Synthesis and alkaline earth metal cation extraction by proton di-ionizable *p-tert*-butylcalix[4]arene-crown-5 compounds in cone, partial-cone and 1,3-alternate conformations

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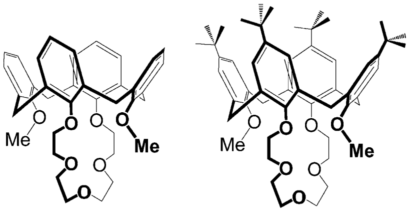
Synthetic strategies for novel, proton di-ionizable *p-tert*-butylcalix[4]arene-crown-5 compounds in cone, partial-cone and 1,3-alternate conformations are reported. Selective linkage of the two diametrical phenolic oxygens in *p-tert*-butylcalix[4]arene with tetraethylene glycol ditosylate gave 1,3-bridged *p-tert*-butylcalix[4]arene-crown-5. The two remaining phenolic units were alkylated using NaH and KH as the bases to give the cone and partial-cone conformers, respectively. Preparation of the 1,3-alternate conformers utilized a different sequence in which O-alkylation was followed by crown ether ring formation. Structures of these new ligands were elucidated by ^{1}H and ^{13}C NMR spectroscopy. These proton-ionizable ligands were tested for their solvent extraction properties toward alkaline earth metal cations. Surprising differences in their extraction behaviors are noted compared to those reported previously for di-ionizable *p-tert*-butylcalix[4]arenecrown-6 analogues.

Introduction

Calixarene-based ligands for complexation of spherical metal ions have received extensive interest in the past two decades. The 1,3-bridged calix[4]arene-crown ethers, in which the two diametrical phenolic oxygens of calix[4]arene are linked by a polyether ring, are important due to their high extraction efficiencies and selectivities for metal ions.[1] Complexation studies with alkali metal cations showed that the selectivity is not only controlled by the cavity size of the crown ether ring, but also by the conformation of the calix[4]arene scaffold. Thus, cone and partial-cone calix[4]arene-crown-4 ligands exhibit very high Na^+/K^+ selectivities,[2] while partial-cone and 1,3-alternate calix[4]arene-crown-5 ligands prefer to bind K^+ instead of Na^+[3–5] and 1,3-alternate calix[4]arene-crown-6 compounds are selective for Cs^+.[6]

The preferred conformation of calix[4]arene-crown-5 ligands for selective binding of K^+ also depends on the *para* substituents, as shown by the conformationally mobile calix[4]arene-crown-5 ligands **1** and **2** (Fig. 1).[5a] The only difference between these two ligands is change of the *para*-substituent from H in **1** to *tert*-butyl in **2**. Although both free ligands exist in cone conformations, a mixture of 1,3-alternate (80%) and partial-cone (20%) conformations is present in the complex of **1** and K^+ and the complex of **2** and K^+ adopts partial-cone and cone conformations with a 3 : 1 ratio.

Introduction of pendant proton-ionizable groups into a calix[4]arene increases extraction efficiency by forming electro-neutral complexes during extraction.[7,8] The first example of a proton-ionizable calix[4]arene-crown ether was reported in 1984 by Ungaro and coworkers.[9] With two carboxylic acid groups, this compound exhibited high efficiency for divalent metal ion extraction (except Mg^{2+}) from water into dichloromethane. The extraction selectivites for Ca^{2+} and Pb^{2+} were better than those of non-ionizable analogues. The remaining one or two phenolic groups in calix[4]arene-crown ether compounds can serve as proton-ionizable groups under strongly basic conditions. In general, the calix[4]arene-crown-5 compounds with one phenolic group showed high selectivities for K^+ and Ca^{2+}, while calix[4]arene-crown-5 and crown-6 extractants with two phenolic groups exhibited remarkable Ca^{2+} selectivity.[10] The *N*-(X)sulfonyl carboxamide group, another type of proton-ionizable function, has been introduced into calix[4]arene-biscrown-6 compounds.[11] These ligands exhibit markedly enhanced extraction efficiency, while retaining high selectivity toward Cs^+ compared with a non-ionizable analogue.



1 **2**

Fig. 1 Conformationally mobile calix[4]arene-crown-5 ligands with different *para*-substituents.

As mentioned previously, the conformations of calix[4]arene ligands play a very important role in extraction selectivity. Although it was reported by Wai and coworkers that a cone *p-tert*-butylcalix[4]arene-crown-6 dicarboxylic acid and the corresponding dihydroxamic acid have high selectivities for Ra^{2+} over light alkaline earth metal cations,[12] no other conformers have been prepared and studied. As part of our program to investigate the effects of both ionizable groups and conformations on the extraction efficiency and selectivity for divalent metal ions, we prepared di-ionizable *p-tert*-butylcalix[4]arene-crown-6 compounds in three conformations (cone, partial-cone and 1,3-alternate).[13] It was found that the cone conformers exhibited

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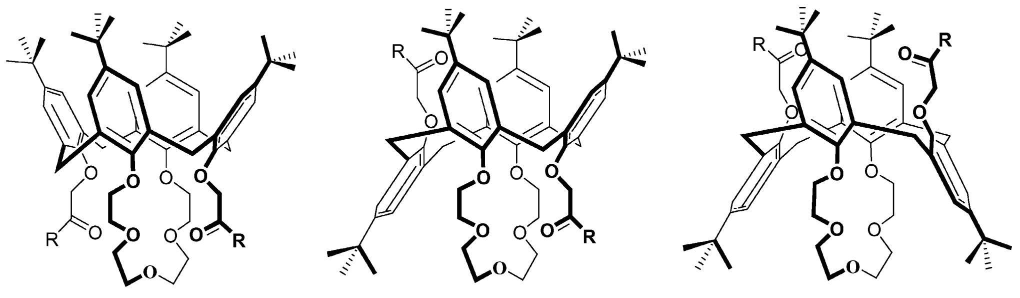


3a-e Cone

4a-e Partial-cone

5a-e 1,3-Alternate

R = OH, $NHSO_2CH_3$, $NHSO_2Ph$, $NHSO_2C_6H_4$-4-NO_2, $NHSO_2CF_3$

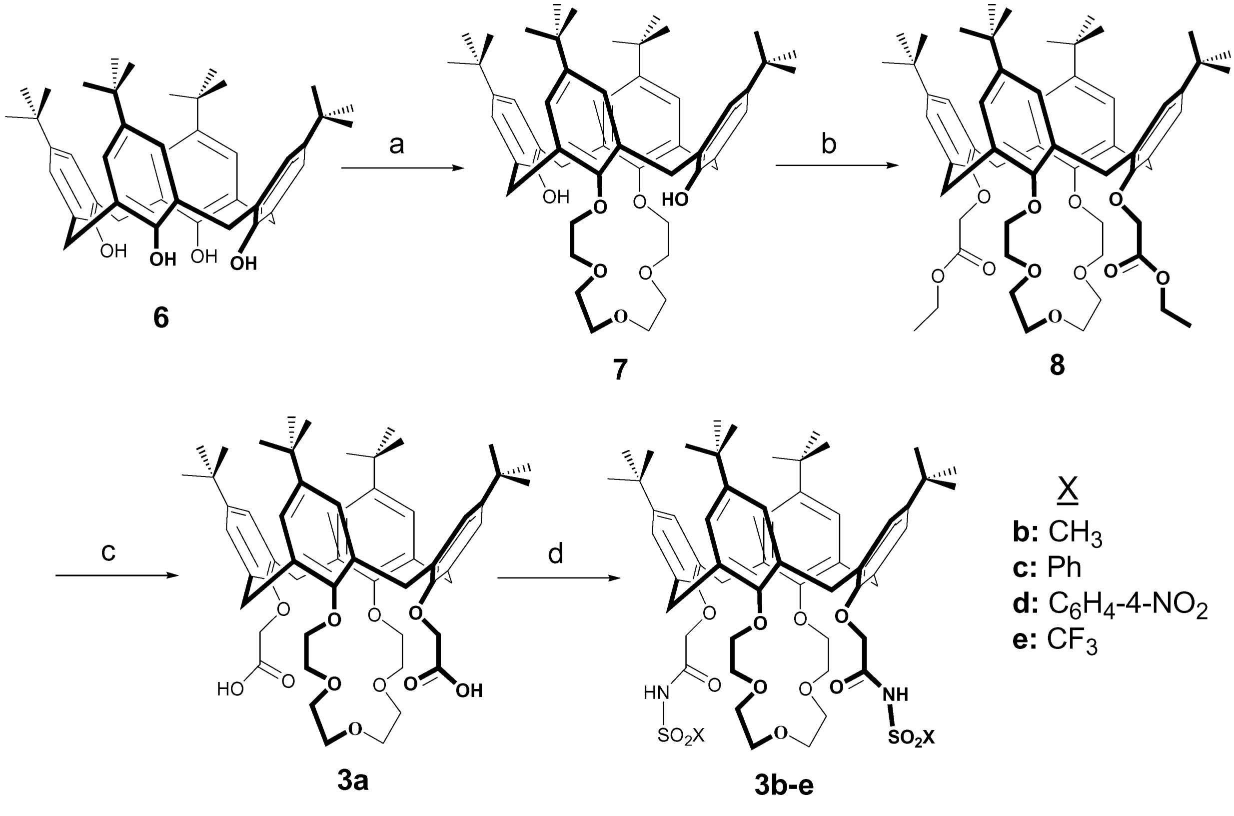
Fig. 2 New proton di-ionizable *p-tert*-butylcalix[4]arene-crown-5 compounds in the cone, partial-cone and 1,3-alternate conformations.

high extraction efficiency and selectivity for Ba^{2+} over Mg^{2+}, Ca^{2+} and Sr^{2+}. In the present work, we report the synthesis of proton di-ionizable *p-tert*-butylcalix[4]arene-crown-5 compounds in the cone, partial-cone and 1,3-alternate conformations (Fig. 2) and their application as extractants for alkaline earth metal cations.

Results and discussion

Synthesis of cone, di-ionizable *p-tert*-butylcalix[4]arene-crown-5 ligands

The synthetic route for the cone conformers is shown in Scheme 1. Since previous strategies for synthesis of 1,3-dihydroxy-*p-tert*-butylcalix[4]arene-crown-5 (**7**) gave only moderate yields (~50%),[3a,14] a procedure reported by Kim *et al.* for the preparation of 1,3-dihydroxycalix[4]arene-crown-5 was adapted.[15] Reaction of *p-tert*-butylcalix[4]arene (**6**) with tetraethylene glycol ditosylate in refluxing MeCN with 1 equivalent of K_2CO_3 gave **7** in 74% yield. Alkylation of **7** with ethyl bromoacetate and NaH in THF at room temperature gave cone diester **8** in 67% yield. Hydrolysis of diester **8** with tetramethylammonium hydroxide (TMAOH) in aqueous THF gave cone di(carboxylic acid) **3a**. The di(carboxylic acid) **3a** was treated with oxalyl chloride in benzene to give the corresponding di(acid chloride), which was reacted with the sodium salt forms of appropriate commercially available sulfonamides to provide **3b–e** in 47–74% yields.



Scheme 1

The cone conformation for ligands **3a–e** was verified by ^{1}H- and ^{13}C-NMR spectroscopy. Table 1 displays the chemical shifts for selected protons in all three conformers. For cone conformers **3a–e**, the methylene bridge (ArCH$_2$Ar) protons show a typical AX pattern, that is two widely separated doublets at δ 4.12–4.36 and 2.95–3.27 for the *exo*- and *endo*-geminal protons, respectively. Both types of protons correlate with a single type of bridge carbon atom at approximately 32 ppm, which is the characteristic chemical shift for bridge carbons with *syn*-orientation. Due to the C$_{2v}$ symmetry, the two ionizable protons give a single peak near 11 ppm and the two OCH$_2$C(O) protons show one singlet at about 5.2 ppm. The aromatic protons (ArH) from the calix[4]arene skeleton appear as two singlets and the *t*-butyl proton signals are two singlets with a 1 : 1 ratio.

Synthesis of partial-cone, di-ionizable *p-tert*-butylcalix[4]arene-crown-5 ligands

Preparation of partial-cone conformers **4a–e** is outlined in Scheme 2. Alkylation of **7** with ethyl bromoacetate in THF using KH (instead of NaH) as the base followed by hydrolysis of the resultant diester with NaOH in aqueous EtOH afforded the partial-cone dicarboxylic acid **4a** in 90% yield. No other conformers were detected. Conversion of **4a** into the corresponding di(acid chloride) with oxalyl chloride was followed by reaction with the sodium salt forms of appropriate sulfonamides to give **4b–e** in 56–88% yields.

Due to reduced symmetry compared with cone conformers (from C$_{2v}$ to C$_s$), the ^{1}H-NMR spectra of the partial-cone conformers are more complex. The two ionizable groups now are non-equivalent. As can be seen from the data in Table 1, the two ionizable protons appear as two singlets at approximately 11 and 8.5 ppm, while the two OCH$_2$C(O) protons are two widely separated singlets. The aromatic protons signals are two singlets and two doublets. The methylene bridge (ArCH$_2$Ar) protons appear as two widely separated doublets (AX pattern) and two closely spaced doublets or singlets (AB pattern). The AX system correlates with *syn*-orientated bridge carbons at about 30 ppm and the AB system correlates with *anti*-orientated bridge carbons at around 38 ppm. The *t*-butyl protons exhibit characteristic patterns of three singlets with a ratio of 1 : 1 : 2. There are significant upfield shifts for the OCH$_2$C(O) protons *anti* to the crown ether rings, as observed in other partial-cone compounds.[3a,14] As shown by the data in Table 1, dramatic upfield shifts ($\Delta\delta$ > 3.1 ppm) are observed the methylene protons of the *anti*-OCH$_2$C(O) groups of ligands **4b–e**. This indicates that these groups are "buried" deeply in the hydrophobic cavity formed by the three surrounding aromatic rings. An exception is the di(carboxylic acid) **4a** with a $\Delta\delta$ value of only 1.35 ppm. Since its diester derivative also has a $\Delta\delta$ value (3.00 ppm) comparable to those observed for **4b–e**, the carboxylic acid group in **4a** must be responsible for its small $\Delta\delta$ value. Conceivably, this results from the smaller size of the carboxylic acid group.

Synthesis of 1,3-alternate, di-ionizable *p-tert*-butylcalix[4]arene-crown-5 ligands

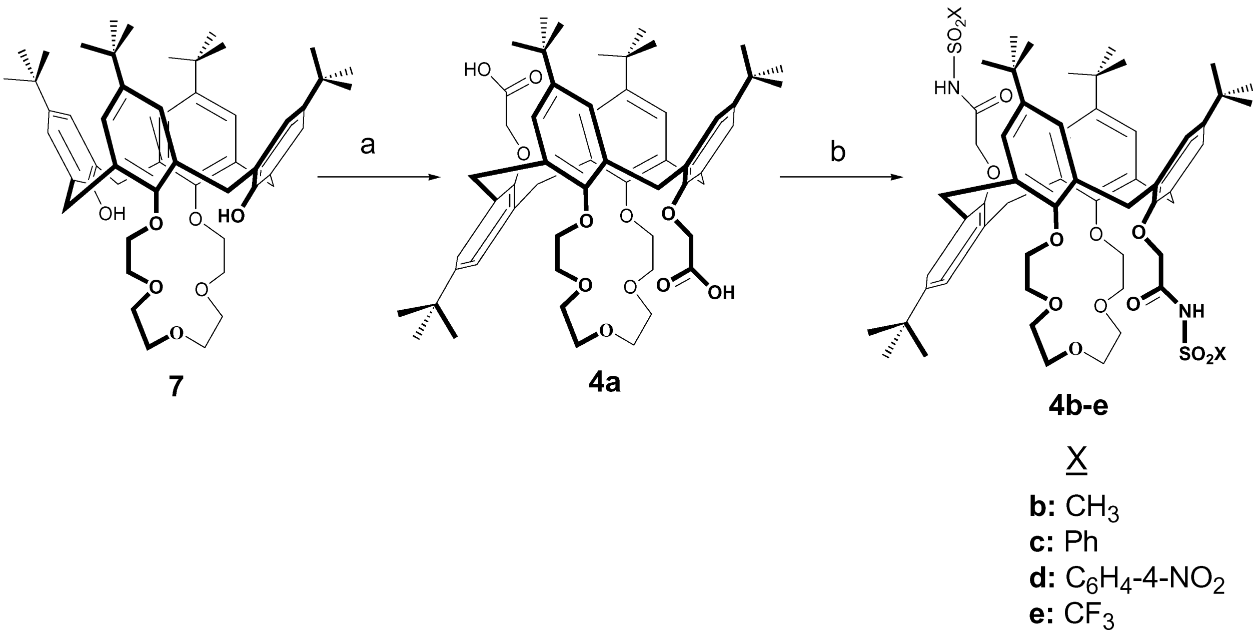
Preparation of 1,3-alternate conformers **5a–e** (Scheme 3) followed the procedure reported for synthesis of the corresponding crown-6 analogues.[13] Thus, alkylation of **6** with *t*-butyl bromoacetate and K$_2$CO$_3$ in refluxing MeCN gave diester **9** in 88% yield. Cyclization of **9** with tetraethylene glycol ditosylate and 1.5 equivalents of Cs$_2$CO$_3$ in refluxing MeCN provided 1,3-alternate diester **10** in 55% yield. Diester **10** was hydrolyzed with NaOH in aqueous EtOH to give the 1,3-alternate di(carboxylic acid) **5a** in 98% yield. (Previously employed conditions for the hydrolysis of the cone diester **8**, *vide infra*, were unsuccessful). Di(carboxylic acid) **5a** was converted into products **5b–e** under the same reaction conditions as those employed for the cone and partial-cone conformers with 57–86% yields.

Due to the increased symmetry of the 1,3-alternate conformers compared with the partial-cone conformers, their ^{1}H-NMR spectra show similar patterns to those of the cone conformers (Table 1). The two ionizable protons exhibit a singlet at around 9 ppm (except for **5e**, 11.26 ppm in d_6-acetone). Both the aromatic and *t*-butyl protons give two singlets that are closer together than those for the cone conformers. Depending on the proton-ionizable

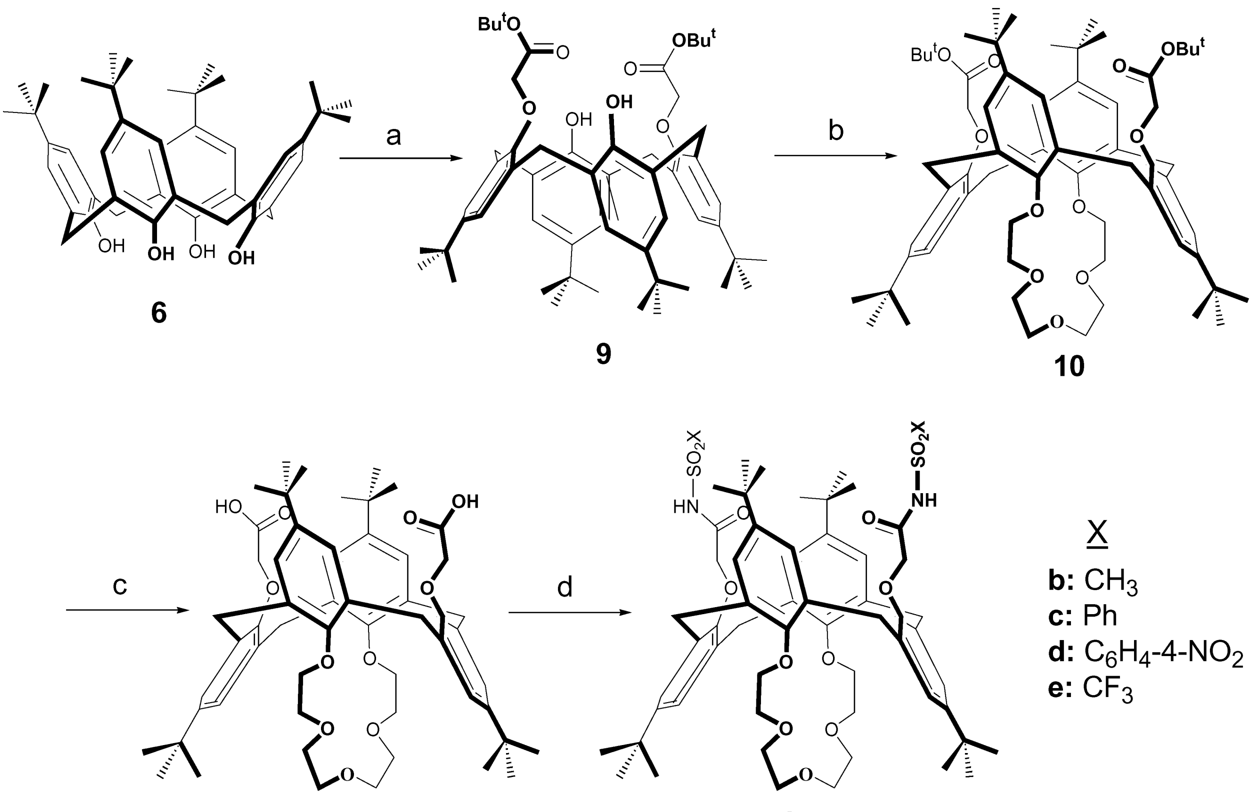
Table 1 Selected proton chemical shifts (ppm) for cone, partial-cone, and 1,3-alternate di-ionizable ligands

Ligand	NH (OH)	ArH	OCH$_2$C(O)	ArCH$_2$Ar	^{t}Bu
3a	11.05	7.13, 6.59	5.29	4.36, 3.27	1.33, 0.83
3b	10.71	7.11, 6.53	5.23	4.36, 3.24	1.32, 0.81
3c	10.76	6.92, 6.42	5.08	4.12, 2.95	1.28, 0.76
3d[a]	11.20	7.06, 6.56	5.27	4.36, 3.06	1.28, 0.82
3e	11.09	7.10, 6.53	5.27	4.26, 3.25	1.32, 0.81
4a	—	7.15, 7.12, 7.11, 6.78	4.83, 3.48 (1.35)[b]	4.41, 3.96, 3.75, 3.27	1.45, 1.26, 1.14
4b	10.88, 8.41	7.23, 7.20, 6.99, 6.92	4.67, 1.49 (3.18)[b]	4.35, 3.85, 3.31	1.44, 1.21, 1.15
4c	10.99, 8.52	7.17, 7.07, 6.86, 6.76	4.48, 1.27 (3.21)[b]	4.08, 3.82, 2.94	1.42, 1.09, 1.00
4d	11.28, 8.62	7.19, 7.06, 6.84, 6.78	4.52, 1.27 (3.25)[b]	4.06, 3.83, 2.95	1.43, 1.06, 1.01
4e	11.53, 8.69	7.25, 7.22, 6.98, 6.92	4.73, 1.48 (3.26)[b]	4.32, 3.83, 3.33	1.44, 1.21, 1.13
5a	—	7.10, 7.02	4.06	3.97, 3.88	1.38, 1.23
5b	8.72	7.11, 7.10	3.47	3.95	1.39, 1.28
5c	9.21	7.09, 7.01	3.03	3.91	1.37, 1.10
5d	9.45	7.11, 7.01	3.09	3.90	1.38, 1.11
5e[a]	11.26	7.21, 7.17	3.41	4.14, 3.99	1.41, 1.26

[a] In d_6-acetone. [b] Chemical shift differences, $\Delta\delta$ (ppm), for *syn*- and *anti*-OCH$_2$C(O) groups shown in parentheses.



Scheme 2

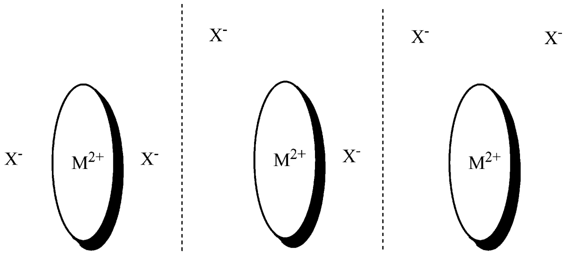


Scheme 3

groups, the methylene bridge ($ArCH_2Ar$) protons are a singlet or quartet or two closely spaced doublets (AB pattern), which correlate with *anti*-orientated bridge carbons ($\delta \sim 39$ ppm). The two $OCH_2C(O)$ protons appears as a singlet at δ 3.03–4.06, with a small upfield shift resulting from the shielding effect of two aromatic rings.

Competitive solvent extraction of alkali metal ions by di-ionizable calix[4]arene-crown-5 ligands 3a–e, 4a–e and 5a–e

The spatial relationship between a crown-complexed divalent metal ion and the two anionic centers formed by side arm ionization of new ligands **3a–e**, **4a–e** and **5a–e** is controlled by the fixed conformations of their calix[4]arene units. As shown in Fig. 3, complex **11** between di-ionized cone calix[4]arene-crown-5 ligands **3a–e** and a divalent metal ion positions an anion on each side of the crown ether unit. Alternatively, the partial-cone di-ionizable calix[4]arene-crown-5 compounds **4a–e** produce complex **12** with one anion in close proximity to the polyether-complexed divalent metal ion and one in a remote location. Finally, both anionic centers in complex **13** formed from the 1,3-alternate di-ionizable calix[4]arene-crown-5 compounds **5a–e** are remote from the complexed divalent metal ion.



11 **12** **13**

Fig. 3 Depiction of spatial relationships between a crown-complexed divalent metal ion and the anionic centers formed by ionization of ligands **3a–e**, **4a–e** and **5a–e**.

To probe the influence of these differing spatial arrangements, as well as crown ether ring size, upon the efficiency and selectivity of divalent metal ion complexation, competitive solvent extraction of alkaline earth metal cations from aqueous solutions into chloroform by ligands **3a–e**, **4a–e** and **5a–e** were performed. Since it has been shown that the selectivity in competitive metal ion extraction may be quite different from that obtained by extrapolating the results of single species extractions,[16] competitive solvent extractions of Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} were utilized in the present investigation.

For competitive solvent extractions of aqueous alkaline earth metal cation solutions (2.0 mM in each) by 1.0 mM solutions of di-ionizable *p-tert*-butylcalix[4]arene-crown-5 ligands **3a–e**, **4a–e** and **5a–e** in chloroform, plots of metal cations loading of the organic phase *vs.* the equilibrium pH of the aqueous phase are presented in Figs. 4 and 6–9. For comparison, previously reported results[13] for corresponding *p-tert*-butylcalix[4]arene-crown-6 dicarboxylic acids are shown in Fig. 5.

Fig. 4 records the results of competitive alkaline earth metal ion solvent extraction by calix[4]arene-crown-5 di(carboxylic acids) **3a**, **4a** and **5a** in the cone, partial-cone and 1,3-alternate conformations, respectively. As can be seen, cone ligand **3a** exhibits high extraction selectivity for Ba^{2+} and Sr^{2+}over Mg^{2+} and Ca^{2+}. On the other hand, partial-cone ligand **4a**, shows high selectivity for Ba^{2+} extraction over other three alkaline earth metal cations and 100% maximum metal loading (for formation of a 1 : 1 metal ion-di-ionized ligand complex) at pH 10. The 1,3-alternate ligand **5a** gives a pronounced extraction selectivity for Ba^{2+} over the other three alkaline earth metal cations, but is neither as effective nor selective an extractant as ligand **4a**. Based upon the pH profiles, the extraction efficiency diminishes in the order **4a** (partial-cone) > **5a** (1,3-alternate) > **3a** (cone). Thus, the most effective and selective extractant is **4a** with the partial-cone conformation in which one ionized group is proximate and the other is remote.

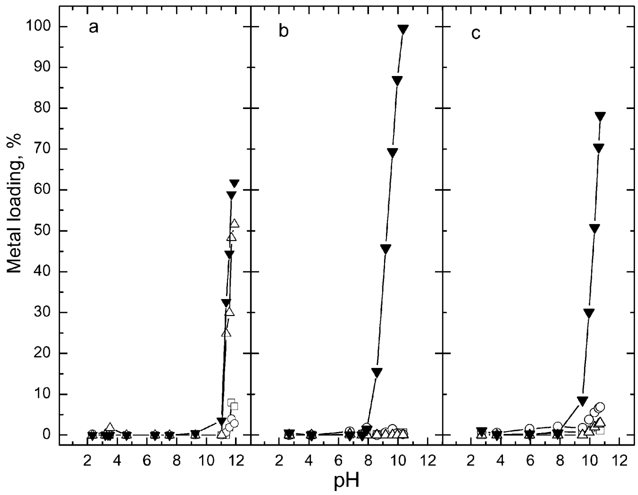


Fig. 4 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by *tert*-butylcalix[4]arene-crown-5 dicarboxylic acids (a) **3a**, (b) **4a**, and (c) **5a**. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}).

The differences between the alkaline earth metal cation extraction results obtained for these *p-tert*-butylcalix[4]arene-crown-5 dicarboxylic acids and those reported previously for the crown-6 analogues in the cone, partial-cone and 1,3-alternate conformations[13] (Fig. 5) are striking. For the crown-6 dicarboxylic acid analogues, the cone isomer was the most effective extractant with a very high extraction selectivity for Ba^{2+} (Fig. 5a) The 1,3-alternate isomer (Fig. 5c) was a much less efficient extractant and gave a selectivity order of $Ba^{2+} > Ca^{2+} \gg Sr^{2+}$, Mg^{2+} and the partial-cone isomer (Fig. 5b) was such a weak extractant that it was impossible to determine its extraction selectivity.

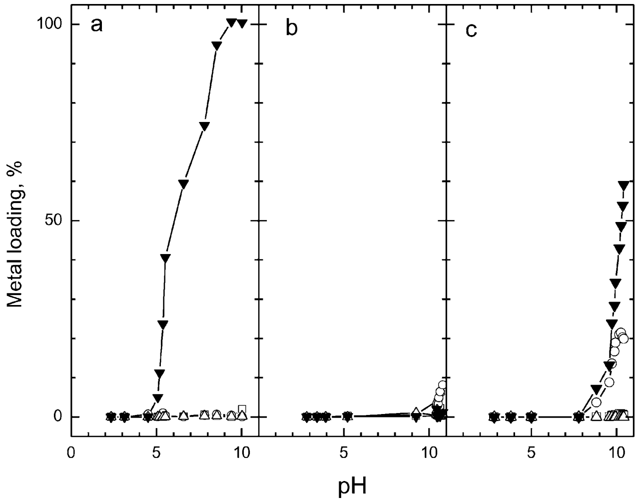


Fig. 5 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by *tert*-butylcalix[4]arene-crown-6 dicarboxylic acids (a) cone, (b) partial-cone, and (c) 1,3-alternate. (□ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}). (Taken from ref. 13).

The only structural difference between the di-ionizable calix[4]arene-crown-5 dicarboxylic acids **3a**, **4a** and **5a** examined in this study and their crown-6 analogues investigated previously[13] is the size of the crown ether ring. Therefore, this must be the causative factor for their markedly different alkaline earth metal cation extraction behaviors. It is known that calix[4]arene-crown-5 compounds are selective for K^+ among the alkali metal cations.[3–5] Since the ionic radius of K^+ (1.52 Å) is very close to that of Ba^{2+} (1.49 Å),[17] it appears that the crown ring size is the dominant factor for extraction of alkaline earth metal cations by the crown-5 rings of **3a**, **4a** and **5a** with positioning of the anionic group relegated to much lesser importance than it was for the crown-6 analogues.

To probe the effect of changing to a different class of ionizable group for which the acidity can be systematically varied, solvent extractions were performed with the calix[4]arene-crown-5 di[*N*-(X)sulfonyl carboxamide] ligands **3b–e**, **4b–e**, and **5b–e** in the cone, partial-cone and 1,3-alternate conformations, respectively.

Results for competitive solvent extractions of alkaline earth metal cations from aqueous solution into chloroform by cone ligands **3b–e** in which the X group is varied CH_3, C_6H_5, C_6H_4-4-NO_2 and CF_3, respectively, are presented in Fig. 6. High Ba^{2+} extraction selectivity is observed for ligands **3b–d** with 100% metals loadings (for formation of 1 : 1 extraction complexes) for ligands **3b–d**. It appears that ligand **3e**, with the strongest electron-withdrawing group, exhibits a maximal metal loading somewhat less than 100%. Presumably this results from the high acidity of ligand **3e** which required the use of 1.0 M HCl for stripping instead of conventional 0.1 M HCl. Unlike the di(carboxylic acid) ligand **3a**, the di[*N*-(X)sulfonyl carboxamide] extractants **3b–e** exhibit very good Ba^{2+}/Sr^{2+} selectivity.

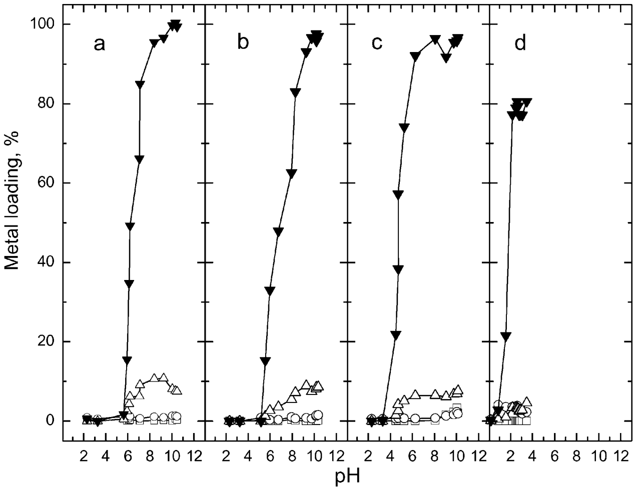


Fig. 6 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by cone *tert*-butylcalix[4]-arene-crown-5 di[*N*-(X)sulfonyl carboxamides] (a) **3b**, (b) **3c**, (c) **3d** and (d) **3e**. (☐ = Mg^{2+}, ○ = Ca^{2+}, △ = Sr^{2+}, ▼ = Ba^{2+}).

Fig. 7 presents the results for competitive alkaline earth metal ion extraction by the partial-cone calix[4]arene-crown-5 di[*N*-(X)sulfonyl carboxamide] ligands **4b–e**. Like the di(carboxylic acid) ligand **4a**, these ligands show very high efficiency (with 100% maximal metal loading) and high selectivity for Ba^{2+} extraction.

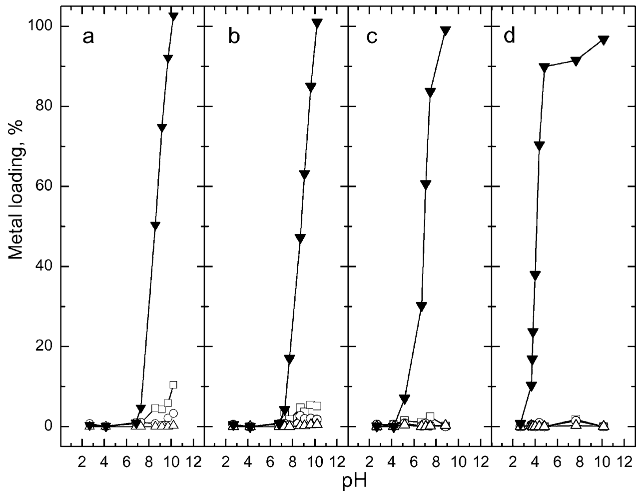


Fig. 7 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by partial-cone *tert*-butylcalix[4]arene-crown-5 di[*N*-(X)sulfonyl carboxamides] (a) **4b**, (b) **4c**, (c) **4d** and (d) **4e**. (☐ = Mg^{2+}, ○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

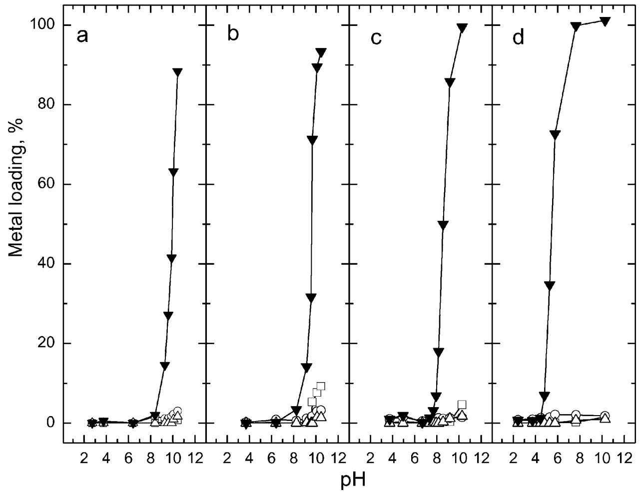


Fig. 8 Percent metals loading *vs.* equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by 1,3-alternate *tert*-butylcalix[4]arene-crown-5 di[*N*-(X)sulfonyl carboxamides] (a) **5b**, (b) **5c**, (c) **5d** and (d) **5e**. (☐ = Mg^{2+},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

Results for competitive solvent extraction of alkaline earth metal cations from aqueous solutions into chloroform by the 1,3-alternate calix[4]arene-crown-5 di(*N*-(X)sulfonyl carboxamide) ligands **5b–e** are presented in Fig. 8. For ligands **5b,d,e**, the Ba^{2+} selectivities are higher than those found for the corresponding di(carboxylic acid) **5a**. For **5c**, significant amounts of Mg^{2+} are transferred into the organic phase when the aqueous phase is highly alkaline. Presumably, this results from formation of colloidal $Mg(OH)_2$.

According to the electron-withdrawing abilities of X in the *N*-(X)sulfonyl carboxamide groups, acidity of the ligands would be expected to increase in the order $CH_3 \sim C_6H_5 < C_6H_4\text{-4-}NO_2 < CF_3$. The pH for half loading, $pH_{0.5}$, is a qualitative measure of ligand acidity. Table 2 presents the $pH_{0.5}$ values for extractants **3b–e**, **4b–e** and **5b–e**. As can be seen, the $pH_{0.5}$ values for a given conformation decrease as the electron-withdrawing ability of X increases. It is interesting to note that for a common X group, the ligand acidity increases uniformly as the conformation is varied in the order: 1,3-alternate < partial-cone < cone. This ordering

Table 2 pH values for half extraction (pH$_{0.5}$) of alkaline earth metal cations by *tert*-butyl-calix[4]arene-crown-5 di[*N*-(X)sulfonyl carboxamide] ligands in the cone (**3b–e**), partial-cone (**4b–e**) and 1,3-alternate (**5b–e**) conformations

	X			
Conformation	CH_3	Ph	C_6H_4-4-NO_2	CF_3
Cone	6.2	6.6	4.7	1.8
Partial-cone	8.4	8.6	6.9	4.1
1,3-Alternate	9.9	9.6	8.5	5.4

is consistent with that expected if proximity of the ionized groups to the polyether-complexed metal ion is an important factor in determining the strength of metal ion binding, as reflected in the extraction propensity of the ligand.

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 ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity INOVA 500 MHz FT-NMR (^{1}H 500 MHz and ^{13}C 126 MHz) spectrometer in $CDCl_3$ with Me_4Si as internal standard unless indicated. 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 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. Tetraethylene glycol ditosylate[18] was prepared according to a literature procedure. Compound **6**[19] was prepared by a reported method. Analytical TLC was performed on Analtech Uniplate silica gel or alumina plates, while silica gel 150 (Mallinckrodt SiliCAR®, 60–200 mesh) was used for column chromatography.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(carboxymethoxy)calix[4]-arene-crown-5 (3a). A mixture of **8** (5.17 g, 5.28 mmol), THF (250 mL), and 10% Me_4NOH (250 mL) was refluxed for 12 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 THF *in vacuo*, di(carboxylic acid) **3a** (4.39 g, 99%) was obtained as a white solid (mp 250–252 °C); Found: C, 72.57; H, 8.00. $C_{56}H_{74}O_{11}$ requires C, 72.86; H, 8.08%; ν_{max}(film)/cm^{-1} 2700–3500 (CO_2H), 1741 (C=O); δ_H 11.05 (2 H, br s, CO_2H), 7.13 (4 H, s, ArH), 6.59 (4 H, s, ArH), 5.29 (4 H, s, OCH_2CO), 4.36 (4 H, d, *J* 12.9, $ArCH_2Ar$), 4.04–4.12 (4 H, m, OCH_2CH_2O), 3.91–3.98 (4 H, m, OCH_2CH_2O), 3.80–3.90 (8 H, m, OCH_2CH_2O), 3.27 (4 H, d, *J* 12.9, $ArCH_2Ar$), 1.33 (18 H, s, $C(CH_3)_3$), 0.83 (18 H, s, $C(CH_3)_3$); δ_C 172.19, 152.93, 151.17, 145.91, 145.44, 134.73, 132.13, 125.64, 125.43, 73.37, 70.36, 70.29, 69.68, 34.12, 33.61, 32.15, 31.65, 30.92.

General procedure for the preparation of cone 5,11,17,23-tetrakis-(1,1-dimethylethyl)-25,27-bis[*N*-(X)sulfonyl carbamoylmethoxy]-calix[4]arene-crown-5 ligands 3b–e. A solution of **3a** (1.43 g, 1.55 mmol) and oxalyl chloride (1.57 g, 12.37 mmol) in benzene (60 mL) was refluxed for 5 h. The solution was evaporated *in vacuo* and the residue was dried under high vacuum for 30 min. The residue was dissolved in THF (20 mL) and added into a mixture of the appropriate sulfonamide (4.65 mmol) and NaH (0.58 g, 24.17 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 (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 either recrystallization or chromatography.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (3b). Recrystallization from CH_2Cl_2-hexanes, yield 48%, white solid, mp 269–271 °C. Found: C, 64.76; H, 7.38; N, 2.39. $C_{58}H_{80}O_{13}N_2S_2$ requires C, 64.66; H, 7.48; N, 2.60%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1715 (C=O); δ_H 10.71 (2 H, s, NH), 7.11 (4 H, s, ArH), 6.53 (4 H, s, ArH), 5.23 (4 H, s, OCH_2CO), 4.36 (4 H, d, *J* 12.6, $ArCH_2Ar$), 4.03–4.13 (4 H, m, OCH_2CH_2O), 3.95–4.01 (4 H, m, OCH_2CH_2O), 3.90–3.95 (4 H, m, OCH_2CH_2O), 3.80–3.90 (4 H, m, OCH_2CH_2O), 3.17–3.30 (10 H, m, $ArCH_2Ar$, CH_3SO_2), 1.32 (18 H, s, $C(CH_3)_3$), 0.81 (18 H, s, $C(CH_3)_3$); δ_C 170.15, 151.85, 151.40, 145.94, 145.21, 135.01, 131.92, 125.61, 124.92, 72.13, 71.02, 70.57, 70.40, 70.36, 69.93, 41.63, 34.12, 33.59, 32.25, 31.64, 30.96.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-benzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (3c). Recrystallization from CH_2Cl_2-hexanes, yield 47%, white solid, mp 274–276 °C. Found: C, 67.86; H, 7.26; N, 2.35. $C_{68}H_{84}O_{13}N_2S_2$ requires C, 67.97; H, 7.05; N, 2.33%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1721 (C=O); δ_H 10.76 (2 H, s, NH), 8.02–8.12 (4 H, m, ArH), 7.60–7.68 (2 H, m, ArH), 7.45–7.54 (4 H, m, ArH), 6.92 (4 H, s, ArH), 6.42 (4 H, s, ArH), 5.08 (4 H, s, OCH_2CO), 4.12 (4 H, d, *J* 12.8, $ArCH_2Ar$), 3.93–4.04 (4 H, m, OCH_2CH_2O), 3.76–3.93 (12 H, m, OCH_2CH_2O), 2.95 (4 H, d, *J* 12.8, $ArCH_2Ar$), 1.28 (18 H, s, $C(CH_3)_3$), 0.76 (18 H, s, $C(CH_3)_3$); δ_C 168.33, 151.75, 151.06, 145.50, 145.02, 139.15, 134.88, 133.66, 131.95, 128.72, 128.34, 125.41, 124.76, 72.04, 70.98, 70.61, 70.50, 70.23, 34.02, 33.51, 32.12, 31.62, 30.91.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (3d). Precipitated from CH_2Cl_2 solution after washing with aq K_2CO_3 solution, yield 74%, light-yellow solid, mp 270–272 °C. Found: C, 62.93; H, 6.32; N, 4.31. $C_{68}H_{82}O_{17}N_4S_2$ requires C, 63.24; H, 6.40; N, 4.34%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1726 (C=O); δ_H (d_6-acetone) 11.20 (2 H, br s, NH), 8.40–8.52 (4 H, m, ArH), 8.26–8.38 (4 H, m, ArH), 7.06 (4 H, s, ArH), 6.56 (4 H, s, ArH), 5.27 (4 H, s, OCH_2CO), 4.35 (4 H, d, *J* 12.6, $ArCH_2Ar$), 3.92–4.08 (8 H, m, OCH_2CH_2O), 3.70–3.92 (8 H, m, OCH_2CH_2O), 3.05 (4 H, d, *J* 12.6, $ArCH_2Ar$), 1.28 (18 H, s, $C(CH_3)_3$), 0.82 (18 H, s, $C(CH_3)_3$); δ_C 169.37, 153.30, 152.45, 151.72, 146.08, 145.52, 145.26, 136.20, 132.92, 130.82, 126.20, 125.66, 124.96, 79.23, 78.96, 78.70, 73.20, 71.56, 71.42, 70.97, 69.25, 34.53, 34.16, 32.77, 31.90, 31.37.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (3e). Chromatography on silica gel with EtOAc as eluent, yield 57%, white solid, mp 200–202 °C. Found: C, 58.57; H, 6.32; N, 2.40. $C_{58}H_{74}O_{13}N_2S_2F_6$ requires C, 58.77; H, 6.29; N, 2.36%. ν_{max}(film)/cm^{-1} 2800–3200 (NH); 1754 (C=O); δ_H 11.09 (2 H, br s, NH), 7.10 (4 H, s, ArH), 6.53 (4 H, s, ArH), 5.27 (4 H, s, OCH_2CO), 4.26 (4 H, d, *J* 12.7, $ArCH_2Ar$), 4.04–4.14 (4 H, m, OCH_2CH_2O), 3.95–4.04 (4 H, m, OCH_2CH_2O), 3.89–3.95 (4H, m, OCH_2CH_2O), 3.80–3.89 (4 H, m, OCH_2CH_2O), 3.26 (4 H, d, *J* 12.9, $ArCH_2Ar$), 1.32 (18 H, s, $C(CH_3)_3$), 0.81 (18 H, s, $C(CH_3)_3$); δ_C 167.35, 151.69, 150.70, 146.35, 145.44, 134.84, 131.81, 125.68, 124.99, 71.77, 71.40, 70.49, 70.26, 32.17, 31.61, 30.92.

Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(carboxymethoxy)-calix[4]arene-crown-5 (4a). A mixture of **7** (8.00 g, 9.91 mmol), THF (250 mL), and KH (2.50 g, 35% dispersion in mineral oil, 21.80 mmol) was stirred under nitrogen at room temperature for 1 h. Ethyl bromoacetate (4.98 g, 29.82 mmol) in THF (50 mL) was added slowly. The reaction mixture was stirred at room temperature for 12 h and quenched with a small amount of water. The THF was evaporated *in vacuo.* To the residue was added 95% EtOH (200 mL), NaOH (2.29 g, 57.25 mmol) and H_2O (50 mL) and the solution was refluxed for 24 h. The EtOH 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 combined organic layers were washed with water (2 × 50 mL) and dried over $MgSO_4$. After evaporation of the CH_2Cl_2 *in vacuo*, the crude product was recrystallized from CH_2Cl_2–MeOH to give **4a** (8.23 g, 90%) as a white solid (mp 189–192 °C). Found: C, 73.09; H, 7.84. $C_{56}H_{74}O_{11}$ requires C, 72.85; H 8.08%; ν_{max}(film)/cm^{-1} 2500–3200 (CO_2H), 1782, 1731 (C=O); δ_H 7.10–7.15 (6 H, m, ArH), 6.78 (2 H, d, *J* 2.3, ArH), 4.83 (2 H, s, *syn*-OCH_2CO), 4.41 (2 H, d, *J* 12.4, $ArCH_2Ar$), 3.95 (2 H, d, *J* 16.7, $ArCH_2Ar$), 3.82–3.90 (6 H, m, OCH_2CH_2O), 3.72–3.78 (4 H, m, OCH_2CH_2O, $ArCH_2Ar$), 3.51–3.66 (6 H, m, OCH_2CH_2O), 3.44–3.51 (4 H, m, OCH_2CH_2O, *anti*-OCH_2CO), 3.27 (2 H, d, *J* 12.4, $ArCH_2Ar$), 1.45 (9 H, s, $C(CH_3)_3$), 1.26 (9 H, s, $C(CH_3)_3$), 1.14 (18 H, s, $C(CH_3)_3$); δ_C 171.99, 168.08, 152.88, 151.18, 150.68, 146.49, 146.26, 134.63, 134.04, 133.13, 131.45, 126.90, 126.15, 125.41, 124.47, 71.76, 71.22, 70.68, 70.51, 70.43, 65.44, 38.94, 34.27, 34.08, 33.90, 31.78, 31.44, 31.10.

General procedure for the preparation of partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis[*N*-(X)-sulfonyl carbamoylmethoxy]calix[4]arene-crown-5 ligands 4b–e. The procedure was the same as that for the cone conformers.

Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (4b). Recrystallization from CH_2Cl_2–MeOH, yield 88%, white solid, mp 272–274 °C. Found: C, 63.65; H, 7.68; N, 2.49. $C_{58}H_{80}O_{13}N_2S_2\cdot0.2CH_2Cl_2$ requires C, 63.87; H, 7.40; N, 2.56%. ν_{max}(film)/cm^{-1} 2800–3200 (NH); 1736 (C=O); δ_H 10.88 (1 H, s, NH), 8.41 (1 H, s, NH), 7.23 (2 H, d, *J* 2.3, ArH), 7.20 (2 H, s, ArH), 6.99 (2 H, s, ArH), 6.92 (2 H, d, *J* 2.3, ArH), 4.67 (2 H, s, *syn*-OCH_2CO), 4.35 (2 H, d, *J* 12.2, $ArCH_2Ar$), 3.72–3.94 (14 H, m, $ArCH_2Ar$, OCH_2CH_2O), 3.62–3.70 (2 H, m, OCH_2CH_2O), 3.54–3.62 (2 H, m, OCH_2CH_2O), 3.36–3.46 (2 H, m, OCH_2CH_2O), 3.31 (2 H, d, *J* 12.2, $ArCH_2Ar$), 3.25 (3 H, s, CH_3SO_2), 2.97 (3 H, s, CH_3SO_2), 1.49 (2 H, s, *anti*-OCH_2CO), 1.44 (9 H, s, $C(CH_3)_3$), 1.21 (9 H, s, $C(CH_3)_3$), 1.15 (18 H, s, $C(CH_3)_3$); δ_C 170.06, 166.23, 152.91, 151.63, 151.43, 147.05, 146.33, 145.72, 136.43, 134.16, 132.58, 131.96, 126.70, 126.46, 125.82, 125.74, 75.23, 72.23, 70.86, 70.55, 70.23, 68.30, 41.35, 41.19, 38.43, 34.19, 34.04, 34.01, 31.61, 31.23, 31.13, 30.74.

Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-benzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (4c). Recrystallization from CH_2Cl_2–MeOH, yield 67%, white solid, mp 177–180 °C. Found: C, 68.28; H, 7.20; N, 2.37. $C_{68}H_{84}O_{13}N_2S_2$ requires C, 67.97; H, 7.05; N, 2.33%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1742, 1731 (C=O); δ_H 10.99 (1 H, s, NH), 8.52 (1 H, s, NH), 8.02–8.12 (2 H, m, ArH), 7.78–7.86 (2 H, m, ArH), 7.61 (1 H, t, *J* 7.4, ArH), 7.44–7.56 (3 H, m, ArH), 7.36 (2 H, t, *J* 7.9, ArH), 7.17 (2 H, s, ArH), 7.07 (2 H, d, *J* 2.3, ArH), 6.86 (2 H, d, *J* 2.2, ArH), 6.76 (2 H, s, ArH), 4.48 (2 H, s, *syn*-OCH_2CO), 4.08 (2 H, d, *J* 12.2, $ArCH_2Ar$), 3.85–3.94 (2 H, m, OCH_2CH_2O), 3.82 (4 H, s, $ArCH_2Ar$), 3.70–3.80 (8 H, m, OCH_2CH_2O), 3.60–3.68 (2 H, m, OCH_2CH_2O), 3.48–3.58 (2 H, m, OCH_2CH_2O), 3.30–3.40 (2 H, m, OCH_2CH_2O), 2.93 (2 H, d, *J* 12.3, $ArCH_2Ar$), 1.42 (9 H, s, $C(CH_3)_3$), 1.27 (2 H, s, *anti*-OCH_2CO), 1.09 (18 H, s, $C(CH_3)_3$), 1.00 (9 H, s, $C(CH_3)_3$); δ_C 168.18, 164.39, 152.64, 152.05, 151.35, 146.91, 145.96, 145.67, 139.02, 138.49, 133.91, 133.61, 133.37, 132.26, 131.39, 128.75, 128.44, 128.39, 126.46, 126.31, 125.91, 125.68, 75.66, 72.25, 71.29, 70.47, 70.26, 68.21, 38.20, 34.17, 33.89, 33.88, 31.56, 31.13, 30.98, 30.35.

Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (4d). Recrystallization from CH_2Cl_2–MeOH, yield 56%, light yellow solid, mp 188–190 °C. Found: C, 62.20; H, 6.47; N, 4.11. $C_{68}H_{82}O_{17}N_4S_2\cdot0.3CH_2Cl_2$ requires C, 62.29; H, 6.32; N, 4.25%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1742, 1732 (C=O); δ_H 11.28 (1 H, s, NH), 8.62 (1 H, s, NH), 8.29–8.35 (2 H, m, ArH), 8.23–8.29 (2 H, m, ArH), 8.18–8.23 (2 H, m, ArH), 8.00–8.05 (2 H, m, ArH), 7.18 (2 H, s, ArH), 7.06 (2 H, d, *J* 2.3, ArH), 6.84 (2 H, d, *J* 2.3, ArH), 6.78 (2 H, s, ArH), 4.52 (2 H, s, *syn*-OCH_2CO), 4.06 (2 H, d, *J* 12.3, $ArCH_2Ar$), 3.69–3.90 (14 H, m, $ArCH_2Ar$, OCH_2CH_2O), 3.62–3.69 (2 H, m, OCH_2CH_2O), 3.50–3.62 (2 H, m, OCH_2CH_2O), 3.30–3.42 (2 H, m, OCH_2CH_2O), 2.95 (2 H, d, *J* 12.3, $ArCH_2Ar$), 1.43 (9 H, s, $C(CH_3)_3$), 1.27 (2 H, s, *anti*-OCH_2CO), 1.06 (18 H, s, $C(CH_3)_3$), 1.01 (9 H, s, $C(CH_3)_3$); δ_C 168.39, 164.82, 152.65, 151.84, 151.29, 150.58, 150.50, 147.09, 146.23, 145.97, 144.41, 143.85, 136.38, 134.02, 132.23, 131.51, 129.97, 129.95, 126.61, 126.40, 125.82, 125.71, 123.89, 123.65, 75.42, 72.34, 70.93, 70.45, 70.22, 68.10, 38.27, 34.23, 33.93, 33.87, 31.60, 31.05, 30.97, 30.48.

Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-trifluoromethanesulfonyl carbzmoylmethoxy)calix[4]arene-crown-5 (4e). Recrystallization from CH_2Cl_2–MeOH, yield 68%, white solid, mp 180–183 °C. Found: C, 58.64; H, 6.47; N, 2.37. $C_{58}H_{74}O_{13}N_2S_2F_6$ requires C, 58.77; H, 6.29; N, 2.36%. ν_{max}(film)/cm^{-1} 2800–3200 (NH); 1775 (C=O); δ_H 11.54 (1 H, br s, NH), 8.69 (1 H, s, NH), 7.25 (2 H, d, *J* 2.9, ArH), 7.22 (2 H, s, ArH), 6.98 (2 H, s, ArH), 6.92 (2 H, d, *J* 2.2, ArH), 4.74 (2 H, s, *syn*-OCH_2CO), 4.31 (2 H, d, *J* 12.2, $ArCH_2Ar$), 3.72–3.94 (14 H, m, $ArCH_2Ar$,

OCH_2CH_2O), 3.56–3.72 (4 H, m, OCH_2CH_2O), 3.39–3.50 (2 H, m, OCH_2CH_2O), 3.32 (2 H, d, *J* 12.3, $ArCH_2Ar$), 1.48 (2 H, s, *anti*-OCH_2CO), 1.44 (9 H, s, $C(CH_3)_3$), 1.21 (18 H, s, $C(CH_3)_3$), 1.13 (9 H, s, $C(CH_3)_3$); δ_C 167.87, 163.01, 152.77, 151.32, 150.98, 147.58, 146.85, 146.30, 136.64, 134.38, 132.17, 131.84, 126.88, 126.82, 125.96, 125.54, 75.25, 72.22, 70.69, 70.50, 70.19, 68.35, 38.52, 34.27, 34.05, 31.64, 31.13, 31.06, 30.69.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(carboxymethoxy)calix[4]arene-crown-5 (5a). A mixture of the diester **10** (5.75 g, 5.55 mmol), NaOH (1.78 g, 44.40 mmol), EtOH (100 mL) and water (30 mL) was refluxed for 12 h. The EtOH 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 combined organic extracts were washed with water (2 × 50 mL) and dried over $MgSO_4$. After evaporation of the CH_2Cl_2 *in vacuo*, **5a** was obtained (5.02 g, 98%) as a white solid (mp 288–291 °C). Found: C, 72.91; H, 8.25. $C_{56}H_{74}O_{11}$ requires C, 72.85; H 8.08%; ν_{max}(film)/cm^{-1} 3415 (CO_2H), 1760 (C=O); δ_H 7.10 (4 H, s, ArH), 7.02 (4 H, s, ArH), 4.06 (4 H, s, OCH_2CO), 3.97 (4 H, d, *J* 17.0, $ArCH_2Ar$), 3.88 (4 H, d, *J* 17.0, $ArCH_2Ar$), 3.56–3.66 (4 H, m, OCH_2CH_2O), 3.43–3.52 (4 H, m, OCH_2CH_2O), 3.36–3.43 (4 H, m, OCH_2CH_2O), 2.92–3.06 (4 H, m, OCH_2CH_2O), 1.38 (18 H, s, $C(CH_3)_3$), 1.23 (18 H, s, $C(CH_3)_3$); δ_C 168.80, 153.42, 151.90, 146.70, 146.63, 132.47, 132.36, 125.86, 125.73, 73.37, 70.89, 70.18, 67.37, 67.18, 38.61, 34.15, 33.93, 31.68, 31.21.

General procedure for the preparation of 1,3-alternate 5,11,17,23-(tetrakis(1,1-dimethylethyl)-25,27-bis[*N*-(X)sulfonyl carbamoylmethoxy]calix[4]arene-crown-5 ligands 5b–e. The procedure was essentially the same as that for the cone conformers.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(*N*-methanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (5b). Chromatography on silica gel with EtOAc as eluent, yield 73%, white solid, mp > 300 °C. Found: C, 64.63; H, 7.66; N, 2.76. $C_{58}H_{80}O_{13}N_2S_2$ requires C, 64.66; H, 7.48; N, 2.60%. ν_{max}(film)/cm^{-1} 3414 (NH); 1760 (C=O); δ_H 8.72 (2 H, s, NH), 7.11 (4 H, s, ArH), 7.10 (4 H, s, ArH), 3.95 (8 H, s, $ArCH_2Ar$), 3.62–3.72 (4 H, m, OCH_2CH_2O), 3.47 (4 H, s, OCH_2CO), 3.36–3.46 (8 H, m, OCH_2CH_2O), 3.17 (6 H, s, CH_3SO_2), 2.90–3.02 (4 H, m, OCH_2CH_2O), 1.39 (18 H, s, $C(CH_3)_3$), 1.28 (18 H, s, $C(CH_3)_3$); δ_C 169.54, 154.10, 152.76, 146.90, 146.07, 133.39, 132.49, 126.50, 126.44, 73.49, 71.18, 70.71, 69.86, 68.04, 41.35, 39.02, 34.17, 34.08, 31.66, 31.22.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(*N*-(benzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (5c). Chromatography on silica gel with CH_2Cl_2–MeOH (50 : 1) as eluent, yield 57%, white solid, mp 275–278 °C. Found: C, 67.79; H, 7.08; N, 2.39. $C_{68}H_{84}O_{13}N_2S_2$ requires C, 67.97; H, 7.05; N, 2.33%. ν_{max}(film)/cm^{-1} 3414 (NH); 1760 (C=O); δ_H 9.21 (2 H, s, NH), 7.98–8.08 (4 H, m, ArH), 7.56–7.66 (2 H, m, ArH), 7.46–7.56 (4 H, m, ArH), 7.09 (4 H, s, ArH), 7.01 (4 H, s, ArH), 3.91 (8 H, s, $ArCH_2Ar$), 3.60–3.70 (4 H, m, OCH_2CH_2O), 3.36–3.48 (8 H, m, OCH_2CH_2O), 3.03 (4 H, s, OCH_2CO), 2.89–2.99 (4 H, m, OCH_2CH_2O), 1.37 (18 H, s, $C(CH_3)_3$), 1.10 (18 H, s, $C(CH_3)_3$); δ_C 168.56, 153.88, 152.61, 147.01, 145.90, 138.58, 133.81, 133.58, 132.79, 128.99, 128.31, 126.75, 126.37, 73.50, 71.19, 69.83, 68.09, 39.01, 34.04, 33.92, 31.64, 31.00.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(*N*-*p*-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (5d). Chromatography on silica gel with CH_2Cl_2–MeOH (100 : 1) as eluent, yield 58%, light yellow solid, mp 276–279 °C. Found: C, 63.55; H, 6.44; N, 4.35. $C_{68}H_{82}O_{17}N_4S_2$ requires C, 63.24; H, 6.40; N, 4.34%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1726, 1703 (C=O); δ_H 9.45 (2 H, s, NH), 8.28–8.38 (4 H, m, ArH), 8.18–8.28 (4 H, m, ArH), 7.11 (4 H, s, ArH), 7.01 (4 H, s, ArH), 3.88 (4 H, d, *J* 17.0, $ArCH_2Ar$), 3.94 (4 H, d, *J* 17.0, $ArCH_2Ar$), 3.60–3.72 (4 H, m, OCH_2CH_2O), 3.36–3.48 (8 H, m, OCH_2CH_2O), 3.09 (4 H, br s, OCH_2CO), 2.88–3.02 (4 H, m, OCH_2CH_2O), 1.38 (18 H, s, $C(CH_3)_3$), 1.11 (18 H, s, $C(CH_3)_3$); δ_C 169.05, 153.94, 152.72, 150.79, 147.04, 146.39, 143.92, 133.69, 132.85, 129.78, 126.70, 126.57, 124.31, 73.50, 71.42, 71.23, 69.77, 68.24, 38.97, 34.10, 33.97, 31.63, 30.94.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(*N*-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-crown-5 (5e). Chromatography on silica gel with hexanes–THF (2 : 1) as eluent, yield 86%, white solid, mp 233–235 °C. Found: C, 59.06; H, 6.44; N, 2.44. $C_{58}H_{74}O_{13}N_2S_2F_6$ requires C, 58.77; H, 6.29; N, 2.36%. ν_{max}(film)/cm^{-1} 2800–3300 (NH); 1764 (C=O); δ_H (d_6-acetone) 11.26 (2 H, br s, NH), 7.21 (4 H, s, ArH), 7.17 (4 H, s, ArH), 4.13 (4 H, d, *J* 16.6, $ArCH_2Ar$), 3.99 (4 H, d, *J* 16.7, $ArCH_2Ar$), 3.58–3.71 (4 H, m, OCH_2CH_2O), 3.46–3.56 (4 H, m, OCH_2CH_2O), 3.25–3.46 (8 H, m, OCH_2CH_2O, OCH_2CO), 2.94–3.12 (4 H, m, OCH_2CH_2O), 1.41 (18 H, s, $C(CH_3)_3$), 1.26 (18 H, s, $C(CH_3)_3$); δ_C 168.66, 155.04, 152.72, 147.14, 146.33, 135.08, 134.36, 127.50, 127.06, 74.46, 71.70, 70.87, 70.17, 68.41, 39.52, 34.64, 34.51, 32.13, 31.55.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,27-dihydroxycalix[4]-arene-crown-5 (7). Under nitrogen, a solution of *p-tert*-butylcalix[4]arene (**6**·toluene) (5.00 g, 6.75 mmol), tetraethylene glycol ditosylate (3.84 g, 7.64 mmol) and K_2CO_3 (1.06 g, 7.64 mmol) in MeCN (300 mL) was refluxed for 24 h. The solution was filtered and the MeCN was evaporated *in vacuo.* The residue was dissolved in CH_2Cl_2 (200 mL) and water (100 mL) was added. The organic phase was separated and washed with 10% aqueous HCl (2 × 100 mL) and water (2 × 100 mL), dried over $MgSO_4$ and evaporated *in vacuo* to give the crude product, which was purified by chromatography on alumina with hexanes–EtOAc (4 : 1) as eluent to give **7** (4.03 g, 74%) as a white solid (mp 244–247 °C, ref. 3a 246–248 °C, ref. 14 245–247 °C); Found: C, 77.04; H, 8.77. $C_{52}H_{70}O_7$ requires C, 77.38; H, 8.74%; ν_{max}(film)/cm^{-1} 3417 (OH); δ_H 7.17 (2 H, s, OH), 7.07 (4 H, s, ArH), 6.75 (4 H, s, ArH), 4.37 (4 H, d, *J* 13.1, $ArCH_2Ar$), 4.07 (8 H, s, OCH_2CH_2O), 3.97 (4 H, t, *J* 5.5, OCH_2CH_2O), 3.84 (4 H, t, *J* 5.5, OCH_2CH_2O), 3.28 (4 H, d, *J* 13.1, $ArCH_2Ar$), 1.31 (18 H, s, $C(CH_3)_3$), 0.91 (18 H, s, $C(CH_3)_3$); δ_C 150.80, 149.76, 146.79, 141.14, 132.48, 127.79, 125.39, 124.93, 71.06, 70.85, 70.35, 33.85, 33.80, 31.73, 31.30, 30.96.

Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(ethoxy-carbonylmethoxy)-calix[4]arene-crown-5 (8). A mixture of **7** (4.64 g, 5.75 mmol) in THF (250 mL) and NaH (0.96 g, 28.76 mmol) was stirred under nitrogen at room temperature for 30 min. Then ethyl bromoacetate (5.76 g, 34.49 mmol) in THF (50 mL) was added slowly. The mixture was stirred at room temperature for 12 h and quenched with a small amount of water (added dropwise). The THF was evaporated *in vacuo.* CH_2Cl_2

(200 mL) and 10% HCl (100 mL) were added to the residue. The organic layer was separated, washed with water (2 × 100 mL), dried over $MgSO_4$ and evaporated *in vacuo.* The residue was purified by chromatography on alumina with hexanes–EtOAc (5 : 1) as eluent to give **8** (3.77 g, 67%) as a white solid (mp 225–227 °C); Found: C, 73.60; H, 8.72. $C_{60}H_{82}O_{11}$ requires C, 73.59; H, 8.44%; ν_{max}(film)/cm^{-1} 1759, 1732 (C=O); δ_H 6.84 (4 H, s, ArH), 6.74 (4 H, s, ArH), 5.08 (4 H, s, OCH_2CO), 4.65 (4 H, d, *J* 12.7, $ArCH_2Ar$), 4.08–4.18 (8 H, m, $OC\mathit{H}_2CH_3$, OCH_2CH_2O), 4.05 (4 H, t, *J* 5.3, OCH_2CH_2O), 3.72–3.78 (4 H, m, OCH_2CH_2O), 3.64–3.70 (4 H, m, OCH_2CH_2O), 3.17 (4 H, d, *J* 12.7, $ArCH_2Ar$), 1.23 (6 H, t, *J* 7.2, $CH_2C\mathit{H}_3$), 1.13 (18 H, s, $C(CH_3)_3$), 1.01 (18 H, s, $C(CH_3)_3$); δ_C 171.14, 153.46, 152.33, 144.80, 144.63, 134.31, 133.57, 125.02, 124.97, 72.75, 71.17, 70.85, 70.56, 70.37, 60.10, 33.85, 33.74, 31.90, 31.45, 31.30, 14.16.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,27-bis(*p-tert*-butoxycarbonylmethoxy)-calix[4]arene (9). A solution of **6**·toluene (10.00 g, 13.50 mmol) and K_2CO_3 (2.10 g, 15.20 mmol) in MeCN (150 mL) was heated at reflux for 0.5 h and *tert*-butyl bromoacetate (6.14 g, 31.48 mmol) was added dropwise. The mixture was refluxed for 24 h. The MeCN was removed *in vacuo* and CH_2Cl_2 (300 mL) and water (100 mL) were added to the residue. The organic layer was washed with 10% HCl (100 mL) and water (2 × 100 mL), dried over $MgSO_4$. The solvent was evaporated *in vacuo.* Purification by chromatography on silica gel with CH_2Cl_2–EtOAc (15 : 1) as eluent to give **9** (10.42 g, 88%) as a white solid (mp 180–182 °C). Found: C, 76.86; H, 8.86. $C_{56}H_{76}O_8$ requires C, 76.68; H, 8.73%; ν_{max}(film)/cm^{-1} 3438 (OH), 1754, 1732 (C=O); δ_H 7.14 (2 H, s, OH), 7.02 (4 H, s, ArH), 6.79 (4 H, s, ArH), 4.58 (4 H, s, OCH_2CO), 4.44 (4 H, d, *J* 13.1, $ArCH_2Ar$), 3.29 (4 H, d, *J* 13.2, $ArCH_2Ar$), 1.54 (18 H, s, $C(CH_3)_3$), 1.27 (18 H, s, $OC(CH_3)_3$), 0.91 (18 H, s, $C(CH_3)_3$); δ_C 168.23, 150.81, 150.47, 146.85, 141.18, 132.39, 127.75, 125.61, 124.99, 82.20, 73.08, 33.87, 33.77, 31.80, 31.66, 31.00, 28.14.

1,3-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis-(*tert*-butoxycarbonylmethoxy)calix[4]arene-crown-5 (10). A solution of **9** (10.00 g, 11.40 mmol), tetraethylene glycol ditosylate (6.27 g, 12.48 mmol), and Cs_2CO_3 (5.57 g, 17.10 mmol) in MeCN (600 mL) was refluxed for 24 h. The MeCN was evaporated *in vacuo* and CH_2Cl_2 (300 mL) and water (100 mL) were added to the residue. The organic layer was separated and washed with 10% HCl (100 mL) and water (2 × 100 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo* to give the crude product, which was purified by chromatography on alumina with CH_2Cl_2–EtOAc (50 : 1) as eluent to give **10** (6.49 g, 55%) as a white solid (mp 115–118 °C). Found: C, 74.18; H, 8.43. $C_{64}H_{90}O_{11}$ requires C, 74.24; H, 8.76%; ν_{max}(film)/cm^{-1} 1757, 1725 (C=O); δ_H 7.13 (4 H, s, ArH), 7.04 (4 H, s, ArH), 4.05 (4 H, d, J 16.0, $ArCH_2Ar$), 3.83 (4 H, d, J 16.0, $ArCH_2Ar$), 3.78 (4 H, s, OCH_2CO), 3.51–3.62 (4 H, m, OCH_2CH_2O), 3.40–3.50 (4 H, m, OCH_2CH_2O), 3.03–3.16 (4 H, m, OCH_2CH_2O), 2.90–3.03 (4 H, m, OCH_2CH_2O), 1.36 (18 H, s, $C(CH_3)_3$), 1.35 (18 H, s, $C(CH_3)_3$), 1.25 (18 H, s, $C(CH_3)_3$); δ_C 169.19, 153.95, 144.48, 143.89, 133.40, 133.30, 127.26, 125.93, 80.70, 72.60, 71.23, 69.99, 69.10, 68.88, 38.92, 33.97, 33.83, 31.69, 31.41, 28.03.

Extraction procedure. An aqueous solution of the alkaline earth metal chlorides with hydroxides for pH adjustment (for **3e**, **4e** and **5e**, 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 (except **3e**, 1.0 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. (For **3e**, the aqueous phase was diluted 100 times prior to ion chromatographic analysis.) 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.

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