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New di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands: synthesis and divalent metal ion extraction

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ABSTRACT

New di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands with elongated side arms in cone, partial-cone, and 1,2-alternate conformations of the calixarene scaffold are prepared and characterized. The acidic groups on the side arms include carboxylic acid and *N*-(X)sulfonyl carboxamide with X variation of −Me, −Ph, $-C_6H_4-4-NO_2$, and $-CF_3$. Solvent extractions of alkaline earth metal cations, Hg^{2+}, and Pb^{2+} from aqueous solutions into chloroform are employed to probe the effects of these structural modifications on the divalent metal ion complexation behavior of the new ligands.

1. Introduction

Calixarenes and crown ethers are both well-known building blocks for the construction of selective metal ion receptors and carriers.[1,2] Of the former class of macrocyclic, multidentate ligands, tetrameric calix[4]arene is particularly well-suited for this purpose because of its accessibility, ease of chemical modification, and cation binding properties. Incorporation of a polyether loop on the lower rim of calix[4]arene not only enhances the cation binding ability of the parent calixarene, but allows for selectivity control through modulation of the crown ether ring size. These hybrid receptors are identified as calixarene-crown ethers or calixcrowns.

Two types of polyether bridges on the lower rim of a calix[4]arene molecule are possible: 1,3-bridging of distal phenolic units and 1,2-bridging of proximal phenolic units.[3] Until recently, studies of calix[4]arene-crown ether compounds have been focused on dialkylated, 1,3-bridged calix[4]arene-crown ethers. Ligands of this type were found to exhibit high binding affinites and selectivities in extractions of alkali and alkaline earth metal cations.[4,5] Much less is known about the properties of regioisomeric 1,2-bridged calix[4]arene-crown ethers, which are more difficult to synthesize. Also, initial investigations suggested that 1,2-bridged calix[4]arene-crown ethers possessed only poor metal cation binding abilities with little selectivity.[6–8]

Of particular interest in our metal ion separations research program are calix[4]arene-crown compounds with two acidic side arms attached to the remaining phenolic oxygens. Such ligands are designed to effectively extract divalent metal ions from aqueous solutions into organic diluents.[9] Extraction proceeds by an ion-exchange mechanism to form an electroneutral di-ionized calixcrown-divalent metal ion complex in the organic phase. This avoids the need for concomitant transfer of a hydrophilic anion from the aqueous phase.

The first example of a di-ionizable calixcrown compound was the cone *p-tert*-butylcalix[4]arene-1,3-crown-5 di(carboxylic acid) **1** (Fig. 1) reported by Ungaro and Pochini in 1984.[4]

Recently, we undertook the synthesis of cone di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown ether ligands **2** (Fig. 2) and their evaluation in divalent metal ion extractions from aqueous solutions into chloroform.[10–14] For this series of ligands, the polyether ring was varied from crown-3 (m=0)[10,15] to crown-4 (m=1)[11,12] to crown-5 (m=2)[13] to crown-6 (m=3).[14] For each polyether ring size, the ionizable groups included both carboxylic acid and *N*-(X)sulfonyl carboxamides for which the acidity can be tuned by variation of the electron-withdrawing ability of X.[16] Surprisingly, di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ether ligands were found to be very effective in competitive alkaline earth metal cation (AEMC)

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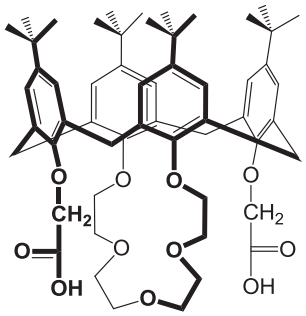

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Fig. 1. First reported di-ionizable calix[4]arene-crown ether **1**.

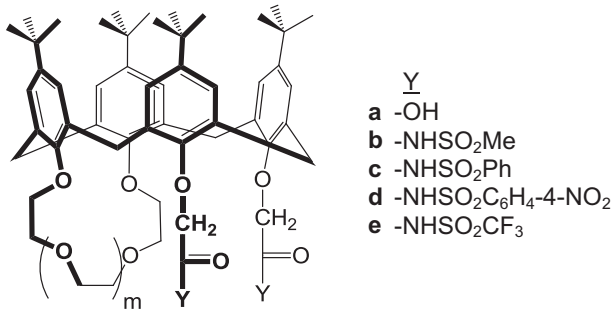


Fig. 2. Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown ether ligands.

the carbonyl group in the proton-ionizable function have been examined in these investigations. The effect of elongating the side arms by increasing the number of methylene groups in the spacer is now explored.

2. Results and discussion

2.1. Geometry optimization of di-ionized calix[4]arene-1,2-crown-4 barium complex

So far, we have been unsuccessful in preparing suitable crystals for solid-state structure determination of a di-ionized *p-tert*-butylcalix[4]arene-1,2-crown-4 complex with Ba^{2+}. To gain insight into the structure of such a complex, the optimized geometry of complex **5** (Fig. 3) was calculated. The ab initio calculations were performed using the Gaussian 03 Revision D.01 suite of programs.[17] For simplification, the four *p-tert*-butyl groups were truncated. The ionizable side arms are $-OCH_2C(O)NHSO_2CH_3$, which has a single methylene group spacer.

The skeleton **3** was assembled using the GausView 4 program, then minimized by semi-empirical methods with the AM1 basis set. The barium complexes were solved using Hartree–Fock theory with custom basis sets: 6-31G-d,p for the atoms C, H, N, O, S; LANL2DZ for barium complex **5**; and LANL2MB for barium complex **4**.[18–20] LANL2MB treats first row elements with the STO-3G basis set, and was chosen for complex **4**, as it required less computational resources, but demonstrated a geometry optimized structure converged with the large number of atoms and a heavy atom, Ba. The LANL2DZ (LANL2MB) basis set utilizes effective core potentials (ECPs) for electrons near the nucleus and incorporates relativistic effects important for heavy atoms. Complex **5** was prepared electrically neutral with nitrogen of the ionized *N*-(methyl)sulfonyl

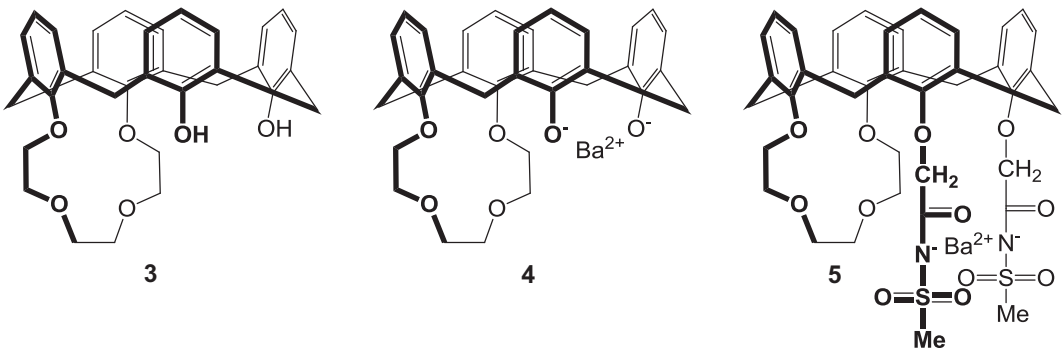


Fig. 3. Structures utilized in geometry optimization of barium complex **5**.

extractions with extraordinarily high selectivity for Ba^{2+}. Since the crown-4 ring is too small to accommodate Ba^{2+}, we envisioned an extraction complex in which the large divalent metal ion perches on the four polyether oxygens with the two ionized side arms coordinating from the opposite side. The Ba^{2+} selectivity in competitive AEMC extraction was found to be lower for analogues with the larger polyether rings of crown-5 and crown-6 and nearly disappeared with smaller crown-3 rings.

In further probing of the reason(s) for the unanticipated selectivity for Ba^{2+} extraction observed with the *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands, the effect of replacing the four *p-tert*-butyl groups on the upper rim with hydrogens was explored.[12] This variation in ligand structure produced some further enhancement in the high selectivity for Ba^{2+} extraction.

To date, only functional side arms of the type $-OCH_2C(O)Y$ with a single methylene group spacer between the phenolic oxygen and carboxamide function formally negative while the barium was formally +2.

The calculated structure for complex **5** is presented in Fig. 4. As can be seen, Ba^{2+} is associated with the two ionized side arms. There is some distance between the four crown ether oxygens and the metal ion. From this calculated structure, the effect of elongating the proton-ionizable side arms remains uncertain.

2.2. Synthesis of di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 compounds with elongated acidic side arms

Since side arms of the type $-OCH_2CH_2C(O)Y$ can undergo retro-Michael cleavage reactions under basic conditions, side arm elongation to include two methylene groups in the spacer was not a viable structural variation. Attention was focused on side arms of $-O(CH_2)_3C(O)Y$ and $-O(CH_2)_4C(O)Y$.

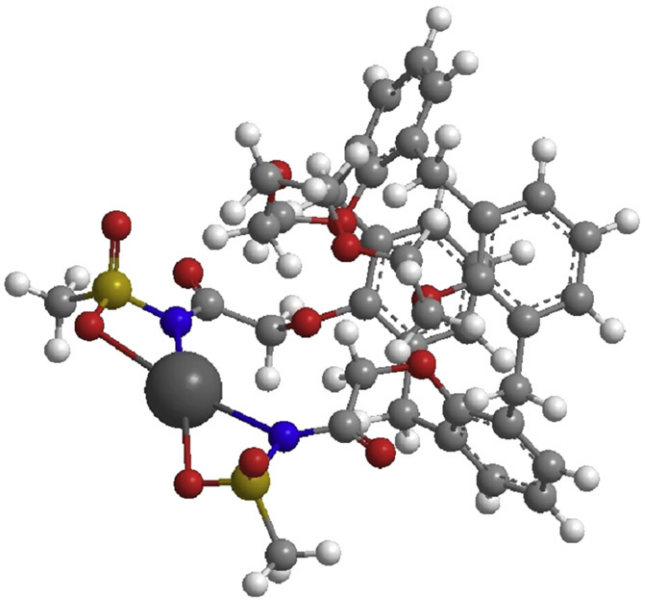
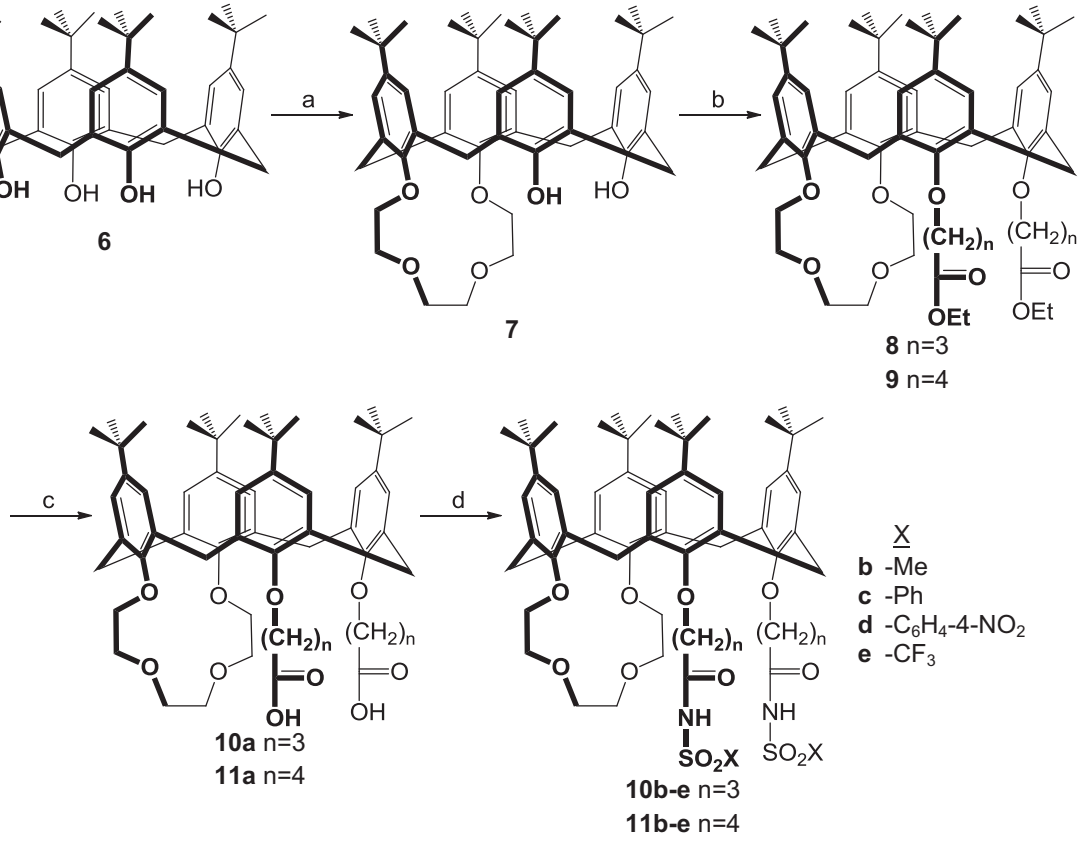


Fig. 4. Geometry optimized structure of barium complex **5**.

2.2.1. Cone di-ionizable p-tert-butylcalix[4]arene-1,2-crown-4 ligands. Synthetic routes to cone di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **10a**–**e** and **11a**–**e** with $-O(CH_2)_3C(O)Y$ and $-O(CH_2)_4C(O)Y$ side arms, respectively, are presented in Scheme 1. Preparation of *p-tert*-butylcalix[4]arene-1,2-crown-4 (**7**) was initially attempted following a literature procedure.[21] We experienced erratic results and yields from this reported procedure and developed an alternative method for synthesis of calixcrown **7**. Reaction of calix[4]arene (**6**) with triethylene glycol ditosylate[22] and 10 equiv of Cs_2CO_3 in MeCN gave the desired *p-tert*-butylcalix[4]arene-1,2-crown (**7**) in 39% yield. Diesters **8** and **9** were synthesized in 57 and 52% yields, respectively, by adding either ethyl bromobutyrate or ethyl bromovalerate to a refluxing mixture of calixcrown **7** and NaH in THF. Diesters **8** and **9** were hydrolyzed by refluxing with 10% aqueous NMe_4OH in THF to give the corresponding di(carboxylic acid)s **10a** and **11a** in quantitative yields. Di(carboxylic acid)s **10a** and **11a** were stirred at room temperature in benzene with oxalyl chloride. The crude di(acid chloride) in THF was added to a mixture of the appropriate sulfonamide and NaH in THF. The *N*-(X)sulfonyl carboxamides **10b**–**e** and **11b**–**e** were obtained in 72–95% yield. Ligands **10d**, **10e**, **11b**, **11d**, and **11e** were isolated as the monosodium salts. Further attempts to protonate the monosodium salts resulted in cleavage of the *N*-(X)sulfonyl carboxamide functionality.

Cone conformations of diesters **8** and **9**, di(carboxylic acid)s **10a** and **11a**, and *N*-(X)sulfonyl carboxamides **10b**–**e** and **11b**–**e** were confirmed by ^1H, ^{13}C, $^1H-^1H$ correlation (COSY), and $^1H-^{13}C$ heteronuclear correlation (HETCOR) NMR spectroscopy. According to the de Mendoza rule,[23] the absence of peaks corresponding to the bridging methylene carbons in the ^{13}C NMR spectra at ~35–40 ppm shows that all four aryl units are *syn* to one another, thus verifying the cone conformation. The *syn* arrangement of the aryl groups in the cone conformation makes the axial and equatorial protons diastereotopic to one another. These methylene protons exhibit a classical AX pattern as widely separated doublets.[24]

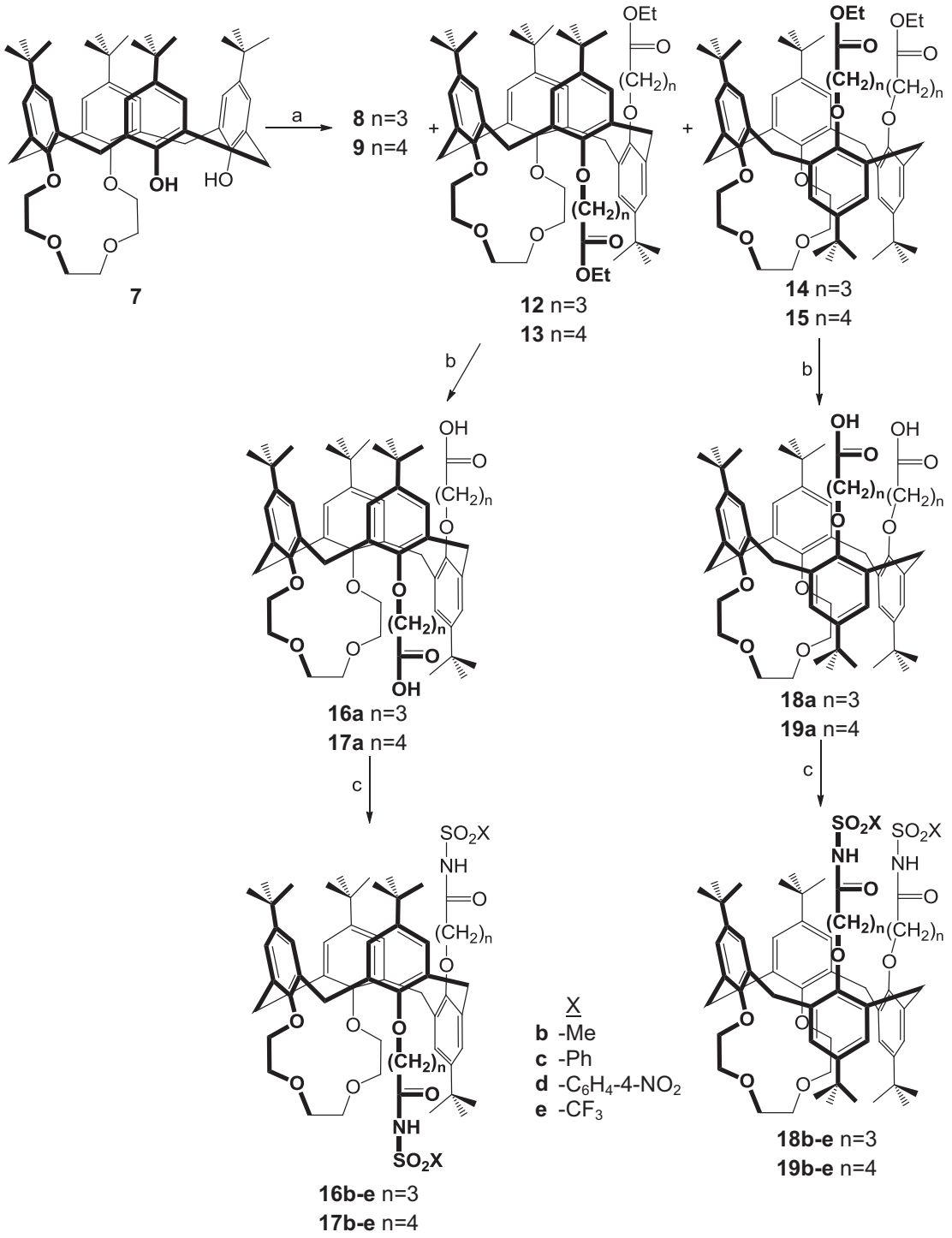
The HETCOR spectra for **10a**–**e** and **11a**–**e** in the cone conformation show a correlation between the bridging methylene carbons and bridging methylene protons (see Supplementary data). These protons correlate with three different types of carbons, proving that the crown ether moiety and the ionizable pendant



Scheme 1. Synthesis of di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **10a**–**e** and **11a**–**e** in the cone conformation. Reagents and conditions: (a) $TsO(CH_2CH_2O)_3Ts$, Cs_2CO_3, MeCN, reflux; (b) $Br(CH_2)_nCO_2Et$ (n=3 or 4), NaH, THF, reflux; (c) 10% aq NMe_4OH, THF, reflux; (d) (i) $(COCl)_2$, C_6H_6, rt; (ii) XSO_2NH_2, NaH, THF, rt.

arms are attached to their respective phenolic oxygens in proximal positions (The presence of three different types of carbons is consistent with the cone conformation.).

2.2.2. Partial-cone and 1,2-alternate di-ionizable p-tert-butylcalix[4] arene-1,2-crown-4 ligands. We sought to identify new conditions whereby alkylation of *p-tert*-butylcalix[4]arene-1,2-crown-4 (**7**) 1,2-alternate conformer (Of the four limiting conformations for calix [4]arene compounds, the 1,2-alternate conformation is the least common.).[25] Nevertheless, we discovered that the three conformers in the diester mixture could be separated easily by column chromatography. This provided the synthetic route by which partial-cone and 1,2-alternate analogues of cone ligands **10a**–**e** and **11a**–**e** were realized (Scheme 2).



Scheme 2. Synthesis of partial-cone and 1,2-alternate di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 compounds **16a**–**e**, **17a**–**e**, **18a**–**e**, and **19a**–**e**. Reagents and conditions: (a) $Br(CH_2)_nCO_2Et$ (n=3 or 4), Cs_2CO_3, MeCN, reflux; (b) 10% aq NMe_4OH, THF, reflux; (c) (i) $(COCl)_2$, C_6H_6, rt; (ii) XSO_2NH_2, NaH, THF, rt.

would give a single non-cone conformer of the diester intermediate. Several attempts gave crude products that contained mixtures of the cone and partial-cone diesters, as well as the rarely encountered

Reaction of **7**, Cs_2CO_3, and ethyl bromobutyrate in MeCN at reflux gave a mixture of cone diester **8**, partial-cone diester **12**, and 1,2-alternate diester **14**. The three regioisomers were separated by

column chromatography. Use of ethyl bromovalerate in place of ethyl bromobutyrate produced a mixture of cone diester **9**, partial-cone diester **13**, and 1,2-alternate diester **15** that was separated by column chromatography.

Diesters **12**–**15** in the partial-cone and 1,2-alternate conformations were refluxed with Me_4NOH in aqueous THF to give the desired di(carboxylic acid)s **16a**, **17a**, **18a**, and **19a** in near-quantitative yields. Each di(carboxylic acid) was stirred with oxalyl chloride in benzene at room temperature to produce the crude di(acid chloride). The di(acid chloride) in THF was added to a mixture of the appropriate sulfonamide and NaH in THF. The partial-cone *N*-(X) sulfonyl carboxamides **16b**–**e** and **17b**–**e** with $-O(CH_2)_3C(O)Y$ and $-O(CH_2)_4C(O)Y$ side arms, respectively, were realized in 39–99% yield. The 1,2-alternate *N*-(X)sulfonyl carboxamides ligands **18b**–**e** and **19b**–**e** with $-O(CH_2)_4C(O)Y$ and $-O(CH_2)_4C(O)Y$ side arms, respectively, were obtained in 69–95%.yield.

Diesters **12**–**15**, di(carboxylic acid)s **16a**, **17a**, **18a**, and **19a**, and *N*-(X)sulfonyl carboxamides **16b**–**e**, **17b**–**e**, **18b**–**e**, and **19b**–**e** were analyzed by ^1H, ^{13}C, COSY, and HETCOR NMR spectroscopy to verify that they were the desired products in the appropriate conformations.

In the ^1H NMR spectra for partial-cone **16b**–**e** and **17b**–**e**, the NH protons appear as widely separated singlets. The downfield singlet at 10.55–11.36 ppm corresponds to the proton on the *syn*-arranged side arm and the more upfield singlet at 8.36–9.35 ppm corresponds to the *anti*-arranged side arm. The three *syn* aryl units of a partial-cone conformer create a 'deshielding' effect that shifts a proton attached to these groups farther downfield compared to those attached to the *anti* aryl unit.

The bridging methylene protons adjacent to *syn*-arranged aryl groups are also diastereotopic, each containing non-equivalent axial and equatorial protons. AX patterns of two widely separated doublets were observed in the ^1H NMR spectrum for the bridging methylene protons adjacent to *syn* aryl units.[24] AB patterns or singlet peaks were also observed for the methylene protons adjacent to *anti*-arranged aryl groups. As expected for compounds in the partial-cone conformation, peaks at 35–40 ppm (*anti*) and 30–31 ppm (*syn*) corresponding to the bridging methylene carbons were observed in the ^{13}C NMR spectra.

Correlations of the bridging methylene groups in partial-cone ligands **16a**–**e** and **17a**–**e** exhibited similar patterns and correlations in their respective ^1H and ^{13}C NMR spectra (see Supplementary data). The peaks for the correlated methylene protons in their ^1H NMR spectra integrated with a 1:1:2 ratio. These three peaks represent the *syn*-arranged aryl groups and the protons adjacent to the *anti*-arranged groups. In the HETCOR spectra, these methylene protons correlate with four different types of carbons, which verify that these compounds are in the partial-cone conformation and contain no symmetry due to the proximal attachment of the crown ether ring.

Compounds **18a**–**e** and **19a**–**e** in the 1,2-alternate conformation exhibited at least two pairs of doublets in their ^1H NMR spectra corresponding to the bridging methylene protons. The two pairs of doublets that always appear are widely separated (AX pattern), and the other methylene protons either appear as a closely spaced AB pattern or a singlet.[24] These correspond to the protons adjacent to *syn* aryl groups and *anti* aryl groups, respectively, and had an integration ratio of 1:1:2.

Bridging methylene carbon peaks typically appear at 35–40 and 30–31 ppm in the ^{13}C NMR spectrum corresponding to the carbon atoms attached to *anti* and *syn* aromatic units, respectively.[23] It was found that the carbon atoms adjacent to *syn* aryl groups appear at 28–29 ppm for these compounds. Selected chemical shifts and splitting patterns are presented in Table S1 in Supplementary data.

The NH protons attached to side arms on aryl groups *syn* to each other but *anti* to the groups containing the 1,2-crown-4 moiety exhibit peaks that appear as singlets. These singlets were relatively upfield (9.17–10.04 ppm) compared to the NH protons in ligands **10a**–**e** and **11a**–**e** in the cone conformation (9.58–12.28 ppm). This is due to the deshielding effect that *syn*-arranged aryl groups have on adjacent substituents.

Compounds **18a**–**e** and **19a**–**e** exhibit similar patterns and correlations in their respective portions of their COSY and HETCOR NMR spectra (see Supplementary data). The spectra further confirm that these ligands are in the 1,2-alternate conformation. The methylene protons correlate with three different types of carbons in the HETCOR spectra, which verifies these compounds are in the 1,2-alternate conformation, there is some symmetry present in these compounds, and the crown ether rings are attached in a proximal fashion.

2.3. Effects of acidic side arm elongation and calixarene unit conformation on divalent metal ion extraction

For comparison with the previously reported[11,12] cone di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **2a**–**e** having $-OCH_2C(O)Y$ side arms, solvent extractions of selected divalent metal ion species from aqueous solutions into chloroform were conducted. These included competitive extractions of hard AEMC (Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+})[11] and single species extractions of intermediate Pb^{2+} and soft Hg^{2+}.[12] Recall that ligands **2a**–**e** with $m=1$ showed high Ba^{2+} selectivity over other AEMC with near 100% metal loadings. These ligands also showed high Pb^{2+} and Hg^{2+} extraction propensities in single species extractions.[12] They extracted >90% of these metal ions except for di(carboxylic acid) **2a**, which gave only about 50% loading with Hg^{2+}.

The extraction procedures were the same as those reported previously[10–14] with the following exception. Since ligands **10d**, **10e**, **11b**, **11d**, and **11e** were obtained as monosodium salts, a modified procedure was employed to ensure removal the Na^+ prior to performing the extractions.

2.3.1. Solvent extraction of AEMC by di-ionizable p-tert-butylcalix[4] arene-1,2-crown-4 ligands. Competitive solvent extraction of aqueous AEMC solutions (2.00 mM in Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) by 1.00 mM solutions of di-ionizable ligands **10a**–**e**, **11a**–**e**, **16a**–**e**, **17a**–**e**, **18a**–**e**, and **19a**–**e** in chloroform was performed. Plots of metal loading of the organic phase versus the equilibrium pH of the aqueous phase are shown in Fig. S7 for cone ligands **10a**–**e** with $-O(CH_2)_3C(O)Y$ side arms and in Fig. S8 for cone ligands **11a**–**e** with $-O(CH_2)_4C(O)Y$ side arms. Immediately apparent is the poor extraction efficiency of these 10 ligands for AEMC. The highest metal cation loading of about 50% was observed with di(carboxylic acid) ligand **10a**. Only di(carboxylic acid) ligands **10a** and **11a** show significant selectivity, in this case for Ca^{2+}. Thus extending the $-OCH_2C(O)Y$ side arms of ligands **2a**–**e** ($n=1$) to $-O(CH_2)_3C(O)Y$ in **10a**–**e** and $-O(CH_2)_4C(O)Y$ in **11a**–**e** destroys the efficient and selective extraction of Ba^{2+}.

Changing the calixarene conformation in the calix[4]arene-1,2-crown-4 ligand from cone to partial-cone or 1,2-alternate varies the spatial relationship between the ionized side arms and the crown-4 ring. For partial-cone ligands **16a**–**e** and **17a**–**e**, one side arm is positioned near to the polyether ring and the other side arm is remote. For the unusual 1,2-alternate conformation in ligands **18a**–**e** and **19a**–**e**, both acidic side arms are directed away from the crown-4 ring.

Plots of metal loading of the organic phase versus the equilibrium pH of the aqueous phase are shown in Fig. S9 for partial-cone ligands **16a**–**e** with $-O(CH_2)_3C(O)Y$ side arms and in Fig. S10 for partial-cone ligands **17a**–**e** with $-O(CH_2)_3C(O)Y$ side arms. Ligands **16a**–**e** are poor AEMC extractants. When the acidic side arms are lengthened by one methylene group, the AEMC extraction efficiencies improve somewhat for ligands **17b** and **17c**, with Ba^{2+} selectivity.

Plots of metal loading of the organic phase versus the equilibrium pH of the aqueous phase are shown in Fig. 5 for 1,2-alternate

ligands **18a**–**e** with $-O(CH_2)_3C(O)Y$ side arms and in Fig. 6 for 1,2-alternate ligands **19a**–**e** with $-O(CH_2)_4C(O)Y$ side arms. Ligands **18a**–**e** are found to be weak and unselective AEMC extractants. When the acid side arms are lengthened by one methylene group, we were surprised by the dramatic change in AEMC extraction behavior. Ligands **19a**–**d** in the 1,2-alternate conformation with $-O(CH_2)_4C(O)Y$ side arms showed the highest AEMC loadings of the six ligand series examined in this study. In comparison, cone **11c** and partial-cone **17c**, the 'second best' in the six-ligand series, reached maximum loadings of only 40%. The sharp contrast of metals loading for the 1,2-alternate conformers over those exhibited by the cone and partial-cone conformers suggests that AEMC coordination is optimized when the ionized extended side arms are spatially close to one another and also to the π-electron cloud of the aromatic rings.

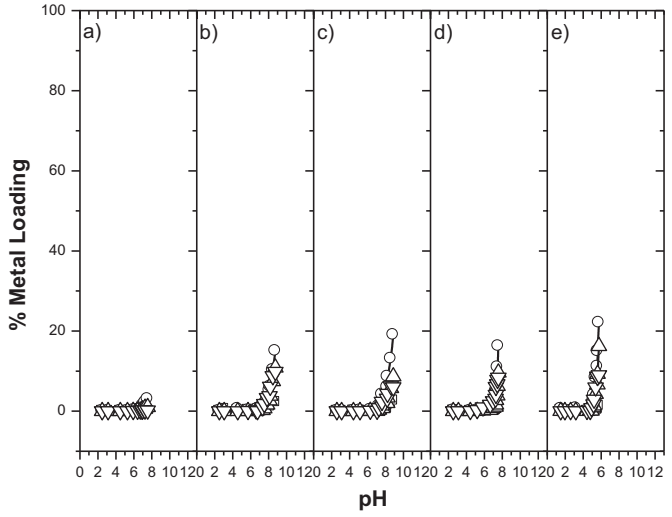


Fig. 5. Percent metal loading versus the equilibrium pH of the aqueous phase for competitive solvent extraction of AEMC into chloroform by 1,2-alternate, di-ionizable calix[4]arene-1,2-crown-4 ligands **18a**–**e** with $-O(CH_2)_3C(O)Y$ side arms. (a) **18a**, (b) **18b**, (c) **18c**, (d) **18d**, (e) **18e** (□=Mg^{2+}, ○=Ca^{2+}, △=Sr^{2+}, ▽=Ba^{2+}).

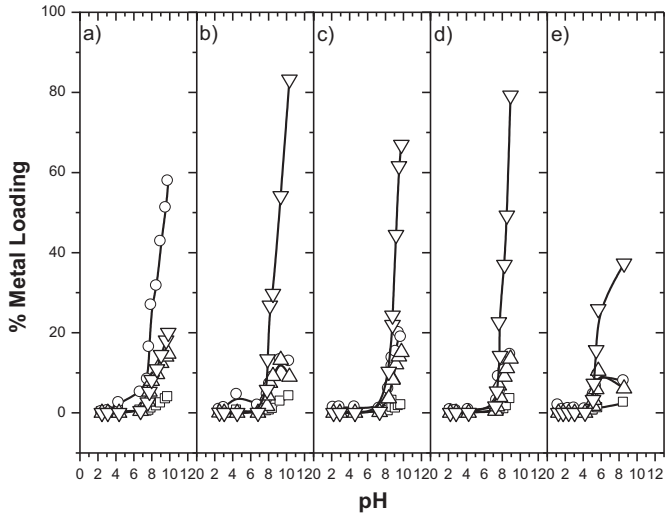


Fig. 6. Percent metal loading versus the equilibrium pH of the aqueous phase for competitive solvent extraction of AEMC into chloroform by 1,2-alternate, di-ionizable calix[4]arene-1,2-crown-4 ligands **19a**–**e** with $-O(CH_2)_4C(O)Y$ side arms. (a) **19a***, (b) **19b***, (c) **19c***, (d) **19d***, (e) **19e*** (□=Mg^{2+}, ○=Ca^{2+}, △=Sr^{2+}, ▽=Ba^{2+}) (data for extractions showing precipitate at higher pHs are excluded).

For di(carboxylic acid) **19a**, the observed Ca^{2+} selectivity indicates preferred complexation of a harder AEMC by the carboxylate-bearing side arms. When the ionized side arm contains *N*-(X)sulfonyl carboxamide groups in **19b**–**d**, the extraction selectivity changes to Ba^{2+}, the softest AEMC in the series.

2.3.2. Solvent extraction of Pb^{2+} by di-ionizable p-tert-butylcalix[4] arene-1,2-crown-4 ligands. In 2007, results for solvent extraction of intermediate Pb^{2+} from aqueous solutions into chloroform by cone ligands **2b**–**e** (with m=1) with short $-OCH_2C(O)NHSO_2X$ side arms were reported.[12] In those single species extractions, Pb^{2+} loadings were very high and exceeded 90% in all cases. The same result was observed for the di(carboxylic acid) ligand **2a**.

From solvent extraction of aqueous Pb^{2+} (1.00 mM) solutions by 0.50 mM chloroform solutions of ligands **10a**–**e**, **11a**–**e**, **16a**–**e**, **17a**–**e**, **18a**–**e**, and **19a**–**e**, plots of Pb^{2+} loading of the organic phase versus the equilibrium pH of the aqueous phase are presented in Figs. 7 and 8.

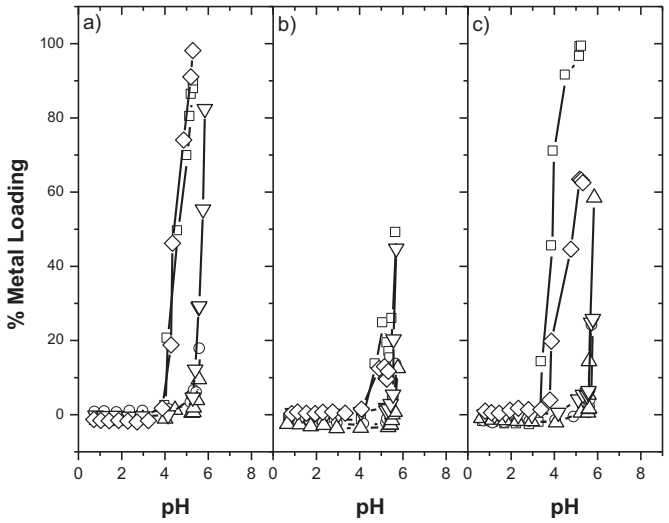


Fig. 7. Percent metal loading versus the equilibrium pH of the aqueous phase for single species solvent extraction of Pb^{2+} into chloroform by di-ionizable calix[4]arene-1,2-crown-4 ligands in three conformations: (a) cone, **10a**–**e***, (b) partial-cone, **16a**–**e**, and (c) 1,2-alternate, **18a**–**e** (□=$-CO_2H$; ○=$-C(O)NHSO_2CH_3$; △=$-C(O)NHSO_2C_6H_5$; ▽=$-C(O)NHSO_2C_6H_4$-4-NO_2; ◇=$-C(O)NHSO_2CF_3$) (data for extractions showing precipitate at higher pHs excluded).

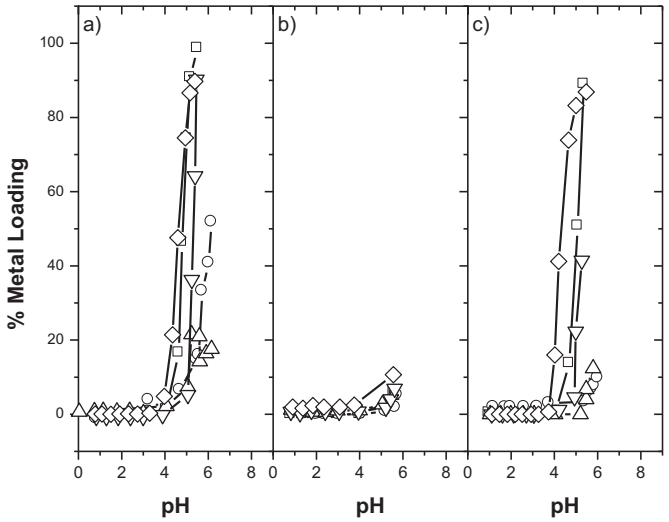


Fig. 8. Percent metal loading versus the equilibrium pH of the aqueous phase for single species solvent extraction of Pb^{2+} into chloroform by di-ionizable calix[4]arene-1,2-crown-4 ligands in three conformations: (a) cone, **11a**–**e**, (b) partial-cone, **5a**–**e***, and (c) 1,2-alternate, **7a**–**e*** (□=$-CO_2H$; ○=$-C(O)NHSO_2Me$; △=$-C(O)NHSO_2Ph$; ▽=$-C(O)NHSO_2C_6H_4$-4-NO_2; ◇=$-C(O)NHSO_2CF_3$) (data for extractions showing precipitate at higher pHs excluded).

Fig. 7 displays the Pb^{2+} extraction results for di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 cone conformers **10a**–**e** (panel a), partial-cone conformers **16a**–**e** (panel b), and 1,2-alternate conformers **18a**–**e** (panel c) with $-O(CH_2)_3C(O)Y$-containing side arms. Ligands **10a**, **10d**, and **10e** with cone conformations and **18a** with a 1,2-alternate conformation were found to be very good Pb^{2+} extractants. Ligand **10e** with a cone conformation reached a maximum loading of 98% and cone di(carboxylic acid) ligand **18a** reached 99%. As a group, the partial-cone ligands **16a-e** were the weakest Pb^{2+} extractants. This suggests that for optimal coordination with Pb^{2+} both acidic side arms should be on the same side of the polyether unit.

Di(carboxylic acid) ligands **10a**, **16a**, and **18a** are as good as, if not better, Pb^{2+} extractants than analogues with *N*-(X)sulfonyl carboxamide functions in the side arms. This change from the AEMC extraction behavior shown in Fig. 6 presumably results from the intermediate hardness/softness of Pb^{2+}.

Fig. 8 presents the extraction results for di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 cone conformers **11a**–**e** (panel a), partial-cone conformers **17a**–**e** (panel b), and 1,2-alternate conformers **19a**–**e** (panel c) with $-O(CH_2)_4C(O)Y$-containing side arms. Similar to the ligands with one less carbon in the side arm, cone ligands **11a**, **11d**, and **11e** and 1,2-alternate ligands **19a** and **19e** were very good Pb^{2+} extractants. Di(carboxylic acid) **11a** in the cone conformation showed the highest Pb^{2+} loading in reaching a maximum loading of 99%.

From comparison of the results presented in Figs. 7 and 8, it is seen that the partial-cone conformers **17a**–**e** were the poorest Pb^{2+} extractants of the six series of di-ionizable calix[4]arene-1,2-crown-4 ligands considered in this study. This is consistent with preferred coordination of Pb^{2+} by two acidic side arms on the same side of the polyether unit.

For the cone series **11** and 1,2-alternate series **19**, the di(carboxylic acid) ligands were as good as, if not better, Pb^{2+} extractants than analogues with *N*-(X)sulfonyl carboxamide functions in the side arms.

2.3.3. Solvent extraction of Hg^{2+} by di-ionizable p-tert-butylcalix[4]arene-1,2-crown-4 ligands. The published results for solvent extraction of soft Hg^{2+} from aqueous solutions into chloroform by cone ligands **2b**–**e** (m=1) with short $-OCH_2C(O)NHSO_2X$ side arms showed high efficiency.[12] In single species solvent extractions, Hg^{2+} loadings were very high and exceeded 90% in all cases. However for the di(carboxylic acid) analogue **2a**, the maximum loading was only about 50%.

From single species solvent extractions of aqueous Hg^{2+} solutions (0.25 mM) by 0.25 mM solutions of di-ionizable ligands **10a**–**e**, **11a**–**e**, **16a**–**e**, **17a**–**e**, **18a**–**e**, and **19a**–**e**, plots of Hg^{2+} loading of the organic phase versus the equilibrium pH of the aqueous phase are presented in Figs. 9 and 10.

Fig. 9 displays the Hg^{2+} extraction results for di-ionizable calix[4]arene-1,2-crown-4 cone conformers **10a**–**e**, partial-cone conformers **16a**–**e**, and 1,2-alternate conformers **18a**–**e** with $-O(CH_2)_3C(O)Y$-containing side arms. Cone ligands **10a**–**e** and 1,2-alternate ligands **18b**–**e** are very good extractants for Hg^{2+}. Cone ligand **10d** reached a maximum loading of 97% and 1,2-alternate ligand **18d** reached 94%. The highest Hg^{2+} loading for the partial-cone series was 75%, exhibited by ligand **16e**. Overall, the extraction efficiency for Hg^{2+} decreases in the order: **10** (cone)>**18** (1.2-alternate)>**16** (partial-cone). These results suggest that the cone conformation gives the best π-cation interactions for extraction of soft Hg^{2+}.

For extractions of Hg^{2+}, the di(carboxylic acid) ligands partial-cone **16a** and 1,2-alternate **18a** perform significantly poorer than ligands **16b**–**e** and **18b**–**e** with *N*-(X)sulfonyl carboxamide functions in the side arms. The hard carboxylate group does not coordinate as well with soft Hg^{2+}.

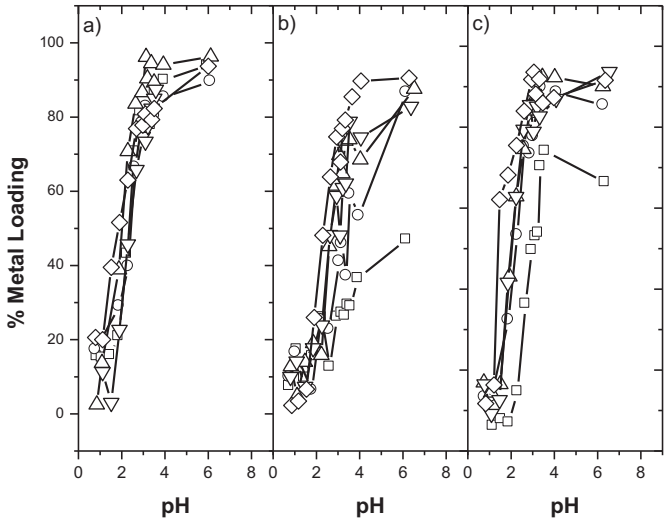


Fig. 9. Percent metal loading versus the equilibrium pH of the aqueous phase for single species solvent extraction of Hg^{2+} into chloroform by di-ionizable calix[4]arene-1,2-crown-4 ligands in three conformations: (a) cone, **10a**–**e**, (b) partial-cone, **16a**–**e**, and (c) 1,2-alternate, **18a**–**e** (□=$-CO_2H$; ○=$-C(O)NHSO_2Me$; △=$-C(O)NHSO_2Ph$; ▽=$-C(O)NHSO_2C_6H_4$-4-NO_2; ◇=$-C(O)NHSO_2CF_3$).

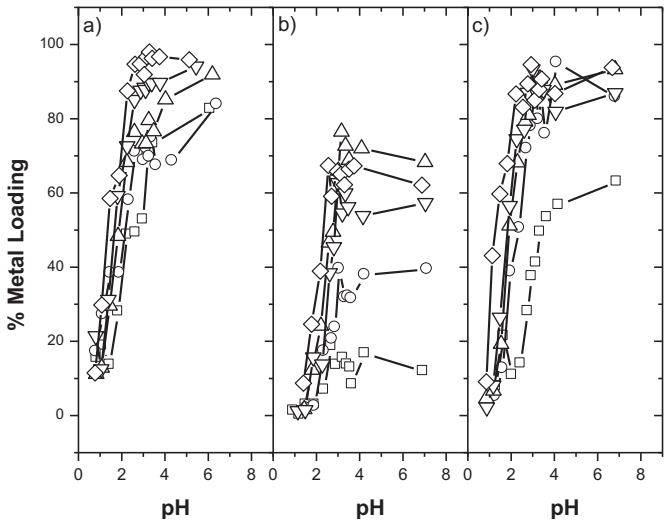


Fig. 10. Percent metal loading versus the equilibrium pH of the aqueous phase for single species solvent extraction of Hg^{2+} into chloroform by di-ionizable calix[4]arene-1,2-crown-4 ligands in three conformations: (a) cone, **11a**–**e**, (b) partial-cone, **17a**–**e**, and (c) 1,2-alternate, **19a**–**e** (□=$-CO_2H$; ○=$-C(O)NHSO_2Me$; △=$-C(O)NHSO_2Ph$; ▽=$-C(O)NHSO_2C_6H_4-4-NO_2$; ◇=$-C(O)NHSO_2CF_3$).

Fig. 10 presents the extraction results for di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 cone conformers **11a**–**e** (panel a), partial-cone conformers **17a**–**e** (panel b), and 1,2-alternate conformers **19a**–**e** with $-O(CH_2)_4C(O)Y$-containing side arms.

Comparison of the extraction profiles shown in Figs. 9 and 10 reveals rather close similarity in the effects of conformation and identity of the acidic group in the side arm. It appears that extending the acidic side arm length by one methylene group results in only minor changes in the efficiency with which Hg^{2+} can be extracted.

3. Conclusions

Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **10a**–**e**, **11a**–**e**, **16a**–**e**, **17a**–**e**, **18a**–**e**, and **19a**–**e** with cone, partial-cone, or unusual 1,2-alternate conformations, elongated side arms, and different groups in the acidic side arms have been synthesized.

The acidic side arms $-O(CH_2)_nC(O)Y$ with n=3 and 4 and Y=−OH, $-NHSO_2Me$, $-NHSO_2Ph$, $-NHSO_2C_6H_4$−4-NO_2, and $-CF_3$. Structures of the new compounds were verified by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy, and combustion analysis.

The influence of these systematic structural variations upon the efficiency and selectivity of divalent metal ion complexation was evaluated by solvent extraction from aqueous solutions into chloroform. Hard AEMC, intermediate Pb^{2+}, and soft Hg^{2+} were utilized to vary the properties of the divalent metal ions being extracted. Results are compared with those published for cone di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **2a**–**e** with short acidic side arms of $-OCH_2C(O)Y$.[11,12]

Ligands **10a**–**e**, **11a**–**e**, **16a**–**e**, **17a**–**e**, and **18a**–**e** showed poor efficiency in competitive AEMC extractions from aqueous solutions into chloroform. Surprisingly, ligands **19b**–**e** with the 1,2-alternate conformation and the longer side arms (n=4) containing *N*-(X) sulfonyl carboxamide groups performed moderately well as AEMC extractants. They exhibited good Ba^{2+} selectivity and moderate-to-high metal loadings. However, their behavior is still surpassed by the high selectivity and efficiency for Ba^{2+} extraction reported previously for ligands **2a**–**e** with m=1. Molecular modeling shows a favorable geometry for Ba^{2+} complexed by cone, di-ionized calix[4]arene-1,2-crown-4 having short side arms.

For single species solvent extractions of intermediate Pb^{2+}, cone ligands **10a**–**e** and **11a**–**e** and 1,2-alternate ligands **18a**–**e** and **19a**–**e** were found to be efficient extractants with maximum loadings of 89–99%. This compares well with ligands **2a**–**e** (m=1) for which metal loadings of >90% were reported.[12] Partial-cone ligands **16a**–**e** and particularly **17a**–**e** are found to be poor extractants for Pb^{2+}.

For single species solvent extractions of soft Hg^{2+}, cone ligands **10a**–**e** and **11a**–**e** and 1,2-alternate *N*-(X)sulfonyl carboxamide ligands **18b**–**e** and **19b**–**e** were found to be effective. Most of these ligands reached maximum Hg^{2+} loadings of >90%. This compares well to ligands **2b**–**e** (m=1), which are reported[12] to reach >90% loading of Hg^{2+}.

Thus, it is found that that the most effective length for the acidic side arms in the di-ionizable calix[4]arene-1,2-crown-4 ligands depends upon the divalent metal ion being extracted. For hard Ba^{2+}, short acidic side arms are clearly the best. For intermediate Pb^{2+} and soft Hg^{2+}, ligands with elongated acidic side arms containing soft *N*-(X)sulfonyl carboxamide functions and cone or 1,2-alternate conformations are as effective as the reported cone ligands **2** (m=1) with short acidic side arms.

4. Experimental

4.1. General

Melting points were determined with a Mel-Temp melting point apparatus. Infrared (IR) spectra were recorded with a Nicolet IR100 FT-IR spectrometer as deposits from CH_2Cl_2 solutions on NaCl plates. The absorptions are expressed in wavenumbers (cm^{-1}). The ^1H and ^{13}C NMR spectra were recorded with a Varian Unity INOVA 500 MHz FT-NMR (^1H at 500 MHz and ^{13}C at 126 MHz) spectrometer at 296 K in $CDCl_3$ with TMS as internal standard. Chemical shifts (δ) are given in parts per million (ppm) downfield from TMS and coupling constant values (J) are given in hertz. Combustion analysis was performed by Desert Analytics Laboratory (now Columbia Analytical Services) of Tucson, Arizona. For compounds **10a**–**e**, **13**, **16a**, **17c**, and **17d**, the combustion analysis results indicated the presence of small amounts of CH_2Cl_2. This was verified by singlets at δ 5.32 in their ^1H NMR spectra. For compounds **11a**, **12**, **17a**, and **19a**, the combustion analysis results indicated the presence of small amounts of EtOAc. This was verified by singlets at δ 2.05, quartets at δ 4.12, and triplets at δ 1.26 in their ^1H NMR spectra.

Reagents were purchased from commercial suppliers and used directly unless otherwise noted. 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 immediately before use. Triethylene glycol ditosylate[22] was prepared according to a literature procedure.

4.2. Synthesis of *p-tert*-butylcalix[4]arene-1,2-crown-4 compounds

*4.2.1. 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxycalix[4]arene-1,2-crown-4 (**7**).* To a suspension of *p-tert*-butylcalix[4]arene (**6**) (5.00 g, 7.71 mmol) in MeCN (500 mL) was added Cs_2CO_3 (25.12 g, 77.10 mmol). The mixture was stirred at room temperature for a 1-h period. A solution of triethylene glycol ditosylate (3.90 g, 8.51 mmol) in MeCN (50 mL) was added to the mixture dropwise over a 1-h period and the mixture was stirred at reflux for 48 h. The solvent was evaporated in vacuo and CH_2Cl_2 was added to the residue. The organic layer was washed with 5% aqueous HCl (100 mL) and water (3×100 mL), then dried over $MgSO_4$. The solvent was evaporated in vacuo and the product was chromatographed on silica gel with hexanes/EtOAc (2:1) as eluent to give white solid **7** (2.29 g, 39% yield) with mp 108–110 °C (lit.[21] mp 110–112 °C).

*4.2.2. General procedure for preparation of cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)(n)-oxy]calix[4]arene-1,2-crown-4 compounds **8** and **9**.* To a solution of **7** (1.00 g, 1.31 mmol) in THF (20 mL) was added NaH (0.13 g, 5.24 mmol) and the mixture was stirred under nitrogen for a 1-h period. A solution of the appropriate alkylating agent (3.93 mmol) in THF (10 mL total volume) was added dropwise via a syringe pump over a 1-h period. The mixture was stirred at reflux for 1 d and then a second portion of the alkylating agent (3.93 mmol) was added dropwise. After refluxing for a total of 2 d, the solvent was evaporated in vacuo and CH_2Cl_2 (30 mL) was added to the residue. The organic layer was washed with 5% aqueous HCl (30 mL) and water (3×30 mL), dried over $MgSO_4$, and evaporated in vacuo. The residue was chromatographed on silica gel with hexanes/EtOAc (10:1) as eluent.

*4.2.2.1. Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)propoxy]calix[4]arene-1,2-crown-4 (**8**).* An off-white solid with mp 57–59 °C was isolated in 57% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1740 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.07 (s, 18H, $C(CH_3)_3$), 1.08 (s, 18H, $C(CH_3)_3$), 1.27 (t, J=7.0 Hz, 6H, CH_3), 2.35 (quintet, J=7.0 Hz, 4H, CH_2CH_2C=O), 2.43–2.60 (m, 4H, CH_2C=O), 3.10, 4.81 (AX, J=12.5 Hz, 4H, $ArCH_2Ar$), 3.14, 4.35 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.15, 4.33 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.70–3.80 (m, 2H, OCH_2CH_2O), 3.80–3.99 (m, 10H, OCH_2, OCH_2CH_2O), 4.16 (q, J=7.0 Hz, 4H, OCH_2CH_3), 4.19–4.24 (m, 2H, OCH_2CH_2O), 4.25–4.32 (m, 2H, OCH_2CH_2O), 6.68–6.89 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.3, 25.6, 30.1, 30.8, 31.2, 31.2, 31.4, 31.4, 33.8, 33.8, 60.3, 70.2, 70.5, 7.3.2, 74.2, 124.9, 125.1, 125.1, 133.5, 133.7, 134.4, 144.5, 144.6, 153.1, 153.2, 173.3. Anal. Calcd for $C_{62}H_{86}O_{10}$: C, 75.12; H, 8.74. Found: C, 74.72; H, 8.66.

*4.2.2.2. Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[4-(ethoxycarbonyl)butoxy]calix[4]arene-1,2-crown-4 (**9**).* A tan oil was isolated in 52% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1739 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.07 (s, 18H, $C(CH_3)_3$), 1.08 (s, 18H, $C(CH_3)_3$), 1.26 (t, J=7.0 Hz, 6H, CH_3), 1.76 (quintet, J=7.5 Hz, 4H, OCH_2CH_2), 2.04 (quintet, J=7.5 Hz, 4H, CH_2CH_2C=O), 2.42 (td, J=7.5, 3.0 Hz, 4H, CH_2C=O), 3.10, 4.75 (AX, J=12.5 Hz, 1H, $ArCH_2Ar$), 3.12, 4.36 (AX, J=12.5 Hz, 1H, $ArCH_2Ar$), 3.14, 4.31 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.68–3.81 (m, 3H, OCH_2), 3.81–3.96 (m, 10H, OCH_2CH_2O), 4.06–4.18 (m, 10H, OCH_2CH_2O), 4.14 (q, J=7.5 Hz,

4H, OCH_2CH_3), 4.25–4.35 (m, 1H, OCH_2), 6.69–6.89 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.3, 21.6, 29.7, 30.2, 30.8, 31.1, 31.4, 33.8, 33.8, 34.2, 60.2, 70.3, 70.6, 73.0, 74.7, 76.7, 124.9, 125.0, 125.0, 133.6, 133.7, 134.2, 144.4, 144.6, 153.1, 153.3, 173.6. Anal. Calcd for $C_{64}H_{90}O_{10}$: C, 75.41; H, 8.90. Found: C, 75.26; H, 9.12.

*4.2.3. Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)propoxy]calix[4]arene-1,2-crown-4 (**10a**).* A solution of diester **8** (7.41 g, 7.48 mmol), 10% aqueous NMe_4OH (250 mL), and THF (250 mL) was refluxed for 1 d, cooled to room temperature, and stirred with 6 N aqueous HCl (150 mL) for a 1-h period. After evaporation of the THF in vacuo, the white precipitate was filtered and dissolved in CH_2Cl_2 (200 mL). The aqueous filtrate was extracted with CH_2Cl_2 (2×200 mL). The combined organic layers were washed with 6 N aqueous HCl until pH=1 and dried over $MgSO_4$. The solvent was evaporated in vacuo to give an off-white solid **10a** (6.67 g, 95%) with mp 157–159 °C. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3684–2406 (OH), 1712 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.07 (s, 18H, $C(CH_3)_3$), 1.08 (s, 18H, $C(CH_3)_3$), 2.31–2.53 (m, 4H, CH_2CH_2C=O), 2.53–2.77 (m, 4H, CH_2C=O), 3.10, 4.86 (AX, J=12.5 Hz, 4H, $ArCH_2Ar$), 3.15, 4.36 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.17, 4.30 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.71–3.80 (m, 2H, OCH_2CH_2O), 3.80–3.92 (m, 8H, OCH_2, OCH_2CH_2O), 3.92–4.00 (m, 2H, OCH_2CH_2O), 4.18–4.30 (m, 4H, OCH_2CH_2O), 6.75–6.87 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 25.3, 29.9, 30.6, 31.1, 31.2, 31.4, 31.4, 33.8, 70.1, 70.6, 73.2, 74.3, 124.9, 125.1, 125.1, 133.4, 133.6, 133.7, 134.7, 144.5, 144.7, 153.0, 153.1, 179.8. Anal. Calcd for $C_{58}H_{78}O_{10}\cdot CH_2Cl_2$: C, 69.46; H, 7.90. Found: C, 69.38; H, 7.97.

*4.2.4. Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)butoxy]calix[4]arene-1,2-crown-4 (**11a**).* A solution of diester **9** (4.51 g, 4.42 mmol), 10% aqueous NMe_4OH (200 mL), and THF (200 mL) was refluxed for 1 d. The solution was cooled to room temperature and stirred with 6 N aqueous HCl (80 mL) for a 1-h period. After evaporation of the THF in vacuo, a white precipitate was filtered and dissolved in CH_2Cl_2 (150 mL). The aqueous filtrate was extracted with CH_2Cl_2 (2×150 mL). The combined organic layers were washed with 6 N aqueous HCl until pH=1 and dried over $MgSO_4$. The solvent was evaporated in vacuo to give white solid **11a** (3.94 g, 93%) with mp 181–182 °C. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3521–1974 (OH), 1707 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.20–1.28 (m, 4H, OCH_2CH_2), 1.30 (s, 18H, $C(CH_3)_3$), 1.34 (s, 18H, $C(CH_3)_3$), 1.36–1.46 (m, 4H, CH_2CH_2C=O), 2.18 (td, J=8.0, 3.0 Hz, 4H, CH_2C=O), 2.75 (quintet, J=5.0 Hz, 2H, OCH_2CH_2O), 3.13, 4.34 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.14, 4.12 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.27–3.51 (m, 10H, OCH_2, OCH_2CH_2O), 3.56–3.72 (m, 4H, OCH_2CH_2O), 3.84 (s, 4H, $ArCH_2Ar$), 6.97–7.03 (m, 4H, ArH), 7.16–7.21 (m, 2H, ArH), 7.23–7.26 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$): δ 20.9, 28.4, 28.7, 29.7, 31.7, 31.8, 33.6, 34.0,34.0, 39.0, 67.9, 69.4, 69.8, 72.0, 125.3, 125.4, 125.5, 125.6, 132.0, 132.1, 133.9, 134.1, 144.2, 144.3, 153.3, 153.8, 180.0. Anal. Calcd for $C_{60}H_{82}O_{10}\cdot 0.5EtOAc$: C, 73.92; H, 8.60. Found: C, 73.97; H, 8.61.

*4.2.5. Cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(N-(X) sulfonyl carbamoyl-propoxy)]calix[4]arene-1,2-crown-4 compounds **10b**–**e**.* Di(carboxylic acid) **10a** (0.50 g, 0.53 mmol) was dried with a benzene azeotrope before addition of oxalyl chloride (0.46 mL, 5.30 mmol) in benzene (50 mL). The solution was stirred at room temperature for a 6-h period. Formation of the di(acid chloride) was confirmed by an IR shift of the C=O absorption from 1712 to 1792 cm^{-1}. The benzene was evaporated in vacuo at ambient temperature to avoid formation of the acid anhydride. The di(acid chloride) residue was subjected to oil-pump vacuum for a 30-min period. The sodium sulfonamidate salt was prepared under nitrogen by dropwise addition of a solution of the appropriate sulfonamide (1.17 mmol) in THF (10 mL) to a mixture of NaH (0.13 g, 5.30 mmol) in THF (10 mL). This mixture was stirred for a 2-h period before the dropwise addition of the di(acid chloride) dissolved in THF (5 mL). The mixture was stirred overnight (3 h for *p*-nitrobenzenesulfonamide) at room temperature after which the solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (30 mL) and H_2O (10 mL) was carefully added. The organic layer was washed with 6 N HCl (30 mL), dried over $MgSO_4$, and evaporated in vacuo. Yields, melting points, spectra, and combustion analysis data for compounds **10b**–**e** are given in Supplementary data.

*4.2.6. 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis[3-(N-(X)sulfonyl carbamoylbutoxy)]calix[4]arene-1,2-crown-4 compounds **11b**–**e**.* Di(carboxylic acid) **11a** (0.50 g, 0.52 mmol) was dried with a benzene azeotrope before addition of oxalyl chloride (0.45 mL, 5.20 mmol) in benzene (50 mL). The solution was stirred at room temperature for a 6-h period. Formation of the di(acid chloride) was confirmed by an IR shift of the C=O absorption from 1712 in **11a** to 1796 cm^{-1}. The benzene was evaporated in vacuo at ambient temperature to avoid formation of the acid anhydride. The di(acid chloride) residue was dried under oil-pump vacuum for a 30-min period. The sodium sulfonamidate salt was prepared under nitrogen by dropwise addition of the appropriate sulfonamide (1.17 mmol) dissolved in THF (10 mL) to a mixture of NaH (0.13 g, 5.20 mmol) in THF (10 mL). The mixture was stirred for a 2-h period before the dropwise addition of the di(acid chloride) dissolved in THF (5 mL). The mixture was stirred overnight at room temperature after which the solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (30 mL) and H_2O (10 mL) was carefully added. The organic layer was washed with 6 N HCl (30 mL), dried over $MgSO_4$, and evaporated in vacuo. Yields, melting points, spectra, and combustion analysis data for compounds **11b**–**e** are given in Supplementary data.

*4.2.7. Preparation of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)propoxy]calix[4]arene-1,2-crown-4 compounds **8**, **12**, and **14** and 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[4-(ethoxycarbonyl)butoxy]calix[4]arene-1,2-crown-4 compounds **11**, **13**, and **15** in cone, partial-cone, and 1,2-alternate conformations.* To a solution of calixcrown **7** (3.60 g, 4.72 mmol) in MeCN (270 mL) was added Cs_2CO_3 (7.70 g, 23.66 mmol). The mixture was stirred under nitrogen for a 1-h period and the appropriate alkylating agent (37.30 mmol) was added in one portion. The mixture was refluxed for 1 d and then quenched with 5% aqueous HCl (70 mL). After evaporation of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 and the organic layer was washed with water (3×), dried over $MgSO_4$, and evaporated in vacuo. The crude product mixture was purified by chromatography on silica gel with hexanes/EtOAc (10:1) as eluent to afford three fractions.

4.2.7.1. With ethyl bromobutyrate as the alkylating agent.

Fraction A. Cone diester **8** was isolated in 41% yield.

*Fraction B. 1,2-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)propoxy]calix[4]arene-1,2-crown-4 (**14**).* The white solid with mp 84–85 °C was isolated in 15% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1736 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.21 (t, J=7.0 Hz, 6H, CH_3), 1.24–1.28 (m, 4H, CH_2CH_2C=O), 1.30 (s, 18H, $C(CH_3)_3$), 1.34 (s, 18H, $C(CH_3)_3$), 1.99–2.16 (m, 4H, CH_2C=O), 2.76 (td, J=10.0, 5.0 Hz, 2H, OCH_2CH_2O), 3.13, 4.35 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.16, 4.13 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.28–3.38 (m, 3H, OCH_2CH_2O), 3.38–3.52 (m, 7H, OCH_2, OCH_2CH_2O), 3.56–3.70 (m, 4H, OCH_2CH_2O), 3.82, 3.88 (AB, J=16.5 Hz, 4H, $ArCH_2Ar$), 4.06 (q, J=7.0 Hz, 4H, OCH_2CH_3), 6.96–7.03 (m, 2H, ArH), 7.03–7.09 (m, 2H, ArH), 7.15–7.22 (m, 2H, ArH), 7.22–7.26 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.2, 28.8, 19.0, 19.7, 30.8, 31.5, 31.6, 31.6, 31.8, 34.0, 34.0, 38.9, 60.1, 67.9, 69.4, 70.0, 71.6, 125.4, 125.5, 125.6, 132.1, 132.2, 133.9, 134.2, 144.3, 144.4, 153.4, 153.8, 173.1.

Anal. Calcd for $C_{62}H_{86}O_{10}\cdot 0.8$EtOAc: C, 73.75; H, 8.77. Found: C, 73.88; H, 8.69.

*Fraction C. Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)propoxy]calix[4]arene-1,2-crown-4 (**12**).* A white solid with mp 63–64 °C was isolated in 22% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1732 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.05 (s, 9H, $C(CH_3)_3$), 1.07 (s, 9H, $C(CH_3)_3$), 1.22–1.28 (m, 6H, CH_3), 1.32 (s, 9H, $C(CH_3)_3$), 1.46 (s, 9H, $C(CH_3)_3$), 1.89 (quintet, J=8.0 Hz, 2H, OCH_2CH_2), 2.10–2.26 (m, 4H, CH_2C=O, OCH_2CH_2), 2.35–2.56 (m, 2H, CH_2C=O), 3.06, 4.36 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.08, 4.05 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.13–4.19 (m, 24H, OCH_2, OCH_2CH_2O, OCH_2CH_3, $ArCH_2Ar$), 6.64–6.74 (m, 2H, ArH), 6.84–6.92 (m, 2H, ArH), 6.98–7.25 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.3, 25.6, 25.8, 30.2, 30.7, 31.0, 31.4, 31.5, 31.7, 33.7, 33.8, 34.1, 34.1, 38.0, 38.1, 60.3, 60.3, 66.8, 69.4, 69.9, 70.6, 70.9, 72.3, 72.6, 73.3, 98.6, 125.2, 125.4, 125.7, 125.8, 125.8, 126.1, 127.2, 128.1, 131.9, 123.2, 123.6, 123.0, 133.1, 133.3, 135.2, 135.5, 143.4, 143.9, 144.1, 145.3, 152.7, 153.3, 153.6, 155.1, 172.9, 173.1. Anal. Calcd for $C_{62}H_{86}O_{10}$: C, 75.12; H, 8.74. Found: C, 74.73; H, 8.18.

4.2.7.2. With ethyl bromovalerate as the alkylating agent.

Fraction A. Cone diester **9** was obtained in 36% yield.

*Fraction B. 1,2-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)butoxy]calix[4]arene-1,2-crown-4 (**15**).* A white solid with mp 48–50 °C was obtained in 16% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1732 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.22 (t, J=7.5 Hz, 6H, CH_3), 1.24–1.28 (m, 4H, OCH_2CH_2), 1.30 (s, 18H, $C(CH_3)_3$), 1.34 (s, 18H, $C(CH_3)_3$), 1.36–1.49 (m, 4H, CH_2CH_2C=O), 2.13 (t, J=8.0 Hz, 4H, CH_2C=O), 2.75 (quintet, J=5.5 Hz, 2H, OCH_2CH_2O), 3.12, 4.35 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.14, 4.14 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.28–3.48 (m, 10H, OCH_2, OCH_2CH_2O), 3.54–3.68 (m, 4H, OCH_2, OCH_2CH_2O), 3.86, 3.82 (AB, J=16.5 Hz, 4H, $ArCH_2Ar$), 4.08 (q, J=7.5 Hz, 4H, OCH_2CH_3), 6.94–7.05 (m, 4H, ArH), 7.12–7.22 (m, 2H, ArH), 7.22–7.29 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.2, 21.1, 28.6, 28.8, 29.0, 29.7, 31.7, 31.8, 33.9, 34.0, 34.0, 39.0, 60.1, 67.9, 69.4, 69.9, 71.9, 125.3, 125.5, 125.6, 132.0, 132.1, 133.9, 134.1, 144.2, 144.3, 153.4, 153.9, 173.4. Anal. Calcd for $C_{64}H_{90}O_{10}\cdot 0.2CH_2Cl_2$: C, 74.40; H, 8.79. Found: C, 74.29; H, 9.02.

*Fraction C. Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(ethoxycarbonyl)butoxy]calix[4]arene-1,2-crown-4 (**13**).* A white solid with mp 77–78 °C was isolated in 20% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 1740 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.02 (s, 9H, $C(CH_3)_3$), 1.04 (s, 9H, $C(CH_3)_3$), 1.22–1.29 (m, 6H, CH_3), 1.34 (s, 9H, $C(CH_3)_3$), 1.45 (s, 9H, $C(CH_3)_3$), 1.55–1.814 (m, 6H, OCH_2CH_2, CH_2CH_2C=O), 1.89 (quintet, J=7.5 Hz, 2H, OCH_2CH_2), 2.32 (t, J=7.5 Hz, 2H, CH_2C=O), 2.37 (t, J=7.5 Hz, 2H, CH_2C=O), 3.05, 4.32 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.06, 4.03 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.38–4.06 (m, 16H, OCH_2, OCH_2CH_2O), 3.65 (s, 4H, $ArCH_2Ar$), 4.14 (q, J=7.5 Hz, 4H, OCH_2CH_3), 6.58–6.68 (m, 2H, ArH), 6.78–6.86 (m, 2H, ArH), 7.07–7.24 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.2, 21.4, 21.6, 29.9, 30.2, 30.3, 30.7, 31.4, 31.4, 31.7, 31.9, 33.7, 33.7, 34.1, 34.1, 34.1, 34.2, 38.0, 38.2, 60.2, 60.3, 66.5, 68.1, 69.4, 70.3, 71.6, 72.4, 72.9, 73.9, 124.1, 125.2, 125.4, 125.7, 125.8, 126.0, 127.1, 128.2, 131.7, 132.1, 132.4, 132.7, 133.0, 133.2, 135.4, 135.6, 143.1, 143.5, 143.8, 145.3, 152.5, 153.4, 153.7, 155.3, 173.3, 173.5. Anal. Calcd for $C_{64}H_{90}O_{10}$: C, 75.41; H, 8.90. Found: C, 75.59; H, 8.54.

*4.2.8. Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)propoxy]calix[4]arene-1,2-crown-4 (**16a**).* The procedure was the same as that employed for preparation of **10a**, but starting from **12**. An off-white solid with mp 113–116 °C was obtained in 88% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3601–2378 (OH), 1705 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.05 (s, 9H, $C(CH_3)_3$), 1.07 (s, 9H, $C(CH_3)_3$), 1.31 (s, 9H, $C(CH_3)_3$), 1.44 (s, 9H, $C(CH_3)_3$), 1.84 (quintet, J=7.5 Hz, 2H, OCH_2CH_2), 2.12–2.24 (m, 2H, OCH_2CH_2), 2.24–2.28 (m, 2H, CH_2C=O), 2.41–2.54 (m, 1H, CH_2C=O), 2.54–2.66 (m, 1H, CH_2C=O), 3.09, 4.28 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.10, 4.02 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.13–4.19 (m, 20H, OCH_2, OCH_2CH_2O, $ArCH_2Ar$), 6.63–6.78 (m, 2H, ArH), 6.86–6.96 (m, 2H, ArH), 7.04–7.30 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$): δ 25.2, 26.1, 29.7, 30.2, 30.5, 31.2, 31.3, 31.4, 31.6, 31.9, 32.0, 33.7, 33.8, 34.1, 34.1, 38.1, 38.2, 67.4, 69.6, 69.8, 69.8, 70.7, 72.1, 72.4, 73.2, 125.2, 125.4, 125.6, 125.8, 126.1, 126.2, 127.1, 127.9, 131.8, 132.1, 132.6, 132.9, 133.3, 133.5, 135.2, 135.3, 143.6, 144.1, 144.2, 145.6, 152.4, 153.0, 153.3, 155.1, 177.1, 178.7. Anal. Calcd for $C_{58}H_{78}O_{10}\cdot 0.4CH_2Cl_2$: C, 72.37; H, 8.19. Found: C, 72.25; H, 8.20.

*4.2.9. Partial-cone 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)butoxy]calix[4]arene-1,2-crown-4 (**17a**).* The procedure was the same as that employed for preparation of **11a**, but starting from **13**. An off-white solid with mp 184–186 °C was obtained in 94% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3548–2015 (OH), 1714 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.02 (s, 9H, $C(CH_3)_3$), 1.04 (s, 9H, $C(CH_3)_3$), 1.34 (s, 9H, $C(CH_3)_3$), 1.45 (s, 9H, $C(CH_3)_3$), 1.63 (quintet, J=7.5 Hz, 2H, CH_2CH_2C=O), 1.71–1.82 (m, 3H, OCH_2CH_2), 1.82–1.96 (m, 1H, OCH_2CH_2), 2.37 (t, J=7.5 Hz, 2H, CH_2C=O), 2.42 (t, J=7.5 Hz, 2H, CH_2C=O), 3.06, 4.26 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.07, 4.02 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.48–4.05 (m, 16H, OCH_2, OCH_2CH_2O), 3.65 (AB, J=7.5 Hz, 2H, $ArCH_2Ar$), 6.58–6.68 (m, 2H, ArH), 6.78–6.88 (m, 2H, ArH), 7.20–7.26 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$): δ 21.1, 22.0, 29.7, 30.1, 30.1, 30.2, 30.5, 31.3, 31.4, 31.7, 31.9, 33.6, 33.7, 33.8, 34.1, 34.1, 34.5, 38.0, 38.1, 66.1, 67.7, 69.3, 69.7, 71.4, 72.3, 72.7, 73.8, 125.2, 125.4, 125.7, 125.8, 126.1, 127.1, 128.1, 131.6, 132.0, 132.4, 132.6, 133.1, 133.3, 135.5, 135.5, 143.2, 143.6, 143.9, 145.5, 152.3, 153.2, 153.5, 155.3, 177.3, 178.8. Anal. Calcd for $C_{60}H_{82}O_{10}\cdot 1.4$EtOAc: C, 72.51; H, 8.64. Found: C, 72.52; H, 8.45.

*4.2.10. 1,2-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)propoxy]calix[4]arene-1,2-crown-4 (**18a**).* The procedure was the same as that employed for preparation of **10a**, but starting from **14**. White solid with mp 172–175 °C was obtained in 84% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3548–2427 (OH), 1711 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.20–1.28 (m, 2H, CH_2CH_2C=O), 1.30 (s, 18H, $C(CH_3)_3$), 1.34 (s, 18H, $C(CH_3)_3$), 1.48–1.60 (m, 2H, CH_2CH_2C=O), 1.95–2.10 (m, 2H, CH_2C=O), 2.10–2.24 (m, 2H, CH_2C=O), 2.79 (td, J=10.0, 5.0 Hz, 2H, OCH_2CH_2O), 3.14, 4.37 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.15, 4.13 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.30–3.38 (m, 2H, OCH_2CH_2O), 3.38–3.45 (m, 6H, OCH_2, OCH_2CH_2O), 3.45–3.53 (m, 2H, OCH_2CH_2O), 3.57–3.72 (m, 4H, OCH_2CH_2O), 3.85 (s, 4H, $ArCH_2Ar$), 6.98–7.05 (m, 4H, ArH), 7.17–7.26 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.2, 28.7, 28.9, 30.6, 31.6, 31.7, 34.0, 34.0, 39.0, 68.0, 39.4, 39.9, 71.4, 125.3, 125.4, 125.6, 125.6, 132.0, 120.0, 133.9, 134.1, 144.3, 144.5, 153.4, 153.5, 179.9. Anal. Calcd for $C_{58}H_{78}O_{10}$: C, 74.49; H, 8.41. Found: C, 74.56; H, 8.39.

*4.2.11. 1,2-Alternate 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(carboxy)butoxy]calix[4]arene-1,2-crown-4 (**19a**).* The procedure was the same as that employed for preparation of **11a**, but starting from **15**. An off-white solid with mp 181–182 °C was obtained in 94% yield. IR (deposit from CH_2Cl_2 solution on a NaCl plate): 3521–2330 (OH), 1707 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.20–1.28 (m, 4H, OCH_2CH_2), 1.30 (s, 18H, $C(CH_3)_3$), 1.34 (s, 18H, $C(CH_3)_3$), 1.36–1.46 (m, 4H, CH_2CH_2C=O), 2.18 (td, J=8.0, 3.0 Hz, 4H, CH_2C=O), 2.75 (quintet, J=5.0 Hz, 2H, OCH_2CH_2O), 3.13, 4.34 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.14, 4.12 (AX, J=12.5 Hz, 2H, $ArCH_2Ar$), 3.27–3.51 (m, 10H, OCH_2, OCH_2CH_2O), 3.56–3.72 (m, 4H, OCH_2CH_2O), 3.84 (s, 4H, $ArCH_2Ar$), 6.97–7.03 (m, 4H, ArH), 7.16–7.21 (m, 2H, ArH), 7.23–7.26 (m, 2H, ArH). ^{13}C ($CDCl_3$): δ 20.9, 28.4, 28.7, 29.7, 31.7, 31.8, 33.6, 34.0, 34.0, 39.0, 67.9, 69.4, 69.8, 72.0,

125.3, 125.4, 125.5, 125.6, 132.0, 132.1, 133.9, 134.1, 144.2, 144.3, 153.3, 153.8, 180.0. Anal. Calcd for $C_{60}H_{82}O_{10}\cdot 0.5$EtOAc: C, 73.92; H, 8.60. Found: C, 73.97; H, 8.61.

*4.2.12. Preparation of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(N-(X)sulfonyl carbamoylpropoxy)]calix[4]arene-1,2-crown-4 compounds **16b–e** and **18b–e** in partial-cone and 1,2-alternate conformations.* The procedure was the same as that employed for synthesizing compounds **10b–e**, but starting from the appropriate di(carboxylic acid) **16a** or **18a**. Yields, melting points, spectra, and combustion analysis data for compounds **16b–e** and **18b–e** are given in Supplementary data.

*4.2.13. Preparation of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis[3-(N-(X)sulfonyl carbamoylbutoxy)]calix[4]arene-1,2-crown-4 compounds **17b–e** and **19b–e** in partial-cone and 1,2-alternate conformations.* The procedure was the same as that employed for synthesizing compounds **11b–e**, but starting from the appropriate di(carboxylic acid) **17a** or **19a**. Yields, melting points, spectra, and combustion analysis data for compounds **17b–e** and **19b–e** are given in Supplementary data.

4.3. Procedures for divalent metal ion extraction

Procedures for competitive alkaline earth metal cation extraction, single species extraction of Pb^{2+}, and single species extraction of Hg^{2+} from aqueous solutions into chloroform have been reported previously.[10–14]

Since ligands **10d**, **10e**, **11b**, **11d**, and **11e** were obtained as monosodium salts, modified procedures were employed to remove the Na^+ before performing extractions with these ligands.

For competitive solvent extraction of AEMC. Into a capped, polypropylene, 15-mL centrifuge tube was placed 3.0 mL of 4.0 M aqueous HCl and 3.0 mL of a 1.0 mM chloroform solution of the ligand. The tube was vortexed with a Glas-Col Multi-Pulse Vortexer for 30 min at room temperature and the tube was centrifuged for 10 min for phase separation with a Becton–Dickinson Clay Adams Brand® Centrifuge. A 2.5-mL portion of the organic phase was removed and added to 2.5 mL of distilled water in a new, 15-mL polypropylene centrifuge tube. The tube was vortexed for 10 min and then centrifuged for 10 min. A 2.0-mL portion of the organic phase was removed for use in the solvent extraction experiment. *For single species solvent extraction of Pb^{2+}*. Into a capped, polypropylene, 15-mL centrifuge tube was placed 3.0 mL of 4 M aqueous HNO_3 and 3.0 mL of a 0.50 mM chloroform solution of the ligand. The tube was vortexed for 30 min and then centrifuged for 10 min. A 2.5-mL portion of the organic phase was removed and added to 2.5 mL of distilled water in a new, 15-mL polypropylene centrifuge tube. The tube was vortexed for 10 min and then centrifuged for 10 min. A 2.0-mL of the organic phase was removed for use in the solvent extraction experiment. *For single species solvent extraction of Hg^{2+}*. Into a capped, polypropylene, 15-mL centrifuge tube was placed 4.0 mL of 4.0 M HNO_3 and 4.0 mL of a 0.25 mM chloroform solution of the ligand. The tube was vortexed for 30 min and then centrifuged for 10 min. A 3.5-mL portion of the organic phase was removed and added to 3.5 mL of distilled water. The tube was vortexed for 10 min and centrifuged for 10 min. A 3.0-mL portion of the organic phase was removed for use in the solvent extraction experiment.

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Supplementary data

^{1}H–^{1}H HETCOR and ^{1}H–^{13}C COSY NMR spectra for new di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-4 ligands **10a**, **17c**, and **18c** (pages S3–S7).

Table S1. Selected ^{1}H NMR and ^{13}C NMR chemical shifts for 1,2-alternate compounds **18a–e** and **19a–e** (page S8).

Yields and characterization data for di-ionizable *p-tert*-butylcalix[4]arene compounds **10b–e**, **11b–e**, **16b–e**, **17b–e**, **18b–e**, and **19b–e** with two elongated, *N*-(X)sulfonyl carboxamide-containing side arms (pages S9–S21).

Fig. S7. Profile for competitive solvent extraction of AEMC into chloroform by cone, di-ionizable calix[4]arene-1,2-crown-4 ligands **10a–e** with $-O(CH_2)_3C(O)Y$ side arms (page S22).

Fig. S8. Profile for competitive solvent extraction of AEMC into chloroform by cone, di-ionizable calix[4]arene-1,2-crown-4 ligands **11a–e** with $-O(CH_2)_4C(O)Y$ side arms (page S22).

Fig. S9. Profile for competitive solvent extraction of AEMC into chloroform by partial-cone, di-ionizable calix[4]arene-1,2-crown-4 ligands **16a–e** with $-O(CH_2)_3C(O)Y$ side arms (page S23).

Fig. S10. Profile for competitive solvent extraction of AEMC into chloroform by partial-cone, di-ionizable calix[4]arene-1,2-crown-4 ligands **17a–e** with $-O(CH_2)_4C(O)Y$ side arms (page S23).

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.09.065.

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