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Di-ionizable calix[4]arene-1,2-crown-5 and -crown-6 ethers in cone conformations: synthesis and divalent metal ion extraction

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Abstract

Two series of di-ionizable calix[4]arene-1,2-crown-5 and -crown-6 ethers in cone conformations are synthesized. The ionizable groups are oxyacetic acid moieties and *N*-(X)sulfonyl oxyacetamide units with X=methyl, phenyl, 4-nitrophenyl, and trifluoromethyl, which 'tunes' their acidity. For competitive solvent extraction of alkaline earth metal cations from aqueous solutions into chloroform, the new ligands with *N*-(X)sulfonyl carbamoyl groups are efficient extractants with Ba^{2+} selectivity. On the other hand, the dicarboxylic acid analogues exhibit little selectivity in extraction of alkaline earth metal cations. For single species extractions of Pb^{2+}, the ligands with both types of ionizable groups show very good extractions abilities. In single species extractions of Hg^{2+}, the *N*-(X)sulfonyl carboxamide ligands are highly efficient, in contrast to the dicarboxylic acid compounds. Influences of the ionizable group identity, the crown ether ring size, and the presence of upper-rim *p-tert*-butyl groups on divalent metal ion extraction are explored.

Keywords: Calixarenes; Crown ethers; Molecular recognition; Solvent extractions

1. Introduction

The development of the field of liquid–liquid separations has been paralleling the progress of coordination chemistry from the use of simple ligands to pre-organized metal ion receptors. The advent of macrocyclic receptors, i.e., crown ethers and calixarenes, produced a second revolution in liquid–liquid separation of metal ions following the monodentate and bidentate extractants, which revolutionized the chemistry for metal ion separations from aqueous solutions, from separatory funnels to the industrial scale.[1] The macrocyclic ligands select cations primarily by their sizes, and the most stable complexes are formed with the closest match between host cavity and cation size.[2] Another important factor is pre-organization of the host macrocyclic molecules. The binding of a specific metal ion by a pre-organized ligand requires only minimal adjustment of the ligand conformation. Since such adjustment is both enthalpically and entropically expensive, this improvement furnishes much more effective and selective metal ion separations.[1,2]

Calix[4]crowns, macrobicyclic compounds that combine calix[4]arene and polyether units, have been widely used as hosts for selective metal ion recognition for more than two decades, since the earliest example of this family, *p-tert*-butylcalix[4]arene-1,3-crown-6-ether, was reported in 1983.[3] The complexation studies of calix[4]arene-crowns have mainly been focused on dialkylated 1,3-bridged calix[4]arene-crown ethers, which were found to exhibit high binding affinity and selectivity in alkali and alkaline earth metal cation extractions.[4] In contrast, very little is known about the ligating ability of the corresponding 1,2-bridged regioisomers, probably because they are more difficult to synthesize. Known members in this category are limited. In general, they exhibit poor binding ability and little selectivity toward metal cations.[5]

Calix[4]arenes with pendant proton-ionizable groups are found to be much more efficient interfacial carriers for metal cations than related unfunctionalized calix[4]arenes with

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phenolic groups on the lower rim.[6] Recently, we have undertaken the synthesis and evaluation of di-ionizable calix[4]-arene-1,2-crown ether ligands as divalent metal ion extractants.[7] Di-ionized calix[4]arene-1,2-crown-4 ethers in the cone conformation were found to be efficient alkaline earth metal cation extractants with extraordinarily high selectivity for Ba^{2+}.[7c] Since the crown ether ring is too small to accommodate Ba^{2+}, we proposed the extraction complex shown in Figure 1. In this complex, the large divalent metal ion is sandwiched between the four polyether ring oxygens on one side and the two ionized groups on the other. In an extension of that study, we have now prepared analogues with larger crown-5 and crown-6 ether rings and evaluated their alkaline earth metal cation extraction abilities. In addition, the efficacy of these new ligands as Hg^{2+} and Pb^{2+} extractants has been assessed.

2. Results and discussion

2.1. Synthetic routes

Calix[4]arene (**1**), tetraethylene glycol dimesylate, and pentaethylene glycol ditosylate were prepared according to reported methods.[8–10] Calix[4]arene-1,2-crown-5 (**2**) and calix[4]aene-1,2-crown-6 (**3**) (Scheme 1) were synthesized by modification of reported procedures.[5f] For the preparation of **2**, the reaction time was extended from 10 to 72 h and tetraethylene glycol ditosylate was replaced with tetraethylene glycol dimesylate, giving a 56% yield. For **3**, the reaction time was extended from 10 to 16 h, increasing the yield by 15%.

Calixcrown **3** was refluxed with ethyl bromoacetate and NaH in THF–DMF (9:1) to give diester **5** in 80% yield. The yield of **5** depended on the amount of calixcrown **3** used in the reaction. The greater the amount of **3** employed, the lower was the percentage yield of diester **5** obtained.

Alkylation of calixcrown **2** was found to be surprisingly difficult. The procedure that was used successfully to alkylate calix[4]arene-1,2-crown-6 (**3**) described above was ineffective. The reaction mixture was brown-black and TLC analysis showed a very complex product mixture. No reaction was evident when KH replaced NaH as the base.

Using DMF as the solvent and performing the reaction at 70 °C for 24 h gave a trace of the desired diester **4**. Extending the reaction time to 72 h gave a 25% yield of diester **4**. A longer reaction time did not increase the yield further. From a small-scale reaction, a 27% yield of diester **4** was obtained when the reaction was performed at 80 °C for 72 h. However, separation and purification of the product were difficult since there were many side products. When large-scale reactions were employed, the average yield of diester **4** dropped to 10–15%.

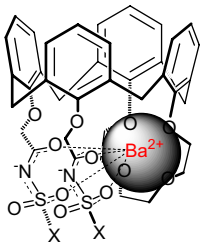


Figure 1. Proposed Ba^{2+} extraction complex with di-ionized *N*-(X)sulfonyl carboxamide calix[4]arene-1,2-crown-4 ligands.

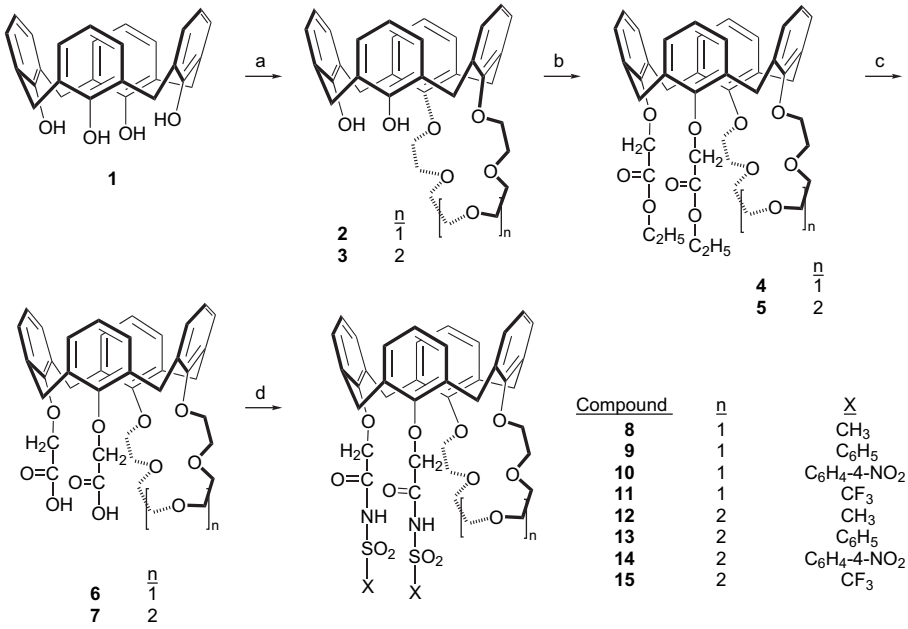
Hydrolysis of calixcrown diesters **4** and **5** with 10% Me_4NOH in H_2O–THF (1:1) gave diacids **6** and **7**, respectively, in nearly quantitative yields. Calixcrown diacids **6** and **7** were converted into the corresponding di(acid chloride)s by reaction with oxalyl chloride in benzene at reflux for 5 h. Formation of the di(acid chloride) was verified by IR spectroscopy with the appearance of a strong carbonyl group absorptions at around 1810 cm^{-1} and the disappearance of the carbonyl group absorptions at about 1750 cm^{-1}. The di(acid chloride)s were reacted with the corresponding sulfonamide anions in THF to afford di-ionizable calixcrowns **8–15** in 41–83% yields.

Structures of the new di-ionizable calyx[4]arene-1,2-crown-5 and -crown-6 ligands were verified by IR spectroscopy, ^1H, and ^{13}C NMR spectroscopy and combustion analysis. Cone conformations of the calix[4]arene units in di-ionizable calixcrowns **6–15** were verified by NMR spectroscopy. There were no peaks between 36 and 40 ppm in the ^{13}C NMR spectrum, revealing that all four benzene rings have *syn* arrangements.[11]

2.2. Competitive solvent extraction of alkaline earth metal cations

Plots of metal ion loadings of the organic phase versus the equilibrium pH of the aqueous phase for competitive solvent extractions of aqueous alkaline earth metal cation (10.0 mM in each) solutions by 1.0 mM solutions of di-ionizable calix[4]arene-1,2-crown-5 ligands **6**, **8–11** in chloroform are presented in Figure 2.[12] Note that the metals loadings were negligible when the aqueous phases were highly acidic. This verifies that the extractants are ineffective in their neutral, non-ionized forms. The di-ionizable calix[4]arene-1,2-crown-5 ligands gave 93–100% maximum metals loadings (for formation of 1:1 di-ionized ligand–metal ion extraction complexes). Although the dicarboxylic acid ligand **6** shows little selectivity (Fig. 2a), the change to *N*-(X)sulfonyl carboxamide acidic functions in ligands **8–11** (Fig. 2b–e) gave extraction selectivity for Ba^{2+} over the other three alkaline earth metal ion species. For ligands **8–11**, the selectivity order was $Ba^{2+}>Sr^{2+}>Ca^{2+}>Mg^{2+}$, the same order as the decreasing metal cation size. With variation of the X group in the order of CH_3, C_6H_5, C_6H_4-4-NO_2, and CF_3, the ligand acidity is expected to increase as the electron-withdrawing power of the X is enhanced. The pH for half loading, $pH_{0.5}$, is a qualitative measure of the ligand acidity. For compounds **8–11**, the $pH_{0.5}$ values are 7.1, 7.0, 6.2, and 4.2, respectively, which is in accord with the electron-withdrawing power of the X group.

For the analogous di-ionizable calix[4]arene-1,2-crown-6 ligands **7** and **12–15** (Fig. 3), less efficient metals loadings (78–83% maximum metals loadings for formation of 1:1



Scheme 1. Synthesis of di-ionizable calix[4]arene-1,2-crown-5 and crown-6 ligands in the cone conformation (**6**–**15**). (a) (i) n=1: $Ms(OCH_2CH_2)_4OMs$, NaH, DMF, 50 °C, 72 h; (ii) n=2: $Ts(OCH_2CH_2)_5OTs$, NaH, DMF, 50 °C, 16 h; (b) (i) n=1: NaH, $BrCH_2CO_2C_2H_5$, DMF, 80 °C, 72 h; (ii) n=2: NaH, $BrCH_2CO_2C_2H_5$, THF–DMF (9:1), reflux, 24 h; (c) (i) 10% $Me_4N^+OH^-$ (aq), THF, reflux, 24 h; (ii) 6 N HCl (aq); (d) (i) ClC(O)C(O)Cl, benzene, reflux, 5 h; (ii) NaH, NH_2SO_2X, THF, rt, 24 h.

di-ionized ligand–metal ion extraction complexes)[12] were observed, compared with their crown-5 analogues. As before, the calixcrown dicarboxylic ligand gave no extraction selectivity (Fig. 3a). All four alkaline earth metal cations are detectably extracted into the chloroform phase with the di(*N*-(X)sulfonyl carboxamide)s **12**–**15** (Fig. 3b–e). The extraction selectivity order was $Ba^{2+}>Sr^{2+}>Ca^{2+}>Mg^{2+}$, the same as those of calix[4]arene-1,2-crown-5 analogues. For compounds **12**–**15**, the $pH_{0.5}$ values were 7.5, 8.1, 6.1, and 3.9, respectively.

When compared with the earlier reported results for alkaline earth metal cation extraction by di-ionizable calix[4]arene-1,2-crown-4 analogues,[7c] it is noted that for the three dicarboxylic acid ligands only the crown-4 ligand exhibits appreciable extraction selectivity. For the calixcrown *N*-(X)sulfonyl oxyacetamides, all show Ba^{2+} extraction selectivity. However, the selectivity is considerably greater with the crown-4 extractant than for the crown-5 and crown-6 analogues. Thus expansion of the polyether ring size to better accommodate Ba^{2+}

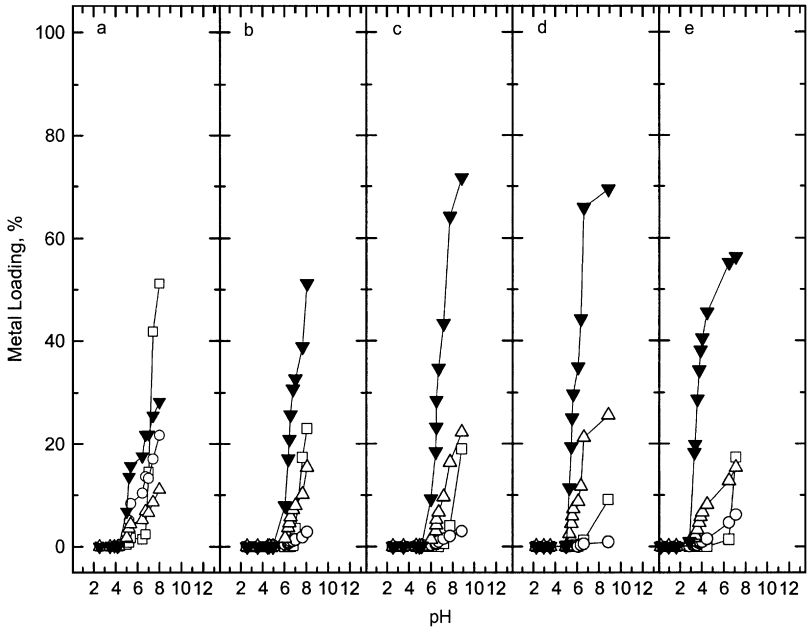


Figure 2. Percent metals loadings versus equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by di-ionizable calix[4]arene-1,2-crown-5 ligands: (a) **6**, (b) **8**, (c) **9**, (d) **10**, and (e) **11** (□=Mg^{2+}; ○=Ca^{2+}; △=Sr^{2+}; ▼=Ba^{2+}).[12]

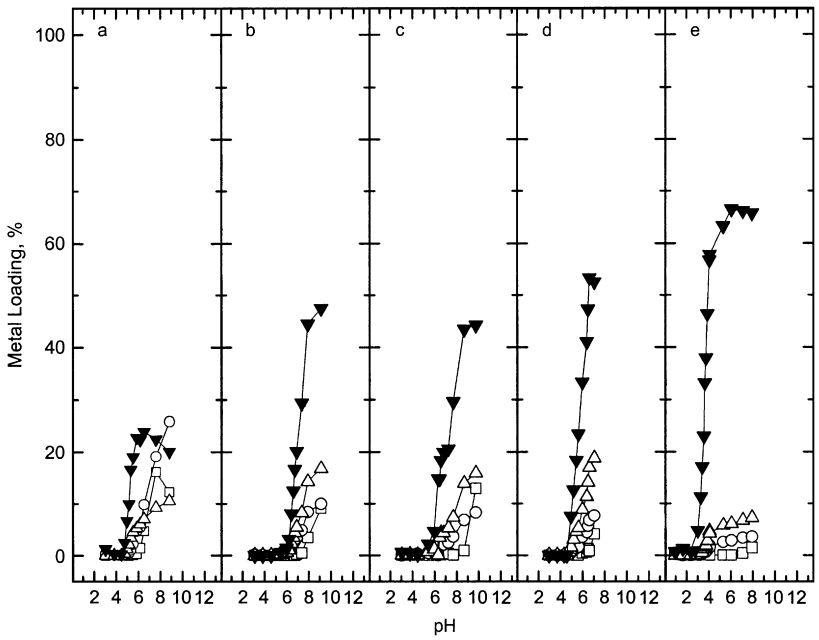


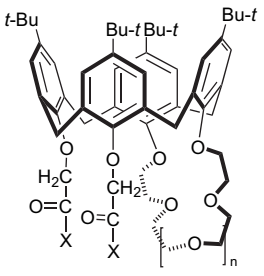
Figure 3. Percent metals loadings versus equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metal ions into chloroform by di-ionizable calix[4]arene-1,2-crown-6 ligands: (a) **7**, (b) **12**, (c) **13**, (d) **14**, and (e) **15** (□=Mg^{2+}; ○=Ca^{2+}; △=Sr^{2+}; ▼=Ba^{2+}).[12]

within the cavity does not lead to improved extraction selectivity.

In previous studies,[7c,13] we found that calix[4]arenes with pendant *N*-(X)sulfonyl carboxamide groups are effective not only in extraction of hard metal cations, but also exhibit high extraction efficiency and selectivity for some intermediate (Pb^{2+}) and soft (Hg^{2+}) metal ions.[13] Therefore, single species solvent extractions of Pb^{2+} and of Hg^{2+} by ligands **6**–**15** and analogues **16**–**25**[7b] (Fig. 4) were performed. For the latter series, the structural modification is introduction of four lipophilic *tert*-butyl groups on the upper rim.

2.3. Solvent extraction of Pb^{2+}

Plots of Pb^{2+} loading of the organic phase versus the equilibrium pH of the aqueous phase for competitive solvent extractions of aqueous $Pb(NO_3)_2$ (1.0 mM) solutions by 0.50 mM solutions of di-ionizable calix[4]arene-1,2-crown-5 ligands **6** and **8**–**11** in chloroform are presented in Figure 5a. All five ligands exhibit high extraction ability toward Pb^{2+} with quantitative or nearly quantitative loading for formation of 1:1 di-ionized ligand–Pb^{2+} extraction complexes. For the *N*-(X)sulfonyl carboxamides **8**–**11**, the extraction efficiency decreases as X is varied in the order: CF_3>4-$NO_2C_6H_4$>CH_3, C_6H_5. This is the order of decreasing electron-withdrawing ability of X.



Compound	n	X
16	1	OH
17	1	$NHSO_2CH_3$
18	1	$NHSO_2C_6H_5$
19	1	$NHSO_2C_6H_4$-4-NO_2
20	1	$NHSO_2CF_3$
21	2	OH
22	2	$NHSO_2CH_3$
23	2	$NHSO_2C_6H_5$
24	2	$NHSO_2C_6H_4$-4-NO_2
25	2	$NHSO_2CF_3$

Figure 4. Di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 and -crown-6 ethers **16**–**25**.

Expanding the polyether ring size from crown-5 to crown-6 produces the extraction profiles shown in Figure 5c for di-ionizable calix[4]arene-1,2-crown-6 ligands **7** and **12**–**15**. In general, it appears that this structural modification leads to less efficient extractants. Only with the dicarboxylic acid extractant **7** and the di(*N*-(X)-sulfonyl carboxamide) ligands with X=CF_3 and 4-$NO_2C_6H_4$ are Pb^{2+} loadings of 90% or greater obtained.

Comparison of the extraction data presented in Figure 5a and b allows the effect of introducing a *p-tert*-butyl group on each aromatic group in the ligands to be assessed. As can be seen, the extraction profiles for di-ionizable *p-tert*-butylcalix[4]arene-1,2-crown-5 ligands **16**–**20** (Fig. 5b) and their di-ionizable calix[4]arene-1,2-crown-5 analogues **6** and **8**–**11** are very similar both in terms of extraction efficiencies and the effect of the X variation for the *N*-(X)sulfonyl carboxamide groups.

Examination of the extraction profiles shown in Figure 5c and d reveals that the addition of four *p-tert*-butyl groups to the upper rim of di-ionizable calix[4]arene-1,2-crown-6 ligands increases the efficiency of Pb^{2+} extraction. For all five of the more lipophilic ligands **21**–**25**, quantitative levels of Pb^{2+} extraction were achieved.

2.4. Solvent extraction of Hg^{2+}

Plots of Hg^{2+} loading of the organic phase versus the equilibrium pH of the aqueous phase for competitive solvent extractions of aqueous $Hg(NO_3)_2$ (0.25 mM) solutions by

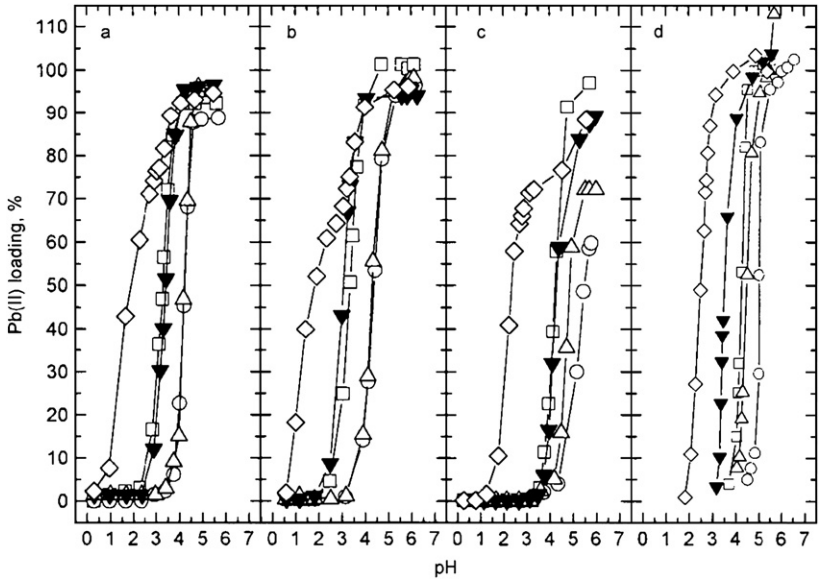


Figure 5. Percent metal loading of the organic phase versus the equilibrium pH of the aqueous phase for single species solvent extraction of Pb^{2+} by ligands: (a) **6** (□), **8** (○), **9** (△), **10** (▼), **11** (◇); (b) **16** (□), **17** (○), **18** (△), **19** (▼), **20** (◇); (c) **7** (□), **12** (○), **13** (△), **14** (▼), **15** (◇); (d) **21** (□), **22** (○), **23** (△), **24** (▼), **25** (◇).

0.25 mM solutions of di-ionizable calix[4]arene-1,2-crown-5 ligands **6** and **8**–**11** in chloroform are presented in Figure 6a. Although the Hg^{2+} extraction efficiency for dicarboxylic acid ligand **6** was only modest, those for the di(*N*-(X)sulfonyl carboxamide) ligands **8**–**11** were very high with quantitative or nearly quantitative Hg^{2+} loading. Contrary to the findings for extractions of alkaline earth metal cations and of Pb^{2+}, the least efficient extraction now was observed when X=CF_3, with little discernable variation for the other three X groups. Presumably this difference arises from the soft nature of Hg^{2+} compared to the other divalent metal ion species examined.

Comparison of the extraction profiles presented in Figure 6a with those for di-ionizable calix[4]arene-1,2-crown-6 compounds **7** and **12**–**15** (Fig. 6c) reveals only minor changes when the polyether rings of the ligands were expanded from crown-5 to crown-6. This contrasts with the results presented earlier for alkaline earth metal cation and Pb^{2+} extractions by the same two series of ligands for which this ring size expansion produced diminished extraction selectivity and/or efficiency.

To examine the influence of lipophilic *p-tert*-butyl groups on the upper rims of both the crown-5 and crown-6 ligands in Hg^{2+}, compare the profiles given in Figure 6b with a and

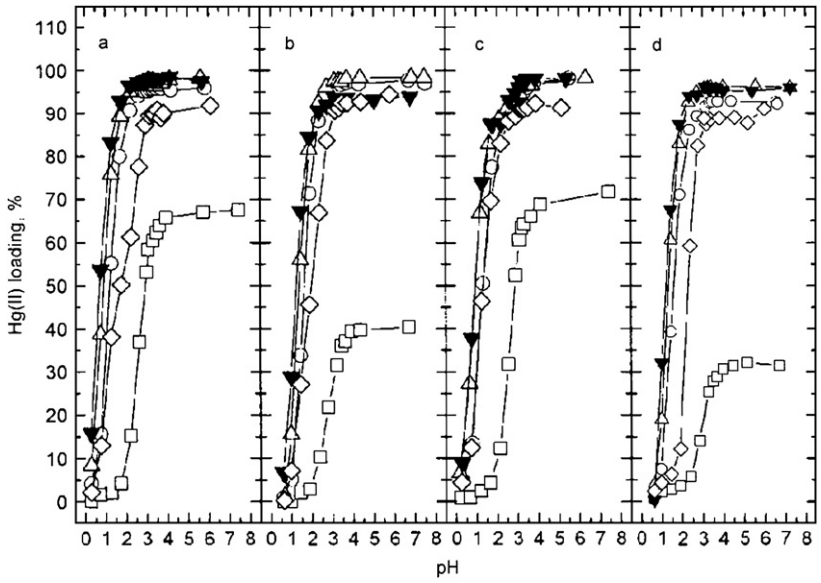


Figure 6. Percent metals loading of the organic phase versus the equilibrium pH of the aqueous phase for single species solvent extraction of Hg^{2+} by ligands: (a) **6** (□), **8** (○), **9** (△), **10** (▼), **11** (◇); (b) **16** (□), **17** (○), **18** (△), **19** (▼), **20** (◇); (c) **7** (□), **12** (○), **13** (△), **14** (▼), **15** (◇); (d) **21** (□), **22** (○), **23** (△), **24** (▼), **25** (◇).

d with c, respectively. With the exception of the *p-tert*-butylcalixarene-1,2-crown-5 and -crown-6 compounds, **16** and **21**, respectively, for which this structural variation is markedly detrimental, the profiles are remarkably similar for the four series of ligands with *N*-(X)sulfonyl carboxamide groups.

3. Experimental

3.1. General

Ligands **16**–**25** were prepared by the reported methods.[7b] Reagents were obtained from commercial suppliers and used directly, unless otherwise noted. THF was dried over sodium wire with benzophenone ketyl as an indicator. DMF was stored over 4 Å molecular sieves. Infrared spectral analyses were performed with a Perkin–Elmer 1600 FTIR spectrophotometer by deposit from CH_2Cl_2 solution onto a NaCl plate. The absorptions are expressed in wavenumbers (cm^{-1}). NMR spectra were measured with a Varian Unity Inova FT-500 spectrometer (499.7 MHz for ^1H and 125.7 MHz for ^{13}C) at 296 K in $CDCl_3$ with TMS as an internal standard. Chemical shifts (δ) are expressed in parts per million downfield from TMS and coupling constants (J) values are given in hertz. Melting points were determined with a Mel-Temp melting point apparatus. Combustion analysis was performed by Desert Analytics Laboratory of Tucson, Arizona.

*3.1.1. 25,26-Bis[(ethoxycarbonyl)methoxy]calix[4]arene-1,2-crown-5 in the cone conformation (**4**)*

To a stirred mixture of NaH (10.00 equiv, 2.04 g, 85 mmol) and DMF (20 mL) in a 250-mL, three-necked flask under nitrogen was added dropwise a solution of 25,26-dihydroxy calix[4]arene-crown-5 (**2**) (1.00 equiv, 4.95 g, 8.50 mmol) in DMF (100 mL). The mixture was stirred for 1 h. A solution of ethyl bromoacetate (8.00 equiv, 11.36 g, 7.54 mL, 68 mmol) in DMF (10 mL) was added over a 1-h period. The mixture was stirred for 72 h at 80 °C. The reaction was quenched by addition of 1 N HCl (20 mL) at 0 °C. The solvent was evaporated in vacuo. CH_2Cl_2 (100 mL) was added to the residue. The resulting organic solution was washed with H_2O (2×100 mL) and dried over $MgSO_4$. After filtration, the filtrate was evaporated in vacuo. The resulting solid was chromatographed on flash silica gel with hexanes–EtOAc (3:2) as eluent to give 1.73 g (27%) of pale yellow solid with a melting point of 51–53 °C. IR: 1757 (C=O), 1266, 1095, 1064 (C–O) cm^{-1}. ^1H NMR: δ 6.73–6.52 (m, 12H, ArH), 4.87 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.75 (s, 4H, OCH_2C(O)), 4.61 (d, J=13.6 Hz, 2H, ArCH_2Ar, *ax*), 4.58 (d, J=15.2 Hz, 1H, ArCH_2Ar, *ax*), 4.22 (q, J=7.1 Hz, 4H, O$CH_2$$CH_3$), 4.30–4.10 (m, 2H, OCH_2), 4.09–3.92 (m, 6H, OCH_2), 3.80–3.59 (m, 8H, OCH_2), 3.23 (d, J=13.4 Hz, 1H, ArCH_2Ar, *eq*), 3.22 (d, J=13.5 Hz, 2H, ArCH_2Ar, *eq*), 3.14 (d, J=13.4 Hz, 1H, ArCH_2Ar, *eq*), 1.29 (t, J=7.2 Hz, 6H, CH_3). ^{13}C NMR: δ 170.1 (C=O), 156.2, 155.6, 135.3, 134.7, 134.6, 128.4, 128.4, 128.3, 128.2, 122.7, 122.3 (Ar), 73.5 (OCH_2), 71.3 (OCH_2C(O)), 71.2, 70.6, 70.3 (OCH_2), 60.5 (O$CH_2$$CH_3$), 31.2, 31.2, 30.6 (Ar$CH_2$Ar), 14.2 ($CH_3$). Anal. Calcd for $C_{44}H_{50}O_{11}\cdot 0.3CH_2Cl_2$: C, 69.37; H, 6.65. Found: C, 69.22; H, 6.77.

*3.1.2. 25,26-Bis[(ethoxycarbony)methoxyl]calix[4]arene-1,2-crown-6 in the cone conformation (**5**)*

A mixture of NaH (10.00 equiv, 0.65 g, 27.1 mmol), 25,26-dihydroxycalix[4]-arene-crown-6 (**3**) (1.00 equiv, 1.70 g, 2.71 mmol), and 45 mL of THF–DMF (9:1) in a 100-mL, one-necked flask under nitrogen was stirred for 30 min. Ethyl bromoacetate (8.00 equiv, 3.62 g, 21.68 mmol) was added to the flask with a syringe. The mixture was refluxed for 24 h. The reaction was quenched by addition of 1 N HCl (10 mL). THF was evaporated in vacuo and 1 N HCl (75 mL) was added to the residue. The resulting aqueous solution was extracted with CH_2Cl_2 (100 mL). The organic layer was separated, washed with H_2O (100 mL), and dried over $MgSO_4$. The CH_2Cl_2 was evaporated in vacuo. The crude product was chromatographed on silica gel with hexanes–EtOAc (1:2) as eluent to give 1.72 g (80%) of pale yellow, viscous oil. IR: 1758 (C=O), 1246, 1093, 1066 (C–O) cm^{-1}. ^1H NMR: δ 6.80–6.30 (m, 12H, ArH), 4.80 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.74 (d, J=16.2 Hz, 2H, OCH_2C(O)), 4.68 (d, J=17.1 Hz, 2H, OCH_2C(O)), 4.65 (d, J=13.7 Hz, 2H, ArCH_2Ar, *ax*), 4.60 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.22 (q, J=7.1 Hz, 4H, O$CH_2$$CH_3$), 4.18–4.07 (m, 4H, OCH_2), 4.07–3.98 (m, 2H, OCH_2), 3.96–3.85 (m, 2H, OCH_2), 3.79–3.60 (m, 12H, OCH_2), 3.24 (d, J=13.7 Hz, 1H, ArCH_2Ar, *eq*), 3.19 (d, J=13.6 Hz, 2H, ArCH_2Ar, *eq*), 3.15 (d, J=13.4 Hz, 1H, ArCH_2Ar, *eq*), 1.30 (t, J=7.1 Hz, 6H, CH_3). ^{13}C NMR: δ 170.0 (C=O), 156.3, 155.6, 135.2, 134.8, 134.8, 134.4, 128.5, 128.4, 128.3, 128.1, 122.8, 122.3 (Ar), 73.2 (OCH_2), 71.2 (OCH_2C(O)), 70.9, 70.9, 70.5, 70.3 (OCH_2), 60.5 (O$CH_2$$CH_3$), 31.4, 31.0, 30.8 (Ar$CH_2$Ar), 14.2 ($CH_3$). Anal. Calcd for $C_{46}H_{54}O_{12}$: C, 69.16; H, 6.81. Found: C, 68.83; H, 7.05.

*3.1.3. 25,26-Bis(carboxymethoxy)calix[4]arene-1,2-crown-5 in the cone conformation (**6**)*

A solution of 25,26-bis[(ethoxycarbonyl)methoxy]calix[4]-arene-crown-5 (**4**) (1.70 g, 2.25 mmol) in THF (20 mL) was mixed with 20 mL of 10% aqueous Me_4NOH. The mixture was refluxed for 24 h. After cooling to room temperature, the reaction was quenched by addition of 6 N HCl (10 mL). The mixture was stirred for 1 h. The organic solvent was evaporated in vacuo and the precipitate was filtered. The precipitate was dissolved in CH_2Cl_2 (50 mL). The aqueous filtrate was extracted with CH_2Cl_2 (2×30 mL). The combined CH_2Cl_2 solutions were dried over $MgSO_4$ and evaporated in vacuo to give 1.51 g (96%) of white solid with a melting point of 128–130 °C. IR: 3500–2700 (br, CO_2H), 1752 (C=O), 1248, 1130, 1058 (C–O) cm^{-1}. ^1H NMR: δ 10.17 (br s, 2H, CO_2H), 7.00–6.50 (m, 12H, ArH), 4.78 (d, J=16.1 Hz, 2H, OCH_2C(O)), 4.65 (d, J=15.9 Hz, 2H, OCH_2C(O)), 4.65 (d, J=15.9 Hz, 1H, ArCH_2Ar, *ax*), 4.61 (d, J=13.8 Hz, 1H, ArCH_2Ar, *ax*), 4.35 (d, J=13.2 Hz, 2H, ArCH_2Ar, *ax*), 4.29–4.15 (m, 2H, OCH_2), 4.15–4.04 (m, 2H, OCH_2), 4.04–3.86 (m, 4H, OCH_2), 3.86–3.73 (m, 4H, OCH_2),

3.73–3.59 (m, 4H, OCH_2), 3.30 (d, J=11.5 Hz, 1H, ArCH_2Ar, *eq*), 3.28 (d, J=13.3 Hz, 2H, ArCH_2Ar, *eq*), 3.18 (d, J=13.2 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 172.0 (C=O), 155.0, 154.7, 135.4, 134.1, 134.0, 133.9, 128.9, 128.9, 128.6, 128.5, 123.8, 123.1 (Ar), 74.6 (OCH_2), 71.6 (OCH_2C(O)), 70.9, 70.4, 69.8 (OCH_2), 31.1, 30.8, 30.4 (ArCH_2Ar). Anal. Calcd for $C_{40}H_{42}O_{11}$: C, 68.76; H, 6.06. Found: C, 68.94; H, 6.11.

3.1.4. 25,26-Bis(carboxymethoxy)calix[4]arene-1,2-crown-6 in the cone conformation (7)

A solution of 25,26-bis[(ethoxycarbonyl)methoxy]calix[4]-arene-crown-6 (**5**) (1.70 g, 2.13 mmol) in THF (30 mL) was mixed with 10% aqueous Me_4NOH (30 mL). The mixture was refluxed for 24 h. After cooling to room temperature, the reaction was quenched by addition of 6 N HCl (15 mL). The mixture was stirred for 1 h. The organic solvent was evaporated in vacuo and the precipitate was filtered. The precipitate was dissolved in CH_2Cl_2 (50 mL). The aqueous filtrate was extracted with CH_2Cl_2 (2×30 mL). The combined CH_2Cl_2 solutions were dried over $MgSO_4$ and evaporated in vacuo to give 1.55 g (98%) of white solid with a melting point of 120–122 °C. IR: 3400–2700 (br, CO_2H), 1757 (C=O), 1273, 1130, 1062 (C–O) cm^{-1}. ^{1}H NMR: δ 10.14 (br s, 2H, CO_2H), 6.99–6.50 (m, 12H, ArH), 4.78 (d, J=16.1 Hz, 2H, OCH_2C(O)), 4.65 (d, J=13.3 Hz, 1H, ArCH_2Ar, *ax*), 4.61 (d, J=16.0 Hz, 2H, OCH_2C(O)), 4.61 (d, J=16.0 Hz, 1H, ArCH_2Ar, *ax*), 4.40 (d, J=13.2 Hz, 2H, ArCH_2Ar, *ax*), 4.28–4.08 (m, 4H, OCH_2), 4.06–3.93 (m, 2H, OCH_2), 3.93–3.83 (m, 2H, OCH_2), 3.83–3.53 (m, 12H, OCH_2), 3.31 (d, J=13.7 Hz, 1H, ArCH_2Ar, *eq*), 3.26 (d, J=13.3 Hz, 2H, ArCH_2Ar, *eq*), 3.20 (d, J=13.3 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 171.7 (C=O), 155.2, 154.7, 135.2, 134.2, 134.2, 133.8, 128.9, 128.9, 128.7, 128.2, 123.8, 123.0 (Ar), 74.3 (OCH_2), 71.6 (OCH_2C(O)), 70.9, 70.8, 70.3, 69.7 (OCH_2), 31.1, 30.7 (ArCH_2Ar). Anal. Calcd for $C_{42}H_{46}O_{12}$: C, 67.91; H, 6.24. Found: C, 67.58; H, 6.54.

3.2. General procedure for the synthesis of 25,26-di(N-(X)sulfonyl carbamoylmethoxy)calix[4]arene-1,2-crown-5 compounds in the cone conformation (8–11)

A solution of 25,26-bis(carboxymethoxy)calix[4]arene-crown-5 (**6**) (1.00 equiv, 1.31 g, 1.875 mmol) in benzene (90 mL) was refluxed with a Dean-Stark trap for 2 h during which 50 mL of benzene was removed. Oxalyl chloride (11.00 equiv, 2.62 g, 1.77 mL, 20.6 mmol) was added to the flask with a syringe and the mixture was refluxed for 5 h under nitrogen. The benzene was evaporated in vacuo to give the corresponding di(acid chloride), which was used directly in the next step. The sulfonamide salt was prepared under nitrogen by adding NaH (10.00 equiv, 0.45 g, 18.75 mmol) and THF (20 mL) to a 3-necked flask. The appropriate sulfonamide (2.2 equiv, 4.12 mmol) in THF (30 mL) was added over a 10-min period. The mixture was stirred for 1.5 h followed by addition of a solution of di(acid chloride) in THF (10 mL). The reaction mixture was stirred for 24 h after which H_2O (10 mL) was added and stirring was continued for 0.5 h. The THF was evaporated in vacuo. CH_2Cl_2 was added to the residue and the resulting solution was dried over $MgSO_4$. After purification by chromatography on silica gel, the product was dissolved in CH_2Cl_2. The solution was shaken with 6 N HCl, dried over $MgSO_4$, and evaporated in vacuo to provide the product as a solid.

3.2.1. 25,26-Bis(N-methanesulfonyl carbamoylmethoxy)-calix[4]arene-1,2-crown-5 in the cone conformation (8)

Compound **8** was chromatographed on silica gel with CH_2Cl_2–MeOH (97:3) as eluent to obtain 0.67 g (42%) of white solid with a melting point of 291–293 °C. IR: 3218 (N–H), 1721 (C=O), 1344, 1140 (SO_2), 1266, 1093, 1057 (C–O) cm^{-1}. ^{1}H NMR: δ 10.22 (s, 2H, NH), 7.00–6.31 (m, 12H, ArH), 4.95 (d, J=16.1 Hz, 2H, OCH_2C(O)), 4.92 (d, J=13.2 Hz, 1H, ArCH_2Ar, *ax*), 4.58 (d, J=16.4 Hz, 2H, OCH_2C(O)), 4.12 (d, J=13.3 Hz, 1H, ArCH_2Ar, *ax*), 4.38 (d, J=13.9 Hz, 2H, ArCH_2Ar, *ax*), 4.20–3.98 (m, 6H, OCH_2), 3.98–3.82 (m, 4H, OCH_2), 3.82–3.65 (m, 6H, OCH_2), 3.35 (s, 6H, CH_3), 3.30 (d, J=13.8 Hz, 2H, ArCH_2Ar, *eq*), 3.27 (d, J=10.7 Hz, 1H, ArCH_2Ar, *eq*), 3.19 (d, J=13.3 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 170.2 (C=O), 155.9, 155.8, 134.8, 134.8, 134.0, 133.1, 129.3, 128.6, 128.6, 128.5, 123.2, 122.8 (Ar), 74.0 (OCH_2), 73.4 (OCH_2C(O)), 69.9, 69.6, 69.4 (OCH_2), 41.5 (CH_3), 31.6, 31.2, 30.6 (ArCH_2Ar). Anal. Calcd for $C_{42}H_{48}O_{13}N_2S_2\cdot 0.1CH_2Cl_2$: C, 58.70; H, 5.64; N, 3.25. Found: C, 58.53; H, 5.71; N, 3.10.

3.2.2. 25,26-Bis(N-benzenesulfonyl carbamoylmethoxy)-calix[4]arene-1,2-crown-5 in the cone conformation (9)

Compound **9** was chromatographed on silica gel with CH_2Cl_2–MeOH (39:1) as eluent to obtain 1.19 g (65%) of white solid with a melting point of 146–147 °C. IR: 3228 (N–H), 1715 (C=O), 1350, 1154 (SO_2), 1265, 1087, 1051 (C–O) cm^{-1}. ^{1}H NMR: δ 10.43 (s, 2H, NH), 8.14 (d, J=7.6 Hz, 4H, ArH), 7.61 (t, J=7.4 Hz, 2H, ArH), 7.50 (t, J=7.8 Hz, 4H, ArH), 7.09–6.10 (m, 12H, ArH), 4.66 (d, J=15.7 Hz, 2H, OCH_2C(O)), 4.48 (d, J=13.5 Hz, 1H, ArCH_2Ar, *ax*), 4.40 (d, J=15.7 Hz, 2H, OCH_2C(O)), 4.38 (d, J=12.9 Hz, 1H, ArCH_2Ar, *ax*), 4.31 (d, J=14.8 Hz, 2H, ArCH_2Ar, *ax*), 4.26–4.11 (m, 2H, OCH_2), 4.11–3.87 (m, 8H, OCH_2), 3.87–3.63 (m, 6H, OCH_2), 3.19 (d, J=13.3 Hz, 1H, ArCH_2Ar, *eq*), 3.12 (d, J=13.7 Hz, 2H, ArCH_2Ar, *eq*), 2.96 (d, J=13.4H, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 168.7 (C=O), 155.9, 155.7, 138.8, 134.9, 134.6, 134.0, 133.9, 132.8, 128.9, 128.9, 128.5, 128.4, 123.0, 122.8 (Ar), 74.4 (OCH_2), 73.2 (OCH_2C(O)), 69.6, 69.4 (OCH_2), 32.1, 31.0, 30.8 (ArCH_2Ar). Anal. Calcd for $C_{52}H_{52}O_{13}N_2S_2$: C, 63.92; H, 5.36; N, 2.87. Found: C, 63.73; H, 5.57; N, 2.85.

3.2.3. 25,26-Bis(N-4-nitrobenzenesulfonyl carbamoylmethoxy)-calix[4]arene-1,2-crown-5 in the cone conformation (10)

Compound **10** was chromatographed on silica gel with CH_2Cl_2–MeOH (39:1) as eluent to give 1.00 g (50%) of yellow solid with a melting point of 246–248 °C. IR: 3237 (N–H), 1720 (C=O), 1534, 1311 (NO_2), 1350, 1153 (SO_2), 1266,

1087, 1055 (C–O) cm^{-1}. ^1H NMR: δ 10.59 (s, 2H, NH), 8.30 (s, 8H, ArH), 6.99–5.60 (m, 12H, ArH), 4.83 (d, J=15.6 Hz, 2H, OCH_2C(O)), 4.60 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.51 (d, J=16.1 Hz, 2H, OCH_2C(O)), 4.40 (d, J=13.2 Hz, 1H, ArCH_2Ar, *ax*), 4.30 (d, J=13.8 Hz, 2H, ArCH_2Ar, *ax*), 4.20–4.09 (m, 2H, OCH_2), 4.05 (d, J=7.8 Hz, 4H, OCH_2), 3.99–3.91 (m, 2H, OCH_2), 3.91–3.84 (m, 2H, OCH_2), 3.84–3.67 (m, 6H, OCH_2), 3.21 (d, J=13.7 Hz, 2H, ArCH_2Ar, *eq*), 3.19 (d, J=9.8 Hz, 1H, ArCH_2Ar, *eq*), 2.96 (d, J=13.6 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 169.0 (C=O), 155.8, 155.5, 150.6, 143.9, 134.6, 133.8, 132.8, 130.0, 129.2, 128.6, 128.4, 124.1, 123.2, 122.9 (Ar), 74.2 (OCH_2), 73.2 (OCH_2C(O)), 69.7, 69.7, 69.5 (OCH_2), 31.9, 31.1, 30.6 (ArCH_2Ar). Anal. Calcd for $C_{52}H_{50}O_{17}N_4S_2$: C, 58.53; H, 4.72; N, 5.25. Found: C, 58.44; H, 4.86; N, 5.05.

*3.2.4. 25,26-Bis(N-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-1,2-crown-5 in the cone conformation (**11**)*

Compound **11** was chromatographed on silica gel with hexanes–EtOAc (1:2) as eluent to give 0.74 g (41%) of white solid with a melting point of 127–129 °C. IR: 3200–2300 (br, N–H), 1752 (C=O), 1372, 1206 (SO_2), 1265, 1135, 1053 (C–O) cm^{-1}. ^1H NMR: δ 10.80 (br s, 2H, NH), 6.65 (br s, 12H, ArH), 4.89 (s, 4H, OCH_2C(O)), 4.78 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.41 (d, J=13.8 Hz, 2H, ArCH_2Ar, *ax*), 4.37 (d, J=13.3 Hz, 1H, ArCH_2Ar, *ax*), 4.23 (br s, 2H, OCH_2), 4.09–3.94 (m, 6H, OCH_2), 3.94–3.84 (m, 4H, OCH_2), 3.84–3.70 (m, 4H, OCH_2), 3.31 (d, J=13.9 Hz, 2H, ArCH_2Ar, *eq*), 3.27 (d, J=13.8 Hz, 1H, ArCH_2Ar, *eq*), 3.23 (d, J=13.2 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 168.4 (C=O), 155.8, 155.3, 135.2, 134.5, 134.0, 132.7, 129.1, 128.8, 128.7, 128.6, 123.4, 123.1 (Ar), 120.5, 117.9 (CF_3), 74.3 (OCH_2), 72.6 (OCH_2C(O)), 69.2, 69.0, 68.7 (OCH_2), 32.3, 31.0, 30.8 (ArCH_2Ar). Anal. Calcd for $C_{42}H_{42}O_{13}N_2S_2F_6$: C, 52.50; H, 4.40; N, 2.92. Found: C, 52.79; H, 4.60; N, 2.97.

*3.3. General procedure for the synthesis of 25,26-di[N-(X)sulfonyl carbamoylmethoxy]calix[4]arene-1,2-crown-6 compounds in the cone conformation (**12–15**)*

A solution of 25,26-bis(carboxymethoxy)calix[4]arene-crown-6 (**7**) (1.00 equiv, 1.68 g, 2.26 mmol) in benzene (90 mL) was refluxed with a Dean-Stark strap for 2 h during which 50 mL of benzene was removed. Oxalyl chloride (11.00 equiv, 3.16 g, 2.14 mL, 24.88 mmol) was added to the flask with a syringe and the mixture was refluxed for 5 h under nitrogen. Benzene was evaporated in vacuo to give the corresponding di(acid chloride), which was used directly in the next step. The sulfonamide salt was prepared under nitrogen by adding NaH (10.00 equiv, 0.54 g, 22.6 mmol) and THF (25 mL) to a three-necked flask. The appropriate sulfonamide (2.2 equiv, 4.97 mmol) in THF (30 mL) was added over a 10-min period. The mixture was stirred for 1.5 h followed by addition of a solution of the di(acid chloride) in THF (10 mL). The reaction mixture was stirred for 24 h after which H_2O (10 mL) was added and stirring was continued for 0.5 h. The THF was evaporated in vacuo. CH_2Cl_2 was added to the residue and the resulting organic solution was dried over $MgSO_4$. After purification by chromatography on silica gel, the product was dissolved in CH_2Cl_2. The solution was shaken with 6 N HCl, dried over $MgSO_4$, and evaporated in vacuo to give the product as a solid.

*3.3.1. 25,26-Bis(N-methanesulfonyl carbamoylmethoxy)-calix[4]arene-1,2-crown-6 in the cone conformation (**12**)*

Compound **12** was chromatographed on silica gel with CH_2Cl_2–MeOH (19:1) as eluent to give 1.44 g (71%) of white solid with a melting point of 126–128 °C. IR: 3220 (N–H), 1712 (C=O), 1343, 1152 (SO_2), 1266, 1084, 1052 (C–O) cm^{-1}. ^1H NMR: δ 10.19 (s, 2H, NH), 7.00–6.20 (m, 12H, ArH), 4.99 (d, J=12.0 Hz, 1H, ArCH_2Ar, *ax*), 4.96 (d, J=16.0 Hz, 2H, OCH_2C(O)), 4.46 (d, J=16.5 Hz, 2H, OCH_2C(O)), 4.46 (d, J=12.0 Hz, 1H, ArCH_2Ar, *ax*), 4.42 (d, J=14.0 Hz, 2H, ArCH_2Ar, *ax*), 4.23–4.12 (m, 2H, OCH_2), 4.08–3.92 (m, 4H, OCH_2), 3.87–3.80 (m, 2H, OCH_2), 3.80–3.67 (m, 10H, OCH_2), 3.67–3.59 (m, 2H, OCH_2), 3.37 (s, 6H, CH_3), 3.28 (d, J=14.0 Hz, 1H, ArCH_2Ar, *eq*), 3.28 (d, J=14.0 Hz, 2H, ArCH_2Ar, *eq*), 3.20 (d, J=14.0 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 169.9 (C=O), 156.0, 155.9, 134.9, 134.3, 134.2, 133.6, 129.3, 128.6, 128.6, 128.3, 123.2, 122.7 (Ar), 73.7 (OCH_2C(O)), 73.6, 70.8, 70.2, 70.0, 69.8 (OCH_2), 41.4 (CH_3), 31.3, 31.0, 30.7 (ArCH_2Ar). Anal. Calcd for $C_{44}H_{52}O_{14}N_2S_2$: C, 58.92; H, 5.84; N, 3.12. Found: C, 58.60; H, 5.80; N, 2.84.

*3.3.2. 25,26-Bis(N-benzenesulfonyl carbamoylmethoxy)-calix[4]arene-1,2-crown-6 in the cone conformation (**13**)*

Compound **13** was chromatographed on silica gel with CH_2Cl_2–MeOH (97:3) as eluent to give 1.92 g (83%) of white solid with a melting point of 107–109 °C. IR: 3231 (N–H), 1716 (C=O), 1350, 1160 (SO_2), 1266, 1088, 1058 (C–O) cm^{-1}. ^1H NMR: δ 10.34 (s, 2H, NH), 8.17 (dd, J=7.3, 1.3 Hz, 4H, ArH), 7.63 (t, J=7.3 Hz, 2H, ArH), 7.54 (t, J=8.0 Hz, 4H, ArH), 6.90–6.20 (m, 12H, ArH), 4.66 (d, J=15.4 Hz, 2H, OCH_2C(O)), 4.56 (d, J=13.8 Hz, 1H, ArCH_2Ar, *ax*), 4.50 (d, J=13.9 Hz, 1H, ArCH_2Ar, *ax*), 4.38 (d, J=13.7 Hz, 2H, ArCH_2Ar, *ax*), 4.38 (d, J=15.4 Hz, 2H, OCH_2C(O)), 4.27–4.15 (m, 2H, OCH_2), 4.15–4.02 (m, 2H, OCH_2), 3.94–3.80 (m, 2H, OCH_2), 3.80–3.65 (m, 6H, OCH_2), 3.65–3.44 (m, 8H, OCH_2), 3.18 (d, J=13.9 Hz, 1H, ArCH_2Ar, *eq*), 3.18 (d, J=13.9 Hz, 2H, ArCH_2Ar, *ax*), 2.95 (d, J=13.9 Hz, 1H, ArCH_2Ar, *ax*). ^{13}C NMR: δ 168.3 (C=O), 156.2, 155.8, 138.7, 135.0, 134.3, 133.9, 133.6, 132.6, 129.1, 129.1, 128.9, 128.7, 128.7, 128.6, 128.2, 123.1, 122.6 (Ar), 74.0 (OCH_2C(O)), 73.9, 71.0, 70.5, 70.4, 70.1 (OCH_2), 31.3, 31.1, 31.0 (ArCH_2Ar). Anal. Calcd for $C_{54}H_{56}O_{14}N_2S_2$: C, 63.52; H, 5.53; N, 2.74. Found: C, 63.19; H, 5.60; N, 2.79.

*3.3.3. 25,26-Bis(N-p-nitrobenzenesulfonyl carbamoylmethoxy)calix[4]arene-1,2-crown-6 in the cone conformation (**14**)*

Compound **14** was chromatographed on silica gel with CH_2Cl_2–MeOH (39:1) as eluent to give 2.03 g (81%) of yellow

solid with a melting point of 183–185 °C. IR: 3226 (N–H), 1725 (C=O), 1537, 1314 (NO_2), 1355, 1194 (SO_2), 1254, 1086, 1052 (C–O) cm^{-1}. ^1H NMR: δ 10.67 (s, 2H, NH), 8.40 (d, J=8.8 Hz, 4H, ArH), 8.36 (d, J=8.8 Hz, 4H, ArH), 6.60 (s, 10H, ArH), 6.48 (s, 2H, ArH), 4.74 (d, J=15.6 Hz, 2H, OCH_2C(O)), 4.57 (d, J=13.9 Hz, 1H, ArCH_2Ar, *ax*), 4.52 (d, J=14.2 Hz, 1H, ArCH_2Ar, *ax*), 4.48 (d, J=15.7 Hz, 2H, OCH_2C(O)), 4.40 (d, J=13.8 Hz, 2H, ArCH_2Ar, *ax*), 4.31–4.18 (m, 2H, OCH_2), 4.16–4.03 (m, 2H, OCH_2), 3.92–3.82 (m, 2H, OCH_2), 3.82–3.67 (m, 6H, OCH_2), 3.66–3.55 (m, 4H, OCH_2), 3.54–3.40 (m, 4H, OCH_2), 3.24 (d, J=13.9 Hz, 2H, ArCH_2Ar, *eq*), 3.22 (d, J=13.7 Hz, 1H, ArCH_2Ar, *eq*), 2.99 (d, J=13.9 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 168.6 (C=O), 156.2, 155.5, 150.7, 143.9, 134.9, 134.1, 133.5, 130.1, 129.2, 128.7, 128.7, 128.2, 124.1, 123.2, 122.7 (Ar), 73.9 (OCH_2), 73.6 (OCH_2C(O)), 70.8, 70.6, 70.4, 70.0 (OCH_2), 31.4, 31.0 (ArCH_2Ar). Anal. Calcd for $C_{54}H_{54}O_{18}N_4S_2$: C, 58.37; H, 4.90; N, 5.04. Found: C, 58.24; H, 4.88; N, 5.03.

*3.3.4. 25,26-Bis(N-trifluoromethanesulfonyl carbamoylmethoxy)calix[4]arene-1,2-crown-6 in the cone conformation (**15**)*

Compound **15** was chromatographed on silica gel with CH_2Cl_2–MeOH (97:3) as eluent to give 1.29 g (57%) of white solid with a melting point of 181–183 °C. IR: 3401 (N–H), 1752 (C=O), 1389, 1215 (SO_2), 1266, 1133, 1055 (C–O) cm^{-1}. ^1H NMR: δ 10.86 (br s, 2H, NH), 7.00–6.20 (m, 12H, ArH), 5.09 (d, J=13.4 Hz, 1H, ArCH_2Ar, *ax*), 4.96 (d, J=16.5 Hz, 2H, OCH_2C(O)), 4.59 (d, J=16.8 Hz, 2H, OCH_2C(O)), 4.42 (d, J=13.7 Hz, 1H, ArCH_2Ar, *ax*), 4.40 (d, J=13.9 Hz, 2H, ArCH_2Ar, *ax*), 4.32–4.14 (m, 2H, OCH_2), 4.06–3.89 (m, 4H, OCH_2), 3.89–3.59 (m, 14H, OCH_2), 3.28 (d, J=14.0 Hz, 2H, ArCH_2Ar, *eq*), 3.26 (d, J=13.6 Hz, 1H, ArCH_2Ar, *eq*), 3.22 (d, J=13.8 Hz, 1H, ArCH_2Ar, *eq*). ^{13}C NMR: δ 168.4 (C=O), 156.1, 155.9, 134.6, 134.6, 134.3, 133.5, 129.2, 128.8, 128.7, 128.3, 123.4, 122.8 (Ar), 120.5, 117.9 (CF_3), 73.4 (OCH_2 and OCH_2C(O)), 70.9, 70.1, 70.0, 69.3 (OCH_2), 31.2, 31.0, 30.6 (ArCH_2Ar). Anal. Calcd for $C_{44}H_{46}O_{14}N_2S_2F_6$: C, 52.59; H, 4.61; N, 2.79. Found: C, 52.28; H, 4.74; N, 2.66.

3.4. Procedure for competitive extraction of alkaline earth metal cations

An aqueous solution of the alkaline earth metal chlorides with hydroxides for pH adjustment (for **11** and **15**, 0.10 M HCl was utilized for pH adjustment) (2.0 mL, 10.0 mM in each alkaline earth metal cation species) and 2.0 mL of 1.0 mM ligand in chloroform in a capped, polypropylene, 15-mL centrifuge tube was vortexed with a Glas-Col Multi-Pulse Vortexer for 10 min at room temperature. The tube was centrifuged for 10 min for phase separation with a Becton–Dickinson Clay Adams Brand® Centrifuge. A 1.5-mL portion of the organic phase was removed and added to 3.0 mL of 0.10 M HCl in a new, 15-mL, polypropylene centrifuge tube. The tube was vortexed for 10 min and centrifuged for 10 min. The alkaline earth metal cation concentrations in the aqueous phase from stripping were determined with a Dionex DX-120 Ion Chromatograph with a CS12A column. The pH of the aqueous phase from the initial extraction step was determined with a Fisher Accumet AR25 pH meter with a Corning 476157 combination pH electrode.

3.5. Procedure for single species extraction of Pb^{2+}

The procedure used for competitive extraction of alkaline earth metal cations was modified, as follows. The organic phase was a 0.50 mM solution of the ligand in chloroform. The aqueous phase contained 1.0 mM $Pb(NO_3)_2$ with the pH adjusted using either HNO_3 or Me_4NOH solutions. For stripping of the extracted Pb^{2+} from the chloroform phase, 1.0 M HNO_3 was utilized. The Pb^{2+} concentrations in the aqueous stripping solutions were determined with a Perkin–Elmer Model 5000 atomic absorption spectrophotometer.

3.6. Procedure for single species extraction of Hg^{2+}

An aqueous solution (3.0 mL) of 0.25 mM $Hg(NO_3)_2$ with HNO_3 or TMAOH for pH adjustment and 3.0 mL of 0.25 mM solution of the ligand in chloroform were placed in a capped, polypropylene, 15-mL centrifuge tube. The mixture was vortexed for 10 min at room temperature. The tube was centrifuged for 10 min for phase separation. A 0.50-mL sample of the aqueous phase was removed and diluted to 5.0 mL with water. A 1.5-mL aliquot of the diluted solution was shaken for 10 min with 3.0 mL of 14 ppm solution of dithizone in chloroform and 1.5 mL of 1.0 M citric acid solution for which the pH had been adjusted using NaOH. The mixture was centrifuged for 10 min. The organic phase was then analyzed by using the absorbance at 496 nm for mercury dithizonate complex with a Shimadzu Model 260 UV–vis spectrophotometer. The pH of the remaining 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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