

Effect of Crown Ring Size and Upper Moiety on the Extraction of s-Block Metals by Ionizable Calixcrown Nano-baskets

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Eight ionizable nano-baskets of cone 25,26-di(carboxymethoxy)calix[4]arene-crown-3,4,5,6 were synthesized and were verified by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy and elemental analysis. The competitive solvent extractions of alkali and alkaline earth metal cations were studied using such nano-baskets. The novelty of this study is including three binding units of calixarene's bowl, crown ether's ring and electron-donor ionizable moieties in a unique scaffold to assess the binding tendency towards the cations. The objective of this work is to study the extraction efficiency, selectivity and $\text{pH}_{1/2}$ of such complexes. The result of solvent extraction experiments indicated that these compounds were effective extractants of alkali and alkaline earth metal cations. Their selectivities were greatly influenced by the acidity of solution and the conformations of the calixcrown. One conformer was selective to Na^+ in $\text{pH} \geq 4$, while the other was highly selective to Ba^{2+} in pH 6 and upper.

Key Words : Nano-basket, Solvent extraction, Calixcrown, Upper rim, s-Block Metals

Introduction

Nano-baskets of calixarenes and calixcrowns are a versatile class of macrocycles, which have been subject to extensive research in development of many extractants, transporters and stationary phases (using gas chromatograph, Teif Gostar Faraz Co.) over the past four decades.¹⁻⁵ Functionalization of calix[4]arenes at both the upper rim and the lower rim has been extensively studied. Attaching donor atoms to the lower rim of a calix[4]arene can improve the binding strength of the parent calixarene dramatically. The two main groups of lower rim functionalized calix[4]arenes are calix[4]arene podands and calixarene-crown ethers.^{6,7} Distal hydroxyl groups can be connected to give 1,3-bridged calix[4]crowns, while connection between proximal hydroxyl groups leads to 1,2-bridged calix[4]crowns.

It is found that the 1,3-bridged calix[4]crowns,⁸ thiacalix[4]biscrowns,⁹ diazocalix[4]dipropyl,¹⁰ diazocalix[4]crown-6,¹⁰ thiacalix[4]biscrown-5 and *p-tert*-butylthiacalix[4]biscrown-5¹¹ exhibit high binding affinity and selectivity toward alkali and alkaline earth metal cations, while the researches on 1,2-bridged calix[4]crowns lag far behind. Combining crown ethers with calix[4]arenes increases the cation binding ability of the parent calixarenes, and control of the selectivity is obtained through modulation of the crown ether size. Attachment of proton-ionizable groups to calixcrowns can further improve their extraction properties because the ionized group not only participates in metal ion coordination, but also eliminates the need to transfer aqueous phase anions into the organic phase. Ungaro *et al.*¹² reported the first di-proton-ionizable calix[4]crown-5 in 1984 and it showed quite high efficiency in extraction of divalent metals from water to dichloromethane. Combining

crown ethers with calix[4]arenes increases the cation binding ability of the parent calixarenes.¹³⁻¹⁵

Zhang *et al.* synthesized di-ionizable *p-tert*-butylcalix[4]-1,2-thiacrown-3 bearing *N*-phenyl-sulfonyl oxyacetamide functions in the lower rim of the cone conformation¹⁶ and calix[4]1,2-crown-3 bearing *N*-phenyl-sulfonyl oxyacetamide functions in the lower rim of the 1,2-alternate conformation¹⁷ and used them for the single species extractions of lead and mercury cations and the competitive solvent extractions of alkali and alkaline earth metals.

Tu *et al.*¹⁸ synthesized di-ionizable calix[4]1,2-crown-4 bearing oxyacetic acid moieties and *N*-phenyl-sulfonyl oxyacetamide functions in the lower rim of the cone conformation and used them for the single species extractions of lead and mercury cations and the competitive solvent extractions of alkaline earth metals. However the competitive solvent extraction of alkali metals was not reported.

Zhou *et al.* synthesized di-ionizable *p-tert*-butylcalix[4]-1,2-crown-5,¹⁹ -1,2-crown-6²⁰ and calix[4]1,2-crown-6²¹ in cone, 1,3-alternate and partial-cone conformations bearing *N*-phenyl-sulfonyl oxyacetamide moieties in the lower rim and used them for competitive solvent extractions of alkaline earth metals. The single species extractions of lead and of mercury cations as well as the competitive solvent extraction of alkali metals were not reported.

Tu *et al.*²² repeated the Zhang's works and presented the synthesis and the competitive solvent extractions of alkaline earth metals, which are reported in references 19 and 20. They also amalgamated the results of reference 21 (the cone conformer) and the a novel synthesis and extraction procedure, in which calix[4]1,2-crown-5 in cone conformation bearing *N*-phenyl-sulfonyl oxyacetamide moieties was used. They reported the results of single species extractions of

mercury and lead cations and the competitive solvent extractions of alkaline earth metals.²³

The selectivity can be affected by the crown ether size, the identity of donor atoms on the crown ether moiety and the conformation of the calixarene platform. To further explore the influence of these factors on the extraction characteristics of *p*-*tert*-butylcalix[4]arene-1,2-crown ethers toward metal ions, series of di-ionizable *p*-*tert*-butylcalix[4]arene-1,2-crown-3 compounds in the cone conformation and the 1,2-alternate conformation, as well as *p*-*tert*-butylcalix[4]arene-1,2-thiacrown-3 in the cone conformation have been synthesized.

There are two kinds of side chain in the calixcrown skeleton that were studied including two ionizable carboxylic acid moieties and the crown-ether moieties. The ionizable moieties not only participate in cooperative metal ion coordination, but also eliminate the need to transfer the anions from the aqueous phase into the organic phase by operating in a cation-exchange mode with the metal cation.²⁴⁻²⁹ In this work, two proton-ionizable function groups were incorporated into calix[4]arene scaffold. A special feature of such modification is that the acidity of the ionizable moiety can be tunable by changing the functional group from hydroxyl to other groups due to different electron-withdrawing abilities of functional group. A wide range of pH environments can be examined when these ionizable groups are incorporated into the calixcrown skeleton. These extractants exhibit excellent extraction selectivity for alkali and alkaline earth metals.

In this work, eight diacid proton-ionizable calixcrowns were synthesized including cone *p*-*tert*-butyl-25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-3 (**10**), cone *p*-*tert*-butyl-25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-4 (**11**), cone *p*-*tert*-butyl-25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-5 (**12**), cone *p*-*tert*-butyl-25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-6 (**13**), cone 25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-3 (**23**), cone

25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-4 (**24**), cone 25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-5 (**25**), and cone 25,26-di(carboxymethoxy) calix[4]arene-1,2-crown-6 (**26**). Competitive solvent extractions of alkali metal cations and alkaline earth metal cations were performed using them, in which 1.0 mM solutions of di-ionizable calix[4]crown ligands in chloroform as well as the plots of cation loading of the organic phase vs. the equilibrium pH of the aqueous phase were presented. In the following, the synthesis and the extraction procedures of eight conformers are presented, respectively. Figure 1 depicted the chemical structure of eight calixcrown scaffolds as extractant agents.

Synthesis Procedure

Reagents were obtained from commercial suppliers and used directly, unless otherwise noted. Acetonitrile (MeCN) was dried over CaH₂ and distilled immediately before use. Tetrahydrofuran (THF) was dried over sodium with benzophenone as an indicator and distilled just before use. Cs₂CO₃ was activated by heating at 150 °C overnight under high vacuum and stored in a desiccator. Melting points were determined with a Mel-Temp melting point apparatus. Infrared (IR) spectra were recorded with a Perkin-Elmer Model 1600 FT-IR spectrometer as deposits from CH₂Cl₂ solution on NaCl plates. The ¹H and ¹³C NMR spectra were recorded with a Varian Unity INOVA 500 MHz FT-NMR (¹H 500 MHz and ¹³C 126 MHz) spectrometer in CDCl₃ with Me₄Si as internal standard unless mentioned otherwise. Chemical shifts (δ) are given in ppm downfield from TMS and coupling constants (*J*) values are in Hz. The synthesis scheme for preparation of cone *p*-*tert*-butyl-25,26-di(carboxymethoxy)calix[4]arene-1,2-crown-3,4,5,6 (**10-13**) and cone 25,26-di(carboxymethoxy)calix[4]arene-1,2-crown-3,4,5,6 (**23-26**) are presented in Figure 2.

Preparation of Diacid Calixcrowns 10-13.

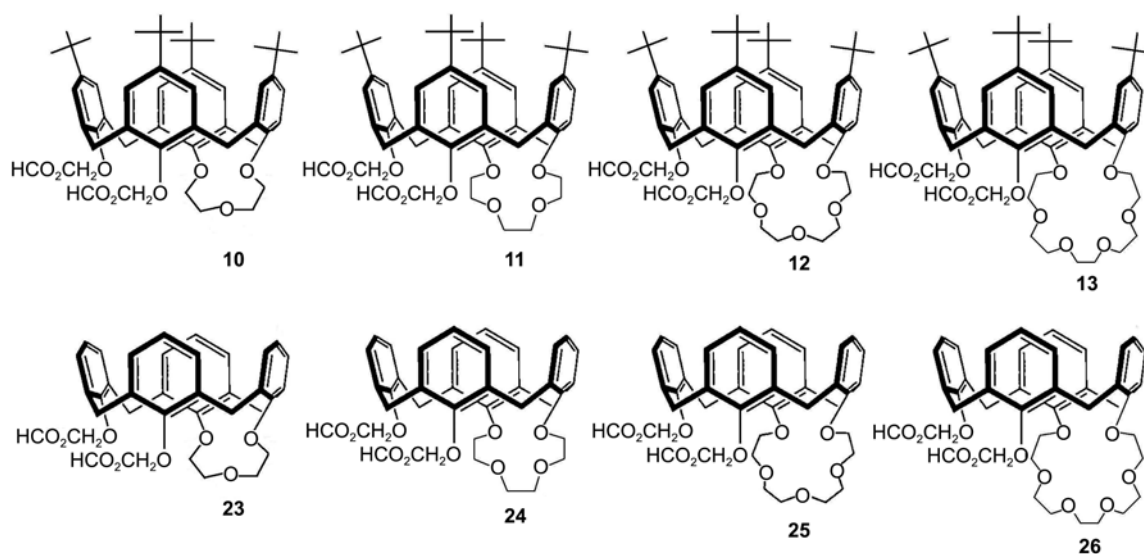


Figure 1. The chemical structure of eight calixcrown scaffolds were synthesized and studied.

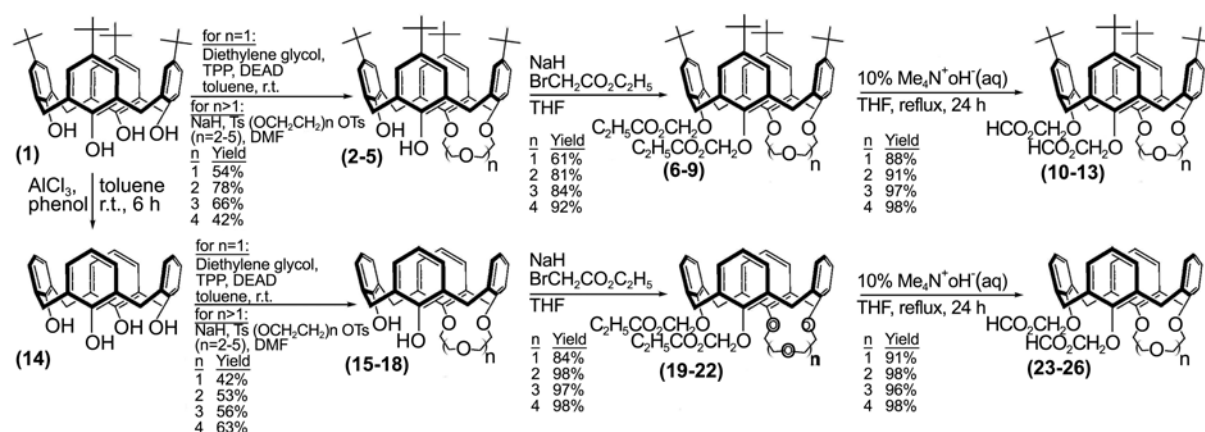


Figure 2. Synthesis of cone *p*-tert-butyl-25,26-di(carboxymethoxy)calix[4]arene-1,2-crown-3,4,5,6 (**10-13**) and cone 25,26-di(carboxymethoxy)calix[4]arene-1,2-crown-3,4,5,6 (**23-26**).

Synthesis of Calixcrown 2: To a mixture of *p*-tert-butylcalix[4]arene (**1**) (6.50 g, 10 mmol), diethylene glycol (1.59 g, 15 mmol) and TPP (8.00 g, 30 mmol) in 200 mL of toluene, a 40% solution of DEAD (5.22 g, 30 mmol) in toluene was added dropwise. The mixture was stirred at room temperature for 0.5 h. Then the solution was evaporated to dryness and the residue was extracted with hexane (3×30 mL) followed by evaporation and subsequent stirring in hexane and ethyl acetate. The precipitate was filtered and the filtrate was purified by chromatography on silica gel with hexane-EtOAc (9:1) as eluent to give a white solid (3.90 g, 54%) with mp 198–199 °C. IR (deposit from CH_2Cl_2 solution on a NaCl plate) $\nu_{\text{max}}/\text{cm}^{-1}$ 3342 (O–H), 1249 and 1124 (C–O); ^1H NMR (CDCl_3): δ 1.20 (s, 18H, CH_3), 1.21 (s, 18H, CH_3), 3.26–3.45 (m, 4H, ArCH_2Ar), 4.01 (t, $J = 10.5$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{O}$), 4.12 (t, $J = 11.0$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{O}$), 4.28–4.46 (m, 7H, $\text{OCH}_2\text{CH}_2\text{O}$, ArCH_2Ar), 4.82 (d, $J = 12.0$ Hz, 1H, ArCH_2Ar), 6.94–7.06 (m, 6H, ArH), 7.15 (d, $J = 2.0$ Hz, 2H, ArH), 8.87 (s, 2H, OH); ^{13}C NMR (CDCl_3): δ 31.30, 31.50, 32.66, 33.01, 33.90, 34.18, 75.32, 125.31, 125.58, 125.60, 126.45, 128.32, 128.84, 129.15, 133.88, 134.62, 142.81, 147.42, 149.14, 150.34. Anal. Calcd for $\text{C}_{48}\text{H}_{62}\text{O}_5$: C, 80.18; H, 8.69. Found: C, 80.08; H, 8.37%.

Synthesis of Calixcrown 3: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxycalix[4]arene-crown-4 in the cone conformation was synthesized as the following. NaH (10.00 eq, 2.13 g, 88.6 mmol), 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27,28-tetrahydroxycalix[4]arene (**1**) (2.00 eq, 11.5 g, 17.72 mmol), and DMF (1150 mL) were added to a 2000 mL, three-necked flask under nitrogen. The mixture was stirred for 1 h. A solution of triethylene glycol ditosylate (1.00 eq, 4.06 g, 8.86 mmol) in DMF (115 mL) was added to the flask over a 1 h period. The mixture was stirred for 48 h at 50 °C. The reaction was quenched by addition of H_2O (50 mL). The DMF was evaporated *in vacuo*. HCl (10%, 1000 mL) was added to the residue and the resulting solution was extracted with EtOAc (1200 mL). The turbid organic layer was separated and the solid was found to be unreacted 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27,28-tetrahydroxycalix[4]arene (**1**) (6.22 g). The

filtrate was evaporated *in vacuo* to give a residue. The residue was dissolved in CH_2Cl_2 and the resulting solution was dried over MgSO_4 . After filtration the CH_2Cl_2 was evaporated *in vacuo*. The crude product was chromatographed on silica gel with hexanes-EtOAc (2:1) as eluent to give 5.26 g (78%) of white solid. ^1H NMR (300 MHz, CDCl_3): δ 8.89 (s, 2H, OH), 7.06 (d, $J = 2.4$, 2H, ArH), 7.02 (d, $J = 2.1$, 2H, ArH), 6.98 (d, $J = 2.4$, 2H, ArH), 6.94 (d, $J = 2.4$, 2H, ArH), 4.66 (d, $J = 12.3$, 1H, ArCH_2Ar , *ax*), 4.29 (d, $J = 12.9$, 3H, ArCH_2Ar , *ax*), 4.26–4.14 (m, 6H, OCH_2), 4.14–3.96 (m, 4H, OCH_2), 3.96–3.84 (m, 2H, OCH_2), 3.36 (d, $J = 12.9$, 2H, ArCH_2Ar , *eq*), 3.35 (d, $J = 12.9$, 2H, ArCH_2Ar , *eq*), 1.21 (s, 18H, CH_3), 1.14 (s, 18H, CH_3).

Synthesis of Calixcrown 4: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxycalix[4]arene-crown-5 in the cone conformation was synthesized as the following. NaH (5.00 eq, 0.18 g, 7.7 mmol) and dry DMF (30 mL) were added into a 250-mL, three-necked flask under nitrogen. A solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27,28-tetrahydroxycalix[4]arene (**1**) (1.00 eq, 1.00 g, 1.54 mmol) in DMF (70 mL) was added to the flask dropwise. The mixture was stirred for 30 minutes. A solution of tetraethylene glycol di-*p*-toluenesulfonate (1.00 eq, 0.77 g, 1.54 mmol) in DMF (30 mL) was added dropwise into the flask. The mixture was stirred for 24 h at 70 °C. The reaction was quenched by addition of 2 N HCl (30 mL) at 0 °C. The DMF was evaporated *in vacuo*. EtOAc (150 mL) and H_2O (150 mL) were added to the residue. The organic layer was separated and washed with H_2O (2×100 mL). The precipitate was filtered and found to be unreacted 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27,28-tetrahydroxycalix[4]arene (**1**). The organic solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel with hexanes-EtOAc (3:2) as eluent to give 0.82 g (66%) of white solid with a melting point of 117–119 °C (lit.: 115–117 °C). IR: 3330 (br, O–H), 1270, 1122, 1058 (C–O) cm^{-1} . ^1H NMR: δ 8.15 (s, 2H, OH), 6.98 (d, $J = 2.3$, 2H, ArH), 6.93 (d, $J = 2.6$, 2H, ArH), 6.92 (s, 4H, ArH), 4.58–4.46 (m, 2H, OCH_2), 4.46 (d, $J = 13.1$, 2H, ArCH_2Ar , *ax*), 4.45 (d, $J = 13.18$, 1H, ArCH_2Ar , *ax*), 4.40 (d, $J = 12.3$, 1H, ArCH_2Ar , *ax*), 4.32–

4.20 (m, 2H, OCH₂), 4.72 (t, $J = 9.3$, 2H, OCH₂), 4.03-3.89 (m, 6H, OCH₂), 3.84-3.73 (m, 2H, OCH₂), 3.70 (dd, $J = 11.0$, 3.0, 2H, OCH₂), 3.31 (d, $J = 12.4$, 1H, ArCH₂Ar, *eq*), 3.30 (d, $J = 13.2$, 2H, ArCH₂Ar, *eq*), 3.26 (d, $J = 13.3$, 1H, ArCH₂Ar, *eq*), 1.16 (s, 18H, CH₃), 1.11 (s, 18H, CH₃). ¹³C NMR: δ 151.42, 149.20, 146.50, 142.00, 133.75, 133.59, 128.82, 128.65, 125.87, 125.67, 125.14, 124.73 (Ar), 75.64, 72.53, 70.76, 70.40 (OCH₂), 34.01, 33.78 (C(CH₃)), 32.15, 31.92 (ArCH₂Ar), 31.49, 31.27 (C(CH₃)), 30.45 (ArCH₂Ar). Anal. Calcd for C₅₂H₇₀O₇: C, 77.38; H, 8.74. Found: C, 77.02; H, 8.76.

Synthesis of Calixcrown 5: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-crown-6-calix[4]arene was synthesized as the following. In a two-necked, round-bottom flask, *p*-tert-butylcalix[4]arene (**1**) (4.00 g, 5.6 mmol) was suspended in dry DMF (500 mL) and NaH (1.33 g, 55.4 mmol) was added. The resulting homogeneous solution was stirred at room temperature for 30 minutes and a solution of pentaethylene glycol di-*p*-toluenesulfonate (2.13 g, 3.9 mmol) dissolved in dry DMF (100 mL) was added over a 2-hour period. The reaction mixture was then stirred at 70 °C for 24 hours. The reaction was quenched by addition of 2 N aqueous HCl (30 mL) and the solvent was evaporated *in vacuo*. The resulting solid was dissolved in CH₂Cl₂ (300 mL) and distilled water (200 mL) was added. After separation, the organic layer was washed with water (2 × 100 mL) and the solvent was evaporated *in vacuo* to afford a solid, which was purified by column chromatography on alumina with EtOAc-hexanes (2:3) as eluent to give 1.99 g (42%) of white solid with mp 202-205 °C: IR: 3340 (OH), 1122, 1052 (C-O) cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.07 (s, 18H), 1.18 (s, 18H), 3.27-3.31 (m, 4H), 3.66-4.20 (m, 18H), 4.26-4.29 (d, $J = 13$ Hz, 1H), 4.32-4.36 (m, 2H), 4.40 (d, $J = 13$ Hz, 2H), 4.46-4.49 (d, $J = 13$ Hz, 1H), 6.87-6.97 (m, 8H), 8.54 (s, 2H); ¹³C NMR (126 MHz, CDCl₃): δ 31.14, 31.24, 31.51, 31.72, 32.48, 33.79, 33.94, 70.66, 70.87, 70.93, 71.40, 74.77, 125.03, 125.07, 125.75, 125.80, 127.71, 128.57, 133.97, 133.61, 141.97, 146.09, 148.91, 151.76. Anal. Calcd. for C₅₄H₇₄O₈: C, 76.20; H, 8.76. Found: C, 76.54; H, 8.90.

Synthesis of Calixcrown 6: *p*-tert-Butylcalix[4]arene-1,2-crown-3 (**2**) (5.00 g, 6.95 mmol) in 50 mL of THF was added dropwise into a mixture of NaH (0.85 g, 35.4 mmol) in 50 mL of THF. After stirring for 2 h, ethyl bromoacetate (6.95 g, 41.7 mmol) was added and the reaction mixture was stirred overnight. The reaction was monitored by TLC. After 48 h, the reaction was quenched by careful addition of dilute HCl and evaporated *in vacuo*. The residue was dissolved in CH₂Cl₂, the solution was washed with dilute HCl and water, dried over MgSO₄, and the solvent was evaporated *in vacuo*. Chromatographic purification on silica gel with hexane-EtOAc (2:8) as eluent gave an oil (3.81 g, 61%). IR (deposit from CH₂Cl₂ solution on a NaCl plate) ν_{\max} /cm⁻¹ 1760 (C=O), 1253 and 1128 (C-O); ¹H NMR (CDCl₃): δ 1.04 (s, 18H, CH₃), 1.12 (s, 18H, CH₃), 1.34 (t, $J = 7.0$ Hz, 6H, OCH₂CH₃), 3.09 (d, $J = 12.0$ Hz, 1H, ArCH₂Ar), 3.18 (d, $J = 12.0$ Hz, 2H, ArCH₂Ar), 3.24 (d, $J = 13.0$ Hz, 1H,

ArCH₂Ar), 3.83-3.92 (m, 2H, OCH₂CH₂O), 4.07 (d, $J = 12.0$, 2H, OCH₂CH₂O), 4.20 (m, 2H, OCH₂CH₂O), 4.27 (q, $J = 7.0$, 4H, OCH₂CH₃), 4.42 (d, $J = 10.5$ Hz, 2H, OCH₂CH₂O), 4.54-4.65 (m, 3H, ArCH₂Ar, OCH₂Ar), 4.88 (d, $J = 15.5$ Hz, 2H, OCH₂CO), 4.96 (d, $J = 12.0$ Hz, 1H, ArCH₂Ar), 6.76-6.84 (m, 4H, ArH), 6.86 (d, $J = 2.5$ Hz, 2H, ArH), 6.92 (d, $J = 2.0$ Hz, 2H, ArH); ¹³C NMR (CDCl₃): δ 14.33, 31.02, 31.32, 31.42, 33.82, 33.88, 53.42, 60.62, 72.03, 73.04, 75.24, 124.35, 125.39, 125.55, 132.72, 134.03, 134.35, 134.81, 144.84, 145.34, 152.88, 152.93, 170.28. Anal. Calcd for C₅₆H₇₄O₉: C, 75.47; H, 8.37. Found: C, 75.22; H, 8.23%.

Synthesis of Calixcrown 7: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy] calix[4]-arene-crown-4 in the cone conformation was synthesized as the following. NaH (8.00 eq, 1.59 g, 66.15 mmol), 5,11,17,23-tetrakis(1,1-dimethyl-ethyl)-25,26-dihydroxycalix[4]-arene-crown-4 (**3**) (1.00 eq, 6.31 g, 8.27 mmol), ethyl bromoacetate (6.00 eq, 8.29 g (5.50 mL), 49.62 mmol), and THF (100 mL) were added to a flask under nitrogen and with a magnetic stirring. The mixture was stirred for 48 h. The reaction was quenched by addition of 10% HCl (22 mL) at 0 °C. The organic solvent was evaporated *in vacuo*. CH₂Cl₂ (200 mL) and H₂O (100 mL) were added to the residue. The separated organic layer was washed with H₂O (2 × 150 mL), dried over MgSO₄, and evaporated *in vacuo*. Methanol was added to the residue to give 5.43 g (70%) of white solid with a melting point of 101-103 °C. IR: 1759 (C=O), 1243, 1124, 1069 (C-O) cm⁻¹. ¹H NMR: δ 6.82-6.79 (m, 8H, ArH), 4.84 (d, $J = 16.2$, 2H, OCH₂C(O)), 4.79 (d, $J = 12.9$, 1H, ArCH₂Ar, *ax*), 4.73 (d, $J = 16.1$, 2H, OCH₂C(O)), 4.64 (d, $J = 12.7$, 3H, ArCH₂Ar, *ax*), 4.36-4.32 (m, 2H, OCH₂), 4.26 (dq, $J = 2.6$, 7.2, 4H, OCH₂CH₃), 4.08-4.02 (m, 4H, OCH₂), 3.98-3.93 (m, 2H, OCH₂), 3.88-3.85 (m, 2H, OCH₂), 3.77-3.74 (m, 2H, OCH₂), 3.21 (d, $J = 12.9$, 1H, ArCH₂Ar, *eq*), 3.17 (d, $J = 12.6$, 2H, ArCH₂Ar, *eq*), 3.12 (d, $J = 12.6$, 1H, ArCH₂Ar, *eq*), 1.32 (t, $J = 7.1$, 6H, OCH₂CH₃), 1.09 (s, 18H, C(CH₃)₃), 1.07 (s, 18H, C(CH₃)₃). ¹³C NMR: δ 170.55 (C=O), 153.23, 153.02, 145.06, 144.84, 134.29, 133.78, 133.65, 132.94, 125.42, 125.38, 125.15, 124.84 (Ar), 72.95 (OCH₂), 71.88 (OCH₂C(O)), 70.06 (OCH₂), 60.53 (OCH₂CH₃), 33.86, 33.82 (C(CH₃)₃), 31.43, 31.37 (C(CH₃)₃), 31.37, 31.15, 30.36 (ArCH₂Ar), 14.26 (OCH₂CH₃). Anal. Calcd for C₅₈H₇₈O₁₀: C, 74.49; H, 8.40. Found: C, 74.40; H, 8.29.

Synthesis of Calixcrown 8: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis[(ethoxycarbonyl)methoxy] calix[4]-arene-crown-5 in the cone conformation was synthesized as the following. NaH (8.00 eq, 2.18 g, 90.72 mmol), 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-dihydroxycalix[4]-arene-crown-5 (**4**) (1.00 eq, 9.15 g, 11.34 mmol), bromoethyl acetate (6.00 eq, 11.36 g (7.54 mL), 68.04 mmol), and THF (150 mL) were added to a flask under nitrogen and with a magnetic stirring. The mixture was stirred for 24 h. The reaction was quenched by addition of 10% HCl (30 mL) at 0 °C. The solvent was evaporated *in vacuo* and CH₂Cl₂ (200 mL) was added to the residue. The separated organic layer

was washed with H₂O (2 × 150 mL), dried over MgSO₄, and evaporated *in vacuo*. The residue was chromatographed on silica gel with hexanes-EtOAc (3:2) as eluent to give 9.32 g (84%) of white solid with a melting point of 212–215 °C. IR: 1762 (C=O), 1248, 1126, 1067 (C-O) cm⁻¹. ¹H NMR: δ 6.81 (d, *J* = 2.2, 2H, ArH), 6.80 (s, 6H, ArH), 4.99 (d, *J* = 12.7, 1H, ArCH₂Ar, *ax*), 4.88 (d, *J* = 16.4, 2H, OCH₂C(O)), 4.81 (d, *J* = 16.4, 2H, OCH₂C(O)), 4.59 (d, *J* = 12.7, 2H, ArCH₂Ar, *ax*), 4.44 (d, *J* = 12.6, 1H, ArCH₂Ar, *ax*), 4.21 (q, *J* = 7.2, 4H, OCH₂CH₃), 4.18–4.06 (m, 6H, OCH₂), 4.01–3.92 (m, 2H, OCH₂), 3.83–3.68 (m, 8H, OCH₂), 3.18 (d, *J* = 12.7, 1H, ArCH₂Ar, *eq*), 3.17 (d, *J* = 12.8, 2H, ArCH₂Ar, *eq*), 3.11 (d, *J* = 12.6, 1H, ArCH₂Ar, *eq*), 1.28 (t, *J* = 7.1, 6H, OCH₂CH₃), 1.08 (s, 18H, C(CH₃)₃), 1.07 (s, 18H, C(CH₃)₃). ¹³C NMR: δ 170.74 (C=O), 153.31, 153.20, 144.85, 144.76, 133.98, 133.67, 133.51, 133.35, 125.27, 125.23, 125.05 (Ar), 73.49 (OCH₂), 71.62 (OCH₂C(O)), 70.96, 70.46, 70.39 (OCH₂), 60.28 (OCH₂CH₃), 33.82, 33.80 (C(CH₃)₃), 31.52 (ArCH₂Ar), 31.41, 31.38 (C(CH₃)₃), 31.29, 30.66 (ArCH₂Ar), 14.22 (OCH₂CH₃). Anal. Calcd for C₆₀H₈₂O₁₁: C, 73.59; H, 8.44. Found: C, 73.99; H, 8.23.

Synthesis of Calixcrown 9: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis((ethoxycarbonyl)methoxy)-27,28-crown-6-calix[4]arene was synthesized as the following. To a solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-calix[4]arene-crown-6 (**5**) (3.80 g, 4.5 mmol) in THF (50 mL) was added NaH (0.83 g, 35.6 mmol) and BrCH₂CO₂Et (2.90 mL, 26.7 mmol) under nitrogen. The reaction mixture was stirred at room temperature for 24 hours and then quenched with 10% aqueous HCl (20 mL). The solvent was evaporated *in vacuo* and CH₂Cl₂ (50 mL) was added to the residue. The organic layer was washed with distilled water (2 × 30 mL) and dried over anhydrous MgSO₄. The solvent was evaporated *in vacuo* to give 4.19 g (92%) of white solid with mp 92–94 °C. IR: 1750 (C=O), 1160, 1022 (C-O) cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 1.07 (s, 18H), 1.08 (s, 18H), 1.30 (t, *J* = 7 Hz, 6H), 3.10–3.22 (m, 4H), 3.66–3.79 (m, 12H), 3.98–4.14 (m, 8H), 4.23 (t, *J* = 7 Hz, 4H), 4.50 (d, *J* = 12.5 Hz, 1H), 4.62 (d, *J* = 13 Hz, 2H), 4.70–4.84 (m, 5H), 6.79 (s, 8H). ¹³C NMR (126 MHz, CDCl₃): δ 14.20, 30.87, 31.17, 31.31, 31.36, 33.76, 33.78, 60.43, 70.05, 70.54, 70.67, 70.75, 71.57, 72.98, 124.96, 125.27, 125.32, 133.19, 133.46, 133.68, 134.03, 144.78, 145.05, 152.94, 153.16, 170.43. Anal. Calcd. for C₆₂H₈₆O₁₂: C, 72.77; H, 8.47; Found: C, 72.54; H, 8.71.

Synthesis of Calixcrown 10: There were no peaks between 35–40 ppm in the ¹³C NMR spectra for compound **10** revealing that all four benzene rings have *syn*-arrangements. In the ¹H NMR spectra for this compound, the bridging methylene protons are split into three pairs of doublets with an integration ratio of 1:2:1. *p*-*tert*-butylcalix[4]arene-1,2-crown-3 diester (**6**) (3.00 g, 3.05 mmol) in 60 mL of THF and 60 mL of 10% Me₄NOH was refluxed overnight. The solvent was evaporated *in vacuo* and the residue was dissolved in 100 mL of CH₂Cl₂. The organic layer was washed with 1 N HCl solution until pH 1, and then washed with 60 mL of brine and 60 mL of water, dried over MgSO₄,

and evaporated *in vacuo* to give a white solid (2.49 g, 88%) with mp 255–256 °C. IR (deposit from CH₂Cl₂ solution on a NaCl plate) ν_{\max} /cm⁻¹ 3217 (O-H), 1761 (C=O), 1203 and 1121 (C-O); ¹H NMR (CDCl₃): δ 1.07 (s, 18H, CH₃), 1.11 (s, 18H, CH₃), 3.12 (d, *J* = 12.0 Hz, 1H, ArCH₂Ar), 3.22–3.36 (m, 3H, ArCH₂Ar), 3.81–3.92 (m, 2H, OCH₂CH₂O), 4.11 (d, *J* = 12.5 Hz, 2H, OCH₂CH₂O), 4.20 (t, *J* = 11.0 Hz, 2H, OCH₂CH₂O), 4.25–4.38 (m, 4H, OCH₂CH₂O, ArCH₂Ar), 4.49 (d, *J* = 13.0 Hz, 1H, ArCH₂Ar), 4.58 (d, *J* = 16.5 Hz, 2H, OCH₂CO), 4.79 (d, *J* = 16.5 Hz, 2H, OCH₂CO), 5.19 (d, *J* = 12.5 Hz, 1H, ArCH₂Ar), 6.83–6.91 (m, 4H, ArH), 6.93 (d, *J* = 2.0 Hz, 2H, ArH), 6.99 (d, *J* = 2.5 Hz, 2H, ArH); ¹³C NMR (CDCl₃): δ 30.30, 30.60, 30.80, 31.24, 31.34, 33.90, 33.98, 53.41, 71.62, 73.63, 124.49, 125.47, 126.11, 126.19, 133.12, 133.25, 133.54, 134.94, 145.45, 146.80, 151.23, 152.71, 171.56. Anal. Calcd for C₅₂H₆₆O₉: C, 74.79; H, 7.97. Found: C, 74.50; H, 7.95%.

Synthesis of Calixcrown 11: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)calix[4]arene crown-4 in the cone conformation was synthesized as the following. A solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis((ethoxycarbonyl)methoxy)calix[4]arene-crown-4 (**7**) (5.43 g, 5.81 mmol) in THF (100 mL) was mixed with 10% aq tetramethylammonium hydroxide (100 mL) and the mixture was refluxed for 24 h. After cooling to room temperature, 6 N HCl (50 mL) was added and the mixture was stirred for 1 h. The THF was evaporated *in vacuo*. The white precipitate in resulting aqueous solution was filtered and dissolved in CH₂Cl₂ (150 mL). The aqueous solution was extracted with CH₂Cl₂ (100 mL). The combined organic CH₂Cl₂ solutions were dried over MgSO₄. The solvent was evaporated to give 4.87 g (95%) of white solid with a melting point of 189–191 °C. IR: 3300–2700 (br, CO₂H), 1748 (C=O), 1265, 1124, 1055 (C-O) cm⁻¹. ¹H NMR: δ 8.51 (br, s, 2H, CO₂H), 6.91 (s, 4H, ArH), 6.85 (d, *J* = 2.0, 2H, ArH), 6.82 (d, *J* = 2.1, 2H, ArH), 5.20 (d, *J* = 12.6, 1H, ArCH₂Ar, *ax*), 4.66 (d, *J* = 15.7, 2H, OCH₂C(O)), 4.57 (d, *J* = 6.5, 2H, OCH₂), 4.53 (d, *J* = 15.7, 2H, OCH₂C(O)), 4.40 (d, *J* = 13.1, 1H, ArCH₂Ar, *ax*), 4.23 (d, *J* = 12.7, 2H, ArCH₂Ar, *ax*), 4.14–4.04 (m, 2H, OCH₂), 3.88–3.59 (m, 8H, OCH₂), 3.26 (d, *J* = 12.7, 3H, ArCH₂Ar, *eq*), 3.11 (d, *J* = 12.4, 1H, ArCH₂Ar, *eq*), 1.09 (s, 18H, C(CH₃)₃), 1.08 (s, 18H, C(CH₃)₃). ¹³C NMR: δ 171.27 (C=O), 152.27, 151.10, 146.62, 145.31, 135.18, 133.64, 133.10, 132.89, 125.80, 125.67, 125.46, 125.14 (Ar), 74.90 (OCH₂), 71.58 (OCH₂C(O)), 70.17, 69.73 (OCH₂), 33.97, 33.87 (C(CH₃)₃), 31.38 (C(CH₃)₃), 31.27 (C(CH₃)₃, ArCH₂Ar), 30.94, 29.53 (ArCH₂Ar). Anal. Calcd for C₅₄H₇₀O₁₀: C, 73.78; H, 8.02. Found: C, 73.87; H, 8.20.

Synthesis of Calixcrown 12: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)calix[4]arene crown-5 in the cone conformation was synthesized as the following. A solution of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis((ethoxycarbonyl)methoxy)calix[4]arene-crown-5 (**8**) (9.23 g, 9.42 mmol) in THF (150 mL) was mixed with 10% aq tetramethylammonium hydroxide (150 mL) and refluxed for 24 h. After cooling to room temperature, 6 N HCl (60

mL) was added to the flask and the mixture was stirred for 1 h. The THF was evaporated *in vacuo*. The white precipitate in resulting aqueous solution was filtered and dissolved in CH_2Cl_2 (150 mL). The aqueous solution was extracted with CH_2Cl_2 (100 mL). The combined organic CH_2Cl_2 solutions were dried over MgSO_4 . The solvent was evaporated *in vacuo* to give 8.18 g (94%) of white solid with a melting point of 262–266 °C. IR: 3363 (br, CO_2H), 1738 ($\text{C}=\text{O}$), 1263, 1091, 1060 ($\text{C}-\text{O}$) cm^{-1} . ^1H NMR: δ 8.03 (br, s, 2H, CO_2H), 6.90 (d, $J = 2.2$, 2H, ArH), 6.88 (d, $J = 2.1$, 2H, ArH), 6.85 (d, $J = 2.2$, 2H, ArH), 6.83 (d, $J = 2.2$, 2H, ArH), 4.60 (d, $J = 12.6$, 1H, ArCH_2Ar , *ax*), 4.57 (s, 4H, $\text{OCH}_2\text{C}(\text{O})$), 4.39 (d, $J = 12.8$, 1H, ArCH_2Ar , *ax*), 4.24 (d, $J = 12.6$, 2H, ArCH_2Ar , *ax*), 4.22–4.05 (m, 4H, OCH_2), 4.02–3.86 (m, 6H, OCH_2), 3.86–3.76 (m, 2H, OCH_2), 3.76–3.55 (m, 4H, OCH_2), 3.25 (d, $J = 12.9$, 1H, ArCH_2Ar , *eq*), 3.24 (d, $J = 12.7$, 2H, ArCH_2Ar , *eq*), 3.16 (d, $J = 12.6$, 1H, ArCH_2Ar , *eq*), 1.08 (s, 36H, CH_3). ^{13}C NMR: 171.25 ($\text{C}=\text{O}$), 152.19, 150.93, 146.64, 145.41, 134.39, 133.57, 133.31, 133.06, 125.73, 125.60, 125.40, 125.14 (Ar), 74.94 (OCH_2), 71.56 ($\text{OCH}_2\text{C}(\text{O})$), 70.86, 70.63, 69.86 (OCH_2), 33.96, 33.87 ($\text{C}(\text{CH}_3)$), 31.35, 31.26 ($\text{C}(\text{CH}_3)$), 30.92, 30.85, 30.48 (ArCH_2Ar). Anal. Calcd for $\text{C}_{56}\text{H}_{74}\text{O}_{11}$: C, 72.86; H, 8.08. Found: C, 73.20; H, 7.80.

Synthesis of Calixcrown 13: 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)-27,28-crown-6-calix[4]arene in the cone conformation was synthesized as the following. Diester 29 (4.00 g, 3.9 mmol) in THF (60 mL) was added to 10% aqueous tetramethylammonium hydroxide (60 mL) and the solution was refluxed for 24 hours. After cooling to room temperature, the reaction mixture was acidified with 6 N aqueous HCl (30 mL) and stirred for one hour. The resulting precipitate was filtered and then dissolved in CH_2Cl_2 (50 mL). The water layer was extracted with CH_2Cl_2 (2 \times 30 mL). The combined CH_2Cl_2 solutions were dried over anhydrous MgSO_4 and the solvent was evaporated *in vacuo* to give 3.67 g (97%) of white solid: mp 238–243 °C; IR: 3416 (CO_2H), 1643 ($\text{C}=\text{O}$), 1124, 1057 ($\text{C}-\text{O}$) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ 1.08 (s, 36H), 3.15–3.26 (m, 4H), 3.64–3.96 (m, 16H), 4.10–4.31 (m, 6H), 4.45–4.65 (m, 6H), 6.82–6.90 (m, 8H), 9.82 (br s, 2H). ^{13}C NMR (126 MHz, CDCl_3): δ 30.71, 30.77, 31.09, 31.25, 31.34, 33.85, 33.93, 69.58, 70.56, 70.76, 70.92, 71.55, 74.52, 124.98, 125.44, 125.57, 125.69, 133.21, 133.30, 133.53, 134.23, 145.35, 146.52, 151.10, 152.30, 171.38. Anal. Calcd. for $\text{C}_{58}\text{H}_{78}\text{O}_{12}$: C, 72.02; H, 8.13; Found: C, 72.13; H, 8.37.

Preparation of Diacid Calixcrowns 23–26.

Synthesis of Calixcrown 14: *p*-tert-Butylcalix[4]arene (1) (10.00 g, 13.5 mmol), toluene (100 mL) and phenol (1.75 g, 18.60 mmol) were added to a flask and the solution was stirred under argon for 10 min. With vigorous mechanical stirring, aluminum trichloride (10.00 g, 75.0 mmol) was added. The mixture was stirred at room temperature for 5 h. The mixture was poured into a 500-mL beaker containing crashed ice (200 g) and extracted with CH_2Cl_2 (400 mL). The organic layer was washed with 1 N HCl (3 \times 100 mL)

and water (2 \times 100 mL), and dried over NaSO_4 . The solvent was evaporated *in vacuo*. Diethyl ether (50 mL) was added to the oily orange residue and the heterogeneous mixture was kept at -15 °C for 1 h. The precipitated solid was filtered and triturated with diethyl ether (100 mL). The mixture was kept at -15 °C for 1 h and filtered to provide 5.54 g (90%) of light yellow powder: mp 314–317 °C (lit 315–318 °C). IR (deposit on NaCl plate from CH_2Cl_2 solution): 3136 (OH) cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ 3.54 (br s, 4H), 4.24 (br s, 4H), 6.73 (t, 4H, $J = 7.6$ Hz), 7.04 (d, 8H, $J = 7.6$ Hz), 10.20 (s, 4H).

Synthesis of Calixcrown 15: To a mixture of calix[4]-arene 14 (6.00 g, 10 mmol), diethylene glycol (1.59 g, 15 mmol) and TPP (8.00 g, 30 mmol) in 200 mL of toluene, a 40% solution of DEAD (5.22 g, 30 mmol) in toluene was added dropwise. The mixture was stirred at room temperature for 1 h. Then the solution was evaporated to dryness and the residue was extracted with hexane (3 \times 30 mL) followed by evaporation and subsequent stirring in hexane and ethyl acetate. The precipitate was filtered and the filtrate was purified by chromatography on silica gel with hexane-EtOAc (9:1) as eluent to give a white solid (2.70 g, 42%) with mp 119–121 °C. IR (deposit from CH_2Cl_2 solution on a NaCl plate) $\nu_{\text{max}}/\text{cm}^{-1}$ 3340 (O-H), 1248 and 1125 ($\text{C}-\text{O}$); ^1H NMR (CDCl_3): δ 3.22–3.48 (m, 4H, ArCH_2Ar), 4.04 (t, $J = 10.5$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{O}$), 4.10 (t, $J = 11.0$ Hz, 2H, $\text{OCH}_2\text{CH}_2\text{O}$), 4.32–4.48 (m, 7H, $\text{OCH}_2\text{CH}_2\text{O}$, ArCH_2Ar), 4.80 (d, $J = 12.0$ Hz, 1H, ArCH_2Ar), 6.96–7.10 (m, 10H, ArH), 7.16 (d, $J = 2.0$ Hz, 2H, ArH), 8.86 (s, 2H, OH); ^{13}C NMR (CDCl_3): δ 33.92, 34.16, 75.30, 125.33, 125.57, 125.61, 126.44, 128.34, 128.82, 129.12, 133.86, 134.60, 142.80, 147.40, 149.16, 150.32. Anal. Calcd for $\text{C}_{32}\text{H}_{30}\text{O}_5$: C, 54.18; H, 4.29. Found: C, 54.06; H, 4.21%.

Synthesis of Calixcrown 16: 25,26-Dihydroxycalix[4]-arene-crown-4 was synthesized as the following. To a mixture of NaH (5.00 eq, 1.80 g, 75 mmol) in DMF (1300 mL) in a 2000 mL, three-necked flask under nitrogen was added dropwise a solution of 25,26,27,28-tetrahydroxycalix[4]arene (14) (1.00 eq, 6.36 g, 15 mmol) in DMF (100 mL). The mixture was stirred for 30 min. A solution of triethylene glycol di-*p*-toluenesulfonate (1.05 eq, 7.22 g, 15.75 mmol) in DMF (100 mL) was added dropwise and the mixture was stirred for 10 h at 70 °C. The reaction was quenched by addition of 1 N HCl (50 mL) at 0 °C. The DMF was removed by mixing with 3 N HCl and CH_2Cl_2 (volume ratio is 1:1:1). The remaining DMF in the organic layer was evaporated under high vacuum. The residue was dissolved in CH_2Cl_2 (350 mL). The resulting organic solution was dried over MgSO_4 . The crude product was chromatographed on silica gel with hexanes-EtOAc (2:1) as eluent to obtain 4.28 g (53%) of white solid with a melting point of 225–227 °C (lit.: 226–228 °C).¹⁰ IR: 3318 (br, O-H), 1259, 1150, 1055 ($\text{C}-\text{O}$) cm^{-1} . ^1H NMR: δ 8.89 (s, 2H, OH), 7.11 (dd, $J = 7.5$, 1.5, 2H, ArH), 7.05–6.90 (m, 8H, ArH), 6.81 (t, $J = 7.57$, 2H, ArH), 6.64 (t, $J = 7.4$, 2H, ArH), 4.71 (d, $J = 12.3$, 1H, ArCH_2Ar , *ax*), 4.38–4.22 (m, 9H (ArCH_2Ar , *ax* (3H) and OCH_2 (6H))), 4.17–4.10 (m, 2H, OCH_2), 4.08–4.01 (m, 2H,

OCH₂), 3.96-3.90 (m, 2H, OCH₂), 3.42 (d, J = 12.33, 1H, ArCH₂Ar, *eq*), 3.41 (d, J = 13.1, 2H, ArCH₂Ar, *eq*), 3.38 (d, J = 13.6, 1H, ArCH₂Ar, *eq*). ¹³C NMR: δ 153.45, 151.14, 134.92, 133.97, 129.21, 129.15, 129.00, 128.85, 128.82, 128.06, 124.99, 120.65 (Ar), 75.67, 71.59, 69.83 (OCH₂), 31.95, 31.78, 29.44 (ArCH₂Ar).

Synthesis of Calixcrown 17: 25,26-Dihydroxycalix[4]-arene-crown-5 was synthesized as the following. To a mixture of NaH (5.00 eq, 2.16 g, 90.0 mmol) and DMF (1300 mL) in a 2000 mL, three-necked flask under nitrogen was added a solution of 25,26,27,28-tetrahydroxycalix[4]-arene (**14**) (1.00 eq, 7.64 g, 18.0 mmol) in DMF (100 mL) over a 1 h period. The mixture was stirred for an additional hour. Tetraethylene glycol dimesylate (2.20 eq, 13.88 g, 39.6 mmol) in DMF (100 mL) was added over a 1-h period. The mixture was stirred at 50 °C for 72 h. The reaction was quenched by addition of H₂O (50 mL) at 0 °C. The DMF was removed by mixing the reaction mixture with 3 N HCl and CH₂Cl₂ (volume ratio is 1:1:1). The remaining DMF in the organic layer was evaporated under high vacuum. Addition of MeOH to the residue generated 5.87 g (56%) of white precipitate with a melting point of 215-217 °C (literature: 216-218 °C).⁷ IR: 3317 (br, OH), 1262, 1128, 1047 (C-O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 8.34 (s, 2H, OH), 7.13-6.87 (m, 8H, ArH), 6.80 (t, J = 7.5, 2H, ArH), 6.60 (t, J = 7.5, 2H, ArH), 4.62-4.41 (m, 6H (ArCH₂Ar, *ax* (4H) and OCH₂ (2H)), 4.41-4.28 (m, 2H, OCH₂), 4.11 (t, J = 9.0, 2H, OCH₂), 4.06-3.88 (m, 6H, OCH₂), 3.87-3.65 (m, 4H, OCH₂), 3.39 (d, J = 12.3, 1H, ArCH₂Ar, *eq*), 3.36 (d, J = 13.5, 2H, ArCH₂Ar, *eq*), 3.32 (d, J = 13.8, 1H, ArCH₂Ar, *eq*).

Synthesis of Calixcrown 18: 25,26-Dihydroxycalix[4]-arene-crown-6 was synthesized as the following. To a mixture of NaH (5.00 eq, 1.58 g, 65.85 mmol) and DMF (1067 mL) in a 2000 mL, three-necked flask under nitrogen was added a solution of 25,26,27,28-tetrahydroxycalix[4]-arene (**14**) (1.00 eq, 5.59 g, 13.17 mmol) in DMF (150 mL) over a 40 min period. The mixture was stirred for 1 h. A solution of pentaethylene glycol di-*p*-toluenesulfonate (2.50 eq, 18.00 g, 32.93 mmol) in DMF (100 mL) was added over a 1 h period. The mixture was stirred overnight at 50-55 °C. The reaction was quenched by addition of H₂O (30 mL). The DMF was removed by mixing the reaction mixture with 3 N HCl and CH₂Cl₂ (volume ratio is 1:1:1). The remaining DMF in the organic layer was evaporated under high vacuum. The residue was chromatographed on silica gel with CH₂Cl₂-acetone (19:1) as eluent to obtain a solid. EtOAc was added to the solid to get 5.18 g (63%) of white precipitate with a melting point of 182-184 °C (literature: 180-182 °C).⁷ IR: 3317 (br, O-H), 1264, 1124, 1050 (C-O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 8.68 (s, 2H, OH), 7.06-6.88 (m, 8H, ArH), 6.76 (t, J = 7.5, 2H, ArH), 6.60 (t, J = 7.5, 2H, ArH), 4.55 (d, J = 12.6, 1H, ArCH₂Ar, *ax*), 4.45 (d, J = 12.9, 2H, ArCH₂Ar, *ax*), 4.44-4.36 (m, 2H, OCH₂), 4.33 (d, J = 13.5, 1H, ArCH₂Ar, *ax*), 4.25-4.14 (m, 2H, OCH₂), 4.13-3.97 (m, 4H, OCH₂), 3.96-3.74 (m, 10H, OCH₂), 3.74-3.61 (m, 2H, OCH₂), 3.66 (d, J = 12.6, 1H, ArCH₂Ar, *eq*), 3.35 (d, J =

13.2, 3H, ArCH₂Ar, *eq*).

Synthesis of Calixcrown 19: Calix[4]arene-1,2-crown-3 (**15**) (4.58 g, 7 mmol) in 50 mL of THF was added dropwise into a mixture of NaH (0.85 g, 35.4 mmol) in 50 mL of THF. After stirring for 1 h, ethyl bromoacetate (6.95 g, 41.7 mmol) was added and the reaction mixture was stirred overnight. The reaction was monitored by TLC. After 48 h, the reaction was quenched by careful addition of dilute HCl and evaporated *in vacuo*. The residue was dissolved in CH₂Cl₂, the solution was washed with dilute HCl and water, dried over MgSO₄, and the solvent was evaporated *in vacuo*. Chromatographic purification on silica gel with hexane-EtOAc (2:8) as eluent gave an oil (1.82 g, 42%). IR (deposit from CH₂Cl₂ solution on a NaCl plate) ν_{\max} /cm⁻¹ 1758 (C=O), 1250 and 1126 (C-O); ¹H NMR (CDCl₃): δ 1.34 (t, J = 7.0 Hz, 6H, OCH₂CH₃), 3.09 (d, J = 12.0 Hz, 1H, ArCH₂Ar), 3.18 (d, J = 12.0 Hz, 2H, ArCH₂Ar), 3.24 (d, J = 13.0 Hz, 1H, ArCH₂Ar), 3.83-3.92 (m, 2H, OCH₂CH₂O), 4.07 (d, J = 12.2, 2H, OCH₂CH₂O), 4.22 (m, 2H, OCH₂CH₂O), 4.27 (q, J = 7.0, 4H, OCH₂CH₃), 4.42 (d, J = 10.5 Hz, 2H, OCH₂CH₂O), 4.51-4.63 (m, 3H, ArCH₂Ar, OCH₂Ar), 4.88 (d, J = 15.5 Hz, 2H, OCH₂CO), 4.98 (d, J = 12.0 Hz, 1H, ArCH₂Ar), 6.78-6.88 (m, 8H, ArH), 6.84 (d, J = 2.5 Hz, 2H, ArH), 6.92 (d, J = 2.0 Hz, 2H, ArH); ¹³C NMR (CDCl₃): δ 14.08, 33.80, 33.86, 53.44, 60.60, 72.02, 73.02, 75.22, 124.36, 125.38, 125.54, 132.74, 134.04, 134.36, 134.80, 144.86, 145.32, 152.86, 152.92, 170.26. Anal. Calcd for C₄₀H₄₂O₉: C, 53.47; H, 4.76. Found: C, 53.20; H, 4.43%.

Synthesis of Calixcrown 20: 25,26-Bis[(ethoxycarbonyl)-methoxy]calix[4]arene-crown-4 in the cone conformation was synthesized as the following. A mixture of NaH (10.00 eq, 2.01 g, 83.92 mmol) and 20 mL of THF-DMF (9:1) in a 250-mL, three-necked flask under nitrogen was stirred for 30 min. A solution of 25,26-dihydroxycalix[4]arene-crown-4 (**16**) (1.00 eq, 4.52 g, 8.39 mmol) in 100 mL of THF-DMF (9:1) was added dropwise. The mixture was stirred for 1 h. Ethyl bromoacetate (8.00 eq, 11.21 g, 7.44 mL, 67.13 mmol) in 10 mL of THF-DMF (9:1) was added to the flask over a 1-h period. The mixture was refluxed for 48 h. The reaction was quenched by addition of 1 N HCl (20 mL) at 0 °C. The organic solvent was evaporated *in vacuo*. The residual aqueous layer was extracted with CH₂Cl₂ (200 mL). The organic solution was washed with H₂O (2 × 150 mL) and then dried over MgSO₄. The solvent was evaporated *in vacuo* to give a solid. The solid was chromatographed on silica gel with hexanes-EtOAc (1:1) as eluent to obtain 5.25 g (88%) of white solid with a melting point of 126-128 °C. IR: 1757 (C=O), 1240, 1094, 1024 (C-O) cm⁻¹. ¹H NMR: δ 6.90-6.30 (m, 12H, ArH), 4.97 (d, J = 13.1, 1H, ArCH₂Ar, *ax*), 4.76 (d, J = 16.2, 2H, OCH₂C(O)), 4.73 (d, J = 15.6, 1H, ArCH₂Ar, *ax*), 4.69 (d, J = 16.2, 2H, OCH₂C(O)), 4.64 (d, J = 13.4, 2H, ArCH₂Ar, *ax*), 4.35-4.19 (m, 6H, OCH₂), 4.19-4.10 (m, 2H, OCH₂), 3.94-3.77 (m, 6H, OCH₂), 3.77-3.67 (m, 2H, OCH₂), 3.24 (d, J = 12.8, 1H, ArCH₂Ar, *eq*), 3.22 (d, J = 13.2, 2H, ArCH₂Ar, *eq*), 3.13-3.11 (d, J = 12.9, 1H, ArCH₂Ar, *eq*), 1.30 (t, J = 7.1, 6H, CH₃). ¹³C NMR: δ 170.10 (C=O), 156.11, 155.61, 135.78, 134.81, 134.54, 134.23,

128.54, 128.49, 128.32, 128.13, 122.79, 122.34 (Ar), 73.49 (OCH₂), 71.14 (OCH₂C(O)), 70.53, 70.16 (OCH₂), 60.53 (OCH₂CH₃), 31.28, 31.15, 29.84 (ArCH₂Ar), 14.22 (CH₃). Anal. Calcd for C₄₂H₄₆O₁₀: C, 70.97; H, 6.52. Found: C, 70.86; H, 6.76.

Synthesis of Calixcrown 21: 25,26-Bis[(ethoxycarbonyl)-methoxy]calix[4]arene-crown-5 in the cone conformation was synthesized as the following. To a stirred mixture of NaH (10.00 eq, 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-dihydroxycalix[4]arene-crown-5 (**17**) (1.00 eq, 4.95 g, 8.50 mmol) in DMF (100 mL). The mixture was stirred for 1 h. A solution of ethyl bromoacetate (8.00 eq, 11.36 g, 7.54 mL, 68 mmol) in DMF (10 mL) was added over a 1 h period. The mixture was stirred for 60 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*. CH₂Cl₂ (100 mL) was added to the residue. The resulting organic solution was washed with H₂O (2 × 100 mL) and dried over MgSO₄. 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 slightly 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* = 13.43, 1H, ArCH₂Ar, *ax*), 4.75 (s, 4H, OCH₂C(O)), 4.61 (d, *J* = 13.6, 2H, ArCH₂Ar, *ax*), 4.58 (d, *J* = 15.2, 1H, ArCH₂Ar, *ax*), 4.22 (q, *J* = 7.1, 4H, OCH₂CH₃), 4.30–4.10 (m, 2H, OCH₂), 4.09–3.92 (m, 6H, OCH₂), 3.80–3.59 (m, 8H, OCH₂), 3.23 (d, *J* = 13.4, 1H, ArCH₂Ar, *eq*), 3.22 (d, *J* = 13.5, 2H, ArCH₂Ar, *eq*), 3.14 (d, *J* = 13.4, 1H, ArCH₂Ar, *eq*), 1.29 (t, *J* = 7.2, 6H, CH₃). ¹³C NMR: δ 170.13 (C=O), 156.24, 155.65, 135.34, 134.67, 134.64, 128.45, 128.42, 128.32, 128.21, 122.70, 122.34 (Ar), 73.50 (OCH₂), 71.31 (OCH₂C(O)), 71.15, 70.56, 70.27 (OCH₂), 60.51 (OCH₂CH₃), 31.25, 31.22, 30.60 (ArCH₂Ar), 14.20 (CH₃). Anal. Calcd. for C₄₄H₅₀O₁₁·0.3CH₂Cl₂: C, 69.37; H, 6.65. Found: C, 69.22; H, 6.77.

Synthesis of Calixcrown 22: 25,26-Bis[(ethoxycarbonyl)-methoxy]calix[4]arene-crown-6 in the cone conformation was synthesized as the following. A stirred mixture of NaH (10.00 eq, 0.65 g, 27.1 mmol), 25,26-dihydroxycalix[4]arene-crown-6 (**18**) (1.00 eq, 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 eq, 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 CH₂Cl₂ (100 mL). The organic layer was separated, washed with H₂O (100 mL), and dried over MgSO₄. The CH₂Cl₂ 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 slightly 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* = 13.43, 1H, ArCH₂Ar, *ax*), 4.74 (d, *J* = 16.2, 2H, OCH₂C(O)), 4.68 (d, *J* = 17.1, 2H,

OCH₂C(O)), 4.65 (d, *J* = 13.7, 2H, ArCH₂Ar, *ax*), 4.60 (d, *J* = 13.43, 1H, ArCH₂Ar, *ax*), 4.22 (q, *J* = 7.1, 4H, OCH₂CH₃), 4.18–4.07 (m, 4H, OCH₂), 4.07–3.98 (m, 2H, OCH₂), 3.96–3.85 (m, 2H, OCH₂), 3.79–3.60 (m, 12H, OCH₂), 3.24 (d, *J* = 13.7, 1H, ArCH₂Ar, *eq*), 3.19 (d, *J* = 13.6, 2H, ArCH₂Ar, *eq*), 3.15 (d, *J* = 13.4, 1H, ArCH₂Ar, *eq*), 1.295 (t, *J* = 7.1, 6H, CH₃). ¹³C NMR: δ 170.00 (C=O), 156.30, 155.58, 135.24, 134.82, 134.81, 134.42, 128.48, 128.44, 128.26, 128.12, 122.75, 122.28 (Ar), 73.18 (OCH₂), 71.15 (OCH₂C(O)), 70.89, 70.87, 70.51, 70.26 (OCH₂), 60.53 (OCH₂CH₃), 31.36, 31.04, 30.81 (ArCH₂Ar), 14.22 (CH₃). Anal. Calcd. for C₄₆H₅₄O₁₂: C, 69.16; H, 6.81. Found: C, 68.83; H, 7.05.

Synthesis of Calixcrown 23: Calix[4]arene-1,2-crown-3 diester (**19**) (2.60 g, 3.05 mmol) in 60 mL of THF and 60 mL of 10% Me₄NOH was refluxed overnight. The solvent was evaporated *in vacuo* and the residue was dissolved in 100 mL of CH₂Cl₂. The organic layer was washed with 1 N HCl solution until pH 1, and then washed with 60 mL of brine and 60 mL of water, dried over MgSO₄, and evaporated *in vacuo* to give a white solid (2.12 g, 91%) with mp 196–200 °C. IR (deposit from CH₂Cl₂ solution on a NaCl plate) ν_{max}/cm⁻¹ 3212 (O-H), 1760 (C=O), 1204 (C-O); ¹H NMR (CDCl₃): δ 3.14 (d, *J* = 12.0 Hz, 1H, ArCH₂Ar), 3.20–3.38 (m, 3H, ArCH₂Ar), 3.80–3.94 (m, 2H, OCH₂CH₂O), 4.12 (d, *J* = 12.5 Hz, 2H, OCH₂CH₂O), 4.22 (t, *J* = 11.0 Hz, 2H, OCH₂CH₂O), 4.22–4.36 (m, 4H, OCH₂CH₂O, ArCH₂Ar), 4.46 (d, *J* = 13.0 Hz, 1H, ArCH₂Ar), 4.56 (d, *J* = 16.5 Hz, 2H, OCH₂CO), 4.78 (d, *J* = 16.5 Hz, 2H, OCH₂CO), 5.18 (d, *J* = 12.5 Hz, 1H, ArCH₂Ar), 6.803–6.92 (m, 8H, ArH), 6.92 (d, *J* = 2.0 Hz, 2H, ArH), 6.98 (d, *J* = 2.5 Hz, 2H, ArH); ¹³C NMR (CDCl₃): δ 31.32, 33.92, 33.96, 53.40, 71.60, 73.64, 124.50, 125.48, 126.10, 126.18, 133.14, 133.23, 133.53, 134.96, 145.46, 146.82, 151.22, 152.74, 171.54. Anal. Calcd for C₃₆H₃₄O₉: C, 51.79; H, 4.10. Found: C, 51.52; H, 4.15%.

Synthesis of Calixcrown 24: 25,26-Bis(carboxymethoxy)calix[4]arene-crown-4 in the cone conformation was synthesized as the following. A solution of 25,26-bis[(ethoxycarbonyl)methoxy]calix[4]arene-crown-4 (**20**) (5.23 g, 7.36 mmol) in THF (65 mL) was mixed with 10% aq tetramethylammonium hydroxide (65 mL) and the solution was refluxed for 24 h. After cooling to room temperature, the reaction was quenched by addition of 6 N HCl (35 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 CH₂Cl₂ (100 mL). The aqueous filtrate was extracted with CH₂Cl₂ (2 × 50 mL). The combined CH₂Cl₂ solutions were dried over MgSO₄ and evaporated *in vacuo* to provide 4.72 g (98%) of white solid with a melting point of 178–180 °C. IR: 3400–2700 (br, CO₂H), 1750 (C=O), 1266, 1098, 1055 (C-O) cm⁻¹. ¹H NMR: δ 10.13 (br, s, 2H, CO₂H), 6.96–6.53 (m, 12H, ArH), 5.23 (d, *J* = 12.9, 1H, ArCH₂Ar, *ax*), 4.85 (d, *J* = 16.1, 2H, OCH₂C(O)), 4.60 (d, *J* = 16.1, 2H, OCH₂C(O)), 4.53 (d, *J* = 13.9, 1H, ArCH₂Ar, *ax*), 4.49 (dd, *J* = 11.5, 4.2, 2H, OCH₂), 4.34 (d, *J* = 13.3, 2H, ArCH₂Ar, *ax*), 4.06 (t, *J* = 9.4, 2H, OCH₂), 3.91–3.63 (m, 8H, OCH₂), 3.34 (d, *J* = 12.9, 1H,

ArCH₂Ar, eq), 3.31 (d, $J = 13.1$, 2H, ArCH₂Ar, eq), 3.14 (d, $J = 13.1$, 1H, ArCH₂Ar, eq). ¹³C NMR: δ 171.90 (C=O), 154.95, 154.76, 136.13, 134.20, 133.96, 133.60, 129.13, 128.96, 128.74, 128.37, 123.86, 123.15 (Ar), 74.82 (OCH₂), 71.62 (OCH₂C(O)), 69.89, 69.80 (OCH₂), 31.11, 29.38 (ArCH₂Ar). Anal. Calcd for C₃₈H₃₈O₁₀·0.4CH₂Cl₂: C, 66.74; H, 5.72. Found: C, 67.02; H, 5.66.

Synthesis of Calixcrown 25: 25,26-Bis(carboxymethoxy)calix[4]arene-crown-5 in the cone conformation was synthesized as the following. A solution of 25,26-bis[(ethoxycarbonyl)methoxy]calix[4]arene-crown-5 (**21**) (1.70 g, 2.25 mmol) in THF (20 mL) was mixed with 20 mL of 10% aq tetramethylammonium hydroxide. 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 CH₂Cl₂ (50 mL). The aqueous filtrate was extracted with CH₂Cl₂ (2 × 30 mL). The combined CH₂Cl₂ solutions were dried over MgSO₄ 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, CO₂H), 1752 (C=O), 1248, 1130, 1058 (C–O) cm⁻¹. ¹H NMR: δ 10.17 (br, s, 2H, CO₂H), 7.00–6.50 (m, 12H, ArH), 4.78 (d, $J = 16.1$, 2H, OCH₂C(O)), 4.65 (d, $J = 15.9$, 2H, OCH₂C(O)), 4.65 (d, $J = 15.9$, 1H, ArCH₂Ar, ax), 4.61 (d, $J = 13.8$, 1H, ArCH₂Ar, ax), 4.35 (d, $J = 13.2$, 2H, ArCH₂Ar, ax), 4.29–4.15 (m, 2H, OCH₂), 4.15–4.04 (m, 2H, OCH₂), 4.04–3.86 (m, 4H, OCH₂), 3.86–3.73 (m, 4H, OCH₂), 3.73–3.59 (m, 4H, OCH₂), 3.30 (d, $J = 11.5$, 1H, ArCH₂Ar, eq), 3.28 (d, $J = 13.3$, 2H, ArCH₂Ar, eq), 3.18 (d, $J = 13.2$, 1H, ArCH₂Ar, eq). ¹³C NMR: δ 171.97 (C=O), 155.04, 154.67, 135.39, 134.11, 134.02, 133.94, 128.94, 128.86, 128.56, 128.46, 123.79, 123.10 (Ar), 74.59 (OCH₂), 71.62 (OCH₂C(O)), 70.89, 70.44, 69.76 (OCH₂), 31.12, 30.83, 30.40 (ArCH₂Ar). Anal. Calcd. for C₄₀H₄₂O₁₁: C, 68.76; H, 6.06. Found: C, 68.94; H, 6.11.

Synthesis of Calixcrown 26: 25,26-Bis(carboxymethoxy)calix[4]arene-crown-6 in the cone conformation was synthesized as the following. A solution of 25,26-bis[(ethoxycarbonyl)methoxy]calix[4]arene-crown-6 (**22**) (1.70 g, 2.13 mmol) in THF (30 mL) was mixed with 10% aq tetramethylammonium hydroxide (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 CH₂Cl₂ (50 mL). The aqueous filtrate was extracted with CH₂Cl₂ (2 × 30 mL). The combined CH₂Cl₂ solutions were dried over MgSO₄ 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, CO₂H), 1757 (C=O), 1273, 1130, 1062 (C–O) cm⁻¹. ¹H NMR: δ 10.14 (br, s, 2H, CO₂H), 6.99–6.50 (m, 12H, ArH), 4.78 (d, $J = 16.1$, 2H, OCH₂C(O)), 4.65 (d, $J = 13.3$, 1H, ArCH₂Ar, ax), 4.61 (d, $J = 16.0$, 2H, OCH₂C(O)), 4.61 (d, $J = 16.0$, 1H, ArCH₂Ar, ax), 4.40 (d, $J = 13.2$, 2H, ArCH₂Ar, ax), 4.28–4.08 (m, 4H, OCH₂), 4.06–3.93 (m, 2H, OCH₂), 3.93–3.83 (m, 2H, OCH₂), 3.83–3.53

(m, 12H, OCH₂), 3.31 (d, $J = 13.7$, 1H, ArCH₂Ar, eq), 3.26 (d, $J = 13.3$, 2H, ArCH₂Ar, eq), 3.20 (d, $J = 13.3$, 1H, ArCH₂Ar, eq). ¹³C NMR: δ 171.74 (C=O), 155.19, 154.72, 135.17, 134.25, 134.19, 133.82, 128.93, 128.86, 128.68, 128.21, 123.76, 123.02 (Ar), 74.30 (OCH₂), 71.64 (OCH₂C(O)), 70.88, 70.75, 70.32, 69.73 (OCH₂), 31.12, 30.67 (ArCH₂Ar). Anal. Calcd. for C₄₂H₄₆O₁₂: C, 67.91; H, 6.24. Found: C, 67.58; H, 6.54.

Extraction Procedures

Upon ionization, the di-ionizable cone calix[4]crowns form metal ion complexes with two anionic centers on the same side of the crown unit. Competitive solvent extractions of alkali metal cations (Li⁺, Na⁺, K⁺, Rb⁺, and Cs⁺) and

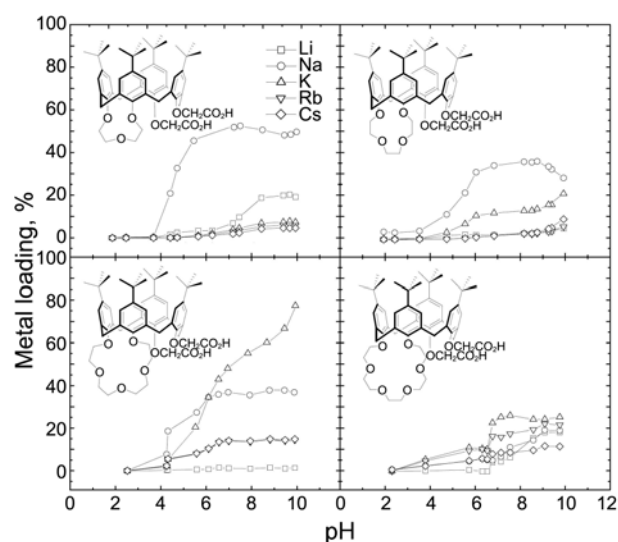


Figure 3. Percent of metals loading vs equilibrium pH of the aqueous phase for competitive solvent extraction of alkali metals into chloroform by conformers **10–13**.

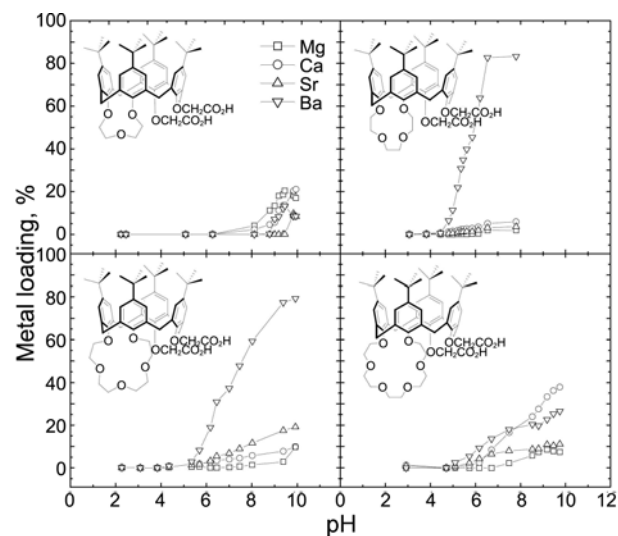


Figure 4. Percent of metals loading vs equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metals into chloroform by conformers **10–13**.

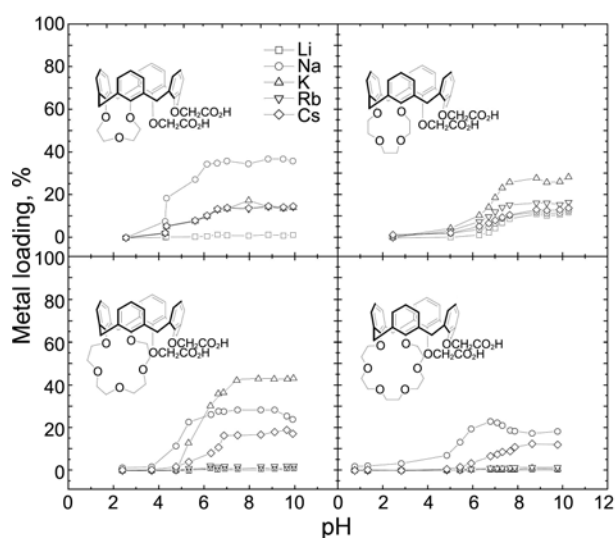


Figure 5. Percent of metals loading vs equilibrium pH of the aqueous phase for competitive solvent extraction of alkali metals into chloroform by conformers **23-26**.

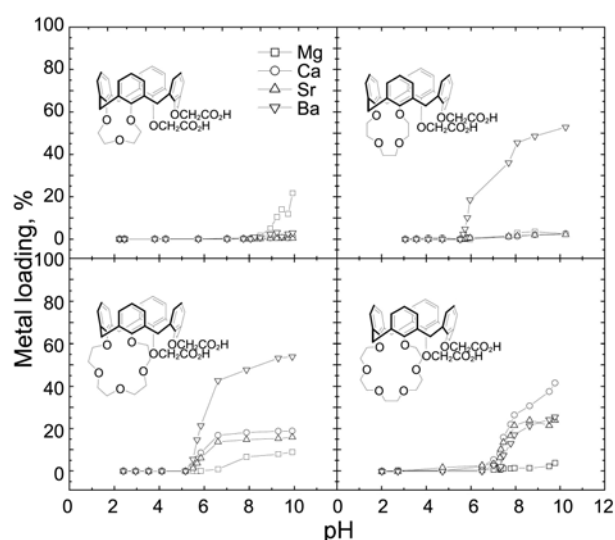


Figure 6. Percent of metals loading vs equilibrium pH of the aqueous phase for competitive solvent extraction of alkaline earth metals into chloroform by conformers **23-26**.

alkaline earth metal cations (Mg^{2+} , Ca^{2+} , Sr^{2+} and Ba^{2+}) were performed by 1.0 mM solutions of di-ionizable calix[4]-crown ligands **10-13** and **23-26** in chloroform, and the plot of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase were obtained, as depicted in Figures 3-6, respectively. All of the extraction experiments were repeated three times and the mean value of the extraction loadings were determined and were presented in the plots.

Competitive Solvent Extractions by Ligand 10. For competitive extraction of such metal cations, di-ionizable 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)-27,28-crown-3-calix[4]arene in the cone conformation (ligand **10**) depicted very different selectivity from its analogues (**11-13**). All five alkali metal cations and four

alkaline earth metal cations were detectably extracted into the chloroform phase and the selectivity order was $\text{Na}^+ \gg \text{Li}^+ > \text{K}^+$, Rb^+ , Cs^+ and $\text{Mg}^{2+} > \text{Ba}^{2+} \approx \text{Ca}^{2+} > \text{Sr}^{2+}$ for ligand **10**, respectively. The pH for half loading, $\text{pH}_{1/2}$, is a measure of the ligand acidity. For compound **10**, the $\text{pH}_{1/2}$ value was obtained to be 4.5 for binding to Na^+ and to be 7.5 for binding to Li^+ , K^+ , Rb^+ and Cs^+ , respectively. The $\text{pH}_{1/2}$ values for binding to alkaline earth metal cations were determined to be in the range of 9.0-9.5. Figures 3 and 4 depicted the plots of alkali and alkaline earth metal ions loading of the organic phase vs. the equilibrium pH of the aqueous phase using ligands **10**, respectively.

Competitive Solvent Extractions by Ligand 11. For competitive solvent extractions of aqueous alkali and alkaline earth metal cations (10.0 mM in each) solutions by 1.0 mM solutions of di-ionizable 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)-27,28-crown-4-calix[4]arene in the cone conformation (ligand **11**) in chloroform, plots of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase are presented in Figures 3 and 4, respectively.

For competitive extraction of alkali and alkaline earth metal cations, ligand **11** exhibited versatile selectivities for such ion species. All five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase. The selectivity order was $\text{Na}^+ > \text{K}^+ > \text{Li}^+$, Rb^+ , Cs^+ and $\text{Ba}^{2+} \gg \text{Ca}^{2+}$, Sr^{2+} , Mg^{2+} for ligand **11**. Moreover, the $\text{pH}_{1/2}$ values were obtained to be around 5.5 for binding to both the alkali and the alkaline earth metal cations.

Competitive Solvent Extraction by Ligand 12. 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)-27,28-crown-5-calix[4]arene in the cone conformation (ligand **12**) also exhibited very different selectivity from its analogues conformers (**10,11,13**). All five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase and the selectivity order was $\text{K}^+ > \text{Na}^+ > \text{Rb}^+ \approx \text{Cs}^+ > \text{Li}^+$ and $\text{Ba}^{2+} > \text{Sr}^{2+} > \text{Ca}^{2+} > \text{Mg}^{2+}$ for ligand **12**, respectively. The $\text{pH}_{1/2}$ values were obtained to be in the range of 4-6 for binding to alkali metal cations. The $\text{pH}_{1/2}$ values for binding to alkaline earth metal cations were determined to be 7. Figures 3 and 4 show the loading plots of alkali and alkaline earth metal cations in the organic phase vs. the equilibrium pH of the aqueous phase using ligands **12**, respectively.

Competitive Solvent Extractions by Ligand 13. For competitive solvent extractions of aqueous alkali and alkaline earth metal cations (10.0 mM in each) solutions by 1.0 mM solutions of di-ionizable 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26-bis(carboxymethoxy)-27,28-crown-6-calix[4]arene in the cone conformation (ligand **13**) in chloroform, plots of metal ions loading of the organic phase vs. the equilibrium pH of the aqueous phase are presented in Figures 3 and 4, respectively. For competitive extraction of alkali and alkaline earth metal cations, ligand **13** exhibited versatile selectivities for such ion species, in which all five alkali metal cations and four alkaline earth metal cations were detectably ex-

tracted into the chloroform phase. The selectivity order was $K^+ > Rb^+ > Na^+ \approx Li^+ > Cs^+$ and $Ba^{2+}, Ca^{2+} > Sr^{2+}, Mg^{2+}$ for ligand **13**. Moreover, the $pH_{1/2}$ value was obtained to be around 7 for binding to alkali and alkaline earth metal cations.

Competitive Solvent Extractions by Ligand 23. For competitive extraction of such alkali and alkaline earth metal cations, di-ionizable cone 25,26-bis(carboxymethoxy)-27,28-crown-3-calix[4]arene (ligand **23**) depicted very different selectivity from its analogues (**24–26**). All five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase and the selectivity order was $Na^+ > K^+, Rb^+, Cs^+ > Li^+$ and $Mg^{2+} > Ba^{2+}, Ca^{2+}, Sr^{2+}$ for ligand **23**, respectively. For compound **23**, the $pH_{1/2}$ value was obtained to be 5 and 9 for binding to alkali and alkaline earth metal cations, respectively. Figures 5 and 6 depicted the plots of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase using ligands **23**, respectively.

Competitive Solvent Extractions by Ligand 24. For competitive solvent extractions of aqueous alkali and alkaline earth metal cations (10.0 mM in each) solutions by 1.0 mM solutions of di-ionizable cone 25,26-bis(carboxymethoxy)-27,28-crown-4-calix[4]arene (ligand **24**) in chloroform, plots of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase are presented in Figures 5 and 6, respectively. For competitive extraction of those cations, ligand **24** exhibited versatile selectivities for alkali and alkaline earth metal ion species, in which all five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase. The selectivity order was $K^+ > Rb^+ > Na^+, Li^+, Cs^+$ and $Ba^{2+} > Ca^{2+}, Sr^{2+}, Mg^{2+}$ for ligand **24**. Moreover, the $pH_{1/2}$ value was obtained to be 7 for binding to alkali and alkaline earth metal cations.

Competitive Solvent Extractions by Ligand 25. For the cone 25,26-bis(carboxymethoxy)-27,28-crown-5-calix[4]arene (ligand **25**), plots of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase are presented in Figures 5 and 6, respectively. The $pH_{1/2}$ value was obtained to be in the range of 5–6 for binding to alkali metals. The $pH_{1/2}$ values for binding to alkaline earth metal cations were determined to be 6. Moreover, all five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase. The selectivity order was $K^+ > Na^+ > Cs^+, Li^+, Rb^+$ and $Ba^{2+} > Ca^{2+} > Sr^{2+} > Mg^{2+}$ for ligand **24**.

Competitive Solvent Extractions by Ligand 26. For the cone 25,26-bis(carboxymethoxy)-27,28-crown-6-calix[4]arene (ligand **26**), plots of metal ion loading of the organic phase vs. the equilibrium pH of the aqueous phase are presented in Figures 5 and 6, respectively. All five alkali metal cations and four alkaline earth metal cations were detectably extracted into the chloroform phase. The selectivity order was $Na^+ > Cs^+ > Li^+, K^+, Rb^+$ and $Ca^{2+} > Ba^{2+}, Sr^{2+} > Mg^{2+}$ for ligand **24**. Moreover, the $pH_{1/2}$ value was obtained to be in the range of 5.5–6.5 for binding to alkali metals. The $pH_{1/2}$

values for binding to alkaline earth metal cations were determined to be 7.5.

Conclusions

Proton di-ionizable diacid conformers of cone 25,26-di(carboxymethoxy)calix[4]arene-27,28-crown-3,4,5,6 (**23–26**), and their analogues including *p-tert*-butyl moieties in the upper rim (**10–13**), were synthesized as potential extractants for alkali and alkaline earth metal cations. The conformations and regio-selectivities of the new ligands were verified by 1H and ^{13}C NMR spectroscopy, IR spectroscopy and elemental analysis.

The upper rim moieties (*p-tert*-butyl-) showed an enhancement in the binding tendency and extraction ability of alkali and alkaline earth metal cations. This was attributed to the fascinating of the inductive charges from aromatic rings to the donor atoms of oxygen in the crown ether and the acid moieties.

By increasing the ring size of crown ether moieties from crown-3 to crown-6, an increasing in the K^+ selectivity was observed. It passed through a maximum using crown-5 moiety and it decreased by more increasing in the ring size. A similar but inverse trend was obtained for Na^+ selectivity.

By increasing the ring size of crown ether moieties, an increasing in the Ba^{2+} selectivity was observed and it decreased by more increasing in the ring size.

Ligand **10** and its analogue (**23**) bearing crown-3 group showed the most selectivity towards Na^+ in pH 4 and upper while, ligand **11** and its analogue (**24**) bearing crown-4 group showed the most selectivity towards Ba^{2+} in pH 6 and upper.

The $pH_{1/2}$ values, which were focused in a broad range of 4–9, were mainly depended to the conformer's structure and less to the trapped cation.

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