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Synthesis of Calix[4]arene Mono and Diamide Derivatives and Selective Complexation of Alkali and Alkaline Earth Cations

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The synthesis of mono and diamide derivatives of the p-tert-butylcalix[4]arenes/calix[4]arenes from the reaction of 5,11,17,23-tetra-tert-butyl-25,27-diethoxycarbonyl-methoxy-26,28-dihydroxycalix[4]arene **1** and 25,27-diethoxycarbonyl-methoxy-26,28-dihydroxycalix[4] arene **2** with various primary amines were reported. The effect of reaction time and steric hindrance of the primary amines used on the reactions have been investigated. All the amide derivatives of calix[4]arene are in a cone conformation according to the ^{1}H-NMR doublet–doublet pattern of the protons of the methylene groups between the aromatic rings. The complexing properties of these compounds toward selected alkali and alkaline earth metal cations are also studied. It has been observed that receptor **8** is a selective extractant for Cs^+ and Sr^{2+} cations.

Keywords: alkali and alkaline earth metal cations; diamide; calix[4]arene; monoamide; solvent extraction

1 Introduction

Numerous studies have been performed to develop efficient separation processes of toxic metals with a solvent extraction technique, which is one of the most commonly used treatment methods to separate and remove metal ions from waste on an industrial scale. In the disposal of waste, an extractant plays a key role on the separation and extraction efficiency. Therefore, the development of an efficient extractant for a target metal ion has received considerable attention in recent years (1).

Calixarenes, cyclic oligomers of phenolic units linked through the ortho positions, are a fascinating class of macrocycles, because of their skeleton simplicity associated with versatile recognition properties both of metallic or organic ions and of neutral molecules (2–5). The capability of being modified at both the lower and upper rims have made this class of synthetic ionophores increasingly attractive for the chemists involved in supramolecular chemistry. Therefore, a variety of sophisticated metal complexing ligands containing calix[4]arene backbone have been designed and synthesized for use as selective metal-ion or organic amines chemosensors (6–21), some of which have been successfully applied in various technologies. The complexation properties of these molecules appear to be highly dependent upon the nature and number of donor atoms and also upon the conformation of the calix[4]arene moiety (22–25). The variety of possible structures and the distinct coordination properties promoted our interest in calixarenes for solvent extraction.

Among the calixarenes that were shown to be particularly effective in metal ion complexation are those in which the substituents contain oxygen donor functions, such as crown ethers (9–12), amides (26–28), esters (29–31) and phosphorylated (32, 33) groups. Izat et al. (34) first reported the synthesis of calixarene ligands for the transport of alkali metal cations. It has been shown that crown ethers and the derivatives of 1,3-alternate calix[4]crown-6 extract Cs^+ ion efficiently from nuclear waste solutions by solvent extraction (35–41).

The family of amide derivatives of calix[4]arenes and their complexes with alkali metal, transition metal and lanthanide ions have been extensively investigated (42, 43). Such nitrogenous calixarenes may show better complexation ability toward alkali and alkaline earth cations. Arnaud-Neu and coworkers reported that tertiary amide derivatives of calix[4]arene show very substantial complexation with both alkali and alkaline earth cations (26, 27). Recently, Chang et al. (28) showed calix[4]arene-derived diamide to be a highly selective ionophore for Ca^{2+}.

In the previous work, we reported (44) the synthesis of *p-tert*-butylcalix[4]arene diamide derivatives by employing the aminolysis reaction of *p-tert*-butylcalix[4]arene diesters in high yields. The complexing properties of these

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compounds toward $Cr_2O_7^{2-}/HCr_2O_7^-$ anions were studied. Herein, we report the syntheses and ion binding properties of new ionophores bearing secondary mono or diamide functions which have often been claimed to act as binding sites in the complexation of certain metals.

2 Experimental

2.1 Materials and General Methods

Melting points were determined on an Electrothermal 9100 apparatus in a sealed capillary and are uncorrected. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$ with TMS as an internal standard. IR spectra were obtained on a Perkin-Elmer 1605 FTIR spectrometer using KBr pellets. UV-Visible spectra were obtained on a Shimadzu 160A UV-Visible recording spectrophotometer. The HPLC measurements were carried out on Agilent 1100 equipment connected with a Zorbax RX-C18 column. Elemental analyses were performed using a Leco CHNS-932 analyzer. FAB-MS spectra were taken on a Varian MAT 312 spectrometer.

Analytical TLC was performed using Merck prepared plates (silica gel 60 F_{254} on aluminum). Flash chromatography separations were performed on a Merck Silica Gel 60 (230–400 Mesh). All reactions, unless otherwise noted, were conducted under a nitrogen atmosphere. All starting materials and reagents used were of standard analytical grade from Fluka, Merck and Aldrich and used without further purification. Toluene was distilled from CaH_2 and stored over sodium wire. Other commercial grade solvents were distilled, and then stored over molecular sieves. The drying agent employed was anhydrous $MgSO_4$. All aqueous solutions were prepared with deionized water that had been passed through a Millipore milli-Q Plus water purification system.

2.2 Synthesis

Compounds **1**–**2** were synthesized according to previously described methods (45, 46). The synthesis of **6**–**9** has been already described by us (44).

2.3 General Procedure for the Synthesis of Compound 3–5 and 10–13

Appropriate primary amine (20.0 mmol) was dissolved in a 1:2 toluene/MeOH mixture (60 mL) and added dropwise into a solution of 5,11,17,23-tetra-*tert*-butyl-25,27-diethoxycarbonylmethoxy-26,28-dihydroxycalix[4]arene **1** *or* 25,27-diethoxycarbonyl-methoxy-26,28-dihydroxycalix[4]arene **2** or (4.0 mmol) in 20 mL toluene with continuous stirring at room temperature for about 30 min. Then, the reaction mixture was refluxed and the reactions were monitored by TLC. After the substrate had been consumed, the solvent was evaporated under reduced pressure and the residue was triturated with MeOH to give a crude product. The crude products were purified by flash chromatography (SiO_2, CH_2Cl_2/Hexane 2:1) and recrystallized from CH_2Cl_2/MeOH.

3: White crystals; yield 61%; mp 269–273°C; IR (KBr): 3378 (OH), 1679 (CO), 1756 (COO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 9.07 (t, 1H, N*H*), 7.79 (s, 2H, O*H*), 7.35 (d, 2H, Ar*H*), 7.06 (m, 3H, Ar*H*), 6.98 (d, 4H, Ar*H*), 6.77 (s, 4H, Ar*H*), 6.63 (m, 4H, Ar*H*), 4.73 (d, 2H, NHCH_2), 4.49 (s, 2H, OCH_2CO), 4.41 (s, 2H, OCH_2CO), 4.19 (d, 2H, $J = 13.2$ Hz, ArCH_2Ar), 4.08 (d, 2H, $J = 13.2$ Hz, ArCH_2Ar), 3.52 (s, 3H, OCH_3), 3.30 (d, 4H, $J = 13.2$ Hz, ArCH_2Ar); ^{13}C-NMR ($CDCl_3$): δ 168.87, 167.30 (*C*=O), 149.76, 149.48, 149.23, 148.80, 147.92, 147.77, 146.29, 132.75, 131.84, 130.75, 130.56, 129.84, 129.12, 128.69, 128.24, 127.58, (Ar*C*), 77.36, 77.05 (O*C*H$_2$), 75.49 (NH*C*H$_2$), 31.68, 31.16, 30.98 (Ar*C*H$_2$Ar), 22.45 (O*C*H$_3$); FAB-MS *m/z*: (666.7) $[M + Na]^+$. Anal. Calcd. for $C_{40}H_{37}NO_7$ (643.72): C, 74.63%; H, 5.79%; N, 2.18%. Found: C, 74.86%; H, 5.48%; N, 2.37%.

4: White crystals; yield 55%; mp 275–278°C; IR (KBr): 3383 (OH), 1687 (CO), 1757 (COO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.98 (t, 1H, N*H*), 7.78 (s, 2H, O*H*), 7.13 (d, 1H, Ar*H*), 6.98 (d, 4H, Ar*H*, ph), 6.85 (q, 4H, Ar*H*, ph), 6.71 (m, 2H, Ar*H, ph*), 6.61 (t, 2H, Ar*H, ph*), 6.27 (d,1H, Ar*H*), 6.17 (t, 1H, Ar*H*), 4.71 (d, 2H, NHCH_2), 4.53 (s, 2H, OCH_2CO), 4.49 (s, 2H, OCH_2CO), 4.21 (d, 2H, $J = 13.2$ Hz, ArCH_2Ar), 4.09 (d, 2H, $J = 13.4$ Hz, ArCH_2Ar), 3.70 (s, 3H, OCH_3), 3.33 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar); ^{13}C-NMR ($CDCl_3$): δ 168.47, 167.12 (*C*=O), 149.88, 149.63, 149.41, 148.96, 148.13, 147.87, 146.69, 133.15, 132.24, 131.18, 130.96, 130.11, 129.62, 128.88, 128.64, 127.93, (Ar*C*), 77.76, 77.25 (O*C*H$_2$), 75.48 (NH*C*H$_2$), 31.73, 31.26, 31.05 (Ar*C*H$_2$Ar), 22.52 (O*C*H$_3$); FAB-MS *m/z*: (656.7) $[M + Na]^+$. Anal. Calcd. for $C_{38}H_{35}NO_8$ (633.69): C, 72.02%; H, 5.57%; N, 2.21%. Found: C, 72.36%; H, 5.39%; N, 2.41%.

5: White crystals; yield 67%; mp 137–140°C; IR (KBr): 3383 (OH), 1685 (CO), 1767 (COO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.98 (t, 1H, N*H*), 7.31 (s, 2H, O*H*), 7.17 (d, 1H, Ar*H*), 6.98 (s, 4H, Ar*H*, ph), 6.75 (s, 2H, Ar*H*, ph), 6.76 (s, 2H, Ar*H*, ph), 6.18 (t, 1H, Ar*H*), 6.29 (d, 1H, Ar*H*), 4.65 (d, 2H, NHCH_2), 4.52 (s, 2H, OCH_2CO), 4.47 (s, 2H, OCH_2CO), 4.20 (d, 2H, $J = 13.2$ Hz, ArCH_2Ar), 4.06 (d, 2H, $J = 13.2$ Hz, ArCH_2Ar), 3.67 (s, 3H, OCH_3), 3.26 (d, 4H, $J = 13.2$ Hz, ArCH_2Ar), 1.21 (s, 18H, C(CH_3)$_3$), 0.93 (s, 9H, C(CH_3)$_3$), 0.90 (s, 9H, C(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$): δ 168.77, 167.32 (*C*=O), 149.91, 149.72, 149.53, 149.07, 148.83, 148.51, 148.26, 147.97, 147.18, 146.89, 132.13, 131.07, 130.71, 129.82, 128.94, 127.89 (Ar*C*), 77.81, 77.33 (O*C*H$_2$), 75.52 (NH*C*H$_2$), 34.37, 34.10, 33.96, 33.62, 33.21, 32.99 (C(*C*H$_3$)$_3$), 31.81, 31.37, 31.12 (Ar*C*H$_2$Ar), 22.51 (O*C*H$_3$); FAB-MS *m/z*: (905.1) $[M + Na]^+$. Anal. Calcd. for $C_{56}H_{67}NO_8$ (882.13): C, 76.25%; H, 7.66%; N, 1.59%. Found: C, 76.03%; H, 7.84%; N, 1.76%.

10: White Crystals; yield 74%; mp 294–297°C; IR (KBr): 3338 (OH), 1680 (CO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.77 (t, 2H, NH), 7.17 (s, 2H, OH), 7.07 (m, 10H, ArH,), 6.95 (d, 4H, ArH), 6.72 (d, 4H, ArH), 6.62 (m, 4H, ArH), 4.50 (d, 4H, NHCH_2), 4.27 (s, 4H, OCH_2CO), 3.65 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 3.24 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar); ^{13}C-NMR ($CDCl_3$): δ 167.85 (C=O), 149.43, 149.20, 148.86, 148.36, 148.04, 136.75, 128.84, 128.40, 127.42, 126.67, 126.80, 126.67 (ArC), 76.79 (OCH_2), 74.53 (NHCH_2), 31.60, 30.89 (ArCH_2Ar); FAB-MS m/z: (741.85) $[M + Na]^+$. Anal. Calcd. for $C_{46}H_{42}N_2O_6$ (718.84): C, 76.86%; H, 5.89%; N, 3.90%. Found: C, 76.68%; H, 5.74%; N, 3.80%.

11: Yellow crystals; yield 73%; mp 278–282°C; IR (KBr): 3314 (OH), 1687 (CO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 9.00 (t, 2H, NH), 7.50 (s, 2H, OH), 7.02 (m, 6H, ArH), 6.80 (d, 4H, ArH, ph), 6.60 (t, 4H, ArH, ph), 6.20–6.25 (m, 4H, ArH, ph), 4.52 (d, 4H, NHCH_2), 4.39 (s, 4H, OCH_2CO), 3.87 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 3.28 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar); ^{13}C-NMR ($CDCl_3$): δ 167.68 (C=O), 149.54, 148.93, 148.56, 148.09, 147.84, 137.16, 132.36, 128.74, 128.35, 127.93, 126.99, 126.23 (ArC), 76.96 (OCH_2), 74.64 (NHCH_2), 31.79, 30.98 (ArCH_2Ar); FAB-MS m/z: (721.74) $[M + Na]^+$. Anal. Calcd. for $C_{42}H_{38}N_2O_8$ (698.76): C, 72.19%; H, 5.48%; N, 4.01%. Found: C, 72.45%; H, 5.34%; N, 4.23%.

12: White crystals; yield 72%; mp 226–230°C; IR (KBr): 3341 (OH), 1679 (CO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.78 (t, 2H, NH), 8.06 (s, 2H, OH), 7.02 (d, 4H, ArH), 6.88 (d, 4H, ArH), 6.85 (t, 2H, ArH), 6.67 (t, 2H, ArH), 4.52 (s, 4H, OCH_2CO), 4.06 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 3.52 (t, 8H, OCH_2CH_2N), 3.38 (t, 4H, NHCH_2CH_2CH_2N), 3.42 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 2.28 (t, 4H, NHCH_2-CH_2CH_2N), 2.15 (m, 8H, OCH_2CH_2N), 1.74 (p, 4H, NHCH_2-CH_2CH_2N); ^{13}C-NMR ($CDCl_3$): δ 167.76 (C=O), 149.28, 148.57, 148.43, 143.27, 132.13, 127.01, 126.18, 125.50 (ArC), 77.12 (OCH_2), 76.85, 76.52, 74.76 (NHCH_2CH_2CH_2-N), 56.19 (OCH_2CH_2N), 53.47 (OCH$_2$CH_2N), 31.58, 30.67 (ArCH_2Ar); FAB-MS m/z: (721.74) $[M + Na]^+$. Anal. Calcd. for $C_{46}H_{56}N_4O_8$ (792.96): C, 69.67%; H, 7.12%; N, 7.07%. Found: C, 69.48%; H, 7.01%; N, 7.24%.

13: White crystals; yield 74%; mp 228–232°C; IR (KBr): 3340 (OH), 1680 (CO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.68 (t, 2H, NH), 8.04 (s, 2H, OH), 6.99 (d, 4H, ArH), 6.88 (d, 4H, ArH), 6.75 (t, 2H, ArH), 6.62 (t, 2H, ArH), 4.52 (s, 4H, OCH_2CO), 4.09 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 3.55 (q, 8H, NHCH_2CH$_2$CH$_2$N), 3.42 (d, 4H, $J = 13.4$ Hz, ArCH_2Ar), 2.38 (t, 4H, NHCH$_2$CH_2CH_2N), 2.29 (q, 8H, NHCH_2CH$_3$), 1.74 (p, 4H, NHCH$_2$CH_2CH_2N), 0.82 (t, 12 H, NCH$_2$CH_3); ^{13}C-NMR ($CDCl_3$): δ 167.82 (C=O), 149.48, 148.86, 148.49, 143.22, 132.40, 127.23, 126.25, 125.64 (ArC), 77.32 (OCH_2), 76.98, 76.70, 74.92 (NHCH_2-CH_2CH_2N), 50.90 (CH$_3$CH_2N), 31.67, 30.96 (ArCH_2Ar), 11.71 (CH$_3$CH$_2$N); FAB-MS m/z: (788) $[M + Na]^+$. Anal. Calcd. for $C_{46}H_{60}N_4O_6$ (765.01): C, 72.22%; H, 7.91%; N, 7.32%. Found: C, 72.40%; H, 7.76%; N, 7.48%.

2.4 Analytical Procedure

Picrate extraction experiments were performed following Pedersen's procedure (47). 10 mL of a 2.5×10^{-5} M aqueous picrate solution and 10 mL of 1×10^{-3} M solution of calixarene in CH_2Cl_2 were vigorously agitated in a stoppered glass tube with a mechanical shaker for 2 min, then magnetically stirred in a thermostated water-bath at 25°C for 1 h, and finally left standing for an additional 30 min. The concentration of picrate ion remaining in the aqueous phase was then determined spectrophotometrically as previously described (19). Blank experiments showed that no picrate extraction occurred in the absence of calixarene. The percent extraction (E%) was calculated as:

$$(E\%) = A_o - A/A_o x100$$

where A_o and A are the initial and final concentrations of the metal picrate before and after the extraction, respectively.

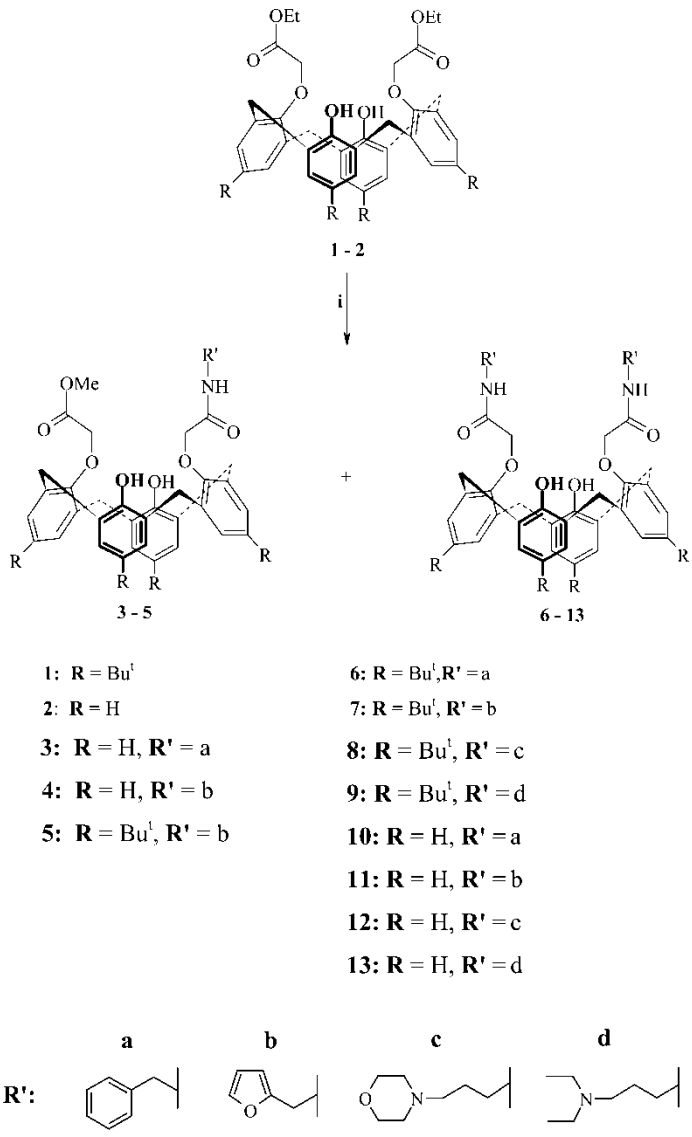
The alkali picrates were prepared as described elsewhere (26) by stepwise addition of a 2.5×10^{-2} M aqueous picric acid solution to a 0.14 M aqueous solution of metal hydroxide, until neutralization which was checked by pH control with a glass electrode. They were then rapidly washed with ethanol and ether before being dried *in vacuo* for 24 h.

3 Results and Discussion

3.1 Design and Synthesis of the New Hosts

The main goal of this work was the development of novel calix[4]arene ionophores bearing amide function that have an effective binding character for the chemically and biologically important metal ions. The synthesis of calix[4]arene amide derivatives can be achieved by following two synthetic pathways: the first is the reaction of acid chloride derivative of calix[4]arene, prepared in two steps starting from calix[4]-arene diester, with a primary amine as reported earlier (18) and the aminolysis (48, 49) reaction of calix[4]arene esters is the second and easy alternative route. The later approach gives better results for the synthesis of calix[4]arene amides, because it encompasses alternative routes, a reduction in the number of synthetic steps, and causes less environmental damage.

The synthetic route for the preparation of calix[4]arene mono and diamide derivatives is described in Scheme 1; 5,11,17,23-tetra-*tert*-butyl-25,27-diethoxycarbonylmethoxy-26,28-dihydroxy- calix[4]-arene **1** or 25,27-diethoxycarbonylmethoxy-26,28-dihydroxycalix[4]arene **2** was refluxed with benzyl amine, furfuryl amine, 3-morpholino-1-propyl amine and 3-diethylamino-1-propyl amine respectively to give corresponding amide derivatives of calix[4]arene **3–5** and **10–13** in 55–74% yields. Toluene-methanol solvent mixture was employed as toluene facilitates the dissolution of diester while methanol is beneficial to transforming the ethyl ester to the more reactive methyl ester prior to aminolysis (50).



Sch. 1. (i) Primary amine, MeOH/Toluene (1:1), reflux.

The new compounds **3–5** and **10–13** were characterized by FTIR, ^{1}H-NMR, ^{13}C-NMR, FAB MS, and elemental analysis. ^{1}H-NMR spectra of the monoamide calix[4]arenes showed a singlet for methoxy protons at 3.52–3.70 ppm for **3–5** while IR spectra showed both characteristic amide and ester carbonyl bands about 1684 cm^{-1} and 1755 cm^{-1}, respectively. ^{1}H-NMR spectra of the calix[4]arene diamide derivatives **10–13** showed only the amide protons at 8.80–9.01 ppm, while IR spectra showed only characteristic amide bands about 1684 cm^{-1} and the disappearance of ester carbonyl band at 1755 cm^{-1}.

The conformational characteristics of calix[4]arenes were conveniently estimated by the splitting pattern of the $ArCH_2Ar$ methylene protons in the ^{1}H and ^{13}C-NMR spectroscopy (2,3). ^{1}H and ^{13}C-NMR data showed that compounds **3–5** and **10–13** have a cone conformation. A typical AB pattern was observed for the methylene bridge $ArCH_2Ar$ protons at 3.30, 4.08 and 4.19 ppm ($J = 13.2$ Hz) for **3**, 3.33, 4.09, and 4.21 ppm ($J = 13.4$ Hz) for **4**, 3.26, 4.06 and 4.20 ppm ($J = 13.2$ Hz) for **5,** 3.24 and 3.65 ppm ($J = 13.4$ Hz) for **10**, 3.28 and 3.87 ppm ($J = 13.4$ Hz) for **11**, 3.42 and 4.06 ppm ($J = 13.4$ Hz) for **12**, 3.42 and 4.09 ppm ($J = 13.4$ Hz) for **13** in ^{1}H-NMR and three signals for mono amide derivatives (**3–5**) and two signals for diamide derivatives (**10–13**) covering a range of δ 31.83–30.98 and 31.79–30.67 ppm, respectively in ^{13}C-NMR. The high field doublets at 3.30 ppm for **3,** 3.33 ppm for **4** and 3.26 ppm for **5**, 3.24 ppm for **10**, 3.28 for **11**, 3.42 ppm for **12** and 3.42 ppm for **13** were assigned to the equatorial protons of methylene groups, whereas the low field signals at 4.08 and 4.19 ppm for **3**, 4.09 and 4.21 ppm for **4**, 4.06 and 4.20 ppm for **5**, 3.65 ppm for **10**, 3.87 for **11**, 4.06 ppm for **12** and 4.09 ppm for **13** were assigned to the axial protons in the ^{1}H-NMR.

3.2 Effect of the Reaction Time and Steric Hindrance

The progress of the reaction was monitored regularly by TLC and HPLC with suitable solvents. The chromatographic analysis showed that the formation of amide derivatives of the calix[4]arenes was affected by the reaction time. This observation allowed us to optimize procedures and yields of amide derivatives by altering the reaction time while maintaining all other parameters unchanged. For example, when the reaction mixture was refluxed for 72 h, monoamide derivative **3** was obtained in 61% yield along with 22% of the diamide derivative **10**. When the reaction was performed under the same conditions for 192 h, it afforded 74% of diamide derivative with only 19% of the monoamide derivative. Similar results were observed for **4** and **5** as shown Table 1.

Steric effects can also play an important role in the aminolysis reaction. The reaction of diester derivative of calix[4]arene **1, 2** with benzyl and furfuryl amines for 72 h produced

Table 1. Aminolysis reaction of calix[4]arene diester derivatives

Starting Material	Time (h)	Product: Monoamide	Yield (%)	Diamide	Yield (%)
1	72	**3**	61	**10**	22
1	72	**4**	55	**11**	23
1	192	**3**	19	**10**	74
1	192	**4**	12	**11**	73
1	72	–	–	**12**	72
1	72	–	–	**13**	74
2	72	–	–	**6**	79
2	72	**5**	67	**7**	13
2	192	**5**	11	**7**	78
2	72	–	–	**8**	76
2	72	–	–	**9**	78

mainly mono amide derivatives. On the other hand, the corresponding reaction with the amine derivatives having a three methylene unit spacer between the bulky moiety and the amine group for 72 h led to the synthesis of the diamide derivatives. The differences between the formation of mono and diamide derivatives from the reaction of calix[4]arene diester with simple amines could be mainly due to steric interactions between the reacting partners. This strategy allowed us to design the synthesis of mono or difunctionalized calix[4]arene derivatives selectively by increasing the chain length of the amine type.

3.3 Two-Phase Solvent Extraction

Ester and amide derivatives of calixarenes are potentially capable of forming complexes with many metal ions. On the basis of previous experience (16–21), we are interested in synthesizing calix[4]arene platform with alkyl amide derivatives on their lower rim that can selectively extract the metal cations from an aqueous phase into the organic phase. Thus, the present work is focused to elaborate the strategic requirements for the two phase extraction measurements. Therefore, the binding abilities of the synthesized ionophores toward some selected metal ions (such as, Li^+, Na^+, K^+, Cs^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) have been evaluated by means of solvent extraction of their metal picrates, and the results are summarized in Table 2.

This data was obtained by using a dichloromethane solution of the receptors **3–13** to extract metal picrates from an aqueous solution. The equilibrium concentration of picrate in the aqueous phase was determined spectrophotomerically from the data given in Table 2, however, it is observed that neither alkali nor alkaline earth metal cations were significantly extracted by the mono amide derivative of calix[4]arenes (**3–5**) and the compounds (**6, 7, 10** and **11**) which do not contain alkyl amino groups. In the literature (51) intramolecular hydrogen bonding between N-H and the facing oxygen atoms of the carbonyl group decreases the metal ion complex ability (Scheme 2). From that result, mono amide derivatives **3–5** and compounds **6**, **7**, **10** and **11** showed less affinity toward these metal cations. Chang et al. (52) reported only very low levels of metal extraction using a tetramer with secondary amide groups. Secondary amides would be expected to engage in intramolecular hydrogen bonds in the cone conformation. These hydrogen bonds would have to dissociate or be disrupted prior to the reception of a guest cation. Such an effect will operate in compounds **6–13**. It has been observed that the compounds **8**, **9**, **12** and **13** are good extractants for alkali and alkaline earth cations. However, better extraction results have been examined by compound **9** and **13** which extracted all of the metal cations more efficiently as compared to compounds **8** and **12**. The higher complexation property of these ionophores (**9** and **13**) is due to the presence of the diethylaminopropyl group which is a less hindered group than the morpholinopropyl group. It is intesesting to note, however, that the diamide derivative **8** showed high selectivity toward Cs^+ and Sr^{2+} ions but the compoud **12** which contains same group (morpholinopropyl) showed a remarkable affinity for Cs^+. The presence of *tert*-butyl groups at the upper rim of compound **8** causes different selectivity. Because the morpholino amide being more rigid might therefore respond less easily to the conformational changes associated with the complexation process.

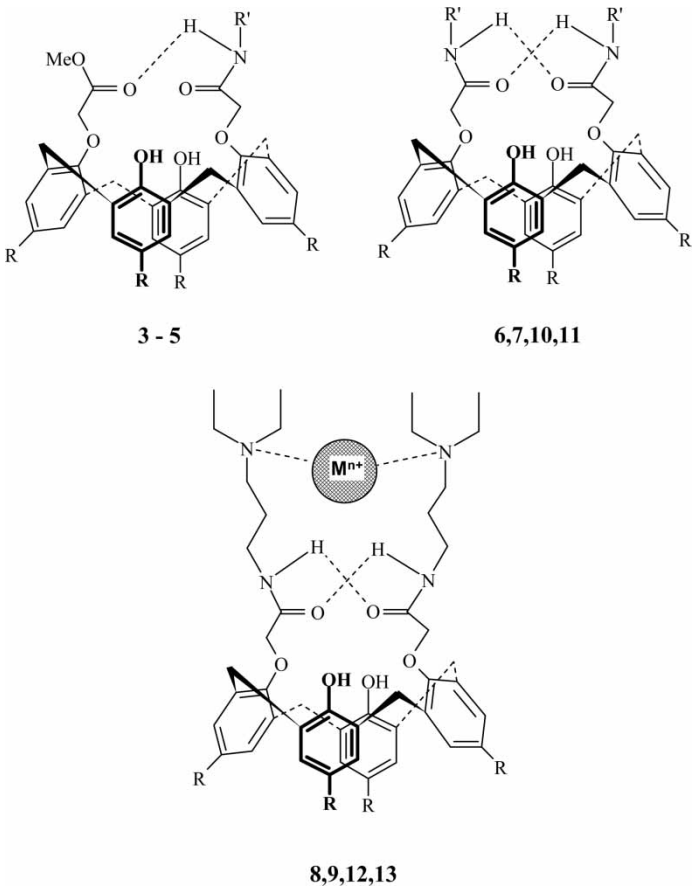
To characterize the extraction ability, the dependence of the distribution coefficient D of the cation between the two phases upon the calixarene concentration was examined. If the general extraction equilibrium is assumed to be given by Equation (1):

$$M^{n+}_{(aq)} + n\text{Pic}^-_{(aq)} + x[L]_{(org)} \rightleftharpoons [M(\text{Pic})_n(L)_x]_{(org)} \qquad (1)$$

Table 2. Extraction of metal picrates with ligands[a]

	Picrate salt extracted (%)							
Compound	Li^+	Na^+	K^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
3	1.93	<0.1	1.2	<0.1	5.92	1.67	2.1	2.34
4	1.12	<0.1	0.9	1.21	7.04	1.88	<0.1	3.71
5	<0.1	<0.1	<0.1	<0.1	3.94	2.54	<0.1	4.3
6	9.2	0.4	6.5	4.0	6.0	5.9	8.1	14.3
7	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
8	40.0	41.1	43.4	76.9	25.8	23.3	73.7	32.9
9	95.6	93.8	95.3	94.2	88.4	90.7	91.9	91.4
10	4.05	<0.1	<0.1	0.3	5.63	1.67	<0.1	3.13
11	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
12	38.4	41.7	44.2	68.8	40.3	24.9	45.3	32.0
13	98.0	95.4	96.4	97.1	93.4	95.7	95.3	94.3

[a]Aqueous phase, [metal nitrate] = 2.5×10^{-5} M; organic phase, dichloromethane, [ligand] = 1×10^{-3} M at 25°C, for 1 h. The percentage extraction is given by [initial aqueous cation] − [final aqueous cation]/[initial aqueous cation] × 100.



Sch. 2. The proposed interactions of ligands with metal cations.

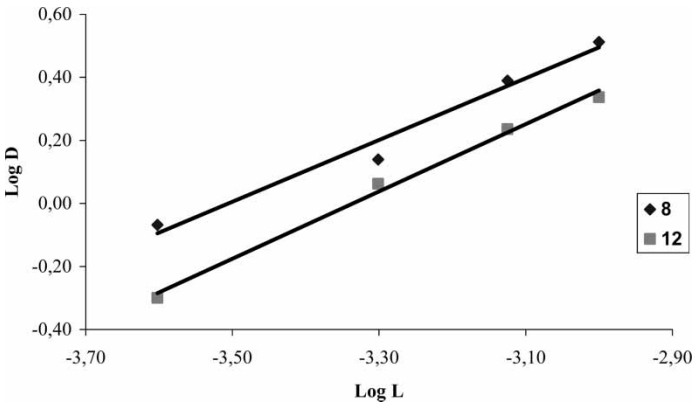


Fig. 1. Log *D* vs. log[L] for the extraction of Cesium picrates by ligands **8** and **12** from an aqueous phase into dichloromethane at 25°C.

the overall extraction equilibrium constant is expressed as Equation (2):

$$K_{ex} = \frac{[M(Pic)_n(L)_x]}{[M^{n+}][Pic^-]^n[L]^x} \quad (2)$$

and the distribution ratio *D* would be defined by:

$$D = \frac{[M(Pic^-)_n(L)_x]}{[M^{n+}]} \quad (3)$$

By introducing *D* into Eq. (2) and taking the log of both sides, Equation (2) can be rewritten as;

$$\log D = \log(K_{ex}[Pic^-]^n) + x\log[L] \quad (4)$$

With these assumptions, a plot of the log *D* vs. log[L] may lead to a straight line with a slope that allows for the determination of the stoichiometry of the extracted species, where [L] is defined as the analytical concentration of the ligand in the organic phase. Figure 1 exhibits the extraction into dichloromethane at different concentrations of **8** and **12** with Cesium picrate. A linear relationship between log D versus log[L] is observed with the slope of the line for extraction of Cs^+ cation by ligands **8** and **12** being approximately equal to 1, suggesting that these ligands **8** and **12** form 1:1 complexes with the Cs^+ cation. From this result we can conclude that Cs^+ is extracted as a 1:1 metal:reagent complex under the experimental conditions (i.e., in the presence of an excess of ligand) according to Equation (5):

$$Cs^+_{(aq)} + Pic^-_{(aq)} + [L]_{(org)} \overset{K_{ex}}{\rightleftarrows} [Cs(Pic)L]_{(org)} \quad (5)$$

The logarithmic extraction constant log *K*ex (*K*ex in mol/L) corresponding to Equation (5) is calculated and the corresponding logarithmic extraction constants are 3.35 for **12** and 3.52 for **8.**

4 Conclusions

In conclusion, the synthesis and complexation ability of calix[4]arene based receptors **3–5** and **10–13** were studied. The effect of reaction time and steric hindrance of the primary amines used on the reactions have been investigated. The spectroscopic data indicated that these compounds adopt the cone conformation. The complexation studies show that compounds **8** and **12** are better extractants for Cs^+ and Sr^{2+} ions compared with other mono and diamide derivatives. The selectivity (Cs^+or Sr^{2+}/Na^+ for **8**) looks promising especially for the treatment of nuclear waste.

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6 References

1. Kakoi, T., Toh, T., Kubota, F., Goto, M., Shinkai, S. and Nakashio, F. (1998) *Analytical Sciences*, **14**, 501–506.
2. Gutsche, C.D. (1983) *Acc. Chem. Res.*, **16**, 161–170.

3. Gutsche, C.D. Calixarenes revisited; The Royal Society of Chemistry: Cambridge, 1998.
4. Yilmaz, M., Memon, S., Tabakci, M. and Bartsch, R.A. New frontiers in polymer research; Topics in Polymer Research. Bregg, R.K. (ed.); Nova Publishers, Inc: New York, Ch. 6, 2006.
5. Takeshita, M. and Shinkai, S. (1995) *Bull. Chem. Soc. Jpn.*, **68**, 1088–1097.
6. Ikeda, A. and Shinkai, S. (1997) *Chem. Rev.*, **97**, 1713–1734.
7. Shinkai, S., Araki, K., Shibata, J., Tsugawa, D. and Manabe, O. (1990) *J. Chem. Soc., Perkin Trans. 1*, 333–337.
8. Shinkai, S. (1993) *Tetrahedron*, **49**, 8933–8968.
9. Thuery, P., Nierlich, M., Lamare, E., Dozol, J.F., Asfari, Z. and Vicens, J. (2000) *J. Inc. Phenom. Mac. Chem.*, **36(4)**, 375–408.
10. Asfari, Z., Harrowfield, J., Thuery, P. and Vicens, J. (2003) *Supramolecular Chemistry*, **15(1)**, 69–77.
11. Bitter, I., Grün, A., Tóth, G., Szöllösy, Á., Horváth, Gy., Ágai, B. and Töke, L. (1996) *Tetrahedron*, **52**, 639–646.
12. Gordon, J.L.M., Böhmer, V. and Vogt, W. (1995) *Tetrahedron Lett.*, **36**, 2445–2448.
13. Oueslati, I., Abidi, R., Thuèry, P. and Vicens, J. (2003) *J. Inc. Phenom. Mac. Chem.*, **47**, 173–178.
14. Kim, J.S., Shon, O.J., Ko, J.W., Cho, M.H., Yu, I.Y. and Vicens, J. (2000) *J. Org. Chem.*, **65(8)**, 2386–2392.
15. McCarrick, M., Wu, B., Harris, S.J., Diamond, D., Barrett, G. and McKervey, M.A. (1993) *J. Chem. Soc., Perkin Trans. 2*, 1963–1968.
16. Memon, S. and Yilmaz, M. (2001) *J. Mol. Struct.*, **595**, 101–109.
17. Memon, S. and Yilmaz, M. (2000) *Sep. Sci. and Tech.*, **35**, 457–467.
18. Memon, S., Akceylan, E., Sap, B., Tabakci, M., Roundhill, D.M. and Yilmaz, M. (2003) *J. Polym. Environ.*, **11**, 67–74.
19. Deligöz, H. and Yilmaz, M. (1995) *Solvent Extr. Ion Exch.*, **13**, 265–270.
20. Kuruoglu, D., Canel, E., Memon, S., Yilmaz, M. and Kilic, E. (2003) *Anal. Sci.*, **19**, 217–221.
21. Erden, S., Demirel, A., Memon, S., Yilmaz, M., Canel, E. and Kılıç, E. (2006) *Sensors and Actuators B*, **113**, 290–296.
22. Arnaud-Neu, F., Barrett, G., Harris, S.J., Owens, M., McKervey, M.A., Schwing-Weill, M.-J. and Schwinte, R. (1993) *Inorg. Chem.*, **32**, 2644–2650.
23. Ghidini, E., Ugozzoli, F., Ungaro, R., Harkema, S., Abu El-Fadl, A. and Reinhoudt, D.N. (1990) *J. Am. Chem. Soc.*, **112**, 6979–6985.
24. Shinkai, S., Otsuka, T., Fugimoto, K. and Matsuda, T. (1990) *Chem. Lett.*, 835–838.
25. Arnaud-Neu, F., Barboso, S., Casnati, A., Pinalli, A., Schwing-Weill, M.J. and Ungaro, R. (2000) *New J. Chem.*, **24**, 967–972.
26. Arnaud-Neu, F., Schwing-Weill, M.J., Ziat, K., Cremin, S., Harris, S.J. and McKervey, M.A. (1991) *New J. Chem.*, **15**, 33–37.
27. Arnaud-Neu, F., Barrett, G., Fanni, S., Marrs, D., McGregor, W., McKervey, M.A., Schwing-Weill, M.-J., Vetrogon, V. and Wechsler, S. (1995) *J. Chem. Soc., Perkin Trans 2*, 453–461.
28. Kim, M.Y. and Chang, S.K. (1998) *J. Org. Chem.*, **63**, 2362–2364.
29. Arduini, A., Pochini, A., Reverberi, S., Ungaro, R., Andreetti, G.D. and Ugozzoli, F. (1986) *Tetrahedron*, **42**, 2089–2100.
30. Arnaud-Neu, F., Collins, E.M., Deasy, M., Ferguson, G., Harris, S.J., Kaitner, B., Lough, A.J., McKervey, M.A., Margues, E., Ruhl, B.L., Schwing-Weill, M. and Seward, E.M. (1989) *J. Am. Chem. Soc.*, **111**, 8681–8691.
31. Iwamoto, K. and Shinkai, S. (1992) *J. Org. Chem.*, **57**, 7066–7073.
32. Yaftian, M.R., Burgard, M., Wieser, C., Dieleman, C.B. and Matt, D. (1998) *Solvent Extr. Ion Exch.*, **16**, 1131–1149.
33. Yaftian, M.R., Burgard, M., Matt, D., Wieser, C. and Dieleman, C. (1997) *J. Incl. Phenom. Macrocycl. Chem.*, **27**, 127–140.
34. Izatt, R.M., Lamb, J.D., Hawkins, R.T., Brown, P.R., Izatt, S.R. and Christensen, J.J. (1983) *J. Am. Chem. Soc.*, **105**, 1782–1785.
35. Asfari, Z., Bressot, C., Rozol, J.F., Rouquette, H., Eymard, S., Lamare, V. and Tourmois, B. (1995) *Anal. Chem.*, **67**, 3133–3139.
36. McDowell, W.J., Case, G.N., McDonough, J.A. and Bartsh, R.A. (1992) *Anal. Chem.*, **64**, 3013–3017.
37. Blausius, E. and Nilles, K.-H. (1984) *Radiochim. Acta*, **359**, 173–182.
38. Mahajan, R.K., Kumar, M., Sharma (nee Bhalla), V. and Kaur, I. (2002) *Talanta*, **58**, 445–450.
39. Gerow, I.H. and Davis, M.V. (1979) *Sep. Sci. Technol.*, **14**, 395–414.
40. Gerow, I.H., Smith, J.E. and Davis, M.V. (1981) *Sep. Sci. Technol.*, **16**, 519–548.
41. Schultz, W.W. and Bray, L.A. (1987) *Sep. Sci. Technol.*, **22**, 191–214.
42. Asfari, Z., Böhmer, V., Harrowfield, J.McB. and Vicens, J. *Calixarenes 2001*; Kluwer Academic Publishers: Dordrecht, 2001.
43. Arnaud-Neu, F. and Schwing-Weill, M.-J. (1997) *Synthetic Metals*, **90**, 157–164.
44. Bozkurt, S., Karakucuk, A., Sirit, A. and Yilmaz, M. (2005) *Tetrahedron*, **61**, 10443–10448.
45. Gutsche, C.D., Iqbal, M. and Stewart, D. (1986) *J. Org. Chem.*, **51**, 742–745.
46. Collins, M., McKervey, M.A., Madigan, E., Moran, M.B., Owens, M., Ferguson, G. and Harris, S.J. (1991) *J. Chem. Soc., Perkin Trans 1*, 3137–3142.
47. Pedersen, C.J. (1968) *J. Fed. Proc. Fed. Am. Soc. Exp. Biol.*, **27**, 1305–1309.
48. Wu, Y., Shen, X., Duan, C., Liu, Y. and Xu, Z. (1999) *Tetrahedron Lett.*, **40(31)**, 5749–5752.
49. Wu, Y., Liu, H., Liu, Y., Duan, C., Hu, J. and Xu, Z. (2000) *J. Incl. Phenom. Macrocycl. Chem.*, **36**, 473–478.
50. Bitter, I., Grün, A., Toth, G., Balázs, B. and Tõke, L. (1997) *Tetrahedron*, **53**, 9799–9812.
51. No, K., Lee, J.H., Yang, S.H., Yu, S.H., Cho, M.H., Kim, M.J. and Kim, J.S. (2002) *J. Org. Chem.*, **67**, 3165–3168.
52. Chang, S.K., Kwon, S.K. and Cho, I. (1987) *Chem. Lett.*, 947–948.