

## Structure Optimization of Di-ionizable Calixarene Nano-baskets for Competitive Solvent Extraction of Alkali and Alkaline Earth Metals

Bahram Mokhtari and Kobra Pourabdollah\*

Department of Chemical Engineering, Shahreza Branch, Islamic Azad University, Shahreza, Iran

\*E-mail: pourabdollah@iaush.ac.ir

Received July 25, 2011, Accepted August 31, 2011

The competitive solvent extractions of alkali and alkaline earth metals by di-ionizable calix[4]arene derivatives were studied using nine conformers of calix[4]arene nano-baskets. The objective of this work is to assess the variation of macrocycle conformation, orientation and position of pendant moieties upon the extraction parameters (extraction efficiency, selectivity and  $\text{pH}_{1/2}$ ) of the complexes. The results revealed that alternation of ring conformation in calixarene scaffold affects the solvent extraction parameters towards alkali and alkaline earth metals, dominantly while changing the orientation of pendant moieties from *ortho*- to *para*- as well as *cis*- to *trans*- analogues depicted no changes in those extraction parameters.

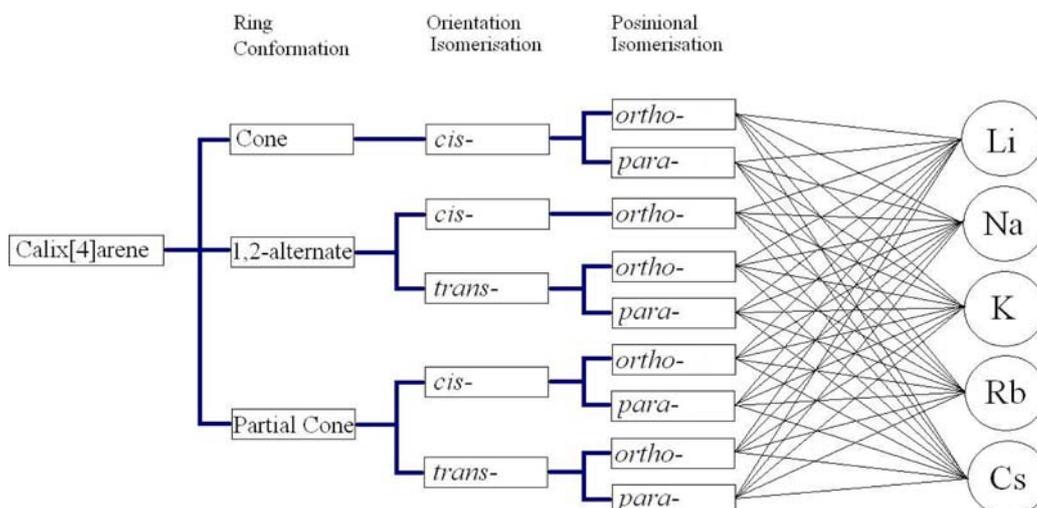
**Key Words :** Solvent extraction, Conformation, Calix[4]arene, Alkali metal

### Introduction

Nano-baskets of calixarenes are a versatile class of macrocycles, which have been subject to extensive research in development of many extractants, transporters and stationary phases over the past four decades.<sup>1-5</sup> In the nineteenth century, Baeyer synthesized them via the reaction of formaldehyde with *p*-substituted phenols in basic or acidic environment.<sup>6</sup> In the 1940s, Zinke and Ziegler discovered that the products possessed cyclic tetrameric structures.<sup>7</sup> In 1975, Gutsche introduced the presently accepted name of calixarene.<sup>8</sup> The small calixarenic cycles, calix[4]arene, possess a bowl-shaped conformation<sup>9</sup> and those with pendent proton-ionizable groups, such as carboxylic acid,<sup>10</sup> phosphinoyl,<sup>11</sup> *N*-sulfonyl carboxamide<sup>12</sup> and hydroxyamic acid<sup>13</sup> have been utilized for solvent extraction of cations.

Ionizable calixarenes than non-ionizable analogues are

more efficient in cation separation owing to charge matching within the resulted complex in the organic phase. There are two kinds of side chain in the calixarene skeleton that were studied including the ionizable sulfonyl carboxamide moieties and the crown ether moieties. The ionizable groups 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. In this work, two proton-ionizable function groups, *N*-phenyl-sulfonyl carboxamide, were incorporated into calix[4]arene scaffold. A special feature of such modification is that the hydrolysis of the *N*-phenyl-sulfonyl carboxamide moiety is tunable by changing the pH of solution. A wide range of pH environments can be examined when these ionizable groups are incorporated into the calixarene skeleton. These extractants exhibit excellent extraction selectivity for alkali and alkaline earth metals.



**Figure 1.** The hierarchical structures of complexes were investigated.

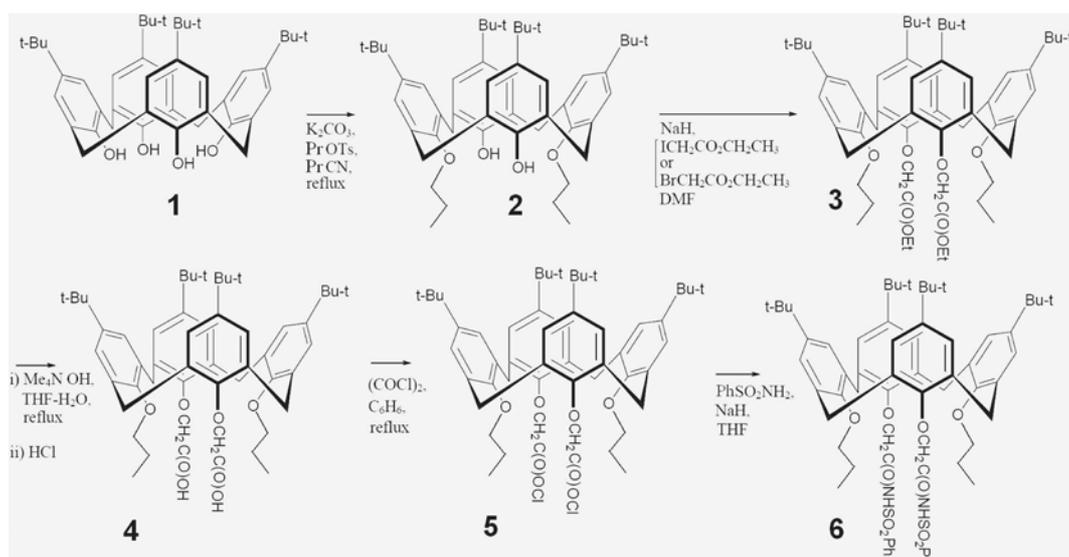


Fig. 2. The synthesis procedure of *p-tert*-calix[4]arenes bearing two N-phenyl sulfonyl carboxamides moieties.

Cations are transferred to the organic phase due to the production of a neutral complex and are analyzed quantitatively in the aqueous phase after back extraction.<sup>14</sup> The loading percentage is equal to the ratio of the extracted amount of metal cation over the initial macrocycle concentration in the organic phase.

In this paper, the competitive solvent extractions of alkali metals from aqueous solutions into chloroform by di-ionizable calix[4]arene derivatives were studied. Figure 1 shows the hierarchical structures of complexes were studied. Nine scaffolds were used to assess the isoconformations upon the extraction efficiency, selectivity and  $\text{pH}_{1/2}$  of complexes.

### The Synthesis Procedure

Novel cone conformer of proton di-ionizable 1,3-dipropoxy-*p-tert*-butylcalix[4]arene ligands were synthesized according to the procedure shown in Figure 2.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-dihydroxy-26,28-di(1-propoxy)calix[4]arene (2).**  $\text{K}_2\text{CO}_3$  (82.93 g, 600 mmol) and *n*-propyl *p*-toluenesulfonate (12.85 g, 60.0 mmol) were added to the suspension of the *p-tert*-butylcalix[4]arene **1** (19.46 g, 30.0 mmol) in 200 mL of dry *n*- $\text{C}_3\text{H}_7\text{CN}$ . The reaction mixture was refluxed for 20 *hr* and then another portion of *n*-propyl *p*-toluenesulfonate (6.43 g, 30.0 mmol) was added. The mixture was heated for another 20 *hr*. After cooling, the reaction mixture was filtered and the solvent was evaporated in *vacuo*. The residue was partitioned between 200 mL of  $\text{CH}_2\text{Cl}_2$  and 200 mL of HCl (1 N). The organic layer was separated, washed with water and evaporated in *vacuo*. The crude product was purified by chromatography on silica gel column with  $\text{CH}_2\text{Cl}_2$ -hexanes (20:1) as eluent to give **2** (88%) as a white solid. The product was recrystallized from *n*- $\text{C}_3\text{H}_7\text{OH}$ - $\text{CH}_2\text{Cl}_2$  in 71% yield; mp 240-242 °C;  $\nu_{\text{max}}$  (film)/ $\text{cm}^{-1}$ : 3800-3200 (OH), 1010 (C-O);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):

$\delta$  0.99 (s, 18H), 1.06 (t,  $J = 7.45$ , 6H), 1.27 (s, 18H), 1.75 (m, 4 H), 3.33 (d,  $J = 12.94$ , 4H), 3.97 (t,  $J = 6.47$ , 4H), 4.30 (d,  $J = 12.82$ , 4H), 6.84 (s, 4H), 7.03 (s, 4H), 7.85 (s, 2 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{c}}$  150.18, 150.30, 146.46, 141.12, 132.88, 127.57, 125.44, 125.30, 33.59, 33.87, 32.12, 31.86, 31.70; Anal. Calc.  $\text{C}_{50}\text{H}_{68}\text{O}_4$ : C, 78.90; H, 9.00; Found: C, 79.10; H, 9.26.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis[(ethoxycarbonyl)methoxy]-26,28-di(1-propoxy)calix[4]arene (3).** 10 mmol 25,27-dipropoxycalix[4]arene (**2**) was added to the suspension of sodium NaH (0.96 g, 40 mmol) in DMF (100 mL), and the mixture was stirred at room temperature. Once the evolution of hydrogen ceased, a solution of ethyl bromoacetate (22 mmol) in DMF (10 mL) was added over a period of 30 min. The mixture was stirred for 3 *hr*, and another portion of ethyl bromoacetate (10 mmol) in DMF (5 mL) was added. The reaction mixture was stirred for another 2 *hr* and the excess of NaH was carefully decomposed by dropwise addition of water. The mixture was diluted with 200 mL HCl (1 N) and was extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 200$  mL). The combined organic extracts were washed with water, dried over  $\text{MgSO}_4$  and evaporated in *vacuo*. The DMF and the unreacted ethyl bromoacetate were removed by distillation under vacuum (60 °C, 1 mm Hg). The residual pale-yellow oil was purified by chromatography on silica gel with hexanes-EtOAc (40:1) as eluent to give the final products **3** in 80% yield as a white solid; mp 108-110 °C;  $\nu_{\text{max}}$  (film)/ $\text{cm}^{-1}$ : 1758 (C=O);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  0.80 (br s, 9H), 1.04 (br s, 9H), 1.26 (t,  $J = 7.20$ , 6H), 1.34 (br d,  $J = 24.78$ , 18H), 2.16 (t,  $J = 8.60$ , 6H), 2.99-5.08 (m, 24H,  $\text{ArCH}_2\text{Ar}$ ,  $\text{OCH}_2\text{CO}_2$ , and  $\text{CH}_2$ ), 6.58-7.24 (m, 8H, ArH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  173.61, 155.95, 153.39, 153.03, 145.92, 143.49, 135.68, 133.93, 132.23, 131.80, 131.55, 127.26, 125.98, 125.33, 124.79, 124.18, 74.16, 72.95, 60.35, 34.09, 33.57, 31.69, 31.22, 26.07; Anal. Calc.  $\text{C}_{58}\text{H}_{80}\text{O}_8$ : C, 76.95; H, 8.91; Found: C, 77.08; H, 8.79.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-**

**25,27-bis(carboxymethoxy)-26,28-di(1-propoxy)calix[4]-arene (4).** A solution of diester **3** (5.0 mmol), THF (150 mL) and 10% aqueous Me<sub>4</sub>NOH (150 mL) was refluxed overnight. The reaction mixture was acidified with HCl (10%) to pH~1. The solvent was removed in *vacuo* and 200 mL CH<sub>2</sub>Cl<sub>2</sub> was added. The organic layer was washed with water, dried over MgSO<sub>4</sub> and evaporated in *vacuo* to give the final product **4** in 96% yield as a white solid; mp 252-254 °C;  $\nu_{\max}$  (film)/cm<sup>-1</sup>: 3320-2410 (CO<sub>2</sub>H), 1712 (C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.60-1.60 (br m, 36H), 2.10-4.16 (br m, 30H), 6.35-4.60 (br m, 8H); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta_c$  180.60, 144.32, 131.88, 125.73, 34.01, 33.95, 31.86, 31.45, 31.12, 29.96, 25.29; Anal. Calcd. C<sub>54</sub>H<sub>72</sub>O<sub>8</sub>·0.6 CH<sub>2</sub>Cl<sub>2</sub>: C, 72.88; H, 8.20; Found: C, 72.74; H, 7.95.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(chlorocarboxymethoxy)-26,28-di(1-propoxy)-calix[4]arene (5).** 2.40 mmol diacid **4** was dried by benzene-azeotropic distillation. Oxalyl chloride (3.04 g, 24.0 mmol) was added to the solution and the reaction mixture was refluxed for 5 hr under nitrogen atmosphere. The solvent was removed in *vacuo* to provide the corresponding acid chloride **5**.

**Synthesis of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27-bis(*N*-phenylsulfonylcarbamoylethoxy)-26,28-di(1-propoxy)calix[4]arene (6).** A solution of the acid chloride **5** in THF (10 mL) was added to a mixture of the appropriate sulfonamide (9.50 mmol) and NaH (0.58 g, 24.0 mmol) in THF (100 mL), and the mixture was stirred under nitrogen at room temperature for 6 hr. Then 2 mL H<sub>2</sub>O was carefully added to decompose the excess NaH. The THF was evaporated in *vacuo* and CH<sub>2</sub>Cl<sub>2</sub> (200 mL) was added to the residue. The organic layer was washed with 200 mL HCl (1 N) and water, was dried over MgSO<sub>4</sub> and was evaporated in *vacuo* to give the crude di-ionizable calix[4]arene. After purification, the product was dissolved in CH<sub>2</sub>Cl<sub>2</sub>, washed with 10% aqueous HCl and water, and dried over MgSO<sub>4</sub>. The solution was evaporated in *vacuo* to give the product **6**. Derivative **6** was obtained in 86% yield after chromatography on silica gel with CH<sub>2</sub>Cl<sub>2</sub>-MeOH (80:1) as eluent. White solid; mp 136-140 °C;  $\nu_{\max}$  (film)/cm<sup>-1</sup>: 3248 (NH), 1722 (C=O), 1362 and 1186 (S=O); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.96 (br s, 18H), 1.24 (br s, 18H), 2.04-4.22 (br m, 26H), 6.20-7.22 (br m, 8H), 7.50 (t, *J* = 7.69, 4H), 7.59 (t, *J* = 7.32, 2H), 8.07 (d, *J* = 7.44, 4H), 9.48 (br s, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta_c$  171.22, 171.02, 155.81, 153.72, 144.53, 138.15, 133.09, 132.60, 129.20, 128.02, 125.09, 72.98, 60.04, 33.96, 33.06, 33.44, 31.94, 31.02, 25.31; Anal. Calc. C<sub>66</sub>H<sub>82</sub>N<sub>2</sub>O<sub>10</sub>S<sub>2</sub>: C, 70.31; H, 7.33; N, 2.48 Found: C, 70.13; H, 7.23; N, 2.59.

Other isoconformers were synthesized using the basic scaffolds of 1,2-alternate and partial-cone.

## Experimental

All of the experiments carried out using nine conformations of di-ionizable *p-tert*-calix[4]arene di-[*N*-(phenyl)-sulfonyl carboxamide]. According to the synthesis proce-

dures that is shown in Figure 2, Two cone conformers (**1** and **2**), three 1,2-alternate conformers (**3-5**), and four partial-cone conformers (**6-9**) were synthesized to extract alkali metals. The *cis/trans* symbols refer to the direction of two di-ionizable moieties and the *ortho/para* depict the relative situation of two di-ionizable moieties.

The alkali metals were loaded into the aqueous solutions by adding stock solutions containing 5 alkali metals. The pH values of the aqueous phases were adjusted using lithium hydroxide and hydrochloric acid solutions. Extraction abilities of nine conformations in thirteen solutions with pH range of 1.0 to 12.0 were determined. The samples contained 2.0 mL of the aqueous phase of 10.0 mM alkali metals and 2.0 mL of 1.00 mM macrocyclic ligand in chloroform. In the stripping step, the organic phase was transferred to a capped conical centrifuge tube and the stripping was involved 5 minutes of mixing and centrifuging. After that, the aqueous phase was diluted for analysis by Dionex DX-120 ion chromatographs with a CS12A column, a conductivity detection and membrane suppression. Base upon the traces in Figure 3, the effect of different isoconformations of di-ionizable calix[4]arene derivatives on the sensitivity (extraction efficiency), selectivity and pH<sub>1/2</sub> values of five alkali metals were determined and compared.

**Standard Solutions.** Lithium chloride (99%), rubidium chloride (99+%) and cesium chloride (99+%) were obtained from Alfa Aesar (Ward Hill, MA). Potassium chloride (99%) and sodium chloride (99%) were purchased from Mallinckrodt (Phillipsburg, NJ). Magnesium chloride hexahydrate (99%), calcium chloride dihydrate (98%), barium chloride dihydrate (99%) and strontium chloride hexahydrate (99%) were obtained from Aldrich. Lithium hydroxide was purchased from Fisher Scientific (Fair Lawn, NJ). Barium hydroxide octahydrate (98%) was purchased from MCB, hydrochloric acid (1.0 N) from J. T. Baker, and sulfuric acid (2.0 N) was obtained from Mallinckrodt. Chloroform was purchased from EM Science and was shaken with deionized water to remove the stabilizing ethanol and stored in the dark.

**Sample Preparation.** The alkali metal cations were loaded into the aqueous solutions by adding stock solutions containing five alkali metal cations. The solutions of five alkali metal cations were made up as lithium, sodium, potassium, rubidium, and cesium chloride solutions (20.0 mM in each). The 20.0 mM lithium hydroxide and 0.01-1.0 M hydrochloric acid solutions were used to adjust the pH values of the aqueous phases.

The alkaline earth metal cations were loaded into the aqueous solutions by adding stock solutions containing 4 alkaline earth metal cations. The blend solutions of alkaline earth metal cations were made up as magnesium, calcium, barium, and strontium chloride solutions (20.0 mM in each). The pH values of the aqueous phases were adjusted using 4.0 mM barium hydroxide and 0.01 M hydrochloric acid solutions.

Extraction ability of calix[4]arene scaffolds were determined in thirteen solutions with pH range of 1.0-12.0. For

each macrocyclic ligand, more than thirteen solutions for competitive solvent extraction of alkali or alkaline earth metals were prepared in 15 mL conical polypropylene centrifuge tubes. The samples contained 2.0 mL of the aqueous phase of 10.0 mM alkali or alkaline earth metals solution and 2.0 mL of 1.00 mM calixarene solution in chloroform.

**Extraction Procedure.** In this research, the solvent extraction procedure as a sample preparation and a preconcentration method was used. The combined aqueous and organic phases were shaken for 5 minutes and were centrifuged for 5 minutes. The pH of the aqueous phase was measured using pH meter with a Corning 476157 combination pH electrode. In the stripping step, 1.5 mL of the organic phase was transferred to a capped conical centrifuge tube containing 3.0 mL of 0.10 M HCl. The stripping involved 5 minutes of mixing and 5 minutes of centrifuging. After that, 1.0 mL of the aqueous phase was diluted to 10.0 mL for analysis by ion chromatography.

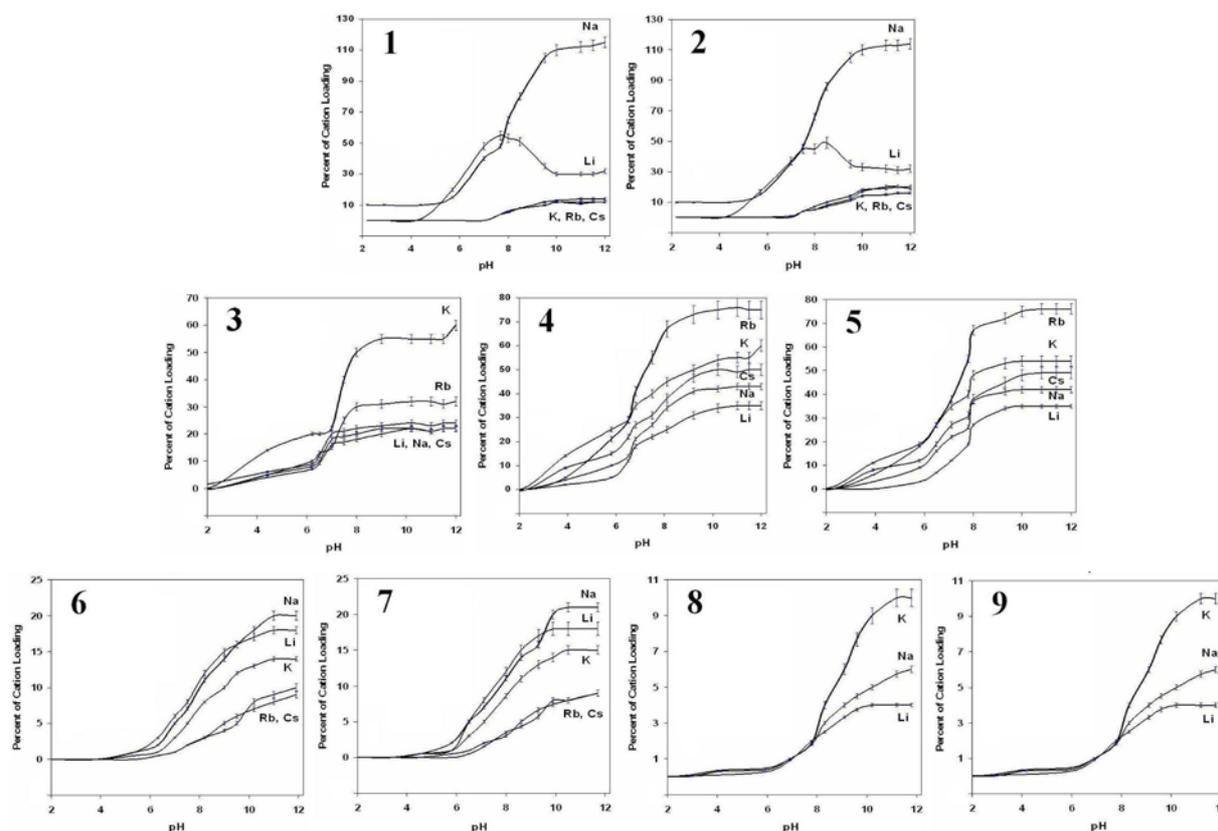
**Ion Chromatographic Analysis.** Determinations of alkali or alkaline earth metals were accomplished by Dionex DX-120 ion chromatographs with a CS12A column, a conductivity detection and membrane suppression. Nitrogen pressure for the eluent was set at 50 psi. The eluent was 0.011 M sulfuric acid after filtration through a Millipore 0.22  $\mu\text{m}$  filtration membrane, while the pump flow rate at 1700 psi was about 1 mL/min. To obtain a stable baseline, the eluent was flowed through the column for 60 minutes and then, 2.0

mL of standard solutions were injected and they were repeated two other times. PeakNet software was used to manipulate the outputs from the ion chromatograph.

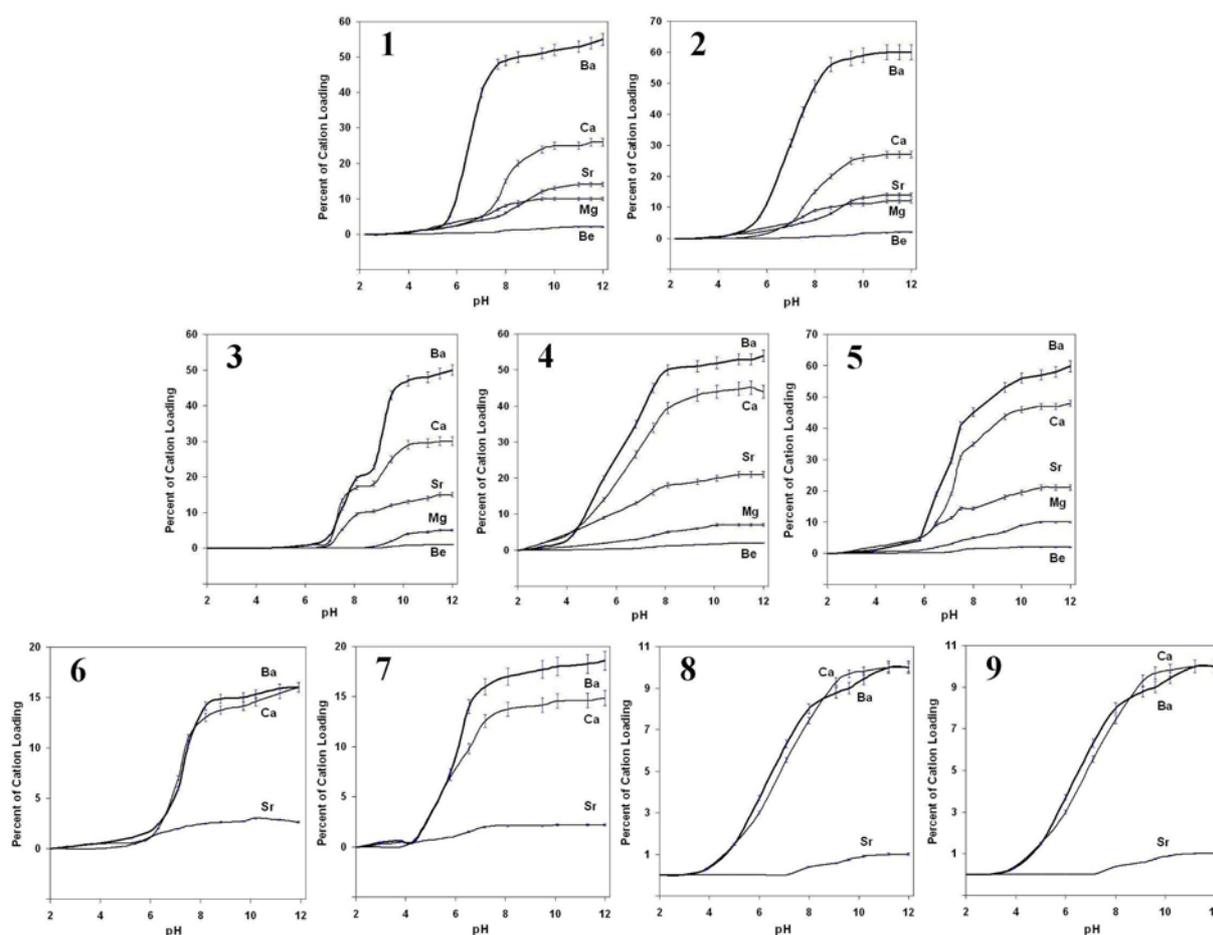
## Results and Discussion

The proton-ionizable groups act as acidity tunable functions with functional group variation. The pH for half loading ( $\text{pH}_{1/2}$ ) was used to measure qualitatively the ligand acidity. Alternating the orientation of pendant moieties from *cis*- to *trans*- as well as *ortho*- to *para*- analogues revealed no changes in the selectivity of macrocyclic ligands. Besides, the cone conformers were selective to sodium and the 1,2-alternate conformers showed a relative selectivity to potassium and rubidium. Figure 3 shows the chemical structure of those nine conformations 1-9 (R group was defined as:  $-\text{NHSO}_2\text{Phenyl}$ ). According to Figure 3, there were not any extractability towards cesium and rubidium in conformers 8 and 9.

The partial-cone conformers were selective to potassium and to one of the lithium or sodium. The lower extraction efficiency of partial-cone conformers than their 1,2-alternate and cone analogues demonstrated that conformation variation had a pronounced influence upon the complexation of alkali metals. The 1,2-alternate conformers showed the widest range of extraction efficiency, which was 4 and 2 times of partial-cone and cone analogues. The extraction efficiency of *cis*- isomers than their *trans*- analogues



**Figure 3.** Loading traces for solvent extractions of alkali metals by isoconformers 1-9. (R:  $\text{NHSO}_2\text{Phenyl}$ ). The cone conformations in the upper row, the 1,2-alternate conformations in the middle row and the partial-cone conformations in the lower row.



**Figure 4.** Loading traces for solvent extractions of alkaline earth metals by isoconformers **1-9**. The cone conformations in the upper row, the 1,2-alternate conformations in the middle row and the partial-cone conformations in the lower row.

revealed that orient variation of pendant moieties had a pronounced influence upon the complexation of alkali metals. The *cis*- isomers presented a middle range of extraction efficiency, while the extraction efficiency for *trans*- analogues was too much high or too much low. The percent of loading, which is related to the sensitivity of extraction method, was compared in *ortho*- isomers and their *para*- analogues. Therefore, variation in position of pendant moieties can have a pronounced influence on the extraction efficiency of alkali metals. The percent of loading in *ortho*- isomers was equal and lower than that of *para*- analogues.

Changing from *ortho*- to *para*- in the pendant moieties showed no changes in the  $pH_{1/2}$  of the resulted complex. The lower  $pH_{1/2}$  of 1,2-alternate conformers than both analogues demonstrated that conformation variation had a pronounced influence upon the complexation of alkali metals. The partial-cone conformers showed the widest range of  $pH_{1/2}$  from 7.5 to 8.7, while this range in cone and 1,2-alternate conformers were determined to be 7.7-8.0 and 6.6-7.0, respectively. The  $pH_{1/2}$  in *cis*- isomers than their *trans*- analogues revealed that orient variation of pendant moieties had an influence upon the complexation of alkali metals. The *cis*- isomers presented a middle range of  $7.0 < pH_{1/2} < 8.0$ , while in the *trans*- analogues it was in  $pH_{1/2} < 7.0$  or

$pH_{1/2} > 8.0$ .

**ortho-Cone Isoconformer 1.** Using the *ortho*-cone di-ionizable *p-tert*-butylcalix[4]arene **1**, the maximum loadings were in the range of 179-197%. The results of competitive solvent extractions by ligand derivative **1** in chloroform are presented in Figure 3. Because of the selective 1:1 binding of  $Na^+$  with the ionizable moieties and unselective binding of other alkali cations with those moieties, the selectivity order for calix[4]arene derivative **1** at pH 8.0 was determined to be as  $Rb^+ & Cs^+ & K^+ < Li^+ \ll Na^+$  and the maximum  $Na^+$  loadings all exceeding 100%. This macrocycle presented a  $Na^+/Li^+$  selectivity of 4 under conditions of high loading. This reveals that the binding of different alkali metal cation species by this derivative was influenced by the pH and the identity of the dangling proton-ionizable moieties. According to Figure 3 for derivative **01**, the amount of  $Li^+$  extracted increased to its maximum loading at pH of 7.5, and then diminished as the pH increased.

Using the *ortho*-cone di-ionizable *p-tert*-butylcalix[4]arene **1**, the maximum loadings were in the range of 85-107%. The results of competitive solvent extractions by ligand derivative **1** in chloroform are presented in Figure 4. Because of the selective 1:1 binding of  $Ba^{2+}$  with the ionizable moieties and unselective binding of other alkaline

earth cations with those moieties, the selectivity order for calix[4]arene derivatives **1** at pH 9.0 was determined to be as  $Mg^{2+} < Sr^{2+} < Ca^{2+} < Ba^{2+}$  and the maximum  $Ba^{2+}$  loadings all exceeding 40%. This macrocycle presented a  $Ba^{2+}/Ca^{2+}$  selectivity of 2 under conditions of high loading. This reveals that the binding of different alkaline earth metal cation species by this derivative was influenced by the pH and the identity of the dangling proton-ionizable moieties.

**para-Cone Isoconformer 2.** Using the *para*-cone di-ionizable *p*-*tert*-butylcalix[4]arene **2**, the maximum loadings were in the range of 197-224%. The results of competitive solvent extractions by this derivative in chloroform are depicted in Figure 3. Owing to the selective 1:1 binding of  $Na^+$  with the ionizable moieties and unselective binding of other alkali cations with those moieties, the selectivity order for calix[4]arene derivative **2** at pH 7.5 was determined to be as  $K^+ & Rb^+ & Cs^+ < Li^+ \ll Na^+$  and the maximum  $Na^+$  loadings all exceeding 100%. This macrocycle presented a  $Na^+/Li^+$  selectivity of 4 under conditions of high loading. According to Figure 3, the amount of  $Li^+$  extracted increased to its maximum loading at pH of 8.5.

Using the *para*-cone di-ionizable *p*-*tert*-butylcalix[4]arene **2**, the maximum loadings were in the range of 97-115%. The results of competitive solvent extractions by ligand derivative **2** in chloroform are depicted in Figure 4. Owing to the selective 1:1 binding of  $Ba^{2+}$  with the ionizable moieties and unselective binding of other alkaline earth metal cations with those moieties, the selectivity order for calix[4]arene derivative **2** at pH 9.0 was determined to be as  $Mg^{2+} < Sr^{2+} < Ca^{2+} < Ba^{2+}$  and the maximum  $Ba^{2+}$  loadings all exceeding 45%. This macrocycle presented a  $Ba^{2+}/Ca^{2+}$  selectivity of 2 under conditions of high loading.

**cis-1,2-alternate Isoconformer 3.** The results of competitive solvent extractions by ligand derivative **3** in chloroform are presented in figure 3. Using the di-ionizable *cis*-1,2-alternate *p*-*tert*-butylcalix[4]arene **3**, the maximum loadings were in the range of 150-183%. Because of the selective 1:1 binding of  $Na^+$  with the ionizable moieties and unselective binding of other alkali cations with those moieties, the selectivity order for calix[4]arene derivative **3** at pH 7.0 was determined to be as  $Li^+ & Na^+ & Cs^+ < Rb^+ \ll K^+$  and the maximum  $K^+$  loadings all exceeding 60%. This macrocycle presented a  $Na^+/Li^+$  selectivity of 2.0 under conditions of high loading.

The results of competitive solvent extractions by ligand derivative **3** in chloroform are presented in Figure 4. Using the di-ionizable *cis*-1,2-alternate *p*-*tert*-butylcalix[4]arene **3**, the maximum loadings were in the range of 95-108%. Because of the selective 1:1 binding of  $Ba^{2+}$  with the ionizable moieties and unselective binding of other alkaline earth metal cations with those moieties, the selectivity order for calix[4]arene derivative **3** at pH 9.0 was determined to be as  $Mg^{2+} < Sr^{2+} < Ca^{2+} < Ba^{2+}$  and the maximum  $Ba^{2+}$  loadings all exceeding 50%. This macrocycle presented a  $Ba^{2+}/Ca^{2+}$  selectivity of 2 under conditions of high loading.

**ortho-trans-1,2-alternate Isoconformer 4.** Using the *ortho-trans*-1,2-alternate di-ionizable *p*-*tert*-butylcalix[4]-

arene **4**, the maximum loadings were in the range of 241-284%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. Owing to the unselective binding of all alkali metal cations with the moieties, the low selectivity order for calix[4]arene derivative **4** at pH 7.5 was determined to be as  $Li^+ < Na^+ & Cs^+ < K^+ < Rb^+$  and the maximum  $Rb^+$  loadings all exceeding 80%. This macrocycle presented an  $Rb^+/K^+$  selectivity of 1.5 in derivative **1** under conditions of high loading.

Using the *ortho-trans*-1,2-alternate di-ionizable *p*-*tert*-butylcalix[4]arene **4**, the maximum loadings were in the range of 112-128%. The results of competitive solvent extractions by ligand derivative **4** in chloroform are presented in Figure 4. Owing to the unselective binding of all alkaline earth metal cations with the moieties, the low selectivity order for calix[4]arene derivative **4** at pH 7.0 was determined to be as  $Mg^{2+} < Sr^{2+} < Ca^{2+} < Ba^{2+}$  and the maximum  $Ba^{2+}$  loadings all exceeding 50%. This macrocycle presented no  $Ba^{2+}/Ca^{2+}$  selectivity but a good  $Ba^{2+}, Ca^{2+}$  versus both  $Sr^{2+}$  and  $Mg^{2+}$  selectivity under conditions of high loading to be 3 and 6, respectively.

**para-trans-1,2-alternate Isoconformer 5.** Using the *para-trans*-1,2-alternate di-ionizable *p*-*tert*-butylcalix[4]arene **5**, the maximum loadings were in the range of 240-294%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. Due to the unselective binding of all alkali metal cations with the di-ionizable moieties, the poor selectivity order for calix[4]arene derivative **5** at pH 8.0 was determined to be as  $Li^+ < Na^+ & Cs^+ < K^+ < Rb^+$  and the maximum  $Rb^+$  loadings all exceeding 80%. This macrocycle showed an  $Rb^+/K^+$  selectivity of 1.5 under conditions of high loading.

Using the *para-trans*-1,2-alternate di-ionizable *p*-*tert*-butylcalix[4]arene **5**, the maximum loadings were in the range of 125-140%. The results of competitive solvent extractions by ligand derivative **5** in chloroform are presented in Figure 4. Due to the unselective binding of all alkaline earth metal cations with the di-ionizable moieties, the poor selectivity order for calix[4]arene derivative **5** at pH 8.0 was determined to be as  $Mg^{2+} < Sr^{2+} < Ca^{2+} < Ba^{2+}$  and the maximum  $Ba^{2+}$  loadings all exceeding 55%. This macrocycle presented small  $Ba^{2+}/Ca^{2+}$  selectivity and a good  $Ba^{2+}, Ca^{2+}$  versus both  $Sr^{2+}$  and  $Mg^{2+}$  selectivity under conditions of high loading to be 3 and 6, respectively.

**ortho-cis-Partial Cone Isoconformer 6.** Using the *ortho-cis* partial-cone di-ionizable *p*-*tert*-butylcalix[4]arene **6**, the maximum loadings were in the range of 57-115%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. The unselective binding of alkali metal cations with the ligand shows no selectivity order for calix[4]arene derivative **6**. The maximum  $Na^+$  loading was exceeding 25%.

This derivative did not show any binding tendency towards  $Mg^{2+}$  and  $Be^{2+}$ . Using the *ortho-cis*-partial cone di-ionizable *p*-*tert*-butylcalix[4]arene **6**, the maximum loadings were in the range of 34-35%. The results of competitive solvent extractions by ligand derivative **6** in chloroform are

presented in Figure 4. The unselective binding of alkaline earth metal cations with the ligand shows no selectivity order of calix[4]arene derivative **6** for  $\text{Ba}^{2+}$  versus  $\text{Ca}^{2+}$  and the selectivity of  $\text{Ba}^{2+}, \text{Ca}^{2+}$  versus  $\text{Sr}^{2+}$  was about 5. The maximum  $\text{Ba}^{2+}$  loadings all exceeding 15%.

**para-cis-Partial Cone Isoconformer 7.** Using the *para-cis* partial-cone di-ionizable *p-tert*-butylcalix[4]arene **7**, the maximum loadings were in the range of 59-112%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. Using this macrocycle, the maximum  $\text{Na}^+$  loading was exceeding 25% and there was a poor selectivity towards the cations.

This derivative did not show any binding tendency towards  $\text{Mg}^{2+}$  and  $\text{Be}^{2+}$ . Using the *para-cis*-partial cone di-ionizable *p-tert*-butylcalix[4]arene **7**, the maximum loadings were in the range of 33-37%. The results of competitive solvent extractions by ligand derivative **7** in chloroform are presented in Figure 4. Using this macrocycle, the maximum  $\text{Ba}^{2+}$  loadings all exceeding 15% and there is a good selectivity toward  $\text{Sr}^{2+}$  and a poor selectivity towards  $\text{Ba}^{2+}$  and  $\text{Ca}^{2+}$  cations.

**ortho-trans-Partial Cone Isoconformer 8.** Using the *ortho-trans* partial-cone **8**, the maximum loadings were in the range of 17-24%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. These derivatives did not show any binding tendency towards  $\text{Cs}^+$  and  $\text{Rb}^+$ . Due to the selective 1:1 binding of  $\text{K}^+$  with the ionizable moieties and unselective binding of other alkali cations, the selectivity order for calix[4]arene derivative **8** at pH 8.0 was determined to be as  $\text{Li}^+ < \text{Na}^+ < \text{K}^+$  and the maximum  $\text{K}^+$  loadings all exceeding 12%. This macrocycle presented a  $\text{K}^+/\text{Li}^+$  selectivity of 3,  $\text{K}^+/\text{Na}^+$  selectivity of 2.0, and  $\text{Na}^+/\text{Li}^+$  selectivity of 1.5 under conditions of high loading. This reveals that the binding of different alkali metal cation species by this derivative was influenced by the pH and the identity of the dangling proton-ionizable moieties.

Using the *ortho-trans*-partial cone **8**, the maximum loadings were in the range of 20-21%. The results of competitive solvent extractions by ligand derivative **8** in chloroform are presented in Figure 4. These derivatives did not show any binding tendency towards  $\text{Mg}^{2+}$  and  $\text{Be}^{2+}$ . Due to the selective 1:1 binding of  $\text{Ba}^{2+}$  with the ionizable moieties and unselective binding of other alkaline earth cations, the selectivity of calix[4]arene derivative **8** at pH 4.0 was  $\text{Sr}^{2+}$  in the presence of  $\text{Ba}^{2+}$  and  $\text{Ca}^{2+}$ . the maximum  $\text{Ba}^{2+}$  and  $\text{Ca}^{2+}$  loadings all exceeding 10%.

**para-trans-Partial Cone Isoconformer 9.** Using the *para-trans* partial-cone di-ionizable *p-tert*-butylcalix[4]arene **9**, the maximum loadings were in the range of 17-22%. The results of competitive solvent extractions by this derivative in chloroform are presented in Figure 3. These derivatives did not show any binding tendency towards  $\text{Rb}^+$  and  $\text{Cs}^+$ . owing to the selective 1:1 binding of  $\text{K}^+$  with the ionizable moieties and unselective binding of other alkali cations, the selectivity order for calix[4]arene derivative **9** at

pH 8.0 was determined to be as  $\text{Li}^+ < \text{Na}^+ < \text{K}^+$  and the maximum  $\text{K}^+$  loadings all exceeding 12%. This macrocycle presented the  $\text{K}^+/\text{Li}^+$ ,  $\text{K}^+/\text{Na}^+$ , and  $\text{Na}^+/\text{Li}^+$  selectivities of 3, 2, and 1.5 under high loading conditions, respectively.

Using the *para-trans*-partial cone di-ionizable *p-tert*-butylcalix[4]arene **9**, the maximum loadings were in the range of 20-23%. The results of competitive solvent extractions by ligand derivative **9** in chloroform are presented in Figure 4. These derivatives did not show any binding tendency towards  $\text{Mg}^{2+}$  and  $\text{Be}^{2+}$ . Owing to the selective 1:1 binding of  $\text{Sr}^{2+}$  with the ionizable moieties and unselective binding of other alkaline earth metal cations, the selectivity order for calix[4]arene derivative **9** at pH 4.0 was determined to be as  $\text{Ba}^{2+}, \text{Ca}^{2+} < \text{Sr}^{2+}$  and the maximum  $\text{Ba}^{2+}$ ,  $\text{Ca}^{2+}$  loadings and  $\text{Sr}^{2+}$  loading all exceeding 10% and 1%, respectively.

## Conclusion

Changing the orientation of pendant moieties from *cis*- to *trans*- as well as *ortho*- to *para*- analogues revealed no changes in the selectivity, extraction efficiency and  $\text{pH}_{1/2}$  of calix[4]arene complexes towards alkali and alkaline earth metals. Besides, alternation of ring conformation (cone, 1,2-alternate and partial cone) showed a pronounced influence upon the solvent extraction of alkali and alkaline earth metal cations.

**Acknowledgments.** This work was supported by Islamic Azad University (Shahreza branch) and Iran Nanotechnology Initiative Council.

## References

1. Mokhtari, B.; Pourabdollah, K.; Dalali, N. *J. Incl. Phenom. Macrocycl. Chem.* **2011**, *69*, 1.
2. Mokhtari, B.; Pourabdollah, K.; Dalali, N. *J. Coord. Chem.* **2011**, *64*, 743.
3. Mokhtari, B.; Pourabdollah, K.; Dallali, N. *J. Radioanal. Nucl. Chem.* **2011**, *287*, 921.
4. Mokhtari, B.; Pourabdollah, K.; Dalali, N. *Chromatographia.* **2011**, *73*, 829.
5. Mokhtari, B.; Pourabdollah, K. *Asian J. Chem.* **2011**, *23*, 1.
6. Baeyer, A. *Chem. Ber.* **1872**, *5*, 280.
7. Zinke, A.; Ziegler, E. *Chem. Ber.* **1944**, *77*, 264.
8. Gutsche, C. D.; Muthukrishnan, R. *J. Org. Chem.* **1978**, *43*, 4905.
9. Maharaj, F.; Craig, D. C.; Scudder, M. L.; Bishop, R.; Kumar, N. *J. Incl. Phenom. Macrocycl. Chem.* **2007**, *59*, 17.
10. Yang, Y.; Cao, X.; Surowiec, K.; Bartsch, R. A. *J. Incl. Phenom. Macrocycl. Chem.* **2011**, *69*, 163.
11. Atanassova, M.; Lachkova, V.; Vassilev, N.; Varbanov, S.; Dukov, I. *J. Incl. Phenom. Macrocycl. Chem.* **2007**, *58*, 173.
12. Zhang, D.; Crawford, J. D.; Bartsch, R. A. *J. Incl. Phenom. Macrocycl. Chem.* **2010**, *66*, 163.
13. Bennouna, L.; Vicens, J.; Asfari, Z.; Yahyaoui, A.; Burgard, M. *J. Incl. Phenom. Macrocycl. Chem.* **2001**, *40*, 95.
14. Rydberg, J.; Cox, M.; Musikas, C.; Choppin, G. R. *Solvent Extraction Principles and Practice*; Dekker, M., Ed.; CRC: New York, U.S.A., 2004; p 20.