Effect of Na^+ on solvent extraction of alkaline earth metal cations by proton-ionizable calix[4]arenes

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Abstract

Metal ion recognition by proton-ionizable calixarenes is often affected by interference from the Na^+ present in many aqueous solutions. To assess the Na^+-effect on calixarene selectivity towards alkaline earth metal cations (AEMC), competitive solvent extraction of Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+} from aqueous solutions into chloroform by di-ionizable calix[4]arene *N*-(trifluoromethylsulfonyl)carboxamides and corresponding carboxylic acids, conformationally mobile and restricted to *cone*, *partial cone* and *1,3-alternate* conformations, was investigated in the absence and in the presence of aqueous-phase Na^+. The extraction selectivities were found to be altered due to contrasting Na^+-induced changes in the AEMC uptake. Observed increases in loadings of smaller AEMC are rationalized by their co-extraction with Na^+.

Keywords: Na^+-effect, selectivity, alkaline earth metal cations, calix[4]arenes, solvent extraction

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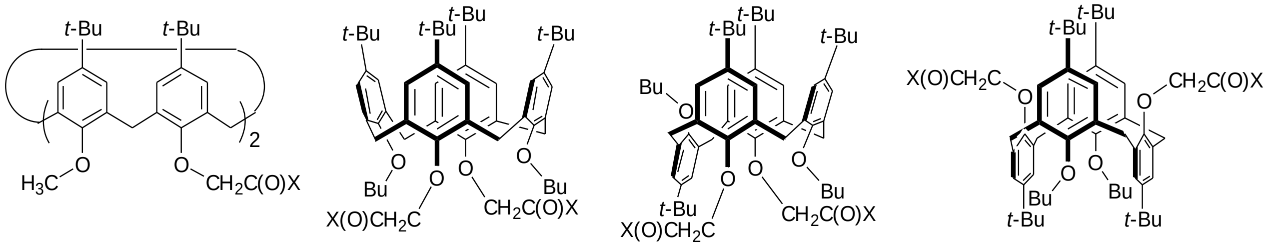
Introduction

Functionalized calixarenes find numerous applications in selective metal ion recognition and separations.[1] For such purposes, calix[4]arenes containing pendent proton-ionizable groups[2] are of special interest since these ligands generally provide stronger binding of cationic species than their neutral analogs. In particular, lower-rim 1,3-disubstituted calix[4]arene *N*-(X-sulfonyl)-carboxamides with "tunable" acidity (achieved by variation of the electron-withdrawing group X) developed by Bartsch and coworkers exhibited efficient and highly selective solvent extraction of the heavy metal species Pb^{2+} [2a] and Hg^{2+},[2b] as well as alkali and alkaline earth metal cations.[2c,2d] Attachment of such proton-ionizable groups to calix[4]-bis(crown-6) moieties yielded ionophores with unique combinations of complexation propensities, such as notably enhanced binding capability towards Cs^+[2e] and selective recognition of Tl^+ in the presence of a large excess of other metal ions.[2f] These findings were employed subsequently in the development of selective fluorescent calixarene-based chemosensors for hazardous heavy metal ions, Hg^{2+},[3a] Cs^+, Tl^+,[3b] and Pb^{2+},[3c] which were obtained by incorporation of a dansyl fluorophore as a part of the proton-ionizable *N*-(X-sulfonyl)carboxamide group. Obviously, the utility of functionalized calixarenes for metal ion recognition is determined by their selectivity.

It should be noted at this point that calix[4]arenes in general, and proton-ionizable ones in particular, possess high affinity for Na^+. For instance, di-ionizable calix[4]arene *N*-(X-sulfonyl)-carboxamides and their parent carboxylic acids in competitive solvent extraction of alkali metal cations exhibit strong preference for Na^+, with loading of this ion exceeding 100% due to formation of complexes with 2:1 Na^+-to-ligand stoichiometry.[2c,2d] Na^+, which is abundant in the environment, including water sources, often interferes with the recognition of other metal ions by calix[4]arenes. Typically, Na^+ competes with targeted metal ions in complexation with calixarenes and thereby suppresses their binding. An example of such behavior is the decrease in extraction of Pb^{2+}[2a] and of Hg^{2+}[2b] into chloroform by calix[4]arene *N*-(X-sulfonyl)carboxamides when Na^+ was present in the aqueous phase. In several publications,[4] Na^+-facilitated enhancement of solvent extraction of Cu^{2+},[4a] lanthanides(III),[4b] Th^{4+} and UO_2^{2+}[4c] by calix[4]arene tetracarboxylates in the *cone* conformation was described. However, information on similar effects for other metal ions, as well as different conformational isomers of calixarenes, remains unavailable to the best of our knowledge.

Herein we present our results for the effect of Na^+ on selectivity in solvent extraction of alkaline earth metal cations (AEMC) by a series of lipophilic, di-ionizable calix[4]arenes **1-8** (Figure 1). The ligands employed in this systematic study vary in the type of acidic functions, *i. e.*, *N*-(trifluoromethylsulfonyl)carboxamide in **1-4** and carboxylic acid in **5-8**. Also, calixarenes **1** and **5** are conformationally mobile, while the others are rigid analogs restricted to the *cone* (**2** and **6**), *partial cone* (*paco*) (**3** and **7**), and *1,3-alternate* (**4** and **8**) conformations.



Flexible
X
1: $NHSO_2CF_3$
5: OH

Cone
X
2: $NHSO_2CF_3$
6: OH

Paco
X
3: $NHSO_2CF_3$
7: OH

1,3-Alternate
X
4: $NHSO_2CF_3$
8: OH

Figure 1. Structures of di-ionizable calix[4]arenes **1-8**.

Results and Discussion

Results from competitive solvent extractions of four AEMC (Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) from basic aqueous solutions (pH 9.8; 10.0 mM in each AEMC) into $CHCl_3$ by 1.00 mM calixarenes **1**-**8** showed that selectivity of the ionophores varies with the type of the proton-ionizable group, as well as the calixarene conformation.[2d] Figure 2 presents the percent AEMC loading for the four calix[4]arene *N*-(trifluoromethylsulfonyl)carboxamide ligands. In the absence of Na^+ in the aqueous phase, flexible ligand **1** and its rigid *cone* **2** and *1,3-alternate* **4** analogs favor Ba^{2+}, while with the *paco* isomer **3**, Ca^{2+} is the best extracted AEMC. Interestingly, **1** and **2** exhibit quite similar AEMC-selectivity patterns, with metal loading increasing gradually from Mg^{2+} to Ca^{2+} to Sr^{2+} to Ba^{2+}. On the other hand, the selectivity trends for **3** and for **4** are unique. For the latter, Ba^{2+} was the only AEMC extracted in appreciable amounts.

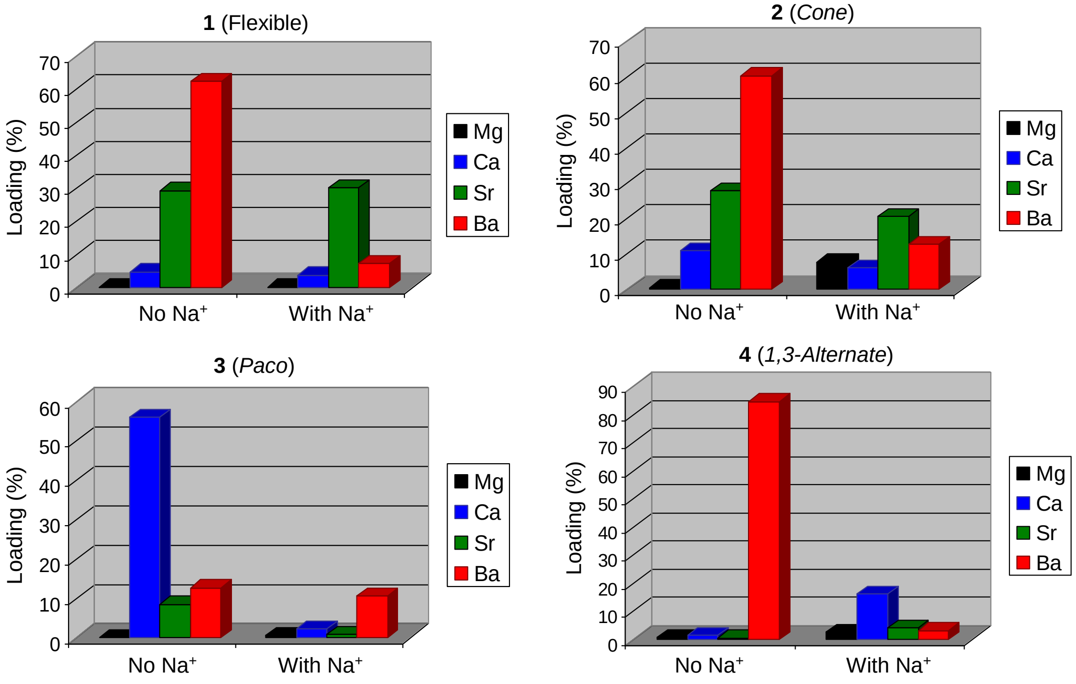


Figure 2. Competitive extraction of AEMC from 10.0 mM aqueous chloride/hydroxide solutions (pH 9.8) into $CHCl_3$ by 1.00 mM calix[4]arene *N*-(trifluoromethylsulfonyl)carboxamides **1**-**4** in the absence and in the presence of 10.0 mM Na^+ in the aqueous phase.

Under otherwise identical conditions, the four calix[4]arene carboxylic acids **5**-**8** (Figure 3) behave differently from the corresponding *N*-(trifluoromethylsulfonyl)carboxamide analogs (Figure 2). In particular, unlike Ba^{2+}-selective **1**, the flexible di(carboxylic acid) **5** exhibits a clear preference for Ca^{2+}. Its AEMC extraction propensity shows significant similarity with that of *paco* calixarene **7**. Interestingly, pairs of rigid calix[4]arene *N*-(trifluoromethylsulfonyl)-

carboxamides and analogous di(carboxylic acids) show similar AEMC extraction selectivities. Thus, the *cone* **2** and **6** and *1,3-alternate* **4** and **8**, to a different extent, favor extraction of Ba^{2+}, while both of the *paco* calixarenes, **3** and **7,** exhibit preference for Ca^{2+}. However, as far as the selectivity patterns of these ionophores are concerned, only in the *1,3-alternate* pair does the behavior of the di(carboxylic acid) closely resemble closely that of the *N*-(trifluoromethylsulfonyl)carboxamide analog (except for the much higher Mg^{2+} loading for the latter).

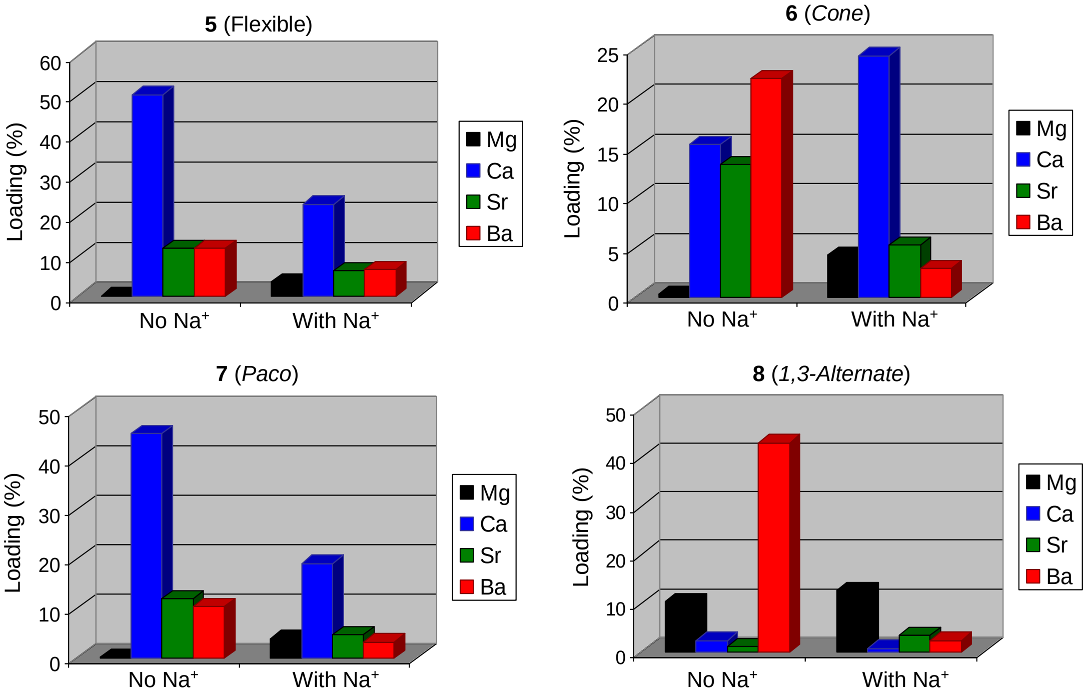


Figure 3. Competitive extraction of AEMC from 10.0 mM aqueous chloride/hydroxide solutions (pH 9.8) into $CHCl_3$ by 1.00 mM calix[4]arene di(carboxylic acids) **5-8** in the absence and in the presence of 10.0 mM Na^+ in the aqueous phase.

Upon addition to the aqueous phase (containing 10.0 mM each of Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) of an equimolar amount of Na^+ under otherwise unchanged conditions, the total AEMC loading for calixarenes **1-8** in generally shows a considerable decline (Table 1). However, the presence of Na^+ has dissimilar effects on the extraction of different AEMC, which results in significant changes in the selectivity patterns for most of the ligands studied herein (Figures 2 and 3 and Table 1).

In particular, decreased efficiency of Ba^{2+} extraction in the presence of Na^+ was observed for nearly all of the calixarenes. This effect is especially dramatic for the ligands that originally exhibited Ba^{2+}-selectivity. Thus, Ba^{2+}-loadings of *1,3-alternate* **4** and **8** diminished by factors of 27 and 17, respectively. For flexible **1** and *cone* **2** and **6**, the diminution factors were (approximately) 9, 5, and 8, respectively. On the other hand, Ba^{2+}-loading of *paco* **3** was scarcely affected by the presence of Na^+ in the aqueous phase. For none of the ligands was Na^+-induced enhancement of Ba^{2+} extraction observed.

Table 1. Effect of aqueous phase Na^+ on the extraction of AEMC into $CHCl_3$ by di-ionizable calix[4]arenes[a]

Calixarene (conformation)	No Na^+		With Na^+	
	Best extracted cation	Total AEMC loading (%)	Best extracted cation	Total AEMC loading (%)
1 (flexible)	Ba^{2+}	96.7	Sr^{2+}	41.3
2 (*cone*)	Ba^{2+}	99.5	Sr^{2+}	47.3
3 (*paco*)	Ca^{2+}	77.4	Ba^{2+}	14.2
4 (*1,3-alternate*)	Ba^{2+}	87.2	Ca^{2+}	26.1
5 (flexible)	Ca^{2+}	74.6	Ca^{2+}	40.0
6 (*cone*)	Ba^{2+}	51.0	Ca^{2+}	36.7
7 (*paco*)	Ca^{2+}	67.9	Ca^{2+}	31.1
8 (*1,3-alternate*)	Ba^{2+}	56.8	Mg^{2+}	19.2

[a] Aqueous phase: 10.0 mM AEMC, 10.0 mM Na^+, pH 9.8. Organic phase: 1.00 mM calixarene in $CHCl_3$.

In contrast, for competitive AEMC extraction in the presence of Na^+, all of the calixarenes but **1** demonstrated increased uptake of Mg^{2+} (which normally is the least extracted AEMC). The most significant enhancements in Mg^{2+} loading were observed for **2**, **5**, and **7** (factors of 26, 28, and 23, respectively). However, Na^+ had an opposite effect on Mg^{2+} extraction by flexible calixarene **1**, for which Mg^{2+} loading decreased by nearly 2-fold.

As far as extractions of Ca^{2+} and Sr^{2+} are concerned, the outcome for the presence of aqueous phase Na^+ varied for the different calixarenes. Thus, Na^+ suppressed the uptake of Ca^{2+} by a majority of the ligands. The most significant, a 25-fold reduction of Ca^{2+} loading, was observed for *paco* **3**, which in the absence of Na^+ showed appreciable selectivity for this AEMC (Figure 2). However, under the same conditions, extraction of Ca^{2+} by *cone* **6** and *1,3-alternate* **4** (both originally selective for Ba^{2+}) improved by factors of 13 and 10, respectively. In the presence of Na^+, extraction of Sr^{2+} was increased for both of the *1,3-alternate* calixarenes (10-fold for **4** and 3-fold for **8**). In contrast, it remained essentially unchanged for ligands **1** and **2** and decreased to different extents for the rest of the calixarenes.

The differing changes in extraction efficiencies of the four AEMC described above resulted in Na^+-induced modification of the selectivity patterns for most of the proton-ionizable calixarenes in this study. Interestingly, due to the Na^+-effect, all of the calix[4]arene *N*-(trifluoromethylsulfonyl)carboxamides altered their AEMC preferences (Table 1). Among the corresponding di(carboxylic acid)s, change of the best extracted AEMC was observed for the *cone* and *1,3-alternate* isomers; whereas it remained the same for the flexible and *paco* analogs.

The observed decline in AEMC loadings for **1**-**8** due to competition with Na^+ is not surprising. Na^+ (Pauling ionic radius of 0.095 Å) is extracted into chloroform very efficiently by both flexible di-ionizable calix[4]arenes **1** and **5** and all three of the rigid conformers **2**-**4**. Nevertheless, this metal ion shows strong preference for *cone* and *paco* geometries of the ligands. Based on ^1H NMR spectroscopic data, complexation with Na^+ in $CDCl_3$ organizes flexible ionophore **1** to the *cone* (about 40%) and *paco* (60%) conformations.[5] Under the same conditions, a *paco* conformation is also favored by Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+} (Pauling ionic radii of 0.065, 0.098, 0.113, and 0.135 Å, respectively). At least 90% of the molecules of flexible **1** adopted this conformation in the complexes with each of the AEMC in $CDCl_3$ solution.[2d] In addition to similar conformational preferences, Na^+ and AEMC tend to form coordinate bonds with oxygen donor atoms of ether, carboxyl and amide groups. In solid-state structures of Na^+ complexes with calix[4]arene amide ligands in the *cone* conformation,[6] the metal ion is positioned nearly symmetrically in the cavity formed by the lower rim phenol and carbonyl oxygens and appears to be a perfect fit for this coordination environment.

On the other hand, the reason for enhancement of AEMC extraction by di-ionizable calixarenes in the presence of Na^+ in the aqueous phase is not as obvious. In earlier publications,[4a,4b] it was proposed that Na^+ coordinated on the lower rim of calix[4]arene carboxylates preorganizes pendent functional groups of the ligand in a way that promotes co-extraction of other appropriately sized metal ions and discourages binding of cations having ionic radii too large to fit in this coordination arrangement. This model was used to explain the Na^+-induced change of extraction selectivity for *cone* calix[4]arene tetra(carboxylic acids) from light, larger lanthanide(III) ions to heavier, smaller ones.[4b]

Adopting a co-extraction hypothesis to justification of the Na^+-effect on the AEMC selectivity for di-ionizable calixarenes **1**-**8**, the following scheme (Figure 4) is suggested. Figure 4a shows a possible Na^+-AEMC co-extraction by a *cone*-shaped calix[4]arene; the *paco* (preferred by both Na^+ and AEMC) and *1,3-alternate* analogs are expected to be capable of similar behavior (Figure 4b). Indeed, as was described above, extraction efficiency for the smallest AEMC, Mg^{2+}, improved in the presence of Na^+ for all of the ligands employed in this study, both flexible and rigid; while uptake of the largest cation, Ba^{2+}, decreased under the same conditions. In terms of the co-extraction model, Mg^{2+} with a smaller ionic radius than Na^+ should be the most appropriate AEMC for coordination by the Na^+-preorganized calixarene (Figure 4). On the other hand, Ba^{2+} is oversized for co-extraction with Na^+ and simply competes with Na^+ in complexation with all of the calixarenes. The other two AEMC, Ca^{2+} (with an ionic radius nearly same as that of Na^+) and Sr^{2+} (larger than Na^+, but significantly smaller than Ba^{2+}), may either compete or be co-extracted with Na^+, depending on the ligand type, which leads to decrease or enhancement, respectively, of the ligand loadings for these metal cations.

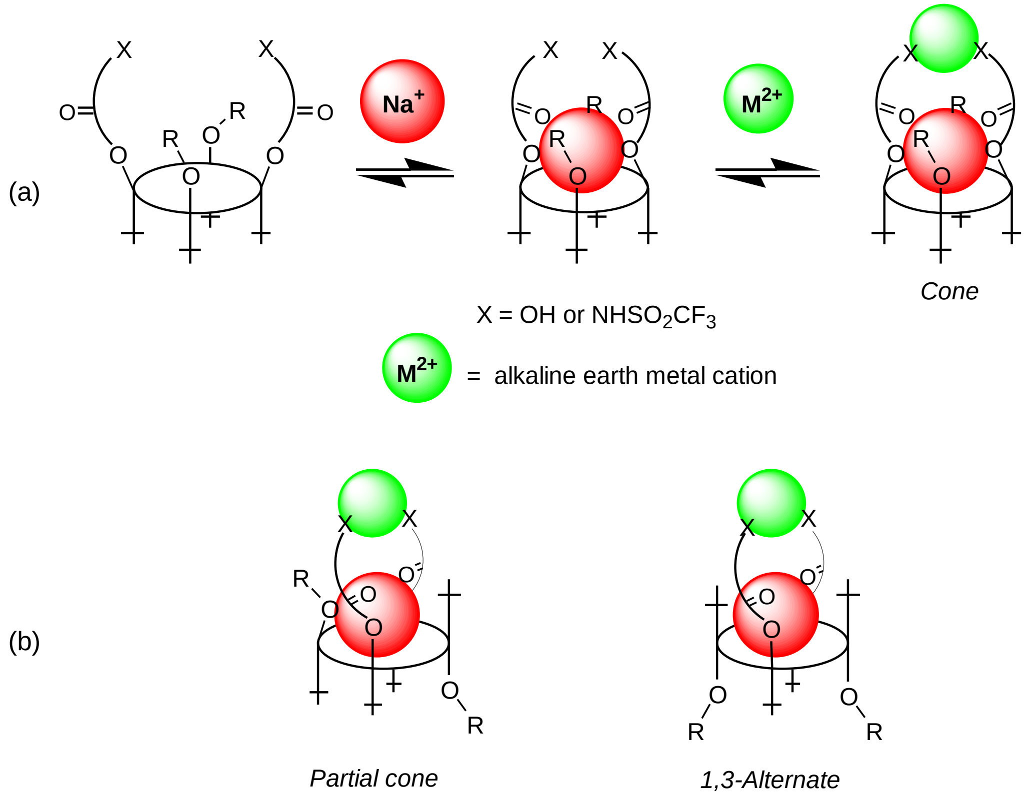


Figure 4. Schematic presentation of a possible Na^+ and AEMC co-extraction with di-ionizable calix[4]arenes **1-8**: (a) shown for a calixarene in the *cone* conformation; (b) analogous structures envisioned for the *partial cone* and *1,3-alternate* calixarenes.

Interestingly, the efficiencies of Ca^{2+} and Sr^{2+} extraction by *1,3-alternate* calixarene isomers (especially **4**) showed a tendency to increase in the presence of Na^+ (Figures 2 and 3). Hence, it was desirable to obtain an additional support for co-extraction of Na^+ and these two AEMC by the *1,3-alternate* ligands. As follows from the scheme in Figure 4, co-extraction of Na^+ and M^{2+} (where M^{2+} is Mg^{2+}, Ca^{2+}, Sr^{2+}, or Ba^{2+}) with a calixarene proceeds via formation of a 1:1:1 stoichiometry complex. Therefore, it was supposed that changes in the formal concentration of the ligand in chloroform at invariable aqueous solution pH and formal metal concentrations may alter the amounts of extracted Na^+ and M^{2+}, but should not affect considerably the molar ratio of the two metal cations in the organic phase after extraction. To test this assumption, competitive extraction of pairs of metal ions, Na^+-Ca^{2+} and Na^+-Sr^{2+}, from 10.0 mM aqueous solutions (pH 11.7) into $CHCl_3$ by *1,3-alternate* calixarene **4** was studied with organic phase ligand concentrations of 0.50 and 1.0 mM. The results obtained are presented in Table 2 as the percent metal loadings of **4** and the corresponding Na^+/M^{2+} loading ratios. These data show that two-fold increase in the formal calixarene concentration had no significant effect on the Na^+/Ca^{2+} and Na^+/Sr^{2+} molar ratios in the organic solution after extraction, which supports the proposal of these metal ions being co-extracted by **4**. In order to establish the real structures of the formed mixed Na^+-AEMC-calixarene complexes, an additional study involving X-ray crystallography would be needed, which is out of the scope of this paper.

Table 2. Competitive extractions of Na^+ and Ca^{2+} and of Na^{2+} and Sr^{2+} from the 10.0 mM aqueous solutions (pH 11.7) into $CHCl_3$ by *1,3-alternate* calix[4]arene *N*-(trifluoromethylsufonyl)-carboxamide **4**

AEMC	Concentration of **4** (mM)	Metal loading (%)		Loading ratio
		Na^+	Ca^{2+}	Na^+/Ca^{2+}
Ca^{2+}	0.50	148.3	27.5	5.4
	1.0	146.6	26.7	5.5
Sr^{2+}		Na^+	Sr^{2+}	Na^+/Sr^{2+}
	0.50	172.4	10.9	15.8
	1.0	174.4	11.9	15.6

Conclusions

AEMC extraction selectivity of di-ionizable calix[4]arene *N*-(trifluoromethylsulfonyl)carboxamides and corresponding carboxylic acids, both flexible and fixed in the *cone*, *paco*, and *1,3-alternate* conformations, may be altered by the presence of aqueous phase Na^+. Unlike the largest metal ion in the series, Ba^{2+}, the percent loading of the smallest Mg^{2+} and, in some cases, of Ca^{2+} and Sr^{2+}, tends to increase, supposedly, as a result of Na^+-AEMC co-extraction via formation of the mixed-metal complex with the calixarene ligand.

Experimental Section

General. Calixarenes used in this study were prepared by published procedures: **1** and **5**,[2a] **2-4**,[2d] **6**,[2b] **7** and **8**.[7] Anhydrous NaCl and alkaline earth metal chlorides from commercial suppliers were dried in an oven according to standard procedures and stored in a desiccator. Alkaline earth metal hydroxides were used as received. Concentrations of Na^+ and AEMC in aqueous solutions were determined with a Dionex DX-120 or Dionex ICS-1000 ion chromatograph. Samples for solvent extraction were shaken with a Glas-Col® Multi-Pulse Vortexer. The pH was measured with a Fisher Scientific Accumet® 50 pH/ion/conductivity meter.

Competitive extraction of AEMC and Na^+. An aqueous solution of 10.0 mM in each of the Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} chlorides/hydroxides at pH 9.8 was extracted by 1.0 mM ligand in $CHCl_3$ by the published procedure.[2d] In the experiments on AEMC extraction in the presence of Na^+, the aqueous phase also contained 10.0 mM NaCl. After extraction, the separated organic phase was stripped with aqueous 0.10 M HCl, and AEMC and Na^+ concentrations in the stripping solution were determined by ion chromatography. The extraction experiments were performed in triplicate; the reported results averages with standard deviations within 5% of the stated values.

For studies of competitive extraction of 10.0 mM binary mixtures Na^+-Ca^{2+} and Na^+-Sr^{2+} by calixarene **4**, the aqueous phase pH was adjusted to 11.7 and the ligand concentrations in $CHCl_3$ were 0.50 and 1.0 mM.

Acknowledgements

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References

1. For example, (a) Ludwig, R. *Fresenius J. Anal. Chem.* **2000**, *367*, 103. (b) *Calixarenes in Action*; Mandolini, L.; Ungaro, R. Eds.; World Scientific, 2000; 284 pp. (c) Ikeda, A.; Shinkai, S. *Chem. Rev*. **1997**, *97*, 1713. (d) Arora, W.; Chawla, H. M.; Singh, S. P. *Arkivoc* **2007**, (ii) 172.
2. (a) Talanova, G. G.; Hwang, H.-S.; Talanov, V. S.; Bartsch, R. A. *Chem. Commun.* **1998**, 419. (b) Talanova, G. G.; Hwang, H.-S.; Talanov, V. S.; Bartsch, R. A. *Chem. Commun.* **1998**, 1329. (c) Talanova, G. G.; Talanov, V. S.; Gorbunova, M. G.; Hwang H.-S.; Bartsch, R. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 2072. (d) Talanova, G. G.; Talanov, V. S.; Hwang H.-S.; Park, C.; Surowiec, K.; Bartsch, R. A. *Org. Biomol. Chem.* **2004**, *2*, 2585. (e) Talanov, V. S.; Talanova, G. G.; Gorbunova, M. G.; Bartsch, R. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 209. (f) Talanova, G, G,; Roper, E. D.; Buie, N. M.; Gorbunova, M. G.; Bartsch, R. A.; Talanov, V. S. *Chem. Commun*. **2005**, 5673.
3. (a) Talanova, G. G.; Elkarim, N. S. A.; Talanov, V. S.; Bartsch, R. A. *Anal. Chem.* **1999**, *71*, 3106. (b) Roper, E. D.; Talanov, V. S.; Gorbunova, M. G.; Bartsch, R. A.; Talanova, G. G. *Anal. Chem*. **2007**, *79*, 1983. (c) Buie, N. M.; Talanov, V. S.; Butcher, R. J.; Talanova, G. G. *Inorg. Chem*. **2008**, *47*(9), 3549.
4. (a) Ohto, K.; Shiratsuchi, K.; Inoue, K.; Goto, M.; Nakashio, F.; Shinkai, S.; Nagasaki, T. *Solv. Extr. Ion Exch*. **1996**, *14*, 459. (b) Ohto, K.; Yano, M.; Inoue, K.; Nagasaki, T.; Goto, M.; Nakashio, F.; Shinkai, S. *Polyhedron* **1997**, *16*, 1655. (c) Montavon, G.; Duplatre, G.; Asfari, Z.; Vicens, J. *Solv. Extr. Ion Exch*. **1997**, *15*, 169.
5. Talanov, V. S.; Hwang, H.-S.; Bartsch, R. A. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1103.

6. (a) Baklouti, L.; Abidi, R.; Thuery, P.; Nierlich, M.; Asfari, Z.; Vicens, J. *J. Incl. Phenom. Macrocycl. Chem.***2001**,*40*(4),323. (b) Moser, A.; Yap, G. P. A.; Detellier, C. *J. Chem. Soc*., *Dalton Trans*. **2002**, 428.
7. Talanov, V. S.; Bartsch, R. A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1957.