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Extraction and complexation of alkali and alkaline earth metal cations by lower-rim calix[4]arene diethylene glycol amide derivatives

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The novel calix[4]arene derivatives, 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis(N-(2-(2-methoxy)ethyl)carbamoyl methoxy)calix[4]arene (1) and 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetra(N,N-bis(2-(2-methoxy)ethyl)carbamoyl methoxy)calix[4]arene (2), were prepared by introducing diethylene glycol subunits at a lower calixarene rim. Complexation affinities of these compounds towards alkali and alkaline earth metal cations were studied at 25 °C in acetonitrile and methanol by means of spectrophotometric, conductometric, and potentiometric titrations. The stability constants of the corresponding complexes with 1:1 (cation:ligand) stoichiometry were determined (in some cases only estimated), and their values obtained by different methods were in good agreement. Much lower stabilities of the complexes with secondary-amide derivative (1) compared to those with tertiary-amide one (2) were observed. That was presumably mostly caused by the presence of intramolecular NH···O=C hydrogen bonds in the former case. It was found that solvent significantly affected the stability of the complexes, whereby the prepared calixarenes showed considerably higher affinities for cations in acetonitrile than in methanol. Generally, the ligands studied showed better binding abilities for alkaline earth than for alkali metal cations. The extraction of metal picrates from water to dichloromethane by complexion of metal ions with ligands 1 and 2 was also investigated. In accordance with the complex stabilities, all cations were extracted fairly well (in some cases even excellently) with tertiary-amide derivative, whereas that was not the case in the extraction experiments with the other ligand studied.

Secondary- 11–13 and tertiary-amide 14–16 calixarene derivatives were shown to have particularly high affinity towards alkali and alkaline earth metal cations. Formation of intramolecular NH···O=C hydrogen bonds in tetrasubstituted secondary-amide derivatives was proven to have strong influence on the binding properties of such ligands. 12,13,17–24 In addition to the above mentioned calixarene size and binding groups nature, its affinity towards metal cations depends strongly on the reaction medium, i.e. on the solvent used. 11–14,17,25–31

Several ethylene glycol-based calixarene derivatives have been reported previously. 1,32–39 The first oxyalkylated p-tert-butylphenol–formaldehyde oligomers (both linear and cyclic) were developed as demulsifiers for petroleum industry. 1 Calixarene crown ethers with ethylene glycol substituents at the lower rim were shown to selectively bind sodium, potassium, and cesium cations. 32,33 Another interesting group of compounds are bis-calixarenes, also known as calix-tubes, which possess two calixarene skeletons bridged by ethylene glycol or various polyethylene glycol (PGE) chains. 34 Calixarene derivatives with a large number of attached (poly)ethylene glycol groups have an increased hydrophilic character, and have found application as agents for extraction of metal cations from aqueous to organic phase. 35–37 In order to optimize the structure of calix[4]arene derivatives for metal-ion biphasic extraction and phase-transition catalysis, Shinkai et al. 35 prepared several amphiphilic calix[4]arene derivatives by introducing hydrophobic groups at the upper calixarene rim.

Introduction
Complexation properties of calixarene derivatives have been extensively studied due to their ability to selectively bind a wide variety of guest species. 1–3 Numerous macrocyclic receptors have been prepared by functionalization of calixarenes at the lower and/or upper rim. By choosing adequate number of phenolic units and appropriate substituents, it has been possible to prepare selective and efficient calixarene hosts for cations, 4,5,6,7 anions, 4,6,7 and neutral species. 4,8–10 The p-tert-butylcalix[4]arene derivatives containing carbonyl groups at the lower rim (ketones, esters, amides) were reported to possess excellent properties for binding alkali, alkaline earth, and transition metal cations. 5,11 Secondary- 11–13 and tertiary-amide 14–16 calixarene derivatives have found application as agents for extraction of metal cations from aqueous to organic phase. 8,9,11–13,17,25–31

Calixarene crown ethers with ethylene glycol substituents at the lower rim were shown to selectively bind sodium, potassium, and cesium cations. 32,33 Another interesting group of compounds are bis-calixarenes, also known as calix-tubes, which possess two calixarene skeletons bridged by ethylene glycol or various polyethylene glycol (PGE) chains. 34 Calixarene derivatives with a large number of attached (poly)ethylene glycol groups have an increased hydrophilic character, and have found application as agents for extraction of metal cations from aqueous to organic phase. 35–37 In order to optimize the structure of calix[4]arene derivatives for metal-ion biphasic extraction and phase-transition catalysis, Shinkai et al. 35 prepared several amphiphilic calix[4]arene derivatives by introducing hydrophobic groups at the upper calixarene rim.
and oligo(ethylene glycol) chains at the lower one. In the
course of an extraction process, the latter hydrophilic groups
penetrate to the aqueous layer, whereas the hydrophobic
calixarene basket remains in a non-polar organic layer. In that
way such compounds can efficiently bind cations in aqueous
phase and transfer them to the organic one. Interestingly,
the length of the hydrophilic chains does not significantly affect
the ligand extraction and phase-transfer catalysis properties.
On the other hand, the receptor can be improved in these
respects by increasing its overall lipophilicity, which can be
accomplished by appending the larger lipophilic functionalities
to the upper calixarene rim. \(^{14}\) Roundhill et al. \(^{36}\) synthesized a
number of polyethylene glycol functionalized calix[4]arenes by
introducing PEG groups at both calixarene rims, and the
obtained compounds were envisaged as potential efficient
metal-ion host molecules and extracting agents. A larger
ethylene glycol-based calix[6]arene derivative \(^{37}\) was
investigated as catalyst and extraction agent for alkali metal
cations, whereby the solvent effect on the ligand abilities was
proven to be of great importance. Shi and Zhang \(^{38}\) reported a
water-soluble \(p\)-tert-butyl-calix[8]arene bearing PGE chains
which was capable of efficiently binding organic molecules and
ions in its hydrophobic cavity. Most recently, pegylated
octopus-shaped calix[4]arenes with different degree of
polyoxyethylation of the lower-rim substituents were
described as promising supramolecular drug delivery
platforms. \(^{39,40}\) To the best of our knowledge, there is only one
calix[4]arene amide derivative bearing diethylene glycol chains
bound to the amide nitrogen atoms reported in the
literature, \(^{41}\) which was studied as anion \(^{42}\) and amino acids
\(^{43–44}\) receptor.

In this work, we present the syntheses of calix[4]arene
amide derivatives with diethylene glycol functionalities
 appended to amide group at the lower rim, and the study of
their complexation affinities towards alkali and alkaline earth
metal cations in two solvents with different solvation and
hydrogen-bonding abilities (methanol, MeOH, and acetonitrile,
MeCN). In addition, the efficiencies of the extraction of cations
from water to chloroform with both ligands has been
investigated and discussed.

**Results and discussion**

**Syntheses**

The syntheses of diethylene glycol calixarenes 1 and 2 were
performed in several reaction steps, as shown in Scheme 1. Compound 1 was prepared via aminolysis (i) of the \(p\)-tert-
butyl-calix[4]arene tetraethyl ester with 2-[2-methoxyethoxy]
ethanamine with 90 % yield, as described in the Experimental
section. Compound 2 was synthesized by the modified method
described previously, using tetra acid chloride \(p\)-tert-
butyl-calix[4]arene, \(^{45}\) starting from the corresponding
tetraester (cone conformation) by (ii) hydrolysis to the
tetraacid, (iii) activation to the acid chloride, and (iv) amide
bond formation (65 % yield). For both compounds an
additional purification step was required to ensure that all of
the ions were removed, and this was done in a similar manner
as described in ref. 46. Details of purification procedure are
described in the Experimental section.

![Scheme 1](image_url)

Calixarene derivatives 1 and 2 were characterized by
spectroscopic methods and mass spectrometry. The \(^1H\) NMR
spectra of compounds 1 and 2 (CDCl\(_3\)) showed the pattern
characteristic of \(p\)-tert-butyl-calix[4]arene in a cone
conformation and approximately \(C_4\) symmetry of
tetrasubstituted calix[4]arene. \(^{19}\) Two singlets appeared, one
corresponding to tert-butyl groups (1.10 ppm, 1.09 ppm) and
another due to the calixarene aromatic protons (6.79 ppm,
6.77 ppm). In addition, two doublets assigned to the equatorial
(3.16 ppm, 3.26 ppm) and axial (4.65 ppm; 5.07 ppm) bridging
methylene protons could be found. In the spectrum of
compound 1, a rather high chemical shift of the amide protons
(7.94 ppm) indicated the presence of intramolecular NH–O=C
hydrogen bonds between the amide groups of the lower-rim
substituents. \(^{19,20}\) The FTIR data were fully in agreement with
NMR results. In the spectrum of 1 the NH stretching band at
3373 cm\(^{-1}\) corresponded to intramolecular hydrogen-bonds
between the amide groups. Positive ESI mass spectra of
compounds 1 and 2 were acquired in acetonitrile. The signals
of singly- \([M+H]^+\) and doubly- \([M+2H]^2+\) protonated ions, as
well as that of adducts with alkali metal cations \([M+Na]^+\),
\([M+H+Na]^+\), and \([M+H+K]^+\) \(^{21}\) were observed (see ESI, Figs. S1
and S2). The \([M+H]^+\) ions of the ligands were isolated and
MS/MS experiments were performed at different collision
energies. Product ion spectra are shown in Figs. S3 and S4
(ESI). The fragmentation of both derivatives was very similar,
the loss of substituent(s) on amide nitrogen atom was
observed as well as the cleavage of C–O bonds, including
phenolic and ether oxygen atoms. The formation of
carbocation was noticed in the case of 2, and the signal at m/z 262 was assigned to the fragment ion C$_{12}$H$_2$N$_4$O$^+$. The proposed fragmentation pathways of 1 and 2 are shown in Schemes S1 and S2 (ESI).

Cation complexation studies

The hypochromic effect on the UV spectra of the acetonitrile solutions of 1 and 2 was observed upon stepwise addition of LiClO$_4$, NaClO$_4$, KClO$_4$, RbNO$_3$, CsNO$_3$, Mg(ClO$_4$)$_2$, Ca(ClO$_4$)$_2$, Sr(ClO$_4$)$_2$, and Ba(ClO$_4$)$_2$ (Figs. S5–S18, ESI) solutions. In addition, an isosbestic point at 256 nm appeared in the case of ligand 1 titrations with Mg(ClO$_4$)$_2$ (Fig. S12, ESI) and Ba(ClO$_4$)$_2$ (Fig. 1). Isosbestic points were also observed in ligand 2 titrations with Rb$^+$ (251 nm), Cs$^+$ (254 nm), and Ba$^{2+}$ (255 nm) (Figs. S10, S11, and S18, ESI).

Linear dependence of absorbance at 277 nm on the amount of cation added up to the ratio n(cation)/n(ligand) = 1, followed by the break in the titration curve, indicated a strong complexation and formation of 1:1 complexes (Fig. 1; the corresponding stability constants could only be estimated, Table 1). This was observed in all above mentioned titrations, except in that of 1 with KClO$_4$ and RbNO$_3$, and those of both 1 and 2 with CsNO$_3$. In the case of complexes K1$^+$ and Cs2$^+$, their stability constants could be determined spectrophotometrically (Fig. 2, Fig. S11, ESI, Table 1). Addition of RbNO$_3$ and CsNO$_3$ into the calixarene derivative 1 acetonitrile solution had no significant effect on its UV spectrum, indicating that under the conditions used no observable complexation took place.

![Figure 1](image1.png)

**Figure 1.** (a) Spectrophotometric titration of 1 (c = 1.89 × 10$^{-4}$ mol dm$^{-3}$) with Ba(ClO$_4$)$_2$ (c = 1.80 × 10$^{-4}$ mol dm$^{-3}$) in acetonitrile. l = 1 cm; t = (25.0 ± 0.1) °C; n(Ba$^{2+}$)/n(1) = 0 (top curve) – 2.57 (bottom curve); the spectra are corrected for dilution. (b) Dependence of absorbance at 277 nm on n(Ba$^{2+}$)/n(1) ratio.

**Figure 2.** (a) Spectrophotometric titration of 1 (c = 2.30 × 10$^{-4}$ mol dm$^{-3}$) with KClO$_4$ (c = 2.24 × 10$^{-4}$ mol dm$^{-3}$) in acetonitrile. l = 1 cm; t = (25.0 ± 0.1) °C; n(K$^+$)/n(1) = 0 (top curve) – 5.93 (bottom curve); the spectra are corrected for dilution. (b) Dependence of absorbance at 277 nm on n(K$^+$)/n(1) ratio. ■ experimental; □ calculated.

To corroborate the findings obtained by spectrophotometry, conductometric titrations of acetonitrile solutions of alkali and alkaline earth cation salts with calixarene derivatives 1 and 2 were carried out (Figs. S19–S33, ESI). In most cases a linear decrease in molar conductivities with the addition of calixarene solutions was recorded up to a break in the titration curve at the molar ratio n(ligand)/n(cation) = 1, indicating, as for spectrophotometric titrations, a strong complexation and formation of 1:1 complexes (example can be seen in Fig. 3). The exceptions were titrations of KClO$_4$ with 1 (Fig. 4) and CsNO$_3$ with 2 (Fig. S25, ESI). By processing the data of these titrations, the stability constants of K1$^+$ and Cs2$^+$ were determined. In all the above cases, decrease in the molar conductivity was due to the lower electric mobility of the larger complexes compared to the free metal cations. Like with spectrophotometric experiments, during the conductometric titrations of RbNO$_3$...
and CsNO₃ acetonitrile solutions with ligand 1 no complexation was observed under the experimental titration conditions.

Figure 3. Conductometric titration of Mg(ClO₄)₂ (c = 1.81 × 10⁻⁴ mol dm⁻³) with 1 (c = 1.90 × 10⁻⁴ mol dm⁻³) in acetonitrile; t = (25.0 ± 0.1) °C.

Figure 4. Conductometric titration of KClO₄ (c = 1.09 × 10⁻⁴ mol dm⁻³) with 1 (c = 1.90 × 10⁻⁴ mol dm⁻³) in acetonitrile; t = (25.0 ± 0.1) °C. ■ experimental; – calculated.

The stability constants of the Na₁⁺ and Na₂⁺ complexes in acetonitrile were too high for spectrophotometric or conductometric determination. For that reason, direct potentiometry using a sodium-selective glass electrode was applied. Potentiometric titration curves for both ligands showed a steep p[Na] jump at the 1:1 n(ligand)/n(cation) ratio, which is in accordance with the results of previously mentioned methods. However, the p[Na] jump was steeper in the case of titration with tertiary-amide derivative 2, indicating a higher stability of the corresponding complex. The jump was even too steep (Fig. S34, ESI) to allow accurate calculation of the Na₂⁺ complex stability constant so it could only be estimated. On the other hand, stability constant of Na₁⁺ complex was determined by processing the corresponding potentiometric titration data (Fig. 5, Table 1).

The spectral changes observed upon the addition of salt solutions to ligand solution in methanol were basically similar to those described above (Figs. S35 – S45, ESI), i.e. the spectra exhibited hypochromic effect and in some cases isosbestic points were observed. For secondary-amide derivative 1 linear dependence of absorbance was observed only upon addition of Ca(ClO₄)₂ solution (Fig S41, ESI), whereas during titration of tertiary-amide derivative 2 such dependence was observed in titrations with all salt solutions, except with RbNO₃ and CsNO₃ (Figs. S39 and S40, ESI).

Figure 5. Potentiometric titration of NaClO₄ (c = 9.78 × 10⁻⁵ mol dm⁻³) with 1 (c = 9.97 × 10⁻⁴ mol dm⁻³) in acetonitrile. V₀(NaClO₄) = 30.3 cm³, i = 0.01 mol dm⁻³ ([C₄H₉]₄NClO₄), t = (25.0 ± 0.1) °C. ■ experimental; – calculated.

Figure 6. (a) Spectrophotometric titration of 1 (c = 1.95 × 10⁻⁴ mol dm⁻³) with Sr(ClO₄)₂ (c = 2.20 × 10⁻⁴ mol dm⁻³) in methanol. l = 1 cm; t = (25.0 ± 0.1) °C; n(Sr²⁺)/n(1) = 0 (top curve) – 4.38 (bottom curve); the spectra are corrected for dilution. (b) Dependence of absorbance at 275 nm on n(Sr²⁺)/n(1) ratio. ■ experimental; – calculated.
Apart from a high-stability complex Ca$^{2+}$, spectrophotometric measurements also showed formation of Na$^{+}$, Ba$^{2+}$ (Figs. S36 and S44, ESI) and Sr$^{2+}$ complexes (Fig. 6). The stability constants of these complexes are given in Table 1. As can be concluded from the described experimental results, calixarene derivative 2 in methanol forms high-stability complexes with most of the investigated cations (the exceptions are Rb$^+$ and Cs$^+$). The determined stability constant of the Rb$^+$ complex is given in Table 1, whereas no observable complexation of cesium cation with ligand 2 took place.

The above results were confirmed by conductometric titrations. By processing of the corresponding data stability constants of the Na$^{+}$, Mg$^{2+}$, Sr$^{2+}$, Ba$^{2+}$, Li$^{2+}$, and Rb$^+$ complexes given in Table 1 were determined (the corresponding titrations are shown in ESI, Figs. S46 – S51). On the other hand, because of their high values, the equilibrium constants for the reactions of formation of the Ca$^{2+}$, Na$^{+}$, K$^+$, Ca$^{2+}$, Sr$^{2+}$, and Ba$^{2+}$ species were only estimated (Table 1; Figs. S52 – S57, ESI). During the conductometric titrations of LiClO$_4$, NaClO$_4$, and RbNO$_3$ with 1 and that of CsNO$_3$ with both ligands in methanol, negligible and irregular changes in molar conductivity were observed indicating that no complexation took place. It should be noted that formation of Mg$^{2+}$ complex was observed conductometrically, although no complexation was detected using spectrophotometry. The stability constant of the Na$^+$ complex in methanol was, like in acetonitrile, too high for spectrophotometric and conductometric determinations. For that reason, it was determined by means of direct potentiometric titration (Fig. 7, Table 1). As stability of the sodium complex with 1 was much lower (Table 1), to determine its stability constant potentiometrically considerably higher concentrations of both ligand and sodium perchlorate were needed. Because of the limited solubility of calixarene 1 in methanol these measurements were not conducted.

$$\text{p}[\text{Na}^+]$$

$$\text{n}(2)/\text{j}[\text{Na}^+]$$

**Figure 7.** Potentiometric titration of NaClO$_4$ (c = 1.00 $\times$ 10$^{-4}$ mol dm$^{-3}$) with 2 (c = 7.13 $\times$ 10$^{-4}$ mol dm$^{-3}$) in methanol. V$_0$(NaClO$_4$) = 30.3 cm$^3$, l = 0.01 mol dm$^{-3}$ ([C$_6$H$_5$O$_2$H]ClO$_4$); T = (25.0 $\pm$ 0.1) °C. ■ experimental, – calculated.

Given the data listed in Table 1, it is evident that the affinity of ligand 2 for alkali and alkaline earth metal cations is much higher than that of ligand 1. The main reason for the difference can be readily explained by taking into account the presence of N–H⋯O=C intramolecular hydrogen bonds in the latter case. Namely, in order for a cation to form a complex with 1, these bonds need to be disrupted to allow reorganization of the amide groups. Amide hydrogen atoms are in fact competing with the cation for the carbonyl oxygen. Tertiary amide derivatives, like 2, do not have the ability to form the aforementioned hydrogen bonds, so no unfavorable competition between the cation and –NH group could take place. Secondary-amide derivative 1 binds smaller Li$^+$ and Na$^+$ cations very well. Its affinity for larger K$^+$ is lower, whereas Rb$^+$ and Cs$^+$ are too large to fit into its hydrophilic cavity. On the other hand, this compound binds all alkaline earth metal cations quite strongly in acetonitrile, as expected due to their size and charge. Tertiary-amide derivative 2 forms highly stable complexes with all cations, except with the largest Cs$^+$ (even in that case the complex stability is moderate). This size- and charge-dependent selectivity is even more pronounced in methanol. As in MeCN, in MeOH both ligands 1 and 2 showed higher affinity towards alkaline earth compared to alkali metal cations (the only exception is complexation with Ba$^{2+}$ because of its relatively large size). However, the complex stabilities in methanol are considerably lower (Table 1). Such a strong solvent influence can be explained by different solvation of all species taking part in complexation reaction, i.e. free cation, free ligand, and the complex. The influence of cation solvation is most pronounced in the case of smallest cations, like Li$^+$ and Mg$^{2+}$. Although they form highly stable complexes with 1 in acetonitrile, the presence of these complexes has been hardly, or not at all, observed in methanol solution. Methanol, as a hydrogen bonding solvent, strongly solvates small cations, thus making substitution of its molecules by ligand binding sites unfavorable. The cation solvation effect is of course present in the complexation of other metal cations, but it is not as dominant as in the cases of Li$^+$ and Mg$^{2+}$. Ligand solvation effect on the studied equilibria should be presumably more pronounced in reactions with 1 than in those with 2. In both cases methanol molecules compete with the cation for binding sites by forming hydrogen bonds with amide carbonyl oxygen atoms. However, contrary to 2, in the case of 1, which is secondary amide derivative, MeCN molecules can (as a proton acceptor) form H-bonds with amide NH groups of the receptor. This in turn leads to disruption of intramolecular N–H⋯O=C hydrogen bonds and to orientation of carbonyl groups favorable for the complexation of metal ion. Obviously the solvation of the complex also plays an important role in determining its thermodynamic stability. However, on the basis of data presented in this paper we cannot say much about this effect.

It should be also mentioned that the process of solvent molecule inclusion into the hydrophobic cavities of calixarenes 1 and 2 and their complexes could occur. This phenomenon is more pronounced in acetonitrile than in methanol, and could be quite important in determining the equilibria of the complexation reactions.12,13,26,48–50
The diethylene glycol calix[4]arene derivatives 1 and 2 were designed and synthesised as compounds comprising hydrophobic and relatively hydrophilic parts as well as binding site which ensure strong complexation of alkali and alkaline earth metal cations. Hence, due to these properties their strong cation binding associated with high extraction abilities was expected. The complexation of alkali and alkaline earth cations by these ligands was studied by several experimental methods. The solvent effect on the complexation reactions was also examined using two solvents with different solvation and hydrogen-bonding abilities, namely acetonitrile and methanol. In both solvents the affinity for binding alkali and alkaline earth metal cations was found to be much higher in the case of tertiary-amide derivative 2 as compared to compound 1 which comprises secondary-amide subunits. That can be explained mostly by taking into account the presence of intramolecular NH–O=C hydrogen bonds in 1, which cannot be formed in 2. In the process of cation complexation, these bonds have to be disrupted, which is energetically quite demanding and therefore significantly reduces the complex stability.

The hydrogen-bonding role is also important for the explanation of the solvent effect on the equilibria of the complexation reactions. Namely, carbonyl-oxygen binding sites of compound 1 are most probably “blocked” by the formation of H-bonds with methanol molecules as a proton donors, whereas such bonds cannot be established with acetonitrile. By considering also the difference in cations solvation in the two solvents, the much higher complex stabilities in MeCN in comparison to MeOH becomes obvious.

In accordance with the above mentioned results, the structural differences between compounds 1 and 2 were shown to be of utmost importance in determining their abilities for extraction of metal cations from water to dichloromethane. Thus, contrary to 1, calix[4]arene derivative 2 was found to be a very good, even excellent extractant of alkali and alkaline earth metal picrates, with 100 % efficiency in the case of sodium cation. Therefore, it can be concluded that, due to its amphiphilic character and strong cation-binding ability, compound 2 can be considered as a promising reagent for the extraction of metal ions from aqueous to organic phase.

### Conclusion

The diethylene glycol calix[4]arene derivatives 1 and 2 were designed and synthesised as compounds comprising hydrophobic and relatively hydrophilic parts as well as binding site which ensure strong complexation of alkali and alkaline earth metal cations. Hence, due to these properties their strong cation binding associated with high extraction abilities was expected. The complexation of alkali and alkaline earth cations by these ligands was studied by several experimental methods. The solvent effect on the complexation reactions was also examined using two solvents with different solvation and hydrogen-bonding abilities, namely acetonitrile and methanol. In both solvents the affinity for binding alkali and alkaline earth metal cations was found to be much higher in the case of tertiary-amide derivative 2 as compared to compound 1 which comprises secondary-amide subunits. That can be explained mostly by taking into account the presence of intramolecular NH–O=C hydrogen bonds in 1, which cannot be formed in 2. In the process of cation complexation, these bonds have to be disrupted, which is energetically quite demanding and therefore significantly reduces the complex stability.

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### Extraction properties

The abilities of compounds 1 and 2 to extract alkali and alkaline earth metal cations from water to dichloromethane were explored according to the procedure described in detail in the Experimental section. As can be seen by inspecting the data in Table 2, secondary-amide derivative 1 moderately extracted sodium, potassium, and calcium picrates from aqueous to organic phase. Other examined picrate salts were extracted poorly (or not at all) by this compound. On the other hand, tertiary-amide derivative 2 was shown to be much better extractant of alkali and alkaline earth metal cations. Most of them were extracted very well (95–100 %) by 2, the exception being rubidium, cesium, and magnesium ions which were not extracted as efficiently. It is interesting to note that extraction efficiency was 100 % in the case of sodium cation, which was not observed earlier with the other calix[4]arene tertiary-amide derivatives.\(^{16,45}\) The results described are obviously directly correlated with the stabilities of the corresponding complexes, i.e. by the structural features of the compounds studied, and their amphiphilic character.

### Table 1 Stability constants for alkali and alkaline earth metal complexes of ligands 1 and 2 in acetonitrile and methanol at 25.0 °C. Uncertainties are given in parentheses as standard errors of the mean (N = 3).

| Cation | log K |
|--------|------|
|        | MeCN | MeOH |
| Li⁺    | >5    | >5   |    |
| Na⁺    | 7.09(3) | >8  | 3.50(5) | 7.45(1) |
| K⁺     | 3.59(5) | >5  | >5    | >5   |
| Rb⁺    | >5    | >5   | >5    | >5   |
| Cs⁺    | >5    | >5   | >5    | >5   |
| Mg²⁺   | >5    | 2.9  | 4.44(3) | 4.27(3) |
| Ca²⁺   | >5    | >5   | >5    | >5   |
| Sr²⁺   | >5    | >5   | >5    | >5   |
| Ba²⁺   | >5    | >5   | >5    | >5   |

\(^{a}\)Spectrophotometric determinations, \(^{b}\)Conductometric determinations,

### Table 2 Extraction percentage (%) of alkali and alkaline earth metal picrates from water into CH₂Cl₂ at 25 °C. Uncertainties are given in parentheses as standard errors of the mean (N = 3).

|       | Li⁺ | Na⁺ | K⁺ | Rb⁺ | Cs⁺ | Mg²⁺ | Ca²⁺ | Sr²⁺ | Ba²⁺ |
|-------|-----|-----|----|-----|-----|------|------|------|------|
| 1     | 2.35(2) | 10.9(2) | 7.8(1) | 3.0(1) | 3.69(6) | 1.7(1) | 6.55(9) | 2.59(6) | 2.3(1) |
| 2     | 96.0(1) | 100.0(1) | 96.96(8) | 75.6(1) | 58.31(8) | 68.4(1) | 99.6(2) | 98.5(2) | 93.3(1) |
Experimental

General

All reagents used in the syntheses were of the best grade commercially available and were not further purified. Solvents were purified by standard procedures. Analytical TLC was performed on silica gel plates (SiO₂, Merck 60 F254). Melting points were determined on a Kofler hot-bench apparatus and were not corrected. ¹H NMR and ¹³C NMR spectra were recorded with Bruker Avance 300 or 600 MHz spectrometer (δ in ppm relative to (CH₃)₄Si as an internal standard, J values are in Hz). IR spectra were recorded by means of ABB Bomem MB102 FTIR spectrometer. MS measurements were conducted on Agilent 6410 Triple Quadrupole mass spectrometer. The salts used for the investigation of calixarene complexation reactions were LiClO₄ (Fluka, p.a. and Sigma Aldrich), NaClO₄ (Sigma Aldrich 98%+), KClO₄ (Merck, p.a.), RbNO₃ (Sigma, 99.7%), CsNO₃ (Sigma, 99.5%), CsCl (Merck, p.a.), Mg(ClO₄)₂ (Aldrich, 99%), Ca(ClO₄)₂ (Aldrich, 99%), Sr(ClO₄)₂ (Aldrich, p.a.), and Ba(ClO₄)₂ (Fluka, p.a.). The solvents, acetonitrile, methanol, water, and dichloromethane (Baker, HPLC Grade and Sigma-Aldrich, 99.9%, Spectrophotometric Grade) were used without further purification. All potentiometric titrations were conducted using a Radiometer P121 (pH) meter, equipped with a Radiometer 805515 combination pH electrode. Glass and Erlenmeyer Flasks were washed with 10% HCl before use. Additional purification step was required to ensure that all of the ions were removed, and that was done in a similar manner as described in ref. 40. Compound 1 was dissolved in methanol followed by addition of deionised water. Subsequently, the solution was heated to evaporate the methanol, leaving a precipitate in the aqueous solution. The precipitated ligand 1 was collected by suction filtration, washed with deionised water, and dried for 12 hours at 110 °C prior to use in physicochemical experiments.

¹H NMR spectra (600 MHz, CDCl₃): δH/ppm = 1.10 (36H, s, (C(CH₃)₃)₂), 3.26 (4H, d, J = 13.3, ArCH₂Ar), 3.35 (12H, s, OCH₃), 3.52–3.62 (32H, m, OCH₂), 4.62 (8H, s, OCH₂CO), 4.65 (4H, d, J = 13.3, ArCH₂Ar), 6.79 (8H, s, ArH), 7.94 (4H, t, J = 6.3, NH). ¹³C NMR spectra (75 MHz, CDCl₃): δC/ppm = 31.33 (C(CH₃)₂), 31.69 (Ar-CH₂Ar), 33.83, (C(CH₃)₃), 39.12 (NHCOCH₂), 58.69 (OCH₃), 69.74 (OCH₃CO), 70.01 (OCH₂CO), 71.88 (NCH₂CH₂O), 74.38 (OCH₂CO), 125.76 (o-Cr-C), 132.74 (m-Cr-C), 145.53 (Ar-Cr-Bu), 153.32 (p-Cr-C), 170.03 (CONH). IR (KBr) vmax/cm⁻¹ = 3373 (s, NH), 2960 (s, CH), 1674 (s, CO amide I), 1542 (m, NH amide II), 1479 (m, CH₂), 1198 (s, COC), 1126 (s, COC). HRMS: m/z [M+H⁺] exact mass, C₇₂H₁₀₀NaO₁₆·H₂O: 1285.7839; found: 1285.7852.

Synthesis of 5,11,17,23-tetra-tert-butyl-25,26,27,28-tetra(N,N-bis(2-(2-methoxyethoxy)ethyl)carbamoylmethoxy)calix[4]arene (2)

Bis[2-(2-methoxyethoxy)ethyl]amine was added to 10 mL of i-butanol. The mixture was kept for several weeks at room temperature. After determining that no calixarene ethyl ester was present in the solution, by means of ¹H NMR spectroscopy, solvent was evaporated and precipitate was dissolved in CH₂Cl₂. The solution was extracted first with HCl (1 mol dm⁻³) and then with water (mixing of water and dichloromethane solution resulted in emulsion which was separated after 1 hour). The solvent was removed under vacuum, the solid residue was dissolved in methanol, water was added in the solution, and compound 1 was precipitated. The precipitate was separated by suction filtration. After drying, a compound 1 was obtained as a white powder.
s, OCH$_3$), 3.43–3.66 (6H, m, OCH$_2$, NCH$_2$), 5.02 (8H, s, OCH$_2$CO), 5.07 (4H, d, J = 12.8, ArCH$_2$Ar), 6.77 (8H, s, ArH). $^1$C NMR (75 MHz, CDCl$_3$): $\delta$ (ppm) = 31.42 (C(H$_2$)), 32.18 (Ar-CH$_2$-Ar), 33.73 (C(CH$_3$)$_3$), 46.60 (NCH$_3$CH$_2$), 47.82 (NCH$_2$CH$_3$), 58.96 (OCH$_3$), 69.74 (OCH$_2$CO), 69.33 (NCH$_2$CH$_2$O), 70.07 (NCH$_3$CH$_2$O), 70.23 (OCH$_3$CH$_2$O), 70.54 (OCH$_3$CH$_2$O), 71.38 (OCH$_2$CH$_2$O), 71.91 (OCH$_2$CH$_3$O), 125.21 (p-Ar-C), 133.58 (m-Ar-C), 144.32 (Ar-C-4-Bu), 153.70 (p-Ar-C), 170.19 (CONH). IR (KBr) $\nu_{\text{max}}$(cm$^{-1}$) = 2953 (s, CH$_3$), 2871 (s, CH$_2$), 1653 (s, CO), 1482 (s, CH$_2$O), 133.58 (C($\text{CH}_3$)$_3$), 144.32 (Ar-C=O), 170.19 (CONH). $\nu_{\text{max}}$(cm$^{-1}$) was calibrated by the incremental addition of NaClO$_4$ (c = 1.0 $\times$ 10$^{-3}$ mol dm$^{-3}$) with solution of ligands or acetonitrile or methanol solution of Et$_4$NCl in picric acid. (c = 1.0 $\times$ 10$^{-3}$ mol dm$^{-3}$) was titrated with a ligand solution (c = 1.0 $\times$ 10$^{-3}$ to 2.5 $\times$ 10$^{-3}$ mol dm$^{-3}$) in a thermostated vessel. The obtained spectroscopic data were processed by the OriginPro 7.5 program. $^{55, 56}$

Picate extractions

Aqueous solutions of metal picates (c$_0$ = 1.5 $\times$ 10$^{-4}$ mol dm$^{-3}$) were prepared in situ by dissolving the metal hydroxide (0.001 mol) in picric acid. (c = 1.5 $\times$ 10$^{-4}$ mol dm$^{-3}$, 25 mL). Solutions (c$_0$ = 2.0 $\times$ 10$^{-3}$ mol dm$^{-3}$) of the calixarene derivatives were prepared in dichloromethane. Equal volumes (5 mL) of the two solutions were shaken vigorously for 20 min in a 100 mL flask. The solutions were left to stand in a thermostated bath at (25.0 $\pm$ 0.1) °C for 24 h until phase separation was complete. The concentration of picate ion in the organic phase was then determined spectrophotometrically as described by Pedersen. $^{58}$ Control blank experiments showed that no picate extraction occurred in the absence of a calixarene. The extraction percentage (%E) has been calculated as %E = [(A$_0$ - A)/A$_0$] $\times$ 100, where A$_0$ and A are the initial and final absorbances of the metal picate at 356 nm before and after the extraction.

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