Ionic recognition by thiacalixarenes: binding of alkali and heavy metal ions by thiacalix[4]arene-bis-crown[n] ethers*

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The binding properties of two thiacalix[4]arene-bis-crown[n] derivatives (n = 5 and 6) were examined through extraction experiments. The stability constants of the resulting complexes in methanol were determined. The replacement of the bridging CH_2 groups by sulfur atoms leads to a strong decrease in both extraction and complexation levels of alkali metal ions but does not affect the selectivity within the series of crown ethers. The stability of complexes with heavy metal ions does not change markedly on passing from thiacalix[4]arene-bis-crown[n] ethers to their calix[4]arene-bis-crown[n] counterparts; therefore no clear-cut conclusions about the possible interactions between these cations and the sulfur atoms can be drawn.

Key words: thiacalixarene-bis-crown[n] ethers, alkali metal ions, heavy metal ions, phase transfer, stability constants.

Thiacalixarenes represent a rather new class of derivatives in which the CH_2 bridges have been replaced by S atoms, resulting in additional coordination sites and a changed dimension of the cavity.[1—3] The ability to form complexes with alkali metal cations has been studied only for *p-tert*-butylthiacalix[4]arene and some of its tetraesters. Data on the extraction of these metals cations by *p-tert*-butylthiacalix[4]arene[4] and by its tetrakis[(ethoxycarbonyl) methoxy]-*O*-derivatives[5] have been reported. In the case of the parent compound (tetra-OH), the extraction is pH-dependent; alkali metal ions are poorly extracted from water into chloroform, the maximum extraction being attained at pH 5.5 for potassium (32%) and at pH 2.2 for lithium (18%). The association constants with alkali metal picrates in $CDCl_3$—CD_3CN were determined by ^1H NMR spectroscopy for tetrakis[(ethoxycarbonyl)methoxy]-*O*-derivatives either with or without *p-tert*-butyl groups.[6] Only the de-*tert*-butylated compound with the 1,3-*alternate* conformation was found to be selective for cesium (the selectivity order is $Cs^+>Rb^+>K^+$), whereas the *p-tert*-butylated counterpart is selective for rubidium (the selectivity order is $Rb^+>K^+>Cs^+$), as confirmed by both extraction and complexation experiments. Later,[7] the ionic recognition properties of two thiacalix[4]arene ketone derivatives and an amide derivative (all three in the 1,3-*alternate* conformation) with respect to alkali, alkaline earth, and some heavy and transition metal ions have been studied. The last-mentioned ligand showed significant complexation with K^+, Rb^+, and Ag^+ ions. A recent publication[8] reports the synthesis and characterization of thiacalix[4]arene ketone derivatives and the influence of their conformations on the extraction properties with respect to alkali metal ions. It was shown that the *cone* conformer exhibits the highest extraction ability toward Na^+, while the *partial cone* and the 1,3-*alternate* conformers are more efficient extractants for the larger K^+ ion.

While considering the high Cs^+/Na^+ selectivity in the extraction of cesium cations with calix[4]arene-crown[6] ethers, Lamare *et al.*[9] reported the synthesis, the crystal structure, and the extraction properties of 1,3-thiacalix[4]arene-bis-crown[n] ethers, namely, compounds **1** (n = 5) and **2** (n = 6).

It was shown experimentally that the thiacalix[4]bis-crown[n] ethers are less efficient than their calixarene counterparts as regards the extraction of these cations from acidic aqueous solutions into 2-nitrophenyl hexyl ether (NPHE). The structure and the dynamic behavior

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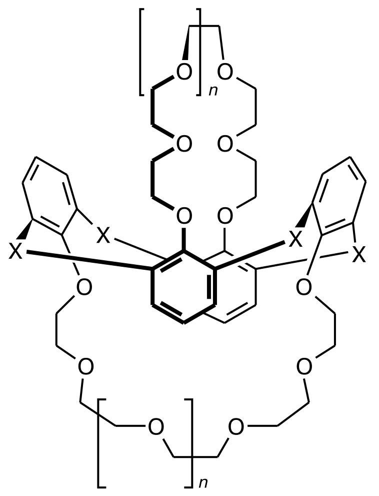

1—4

X = S, *n* = 0 (**1**), 1 (**2**)
X = CH$_2$, *n* = 0 (**3**), 1 (**4**)

of hypothetical alkali metal ion complexes were studied by molecular modeling. It was found that the cesium cation is located close to the thiacalixarene cavity and does not interact strongly with the crown unit, which functions only partially as a ligand. These results demonstrate that the size of the calixarene cavity in the 1,3-*alternate* conformation plays a key role in the remarkable affinity of these molecules for cesium. More recently, the synthesis of 1,3-*alternate* thiacalix[4]bis-crown[n] ethers with n = 4—7 has been reported.[10] The ability of these crown ethers to extract metal cations is lower than that of conventional calix[4]bis-crown[n] ethers. X-Ray diffraction data confirmed the results of molecular modeling[9] and made it possible to attribute the lower extraction ability to weaker electrostatic interactions of the polyether oxygen atoms and to decreased π-interactions. The researchers cited[10] also noted a more rapid metal ion shuttling through the 1,3-*alternate* thiacalix[4]crown[n] ether tubes compared to usual calix[4]crown[n] ethers, probably because the metal ions are less strongly bound in the complex.

A different synthesis of *p-tert*-butyl and *p*-H-thiacalix[4]bis-crown[n] ethers and their SO, and SO$_2$ derivatives has been reported.[11] The binding abilities have been assessed in experiments on solvent extraction of alkali metal picrates from water into chloroform. Compound **1** selectively extracts K$^+$ and Rb$^+$ ions, whereas compound **2** is selective with respect to cesium. Moderate results on the extraction of alkali metal and silver cations have been reported for *p-tert*-butylcalix[4]bis-crown-5.[12]

Here we report the first results on the binding properties of ligands **1** and **2** toward the whole series of alkali metal ions and four heavy metal ions (Ag$^+$, Pb^{2+}, Hg^{2+}, and Cd^{2+}). Two approaches were used, namely, experiments on the phase transfer of metal picrates from water into dichloromethane and determination of the stability constants of the complexes in methanol. New data on the extraction and complexation of heavy metal ions with both calix[4]bis-crown[n] ethers **3** and **4** were also obtained for comparison.

Experimental

The solvents, methanol (Carlo Erba) and dichloromethane (Prolabo, RP Normapur), were used without further purification.

All ligands were synthesized as described previously.[9,13] Solutions of ligands were prepared in the presence of a supporting electrolyte, namely, Et$_4$NCl (Fluka, purum), Et$_4$NBF$_4$ (Fluka, puriss.), or Et$_4$NNO$_3$ (Acros), depending on the nature of the metal salt.

The metal salts used in the complexation experiments included commercial alkali metal ion chlorides, LiCl (Fluka, MicroSelect), NaCl (Merck, p.a.), KCl (Merck, p.a.), RbCl (Merck, p.a.), and CsCl (Fluka, puriss.); silver tetrafluoroborate, AgBF$_4$, H$_2$O (Merck, p.a.); cadmium, lead, and mercury nitrates, Cd(NO$_3$)$_2$·4H$_2$O (Merck, p.a.), Pb(NO$_3$)$_2$ (Merck, p.a.), and Hg(NO$_3$)$_2$·H$_2$O (Prolabo, p.a.). All stock solutions (except those of alkali metal ions) were standardized by classical titrations using EDTA and the appropriate colored indicators; in the case of Ag$^+$, potentiometric titration with NaCl was used.

Alkali metal,[14] silver,[15] and lead and cadmium[16] picrates used for extraction experiments were obtained as described previously. Mercury picrate was prepared by the reaction of picric acid with mercuric oxide.

Extraction. Extraction experiments were performed by mixing two equal volumes (2 mL) of an organic and an aqueous phase. The concentrations of the metal ion in the aqueous phase (C_M) and that of the calixarene in the organic phase (C_L) were identical ($2.5 \cdot 10^{-4}$ mol L^{-1}). The procedure has been described in detail previously.[14] The values listed in Tables 1 and 3 are average values of the results obtained in n (at least, three) independent experiments with their standard deviation σ_{n-1}.

Determination of stability constants. The stability constants β were mainly determined using UV absorption spectrophotometry by monitoring the changes in the spectra of the ligands induced by complexation. The experimental procedure has been reported previously.[14] The experimental data were interpreted using known programs.[17,18] The typical ligand concentration

Table 1. Degree of extraction (E) of alkali metal picrates from water into dichloromethane at 20 °C and logarithms of the stability constants (log β) of alkali metal complexes with thiacalix[4]bis-crown[n] ethers in methanol (Et$_4$NCl or Et$_4$NNO$_3$, 10^{-2} mol L^{-1} as the supporting electrolyte) at 25 °C

Cation	*E* (%)		logβ	
	1	**2**	**1**	**2**
Li$^+$	2.3±0.3	≤1	≤1	≤1
Na$^+$	2.6±0.4	1.69±0.06	1.18±0.01	1.11±0.01
K$^+$	19.74±0.08	2.8±0.4	4.7±0.3	2.67±0.01
Rb$^+$	22.0±0.9	3.8±1	5.23±0.06	3.56±0.06
Cs$^+$	5.6±0.7	17.5±0.6	2.7±0.3	4.7±0.2

Table 2. Degree of extraction (*E*) of heavy metal picrates from water into dichloromethane by thiacalix[4]bis-crown[n] ethers and the corresponding calix[4]bis-crown[n] ethers at 20 °C

Cation	1	2	3	4
Ag^+	10.3±0.4	8.6±0.4	45.7±0.2[19]	40.6±0.1[19]
Cd^{2+}	2.8±0.3	≤1	5.3±0.1	1.8±0.2
Pb^{2+}	1.8±0.1	1.8±0.1	3.8±0.1	1.4±0.2
Hg^{2+}	6.8±0.1	2.7±0.1	4.4±0.2	13±1

was $C_L = 3 \cdot 10^{-5}$ mol L^{-1} and the ratio of metal to ligand concentrations at the end of the titration (*R*) ranged from 2 to 400, depending on the complex stability. The spectra were recorded in the 220 to 300 nm range. The complexation with metal ions generally leads to a decrease in the intensity of the major absorption band of the ligand. Figure 1 illustrates the complexation of Cs^+ with ligand **2**.

The stability constants of silver complexes were also determined by potentiometry according to the following procedure: using a 2 mL microburette, the ligand was added to a solution of $AgBF_4$ with the known concentration C_{Ag}. Before each experiment, the working silver electrode was calibrated by adding small volumes of a concentrated solution of $AgBF_4$ in methanol to 10 mL of a 0.01 *M* solution of Et_4NBF_4 in the same solvent. The measurements were interpreted using known software.[17]

Results and Discussion

Alkali metal ions. The extraction and complexation data are listed in Table 1 and illustrated in Fig. 2. The corresponding values for the related calix[4]arene-bis-crown ethers **3** and **4** are given for comparison.[19]

The replacement of the bridging CH_2 groups by sulfur atoms results in a significant decrease in the extraction level. For instance, the degree of extraction of K^+ ions drops from 77.8 in the case of crown ether **3** to only 19.74 for crown ether **1**, while that of Cs^+ decreases from 59 for compound **4** to 17.5 for compound **2**. However the selectivity profile remains more or less the same. Both ligands **1** and **2** virtually do not extract Li^+ and Na^+; however, ligand **1** is selective for K^+ and Rb^+, while ligand **2**, for Cs^+. These results confirm the data obtained previously[9—11] under different conditions for alkali metal nitrates and picrates with both ligands, and especially the fact that ligand **1** is a less efficient extractant for cesium ions than crown ether **2**.

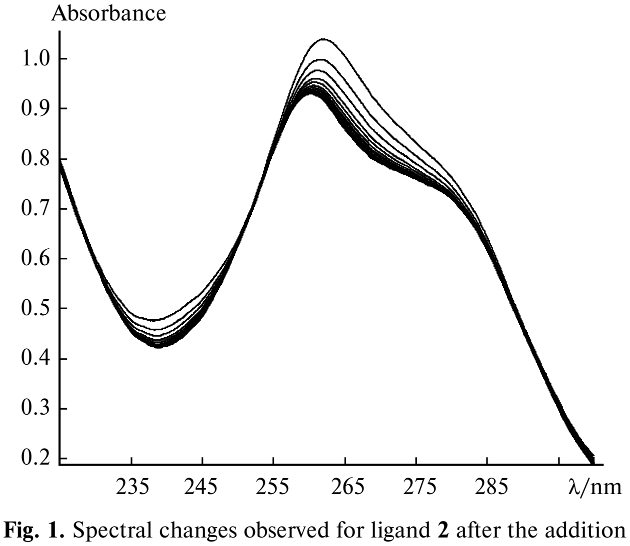

Fig. 1. Spectral changes observed for ligand **2** after the addition of cesium chloride; $C_L = 3 \cdot 10^{-5}$ mol L^{-1}, $0 \le R = C_M/C_L \le 3$.

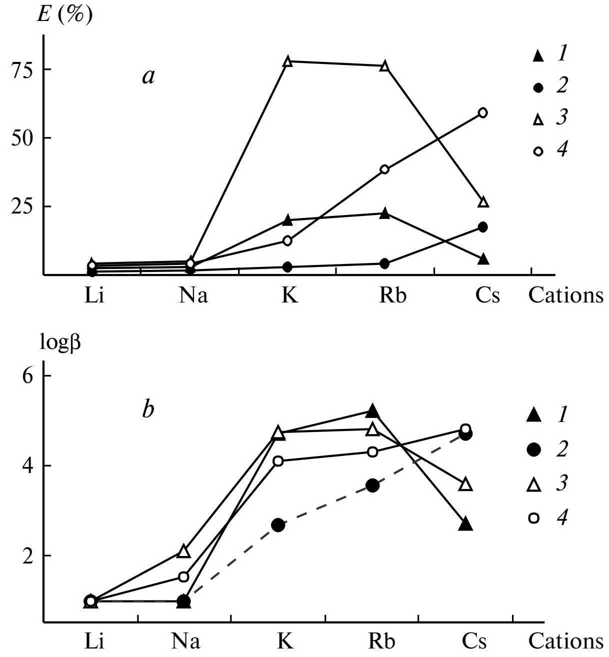

Fig. 2. Variation of the degree of extraction *E* (%) of alkali metal picrates (*a*) and logarithms of the stability constants (logβ) (*b*) of alkali metal complexes with thiacalix[4]bis-crown[n] ethers **1** and **2** and the corresponding calix[4]bis-crown[n] ethers **3** and **4** (data were taken from Ref. 19 except for those for Cs^+. The stability constant of the Cs^+ complex with ligand **3** in methanol was determined once again in this study: $\log \beta = 3.5 \pm 0.1$).

The data of spectrophotometric titration of both ligands **1** and **2** with any alkali metal ions, except for Li^+, indicated the formation of only mononuclear complexes, despite the presence of two potential chelation sites. In the case of Li^+, no spectral changes were observed during the titration with either of the ligands, indicating the absence of complexation with this cation.

The profiles of complexation selectivity exactly coincide with the extraction profiles with a slightly higher selectivity with respect to rubidium over potassium in the case of crown ether **1** and a pronounced affinity of crown ether **2** for cesium. The extraction and complexation selectivities Cs^+/M^+ expressed as the ratios $S^E{}_{Cs/M}$ of the degrees of extraction of the two cations and the differences $S^C{}_{Cs/M} = \log\beta_{CsL+} - \log\beta_{ML+}$ are given in Table 3.

Table 3. Extraction ($S^{E}_{Cs/M} = E(Cs^+)/E(M^+)$) and complexation ($S^{C}_{Cs/M} = \log\beta_{Cs^+} - \log\beta_{M^+}$) selectivities for thiacalix[4]bis-crown [n] ethers and calix[4]bis-crown[n] ethers

M^+	$S^{E}_{Cs/M}$		$S^{C}_{Cs/M}$	
	2	**4**	**2**	**4**
Na^+	10.4	14.4	3.6	3.3
K^+	6.3	4.9	2.0	0.7
Rb^+	4.6	1.5	1.1	0.5

It can bee seen that the Cs^+/Na^+ complexation selectivities of crown ethers **2** and **4** are of the same order of magnitude, whereas the Cs^+/Rb^+ and Cs^+/K^+ selectivities are much higher for compound **2** than for **4**. The same trends are observed for the corresponding extraction selectivities, although the Cs^+/Na^+ selectivity is lower for **2** than for **4**. This is due to a more pronounced decrease in the degree of extraction for Cs^+ compared to that for Na^+ on going from compound **4** to **2**. These findings are consistent with the enlargement of the cavity of the ligands upon introduction of the sulfur atoms. Data of molecular dynamic simulation in combination with the crystal structure data for the ligands have shown that the size of the cavity in compounds **1** and **2** dictated by the presence of sulfur bridges is larger than that in the parent calixarenes (the average S...S distance is longer than the $CH_2...CH_2$ distance by 0.5 Å).[9] Thus, whereas the geometry of **2** still fits the size of Cs^+, for smaller cations like Rb^+ and K^+, this ligand becomes less adapted than **4**.

The size effect can also be clearly seen by comparing the behaviors of the thiacalix[4]bis-crown ether **1** and the corresponding calix[4]bis-crown ether **3**. The complex formation with Na^+ ions becomes less efficient (the stability constant decreases from 2.10 to 1.18 log units), whereas the K^+ complexes with both ligands have equal stabilities. In the case of crown ether **1**, the maximum stability is found for the Rb^+ complex, which is more stable than the similar complex with ligand **3**. The decrease in the stability constant observed for Cs^+ is in line with the fact that the size of the ligand may prove too small for this cation.

Table 4. Logarithms of the stability constants (log*β*) of heavy metal complexes with thiacalix[4]bis-crown ethers and the corresponding calix[4]bis-crown[n] ethers in methanol (Et_4NCl or Et_4NNO_3, 10^{-2} mol L^{-1} as the supporting electrolyte) at 25 °C

Cation	Composition	1	2	3	4
Ag^+	1 : 1	5.1±0.3	3.57±0.04*	5.58±0.01[19]	4.5±0.1[19]
	2 : 1			9.34±0.01[19]	
Cd^{2+}	1 : 1	2.4±0.7	2.5±0.5	2.59±0.01	1.79±0.08
Pb^{2+}	1 : 1	2.3±0.4	2.6±0.4	2.19±0.01	1.86±0.04
Hg^{2+}	1 : 1	2.6±0.6	2.2±0.5	1.75±0.01	2.3±0.1

* Average values of the spectrophotometric and potentiometric measurements.

Heavy metal ions. The degrees of extraction of Ag^+, Cd^{2+}, Pb^{2+}, and Hg^{2+} picrates from water into dichloromethane by the two thiacalix[4]bis-crown[n] ethers and their two calixarene counterparts are listed in Table 2. The thiacalix[4]bis-crown[n] ethers do not provide efficient extraction of the heavy metal ions. The highest degrees of extraction, which hardly exceed 10%, were obtained for silver picrate with the two ligands (E = 10.3% for ligand **1** and E = 8.6% for ligand **2**) and for mercury picrate with ligand **1** (E = 6.8%). Actually, calix[4]bis-crown[n] ethers are much better extractants for Ag^+ ions than the sulfur-containing derivatives: their E values being higher than 40%, whereas the degrees of extraction of Cd^{2+}, Pb^{2+}, and Hg^{2+} ions are relatively low and are of the same order of magnitude.[20]

The data on complexation in MeOH (Table 4) indicate the formation of 1 : 1 complexes, as in the case of alkali metal ions. The stabilities of these complexes are generally consistent with the extraction data, because ligands **1** and **2** form the most stable complexes with Ag^+ ions (logβ = 5.1 and 3.6, respectively). These complexes are, however, less stable than the complexes with ligands **3** and **4**.

The stabilities of Cd^{2+}, Pb^{2+}, and Hg^{2+} complexes with both ligands are nearly equal to within the experimental error. The stabilities of these complexes also do

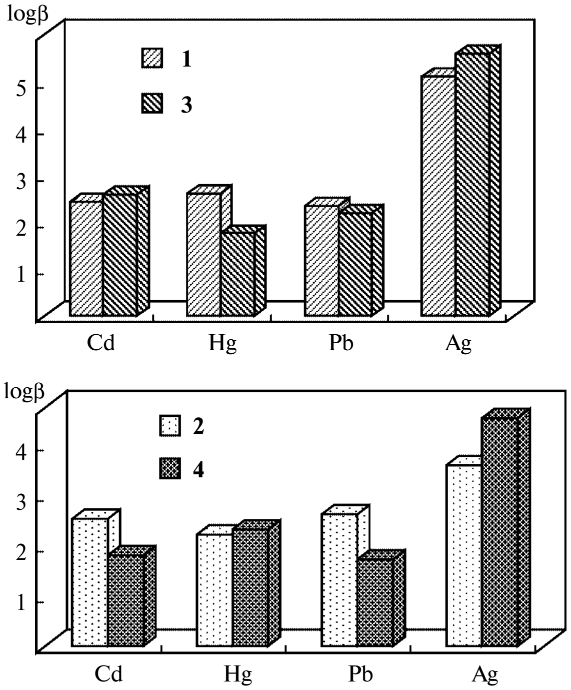

Fig. 3. Comparison of the stability (logβ) of heavy metal complexes with thiacalix[4]bis-crown[n] ethers **1** and **2** and with the corresponding calix[4]bis-crown[n] ethers **3** and **4**.

not differ much from those of complexes formed by the corresponding calixarenes (see Fig. 3), although the Cd^{2+} and Pb^{2+} complexes with ligand **2** and the Hg^{2+} complex with ligand **1** are significantly more stable. These differences may result from the competition between two opposite effects, namely, a favorable effect of interaction with the bridging sulfur atoms and an unfavorable size effect related to the larger size of the thiacalix[4]bis-crown[n] ether cavity, less adapted for complexation than that of the corresponding calix[4]bis-crown[n] ethers.

The results of both extraction and complexation experiments show that the introduction of sulfur atoms in place of the bridging CH_2 groups entails a decrease in the affinity for alkali metal ions without significant changes in the selectivity trend within the series. The enhanced selectivity of cesium over the potassium and rubidium ions attracts attention. These results may be explained by the increase in the cavity size due to the presence of the sulfur atoms. Like calix[4]bis-crown[n] ethers, thiacalix[4]bis-crown[ethers] are not efficient extractants for heavy metal ions, except for Ag^+.

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