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Complexation and transport of alkali, alkaline earth, transition and heavy metal cations by *p-tert*-butyldihomooxacalix[4]arene tetra(diethyl)amide

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The binding properties of the tetra(diethyl)amide (**2**) derived from *p-tert*-butyldihomooxacalix[4]arene, in the cone conformation, towards alkali, alkaline earth, transition (Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}) and heavy (Ag^+, Cd^{2+}, Hg^{2+} and Pb^{2+}) metal cations have been established by extraction studies of metal picrates from an aqueous solution into dichloromethane, transport experiments with the same salts through a dichloromethane membrane and stability constant measurements in methanol. Results concerning the calorimetric study of Na^+ and K^+ complexes in methanol are presented. The affinity of **2** for some cations (Na^+, K^+, Ba^{2+}, Ag^+ and Zn^{2+}) has been investigated by ^1H NMR spectrometry, as well. The results are compared to those obtained with the analogous calix[4]arene tetraamide derivative **3**. Amide **2** displays a preference for the alkali cations (mainly Na^+ and K^+) in contrast to amide **3** that prefers the alkaline earth cations. Ag^+ and Cd^{2+} soft Lewis acids are also strongly bound by both amides. ^1H NMR titrations confirm the formation of 1:1 complexes between **2** and all cations studied, also suggesting that they should be located inside the cavity defined by the phenoxy and carbonyl oxygen atoms. **2** shows transport rates that do not follow the same trends as the stability constants or extraction percentages; it can therefore be characterized as a selective receptor.

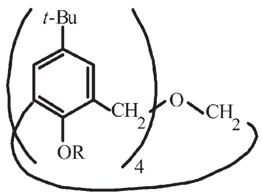
Introduction

Calixarene-based molecules[1–4] have received intense attention in the last few years. One of the most important features of these compounds is their diversity. Calixarenes find applications as selective binders and carriers, as analytical sensors, as catalysts and as model structures for biomimetic studies.

In the field of host-guest chemistry, many studies have focused on the binding ability of calixarene derivatives with carbonyl groups at their lower rims towards metal ions, predominantly alkali and alkaline earth,[5a] but also transition and heavy metal cations.[5b] Several functionalised calix[*n*]arenes (mainly $n = 4$,[6–20] but also $n = 6$[12,19,21–23] and $n = 8$,[6,12,21,22] homo-[24] and homooxacalixarenes[25,26]) with primary, secondary and tertiary amide groups have been studied extensively, both in solution and in the solid state. It is understood from these studies that tertiary amides are strong complexation agents for alkali, alkaline earth and some transition metal cations. The diethylamide residue has been the most studied, since the first synthesis of the *p-tert*-butylcalix[4]arene tetraamide derivative **3**, in 1988.[27]

Dihomooxacalix[4]arenes, with a larger cavity than the calix[4]arenes, but still possessing a true cone conformation, are potential host molecules for larger cations. For a few years, we have been synthesising dihomooxacalix[4]arene derivatives with carbonyl group containing substituents on the lower rim. The binding properties of such compounds bearing ketone[28,29] and ester[29,30] groups towards alkali, alkaline earth and some transition and heavy metal cations have been reported. In the course of these studies, we synthesised the tetra(diethyl)amide derivative **2**[31] from *p-tert*-butyldihomooxacalix[4]arene (**1**), in the cone conformation.

In the present work we report the binding properties of ligand **2** towards alkali, alkaline earth, transition (Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}) and heavy (Ag^+, Cd^{2+}, Hg^{2+} and Pb^{2+}) metal cations. This has been established by extraction studies of metal picrates from an aqueous solution into dichloromethane, transport experiments with the same salts through a dichloromethane membrane and by determination of stability constants in methanol based on



1 R = H

2 R = $CH_2CON(Et)_2$

4 R = CH_2COPh

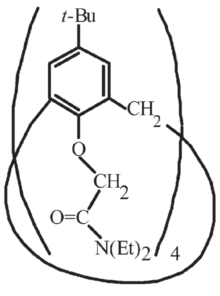


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Table 1 Percentage extraction (% *E*)[a] and stability constants (log β)[b] of alkali and alkaline earth metal complexes at 25 °C

		Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
Ionic radius[c] /Å		0.78	0.98	1.33	1.49	1.65	0.78	1.06	1.27	1.43
2	% *E*	71	96	99	92	66	14	93	90	91
	log β	3.81 ± 0.03	7.23 ± 0.06[f]	6.73 ± 0.01[f]	4.8 ± 0.1	4.36 ± 0.04	2.6 ± 0.1	5.0 ± 0.3[f]	4.92 ± 0.07	4.4 ± 0.2
3[d]	% *E*	63	96	74	24	12	9	98	86	74
	log β	3.9	7.9[f]	5.8[f]	3.8	2.4	1.2	≥9[f]	≥9[f]	7.2[f]
4[e]	% *E*	62	68	70	55	26	14	9.6	17	57
	log β	2.3	3.7	4.0	3.7	2.2	4.0	4.0	4.5	4.9

[a] Values with uncertainties less than 5%. [b] Standard deviation σ_{n-1} on the mean of several experiments. Spectrophotometric measurements, unless noted otherwise. [c] See Ref. 42. [d] Data taken from Ref. 20. [e] Data taken from Ref. 28. [f] Determined by potentiometry.

UV-spectrophotometric titrations and competitive potentiometry. Calorimetric studies of Na^+ and K^+ complexes of compound **2** in methanol have also been performed. Finally, the affinity of **2** for some cations has also been investigated by ^{1}H NMR spectrometry. The results are compared to those obtained with calix[4]arene tetraamide derivative **3**, in order to analyse the effects of the extra oxygen and carbon atoms present in the macrocyclic ring of **2**, namely on its conformational flexibility.

Results and discussion

Extraction and complexation studies

Alkali and alkaline earth metal cations. The results of phase transfer were obtained by the standard picrate method.[32] These data, expressed as a percentage of cation extracted (% *E*), for tetraamide **2** are given in Table 1. Logarithms of the stability constants of the 1:1 complexes formed with **2** are also collected in Table 1. The corresponding values for tetraamide **3**[20] and tetraphenylketone **4**[28] are included for comparison. Extraction and complexation results towards alkali and alkaline earth cations *versus* their ionic radius are illustrated in Figs. 1 and 2, respectively.

Amide **2** shows very high extraction levels for all the cations (except for Mg^{2+}) and higher than compound **3** (except for Ca^{2+} and except for Na^+ where the value is the same). This difference is greater for the larger cations Rb^+ and Cs^+ and, to a lesser extent, for K^+. In the alkali series, **2** displays a plateau selectivity for cations Na^+, K^+ and Rb^+ with a very slight maximum for K^+. This behaviour is consistent with its larger cavity size compared with that of amide **3**, which presents a peak selectivity for Na^+.

The complexation profile of **2** (Fig. 2) is almost the same as that observed in extraction. Na^+ is now the best complexed cation (log $\beta = 7.23$) with a small preference over K^+ (log $\beta = 6.73$). Li^+ is too small to form strong complexes with ligand **2**, exhibiting the lowest log β (3.81) within the alkali series. This value is on the same order of magnitude as that of the **3**-Li^+ complex (log $\beta = 3.9$). In the case of Cs^+, the largest alkali cation, ligand **2** shows an increase in stability constant of nearly 2 log units (log $\beta = 4.36$) relative to ligand **3** (log $\beta = 2.4$). While derivative **3**, more rigid, shows a notorious selectivity in favour of Na^+, with **2** this selectivity is less evident. Due to the oxygen bridge, the dihomooxa derivative is a more flexible molecule, being able to undergo more pronounced conformational changes, present in the complexation process. The three larger alkali cations are favoured, both in extraction and stability constants.

A preliminary calorimetric study of the complexation of Na^+ and K^+ cations with ligand **2** led to the corresponding values of $-\Delta G$, $-\Delta H$ and $T\Delta S$ listed in Table 2. The stabilisation of both complexes appears to be entirely enthalpy controlled, $-\Delta H$ being strongly positive and $T\Delta S$ close to zero. The lower stability of the K^+ complex, and hence the Na^+/K^+ selectivity of **2** is due to a more favourable enthalpy term with Na^+. In the case of Na^+, $-\Delta H$ and $T\Delta S$ values are of the same order of magnitude with both ligands **2** and **3**, taking into consideration the experimental error. With K^+, $-\Delta H$ values are not significantly different for both ligands. Thus, the less unfavourable entropy term $T\Delta S$ is responsible for the higher stability of the complex with **2** and consequently for the weaker Na^+/K^+ selectivity of **2** as compared to **3**. This may be related to the larger size and greater flexibility of **2**. Work is in progress with other cations.

In the alkaline earth series, extraction is much more efficient for Ca^{2+}, Sr^{2+} and Ba^{2+} compared with the very low level towards Mg^{2+} with both ligands (see Table 1). However,

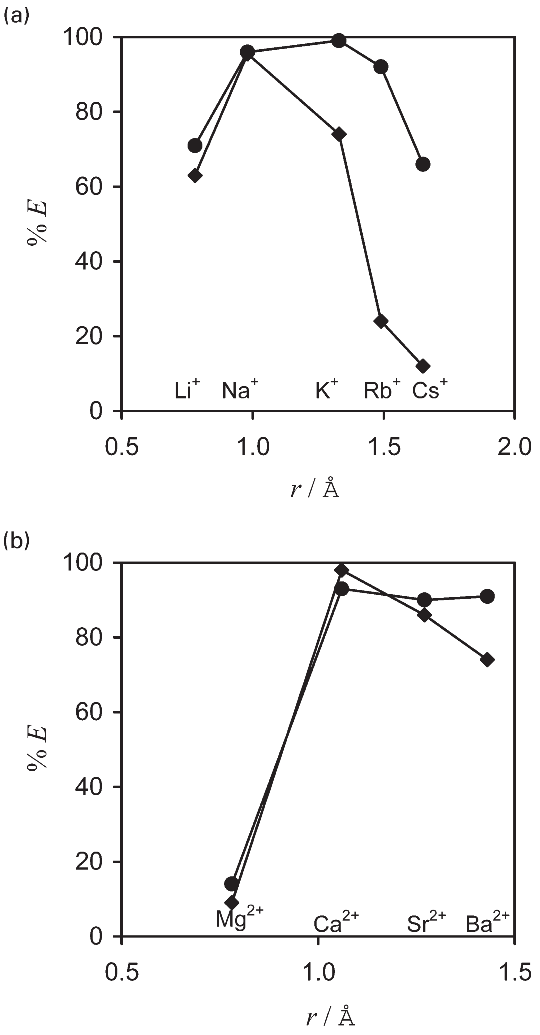


Fig. 1 Percentage extraction (% *E*) of metal picrates into CH_2Cl_2 at 25 °C *vs.* the cation ionic radius (*r*) for amides **2** (●) and **3** (◆): (a) alkali and (b) alkaline earth metals.

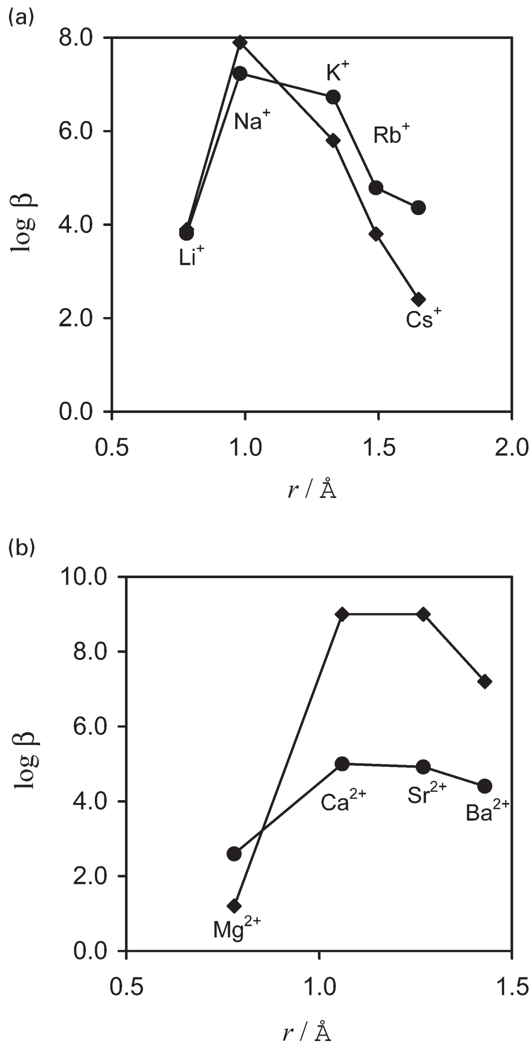


Fig. 2 Logarithms of the stability constants (log β) of metal cation complexes in methanol *vs.* the cation ionic radius (r) for amides **2** (●) and **3** (◆): (a) alkali and (b) alkaline earth metals.

2 practically does not discriminate between this triad of cations. A similar trend is reflected in complexation, with ligand **2** showing a small preference for Ca^{2+} (log $\beta = 5.0$) and Sr^{2+} (log $\beta = 4.92$) over Ba^{2+} (log $\beta = 4.4$). The stability constants are higher for **3** than for **2**, and also the Ca^{2+}/Mg^{2+} selectivity is much more pronounced with that ligand.

As observed for tetraamide **3** relative to other calix[4]arene derivatives containing ester and ketone groups,[20] the presence of the tertiary amide groups in ligand **2** also enhances the complexing ability with respect to the tetraphenylketone derivative **4**.[28] Both dihomooxa derivatives show, however, similar complexation profiles towards alkali cations, but different behaviours for the alkaline earth cations. As summarised in Table 3, diethylamide **2** displays a preference for monovalent cations, in contrast to diethylamide **3** (with the exception of Li^+, which is preferred to Mg^{2+}) and phenylketone **4**.

Table 2 Thermodynamic parameters of complexation of alkali complexes with ligands **2** and **3** in methanol at 25 °C

Ligand	Parameter/kJ mol^{-1}	Na^+	K^+
2	$-\Delta G$	41.2 ± 0.3	38.40 ± 0.06
	$-\Delta H$	46 ± 4	38.1^b
	$T\Delta S$	-5 ± 4	0
3^a	$-\Delta G$	45	33.1
	$-\Delta H$	50.6	42.4
	$T\Delta S$	−6	−9.3

[a] Data taken from Ref. 16. [b] Single experiment.

Table 3 Complexation selectivities, $S = \beta_{LM1}{}^{n+}/\beta_{LM2}{}^{n+}$, for compounds **2**, **3** and **4**

Ligand	Li^+/Mg^{2+}	Na^+/Ca^{2+}	K^+/Sr^{2+}	Rb^+/Ba^{2+}
2	16.2	170	65	2.45
3	501	≤ 0.08	$\leq 6 \times 10^{-4}$	4×10^{-4}
4	0.02	0.50	0.32	0.06

Transition and heavy metal cations. The percentage of cations extracted and the logarithms of the stability constants of the 1:1 complexes formed with ligand **2** are presented in Table 4 and Figs. 3 and 4. Some values for ligands **3**[19] and **4**[29] are also included.

Extraction data reveal that tetraamide **2** is a very good phase transfer agent for heavy cations and a good phase transfer agent for all the transition cations. **2** shows a strong preference for Ag^+ (98% E) closely followed by Pb^{2+} (92% E) and Cd^{2+} (88% E). These values are similar to those obtained with ligand **3** (Table 4). Within the transition cations, Mn^{2+} is the best extracted (76%), followed by Ni^{2+} (50%) and Cu^{2+} (48%). Cu^{2+} cations are better extracted by amide **2** (48%) than by amide **3** (14%).

Figs. 3 and 4 show that the complexation profile reflects that observed in extraction, except for Ni^{2+}. Ligand **2** displays a high selectivity for Ag^+ (log $\beta = 7.0$) and also, although to a lesser extent, for Mn^{2+} (log $\beta = 5.8$) and Cd^{2+} (log $\beta = 5.7$). Ni^{2+} is the least complexed cation, with log $\beta = 2.1$.

If we compare these results with those obtained in extraction with phenylketone **4**,[29] ligand **2** is a much stronger binder as well. This is even more marked with the heavy cations Cd^{2+}, Hg^{2+} and Pb^{2+}. However, the extraction levels for Ag^+ are the highest with both dihomooxa derivatives and the values obtained for Cu^{2+} are also almost the same.

As observed by us before for ester, ketone[29] and amide[19] derivatives containing hard oxygen donor atoms, **2** also shows a clear preference for soft Lewis acids[33] like Ag^+ and Cd^{2+}.

Proton NMR studies

Further information on the cation binding behaviour of amide **2** was obtained by ^1H NMR titration experiments. The cations studied were Na^+, K^+ (thiocyanates), Ba^{2+}, Ag^+ and Zn^{2+} (triflates), and in all cases the experimental data were also consistent with the formation of only 1:1 complexes.

Variable amounts of the salts were added to **2** and the proton spectra were recorded after each addition. These titrations indicate similar behaviours for Na^+, K^+, Ag^+ and Ba^{2+}. With [salt]/[ligand] ratios lower than 1, both signals of the complexed and uncomplexed ligand are present and sharp in the spectra (Fig. 5 shows the spectra for K^+ as an example), indicating that on the NMR time scale the exchange rate between the two species is slow at room temperature. With 1:1 ratios, all the signals for the free ligand disappeared and those of the complexed ligand remain unchanged after subsequent additions of the salt, indicating a 1:1 metal-to-ligand stoichiometry. For Zn^{2+} the signals of the complexed and uncomplexed ligand are also present, but they are broad (Fig. 6, spectrum b), indicating a faster exchange rate and consequently a higher affinity of **2** for the previous four cations than for Zn^{2+}. This is in agreement with the extraction results. However, the stability constant for Ba^{2+} (log $\beta = 4.4$) is nearly the same as that for Zn^{2+} (log $\beta = 4.5$). In fact, the **2**-Ba^{2+} proton NMR spectrum is slightly different from the other three (Na^+, K^+, Ag^+) spectra, in particular the peaks in the

Table 4 Percentage extraction (% *E*)[a] and stability constants (log *β*)[b] of transition and heavy metal complexes at 25 °C

Ligand		Mn^{2+}	Fe^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Ag^{+}	Cd^{2+}	Hg^{2+}	Pb^{2+}
2	% *E*	76	43	35	50	48	39	98	88	74	92
	log *β*	5.8 ± 0.2	—	3.40 ± 0.01	2.1 ± 0.3	4.50 ± 0.04	4.5 ± 0.1	7.0 ± 0.1[c]	5.7 ± 0.1	3.4 ± 0.1	5.0 ± 0.1
3[d]	% *E*	—	—	—	—	14	—	99	97	—	97
4[e]	% *E*	8.0	11	4.0	5.5	39	19	74	13	10	9.1

[a] Values with uncertainties less than 5%. [b] Spectrophotometric measurements, unless otherwise stated. [c] Determined by potentiometry. [d] Data taken from Ref. 19. [e] Data taken from Ref. 29.

methylene region are less overlapped. This situation is also observed in the **2**-Zn^{2+} complex spectrum (Fig. 6).

^1H NMR data of the free and complexed ligand **2** are collected in Table 5.

Complexation of the five cations affects all the proton chemical shifts in the ligand. The largest variations are recorded for the bridging axial methylene protons ($ArCH_2Ar$) and by the oxygen bridge equatorial methylene protons (CH_2OCH_2), which move upfield, and by the aromatic protons, which move downfield. Also the methylene protons of the OCH_2CO groups undergo large shift variations, being upfield in the case of the monovalent cations (Na^+, K^+ and Ag^+) and downfield for the divalent ones (Ba^{2+} and Zn^{2+}). The smallest variations are observed for the protons of the $N(CH_2CH_3)_2$ and *tert*-butyl groups. Similar observations have been made for closely related calix[4]arene derivatives with Na^+,[6,11,34,35] Ag^+,[29,35] and Ba^{2+},[36] and also for the dihomooxaketone **4** with Ag^+.[29]

A more detailed examination of the spectral changes upon complexation shows that the axial methylene proton (H3) of the CH_2 bridge opposite to the bridging oxygen atom (Scheme 1) experiences a very large upfield shift ($\Delta\delta > 0.50$), almost three times the shift observed for the axial methylene protons H5 ($\Delta\delta \cong 0.20$). The exception is for the complexation with Ba^{2+}, which shows very large upfield shifts for both axial protons ($\Delta\delta = 0.86$ and 0.61).

As observed for other calixarene derivatives,[6,11,29,34,36] the variation in chemical shift experienced by the equatorial methylene protons ($ArCH_2Ar$) is downfield and much smaller than that of the axial protons, but the CH_2OCH_2 resonances behave differently, as reported before for ketone **4**.[29] The axial and equatorial methylene protons of the oxygen bridge move upfield and the equatorial protons experience a larger shift variation ($\Delta\delta \cong 0.45$) than the axial ones ($\Delta\delta \cong 0.11$). In the case of Ba^{2+} and Zn^{2+} cations, the axial protons even show a small downfield shift ($\Delta\delta = 0.04$ and 0.11, respectively). These results suggest that the oxygen bridge conformation changes significantly upon complexation, with the equatorial protons undergoing a higher shielding effect.

The downfield shift for the aromatic protons indicates the involvement of the phenolic oxygens in complexation, as reported by Ungaro *et al.*[34] The largest upfield shifts shown by the complexed ligand protons adjacent to the oxygen donor atoms can be explained in terms of variations of both shielding and deshielding effects of the aromatic rings and carbonyl groups upon cation binding to those donor atoms. Therefore, this suggests that all five cations must be inside the cavity defined by the phenoxy and carbonyl oxygen atoms.

Although comparable spectral changes had been observed for complexation of all cations, ligand **2** showed a slight discrimination between the monovalent and the divalent ones. This seems to indicate that the dimensions of the ionophoric cavity and the arrangement of the donor atoms in ligand **2** are best suited to those monovalent cations, but still allow the inclusion of the smallest Zn^{2+} or the biggest Ba^{2+} cations, through more extensive conformational rearrangements.

Ion transport

Transport experiments were carried out in a CH_2Cl_2 liquid membrane system, similar to that employed by Lamb *et al.*[37] Tables 6 and 7 present the transport rates *V* for compound **2**.

These results show that amide **2** ranges from being an inefficient to a reasonably good neutral carrier for all the cations studied. **2** displays a transport rate sequence the reverse of that for the stability constants and for the efficiency of extraction. Whereas K^+ and Na^+ are the most extracted and efficiently complexed cations, they become the most slowly transported ones. The opposite is observed with Cs^+ and Li^+, which being the least bound cations are the fastest transported ones. **2** presents good Cs^+/Na^+ and Cs^+/K^+ transport selectivities ($S = V_{M1}{}^{n+}/V_{M2}{}^{n+} = 16.1$ and 21.5, respectively).

With alkaline earth metal cations a similar situation is observed. Mg^{2+} is now the best carried cation, even showing

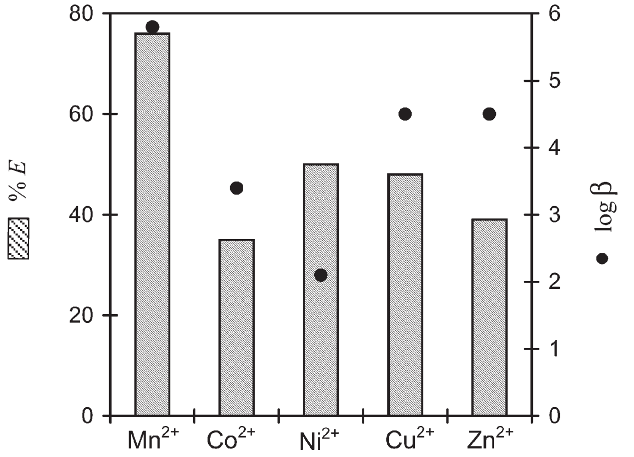


Fig. 3 Percentage extraction (% *E*) and stability constants (log *β*) of transition metal complexes at 25 °C for amide **2**.

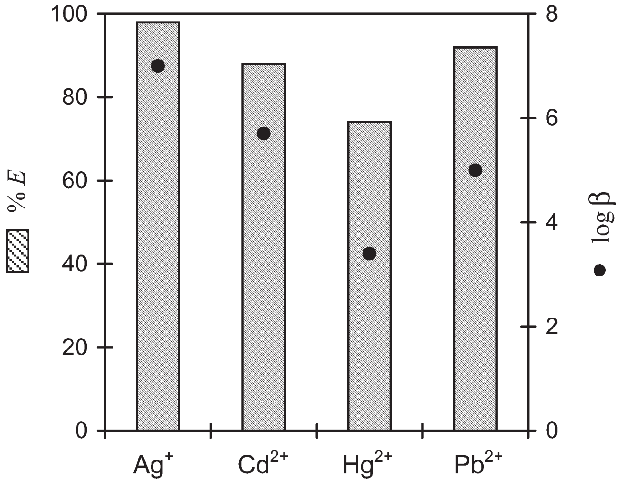


Fig. 4 Percentage extraction (% *E*) and stability constants (log *β*) of heavy metal complexes a 25 °C for amide **2**.

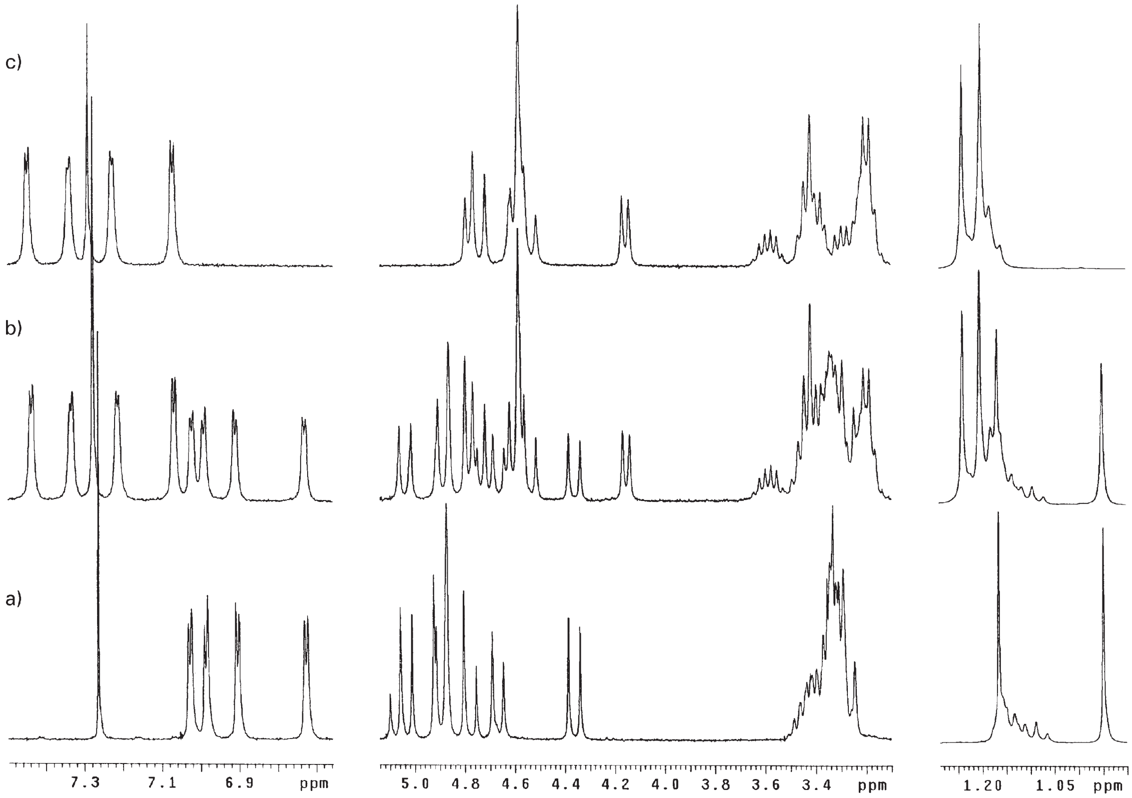


Fig. 5 300 MHz ^{1}H NMR spectra of **2** in $CDCl_3$ at 22 °C: (a) free ligand, (b) upon addition of 0.5 and (c) 1 equiv of KSCN.

the highest transport rate (1.9 µmol h^{-1}) in this work, in contrast to both extraction and complexation processes, where it is the worst bound cation. Amide **2** exhibits very selective transport for Mg^{2+} with respect to Ca^{2+} ($S_{Mg^{2+}/Ca^{2+}} = 90.5$).

The same situation is observed for the four transition and heavy metal cations studied: Ag^+ and Cd^{2+} are the most extracted and complexed cations, but they show very small transport rates when compared to those of Cu^{2+} and Zn^{2+}, both less strongly bound cations.

Based on the classification of ligands as selective carriers (the most efficiently bound cation is also the fastest transported) or selective receptors (the best bound cation is the most slowly transported one) proposed by Lehn,[38] amide **2** is a selective receptor. This is indicated from the negative

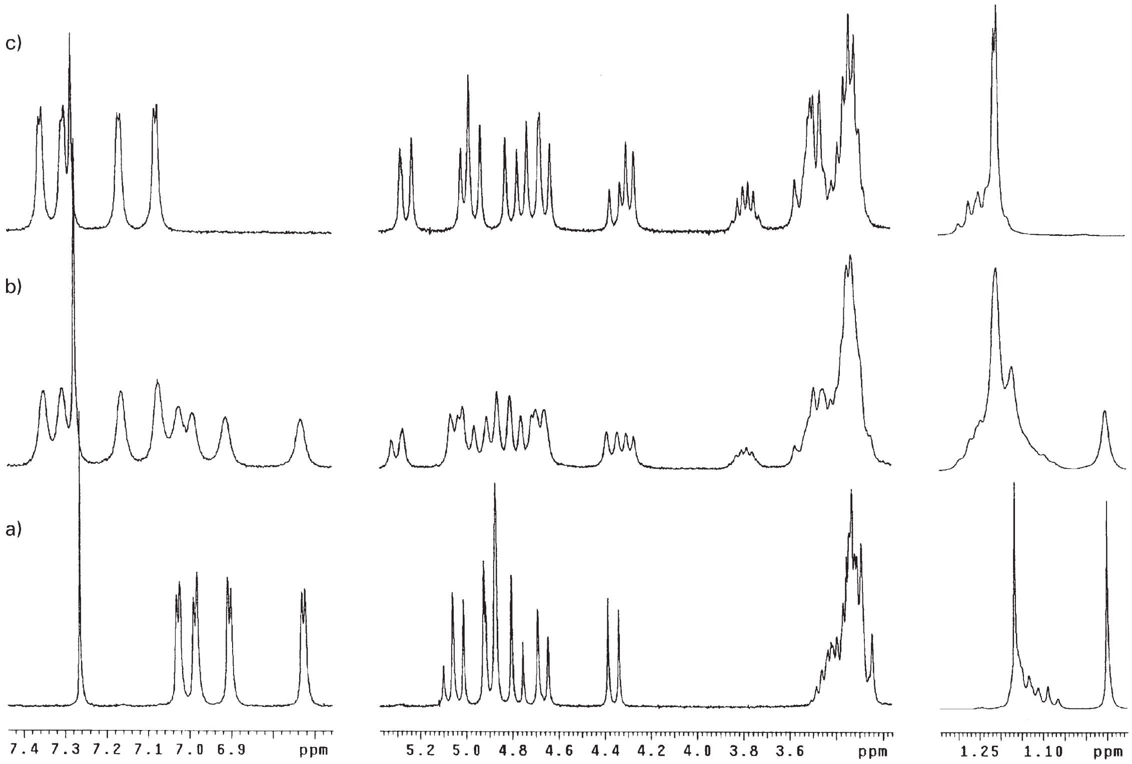


Fig. 6 300 MHz ^{1}H NMR spectra of **2** in $CDCl_3$ at 22 °C: (a) free ligand, (b) upon addition of 0.5 and (c) 1 equiv of $Zn(SO_3CF_3)_2$.

Table 5 Relevant proton chemical shifts (δ) of ligand **2** and its metal complexes

		$ArCH_2Ar$		CH_2OCH_2			
	t-Bu	eq	ax	eq	ax	OCH_2CO	ArH
2	0.95, 1.17	3.27, 3.31	4.91, 5.08	4.67	4.89	4.36, 4.78, 4.90, 5.04	6.72, 6.90, 6.99, 7.02
2 + Na^+	1.18, 1.23	3.39, 3.41	4.70, 4.54	4.23	4.76	4.65, 4.72, 4.74, 4.79	7.07, 7.21, 7.28, 7.42
2 + K^+	1.20, 1.24	3.36–3.47	4.74, 4.59	4.16	4.78	4.54, 4.59[a], 4.60	7.07, 7.23, 7.34, 7.45
2 + Ag^+	1.20, 1.24	3.39, 3.41	4.72, 4.57	4.24	4.74	4.61, 4.67, 4.70[a]	7.08, 7.19, 7.29, 7.41
2 + Ba^{2+}	1.17, 1.21	3.53–3.68	4.30, 4.22	4.18	4.93	4.46, 4.62, 4.97, 5.25	7.08, 7.38, 7.43, 7.50
2 + Zn^{2+}	1.20, 1.21	3.45–3.54	4.66, 4.35	4.29	5.00	4.71, 4.80, 4.96, 5.26	7.08, 7.17, 7.30, 7.36

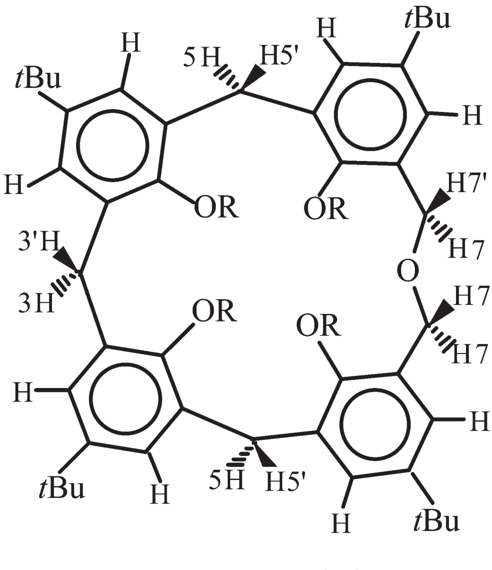
[a] Singlet corresponding to four protons.

slope in the plot of transport rates *versus* stability constants (Fig. 7).

Diethylamide **2** behaves as phenylketone **4**[28,29] and also as diethylamide **3**,[17] although for the latter the conditions and the experimental apparatus used were different, as well as the anion (thiocyanate). Dihomooxaamide **2** is a worse carrier than dihomooxaketone **4**, whereas the opposite trend is observed in complexation and in extraction.

Conclusions

Extraction studies from an aqueous solution into CH_2Cl_2 and stability constant measurements in methanol have shown that the dihomooxaamide **2** shows very high affinities for the alkali cations, in contrast to amide **3** that prefers the alkaline earth cations. Amide **2** displays a preference for Na^+ and K^+, but the largest Rb^+ and Cs^+ cations are also well-bound. Due to the oxygen bridge, **2** is a more flexible and larger molecule compared to **3**. Thus, **2** prefers the larger cations, being a less selective ligand. Amide **2** is a strong binder for most of the transition and heavy metal cations. It shows a strong preference for Ag^+, Cd^{2+}, Pb^{2+} and Mn^{2+}. The results for both amides have shown that, although these ligands bear hard oxygen donor atoms, they display a strong affinity towards soft metal cations, like Ag^+ and Cd^{2+}. Amide **2** forms 1:1 complexes with all cations and ^1H NMR titration experiments suggested that they should be encapsulated into the cavity defined by the phenoxy and carbonyl oxygen atoms. **2** is a poor neutral carrier, showing a transport rate sequence the reverse of that for the stability constants and for the efficiency of extraction. Hence, **2** is a selective receptor, as is amide **3**.



R = $CH_2CON(Et)_2$

Scheme 1

Table 6 Transport rate (V/μmol h^{-1}) of alkali and alkaline earth picrates through a CH_2Cl_2 liquid membrane at 25 °C[a]

	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
2	1.2	0.08	0.06	0.26	1.3	1.9	0.021	0.017	0.036
4[b]	1.8	0.17	0.21	0.8	2.7	0.06	1.5	0.7	0.15

[a] Reproducibility of ±10%. [b] Data taken from Ref. 28.

Experimental

Extraction studies

Ligand **2** was synthesized in a previous work.[31]

Solutions of the metal picrate in water and of the calixarene in CH_2Cl_2 (5 mL each of 2.5×10^{-4} M solutions) were vigorously shaken for 2 min and then thermostatted in a water bath with mechanical stirring, at 25 °C overnight. After complete phase separation, the concentration of picrate ion in the aqueous phase was determined spectrophotometrically

Table 7 Transport rate (V/μmol h^{-1}) of some transition and heavy metal picrates through a CH_2Cl_2 liquid membrane at 25 °C[a]

	Cu^{2+}	Zn^{2+}	Ag^+	Cd^{2+}
2	1.0	0.9	0.08	0.07
4[b]	0.21	0.049	0.8	0.08

[a] Reproducibility of ±10%. [b] Data taken from Ref. 29.

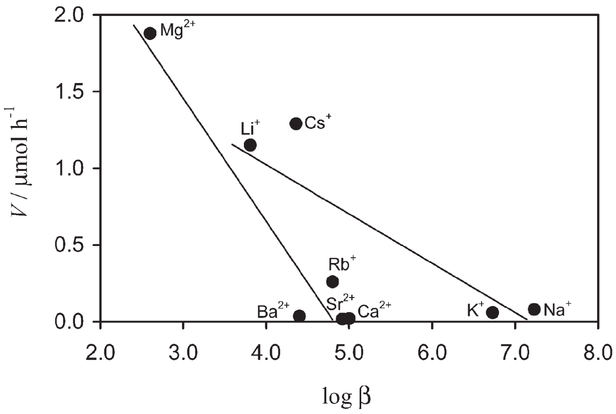


Fig. 7 Correlations between transport rate (V/μmol h^{-1}) of metal picrates and log β for amide **2**.

($\lambda_{max} = 354$ nm). For each cation-calixarene system, the absorbance measurements were repeated four times. Blank experiments showed that no picrate extraction occurred in the absence of the calixarene derivative. The details of metal picrate preparation have already been described.[28,29]

Determination of stability constants

The stability constants β, defined as the concentration ratio $[ML^{n+}]/[M^{n+}][L]$ (where M^{n+} = cation and L = ligand) were determined in methanol (Carlo Erba, 99.9%, used without further purification) by UV absorption spectrophotometry at 25 °C and at 0.01 M ionic strength provided by Et_4NCl (Fluka purum), according to the procedure already described.[20] The ligand concentrations ranged between 2.5×10^{-4} and 5×10^{-4} M and the spectra were treated using the program SPECFIT.[39] When log β was superior to 5, competitive potentiometry involving Ag^+ as an auxiliary cation was performed, as already described.[20] The data were treated using the program SIRKO.[40]

The salts used for spectrophotometry were chlorides (LiCl Fluka purum; RbCl Merck suprapur; CsCl Fluka puriss; $MgCl_2$, $SrCl_2$, $BaCl_2$ and $MnCl_2$ Merck p.a.; $CdCl_2$, $HgCl_2$ and $PbCl_2$ Prolabo rectapur) or perchlorates [$Co(ClO_4)_2$, $Ni(ClO_4)_2$ and $Cu(ClO_4)_2$ Fluka purum; $Zn(ClO_4)_2$ Johnson Matthey Alfa products]. The salts used for potentiometry were perchlorates [Et_4NClO_4, $NaClO_4$, $Ca(ClO_4)_2$ Fluka purum; $KClO_4$ Prolabo p.a.] and $AgBF_4$ (Riedel-de Haën). All these salts were dried under vacuum for 24 h before use.

The concentrations of the cation solutions, except for the alkali cations, were analysed by a Varian Liberty 220 (ICP-AES) spectrometer. The concentration of the Ag^+ solution was determined by potentiometry with addition of NaCl.

Calorimetric measurements

The calorimetric determinations were made in methanol at 25 °C using a precision Isoperibol titration calorimeter (Tronac 450, Orem, Utah). The experimental procedure has already been reported in detail elsewhere.[16] The salt solutions (1.4×10^{-2} M) were titrated into a 50 mL solution of the calixarene (5×10^{-4} M). The measured heat was directly related to the complexation enthalpy ΔH, because log β is known to be higher than 5. Knowing $\Delta G = -RT \ln\beta$, $T\Delta S$ values were derived from the expression $\Delta G = \Delta H - T\Delta S$.

The accuracy of the calorimetric measurements was checked by determining the enthalpy of complexation of Na^+ with 18-crown-6 in methanol. The calculated value ($\Delta H = -35.3$ kJ mol^{-1}) was in good agreement with the literature data ($\Delta H = -34.0$ kJ mol^{-1}).[41]

^{1}H NMR titration experiments

Several aliquots (up to 2–3 equiv) of the salt solutions (NaSCN, KSCN and Ba, Ag and Zn triflates, 1 M) in CD_3OD were added to $CDCl_3$ solutions (2×10^{-2} M) of ligand **2** directly in the NMR tube, with a 25 µL syringe. The spectra were recorded on a Varian Unity 300 spectrometer after each addition of the salts; the temperature of the NMR probe was kept constant at 22 °C.

Transport experiments

The ion transport across a liquid membrane was done using an apparatus similar to that employed by Lamb *et al.*[37] The membrane phase (50 mL of a 7×10^{-5} M solution of the calixarene in CH_2Cl_2), the receiving phase (25 mL of doubly distilled and deionised water) and the source phase (7 mL of a 5×10^{-3} M aqueous solution of metal picrate), were placed in a thermostatted vessel. The apparatus was maintained at 25 °C and the phases stirred at 150 rpm. The experiments were repeated at least three times. The appearance of the picrate ion in the receiving phase was followed by UV spectrophotometry at regular time intervals. Experiments with no carrier present were performed, indicating no transport of metal picrates. The experimental procedure has already been described in detail elsewhere.[28]

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