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Synthesis, Complexation, and Membrane Transport Studies of 1,3-Alternate Calix[4]arene-crown-6 Conformers: A New Class of Cesium Selective Ionophores

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Abstract: 1,3-Dialkoxycalix[4]arene-crown-6 ionophores (**4a−d**) are obtained in the fixed 1,3-alternate conformation in 63−85% yield by the reaction of the corresponding 1,3-dialkoxycalix[4]arenes **3a−d** with pentaethylene glycol ditosylate in CH_3CN in the presence of Cs_2CO_3. The corresponding cone conformer of the diisopropyl derivative (**6**) was synthesized *via* selective demethylation of the 1,3-dimethoxycalix-crown (**2a**) and subsequent dialkylation. Extraction experiments with alkali picrates reveal a strong preference of ligands **4** for Cs^+. Thermodynamic parameters obtained for the complexation of **4a** show that the high stability constant in MeOH ($\log\beta = 6.4 \pm 0.4$) is reflected mainly in the large $-\Delta H_c$ value of 50.2 ± 0.2 kJ·mol^{-1}. The entropy of complexation ($T\Delta S_c = -15$ kJ·mol^{-1}), less negative than for other crown ethers, is explained in terms of preorganization of **4a**. The X-ray structure of the cesium picrate·**4a** complex shows clearly that the cation is positioned between the two aromatic rings with short Cs−C distances of 3.49 and 3.69 Å, respectively. ^1H NMR spectroscopy confirms this type of structure in solution. Ligands **4** incorporated in supported liquid membranes transport Cs^+ cations with a high preference over Na^+. By the application of an anion gradient, traces of Cs^+ can be removed (≥99.8%) from acidic solutions (pH = 0) that contain 4 M of $NaNO_3$.

Introduction

The present work had its beginning with the studies of Ungaro and co-workers[1] involving the use of calixarenes[2] as building blocks or molecular platforms for the construction of metal ion ligands.[3] It is now well-established that the efficiency and selectivity in metal ion binding by calixarene ionophores depends not only on the ring size of the calix but also on the nature of the binding groups attached and, especially for calix[4]arene derivatives, on the conformation of the macrocycle (cone, partial cone, 1,3-alternate, 1,2-alternate).

Ungaro and co-workers have previously reported the synthesis, structure, and complexing properties of several stereoisomers of 1,3-dialkoxy-*p*-*tert*-butylcalix[4]arene-crown-5,[4] a new class of potassium selective ligands. Their ionophoric properties[5] as well as their selectivity in metal detection by ion-selective field effect transistors[6] strongly depend on the stereochemistry around the binding region. Interestingly, Yamamoto and Shinkai[7] have reported that the corresponding calix[4]arene-crown-4, with a shorter polyethylene glycol bridge, shows a very high *inverse* K^+/Na^+ selectivity in ion-selective electrodes.

We have investigated the combination of calix[4]arenes and crown ether bridges for the problem of selective removal of $^{137}Cs^+$ from medium level radioactive waste, an important environmental and technological problem.[8,9] The objective was to selectively extract long-lived ^{137}Cs isotopes from an aqueous solution containing 1 M HNO_3 and 4 M $NaNO_3$.

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(1) Bocchi, V.; Fiona, D.; Pochini, A.; Ungaro, R. *Tetrahedron* **1982**, *38*, 373−378.

(2) For recent review articles and books on calixarenes, see: (a) Gutsche, C. D. *Calixarenes, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, U.K., 1989; Vol. 1. (b) *Calixarenes, A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer, Academic Publishers: Dordrecht, The Netherlands, 1991. (c) Gutsche, C. D. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: New York, 1991; Vol. 4, pp 27−63. (d) Van Loon, J.-D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proced. Int.* **1992**, *24*, 437−462. (e) Shinkai, S. *Tetrahedron* **1993**, *40*, 8933−8968. (f) Böhmer, V. *Angew. Chem.* **1994**, in press. (g) Pochini, A.; Ungaro, R. In *Comprehensive Supramolecular Chemistry*; Vögtle, F., Ed.; Pergamon Press, in press; Vol. 2.

(3) For recent review articles on the inclusion properties of calixarenes, see: Ungaro, R.; Pochini, A. in ref 2b, pp 127−147. Ungaro, R.; Pochini, A. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Eds.; VCH: Weinheim, Germany, 1991; pp 57−81. Andreetti, G. D.; Ugozzoli, F.; Ungaro, R.; Pochini, A. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., Mac Nicol, D. D., Eds.; Oxford University Press: New York, 1991; Vol. **4**, pp 64−125. Van Doorn, A. R.; Verboom, W.; Reinhoudt, D. N. In *Adv. Supramol. Chem.* **1993**, *3*, 160−206. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. In *Computational Approaches in Supramolecular Chemistry*; Wipff, G., Ed.; Kluwer Academic, Publishers: Dordrecht, The Netherlands, 1994; pp 277−300.

(4) (a) Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.-E.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567−7575. (b) Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A. A; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 6979−6985.

(5) Nijenhuis, W. F.; Buitenhuis, E. G.; de Jong, F.; Sudhölter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 7963−7968.

(6) Brzozka, Z.; Lammerink, B.; Reinhoudt, D. N.; Ghidini, E.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1037−1040.

(7) Yamamoto, J.; Shinkai, S. *Chem. Lett.* **1994**, 1115−1118.

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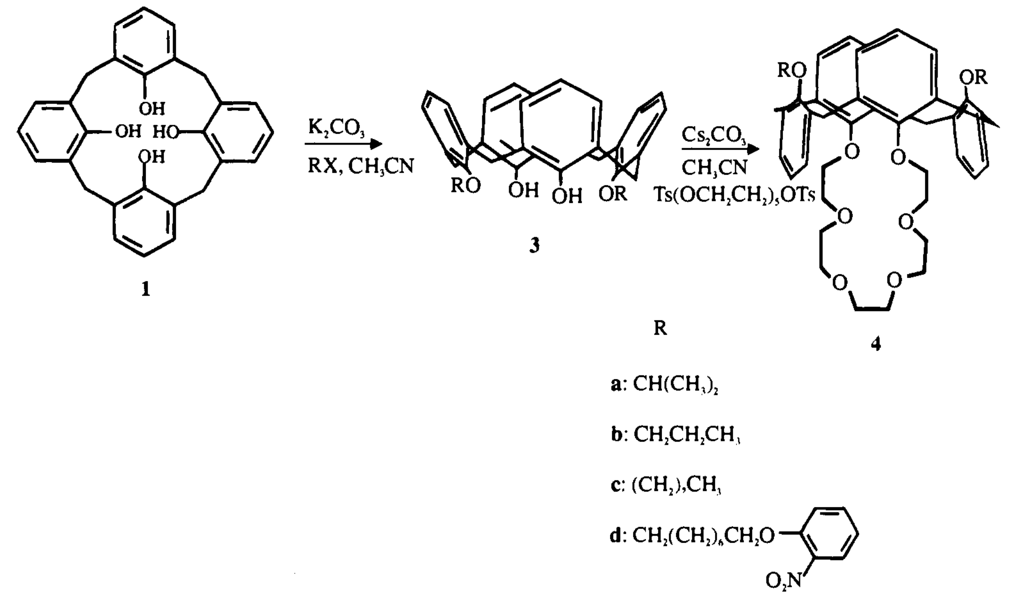
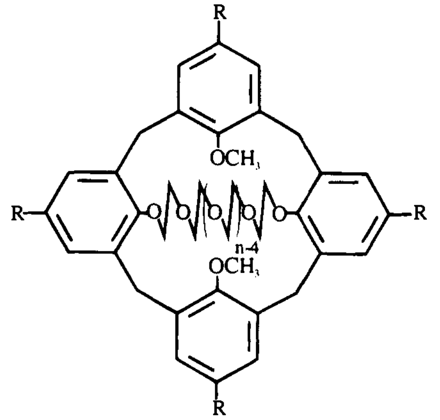
Scheme 1





2a: n = 6, R = H

b: n = 6, R = t-Bu

c: n = 5, R = H

d: n = 7, R = H

In this paper we report that 1,3-dialkoxycalix[4]arene-crown-6 derivatives, when they are fixed in the 1,3-alternate conformation, are exceptionally selective ionophores for cesium cations. The properties of these new ligands have been assessed by NMR, two-phase solvent extraction, thermodynamic studies in solution, and X-ray crystal structure determination of their cesium complexes. Their application in supported liquid membranes revealed that it is possible to remove cesium salts selectively from strongly acidic solutions that contain 4 M $NaNO_3$. By anion-driven transport against the concentration gradient ≥99.8% of traces of cesium can be removed within 24 h.

Results and Discussion

Synthesis and Conformational Properties of the Ionophores. The X-ray crystal structure of the cesium picrate complex of the 1,3-dimethoxycalix[4]arene-crown-6 (**2a**) revealed that this conformationally mobile ligand adopts a 1,3-alternate conformation in the complex.[10] Therefore further work focused on the synthesis of calix[4]crown-6 derivatives having a *fixed* 1,3-alternate structure. Previously Reinhoudt and coworkers have shown that the reaction of calix[4]arenes with alkylating agents in CH_3CN in the presence of Cs_2CO_3 is a well established method to obtain tetraalkoxycalix[4]arenes fixed in the 1,3-alternate conformation.[11] When we applied this method (Scheme 1) to 1,3-dialkoxycalix[4]arenes (**3**), prepared from calix[4]arene **1** with alkyl halides in CH_3CN in the presence of K_2CO_3, we obtained the calix[4]crown-6 ethers (**4**) in a fixed 1,3-alternate conformation. No other isomers were isolated. Possibly the cyclization reaction to give the 1,3-alternate conformers is favored by the cesium template ions. All compounds **4** are blocked in the 1,3-alternate conformation as inferred from the ^1H NMR spectra which exhibit a singlet around δ 3.8 for the bridging methylene groups of the calix[4]arene moiety. The ^{13}C NMR spectra show one signal around 38 ppm, characteristic for *anti*oriented nuclei in the calix.[12] The 1,3-diisopropoxy cone isomer (**6**) was synthesized via **5** by first bridging calix[4]arene **1** with pentaethylene glycol ditosylate in benzene with KO*t*-Bu as the base. The yield of 1,3-dihydroxycalix[4]arene-crown-6 was only 34%. An alternative route (Scheme 2) to **5** involves the reaction of 1,3-dimethoxycalix[4]arene-crown-6 (**2a**) with trimethylsilyl iodide that produces **5** in 84%. This very selective demethylation procedure[13] seems not to affect the crown ether moiety and may provide a general method for the synthesis of dihydroxycalix[4]arene-crown ethers

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(8) *Radioactive Waste Management and Disposal*; Cecille, L., Ed.; Elsevier Science Publisher: London, New York, 1991.

(9) McDowell, W. J.; Case, G. N.; McDonough, J. A.; Bartsch, R. A. *Anal. Chem.* **1992**, *64*, 3013–3017.

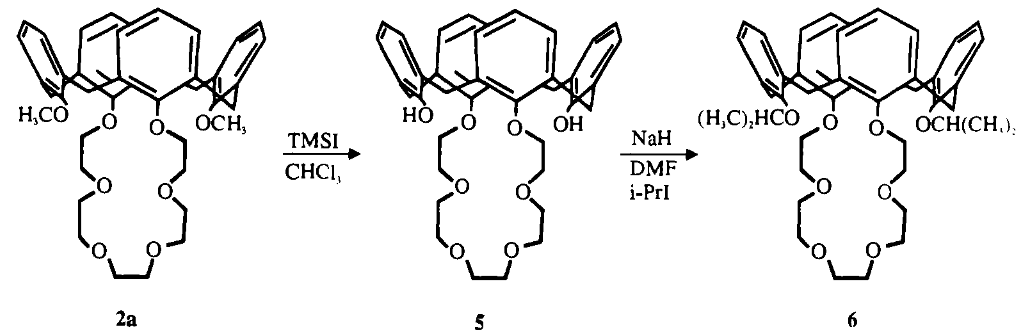
(10) Ungaro, R.; Casnati, A.; Ugozzoli, F.; Pochini, A.; Dozol, J.-F.; Hill, C.; Rouquette, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1506–1509.

(11) Verboom, W.; Datta, S.; Asfari, Z.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1992**, *57*, 5394–5398.

(12) Molins, M. A.; Nieto, P. M.; Sanchez, C.; Prados, P.; de Mendoza, J.; Pons, M. O. *J. Org. Chem.* **1992**, *57*, 6924–6931.

(13) Casnati, A.; Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R. *Tetrahedron* **1991**, *47*, 2221–2228.

Scheme 2



2a **5** **6**

Table 1. Conformers Distribution and NMR Aromatic Signals for Compound **2a** in Different Solvents at −25 °C

solvent	conformation	%	ArH
CD_3CN	cone	50	7.18 (d), 6.90 (t), 6.52 (d), 6.42 (t)
	partial cone	35	7.17, 7.14, 6.93−6.88, 6.56
	1,3-alternate	15	7.32 (d), 7.09 (d), 7.00 (t), 6.84 (t)
$CDCl_3$	cone	60	7.19 (d), 6.97 (t), 6.40 (m)
	partial cone	25	7.24, 7.21, 6.97, 6.61(t), 6.56(dd), 6.43
	1,3-alternate	15	7.33 (d), 7.11 (d), 6.99 (t), 6.85 (t)
CD_3OD[a]	cone	64	7.11 (d), 6.87 (t), 6.30 (m)

[a] At +25 °C.

Table 2. Extraction Percentage of Alkali Picrates by Calix-crowns, from Water to Dichloromethane, at 20 °C

ligands	Li^+	Na^+	K^+	Rb^+	Cs^+
2a	0.4 ± 0.2	0.67 ± 0.07	1.0 ± 0.1	2.3 ± 0.2	6.3 ± 0.2
2b	1.4 ± 0.2	1.6 ± 0.4	2.2 ± 0.3	3.1 ± 0.5	19.0 ± 0.7
2c	2 ± 0.4	1.6 ± 0.3	10 ± 1	8.9 ± 0.9	2.8 ± 0.3
4a	3.0 ± 0.4	2.4 ± 0.1	15.8 ± 0.5	43.8 ± 0.7	64.5 ± 0.7
4b	2.5 ± 0.5	2.6 ± 0.6	13.8 ± 0.4	41.7 ± 0.3	63.5 ± 0.3
4c	2.1 ± 0.3	2.2 ± 0.3	13.4 ± 0.8	40.0 ± 0.9	63.9 ± 0.3
2d	0.5 ± 0.4	0.21 ± 0.08	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.1
6	≤0.2	≤0.2	≤0.2	≤0.2	≤0.2

which are difficult to obtain by direct bridging.[4b,14] The reaction of **5** with isopropyl bromide in DMF with NaH as the base, a standard procedure for the synthesis of *cone conformers*,[15] produced **6** in 73% yield. In the ^1H NMR spectrum the $ArCH_2$-Ar protons of **6** give an AX system (δ 3.14 and 4.38 ppm) and in the ^{13}C NMR a triplet ($\delta_c = 31.6$ ppm), which are both typical for a fixed cone conformation.[12] The conformationally mobile 1,3-dimethoxycalix[4]arene-crown ethers (**2**) were synthesized from the 1,3-dimethoxycalix[4]arenes and the appropriate polyethylene glycol ditosylates. They are conformationally mobile in solution; detailed VT-^1H NMR studies have been performed only on compound **2a** in two different solvents CD_3CN and $CDCl_3$. The room temperature ^1H NMR spectrum of **2a** is composed of sharp and broad peaks in all regions, which indicate the presence of three conformations, one of which (the cone) is kinetically stable (on the 400 MHz time scale) whereas the other two are in rapid equilibrium. At $T = -25$ °C the signals of the three conformations are clearly visible in both solvents, and by integration of the aromatic region their relative abundance was established (Table 1).

In both solvents the thermodynamically most stable conformer of **2a** is the cone, followed by partial cone and 1,3-alternate. The cone conformation is also the most stable for compounds **2b−d**; a "flattened cone" structure has been found in the solid state for the 1,3-dimethoxy-*p-tert*-butylcalix[4]arene-crown-5.[4b]

Complexation Studies

A first estimation of the ionophoric properties of ligands **2**, **4**, and **6** was accomplished by the picrate extraction method developed by Pedersen.[16] The results are reported in Table 2. We also determined association constants in wet $CHCl_3$, using the picrate extraction method reported by Lein and Cram[17] which is more quantitative and allows a direct comparison of the ionophoric properties of compound **2a,b**, **4a,b**, and **6** with other lipophilic alkali metal ion complexing agents,[18] including other calix-crowns.[4] The results of these studies are reported in Table 3. Both types of experiments reveal a high preference of ligands **4** fixed in the 1,3-alternate conformation for Cs^+. The corresponding cone conformer **6** hardly extracts or binds Cs^+.

Complexation data (logβ) for conformationally mobile calix-crowns-6 (**2a,b**) and for compounds **4a** and **4b**, blocked in the 1,3-alternate conformation and alkali metal cations in MeOH are reported in Table 4 and Figure 1. These data were obtained by UV absorption spectrophotometry and by competitive potentiometric measurements. The logβ values for the silver complexes are also reported as their determination was necessary for the interpretation of the competitive potentiometric measurements. Table 5 reports the thermodynamic parameters (ΔH_c and $T\Delta S_c$) for the complexation, determined by calorimetry.

There is full agreement between the extraction and the complexation data for the calix-crowns reported. Among the conformationally mobile 1,3-dimethoxy compounds **2** the crown-5 (**2c**) shows selectivity for potassium ion, the calix-crown-7 (**2d**) is completely unselective and quite inefficient, whereas the crowns-6 (**2a** and **2b**) show selectivity for cesium cation. The *tert*-butyl derivative **2b** is slightly more efficient than the unsubstituted analog **2a**.

A dramatic increase in the binding and extraction of cesium cation is observed for all ligands in the *1,3-alternate* conformation.

A stereochemical dependence of alkali metal ion complexation was previously observed in potassium selective ionophores, the 1,3-diethoxy-*p-tert*-butylcalix[4]arene-crowns-5,[4b] but the difference between cone and partial cone or 1,3-alternate conformers was not as large as that observed in this case for the two conformers **6** (cone) and **4a** (1,3-alternate). Probably the presence of two bulky isopropoxy groups decreases for steric reasons, the already low binding ability of the cone isomer, especially toward the larger cations. Interestingly all calix[4]arene-crowns-6 in the 1,3-alternate conformation (**4**) do not

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(14) Yamamoto, H.; Sakaki, T.; Shinkai, S. *Chem. Lett.* **1994**, 469−472.

(15) Groenen, L. C.; Rüel, B. H. M.; Casnati, A.; Timmerman, P.; Verboom, W.; Harkema, S.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Tetrahedron Lett.* **1991**, *32*, 2675−2678.

(16) Pedersen, C. J. *Fed. Proc. Fed. Am. Soc. Expl. Biol.* **1968**, *27*, 1305−1309

(17) (a) Lein, G. M.; Cram, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 448−455. (b) Helgeson, R. C.; Weisman, G. R.; Toner, J. L.; Tarnowski, T. L.; Chau, L.; Mayer, J. M.; Cram, D. J. *J. Am. Chem, Soc.* **1979**, *101*, 4928−4941.

(18) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1039−1057.

Table 3. Association Constants (K_a) and Binding Free Energies ($-\Delta G$) of Complexes of Hosts with Alkali Picrates in $CHCl_3$ Saturated with H_2O at 22 °C[a]

	$\log K_a$					$-\Delta G$ (kJ mol^{-1})				
ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	Li^+	Na^+	K^+	Rb^+	Cs^+
4a	*b*	5.2	6.4	7.9	8.8	<24	29.2	36.8	44.6	49.4
4b	5.5	5.1	6.8	7.7	8.6	31.2	28.7	36.9	43.7	48.4
2a	*b*	4.3	4.2	5.2	6.0	<24	24.3	26.2	29.6	33.8
2b	4.7	4.6	5.2	5.3	6.5	26.8	26.4	29.7	30.6	37.3
6	<4	<4	<4	<4	<4	<24	<24	<24	<24	<24

[a] The association constants were determined as described by Cram et al.;[17a] the precision of the method is as described by Cram et al.[17b] [b] Not determined.

Table 4. Complexation Data ($\log\beta$)[a] of Some Calix[4]arene-crown-6 and Alkali Metal Cations, in MeOH, at 25 °C, I = 0.01 M (Et_4NCl or Et_4NClO_4)

ligands	Li^+	Na^+	K^+	Rb^+	Cs^+	Ag^+
4a	$\leq 1^b$	$\leq 1^b$	$4.5 \pm 0.1^{b,c}$	5.93 ± 0.06^c	6.1 ± 0.2^c	4.52 ± 0.09^c
4b	$\leq 1^b$	$\leq 1^b$	4.3 ± 0.2^c	5.96 ± 0.01^c	6.4 ± 0.2^c	4.6 ± 0.09^c
2a	$\leq 1^b$	$\leq 1^b$	2.13 ± 0.08^b	3.18 ± 0.03^b	4.2 ± 0.2^b	
2b	$\leq 1^b$	$\leq 1^b$	2.54 ± 0.08^b	3.5 ± 0.3^b	4.6 ± 0.1^b	

[a] Standard deviation σ_{n-1} of the mean of a minimum of two experiments. [b] UV absorption spectrophotometric measurements. [c] Direct or competitive (with Ag^+) potentiometric measurements.

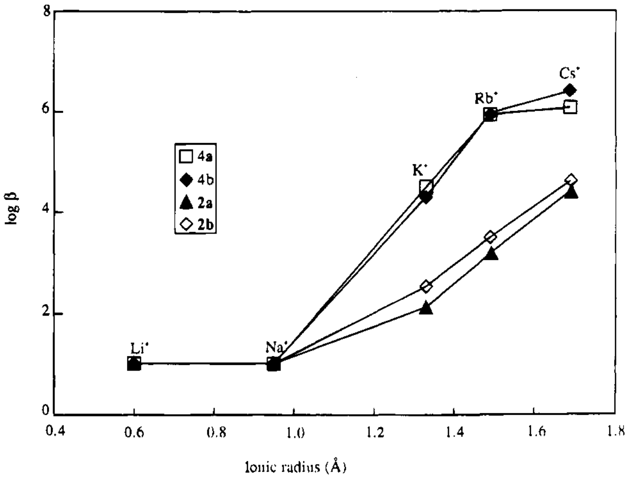

Figure 1. Stability constants ($\log\beta$) for complexes of alkali metal cations and calix-crowns in methanol (data from Table 4).

complex efficiently small cations such as lithium and sodium and therefore their Cs^+/Na^+ selectivity is very high ($\Delta\log\beta \geq 5$). This is an important finding, since for the removal of cesium ion from radioactive waste a very high Cs^+/Na^+ selectivity is required.[8]

Calorimetric measurements were carried out to better understand the selectivity observed and the difference between "mobile" compounds (**2a**,**b**) and those preorganized in the 1,3-alternate structure exemplified by **4a**. Although the interpretation of the results, reported in Table 5, is rather complex due to the concomitant operation of several effects, some interesting features emerge from the data. The high efficiency of ligand **4a** in the complexation of cesium ion is controlled by the enthalpy term, which is one of the highest values found for a synthetic ligand toward cesium in MeOH.[19a] This value is not so much counterbalanced by the entropy term ($T\Delta S_c$) which is less negative than with other cyclic ligands, such as 18-crown-6 and 21-crown-7.[19b] The slightly less negative value found for the entropy term can be explained by the preorganization of the ligand in the 1,3-alternate conformation, where only a small part of the crown ether moiety is rather flexible. Only this flexibility is lost during complex formation with the large cesium ion, which fits very well, according to CPK models and to X-ray analysis, into the cavity created by the polyether ring and by the aromatic nuclei, thus explaining the slightly lower negative value (−15 ± 1 kJ·mol^{-1}) found for the $T\Delta S_c$ term compared, for example, with the cesium complex of 18-crown-6 ($T\Delta S_c$ = −19.8 kJ·mol^{-1}) and of 21-crown-7 ($T\Delta S_c$ = −18.1 kJ·mol^{-1}).[19b] Going toward smaller cations such as Rb^+ and especially K^+ the $-\Delta H_c$ decreases and the $T\Delta S_c$ becomes even positive for K^+. This behavior is very different from that of other crown ether complexes for which the $T\Delta S_c$ terms are usually negative[19] and indicates that these cations are not interacting strongly (because of a non-perfect fit) with all the available binding sites, but probably only with the two opposite aromatic nuclei and the upper part of the crown close to the phenolic oxygen atoms. The high Cs^+/Na^+ selectivity observed with these ligands finds its origin in the fact that the crown ether moiety, whose size is intermediate between a 18-crown-6 and a 21-crown-7, fits the cesium cation very well, while it cannot wrap around the smaller cations due to the steric hindrance of the calix skeleton.

Also in the case of the conformationally mobile compounds **2a** and **2b** the stability of the cesium complex is enthalpy controlled as $-\Delta H_c > 0$ and $T\Delta S_c \leq 0$.

The comparison of the thermodynamic parameters of the cesium complexes of ligand **4a** and the conformationally mobile analogue **2a** reveals some interesting features. Since ligand **2a** exists in MeOH solution mainly in the cone conformation (*vide supra*) and adopts a 1,3-alternate structure in solution (*vide infra*) and in the solid state[10] upon complexation with Cs^+, one would have expected that this interconversion should be payed for mainly in terms of entropy rather than enthalpy. This is not the case, since the $T\Delta S_c$ term for the **2a**·Cs^+ complex is 0 kJ·mol^{-1} and is much more favorable than the corresponding value for **4a**·Cs^+ (−15 kJ·mol^{-1}). On the other hand, the former complex is enthalpically less stable ($-\Delta H_c$ = 23 kJ·mol^{-1}) compared with the latter ($-\Delta H_c$ = 50.2 kJ·mol^{-1}). This result can be explained in terms of solvation effects. The cone conformation of calix-crown **2a**, being more polar and less preorganized, is more exposed to solvation than the less polar and fixed 1,3-alternate conformation. The desolvation which must occurr during the complexation process with cesium ion should enhance the $T\Delta S_c$ term and decrease the $-\Delta H_c$ term in ligand **2a** compared with the ligand **4a**, a result which is indeed observed. The higher efficiency and Cs^+ selectivity shown by ligands **4**, blocked in 1,3-alternate conformation, therefore can be explained by invoking the concept of preorganization which clearly includes, in Cram's definition,[18] the solvation effect.

The similar $\log\beta$ values for **2a**·Cs^+ and **2b**·Cs^+ would normally suggest that these complexes are thermodynamically quite similar; however, this is not the case. When the individual thermodynamic contributions are examined, they are very different for the two complexes, *i.e.* $-\Delta H_c$ is more positive and

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(19) (a) Inoue, Y.; Liu, Y.; Hakushi, T. In *Cation Binding by Macrocycles*; Inoue, Y., Gokel, G. W., Eds.; M. Dekker: New York, 1990; pp 1−110. (b) Lamb, J. D.; Izatt, R. M.; Swain, C. S.; Christensen, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 475−479.

Table 5. Thermodynamic Parameters of Complexation in Methanol, at 298 K [ΔH_c ($kJ \cdot mol^{-1}$), ΔG ($kJ \cdot mol^{-1}$), $T\Delta S$ ($kJ \cdot mol^{-1}$), and ΔS_c ($J \cdot K^{-1} \cdot mol^{-1}$)][a]

	4a				**2a**	**2b**	18C6[b]	21C7[b]
Ligands	Ag^+	K^+	Rb^+	Cs^+	Cs^+	Cs^+	Cs^+	Cs^+
log*K*	4.52 ± 0.09	4.5 ± 0.1	5.93 ± 0.06	6.1 ± 0.2	4.2 ± 0.2	4.6 ± 0.1	4.79 ± 0.05	5.01 ± 0.01
$-\Delta G_c$	25.8 ± 0.5	25.6 ± 0.6	33.8 ± 0.3	35 ± 1	24 ± 1	26.2 ± 0.6	27.3 ± 0.3	28.56 ± 0.06
$-\Delta H_c$	13.5 ± 0.4	18.1 ± 0.4	40 ± 2	50.2 ± 0.4	23 ± 1	36 ± 3	47.2 ± 0.3	46.73 ± 0.04
$T\Delta S_c$	12.3 ± 0.9	7 ± 1	−6 ± 2	−15 ± 1	0 ± 2	−10 ± 4	−19.8 ± 0.6	−18.1 ± 0.1
ΔS_c	41 ± 3	25 ± 3	−21 ± 6	−52 ± 3	2 ± 6	−30 ± 10		

[a] Standard deviation σ_{n-1} on the mean of *n* experiments ($2 \le n \le 4$). [b] From ref 19b.

$T\Delta S_c$ more negative with **2b** than with **2a**. The structures of the two complexes in solution seem to be similar (*vide infra*), showing the calix to be in the 1,3-alternate conformation. The large difference in the $-\Delta H_c$ values for the complexes can be attributed to the better fitting of the cesium cation inside the binding pocket constituted by the aromatic nuclei and the crown ether ring and to the enhanced basicity of the aromatic nuclei and the oxygens involved in complexation with consequently a stronger interaction with the cation. Another hypothesis which could explain the difference in both entropy and enthalpy terms is the lower solvation of the calixarene cavity of ligand **2b**, which would result upon complexation in a more favorable variation in enthalpy and in a less favorable change in entropy as observed. This effect could hide a possible favorable entropy contribution arising by a higher desolvation of the crown imposed by the *tert*-butyl groups.

Solution and Solid State Structure of Alkali Metal Complexes. The ^1H NMR spectrum of the 1:1 complex between the conformationally mobile calix-crown **2a** and Cs^+ picrate in CD_3CN or CD_3OD is very different from that of the free ligand previously discussed. Of the three conformations present in the free ligand **2a**, only the least stable 1,3-alternate conformation is detected (>95%) in the cesium complex. This is clearly indicated by the disappearance of the two doublets (AX system) of the bridging methylenes ($ArCH_2Ar$) of the cone isomer and of the broad signals attributed to other conformations (Figure 3b). Upon complexation all these signals merge in a singlet around 3.7 ppm which is typical for a symmetrical 1,3-alternate calix[4]arene conformation (Figure 2c). The same behavior is shown by the *p*-*tert*-butyl derivative **2b**.

These results are in full agreement with the X-ray crystal structure of the cesium complex of ligand **2a** which shows the calix in a 1,3-alternate conformation.[10] A completely different behavior is shown by the sodium complex of ligand **2a** whose ^1H NMR spectrum (Figure 2a) shows (at >80% complexation) the presence of only the cone conformation.

The X-ray crystal structure of the cesium picrate complex of ligand **4a** is given in Figure 3, whereas in Table 6 the most relevant bond distances observed in the coordination sphere of the complexed cation are reported, together with the corresponding values previously reported for the cesium picrate complex of ligand **2a**. In both structures there is clear evidence for the participation of the aromatic nuclei in complexation. In the **4a**·CsPic complex (Figure 3) the cation interacts in η^3 fashion with the rotated nucleus D and in the η^2 with the opposite nucleus B. The Cs−C contacts which range from 3.486(8) to 3.69(1) Å, are not very different from the corresponding values observed in the **2a**·CsPic complex (Table 6)[10] and compare very well with those reported for systems were cesium−arene interactions have been documented.[20] Interestingly the shortest Cs−O distances are found for the oxygens O(1), O(4), O(1A), and O(1C) of the upper part of the crown moiety close to the aromatic nuclei thus indicating, in agreement with the thermodynamic data, that the binding pocket constituted by these oxygen atoms and by the two rotated aromatic nuclei contributes most to the complexation. Surprisingly, the picrate anion is interacting with the complexed cesium cation not through the phenolic oxygen but only through one nitro group in the *ortho* position (O1P). This is the most relevant difference between the X-ray crystal structure shown in Figure 3 and that reported previously for the **2a**·CsPic where the phenolate anion of the picrate is also coordinated to the cesium cation.

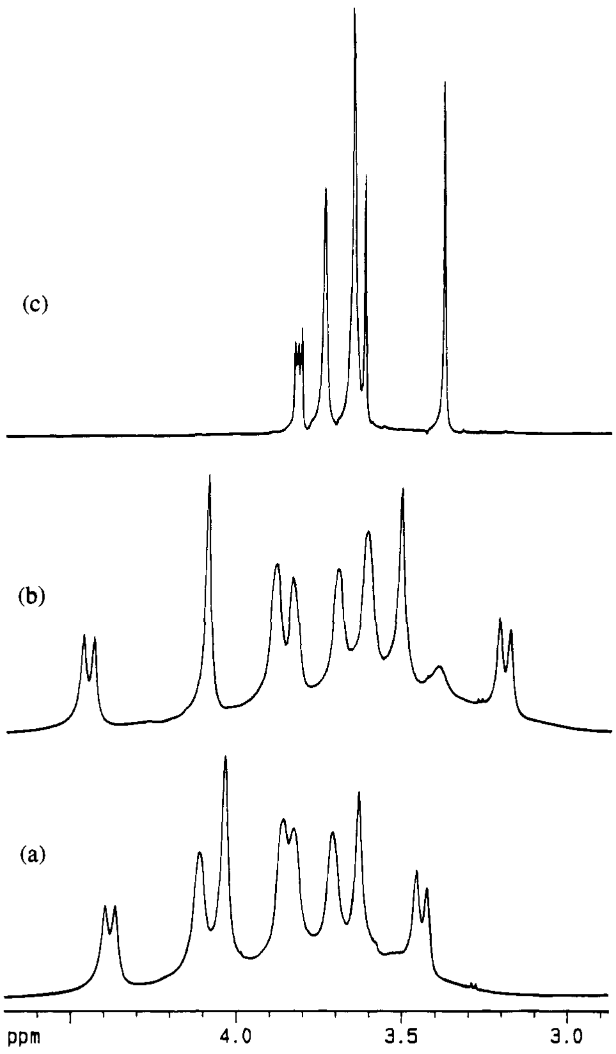

Figure 2. ^1H NMR spectra (400 MHz in CD_3CN) of (a) the **2a**·NaPic complex, (b) the free ligand **2a**, and (c) the **2a**·CsPic complex.

To verify the presence of cation/π interactions in solution, we measured the ^1H NMR spectra of several metal ion complexes of ligand **4a** in CD_3OD (Table 7) because this ligand shows a very high Cs^+/Na^+ selectivity especially in MeOH. Since **4a** is fixed in the 1,3-alternate structure, the spectra of

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[20] Gregory, K.; Bremer, M.; von Ragué Schleyer, P.; Klusener, P. A. A.; Brandsma, L. *Angew. Chem.* **1989**, *101*, 1261−1263. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159−1161.

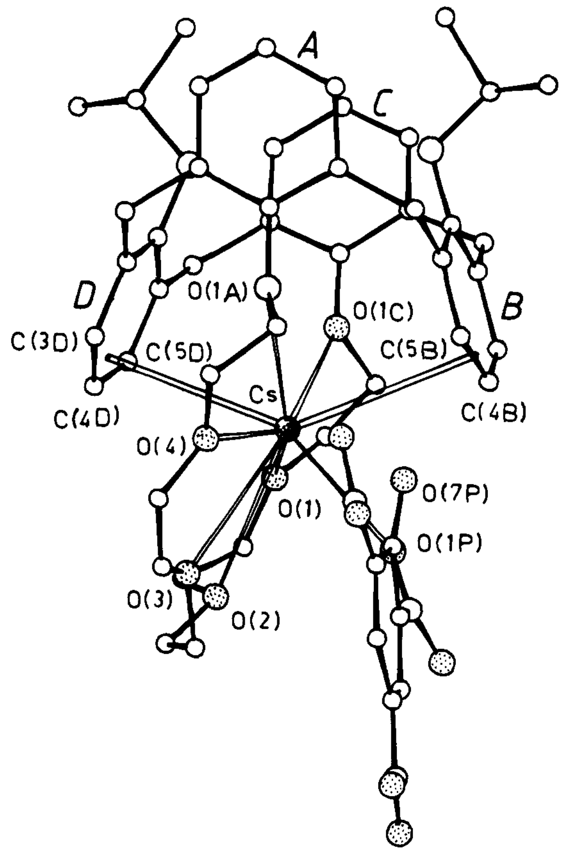

Figure 3. X-ray crystal structure of the **4a**·CsPic complex.

Table 6. Relevant Interatomic Distances (Å) Observed in Complex **4a**·CsPic Compared with the Corresponding Values Observed in **2a**·CsPic[a]

	4a·CsPic	**2a**·CsPic	
Cs–O(1A)	3.189(5)	3.319(5)	3.468(5)
Cs–O(1C)	3.188(5)	3.300(5)	3.269(4)
Cs–O(1)	3.245(6)	3.212(5)	3.294(5)
Cs–O(2)	3.475(7)	3.333(6)	3.398(6)
Cs–O(3)	3.276(9)	3.67(1)	3.401(7)
Cs–O(4)	3.100(5)	3.265(9)	3.196(7)
Cs–C(3D)	3.676(7)	3.548(9)	3.588(8)
Cs–C(4D)	3.486(8)	3.43(1)	3.354(7)
Cs–C(5D)	3.563(7)	3.649(9)	3.566(7)
Cs–C(4B)	3.58(1)	3.568(7)	3.422(7)
Cs–C(5B)	3.69(1)	3.684(8)	3.549(7)
Cs–O(1P)	3.083(7)	3.413(9)	3.361(1)
Cs–O(7P)		3.094(6)	3.143(6)

[a] In the dimethoxycalix[4]arene-crown-6 CsPic complex, two independent molecules were found.[10]

their complexes should be sensitive mainly to the interactions with the cations and not to the conformational rearrangement of the calix, as in the case of the flexible ligands **2a** and **2b**. The high stability constants ($4.5 \leq \log\beta \leq 6.1$) found in MeOH for this ligand and Ag^+, K^+, Rb^+, and Cs^+ cations (Table 4) ensure that at room temperature and at 1.5×10^{-2} M concentration of host and metal nitrate, the complex is >96% formed and only the signals which refer to this species are observed.

The signal assignment of the protons to the two different pairs of aromatic rings has been made on the basis of NOESY experiments with the free ligand **4a** and its Ag^+ complex. In the latter, strong through space correlations of all crown ether protons with the doublet at 7.58 ppm and the triplet at 6.96 ppm indicate that these signals belong to the aromatic rings bearing the isopropyl groups. The X-ray crystal structure of the cesium complex of ligand **4a** shows (Figure 3) that the oxygen atoms of the rotated aromatic nuclei bearing the isopropoxy groups are not involved in complexation. However, the aromatic protons in para and meta position of these nuclei experience a large downfield shift upon complexation (Table 7). The largest shift is observed for the doublet of the meta protons and it is maximum for Ag^+ ($\Delta\delta = +0.52$ ppm), whereas for alkali metal ions it follows the charge density order (K^+, +0.23 ppm; Rb^+, +0.19 ppm; and Cs^+, +0.13 ppm). All these observations suggest that also in solution, as observed in the solid state, the complexed cations interact not only with the crown ether moiety but also with the two rotated aromatic nuclei (cation/π interaction) of the 1,3-alternate conformation.[21]

Membrane Transport. Previously, Reinhoudt and coworkers have described the carrier-mediated transport of alkali metal and guanidinium cations through bulk liquid membranes[22] (BLM) and supported liquid membranes (SLM).[5,23–25] The main advantage of SLM's over the bulk liquid membrane (BLM) is that much less carrier is needed because of the much smaller membrane volume. The mechanism of carrier-mediated transport through liquid membranes and the use of macrocyclic carriers in SLM's have been reviewed recently.[23,24] We have used *o*-nitrophenyl octyl ether (NPOE) as the membrane solvent; because of the high polarity of NPOE ($\epsilon = 24$) the salt is present as free ions. We have reported a mathematical model[5] which describes the initial flux as a function of the diffusion constant of the complex (D_M), the product (K_{ex}) of the association constant of the complex in the membrane and the partition coefficient of the salt, the concentration of salt (a) in the aqueous phase and of the carrier (L_0) in the membrane phase, and the thickness of the membrane (d):

$$J = \frac{D_M}{2d}\left\{-K_{ex}a^2 + K_{ex}a^2\sqrt{1 + \frac{4L_0}{K_{ex}a^2}}\right\}$$

In this model a few assumptions were made: (i) The carrier is confined to the membrane phase. (ii) The salt is present as free ions. (iii) The transport is diffusion limited. The model was already shown to be valid in the carrier-mediated transport of Na^+, K^+, and guanidinium ions.[25]

Single Cation Transport. To verify that the carriers **4** were not leaching from the membrane, cesium fluxes were measured for 24 h with carriers **4a** and **4d**, after which both the source phase and the receiving phase were replaced. The cesium flux remained constant (Table 8) even after several replacements. Therefore, we concluded that the carriers are not leaching from the membrane.

To obtain the extraction constant K_{ex} and the diffusion coefficient D_M, a series of experiments were performed with **4a–d** in which the cesium concentration in the source phase was varied (Figure 4). The cesium fluxes for **4a–d** are given in Table 9. With the model mentioned above, the extraction constant K_{ex} and the diffusion coefficient D_M were calculated (Table 10). To verify that in all cases the transport is diffusion limited, the thickness of the membrane was varied. The flux as a function of the membrane thickness is shown in Figure 5. The intercept is zero within experimental error, which implies

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(21) For similar observations in other calixarene systems see: Ikeda, A.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 3102–3110.

(22) Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N.; van Eerden, J.; Harkema, S. *J. Org. Chem.* **1989**, *54*, 1000–1005.

(23) Visser, H. C.; Reinhoudt, D. N.; de Jong, F. *Chem. Soc. Rev.* **1994**, 75–81.

(24) van Straaten-Nijenhuis, W. F.; de Jong, F.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 317–324.

(25) Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R.; Nijenhuis, W. F.; de Jong, F.; Reinhoudt, D. N. *Isr. J. Chem.* **1992**, *32*, 79–87.

Table 7. ^{1}H NMR Data for Ligand **4a** and Its Metal Nitrate Complexes in CD_3OD at 25 °C

compound	H_{meta}[a]	H_{meta}[b]	H_{para}[a]	H_{para}[b]	$CHMe_2$	$ArCH_2Ar$[c]	OCH_2[d]	$CH(CH_3)_2$
4a	7.06	7.02	6.79	6.77	4.29	3.83, 3.77	3.68 (s, 4), 3.65 (m, 4), 3.53 (m, 4), 3.34 (s, 8)	0.91
4a·Na^+	7.09	7.07	6.81	6.78	4.33	3.85, 3.78	3.74 (s, 4), 3.72 (m, 4), 3.67 (m, 4), 3.63 (m, 4), 3.57 (m, 4)	0.93
4a·K^+	7.29	7.16	6.94	6.86	4.50	3.87, 3.80	3.95 (m, 4), 3.78 (m, 16)	1.04
4a·Rb^+	7.25	7.16	6.93	6.84	4.49	3.87, 3.78	3.92 (m, 4), 3.79 (m, 4), 3.78 (s, 8), 3.75 (s, 4)	1.06
4a·Cs^+	7.19	7.17	6.93	6.83	4.47	3.86, 3.77	3.90 (m, 4), 3.74 (s, 8), 3.72 (m, 4), 3.71 (s, 4)	1.06
4a·Ag^+	7.58	7.06	6.96	6.71	4.51	3.76, 3.67	4.09–4.04 (m, 12), 3.94 (m, 8)	1.32

[a] Aromatic protons of propoxy-substituted rings. [b] Aromatic protons of the rings bearing the crown ether; H_{meta} = doublet, H_{para} = triplet. [c] AB system. [d] Multiplicity and number of protons in parentheses.

Table 8. $CsNO_3$ Flux ($\times 10^{-7}$ mol·m^{-2}·s^{-1}) upon Replacement of the Aqueous Phases[a]

	no. of replacements			
compd	0	1	2	3
4a	2.89	3.47	3.14	3.10
4d	2.86	2.72	2.90	2.81

[a] [Carrier]$_m$ = 0.01 M. Source phase: 0.25 M $CsNO_3$.

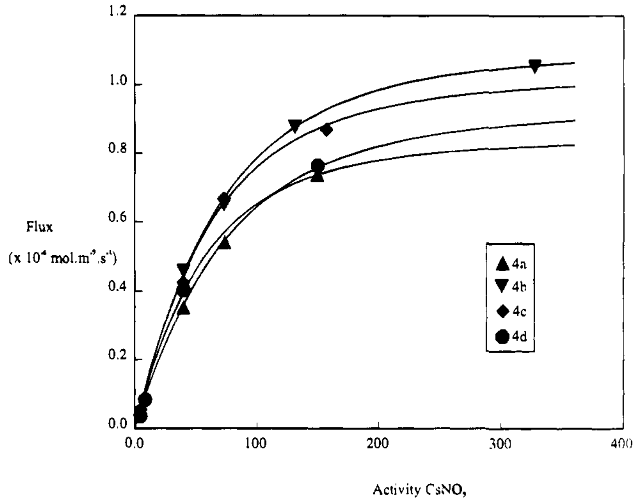

Figure 4. $CsNO_3$ flux as a function of the salt activity in the source phase for carriers **4a–d**. [Carrier]$_m$ = 1 × 10^{-2} M; T = 298 K. The lines drawn are calculated to the model; the points are measured values.

Table 9. $CsNO_3$ Fluxes over 24 h,[a] Calculated Extraction Constants, and Diffusion Coefficients for Different Carriers in NPOE

compd	flux (mol·m^{-2}·s^{-1})	K_{ex} (M^{-1})	D_M (m^2·s^{-1})
4a	3.53 × 10^{-7}	1.46	9.67 × 10^{-12}
4b	4.49 × 10^{-7}	1.73	1.11 × 10^{-11}
4c	4.27 × 10^{-7}	2.13	1.01 × 10^{-11}
4d	4.05 × 10^{-7}	2.56	8.50 × 10^{-12}

[a] Carrier concentration 0.01 M in NPOE. Source phase 0.05 M $CsNO_3$, T = 298 K.

that the transport is diffusion limited and that there is no additional resistance due to slow rates of cation release.

The measured sodium cation fluxes of **4a–d** were hardly higher than the blank fluxes.

Uphill Transport. Cussler et al.[26] have shown that common-ion pumping can be used to transport a salt against its concentration gradient. When a secondary salt with the same anion and a low extraction constant is present in large excess, the anion gradient acts as a "pump" for the primary salt. The properties of carriers **4**, having high affinity for cesium and showing no significant sodium transport, are ideal for removing traces of cesium salts out of a solution with a high sodium concentration. Using 0.01 M carrier solutions of **4a–d** in NPOE, from a mixture of 1 × 10^{-3} M $CsNO_3$/1 M $NaNO_3$, within 4 days 71–87% of the cesium was transported (Figure 6). The Cs^+/Na^+ ratios obtained in the receiving phase varied from 7650 (**4d**) to 13650 (**4b**, Table 10). The flux increased with increasing carrier concentration, as can be seen from Figure 7. Carrier **4d**, designed to be highly soluble in NPOE, showed the highest cesium flux when 18 wt % of **4d** (0.16 M) in NPOE was used. At even higher carrier concentrations, the flux decreases, probably because the viscosity in the membrane becomes too high. To compare **4b–d**, a carrier concentration of 0.05 M was chosen (**4a** did not completely dissolve in NPOE at this concentration). As can be seen from Figure 6, virtually all cesium was removed from the source phase within 4 days. The Cs^+/Na^+ ratios varied from 2200 to almost 3800 (Table 10). Using conditions to simulate the saline mixture present in medium level nuclear waste solutions (1 × 10^{-3} M $CsNO_3$, 4 M $NaNO_3$, 1 M HNO_3) and again a carrier concentration of 0.05 M in NPOE, virtually all cesium was removed from the source phase, even within 24 h (see Figure 8). The Cs^+/Na^+ ratios varied from 400 to 500 (Table 11).

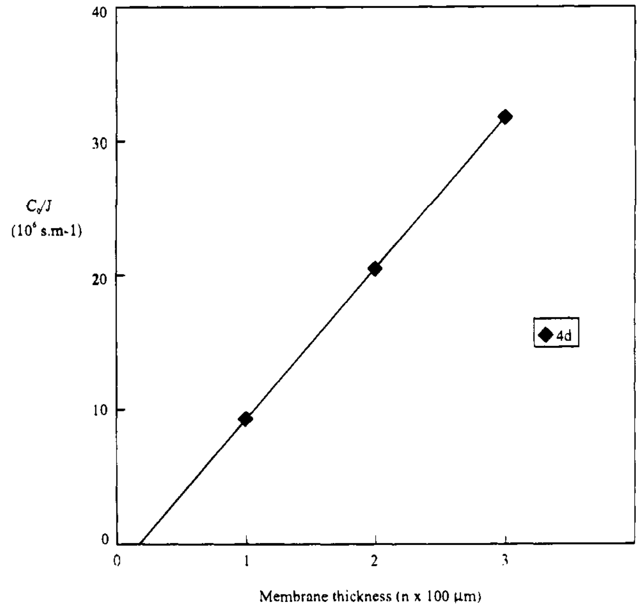

Figure 5. Influence of the membrane thickness (n × 100 μm) on C_0/J for carrier **4d**. [Carrier]$_m$ = 1 × 10^{-2} M. The source phase was 1 × 10^{-1} M $CsNO_3$, T = 298 K.

Experimental Section[27]

Melting points were determined with an Electrothermal melting point apparatus in a sealed capillary and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker AMX400 (^{1}H: 400 MHz) and AC300 (^{1}H: 300 MHz; ^{13}C: 75 MHz) spectrometers of the Centro Interdipartimentale di Misure (C.I.M.) of the University of Parma and with a Bruker AC250F (^{1}H: 250 MHz) spectrometer with Me_4Si as internal standard. Mass spectra were obtained either with a Finnigan

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(26) Caracciolo, F.; Cussler, E. L.; Evans, D. F. *AIChE J.* **1975**, *21*, 160.

(27) The name calix[4]arene is used instead of the official CA name: pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,26,27,28-tetrol.

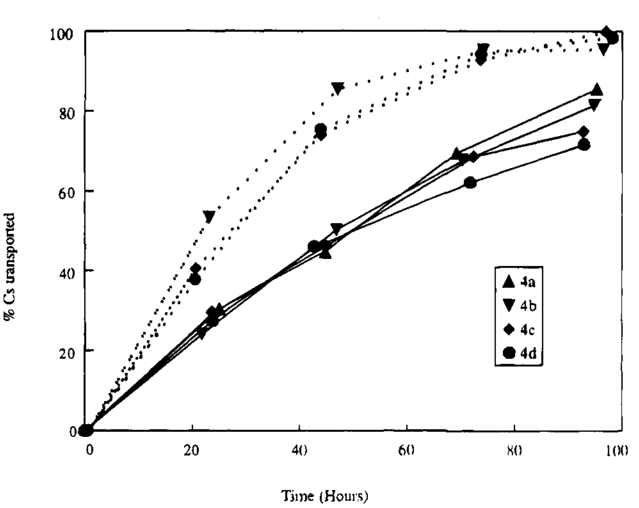

Figure 6. Transport rates of $CsNO_3$ as a function of time for carriers **4a**–**d**. Solid lines: $[\text{carrier}]_m = 1 \times 10^{-2}$ M. Dashed lines: $[\text{carrier}]_m = 5 \times 10^{-2}$ M. The source phase consisted of a mixture of 1×10^{-3} M $CsNO_3$ and 1 M $NaNO_3$. Membrane thickness, 100 μm; $T = 298$ K.

Table 10. Percentage of Transported Cations and the Cs^+/Na^+ Ratio in the Receiving Phase after 96 h[a]

entry	compd	[carrier]	% Cs^+	% Na^+	overall $[Cs^+]/[Na^+]$[b]
1	**4a**	0.01	85.3	0.0073	11750
2	**4b**	0.01	81.2	0.0059	13650
3	**4c**	0.01	74.9	0.0090	8350
4	**4d**	0.01	71.7	0.0094	7650
5	**4b**	0.05	94.4	0.025	3800
6	**4c**	0.05	100	0.048	2200
7	**4d**	0.05	97.6	0.0414	2350

[a] $T = 298$ K. $[Cs^+]/[Na^+]$ ratio in the source phase: $1{:}10^3$ (1×10^{-3} M $CsNO_3$, 1 M $NaNO_3$). [b] $[Cs^+]/[Na^+] \times 10^3$ after 96 h.

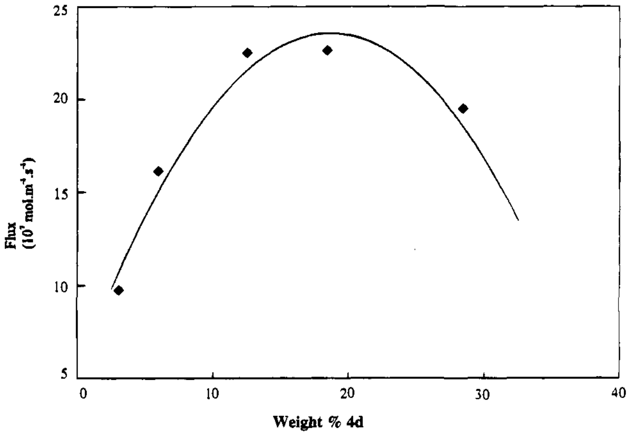

Figure 7. $CsNO_3$ flux as a function of [**4d**] in NPOE. The source phase was 1×10^{-1} M $CsNO_3$. Membrane thickness, 100 μm, $T = 298$ K.

MAT90 spectrometer (FAB using 3-nitrobenzyl alcohol as a matrix) or with a Finnigan MAT SSQ710 spectrometer (DCI using methane as the ionizing gas).

CH_3CN was dried over molecular sieves (3 Å). Petroleum ether refers to the fraction boiling at 60–80 °C. 2-(1-(8-Bromooctyl)oxy)-nitrobenzene[28] and penta- and hexaethylene glycol ditosylate[29] were prepared according to literature procedures. Analytical TLC were performed on precoated silica gel plates (SiO_2, Merck, 60 F_{254}), while silica gel 60 (SiO_2, Merck, particle size 0.040–0.063 mm, 230–240

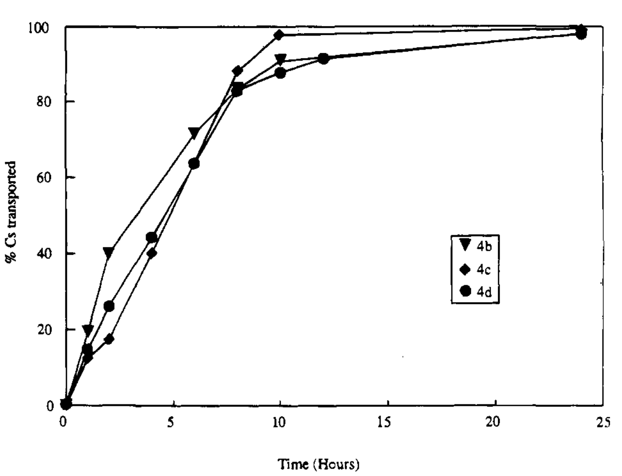

Figure 8. Transport rates of $CsNO_3$ as a function of time for carriers **4b**–**d**. $[\text{Carrier}]_m = 5 \times 10^{-2}$ M. The source phase consisted of a mixture of 1×10^{-3} M $CsNO_3$, 4 M $NaNO_3$, and 1 M HNO_3. Membrane thickness, 100 μm, $T = 298$ K.

Table 11. Percentage of Transported Cations and the Cs^+/Na^+ Ratio in the Receiving Phase after 24 h[a]

compd	% Cs^+	% Na^+	overall $[Cs^+]/[Na^+]$[b]
4b	97.9	0.23	423
4c	99.5	0.20	496
4d	98.1	0.25	392

[a] $[\text{Carrier}]_m = 0.05$ M, $T = 298$ K. $[Cs^+]/[Na^+]/[H^+]$ ratio in the source phase: 1:4000:1000 (1×10^{-3} M $CsNO_3$, 4 M $NaNO_3$, 1 M HNO_3). [b] $\{[Cs^+]/[Na^+]\}(4 \times 10^3)$ after 24 h.

Table 12. Experimental Data for the X-ray Diffraction Studies of **4a**·CsPic

formula	$C_{50}H_{65}CsN_3O_{15}$
cryst syst	monoclinic
space group	$P2_1/n$
cell parameters at 295 K[a]	
a, Å	20.289(6)
b, Å	10.949(3)
c, Å	22.107(6)
α, deg	90
β, deg	97.28(2)
γ, deg	90
V, Å^3	4871(2)
Z	4
D_{calcd}, g cm^{-3}	1.462
F(000)	2208
mol wt	1071.91
linear abs coeff, cm^{-1}	65.37
diffractometer	Siemens AED
scan type	$\theta/2\theta$
scan speed, deg/min	3-12
scan width, deg	$(\theta - 0.65),[\theta + (0.65 + \Delta\lambda\lambda^{-1})\tan\theta]$
radiation	Cu Kα (1.54178 Å)
2θ range, deg	6/130
no. of reflcns measd	$\pm h, +k, +l$
total data measd	9007
criterion for obsn	$I \geq 2\sigma \geq (I)$
no. of obsd data measd	4987
no. of unique obsd data	4839
agreement between equivalent obsd reflcns	0.08
no. of variables	631
max Δ/σ on last cycle	0.07
$R = \Sigma\lvert\Delta F\rvert/\Sigma\lvert F_o\rvert$	0.064
$R_w = \Sigma w^{1/2}\Delta F\lvert/\Sigma w^{1/2}\lvert F_o\rvert$	0.064
GOF $= [\Sigma w\lvert\Delta F\rvert^2/(\text{NO} - \text{NV})]^{1/2}$	0.87

[a] Unit cell parameters were obtained by least-squares analysis of the setting angles of 30 carefully centered reflections chosen from diverse regions of reciprocal space.

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(28) Visser, H. Supported Liquid Membranes with Improved Membrane Stability: Kinetics and Mechanisms of Carrier Mediated Salt Transport, Dutch Ph.D. Thesis, 1994, ISBN 90-9007142-3.

(29) Ouchi, M.; Inoue, Y.; Kanzaki, T.; Hakushi, T. *J. Org. Chem.* **1984**, *49*, 1408–1412.

mesh) was used for preparative column chromatography. 25,26,27,28-Tetrahydroxy-*p-tert*-butylcalix[4]arene,[30a] tetrahydroxycalix[4]arene,[30b] 25,27-dimethoxycalix[4]arene,[31] and 25,27-bis(2-propyloxy)calix[4]arene[32] were prepared as described in the literature.

In NMR spectra, the "Ar" notation indicates the aromatic nuclei of the calixarene backbone, considering the phenol oxygen as the main substituent to which the ipso, ortho, meta, and para positions refer. For compounds **3d** and **4d** "Ph" refers to the nitrated aromatic nuclei.

25,27-Bis(1-propyloxy)calix[4]arene (3b). To a suspension of calix[4]arene **1** (3.0 g, 7.06 mmol) in CH_3CN (200 mL) were added 1-iodopropane (4.79 g, 28.2 mmol) and K_2CO_3 (3.9 g, 28.2 mmol) and the reaction mixture was stirred under reflux for 24 h. The solvent was then removed under reduced pressure and the residue quenched with 100 mL of 10% HCl and 100 mL of CH_2Cl_2. The organic phase was separated and washed twice with distilled water (2 × 100 mL). CH_2Cl_2 was dried over Mg_2SO_4 and distilled off to afford a solid which was crystallized from 1/5 CH_2Cl_2–MeOH to give pure compound **3b**: yield 64%; mp 268–270 °C; ^1H NMR ($CDCl_3$) δ 8.32 (s, 2H, OH), 7.10 and 6.95 (d, J = 7.5 Hz, 4H each, ArH meta), 6.78 and 6.70 (t, J = 7.5 Hz, 2H each, ArH para), 4.38 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 4.02 (t, J = 6.2 Hz, 4H, $OC\mathit{H}_2CH_2CH_3$), 3.43 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 2.13 (m, 4H, $OCH_2C\mathit{H}_2CH_3$), 1.36 (t, J = 7.3 Hz, $OCH_2CH_2C\mathit{H}_3$); ^{13}C NMR ($CDCl_3$) δ 153.3, 151.9 (s, Ar ipso), 133.4, 128.9 (s, Ar ortho), 128.4, 128.1 (d, Ar meta), 125.2 (d, Ar para), 78.2 (t, $O\mathit{C}H_2CH_2CH_3$), 31.4 (t, $ArCH_2Ar$), 23.4 (t, $OCH_2\mathit{C}H_2CH_3$), 10.8 (q, $OCH_2CH_2\mathit{C}H_3$); MS (DCI), *m/e* 509.1 ((M + H)$^+$ calcd 508.3). Anal. Calcd for $C_{34}H_{36}O_4$: C, 80.29; H, 7.13. Found: C, 80.34; H, 7.07.

25,27-Bis(1-octyloxy)calix[4]arene (3c). A suspension of calix[4]arene **1** (5.0 g, 11.6 mmol), K_2CO_3 (3.9 g, 28.2 mmol), and 1-iodooctane (6.20 g, 25.8 mmol) in CH_3CN (250 mL) was stirred under reflux for 5 days. The reaction mixture was then quenched as reported for compound **3b**. Pure **3c** was obtained by crystallization from hexane: yield 52%; mp 115–117 °C; ^1H NMR ($CDCl_3$) δ 8.25 (s, 2H, OH), 7.06 (d, J = 7.4 Hz, 4H, ArH meta), 6.92 (d, J = 5.9 Hz, 4H, ArH meta), 6.74 (t, J = 5.9 Hz, 2H, ArH para), 6.65 (t, J = 7.4 Hz, 2H, ArH para), 4.33 (d, J = 13.1 Hz, 4H, $ArCH_2Ar$), 4.00 (t, J = 6.6 Hz, 4H, $OC\mathit{H}_2R$), 3.38 (d, J = 13.1 Hz, 4H, $ArCH_2Ar$), 1.30 (m, 24H, $OCH_2(C\mathit{H}_2)_6CH_3$), 0.91 (t, J = 6.8 Hz, $OCH_2(CH_2)_6C\mathit{H}_3$)); ^{13}C NMR ($CDCl_3$) δ 153.6, 152.6 (s, Ar ipso), 133.0, 129.1 (s, Ar ortho), 128.7, 128.5 (d, Ar meta), 125.5, 119.2 (d, Ar para), 77.3 (t, $O\mathit{C}H_2R$), 32.2, 31.7, 30.3, 29.8, 29.6, 26.3, 23.0 (t, $OCH_2(\mathit{C}H_2)_6CH_3$ and $ArCH_2Ar$), 14.4 (q, $OCH_2(CH_2)_6\mathit{C}H_3$); MS (DCI), *m/e* 649 ((M + H)$^+$ calcd 648.5). Anal. Calcd for $C_{44}H_{56}O_4$: C, 81.45; H, 8.69. Found: C, 81.53; H, 8.58.

25,27-Bis[1-(8-((2-nitrophenyl)oxy)octyl)oxy]-26,28-dihydroxycalix[4]arene (3d). A suspension of calix[4]arene (4.61 g, 10.87 mmol), K_2CO_3 (1.50 g, 10.87 mmol), and 2-(1-(8-bromooctyl)oxy)nitrobenzene (7.90 g, 23.9 mmol) was stirred overnight under reflux, then quenched and treated as described above for compound **3b**. The product was purified by column chromatography (SiO_2: first elution with 1/1 hexane–CH_2Cl_2 to remove some starting material, then with CH_2Cl_2) and obtained as an amorphous solid: yield 57%; mp 54–56 °C; ^1H NMR ($CDCl_3$) δ 8.20 (s, 2H, OH), 7.76 (dd, J = 8.1 and 1.6 Hz, 2H, PhH-3), 7.42 (dt, J = 7.9 and 1.6 Hz, 2H, PhH-5), 7.1–6.8 (m, 12H, ArH and PhH-4,6), 6.75–6.55 (m, 4H, ArH para), 4.30 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 4.1–3.9 (m, 8H, OCH_2), 3.36 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 2.15–1.35 (m, 24H, CH_2); ^{13}C NMR ($CDCl_3$) δ 153.4, 152.5, 152.0 (s, ArC-O and PhC-O), 139.9 (s, PhC-NO_2), 134.0, 128.9, 128.4, 125.5, 125.2, 120.0, 118.9, 114.4 (Ar and Ph), 133.2, 128.2 (s, Ar ortho), 76.6 (t, $ArOCH_2$), 69.6 (t, $PhOCH_2$), 31.4, 30.0, 29.3, 29.2, 29.0, 25.8 (t, $ArCH_2Ar$ and CH_2); MS (FAB), *m/e* 923.6 ((M + H)$^+$ calcd 923.5). Anal. Calcd for $C_{56}H_{62}N_2O_{10}$: C, 72.86; H, 6.77; N, 3.03. Found: C, 72.99; H, 6.85; N, 3.30.

General Procedure for the Synthesis of 25,27-Dialkoxycalix[4]arene-crown-*n* (*n* = 5–7). 25,27-Dialkoxycalix[4]arene **3** (2.28 mmol) was dissolved in CH_3CN (400 mL) and added to an excess of Cs_2CO_3 (2.93 g, 9 mmol) and tetra-, penta-, or hexaethylene glycol di-*p*-toluenesulfonate (2.5 mmol) under nitrogen atmosphere. The reaction mixture was refluxed for 16–24 h. Then CH_3CN was removed under reduced pressure and the residue extracted with 70 mL of CH_2Cl_2 and 70 mL of 10% HCl. The organic phase was separated and washed twice with water, and the solvent was distilled off. After purification, 25,27-dialkoxycalix[4]arene-crown-*n* **2** and **4** (*n* = 5–7) were obtained in 63–85% yield.

25,27-Dimethoxycalix[4]arene-crown-6 (2a) was crystallized from the oily residue with 1/5 CH_2Cl_2–MeOH: yield 78%; mp 180–181 °C; ^1H NMR ($CDCl_3$) selected sharp signals δ 7.16 (d, J = 7.4 Hz, 4H, ArH meta), 6.94 (t, J = 7.4 Hz, 2H, ArH para), 6.35 (s, 6H, ArH), 4.46 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$), 4.08 (s, 6H, OCH_3), 3.93 (s, 8H, $ArOC\mathit{H}_2C\mathit{H}_2OCH_2CH_2OCH_2$), 3.81 (m, 4H, $ArOCH_2CH_2OC\mathit{H}_2CH_2OCH_2$), 3.71 (m, 4H, $ArOCH_2CH_2OCH_2C\mathit{H}_2OCH_2$), 3.61 (s, 4H, $ArOCH_2CH_2OCH_2CH_2OC\mathit{H}_2$), 3.19 (d, J = 12.9 Hz, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ selected signals 159.3, 153.4 (s, Ar ipso), 137.0, 133.4 (s, Ar ortho), 128.6, 127.5 (d, Ar meta), 122.4 (d, Ar para), 74.2, 71.2, 71.0, 70.8 (t, OCH_2), 61.2 (q, OCH_3), 30.8 (t, $ArCH_2Ar$); MS (DCI), *m/e* 655.5 (M$^+$ calcd 654.3). Anal. Calcd for $C_{40}H_{46}O_8$: C, 73.37; H, 7.08. Found: C, 73.50; H, 7.20.

25,27-Dimethoxycalix[4]arene-crown-5 (2c) was crystallized from MeOH: yield 85%; mp 220–221 °C; ^1H NMR ($CDCl_3$) δ 7.13 (d, J = 7.3 Hz, 4H, ArH meta), 6.90 (t, J = 7.3 Hz, 2H, ArH para), 6.53 (d, 4H, J = 7.5 Hz, ArH meta), 6.43 (t, J = 7.5 Hz, 2H, Ar para), 4.42 (d, J = 12.5 Hz, 4H, $ArCH_2Ar$), 4.13 (s, 6H, OCH_3), 3.99 (m, 4H, $ArOC\mathit{H}_2CH_2OCH_2CH_2$), 3.93 (m, 4H, $ArOCH_2C\mathit{H}_2OCH_2CH_2$), 3.75 (m, 4H, $ArOCH_2CH_2OC\mathit{H}_2CH_2$), 3.58 (m, 4H, $ArOCH_2CH_2OCH_2C\mathit{H}_2$), 3.20 (d, J = 12.5 Hz, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 159.3 and 155.4 (s, Ar ipso), 138.9 and 136.7 (s, Ar ortho), 128.4 and 127.7 (d, Ar meta), 122.6 and 122.4 (d, Ar para), 73.0, 71.5, 71.0, 70.8 (t, OCH_2), 61.2 (q, OCH_3), 31.2 (t, $ArCH_2Ar$); MS (DCI), *m/e* 610.2 (M$^+$ calcd 610.3). Anal. Calcd for $C_{38}H_{42}O_7$: C, 74.74; H, 6.92. Found: C, 74.63; H, 6.93.

25,27-Dimethoxycalix[4]arene-crown-7 (2d) was crystallized from 1/5 CH_2Cl_2–MeOH: yield 75%; mp 121–122 °C; ^1H NMR ($CDCl_3$) selected sharp signals δ 7.14 (d, J = 7.4 Hz, 4H, Ar meta), 6.92 (t, J = 7.4 Hz, 2H, Ar para), 6.32 (s, 6H, ArH), 4.51 (d, J = 13.0 Hz, 4H, $ArCH_2Ar$), 4.03 (s, 6H, $ArOCH_3$), 3.85–3.39 (m, 24H, OCH_2), 3.17 (d, J = 13.0 Hz, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) selected signals δ 155.9, 155.3 (s, Ar ipso), 137.0, 133.4, 131.0 (s, Ar ortho), 128.5, 127.2 (d, Ar meta), 122.2, 121.9, 121.5 (d, Ar para), 74.2, 72.9, 71.1, 70.9, 70.7, 70.6 (t, OCH_2), 60.8 (q, OCH_3), 36.0 and 30.6 (t, $ArCH_2Ar$); MS (DCI), *m/e* 698.0 (M$^+$ calcd 698.3). Anal. Calcd for $C_{42}H_{50}O_9$: C, 72.18; H, 7.21. Found: C, 72.10; H, 7.30.

25,27-Bis(2-propyloxy)calix[4]arene-crown-6, 1,3-alternate (4a), was crystallized from EtOH: yield 85%; mp 197–198 °C; ^1H NMR ($CDCl_3$) δ 7.07 (d, J = 7.5 Hz, 4H, ArH meta), 7.03 (d, J = 7.4 Hz, 4H, ArH meta), 6.82 (t, J = 7.5 Hz, 2H, Ar para), 6.80 (t, J = 7.4 Hz, 2H, ArH para), 4.24 (ept, J = 6.3 Hz, 2H, $OC\mathit{H}(CH_3)_2$), 3.83 and 3.76 (d, J = 15.7 Hz, 4H each, $ArCH_2Ar$), 3.73 (s, 4H, $ArO(CH_2CH_2O)_2C\mathit{H}_2$), 3.68 (t, J = 4.1 Hz, 4H, $ArOC\mathit{H}_2CH_2OCH_2CH_2OCH_2$), 3.53 (t, J = 4.1 Hz, 4H, $ArOCH_2C\mathit{H}_2OCH_2CH_2OCH_2$), 3.46 (t, J = 6.0 Hz, 4H, $ArOCH_2CH_2OC\mathit{H}_2CH_2OCH_2$), 3.34 (t, J = 6.0 Hz, 4H, $ArOCH_2CH_2OCH_2C\mathit{H}_2OCH_2$), 0.91 (d, J = 6.3 Hz, 12H, $OCH(C\mathit{H}_3)_2$); ^{13}C NMR ($CDCl_3$) δ 156.8, 154.9 (s, Ar ipso), 134.6, 133.6 (s, Ar ortho), 130.3, 129.7 (d, Ar meta), 121.8, 121.6 (d, Ar para), 70.5 (d, $ArO\mathit{C}H$), 71.2, 71.1, 71.0, 70.0, 69.3 (t, OCH_2), 38.9 (t, $ArCH_2Ar$), 21.9 (q, CH_3); MS (DCI), *m/e* 710.1 (M$^+$ calcd 710.4). Anal. Calcd for $C_{44}H_{54}O_8$: C, 74.33; H, 7.65. Found: C, 74.21; H, 7.78.

25,27-Bis(1-propyloxy)calix[4]arene-crown-6, 1,3-alternate (4b) was crystallized from MeOH: yield 80%; mp 140–141 °C; ^1H NMR ($CDCl_3$) δ 7.10 (d, J = 7.2 Hz, 4H, ArH meta), 7.03 (d, J = 7.6 Hz, 4H, ArH meta), 6.84 (t, J = 7.2 Hz, 2H, ArH para), 6.80 (t, J = 7.6 Hz, 2H, ArH para), 3.78 (s, 8H, $ArCH_2Ar$), 3.73 (s, 4H, $ArO(CH_2CH_2O)_2C\mathit{H}_2$), 3.68 (t, J = 5.0 Hz, 4H, $ArOC\mathit{H}_2CH_2O$), 3.62 (t, J = 6.0 Hz, 4H, $OC\mathit{H}_2CH_2CH_3$), 3.52 (t, J = 5.0 Hz, 4H, $ArOCH_2C\mathit{H}_2OCH_2CH_2OCH_2$), 3.45–3.40 (m, 8H, $ArOCH_2CH_2OC\mathit{H}_2C\mathit{H}_2OCH_2$), 1.32 (m, 4H, $OCH_2C\mathit{H}_2CH_3$), 0.73 (t, J = 7.2 Hz, 6H, $OCH_2CH_2C\mathit{H}_3$); ^{13}C NMR ($CDCl_3$) δ 156.9, 156.5 (s, Ar ipso), 134.0, 133.7 (s, Ar ortho), 129.8, 129.7 (d, Ar meta), 122.0 (d, Ar para), 72.1, 71.2, 71.0, 69.9 (t, OCH_2),

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(30) (a) Gutsche C. D. *Org. Synth.* **1989**, *68*, 234–246. (b) Gutsche, C. D.; Lin, L.-G. *Tetrahedron* **1986**, *42*, 1633–1640.

(31) van Loon, J. D.; Arduini, A.; Coppi, L.; Verboom, W.; Ungaro, R.; Pochini, A.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, *55*, 5639–5646.

(32) Casnati, A.; Comelli, E.; Fabbi, M.; Bocchi, V.; Mori, G.; Ugozzoli, F.; Manotti Lanfredi, A. M.; Pochini, A.; Ungaro, R. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 384–392.

37.9 (t, $ArCH_2Ar$), 22.7 (t, $OCH_2CH_2CH_3$), 10.1 (q, CH_3); MS (DCI), *m/e* 710.2 (M^+ calcd 710.4). Anal. Calcd for $C_{44}H_{54}O_8$: C, 74.33; H, 7.65. Found: C, 74.25; H, 7.73.

25,27-Bis(1-octyloxy)calix[4]arene-crown-6, 1,3-alternate (4c), was obtained by column chromatography on silica gel (eluent: 1/1 hexane–EtOAc) and crystallized from MeOH: yield 70%; mp 94–95 °C; ^1H NMR ($CDCl_3$) δ 7.12 (d, J = 7.5 Hz, 4H, ArH meta), 7.08 (d, J = 7.5 Hz, 4H, ArH meta), 6.83 (t, J = 7.5 Hz, 2H, ArH para), 6.77 (t, J = 7.5 Hz, 2H, ArH para), 3.78 (s, 8H, $ArCH_2Ar$), 3.71 (s, 4H, $ArO(CH_2CH_2O)_2CH_2$), 3.66 (t, J = 4.6 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.60 (t, J = 6.0 Hz, 4H, $OCH_2(CH_2)_6CH_3$), 3.49 (t, J = 4.6 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.40 (m, 8H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 1.36–1.15 (m, 24H, $OCH_2(CH_2)_6CH_3$), 0.92 (t, J = 7.1 Hz, 6H, $OCH_2(CH_2)_6CH_3$); ^{13}C NMR ($CDCl_3$) δ 157.0, 156.6 (s, Ar ipso), 134.1, 133.8 (s, Ar ortho), 129.8, 129.7 (d, Ar meta), 122.2 (d, Ar para), 71.3, 71.1, 71.0, 70.7, 69.9 (t, OCH_2), 38.0 (t, $ArCH_2Ar$), 32.0, 29.8, 29.5, 29.4, 25.9, 22.8 (t, $ArOCH_2(CH_2)_6CH_3$), 14.3 (q, CH_3); MS (DCI), *m/e* 850.2 (M^+ calcd 850.5). Anal. Calcd for $C_{54}H_{74}O_8$: C, 76.20; H, 8.76. Found: C, 76.08; H, 8.83.

25,27-Bis[1-(8-((2-nitrophenyl)oxy)octyl)oxy]calix[4]arene-crown-6, 1,3-alternate (4d). Pure compound **4d** was obtained by column chromatography (SiO_2: 1/3 petroleum ether–EtOAc) as a yellow oil which slowly crystallized upon standing: yield 63%; mp 51–52 °C; ^1H NMR ($CDCl_3$) δ 7.79 (dd, J = 7.6 and 1.7 Hz, 2H, PhH-3), 7.48 (dt, J = 7.9 and 1.7 Hz, 2H, PhH-5), 7.15–6.9 (m, 12H, ArH and PhH-4,6), 6.9–6.7 (m, 4H, ArH), 4.09 (t, J = 6.4 Hz, 4H, $PhOCH_2$), 3.78 (s, 8H, $ArCH_2Ar$), 3.7–3.3 (m, 24H, OCH_2), 1.95–1.1 (m, 24H, CH_2); ^{13}C NMR ($CDCl_3$) δ 156.9, 156.5, 152.5 (s, ArC-O and PhC-O), 140.0 (s, PhC-NO_2), 134.0, 129.8, 129.6, 125.5, 122.1, 120.0, 114.4 (Ar and Ph), 77.3 (t, $ArOCH_2$), 71.2, 71.1, 71.0, 70.5, 69.8, 69.6 (t, OCH_2CH_2O and $PhOCH_2$), 37.9 (t, $ArCH_2Ar$), 29.6, 29.4, 29.3, 29.0, 25.9, 25.8 (t, CH_2); MS (FAB), *m/e* 1125.3 ($(M + H)^+$, calcd 1124.6). Anal. Calcd for $C_{66}H_{80}N_2O_{14}$: C, 70.44; H, 7.17; N, 2.49. Found: C, 70.59; H, 7.17; N, 2.48.

25,27-Dihydroxycalix[4]arene-crown-6 (5). To a solution of compound **2a** (0.5 g, 0.76 mmol) in 30 mL of $CHCl_3$ was added iodotrimethylsilane (0.22 mL, 1.52 mmol) under N_2. The reaction mixture was refluxed for 2 h, then quenched with 10% HCl (50 mL) and transferred to a separatory funnel. The organic phase was separated and washed with a saturated solution of $Na_2S_2O_3$ (30 mL) and with water (2 × 50 mL). $CHCl_3$ was removed under reduced pressure and the product crystallized from MeOH: yield 84%; mp 224–225°C; IR-(KBr) υ_{max} 3360 (bs, OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.49 (s, 2H, OH), 7.07 (d, J = 7.6 Hz, 4H, ArH meta), 6.83 (d, J = 7.6 Hz, 4H, ArH meta), 6.70 (t, J = 7.6 Hz, 2H, ArH para), 6.68 (t, J = 7.6 Hz, 2H, ArH para), 4.42 (d, J = 13.1 Hz, 4H, $ArCH_2Ar$), 4.15 (t, J = 4.8 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 4.01 (t, J = 4.8 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.93 (t, J = 4.8 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.84 (t, J = 4.8 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.70 (s, 4H, $ArO(CH_2CH_2O)_2CH_2$), 3.36 (d, J = 13.1 Hz, 4H, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 153.3, 152.1 (s, Ar ipso), 133.1, 128.2 (s, Ar ortho), 129.0, 128.5 (d, Ar meta), 125.3, 118.9 (d, Ar para), 76.4, 71.6, 71.0, 69.9 (t, OCH_2), 31.1 (t, $ArCH_2Ar$); MS (DCI), *m/e* 626.0 (M^+ calcd 626.3). Anal. Calcd for $C_{38}H_{42}O_8$: C, 72.83; H, 6.75. Found: C, 72.77; H, 6.87.

25,27-Bis(2-propyloxy)calix[4]arene-crown-6, Cone (6). To a solution of calix[4]arene-crown-6 **5** (0.35g, 0.56 mmol) in 25 mL of dry DMF were added NaH (50% in oil, 0.27 mg, 1.12 mmol) and 2-iodopropane (1.90 g, 11.2 mmol) under nitrogen. The reaction mixture was stirred at room temperature for 8 h. Then 50 mL of 10% HCl were slowly added, and the resulting solid was filtered and washed with water (50 mL) on a buchner. Pure product **6** was obtained by recrystallization from MeOH: yield 73%; mp 172–174°C; ^1H NMR ($CDCl_3$) δ 7.12 (d, J = 7.5 Hz, 4H, ArH meta), 6.94 (t, J = 7.5 Hz, 2H, ArH para), 6.18 (t, J = 7.4 Hz, 2H, ArH para), 6.03 (d, J = 7.4 Hz, 4H, ArH meta), 4.38 (d, J = 13.6 Hz, 4H, $ArCH_2Ar$), 4.26 (t, J = 7.7 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 4.04 (t, J = 7.7 Hz, 4H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.92 (ept, J = 6.0 Hz, 2H, $OCH(CH_3)_2$), 3.73 (s, 8H, $ArOCH_2CH_2OCH_2CH_2OCH_2$), 3.69 (s, 4H, $ArO(CH_2CH_2O)_2CH_2$), 3.14 (d, J = 13.6 Hz, 4H, $ArCH_2Ar$), 1.34 (d, J = 6.0 Hz, 12H, $OCH(CH_3)_2$); ^{13}C NMR ($CDCl_3$) δ 158.3, 153.3 (s, Ar ipso), 137.0, 133.7 (s, Ar ortho), 129.1, 127.2 (d, Ar meta), 122.1, 121.9 (d, Ar para), 76.7 (d, ArOCH), 72.4, 71.1, 70.8, 69.8 (t, OCH_2), 31.6 (t, $ArCH_2Ar$), 22.4 (q, CH_3); MS (DCI), *m/e* 710.8 (M^+ calcd 710.4). Anal. Calcd for $C_{44}H_{54}O_8$: C, 74.33; H, 7.65. Found: C, 74.22; H, 7.78.

Picrate Extraction Measurements. Picrate extraction experiments (Table 2) were performed following Pedersen's procedure:[16] 5 mL of a 2.5 × 10^{-4} M aqueous picrate solution and 5 mL of a 2.5 × 10^{-4} M solution of calixarene in CH_2Cl_2 were vigorously agitated in a stoppered glass tube with a mechanical shaker for 2 min, then magnetically stirred in a thermostatted water-bath at 20 ± 0.1 °C for 30 min, and finally left standing for an additional 30 min. The concentration of picrate ion remaining in the aqueous phase was then determined spectrophotometrically as previously described.[33] Blank experiments showed that no picrate extraction occurred in the absence of calixarene.

For data reported in Table 3 Cram's procedure[17] was followed using EtOH-free $CHCl_3$ instead of $CDCl_3$. The alkali picrates were prepared as described elsewhere[33,34] by stepwise addition of a 2.0 × 10^{-2} M aqueous picric acid solution to a 0.14 M aqueous solution of metal hydroxide, until neutralization which was checked by pH control with a glass electrode. They were then rapidly washed with EtOH and ether before being dried *in vacuo* for 24 h.

Stability Constant Measurements. The stability constants β, equal to the concentration ratios $[ML^+]/[M^+][L]$ (M^+ = cation, L = ligand), were determined in pure MeOH (Carlo Erba p.a.) by spectrophotometry and/or competitive potentiometry with Ag^+ as an auxiliary cation.

The ionic strength was maintained at 0.01 M in all cases by use of Et_4NCl (Fluka, purum) for the spectrophotometric measurements and by use of Et_4NClO_4 (Fluka, purum) for the potentiometric measurements. Et_4NCl and Et_4NClO_4 were recrystallized twice from acetone and from water, respectively, and after washing with acetone they were dried *in vacuo* at room temperature for 48 h.

The metallic salts used for spectrophotometry were chlorides: LiCl (Fluka, puriss.), NaCl (Prolabo, Normapur), KCl (Merck, p.a.), RbCl (Fluka, puriss.), and CsCl (Merck, puriss.). The following perchlorates, $AgClO_4$ (Fluka, puriss.), $KClO_4$ (Prolabo, Normapur), $RbClO_4$ (Sigma), and $CsNO_3$ (Fluka, purum), were employed for potentiometric measurements.

The spectrophotometric technique has been described in detail elsewhere.[35] For each cation, several solutions were prepared with a constant ligand concentration (from 5 × 10^{-5} to 2.5 × 10^{-4} M) and increasing concentrations of metallic salt. The spectra were recorded for each solution between 240 and 295 nm with a Shimadzu UV-2101 PC, using Supracil cuves of 1 or 2 cm path length, thermoregulated at 25 ± 0.1 °C. The spectral changes in this wavelength range were significant enough to be exploited by a multiwavelength numerical treatment (program Letagrop-Spefo),[36] which yielded the stability constants and the molar extinction coefficients of the complexes.

The competitive potentiometric measurements have also been described elsewhere.[33] They were performed with the following electrochemical cell:

$$\mathrm{Ag(s)/AgClO_4},\ C_{\mathrm{Ag^+}},\ C_{\mathrm{M^+}}\quad \mathrm{Et_4NClO_4//Et_4NClO_4}\ 10^{-2}\ \mathrm{M//AgClO_4}\ 10^{-2}\ \mathrm{M/Ag(s)}$$

using silver rod electrodes (Metrohm) connected to a Tacussel LPH 430T millivoltmeter as working and reference electrodes. Reference and measurement cells were thermoregulated at 25 ± 0.1 °C. Prior to each measurement, the working electrode was calibrated by incremental addition of a $AgClO_4$ solution ($C^{\circ}_{\mathrm{Ag}} \approx 1 \times 10^{-3}$ M) to 10 mL of a 1 × 10^{-2} M Et_4NClO_4 solution containing the required cation ($C_M \approx 1 \times 10^{-4}$ M). After calibration, when $C_{Ag} \approx C_M$, a ligand solution ($C^{\circ}_L = 1 \times 10^{-3}$ M) was progressively added up to $R = C_L/(C_{Ag} + C_M) \approx$

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(33) Arnaud-Neu, F.; Schwing-Weill, M. J.; Ziat, K.; Cremin, S.; Harris, S. J.; McKervey, M. A. *New J. Chem.* **1991**, *15*, 33–37.

(34) Arnaud-Neu, F.; Cremin, S.; Cunningham, D.; Harris, S. J.; McArdle, P.; McKervey, M. A.; McManus, M.; Schwing-Weill, M. J.; Ziat, K. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1991**, *10*, 329–339.

(35) Arnaud-Neu, F.; Collins, E.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M. J.; Seward, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 8681–8691.

(36) Sillen, L. G.; Warnqvist, B. *Ark. Kemi* **1968**, *31*, 377–390.

1. Measurements were numerically treated by the program Miniquad,[37] taking into account the stability constant of the corresponding silver complex obtained by direct potentiometry.

Thermodynamic Parameter Determination. The enthalpies of complexation were determined by calorimetry at 25 °C, using a precision isoperibol titration calorimeter (Tronac 450, Orem, Utah). The general experimental procedure and calculations have already been described.[38] For solubility reasons, a solution of the chloride salt of the required cation was titrated into a ligand solution ($3 \times 10^{-4} \leq C_L \leq 9 \times 10^{-4}$ M) until $C_M/C_L \approx 2$. In the case of the complexes of **4a** with Cs^+ and Rb^+, the number of moles of metallic salt added to the ligand solution is equal to the number of moles of complex formed and the measured heat is directly related to the complexation enthalpy ΔH_c. ΔS_c could then be derived from the expression $\Delta G_c = \Delta H_c - T\Delta S_c$, knowing $\Delta G_c = -RT \log\beta$. In the case of less stable complex **2a**·Cs^+, $\log\beta$ and ΔH_c have been refined simultaneously using program FS101 from Tronac and the general program SIRKO.[39] The two programs gave the same results and the average value of $\log\beta = 4.16$ thus obtained and corresponding to two experiments is in excellent agreement with the value found by spectrophotometry. In the case of the complexes formed by **4** with K^+ and Ag^+, and by **2b** with Cs^+, the ΔH_c values were obtained with the general program SIRKO fixing the $\log\beta$ at the values obtained by spectophotometry or potentiometric experiments.

X-ray Crystal Structure Analysis of the Complex 4a·CsPic. The crystal data and the most significant details of the X-ray experiments are reported in Table 12. X-ray measurements were carried out at 293 K using Ni filtered Cu-K_α radiation. The diffractometer intensity was monitored by means of three reflections measured every hundred reflections. No decay was observed. The intensities were determined by profile analysis according to Lehman and Larsen[40] and corrected for Lorentz and polarization.

The structure solution was obtained by Direct Methods using SHELX86[41] and refined by blocked full-matrix least-squares methods (482 + 149 parameters) using SHELX76.[42] All the non-hydrogen atoms have been refined anisotropically. Hydrogen atoms have been added at calculated positions (C−H = 1.0 Å) and treated as riding atoms with single common isotropic displacement parameters. The atomic scattering factors of the non-hydrogen atoms were taken from Cromer and Waber.[43] The values of $\Delta f'$ and $\Delta f''$ were those of Cromer.[44] The geometrical calculations were obtained by PARST.[45] All the crystallographic calculations were performed on the Gould Encore 91 of the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. Parma, Italy.

Membrane Transport. The polymeric film Accurel was obtained from Enka Membrana. *o*-Nitrophenyl *n*-octyl ether (NPOE) was purchased from Fluka and was used without further purification. $NaNO_3$ and $CsNO_3$ were of analytical grade and were obtained from Janssen Chimica. The transport experiments were carried out in the permeation cell consisting of two identical cylindrical compartments (half-cell volume ca. 50 mL; effective membrane area ca. 13.5 cm^2). Details of this cell have been described elsewhere.[46] Aqueous solutions of $CsNO_3$ and $NaNO_3$ were used as the source phase. Doubly distilled and deionized water was used as the receiving phase. Supported liquid membrane consisted of a thin microporous polypropylene film (Accurel, thickness $d = 100\ \mu$m, porosity 64%) immobilizing the solution of the carrier in NPOE. The measurements were performed at 25 ± 0.1 °C at least in duplicate. The transported nitrate salts were determined by monitoring the conductivity (Radiometer CDM83 conductivity meter and Unicam 9550/60 electrode with a cell constant of 0.95 cm^{-1}) of the receiving phase as a function of time in the case of single ion transport and by atomic absorption in the case of competitive transport. The standard deviation in the transport measurements is about 15%. Salt activities were calculated according to Debye−Hückel theory.[47]

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Supplementary Material Available: Tables SI through SIV giving atomic coordinates, displacement parameters, hydrogen atom coordinates, bond lengths, and angles for **4a**·CsPic (11 pages) listing of the observed and calculated structure factors (29 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(37) Sabatini, A.; Vacca, A.; Gans, P. *Talanta* **1974**, *21*, 53−77.

(38) Arnaud-Neu, F.; Barret, G.; Fanni, S.; Marss, D.; McGregor, W.; McKervey, M. A.; Schwing-Weill, M. J.; Wechsler, S. *J. Chem. Soc., Perkin Trans 2*, submitted for publication.

(39) Vetrogon, V. I.; Lukyanenko, N. G.; Schwing-Weill, M.-J.; Arnaud-Neu, F. *Talanta*, in press.

(40) Lehman, M. S.; Larsen, F. K. *Acta Crystallogr., Sect. A* **1974**, *30*, 580−584.

(41) Sheldrick, G. M. SHELX86; Program for Crystal Structure Solutions, University of Göttingen, Germany, 1986.

(42) Sheldrick, G. M. SHELX76; Program for Crystal Structure Solutions, University of Göttingen, Germany, 1976.

(43) Cromer, D. T.; Waber, J. J. *International Tables for X-ray Crystallography*; The Kinoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2.B.

(44) Cromer, D. T. *International Tables for X-ray Crystallography*; The Kinoch Press: Birmingham, England, 1974; Vol. IV, Table 2.3.1.

(45) Nardelli, M. PARST *Comput. Chem.* **1983**, *7*, 95−98.

(46) Stolwijk, T. B.; Sudhölter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1987**, *109*, 7042−7047.

(47) Meier, P. C. *Anal. Chim. Acta* **1982**, *136*, 363−368.