Quinoline-Containing Calixarene Fluoroionophores: A Combined NMR, Photophysical and Modeling Study

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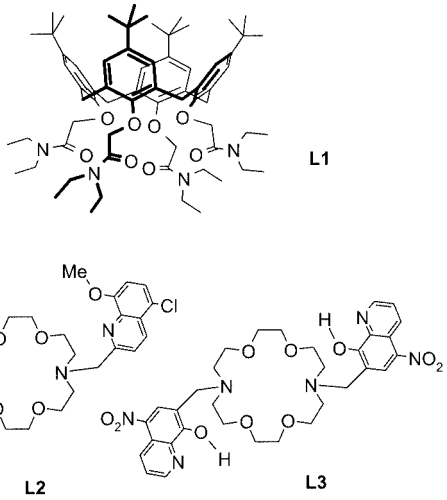
The 8-alkoxy-5-chloroquinoline fluorophore was appended at the lower rim of a calix[4]arene triamide with two different orientations. In ligand **1** the quinoline part is linked to the calixarene skeleton through the pyridine C^2 atom, while in **2** it is linked through the phenolic oxygen atom of the chromophore. The binding properties of both ligands, investigated in chloroform and methanol solutions, indicate that they are efficient fluoroionophores, with selectivity for sodium and strontium ions among alkali and alkaline earth metal ions. Combined NMR, photophysical, and modeling studies disclosed the peculiar conformational and coordination features of monovalent and divalent metal ion complexes. Lanthanide metal ion complexes were prepared and studied in acetonitrile solution showing good luminescence in the case of Nd^{3+}, Yb^{3+}, and Er^{3+} ions.

Introduction

In recent years, the synthesis, characterisation, and application of fluorescent labels and sensors have been the focus of much attention,[1,2] supported by the great sensitivity and versatility offered by luminescence spectroscopy. The use of these devices has allowed complex analytical problems to be tackled in growing fields with large social and economic impacts, such as medical diagnostics, environmental sciences, and cell biology.[3−5] In order to convert a ligand of known selectivity into a chromoionophore, luminophores (chromophores) are usually introduced in suitable positions on the ligand skeleton. 8-Alkoxy- or 8-hydroxyquinolines have been appended through positions 2 or 7 on different azacrown ethers, producing a series of ligands showing a K^+ and Ba^{2+} selectivity among the alkali and alkaline earth metal ions. These ligands also allowed the analytical determination of Mg^{2+} in very dilute solutions by means of UV/Vis spectrophotometry.[6−8] More recently, the complexing properties of some of these compounds have been investigated in more detail using fluorescence.[9−12] Compound **L2** selectively responds to Cd^{2+} with a large increase in fluorescence, while **L3** responds to Hg^{2+}, thus giving effective ligands potentially useful as chemosensors.



Calixarenes[13] have been widely used as building blocks for the synthesis of ionophores either of the podand type[14] or macrobicyclic as the calixcrowns,[15] which show efficiency and selectivity according to the calixarene ring size and conformation.[16] The tetramide of *p-tert*-butylcalix[4]arene **L1**[17] is probably one of the most studied calixarene ligands since it binds alkali and alkaline earth metal ions with association constants comparable to or higher than

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those of cryptands.[18,19] Tetramide **L1** has also been used to encapsulate lanthanide ions efficiently,[20] indicating the potential of calixarene ligands to form luminescent complexes, a topic of great interest in several areas of chemical technology.[21−24] Several chromoionophores based on calixarenes are known, decorated with a variety of luminophores.[25] The 8-alkoxyquinoline moiety has been very recently introduced on calix[4]-[26] or calix[6]arene,[27] but the cation-binding properties of the resulting ligands are very poor since no other binding group is present.

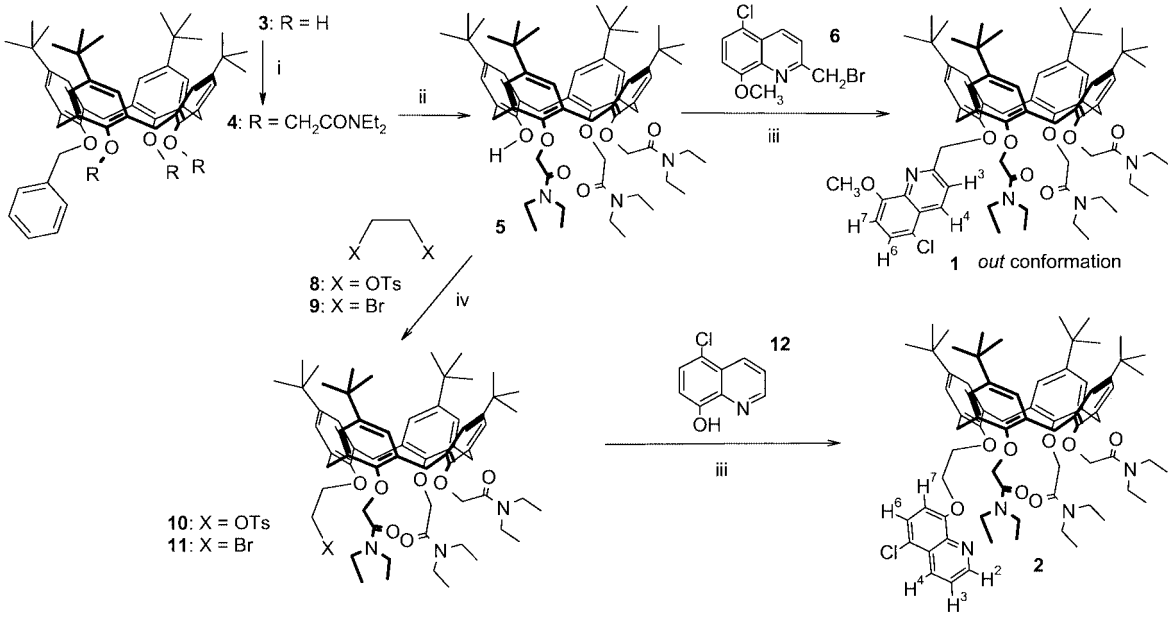
In this paper we report our efforts at syntheses intended to introduce alkoxyquinoline luminophores onto the lower rim of a calix[4]arene also bearing three acetamide binding groups, together with the complexation properties of the ligands towards spherical cations and the results of photophysical studies on free ligands and their complexes.

Results and Discussion

Synthesis of the Ligands

As the basic calix[4]arene ionophore to be converted into a quinoline-containing chromoionophore, we selected the triamide **5**, which bears three acetamide chelating groups at the lower rim. In this way, the free phenolic hydroxy group still present could be used to anchor the desired fluorophore. The triamide of *p-tert*-butylcalix[4]arene triamide **5** was previously prepared[28] in 23% yield using the BaO/$Ba(OH)_2$ method.[29] However, we preferred an indirect procedure (see Scheme 1) which takes advantage of the selective protection as benzyl ether of one of the phenolic OH groups of *p-tert*-butylcalix[4]arene. The monobenzyl ether **3**[30] was alkylated using α-chloroacetamide under conditions that ensure that the pure *cone* isomer is obtained (NaH, DMF).[31,32] Compound **4** was then debenzylated by transfer hydrogenation using $Pd(OH)_2$/C and cyclohexene,[33] yielding the triamide **5** in 75% overall yield from compound **3**. A similar strategy, which exploits the monoallyl *p-tert*-butylcalix[4]arene, was recently reported by Reinhoudt and coworkers.[34] Compound **5** was then alkylated with a slight excess of 2-(bromomethyl)-5-chloro-8-methoxyquinoline (**6**) and NaH in dry DMF at room temperature, giving compound **1** in 50% yield. The introduction of the quinoline moiety was confirmed by the presence in the ^{1}H NMR spectrum of four doublets in the aromatic region for the quinoline (Q) protons and of two singlets at δ = 5.39 and 4.03 ppm for the OCH_2Q and OMe groups, respectively. The presence of two AX systems (4 H each; δ = 5.07, 3.24 ppm, J = 12.8 Hz; δ = 4.86, 3.15 ppm, J = 12.8 Hz) in the ^{1}H NMR spectrum and of two triplets (δ = 32.1 and 31.6 ppm) in the ^{13}C NMR spectrum for the methylene bridge $ArCH_2Ar$ indicates that the macrocycle is locked in the *cone* conformation.[35,36] This conformation allows the quinoline moiety to be adjacent to the three acetamide groups and therefore in close proximity to the complexed metal ion. A more detailed structural analysis of ligand **1** is given in connection with the complexation studies (vide infra).

Since we were also interested to study how the complexation and photophysical properties would be affected by changing the orientation of the quinoline nucleus, we synthesised compound **2** where the chromophore is linked through the phenolic oxygen atom. The triamide **5** was first treated with a 12-fold excess of ethylene glycol ditosylate (**8**) in order to avoid the formation of double calixarenes[34] and the tosylate **10** isolated in 65% yield. The use of 1,2-dibromoethane (**9**) (100-fold excess) as alkylating agent gave a higher yield (84%) and an easier procedure for the iso-



Scheme 1. Reagents and conditions: (i) NaH, $ClCH_2CONEt_2$, NaI, DMF dry, 80 °C; (ii) $Pd(OH)_2$/C, C_6H_{10}, EtOH, 80 °C; (iii) NaH, DMF dry, room temp.; (iv) K_2CO_3, CH_3CN dry, 80 °C

lation of the corresponding bromide **11**. The subsequent coupling reaction with 5-chloro-8-hydroxyquinoline (**12**) gave **2** in 30% yield. The ^{1}H NMR spectrum in $CDCl_3$ of the bromo compound **11** shows a singlet of 4 protons at δ = 4.22 ppm for the OCH_2CH_2Br methylene groups which could be compatible with the presence of a double calixarene. However, the presence of two triplets in the ^{13}C NMR spectrum at δ = 73.6 ppm (OCH_2) and δ = 31.4 ppm (CH_2Br), which correlate with the ^{1}H NMR singlet at δ = 4.22 ppm in a two-dimensional HSBC (^{1}H, ^{13}C correlation) experiment, proves that the protons of the two methylene groups are isochronous. The identity of compound **11** was also proved by the mass spectrum, which shows the molecular mass and the typical pattern of a monobromo-substituted compound. Like compound **1**, compound **2** is also present in the *cone* conformation as proved by the presence of two AX systems (4 H each; δ = 5.09, 3.18 ppm, J = 14.1 Hz; δ = 4.75, 3.16 ppm, J = 12.8 Hz) in the ^{1}H NMR spectrum and of two triplets (δ = 31.8 and 30.9 ppm) in the ^{13}C NMR spectrum for the methylene bridges $ArCH_2Ar$.

Structural and Spectroscopic Characterisation of the Free Ligands

A careful examination of the HSBC experiment (see Figure S1a of the Supporting Information) of ligand **1** in $CDCl_3$ allowed us to correctly assign the resonance of its H^3 and H^4 protons. The peaks at δ = 123.2 and 134.1 ppm were assigned to the C^3 and C^4 carbon atoms, respectively, in good agreement with the estimated values and with those of 5-chloro-8-methoxy-2-methylquinoline (**7**). Surprisingly, the peak at δ = 123.2 ppm (C^3) correlates with the proton signal at δ = 8.80 ppm (H^3) while the carbon signal at δ = 134.1 ppm (C^4) correlates with the proton signal at δ = 8.54 ppm (H^4), making the proton assignment unambiguous. This was also confirmed by the presence of a strong NOE peak (see Figure S1b of the Supporting Information) between the doublet at δ = 8.80 ppm (H^3) and the singlet of the methylene protons in position 2 of the quinoline (CH_2Q).

These data indicate that the signal for H^3 in compound **1** is strongly shifted downfield (Δδ = +1.37 ppm) from the value of δ = 7.43 ppm found for **7**. Quite intense NOEs are also present between H^3 and the methylene protons in an α-position to the amide carbonyl groups ($CH_2^{am}CO$, H^{am}) and between H^4 and the NCH_2 protons, suggesting that the quinoline is adopting an "out" conformation (see Scheme 1) with its N and O atoms pointing outwards and the H^4 and H^3 protons towards the amide carbonyl groups. The surprising downfield shift experienced by H^3 indicates a possible interaction with the carbonyl groups in a non-classical hydrogen bond. Interestingly, this interaction seems to be quite important since in CD_3CN and CD_3OD solutions we observed analogous shifts of H^3 (Table 1) and similar NOE peaks with the acetamide chains. In contrast, none of these remarkable shifts were present for the free ligand **2** (Table 2) which shows only a moderate downfield shift of H^7 (δ = 7.52 ppm) compared to the estimated value (δ = 6.89 ppm) or to that observed in compound **7** (δ =

Table 2. Chemical shifts and complexation-induced shift (CIS) [ppm][a] of the quinoline protons in the free ligand **2** and its complexes (300 MHz, 300 K)

Proton	Calcd.[b]	**2** ($CDCl_3$)	**2** (CD_3OD)	[**2**·Na] (CD_3OD)	[**2**·Ca] (CD_3OD)
H^7	6.89	7.52	7.63	7.42 (−0.21)	7.28 (−0.35)
H^6	7.51	7.55	7.63	7.66 (+0.03)	7.72 (+0.09)
H^4	8.53	8.49	8.64	8.63 (−0.01)	8.76 (+0.12)
H^3	7.46	7.49	7.70	7.70 (+0.00)	7.85 (+0.05)
H^2	8.95	8.90	8.89	8.92 (+0.03)	8.88 (−0.01)

[a] The − sign indicates an upfield shift, while the + sign indicates a downfield one. [b] Calculated for 5-chloro-8-ethoxyquinoline using the additivity rules.

Table 1. Chemical shifts and complexation-induced shift (CIS) [ppm][a] of the quinoline protons for the free ligand **1** in different solvents and its complexes (300 MHz, 300 K)

Proton	**7** ($CDCl_3$)	Calcd.[b]	**1** ($CDCl_3$)	**1** (CD_3CN)	**1** (CD_3OD)	[**1**·Na] (CD_3OD)	[**1**·K] (CD_3OD)	[**1**·Ca] (CD_3OD)	**1** + TFA (CD_3OD)
H^7	6.95	6.88	6.93	7.08	7.19	7.16 (−0.03)	7.27 (+0.08)	7.37 (+0.18)	7.63 (+0.44)
H^6	7.46	7.47	7.48	7.56	7.63	7.63 (0.00)	7.68 (+0.05)	7.75 (+0.12)	8.00 (+0.37)
H^4	8.42	8.47	8.54	8.59	8.74	8.54 (−0.20)	8.57 (−0.17)	8.49 (−0.25)	9.60 (+0.86)
H^3	7.43	7.32	8.80	9.11	9.06	8.19 (−0.87)	7.47 (−1.59)	6.79 (−2.27)	9.32 (+0.26)
CH_2Q	−	4.96	5.39	5.27	5.34	5.58 (+0.24)	5.46 (+0.12)	5.68 (+0.34)	5.84 (+0.50)
OCH_3	4.07	3.73	4.03	4.01	4.07	3.98 (−0.09)	4.13 (+0.06)	4.15 (+0.08)	4.24 (+0.17)

[a] The − sign indicates an upfield shift, while the + sign indicates a downfield one. [b] Calculated for 5-chloro-2-methoxy-8-(methoxymethyl)quinoline using the additivity rules.

6.95 ppm),[37] but no significant NOE peak in the NOESY two-dimensional spectra.

The conformational properties of the free ligands **1** and **2** were also studied by semiempirical calculations. The optimised geometry of **1** [see a) in Figure 1] shows the calixarene aromatic nuclei in a *cone* structure with approximate four-fold symmetry and confirms the "out" conformation also observed in solution by NMR techniques. All the phenolic and amide oxygen atoms point towards the interior of the hydrophilic cavity created at the lower rim, while the quinoline nitrogen atom and the methoxy group are pointing towards the exterior. This is due to a quite strong intramolecular C−H···O hydrogen bond (H···O 1.843 Å) between the H^3 atom of the quinoline moiety and the amide oxygen atom of the adjacent amide chain as shown in Figure 1 [a), left]. The molecular electrostatic potential (MEP) mapped onto the molecular surface indicates the strong negative value of the MEP on the oxygen atom and the positive value on H^3 involved in hydrogen bonding.

The minimum conformation adopted by **2** is quite different. The optimised geometry of the equilibrium conformer [Figure 1, b)] shows that the calixarene basket is in a *flattened cone* conformation with nearly C_s symmetry. The H^7 atom of the quinoline points towards the carbonyl oxygen atom of the adjacent amide chain but this intramolecular hydrogen bond is much weaker (H···O 2.51 Å) than in **1**.

In methanol and acetonitrile solutions the two chromoionophores **1** and **2** show similar but not equal absorption spectra in the 240−360-nm region. Moreover, these spectra are somewhat different from the one observed for the model compound, 5-chloro-8-methoxy-2-methylquinoline (**7**). In particular, the following differences can be observed: (i) the presence in the 260−280 nm region of an absorption band that could be attributed to the π−π* transition involving the aromatic rings of the calixarene[38] and (ii) a different shape of the band typical of the methoxyquinoline chromophore in the 280−360 nm range.[12]. It is worth noting that the excitation spectra strictly match the absorption ones, indicating that excitation over the whole 240−380 nm region leads to the population of the fluorescent excited state with unitary efficiency, as also occurs when in **1** and **2** the calixarene chromophore is excited. This finding is clear evidence of an efficient energy transfer process between the two parts of the system. This conclusion is also supported by the lack of any luminescence attributable to the calixarene skeleton.[38] The fluorescence of compounds **1**, **2**, and **7** at room temperature in both solvents (Table 3) shows a large and nonstructured band around 400 nm, generally quite intense ($\Phi > 0.1$), with the single exception of **1** in methanol solution. The fluorescence maximum depends on the solvent and on the nature of the compound.

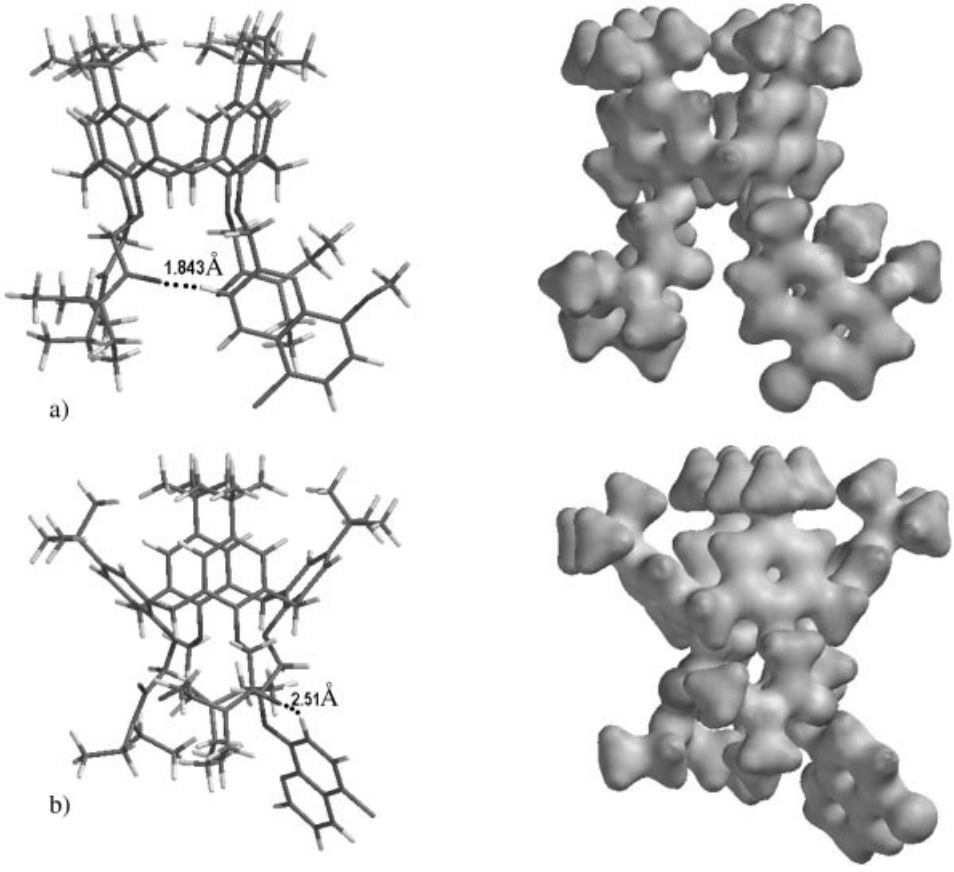


Figure 1. Minimised molecular structure of a) ligand **1** and b) ligand **2**; left: stick representation showing the hydrogen bond (black dots) between quinoline hydrogen atoms and the adjacent amide carbonyl group; right: MEP mapped onto the isodensity surface at 0.08 e/a.u.^{3} (for coloured pictures see Figure S2 in the Supporting Information; see also footnote on the first page of this article)

Table 3. Room-temperature photophysical properties of the hosts **1** and **2** and their reference compound **7**

		Absorption		Fluorescence		
	Solvent	λ_{max} [nm]	ε [$M^{-1}\cdot cm^{-1}$]	λ_{max} [nm]	τ [ns]	Φ
1	CH_3CN	310	3650	394	4.0	0.17
		248	40350			
1	MeOH	312	3650	415	3.9	0.12
		249	42900			
2	CH_3CN	322	4300	408	7.8	0.30
		241	37200			
2	MeOH	324	4590	410	5.8	0.21
		243	38400			
7	CH_3CN	308	3450	397	7.7	0.31
		247	30300			
7	MeOH	308	2900	410	3.5	0.20
		247	27500			

This behaviour can be conveniently compared with that found for the lariat crown ether **L2**, possessing two 8-methoxyquinoline units, which in methanol solution has a fluorescence band with a similar energy (λ_{max} = 420 nm) but with a much smaller quantum yield (0.007). The relatively low quantum yield of uncomplexed 8-hydroxyquinoline derivatives has usually been explained as involving the occurrence in the excited state of inter- (involving the solvent) and intramolecular proton-transfer processes, leading to a nonradiative deactivation to the ground state. In the cases of **1**, **2**, **7**, and **L2**, an intramolecular proton-transfer process is obviously impossible, while an intermolecular process can only occur in the protic methanol. This could be the reason why the quantum yields in methanol solution of **1**, **2**, and **7** are always lower than those found in acetonitrile. The occurrence of electron-transfer processes involving the nitrogen atoms of the crown is in turn the most plausible explanation for the lower quantum yield shown by **L2** compared with **1**, **2**, and **7**. The slightly different photophysical behaviours among **1**, **2**, and **7** can be accounted for by the different environment experienced by the methoxyquinoline chromophore, whose lower-energy excited state, having a charge-transfer character, is sensitive to the environmental conditions. In particular, the lower quantum yield in both solvents shown by **1** can be explained by the intramolecular C−H···O hydrogen bond between the H^3 atom of the quinoline and the amide oxygen of the adjacent amide, as found with molecular modeling.

Complexation of Alkali and Alkaline Earth Metal Ions

The binding properties of ligands **1** and **2** towards alkali and alkaline earth metal ions were evaluated by determining three different sets of data: (i) extraction percentages (*E*%) of metal ion picrates from water to dichloromethane using Pedersen's procedure[39] (see Table S1 of the Supporting Information), (ii) association constants in $CHCl_3$ by Cram's method (see Table S2 of the Supporting Information) and (iii) association constants in MeOH by spectrophotometry (Table 4). All these data are concordant in showing that both ligands **1** and **2** are selective for sodium ion. Triamides **1**, **2**, and **4** are able to bind alkali and alkaline earth cations but less efficiently than the tetramide **L1**, thus indicating that the substitution of one acetamide binding group with a less donating group causes a significant decrease in the binding properties of *cone* calix[4]arene amide ligands. This effect is more important for alkaline earth metal ions which, being harder than alkali cations, require extremely efficient ligands if they are to be dehydrated and extracted. Moreover, ligands **1** and **2** are only slightly better than **4**, indicating that the presence of the two additional binding sites (pyridine nitrogen atom and anisole oxygen atom) of the quinoline nuclei does not play an important role. As for ligand **L1**, the selectivity of ligands **1** and **2** is for sodium within alkali metal ions while it is shifted to strontium among the alkaline earth metal ions. The association constants (K_a) of complexes of ligands **1**, **2**, and **4** with alkali metal picrates in $CHCl_3$ (Table S2 of the Supporting Information) confirm that the triamides are still sodium-selective but are less efficient ligands than tetramide **L1**.[40] The complexes of potassium, rubidium, and caesium ions with **1**, **2**, and **4** show nearly the same stability, indicating lower size selectivity for these ligands compared to **L1**. The association constants of hosts **1** and **2** with a variety of alkali, alkaline earth, and transition metal ions were also evaluated in methanol using spectrophotometry and spectrofluorimetry (Table 4). As far as **1** is concerned, addition of up to 5 equiv. of Cs^+, Mg^{2+}, Zn^{2+}, Eu^{3+}, Er^{3+}, Nd^{3+}, and Yb^{3+} to a solution containing this host did not cause any appreciable change in the photophysical properties of the host. This finding can in principle indicate either a negligible interaction of the metal ion with the appended chromophore or a small association constant. Changes were instead observed with the ions reported in Table 4. In particular, a red shift of the absorption bands and a red shift and quenching of the luminescence were observed in all cases, with the exception of the potassium complex, which exhibits a 30% luminescence increase. In the series of the alkali and alkaline earth metal ions, the strongest changes in the fluorescence intensity were detected with the ions possessing the highest charge density, and in particular with Ca^{2+}, while the highest affinity was found for Na^+, leading to a good sodium-over-potassium selectivity.

Table 4. Association constants and fluorescence properties in methanol solutions at 298 K of the complexes of the hosts **1** and **2** with different metal ions

	log K_a	λ_{max} [nm]	I_{rel}
[**1**·Na^+]	7.0 ± 0.8	418	95
[**1**·K^+]	3.8 ± 0.1	417	134
[**1**·Ca^{2+}]	5.0 ± 0.1	434	6
[**1**·Sr^{2+}]	5.7 ± 0.2	435	22
[**1**·Ba^{2+}]	5.5 ± 0.1	433	66
[**1**·Cd^{2+}]	4.0 ± 0.1	425	28
[**2**·Ca^{2+}]	5.4 ± 0.1	414	200
[**2**·Sr^{2+}]	5.7 ± 0.2	406	217
[**2**·Ba^{2+}]	5.2 ± 0.1	406	223
[**2**·Cd^{2+}]	5.6 ± 0.1	405	126

The host **2** shows a quite different behaviour since the changes observed in the absorption spectra were almost negligible with all metal ions. As far as fluorescence spectra are concerned, no changes were detected with alkali metal ions, while the fluorescence intensity doubled upon complexation with alkaline earth metal ions, with only minor differences among the various complexes, and a smaller increase was observed for the Cd^{2+} complex. In addition, the shifts of the fluorescence maximum of this host with all the ions studied are much smaller than those noticed for **1** and, even more important, in the opposite direction. These findings are in agreement with a prevalent coordination of the methoxyquinoline chromophore through the nitrogen atom in **1**, and through the oxygen atom in **2**. In fact, it is well known that the lowest energy band of neutral hydroxyquinoline derivatives is associated with a $\pi-\pi^*$ transition, in which substantial charge density is transferred from the oxygen atom to the nitrogen atom.[41] Coordination through the oxygen atom, lowering its electronic density, causes an increase of the energy of the lowest excited state and a blue shift of the relative band in the absorption and emission spectra; the reverse is expected when the nitrogen atom is involved.[42] In principle, the negligible differences in the absorption and luminescence spectra observed upon addition of alkali metal ions could be attributed to (i) a very small association constant in these experimental conditions or (ii) a negligible effect on the photophysical properties upon coordination of the metal ion. To rule out the first hypothesis, we performed competition experiments, titrating a methanol solution containing equimolar amounts of the ligand **2** and Ca^{2+} ions, which showed, as expected, a luminescence intensity about twofold more intense than that observed for the free ligand. The addition of sodium caused a decrease of the luminescence intensity, although it was necessary after each addition to wait some hours to reach equilibrium. The addition of 1 equiv. of sodium ion was sufficient to bring the luminescence intensity to a value very close to that of the ligand alone, as expected in the case of the formation of the sodium complex. This finding indicates that the complex with Na^+ ion does form, with an association constant much higher than that observed for the formation of the Ca^{2+} complex. The interactions between the metal ion and the chromophore are, however, not strong enough to induce monitorable changes in the photophysical properties of the latter.

Structure of the Complexes

To obtain more insights into the structure of the complexes of ligands **1** and **2** we recorded the ^1H NMR spectra of the free ligands and of their sodium and potassium thiocyanate or calcium perchlorate complexes in CD_3OD solution (see Figures S3−S9 of the Supporting Information). According to the association constants determined in methanol by spectrophotometry, in the concentration conditions used for the NMR experiments ([ligand] = 1×10^{-3} M; [salt] = 5×10^{-3} M) at least 95% of the ligand is complexed with the metal ion. Moreover, since the exchange rate between the free and complexed ligand is slow compared to the NMR time scale, we could also verify that no signals of the uncomplexed macrocycles were present under these conditions. Upon complexation of sodium, potassium, or calcium, the signals of the protons of both ligands **1** and **2** undergo pronounced shifts. Particularly diagnostic are those of the aromatic protons of the macrocycle (ArH), of the OCH_2CO and of the axial protons of the methylene bridge ($ArCH_2Ar$) which indicate that, for both ligands, the metal ion is positioned inside the hydrophilic cavity created at the lower rim of the calixarene, coordinated by the four calixarene phenolic oxygen atoms and by the three carbonyl groups.[17,43] However, the behaviour of the fluorophore in the two ligands is quite different. In ligand **1**, upon complexation, large shifts are observed for all the signals of the quinoline protons, which made their assignment difficult. However, by combining NOESY and HSQC data we could unambiguously assign all the peaks of the quinoline protons in all complexes (Table 1 and Figure 2).

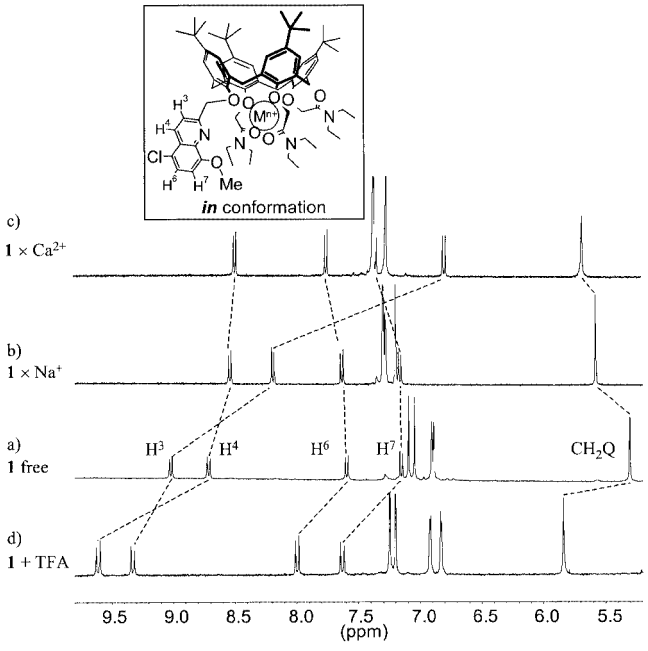


Figure 2. Portions of the ^1H NMR spectra (CD_3OD, 300 MHz, 300 K) of: a) ligand **1**, b) its sodium complex, c) its calcium complex, and d) **1** with an excess of TFA

The signals of H^6, H^7, CH_2Q and OCH_3 are shifted to lower field, as expected by the coordination of a quinoline nucleus to a metal ion and as reported for quinoline-substituted crown ethers.[7] On the contrary, the signals of H^4 and especially H^3 experience marked upfield shifts (CIS = −0.17 to −2.27 ppm) which depend on the complexed cation. This behaviour must be ascribed to anisotropic effects, since the protonation of the quinoline nitrogen atom of **1** with an excess of trifluoroacetic acid (TFA) shifts all the signals downfield (Table 1 and Figure 2). It is therefore reasonable to suppose that, in order to complex a cation through its N and O atoms, the quinoline nucleus has to rearrange to an "in" conformation (Figure 2) which causes the breaking of the intramolecular H-bonding observed in

the free ligand **1** and brings the H^3 and H^4 protons into the shielding cone of the aromatic nucleus of the calixarene. In support of the metal ion coordination by the chromophore, we also observed strong correlations between the OCH_3 protons and those of the methylene and methyl groups of the NCH_2CH_3 amide groups in the NOESY spectrum of [**1**·Ca^{2+}]. The shifts experienced by ligand **2** upon metal ion complexation (Table 2) are less pronounced. The signal of the quinoline proton closer to the calixarene skeleton (H^7) shifts upfield (CIS = −0.21 to −0.35 ppm) in the sodium and calcium complexes indicating a possible anisotropic effect of the aromatic and/or carbonyl groups of the macrocycle. The low-field shifts (CIS = +0.03 to +0.12 ppm) shown by the signals of all the other protons of the quinoline seem to indicate that the chromophore is coordinated to the metal ion in these complexes also. As for the free ligands **1** and **2** (vide supra), to obtain more insights into the structures of the cationic complexes [**1**·Ca^{2+}] and [**2**·Ca^{2+}], we performed a geometry optimisation by semiempirical calculations at the PM3 level. In the [**1**·Ca^{2+}] complex [see a), Figure 3] the calcium ion is nona-coordinate in the form of a square antiprism capped on the upper regular face. The square antiprism is created by the four phenolic oxygen atoms (Ca···O 2.441−2.677 Å), the three amide oxygen atoms (Ca···O 2.425−2.656 Å), and the quinoline N atom (Ca···N 2.627 Å). The ninth coordination site is the oxygen atom of the methoxy group at the quinoline moiety (Ca···O 2.642 Å). In the [**2**·Ca^{2+}] complex [see b), Figure 3] the metal ion is octa-coordinate in the form of a square antiprism to the four phenolic (Ca···O 2.474−2.581 Å) and to the three amide oxygen atoms (Ca···O 2.408−2.490 Å), and to the oxygen atom in the 9-position of the quinoline moiety (Ca···O 2.625 Å). The quinoline nucleus brings its nitrogen atom almost along the axis of the calix at 2.971 Å from the metal centre. This distance is 0.25 Å (9.1%) longer than the longest Ca···N bond (2.721 Å) found in the Cambridge Crystallographic Database, and related to a calcium dibromide [2.2.2]cryptate.[44] This could suggest that the metal ion is (weakly) nona-coordinated in the form of a square antiprism capped on the lower regular face, but the spectroscopic data reported above indicate the absence of such Ca^{2+}−N interaction.

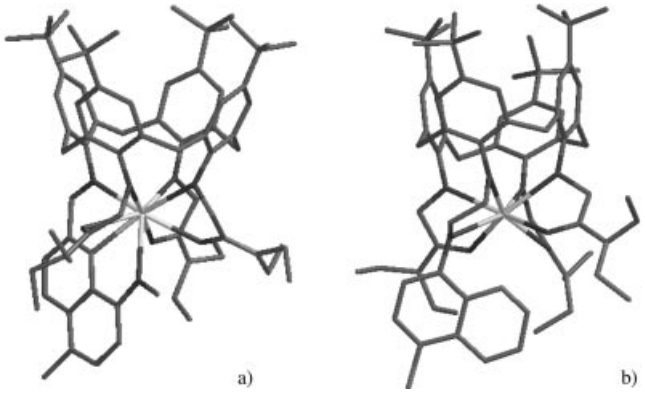


Figure 3. Perspective views of the minimised structures of: a) [**1**·Ca^{2+}] and b) [**2**·Ca^{2+}] complexes (for coloured models see Figure S10 in the Supporting Information)

As discussed above, all these findings are in agreement with the results obtained by photophysical investigations, which suggest a different coordination mode for **1** and **2**. In particular, in the latter, the methoxyquinoline chromophore was postulated to coordinate the metal ion mainly via the oxygen atom, as supported by NMR experiments and by molecular modeling.

Complexation of Lanthanide Ions

We also attempted to prepare complexes of different luminescent lanthanide ions with **1** and **2**, in order to study their photophysical properties. Since the complexes of **1** and **2** are not stable in methanol solution, as observed during the titration experiments described above, we added the nitrate salts of Gd^{3+}, Eu^{3+}, Nd^{3+}, Yb^{3+}, and Er^{3+} to acetonitrile solutions of the two ligands. Upon addition of Gd^{3+} ions to both hosts **1** and **2**, we observed a quenching of the fluorescence band around 400 nm, which was almost complete in the case of **1**.

Complexation with the Gd^{3+} ion, which does not possess a low-energy excited state, does not offer new energy-transfer pathways for the deactivation of the quinoline-centred fluorescence. In the case of **1**, the strong quenching observed is in line with the results observed in methanol solution with the alkali and alkaline earth metal ions, where the fluorescence decrease was correlated to the charge density of the ion. A similar result was also observed upon addition of Eu^{3+} ions. In this case, however, charge- and energy-transfer processes involving the metal ion could, in theory, be feasible, since europium can be reduced at low potential and possesses excited states at lower energy than the singlet state of the methoxyquinoline unit. It was not possible, however, to observe metal-centred emission, indicating either that the energy transfer to the ion is not efficient or that an even lower charge-transfer excited state is present in the assembly. On the contrary, if Nd^{3+}, Yb^{3+} or Er^{3+} are added to a solution of **1** and **2**, the quenching of the methoxyquinoline luminescence is accompanied by an increase of the metal-centred luminescence typical of each ion, indicating that in these cases an efficient energy transfer occurs. As can be seen from Figures 4 and 5, the structure of the luminescence band, in particular of the Yb^{3+} complex, depends on the host, indicating a different coordination mode between the host and the metal ion, as also found for alkali and alkaline earth metal ions in methanol solution.

Conclusion

The introduction of 8-alkoxy-5-chloroquinoline at the lower rim of the triamide of *p*-*tert*-butylcalix[4]arene led to the synthesis of two novel fluoroionophores. Ligand **1**, with the chromophore linked to the calixarene through the 2-position of the quinoline nucleus, shows peculiar spectroscopic properties. NMR spectroscopic data, fluorescence and semiempirical calculations indicate that the H^3 proton

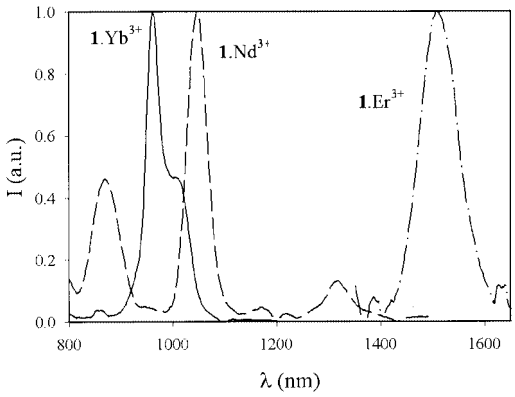


Figure 4. Fluorescence spectra (λ_{exc} = 320 nm) of the complexes of **1** with Yb^{3+}, Nd^{3+}, and Er^{3+} in acetonitrile solution at room temperature

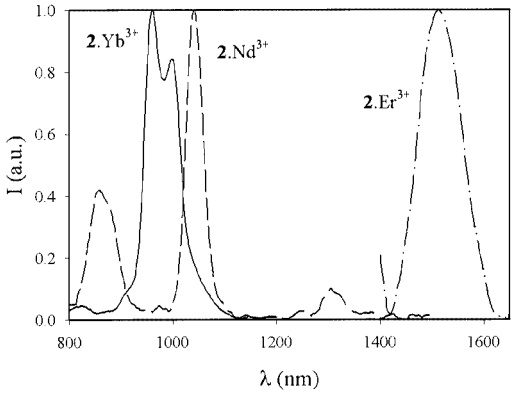


Figure 5. Fluorescence spectra (λ_{exc} = 320 nm) of the complexes of **2** with Yb^{3+}, Nd^{3+}, and Er^{3+} in acetonitrile solution at room temperature

of the quinoline is strongly hydrogen-bonded to one of the adjacent amide carbonyl groups. Contrary to what was observed with quinoline-functionalised crown ethers, no changes in the absorption or emission spectra were observed for either ligand **1** or **2** with Hg^{2+}, Mg^{2+}, and Zn^{2+} metal ions. Alkali and alkaline earth metal ion complexes of **1** usually show a bathochromic shift and a quenching of the fluorescence band with respect to the free ligand; on the contrary, the corresponding complexes of **2** present hypsochromic shifts of λ_{max} and an increase of fluorescence intensities for alkaline earth cation complexes. NMR spectroscopic data and semiempirical calculations also support the hypothesis that this difference in the photophysical properties is due to a different mode of coordination of the quinoline nucleus to the metal ion. In the complexes of **1** both the quinoline N and O atoms are coordinated while in complexes of **2** the N atom is too far from the metal ion. Ligands **1** and **2** do not form complexes with lanthanide ions in methanol but in acetonitrile complexation with Nd^{3+}, Yb^{3+}, and Er^{3+} causes the quenching of fluorescence, accompanied by an increase in the metal-centred luminescence, which indicates that an efficient energy transfer occurs, this feature being of particular interest for practical applications.

Experimental Section

General Remarks: Melting points were determined with an Electrothermal apparatus in sealed capillaries under nitrogen. ^1H and ^{13}C NMR spectra were recorded with Bruker spectrometers AC300 (^1H: 300 MHz; ^{13}C: 75 MHz) or AVANCE 300 (^1H: 300 MHz; ^{13}C: 75 MHz) with TMS as internal standard. Mass spectra were obtained in the ESI mode with Micromass 4LCZ or in the CI (CH_4) mode with Finnigan Mat SSQ710 spectrometers. UV/Vis spectra were recorded with a Perkin−Elmer Lambda Bio 20 spectrophotometer. TLC was performed on precoated silica gel Merck 60 F_{254} or neutral alumina Merck 60 F_{254} (type E) plates. All solvents were purified by standard procedures; dry solvents were obtained by literature methods and stored over molecular sieves. All the reactions were carried out under nitrogen. 25-Monobenzyloxy-*p*-*tert*-butylcalix[4]arene[30] was prepared according to a literature method.

25-Benzyloxy-26,27,28-tris{[(diethylamino)carbonyl]methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)calix[4]arene (4): A stirred solution of NaI (2.16 g, 14.41 mmol) and $ClCH_2CONEt_2$ (1.98 mL, 14.41 mmol) in dry DMF (20 mL) was heated at 80 °C for 30 min. After cooling to room temperature, compound **3** (1.78 g, 2.4 mmol) and NaH (60% in oil, 1.92 g, 48 mmol) were added. The reaction mixture was heated at 80 °C for 2 d and then (***CAREFULLY!***) quenched with HCl (50 mL of 1 N solution). The white solid formed was filtered through a Buchner funnel and dissolved in CH_2Cl_2 (40 mL). The organic layer was washed with 1 N HCl (5 × 50 mL) and distilled water (5 × 50 mL). CH_2Cl_2 was removed from the organic phase using a rotavapor and the crude product obtained was purified by column chromatography using an elution gradient (SiO_2; EtOAc/MeOH, 95:5 to EtOAc/MeOH/Et_3N, 8:2:1). Yield: 2.25 g (87%). M.p. 206 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.52−7.50 (m, 2 H, PhH_{ortho}), 7.26−7.24 (m, 3 H, PhH_{meta} and PhH_{para}), 6.77−6.72 (m, 8 H, ArH), 5.05 (d, *J* = 12.7 Hz, 2 H, $ArCH_{ax}HAr$), 5.04 (s, 2 H, $ArOCH_2Ph$), 5.00 (s, 2 H, $ArOCH_2CO$), 4.83 (d, *J* = 14.8 Hz, 2 H, ArOCHHCO), 4.66 (d, *J* = 12.8 Hz, 2 H, $ArCH_{ax}HAr$), 4.65 (d, *J* = 12.3 Hz, 2 H, ArOCHHCO), 3.43−3.33 (m, 12 H, NCH_2CH_3), 3.18 (d, *J* = 12.7 Hz, 2 H, $ArCH_{eq}HAr$), 3.08 (d, *J* = 12.8 Hz, 2 H, $ArCH_{eq}HAr$), 1.20−1.01 (m, 18 H, NCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.8, 168.7 (s, C=O), 153.5, 152.9 (s, Ar *ipso*), 144.4, 144.2 (s, Ar *para*), 138.9 (s, Ar *ipso*), 133.9, 133.7, 133.5, 133.3 (s, Ar *ortho*), 129.8, 127.7, 127.2 (s, Ph), 125.1, 124.8 (d, Ar *meta*), 76.8 (t, OCH_2Ph), 71.4, 71.2 (t, $ArOCH_2CO$), 40.6, 40.4. 39.7, 39.5 (t, NCH_2CH_3), 33.7 [s, $C(CH_3)_3$], 31.8 (t, $ArCH_2Ar$), 31.4, 31.3 [q, $C(CH_3)_3$], 14.3, 14.2, 13.0 (q, NCH_2CH_3) ppm. MS (CI): *m*/*z* = 1078.5 (100) [M + H^+]. $C_{69}H_{95}N_3O_7$ (1078.53): calcd. C 76.84, H 8.88, N 3.90; found C 76.79, H 8.93, N 3.96.

25,26,27-Tris{[(diethylamino)carbonyl]methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)-28-hydroxycalix[4]arene (5): A suspension of monobenzyl ether **4** (0.5 g, 0.46 mmol) and $Pd(OH)_2/C$ (0.05 g, 20% w/w, Pearlman's catalyst) in EtOH/cyclohexene (20 mL of a 1:1 mixture) were heated at 80 °C in a Schlenk tube for 2 d. The reaction mixture was filtered through a Celite bed, the solvent removed under reduced pressure, and the product crystallised from CH_3CN. Yield: 0.39 g (87%). M.p. 225−227 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.78 (s, 1 H, ArOH), 6.94 (s, 2 H, ArH), 6.88 (s, 2 H, ArH), 6.68 (d, *J* = 6.7 Hz, 4 H, ArH), 5.12 (s, 2 H, $ArOCH_2CO$), 5.08 (d, *J* = 12.8 Hz, 2 H, $ArCH_{ax}HAr$), 5.03 (d, *J* =

13.9 Hz, 2 H, $ArOCH_AHCO$), 4.54 (d, J = 13.9 Hz, 2 H, $ArOCHH_BCO$), 4.50 (d, J = 12.8 Hz, 2 H, $ArCH_{ax}HAr$), 3.43−3.33 (m, 12 H, NCH_2CH_3), 3.26−3.17 (m, 4 H, $ArCH_{eq}HAr$), 1.20 [s, 9 H, $C(CH_3)_3$], 1.18 [s, 9 H, $C(CH_3)_3$], 1.25−0.94 (m, 18 H, NCH_2CH_3), 0.95 [s, 18 H, $C(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.5, 168.1 (s, C=O), 154.0, 152.7, 150.5 (s, Ar *ipso*), 145.5, 144.8, 140.3 (s, Ar *para*), 134.4, 133.2, 133.0, 127.6 (s, Ar *ortho*) 125.8, 125.4, 125.1, 124.7 (d, Ar *meta*), 72.6, 71.2 (t, $ArOCH_2CO$), 41.0, 40.0 (t, NCH_2CH_3), 33.7 [s, $C(CH_3)_3$], 32.2 (t, $ArCH_2Ar$), 31.6, 31.5, 31.2 [q, $C(CH_3)_3$], 14.3, 13.0 (q, NCH_2CH_3) ppm. MS (CI): m/z = 988.4 (100), $[M + H^+]$. $C_{62}H_{89}N_3O_7$ (988.41): calcd. C 75.34, H 9.08, N 4.25; found C 75.28, H 9.15, N 4.31.

5-Chloro-8-methoxy-2-methylquinoline (7): Compound **7** was obtained according to a literature procedure.[45] The crude reaction mixture was purified by column chromatography using an elution gradient (SiO_2; EtOAc/hexane, 7:3 to EtOAc/hexane, 1:1). Yield: 20%. M.p. 93 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.42 (d, J = 8.7 Hz, 1 H, QH^4), 7.46 (d, J = 8.4 Hz, 1 H, QH^6), 7.43 (d, J = 8.7 Hz, 1 H, QH^3), 6.95 (d, J = 8.4 Hz, 1 H, 1 H, QH^7), 4.07 (s, 3 H, OCH_3), 2.82 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.6 (s, C^2), 153.9 (s, C^8), 140.1 (s, C^9), 132.9 (d, C^4), 125.3 (d, C^6), 125.1 (s, C^1), 123.2 (s, C^3), 122.0 (s, C^5), 107.4 (d, C^7), 56.0 (q, OCH_3), 25.4 (q, CH_3) ppm. MS (CI): m/z = 206.9 (95) $[M^+]$, 208.9 (100) $[M + 2]^+$.

2-(Bromomethyl)-5-chloro-8-methoxyquinoline (6): The mono(bromomethyl) derivative **6** was obtained according to a literature procedure[7] and the crude reaction mixture purified by column chromatography using an elution gradient (SiO_2; EtOAc/hexane, 8:3 to EtOAc/hexane, 7:3). Yield: 45%. M.p. 151−153 °C. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 156.6 (s, C^2), 154.4 (s, C^8), 134.4 (d, C^4), 133.8 (s, C^9), 126.8 (d, C^6), 122.7 (d, C^3), 122.2 (s, C^1), 121.8 (s, C^5), 108.1 (d, C^7), 56.3 (q, OCH_3), 34.0 (t, CH_2Br) ppm. MS (CI): m/z = 286.1 (45) $[M + H]^+$, 288.2 (55) $[M + H + 2]^+$, 290 (15) $[M + H + 4]^+$.

28-[(5-Chloro-8-methoxyquinolin-2-yl)methoxy]-25,26,27-tris-{[(diethylamino)carbonyl]methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)calix[4]arene (1): A solution of triamide **5** (0.3 g, 0.3 mmol) and NaH (60% in oil, 0.048 g, 1.2 mmol) in dry DMF (10 mL) was stirred at room temperature for 30 min and then (bromomethyl)quinoline **6** (0.104 g, 0.36 mmol) was added. After 5 h, the reaction mixture was quenched (***CAREFULLY!***) by addition of HCl (10 mL of a 1 N solution) and CH_2Cl_2 (25 mL). The organic layer was separated and the aqueous phase extracted with another portion of CH_2Cl_2 (25 mL). The combined organic layers were washed with H_2O (40 mL) and the solvent removed under reduced pressure. Pure compound **1** was obtained by recrystallisation from MeOH. Yield: 0.18 g (50%). M.p. 201−203 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.84 (d, J = 8.7 Hz, 1 H, QH^4), 8.55 (d, J = 8.7 Hz, 1 H, QH^3), 7.48 (d, J = 8.3 Hz, 1 H, QH^6), 6.94 (d, J = 8.3 Hz, 1 H, QH^7), 6.81 (s, 8 H, ArH), 5.39 (s, 2 H, $ArOCH_2Q$), 5.07 (d, J = 12.8 Hz, 2 H, $ArCH_{ax}HAr$), 4.99 (s, 2 H, $ArOCH_2CO$), 4.94 (d, J = 15 Hz, 2 H, $ArOCH_AHCO$), 4.86 (d, J = 12.8 Hz, 2 H, $ArCH_{ax}HAr$), 4.75 (d, J = 15 Hz, 2 H, $ArOCHH_BCO$), 4.03 (s, 3 H, OCH_3), 3.40−3.20 (m, 12 H, NCH_2CH_3), 3.28−3.11 (m, 4 H, $ArCH_{eq}HAr$), 1.09 [s, 9 H, $C(CH_3)_3$], 1.08 [s, 9 H, $C(CH_3)_3$], 1.25−0.94 (m, 18 H, NCH_2CH_3), 1.04 [s, 18 H, $C(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.5 (s, C=O), 156.6 (s, C^2), 154.4 (s, C^8), 153.7, 153.5, 153.3 (s, Ar *ipso*), 144.7, 144.5, 144.4 (s, Ar *para*), 139.7 (s, C^9), 134.1 (d, C^4), 133.9, 133.4, 133.3, 132.9 (d, Ar *ortho*), 126.3 (d, C^6), 125.5, 125.4, 125.3, 125.2 (d, Ar *meta*), 123.2 (d, C^3), 122.1 (s, C^1), 121.9 (s, C^5), 107.3 (d, C^7), 78.5 (t, $ArOCH_2Q$), 71.9 (t, $ArOCH_2CO$), 71.5 (t, $ArOCH_2CO$), 56.2 (q, OCH_3), 40.6 (t, NCH_2CH_3), 39.7 (t, NCH_2CH_3), 33.8 [s, $C(CH_3)_3$], 32.1 (t, $ArCH_2Ar$), 31.6 (t, $ArCH_2Ar$), 31.4 [q, $C(CH_3)_3$], 14.1 (q, CH_3), 12.9 (q, CH_3) ppm. MS (CI): m/z = 1192.9 (100) $[M^+]$, 1194.8 (45) $[M + 2]^+$. $C_{73}H_{97}ClN_4O_8$ (1194.05): calcd. C 73.43, H 8.19, N 4.69; found C 73.39, H 8.22, N 4.76.

25,26,27-Tris{[(diethylamino)carbonyl]methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)-28-[2-(tosyloxy)ethyl]calix[4]arene (10): A suspension of triamide **5** (0.3 g, 0.3 mmol) and Na_2CO_3 (0.26 g, 2.43 mmol) in dry CH_3CN (30 mL) was heated at 80 °C for 30 min and then diethylene glycol ditosylate (**8**) (1.23 g, 3.64 mmol) was added. After 4 d of heating at 80 °C the solvent was removed under reduced pressure and the residue quenched with HCl (30 mL of a 0.1 N solution). This water phase was extracted twice with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with water. After removal of the solvent using a rotavapor, the residue was submitted to column chromatography (neutral Al_2O_3; EtOAc/Et_2O/Et_3N, 9:4:0.4) to give compound **10** as a mixture of metal ion complexes. This solid was then dissolved in CH_2Cl_2, washed four times with distilled water, and the solvent removed under reduced pressure to give metal ion free compound **10**. Yield: 0.23 g (65%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.72 (d, J = 8.4 Hz, 2 H, TosH), 7.25 (d, J = 8.4 Hz, 2 H, TosH), 7.00 (s, 2 H, ArH), 6.97 (s, 2 H, ArH), 6.58 (d, J = 2.4 Hz, 2 H, ArH), 6.48 (d, J = 2.4 Hz, 2 H, ArH), 5.16 (s, 2 H, $ArOCH_2CO$), 5.11 (d, J = 14.1 Hz, 2 H, $ArOCH_AHCO$), 4.81 (t, J = 5.6 Hz, 2 H, OCH_2CH_2OTs), 4.77 (d, J = 14.1 Hz, 2 H, $ArCH_{ax}HAr$), 4.58 (d, J = 14.1 Hz, 2 H, $ArOCHH_BCO$), 4.58 (d, J = 14.1 Hz, 2 H, $ArCH_{ax}HAr$), 4.34 (t, J = 5.6 Hz, 2 H, OCH_2CH_2Tos), 3.46−3.32 (m, 12 H, NCH_2CH_3), 3.24−3.12 (m, 4 H, $ArCH_{eq}HAr$), 2.41 (s, 3 H, CH_3Tos), 1.26 [s, 9 H, $C(CH_3)_3$], 1.25 [s, 9 H, $C(CH_3)_3$], 1.29−1.08 (m, 18 H, NCH_2CH_3), 0.88 [s, 18 H, $C(CH_3)_3$] ppm. MS (ESI): m/z = 1208.7 (100) $[M + Na^+]$. $C_{71}H_{99}N_3O_{10}S$ (1186.65): calcd. C 71.86, H 8.41, N 3.54; found C 71.82, H 8.48, N 3.58.

28-(2-Bromoethoxy)-25,26,27-tris{[(diethylamino)carbonyl]-methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)calix[4]arene (11): A solution of triamide **5** (0.3 g, 0.30 mmol), K_2CO_3 (0.34 g, 2.4 mmol) and dibromoethane (**9**) (5.7 g, 30.3 mmol) was heated at 80 °C for 24 h in a Schlenk tube. The solvent was then removed under reduced pressure and the residue dissolved in CH_2Cl_2 (30 mL). The organic layer was washed twice with water (2 × 30 mL), the solvent removed under reduced pressure, and the resulting brownish oil thoroughly dried under high vacuum. Yield: 0.28 g (84%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.08 (s, 2 H, ArH), 7.07 (s, 2 H, ArH), 6.57 (d, J = 2.4 Hz, 2 H, ArH), 6.42 (d, J = 2.4 Hz, 2 H, ArH), 5.16 (s, 2 H, $ArOCH_2CO$), 5.12 (d, J = 12.6 Hz, 2 H, $ArCH_{ax}HAr$), 4.78 (d, J = 13.1 Hz, 2 H, $ArOCH_AHCO$), 4.54 (d, J = 12.6 Hz, 2 H, $ArCH_{ax}HAr$), 4.41 (d, J = 13.1 Hz, 2 H, $ArOCH_BHCO$), 4.22 (s, 4 H, OCH_2CH_2Br), 3.51−3.28 (m, 12 H, NCH_2CH_3), 3.25−3.13 (m, 4 H, $ArCH_{eq}HAr$), 1.29 [s, 9 H, $C(CH_3)_3$], 1.18 [s, 9 H, $C(CH_3)_3$], 1.30−1.08 (m, 18 H, NCH_2CH_3), 0.84 [s, 18 H, $C(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.7, 168.2 (s, C=O), 155.9, 153.8, 153.1 (s, Ar *ipso*), 146.0, 145.0 (s, Ar *para*), 136.1, 135.2, 132.5, 132.3 (d, Ar *ortho*), 126.2, 125.9, 125.5, 124.9 (d, Ar *meta*), 73.6 (t, OCH_2CH_2Br), 73.2 (t, $ArCH_2CO$), 72.8 (t, $ArCH_2CO$), 41.9, 41.1, 40.7, 40.2 (t, NCH_2CH_3), 34.5, 34.4, 34.0 [s, $C(CH_3)_3$], 32.1 [q, $C(CH_3)_3$], 31.9, 31.7 (t, $ArCH_2Ar$), 31.4 (t, OCH_2CH_2Br), 14.9, 13.6 (q, NCH_2CH_3) ppm. MS (CI): m/z = 1095.5 (40) $[M + 2]^+$, 1093.5 (100) $[M^+]$. $C_{64}H_{92}BrN_3O_7$ (1095.36): calcd. C 70.18, H 8.47, N 3.84; found C 70.24, H 8.51, N 3.86.

28-[2-(5-Chloroquinolin-8-yloxy)ethoxy]-25,26,27-tris{[(diethylamino)carbonyl]methoxy}-5,11,17,23-tetrakis(1,1-dimethylethyl)-calix[4]arene (2): A suspension of bromo derivative **11** (0.48 g, 0.44 mmol) and K_2CO_3 (0.06 g, 0.88 mmol) in dry CH_3CN (30 mL) was heated at 80 °C for 30 min and then 5-chloro-8-hydroxyquinoline (**12**) (0.08 g, 0.44 mmol) added. After 3 d of heating at 80 °C, the solvent was removed under reduced pressure and H_2O (30 mL) was added. This aqueous layer was extracted twice with CH_2Cl_2 (2 × 30 mL) and the solvent removed from the combined organic extracts. The product was obtained by column chromatography using an elution gradient (SiO_2; EtOAc to EtOAc/MeOH, 9:1 to EtOAc/MeOH, 7:3). After the chromatography, the product was dissolved in CH_2Cl_2 and washed three times with distilled water in order to decomplex the ligand from metal ion salts. Yield: 0.16 g (30%). M.p. 185−187 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.90 (dd, *J* = 4.22, *J* = 1.76 Hz, 1 H, QH^2), 8.49 (dd, *J* = 7.8, *J* = 0.8 Hz, 1 H, QH^4), 7.55 (d, *J* = 8.7 Hz, 1 H, QH^6), 7.52 (d, *J* = 8.7 Hz, 1 H, QH^7), 7.49 (dd, *J* = 7.6, *J* = 4.2 Hz, 1 H, QH^3), 7.01 (s, 2 H, ArH), 7.00 (s, 2 H, ArH), 6.60 (d, *J* = 2.4 Hz, 2 H, ArH), 6.53 (d, *J* = 2.4 Hz, 2 H, ArH), 5.21 (s, 2 H, $ArOCH_2CO$), 5.09 (d, *J* = 14.1 Hz, 2 H, $ArCH_{ax}HAr$), 5.03 (t, *J* = 4.9 Hz, 3 H, OCH_2CH_2OQ), 4.80 (d, *J* = 12.7 Hz, 2 H, $ArOCH_AHCO$), 4.75 (d, *J* = 14.1 Hz, 2 H, $ArCH_{ax}HAr$), 4.58 (d, *J* = 12.7 Hz, 2 H, $ArOCHH_BCO$), 4.59 (t, *J* = 4.9 Hz, 2 H, OCH_2CH_2Q), 3.41−3.23 (m, 12 H, NCH_2CH_3), 3.21−3.14 (m, 4 H, $ArCH_{eq}HAr$), 1.25 [s, 9 H, $C(CH_3)_3$], 1.08 [s, 9 H, $C(CH_3)_3$], 1.25−0.94 (m, 18 H, NCH_2CH_3), 0.90 [s, 18 H, $C(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.5, 168.2 (s, C=O), 154.8, 154.4, 154.1 (s, Ar *ipso*), 153.2 (s, C^8), 149.1 (d, C^2), 145.1 144.5 (s, Ar *para*), 140.9 (s, C^9), 135.3, 134.7, 132.5, 132.1 (d, Ar *ortho*), 132.6 (d, C^4), 127.0 (d, C^6), 126.9 (s, $C^{1\circ}$), 125.7, 125.4, 125.1, 124.8 (d, Ar *meta*), 121.9 (d, C^3), 121.1 (s, C^5), 109.9 (d, C^7), 72.4 (t, $ArOCH_2CH_2OQ$), 71.7, 70.9 (t, $ArOCH_2CO$), 56.2 (q, OCH_3), 67.8 (t, $ArOCH_2CH_2OQ$), 40.9, 40.8, 39.9, 39.6 (t, NCH_2CH_3), 33.9, 33.7 [s, $C(CH_3)_3$], 31.8, 30.9 (t, $ArCH_2Ar$), 31.6, 31.2 [q, $C(CH_3)_3$], 14.3, 13.1, 12.9 (t, NCH_2CH_3) ppm. MS (CI): *m/z* = 1193.5 (100) [M + H^+]. $C_{73}H_{97}ClN_4O_8$ (1194.05): calcd. C 73.43, H 8.19, N 4.69; found C 73.47, H 8.22, N 4.75.

Metal Picrate Extraction: The percentages of extraction of metal picrates (*E*%) from water into dichloromethane, at 20 ± 0.1 °C, were determined from the absorbance at 354 nm of the picrate anion remaining in the aqueous phase after extraction. The same concentration (2.5×10^{-4} M) was used for the ligand in the organic phase and the picrate salt in the aqueous phase as already described in detail.[39]

2D NMR Experiments: 2D NMR spectra were acquired with a 300 MHz Bruker Avance instrument with the standard COSYGPQF, GRASP-HSBC and NOESYPH pulse sequences supplied with the Bruker software. The mixing times used in the NOESYPH experiments were 650 ms.

Photophysical Studies: Photophysical experiments were conducted in 5×10^{-5} to 5×10^{-4} M methanol and acetonitrile (Merck Uvasol) solutions at room temperature. Absorption spectra were recorded with a Perkin−Elmer Lambda 16 spectrophotometer. Uncorrected emission spectra and corrected excitation spectra were obtained with a Perkin-Elmer LS50 spectrofluorimeter. Corrections for instrumental response, inner filter effects, and phototube sensitivity were performed as described previously.[46]

Semiempirical Calculations: All geometry optimisation calculations were performed with the SPARTAN'02 program (Release 1.02). The equilibrium conformers were first obtained by the Monte Carlo method using the MMFF molecular mechanics force field. The obtained structures were then minimised using the semiempirical·molecular orbital method in the PM3 model.[47] The geometry of the calcium complexes were directly optimised by the semiempirical method in the PM3 model. Each stationary point was characterised as a minimum or a transition state by frequencies calculation.

Supporting Information: This material (see footnote on the first page of this article or from the authors) contains portions of the HSBC and NOESYPH spectra of compound **1** in $CDCl_3$, ^{1}H NMR spectra in methanol of compounds **1**, **2**, and of their Na^+ and Ca^{2+} complexes, coloured minimised molecular structures of the free ligands and of their Ca^{2+} complexes, a table with the extraction percentages of alkali and alkaline earth picrates from H_2O to CH_2Cl_2 by calix[4]arene amides (**1**, **2**, **4**, **L1**), and association constants and binding free energies of complexes of calixarene amide ligands (**1**, **2**, **4**, **L1**) with alkali picrates in $CHCl_3$ saturated with H_2O.

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