A new calix[4]arene-based fluorescent sensor for sodium ion

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A new calix[4]arene with three ester groups and an appended naphthalenic fluorophore has been synthesized; investigation of its photophysical and complexing properties towards alkali and alkaline-earth metal ions reveals a high selectivity for Na+ in water–ethanol mixtures.

Considerable effort is being devoted to the design of a fluorescent sensor for metal ions.[1–4] Progress has still to be made in relation to the selectivity exhibited towards a given ion. Calixarenes with appropriate appended groups are good candidates because they have been shown to be highly specific ligands[5] and their potential applications as sensing agents have received increasing interest.[6] In particular, several calixarene-based fluorescent sensors have already been designed.[7]

In the present work, a novel calix[4]arene containing three ester groups and an appended naphthalenic fluorophore is described. Calix[4]arene tetraesters have been previously shown to be of interest as complexing agents of alkali metal ions.[8] In view of our previous studies on crowned-coumarin sensors, based on cation-enhancement of photoinduced charge transfer,[9] we have chosen as a fluorophore 6-acyl-2-methoxynaphthalene (AMN) which includes an electron-donating substituent (methoxy group) conjugated to an electron-withdrawing substituent (carbonyl group). It undergoes intramolecular charge transfer upon excitation and is thus expected to be environmentally sensitive. As for crowned coumarins, the fluorophore is linked to calix[4]arene so that the carbonyl group participates in the complexation process (Scheme 1). Consequently, cation binding results in the enhancement of photoinduced charge transfer with concomitant marked changes of photophysical characteristics.

Calix[4]arene **2**‡ was prepared in three steps. 6-Choroacyl-2-methoxynaphthalene was obtained by Friedel–Craft acylation between methoxynaphthalene and chloroacetyl chloride in nitrobenzene.[10] 4-*tert*-Butylcalix[4]arene was mono-alkylated using 2 equiv. of 6-chloroacyl-2-methoxynaphthalene and 2 equiv. of $KHCO_3$ in acetone. The remaining three phenolic groups were later functionnalized using 4 equiv. of ethyl bromoacetate and 2 equiv. of K_2CO_3 in acetone.[8] The cone conformation was confirmed by NMR.[11]
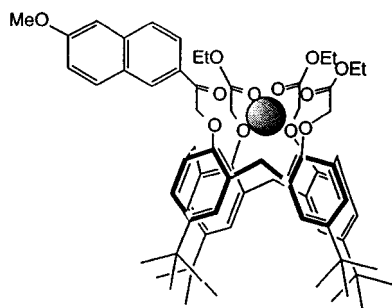
Scheme 1
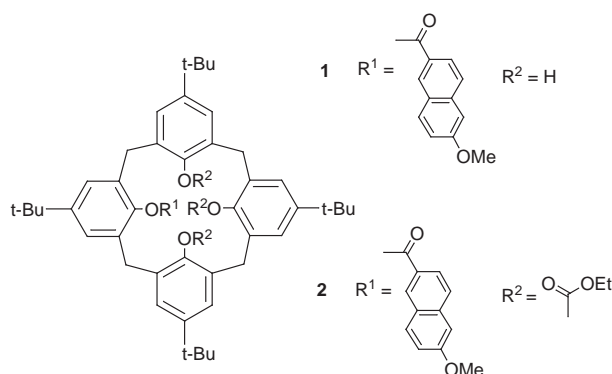
The effects upon addition of Li+, Na+, K+, Mg2+ and Ca2+ perchlorates to **2** were first examined in acetonitrile solution. The absorption and fluorescence spectra of **2** and its complexes with Li+, Na+, K+ and Ca2+ are shown in Fig. 1 and 2, respectively. The spectra of the Mg2+ complex are not shown because full complexation was still not achieved upon addition of $Mg(ClO_4)_2$ at a concentration of 0.04 M. An increase in the molar absorption coefficients together with red shifts of the absorption and emission spectra are observed upon cation binding, as expected from the cation-induced enhancement of the electron-withdrawing character of the carbonyl; the higher the charge density of the cation, the larger the observed effects. The red shifts of the emission spectrum are 45 and 61 nm upon complexation of Na+ and Ca2+, respectively.

Moreover, the fluorescence quantum yield, which is very low for **2** (1.24×10^{-3}), drastically increases upon cation binding (*e.g.* 0.68 for Ca2+). The enhancement factors are 16, 35, 250, 550, for K+, Na+, Li+, Ca2+, respectively, again following the trend in charge density. Such an enhancement can be tentatively explained in terms of the relative locations of the singlet ππ* and nπ* states. For a ketone like **2**, some nπ* character is expected for the lowest excited singlet state.[12] This results in an efficient intersystem crossing to the triplet state and consequently a low fluorescence quantum yield. In the presence of cation which strongly interacts with the lone pair of the carbonyl group, the nπ* state is likely to be shifted to higher energy so that the lowest excited state becomes ππ*.

In ethanol, we first note that the fluorescence quantum yield of **2** is 2.5×10^{-3}, *i.e.* 2 times larger than in acetonitrile. This solvent dependency of the quantum yield, which increases with increasing solvent polarity, supports the existence of a low lying nπ* state in the absence of a cation. The cation-induced photophysical changes in ethanol follow the same trends as in acetonitrile, but they were found to be weaker upon addition of Li+, Mg2+ and Ca2+ and subsequently it was impossible to measure the spectral characteristics and the fluorescence quantum yields of the relevant complexes in this solvent. The fluorescence quantum yield increases by a factor of 15 and 38 upon binding of K+ and Na+, respectively.
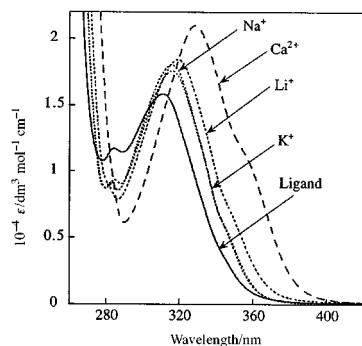
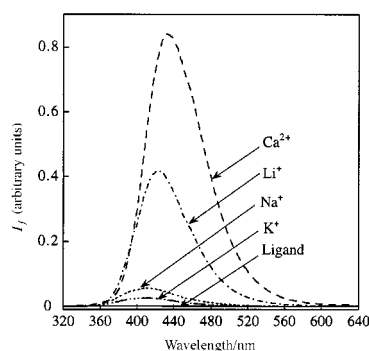**Fig. 1** Absorption spectra of ligand **2** and its complexes in acetonitrile.

Fig. 2 Corrected fluorescence spectra of ligand **2** and its complexes in acetonitrile. Excitation wavelength 320 nm.

Table 1 Stability constants of the complexes of **3** in acetonitrile, ethanol and ethanol–water mixtures

Solvent	Cation	$\log\beta$
MeCN	Li+	6.32 ± 0.07^a
	Na+	6.28 ± 0.06^a
	K+	4.74 ± 0.03^a
	Mg2+	2.06 ± 0.04^a
	Ca2+	5.30 ± 0.06^a
EtOH	Li+	0.9 ± 0.08^a
	Na+	14.3^b
	K+	2.87 ± 0.03^a
	Mg2+	1.82 ± 0.06^a
	Ca2+	1.25 ± 0.03^a
EtOH–H$_2$O	Na+	3.87 ± 0.05^a
(80:20 v/v)	K+	1.17 ± 0.05^a
EtOH–H$_2$O	Na+	3.04 ± 0.07^a
(60:40 v/v)	K+	0^a ($\beta = 0.75 \pm 0.3$)

^{a} 1:1 stoichiometry for the complex. ^{b} 1:2 stoichiometry, $\log K_{11} = 4.6 \pm 0.1$ (M + L $\rightleftharpoons$ ML), $\log K_{12} = 9.7 \pm 0.1$ (ML + L $\rightleftharpoons$ ML$_2$), $\beta = K_{11}K_{12}$.

We then examined the stability of the complexes and their selectivity. The stability constants of the complexes in acetonitrile, ethanol and water/ethanol mixtures are reported in Table 1. In acetonitrile, the values of the stability constants are consistent with those previously reported for the analogous tetraethyl *p-tert*-butylcalix[4]arene tetraacetate and tetraphenyl *p-tert*-butylcalix[4]arene tetraketone.[8] As expected, the stability of the complexes is lower in ethanol. In the case of Na+, the titration curve could not be satisfactorily fitted under the assumption of a 1:1 complex. Careful analysis of the evolution of the absorption spectra revealed that a 2:1 complex and a 1:1 complex with sodium were successively formed upon addition of Na+.§

We then studied the ion-response of **2** in the presence of water since in most applications the metal ions to be detected are in aqueous solutions. Although, **2** is not soluble in water, this is not considered to be a drawback as our eventual aim is to design an optical-fibre device in which **2** will be immobilized in a polymer

or sol–gel film. Furthermore, insolubility in water is preferable so as to minimize leakage. Meanwhile, in order to test the response of **2** in aqueous environments, we measured the stability constants in ethanol–water mixtures. The maximum water content which facilitates sufficient solubility of **2** is 40% by volume. Values are reported in Table 1. It is worth noting, that, in the presence of water, the 2:1 complex with Na+ is no longer observed. The stability constant decreases as the water content increases, as expected, but it appears to level off. It is remarkable that the stability constant of the Na+ complex in ethanol–water (60:40 v/v) is *ca.* 1300; this is suitable for measuring sodium ion concentrations in the mmolar range. In the same ethanol–water mixture, the stability constant of the K+ complex is *ca.* 1. Therefore, selectivity Na+/K+ (expressed by the ratio of the stability constants) is *ca.* 1300. Moreover, it should be emphasized that the other cations used in this study (Li+, Mg2+ and Ca2+) have negligible effects. Finally, it is remarkable that the fluorescence quantum yield of the sodium complex in ethanol–water (60:40 v/v) is 0.11, *i.e.* 30 times larger than that of the free ligand.

The next step of this investigation will be the synthesis of calix[4]arenes with four appended chromophores along the same design principles. The molar absorption coefficient will therefore be four times larger and additional cation-induced photophysical effects are expected.

Notes and references

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‡ The typical experimental procedures for **1** and **2** will be reported elsewhere together with elemental analysis and NMR data.
§ The constants of the successive equilibria K_{11} and K_{12} were determined using the Specfit software version 211 (Spectrum Software Associates).

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