Selective detection of cesium by a water-soluble fluorescent molecular sensor based on a calix[4]arene-bis(crown-6-ether)†

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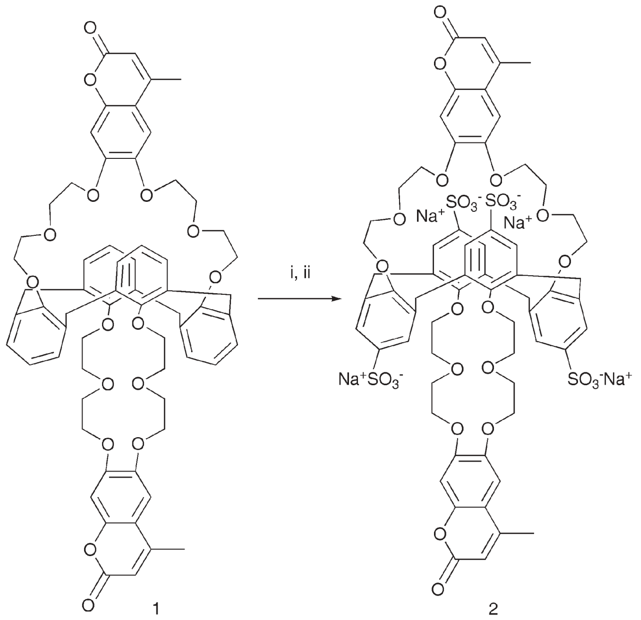
A tetrasulfonated calixarene with two appended crowns, each including a dioxycoumarin fluorophore, is highly soluble in water and shows excellent selectivity for cesium ions.

There is a significant need for the development of sensors able to selectively detect cesium ions. The major source of cesium involves nuclear waste materials and its toxicity is due to its ability to replace potassium in muscles and red cells. In nuclear waste, cesium must be detected in a medium where sodium and potassium are present in a large excess.[1] Various methods were reported for the determination of cesium, including atomic absorption spectroscopy,[2] radioanalysis[3] and ion-selective electrodes (ISEs).[4] Recent developments using ISEs were aimed at obtaining very low detection limits.[4c] Those analytical methods have different disadvantages, since they require expensive instruments and/or controlled experimental conditions. In contrast, fluorescent molecular sensors of ions (fluoroionophores), consisting of fluorophores linked to recognition moieties (ionophores),[5] offer many advantages in terms of sensitivity, selectivity and low cost.[6] In order to achieve good selectivity, the choice of the ionophore is of major importance, and in this respect, 1,3-alternate calix[4]arene-bis(crown-6-ether) exhibits remarkable selectivity[7] towards Cs^+ *versus* Na^+ and to a lesser extent *versus* K^+. It was extensively used for solvent extraction from nuclear waste solutions.[8]

Cesium-selective fluoroionophores, consisting of calix[4]arene-bis(crown-6-ether) with appended cyanoanthracenes, were previously reported by Dabestani *et al.*[9] We described the synthesis, the binding and photophysical properties of **1**, a calix[4]arene-bis(crown-6-ether) with a dioxycoumarin fluorophore inserted in both crowns.[10] Such fluorescent molecular sensors have limitations for practical applications due to their poor solubility in water. In order to render compound **1** soluble in water, we used the method of Lemaire and coworkers to introduce sulfonate groups[11] leading to calixarene **2**. We report here the synthesis together with the photophysical and complexing properties of this compound.

Calixarene **2** was thus synthesized by chlorosulfonylation‡ followed by hydrolysis of the chlorosulfonyl groups§ (Scheme 1). The absorption and emission spectra of **2** do not depend on the pH (from pH 6 to 9). This compound is strongly fluorescent in water with a fluorescence quantum yield Φ_F of 0.40. Addition of sodium ions to a solution of **2** in lutidine buffer does not induce any effect on the emission spectrum up to a concentration of 25 mM. The concentration must attain 50 mM to observe significant changes. Therefore, it is possible to use a MES buffer (50 mM) adjusted at pH 7 with NaOH (25 mM) without any trouble due to the presence of the added sodium ions at a concentration of 25 mM. In this medium, addition of cesium acetate induces a 10 nm bathochromic shift of the absorption spectra (Fig. 1) and an enhancement of the fluorescence intensity (Fig. 2). A linear response of the fluorescence intensity as a function of cesium concentration was observed from 0 to 0.1 mM. The detection limit calculated as three times the standard deviation of the background noise was found to be 3.7 μM. The observed shift of the absorption spectra allows a ratiometric measurement: the ratio of the fluorescence intensities at 420 nm for two excitation wavelengths, *I*(360)/*I*(320), provides a better sensitivity (see the curve in the ESI†): a detection limit of 0.3 μM was found under these conditions. Such a detection limit is of the same order of magnitude as that observed with cesium fluoroionophores soluble in organic solvents,[9,10] but it is unprecedented for a water-soluble fluoroionophore.



Scheme 1 Synthesis of the tetrasulfonated calixarene **2**: (i) HSO_3Cl, $CHCl_3$, −10 °C to RT, 2 h, 87%; (ii) H_2O, pyridine, $NaHCO_3$, RT, 92%.

Analysis of the absorption spectra at various cesium concentrations by means of the SPECFIT programme led to the following

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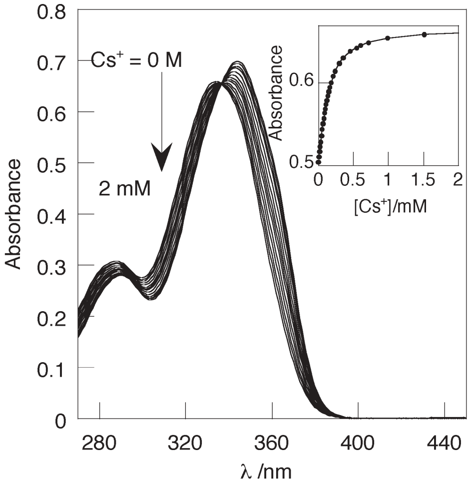

Fig. 1 Absorption spectra of **2** (33 μM) in the presence of increasing concentration of Cs^+ in MES–NaOH buffer pH 7. Inset: titration curve at 365 nm.

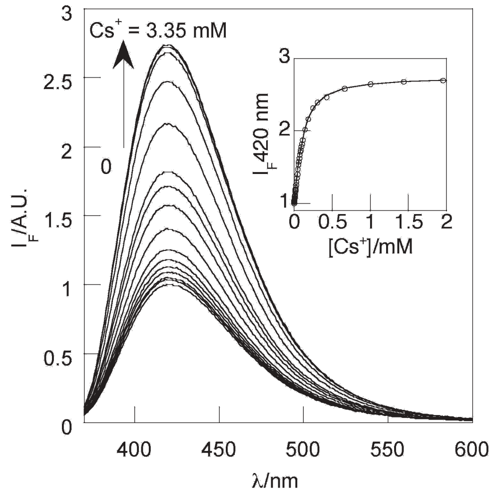

Fig. 2 Corrected emission spectra of **2** (2.6 μM) in the presence of increasing concentration of Cs^+ in MES–NaOH buffer pH 7. Excitation at 365 nm. Inset: titration curve at 420 nm.

stability constants of the two complexes, 1 : 1 and 2 : 1 (metal–ligand): log K_{11} = 4.10 ± 0.04, log K_{21} = 3.82 ± 0.05. The values obtained from emission data gave the same values within the experimental error, which does not necessarily mean that the stability constants of the complexes is the same in the ground and excited states, but that the complexation equilibrium in the excited state is not reached during the lifetime of this excited state (3.5 ns).

It should be noted that, in contrast to the non-sulfonated calix[4]arene-bis(crown-6-ether) **1**, for which an anticooperative effect was observed on binding with a second cation (as a result of the repulsion of the two cations),[10] the ratio K_{21}/K_{11} ($\sim$0.55 ± 0.30) is close to the statistical value of 1/4 that would be observed if the two binding sites were identical and independent.[12] This means that there is no electrostatic repulsion between the two bound cations because of the shielding effect of the sulfonate groups. The SPECFIT programme also provides the absorption and the emission spectra of the 1 : 1 and 2 : 1 complexes that are displayed in Fig. 3. The absorption spectrum of the 1 : 1 complex is the half sum of the spectrum of the free ligand and that of the 2 : 1 complex, which clearly proves that the two binding sites have the same affinities for cations.

It is of major importance to note that, in the complexes, electrostatic attraction brings the two sulfonate groups close to a cesium ion that is coordinated to the oxygen atoms at the 6- and 7-positions of the coumarin. Consequently, in the vicinity of these oxygen atoms, there is an overall negative charge (equal to that of an electron) that reinforces the electron-donating character of these atoms, explaining the observed red shift of the absorption spectrum.

The enhancement of the fluorescence intensity upon cesium binding can be explained in the same way. It should be indeed recalled that coumarin itself (*i.e.* without any substituent on the phenyl ring) is very poorly fluorescent and that introduction of electron-donating methoxy groups at the 6- and 7-positions leads to intense fluorescence, as a consequence of an intramolecular charge transfer from these groups to the lactone carbonyl group (acceptor).[13] In calixarene **1**, the decrease in fluorescence intensity upon cesium binding was explained by the reduction in the electron-donating character of the coumarinic oxygen atoms at the 6- and 7-positions. On the contrary, in the complexes of calixarene **2** with cesium ion, the electron-donating character is reinforced by the negative charge appearing in the vicinity of the oxygen atoms, which leads to an increase in fluorescence intensity. In line with this increase, the lifetime of the excited state increases from 3.51 ± 0.05 ns for the free ligand to 3.73 ± 0.05 ns for the 2 : 1 complex.

^{1}H-NMR studies of the 2 : 1 complex confirm the enhancement of the electron-donating character of the coumarinic oxygen atoms upon complexation with cesium. In fact, a considerable upfield shift is observed for one of the aromatic protons of the coumarin close to the oxygen of the crown ether. In contrast, the aromatic protons of the calix[4]arene moved downfield by 0.11 ppm, owing to π-metal interaction between the cesium ion and the phenyl ring of the calixarene.

It is of interest to compare the effects of cesium ion with the effect of a double-charged cation like magnesium ion. A decrease in fluorescence intensity upon addition of Mg^{2+} was observed. Indeed, the two positive charges of this cation are compensated by the two negative charges of the sulfonate groups, so that no net

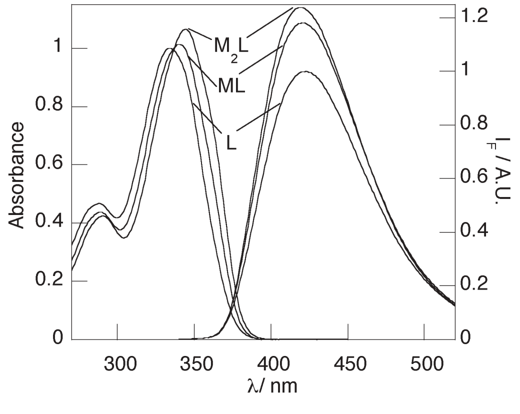

Fig. 3 Absorption and emission spectra of **2** and its 1 : 1 and 2 : 1 complexes with Cs^+ calculated from the titration data using the SPECFIT programme in MES–NaOH buffer pH 7.

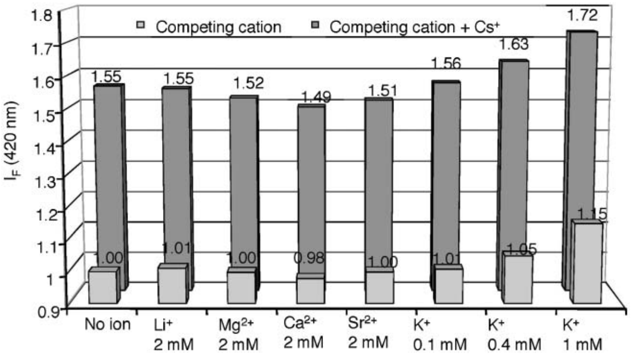

Fig. 4 Fluorescence intensity at 420 nm $I_F(420)$ of 2 (2.6 μM) in MES–NaOH buffer pH 7, in the presence of Cs^+ (0.055 mM, 1 ppm) and various interfering cations.

charge appears in the vicinity of the oxygen atoms of the coumarin and there is no concomitant fluorescence enhancement.

The photophysical effects of cesium binding require further attention. Upon excitation, the redistribution of charges on the atoms involved in the photoinduced intramolecular charge transfer and in the coordination is likely to result in motions of the bound cations, as previously observed with the complexes with calixarene **1**.[10b] The situation is more complicated with calixarene **2**, because of the presence of the sulfonate groups. In particular, a slight blue shift of the emission spectrum upon cesium binding was observed instead of a red shift because of possible compensation effects between the reduction in charge density of the oxygen atoms of the coumarin at the 6- and 7- positions due to intramolecular charge transfer, and the increase in charge density due to the vicinity of an overall negative charge. Moreover, the redistribution of charges is likely to be not strictly the same when one or two cations are present in the complex; interactions in the excited states between the two cations within the 2 : 1 complex may occur with possible effects on emission spectra. In fact, in contrast to the absorption spectrum, the emission spectrum of the 1 : 1 complex was found to be significantly different from the half sum of the spectra of the free ligand and the 2 : 1 complex (see Fig. 3).

Finally, let us examine now the selectivity of **2** for Cs^+ with respect to other cations such as K^+, Ca^{2+}, Li^+, Mg^{2+}. Except for K^+, the stability constants of the complexes with these ions are too low to be determined and the competition–based fluorescence effect profiles for these metal ions (Fig. 4) show significant interference with these competing cations under these conditions. The value of K_{11} for the K^+ complex was found to be 51 ($\log K_{11}$ = 1.71), i. e. much lower than for Cs^+. The selectivity towards Cs^+ versus K^+ (expressed as the ratio of the stability constants) is thus larger than 250.¶

In conclusion, the new water soluble calix[4]arene-bis(crown-6-ether) fluoroionophore can detect cesium ion very efficiently and selectively in water.

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Notes and references

‡ Synthetic procedure for the preparation of the tetrachlorosulfonylated intermediate: to a solution of **1** (234 mg, 0.21 mmol) in $CHCl_3$ (3 mL) was added dropwise HSO_3Cl (0.56 ml, 8.48 mmol) at −10 °C. After 3 h at room temperature, the brownish reaction mixture was poured into an ice-water solution. Saturated aqueous NaCl solution was added (20 ml). Extraction with EtOAc, drying over $MgSO_4$ and solvent removal gave 280 mg of a white solid. By addition of isopropanol, pure tetrachlorosulfonylated calixarene was collected by filtration as a white powder (271 mg, 87%); δ_H (300 MHz, $(CD_3)_2CO$) 2.46 (6H, br s), 3.22 (8H, t, J 6.3 Hz, OCH_2CH_2O), 3.76–3.93 (16H, m), 4.06–4.23 (8H, m), 4.48 (8H, br s), 6.17 (2H, d, J 0.7 Hz), 6.90 (2H, s), 7.23 (2H, s), 8.12 (8H, d, J 3.7 Hz); elemental analysis for $C_{64}H_{60}Cl_4O_{24}S_4$ (1483.22): calcd C 51.83, H 4.08; found C 51.41, H 4.35.

§ Synthetic procedure for the preparation of compound **2**: tetrachlorosulfonylated calixarene (247 mg, 0.17 mmol) was dissolved in pyridine (2 ml) and water (0.25 ml) was added. The reaction mixture was stirred during 2 h at room temperature. After removal of the solvent, 0.1 ml of water was added. The solution was neutralized to pH = 7 by titration with 10% $NaHCO_3$ aqueous solution and acetone was added. The resulting precipitate was filtered and compound **2** (229 mg, 92%) was obtained after recrystallisation in acetone–water as a white powder; mp > 260 °C ; δ_H (300 MHz, (D_2O)) 2.45 (6H, m, CH_3), 3.15–3.35 (8H, m), 3.60–3.75 (8H, m), 3.75–3.85 (4H, m), 3.88–3.96 (4H, m), 4.07 (8H, br s), 4.11–4.27 (8H, m), 6.23 (2H, s), 7.03 (2H, s), 7.29 (2H, s), 7.60 (8H, s); δ_C (75 MHz, D_2O) 18.9 (CH_3), 37.7 ($Ar–CH_2–Ar$); 69.1, 69.5, 69.7, 69.8, 70.4, 70.9, 71.0 ($O–CH_2$); 103.0, 111.3 (CH_{ar}); 113.3 (C_q), 114.5, 127.5 (CH_{ar}); 134.6, 134.7, 138.3, 138.4, 146.0, 150.4, 154.1, 157.5, 159.2, 162.2, 165.9 (C_q); m/z (ESI^-): 724.9 ($[M–2Na]^{2-}$), 475.6 ($[M–3Na]^{3-}$), 351.0 ($[M–4Na]^{4-}$)

¶ The complexation constants were determined by global analysis of the evolution of all the absorption or fluorescence spectra by using the Specfit Global Analysis System V3.0 for 32-bit Window system.

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