A Novel Calix[4]arene Tetraester with Fluorescent Response to Complexation with Alkali Metal Cations

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A new metal sensing compound, a calix[4]arene having four anthracene moieties on the lower rim has been synthesized; the intensity of its fluorescence spectrum is markedly affected by alkali metal ion complexation.

Optical detection methods have received increasing attention for chemical trace analyses especially for selective determination of clinically important species. Spectroscopic detection of metal ions is of great importance both in classical analytical chemistry and in the molecular design of ion sensors involving optical signal transformation. The inherently sensitive nature of fluorescence signally makes it an attractive option, particularly when combined with a selective complexing process involving the target species.[1]

Calixarenes are useful building blocks in the design of novel host molecules.[2,3] Calixarene derivatives incorporating ionophoric functional groups linked by the phenolic oxygen atoms exhibit some excellent properties as neutral receptors for metal ions: they form stable complexes and show sharp size related selectivity because of their well preorganized ionophoric groups.[4–6] This led us to prepare fluorescent calixarenes by incorporation of aromatic fluorophores into the basic calixarene skeleton.

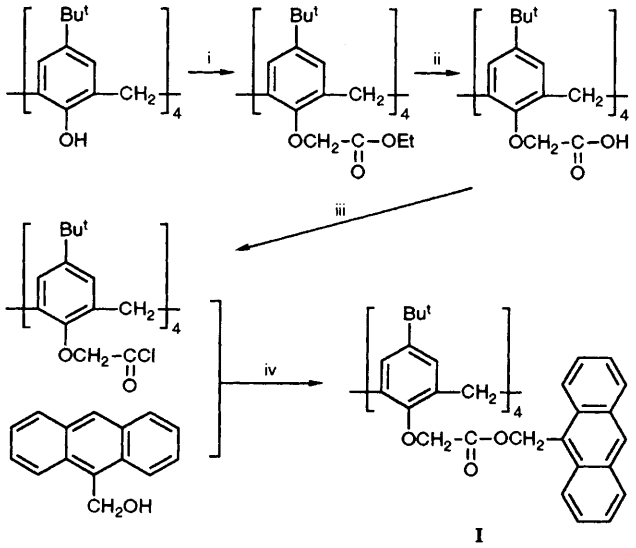
Herein, we report the synthesis and spectroscopic study of a new calix[4]arene designed to combine the specific complexing ability of calix[4]arenes for alkali metal ions with the photophysical behaviour of the anthracene moiety. We have chosen anthracene because it is an efficient fluorophore,[7] particularly suited to reflect intramolecular interactions which

should occur with our systems on complexation with metal ions. With these objectives in mind, we have synthesized compound **I**, a calix[4]arene tetraester in which four anthracene units are introduced at the lower rim. During the course of our work, Jin *et al.* have published work on a calix[4]arene sodium sensor containing two pyrene moieties on the lower rim.[8]

The fluorescent calix[4]arene **I** (m.p. 105.5–109.0 °C) was synthesized by the method shown in Scheme 1. The structure and purity of **I** were confirmed by IR and ^{1}H NMR spectroscopy and elemental analysis.†

Previous to the spectroscopy study, ^{1}H NMR titration experiments, were carried out in order to examine the complexing ability of **I**. The ^{1}H NMR spectra were recorded in both the absence and presence of Na^+ since it has been shown that the tetramethyl *p-tert*-butylcalix[4]arene tetraacetate exhibits a high selectivity and complexing ability towards Na^+.[8–11] ^{1}H NMR spectra were obtained from 5.1 mmol dm^{-3} solutions of **I** in $CDCl_3$; ^{1}H NMR titrations were performed by adding incremental amounts of MSCN in CD_3OD (M = Na^+, K^+) at 25 °C.

In the absence of NaSCN, compound **I** possesses the cone conformation as evidenced by the splitting pattern of the $ArCH_2Ar$ methylene protons [Fig. 1(*a*)]. When NaSCN is added directly to the $CDCl_3$ solutions of **I**, the signals in the ^{1}H NMR spectrum change greatly. With a salt/**I** ratio of less than 1 [Fig. 1(*b*)], signals for both complexed and uncomplexed ligand were present in the spectrum, indicating that on the NMR timescale the exchange rate between the two species was slower at room temperature. Upon reaching a 1:1 stoichiometry [Fig. 1(*c*)] all the signals for the free ligand disappeared and an increase in the salt/**I** ratio beyond unity produced no further spectral shifts. Complexation affects the proton chemical shifts in the ligand, the largest change being experienced by the aromatic protons (0.47 ppm downfield). This downfield shift of the aromatic protons suggests that the phenoxy oxygen atoms are involved in complexation. This finding indicates a 1:1 stoichiometry for the NaSCN complex with **I**, and shows that the incorporation of four anthracene molecules does not hamper the calixarene's Na^+ binding ability.



I

Scheme 1 *Reagents*: i, $BrCH_2CO_2Et$, K_2CO_3 in acetone; ii, KOH, H_2O, EtOH, HCl; iii, $SOCl_2$; iv, pyridine, tetrahydrofuran

† *^{1}H NMR data* for **I** ($CDCl_3$, 25 °C): δ 1.05 (s, 36H, CMe_3), 2.85 (d, 4H H_B, $ArCH_2Ar$), 4.65 (d, 4H H_A, $ArCH_2Ar$), 4.70 (s, 8H, OCH_2CO_2), 6.10 (s, 8H, anthr-CH_2), 6.60 (s, 8H, ArH), 7.31–8.30 (m, 36H, anthracene).

The fluorescence emission spectra of **I** (5×10^{-6} mol dm^{-3} in $CHCl_3$) exhibits a monomer emission characterised by a fluorescence maximum at 418 nm (excitation 388 nm) and two bands at 391 and 443 nm (Fig. 2). Two contrasting situations emerged when we examined the effect of adding incremental amounts of lithium, sodium or potassium thiocyanate (in MeOH) to **I** in $CHCl_3$. When Li^+ or Na^+ is added, the fluorescence intensity of the entire spectrum decreases markedly with increasing salt concentration [Fig. 2(*A*)]. In contrast, we have found that the addition of KSCN has a different effect. As shown in Fig. 2(*B*), the maximum emission (*ca.* 418 nm) decreases with increasing KSCN concentration whereas the emission at 443 nm increases, with an isoemissive point at λ 432 nm. This particular effect caused by changing the K^+ concentration could be used advantageously for quantimetric determination of this ion in nonaqueous solution. Furthermore, the fact that the intensity remains constant when varying the concentration of K^+ at λ 432 nm (isoemissive point) can be used to calculate the concentration of Li^+ or Na^+ at different background K^+ concentrations in which a proportional decrease of the emission intensity is observed as the concentration of either of these ions is increased.

The difference in behaviour obtained with K^+ relative to that observed with Li^+ and Na^+ is not easy to interpret. The ^{1}H NMR of **I** in the presence of KSCN (Fig. 3) indicates that **I** forms a complex with K^+ with retention of cone conformation

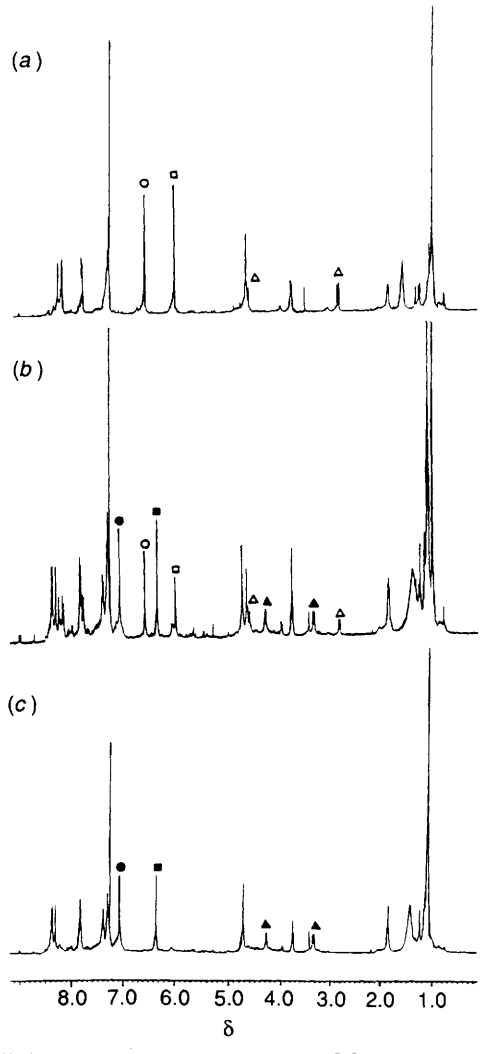


Fig. 1 ^{1}H NMR spectra of the fluorescent calix[4]arene **I** in $CDCl_3$ at 25 °C. (*a*) *R* = [NaSCN]/[**I**] = 0, (*b*) *R* = 0.5, (*c*) *R* = 1, where [**I**] = 5.1 mmol dm^{-3}. Aliquots from CD_3OD solution of 1 mol dm^{-3} NaSCN were added directly to a $CDCl_3$ solution of **I** in an NMR tube; (○, ● = ArH; △, ▲ = $ArCH_2Ar$; □, ■ = anthracene-CH_2).

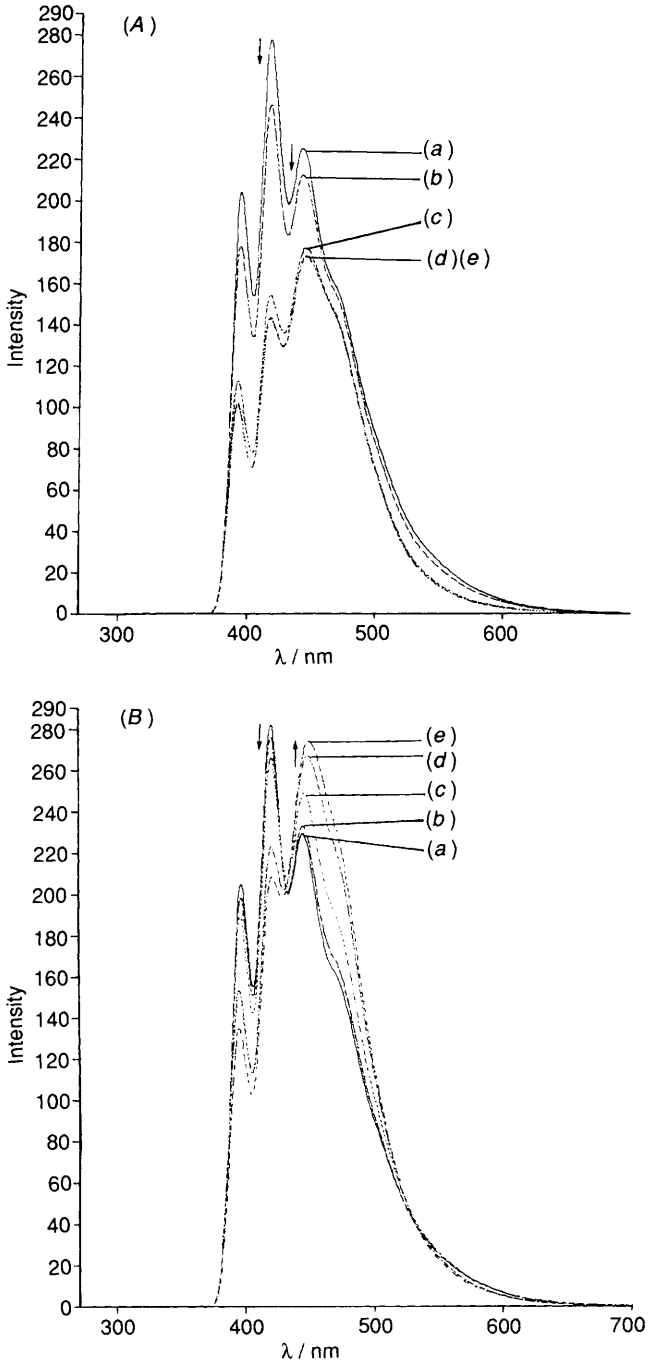


Fig. 2 Fluorescence spectra of **I** (5.00×10^{-6} mol dm^{-3}) in chloroform at different concentrations of NaSCN (*A*) and KSCN (*B*). [MeSCN] = (*a*) 0, (*b*) 1.0×10^{-6}, (*c*) 4.0×10^{-6}, (*d*) 6.0×10^{-6}, (*e*) 8.0×10^{-6} mol dm^{-3}. The spectra were measured with excitation at 388 nm.

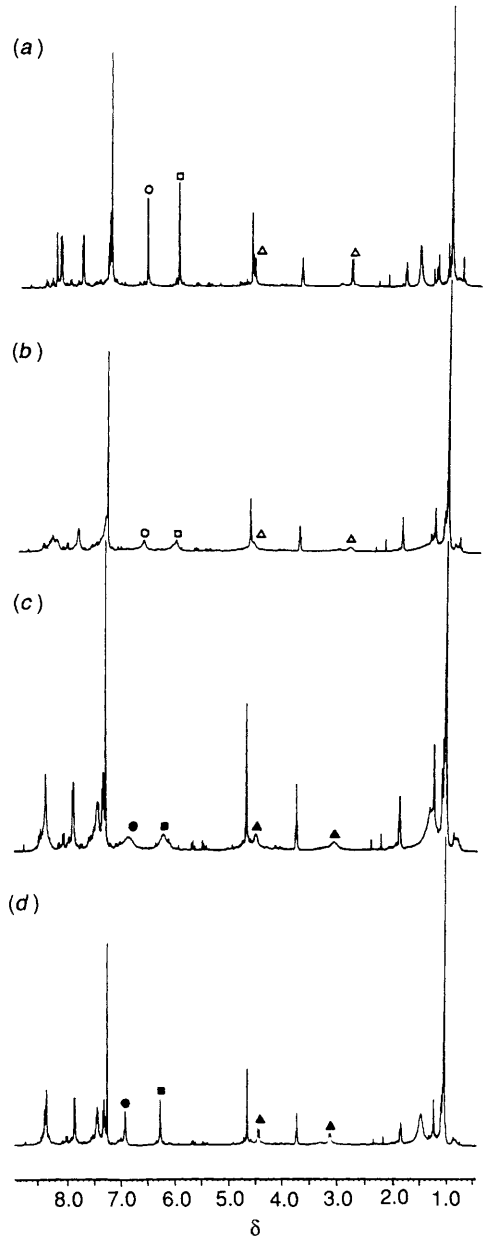


Fig. 3 ^{1}H NMR spectra of the fluorescent calix[4]arene **I** in $CDCl_3$ at 25 °C. (*a*) R = [KSCN]/[**I**] = 0, (*b*) $R = 0.5$, (*c*) $R = 1$, (*d*) $R = 2$, where [**I**] = 5.1 mmol dm^{-3} (○, ● = ArH; △, ▲ = $ArCH_2Ar$; □, ■ = anthracene-CH_2).

(as with Na^+); but some differences were apparent between K^+ and Na^+ complexation by a closer examination of the ^{1}H NMR spectra by titration with respective thiocyanate salts. Thus, for K^+/**I** molar ratio of 0.5 a decrease in the signals corresponding to the free ligand is produced, with no new signals for the complexed species [Fig. 3(*b*)] whereas signals for both complexed and uncomplexed were present for the same relative quantity of Na^+ [Fig. 1(*b*)]. Upon reaching K^+/**I** molar ratio of 1 [Fig. 3(*c*)], the signals of the free ligand disappear and those corresponding to the K^+ complex start to appear and continue to increase in intensity until K^+/**I** molar ratio of 2 [Fig. 3(*d*)]. Additionally, a comparison between both NMR spectra of **I**–metal salt reveals that the proton chemical shifts relative to the free ligand are much larger in the Na^+ complexation compared with potassium (downfield shift aromatic proton: 0.47 ppm with Na^+, 0.34 ppm with K^+; H_B of AB methylene $ArCH_2Ar$ quartet: 0.47 ppm with Na^+, 0.28 ppm with K^+ and upfield shift H_A of AB methylene $ArCH_2Ar$ quartet: 0.39 ppm with Na^+ and 0.25 ppm with K^+).

The NMR data alone may suggest formation of a 1:2 ligand–ion complex in the case of potassium. Quenching of fluorescence arising from complexation of ligand with Na^+ may arise from interaction of four anthracene moieties brought in closer proximity to one another.

Enhancement of the longer wavelength emission spectrum of ligand complexed with K^+ is more difficult to explain. Similar perturbation differences on fluorescence have been noted by K^+ complexation of 2,3-naphtho-20-crown-6 (quenching) and its closely related 1,8-naphtho-21-crown-6 (enhancement).[12]

We propose to examine similarly derivatised dioxacalixarene[13] or calix[5]arenes[14] with larger polar cavities more suited to K^+. Additionally, we hope to examine the modifica-

tion of fluorescence of substituted anthracene calixarene ester derivatives[15] by complexation with alkali metal ions.

In conclusion, compound **I** designed using the calix[4]arene skeleton shows interesting optical responses to K^+, Li^+ and Na^+, which could form the basis of an optical sensor for the determination of these ions.

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