Novel Chromogenic Ligands for Lithium and Sodium based on Calix[4]arene Tetraesters

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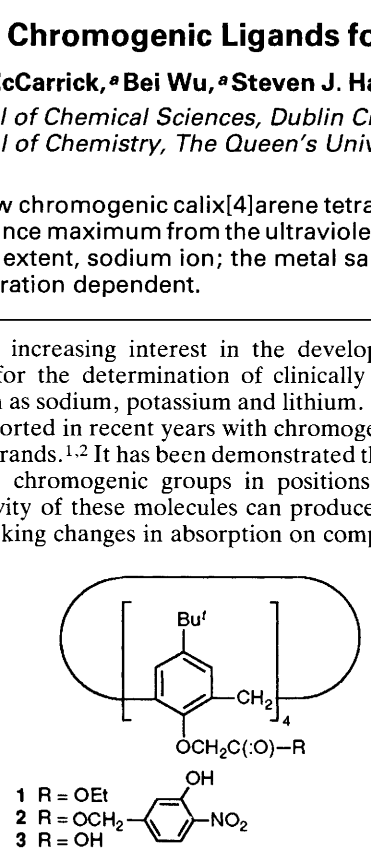
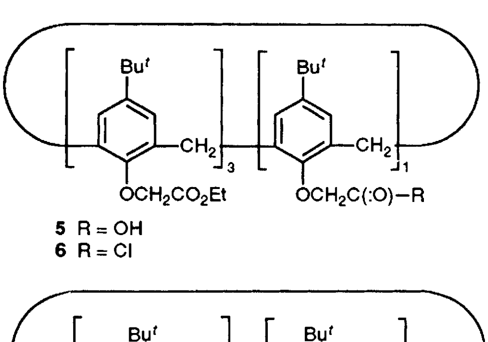
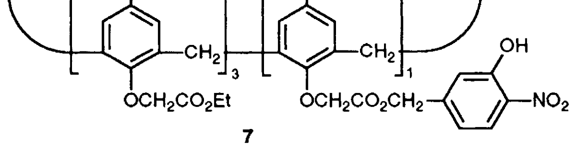
Two new chromogenic calix[4]arene tetraesters bearing nitrophenol residues display a striking cation-selective shift in absorbance maximum from the ultraviolet to the visible region in the presence of base upon addition of lithium ion or, to a lesser extent, sodium ion; the metal salt causes a change from colourless to yellow, the colour density being concentration dependent.

There is increasing interest in the development of optical sensors for the determination of clinically important metal ions such as sodium, potassium and lithium. Some success has been reported in recent years with chromogenic crown ethers and spherands.[1,2] It has been demonstrated that attachment of ionisable chromogenic groups in positions adjacent to the polar cavity of these molecules can produce materials which show striking changes in absorption on complexation.







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Incorporation of a metal cation into the cavity is accompanied by deprotonation and it is the latter process that produces the optical response. The same principle of deprotonation has been applied in recent attempts to design a chromogenic

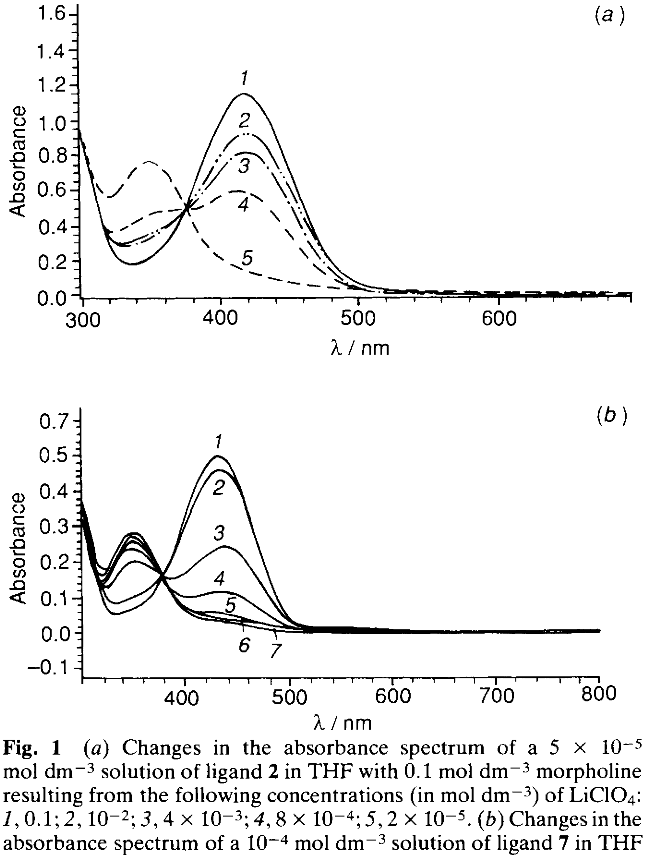

Fig. 1 (*a*) Changes in the absorbance spectrum of a 5×10^{-5} mol dm^{-3} solution of ligand **2** in THF with 0.1 mol dm^{-3} morpholine resulting from the following concentrations (in mol dm^{-3}) of LiClO$_4$: *1*, 0.1; *2*, 10^{-2}; *3*, 4×10^{-3}; *4*, 8×10^{-4}; *5*, 2×10^{-5}. (*b*) Changes in the absorbance spectrum of a 10^{-4} mol dm^{-3} solution of ligand **7** in THF with 0.2 mol dm^{-3} morpholine resulting from the following concentrations (in mol dm^{-3}) of LiClO$_4$; *1*, 0.1; *2*, 10^{-2}; *3*, 10^{-3}; *4*, 10^{-4}; *5*, 10^{-5}; *6*, 10^{-6}. Trace *7* is the spectrum of the ligand without LiClO$_4$.

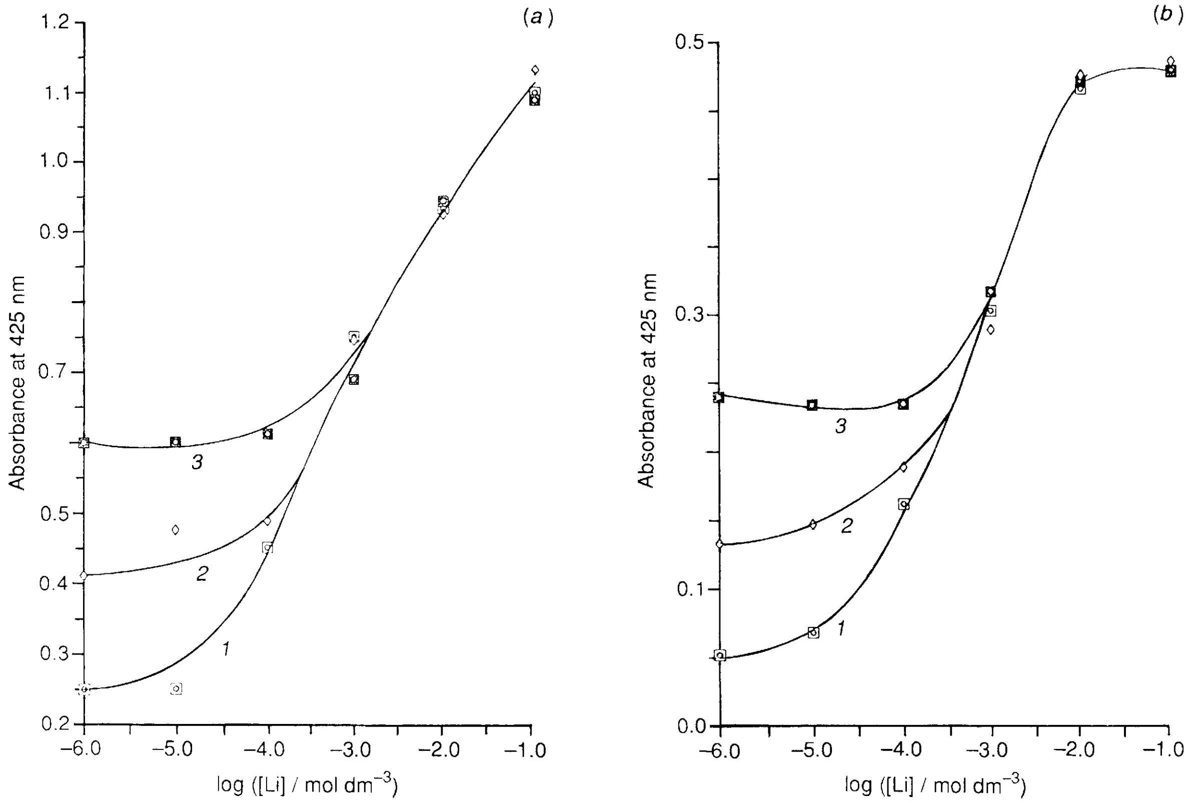

Fig. 2 Optical response of (*a*) 5×10^{-5} mol dm^{-3} ligand **2**, 0.1 mol dm^{-3} morpholine in THF; (*b*) 10^{-4} mol dm^{-3} ligand **7**, 0.2 mol dm^{-3} morpholine in THF, to lithium in the presence of fixed levels of sodium. [Na]/mol dm^{-3}: curve *1*, 0; **2**, 0.001; *3*, 0.01. From these data, an approximate selectivity coefficient ($K_{\mathrm{Li,Na}}$) can be calculated from the concentrations of the ions at the intercepts *via* the expression $K_{\mathrm{Li,Na}} = C_{\mathrm{Na}}/C_{\mathrm{Li}}$:

Ligand	2	2	7	7
[Na$^+$]/mol dm^{-3}	10^{-2}	10^{-3}	10^{-2}	10^{-3}
$K_{\mathrm{Li,Na}}$	25.1	11.2	34.7	14.7

calix[4]arene which is specific for lithium.[3] This report by Shinkai and coworkers on the design of an ion-selective chromogenic calixarene which is based on the azo chromophore prompts us to describe a new chromogenic calix[4]arene in which a nitrophenol is used as the chromogenic group in the assembly.

Fluorescence spectrophotometric determination has also been investigated for metal ion analysis. Fluorescent ionophores of cyclic and non-cyclic polyethers,[4,5] and, more recently, of a calix[4]arene,[6] have been synthesized and reported to produce a marked increase in fluorescence in the presence of lithium ions in the case of the former, and sodium ions in the latter.

We now present results obtained with two new chromogenic ligands based on calix[4]arenes which could form the basis of an optical sensor for lithium. Calix[4]arene esters of type **1** are efficient ionophores for alkali cations and have been incorporated into ion-selective electrodes for sodium, potassium and caesium.[7,8] In the tetramer ester series, stability constant measurements show that the selectivity of complexation favours sodium in methanol whereas lithium is favoured in acetonitrile. Our objective was to place an ionisable chromophoric group in the neighbourhood of the ester podands of a calix[4]arene tetraacetate, so as to produce a significant change in absorbance on metal complexation. Given the known potentiometric selectivity of the calixarene tetramers, it was anticipated that this would lead to a corresponding optical selectivity for these ions.

Ligand **2** was prepard from the known *p-tert*-butylcalix[4]arenetetraacetic acid **3**.[9] Treatment with thionyl chloride furnished the tetraacid chloride **4** which on exposure to 3-hydroxyl-4-nitrobenzyl alcohol in tetrahydrofuran containing triethylamine furnished **2** in 76% yield (m.p. 76–78 °C). In a similar fashion, triester monoacid **5**[10] was transformed, *via* acid chloride **6**, into ligand **7**, m.p. 117–119 °C in 60% yield.

For investigation of the effect of the optical response of the ligands to addition of alkali metal ions, each was dissolved in tetrahydrofuran (THF: 5×10^{-5} mol dm^{-3} for **2** and 10^{-4} mol dm^{-3} for **7**) and morpholine added (40 mm^3 for **2** and 90 mm^3 for **7**) to 5 cm^3 aliquots of these solutions. Incremental amounts of lithium perchlorate were then added to each solution, producing the UV–VIS spectral changes recorded in Fig. 1(*a*) and (*b*). It is clear that addition of lithium perchlorate causes a large change in the absorbance spectrum of both ligands, with maximum absorbance around 420 nm and an isosbestic point at 370 nm in the case of ligand **2**, and maximum absorbance at around 430 nm and an isosbestic point at 375 nm in the case of ligand **7**. Similar experiments with lithium chloride produced the same spectral response. A significantly lower response was observed on addition of potassium ion. The crucial role played by the base in generating the optical response was confirmed by the total lack of spectral changes on addition of metal salts in the absence of morpholine. Deprotonation of the phenol is therefore an integral part of the process and the fact that an optical response is also found with the monophenol ligand **7** indicates that one deprotonation is sufficient for the effect to be observed.

The optical response of the two ligands for lithium in the presence of fixed background concentrations of sodium is illustrated in Fig. 2(*a*) (ligand **2**) and Fig. 2(*b*) (ligand **7**). These results suggest that ligand **7** is more selective for lithium than **2** under the conditions employed, though these have yet to be optimised. From similar experiments, potassium ions have been found to have no significant effect unless present at concentrations above 10^{-2} mol dm^{-3}.

Chromoionophores such as these will have important applications in the future in the development of optical sensors and colorimetric reagents for the determination of these ions, particularly in body fluids. While the selectivity demonstrated for lithium against sodium is somewhat lower than desirable for lithium determinations in blood (*ca.* 150), the lack of response to potassium ions suggests that ligand **7** in particular may be useful for sodium determinations in the absence of lithium.

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