## Selective Chromogenic Reagents based upon Phenolic Cryptands

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Chloroform solutions of the chromoionophore **4c**, which has been synthesised by a simple procedure from diaza-15-crown-5 **2a**, extract lithium cations from aqueous solutions in the pH range 7–8 with very high selectivity as compared with the extraction of sodium, potassium, magnesium and calcium; the related reagent **5** shows moderate selectivity for sodium.

A number of highly selective ionophores for lithium have been reported, which have, for the most part, been based upon 14-crown-4 derivatives and some of which have provided the basis for lithium selective electrodes<sup>1</sup> with Li<sup>+</sup>: Na<sup>+</sup> selectivity ratios of up to 1500:1. Selective chromogenic reagents for lithium have been rather less successful although a number of examples have been reported<sup>2</sup> and in one case<sup>3</sup> a high Li<sup>+</sup>: Na<sup>+</sup> selectivity ratio has been reported for complexation in methanol. Ion selective electrodes for sodium are well established, a number of chromogenic agents have been described and high Na+: K+ selectivity4,5 has been reported for reagents based upon a spherand and a cryptahemispherand. In this communication we report a new chromogenic reagent that shows very high selectivity for lithium and a related reagent that shows moderate selectivity for sodium. Both compounds can be obtained by very simple procedures from commercially available diaza-crown ethers.

The ready availability<sup>6</sup> of the phenolic cryptands 1 by the reaction of diaza-crown ethers 2 with the dihalide 3 suggested that chromogenic reagents based upon these cryptand structures should be investigated. Reaction of the phenols 1 with

aryldiazonium salts gave the azophenolic cryptands 4a-c and 5 as outlined in Scheme 1. The products 4a-c and 5 had spectroscopic properties (NMR, mass and absorption spectra) in accord with the assigned structures, although in aqueous solution there may be a proportion of the phenylhydrazone tautomer (*cf.* ref. 7).

Chloroform solutions of compounds **4a** and **4b** extract lithium from an aqueous solution of lithium chloride at pH 9





Scheme 1 Synthesis of azophenolic cryptands 4 and 5. Reagents and conditions (yields): i, reflux in MeCN ca. 24 h (1a 86%, 1b 82%); ii,  $ArN_2^+$  Cl<sup>-</sup>, 0 °C (4a 50%, 4b 83%, 4c 85%, 5 80%)



**Fig. 1** Absorption spectrum (300–700 nm) of cryptand 4c in CHCl<sub>3</sub> (8.14  $\times$  10<sup>-5</sup> mol dm<sup>-3</sup>) after equilibration with an equal volume of aqueous LiCl at pH 7.0 [tris(hydroxymethyl)methylamine–HCl buffer] at concentrations of 0.01, 0.025, 0.05, 0.075, 0.1, 0.25, 0.50 and 1.0 mol dm<sup>-3</sup>. The absorbance at 406 nm corresponds to the free cryptand and at 534 nm to the lithium complex.



**Fig. 2** Absorption spectrum (300–800 nm) of cryptand **4c** in CHCl<sub>3</sub> (5.15  $\times$  10<sup>-5</sup> mol dm<sup>-3</sup>) after equilibration with equal volumes of aqueous (*a*) LiCl (1.0 mol dm<sup>-3</sup>), (*b*) NaCl (1.0 mol dm<sup>-3</sup>) and (*c*) KCl (1.0 mol dm<sup>-3</sup>) at pH 9.0 [tris(hydroxymethyl)methylamine–HCl buffer]. Under these conditions there is no detectable response to either Na<sup>+</sup> or K<sup>+</sup> as indicated by (*d*) the absorbance of the free cryptand.

but they are not sufficiently acidic to function as useful chromogenic reagents in the pH range 7–8. The more acidic *p*-nitrophenylazophenol **4c** extracts lithium from aqueous solution in the pH range 7–9 with a considerable change in its absorption spectrum as shown in Fig. 1. It also shows very high selectivity for lithium as compared with sodium and potassium, neither of which gives a measurable response in this pH range even at concentrations as high as 1 mol dm<sup>-3</sup> (see Fig. 2). Details of extraction coefficients are given in Table 1, the

Table 1 Extraction coefficients<sup>a</sup> for chromoionophores 4c and 5

Compound	pH/±0.1	Cation	$\log_{10}K_{\rm e}/\pm0.2^d$
<b>4c</b> <sup>b</sup>	7.7	Li+	-6.9
	8.2	Li+	-7.0
	9.3	Li+	-7.2
5 <sup>c</sup>	6.9	Na+	-6.5
	8.1	Na+	-6.6
	9.3	Na+	-6.7
	9.4	K+	-9.3
	9.2	Li+	-9.6
	9.1	Ca <sup>2+</sup>	-7.9

<sup>*a*</sup> For a solution of **4c** or **5** at *ca*.  $10^{-5}$  to  $10^{-4}$  mol dm<sup>-3</sup> in CHCl<sub>3</sub> and solutions of M<sup>+</sup> at  $10^{-4}$  to 1 mol dm<sup>-3</sup> in water using a tris(hydroxy-methyl)methylamine–HCl buffer.  $K_e$  is based upon changes in absorption at 406 and 534 nm for **4c** and Li<sup>+</sup>, 402 and 554 nm for **5** and Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup>, and 402 and 500 nm for **5** and Ca<sup>2+</sup>. <sup>*b*</sup> No measurable response for Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup> and Ca<sup>2+</sup> in the pH range 7–9 up to 1 mol dm<sup>-3</sup> concentration of the metal salts. <sup>*c*</sup> No measurable response for Mg<sup>2+</sup> in the pH range 7–9 up to 1 mol dm<sup>-3</sup> concentration of the metal salts. <sup>*c*</sup> No measurable response for Mg<sup>2+</sup> in the pH range 7–9 up to 1 mol dm<sup>-3</sup> concentration of the metal salts. <sup>*c*</sup> No measurable response for Mg<sup>2+</sup> in the pH range 7–9 up to 1 mol dm<sup>-3</sup> concentration of the metal salts. <sup>*c*</sup> Me = [H<sup>+</sup>]<sub>aq</sub>[M<sup>+</sup>Cl<sup>-</sup>]<sub>org</sub>/[M<sup>+</sup>]<sub>aq</sub><sup>-</sup>[ClH]<sub>org</sub> (where the subscripts aq and org refer to the aqueous and organic phases, respectively and ClH refers to the ionisable chromo-ionophore).



Fig. 3 Absorption spectrum (300–800 nm) of cryptand 5 in CHCl<sub>3</sub> (2.79  $\times$  10<sup>-5</sup> mol dm<sup>-3</sup>) after equilibration with equal volumes of aqueous (a) NaCl (0.005 mol dm<sup>-3</sup>), (b) KCl (1.0 mol dm<sup>-3</sup>) and (c) LiCl (1.0 mol dm<sup>-3</sup>) at pH 9.0 [tris(hydroxymethyl)methylamine–HCl buffer]

Li<sup>+</sup>:Na<sup>+</sup> selectivity ratio is *ca*. 10<sup>4</sup> or greater on the basis of the spectroscopic response at pH 9 (response to  $10^{-4}$  mol dm<sup>-3</sup> Li<sup>+</sup> greater than response to 1 mol dm<sup>-3</sup> Na<sup>+</sup>).

The larger cavity of the *p*-nitrophenylazophenol 5 is more appropriate for sodium complexation and within the pH range 7-8 this compound shows moderately high selectivity for sodium extraction as compared with lithium (ratio of  $K_{es}$  for Na<sup>+</sup>: Li<sup>+</sup> ca. 800) and for sodium as compared with potassium (ratio of  $K_{es}$  for Na<sup>+</sup>: K<sup>+</sup> ca. 400), the selectivity at pH 9 is illustrated in Fig. 3. The response of chromoionophore 5 to calcium is more significant (ratio of  $K_{es}$  for Na<sup>+</sup> : Ca<sup>2+</sup> ca. 16), although in this case the absorption maximum of the Ca<sup>2+</sup> complex is at a rather shorter wavelength (see data in Table 1). Although relatively modest, this selectivity compares well with that shown by chromogenic reagents based upon spherand systems.<sup>4,8</sup> The lithium salt 6b and the sodium salt 6c/7c had spectroscopic properties (1H and 13C NMR) in accord with the proposed structures, in particular the <sup>1</sup>H spectra (400 MHz) are in accord with the conformations shown diagramatically in 6 and 7 in which the NCH<sub>2</sub>CH<sub>2</sub>O and OCH<sub>2</sub>CH<sub>2</sub>O units have a gauche relationship between the heteroatoms and the aromatic ring lies parallel to the macrocycle. Although the process  $6a \rightleftharpoons 7a$  is fast on the NMR time scale for the free chromoionophore 5 this process is slow on the NMR time scale for the sodium salt 6c/7c. On the other hand the chromoionophore 4c appears to adopt only the conformation 6 for both the free chromoionophore 6a and the lithium salt 6b.

The chromoionophores 4c and 5 are promising compounds for use in optical fibre sensors for Li<sup>+</sup> and Na<sup>+</sup> and structural modification to enhance lipophilicity and sensitivity should



**b**; X = O<sup>-</sup>Li<sup>+</sup>, n = 1 **c**; X = O<sup>-</sup>Na<sup>+</sup>, n = 2

improve their performance. They also show an interesting relationship to chromogenic cryptahemispherands<sup>5</sup> and cryptands<sup>7,9</sup> which, although highly selective for Na<sup>+</sup> and K<sup>+</sup>, require more elaborate synthetic procedures. The advantage of using cryptand structures<sup>10</sup> for cation recognition by chromoionophores is exemplified by these compounds and also by a bridged calixarene derivative which shows<sup>11</sup> very high selectivity for K<sup>+</sup> (ratio of  $K_e$ s for K<sup>+</sup> : Na<sup>+</sup> ca. 1200).

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