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Chromoionophores with High Lithium and Sodium Selectivity

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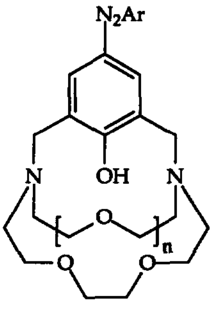
Abstract The new phenolic cryptand reagents **2a** and **2b** are readily prepared and have very high selectivity for Li^+ and Na^+ respectively.

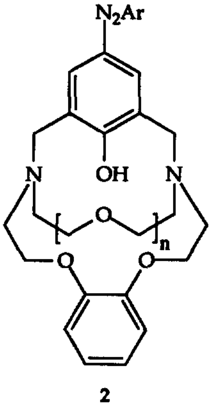
The development of a simple route to phenolic cryptands[1] led to the synthesis of two new chromoionophores **1a** and **1b** which showed[2] very promising properties for use in optical fibre sensors of a type that has been described.[3#] The requirements for the sensing chromogenic reagent include (i) low water solubility to avoid loss of reagent from the fibre tip, (ii) adequate sensitivity to respond to the sensed cation at mM concentrations, and (iii) high selectivity for the sensed cation as compared with other cations likely to be present in the sample. Thus for sensing Li^+ or Na^+ in samples of biological origin the reagent should not respond to other alkali metal cations or to Ca^{2+} and Mg^{2+}.



1

a, n = 1

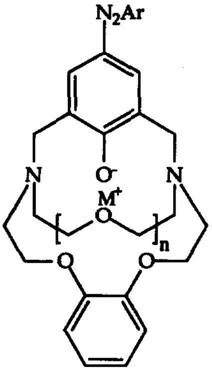
b, n = 2



2

a, n = 1

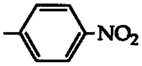
b, n = 2



3

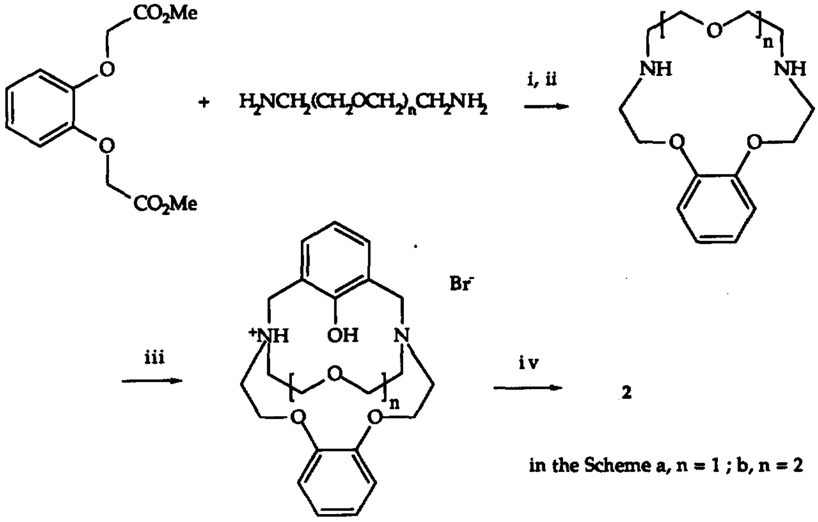
a, n = 1, M = Li

b, n = 2, M = Na

in 1 - 3 Ar = 

[#] The chromogenic reagent is absorbed onto 200 mesh XAD2 polystyrene resin from a solution in an organic solvent such as chloroform or methanol. The coated polystyrene is then held in place at the tip of an optical fibre by a porous membrane.

The chromoionophore **1a**, which responds virtually exclusively to Li^+, is partly extracted into aqueous solutions at pH 7 and the chromoionophore **1b**, which responds to Na^+, has less than optimum selectivity[2] in the presence of Ca^{2+}. Search[§] through the available conformations of **1b** and its Na^+ complex reveals that the macrocycle of the free phenol has a lower steric energy when one of the C-C bonds adopts an anti-conformation rather than the gauche-conformation required for the formation of the complex. This situation is commonly encountered in crown ether and cryptand chemistry and may be rectified[4] by replacing one or more of the $-OCH_2CH_2O-$ units of the macrocycle with a rigid catechol unit. This replacement, exemplified by the structures **2a** and **2b**, is also expected to enhance the lipophilicity of the chromogenic reagents in accord with the need for low water solubility.



in the Scheme a, n = 1 ; b, n = 2

Reagents (yields) :- i, MeOH, RT (a 53%, b 63%); ii, a $BH_3 . SMe_2$, THF, Δ (83%), b, $LiAlH_4$, THF, Δ (54%); iii, 2,6-bisbromomethylanisole, CH_3CN, Δ, 48 h (a 51%, b 70%); iv, p-nitrophenyldiazonium chloride, NaOH, H_2O, EtOH, -5°C then RT (a 56%, b 88%).

Scheme Synthesis of Chromoionophores **2a** and **2b**

This modification was readily achieved and compounds **2a** and **2b** were prepared by the route outlined in the Scheme (the yields that are given have not been optimised). The new chromoionophores were isolated as their lithium and sodium complexes **3a** and **3b** from which the parent phenol could be regenerated by repeatedly washing a solution in an organic solvent with water at pH 7. The chromogenic cryptands **2a** and **2b** were evaluated by examining the extraction of alkali metal cations from aqueous solution in the pH range

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[§] Using the molecular modelling programs QUANTA and CHARMm (Molecular Simulations Inc)

7-9, the results of this investigation are summarised in the Table which also gives the corresponding data for reagents **1**.

Table Extraction Coefficients[a,e] and Selectivities for Chromoionophores **1** and **2**

	$\log_{10}K_e$ (±0.2)[b]	
Host	Compound **1a**	Compound **2a**
Cation	Li^+	Li^+
pH 7	-6.9	-6.9
pH 8	-7.0	-7.3
pH 9	-7.2	-7.3
λ[c,d]	534	528

		$\log_{10}K_e$ (±0.2)[b]				$\log_{10}K_e$ (±0.2)[b]		
Host		Compound **1b**				Compound **2b**		
Cation	Li^+	Na^+	K^+	Ca^{2+}	Li^+	Na^+	K^+	Ca^{2+}
pH 7		-6.5				-5.8		
pH 8		-6.6				-5.8		
pH 9	-9.6	-6.7	-9.3	-7.9	-9.5	-5.8	-9.6	-9.4
λ[c,d]	554	554	554	500	528	546	560	500

[a] For a solution of the chromoionophore at ca 10^{-5} to 10^{-4} mol dm^{-3} in $CHCl_3$ and solutions of M^+ at 10^{-4} to 1 mol dm^{-3} in water using a tris(hydroxymethyl)methylamine-HCl buffer.

[b] $K_e = [H^+]_{aq}.[M^+Cl^-]_{org}/[M^+]_{aq}.[ClH]_{org}$ (where the subscripts aq and org refer to aqueous and organic phases respectively and ClH refers to the ionisable chromoionophore.

[c] λ (nm) used for calculating $[M^+Cl^-]_{org}$, in general M=Li gives λ_{max} ca 530 nm, M=Na gives λ_{max} ca 550 nm, M=K gives λ_{max} ca 560 nm, and M=Ca gives λ_{max} ca 500 nm.

[d] λ_{max} ca 400 nm used for calculating $[ClH]_{org}$.

[e] Compounds **1a** and **2a** give no measurable response to Na^+, K^+, Mg^{2+}, and Ca^{2+} in the pH range 7-9 up to 1 mol dm^{-3} concentrations of the metal salts. Compounds **1b** and **2b** give no measurable response to Mg^{2+} in the pH range 7-9 up to 1 mol dm^{-3} concentrations of the metal salts.

The bridged diaza-15-crown-5 **2a** shows the same very high selectivity for Li^+ that is shown by **1a** with very nearly the same value of K_e, however reagent **2a** is completely insoluble in the aqueous phase at pH 7. The bridged diaza-18-crown-6 **2b** shows significantly enhanced selectivity for Na^+ as compared with reagent **1b**, primarily as a result of selectively enhanced sensitivity for Na^+. This result is in accord with a search through a large number of conformations of the reagent **2b** and its Na^+ complex **3b** which shows that a unique low energy conformation of **2b** (with steric energy >2 kcal mol^{-1} lower than any other conformation) has all the C-C bonds of the macrocycle in a gauche conformation and corresponds to a conformation of the complex **3b** of low steric energy. Thus this increased selectivity of chromoionophore **2b** appears to be a consequence of increased preorganisation brought about by the fused aromatic ring.

The two new chromoionophores **2a** and **2b** have ideal properties for use in optical fibre sensors for Li^+ and Na^+ in the pH range 7-9 and compare very favourably, both in performance and ease of synthesis, with other chromoionophores that have been reported[5,6] to show selectivity for Li^+ and Na^+.

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