A Highly Selective Chromoionophore for Potassium Based upon a Bridged Calix[4]arene

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The chromoionophores **9** and **10** in chloroform extract potassium ions from aqueous solutions in the pH range 7–9 with high selectivity as compared with sodium (K_e^{K+}/K_e^{Na+} *ca.* 1000), magnesium and calcium (no detectable extraction) ions.

The use of optical fibre sensors to measure the concentration of cations in biological fluids,[1] particularly blood, requires measurement of K^+ concentrations (*ca.* 4 mmol dm^{-3}) in the presence of much higher concentrations of Na^+ (145 mmol dm^{-3}) and comparable concentrations of Mg^{2+} (1.5 mmol dm^{-3}) and Ca^{2+} (1.8 mmol dm^{-3}). The use of the ionisable chromoionophore **1**[2] in an optical fibre sensor was reported some time ago,[3] but this compound has inadequate K^+/Na^+ selectivity (*ca.* 6:1) and it also responds[4] to Ca^{2+}. The chromoionophore **2** shows much higher selectivity for K^+/Na^+ (*ca.* 120) and it does not respond to Ca^{2+} or Mg^{2+} but the synthetic route to **2** is inconveniently long.[5]

The bridged calixarenes **3** have been reported[6] to show exceptionally high K^+/Na^+ selectivity (up to $10^4:1$) and they have been examined as ion carriers for electrochemical K^+ sensors. The modification of structure **3** to give an ionisable chromoionophore appeared to be a promising approach to a selective optical fibre-based sensor for K^+ and the results of such a study are reported in this communication.

The target chromoionophore **9** was selected by analogy with compounds **1** and **2**; the synthesis of **9**, which exemplifies a general synthetic route to compounds of this type, is summarised in Scheme 1. The tribenzoate **4**[7] proved to be a good starting point for the synthesis of the allyl methyl ether **5**; the selective allylation reaction is based upon the known tendency for the development of this dialkylation pattern under the selected reaction conditions.[8] The bridging reaction **5** → **6** proceeded in good yield, and deprotection to give monomethyl ether **7**, followed by oxidation with thallium(III) nitrate,[9] gave quinone **8**, which was always accompanied by a low yield of the corresponding *p*-nitrophenol. Reaction of **8**

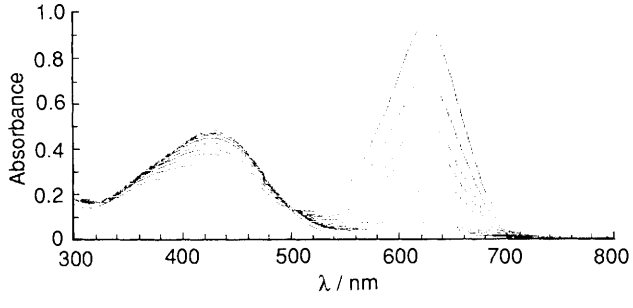


Fig. 1 Absorption spectra of calixarene derivative **9** (*ca.* 3×10^{-5} mol dm^{-3} in $CHCl_3$) showing the effect of K^+ extraction from aqueous solutions of KCl at pH 8. The spectra correspond to K^+ concentrations 0.0, 0.002, 0.005, 0.01, 0.024, 0.05, 0.1, 0.2, 0.4 and 1.0 mol dm^{-3}. The chromoionophore **9** shows absorbance centred at 437 nm and the K^+ salt **13**, M = K^+, shows absorbance centred at 628 nm.

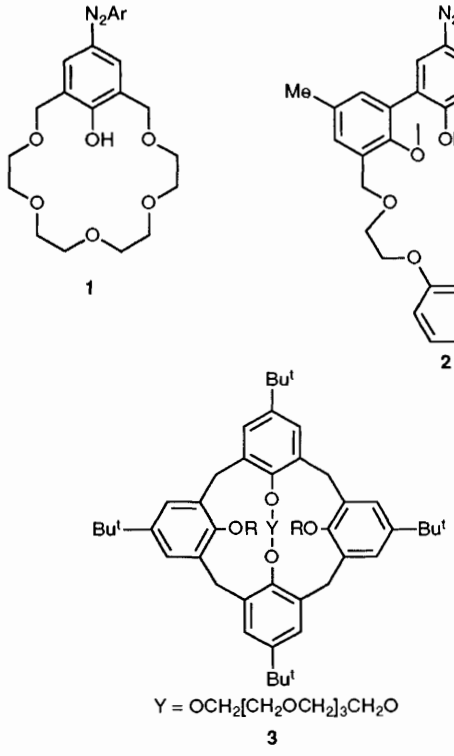
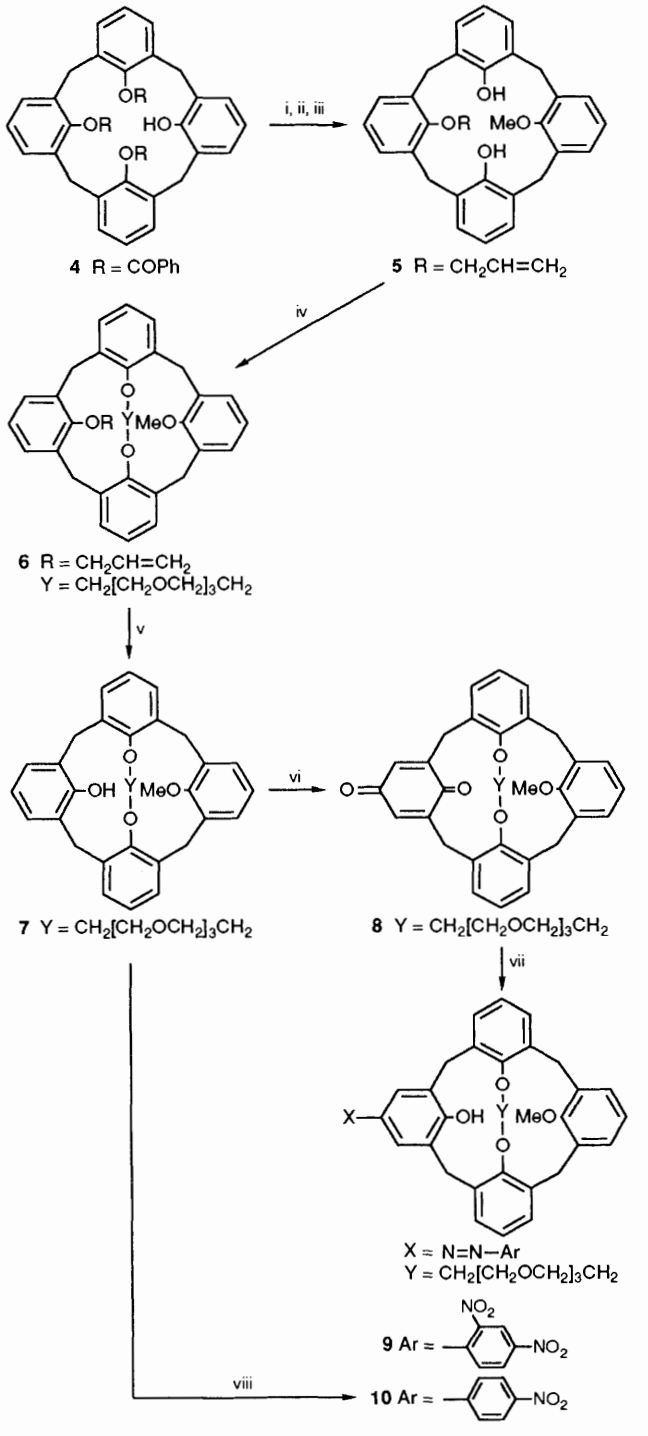


Table 1 Extraction coefficients[a] for chromoionophores **9** and **10**

pH	Cation[b]	K_e[c] for **9**[d]	K_e[c] for **10**[e]
7.0	K^+	2.9×10^{-7}	$<0.1 \times 10^{-7}$
	Rb^+	0.2×10^{-7}	
8.0	K^+	2.6×10^{-7}	0.5×10^{-8}
	Rb^+	1.6×10^{-8}	
9.0	Na^+	0.2×10^{-9}	
	K^+	2.3×10^{-7}	*ca.* 5×10^{-9}
	Rb^+	1.5×10^{-8}	

[a] For a solution of **9** or **10** at *ca.* 3×10^{-5} 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. K_e is based upon changes in absorbance at 436 and 628 nm for **9** and 408 and 590 nm for **10**. [b] No measurable results for Li^+, Cs^+, Mg^{2+} and Ca^{2+} in the pH range 7–9 up to 1 mol dm^{-3} concentration of the metal salts. [c] $K_e = [H^+]_{aq}.[K^+Cl^-]_{org}/[K^+]_{aq}.[ClH]_{org}$ (where the subscripts aq and org refer to the aqueous and organic phases respectively and ClH refers to the ionisable chromoionophore). [d] Compound **9** has λ_{max} 437 nm (ε_{max} 22×10^3) in $CHCl_3$. [e] Compound **10** has λ_{max} 408 nm (ε_{max} 26×10^3) in $CHCl_3$.

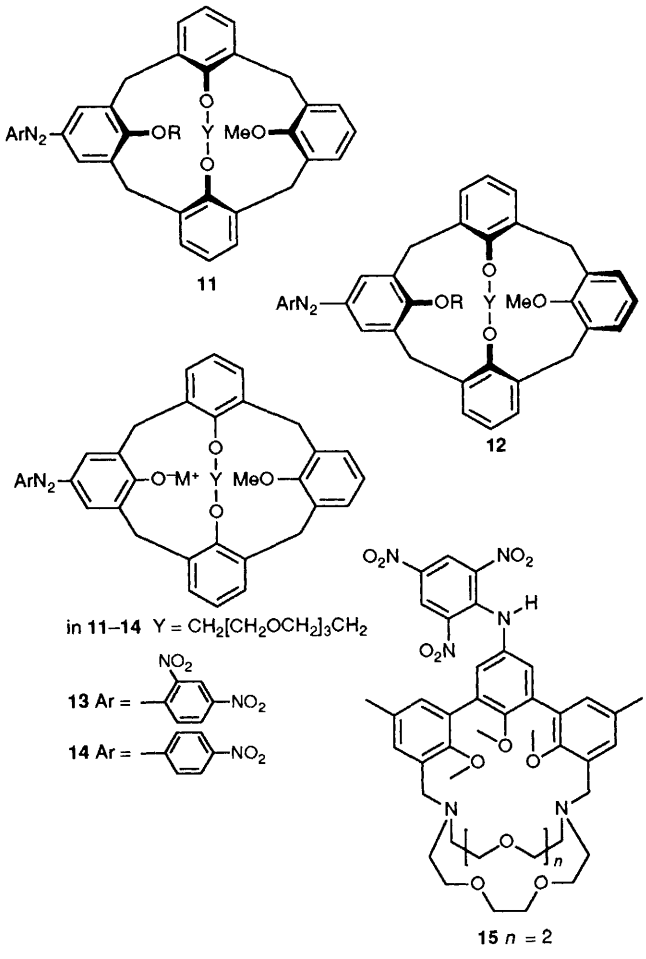


Scheme 1 Synthesis of chromoionophores **9** and **10**. *Reagents* (yields): i, MeI, NaH, tetrahydrofuran (THF) (75%); ii, NaOH, THF, EtOH, H_2O (86%); iii, CH_2=$CHCH_2Br$, K_2CO_3, Me_2CO (56%); iv, $TsOCH_2(CH_2OCH_2)_3CH_2OTs$, $KOBu^t$, toluene, reflux, 24 h (80%); v, TsOH, 10% Pd/C, EtOH, 5 days, room temp. (78%); vi, $Tl(NO_3)_3.3H_2O$, MeOH, EtOH, $CHCl_3$, 10 min, room temp. (58%); vii, 2,4-dinitro- or 4-nitro-phenylhydrazine, H_2SO_4, EtOH, $CHCl_3$, 2 h, room temp. (70 or 47%); viii, *p*-nitrophenyldiazonium chloride, aq. NaOH, 0 °C, 30 min (53%). Ts = *p*-$MeC_6H_4SO_2$.

with 2,4-dinitrophenylhydrazine gave azophenol **9**. Alternatively, the analogous 4′-nitroazophenol **10** could be obtained by reaction of quinone **8** with *p*-nitrophenylhydrazine or reaction of monomethyl ether **7** with *p*-nitrophenyldiazonium chloride.

The ^1H NMR spectra of the calixarene-based chromoionophores **9** and **10** showed signals which could be assigned to a major and a minor conformation. These are probably the cone **11** and partial cone **12** conformations which have been identified[10] for bridged calixarenes **3**, but the reduced symmetry of **9** and **10**, as compared with **3**, does not permit distinction between these two possibilities on the basis of the ^1H NMR data. Molecular mechanics calculations, using the programs QUANTA and CHARMm supplied by Polygen Corporation, support these conclusions and further suggest that the partial cone conformations are lower in steric energy than cone conformations in both the free and complexed state.

Both **9** and **10** extracted K^+ ions from aqueous solutions into chloroform with a colour change associated with the formation of the salts **13** and **14**; changes in the absorption spectrum of chromoionophore **9** are shown in Fig. 1. Data from these extraction experiments, summarised in Table 1 show that compounds **9** and **10** are both highly selective chromoionophores for K^+ in the presence of the other physiologically



important ions Na^+, Mg^{2+} and Ca^{2+}. The extraction shows the expected pH dependence since it involves extraction of a proton into the aqueous phase; it is therefore convenient to present results in terms of the extraction coefficient K_e (defined in footnote *c* to the Table) which is pH independent. Both chromoionophores **9** and **10** show adequate sensitivity for measuring K^+ at physiological concentrations and pH. We note that the pK_a of the azophenol chromophore can be adjusted over 2–3 orders of magnitude by changing the substitution pattern in the group Ar (see **9** and **10**) with a corresponding change in sensitivity to K^+ at a given pH.

The chromoionophores **9** and **10** are very promising compounds for use in optical fibre sensors for K^+ of the type that have been described in an earlier publication[3] and preliminary experiments[11] show that the high K^+/Na^+ selectivity is retained under these conditions. The ionisable chromoionophore **15**, based upon a cryptahemispherand, also shows[12] a very high selectivity for K^+ as compared with other physiologically important cations, but from its reported properties it appears to be less suitable for use in an optical fibre sensor than compounds **9** and **10**.

Received, 15th January 1992; Com. 2/00237J

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