A Chromogenic Crown Ether as a Sensing Molecule in Optical Sensors for the Detection of Hard Metal Ions

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A new chromogenic crown ether based on a merocyanine dye and a phenolic crown ether shows a striking selectivity for calcium or barium complexation and has a potential use in optical sensors.

In the last decade many chromogenic crown ethers have been synthesised.[1—3] Sutherland *et al.*[4] have reported the use of a chromoionophore in an optical sensor. Recently Cram *et al.* have reported an interesting new chromogenic spherand.[5] We are currently investigating the application of chromoionophores in optochemical sensors based on the surface plasmon phenomenon.[†] For this application prerequisites are a high extinction coefficient ($\varepsilon > 10^5$ l mol^{-1} cm^{-1}), absorption at a wavelength as high as possible, and a colour change of about half the bandwidth.[9] However, the extinction coefficients of the reported chromoionophores are too low ($\varepsilon < 5 \times 10^4$ l mol^{-1} cm^{-1}), as are their absorption wavelengths ($\lambda_{\text{max.}}$ <550 nm), or else they do not show colour change or selectivity. Chromophores that may meet all the requirements include cyanine dyes, merocyanines, and triphenylmethanes. The ionophore should be in conjugation with the chromophore in order for a large enough colour change to occur upon complexation.

The synthesis of a chromogenic crown ether (**4**) that meets all the criteria is shown in Scheme 1. 20-Bromo-17-(prop-2-enyloxy)-2,5,8,11,14-pentaoxa[15]metacyclophane (**1**) was synthesised as we have described previously for a series of similar crown ethers.[10] The 20-formyl analogue (**2**) was prepared from (**1**) by lithiation with n-butyl-lithium at −70 °C and subsequent reaction with dimethyl formamide at −70 °C followed by hydrolysis.[11] Compound (**2**) was deallylated with 5% palladium–carbon in methanol–water (80 : 20) to give the

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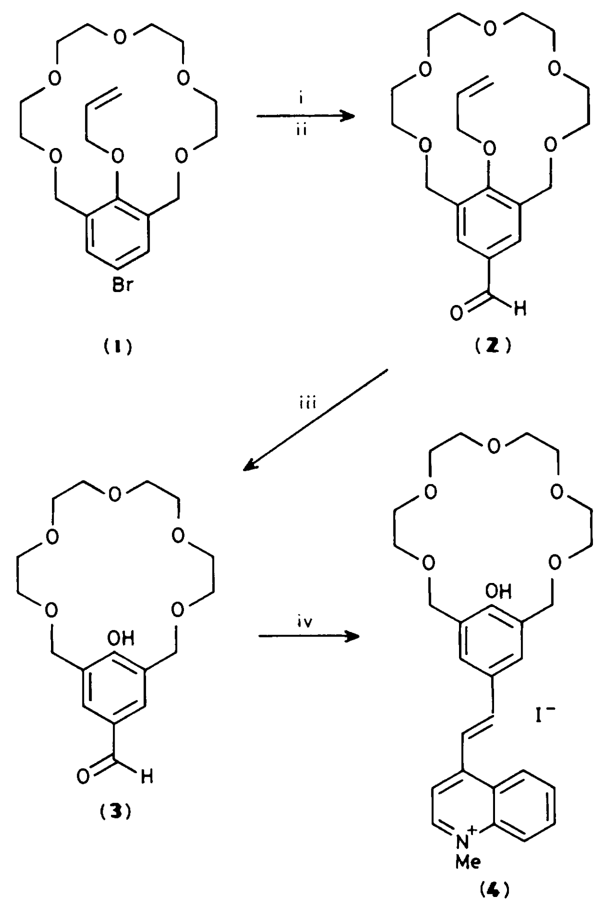
[†] A surface plasmon is an electromagnetic wave propagated at the interface between certain metals (usually silver or gold) and a dielectric material.[6] The propagation constant of this plasmon depends on the properties (refractive index, absorption, and thickness) of the dielectric material. This dependence has been applied in optical sensors by Liedberg *et al.*[7] and Kreuwel *et al.*[8] We prefer to use a dye because of its absorption band. As a consequence of this absorption band the refractive index can change markedly.



Scheme 1. *Reagents*: i, Bu^nLi; ii, DMF; iii, Pd–C, $MeOH–H_2O$, H^+; iv, EtOH, piperidine, 1,4-dimethylquinolinium iodide; yields: (**2**) 35%, (**3**) 80%, (**4**) 40%.

17-hydroxy compound (**3**). Compound (**3**) was coupled under basic conditions with 1,4-dimethylquinolinium iodide (from 4-methylquinoline and methyl iodide) to yield 4-[2-(17-hydroxy-2,5,8,11,14-pentaoxo[15]metacyclophan-20-yl)-ethenyl]-1-methylquinolinium iodide (**4**).‡

The absorption spectra of (**4**) ($\lambda_{max.}$ 430 nm) and its deprotonated form ($\lambda_{max.}$ 610 nm) differ greatly (Figure 1). The maximum of the calcium complex is intermediate between those of protonated and deprotonated forms (520 nm). This indicates that the Ca^{2+} ion is in close contact with the phenolate anion.

Table 1. Complexation constants K_a for 1:1 complexation of compound (**4**) and two simple crown ethers with some group 1 and 2 cations in neutral and in basic methanol.[a]

	$10^{-3} K_a$/l mol^{-1} (±10%)			
Salt	A	B	15-C-5[b]	18-C-6[b]
LiSCN	<1	<1	0.02	0
NaSCN	1.0	15	2.0	25
KSCN	3.2	155	2.5	1260
MgTf[c]	<1	<1		
$CaCl_2$	100	63	0.20	7.9
$Ba(ClO_4)_3$	100	32		11000

[a] Complexation is always 1:1 at low concentrations; at higher concentrations several complexes can exist; A, in methanol; B, in methanol with piperidine [piperidine: (**4**) 16000:1]. [b] 15-C-5 = 15-crown-5; 18-C-6 = 18-crown-6; K_a values from Izatt *et al.*[13] [c] MgTf = magnesium trifluoromethanesulphonate.

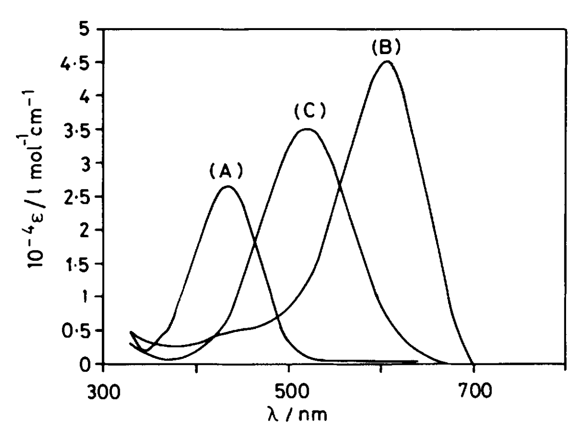


Figure 1. Absorption spectra of (A) compound (**4**), (B) the deprotonated form of (**4**), and (C) the calcium complex of (**4**) in methanol.

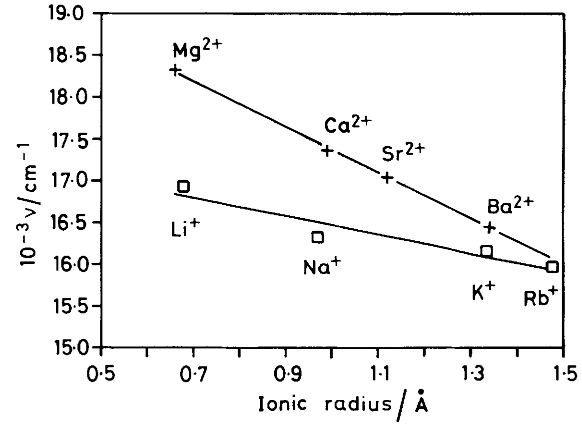


Figure 2. Absorption maximum as a function of the ionic radius of the complexed cation [solvent dichloromethane–methanol (96:4)].

The wavelength at which maximum absorption occurs and the extinction coefficient at this wavelength depend on the solvent. In methanol the extinction coefficient is relatively low ($\lambda_{max.}$ 435 nm; ε 2.7×10^4 l mol^{-1} cm^{-1}); however it is high in propan-2-ol ($\lambda_{max.}$ 610 nm; ε 1.26×10^5 l mol^{-1} cm^{-1}). This means that in propan-2-ol compound (**4**) meets all the requirements for our sensor application.

In complexation experiments we found a linear relationship between the frequency at which maximum absorption occurs and the ionic radius of the complexed cation (Figure 2). The

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‡ Spectroscopic analyses confirm the structures: (**1**) 80 MHz ^1H n.m.r. δ 3.5 (m, 16 H, OCH_2CH_2O), 4.15 and 4.85 (AB, 4 H, *J* 10.5 Hz, $ArCH_2O$), 4.5—6.5 (m, 5 H, allyl), and 7.3 (s, 2 H, ArH); (**2**) 200 MHz ^1H n.m.r. δ 3.3—3.8 (m, 16 H, OCH_2CH_2O), 4.36 and 4.96 (AB, 4 H, *J* 10.5 Hz, $ArCH_2O$), 4.9—6.4 (m, 5 H, allyl), 7.81 (s, 2 H, ArH), and 9.93 (s, 1 H, COH); i.r. $\nu_{max.}$ 1690 cm^{-1} (C=O); (**3**) 200 MHz ^1H n.m.r. δ 3.6—3.8 (m, 16 H, OCH_2CH_2O), 4.73 (s, 4 H, $ArCH_2O$), 7.67 (s, 2 H, ArH), and 9.82 (s, 1 H, -COH); i.r. $\nu_{max.}$ 1690 cm^{-1} (C=O); (**4**) m.p. 192—194 °C, satisfactory elemental analyses were obtained, ^1H n.m.r. δ 3.5—3.9 (m, 16 H, OCH_2CH_2O), 4.42 (s, 2 H, $ArCH_2O$), 4.64 (s, 2 H, $ArCH_2O$), 7.4—9.3 (several signals, 8 H, ArH), 7.62 (d, 1 H, *J* 15.8 Hz, CH=C*H*), 7.84 (d, 1 H, *J* 15.8 Hz, C*H*=CH), and 8.65 (s, 1 H, OH).

slope for monovalent cations is different from that for the bivalent species. Complexes with group 1 cations absorb light at high wavelengths (580—610 nm). The spectra of these complexes are almost the same as the spectrum of the deprotonated form of (**4**). Complexes with group 2 cations absorb light at lower wavelengths (520—580 nm). Thus bivalent cations cause a larger shift of absorption maximum than monovalent cations.

Complexation constants in methanol for 1 : 1 complexation of several cations with compound (**4**) have been determined spectrophotometrically (Table 1). The values were calculated by the Benesi–Hildebrand method.[12] For comparison the association constants of 15-crown-5 and 18-crown-6 with group 1 and group 2 cations are also shown. The results indicate that in neutral methanol compound (**4**) is selective for Ca^{2+} and Ba^{2+} with respect to Li^+, Na^+, K^+, and Mg^{2+}. In basic methanol there is some selectivity for potassium over calcium. Association constants of (**4**) with group 1 and group 2 cations are usually higher than those of 15-crown-5, but lower than those of 18-crown-6. Only calcium forms a stronger complex with (**4**) than with 18-crown-6.

From these results we conclude that compound (**4**) meets the requirements for our sensor application. Work on the immobilisation of this compound at the sensor surface is in progress.

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