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Synthesis and Optical Investigation of Chromogenic 1,3-Calix[4]crowns

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Chromogenic 1,3-calix[4](crown-5 and -6) ethers containing azophenol and indophenol signalling groups were synthesized and their optical recognition toward alkali and alkaline earth metal cations was investigated by UV–visible spectrophotometry. A calcium ion preference was found to be characteristic of most ligands. A calix[4]crown-5 indolo-spiropyran derivative was also prepared to study the photoisomerization equilibrium of the spiropyran–merocyanine system.

Keywords: Calixcrowns; Chromoionophores; Optical recognition; Calcium selectivity

INTRODUCTION

In the past decade a large number of supramolecules combining the unique properties of calixarenes and crowns have been described [1,2] and applied in analytical and separation chemistry [3,4]. The first syntheses connected with comprehensive binding studies of the distally bridged 1,3-calix[4](crown-5 and -6) ethers **I** and **II** (Fig. 1) were reported by the Ungaro and Reinhoudt groups [5,6]. The authors have claimed K^+ selectivity for the crown-5 derivatives **I** and Cs^+ selectivity for the crown-6 compounds **II**, disclosing the strong dependence of their efficiency on the nature of groups R and on the stereochemistry around the binding region. To facilitate the monitoring of the binding process, in several cases chromophore or fluorophore groups were introduced into the calixcrown molecules. These ionophores may have potential in the development of optical devices, such as optodes for the determination of cations in biological fluids or in radioactive wastes [7–11]. Utilizing the potassium selectivity of calix[4](crown-5) molecules, Sutherland and co-workers synthesized the chromogenic version of ligands **I** by introducing one azophenol moiety into the calixarene core. Thus, proton-ionizable calix[4](crown-5) ligands **3a**,**b** (Fig. 1) were obtained exhibiting excellent K^+/Na^+ selectivities associated with coloration in solvent extraction experiments in the pH range 7–9 [10]. Interestingly, loss of the characteristic monovalent alkali cation preference of calix[4]-(crown-5) ligands was observed with the fluorogenic compound **4**, which contains two *p*-(benzthiazol-2-yl)-phenol signalling groups; instead, a remarkable Ca^{2+} selectivity was measured in homogeneous basic solutions [11]. It is more surprising, however, that the bis(4-nitrophenylazo)-coupled 1,3-calix[4]crown-6 **5** was also reported to exhibit Ca^{2+} selectivity even under neutral conditions [12].

As part of our ongoing programme to synthesize chromoionophores for developing optical sensors, we have studied the optical properties of different chromophore groups (2,4-dinitrophenylazo, pyridinium, indophenol) introduced into various calix[4]-arenes including bridged derivatives [13–16]. We report here the synthesis of some chromogenic 1,3-calix[4](crown-5 and -6) ethers **6**–**8** and **10**, and their optical behaviour in the presence of alkali and alkaline earth metal cations is also demonstrated. In addition, the photochromic indolo-spiropyran derivative **11** was prepared. Photochromic materials, especially spiro[2*H*]-1-benzopyrans have attracted much attention recently because of their potential applications as optical filters, switches, memories

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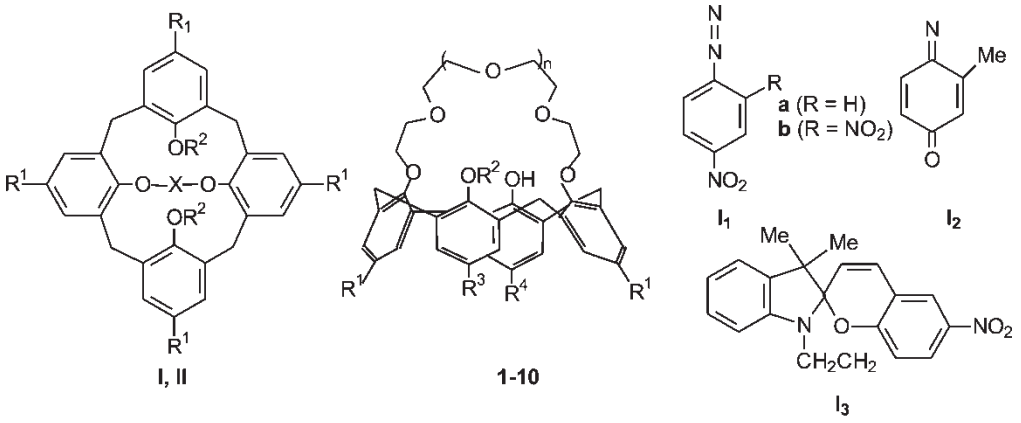


I X = $(CH_2CH_2O)_3CH_2CH_2$
II X = $(CH_2CH_2O)_4CH_2CH_2$
R^1 = H, Bu^t, R^2 = Me. Et, i-Pr
1a (R^1, R^2, R^3, R^4 = H, n = 1)
1b (R^1, R^3, R^4 = Bu^t, R^2 = H, n = 1)
2 (R^1, R^2, R^3, R^4, = H, n = 2)
3a (R^1, R^3 = H, R^2 = Me, R^4 = I_1a, n = 1)
3b (R^1, R^3 = H, R^2 = Me, R^4 = I_1b, n = 1)
5 (R^1, R^2 = H, R^3, R^4 = I_1a, n = 2)
6 (R^1, R^2 = H, R^3, R^4 = I_1b, n = 1)
7 (R^1, R^2 = H, R^3, R^4 = I_1b, n = 2)
8 (R^1, R^2 = H, R^3, R^4 = I_2, n = 1)
9a (R^1, R^3, R^4 = H, R^2 = CH_2COOEt, n = 1)
9b (R^1, R^3, R^4 = Bu^t, R^2 = CH_2COOEt, n = 1
10 (R^1, R^3 = H, R^2 = CH_2COOEt, R^4 = I_1b, n = 1)

FIGURE 1 Survey of 1,3-calix[4](crown-5 and -6) ethers and chromoionophores.

and other optical devices [17]. Upon UV irradiation the spiropyran ring is converted to its coloured merocyanine form by cleavage of the C–O bond. The process is reversed either thermally or by irradiation with visible light. The stability of the merocyanine form can be influenced by attaching a crown ether moiety to the spiropyran skeleton, thus the photoisomerization is controlled by complexing alkali cations [18–20]. To our knowledge, until now calixcrown–spiropyran conjugates have not been reported in the literature. The easily available host **11** was chosen to study how the equilibrium between the uncoloured spiropyran and the coloured merocyanine form is affected by the complexation with mono- and divalent cations.

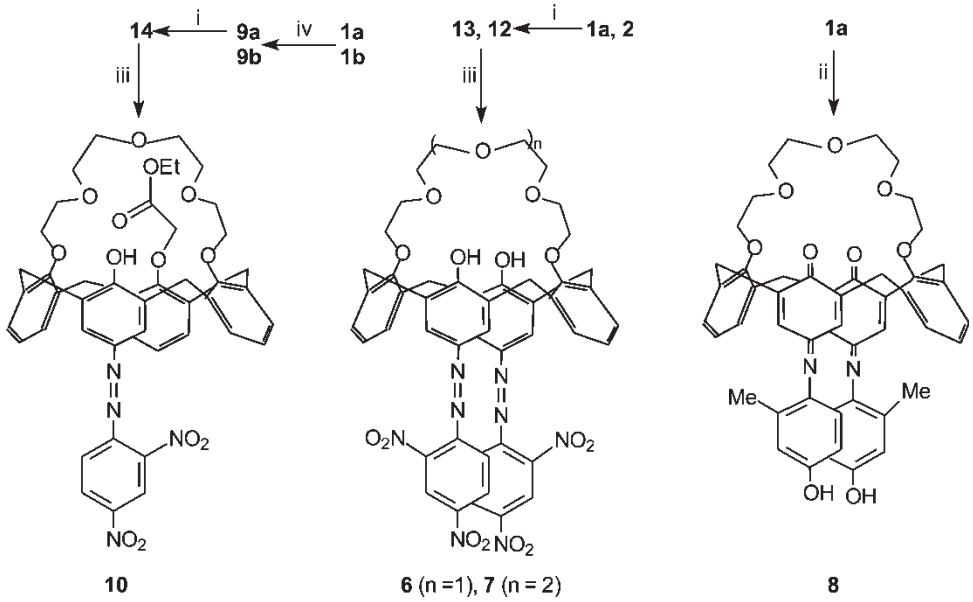
RESULTS AND DISCUSSION

To provide further evidence for the alteration of the binding selectivity pattern in this special class of calixcrowns, we first prepared analogous calixcrown-5 and crown-6 compounds supplied with two 2,4-dinitrophenylazo (**6**, **7**) and indophenol (**8**) indicator moieties, respectively. Ligand **10**, containing an additional ethoxycarbonyl(methoxy) arm (an ester analogue of Sutherland's **3b**), was also synthesized, as outlined in Scheme 1.

Thus, azo compounds **6**, **7** and **10** were obtained by the $Tl(NO_3)_3$-mediated oxidation of calixcrowns **1a**, **2** or **9a** to diquinones **12**, **13** and monoquinone **14**, respectively, followed by condensation with 2,4-dinitrophenyl hydrazine (DNPH) [21]. Indophenol **8** was prepared by the oxidative treatment of **1a** with $K_3Fe(CN)_6$ and 4-amino-*m*-cresol under basic conditions [16].

Each chromogenic molecule exists in the *cone* conformation as reflected by the characteristic ^{13}C signals ($ArCH_2Ar$ δ 30.4–32.4 ppm). We have previously studied the tautomerization of the indophenol moiety in different capped calixarenes by NMR methods [16]. A solvent-dependent process affording an equilibrium of the *exo*-quinoid and the *endo*-quinoid tautomers (in the latter case the semiquinone moiety constitutes a part of the calixarene core) has been observed (Fig. 2).

Theoretically, compound **8**, in which two indophenol units are available, may exist in three tautomeric forms: *exo*-, *endo*- and *exo*/*endo*-quinoid structures referring to the position of the quinoneimine subunits. In the *endo* tautomer, however, the two opposite arylimino groups can occupy *anti* (inherently chiral) and *syn* (achiral) arrangements that can be distinguished because the rate of the *E*/*Z* isomerization is very slow at ambient temperature (the free enthalpy of activation $\Delta G^{\ddagger} > 21.5$ kcal/mol measured for an analogous calixindophenol) [16]. In the first case all the four $ArCH_2Ar$ methylene groups are diastereotopic, whereas in the achiral arrangement by pairs, two are equivalent. In the chiral *exo*/*endo*-quinoid tautomer, all four methylenes are again diastereotopic, but both of the *endo*- and *exo*-quinoid moieties should exhibit different chemical shifts, resulting in



SCHEME 1 Synthesis of chromogenic calixcrowns. Reagents and conditions: (i) $Tl(NO_3)_3{\cdot}3H_2O$, $CHCl_3$, EtOH, rt; (ii) 2-amino-*m*-cresol, aq. $K_3Fe(CN)_6$, DBU, MeCN; (iii) 2,4-DNPH, $CHCl_3$, EtOH, H^+, rt; (iv) $BrCH_2COOEt$, BaO, DMF.

an increased number of signals. On the basis of these considerations the structure of indophenol **8** in acetone-d_6 and methanol-d_4 was assigned exclusively to the *endo*-quinoid tautomer as reflected by the ^1H NMR and ^{13}C spectra (four AB doublets for the CH_2 protons, see Fig. 4). In Fig. 1 $\mathbf{I}_2$ is depicted as an *exo*-quinoid tautomer for the sake of the general formula.

Preliminary Complexation Studies with Chromogenic Hosts 6–8 and 10

The binding properties of the target compounds were studied by UV–visible spectrophotometry in acetone solution ($[L] = 5 \times 10^{-5}$ M). The absorption maxima ($\lambda_{max}L$) of the azophenol hosts **6**, **7** and **10** appeared in the region 414–422 nm, while that of the indophenol **8** was detected at 522 nm. When a 100-fold excess of triethylammonium (TEA) had been added, the intensities of these bands decreased due to deprotonation, and new bands characteristic of the phenolates appeared at longer wavelengths ($\lambda_{max}L^-$). The spectra were then measured in the presence of 100-fold excess of alkali (Li^+, Na^+, K^+, Cs^+), Ca^{2+} and Mg^{2+} perchlorate salts alone ($\lambda_{max}L + M^+$), followed by the addition of excess of TEA ($\lambda_{max}L^- + M^+$). The wavelength changes $\Delta\lambda_1 = \lambda_{max}(L + M^+) - \lambda_{max}L$ and $\Delta\lambda_2 = \lambda_{max}L^- - \lambda_{max}(L^- + M^+)$ are summarized in Table I.

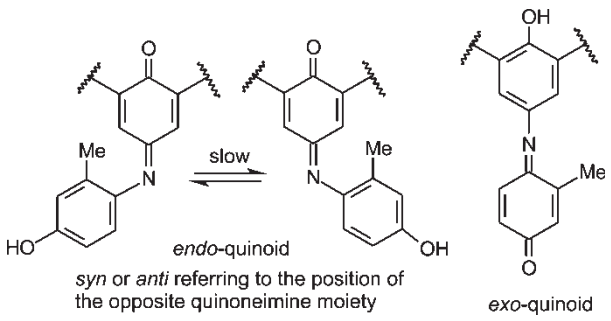


FIGURE 2 Tautomeric forms of calix-bis(indophenols).

Complexation under Neutral Conditions

Upon the addition of metal salts alone, the absorbances of azo dyes **6**, **7** and **10** were generally increased and the λ_{max1} values were shifted ($\Delta\lambda_1 = 8$–56 nm), displaying a shoulder (Table I). In addition, phenolate bands (λ_2) with weak intensities appeared in all of the spectra due to the complexation-induced partial dissociation of the acidic phenol moieties. These spectral changes, however, indicated negligible complexation. Although the related bis(4-nitrophenylazo)-crown-6 **5** was reported to selectively exhibit a 150-nm bathochromic shift on addition of Ca^{2+} in MeCN [12], our analogous bis(2,4-dinitrophenylazo) derivative **7** showed no response towards any cations, including Ca^{2+}, in either acetone or MeCN. Apart from the behaviour of azo dyes, the indophenol host **8** exhibited a highly selective optical response to Ca^{2+} (54-nm shift) and its spectrum was not affected by monovalent cations (Table I). Although Mg^{2+} produced a shift of 26 nm, no responses were detected below 10-fold excess of the salt. Titration of Ca^{2+} into a solution of host **8** produced wavelength changes with an isobestic point

TABLE I Optical responses of **6**–**8** and **10** (5×10^{-5} M) to TEA and different metal salts (5×10^{-3} M) in acetone

	Metal-induced wavelength changes							
	λ_{max1} (nm) L	λ_{max2} (nm) L^-	$\Delta\lambda_1/\Delta\lambda_2$					
			Li^+	Na^+	K^+	Cs^+	Ca^{2+}	Mg^{2+}
6	414	622	10/2	26/6	44/2	NM	44/−14	4
7	418	646	0/−4	−6/4	−8/4	28/−44	28/−44	−4
8	522	670	4	8	0	NM	54	26
10	422	620	−8/−6	28/0	28/0	0/0	56/−62	2

NM, not measured

at 426 nm (Fig. 3). The association constant calculated for 1:1 complex stoichiometry from the linear Benessi-Hildebrand plot was $K_{ass} = 1.5 \times 10^4\,M^{-1}(\pm 10\%)$.

The structural background of the coloration process was studied by ^1H and ^{13}C NMR and ligand **8** was found to retain the *endo*-quinoid tautomeric structure in the presence of Ca^{2+} As can be seen in Fig. 4, the ^{13}C signal of the quinone carbonyls is shifted downfield by 3.5 ppm, indicating an interaction with the Ca^{2+} entrapped by the crown loop. This effect induces an electron flux in the direction of the binding site (the chemical shifts of the diastereotopic methylene and aromatic protons are averaged), facilitating the dissociation of the phenolic OH, which is reflected by the bathochromic band shift in the visible spectrum.

Complexation under Basic Conditions

The partial dissociation of the proton-ionizable chromoionophores **6**, **7** and **10** affected by TEA went to completion upon the addition of metal salts, affording large intensity enhancements of the phenolate bands with different $\Delta\lambda_2$ shifts. Analysis of the spectral data revealed that Li^+, Na^+ and K^+ did not cause significant wavelength changes with any of the ligands. By contrast, all of the hosts responded to calcium, resulting in hypsochromic shifts, which were more pronounced with ligands **7** (−44 nm) and **10** (−62 nm). Interestingly, the former gave the same shift upon addition of caesium (Table I). We assume these large shifts can be attributed to strong binding accompanied by negative halochromism, the magnitude of which depends partly on the positive charge density of the cations and partly on the tightness of the phenolate–cation ion pair formed upon complexation. Because of the more distinct optical response to Ca^{2+}, ligand **10** was chosen for further evaluation. The solution of host **10** was titrated with various amounts of Ca^{2+} and the λ_{max2} values were gradually shifted from 620 to 558 nm with increasing absorbances, reaching the final point at 1:1 complex stoichiometry (Fig. 5). Further spectral changes was not observed even with 10-fold excess of Ca^{2+}. However, depending on the molar ratios, two series of spectra with a break-point at about 0.5 equiv of Ca^{2+} can be observed, which may refer to two equilibria with 2:1 followed by 1:1 **10**/Ca^{2+} complex stoichiometry. Although we have no structural evidence for the complexed species, the spectral data allow some conclusions to be drawn. At high ligand/cation ratios the Ca^{2+} ion is bound by 2 mol of **10**, involving primarily the ethoxycarbonyl(methoxy) sites, while the remote TEA–phenolate ion pair is stabilized to some extent by the crown ring. Consequently, the phenolate is scarcely affected by the calcium ion in this process,

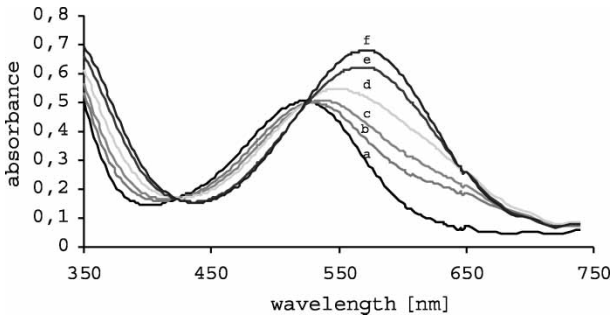


FIGURE 3 Spectral changes of **8** (5×10^{-5} M, acetone) upon the addition of various amount of Ca^{2+}; $Ca(ClO_4)_2$ equivalents: 0 (a), 0.25 (b), 0.5 (c), 1 (d), 2 (e), 5 (f).

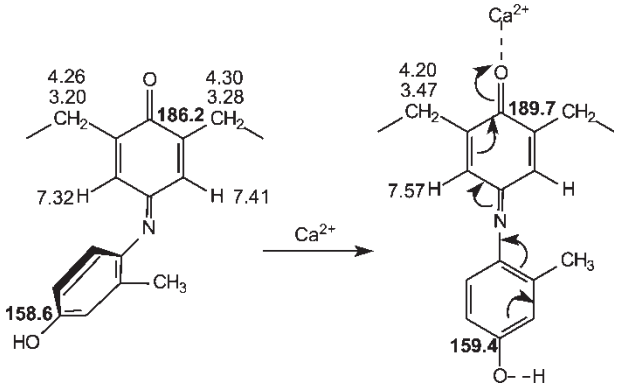


FIGURE 4 ^1H and ^{13}C chemical shifts of the indophenol chromophore in ligand **8** upon the complexation with Ca^{2+}.

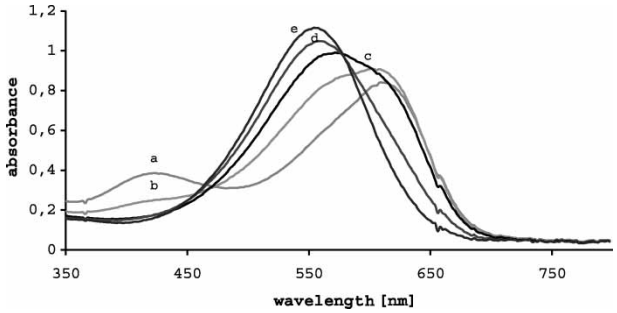


FIGURE 5 Spectral changes of **10** (5×10^{-5} M, acetone) upon the addition TEA (5×10^{-3} M) and various amount of Ca^{2+}; $Ca(ClO_4)_2$ equivalents: 0.2 (a), 0.4 (b), 0.6 (c), 0.8 (d), 1 (e).

as reflected by the insignificant band shifts from 620 to 610 nm (Fig. 5a,b).

When the Ca^{2+} equivalents are increased, the λ_{max} values are further shifted up to 568 nm referring to 1:1 stoichiometry (Fig. 5c–e). In this species the calcium ion is complexed by the macrocyclic ring forming a strong ion pair with the phenolate oxygen (displacing the TEA cation), as reflected by the large (62 nm) hypsochromic shift in the visible spectra. Further quantitative studies of these equilibria are in progress.

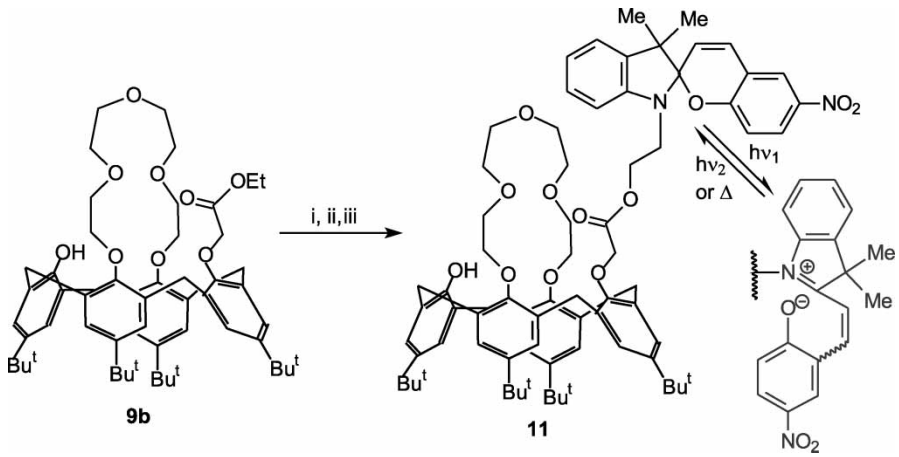
Photochromic Indolo-spiropyran Derivative 11

The introduction of an indolo-spirobenzopyran moiety into the calixcrown molecule was designed via the alcoholic part of ester **9b** in a three-step procedure using known reactions. First, **9b** was hydrolysed to the respective acid, followed by chlorination with oxalyl chloride to the acid chloride, which was then condensed with 2-(3,3′-dimethyl-6-nitro-3′*H*-spiro[chromene-2,2′-indol]-1′-yl)-ethanol ($\mathbf{I}_3$-OH) [22] to obtain host **11** (Scheme 2).

We recently published the photochromic properties of compound **11** without giving experimental details of the preparation [23]. A brief account of the spectroscopic evaluation is now given. The UV–visible spectra of **11** taken with the samples kept in the dark (no visible bands) and then 2, 15 and 60 min after a short illumination with UV light (the 365-nm line of a 200-W high-pressure mercury arc lamp) clearly showed the photochromism: under irradiation a series of spectra were obtained with absorption maxima of increasing intensity at 540 nm (EtOH) and 561 nm (MeCN), respectively, characteristic of the merocyanine form. The maximum of the visible band decayed slowly, indicating the regeneration of the original spiropyran form. The equilibrium constants of the conversion of spiropyran to merocyanine were calculated: $K_e = (1.1 \pm 0.3) \times 10^{-2}$ (EtOH) and $(3.4 \pm 1.5) \times 10^{-3}$ (MeCN) [22]. This means that the rate of ring closure is slower in EtOH than in MeCN, which points to the stabilizing effect of the protic ethanol on the polar merocyanine form.

Binding experiments were then conducted with various metal salts to assess whether the equilibrium of photoisomerization was influenced by the different complexing properties of the cations. We expected that the equilibrium would be shifted by complexation to the polar merocyanine form stabilized by the interaction between the complexed cation and the merocyanine–phenolate anion.

The results were disappointing: significant changes in the K_e values and straightforward relationships in terms of the cations were not found. We assume that the signalling unit in **11** is too far from the complexing site so that the merocyanine-phenolate (shown in red in Scheme 2) cannot interact with the complexed cation. In general, some increase in the stability of the merocyanine form was observed but it was due to the large excess of the external cations and not to the complexed cations. Synthesis of a new calixcrown ligand in which the spiropyran moiety is attached



SCHEME 2 Synthesis of indolo-spirobenzopyran **11**. Reagents and conditions: (i) aq. KOH, EtOH, rfl, H^+; (ii) $(COCl)_2$, $CHCl_3$, rfl; (iii) $\mathbf{I}_3$-OH, Et_3N, DMAP cat., CH_2Cl_2, rt.

directly to the binding site via the benzopyran subunit is currently under way in our laboratory.

CONCLUSIONS

Several proton-ionizable 1,3-calix[4](crown-5 and -6) ethers containing 2,4-dinitrophenylazo and indophenol chromophores were synthesized and their binding selectivities evaluated towards alkali and alkaline earth metal cations by UV–visible spectroscopic measurements. The alteration of the K^+ preference to Ca^{2+} with calix(crown-5) ethers was supported by recent examples. Indophenol **8** in neutral medium and the ester-armed azo dye **10** in basic medium exhibited selective optical responses to Ca^{2+}. The crown-6 host **7** was found to respond similarly to Cs^+ and Ca^{2+} under basic conditions. The photochromic calix[4]crown-5 indolo-spiropyran conjugate **11** was prepared for the first time and found to display photochromism. The equilibrium of the spiropyran–merocyanine photoisomerization, however, was not influenced by the complexation with metal cations, presumably because of structural reasons.

EXPERIMENTAL

Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) at 500/125 MHz on a Bruker Avance DRX-500 spectrometer. UV–visible spectra of the chromoionophores were recorded on an HP 8452A spectrophotometer. For kinetic and equilibrium measurements of the spiropyran-merocyanine system **11**, a Cintra 10e UV–visible spectrophotometer was used. Precoated silica gel plates (Merck 60 F_{254}) were used for analytical TLC and Kieselgel 60 for column chromatography. All chemicals were reagent grade and used without further purification. Calixcrowns **1a**, **1b** and **2** [24] and I_3-OH [22] were prepared as described in the literature.

General Procedure for the Synthesis of Azo Derivatives 6, 7 and 10

Compound **1a**, **2** or **9a** (0.75 mmol) in $CHCl_3$ (15 ml) was added to a mixture of $Tl(NO_3)_3{\cdot}3H_2O$ (2.0 g, 4.5 mmol for **1a** and **2**; 1.0 g, 2.25 mmol for **9a**) in dry MeOH (20 ml) and EtOH (55 ml), and the solution stirred for 1 h at ambient temperature. The solution was then diluted with water (70 ml), acidified with 10% aqueous HCl and extracted with 3×50 ml $CHCl_3$. The organic phase was washed with water, dried (Na_2SO_4) and evaporated to give crude diquinones **12** and **13** (0.7 mmol, mixture of conformers) and monoquinone **14** (0.7 mmol; the analytical sample was purified by chromatography with 9:1 toluene/MeOH). These compounds, without purification, were allowed to react overnight with 2,4-dinitrophenyl hydrazine (0.3 g, 1.5 mmol for **12** and **13**; 0.16 g, 0.8 mmol for **14**) in a mixture of CH_2Cl_2 (15 ml), EtOH (5 ml) and one drop of 6 M HCl at ambient temperature, resulting in the formation of compounds **6** (0.37 g, 51%), **7** (0.23 g, 30%) and **10** (0.27 g, 42%) as red crystals after column chromatography on silica (eluent: toluene/MeOH 9:1).

Compound **6** (*cone*): mp 232–235°C; ^{1}H NMR: δ 8.94 (s, 2H, O*H*), 8.77 (s, 2H, Ph*H*), 8.49 (dd, 2H, Ph*H*), 7.84 (d, 2H, Ph*H*), 7.82 (s, 4H, Ar*H*), 6.96 (d, 4H, *m*-Ar*H*), 6.82 (t, 2H, *p*-Ar*H*), 4.51 and 3.55 (d + d, 4 + 4H, *J* 13.1 Hz, ArCH_2Ar), 4.19 (m, 4H, OCH_2), 4.12 (m, 4H, OCH_2), 3.94 (m, 4H, OCH_2), 3.86 (m, 4H, OCH_2); ^{13}C NMR δ 160.1, 152.1, 146.3, 132.4, 129.8, 129.4, 126.0, 126.0 (Ar), 149.5, 147.0, 146.6, 127.8, 120.3, 120.3 (Ph), 77.0, 71.4, 71.4, 70.3 (O*C*H_2), 31.2 (Ar*C*H_2Ar); anal. calcd for $C_{48}H_{42}N_8O_{15}$ (970.90): C, 59.38; H, 4.36, found: C, 59.61; H, 4.32%.

Compound **7** (*cone*): mp 179–182°C; ^{1}H NMR: δ 8.77 (s, 2H, Ph*H*), 8.74 (s, 2H, O*H*), 8.49 (dd, 2H, Ph*H*), 7.84 (d, 2H, Ph*H*), 7.82 (s, 4H, Ar*H*), 6.94 (d, 4H, *m*-Ar*H*), 6.79 (t, 2H, *p*-Ar*H*), 4.50 and 3.54 (d + d, 4 + 4H, *J* 13.2 Hz, ArCH_2Ar), 4.23 (m, 4H, OCH_2), 4.03 (m, 4H, OCH_2), 3.90 (m, 4H, OCH_2), 3.83 (m, 4H, OCH_2), 3.67 (s, 4H, OCH_2); ^{13}C NMR δ160.0, 152.1, 146.3, 132.4, 129.7, 129.5, 126.0, 126.0 (Ar), 149.5, 147.0, 146.7, 127.8, 120.4, 120.3 (Ph) 76.7, 71.8, 71.2, 71.2, 70.0 (O*C*H_2), 31.2 (Ar*C*H_2Ar); anal. calcd for $C_{50}H_{46}N_8O_{16}$ (1014.95): C, 59.17; H, 4.57, found: C, 59.41; H, 4.60%.

Compound **10** (*cone*): mp 229–231°C; ^{1}H NMR (acetone-d_6): δ 8.86 (d, 1H, *J* 2.4 Hz, Ph*H*), 8.64 (dd, 1H, *J* 8.9, 2.4 Hz, Ph*H*), 7.97 (d, 1H, *J* 8.9 Hz, Ph*H*), 7.87 (s, 2H, *m*-Ar*H*), 7.21 (d, 2H, *m*-Ar*H*), 6.88 (t, 1H, *p*-Ar*H*), 6.82 (d, 2H, *m*-Ar*H*), 6.81 (d, 2H, *m*-Ar*H*), 6.58 (t, 2H, *p*-Ar*H*), 5.34 (s, 2H, OCH_2CO), 4.93 and 3.37 (d + d, 2 + 2H, *J* 12.8 Hz, ArCH_2Ar), 4.65 and 3.54 (d + d, 2 + 2H, *J* 13.3 Hz, ArCH_2Ar), 4.22 and 3.96 (d + t, 2 + 2H, OCH_2), 4.20 and 3.90 (t + m, 2 + 2H, OCH_2), 3.91 (m, 4H, OCH_2), 3.80 and 3.76 (m + m, 2 + 2H, OCH_2), 4.20 (q, 2H, OCH_2CH$_3$), 1.28 (t, 3H, OCH$_2$CH_3); ^{13}C NMR δ 171.7 (C═O), 161.5, 156.6, 154.8, 146.7, 136.8, 135.0, 133.3, 130.9, 130.2, 130.0, 129.6, 126.4, 125.0, 124.5 (Ar), 149.8, 148.1, 147.6, 128.9, 121.2, 120.9 (Ph), 76.7, 71.9, 71.5, 71.1 (O*C*H_2), 71.5 (O*C*H_2CO) 61.1 (O*C*H_2CH$_3$), 32.4, 31.4 (Ar*C*H_2Ar), 14.7 (OCH$_2$*C*H$_3$); anal. calcd for $C_{46}H_{46}N_4O_{13}$ (862.89): C, 64.03; H, 5.37, found: C, 63.78 H, 5.34%.

Compound **14** (*cone*): mp 128–130°C; ^{1}H NMR: δ 6.94 (d, 2H, Ar*H*), 6.80 (d, 2H, Ar*H*), 6.76–6.69 (m, 5H, Ar*H*), 6.74 (s, 2H, C*H*), 4.97 (s, 2H, OCH_2CO), 4.58 and 3.24 (d + d, 4 + 4H, *J* 13.5 Hz, ArCH_2Ar), 4.18 and 3.99 (m + m, 2 + 2H, OCH_2), 3.98 and 3.73 (m + m, 2 + 2H, OCH_2), 3.94 and 3.54

(m + m, 2 + 2H, OCH_2), 3.75 and 3.68 (m + m, 2 + 2H, OCH_2), 4.07 (q, 2H, OCH_2CH$_3$), 4.07 (t, 3H, OCH$_2$CH_3); ^{13}C NMR δ 188.6, 186.7 (*C*=O), 170.4, (*C*O$_2$Et), 156.6, 155.0, 135.8, 135.1, 133.5, 131.9, 130.1, 129.3, 128.7, 128.5, 123.4, 123.3 (Ar), 72.1, 71.4, 70.7, 70.0 (OC H$_2$), 70.7 (OC H$_2$CO), 60.4 (OC H$_2$CH$_3$), 31.8 (ArC H$_2$Ar), 14.3 (OCH$_2$C H$_3$); anal. calcd for $C_{40}H_{42}O_{10}$ (682.76): C, 70.37; H, 6.20, found: C, 70.61; H, 6.16%.

Synthesis of Indophenol 8

To a MeCN (80 ml) solution of **1a** (0.58 g, 1 mmol), 4-amino-*m*-cresol (0.5 g, 4 mmol) and DBU (3 ml, 20 mmol) was added $K_3Fe(CN)_6$ (2.64 g, 8 mmol) dissolved in 8 ml water and the mixture stirred for 24 h at room temperature. The solvent was then removed under reduced pressure, the residue was dissolved in $CHCl_3$, thoroughly washed with water, and dried to afford **8** (0.20 g, 24%) as dark red crystals after column chromatography on silica (eluent: CH_2Cl_2/MeOH 8:2) (*cone*): mp > 350°C; ^{1}H NMR (methanol-d_4): δ 7.34 (s, 2H, Ar*H*), 7.15 (s, 2H, Ar*H*), 6.82 (d, 2H, Ar*H*), 6.82 (s, 2H, Ph*H*), 6.72 (d, 2H, Ph*H*), 6.68 (t, 2H, *p*-Ar*H*), 6.64 (d, 2H, Ar*H*), 6.60 (d, 2H, Ph*H*), 4.31 and 3.20 (d + d, 1 + 1H, *J* 12.8 Hz, ArCH_2A*r*), 4.26 and 3.06 (d + d, 1 + 1H, *J* 12.2 Hz, ArCH_2Ar), 4.29 and 3.23 (d + d, 1 + 1H, *J* 12.2 Hz, ArCH_2Ar), 4.24 and 3.04 (d + d, 1 + 1H, *J*12.7 Hz, ArCH_2A*r*), 3.99 (m, 4H, OCH_2), 3.96 (m, 4H, OCH_2), 3.86 (m, 4H, OCH_2), 3.77 (m, 4H, OCH_2), 2.23 (s, 6H, CH_3); ^{13}C NMR δ 187.5 (C=O), 155.4 (C=N–), 158.5, 158.3 132.8, 132.6, 130.1, 130.0, 125.2 (Ar), 155.4, 142.4, 134.6, 123.1, 118.8, 114.2 (Ph), 145.4, 146.3 (*C*), 138.7, 125.9 (*C*H), 74.6, 72.3, 71.7, 71.3 (OC H$_2$), 31.2, 30.8 (ArC H$_2$Ar), 18.6 (*C* H$_3$); FAB-MS *m*/*z*: 859.9 $[M + K]^+$; anal. calcd for $C_{50}H_{48}N_2O_9$ (820.93): C, 73.15; H, 5.89, found: C, 73.42; H, 5.91%.

Synthesis of Calixcrown Esters 9a and 9b

A mixture of **1a** or **1b** (2 mmol), ethyl bromoacetate (0.50 g, 3 mmol) and BaO (0.46 g, 3 mmol) in 20 ml DMF was stirred at 80°C overnight. The solvent was evaporated under reduced pressure, the residue was dissolved in CH_2Cl_2 (30 ml), washed with water, dried (Na_2SO_4) and then evaporated to dryness. The residue was triturated with methanol and filtered to give **7a** (0.82 g, 62%) and **7b** (1.06 g, 60%) as white solids.

Compound **9a** (*cone*): mp 172–175°C; ^{1}H NMR: δ 7.14 (d, 2H, Ar*H*), 7.08 (d, 2H, Ar*H*), 6.93 (t, 2H, Ar*H*), 6.69 (d, 2H, Ar*H*), 6.67 (d, 2H, Ar*H*), 6.56 (t, 2H, Ar*H*), 5.30 (s, 2H, OCH_2CO), 4.85 and 3.33 (d + d, 2 + 2H, *J* 12.9 Hz, ArCH_2Ar), 4.53 and 3.32 (d + d, 2 + 2H, *J* 13.2 Hz, ArCH_2Ar), 4.18 (q, 2H, OCH_2CH$_3$), 4.16 (m, 2H, OCH_2), 4.10 (m, 2H, OCH_2), 3.93 (m, 8H, OCH_2), 3.79 (m, 4H, OCH_2), 1.29 (t, 3H, OCH$_2$CH_3); anal. calcd for $C_{40}H_{44}O_9$ (668.78): C, 71.84; H, 6.63, found: C, 71.57; H, 6.66%.

Compound **9b** (*cone*): mp 217–220°C; ^{1}H NMR: δ 7.11 (s, 2H, Ar*H*), 7.05 (s, 2H, Ar*H*), 6.64 (s, 4H, Ar*H*), 5.18 (s, 2H, OCH_2CO), 4.81 and 3.26 (d + d, 2 + 2H, *J* 12.7 Hz, ArCH_2Ar), 4.48 and 3.23 (d + d, 2 + 2H, *J* 13.1 Hz, ArCH_2Ar), 4.21 (q, 2H, OCH_2CH$_3$), 4.15 (d, 2H, OCH_2), 4.08 (t, 2H, OCH_2), 3.97 (m, 4H, OCH_2), 3.90 (m, 4H, OCH_2), 3.84 (m, 2H, OCH_2), 3.76 (m, 2H, OCH_2), 1.29 (t, 3H, OCH$_2$CH_3), 1.31 (s, 18H, C(CH_3)$_3$), 0.87 (s, 18H, C(CH_3)$_3$); anal. calcd for $C_{56}H_{76}O_9$ (893.21): C, 75.30; H, 8.58, found: C, 75.06; H 8.55%.

Synthesis of Indolo-spiropyran 11

A mixture of **9b** (0.89 g, 1 mmol) and KOH (0.7 g, 12.5 mmol) in EtOH (10 ml) was refluxed for 3 h, then acidified with aqueous HCl, filtered and washed with water. The crude and dried carboxylic acid thus formed (0.43 g, 0.5 mmol) was treated with $(COCl)_2$ (0.5 ml, 5.9 mmol) in $CHCl_3$ (15 ml) at boiling temperature (1 h), evaporated to dryness to give crude acid chloride, which was allowed to react with I_3-OH (0.18 g, 0.5 mmol) in the presence of Et_3N (0.5 ml, 3.6 mmol) and DMAP catalyst (0.03 g) in CH_2Cl_2 (10 ml) at ambient temperature (24 h). After standard work-up the product was chromatographed on silica (eluent: EtOAc) to give **11** as purple crystals (0.20 g, 33%) (*cone*): mp: 106–109°C; ^{1}H NMR: δ 8.03 (dd, 1H, Ar*H*-NO$_2$), 8.00 (s, 1H, Ar*H*-NO$_2$), 7.21 (t, 1H, spiro-Ar*H*), 7.15 (s, 1H, Ar*H*), 7.11 (d, 1H, spiro-Ar*H*), 7.10 (s, 2H, Ar*H*), 7.05 (s, 1H, Ar*H*), 6.92 (t, 1H, spiro-Ar*H*), 6.81 (d, 1H, *J* 10.4 Hz, C*H*=), 6.77 (s, 1H, Ar*H*), 6.74 (d, 1H, Ar*H*-NO$_2$), 6.68 (d, 1H, spiro-Ar*H*), 6.63 (s, 2H, Ar*H*), 6.60 (s, 1H, Ar*H*), 5.81 (d, 1H, *J* 10.4 Hz, C*H*=), 5.19 and 5.12 (d + d, 1 + 1H, *J* 17.0 Hz, OCH$_2$CO), 4.81 and 3.24 (d + d, 1 + 1H, *J* 12.7 Hz, ArCH_2Ar), 4.67 and 3.20 (d + d, 1 + 1H, *J* 12.8 Hz, ArCH_2Ar), 4.46 and 3.32 (d + d, 1 + 1H, *J* 12.9 Hz, ArCH_2Ar), 4.45 and 3.24 (d + d, 1 + 1H, *J* 12.9 Hz, ArCH_2Ar), 4.34 and 4.25 (m, 1 + 1H, CO$_2$CH_2), 4.13 and 3.98 (m + m, 2 + 2H, OCH_2), 4.10 (m, 1H, OCH_2), 4.04 (m, 1H, OCH_2), 3.92–3.66 (m, 10H, OCH_2), 3.49 and 3.39 (m + m, 1 + 1H, NCH_2), 1.33 (s, 9H, C(CH_3)$_3$), 1.32 (s, 9H, C(CH_3)$_3$), 1.29 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.88 (s, 9H, C(CH_3)$_3$), 0.87 (s, 9H, C(CH_3)$_3$); ^{13}C NMR δ 152.8, 151.1, 151.0, 146.7, 145.8, 145.7, 135.4, 135.0, 132.7, 132.4, 132.2, 125.9, 125.3, 125.2, 125.0, 124.9, 124.8 (Ar), 159.3, 141.2, 126.8, 122.8, 118.5, 115.6 (Ar-NO$_2$), 146.7, 135.8, 127.9, 121.8, 120.0, 106.7 (spiro-Ar), 128.3, 121.7 (*C*H=), 106.3 (NC), 75.3, 70.9, 70.8, 70.6 (OC H$_2$), 70.1 (OC H$_2$CO) 62.2 (CO$_2$*C* H$_2$), 52.7 (*C*(CH$_3$)$_2$), 42.3 (NC H$_2$), 34.1, 32.8,

33.7 ($C(CH_3)_3$), 31.8, 31.3 ($ArCH_2Ar$), 31.8, 31.7, 31.0 ($C(CH_3)_3$), 25.9, 19.9 (CH_3); anal. calcd for $C_{74}H_{90}N_2O_{12}$ (1199.53): C, 74.10; H, 7.56, found: C, 73.82; H, 7.59%.

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