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Substituent Tuning of Photoreversible Lithium Chelating Agents

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ABSTRACT

Strategically placed substituents on crowned indolospirobenzopyran rings can be used to tune their chelating ability in order to obtain photoreversible lithium binding agents.

1 INTRODUCTION

There is a growing interest in the development of reversible metal chelating agents in which chelation can be switched on and off by exposure to light of different wavelengths. A popular substrate for such studies is the indolospirobenzopyran system **1**, and its analogues, since these have well-documented photochromic properties[1,2] and, on exposure to short wavelength light, can isomerise to the open merocyanine forms, such as **2**.

The first photochromic chelating agent, **3**, was reported in 1965 by Phillips *et al.*[3] The masked 8-hydroxyquinoline group in this molecule proved to form extremely stable metal complexes that overpowered the reversible photochromic effect, the complexed merocyanine form being unaffected by exposure to visible light. More recently, Kimura *et al.*[4–6] have reported that the crowned spiropyran **4a** compexes with lithium perchlorate in aprotic solvents, such as acetonitrile, but that as is the case for **3**, the chelation catalyses the thermal (i.e. dark) opening of the pyran ring to give the merocyanine metal complex **6a** (Scheme 1); however, for the homologue **4d**, in which the crown group itself can fully satisfy the

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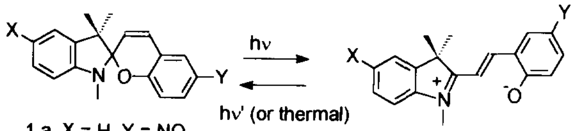

1 a, X = H, Y = NO_2
b, X = NO_2, Y = NO_2
c, X = CF_3, Y = NO_2

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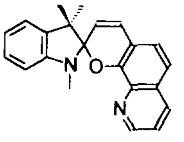

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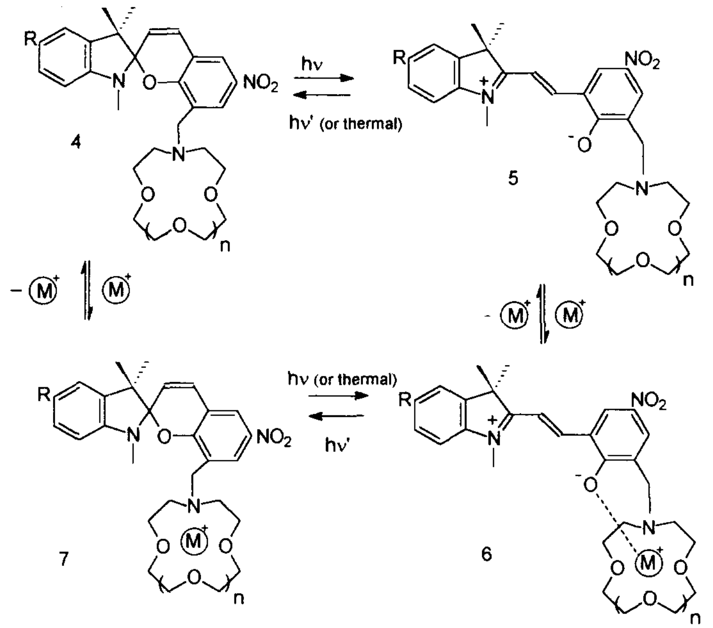
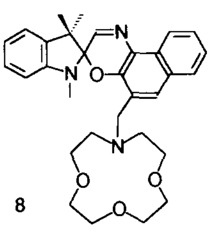
chelating requirements of the lithium ion, the presence or absence of this cation hardly affects its photochromic behaviour. The spironaphthoxazine **8** behaves similarly to **4a** but, in this case, irradiation of the coloured merocyanine complex with visible light partially reconverts it to the closed pyran form, presumed to be accompanied by a switching off of chelation, although this was not confirmed by kinetic studies; in the dark the colourless form thermally reopens to the merocyanine complex.[7] Some variations on this theme, such as placing the metal chelating ligand on the indolo-nitrogen, as in compound **9**, have also been reported.[8–11]

Although such thermal–photochemical cycles are of interest in certain applications, means for eliminating the dark (thermal) processes (see Scheme 1) and for tuning the overall equilibrium of the isomerisation



a, R = H, n = 1
b, R = NO_2, n = 1
c, R = CF_3, n = 1
d, R = H, n = 2

Scheme 1



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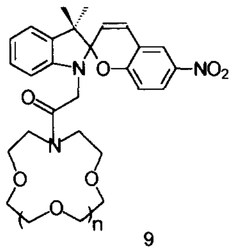

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would open up truly photoreversible systems. In order to prepare such systems, attention has to be paid to the following points.

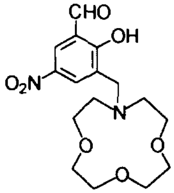
(a) Obtaining the right balance (position of the equilibria) between the isomeric forms, for example to avoid the chelating interactions or solvent effects tipping the equilibrium too far to one side, namely from **4** to the open chelated form **6**. Presumably, in the case cited above, formation of the open form proceeds by two thermal steps, a pre-equilibrium involving formation of the weakly complexed species **7**, followed by ring opening to give the more strongly complexed and thus thermodynamically preferred merocyanine isomer, **6**, in which the cation is also stabilised by the phenolate oxygen.

(b) Decreasing the rate of the dark (thermal) equilibration processes between the open and closed forms by increasing the activation energy barriers.

The former problem, the position of the equilibria, can be tackled by the addition of appropriately placed substituents that change the electronic demands on the parent system[12] and our attempts to achieve this are the subject of this paper.

2 RESULTS AND DISCUSSION

The crowned spiropyrans **4a**, **b** and **c**, and their uncrowned reference compounds **1a**, **b** and **c**, have been prepared by standard procedures. Thus, the crowned spiropyrans were prepared by condensation of the crowned salicylaldehyde **10** with the appropriate indolenine **11**.[5] These



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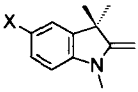

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TABLE 1
Effect of Alkali Cations on the Photochromic Behaviour of Compounds **4b** and **4c**[a]

	M^{n+}	*Dark*[b]	*UV*	*Visible*	*Ratio UV:Vis*	*Comments*
4b	—	0·015	0·03	0·00(1)	—	Very weak photochromicity
4b	Li^+	0·015	0·13	0·01(3)	10	Photochromic; UV on/ visible off
4b	Na^+	0·01	0·02	0·01	2	Poor photochromicity
4b	K^+	0·01	0·015	0·01	1·5	Very weak photochromicity
4c	—	0·01	0·05	0·00(5)	—	Weak photochromicity
4c	Li^+	0·12	0·27	0·03	9	Photochromic; UV on/ visible off/ dark partly on
4c	Na^+	0·03	0·13	0·03	4	Some photochromicity
4c	K^+	0·02	0·11	0·01	11	Some photochromicity

[a] Solutions 10^{-5}M with cations as perchlorates at 0·2 M in acetonitrile. Values are normalised absorbances of λ_{max} in the region 540–560 nm.
[b] See text for details of exposure regimes.

have different electronic substituents on the indole ring, and the nitro compounds (series **b**) and the trifluoromethyl derivatives (series **c**) were chosen because previous studies have shown that they prefer to stay in the closed form compared with the ‘unsubstituted’ series **a**. For example, with acid, which catalyses ring opening, **1b** and **c** were not readily converted to the protonated open isomers **12**, whereas the unsubstituted compound, **1a**, is affected.[13] They also show poor photochromic properties, the closed spiropyran form being preferred. The electron attracting properties of the nitro and trifluoromethyl substituents destabilise formation of the positive charge carried in the iminium form of the open isomer **2**.

The photochromic studies were principally carried out in aprotic solvents using the metal perchlorates of Li^+, Na^+ and K^+, with Na^+ and K^+ ions for reference. The position of equilibrium was measured by UV spectroscopy (Table 1). Freshly prepared solutions of the reagents (1×10^{-5} M) were examined after adding the metal salt, allowing equilibration in the dark for 1 h, exposing the solution to ultraviolet light for 1 min and measuring the UV spectrum, and then exposing the solution to white light for 3 min before finally remeasuring the spectrum. Where relevant, the reversibility of the the systems was examined by repetition of the cycle.

Control studies on the uncrowned spiropyrans **1a**, **b** and **c** showed that the cations had very little effect on the position of the equilibria and, for derivatives **1b** and **1c**, the thermodynamically favoured isomer was still the closed, pyran form **1** rather than the merocyanine form **2**.

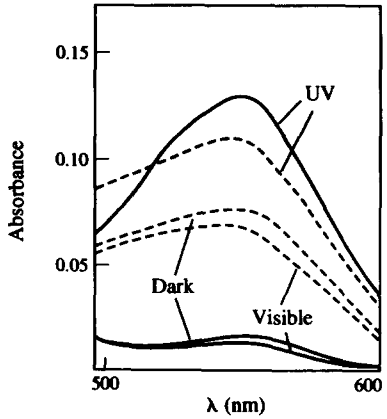

Fig. 1. Photochromic properties of compound **4**: – – – –, **4a** in THF; ——, **4b** in acetonitrile; both at 10^{-5} M and [Li^+] at 0·2 M; see text for details of exposure regimes.

Initial studies in the crowned series were with the known unsubstituted spiropyran **4a**.[4,5] In the absence of metal ions this exhibited photochromic properties very similar to those of the model system **1a**. Addition of Li^+ (up to 20 000× 0·2M tetrahydrofuran) in the dark caused an immediate shift to the open form (*c.* 50%) (Fig. 1); further addition of Li^+ had little effect on the dark equilibrium. Irradiating with UV light caused a moderate increase in the amount of open form present, while irradiation with visible light only effected a shift back to the 'dark' equilibrium position. With acetonitrile as solvent more of the open form was observed under all conditions. Compared with the behaviour of the parent spiropyran **1a**, the lithium cations, as expected, moved the photochromic equilibrium well over to the open merocyanine form, the thermodynamically more stable isomer; visible light was insufficient to reverse this effect. These observations are consistent with those reported previously.[4,6]

As argued above, the presence of an electron withdrawing group *para* to the indolic nitrogen atom, namely at position 5', as in **4b**, should counteract this tendency towards ring-opening. In the absence of Li^+ cations, the spiropyran **4b** showed virtually no photochromic behaviour (Table 1). Upon addition of Li^+ only a very small shift to the coloured form occurred in the dark but photochromic behaviour was observed, with the formation of an absorption at λ_{max} 550 nm, after exposure to UV light; this was completely reversed by exposure to visible light (Fig. 1). Since the presence of Li^+ cations had no effect when using the uncrowned spiropyran **1b**, they must help to stabilise the formation of the coloured merocyanine isomer by chelation to the aza-crown group. The effect of Li^+ ions could be 'titrated'; after exposure to UV light, little effect was observed until the Li^+ concentration exceeded 10·3 M (Fig. 2). The

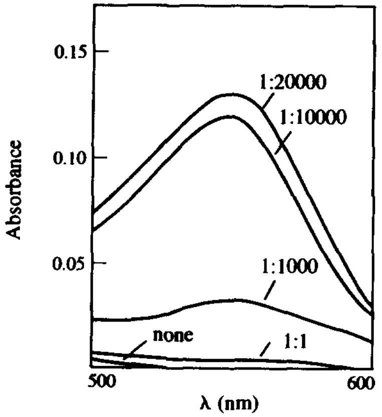

Fig. 2. Change in UV behaviour of **4b**, at 10^{-5} M, on addition of Li^+; acetonitrile solutions, molar ratios of Li^+ given.

estimated binding constant for chelation by the merocyanine form is thus in the region of $\geq 10^2$ times that of the closed form.

As expected, the presence of water attenuates the photochromic behaviour of **1c** and, in 1 : 1 aqueous acetonitrile in the presence of Li^+, only about 40% of the merocyanine formed on irradiation with UV light, although this was again reversed with visible light.

The trifluoromethyl derivative **4c** exhibited photochromic properties similar to, but less pronounced than, those of **4b**. In the absence of cations this shows a partial tendency to open (see Table 1) but, either thermally or in the presence of visible light, this was reversed to give the closed form. Addition of Li^+ caused a larger shift to the open form than that observed with **1c**, although the equilibrium could be reversibly shifted in either direction by exposure to UV and visible light.

Important trends were established using the reference cations Na^+ and K^+. For both **1c** and **1d** only relatively small perturbations were observed with either of these ions; this contrasts with the behaviour in the presence of Li^+, which supports the selectivity for the latter (Table 1, absorption ratios). Our results, and the ^{7}Li NMR results and ion extraction results reported by Kimura *et al.*[4-6] support the explanation involving specific binding of the aza-crown to these cations, which is stronger in the merocyanine form **6** than in the colourless closed form **7** (Scheme 1). Figure 1 illustrates the improvement in the photochromic properties of these systems that can be obtained by the inclusion of the appropriately sited electron withdrawing group. Thermal conversion of the coloured form to the dark equilibrium position was observed, although these processes were relatively slow at room temperature; further work to quantify these effects is in progress.

Larger changes in the equilibrium positions of **4b** were induced by divalent cations such as Ca^{2+}, Mg^{2+} and Ba^{2+}. In particular, Mg^{2+} and Ba^{2+} ions converted compounds **4b** and **4c** into photochromically reversible systems. It is likely that, under the aprotic conditions used, this is also due to the formation of chelates between the substrates and the cations, although further work is required to prove this hypothesis.

These results allow for both an essentially clean switching 'on' and 'off' of metal chelation by exposure to a light cycle, using the substituted systems **4b** and **c**, as compared with the partial effects reported for the unsubstituted indolenine derivative **4a**.

3 EXPERIMENTAL

Preparation of the indolenines **1a–c** was as described previously.[12]

The crowned indolenines **4a–c** were prepared following the method described by Kimura *et al.*[5]

1′,3′,3′-Trimethyl-6-nitro-8-[10-(1,4,7-trioxa-10-azacyclododecyl)methyl]-spiro[2H-1-benzopyran-2,2′-indolenine] **1a**, showed m.p. 134°C (lit.[5] 134°C), m/z 509 (M^+ 100%), 464 (10), 408 (30), 336 (35), 158 (25).

1′,3′,3′-Trimethyl-5′,6-dinitro-8-[10-(1,4,7-trioxa-10-aza-cyclododecyl)-methyl]spiro[2H-1-benzopyran-2,2′-indolenine] **1b** was obtained by the condensation of 2-methylene-1,3,3-trimethyl-5-nitro-indolenine,[14] **11** (X = NO_2), with the crowned salicylaldehyde[5] **10** in refluxing ethanol. The title product was obtained in 14% yield, m.p. 139–140°C, as a tan coloured powder; ν_{max} ($CHCl_3$) 2950, 1650, 1610, 1515, 1320 cm^{-1}; δ_H ($CDCl_3$) 8·6–6·2 (5H, m, Ar-H), 7·0 and 5·80 (2H, d, J 10·3 Hz, CH=CH), 4·7 (2H, broad s, $ArCH_2N$), 4·6 (8H, broad s, OCH_2), 4·5 (4H, m, OCH_2CH_2N), 3·8 (3H, s, NCH_3), 3·6 (4H, m, NCH_2CH_2O), 2·33 (3H, s, CH_3), 2·20 (3H, s, CH_3); m/z (%) 355 (M^+ 174, 100). Found: C, 58·6; H, 6·1; N, 9·7% ($C_{28}H_{34}N_4O_8H_2O$ requires C, 58·7; H, 6·3; N, 9·8%).

5′-Trifluoromethyl-1′,3′,3′-trimethyl-6-nitro-8-[10-(1,4,7-trioxa-10-aza-cyclododecyl)methyl]spiro[2H-1-benzopyran-2,2′-indolenine] **1c** was obtained by the condensation of 5-trifluoromethyl-2-methylene-1,3,3-trimethylindolenine,[15] **11** (X = CF_3) with the crowned salicylaldehyde **10** in refluxing ethanol. The title product was obtained in 90% yield, as an amorphous yellow solid, ν_{max} ($CHCl_3$) 3000–2800, 1615, 1515, 1325 cm^{-1}; δ_H 9·5–7·5 (5H, m, Ar—H), 6·70 and 5·85 (2H, d, J 10·6 Hz, CH=CH), 4·6 (8H, broad s, OCH_2CH_2O), 4·40 (2H, s, $ArCH_2N$), 4·40 (4H, m, OCH_2CH_2N), 3·70 (3H, s, NCH_3), 3·60 (4H, broad s, OCH_2CH_2N), 2·25 (3H, s, CH_3), 2·20 (3H, s, CH_3); m/z (%) 577 (M^+ 38), 226 (100). Found:

C, 56·3; H, 5·50, N, 6·5% ($C_{29}H_{34}F_3N_3O_6H_2O$ requires C, 56·7; H, 6·2; N, 6·85%).

The photochromic properties of these compounds were explored by making up solutions in the dark in freshly dried and redistilled solvents, generally tetrahydrofuran and acetonitrile. Perchlorate salts were dried over P_2O_5 for several days before use. Solutions were placed in a stoppered 1 cm cuvette at room temperature (20–23°C) and allowed to equilibrate for 1 h before measurement of their UV/visible absorption curves (dark curves). The solutions were then irradiated with UV light from a steady power source for 1 min. The UV light source was a 200 W mercury–xenon lamp, focussed in a LOT-Oriel air-cooled lamp housing, with filters to remove light <300 nm and >500 nm. The UV absorption was measured (UV curve) then the cuvette was exposed to a visible light source for 3 min, using a 100 W tungsten spotlight, and the UV absorption spectrum (visible curve) remeasured. The solutions were recycled a second time to ensure reproducible results were obtained.

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