Spectroscopic detection of diols and sugars by a colour change in boronic acid-appended spirobenzopyrans

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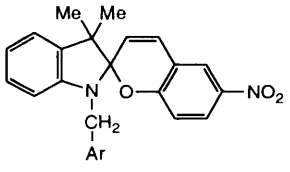
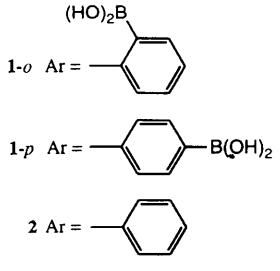
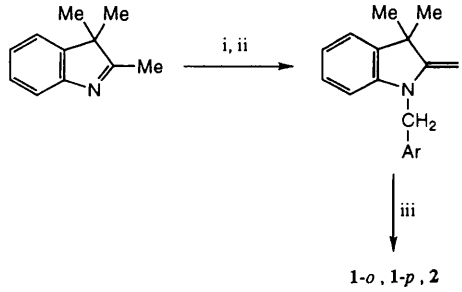
Boronic acid-appended spiropyrans have been synthesized in order to detect diols and sugars by a colour change: only when the boron atom could intramolecularly interact with the tertiary amine in the spiropyran moiety, did added diols and sugars change the shift of the spiropyran–merocyanine equilibrium, which was visually detectable as a colour change.

Spiropyran (SP) derivatives undergo reversible solvatochromic and photochromic isomerization to the corresponding zwitterionic merocyanine (MC) form. Because of their unique physical and chemical properties, extensive studies have been devoted to their applications in the photocontrol of membrane transport,[1,2] membrane potentials,[3–6] polymer rheology,[7,8] metal-sensing,[9,10] *etc.* We recently found that boronic acid derivatives are very useful in capturing diols and sugars in aqueous solution and the tertiary amine frequently exerts a crucial effect on the binding process through the boron–amine interaction.[11] We noticed that SP–MC interconversion occurs with the appearance and disappearance of a tertiary amine in the spiropyran ring. This gave us the idea that if a boronic acid group is introduced into the appropriate position where the boronic acid can intramolecularly interact with the tertiary amine, it follows that diol- and sugar-binding processes would be controlled in conjugation with SP–MC interconversion. With these objects in mind we synthesized **1**-*o* for which the boron–nitrogen interaction is expected and **1**-*p* for which it is not. Compound **2** was used as a reference compound without such sugar-binding functions.





† **1**-*o*: mp 193–194 °C; ν_{max}/cm^{-1} 3400 (OH), 1510 (NO) and 1340 (BO); δ_H(250 MHz; [$^2H_6$]DMSO; Me_4Si; 25 °C) 1.24 (6 H, s, Me), 4.47 (2 H, q, NCH_2), 6.03 and 6.24 (1 H each, d each, CH=CH), 6.76–8.18 (11 H, m, ArH) and 8.11 [2 H, s, $B(OH)_2$] (Found: C, 68.0; H, 5.0; N, 6.4. $C_{25}H_{23}N_2O_5$ requires C, 67.88; H, 5.24; N, 6.33%). **1**-*p*: mp (decomp.) 280 °C; ν_{max}/cm^{-1} 3400 (OH), 1510 (NO) and 1330 (BO); δ_H(250 MHz; [$^2H_6$]DMSO; Me_4Si; 25 °C) 1.25 (6 H, s, Me), 4.30 (2 H, q, NCH_2), 6.10 and 6.24 (1 H each, d each, CH=CH), 7.23–8.21 (11 H, m, ArH) and 8.01 [2 H, s, $B(OH)_2$] (Found: C, 68.4; H, 5.3; N, 6.1. $C_{25}H_{23}N_2O_5 \cdot 0.1C_6H_{14}$ requires C, 68.18; H, 5.52; N, 6.21%). **2**: mp 156–158 °C; ν_{max}/cm^{-1} 1510 (NO); δ_H(250 MHz; $CDCl_3$; Me_4Si; 25 °C) 1.30 and 1.34 (3 H each, s each, Me), 4.35 (2 H, q, NCH_2), 5.92 and 6.35 (1 H each, d each, CH=CH) and 7.23–8.21 (12 H, m, ArH) (Found: C, 74.7; H, 5.6; N, 6.9. $C_{25}H_{22}N_2O_3 \cdot 0.2H_2O$ requires C, 74.67; H, 5.63; N, 6.97%).



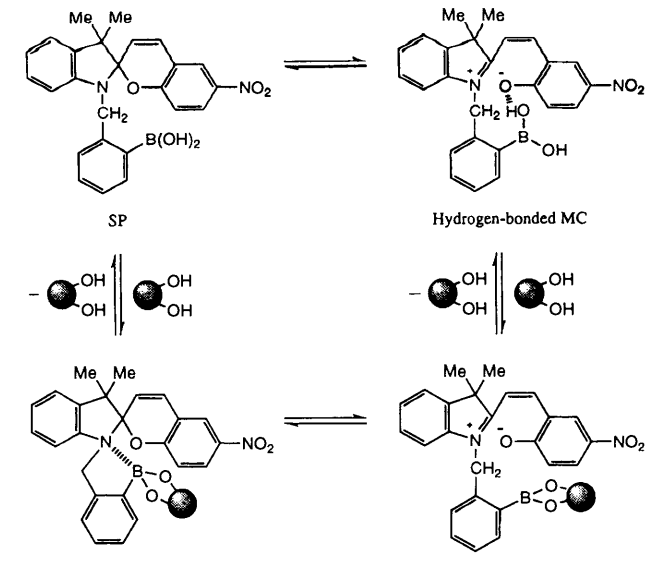
Scheme 1 *Reagents and conditions:* i, $ArCH_2Br$, MeCN, reflux; ii, NaOH, H_2O, room temp.; iii, 5-nitrosalicylaldehyde, EtOH, reflux

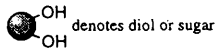
These compounds were synthesized according to Scheme 1 and identified by IR and ^1H NMR spectral evidence and elemental analyses.†

First, we examined the solvent effect on the SP–MC equilibria. In solution they gave a purple colour assignable to the MC form (in acetonitrile, λ_{max} 552 nm for **1**-*o*, 570 nm for **1**-*p* and 552 nm for **2**) and the absorbance increased with increasing solvent polarity: *e.g.* the absorbance was linearly correlated with $E_T(30)$. When compared in acetonitrile, the absorbance increased in the order of **1**-*o* (ε_{552} = 470) > **1**-*p* (ε_{570} = 240) > **2** (ε_{552} = 240 dm^3 mol^{-1} cm^{-1}). Although the reason for this order is not clear, we believe that the hydrogen-bonding interaction between the boronic acid and the phenolate anion stabilizes the MC form in **1**-*o* (Scheme 2). As shown in Fig. 1, the MC band in **1**-*o* was scarcely affected by the addition of mono-ols, but decreased markedly with increasing diol concentrations. Such a spectral change induced by diols was not observed for **1**-*p* (except with catechol)‡ and **2** (Fig. 2). The results indicate that diols bound to the boronic acid in **1**-*o* can push the equilibrium to the SP form. It is already established that the acidity of boronic acids is intensified through diol complexation. In the present system the boron–nitrogen interaction is possible only in the SP form of **1**-*o*. One can thus conclude that in the presence of diols the SP form is more stable owing to the effect of the stronger boron–nitrogen interaction (Scheme 2).

The MC form can be generated by UV-light irradiation. When the acetonitrile solution of **1**-*o* or **2** was photoirradiated [400 W high-pressure Hg-lamp, Toshiba UV-D35 filter (290 < λ/nm < 400)], the solution reached the photostationary

‡ As shown in Fig. 2, the MC fraction in **1**-*p* is not affected by the addition of diols, but decreases only in the presence of catechol. The most likely rationale for the exceptional behaviour of catechol is the intermolecular boron–nitrogen interaction which becomes possible, for example, when the **1**-*p*–catechol complex forms a dimer. To corroborate this hypothesis we repeated the plot in Fig. 2 at different **1**-*p* concentrations. The result showed that the MC fraction decreases with increasing **1**-*p* concentration. The finding is in line with the above-mentioned hypothesis.





Scheme 2

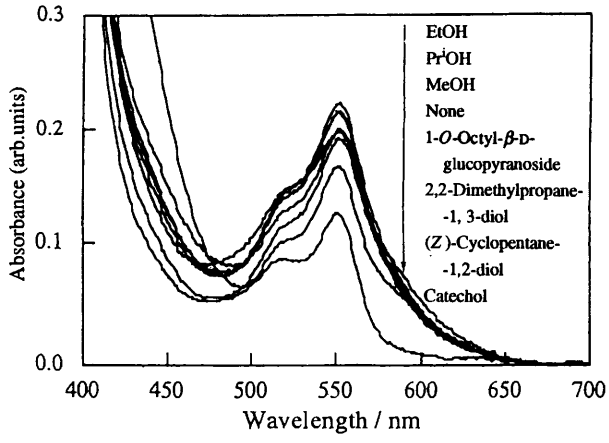


Fig. 1 Absorption spectra changes of **1**-*o* (5.0×10^{-4} mol dm^{-3}) by added diol or sugar (0.10 mol dm^{-3}) in acetonitrile at 25 °C

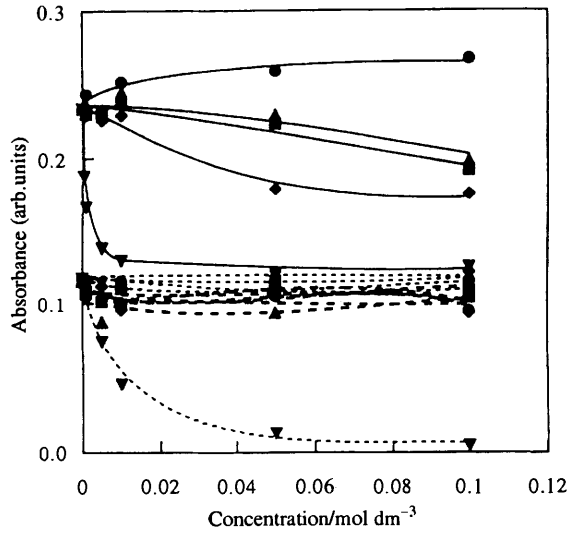


Fig. 2 Plots of A_{552} (**1**-*o* and **2**) or A_{570} (**1**-*p*) *vs.* diol or sugar concentration in acetonitrile at 25 °C: [**1**-*o*] = [**1**-*p*] = [**2**] = 5.0×10^{-4} mol dm^{-3}; ● EtOH, ▲ 1-*O*-octyl-β-D-glucopyranoside, ■ 2,2-dimethylpropane-1,3-diol, ◆ (*Z*)-cyclopentane-1,2-diol, ▼ catechol. **1**-*o*, **1**-*p* and **2** are shown by solid lines, dotted lines and bold dotted lines, respectively.

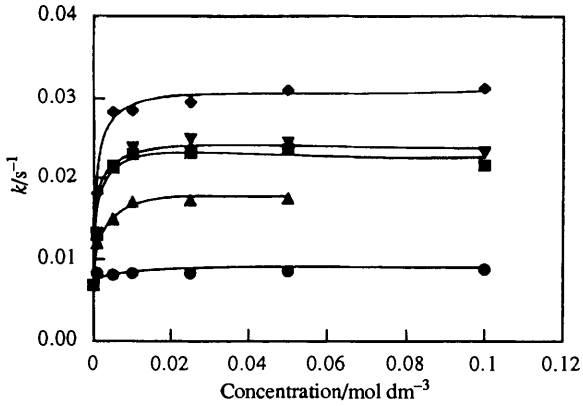


Fig. 3 Plots of k *vs.* diol or sugar concentration in acetonitrile at 25 °C; [**1**-*o*] = 5.0×10^{-4} mol dm^{-3}; ● pinacol, ▲ 1-*O*-octyl-β-D-glucopyranoside, ■ 2,2-dimethylpropane-1,3-diol, ◆ (*Z*)-cyclopentane-1,2-diol, ▼ propane-1,3-diol

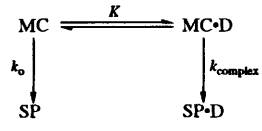
Table 1 K and $k_{complex}$ for diols and sugar with **1**-*o*

Diols and sugar	K/dm^{-3} mol^{-1}	$k_{complex}/10^{-2}$ s^{-1}
None	—	(k_0 = 0.68)
Pinacol	*ca.* 50[a]	*ca.* 0.70[a]
1-*O*-Octyl-β-D-glucopyranoside	470	1.84
Propane-1,3-diol	520	2.59
2,2-Dimethylpropane-1,3-diol	510	2.44
(*Z*)-Cyclopentane-1,2-diol	850	3.16
Catechol	*ca.* 8.0×10^3[b]	*ca.* 7.00[b]

[a] The absorbance change induced by the pinacol addition was so small that we could not determine these parameters precisely. [b] The kinetic process was so fast that we could not determine these parameters precisely.

state in 20 min. In the dark this band decreased following first-order kinetics as the thermodynamic equilibrium was approached. As shown in Fig. 3, the first-order rate constant k increased with increasing diol concentrations giving further support for the diol-bound SP being more stable than SP, owing to the strengthened boron–nitrogen interaction. The stabilization of the final state should accelerate the thermal reaction from MC to SP. On the other hand, the value of k for **2** was scarcely affected by the addition of diols.

We analysed the concentration dependence according to Scheme 3. The kinetics of the reaction system shown in Scheme



MC: merocyanine form
SP: spiropyran form
D: diol or sugar

Scheme 3 §

3 can be expressed as $k_0/(k_0 - k) = (qK[\text{diol}])^{-1} + q^{-1}$ where k_0 and K are the first-order rate constant in the absence of diol and the association constant for MC (= [MC–diol]/[MC]-[diol]), respectively, and q is $1 - (k_{complex}/k_0)$.[12] The plots

§ Here, there are two possibilities: (*i*) the rate-determining conversion of MC to MC–D followed by the fast isomerization of MC–D to SP–D and (*ii*) as illustrated in Scheme 3, the fast equilibrium between MC and MC–D followed by the slow conversion of MC–D to SP–D. We have found that the complexation equilibria between diols and boronic acids are very fast. Furthermore, it is hardly conceivable that the absorbance change is observed for the conversion of MC to MC–D because the absorption spectra of these two species should be similar. These considerations support the view that (*ii*) is the mechanism occurring in the present system.

showed a good linear relationship, from which the K and $k_{complex}$ values were estimated. Examination of Table 1 reveals that there exists one general rule which governs the effect of added diols on the SP–MC equilibrium, *i.e.* the diol which can efficiently reduce the MC absorbance in Fig. 2 possesses large K and $k_{complex}$ values. This means that when the more stable boronate complex is formed between **1**-*o* and diol, the boron atom becomes more acidic and the SP form is stabilized by the intensified boron–nitrogen interaction. The largest effect is observed with catechol. It is difficult to find a general rule governing the correlation between the diol structure and the boronic acid affinity. We noticed from examination of Table 1, however, that the diol which has two OH groups preorganized into the *cis* orientation shows a high boronic acid affinity.

In conclusion, the present study shows that the concentration of diols and sugars can be detected by a colour change in the SP–MC equilibrium of boronic acid-appended spirobenzopyrans. Also significant is the control of the isomerization rate by these compounds. As described in the introduction, the SP–MC equilibrium is a potential chromism with a number of practical applications. We believe that these functions are efficiently controlled by diols and sugars and the facile sensing using the colour change becomes possible.

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