Synthesis of photochromic 6′-sulfanyl substituted-spiro[indoline-naphthoxazines]

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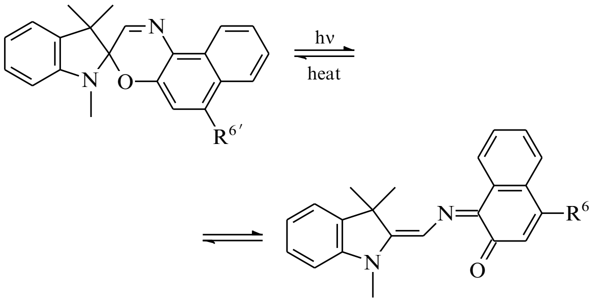
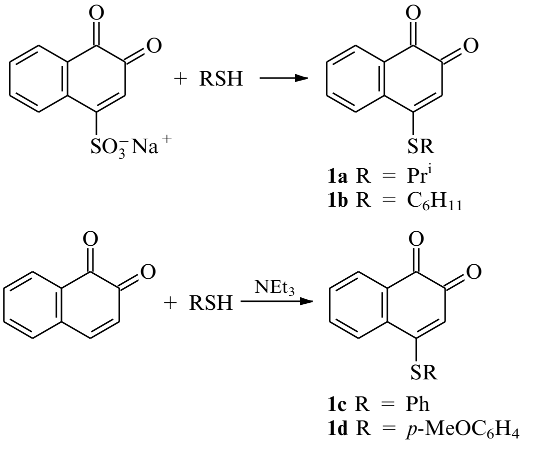
The unexpected synthesis of photochromic spiro{indoline-naphth[1,2-*b*]oxazines} in high-yield during the reaction of Fisher's base with mixture of oximes of 4-sulfanyl substituted-1,2-naphthoquinones is described.

Photochromic compounds can be considered as reversible potential dyes under light induction (Scheme 1). The spiro[indoline-naphthoxazine] series presents a good compromise between photochromic properties (colour efficiency, stability of the coloured open form and resistance towards photodegradation), giving rise to fundamental and technological interests.[1,2] We have investigated the substitution of the 6′-position by an alkyl- (or aryl-) sulfanyl group, this position being one of the most efficient in the modulation of photochromic parameters, particularly on the absorption wavelength.[3,4]



Scheme 1 Photochromic equilibrium in the spironaphthoxazine series.

Two approaches were developed for the synthesis of thiosubstituted naphthoquinones **1a**–**d** (Scheme 2).

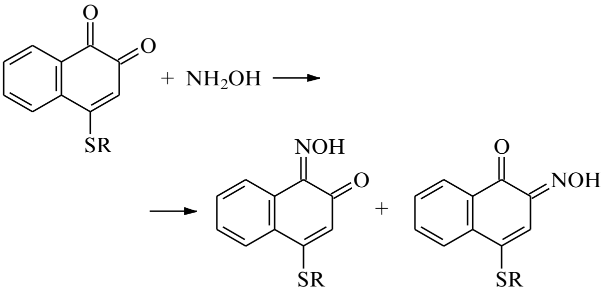


1a R = Pr^i
1b R = C_6H_{11}

1c R = Ph
1d R = *p*-$MeOC_6H_4$

Scheme 2 Synthesis of 4-alkyl- (aryl-) sulfanyl substituted 1,2-naphthoquinones.

The oximation of 1,2-naphthoquinones **1a**–**d** with hydroxylamine hydrochloride in pyridine gave the corresponding oximinonaphthoquinones (Scheme 3). This reaction was not regioselective, and both the 1- and 2-oximinonaphthoquinones were obtained.



2a R = Pr^i
2b R = C_6H_{11}
2c R = Ph
2d R = *p*-$MeOC_6H_4$

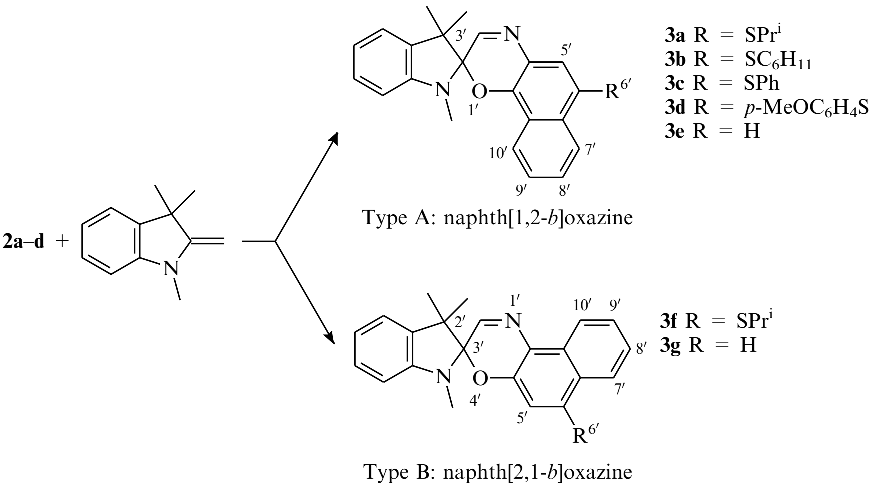
Scheme 3 Oximation of 1,2-naphthoquinones.

The regioselectivity of the reaction was investigated by ^1H NMR, and the 2-oximinonaphthoquinone was found to be the major isomer (2-oximinonaphthoquinone : 1-oximinonaphthoquinone = 75 : 25; 80 : 20; 90 : 10; 90 : 10, respectively for **2a**, **2b**, **2c** and **2d**).

The oximinonaphthoquinones were obtained as an unseparable mixture and were directly used to undergo a condensation reaction with 2-methyleneindoline. In general, the condensation of the latter with 2-oximinonaphthoquinones is much less effective than the condensation with the 1-oximinonaphthoquinone, and the formation of type B spiro{indoline-naphth[2,1-*b*]oxazines} was expected (Scheme 4).

In all the condensation experiments the formation of a major product was effectively observed. Small amounts of a by-product were detected (about 15% according to the NMR spectra) when R = C_6H_{11} and Pr^i. The latter substitution compound was isolated and characterized. The comparative ^1H NMR analysis of both compounds obtained for R = Pr^i and the comparison with the spectra of the unsubstituted spirooxazine **3e** and **3g** allow us to assign (unexpectedly) a type A structure to the major compound (**3a**) and the type B structure to the minor compound (**3f**). The main difference observed in the ^1H NMR spectra of **3a** and **3f** is related to the 5′-hydrogen atom (δ 7.83 for **3a** and δ 7.11 for **3f**). These values are more compatible with those measured in the case of spiro{indoline-naphth[1,2-*b*]oxazine} (type A, δ 7.40 for **3e**). As a matter of fact, the chemical shifts observed generally for spiro{indoline-naphth[2,1-*b*]oxazine} (type B) range from δ 6.4–7.5 when the naphtho moiety is substituted in the 6′-position by electron releasing groups[3,5] or electron withdrawing groups,[4] respectively.

Moreover, evidence for the validity of the proposed structures was given by X-ray analysis for compounds **3a** and **3b** (Figures 1, 2).[†] Indoline and naphthoxazine fragments of molecules **3a** and **3b** are nonplanar and orthogonal to each other [bending angles N(2)···C(20) = 25.6° (**3a**), 28.2° (**3b**),



Scheme 4 Synthesis of sulfanyl substituted-spironaphthoxazines.

O(1)···C(2) = 12.1(1)° (**3a**), 16.9(2)° (**3b**), O(1)···N(1) = 7.0(1)° (**3a**), 8.5(2)° (**3b**)]. Orientation of the sulfanyl substituents is characterized by the torsion angles C(6)C(7)S(1)C(23) 55.6(1)° (**3a**) and 33.7(1)° (**3b**).

The photochromic characteristics (colourability A_0, fading rate constant k_Δ and absorption wavelength $\lambda_{\max}$) were measured by flash photolysis coupled to a fast spectrometer.[6] Results obtained for spironaphthoxazines of type A and B are summarized in Table 1.

For naphth[1,2-*b*]oxazines (type A), substitution by an alkyl- (or aryl-) sulfanyl group involved a large increase in the colourability (compared to the values obtained with compound **3e**). Moreover, a bathochromic shift of about 20 nm for all the sulfanyl substituted compounds was observed.

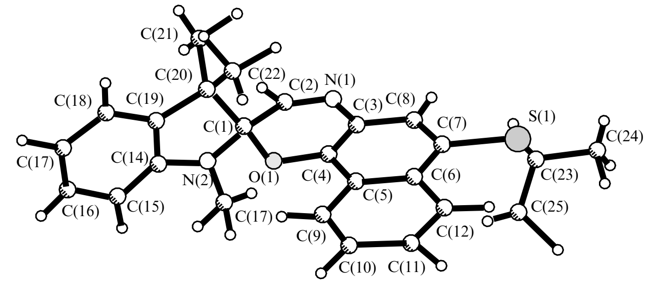


Figure 1 Ortep II drawing of the molecule **3a** with thermal ellipsoids of 50% probability.

Table 1 Spectrokinetic parameters of spironaphthoxazines **3a**–**g** (unsubstituted compounds **3e** and **3g** are given as reference).

Compound **3**	A_0	k_Δ/s^{-1}	$\lambda_{\max}$ (sh)/nm
a	1.07	0.23	600 (628)
b	0.90	0.19	(415) 611
c	1.18	0.17	(412) 603 (640)
d	1.05	0.26	602 (635)
e	0.18	0.95	580 (612)
f	3.20	0.18	(554) 588
g	1.08	0.54	(564) 594

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† *Crystal data* for **3a**: $C_{25}H_{27}N_2OS$, monoclinic, space group $P2_1/c$, $a = 12.411(2)$, $_3$ $b = 13.790(3)$, $c = 12.831(3)$ A, $\beta = 95.02(3)°$, $V = 2187.6(8)$ A , $D_c = 1.222$ g cm^{-3}, $Z = 4$. The intensities of 2529 reflections (963 observed): I_{hkl} were measured on a KM-4 diffractometer (graphite monochromated λMo-Kα, $\lambda = 0.71069$ nm) using the $\theta/2\theta$ scan technique ($2\theta < 44°$). The structure was solved by direct methods and refined by a full-matrix least-squared method in an anisotropic approximation for all atoms. The final R_F was 0.035 for 963 reflections.

3b: $C_{28}H_{30}N_2OS$, monoclinic, space group $P2_1/c$, $a = 15.366(3)$, $b = 11.926(2)$, $c = 13.514(3)$ A, $\beta = 106.16(3)°$, $V = 2378.7(8)$ A , $D_c = 1.236$ g cm^{-3}, $Z = 4$. The intensities of 4295 reflcections (2451 observed): I_{hkl} were measured on a KM-4 diffractometer (graphite monochromated λMo-Kα, $\lambda = 0.71069$ nm) using the $\theta/2\theta$ scan technique ($2\theta < 54°$). The structure was solved by direct methods and refined by a full-matrix least-squared method in an anisotropic approximation for all atoms. The final R_F was 0.050 for 2451 reflections.

All calculations were performed on IBM PC using SHELX software. Full lists of bond lengths, bond angles, atomic coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Notice to Authors', *Mendeleev Communications*, 1996, Issue 1. Any request to the CCDC for data should quote the full literature citation and the reference number 1135/09.

‡ *Typical procedure for the oximation of 4-alkyl(aryl)sulfanyl substituted-1,2-naphthoquinones.* 4-Isopropylsulfanyl-1,2-naphthoquinone[7] (0.93 g, 4 mmol) was dissolved in 20 ml of pyridine–ethanol (80 : 20), and a solution of hydroxylamine hydrochloride (0.31 g, 4.5 mmol) in the same solvent (20 ml) was added dropwise. The reaction mixture was heated for 2 h at 80 °C, and the solvent removed *in vacuo*. The residue was subjected to column chromatography on silica gel eluting with dichloromethane–ethyl acetate (70 : 30). The product was obtained as an unseparable mixture of 1- and 2-oximino naphthoquinone isomers. Global yield 30%.

§ *Typical procedure for the synthesis of spironaphthoxazines* **3a**–**g**. A solution of 4-isopropylsulfanyl-1- and 2-oximino-naphthoquinones (1 g, 4 mmol) in trichlorethylene (20 ml) was refluxed for 2 h. The solvent was removed *in vacuo* and the residue was subjected to column chromatography on silica using hexane–ethyl acetate (70 : 30) as eluent. Total yield 30%.

¶ 6′-Isopropylsulfanyl-1,3,3-trimethylspiro{indoline-2,3′-[3*H*]naphth-[2,1-*b*][1,4]oxazine} **3f**: yield 4.5%, mp 111–112 °C; δ_H (250 MHz; CDCl$_3$) 1.27–1.35 [d, 12H, CH(C*H*$_3$)$_2$ and C(CH$_3$)$_2$]; 2.77 (s, 3H, NCH$_3$); 3.46 [m, 1H, C*H*(CH$_3$)$_2$, *J* 6.7 Hz]; 6.58 (d, 1H, H$_7$, *J* 8.2 Hz); 6.91 (dd, 1H, H$_5$, *J* 7.4 Hz); 7.09 (d, 1H, H$_4$); 7.11 (s, 1H, H$_5$); 7.23 (ddd, 1H, H$_6$ *J* 7.7, 1.2 Hz); 7.43 (ddd, 1H, H$_{8'}$, *J* 6.8, 1.3 Hz); 7.59 (d, 1H, H$_{g'}$, *J* 6.9, 1.2 Hz); 7.72 (s, 1H, H$_{2'}$); 8.27 (d, 1H, H$_{7'}$, *J* 8.5 Hz); 8.58 (d, 1H, H$_{10'}$, *J* 8.1, 0.5 Hz); δ_C (62.5 MHz; CDCl$_3$) 20.9; 25.5 [2q, C(*C*H$_3$)$_2$]; 23.2 [q, CH(*C*H$_3$)$_2$]; 30.0 (q, NCH$_3$); 37.7 [d, *C*H(CH$_3$)$_2$]; 52.0 (s, C$_3$); 99.2 (s, C$_2$); 107.2 (d, C$_7$); 119.9 (d, C$_5$); 121.5 (d, C$_4$); 122.0 (d, C$_{10'}$); 124.3 (d, C$_{9'}$); 125.0 (d, C$_{7'}$); 127.3 (d, C$_{8'}$); 128.0 (d, C$_6$); 150.3 (d, C$_{2'}$).

6′-Isopropylsulfanyl-1,3,3-trimethylspiro{indoline-2,2′-[2*H*]naphth-[2,1-*b*][1,4]oxazine} **3a**: yield 25.5%, mp 124–126 °C. After chromatography, the product was recrystallized from methanol; δ_H (250 MHz; CDCl$_3$) 1.29 [d, 6H, CH(C*H*$_3$)$_2$, *J* 6.7 Hz]; 1.35–1.36 [s, 6H, C(CH$_3$)$_2$]; 2.77 (s, 3H, NCH$_3$); 3.46 [m, 1H, C*H*(CH$_3$)$_2$, *J* 6.7 Hz]; 6.58 (d, 1H, H$_7$; *J* 7.7 Hz); 6.91 (dd, 1H, H$_5$, *J* 7.4 Hz); 7.09 (d, 1H, H$_4$, *J* 6.3 Hz); 7.23 (dd, 1H, H$_6$, *J* 7.6, 1.2 Hz); 7.38 (dd, 1H, H$_{8'}$, *J* 8.2, 1.1 Hz); 7.53 (dd, 1H, H$_6$, *J* 7.6, 1.2 Hz); 7.70 (s, 1H, H$_{3'}$); 7.83 (s, 1H, H$_{5'}$); 8.01 (d, 1H, H$_{7'}$, *J* 8.1 Hz); 8.45 (d, 1H, H$_{10'}$, *J* 8.5 Hz); δ_C (62.5 MHz; CDCl$_3$) 23.5 (q, CH$_3$); 23.5 (q, CH$_3$); 25.7 (q, CH$_3$); 29.8 (q, NCH$_3$); 39.6 [d, *C*H(CH$_3$)$_2$]; 51.8 (s, C$_3$); 99.4 (s, C$_2$); 107.3 (d, C$_7$); 119.9 (d, C$_5$); 121.5 (d, C$_4$); 122.3 (d, C$_{7'}$); 125.8 (d, C$_{8'}$); 126.3 (d, C$_{10'}$); 127.6 (d, C$_{9'}$); 128.0 (d, C$_6$); 133.4 (d, C$_{5'}$); 152.5 (d, C$_{3'}$).

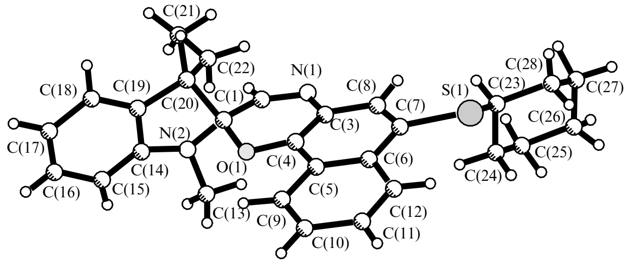

Figure 2 Ortep II drawing of the molecule **3b** with thermal ellipsoids of 50% probability.

For naphth[2,1-*b*]oxazine (type B), spironaphthoxazine **3f** exhibits also a good value of colourability, which is 3 times increased (compound **3g** being kept as the reference). Substitution by an isopropylsulfanyl group involves, in the case of **3f**, a slight hypsochromic shift of about 6 nm.

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