Synthesis and structure of spirooxazines of the thieno[3,2-b]pyrroline series

Valerii Z. Shirinian[a], Mikhail M. Krayushkin[a*], Denis M. Nikalin[a], Alexey A. Shimkin[a], Lyudmila G. Vorontsova[a], and Zoya A. Starikova[b]

[a] N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp., 47, 119991 Moscow, Russian Federation
[b] A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 117813 Moscow, Russian Federation
E-mail: mkray@mail.ioc.ac.ru

Abstract

A series of spironaphthoxazines based on thieno[3,2-b]pyrroline derivatives were synthesized and their structures were studied by ^{1}H NMR spectroscopy, mass spectrometry, and X-ray diffraction. Comparative analysis of the spatial structures of spirooxazines of the thieno[3,2-b]pyrroline and indoline series was performed.
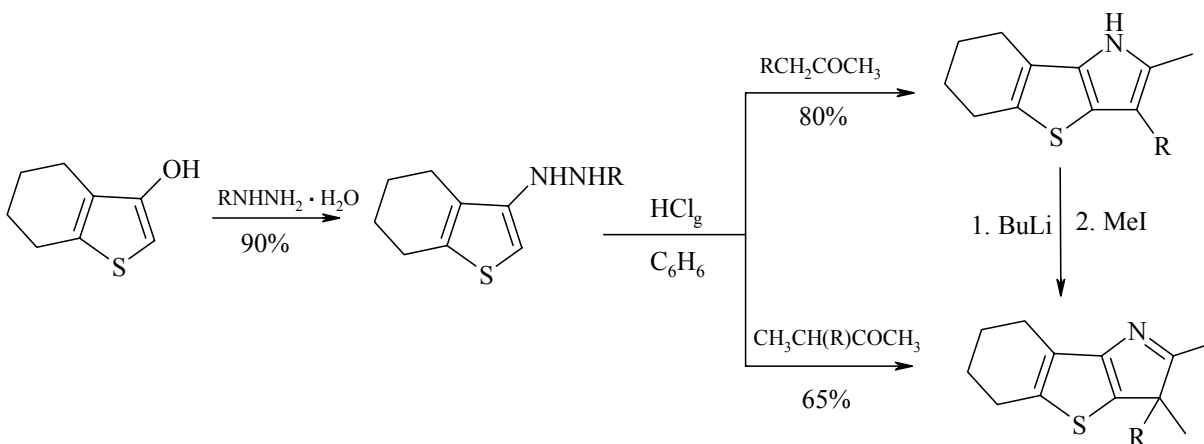
Keywords: Thieno[3,2-b]pyrroles, spirooxazines, Fischer reaction, thieno[3,2-b]pyrrolenines, X-ray diffraction analysis, Fischer's salt

Introduction

Organic photochromes are widely used in various fields of science and engineering, in particular, for the design of light filters, optically controlled molecular switches, photochromic organic media for optical information recording and processing, etc. Among various classes of photochromic substances, spirooxazines (SPO) are distinguished by high sensitivity and resolving power.[1-4] The vast majority of known spirooxazines belong to the indoline series. It appeared of interest to prepare close analogs of these compounds containing the thieno[3,2-b]pyrrole heterocyclic systems instead of the indole system. Similar replacement of the benzene ring by a less aromatic and electron rich thiophene ring in photochromic compounds can give rise to new valuable properties and induce further chemical modification of products.

Thienopyrrolenine derivatives are the key compounds for the preparation of spiropyrans and spirooxazines of the thienopyrroline series. Before our studies, only a few examples of thienopyrrolenines have been described in the literature; these were prepared in low yields from tin salts of aminothiophenes according to the Bishler reaction.[5,6] It should be noted that the starting aminothiophenes are rather unstable and difficult to obtain.

As a continuation of our studies [7-9] on the development of convenient methods for the synthesis of photochromic compounds based on thiophene derivatives, we recently elaborated effective methods for the synthesis of thienopyrroles and thienopyrrolenines according to the Fischer reaction (Scheme 1).[10,11] As the starting compounds for the synthesis of the last-mentioned products, we used readily available β-hydroxythiophene derivatives. The Fischer reaction is widely used to prepare indole and indolenine derivatives;[12-14] however, before our studies it had not been used for the synthesis of thieno[3,2-*b*]pyrrolenines.
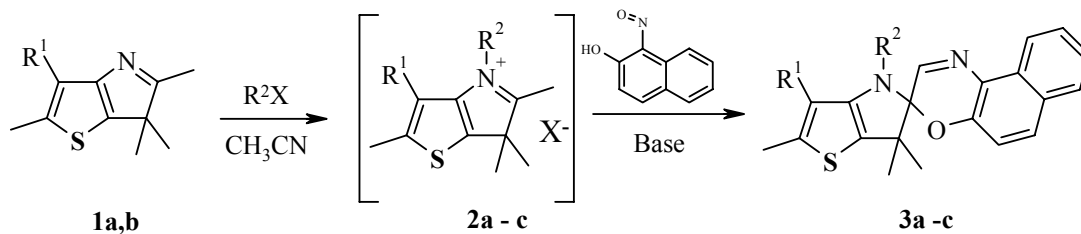

Scheme 1

This paper gives an account of the synthesis and structure of spirooxazines based on thieno[3,2-*b*]pyrrolenine derivatives.

Results and Discussion

Spirooxazines **3a-c** of the thienopyrroline series were prepared via the classical route (Scheme 2) from the appropriate thienopyrrolenines **1a,b** whose synthesis has been reported in detail.[10,11] The first stage includes refluxing of compounds **1a, b** with alkylating agents in acetonitrile to give thienopyrroline analogs of Fischer's salts **2a-c**. Due to the difficulty of purification, these quaternary salts were not characterized. The condensation of the thienopyrrolines (obtained *in*
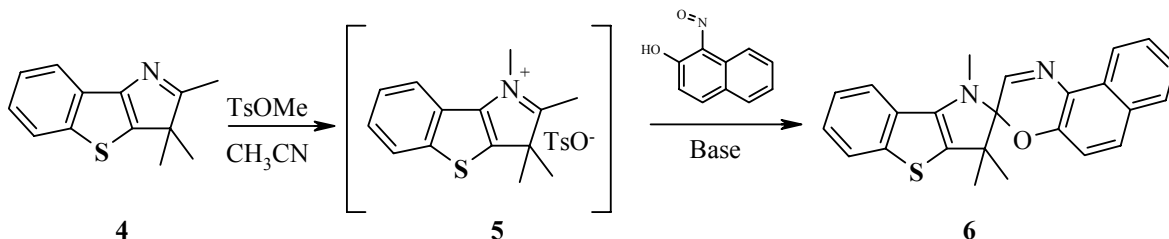
situ by treatment of these salts with bases) with 1-nitroso-2-naphthol results in the desired spirooxazines.

1a, R^1 = H; 1b, R^1 = COOMe; 2a, R^1 = H, R^2 = Me, X = TsO;
2b, R^1 = H, R^2 = Et, X = I; 2c, R^1 = COOMe, R^2 = Me, X = TfO;
3a, R^1 = H, R^2 = Me; 3b, R^1 = H, R^2 = Et; 3c, R^1 = COOMe, R^2 = Me;
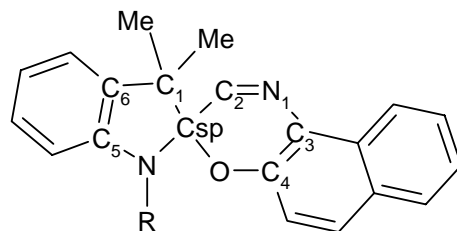
Scheme 2

Similarly, benzo[*b*]thieno[3,2-*b*]pyrrolenine **4** was converted into spirooxazine **6** (Scheme 3).

Scheme 3

The structures of the spirooxazines of the thienopyrroline series were established by ^{1}H NMR spectroscopy, mass spectrometry, and elemental analysis; those for compounds **3b** and **6** were also confirmed by X-ray diffraction. As expected, a typical feature of the ^{1}H NMR spectra is the presence of two singlets at 1.30 – 1.50 ppm, corresponding to two geminal methyl groups and a singlet at 7.6 – 7.9 ppm, typical of the imine proton of the oxazine ring.

Thienopyrroline spirooxazines have been unknown previously; therefore, it appeared pertinent to compare the spatial structures of the compounds obtained with spirooxazines of the indoline series **SPO1** and **SPO2**, whose X-ray diffraction analysis had been reported.[15,16] (To make the comparison of molecular parameters more convenient, we give a general atom numbering in Scheme 4).

SPO1. R = Me;   **SPO2.** R = (CH$_2$)$_2$COOH

Scheme 4

The general view of molecules **3b** and **6** is shown in Figs. 1 and 2. The X-ray diffraction data, the atom coordinates, and thermal and geometric parameters are deposited at the Cambridge Crystallographic Data Centre under the registration numbers 249951 (**3b**) and 249952 (**6**). Analysis of the spatial structures of these molecules shows that the key structural features resemble those of the previously studied spirooxazines.[15-18] The spiro unit is tetrahedral. The thienopyrroline fragment in compound **3b** and, correspondingly, the benzothienopyrroline fragment in molecule **6** are virtually orthogonal to the naphthoxazine fragment: the dihedral angle between the corresponding planes is ~ 89.50°. The pyrroline rings in both molecules, as in the SPO of the indoline series, have an envelope conformation. The folding angle along the N….C1 line in molecule **3b** equals 24.23°, while that in **6** is 32.15°. These data fall in the range of values found in the previously studied compounds of this type (24.1 – 39.9°).[12-16,18] The deviation of the C$_{sp}$ spiro atom in compounds **3b** and **6** from the averaged plane of atoms of the thienopyrroline (benzothienopyrroline) ring is equal to 0.348 Å (0.496 Å).
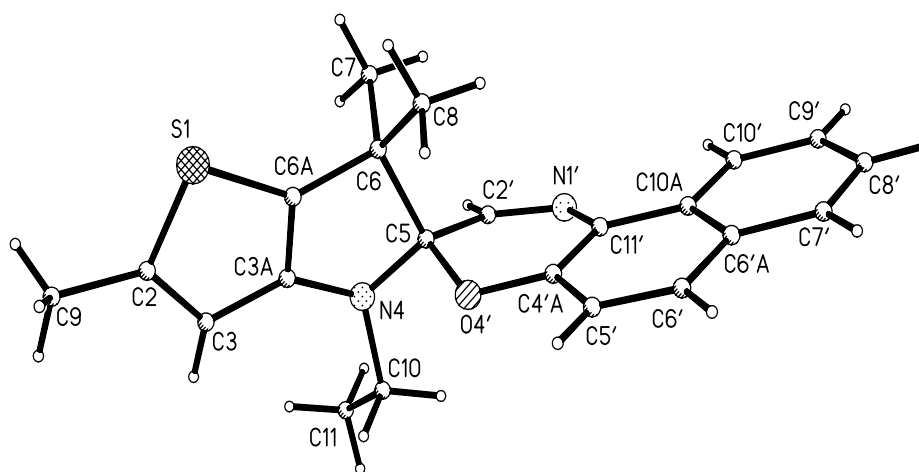

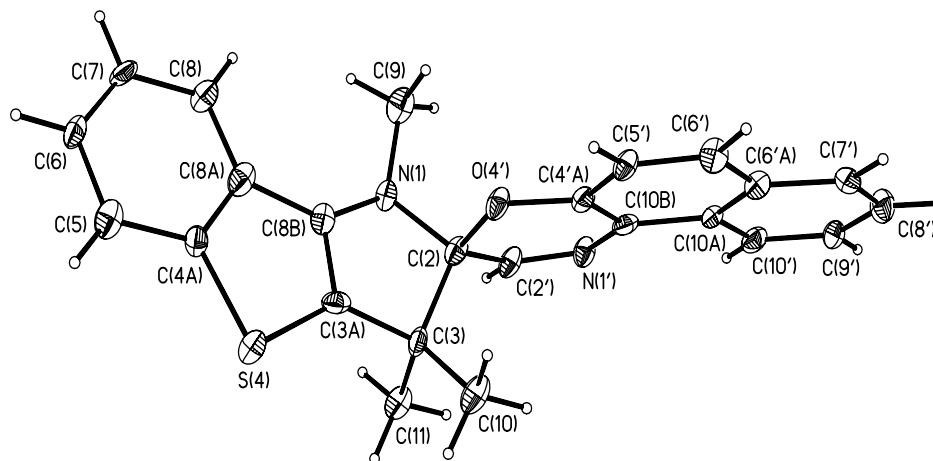**Figure 1.** Structure of molecule **3b** and atom numbering.

Figure 2. Structure of molecule **6** and atom numbering.

Important characteristics of spirooxazines are the Csp–N and the Csp–O bond lengths, which mainly determine the reactivity of compounds under photoirradiation. Table 1[*] presents the bond lengths for the most important rings, e.g. the pyrrole and oxazine rings, attached to a spiro unit for molecules **3b** and **6** and for the related structural analogs of the indoline series, **SPO1** and **SPO2**. It is known that the Csp–N bond in photochromic spirooxazines is markedly shortened, while the Csp–O bond is elongated in comparison with the standard values (C–N, 1.47 – 1.48 Å; C–O, 1.41-1.43Å).[19] It can be seen from Table **1** that in compounds **3b**, **SPO1**, and **SPO2**, the Csp–N bonds are shorter than the single C–N bond; however, in molecule **6**, this corresponds to an ordinary single bond. The Csp–O bonds in all molecules are elongated with respect to the standard value to almost the same extent. Note that the C5 – C6 bonds in molecules **3b** and **6** are shortened in comparison with the corresponding bonds in the structures of **SPO1** and **SPO2**, which is due to condensation of the pyrroline rings with thiophene ring, instead of the benzene one. The others bonds in the presented structures coincide to within the determination error (~0.003 Å). The bond angles in the structures under study differ by not more than 2-3°.

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[*] The atom numbering in Tables 1 and 2 corresponds to Scheme 2.

Table 1. Bond lengths in spirooxazines **3b**, **6**, **SPO1**, and **SPO2**

Bond	Bond length, (R, Å)			
	3b	**6**	**SPO1**	**SPO2**
C_{sp}-N	1.437	1.469	1.437	1.436
C_{sp}- O	1.460	1.456	1.456	1.455
C_{sp}-C1	1.588	1.559	1.567	1.548
C_{sp}-C2	1.512	1.501	1.507	1.504
C1-C6	1.505	1.529	1.510	1.503
C6-C5	1.338	1.343	1.384	1.366
C5-N	1.416	1.412	1.402	1.414
N1-C2	1.272	1.275	1.276	1.267
N1-C3	1.407	1.411	1.411	1.417
C3-C4	1.376	1.382	1.370	1.366
C4-O	1.369	1.365	1.372	1.362

Table 2. Torsion angles of spirooxazines **3b**, **6**, **SPO1** and **SPO2**

Torsion angle	The magnitude (ψ, deg)			
	3b	**6**	**SPO1**	**SPO2**
C_{sp}C1C6C5	17.40	19.50	19.30	19.61
C1C6C5N	-2.50	-0.80	-1.54	-2.80
C6C5N C_{sp}	-15.90	-19.90	-19.13	-17.24
C5N C_{sp}C1	26.40	31.40	30.35	28.80
N C_{sp}C1C6	-25.90	-30.20	-29.12	-28.62
O C_{sp}C2N1	25.40	13.10	22.00	16.90
C_{sp}C2N1C3	-2.70	-1.30	-3.74	-3.30
C2N1C3C4	-13.90	-6.80	-9.48	-7.80
N1C3C4O	4.80	1.60	1.73	3.40
C3C4O C_{sp}	20.50	11.50	18.90	11.88
C4O C_{sp}C2	-32.70	-17.40	-28.05	-20.12

Another important characteristic of spirooxazines are the torsion angles in the pyrroline and oxazine rings. These parameters are important, as they reflect the degree of ring distortion caused by steric non-valence interactions between substituents,[17,20] thus indicating a change in the mutual orientation of the LEP orbital (n) of the N atom and the σ* orbital of the C–O spiro bond, which largely determines the degree of the n-σ* interaction in the electronically excited state of spirooxazines. Table 2 presents the torsion angles for the SPO of the pyrroline and indoline series. First of all, attention is drawn by the similarity of the torsion angles in the pyrroline

fragment: they differ by not more than 3°. This implies that the conformation of the pyrroline ring depends on neither the substituent at the N atom nor the nature of the ring to which it is fused. Conversely, the oxazine fragment is more labile: the replacement of the methyl group by an ethyl group or by a propionic acid residue increases the torsion angles by 9 – 12°. As a consequence, the whole naphthoxazine fragment in molecules **3b** and **SPO1** acquires a twisted conformation, which will be apparently reflected in the spectroscopic characteristics of these compounds.

Thus, we synthesized the first spironaphthoxazines of the thieno[3,2-*b*]pyrroline series and studied their structures by ^{1}H NMR spectroscopy, mass spectrometry, and X-ray diffraction analysis. Comparative analysis of the spatial structure of spirooxazines of the thieno[3.2-*b*]pyrroline and indoline series was performed. It was shown that the structure of spironaphthoxazines based on thienopyrroline are similar to the structures of spirooxazines of the indoline series.

Experimental Section

General Procedures. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-250 and Bruker AM-300 CDCl$_3$ spectrometers and the EI mass spectra were run on a Kratos instrument (70 eV) with direct sample injection into the ion source. Melting points were measured on a Boetius hot stage and were not corrected. The completion of the reactions was detected using TLC (Silufol UV-254, elution with petroleum ether (60–80°C) – ethyl acetate, 12:1). Column chromatography was performed using Acros silica gel (C.A.S.-7631-86-9) (0.060–0.200). 2,5,6,6-Tetramethyl-6*H*-thieno[3,2-*b*]pyrrole **1a**,[10] ethyl 2,5,6,6-tetramethyl-6*H*-thieno[3,2-*b*]pyrrole-3-carboxylate **1b**,[11] and 2,3,3-trimethylbenzo[*b*]thieno[3,2-*b*]pyrrolenine **4**[11] were prepared by the procedures we developed previously. Commercially available (Merck, Acros, Aldrich) samples of 1-nitroso-2-naphthol, triethylamine, methyl tosylate, N-methylpyrrolidine, and anhydrous (99.9 %) acetonitrile, methanol, and ethanol were used.

Preparation of spironaphthoxazines-general procedure
A solution of the thienopyrrolenine (2.5 mmol) and the alkylating agent (2.6 mmol) in 10 mL of anhydrous acetonitrile was refluxed for 1 – 5 h under argon. The solvent was evaporated and anhydrous alcohol (10 ml), 1-nitroso-2-naphthol (0.38 g, 2.2 mmol), and a base (2.2 mmol) were added. The reaction mixture was refluxed for 30 – 45 min and cooled, and the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel using a 12:1 petroleum ether – ethyl acetate mixture as the eluent.

2,4,6,6-Tetramethylspiro(thieno[3,2-*b*]pyrroline-5,3′-[3*H*]naphtho [2,1-*b*][1,4]oxazine) (3a).
Methyl tosylate was used as the alkylating agent; the refluxing time was 1 h; ethanol served as the solvent and N-methylpyrrolidine, as the base. Yield 18%, yellowish solid. M.p. = 137-139°C (138-140°C[10]).

2,6,6-Trimethyl-4-ethylspiro(thieno[3,2-*b*]pyrroline-5,3′-[3*H*]naphtho[2,1-*b*][1,4]oxazine) (3b). Ethyl iodide was used as the alkylating agent; the refluxing time was 5 h; methanol served as the solvent and N-methylpyrrolidine, as the base. Yield 16%, pale yellow solid. M.p. = 109-110°C (110-112°C[10]).

2,4,6,6-Tetramethyl-3-carbomethoxyspiro(thieno[3,2-*b*]pyrroline-5,3′-[3*H*]naphtho[2,1-*b*][1,4]oxazine (3c). Methyl triflate was used as the alkylating agent; the refluxing time was 1 h; ethanol served as the solvent and N-methylpyrrolidine, as the base. Yield 40%, yellowish solid. M.p. = 140-142°C (hexane). IR (KBr) 1716, 1620, 1592, 1512, 1408, 1268, 1228, 1080, 1064, 1036, 1000 cm^{-1}. ^{1}H NMR (CDCl$_3$, 250 MHz) δ 1.31 (3H, s, C(CH$_3$)$_2$); 1.37 (3H, s, C(CH$_3$)$_2$); 2.62 (3H, s, Me); 2.85 (3H, s, N-Me); 3.87 (3H, s, CO$_2$Me); 7.09 (1H, d, CH$_{naphth}$, J = 8.5 Hz); 7.35-7.75 (4H, m, CH$_{naphth}$); 7.77 (1H, s, CH=N); 8.56 (1H, d, CH$_{naphth}$, J = 8.5 Hz). ^{13}C NMR (CDCl$_3$, 62.9 MHz) δ 17.28 (CH$_{3thioph}$); 22.25, 25.44 (C(CH$_3$)$_2$); 32.55 (N-CH$_3$); 51.50 (COOCH$_3$); 51.84 (C(CH$_3$)$_2$); 102.93 (NCO); 116.66, 117.48, 121.59, 122.73, 122.96, 124.28, 127.19, 127.82, 129.38, 130.38, 130.95, 143.85, 148.13, 148.19 (C$_{arom}$); 150.59 (CH=N); 164.09 (COOCH$_3$). MS, *m/z*: 406 [M]$^+$. Found (%): C, 68.05; H, 5.58; N, 7.09. C$_{23}$H$_{22}$N$_2$O$_3$S. Calculated (%): C, 67.96; H, 5.46; N, 6.89.

2,3-Dihydrospiro[1,3,3-trimethyl-1*H*-1-benzothieno[3,2-*b*]pyrrole-2,3′-[3*H*]-naphtho[2,1-*b*][3,4]oxazine] (6). Methyl tosylate was used as the alkylating agent; the refluxing time was 1 h; ethanol served as the solvent and triethylamine was the base. Yield 25%, pale yellow crystals. M.p. = 225-227°C (petroleum ether − benzene). IR (KBr) 1624, 1592, 1508, 1404, 1268, 1236, 1080, 1060, 1028, 1000 cm^{-1}. ^{1}H NMR (CDCl$_3$, 250 MHz) δ 1.42 (s, 3H, CH$_3$), 1.46 (s, 3H, CH$_3$); 3.10 (s, 3H, NCH$_3$); 7.10 (d, 1H, H$_{arom}$, J = 8.5 Hz), 7.27 (t, 1H, H$_{arom}$, J = 7.9 Hz), 7.34 (t, 1H, H$_{arom}$, J = 7.2 Hz), 7.42 (t, 1H, H$_{arom}$, J = 7.9 Hz), 7.60 (t, 1H, H$_{arom}$, J = 7.2 Hz), 7.71 (d, 1H, H$_{arom}$, J = 8.5 Hz), 7.74 − 7.76 (m, 4H, 3H$_{arom}$ + CH=N); 8.60 (d, 1H, H$_{arom}$, J = 8.5 Hz). ^{13}C NMR (CDCl$_3$, 50.3 MHz) δ 22.01, 24.92 (2C(CH$_3$)$_2$); 32.20 (NCH$_3$); 52.93 (C(CH$_3$)$_2$); 102.85 (NCO); 116.73, 120.42, 121.67, 123.49, 124.22, 124.35, 124.52, 127.24, 127.86, 130.45 (CH$_{arom}$); 123.00, 124.44, 126.10, 128.48, 129.51, 131.02, 143.64, 144.00 (C$_{arom}$); 150.29 (CH = N). MS, *m/z*: 384 [M]$^+$. No elemental analysis could be obtained due to the sensitivity of the compound to light.

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