New mesoionic systems of the azolopyridine series
1. Synthesis and structures of thiazolo[3,2-*a*]pyridinium 2-thiolates

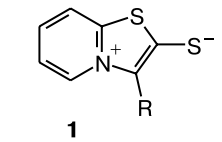
E. V. Babaev, V. B. Rybakov, I. A. Orlova, A. A. Bush, K. V. Maerle, and A. F. Nasonov*

Department of Chemistry, M. V. Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax: +7 (095) 932 8846. E-mail: babaev@org.chem.msu.su

A procedure was developed for the synthesis of representatives of the previously unknown bicyclic mesoionic thiazolo[3,2-*a*]pyridinium 2-thiolate system by the reaction of 2-X-*N*-phenacylpyridinium salts (X = Cl, SMe) with CS_2 in the presence of Et_3N. The three-dimensional structure of 3-(*p*-nitrobenzoyl)thiazolo[3,2-*a*]pyridinium 2-thiolate was established by X-ray diffraction analysis.

Key words: mesoionic heterocycles, cycloaddition, *N*-phenacylpyridinium ylides, carbon disulfide.

Up to now, bicyclic mesoionic thiazolopyridines **1** have not been known although their monocyclic prototypes **2** as well as tri- and tetracyclic analogs (**3**, **4**) have been studied in sufficient detail.[1]



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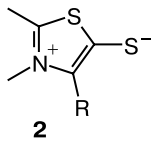

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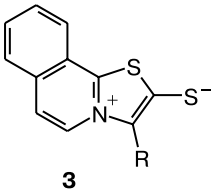

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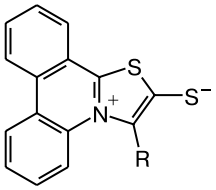

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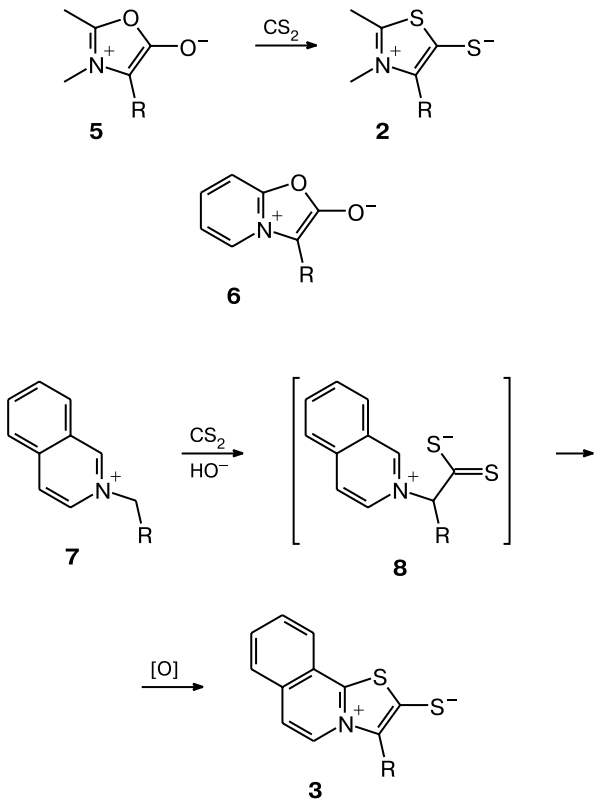
The most general approach to the synthesis of compounds of classes **2—4** (Scheme 1) involves the reactions of carbon disulfide with typical 1,3-dipoles, *viz.*, munchnones **5** [2—4] or ylides based on isoquinolinium salts **7**.[5—10]

Both these reactions are unsuitable for the construction of bicyclic skeleton **1**. For example, oxazolopyridine **6** (bicyclic analog of munchnone **5**) is very stable, does not exhibit properties of 1,3-dipoles in reactions with dipolarophiles,[1,11] and cannot undergo the transformation into system **1** under the action of carbon disulfide. In turn, compounds **9**, which are pyridinium analogs of salts **7**, readily react with carbon disulfide to give stable enethiol betaines **10** and their salts **11**. However, this

Scheme 1



reaction is terminated in the step of formation of the above-mentioned adducts[6] (Scheme 2).

Reagents **9—11** are widely used for the synthesis of various acyclic and heterocyclic derivatives.[12—14] How-

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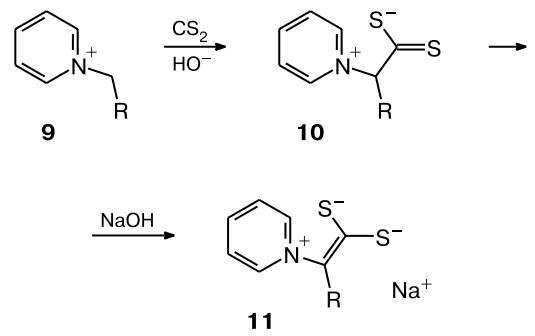
Scheme 2

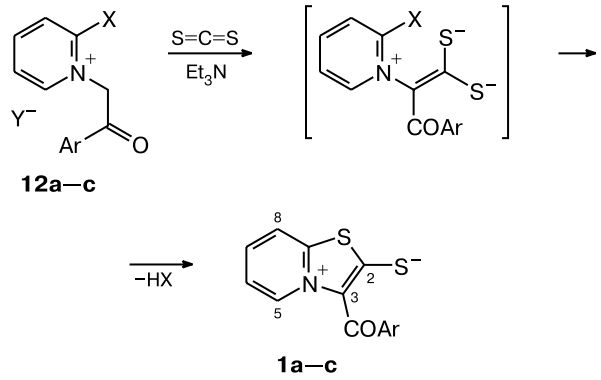


ever, in none of the cases did the closure of the thiazole ring giving rise to system **1** occur.

The difference in the behavior of intermediates **8** and **10** is, apparently, attributed to a larger π-deficiency of the isoquinolinium ring compared to the pyridinium ring. An increase in the electron deficiency of the pyridinium ring (by introducing an electron-withdrawing group in the β position or a leaving group in the α position of pyridine) could make possible the transformation of pyridines **9—11** into thiazolopyridines **1**.

We found that *N*-phenacylpyridinium salts **12** bearing the halogen atom or the methylthio group in the α position of the pyridine ring reacted with carbon disulfide in the presence of Et_3N to form compounds possessing a bicyclic skeleton of type **1** (Scheme 3).

Scheme 3



1, 12: Ar = *p*-Br—Ph (**a**), *p*-NO_2—Ph (**b**), *p*-Cl—Ph (**c**).
12: X = SMe, Y = I (**a**); X = Cl, Y = Br (**b, c**).

The reaction of 2-methylthiopyridinium salt **12a** proceeded most readily to give product **1a** within a few minutes; the yield of the product was close to 100%. The reactions of 2-chloropyridinium salts **12b,c** afforded products **1b,c** in yields of no higher than 20—40%, and these products required additional purification. Mesoionic heterocycles **1a—c** are poorly soluble in acetone, have high melting points, and are colored from yellow to orange-red.

The ^1H NMR spectra of products **1a—c**, unlike the spectra of the starting pyridinium salts **12**, have no signals of the CH_2 groups (a signal of the SCH_3 group is also absent). The most pronounced feature of the spectra is the presence of the characteristic low-field doublet of the H(5) proton at δ 9.4—9.7 (the remaining signals are observed in the δ region of 7.6—8.2). Such a substantial downfield shift caused by the influence of the magnetically anisotropic acyl group at position 3 (the peri effect) is typical also of other isostructural analogs of compounds **1**.[15] In the mass spectrum of compound **1b**, the most intense peaks correspond to the molecular ion and fragments formed upon elimination of CO, the nitro group, and carbon disulfide.

The bicyclic structure of compounds **1a—c** was unambiguously established by X-ray diffraction analysis of compound **1b** (Fig. 1, Table 1). According to the results of X-ray diffraction study, the bicyclic fragment is planar to within 0.029(4) Å. The S(2) and C(10) atoms are virtually in this plane, whereas the O(10) atom deviates from the plane by almost 0.5 Å, although the dihedral angle between the carbonyl group and the bicyclic fragment is not-too-large (~20°). The benzene ring of the nitrobenzoyl

Table 1. Crystallographic data and characteristics of X-ray diffraction study for **1b**

Molecular formula	$C_{14}H_8N_2O_3S_2$
Molecular weight	316.34
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	5.030(3)
b/Å	22.239(9)
c/Å	12.123(6)
α/deg	90
β/deg	97.56(4)
γ/deg	90
V/Å^3	1344.3(12)
Z	4
d_{calc}/g cm^{-3}	1.563
μ/mm^{-1}	0.407
Scan range, θ/deg	1.83—25.99
Ranges of indices	$-6 \le h \le 6$
	$0 \le k \le 27$
	$0 \le l \le 14$
Number of measured reflections	2633
	(R_{int} = 0.0559)
Number of parameters in refinement	191
GOOF	0.918
R_1/wR_2 [$I > 2\sigma(I)$]	0.0599/0.0583
R_1/wR_2 (based on all reflections)	0.1962/0.0849
Extinction	0.0004(3)
$\Delta\rho_{max}/\Delta\rho_{min}$, e Å^{-3}	0.249/−0.237

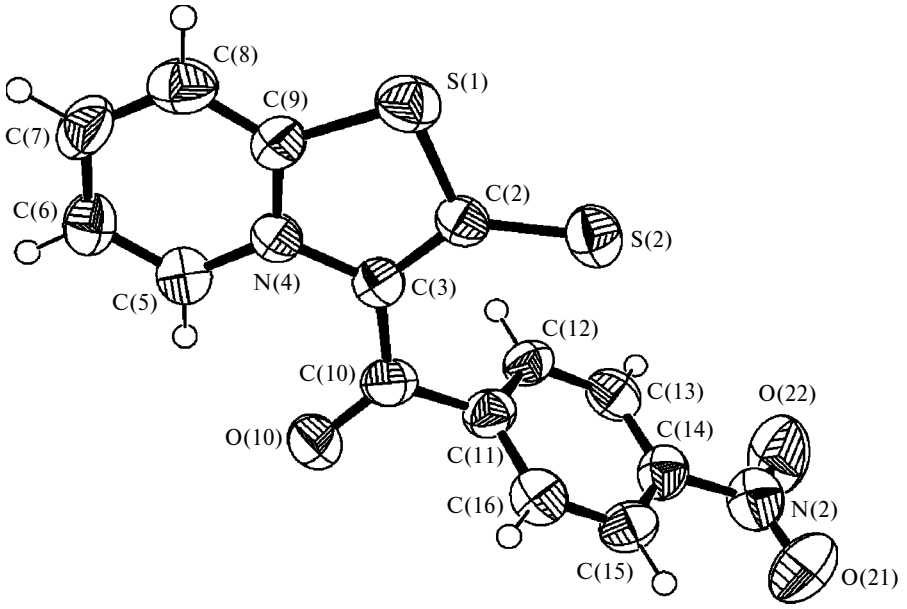


Fig. 1. Molecular structure of **1b** and the atomic numbering scheme (thermal ellipsoids are drawn at the 50% probability level).

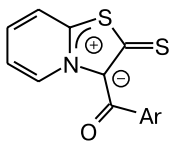
fragment is also planar within 0.025(4) Å, the carbonyl group being twisted with respect to the benzene ring by almost 60°, whereas the nitro group is virtually in the plane of the ring (the twist angle is 3.7°). In other words, the carbonyl group is conjugated with the C(3)=C(2)—S(2) fragment and is not conjugated with the nitrophenyl fragment.

Analysis of three C—S bond lengths and three C—N bond lengths (Table 2) revealed the unusual structural feature of the bicycle. In the thiazole fragment, the S(1)—C(9) bond (1.701(5) Å) is much shorter than the S(1)—C(2) bond (1.753(5) Å), which indicates that the former bond is conjugated with the lone electron pair of the bridging nitrogen atom, whereas the S(1)—C(2) bond is not involved in any conjugation. The exocyclic S(2)—C(2) bond has the shortest length (1.658(5) Å) and is, in fact, a double bond. Consequently, it is incorrect to represent mesoionic system **1** as a structure with the single S(2)—C(2) bond (and the negative charge on the S(2) atom).

Table 2. Selected interatomic distances *d* (Å) in the structure of **1b**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(9)	1.701(5)	C(10)—O(10)	1.244(5)
S(1)—C(2)	1.753(5)	C(10)—C(11)	1.475(6)
C(2)—C(3)	1.408(6)	C(11)—C(16)	1.368(6)
C(2)—S(2)	1.658(5)	C(11)—C(12)	1.395(6)
C(3)—N(4)	1.423(6)	C(12)—C(13)	1.385(6)
C(3)—C(10)	1.449(6)	C(13)—C(14)	1.385(6)
N(4)—C(9)	1.344(5)	C(14)—C(15)	1.375(6)
N(4)—C(5)	1.362(5)	C(14)—N(2)	1.471(7)
C(5)—C(6)	1.371(6)	C(15)—C(16)	1.360(6)
C(6)—C(7)	1.388(6)	N(2)—O(22)	1.206(5)
C(7)—C(8)	1.377(7)	N(2)—O(21)	1.221(6)
C(8)—C(9)	1.383(7)		

The bridging C(9)—N(4) bond (1.34 Å) is the shortest C—N bond, which is consistent with delocalization of the positive charge over the N(4)—C(9)—S(1) fragment. The C(3)—N(4) bond (1.42 Å) is the longest C—N bond. In our opinion, this fact is indicative of the ylide character of compound **1b** and, presumably, of the point localization of the negative charge on the C(3) atom. This assumption is supported by the abnormally large C(3)—C(2) and C(3)—C(10) bond lengths (1.40 and 1.45 Å, respectively). Therefore, the ylide carbon atom C(3) is involved in conjugation with neither the carbonyl group nor the exocyclic C(2)—S(2) double bond. Based on these characteristic features, we concluded that the structural formula **A** most adequately reflects the structures of compounds **1a—c**.



A

The above-presented distribution of the single and double bonds in the skeleton of the bicycle is additionally confirmed by the dienic character of the six-membered fragment. Actually, the C(5)—C(6) (1.371(6) Å) and C(7)—C(8) (1.377(7) Å) bonds are substantially shorter than the C(6)—C(7) bond (1.388(6) Å). A comparative analysis and detailed discussion of this phenomenon in the series of condensed munchnones will be published elsewhere.

Experimental

The ^{1}H NMR spectra (δ) were recorded on a Bruker AC 400 instrument. The mass spectrum was obtained on an MS5988 instrument. The starting pyridinium salts **12a**,[16] **12b**,[17] and **12c** [18] were synthesized according to known procedures.

Reactions of salts 12a—c with carbon disulfide (general procedure). Triethylamine (2 mL) was added to a suspension of pyridinium salt **12a—c** (1 mmol) and carbon disulfide (1 mL) in acetonitrile (5 mL) with vigorous stirring. The reaction mixture was kept at room temperature for 12 h. The precipitate that formed was filtered off and washed with a small amount of water to prepare the corresponding compounds **1a—c**.

3-(*p*-Bromobenzoyl)thiazolo[3,2-*a*]pyridinium 2-thiolate (1a) was prepared from 1-(*p*-bromophenacyl)-2-methylthiopyridinium iodide **12a** as a bright-yellow powder in 93% yield, m.p. 240—241 °C. Found (%): N, 3.95. $C_{14}H_8BrNOS_2$. Calculated (%): N, 4.00. ^{1}H NMR (DMSO-d_6 + CCl_4), δ: 9.45 (d, 1 H, H(5), J = 6.0 Hz); 8.27 (d, 1 H, H(8)); 7.92 (m, 1 H, H(7)); 7.75 (m, 2 H, ArH); 7.62 (m, 1 H, H(6)); 7.55 (m, 2 H, ArH).

3-(*p*-Nitrobenzoyl)thiazolo[3,2-*a*]pyridinium 2-thiolate (1b) was prepared from 2-chloro-1-(*p*-nitrophenacyl)pyridinium bromide **12b** as orange-red crystals. The yield of the crude product was 47%. After recrystallization, the yield was 22%, m.p. 275 °C (from acetone). ^{1}H NMR (DMSO-d_6 + CCl_4), δ: 9.73 (d, 1 H, H(5), J = 6.6 Hz); 8.23 (d, 2 H, ArH); 8.20 (m, 1 H, H(8)); 8.00 (m, 1 H, H(7)); 7.91 (m, 2 H, ArH); 7.70 (m, 1 H, H(6)). MS, m/z: 316 $[M]^+$ (37.03), 287 (100), 269 (10.85), 241 (49.0). Results of single-crystal X-ray diffraction analysis of compound **1b** are given in Tables 1—3.

3-(*p*-Chlorobenzoyl)thiazolo[3,2-*a*]pyridinium 2-thiolate (1c) was prepared from 1-(*p*-chlorophenacyl)-2-chloropyridinium bromide **12c** as an orange powder. The yield of the crude product was 36%. After chromatography on silica gel (100 : 1 chloroform—methanol mixture as the eluent), the yield was 20%, m.p. 239—241 °C. Found (%): N, 4.53. $C_{14}H_8ClNOS_2$. Calculated (%): N, 4.58. ^{1}H NMR (DMSO-d_6 + CCl_4): 9.34 (d, 1 H, H(5), J = 5.8 Hz); 8.20 (d, 1 H, H(8), J = 7.7 Hz); 7.97 (m, 1 H, H(7)); 7.84 (m, 2 H, ArH); 7.65 (m, 1 H, H(6)); 7.49 (m, 2 H, ArH). ^{1}H NMR ($CHCl_3$), δ: 9.55 (d, 1 H, H(5), J = 6.6 Hz); 7.88 (m, 2 H, ArH); 7.74 (m, 2 H, H(6), H(8)); 7.46—7.40 (m, 3 H, H(7), ArH).

Table 3. Selected bond angles (ω) in the structure of **1b**

Angle	ω/deg	Angle	ω/deg
C(9)—S(1)—C(2)	92.6(3)	C(8)—C(9)—S(1)	127.0(5)
C(3)—C(2)—S(2)	133.9(4)	O(10)—C(10)—C(3)	122.7(5)
C(3)—C(2)—S(1)	108.8(4)	C(3)—C(10)—C(11)	119.0(5)
S(2)—C(2)—S(1)	117.2(3)	O(10)—C(10)—C(11)	118.2(5)
C(2)—C(3)—N(4)	112.5(5)	C(16)—C(11)—C(12)	119.7(5)
C(2)—C(3)—C(10)	126.2(5)	C(16)—C(11)—C(10)	120.8(5)
N(4)—C(3)—C(10)	121.1(4)	C(12)—C(11)—C(10)	119.3(5)
C(9)—N(4)—C(5)	120.0(4)	C(13)—C(12)—C(11)	119.1(5)
C(9)—N(4)—C(3)	113.5(4)	C(14)—C(13)—C(12)	118.5(6)
C(5)—N(4)—C(3)	126.3(5)	C(15)—C(14)—C(13)	122.7(6)
N(4)—C(5)—C(6)	120.5(5)	C(15)—C(14)—N(2)	119.5(6)
C(5)—C(6)—C(7)	120.5(5)	C(13)—C(14)—N(2)	117.8(6)
C(8)—C(7)—C(6)	117.7(5)	C(16)—C(15)—C(14)	117.3(5)
C(7)—C(8)—C(9)	120.8(5)	O(22)—N(2)—O(21)	123.3(6)
N(4)—C(9)—C(8)	120.4(5)	O(22)—N(2)—C(14)	118.8(6)
N(4)—C(9)—S(1)	112.6(4)	O(21)—N(2)—C(14)	117.9(6)

X-ray diffraction analysis. The intensities of reflections for a single crystal of **1b** were measured at room temperature on a CAD-4 diffractometer[19] (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω scanning technique). The unit cell parameters were determined and refined based on 25 reflections in the θ angle range of 12.5—14.5°. The main parameters of X-ray study and crystallographic characteristics are given in Table 1. No absorption correction was applied because of the low linear absorption coefficients and small sizes of the crystals of **1b**. The experimental data were preliminarily processed using the WinGX program package.[20] All subsequent calculations were carried out using the SHELX97 program package.[21] The crystal structure was solved by direct methods and refined by the full-matrix least-squares method with anisotropic thermal parameters for all nonhydrogen atoms. The hydrogen atoms were placed in geometrically calculated positions and refined using the riding model. The selected interatomic distances and bond angles are given in Tables 2 and 3, respectively. The crystallographic data for the structure of **1b** were deposited with the Cambridge Structural Database. The molecular structure of compound **1b**, which was drawn with the use of the ORTEP-3 program,[22] and the atomic numbering scheme are shown in Fig. 1.

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