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# SYNTHESIS AND PROPERTIES OF SUBSTITUTED ISOXAZOLO[3',4':4,5]-THIENO[2,3-*b*]PYRIDINES

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*We synthesized derivatives of a novel heterocyclic system, isoxazolo[3',4':4,5]thieno[2,3-b]pyridine by sequential conversions in three steps: isomerization of 2-(2-R-ethylthio-2-oxo)-3-pyridyl cyanides obtained by alkylation from substituted 3-cyano-2(1H)-pyridinethiones by α-halomethyl ketones in alkaline medium, to form 3-aminothieno[2,3-b]pyridines; diazotization of the amino group followed by nucleophilic substitution of the diazonium group by an azido group, bypassing the step of isolating the diazonium salts; and thermolysis of the azides formed.*

**Keywords:** 3-aminothieno[2,3-*b*]pyridines, 3-azidothieno[2,3-*b*]pyridines, isoxazolo[3',4':4,5]thieno-[2,3-*b*]pyridines, 2-(2-R-ethylthio-2-oxo)-3-pyridyl cyanides, 3-cyano-2(1H)pyridinethiones.

3-Cyano-2(1H)-pyridinethiones are widely used for synthesis of polycondensed heteroaromatic systems [1-4]. We previously obtained compounds containing pyridine, thiophene, and oxazole rings in their structure [5]. The aim of this work was directed synthesis of isoxazolo[3',4':4,5]thieno[2,3-*b*]pyridines and a study of their physicochemical characteristics.

As the starting materials for constructing the tricyclic system, we used substituted 3-cyano-2(1H)-pyridinethiones **1-3** and α-halomethyl ketones **4a-g**.

The reaction of pyridinethiones **1-3** with ketones **4a-g** was carried out in the presence of a two-fold amount of KOH to bind the evolved hydrogen halide and to ensure Thorpe–Ziegler cyclization of intermediates **5** to form thienopyridines **6**. The alkylation products **5**, as shown in our papers [6, 7], can be isolated in pure form and characterized, but in this case they were not the object of our investigation.

3-Aminothieno[2,3-*b*]pyridines **6** are bright yellow crystals which are quite soluble in polar solvents, and insoluble in water and alkanes; their physicochemical characteristics are given in Table 1. The characteristics of compounds **6a,d,g**, which we synthesized earlier, are given in [6-8].

The IR and $^1$H NMR spectral data were the most informative for establishing the structure of thienopyridines **6** (Table 1). Thus in the IR spectra of compounds **6**, there are no absorption bands for the nitrile group in the 2240-2215 cm$^{-1}$ region or from the C=S group of the thioamide at 1215-1220 cm$^{-1}$, typical of compounds **1-3**, and two absorption bands appear for the stretching vibrations of the N–H bond of the amino group at 3520-3340 cm$^{-1}$ and 3315-3230 cm$^{-1}$, and also an absorption band for the conjugated carbonyl group at 1605-1590 cm$^{-1}$. In the $^1$H NMR spectra there are signals from all the protons, and a broadened singlet for the protons of the amino group is observed in the 7.32-8.17 ppm region.

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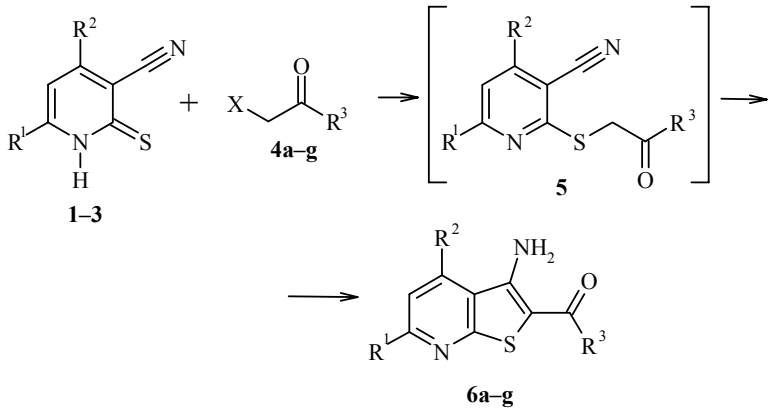
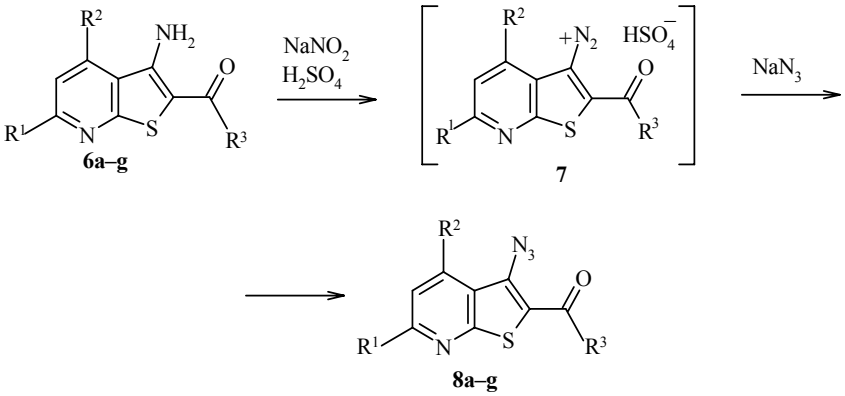


**1**, **6a**, **6d-g** $R^1$ = Me, $R^2$ = $CH_2OMe$; **2**, **6b** $R^1$ = $CH_2OMe$, $R^2$ = Me; **3**, **6c** $R^1$ = $R^2$ = Me;
**4a-c**, **6a-c** $R^3$ = Ph; **4d**, **6d** $R^3$ = $C_6H_4Br$-4; **4e**, **6e** $R^3$ = $C_6H_3Cl_2$-2,4; **4f**, **6f** $R^3$ = $C_6H_3F_2$-2,4;
**4g**, **6g** $R^3$ = $Ad^1$

Diazotization of 3-aminothienopyridines **6** was carried out in acetic acid medium in the presence of conc. $H_2SO_4$, which ensured good solubility of the starting components at sufficiently low temperatures (5-7°C). The low basicity of 2-acyl-substituted aminothienopyridines in the diazotization reaction enables a sufficiently large amount of free amine to exist in the equilibrium mixture, as needed for efficient reaction. The diazonium salts **7a-g** obtained in the solutions, immediately after removal of the excess nitrous acid, underwent a nucleophilic substitution reaction with a concentrated aqueous solution of sodium azide.



**8a**, **8d–g** $R^1$ = Me, $R^2$ = $CH_2OMe$; **8b** $R^1$ = $CH_2OMe$, $R^2$ = Me; **8c** $R^1$ = $R^2$ = Me; **8a–c** $R^3$ = Ph;
**8d** $R^3$ = $C_6H_4Br$-4; **8e** $R^3$ = $C_6H_4Cl_2$-2,4; **7f**, **8f** $R^3$ = $C_6H_4F_2$-2,4; **8g** $R^3$ = $Ad^1$

The 2-acyl-3-azidothieno[2,3-*b*]pyridines (**8**) obtained are crystalline compounds ranging from pale cream to light yellow in color and darkening in air, with decomposition temperatures in the range 114-128°C (Table 2).

The structure of pyridines **8** is supported by the IR, $^1$H NMR, and mass spectral data (Tables 2, 3, 6). In the IR spectra of products **8**, we see the typical very intense absorption band for the azide group at 2105-2125 $cm^{-1}$. Replacing the amino group with an azide group leads to a shift of the absorption bands for the carbonyl group toward the higher frequency region by 40 $cm^{-1}$ on the average, to 1625-1660 $cm^{-1}$ (Table 4). In the $^1$H NMR spectra, compared with the spectra for the starting aminothienopyridines **6**, the signal from the protons of the amino group are missing; the signal from the proton of the pyridine cycle is shifted downfield ($\Delta\delta$ = 0.25-0.35 ppm).

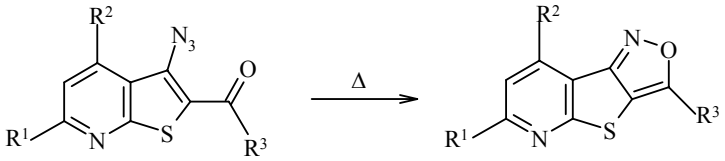
TABLE 1. Physicochemical Characteristics of Substituted 3-Aminothieno[2,3-*b*]pyridines **6a-g**

| Compound | Empirical formula | Found, % / Calculated, % | | | mp, °C | IR spectrum, ν, $cm^{-1}$ | | $^1$H NMR spectrum, δ, ppm (*J*, Hz) | | | | | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | C | H | N | | $NH_2$ | C=O | $CH_3$, s | $OCH_3$, s | $CH_2O$, s | $H_{Py}$, s | $NH_2$, s | Other protons | |
| **6a** | $C_{17}H_{16}N_2O_2S$ | 65.25 / 65.36 | 5.15 / 5.16 | 8.94 / 8.97 | 137-138 | 3465, 3260 | 1595 | 2.66 | 3.45 | 4.80 | 7.01 | 8.10 | 7.27-7.90 (5H, m, $H_{Ph}$) | 92 |
| **6b** | $C_{17}H_{16}N_2O_2S$ | 65.20 / 65.36 | 5.14 / 5.16 | 9.05 / 8.97 | 126-127 | 3480, 3305 | 1590 | 2.84 | 3.41 | 4.53 | 7.22 | 7.98 | 7.50-7.76 (5H, m, $H_{Ph}$) | 90 |
| **6c** | $C_{16}H_{14}N_2OS$ | 68.20 / 68.06 | 5.01 / 5.00 | 9.94 / 9.92 | 203-204 | 3520, 3310 | 1590 | 2.53, 2.78 | — | — | 7.05 | 7.96 | 7.50-7.75 (5H, m, $H_{Ph}$) | 89 |
| **6d** | $C_{17}H_{15}BrN_2O_2S$ | 52.01 / 52.18 | 3.81 / 3.86 | 7.12 / 7.16 | 135-136 | 3340, 3230 | 1605 | 2.66 | 3.45 | 4.80 | 7.00 | 8.17 | 7.62 (2H, d, $^3J$ = 8.1, 2,6-$H_{Ar}$); 7.82 (2H, d, $^3J$ = 8.1, 3,5-$H_{Ar}$) | 93 |
| **6e** | $C_{17}H_{14}Cl_2N_2O_2S$ | 53.64 / 53.55 | 3.69 / 3.70 | 7.37 / 7.35 | 185-186 | 3400, 3298 | 1595 | 2.57 | 3.42 | 4.86 | 7.28 | 8.11 | 7.50-7.55 (2H, m, 5,6-$H_{Ar}$); 7.71 (1H, d, $^4J$ = 2.2, 3-$H_{Ar}$) | 90 |
| **6f** | $C_{17}H_{14}F_2N_2O_2S$ | 58.72 / 58.61 | 4.05 / 4.05 | 8.05 / 8.04 | 169-170 | 3410, 3310 | 1595 | 2.58 | 3.43 | 4.87 | 7.28 | 8.07 | 7.20 (1H, d. d, $^4J$ = 2.7, 3-$H_{Ar}$); 7.33 (1H, d, $^3J$ = 8.6, $^4J$ = 2.7, 5-$H_{Ar}$); 7.63 (1H, d, $^3J$ = 8.6, 6-$H_{Ar}$) | 92 |
| **6g** | $C_{21}H_{26}N_2O_2S$ | 68.22 / 68.08 | 7.11 / 7.07 | 7.50 / 7.56 | 176-177 | 3370, 3250 | 1600 | 2.80 | 3.48 | 4.63 | 7.13 | 7.32 | 1.79-1.90 (6H, m, $H_{Ad}$); 2.06-2.20 (9H, m, $H_{Ad}$) | 96 |

TABLE 2. Some Physicochemical Characteristics of 2-Acyl-3-azidothieno-[2,3-*b*]pyridines **8a-g**

| Compound | Empirical formula | Found, % / Calculated, % | | | T. decomp., °C | IR spectrum, ν, cm$^{-1}$ | | Yield, % |
|---|---|---|---|---|---|---|---|---|
| | | C | H | N | | $N_3$ | C=O | |
| **8a** | $C_{17}H_{14}N_4O_2S$ | 60.55 / 60.34 | 4.19 / 4.17 | 16.50 / 16.56 | 115-117 | 2110 | 1625 | 74 |
| **8b** | $C_{17}H_{14}N_4O_2S$ | 60.39 / 60.34 | 4.18 / 4.17 | 16.52 / 16.56 | 114-115 | 2110 | 1625 | 79 |
| **8c** | $C_{16}H_{12}N_4OS$ | 62.39 / 62.32 | 3.93 / 3.92 | 18.10 / 18.17 | 118-119 | 2115 | 1630 | 78 |
| **8d** | $C_{17}H_{13}BrN_4O_2S$ | 49.00 / 48.93 | 3.16 / 3.14 | 13.36 / 13.43 | 126-128 | 2105 | 1625 | 75 |
| **8e** | $C_{17}H_{12}Cl_2N_4O_2S$ | 50.32 / 50.13 | 2.98 / 2.97 | 13.60 / 13.69 | 122-124 | 2125 | 1640 | 83 |
| **8f** | $C_{17}H_{12}F_2N_4O_2S$ | 54.70 / 54.54 | 3.25 / 3.23 | 14.91 / 14.97 | 118-119 | 2125 | 1640 | 73 |
| **8g** | $C_{21}H_{24}N_4O_2S$ | 63.81 / 63.61 | 6.13 / 6.10 | 14.06 / 14.13 | 120-122 | 2125 | 1635 | 82 |

The carbonyl group located adjacent to the azide group accelerates the process of decomposition of the azide in the presence of π-conjugation, due to formation of a transition state in which nucleophilic attack by the unshared electron pair of the oxygen atom occurs at the nitrogen atom in the plane of the molecule, which promotes formation of oxazoles [9, 10]. A similar pattern is observed in the case of thermolysis of 2-acyl-3-azidothienopyridines **8a-g**, leading to formation of derivatives of a novel heteroaromatic system: isoxazolo[3',4':4,5]thieno[2,3-*b*]pyridine **9**.




**8a–g** **9a–g**

**8a**, **8d-g, 9a**, **9d-g** $R^1$ = Me, $R^2$ = $CH_2OMe$; **8b**, **9b** $R^1$ = $CH_2OMe$, $R^2$ = Me; **8c**, **9c** $R^1$ = $R^2$ = Me; **8a-c, 9a-c** $R^3$ = Ph; **8d**, **9d** $R^3$ = $C_6H_4Br$-4; **8e, 9e** $R^3$ = $C_6H_3Cl_2$-2,4; **8f, 9f** $R^3$ = $C_6H_3F_2$-2,4; **8g, 9g** $R^3$ = Ad[1]

TABLE 3. $^1$H NMR Spectra of Some of the Synthesized 2-Acyl-3-azidothieno[2,3-*b*]pyridines **8**

| Compound | $^1$H NMR spectrum, δ, ppm (*J*, Hz) | | | | |
|---|---|---|---|---|---|
| | $CH_3$, s | $CH_3O$, s | $CH_2O$, s | $H_{Py}$, s | Other protons |
| **8a** | 2.50 | 3.38 | 4.76 | 7.26 | 7.07-7.62 (5H, m, $H_{Ph}$) |
| **8d** | 2.64 | 3.51 | 5.05 | 7.46 | 7.80 (2H, d, $^3J$ = 8.1, 2,6-$H_{Ar}$); 7.87 (2H, d, $^3J$ = 8.1, 3,5-$H_{Ar}$) |
| **8e** | 2.63 | 3.50 | 5.03 | 7.46 | 7.63 (1H, d, $^3J$ = 8.3, 6-$H_{Ar}$); 7.74 (1H, dd, $^3J$ = 8.3, $^4J$ = 2.2, 5-$H_{Ar}$); 7.79 (1H, d, $^4J$ = 2.2, 3-$H_{Ar}$) |
| **8f** | 2.62 | 3.49 | 5.03 | 7.45 | 7.24-7.90 (3H, m, $H_{Ar}$) |
| **8g** | 2.62 | 3.47 | 4.98 | 7.40 | 1.70-1.82 (6H, m, $H_{Ad}$), 2.00-2.15 (9H, m, $H_{Ad}$) |

TABLE 4. Physicochemical Characteristics of Compounds **9**

| Compound | Empirical formula | Found, % / Calculated, % | | | mp, °C | Yield, % |
|---|---|---|---|---|---|---|
| | | C | H | N | | |
| **9a** | $C_{17}H_{14}N_2O_2S$ | 65.93 / 65.79 | 4.50 / 4.55 | 9.07 / 9.03 | 183-184 | 81 |
| **9b** | $C_{17}H_{14}N_2O_2S$ | 65.95 / 65.79 | 4.52 / 4.55 | 9.05 / 9.03 | 176-177 | 77 |
| **9c** | $C_{16}H_{12}N_2OS$ | 68.66 / 68.55 | 4.29 / 4.31 | 10.02 / 9.99 | 202-203 | 84 |
| **9d** | $C_{17}H_{13}BrN_2O_2S$ | 52.29 / 52.45 | 3.36 / 3.37 | 7.18 / 7.20 | 259-260 | 83 |
| **9e** | $C_{17}H_{12}Cl_2N_2O_2S$ | 53.72 / 53.84 | 3.18 / 3.19 | 7.39 / 7.39 | 242-243 | 72 |
| **9f** | $C_{17}H_{12}F_2N_2O_2S$ | 59.00 / 58.95 | 3.50 / 3.49 | 8.11 / 8.09 | 233-234 | 78 |
| **9g** | $C_{21}H_{24}N_2O_2S$ | 68.30 / 68.45 | 6.55 / 6.56 | 7.58 / 7.60 | 191-192 | 83 |

The reaction of decomposition of azides **8a-g** was carried out in *m*-xylene at the boiling point of the solvent. The process was completed with approximately 30 min of boiling (according to TLC data). The isoxazolothienopyridines **9a-g** were isolated from the reaction mixture in 72 to 83% yields.

Products **9** are colorless crystalline compounds that are insoluble in water, alkanes, and ether and are soluble in haloalkanes. Some physicochemical characteristics of compounds **9** are given in Tables 4 and 5.

We note that the sets of major lines in the mass spectra of isoxazolothienopyridines **9** and the corresponding azides **8** are identical (Table 6). This allows us to say that extrusion of the nitrogen molecule from the molecular ion of the azides is accompanied by rearrangement to the corresponding isoxazole radical ion ($\Phi_1$). Further $\Phi_{M^+}$ fragmentation processes do not depend on the route by which this species is obtained: directly from the isoxazolothienopyridine molecule, or as a result of decomposition of the azide molecular ion. The major directions of fragmentation of the molecular ion for compounds **8** and **9** are given in Fig. 1.

Some of the priority directions for decomposition of isoxazolo[3',4':4,5]thieno[2,3-*b*]pyridines containing a methoxymethyl fragment is ejection of a formaldehyde molecule, accompanied by formation of an $\Phi_2$ radical cation ($M^+$ for the compound **9c**). Upon abstraction of a methoxymethyl group, the cations $\Phi_3$ ($CH_2{=}O^+{-}CH_3$) and $\Phi_4$ are formed. Further fragmentation of the $\Phi_2$ radical cation can occur along two routes: a) cleavage of a methyl radical to form the $\Phi_4$ cation; b) dissociation, leading to the cation $\Phi_5$, the decomposition products of which (the cations $\Phi_6$, $\Phi_7$, $\Phi_8$) give the most intense signals in the mass spectrum.

Another direction for fragmentation of $M^+$ ($\Phi_1$) includes cleavage of a methyl radical, rearrangement of the cation $\Phi_9$ formed with transfer of a portion to the pyridine nitrogen atom (the rearranged ion $\Phi_{9a}$) followed by extrusion of a carbon monoxide molecule. Fragmentation of the $\Phi_{10}$ cation leads to formation of methylnicotinonitrile and the unstable cation $\Phi_5$.

Thus the mass spectral fragmentation of 2-acyl-3-azidothieno[2,3-*b*]pyridines **8** and isoxazolo[3',4':4,5]thieno[2,3-*b*]pyridines **9** occurs according to a common scheme. In the initial fragmentation step, the methoxymethyl group of the molecule undergoes decomposition.

According to a quantum chemical study of the structure of 6-methyl-8-methoxymethyl-3-phenylisoxazolo[3',4':4,5]thieno[2,3-*b*]pyridine (**9a**) (AM1 method), combining three different types of heterocycles in the same molecule leads to significant changes in the interatomic distances in the aromatic system compared with the corresponding bonds of the isolated rings. An interesting feature is the fact that the common bonds for the heterocycles become longer than in the isolated systems (Fig. 2, Table 7).

TABLE 5. Spectral Characteristics of 3-R-Isoxazolo[3',4':4,5]thieno[2,3-*b*]pyridines **9**

| Compound | UV spectrum, $\lambda_{max}$, nm (log ε) | IR spectrum, ν, $cm^{-1}$, C=C, C=N | $^1$H NMR spectrum, δ, ppm (*J*, Hz) | | | | |
|---|---|---|---|---|---|---|---|
| | | | $-CH_3$, s | $-O-CH_3$, s | $-CH_2-O-$, s | $H_{Py}$, s | Other protons |
| **9a** | 212(4.33), 221(4.26)<br>245(4.19), 254(4.18)<br>288(4.53), 335(3.90) | 1600 | 2.65 | 3.54 | 4.87 | 7.41 | 7.45-7.83 (5H, m, $H_{Ph}$) |
| **9b** | 212(4.32), 222(4.26)<br>245(4.13), 257(4.07)<br>287(4.43), 337(3.87) | 1605 | 2.81 | 3.46 | 4.60 | 7.46 | 7.51-7.84 (5H, m, $H_{Ph}$) |
| **9c** | — | 1600 | 2.60<br>2.75 | — | — | 7.30 | 7.52-7.83 (5H, m, $H_{Ph}$) |
| **9d** | 210(4.12), 227(3.96)<br>247(3.90), 256(3.93)<br>292(4.34), 336(4.14) | 1605 | 2.72 | 3.61 | 5.01 | 7.28 | 7.42 (2H, d, $^3J$ = 8.1, 3,5-$H_{Ar}$); 7.71 (2H, d, $^3J$ = 8.1, 2,6-$H_{Ar}$) |
| **9e** | — | 1600 | 2.64 | 3.50 | 4.91 | 7.46 | 7.67 (1H. dd, $^3J$ = 8.3, $^4J$ = 2.2, 5-HAr);<br>7.89 (1H, d, $^3J$ = 8.3, 6-$H_{Ar}$); 7.95 (1H, d, $^4J$ = 2.2, 3-$H_{Ar}$) |
| **9f** | 207(4.54), 225(4.24)<br>242(4.16), 253(4.03)<br>287(4.56), 388(3.89) | 1605 | 2.66 | 3.52 | 4.91 | 7.46 | 7.33 (1H, d, $^4J$ = 2.7, 3-$H_{Ar}$); 7.48 (1H, dd, $^3J$ = 8.6,<br>$^4J$ = 2.7, 5-HAr); 8.08 (1H, d, $^3J$ = 8.6, 6-HAr) |
| **9g** | 212(4.02), 221(4.10)<br>238(4.00), 244(4.06)<br>275(4.39), 322(3.57) | 1603 | 2.67 | 3.58 | 4.93 | 7.38 | 1.83 (6H, m, $H_{Ad}$); 2.24 (9H, m, $H_{Ad}$) |

TABLE 6. Values of *m/z* ($I_{rel}$, %) and Basic Characteristics of Ions in Mass Spectra of 3-Azidothieno[2,3-*b*]pyridines (**8**) and Isoxazolothienopyridines (**9**)

| Compound | $M^+_{(azide)}$ | $\Phi_1$ | $\Phi_2$ | $\Phi_3$ | $\Phi_4$ | $\Phi_5$ | $\Phi_6$ | $\Phi_7$ | $\Phi_8$ | $\Phi_9$ | $\Phi_{10}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **8a** | 338 (1.4) | 310 (5.1) | 280 (9.8) | 45 (13.0) | 265 (—) | 149 (1.0) | 105 (78.0) | 121 (18.5) | 77 (100) | 295 (36.6) | 267 (—) |
| **8d*** | 417 (—) | 388 (5.5) | 359 (8.0) | 45 (37.8) | 344 (—) | 228 (—) | 183 (100) | 199 (28.7) | 155 (54.5) | 373 (17.8) | 342 (—) |
| **8f** | 374 (5.4) | 346 (8.0) | 316 (14.1) | 45 (13.6) | 301 (—) | 185 (—) | 141 (100) | 157 (16.6) | 113 (34.4) | 331 (51.3) | 303 (10.2) |
| **8g** | 396 (4.0) | 368 (30.6) | 338 (22.0) | 45 (14.9) | 323 (—) | 207 (—) | 163 (—) | 179 (—) | 135 (100) | 353 (16.6) | 325 (9.7) |
| **9a** | — | 310 (22.1) | 280 (16.5) | 45 (11.5) | 265 (—) | 149 (—) | 105 (81.9) | 121 (17.3) | 77 (100) | 295 (51.2) | 267 (5.1) |
| **9b** | — | 310 (31.5) | 280 (100) | 45 (5.4) | 265 (3.0) | 149 (0.4) | 105 (24.4) | 121 (6.8) | 77 (24.1) | — | — |
| **9c** | — | 280 (100) | 280 (100) | — | 265 (2.2) | 149 (0.4) | 105 (18.5) | 121 (7.4) | 77 (25.8) | — | — |
| **9d*** | — | 388 (35.5) | 359 (18.0) | 45 (7.0) | 344 (—) | 228 (—) | 183 (100) | 199 (20.4) | 155 (70.0) | 373 (29.0) | 342 (—) |
| **9f** | — | 346 (54.4) | 316 (38.1) | 45 (7.0) | 301 (7.0) | 185 (—) | 141 (100) | 157 (17.6) | 113 (29.8) | 331 (97.0) | 303 (19.8) |
| **9g** | — | 368 (64.6) | 338 (49.0) | 45 (13.0) | 323 (3.9) | 207 (—) | 163 (6.7) | 179 (—) | 135 (100) | 353 (27.8) | 325 (17.5) |

* The *m/z* values are given for fragments containing the lighter bromine isotope.

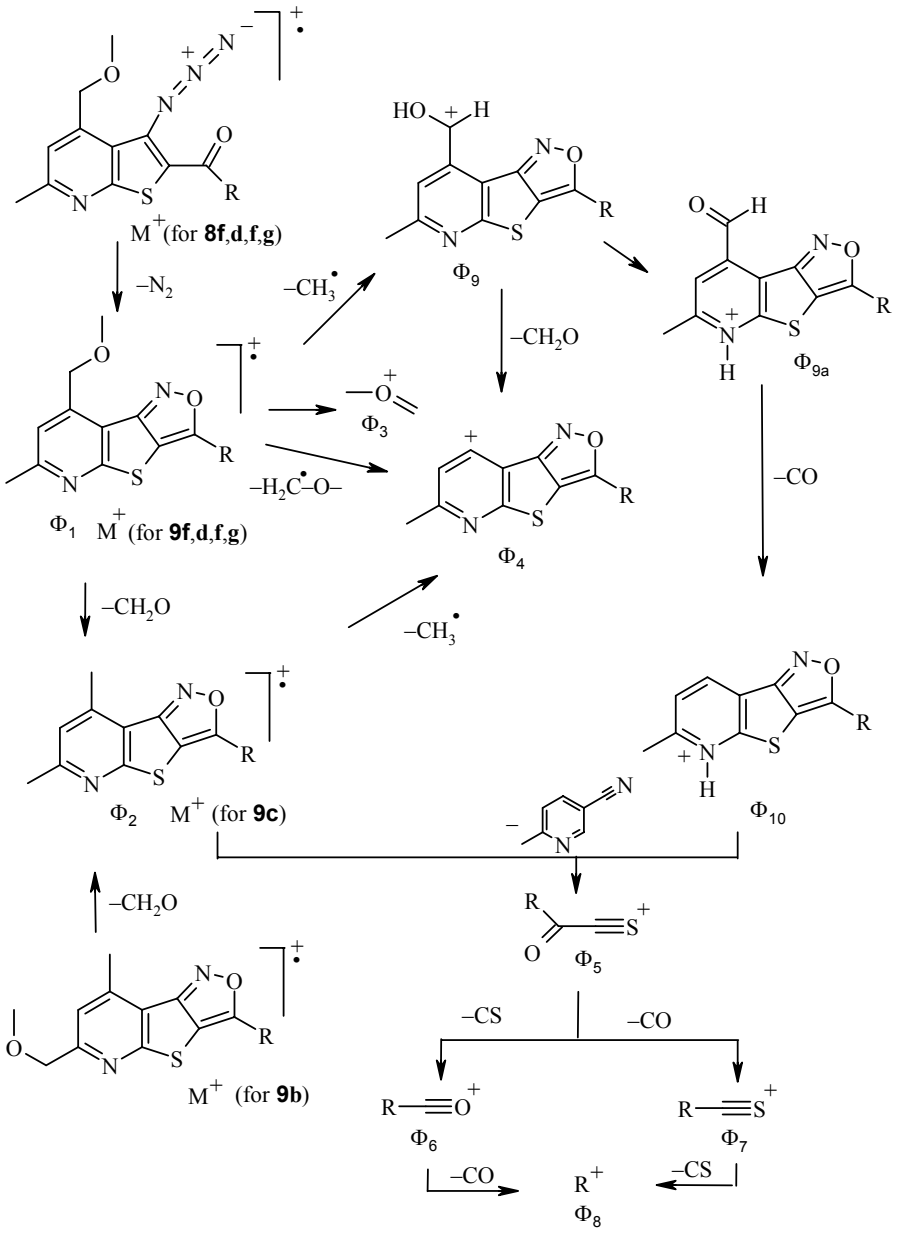



Fig. 1. Major fragmentation routes for 3-azidothieno[2,3-*b*]pyridines **8** and isoxazolothienopyridines **9**.

TABLE 7. Interatomic Distances (*d*, Å) in the Isoxazolothienopyridine **9a** Molecule

| Bond | Heterocyclic system | Isolated heterocycle | Bond | Heterocyclic system | Isolated heterocycle |
|---|---|---|---|---|---|
| N(1)–C(1) | 1.357 | 1.347 | C(6)–C(7) | 1.490 | 1.377 (Tf)<br>1.462 (Isox) |
| C(1)–C(2) | 1.416 | 1.407 | C(7)–S | 1.667 | 1.672 |
| C(2)–C(3) | 1.398 | 1.396 | S–C(5) | 1.736 | 1.672 |
| C(3)–C(4) | 1.398 | 1.396 | C(6)–N(2) | 1.341 | 1.342 |
| C(4)–C(5) | 1.435 | 1.407 (Py)<br>1.377 (Tf) | N(2)–O(1) | 1.320 | 1.320 |
| C(5)–N(1) | 1.343 | 1.347 | O(1)–C(8) | 1.428 | 1.411 |
| C(4)–C(6) | 1.438 | 1.342 | C(8)–C(7) | 1.381 | 1.379 |

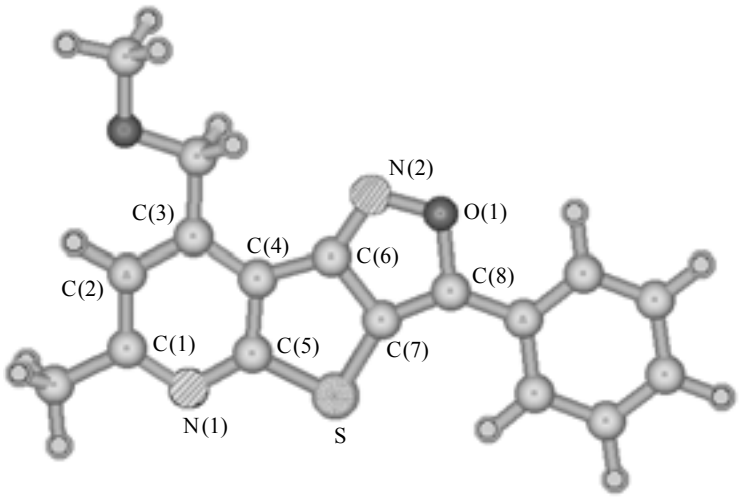



Fig. 2. Projection of the spatial structure of compound **8a**, obtained by the AM1 method.

## EXPERIMENTAL

The UV spectra were recorded on a Specord UV-vis and a Specord M-40 in the 200-700 nm range in quartz cuvets of thickness 10 mm in ethanol; the IR spectra were recorded on a Specord 71 IR-20 in the 3600-650 $cm^{-1}$ range, NaCl prisms, KBr. The crystalline substances were recorded as a suspension in vaseline oil. The $^1H$ NMR spectra were recorded on a Bruker WM-250 (250 MHz) in DMSO-$d_6$, internal standard HMDS. The mass spectra were obtained on a Varian CH-6 with ionizing potential 70 eV and temperatures 50-180°C.

**3-Amino-2-benzoyl-6-methoxymethyl-4-methylthieno[2,3-*b*]pyridine (6b).** An 10% aqueous solution of KOH (5.6 ml, 0.01 mol) was added to a suspension of 3-cyano-2(1H)-pyridinethione **2** (1.94 g, 0.01 mol) in DMF (20 ml). Then phenacyl bromide (1.99 g, 0.01 mol) was added with stirring; the mixture was held for 10-15 min at room temperature. Then another 5.6 ml of a 10% aqueous KOH solution was added, and the reaction mixture was stirred for 20 min; then the precipitate formed was separated, washed successively with water and a 1:1 ethanol–water mixture, and dried in air. The filtrate was diluted with a two-fold amount of water, the flocculent precipitate was separated and washed with water and then recrystallized from ethanol. Compounds **6a,c-g** were obtained similarly.

**3-Azido-2-benzoyl-4-methoxymethyl-6-methylthieno[2,3-*b*]pyridine (8a).** Conc. $H_2SO_4$ (0.6 ml) was added to a solution of compound **6a** (1.69 g, 0.005 mol) in glacial acetic acid (12 ml). The reaction mixture was cooled in an ice bath down to +5 to +8°C and a solution of sodium azide (0.48 g, 0.007 mol) in water (2 ml) was slowly added in small portions. The mixture was stirred for 20 min and then the excess nitrous acid was neutralized with urea (monitored using starch/iodide indicator paper), and a solution of sodium azide (0.46 g, 0.007 mol) in water (2 ml) was added dropwise over a 10 min period. Stirring was continued for one hour. Then the reaction mass was slowly poured into water with finely shaved ice. The precipitate of azide **6a** was separated, washed on the filter with cold water until the wash water tested neutral, and then it was dried over concentrated sulfuric acid. The 2-acyl-3-azidothieno[2,3-*b*]pyridines **8b-g** was obtained similarly.

**8-Methoxymethyl-6-methyl-3-phenylisoxazolo[3',4':4,5]thieno[2,3-*b*]pyridine (9a).** Compound **8a** (1.69 g, 0.005 mol) was boiled for 30 min in *m*-xylene (30 ml). Then the solution was cooled down to room temperature, diluted with hexane (40 ml) (petroleum ether). The precipitated crystals of isoxazolothienopyridine were separated, washed with hexane, and dried in air. They were purified by recrystallization from DMF. Compounds **9b-g** were obtained by a similar procedure.

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