Heterocycles with a β-nitroenamine fragment
3.* Synthesis of 3-amino-2-nitrothieno[2,3-*b*]pyridines. Crystal and molecular structure of 3-amino-4-methyl-2-nitro-6-trifluoromethylthieno[2,3-*b*]pyridine

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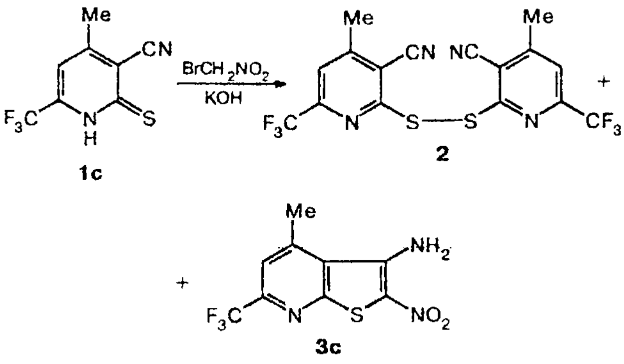
The reaction of 3-cyanopyridine-2(1*H*)-thiones with bromonitromethane in the presence of triethylamine results in 3-amino-2-nitrothieno[2,3-*b*]pyridines. The crystal and molecular structure of one of the reaction products was established by X-ray diffraction analysis.

Key words: 3-cyanopyridine-2(1*H*)-thiones, bromonitromethane, 3-amino-2-nitrothieno[2,3-*b*]pyridines, X-ray diffraction analysis.

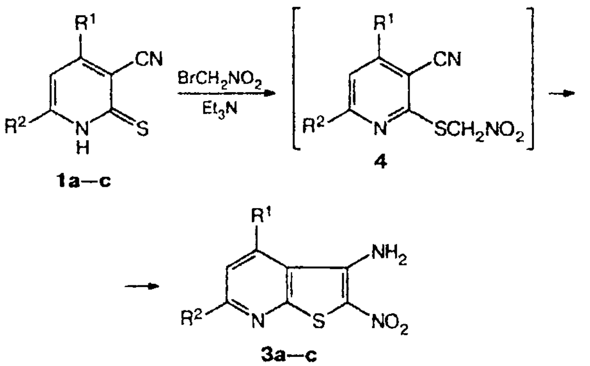
Earlier,[2] it was shown that 3-cyanopyridine-2-thiones react with bromonitromethane in the presence of aqueous alkali to give, as with halocarbonyl compounds, 3-amino-2-nitrothieno[2,3-*b*]pyridines. However, we found that reaction of bromonitromethane with pyridinethione **1c** in aqueous DMF in the presence of an equimolar amount of KOH results in a mixture of disulfide **2** and thienopyridine **3c** where the disulfide prevails (Scheme 1).

Scheme 1



When the reaction was carried out in EtOH in the presence of an equimolar amount of Et_3N, only thienopyridines **3a—c** were formed. Probably, initially *S*-alkylation occurs to give cyanopyridines **4**. However, these intermediates could not be isolated.

Scheme 2



	1a, 3a	**1b, 3b**	**1c, 3c**
R^1	Me	CF_3	Me
R^2	Me	Me	CF_3

Such a strong dependence of the reaction pathway on the nature of the base and the medium is probably explained by the fact that alkali can detach the proton from pyridinethione to give the corresponding anion, which further reduces bromonitromethane (*i.e.*, enters into the Zinin reaction), while triethylamine only binds HBr evolved in the formation of pyridines **4**.

The structures of the compounds obtained were established by ^1H NMR and IR spectroscopy (Table 1).

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* For Part 2, see Ref. 1.

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Table 1. Characteristics of thienopyridines **3a—c**

Compound	Yield (%)	M.p. /°C	Found/Calculated (%) C	H	N	Molecular formula	IR, ν/cm^{-1}	^{1}H NMR, δ
3a	53	269—270	48.21 48.42	4.32 4.06	18.71 18.82	$C_9H_9N_3O_2S$	3450—3300 (NH_2), 1630—1610 (CO), 1550 $\nu_{as}(NO_2)$	2.55 (s, CH_3); 2.78 (s, CH_3); 7.2 (s, CH); 8.4 (br.s, NH_2)
3b	42	235—237	38.11 38.99	2.24 2.18	15.18 15.16	$C_9H_6F_3N_3O_2S$	3450—3300 (NH_2), 1625 (CO), 1545 $\nu_{as}(NO_2)$	2.6 (s, CH_3); 7.8 (s, CH); 8.3 (br.s, NH_2)
3c	63	203—204	39.10 38.99	2.12 2.18	15.28 15.16	$C_9H_6F_3N_3O_2S$	3400—3300 (NH_2), 1610 (CO), 1520 $\nu_{as}(NO_2)$	2.9 (s, CH_3); 7.7 (s, CH); 8.4 (br.s, NH_2)

To confirm these structures, compound **3c** was studied by X-ray diffraction analysis. Figure 1 illustrates the general view of the molecule. Bond lengths and bond angles are listed in Tables 2 and 3, respectively. As in the molecule of 3-amino-4-methyl-6-trifluoromethylthieno[2,3-*b*]pyridine-2-carboxanilide studied earlier,[3] the thienopyridine fragment in compound **3c** is planar (the dihedral angle between the planes of the heterocycles is equal to 1.5°). It can be seen from Fig. 1 that the NO_2 and NH_2 groups also lie in the heterocycle plane, which results in formation of a strong intramolecular N(10)—H(102)...O(1) hydrogen bond with the following parameters: N(10)...O(1) 2.705(3) Å, N(10)—H(102) 0.85(2) Å, H(102)...O(1) 2.07(2) Å, N(10)—H(102)...O(1) 131(2)°. The planar structure of the N(10)—C(3)=C(2)—N(11)—O(1) fragment (the deviation of the atoms from the average plane does not exceed 0.012 Å) is favorable for conjugation. Thus, the N(10)—C(3) and C(2)—N(11) valence distances (1.331(3) and 1.383(3) Å, respectively) are much shorter than the usual ones (the conjugated C(sp^2)—N(sp^2) and C(sp^2)—NO_2 bond lengths are equal to 1.336 and 1.468 Å, respectively),[4] while the C(2)=C(3) (1.399(4) Å) and N(11)—O(1) bonds (1.256(3) Å) are significantly longer (the standard values of the C(sp^2)=C(sp^2) and N(sp^2)—O (in the NO_2 group) bond lengths are equal to 1.331 and 1.218 Å, respectively).[4] A similar rearrangement of bond lengths with formation of a strong intramolecular H-bond was established by us earlier[5] for the same fragment of substituted 2-amino-3-nitropyran.

An analysis of crystal package in compound **3c** showed the presence of an intermolecular S(1)...F(1) (0.5 + *x*, *y*,

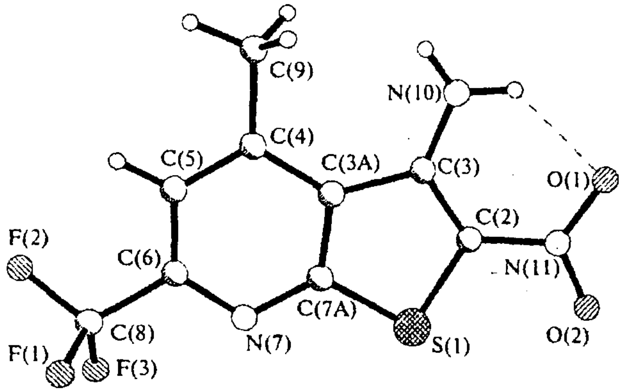

Fig. 1. General view of molecule **3c**. The intramolecular N—H...O hydrogen bond is indicated by a dotted line.

Table 2. Bond lengths (*d*) in molecule **3c**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(7A)	1.736(2)	N(7)—C(7A)	1.336(3)
S(1)—C(2)	1.737(2)	N(10)—C(3)	1.331(3)
O(1)—N(11)	1.256(3)	N(11)—C(2)	1.383(3)
O(2)—N(11)	1.245(3)	C(2)—C(3)	1.399(4)
F(1)—C(8)	1.33(2)	C(3)—C(3A)	1.450(3)
F(2)—C(8)	1.371(13)	C(3A)—C(4)	1.411(3)
F(3)—C(8)	1.271(11)	C(3A)—C(7A)	1.416(3)
F(1')—C(8)	1.33(3)	C(4)—C(5)	1.383(3)
F(2')—C(8)	1.21(3)	C(4)—C(9)	1.507(4)
F(3')—C(8)	1.41(2)	C(5)—C(6)	1.385(3)
N(7)—C(6)	1.333(3)	C(6)—C(8)	1.510(3)

Table 3. Bond angles (ω) in molecule **3c**

Angle	ω/deg	Angle	ω/deg
C(7A)—S(1)—C(2)	88.6(1)	N(7)—C(6)—C(5)	125.3(2)
C(6)—N(7)—C(7A)	114.4(2)	N(7)—C(6)—C(8)	113.8(2)
O(2)—N(11)—O(1)	122.4(2)	C(5)—C(6)—C(8)	120.8(2)
O(2)—N(11)—C(2)	118.3(2)	N(7)—C(7A)—C(3A)	125.6(2)
O(1)—N(11)—C(2)	119.3(2)	N(7)—C(7A)—S(1)	119.7(2)
N(11)—C(2)—C(3)	126.0(2)	C(3A)—C(7A)—S(1)	114.7(2)
N(11)—C(2)—S(1)	117.8(2)	F(3)—C(8)—F(1)	107.8(10)
C(3)—C(2)—S(1)	116.1(2)	F(2')—C(8)—F(1')	108(2)
N(10)—C(3)—C(2)	124.5(2)	F(3)—C(8)—F(2)	106.3(6)
N(10)—C(3)—C(3A)	125.8(2)	F(1)—C(8)—F(2)	105.6(10)
C(2)—C(3)—C(3A)	109.7(2)	F(2')—C(8)—F(3')	108.5(13)
C(4)—C(3A)—C(7A)	117.8(2)	F(1')—C(8)—F(3')	103(2)
C(4)—C(3A)—C(3)	131.3(2)	F(2')—C(8)—C(6)	114.4(10)
C(7A)—C(3A)—C(3)	110.9(2)	F(3)—C(8)—C(6)	114.1(5)
C(5)—C(4)—C(3A)	116.4(2)	F(1)—C(8)—C(6)	110.9(7)
C(5)—C(4)—C(9)	120.4(2)	F(1')—C(8)—C(6)	111.0(12)
C(3A)—C(4)—C(9)	123.1(2)	F(2)—C(8)—C(6)	111.6(5)
C(4)—C(5)—C(6)	120.4(2)	F(3')—C(8)—C(6)	111.8(7)

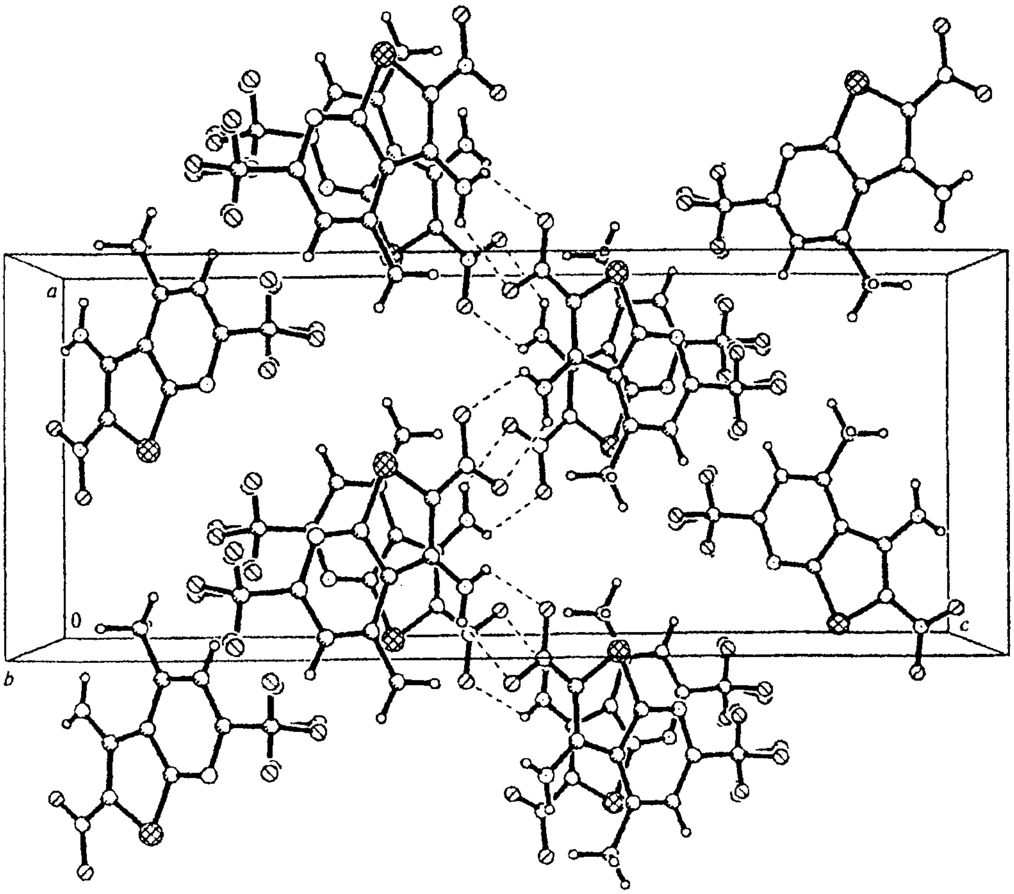

Fig. 2. The *ac* projection of crystal structure **3c**. The intermolecular N—H...O hydrogen bonds are indicated by the dotted lines.

0.5 − z) nonvalence contact (3.202(4) Å), which is comparable with the sum of the van der Waals radii of these atoms.[6]

In the crystal, the intermolecular hydrogen bonds N(10)—H(101)...O(1) (−0.5 + x, −0.5 − y, 1 − z) [N(10)...O(1) 2.966(4) Å, N(10)—H(101) 0.86(2) Å, H(101)...O(1) 2.34(2) Å, N(10)—H(101)...O(1) 129(2)°] and N(10)—H(102)...O(2) (−0.5 + x, −0.5 − y, 1 − z) [N(10)...O(2) 2.970(4) Å, N(10)—H(102) 0.85(2) Å, H(102)...O(2) 2.39(2) Å, N(10)—H(102)...O(2) 126(2)°] combine molecules **3c** into infinite chains (Fig. 2).

Experimental

^{1}H NMR spectra were recorded on a Bruker WM-250 instrument (250 MHz) in DMSO-d_6. IR spectra were recorded on a Perkin—Elmer 457 instrument (KBr).

Synthesis of thienopyridines 3a—c (general procedure). Bromonitromethane (1.4 g) was added dropwise at 0 °C to a solution of pyridinethione **1a—c** (0.01 mol) in 40 mL of ethanol and triethylamine (1.4 g). The reaction mixture was stirred for 48 h, the solvent was removed, and the residue was washed with water and recrystallized from DMF.

Synthesis of disulfide (2). 10% KOH (5 mL) and then bromonitromethane (1.4 g) were added with stirring to a solution of pyridinethione **1a** (0.01 mol) in 10 mL of DMF. The reaction mixture was left for three days. Then it was poured into water, and the precipitate that formed was filtered off. Disulfide **2** was isolated by column chromatography on SiO_2. Yield 0.29 g (13%), m.p. 245 °C. ^{1}H NMR (DMSO), δ: 2.65 (s, 3 H, CH_3); 8.0 (s, 1 H, CH). MS (EI, 70 eV), m/z: 434 $[M]^+$.

X-ray diffraction analysis. The crystals of **3c** ($C_9H_6F_3N_3O_2S$) are rhombic, a = 9.766(2) Å, b = 9.124(5) Å, c = 24.211(6) Å, V = 2157(1) Å^3, d_{calc} = 1.707 g cm^{-3} (25 °C), Z = 8, space group *Pbca*. The unit cell parameters and the intensity data were measured from 2804 reflections on a Siemens P3/PC four-circle automatic diffractometer (λ(Mo-Kα), graphite monochromator, θ/θ scanning until θ_{max} = 28°). The structure was solved by the direct method with location of all nonhydrogen atoms and refined by the full-matrix least-squares method in the anisotropic approximation for nonhydrogen atoms. All hydrogen atoms were located in an objective manner by differential Fourier syntheses and refined isotropically. The trifluoromethyl group was disordered in two positions with different occupancy factors (2 : 1). The final residuals R_1 = 0.051 from 1767 independent reflections with $I > 2T$, wR_2 = 0.119 from 2728 reflections. All computations were performed with the SHELXTL PLUS and SHELXTL-93 programs (PC version). Atomic coordinates and isotropic equivalent (isotropic for H atoms) thermal parameters are given in Table 4.

Table 4. Atomic coordinates ($\times 10^4$) and isotropic equivalent (isotropic for H atoms) thermal parameters in molecule **3c**

Atom	*x*	*y*	*z*	$U/Å^2$
S(1)	4789(1)	484(1)	3789(1)	43(1)
O(1)	4188(2)	−2351(2)	4940(1)	61(1)
O(2)	6026(2)	−1388(2)	4568(1)	66(1)
F(1)	1778(23)	2364(18)	1988(7)	81(4)
F(2)	582(11)	3982(13)	2419(4)	60(2)
F(3)	2745(11)	4112(10)	2398(4)	75(3)
F(1')	1999(43)	2393(31)	1989(13)	61(5)
F(2')	698(26)	3826(29)	2378(9)	87(7)
F(3')	2842(17)	4228(17)	2424(7)	42(3)
N(7)	3117(2)	1941(2)	3115(1)	38(1)
N(10)	1724(3)	−1372(3)	4588(1)	51(1)
N(11)	4758(2)	−1488(2)	4607(1)	50(1)
C(2)	3959(3)	−620(3)	4268(1)	42(1)
C(3)	2527(3)	−595(3)	4254(1)	39(1)
C(3A)	2067(2)	387(2)	3821(1)	35(1)
C(4)	740(2)	770(2)	3641(1)	39(1)
C(5)	662(3)	1721(3)	3198(1)	40(1)
C(6)	1844(2)	2253(2)	2954(1)	36(1)
C(7A)	3196(2)	1019(2)	3542(1)	36(1)
C(8)	1774(3)	3191(3)	2441(1)	42(1)
C(9)	−545(3)	174(4)	3902(1)	53(1)
H(5)	−205(26)	1996(28)	3051(10)	45(7)
H(91)	−566(29)	365(31)	4294(13)	58(8)
H(92)	−600(32)	−889(35)	3881(12)	59(9)
H(93)	−1397(34)	627(32)	3737(12)	64(9)
H(101)	843(34)	−1370(29)	4554(11)	45(7)
H(102)	2128(32)	−1987(35)	4797(13)	60(9)

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