Chemistry of Heterocyclic Compounds, Vol. 30, No. 9, 1994

REACTIONS OF POLYHALOPYRIDINES. 8.* REACTIONS OF POLYCHLOROTRIFLUOROMETHYL-PYRIDINES WITH SODIUM N,N-DIMETHYLDITHIOCARBAMATE. STRUCTURE OF THE 8-TRIFLUOROMETHYLBIS-1,3-DITHIOLO-[4,5-b:4′,5′-e]-PYRIDINE-2,6-DIONE MOLECULE

A. M. Sipyagin and Z. G. Aliev

The reaction of the isomeric tetrachloro-α-, β-, and γ-trifluoromethylpyridines and of 3,4,5-trichloro-2-trifluoromethylpyridine with sodium N,N-dimethyldithiocarbamate dihydrate has been studied. In the case of the α- and γ-isomers an intramolecular cyclization with the formation of 1,3-dithiol-2-one derivatives occurs and the remaining compounds give only products of mono- or disubstitution of chlorine atoms by a dithiocarbamate fragment at positions 4 or 6 of the pyridine ring. The structure of the compounds synthesized was proved using ^{13}C NMR and X-ray crystallographic analysis.

We reported previously a new method of synthesizing the 1,3-dithiolo[4,5-c]pyridine and bis-1,3-dithiolo[4,5-b:4′,5′e]-pyridine systems from N,N-dialkyldithiocarbamate derivatives of chlorocyanopyridines. It was shown that nucleophilic attack by the N,N-dialkyldithiocarbamate anion occurs initially at positions 2 or 4 of the pyridine ring. The chlorine atoms at $C_{(3)}$ and $C_{(5)}$, which are activated by the acceptor cyano group, then underwent an intramolecular substitution by the negatively charged sulfur atom of the dithiocarbamate fragment [1].

The isomeric α-, β-, and γ-trifluoromethyl-tetrachloropyridines (I) [2] and 2-trifluoromethyl-3,4,5-trichloropyridine (II) may serve as interesting models for the further development of methods of obtaining annelated heterocyclic compounds containing pyridine using intramolecular nucleophilic reactions. It is known that the presence of a CH_3 group in the position para to chlorine in a benzene nucleus accelerates significantly its replacement by nucleophilic reagents. Similar effects are also observed for the ortho and meta positions, but in these cases the lability of the chlorine atoms is reduced by factors of 2 and 10 respectively [3]. Consequently, in reactions of compound (I) with sodium N,N-dimethyldithiocarbamate the presence of a CF_3 group in the α position of the pyridine ring [compound (Ia)] must facilitate significantly the cyclization of the 4-N,N-dimethyldithiocarbamate derivative (IIa) at position 5. A trifluoromethyl substituent in the β position [compound (Ib)] must activate positions 2 and 4 simultaneously with the nitrogen atom of the pyridine ring, thereby accelerating the substitution of both the $Cl_{(2)}$ and $Cl_{(4)}$ atoms but not the occurrence of intramolecular processes. A CF_3 group in the γ position creates favorable conditions for intramolecular cyclization at positions 3 and 5. It must be noted that the trifluoromethyl group exerts a weaker electron-accepting effect than the cyano group [4], consequently it is expected that the dithiocarbamate derivatives (II) will be less reactive in intramolecular nucleophilic reactions (which have been described previously for CN substituted choloropyridines) [1].

We have carried out the reaction of compounds (Ia-c) and (II) with sodium N,N-dimethyldithiocarbamate in acetone. It turned out that compound (Ia), unlike its cyano analog [1], initially gives a yellow thermally unstable derivative, probably the dithiocarbamate (III), which has no sharp melting point and is converted on boiling in acetone for 0.5 h into 4,7-dichloro-6-trifluoromethyl-1,3-dithiolo[4,5-c]pyridine-2-one (IV). The mechanism of forming the 1,3-dithiol-2-one fragment was discussed previously in [1].

*See [6] for part 7.

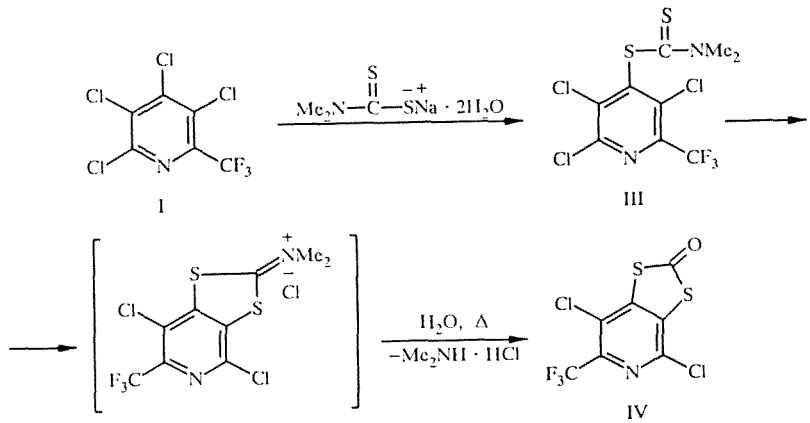
Institute of Chemical Physics, Chernogolovka, Russian Academy of Sciences, Chernogolovka 142432. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1278-1284, September, 1994. Original article submitted June 25, 1994.

 0009-3122/94/3009-1110$12.50 ©1995 Plenum Publishing Corporation

TABLE 1. ^{13}C NMR Spectra of the Compounds Synthesized

Compound	Pyridine carbon atoms					CF_3	Other carbon atoms
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$		
Ia	142.6 q, $^2J_{CF}$ = 36.1 Hz	129,4	145,8	134,2	147,4	119.8 q, J_{CF} = 274.3 Hz	—
IV	141.2 q, $^2J_{CF}$ = 35 Hz	133,5	140,3	122,7	147,1	119.8 q, J_{CF} = 274 Hz	182,0 (C=O)
II	144.6 q, $^2J_{CF}$ = 35 Hz	131,3	144,5	135,6	147,0	121.1 q, J_{CF} = 274 Hz	—
V	143.8 q, $^2J_{CF}$ = 35 Hz	137,3	143,6	142,1	146,5	120.7 q, J_{CF} = 274 Hz	42,5; 45,3 (NMe_2); 188,2 (C=S)
Ib	146,3	123.2 q, $^2J_{CF}$ = 43.5 Hz	145,6	131,0	151,6	121.0 q, J_{CF} = 276.5 Hz	—
VI	146,1	128.1 q, $^2J_{CF}$ = 34.5 Hz	145,3	138,0	151,4	121.3 q, J_{CF} = 275.2 Hz	42,6; 45,2 (NMe_2); 188,7 (C=S)
VII*	146,7	127.8 q, $^2J_{CF}$ = 35 Hz	143,7	141,4	156,7	121.5 q, J_{CF} = 275.1 Hz	42,6; 43,6; 44,7; 45,2 ($2NMe_2$); 187,2; 189,2 (C=S)
Ic	148,0	128,5	137.3 q, $^2J_{CF}$ = 31.8 Hz	128,5	148,0	120.7 q, J_{CF} = 277.2 Hz	—
IX	153,0	134,9	131.1 q, $^2J_{CF}$ = 35 Hz	130,0	155,2	121.3 q, J_{CF} = 275.8 Hz	43,0; 45,1 (NMe_2); 184,8 (C=O); 190,0 (C=S)
X	155,0	126,4	125.8 q, $^2J_{CF}$ = 35 Hz	126,4	155,0	121.6 q, J_{CF} = 275 Hz	183,7 (C=O)

*The numbering of atoms is analogous to (VI).



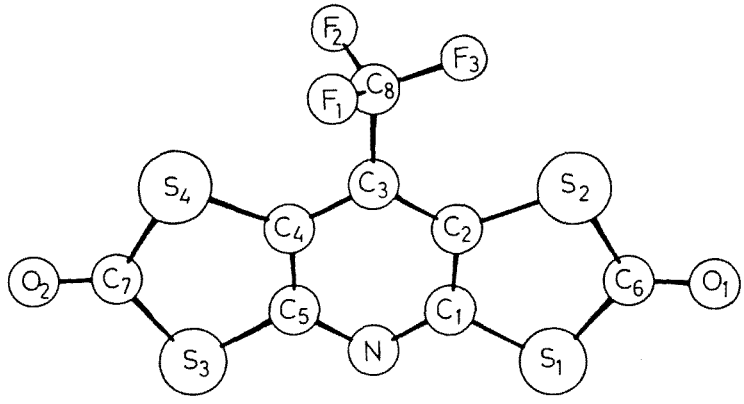
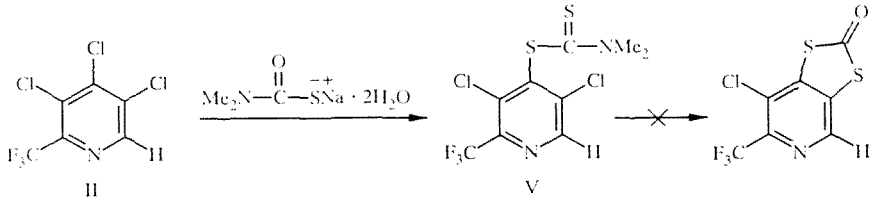


Fig. 1. Structure of the 8-trifluoromethylbis-1,3-dithiolo[4,5-b:4′,5′-e]pyridine-2,6-dione molecule.

The decision on the location of the dithiole ring was made on the basis of a comparative analysis of the NMR spectra of compounds (Ia) and (IV) (Table 1), and also by analogy with the X-ray crystallographic data on the cyano analog[1]. Significant displacements of 5.5 and 11.5 ppm towards high field were observed for the signals of the $C_{(4)}$ and $C_{(5)}$ carbon atoms respectively in the spectrum of compound (IV), and are explained by the significant electron-donating effect of the sulfur atom. In addition, a displacement towards high field was characteristic for the $C_{(3)}$ signal of compound (IV) though the positions of the $C_{(2)}$ and $C_{(6)}$ peaks were displaced less significantly. A signal for a carbonyl carbon atom at 182 ppm was also present in the spectrum of compound (IV).

A stable derivative (V) is formed on reacting compound (II) with sodium dimethyldithiocarbamate in acetone. Compound (V) does not undergo any significant changes on boiling in organic solvents at temperatures up to 100°C.



Yellow crystals of compound (V) were obtained in all experiments and had a sharp melting point with a 1-2°C range.

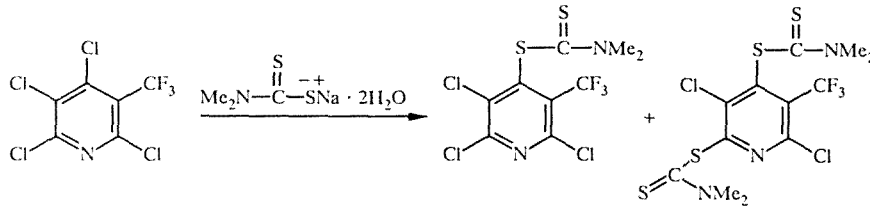
Signals were present in the ^{13}C NMR spectrum of compound (V) for methyl carbon atoms and for a thiocarbonyl group characteristic of the dimethyldithiocarbamate substituent. A displacement of 6-6.5 ppm towards low field compared with the initial chloropyridine (II) was observed for the $C_{(3)}$ and $C_{(5)}$ signals with an insignificant change in the position of the peaks for $C_{(2)}$, $C_{(4)}$, and $C_{(6)}$, which is a characteristic of the 4-N,N-dialkyldithiocarbamates of polychloropyridines [1].

Our proposals on the possibility of carrying out nucleophilic cyclizations at the activated 5 position of the pyridine by the reaction of compound (Ia) with sodium N,N-dimethyldithiocarbamate were therefore confirmed completely. In addition, the reduction of electron-accepting properties of one α substituent hinders the carrying out of a second intramolecular reaction in the substituted 3,4,5,6-tetrachloropyridine and leads to the need for thermal stimulation of these processes. A 1,3-dithiole derivative is not generally formed when a second substituent, such as the $Cl_{(6)}$, is replaced by hydrogen.

The proposals on the orientating effect of the CF_3 substituent in compound (Ib) were confirmed in full by experiment. Reaction with a 50% excess of sodium N,N-dimethyldithiocarbamate gave a mixture of two compounds, the products of mono- and disubstitution with a predominance of the latter. Study of the ^{13}C NMR spectra confirmed the formation of 4 (VI) and 2,4 (VII) substituted dithiocarbamates. Signals were observed in the spectrum of compound (VI) which are characteristic of the dimethyl-dithiocarbamate substituent. In the pyridine portion of the spectrum the picture was characteristic of 4 derivatives of this nucleus, viz., a displacement of 5-7 ppm towards low field for the signals of the $C_{(3)}$ and $C_{(5)}$ atoms with an insignificant change in the position for the $C_{(2)}$, $C_{(4)}$, and $C_{(6)}$ peaks. The presence of a second dithiocarbamate group at position 2 leads to signal displacement for $C_{(2)}$ of 5 ppm and $C_{(3)}$ of 3.4 ppm towards low field, and for $C_{(4)}$ of 1.6 ppm towards high field. The positions of the $C_{(5)}$ and $C_{(6)}$ peaks underwent almost no change.

TABLE 2. Bond Lengths in Compound (X)

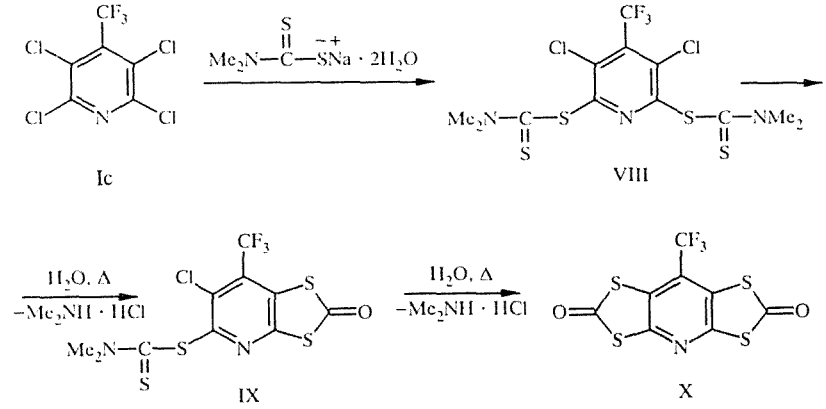
Bond	d, Å	Bond	d, Å
$S_{(1)}—C_{(6)}$	1,751(7)	$S_{(2)}—C_{(2)}$	1,755(5)
$S_{(1)}—C_{(1)}$	1,757(6)	$S_{(2)}—C_{(6)}$	1,774(7)
$S_{(3)}—C_{(5)}$	1,742(6)	$S_{(4)}—C_{(4)}$	1,755(6)
$S_{(3)}—C_{(7)}$	1,783(7)	$S_{(4)}—C_{(7)}$	1,774(8)
$O_{(1)}—C_{(6)}$	1,213(8)	N—$C_{(1)}$	1,322(8)
$O_{(2)}—C_{(7)}$	1,191(8)	N—$C_{(5)}$	1,329(7)
$C_{(1)}—C_{(2)}$	1,394(8)	$C_{(2)}—C_{(3)}$	1,396(8)
$C_{(3)}—C_{(4)}$	1,389(8)	$C_{(3)}—C_{(8)}$	1,493(9)
$C_{(4)}—C_{(5)}$	1,397(8)	$C_{(8)}—F_{(5)}$	1,183(14)
$C_{(8)}—F_{(2)}$	1,221(15)	$C_{(8)}—F_{(1)}$	1,359(17)
$C_{(8)}—F_{(3)}$	1,338(13)	$C_{(8)}—F_{(4)}$	1,366(14)
$C_{(8)}—F_{(6)}$	1,345(20)		



Ib VI VII

All attempts to bring about thermal cyclization of compounds (VI) and (VII) (heating to 100°C in various solvents) were unsuccessful, only the initial compounds were determined in solution.

The presence of a CF_3 substituent at position 4 in a tetrachloropyridine [compound (Ic)] proved to be totally adequate for the activation of the $Cl_{(3)}$ and $Cl_{(5)}$ atoms and they participated in a second intramolecular substitution of the 2,6-dithiocarbamate intermediate (VIII) leading to the formation of the tricyclic compound (X). The product of substitution of one chlorine atom (IX) was the second substance isolated from the reaction mixture.



Ic VIII IX X

Signals in the ^{13}C NMR spectrum of compound (IX) were readily identified as being characteristic of the dithiocarbamate (43.0 and 43.1 ppm CH_3 and 190.0 ppm C=S) and dithiolone (184.8 ppm C=O) fragments. In addition the latter is determined in the IR spectra by the presence of the carbonyl group absorption band at 1720 cm^{-1}. The majority of the signals of the pyridine ring carbon atoms were displaced towards low field compared to the initial (Ic) and only the one signal for $C_{(4)}$ was displaced by 6.2 ppm towards high field. Analysis of the NMR spectra of compound (X) confirmed the symmetrical structure of the molecule. There were three signals for the carbon atoms of the pyridine ring. The signals for $C_{(2)}$ and $C_{(6)}$ were displaced by 7 ppm towards low field and the $C_{(3)}$, $C_{(4)}$, and $C_{(5)}$ signals were displaced towards high field. In addition, only one signal for the carbon of a C=O group was present in the spectrum. The structure of the compound

TABLE 3. Valence Angles in Compound (X)

Bond	ω	Bond	ω
$C_{(1)}$—$S_{(1)}$—$C_{(6)}$	95,2(3)	$C_{(2)}$—$S_{(2)}$—$C_{(6)}$	95,7(3)
$C_{(5)}$—$S_{(3)}$—$C_{(7)}$	95,3(3)	$C_{(4)}$—$S_{(4)}$—$C_{(7)}$	96,3(3)
$C_{(1)}$—N—$C_{(5)}$	116,4(5)	N—$C_{(1)}$—$C_{(2)}$	124,8(6)
$S_{(1)}$—$C_{(1)}$—N	117,3(5)	$S_{(1)}$—$C_{(1)}$—$C_{(2)}$	117,84(5)
$C_{(1)}$—$C_{(2)}$—$C_{(3)}$	118,7(5)	$S_{(2)}$—$C_{(2)}$—$C_{(3)}$	125,5(4)
$S_{(2)}$—$C_{(2)}$—$C_{(1)}$	115,8(4)	$C_{(2)}$—$C_{(3)}$—$C_{(4)}$	116,8(5)
$C_{(4)}$—$C_{(3)}$—$C_{(8)}$	121,4(6)	$C_{(2)}$—$C_{(3)}$—$C_{(8)}$	121,8(6)
$C_{(3)}$—$C_{(4)}$—$C_{(5)}$	119,7(6)	$S_{(4)}$—$C_{(4)}$—$C_{(5)}$	115,7(4)
$S_{(4)}$—$C_{(4)}$—$C_{(3)}$	124,7(5)	N—$C_{(5)}$—$C_{(4)}$	123,6(5)
$S_{(3)}$—$C_{(5)}$—N	117,9(4)	$S_{(3)}$—$C_{(5)}$—$C_{(4)}$	118,5(5)
$S_{(1)}$—$C_{(6)}$—$O_{(1)}$	124,1(6)	$S_{(1)}$—$C_{(6)}$—$S_{(2)}$	115,4(4)
$S_{(2)}$—$C_{(6)}$—$O_{(1)}$	120,6(6)	$S_{(3)}$—$C_{(7)}$—$S_{(4)}$	114,3(4)
$S_{(4)}$—$C_{(7)}$—$O_{(2)}$	122,4(6)	$S_{(3)}$—$C_{(7)}$—$O_{(2)}$	123,3(6)
$C_{(3)}$—$C_{(8)}$—$F_{(1)}$	108,4(9)	$C_{(3)}$—$C_{(8)}$—$F_{(2)}$	113,8(9)
$C_{(3)}$—$C_{(8)}$—$F_{(3)}$	112,6(7)	$C_{(3)}$—$C_{(8)}$—$F_{(4)}$	108,4(8)
$C_{(3)}$—$C_{(8)}$—$F_{(5)}$	117,0(9)	$C_{(3)}$—$C_{(8)}$—$F_{(6)}$	113,0(1)
$F_{(1)}$—$C_{(8)}$—$F_{(2)}$	112,4(1,4)	$F_{(1)}$—$C_{(8)}$—$F_{(3)}$	100,7(1,4)
$F_{(2)}$—$C_{(8)}$—$F_{(3)}$	108,3(1,2)	$F_{(4)}$—$C_{(8)}$—$F_{(5)}$	106,7(1,6)
$F_{(4)}$—$C_{(8)}$—$F_{(6)}$	97,1(1,4)	$F_{(5)}$—$C_{(8)}$—$F_{(6)}$	112,4(1,8)

TABLE 4. Coordinates of Atoms ($\times 10^4$) in Compound (X)

Atom	x	y	z
$S_{(1)}$	0,3633(2)	0,2190(1)	0,0601(2)
$S_{(2)}$	0,4389(2)	0,4147(1)	0,1381(2)
$S_{(3)}$	0,8432(2)	0,1005(1)	0,5067(2)
$S_{(4)}$	0,9476(2)	0,2894(1)	0,6149(2)
$F_{(1)}$	0,8741(12)	0,4690(10)	0,4004(24)
$F_{(2)}$	0,7372(32)	0,4662(10)	0,5720(20)
$F_{(3)}$	0,6460(19)	0,5118(6)	0,3373(24)
$F_{(4)}$	0,6144(16)	0,4906(10)	0,4720(33)
$F_{(5)}$	0,7711(45)	0,4985(12)	0,3361(26)
$F_{(6)}$	0,8363(24)	0,4556(13)	0,5786(27)
$O_{(1)}$	0,2052(6)	0,3587(4)	-0,0908(6)
$O_{(2)}$	1,0891(6)	0,1401(4)	0,7398(7)
N	0,6078(6)	0,1721(3)	0,2911(6)
$C_{(1)}$	0,5273(7)	0,2426(4)	0,2177(7)
$C_{(2)}$	0,5638(6)	0,3340(4)	0,2552(7)
$C_{(3)}$	0,6931(7)	0,3541(4)	0,3808(8)
$C_{(4)}$	0,7790(7)	0,2804(4)	0,4573(7)
$C_{(5)}$	0,7318(7)	0,1915(4)	0,4094(7)
$C_{(6)}$	0,3140(8)	0,3337(8)	0,0166(8)
$C_{(7)}$	0,9330(8)	0,1703(5)	0,6396(8)
$C_{(8)}$	0,7365(9)	0,4502(5)	0,4318(10)

(X) molecular was confirmed by x-ray crystallographic analysis (see Fig. 1). The molecule is planar. The trifluoromethyl group is randomized at two positions each half populated with a turn about the $C_{(3)}-C_{(8)}$ bond of 60°C. The orientation of the CF_3 group is such that one of the fluorine atoms lies in the plane of the molecule. Bond lengths (Table 2) and valence angles (Table 3) have the usual values for the corresponding bonds and require no comment.

A general method has been developed for obtaining derivatives of 1,3-dithiolo[4,5-c]pyridine and bis-1,3-dithiolo[4,5-b:4′,5′-e]pyridine. It is based on the reaction of tetrachloropyridines containing accepting substituents in positions 2 or 4 (more accepting than a chlorine atom) with sodium N,N-dialkyldithiocarbamates.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-80 instrument in Nujol. The ^{13}C NMR spectra were drawn on a Bruker AC 200 instrument with an operating frequency of 50 MHz in $CDCl_3$ solution, internal standard was TMS. Experi-

mental data totalling 1044 independent reflections were obtained on a DAR-UM automatic diffractometer with CuKα radiation and a graphite monochromator. The structure was determined by the direct statistical method and refined in a full-matrix anisotropic approach to R = 0.060. All calculations were carried out with the AREN set of programs [5]. The coordinates of atoms are given in Table 4.

4,7-Dichloro-6-trifluoromethyl-1,3-dithiolo[4,5-c]pyridine-2-one (IV) $C_7Cl_2F_3NOS_2$. A solution of sodium N,N-dimethyldithiocarbamate dihydrate (2.3 g, 0.013 mole) in acetone (70 ml) was added with stirring to a solution of compound (Ia) (2.83 g, 0.01 mole) in acetone (50 ml). The reaction mixture was boiled under reflux for 0.5 h, then cooled, and filtered. The filtrate was evaporated in vacuum and the residue chromatographed on a column of silica gel (eluent was benzene–hexane, 1:4). Compound (IV) (2.39 g: 78%) was obtained as white crystals of mp 70-71.5°C (hexane).

3,5-Dichloro-2-trifluoromethyl-4-pyridyl N,N-Dimethyldithiocarbamate (V) $C_9H_7Cl_2F_3N_2S_2$. Sodium N,N-dimethyl-dithiocarbamate (2 g, 0.01 mole) was added with stirring at room temperature to a solution of compound (II) (1.25 g, 0.005 mole) in acetone (25 ml) and the mixture stirred for 5 h. The solvent was removed in vacuum and the residue chromatographed on a column of silica gel (eluent was benzene–hexane, 3:1). Compound (V) (1.51 g, 90%) was obtained as yellow crystals of mp 96-97.5°C (from hexane).

Reaction of Compound (Ib) with Sodium N,N-Dimethyldithiocarbamate Dihydrate. The reagent (1.35 g, 0.0075 mole) dissolved in acetone (75 ml) was added at room temperature to a solution of compound (Ib) (1.42 g, 0.005 mole) in acetone (25 ml). The reaction mixture was stirred for 2 h, the solvent removed in vacuum, and the residue chromatographed on a column of silica gel (eluent was benzene). The monosubstituted compound (VI) was eluted initially and then the disubstituted product (VI). After removal of the solvent compounds (VI) (0.5 g) and (VII) (0.65 g) were obtained.

2,5,6-Trichloro-3-trifluoromethyl-4-pyridyl N,N-Dimethyldithiocarbamate (VI) $C_9H_6Cl_3F_3N_2S_2$. Yellow crystals of mp 146-148°C (hexane).

3,6-Dichloro-5-trifluoromethyl-2,4-pyridodiyl Bis(N,N-dimethyldithiocarbamate) (VII) $C_{12}H_6Cl_2F_3N_3S_4$. Yellow crystals of mp 140°C (with decomposition).

Reaction of Compound (Ic) with Sodium N,N-Dimethyldithiocarbamate Dihydrate. A solution of the reagent (1.79 g, 0.001 mole) in acetone (100 ml) was added with stirring to a solution of compound (Ic) (1.42 g, 0.005 mole) in acetone (25 ml). The reaction mixture was boiled under reflux for 6 h. The solvent was removed in vacuum and the residue chromatographed on a column of silica gel (eluent was benzene–hexane, 1:2). Compound (X) (0.4 g) was obtained after removing the solvent. Subsequent elution with a 1:1 benzene–hexane mixture gave compound (IX) (0.2 g).

6-Chloro-2-oxo-7-trifluoromethyl-1,3-dithiolo[4,5-b]-5-pyridyl N,N-dimethyldithiocarbamate (IX) $C_{10}H_6ClF_3N_2OS_2$. Yellow crystals of mp 150°C (with decomposition).

8-Trifluoromethyl-bis-1,3-dithiolo[4,5-b:4′,5′-e]pyridine-2,6-dione (X) $C_8F_3NO_2S_2$. Yellow crystals of mp 160.5-161.5°C (from methanol).

The crystals of compound (X) were monoclinic with the following crystallographic parameters: a = 8.982(2), b = 14.628(3), c = 8.561(2) Å, β = 104.90(4)°, V = 1087.0 Å^3, M = 327.33, d = 2.000 g/cm^3, Z = 4.

REFERENCES

1. A. M. Sipyagin and Z. G. Aliev, Khim. Geterotsikl. Soedin., No. 9, 1207 (1993).
2. A. M. Sipyagin and B. V. Kunshenko, Khim. Geterotsikl. Soedin., No. 5, 657 (1994).
3. S. M. Shein and A. V. Evstifeeva, Zh. Obshch. Khim., **38,** 492 (1968).
4. L. M. Yagupol'skii, Aromatic and Heterocyclic Compounds with Fluorine-Containing Substituents [in Russian], Naukova Dumka, Kiev (1988).
5. V. I. Andrianov, Kristallografiya, **32,** No. 1, 228 (1987).
6. A. M. Sipyagin, V. V. Kolchanov, and N. N. Sveshnikov, Khim. Geterotsikl. Soedin., No. 5, 660 (1994).