Chemistry of Heterocyclic Compounds, Vol. 37, No. 10, 2001

STEREOSELECTIVE SYNTHESIS AND ALKYLATION OF N-METHYLMORPHOLINIUM 4,5-*trans*-4-(2-CHLOROPHENYL)-3-CYANO-6-HYDROXY-5-(2-THENOYL)-6-TRIFLUOROMETHYL-1,4,5,6-TETRAHYDROPYRIDINE-2-THIOLATE. MOLECULAR AND CRYSTAL STRUCTURE OF 4,5-*trans*-4-(2-CHLOROPHENYL)-3-CYANO-6-HYDROXY-2-METHALLYLTHIO-5-(2-THENOYL)-6-TRIFLUOROMETHYL-1,4,5,6-TETRAHYDROPYRIDINE

S. G. Krivokolysko[1], V. D. Dyachenko[1], A. N. Chernega[2], and V. P. Litvinov[3]

The condensation of 2-chlorobenzaldehyde with cyanothioacetamide and 2-thenoyltrifluoroacetone in the presence of N-methylmorpholine takes place stereoselectively and leads to the formation of N-methylmorpholinium 4,5-trans-4-(2-chlorophenyl)-3-cyano-6-hydroxy-5-(2-thenoyl)-6-trifluoromethyl-1,4,5,6-tetrahydropyridine-2-thiolate. The latter was used to synthesize the corresponding 2-alkylthiotetrahydropyridines. The structure of 4,5-trans-4-(2-chlorophenyl)-3-cyano-6-hydroxy-2-methallylthio-5-(2-thenoyl)-6-trifluoromethyl-1,4,5,6-tetrahydropyridine was determined by X-ray crystallographic analysis.

Keywords: 2-thenoyltrifluoroacetone, tetrahydropyridines, 2-chlorobenzaldehyde, cyanothioacetamide, alkylation, condensation.

The reaction of benzoyltrifluoroacetone with 2-thienylmethylenecyanoselenoacetamide was used successfully for the synthesis of 3,4-*trans*-5-benzoyl-3-cyano-4-(2-thenoyl)-6-trifluoromethyl-3,4-dihydropyridine-2(1H)-selenone [1]. At the same time partially hydrogenated sulfur-containing pyridines with a trifluoromethyl group are unknown [2].

We established that the reaction of 2-chlorobenzaldehyde (**1**), cyanothioacetamide (**2**), and 2-thenoyltrifluoroacetone (**3**) in ethanol (~20°C) in the presence of N-methylmorpholine takes place stereoselectively with the formation of N-methylmorpholinium 4,5-*trans*-4-(2-chlorophenyl)-3-cyano-6-

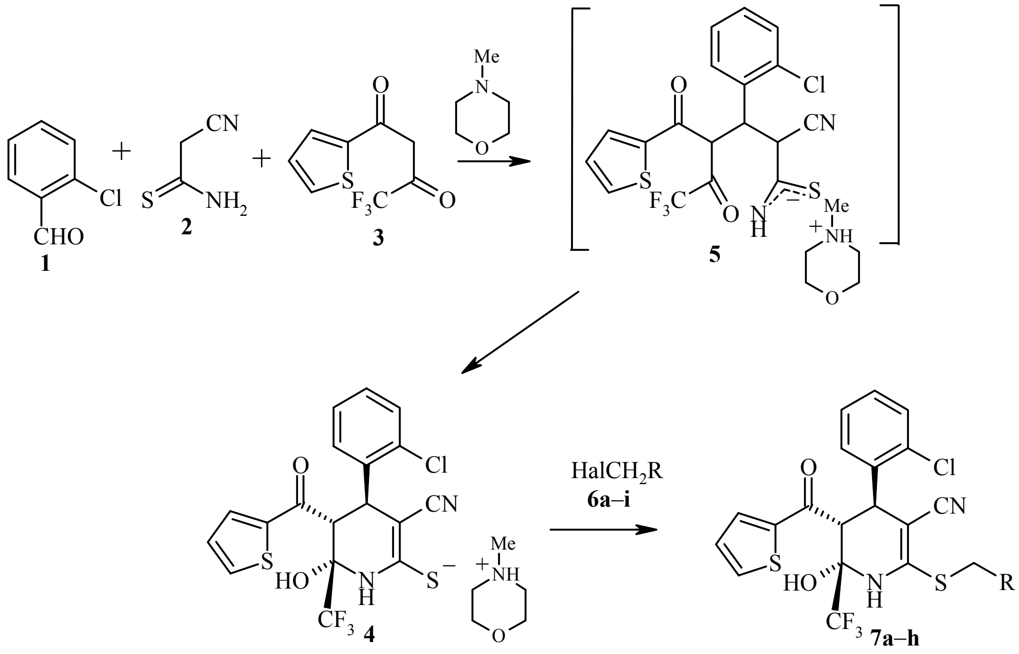
---

[1] Taras Shevchenko Lugansk State Pedagogical University, Lugansk 91011, Ukraine; e-mail: kgb@lgpi.lugansk.ua. [2] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev. [3] N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow; e-mail: vpl@cacr.ioc.ac.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1324-1331, October, 2001. Original article submitted May 18, 1999. Revision submitted January 7, 2000.

0009-3122/01/3710-1208$25.00©2001 Plenum Publishing Corporation

hydroxy-5-(2-thenoyl)-6-trifluoromethyl-1,4,5,6-tetrahydropyridine-2-thiolate (**4**). It is clear that the regioselectivity of the reaction is determined in the intermediate **5**. During the alkylation of the salt **4** by the halides **6** the corresponding sulfides **7** were obtained.

The structure of compounds **4**, **7** was confirmed by the results of elemental analysis and by physicochemical methods (Experimental, Tables 1 and 2). Thus, the ^1H NMR spectra of these compounds contain the signals for the protons of all the substituents, the NH group, and the N-methylmorpholinium cation. The signals of the 4-H and 5-H protons are represented by broad doublets in the regions of 4.80-4.92 and 3.93-4.40 ppm with spin–spin coupling constant ^3J = 10-14 Hz and also by a broad signal in the region of 4.30-4.43 ppm.



6, **7** **a** Hal = I, R = H; **b** Hal = I, R = Me; **c** Hal = Cl, R = COOMe; **d** Hal = Cl, R = COOEt;
e Hal = Cl, R = C(Me)=CH_2; **f** Hal = Cl, R = Ph; **g** Hal = Cl, R = $CONH_2$; **h** Hal = Cl,
R = 4-BrC_6H_4NHCO; **i** Hal = Br, R = COPh

The integral intensity ratio of the above-mentioned doublets and of the broad signal is ~2:1. The presented data indicate that compounds **4** and **7** represent a mixture of conformers (A and B), in which the conformer A with the *trans*-diaxial arrangement of the 4-H and 5-H protons predominates.

In order to explain the ^1H NMR data and to establish unambiguously the structure of the tetrahydropyridines **4** and **7** an X-ray crystallographic analysis of compound **7e** was undertaken (Fig. 1, Table 3; the numbering of the atoms in the names and in the ^1H NMR spectra presented in Table 1 does not conform to IUPAC nomenclature).

The central heterocycle $N_{(1)}C_{(1-5)}$ is nonplanar (the deviations of the atoms from the mean-square plane are 0.07-0.31 Å) and has a half-chair conformation; the $N_{(1)}C_{(1-3)}$ atoms are coplanar within 0.001 Å, while the $C_{(4)}$ and $C_{(5)}$ atoms project from this plane by -0.47 and 0.23 Å. The torsion angles in this heterocycle $N_{(1)}C_{(1)}C_{(2)}C_{(3)}$ 0.3, $C_{(1)}C_{(2)}C_{(3)}C_{(4)}$ 18.6, $C_{(2)}C_{(3)}C_{(4)}C_{(5)}$ -45.6, $C_{(3)}C_{(4)}C_{(5)}N_{(1)}$ 55.8, $C_{(4)}C_{(5)}N_{(1)}C_{(1)}$ -38.6, $C_{(5)}N_{(1)}C_{(1)}C_{(2)}$ 10.5° are close to those found in cyclohexene and its derivatives [3].

TABLE 1. The ^{1}H NMR Spectra of the Synthesized Compounds **7a-i**

Compound	Chemical shifts, δ, ppm, SSCC (J), Hz*
7a	2.52 (s, SMe); 4,25 (br. d, $^3J = 11.4$, 5-H$_A$); 4.35 (br. s, 4-H$_B$ and 5-H$_B$); 4.88 (br. d, $^3J = 11.4$, 4-H$_A$); 7.15 and 7.87 (two m, Ar and Het); 7.43 (s, OH); 8.20 (s, NH)
7b	1.28 (t, $^3J = 6.5$, Me); 3.01 and 3.07 (two d, $^3J = 6.5$, SCH$_2$); 4.20 (br. d, $^3J = 14.0$, 5-H$_A$); 4.33 (br. s, 4-H$_B$ and 5-H$_B$); 4.89 (br. d, $^3J = 14.0$, 4-H$_A$); 7.15 and 7.87 (two m, Ar and Het); 7.42 (s, OH); 8.27 (s, NH)
7c	3.73 (s, Me); 4.00 (s, SCH$_2$); 4.22 (br. d, $^3J = 11.8$, 5-H$_A$); 4.41 (br. s, 4-H$_B$ and 5-H$_B$); 4.85 (br. d, $^3J = 11.8$, 4-H$_A$); 7.16 and 7.90 (two m, Ar and Het); 7.51 (s, OH); 8.31 (s, NH)
7d	1.25 (t, $^3J = 6.6$, Me); 3.99 (s, SCH$_2$); 4.18 (q, $^3J = 6.6$, OCH$_2$); 4.30 (br. d, $^3J = 13.0$, 5-H$_A$); 4.33 (br. s, 4-H$_B$ and 5-H$_B$); 4.87 (br. d, $^3J = 13.0$, 4-H$_A$); 7.13, 7.71 and 7.89 (three m, Ar and Het); 7.50 (s, OH); 8.31 (s, NH)
7e	1.85 (s, Me); 3.62 and 3.72 (two d, $^2J = 8.0$, SCH$_2$); 4.16 (br. d, $^3J = 12.0$, 5-H$_A$); 4.43 (br. s, 4-H$_B$ and 5-H$_B$); 4.86 (br. d, $^3J = 12.0$, 4-H$_A$); 4.98 (s, =CH$_2$); 7.15 m, 7.65 m and 7.88 d, $^3J = 4.8$ (Ar and Het); 7.42 (s, OH); 8.24 (s, NH)
7f	3.93 (br. d, $^3J = 11.7$, 5-H$_A$); 4.26 and 4.34 (two d, $^2J = 12.8$, SCH$_2$); 4.38 (br. s, 4-H$_B$ and 5-H$_B$); 4.80 (br. d, $^3J = 11.7$, 4-H$_A$); 7.13 m, 7.41 m, 7.75 m and 7.88 d, $^3J = 4.7$ (Ar and Het); 7.49 (s, OH); 8.42 (s, NH)
7g	3.63 and 3.73 (two d, $^2J = 15.4$, SCH$_2$); 4.38 (br. d, $^3J = 12.5$, 5-H$_A$); 4.42 (br. s, 4-H$_B$ and 5-H$_B$); 4.87 br. d, $^3J = 12.5$, 4-H$_A$); 7.12 m and 7.87 d, $^3J = 4.9$ (Ar and Het); 7.46 (s, OH); 7.74 and 8.05 (two br. s, CONH$_2$); 10.04 (s, NH)
7h	3.91 and 3.97 (two d, $^2J = 15.5$, SCH$_2$); 4.40 (br. d, $^3J = 12.0$, 5-H$_A$); 4.43 (br. s, 4-H$_B$ and 5-H$_B$); 4.90 (br. d, $^3J = 12.0$, 4-H$_A$); 7.13 m, 7.58 br. s and 7.89 m (Ar, Het and OH); 9.19 (s, NH); 10.69 (s, CONH)
7i	4.32 (br. d, $^3J = 10.0$, 5-H$_A$); 4.36 (br. s, 4-H$_B$ and 5-H$_B$); 4.81 (s, SCH$_2$); 4.92 (br. d, $^3J = 10.0$, 4–H$_A$); 7.16, 7.66 and 7.95 (three m, Ar, Het and OH); 8.33 (s, NH)

---

* The integral intensity of the protons of compounds **7** corresponds to the proposed formulas and to the ratio of the conformers A and B.

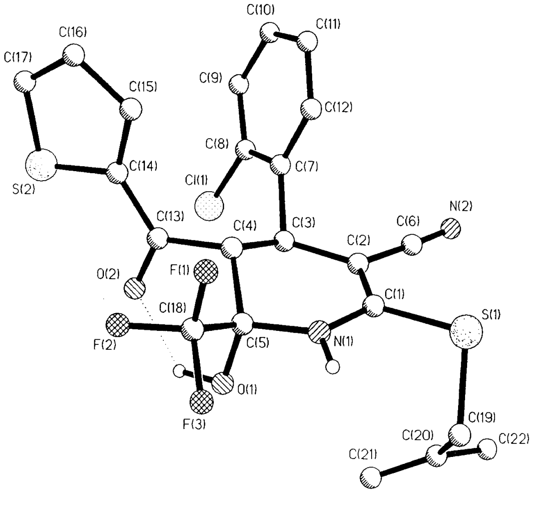


Fig. 1. General view of the molecule of compound **7e** with the numbering of the atoms. Of the hydrogen atoms only H$_{(1)}$ and H$_{(2)}$ are shown.

TABLE 2. The Characteristics of the Synthesized Compounds **7a-i**

Compound	Empirical formula	Found, % / Calculated, % C	H	N	S	mp, °C	IR spectrum, ν, cm^{-1}	Yield, %
7a	$C_{19}H_{14}ClF_3N_2O_2S_2$	49.93 49.73	3.25 3.08	5.77 6.10	13.71 13.97	215-217	3250-3390 (NH, OH), 2200 (CN), 1635 (CO)	78
7b	$C_{20}H_{16}ClF_3N_2O_2S_2$	50.56 50.76	3.68 3.41	5.71 5.92	13.74 13.56	179-181	3150-3330 (NH, OH), 2205 (CN), 1635, 1655 (CO)	75
7c	$C_{21}H_{16}ClF_3N_2O_4S_2$	48.95 48.79	3.33 3.12	5.11 5.42	12.68 12.41	163-165	3210-3375 (NH, OH), 2205 (CN), 1620, 1660, 1736 (CO)	67
7d	$C_{22}H_{18}ClF_3N_2O_4S_2$	49.99 49.77	3.13 3.42	5.44 5.28	11.78 12.08	104-106	3180-3360 (NH, OH), 2195 (CN), 1635, 1665, 1740 (CO)	81
7e	$C_{22}H_{18}ClF_3N_2O_2S_2$	52.73 52.96	3.85 3.64	5.78 5.61	12.62 12.85	164-166	3210-3330 (NH, OH), 2202 (CN), 1630, 1675 (CO)	83
7f	$C_{25}H_{18}ClF_3N_2O_2S_2$	56.33 56.13	3.52 3.36	5.42 5.24	11.71 11.99	188-190	3240, 3390 (NH, OH), 2195 (CN), 1620, 1680 (CO)	67
7g	$C_{20}H_{15}ClF_3N_3O_3S_2$	47.97 47.86	3.23 3.01	8.47 8.37	12.53 12.78	239-241	3120-3360 (NH, OH), 2204 (CN), 1620, 1650, 1702 (CO)	88
7h	$C_{26}H_{18}BrClF_3N_3O_3S_2$	47.82 47.54	2.92 2.76	6.19 6.40	9.81 9.76	243-245	3210-3300 (NH, OH), 2190 (CN), 1650, 1690 (CO)	93
7i	$C_{26}H_{18}ClF_3N_2O_3S_2$	55.72 55.47	3.29 3.22	5.21 4.98	11.53 11.39	124-126	3240, 3390 (NH, OH), 2195 (CN), 1620, 1680 (CO)	77

We note that in related compounds [4] the central $N_{(1)}C_{(1-5)}$ ring is appreciable flatter on account of $n(N_{(1)})$–$\pi^*(C_{(5)}{=}O)$ conjugation. The "torsion angle" ψ (the pseudotorsion angle between the $C_{(1)}$–$C_{(2)}$ and $C_{(4)}$–$C_{(5)}$ bonds [3]) amounts to 27.2°. As a result of conjugation between the unshared electron pair of the $N_{(1)}$ atom and the π system of the $C_{(1)}{=}C_{(2)}$ bond the interatomic $N_{(1)}$–$C_{(1)}$ separation of 1.361(9) Å is substantially shortened compared with the range of 1.43-1.45 Å characteristic of ordinary $N(sp^2)$–$C(sp^2)$ bonds [5, 6]. The hydrogen atoms $H_{(3)}$ and $H_{(4)}$ are *trans*-diaxial (torsion angle $H_{(3)}C_{(3)}C_{(4)}H_{(4)}$ -170.8°). The values of the torsion angle $C_{(7)}C_{(3)}C_{(4)}C_{(13)}$ 65 and 78°, the bond lengths $Cl_{(1A)}$–$C_{(8)}$ 1.638(7) and $Cl_{(1B)}$–$C_{(12)}$ 1.455(9) Å, and the bond angles $Cl_{(1A)}$–$C_{(8)}$–$C_{(7)}$ 122.4(6) and $Cl_{(1B)}$–$C_{(12)}$–$C_{(7)}$ 129.2(7)°, $Cl_{(1A)}$–$C_{(8)}$–$C_{(9)}$ 115.8(6) and $Cl_{(1B)}$–$C_{(12)}$–$C_{(11)}$ 106.3(7)° confirm the existence of two conformational isomers A and B for the investigated compound, formed as a result

TABLE 3. The Bond Lengths (*d*) and Bond Angles (ω) in the Molecule of Compound **7e**

Bond	*d*, Å	Angle	ω, deg
$S_{(1)}-C_{(1)}$	1.753(7)	$C_{(1)}-S_{(1)}-C_{(19)}$	100.7(4)
$S_{(1)}-C_{(19)}$	1.815(9)	$C_{(14)}-S_{(2)}-C_{(17)}$	91.3(5)
$S_{(2)}-C_{(14)}$	1.714(7)	$C_{(1)}-N_{(1)}-C_{(5)}$	121.5(6)
$S_{(2)}-C_{(17)}$	1.662(11)	$N_{(1)}-C_{(1)}-C_{(2)}$	121.9(6)
$N_{(1)}-C_{(1)}$	1.361(9)	$C_{(1)}-C_{(2)}-C_{(3)}$	122.7(6)
$N_{(1)}-C_{(5)}$	1.436(9)	$C_{(2)}-C_{(3)}-C_{(4)}$	109.3(5)
$C_{(1)}-C_{(2)}$	1.343(9)	$C_{(3)}-C_{(4)}-C_{(5)}$	110.9(6)
$C_{(2)}-C_{(3)}$	1.521(9)	$N_{(1)}-C_{(5)}-C_{(4)}$	109.6(6)
$C_{(3)}-C_{(4)}$	1.55(1)	$N_{(2)}-C_{(6)}-C_{(2)}$	177.1(8)
$C_{(4)}-C_{(5)}$	1.53(1)	$S_{(2)}-C_{(14)}-C_{(15)}$	111.9(6)
$C_{(14)}-C_{(15)}$	1.383(11)	$C_{(14)}-C_{(15)}-C_{(16)}$	110.3(8)
$C_{(15)}-C_{(16)}$	1.422(12)	$C_{(15)}-C_{(16)}-C_{(17)}$	112.3(9)
$C_{(16)}-C_{(17)}$	1.345(14)	$S_{(2)}-C_{(17)}-C_{(16)}$	114.2(7)

of the initial rotation of the benzene ring about the ordinary $C_{(3)}-C_{(7)}$ bond. The benzene ring $C_{(7-12)}$ in the molecule of **7e** is rotated by 73.2° in relation to the mean-square plane of the $N_{(1)}C_{(1-5)}$ ring, and the $S_{(2)}O_{(2)}C_{(13-17)}$ and $S_{(1)}C_{(1)}C_{(19)}$ groups form dihedral angles of 85.2 and 58.6° with the central heterocycle. In turn, the $C_{(19-21)}$ bond system is rotated significantly in relation to the $S_{(1)}C_{(1)}C_{(19)}$ group. (The corresponding dihedral angle amounts to 77.3°.) The bond lengths $S_{(1)}-C_{(1)}$ 1.753(7) and $S_{(1)}-C_{(13)}$ 1.815(9) Å and the bond angle $C_{(1)}-S_{(1)}-C_{(13)}$ 100.7(4)° are close to the corresponding values found in the molecules of known tetrahydropyridines [4]. A particular feature of the structure of compound **7e** is the fairly strong [7] intramolecular hydrogen bond $O_{(1)}-H_{(2)}\cdots O_{(2)}$, which closes the six-membered ring $C_{(4)}C_{(5)}O_{(1)}H_{(2)}O_{(2)}C_{(13)}$. The geometric parameters of this bond are as follows: $O_{(1)}\cdots O_{(2)}$ 2.668(9), $O_{(1)}-H_{(2)}$ 1.08(12), $O_{(2)}\cdots H_{(2)}$ 1.85(12) Å, $O_{(1)}H_{(2)}\cdots O_{(2)}$ 130(6)°. (The statistical mean value of the O···O distance for hydrogen bonds of the O–H···O type is 2.72 [8].) In the crystal the molecules of compound **7e** are linked into infinite chains by means of relatively weak $N_{(1)}-H_{(1)}\cdots N_{(2)}$ hydrogen bonds (Fig. 2).

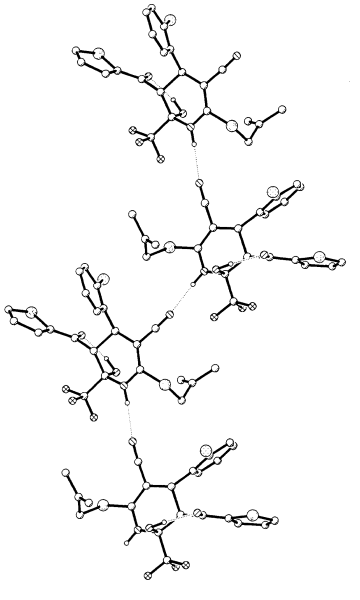


Fig. 2. A *bc* projection of the crystal structure of **7e**. (The dotted lines represent the hydrogen bonds.)

TABLE 4. The Coordinates of the Atoms and the Equivalent Isotropic Temperature Factors (U_{eq}) in the Structure of **7e**

Atom	*x*	*y*	*z*	U_{eq}, Å^2
$\text{Cl}_{(1A)}$*	0.8697(3)	0.6176(2)	0.3717(3)	0.0898
$\text{Cl}_{(1B)}$	0.6238(8)	0.4422(7)	0.0406(7)	0.0988
$\text{S}_{(1)}$	0.43073(14)	0.30844(15)	0.23798(16)	0.0590
$\text{S}_{(2)}$	1.09186(17)	0.42822(19)	0.3163(2)	0.0823
$\text{F}_{(1)}$	0.7779(5)	0.1584(4)	0.2213(5)	0.0884
$\text{F}_{(2)}$	0.9035(4)	0.1841(4)	0.3654(5)	0.0862
$\text{F}_{(3)}$	0.7660(4)	0.1078(3)	0.3744(5)	0.0943
$\text{O}_{(1)}$	0.7722(5)	0.2889(4)	0.4559(4)	0.0671
$\text{O}_{(2)}$	0.9340(4)	0.3890(5)	0.4285(5)	0.0740
$\text{N}_{(1)}$	0.6335(5)	0.2597(5)	0.2999(5)	0.0522
$\text{N}_{(2)}$	0.4729(6)	0.5657(5)	0.2201(7)	0.0739
$\text{C}_{(1)}$	0.5661(5)	0.3348(5)	0.2704(5)	0.0436
$\text{C}_{(2)}$	0.6012(5)	0.4237(5)	0.2641(5)	0.0431
$\text{C}_{(3)}$	0.7181(5)	0.4476(5)	0.2889(5)	0.0439
$\text{C}_{(4)}$	0.7809(5)	0.3553(5)	0.2829(5)	0.0443
$\text{C}_{(5)}$	0.7458(6)	0.2733(5)	0.3431(6)	0.0523
$\text{C}_{(6)}$	0.5281(6)	0.5011(6)	0.2399(6)	0.0546
$\text{C}_{(7)}$	0.7417(5)	0.5222(5)	0.2098(5)	0.0531
$\text{C}_{(8)}$	0.8107(6)	0.5961(6)	0.2434(6)	0.0834
$\text{C}_{(9)}$	0.8373(7)	0.6566(6)	0.1701(9)	0.0927
$\text{C}_{(10)}$	0.7892(9)	0.6428(7)	0.0631(9)	0.1196
$\text{C}_{(11)}$	0.7193(9)	0.5709(7)	0.0265(6)	0.1115
$\text{C}_{(12)}$	0.6988(6)	0.5127(5)	0.1009(6)	0.0991
$\text{C}_{(13)}$	0.8984(6)	0.3792(5)	0.3292(7)	0.0547
$\text{C}_{(14)}$	0.9644(5)	0.3900(5)	0.2599(7)	0.0527
$\text{C}_{(15)}$	0.9420(6)	0.3741(6)	0.1496(7)	0.0663
$\text{C}_{(16)}$	1.0325(9)	0.3935(8)	0.1149(9)	0.0914
$\text{C}_{(17)}$	1.1151(8)	0.4238(7)	0.197(1)	0.0890
$\text{C}_{(18)}$	0.7975(7)	0.1801(6)	0.3237(8)	0.0656
$\text{C}_{(19)}$	0.4235(7)	0.2595(7)	0.3659(8)	0.0775
$\text{C}_{(20)}$	0.4535(7)	0.3277(7)	0.4562(7)	0.0711
$\text{C}_{(21)}$	0.546(1)	0.322(1)	0.5310(9)	0.1089
$\text{C}_{(22)}$	0.3781(9)	0.403(1)	0.460(1)	0.1119
$\text{H}_{(1)}$	0.605(7)	0.200(7)	0.306(7)	0.09(3)
$\text{H}_{(2)}$	0.846(9)	0.326(8)	0.49(1)	0.13(4)

---

* The $\text{Cl}_{(1)}$ atom is randomized between the two positions A and B with occupations 0.72 and 0.28 respectively.

The principal geometric parameters of these H bonds are as follows: $\text{N}_{(1)}\text{–H}_{(1)}$ 0.93(9), $\text{N}_{(1)}\cdots\text{N}_{(2)}$ 3.043(9), $\text{N}_{(2)}\cdots\text{H}_{(1)}$ 2.13(9) Å, $\text{N}_{(1)}\text{H}_{(1)}\cdots\text{O}_{(1)}$ 167(6)°. (The typical value of the N···N distance for H bonds of the N–H···N type is 2.98 Å [8].)

EXPERIMENTAL

The IR spectra were recorded in vaseline oil on an IKS-29 spectrophotometer. The NMR spectra were recorded on a Bruker AM-300 instrument (300 MHz) (for compounds **7a-c**,**h**,**i**) and a Bruker WP-100 SY instrument (100 MHz) (for compounds **4**, **7d-g**) in DMSO-d_6 with TMS as internal standard. The reaction and the individuality of the products were monitored by TLC on Silufol UV-254 plates (eluent 3:5 acetone–hexane).

N-Methylmorpholinium 4,5-*trans*-4-(2-Chlorophenyl)-3-cyano-6-hydroxy-5-(2-thenoyl)-6-trifluoromethyl-1,4,5,6-tetrahydropyridine-2-thiolate (4). To a mixture of 2-chlorobenzaldehyde **1** (2.25 ml, 20 mmol) and three drops of N-methylmorpholine in ethanol (30 ml) at 20°C while stirring we added successively cyanothioacetamide **2** (2 g, 20 mmol), after 5 min 2-thenoyltrifluoroacetone **3** (4.44 g, 20 mmol), and a further portion of N-methylmorpholine (2.52 ml, 25 mmol). After 2 h the precipitate was filtered off and washed with acetone. We obtained 9.94 g (91%) of the salt **4**; mp 168-170°C. IR spectrum, cm^{-1}: 3195, 3330-3420 (N^+H, NH, OH), 2175 (CN), 1620 (CO). ^1H NMR spectrum, δ, ppm, J (Hz): 2.69 (3H, s, NMe); 3.03 (4H, m, CH_2NCH_2); 3.76 (4H, m, CH_2OCH_2); 4.20 (2/3H, br. d, $^3J = 12.2$, 5-H_A); 4.50 (2/3H, br. s, 4-H_B and 5-H_B); 4.81 (2/3H, br. d, $^3J = 12.2$, 4-H_A); 7.10, 7.67, and 7.89 (9H, three m, Ar, Het, OH, and NH). (The signal of N^+H does not appear on account of deuteroexchange.) Found, %: C 50.82; H 4.11; N 7.94; S 11.92. $C_{23}H_{23}ClF_3N_3O_3S_2$. Calculated, %: C 50.59; H 4.25; N 7.70; S 11.74.

4,5-*trans*-4-(2-Chlorophenyl)-3-cyano-6-hydroxy-2-R-methylthio-5-(2-thenoyl)-6-trifluoromethyl-1,4,5,6-tetrahydropyridines (7a-i). To a suspension of the salt **4** (2.73 g, 5 mmol) in 80% ethanol (30 ml) while stirring we added a 10% solution of potassium hydroxide (2.8 ml, 5 mmol) and after 5 min the corresponding halide **6** (5 mmol). After 3 h the precipitate was filtered off and washed with ethanol and hexane. The characteristics of compounds **7** are given in Tables 1 and 2.

X-ray Crystallographic Analysis of a Single Crystal of Compound 7e. A single crystal (0.21×0.33×0.38 mm) was investigated at 18°C on an Enraf-Nonius CAD-4 automatic four-circle diffractometer (CuKα radiation, ratio of scan rates $\omega/2\theta = 1.2$, $\theta_{max} = 60°$, segment of sphere $0 \leq h \leq 14$, $0 \leq k \leq 15$, $-14 \leq l \leq 14$). In all 3741 reflections were collected, of which 3406 were symmetrically independent. The crystals of compound **7e** are monoclinic, $a = 13.218(2)$, $b = 14.047(5)$, $c = 12.894(7)$ Å, $\beta = 107.10(3)°$, $V = 2288.2$ Å^3, M = 498.97, $Z = 4$, $d_{calc} = 1.45$ g/cm^3, $\mu = 35.97$ cm^{-1}, space group $P2_1/c$. The structure was interpreted by the direct method and refined by least-squares treatment in full-matrix anisotropic approximation using the CRYSTALS software [9]. In the refinement 2195 reflections with $I > 4(I)$ were used (306 refined parameters, number of reflections per parameter 7.2). The positions of most of the hydrogen atoms were calculated by geometry, and these atoms were included in the calculation with fixed position and temperature parameters. Only the $H_{(1)}$ and $H_{(2)}$ atoms, attached to the $N_{(1)}$ and $O_{(1)}$ atoms respectively, were revealed objectively from the difference synthesis and refined isotropically. Allowance for absorption in the crystal was made by an azimuthal scan [10]. The Chebyshev weighting scheme with parameters 2.50, -1.79, 1.07, and -1.30 was used during refinement. The final values of the convergence factors were $R = 0.076$ and $R_w = 0.085$, GOF = 1.079. The atomic coordinates are given in Table 4.

The work was carried out with financial support from the Russian Fundamental Research Fund (project No. 99-03-32965).

REFERENCES

1. V. P. Litvinov and V. D. Dyachenko, *Dokl. Akad. Nauk*, **352**, 636 (1997).
2. V. P. Litvinov, *Izv. Akad. Nauk, Ser. Khim.*, 2123 (1998).
3. A. N. Vereshchagin, *Usp. Khim.*, **52**, 1879 (1983).
4. S. G. Krivokolysko, V. D. Dyachenko, E. B. Rusanov, and V. B. Litvinov, *Khim. Geterotsikl. Soedin.*, 1076 (2001).
5. R. W. Alder, N. C. Goode, T. J. King, J. M. Mellor, and B. W. Miller, *J. Chem. Soc. Chem. Commun.*, 5, 173 (1976).
6. M. Burke-Laing and M. Laing, *Acta Crystallogr. (B)*, **32**, 3216 (1976).
7. P. Gilli, V. Bertolasi, V. Ferretti, and G. Gilli, *J. Am. Chem. Soc.*, **116**, 909 (1994).

8. L. N. Kuleshova and P. M. Zorkii, *Acta crystallogr. (B)*, **37**, 1363 (1981).
9. D. J. Watkin, C. K. Prout, J. R. Carruthers, and P. W. Betteridge, *Crystals*, Issue 10, Chemical Crystallography Laboratory, University of Oxford (1996).
10. A. C. T. North, D. C. Phillips, F. Scott, and F. S. Mathews, *Acta crystallogr. (A)*, **24**, 351 (1968).
11. J. R. Carruthers and D. J. Watkin, *Acta crystallogr. (A)*, **35**, 698 (1979).