Reaction of perfluoro-2-methylpent-2-en-3-yl isothiocyanate with methylamine

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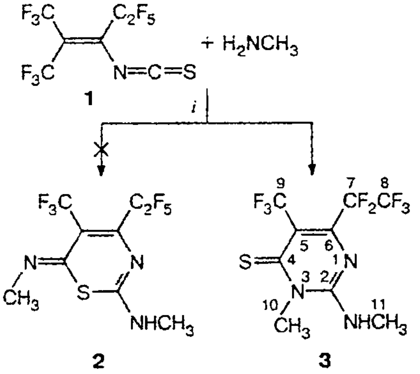
3-Methyl-2-methylamino-6-pentafluoroethyl-5-trifluoromethyl-3*H*-pyrimidine-4-thione was synthesized by treatment of perfluoro-2-methylpent-2-en-3-yl isothiocyanate with methylamine. The molecular structure of this pyrimidine-4-thione was studied by X-ray diffraction analysis.

Key words: intramolecular nucleophilic cyclization, recyclization, X-ray diffraction analysis, NMR spectroscopy.

Previously, it has been shown that treatment of perfluoro-2-methylpent-2-en-3-yl isothiocyanate (**1**) with secondary amines (diisopropylamine[1] or morpholine and piperidine[2]) results in the formation of 2-substituted perfluoro-4-ethyl-5-methyl-6*H*-1,3-thiazines, which contain two active fluorine atoms in position 6. These compounds are readily converted into 2-substituted perfluoro-4-ethyl-5-methyl-6*H*-1,3-thiazin-6-ones on storage in humid air. It may be expected that, if the reaction of compound **1** with primary amines occurs similarly to the reaction with secondary amines, then in the presence of excess primary amine, 2,6-disubstituted pentafluoroethyl-6*H*-1,3-thiazines would be formed; for example, in the case of methylamine, the reaction would yield 2-methylamino-6-methylimino-4-pentafluoroethyl-5-trifluoromethyl-6*H*-1,3-thiazine (**2**). However, we found that the reaction of compound **1** with excess methylamine in diglyme affords 3-methyl-2-methylamino-6-pentafluoroethyl-5-trifluoromethyl-3*H*-pyrimindine-4-thione (**3**) rather than compound **2**.



i. NEt$_3$, diglyme, 60 °C, 4 h

The IR and ^{1}H NMR spectra and mass spectrometry data confirm the structure attributed to compound **3**. To determine precisely the characteristic features of the conformation of compound **3**, it was studied by X-ray diffraction analysis (Fig. 1, Table 1). The molecule of compound **3** as a whole is planar, and the deviations of the atoms of the pyrimidine ring from its plane do not exceed ±0.047(2) Å. Apparently, steric interactions between the substituents in positions 4, 5, and 6 lead to marked deviations of the S(13), C(9), and C(7) atoms from the plane of the ring, *viz.*, 0.260(4), −0.185(5), and

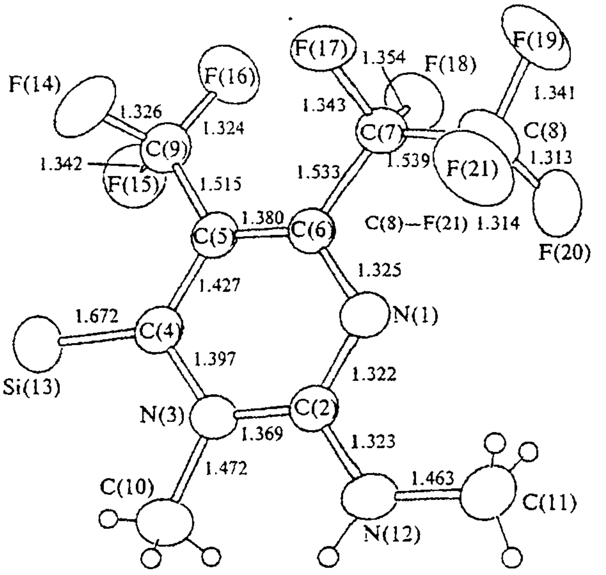


Fig. 1. Crystal structure of compound **3** according to X-ray structural analysis. The errors in the presented bond lengths are 0.003—0.004 Å.

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Table 1. Coordinates ($\times 10^4$) and equivalent thermal factors ($\times 10^3$/Å) for nonhydrogen atoms of compound **3**.

Atom	*x/a*	*y/b*	*z/c*	U_{eq}
N(1)	1789(2)	8606(2)	4055(1)	36(1)
C(2)	1495(2)	9309(3)	3469(2)	36(1)
N(3)	2093(2)	9982(3)	2996(1)	38(1)
C(4)	3056(2)	9943(3)	3109(2)	37(1)
C(5)	3362(2)	9057(3)	3698(2)	37(1)
C(6)	2700(2)	8490(3)	4164(2)	34(1)
C(7)	2898(2)	7705(3)	4889(2)	39(1)
C(8)	2051(3)	7437(4)	5393(2)	54(1)
C(9)	4401(2)	8815(4)	3781(2)	53(1)
C(10)	1708(3)	10775(6)	2367(2)	60(1)
C(11)	−81(3)	8701(6)	3854(3)	65(1)
N(12)	584(2)	9394(3)	3361(2)	47(1)
S(13)	3748(1)	10946(1)	2584(1)	52(1)
F(14)	4866(1)	9935(3)	4011(1)	77(1)
F(15)	4797(1)	8422(2)	3140(1)	72(1)
F(16)	4599(1)	7782(3)	4246(2)	89(1)
F(17)	3512(1)	8411(2)	5309(1)	61(1)
F(18)	3254(1)	6414(2)	4755(1)	55(1)
F(19)	2368(2)	6829(2)	6015(1)	76(1)
F(20)	1447(2)	6569(2)	5096(1)	69(1)
F(21)	1633(2)	8606(2)	5588(1)	72(1)

0.146(4) Å, respectively. According to the Cambridge Crystallographic Database,[3] the only monocyclic compound with a 3*H*-pyrimidine-4-thione fragment that has been studied by X-ray diffraction is 2-amino-5-cyano-4-methylthio-6(1*H*)-pyrimidinethione **4**.[4] The bond lengths in compounds **3** and **4** coincide except for the lengths of the N(3)—C(4), C(4)—C(5), and C(5)—C(6) bonds, which are equal to 1.397(3), 1.427(4), and 1.380(4) and 1.373(3), 1.402(4), and 1.411(4) Å, respectively. Nevertheless, notice that the lengths of these bonds fall within the range specified for these bonds in a (3*H*)-pyrimidine-4-thione fragment in the Cambridge Database. In the crystal, molecules of **3** form chains directed along the *a* axis; in these chains, the molecules of **3** are joined through N—H...S hydrogen bonds (parameters: N(12)...S(13) 3.469(3), H(N(12)...S(13) 2.78(4) Å, N(12)—H...S(13) 137(4)°, see Fig. 1).

It can be assumed that compound **3** is formed by the following pathway. First, methylamine attacks the carbon atom of the N=C=S group to give anion **A**, which is stabilized by abstracting a fluoride ion and is thus converted into compound **5** (Scheme 1). Under the conditions of basic catalysis (triethylamine), compound **5** generates anion **B**, which undergoes an intramolecular nucleophilic cyclization to give anion **C**; when this anion eliminates a fluoride anion, this yields compound **6**. This compound contains a very active fluorine atom at the multiple bond and reacts with methylamine to give compound **7**. Recyclization of this compound occurring *via* intermediate **D** affords compound **3**. Recyclizations of this sort are well known, for example, in the series of pyrimidines.[5]

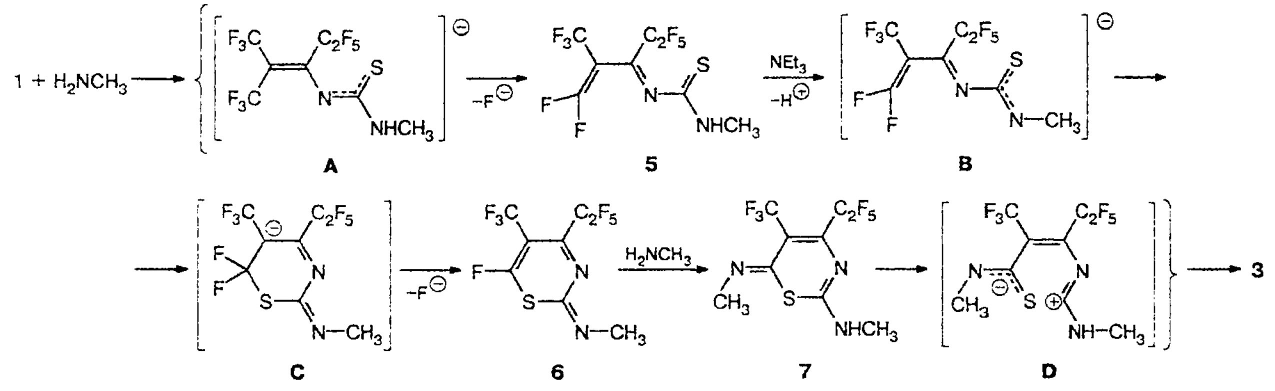
Thus, the reaction of primary amines with compound **1**, unlike that of secondary amines, leads to 3-methyl-2-methylamino-6-pentafluoroethyl-5-trifluoromethyl-3*H*-pyrimidine-4-thione rather than to 2-substituted derivatives of perfluoro-4-ethyl-5-methyl-6*H*-1,3-thiazine.

Experimental

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker WP 200SY spectrometer (200.50 and 188 MHz, respectively) with respect to internal tetramethylsilane and C_6F_6 (J_{C-H} spin-spin coupling constants were not measured). The IR spectrum was recorded on a Specord M-80 spectrophotometer (CCl_4); the electronic spectrum was run on a Specord UV VIS spectrophotometer in ethanol; mass spectra were obtained on a VG 707 OE chromato-mass spectrometer at an ionization energy of 70 eV.

3-Methyl-2-methylamino-6-pentafluoroethyl-3*H*-5-trifluoromethylpyrimidine-4-thione (3). Triethylamine (1.5 g, 0.015 mol) and then compound **1** (5.1 g, 0.015 mol) were added with stirring to methylamine (0.95 g, 0.03 mol) in 25 mL of diglyme cooled with ice water. The orange-colored mixture was stirred for 4 h at 40 °C, poured into water, and extracted with $CHCl_3$. The extract was washed with water and dried with $CaCl_2$. After evaporation of the solvent *in vacuo*, the residue was recrystallized from an MeCN—CH_2Cl_2 mixture (1 : 10). The yield of compound **3** was 4.6 g (90%), m.p. 194—195 °C. IR (CCl_4, 5%), ν/cm^{-1}: 3387, 2954 (C—H);

Scheme 1



1600, 1548 (C=C, C=N); 1525 (C=S); 1458 (C—N); 1433, 1406 (CH_3—N); 1357 (CH_3—N); 1226—1213 (C—F); 1130 (C=S). UV (EtOH), λ_{max}/nm: 232 (ε 23200), 281 (ε 11600), 366 (ε 10000). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 341 $[M]^+$ (100), 326 $[M-CH_3]^+$ (16.89), 322 $[M-F]^+$ (9.57), 311 $[M-NHCH_3]^+$ (3.31), 307 $[M-CH_3-F]^+$ (0.51), 272 $[M-CF_3]^+$ (6.48), 257 $[M-CH_3-CF_3]^+$ (6.45), 242 $[M-CF_3-NHCH_3]^+$ (1.15), 222 $[M-C_2F_5]^+$ (4.17), 119 $[C_2F_5]^+$ (1.79), 69 $[CF_3]^+$ (6.69), 30 $[NHCH_3]^+$ (24.05). Found: m/z = 341.02277, for $C_9H_7F_8N_3S$, calculated: m/z = 341.02328. Found (%): C, 31.06, 31.38; H, 2.12, 1.98; F, 44.93, 45.12; N, 11.68; S, 9.50, 9.20. Calculated (%): C, 31.67; H, 2.05; F, 44.57; N, 12.32; S, 9.38. ^{1}H NMR ($CDCl_3$), δ: 3.75 (s, 3 H, NH—CH_3, H(11)); 2.95 (s, 3 H, CH_3, H(10)). ^{13}C NMR ($CDCl_3$), δ: 183.6 (C(4)); 153.2 (C(2)); 147.7 (C(6), $^2J_{C-F}$ = 29.6 Hz); 122.5 (C(9), $^1J_{C-F}$ = 270.1 Hz); 118.6 (C(8), $^1J_{C-F}$ = 286.5 Hz, $^2J_{C-F}$ = 35.8 Hz); 115.1 (C(5), $^2J_{C-F}$ = 32.4 Hz); 111.8 (C(7), $^1J_{C-F}$ = 260.8 Hz, $^2J_{C-F}$ = 35.1 Hz); 33.7 (C(10)); 28.9 (C(11)). ^{19}F NMR ($CDCl_3$), δ: 104.1 (F(9), 3 F); 82.7 (F(8), 3 F); 51.1 (F(7), 2 F).

X-ray structural study of a single crystal of compound 3 was carried out on a SYNTEX $P2_1$ diffractometer (Cu-Kα-radiation with a graphite monochromator). The crystals of compound 3 are rhombic, a = 14.342(2), b = 9.532(2), c = 18.050(3) Å, V = 2467.6(7) Å, space group *Pbca*, Z = 8, $C_9H_7F_8N_3S$, μ = 3.335 mm^{-1}, d_{calc} = 1.837 g cm^{-3}. The intensities of 2147 independent reflections with $2\theta < 134°$ were measured by $\theta/2\theta$-scanning. A correction for the absorption over the crystal faces (transmission 0.33—0.62) was introduced. The structure was solved by the direct method using the SHELXS-86 program. The final refinement of the structural parameters was performed by the least-squares method in the full-matrix anisotropic (or isotropic for the H atoms) approximation using the SHELXL-93 program to $_wR_2$ = 0.1265 for all F^2 (R = 0.0442 for 1576$F > 4\sigma$, 219 parameters). The coordinates and the equivalent heat factors for nonhydrogen atoms are presented in Table 1.

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