Synthesis of (2*E*)-2-(tetrafluoroethylidene)-3,3-bis(trifluoromethyl)-2,3-dihydrothiazolo[3,2-*a*]benzimidazole

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The reaction of benzimidazoline-2-thione with perfluoro-2-methylpent-2-ene in the presence of triethylamine afforded (2*E*)-2-(tetrafluoroethylidene)-3,3-bis(trifluoromethyl)-2,3-dihydrothiazolo[3,2-*a*]benzimidazole whose structure was confirmed by X-ray diffraction analysis. The reaction pathways are discussed.

Key words: heterocyclization, nucleophilic substitution, X-ray diffraction analysis.

One of procedures for the preparation of perfluoroalkyl-substituted heterocyclic compounds involves the reactions of binucleophilic reagents with internal perfluoroolefins.[1] In the case of nucleophiles, which contain two potential nucleophilic centers of the **a**—**b**—**c** type bearing a charge on the atom **a** and a lone electron pair on the atom **c**, intramolecular nucleophilic cyclization proceeds in the presence of bases. For example, the reactions of thiourea[2] or sodium azide[3] with perfluoro-2-methylpent-2-ene or of potassium ethyl xanthate[4] with hexafluoropropylene gave rise to five-membered heterocyclic compounds.

In the present study, we examined the reaction of benzimidazoline-2-thione with perfluoro-2-methylpent-2-ene.

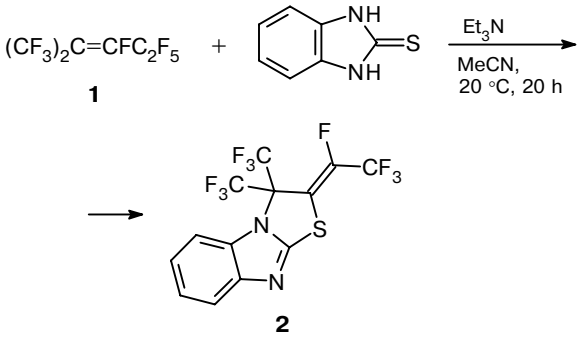
Results and Discussion

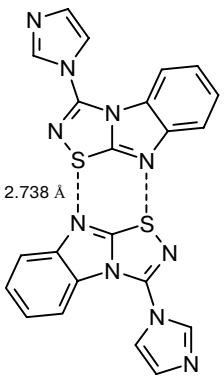
In studies on the synthesis of potential biologically active compounds containing the perfluoro-5-ethylidene-4,4-dimethyl-2-thiazoline fragment, we demonstrated that the reaction of benzimidazoline-2-thione with perfluoro-2-methylpent-2-ene (**1**) in the presence of triethylamine afforded (2*E*)-2-(tetrafluoroethylidene)-3,3-bis(trifluoromethyl)-2,3-dihydrothiazolo[3,2-*a*]benzimidazole (**2**) (Scheme 1). Previously, an analogous heterocyclic system has been prepared by the reactions of 4,5-diphenylimidazoline-2-thione and benzimidazoline-2-thione with hexafluoropropylene oxide[5] and by the reaction of benzimidazoline-2-thione with dibromoethane.[6]

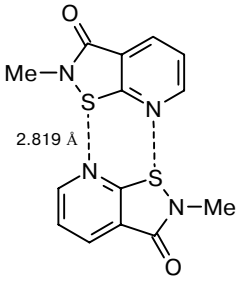
The structure of compound **2** was confirmed by the data from ^1H, ^{13}C, and ^{19}F NMR spectroscopy and X-ray diffraction analysis.

According to the X-ray diffraction data, two crystallographically independent molecules of compound **2** in the crystal (Fig. 1) are linked in dimers through rather strong secondary bonds formed by the S and N atoms (the sum of the van der Waals radii of these atoms is 3.32 Å[7]). Earlier, analogous interactions have been found in the crystals of 3-(imidazol-1-yl)-1,2,4-thiadiazolo[4,5-*a*]benzimidazole[8] and 2-methylisothiazolo[5,4-*b*]pyridin-3(2*H*)-one.[9]

Scheme 1







The bond lengths and bond angles in two independent molecules are virtually equal (to within the experimental error) to the standard values.[10] The core of molecule **2** is nearly planar (the average deviation of the atoms of the core, including the exocyclic double bond, from the mean plane is ±0.04 Å). The Cambridge

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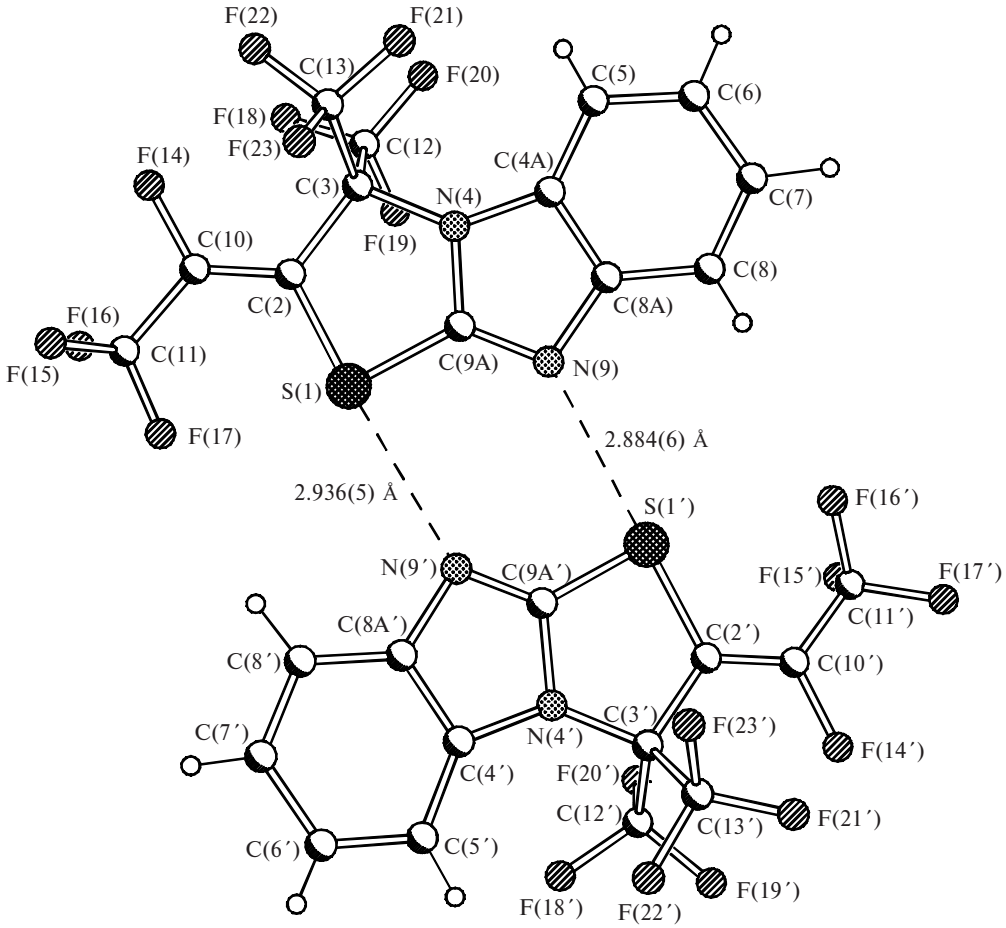
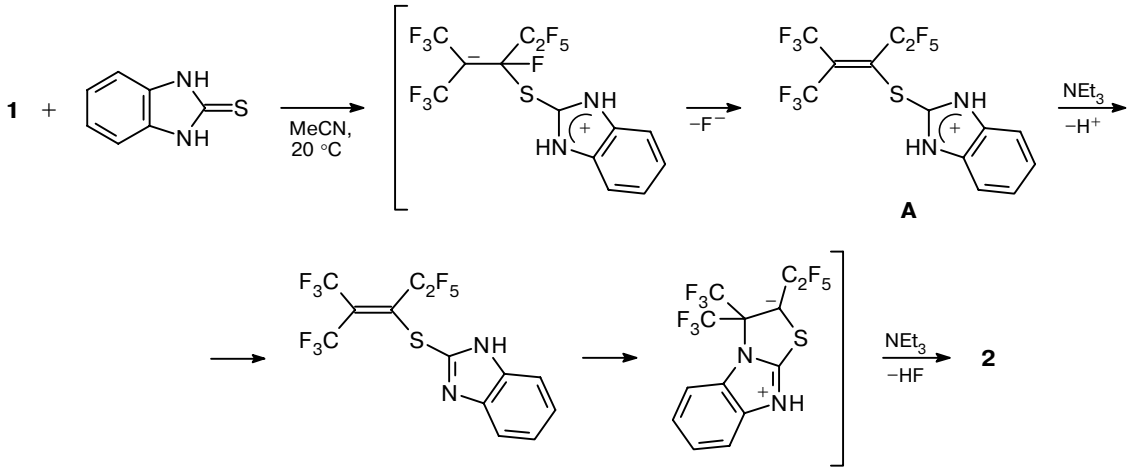


Fig. 1. Crystal structure containing two independent molecules of compound **2** based on X-ray diffraction data.

Structural Database[11] contains the data on 2-(3-hydroxy-3-methyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazol-2-yl)ethyl *N*-(4-fluorophenyl)carbamate possessing a similar core[12] in which the bond lengths are similar to those of compound **2**. However, the thiazolidine fragment in the former compound, unlike that in molecule **2**, is nonplanar and adopts a conformation intermediate between *twist* and *envelope* due, apparently, to the absence of the exocyclic double bond.

We found the optimum conditions of the synthesis of compound **2**. It can be suggested that the addition of benzimidazoline-2-thione to compound **1** gave rise ini-

Scheme 2



tially to cation **A**, which was then deprotonated upon addition of triethylamine, while the intermediate that formed underwent intramolecular heterocyclization to form compound **2** (Scheme 2).

The use of acetonitrile as the solvent makes it possible to obtain initially kinetic product **A** (which is, apparently, associated with the weak tendency of MeCN to proton transfer and the low solubility of benzimidazoline-2-thione in this solvent) followed by activation of the second nucleophilic center.

To summarize, we synthesized fused polycyclic heterocyclic compound **2** with the use of perfluoro-2-methylpent-2-ene and the ambident nucleophile, *viz.*, benzimidazoline-2-thione.

Experimental

The ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker WP-200 SY spectrometer (200, 50, and 188 MHz, respectively) relative to Me_4Si and C_6F_6 as the internal standards (the spin-spin coupling constants J_{C-H} were not measured). The IR spectra were measured on a Specord M-80 spectrometer (in CCl_4). The mass spectra were obtained on a VG 707 OE GL-mass spectrometer (EI, 70 eV).

We used acetonitrile of reagent grade, which was dried by successive distillation over P_2O_5 and CaH_2, triethylamine of reagent grade, which was stored over granulated KOH and then distilled over sodium, and benzimidazoline-2-thione of reagent grade, which was recrystallized from benzene.

X-ray diffraction study of compound 2 was carried out on a SYNTEX $P2_1$ diffractometer (Cu-Kα radiation, graphite monochromator). To prevent damage in the course of X-ray data collection, the single crystal was placed in a polyethylene capillary. Crystals of compound **2** are monoclinic, $a = 32.244(8)$, $b = 11.264(2)$, $c = 18.687(5)$ Å, $\beta = 119.95(2)°$, $V = 5881(2)$ Å^3, space group $C2/c$, $Z = 16$, $C_{13}H_4F_{10}N_2S$, $\mu = 3.120$ mm^{-1}, $d_{calc} = 1.853$ g cm^{-3}. A total of 3900 independent reflections with $2\theta < 120°$ were measured using the ω scanning technique. The intensities of the reflections were corrected taking into account the decay of the intensities of the check reflections to 75%. The absorption corrections for the crystal habitus (transmission was 0.19—0.44) and then using the DIFABS program (the correction was 0.81—1.23) were made. The structure was solved by the direct method using the SHELXS-86 program package and refined by the least-squares method in the anisotropic-isotropic (for H atoms) approximation using the SHELXL-97 program package to $wR_2 = 0.1878$, $S = 0.591$ for all reflections and to $R = 0.064$ for 1759 reflections with $F > 4\sigma$ (502 parameters were refined). The atomic coordinates and the equivalent thermal parameters of the nonhydrogen atoms in two independent molecules were deposited with the Cambridge Structural Database.

Perfluoro-2-methylpent-2-ene (1). Anhydrous MeCN (200 mL), CsF (3 g) of reagent grade, which was preliminarily calcined at 400 °C for 6 h, and the product FOL-62 purchased from JSC Galogen (Perm, Russia), which consisted of perfluoro-4-methylpent-2-ene (98%) and perfluoro-2-methylpent-2-ene (~2%) and which was kept over $CaCl_2$ for 24 h before use, were successively placed in a 2-L flask equipped with an efficient reflux condenser with a calcium-chloride tube. The reaction mixture was refluxed for 34 h with intense stirring using a magnetic stirrer and then cooled to ~20 °C. The lower fluorocarbon layer was separated, washed with H_2O, dried over $CaCl_2$, and distilled, the first 50 mL of the distillate being discarded. Subsequent distillation afforded perfluoro-2-methylpent-2-ene (950 mL) with b.p. 51 °C and the purity of 98.5—99.5% (GLC).

(2*E*)-2-(Tetrafluoroethylidene)-3,3-bis(trifluoromethyl)-2,3-dihydrothiazolo[3,2-*a*]benzimidazole (2). A solution of compound **1** (2.8 g, 9 mmol) and benzimidazoline-2-thione (1.4 g, 9 mmol) in MeCN (10 mL) was stirred at ~20 °C for 20 h. Then NEt_3 (2.02 g, 20 mmol) was added. The reaction mixture was stirred at 50 °C for 1 h, poured into water, extracted with $CHCl_3$, and dried with $CaCl_2$. The solvent was distilled off on a rotary vacuum evaporator and the solid residue was recrystallized from CH_2Cl_2. After sublimation (80 °C, 13 Torr), compound **2** was obtained in a yield of 3.3 g (79.5%), m.p. 89—90 °C. IR (CCl_4, 5%), ν/cm^{-1}: 3025 (C—H); 1660, 1610 (C=C); 1520 (C_6H_4); 1445 (C—N); 1345, 1325 (C—N); 1200—1270 (C—F); 1150 (C=S). UV (EtOH), λ_{max}/nm: 210 (ε 54000), 244 (ε 14400), 280 (ε 10600), 288 (ε 10800). MS, m/z (I_{rel} (%)): 410 $[M]^+$ (100), 391 $[M - F]^+$ (9.29), 341 $[M - CF_3]^+$ (62.09), 293 $[M - CF_3, N{=}C{=}S]^+$ (15.88), 214 $[M - 2\ CF_3, N{=}C{=}S]^+$ (16.71), 146 $[M - 3\ CF_3, N{=}C{=}S]^+$ (10.70), 134 $[C_6H_4NCS]^+$ (3.90), 102 $[C_6H_4NC]^+$ (3.34), 90 $[C_6H_4N]^+$ (5.53), 69 $[CF_3]^+$ (6.28), 39. Found: $m/z = 409.99410$ $[M^+]$. $C_{13}H_4F_{10}N_2S$. Calculated: $M = 409.99354$. ^1H NMR ($CDCl_3$), δ: 7.63 (m, 1 H, H(8)); 7.43 (m, 1 H, H(5)); 7.28 (m, 2 H, H(6), H(7)). ^{13}C NMR ($CDCl_3$), δ_C: 152 (C(9A)); 148.9 (C(4A)); 141.6 (CF=, $^1J_{C-F} = 278$ Hz, $^2J_{C-F} = 41.7$ Hz); 133.2 (C(8A)); 125.1 (C(2), $^2J_{C-F} = 32.6$ Hz); 124.1 (C(7)); 123.8 (C(6)); 121.4 (3,3-$(CF_3)_2$, $^1J_{C-F} = 290.8$ Hz); 119.9 (C(5)); 118 ($C\underline{F}_3$—CF=, $^1J_{C-F} = 275$ Hz, $^2J_{C-F} = 39.6$ Hz); 112.5 (C(8)); 76.9 (C(3), $^2J_{C-F} = 31.9$ Hz). ^{19}F NMR ($CDCl_3$), δ_F: 95.8 (d, 6 F, 3,3-$(CF_3)_2$, $J_{FF} = 28.5$ Hz); 95.5 (d, 3 F, CF_3—CF=, $J_{FF} = 8$ Hz); 55.6 (q, 1 F, C$\underline{F}$=, $J_{FF} = 28.5$ and 8 Hz).

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