Synthesis of 4,5-dihydrothiazole derivatives by the reaction of perfluoro-2-methylpent-2-en-3-yl isothiocyanate with ambident N,O- and N,S-nucleophiles

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The reactions of perfluoro-2-methylpent-2-en-3-yl isothiocyanate with ambident N,O- and N,S-nucleophiles (thiazole-2-thione, pyridine-2-thione, 2-hydroxypyridine, benzothiazole-2-thione, benzoxazole-2-thione, 3,4,5,6-tetrahydropyrimidine-2-thione) in the presence of triethylamine yield only 2-*N*-substituted 4,5-dihydrothiazole derivatives. The molecular structures of three products were determined by X-ray diffraction analysis. The reaction pathways are discussed.

Key words: nucleophilic substitution, heterocyclization, perfluoro-2-methylpent-2-en-3-yl isothiocyanate, heterocumulenes, regioselectivity, NMR spectroscopy, X-ray diffraction analysis.

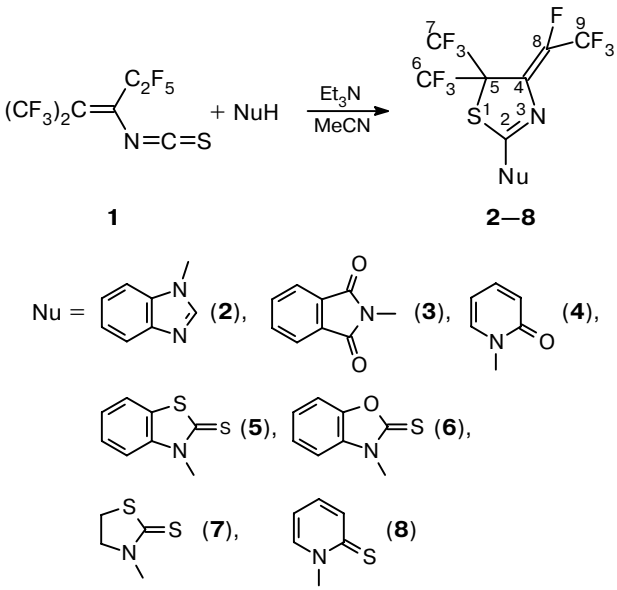
Heterocyclic compounds account for a substantial part of the current pesticides[1] and drugs.[2] Since fluorination can appreciably enhance their biological activity,[3,4] a great number of perfluoroalkylated heterocycles have been synthesized.[5—7] The methods of direct fluorination of polyfunctional compounds are advanced insufficiently, and so far the most productive approach is based on the use of fluorinated synthetic blocks and binucleophilic reagents.[8] The presence of a heterocumulene residue (for example, the isothiocyanate N=C=S group) at the double bond allows mononucleophiles to be used for constructing a heterocyclic system. Previously, it was shown that the action of, *e.g.*, dialkylamines or cyclic secondary amines on isothiocyanate derivatives of perfluoroolefins results in the formation of a fluorine-containing six-membered heterocycle (6*H*-[1,3]thiazine),[9] whereas the reactions with azoles[10] and carbazole and phenothiazine[11] yield a five-membered heterocycle (4,5-dihydrothiazole).

In the present work, the reactions of perfluoro-2-methylpent-2-en-3-yl isothiocyanate (**1**) with a series of ambident heterocyclic N,O- and N,S-nucleophiles are studied with the aim to prepare biologically active compounds and determine the most reactive nucleophilic center.

According to our data,[10,11] one could expect that compound **1** would react with N-nucleophiles to give a five-membered heterocycle (4,5-dihydrothiazole). Indeed, it was shown that the reactions of **1** with benzimidazole (in the presence of triethylamine) and potassium phthalimide afford compounds **2** and **3** (Scheme 1).

Since the other reagents involved have two or more potential nucleophilic centers, the main problem was to find out which center is responsible for the formation of the final products.

Scheme 1



It was found that the reaction of compound **1** with 2-hydroxypyridine in the presence of Et_3N in MeCN yields compound **4**. The precise structure of the latter was determined by X-ray diffraction analysis (Fig. 1). The X-ray data show that the ring of 4,5-dihydrothiazole is not completely planar, the C(5) atom deviating from the plane of the other four atoms by 0.102(3) Å. Note that the S—C$(CF_3)_2$ bond is longer (1.852(2) Å) than

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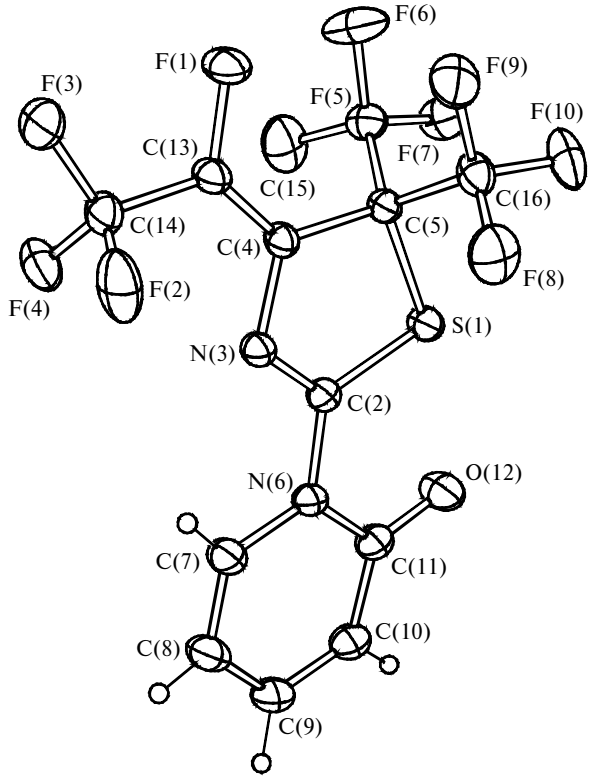


Fig. 1. Spatial structure of 1-[4(*E*)-(1,2,2,2-tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-1*H*-pyridin-2-one (**4**) according to the X-ray diffraction data.

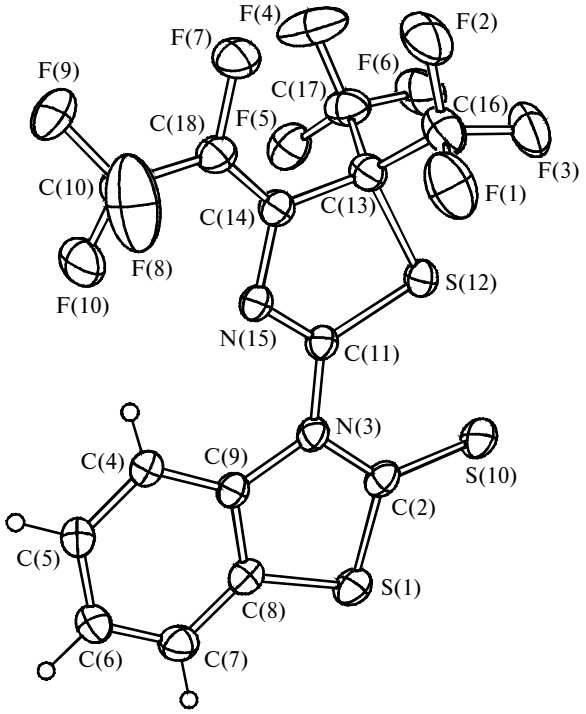


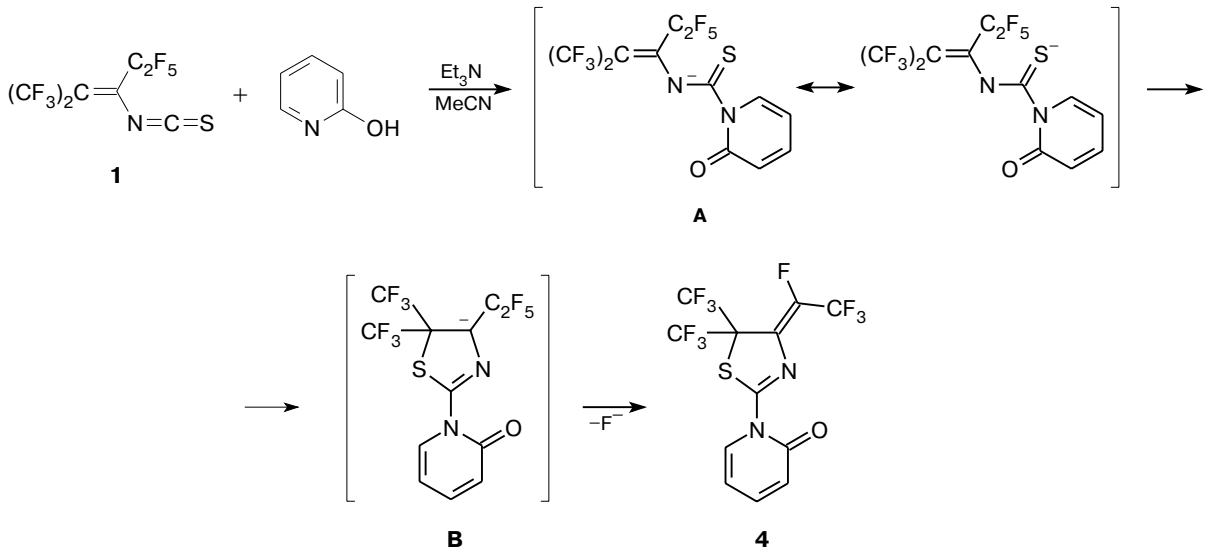
Fig. 2. Spatial structure of 3-[4(*E*)-(1,2,2,2-tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-3*H*-benzothiazole-2-thione (**5**) according to the X-ray diffraction data.

the bond length (1.817(8) Å) averaged over three compounds[11] containing the 2-amino-4-ethylidene-4,5-dihydrothiazole fragment. The six-membered ring of molecule **4** contains the localized bonds, which is characteristic of the 2-pyridone fragment.

One can assume that compound **4** is formed according to Scheme 2. Apparently, the N-nucleophilic center of 2-hydroxypyridine initially attacks the C atom of the N=C=S group to give anion **A**.

This is followed by intramolecular nucleophilic cyclization resulting, through carbanion **B**, in compound **4**.

Scheme 2



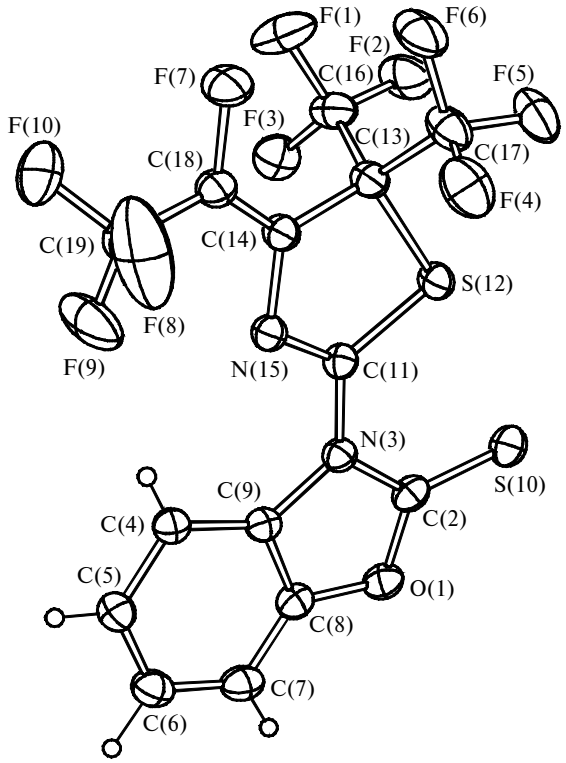
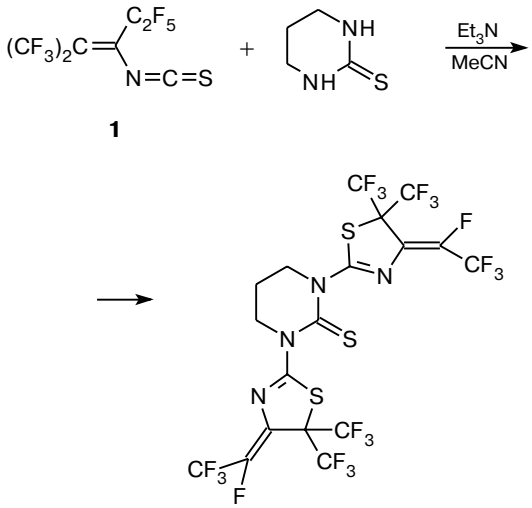


Fig. 3. Spatial structure of 1-[4(*E*)-(1,2,2,2-tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-3*H*-benzoxazole-2-thione (**6**) according to the X-ray diffraction data.

The reactions of compound **1** with benzothiazole-2-thione and benzoxazole-2-thione in the presence of triethylamine in MeCN yield compounds **5** and **6**, respectively. Their structures were confirmed by data from ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy, mass spectrometry, and X-ray diffraction analysis (Figs. 2 and 3). The structures of compounds **5** and **6** are very close. The benzothiazoline fragment is planar with an accuracy of ±0.013(2) Å, while the benzoxazoline fragment, with an accuracy of ±0.008(2) Å. The 4,5-dihydrothiazole ring in **5** and **6** is not quite planar, the C(13) atom deviating from the plane of the other four atoms by 0.118(5) and 0.165(5) Å. However, this ring is nearly in the plane of the bicyclic framework; the interplanar C(9)—N(3)—C(11)—N(15) angles are equal to 9.03(9)° and 9.76(9)°, respectively. It should be noted that the C=S bond in **6** is shorter (1.621(3) Å) than that in **5** (1.641(3) Å), which correlates with the average bond lengths (1.650(14) and 1.630(9) Å) for four derivatives of benzothiazoline-2-thione and for five derivatives of benzoxazoline-2-thione borrowed from the Cambridge Crystallographic Database.[12] At the same time, the C(2)—N(3) bond (1.395(4) and 1.387(4) Å in **5** and **6**, respectively) is longer than the average bond lengths (1.372(33) and 1.369(21) Å) in the aforementioned derivatives, while the S(1)—C(2) (1.711(3) Å) and O(1)—C(2) bonds (1.353(4) Å) are shorter than the average bond values (1.747(12) and 1.371(15) Å). It is also noteworthy that the S—$C(CF_3)_2$ bond is longer (1.868(3) Å in **5** and 1.858(3) Å in **6**) than the bond length (1.817(8) Å) averaged over three compounds[11] containing the 2-amino-4-ethylidene-4,5-dihydrothiazole fragment.

It was found that compound **1** reacts with thiazole-2-thione and pyridine-2-thione in the presence of Et_3N in MeCN at −10 °C to give 2-*N*-substituted 2-[4-(tetrafluoroethylidene]-5,5-bis(trifluoromethyl)-4,5-dihydrothiazoles (**7** and **8**, respectively). The reaction of compound **1** with 3,4,5,6-tetrahydropyrimidine-2-thione in the presence of Et_3N in MeCN at −20 °C yields product **9**, whose structure suggests that compound **1** is attacked by both N-nucleophilic centers (Scheme 3).

Scheme 3



The structures of compounds **7**—**9** were confirmed by data from ^{1}H, ^{13}C, and ^{19}F NMR and IR spectroscopy and mass spectrometry. Earlier, we noted that the chemical shift of the F(8) atom depends on the character of the heteroatom directly bonded to the C(2) atom in the 4,5-dihydrothiazole ring. In the case of nitrogen, the chemical shift of the F(8) atom in the ^{19}F NMR spectrum is 29—30 ppm. The formation of compounds **7**—**9** is due to the attack of the N-nucleophilic center on the C atom of the N=C=S group. If there are two such centers (as in 3,4,5,6-tetrahydropyrimidine-2-thione), both of them can attack the C atom of the N=C=S group.

Some chemical properties of compounds **2**—**6** proposed as reagents for combinatorial chemistry were published earlier.[13]

Thus, the reactions of N,O- and N,S-ambident nucleophiles with perfluoro-2-methylpent-2-en-3-yl isothiocyanate give exclusively 2-*N*-substituted 4,5-dihydrothiazoles.

Experimental

^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker WP 200 SY spectrometer (200 (^1H), 50 (^{13}C), and 188 MHz (^{19}F)); the chemical shifts are referenced to TMS and C_6F_6 as the internal standards (J_{C-H} was not measured). IR spectrum was recorded on a Specord M-80 spectrophotometer (CCl_4); the electronic absorption spectrum was recorded on a Specord UV VIS spectrophotometer in EtOH; mass spectra were recorded on a VG 707 OE GLC-MS instrument (ionizing voltage 70 eV).

1-[4(*E*)-1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-1*H*-benzimidazole (2). A mixture of compound **1** (3.4 g, 0.01 mol), benzimidazole (1.18 g, 0.01 mol), and triethylamine (2.02 g, 0.02 mol) in 10 mL of MeCN was stirred at ~20 °C for 1 h and then heated at 45 °C for 3 h. The reaction mixture was poured into water, and the voluminous precipitate that formed was filtered off and dissolved in CH_2Cl_2. The resulting solution was dried with $MgSO_4$. The solvent was removed, and the residue was purified by column chromatography on silica gel in CH_2Cl_2. The yield of compound **2** was 3.9 g (89%), m.p. 118—119 °C (from hexane). IR, ν/cm^{-1}: 1160—1270 (C—F), 1355 (C—N), 1450 (C—N), 1510 (C=C arom.), 1600, 1615 (C=N), 1690 (C=C), 3040 (C—H). UV (EtOH), λ_{max}/nm: 250 (ε 36900), 307 (ε 30300). MS, *m/z* (I_{rel} (%)): 437 $[M]^+$ (100), 418 $[M - F]^+$ (13), 368 $[M - CF_3]^+$ (41), 301 $[M - F - C_7H_5N_2]^+$ (1), 299 $[M - 2\ CF_3]^+$ (15), 175 $[C_8H_5N_3S]^+$ (11), 143 $[C_8H_5N_3]^+$ (11), 117 $[C_7H_5N_2]^+$ (2), 102 $[C_7H_4N]^+$ (16), 76 $[C_6H_4]^+$ (4), 69 $[CF_3]^+$ (14). Found, *m/z*: 437.0034. $C_{14}H_5F_{10}N_3S$. Calculated: 437.0044. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 98.8 (d, 6 F, F(6,7), J = 22 Hz); 96.6 (d, 3 F, F(9), J = 7 Hz); 29.2 (septet.q, 1 F, F(8), J = 22 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 160.3 (C(10)); 154.8 (C(2), $^4J_{C-F}$ = 9.9 Hz); 145.2 (C(8), $^1J_{C-F}$ = 266.5 Hz, $^2J_{C-F}$ = 39.8 Hz); 144.1 (C(11)); 142.6 (C(16)); 133.8 (C(4), $^2J_{C-F}$ = 29.8 Hz); 126.0 (C(12)); 125.8 (C(15)); 122.5 (C(9), $^1J_{C-F}$ = 283.8 Hz); 122.0 (C(6), C(7), $^1J_{C-F}$ = 285.1 Hz); 120.7 (C(14)); 117.1 (C(13)); 74.0 (C(5), $^2J_{C-F}$ = 27.8 Hz).

2-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]isoindole-1,3-dione (3). Potassium phthalimide (2.78 g, 15 mmol) was added at ~20 °C to a solution of compound **1** (5.09 g, 15 mmol) in 15 mL of MeCN. The reaction mixture was stirred at 70 °C for 4 h and then cooled to ~20 °C. The precipitate of KF that formed was filtered off, and the solution was concentrated *in vacuo*. The products were extracted from the residue with hot hexane (2×35 mL). The extract was cooled, and the precipitate that formed was filtered off and sublimed *in vacuo* at 120 °C (0.02 Torr) to give compound **3** (3.45 g, 49%), m.p. 126—127 °C (from hexane). IR, ν/cm^{-1}: 1150—1270 (C—F), 1350 (C—O), 1590 (C=C arom.), 1615 (C=N), 1690 (C=C), 1740, 1800 (C=O), 3000 (C—H). MS, *m/z* (I_{rel} (%)): 466 $[M]^+$ (86), 447 $[M - F]^+$ (14), 119 $[C_2F_5]^+$ (7), 104 $[C_7H_4O]^+$ (38), 100 $[CF_2{=}CF_2]^+$ (2), 76 $[C_6H_4]^+$ (27), 69 $[CF_3]^+$ (35). Found, *m/z*: 465.9829. $C_{15}H_4F_{10}N_2O_2S$. Calculated: 465.9834. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 96.4 (d, 6 F, F(6), F(7), J = 22 Hz); 96.0 (d, 3 F, F(9), J = 7 Hz); 30.2 (septet.q, 1 F, F(8), J = 22 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 163.0 (C(10)); 151.8 (C(2), $^4J_{C-F}$ = 9.9 Hz); 146.9 (C(8), $^1J_{C-F}$ = 269.5 Hz, $^2J_{C-F}$ = 39.9 Hz); 136.2 (C(11)); 130.7 (C(12)); 125.0 (C(13)); 122.2 (C(9), $^1J_{C-F}$ = 281.1 Hz); 122.1 (C(6), C(7), $^1J_{C-F}$ = 281.1 Hz); 115.8 (C(8), $^2J_{C-F}$ = 36.1 Hz); 70.9 (C(5), $^2J_{C-F}$ = 31.8 Hz).

1-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-1*H*-pyridin-2-one (4). A solution of 2-hydroxypyridine (1.43 g, 0.015 mol) and triethylamine (1.52 g, 0.015 mol) in 10 mL of MeCN was added with stirring at ~20 °C to a solution of compound **1** (5.09 g, 0.015 mol) in 15 mL of MeCN. The reaction mixture was stirred at ~20 °C for 1 h, then heated at 45 °C for 3 h, cooled, and concentrated *in vacuo* (water-jet pump). The product was extracted from the residue with boiling hexane (2×30 mL). The extract was cooled, and the precipitate that formed was filtered off and sublimed *in vacuo* at 88 °C (0.02 Torr) to give compound **4** (3.77 g, 61%), m.p. 75—76 °C (from hexane). IR, ν/cm^{-1}: 1150—1260 (C—F), 1350 (C—O), 1450 (C—N), 1540 (C=C arom.), 1570 (C=N), 1615 (C=N), 1600 (C=C), 1670 (C=O), 3060 (C—H). MS, *m/z* (I_{rel} (%)): 414 $[M]^+$ (51), 395 $[M - F]^+$ (6), 345 $[M - CF_3]^+$ (9), 336 $[M - C_5H_4N]^+$ (1), 182 $[(CF_3)_2CS]^+$ (1), 119 $[C_2F_5]^+$ (3), 100 $[CF_2{=}CF_2]^+$ (1), 94 $[C_5H_4NO]^+$ (3), 78 $[C_5H_4N]^+$ (100), 69 $[CF_3]^+$ (19). Found, *m/z*: 413.9891. $C_{12}H_4F_{10}N_2OS$. Calculated: 413.9885. ^1H NMR, δ: 8.34 (dd, H(14), J = 7.0 and 2.0 Hz); 7.50 (td, H(12), J = 7.0 and 2.0 Hz); 6.71 (d, H(11), J = 2.0 Hz); 6.45 (td, H(13), J = 7.0 and 2.0 Hz). ^{19}F NMR ($(CD_3)_2CO$), δ_F: 95.9 (d, 6 F, F(6), F(7), J = 22 Hz); 95.8 (d, 3 F, F(9), J = 7 Hz); 29.7 (septet.q, 1 F, F(8), J = 22 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 161.8 (C(10)); 143.4 (C(2), $^4J_{C-F}$ = 9.9 Hz); 146.4 (C(8), $^1J_{C-F}$ = 269.3 Hz, $^2J_{C-F}$ = 39.7 Hz); 131.0 (C(11)); 130.6 (C(14)); 121.1 (C(13)); 122.4 (C(9), $^1J_{C-F}$ = 283.7 Hz); 122.3 (C(6), C(7), $^1J_{C-F}$ = 283.7 Hz); 116.0 (C(4), $^2J_{C-F}$ = 37.3 Hz); 109.1 (C(12)); 72.0 (C(5), $^2J_{C-F}$ = 29.0 Hz).

3-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-3*H*-benzothiazole-2-thione (5). Compound **1** (0.68 g, 2 mmol) was added with stirring at ~20 °C to a solution of benzothiazole-2-thione (0.34 g, 2 mmol) and triethylamine (0.2 g, 2 mmol) in 5 mL of MeCN. The reaction mixture was kept for 2 h. The precipitate that formed was filtered off, and the solution was concentrated *in vacuo* (water-jet pump). The residue was sublimed at 130 °C (0.01 Torr) to give compound **5** (0.81 g, 83%), m.p. 154—156 °C. Found (%): N, 5.17; S, 19.80; 20.10. $C_{14}H_4F_{10}N_2S_3$. Calculated (%): N, 5.76; S, 19.75. IR, ν/cm^{-1}: 1150—1270 (C—F), 1350 (C—N), 1450 (C—N), 1550 (C=C arom.), 1585 (C=N), 1620, 1670 (C=C), 3040 (C—H). Found, *m/z*: 485.9371. Calculated: 485.9377. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 95.8 (d, 6 F, F(6), F(7), J = 20.5 Hz); 95.6 (d, 3 F, F(9), J = 7 Hz); 31.2 (septet.q, 1 F, F(8), J = 20.5 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 193.3 (C(10)); 158.7 (C(2), $^4J_{C-F}$ = 10.7 Hz); 144.8 (C(8), $^1J_{C-F}$ = 266.8 Hz, $^2J_{C-F}$ = 39.6 Hz); 139.7 (C(16)); 130.5 (C(4), $^2J_{C-F}$ = 23.4 Hz); 127.3 (C(13), C(14)); 126.6 (C(11)); 122.4 (C(6), C(7), $^1J_{C-F}$ = 283.8 Hz); 121.5 (C(15)); 118.8 (C(9), $^1J_{C-F}$ = 273.9 Hz, $^2J_{C-F}$ = 23.4 Hz); 118.3 (C(12)); 74.0 (C(5), $^2J_{C-F}$ = 27.8 Hz).

1-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-3*H*-benzoxazole-2-thione (6). Compound **1** (0.68 g, 2 mmol) was added with stirring at ~20 °C to a mixture of benzoxazole-2-thione (0.3 g, 2 mmol) and triethylamine (0.2 g, 2 mmol) in 5 mL of MeCN. The reaction mixture was kept for 2 h. The precipitate that formed was filtered off, and the solution was concentrated *in vacuo* (water-jet pump). The residue was sublimed at 120 °C (0.01 Torr) to give compound **6** (0.76 g, 81%), m.p. 183—184 °C (from hexane). Found (%): C, 35.86; 36.00; H, 1.10; 1.29; N, 5.69; S, 13.66; 13.36. $C_{14}H_4F_{10}N_2OS_2$. Calculated (%): C, 35.74; H, 0.85; N, 5.96; S, 13.62. IR, ν/cm^{-1}: 1150—1270 (C—F), 1350 (C—O), 1470 (C—N), 1570 (C=C arom.), 1600 (C=N),

1610 and 1690 (C=C), 3040 (C—H). Found, *m/z*: 469.9591. Calculated: 469.9605. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 95.9 (d, 6 F, F(6), F(7), J = 21.5 Hz); 95.6 (d, 3 F, F(9), J = 7 Hz); 30.0 (septet.q, 1 F, F(8), J = 21.5 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 179.0 (C(10)); 157.7 (C(2), $^4J_{C-F}$ = 10.7 Hz); 144.9 (C(8), $^1J_{C-F}$ = 266.8 Hz, $^2J_{C-F}$ = 39.6 Hz); 147.1 (C(16)); 142.7 (C(11)); 132.5 (C(4), $^2J_{C-F}$ = 23.4 Hz); 127.3 (C(15)); 125.6 (C(12)), 119.6 (C(6), C(7), $^1J_{C-F}$ = 283.8 Hz); 118.9 (C(9), $^1J_{C-F}$ = 273.9 Hz, $^2J_{C-F}$ = 23.4 Hz); 110.1 (C(13), C(14)); 70.1 (C(5), $^2J_{C-F}$ = 25.8 Hz).

3-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-4,5-dihydrothiazol-2-thione (7). A mixture of thiazole-2-thione (0.3 g, 25.7 mmol) and triethylamine (7.8 g, 77.2 mmol) in 15 mL of MeCN was added with stirring at 0 °C to a solution of compound **1** (8.7 g, 25.7 mmol) in 20 mL of MeCN. The reaction mixture was kept at this temperature for 1 h and at ~20 °C for 1 h and then heated at 60 °C for 1 h. Then, it was poured into water and acidified with 5% HCl, and the product was extracted with CH_2Cl_2. The extract was dried with $CaCl_2$ and concentrated, and the residue was chromatographed on silica gel in CH_2Cl_2—hexane (1 : 1). The yield of compound **7** was 8.4 g (74.7%), b.p. 78—79 °C (3 Torr). IR, ν/cm^{-1}: 1196—1277 (C—F), 1358 (C—O), 1378 (C=S), 1558 (C=N), 1682 (C=C), 2960 (C—H). UV (EtOH), λ_{max}/nm: 304 (ε 18600), 337 (ε 15200). MS, *m/z* (I_{rel} (%)): 438 $[M]^+$ (100), 419 $[M - F]^+$ (10), 369 $[M - CF_3]^+$ (3), 176 $[C_4H_4N_2S_3]^+$ (9), 150 $[C_3H_4NS_3]^+$ (6), 118 $[C_3H_4NS_2]^+$ (3), 86 $[C_3H_4NS]^+$ (2), 72 $[C_3H_5S]^+$ (45), 69 $[CF_3]^+$ (26). Found, *m/z*: 437.9383. $C_{10}H_4F_{10}N_2S_3$. Calculated: 437.9377. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 96.9 (d, 6 F, F(6), F(7), J = 22.5 Hz); 96.6 (d, 3 F, F(9), J = 7 Hz); 28.0 (septet.q, 1 F, F(8), J = 22.5 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 179.0 (C(10)); 157.9 (C(2), $^4J_{C-F}$ = 10.2 Hz); 144.2 (C(8), $^1J_{C-F}$ = 265.5 Hz, $^2J_{C-F}$ = 39.5 Hz); 130.7 (C(4), $^2J_{C-F}$ = 27.7 Hz); 122.3 (C(6), C(7), $^1J_{C-F}$ = 284.1 Hz); 118.7 (C(9), $^1J_{C-F}$ = 274.1 Hz, $^2J_{C-F}$ = 37.4 Hz); 70.1 (C(5), $^2J_{C-F}$ = 30.5 Hz); 57.3 (C(11), C(12)).

1-[4(*E*)-(1,2,2,2-Tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-1*H*-pyridine-2-thione (8). A mixture of pyridine-2-thione (2.5 g, 22.4 mmol) and triethylamine (6.8 g, 67.3 mmol) in 15 mL of MeCN was added with stirring and cooling with ice water to a solution of compound **1** (7.6 g, 22.4 mmol) in 20 mL of MeCN. The reaction mixture was kept at this temperature for 1 h and at ~20 °C for 1 h and then heated at 60 °C for 1 h. It was then poured into water and acidified with 5% HCl, and the product was extracted with CH_2Cl_2. The extract was dried with $CaCl_2$ and concentrated, and the residue was chromatographed on silica gel in CH_2Cl_2—hexane (1 : 1). The yield of compound **8** was 7.4 g (76.7%), m.p. 65—66 °C. IR, ν/cm^{-1}: 1165—1260 (C—F), 1355 (C=S), 1419, 1457 (C—N), 1523 (C=C$_{Ar}$), 1578 (C=N), 1631 (C=C), 3050 (C—H). UV (EtOH), λ_{max}/nm: 255 (ε 9300), 311 (ε 21000). MS, *m/z* (I_{rel} (%)): 430 $[M]^+$ (78), 411 $[M - F]^+$ (6), 361 $[M - CF_3]^+$ (3), 168 $[C_6H_4NS_2]^+$ (32), 142 $[C_5H_4NS_2]^+$ (100), 122 $[C_6H_4NS]^+$ (1), 119 $[C_2F_5]^+$ (1), 110 $[C_5H_4NS]^+$ (13), 78 $[C_5H_4]^+$ (99), 69 $[CF_3]^+$ (12). Found, *m/z*: 429.9656. $C_{12}H_4F_{10}N_2S_2$. Calculated: 429.9656. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 96.9 (d, 6 F, F(6), F(7), J = 22.5 Hz); 96.6 (d, 3 F, F(9), J = 7 Hz); 28.0 (septet.q, 1 F, F(8), J = 22.5 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 170.1 (C(10)); 148.9 (C(2), $^4J_{C-F}$ = 10.2 Hz); 147.5 (C(11)); 144.8 (C(8), $^1J_{C-F}$ = 267.7 Hz, $^2J_{C-F}$ = 39.9 Hz); 137.6 (C(14)); 134.1 (C(4), $^2J_{C-F}$ = 26.9 Hz); 122.7 (C(13)); 122.6 (C(13)); 121.8 (C(6), C(7), $^1J_{C-F}$ = 283.6 Hz); 118.0 (C(9), $^1J_{C-F}$ = 273.9 Hz, $^2J_{C-F}$ = 37.4 Hz); 68.9 (C(5), $^2J_{C-F}$ = 30.9 Hz, $^4J_{C-F}$ = 4.7 Hz).

1,3-Bis[4(*E*)-(1,2,2,2-tetrafluoroethylidene)-5,5-bis(trifluoromethyl)-4,5-dihydrothiazol-2-yl]-tetrahydropyrimidine-2-thione (9). A mixture of 3,4,5,6-tetrahydropyrimidine-2-thione (2.5 g, 21.5 mmol) and triethylamine (6.5 g, 64.3 mmol) in 15 mL of MeCN was added with stirring and cooling with ice water to a solution of compound **1** (7.3 g, 21.5 mmol) in 20 mL of MeCN. The reaction mixture was kept at this temperature for 1 h and at ~20 °C for 1 h and then heated at 60 °C for 1 h. It was then poured into water and acidified with 5% HCl, and the product was extracted with CH_2Cl_2. The extract was dried with $CaCl_2$ and concentrated, and the residue was chromatographed on silica gel in CH_2Cl_2—hexane (1 : 1). The yield of compound **9** was 6.1 g (75.3%), m.p. 183—184 °C (from CH_2Cl_2). IR, ν/cm^{-1}: 1160—1267 (C—F), 1361 (C=S), 1392, 1415 (C—N), 1477 (C—N), 1562 (C=N), 1687 (C=C), 3050 (C—H). UV (EtOH), λ_{max}/nm: 231 (ε 53900), 325 (ε 33100). MS, *m/z* (I_{rel} (%)): 754 $[M]^+$ ($C_{11}H_6F_{10}N_3S_2$) (59), 735 $[M - F]^+$ (12), 685 $[M - CF_3]^+$ (1), 434 $[M - C_7F_{10}NS]^+$ (100), 406 $[M - C_7F_{10}NS - CH_2N]^+$ (14), 375 406 $[M - C_7F_{10}NS - S{=}C{=}NH]^+$ (14), 362 406 $[M - C_7F_{10}NS - S{=}C{=}NCH_2]^+$ (1), 348 406 $[M - C_7F_{10}NS - S{=}C{=}NC_2H_4]^+$ (7), 320 $[C_7F_{10}NS]^+$ (2), 119 $[C_2F_5]^+$ (1), 113 $[C_4H_5N_2S]^+$ (3), 100 $[CF_2{=}CF_2]^+$ (17), 86 $[S{=}C{=}N\text{-}C_2H_4]^+$ (2), 72 $[S{=}C{=}NCH_2]^+$ (32), 69 $[CF_3]^+$ (16), 59 $[S{=}C{=}NH]^+$ (4), 44 $[C_2H_3N]^+$ (41), 28 $[CH_2{=}N]^+$ (24). Found, *m/z*: $[M - C_7F_{10}NS]^+$ 433.9832. Calculated: 433.9843. ^{19}F NMR ($(CD_3)_2CO$), δ_F: 96.7 (d, 6 F, F(6), F(7), J = 21.5 Hz); 96.6 (d, 3 F, F(9), J = 7 Hz); 28.0 (septet.q, 1 F, F(8), J = 21.5 and 7 Hz). ^{13}C NMR (CD_2Cl_2), δ_C: 179.6 (C(10)); 162.1 (C(2), $^4J_{C-F}$ = 10.9 Hz); 144.1 (C(8), $^1J_{C-F}$ = 254.8 Hz, $^2J_{C-F}$ = 29.9 Hz); 130.2 (C(4), $^2J_{C-F}$ = 27.8 Hz); 121.6 (C(6), C(7), $^1J_{C-F}$ = 283.5 Hz); 118.4 (C(9), $^1J_{C-F}$ = 273.8 Hz, $^2J_{C-F}$ = 37.3 Hz); 76.9 (C(5), $^2J_{C-F}$ = 32.7 Hz, $^4J_{C-F}$ = 4.7 Hz); 50.2 (C(11), C(12), C(13)).

X-ray diffraction analysis of single crystals 4—6 was carried out on a Bruker P4 diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scan mode, 2θ < 50°). Absorption corrections were applied by the integration method. The structures were solved by the direct method and refined in the full-matrix anisotropic-isotropic (for H atoms) approximation with the use of the SHELXTL program package.

The crystals of compound **4** are monoclinic: a = 6.3084(3), b = 11.3803(6), c = 20.739(1) Å, β = 94.612(4)°, V = 1484.1(1) Å^3, space group $P2_1/c$, $C_{12}H_4F_{10}N_2OS$, M = 414.23, Z = 4, d_{calc} = 1.854 g cm^{-3}, μ = 0.339 mm^{-1}, crystal size 0.12×0.20×0.70 mm, transmission 0.90—0.96. The intensities of 2624 independent reflections were measured. The final residual is wR_2 = 0.1136 (S = 1.015) for all reflections (R = 0.0406 for 2173 $F_0 > 4\sigma(F)$).

The crystals of compound **5** are triclinic: a = 7.5423(5), b = 9.2608(6), c = 13.377(1) Å, α = 90.904(6), β = 95.623(6), γ = 112.89(5)°, V = 855.1(1) Å^3, space group $P\bar{1}$, $C_{14}H_4F_{10}N_2S_3$, M = 486.37, Z = 2, d_{calc} = 1.889 g cm^{-3}, μ = 0.541 mm^{-1}, crystal size 0.18×0.36×0.84 mm, transmission 0.81—0.91. The intensities of 2982 independent reflections were measured. The final residual is wR_2 = 0.1324 (S = 1.034) for all reflections (R = 0.0460 for 2375 $F_0 > 4\sigma(F)$).

The crystals of compound **6** are triclinic: a = 7.7366(5), b = 8.9698(6), c = 13.2589(7) Å, α = 83.168(5), β = 84.723(5), γ = 65.439(4)°, V = 830.00(9) Å^3, space group $P\bar{1}$, $C_{14}H_4F_{10}N_2OS_2$, M = 470.31, Z = 2, d_{calc} = 1.882 g cm^{-3}, μ = 0.437 mm^{-1}, crystal size 0.14×0.26×1.14 mm, transmission 0.86—0.94. The intensities of 2942 independent reflections were measured. The final residual is wR_2 = 0.1521 (S = 1.079) for all reflections (R = 0.0503 for 2445 $F_0 > 4\sigma(F)$).

The atomic coordinates have been deposited with the Cambridge Crystallographic Database.

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