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Fluorine-Containing Heterocycles: XVI.* Reactions of Tetrafluorobenzoyl Isothiocyanate with Hydrazines and Their Derivatives

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Abstract—Fluorinated derivatives of 4*H*-1,3-benzothiazin-4-one, [1,2,4]triazolo[4,3-*a*]pyrimidine, [1,2,4]triazolo[3,4-*b*][1,3]benzazoles, and 1,5-dihydro-1,2,4-triazole-5-thione were synthesized by addition of hydrazines and their derivatives to tetrafluorobenzoyl isothiocyanate, followed by cyclization of intermediate thiosemicarbazides.

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Fluorine-containing heterocycles are widely used as technical materials, pesticides, and effective medical agents due to unique properties of fluorine atoms in organic molecules [2]. We previously showed that polyfluorobenzoyl isothiocyanates are promising as building blocks for the preparation of fluorinated 4*H*-1,3-benzothiazin-4-ones [1, 3, 4]. With a view to synthesize new fluorine-containing heterocycles, in the present work we examined reactions of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) with aryl- and hetarylhydrazines and some hydrazine derivatives (hydrazides, thiosemicarbazides, and hydrazones).

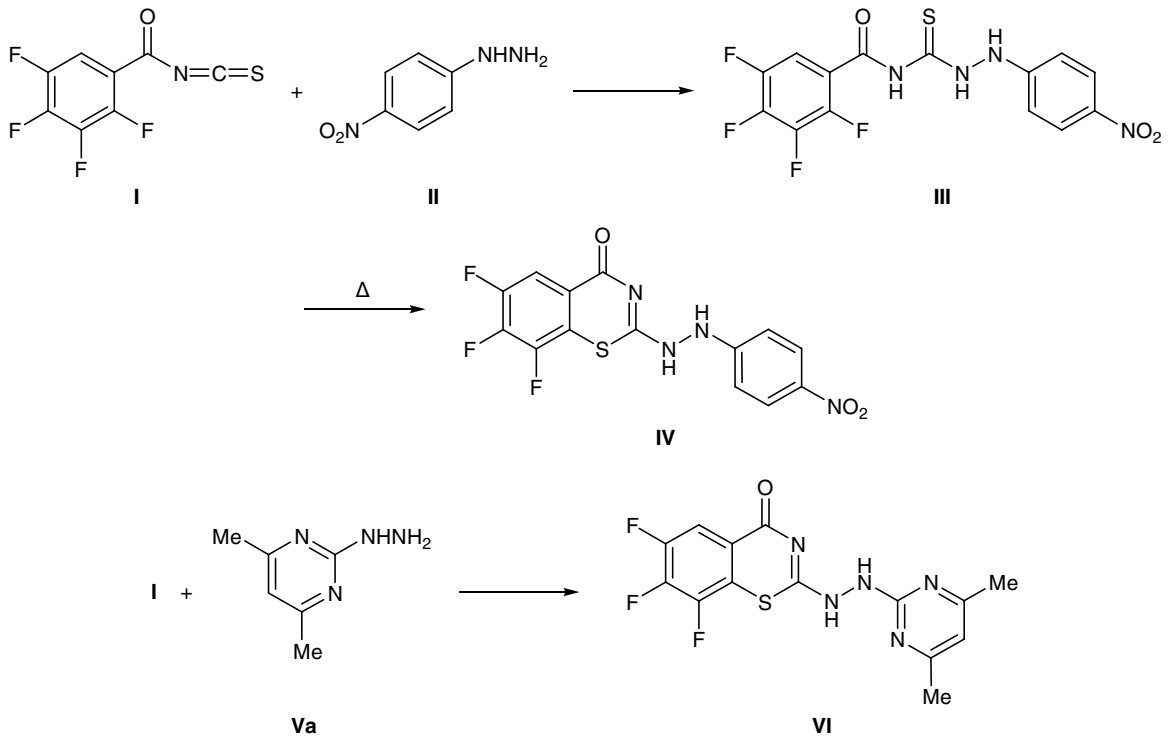
There are data on reactions of benzoyl isothiocyanate with alkyl- and arylhydrazines, which lead to the formation of the corresponding dihydrotriazolethiones via condensation of intermediate thiosemicarbazides [5]. The presence of a fluorine atom in the *ortho* position of the benzene ring in benzoyl isothiocyanate could give rise to alternative cyclization pathways, e.g., those leading to the formation of 1,3-thiazine or pyrimidine systems which attract interest due to their chemical and biological properties [6–8].

Only a few published data are available on reactions of benzoyl isothiocyanates with hydrazine derivatives. The reaction of benzoyl isothiocyanate with isonicotinic acid hydrazide gave 1-isonicotinoyl-4-acylthiosemicarbazides which showed a strong bacteriostatic activity [9, 10]. Durant [11] obtained 1,3,5-oxadiazinethiones by reaction of benzoyl isothiocyanate with *N*′-substituted hydrazones.

We found that *p*-nitrophenylhydrazine (**II**) smoothly adds to tetrafluorobenzoyl isothiocyanate (**I**) on heating in boiling acetonitrile (reaction time 30 min) to give 84% of thiosemicarbazide **III** (Scheme 1). The ^{1}H NMR spectrum of compound **III** confirmed the presence in its molecule of an aryl fragment and three NH groups; it also contained a one-proton multiplet at δ 7.65 ppm, which is typical of tetrafluorobenzoyl substituent. Compound **III** was subjected to cyclization by heating in boiling dimethyl sulfoxide over a period of 15 min; as a result, 1,3-benzothiazinone **IV** was isolated. Compound **IV** showed in the ^{1}H NMR spectrum signals from protons in the nitrophenyl fragment and two NH signals, while the 5-H signal appeared as a double doublet of doublets at δ ~8.00 ppm. In the mass spectrum of 2-(*p*-nitrophenylhydrazino)-4*H*-1,3-benzothiazin-4-one (**IV**), the molecular ion peak had the maximal intensity; in addition, an ion peak with *m*/*z* 190 (I_{rel} 38%; $[M - ArNHNHCN]^+$) was present, which is typical of 2-substituted 6,7,8-trifluoro-4*H*-1,3-benzothiazin-4-ones [1]. These findings indicate that the intramolecular cyclization of **III** involved the *ortho*-fluorine atom rather than the carbonyl group.

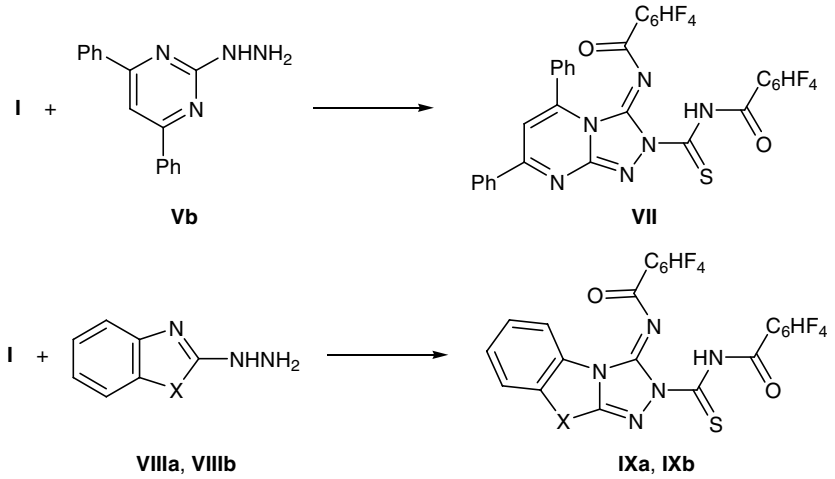
* For communication XV, see [1].

Scheme 1.



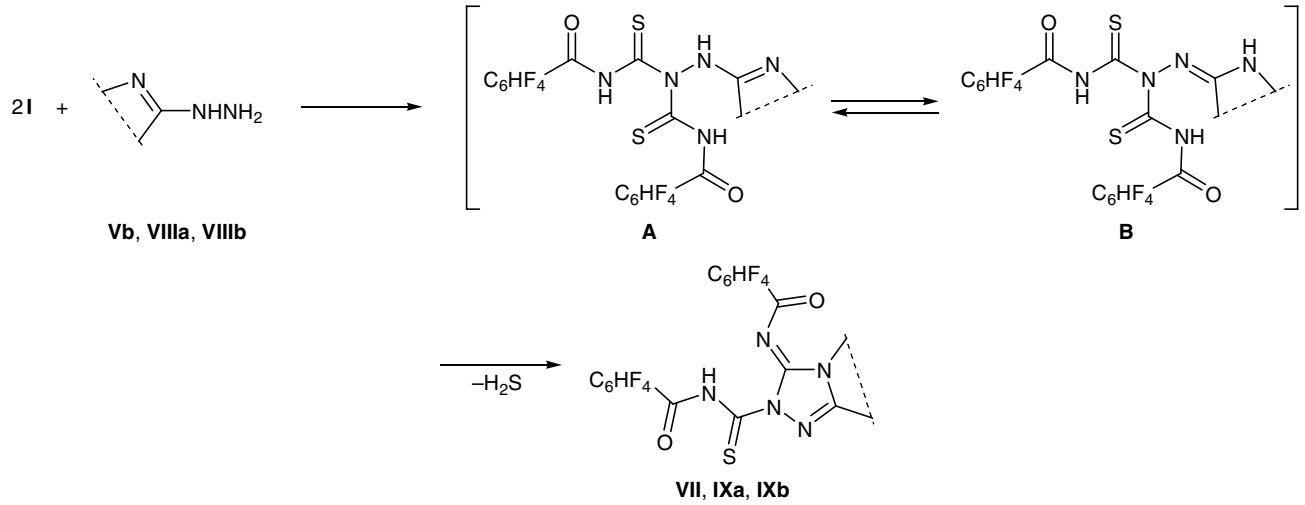
2,3,4,5-Tetrafluorobenzoyl isothiocyanate (**I**) is capable of reacting with hetarylhydrazines to give not only benzothiazinone derivatives like **IV**. Intramolecular cyclization of intermediates like **III** can occur with participation of the endocyclic nitrogen atom in the hydrazine fragment. In fact, by heating compound **I** with 4,6-dimethylpyrimidin-2-ylhydrazine **Va** in boiling acetonitrile over a period of 1 h we obtained fluorine-containing 2-(4,6-dimethylpyrimidin-2-yl)-4*H*-1,3-benzothiazin-4-one (**VI**) (Scheme 1). The ^{1}H NMR spectrum of **VI** contained a multiplet signal at δ 7.94 ppm from the 5-H proton and signals from two NH groups and 4,6-dimethylpyrimidine fragment. In the ^{19}F NMR spectrum of **VI**, multiplets belonging to three fluorine atoms were present. The base peak in the mass spectrum of compound **VI** was that corresponding to the 2-(4,6-dimethylpyrimidin-2-yl)hydrazine-1-carbonitrile fragment (*m*/*z* 163). Fragmentation of 2-substituted 6,7,8-trifluoro-4*H*-1,3-benzothiazin-4-ones is usually characterized by elimination of RCN as

Scheme 2.



X = S (**a**), NH (**b**).

Scheme 3.



Vb, **VIIIa**, **VIIIb** **A** **B** **VII**, **IXa**, **IXb**

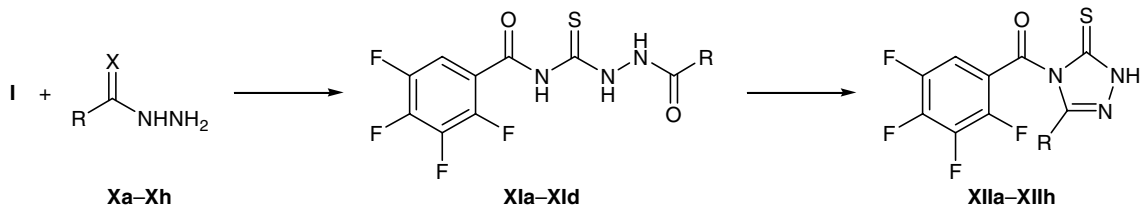
the main decomposition pathway (the corresponding peak in the mass spectrum has the maximal intensity) [1–3]; elimination of RNHCN as the main fragmentation pathway of 2-aminopyrido[3,2-*e*]thiazin-4-ones was reported in [12].

4,6-Diphenylpyrimidin-2-ylhydrazine (**Vb**) reacted with isothiocyanate **I** in boiling acetonitrile in a different way, and the product was substituted [1,2,4]-triazolo[4,3-*a*]pyrimidine **VII** (Scheme 2); the structure of **VII** was proved by the ^{1}H and ^{19}F NMR and mass spectra (see Experimental). Likewise, the reactions of 1,3-benzazol-2-ylhydrazines **VIIIa** and **VIIIb** with tetrafluorobenzoyl isothiocyanate gave fused triazoles **IXa** and **IXb**, respectively (Scheme 2), whose structure was confirmed by spectral data.

Most probably, the formation of triazoles **VII** and **IX** involved addition of the primary amino group in the hydrazine at the N=C bond of isothiocyanate **I**, and the subsequent intramolecular condensation is accompanied by elimination of hydrogen sulfide, as shown in Scheme 3. We failed to convert compounds **VII** and **IX** into the corresponding 1,3-benzothiazin-4-ones by heating in diphenyl ether, DMSO, or toluene in the presence of triethylamine.

It might be expected that fluorine-containing 2-substituted 4*H*-1,3-benzothiazin-4-one can be prepared by condensation of isothiocyanate **I** with hydrazides **Xa**–**Xd** or thiosemicarbazides **Xe**–**Xh** via intramolecular replacement of the *ortho*- fluorine atom in **I**. However, the isolated products were dihydrotriazolethiones **XII**, i.e., the cyclization followed a different pattern. The addition of hydrazides **Xa**–**Xd** to tetrafluorobenzoyl isothiocyanate (**I**) smoothly occurred in boiling acetonitrile (reaction time 1 h), and the yields of benzoylthiosemicarbazides **XIa**–**XId** ranged from 83 to 92% (Scheme 4); the structure of compounds **XIa**–**XId** was confirmed by the ^{1}H NMR data. We failed to effect cyclization of **XIa**–**XId** by heating in boiling toluene in the presence of a base or by heating in dimethylformamide [1, 3, 4]. The only effective route to triazole derivatives **XIIa**–**XIId** was heating of compounds **XIa**–**XId** in diphenyl ether over a period of 2 h; the structure of **XIIa**–**XIId** was confirmed by the ^{1}H NMR and mass spectra. The ^{1}H NMR spectra of these compounds contained signals from protons in the phenyl or pyridyl fragment and a multiplet at δ 7.58–7.76 ppm due to proton in the tetrafluorophenyl group, while only one signal from NH proton was present

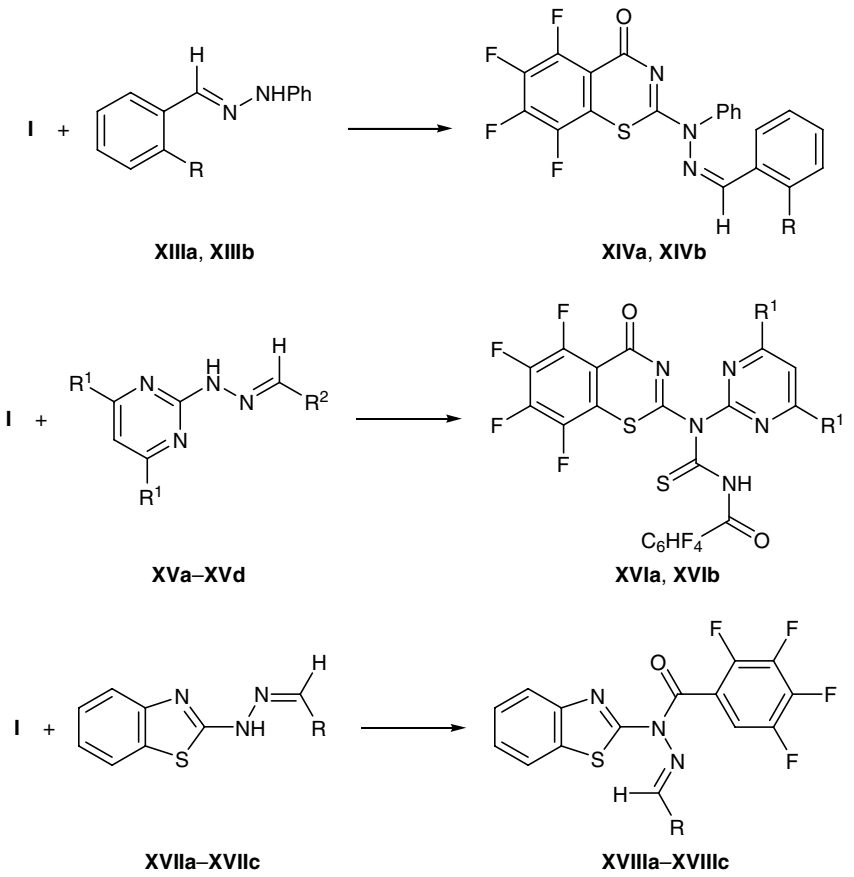
Scheme 4.



Xa–**Xh** **XIa**–**XId** **XIIa**–**XIIh**

X = O, R = Ph (**a**), *m*-$O_2NC_6H_4$ (**b**), pyridin-3-yl (**c**), pyridin-4-yl (**d**); X = S, R = pyrrolidin-1-yl (**e**), piperidino (**f**), morpholino (**g**), thiomorpholino (**h**).

Scheme 5.



XIII, **XIV**, R = H (**a**), OH (**b**); **XV**, R^1 = Me, R^2 = Ph (**a**), 2-furyl (**b**); R^1 = Ph, R^2 = Ph (**c**), 4-$MeOC_6H_4$ (**d**); **XVI**, R^1 = Me (**a**), Ph (**b**); **XVII**, **XVIII**: R = Ph (**a**), 4-$MeOC_6H_4$ (**b**), 2-furyl (**c**).

(against three NH signals in the spectra of initial compounds **XI**). The most abundant ion in the mass spectra of **XIIa**–**XIId** was $[C_6HF_4CO]^+$ with *m*/*z* 177; this means that the cyclization involved the carbonyl group in the hydrazide rather than tetrafluorobenzoyl fragment. The formation of dihydrotriazolethiones in reactions of benzoyl isothiocyanate with monoalkyl-substituted hydrazines was reported previously [5]. By heating isothiocyanate **I** with thiosemicarbazides **Xe**–**Xh** in boiling acetonitrile for 1 h we obtained 73–81% of triazolethiones **XIIe**–**XIIh** whose structure was confirmed by the ^{1}H NMR and mass spectra.

We anticipated that reactions of 2,3,4,5-tetrafluorobenzoylisothiocyanate (**I**) with hydrazones derived from aromatic and heterocyclic aldehydes will give rise to new fluorine-containing 2-substituted 1,3-benzothiazin-4-ones. *N*-Benzylidene-*N*′-phenylhydrazines **XIIIa** and **XIIIb** reacted with isothiocyanate **I** in acetonitrile (1 h) to give compounds **XIVa** and **XIVb**, and we failed to isolated intermediate addition product (Scheme 5). The structure of **XIVa** and **XIVb** was consistent with their ^{1}H and ^{19}F NMR and mass spectra. Fluorine-containing 1,3-benzothiazinones **XVIa** and **XVIb** were formed under analogous conditions (boiling acetonitrile, 1 h) in the reactions of isothiocyanate **I** with hydrazones **XVa**–**XVd** derived from 4,6-dimethyl- or 4,6-diphenylpyrimidin-2-ylhydrazine and benzaldehyde or furan-2-carbaldehyde. Presumably, the observed reaction pattern is favored by electron-withdrawing properties of the pyrimidine fragment, which promotes amine–nitrile cleavage of the hydrazonium salt formed as a result of protonation of benzothiazinone **XIV** with HF. Analogous decomposition of *N*,*N*-disubstituted hydrazones have been reported [13, 14]. 2-Hetarylamino-1,3-benzothiazinone then reacts with the second isothiocyanate molecule to give compound **XVI**.

The structure of 1,3-benzothiazin-4-ones **XVIa** and **XVIb** was confirmed by the ^{1}H and ^{19}F NMR and mass spectra. In the ^{1}H NMR spectra of **XVIa** and

XVIb we observed signals from protons in the pyrimidine fragment, tetrafluorobenzoyl residue, 5-H in the benzothiazine ring, and NH group. Compound **XVIb** displayed in the ^{19}F NMR spectra multiplets from seven fluorine atoms. The base peak in the mass spectra of **XVIa** and **XVIb** was that belonging to the C_6HF_4 fragment (*m*/*z* 177, $[M - RCN]^+$); this ion is typical of trifluoro-substituted 1,3-benzothiazinones.

Benzothiazolylhydrazones **XVIIa**–**XVIIc** derived from 1,3-benzothiazol-2-ylhydrazine reacted with isothiocyanate **I** in a way similar to 2-aminobenzotiazoles [1]. Instead of addition of the hydrazone NH group at the N=C bond of isothiocyanate, replacement of the N=C=S group occurred to give compounds **XVIIIa**–**XVIIIc** (Scheme 5).

Thus our results show that the direction of reactions of hydrazones with tetrafluorobenzoyl isothiocyanate depends on the nature of the hydrazine component. These reactions provide a convenient synthetic route to substituted 4,5-dihydro-1*H*-1,2,4-triazole-5-thiones and 4*H*-1,3-benzothiazin-4-ones.

EXPERIMENTAL

The ^1H NMR spectra were recorded on Bruker WM-250 and Bruker DRX-400 spectrometers operating at 250.14 and 400.13 MHz, respectively. The ^{19}F NMR spectra were measured on a Bruker DRX-500 instrument at 376.45 MHz. Tetramethylsilane (^1H) and hexafluorobenzene (^{19}F) were used as internal references, and DMSO-d_6, as solvent. The mass spectra were obtained on a Varian MAT 311A spectrometer (accelerating voltage 3 kV, cathode emission current 300 μA, energy of ionizing electrons 70 eV, direct sample admission into the ion source).

2,3,4,5-Tetrafluoro-*N*-[2-(4-nitrophenyl)hydrazinocarbothioyl]benzamide (III). A solution of 0.46 g (6 mmol) of ammonium thiocyanate in 15 ml of acetonitrile was added to a solution of 1.28 g (6 mmol) of tetrafluorobenzoyl chloride in 2.5 ml of toluene. The mixture was kept for 5 min at 40°C, the precipitate of ammonium chloride was filtered off, and the filtrate was added to a solution of 0.45 g (2.9 mmol) of *p*-nitrophenylhydrazine in 10 ml of acetonitrile. The mixture was heated for 30 min under reflux and cooled, and the light yellow precipitate was filtered off and recrystallized from ethanol. Yield 0.92 g (84%), mp 168–170°C. ^1H NMR spectrum, δ, ppm: 6.89 d (2H, 2-H, 6-H, ^3J = 7.4 Hz), 7.65 m (6'-H), 8.08 d (2H, 3-H, 5-H, ^3J = 7.4 Hz), 9.4 br.s (1H, NH), 11.8 br.s (1H, NH), 11.9 br.s (1H, NH). Found, %: C 41.53; H 2.16; N 14.85. $C_{13}H_8F_4N_4O_3S$. Calculated, %: C 41.49; H 2.13; N 14.89.

6,7,8-Trifluoro-2-[2-(*p*-nitrophenyl)hydrazino]-4*H*-1,3-benzothiazin-4-one (IV). A solution of 0.5 g (1.3 mmol) of compound **III** in 5 ml of dimethyl sulfoxide was heated for 15 min under reflux. The mixture was cooled, and the precipitate was filtered off and washed with ethanol and diethyl ether. Yield 0.44 g (91%), mp > 250°C. ^1H NMR spectrum, δ, ppm: 7.02 d (2H, 2'-H, 6'-H, ^3J = 9.2 Hz), 8.00 d.d.d (1H, 5-H, ^3J = 10.1, ^4J = 7.9, ^5J = 1.8 Hz), 8.05 d (2H, 3'-H, 5'-H, ^3J = 9.2 Hz), 9.7 br.s (1H, NH), 10.2 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 368 $[M]^+$ (100), 218 (14), 216 (12), 206 (11), 191 (26), 190 (38), 162 (24), 150 (21), 122 (23), 92 (12), 91 (12), 90 (14), 76 (11), 64 (13), 63 (12). Found, %: C 42.43; H 1.95; N 15.20. $C_{13}H_7F_3N_4O_3S$. Calculated, %: C 42.39; H 1.90; N 15.22.

2-[(4,6-Dimethylpyrimidin-2-yl)hydrazino]-6,7,8-trifluoro-4*H*-1,3-benzothiazin-4-one (VI). A solution of 8 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in acetonitrile (prepared as described above) was added to a suspension of 0.55 g (4 mmol) of 4,6-dimethylpyrimidin-2-ylhydrazine (**Va**) in 10 ml of anhydrous acetonitrile. The mixture was stirred for 30 min at room temperature, heated for 1 h under reflux, and evaporated to 1/4 of the initial volume. The precipitate was filtered off and recrystallized from DMSO. Yield 0.95 g (67%), mp > 250°C. ^1H NMR spectrum, δ, ppm: 2.28 s (6H, CH_3), 6.58 s (1H, 5'-H), 7.94 d.d.d (1H, 5-H, ^3J = 10.0, ^4J = 7.8, ^5J = 2.0 Hz), 11.0 br.s (1H, NH), 11.9 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 9.48 m (1F), 26.70 m (1F), 26.93 m (1F). Mass spectrum, *m*/*z* (I_{rel}, %): 353 $[M]^+$ (85), 191 (30), 190 (20), 164 (10), 163 (100), 162 (21), 123 (35), 109 (12), 108 (40), 107 (15), 96 (15), 93 (14), 67 (30), 66 (11). Found, %: C 47.64; H 2.81; N 19.78. $C_{14}H_{10}F_3N_5OS$. Calculated, %: C 47.59; H 2.85; N 19.82.

***N*-{5,7-Diphenyl-2-(2,3,4,5-tetrafluorobenzoylaminocarbothioyl)-2*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-3-ylidene}-2,3,4,5-tetrafluorobenzamide (VII).** A solution of 6 mmol of isothiocyanate **I** in acetonitrile (prepared as described above) was added to a suspension of 0.92 g (3 mmol) of 4,6-diphenylpyrimidin-2-ylhydrazine (**Vb**) in 10 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature,

heated for 1 h under reflux, and cooled, and the precipitate was filtered off and recrystallized from DMSO. Yield 1.6 g (76%), mp 274–276°C. ^{1}H NMR spectrum, δ, ppm: 7.52 m (4H, H_{arom}), 7.62 m (2H, H_{arom}), 7.81 m (2H, 6'-H, 6''-H), 8.42 m (2H, H_{arom}), 8.44 m (2H, H_{arom}), 8.74 s (1H, 5-H), 13.2 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 7.49 m (1F), 8.00 m (1F), 12.13 m (1F), 12.58 m (1F), 22.98 m (1F), 24.00 m (1F), 24.46 m (1F), 24.71 m (1F). Mass spectrum, *m*/*z* (I_{rel}, %): 698 $[M]^+$ (17), 549 (15), 231 (33), 189 (39), 177 (100), 149 (24), 129 (27), 77 (12). Found, %: C 54.98; H 1.99; N 12.07. $C_{32}H_{14}F_8N_6O_2S$. Calculated, %: C 55.02; H 2.02; N 12.03.

2,3,4,5-Tetrafluoro-*N*-{2-(2,3,4,5-tetrafluorobenzoylaminocarbothioyl)-2,3-dihydro[1,2,4]triazolo-[3,4-*b*][1,3]benzothiazol-3-ylidene}benzamide (IXa). A solution of 9 mmol of isothiocyanate **I** in acetonitrile (prepared as described above) was added to a suspension of 0.74 g (4.5 mmol) of 1,3-benzothiazol-2-ylhydrazine (**VIIIa**) in 10 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, and cooled, and the precipitate was filtered off and recrystallized from DMSO. Yield 2.1 g (78%), mp 253–255°C. ^{1}H NMR spectrum, δ, ppm: 7.50 m (1H, benzothiazole), 7.60 m (1H, benzothiazole), 7.94 m (1H, 6'-H), 8.00 m (1H, benzothiazole), 8.19 m (1H, 6''-H), 8.24 m (1H, benzothiazole), 13.8 br.s (1H, NH). ^{19}F NMR spectrum, δ, ppm: 7.78 m (1F), 8.10 m (1F), 12.64 m (1F), 13.09 m (1F), 24.09 m (1F), 24.22 m (1F), 24.72 m (1F), 24.97 m (1F). Mass spectrum, *m*/*z* (I_{rel}, %): 601 $[M]^+$ (15), 451 (35), 177 (100), 149 (20), 134 (10). Found, %: C 45.96; H 1.19; N 11.61. $C_{23}H_7F_8N_5O_2S_2$. Calculated, %: C 45.92; H 1.16; N 11.65.

2,3,4,5-Tetrafluoro-*N*-{2-(2,3,4,5-tetrafluorobenzoylaminocarbothioyl)-2,3-dihydro[1,2,4]triazolo-[3,4-*b*]benzimidazol-3-ylidene}benzamide (IXb) was synthesized in a similar way. Yield 71%, mp 284–286°C. ^{1}H NMR spectrum, δ, ppm: 7.33 m (2H, benzimidazole), 7.68 m (2H, benzimidazole), 7.93 m (1H, 6'-H), 8.03 m (1H, 6''-H), 13.1 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 584 $[M]^+$ (15), 451 (31), 177 (100), 149 (25). Found, %: C 47.22; H 1.33; N 14.41. $C_{23}H_8F_8N_6O_2S$. Calculated, %: C 47.26; H 1.37; N 14.38.

***N*-(2-Benzoylhydrazinocarbothioyl)-2,3,4,5-tetrafluorobenzamide (XIa).** A solution of 8 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in 10 ml of anhydrous acetonitrile was added to a solution of 0.54 g (4 mmol) of benzohydrazide (**Xa**) in 8 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, cooled, and evaporated, and the residue was washed with ethanol and recrystallized from DMSO. Yield 1.37 g (92%), mp 176–178°C. ^{1}H NMR spectrum, δ, ppm: 7.51 m (3H, H_{arom}), 7.67 m (1H, 6'-H), 7.93 m (2H, H_{arom}), 11.0 br.s (1H, NH), 12.0 br.s (1H, NH), 12.1 br.s (1H, NH). Found, %: C 48.55; H 2.47; N 11.30. $C_{15}H_9F_4N_3O_2S$. Calculated, %: C 48.52; H 2.44; N 11.32.

Compounds **XIb**–**XId** were synthesized in a similar way.

2,3,4,5-Tetrafluoro-*N*-[2-(3-nitrobenzoyl)hydrazinocarbothioyl]benzamide (XIb). Yield 86%, mp 206–208°C. ^{1}H NMR spectrum, δ, ppm: 7.56 m (1H, 6'-H), 7.80 t (1H, 5-H, ^3J = 7.9 Hz), 8.36 m (2H, 4-H, 6-H), 8.81 m (1H, 2-H), 10.6 br.s (1H, NH), 11.0 br.s (1H, NH), 12.5 br.s (1H, NH). Found, %: C 45.30; H 1.94; N 13.44. $C_{15}H_8F_4N_4O_4S$. Calculated, %: C 45.27; H 1.92; N 13.46.

2,3,4,5-Tetrafluoro-*N*-[2-(pyridin-3-ylcarbonyl)-hydrazinocarbothioyl]benzamide (XIc). Yield 83%, mp 177–179°C. ^{1}H NMR spectrum, δ, ppm: 7.49 m (1H, 5-H), 7.67 m (1H, 6'-H), 8.24 m (1H, 6-H), 8.72 m (1H, 4-H), 9.06 m (1H, 2-H), 11.3 br.s (1H, NH), 12.0 br.s (1H, NH), 12.1 br.s (1H, NH). Found, %: C 45.20; H 2.18; N 15.03. $C_{14}H_8F_4N_4O_2S$. Calculated, %: C 45.17; H 2.16; N 15.05.

2,3,4,5-Tetrafluoro-*N*-[2-(pyridin-4-ylcarbonyl)-hydrazinocarbothioyl]benzamide (XId). Yield 91%, mp 172–174°C. ^{1}H NMR spectrum, δ, ppm: 7.82 m (3H, 6'-H, 2-H, 6-H), 8.73 m (2H, 3-H, 5-H), 11.4 br.s (1H, NH), 12.0 br.s (1H, NH), 12.4 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 372 (13) $[M]^+$, 177 (87), 149 (29), 106 (100), 78 (55), 51 (25). Found, %: C 45.16; H 2.14; N 15.08. $C_{14}H_8F_4N_4O_2S$. Calculated, %: C 45.17; H 2.16; N 15.05.

3-Phenyl-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIa). A solution of 1.1 g (2.96 mmol) of compound **XIa** in 2 g of diphenyl ether was heated for 3 h under reflux. After cooling, the precipitate was filtered off and recrystallized from DMSO. Yield 0.89 g (85%), mp 225–227°C. ^{1}H NMR spectrum, δ, ppm: 7.51 m (3H, H_{arom}), 7.74 m (1H, 6'-H), 7.93 m (2H, H_{arom}), 13.4 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 353 (25) $[M]^+$, 177 (100), 149 (23), 121 (15). Found, %: C 50.95; H 1.98; N 11.87. $C_{15}H_7F_4N_3OS$. Calculated, %: C 50.99; H 2.00; N 11.89.

Compounds **XIIb–XIId** were synthesized in a similar way.

3-(3-Nitrophenyl)-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIb). Yield 69%, mp 194–196°C. ^{1}H NMR spectrum, δ, ppm: 7.58 m (1H, 6''-H), 7.79 t (1H, 5'-H, ^3J = 7.9 Hz), 8.39 m (2H, 4'-H, 6'-H), 8.81 m (1H, 2'-H), 13.2 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 398 (1.2) $[M]^+$, 177 (100), 149 (39), 104 (28), 76 (20). Found, %: C 45.21; H 1.51; N 14.09. $C_{15}H_6F_4N_4O_3S$. Calculated, %: C 45.23; H 1.52; N 14.07.

3-(Pyridin-3-yl)-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIc). Yield 77%, mp 234–236°C. ^{1}H NMR spectrum, δ, ppm: 7.53 m (1H, 5'-H), 7.76 m (1H, 6''-H), 8.30 m (1H, 6'-H), 8.67 m (1H, 4'-H), 9.21 m (1H, 2'-H), 13.4 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 354 (19) $[M]^+$, 177 (100), 149 (24). Found, %: C 47.49; H 1.74; N 15.79. $C_{14}H_6F_4N_4OS$. Calculated, %: C 47.46; H 1.71; N 15.81.

3-(Pyridin-4-yl)-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIId). Yield 76%, mp 240–242°C. ^{1}H NMR spectrum, δ, ppm: 7.75 m (1H, 6''-H), 7.88 m (2H, 2'-H, 6'-H), 8.74 m (2H, 3'-H, 5'-H), 13.7 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 354 (21) $[M]^+$, 177 (100), 149 (26). Found, %: C 47.47; H 1.73; N 15.80. $C_{14}H_6F_4N_4OS$. Calculated, %: C 47.46; H 1.71; N 15.81.

3-(Pyrrolidin-1-yl)-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIe). A solution of 6 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in 9 ml of anhydrous acetonitrile was added to a solution of 0.43 g (3 mmol) of pyrrolidine-1-carbothiohydrazide (**Xe**) in 7 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, cooled, and evaporated, and the residue was washed with ethanol and recrystallized from DMSO. Yield 0.76 g (73%), mp >250°C. ^{1}H NMR spectrum, δ, ppm: 2.02 m [4H, $(CH_2)_2$], 3.42 m [4H, $N(CH_2)_2$], 7.56 m (1H, 6''-H), 12.9 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 346 (100) $[M]^+$, 327 (12), 326 (11), 318 (30), 304 (10), 177 (87), 149 (38), 114 (79), 100 (32), 99 (20), 72 (70), 70 (18), 69 (17), 55 (53). Found, %: C 45.08; H 2.87; N 16.25. $C_{13}H_{10}F_4N_4OS$. Calculated, %: C 45.11; H 2.91; N 16.19.

Compounds **XIIf–XIIh** were synthesized in a similar way.

3-Piperidino-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIf). Yield 76%, mp 188–190°C. ^{1}H NMR spectrum, δ, ppm: 1.67 m [6H, $(CH_2)_3$], 3.44 m [4H, $N(CH_2)_2$], 7.65 m (1H, 6''-H), 12.8 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 360 (86) $[M]^+$, 331 (33), 304 (18), 177 (100), 149 (32), 128 (43), 84 (20), 83 (78), 72 (75), 69 (60), 55 (40). Found, %: C 46.71; H 3.28; N 15.38. $C_{14}H_{12}F_4N_4OS$. Calculated, %: C 46.67; H 3.33; N 15.36.

3-Morpholino-4-(2,3,4,5-tetrafluorobenzoyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIg). Yield 79%, mp 218–220°C. ^{1}H NMR spectrum, δ, ppm: 3.43 m [4H, $N(CH_2)_2$], 3.75 m [4H, $O(CH_2)_2$], 7.66 m (1H, 6''-H), 12.9 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 362 (55) $[M]^+$, 305 (46), 177 (100), 130 (31), 86 (40). Found, %: C 43.11; H 2.75; N 15.41. $C_{13}H_{10}F_4N_4O_2S$. Calculated, %: C 43.10; H 2.78; N 15.46.

4-(2,3,4,5-Tetrafluorobenzoyl)-3-thiomorpholino-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (XIIh). Yield 81%, mp 176–178°C. ^{1}H NMR spectrum, δ, ppm: 2.72 [4H, $S(CH_2)_2$], 3.80 [4H, $N(CH_2)_2$], 7.65 m (1H, 6''-H), 12.9 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 378 (20) $[M]^+$, 306 (17), 305 (100), 177 (57), 149 (15), 69 (16). Found, %: C 41.22; H 2.69; N 14.75. $C_{13}H_{10}F_4N_4OS_2$. Calculated, %: C 41.27; H 2.66; N 14.81.

2-(2-Benzylidene-1-phenylhydrazino)-6,7,8-trifluoro-4*H*-1,3-benzothiazin-4-one (XIVa). A solution of 9 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in 12 ml of anhydrous acetonitrile was added to a solution of 0.54 g (4.5 mmol) of compound **XIIIa** in 9 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, cooled, and evaporated, and the residue was washed with ethanol and recrystallized from DMSO. Yield 1.50 g (81%), mp 285–287°C. ^{1}H NMR spectrum, δ, ppm: 7.38 m (2H, H_{arom}), 7.46 m (3H, H_{arom}), 7.57 s (1H, CH=N), 7.65 m (2H, H_{arom}), 7.69 m (3H, H_{arom}), 7.97 d.d.d (1H, 5-H, ^3J = 10.0, ^4J = 7.8, ^5J = 2.3 Hz), 13.2 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 411 (19) $[M]^+$, 335 (19), 334 (100), 308 (14), 191 (17), 190 (20), 162 (22), 118 (77), 77 (51), 51 (14). Found, %: C 61.26; H 2.89; N 10.25. $C_{21}H_{12}F_3N_3OS$. Calculated, %: C 61.31; H 2.94; N 10.21.

6,7,8-Trifluoro-2-[2-(2-hydroxybenzylidene)-1-phenylhydrazino]-4*H*-1,3-benzothiazin-4-one (XIVb) was synthesized in a similar way. Yield 85%, mp 278–280°C. ^{1}H NMR spectrum, δ, ppm: 6.83 m

(2H, H_{arom}), 7.23 (1H, H_{arom}), 7.38 m (2H, H_{arom}), 7.71 m (3H, H_{arom}), 7.81 m (1H, H_{arom}), 7.88 s (1H, CH=N), 7.95 d.d.d (1H, 5-H, ^3J = 10.0, ^4J = 7.8, ^5J = 2.3 Hz), 9.83 s (1H, OH). ^{19}F NMR spectrum, δ_F, ppm: 9.46 m (1F), 25.58 m (1F), 27.63 d.d.d (1F, J = 22.3, 10.8, 5.1 Hz). Mass spectrum, m/z (I_{rel}, %): 427 (10) $[M]^+$, 334 (28), 308 (30), 191 (25), 190 (20), 162 (18), 119 (23), 118 (100), 91 (19), 77 (16), 65 (10). Found, %: C 58.97; H 2.76; N 9.88. $C_{21}H_{12}F_3N_3O_2S$. Calculated, %: C 59.02; H 2.81; N 9.84.

1-(4,6-Dimethylpyrimidin-2-yl)-3-(2,3,4,5-tetrafluorobenzoyl)-1-(6,7,8-trifluoro-4-oxo-4*H*-1,3-benzothiazin-2-yl)thiourea (XVIa). A solution of 9 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in 12 ml of anhydrous acetonitrile was added to a suspension of 1.0 g (4.5 mmol) of 1-benzylidene-2-(4,6-dimethylpyrimidin-2-yl)hydrazine (**XVa**) in 12 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, cooled, and evaporated, and the residue was washed with ethanol and recrystallized from DMSO. Yield 1.8 g (70%), mp 202–204°C. ^{1}H NMR spectrum, δ, ppm: 2.58 s (3H, CH_3), 2.64 s (3H, CH_3), 7.44 s (1H, 5'-H), 7.78 m (2H, C_6HF_4), 13.2 br.s (1H, NH). Mass spectrum, m/z (I_{rel}, %): 574 (22) $[M]^+$, 425 (29), 177 (100), 149 (22), 107 (23), 105 (11), 67 (16). Found, %: C 46.04; H 1.78; N 12.17. $C_{22}H_{10}F_7N_5O_2S_2$. Calculated, %: C 45.99; H 1.74; N 12.20.

In the reaction of isothiocyanate **I** with 1-(4,6-dimethylpyrimidin-2-yl)-2-(2-furylmethylidene)hydrazine (**XVb**), the yield of compound **XVIa** was 67%.

1-(4,6-Diphenylpyrimidin-2-yl)-3-(2,3,4,5-tetrafluorobenzoyl)-1-(6,7,8-trifluoro-4-oxo-4*H*-1,3-benzothiazin-2-yl)thiourea (XVIb) was synthesized in a similar way from isothiocyanate **I** and 1-benzylidene-2-(4,6-diphenylpyrimidin-2-yl)hydrazine (**XVc**). Yield 73%, mp 275–277°C. ^{1}H NMR spectrum, δ, ppm: 7.53 m (2H, H_{arom}), 7.62 m (4H, H_{arom}), 7.78 m (2H, C_6HF_4), 8.43 m (2H, H_{arom}), 8.45 m (2H, H_{arom}), 8.74 s (1H, 5'-H), 13.2 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 7.51 m (1F), 7.95 m (1F), 12.24 m (1F), 22.95 m (1F), 24.04 m (1F), 24.68 m (2F). Mass spectrum, m/z (I_{rel}, %): 698 (20) $[M]^+$, 549 (16), 231 (30), 189 (35), 177 (100), 149 (20), 129 (24). Found, %: C 55.05; H 1.97; N 10.07. $C_{32}H_{14}F_7N_5O_2S_2$. Calculated, %: C 55.10; H 2.02; N 10.04.

In the reaction of isothiocyanate **I** with 1-(4,6-dimethylpyrimidin-2-yl)-2-(4-methoxybenzylidene)hydrazine (**XVd**), the yield of compound **XVIb** was 69%.

***N*-(1,3-Benzothiazol-2-yl)-*N'*-benzylidene-2,3,4,5-tetrafluorobenzohydrazide (XVIIIa).** A solution of 6 mmol of 2,3,4,5-tetrafluorobenzoyl isothiocyanate (**I**) in 9 ml of anhydrous acetonitrile was added to a suspension of 0.75 g (3 mmol) of 1-(1,3-benzothiazol-2-yl)-2-benzylidenehydrazine (**XVIIa**) in 10 ml of anhydrous acetonitrile. The mixture was kept for 30 min at room temperature, heated for 1 h under reflux, cooled, and evaporated, and the residue was washed with ethanol and recrystallized from DMSO. Yield 1.1 g (75%), mp 147–149°C. ^{1}H NMR spectrum, δ, ppm: 7.40–7.65 m (7H, C_6H_5, benzothiazole), 7.73 m (1H, C_6HF_4), 7.93 m (1H, benzothiazole), 8.06 m (1H, benzothiazole), 9.05 s (1H, CH=N). Mass spectrum, m/z (I_{rel}, %): 429 (21) $[M]^+$, 326 (13), 252 (32), 224 (20), 223 (26), 177 (100), 149 (36), 77 (10). Found, %: C 58.69; H 2.52; N 9.83. $C_{21}H_{11}F_4N_3OS$. Calculated, %: C 58.74; H 2.56; N 9.79.

Compounds **XVIIIb** and **XVIIIc** were synthesized in a similar way.

***N*-(1,3-Benzothiazol-2-yl)-2,3,4,5-tetrafluoro-*N'*-(4-methoxybenzylidene)benzohydrazide (XVIIIb).** Yield 82%, mp 190–192°C. ^{1}H NMR spectrum, δ, ppm: 6.96 d (2H, 3'-H, 5'-H, ^3J = 8.5 Hz), 7.47 m (2H, benzothiazole), 7.62 d (2H, 2'-H, 6'-H, ^3J = 8.5 Hz), 7.67 m (1H, C_6HF_4), 7.87 m (1H, benzothiazole), 8.05 m (1H, benzothiazole), 8.94 s (1H, CH=N). Mass spectrum, m/z (I_{rel}, %): 459 (18) $[M]^+$, 326 (34), 282 (12), 223 (17), 177 (100), 150 (13), 149 (30), 77 (10). Found, %: C 57.47; H 2.78; N 9.18. $C_{22}H_{13}F_4N_3O_2S$. Calculated, %: C 57.52; H 2.83; N 9.15.

***N*-(1,3-Benzothiazol-2-yl)-2,3,4,5-tetrafluoro-*N'*-(2-furylmethylidene)benzohydrazide (XVIIIc).** Yield 77%, mp 138–140°C. ^{1}H NMR spectrum, δ, ppm: 6.59 d.d (1H, 2'-H, ^3J = 3.8, 2.2 Hz), 6.97 d (1H, 1'-H, ^3J = 3.8 Hz), 7.55 m (2H, benzothiazole), 7.76 d (1H, 3'-H, ^3J = 2.2 Hz), 8.00 m (2H, benzothiazole), 9.02 s (1H, CH=N). Mass spectrum, m/z (I_{rel}, %): 419 (17) $[M]^+$, 326 (14), 242 (17), 186 (31), 177 (100), 149 (32), 52 (13). Found, %: C 54.33; H 2.11; N 10.06. $C_{19}H_9F_4N_3O_2S$. Calculated, %: C 54.37; H 2.15; N 10.02.

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