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Efficient synthesis of tri- and difluoroacetyl hydrazides as useful building blocks for non-symmetrically substituted, fluoroalkylated 1,3,4-oxadiazoles

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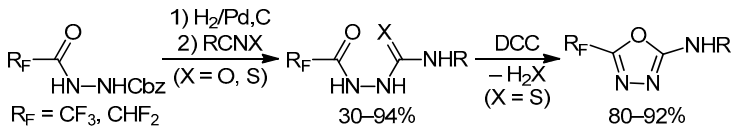


A convenient and efficient approach to 2-arylamino-5-fluoroalkyl-1,3,4-oxadiazoles has been established *via* heterocyclization of tri- and difluoroacetylated thiosemicarbazides using dicyclohexylcarbodiimide. A heterocyclization performed with selected thiosemicarbazides under basic conditions led to 4-aryl-5-fluoroalkyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thiones in moderate yields. The starting fluoroacetylated thiosemicarbazides were prepared by fluoroacetylation of benzyloxycarbonyl-protected hydrazine with a corresponding anhydride, followed by hydrogenolytic deprotection and reaction with arylisothiocyanates. Fluoroacetylated semicarbazides were prepared similarly, but all attempts to achieve their heterocyclization were unsuccessful.

Keywords: fluoroalkylated heterocycles, hydrazides, 1,3,4-oxadiazoles, protected hydrazines, 1,2,4-triazole-3-thiones, heterocyclization.

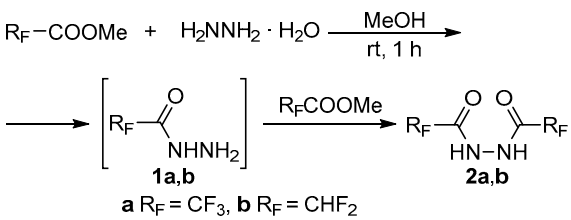
Fluorine-containing heterocyclic compounds are widely applied as biologically active substances for the preparation of new drugs, agrochemicals, and materials with special properties.[1] The development of methods for stereoselective synthesis of diverse fluorinated *N*-heterocycles is also of current interest.[2] Among heterocyclic systems which attract great attention, an important class comprises 1,3,4-oxadiazole derivatives[3] including fluorinated examples.[4]

Hydrazides of carboxylic acids (carbohydrazides) are known as versatile building blocks used for the preparation of heterocyclic compounds with diverse ring size. The target heterocycles can be synthesized starting either from substituted carbohydrazides or their derivatives, such as hydrazones, semicarbazides, thiosemicarbazides, etc.[5] A known method for the preparation of 1,3,4-oxadiazoles is the treatment of semicarbazides derived from carbohydrazides with sulfuric acid[6] or another acidic agent. Alternatively, 1,3,4-oxadiazoles can be obtained directly from carbohydrazides by the reaction with orthoesters.[7]

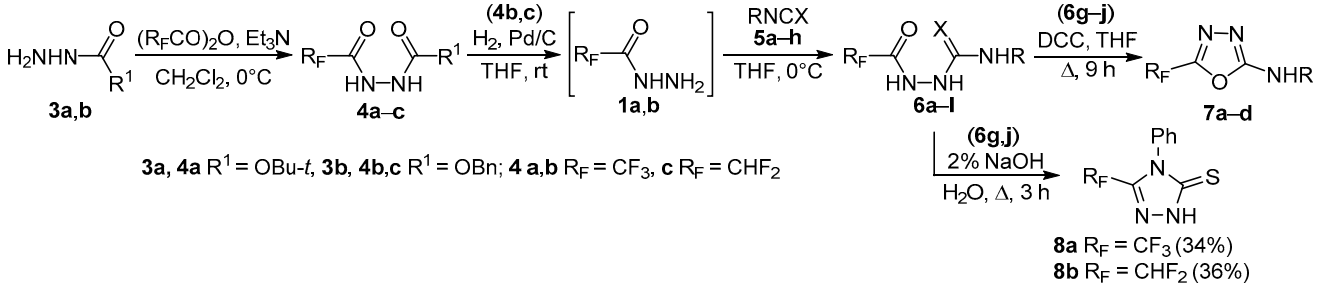
Due to our continuing interest in the development of methods for fluoroalkylation and the synthesis of fluorinated heterocycles,[8] we focused attention on the exploration of the relatively little known tri- and difluoroacetyl hydrazides **1a**,**b** as potential precursors for the preparation of fluorinated 1,3,4-oxadiazoles. The method selected for the synthesis of the latter was heterocyclization of semicarbazides of fluorinated carbohydrazides using sulfuric acid. In addition, analogous heterocyclizations could be performed starting with thiosemicarbazides and selenosemicarbazides.

Typically, the access to carbohydrazides is based on the reaction of the corresponding carboxylic esters with an equimolar amount of hydrazine hydrate.[5] In our case, the treatment of methyl trifluoroacetate with 1.0–5.0 equivalents of hydrazine hydrate in methanolic solution led to bis(trifluoroacetyl)hydrazine (**2a**) as a single product (Scheme 1). Its structure was confirmed by the ESI-MS registered for the crude product, which displayed a single signal for *m*/*z* 223. Increasing the excess of hydrazine

Scheme 1



Scheme 2



hydrate to 1:10 or 1:20 resulted in a mixture of comparable amounts of compounds **2a** and **1a** or in the exclusive formation of compound **1a**, respectively. Apparently, the initially formed compound **1a** reacts rapidly with the starting ester yielding bis-adduct **2a** as the final product. The formation of the analogous product **2b** was observed using methyl difluoroacetate in the reaction with hydrazine hydrate.

In the course of the attempted synthesis of compound **1a**, the tested protocol with 20-fold excess of hydrazine hydrate was practically useless, as the expected product could not be efficiently separated from the excess of hydrazine hydrate. In the light of the presented results, the reported syntheses of compound **1a** from trifluoroacetates and hydrazine hydrate used in nearly equimolar amounts seem to be non-reproducible protocols.[9] However, instability of compound **1a** was observed during the storage of the isolated product already at room temperature.[9a]

For that reason, the Boc- and Cbz-protected hydrazines **3a** and **3b**, respectively, were prepared and converted into the *N*-protected non-symmetrical tri- and difluoroacetyl hydrazines **4a**–**c** by treatment with tri- or difluoroacetic anhydride (Scheme 2). Similar approaches for the synthesis of compound **1a** based on the application of *N*-Boc-protected hydrazine have been only rarely reported.[10]

However, the attempted deprotection of the Boc-hydrazide **4a** performed typically by treatment with trifluoroacetic acid in CH_2Cl_2 at 0°C or with HCl in dioxane at 0°C yielded exclusively the symmetrical product **2a**. On the other hand, hydrogenolysis of compounds **4b** and **4c** over Pd/C in THF at room temperature afforded the desired tri- and difluoroacetyl hydrazides **1a** and **1b**, respectively, as the sole products (Scheme 2). In the case of compound **1a**, the attempted isolation led again to its conversion into the symmetrical diacylhydrazine **2a**. Therefore, freshly prepared compounds **1a** and **1b** in THF solution were treated with isocyanates, isothiocyanates, and isoselenocyanates **5** (X = O, S, Se, respectively, Scheme 2). The most reactive isocyanates **5a**–**d** formed the expected semicarbazides **6a**–**f** in high yields (Scheme 2, Table 1). Similarly, aromatic isothiocyanates **5e**–**h** gave thiosemicarbazides **6g**–**j** in good yields, and only in the case of the less reactive cyclohexylisothiocyanate the corresponding products **6k** and **6l** were formed in low yields and could not be isolated in pure form. Finally, the attempted reactions of compounds **1a**,**b** with phenyl isoselenocyanate led to black-colored, complex mixtures of unidentified products.

First experiments aimed at the preparation of fluorinated 1,3,4-oxadiazoles were performed with compound **6a** using ethyl orthoacetate and catalytic amounts of *p*-TsOH, but in this case, a complex mixture of unidentified products was formed. Similarly, treatment of compound **6a** with concd. H_2SO_4 led to the same result. Finally, the reaction of thiosemicarbazides **6g**–**j** with DCC in boiling THF afforded selectively 2-amino-1,3,4-oxadiazoles **7a**–**d** in excellent yields (Scheme 2, Table 2). Analytically pure products were isolated after flash column chromatography. Their structures were established by means of spectroscopic methods. For example, the ^{13}C NMR spectrum of compound **7a** revealed a singlet for the C-2 atom at 161.7 ppm and a quartet for the C-5 atom with $^2J_{CF}$ = 42.9 Hz at 147.9 ppm. The characteristic quartet with $^1J_{CF}$ = 268.1 Hz at 116.8 ppm was attributed to the CF_3 group. In addition, the ^{19}F NMR spectrum showed the signal of the CF_3 group at –64.6 ppm.

Table 1. Reactants and product yields in the synthesis of *N*-acylated semicarbazides **6a**–**f** and thiosemicarbazides **6g**–**l**

Hydrazide	R_F	Reagent	R	X	Product	Yield, %
1a	CF_3	**5a**	Ph	O	**6a**	88
1a	CF_3	**5b**	4-FC_6H_4	O	**6b**	91
1a	CF_3	**5c**	4-$MeOC_6H_4$	O	**6c**	86
1a	CF_3	**5d**	*c*Hex	O	**6d**	93
1b	CHF_2	**5a**	Ph	O	**6e**	90
1b	CHF_2	**5d**	*c*Hex	O	**6f**	94
1a	CF_3	**5e**	Ph	S	**6g**	77
1a	CF_3	**5f**	4-FC_6H_4	S	**6h**	74
1a	CF_3	**5g**	4-$MeOC_6H_4$	S	**6i**	68
1b	CHF_2	**5e**	Ph	S	**6j**	80
1a	CF_3	**5h**	*c*Hex	S	**6k**	ca. 30*
1b	CHF_2	**5h**	*c*Hex	S	**6l**	ca. 30*

* Symmetrical *N*,*N*'-bis(trifluoroacetyl)hydrazine (**2a**) and *N*,*N*'-bis(difluoroacetyl)hydrazine (**2b**) were formed as by-products, and separation of these mixtures could not be achieved. The yields of compounds **6k** and **6l** were estimated based on the registered ^{19}F NMR spectra and the calculated ratios of **6k**/**2a** and **6l**/**2b**, respectively.

Table 2. Yields of fluoroalkylated 2-amino-1,3,4-oxadiazoles **7a**–**d**

Thiosemicarbazide	R_F	R	1,3,4-Oxadiazole	Yield, %
6g	CF_3	Ph	**7a**	92
6h	CF_3	4-FC_6H_4	**7b**	95
6i	CF_3	4-$MeOC_6H_4$	**7c**	80
6j	CHF_2	Ph	**7d**	82

It is worth mentioning that an efficient method to obtain 2-amino-1,3,4-oxadiazoles comprises the reaction of thiosemicarbazides of type **6g**–**l** or analogous with TsCl and pyridine.[11] In some cases, the same product could be obtained from the corresponding semicarbazide, albeit in significantly lower yield and after longer reaction time. The reported formation of compound **7a** as the exclusive product was confirmed also in our laboratory.

In an extension of the study, fluorinated thiosemicarbazides **6g** and **6j** were heated in an aqueous solution of NaOH (2%), and 1,2,4-triazole-3-thiones **8a** and **8b**, respectively, were obtained in moderate yields (Scheme 2). This observation confirms the behavior of thiosemicarbazides under basic conditions.[12] Again, the attempted cyclization of the corresponding semicarbazides **6a**–**f** (X = O) under analogous conditions was unsuccessful.

The present study has shown that, in addition to other methods for the preparation of 2-amino-1,3,4-oxadiazoles based on the heterocyclization of semicarbazides, the corresponding thiosemicarbazides, including fluorinated derivatives, can also be used for this purpose. The heterocyclization of fluorinated thiosemicarbazides can be efficiently performed using DCC as the activating and H_2S-binding reagent. This protocol supplements the already reported method with *p*-TsCl and pyridine in THF solution.[11] According to our observation, yields of the final products are comparable in both methods. However, the elimination of pyridine (or triethylamine) as an additional component of the reaction mixture can be considered as an advantageous feature of the present protocol. In both procedures, the heterocyclization occurs chemoselectively *via* the conversion of the more nucleophilic C=S function into a good leaving group and the subsequent nucleophilic attack of the oxygen atom leading to 2-amino-1,3,4-oxadiazoles as the final products. This type of chemoselectivity is preserved also in thiosemicarbazides containing an electron-deficient R_FCO group. Another method for the synthesis of symmetrical 2,5-bis-(perfluoroalkyl)-substituted 1,3,4-oxadiazoles from 1,2-diacylhydrazines, prepared stepwise by twofold acylation of hydrazine, is the cyclization by treatment with $POCl_3$ as activating and dehydrating agent.[9b] This approach can be considered as a pioneering method for the synthesis of 1,3,4-oxadiazoles.[13]

The presented method for the preparation of fluorinated 2-amino-1,3,4-oxadiazoles requires an efficient access to fluorinated monoacetylhydrazines. Our study showed that they can be synthesized from Cbz-protected hydrazine and the corresponding fluorinated acetanhydrides. After the deprotection, the obtained carbohydrazides have to be reacted immediately with isocyanates or isothiocyanates to give the required semicarbazides and thiosemicarbazides, respectively. Otherwise they undergo spontaneous disproportionation yielding symmetrical 1,2-diacylhydrazines, which are of limited importance for further applications.

Experimental

IR spectra were recorded on a NEXUS FT-IR spectrophotometer in KBr pellets. The ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance III 600 spectrometer (600, 150, and 565 MHz, respectively) in DMSO-d_6, using the solvent signal as reference (2.50 and 39.51 ppm for ^{1}H and ^{13}C nuclei, respectively). Assignments of signals in ^{13}C NMR spectra were made using ^{1}H–^{13}C HMQC and HMBC techniques. ESI mass spectra were obtained using a Varian 500 MS LS Ion Trap spectrometer. High-resolution mass spectra (electron ionization) were obtained on a Finningan MAT-95 spectrometer. Elemental analyses were recorded on an Elementar vario Micro cube apparatus. Melting points were determined on a Melt-Temp II apparatus (Aldrich) in capillaries.

All solvents were used as commercial products. Methyl trifluoroacetate, methyl difluoroacetate, trifluoroacetic acid anhydride, and difluoroacetic acid anhydride, were purchased from Fluorochem. Chloroform was dried over P_2O_5 and freshly distilled prior to use. Tetrahydrofuran was dried over sodium in the presence of benzophenone and freshly distilled from the violet-colored solution prior to use. Anhydrous ethanol was dried over calcium oxide and CH_2Cl_2 over calcium hydride. (*tert*-Butoxycarbonyl)-hydrazine (**3a**)[14a] and (benzyloxycarbonyl)hydrazine (**3b**)[14b] were obtained according to the known protocols.

Synthesis of the symmetrical 1,2-bis(trifluoroacetyl)-hydrazine (2a). Ethyl trifluoroacetate (142 mg, 1.0 mmol) was added dropwise to the solution of hydrazine hydrate (50 mg, 1.0 mmol) in MeOH (~5.0 ml). The reaction mixture was stirred over 1 h at room temperature. Next, the solvent was evaporated, and the solid product was recrystallized from EtOH. Yield 160 mg (71%), mp 173–175°C (EtOH) (mp 176°C[9b]). IR spectrum, ν , cm^{-1}: 3346 (N–H, w), 3293 (w), 3213 (w), 3142 (w), 2989 (m), 2957 (w), 2858 (w), 2756 (w), 1612 (C=O, vs), 1520 (w), 1414 (m), 1203 (vs), 1190 (vs), 1146 (vs), 1098 (s), 973 (m). ^{1}H NMR spectrum, δ, ppm: 7.45 (2H, br. s, 2NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 118.1 (q, $^1J_{CF}$ = 284.4, $2CF_3$); 159.1 (q, $^2J_{CF}$ = 31.0, 2C=O). ^{19}F NMR spectrum, δ, ppm: –72.9 (6F, s, $2CF_3$). Found, *m*/*z*: 224.0013 $[M]^+$. $C_4H_2F_3N_2O_2$. Calculated, *m*/*z*: 224.0015.

Reactions of protected hydrazines 3a,b with fluorinated acid anhydrides (General method). A solution of $BocNHNH_2$ (**3a**) (3.0 mmol, 498 mg) or $CbzNHNH_2$ (**3b**) (3.0 mmol, 396 mg) in anhydrous CH_2Cl_2 (~30 ml) was placed in an ice bath (~0°C). Next, triethylamine (4.5 mmol, 455 mg) was added, and after ca. 20 min, the appropriate fluorinated anhydride (3.2 mmol) was added dropwise while cooling the reaction flask in an ice bath. The reaction mixture was stirred at room temperature for 2 h. Then the solvent was evaporated, and the crude products were purified by column chromatography (SiO_2, hexane–AcOEt, 1:1). Analytically pure samples were obtained after crystallization from an appropriate solvent.

***tert*-Butyl 2-(trifluoroacetyl)hydrazinecarboxylate (4a)**. Yield 608 mg (89%), colorless crystals, mp 129–131°C (Et_2O–hexane) (mp 130–132°C[10a]). IR spectrum, ν , cm^{-1}: 3294 (N–H, br., s), 3196 (N–H, br., m), 3031 (m), 3000 (m), 2989 (m), 2914 (w), 1741 (C=O, s), 1690 (C=O, vs), 1571 (w), 1506 (s), 1457 (w), 1400 (w), 1369 (m), 1247 (s), 1207 (vs), 1162 (s), 1137 (s), 1052 (w), 1024 (w), 901 (w), 857 (w), 732 (m), 675 (w). ^{1}H NMR spectrum, δ, ppm:

1.43 (9H, s, $3CH_3$); 9.28 (1H, s, NH); 11.23 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 28.4 ($3CH_3$); 80.6 ($\underline{C}(CH_3)_3$); 116.3 (q, $^1J_{CF}$ = 286.5, CF_3); 154.9 (C=O); 156.7 (q, $^2J_{CF}$ = 35.1, $CF_3\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm: –74.0 (3F, s, CF_3). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 227 $[M–H]^-$ (100%). Found, %: C 37.02; H 4.96; N 12.30. $C_7H_{11}F_3N_2O_3$. Calculated, %: C 36.85; H 4.86; N 12.28.

Benzyl 2-(trifluoroacetyl)hydrazinecarboxylate (4b). Yield 605 mg (77%), colorless crystals, mp 109–111°C (Et_2O–hexane) (mp 106–108°C[10b]). IR spectrum, ν, cm^{-1}: 3335 (N–H, br., m), 3268 (N–H, br., m), 3041 (m), 2968 (w), 2915 (w), 1761 s (C=O), 1689 s (C=O), 1549 (m), 1511 (m), 1357 (w), 1243 (vs), 1209 (vs), 1158 (s), 1046 (w), 969 (w), 746 (m), 697 (m). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.14 (2H, s, CH_2); 7.35–7.39 (5H, m, H Ph); 9.75 (1H, br. s, NH); 11.44 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 66.9 (CH_2); 116.3 (q, $^1J_{CF}$ = 286.5, CF_3); 128.4, 128.6, 128.9 (C Ph); 136.7 (C-1 Ph); 155.8 (C=O); 156.7 (q, $^2J_{CF}$ = 35.8, $CF_3\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –74.0 (3F, s, CF_3). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 261 $[M–H]^-$ (100). Found, %: C 45.67; H 3.56; N 10.85. $C_{10}H_9F_3N_2O_3$. Calculated, %: C 45.81; H 3.46; N 10.68.

Benzyl 2-(difluoroacetyl)hydrazinecarboxylate (**4c**). Yield 682 mg (93%), colorless crystals, mp 116–117°C (Et_2O–hexane). IR spectrum, ν , cm^{-1}: 3316 (2N–H, br., s), 3091 (w), 3064 (w), 3040 (w), 3017 (w), 2996 (w), 2965 (w), 2903 (w), 1739 s (C=O), 1683 (C=O, s), 1546 (m), 1506 (m), 1464 (w), 1384 (w), 1358 (w), 1257 (m), 1205 (w), 1106 (w), 1056 (m), 960 (w), 750 (m), 701 (m), 580 (m). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.13 (2H, s, CH_2); 6.37 (1H, t, $^2J_{HF}$ = 52.9, CHF_2); 7.35–7.39 (5H, m, H Ph); 9.51 (1H, s, NH); 10.74 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 66.7 (CH_2); 108.6 (t, $^1J_{CF}$ = 245.4, CHF_2); 128.4, 128.5, 128.9 (C Ph); 136.9 (C-1 Ph); 156.0 (C=O); 162.3 (t, $^2J_{CF}$ = 25.0, $CHF_2\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –126.8 (2F, d, $^2J_{HF}$ = 52.9, CHF_2). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 267 $[M+Na]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 243 $[M–H]^-$ (100). Found, %: C 49.32; H 4.13; N 11.60. $C_{10}H_{10}F_2N_2O_3$. Calculated, %: C 49.19; H 4.13; N 11.47.

Preparation of fluorinated acid hydrazides *via* hydrogenolysis of *N*'-(benzyloxy)carbohydrazides 4b,c and their reactions with isocyanates and isothiocyanates (General method). A portion of the catalyst (10% Pd/C (60 mg)) was added to a solution of the CBz-protected carbohydrazide **4b**,**c** (2.0 mmol) in anhydrous THF (~50 ml). Next, the reaction flask was equipped with a septum, a long syringe, and a balloon filled with hydrogen. Progress of the reaction was monitored by TLC (SiO_2, hexane–AcOEt, 1:1), and as soon as the reaction was finished, the solution was filtered through a Celite pad. Next, the appropriate isocyanate **5a**–**d** or isothiocyanate **5e**–**h** (2.2 mmol) was added dropwise to the filtrate while cooling the reaction flask in an ice bath (~0°C). The mixture was stirred overnight at room temperature. After evaporation of the solvent, the crude products were purified by column chromatography (SiO_2, hexane, then with increasing amount (40–90%) of AcOEt in hexane). Semicarbazides **6a**–**f** and thiosemicarbazides **6g**–**j** were obtained as amorphous solids by trituration with Et_2O.

***N*-Phenyl-2-(trifluoroacetyl)hydrazinecarboxamide (6a)**. Yield 436 mg (88%), colorless crystals, mp 176–178°C (mp 265.8–266.6[11]). IR spectrum, ν, cm^{-1}: 3297 (3N–H, br., vs), 3057 (m), 2890 (w), 1727 (C=O, vs), 1667 (C=O, vs), 1608 (s), 1574 (s), 1558 (m), 1360 (m), 1317 (m), 1303 (m), 1216 (s), 1189 (vs), 1165 (vs), 1128 (s), 1078 (w), 1044 (w), 1033 (w), 920 (m), 857 (w), 745 (m), 695 (m), 633 (m), 581 (w). ^{1}H NMR spectrum, δ, ppm: 6.98–7.00 (1H, m, H Ph); 7.26–7.29 (2H, m, H Ph); 7.45–7.46 (2H, m, H Ph); 8.44 (1H, br. s, NH); 8.96 (1H, br. s, NH); 11.24 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 116.5 (q, $^1J_{CF}$ = 289.4, CF_3); 119.1, 122.7, 129.1 (C Ph); 139.8 (C-1 Ph); 154.7 (C=O); 156.8 (q, $^2J_{CF}$ = 34.8, $CF_3\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm: –73.6 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 248 $[M+H]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 246 $[M–H]^-$ (100). Found, *m/z*: 247.0571 $[M]^+$. $C_9H_8F_3N_3O_2$. Calculated, *m/z*: 247.0563.

***N*-(4-Fluorophenyl)-2-(trifluoroacetyl)hydrazinecarboxamide (6b)**. Yield 483 mg (91%), colorless crystals, mp 190–191°C. IR spectrum, ν, cm^{-1}: 3378 (N–H, br., m), 3319 (N–H, br., m), 3227 (N–H, br., m), 3065 (w), 2908 (w), 1720 (m), 1690 (C=O, s), 1664 (C=O, s), 1620 (w), 1571 (s), 1514 (s), 1411 (w), 1363 (w), 1277 (w), 1219 (s), 1198 (s), 1170 (s), 1124 (w), 1099 (w), 1053 (w), 1015 (w), 923 (w), 832 (w), 793 (w), 739 (w), 635 (w). ^{1}H NMR spectrum, δ, ppm: 7.10–7.13 (2H, m, H Ar); 7.45–7.48 (2H, m, H Ar); 8.49 (1H, br. s, NH); 9.04 (1H, br. s, NH); 11.23 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 115.6, 115.7 (C Ar); 116.4 (q, $^1J_{CF}$ = 286.6, CF_3); 136.1 (C-1 Ar); 154.8 (C=O); 157.1 (q, $^2J_{CF}$ = 35.7, $F_3C\underline{C}$=O); 158.0 (d, $^1J_{CF}$ = 237.0, C-4 Ar). ^{19}F NMR spectrum, δ, ppm: –117.3 (1F, s, CF); –73.7 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 266 $[M+H]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 264 $[M–H]^-$ (100). Found, *m/z*: 265.0473 $[M]^+$. $C_9H_7F_4N_3O_2$. Calculated, *m/z*: 265.0469.

***N*-(4-Methoxyphenyl)-2-(trifluoroacetyl)hydrazinecarboxamide (6c)**. Yield 475 mg (86%), colorless crystals, mp 186–188°C. IR spectrum, ν, cm^{-1}: 3289 (3N–H, br., vs), 3146 (w), 3088 (w), 3056 (w), 3008 (w), 2954 (w), 2914 (w), 2837 (w), 1728 (C=O, s), 1668 (C=O, vs), 1608 (s), 1575 (s), 1540 (m), 1515 (s), 1465 (w), 144 (w), 1361 (w), 1304 (w), 1251 (s), 1218 (s), 1190 (s), 1173 (vs), 1128 (s), 1104 (m), 1031 (m), 920 (m), 836 (m), 799 (w), 836 (m), 739 (m), 636 (m). ^{1}H NMR spectrum, δ, ppm: 3.72 (3H, s, CH_3); 6.85–6.88 (2H, m, H Ar); 7.33–7.36 (2H, m, H Ar); 8.36 (1H, br. s, NH); 8.79 (1H, br. s, NH); 11.18 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 55.6 (OCH_3); 114.4, 114.5, 120.4, 120.5 (C Ar); 116.4 (q, $^1J_{CF}$ = 286.6, CF_3); 132.7 (C-1 Ar); 155.0 (C-4 Ar); 155.2 (C=O); 157.0 (q, $^2J_{CF}$ = 35.4, $CF_3\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm: –73.7 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 300 $[M+Na]^+$ (100); 278 $[M+H]^+$ (75). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 276 $[M–H]^-$ (100). Found, *m/z*: 277.0673 $[M]^+$. $C_{10}H_{10}F_3N_3O_3$. Calculated, *m/z*: 277.0669.

***N*-Cyclohexyl-2-(trifluoroacetyl)hydrazinecarboxamide (6d)**. Yield 471 mg (93%), colorless crystals, mp 151–152°C. IR spectrum, ν, cm^{-1}: 3331 (N–H, br., m), 3267 (2N–H, br., m),

3116 (w), 3027 (w), 2935 (m), 2858 (m), 1748 (C=O, s), 1675 (C=O, s), 1636 (m), 1589 (m), 1551 (w), 1489 (w), 1465 (w), 1456 (w), 1358 (w), 1317 (w), 1253 (m), 1239 (m), 1204 (s), 1164 (s), 1133 (m), 1078 (m), 1018 (w), 914 (w), 891 (w), 795 (w), 737 (m), 656 (w). ^{1}H NMR spectrum, δ, ppm: 1.11–1.30 (5H, m) and 1.54–1.76 (5H, m, 5CH_2); 3.39–3.40 (1H, m, CH); 6.38 (1H, br. s, NH); 7.99 (1H, br. s, NH); 11.02 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 25.0, 25.6, 33.3 (5 CH_2); 48.8 (CH); 116.4 (q, $^1J_{CF}$ = 286.5, CF_3); 156.5 (C=O); 156.9 (q, $^2J_{CF}$ = 35.5, $CF_3\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm: –73.7 (3F, s, CF_3). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 276 $[M+Na]^+$ (100), 254 $[M+H]^+$ (25). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 252 $[M–H]^–$ (100). Found, *m*/*z*: 253.1028 $[M]^+$. $C_9H_{14}F_3N_3O_2$. Calculated, *m*/*z*: 253.1033.

2-(Difluoroacetyl)-*N*-phenylhydrazinecarboxamide (6e). Yield 410 mg (90%), colorless crystals, mp 172–174°C. IR spectrum, ν, cm^{-1}: 3366 (N–H, br., s), 3300 (N–H, br., s), 3199 (N–H, br., s), 3099 (m), 3039 (m), 2926 (w), 2857 (w), 1946 (w), 1929 (w), 1717 (C=O, vs), 1693 (C=O, vs), 1600 (vs), 1564 (s), 1498 (s), 1444 (s), 1383 (w), 1320 (m), 1254 (m), 1218 (m), 1174 (m), 1151 (w), 1109 (s), 973 (w), 906 (w), 837 (w), 745 (s), 692 (m), 645 (m). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.32 (1H, t, $^1J_{CF}$ = 52.1, CHF_2); 6.96–6.98 (1H, m, H Ph); 7.25–7.27 (2H, m, H Ph); 7.43–7.45 (2H m, H Ph); 8.39 (1H, br. s, NH); 8.89 (1H, br. s, NH); 10.64 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 108.4 (t, $^1J_{CF}$ = 244.5, CHF_2), 118.8, 122.2, 128.8 (C Ph); 139.0 (C-1 Ph); 154.7 (C=O); 161.9 (t, $^2J_{CF}$ = 25.2, $CHF_2\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –126.5 (2F, d, $^2J_{FH}$ = 52.1, CHF_2). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 252 $[M+Na]^+$ (100). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 228 $[M–H]^–$ (100). Found, *m*/*z*: 229.0664 $[M]^+$. $C_9H_9F_2N_3O_2$. Calculated, *m*/*z*: 229.0657.

***N*-Cyclohexyl-2-(difluoroacetyl)hydrazinecarboxamide (6f)**. Yield 442 mg (94%), colorless crystals, mp 178–179°C. IR spectrum, ν, cm^{-1}: 3391 (N–H, br., m), 3351 (N–H, s), 3231 (N–H, s), 3104 (w), 3038 (w), 2935 (s), 2856 (m), 1731 (C=O, s), 1656 (C=O, vs), 1564 (vs), 1464 (w), 1454 (m), 1399 (w), 1370 (w), 1346 (w), 1320 (w), 1277 (w), 1258 (w), 1238 (m), 1190 (w), 1125 (s), 1095 (m), 1076 (m), 978 (w), 967 (w), 893 (w), 845 (w), 824 (w), 773 (w), 670 (w), 639 (w). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.13–1.28 (5H, m) and 1.65–1.76 (5H, m, 5CH_2); 3.31–3.42 (1H, m, CH); 6.26 (1H, t, $^1J_{CF}$ = 53.2, CHF_2); 6.28 (1H, br. s, NH); 7.88 (1H, br. s, NH); 10.44 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 25.0, 25.7, 33.4 (5 CH_2); 48.6 (CH); 108.6 (t, $^1J_{CF}$ = 244.2, CHF_2); 156. 8 (C=O); 162.0 (t, $^2J_{CF}$ = 25.2, $CHF_2\underline{C}$=O). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –126.5 (2F, d, $^2J_{FH}$ = 53.2, CHF_2). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 258 $[M+Na]^+$ (100), 236 $[M+H]^+$ (50). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 234 $[M–H]^–$ (100). Found, *m*/*z*: 235.1133 $[M]^+$. $C_9H_{15}F_2N_3O_2$. Calculated, *m*/*z*: 235.1127.

***N*-Phenyl-2-(trifluoroacetyl)hydrazinecarbothiamide (6g)**. Yield 405 mg (77%), colorless crystals, mp 128–129°C (mp 132.0–133.0°C[15]). IR spectrum, ν, cm^{-1}: 3310 (N–H, br., m), 3158 (2N–H, br., s), 3034 (m), 2891 (w), 1735 (C=O, vs), 1628 (w), 1594 (m), 1538 (s), 1520 (s), 1498 (m), 1487 (m), 1451 (m), 1418 (w), 1362 (w), 1270 (w), 1217 (s), 1166 (vs), 1155 (vs), 1117 (m), 1029 (w), 1005 (w), 935 (w), 898 (w), 745 (m), 697 (m), 638 (w), 615 (w), 526 (m). ^{1}H NMR spectrum, δ, ppm: 7.18–7.46 (5H, m, H Ph); 9.75 (2H, br. s, 2NH); 11.52 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 116.8 (q, $^1J_{CF}$ = 291.7, CF_3); 125.6 (C-1 Ph); 128.7, 139.4 (C Ph); 155.8 (q, $^2J_{CF}$ = 30.0, $CF_3\underline{C}$=O); 179.9 (C=S). ^{19}F NMR spectrum, δ, ppm: –73.6 (s, CF_3). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 286 $[M+Na]^+$ (100), 264 $[M+H]^+$ (75). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 262 $[M–H]^–$ (100). Found, *m*/*z*: 263.0342 $[M]^+$. $C_9H_8F_3N_3OS$. Calculated, *m*/*z*: 263.0334.

***N*-(4-Fluorophenyl)-2-(trifluoroacetyl)hydrazinecarbothiamide (6h)**. Yield 415 mg (74%), colorless crystals, mp 138–139°C. IR spectrum, ν, cm^{-1}: 3238 (3N–H, br., s), 3148 (w), 3063 (m), 1726 (C=O, m), 1616 (w), 1559 (m), 1518 (m), 1416 (w), 1362 (m), 1304 (w), 1249 (w), 1208 (m), 1191 (m), 1170 (m), 1126 (w), 1097 (w), 918 (w), 830 (w), 803 (w), 743 (w), 691 (w). ^{1}H NMR spectrum, δ, ppm: 7.17–7.20 (2H, m, H Ar); 7.45 (2H, m, H Ar); 9.85 (2H, br. s, 2NH); 11.53 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 116.0, 115.5 (C Ar); 116.9 (q, $^1J_{CF}$ = 289.5, CF_3); 136.1 (C-1 Ar); 157.3 (q, $^2J_{CF}$ = 35.7, $F_3C\underline{C}$=O); 158.1 (d, $^1J_{CF}$ = 237.1, C-4 Ar); 178.1 (C=S). ^{19}F NMR spectrum, δ, ppm: –117.3 (1F, s, CF); –73.4 (3F, s, CF_3). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 282 $[M+H]^+$ (100). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 280 $[M–H]^–$ (100). Found, *m*/*z*: 281.0243 $[M]^+$. $C_9H_7F_4N_3OS^+$. Calculated, *m*/*z*: 281.0240.

***N*-(4-Methoxyphenyl)-2-(trifluoroacetyl)hydrazinecarbothiamide (6i)**. Yield 401 mg (68%), colorless crystals, mp 140–141°C. IR spectrum, ν, cm^{-1}: 3214 (3N–H, br., s), 3046 (w), 2966 (w), 2943 (w), 2918 (w), 2845 (w), 1716 (C=O, m), 1613 (w), 1589 (w), 1545 (m), 1516 (m), 1469 (w), 1357 (m), 1302 (w), 1240 (m), 1215 (m), 1187 (m), 1168 (m), 1130 (w), 1101 (w), 1028 (m), 925 (m), 841 (w), 783 (w), 742 (w), 688 (w), 658 (w). ^{1}H NMR spectrum, δ, ppm: 3.77 (3H, s, CH_3); 6.93–6.94 (2H m, H Ar); 7.26–7.27 (2H, m, H Ar); 9.73 (1H, br. s, NH); 9.88 (1H, br. s, NH); 11.47 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 55.7 (OCH_3); 114.0, 132.1 (C Ar); 127.8 (C-1 Ar); 116.4 (q, $^2J_{CF}$ = 286.5, CF_3); 156.8 (q, $^2J_{CF}$ = 35.7, $CF_3\underline{C}$=O); 157.5 (C-4 Ar); 181.9 (C=S). ^{19}F NMR spectrum, δ, ppm: –73.6 (3F, s, CF_3). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 294 $[M+H]^+$ (100). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 292 $[M–H]^–$ (100). Found, *m*/*z*: 293.0437 $[M]^+$. $C_{10}H_{10}F_3N_3OS$. Calculated, *m*/*z*: 293.0440.

2-(Difluoroacetyl)-*N*-phenylhydrazinecarbothiamide (6j). Yield 394 mg (80%), colorless crystals, mp 143–144°C. IR spectrum, ν, cm^{-1}: 3284 (N–H, br., s), 3163 (2N–H, br., vs), 3033 (m), 2886 (w), 1725 (C=O, vs), 1592 (w), 1523 (s), 1500 (s), 1452 (m), 1374 (w), 1335 (w), 1290 (w), 1241 (w), 1201 (m), 1150 (s), 1120 (m), 1090 (s), 1027 (w), 1004 (w), 970 (w), 935 (w), 911 (w), 820 (w), 742 (m), 697 (s), 668 (w), 636 (w), 616 (w). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.30 (1H, t, $^2J_{CF}$ = 50.8, CHF_2); 7.19–7.43 (5H, m, H Ph); 9.79 (2H, br. s, 2NH); 10.91 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 108.6 (t, $^1J_{CF}$ = 244.8, CHF_2); 125.8 (C-1 Ph); 128.7, 139.4 (C Ph); 162.3 (t, $^2J_{CF}$ = 25.0, $CHF_2\underline{C}$=O); 181.4 (C=S). ^{19}F NMR spectrum,

δ, ppm (*J*, Hz): –126.9 (2F, d, $^2J_{FH}$ = 50.8, CHF_2). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 268 $[M+23]^+$ (100), 246 $[M+H]^+$ (50). Found, *m/z*: 245.0312 $[M]^+$. $C_9H_9F_2N_3OS$. Calculated, *m/z*: 245.0429.

Cyclization of thiosemicarbazides 6g–j to 1,3,4-oxadiazoles 7a–d (General method). Method A. Dicyclohexylcarbodiimide (305 mg, 1.48 mmol) was added to a solution of the appropriate thiosemicarbazide **6g–j** (1.0 mmol) in anhydrous THF (~15 ml). The mixture was heated at reflux for 9 h, and then the solvent was evaporated. The obtained crude products were purified by column chromatography (SiO_2, hexane–Et_2O, 6:4).

Method B. Tosyl chloride (229 mg, 1.20 mmol) and Et_3N (222 mg, 2.20 mmol) were added to a solution of thiosemicarbazide **7g** (263 mg, 1.0 mmol) in *N*-methylpyrrolidin-2-one (NMP, 8 ml). The mixture was stirred for 3 h at room temperature, and, afterwards, H_2O (~10 ml) and CH_2Cl_2 (15 ml) were added. The organic layer was separated and the aqueous layer was washed with dichloromethane (2×15 ml). The organic layers were combined, dried over anhydrous Na_2SO_4, and filtered. Then the solvent was evaporated, and the product was purified by column chromatography (SiO_2, hexane–Et_2O, 6:4).

***N*-Phenyl-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (7a)**. Yield 210 mg (92%, method A), 140 mg (61%, method B), colorless crystals, mp 129–131°C (Et_2O–hexane) (mp 125.7–128.5°C[11]). IR spectrum, ν, cm^{-1}: 3186 (w), 3082 (w), 2996 (w), 2944 (w), 2879 (w), 1676 (s), 1603 (m), 1588 (m), 1503 (m), 1407 (w), 1346 (w), 1333 (w), 1231 (w), 1210 (m), 1165 (m), 1142 (m), 1119 (m), 1058 (w), 1032 (w), 968 (w), 890 (w), 729 (w), 749 (m), 688 (w), 627 (w). ^{1}H NMR spectrum, δ, ppm: 7.08–7.10 (1H, m, H Ph); 7.40–7.42 (2H, m, H Ph); 7.56–7.57 (2H, m, H Ph); 11.1 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 116.8 (q, $^1J_{CF}$ = 268.1, CF_3); 118.2, 123.4, 129.7 (C Ph); 138.1 (C-1 Ph); 147.9 (q, $^2J_{CF}$ = 42.9, $\underline{C}CF_3$); 161.7 (C-2). ^{19}F NMR spectrum, δ, ppm: –64.6 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 230 $[M+H]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 228 $[M–H]^–$ (100). Found, *m/z*: 229.0459 $[M]^+$. $C_9H_6F_3N_3O$. Calculated, *m/z*: 229.0457.

***N*-(4-Fluorophenyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (7b)**. Yield 219 mg (95%, method A), colorless crystals, mp 147–149°C (Et_2O–hexane). IR spectrum, ν, cm^{-1}: 3337 (w), 3191 (w), 3074 (w), 2998 (w), 2945 (w), 2874 (w), 1679 (s), 1668 (s), 1607 (m), 1596 (m), 1511 (vs), 1441 (w), 1387 (m), 1328 (m), 1232 (s), 1164 (m), 1116 (s), 1057 (m), 968 (w), 830 (m), 750 (m). ^{1}H NMR spectrum, δ, ppm: 7.24–7.27 (2H, m, H Ar); 7.58–7.61 (2H, m, H Ar); 11.11 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 116.8 (q, $^1J_{CF}$ = 268.0, CF_3); 116.2, 116.3, 119.8, 119.9 (C Ar); 134.5 (C-1 Ar); 147.9 (q, $^2J_{CF}$ = 43.0, $\underline{C}CF_3$), 158.4 (d, $^1J_{CF}$ = 238.0, C-4 Ar), 161.7 ($\underline{C}$-2). ^{19}F NMR spectrum, δ, ppm: –120.2 (1F, s, CF); –64.5 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 248 $[M+H]^+$ (100). Found, *m/z*: 247.0369 $[M]^+$. $C_9H_5F_4N_3O$. Calculated, *m/z*: 247.0363.

***N*-(4-Methoxyphenyl)-5-(trifluoromethyl)-1,3,4-oxadiazol-2-amine (7c)**. Yield 193 mg (80%, method A), colorless crystals, mp 153–154°C (Et_2O–hexane). IR spectrum, ν, cm^{-1}: 3281 (m), 3131 (w), 3061 (w), 3008 (w), 2954 (w), 2920 (w), 2836 (w), 1632 (vs), 1586 (s), 1540 (m), 1518 (s), 1457 (m), 1426 (m), 1383 (s), 1229 (s), 1171 (s), 1133 (s), 1060 (m), 1034 (m), 987 (w), 831 (w). ^{1}H NMR spectrum, δ, ppm: 3.75 (3H, s, OCH_3); 6.98–6.99 (2H, m, H Ar); 7.48–7.49 (2H, m, H Ar); 10.85 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 55.7 (OCH_3); 114.9, 119.9 (C Ar); 116.8 (q, $^1J_{CF}$ = 267.9, CF_3); 131.2 (C-1 Ar); 147.6 (q, $^2J_{CF}$ = 42.7, $\underline{C}CF_3$); 155.7 (C-4 Ar); 162.0 (C-2). ^{19}F NMR spectrum, δ, ppm: –64.5 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 260 $[M+H]^+$ (100). Found, *m/z*: 259.0564 $[M]^+$. $C_{10}H_8F_3N_3O_2$. Calculated, *m/z*: 259.0563.

5-(Difluoromethyl)-*N*-phenyl-1,3,4-oxadiazol-2-amine (7d). Yield 160 mg (82%, method A), colorless crystals, mp 157–158°C (Et_2O–hexane). IR spectrum, ν, cm^{-1}: 3329 (w), 3252 (w), 3189 (w), 3073 (w), 3023 (m), 2955 (m), 2882 (m), 2748 (w), 2660 (w), 1668 (s), 1602 (s), 1589 (s), 1504 (s), 1479 (m), 1394 (w), 1375 (m), 1355 (m), 1292 (m), 1230 (w), 1108 (m), 1050 (s), 987 (m), 885 (w), 838 (m), 748 (s), 730 (m), 686 (m). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.07 (1H, t, $^2J_{HF}$ = 7.2, CHF_2); 7.38–7.40 (3H, m, H Ph); 7.57–7.59 (2H, m, H Ph); 10.87 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 107.1; (t, $^1J_{CF}$ = 235.2, CHF_2); 117.9, 123.0, 129.6 (C Ph); 138.5 (C-1 Ph); 153.2 (t, $^2J_{CF}$ = 28.6, $\underline{C}CHF_2$); 161.7 (C-2). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –119.9 (2F, d, $^2J_{FH}$ = 51.4, CHF_2). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 274 $[M+Na]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 250 $[M–H]^–$ (100). Found, *m/z*: 211.0561 $[M]^+$. $C_9H_7F_2N_3O$. Calculated, *m/z*: 211.0552.

Cyclization of thiosemicarbazides 6g,i to 1,2,4-triazole-3-thiones 8a,b (General method). An aqueous solution of NaOH (2%, ~2 ml) and an appropriate thiosemicarbazide **6g**,**i** were heated at reflux for 3 h. Next, the reaction mixture was neutralized with acetic acid, the product was extracted with AcOEt (3×25 ml), and the combined organic layers were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude products were purified by column chromatograpy (SiO_2, hexane–AcOEt, 6:4).

4-Phenyl-5-(trifluoromethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8a).[16] Yield 42 mg (34%), pale-yellow crystals, mp 170–172°C. IR spectrum, ν, cm^{-1}: 3145 (m), 3091 (m), 3033 (m), 2911 (m), 2853 (m), 2741 (m), 1597 (m), 1498 (s), 1474 (s), 1446 (s), 1458 (s), 1344 (w), 1277 (s), 1238 (s), 1219 (s), 1176 (s), 1149 (s), 1093 (m), 1036 (m), 984 (m), 775 (m). ^{1}H NMR spectrum, δ, ppm: 7.50–7.51 (2H, m, H Ph); 7.59–7.60 (3H, m, H Ph); 14.69 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 117.1 (q, $^1J_{CF}$ = 269.1, CF_3); 128.9, 129.9, 130.8 (C Ph); 132.9 (C-1 Ph); 140.7 (q, $^2J_{CF}$ = 39.9, $\underline{C}CF_3$), 171.3 (C=S). ^{19}F NMR spectrum, δ, ppm: – 62.7 (3F, s, CF_3). Mass spectrum (ESI+), *m/z* (I_{rel}, %): 246 $[M+H]^+$ (100). Mass spectrum (ESI–), *m/z* (I_{rel}, %): 244 $[M–H]^–$ (100). Found, *m/z*: 245.0234 $[M]^+$. $C_9H_6F_3N_3S$. Calculated, *m/z*: 245.0229.

5-Difluoromethyl-4-phenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (8b).[16] Yield 41 mg (36%), colorless crystals, mp 187–189°C. IR spectrum, ν , cm^{-1}: 3249 (w), 3149 (w), 3089 (m), 3037 (m), 2999 (w), 2902 (m), 2848 (m), 2745 (m), 1594 (w), 1541 (m), 1497 (s), 1487 (s), 1435 (m), 1340 (w), 1323 (m), 1270 (s), 1229 (m), 1193 (w), 1176

(w), 1126 (m), 1077 (s), 1056 (s), 1015 (w), 823 (m), 776 (m), 738 (w), 724 (w), 690 (m). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.04 (1H, t, $^2J_{HF}$ = 51.6, CHF_2); 7.46–7.47 (2H, m, H Ph); 7.57–7.62 (3H, m, H Ph); 14.41 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 107.8 (t, $^1J_{CF}$ = 235.9, CHF_2); 128.7, 129.8, 130.4 (C Ph); 133.3 (C-1 Ph); 144.9 (t, $^2J_{CF}$ = 27.9, $CHF_2\underline{C}$); 170.5 (C=S). ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –119.2 (2F, d, $^2J_{FH}$ = 50.8, CHF_2). Mass spectrum (ESI+), *m*/*z* (I_{rel}, %): 228 $[M+H]^+$ (100). Mass spectrum (ESI–), *m*/*z* (I_{rel}, %): 226 $[M–H]^-$ (100). Found, *m*/*z*: 227.0329 $[M]^+$. $C_9H_7F_2N_3S$. Calculated, *m*/*z*: 227.0323.

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