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Dedicated to Full Member of the Russian Academy of Sciences O.N. Chupakhin on his 70th Anniversary

Synthesis of 7-Alkyl(aryl)-6-alkoxycarbonyl-5-fluoroalkyl-1,2,4-tri(tetr)azolo[1,5-*a*]pyrimidines

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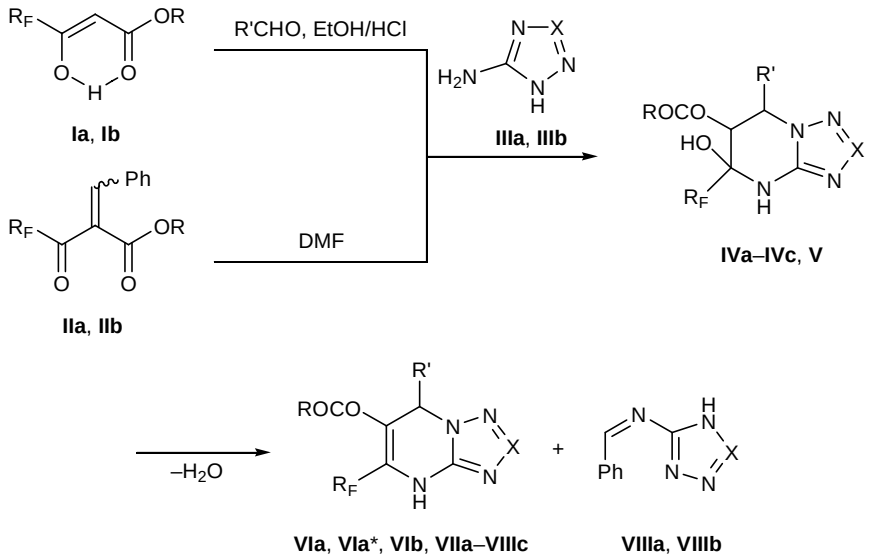
Abstract—Fluorinated 3-oxo esters react with aldehydes and 3-amino-1,2,4-triazoles and 5-aminotetrazoles to give, respectively, 7-alkyl(aryl)-6-alkoxycarbonyl-5-fluoroalkyl-1,2,4-triazolo[1,5-*a*]pyrimidines and -tetrazolo[1,5-*a*]pyrimidines. The same heterocyclic products can be obtained by reaction of 2-benzylidene-2-fluoroacyl esters with the corresponding aminoazoles.

1,2,3,4-Tetrahydropyrimidin-2-one derivatives attract interest as potential biologically active compounds. Specifically, some 1,2,3,4-tetrahydropyrimidin-2-ones which are isosteric to known drugs of the Nifedipine series were shown to exhibit a strong antihypertensive effect [1]. Tetrahydropyrimidin-2-ones can be prepared by Biginelli's three-component condensation of 3-oxo esters, aldehydes, and urea derivatives [2] or via Etwal's modification through 2-arylmethylene-3-oxo esters [3]. Fluoroalkyl-containing 1,3-dicarbonyl compounds react with benzaldehyde and urea (or thiourea) to afford hexahydropyrimidin-2-ones [4, 5] instead of the expected tetrahydropyrimidin-2-ones. We have found no published data on reactions of aminoazoles with aldehydes and fluorinated 3-oxo esters, while nonfluorinated analogs are widely used for the synthesis of fused azolopyrimidines [6–9].

In the present work we studied synthetic routes to tri- and tetrazolo[1,5-*a*]pyrimidines on the basis of fluoroalkyl-containing 3-oxo esters and their derivatives according to Biginelli's reaction. We have found that reactions of fluoroalkyl-containing 3-oxo esters **Ia** and **Ib** with aldehydes and 3-amino-1,2,4-triazole (**IIIa**) or 5-aminotetrazole (**IIIb**) lead to formation of the corresponding tri- and tetrazolopyrimidines **IVa**–**IVc**, **V**, **VIa**, **VIb**, and **VIIa**–**VIIc** (Scheme 1). As aldehyde component we used benzaldehyde, *p*-methoxybenzaldehyde, and acetaldehyde. Heterocycles **VIa**, **VIb**, **VIIa**, and **VIIb** were also synthesized by cyclocondensation of 2-benzylidene-2-fluoroacyl esters **IIa** and **IIb** with aminoazoles **IIIa** and **IIIb**; in these cases, the yields were greater. Lower yields of the target products in the three-component condensation are explained by greater contribution of various side processes. For example, we isolated *N*-benzylideneamino derivatives **VIIIa** and **VIIIb** as by-products which were formed by condensation of aldehydes with aminoazoles.

Unlike transformations of fluorinated 1,3-dicarbonyl compounds in reactions with urea and thiourea [4, 5], the major products isolated in the reactions of 3-oxo esters **Ia** and **Ib** with aminoazoles **IIIa** and **IIIb** were substituted dihydrotri- and -tetrazolopyrimidines **VIa**, **VIb**, and **VIIa**–**VIIc**. However, in some cases we succeeded in obtaining tetrahydroazolopyrimidines **IVa** and **IVb** which contained a hydroxy group in the geminal position with respect to the fluorinated substituent. Tetrahydroazolopyrimidines **IVc** and **V** were the only products isolated in the condensation of 3-oxo ester **Ia** with acetaldehyde and amines **IIIa** and **IIIb**. Heating of compounds **IVa** and **IVb** in boiling toluene in the presence of *p*-toluenesulfonic acid with removal of the liberated water by azeotropic

Scheme 1.

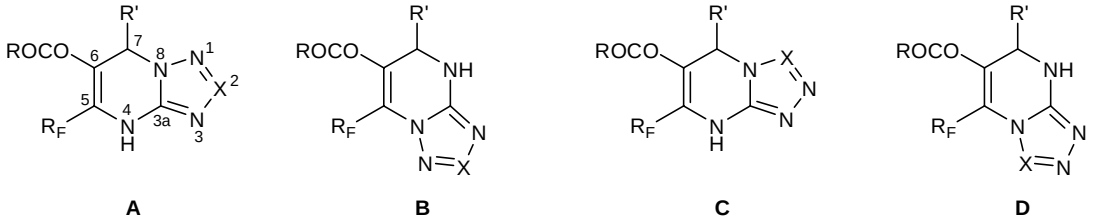


Ia, **IIa**, **IVa**–**IVc**, **V**, **VIa**, **VIa***, **VIIa**, **VIIc**, R_F = CF_3, R = Et; **Ib**, **IIb**, **VIb**, **VIIb**, R_F = $H(CF_2)_2$, R = Me; **IVa**, **VIa**, **VIa***, **VIb**, **VIIa**, **VIIb**, R' = Ph; **IVc**, **V**, R' = Me; **IVb**, **VIIc**, R' = 4-$MeOC_6H_4$; **IIIa**, **V**, **VIa**, **VIa***, **VIb**, **VIIIa**, X = CH; **IIIb**, **IVa**–**IVc**, **VIIa**–**VIIc**, **VIIIb**, X = N.

distillation afforded dihydrotetrazolopyrimidines **VIIa** and **VIIc**.

Theoretically, the above cyclocondensations with 5-aminotetrazole could lead to formation of two regioisomeric heterocyclic products **A** and **B** (X = N), and from 3-amino-1,2,4-triazole (**IIIa**), four isomers **A**–**D** (X = CH) could be obtained. These structures cannot be distinguished on the basis of the ^{1}H and ^{19}F NMR and IR spectra. Isotopically labeled compounds are widely used in the determination of molecular structure [10]. We have synthesized [^{15}N]-labeled triazolopyrimidine **VIa*** from 3-oxo ester **Ia**, benzaldehyde, and 1-[^{15}N]-3-amino-1,2,4-triazole (**IIIa***) (^{15}N concentration ~43%). In the ^{1}H NMR spectrum of compound **VIa***, the 2-H signal appeared as a doublet at δ 7.78 ppm, $J(^1H–^{15}N)$ = 15.3 Hz, indicating the presence of ^{15}N isotope. The intensity ratio of the 2-H resonance signals corresponding to the labeled (doublet) and unlabeled (singlet) molecules was consistent with the initial ^{15}N concentration (~ 43%) in triazolopyrimidine **VIa***. The structure of **VIa*** was established by ^{13}C NMR spectroscopy. The C^7 signal appeared in the spectrum as a doublet at δ_C 60.06 ppm due to coupling with ^{15}N, $^2J(^{13}C–^{15}N)$ = 4.9 Hz, which can occur only in the [1,5-*a*]-fused isomer (**A**). Comparison of the ^{19}F and ^{13}C NMR data for **VIa**, **VIb**, and **VIIa** led us to conclude that these compounds also have structure **A**.

Tetrahydrotri- and -tetrazolo[1,5-*a*]pyrimidines **IVa**–**IVc** and **V** possess three asymmetric carbon atoms; therefore, four diastereoisomers (and, in addition, four respective enantiomers) are possible. According to the NMR data, compounds **IVa** and **IVb** having aryl substituents on C^7 exist as a single diastereoisomer. Taking into account high conformational energies of the phenyl [ΔG(Ph) = 12.1 kJ/mol] and ethoxycarbonyl groups [ΔG(COOEt) = 5.3 kJ/mol], the most favorable conformation is that in which the above groups occupy equatorial positions [11]. This also follows from the coupling constant $J_{6,7}$ = 11.3–11.8 Hz, which corresponds to axial orientation of the 6-H and 7-H protons [12]. The conformational energies of CF_3



[$\Delta G(CF_3)$ = 8.8 kJ/mol] and OH groups [ΔG(OH) = 2.2 kJ/mol] in substituted cyclohexanones [11] suggest preferential equatorial orientation of the trifluoromethyl group. Moreover, in keeping with the X-ray diffraction data, just the same arrangement of the trifluoromethyl and hydroxy groups is typical of ethyl 2-oxo-4-phenyl-6-trifluoromethyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate [4] and dimethyl 2,6-dihydroxy-2,6-bis(1,1,2,2-tetrafluoroethyl)-4-phenyltetrahydropyran-3,5-dicarboxylate [13].

The ^{1}H and ^{19}F NMR spectra of 7-methyl-substituted tetrahydroazolo[1,5-*a*]pyrimidines **IVc** and **V** contained a double set of signals, indicating that they exist in solution (DMSO-d_6) as two diastereoisomers **E** and **E'** [ratio 3:2 (**IVc**) and 9:1 (**V**)]. The 6-H and 7-H signals of the major diastereoisomer (**E**) appear in the ^{1}H NMR spectra of **IVc** and **V** as doublets with J = 11.3 Hz, corresponding to diaxial orientation of these protons. Analogous signals from the minor diastereoisomer (**E'**) are also split into doublets but with a smaller coupling constant, J = 4.5–4.6 Hz, which indicates than one proton is equatorial while the other is axial [12]. In addition, the 6-H proton in isomers **E'** is coupled with the OH proton through four bonds (^4J = 1.2–1.3 Hz, *W*-coupling). This means that the ethoxycarbonyl group in **E'** occupies axial position and that the neighboring 6-H proton is equatorial. Comparison of the conformational energies of the ethoxycarbonyl and methyl groups [ΔG(Me) = 7.1 kJ/mol] also suggests preferential change of orientation of the carbonyl-containing substituent [11].

Thus our results showed that the cyclocondensation of fluorinated 3-oxo esters **I** and aldehydes (or 2-benzylidene-2-fluoroacyl esters **II**) with aminoazoles **IIIa** and **IIIb** is regioselective and that the resulting bicyclic compounds belong to a single heterocyclic system.

EXPERIMENTAL

The IR spectra were recorded in the range from 400 to 4000 cm^{-1} on a Perkin–Elmer Spectrum-1 Fourier spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Bruker DRX-400 spectrometer at 400 MHz. The ^{19}F NMR spectra were obtained on Tesla BS-587A (75.3 MHz) and Bruker DRX-400 (376 MHz) instruments using C_6F_6 as reference. The ^{13}C NMR spectra were run on a Bruker DRX-400 spectrometer (100 MHz, TMS). DMSO-d_6 was used as solvent. Elemental analysis was performed on a Carlo Erba CHNS-O EA 1108 analyzer. The ^{13}C NMR spectra of compounds **VIa***, **VIb**, and **VIIa** are given in table.

2-Benzylidene-2-fluoroacyl esters **IIa** and **IIb** were synthesized by the procedures reported in [13, 14], and labeled 1-[^{15}N]-3-amino-1,2,4-triazole was prepared as described in [10].

Azolo[1,5-*a*]pyrimidines IV–VII (*general procedure***).** *a*. A mixture of 0.01 mol of 3-oxo ester **I**, 0.01 mol of benzaldehyde, *p*-methoxybenzaldehyde, or acetaldehyde, and 0.01 mol of 3-amino-1,2,4-triazole or 5-aminotetrazole in 20 ml of ethanol containing a catalytic amount of hydrochloric acid was heated for 12 h under reflux. The mixture was evaporated, and the precipitate was washed with hot water and recrystallized from ethanol.

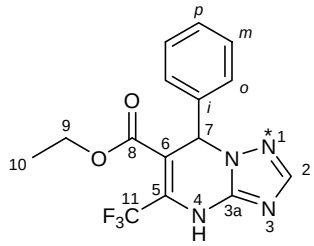
b. A mixture of 0.01 mol of 2-benzylidene-3-oxo ester **II** and 0.01 mol of 3-amino-1,2,4-triazole, 5-aminotetrazole, or 1-[^{15}N]-3-amino-1,2,4-triazole (43% of ^{15}N) in 10 ml of DMF was stirred for 12–14 h at 70°C. The mixture was poured into cold water, and the precipitate was filtered off, washed with hot water, and recrystallized from ethanol.

c. *p*-Toluenesulfonic acid, 0.05 g, was added to a solution of 0.01 mol of azolopyrimidine **IVa** or **IVb** in 100 ml of benzene, and the mixture was heated for 8 h with simultaneous removal of water as azeotrope with benzene. The solution was filtered while hot, the filtrate was evaporated, and the precipitate was recrystallized from ethanol.

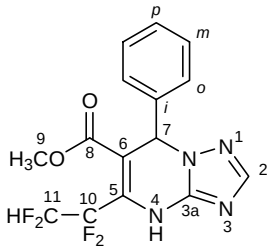
Ethyl 5-hydroxy-7-phenyl-5-trifluoromethyl-4,5,6,7-tetrahydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate (IVa). Yield (*a*) 1.68 g (47%), mp 201–202°C. IR spectrum, ν, cm^{-1}: 3455, 3174 (NH, OH); 1720 (C=O); 1624, 1551 (C=C, C=N); 1080–1204 (C–F). ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.57 d (1H, 6-H, J = 11.8 Hz), 3.88 d.q and 3.86 d.q (1H each, $OC\mathbf{H}_2CH_3$, J = 10.8, 7.1 Hz), 5.63 d (1H, 7-H, J = 11.8 Hz), 7.40–7.47 m (5H, C_6H_5), 7.99 s (1H, NH), 9.57 s (1H, OH). ^{19}F NMR spectrum, δ_F, ppm: 82.71 s (CF_3). Found, %: C 46.89; H 3.93; F 15.97; N 19.50. $C_{14}H_{14}F_3N_5O_3$. Calculated, %: C 47.07; H 3.95; F 15.95; N 19.60.

Ethyl 5-hydroxy-7-(4-methoxyphenyl)-5-trifluoromethyl-4,5,6,7-tetrahydrotetrazolo[1,5-*a*]-pyrimidine-6-carboxylate (IVb). Yield (*a*) 2.05 g (53%), mp 179–180°C. IR spectrum, ν, cm^{-1}: 3451, 3175 (NH, OH); 1713 (C=O); 1613, 1518 (C=C, C=N); 1152–1206 (C–F). ^{1}H NMR spectrum, δ, ppm:

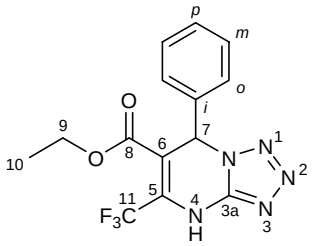
^{13}C NMR spectra of azolo[1,5-*a*]pyrimidines **VIa***, **VIb**, and **VIIa** in DMSO-d_6



VIa*



VIb



VIIa

Atom	Chemical shifts δ_C, ppm		
	VIa*	**VIb**	**VIIa**
C^2	150.17 br.s	150.44 br.s	–
C^{3a}	146.62 br.s	146.65	148.40 br.s
C^5	131.18 br.q (J_{CF} = 34.2 Hz)	133.96 br.t (J_{CF} = 28.0 Hz)	130.14 br.q (J_{CF} = 36.3 Hz)
C^6	104.42	103.86	105.90 q (J_{CF} = 2.5 Hz)
C^7	60.06 (J_{CH} = 4.9 Hz)	59.90	61.32
C^8	162.98	164.11	162.51 br.s
C^9	60.93	52.15	59.54
C^{10}	13.36	112.76 t.t (J_{CF} = 255.7, 27.6 Hz)	13.32
C^{11}	119.94 q (J_{CF} = 276.1 Hz)	109.64 t.t (J_{CF} = 251.4, 30.2 Hz)	119.76 q (J_{CF} = 276.1 Hz)
C^i	139.33	139.75	137.93
C^o	127.22	126.90	127.70
C^m	128.66	128.76	129.31
C^p	128.66	128.63	128.97

0.90 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.57 d (1H, 6-H, J = 11.8 Hz), 3.74 s (3H, OCH_3), 3.89 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 5.58 d (1H, 7-H, J = 11.8 Hz), 6.93–6.97 m (4H, C_6H_4), 7.97 s (1H, NH), 9.54 s (1H, OH). ^{19}F NMR spectrum, δ_F, ppm: 82.71 s (CF_3). Found, %: C 46.45; H 4.17; F 14.69; N 18.12. $C_{15}H_{16}F_3N_5O_4$. Calculated, %: C 46.52; H 4.16; F 14.72; N 18.08.

Ethyl 5-hydroxy-7-methyl-5-trifluoromethyl-4,5,6,7-tetrahydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate (IVc). Yield (*a*) 1.26 g (43%), mp 156–158°C. IR spectrum, ν, cm^{-1}: 3225, 3193 (NH, OH); 1740 (C=O); 1617, 1539 (C=C, C=N); 1087–1206 (C–F). ^{1}H NMR spectrum, δ, ppm (mixture of stereoisomers **E** and **E'**, 3:2): **E**: 1.21 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 1.61 d (3H, CH_3, J = 6.3 Hz), 3.20 d (1H, 6-H, J = 11.3 Hz), 4.18 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.63 d.q (1H, 7-H, J = 11.3, 6.3 Hz), 7.79 s (1H, NH), 9.38 s (1H, OH); **E'**: 1.07 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 1.61 d (3H, CH_3, J = 6.3 Hz), 3.30 d.d (1H, 6-H, J = 4.5, 1.3 Hz), 4.03 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.39 d.q (1H, 7-H, J = 6.3, 4.5 Hz), 7.59 s (1H, NH), 8.80 br.d (1H, OH, J = 1.3 Hz). ^{19}F NMR spectrum, δ_F, ppm (mixture of stereoisomers **E** and **E'**, 3:2): **E**: 82.51 s (CF_3); **E'**: 82.49 s (CF_3). Found, %: C 36.65; H 4.12; F 19.28; N 23.70. $C_9H_{12}F_3N_5O_3$. Calculated, %: C 36.62; H 4.10; F 19.31; N 23.72.

Ethyl 5-hydroxy-7-methyl-5-trifluoromethyl-4,5,6,7-tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (V). Yield (*a*) 2.00 g (68%), mp 183–185°C. IR spectrum, ν, cm^{-1}: 3221, 3130, 3103 (NH, OH); 1746 (C=O); 1621, 1557 (C=N); 1096–1195 (C–F). ^{1}H NMR spectrum, δ, ppm (mixture of stereoisomers **E** and **E'**, 9:1): **E**: 1.20 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 1.46 d (3H, CH_3, J = 6.4 Hz), 3.01 d (1H, 6-H, J = 11.3 Hz), 4.16 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.39 d.q (1H, 7-H, J = 11.3, 6.4 Hz), 7.55 s (1H, NH), 7.56 s (1H, 2-H), 8.69 s (1H, OH); **E'**: 1.05 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 1.44 d (3H, CH_3, J = 6.4 Hz), 3.17 d.d (1H, 6-H, J = 4.6, 1.2 Hz), 4.02 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.39 d.q (1H, 7-H, J = 6.4, 4.6 Hz), 7.50 s (1H, 2-H), 7.59 s (1H, NH), 8.80 br.d

(1H, OH, J = 1.2 Hz). ^{19}F NMR spectrum, δ_F, ppm (mixture of stereoisomers **E** and **E'**, 9:1): **E**: 82.33 s (CF_3); **E'**: 82.29 s (CF_3). Found, %: C 40.89; H 4.38; F 19.38; N 19.13. $C_{10}H_{13}F_3N_4O_3$. Calculated, %: C 40.82; H 4.45; F 19.37;N 19.04.

Ethyl 7-phenyl-5-trifluoromethyl-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (VIa). Yield (*a*) 1.86 g (55%), (*b*) 2.33 g (69%); mp 157–159°C. IR spectrum, ν, cm^{-1}: 3200 (NH); 1710 (C=O); 1600, 1559 (C=C, C=N); 1100–1200 (C–F). ^{1}H NMR spectrum, δ, ppm: 1.08 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 4.01 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.36 q (1H, 7-H, J_{HF} = 1.4 Hz), 7.22–7.36 m (5H, C_6H_5), 7.61 s (1H, 2-H), 11.44 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 99.64 d (CF_3, J_{FH} = 1.4 Hz). Found, %: C 53.19; H 3.79; F 16.81; N 16.66. $C_{15}H_{13}F_3N_4O_2$. Calculated, %: C 53.26; H 3.87; F 16.84; N 16.56.

Ethyl 7-phenyl-5-trifluoromethyl-4,7-dihydro-[1-^{15}N][1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (VIa*). Yield (*b*) 2.03 g (60%), mp 155–157°C. IR spectrum, ν, cm^{-1}: 3203 (NH); 1711 (C=O); 1600, 1558 (C=C, C=N); 1100–1200 (C–F). ^{1}H NMR spectrum, δ, ppm: 1.01 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.99 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.43 q (1H, 7-H, J_{HF} = 1.4 Hz), 7.23–7.76 m (4H, C_6H_5), 7.78 d [1H, 2-H, $J(^1H–^{15}N)$ = 15.3 Hz], 11.65 b.s (1H, NH).

Methyl 7-phenyl-5-(1,1,2,2-tetrafluoroethyl)-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (VIb). Yield (*a*) 1.60 g (45%), (*b*) 2.24 g (63%); mp 197–199°C. IR spectrum, ν, cm^{-1}: 3462, 1624 (NH); 1712 (C=O); 1580, 1570, 1545 (C=C, C=N); 1115–1205 (C–F). ^{1}H NMR spectrum, δ, ppm: 3.58 s (3H, OCH_3), 6.39 t (1H, 7-H, J_{HF} = 1.4 Hz), 6.87 d.d.d.d [1H, $H(CF_2)_2$, J_{HF} = 53.0, 53.5, 6.7, 5.0 Hz], 7.21–7.36 m (5H, C_6H_5), 7.61 s (1H, 2-H), 11.45 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 25.69 m (2F, HCF_2, *AB* system, Δ_{AB} = 0.26 ppm, J_{AB} = 300.0, J_{FH} = 53.0, 53.5, 6.7, 5.0 Hz), 44.21 br.d (1F, CF_2, J_{FF} = 263.0 Hz), 47.35 br.d (1F, CF_2, J_{FF} = 263.0 Hz). Found, %: C 50.28; H 3.39; F 20.98; N 15.79. $C_{15}H_{12}F_4N_4O_2$. Calculated, %: C 50.57; H 3.36; F 21.32; N 15.73.

Ethyl 7-phenyl-5-trifluoromethyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate (VIIa). Yield (*a*) 1.69 g (50%), (*b*) 2.47 g (73%), (*c*) 3.29 g (97%); mp 194–196°C. IR spectrum, ν, cm^{-1}: 3462, 3173 (NH); 1712 (C=O); 1624, 1549 (C=C, C=N); 1070–1235 (C–F). ^{1}H NMR spectrum, δ, ppm: 0.99 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 4.00 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.82 q (1H, 7-H, J_{HF} = 1.5 Hz), 7.36–7.44 m (5H, C_6H_5), 12.01 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 100.49 d (CF_3, J_{FH} = 1.5 Hz). Found, %: C 49.63; H 3.72; F 16.68; N 20.81. $C_{14}H_{12}F_3N_5O_2$. Calculated, %: C 49.57; H 3.57; F 16.79; N 20.64.

Methyl 7-phenyl-5-(1,1,2,2-tetrafluoroethyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate (VIIb). Yield (*a*) 1.75 g (49%), (*b*) 2.00 g (56%), (*c*) 3.50 g (98%); mp 185–186°C. IR spectrum, ν, cm^{-1}: 3430, 1590 (NH); 1720 (C=O); 1590, 1540 (C=C, C=N); 1060–1200 (C–F). ^{1}H NMR spectrum, δ, ppm: 3.57 s (3H, CH_3), 6.77 s (1H, 7-H), 6.87 t.d.d [1H, $H(CF_2)_2$, J_{HF} = 53, 7.4, 4.0 Hz], 7.29–7.41 m (5H, C_6H_5), 11.84 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 26.05 d.t (2F, HCF_2, J_{FH} = 53, J_{FF} = 8.7 Hz), 46.04 m (2F, CF_2, *AB* system, Δ_{AB} = 4.15 ppm, J_{AB} = 267.5, J_{FF} = 8.7, J_{FH} = 7.4 Hz). Found, %: C 46.88; H 3.16; F 20.97; N 19.37. $C_{14}H_{11}F_4N_5O_2$. Calculated, %: C 47.07; H 3.10; F 21.27; N 19.60.

Ethyl 7-(4-methoxyphenyl)-5-trifluoromethyl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-6-carboxylate (VIIc). Yield (*a*) 1.47 g (40%), mp 184–186°C. IR spectrum, ν, cm^{-1}: 3452 (NH); 1718 (C=O); 1615, 1518 (C=C, C=N); 1080–1206 (C–F). ^{1}H NMR spectrum, δ, ppm: 1.02 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.77 s (3H, OCH_3), 4.00 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.75 q (1H, 7-H, J_{HF} = 1.5 Hz), 7.25–7.41 m (4H, C_6H_4), 11.94 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 100.48 d (CF_3, J_{FH} = 1.5 Hz). Found, %: C 48.72; H 3.80; F 15.39; N 18.98. $C_{14}H_{12}F_3N_5O_2$. Calculated, %: C 48.78; H 3.82; F 15.43; N 18.96.

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