A Convenient Approach to 4,7-Dihydrotetrazolo [5,1-*c*][1,2,4]triazine Synthesis

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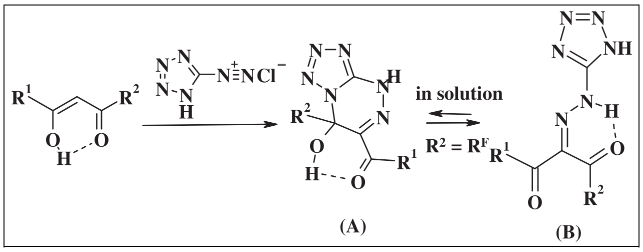

Azo coupling of 1,3-dicarbonyl compounds with tetrazolyl-5-diazonium chloride is used to develop a convenient one-step procedure for the synthesis of 4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazines. In contrast to nonfluorinated analogs, 7-hydroxy-7-polyfluoroalkyl-4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazines undergo a ring-chain isomerism resulting from the cleavage at the C7-N7a bond. A distinctive feature of nonfluorinated 4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazines is the possibility to dehydration, which is accompanied by an azide rearrangement due to the tetrazole ring cleavage with the formation of tetrazolo[1,5-*b*][1,2,4]triazines.

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INTRODUCTION

Tetrazolotriazine systems have recently attracted great attention due to the ability of exhibiting biologically active properties. As a case in point, fused 1,2,4-triazine derivatives have potential application as herbicides or plant growth regulators for the control of undesired plants or vegetation [1]. Tetrazolotriazines have isosteric structure similar to purines, which are directly responsible for breaking metabolism and inhibiting protein biosynthesis.

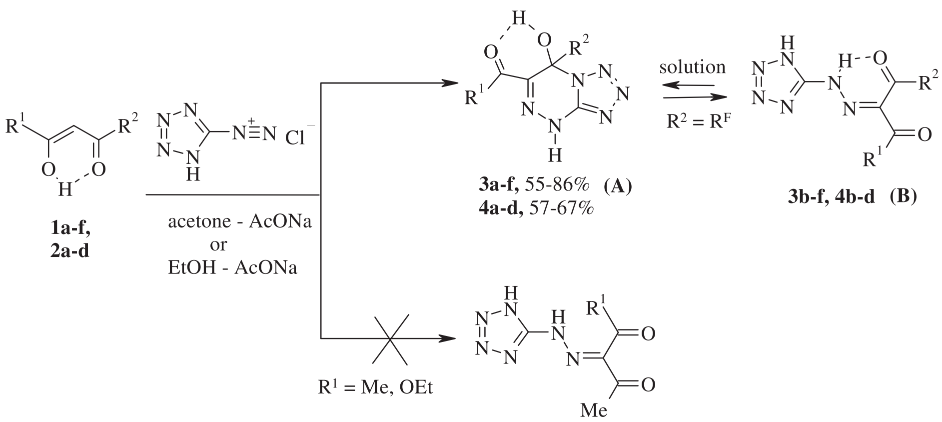
Five such ring systems of fused tetrazolo-[1,2,4] and [1,3,5]triazine systems including tetrazolo[1,5-*b*][1,2,4] triazine, tetrazolo[5,1-*c*][1,2,4]triazine, tetrazolo[5,1-*f*] [1,2,4]triazine, tetrazolo[1,5-*d*][1,2,4]triazine, and tetrazolo[1,5-*a*][1,3,5]triazine have been described [2–4]. The favored approach for their synthesis has so far been based on intramolecular cyclization of appropriate azidotriazines which were mainly obtained from hydrazine derivatives by nitrous acid or by nucleophilic displacement of a halogen-substituted compound by sodium azide [4].

Despite extensive studies on tetrazolo[1,5-*b*][1,2,4]triazines and other systems [5–10], there is still a lack of information on the synthesis of tetrazolo[5,1-*c*][1,2,4]triazines, which is generally limited to the preparation of condensed heterocycles with naphthalene [11] and benzene [12–15]. Attempts to generate such initial bicyclic systems have had little success since the reaction of sodium (5-mercaptotetrazol-1-yl)acetate and *N*-arylhydrazonoyl chloride followed by intramolecular cyclization gives 4,7-dihydroterazolo[5,1-*c*][1,2,4]triazines in medium yields [16]. Ethyl 7-aminotetrazolo[5,1-*c*][1,2,4] triazine-6-carboxylate is formed *via* cyclization of 2-cyano-2-(tetrazol-5-ylhydrazono)acetate [17], and 6-methyltetrazolo [5,1-*c*][1,2,4]triazin-7(4*H*)-ones are obtained from hydrazono derivatives [18].

Moreover, the reactions of tetrazolyl diazonium salts with CH-active methylene compounds produce tetrazolo [1,5-*b*][1,2,4]triazines rather than tetrazolo[5,1-*c*][1,2,4] triazines [19–22] due to the cleavage of a tetrazole ring *via* azide derivatives.

Our previous study showed the structure of hetaryl component to exert determinative influence on the result of azo coupling between fluoroalkyl-containing 1,3-dicarbonyl compounds and hetaryldiazonium salts. Thus, the reactions of polyfluoroalkyl-containing 1,3-diketones and 3-oxo esters with hetaryldiazonium chlorides having the fragment NH in α-position (1,2,4-triazolyl-3-, 4-ethoxycarbonylpyrazolyl-3-, and 4-ethoxycarbonylimidazolyl-5-diazonium chlorides) [23–25] gave the stable 4-hydroxy-4-polyfluoroalkyl-1,4-dihydroazolo[5,1-*c*][1,2,4]triazines rather than expected open-chain 2-hetarylhydrazono-1,3-dicarbonyl compounds. At the same time, antipyrinyldiazonium salt in these reactions resulted in 2-antipyrinylhydrazono-1,3-dicarbonyl compounds [26]. We also carried out azo coupling of fluoroalkyl-containing 1,3-diketones **1** and 3-oxo esters **2** with tetrazolyl-5-diazonium chloride.

Scheme 1. Azo coupling of 1,3-dicarbonyl compounds with tetrazolyl-5-diazonium chloride.



1, **3**: R^1 = Me, R^2 = Me (**a**), CF_3 (**b**), C_3F_7 (**c**), C_4F_9 (**d**); R^1 = Ph, R^2 = CF_3 (**e**), C_3F_7 (**f**).
2, **4**: R^1= OEt, R^2 = Me (**a**), CF_3 (**b**); R^1 = OMe, R^2 = $H(CF_2)_2$ (**c**), C_4F_9 (**d**).

Transformations of tetrazolyl-5-diazonium salt with acetylacetone [27] and ethyl acetoacetate [28] were shown to form the corresponding 2-tetrazolylhydrazono-1,3-dicarbonyl compounds, with their structure having been confirmed by elemental analysis only.

RESULTS AND DISCUSSION

To contribute to the gained understanding, we have conducted a detailed study of the reactions of fluoroalkyl-containing 1,3-diketones **1b–f** and 3-oxo esters **2b–d** with terazolyl-5-diazonium chloride. This transformation was carried out in ethanol in the presence of sodium acetate at a low temperature for 1,3-diketones **1**; however, acetone proved better in the case of 3-oxo esters **2**. For comparison, we have carried out similar transformationsof nonfluorinated 1,3-dicarbonyl compounds (acetylacetone **1a** and ethyl acetoacetate **2a**) (Scheme 1).

The structure of isolated products has been studied by IR and NMR spectroscopy as well as by X-ray analysis, because elemental analysis can suppose either a linear structure of 2-tetrazolylhydrazono-1,3-dicarbonyl compounds **B** or isomeric bicyclic structure of 7-hydroxy-7-polyfluoroalkyl-4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazines **A** for the compounds **3a–f**, **4a–d**.

In accordance with the X-ray diffraction data, compound **3e** has the structure of 6-benzoyl-7-hydroxy-7-trifluoromethyl-4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazine in crystal. There is an intramolecular hydrogen bond between oxygen O2 of benzoyl group and hydrogen H1 of the hydroxyl fragment in the molecule. Thus, the distance O2···H1—2.47(2) Å, angles O1H1O2—99(2), C9O1H1—114(2)° (Fig. 1). The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 795103.

The comparative analysis of IR spectra of the products **3b–f**, **4b–d** has revealed their uniformity. A characteristic feature is the presence of two very strong absorption bands at 3252–3234 and 3218–3206 cm^{-1} due to the stretching vibrations of OH and NH groups, as well as one high-frequency absorption band of the carbonyl group (ν 1714–1707 cm^{-1} for alkoxycarbonyl-substituted compounds **4b–d**, ν 1693–1690 cm^{-1} for acetyl-substituted products **3b–d**, and ν 1643–1639 cm^{-1} for benzoyl-substituted products **3e,f**). The above data indicate that all compounds **3b–f, 4b–d** have the structure of bicyclic isomer **A** in a solid state. Besides, the absorption band shift of the carbonyl fragment in a low-frequency field (in comparison with the values typical for these groups) can be explained by forming an intramolecular hydrogen bond with OH group. Of particular note is that IR spectra of the nonfluorinated products **3a** and **4a** are very similar to those of fluoroalkyl-containing analogs. In this

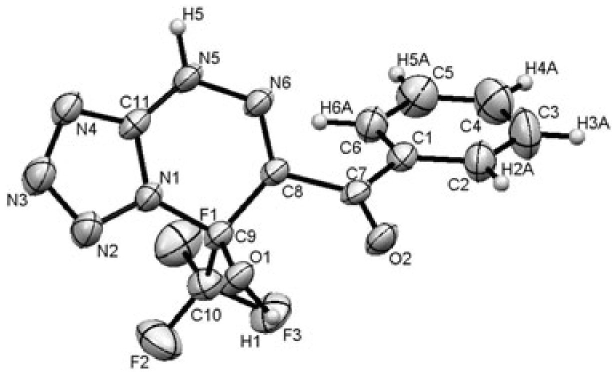


Figure 1. The ORTEP view of compound **3e**.

Table 1

Isomer composition of compounds **3** and **4** according to NMR spectroscopy data.

Compounds	R^1	R^2	Solvents	Isomer fraction (%)	
				B	*A*
3a	Me	Me	$(CD_3)_2SO$, Py-d_5	–	100
3b	CF_3	Me	$(CD_3)_2SO$	15	85
3c	C_3F_7	Me	$(CD_3)_2SO$	87	13
3d	C_4F_9	Me	$(CD_3)_2SO$,	88	12
			CD_3OD	84	16
			CD_3CN	82	18
			$(CD_3)_2CO$	89	11
3e	CF_3	Ph	$(CD_3)_2SO$, CD_3CN, $(CD_3)_2CO$, CD_3OD	–	100
			Py-d_5	3	97
3f	C_3F_7	Ph	$(CD_3)_2SO$	54	46
4a	Me	OEt	$(CD_3)_2SO$, Py-d_5	–	100
4b	CF_3	OEt	$(CD_3)_2SO$	–	100
			Py-d_5	2	98
4c	$H(CF_2)_2$	OMe	$(CD_3)_2SO$	–	100
			Py-d_5	15	85
4d	C_4F_9	OMe	$(CD_3)_2SO$	–	100
			Py-d_5	18	82

way, the compounds **3a–f** and **4a–d** exist in a solid state as the bicyclic form **A**.

The structure of products **3a–f** and **4a–d** in solutions has been studied using NMR spectroscopy. The ^{1}H-NMR and ^{19}F-NMR spectra of fluorinated compounds **3e** and **4b–d** in DMSO-d_6 contain one set of signals of one isomer, whereas the ^{1}H-NMR and ^{19}F-NMR spectra of products **3b–d,f** are characterized by a double set of signals corresponding to both (Table 1).

The ^{1}H-NMR spectra do not give convincing arguments for the choice of either cyclic or open-chain structure of the products **3b–f** and **4b–d** due to the spectral parameter proximity of tetrazolotriazines **A** and tetrazolylhydrazones **B**.

The use of ^{19}F-NMR spectroscopy data appears more convenient, since the neighboring carbon atoms make chemical shifts of fluorine atoms in α-CF_3 or α-CF_2 groups in the open-chain 2-(het)arylhydrazono-1,3-dicarbonyl compounds and cyclic dihydroazolotriazines different. In accordance with the literature data [23–25], the signals of fluorine atoms in α-CF_3 or α-CF_2 groups attached to sp^3-hybridized carbon atom in azolotriazines **A** are observed in a stronger field {δ(α-CF_3) 83–85, δ(α-CF_2) 45 ppm} compared to those in (het)arylhydrazones **B**, where α-CF_3 or α-CF_2 groups are connected to sp^2-hybridized carbon atom {δ(α-CF_3) 90–93, δ(α-CF_2) 49–52 ppm} [29].

The ^{19}F-NMR spectra of compounds **4b–d**, containing alkoxycarbonyl substituent, have indicated them to exist in the **A** form in DMSO-d_6 independently of the polyfluoroalkyl fragment structure (Table 1). In contrast, the compounds **3b–d**, having the acetyl substituent, are revealed as a mixture of the open-chain **B** and cyclic **A** isomers. The fraction of isomer **B** increases with the growth of polyfluoroalkyl chain. The isomer **B** portion is 15% in the case of trifluoromethyl-substituted product **3b**, and amounts up to as much as 87 and 88% for heptafluoropropyl and nonafluorobutyl analogs **3c,d**, respectively (Table 1).

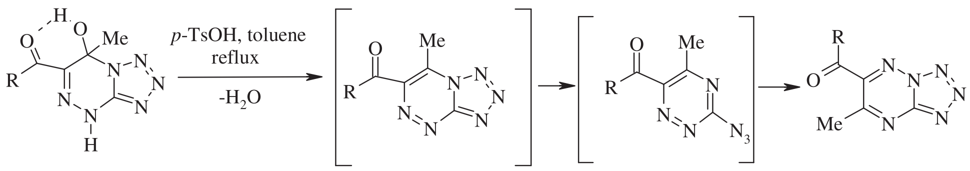
The product **3e** bearing trifluoromethyl and phenyl substituents exists in the cyclic form **A** in the DMSO-d_6 solution, whereas the compound **3f** combining bulk heptafluoropropyl and phenyl substituents is a mixture of **A** and **B** isomers in the ratio 1:1.

The choice of a structure is based on the ^{13}C-NMR spectroscopy data for the nonfluorinated products **3a** and **4a**. Thus, the carbon atom of an acetyl fragment being responsible for isomeric transformations indicates characteristic chemical shift in the ^{13}C-NMR spectra. The ^{13}C-NMR spectra of compounds **3a** and **4a** have been found to contain the only signal of the carbonyl carbon atom at 194 ($\underline{C}$OMe) and 161 ($\underline{C}O_2Et$) ppm, respectively, while in 2-(het)arylhydrazono-1,3-dicarbonyl compounds two of these signals {δ 164 ($\underline{C}O_2Et$) [30] or 196 ($\underline{C}$OMe) [29] and 197 ($\underline{C}$OMe) [29, 30] ppm} are observed. In addition, the spectra contain a signal of sp^3-hybridized carbon at δ 81.7 ppm indicating the cyclic form **A** of the compound **3a** and **4a** in a DMSO-d_6 solution [29, 30].

The compounds **3a** and **4a** have identical mp to the previously obtained substances [27, 28] and had been reported to be of open-chain form. However, with the help of spectral characteristics we showed them to have the cyclic structure indeed.

Thus, ^{1}H-NMR, ^{19}F, and IR spectroscopy as well as X-ray analysis data have allowed us to conclude that the products of azo coupling of both fluoroalkyl-containing and nonfluorinated 1,3-diketones **1**, 3-oxo esters **2** with tetrazolyl-5-diazonium chloride are 7-hydroxy-7-(polyfluoro)alkyl-4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazines **3a–e, 4a–d**.

Scheme 2. Dehydration of substance **3a** and **4a**.



3a, 4a

To study the solvent effect on the ring-chain isomerism of heterocycles **3b–f, 4b–d**, the ^{19}F-NMR spectra are registered for the compounds **3d,e** in $(CD_3)_2CO$, CD_3CN, CD_3OD, and Py-d_5 (Table 1). The ^{19}F-NMR spectroscopy method is selected as the most informative and allowing to distinguish between the **A** cyclic and **B** open-chain forms.

In contrast to acetyl- and benzoyl-substituted dihydrotetrazolotriazines **3b–f**, alkoxy-containing analogs **4b–d** are shown to be less subjected to ring-chain isomerism. The trace amounts of open-chain isomer **B** (2%) is revealed in the trifluoromethyl-substituted product **4b** when the ^{19}F-NMR spectrum is recorded in Py-d_5. The tendency to disclose is more pronounced in the case of compound **4d** having nonafluorobutyl substituent, because the spectrum shows 18% of the form **B** in Py-d_5.

The formation of open-chain isomers takes place in all cases independently of the fluoroalkyl group structure. Being a fairly strong base (pK_a 5.23 [31]), pyridine is capable of abstracting a proton from the hydroxy group of dihydrotetrazolotriazines **A**. Stabilization of the resulting deprotonated intermediate occurs *via* cleavage of tetrazine ring followed by the formation of 2-tetrazolylhydrazones **B**.

The nonfluorinated analogs **3a** and **4a** are not subjected to ring-chain isomerism in comparison with polyfluoroalkyl-containing heterocycles **3b–f** and **4b–d** since their ^{1}H-NMR spectra in Py-d_5 contain one set of signals corresponding to the cyclic isomer **A**.

We did not observe any dehydration effect of the fluoroalkyl-containing compounds **3b–f** and **4b–d** either by heating in acetic acid or boiling toluene in the presence of dehydrating agents. However, we succeeded in dehydrating the nonfluorinated derivatives **3a** and **4a** by refluxing in toluene in the presence of *p*-toluenesulfonic acid (Scheme 2).

The structure of 6-acetyl-7-methyltetrazolo[1,5-*b*][1,2,4] triazine **5a** has been proved by the X-ray diffraction analysis (Fig. 2). The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 804972).

The elimination of water molecule and subsequent aromatization of heterocycle allowed the cleavage of a tetrazole ring. As a result, we have obtained 7-methyltetrazolo [1,5-*b*][1,2,4]triazines instead of 7-methyltetrazolo[5,1-*c*] [1,2,4]triazines *via* azide rearrangement in accordance with the literature data [19–22] (Scheme 1).

CONCLUSIONS

To sum up, we have developed a simple and efficient method for the synthesis of 4,7-dihydrotetrazolo[5,1-*c*] [1,2,4]triazines bearing ester or acyl(aroyl) fragments. The fluorinated heterocycles **3b–f** and **4b–d** in the solid state are found to exist in the dihydrotetrazolotriazine form **A**, that capable to undergo ring-chain isomerism as a result of C7-N7a bond cleavage in solution. This is typical for the previously obtained 4-hydroxy-4-polyfluoroalkyl-1,4-dihydroazolo[5,1-*c*][1,2,4]triazines [23–25]. These heterocycles have been found to exist mainly (>70%) as the cyclic isomer **A** in solution. In contrast, the open-chain form **B** dominates in 4,7-dihydrotetrazolo[5,1-*c*][1,2,4] triazines having "long" polyfluroalkyl and acetyl fragments (compounds **3c,d**). In this case, the fraction of the open isomer **B** comes up to 90% (Table 1).

EXPERIMENTAL

Melting points were measured in the open capillaries on "Stuart SMP30" melting point apparatus. The IR spectra were recorded on "Perkin-Elmer Spectrum One FTIR" and "Thermo Nicolet 6700 FTIR" spectrometers at 4000–400 cm^{-1} using the "Frustrated total internal reflection" method. The ^{1}H-NMR and ^{13}C-NMR spectra were registered on "Bruker DRX-400" spectrometer (^{1}H, 400; ^{13}C, 100.6 MHz) relative to $SiMe_4$. The ^{19}F-NMR spectra were obtained on "Bruker DRX-400" spectrometer (^{19}F, 376 MHz) using C_6F_6 as an internal standard. The solvent is DMSO-d_6 unless otherwise stated. The microanalyses were carried out on "Perkin-Elmer PE 2400" series II elemental analyzer.

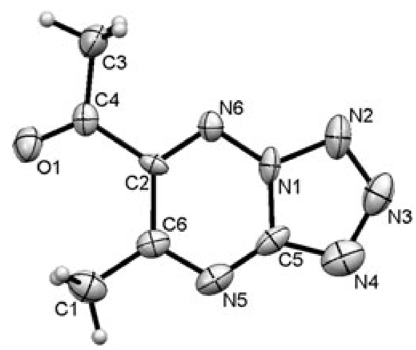


Figure 2. The ORTEP view of compound **5a**.

A single crystal of azoloazine **3e** (Fig. 2) was obtained by crystallization from the ethanol [**5a** from CH_2Cl_2 (Fig. 2)]. The X-ray studies were performed on "Xcalibur 3 CCD" diffractometer [graphite monochromator, ω (ϕ/ω for **5a**) scanning, λMoK_α 0.71073 Å radiation, *T* 295(2) K (130(2) K for **5a**)]. The registration of absorption was carried out analytically by the model of multifacet crystal using a program "CrysAlis RED 1.171.29.9. The crystal structures were solved by direct methods followed by Fourier synthesis with SHELXS-97 [32] and refined with full-matrix least-squares methods for all nonhydrogen atoms with SHELXL-97 software packages [32].

Crystallographic data for compound **3e**: $C_{11}H_7F_3N_6O_2$, *M* 312.23, space group *P(2)1*, monoclinic, *a* 9.128(3), *b* 7.102(5), *c* 10.576(3) Å, α, γ 90°, β 113.67(3)°, *V* 627.9(4) Å^3, *Z* 2, D_{calc} 1.651 g cm^{-3}, μ 0.149 mm^{-1}, 3653 reflection measured, 1653 unique reflections which were used in all calculations. The final *R* is 0.030, number of refined parameters 207. CCDC 795103 contains the supplementary crystallographic data for this compound [33].

Crystallographic data for compound **5a**: $C_6H_6N_6O$, *M* 178.17, space group $P2_1/c$, monoclinic, *a* 13.845(1), *b* 6.310(4), *c* 9.439 (1) Å, α, γ 90°, β 108.44(1)°, *V* 782.3(2) Å^3, *Z* 4, D_{calc} 1.513 g cm^{-3}, μ 0.114 mm^{-1}, 5428 reflection measured, 1934 unique reflections which were used in all calculations. The final *R* is 0.030, number of refined parameters 217. CCDC 804972 contains the supplementary crystallographic data for this compound.*

Initial fluorinated 1,3-dicarbonyl compounds **1b–f** and **2b–d** were synthesized according to the procedure described in [34, 35].

General procedure for 7-hydroxy-7-(polyfluoro)alkyl-4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazine (3a–f, 4a–d) synthesis. A two-necked stainless-steel flask equipped with a stirrer and a dropping funnel was charged with 0.5 g of 5-aminotetrazole (10 mmol), a mixture of concentrated hydrochloric acid (2.5 mL) and water (60 mL) was added. The resulting solution was cooled to 0°C and 0.7 g sodium nitrite in 3 mL of water was slowly added dropwise under vigorous stirring. The resulting mixture was stirred for 30 min on 0°C, and the obtained tetrazolyldiazonium salt was added to a solution of 5.5 g sodium acetate and 10 mmol of corresponding 1,3-diketiones **1a–f** or 3-oxo esters **2a–d** in 30 mL ethanol (or acetone for compounds **4**) under stirring at 5°C. By the end of addition procedure, crystals began separate from the solution and the precipitate was filtered off; aqueous ethanol (50%) was used for washing of products **3a–f**. In the case of compounds **4a–d** reaction mixture was extracted by diethyl ether. The solvent was evaporated. The residue was recrystallized from an appropriate solvent.

6-Acetyl-7-hydroxy-7-methyl-4,7-dihydrotetrazolo[5,1-c][1,2,4] triazine (3a). Yield 55%, light-green crystals, mp 158–160°C decomp. (163–164°C decomp. [27]). ^{1}H-NMR: **A**, 100%: 2.21 and 2.40 both s (6H, 2 Me), 7.80 s (1H, NH), 13.20 s (1H, OH) ppm. ^{1}H-NMR (Py-d_5): **A**, 100%: 2.56 and 2.74 both s (6H, 2 Me) ppm. ^{13}C-NMR: **A**, 100%: 25.08, 26.77 (both Me), 81.71 (C^4), 139.18 (C^3), 146.43 (C^{7a}), 194.81 (C=O) ppm. IR: 3251, 3199 (OH, NH^{str}), 1673 (C=O), 1549 (NH^{bend}, C=N, N=N) cm^{-1}. Anal. calcd for $C_6H_8N_6O_2$: C 36.74, H 4.11, N 42.84%. Found: C 36.39, H 4.01, N 42.53%.

6-Acetyl-7-hydroxy-7-trifluoromethyl-4,7-dihydrotetrazolo [5,1-c][1,2,4]triazine (3b). Yield 63%, gray powder, mp 173–175°C. ^{1}H-NMR: **A**, 85%: 2.46 s (3H, Me), 9.79 s (1H, NH), 14.04 s (1H, OH); **B**, 15%: 2.25 s (3H, Me), 8.15 s (1H, NH), 14.04 s (1H, NNH) ppm. ^{19}F-NMR: **A**, 85%: 85.53 s (CF_3); **B**, 15%: 92.45 s (CF_3) ppm. IR: 3238, 3206, 3138 (OH, NH^{str}), 1693 (C=O), 1612, 1552, 1538 (NH^{bend}, C=N, N=N), 1202–1147 (C-F) cm^{-1}. Anal. calcd for $C_6H_5F_3N_6O_2$: C 28.81, H 2.10, N 33.70%. Found: C 28.81, H 2.01, N 33.60%.

6-Acetyl-7-heptafluoropropyl-7-hydroxy-4,7-dihydrotetrazolo [5,1-c][1,2,4]triazine (3c). Yield 86%, gray powder, mp 156–157°C. ^{1}H-NMR: **A**, 13%: 2.45 s (3H, Me), 9.94 s (1H, NH), 14.17 s (1H, OH); **B**, 87%: 2.23 s (3H, Me), 8.16 s (1H, NH), 14.17 s (1H, NNH) ppm. ^{19}F-NMR: **A**, 13%: 36.90 m (2F, β-CF_2, AB system, J_{AB} 293.7, $\Delta\nu_{AB}$ 170.8 Hz), 45.90 m (2F, α-CF_2, AB system, J_{AB} 281.8, $\Delta\nu_{AB}$ 763.2 Hz), 82.44 t (3F, CF_3, $^3J_{F,F}$ 11.1 Hz); **A**, 87%: 38.70 m (2F, β-CF_2), 50.77 m (2F, α-CF_2), 82.67 t (3F, CF_3, $^3J_{F,F}$ 9.3 Hz). IR: 3242, 3208, 3135 (OH, NH^{str}), 1690 (C=O), 1614, 1555, 1532 (NH^{bend}, C=N, N=N), 1231–1124 (C-F). Anal. calcd for $C_8H_5F_7N_6O_2$: C 27.47 H 1.42, N 23.76%. Found: C 27.44, H 1.44, N 24.00%.

6-Acetyl-7-hydroxy-7-nonafluorobutyl-4,7-dihydrotetrazolo [5,1-c][1,2,4]triazines (3d). Yield 75%, gray powder, mp 145-147°C. ^{1}H-NMR: **A**, 20%: 2.50 s (3H, Me), 9.96 s (1H, NH), 14.16 s (1H, OH); **B**, 80%: 2.23 s (3H, Me_3), 8.16 s (1H, NH), 14.16 s (1H, NNH) ppm. ^{19}F-NMR: **A**, 20%: 37.07 m (2F, γ-CF_2), 40.17 m (2F, β-CF_2), 45.57 m (2F, α-CF_2, AB system, J_{AB} 279, $\Delta\nu_{AB}$ 753 Hz), 82,24 m (3F, CF_3); **B**, 80%: 37.57 m (2F, γ-CF_2), 42.06 m (2F, β-CF_2), 51.25 m (2F, α-CF_2), 82,29 m (3F, CF_3) ppm. ^{19}F-NMR (CD_3OD): **A**, 16%: 38.25 m (2F, γ-CF_2), 42.02 m (2F, β-CF_2), 46.90 m (2F, α-CF_2, AB system, J_{AB} 288, $\Delta\nu_{AB}$ 588 Hz), 82.93 t.m (3F, CF_3, $^3J_{F,F}$ 10.8 Hz); **B**, 84%: 38.65 m (2F, γ-CF_2), 43.44 m (2F, β-CF_2), 52.03 m (2F, α-CF_2), 82.83 tt (3F, CF_3, $^3J_{F,F}$ 10.1, $^4J_{F,F}$ 2.3 Hz) ppm. ^{19}F-NMR (CD_3CN): **A**, 18%: 38.02 m (2F, γ-CF_2), 41.35 m (2F, β-CF_2), 44.98 m (2F, α-CF_2, AB system, J_{AB} 288, $\Delta\nu_{AB}$ 569 Hz), 82.76 m (CF_3), **B**, 82%: 38.42 m (2F, γ-CF_2), 43.06 m (2F, β-CF_2), 51.66 m (2F, α-CF_2), 82.82 tt (3F, CF_3, $^3J_{F,F}$ 10.1, $^4J_{F,F}$ 2.5 Hz) ppm. ^{19}F-NMR ($(CD_3)_2CO$): **A**, 11%: 38.12 m (2F, γ-CF_2), 41.65 m (2F, β-CF_2), 46.05 Mm (2F, α-CF_2, AB system, J_{AB} 289, $\Delta\nu_{AB}$ 602 Hz), 82.77 m (CF_3); **B**, 89%: 38.55 m (2F, γ-CF_2), 43.22 m (2F, β-CF_2), 51.99 m (2F, α-CF_2), 82.86 t.m (3F, CF_3, $^3J_{F,F}$ 10.1 Hz) ppm. IR: 3241, 3206, 3135 (OH, NH^{str}), 1693 (C=O), 1613, 1555, 1533 (NH^{bend}, C=N, N=N), 1242–1135 (C-F) cm^{-1}. Anal. calcd for $C_9H_5F_9N_6O_2$: C 27.05 H 1.25, N 20.79%. Found: C 27.01, H 1.26, N 21.00%.

6-Benzoyl-7-hydroxy-7-trifluoromethyl-4,7-dihydrotetrazolo [5,1-c][1,2,4]triazine (3e). Yield 84%, gray powder, mp 159–160°C. ^{1}H-NMR: **A**, 100%: 7.86–7.55 m (5H, Ph), 10.14 s (1H, NH), 13.94 s (1H, OH) ppm. ^{19}F-NMR: **A**, 100%: 85.40 s (CF_3) ppm. ^{19}F-NMR (CD_3OD): **A**, 100%: 85.03 s (CF_3) ppm. ^{19}F-NMR (CD_3CN): **A**, 100%: 84.10 s (CF_3) ppm. ^{19}F-NMR ($(CD_3)_2CO$): **A**, 100%: 85.08 s (CF_3) ppm. ^{19}F-NMR (Py-d_5): **A**, 97%: 84.73 s (CF_3); **B**, 3%: 88.57 s (CF_3) ppm. IR: 3234, 3206, 3137 (OH, NH^{str}), 1639 (C=O), 1610, 1593, 1576, 1553, 1536 (NH^{bend}, C=N, C=C, N=N), 1176–1129 (C-F) cm^{-1}. Anal. calcd for $C_{11}H_7F_3N_6O_2$: C 44.54, H 2.27, N 26.64%. Found: C 42.32, H 2.26, N 26.92%.

6-Benzoyl-7-heptafluoropropyl-7-hydroxy–4,7-dihydrotetrazolo [5,1-c][1,2,4]triazine (3f). Yield 86%, gray powder, mp 133–134°C. ^{1}H-NMR: 7.84–7.39 m (5H, Ph), **A**, 46%: 10.29 s (1H, NH), 13.99 s (1H, OH); **B**, 54%: 8.86 s (1H, NH), 14.51 s (1H, NNH) ppm. ^{19}F-NMR: **A**, 46%: 37.89 m (2F, β-CF_2), 45.13 m (2F, α-CF_2, AB system, J_{AB} 288, $\Delta\nu_{AB}$ 511 Hz), 82.42 t (3F, CF_3, $^3J_{F,F}$ 10.8 Hz); **B**, 54%: 38.46 m (2F, β-CF_2), 50.15 m (2F, α-CF_2), 82.58 t (3F, CF_3, $^3J_{F,F}$ 9.2 Hz) ppm. IR: 3236, 3210, 3137 (OH, NH^{str}), 1644 (C=O), 1612, 1594, 1579, 1558, 1533 (NH^{bend}, C=N, C=C, N=N), 1242–1125 (C-F) cm^{-1}. Anal. calcd for $C_{13}H_7F_7N_6O_2$: C 37.54 H 1.92, N 20.39%. Found: C 37.88, H 1.71, N 20.39%.

Ethyl-7-hydroxy-7-methyl-4,7-dihydrotetrazolo[5,1-c][1,2,4] triazine-6-carboxylate (4a). Yield 65%, yellow powder, mp 142–143°C (140–141°C [28]). ^{1}H-NMR: **A**, 100%: 1.29 t (3H, OCH$_2$Me, $^3J_{H,H}$ 7.1 Hz), 2.22 s (3H, Me), 4.26 q (2H, OCH$_2$Me, $^3J_{H,H}$ 7.1 Hz), 7.96 s (1H, NH), 13.12 s (1H, OH) ppm. ^{1}H-NMR (Py-d_5): **A,** 100%: 1.38 t (3H, OCH$_2$Me, $^3J_{H,H}$ 7.0 Hz), 2.47 s (3H, Me), 4.32 q (2H, OCH$_2$Me, $^3J_{H,H}$ 7.0 Hz) ppm. ^{13}C-NMR: **A**, 100%: 13.98, 25.43 (both Me), 61.10 (CH$_2$Me), 81.75 (C^4), 133.31 (C^3), 146.42 (C^{7a}), 161.53 (C=O) ppm. IR: 3271, 3225 (OH, NH^{str}), 1696 (CO$_2$Et), 1567, 1540 (NH^{bend}, C=N, N=N) cm^{-1}. Anal. calcd for $C_7H_{10}N_6O_3$: C 37.17, H 4.46, N 37.15%. Found: C 36.92, H 4.51, N 36.97%.

Ethyl-7-hydroxy-7-trifluoromethyl-4,7-dihydrotetrazolo[5,1-c] [1,2,4]triazine-6-carbo-xylate (4b). Yield 57%, light-yellow powder, mp 124–125°C. ^{1}H-NMR: **A**, 100%: 1.25 t(3H, OCH$_2$Me, $^3J_{H,H}$ 7.1 Hz), 4.31 q (2H, OCH$_2$Me, $^3J_{H,H}$ 7.1 Hz), 10.06 s (1H, NH), 14.06 s (1H, OH) ppm. ^{19}F-NMR: **A**, 100%: 85.02 s (CF$_3$) ppm. ^{19}F-NMR (Py-d_5): **A**, 96%: 84.55 s (CF$_3$); **B**, 4% 88.53 s (CF$_3$) ppm. IR: 3248, 3217, 3142 (OH, NH^{str}), 1707 (CO$_2$Et), 1615, 1559, 1531 (NH^{bend}, C=N, N=N), 1209–1142 (C-F) cm^{-1}. Anal. calcd for $C_7H_7F_3N_6O_3$: C 30.26 H 2.32, N 20.05%. Found: C 30.01, H 2.52, N 20.34%.

Methyl-7-hydroxy-7-(1,1,2,2-tetrafluoroethyl)-4,7-dihydrotetrazolo [5,1-c][1,2,4]tri-azine-6-carboxylate (4c). Yield 58%, yellow powder, mp 123–124°C. ^{1}H-NMR: **A**, 100%: 3.83 s (3H, OMe), 6.83 tt (1H, H(CF$_2$)$_2$, $^2J_{H,F}$ 50.5, $^3J_{H,F}$ 5.7 Hz), 9.85 s (1H, NH), 13.89 s (1H, OH) ppm. ^{19}F-NMR: **A**, 100%: 27.05 m (2F, HCF$_2$, AB system, $^2J_{H,F}$ 50.5, J_{AB} 306, $\Delta\nu_{AB}$ 223 Hz), 38.02 m (2F, CF$_2$, AB system, J_{AB} 270, $\Delta\nu_{AB}$ 503 Hz) ppm. ^{19}F-NMR (Py-d$_5$): **A**, 85%: 27.53 m (2F, HCF$_2$, AB system, $^2J_{H,F}$ 51.9, J_{AB} 300, $\Delta\nu_{AB}$ 537 Hz), 37.88 m (2F, CF$_2$, AB system, J_{AB} 268, $\Delta\nu_{AB}$ 822 Hz); **B**, 15%: 26.93 dt (2F, HCF$_2$, $^2J_{H,F}$ 53.7, $^3J_{F,F}$ 8.4), 42.42 m (2F, CF$_2$) ppm. IR: 3247, 3198, 3136 (OH, NH^{str}), 1712 (CO$_2$Me), 1626, 1560, 1534 (NH^{bend}, C=N, N=N), 1153–1112 (C-F) cm^{-1}. Anal. calcd for $C_7H_6F_4N_6O_3$: C 27.91 H 1.97, N 27.97%. Found: C 28.2, H 2.03, N 28.19%.

Methyl-7-hydroxy-7-nonafluorobutyl-4,7-dihydrotetrazolo[5,1-c] [1,2,4]triazine-6-carboxylate (4d). Yield 63%, gray powder, mp 125–127°C ^{1}H-NMR: **A**, 100%: 3.84 s (3H, OMe), 10.26 s (1H, NH), 14.05 s (1H, OH) ppm. ^{19}F-NMR: **A**, 100%: 37.05 m (2F, γ-CF$_2$), 40.09 m (2F, β-CF$_2$, AB system, J_{AB} 301, $\Delta\nu_{AB}$ 137 Hz), 45.71 m (2F, α-CF$_2$, AB system, J_{AB} 280, $\Delta\nu_{AB}$ 481 Hz), 82.28 tm (3F, CF$_3$, $^3J_{F,F}$ 9.6 Hz) ppm. ^{19}F-NMR (Py-d$_5$): **A**, 82%: 37.02 m (2F, γ-CF$_2$), 40.84 m (2F, β-CF$_2$, AB system, J_{AB} 299, $\Delta\nu_{AB}$ 180 Hz), 45.44 m (2F, α-CF$_2$, AB system, J_{AB} 286, $\Delta\nu_{AB}$ 427 Hz), 81.86 m (3F, CF$_3$); **B**, 18%: 37.88 m (2F, γ-CF$_2$), 42.12 m (2F, β-CF$_2$), 51.97 m (2F, α-CF$_2$), 81.86 m (3F, CF$_3$) ppm. IR: 3252, 3217, 3146 (OH, NH^{str}), 1754, 1714 (CO$_2$Me), 1622, 1562, 1537 (NH^{bend}, C=N, N=N), 1206–1136 (C-F) cm^{-1}. Anal. calcd for $C_9H_5F_9N_6O_3$: C 26.23 H 1.07, N 20.02%. Found: C 25.98, H 1.21, N 20.19%.

General procedure for dehydration. A mixture of 2 mmol 4,7-dihydrotetrazolo[5,1-*c*][1,2,4]triazine (**3a, 4a**) and 100 mg *p*-toluenesulfonic acid (0.5 mmol) in absolute toluene (10 mL) refluxed with azeotropic distillation of water for 2–3 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (on Merck 60 silica gel, eluent: CH$_2$Cl$_2$).

6-Acetyl-7-methyltetrazolo[1,5-b][1,2,4]triazine (5a). Yield 76%, pale-yellow crystals, mp 131–132°C. ^{1}H-NMR: **A**, 100%: 2.74 and 2.88 both s (6H, 2 Me) ppm. ^{13}C-NMR: **A**, 100%: 24.75, 27.41 (both Me), 145.31 (C^3), 148.06 (C^{7a}), 163.30 (C^4), 195.50 (C=O) ppm. IR: 1713 (C=O), 1643, 1576, 1476, 1419 (C=C, C=N, N=N) cm^{-1}. Anal. calcd for $C_6H_6N_6O$: C 40.45, H 3.39, N 47.17%. Found: C 40.80, H 3.20, N 47.11%.

Ethyl 7-methyltetrazolo[1,5-b][1,2,4]triazine-6-carboxylate (6a). Yield 60%, yellow oil. ^{1}H-NMR: **A**, 100%: 1.40 t (3H, Me, $^3J_{H,H}$ 7.1 Hz), 2.92 s (3H, Me), 4.51 q (2H, CH$_2$, $^3J_{H,H}$ 7.1 Hz) ppm. IR: 1795 (C=O), 1650, 1580, 1470, 1425 (C=C, C=N, N=N) cm^{-1}. Anal. calcd for $C_7H_8N_6O_2$: C 40.39, H 3.87, N 40.37%. Found: C 40.52, H 3.60, N 40.15%.

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