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Synthesis of Amino Derivatives of Triazolopyrimidine

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Abstract—Heterocyclization of 1-(4,6-dimethylpyrimidin-2-yl)-4-R-thiosemicarbazides by the action of methyl iodide in ethanol in the presence of sodium acetate is accompanied by Dimroth rearrangement leading to the formation of 5,7-dimethyl-2-R-amino[1,2,4]triazolo[1,5-*a*]pyrimidines. Analogous heterocyclization of 4-aryl-1-(4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)thiosemicarbazides gives 3-arylamino-7-methyl-5-oxo-[1,2,4]triazolo[4,3-*a*]pyrimidines. The presence in the pyrimidine ring of a carbonyl group capable of forming hydrogen bond with protons of the amino group stabilizes the molecule, thus hampering the Dimroth rearrangement.

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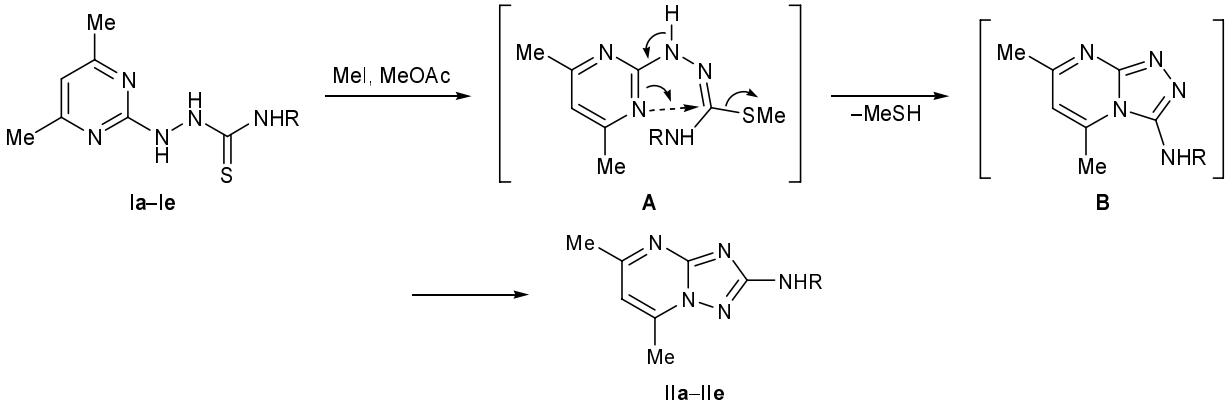
Fused heterocyclic systems including a pyrimidine ring, in particular triazolopyrimidines, can be regarded as synthetic analogs of natural compounds; therefore, they attract interest as potential physiologically active substances. [1,2,4]Triazolo[4,3-*a*]pyrimidines can be obtained by cyclizations of 2-hydrazinopyrimidines with aliphatic carboxylic acids, their esters, anhydrides, and chlorides [1–5], as well as with ortho esters [6, 7] or phosgene [3]. 2-Hydrazinopyrimidines are known to react with cyanogen bromide [3] to give the corresponding amino derivatives, while their reactions with carbon disulfide or isothiocyanates [1, 2, 4, 8] lead to the formation of sulfanyl-substituted triazolopyrimidines; in the latter case the process involves intermediate formation of 1-(pyrimidin-2-yl)thiosemicarbazides [1, 9]. When the reaction is carried out under severe conditions or in strongly acidic or strongly basic medium, the cyclization may be accompanied by the Dimroth rearrangement to give [1,2,4]triazolo-[1,5-*a*]pyrimidines as final products [1, 2, 10, 11].

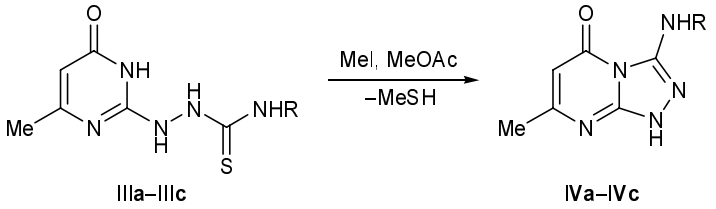
In the present work we showed that 1-(pyrimidin-2-yl)thiosemicarbazides are converted into 2-aminotriazolopyrimidine derivatives by the action of methyl iodide. 4-Aryl(or alkyl)-1-(4,6-dimethylpyrimidin-2-yl)thiosemicarbazides **Ia**–**Ie** reacted with methyl iodide in boiling methanol in the presence of sodium acetate to give the corresponding 2-R-amino-5,7-dimethyl[1,2,4]triazolo[1,5-*a*]pyrimidines **IIa**–**IIe** in

Scheme 1.



R = Ph (**a**), 4-$MeOC_6H_4$ (b), 4-$EtOCOC_6H_4$ (**c**), CH_2=$CHCH_2$ (**d**), Me (**e**).

Scheme 2.



R = Ph (**a**), 4-$MeOC_6H_4$ (b), 4-$EtOCOC_6H_4$ (**c**).

high yield (Scheme 1). It should be emphasized that no sulfanyl-substituted triazolopyrimidines were formed in these reactions, though such compounds were the major products of the thermal cyclization of analogous substrates in the absence of methyl iodide and sodium acetate [1, 9].

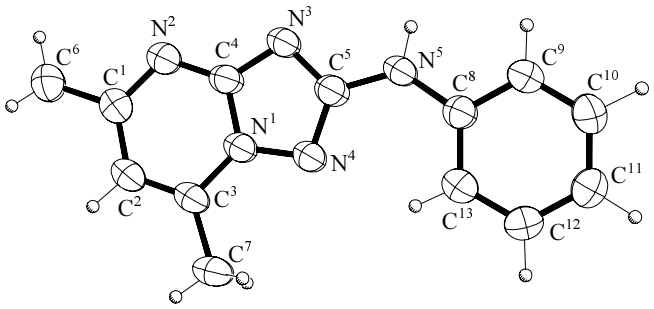


Fig. 1. Structure of the molecule of 5,7-dimethyl-2-phenylamino[1,2,4]triazolo[1,5-*a*]pyrimidine (**IIa**) according to the X-ray diffraction data. Principal bond lengths (Å) and bond angles (deg): N^1–N^4 1.370(2), N^1–C^3 1.360(3), N^1–C^4 1.370(2), N^2–C^1 1.331(3), N^2–C^4 1.336(3), N^3–C^4 1.333(2), N^3–C^5 1.353(3), N^4–C^5 1.339(2), N^5–C^5 1.362(3), N^5–C^8 1.395(3), C^1–C^2 1.401(3), C^2–C^3 1.355(3); $C^3N^1C^4$ 122.3(2), $N^4N^1N^4$ 111.1(2), $C^1N^2C^4$ 116.5(2), $C^4N^3C^5$ 103.1(2), $N^1N^4C^5$ 100.3(2), $C^5N^5C^8$ 129.1(2).

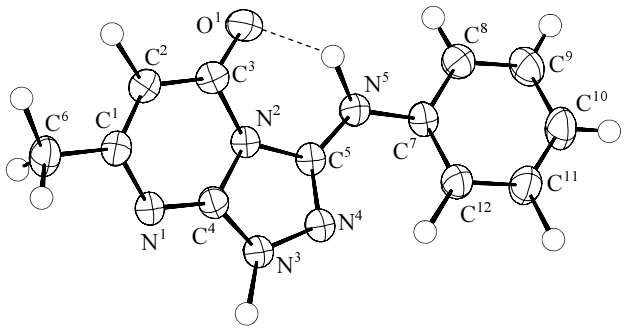


Fig. 2. Structure of the molecule of 7-methyl-3-phenylamino-[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (**IVa**) according to the X-ray diffraction data. Principal bond lengths (Å) and bond angles (deg): N^1–C^1 1.362(2), N^1–C^4 1.330(2), N^2–C^3 1.425(2), N^2–C^4 1.371(2), N^2–C^5 1.395(2), N^3–N^4 1.394(2), N^3–C^4 1.323(2), N^4–C^5 1.307(2), N^5–C^5 1.356(2), N^5–C^7 1.408(2); $C^1N^1C^4$ 114.8(1), $C^3N^2C^4$ 122.0(1), $C^4N^2C^5$ 106.0(1), $N^4N^3C^4$ 111.4(1), $N^3N^4C^5$ 104.7(1), $C^5N^5C^7$ 126.7(1).

Presumably, the first stage in the process is alkylation of the sulfur atom with formation of *S*-methyl derivative **A** which undergoes intramolecular cyclization with elimination of methanethiol molecule. The subsequent Dimroth rearrangement of intermediate **B** gives final product **II** (Scheme 1).

The nitrogen atoms in the pyrimidine ring of unsymmetrically substituted (4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)hydrazines (or the corresponding thiosemicarbazides) are nonequivalent; therefore, analogous cyclization of these compounds could give rise to two types of triazolopyrimidine derivatives. However, 4-aryl-1-(4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)thiosemicarbazides **IIIa**–**IIIc** reacted with methyl iodide in the presence of sodium acetate to give exclusively 3-arylamino-7-methyl-5-oxo[1,2,4]triazolo-[4,3-*a*]pyrimidines **IVa**–**IVc** (Scheme 2); i.e., only the N^1 atom in the pyrimidine ring was involved in the heterocyclization. The carbonyl group in the pyrimidine ring is capable of forming intramolecular hydrogen bond with protons of the amino group; this hydrogen bond stabilizes triazolopyrimidine molecule **IV** and hampers Dimroth rearrangement. Our results are very consistent with published data [1].

The ^{1}H NMR spectra of compounds **IIa**–**IIe** contain signals from protons in the pyrimidine ring at δ 6.48–6.95 ppm, amino group (ArNH or AlkNH) at δ 9.06–9.78 or 5.99–7.03 ppm, respectively, and two singlets from the methyl protons at δ 2.51 and 2.62–2.68 ppm; a considerable nonequivalence of the methyl protons confirms formation of a fused bicyclic system. On the other hand, the spectra contained no signals from protons on the nitrogen atoms in positions *1* and *2* of thiosemicarbazide, which were present in the spectra of initial compounds **Ia**–**Ie** (δ 8.71–9.87 ppm). The ^{1}H NMR spectra of **IVa**–**IVc** lacked signal from the pyrimidine N^1H proton, typical of initial compounds **IIIa**–**IIIc** (δ 10.31–10.34 ppm), but a signal from the triazole NH proton appeared at δ 13.20–13.23 ppm.

The structure of compounds **IIa** and **IVa** was proved by X-ray analysis. Figures 1 and 2 show the

structures of molecules **IIa** and **IVa**, respectively; their principal geometric parameters are also given. The bicyclic system N^1–N^4C^1–C^5 in both molecules is planar: deviations of atoms from the mean-square plane do not exceed 0.017 Å, and the dihedral angles between the $N^1N^2C^1C^2C^3C^4$ and $N^2N^3N^4C^4C^5$ rings are 0.3° (**IIa**) and 1.2° (**IVa**). The benzene ring is almost coplanar to the bicyclic system: the corresponding dihedral angles are 9.3° and 9.2° for molecules **IIa** and **IVa**, respectively. The N^5 atom has a planar–trigonal bond configuration: the sum of the bond angles at that atom is 359.4° for **IIa** and 359.9° for **IVa**. Conjugation between the unshared electron pair on N^5 and π systems of the bicyclic fragment and benzene ring leads to shortening of the N^5–C^5 and N^5–C_{arom} bonds [1.362(3) and 1.395(3) Å in molecule **IIa**; 1.356(2) and 1.408(2) Å in **IVa**] relative to the standard length of purely single N_{sp2}–C_{sp2} bond (1.43–1.45 Å [12, 13]).

Molecules **IIa** in crystal form centrosymmetric dimers via intermolecular hydrogen bonds N^5–H···N^3 with the following parameters: N···N 3.057, N–H 0.86(2), H···N 2.21(2) Å; ∠NHN 171(2)° (Fig. 3). The molecular structure of **IVa** is characterized by formation of intramolecular hydrogen bond N^5–H···O^1 [N···O 2.834(2), N–H 1.02(2), O···H 2.12(2) Å, ∠OHN 134(2)°] that closes the six-membered ring $O^1C^3N^2C^5N^5H^5$. Molecules **IVa** in crystal are linked into centrosymmetric dimers via fairly strong [14] intermolecular hydrogen bonds N^3–H···N^1 [N···N 2.814(2), N–H 1.02(2), N···H 1.81(4) Å, ∠NHN 156(2)°] (Fig. 4).

EXPERIMENTAL

The IR spectra of compounds **I**–**IV** were recorded in KBr on a UR-20 spectrometer. The ^{1}H NMR spectra were obtained on a Varian VXR-300 spectrometer at 300 MHz from solutions in DMSO-d_6 containing tetramethylsilane as internal reference.

The X-ray diffraction data for single crystals of compounds **IIa** and **IVa** were acquired at room temperature on an Enraf–Nonius CAD-4 automatic four-circle diffractometer. The principal crystallographic parameters and refinement details are given in table. Both structures were solved by the direct method and were refined by the least-squares procedure in full-matrix anisotropic approximation using CRYSTALS [15] and SHELXTL software packages [16]. All hydrogen atoms were visualized by the difference synthesis of electron density, and their positions were refined in isotropic approximation. The structure of **IIa** was refined using a weight scheme with $w = 1/\sigma^2 Fo^2 + (0.1000P)^2$, where $P = (Fo^2 + 2Fc^2)/3$. Chebyshev's weight scheme [17] with five parameters (2.68, 1.81, 2.57, 0.48, and 0.71) was used in the refinement of **IVa**. Absorption by the crystals of **IIa** and **IVa** was taken into account by the azimuthal scanning technique [18]. The complete sets of crystallographic data for compounds **IIa** and **IVa** were deposited to the

Crystallographic data for compounds **IIa** and **IVa**

Parameter	Compound **IIa**	Compound **IVa**
Irradiation	λCuK_α	λMoK_α
θ_{mzx}, deg	28	68
Spherical segment	$0 \le h \le 10$	$0 \le h \le 10$
	$-9 \le k \le 10$	$0 \le k \le 6$
	$-14 \le l \le 14$	$-29 \le l \le 29$
Crystal habit, mm	0.25×0.31×0.37	0.25×0.31×0.37
a, Å	7.623(2)	8.464(7)
b, Å	8.105(2)	5.411(2)
c, Å	11.146(2)	24.370(8)
α, deg	90.0	78.33(3)
β, deg	92.67(5)	75.85(3)
γ, deg	90.0	64.12(3)
V, Å^3	1115(1)	597.2(2)
M	241.3	239.3
Z	4	2
d_{calc}	1.44	1.33
μ, cm^{-1}	7.68	0.86
F(000)	505	252
Space group	$P2_1/n$ (no. 14)	$P\bar{1}$ (no. 2)
Number of reflections		
total	2427	3085
independent	2029	2871
used in the refinement	1668, $I > 3\sigma(I)$	1717, $I > 2\sigma(I)$
R_{int}	0.023	0.039
Number of refined parameters	207	215
R	0.038	0.058
R_w	0.040	
$R_w(F^2)$		0.1429
GOF	0.977	0.945
$\Delta\rho_{max}$	0.44	0.19
$\Delta\rho_{min}$	–0.37	–0.31

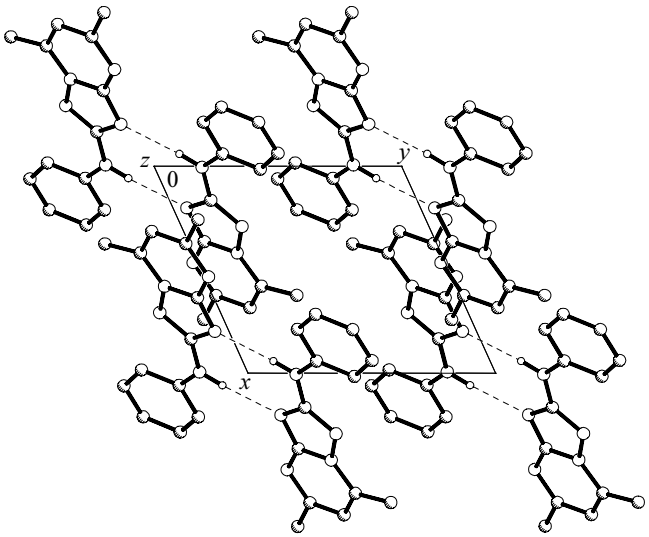


Fig. 3. Crystal packing of compound **IIa** (projection onto the *ab* plane). Intermolecular hydrogen bonds N–H···N are shown with dashed lines.

Cambridge Crystallographic Data Center (entry nos. 246490 and 246489).

2-Hydrazino-4,6-dimethylpyrimidine was synthesized by the procedure reported in [8], and 2-hydrazino-6-methylpyrimidin-4(3*H*)-one was obtained as described in [5].

1-(4,6-Dimethylpyrimidin-2-yl)-4-R-thiosemicarbazides Ia–Ie (*general procedure***).** 2-Hydrazino-4,6-dimethylpyrimidine, 1.38 g (0.01 mol), was dissolved in 50 ml of ethanol on heating, the solution was cooled to 45–50°C, and a solution of 0.015 mol of the corresponding isothiocyanate in 20 ml of ethanol was added. The mixture was left to stand for 24 h at room temperature, and the precipitate was filtered off and washed with ethanol and diethyl ether.

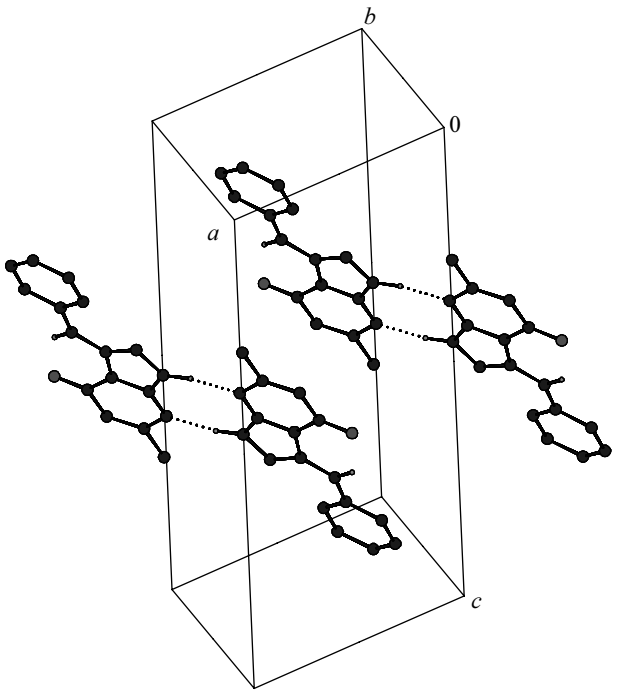


Fig. 4. Crystal packing of compound **IVa**. Intermolecular hydrogen bonds N–H···N are shown with dotted lines.

1-(4,6-Dimethylpyrimidin-2-yl)-4-phenylthiosemicarbazide (Ia). Yield 2.10 g (77%), mp 199–201°C. IR spectrum, ν, cm^{-1}: 3210, 3010 (NH); 1610, 1580, 1550 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 2.28 s (6H, CH_3); 6.66 s (1H, CH); 7.10 t (1H, H_{arom}, J = 7.2 Hz); 7.28 t (2H, H_{arom}, J = 7.2 Hz); 7.53 d (2H, H_{arom}, J = 7.5 Hz); 8.90 m, 9.62 m, and 9.66 m (3H, NH). Found, %: C 57.03; H 5.49; N 25.57; S 11.68. $C_{13}H_{15}N_5S$. Calculated, %: C 57.12; H 5.53; N 25.62; S 11.73.

1-(4,6-Dimethylpyrimidin-2-yl)-4-(4-methoxyphenyl)thiosemicarbazide (Ib). Yield 2.94 g (97%), mp 185–187°C. IR spectrum, ν, cm^{-1}: 3300–3000 (NH); 1620, 1585, 1480 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 2.28 s (6H, CH_3); 3.73 s (3H, OCH_3); 6.64 s (1H, CH); 6.85 d (2H, H_{arom}, J = 8.4 Hz); 7.35 d (2H, H_{arom}, J = 8.4 Hz); 8.87 m, 9.50 m, and 9.54 m (3H, 3NH). Found, %: C 55.40; H 5.61; N 23.03; S 10.49. $C_{14}H_{17}N_5OS$. Calculated, %: C 55.43; H 5.65; N 23.08; S 10.57.

Ethyl 4-{[2-(4,6-dimethylpyrimidin-2-yl)hydrazino]carbonothioylamino}benzoate (Ic). Yield 3.04 g (88%), mp 108–110°C. IR spectrum, ν, cm^{-1}: 3390, 3220, 3070 (NH); 1715 (C=O); 1620, 1585, 1550 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.31 t (3H, $CH_2C\mathbf{H}_3$, J = 6.9 Hz); 2.28 s (6H, CH_3); 4.29 q (2H, CH_2, J = 7.2 Hz); 6.66 s (1H, CH); 7.83 d (2H, H_{arom}, J = 8.7 Hz); 7.88 d (2H, H_{arom}, J = 8.7 Hz); 8.90 m, 9.80 m, and 9.87 m (3H, NH). Found, %: C 55.53; H 5.47; N 20.19; S 9.13. $C_{16}H_{19}N_5O_2S$. Calculated, %: C 55.63; H 5.54; N 20.27; S 9.28.

4-Allyl-1-(4,6-dimethylpyrimidin-2-yl)thiosemicarbazide (Id). Yield 2.23 g (94%), mp 232–233°C. IR spectrum, ν, cm^{-1}: 3240, 3000, 2960 (NH); 1615, 1565 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.26 s (6H, CH_3), 4.08 t (2H, CH_2, J = 5.7 Hz), 5.00 d (1H, CH, J = 10.2 Hz), 5.13 d (1H, CH, J = 17.1 Hz), 5.74–5.87 m (1H, CH), 6.63 s (1H, CH), 8.06 t (1H, NH, J = 5.7 Hz), 8.76 m (1H, NH), 9.24 m (1H, NH). Found, %: C 50.47; H 6.29; N 29.39; S 13.47. $C_{10}H_{15}N_5S$. Calculated, %: C 50.61; H 6.37; N 29.51; S 13.51.

1-(4,6-Dimethylpyrimidin-2-yl)-4-methylthiosemicarbazide (Ie). Yield 2.07 g (98%), mp 230–

232°C. IR spectrum, ν, cm^{-1}: 3240, 3070, 3010 (NH); 1610, 1590 (C=N). ^1H NMR spectrum, δ, ppm: 2.25 s (6H, CH_3), 2.84 d (3H, CH_3, J = 4.5 Hz), 6.61 s (1H, CH), 7.94 q (1H, NH, J = 3.9 Hz), 8.71 m (1H, NH), 9.17 m (1H, NH). Found, %: C 45.34; H 6.18; N 33.02; S 15.13. $C_8H_{13}N_5S$. Calculated, %: C 45.48; H 6.20; N 33.15; S 15.18.

5,7-Dimethyl-2-R-amino[1,2,4]triazolo[1,5-*a*]-pyrimidines IIa–IIc (*general procedure*). A mixture of 5 mmol of thiosemicarbazide **Ia**–**Ic**, 0.62 g (7.5 mmol) of sodium acetate, and 0.47 ml (7.5 mmol) of methyl iodide in 50 ml of ethanol was heated for 1–1.5 h under reflux. The solution was evaporated by half and was left to stand for 5–7 days for crystallization. The precipitate was filtered off and washed on a filter with ethanol and diethyl ether.

5,7-Dimethyl-2-phenylamino[1,2,4]triazolo-[1,5-*a*]pyrimidine (IIa). Yield 0.87 g (73%), mp 275–276°C. IR spectrum, ν, cm^{-1}: 3120 (NH); 1625, 1585, 1535, 1475 (C=N, C=C_{arom}). ^1H NMR spectrum, δ, ppm: 2.51 s and 2.68 s (3H each, CH_3), 6.90 t (1H, H_{arom}, J = 7.5 Hz), 6.95 s (1H, CH), 7.29 t (2H, H_{arom}, J = 8.1 Hz), 7.73 d (2H, H_{arom}, J = 8.4 Hz), 9.74 s (1H, NH). Found, %: C 65.19; H 5.39; N 29.14. $C_{13}H_{13}N_5$. Calculated, %: C 65.26; H 5.48; N 29.27.

5,7-Dimethyl-2-(4-methoxyphenylamino)[1,2,4]-triazolo[1,5-*a*]pyrimidine (IIb). Yield 1.04 g (77%), mp 253–255°C. IR spectrum, ν, cm^{-1}: 3080 (NH); 1620, 1580, 1520, 1470 (C=N, C=C_{arom}). ^1H NMR spectrum, δ, ppm: 2.50 s and 2.66 s (3H each, CH_3), 3.72 s (3H, OCH_3), 6.89 d (2H, H_{arom}, J = 8.7 Hz), 6.93 s (1H, CH), 7.63 d (2H, H_{arom}, J = 8.7 Hz), 9.54 s (1H, NH). Found, %: C 62.37; H 5.58; N 26.00. $C_{14}H_{15}N_5O$. Calculated, %: C 62.44; H 5.61; N 26.01.

Ethyl 4-(5,7-dimethyl[1,2,4]triazolo[1,5-*a*]pyrimidin-2-ylamino)benzoate (IIc). Yield 0.95 g (61%), mp 212–214°C. IR spectrum, ν, cm^{-1}: 3320, 3010 (NH); 1720 (C=O); 1640, 1620, 1565 (C=N, C=C_{arom}). ^1H NMR spectrum, δ, ppm: 1.29 t (3H, $CH_2C\mathbf{H}_3$, J = 6.9 Hz), 2.51 s and 2.62 s (3H each, CH_3), 4.25 q (2H, CH_2, J = 6.9 Hz), 6.82 s (1H, CH), 6.84 d (2H, H_{arom}, J = 9.0 Hz), 7.82 d (2H, H_{arom}, J = 8.7 Hz), 9.07 s (1H, NH). Found, %: C 61.62; H 5.43; N 22.45. $C_{16}H_{17}N_5O_2$. Calculated, %: C 61.72; H 5.50; N 22.49.

2-Allylamino-5,7-dimethyl[1,2,4]triazolo[1,5-*a*]-pyrimidine (IId). A mixture of 1.19 g (5 mmol) of thiosemicarbazide **Id**, 0.62 g (7.5 mmol) of sodium acetate, and 0.47 ml (7.5 mmol) of methyl iodide in 50 ml of ethanol was heated for 1–1.5 h under reflux. The resulting solution was evaporated to dryness, and a solution of 0.97 g (7 mmol) of potassium carbonate in 20 ml of water was added to the residue. The undissolved material was filtered off and washed on a filter with ethanol–diethyl ether (1:1). Yield 0.28 g (28%), mp 142–144°C. IR spectrum, ν, cm^{-1}: 3290, 3090 (NH); 1605 (C=N). ^1H NMR spectrum, δ, ppm: 2.46 s and 2.58 s (3H each, CH_3), 3.91 t (2H, CH_2, J = 5.7 Hz), 5.08 d (1H, CH, J = 11.7 Hz), 5.23 d (1H, CH, J = 17.7 Hz), 5.89–6.02 m (1H, CH), 6.83 s (1H, CH), 7.03 t (1H, NH, J = 6.0 Hz). Found, %: C 58.97; H 6.38; N 34.49. $C_{10}H_{13}N_5$. Calculated, %: C 59.10; H 6.45; N 34.46.

5,7-Dimethyl-2-methylamino[1,2,4]triazolo-[1,5-*a*]pyrimidine (IIe). A mixture of 1.06 g (5 mmol) of thiosemicarbazide **Ie**, 0.62 g (7.5 mmol) of sodium acetate, and 0.47 ml (7.5 mmol) of methyl iodide in 50 ml of ethanol was heated for 1–1.5 h under reflux. The solution was evaporated, and the residue (partially tarry) was ground with 10 ml of ethyl acetate and left to stand for crystallization. The product was filtered off and recrystallized from acetone. Yield 0.26 g (29%), mp 182–184°C (from acetone). IR spectrum, ν, cm^{-1}: 3470 (NH); 1640, 1590, 1550 (C=N). ^1H NMR spectrum, δ, ppm: 2.38 s and 2.76 s (3H each, CH_3), 2.86 d (3H, CH_3, J = 5.1 Hz), 5.98 q (1H, NH, J = 4.8 Hz), 6.48 s (1H, CH). Found, %: C 54.13; H 6.19; N 39.46. $C_8H_{11}N_5$. Calculated, %: C 54.22; H 6.26; N 39.52.

1-(4-Methyl-6-oxo-1,6-dihydropyrimidin-2-yl)-4-R-thiosemicarbazides IIIa and IIIb (*general procedure*). A mixture of 1.40 g (0.01 mol) of 2-hydrazino-6-methylpyrimidin-4(3*H*)-one and 0.015 mol of phenyl or 4-methoxyphenyl isothiocyanate in 100 ml of ethanol was heated for 30–45 min under reflux. The precipitate was filtered off and washed with ethanol and diethyl ether.

1-(4-Methyl-6-oxo-1,6-dihydropyrimidin-2-yl)-4-phenylthiosemicarbazide (IIIa). Yield 2.53 g (92%), mp 282–285°C. IR spectrum, ν, cm^{-1}: 3280, 3050, 2840 (NH); 1720 (C=O); 1670, 1575, 1455 (C=N, C=C_{arom}). ^1H NMR spectrum, δ, ppm: 2.10 s (3H, CH_3), 5.47 br.s (1H, CH), 7.13 t (1H, H_{arom}, J = 7.5 Hz), 7.32 t (2H, H_{arom}, J = 7.8 Hz), 7.60 d (2H, H_{arom}, J = 7.8 Hz), 9.62–10.31 m (4H, NH). Found, %: C 52.13; H 4.69; N 25.47; S 11.51. $C_{12}H_{13}N_5OS$. Calculated, %: C 52.35; H 4.76; N 25.44; S 11.65.

4-(4-Methoxyphenyl)-1-(4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)thiosemicarbazide (IIIb). Yield 2.90 g (95%), mp 281–283°C. IR spectrum, ν, cm^{-1}: 3285, 3210, 3045, 2980 (NH); 1725 (C=O); 1665, 1570, 1470, 1440 (C=N, C=C_{arom}). ^1H NMR spectrum, δ, ppm: 2.08 s (3H, CH_3), 3.76 s (3H, OCH_3), 5.50 br.s

(1H, CH), 6.90 d (2H, H_{arom}, J = 9.0 Hz), 7.41 d (2H, H_{arom}, J = 7.8 Hz), 9.19–10.34 m (4H, NH). Found, %: C 51.06; H 4.81; N 22.83; S 10.43. $C_{13}H_{15}N_5O_2S$. Calculated, %: C 51.13; H 4.95; N 22.94; S 10.50.

Ethyl 4-{[2-(4-methyl-6-oxo-1,6-dihydropyrimidin-2-yl)hydrazino]carbonothioylamino}benzoate (IIIc). A solution of 1.40 g (0.01 mol) of 2-hydrazino-6-methylpyrimidin-4(3*H*)-one and 3.11 g (0.015 mol) of ethyl 4-isothiocyanatobenzoate in 100 ml of ethanol was stirred for 2–3 days at 30–40°C. The mixture was then heated to the boiling point, and thiosemicarbazide **IIIc** was filtered off from the hot mixture and washed with ethanol and diethyl ether on a filter. Yield 3.02 g (87%), mp 288–290°C. IR spectrum, ν, cm^{-1}: 3280, 3050, 2850 (NH); 1725 (C=O); 1665, 1630, 1605, 1585, 1470, 1440 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, $CH_2C\mathbf{H}_3$, J = 7.2 Hz), 2.10 s (3H, CH_3), 4.32 q (2H, CH_2, J = 7.2 Hz), 5.49 br.s (1H, CH), 7.86–7.94 m (4H, H_{arom}), 9.60–10.34 m (4H, NH). Found, %: C 51.73; H 4.87; N 20.07; S 9.14. $C_{15}H_{17}N_5O_3S$. Calculated, %: C 51.86; H 4.93; N 20.16; S 9.23.

3-R-amino-7-methyl[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-ones IVa–IVc (*general procedure***).** A mixture of 5 mmol of thiosemicarbazide **IIIa**–**IIIc**, 0.62 g (7.5 mmol) of sodium acetate, and 0.47 ml (7.5 mmol) of methyl iodide in 50 ml of ethanol was heated for 1–1.5 h under reflux. The precipitate was filtered off and washed on a filter with ethanol and diethyl ether.

7-Methyl-3-phenylamino[1,2,4]triazolo[4,3-*a*]-pyrimidin-5(1*H*)-one (IVa). Yield 0.94 g (78%), mp >320°C (from EtOH–DMSO). IR spectrum, ν, cm^{-1}: 3320 (NH); 1710 (C=O); 1660, 1620, 1585 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H, CH_3), 5.60 s (1H, CH), 7.00 t (1H, H_{arom}, J = 7.5 Hz), 7.35 t (2H, H_{arom}, J = 7.5 Hz), 7.61 d (2H, H_{arom}, J = 8.7 Hz), 9.42 s (1H, NH), 13.20 br.s (1H, NH). Found, %: C 59.69; H 4.59; N 29.04. $C_{12}H_{11}N_5O$. Calculated, %: C 59.74; H 4.60; N 29.03.

3-(4-Methoxyphenylamino)-7-methyl[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (IVb). Yield 1.09 g (80%), mp >320°C (from EtOH–DMSO). IR spectrum, ν, cm^{-1}: 3300 (NH); 1710 (C=O); 1660, 1620, 1590, 1530, 1430 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 2.24 s (3H, CH_3), 3.75 s (3H, OCH_3), 5.60 s (1H, CH), 6.94 d (2H, H_{arom}, J = 8.7 Hz), 7.55 d (2H, H_{arom}, J = 8.4 Hz), 9.24 s (1H, NH), 13.13 br.s (1H, NH). Found, %: C 57.39; H 4.82; N 25.74. $C_{13}H_{13}N_5O_2$. Calculated, %: C 57.56; H 4.83; N 25.82.

Ethyl 4-(7-methyl-5-oxo-1,5-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-3-ylamino)benzoate (IVc). Yield 1.10 g (70%), mp 277–279°C (from EtOH). IR spectrum, ν, cm^{-1}: 3320–3280 (NH); 1720, 1700 (C=O); 1615, 1580, 1530 (C=N, C=C_{arom}). ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, $CH_2C\mathbf{H}_3$, J = 7.2 Hz), 2.26 s (3H, CH_3), 4.30 q (2H, CH_2, J = 7.2 Hz), 5.62 s (1H, CH), 7.74 d (2H, H_{arom}, J = 9.0 Hz), 7.94 d (2H, H_{arom}, J = 8.7 Hz), 9.70 s (1H, NH), 13.23 br.s (1H, NH). Found, %: C 57.42; H 4.73; N 22.28. $C_{15}H_{15}N_5O_3$. Calculated, %: C 57.50; H 4.83; N 22.35.

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