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Synthesis of Fused Triazolothienopyrimidine Derivatives

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Abstract—Reactions of substituted 1-(thieno[2,3-*d*]pyrimidin-2-yl)-4-arylthiosemicarbazides with methyl iodide led to the formation of fused triazolothienopyrimidine derivatives.

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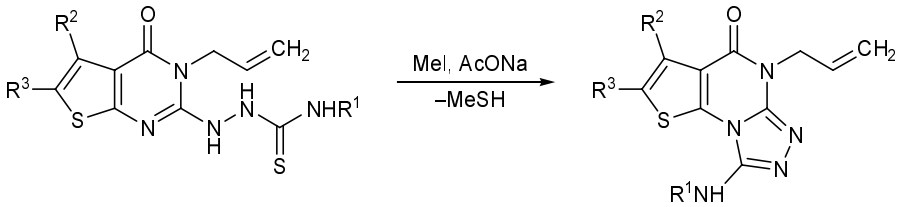
Fused heterocyclic systems including a 1,2,4-triazole ring are usually obtained by appending the latter to various nitrogen-containing heterocycles through appropriate α-hydrazino-substituted derivatives [1]. For example, [1,2,4]triazolothienopyrimidines were synthesized by heating 2-hydrazinothienopyrimidines with ortho esters [2–4] or carboxylic acids [5, 6]. Carboxylic acid anhydrides were also used in such cyclizations [3, 7, 8].

In the present article we describe heterocyclization of *N*-aryl-2-(3-allyl-4-oxo-3,4-dihydrothieno[2,3-*d*]-pyrimidin-2-yl)hydrazine-1-carbothioamides **I** and **II** by the action of methyl iodide in boiling ethanol in the presence of sodium acetate. The heterocyclization involves the only unsubstituted nitrogen atom in position *1* of the pyrimidine ring and leads to the formation of angularly fused 1-arylamino-4,5-dihydrothieno[2,3-*d*]-[1,2,4]triazolo[3,4-*b*]pyrimidin-5-ones **III** and **IV** (Scheme 1). Analogous cyclization of *N*-aryl-2-(thienopyrimidin-2-yl)hydrazine-1-carbothioamides **V** and **VI** occurs at the N^3 atom of the pyrimidine ring to give linearly fused 3-arylamino-4,5-dihydrothieno-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5-ones **VII** and **VIII** (Scheme 2). It should be noted that 4-alkylthiosemicarbazides **Vd** and **Ve** failed to undergo intramolecular ring closure by the action of methyl iodide.

Presumably, the first step of the process is alkylation of the sulfur atom in thiosemicarbazides **I**, **II**, **V**, and **VI**, and methylsulfanyl derivatives thus formed undergo intramolecular cyclization with elimination of methanethiol to give the corresponding triazolothienopyrimidines as final products.

The ^{1}H NMR spectra of the cyclization products considerably differed from the spectra of initial thiosemicarbazides. Compounds **I**, **II**, **V**, and **VI** showed in the ^{1}H NMR spectra three signals in the region δ 8.20–9.99 ppm from the NH protons in the thiosemicarbazide fragment, whereas the spectra of angular cyclization products **III** and **IV** contained one singlet at δ 8.49–9.35 ppm from the arylamino NH group; linearly fused triazolothienopyrimidines **VII** and **VIII** gave rise to two NH singlets at δ 9.42–10.02 (ArNH) and 13.00–13.35 ppm (N^1H).

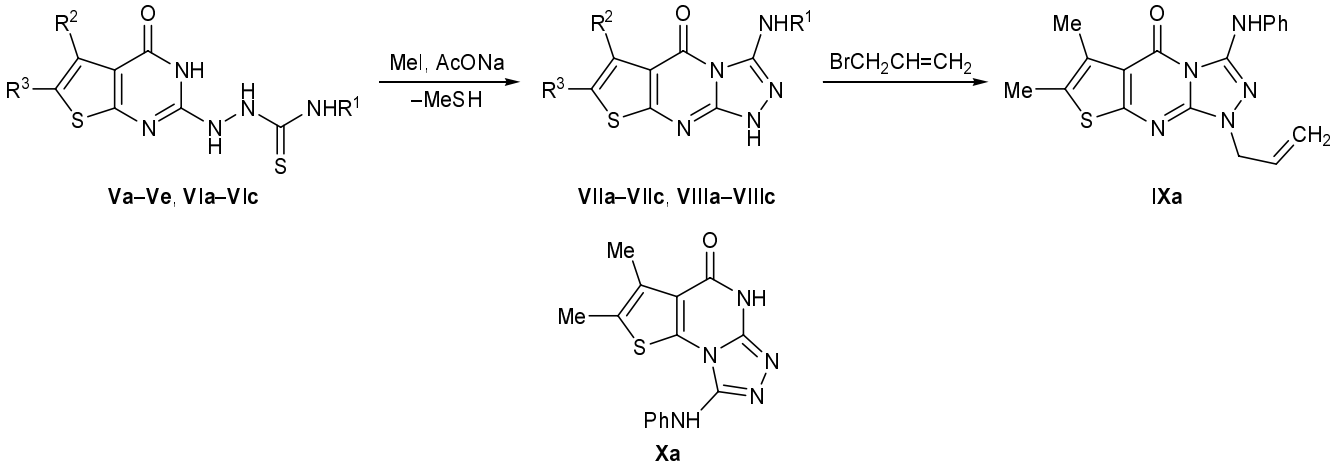
Scheme 1.



Ia–Ic, **IIa–IIc** **IIIa–IIIc**, **IVa–IVc**

R^1 = Ph (**a**), 4-$MeOC_6H_4$ (**b**), 4-$EtOCOC_6H_4$ (**c**); **I**, **III**, $R^2R^3 = (CH_2)_4$; **II**, **IV**, $R^2 = R^3$ = Me.

Scheme 2.



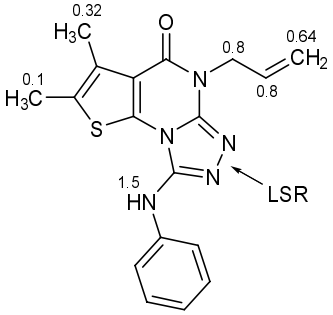
R^1 = Ph (**a**), 4-$MeOC_6H_4$ (**b**), 4-$EtOCOC_6H_4$ (**c**), CH_2=$CHCH_2$ (**d**), Me (**e**); **V**, **VII**, $R^2R^3 = (CH_2)_4$; **VI**, **VIII**, $R^2 = R^3$ = Me.

Allyl bromide reacted with compound **VIIIa** at the N^1 atom of the triazole ring. This follows from the fact that the ^{1}H NMR spectrum of the alkylation product, compound **IXa**, contained no NH signal (δ 13.18 ppm in the spectrum of **VIIIa**). The linearly fused structure of compound **VIIIa** is confirmed by the fact that the product of its alkylation with allyl bromide is not identical to compound **IVa**, which would be obtained by alkylation of the corresponding angular isomer (**Xa**).

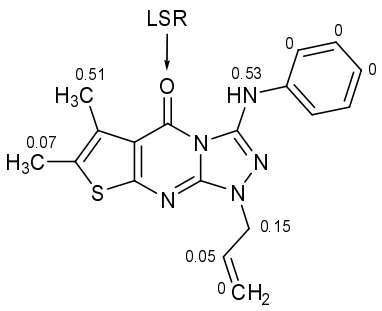
An additional proof for the assumed structure of compound **IXa** was obtained by measuring its ^{1}H NMR spectrum, as well as the spectrum of its angularly fused isomer **IVa**, in the presence of a lanthanide shift reagent (LSR), $Eu(fod)_3$. The lanthanide-induced shifts are given below.

Molecules **IXa** and **IVa** possess several possible centers capable of coordinating LSR: carbonyl oxygen atom, amino nitrogen atom, and endocyclic nitrogen atoms. The probability for coordinating LSR is determined mainly by spatial accessibility of the respective center. It is known that secondary aromatic amines weakly coordinate LSR, for the lone electron pair on the nitrogen atom is shielded by aromatic group. Therefore, no LSR coordination at the ArNH nitrogen atom should occur in both compounds. The carbonyl oxygen atoms in molecules **IXa** and **IVa** are comparable in their spatial accessibility. In addition, molecule **IVa** contains a more accessible nitrogen atom in the triazole ring, so that this compound was expected to exhibit larger lanthanide-induced shifts as compared to **IXa**. In fact, the experimental data were in agreement with the expectations. Thus comparison of the lanthanide-induced shifts confirmed the structure of **IXa**.

The structure of compound **IVb** was proved by X-ray analysis (Fig. 1). The tricyclic system $S^1N^{1-4}C^{1-7}$ is almost planar: deviations of particular atoms from the mean-square plane do not exceed 0.037 Å, and the dihedral angles between the central pyrimidine ring $N^1N^2C^{3-6}$ and five-membered rings S^1C^{1-4} and $N^{2-4}C^6C^7$ are as small as 2.2 and 3.4°, respectively. On the other hand, the benzene ring C^{13}–C^{18} is almost orthogonal to the tricyclic system for steric reasons: the corresponding dihedral angle is 79.6°. The bond length distribution in the fused tricyclic system sug-



IVa



IXa

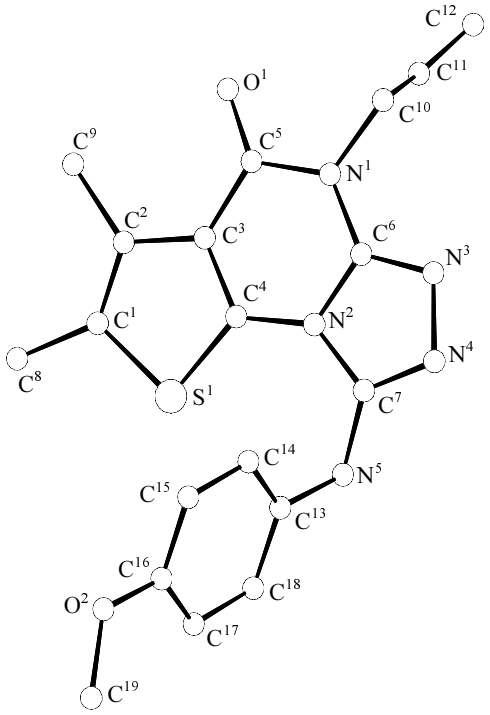


Fig. 1. Structure of the molecule of 4-allyl-1-(4-methoxyphenylamino)-6,7-dimethylthieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-one (**IVb**) according to the X-ray diffraction data (hydrogen atoms are not shown). Principal bond lengths (Å) and bond angles (deg): S^1–C^1 1.747(2), S^1–C^4 1.706(2), N^1–C^5 1.395(3), N^1–C^6 1.378(2), N^2–C^4 1.394(2), N^2–C^6 1.371(2), N^2–C^7 1.390(2), N^3–N^4 1.408(2), N^3–C^6 1.301(3), N^4–C^7 1.305(2), N^5–C^7 1.366(2), N^5–C^{13} 1.430(3); $C^1S^1C^4$ 90.84(9), $C^5N^1C^6$ 122.6(2), $C^4N^2C^6$ 120.4(2), $N^4N^3C^6$ 105.6(2), $N^3N^4C^7$ 108.5(2), $S^1C^1C^2$ 112.4(2), $C^1C^2C^3$ 122.6(2), $C^2C^3C^4$ 112.1(2), $C^2C^3C^5$ 126.7(2), $C^4C^3C^5$ 121.3(2), $S^1C^4C^3$ 112.9(1), $N^2C^4C^3$ 119.9(2), $N^1C^5C^3$ 115.6(2), $N^1C^6N^2$ 120.6(2), $N^1C^6N^3$ 127.5(2), $N^2C^7N^4$ 109.6(2).

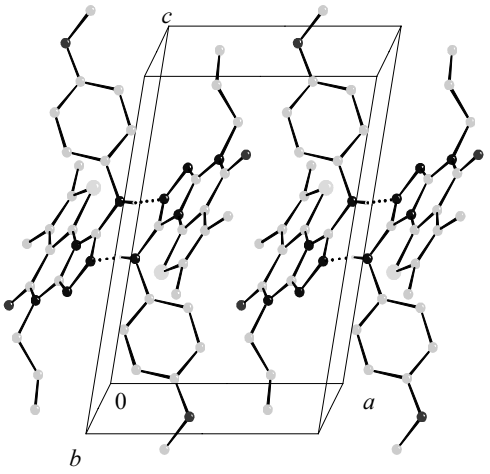


Fig. 2. Packing of molecules of 4-allyl-1-(4-methoxyphenylamino)-6,7-dimethylthieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-one (**IVb**) in crystal. Intermolecular hydrogen bonds N^5–H···N^4 are shown with dotted lines.

gests considerable delocalization of electron density [9]. Molecules of **IVb** in crystal are linked through medium-strength [10] intermolecular hydrogen bonds N^5–H···N^4 [N^5···N^4 3.012(2), N^4···H 2.16, N^5–H 0.86(3) Å; ∠N^4HN^5 169.6(1.7)°] to form centrosymmetric dimers (Fig. 2). The structure of compound **IVb** indicates that the cyclization of thiosemicarbazides **I**, **II**, **V**, and **VI** does not involve Dimroth rearrangement which is known to accompany analogous transformations in some cases [1].

EXPERIMENTAL

The IR spectra of compounds **I**–**IX** were recorded in KBr on a UR-20 spectrometer. The ^{1}H NMR spectra were measured on Varian VXR-300 (300 MHz; DMSO-d_6) and Mercury-400 instruments (400 MHz; **IVa** and **XIa**; $CDCl_3$) using tetramethylsilane as internal reference.

The X-ray diffraction study of a single crystal of compound **IVb** (0.46×0.49×0.49 mm) was performed at room temperature on an Enraf–Nonius CAD-4 automatic four-circle diffractometer (CuK_α irradiation, λ 1.54178 Å; scan rate ratio 2θ/ω = 1.2, θ_{max} 65°; spherical segment $0 \le h \le 9$, $-10 \le k \le 10$, $-14 \le l \le 14$). Total of 3404 reflections were measured. Triclinic crystals with the following unit cell parameters: a = 8.338(1), b = 9.362(2), c = 12.292(2) Å; α = 87.84(1), β = 78.06(1), γ = 84.47(1)°; V = 934.3 Å^3; M 381.5; Z = 2; d_{calc} = 1.36 g/cm^3; μ = 17.5 cm^{-1}; F(000) = 400.0; space group $P1$ (no. 2). The structure was solved by the direct method and was refined by the least-squares procedure in full-matrix anisotropic approximation using CRYSTALS software package [11]; 3164 reflections with $I > 3\sigma(I)$ were used in the refinement (248 refined parameters, 12.6 reflections per parameter). All hydrogen atoms were visualized from the difference synthesis of electron density and were included in the refinement procedure with fixed positional and thermal factors. Only the H^5 atom involved in intermolecular hydrogen bond was refined in isotropic approximation. Chebyshev's weight scheme [12] with five parameters (1.08, –1.54, –0.35, –1.09, –0.45) was applied. The final divergence factors were R = 0.050, R_W = 0.050, GOF 1.029. The residual electron density from the Fourier difference series was 0.28 and –0.42 e/Å^3. Absorption by the crystal was taken into account by the azimuthal scanning technique [13]. The complete set of crystallographic data for compound **IVb** was deposited to the Cambridge Crystallographic Data Center (entry no. 276260).

***N*-R^1-2-(5-R^2-6-R^3-3-allyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazine-1-carbothioamides I and II (*general procedure*).** A solution of 0.015 mol of the corresponding isothiocyanate in 20 ml of ethanol was added to 0.01 mol of 5-R^2-6-R^3-3-allyl-2-hydrazinothieno[2,3-*d*]pyrimidin-4(3*H*)-one in 50 ml of ethanol. The mixture was left to stand for 12 h, and the precipitate was filtered off and washed with ethanol and diethyl ether.

2-(3-Allyl-4-oxo-5,6-tetramethylene-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-*N*-phenylhydrazine-1-carbothioamide (Ia). Yield 3.37 g (82%), mp 177–179°C. IR spectrum, ν, cm^{-1}: 3130, 3170, 2950 (NH); 1680 (C=O); 1615, 1575 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.76 m (4H, CH_2); 2.65–2.81 m (4H, CH_2); 4.66 d (2H, CH_2, J = 2.4 Hz); 5.06 d (1H, CH, J = 18.0 Hz); 5.14 d (1H, CH, J = 9.9 Hz); 5.86–6.00 m (1H, CH); 7.16 t (1H, H_{arom}, J = 7.8 Hz); 7.33 t (2H, H_{arom}, J = 8.1 Hz); 7.42–7.44 m (2H, H_{arom}); 9.31 s, 9.61 s, and 9.76 s (1H each, NH). Found, %: C 58.31; H 5.11; N 16.93; S 15.47. $C_{20}H_{21}N_5OS_2$. Calculated, %: C 58.37; H 5.14; N 17.02; S 15.58.

2-(3-Allyl-4-oxo-5,6-tetramethylene-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-*N*-(4-methoxyphenyl)-hydrazine-1-carbothioamide (Ib). Yield 3.75 g (85%), mp 176–178°C (from alcohol). IR spectrum, ν, cm^{-1}: 3260, 2960 (NH); 1690 (C=O); 1550 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.76 m (4H, CH_2); 2.65–2.81 m (4H, CH_2); 3.74 s (3H, OCH_3); 4.66 d (2H, CH_2, J = 3.6 Hz); 5.05 d (1H, CH, J = 17.7 Hz); 5.13 d (1H, CH, J = 10.2 Hz); 5.87–5.98 m (1H, CH); 6.89 d (2H, H_{arom}, J = 9.0 Hz); 7.26 d (2H, H_{arom}, J = 6.9 Hz); 9.29 s, 9.53 s, and 9.66 s (1H each, NH). Found, %: C 57.04; H 5.19; N 15.76; S 14.39. $C_{21}H_{23}N_5O_2S_2$. Calculated, %: C 57.12; H 5.25; N 15.86; S 14.52.

Ethyl 4-{[2-(3-allyl-4-oxo-5,6-tetramethylene-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazino]-carbonothioylamino}benzoate (Ic). Yield 4.11 g (85%), mp 174–176°C. IR spectrum, ν, cm^{-1}: 3325, 3250, 3170, 2960 (NH); 1730, 1710 (C=O); 1615, 1560 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.31 t (3H, CH_3, J = 7.5 Hz); 1.72–1.77 m (4H, CH_2); 2.65–2.81 m (4H, CH_2); 4.30 q (2H, CH_2, J = 6.9 Hz); 4.67 m (2H, CH_2); 5.05 d (1H, CH, J = 18.0 Hz); 5.15 d (1H, CH, J = 9.9 Hz); 5.86–5.98 m (1H, CH); 7.72 d (2H, H_{arom}, J = 7.8 Hz); 7.92 d (2H, H_{arom}, J = 8.7 Hz); 9.34 s, 9.79 s, and 9.99 s (1H each, NH). Found, %: C 57.07; H 5.13; N 14.38; S 13.18. $C_{23}H_{25}N_5O_3S_2$. Calculated, %: C 57.12; H 5.21; N 14.48; S 13.26.

2-(3-Allyl-5,6-dimethyl-4-oxo-3,4-dihydrothieno-[2,3-*d*]pyrimidin-2-yl)-*N*-phenylhydrazine-1-carbothioamide (IIa). Yield 2.78 g (72%), mp 183–184°C. IR spectrum, ν, cm^{-1}: 3330, 3250, 3180 (NH); 1710 (C=O); 1620, 1560 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3); 2.32 s (3H, CH_3); 4.67 m (2H, CH_2); 5.07 d (1H, CH, J = 17.7 Hz); 5.15 d (1H, CH, J = 11.1 Hz); 5.86–5.99 m (1H, CH); 7.16 t (1H, H_{arom}, J = 6.9 Hz); 7.33 t (2H, H_{arom}, J = 8.4 Hz); 7.43–7.45 m (2H, H_{arom}); 9.32 s, 9.63 s, and 9.77 s (1H each, NH). Found, %: C 56.02; H 4.93; N 18.14; S 16.57. $C_{18}H_{19}N_5OS_2$. Calculated, %: C 56.08; H 4.97; N 18.17; S 16.64.

1-(3-Allyl-5,6-dimethyl-4-oxo-3,4-dihydrothieno-[2,3-*d*]pyrimidin-2-yl)-*N*-(4-methoxyphenyl)hydrazine-1-carbothioamide (IIb). Yield 3.37 g (81%), mp 164–166°C. IR spectrum, ν, cm^{-1}: 3360, 3270, 3170 (NH); 1710 (C=O); 1610, 1560 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3); 2.32 s (3H, CH_3); 3.74 s (3H, OCH_3); 4.66 d (2H, CH_2, J = 3.6 Hz); 5.07 d (1H, CH, J = 17.1 Hz); 5.14 d (1H, CH, J = 10.5 Hz); 5.88–5.97 m (1H, CH); 6.89 d (2H, H_{arom}, J = 9.0 Hz); 7.27 d (2H, H_{arom}, J = 6.9 Hz); 9.27 s, 9.53 s, and 9.64 s (1H each, NH). Found, %: C 54.67; H 5.01; N 16.72; S 15.43. $C_{19}H_{21}N_5O_2S_2$. Calculated, %: C 54.92; H 5.09; N 16.85; S 15.43.

Ethyl 4-{[2-(3-allyl-5,6-dimethyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazino]carbonothioylamino}benzoate (IIc). Yield 1.65 g (36%), mp 128–130°C. IR spectrum, ν, cm^{-1}: 3240, 3010 (NH); 1720, 1700 (C=O); 1620, 1575 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.31 t (3H, CH_3, J = 6.9 Hz); 2.28 s (3H, CH_3); 2.33 s (3H, CH_3); 4.30 q (2H, CH_2, J = 7.2 Hz); 4.68 m (2H, CH_2); 5.07 d (1H, CH, J = 16.8 Hz); 5.16 d (1H, CH, J = 10.5 Hz); 5.86–6.00 m (1H, CH); 7.73 d (2H, H_{arom}, J = 7.2 Hz); 7.92 d (2H, H_{arom}, J = 8.4 Hz); 9.32 s, 9.80 s, and 9.97 s (1H each, NH). Found, %: C 55.03; H 5.01; N 15.27; S 14.02. $C_{21}H_{23}N_5O_3S_2$. Calculated, %: C 55.12; H 5.07; N 15.31; S 14.02.

1-(R^1-amino)-6-R^2-7-R^3-thieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-ones III and IV (*general procedure*). A suspension of 5 mmol of thiosemicarbazide **I** or **II**, 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 h under reflux. The precipitate was filtered off and washed on a filter with ethanol and diethyl ether.

4-Allyl-1-phenylamino-6,7-tetramethylene-thieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-

one (IIIa). Yield 1.25 g (66%), mp 215–217°C (from ethanol). IR spectrum, ν, cm^{-1}: 3190, 2960 (NH); 1690 (C=O); 1610, 1570 (C=N). ^1H NMR spectrum, δ, ppm: 1.75 m (4H, CH_2), 2.67–2.88 m (4H, CH_2), 4.73 d (2H, CH_2, J = 4.8 Hz), 5.20 d (1H, CH, J = 10.2 Hz), 5.27 d (1H, CH, J = 17.1 Hz), 5.93–6.05 m (1H, CH), 6.82–6.87 m (3H, H_{arom}), 7.20 t (2H, H_{arom}, J = 7.5 Hz), 8.70 s (1H, NH). Found, %: C 63.61; H 5.02; N 18.49; S 8.38. $C_{20}H_{19}N_5OS$. Calculated, %: C 63.64; H 5.07; N 18.55; S 8.49.

4-Allyl-1-(4-methoxyphenylamino)-6,7-tetramethylenethieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-one (IIIb). Yield 1.63 g (80%), mp 168–170°C (from ethanol). IR spectrum, ν, cm^{-1}: 3240, 2960 (NH); 1690 (C=O); 1610, 1560 (C=N). ^1H NMR spectrum, δ, ppm: 1.75 m (4H, CH_2), 2.68–2.88 m (4H, CH_2), 3.68 s (3H, OCH_3), 4.72 d (2H, CH_2, J = 4.8 Hz), 5.19 d (1H, CH, J = 11.7 Hz), 5.25 d (1H, CH, J = 17.4 Hz), 5.92–6.04 m (1H, CH), 6.81 s (4H, H_{arom}), 8.49 s (1H, NH). Found, %: C 61.87; H 5.16; N 17.09; S 7.82. $C_{21}H_{21}N_5O_2S$. Calculated, %: C 61.90; H 5.19; N 17.19; S 7.87.

Ethyl 4-(4-allyl-6,7-tetramethylene-5-oxo-4,5-dihydrothieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-1-ylamino)benzoate (IIIc). Yield 1.51 g (67%), mp 183–185°C (from ethanol). IR spectrum, ν, cm^{-1}: 2960 (NH); 1720, 1690 (C=O); 1610, 1570 (C=N). ^1H NMR spectrum, δ, ppm: 1.29 t (3H, CH_3, J = 6.9 Hz), 1.74 m (4H, CH_2), 2.67–2.89 m (4H, CH_2), 4.25 q (2H, OCH_2, J = 7.2 Hz), 4.74 d (2H, CH_2, J = 5.4 Hz), 5.21 d (1H, CH, J = 10.2 Hz), 5.28 d (1H, CH, J = 17.1 Hz), 5.93–6.05 m (1H, CH), 6.90 d (2H, H_{arom}, J = 9.0 Hz), 7.81 d (2H, H_{arom}, J = 8.7 Hz), 9.32 s (1H, NH). Found, %: C 61.39; H 5.04; N 15.49; S 7.09. $C_{23}H_{23}N_5O_3S$. Calculated, %: C 61.45; H 5.16; N 15.58; S 7.13.

4-Allyl-6,7-dimethyl-1-(phenylamino)thieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-one (IVa). Yield 1.02 g (58%), mp 235–237°C (from ethanol). IR spectrum, ν, cm^{-1}: 3230, 3190, 3125, 3050 (NH); 1675 (C=O); 1595 (C=N). ^1H NMR spectrum, δ, ppm: in DMSO-d_6: 2.30 s (3H, CH_3), 2.37 s (3H, CH_3), 4.74 d (2H, CH_2, J = 5.4 Hz), 5.20 d (1H, CH, J = 10.8 Hz), 5.27 d (1H, CH, J = 17.1 Hz), 5.93–6.06 m (1H, CH), 6.83–6.88 m (3H, H_{arom}), 7.20 t (2H, H_{arom}, J = 7.5 Hz), 8.73 s (1H, NH); in $CDCl_3$: 2.29 s (3H, CH_3), 2.44 s (3H, CH_3), 4.85 d (2H, CH_2, J = 4.0 Hz), 5.30 d (1H, CH, J = 12.0 Hz), 5.44 d (1H, CH, J = 16.0 Hz), 6.01–6.10 m (1H, =CH), 6.81–6.88 m (3H, H_{arom}), 7.12 t (2H, H_{arom}, J = 8.0 Hz), 7.45 br.s (1H, NH); in $CDCl_3$/LSR: 2.45 s (3H, CH_3), 2.76 s (3H, CH_3), 5.65 d (2H, CH_2, J = 4.0 Hz), 6.04–6.16 m (2H, $=CH_2$), 6.85–7.16 m (6H, H_{arom}, CH), 8.95 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.71, 13.05, 43.96, 115.65, 118.04, 118.08, 120.83, 128.71, 129.79, 130.21, 132.20, 137.23, 143.87, 144.78, 147.17, 156.41. Found, %: C 61.49; H 4.78; N 19.87; S 9.09. $C_{18}H_{17}N_5OS$. Calculated, %: C 61.52; H 4.88; N 19.93; S 9.12.

4-Allyl-1-(4-methoxyphenylamino)-6,7-dimethylthieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-5(4*H*)-one (IVb). Yield 1.35 g (71%), mp 207–209°C (from ethanol). IR spectrum, ν, cm^{-1}: 3210, 2960 (NH); 1695 (C=O); 1625, 1600 (C=N). ^1H NMR spectrum, δ, ppm: 2.31 s (3H, CH_3), 2.37 s (3H, CH_3), 3.68 s (3H, OCH_3), 4.72 d (2H, CH_2, J = 5.4 Hz), 5.19 d (1H, CH, J = 10.2 Hz), 5.26 d (1H, CH, J = 17.7 Hz), 5.91–6.05 m (1H, CH), 6.82 s (4H, H_{arom}), 8.51 s (1H, NH). Found, %: C 59.78; H 4.95; N 18.27; S 8.39. $C_{19}H_{19}N_5O_2S$. Calculated, %: C 59.83; H 5.02; N 18.36; S 8.41.

Ethyl 4-(4-allyl-6,7-dimethyl-5-oxo-4,5-dihydrothieno[2,3-*d*][1,2,4]triazolo[3,4-*b*]pyrimidin-1-ylamino)benzoate (IVc). Yield 1.31 g (62%), mp 192–193°C (from ethanol). IR spectrum, ν, cm^{-1}: 3000, 2950 (NH); 1720, 1690 (C=O); 1615, 1580 (C=N). ^1H NMR spectrum, δ, ppm: 1.29 t (3H, CH_3, J = 7.2 Hz), 2.31 s (3H, CH_3), 2.38 s (3H, CH_3), 4.25 q (2H, CH_2, J = 6.9 Hz), 4.75 d (2H, CH_2, J = 4.8 Hz), 5.21 d (1H, CH, J = 10.2 Hz), 5.29 d (1H, CH, J = 17.7 Hz), 5.94–6.06 m (1H, CH), 6.92 d (2H, H_{arom}, J = 8.4 Hz), 7.82 d (2H, H_{arom}, J = 8.4 Hz), 9.35 s (1H, NH). Found, %: C 59.49; H 4.91; N 16.46; S 7.49. $C_{21}H_{21}N_5O_3S$. Calculated, %: C 59.56; H 5.00; N 16.54; S 7.57.

***N*-R^1-2-(5-R^2-6-R^3-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazine-1-carbothioamides V and VIa–VIc** were described in [14].

***N*-R^1-2-(5-R^2-6-R^3-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazine-1-carbothioamides Vd and Ve (*general procedure*).** A solution of 0.015 mol of the corresponding isothiocyanate in 20 ml of ethanol was added to a suspension of 2.36 g (0.01 mol) of 2-hydrazino-5,6-tetramethylenethieno[2,3-*d*]pyrimidin-4(3*H*)-one in 50 ml of ethanol. The mixture was heated for 2 h under reflux and cooled, and the precipitate was filtered off and washed with ethanol and diethyl ether.

***N*-Allyl-2-(4-oxo-5,6-tetramethylene-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)hydrazine-1-car-**

bothioamide (Vd). Yield 3.29 g (72%), mp > 300°C. IR spectrum, ν, cm^{-1}: 3320, 3180, 2965 (NH); 1685 (C=O); 1630, 1565 (C=N). ^1H NMR spectrum, δ, ppm: 1.75 m (4H, CH_2), 2.63–2.78 m (4H, CH_2), 4.09 m (2H, CH_2), 5.03 d (1H, CH, J = 9.0 Hz), 5.14 d (1H, CH, J = 17.1 Hz), 5.55–5.58 m (1H, CH), 8.36 m (1H, NH), 8.46 m (1H, NH), 9.31 (1H, NH), 11.01 br.s (1H, NH). Found, %: C 50.06; H 5.09; N 20.85; S 19.16. $C_{14}H_{17}N_5OS_2$. Calculated, %: C 50.13; H 5.11; N 20.88; S 19.12.

***N*-Methyl-2-(4-oxo-5,6-tetramethylene-3,4-dihydrothieno[2,3-*d*]pyrimi-din-2-yl)hydrazine-1-carbothioamide (Ve).** Yield 3.00 g (97%), mp > 300°C. IR spectrum, ν, cm^{-1}: 3320, 3190, 2960 (NH); 1685 (C=O); 1630, 1570 (C=N). ^1H NMR spectrum, δ, ppm: 1.75 m (4H, CH_2), 2.63–2.78 m (4H, CH_2), 2.78 d (3H, CH_3, J = 4.5 Hz), 8.20 m (1H, NH), 8.46 m (1H, NH), 9.25 m (1H, NH), 11.01 br.s (1H, NH). Found, %: C 46.46; H 4.84; N 22.62; S 20.67. $C_{12}H_{15}N_5OS_2$. Calculated, %: C 46.58; H 4.89; N 22.63; S 20.73.

3-(R^1-Amino)-6-R^2-7-R^3-thieno[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyri-midin-5(1*H*)-ones VII and VIII were synthesized as described above for compounds **III** and **IV**.

3-Phenylamino-6,7-tetramethylenethieno[2,3-*d*]-[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (VIIa). Yield 1.21 g (72%), decomposition point 323–327°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3240, 3190 (NH); 1670 (C=O); 1610, 1580 (C=N). ^1H NMR spectrum, δ, ppm: 1.78 m (4H, CH_2), 2.61–2.84 m (4H, CH_2), 7.02 t (1H, H_{arom}, J = 7.5 Hz), 7.36 t (2H, H_{arom}, J = 7.8 Hz), 7.60 d (2H, H_{arom}, J = 8.1 Hz), 9.66 s and 13.16 br.s (1H each, NH). Found, %: C 60.61; H 4.39; N 20.52; S 9.62. $C_{17}H_{15}N_5OS$. Calculated, %: C 60.52; H 4.48; N 20.76; S 9.50.

3-(4-Methoxyphenylamino)-6,7-tetramethylene-thieno[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (VIIb). Yield 1.49 g (81%), mp 322–324°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3260, 2950 (NH); 1680 (C=O); 1610, 1580 (C=N). ^1H NMR spectrum, δ, ppm: 1.79 m (4H, CH_2), 2.62–2.85 m (4H, CH_2), 3.74 s (3H, OCH_3), 6.93 d (2H, H_{arom}, J = 9.0 Hz), 7.53 d (2H, H_{arom}, J = 9.0 Hz), 9.43 s and 13.00 s (1H each, NH). Found, %: C 58.73; H 4.56; N 19.01; S 8.73. $C_{18}H_{17}N_5O_2S$. Calculated, %: C 58.84; H 4.66; N 19.06; S 8.73.

Ethyl 4-(5-oxo-6,7-tetramethylene-1,5-dihydrothieno[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-3-ylamino)benzoate (VIIc). Yield 1.88 g (92%), mp 228–230°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3210, 2960 (NH); 1725, 1690 (C=O); 1615, 1585 (C=N). ^1H NMR spectrum, δ, ppm: 1.32 t (3H, CH_3, J = 6.9 Hz), 1.78 m (4H, CH_2), 2.60–2.83 m (4H, CH_2), 4.28 q (2H, CH_2, J = 6.9 Hz), 7.65 d (2H, H_{arom}, J = 9.0 Hz), 7.91 d (2H, H_{arom}, J = 8.1 Hz), 9.91 s and 13.21 s (1H each, NH). Found, %: C 58.59; H 4.65; N 17.03; S 7.72. $C_{20}H_{19}N_5O_3S$. Calculated, %: C 58.67; H 4.68; N 17.10; S 7.83.

6,7-Dimethyl-3-phenylaminothieno[2,3-*d*][1,2,4]-triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (VIIIa). Yield 1.18 g (76%), decomposition point 326–330°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3250, 3210 (NH); 1665 (C=O); 1615, 1585 (C=N). ^1H NMR spectrum, δ, ppm: 2.25 s and 2.36 s (3H each, CH_3), 7.04 t (1H, H_{arom}, J = 7.6 Hz), 7.35 t (2H, H_{arom}, J = 7.8 Hz), 7.59 d (2H, H_{arom}, J = 8.1 Hz), 9.66 s and 13.16 br.s (1H each, NH). Found, %: C 57.93; H 4.18; N 22.37; S 10.45. $C_{15}H_{13}N_5OS$. Calculated, %: C 57.86; H 4.21; N 22.49; S 10.30.

3-(4-Methoxyphenylamino)-6,7-dimethylthieno-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (VIIIb). Yield 1.19 g (70%), mp 289–291°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3090, 2970, 2850 (NH); 1690 (C=O); 1620, 1580 (C=N). ^1H NMR spectrum, δ, ppm: 2.25 s and 2.35 s (3H each, CH_3), 3.74 s (3H, OCH_3), 6.93 d (2H, H_{arom}, J = 9.0 Hz), 7.53 d (2H, H_{arom}, J = 9.0 Hz), 9.46 s and 13.00 s (1H each, NH). Found, %: C 56.26; H 4.40; N 20.49; S 9.37. $C_{16}H_{15}N_5O_2S$. Calculated, %: C 56.29; H 4.43; N 20.51; S 9.39.

Ethyl 4-(6,7-dimethyl-5-oxo-1,5-dihydrothieno-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-3-ylamino)-benzoate (VIIIc). Yield 1.82 g (95%), mp 316–318°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3330, 3210 (NH); 1730, 1690 (C=O); 1615, 1580 (C=N). ^1H NMR spectrum, δ, ppm: 1.32 t (3H, $CH_2C\mathbf{H}_3$, J = 7.2 Hz), 2.25 s and 2.35 s (3H each, CH_3), 4.28 q (2H, OCH_2, J = 7.2 Hz), 7.70 d (2H, H_{arom}, J = 8.7 Hz), 7.93 d (2H, H_{arom}, J = 8.7 Hz), 10.00 s and 13.31 s (1H each, NH). Found, %: C 56.27; H 4.39; N 18.13; S 8.28. $C_{18}H_{17}N_5O_3S$. Calculated, %: C 56.38; H 4.47; N 18.27; S 8.36.

1-Allyl-6,7-dimethyl-3-phenylaminothieno-[2,3-*d*][1,2,4]triazolo[4,3-*a*]-pyrimidin-5(1*H*)-one (IXa). A solution of 0.17 ml (2 mmol) of allyl bromide in 5 ml of DMF was added under stirring to a suspension of 0.62 g (2 mmol) of compound **VIIIa** and 0.28 g (2 mmol) of potassium carbonate in 20 ml of DMF. The mixture was heated for 12 h at 60°C, and the

precipitate was filtered off and washed on a filter with hot ethanol and diethyl ether. Yield 0.26 g (37%), mp 231–232°C (from ethanol–DMSO). IR spectrum, ν, cm^{-1}: 3300 (NH); 1680 (C=O); 1650, 1590 (C=N). ^1H NMR spectrum, δ, ppm: in DMSO-d_6: 2.30 s and 2.39 s (3H each, CH_3), 4.71 d (2H, CH_2, J = 5.1 Hz), 5.26–5.33 m (2H, =CH_2), 5.95–6.07 m (1H, =CH), 7.05 t (1H, H_{arom}, J = 7.2 Hz), 7.39 d (2H, H_{arom}, J = 8.1 Hz), 7.63 d (2H, H_{arom}, J = 8.1 Hz), 9.75 s (1H, NH); in $CDCl_3$: 2.33 s and 2.45 s (3H each, CH_3), 4.75 d (2H, CH_2, J = 4.0 Hz), 5.32–5.54 m (2H, =CH_2), 5.90–6.20 m (1H, =CH), 7.06 t (1H, H_{arom}, J = 8.0 Hz), 7.37 d (2H, H_{arom}, J = 8.0 Hz), 7.56 d (2H, H_{arom}, J = 8.0 Hz), 9.81 s (1H, NH); in $CDCl_3$/LSR: 2.40 s and 2.96 s (3H each, CH_3), 4.81 d (2H, CH_2, J = 4.0 Hz), 5.33–5.54 m (2H, =CH_2), 6.05–6.35 m (1H, =CH), 7.05 m (1H, H_{arom}), 7.35 m (2H, H_{arom}), 7.54 m (2H, H_{arom}), 10.34 s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.84, 13.35, 48.86, 118.26, 118.71, 122.82, 123.66, 127.91, 129.55, 129.64, 132.32, 138.82, 143.20, 146.02, 156.41. Found, %: C 61.47; H 4.81; N 19.83; S 9.04. $C_{18}H_{17}N_5OS$. Calculated, %: C 61.52; H 4.88; N 19.93; S.12.

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