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Synthesis of Methyl 7-Aryl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylates and Their Reaction with Hydrazine Hydrate

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Abstract—Fusion of methyl 4-(2-thienyl)-2,4-dioxobutanoate with 1*H*-tetrazol-5-amine monohydrate and aromatic aldehyde gave methyl 7-aryl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylates which reacted with an equimolar amount of hydrazine hydrate at 180–190°C under solvent-free conditions to produce 9-aryl-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-ones.

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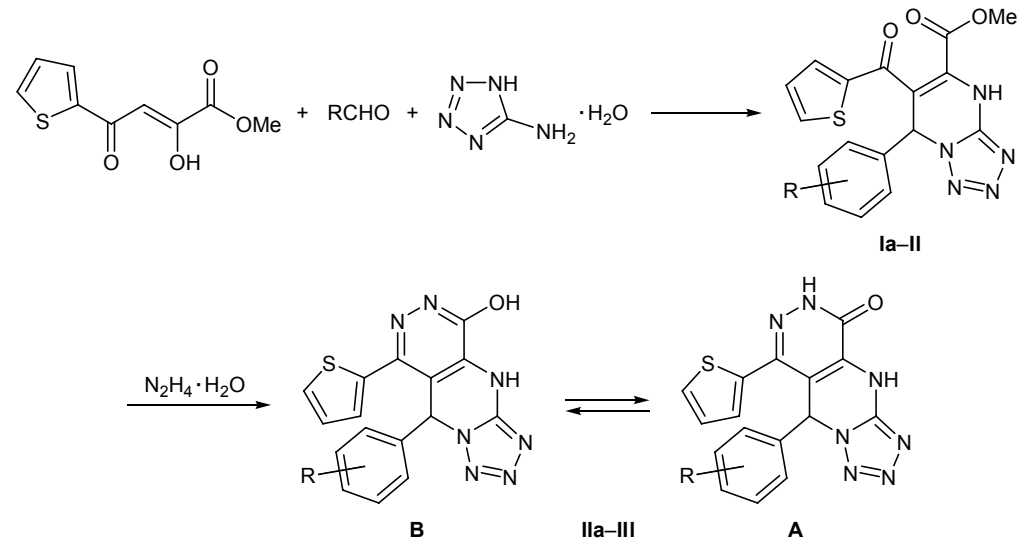
Three-component condensation of methyl 4-R-2,4-dioxobutanoates with aromatic aldehyde and 5-aminotetrazole gives methyl 6-acyl-7-aryl-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylates [1–4]. While continuing our studies on such reactions with 4-hetaryl-2,4-dioxobutanoic acid esters with a view to search for new biologically active compounds among tetrazole derivatives we examined three-component condensation of methyl 4-(2-thienyl)-2,4-dioxobutanoate with 5-aminotetrazole and aromatic aldehydes. By heating the reactants at 130–140°C under solvent-free conditions we obtained the corresponding methyl 7-aryl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylates **Ia**–**Il** (Scheme 1).

Compounds **Ia**–**Il** were isolated as colorless crystalline substances which were readily soluble in DMSO and DMF, soluble in glacial acetic acid on heating, poorly soluble in ethanol, and insoluble in water, diethyl ether, and chloroform. Compounds **Ia**–**Il** displayed in the ^{1}H NMR spectra a three-proton singlet at δ 3.38–3.40 ppm from the methoxy group in position *5* of the heteroring, a singlet at δ 6.59–7.12 ppm from the 7-H proton, a set of signals in the region δ 6.38–7.42 ppm from aromatic protons, signals from protons in the thiophene ring (a triplet at δ 6.89–7.36 ppm and two doublets at δ 7.40–7.67 and 7.81–7.95 ppm), and a downfield singlet at δ 11.02–11.50 ppm from the NH proton in position *4* of the heteroring. The IR spectra of **Ia**–**Il** contained absorption bands belonging to stretching vibrations of the ketone carbonyl group at 1624–1644 cm^{-1}, ester carbonyl group at 1728–1744 cm^{-1}, and N–H bond at 3112–3360 cm^{-1}.

The presence of a γ-dicarbonyl fragment in molecules **Ia**–**Il** makes them convenient for building up fused heterocyclic systems. Reaction of compounds **Ia**–**Il** with an equimolar amount of hydrazine hydrate at 180–190°C under solvent-free conditions led to the formation of 9-aryl-8-(2-thienyl)-4,9-dihydrotetrazolo-[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-ones **IIa**–**IIl** (Scheme 1). Compounds **IIa**–**IIl** are potentially tautomeric, and they can exist as structures **A** and **B**. On the basis of spectral data they were assigned lactam structure **A**. In the ^{1}H NMR spectra of **IIa**–**IIl** we observed a singlet from 9-H at δ 7.00–7.17 ppm, a multiplet centered at δ 6.95–7.24 ppm due to aromatic protons, signals from protons in the thiophene ring (a triplet at δ 6.15–6.98 ppm and two doublets at δ 6.54–7.42 and 7.30–7.55 ppm), a singlet from N^{4}H at δ 11.44–

Scheme 1.



R = 4-HO-3-MeO (**a**), 4-HO-3-EtO (**b**), 3-HO (**c**), 4-HO (**d**), 3,4-$(MeO)_2$ (**e**), 2,4-$(MeO)_2$ (**f**), 2,5-$(MeO)_2$ (**g**), 2,4-Cl_2 (**h**), 4-*i*-Pr (**i**), 4-MeOCO (**j**), 4-*t*-Bu (**k**), 4-EtO (**l**).

11.85 ppm, and a singlet from N^6H at δ 13.18–13.42 ppm. The IR spectra of **IIa**–**III** contained absorption bands due to stretching vibrations of the ketone carbonyl group at 1618–1670 cm^{-1} and N–H bonds at 3120–3264 cm^{-1}.

The molecular and crystalline structures of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate [4] were determined by X-ray analysis of a single crystal which was obtained by slow crystallization from ethanol. The bicyclic fragment in the molecule of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Fig. 1) is bent along the $N^5\cdots C^4$ axis. The dihedral angle between the $C^4C^3C^2N^5$ and $N^1N^2N^3N^4N^5C^1C^4$ planes is 11°, the maximal deviation of atoms from the mean-square planes being 0.015 Å. The endocyclic double bonds are localized without appreciable conjugation effect. All bond lengths and bond angles fall into the corresponding standard ranges. Packing of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate molecules in crystal is primarily determined by formation of intermolecular hydrogen bonds NH···N which give rise to dimers, the interatomic distance $N^5\cdots N^4$ being 2.889(3) Å [$-x + 1$, $-y + 1$, $-z + 2$] (Fig. 2).

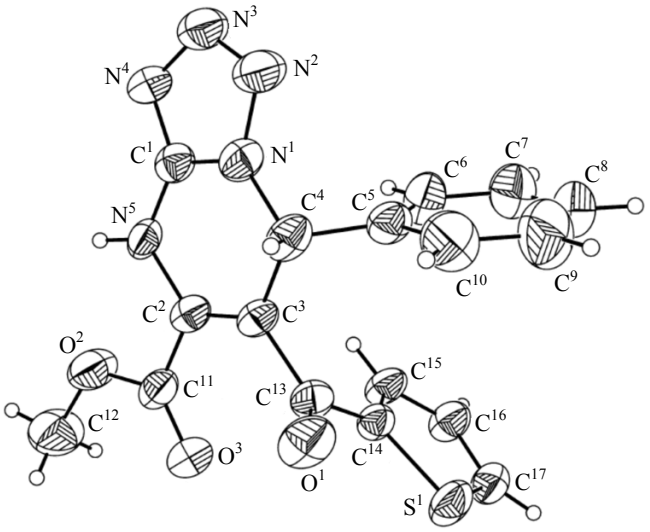


Fig. 1. Structure of the molecule of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

EXPERIMENTAL

The IR spectra were recorded on a Specord M80 spectrometer from samples dispersed in mineral oil. The ^1H NMR spectra were measured on a Bruker DRX 500 instrument at 500.13 MHz from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were recorded on an INCOS 50 spectrometer.

X-Ray analysis of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate. The X-ray diffraction data were acquired on an Xcalibur 3 automatic diffractometer with a CCD

detector acording to standard procedure [MoK_α irradiation, graphite monochromator, ω-scanning, temperature 295(2) K] from a 0.26×0.08×0.02-mm colorless needle-shaped crystal. No correction for absorption was introduced. The structure was solved by the direct method and was refined by the full-matrix least-squares procedure (by F^2) in anisotropic approximation for all non-hydrogen atoms using SHELXTL-97 software package [5]. The positions of hydrogen atoms were determined from the spatial electron density peaks and were refined in isotropic approximation according to the riding model. Triclinic crystal system, space group *P*-1; unit cell parameters: a = 5.9618(9), b = 10.9349(16), c = 13.1581(17) Å; α = 96.821(11)°, β = 97.889(11)°, γ = 91.868(12)°; V = 842.6(2) Å^3; Z = 2. $C_{17}H_{13}N_5O_3S$. Total of 4018 reflection intensities were measured in the range $3.15 < \theta < 26.37°$, 3280 reflections were independent (R_{int} = 0.0470), and 1312 reflections were characterized by $I > 2\sigma(I)$ (235 calculated parameters). The completeness for θ = 25.50° was 95.7%. The low reflectance of the needle-shaped crystal related to its small scattering volume, made it impossible to match a satisfactory weight scheme (S = 0.805). The final divergence factors were R_1 = 0.0407, wR_2 = 0.0326 [for reflections with $I > 2\sigma(I)$] and R_1 = 0.1463, wR_2 = 0.0378 (for all reflections). The maximal and minimal residual electron densities were 0.178 and –0.218 eÅ^{-3}, respectively. The X-ray diffraction data for methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate were deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 826877) and are available at *http://www.ccdc.cam.ac.uk/*.

Methyl 7-(4-hydroxy-3-methoxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ia). A mixture of 0.01 mol of methyl 4-(2-thienyl)-2,4-dioxobutanoate, 0.01 mol of 1*H*-tetrazol-5-amine monohydrate, and 0.01 mol of 4-hydroxy-3-methoxybenzaldehyde was heated for 30 min at 130–140°C until gaseous products no longer evolved. The mixture was cooled to room temperature and treated with ethanol, and the precipitate was filtered off and recrystallized from glacial acetic acid. Yield 2.21 g (53%), mp 234–237°C. IR spectrum, ν, cm^{-1}: 3542 (OH), 3360 (NH), 1728 (C=O, ester), 1632 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.38 s (3H, $COOCH_3$), 3.58 s (3H, OCH_3), 6.59 s (1H, 7-H), 6.77 m (3H, H_{arom}); 7.00 t, 7.60 d, and 7.86 d (3H, 2-thienyl); 9.00 s (1H, OH), 11.17 s (1H, NH). Found, %: C 52.15, 52.35; H 3.56, 3.59; N 16.89, 16.92. $C_{18}H_{15}N_5O_5S$. Calculated, %: C 52.30; H 3.66; N 16.94.

Compounds **Ib**–**Il** were synthesized according to a similar procedure.

Methyl 7-(3-ethoxy-4-hydroxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ib). Yield 2.35 g (55%), mp 229–231°C. IR spectrum, ν, cm^{-1}: 3472 (OH), 3360 (NH), 1728 (C=O, ester), 1624 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.20 t and 3.87 q (3H and 2H, OEt), 3.39 s (3H, OCH_3), 6.60 s (1H, 7-H), 6.75 m (3H, H_{arom}); 7.00 t, 7.60 d, 7.85 d (3H, 2-thienyl); 8.94 s (1H, OH), 11.16 s (1H, NH). Found, %: C 53.38, 53.35; H 3.96, 3.99; N 16.32, 16.36. $C_{19}H_{17}N_5O_5S$. Calculated, %: C 53.39; H 4.01; N 16.38.

Methyl 7-(3-hydroxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ic). Yield 2.26 g (59%), mp 212–213°C. IR spectrum, ν, cm^{-1}: 3552 (OH), 3200 (NH), 1744 (C=O, ester), 1636 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.40 s (3H, OCH_3), 6.55 m (4H, H_{arom}), 6.70 s (1H, 7-H); 7.00 t, 7.55 d, 7.85 d (3H, 2-thienyl); 9.40 s (1H, OH), 11.30 s (1H, NH). Found, %: C 53.28, 53.25; H 3.46, 3.49; N 18.32, 18.23. $C_{17}H_{13}N_5O_4S$. Calculated, %: C 53.26; H 3.42; N 18.27.

Methyl 7-(4-hydroxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Id). Yield 1.98 g (51%), mp 241–243°C. IR spectrum,

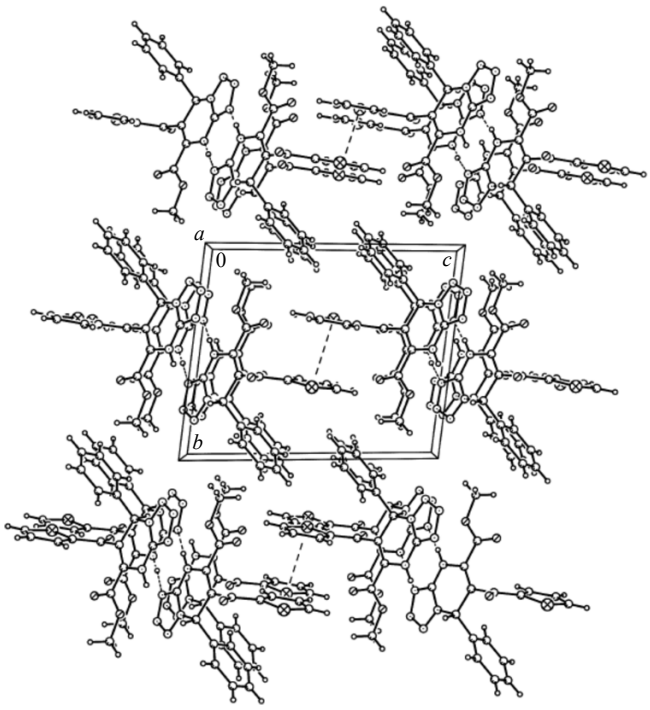


Fig. 2. A fragment of crystal packing of methyl 7-phenyl-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate.

ν, cm^{-1}: 3500 (OH), 3328 (NH), 1736 (C=O, ester), 1632 (C=O). ^1H NMR spectrum, δ, ppm: 3.40 s (3H, OCH_3), 6.75 s (1H, 7-H), 6.60 m (4H, H_{arom}); 7.10 t, 7.65 d, 7.95 d (3H, 2-thienyl); 9.55 s (1H, OH), 11.30 s (1H, NH). Found, %: C 53.26, 53.25; H 3.45, 3.42; N 18.22, 18.24. $C_{17}H_{13}N_5O_4S$. Calculated, %: C 53.27; H 3.41; N 18.26.

Methyl 7-(3,4-dimethoxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ie). Yield 2.11 g (49%), mp 239–241°C. IR spectrum, ν, cm^{-1}: 3280 (NH), 1744 (C=O, ester), 1628 (C=O). ^1H NMR spectrum, δ, ppm: 3.38 s (3H, $COOCH_3$), 3.58 s (3H, OCH_3), 3.62 s (3H, OCH_3), 6.77 s (1H, 7-H), 6.70 m (3H, H_{arom}); 7.03 t, 7.67 d, 7.82 d (3H, 2-thienyl); 11.22 s (1H, NH). Found, %: C 53.32, 53.37; H 4.04, 4.03; N 16.32, 16.34. $C_{19}H_{17}N_5O_5S$. Calculated, %: C 53.39; H 4.01; N 16.38.

Methyl 7-(2,4-dimethoxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (If). Yield 1.96 g (45%), mp 211–213°C. IR spectrum, ν, cm^{-1}: 3112 (NH), 1744 (C=O, ester), 1632 (C=O). ^1H NMR spectrum, δ, ppm: 3.38 s (3H, $COOCH_3$), 3.59 s (3H, OCH_3), 3.64 s (3H, OCH_3), 6.78 s (1H, 7-H), 6.38 m (3H, H_{arom}); 7.00 t, 7.40 d, 7.81 d (3H, 2-thienyl); 11.02 s (1H, NH). Found, %: C 53.33, 53.36; H 4.05, 4.04; N 16.33, 16.35. $C_{19}H_{17}N_5O_5S$. Calculated, %: C 53.39; H 4.01; N 16.38.

Methyl 7-(2,5-dimethoxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ig). Yield 2.99 g (70%), mp 216–218°C. IR spectrum, ν, cm^{-1}: 3112 (NH), 1744 (C=O, ester), 1632 (C=O). ^1H NMR spectrum, δ, ppm: 3.38 s (3H, $COOCH_3$), 3.58 s (3H, OCH_3), 3.68 s (3H, OCH_3), 6.77 s (1H, 7-H), 6.82 m (3H, H_{arom}); 7.00 t, 7.42 d, 7.81 d (3H, 2-thienyl); 11.08 s (1H, NH). Found, %: C 53.35, 53.34; H 4.06, 4.02; N 16.35, 16.36. $C_{19}H_{17}N_5O_5S$. Calculated, %: C 53.39; H 4.01; N 16.38.

Methyl 7-(2,4-dichlorophenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ih). Yield 2.59 g (59%), mp 232–235°C. IR spectrum, ν, cm^{-1}: 3250 (NH), 1740 (C=O, ester), 1640 (C=O). ^1H NMR spectrum, δ, ppm: 3.40 s (3H, $COOCH_3$), 7.12 s (1H, 7-H); 7.25 t, 7.66 d, 7.90 d (3H, 2-thienyl); 7.42 m (3H, H_{arom}), 11.50 s (1H, NH). Found, %: C 46.84, 46.85; H 2.56, 2.52; N 16.06, 16.04. $C_{17}H_{11}Cl_2N_5O_3S$. Calculated, %: C 46.80; H 2.54; N 16.05.

Methyl 7-(4-isopropylphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ii). Yield 2.38 g (58%), mp 245–246°C. IR spectrum, ν, cm^{-1}: 3220 (NH), 1728 (C=O, ester), 1640 (C=O). ^1H NMR spectrum, δ, ppm: 1.07 m and 1.13 m [6H, $CH(CH_3)_2$], 2.75 m [1H, $(CH_3)_2CH$], 3.40 s (3H, OCH_3), 6.76 s (1H, 7-H); 6.89 t, 7.56 d, 7.83 d (3H, 2-thienyl); 7.11 m (4H, H_{arom}), 11.30 s (1H, NH). Found, %: C 58.64, 58.63; H 4.66, 4.67; N 17.11, 17.15. $C_{20}H_{19}N_5O_3S$. Calculated, %: C 58.67; H 4.68; N 17.10.

Methyl 7-(4-methoxycarbonylphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ij). Yield 2.41 g (56%), mp 251–252°C. IR spectrum, ν, cm^{-1}: 3320 (NH), 1728 (C=O, ester), 1644 (C=O). ^1H NMR spectrum, δ, ppm: 3.40 s and 3.77 s (3H each, OCH_3), 6.91 s (1H, 7-H), 7.06 m (4H, H_{arom}); 7.36 t, 7.62 d, 7.83 d (3H, 2-thienyl); 11.39 s (1H, NH). Found, %: C 53.65, 53.63; H 3.54, 3.57; N 16.49, 16.45. $C_{19}H_{15}N_5O_5S$. Calculated, %: C 53.64; H 3.55; N 16.46.

Methyl 7-(4-*tert*-butylphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Ik). Yield 2.36 g (55%), mp 241–243°C. IR spectrum, ν, cm^{-1}: 3220 (NH), 1736 (C=O), 1644 (C=O). ^1H NMR spectrum, δ, ppm: 1.17 s (9H, *t*-Bu), 3.40 s (3H, OCH_3), 6.76 s (1H, 7-H); 7.02 t, 7.59 d, 7.85 d (3H, 2-thienyl); 7.16 m (4H, H_{arom}), 11.31 s (1H, NH). Found, %: C 59.61, 59.60; H 5.01, 5.03; N 16.52, 16.55. $C_{21}H_{21}N_5O_3S$. Calculated, %: C 59.56; H 5.0; N 16.54.

Methyl 7-(4-ethoxyphenyl)-6-(2-thenoyl)-4,7-dihydrotetrazolo[1,5-*a*]pyrimidine-5-carboxylate (Il). Yield 2.15 g (52%), mp 246–247°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1728 (C=O, ester), 1644 (C=O). ^1H NMR spectrum, δ, ppm: 1.25 t and 3.90 q (3H and 2H, OEt), 3.40 s (3H, OCH_3), 6.75 s (1H, 7-H); 7.00 t, 7.60 d, 7.86 d (3H, 2-thienyl); 7.10 m (4H, H_{arom}), 11.40 s (1H, NH). Found, %: C 55.48, 55.51; H 4.12, 4.14; N 17.05, 17.07. $C_{19}H_{17}N_5O_4S$. Calculated, %: C 55.47; H 4.16; N 17.02.

9-(4-Hydroxy-3-methoxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIa). A mixture of 0.01 mol of compound **Ia** and 0.01 mol of hydrazine hydrate was heated for 5–10 min at 180–190°C until gaseous products no longer evolved. The mixture was cooled to room temperature and treated with ethanol, and the precipitate was filtered off and recrystallized from glacial acetic acid. Yield 2.09 g (53%), mp >300°C. IR spectrum, ν, cm^{-1}: 3208 (NH, OH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 3.55 s (3H, OCH_3); 6.53 t, 7.35 d, 7.42 d (3H, 2-thienyl); 7.0 s (1H, 9-H), 7.04 m

(3H, H_{arom}), 9.00 s (1H, OH), 11.56 s (1H, N^4H), 13.28 s (1H, N^6H). Found, %: C 51.66, 51.68; H 3.32, 3.34; N 24.82, 24.84. $C_{17}H_{13}N_7O_3S$. Calculated, %: C 51.64; H 3.31; N 24.80.

Compounds **IIb–III** were synthesized in a similar way.

9-(3-Ethoxy-4-hydroxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIb). Yield 2.29 g (56%), mp 286–288°C. IR spectrum, ν, cm^{-1}: 3208 (NH, OH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 1.20 t and 3.80 q (3H and 2H, OEt), 6.95 m (3H, H_{arom}); 6.54 t, 7.35 d, 7.47 d (3H, 2-thienyl); 7.00 s (1H, 9-H), 9.00 s (1H, OH), 11.65 s (1H, N^4H), 13.29 s (1H, N^6H). Mass spectrum, *m*/*z* (I_{rel}, %): 409 (14.31) $[M]^+$, 348 (100) $[C_{16}H_{11}N_7OS]^+$, 272 (33.93) $[C_{10}H_7N_7OS]^+$. Found, %: C 52.83, 52.85; H 3.65, 3.67; N 23.97, 23.99. $C_{18}H_{15}N_7O_3S$. Calculated, %: C 52.81; H 3.69; N 23.95.

9-(3-Hydroxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIc). Yield 2.22 g (61%), mp 295–297°C. IR spectrum, ν, cm^{-1}: 3220 (NH, OH), 1676 (C=O). ^1H NMR spectrum, δ, ppm: 6.32 t, 6.54 d, 7.34 d (3H, 2-thienyl); 7.03 m (4H, H_{arom}), 7.10 s (1H, 9-H), 9.40 s (1H, OH), 11.75 s (1H, N^4H), 13.34 s (1H, N^6H). Found, %: C 52.62, 52.64; H 3.04, 3.06; N 26.85, 26.87. $C_{16}H_{11}N_7O_2S$. Calculated, %: C 52.60; H 3.03; N 26.83.

9-(4-Hydroxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IId). Yield 2.19 g (60%), mp 304–306°C. IR spectrum, ν, cm^{-1}: 3264 (NH, OH), 1680 (C=O). ^1H NMR spectrum, δ, ppm: 6.50 t, 6.75 d, 7.30 d (3H, 2-thienyl); 7.02 m (4H, H_{arom}), 7.06 s (1H, 9-H), 9.45 s (1H, OH), 11.65 s (1H, N^4H), 13.29 s (1H, N^6H). Found, %: C 52.62, 52.63; H 3.03, 3.04; N 26.84, 26.85. $C_{16}H_{11}N_7O_2S$. Calculated, %: C 52.61; H 3.02; N 26.84.

9-(3,4-Dimethoxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIe). Yield 2.45 g (60%), mp 274–276°C. IR spectrum, ν, cm^{-1}: 3150 (NH), 1676 (C=O). ^1H NMR spectrum, δ, ppm: 3.57 s (3H, OCH_3), 3.64 s (3H, OCH_3); 6.30 t, 6.57 d, 7.30 d (3H, 2-thienyl); 7.04 m (3H, H_{arom}), 7.16 s (1H, 9-H), 11.53 s (1H, N^4H), 13.18 s (1H, N^6H). Found, %: C 52.82, 52.84; H 3.67, 3.70; N 23.96, 23.98. $C_{18}H_{15}N_7O_3S$. Calculated, %: C 52.81; H 3.69; N 23.95.

9-(2,4-Dimethoxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:l,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIf). Yield 2.24 g (55%), mp 291–293°C. IR spectrum, ν, cm^{-1}: 3120 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 3.50 s (3H, OCH_3), 3.62 s (3H, OCH_3); 6.30 t, 6.55 d, 7.41 d (3H, 2-thienyl); 7.17 s (1H, 9-H), 7.04 m (3H, H_{arom}), 11.56 s (1H, N^4H), 13.21 s (1H, N^6H). Mass spectrum, *m*/*z* (I_{rel}, %): 409 (12.38) $[M]^+$, 350 (100) $[C_{16}H_{11}N_7OS]^+$, 272 (6.93) $[C_{10}H_7N_7OS]^+$. Found, %: C 52.80, 52.81; H 3.67, 3.69; N 23.96, 23.97. $C_{18}H_{15}N_7O_3S$. Calculated, %: C 52.82; H 3.68; N 23.96.

9-(2,5-Dimethoxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIg). Yield 2.54 g (62%), mp 290–293°C. IR spectrum, ν, cm^{-1}: 3144 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 3.40 s (1H, OCH_3), 3.50 s (3H, OCH_3); 6.15 t, 6.68 d, 7.39 d (3H, 2-thienyl); 7.08 m (3H_{arom}), 7.15 s (1H, 9-H), 11.61 s (1H, N^4H), 13.22 s (1H, N^6H). Mass spectrum, *m*/*z* (I_{rel}, %): 409 (11.31) $[M]^+$, 350 (100) $[C_{16}H_{11}N_7OS]^+$, 77 (7.41) $[C_6H_5]^+$. Found, %: C 52.83, 52.84; H 3.68, 3.71; N 23.96, 23.97. $C_{18}H_{15}N_7O_3S$. Calculated, %: C 52.81; H 3.69; N 23.95.

9-(2,4-Dichlorophenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIh). Yield 2.75 g (66%), mp 298–299°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 6.98 t, 7.42 d, 7.47 d (3H, 2-thienyl); 7.12 s (1H, 9-H), 7.24 m (3H, H_{arom}), 11.85 s (1H, N^4H), 13.34 s (1H, N^6H). Found, %: C 45.93, 45.94; H 2.16, 2.19; N 23.48, 23.47. $C_{16}H_9ClN_7OS$. Calculated, %: C 45.95; H 2.17; N 23.44.

9-(4-Isopropylphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIi). Yield 2.54 (65%), mp 296–298°C. IR spectrum, ν, cm^{-1}: 3152 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 1.09 d [6H, $(CH_3)_2CH$], 2.77 m [1H, $(CH_3)_2CH$]; 6.80 t, 7.30 d, 7.40 d (3H, 2-thienyl); 7.15 s (1H, 9-H), 7.10 m (4H, H_{arom}), 11.73 s (1H, N^4H), 13.31 s (1H, N^6H). Found, %: C 58.32, 58.34; H 4.36, 4.38; N 25.06, 25.07. $C_{16}H_{17}N_7OS$. Calculated, %: C 58.30; H 4.39; N 25.05.

Methyl 4-[5-oxo-8-(2-thienyl)-4,5,6,9-tetrahydrotetrazolo[1′,5′:1,2]pyrimido[4,5-*d*]pyridazin-9-yl]-benzoate (IIj). Yield 2.64 g (65%), mp >300°C. IR spectrum, ν, cm^{-1}: 3250 (NH), 1665 (C=O). ^1H NMR spectrum, δ, ppm: 3.80 s (3H, OCH_3); 6.80 t, 7.40 d, 7.55 d (3H, 2-thienyl); 7.10 s (1H, 9-H), 7.20 m (4H, H_{arom}), 11.60 s (1H, N^4H), 13.20 s (1H, N^6H). Found, %: C 53.03, 53.04; H 3.24, 3.27; N 24.08, 24.09. $C_{18}H_{13}N_7O_3S$. Calculated, %: C 53.07; H 3.22; N 24.07.

9-(4-*tert*-Butylphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′ : 1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (IIk). Yield 2.67 g (66%), mp 304–306°C. IR spectrum, ν, cm^{-1}: 3200 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 1.15 s (9H, *t*-Bu); 6.74 t, 7.31 d, 7.41 d (3H, 2-thienyl); 7.07 m (4H, H_{arom}), 7.14 s (1H, 9-H), 11.44 s (1H, N^4H), 13.25 s (1H, N^6H). Mass spectrum, *m*/*z* (I_{rel}, %): 405 (14.31) $[M]^+$, 350 (100) $[C_{16}H_{11}N_7OS]^+$, 272 (17.62) $[C_{10}H_7N_7OS]^+$, 134 (33.33) $[t\text{-}BuC_6H_5]^+$. Found, %: C 59.23, 59.24; H 4.75, 4.76; N 24.13, 24.19. $C_{20}H_{19}N_7OS$. Calculated, %: C 59.24; H 4.72; N 24.18.

9-(4-Ethoxyphenyl)-8-(2-thienyl)-4,9-dihydrotetrazolo[1′,5′ : 1,2]pyrimido[4,5-*d*]pyridazin-5(6*H*)-one (III). Yield 1.88 g (61%), mp 273–275°C. IR spectrum, ν, cm^{-1}: 3110 (NH), 1672 (C=O). ^1H NMR spectrum, δ, ppm: 1.30 t and 3.90 q (3H, 2H, OEt); 6.85 t, 7.35 d, 7.45 d (3H, 2-thienyl); 7.10 m (4H, H_{arom}), 7.14 s (1H, 9-H), 11.78 s (1H, N^4H), 13.42 s (1H, N^6H).

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