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Structure of Reaction Products of Substituted [1,3]Thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones with Amines and Hydrazines

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Abstract—Reactions of 2-(4-methylphenyl)[1,3]triazolo[3,2-*b*][1,2,4]thiazol-6(5*H*)-one and 5-benzylidene-2-(4-methylphenyl)[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-one with amines and hydrazines of diverse structures were studied. The structure of the reaction products was established.

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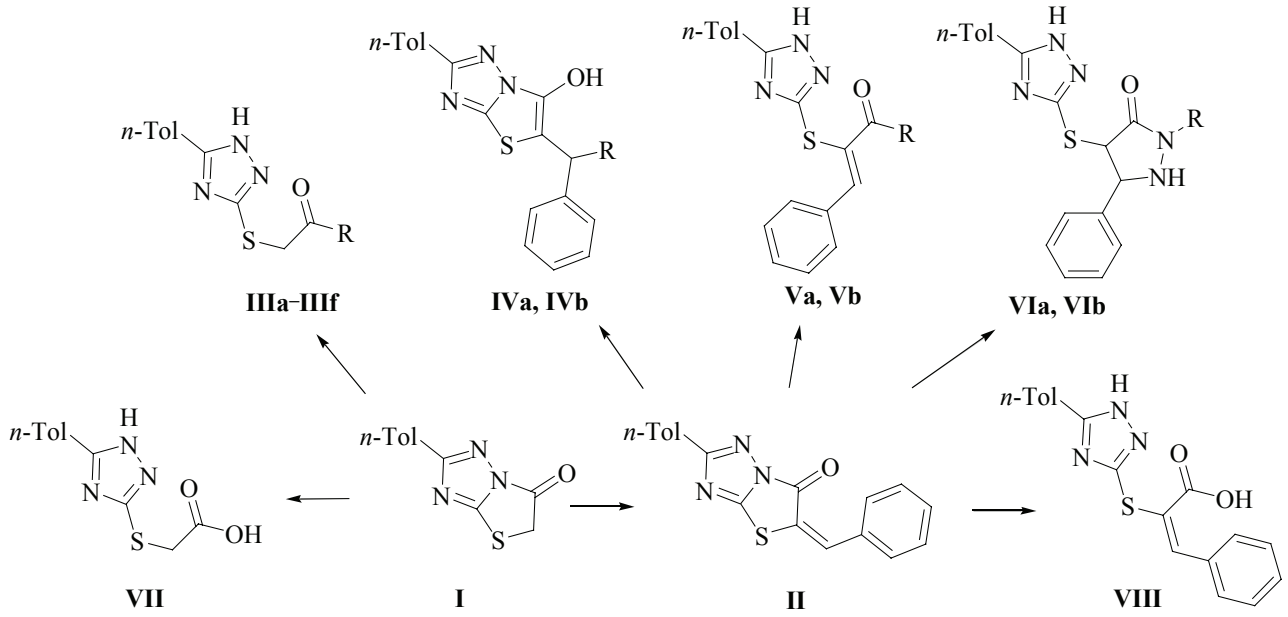
The development of preparation methods of new derivatives of 1,2,4-triazolethiones is an urgent problem since these compounds possess a wide range of physiological activity exhibiting analgesic, vasodilatory, antitumor, bactericidal, and sedative action [1–3].

A special interest is directed to the chemical properties of **[**1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones obtained by a cyclocondensation of 1,2,4-triazole-3-thiones with haloacetic acids, and also of the reaction products of the latter with aldehydes, 5-benzylidene[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones. The published data on the reactions of these heterocyclic systems with amines of various structures are ambiguous. It is reported in [4, 5] on the opening of the lactam ring of the [1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones under the action of aromatic amines and hydrazines with the formation of the corresponding thioacetamides. In the reaction of 5-benzylidene[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones with secondary amines no opening of te lactam ring occurs, and the products of Michael 1,4-addition are formed where an intramolecular hydrogen bond exists between the nitrogen atom of the added amine and the proton of the enol hydroxy group [6–10]. A prolonged heating of [1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones with substituted hydrazines in acetic acid resulted in tricyclic compounds, 3,3a-dihydro-2*H*-pyrazolo[3',4':4,5][1,3]thiazolo[3,2-*b*][1,2,4]triazoles [11].

We formerly proved for the first time by XRD method by an example of 5-(4-methylphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione that the cyclocondensation of triazolethiones with haloacetic acids proceeded regiospecifically with the formation of 2-(4-methylphenyl)[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-one (**I**) and not the isomeric 3-(4-methylphenyl)[1,3]thiazolo[2,3-*c*][1,2,4]triazol-5(6*H*)-one [12]. In the present study we examined the structures of the products of the reactions of [1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones and 5-benzylidene[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones with diverse amines (primary and secondary, cycloaliphatic and heterocyclic) and hydrazines. As model compounds substances **I, II** were used.

The reactions of compound **I** in dioxane with amines (piperidine, morpholine, cyclohexylamine, pyridin-3-ylmethanamine) and hydrazine hydrate at room temperature, and with 3-(trifluoromethyl)aniline at boiling led to the rupture of the C–N bond of the lactam ring and to the formation of the corresponding amides of thioacetic acid **IIIa–IIIf** in 77–91% yields. The reactions of compound **II** with hydrazines, primary and secondary amines at room temperature in dioxane afforded three different com-



III, R = $N(CH_2CH_2)_2CH_2$ (**a**), $N(CH_2CH_2)_2O$ (**b**), $NHCH(CH_2)_5$ (**c**), Py-3-CH_2NH (**d**), $NHNH_2$ (**e**), 3-$CF_3C_6H_4NH$ (**f**); **IV**, R = $N(CH_2CH_2)_2CH_2$ (**a**), $N(CH_2CH_2)_2O$ (**b**); **V**, R = $NHCH(CH_2)_5$ (**a**), Py-3-CH_2NH (**b**); **VI**, R = H (**a**), 4-$CH_3OC_6H_4$ (**b**).

pounds **IV–VI**, whose structure was established from the combination of IR, NMR, and mass spectra. No reaction occurred with aromatic amines even at prolonged boiling.

In the ^{1}H NMR spectra of compounds **IIIa–IIIf** a characteristic downfield signal is observed from the proton of the NH group of the triazole ring in the region 14.0–14.5ppm, which due to the prototropic ring tautomerism [13] appears as two contiguous broadened singlets. In the spectra of compounds **IIIa, IIId, IIIf**, **Va, Vb, VIa** an expected signal of the amide proton is observed. Under the electron impact compounds **III–VI** give as a rule the most intensive ions corresponding to the fragment of the lactam ring [319^+ (**II**)], or to the thiazole fragment formed at the rupture of the S–C bond (191^+).

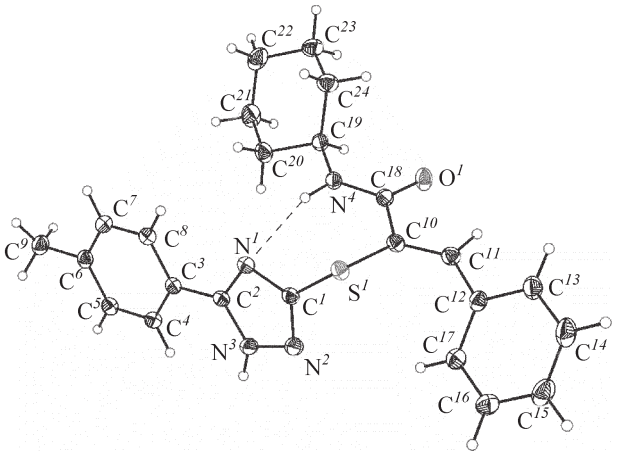
In order to refine the data on the structure of addition products of amines and hydrazines the alkaline hydrolysis was performed of compounds **I, II** providing the corresponding derivatives of thioacetic acids **VII, VIII**. The ^{1}H NMR spectra of compounds **VII, VIII** contain characteristic signals of CH_2 and =CH– groups in the regions 3.94 and 8.09 ppm respectively, and also of the protons of NH groups in the region 14.0–14.5 ppm and COOH in the region 12.5–13.0 ppm.

The structure of the reaction products obtained with the substrate **II** was difficult to establish unambiguously using only spectral data since in the IR spectra the bands of the NH groups of the triazole ring and of the OH group of the enol form may appear in the same region (3200–3100 cm^{-1}), and in the ^{1}H NMR spectrum the proton signals of these groups are observed in a weak field (14.0–14.5 ppm) and easily exchange with water present in the deuterated solvent. Attempting to clear the structure of compound **IVa** we registered 2D spectra ROESY and HMBC, but due to the formation of a strong intramolecular hydrogen bond between the nitrogen atom of the piperidine fragment and the enol proton of the OH group we failed to obseve the expected cross-peaks of the aliphatic protons (the proton signals from the CH_2 group were observed as five broadened singlets)**.** This hydrogen bond is absent in compound **Va** indicating the formation of the corresponding amide derivative as confirms the presence in the ^{1}H NMR spectrum of the signals of the amide hydrogen (7.88 ppm) in the form of a broadened doublet (*J* 3.3 Hz). The structure of compound **Va** was unambiguously proved by XRD analysis. The general view of the molecule of compound **Va** is shown in the figure.

All aromatic rings in the molecule are planar, the cyclohexane fragment is present in the usual chair conformation. The toluene and triazole fragments are located in the same plane and are conjugated, as indicates the length of the C^2–C^3 bond (see the table) that is somewhat shorter than the average value for the conjugated systems (1.476 Å) [14]. The distribution of the bond lengths in the triazole shows precisely that the proton is bound to the

General view of the molecule *N*-cyclohexyl-2-{[5-(4-methylphenyl)-1*H*-1,2,4-triazol-3-yl]sulfanyl}-3-phenylprop-2-enamide (**Va**) the atoms presented as thermal ellipsoids of 50% probability

Bond	Length, Å	Bond	Length, Å
N^4–C^{18}	1.330(2)	N^1–C^1	1.363(2)
C^{10}–C^{18}	1.509(2)	N^2–C^1	1.325(2)
C^{10}–C^{11}	1.345(2)	N^2–N^3	1.364(2)
C^{11}–C^{12}	1.472(2)	N^3–C^2	1.349(2)
C^2–C^3	1.467(2)	N^1–C^2	1.334(2)



Lengths of some bonds in compound **Va**

atom N^3, as has been localized from the difference map of the electron density. The fragment N^4–$C^{18}(O^1)$–C^{10}=C^{11} is planar and is not conjugated with the benzene ring, the torsion angle $C^{10}C^{11}C^{12}C^{13}$ is –143.0(2)°. The conjugation is however absent also in this planar fragment: The bond C^{10}–C^{18} (see the table) is considerably longer then the average value for the conjugated systems (1.464 Å [14]). The N^4 and O^1 atoms of the amide group are involved in the formation of hydrogen bonds. The intramolecular hydrogen bond N^4–H^4···N^1 [N···N 3.022(2), H···N 2.18 Å, NHN angle 156°] apparently stabilizes the conformation observed in the crystal structure of compound **Va**. The bond N^3–H^3···O^1 [N···O 2.732(2), H···O 1.83 Å, NHO angle 176°] connects the molecules into chains parallel to the *b* axis. The other intermolecular interactions in the crystals are governed by the van der Waals forces.

In the ^{1}H NMR spectrum of compound **VIa** obtained by the reaction of compound **II** with hydrazine hydrate гидратом signals of four protons are observed in a wide range of chemical shifts (4.3–9.7 ppm), and three among them are connected in pairs by common vicinal coupling constants. It indicates the formation of a pyrazolidone ring with the prevalence of the keto form. In the spectrum of compound **VIb** only signals of two protons appear as a doublet and a triplet, and the downfield signal is absent. It means that in the formed pyrazolidone ring the *para*-methoxyphenyl substituent is attached to the amide nitrogen atom.

It is presumable from the existing spectral data that the formation of compounds **VIa, VIb** occurs primarily by 1,4-addition of hydrazine along Michael reaction followed by the opening of the lactam ring and simultaneous cyclization to pyrazolidone. The first stage of the reaction apparently proceeds analogously to the conversion of compound **II** into **IV**.

Thus it was shown by the example of compounds **I, II** that **[**1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-ones in reactions with amines form reaction products of diverse structures in keepimg with the nature and the structure of the reagent. In the reaction of 5-benzylidene[1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-one (**II**) with secondary amines stable structures **IV** are formed without the opening of the lactam ring; these structures may be regarded as intramolecular zwitter-ions. In reactions with primary amines and hydrazines the lactam ring is openedwith the formation of the corresponding amides **V** and pyrazolidones **VI**. Amides **III** are formed also in the reactions between amines of various nature and hydrazine and [1,3]thiazolo[3,2-*b*][1,2,4]triazol-6(5*H*)-one (**I**).

EXPERIMENTAL

NMR spectra were registered on a spectrometer Bruker DRX-500 [500.13 (^{1}H), 125.75 MHz (^{13}C)] in DMSO-d_6 at 30°C. As internal reference for measuring the chemical shifts was used the signal of tetramethylsilane (Institute of Organic Chemistry, Russian Academy of Sciences, Moscow). The registering of 2D spectra was carried out by standard Bruker procedures.

Mass spectra were measured on a GC-MS instrument Finnigan MAT INCOS 50, electron impact, ionizing electrons energy 70 eV, ionizing chamber temperature 100–220°C (Institute of Organic Chemistry, Russian Academy of Sciences, Moscow).

IR spectra were recorded on a Fourier spectrophotometer Perkin Elmer in the range 700–4000 cm^{-1} from mulls of substances in mineral oil between KBr plates.

XRD analysis was carried out in the Institute of Organoelemental Compounds, Russian Academy

of Sciences, Moscow. The experimental intensity of reflections were measured on a diffractometer Smart Apex2 CCD, λ(MoK_α) 0.71073 Å, graphite monochromator, ω-scanning at 100 K. The processing of the arrays of the measured intensities was performed along the program APEX2. The structures were solved by the direct method and refined by full-matric least-squares method in the anisotropic approximation for nonhydrogen atoms with respect to F^2_{hkl}. The hydrogen atoms were placed in the geometrically calculated positions and refined in the rider model [U_{iso}(H) = nU_{eq}(C)], where n = 1.5 for carbon atoms of methyl groups, 1.2 for the other carbon atoms. The solution and refining of the structure were carried out by SHELXTL software. The X-ray structural analysis data have been deposited in the Cambridge Crystallographic Data Center (CCDC no. 972922).

Compounds IIIa–IIIf, IVa, IVb, Va, V, VIa, VIb. *General procedure.* Into a flask equipped with a stirrer to a solution of 10 mmol of compound **I** or **II** in 50 mL of dioxane was added 12 mmol of primary secondary amine or hydrazine. The reaction mixture was stirred for 1 h at room temperature (in the case of aromatic amine, 2 h at boiling), then the mixture was poured in water, the separated precipitate was filtered off, washed with water on the filter, and dried.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-1-(piperidin-1-yl)ethanone (IIIa). Yield 2.43 g (77%), mp 178.5–181.5°C (decomp.). IR spectrum, ν, cm^{-1}: 3159 (NH), 1622 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.43 br.s (2H, CH_2), 1.55 br.s (4H, CH_2), 2.35 s (3H, CH_3), 3.45 br.s (4H, NCH_2), 4.20 br.s (2H, SCH_2), 7.31 br.d (2H, H$^{3''',5'''}$, *J* 8.0 Hz), 7.85 d (2H, H$^{2''',6'''}$, *J* 8.0 Hz), 14.26 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 316 [M]$^+$ (24), 191 (23), 126 (100), 118 (19), 116 (16), 112 (20), 97 (81), 91 (17), 83 (92). Found, %: C 60.65; H 6.26; N 17.68. $C_{16}H_{20}N_4OS$. Calculated, %: C 60.73; H 6.37; N 17.71. *M* 316.43.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-1-(morpholin-4-yl)ethanone (IIIb). Yield 2.58 g (81%), mp 215–217°C. IR spectrum, ν, cm^{-1}: 3157 (NH), 1623 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.35 s (3H, CH_3), 3.46 t (2H, CH, *J* 4.5 Hz), 3.56 t (4H, CH_2, *J* 4.5 Hz), 3.62 t (2H, CH_2, *J* 4.5 Hz), 4.20 br.s (2H, CH_2), 7.32 br.s (2H, H$^{3''',5'''}$), 7.86 d (2H, H$^{2''',6'''}$, *J* 8.0 Hz), 14.03 s, 14.32 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.86, 45.90, 65.90, 125.58, 125.85, 129.23, 129.46, 138.76, 151.81, 160.39, 165.53. Mass spectrum, *m*/*z* (I_{rel}, %): 318 [M]$^+$ (20), 191 (94), 128 (54), 118 (63), 117 (50), 86 (100), 56 (58). Found, %: C 59.47; H 5.62; N 17.55. $C_{15}H_{18}N_4O_2S$. Calculated, %: C 56.59; H 5.70, N 17.60. *M* 318.40.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-*N*-cyclohexylacetamide (IIIc). Yield 3 g (91%), mp 207–209°C. IR spectrum, ν, cm^{-1}: 3300 (NH), 1638 (C=O), 1549 (NHC=O). ^{1}H NMR spectrum, δ, ppm: 1.06 m (1H, CH_2), 1.18 d.t (4H, CH_2, *J* 10.0 Hz), 1.49 br.d (1H, CH_2, *J* 11.5 Hz), 1.55–1.63 m (4H, CH_2), 2.36 s (3H, CH_3), 3.52 br.s (1H, CHN), 3.82 s (2H, CH_2S), 7.31 br.s (2H, H$^{3''',5'''}$), 7.84 d (2H, H$^{2''',6'''}$, *J* 7.9 Hz), 7.97 br.s (1H, NH), 14.31 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 330 *[M]*$^+$ *(18), 248 (21),* 232 (32), 191 (25), 140 (100), 118 (53), 99 (81), 82 (89). Found, %: C 61.27; H 6.82; N 16.55. $C_{15}H_{18}N_4O_2S$. Calculated, %: C 61.79; H 6.71; N 16.95. *M* 330.46.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-*N*-(pyridin-3-ylmethyl)acetamide (IIId). Yield 2.95 g (87%), mp 141–144°C. IR spectrum, ν, cm^{-1}: 3320 (NH), 1622 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.36 s (3H, CH_3), 3.95 s (2H, SCH_2), 4.33 d (2H, NCH_2, *J* 5.9 Hz), 7.22 d.d (1H, H$^{5'}$, *J* 4.5, *J* 7.5 Hz), 7.31 d (2H, H$^{3'''',5''''}$, *J* 8.0 Hz), 7.62 br.d (1H, H$^{4'}$, *J* 7.5 Hz), 7.83 d (2H, H$^{2'''',6''''}$, *J* 8.0 Hz), 8.42 d (1H, H$^{6'}$, *J* 4.5 Hz), 8.47 br.s (1H, H$^{2'}$), 8.77 br.t (1H, NH, *J* 5.9 Hz), 14,35 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 339 [M]$^+$ (98), 325 (21), 266 (15), 231 (22), 205 (73), 192 (74), 191 (20), 172 (21), 162 (32), 149 (54), 135 (55), 118 (84), 108 (53), 107 (56), 92 (62), 91 (100), 88 (27), 65 (84). Found, %: C 59.96; H 4.96; N 20.55. $C_{11}H_{13}N_5OS$. Calculated, %: C 60.16; H 5.05; N 20.63. *M* 339.42.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (IIIe). Yield 2.18 g (83%), mp 72–75°C. IR spectrum, ν, cm^{-1}: 3307 (NH), 1659 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 3.82 s (1H, SCH_2), 4.26 br.s (2H, NH_2), 7.30 d (2H, H$^{3''',5'''}$, *J* 8.0 Hz), 7.84 d (2H, H$^{2''',6'''}$, *J* 8.0 Hz), 9.26 br.s (1H, NH), 14.23 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 263 [M]$^+$ (95), 232 (63), 204 (55), 192 (61), 191 (100), 118 (66), 117 (46), 91 (50), 65 (26). Found, %: C 50.08; H 4.86; N 26.53. $C_{11}H_{13}N_5OS$. Calculated, %: C 50.18; H 4.98; N 26.60. *M* 263.32.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-*N*-[3-(trifluoromethyl)phenyl]acetamide (IIIf). Yield 3.57 g (91%), mp 168–170°C (benzene–ethanol). IR spectrum, ν, cm^{-1}: 3268, 3208 (NH), 1682 (C=O), 1556 (NH–C=O). ^{1}H NMR spectrum, δ, ppm:

2.35 s (3H, CH_3), 4.12 br.s (2H, SCH_2), 7.38 br.s (2H, $H^{3'''',5''''}$), 7.42 br.d (1H, $H^{4'}$, *J* 7.9 Hz), 7.57 t (1H, $H^{5'}$, *J* 7.9 Hz), 7.78 br.d (1H, $H^{6'}$, *J* 7.9 Hz), 7.83 d (2H, $H^{2'''',6''''}$, *J* 8.0 Hz), 8.08 s (1H, $H^{2'}$), 10.63 br.s (1H, NH), 14.13 and 14.39 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 392 $[M]^+$ (20), 232 $[M - (NH–C_7H_4F_3)]^+$ (18), 205 (100), 172 (21), 160 (17), 118 (51), 118 (25), 117 (25), 91 (15). Found, %: C 54.98; H 3.76; N 14.24. $C_{18}H_{15}F_3N_4OS$. Calculated, %: C 55.10; H 3.85; N 14.28. *M* 392.41.

2-(4-Methylphenyl)-5-[phenyl(piperidin-1-yl) methyl][1,3]thiazolo[3,2-*b*][1,2,4]triazol-6-ol (IVa). Yield 3.75 g (93%), mp 195–197°C (decomp.). IR spectrum, ν, cm^{-1}: 3149 (OH), 1599 (C=N). ^1H NMR spectrum, δ, ppm: 1.34 br.s (2H, CH_2), 1.53 br.s (2H, CH_2), 1.59 br.s (2H, CH_2) , 2.36 s (3H, CH_3), 3.30 br.s (2H, CH_2), 3.64 br.s (2H, SCH_2), 6.92 s (1H, NCH), 7.33 d (2H, $H^{3',5'}$, *J* 8.0 Hz), 7.37 t (1H, $H^{4''}$, *J* 7.7 Hz), 7.46 t (2H, $H^{3'',5''}$, *J* 7.7 Hz), 7.63 d (2H, $H^{2'',6''}$, *J* 7.7 Hz), 7.86 d (2H, $H^{2',6'}$, *J* 8.0 Hz). ^{13}C NMR spectrum, δ, ppm: 21.0, 24.08, 24.92, 25.34, 42.37, 48.18, 66.41, 125.91, 129.66, 129.30, 128.53, 128.43, 128.34, 130.65, 134.61, 140.02, 165.28. Mass spectrum, *m*/*z* (I_{rel}, %): 404 $[M]^+$ (12), 371 (25), 319 (51), 293 (22), 214 (100), 191 (41). Found, %: C 68.17; H 5.90; N 13.82. $C_{23}H_{24}N_4OS$. Calculated, %: C 68.29; H 5.98; N 13.85. *M* 404.54.

2-(4-Methylphenyl)-5-[morpholin-4-yl(phenyl) methyl][1,3]thiazolo[3,2-*b*][1,2,4]triazol-6-ol (IVb). Yield 3.90 g (96%), mp 166–168°C (decomp.). IR spectrum, ν, cm^{-1}: 3159 (OH), 1599 (C=N). ^1H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.37 br.s (2H, NCH_2), 3.46 br.s (2H, NCH_2), 3.64 br.s (2H, OCH_2), 3.73 br.d (2H, OCH_2), 6.94 s (1H, NCH), 7.30 d (2H, $H^{3',5'}$, *J* 8.0 Hz), 7.36 t (1H, $H^{4''}$, *J* 7.6 Hz), 7.44 t (2H, $H^{3'',5''}$, *J* 7.6 Hz), 7.63 d (2H, $H^{2'',6''}$, *J* 7.6 Hz), 7.84 d (2H, $H^{2',6'}$, *J* 8.0 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 406 $[M]^+$ (44), 373 (16), 320 (100), 293 (18), 216 (34), 191 (33), 160 (23), 134 (42), 131 (20), 117 (21), 102 (12), 90 (5). Found, %: C 59.88; H 5.38; N 13.75. $C_{22}H_{22}N_4O_2S$. Calculated, %: C 65.00; H 5.46; N 13.78. *M* 406.51.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-3-phenyl-*N*-cyclohexylprop-2-enamide (Va). Yield 3.39 g (81%), mp 201–204°C (decomp.). IR spectrum, ν, cm^{-1}: 3320 (NH), 1625 (C=O), 1541 (NH–C=O). ^1H NMR spectrum, δ, ppm: 1.06 m (1H, CH_2), 1.18 d.t (4H, CH_2, *J* 7.0, *J* 10.0 Hz), 1.49 br.d (1H, CH_2, *J* 11.5), 1.55–1.63 m (4H, CH_2), 2.35 s (3H, CH_3), 3.52 br.s (1H, NCH), 7.32 d (2H, $H^{3'''',5''''}$, *J* 7.7 Hz), 7.38 t (1H, $H^{4'}$, *J* 7.4 Hz), 7.46 t (2H, $H^{3',5'}$, *J* 7.4 Hz), 7.67 s (1H, C=CH), 7.73 d (2H, $H^{2',6'}$, *J* 7.4 Hz), 7.82 d (2H, $H^{2'''',6''''}$, *J* 7.7 Hz), 7.88 d (1H, NH, *J* 3.3 Hz) 14.45 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 418 $[M]^+$ (15), 320 $[M - (NH - C_6H_{11})]^+$ (12), 292 $[M - (CONH –C_6H_{11})]$ (17), 228 (100), 191 (97), 161 (10), 146 (24), 134 (66), 118 (46), 98 (49). Found, %: C 68.75; H 6.19; N 13.33. $C_{24}H_{26}N_4OS$. Calculated, %: C 68.87; H 6.26; N 13.39. *M* 418.57.

2-{[3-(4-Methylphenyl)-1*H*-1,2,4-triazol-5-yl] sulfanyl}-*N*-(pyridin-3-ylmethyl)-3-phenylprop-2-enamide (Vb). Yield 3.25 g (76%), mp 203–206°C (decomp.). IR spectrum, ν, cm^{-1}: 3253 (NH), 1634 (C=O), 1538 (NH-C=O). ^1H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 4.35 d (2H, NCH_2, *J* 6.0 Hz), 7.01 d.d (1H, $H^{5''}$, *J* 4.8, *J* 7.7 Hz), 7.33 d (2H, $H^{3'''',5''''}$, *J* 8.0 Hz), 7.40 t (1H, $H^{4'}$, *J* 7.6 Hz), 7.45 d (1H, $H^{4''}$, *J* 7.7 Hz), 7.46 t (2H, $H^{3',5'}$, *J* 7.6 Hz), 7.75 d (2H, $H^{2'',6''}$, *J* 7.6 Hz), 7.80 d (2H, $H^{2'''',6''''}$, *J* 8.0 Hz), 7.89 s (1H, CH=C), 8.31 br.d (1H, $H^{6''}$, *J* 4.7 Hz), 8.40 br.s (1H, $H^{2''}$), 8.91 t (1H, NH, *J* 6.0 Hz), 14.22 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 427 *[M]*$^+$ *(36)*, 395 (15), 336 (17), 319 (24), 237 (100), 191 (57), 134 (47), 118 (44), 92 (79), 80 (40). Found, %: C 67.35; H 4.88; N 16.32. $C_{24}H_{21}N_5OS$. Calculated, %: C 67.43; H 4.95; N 16.38. *M* 427.53.

4-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-5-phenylpyrazolidin-3-one (VIa). Yield 3.02 g (86%), mp 168.5–171°C (decomp.). IR spectrum, ν, cm^{-1}: 3236 (NH), 1668 (C=O). ^1H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 4.38 d (1H, H^4, *J* 6.2 Hz), 4.70 d.d (1H, H^5, *J* 6.2, *J* 7.6 Hz), 5.98 d (1H, H^1, *J* 7.6 Hz), 7.28 t (1H, $H^{4'}$, *J* 7.6 Hz), 7.35 t (2H, $H^{3',5'}$, *J* 7.6 Hz), 7.36 d (2H, $H^{3'''',5''''}$, *J* 7.8 Hz), 7.57 d (2H, $H^{2',6'}$, *J* 7.6 Hz), 7.84 d (2H, $H^{2'''',6''''}$, *J* 7.8 Hz), 9.70 br.s (1H, H^2), 14.20 s, 14.46 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 351 $[M]^+$ (3), 320 $[M - (NH - NH_2)]^+$ (12), 319 (6), 228 (9), 191 (100), 160 (42), 131 (28), 118 (36), 103 (40), 91 (25). Found, %: C 61.45; H 4.76; N 19.87. $C_{18}H_{17}N_5OS$. Calculated, %: C 61.52; H 4.88; N 19.93. *M* 351.43.

2-(4-Methoxyphenyl)-4-{[3-(4-methylphenyl)-1*H*-1,2,4-triazol-5-yl]sulfanyl}-5-phenylpyrazolidin-3-one (VIb). Yield 2.49 g (55%), mp 212–214°C. IR spectrum, ν, cm^{-1}: 3197 (NH), 1659 (C=O). ^1H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 3.76 s (3H, OCH_3), 5.20 d.d (1H, H^4, *J* 6.4, *J* 7.2 Hz), 5.41 d (1H, H^5, *J* 7.2 Hz), 6.99 d (2H, $H^{3',5'}$, *J* 8.9 Hz), 7.15 d (1H, H^1, *J* 6.4 Hz), 7.19 d (2H, $H^{3'''',5''''}$, *J* 8.0 Hz), 7.27 t (2H, $H^{3'',5''}$, *J* 7.7 Hz), 7.29 t (1H, $H^{4''}$, *J* 7.7 Hz), 7.35 d (2H, $H^{2'',6''}$, *J* 7.7 Hz), 7.79 d (2H, $H^{2',6'}$, *J* 8.9 Hz), 7.84 d (2H, $H^{2'''',6''''}$, *J* 8.0 Hz), 14.42 s

(1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 457 *[M]*$^+$ *(2)*, 319 (19), 267 (72), 250 (25), 191 (56), 131 (67), 122 (62), 107 (51), 103 (100), 91 (57), 80 (65). Found, %:C 65.46; H 4.96; N 15.26. $C_{25}H_{23}N_5O_2S$. Calculated, %: C 65.63; H 5.07; N 15.31. *M* 457.56.

Compounds VII, VIII. Into a flask equipped with a stirrer and a thermometer to a solution of 10 mmol of compound **I** or **II** in 50 mL of water was added 30 mmol of NaOH. The reaction mixture wasboiled till a formation of a transparent solution (30 min or 3 h respectively, the mixture was cooled, HCl was added to pH 4–5, the separated precipitate was filtered off, washed with water on the filter, and dried.

{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}acetic acid (VII). Yield 2.46 g (95%), mp 149.5–150.5°C. IR spectrum, ν, cm^{-1}: 3174 (NH), 1682 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.94 s (2H, CH_2), 7.28 d (2H, $H^{3'',5''}$, *J* 7.8 Hz), 7.83 d (2H, $H^{2'',6''}$, *J* 7.8 Hz), 12.81 br.s (1H, COOH), 14.24 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 241 [M]$^+$ (1), 249 (2), 205 (28), 172 (7), 118 (17), 117 (19), 116 (10), 91 (6), 43 (100). Found, %: C 52.57; H 4.57; N 16.73. $C_{11}H_{11}N_3O_2S$. Calculated, %: C 53.00; H 4.45; N 16.86. *M* 249.29.

2-{[5-(4-Methylphenyl)-1*H*-1,2,4-triazol-3-yl] sulfanyl}-3-phenylprop-2-enoic acid (VIII). Yield 2.83 g (84%), mp 224–226°C. IR spectrum, ν, cm^{-1}: 3262 (NH), 1681 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 7.32 br.d (1H, $H^{3''',5'''}$, *J* 8.0 Hz), 7.43 t (1H, $H^{4'}$, *J* 7.0 Hz), 7.47 t (2H, $H^{3',5'}$, *J* 7.0 Hz), 7.79 d (2H, $H^{2',6'}$, *J* 7.0 Hz), 7.82 d (2H, $H^{2''',6'''}$, *J* 8.0 Hz), 8.09 s (1H, CH), 12.80 s (1H, COOH), 14.39 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 337 [M]$^+$ (2), 292 (10), 191 (100), 134 (56), 118 (37), 117 (21), 91 (35). Found, %: C 63.96; H 4.39; N 12.41. $C_{18}H_{15}N_3O_2S$. Calculated, %: C 64.08; H 4.48; N 12.45. *M* 337.40.

REFERENCES

1. Uzgören-Baran, A., Tel, B.C., Sarýgöl, D., Öztürk, E.Ý., Kazkayas, Ý., Okay, G., Ertan, M., and Tozkoparan, B., *Eur. J. Med. Chem.,* 2012, vol. 57, p. 398.
2. Micheli, F., Arista, L., Bonanomi, G., Blaney, F.E., Braggio, S.A., Capelli, M., Checchia, A., Damiani, F., Di-Fabio, R., Fontana, S., Gentile, G., Griffante, C., Hamprecht, D., Marchioro, C., Mugnaini, M., Piner, J., Ratti, E., Tedesco, G., Tarsi, L., Terreni, S., Worby, A., Ashby, C.R. Jr., and Heidbreder, C., *J. Med. Chem.,* 2010, vol. 53, p. 374.
3. Doğdaş, E., Tozkoparan, B., Kaynak, F.B., Eriksson, L., Küpeli, E., Yeşilada, E., and Ertan, M., *Arz.-Forsch. (Drug, Res*.)., 2007, vol. 57, p. 196.
4. Ali, M.I., Mostafa, A.B., and Soliman, A.A., *J. Prakt. Chem.,* 1976, vol. 318, p. 12.
5. Ali, M.I. and Soliman, A.A.-W., *J. Prakt. Chem.,* 1983, vol. 325, p. 869.
6. Tozkoparan, B., Akgun, H., Ertan, M., and Rubsemann, K., *Arch. Pharm.,* 1995, vol. 328, p. 169.
7. Tozkoparan, B., Ayhan, Kilcigil, G., Ertan, R., Ertan, M., Kelicen, P., and Demirdamar, R., *Arz.-Forsch. (Drug, Res.).,* 1999, vol. 49, no. II, p. 1006.
8. Tozkoparan, B., Aktay, G., Yesilada, E., and Ertan, M., *Arz.-Forsch. (Drug, Res.).,* 2001, 51, vol. I, p. 470.
9. Sarhan, Abdelwareth, A.O., ElSherif, Hassan, A.H., Mahmoud, Abdalla, M., Habib, and Osama, M.A., *J. Heterocycl. Chem*., 2008, vol. 45, p. 897.
10. Tozkoparan, B., Gokhan, N., Kupeli, E., Yeilada, E., Ertan, M. *Arz.-Forsch. (Drug, Res.).,* 2004, vol. 54, p. 35.
11. Mohan, J., *Indian, J. Chem. B: Org. Chem. Include. Med. Chem.,* 1998, vol. 37, p. 953.
12. Rzhevskii, A.A., Gerasimova, N.P., Alov, E.M., Kozlova, O.S., Danilova, A.S., Khapova, S.A., Suponitskii, K.Yu. *Izv. Akad. Nauk, Ser. Khim.,* 2012, p. 2116.
13. Minkin, V.I., Garnovskii, A.D., Elguero, J., Katritzky, A.R., and Denisko, O.V., *Adv. Heterocyclic, Chem.,* 2000, vol. 76, p. 157.
14. Allen, F.H., Kennard, O., Watson, D.G., Brammer, L., Orpen, A.G., and Taylor, R., *J. Chem. Soc., Perkin Trans. II*, 1987, p. 1.