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Alkylation of 1,2,4-Triazole-3-thiols with Haloalkanoic Acid Esters

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Abstract—Alkylation of 4,5-disubstituted 4*H*-1,2,4-triazole-3-thiols with methyl chloroformate and ethyl chloroacetate chemoselectively afforded the corresponding *S*-alkyl derivatives, whereas the alkylation of 5-benzyl-4-phenyl-4*H*-1,2,4-triazole-3-thiol with methyl 3-bromopropanoate gave an inseparable mixture of S- and N-alkylation products. Hydrazinolysis of *S*-(5-benzyl-4-phenyl-4*H*-1,2,4-triazol-3-yl) methyl carbonothioate involved anomalous cleavage with formation of the initial 4,5-disubstituted 1,2,4-triazole and methyl hydrazinecarboxylate.

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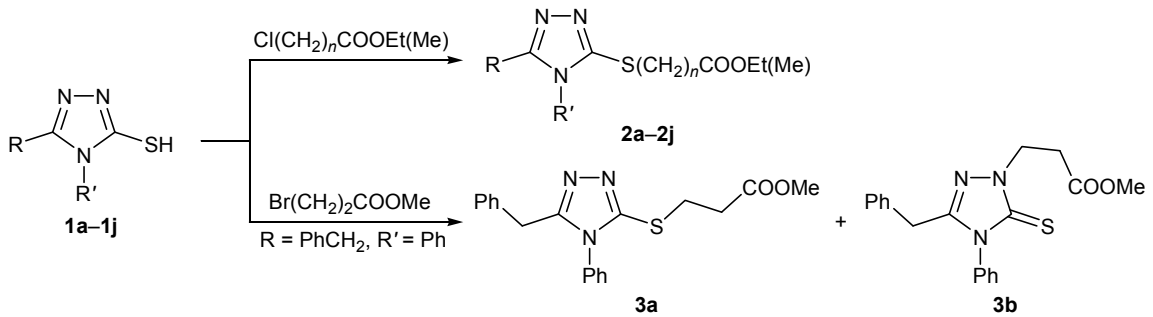
Azole rings are structural fragments of many biologically active compounds which have found applications in pharmacology and medicine. Among the azole series, 1,2,4-triazoles have attracted great interest; some 1,2,4-triazoles are used in medical practice as antifungal and antimicrobial drugs (examples are isavuconazole, paclobutrazol, epoxiconazole, tebuconazole, flusilazole, etc.). Recent studies have shown that 1,2,4-triazole derivatives exhibit a broad spectrum of biological activity and that the nature of substituent on the base ring is the main factor determining their properties. Di- and trisubstituted 1,2,4-triazoles were reported to display antibacterial [1–3], antifungal [4, 5], antitumor [6, 7], anti-inflammatory [8, 9], fungicidal [10, 11], and herbicidal properties [12, 13], inhibit HIV-1 [14], etc. Apart from biological studies, extensive search for new methods of synthesis of 1,2,4-triazoles [15] and their derivatives is performed [16, 17]. Undoubtedly, research in this field is important.

1,2,4-Triazolethiols are known to react with benzyl and benzoyl halides under basic conditions to give exclusively the corresponding S-substituted products [18]. With the goal of extending the series of available

Scheme 1.



1, R′ = Ph, R = $HOCH_2CH_2CH_2$ (**a**), 4-BrC_6H_4 (**b**), Ph (**c**), pyridin-3-yl (**d**), 2-$MeOC_6H_4$ (**e**); R = 2-$MeOC_6H_4$, R′ = CH_2=$CHCH_2$ (**f**); R = 2-MeC_6H_4, R′ = Ph (**g**), CH_2=$CHCH_2$ (**h**); R′ = Ph, R = Fu (**i**), $PhCH_2$ (**j**); **2**, *n* = 1: R′ = Ph, R = $HOCH_2CH_2$ (**a**), 4-BrC_6H_4 (**b**), Ph (**c**), pyridin-3-yl (**d**), 2-$MeOC_6H_4$ (**e**); R = 2-$MeOC_6H_4$, R′ = CH_2=$CHCH_2$ (**f**); R = 2-MeC_6H_4, R′ = Ph (**g**), CH_2=$CHCH_2$ (**h**); R = Fu, R′ = Ph (**i**); *n* = 0, R = $PhCH_2$, R′ = Ph (**j**).

1,2,4-triazoles, in this work we studied the reactions of 4,5-disubstituted 1,2,4-triazole-3-thioles with ethyl chloroacetate, methyl chloroformate, and methyl 3-bromopropanoate. According to the ^{1}H and ^{13}C NMR and X-ray diffraction data (Figs. 1, 2), esters **2a**–**2j** were the only products in the reactions of 1,2,4-triazoles **1a**–**1j** with ethyl chloroacetate and methyl chloroformate (Scheme 1).

The alkylation of **1j** with methyl 3-bromopropanoate led to the formation of an inseparable mixture of two compounds **3a** and **3b** (according to the TLC data). Presumably, this result is determined by relatively high reactivity of the alkylating agent which is capable of reacting with both tautomers of **1j** on prolonged heating. The ^{1}H NMR spectrum of the product mixture clearly showed triplet signals due to protons of methylene groups attached to sulfur and nitrogen at δ 3.31 and 4.43 ppm, respectively. The signals were assigned with account taken of the chemical shift of the SCH_2 protons in **2a** (δ 3.92 ppm) whose structure was unambiguously determined by X-ray analysis, as well as of our previous data according to which CH_2 protons in *N*-alkyl derivatives resonate in the region δ 4.27–4.33 ppm [19, 20].

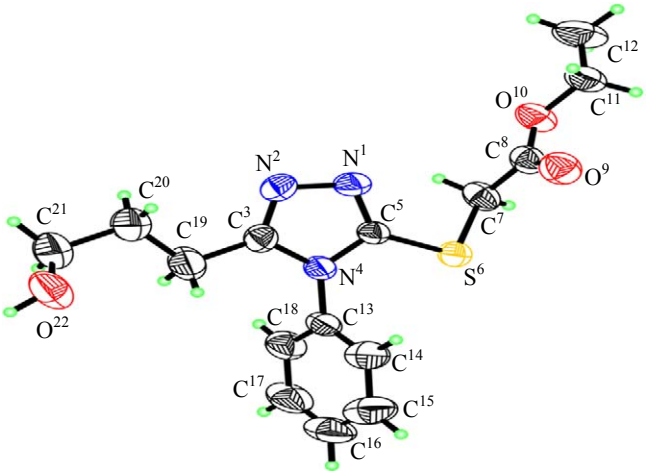


Fig. 1. Structure of the molecule of ethyl {[5-(3-hydroxypropyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (**2a**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

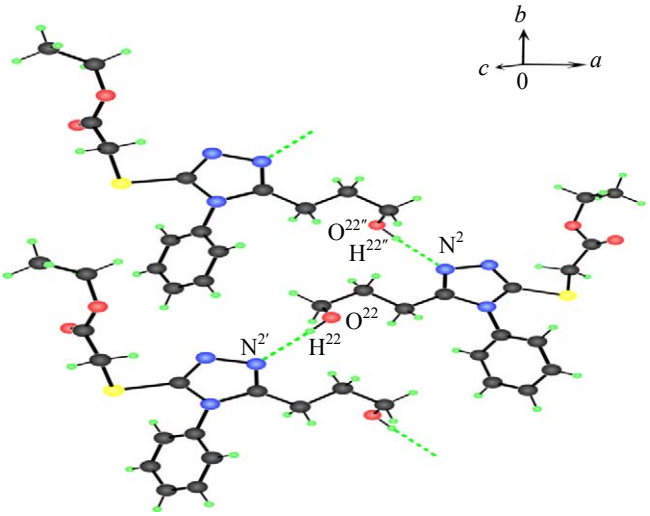
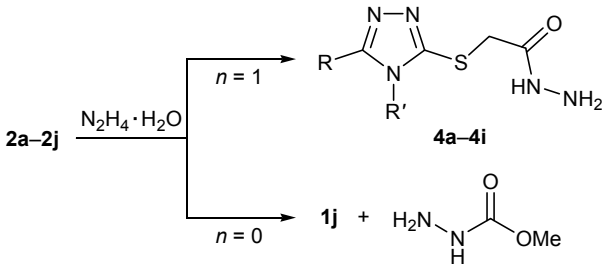


Fig. 2. Hydrogen-bonded chain formed by molecules of ethyl {[5-(3-hydroxypropyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]-sulfanyl}acetate (**2a**) in crystal along the [0 1 0] axis; symmetry operation: *i*: –*x*, 0.5 + *y*, 0.5 – *z*; *ii*: –*x*, 0.5 + *y*, *z*. Hydrogen bonds are shown with dashed lines.

Compounds **2a**–**2j** are convenient substrates for further modification. The reaction of **2a**–**2i** with hydrazine hydrate afforded the corresponding hydrazides **4a**–**4i** in high yield. Surprisingly, in the reaction of **2j** with hydrazine hydrate we isolated initial triazole **1j** and methyl hydrazinecarboxylate (Scheme 2). The most probable reason for anomalous splitting of **2j** is that polar ester group in its molecule is directly linked to the sulfur atom, and nucleophilic attack promotes cleavage of weaker C–S bond with formation of initial thiol and hydrazinecarboxylate.

Scheme 2.



4, R′ = Ph, R = $HOCH_2CH_2CH_2$ (**a**), 4-BrC_6H_4 (**b**), Ph (**c**), pyridin-3-yl (**d**), 2-$MeOC_6H_4$ (**e**); R = 2-$MeOC_6H_4$, R′ = CH_2=$CHCH_2$ (**f**); R = 2-MeC_6H_4, R′ = Ph (**g**), CH_2=$CHCH_2$ (**h**); R = Fu, R′ = Ph (**i**).

Thus, it is advisable to alkylate 4,5-disubstituted 1,2,4-triazoles with α-halo esters. The reaction is chemoselective and is complete in a short time with high yields of the final products.

Biological testing has shown the absence of antibacterial or antimicrobial activity of compounds **2a**–**2i** and generally weak antibacterial activity of **4a**–**4i**. Among the latter, compounds **4a** and **4d** showed a moderate activity against gram-positive (*St. epidermidis*) and gram-negative bacteria (*E. coli*); therefore, they deserve some attention, and search for new biologically active compounds in the series of 1,2,4-triazoles is reasonable.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-300 spectrometer at 300 and 75 MHz, respectively, using DMSO–CCl_4 (1:3) as solvent. The melting points were measured on a Boetius micro hot stage. Analytical thin-layer chromatography was performed on Silufol UV-254 plates; spots were visualized by treatment with iodine vapor.

The X-ray diffraction data for compound **2a** were obtained at room temperature on an Enraf–Nonius CAD-4 automated diffractometer (Mo K_α radiation, graphite monochromator, θ/2θ scanning). The unit cell parameters (monoclinic crystal system) were determined and refined from 24 reflections in the range $14.00 < \theta < 14.92°$. The structure was solved by the direct method. A correction for absorption was applied by the ψ-scan method [21]. The positions of hydrogen atoms were calculated geometrically and were refined according to the riding model assuming C–H bond length 0.93–0.97 Å and $U_{iso}(H) = 1.2–1.5U_{eq}(C)$. The structure was refined by the full-matrix least-squares method in anisotropic approximation for non-hydrogen atoms and isotropic for hydrogens. All calculations were performed using SHELXTL [22].

Both aromatic rings in molecule **2a** (1,2,4-triazole and phenyl) are almost ideally planar; the maximum deviations of atoms from the mean-square planes does not exceed 0.0047(2) and 0.0066(2) Å, respectively. The 1,2,4-triazole and phenyl ring planes form a dihedral angle of 73.694(4)°. Analysis of thermal vibration ellipsoids and Fourier difference maps indicated the possibility of statistical disordering of the ester group (O^{10}, C^{11}, C^{12}). The final structural model was refined with account taken of disordered positions with populations of 30 and 70%. Molecules **2a** in crystal are linked through $O^{22}–H^{22}\cdots N^2$ hydrogen bonds [2.886(3) Å] to form infinite chains along the [0 1 0] axis, and the chains form a three-dimensional network via van der Waals interactions. The X-ray diffraction data for compound **2a** were deposited to the Cambridge Crystallographic Data Centre (CCDC entry no. 1410455).

Alkylation of 4,5-disubstituted 4*H*-1,2,4-triazole-3-thiols 1a–1j with halo esters (*general procedure*). A mixture of 0.01 mol of 1,2,4-triazole **1a**–**1j**, 0.006 mol of anhydrous potassium carbonate, and 0.01 mol of the corresponding halo ester in 15 mL of anhydrous acetone was stirred for 1 h at room temperature and for 10 h at 50–60°C. The solvent was removed, the crystalline residue was treated with water, and the precipitate was filtered off, washed with water, dried, and recrystallized.

Ethyl {[5-(hydroxypropyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2a). Yield 65%, mp 71–72°C (from H_2O–EtOH, 3:1), R_f 0.56 (EtOH–PhH–hexane, 1:3:3). ^{1}H NMR spectrum, δ, ppm: 1.26 t (3H, $CH_2C\mathbf{H}_3$, J = 7.14 Hz), 1.76 t.t (2H, $C\mathbf{H}_2CH_2OH$, J = 7.5, 6.2 Hz), 2.58 t (2H, 5-CH_2, J = 7.5 Hz), 3.42 t.d (2H, $C\mathbf{H}_2OH$, J = 6.2, 4.5 Hz), 3.93 s (2H, SCH_2), 4.14 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.18 br.t (1H, OH, J = 4.5 Hz), 7.35–7.49 m (2H, H_{arom}), 7.52–7.62 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 21.2, 29.2, 33.7, 59.5, 60.7, 126.8, 129.3, 129.4, 132.8, 148.3, 155.2, 167.2. Found, %: C 56.10; H 6.00; N 13.14; S 10.03. $C_{15}H_{19}N_3O_3S$. Calculated, %: C 56.06; H 5.96; N 13.07; S 9.98.

Ethyl {[5-(4-bromophenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2b). Yield 88%, mp 158°C (from H_2O–EtOH, 2:1), R_f 0.52 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 4.03 s (2H, SCH_2), 4.17 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 7.25–7.30 m (2H, H_{arom}), 7.32–7.39 m (2H, H_{arom}), 7.41–7.46 m (2H, H_{arom}), 7.53–7.58 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 33.6, 40.0, 60.8, 123.2, 125.4, 126.9, 129.1, 129.5, 131.0, 133.4, 150.8, 152.9, 167.0. Found, %: C 51.64; H 3.92; Br 19.15; N 10.49; S 7.72. $C_{18}H_{16}BrN_3O_2S$. Calculated, %: C 51.68; H 3.86; Br 19.10; N 10.45; S 7.67.

Ethyl [(4,5-diphenyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]acetate (2c). Yield 98%, mp 178–180°C (from H_2O–EtOH, 2:5), R_f 0.50 (EtOH–PhH, 2:5). ^{1}H NMR spectrum, δ, ppm: 1.28 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 4.00 s (2H, SCH_2), 4.15 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.95–7.39 m (6H, H_{arom}), 7.45–7.60 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 33.7, 39.0, 39.2, 60.7, 115.9, 117.4, 120.8, 131.3, 131.5, 131.6, 148.6, 152.8, 156.5, 167.2. Found, %: C 63.74; H 5.00; N 12.45; S 9.40. $C_{18}H_{17}N_3O_2S$. Calculated, %: C 63.70; H 5.05; N 12.38; S 9.45.

Ethyl {[4-phenyl-5-(pyridin-3-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2d). Yield 88%, mp 138°C (from H_2O–EtOH, 2:1), R_f 0.48 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 1.30 t (3H, CH_3, J = 7.1 Hz), 4.06 s (2H, SCH_2), 4.18 q (2H, OCH_2, J = 7.1 Hz), 7.27 d.d (1H, C_5H_4N, J = 7.9, 4.8 Hz), 7.37–7.44 m (2H, H_{arom}), 7.53–7.60 m (4H, H_{arom}), 7.68 d.t (1H, C_5H_4N, J = 7.9, 1.9 Hz), 8.49–8.54 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 33.7, 40.0, 60.8, 122.6, 126.2, 127.0, 129.6, 129.8, 133.1, 134.4, 147.9,

149.7, 151.1, 151.7, 167.0. Found, %: C 60.02; H 4.80; N 16.50; S 9.46. $C_{17}H_{16}N_4O_2S$. Calculated, %: C 59.98; H 4.74; N 16.46; S 9.42.

Ethyl {[5-(methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2e). Yield 89%, mp 162°C (from H_2O–EtOH, 2:3), R_f 0.57 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 1.26 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.81 s (3H, OCH_3), 4.03 s (2H, SCH_2), 4.17 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 7.25–7.30 m (2H, H_{arom}), 7.32–7.39 m (2H, H_{arom}), 7.41–7.46 m (2H, H_{arom}), 7.53–7.58 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 33.6, 39.8, 40.0, 60.8, 96.5, 123.2, 124.8, 125.4, 126.9, 129.0, 129.5, 131.2, 133.4, 150.8, 155.9, 167.0. Found, %: C 61.82; H 5.14; N 11.43; S 8.65. $C_{19}H_{19}N_3O_3S$. Calculated, %: C 61.77; H 5.18; N 11.37; S 8.68.

Ethyl {[5-(2-methoxyphenyl)-4-(prop-2-en-1-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2f). Yield 88%, mp 75–76°C (from PhH), R_f 0.52 (EtOH–PhH–hexane, 1:3:3). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 3.84 s (3H, OCH_3), 4.03 s (2H, SCH_2), 4.18 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.41 d.t (2H, NCH_2, J = 5.3, 1.6 Hz), 4.93 d.q (1H, $=CH_2$, J = 17.1, 1.6 Hz), 5.14 d.q (1H, $=CH_2$, J = 10.3, 1.6 Hz), 5.74 d.d.t (1H, =CH, J = 17.1, 10.3, 5.3 Hz), 7.05 t.d (1H, H_{arom}, J = 7.4, 0.9 Hz), 7.10 d.d (1H, H_{arom}, J = 8.4, 0.9 Hz), 7.33 d.d (1H, H_{arom}, J = 7.4, 1.8 Hz), 7.50 d.d.d (1H, H_{arom}, J = 8.4, 7.4, 1.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.6, 34.5, 46.1, 54.9, 60.8, 110.9, 115.9, 117.4, 120.8, 131.3, 131.5, 131.6, 148.6, 152.8, 156.5, 167.2. Found, %: C 57.68; H 5.80; N 12.65; S 9.65. $C_{16}H_{19}N_3O_3S$. Calculated, %: C 57.64; H 5.74; N 12.60; S 9.62.

Ethyl {[5-(2-methylphenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2g). Yield 95%, mp 80–81°C (from H_2O–EtOH, 8:5), R_f 0.59 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 2.28 s (3H, CH_3), 4.03 s (2H, SCH_2), 4.18 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 6.97–7.41 m (6H, H_{arom}), 7.46–7.63 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 20.7, 33.7, 60.7, 125.1, 125.5, 127.6, 128.2, 129.7, 129.8, 130.1, 133.7, 137.1, 149.7, 167.6. Found, %: C 64.62; H 5.38; N 11.55; S 9.00. $C_{19}H_{19}N_3O_2S$. Calculated, %: C 64.57; H 5.42; N 11.89; S 9.07.

Ethyl {[5-(2-methylphenyl)-4-(prop-2-en-1-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2h). Yield 70%, viscous material, R_f 0.50 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 2.28 s (3H, CH_3), 4.03 s (2H, SCH_2), 4.18 q (2H, $C\mathbf{H}_2CH_3$, J = 7.1 Hz), 4.39 d.t (2H, NCH_2, J = 5.3, 1.6 Hz), 4.90 d.q (1H, $=CH_2$, J = 17.1, 1.6 Hz), 5.12 d.q (1H, $=CH_2$, J = 10.3, 1.6 Hz), 5.74 d.d.t (1H, =CH, J = 17.1, 10.3, 5.3 Hz), 6.97–7.41 m (1H, H_{arom}), 7.46–7.63 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 20.7, 33.7, 39.0, 60.7, 124.4, 115.9, 117.4, 120.8, 131.3, 131.5, 131.6, 148.6, 152.8, 156.5, 167.2. Found, %: C 60.58; H 6.07; N 13.30; S 10.05. $C_{16}H_{19}N_3O_2S$. Calculated, %: C 60.54; H 6.03; N 13.24; S 10.10.

Ethyl {[5-(furan-2-yl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetate (2i). Yield 85%, mp 124–125°C (from H_2O–EtOH, 2:3), R_f 0.56 (EtOH–PhH, 1:7). ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, CH_3, J = 6.7 Hz), 4.02 s (2H, SCH_2), 4.17 q (2H, OCH_2, J = 7.1 Hz), 6.22 d (1H, Fu, J = 3.97 Hz), 6.37–6.42 m (1H, Fu), 7.38–7.44 m (2H, H_{arom}), 7.50–7.53 m (1H, Fu), 7.57–7.62 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 33.7, 60.8, 110.6, 110.8, 123.3, 127.1, 129.8, 133.1, 140.9, 143.5, 146.9, 150.1, 166.9. Found, %: C 58.30; H 4.70; N 12.83; S 9.85. $C_{16}H_{15}N_3O_3S$. Calculated, %: C 58.34; H 4.59; N 12.76; S 9.74.

***S*-(5-Benzyl-4-phenyl-4*H*-1,2,4-triazol-3-yl) *O*-methyl carbonothioate (2j).** Yield 71%, mp 143°C (from Et_2O), R_f 0.51 (EtOH–PhH, 1:10). ^{1}H NMR spectrum, δ, ppm: 3.85 s (2H, $PhC\mathbf{H}_2$), 4.04 s (3H, CH_3), 6.83–6.98 m (2H, H_{arom}), 7.05–7.24 m (5H, H_{arom}), 7.36–7.54 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 31.3, 53.8, 126.5, 127.7, 128.2, 128.8, 129.1, 132.9, 133.0, 148.2, 150.7, 169.7. Found, %: C 63.60; H 5.10; N 12.30; S 9.50. $C_{18}H_{17}N_3O_2S$. Calculated, %: C 63.70; H 5.05; N 12.38; S 9.45.

Compounds 3a and 3b (inseparable mixture**).** Following the general alkylation procedure, the reaction of 0.01 mol of 5-benzyl-4-phenyl-4*H*-1,2,4-triazole-3-thiol with 0.01 mol of methyl 3-bromopropanoate in the presence of 0.006 mol of anhydrous potassium carbonate gave 2.9 g of a crystalline product. After repeated fractional recrystallization, the product contained two compounds **3a** and **3b** (TLC) with fairly similar R_f values.

Compounds 4a–4i (*general procedure***).** Hydrazine hydrate, 15 mmol (85% solution), was added to a mixture of 10 mmol of ester **2a**–**2i** and 20 mL of ethanol, and the mixture was stirred for 2 h at room temperature and for 8 h at 50–60°C. The solvent was removed, and the crystalline residue was washed with water, dried, and recrystallized.

2-{[5-(3-Hydroxypropyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4a). Yield 70%, mp 149–150°C (H_2O–EtOH, 3:2), R_f 0.50 (EtOH–PhH, 1:7). ^{1}H NMR spectrum, δ, ppm: 2.58 t (2H,

5-CH_2, J = 7.5 Hz), 3.36–3.49 m (2H, C**H**$_2$$CH_2$OH), 3.93 s (2H, SCH_2), 4.14 q (2H, C**H**$_2$OH, J = 7.14 Hz), 4.18 br.s (1H, OH), 6.10 d (1H, NH_2, J = 3.17 Hz), 6.29 d (1H, NH_2, J = 5.6 Hz), 7.28–7.49 m (2H, H_{arom}), 7.49–7.73 m (3H, H_{arom}), 9.28 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 21.3, 29.2, 33.7, 59.5, 126.9, 129.3, 132.9, 149.2, 155.2, 156.5, 156.9, 167.2. Found, %: C 50.85; H 5.52; N 22.83; S 9.04. $C_{13}H_{17}N_5O_2S$. Calculated, %: C 50.80; H 5.57; N 22.78; S 9.00

2-{[5-(4-Bromophenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4b). Yield 91%, mp 230–232°C (from EtOH), R_f 0.55 (EtOH–benzene, 1:9). ^{1}H NMR spectrum, δ, ppm: 3.87 s (2H, SCH_2), 4.09 br.s (2H, NH_2), 7.25–7.30 m (2H, H_{arom}), 7.41–7.46 m (2H, H_{arom}), 7.52–7.57 m (5H, H_{arom}), 9.29 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.8, 60.8, 123.1, 125.5, 127.1, 129.1, 129.5, 131.1, 133.5, 151.6, 152.9, 165.8. Found, %: C 47.58; H 3.52; N 17.37; S 7.88. $C_{16}H_{14}N_5OS$. Calculated, %: C 47.53; H 3.49; N 17.32; S 7.93.

2-[(4,5-Diphenyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]-acetohydrazide (4c). Yield 97%, mp 201–203°C (from H_2O–EtOH, 1:5), R_f 0.55 (EtOH–PhH, 2:5). ^{1}H NMR spectrum, δ, ppm: 3.78 s (2H, SCH_2), 3.98 br.s (2H, NH_2), 6.90–7.30 m (6H, H_{arom}), 7.44–7.59 m (4H, H_{arom}), 9.27 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.7, 60.7, 115.9, 117.4, 120.8, 131.3, 131.6, 148.6, 151.3, 152.8, 156.5, 167.2. Found, %: C 59.10; H 4.60; N 21.57; S 9.90. $C_{16}H_{15}N_5OS$. Calculated, %: C 59.06; H 4.65; N 21.52; S 9.85.

2-{[4-Phenyl-5-(pyridin-3-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4d). Yield 90%, mp 225°C (from H_2O–EtOH, 1:5), R_f 0.55 (EtOH–PhH–hexane, 3:3:1). ^{1}H NMR spectrum, δ, ppm: 3.87 s (2H, SCH_2), 4.12 br.s (2H, NH_2), 7.27 d.d (1H, C_5H_4N, J = 7.8, 4.8 Hz), 7.38–7.43 m (2H, H_{arom}), 7.53–7.60 m (3H, H_{arom}), 7.66 d.d.d (1H, C_5H_4N, J = 7.8, 2.1, 1.8 Hz), 8.51 d.t (1H, C_5H_4N, J = 4.8, 1.8 Hz), 8.53 d (1H, C_5H_4N, J = 2.1 Hz), 9.29 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.7, 60.9, 115.9, 117.8, 121.8, 131.4, 131.7, 148.6, 149.7, 151.2, 152.8, 156.5, 167.4. Found, %: C 55.15; H 4.40; N 25.80; S 9.95. $C_{15}H_{14}N_6OS$. Calculated, %: C 55.20; H 4.32; N 25.75; S 9.82.

2-{[5-(2-Methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4e). Yield 90%, mp 170°C (from H_2O–EtOH, 2:3), R_f 0.58 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 3.81 s (3H, OCH_3), 4.03 s (2H, SCH_2), 4.10 br.s (2H, NH_2), 7.30–7.35 m (2H, H_{arom}), 7.32–7.39 m (2H, H_{arom}), 7.41–7.46 m (2H, H_{arom}), 7.53–7.58 m (3H, H_{arom}), 9.31 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 60.8, 117.2, 123.2, 124.8, 125.4, 126.9, 129.0, 129.5, 131.2, 133.4, 150.8, 155.9, 167.0. Found, %: C 57.50; H 4.75; N 19.75; S 8.98. $C_{17}H_{17}N_5O_2S$. Calculated, %: C 57.45; H 4.82; N 19.70; S 9.02.

2-{[5-(2-Methoxyphenyl)-4-(prop-2-en-1-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4f). Yield 92%, mp 82–84°C (from H_2O–EtOH, 3:2), R_f 0.55 (EtOH–PhH–hexane, 1:3:1). ^{1}H NMR spectrum, δ, ppm: 3.83 s (3H, OCH_3), 4.10 br.s (2H, NH_2), 4.41 d.t (2H, NCH_2, J = 5.2, 1.7 Hz), 4.91 d.q (1H, =CH_2, J = 17.2, 1.7 Hz), 5.11 d.q (1H, =CH_2, J = 17.2, 1.7 Hz), 5.75 d.d.t (1H, =CH, J = 17.1, 10.3, 5.3 Hz), 7.32–7.51 m (4H, H_{arom}), 9.34 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 34.7, 46.2, 55.1, 110.9, 115.9, 117.5, 120.2, 131.4, 131.5, 131.6, 149.5, 152.9, 156.7, 166.1. Found, %: C 52.70; H 5.33; N 22.00; S 10.00. $C_{14}H_{17}N_5OS$. Calculated, %: C 52.65; H 5.37; N 21.93; S 10.04.

2-{[5-(2-Methylphenyl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4g). Yield 70%, mp 112–113°C (from H_2O–EtOH, 3:2), R_f 0.58 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 4.03 s (2H, SCH_2), 4.10 br.s (2H, NH_2), 6.97–7.41 m (6H, H_{arom}), 7.46–7.63 m (3H, H_{arom}), 9.30 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.7, 60.7, 124.4, 115.9, 117.4, 120.8, 131.3, 131.5, 131.6, 148.6, 152.8, 156.5, 167.2. Found, %: C 60.20; H 5.10; N 20.70; S 9.50. $C_{17}H_{17}N_5OS$. Calculated, %: C 60.16; H 5.05; N 20.63; S 9.45.

2-{[5-(2-Methylphenyl)-4-(prop-2-en-1-yl)-4*H*-1,2,4-triazol-3-yl]sulfanyl}acetohydrazide (4h). Yield 70%, mp 70–71°C (from H_2O–EtOH, 12:10), R_f 0.60 (EtOH–PhH, 1:5). ^{1}H NMR spectrum, δ, ppm: 2.90 s (3H, CH_3), 4.09 br.s (2H, NH_2), 4.39 d.t (2H, NCH_2, J = 5.3, 1.6 Hz), 4.90 d.q (1H, =CH_2, J = 17.1, 1.6 Hz), 5.09 d.q (1H, =CH_2, J = 17.1, 1.6 Hz), 5.72 d.d.t (1H, =CH, J = 17.1, 10.3, 5.3 Hz), 7.30–7.50 m (4H, H_{arom}), 9.34 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 34.7, 46.2, 55.1, 110.9, 115.9, 117.5, 120.2, 131.4, 131.5, 131.6, 149.5, 152.9, 156.7, 166.1. Found, %: C 55.45; H 5.70; N 23.15; S 10.52. $C_{14}H_{17}N_5OS$. Calculated, %: C 55.42; H 5.65; N 23.08; S 10.57.

2-{[5-(Furan-2-yl)-4-phenyl-4*H*-1,2,4-triazol-3-yl]sulfanyl]acetohydrazide (4i). Yield 90%, mp 111–112°C (from H_2O–EtOH, 1:1), R_f 0.50 (EtOH–PhH, 1:7). ^{1}H NMR spectrum, δ, ppm: 3.84 s (2H, CH_2), 4.08 br.s (2H, NH_2), 6.13 d (1H, Fu, J = 3.97 Hz), 6.39 d (1H, Fu, J = 3.97 Hz), 7.39–7.45 m (2H, H_{arom}),

7.52 s (1H, Fu), 7.57–7.62 m (3H, H_{arom}), 9.28 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.9, 110.5, 110.8, 123.4, 127.2, 129.3, 129.7, 134.2, 141.0, 143.5, 150.9, 166.7. Found, %: C 53.40; H 5.80; N 22.30; S 10.25. $C_{14}H_{13}N_5O_2S$. Calculated, %: C 53.45; H 5.70; N 22.21; S 10.17.

Hydrazinolysis of *S*-(5-benzyl-4-phenyl-4*H*-1,2,4-triazol-3-yl) *O*-methyl carbonothioate. Following the general procedure for the synthesis of **4a**–**4i**, the reaction of 5 mmol of **2j** with 7.5 mmol of 85% hydrazine hydrate in 10 mL of ethanol gave a crystalline solid which was filtered off, washed with water, and recrystallized. The product was identified as 5-benzyl-4-phenyl-4*H*-1,2,4-triazole-3-thiol, mp 196–198°C [23]. The filtrate was treated with methylene chloride, the extract was dried and evaporated, and the residue was distilled under reduced pressure, bp 111–113°C (22 mm), mp 47–48°C [24].

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