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Synthesis of New 4,5-Substituted 4*H*-1,2,4-Triazole-3-thiols and Their Sulfanyl Derivatives

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Abstract—Reaction of hydrazides of 4-alkoxybenzoic acids with benzyl isothiocyanate followed by cyclization with thiosemicarbazide afforded a series of new 4,5-substituted 4*H*-1,2,4-triazole-3-thiols. *S*-Alkylation of the latter led to the formation of the corresponding 4,5-substituted sulfanyl derivatives of 4*H*-1,2,4-triazoles.

Keywords: 1,2,4-triazole-3-thiol, thiosemicarbazide, benzyl isothiocyanate, *S*-alkylation, halogenated carboxylic acids, chloroethanol, chloroacetamide

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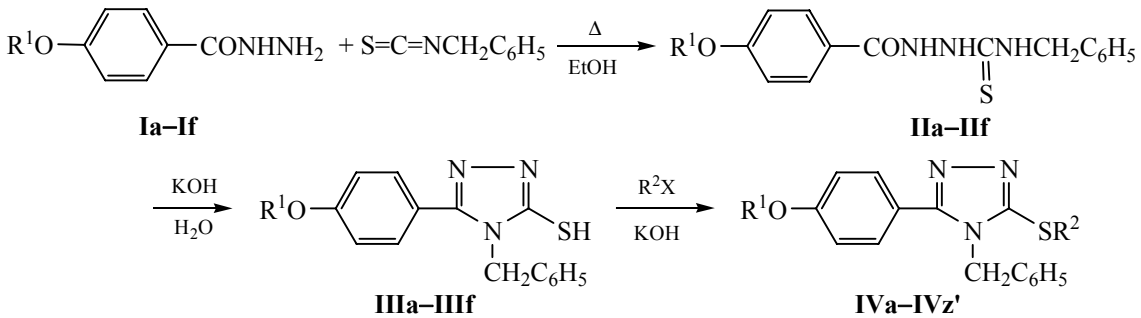
Previously, we have reported the synthesis of a number of alkoxyphenyl-, alkoxyphenethyl- and benzofuryl derivatives of 4*H*-1,2,4-triazoles, which have shown high antitumor activity [1–6]. In this work we prepared new 4-benzyl-1,2,4-triazole-3-thiol derivatives. In addition, the substitution reaction of the hydrogen of SH-group with various halides was studied.

Synthesis of the target compounds was carried out as Scheme 1.

1,4-Substituted thiosemicarbazides **IIa**–**IIf** were obtained by boiling hydrazides of 4-alkoxybenzoic acids **Ia**–**If** with benzylisothiocyanate in ethanol. Cyclization of thiosemicarbazides **IIa**–**IIf** into 5-(4-

Scheme 1.



Ia–If **IIa–IIf** **IIIa–IIIf** **IVa–IVz'**

I–**III**, R^1 = CH_3 (**a**), C_2H_5 (**b**), C_3H_7 (**c**), *i*-C_3H_7 (**d**), C_4H_9 (**e**), *i*-C_4H_9 (**f**); **IV**, R^1 = CH_3, R^2 = CH_2COOH (**a**); R^1 = CH_3, R^2 = $CH(CH_3)COOH$ (**b**); R^1 = CH_3, R^2 = $CH(C_4H_9)COOH$ (**c**); R^1 = C_2H_5, R^2 = CH_2COOH (**d**); R^1 = C_2H_5, R^2 = $CH(CH_3)$·COOH (**e**); R^1 = C_2H_5, R^2 = $CH(C_4H_9)COOH$ (**f**); R^1 = C_3H_7, R^2 = CH_2COOH (**g**); R^1 = C_3H_7, R^2 = $CH(CH_3)COOH$ (**h**); R^1 = C_3H_7, R^2 = $CH(C_4H_9)COOH$ (**i**); R^1 = *i*-C_3H_7, R^2 = CH_2COOH (**j**); R^1 = *i*-C_3H_7, R^2 = $CH(CH_3)COOH$ (**k**); R^1 = *i*-C_3H_7, R^2 = $CH(C_4H_9)COOH$ (**l**); R^1 = C_4H_9, R^2 = CH_2COOH (**m**); R^1 = C_4H_9, R^2 = $CH(C_4H_9)COOH$ (**n**); R^1 = *i*-C_4H_9, R^2 = CH_2COOH (**o**); R^1 = CH_3, R^2 = CH_2CH_2OH (**p**); R^1 = C_2H_5, R^2 = CH_2CH_2OH (**q**); R^1 = C_3H_7, R^2 = CH_2CH_2OH (**r**); R^1 = *i*-C_3H_7, R^2 = CH_2CH_2OH (**s**); R^1 = C_4H_9, R^2 = CH_2CH_2OH (**t**); R^1 = *i*-C_4H_9, R^2 = CH_2CH_2OH (**u**); R^1 = CH_3, R^2 = CH_2CONH_2 (**v**); R^1 = C_2H_5, R^2 = CH_2CONH_2 (**w**); R^1 = C_3H_7, R^2 = CH_2CONH_2 (**x**); R^1 = *i*-C_3H_7, R^2 = CH_2CONH_2 (**y**); R^1 = C_4H_9, R^2 = CH_2CONH_2 (**z**); R^1 = *i*-C_4H_9, R^2 = CH_2CONH_2 (**z'**).

alkoxyphenyl)-4-benzyl-4*H*-1,2,4-triazole-3-thiols **IIIa**–**IIIf** was performed by heating the reaction mixture in a 4.5% aqueous solution KOH followed by acidification with acetic acid. *S*-Alkylation of 1,2,4-triazole-3-thiols **IIIa**–**IIIf** was carried out with chloroacetic, 2-bromopropionic and 2-bromocaproic acids in a threefold excess of aqueous KOH or chloroethanol and chloroacetamide in alcoholic solution of an equimolar amount of KOH.

Triazole thiols **IIIa**–**IIIf** and *S*-substituted triazoles **IVa**–**IVz'** were white crystalline substances. Their composition and structures were confirmed by elemental analysis and ^{1}H NMR spectroscopy (see Experimental).

EXPERIMENTAL

^{1}H NMR spectra of DMSO-d_6 solutions were recorded on a Mercury-300 spectrometer relative to internal TMS operating at 300 MHz. Melting points were measured on a Boetius heating block. TLC was performed on Silufol UV-254 plates eluting with the mixtures benzene–acetone, 1 : 3 (**IIa**–**IIf**), benzene–acetone, 2 : 1 (**IIIa**–**IIIf**), benzene–ethanol, 1.5 : 1 (**IVa**–**IVo**), and benzene–acetone–ethanol, 1 : 1 : 0.1 (**IVp**–**IVz'**), developing with UV light.

1-(4-Alkoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazides (IIa–IIf). A mixture of 10 mmol of hydrazides of 4-alkoxybenzoic acids **Ia**–**If** and 10 mmol of benzyl isothiocyanate in 30 mL of ethanol was refluxed for 5.4 h. The resulting crystals were filtered off and recrystallized from ethanol.

1-(4-Methoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IIa). Yield 84%, mp 202–203°C, R_f 0.64. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 3.82 s (3H, CH_3), 4.77 d (2H, $NHCH_2$, *J* 6.0), 6.87–6.92 m (2H, ArH), 7.88–7.94 m (2H, ArH), 7.15–7.36 m (5H, ArH), 8.29 br.t (1H, NH, *J* 6.0), 9.05 br.s (1H, NH), 9.99 br.s (1H, NH). Found, %: N 13.45; S 10.37. $C_{16}H_{17}N_3O_2S$. Calculated, %: N 13.32; S 10.16.

1-(4-Ethoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IIb). Yield 90%, mp 196–197°C, R_f 0.65. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.43 t (3H, $OCH_2\underline{CH_3}$), 4.09 q (2H, $O\underline{CH_2}CH_3$, *J* 6.9), 4.78 d (2H, $NH\underline{CH_2}$, *J* 6.0), 6.87–6.92 m (2H, ArH), 7.87–7.93 m (2H, ArH), 7.15–7.36 m (5H, ArH), 8.29 br.t (1H, $\underline{NH}CH_2$, *J* 6.0), 9.06–10.01 br.s (2H, NHNH). Found, %: N 12.56; S 9.86. $C_{17}H_{19}N_3O_2S$. Calculated, %: N 12.75; S 9.73.

1-(4-Propoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IIc). Yield 80%, mp 185–186°C, R_f 0.67. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.04 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.4), 1.74–1.85 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.94 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 4.77 t (2H, $NH\underline{CH_2}$, *J* 6.0), 6.85–6.90 m (2H, ArH), 7.31–7.35 m (2H, ArH), 7.09–7.12 m (2H, ArH), 7.18–7.29 m (3H, Ar), 7.22 br.s (1H, NH), 9.03–9.98 br.s (2H, NHNH). Found, %: N 12.56; S 9.58. $C_{18}H_{21}N_3O_2S$. Calculated, %: N 12.23; S 9.33.

1-(4-Isopropoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IId). Yield 90%, mp 197–198°C, R_f 0.65. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.34 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 4.66 septet [1H, $O\underline{CH}\cdot(CH_3)_2$, *J* 6.0], 4.77 d (2H, $NH\underline{CH_2}$, *J* 6.0), 6.85–6.90 m (2H, ArH), 7.86–7.91 m (2H, ArH), 7.15–7.21 m (1H, ArH), 7.24–7.35 m (4H, ArH), 8.26 br.t (1H, NH), 9.19 br.s (1H, NH), 10.09 br.s (1H, NH). Found, %: N 12.44; S 9.12. $C_{18}H_{21}N_3O_2S$. Calculated, %: N 12.23; S 9.33.

1-(4-Buthoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IIe). Yield 98%, mp 177–178°C, R_f 0.68. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.00 t [3H, $O(CH_2CH_2CH_2\underline{CH_3}$, *J* 7.4], 1.52 m (2H, $OCH_2CH_2\underline{CH_2}CH_3$), 1.77 m (2H, $OCH_2\underline{CH_2}CH_2CH_3$), 4.02 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 4.77 d (2H, $NH\underline{CH_2}$, *J* 6.0), 6.89–7.15 m (2H, ArH), 7.22–7.35 m (2H, ArH), 7.15–7.24 m (1H, ArH), 7.26–7.35 m (4H, ArH), 8.25 br.t (1H, NH), 9.16 br.s (1H, NH), 10.08 br.s (1H, NH). Found, %: N 11.96; S 8.75. $C_{19}H_{23}N_3O_2S$. Calculated, %: N 11.75; S 8.96.

1-(4-Isobuthoxyphenyl)carbonyl-4-benzyl-3-thiosemicarbazide (IIe). Yield 90%, mp 196–197°C, R_f 0.67. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.04 d [6H, $OCH_2CH(\underline{CH_3})_2$, *J* 6.6], 2.08 m [1H, $OCH_2\underline{CH}(CH_3)_2$, *J* 6.6], 3.78 d [2H, $O\underline{CH_2}CH(CH_3)_2$, *J* 6.6], 4.77 d (2H, $NH\underline{CH_2}$, *J* 6.0), 6.87–6.92 m (2H, ArH), 7.87–7.92 m (2H, ArH), 7.14–7.21 m (1H, ArH), 7.24–7.35 m (4H, ArH), 8.27 br.t (1H, NH, *J* 6.0), 9.18 br.s (1H, NH), 10.09 br.s (1H, NH). Found, %: N 11.89; S 8.68. $C_{19}H_{23}N_3O_2S$. Calculated, %: N 11.75; S 8.96.

5-(4-Alkoxyphenyl)-4-benzyl-4*H*-1,2,4-triazole-3-thiols (IIIa–IIIf). A mixture of 10 mmol of thiosemicarbazide **IIa**–**IIf**, 1 g of KOH, and 50 mL of water was refluxed for 2 h. After cooling the mixture was treated with acetic acid. The precipitate was filtered off, washed with water, dried, and recrystallized from 70% aqueous ethanol.

4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIIa). Yield 94%, mp 205–206°C, R_f 0.69. ^{1}H

NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 3.82 s (3H, OCH_3), 5.28 s (2H, NCH_2), 6.87–6.92 m (2H, ArH), 7.32–7.37 m (2H, ArH), 7.08–7.12 m (2H, ArH), 7.18–7.30 m (3H, ArH), 13.78 br.s (1H, SH). Found, %: N 14.37; S 10.96. $C_{16}H_{15}N_3OS$. Calculated, %: N 14.13; S 10.78.

4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIIb). Yield 98%, mp 203–204°C, R_f 0.68. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 4.06 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 13.71 br.s (1H, SH). Found, %: N 13.61; S 10.46. $C_{17}H_{17}N_3OS$. Calculated, %: N 13.49; S 10.29.

4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIIc). Yield 90%, mp 180–181°C, R_f 0.67. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.04 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.4), 1.74–1.86 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.94 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 5.28 s (2H, NCH_2), 6.85–6.90 m (2H, ArH), 7.31–7.35 m (2H, ArH), 7.09–7.13 m (2H, ArH), 7.18–7.29 m (3H, ArH), 13.72 br.s (1H, SH). Found, %: N 12.72; S 9.62. $C_{18}H_{19}N_3OS$. Calculated, %: N 12.91; S 9.85.

4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIId). Yield 94%, mp 210–211°C, R_f 0.70. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.33 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 4.61 septet [1H, $O\underline{CH}\cdot(CH_3)_2$, *J* 6.0], 5.28 s (2H, NCH_2), 6.82– 6.87 m (2H, ArH), 7.29–7.34 m (2H, ArH), 7.08–7.12 m (2H, ArH), 7.18–7.29 m (3H, ArH), 13.77 br.s (1H, SH). Found, %: N 12.74; S 9.66. $C_{18}H_{19}N_3OS$. Calculated, %: N 12.91; S 9.85.

4-Benzyl-5-(4-buthoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIIe). Yield 85%, mp 185–186°C, R_f 0.69. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.99 t (3H, $OCH_2CH_2CH_2\underline{CH_3}$, *J* 7.3), 1.44–1.57 m (2H, $OCH_2CH_2\cdot\underline{CH_2}CH_3$), 1.71–1.81 m (2H, $OCH_2\underline{CH_2}CH_2CH_3$), 3.98 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 5.24 s (2H, NCH_2), 6.89–6.93 m (2H, ArH), 7.39–7.44 m (2H, ArH), 7.00–7.05 m (2H, ArH), 7.23–7.35 m (3H, ArH), 13.76 br.s (1H, SH). Found, %: N 12.55; S 9.67. $C_{19}H_{21}N_3OS$. Calculated, %: N 12.37; S 9.44.

4-Benzyl-5-(4-isobethoxyphenyl)-4*H*-1,2,4-triazole-3-thiol (IIIf). Yield 88%, mp 205–206°C, R_f 0.65. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.03 d [6H, $OCH_2CH(\underline{CH_3})_2$, *J* 6.6], 2.07 m [1H, $OCH_2\underline{CH}(CH_3)_2$, *J* 6.6], 3.74 d [2H, $O\underline{CH_2}CH(CH_3)_2$, *J* 6.6], 5.28 s (2H, NCH_2), 6.85–6.90 m (2H, ArH), 7.31–7.35 m (2H, ArH), 7.09–7.13 m (2H, ArH), 7.19–7.30 m (3H, ArH), 13.76 br.s (1H, SH). Found, %: N 12.61; S 9.72. $C_{19}H_{21}N_3OS$. Calculated, %: N 12.37; S 9.44.

Substituted triazol-3-ylsulfanylacetic, -propionic, and -hexanoic acids (IVa–IVo). A mixture of 6 mmol of KOH, 30 mL of water, 2 mmol of triazole-3-thiol **IIIa–IIIf**, and 2 mmol of the corresponding carboxylic acid was refluxed for 2 h. The mixture was filtered and treated with acetic acid. The precipitate was filtered off, washed with water, dried, and recrystallized from ethanol.

[4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVa). Yield 85%, mp 195–196°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 3.81 s (3H, OCH_3), 3.85 s (2H, SCH_2), 5.25 s (2H, NCH_2), 6.84–7.02 m (4H, ArH), 7.20–7.35 m (3H, ArH), 7.40–7.46 m (2H, ArH), 13.75 br.s (1H, COOH). Found, %: N 11.63; S 9.31. $C_{18}H_{17}N_3O_3S$. Calculated, %: N 11.82; S 9.02.

2-[4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]propionic acid (IVb). Yield 83%, mp 139–140°C, R_f 0.53. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.58 d (3H, $SCH\underline{CH_3}$, *J* 7.1), 3.82 s (3H, OCH_3), 4.19 q (1H, $S\underline{CH}CH_3$, *J* 7.1), 5.25 s (2H, NCH_2), 6.88–7.00 m (4H, ArH), 7.21–7.37 m (3H, ArH), 7.41–7.47 m (2H, ArH), the signal of COOH group was not observed due to broadening. Found, %: N 11.25; S 8.77. $C_{19}H_{19}N_3O_3S$. Calculated, %: N 11.37; S 8.67.

2-[4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]hexanoic acid (IVc). Yield 87%, mp 133–134°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.93 t (3H, $CH_2CH_2CH_2\underline{CH_3}$, *J* 7.0), 1.29–1.47 m (4H, $CH_2\underline{CH_2}\underline{CH_2}CH_3$), 1.79–1.99 m (2H, $\underline{CH_2}CH_2CH_2CH_3$), 3.82 s (3H, OCH_3), 4.07 d. d (1H, SCH, *J* 7.3), 5.25 s (2H, NCH_2), 6.91–6.99 m (4H, ArH), 7.22–7.34 m (3H, ArH), 7.41–7.46 m (2H, ArH), the signal of COOH group was not observed due to broadening. Found, %: N 10.45; S 7.92. $C_{22}H_{25}N_3O_3S$. Calculated, %: N 10.21; S 7.79.

[4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVd). Yield 85%, mp 170–171°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 3.85 s (2H, SCH_2), 4.08 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.96–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 13.75 br.s (1H, COOH). Found, %: N 11.64; S 8.84. $C_{19}H_{19}N_3O_3S$. Calculated, %: N 11.37; S 8.67.

2-[4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]propionic acid (IVe). Yield 82%, mp 132–133°C, R_f 0.56. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 1.58 d (3H, $SCH\underline{CH_3}$, *J* 7.2), 4.06 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 4.19 q (1H, SCH, *J* 7.2), 5.25 s (2H, NCH_2), 6.89–7.00 m (4H, ArH), 7.22–7.34 m (3H, ArH), 7.38–7.45 m (2H, ArH), 12.63 br.s (1H, COOH). Found, %: N 10.76; S 8.58. $C_{20}H_{21}N_3O_3S$. Calculated, %: N 10.95; S 8.36.

2-[4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]hexanoic acid (IVf). Yield 75%, mp 140–141°C, R_f 0.54. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.93 t (3H, $CH_2CH_2CH_2\underline{CH_3}$, *J* 7.0), 1.30–1.47 m (4H, $CH_2\underline{CH_2CH_2}CH_3$), 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 1.79–1.99 m (2H, $SCH\underline{CH_2}$), 4.06 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 4.07 t (1H, SCH, *J* 6.7), 5.25 s (2H, NCH_2), 6.88–6.99 m (4H, ArH), 7.22–7.35 m (3H, ArH), 7.39–7.45 m (2H, ArH), 12.5 br.s (1H, COOH). Found, %: N 9.98; S 7.75. $C_{23}H_{27}N_3O_3S$. Calculated, %: N 9.87; S 7.53.

[4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVg). Yield 92%, mp 167–168°C, R_f 0.55. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.93 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.1), 1.28 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.94 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 4.06 d. d (2H, SCH_2), 5.25 s (2H, NCH_2), 6.88–6.93 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.94–6.99 m (2H, ArH), 7.21–7.33 m (3H, ArH), 12.68 br.s (1H, COOH). Found, %: N 10.76; S 8.62. $C_{20}H_{21}N_3O_3S$. Calculated, %: N 10.95; S 8.36.

2-[4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]propionic acid (IVh). Yield 75%, mp 130–131°C, R_f 0.69. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.05 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.4), 1.58 d (3H, $SCH\underline{CH_3}$, *J* 7.2), 1.74–1.86 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.95 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 4.19 q (1H, $S\underline{CH}CH_3$, *J* 7.2), 5.25 s (2H, NCH_2), 6.86–6.99 m (4H, ArH), 7.21–7.35 m (3H, ArH), 7.39–7.45 m (2H, ArH), 13.75 br.s (1H, COOH). Found, %: N 10.68; S 8.71. $C_{21}H_{23}N_3O_3S$. Calculated, %: N 10.57; S 8.86.

2-[4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]hexanoic acid (IVi). Yield 91%, mp 102–103°C, R_f 0.57. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.92 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.1), 1.04 t (3H, $CH_2CH_2CH_2\underline{CH_3}$, *J* 7.4), 1.28–1.47 m and 1.74–1.95 m (8H, $OCH_2\underline{CH_2}CH_3$, $\underline{CH_2CH_2CH_2}CH_3$), 3.94 t (2H, $\underline{OCH_2}CH_2CH_3$, *J* 6.5), 4.06 d. d (1H, SCH, *J* 7.2, 6.5), 5.25 s (2H, NCH_2), 6.88–6.93 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.94–6.99 m (2H, ArH), 7.21–7.33 m (3H, ArH), the signal of COOH group was not observed due to broadening. Found, %: N 9.36; S 7.45. $C_{24}H_{29}N_3O_3S$. Calculated, %: N 9.55; S 7.29.

[4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVj). Yield 92%, mp 141–142°C, R_f 0.55. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.34 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 3.84 s (2H, SCH_2), 4.61 septet [1H, $O\underline{CH}(CH_3)_2$, *J* 6.0], 5.28 s (2H, NCH_2), 6.82–6.87 m (2H, ArH), 7.29–7.34 m (2H, ArH), 7.08–7.12 m (2H, ArH), 7.18–7.29 m (3H, ArH), 12.57 br.s (1H, COOH). Found, %: N 10.66; S 8.58. $C_{20}H_{21}N_3O_3S$. Calculated, %: N 10.95; S 8.36.

2-[4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]propionic acid (IVk). Yield 85%, mp 124–126°C, R_f 0.50. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.33 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 1.58 d (3H, $SCH\underline{CH_3}$, *J* 7.2), 4.19 q (1H, $S\underline{CH}CH_3$, *J* 7.2), 4.61 septet [1H, $O\underline{CH}(CH_3)_2$, *J* 6.0], 5.25 s (2H, NCH_2), 6.82–6.88 m (2H, ArH), 7.29–7.34 m (2H, ArH), 7.08–7.12 m (2H, ArH), 7.18–7.29 m (3H, ArH), the signal of COOH group was not observed due to broadening. Found, %: N 10.78; S 8.98. $C_{21}H_{23}N_3O_3S$. Calculated, %: N 10.57; S 8.86.

2-[4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]hexanoic acid (IVl). Yield 80%, mp 69–70°C, R_f 0.69. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.93 t (3H, $CH_2CH_2CH_2\underline{CH_3}$, *J* 7.0), 1.30–1.47 m (4H, $\underline{CH_2CH_2}CH_3$), 1.33 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 1.79–1.99 m (3H, $SCH\underline{CH_2}$), 4.07 t (1H, $S\underline{CH}CH_2$, *J* 6.7), 5.25 s (2H, NCH_2), 6.88–6.99 m (4H, ArH), 7.22–7.35 m (3H, ArH), 7.39–7.45 m (2H, ArH), 12.5 br.s (1H, COOH). Found, %: N 9.77; S 7.48. $C_{24}H_{29}N_3O_3S$. Calculated, %: N 9.55; S 7.29.

[4-Benzyl-5-(4-buthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVm). Yield 85%, mp 70–72°C, R_f 0.57. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.99 t (3H, $OCH_2CH_2CH_2\underline{CH_3}$, *J* 7.3), 1.44–1.57 m (2H, $OCH_2CH_2\underline{CH_2}CH_3$), 1.71–1.81 m (2H, $OCH_2\underline{CH_2}CH_2CH_3$), 3.95 m (1H, SCH_2), 3.98 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 5.24 s (2H, NCH_2), 6.89–6.93 m (2H, ArH), 7.39–7.44 m (2H, ArH), 7.00–7.05 m (2H, ArH), 7.23–7.35 m (3H, ArH), 12.66 br.s (1H, COOH). Found, %: N 10.79; S 8.27. $C_{21}H_{23}N_3O_3S$. Calculated, %: N 10.57; S 8.06.

2-[4-Benzyl-5-(4-buthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]hexanoic acid (IVn). Yield 87%, mp 79–80°C, R_f 0.50. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.93 t (3H, $CH_2CH_2CH_2\underline{CH_3}$, *J* 7.0), 0.99 t

(3H, $OCH_2CH_2CH_2\underline{CH_3}$, *J* 7.4), 1.30–1.47 m (4H, $CH_2\underline{CH_2}\cdot\underline{CH_2}CH_3$), 1.43–1.56 m (2H, $OCH_2CH_2\underline{CH_2}CH_3$), 1.70–1.80 m (2H, $OCH_2\underline{CH_2}CH_2CH_3$), 1.79–1.99 m (2H, $SCH\underline{CH_2}$), 3.98 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 4.07 d. d (1H, $S\underline{CH}CH_2$, J 7.3, 6.6), 5.25 s (2H, NCH_2), 6.91–6.99 m (4H, ArH), 7.22–7.34 m (3H, ArH), 7.41–7.46 m (2H, ArH), 12.59 br.s (1H, COOH). Found, %: N 9.45; S 7.27. $C_{25}H_{31}N_3O_3S$. Calculated, %: N 9.26; S 7.06.

[4-Benzyl-5-(4-isobuthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetic acid (IVo). Yield 98%, mp 155–156°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.03 t [6H, $CH_2CH(\underline{CH_3})_2$, *J* 6.6], 2.08 m [1H, $CH_2\underline{CH}(CH_3)_2$, *J* 6.6], 3.75 d [2H, $O\underline{C}H_2CH(CH_3)_2$, *J* 6.6], 3.95 s (2H, SCH_2), 5.25 s (2H, NCH_2), 6.88–6.94 m (2H, ArH), 7.36–7.43 m (2H, ArH), 6.97–7.02 m (2H, ArH), 7.22–7.35 m (3H, ArH), 12.65 br.s (1H, COOH). Found, %: N 10.78; S 8.29. $C_{21}H_{23}N_3O_3S$. Calculated, %: N 10.57; S 8.06.

Substituted 4*H*-1,2,4-triazol-3-sulfanylethanols (IVp–IVu) and 4*H*-1,2,4-triazol-3-ylsulfanylacetamides (IVv–IVz'). A mixture of 1.0 mmol of KOH in 20 mL of ethanol, 10 mmol of triazole-3-thiol **IIIa**–**IIIf**, and 10 mmol of chloroethanol or chloroacetamide was refluxed for 45–60 min. After cooling, water was added, and the mixture was left standing overnight. The formed crystals were filtered off, dried, and recrystallized from 70% aqueous ethanol.

2-[4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVp). Yield 63%, mp 177–178°C, R_f 0.50. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 3.25 t (2H, SCH_2), 3.71 t.d (2H, $\underline{CH_2}OH$, *J* 6.4, 5.7), 3.80 s (3H, OCH_3), 4.75 t (1H, OH, *J* 5.7), 5.20 s (2H, NCH_2), 6.87–6.93 m (2H, ArH), 7.38–7.43 m (2H, ArH), 6.96–7.02 m (2H, ArH), 7.22–7.34 m (3H, ArH). Found, %: N 12.48; S 9.54. $C_{18}H_{19}N_3O_2S$. Calculated, %: N 12.30; S 9.39.

2-[4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVq). Yield 78%, mp 116–117°C, R_f 0.55. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 3.24 t (2H, SCH_2, *J* 6.4), 3.71 t.d (2H, $\underline{CH_2}OH$, *J* 6.4), 4.06 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 4.75 t (1H, OH, *J* 5.7), 5.20 s (2H, NCH_2), 6.88–6.93 m (2H, ArH), 7.38–7.43 m (2H, ArH), 6.96–7.02 m (2H, ArH), 7.23–7.34 m (3H, ArH). Found, %: N 11.64; S 8.82. $C_{19}H_{21}N_3O_2S$. Calculated, %: N 11.82; S 9.02.

2-[4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVr). Yield 98%, mp 89–90°C, R_f 0.59. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.04 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.4), 1.74–1.86 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.27 t (2H, SCH_2), 3.72 t.d (2H, $\underline{CH_2}OH$, *J* 6.4, 5.7), 3.95 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 4.74 t (1H, OH, *J* 5.7), 5.28 s (2H, NCH_2), 6.85–6.90 m (2H, ArH), 7.31–7.35 m (2H, ArH), 7.09–7.13 m (2H, ArH), 7.18–7.29 m (3H, ArH). Found, %: N 11.57; S 8.86. $C_{20}H_{23}N_3O_2S$. Calculated, %: N 11.37; S 8.67.

2-[4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVs). Yield 67%, mp 102–103°C, R_f 0.63. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.33 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 3.25 t (2H, SCH_2), 3.74 t.d (2H, $\underline{CH_2}OH$, *J* 6.4), 4.61 septet [1H, $O\underline{CH}(CH_3)_2$, *J* 6.0], 5.28 s (2H, NCH_2), 4.75 t (1H, OH, *J* 5.7), 6.82–6.87 m (2H, ArH), 7.29–7.34 m (2H, ArH), 7.08–7.12 m (2H, ArH), 7.18–7.29 m (3H, ArH). Found, %: N 11.64; S 8.95. $C_{20}H_{23}N_3O_2S$. Calculated, %: N 11.37; S 8.67.

2-[4-Benzyl-5-(4-buthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVt). Yield 92%, mp 67–68°C, R_f 0.60. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.99 t (3H, $OCH_2CH_2CH_2\underline{CH_3}$, *J* 7.3), 1.44–1.56 m (2H, $OCH_2CH_2\underline{CH_2}CH_3$), 1.71–1.81 m (2H, $OCH_2\cdot\underline{CH_2}CH_2CH_3$), 3.72 t.d (2H, $\underline{CH_2}OH$, *J* 6.4), 3.85 s (2H, SCH_2), 3.98 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 4.75 t (1H, OH, *J* 5.7), 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.38–7.44 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH). Found, %: N 11.30; S 8.54. $C_{21}H_{25}N_3O_2S$. Calculated, %: N 10.95; S 8.36.

2-[4-Benzyl-5-(4-isobuthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanol (IVu). Yield 98%, mp 125–126°C, R_f 0.59. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.03 d [6H, $OCH_2CH(\underline{CH_3})_2$, *J* 6.6], 2.08 m [1H, $OCH_2\underline{CH}(CH_3)_2$, *J* 6.6], 3.25 t (2H, SCH_2, *J* 6.4), 3.71 t.d (2H, $\underline{CH_2}OH$, *J* 6.4, 5.7), 3.75 d [2H, $O\underline{CH_2}CH\cdot(CH_3)_2$, *J* 6.6], 4.76 t (1H, OH, *J* 5.7), 5.20 s (2H, NCH_2), 6.88–6.94 m (2H, ArH) and 7.36–7.43 m (2H, ArH), 6.97–7.02 m (2H, ArH), 7.22–7.34 m (3H, ArH). Found, %: N 10.72; S 8.67. $C_{21}H_{25}N_3O_2S$. Calculated, %: N 10.95; S 8.36.

[4-Benzyl-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVv). Yield 70%, mp 201–202°C, R_f 0.62. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 3.83 s (3H, OCH_3), 3.85 s (2H, SCH_2), 5.25 s (2H, NCH_2), 6.92–7.05 m (4H, ArH), 7.23–7.35 m (3H, ArH), 7.41–7.46 m (2H, ArH), 6.95 br.s and 7.54 br.s (2H, NH2). Found, %: N 15.62; S 9.26. $C_{18}H_{18}N_4O_2S$. Calculated, %: N 15.80; S 9.04.

[4-Benzyl-5-(4-ethoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVw). Yield 83%, mp 164–165°C, R_f 0.70. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.41 t (3H, $OCH_2\underline{CH_3}$, *J* 7.0), 3.85 s (2H, SCH_2), 4.06 q (2H, $O\underline{CH_2}CH_3$, *J* 7.0), 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 6.96 br.s and 7.55 br.s (2H, NH_2). Found, %: N 15.45; S 8.82. $C_{19}H_{20}N_4O_2S$. Calculated, %: N 15.20; S 8.70.

[4-Benzyl-5-(4-propoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVx). Yield 90%, mp 135–136°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.92 t (3H, $OCH_2CH_2\underline{CH_3}$, *J* 7.4), 1.74–1.86 m (2H, $OCH_2\underline{CH_2}CH_3$), 3.86 s (2H, SCH_2), 3.94 t (2H, $O\underline{CH_2}CH_2CH_3$, *J* 6.5), 5.28 s (2H, NCH_2), 6.85–6.94 m (2H, ArH), 7.31–7.34 m (2H, ArH), 7.09–7.13 m (2H, ArH), 7.18–7.29 m (3H, ArH), 6.96 br.s and 7.55 br.s (2H, NH_2). Found, %: N 14.48; S 8.65. $C_{20}H_{22}N_4O_2S$. Calculated, %: N 14.64; S 8.38.

[4-Benzyl-5-(4-isopropoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVy). Yield 80%, mp 171–172°C, R_f 0.59. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.33 d [6H, $OCH(\underline{CH_3})_2$, *J* 6.0], 3.85 s (2H, SCH_2), 4.61 septet [1H, $O\underline{CH}(CH_3)_2$, *J* 6.0], 5.25 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.32–7.34 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 6.94 br.s and 7.54 br.s (2H, NH_2). Found, %: N 14.72; S 8.58. $C_{20}H_{22}N_4O_2S$. Calculated, %: N 14.64; S 8.38.

[4-Benzyl-5-(4-buthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVz). Yield 85%, mp 119–120°C, R_f 0.60. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 0.99 t (3H, $OCH_2CH_2CH_2\underline{CH_3}$, *J* 7.3), 1.44–1.56 m (2H, $OCH_2CH_2\underline{CH_2}CH_3$), 1.71–1.81 m (2H, $OCH_2\underline{CH_2}CH_2CH_3$), 3.85 s (2H, SCH_2), 3.98 t (2H, $O\underline{CH_2}CH_2CH_2CH_3$, *J* 6.4), 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.39–7.44 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 6.94 br.s and 7.54 br.s (2H, NH_2). Found, %: N 14.35; S 8.41. $C_{21}H_{24}N_4O_2S$. Calculated, %: N 14.13; S 8.08.

[4-Benzyl-5-(4-isobuthoxyphenyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide (IVz'). Yield 73%, mp 137–138°C, R_f 0.58. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 1.03 d [6H, $OCH_2CH(\underline{CH_3})_2$, *J* 6.6], 2.07 m [1H, $OCH_2\underline{CH}(CH_3)_2$, *J* 6.6], 3.25 s (2H, SCH_2), 3.74 d [2H, $O\underline{CH_2}CH(CH_3)_2$, *J* 6.6], 5.24 s (2H, NCH_2), 6.89–6.94 m (2H, ArH), 7.36–7.44 m (2H, ArH), 6.99–7.04 m (2H, ArH), 7.23–7.35 m (3H, ArH), 6.94 br.s and 7.54 br.s (2H, NH_2). Found, %: N 14.38; S 7.55. $C_{21}H_{24}N_4O_2S$. Calculated, %: N 14.13; S 8.08.

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