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Synthesis of 1,2,4-Triazole-3-thiols and Their S-Substituted Derivatives

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Abstract—New 1,2,4-triazole-3-thiols were synthesized by reactions of the corresponding carboxylic acid hydrazides with isothiocyanates and subsequent cyclization of intermediate 1,4-substituted thiosemicarbazides. Alkylation of 1,2,4-triazole-3-thiols with benzyl chlorides and bromacetophenones gave only S-substituted derivatives.

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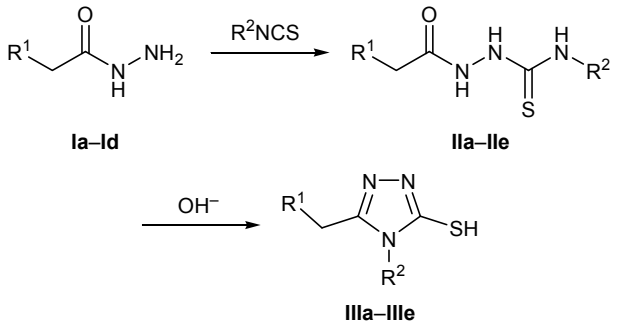
Biological studies on synthetic analogs of naturally occurring heterocyclic compounds showed that most of them exhibit a broad spectrum of biological activity. Among compounds of this series, of particular interest are 1,2,4-triazoles which are mostly of synthetic origin. Some 1,2,4-triazole derivatives exhibit hypotensive effect [1] and possess antitumor [2], fungicidal [3], antibacterial [4], and other kinds of biological activity.

While searching for new useful properties in the series of 1,2,4-triazoles we synthesized their new derivatives. Reactions of carboxylic acid hydrazides **Ia**–**Id** with allyl, phenyl, and furfurylmethyl isothiocyanates gave 1,4-disubstituted thiosemicarbazides **IIa**–**IIe**. Optimal conditions for this reaction were found. The best results were obtained by heating the initial reactants in ethanol for a short time [5]. Compounds **IIa**–**IIe** underwent intramolecular cyclization in alkaline medium to form targeted 3,4-disubstituted 1,2,4-triazole-3-thiols **IIIa**–**IIIe**. It is advisable to carry out this reaction with the use of 10% aqueous sodium or potassium hydroxide. The cyclization was complete in 4 h, and compounds **IIIa**–**IIIe** were formed in high yield [6] (Scheme 1).

From the viewpoint of biological activity, synthesis of 1,2,4-triazole-3-thiol derivatives substituted at the sulfur atom seemed to be promising. For instance, biological effects of compounds possessing free and substituted thiol groups could be compared. 3,4-Disubstituted 1,2,4-triazole-3-thiols **IIIa**–**IIIe** were subjected to alkylation with various halogen derivatives, specifically with substituted benzyl chlorides and bromoacetophenones (Scheme 2). The optimal conditions for the alkylation with benzyl chlorides included the use of anhydrous acetone as solvent and anhydrous potassium carbonate as base and prolonged heating (10 h). The reactions of **III** with bromoacetophenones were complete in 2 h in the absence of a base.

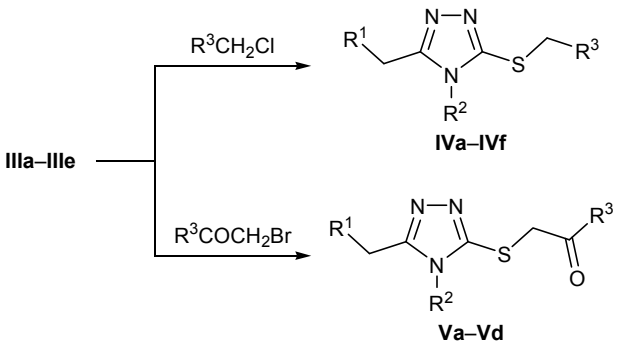
Scheme 1.



I, R^1 = 2,4-$Cl_2C_6H_3O$ (**a**), 4-Cl-2-MeC_6H_3O (**b**), PhO (**c**), *i*-Pr (**d**); **II**, **III**, R^1 = 2,4-$Cl_2C_6H_3O$, R^2 = CH_2=$CHCH_2$ (**a**), Ph (**b**); R^1 = 4-Cl-2-MeC_6H_3O, R^2 = CH_2=$CHCH_2$ (**c**); R^1 = PhO, R^2 = Ph (**d**); R^1 = *i*-Pr, R^2 = 2-furylmethyl (**e**).

[†] Deceased.

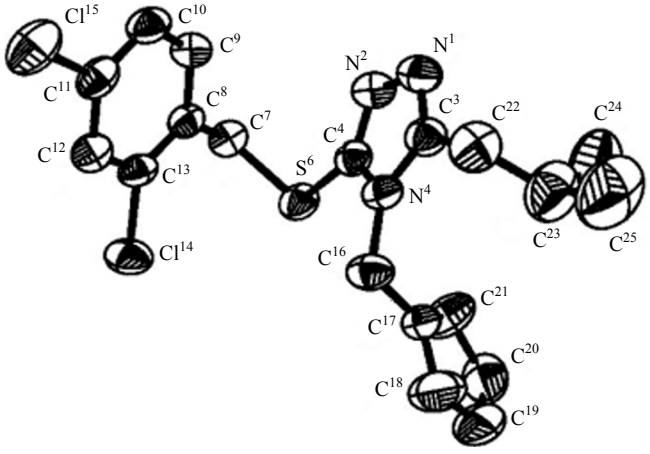
Scheme 2.



IV, R^1 = 2,4-$Cl_2C_6H_3O$, R^2 = Ph, R^3 = 3,4-$Cl_2C_6H_3$ (**a**), 2,4-$Cl_2C_6H_3$ (**b**); R^1 = 4-Cl-2-MeC_6H_3O, R^2 = CH_2=$CHCH_2$, R^3 = 2,4-$Cl_2C_6H_3$ (**c**); R^1 = *i*-Pr, R^2 = 2-furylmethyl, R^3 = 2,4-$Cl_2C_6H_3$ (**d**); R^1 = PhO, R^2 = Ph, R^3 = 2,4-$Cl_2C_6H_3$ (**e**), 3,4-$Cl_2C_6H_3$ (**f**); **V**, R^1 = 2,4-$Cl_2C_6H_3O$, R^2 = Ph, R^3 = Ph (**a**), 4-$O_2NC_6H_4$ (**b**); R^1 = PhO, R^2 = R^3 = Ph (**c**), R^2 = Ph, R^3 = 4-$O_2NC_6H_4$ (**d**).

We previously found [7] that 1,2,4-triazole-3-thiols in solution give rise to thione–thiol tautomeric equilibrium; therefore, the alkylation may involve both endocyclic nitrogen atom and exocyclic sulfur atom with formation of N- and S-substituted isomers. We examined alkylation of compounds **III** in different solvents, such as acetonitrile, acetone, and aqueous acetone. In all cases, the products obtained under different conditions were identical (no depression of the melting point was observed on mixing). The structure of compound **IVd** as S-substituted 1,2,4-triazole-3-thiol was unambiguously proved by X-ray analysis (see figure).

Preliminarily tests of compounds **IIIe** and **IVd** for antioxidant activity revealed that the latter exerts stabilizing effect on red blood cell membranes. Compound **IIIe** showed no stabilizing effect under analogous conditions, presumably due to the presence of free thiol group in its molecule.



Structure of the molecule of 3-(2,4-dichlorobenzylsulfanyl)-4-(2-furylmethyl)-5-isobutyl-4*H*-1,2,4-triazole (**IVd**) according to the X-ray diffraction data.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet FTIR Nexus spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Varian Mercury-300 spectrometer (300 MHz) using $CDCl_3$ as solvent. Thin-layer chromatography was performed on Silufol UV-254 plates; spots were visualized by treatment with iodine vapor. The melting points were determined on a Boetius melting point apparatus. Initial carboxylic acid hydrazides **Ia**–**Ie** were synthesized according to the procedure described in [8].

X-Ray analysis of 3-(2,4-dichlorobenzylsulfanyl)-4-(2-furylmethyl)-5-isobutyl-4*H*-1,2,4-triazole (IVd). The unit cell parameters (monoclinic crystal system) were measured on an Enraf–Nonius CAD-4 automatic diffractometer at room temperature and were refined by 22 reflections (spherical segment $10° < \theta < 13°$): a = 18.897(4), b = 5.939(1), c = 17.134(3) Å; β = 98.25(3)°; V = 1902.9(7) Å^3; Z = 4; space group $P2_1/c$ The X-ray diffraction data were acquired using the same instrument. Intensities of 11489 reflections were measured in the range $0 \le h \le 24$, $-8 \le k \le 8$, $-26 \le l \le 26$, θ_{max} = 30° (MoK_α irradiation, graphite monochromator). All calculations were performed using SHELXTL software package [9]. Averaging of symmetry-equivalent reflections left an array consisting of 5562 nonequivalent reflections (R = 0.08), 2719 of which were characterized by $I > 2\sigma(I)$. The structure was solved by the direct method; the coordinates of hydrogen atoms were determined from the Fourier difference syntheses. The structure was refined by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms and isotropic approximation for hydrogen atoms; the final divergence factor was R = 0.062, S = 1.008.

1,4-Disubstituted tiosemicarbazides IIa–IIe (*general procedure*). A solution of 0.06 mol of allyl, phenyl, or 2-furylmethyl isothiocyanate in 30 ml of ethanol was added to a solution of 0.06 mol of carboxylic acid hydrazide **Ia**–**Id** in 30 ml of ethanol. The mixture was thoroughly mixed, left to stand for 1 h at room temperature, and heated for 2 h under reflux. After cooling, the precipitate was filtered off, dried, and recrystallized from ethanol or aqueous ethanol.

4-Allyl-1-(2,4-dichlorophenoxyacetyl)thiosemicarbazide (IIa). Yield 97%, mp 162–164°C (from ethanol–water, 1:3), R_f 0.59 (ethanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3200–3300 (NH), 3050 (C–H_{arom}), 1680 (C=O), 1640 (C=C), 1600, 1610 (C=C_{arom}), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 4.15 s (2H, NCH_2), 4.65 s (2H, OCH_2), 5.20 d and 5.25 d (1H each, =CH_2), 5.90 q (1H, =CH), 7.10 m (1H, H_{arom}), 7.25 m (1H, H_{arom}), 7.55 m (1H, H_{arom}), 9.40 s (2H, NH), 9.90 s (1H, NH). Found, %: C 43.25; H 3.75; Cl 21.35; N 12.70; S 9.45. $C_{12}H_{13}Cl_2N_3O_2S$. Calculated, %: C 43.11; H 3.89; Cl 21.26; N 12.57; S 9.58.

1-(2,4-Dichlorophenoxyacetyl)-4-phenylthiosemicarbazide (IIb). Yield 91%, mp 159–160°C (from ethanol–water, 1:3), R_f 0.65 (ethanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3200–3300 (NH), 3080 (C–H_{arom}), 1690 (C=O), 1600 (C=C_{arom}), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 4.70 s (2H, OCH_2), 7.20–7.40 m and 7.60 m (8H, H_{arom}), 9.10 s (1H, NH), 9.30 m (2H, NH). Found, %: C 48.55; H 3.45; Cl 19.25; N 11.45; S 8.55. $C_{15}H_{13}Cl_2N_3O_2S$. Calculated, %: C 48.65; H 3.51; Cl 19.19; N 11.35; S 8.65.

4-Allyl-1-(4-chloro-2-methylphenoxyacetyl)thiosemicarbazide (IIc). Yield 80%, mp 174–175°C (from ethanol), R_f 0.54 (etanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3200–3300 (NH), 3080 (C–H_{arom}), 1690 (C=O), 1645 (C=C), 1600 (C=C_{arom}), 1200 (COC), 750 (C–Cl). ^1H NMR spectrum, δ, ppm: 2.25 s (3H, CH_3), 4.15 d (2H, NCH_2), 4.60 s (2H, OCH_2), 5.20 d and 5.25 d (1H each, =CH_2), 5.85 q (1H, =CH), 6.90 m (1H, H_{arom}), 7.20 m (1H, H_{arom}), 7.35 m (1H, H_{arom}), 9.30 s (2H, NH), 9.85 s (1H, NH). Found, %: C 49.90; H 5.00; Cl 11.45; N 13.50; S 10.10. $C_{13}H_{16}ClN_3O_2S$. Calculated, %: C 49.76; H 5.10; Cl 11.32; N 13.40; S 10.21.

1-Phenoxyacetyl-4-phenylthiosemicarbazide (IId). Yield 95%, mp 133–134°C (from ethanol), R_f 0.66 (ethanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3180–3300 (NH), 3050 (C–H_{arom}), 1690 (C=O), 1610 (C=C_{arom}), 1180 (COC). ^1H NMR spectrum, δ, ppm: 4.60 s (2H, OCH_2), 6.80 m (1H, H_{arom}), 6.95 m (2H, H_{arom}), 7.00 m (1H, H_{arom}), 7.20 m (2H, H_{arom}), 7.35 m (2H, H_{arom}), 7.70 m (2H, H_{arom}), 9.45 s (2H, NH), 10.15 s (1H, NH). Found, %: C 59.95; H 4.85; N 14.05; S 10.75. $C_{15}H_{15}N_3O_2S$. Calculated, %: C 59.80; H 4.98; N 13.95; S 10.63.

4-(2-Furylmethyl)-1-(3-methyl-1-oxobutyl)thiosemicarbazide (IIe). Yield 83%, mp 153–154°C (from ethanol–water, 1:1), R_f 0.50 (ethanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3190–3280 (NH), 3050 (C–H_{arom}), 1690 (C=O), 1650 (C=C), 1215 (COC). ^1H NMR spectrum, δ, ppm: 0.90 t (6H, CH_3), 1.95 q [1H, C**H**$(CH_3)_2$], 2.15 d (2H, CH_2CO), 5.40 d (2H, NHC**H**$_2$), 6.30 s (1H, =CH), 6.45 s (1H, =CH), 7.60 s (1H, =CH), 8.45 t (1H, N**H**CH_2), 8.50 s (1H, NH), 9.55 s (1H, NH). Found, %: C 51.85; H 6.45; N 16.60; S 12.45. $C_{11}H_{17}N_3O_2S$. Calculated, %: C 51.77; H 6.67; N 16.47; S 12.55.

4,5-Disubstituted 4*H*-1,2,4-triazole-3-thiols IIIa–IIIe (*general procedure*). 1,4-Disubstituted thiosemicarbazide, 0.04 mol, was dissolved in a solution of 3.4 g (0.06 mol) of potassium hydroxide in 30.6 ml of water, the mixture was heated for 4 h on a boiling water bath, cooled, and acidified with dilute (1:1) hydrochloric acid to pH 2–3, and the precipitate was filtered off, washed with water, dried, and recrystallized from appropriate solvent.

4-Allyl-5-(2,4-dichlorophenoxymethyl)-4*H*-1,2,4-triazole-3-thiol (IIIa). Yield 86%, mp 140°C (from ethanol–water, 2:1), R_f 0.60 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3050 (C–H_{arom}), 2740 (SH), 1640 (C=C), 1610, 1600 (C=C_{arom}), 1540 (C=N), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 5.00 d (2H, NCH_2), 5.25 d (1H, =CH_2), 5.35 d (2H, OCH_2), 5.45 d (1H, =CH_2), 6.10 q (1H, =CH), 7.35 m (1H, H_{arom}), 7.45 m (1H, H_{arom}), 7.50 m (1H, H_{arom}), 13.90 s (1H, SH). Found, %: C 45.65; H 3.30; Cl 22.35; N 13.40; S 10.20. $C_{12}H_{11}Cl_2N_3OS$. Calculated, %: C 45.57; H 3.48; Cl 22.47; N 13.29; S 10.13.

5-(2,4-Dichlorophenoxymethyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (IIIb). Yield 93%, mp 191–192°C (from ethanol–water, 5:1), R_f 0.66 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080 (C–H_{arom}), 2750 (SH), 1610, 1600 (C=C_{arom}), 1545 (C=N), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 5.10 s (2H, OCH_2), 7.30 m (1H, H_{arom}), 7.45 m (2H, H_{arom}), 7.55 m (2H, H_{arom}), 7.60 m (3H, H_{arom}), 13.95 s (1H, SH). Found, %: C 51.25; H 3.05; Cl 20.30; N 12.05; S 8.95. $C_{15}H_{11}Cl_2N_3OS$. Calculated, %: C 51.14; H 3.13; Cl 20.17; N 11.93; S 9.09.

4-Allyl-5-(4-chloro-2-methylphenoxymethyl)-4*H*-1,2,4-triazole-3-thiol (IIIc). Yield 89%, mp 114–115°C (from ethanol–water, 2:1), R_f 0.64 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080 (C–H_{arom}), 2750 (SH), 1640 (C=C), 1600 (C=C_{arom}), 1540 (C=N), 1200 (COC), 750 (C–Cl). ^1H NMR spectrum, δ, ppm: 2.10 s (3H, CH_3), 5.00 d (2H, NCH_2), 5.25 d (2H, OCH_2), 5.20 d and 5.40 d (1H each, =CH_2), 6.00 q (1H, =CH), 6.85 m (1H, H_{arom}), 7.20 m (1H, H_{arom}),

7.35 m (1H, H_{arom}), 13.85 s (1H, SH). Found, %: C 52.90; H 4.60; Cl 12.15; N 14.35; S 10.70. $C_{13}H_{14}ClN_3OS$. Calculated, %: C 52.79; H 4.74; Cl 12.01; N 14.21; S 10.83.

5-Phenoxymethyl-4-phenyl-4*H*-1,2,4-triazole-3-thiol (IIId). Yield 96%, mp 170–172°C (from ethanol–water, 2:1), R_f 0.58 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3050 (C–H_{arom}), 2750 (SH), 1610 (C=C_{arom}), 1550 (C=N), 1180 (COC). ^1H NMR spectrum, δ, ppm: 5.25 s (2H, OCH_2), 6.85 m (3H, H_{arom}), 7.00 m (1H, H_{arom}), 7.20 m (2H, H_{arom}), 7.45 m (2H, H_{arom}), 7.50 m (2H, H_{arom}), 13.95 s (1H, SH). Found, %: C 63.50; H 4.70; N 14.95; S 11.20. $C_{15}H_{13}N_3OS$. Calculated, %: C 63.60; H 4.59; N 14.84; S 11.31.

4-(2-Furylmethyl)-5-isobutyl-4*H*-1,2,4-triazole-3-thiol (IIIe). Yield 73%, mp 135–136°C (from ethanol–water, 1:3), R_f 0.67 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080 (C–H), 2740 (SH), 1650 (C=C), 1550 (C=N), 1215 (COC). ^1H NMR spectrum, δ, ppm: 0.95 d (6H, CH_3), 1.85 m [1H, C**H**$(CH_3)_2$], 2.60 d (2H, CHC**H**$_2$), 4.75 s (2H, CH_2N), 6.00 d (1H, CH=), 6.45 d (1H, CH=), 7.50 t (1H, CH=), 13.25 s (1H, SH). Found, %: C 55.80; H 6.15; N 17.01; S 13.40. $C_{11}H_{15}N_3OS$. Calculated, %: C 55.70; H 6.33; N 17.72; S 13.50.

3-Benzylsulfanyl-1,2,4-triazoles IVa–IVf (*general procedure*). Anhydrous potassium carbonate, 0.7 g, was added to a mixture of 5 mmol of 3,4-disubstituted 1,2,4-triazole-3-thiol **III** and 5 mmol of the corresponding substituted benzyl chloride in 20 ml of anhydrous acetone. The mixture was heated for 10 h under reflux and evaporated, the residue was cooled, treated with 30 ml of water, and extracted with 70 ml of diethyl ether, the extract was washed with water and dried over anhydrous magnesium sulfate, the solvent was removed, and the crystalline residue was purified by recrystallization.

3-(3,4-Dichlorobenzylsulfanyl)-5-(2,4-dichlorophenoxymethyl)-4-phenyl-4*H*-1,2,4-triazole (IVa). Yield 75%, mp 75–76°C (from hexane), R_f 0.57 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1610, 1600 (C=C_{arom}), 1545 (C=N), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 4.00 s (2H, SCH_2), 5.05 s (2H, OCH_2), 6.90 m (3H, H_{arom}), 7.20 m (2H, H_{arom}), 7.30 m (1H, H_{arom}), 7.60 m (4H, H_{arom}), 7.70 m (1H, H_{arom}). Found, %: C 51.80; H 2.80; Cl 27.90; N 8.35; S 6.15. $C_{22}H_{15}Cl_4N_3OS$. Calculated, %: C 51.66; H 2.94; Cl 27.79; N 8.23; S 6.26.

3-(2,4-Dichlorobenzylsulfanyl)-5-(2,4-dichlorophenoxymethyl)-4-phenyl-4*H*-1,2,4-triazole (IVb). Yield 80%, mp 126–127°C (from ethanol), R_f 0.60 (ethanol–benzene, 1:5). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1610, 1600 (C=C_{arom}), 1540 (C=N), 1210 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 4.45 s (2H, SCH_2), 5.10 s (2H, OCH_2), 7.20 m (4H, H_{arom}), 7.30 m (2H, H_{arom}), 7.60 m (4H, H_{arom}), 7.70 m (1H, H_{arom}). Found, %: C 51.50; H 3.05; Cl 27.65; N 8.30; S 6.35. $C_{22}H_{15}Cl_4N_3OS$. Calculated, %: C 51.66; H 2.94; Cl 27.79; N 8.23; S 6.26.

4-Allyl-3-(4-chloro-2-methylphenoxymethyl)-5-(2,4-dichlorobenzylsulfanyl)-4*H*-1,2,4-triazole (IVc). Yield 85%, mp 85°C (from hexane), R_f 0.61 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1640 (C=C), 1610 (C=C_{arom}), 1540 (C=N), 1180 (COC), 750 (C–Cl). ^1H NMR spectrum, δ, ppm: 2.15 s (3H, CH_3), 4.45 s (2H, SCH_2), 4.55 s (2H, OCH_2), 4.90 d and 5.15 d (1H each, CH_2=), 5.20 s (2H, C**H**$_2$CH=), 5.90 m (1H, CH=), 7.10 m (4H, H_{arom}), 7.40 m (2H, H_{arom}). Found, %: C 52.95; H 3.85; Cl 23.30; N 9.30; S 7.15. $C_{20}H_{18}Cl_3N_3OS$. Calculated, %: C 52.81; H 3.96; Cl 23.43; N 9.24; S 7.04.

3-(2,4-Dichlorobenzylsulfanyl)-4-(2-furylmethyl)-5-isobutyl-4*H*-1,2,4-triazole (IVd). Yield 69%, mp 69–70°C (from hexane), R_f 0.52 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080 (C–H_{arom}), 3050 (C–H), 1650 (C=C), 1610, 1600 (C=C_{arom}), 1550 (C=N), 1215 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 0.90 s (6H, CH_3), 1.80 m [1H, C**H**$(CH_3)_2$], 2.50 d (2H, CHC**H**$_2$), 4.50 s (2H, SCH_2), 4.85 s (2H, NCH_2), 6.00 s (1H, CH=), 6.40 s (1H, CH=), 7.10 m (1H, C_6H_3), 7.25 m (1H, C_6H_3), 7.60 s (1H, CH=), 7.70 m (1H, C_6H_3). Found, %: C 54.45; H 4.90; Cl 17.80; N 10.20; S 7.95. $C_{18}H_{19}Cl_2N_3OS$. Calculated, %: C 54.55; H 4.80; Cl 17.93; N 10.61; S 8.08.

3-(2,4-Dichlorobenzylsulfanyl)-5-phenoxymethyl-4-phenyl-4*H*-1,2,4-triazole (IVe). Yield 88%, mp 108–109°C (from ethanol–water, 10:1), R_f 0.64 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1610, 1600 (C=C_{arom}), 1550 (C=N), 1180 (COC), 720 (C–Cl). ^1H NMR spectrum, δ, ppm: 4.40 s (2H, SCH_2), 5.05 s (2H, OCH_2), 7.00 m (2H, H_{arom}), 7.05 m (1H, H_{arom}), 7.15 m (1H, H_{arom}), 7.30 m (1H, H_{arom}), 7.35 m (2H, H_{arom}), 7.50–7.70 m (6H, H_{arom}). Found, %: C 59.65; H 4.00; Cl 16.20; N 9.60; S 7.15. $C_{22}H_{17}Cl_2N_3OS$. Calculated, %: C 59.73; H 3.85; Cl 16.06; N 9.50; S 7.24.

3-(3,4-Dichlorobenzylsulfanyl)-5-phenoxymethyl-4-phenyl-4*H*-1,2,4-triazole (IVf). Yield 80%, mp 126–127°C (from ethanol), R_f 0.60 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3050, 3080 (C–H_{arom}), 1600, 1615 (C=C_{arom}), 1550 (C=N), 1180

(COC), 730 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 4.40 s (2H, SCH_2), 5.00 s (2H, OCH_2), 6.90 m (3H, H_{arom}), 7.20 m (2H, H_{arom}), 7.30 m (4H, H_{arom}), 7.50 m (4H, H_{arom}). Found, %: C 59.85; H 3.70; Cl 16.15; N 9.65; S 7.15. $C_{22}H_{17}Cl_2N_3SO$. Calculated, %: C 59.73; H 3.85; Cl 16.06; N 9.50; S 7.24.

3-(Phenacylsulfanyl)-4*H*-1,2,4-triazoles Va–Vd (*general procedure*). A mixture of 5 mmol of 3,4-disubstituted 1,2,4-triazole-3-thiol **IIIb** or **IIId** and 5 mmol of bromoacetophenone or 4-nitro-ω-bromoacetophenone in 15 ml of anhydrous acetone was stirred for 0.5 h at room temperature and for 2 h on heating under reflux. The solvent was removed, the residue was cooled, treated with water, and made alkaline by adding aqueous ammonia to pH 8–9, and the precipitate was filtered off, washed with water, dried, and recrystallized.

2-[5-(2,4-Dichlorophenoxymethyl)-4-phenyl-4*H*-1,2,4-triazol-3-ylsulfanyl]-1-phenylethanone (Va). Yield 79%, mp 157–158°C (from ethanol), R_f 0.63 (ethanol–benzene, 1:4). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1730 (C=O), 1600, 1610 (C=C_{arom}), 1540 (C=N), 1210 (COC), 720 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 4.90 s (2H, SCH_2), 5.15 s (2H, OCH_2), 7.20 m (2H, H_{arom}), 7.30 m (1H, H_{arom}), 7.45–7.60 m (8H, H_{arom}), 8.05 m (2H, H_{arom}). Found, %: C 58.85; H 3.55; Cl 15.00; N 9.05; S 6.70. $C_{23}H_{17}Cl_2N_3OS$. Calculated, %: C 58.72; H 3.62; Cl 15.11; N 8.94; S 6.81.

2-[5-(2,4-Dichlorophenoxymethyl)-4-phenyl-4*H*-1,2,4-triazol-3-ylsulfanyl]-1-(4-nitrophenyl)ethanone (Vb). Yield 90%, mp 180–181°C (from ethanol), R_f 0.62 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1735 (C=O), 1650, 1600 (C=C_{arom}), 1545 (C=N), 1210 (COC), 720 (C–Cl). ^{1}H NMR spectrum, δ, ppm: 4.95 s (2H, SCH_2), 5.05 s (2H, OCH_2), 7.20 m (2H, H_{arom}), 7.30 m (1H, H_{arom}), 7.45–7.60 m (5H, H_{arom}), 8.30 m (4H, H_{arom}). Found, %: C 53.65; H 3.05; Cl 13.85; N 10.95; S 6.05. $C_{23}H_{16}Cl_2N_4O_4S$. Calculated, %: C 53.59; H 3.11; Cl 13.79; N 10.87; S 6.21.

2-[5-(Phenoxymethyl)-4-phenyl-4*H*-1,2,4-triazol-3-ylsulfanyl]-1-phenylethanone (Vc). Yield 77%, mp 80–51°C (from ethanol), R_f 0.60 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3050 (C–H_{arom}), 1730 (C=O), 1600 (C=C_{arom}), 1540 (C=N), 1200 (COC). ^{1}H NMR spectrum, δ, ppm: 4.95 s (2H, SCH_2), 5.20 s (2H, OCH_2), 7.20 m (2H, H_{arom}), 7.30 m (3H, H_{arom}), 7.45–7.60 m (8H, H_{arom}), 8.05 m (2H, H_{arom}). Found, %: C 68.55; H 4.65; N 10.65; S 7.85. $C_{23}H_{19}N_3O_2S$. Calculated, %: C 68.83; H 4.74; N 10.47; S 7.98.

1-(4-Nitrophenyl)-2-[5-(phenoxymethyl)-4-phenyl-4*H*-1,2,4-triazol-3-ylsulfanyl]ethanone (Vd). Yield 95%, mp 195–196°C (from ethanol), R_f 0.71 (ethanol–benzene, 1:6). IR spectrum, ν, cm^{-1}: 3080, 3050 (C–H_{arom}), 1735 (C=O), 1610, 1600 (C=C_{arom}), 1540 (C=N), 1200 (COC). ^{1}H NMR spectrum, δ, ppm: 4.85 s (2H, SCH_2), 5.40 s (2H, OCH_2), 6.95 m and 7.00–7.05 m (3H, H_{arom}), 7.30–7.50 m (5H, H_{arom}), 7.55–7.64 m (4H, H_{arom}), 7.94 m (2H, H_{arom}). Found, %: C 61.95; H 3.95; N 12.65; S 7.00. $C_{23}H_{18}N_4O_4S$. Calculated, %: C 61.88; H 4.04; N 12.56; S 7.18.

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