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SYNTHESIS OF AZOLES FROM 3-[(3-HYDRAZINO-3-OXOPROPYL)ANILINO]- AND 3-[(3-HYDRAZINO-3-OXOPROPYL)-4-METHYLANILINO]PROPANE HYDRAZIDES

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Condensation of 3-[(3-hydrazino-3-oxopropyl)anilino]- and 3-[(3-hydrazino-3-oxopropyl)-4-methylanilino]propane hydrazides with 2,4-pentanedione, phenyl isocyanate or phenyl isothiocyanate (with subsequent work up of the semicarbazides obtained by base), and carbon disulfide gave respectively: 1-(3,5-dimethyl-1H-1-pyrazolyl)-3-[3-(3,5-dimethyl-1H-1-pyrazolyl)-3-oxopropylanilino]-1-propanone, 3-(2-{[2-(5-oxo-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-5-one and its thio analog, and 5-(2-{[2-(2-thioxo-2,3-dihydro-1,3,4-oxadiazol-5-yl)ethyl]anilino}ethyl)-2,3-dihydro-1,3,4-oxadiazole-2(3H)-thione plus their methyl derivatives.

Keywords: hydrazides, 1,3,4-oxadiazoles, pyrazoles, 1,2,4-triazoles, cyclization.

1,2,3-Triazoles, oxa- and thiadiazoles have a broad spectrum of biological activity. A widely known method for the synthesis of diazoles is the cyclization of hydrazine derivatives with the dicarbonyl compounds acetylacetone or acetoacetic ester. In a series of studies carboxylic acid hydrazides have been used as the azo component [1-3].

The aim of this work was a study of the possible reaction of 3-[(3-hydrazino-3-oxopropyl)anilino]- and 3-[(3-hydrazino-3-oxopropyl)-4-methylanilino]propane hydrazides to give compounds with two pyrazole, oxadiazole, or triazine rings in their structure.

Refluxing the dihydrazides **1** with 2,4-pentanedione causes condensation to 1-(3,5-dimethyl-1H-1-pyrazolyl)-3-[3-[3,5-dimethyl-1H-1-pyrazolyl]-3-oxopropylanilino]-1-propanone (**2a**) or its 4-methyl analog **2b**. Formation of the pyrazole rings was confirmed by the presence of two methyl group singlets at 2.17 and 2.47 or 2.14 and 2.19 ppm and a methine singlet at 6.18 and 5.75 ppm in their ^{1}H NMR spectra. The carbon atom signals for the pyrazole rings were fully in agreement with analogous signals given for substituted pyrazoles [4-6]. Reaction of the dihydrazides **1** with phenyl isocyanate or phenyl isothiocyanate in methanol gave the hydrazinocarboxamide **3** and hydrazinocarbothioamide **4** derivatives, cyclization of which in basic medium gave 3-(2-{[2-(5-oxo-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4-phenyl-4,5-dihydro-3H-1,2,4-triazol-5-one (**5a**) or its methyl derivative **5b** and the thio analogs **6**. In the reaction of dihydrazides **1** with phenyl isocyanate, crystals of the semicarbazides **3** began to appear after 15 min heating while phenyl isothiocyanate required more prolonged heating. The ^{1}H NMR spectra of the semicarbazides **3** and

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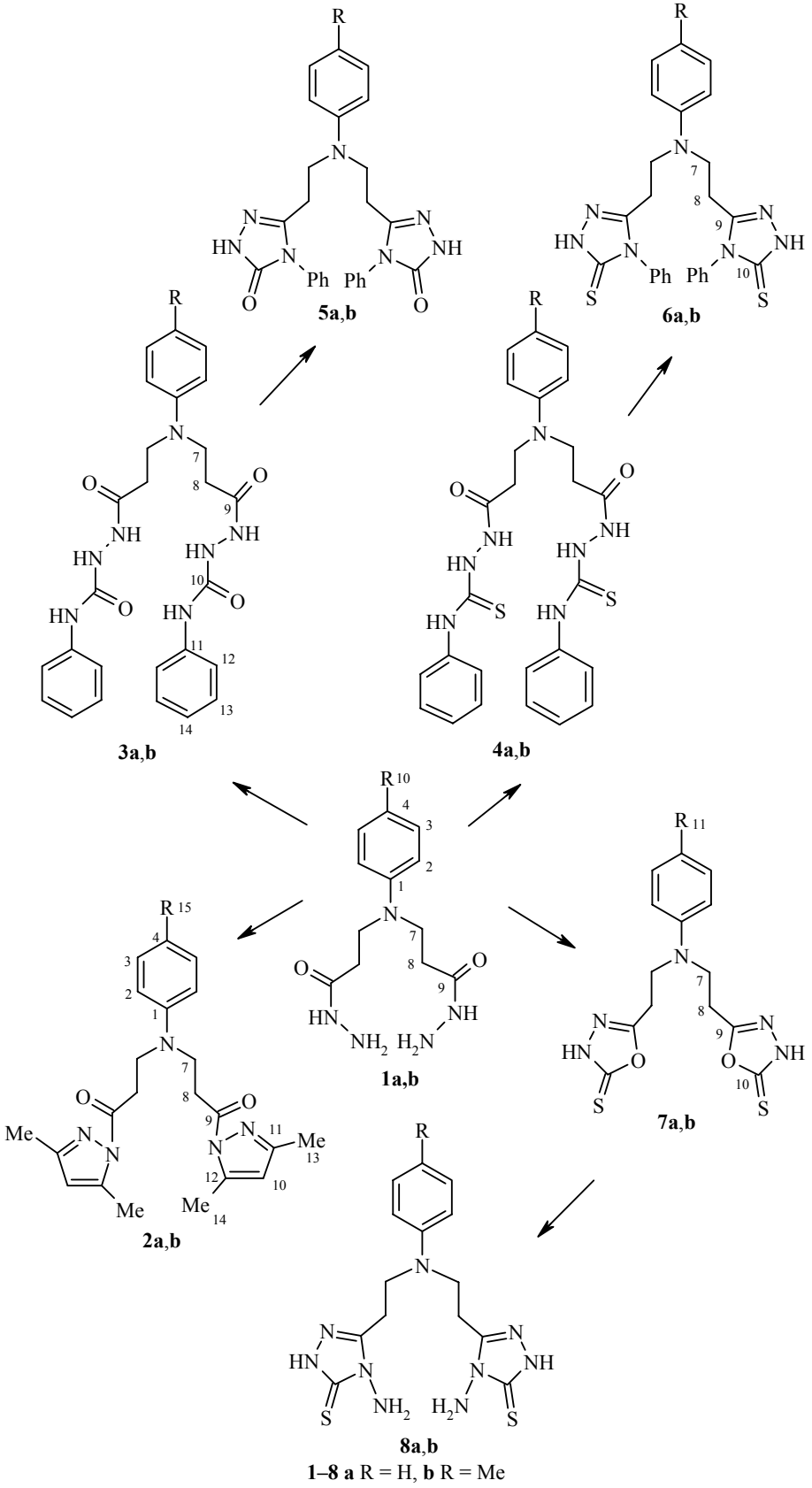

5a,**b**

6a,**b**

3a,**b**

4a,**b**

1a,**b**

7a,**b**

2a,**b**

8a,**b**

1–8 a R = H, **b** R = Me

thiosemicarbazides **4** showed a set of signals for the protons of the phenyl radical and the absence of the signals for primary amino group protons present in the hydrazide **1**. The triazole ring proved to have a marked deshielding effect on the hydrogen atoms of the neighboring methylene group as a result of which the signals in the ^{1}H NMR spectra of compounds **5, 6** are found 0.19 and 0.31 ppm to lower field than the corresponding signals in the starting dihydrazides **1** [7]. The 1,3,4-oxadiazole-2(3H)-thiones **7** were prepared [3] by refluxing the hydrazides **1** with carbon disulfide in basic alcoholic medium and subsequent cyclization of the potassium salts of the hydrazinocarbodithioates formed using hydrochloric acid (without their isolation). The oxadiazole-2(3)-thiones **7** were separated from the reaction mixture as a difficult to crystallize mass. Methanol, ethanol, and butanol were used as solvent in this reaction, the best yield being obtained with ethanol. It is known [8, 9] that the nitrogen atom in 1,3,4-oxadiazole-2(3H)-thiones can be exchanged for an alkylamino group using aliphatic amines. Refluxing the oxadiazolethiones **7** with aniline in dioxane for 16 h did not give the phenyl derivative **6**. Treatment of the 1,3,4-oxadiazole-2(3H)-thiones **7** with hydrazine in refluxing dioxane caused exchange of the oxygen atom for a nitrogen and gave 4-amino-3-{2-[4-amino-5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-ylethyl-anilino]ethyl}-4,5-dihydro-1H-1,2,4-triazol-5-thione (**8a**) and its methyl derivative **8b**. The ^{1}H NMR spectra of compound **8** shows singlet signals for the amino groups at 5.67 and 5.63 ppm respectively and NH signals at 13.56 ppm typical of 1,3,4-oxadiazole-2-thiones.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Varian 300 instrument (300 and 75 MHz respectively) using TMS as internal standard and DMSO-d_6 as solvent. IR spectra were taken on a Perkin-Elmer Spectrum Bx FT-IR spectrometer for KBr tablets. Mass spectra were recorded on a Waters Micromass ZQ 2000 instrument using chemical ionization. Monitoring of the reaction course and purity of the compounds prepared was carried out using TLC on Silufol 254 and Silufol UV-254 plates.

1-(3,5-Dimethyl-1H-1-pyrazolyl)-3-[3-(3,5-dimethyl-1H-1-pyrazolyl)-3-oxopropylanilino]-1-propanone (2a). A mixture of the dihydrazide **1a** (1.325 g, 5 mmol), methanol (50 ml), 2,4-pentanedione (2 ml, 2.0 g, 20 mmol), and HCl (2M, 1 ml) was refluxed for 4 h, cooled, and water (50 ml) was added. The oily layer produced was separated and crystallized from methanol to give compound **2a** (1.32 g, 42%) with mp 112-113ºC. IR spectrum, ν, cm^{-1}: 1722 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.17, 2.47 (12H, 2s, CH_3); 3.29 (4H, t, *J* = 7.05, $COCH_2$); 3.75 (4H, t, *J* = 7.05, NCH_2); 6.18 (2H, s, CH=); 6.65 (1H, t, *J* = 7.2, H-4 Ar); 6.82 (2H, d, *J* = 7.9, H-2,6 Ar); 7.19 (2H, t, *J* = 7.9, H-3,5 Ar). ^{13}C NMR spectrum, δ, ppm: 171.96 (C-9); 151.36 (C-11); 146.71 (C-1); 143.07 (C-12), 129.14 (C-3); 115.97 (C-4); 112.04 (C-2); 111.08 (C-10); 45.99 (C-7); 33.13 (C-8); 14.39 (C-14); 13.97 (C-13). Mass spectrum (20 eV), *m/z* (I_{rel}, %): 394 $[M+H]^+$ (50). Found, %: C 67.36; H 6.87; N 17.65. $C_{22}H_{27}N_5O_2$. Calculated, %: C 67.15; H 6.92; N 17.80.

1-(3,5-Dimethyl-1H-1-pyrazolyl)-3-[3-(3,5-dimethyl-1H-1-pyrazolyl)-4-methylanilino-3-oxopropyl]-1-propanone (2b) was prepared similarly to compound **2a** from the dihydrazide **1b** (1.395 g, 5 mmol). Yield 0.75 g (36%); mp 117-118ºC. IR spectrum, ν, cm^{-1}: 1728 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.14 (3H, s, 4-CH_3); 2.19, 2.22 (12H, 2s, CH_3); 3.54 (4H, t, *J* = 7.0, $COCH_2$); 3.61 (4H, t, *J* = 7.0, NCH_2); 5.75 (2H, s, CH=); 6.64 (2H, d, *J* = 8.5, H-2,6 Ar); 7.02 (2H, t, *J* = 8.5, H-3,5 Ar). ^{13}C NMR spectrum, δ, ppm: 172.04 (C-9); 151.93 (C-11); 144.49 (C-1); 142.64 (C-12); 129.62 (C-3); 124.89 (C-4); 112.58 (C-2); 103.09 (C-10); 51.27 (C-7); 46.30 (C-8); 31.58 (C-15); 19.78 (C-14); 11.83 (C-13). Mass spectrum (30 eV), *m/z* (I_{rel}, %): 408 $[M+H]^+$ (40). Found, %: C 67.52; H 6.95; N 17.01. $C_{23}H_{29}N_5O_2$. Calculated, %: C 67.79; H 7.17; N 17.19.

N-Phenyl-2-[3-({3-[2-(anilinocarbonyl)hydrazino]-3-oxopropyl}anilino)propanoyl]-1-hydrazinocarboxamide (3a). Phenyl isocyanate (1.19 ml, 10 mmol) was added to a hot solution of dihydrazide **1a** (1.325 g, 5 mmol) in methanol (50 ml). The mixture was refluxed until a precipitate appeared, cooled, the crystals filtered off, washed with methanol, and recrystallized from methanol. Yield 1.5 g (59%);

mp 203-204ºC. IR spectrum, ν, cm^{-1}: 1717 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.35 (4H, t, *J* = 7.2, CH_2CO); 3.61 (4H, t, *J* = 7.2, CH_2N); 6.66 (1H, t, *J* = 7.2, H-4 Ar); 6.78 (2H, d, *J* = 8.1, H-2,6 Ar); 6.99 (2H, t, *J* = 8.1, H-3,5 Ar); 7.19-7.30 (10H, m, H Ar); 8.07 (2H, s, NHNHCO); 8.75 (2H, s, NHNHCO); 9.78 (2H, s, NH Ar). ^{13}C NMR spectrum, δ, ppm: 170.58 (C-9); 155.22 (C-10); 146.81 (C-1); 139.51 (C-11); 129.20 (C-3); 128.58 (C-13); 121.82 (C-14); 118.41 (C-4); 115.76 (C-12); 111.78 (C-2); 46.40 (C-7); 31.22 (C-8). Mass spectrum (35 eV), *m/z* (I_{rel}, %): 504 $[M+H]^+$ (40). Found, %: C 61.83; H 5.67; N 19.50. $C_{26}H_{29}N_7O_4$. Calculated, %: C 62.02; H 5.80; N 19.47.

N-Phenyl-2-[3-({3-[2-(anilinocarbonyl)hydrazino]-3-oxopropyl}-4-methylanilino)propanoyl]-1-hydrazinocarboxamide (3b) was prepared similarly to compound **3a** from dihydrazide **1b** (2.79 g, 10 mmol) and phenylisocyanate (2.38 g, 20 mmol). Yield 4.0 g (77%); mp 201-202ºC. IR spectrum, ν, cm^{-1}: 1670 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.18 (3H, s, 4-CH_3); 2.38 (4H, t, *J* = 7.2, CH_2CO); 3.58 (4H, t, *J* = 7.2, CH_2N); 7.19 (2H, d, *J* = 8.5, H-3,5 Ar); 6.63 (2H, d, *J* = 8.5, H-2,6 Ar); 6.86-7.11 (10H, m, H Ar); 7.98 (2H, s, NHNHCO); 8.73 (2H, s, NHNHCO); 9.74 (2H, s, NH Ar). ^{13}C NMR spectrum, δ, ppm: 170.06 (C-9); 155.37 (C-10); 144.94 (C-1); 139.68 (C-11); 129.63 (C-3); 128.60 (C-13); 124.26 (C-4); 121.80 (C-14); 115.75 (C-12); 112.49 (C-2); 46.51 (C-7); 31.22 (C-8); 31.58 (C-15). Mass spectrum (15 eV), *m/z* (I_{rel}, %): 518 $[M+H]^+$ (100). Found, %: C 63.07; H 5.59; N 18.70. $C_{27}H_{31}N_7O_4$. Calculated, %: C 62.65; H 6.04; N 18.94.

N-Phenyl-2-[3-({3-[2-(anilinothiocarbonyl)hydrazino]-3-oxopropyl}anilino)propanoyl]-1-hydrazinocarbothioamide (4a). A mixture of **1a** (1.325 g, 5 mmol), methanol (50 ml), and phenyl isothiocyanate (1.32 ml, 1.49 g, 11 mmol) was refluxed for 4 h, a solution of KOH (20%, 20 ml) was added, and the product was refluxed for a further 20 min. It was cooled and the crystals produced were filtered off, washed with ether, and crystallized from a mixture of DMF and water. Yield 1.93 g (67%); mp 160-161ºC. IR spectrum, ν, cm^{-1}: 3199 (NH), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.27 (4H, t, *J* = 7.05, $COCH_2$); 3.64 (4H, t, *J* = 7.05, CH_2N); 6.67 (1H, t, *J* = 7.05, H-4 Ar); 6.81 (2H, d, *J* = 8.2, H-2,6 Ar); 7.17 (2H, t, *J* = 8.2, H-3,5 Ar); 7.18-7.26 (10H, m, H Ar); 9.62 (4H, s, NHNHCO); 10.04 (2H, br. s, NH Ar). ^{13}C NMR spectrum, δ, ppm: 180.96 (C-10); 170.62 (C-9); 146.85 (C-1); 139.04 (C-11); 129.24 (C-3); 128.07 (C-13); 125.19 (C-14); 118.65 (C-4); 115.87 (C-12); 111.94 (C-2); 46.19 (C-7); 31.25 (C-8). Mass spectrum (30 eV), *m/z* (I_{rel}, %): 536 $[M+H]^+$ (100). Found, %: C 57.93; H 5.75; N 17.96. $C_{26}H_{29}N_7O_2S_2$. Calculated, %: C 58.29; H 5.46; N 18.30.

N-Phenyl-2-[3-({3-[2-(anilinothiocarbonyl)hydrazino]-3-oxopropyl}4-methylanilino)propanoyl]-1-hydrazinocarbothioamide (4b) was prepared similarly to compound **4a** from dihydrazide **1b** (1.395 g, 5 mmole) and phenylisothiocyanate (1.32 ml, 1.49 g, 11 mmol). Yield 1.1 g (41%), mp 168-169ºC. IR spectrum, ν, cm^{-1}: 3162 (NH), 1702 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.16 (3H, s, 4-CH_3); 2.35 (4H, t, *J* = 7.05, $COCH_2$); 3.58 (4H, t, *J* = 7.05, CH_2N); 6.96 (2H, d, *J* = 8.1, H-2,6 Ar); 7.05 (2H, dd, *J* = 7.3, *J* = 8.1, H-3,5 Ar); 7.25-7.34 (10H, m, H Ar); 9.59, 9.54 (4H, s, NHNHCO); 10.00 (2H, s, NH Ar). ^{13}C NMR spectrum, δ, ppm: 181.96 (C-10); 170.59 (C-9); 144.83 (C-1); 139.69 (C-11); 130.47 (C-14); 128.04 (C-13); 127.78 (C-12); 125.75 (C-4); 124.64 (C-3); 112.47 (C-2); 50.43 (C-7); 31.25, 30.89 (C-8); 20.64 (C-15). Mass spectrum (45 eV), *m/z* (I_{rel}, %): 550 $[M+H]^+$ (60**)**. Found, %: C 58.96; H 6.09; N 17.57. $C_{27}H_{31}N_7O_2S_2$. Calculated, %: C 58.99; H 5.68; N 17.83.

3-(2-{[2-(5-Oxo-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-5-one (5a). A solution of hydrazinocarboxamide **3a** (1.3 g, 2.6 mmol) in KOH solution (20%, 20 ml) was refluxed for 1 h. The reaction mixture was cooled, conc. HCl was added to pH 4, and the precipitated crystals were filtered, washed with water, and recrystallized from a mixture of DMF and water. Yield 1.0 g (80%); mp 190-191ºC. IR spectrum, ν, cm^{-1}: 3166 (NH), 1707 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.46 (4H, t, *J* = 7.2, CH_2CN); 3.25 (4H, t, *J* = 7.2, CH_2N); 6.56 (1H, t, *J* = 7.2, H-4 Ar); 6.71 (2H, d, *J* = 7.2, H-2,6 Ar); 6.99 (2H, t, *J* = 7.2, H-3,5 Ar); 7.28-7.57 (10H, m, H Ar); 11.74 (2H, s, NNH). ^{13}C NMR spectrum, δ, ppm: 154.28 (C-10); 145.99 (C-1); 144.97 (C-9); 132.73 (C-3); 129.44 (C-11); 129.09 (C-14); 128.66 (C-13); 127.50 (C-12); 115.78 (C-4); 110.93 (C-2); 46.63 (C-7); 23.57 (C-8). Mass spectrum (30 eV), *m/z* (I_{rel}, %): 468 $[M+H]^+$ (40). Found, %: C 67.10; H 5.40; N 20.64. $C_{26}H_{25}N_7O_2$. Calculated, %: C 66.79; H 5.39; N 20.97.

3-(2-{4-Methyl[2-(5-oxo-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4-phenyl-4,5-dihydro-1H-1,2,4-triazol-5-one (5b) was prepared similarly to compound **5a** from hydrazinocarboxamide **3b** (0.63 g, 1.3 mmol). Yield 0.48 g (83%); mp 246-247ºC. IR spectrum, ν, cm^{-1}: 3156 (NH), 1722 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (3H, s, 4-CH_3); 2.48 (4H, t, *J* = 7.2, CH_2CN); 3.59 (4H, t, *J* = 7.2, CH_2N); 6.75 (2H, d, *J* = 8.5, H-3,5 Ar); 6.95 (2H, d, *J* = 8.5, H-2,6 Ar); 7.24-7.51 (10H, m, H Ar); 11.84 (2H, s, NNH). ^{13}C NMR spectrum, δ, ppm: 154.15 (C-10); 144.09 (C-1); 143.62 (C-9); 132.50 (C-3); 129.95 (C-11); 129.41 (C-14); 128.65 (C-13); 127.32 (C-12); 125.23 (C-4); 109.96 (C-2); 59.53 (C-7); 43.89 (C-8); 20.06 (C-15). Mass spectrum (20 eV), *m*/*z* (I_{rel}, %): 482 $[M+H]^+$ (60). Found, %: C 67.21; H 5.38; N 20.34. $C_{27}H_{27}N_7O_2$. Calculated, %: C 67.34; H 5.65; N 20.36.

4-Phenyl-3-(2-{[2-(4-phenyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4,5-dihydro-1H-1,2,4-triazol-5-thione (6a). Compound **4a** (0.54 g, 1 mmol) and KOH solution (20%, 20 ml) were refluxed for 5 h. After cooling to room temperature, conc. HCl was added to pH 4 and the precipitated crystals were filtered off, washed with water, and recrystallized from a mixture of DMF and water. Yield 0.4 g (89%); mp 228-229ºC. IR spectrum, ν, cm^{-1}: 3296 (NH), 1670 (C=O), 1540, 1468 (C=S). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.45 (4H, t, *J* = 7.05, CH_2CN); 3.54 (4H, t, *J* = 7.05, CH_2N); 6.68 (1H, t, *J* = 8.3, H-4 Ar); 6.79 (2H, d, *J* = 8.3, H-2,6 Ar); 7.12 (2H, t, *J* = 8.3, H-3,5 Ar); 7.28-7.47 (10H, m, H Ar); 13.71 (2H, s, NNHC=S). ^{13}C NMR spectrum, δ, ppm: 167.61 (C-10); 146.91 (C-1); 133.52 (C-9); 129.35 (C-3); 129.68 (C-11); 129.63 (C-13); 128.31 (C-14); 122.99 (C-12); 118.78 (C-4); 112.01 (C-2); 46.86 (C-7); 44.89 (C-8). Mass spectrum (20 eV), *m*/*z* (I_{rel}, %): 500 $[M+H]^+$ (100). Found, %: C 62.35; H 4.91; N 19.43. $C_{26}H_{25}N_7S_2$. Calculated, %: C 62.50; H 5.04; N 19.62.

3-(2-{4-Methyl[2-(4-phenyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]anilino}ethyl)-4-phenyl-4,5-dihydro-1H-1,2,4-triazole-3-thione (6b). The hydrazinocarbothioamide **4b** (0.625 g, 1.3 mmol) was refluxed for 1 h with KOH solution (20%, 20 ml). After cooling to room temperature conc. HCl was added to pH 4 and the precipitated crystals were filtered off, washed with water, and crystallized from methanol. Yield 0.48 g (82%); mp 262-263ºC. IR spectrum, ν, cm^{-1}: 1500, 1452 (C=S). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.09 (3H, s, 4-CH_3); 2.49 (4H, t, *J* = 7.05, CH_2CN); 3.39 (4H, t, *J* = 7.05, CH_2N); 5.92 (2H, d, *J* = 8.5, H-2,6 Ar); 6.73 (2H, d, *J* = 8.5, H-3,5 Ar); 7.37-7.56 (10H, m, H Ar); 13.77 (2H, s, NNHC=S). ^{13}C NMR spectrum, δ, ppm: 167.55 (C-10); 143.60 (C-1); 133.47 (C-9); 129.52 (C-3); 129.46 (C-11); 129.41 (C-13); 128.29 (C-14); 124.54 (C-4); 122.97 (C-12); 111.28 (C-2); 46.95 (C-7); 44.91 (C-8); 20.60 (C-15). Mass spectrum (70 eV), *m*/*z* (I_{rel}, %): 514 $[M+H]^+$ (40). Found, %: C 62.99; H 5.25; N 18.85. $C_{27}H_{27}N_7S_2$. Calculated, %: C 63.13; H 5.30; N 19.09.

5-(2-{[2-(2-Thioxo-2,3-dihydro-1,3,4-oxadiazol-5-yl)ethyl]anilino}ethyl)-2,3-dihydro-1,3,4-oxadiazole-2-thione (7a). CS_2 (5.7 g, 4.5 ml, 75 mmol) was added dropwise with stirring to a solution of KOH (2.8 g, 50 mmol) in ethanol (75 ml) and stirred for 15 min at 20ºC. Dihydrazide **1a** (13.25 g, 50 mmol) in ethanol (50 ml) was added to the solution obtained and the product was stirred at reflux for 24 h. The liquid fraction was distilled off, the residue was dissolved in water (150 ml), HCl added to pH 3-4, and the mass produced was separated, and was washed with and crystallized from methanol. Yield 11.8 g (69%); mp 167-168ºC. IR spectrum, ν, cm^{-1}: 3179 (NH), 1505 (C=S). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.43 (4H, t, *J* = 7.1, CH_2CN); 3.01 (4H, t, *J* = 7.1, CH_2N); 6.64-6.91 (5H, m, H Ar); 9.97, 10.12 (2H, 2s, NN H). ^{13}C NMR spectrum, δ, ppm: 177.69 (C-10); 162.44 (C-9), 146.18 (C-1); 129.32 (C-3); 116.13 (C-4); 112.02 (C-2); 46.89 (C-7); 32.20 (C-8). Mass spectrum (20 eV), *m/z* (I_{rel}, %): 350 $[M+H]^+$ (30). Found, %: C 47.75; H 3.90; N 19.86. $C_{14}H_{15}N_5O_2S_2$. Calculated, %: C 48.14; H 4.30; N 20.06.

5-(2-{4-Methyl[2-(2-thioxo-2,3-dihydro-1,3,4-oxadiazol-5-yl)ethyl]anilino}ethyl)-2,3-dihydro-1,3,4-oxadiazole-2-thione (7b) was prepared similarly to compound **7a** from KOH solution (1.4 g, 25 mmol) in ethanol (50 ml), CS_2 (3.8 gm, 3 ml, 50 mmol), and the dihydrazide **1b** (6.97 g, 25 mmol) in ethanol (50 ml). Yield 1.4 g (11%), mp 166-167ºC. IR spectrum, ν, cm^{-1}: 3175 (NH), 1507 (C=S). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.20 (3H, s, 4-CH_3); 2.54 (4H, t, *J* = 7.1, CH_2CN); 3.48 (4H, t, *J* = 7.1, CH_2N); 6.63-7.04 (5H, m, H Ar);

10.02, 10.18 (2H, 2s, NNH). ^{13}C NMR spectrum, δ, ppm: 177.73 (C-10); 162.69 (C-9), 144.96 (C-1); 129.47 (C-3); 124.27 (C-4); 111.81 (C-2); 47.01 (C-7); 32.48 (C-8); 19.85 (C-11). Mass spectrum (20 eV), *m/z* (I_{rel}, %): 364 $[M+H]^+$ (30). Found, %: C 49.25; H 4.98; N 18.93. $C_{15}H_{17}N_5O_2S_2$. Calculated, %: C 49.57; H 4.71; N 19.27.

4-Amino-3-{2-[4-amino-(5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethylanilino]ethyl}-4,5-dihydro-1H-1,2,4-triazole-5-thione (8a). A mixture of the oxadiazolethione **7a** (3.49 g, 10 mmol), NH_2NH_2 (1.5 g, 30 mmol), and dioxane (20 ml) was refluxed for 10 h and a solution of KOH (10%) was added to pH 10. The basic solution was filtered and the filtrate was acidified with HCl to pH 3. The precipitate was filtered off, washed with cold water to neutral reaction, and crystallized from ethanol. Yield 2.5 g (66%); mp 200-201ºC. IR spectrum, ν, cm^{-1}: 1722 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.24 (4H, t, *J* = 7.3, CH_2CN); 3.53 (4H, t, *J* = 7.3, CH_2N); 6.64-6.97 (5H, m, H Ar); 5.67 (4H, s, $2NH_2$); 13.56 (2H, s, 2NH). ^{13}C NMR spectrum, δ, ppm: 165.87 (C-10); 146.73 (C-1); 143.59 (C-9); 129.26 (C-3); 115.92 (C-4); 111.75 (C-2); 47.75 (C-7); 22.53 (C-8). Mass spectrum (20 eV), *m/z* (I_{rel}, %): 378 $[M+H]^+$ (40). Found, %: C 44.89; H 5.48; N 32.95. $C_{14}H_{19}N_9S_2$. Calculated, %: C 44.54; H 5.07; N 33.39.

4-Amino-3-{2-[4-amino-(5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl-4-methylanilino]ethyl}-4,5-dihydro-1H-1,2,4-triazole-5-thione (8b) was prepared similarly to compound **8a** from the oxadiazolethione **7b** (1.82 g, 5 mmol), NH_2NH_2 (0.76 g, 15 mmol), and dioxane (20 ml). Yield 2.5 g (66%); mp 165-166ºC. IR spectrum, ν, cm^{-1}: 1722 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.20 (3H, s, 4-CH_3); 2.91 (4H, t, *J* = 7.2, CH_2CN); 3.66 (4H, t, *J* = 7.2, CH_2N); 6.78-7.03 (4H, m, H Ar); 5.63 (4H, s, $2NH_2$); 13.56 (2H, s, 2NH). ^{13}C NMR spectrum, δ, ppm: 165.91 (C-10); 144.48 (C-1); 143.61 (C-9); 129.76 (C-3); 124.36 (C-4); 112.14 (C-2); 48.00 (C-7); 22.55 (C-8); 19.88 (C-11). Mass spectrum (20 eV), *m/z* (I_{rel}, %): 392 $[M+H]^+$ (60). Found, %: C 44.89; H 5.48; N 32.95. $C_{15}H_{21}N_9S_2$. Calculated, %: C 44.54; H 5.07 N 33.39.

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