Heteroatom Chemistry
Volume 20, Number 7, 2009

Synthesis of Novel 1,3-Substituted 1*H*-[1,2,4]-Triazole-3-Thiol Derivatives

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Received 2 May 2009

ABSTRACT: *By means of regioselective S-alkylation of 1H-1,2,4-triazole-3-thiol (***1***), a series of S-substituted derivatives* **2a**–**j** *were synthesized. In certain conditions, the reaction of* **2** *with arylsulfochlorides, arylisocyanates, and quaternary ammonium salts of azines corresponding compounds were obtained 1-arylsulfonyl- (***3a**–**d***), 1-arylcarbonamido-* **(4a,b),** *and 1-azinyl-1,2,4- (***6a**–**p***) triazoles. Structures of compounds were confirmed by* ^1H *NMR and elemental analyses.* © 2010 Wiley Periodicals, Inc. Heteroatom Chem 20:405–410, 2009; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20565

INTRODUCTION

1,2,4-Triazole derivatives represent one of the most interesting and important classes of compounds, possessing a wide spectrum of biological activity. Thus, some carbonamido(carboxy)methylthio-4-amino-1,2,4-triazoles and products of their intramolecular cyclization with antituberculosis activity [1], 5-aryl-substituted 1,2,4-triazol-3-thiols, having anti-inflammatory properties [2], diverse derivatives having antibacterial, antifungal, hypoglycemic, antihypertensive, and analgesic activities [3–10], and a series of 3,5-substituted 1,2,4-triazoles with expressed fungicide [11] and herbicide activities [12–14] are described.

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The purpose of the present research was to synthesize new 1*H*-1,2,4-triazole-3-thiol derivatives, by regioselective substitution in positions 1 and 3 of heterocycle and further study of physiological activity of the obtained substances.

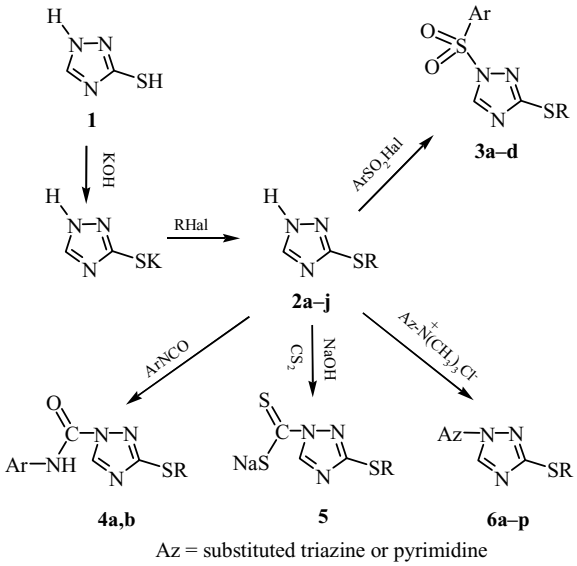
RESULTS AND DISCUSSION

Initial 1*H*-1,2,4-triazole-3-thiol **1** can be obtained in various tautomeric forms with 3-thiol or 3-thion groups and depending on localization of hydrogen atom at three different nitrogen atoms of heterocycle. However, it has been established that under action of halogen derivatives at 20°C in water or at short-term heating in acetone proceeds only 3-S-substitution (**2a–j**, Scheme 1).

For the benefit of it, the data of ^{1}H NMR spectra are verified. Thus, the chemical shift values of 5-H singlet (8.10–8.20 ppm) specify that alkylation proceeds without infringement of heterocycle aromaticity, and signal of a mobile proton (13,7–13.8 ppm) corresponds to the NH group. Hence, the structures with the thion group in the third position of triazole are excluded. The chemical shifts of alkyl groups attached to heteroatom also agree with S-substitution. These conclusions conform to those data that were reviewed in [15–18].

Some authors established that N-alkylation of azoles successfully proceeds in biphase catalytic systems [19,20]; however, in the case of triazole derivatives, the yields of obtained compounds do not exceed 43%–68%.

In our investigation, it was shown that N-substitution of obtained compounds by action of



SCHEME 1

arylsulfochlorides easily proceeds in benzene, using triethylamine as a hydrogen chloride acceptor (**3a–d**), and in the presence of catalytic amounts of pyridine these compounds form with arylisocyanates 1-*N*-arylcarbonamido derivatives (**4a,b**). From compound **2b** under action of carbon disulfide and in the presence of caustic soda in benzene, sodium *N*-dithiocarbamate (**5**) was formed. Compounds **2a–j** in acetone in the presence of caustic potash easily interact with azinyl-2(4)-trimethyl ammonium chlorides and form corresponding **6a–p** compounds (Scheme 1).

Compounds **2** can exist in three different tautomeric forms, depending on the hydrogen atom attachment. In ^{1}H NMR spectra of these compounds, signals of NH and 5-H are widened, the spin–spin interaction between them is invisible, and during heating the signals are narrowed. This effect can be explained on the basis of the "fast" (in comparison with a temporary NMR scale) exchange of a mobile proton between the nitrogen atoms of heterocycle. At the same time, the signals of 5-H in ^{1}H NMR spectra of compounds **3–6** undergo low-field shift at 0.85–1.0 ppm in comparison with compounds **2**, which agree with 1-N or 4-N-substitution. The last mechanism is excluded because the signals of the 5-CH_2 group should be observed in ^{1}H NMR spectra. For this reason for compounds **3–6**, the structure with 1-N-substitution is attributed.

EXPERIMENTAL

The ^{1}H NMR spectra were determined by Varian mercury-300 spectrometer, in the mixture of solvents DMSO-d_6 and CCl_4 (1:3), using tetramethylsilane as internal standard. The reaction course control and individuality of the received substances were checked by using the TLC method and acetone–hexane mixture (2:1) as eluent. Melting points are uncorrected. Initial 1*H*-[1,2,4]-triazole-3-thiol **1** and quaternary ammonium salts for synthesis of **6a–p** were prepared as described, respectively, in [21] and [22].

Synthesis of Compounds **2a–g** *(Prepared from* **1***)*

General Procedure. To a solution of potassium salt of 1*H*-[1,2,4]-triazole-3-thiol (0.01 mol, 1.4 g) in 5 mL water at 0°C, 0.01 mol alkyl halide was added dropwise with continuous stirring, and the mixture was allowed to stand at 20°C for 24 h. Then the mixture was diluted with water (5 mL), the residue of a product filtered off, washed with water, and dried in the air. The resulting compound was purified by recrystallization from hexane: benzene (1:1).

*3-Methylsulfanyl-1H-1,2,4-triazol (***2a***).* The compound was obtained in 74% yield as a white crystal; mp 104–106°C; ^{1}H NMR δ (ppm): 2.43 (3H, s, SCH_3); 8.15 (1H, w.s, 5-H); 13.70 (1H, w.s, NH); elemental anal. (%), Calcd for $C_3H_5N_3S$: N, 36.52; S, 27.83; Found: N, 36.33; S, 28.09.

*(1H-1,2,4-Triazol-3-yl-sulfanyl)-acetic acid methyl ester (***2b***).* The compound was obtained in 81% yield as a white crystal; mp 119–121°C; ^{1}H NMR δ (ppm): 3.70 (3H, s, OCH_3); 3.91 (2H, s, SCH_2); 8.10 (1H, w.s, CH); 13.80 (1H, w.s, NH); elemental anal. (%), Calcd for $C_5H_7N_3OS$: N, 24.28; S, 18.50; Found: N, 24.04; S, 18.24.

*(1H-1,2,4-Triazol-3-yl-sulfanyl)-acetic acid ethyl ester (***2c***).* The compound was obtained in 76% yield as a white crystal; mp 55–57°C; ^{1}H NMR δ (ppm): 1.27 (3H, t, J = 6.9, $CH_2\underline{CH_3}$); 3.93 (2H, s, SCH_2); 4.16 (2H, q, J = 6.9, $\underline{CH_2}CH_3$); 8.14 (1H, w.s, 5-H); 13.70 (1H, w.s, NH); elemental anal. (%), Calcd for $C_6H_9N_3OS$: N, 22.46; S, 17.11; Found: N, 22.21; S, 17.32.

*2-(1H-1,2,4-Triazol-3-yl-sulfanyl)-acetamide (***2d***).* The compound was obtained in 79% yield as a white crystal; mp 164–166°C; ^{1}H NMR δ (ppm): 3.85 (2H, s, SCH_2); 6.95 and 7.37 (2H, w.s, NH_2); 8.15 (1H, w.s, CH); 13.75 (1H, w.s, NH); elemental anal. (%), Calcd for $C_4H_6N_4OS$: N, 35.44; S, 20.25; Found: N, 35.18; S, 19.97.

*3-(1H-1,2,4-Triazol-3-yl-sulfanyl)-pentane-2,4-dione (**2e**).* The compound was obtained in 65% yield as a white crystal; mp 114–115°C; ^{1}H NMR δ (ppm): 2.35 [6H, s, $(CH_3)_2$]; 8.20 (1H, s, 5-H); 13.80 (1H, w.s, NH); 17.10 (1H, s, OH-enol); elemental anal. (%), Calcd for $C_7H_9N_3O_2S$: N, 21.05; S, 16.08; Found: N, 20.88; S, 16.37.

*3-Benzylsulfanyl-1H-1,2,4-triazole (**2f**).* The compound was obtained in 83% yield as a white crystal; mp 80–82°C; ^{1}H NMR δ (ppm): 3.83 (2H, s, SCH_2); 7.17–7.45 (5H, m, C_6H_5); 8.12(1H, w.s, 5-H); 13.80 (1H, w.s, NH); elemental anal. (%), Calcd for $C_9H_9N_3S$: N, 21.99; S, 16.75; Found: N, 22.17; S, 16.48.

*3-(4-Chloro-benzylsulfanyl)-1H-1,2,4-triazole (**2g**).* The compound was obtained in 87% yield as a white crystal; mp 132–134°C; ^{1}H NMR δ (ppm): 3.85 (2H, s, SCH_2); 7.32–7.50 (4H, m, C_6H_4); 8.15 (1H, w.s, 5-H); 13.80 (1H, w.s, NH); elemental anal. (%), Calcd for $C_9H_8ClN_3S$: N, 18.63; S, 14.19; Found: N, 18.41; S, 13.88.

Synthesis of Compounds **2h–j** *(Prepared from* **I***)*

General Procedure. To a suspension of potassium salt of 1*H*-[1,2,4]-triazole-3-thiol (0.01 mol, 1.4 g) in 10 mL acetone, 0.01 mol aryloxyethyl bromide was added dropwise with continuous stirring, and the resulting mixture was allowed to stand at 50–60°C for 3 h. The potassium bromide was filtered off, and after evaporation and processing with water the residue was filtered off. The resulting compounds were purified by recrystallization from hexane: benzene (1:1).

*3-(2-Phenoxy-ethyl-sulfanyl)-1H-1,2,4-triazole (**2h**).* The compound was obtained in 88% yield as a white crystal; mp 87–89°C; ^{1}H NMR δ (ppm): 3.55 (2H, t, J = 7.1, SCH_2); 4.25 (2H, t, J = 7.1, OCH_2); 6.70–7.00 (5H, m, C_6H_5); 8.10 (1H, s, 5-H), 13.75 (1H, w.s, NH); elemental anal. (%), Calcd for $C_{10}H_{11}N_3OS$: N, 19.00; S, 14.48; Found: N, 19.21; S, 14.11.

*3-(2-o-Tolyloxy-ethylsulfanyl)-1H-1,2,4-triazole (**2i**).* The compound was obtained in 93% yield as a white crystal; mp 86–88°C; ^{1}H NMR δ (ppm): 2.20 (3H, s, CH_3); 3.52 (2H, t, J = 7.1, SCH_2); 4.25 (2H, t, J = 7.1, OCH_2); 6.75–7.05 (4H, m, C_6H_4), 8.16 (1H, w.s, 5-H); 13.7(1H, w.s, NH); elemental anal. (%), Calcd for $C_{11}H_{13}N_3OS$: N, 17.87; S, 13.62; Found: N, 17.60; S, 14.00.

*3-(2-p-Tolyloxy-ethylsulfanyl)-1H-1,2,4-triazole (**2j**).* The compound was obtained in 86% yield as a white crystal; mp 104–106°C; ^{1}H NMR δ (ppm): 2.26 (3H, s, CH_3); 3.50 (2H, t, J = 7.1, SCH_2); 4.28 (2H, t, J = 7.1, OCH_2); 6.8–7.03 (4H, m,C_6H_4), 8.20 (1H, w.s, 5-H); 13.7 (1H, w.s, NH); elemental anal. (%), Calcd for $C_{11}H_{13}N_3OS$: N, 17.87; S, 13.62; Found: N, 17.45; S, 13.91.

Synthesis of Compounds **3a–d**

General Procedure. To a solution of 0.01 mol arylsulfochloride in 10 mL benzene at 7–10°C, 1.4 mL (0.01 mol) of triethylamine in 10 mL benzene was added dropwise with continuous stirring, and 1.7 g (0.01 mol) of compound **2b** was then added. The resulting mixture was boiled for 4 h; then was allowed to cool at room temperature, and triethylamine hydrochloride was filtered off. The filtrate was evaporated, and the residue was washed with aqueous sodium hydrocarbonate solution (5%), and desired compounds **3a–d** were filtered off.

*(1-Benzenesulfonyl-1H-1,2,4-triazol-3-ylsulfanyl)-acetic acid methyl ester (**3a**).* The compound was obtained in 90% yield as a white crystal; mp 79–81°C; ^{1}H NMR δ (ppm): 3.58 (3H, s, OCH_3); 4.04 (2H, s, SCH_2); 7.80 and 8.10 (4H, m,C_6H_4); 9.37 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{11}H_{11}N_3O_4S_2$: N, 13.42; S, 20.45; Found: N, 13.18; S, 20.66.

*[1-(4-Chloro-benzenesulfonyl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**3b**).* The compound was obtained in 91% yield as a white crystal; mp 126–128°C; ^{1}H NMR δ (ppm): 3.63 (3H, s, OCH_3); 3.90 (2H, s, SCH_2); 7.50–8.05 (4H, m,C_6H_4); 9.05 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{11}H_{10}ClN_3O_4S_2$: N, 12.09; S, 18.42; Found: N, 12.30; S, 18.18.

*[1-(Toluene-4-sulfonyl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**3c**).* The compound was obtained in 72% yield as a white crystal; mp 90–91°C; ^{1}H NMR δ (ppm): 2.48 (3H, s, CH_3); 3.65 (3H, s, OCH_3); 3.92 (2H, s, SCH_2); 7.45–7.93 (4H, m,C_6H_4); 9.0 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{12}H_{13}N_3O_4S_2$: N, 12.84; S, 19.57; Found: N, 13.11; S, 19.81.

*[1-(2,5-Dimethyl-benzenesulfonyl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**3d**).* The compound was obtained in 90% yield as a white crystal; mp 100–102°C; ^{1}H NMR δ (ppm): 2.40 and 2.47 [6H, s,s, 2- and 5-CH_3); 3.62 (3H, s, OCH_3); 3.90 (2H, s, SCH_2); 7.38–7.85 (3H, m,C_6H_3); 9.02 (1H, s,

5-H); elemental anal. (%), Calcd for $C_{13}H_{15}N_3O_4S_2$: N, 12.32; S, 18.77; Found: N, 12.08; S, 19.09.

Synthesis of Compounds **4a,b**

General Procedure. A mixture of compound **2b** (0.01 mol, 1.7 g) and arylisocyanate (0.01 mol) in benzene (20 ml) in the presence of catalytic amounts of pyridine was boiled for 3 h. The resulting mixture was filtered, and the filtrate was evaporated. The residues of compounds **4a,b** were recrystallized from ethanol (50%).

*(1-Phenylcarbamoyl-1H-1,2,4-triazol-3-ylsulfanyl)-acetic acid methyl ester (**4a**).* The compound was obtained in 69% yield as a white crystal; mp 95–97°C; ^{1}H NMR δ (ppm): 3.70 (3H, s, OCH_3); 4.07 (2H, s, SCH_2); 7.10–7.72 (5H, m, C_6H_5); 9.02 (1H, s, 5-H); 10.23 (1H, w.s, NH); elemental anal. (%), Calcd for $C_{12}H_{12}N_4O_3S$: N, 19.18; S, 10.96; Found: N, 19.38; S, 10.69.

*[1-(4-Chloro-phenylcarbamoyl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**4b**).* The compound was obtained in 81% yield as a white crystal; mp 123–124°C; ^{1}H NMR δ (ppm): 3.73 (3H, s, OCH_3); 4.10 (2H, s, SCH_2); 7.48–8.03 (4H, m, C_6H_4); 9.05 (1H, s, 5-H); 10.23 (1H, w.s, NH); elemental anal. (%), Calcd for $C_{12}H_{11}ClN_4O_3S$: N, 17.15; S, 9.80; Found: N, 17.43; S, 10.09.

Synthesis of Compound **5**

*Sodium salt of 3-methylsulfanyl-1,2,4-triazole-1-carbodithioic acid (**5**).* To a suspension of NaOH (0.011 mol, 0.44 g) in absolute benzene (10 mL), carbon bisulfide (0.011 mol, 0.66 g) was added dropwise followed by the slow addition of compound **2a** (0.01 mol, 1.15 g). The mixture was vigorously stirred at 20°C and was allowed to stand overnight. Benzene was decanted, the reaction mass was rubbed with hexane, and the desired compound **5** was filtered off and washed with ether. The compound was obtained in 78% yield as a white crystal; mp 72–74°C; ^{1}H NMR δ (ppm): 2.43 (3H, s, SCH_3); 7.60 (1H, s, CH); elemental anal. (%), Calcd for $C_4H_9N_3S_3Na$: N, 19.72; S, 45.07; Found: N, 19.44; S, 44.68.

Synthesis of Compounds **6a–p**

General Procedure. To a suspension of N-potassium salt of **2** (0.01 mol), azinyl-2-trimethylammonium chloride (0.01 mol) was added with continuous stirring at 20°C for 1 h, then at 45–50°C for 3–4 h, until all the trimethylamine was evaporated. The resulting suspension was evaporated; the residue washed with water and filtered off. The desired compounds **6a–p** were recrystallized from toluene or /hexane: benzene (1:2).

*2,4-Bis-dimethylamino-6-(3-methylsulfanyly-1H-1,2,4-triazol-1-yl)-1,3,5-triazine (**6a**).* The compound was obtained as a white crystal; prepared from **2a**; yield: 89%, mp 138–140°C; ^{1}H NMR δ (ppm): 2.62 (3H, s, SCH_3); 3.18 and 3.22 [6H, s,s, $N(CH_3)_4$]; 9.08 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{10}H_{16}N_8S$: N, 40.00; S, 11.43; Found: N, 39.75; S, 11.10.

*2,4-Diethylamino-4-methylamino-6-(3-methylsulfanyl-1H-1,2,4-triazol-1-yl)-1,3,5-triazine (**6b**).* The compound was obtained as a white crystal; prepared from **2a**; yield: 90%, mp 134–136°C; ^{1}H NMR δ (ppm): 1.20 (3H, t, $J = 7.0$, $\underline{CH_3}CH_2$); 2.60 and 2.65 (5:1) (2H, s,s, SCH_3); 2.88 and 2.95 (5:1) (3H, d.d, $J = 5.6$, NCH_3); 3.63 (2H, m, $CH_3\underline{CH_2}$); 7.05 and 7.68 (5:1) (1H, w.q, $J = 5.6$, NH); 9.03 and 9.07 (5:1) (1H, s,s, 5-H)*; elemental anal. (%), Calcd for $C_{11}H_{18}N_8S$: N, 38.49; S, 11.00; Found: N, 38.12; S, 11.39.

*2-Methoxy-4-methyl-6-(3-methylsulfanyl-1H-1,2,4-triazol-1-yl)-pyrimidine (**6c**).* The compound was obtained as a white crystal; prepared from **2a**; yield: 72%, mp 132–134°C; ^{1}H NMR δ (ppm): 2.50 (3H, s, CH_3); 2.64 (2H, s, SCH_3); 4.06 (3H, s, OCH_3); 6.62 (1H, s, CH-pyrim.); 9.13 (1H, s, 5-H); elemental anal. (%), Calcd for $C_9H_{11}N_5OS$: N, 29.54; S, 13.50; Found: N, 29.33; S, 13.21.

*[1-(2,4-Bis-dimethylamino-1,3,5-triazine-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**6d**).* The compound was obtained as a white crystal; prepared from **2b**, yield: 82%, mp 147–148°C; ^{1}H NMR δ (ppm): 3.18 and 3.23 [6H, ss, $N(CH_3)_4$]; 3.73 (3H, s, OCH_3); 4.00 (2H, s, SCH_2); 9.10 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{12}H_{18}N_8O_2S$: N, 33.14; S, 9.48; Found: N, 32.89; S, 9.71.

*[1-(2-Dimethylamino-4-pyrrolidin-1-yl-1,3,5-triazine-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**6e**).* The compound was obtained as a white crystal; prepared from **2b**, yield: 82%, mp 131–133°C; ^{1}H NMR δ (ppm): 1.85 (4H, m, CH_2CH_2); 3.15 and 3.20 [6H, s,s $N(CH_3)_2$]; 3.55–3.65 [4H, m, $N(CH_2)_2$]; 3.73 (3H, s, OCH_3); 4.00 (2H, s, SCH_2); 9.08 (1H, s, 5-H) *; elemental anal. (%), Calcd for $C_{14}H_{20}N_8O_2S$: N, 30.77; S, 8.79; Found: N, 31.09; S, 9.10.

*[1-(4-Methyl-6-pyrrolidin-1-yl-pyrimidin-2-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid methyl ester (**6f**).* The compound was obtained as a white crystal; prepared from **2b**, yield: 80%, mp 132–134°C; ^{1}H NMR δ (ppm): 2.00 (4H, w.m, CH_2CH_2); 2.38 (3H, s, CH_3); 3.38–3.65 [4H, w.m, $N(CH_2)_2$]; 3.75 (3H, s, OCH_3); 4.02 (2H, s, SCH_2); 6.20 (1H, s, CH-pyrim); 9.03 (1H, s, 5-H) *; elemental anal. (%), Calcd for $C_{14}H_{18}N_6O_2S$: N, 25.15; S, 9.58; Found: N, 24.87; S, 9.22.

*[1-(2-Amino-4-methyl-pyrimidin-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid ethyl ester (**6g**).* The compound was obtained as a white crystal; prepared from **2c**, yield: 78%, mp 133–135°C; ^{1}H NMR δ (ppm): 1.28 (3H, t, J = 7.1, $CH_2\underline{CH_3}$); 2.35 (3H, s, CH_3-cycL.); 3.98 (2H, s, SCH_2); 4.15 (2H, q, J = 7.1, $\underline{CH_2}CH_3$); 6.08 (2H, w.s, NH_2); 6.79 (1H, s, CH-pyrim.); 9.05 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{11}H_{14}N_6O_2S$: N, 28.57; S, 10.88; Found: N, 28.81; S, 11.19.

*[1-(4-Methyl-6-phenoxy-pyrimidin-2-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetic acid ethyl ester (**6h**).* The compound was obtained as a white crystal; prepared from **2c**, yield: 63%, mp 108–110°C; ^{1}H NMR δ (ppm): 1.27 (3H, t, J = 7.1, $CH_2\underline{CH_3}$); 2.55 (3H, s, CH_3-cycL.); 3.98 (2H, s, SCH_2); 4.15 (2H, q, J = 7.1, $\underline{CH_2}CH_3$); 6.76 (1H, s, CH-pyrim.); 7.20–7.55 (5H, m, C_6H_5); 8.85 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{17}H_{17}N_5O_3S$: N, 18.87; S, 8.63; Found: N, 18.65; S, 8.36.

*2-[1-(2,4-Bis-dimethylamino-1,3,5-triazine-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetamide (**6i**).* The compound was obtained as a white crystal; prepared from **2d**, yield: 93%, mp 180–182°C; ^{1}H NMR δ (ppm): 3.18 and 3.21 [6H, s,s, $N(CH_3)_4$]; 3.80 (2H, s, SCH_2); 6.95 and 7.35 (2H, w,s, NH_2); 9.13 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{11}H_{17}N_9OS$: N, 39.01; S, 9.91; Found: N, 39.30; S, 10.22.

*2-[1-(2-Dimethylamino-4-methoxy-1,3,5-triazine-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetamide (**6j**).* The compound was obtained as a white crystal; prepared from **2d**, yield: 80%, mp 185–186°C; ^{1}H NMR δ (ppm): 3.22 and 3.30 [6H, s,s, $N(CH_3)_4$]; 3.85 (2H, s, SCH_2); 4.00 (3H, s, OCH_3); 6.95 and 7.38 (2H, w.s, NH_2); 9.20 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{10}H_{14}N_8O_2S$: N, 36.13; S, 10.32; Found: N, 36.34; S, 10.59.

*2-[1-(2-Methylamino-4-piperidine-1-yl-1,3,5-triazine-6-yl)-1H-1,2,4-triazol-3-ylsulfanyl]-acetamide (**6k**).* The compound was obtained as a white crystal; prepared from **2d**, yield: 85%, mp 245–247°C; ^{1}H NMR δ (ppm): 1.55–1.73 [6H, m, $(CH_2)_3$]; 2.87 and 2.95 (5:1) (6H, d, J = 5.8); 3.80 (2H, s, SCH_2); 3.75–3.86 [4H, m, $N(CH_2)_2$]; 6.98 and 7.36 (2H, w.s, NH_2); 7.10 and 7.78 (1:5) (1H, q, J = 5.8, NH); 9.10 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{13}H_{19}N_9OS$: N, 36.10; S, 9.17; Found: N, 36.35; S, 9.40.

*1-(2,4-Bis-dimethylamino-1,3,5-triazine-6-yl)-3-benzylsulfanyl-1H-1,2,4-triazol (**6l**).* The compound was obtained as a white crystal; prepared from **2f**, yield: 90%, mp 125–127°C; ^{1}H NMR δ (ppm): 3.20 and 3.28 [6H, s,s, $N(CH_3)_4$]; 4.40 (2H, s, SCH_2); 7.15–7.45 (5H, m, C_6H_5); 9.10 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{16}H_{19}N_8S$: N, 31.55; S, 9.01; Found: N, 31.71; S, 8.78.

*1-(2-Methylamino-4-dimethylamino-1,3,5-triazine-6-yl)-3-benzylsulfanyl-1H-1,2,4-triazol (**6m**).* The compound was obtained as a white crystal; prepared from **2f**, yield: 91%, mp 194–196°C; ^{1}H NMR δ (ppm): 2.90 and 2.95 (5:1) (6H, d.d, J = 5.9, NCH_3); 3.22 [6H, w.s, $N(CH_3)_2$]; 4.40 and 4.42 (2H, s, SCH_2); 7.10 and 7.65 (1:5) (1H, q, J = 5.9, NH); 7.18–7.43 (5H, m, C_6H_5); 9.08 and 9.10 (5:1) (1H, s,s, 5-H)*; elemental anal. (%), Calcd for $C_{15}H_{18}N_8S$: N, 32.75; S, 9.36; Found: N, 32.54; S, 9.69.

*1-(2-Amino-4-methyl-pyrimidin-6-yl)-3-benzylsulfanyl-1H-1,2,4-triazol (**6n**).* The compound was obtained as a white crystal; prepared from **2f**, yield: 89%, mp 222–224°C; ^{1}H NMR δ (ppm): 2.37 (3H, s, CH_3); 4.40 (2H, s, SCH_2); 6.42 (2H, w.s, NH_2); 6.80 (1H, s, CH-pyrim); 7.18–7.45 (5H, m, C_6H_5); 9.05 (1H, s, 5-H); elemental anal. (%), Calcd for $C_{14}H_{14}N_6S$: N, 28.19; S, 10.74; Found: N, 27.89; S, 10.36.

*1-(2,4-Bis-dimethylamino-1,3,5-triazine-6-yl)-2-p-tolyloxy-ethylsulfanyl-1H-1,2,4-triazol (**6o**).* The compound was obtained as a white crystal; prepared from **2j**, yield: 90%, mp 134–136°C; ^{1}H NMR δ (ppm): 2.26 (3H, s, CH_3); 3.18 and 3.24 [6H, s,s $N(CH_3)_4$]; 3.50 (2H, t, J = 7.1, SCH_2); 4.28 (2H, t, J = 7.1, OCH_2); 6.80–7.05 (4H, m, C_6H_4); 9.10 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{18}H_{24}N_8OS$: N, 28.00; S, 8.00; Found: N, 28.27; S, 8.32.

*1-(2,4-di-Pyrrolidin-1-yl-1,3,5-triazine-6-yl)-2-p-tolyloxy-ethylsulfanyl-1H-1,2,4-triazol (**6p**).* The compound was obtained as a white crystal; prepared from **2j**, yield: 87%, mp 135–137°C; ^{1}H NMR δ (ppm): 1.95 [8H, m, $(CH_2)_4$]; 2.25 (3H, s, CH_3);

3.46–3.70 [8H, m, $N(CH_2)_4$]; 3.50 (2H, t, $J = 7.1$, SCH_2); 4.28 (2H, t, $J = 7.1$, OCH_2); 6.78–7.03 (4H, m, C_6H_4); 9.07 (1H, s, 5-H)*; elemental anal. (%), Calcd for $C_{22}H_{28}N_8OS$: N, 24.78; S, 7.08; Found: N, 25.10; S, 7.41.

Note: * Two groups of signals in ^1H NMR spectra are caused by the presence of conformational isomers as a result of internal rotation of N-alkyl groups around the N-C bond [23].

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