DOI 10.1007/s10593-015-1678-5

*Chemistry of Heterocyclic Compounds* **2015**, *51*(2), 176–186

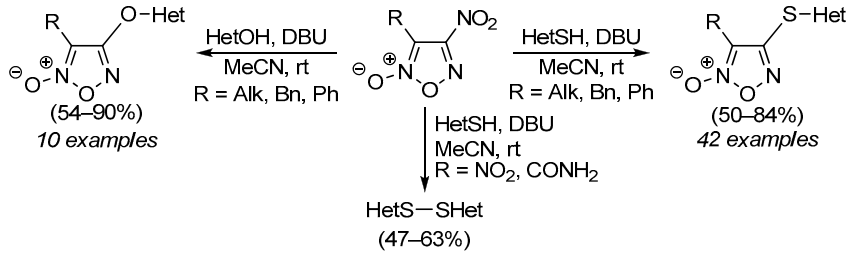
# Synthesis of hetarylsulfanyl- and hetaryloxyfuroxans by nucleophilic substitution of nitro group in nitrofuroxans with heterocyclic thiol and hydroxy derivatives*

**Leonid L. Fershtat[1], Margarita A. Epishina[1], Alexander S. Kulikov[1], Marina I. Struchkova[1], Nina N. Makhova[1]***

[1] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky Ave., Moscow 119991, Russia; e-mail: mnn@ioc.ac.ru*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2015, *51*(2), 176–186

Submitted January 13, 2015
Accepted January 28, 2015




We report a general method for the synthesis of previously unknown heterocyclic systems containing furoxan and heterocyclic fragments linked by S- and O-bridges, based on nucleophilic substitution of nitro group in 4-nitrofuroxans with HetS and HetO groups introduced by reactions with hetarylthiols and hydroxy heterocycles in 1,8-diazabicyclo[5.4.0]undec-7-ene/MeCN system at room temperature. We showed that hetarylthiols reacted with 4-nitrofuroxans containing aliphatic, benzyl, and aromatic substituents at the ring C-3 atom, allowing to obtain a library of previously unknown hetarylsulfanylfuroxans, while the reaction with hydroxy heterocycles was successful only in the case of 4-nitro-3-phenylfuroxan, the rest of the nitrofuroxans showing low reactivity, and substitution products could be obtained only in certain cases. 4-Nitrofuroxans with electron-withdrawing substituents ($NO_2$, $CONH_2$) acted as oxidants, forming 1,2-di(hetaryl)disulfides.

**Keywords**: hetaryloxyfuroxans, hetarylthiols, hydroxyheterocycles, 4-nitrofuroxans, disulfide bridges, hetarylsulfanylfuroxan library, nucleophilic substitution.

At the end of the 20th century it was established that nitric oxide (NO) is one of ubiquitous and crucial regulator molecules for cellular metabolism, affecting various physiological and pathophysiological processes. Nitric oxide participates in the regulation of vasoconstriction, inhibits thrombocyte aggregation and adhesion to blood vessel walls, acts on the central and autonomic nervous systems, regulating respiratory, digestive, urinary and reproductive functions.[2–11]

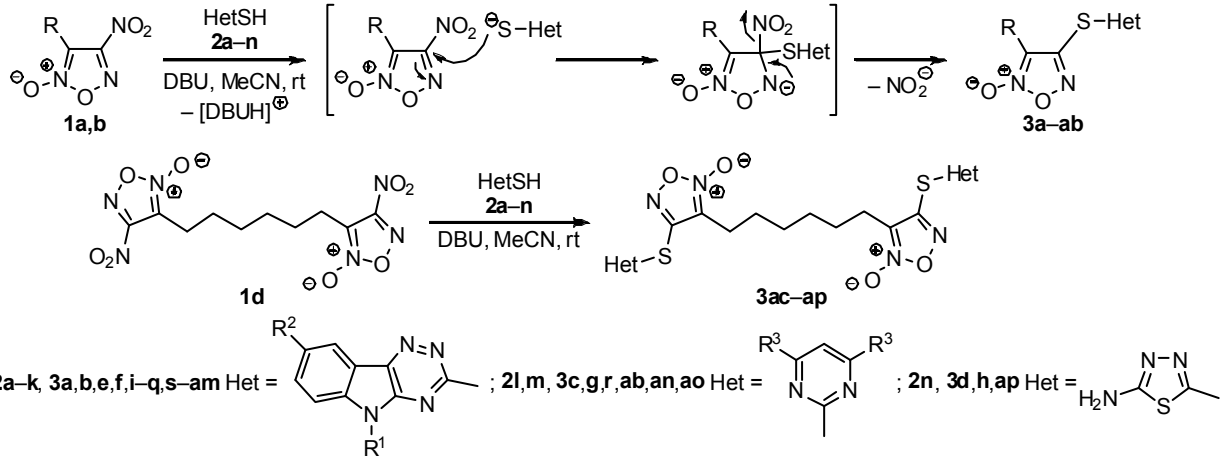
Therefore, one of the most active areas of medicinal chemistry is the search for compounds capable of releasing NO in the body, either enzymatically, or independently of NO synthases. Several drugs are currently available that act by releasing NO (exogenous NO), first of all, nitrates, nitrate esters, and nitrites (nitroglycerin, nitrosorbide, isosorbide mononitrate, amyl nitrite, etc.), which are used as vasodilators. Many different types of compounds have been synthesized and tested as NO donors (guanidines, nitramines, oximes, mesoionic systems, heterocyclic *N*-oxides, and others).[12,13] 1,2,5-Oxadiazole 2-oxides (furoxans) are also known as compounds capable of NO release *in vivo*.[14–16]

One of the approaches to the preparation of new pharmacologically active compounds involves the addition of a furoxan ring as potential NO donor to molecules with known pharmacological activity. Such a strategy has been widely used by the Italian chemist A. Gasco with positive results.[17–19] Thus, the goal of our current work was the development of a general method for the synthesis of previously unknown heterocyclic systems, with sulfur or oxygen linkers connecting a furoxan system to various heterocyclic pharmacophores.

Recently we developed a new, simple and effective method for the synthesis of previously practically

* A brief report is available.[1]

**Scheme 1**




**1a**, **3a–c**,**i–r** R = Ph; **1b**, **3e–h**,**s–ab** R = Bn;
**2a**, **3a**,**e**,**ac** $R^1$ = H; **2b**,**j**,**k**, **3b**,**f**,**p**,**q**,**z**,**aa**,**ad**,**al**,**am** $R^1$ = Me; **2c**, **3i**,**s**,**ae** $R^1$ = Et; **2d**, **3j**,**t**,**af** $R^1$ = *n*-Pr; **2e**, **3k**,**u**,**ag** $R^1$ = *i*-Pr;
**2f**,**3l**,**v**,**ah** $R^1$ = *n*-Bu; **2g**, **3m**,**w**,**ai** $R^1$ = Bn; **2h**, **3n**,**x**,**aj** $R^1$ = $CH_2CH_2Ph$; **2i**, **3o**,**y**,**ak** $R^1$ = All;
**2a–i**, **3a**,**b**,**e**,**f**,**i–o**,**s–y**,**ac** $R^2$ = H; **2j**, **3p**,**z**,**al** $R^2$ = $NO_2$; **2k**, **3q**,**aa**,**am** $R^2$ = Br; **2l**, **3c**,**g**,**an** $R^3$ = $NH_2$; **2m**, **3r**,**ab**,**ao** $R^3$ = Me

unavailable 3-alkyl- and 3-aryl-4-nitrofuroxans **1a**,**b**,**d**, enabling the preparation of these compounds in significant quantities.[20] Therefore, in this work we planned to perform nucleophilic substitution of nitro group with hetarylsulfanyl and hetaryloxy fragments by treating 4-nitrofuroxans with hetarylthiols and hydroxy derivatives of heterocycles in the presence of bases.

In the first experiments, we used hetarylthiols **2**, while the starting 4-nitrofuroxans contained phenyl, benzyl, aliphatic, and various electron-withdrawing substituents at the C-3 atom of 1,2,5-oxadiazole ring: Ph (compound **1a**), Bn (compound **1b**), $NO_2$ (compound **1c**), 4-nitro-3-[6-(4-nitrofuroxan-3-yl)hexyl] (compound **1d**), and $CONH_2$ (compound **1e**), which were synthesized according to known procedures.[20–22] The heterocyclic thiols **2a**–**m** have been described in the literature,[23–25] while the thiol **2n** is commercially available. All the investigated thiols **2a**–**n** possess some types of pharmacological activity. Thus, derivatives of indolotriazinethiols **2a**–**k** have been characterized as a new series of compounds with pronounced antiparasitic[23] and antihypoxic[26] activity. The diaminopyrimidinethiol **2l** in combination with gold nanoparticles shows a wide range of antibacterial activity,[27] dimethylpyrimidinethiol **2m** may serve as an effective inhibitor of certain metal-containing enzymes,[28] while 5-amino-1,3,4-thiadiazole-2-thiol **2n** is a strong inhibitor of carbonic anhydrase IX, and thus a potential anticancer agent.[29]

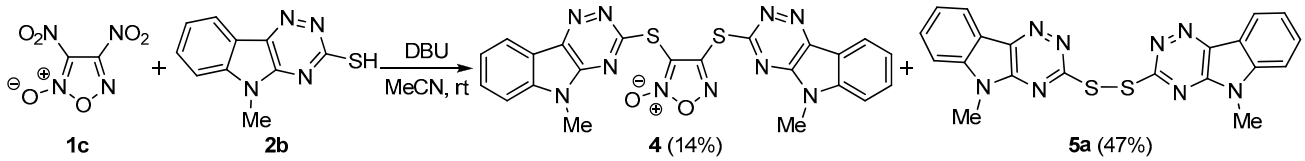
As a part of this study, we were interested in evaluating the reactivity of 4-nitrofuroxans **1a**–**e** towards nucleophilic substitution of nitro group with hetarylsulfanyl and hetaryloxy fragments, depending on the structure of substituents at the C-3 atom of furoxan ring and the type of heterocyclic fragment in the starting nucleophiles. We previously demonstrated the general possibility of nitro group substitution in 4-nitrofuroxans with heterocyclic thiols,[1] using the model reaction of 4-nitro-3-phenylfuroxan (**1a**) with triazinethiol **2a**. In order to find the optimum conditions for this process, we used various bases and reaction media: KOH/DMF, $K_2CO_3$/DMF, $K_2CO_3$/acetone, $Et_3N$/MeCN, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/MeCN, DBU/[bmim]$BF_4$, [bmim]OH/DMF, and [bmim]OH/[bmim]$BF_4$ ([bmim]–butylmethylimidazolium). The first representative of hetarylsulfanylfuroxans **3a** was obtained only in the DBU/MeCN system at room temperature in 65% yield. These optimized conditions were used for the preparation of several additional hetarylsulfanylfuroxan representatives **3b**–**h** from nitrofuroxans **1a**,**b** and thiols **2a**,**b**,**l**,**n** (Scheme 1).[1]

The nucleophilic substitution of nitro group in nitrofuroxans with HetS fragments can be formally considered as nucleophilic aromatic substitution according to $S_NAr$ mechanism. However, the formation of Meisenheimer-type complex in furoxan ring is unlikely, because both double bonds in the ring are strictly fixed, while the O(1)–N(2) bond is close to ordinary.[30] We can assume that the negative charge arising after attack by thiolate ion at the nitrofuroxan C-4 atom is localized on the ring N-5 atom, followed by elimination of $NO_2$ anion and formation of the final hetarylsulfanylfuroxan **3** (Scheme 1). An analogous mechanism was proposed by us earlier.[31]

As previously shown,[1] the substitution of nitro group in 4-nitro-3-phenylfuroxan (**1a**) occurred faster and with higher yields than in 3-benzyl-4-nitrofuroxan (**1b**). In contrast to furoxans **1a**,**b**, the nucleophilic substitution in 3,4-dinitrofuroxan (**1c**) could be achieved only with thiol **2b**, and even the product **4** of nucleophilic substitution at both nitro groups was obtained in low yield (14%) (Scheme 2). The major product of this reaction was disulfide **5a**, i.e., dinitrofuroxan **1c** played the role of an oxidant in this reaction.

In the current work, we continued the study of nucleophilic nitro group substitution in 4-nitrofuroxans **1a**,**b** by reaction with other hetarylthiols **2c**–**k**,**m**, as well as observed the behavior of 1,6-bis(4-nitrofuroxan-3-yl) hexane (**1d**) and 4-nitrofuroxan-3-carboxamide (**1e**) in this reaction. Nitrofuroxans **1a**,**b** successfully reacted with thiols **2c**–**k**,**m** under the previously found conditions (equimolar

**Scheme 2**




ratio of reactants and DBU in MeCN at 20°C), giving the hetarylsulfanylfuroxans **3i–ab**, and the same reactivity trend towards nucleophilic substitution was observed – the reaction with 4-nitrofuroxan **1a** occurred faster (control by TLC) and gave higher yields of substitution products than the reaction with nitrofuroxan **1b** (Scheme 1). At the same time, indolotriazinethiols **2c–k** were found to be more reactive compared to the dimethylpyrimidinethiol **2m**. The reaction of nitrofuroxan **1a** with hetarylthiols **2c–k** was finished in 8 h with the formation of hetarylsulfanylfuroxans **3i–q** in 70–84% yields, while the reaction with hetarylthiol **2m** required 30 h, and the yield of hetarylsulfanylfuroxan **3r** was merely 53%. Similar results were obtained also in the reaction of 3-benzyl-4-nitrofuroxan (**1b**) with hetarylthiols **2c–m**. While the reaction of compound **1b** with thiols **2c–k** was accomplished in 10 h, giving the hetarylsulfanylfuroxans **3s–z** and **3aa** in 61-76% yields, the reaction with thiol **2m** required stirring for 48 h, while the hetarylsulfanylfuroxan **3ab** was obtained in only 35% yield.

The nucleophilic substitution of nitro groups in 3,3'-(hexane-1,6-diyl)bis(4-nitrofuroxan) (**1d**), containing two nitrofuroxan fragments linked by a hexamethylene chain, predictably was even slower than the reaction of benzylnitrofuroxan **1b** (Scheme 1). Besides that, effective substitution of both nitro groups in the starting substrate **1d** required a 20% molar excess of thiol with respect to 1 mol of furoxan **1d**. As in the previous cases, the most reactive were derivatives of indolotriazinethiols **2a–k**. The completion of these reactions took 48 h, giving the hetarylsulfanylfuroxans **3ac–an** in up to 70% yields, while completing the reaction with dimethylpyrimidinethiol **2m** and aminothiadiazolethiol **2n** required longer time (90 and 120 h, respectively), while the yields of compounds **3ao** and **3ap** were 34% and 51%, respectively.

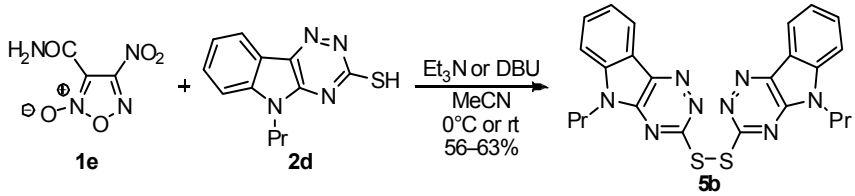
An interesting feature was observed during the reaction of 4-nitrofuroxan-3-carboxamide (**1e**) with indolotriazinethiol **2d**. Instead of the expected nitro group substitution product, we obtained the disulfide **5b**. Variation of base ($Et_3N$ versus DBU), and the reaction temperature (0–20°C) had no effect on the direction of reaction, while the yield of compound **5b** changed insignificantly (Scheme 3), pointing to the oxidizing properties of nitrofuroxan **1e**. The presence of electron-withdrawing substituents ($NO_2$, $CONH_2$) at the C-3 atom of furoxan ring apparently increased the oxidizing properties of 4-nitrofuroxans. However, the tendency to form disulfide was observed only in the reaction of compound **1e** with indolotriazine **2d**. The reaction of nitrofuroxan **1e** with pyrimidinethiols **2l**,**m** and aminothiadiazolethiol **2n** was not successful – all experiments failed to produce nitro group substitution products or the respective disulfides, but thiols **2l–n** were recovered unchanged from the reaction mixtures.

In order to study the nucleophilic substitution of nitro group in nitrofuroxans with hetaryloxy fragments, 4-nitrofuroxans **1a–c** were treated with some heterocyclic hydroxy derivatives **6a–e**.

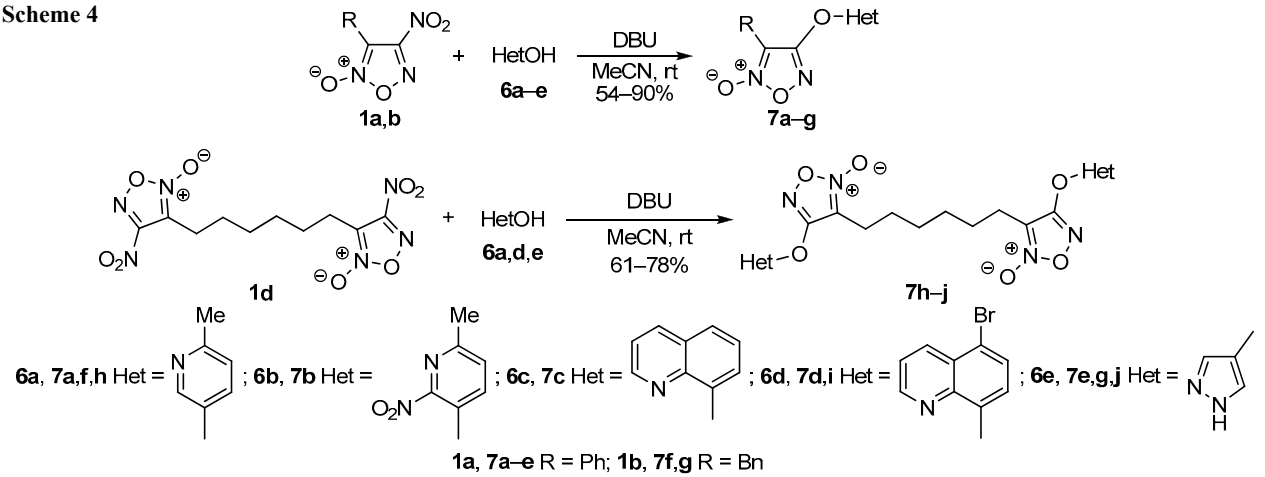
The optimum conditions found for the reaction with thiols (DBU/MeCN) were also effective for the reaction of nitrofuroxans **1a–c** with hydroxy heterocycles **6** (Scheme 4). As in the case with hetarylthiols **2**, 4-nitro-3-phenylfuroxan (**1a**) was the most reactive nitrofuroxan in nucleophilic substitution reactions with hydroxy heterocycles. Pyridine derivatives **6a**,**b** were the most reactive nucleophiles among the hydroxy heterocycles used (reaction time 2 h), while the quinoline derivatives **6c**,**d** gave slower reactions (reaction time 8 h), and the reaction with hydroxypyrazole **6e** was the most difficult (48 h). The respective 4-hetaryloxy-3-phenylfuroxans **7a–e** were obtained in high yields (68–90%). However, in the cases of 3-benzyl-4-nitrofuroxan (**1b**) and bisnitrofuroxan **1d** the reaction was no longer universally applicable. Thus, the nitrofuroxan **1b** in reactions with hydroxy heterocycles **6a**,**e** gave only two types of hetarylfuroxan ethers **7f**,**g** in 72 and 54% yields, respectively. The reaction of furoxan **1d** was successful only with three nucleophiles **6a**,**d**,**e**, giving the respective compounds **7h–j** in fair yields (61–78%), while the reaction time increased from 4 h to 48 h in the series of compound **6a** (4 h), compound **6d** (12 h), and compound **6e** (48 h). The lower reactivity of hydroxy heterocycles was apparently associated with their weaker nucleophilicity compared to the nucleophilicity of hetarylthiols.

The structure of the synthesized hetarylsulfanylfuroxans **3i–ap** and hetaryloxyfuroxans **7a–j** was confirmed by a data set that consisted of elemental analysis, $^1H$ and $^{13}C$ NMR spectroscopy, and high-resolution mass spectrometry. The obtained polyheterocyclic structures had very poor solubility even in highly polar solvents. For this reason, the

**Scheme 3**



**Scheme 4**




reaction products were precipitated from solution with water and carefully washed on filter with water to remove salts, followed by washing with acetonitrile to remove possible organic impurities. Besides that, the poor solubility of the synthesized compounds explains the broadened shape of all $^1$H NMR signals. The hetarylsulfanylfuroxans **3i**–**ap** and hetaryloxyfuroxans **7a**–**j** were found to obey a general rule applicable to all furoxans: the difference of $^{13}$C NMR chemical shifts for the furoxan ring was ~40 ppm, that could be explained by the increased electron density on the ring C-3 atoms due to resonance coupling with the *N*-oxide fragment.[32]

Thus, our study of nucleophilic nitro group substitution in 4-nitrofuroxans with hetarylthiol and hetaryloxy fragments allowed to identify the optimal conditions for the formation of hetaryl thiolate anion (DBU/MeCN), which were effective also for the formation of hetaryloxy anion, allowing to develop a general method for the synthesis of previously unknown heterocyclic systems containing a furoxan ring linked to a heterocyclic fragment by S- and O-bridges. The effects of substituents at the furoxan ring C-3 atom and the starting hetarylthiol structure on the reaction outcome were established. Nucleophilic substitution with hetarylthiols was successful for 4-nitrofuroxans with phenyl, benzyl, and aliphatic substituents. With electron-withdrawing substituent ($NO_2$, $CONH_2$) at this position, 4-nitrofuroxans reacted as oxidizers with indolotriazine thiols, resulting in oxidative formation of a disulfide bridge. In the case of less nucleophilic hydroxy heterocycles, only 4-nitro-3-phenylfuroxan gave nucleophilic substitution products. Other nitrofuroxans participated in nucleophilic substitution reactions with heterocyclic hydroxy compounds only in certain cases. Among the studied hetarylthiols, indolotriazine thiols were the most active in nucleophilic substitution reactions of 4-nitrofuroxan nitro groups, while 3-hydroxy-6-methylpyridine was the most active among heterocyclic hydroxy derivatives. The overall practical result of this study was the preparation of a library of previously unknown hetarylsulfanylfuroxans.

## Experimental

$^1$H and $^{13}$C NMR spectra were acquired on a Bruker AM-300 spectrometer (300 and 75 MHz, respectively) in DMSO-$d_6$. The residual solvent proton signals (2.50 ppm) and $^{13}$C signals (39.5 ppm) were used as internal standards. High-resolution mass spectra were recorded on a Bruker micrOTOF II instrument with electrospray ionization (ESI). Elemental analysis was performed on Perkin–Elmer 2400 and EuroVector EA instruments. The bromine content was determined gravimetrically. Melting points were determined on a Sanyo Gallenkamp apparatus. The reaction progress was controlled by TLC on Merck 60 $F_{254}$ silica gel plates (visualization under 254 nm UV light).

The starting nitrofuroxans **1a**,**b**,**d**,[20] **1c**,[21] and **1e**,[22] as well as the heterocyclic thiols **2a**–**g**,**i**–**m**[23–25] were obtained according to published methods. 5-Amino-1,3,4-thiadiazole-2-thiol (**2n**), hydroxy heterocycles **6a**–**d**, and DBU were commercially available (Acros). Acetonitrile was purified by refluxing with $P_2O_5$ until the solvent no longer changed color after adding a fresh portion of $P_2O_5$, then distilled over anhydrous potassium carbonate.

**5-(2-Phenylethyl)-5*H*-[1,2,4]triazino[5,6-*b*]indole-3-thiol (2h)**. A suspension of 1-(2-phenylethyl)isatin[33] (25.1 g, 0.100 mol) in water (400 ml) was stirred at room temperature and treated by the addition of thiosemicarbazide (9.56 g, 0.105 mol) and $K_2CO_3$ (20.7 g, 0.150 mol). The reaction mixture was refluxed for 4 h until complete dissolution of the starting isatin and for additional 1 h, then filtered while hot to remove insoluble impurities. The obtained filtrate was cautiously acidified with 10% HCl (accompanied by evolution of hydrogen sulfide) to pH 1, the precipitate formed was filtered off, washed with water, and air-dried. Yield 26.62 g (87%), yellow powder, mp 279–281°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.08 (2H, t, $^3J$ = 7.4, $NCH_2C\underline{H}_2$); 4.42 (2H, t, $^3J$ = 7.4, $NCH_2$); 7.17–7.23 (5H, m, H Ph); 7.34 (1H, t, $^3J$ = 7.4, H Het); 7.50–7.62 (2H, m, H Het); 7.97 (1H, d, $^3J$ = 7.6, H Het); 14.48 (1H, br. s, SH). $^{13}$C NMR spectrum, δ, ppm: 34.3 ($NCH_2\underline{C}H_2$); 43.3 ($NCH_2$); 112.8, 118.2, 122.7, 124.4, 127.5, 129.3, 129.8, 132.7, 136.1, 138.9, 144.4, 148.9 (C Ph, C Het); 180.1 (CS).

Found, % C 66.60; H 4.63; N 18.27; S 10.50. $C_{17}H_{14}N_4S$. Calculated, %: C 66.64; H 4.61; N 18.29; S 10.46.

**Preparation of hetarylsulfanylfuroxans 3i–ab** (General method). DBU (0.15 ml, 1 mmol) was added at room temperature to a stirred suspension of the respective thiol **2c–k**,**m** (1 mmol) in anhydrous MeCN (2 ml). Furoxan **1a** or **1b** was added to the obtained mixture after 10 min and the reaction mixture was stirred for 8–48 h until complete conversion of the starting furoxan **1a** or **1b** (control by TLC, eluent $CHCl_3$). The mixture was then treated with $H_2O$ (10 ml). The precipitate that formed was filtered off, carefully washed with water, acetonitrile (~1 ml), and air-dried.

**5-Ethyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3i)**. Yield 319 mg (82%), orange powder, mp 162–164°C. $^1$H NMR spectrum, δ, ppm: 1.28 (3H, br. s, $CH_3$); 4.29 (2H, br. s, $CH_2$); 7.47 (4H, br. s, H-3,4,5 Ph, H); 7.81 (2H, br. s, H-2,6 Ph); 7.94 (2H, br. s, H); 8.32 (1H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 13.1 ($CH_3$); 36.3 ($CH_2$); 111.6 (C-3 furoxan); 116.4, 117.0, 122.1, 123.3, 127.8, 129.0, 129.3, 131.0, 131.8, 141.0, 142.2, 145.5, 163.2 (C Ph, C Het); 149.8 (C-4 furoxan). Found, *m*/*z*: 391.0968 $[M+H]^+$. $C_{19}H_{15}N_6O_2S$. Calculated, *m*/*z*: 391.0972. Found, %: C 58.41; H 3.66; N 21.48; S 8.23. $C_{19}H_{14}N_6O_2S$. Calculated, %: C 58.45; H 3.61; N 21.53; S 8.21.

**3-[(5-Oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5-propyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3j)**. Yield 339 mg (84%), yellow powder, mp 171–173°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.78 (3H, br. s, $CH_3$); 1.73 (2H, br. s, $CH_3C\underline{H}_2$); 4.20 (2H, br. s, $NCH_2$); 7.48 (5H, br. s, H Ph); 7.82 (2H, br. s, H Het); 7.94 (1H, br. s, H Het); 8.33 (1H, d, $^3J$ = 7.2, H Het). $^{13}$C NMR spectrum, δ, ppm: 11.3 ($CH_3$); 21.1 ($CH_3\underline{C}H_2$); 42.8 ($NCH_2$); 111.7 (C-3 furoxan); 116.4, 117.0, 122.0, 122.1, 123.3, 127.7, 129.0, 131.1, 131.8, 141.5, 142.1, 146.0, 163.4 (C Ph, C Het); 149.7 (C-4 furoxan). Found, *m*/*z*: 405.1126 $[M+H]^+$. $C_{20}H_{17}N_6O_2S$. Calculated, *m*/*z*: 405.1128. Found, %: C 59.32; H 4.05; N 20.72; S 7.97. $C_{20}H_{16}N_6O_2S$. Calculated, %: C 59.39; H 3.99; N 20.78; S 7.93.

**5-Isopropyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)-sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3k)**. Yield 323 mg (80%), yellow powder, mp 134–136°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.47 (6H, d, $^3J$ = 6.4, $CH(C\underline{H}_3)_2$); 4.95–4.99 (1H, m, $C\underline{H}(CH_3)_2$); 7.45 (5H, br. s, H); 7.75 (1H, t, $^3J$ = 7.6, H Het); 7.91 (2H, m, H Het); 8.30 (1H, d, $^3J$ = 7.3, H Het). $^{13}$C NMR spectrum, δ, ppm: 19.4, 19.7 ($2CH_3$); 46.6 ($\underline{C}H(CH_3)_2$); 112.1 (C-3 furoxan); 116.2, 117.1, 121.7, 121.9, 123.0, 127.6, 128.9, 131.0, 131.6, 140.6, 142.1, 145.4, 162.9 (C Ph, C Het); 149.7 (C-4 furoxan). Found, %: C 59.34; H 4.03; N 20.70; S 7.96. $C_{20}H_{16}N_6O_2S$. Calculated, %: C 59.39; H 3.99; N 20.78; S 7.93.

**5-Butyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3l)**. Yield 330 mg (79%), yellow powder, mp 178–180°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.80 (3H, br. s, $CH_3$); 1.14 (2H, br. s, $CH_3C\underline{H}_2$); 1.65 (2H, br. s, $NCH_2C\underline{H}_2$); 4.19 (2H, br. s, $NC\underline{H}_2$); 7.45 (4H, br. s, H-3,4,5 Ph, H); 7.79 (2H, br. s, H-2,6 Ph); 7.91 (2H, br. s, H Het); 8.30 (1H, d, $^3J$ = 6.7, H Het). $^{13}$C NMR spectrum, δ, ppm: 13.2 ($CH_3$); 19.4 ($CH_3\underline{C}H_2$); 29.5 ($NCH_2\underline{C}H_2$); 42.3 ($NCH_2$); 111.5 (C-3 furoxan); 116.1, 116.9, 121.8, 122.0, 123.2, 127.6, 128.9, 130.9, 131.7, 141.2, 141.9, 144.8, 163.4 (C Ph, C Het); 148.9 (C-4 furoxan). Found, *m*/*z*: 419.1273 $[M+H]^+$. $C_{21}H_{19}N_6O_2S$. Calculated, *m*/*z*: 419.1285. Found, %: C 60.30; H 4.28; N 20.11; S 7.70. $C_{21}H_{18}N_6O_2S$. Calculated, %: C 60.27; H 4.34; N 20.08; S 7.66.

**5-Benzyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3m)**. Yield 334 mg (74%), orange powder, mp 193–195°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 5.46 (2H, s, $NCH_2$); 7.25 (5H, s, H Ph); 7.42 (3H, br. s, H-3,4,5 3-Ph); 7.50 (2H, br. s, H-2,6, 3-Ph); 7.76 (1H, br. s, H Het); 7.88 (2H, br. s, H Het); 8.34 (1H, d, $^3J$ = 8.4, H Het). $^{13}$C NMR spectrum, δ, ppm: 44.6 ($NCH_2$); 111.9 (C-3 furoxan); 117.2, 122.1, 123.6, 127.6, 127.8, 128.0, 128.8, 129.0, 131.0, 131.9, 132.7, 135.5, 138.4, 141.7, 142.5, 144.7, 163.1 (C Ph, C Het); 149.1 (C-4 furoxan). Found, *m*/*z*: 453.1119 $[M+H]^+$. $C_{24}H_{17}N_6O_2S$. Calculated, *m*/*z*: 453.1128. Found, %: C 63.66; H 3.54; N 18.52; S 7.13. $C_{24}H_{16}N_6O_2S$. Calculated, %: C 63.70; H 3.56; N 18.57; S 7.09.

**3-[(5-Oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5-(2-phenylethyl)-5*H*-[1,2,4]triazino[5,6-*b*]indole (3n)**. Yield 326 mg (70%), bright-orange powder, mp 200–202°C. $^1$H NMR spectrum, δ, ppm: 2.97 (2H, br. s, $NCH_2C\underline{H}_2$); 4.42 (2H, br. s, $NCH_2$); 6.99 (2H, br. s, HPh); 7.11 (3H, br. s, H Ph); 7.45 (4H, br. s, H-3,4,5 3-Ph, H Het); 7.76 (2H, br. s, H-2,6 3-Ph); 7.91 (2H, br. s, H Het); 8.27 (1H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 33.4 ($NCH_2\underline{C}H_2$); 42.7 ($N\underline{C}H_2$); 111.8 (C-3 furoxan); 116.3, 116.7, 121.8, 123.2, 126.5, 127.6, 128.0, 128.2, 128.5, 128.9, 130.9, 131.6, 137.6, 141.0, 141.8, 145.7, 163.2 (C Ph, C Het); 149.3 (C-4 furoxan). Found, *m*/*z*: 467.1281 $[M+H]^+$. $C_{25}H_{19}N_6O_2S$. Calculated, *m*/*z*: 467.1285. Found, %: C 64.39; H 3.86; N 17.97; S 6.90. $C_{25}H_{18}N_6O_2S$. Calculated, %: C 64.36; H 3.89; N 18.01; S 6.87.

**5-Allyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3o)**. Yield 293 mg (73%), bright-yellow powder, mp 172–174°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 4.87 (2H, br. s, $NCH_2$); 5.03 (1H, d, $^3J$ = 10.1, $CH=C\underline{H}_2$); 5.16 (1H, d, $^3J$ = 10.1, $CH=C\underline{H}_2$); 5.88–5.93 (1H, m, $CH_2C\underline{H}=CH_2$); 7.40–7.45 (5H, m, H Ph); 7.72 (2H, t, $^3J$ = 6.1, H Het); 7.88 (1H, d, $^3J$ = 6.2, H Het); 8.29 (1H, d, $^3J$ = 7.5, H Het). $^{13}$C NMR spectrum, δ, ppm: 43.3 ($NCH_2$); 111.7 (C-3 furoxan); 116.9, 117.2, 117.8, 121.9, 123.3, 127.7, 128.8, 130.8, 131.1, 131.2, 131.4, 131.7, 141.1, 142.0, 163.2 (C Ph, C Het, $CH=CH_2$); 149.6 (C-4 furoxan). Found, *m*/*z*: 403.0947 $[M+H]^+$. $C_{20}H_{15}N_6O_2S$. Calculated, *m*/*z*: 403.0972. Found, %: C 59.73; H 3.53; N 20.84; S 7.99. $C_{20}H_{14}N_6O_2S$. Calculated, %: C 59.69; H 3.51; N 20.88; S 7.97.

**5-Methyl-8-nitro-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3p)**. Yield 320 mg (76%), red powder, mp 191–193°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.79 (3H, s, $NCH_3$); 7.43–7.49 (5H, m, H Ph); 8.02 (1H, d, $^3J$ = 8.4, H Het); 8.64 (1H, d, $^3J$ = 8.4, H Het); 9.08 (1H, s, H Het). $^{13}$C NMR spectrum, δ, ppm: 28.7 ($NCH_3$); 111.6 (C-3 furoxan); 116.7, 121.8, 123.2, 126.5, 127.6, 128.2, 128.9, 130.9, 131.6, 141.0, 145.7, 163.1, 165.0 (C Ph, C Het); 149.7 (C-4 furoxan). Found, *m*/*z*: 422.0652 $[M+H]^+$. $C_{18}H_{12}N_7O_4S$. Calculated, *m*/*z*:

422.0666. Found, %: C 51.26; H 2.68; N 23.25; S 7.63. $C_{18}H_{11}N_7O_4S$. Calculated, %: C 51.30; H 2.63; N 23.27; S 7.61.

**8-Bromo-5-methyl-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3q)**. Yield 359 mg (79%), orange powder, mp 198–200°C. $^1$H NMR spectrum, δ, ppm: 3.68 (3H, s, NC$\underline{H}_3$); 7.43 (3H, br. s, H-3,4,5 Ph); 7.73 (2H, br. s, H-2,6 Ph); 7.89 (2H, br. s, H Het); 8.40 (1H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 28.2 ($NCH_3$); 109.2 (C-3 furoxan); 114.0, 115.8, 119.3, 122.4, 124.5, 128.3, 129.4, 131.4, 134.5, 141.4, 141.8, 146.6, 164.2 (C Ph, C Het); 150.1 (C-4 furoxan). Found, *m/z*: 456.9904 $[M(^{81}Br)+H]^+$, 454.9923 $[M(^{79}Br)+H]^+$. $C_{18}H_{12}BrN_6O_2S$. Calculated, *m/z*: 456.9900, 454.9920. Found, %: C 47.44; H 2.46; Br 17.50; N 18.43; S 7.03. $C_{18}H_{11}BrN_6O_2S$. Calculated, %: C 47.48; H 2.44; Br 17.55; N 18.46; S 7.04.

**4,6-Dimethyl-2-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl) sulfanyl]pyrimidine (3r)**. Yield 159 mg (53%), yellow powder, mp 161–163°C. $^1$H NMR spectrum, δ, ppm: 2.21 (6H, s, $2CH_3$); 6.99 (1H, s, H Het); 7.47 (3H, br. s, H-3,4,5 Ph); 7.72 (2H, br. s, H-2,6 Ph). $^{13}$C NMR spectrum, δ, ppm: 23.1, 23.3 ($2CH_3$), 111.8 (C-3 furoxan); 117.6, 117.8, 122.3, 127.5, 128.7, 130.7, 167.8 (C Ph, C Het); 151.6 (C-4 furoxan). Found, *m/z*: 301.0728 $[M+H]^+$. $C_{14}H_{13}N_4O_2S$. Calculated, *m/z*: 301.0754. Found, %: C 56.03; H 3.98; N 18.62; S 10.72. $C_{14}H_{12}N_4O_2S$. Calculated, %: C 55.99; H 4.03; N 18.65; S 10.68.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-ethyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3s)**. Yield 303 mg (75%), yellow powder, mp 229–231°C. $^1$H NMR spectrum, δ, ppm: 1.32 (3H, br. s, $CH_2C\underline{H}_3$); 4.16 (2H, br. s, $C\underline{H}_2Ph$); 4.36 (2H, br. s, $C\underline{H}_2CH_3$); 7.32 (5H, s, H Ph); 7.50–7.56 (1H, m, H Het); 7.79–7.86 (2H, m, H Het); 8.33–8.37 (1H, m, H Het). $^{13}$C NMR spectrum, δ, ppm: 12.4 ($CH_3$); 28.9 ($\underline{C}H_2Ph$); 37.7 ($NCH_2$); 110.2 (C-3 furoxan); 116.3, 116.9, 122.4, 124.5, 127.9, 129.2, 129.8, 131.3, 132.1, 141.4, 142.1, 144.8, 162.7 (C Ph, C Het); 149.9 (C-4 furoxan). Found, *m/z*: 405.1106 $[M+H]^+$. $C_{20}H_{17}N_6O_2S$. Calculated, *m/z*: 405.1128. Found, %: C 59.37; H 4.01; N 20.83; S 7.90. $C_{20}H_{16}N_6O_2S$. Calculated, %: C 59.39; H 3.99; N 20.78; S 7.93.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-propyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3t)**. Yield 318 mg (76%), dark-yellow powder, mp 239–241°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.32 (3H, t, $^3J$ = 7.1, $CH_3$); 1.34–1.41 (2H, m, $CH_3C\underline{H}_2$); 4.14 (2H, t, $^3J$ = 6.2, $NC\underline{H}_2$); 4.39 (2H, s, $C\underline{H}_2Ph$); 7.37 (5H, s, H Ph); 7.50 (1H, t, $^3J$ = 5.9, H Het); 7.71–7.77 (2H, m, H Het); 8.37 (1H, d, $^3J$ = 7.7, H Het). $^{13}$C NMR spectrum, δ, ppm: 10.5 ($CH_3$); 20.7 ($CH_3\underline{C}H_2$); 29.1 ($\underline{C}H_2Ph$); 42.6 ($N\underline{C}H_2$); 111.4 (C-3 furoxan); 116.9, 121.8, 123.1, 124.6, 128.1, 128.7, 129.3, 131.4, 132.9, 141.1, 141.6, 146.5, 164.1 (C Ph, C Het); 149.9 (C-4 furoxan). Found, *m/z*: 419.1264 $[M+H]^+$. $C_{21}H_{19}N_6O_2S$. Calculated, *m/z*: 419.1285. Found, %: C 60.23; H 4.32; N 20.06; S 7.69. $C_{21}H_{18}N_6O_2S$. Calculated, %: C 60.27; H 4.34; N 20.08; S 7.66.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-isopropyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3u)**. Yield 301 mg (72%), yellow powder, mp 163–165°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (6H, d, $^3J$ = 6.6, $CH(C\underline{H}_3)_2$); 4.26 (2H, s, $C\underline{H}_2Ph$); 4.81–4.89 (1H, m, $C\underline{H}(CH_3)_2$); 7.29 (5H, s, H Ph); 7.50 (1H, d, $^3J$ = 7.1, H Het); 7.72–7.78 (2H, m, H Het); 8.38 (1H, d, $^3J$ = 7.2, H Het). $^{13}$C NMR spectrum, δ, ppm: 18.5, 18.9 ($2CH_3$); 29.6 ($\underline{C}H_2Ph$); 47.2 ($\underline{C}H(CH_3)_2$); 111.7 (C-3 furoxan); 116.0, 117.6, 121.2, 121.7, 123.6, 127.3, 129.4, 131.5, 131.9, 141.2, 142.4, 145.7, 163.6 (C Ph, C Het); 149.9 (C-4 furoxan). Found, *m/z*: 419.1271 $[M+H]^+$. $C_{21}H_{19}N_6O_2S$. Calculated, *m/z*: 419.1285. Found, %: C 60.26; H 4.37; N 20.05; S 7.65. $C_{21}H_{18}N_6O_2S$. Calculated, %: C 60.27; H 4.34; N 20.08; S 7.66.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-butyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3v)**. Yield 263 mg (61%), dark-yellow powder, mp 194–196°C. $^1$H NMR spectrum, δ, ppm: 0.66 (3H, br. s, $CH_3$); 1.23 (2H, br. s, $CH_3C\underline{H}_2$); 1.72 (2H, br. s, $NCH_2C\underline{H}_2$); 4.14 (2H, br. s, $NCH_2$); 4.33 (2H, s, $C\underline{H}_2Ph$); 7.38 (5H, s, H Ph); 7.56 (1H, br. s, H Het); 7.79 (2H, br. s, H Het); 8.42 (1H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 13.7 ($CH_3$); 19.8 ($CH_3\underline{C}H_2$); 28.9, 29.8 ($\underline{C}H_2Ph$, $NCH_2\underline{C}H_2$); 42.1 ($NCH_2$); 110.1 (C-3 furoxan); 115.3, 116.7, 121.1, 122.6, 123.9, 127.8, 129.3, 130.7, 131.8, 141.0, 141.6, 145.3, 163.8 (C Ph, C Het); 149.6 (C-4 furoxan). Found, *m/z*: 433.1429 $[M+H]^+$. $C_{22}H_{21}N_6O_2S$. Calculated, *m/z*: 433.1441. Found, %: C 61.07; H 4.71; N 19.41; S 7.44. $C_{22}H_{20}N_6O_2S$. Calculated, %: C 61.10; H 4.66; N 19.43; S 7.41.

**5-Benzyl-3-[(4-benzyl-5-oxido-1,2,5-oxadiazol-3-yl)-sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3w)**. Yield 303 mg (65%), orange powder, mp 241–243°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 4.21 (2H, s, $C\underline{H}_2Ph$); 5.35 (2H, br. s, $NC\underline{H}_2$); 6.69 (3H, br. s, $NCH_2C_6\underline{H}_5$); 6.92 (2H, br. s, $NCH_2C_6\underline{H}_5$); 7.34 (5H, s, H Ph); 7.52 (1H, d, $^3J$ = 7.6, H Het); 7.71–7.75 (2H, m, H Het); 8.38 (1H, d, $^3J$ = 7.6, H Het). $^{13}$C NMR spectrum, δ, ppm: 29.1 ($\underline{C}H_2Ph$); 44.4 ($N\underline{C}H_2$); 111.4 (C-3 furoxan); 116.6, 122.4, 123.2, 127.2, 127.4, 127.9, 128.6, 129.1, 131.4, 131.8, 132.6, 135.3, 137.9, 140.4, 141.8, 145.2, 163.6 (C Het); 149.7 (C-4 furoxan). Found, *m/z*: 467.1267 $[M+H]^+$. $C_{25}H_{19}N_6O_2S$. Calculated, *m/z*: 467.1285. Found, %: C 64.34; H 3.88; N 18.05; S 6.86. $C_{25}H_{18}N_6O_2S$. Calculated, %: C 64.36; H 3.89; N 18.01; S 6.87.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-(2-phenylethyl)-5*H*-[1,2,4]triazino[5,6-*b*]indole (3x)**. Yield 326 mg (68%), orange powder, mp 174–176°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.88 (2H, br. s, $NCH_2C\underline{H}_2$); 4.18 (2H, s, $C\underline{H}_2Ph$); 4.45 (2H, br. s, $NCH_2$); 6.85 (3H, br. s, $(CH_2)_2C_6\underline{H}_5$); 6.97 (2H, br. s, $(CH_2)_2C_6\underline{H}_5$); 7.29 (5H, s, $CH_2C_6\underline{H}_5$); 7.46 (1H, br. s, H Het); 7.74 (2H, br. s, H Het); 8.33 (1H, d, $^3J$ = 7.2, H Het). $^{13}$C NMR spectrum, δ, ppm: 29.0 ($\underline{C}H_2Ph$); 33.3 ($NCH_2\underline{C}H_2$); 42.6 ($NCH_2$); 111.5 (C-3 furoxan); 116.9, 121.8, 123.0, 126.3, 128.0, 128.2, 128.3, 128.4, 129.1, 129.6, 129.9, 131.4, 137.4, 141.0, 141.8, 146.4, 164.3 (C Het); 149.4 (C-4 furoxan). Found, *m/z*: 481.1426 $[M+H]^+$. $C_{26}H_{21}N_6O_2S$. Calculated, *m/z*: 481.1441. Found, %: C 65.01; H 4.18; N 17.50; S 6.65. $C_{26}H_{20}N_6O_2S$. Calculated, %: C 64.98; H 4.20; N 17.49; S 6.67.

**5-Allyl-3-[(4-benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (3y)**. Yield 245 mg (59%), bright-yellow powder, mp 188–190°C. $^1$H NMR

spectrum, δ, ppm (*J*, Hz): 4.23 (2H, s, C$\underline{H}_2$Ph); 4.82 (2H, br. s, NC$\underline{H}_2$); 5.05 (1H, d, $^3J$ = 10.3, CH=C$\underline{H}_2$); 5.19 (1H, d, $^3J$ = 10.3, CH=C$\underline{H}_2$); 5.62–5.68 (1H, m, $CH_2C\underline{H}$=$CH_2$); 7.33 (5H, s, H Ph); 7.51 (2H, t, $^3J$=7.6, H Het); 7.74 (1H, d, $^3J$ = 7.7, H Het); 8.39 (1H, d, $^3J$ = 7.9, H Het). $^{13}$C NMR spectrum, δ, ppm: 28.9 (C$\underline{H}_2$Ph); 43.6 (NC$\underline{H}_2$); 110.9 (C-3 furoxan); 116.7, 117.3, 117.9, 122.9, 123.8, 127.8, 128.4, 130.2, 131.0, 131.3, 131.5, 131.9, 141.4, 142.6 163.0 (C Het, CH=$CH_2$); 149.8 (C-4 furoxan). Found, *m/z*: 417.1114 $[M+H]^+$. $C_{21}H_{17}N_6O_2S$. Calculated, *m/z*: 417.1128. Found, %: C 60.59; H 3.85; N 20.14; S 7.72. $C_{21}H_{16}N_6O_2S$. Calculated, %: C 60.56; H 3.87; N 20.18; S 7.70.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-5-methyl-8-nitro-5*H*-[1,2,4]triazino[5,6-*b*]indole (3z)**. Yield 283 mg (65%), red powder, mp 196–198°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.84 (3H, s, NC$\underline{H}_3$); 4.18 (2H, s, C$\underline{H}_2$Ph); 7.31 (5H, s, H Ph); 7.92 (1H, d, $^3J$ = 8.1, H Het); 8.56 (1H, d, $^3J$ = 8.1, H Het); 8.94 (1H, s, H Het). $^{13}$C NMR spectrum, δ, ppm: 28.1 ($NCH_3$); 29.7 (C$\underline{H}_2$Ph); 111.3 (C-3 furoxan); 115.9, 121.4, 123.1, 126.8, 127.7, 128.5, 129.3, 130.7, 131.8, 140.3, 145.2, 163.5 (C Het); 149.8 (C 4 furoxan); 165.8 ($CNO_2$). Found, *m/z*: 436.0807 $[M+H]^+$. $C_{19}H_{14}N_7O_4S$. Calculated, *m/z*: 436.0823. Found, %: C 52.43; H 2.98; N 22.48; S 7.37. $C_{19}H_{13}N_7O_4S$. Calculated, %: C 52.41; H 3.01; N 22.52; S 7.36.

**3-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)sulfanyl]-8-bromo-5-methyl-5*H*-[1,2,4]triazino[5,6-*b*]indole (3aa)**. Yield 338 mg (72%), dark-yellow powder, mp 204–206°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.66 (3H, s, NC$\underline{H}_3$); 4.19 (2H, s, C$\underline{H}_2$Ph); 7.29 (5H, s, H Ph); 7.64 (1H, d, $^3J$ = 8.6, H Het); 7.88 (1H, d, $^3J$ = 8.6, H Het); 8.22 (1H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 28.2 ($NCH_3$); 29.3 (C$\underline{H}_2$Ph); 110.3 (C-3 furoxan); 114.2, 116.7, 119.9, 122.1, 125.7, 128.7, 129.3, 131.0, 134.7, 141.2, 141.8, 145.8, 163.7 (C Het); 149.7 (C-4 furoxan). Found, *m/z*: 471.0052 $[M(^{81}Br)+H]^+$, 469.0071 $[M(^{79}Br)+H]^+$. $C_{19}H_{14}BrN_6O_2S$. Calculated, *m/z*: 471.0056, 469.0077. Found, %: C 48.59; H 2.83; Br 16.99; N 17.87; S 6.85. $C_{19}H_{13}BrN_6O_2S$. Calculated, %: C 8.62; H 2.79; Br 17.03; N 17.91; S 6.83.

**4,6-Dimethyl-2-[(4-benzyl-5-oxido-1,2,5-oxadiazol-3-yl)-sulfanyl]pyrimidine (3ab)**. Yield 110 mg (35%), yellow powder, mp 169–171°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.14 (6H, s, $2CH_3$); 4.24 (2H, s, C$\underline{H}_2$Ph); 6.87 (1H, s, H Het); 7.36 (5H, s, H Ph). $^{13}$C NMR spectrum, δ, ppm: 22.4, 22.5 ($2CH_3$); 28.8 (C$\underline{H}_2$Ph); 111.3 (C-3 furoxan); 115.2, 117.4, 122.8, 126.9, 128.4, 129.9, 166.3 (C Ph, C Het); 150.2 (C-4 furoxan). Found, *m/z*: 315.0894 $[M+H]^+$. $C_{15}H_{15}N_4O_2S$. Calculated, *m/z*: 315.0910. Found, %: C 57.28; H 4.50; N 17.79; S 10.24. $C_{15}H_{14}N_4O_2S$. Calculated, %: C 57.31; H 4.49; N 17.82; S 10.20.

**Preparation of compounds 3ac–ap** (General method). DBU (0.33 ml, 2.2 mmol) was added dropwise at room temperature to a stirred suspension of the respective thiol **2a**–**n** (2.2 mmol) in anhydrous MeCN (4 ml). The obtained mixture was stirred for 15 min and then furoxan **1d** (0.34 g, 1.0 mmol) was added. The reaction mixture was further stirred for 48–120 h until complete conversion of the starting furoxan **1d** (control by TLC, eluent $CHCl_3$). The reaction mixture was then diluted with $H_2O$ (20 ml). The precipitate formed was filtered off, carefully washed with water, 0.75 N NaOH, then again with water, acetonitrile (~1 ml), and air-dried.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5*H*-[1,2,4]triazino-[5,6-*b*]indole) (3ac)**. Yield 412 mg (63%), orange powder, mp 239–241°C. $^1$H NMR spectrum, δ, ppm: 1.19 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.58 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.57 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 7.56 (2H, br. s, H Het); 7.82 (4H, br. s, H Het); 8.34 (2H, br. s, H Het); 12.94 (2H, br. s, 2NH). $^{13}$C NMR spectrum, δ, ppm: 21.4 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.6 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.9 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 111.2 (C-3 furoxan); 121.3, 122.5, 122.9, 126.8, 133.9, 140.7, 142.4, 145.5, 163.8 (C Het); 151.2 (C-4 furoxan). Found, *m/z*: 655.1388 $[M+H]^+$. $C_{28}H_{23}N_{12}O_4S_2$. Calculated, *m/z*: 655.1401. Found, %: C 51.45; H 3.43; N 25.60; S 9.84. $C_{28}H_{22}N_{12}O_4S_2$. Calculated, %: C 51.37; H 3.39; N 25.67; S 9.80.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-methyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ad)**. Yield 375 mg (55%), orange powder, mp 187–189°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.53 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.75 (10H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$, $2NC\underline{H}_3$); 7.51 (2H, d, $^3J$ = 7.6, H Het); 7.79 (4H, br. s, H Het); 8.30 (2H, d, $^3J$ = 7.6, H Het). $^{13}$C NMR spectrum, δ, ppm: 22.0 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.8 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.5 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 28.2 ($NCH_3$), 109.4 (C-3 furoxan); 121.8, 122.4, 123.3, 125.6, 131.7, 140.3, 141.6, 144.7, 163.6 (C Het); 152.4 (C-4 furoxan). Found, *m/z*: 683.1697 $[M+H]^+$. $C_{30}H_{27}N_{12}O_4S_2$. Calculated, *m/z*: 683.1714. Found, %: C 52.81; H 3.79; N 24.60; S 9.44. $C_{30}H_{26}N_{12}O_4S_2$. Calculated, %: C 52.78; H 3.84; N 24.62; S 9.39.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-ethyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ae)**. Yield 483 mg (68%), yellow powder, mp 196–198°C. $^1$H NMR spectrum, δ, ppm: 1.21–1.28 (10H, m, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$, $2C\underline{H}_3$); 1.55 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.54 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.27–4.32 (4H, m, $2NCH_2$); 7.55–7.59 (2H, m, H Het); 7.79–7.85 (4H, m, H Het); 8.33–8.36 (2H, m, H Het). $^{13}$C NMR spectrum, δ, ppm: 13.6 ($CH_3$); 21.7 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.9 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 28.6 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 36.9 ($2CH_2$); 111.6 (C-3 furoxan); 121.1, 122.6, 123.7, 125.2, 130.3, 140.7, 141.9, 144.2, 163.8 (C Het); 150.1 (C-4 furoxan). Found, *m/z*: 711.2027 $[M+H]^+$. $C_{32}H_{31}N_{12}O_4S_2$. Calculated, *m/z*: 711.2027. Found, %: C 54.01; H 4.29; N 23.61; S 8.98. $C_{32}H_{30}N_{12}O_4S_2$. Calculated, %: C 54.07; H 4.25; N 23.65; S 9.02.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-propyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3af)**. Yield 480 mg (65%), light-yellow powder, mp 210–212°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.68 (6H, br. s, $2CH_3$); 1.14 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.50 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 1.65 (4H, br. s, $2CH_3C\underline{H}_2$); 3.51 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.33 (4H, br. s, $2NCH_2$); 7.81 (4H, br. s, H Het); 7.94 (2H, br. s, H Het); 8.33 (2H, d, $^3J$ = 7.1, H Het). $^{13}$C NMR spectrum, δ, ppm: 11.2 ($CH_3$); 20.4 ($CH_3\underline{C}H_2$); 22.1 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.4 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 29.7 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 43.4

($NCH_2$); 110.4 (C-3 furoxan); 116.4, 122.0, 122.5, 123.7, 131.6, 141.1, 141.9, 146.6, 163.9 (C Het); 149.9 (C-4 furoxan). Found, *m/z*: 739.2329 $[M+H]^+$. $C_{34}H_{35}N_{12}O_4S_2$. Calculated, *m/z*: 739.2340. Found, %: C 55.32; H 4.59; N 22.72; S 8.70. $C_{34}H_{34}N_{12}O_4S_2$. Calculated, %: C 55.27; H 4.64; N 22.75; S 8.68.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-isopropyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ag)**. Yield 421 mg (57%), light-yellow powder, mp 158–160°C. $^1$H NMR spectrum, δ, ppm: 1.23 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.45 (16H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$, $2CH_3$); 3.56 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.74–4.80 (2H, m, $2C\underline{H}(CH_3)_2$); 7.48 (2H, br. s, H Het); 7.71 (4H, br. s, H Het); 8.34 (2H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 19.3, 19.7 ($CH_3$); 21.8 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.0 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.5 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 46.5 ($\underline{C}H(CH_3)_2$); 111.7 (C-3 furoxan); 112.1, 117.0, 121.8, 122.9, 131.3, 140.6, 141.7, 146.0, 163.4 (C Het); 149.3 (C-4 furoxan). Found, %: C 55.25; H 4.68; N 22.73; S 8.74. $C_{34}H_{34}N_{12}O_4S_2$. Calculated, %: C 55.27; H 4.64; N 22.75; S 8.68.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-butyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ah)**. Yield 536 mg (70%), yellow powder, mp 197–199°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.86 (6H, br. s, $2CH_3$); 1.17 (8H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$, $2CH_3C\underline{H}_2$); 1.61 (8H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$, $2NCH_2C\underline{H}_2$); 3.68 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.14 (4H, br. s, $2NCH_2$); 7.49 (2H, br. s, H Het); 7.87 (4H, br. s, H Het); 8.26 (2H, d, $^3J$ = 6.9, H Het). $^{13}$C NMR spectrum, δ, ppm: 13.7 ($CH_3$); 19.8 ($CH_3\underline{C}H_2$); 22.4 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.7 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 29.8 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 31.4 ($NCH_2\underline{C}H_2$); 43.8 ($NCH_2$); 110.3 (C-3 furoxan); 116.1, 116.9, 121.8, 123.2, 131.7, 141.2, 141.9, 144.8, 163.7 (C Het); 149.7 (C-4 furoxan). Found, *m/z*: 767.2639 $[M+H]^+$. $C_{36}H_{39}N_{1\text{-}2}O_4S_2$. Calculated, *m/z*: 767.2653. Found, %: C 56.43; H 5.02; N 21.88; S 8.39. $C_{36}H_{38}N_{12}O_4S_2$. Calculated, %: C 56.38; H 4.99; N 21.92; S 8.36.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-benzyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ai)**. Yield 450 mg (54%), orange powder, mp 206–208°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.18 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.52 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.64 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 5.32 (4H, s, $2NC\underline{H}_2Ph$); 7.29 (10H, s, $2NCH_2C_6\underline{H}_5$); 7.73 (2H, br. s, H Het); 7.94 (4H, br. s, H Het); 8.32 (2H, d, $^3J$ = 8.2, H Het). $^{13}$C NMR spectrum, δ, ppm: 20.3 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.6 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 29.1 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 44.9 ($NCH_2$); 110.2 (C-3 furoxan); 116.1, 117.2, 122.1, 123.6, 128.0, 128.8, 129.0, 131.9, 132.7, 141.7, 142.5, 144.7, 163.7 (C Het); 149.9 (C-4 furoxan). Found, *m/z*: 835.2322 $[M+H]^+$. $C_{42}H_{35}N_{12}O_4S_2$. Calculated, *m/z*: 835.2340. Found, %: C 60.38; H 4.07; N 20.09; S 7.73. $C_{42}H_{34}N_{12}O_4S_2$. Calculated, %: C 60.42; H 4.10; N 20.13; S 7.68.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-(2-phenylethyl)-5*H*-[1,2,4]triazino[5,6-*b*]indole) (3aj)**. Yield 414 mg (48%), orange powder, mp 213–215°C. $^1$H NMR spectrum, δ, ppm: 1.13 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.58 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 2.33 (4H, br. s, $2NCH_2C\underline{H}_2$); 3.73 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.22 (4H, br. s, $2NCH_2$); 6.71 (6H, br. s, $2CH_2C_6\underline{H}_5$); 6.92 (4H, br. s, $2CH_2C_6\underline{H}_5$); 7.47 (2H, br. s, H Het); 7.73 (4H, br. s, H Het); 8.36 (2H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 21.9 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.6 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 28.3 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 32.1 ($NCH_2\underline{C}H_2$); 44.2 ($NCH_2$); 111.6 (C-3 furoxan); 117.2, 122.0, 123.3, 127.1, 127.8, 128.0, 128.7, 131.5, 135.2, 140.9, 141.8, 146.4, 164.4 (C Het); 149.5 (C-4 furoxan). Found, %: C 61.20; H 4.51; N 19.45; S 7.46. $C_{44}H_{38}N_{12}O_4S_2$. Calculated, %: C 61.24; H 4.44; N 19.48; S 7.43.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-allyl-5*H*-[1,2,4]triazino[5,6-*b*]-indole) (3ak)**. Yield 308 mg (42%), bright-yellow powder, mp 174–176°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.19 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.62 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.71 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 4.82 (4H, br. s, $NC\underline{H}_2$); 5.04 (2H, d, $^3J$ = 10.2, $CH{=}C\underline{H}_2$); 5.19 (2H, d, $^3J$ = 10.2, $CH{=}C\underline{H}_2$); 5.66–5.72 (2H, m, $CH_2C\underline{H}{=}CH_2$); 7.48–7.52 (4H, m, H Het); 7.69–7.75 (2H, m, H Het); 8.40 (2H, d, $^3J$ = 6.7, H Het). $^{13}$C NMR spectrum, δ, ppm: 21.6 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.7 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 29.1 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 43.5 ($NCH_2$); 109.4 (C-3 furoxan); 116.7, 117.4, 118.6, 121.7, 123.6, 127.1, 131.3, 131.8, 141.7, 142.6, and 163.6 (C Het, $\underline{C}H{=}\underline{C}H_2$); 149.8 (C-4 furoxan). Found, *m/z*: 735.2013 $[M+H]^+$. $C_{34}H_{31}N_{12}O_4S_2$. Calculated, *m/z*: 735.2027. Found, %: C 55.54; H 4.17; N 22.93; S 8.69. $C_{34}H_{30}N_{12}O_4S_2$. Calculated, %: C 55.57; H 4.12; N 22.87; S 8.73.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(5-methyl-8-nitro-5*H*-[1,2,4]triazino-[5,6-*b*]indole) (3al)**. Yield 486 mg (63%), orange powder, mp 132–134°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.58 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.63 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 3.86 (6H, s, $2NCH_3$); 8.07 (2H, d, $^3J$ = 8.0, H Het); 8.56 (2H, d, $^3J$ = 8.0, H Het); 9.01 (2H, s, H Het). $^{13}$C NMR spectrum, δ, ppm: 21.2 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.9 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 28.3 ($NCH_3$); 29.7 ($\underline{C}H(CH_2)_4\underline{C}H_2$); 109.3 (C-3 furoxan); 116.7, 121.8, 126.5, 127.6, 131.6, 141.0, 145.7, 163.4 (C Het); 149.9 (C-4 furoxan); 165.7 ($CNO_2$). Found, *m/z*: 773.1402 $[M+H]^+$. $C_{30}H_{25}N_{14}O_8S_2$. Calculated, *m/z*: 773.1416. Found, %: C 46.60; H 3.17; N 25.32; S 8.34. $C_{30}H_{24}N_{14}O_8S_2$. Calculated, %: C 46.63; H 3.13; N 25.38; S 8.30.

**3,3'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(8-bromo-5-methyl-5*H*-[1,2,4]triazino[5,6-*b*]indole) (3am)**. Yield 420 mg (50%), dark-yellow powder, mp 183–185°C. $^1$H NMR spectrum, δ, ppm: 1.19 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.53 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 3.55 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 3.78 (6H, s, $2NCH_3$); 7.97 (4H, br. s, H Het); 8.43 (2H, br. s, H Het). $^{13}$C NMR spectrum, δ, ppm: 21.1 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.6 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 28.6 ($NCH_3$); 29.1 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 109.8 (C-3 furoxan); 114.3, 115.9, 118.4, 124.8, 133.8, 141.1, 141.7, 145.4, 164.0 (C Het); 149.7 (C-4 furoxan). Found, %: C 42.91; H 2.93; Br 18.98; N 19.96; S 7.60. $C_{30}H_{24}Br_2N_{12}O_4S_2$. Calculated, %: C 42.87; H 2.88; Br 19.01; N 20.00; S 7.63.

**2,2'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(4,6-diaminopyrimidine) (3an)**. Yield 299 mg (56%), yellow powder, mp 177–179°C. $^1$H NMR spectrum, δ, ppm: 1.27 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.60

(4H, br. s, $CH_2CH_2(CH_2)_2CH_2CH_2$); 3.47 (4H, br. s, $CH_2(CH_2)_4CH_2$); 5.19 (2H, s, H Het); 6.21 (8H, s, $4NH_2$). $^{13}$C NMR spectrum, δ, ppm: 18.9 ($(CH_2)_2(CH_2)_2(CH_2)_2$); 24.9 ($CH_2CH_2(CH_2)_2CH_2CH_2$); 29.3 ($CH_2(CH_2)_4CH_2$); 79.8 (CH Het); 111.3 (C-3 furoxan); 151.9 (C-4 furoxan); 163.7 ($CNH_2$); 166.9 (CS). Found, *m/z*: 535.1378 $[M+H]^+$. $C_{18}H_{23}N_{12}O_4S_2$. Calculated, *m/z*: 535.1401. Found, %: C 40.40; H 4.19; N 31.38; S 11.97. $C_{18}H_{22}N_{12}O_4S_2$. Calculated, %: C 40.44; H 4.15; N 31.44; S 12.00.

**2,2'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(4,6-dimethylpyrimidine) (3ao)**. Yield 180 mg (34%), bright-yellow powder, mp 182–184°C. $^1$H NMR spectrum, δ, ppm: 1.22 (4H, br. s, $(CH_2)_2(CH_2)_2(CH_2)_2$); 1.54 (4H, br. s, $CH_2CH_2(CH_2)_2CH_2CH_2$); 2.21 (12H, s, $4CH_3$); 3.54 (4H, br. s, $CH_2(CH_2)_4CH_2$); 6.99 (2H, s, 2CH Het). $^{13}$C NMR spectrum, δ, ppm: 18.8 ($(CH_2)_2(CH_2)_2(CH_2)_2$); 22.6, 22.8 ($CH_3$); 24.1 ($CH_2CH_2(CH_2)_2CH_2CH_2$); 29.6 ($CH_2(CH_2)_4CH_2$); 110.3 (C-3 furoxan); 117.8, 127.5 (C Het); 152.4 (C-4 furoxan); 166.2 (CS). Found, *m/z*: 531.1576 $[M+H]^+$. $C_{22}H_{27}N_8O_4S_2$. Calculated, *m/z*: 531.1591. Found, %: C 49.82; H 4.91; N 21.10; S 12.11. $C_{22}H_{26}N_8O_4S_2$. Calculated, %: C 49.80; H 4.94; N 21.12; S 12.09.

**2,2'-{(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)sulfanediyl]}bis(1,3,4-thiadiazol-2-amine) (3ap)**. Yield 264 mg (51%), dark-yellow powder, mp 285–287°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (4H, br. s, $(CH_2)_2(CH_2)_2(CH_2)_2$); 1.57 (4H, br. s, $CH_2CH_2(CH_2)_2CH_2CH_2$); 3.42 (4H, br. s, $CH_2(CH_2)_4CH_2$); 7.97 (4H, br. s, $2NH_2$). $^{13}$C NMR spectrum, δ, ppm: 19.6 ($(CH_2)_2(CH_2)_2(CH_2)_2$); 23.9 ($CH_2CH_2(CH_2)_2CH_2CH_2$); 28.6 ($CH_2(CH_2)_4CH_2$); 109.6 (C-3 furoxan); 153.2 (C-4 furoxan); 160.2 ($CNH_2$); 172.8 (SCS). Found, *m/z*: 517.0306 $[M+H]^+$. $C_{14}H_{17}N_{10}O_4S_4$. Calculated, *m/z*: 517.0311. Found, %: C 32.52; H 3.08; N 27.15; S 24.80. $C_{14}H_{16}N_{10}O_4S_4$. Calculated, %: C 32.55; H 3.12; N 27.11; S 24.83.

**1,2-Bis(5-propyl-5*H*-[1,2,4]triazino[5,6-*b*]indol-3-yl) disulfide (5b)**. A suspension of thiol **2d** (0.17 g, 0.7 mmol) in anhydrous MeCN (2 ml) was stirred and treated with $Et_3N$ (0.10 ml, 0.7 mmol) or DBU (0.11 ml, 0.7 mmol). Furoxan **1e** was added to the obtained mixture after 10 min, and stirring was continued for 40 min until complete conversion of the starting furoxan **1e** (control by TLC, eluent $CHCl_3$). The reaction mixture was then diluted with $H_2O$ (10 ml), the precipitate formed was filtered off, washed with water and acetonitrile, and air-dried. Yield 190–210 mg (56–63%), bright-red powder that remained unchanged upon heating to 300°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 0.90 (6H, t, $^3J$ = 6.8, $2CH_3$); 1.72–1.77 (4H, m, $2CH_3CH_2$); 4.03–4.07 (4H, m, $2NCH_2$); 7.75 (2H, br. s, H Het); 7.90 (4H, br. s, H Het); 8.35 (2H, d, $^3J$ = 7.3, H Het). $^{13}$C NMR spectrum, δ, ppm: 11.2 ($CH_3$); 20.7 ($CH_3CH_2$); 42.0 ($NCH_2$); 117.0, 117.8, 120.9, 122.7, 123.1, 130.7, 141.7, 143.9, 154.0 (C). Found, *m/z*: 487.1491 $[M+H]^+$. $C_{24}H_{23}N_8S_2$. Calculated, *m/z*: 487.1482.

**Preparation of hetaryloxyfuroxans 7a–j** (General method). DBU (0.15 ml, 1 mmol) was added dropwise at room temperature to a stirred solution of the respective hydroxy heterocycle **6a–e** (1 mmol) in anhydrous MeCN (2 ml). The obtained solution was treated after 10 min by the addition of furoxan **1a** or **1b** (1 mmol) or furoxan **1d** (0.5 mmol) and stirred for 2–48 h until complete conversion of the starting furoxan (control by TLC, eluent $CHCl_3$). The reaction mixture was then diluted with $H_2O$ (10 ml). The precipitate formed was filtered off, carefully washed with water, and air-dried.

**2-Methyl-5-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)-oxy]pyridine (7a)**. Yield 242 mg (90%), white powder, mp 102–104°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.53 (3H, s, $CH_3$); 7.42 (1H, d, $^3J$ = 8.4, H-4 Het); 7.61–7.66 (3H, m, H-3,4,5 Ph); 7.92 (1H, d, $^3J$ = 8.4, H-3 Het); 8.11 (2H, d, $^3J$ = 6.8, H-2,6 Ph); 8.67 (1H, s, H-6 Het). $^{13}$C NMR spectrum, δ, ppm: 23.4 ($CH_3$); 108.2 (C-3 furoxan); 121.6, 124.0, 126.7, 128.5, 129.1, 130.9, 141.1, 147.6, 162.3 (C Ph, C Het); 156.3 (C-4 furoxan). Found, *m/z*: 270.0877 $[M+H]^+$. $C_{14}H_{12}N_3O_3$. Calculated, *m/z*: 270.0873. Found, %: C 62.49; H 4.05; N 15.57. $C_{14}H_{11}N_3O_3$. Calculated, %: C 62.45; H 4.12; N 15.61.

**6-Methyl-2-nitro-3-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)oxy]pyridine (7b)**. Yield 254 mg (81%), bright-yellow powder, mp 141–143°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.62 (3H, s, $CH_3$); 7.62–7.66 (3H, m, H-3,4,5 Ph); 7.91 (1H, d, $^3J$ = 8.4, H-4 Het); 8.07 (2H, d, $^3J$ = 6.4, H-2,6 Ph); 8.44 (1H, d, $^3J$ = 8.4, H-3 Het). $^{13}$C NMR spectrum, δ, ppm: 22.9 ($CH_3$); 107.9 (C-3 furoxan); 121.1, 126.5, 129.1, 130.8, 131.1, 134.7, 138.8, 147.5, 161.4 (C Ph, C Het); 156.5 (C-4 furoxan). Found, %: C 53.47; H 3.23; N 17.77. $C_{14}H_{10}N_4O_5$. Calculated, %: C 53.51; H 3.21; N 17.83.

**8-[(5-Oxido-4-phenyl-1,2,5-oxadiazol-3-yl)oxy]quinoline (7c)**. Yield 250 mg (82%), light-yellow powder, mp 167–169°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 7.63–7.75 (5H, m, H-3,4,5 Ph, H-3,6 Het); 7.98 (1H, d, $^3J$ = 7.4, H-4 Het); 8.04 (1H, d, $^3J$ = 7.4, H-5 Het); 8.25 (2H, d, $^3J$ = 7.1, H-2,6 Ph); 8.52 (1H, d, $^3J$ = 8.2, H-7 Het); 8.93 (1H, br. s, H-2 Het). $^{13}$C NMR spectrum, δ, ppm: 108.0 (C-3 furoxan); 120.9, 121.8, 122.6, 126.6, 126.8, 127.1, 129.2, 129.6, 131.0, 136.5, 139.2, 148.4, 163.0 (C Ph, C Het); 151.2 (C-4 furoxan). Found, %: C 66.83; H 3.69; N 13.72. $C_{17}H_{11}N_3O_3$. Calculated, %: C 66.88; H 3.63; N 13.76.

**5-Bromo-8-[(5-oxido-4-phenyl-1,2,5-oxadiazol-3-yl)-oxy]quinoline (7d)**. Yield 334 mg (87%), yellow powder, mp 188–190°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 7.61–7.68 (3H, m, H-3,4,5 Ph); 7.78–7.83 (1H, m, H-3 Het); 7.97 (1H, d, $^3J$ = 8.2, H-6 Het); 8.11 (1H, d, $^3J$ = 8.2, H-7 Het); 8.22 (2H, d, $^3J$ = 6.4, H-2,6 Ph); 8.60 (1H, d, $^3J$ = 8.6, H-4 Het); 9.00 (1H, d, $^3J$ = 8.6, H-2 Het). $^{13}$C NMR spectrum, δ, ppm: 108.6 (C-3 furoxan); 119.1, 121.6, 121.9, 124.1, 126.7, 128.3, 129.2, 130.3, 131.1, 135.6, 140.0, 148.2, 163.4 (C Ph, C Het); 152.1 (C-4 furoxan). Found, *m/z*: 407.9778 $[M(^{81}Br)+Na]^+$, 405.9798 $[M(^{79}Br)+Na]^+$. $C_{17}H_{10}BrN_3NaO_3$. Calculated, *m/z*: 407.9777, 405.9798. Found, %: C 53.11; H 2.67; Br 20.74; N 10.88. $C_{17}H_{10}BrN_3O_3$. Calculated, %: C 53.15; H 2.62; Br 20.80; N 10.94.

**3-Phenyl-4-(1*H*-pyrazol-4-yloxy)-1,2,5-oxadiazole 2-oxide (7e)**. Yield 166 mg (68%), white powder, mp 70–72°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 7.54 (3H, br. s, H-3,4,5 Ph); 8.07 (2H, d, $^3J$ = 6.6, H-2,6 Ph); 8.26

(1H, s, H-5 Het); 8.73 (1H, s, H-3 Het); 12.92 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 107.9 (C-3 furoxan); 126.5, 128.7, 129.0, 130.9 (C Ph); 135.8, 138.5, 161.1 (C Het); 151.9 (C-4 furoxan). Found, *m/z*: 243.0575 $[M–H]^+$. $C_{11}H_7N_4O_3$. Calculated, *m/z*: 243.0513. Found, %: C 54.07; H 3.34; N 22.89. $C_{11}H_8N_4O_3$. Calculated, %: C 54.10; H 3.30; N 22.94.

**5-[(4-Benzyl-5-oxido-1,2,5-oxadiazol-3-yl)oxy]-2-methylpyridine (7f)**. Yield 204 mg (72%), white powder, mp 77–79°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.55 (3H, s, $CH_3$); 4.12 (2H, s, $C\underline{H}_2Ph$); 7.34 (5H, s, H Ph); 7.44 (1H, d, $^3J$ = 8.6, H-4 Het); 7.88 (1H, d, $^3J$ = 8.6, H-3 Het); 8.63 (1H, s, H-6 Het). $^{13}$C NMR spectrum, δ, ppm: 23.1 ($CH_3$), 29.6 ($\underline{C}H_2Ph$); 108.9 (C-3 furoxan); 121.9, 124.6, 126.8, 128.3, 129.3, 130.6, 141.2, 147.4, 162.1 (C Ph, C Het); 149.3 (C-4 furoxan). Found, %: C 63.64; H 4.58; N 14.86. $C_{15}H_{13}N_3O_3$. Calculated, %: C 63.60; H 4.63; N 14.83.

**3-Benzyl-4-(1*H*-pyrazol-4-yloxy)-1,2,5-oxadiazole 2-oxide (7g)**. Yield 139 mg (54%), white powder, mp 66–68°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 4.17 (2H, s, $C\underline{H}_2Ph$); 7.31 (5H, s, H Ph); 8.21 (1H, s, H-5 Het); 8.69 (1H, s, H-3 Het); 12.87 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 29.2 ($\underline{C}H_2Ph$); 110.8 (C-3 furoxan); 126.8, 128.5, 129.3, 131.8 (C Ph); 135.2, 138.9, 161.3 (C Het); 149.6 (C-4 furoxan). Found, %: C 55.76; H 3.93; N 21.66. $C_{12}H_{10}N_4O_3$. Calculated, %: C 55.81; H 3.90; N 21.70.

**3,3'-(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)oxy]}bis(6-methylpyridine) (7h)**. Yield 183 mg (78%), white powder, mp 92–94°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (4H, br. s, $CH_2CH_2C\underline{H}_2C\underline{H}_2CH_2CH_2$); 1.64 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 2.53 (6H, s, $2CH_3$); 2.62 (4H, br. s, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 7.37 (2H, d, $^3J$ = 8.6, H-4 Het); 7.81 (2H, d, $^3J$ = 8.6, H-3 Het); 8.56 (2H, s, H-6 Het). $^{13}$C NMR spectrum, δ, ppm: 21.3 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 23.4 ($2CH_3$); 24.1 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.8 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 109.8 (C-3 furoxan); 124.0, 128.1, 140.8, 147.6, 163.1 (C Het); 156.1 (C-4 furoxan). Found, %: C 56.44; H 5.09; N 17.98. $C_{22}H_{24}N_6O_6$. Calculated, %: C 56.40; H 5.16; N 17.94.

**8,8'-(Hexane-1,6-diyl)bis[(5-oxido-1,2,5-oxadiazole-4,3-diyl)oxy]}bis(5-bromoquinoline) (7i)**. Yield 247 mg (71%), yellow powder, mp 173–175°C. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.42 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.77 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 2.71 (4H, t, $^3J$=6.8, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 7.69–7.74 (2H, m, H-3 Het); 7.80 (2H, d, $^3J$ = 8.1, H-6 Het); 8.02 (2H, d, $^3J$ = 8.1, H-7 Het); 8.51 (2H, d, $^3J$ = 8.3, H-4 Het); 8.91 (2H, br. s, H-2 Het). $^{13}$C NMR spectrum, δ, ppm: 21.4 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.1 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.8 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 109.6 (C-3 furoxan); 118.8, 121.3, 123.9, 128.1, 130.1, 135.3, 139.9, 148.2, 163.8 (C Het); 151.6 (C-4 furoxan). Found, %: C 48.11; H 3.24; Br 22.85; N 11.99. $C_{28}H_{22}Br_2N_6O_6$. Calculated, %: C 48.16; H 3.18; Br 22.88; N 12.03.

**3,3'-(Hexane-1,6-diyl)bis[(4-(1*H*-pyrazol-4-yloxy)-1,2,5-oxadiazole] 2,2'-dioxide (7j)**. Yield 127 mg (61 %), white powder, mp 91–93°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (4H, br. s, $(CH_2)_2(C\underline{H}_2)_2(CH_2)_2$); 1.69 (4H, br. s, $CH_2C\underline{H}_2(CH_2)_2C\underline{H}_2CH_2$); 2.76 (4H, t, $^3J$=6.6, $C\underline{H}_2(CH_2)_4C\underline{H}_2$); 8.19 (2H, s, H-5 Het); 8.67 (2H, s, H-3 Het); 12.96 (2H, br. s, 2NH). $^{13}$C NMR spectrum, δ, ppm: 21.3 ($(CH_2)_2(\underline{C}H_2)_2(CH_2)_2$); 24.4 ($CH_2\underline{C}H_2(CH_2)_2\underline{C}H_2CH_2$); 27.9 ($\underline{C}H_2(CH_2)_4\underline{C}H_2$); 109.2 (C-3 furoxan); 134.6, 138.1, 160.3 (C Het); 151.2 (C-4 furoxan). Found, %: C 45.89; H 4.37; N 26.81. $C_{16}H_{18}N_8O_6$. Calculated, %: C 45.93; H 4.34; N 26.78.

*The work was performed with financial support from the Russian Science Foundation (grant 14-50-00126).*

## References


1. Fershtat, L. L.; Epishina, M. A.; Kulikov, A. S.; Makhova, N. N. *Mendeleev Commun.* **2015**, *25*, 36.
2. Furchgott, R. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1870.
3. Murad, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1856.
4. Ignarro, L. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 1882.
5. Gasco, A.; Fruttero, R.; Sorba, G.; Di Stilo, A.; Calvino, R. *Pure Appl. Chem.* **2004**, *76*, 973.
6. Cena, C.; Bertinaria, M.; Boschi, D.; Giorgis, M.; Gasco, A. *ARKIVOC* **2006**, (vii), 301.
7. Jovene, C.; Chugunova, E. A.; Goumont, R. *Mini-Rev. Med. Chem.* **2013**, *13*, 1089.
8. Willmot, M.; Gray, L.; Gibson, C.; Murphy, S.; Bath, P. M. *Nitric Oxide* **2005**, *12*, 141.
9. Miller, M. R.; Megson, I. L. *Br. J. Pharmacol.* **2007**, *151*, 305.
10. Huerta, S.; Chilka, S.; Bonavida, B. *Int. J. Oncol.* **2008**, *33*, 909.
11. Roberts, B. W.; Mitchell, J.; Kilgannon, J. H.; Chansky, M. E.; Trzeciak, S. *Shock* **2013**, *39*, 229.
12. Granik, V. G.; Grigoriev, N. B. *Nitric oxide (NO). New Route to Drug Design* [in Russian]; Vuzovskaya Kniga: Moscow, 2004, p. 180.
13. *Nitric Oxide Donors: For Pharmaceutical and Biological Applications*; Wang, P. G.; Cai, T. B.; Taniguchi, N., Eds.; Wiley-VCH: Weinheim, 2005, p. 13.
14. Ferioli, R.; Folco, G. C.; Ferretti, C.; Gasco, A. M.; Medana, C.; Fruttero, R.; Civelli, M.; Gasco, A. *Brit. J. Pharm.* **1995**, *114*, 816.
15. Kots, A. Ya.; Grafov, M. A.; Khropov, Yu. V.; Betin, V. L.; Belushkina, N. N.; Busygina, O. G.; Yazykova, M. Yu.; Ovchinnikov, I. V.; Kulikov, A. S.; Makhova, N. N.; Medvedeva, N. A.; Bulargina, T. V.; Severina, I. S. *Brit. J. Pharm.* **2000**, *129*, 1163.
16. Bussygina, O. G.; Pyatakova, N. V.; Khropov, Yu. V.; Ovchinnikov, I. V.; Makhova, N. N.; Severina, I. S. *Biochemistry (Moscow)* **2000**, *65*, 457. [*Biokhimiya* **2000**, *65*, 540.]
17. Lazzarato, L.; Cena, C.; Rolando, B.; Marini, E.; Lolli, M. L.; Guglielmo, S.; Guaita, E.; Morini, G.; Coruzzi, G.; Fruttero, R.; Gasco, A. *Bioorg. Med. Chem.* **2011**, *19*, 5852.
18. Borretto, E.; Lazzarato, L.; Spallotta, F.; Cencioni, C.; D'Alessandra, Yu.; Gaetano, C.; Fruttero, R.; Gasco, A. *ACS Med. Chem. Lett.* **2013**, *4*, 994.
19. Guglielmo, S.; Cortese, D.; Vottero, F.; Rolando, B.; Kommer, V. P.; Williams, D. L.; Fruttero, R.; Gasco, A. *Eur. J. Med. Chem.* **2014**, *84*, 135.
20. Fershtat, L. L.; Struchkova, M. I.; Goloveshkin, A. S.; Bushmarinov, I. S.; Makhova, N. N. *Heteroat. Chem.* **2014**, *25*, 226.
21. Ovchinnikov, I. V.; Makhova, N. N.; Khmel'nitskii, L. I. *Russ. Chem. Bull., Int. Ed.* **1995**, *44*, 702. [*Izv. Akad. Nauk, Ser. Khim.* **1995**, 722.]
22. Kulikov, A. S.; Ovchinnikov, I. V.; Molotov, S. I.; Makhova, N. N. *Russ. Chem. Bull., Int. Ed.* **2003**, *52*, 1822. [*Izv. Akad. Nauk, Ser. Khim.* **2003**, 1727.]
23. Sharma, R.; Pandey, A. K.; Shivahare, R.; Srivastava, K.; Gupta, S.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 298.
24. Mohebbi, S.; Falcón-Pérez, J. M.; González, E.; Millet, O.;

Mato, J. M.; Kobarfard, F. *Chem. Pharm. Bull.* **2012**, *60*, 70.
25. Goswami S.; Jana S.; Dey S.; Adak A. K. *Aust. J. Chem.*, **2007**, *60*, 120.
26. Tomchin, A. B.; Uryupov, O. Yu.; Zhukova, T. I.; Kuznetsova, T. A.; Kostycheva, M. V.; Smirnov, A. V. *Pharm. Chem. J.* **1997**, *31*, 125. [*Khim.-Pharm. Zh.* **1997**, *31*(3), 19.]
27. Zhao, Y.; Chen, Z.; Chen, Y.; Xu, J.; Li, J.; Jiang, X. *J. Am. Chem. Soc.* **2013**, *135*, 12940.
28. Jacobsen, J. A.; Fullagar, J. L.; Miller, M. T.; Cohen S. M. *J.Med.Chem.* **2011**, *54*, 591.
29. Almajan, G. L.; Innocenti, A.; Puccetti, L.; Manole, G.; Barbuceanu, S.; Saramet, I.; Scozzafava, A.; Supuran, C. T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2347.
30. Khmel'nitskii, L. I.; Novikov, S. S.; Godovikova, T. I. *Chemistry of Furoxans. Structure and Synthesis* [in Russian]; Nauka: Moscow, 1996, p. 26.
31. Finogenov, A. O.; Ovchinnikov, I. V.; Kulikov, A. S.; Makhova, N. N. *Russ. Chem. Bull*., *Int. Ed.* **2012**, *61*, 472. [*Izv. Akad. Nauk*, *Ser. Khim.* **2012**, 469.]
32. Khmel'nitskii, L. I.; Novikov, S. S.; Godovikova, T. I. *Chemistry of Furoxans. Structure and Synthesis* [in Russian]; Nauka: Moscow, 1996, p. 67
33. Zhao, P.; Li, Y.; Gao, G.; Wang, S.; Yan, Y.; Zhan, X.; Liu, Z.; Mao, Z.; Chen, S.; Wang, L. *Eur. J. Med. Chem.* **2014**, *86*, 165.