DOI 10.1007/s10593-019-02607-1

Chemistry of Heterocyclic Compounds **2019**, *55*(12), 1233–1244

3-Amino-4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]furazan – a multifunctional synthon for the synthesis of 1,2,5-oxadiazole derivatives

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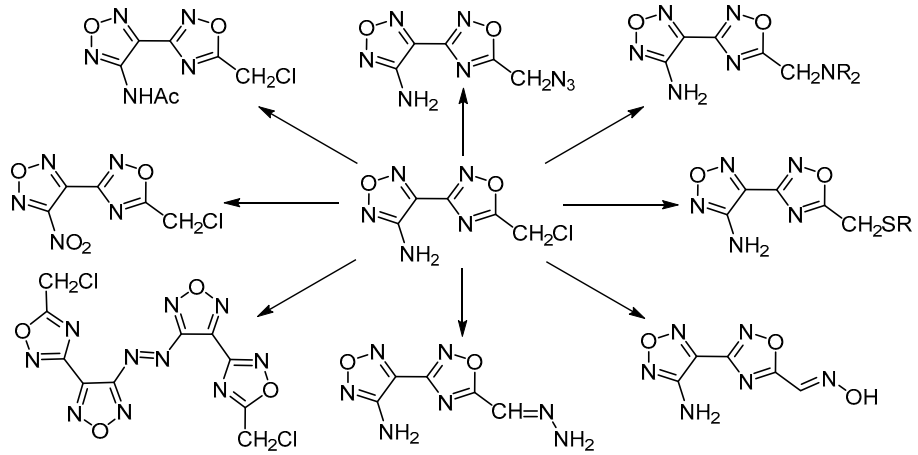
Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2019, *55*(12), 1233–1244

Submitted January 19, 2019
Accepted after revision October 21, 2019



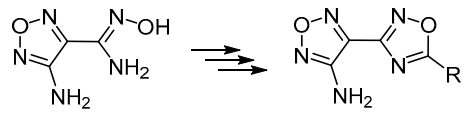
The chemical properties of 3-amino-4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]furazan were scrutinized: acylation of the amino group and its oxidation to azo and nitro groups, reactions of the chloromethyl group with N- and S-nucleophilic reagents, as well as reactions of transformation of the 1,2,4-oxadiazole ring.

Keywords: chloromethyl, furazan, 1,2,4-oxadiazole, 1,2,5-oxadiazole, oxidation.

Oxadiazole derivatives are widely utilized in various fields of chemistry: organic synthesis,[1] medicinal chemistry,[2–8] in design of new materials.[5,9] 4-Aminofurazan-3-carboxylic acid amidoxime (**1**) is widely used in the synthesis of polyfunctional derivatives of furazan (1,2,5-oxadiazole), which was the subject of a special review.[10] A number of studies were devoted to cyclization of the amidoxime moiety of compound **1** into 1,2,4-oxadiazole ring (Scheme 1).[11–17] Some derivatives of substituted 3-amino-4-(1,2,4-oxadiazol-3-yl)furazan **2** exhibit antimycobacterial activity against *Mycobacterium tuberculosis*[18] and are PI3K phosphoinositide 3-kinase inhibitors.[19] Based on the 4-(1,2,4-oxadiazol-3-yl)furazan skeleton, a number of energetic compounds were also synthesized.[7,16,17, 20–24]

In continuation of our studies of derivatives of compound **2**,[14,25] this work describes the reactivity of

Scheme 1

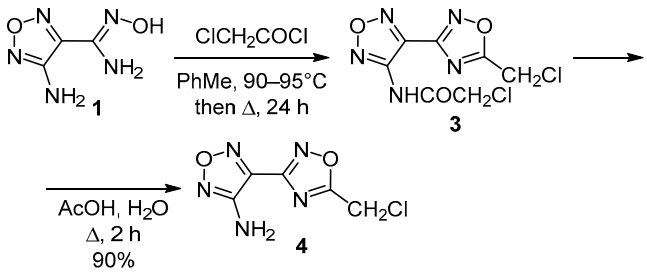


1 **2a** R = H **b** R = Me

4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (**4**)[26] which we previously obtained from 4-aminofurazan-3-carboxylic acid amidoxime (**1**) *via* chloroacetamide intermediate **3** (Scheme 2). There are three potential reaction centers in furazan **4**: amino group, chloromethyl group, and 1,2,4-oxadiazole ring. The latter can enter into both the ring opening reactions and reactions of transformation into other heterocyclic systems[8,29,30] due to the reduced aromaticity,[11,13,27] as well as the small "π"

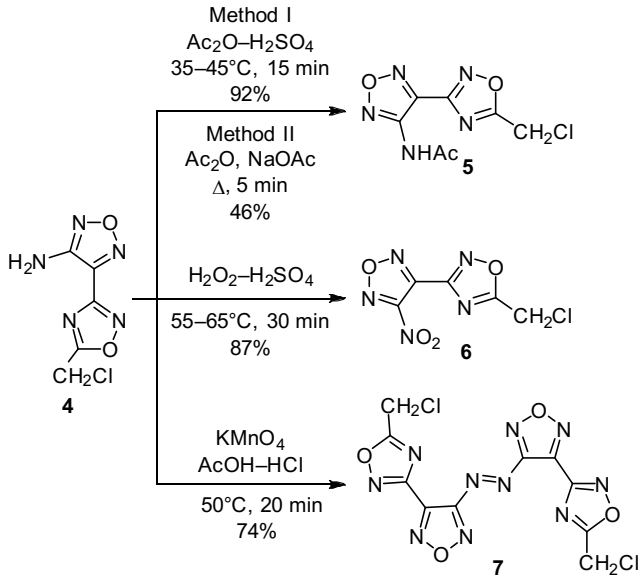
character of the N–O bond of the 1,2,4-oxadiazole ring.[28] Based on this, we studied some reactions involving the indicated reaction centers of compound **4**.

Scheme 2



Compound **4** enters into a number of amino group-specific reactions for aminofurazan derivatives. The acylation reaction of compound **4** in the presence of Ac_2O and a catalytic amount of concentrated H_2SO_4 proceeds under mild conditions with the formation of the corresponding *N*-acetyl derivative **5**. Using NaOAc as a catalyst requires harsher reaction conditions (heating under reflux) and leads to a lower yield of product **5**. Oxidation of the amino group of aminofurazans with H_2O_2-based mixtures is the main method for the synthesis of 3-nitrofurazans.[31,32] We used one of the most accessible and effective mixtures, H_2O_2–H_2SO_4 (at temperatures above 45°C), to obtain 4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]-3-nitrofurazan (**6**).[14,25,33] It is known that the oxidation of aminofurazans with $KMnO_4$ in the presence of HCl is used in the synthesis of azofurazans.[1] Similar to the oxidative dimerization of other 3-amino-4-(1,2,4-oxadiazol-3-yl)furazans to the corresponding azo derivatives,[14,25] oxidation of compound **4** with $KMnO_4$ in an AcOH–HCl mixture at 50°C leads to the formation of azo derivative **7** in 74% yield (Scheme 3).

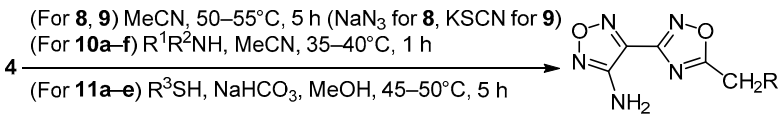
Scheme 3

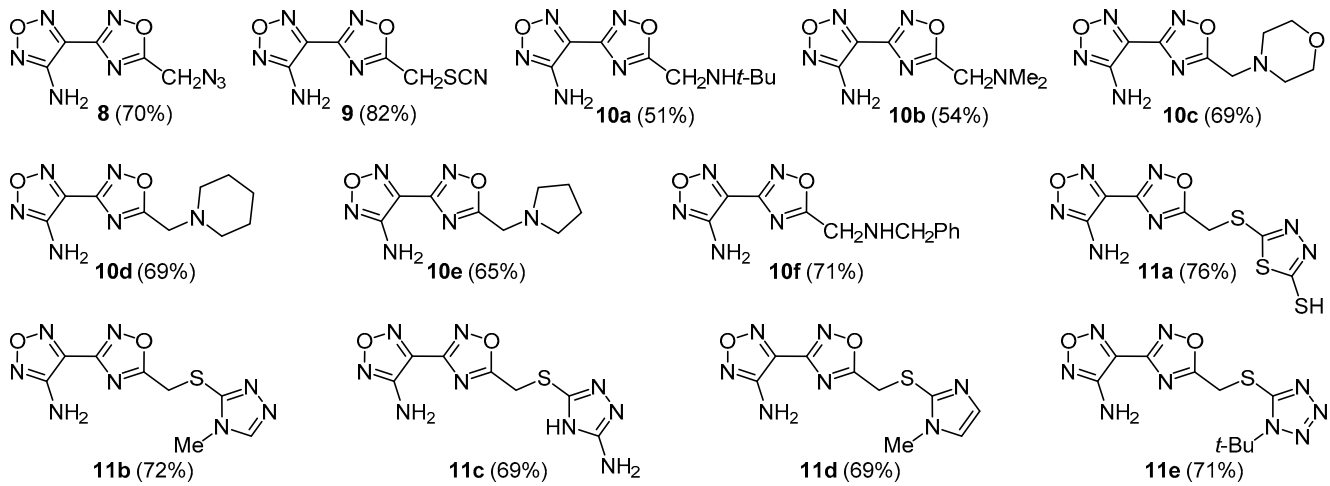


It is well known that the chlorine atom in 1,2,4-oxadiazole chloromethyl derivatives can be substituted by N-, O-, and S-nucleophiles.[34] Indeed, the reaction of compound **4** with reagents such as NaN_3 and KSCN leads to the formation of the corresponding azides **8** and thiocyanates **9**. Substitution of chlorine also occurs when reacting with a number of primary and secondary amines and heterocyclic thiols (Scheme 4).

It should be noted that, while the ^{13}C NMR spectra of compounds **8**, **9**, **10a**–**f**, **11a**–**e**, in particular, the signals of the C–3 and C–4 atoms of the furazan ring at 155.7–155.9 and 137.3–140.1 ppm, respectively, and the signals of C-3' and C-5' atoms of the 1,2,4-oxadiazole ring at 155.9–159.8 and 177.1–181.7 ppm, respectively, are consistent with the spectra of compounds **2**–**7** and with literature data,[35–37] for

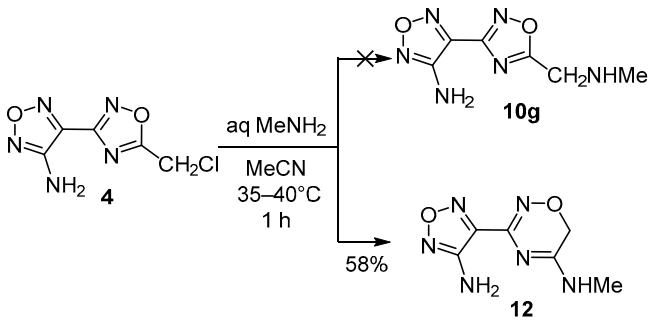
Scheme 4





the product isolated as a result of the reaction of furazan **4** with $MeNH_2$, the signal of the carbon atom C-5' of the starting 1,2,4-oxadiazole ring is significantly shifted upfield (177.0 → 155.6 ppm), and the signal of methylene group experiences downfield shift (33.9 → 61.5 ppm). Thus, the reaction with $MeNH_2$ affects not only the chloromethyl group, but also leads to the transformation of the 1,2,4-oxadiazole ring. In this case, the formation of 3-(4-amino-1,2,5-oxadiazol-3-yl)-*N*-methyl-6*H*-1,2,4-oxadiazin-5-amine (**12**) is observed (Scheme 5). A similar transformation was previously observed when studying the properties of 5-chloromethyl-3-(5-nitrofuran-2-yl)-1,2,4-oxadiazole.[38]

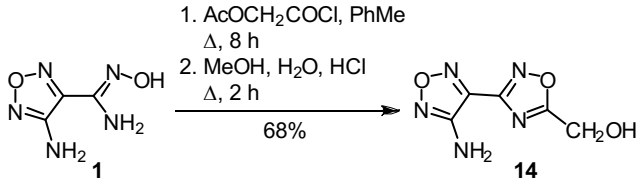
Scheme 5



Hydrolysis of 3-amino-4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]furazan (**4**) under mild conditions (K_2CO_3, EtOH, 30°C) produces 1,2,4-oxadiazine **13**, the product of the transformation of the 1,2,4-oxadiazole ring, instead of the expected hydroxymethyl compound **14** (Scheme 6). The structure of the obtained compound was established on the basis of ^{13}C NMR spectroscopy data. In the ^{13}C NMR spectrum of compound **13**, the signal of the C-5' carbon atom of the starting 1,2,4-oxadiazole ring is significantly shifted upfield (177.0 → 144.4 ppm), and the signal of the methylene group of the side chain experiences downfield shift (33.9 → 67.7 ppm), which corresponds to the previously described NMR spectra of 1,2,4-oxadiazin-6(5*H*)-ones.[39]

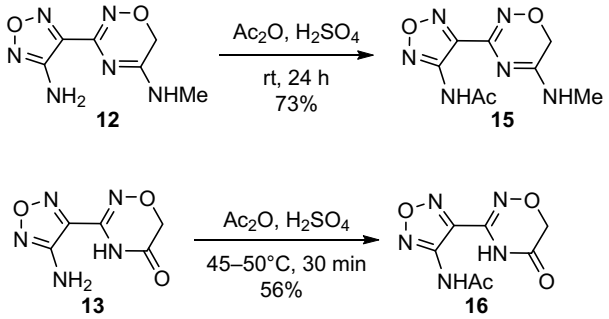
To prove the direction of the hydrolysis reaction of compound **4** toward the formation of oxadiazine **13**, we synthesized hydroxymethyl derivative **14** *via* the reaction of amidoxime **1** with an excess of acetoxyacetyl chloride and subsequent hydrolysis (Scheme 7). The main difference between the ^{13}C NMR spectra of the obtained compound **14** and 1,2,4-oxadiazine **13** is the location of the signal of the C-5' carbon atom, 180.9 and 144.4 ppm, respectively.

Scheme 7



The acylation of compounds **12** and **13** by Ac_2O in the presence of H_2SO_4 proceeds at the amino group of the furazan ring, which leads to the formation of the corresponding 3-acetylaminofurazans **15** and **16** (Scheme 8).

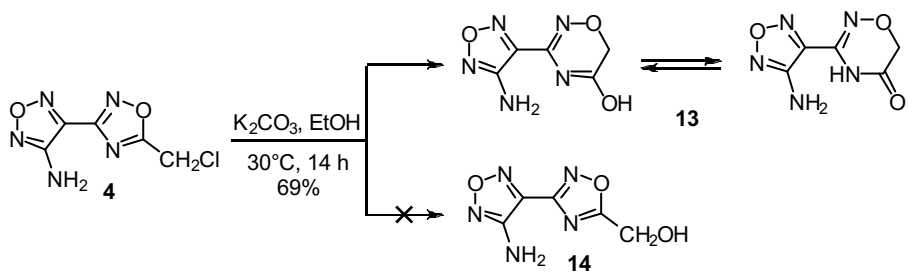
Scheme 8



Under more severe conditions (K_2CO_3, MeOH–H_2O upon heating; KOH–MeOH, KOH–H_2O at room temperature) hydrolysis of chloromethyl derivative **4** leads to the opening of the 1,2,4-oxadiazole ring. The final hydrolysis product was identified by us as ({[amino(4-amino-1,2,5-oxadiazol-3-yl)methylidene]amino}oxy)acetic acid (**17**). A probable reaction mechanism is shown in Scheme 9. The acylation of compound **17** by Ac_2O to give diacetylamine **18** confirms the presence of two amino groups in the starting substrate. The IR and ^1H and ^{13}C NMR spectra of compound **17** are identical to the spectra of the compound obtained by alkylation of amidoxime **1** in the presence of ethyl chloroacetate followed by hydrolysis (Scheme 10).

We previously showed that the reaction of compound **4** with hydrazine leads to a very uncharacteristic oxidation of the chloromethyl group to the azomethine group resulting in the formation of hydrazone **19** (Scheme 11).[26] Several cases are described in the literature when such reactions were observed only for 6-chloromethylpurine,[40] derivatives of phenacyl bromide,[41] and 4-chloro-2-chloromethyl-6-pyrimidones;[42] a possible mechanism of this reaction was proposed.[35–37] We have now shown that treatment of compound **4** with phenylhydrazine also produces

Scheme 6



Scheme 9

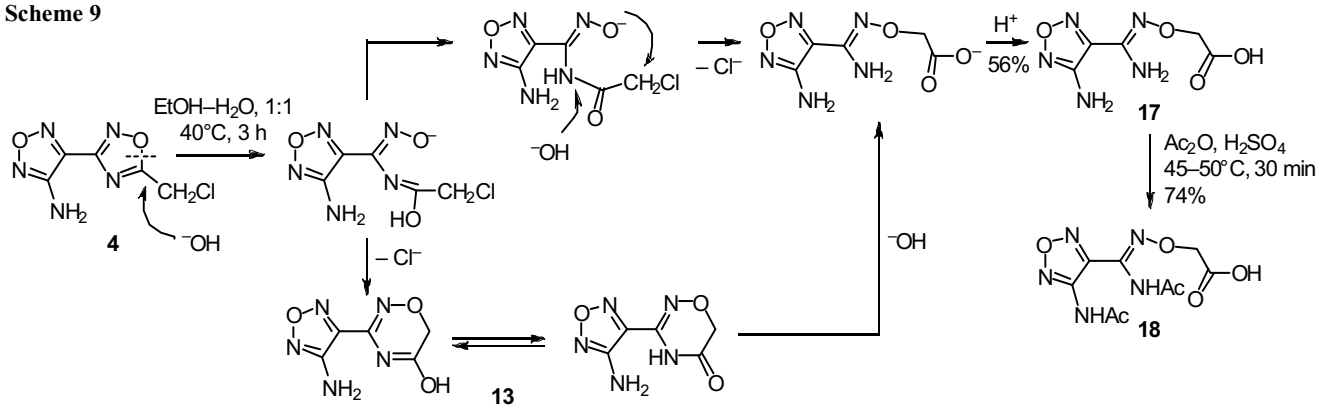
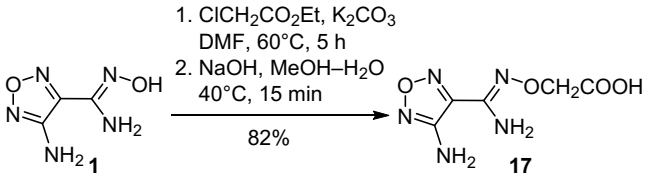
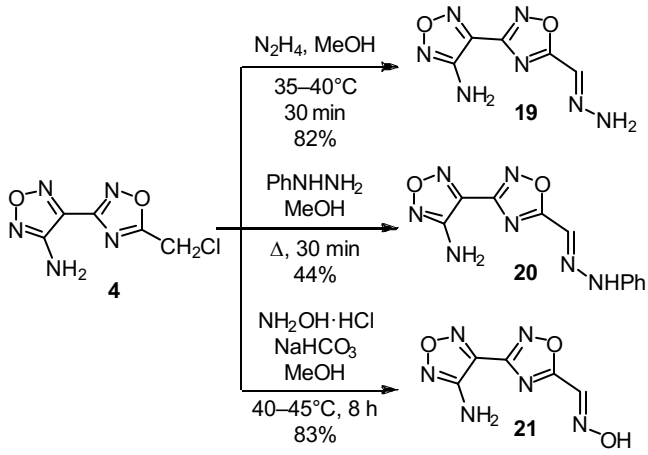


Схема 10



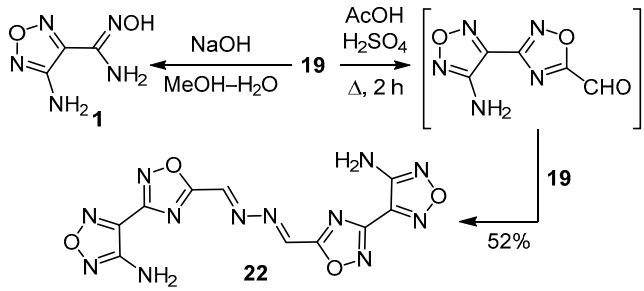
Scheme 11



hydrazone **20**, and the reaction of compound **4** with hydroxylamine leads to a similar result, the formation of oxime **21** (Scheme 11).

^{1}H and ^{13}C NMR spectra of compounds **19**–**21** confirm their structures. Chemical shifts of the signals of carbon atoms in the ^{13}C NMR spectra of the obtained compounds indicate the retention of the linked furazan (C-3, 155.9 ppm; C-4, 137.4–137.6 ppm) and 1,2,4-oxadiazole rings (C-3', 159.3–159.7 ppm; C-5', 172.1–174.7 ppm). ^{1}H NMR spectra demonstrate the absence of a methylene group and the presence of an azomethine fragment (7.67, 7.91, 8.47 ppm). Despite the presence of an amino group, compounds **19** and **21** proved to be inert in the reaction with carbonyl compounds (Me_2CO or PhCHO in EtOH–AcOH). Under more severe conditions in the presence of H_2SO_4, attempts to condense compound **19** with carbonyl compounds (as well as in their absence) led to the formation of bishydrazone (azine) **22**, which was insoluble in the reaction medium. As a result of treating compound **19** (as

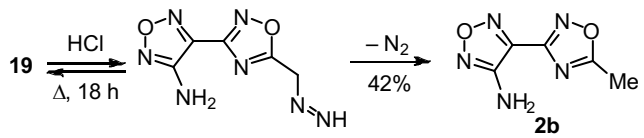
Scheme 12



well as compound **21**) with aqueous NaOH, the opening of the 1,2,4-oxadiazole ring and the formation of amidoxime **1** took place (Scheme 12).

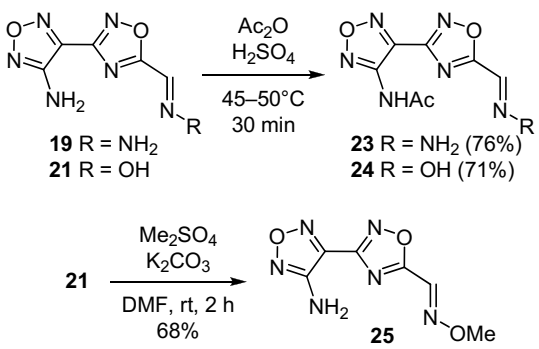
Prolonged heating of hydrazone **19** with HCl leads to a very unusual version of the Wolff–Kishner[43] reduction of the carbonyl group with the formation of 4-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (**2b**) (Scheme 13).

Scheme 13



Acylation of compounds **19** and **21** under mild conditions (Ac_2O, H^+, 20–25°C) occurs at the amino group of the furazan ring and leads to the formation of acylamines **23** and **24** (Scheme 14). Heating the reaction mixture to its boiling point leads to resinification and the formation of a complex mixture of unidentified products. The oxime

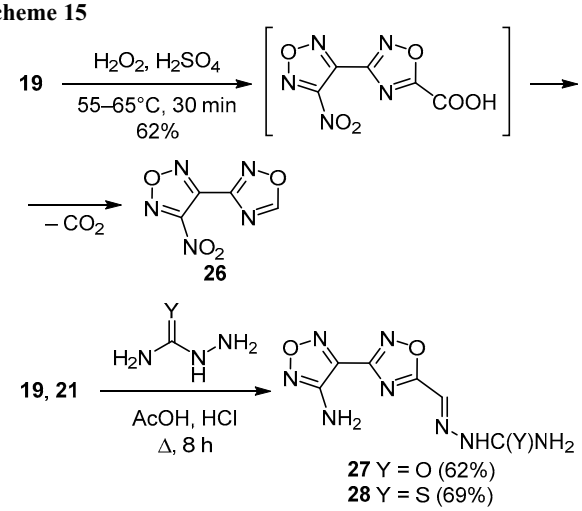
Scheme 14



group of compound **21** is alkylated at the oxygen atom with dimethyl sulfate to form methoxyimine **25**.

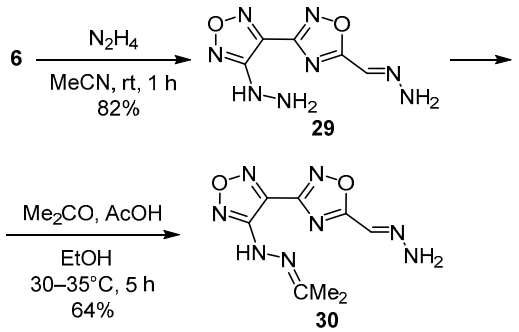
The oxidation of the furazan amino group of compound **19** to the nitro group with H_2O_2–H_2SO_4 is accompanied by oxidative hydrolysis of the hydrazonomethyl fragment followed by decarboxylation to form 3-nitro-4-(1,2,4-oxadiazol-3-yl)furazan (**26**) (Scheme 15). The presence of the azomethine fragment in compounds **19** and **21** is also confirmed by their transamination reactions with semicarbazide and thiosemicarbazide leading to the formation of the corresponding products **27**, **28**.

Scheme 15



The reaction of 4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]-3-nitrofurazan (**6**) with hydrazine is accompanied not only by the substitution of the nitro group for hydrazine group, but also similar to the above-described conversion of the chloromethyl group to form hydrazone **29**. In this case, the condensation of the obtained compound with Me_2CO affects only the more nucleophilic furazan hydrazine group to form product **30** (Scheme 16).

Scheme 16



Our studies of the chemical properties of 3-amino-4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]furazan show that the compound under consideration is a promising multifunctional synthon for the preparation of previously inaccessible furazan derivatives. It was shown that the reactivity of the amino group of the furazan ring is predictable, while the behavior of the chloromethyl substituent is less clear and may be accompanied by transformation of the 1,2,4-oxadiazole ring.

Experimental

IR spectra were registered on an FSM-1201 FT spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker DRX-400 spectrometer (400 and 100 MHz, respectively) in DMSO-d_6, using residual solvent signals (2.51 ppm for ^{1}H nuclei, 39.96 ppm for ^{13}C nuclei) to assign chemical shifts. The assignment of signals in the ^{13}C NMR spectra was based on the spectra of similar compounds. Mass spectra were recorded on a Finnigan MAT Incos 50 spectrometer (EI ionization, 70 eV). High-resolution mass spectra were recorded on a Bruker micrOTOF II mass spectrometer (electrospray ionization). Elemental analysis was performed on a PerkinElmer Series II 2400 Elemental analyzer. Melting points were determined in an open capillary. Monitoring of the reaction progress and assessment of the purity of synthesized compounds were done by HPLC on a Shimadzu Series 20 chromatograph with a diode array detector (column Luna C18(2) 250 × 4.6 mm, particle size 5 μm), mobile phase MeOH–H_2O, 3:1, thermostat and detector temperature 40°C, detection at 209, 230, and 254 nm.

Compounds **2a**,[10] **2b**,[14] **3**,[26] **4**[26] were synthesized according to literature methods.

4-(1,2,4-Oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (2a).[10] IR spectrum, ν, cm^{-1}: 3438, 2971, 2918, 2743, 2682, 1636, 1603, 1483, 1470, 1429, 1417, 1320, 1223, 1170, 1092, 1078, 1056, 1011, 997, 860, 704, 626, 611. ^{1}H NMR spectrum, δ, ppm: 6.50 (2H, s, NH_2); 10.00 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 137.4 (C-4); 156.0 (C-3); 158.6 (C-3'); 168.7 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 154 $[M+1]^+$ (3), 153 $[M]^+$ (100), 123 $[M–NO]^+$ (23), 96 (94), 69 (19), 58 $[NHCNOH]^+$ (90), 53 (28), 42 (15), 30 $[NO]^+$ (55), 29 $[CHO]^+$ (41).

4-(5-Methyl-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (2b).[14] IR spectrum, ν, cm^{-1}: 3469, 3362, 2922, 2852, 2362, 1804, 1630, 1584, 1547, 1480, 1463, 1429, 1385, 1260, 1150, 1087, 1044, 1016, 978, 956, 925, 911, 862, 768, 737, 713, 693, 654, 577, 515, 458, 403. ^{1}H NMR spectrum, δ, ppm: 2.74 (3H, s, CH_3); 6.44 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 12.4 (CH_3); 137.4 (C-4); 155.8 (C-3); 155.9 (C-3'); 179.0 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 167 $[M]^+$ (19), 110 (14), 43 (100), 42 $[CNO]^+$ (14), 32 (19), 30 [NO] $(21)^+$.

3-Chloro-*N*-{4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-yl}acetamide (3).[26] IR spectrum, ν, cm^{-1}: 3340, 3005, 2950, 1704 (C=O), 1619, 1587, 1555, 1538, 1429, 1404, 1328, 1310, 1302, 1275, 1229, 1153, 1014, 970, 930, 906, 869, 820, 784, 770, 636, 619, 599, 566, 490. ^{1}H NMR spectrum, δ, ppm: 11.4 (1H, s, NH); 5.27 (2H, s, CH_2); 4.46 (2H, s, CH_2). ^{13}C NMR spectrum, δ, ppm: 33.9 (CH_2); 42.9 (CH_2); 141.5 (C-4); 150.0 (C-3); 159.1 (C-3'); 177.1 (C-5'); 166.3 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 279 $[M(^{37}Cl)]^+$ (2), 277 $[M(^{35}Cl)]^+$ (4), 230 (14), 228 $[M–CH_2Cl]^+$ (43), 201 $[M–COCH_2Cl]^+$ (15), 144 (13), 79 $[COCH_2{}^{37}Cl)]^+$ (25), 77 $[COCH_2{}^{35}Cl)]^+$ (83), 51 $[CH_2{}^{37}Cl)]^+$ (35), 49 $[CH_2{}^{35}Cl)]^+$ (100), 42 $[CH_2CO]^+$ (43), 30 $[NO]^+$ (64).

4-[5-(Chloromethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (4).[26] IR spectrum, ν, cm^{-1}: 3469, 3013, 2963, 2921, 1629, 1605, 1587, 1551, 1465, 1428, 1388,

1294, 1273, 1145, 1014, 977, 943, 905, 763, 703, 641, 575, 567, 441, 413, 402. ^{1}H NMR spectrum, δ, ppm: 5.26 (2H, s, CH_2); 6.40 (2H, br. s, CH_2). ^{13}C NMR spectrum, δ, ppm: 33.9 (CH_2); 137.3 (C-4); 155.9 (C-3); 159.8 (C-3'); 177.0 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 203 $[M(^{37}Cl)]^+$ (11), 201 $[M(^{35}Cl)]^+$ (35), 146 (30), 144 $[M–NHCNO]^+$ (100), 77 (34), 69 (37), 58 $[NHCNOH]^+$ (95), 54 (18), 53 (40), 51 (22), 49 (57), 42 (32), 30 $[NO]^+$ (79).

***N*-{4-[5-(Chloromethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-yl}acetamide (5)**. Method I. Concentrated H_2SO_4 (1 drop, ~0.03 ml) was added to a solution of compound **4** (1.00 g, 5.00 mmol) in Ac_2O (5 ml, 0.46 mol). An exothermic reaction was observed with the formation of a precipitate. The reaction mixture was stirred at 35–45°C for 15 min, then MeOH (20 ml) was added, and the solvent was evaporated under reduced pressure. The residue was recrystallized from MeOH. Yield 1.10 g (92%), white crystals, mp 99−100°C.

Method II. Anhydrous NaOAc (0.10 g, 1.20 mmol) was added to a solution of compound **4** (1.00 g, 5.00 mmol) in Ac_2O (5 ml, 0.46 mol). The reaction mixture was brought to a boil and heated under reflux for 5 min (longer heating led to resinification of the reaction mixture). Then it was cooled to room temperature, H_2O (20 ml) was added, and left overnight. The formed precipitate was filtered off and recrystallized from MeOH. Yield 0.55 g (46%), light-brown crystals, mp 98−99.5°C. IR spectrum, ν, cm^{-1}: 3318, 3032, 2974, 2857, 1742 (C=O), 1713, 1614, 1589, 1551, 1518, 1372, 1324, 1244, 1220, 1157, 1147, 1043, 1018, 971, 905, 760, 752, 606, 598, 575, 509. ^{1}H NMR spectrum, δ, ppm: 2.12 (3H, s, CH_3); 5.27 (2H, s, CH_2); 11.20 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 23.2 (CH_3); 33.9 (CH_2); 141.8 (C-4); 150.5 (C-3); 159.3 (C-3'); 169.8 (C=O); 176.9 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 245 $[M(^{37}Cl)]^+$ (4), 243 $[M(^{35}Cl)]^+$ (10), 215 (18), 203 (33), 201 $[M–CH_2CO]^+$ (100), 144 (19), 43 $[CH_3CO]^+$ (46). Found, %: C 34.23; H 2.75; N 28.47. $C_7H_6ClN_5O_3$. Calculated, %: C 34.51; H 2.48; N 28.75.

5-(Chloromethyl)-3-(4-nitro-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazole (6). Compound **4** (20 g, 0.10 mol) was added in 4–5-g portions to an oxidizing mixture prepared from 36% aqueous H_2O_2 (30 ml, ~0.30 mol) and 94−96% H_2SO_4 (40 ml, ~0.75 mol), keeping the temperature of the reaction mixture at 55−65°C. At the end of the exothermic reaction, the mixture was stirred at the same temperature for 30 min. After cooling to room temperature, H_2O (500 ml) was added, and the mixture was extracted with CH_2Cl_2 (2×50 ml). The organic layer was washed with H_2O (4×100 ml), dried over $MgSO_4$, and evaporated under reduced pressure. Yield 20.1 g (87%), light-yellow oil, n_D 1.524. IR spectrum, ν, cm^{-1}: 3036, 2974, 1603, 1568, 1441, 1369, 1312, 1295, 1117, 1038, 1016, 970, 934, 891, 825, 756. ^{1}H NMR spectrum, δ, ppm: 4.89 (2H, s, CH_2). ^{13}C NMR spectrum, δ, ppm: 32.9 (CH_2); 139.1 (C-4); 158.5 (C-3); 156.9 (C-3'); 176.9 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 234 $[M(^{37}Cl)+1]^+$ (1), 233 $[M(^{37}Cl)]^+$ (17), 232 $[M(^{35}Cl)+1]^+$ (5), 231 $[M(^{35}Cl)]^+$ (48), 51 (10), 49 (28), 46 $[NO_2]^+$ (100), 30 $[NO]^+$ (88). Found, *m/z*: 231.9861 $[M+H]^+$. $C_5H_3ClN_5O_4$. Calculated, *m/z*: 231.9868.

3,3'-[Diazene-1,2-diyldi-(1,2,5-oxadiazole-4,3-diyl)]bis-[5-(chloromethyl)-1,2,4-oxadiazole] (7). Compound **4** (2.00 g, 10 mmol) was added to a mixture of AcOH (25 ml) and 35% HCl (25 ml), and the whole was heated to 30–35°C. $KMnO_4$ (1.38 g, 10 mmol) was added to the resulting suspension with stirring. The reaction mixture was heated to 50°C and stirred for 20 min, then cooled to room temperature, the $KMnO_4$ residue was neutralized by the addition of a small amount of a 30% aqueous H_2O_2. The reaction mixture was diluted with H_2O (50 ml), the precipitate formed was filtered off and recrystallized from AcOH. Yield 1.78 g (74%), orange-yellow crystals, mp 116–117°C. IR spectrum, ν, cm^{-1}: 3042, 3018, 2970, 1584, 1451, 1432, 1423, 1349, 1277, 1245, 1143, 1032, 1014, 969, 922, 903, 871, 788, 773, 767, 760, 710, 698, 648, 596, 486. ^{1}H NMR spectrum, δ, ppm: 5.26 (4H, s, $2CH_2$). ^{13}C NMR spectrum, δ, ppm: 33.9 (CH_2); 141.5 (C-4); 162.2 (C-3); 158.6 (C-3'); 177.5 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 402 $[M(^{37}Cl)]^+$ (2), 401 (2), 400 $[M(^{35}Cl,^{37}Cl)]^+$ (13), 399 (3), 398 $[M(^{35}Cl)]^+$ (21), 351 (34), 349 (100), 213 (35), 49 (22), 30 $[NO]^+$ (85). Found, *m/z*: 398.9859 $[M+H]^+$. $C_{10}H_5Cl_2N_{10}O_4$. Calculated, *m/z*: 398.9867.

4-[5-(Azidomethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (8). NaN_3 (0.90 g, 14 mmol) was added to a solution of compound **4** (2.00 g, 10 mmol) in MeCN (25 ml), and the mixture was stirred at 50–55°C for 5 h. Then the reaction mixture was poured into H_2O (50 ml), the precipitate formed was filtered off and recrystallized from MeOH. Yield 1.45 g (70%), white crystals, mp 118–119°C. IR spectrum, ν, cm^{-1}: 3468, 2921, 2853, 2216 (N_3), 2121 (N_3), 1627, 1603, 1558, 1469, 1389, 1340, 1306, 1282, 1191, 1149, 1014, 973, 909, 796, 569, 448, 413. ^{1}H NMR spectrum, δ, ppm: 5.08 (2H, s, CH_2); 6.49 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 47.8 (CH_2); 137.7 (C-4); 155.9 (C-3); 156.0 (C-3'); 177.1 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 210 $[M+2]^+$ (1), 209 $[M+1]^+$ (9), 208 $[M]^+$ (100), 151 (50), 96 (20), 69 (37), 58 (46), 54 (20), 53 (44), 42 (28), 30 $[NO]^+$ (81), 28 $[N_2]^+$ (97). Found, *m/z*: 209.0522 $[M+H]^+$. $C_5H_5N_8O_2$. Calculated, *m/z*: 209.0530.

[3-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazol-5-yl]-methyl thiocyanate (9). Finely ground KSCN (1.26 g, 13.00 mmol) was added to a solution of compound **4** (2.00 g, 10.00 mmol) in MeCN (25 ml). The mixture was stirred at 50–55°C for 5 h, then poured into H_2O (50 ml); the precipitate formed was filtered off and recrystallized from MeOH. Yield 1.84 g (82%), light-beige amorphous powder, mp 97–98°C. IR spectrum, ν, cm^{-1}: 3464, 3329, 3014, 2922, 2853, 2157 (CN), 1631, 1603, 1585, 1560, 1462, 1292, 1241, 1140, 1007, 965, 935, 875, 576. ^{1}H NMR spectrum, δ, ppm: 4.93 (2H, s, CH_2); 6.51 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 27.4 (CH_2); 112.4 (SCN); 137.3 (C-4); 155.9 (C-3); 159.8 (C-3'); 177.2 (C-5'). Mass spectrum, *m/z* (I_{rel}, %): 224 $[M]^+$ (13), 194 $[M–NO]^+$ (12), 165 $[M–HSCN]^+$ (70), 109 (31), 108 (23), 72 $[CH_2SCN]^+$ (45), 69 (15), 58 $[SCN]^+$ (100), 52 (33), 45 (21), 42 $[CNO]^+$ (25), 30 $[NO]^+$ (50). Found, *m/z*: 225.0180 $[M+H]^+$. $C_6H_5N_6O_2S$. Calculated, *m/z*: 225.0189.

Synthesis of compounds 10a–f and 12 in the reaction of 4-[5-(chloromethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadi-

azol-3-amine (4) with amines (General method). The corresponding amine (22 mmol) (Me_2NH was used as a 30% aqueous solution) was added to a solution of compound **4** (2.00 g, 10.00 mmol) in MeCN (25 ml), and the mixture was stirred at 35–40°C for 1 h. The solvent and excess amine were distilled off under reduced pressure. H_2O (50 ml) was added to the obtained residue, the insoluble precipitate was filtered off and recrystallized from MeOH.

4-{5-[(*tert*-Butylamino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (10a) was obtained in the reaction of compound **4** with *t*-$BuNH_2$. Yield 1.21 g (51%), small irregularly shaped plates, mp 113–114°C. IR spectrum, ν, cm^{-1}: 3388, 3309, 3122, 2966, 1640, 1585, 1558, 1467, 1459, 1392, 1372, 1231, 1146, 1118, 1015, 975, 926, 907, 840, 785, 765, 580, 423. ^{1}H NMR spectrum, δ, ppm: 1.07 (9H, s, $C(CH_3)_3$); 4.11 (2H, s, CH_2); 6.49 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 28.9 (CH_3); 39.1 ($C(CH_3)_3$); 51.0 (CH_2); 137.5 (C-4); 155.9 (C-3); 159.2 (C-3'); 181.7 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 238 $[M]^+$ (<1), 224 $[M–CH_2]^+$ (17), 223 $[M–CH_3]^+$ (100), 165 (16), 70 (74), 57 (16), 41 (16), 30 $[NO]^+$ (28). Found, *m*/*z*: 239.1259 $[M+H]^+$. $C_9H_{15}N_6O_2$. Calculated, *m*/*z*: 239.1251.

4-{5-[(Dimethylamino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (10b) was obtained in the reaction of compound **4** with Me_2NH. Yield 1.13 g (54%), light-beige amorphous powder, mp 98–99°C. IR spectrum, ν, cm^{-1}: 3470, 3451, 3310. 3156, 1630, 1587, 1557, 1467, 1360, 1146, 1013, 968, 854, 576, 402. ^{1}H NMR spectrum, δ, ppm: 6.48 (2H, s, NH_2); 4.07 (2H, s, CH_2); 2.36 (6H, s, $2CH_3$). ^{13}C NMR spectrum, δ, ppm: 44.8 (CH_3); 53.1 (CH_2); 137.5 (C-4); 155.9 (C-3); 159.2 (C-3'); 181.7 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 210 $[M]^+$ (3), 167 $[M–CH_2=NCH_3]^+$ (20), 151 (23), 137 (32), 110 (23), 58 $[HNCNOH]^+$ (100), 44 $[NMe_2]^+$ (50), 42 $[CNO]^+$ (38). Found, *m*/*z*: 211.0943 $[M+H]^+$. $C_7H_{11}N_6O_2$. Calculated, *m*/*z*: 211.0938.

4-[5-(Morpholin-4-ylmethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (10c) was obtained in the reaction of compound **4** with morpholine. Yield 1.74 g (69%), white crystals, mp 184–185°C. IR spectrum, ν, cm^{-1}: 3444, 3285, 3154, 2973, 2920, 2873, 2837, 1628, 1583, 1561, 1459, 1415, 1348, 1333, 1308, 1205, 1170, 1107, 1067, 1041, 1005, 973, 967, 921, 907, 863, 818, 712, 682, 617, 578, 524, 478, 446. ^{1}H NMR spectrum, δ, ppm: 2.53–2.61 (4H, m, $(CH_2)_2O$); 3.57–3.63 (4H, m, $(CH_2)_2N$); 4.06 (2H, s, CH_2); 6.48 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 52.6 ($(CH_2)_2N$); 52.9 (CH_2); 66.5 ($(CH_2)_2O$); 137.5 (C-4); 155.9 (C-3); 159.3 (C-3'); 178.2 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 252 $[M]^+$ (1), 222 $[M–NO]^+$ (1), 137 (64), 109 (21), 56 (32), 42 (40), 41 (19), 30 $[NO]^+$ (25). Found, *m*/*z*: 253.1036 $[M+H]^+$. $C_9H_{13}N_6O_3$. Calculated, *m*/*z*: 253.1044.

4-[5-(Piperidin-1-ylmethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (10d) was obtained in the reaction of compound **4** with piperidine. Yield 1.74 g (69%), white crystals, mp 121–122°C. IR spectrum, ν, cm^{-1}: 3469, 2922, 2853, 1726, 1638, 1543, 1506, 1315, 1144, 1112, 1038, 1001, 963, 899, 862, 764, 570, 433, 405. ^{1}H NMR spectrum, δ, ppm: 1.32–1.40 (2H, m, CH_2); 1.49–1.54 (4H, m, $2CH_2$); 2.45–2.55 (4H, m, $N(CH_2)_2$); 4.00 (2H, s, CH_2); 6.47 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 23.8 (CH_2); 25.9 (CH_2); 53.2 (NCH_2); 55.8 ($N(CH_2)_2$); 137.5 (C-4); 155.9 (C-3); 159.2 (C-3'); 178.6 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 249 $[M–1]^+$ (2), 137 (12), 98 $[(CH_2)_5NCH_2]^+$ (28), 97 (24), 96 (18), 84 $[(CH_2)_5N]^+$ (100), 42 (21), 41 (18). Found, *m*/*z*: 251.1259 $[M+H]^+$. $C_{10}H_{15}N_6O_2$. Calculated, *m*/*z*: 251.1251.

4-[5-(Pyrrolidin-1-ylmethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (10e) was obtained in the reaction of compound **4** with pyrrolidine. Yield 1.53 g (65%), beige crystals, mp 87–88°C. IR spectrum, ν, cm^{-1}: 3448, 2921, 2802, 1627, 1461, 1420, 1394, 1350, 1171, 1116, 1043, 1003, 968, 905, 879, 572. ^{1}H NMR spectrum, δ, ppm: 1.71 (4H, s, $(CH_2)_2$); 2.62 (4H, s, $N(CH_2)_2$); 4.11 (2H, s, CH_2); 6.46 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 23.8 ($(CH_2)_2$); 49.6 (NCH_2); 53.5 ($N(CH_2)_2$); 137.4 (C-4); 155.9 (C-3); 159.3 (C-3'); 179.0 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 235 $[M–1]^+$ (<1), 193 (1), 84 $[CH_2N(CH_2)_4]^+$ (42), 83 (40), 70 $[N(CH_2)_4]^+$ (100), 55 (22), 42 $[CH_2NCH_2]^+$ (46). Found, *m*/*z*: 237.1088 $[M+H]^+$. $C_9H_{13}N_6O_2$. Calculated, *m*/*z*: 237.1095.

4-{5-[(Benzylamino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (10f) was obtained in the reaction of compound **4** with $BnNH_2$. Yield 1.93 g (71%), beige crystals, mp 102–103°C. IR spectrum, ν, cm^{-1}: 3467, 3332, 3308, 2920, 2857, 163, 1551, 1455, 1153, 1115, 1023, 1005, 967, 901, 806, 737, 696, 580, 522. ^{1}H NMR spectrum, δ, ppm: 3.82 (2H, s, CH_2); 4.13 (2H, s, CH_2); 6.51 (2H, s, NH_2); 7.22–7.37 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 43.9; 55.5; 127.3 (C-4 Ph); 128.5 (C-3,5 Ph); 128.6 (C-2,6 Ph); 137.4 (C-1 Ph); 140.1 (C-4); 155.9 (C-3); 159.2 (C-3'); 180.7 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 271 $[M–1]^+$ (1), 137 (10), 118 $[PhCH=NCH_2]^+$ (39), 117 (16), 106 $[C_7H_7NH]^+$ (100), 91 $[C_7H_7]^+$ (78), 70 (21). Found, *m*/*z*: 273.1102 $[M+H]^+$. $C_{12}H_{13}N_6O_2$. Calculated, *m*/*z*: 273.1095

3-(4-Amino-1,2,5-oxadiazol-3-yl)-*N*-methyl-6*H*-1,2,4-oxadiazin-5-amine (12) was obtained in the reaction of compound **4** with $MeNH_2$. Yield 1.14 g (58%), white crystals, mp 195–196°C. IR spectrum, ν, cm^{-1}: 3432, 3327, 3163, 3108, 2920, 2884, 1619, 1517, 1406, 1189, 1086, 993, 947, 906, 860, 570. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.91 (3H, d, *J* = 4.8, CH_3); 4.26 (2H, s, CH_2); 6.29 (2H, s, NH_2); 8.51 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 27.3 (CH_3); 61.5 (C-6'); 142.6 (C-4); 153.7 (C-3); 159.3 (C-3'); 155.6 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 197 $[M+1]^+$ (5), 196 $[M]^+$ (63), 139 $[M–CH_2=CHNO]^+$ (90), 82 (11), 68 (14), 58 (13), 57 (40), 56 $[CH_2CNO]^+$ (100), 55 (33), 54 (20), 53 (29), 42 $[CNO]^+$ (57), 41 (33), 30 $[NO]^+$ (48). Found, *m*/*z*: 197.0774 $[M+H]^+$. $C_6H_9N_6O_2$. Calculated, *m*/*z*: 197.0782.

Synthesis of compounds 11a–e (General method). $NaHCO_3$ (1.68 g, 20 mmol) and the corresponding thiol (11 mmol) were added to a solution of compound **4** (2.00 g, 10 mmol) in MeOH (35 ml). The mixture was stirred at 45–50°C for 5 h, then poured into H_2O (50 ml); the precipitate formed was filtered off and recrystallized from AcOH.

5-({[3-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazol-5-yl]methyl}sulfanyl)-1,3,4-thiadiazole-2-thiol (11a) was obtained in the reaction of compound **4** with 1,3,4-thiadiazole-2,5-dithiol. Yield 2.39 g (76%), white crystals, mp 215–216°C. IR spectrum, ν, cm^{-1}: 3438, 3339, 2921, 2853, 1630, 1603, 1585, 1490, 1443, 1380, 1254, 1238, 1145, 1114 (C=S), 1047, 715, 479. ^{1}H NMR spectrum, δ, ppm: 4.95 (2H, s, CH_2); 6.47 (2H, br. s, NH_2); 14.70 (1H, br. s, SH). ^{13}C NMR spectrum, δ, ppm: 27.7 (CH_2); 137.3 (C-4); 155.9 (C-3); 159.7 (C-3'); 177.9 (C-5'); 189.2 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 315 $[M]^+$ (23), 258 (18), 150 (14), 109 (10), 77 (16), 76 (35), 73 (28), 64 (35), 60 (24), 59 (64), 58 (54), 53 (39), 46 (54), 45 $[CHS]^+$ (100), 44 (21), 43 $[CHNO]^+$ (37), 42 $[CNO]^+$ (45), 30 (67), 29 (71). Found, *m*/*z*: 315.9748 $[M+H]^+$. $C_7H_6N_7O_2S_3$. Calculated, *m*/*z*: 315.9740. According to the ^{13}C NMR spectrum, the compound is in the thione form.

4-(5-{[(4-Methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]methyl}-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (11b) was obtained in the reaction of compound **4** with 4-methyl-1,2,4-triazole-3-thiol. Yield 2.02 g (72%), white needles, mp 210–211°C. IR spectrum, ν, cm^{-1}: 3449, 3269, 3238, 3119, 2972, 2929, 1633, 1585, 1554, 1519, 1466, 1429, 1395, 1333, 1244, 1212, 1172, 1148, 1011, 969, 929, 911, 880, 692, 644, 413. 1H NMR spectrum, δ, ppm: 3.62 (3H, s, CH_3); 4.82 (2H, s, CH_2); 6.44 (2H, s, NH_2); 8.59 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 28.0 (CH_3); 31.5 (CH_2); 137.3 (C-4); 147.2; 147.6; 155.9 (C-3); 159.6 (C-3'); 178.3 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 281 $[M+1]^+$ (1), 280 $[M]^+$ (4), 223 (44), 129 (13), 115 (98), 84 (14), 58 (15), 56 (16), 55 (30), 42 $[CNO]^+$ (100), 30 $[NO]^+$ (26). Found, *m*/*z*: 281.0571 $[M+H]^+$. $C_8H_9N_8O_2S$. Calculated, *m*/*z*: 281.0564.

4-(5-{[(4-Amino-4*H*-1,2,4-triazol-3-yl)sulfanyl]methyl}-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (11c) was obtained in the reaction of compound **4** with 5-amino-1,2,4-triazole-3-thiol. Yield 1.94 g (69%), orange crystals, mp 187–188°C. IR spectrum, ν, cm^{-1}: 3471, 3400, 3380, 3316, 3178, 3128, 2954, 2919, 1649, 1633, 1608, 1583, 1558, 1498, 1472, 1382, 1347, 1275, 1236, 1159, 1119, 1077, 1057, 1017, 975, 910, 870, 766, 739, 711, 654, 569, 542, 517, 498, 472, 410. ^{1}H NMR spectrum, δ, ppm: 4.68 (2H, s, CH_2); 6.14 (2H, s, NH_2); 6.46 (2H, s, NH_2); 12.10 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 26.1 (CH_2); 137.4 (C-4); 154.4; 155.8 (C-3); 158.1; 159.6 (C-3'); 179.4 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 282 $[M+1]^+$ (1), 281 $[M]^+$ (7), 224 (35), 129 (16), 128 (14), 116 (60), 86 (21), 85 (34), 70 (16), 58 (23), 45 (26), 43 $[CHNO]^+$ (100), 42 $[CNO]^+$ (25), 30 $[NO]^+$ (35). Found, *m*/*z*: 282.0521 $[M+H]^+$. $C_7H_8N_9O_2S$. Calculated, *m*/*z*: 282.0516.

4-(5-{[(1-Methyl-1*H*-imidazol-2-yl)sulfanyl]methyl}-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (**11d**) was obtained in the reaction of compound **4** with 1-methyl-imidazole-2-thiol. Yield 1.92 g (69%), white amorphous powder, mp 218–219°C. IR spectrum, ν, cm^{-1}: 3463, 3353, 3178, 3135, 3112, 1854, 1627, 1595, 1462, 1407, 1283, 1175, 1132, 1028, 977, 862, 764, 746, 692, 490, 434. ^{1}H NMR spectrum, δ, ppm: 3.52 (3H, s, CH_3); 4.38 (2H, s, CH_2); 6.39 (2H, s, NH_2); 6.97 (1H, s, CH); 7.26 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 29.1 (CH_2); 33.4 (CH_3); 124.4 (CH); 129.4 (CH); 138.7 (C-4); 139.5; 155.7 (C-3); 155.9 (C-3'); 177.2 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 279 $[M]^+$ (1), 278 $[M–1]^+$ (9), 221 $[M–SCN]^+$ (40), 115 (11), 114 [1-methylimidazole-2-thiol]$^+$ (100), 72 (11). Found, *m*/*z*: 280.0608 $[M+H]^+$. $C_9H_{10}N_7O_2S$. Calculated, *m*/*z*: 280.0611.

4-(5-{[(1-*tert*-Butyl-1*H*-tetrazol-5-yl)sulfanyl]methyl}-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (11e) was obtained in the reaction of compound **4** with 1-*tert*-butyl-tetrazole-5-thiol. Yield 2.3 g (71%), light-brown amorphous powder, mp 124–125°C. IR spectrum, ν, cm^{-1}: 3469, 3461, 3355, 3316, 2981, 2923, 1626, 1603, 1583, 1550, 1397, 1377, 1220, 1145, 1137, 1106, 973, 929, 595, 581. ^{1}H NMR spectrum, δ, ppm: 1.69 (9H, s, $C(CH_3)_3$); 5.13 (2H, s, CH_2); 6.46 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 28.5 (CH_2); 28.7 (CH_3); 61.9 ($C(CH_3)_3$); 137.3 (C-4); 151.2 (tetrazole); 155.8 (C-3); 159.6 (C-3'); 178.0 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 323 $[M]^+$ (22), 268 (20), 267 $[M–C_4H_8]^+$ (26), 210 (24), 167 (92), 137 (20), 109 (17), 57 $[CMe_3]^+$ (100), 41 (23). Found, *m*/*z*: 324.0980 $[M+H]^+$. $C_{10}H_{14}N_9O_2S$. Calculated, *m*/*z*: 324.0986.

3-(4-Amino-1,2,5-oxadiazol-3-yl)-6*H*-1,2,4-oxadiazin-5-ol (13). Chloromethyl derivative of compound **4** (1.0 g, 5.0 mmol) was added to a mixture of K_2CO_3 (1.5 g, 10.9 mmol) and EtOH (30 ml). The reaction mixture was stirred at 30°C for 14 h, then it was filtered from inorganic salts. The filtrate was acidified with concentrated HCl (pH 1), H_2O (30 ml) was added, and evaporated under reduced pressure to 1/2 of the initial volume. The precipitate was filtered off and recrystallized from MeOH–H_2O, 1:1 mixture. Yield 0.63 g (69%), white amorphous powder, mp 225–226°C. IR spectrum, ν, cm^{-1}: 3456, 3410, 3320, 3208, 3142, 1727, 1642, 1547, 1467, 1363, 1344, 1312, 1049, 1001, 971, 952, 917, 862, 774, 571, 517, 467. ^{1}H NMR spectrum, δ, ppm: 4.53 (2H, s, CH_2); 6.40 (2H, s, NH_2); 11.90 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 67.7 (C-6'); 138.6 (C-4); 144.4 (C-5'); 155.2 (C-3); 164.8 (C-3'). Mass spectrum, *m*/*z* (I_{rel}, %): 184 $[M+1]^+$ (1), 183 $[M]^+$ (38), 126 (57), 98 (56), 96 (100), 71 (20), 69 (27), 68 (16), 54 (41), 53 (60), 43 $[HCNO]^+$ (21), 42 $[CNO]^+$ (55), 30 $[NO]^+$ (91). Found, *m*/*z*: 184.0472 $[M+H]^+$. $C_5H_6N_5O_3$. Calculated, *m*/*z*: 184.0465.

[3-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazol-5-yl]-methanol (14). Amidoxime **1** (3.0 g, 21 mmol) was added with stirring to PhMe (50 ml), then acetoxyacetyl chloride (6.7 ml, 63 mmol) was added. The reaction mixture was brought to a boil and heated under reflux for 8 h, then cooled to room temperature, and evaporated under reduced pressure. The residue was dissolved in MeOH (20 ml), H_2O (10 ml) and HCl (1 ml) were added, and the mixture was heated under reflux for 2 h. The solvent was evaporated under reduced pressure, the residue was recrystallized from MeOH. Yield 2.6 g (68%), white powder, mp 161–162°C. IR spectrum, ν, cm^{-1}: 3468, 3382, 3321, 1642, 1583, 1557, 1467, 1434, 1400, 1376, 1243, 1211, 1155, 1090, 1028, 1019, 975, 906, 875, 766, 741, 579, 523, 465, 437. ^{1}H NMR spectrum, δ, ppm: 4.88 (2H, s, CH_2); 6.20 (1H, br. s, OH); 6.49 (2H, br. s, NH_2). ^{13}C NMR spectrum, δ, ppm: 55.6; 137.5 (C-4); 155.9 (C-3); 159.3 (C-3'); 180.9 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 184 $[M+1]^+$ (2), 183 $[M]^+$

(28), 126 (99), 69 $[HNCNCO]^+$ (26), 58 $[HNCNOH]^+$ (34), 31 $[CH_2OH]^+$ (100), 30 $[NO]^+$ (40), 28 $[CHNH]^+$ (39). Found, *m*/*z*: 184.0473 $[M+H]^+$. $C_5H_6N_5O_3$. Calculated, *m*/*z*: 184.0465.

***N*-{4-[5-(Methylamino)-6*H*-1,2,4-oxadiazin-3-yl]-1,2,5-oxadiazol-3-yl}acetamide (15)**. Concentrated H_2SO_4 (0.05 g, 1.0 mmol) was added to a solution of compound **12** (1.00 g, 5.1 mmol) in Ac_2O (2 ml, 21.0 mmol). The reaction mixture was stirred at room temperature for 24 h, then MeOH (1 ml) was added. The formed precipitate was filtered off and recrystallized from MeOH. Yield 0.89 g (73%), white amorphous powder, mp 247–248°C. IR spectrum, ν, cm^{-1}: 3323, 3212, 2924, 1712, 1621, 1599, 1546, 1524, 1407, 1395, 1375, 1314, 1286, 1237, 1183, 1022, 996, 948, 898, 880, 847, 719, 681, 658, 605, 594, 533, 489. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.17 (3H, s, CH_3); 2.92 (3H, d, *J* = 4.7, $NHCH_3$); 4.28 (2H, s, CH_2); 8.61 (1H, s, NH); 10.30 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 23.9 ($CO\underline{C}H_3$); 27.4 ($NHCH_3$); 61.5 (C-6'); 144.7 (C-4); 149.6 (C-3); 152.6 (C-5'); 159.4 (C-3'); 168.4 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 238 $[M]^+$ (4), 139 (18), 57 (18), 56 (98), 55 (11), 53 (29), 46 (33), 44 $[CH_3NHCH_2]^+$ (10), 43 $[CH_3CO]^+$ (40), 42 $[CH_2CO]^+$(54), 41 (24), 31 (34), 30 $[NO]^+$ (100), 29 $[CH_2NH]^+$ (57), 27 $[HCN]^+$ (24). Found, *m*/*z*: 239.0895 $[M+H]^+$. $C_8H_{11}N_6O_3$. Calculated, *m*/*z*: 239.0887.

***N*-[4-(5-Oxo-5,6-dihydro-4*H*-1,2,4-oxadiazin-3-yl)-1,2,5-oxadiazol-3-yl]acetamide (16)**. Compound **13** (0.91 g, 5 mmol) and concentrated H_2SO_4 (0.05 g, 1 mmol) were successively added with stirring to Ac_2O (2 ml, 21 mmol). The reaction mixture was stirred at 45–50°C for 30 min, then MeOH (5 ml) was added, and the solvent was evaporated under reduced pressure. The residue was washed with H_2O, hot (~60°C) MeOH (10 ml) was added, followed by hot H_2O dropwise (until crystallization started), then cooled to room temperature. The precipitate was filtered off and recrystallized from MeOH. Yield 0.63 g (56%), white crystals, mp 231–232°C. IR spectrum, ν, cm^{-1}: 3310, 3239, 3194, 3138, 3103, 1737, 1720, 1706, 1532, 1456, 1396, 1363, 1354, 1294, 1229, 1121, 1058, 1016, 999, 954, 914, 879, 852, 787, 664, 642, 602, 592, 583, 514. ^1H NMR spectrum, δ, ppm: 2.14 (3H, s, CH_3); 4.47 (2H, s, CH_2); 10.90 (1H, s, NH); 11.80 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 23.4 (CH_3); 67.2 (C-6'); 142.1 (C-4); 143.7 (C-5'); 149.9 (C-3); 165.3 (C-3'); 169.3 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 225 $[M]^+$ (2), 195 $[M–NO]^+$ (29), 183 $[M–CH_2CO]^+$ (18), 153 (100), 126 (23), 96 (25), 43 $[CH_3CO]^+$ (26). Found, *m*/*z*: 226.0578 $[M+H]^+$. $C_7H_8N_5O_4$. Calculated, *m*/*z*: 226.0571.

({[Amino(4-amino-1,2,5-oxadiazol-3-yl)methylidene]-amino}oxy)acetic acid (17). Compound **4** (2.0 g, 10 mmol) was added to a solution of NaOH (1.2 g, 30 mmol) in EtOH–H_2O, 1:1 (50 ml). The reaction mixture was stirred at 40°C for 3 h, then cooled to room temperature. The solvent was evaporated under reduced pressure, the residue was dissolved in H_2O (10 ml) and acidified with concentrated HCl (pH 1). The formed precipitate was filtered off and recrystallized from H_2O. Yield 0.63 g (56%), white crystals, mp 191–192°C. IR spectrum, ν, cm^{-1}: 3848, 3834, 3470, 3414, 3357, 3175, 2920, 2763, 2650, 2569, 1729, 1656, 1452, 1254, 1194, 1118, 972, 908, 875, 808, 726, 677, 538, 419. ^1H NMR spectrum, δ, ppm: 4.67 (2H, s, CH_2); 6.26 (2H, s, NH_2); 6.57 (2H, s, NH_2); 12.71 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 70.9 (CH_2); 140.0 (C-4); 144.5 (C=N); 154.9 (C-3); 171.5 (COOH). Mass spectrum, *m*/*z* (I_{rel}, %): 202 $[M+1]^+$ (7), 201 $[M]^+$ (89), 144 (40), 98 (100), 84 $[H_2NC_2N_2O]^+$ (18), 70 (26), 68 (40), 55 (52), 54 (36), 53 (38), 45 $[COOH]^+$ (28), 43 $[HNCNH_2]^+$ (67), 42 $[CNO]^+$ (26), 31 (21), 30 (67), 29 (30), 28 (55). Found, *m*/*z*: 202.0578 $[M+H]^+$. $C_5H_8N_5O_4$. Calculated, *m*/*z*: 202.0571.

Preparation of compound **17** from amidoxime **1**. Ethyl chloroacetate (2.60 g, 22 mmol) and K_2CO_3 (4.20 g, 30 mmol) were added to a solution of amidoxime **1** (2.86 g, 20 mmol) in DMF (20 ml). The reaction mixture was stirred at 60°C for 5 h, then H_2O (50 ml) was added. The formed precipitate was filtered off, washed with H_2O, and dissolved in MeOH (20 ml). 5% Aqueous NaOH (20 ml, 25 mmol) was added to the solution, the mixture was heated to 40°C and stirred at this temperature for 15 min. The solvent was evaporated under reduced pressure to 1/2 of the original volume and acidified with concentrated HCl (pH 1). The formed precipitate was filtered off and recrystallized from H_2O. Yield 3.3 g (82%). The analytical and spectral characteristics of compounds **17** obtained by different methods were identical.

[({(Acetylamino)[4-(acetylamino)-1,2,5-oxadiazol-3-yl]-methylidene}amino)oxy]acetic acid (18). Compound **17** (1.00 g, 5 mmol) and concentrated H_2SO_4 (0.05 g, 1 mmol) were successively added with stirring to Ac_2O (2 ml, 2.16 g, 21 mmol). The reaction mixture was stirred at 45–50°C for 30 min, then H_2O (5 ml) was added, and the solvent was evaporated under reduced pressure. The residue was washed with cold H_2O (20 ml) and recrystallized from MeOH. Yield 2.11 g (74%), white amorphous powder, mp 210–211°C. IR spectrum, ν, cm^{-1}: 3401, 3273, 2921, 2853, 1735, 1695, 1638, 1606, 1524, 1395, 1375, 1253, 1099, 1038, 903, 888, 747, 691, 674, 663, 588, 569, 502. ^1H NMR spectrum, δ, ppm: 2.05 (3H, s, CH_3); 2.08 (3H, s, CH_3); 3.35 (1H, br. s, COOH); 4.67 (2H, s, CH_2); 10.64 (1H, s, NH); 10.91 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 23.0 (CH_3); 23.1 (CH_3); 71.3 (CH_2); 136.5 (C-4); 145.0 (C=N); 150.3 (C-3); 169.1 (C=O); 169.2 (C=O); 170.8 (COOH). Mass spectrum, *m*/*z* (I_{rel}, %): 285 $[M]^+$ (2), 243 $[M–CH_2CO]^+$ (24), 154 (45), 153 (59), 126 (25), 98 (42), 96 (56), 70 (37), 69 (17), 55 (16), 54 (21), 53 (23), 43 $[CH_3CO]^+$ (100), 30 (38), 29 $[CHO]^+$ (26). Found, *m*/*z*: 286.0790 $[M+H]^+$. $C_9H_{12}N_5O_6$. Calculated, *m*/*z*: 286.0782.

4-[5-(Hydrazinylidenemethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (19). Hydrazine hydrate (9.2 g, 0.18 mol) was added with stirring at 35–40°C to a solution of chloromethyl derivative **4** (16.0 g, 0.08 mol) in MeOH (100 ml). After the exothermic reaction subsided, the reaction mixture was stirred at 40°C for 30 min, then evaporated under reduced pressure to 1/2 of the initial volume. Hot (70–80°C) H_2O (100 ml) was added and, with stirring, cooled to room temperature. The precipitate was filtered off, washed with H_2O (2×50 ml) and recrystallized

from AcOH. Yield 12.8 g (82%), white amorphous powder, mp 231–232°C. IR spectrum, ν, cm^{-1}: 3469, 3367, 1633, 1599, 1553, 1465, 1385, 1367, 1309, 1262, 1151, 970, 928, 900, 862, 829, 769, 738, 575, 444. ^{1}H NMR spectrum, δ, ppm: 6.39 (2H, s, NH_2); 7.67 (1H, s, CH); 8.93 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 117.3; 137.6 (C-4); 155.9 (C-3); 159.3 (C-3'); 174.9 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 196 $[M+1]^+$ (1), 195 $[M]^+$ (22), 138 (47), 69 (14), 53 (16), 43 $[CH=NNH_2]^+$ (100), 42 (30), 30 $[NO]^+$ (26). Found, *m*/*z*: 196.0585 $[M+H]^+$. $C_5H_6N_7O_2$. Calculated, *m*/*z*: 196.0577. Found, %: C 30.62; H 2.64; N 50.43. $C_5H_5N_7O_2$. Calculated, %: C 30.77; H 2.58; N 50.24.

Synthesis of 4-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazol-3-amine (2b) from compound 19. Compound **19** (2.0 g, 10 mmol) was added to concentrated HCl (10 ml). The reaction mixture was heated under reflux until the starting compound was completely dissolved (about 18 h), then evaporated under reduced pressure. The residue was dissolved in boiling H_2O (20 ml). The solution was cooled to 5°C, the precipitate was filtered off and recrystallized from MeOH. Yield 0.7 g (42%). Analytical and spectral characteristics were identical to those described previously.[14]

4-{5-[(2-Phenylhydrazinylidene)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (20). Phenylhydrazine (3.4 g, 31 mmol) was added with stirring at room temperature to a solution of chloromethyl derivative **4** (2.0 g, 10 mmol) in MeOH (100 ml). The reaction mixture was brought to a boil and heated under reflux for 30 min, then H_2O (100 ml) was added, acidified with concentrated HCl (pH 1) and left for 16 h. The formed precipitate was filtered off, washed with H_2O (2×50 ml), and recrystallized from MeOH. Yield 1.2 g (44%), yellow amorphous powder, mp 250–251°C. IR spectrum, ν, cm^{-1}: 3465, 3344, 3272, 1638, 1588, 1556, 1512, 1497, 1446, 1397, 1359, 1338, 1262, 1197, 1176, 1156, 997, 969, 902, 891, 870, 785, 768, 758, 692, 643, 594, 506. ^{1}H NMR spectrum, δ, ppm: 6.50 (2H, s, NH_2); 6.97–7.37 (5H, m, H Ph); 7.91 (1H, s, CH); 11.80 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 114.1 (C Ph); 118.7 (CH=N); 122.6 (C Ph); 130.0 (C Ph); 137.6 (C-4); 143.3 (C Ph); 155.9 (C-3); 159.6 (C-3'); 174.1 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 273 $[M+2]^+$ (1), 272 $[M+1]^+$ (15), 271 $[M]^+$ (96), 92 $[C_6H_5NH]^+$ (26), 91 $[C_6H_5N]^+$ (42), 77 $[C_6H_5]^+$ (100), 65 (37), 39 (11). Found, %: C 48.25; H 3.78; N 36.52. $C_{11}H_9N_7O_2$. Calculated, %: C 48.71; H 3.34; N 36.15.

4-{5-[(Hydroxyimino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (21). $NH_2OH·HCl$ (8.34 g, 0.12 mol) and $NaHCO_3$ (12.60 g, 0.15 mol) were added to a solution of compound **4** (10.00 g, 0.05 mol) in MeOH (70 ml). The reaction mixture was stirred at 40–45°C for 8 h, then H_2O (100 ml) was added. The formed precipitate was filtered off, washed with H_2O (2×50 ml), and recrystallized from AcOH. Yield 8.13 g (83%), white amorphous powder, mp 182–183°C. IR spectrum, ν, cm^{-1}: 3600, 3458, 3330, 3017, 2920, 2896, 1627, 1598, 1583, 1564, 1505, 1423, 1353, 1346, 1269, 1174, 1047, 998, 969, 912, 875, 822, 769, 580, 499, 447. ^{1}H NMR spectrum, δ, ppm: 6.49 (2H, s, NH_2); 8.47 (1H, s, CH); 13.30 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 135.8; 137.4 (C-4); 155.9 (C-3); 159.7 (C-3'); 172.1 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 197 $[M+1]^+$ (4), 196 $[M]^+$ (35), 139 $[M–NHCNO]^+$ (100), 30 $[NO]^+$ (27). Found, *m*/*z*: 197.0427 $[M+H]^+$. $C_5H_5N_6O_3$. Calculated, *m*/*z*: 197.0418. Found, %: C 30.51; H 2.14; N 42.71. $C_5H_4N_6O_3$. Calculated, %: C 30.62; H 2.06; N 42.85.

4,4'-[1,2-Hydrazine-1,2-diylidenebis(methylylidene-1,2,4-oxadiazole-5,3-diyl)]bis(1,2,5-oxadiazol-3-amine) (22). Concentrated H_2SO_4 (0.05 g, 1 mmol) was added to a solution of compound **19** (2.00 g, 10 mmol) in AcOH (10 ml), and the mixture was heated under reflux for 2 h. The reaction mixture was cooled to room temperature, the precipitate was filtered off and recrystallized from AcOH. Yield 0.93 g (52%), light-beige amorphous powder, mp 286–287°C (decomp.). IR spectrum, ν, cm^{-1}: 3454, 3326, 3296, 3216, 1630, 1535, 1519, 1424, 1387, 1373, 1351, 1303, 1236, 1175, 1153, 1006, 969, 810, 578, 561, 467, 418. ^{1}H NMR spectrum, δ, ppm: 6.51 (4H, s, $2NH_2$); 8.10 (2H, s, 2CH). ^{13}C NMR spectrum, δ, ppm: 126.4; 137.3 (C-4); 155.9 (C-3); 159.9 (C-3'); 173.3 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 358 $[M]^+$ (1), 328 $[M–NO]^+$ (<1), 194 (60), 43 (100), 28 (30), 18 (25). Found, %: C 33.67; H 1.95; N 46.75. $C_{10}H_6N_{12}O_4$. Calculated, %: C 33.53; H 1.69; N 46.92.

***N*-{4-[5-(Hydrazinylidenemethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-yl}acetamide (23)**. Compound **19** (1.00 g, 5 mmol) and concentrated H_2SO_4 (0.05 g, 1 mmol) were successively added at room temperature to Ac_2O (2 ml, 2.16 g, 21 mmol). The reaction was accompanied by a noticeable exothermic effect, and a precipitate formed after 5 min. The reaction mixture was stirred at 45–50°C for 30 min, cooled to room temperature, the precipitate was filtered off and recrystallized from MeOH. Yield 0.90 g (76%), white amorphous powder, mp 226–227°C. IR spectrum, ν, cm^{-1}: 3398, 3222, 3166, 3033, 2934, 1698, 1592, 1531, 1369, 1315, 1254, 1158, 1129, 968, 910, 690, 660, 596, 583. ^{1}H NMR spectrum, δ, ppm: 2.12 (3H, s, CH_3); 8.08 (1H, s, CH); 11.20 (2H, s, NH_2); 12.10 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 23.2 (CH_3); 126.3 (CH=N); 141.7 (C-4); 150.5 (C-3); 159.4 (C-3'); 169.8 (C=O); 173.3 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 237 $[M]^+$ (12), 236 $[M–H]^+$ (100), 194 $[M–CH_3CO]^+$ (62), 167 (10), 111 (10), 43 (48) $[CH_3CO]^+$. Found, %: C 35.21; H 3.08; N 41.62. $C_7H_7N_7O_3$. Calculated, %: C 35.45; H 2.97; N 41.34.

***N*-(4-{5-[(Hydroxyimino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-yl)acetamide (24)** was obtained from compound **21** (0.93 g, 5.3 mmol) by the method described for furazan **23** synthesis at room temperature. Yield 0.85 g (71%), light-yellow amorphous powder, mp 167–168°C. IR spectrum, ν, cm^{-1}: 3605, 3497, 3345, 3248, 1727, 1711, 1581, 1534, 1370, 1360, 1338, 1310, 1257, 1169, 1054, 1039, 1017, 1001, 970, 939, 826, 798, 768, 645, 596. ^{1}H NMR spectrum, δ, ppm: 2.12 (3H, s, CH_3); 8.48 (1H, s, CH); 11.14 (1H, s, NH); 13.25 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 23.2 (CH_3); 135.9 (CH=N); 141.7 (C-4); 150.5 (C-3); 159.3 (C-3'); 169.8 (C=O); 172.1 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 239 $[M+1]^+$ (2), 238 $[M]^+$ (7), 210

(17), 196 $[M–CH_2CO]^+$ (100), 139 (56), 72 (20), 43 $[CH_3CO]^+$ (57), 30 $[NO]^+$ (25). Found, *m*/*z*: 239.0515 $[M+H]^+$. $C_7H_7N_6O_4$. Calculated, *m*/*z*: 239.0523.

4-{5-[(Methoxyimino)methyl]-1,2,4-oxadiazol-3-yl}-1,2,5-oxadiazol-3-amine (25). Finely ground K_2CO_3 (1.40 g, 10 mol) was added to a solution of oxime **21** (1.00 g, 5 mmol) in DMF (40 ml), and Me_2SO_4 (0.88 g, 7 mmol) was added with stirring at 15–20°C. The reaction mixture was stirred at room temperature for 2 h and evaporated under reduced pressure. H_2O (50 ml) was added to the residue, the formed precipitate was filtered off and recrystallized from MeOH. Yield 0.81 g (68%), light-yellow crystals, mp 118–119°C. IR spectrum, ν, cm^{-1}: 3457, 3330, 3024, 2949, 1630, 1620, 1424, 1357, 1174, 1063, 1003, 969, 936, 908, 873, 799, 578, 515. ^{1}H NMR spectrum, δ, ppm: 4.12 (3H, s, CH_3); 6.50 (2H, s, NH_2); 8.63 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 64.2 (OCH_3); 136.4 (CH=N); 137.7 (C-4); 155.9 (C-3); 159.8 (C-3'); 172.1 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 211 $[M+1]^+$ (2), 210 $[M]^+$ (15), 153 (100), 86 (25), 69 (14), 58 $[HCNOMe]^+$ (29), 53 (14), 30 $[NO]^+$ (24). Found, *m*/*z*: 211.0581 $[M+H]^+$. $C_6H_7N_6O_3$. Calculated, *m*/*z*: 211.0574.

3-(4-Nitro-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazole (26) was prepared using an oxidizing mixture, prepared from 36% aqueous H_2O_2 (4 ml, ~40 mmol) and 94−96% H_2SO_4 (5 ml, ~94 mmol), and 4-[5-(hydrazinylidenemethyl)-1,2,4-oxadiazol-3-yl]-1,2,5-oxadiazol-3-amine (**19**) (2 g, 10 mmol) by the method described for furazan **6** synthesis. Yield 0.98 g (54%), colorless roundish crystals. HPLC and spectral characteristics of the compound match those previously described.[24] IR spectrum, ν, cm^{-1}: 3430, 3138, 1609, 1564, 1539, 1505, 1422, 1408, 1307, 1270, 1116, 1035, 965, 910, 883, 823, 773, 742, 616, 586, 475, 418, 404. ^{1}H NMR spectrum, δ, ppm: 10.1 (1H, s, CH). ^{13}C NMR spectrum, δ, ppm: 141.1 (C-4); 156.5 (C-3'); 160.0 (C-3); 169.2 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 183 $[M]^+$ (1), 137 $[M–NO_2]^+$ (2), 77 (22), 46 $[NO_2]^+$ (100), 38 (13), 30 $[NO]^+$ (99).

2-{[3-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazol-5-yl]methylidene}hydrazinecarboxamide (27). Compound **19** (1.0 g, 5.0 mmol), semicarbazide hydrochloride (0.8 g, 7.2 mmol) were added to a mixture of AcOH (20 ml) and concentrated HCl (10 ml). The reaction mixture was heated under reflux for 8 h, H_2O (50 ml) was added, and cooled to room temperature. The precipitate was filtered off and recrystallized from AcOH. Yield 0.8 g (62%), fine white crystals, mp 282–283°C (decomp.). IR spectrum, ν, cm^{-1}: 3488, 3438, 3373, 3287, 3231, 3194, 3103, 3013, 2921, 1707, 1639, 1619, 1586, 1439, 1421, 1356, 1307, 1192, 1000, 972, 919, 802, 736, 586, 508, 472. ^{1}H NMR spectrum, δ, ppm: 6.51 (2H, s, NH_2); 6.80 (2H, s, NH_2); 7.99 (1H, s, CH); 11.33 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 123.0 (CH=N); 137.3 (C-4); 155.7 (C=O); 156.0 (C-3); 159.7 (C-3'); 173.2 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 238 $[M]^+$ (4), 195 (13), 194 (100) $[M–CONH_2]^+$, 138 (26), 44 $[H_2NCO]^+$ (32), 43 $[HNCO]^+$ (37), 42 (13). Found, %: C 30.41; H 2.68; N 46.91. $C_6H_6N_8O_3$. Calculated, %: C 30.26; H 2.54; N 47.05.

2-{[3-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazol-5-yl]methylidene}hydrazinecarbothioamide (28) was obtained from compound **19** (1.0 g, 5.0 mmol) and thiosemicarbazide (0.6 g, 6.5 mmol) by the method described for the synthesis of furazan **27**. Yield 0.88 g (69%), light-beige amorphous powder, mp 286–287°C (decomp.). IR spectrum, ν, cm^{-1}: 3445, 3394, 3320, 3279, 3173, 1633, 1615, 1597, 1511, 1469, 1428, 1355, 1275, 1176, 1127, 1061, 999, 968, 904, 875, 853, 788, 767, 629, 574, 482, 403. ^{1}H NMR spectrum, δ, ppm: 6.49 (2H, s, NH_2); 8.16 (2H, s, NH_2); 8.81 (1H, s, CH); 12.27 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 125.2 (N=CH); 137.3 (C-4); 156.0 (C-3); 159.8 (C-3'); 173.0 (C-5'); 179.6 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 254 $[M]^+$ (100), 199 (32), 194 $[M–CNS]^+$ (45), 164 $[M–CNS–NO]^+$ (26), 154 (20), 138 (29), 116 (40), 102 $[H_2NCSNHN=CH]^+$ (27), 85 (27), 60 (48), 53 (27), 42 $[H_2NCN]^+$ (15). Found, %: C 28.39; H 2.53; N 43.97. $C_6H_6N_8O_2S$. Calculated, %: C 28.35; H 2.38; N 44.08.

5-(Hydrazinylidenemethyl)-3-(4-hydrazinyl-1,2,5-oxadiazol-3-yl)-1,2,4-oxadiazole (29). A solution of compound **6** (1.15 g, 5 mmol) in MeCN (5 ml) was added with stirring at 20°C to a solution of hydrazine hydrate (1.20 g, 24 mmol) in MeCN (30 ml). The reaction mixture was stirred at room temperature for 1 h, diluted with H_2O (50 ml). The precipitate was filtered off and recrystallized from AcOH. Yield 0.87 g (82%), white powder, mp 207–208°C (decomp.). IR spectrum, ν, cm^{-1}: 3413, 3326, 3234, 2920, 2851, 1661, 1588, 1562, 1446, 1323, 1295, 1241, 1175, 1127, 995, 968, 948, 920, 882, 859, 825, 768, 429. ^{1}H NMR spectrum, δ, ppm: 4.59 (2H, s, NH_2); 7.31 (1H, s, NH); 7.68 (1H, s, NH); 8.97 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 117.2 (C=N); 136.3 (C-4); 159.1 (C-3); 159.6 (C-3'); 174.9 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 210 $[M]^+$ (2), 181 $[M–NNH]^+$ (4), 138 $[M–H_2NNCNO]^+$ (12), 71 $[HNN=CNO]^+$ (22), 69 (11), 43 $[CH=NNH_2]^+$ (100), 42 $[CNO]^+$ (28), 31 $[NHNH_2]^+$ (18), 30 $[NO]^+$ (42), 29 $[CHO]^+$ (21), 28 (21). Found, *m*/*z*: 211.0693 $[M+H]^+$. $C_5H_7N_8O_2$. Calculated, *m*/*z*: 211.0686.

5-(Hydrazinylidenemethyl)-3-{4-[2-(propan-2-ylidene)-hydrazinyl]-1,2,5-oxadiazol-3-yl}-1,2,4-oxadiazole (30). Compound **29** (0.7 g, 3.3 mol) was added to a mixture of 95% EtOH (10 ml), AcOH (1 ml), and acetone (1 ml, 9.0 mmol). The reaction mixture was stirred at 30–35°C for 5 h, then diluted with H_2O (30 ml). The precipitate was filtered off and recrystallized from MeOH. Yield 0.53 g (64%), white amorphous powder, mp 213–214°C. IR spectrum, ν, cm^{-1}: 3414, 3313, 3216, 1619, 1586, 1571, 1430, 1369, 1311, 1229, 1156, 967, 921, 873, 768. ^{1}H NMR spectrum, δ, ppm: 1.94 (3H, s, CH_3); 1.98 (3H, s, CH_3); 7.69 (1H, s, N=CH); 8.69 (1H, NH); 9.01 (2H, s, NH_2). ^{13}C NMR spectrum, δ, ppm: 16.7 (CH_3); 29.0 (CH_3); 117.1 (N=CH); 136.8 (C-4); 154.3 (N=<u>C</u>Me$_2$); 155.0 (C-3); 159.1 (C-3'); 174.9 (C-5'). Mass spectrum, *m*/*z* (I_{rel}, %): 251 $[M+1]^+$ (12), 250 $[M]^+$ (87), 221 (23), 220 (16), 191 (17), 176 (28), 138 (26), 98 (17), 83 (41), 71 $[Me_2CNNH]^+$ (21), 69 (16), 56 (87), 43 $[CH=NNH_2]^+$ (100), 42 $[CNO]^+$ (72), 41 (43), 39 (23), 30 $[NO]^+$ (51), 29 $[CHO]^+$ (23), 28 (37). Found, *m*/*z*: 251.1006 $[M+H]^+$. $C_8H_{11}N_8O_2$. Calculated, *m*/*z*: 251.0999.

References

1. Sheremetev, A. B.; Machova, N. N.; Friedrichsen, W. In *Advances in Heterocyclic Chemistry*; Katritzky, A., Ed.; Elsevier: New York, 2001, Vol. 78, p. 65.
2. Jakopin, Z.; Dolenc, M. S. *Curr. Org. Chem.* **2008**, *12*, 850.
3. Bostrom, J.; Hogner, A.; Llinas, A.; Wellner, E.; Plowright, A. T. *J. Med. Chem.* **2012**, *55*, 1817.
4. Abdel-Wahab, B. F.; Mohamed, H. A.; Khidre, R. E.; El-Mansy, M. F. *J. Heterocycl. Chem*. **2014**, *51*, 1215.
5. Pace, A.; Buscemi, S.; Piccionello, A. P.; Pibiri, I. In *Advances in Heterocyclic Chemistry*; Scriven, E. F. V.; Ramsden, C., Eds.; Elsevier: New York, 2015, Vol. 116, p. 85.
6. Fershtat, L. L.; Makhova, N. N. *Russ. Chem. Rev.* **2016**, *85*, 1097. [*Usp. Khim.* **2016**, *85*, 1097.]
7. Sun, Q.; Shen, C.; Li, X.; Lu, M. *J. Mater. Chem*. *A* **2017**, *5*, 11063.
8. Piccionello, A. P.; Pace, A.; Buscemi, S. *Chem. Heterocycl. Compd*. **2017**, *53*, 936. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 936.]
9. Tang, Y.; Imler, G. H.; Parrish, D. A.; Shreeve, J. M. *Org. Lett.* **2018**, *20*, 8039.
10. Stepanov, A. I.; Sannikov, V. S.; Dashko, D. V.; Astrat'ev, A. A. *Izv. SPbGTI(TU)* [in Russian] **2014**, *25*, 32.
11. Andrianov, V. G.; Eremeev, A. V. *Chem. Heterocycl. Compd*. **1984**, 937. [*Khim. Geterotsikl. Soedin.* **1984**, 1155.]
12. Yarovenko, V. N.; Shirinyan, V. Z.; Zavarzin, I. V.; Krayushkin, M. M. *Russ. Chem. Bull*. **1994**, *43*, 114. [*Izv. Akad. Nauk, Ser. Khim.* **1994**, 118.]
13. Shaposhnikov, S. D.; Korobov, N. V.; Sergievskii, A. V.; Pirogov, S. V.; Mel'nikova, S. F.; Tselinskii, I. V. *Russ. J. Org. Chem*. **2002**, *38*, 1351. [*Zh. Org. Khim.* **2002**, *38*, 1405.]
14. Stepanov, A. I.; Sannikov, V. S.; Dashko, D. V.; Astrat'ev, A. A. *Izv. SPbGTI(TU)* [in Russian] **2014**, *26*, 42.
15. Sheremetev, A. B.; Dmitriev, D. E.; Lagutina, N. K.; Raihstat, M. M.; Kiselyov, A. S.; Semenova, M. N.; Ikizalp, N. N.; Semenov, V. V. *Mendeleev Commun*. **2010**, *20*, 132.
16. Wei, H.; He, C.; Zhang, J.; Shreeve, J. M. *Angew. Chem.*, *Int. Ed.* **2015**, *54*, 9367.
17. Pagoria, P. F.; Zhang, M.-X., Zuckerman, N. B.; DeHope, A. J.; Parrish, D. A. *Chem. Heterocycl. Compd*. **2017**, *53*, 760. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 760.]
18. Kataria, A.; Singh, J.; Kundu, B. *J. Cell. Biochem*. **2019**, *120*, 143.
19. Giordanetto, F.; Kull, B.; Dellsen, A. *Bioorg. Med. Chem. Lett*. **2011**, *21*, 829.
20. Tsyshevsky, R.; Pagoria, P.; Zhang, M.; Racoveanu, A.; Parrish, D. A.; Smirnov, A. S.; Kuklja, M. M. *J. Phys. Chem. C* **2017**, *121*, 23853.
21. He, C.; Imler, G. H.; Parrish, D. A.; Shreeve, J. M. *J. Mater. Chem. A* **2018**, *6*, 16833.
22. Wang, B.; Xiong, H.; Cheng, G.; Zhang, Z.; Yang, H. *New J. Chem*. **2018**, *42*, 19671.
23. Wang, Q.; Shao, Y.; Lu, M. *Cryst. Growth Des.* **2018**, *18*, 6150.
24. Johnson, E. C.; Bukowski, E. J.; Sabatini, J. J.; Sausa, R. C.; Byrd, E. F. C.; Garner, M. A.; Chavez, D. E. *ChemPlusChem* **2019**, *84*, 319.
25. Stepanov, A. I.; Sannikov, V. S.; Dashko, D. V.; Roslyakov, A. G.; Astrat'ev, A. A.; Stepanova, E. V. *Chem. Heterocycl. Compd*. **2015**, *51*, 350. [*Khim. Geterotsikl. Soedin.* **2015**, *51*, 350.]
26. Stepanova, E. V., Stepanov, A. I. *Izv. vyssh. uchebn. zaved. Khim. Khim. Tekhnol.* [in Russian] **2017**, *60*, 26.
27. Pace, A.; Pierro, P. *Org. Biomol. Chem*. **2009**, *7*, 4337.
28. Paoloni, L.; Cignitti, M. *Tetrahedron* **1968**, *24*, 485.
29. Ruccia, M.; Vivona, N.; Spinelli, D. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R.; Boulton, A. J., Eds.; Elsiver: New York, 1981, Vol. 29, p. 141.
30. Tyrkov, A. G. *Izv. vyssh. uchebn. zaved. Khim. Khim. Tekhnol.* [in Russian] **2003**, *46*, 3.
31. Novikova, T. S.; Mel'nikova, T. M.; Kharitonova, O. V.; Kulagina, V. O.; Aleksandrova, N. S.; Sheremetev, A. B.; Pivina, T. S.; Khmel'nitskii, L. I.; Novikov, S. S. *Mendeleev Commun*. **1994**, *4*, 138.
32. Lotmentsev, Y. M.; Kondakova, N. N.; Bakeshko, A. V.; Kozeev, A. M.; Sheremetev, A. B. *Chem. Heterocycl. Compd*. **2017**, *53*, 740. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 740.]
33. Stepanov, A. I.; Sannikov, V. S.; Dashko, D. V.; Roslyakov, A. G.; Astrat'ev, A. A.; Stepanova, E. V. *Chem. Heterocycl. Compd*. **2017**, *53*, 746. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 746.]
34. Aitken, R. A.; Argyropoulos, N. G.; Bansal, R. K.; Begtrup, M.; Bradley, P. In *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Georg Thieme Verlag, 2014, Vol. 13, p. 171.
35. Hemming, K. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Eds.; Elsevier, 2008, Vol. 5, p. 243.
36. Johnson, E. C.; Sabatini, J. J.; Chavez, D. E.; Sausa, R. C.; Byrd, E. F. C.; Wingard, L. A.; Guzman, P. E. *Org. Process Res. Dev.* **2018**, *22*, 736.
37. Dmitriev, D. E.; Strelenko, Yu. A.; Sheremetev, A. B. *Russ. Chem. Bull.*, *Int. Ed.* **2013**, *62*, 504. [*Izv. Akad. Nauk, Ser. Khim.* **2013**, 503.]
38. Crovetti, A. J.; Von Esch, A. M.; Thill, R. J. *J. Heterocycl. Chem*. **1972**, *9*, 435.
39. Durust, Y. *Magn. Reson. Chem*. **1998**, *36*, 878.
40. Giner-Sorolla, A.; Bendich, A. *J. Org. Chem*. **1966**, *31*, 4239.
41. Hauptmann, S.; Kluge, M.; Seidig, K.-D.; Wilde, H. *Angew. Chem.*, *Int. Ed*. **1965**, *4*, 688.
42. Elvidge, J. A.; Zaidi, N. A. *J. Chem. Soc. C* **1968**, 2188.
43. Kishner, N. *J. Russ. Phys. Chem. Soc.* **1911**, *43*, 582.