Chemistry of Heterocyclic Compounds, Vol. 50, No. 1, April, 2014 (Russian Original Vol. 50, No. 1, January, 2014)

REACTION OF 2-ARYL-4-CYANO-1,3-OXAZOLE-5-SULFONYL CHLORIDES WITH 5-AMINO-1*H*-PYRAZOLES AND 5-AMINO-1*H*-1,2,4-TRIAZOLE

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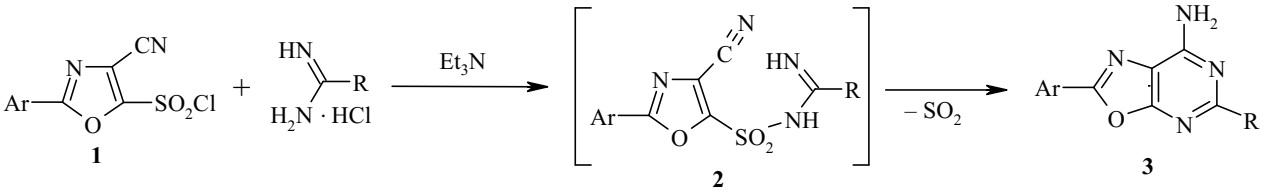
The reaction of 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chlorides with 5-amino-3-R-1H-pyrazoles and 5-amino-1H-1,2,4-triazole gave 5-[(3-R-5-amino-1H-pyrazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles and 5-[(5-amino-1H-1,2,4-triazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles. The action of sodium hydride on these carbonitriles leads to the elimination of sulfur dioxide and cyclocondensation to give new heterocyclic systems, namely, [1,3]oxazolo[5,4-d]pyrazolo[1,5-a]-pyrimidine and [1,3]oxazolo[5,4-d][1,2,4]triazolo[1,5-a]pyrimidine.

Keywords: 5-amino-1*H*-pyrazole, 5-amino-1*H*-1,2,4-triazole, 4-cyano-1,3-oxazole-5-sulfonyl chloride, [1,3]oxazolo[5,4-*d*]pyrazolo[1,5-*a*]pyrimidin-9-amine, [1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-9-amine, sodium hydride.

The rapid development of the chemistry of functional derivatives of 1,3-oxazole in recent decades is attributed to the finding of many bioactive 1,3-oxazole compounds among natural products [1-3]. Such compounds include the antibiotics virginiamycin, madumycin II, griseoviridin, dendroamide A etc., possessing not only strong bactericidal but also antiblastic activity [3-7]. 1,3-Oxazole-4-carbonitriles also display various biological activity [8-11]. Furthermore, these compounds are convenient substrates for the synthesis of other heterocyclic systems [12-14].



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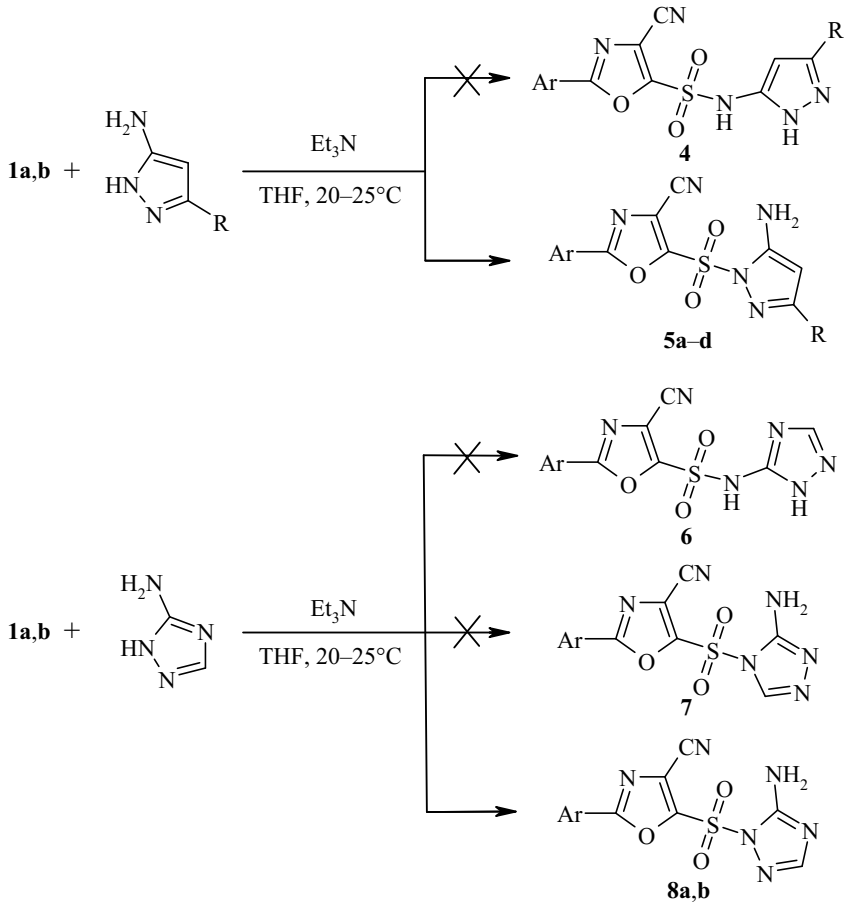
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 84-95, January, 2014. Original article submitted January 2, 2014.

 0009-3122/14/5001-0076

In recent work [15], we found that the reaction of available 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chlorides **1** with amidines in the presence of Et_3N proceeding through intermediates **2** at 20-25°C in THF gives 7-amino-2-aryl-1,3-oxazolo[5,4-*d*]pyrimidines **3**.

We have now studied the similar reaction of oxazoles **1** with 3-R-5-amino-1*H*-pyrazoles and 5-amino-1*H*-1,2,4-triazole, which contain an amidine fragment. This reaction gives *N*-azolylsulfonation products, which were isolated in 70-88% yield as pure compounds and characterized by elemental analysis and LC/MS (Tables 1 and 2). As indicated in the literature [16-21], the formation of two compounds (**4** and **5**) is possible in the reaction of oxazoles **1** with 3-R-5-amino-1*H*-pyrazoles, while three alternative structures (**6**-**8**) may be formed in the reaction with 5-amino-1*H*-1,2,4-triazole.



1, **8 a** Ar = Ph, **b** Ar = 4-MeC_6H_4;
5 a Ar = Ph, R = Me; **b** Ar = R = Ph; **c** Ar = 4-MeC_6H_4, R = Me; **d** Ar = 4-MeC_6H_4, R = Ph

It is difficult to determine which of these alternative structures is formed using only IR and NMR spectroscopy. Furthermore, we cannot exclude the participation of the nitrile fragment in this reaction since there is no CN group absorption band at 2220-2240 cm^{-1} in the IR spectra of the reaction products. Thus, an X-ray structural analysis was carried out, which showed unequivocally that these products are sulfonylamides **5** and **8**.

The major bond lengths and valence angles in 4-cyano-2-phenyl-1,3-oxazole fragment of carbonitrile **5b** (Fig. 1) are virtually identical to the corresponding values for related structures containing this fragment [22, 23]. Thus, the C(1)–N(1) (1.293(3) Å) and C(2)–C(3) bond lengths (1.345(2) Å) are only slightly greater than the lengths of the standard C=N (1.28 Å) and C=C double bonds (1.33 Å), while the other bond lengths in the oxazole ring have values characteristic for delocalized bonds. The 2-phenyl-1,3-oxazole fragment itself is planar and the mean deviation of the atoms from the plane is only 0.0297 Å. The 5-amino-3-phenylpyrazole fragment

is also almost planar (the mean deviation of the atoms from the plane is 0.050 Å) and forms a dihedral angle of 74.98(6)° with the 2-phenyl-1,3-oxazole fragment. We should note that the sulfur atom deviates from both the 2-phenyl-1,3-oxazole and 5-amino-3-phenylpyrazole fragments by -0.1333(27) and 0.7306(20) Å, respectively. The sum of the valence angles at the atom N(3) is 354.38(17)°.

The lengths of the S–C and S–N bonds are 1.742(2) and 1.6562(18) Å, which is characteristic for such compounds. The crystal features a shortened N(5)–H···O(2) contact, which may be considered as an intramolecular hydrogen bond with the following parameters: N(5)···O(2), 2.833(3) Å; N(5)–H–O(2), 121(2)°. There is also a very weak intermolecular N(5)–H···N(4a) hydrogen bond with parameters: N(5)···N(4), 3.146(3) Å; N(5)–H–N(4), 160(2)°. (The letter a indicates the nitrogen atom related to the base atoms by the symmetry operation 0.5-*x*, *y*-0.5, *z*).

The major bond lengths and valence angles in the 4-cyano-2-phenyl-1,3-oxazole fragment in carbonitrile **8a** (Fig. 2) are virtually identical to the corresponding values for carbonitrile **5b**. The 2-phenyl-1,3-oxazole fragment itself is planar, while the mean deviation of the atoms from the plane is 0.0412 Å. The 5-amino-1,2,4-traizole ring is planar (the mean deviation of the atoms from the plane is only 0.008 Å) and forms a dihedral angle of 86.98(5)° with the 2-phenyl-1,3-oxazole fragment. The sulfur atom in carbonitrile **8a** deviates from the planes of the 2-phenyl-1,3-oxazole and 1,2,4-triazole rings by 0.0777(17) and 0.3648(28) Å, respectively. These values are somewhat less than for these parameters in carbonitrile **5b**. The configuration of the N(3) atom in carbonitrile **8a** is also more compressed and the sum of the valence angles at this atom is 357.31(16)°.

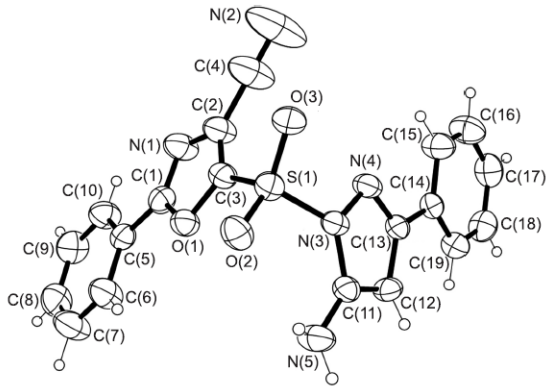


Fig. 1. Molecular structure of carbonitrile **5b** with representation of the atoms by thermal vibration ellipsoids of 50% probability.

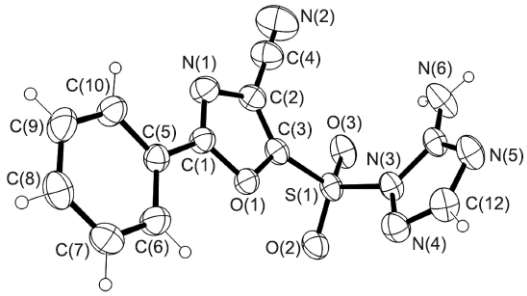
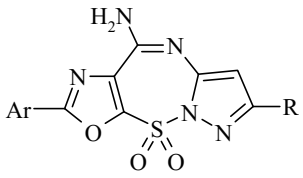


Fig. 2. Molecular structure of carbonitrile **8a** with representation of the atoms by thermal vibration ellipsoids of 50% probability.

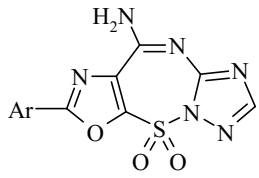
A shortened N(6)–H···O(3) contact is observed in the crystal of carbonitrile **8a**, which may be considered as an intramolecular hydrogen bond with the following parameters: N(6)···O(3), 2.875(2) Å; N(6)–H–O(3), 125.1(19)°. There is also a weak intermolecular N(6)–H···N(5b) hydrogen bond with the

following parameters: N(6)···N(5), 3.031(3) Å; N(6)–H–N(5), 168(2)°. (The letter b indicates the nitrogen atom related to the base atoms by the symmetry operation 1-*x*, 2-*y*, 2-*z*).

5-[(5-Amino-3-R-1*H*-pyrazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles **5a-d** and 5-[(5-amino-1*H*-1,2,4-triazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles **8a**,**b** contain an electrophilic nitrile group and nucleophilic primary amino group. Thus, these compounds can form seven-membered thiadiazepine rings **A** and **B** (see analogies [17, 24]).

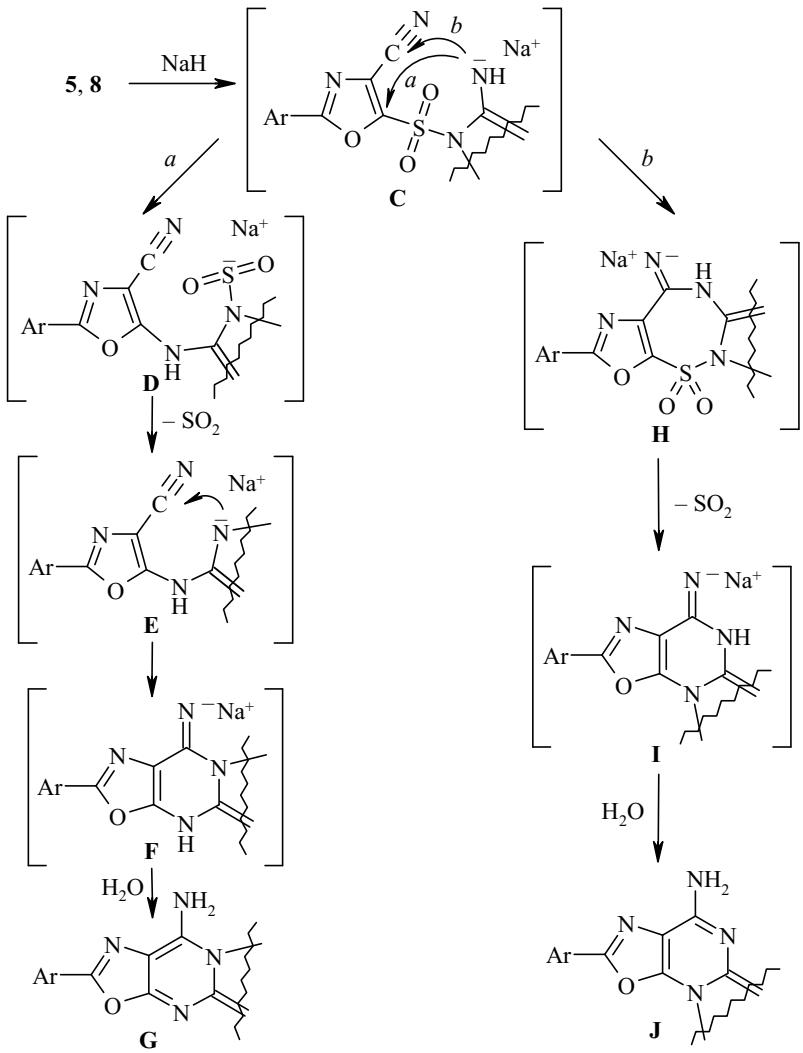


A



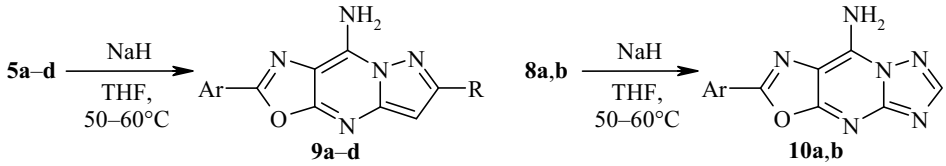
B

In order to check this proposal, carbonitriles **5a-d** and **8a**,**b** were treated with NaH in tetrahydrofuran similar to the method described in our previous work [25]. Elemental analysis indicated that this reaction does not give products containing sulfur. The ^{1}H and ^{13}C NMR spectral and LC/MS data (Tables 1 and 2) indicate that the reaction is accompanied by the elimination of sulfur dioxide and formation of an oxazolopyrimidine



system fused to a pyrazole or triazole ring. Initially, intermediate **C** probably is formed with a negative charge on the exocyclic nitrogen atom. This intermediate can convert to final products **G** and **J** through two pathways. Pathway *a* presupposes initial attack of the C-5 atom in the oxazole ring by the nucleophilic nitrogen atom and formation of intermediate **D**. Subsequent loss of sulfur dioxide by analogy of the data in the literature [26] leads to salt **F**. Then, this intermediate salt reacts with water to yield product **G**. Through pathway *b*, the nitrogen atom in structure **C** initially attacks the electrophilic site of the CN group to give thiadiazepine intermediate **H**, which then converts through intermediate **I** to yield product **J**.

The chain of transformations **C→D→E→F→G** presupposes formation of a linear tricyclic system, while the chain **C→H→I→J** presupposes formation of an angular system. We should note that we have already obtained a compound with angular structure **J** [25] but its spectral characteristics are not in accord with our product with structure **9b**. Thus, we favor the former variant with formation of new heterocyclic systems: 6-R-2-aryl[1,3]oxazolo-[5,4-*d*]pyrazolo[1,5-*a*]pyrimidin-9-amines **9a-d** and 2-aryl[1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-9-amines **10a**,**b**.



9 a Ar = Ph, R = Me; **b** Ar = R = Ph; **c** Ar = 4-MeC_6H_4, R = Me;
d Ar = 4-MeC_6H_4, R = Ph; **10 a** Ar = Ph, **b** 4-MeC_6H_4

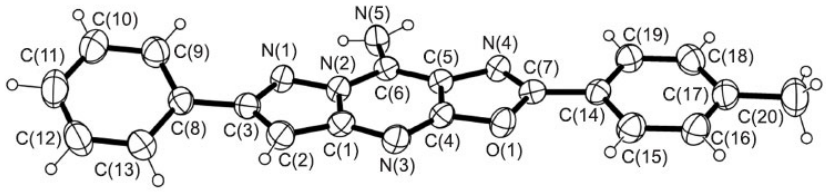


Fig. 3. Molecular structure of pyrimidinamine **9d** with representation of the atoms by thermal vibration ellipsoids of 50% probability.

The ^{1}H NMR spectra of these compounds show characteristic singlets for the pyrazole protons in compounds **9a-d** (6.14-6.86 ppm) and triazole protons in compounds **10a**,**b** (8.42, 8.45 ppm, respectively). The presence of a primary amino group in pyrimidinamines **9a-d** and **10a**,**b** was confirmed by finding a broadened singlet at 8.63-9.15 ppm in the region characteristic for this group. X-ray structural analysis was carried out for pyrimidinamines **9d** (Fig. 3) and **10b** (Fig. 4) to obtain unequivocal proof of the structures of these compounds and determine their special features.

The major bond lengths and valence angles in the central tricyclic fragment in compound **9d** (Fig. 3) are characteristic for conjugated heterocyclic systems, and, on the whole, the geometrical characteristics are similar to those for previously studied simpler heterocyclic systems [27, 28]. Thus, the valence angles for the five-membered heterocycles fall in the range 103.52(13)-114.84(14)°, while these values for the pyrimidine ring are 111.34(14)-130.48(15)°. The distribution of the endocyclic angles in the central fragment are somewhat unusual, which leads to their pairwise enhancement: N(3)–C(1)–C(2), 132.78(15)°; N(3)–C(4)–O(1), 122.55(14)°; N(1)–N(2)–C(6), 123.22(13)°; C(6)–C(5)–N(4), 131.67(14)°.

The C(6)–N(5) bond is considerably shorter (1.326(2) Å) than the standard C–N single bond (1.45 Å) due to strong conjugation of the lone electron pair of the N(5) atom with the heterocyclic π-electron system. The sum of the valence angles at the N(5) atom is 359.6(18)°.

As we might have expected, the central tricyclic fragment is virtually planar (the mean-square deviation of the atoms from the plane is only 0.028 Å), while the phenyl and 4-methylphenyl substituents are twisted relative to the tricyclic fragment by 27.93(5) and 7.74(5)°, respectively.

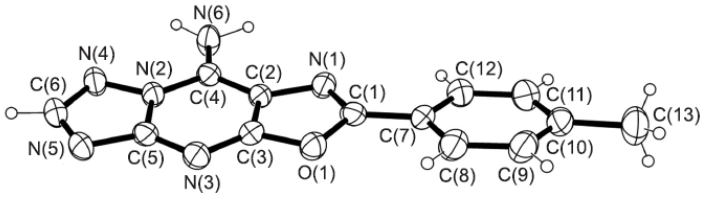


Fig. 4. Molecular structure of pyrimidinamine **10b** with representation of the atoms by thermal vibration ellipsoids of 50% probability.

Intermolecular N(5)–H···N(3a) and N(5)–H(2N)···N(4b) hydrogen bonds are formed in the crystal with the following parameters: N(5)···N(3a), 3.018(2) Å; N(5)–H–N(3a), 142.0(17)°; N(5)···N(4b), 3.074(2)Å, N(5)–H(2N)–N(4b), 158.8(17)°. (The letters a and b indicate nitrogen atoms related to the base atoms by symmetry operations *x*, 1-*y*, *z*+0.5 and -*x*, *y*, 1.5-*z*, respectively.

The major bond lengths and valence angles in the central tricyclic fragment of pyrimidinamine **10b** (Fig. 4) are similar to those for pyrimidinamine **9d** and are characteristic for conjugated heterocyclic systems. Thus, the valence angles in the five-membered heterocycles fall in a somewhat broader range than in pyrimidinamine **9d**, 100.65(17)-117.71(19)°, while these values for the pyrimidine ring are 109.67(17)-130.78(19)°. As in the case of compound **9d**, the C(4)–N(6) bond is shorter (1.324(3) Å) than the standard C–N single bond due to strong conjugation of the lone electron pair of the N(6) atom with the heterocyclic π-electron system. The sum of the valence angles at the N(5) atom is 359.6(18)°. The central tricyclic fragment is virtually planar (the mean-square deviation of the atoms from the plane is only 0.016 Å), while the aryl substituent is twisted relative to the central fragment by 9.0(5)°.

Intermolecular N(6)–H(1N)···N(5a) hydrogen bonds are found in the crystal with the following parameters: N(6)···N(5a), 2.872(3) Å, N(6)H(1N)N(5a), 174.8(18)°. (The letter a indicates the nitrogen atom related to the base atoms by the symmetry operation 0.5+*x*, 0.5-*y*, *z*+0.5).

Thus, our study showed that the reaction of 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chlorides with 3-R-5-amino-1*H*-pyrazoles and 5-amino-1*H*-1,2,4-triazoles proceeds regioselectively at the ring nitrogen atom N-1. The products obtained upon the action of sodium hydride give new heterocyclic systems, namely, [1,3]oxazolo[5,4-*d*]pyrazolo[1,5-*a*]pyrimidine and [1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine, whose structures were confirmed by X-ray structural analysis.

EXPERIMENTAL

IR spectra were recorded on a Vertex 70 spectrometer in KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer (500 and 125 MHz, respectively) in DMSO-d_6 with TMS as internal standard. The LC/MS spectra were recorded with an Agilent 1100 Series chromatograph equipped with a diode matrix and Agilent LC/MSD SL mass-selective detector using a 4.6×15-mm column packed with Zorbax SB-C18 (1.8 μm) and solvents: A) 95:5 MeCN–H_2O, 0.1% CF_3CO_2H, and B) 0.1% aqueous CF_3CO_2H. The eluent flow rate was 3 ml/min. The injection volume was 1 μl. The UV detectors recorded at 215, 254, and 285 nm. The chemical ionization spectra were recorded at atmospheric pressure. Elemental analysis was carried out in the Analytical Laboratory of the Institute of Bioorganic and Petrochemistry

TABLE 1. Physicochemical Characteristics of Compounds **5a-d**, **8a**,**b**, **9a-d**, and **10a**,**b**

Compound	Empirical formula	Found, % / Calculated, %				Mp*, °C	Yield, %
		C	H	N	S		
5a	$C_{14}H_{11}N_5O_3S$	51.08 / 51.06	3.32 / 3.37	21.18 / 21.26	9.75 / 9.74	172-174	70
5b	$C_{19}H_{13}N_5O_3S$	58.21 / 58.30	3.40 / 3.35	17.95 / 17.89	8.14 / 8.19	205-206	78
5c	$C_{15}H_{13}N_5O_3S$	52.39 / 52.47	3.77 / 3.82	20.52 / 20.40	9.35 / 9.34	200-201	85
5d	$C_{20}H_{15}N_5O_3S$	59.18 / 59.25	3.79 / 3.73	17.37 / 17.27	7.89 / 7.91	202-203	88
8a	$C_{12}H_8N_6O_3S$	45.49 / 45.57	2.50 / 2.55	26.65 / 26.57	10.13 / 10.14	210-211	74
8b	$C_{13}H_{10}N_6O_3S$	47.15 / 47.27	3.12 / 3.05	25.58 / 25.44	9.75 / 9.71	209-210	76
9a	$C_{14}H_{11}N_5O$	63.30 / 63.39	4.15 / 4.18	26.46 / 26.40	—	262-264	53
9b	$C_{19}H_{13}N_5O$	69.70 / 69.72	4.00 / 4.00	21.42 / 21.39	—	>300	60
9c	$C_{15}H_{13}N_5O$	64.49 / 64.51	4.61 / 4.69	25.13 / 25.07	—	299-300	54
9d	$C_{20}H_{15}N_5O$	70.31 / 70.37	4.39 / 4.43	20.49 / 20.52	—	>300	55
10a	$C_{12}H_8N_6O$	57.05 / 57.14	3.11 / 3.20	33.45 / 33.32	—	>300	50
10b	$C_{13}H_{10}N_6O$	58.51 / 58.64	3.75 / 3.79	31.71 / 31.56	—	>300	53

*Recrystallization solvents: acetonitrile for compounds **5a**,**b**, **8a**,**b**, and **9a**, ethanol for compounds **5c**,**d**, and 1:1 acetonitrile–DMF for compounds **9b-d** and **10a**,**b**.

of the National Academy of Sciences of Ukraine. The carbon and hydrogen contents were determined using the Pregl gravimetric method, while nitrogen was determined using the Dumas gasometric micromethod. Sulfur was determined by the Scheininger titrimetric method [29]. Melting points were determined on a Fisher–Johns instrument. The reaction course and purity of the products were monitored by thin-layer chromatography on Silufol UV-254 plates using 9:1 chloroform–methanol as the eluent with visualization by UV light.

Starting 2-aryl-4-cyano-1,3-oxazolo-5-sulfonyl chlorides **1a**,**b** were obtained according to our previous procedure [30]. 3-R-5-Amino-1*H*-pyrazoles were obtained according to Grandberg et al. [31]. Commercial samples of 5-amino-1*H*-1,2,4-triazole and NaH were obtained from Aldrich.

5-[(5-Amino-3-R-1*H*-pyrazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles 5a-d (General Method). A solution of 5-amino-3-methyl-1*H*-pyrazole (4 mmol) or 5-amino-3-phenyl-1*H*-pyrazole in anhydrous THF (10 ml) and Et_3N (0.405 g, 4 mmol) was added with stirring to a solution of sulfonyl chloride **1a**,**b** (4 mmol) in anhydrous THF (15 ml). The reaction mixture was maintained for 12 h at 20-25°C. The precipitate was filtered off, and the solvent was removed at reduced pressure. The residue was treated with water (20 ml). The precipitate formed was filtered off, washed with water (10 ml), dried, and purified by recrystallization.

Compound 5a. ^{13}C NMR spectrum, δ, ppm: 12.8 (CH_3); 88.6; 109.4; 118.4 (CN); 123.1; 127.0; 129.2; 133.2; 148.7; 152.5; 158.0; 163.7.

TABLE 2. Spectral Characteristics of Compounds **5a-d**, **8a**,**b**, **9a-d**, and **10a**,**b**

Compound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz)	Mass spectrum, *m/z* $[M+H]^+$
5a	1167, 1209, 1331, 1393, 1448, 1545, 1594, 1634; 3303, 3472 (NH_2)	2.02 (3H, s, CH_3); 5.28 (1H, s, CH pyrazole); 6.45 (2H, s, NH_2); 7.62-7.74 (3H, m, H Ar); 8.00 (2H, d, *J* = 6.8, H Ar)	330
5b	1172, 1200, 1330, 1404, 1449, 1480, 1547, 1568, 1621; 3315, 3460 (NH_2)	5.88 (1H, s, CH pyrazole); 6.66 (2H, s, NH_2); 7.42-7.44 (3H, m, H Ar); 7.61-7.70 (3H, m, H Ar); 7.77 (2H, d, *J* = 6.5, H Ar); 7.98 (2H, d, *J* = 8.0, H Ar)	392
5c	1166, 1205, 1267, 1329, 1405, 1494, 1550, 1582, 1637; 3142, 3448 (NH_2)	2.05 (3H, s, CH_3); 2.41 (3H, s, CH_3); 5.23 (1H, s, CH pyrazole), 6.41 (2H, s, NH_2); 7.45 (2H, d, *J* = 7.6, H Ar); 7.89 (2H, d, *J* = 7.6, H Ar)	344
5d	1171, 1201, 1327, 1401, 1477, 1494, 1570, 1622; 3328, 3470 (NH_2)	2.38 (3H, s, CH_3); 5.86 (1H, s, CH pyrazole); 6.57 (2H, s, NH_2); 7.39-7.44 (5H, m, H Ar); 7.74-7.76 (2H, m, H Ar); 7.88 (2H, d, *J* = 7.6, H Ar)	406
8a	1176, 1218, 1283, 1336, 1425, 1481, 1516, 1548, 1647, 1603; 3148, 3387 (NH_2)	7.63-7.73 (5H, m, H Ar, NH_2); 7.79 (1H, s, CH triazole); 7.88 (2H, d, *J* = 6.8, H Ar)	317
8b	1137, 1174, 1217, 1280, 1332, 1428, 1492, 1516, 1551, 1609, 1647; 3160, 3391 (NH_2)	2.42 (3H, s, CH_3); 7.46 (2H, d, *J* = 7.6, H Ar); 7.70 (2H, s, NH_2); 7.78 (1H, s, CH triazole); 7.92 (2H, d, *J* = 7.6, H Ar)	331
9a	1071, 1263, 1280, 1360, 1563, 1521, 1675, 2924; 3116, 3301 (NH_2)	2.42 (3H, s, CH_3); 6.15 (1H, s, CH pyrazole); 7.60-7.62 (5H, m, H Ar); 8.09-8.11 (2H, m, H Ar); 8.63 (2H, br. s, NH_2)	266
9b	1051, 1262, 1282, 1362, 1446, 1560, 1612, 1681; 3153, 3306 (NH_2)	6.86 (1H, s, CH pyrazole); 7.45-7.52 (3H, m, H Ar); 7.62-7.64 (3H, m, H Ar); 8.10-8.13 (4H, m, H Ar); 8.77 (2H, br. s, NH_2)	328
9c	1047, 1265, 1280, 1361, 1501, 1563, 1621, 1677, 2919; 3126, 3303 (NH_2)	2.34 (3H, s, CH_3); 2.36 (3H, s, CH_3); 6.14 (1H, s, CH pyrazole); 7.40 (2H, d, *J* = 7.6, H Ar); 7.99 (2H, d, *J* = 7.6, H Ar); 8.64 (2H, br. s, NH_2)	280
9d	1051, 1262, 1361, 1442, 1502, 1562, 1620, 1675; 3139, 3299 (NH_2)	2.42 (3H, s, CH_3); 6.86 (1H, s, CH pyrazole); 7.43-7.55 (5H, m, H Ar); 8.08 (2H, d, *J* = 7.6, H Ar); 8.12 (2H, d, *J* = 7.6, H Ar); 8.72 (2H, br. s, NH_2)	342
10a	1044, 1277, 1372, 1409, 1478, 1543, 1599, 1679; 3334 (NH_2)	7.63 (3H, s, H Ar); 8.14 (2H, s, H Ar); 8.42 (1H, s, CH triazole); 8.97 (2H, br. s, NH_2)	253
10b	1045, 1224, 1280, 1412, 1543, 1598, 1682, 2925; 3092, 3345 (NH_2)	2.41 (3H, s, CH_3); 7.41 (2H, d, *J* = 7.6, H Ar); 8.01 (2H, d, *J* = 7.6, H Ar); 8.45 (1H, s, CH triazole); 9.15 (2H, br. s, NH_2)	267

Compound 5c. ^{13}C NMR spectrum, δ, ppm: 14.0 (CH_3); 21.4 (CH_3); 89.4; 110.1; 119.1 (CN); 121.0; 127.5; 130.3; 144.4; 148.8; 152.9; 158.3; 164.3.

5-[(5-Amino-1*H*-1,2,4-triazol-1-yl)sulfonyl]-2-aryl-1,3-oxazole-4-carbonitriles 8a,b (General Method) were obtained similar to oxazoles **5a-d** from sulfonyl chlorides **1a**,**b** and 5-amino-1*H*-1,2,4-triazole.

Compound 8a. ^{13}C NMR spectrum, δ, ppm: 110.0; 120.1 (CN); 123.8; 127.7; 129.7; 133.8; 148.2; 154.4; 157.5; 164.5.

6-R-2-Aryl[1,3]oxazolo[5,4-*d*]pyrazolo[1,5-*a*]pyrimidin-9-amines 9a-d (General Method). NaH (0.048 g, 2 mmol) was added with stirring to a solution of oxazole **5a-d (**2 mmol) in anhydrous THF (15 ml). The reaction mixture was stirred for 2 h at 20-25°C. The temperature was then raised to 50-60°C. The mixture

was maintained at this temperature for 0.5 h. The suspension was left overnight and then treated with water (20 ml). The precipitate formed was filtered off, washed with water (10 ml), dried, and purified by recrystallization.

Compound 9a. ^{13}C NMR spectrum, δ, ppm: 14.7 (CH_3); 92.5; 105.2; 126.6; 129.5; 131.5; 142.0; 144.3; 148.0; 154.0; 156.7; 160.2.

Compound 9c. ^{13}C NMR spectrum, δ, ppm: 14.7 (CH_3); 21.2 (CH_3); 92.4; 105.2; 123.9; 126.6; 130.0; 141.6; 141.8; 148.0; 153.9; 157.0; 160.2.

2-Aryl[1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-9-amines 10a,b (General Method) were obtained analogously to pyrimidinamines **9a-d** from oxazoles **8a**,**b.**

Compound 10a. ^{13}C NMR spectrum, δ, ppm: 107.9; 126.6; 127.2; 129.8; 132.2; 143.4; 154.3; 155.0; 158.3; 163.2.

X-ray structural study of compounds 5b, 8a, 9d, and 10b was carried out at room temperature on a Bruker Smart Apex II diffractometer with λMoKα radiation and a graphite monochromator. The structures were solved by the direct method and refined by the method of least squares using the Bruker SHELXTL programs [32].

The unit cell parameters for orthorhombic crystals of compound **5b** ($C_{19}H_{13}N_5O_3S$, *M* 391.4), space group *Pbcn*: *a* 21.1512(7), *b* 11.4815(4), *c* 14.6393(5) Å; *V* 3555.1(2) Å^3; *Z* 8; d_{calc} 1.463 g/cm^3; μ 0.215 mm^{-1}; *F*(000) 1616. We used a monocrystal of compound **5b** with linear dimensions 0.10×0.11×0.1 mm. A set of 33272 reflections was recorded (θ_{max} 26.49°, sphere segment $-26 \le h \le 25$, $-14 \le k \le 14$, $-18 \le l \le 18$), of which 3676 reflections were independent (R_{int} 0.0585). A correction for absorption was introduced by the multiscanning method using the SADABS program (T_{min}/T_{max} = 0.7570/0.9697). The hydrogen atoms were determined objectively from the Fourier difference map and refined isotropically. A total of 2454 reflections with $I > 2\sigma(I)$ were used in the refinement (306 refined parameters, 8.0 reflections per parameter). We used the weighting scheme $\omega = 1/[\sigma^2(F_o^2) + (0.0212P)^2 + 3.088P]$, where $P = (F_o^2 + 2F_c^2)/3$. The final probability factors: $R_1(F)$ 0.0418, $wR_2(F^2)$ 0.0781 for reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0771, $wR_2(F^2)$ 0.0925, *GOOF* 0.973 over all reflections. A correction for isotropic extinction 0.00143(15) was taken into account. The residual electron density from the Fourier difference map after the final refinement cycle was 0.22 and -0.35 e/Å^3. The complete crystallographic data set was deposited at the Cambridge Crystallographic Data Center (CCDC deposit 919590).

The unit cell parameters of monoclinic crystals of oxazole **8a** ($C_{12}H_8N_6O_3S$, *M* 316.30), space group $P2_1/n$: *a* 9.5927(6), *b* 11.6543(7), *c* 12.3822(8) Å; β 103.073(3)°; *V* 1348.41(15) Å^3; *Z* 4; d_{calc} 1.558 g/cm^3; μ 0.264 mm^{-1}; *F*(000) 648. We used a monocrystal of compound **8a** with linear dimensions 0.10×0.11×0.10 mm. A set of 18299 reflections was recorded (θ_{max} 26.54°, sphere segment $-11 \le h \le 12$, $-14 \le k \le 14$, $-15 \le l \le 14$), of which 2800 reflections were independent (R_{int} 0.0355). A correction for absorption was introduced using the multi-scanning method with the SADABS program (T_{min}/T_{max} = 0.8487/0.9741). The hydrogen atoms were found objectively from the Fourier difference map and refined isotropically. A total of 2227 reflections with $I > 2\sigma(I)$ were used in the refinement (231 refined parameters, 9.6 reflections per parameter). We used the weighting scheme $\omega = 1/[\sigma^2(F_o^2) + (0.0423P)^2 + 0.6192P]$, where $P = (F_o^2 + 2F_c^2)/3$. The final probability factors $R_1(F^2)$ 0.0367, $wR_2(F^2)$ 0.0866 for reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0511, $wR_2(F^2)$ 0.0965, *GOOF* 1.043 for all the reflections. The residual electron density from the Fourier difference map after the final refinement cycle was 0.21 and -0.38 e/Å^3. The complete crystallographic data set was deposited at the Cambridge Crystallographic Data Center (CCDC deposit 919588).

The unit cell parameters of monoclinic crystals of pyrimidinamine **9d** ($C_{20}H_{15}N_5O$, *M* 341.37), space group *C*2/*c*: *a* 36.3582(10), *b* 7.2706(3), *c* 12.9087(4) Å; β 105.637(2)°; *V* 3286.07(19) Å^3; *Z* 8; d_{calc} 1.38 g/cm^3; μ 0.09 mm^{-1}; *F*(000) = 1424. We used a monocrystal of compound **9d** with linear dimensions 0.50×0.20×0.14 mm. A set of 16806 reflections was recorded (θ_{max} 27.48°, sphere segment $-46 \le h \le 46$, $-9 \le k \le 9$, $-16 \le l \le 16$), of which 3781 reflections were independent (R_{int} 0.0528). A correction for absorption was introduced using the multiscanning method with the SADABS program (T_{min}/T_{max} = 0.7541/0.9875). The positions of the hydrogen atoms at the carbon

atoms were calculated geometrically and refined using the rider model, while the positions of the hydrogen atoms at the N(5) atom were found objectively from the Fourier difference map and refined isotropically. A total of 2412 reflections with $I > 2\sigma(I)$ were used in the refinement (243 refined parameters, 9.9 reflections per parameter). We used the weighting scheme $\omega = 1/[\sigma^2(F_o^2) + (0.0579P)^2 + 0.1453P]$, where $P = (F_o^2 + 2F_c^2)$. The final probability factors $R_1(F)$ 0.0498, $wR_2(F^2)$ 0.1127 for reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0874 and $wR_2(F^2)$ 0.1253, *GOOF* 1.039 for all the reflections. The residual electron density from the Fourier difference map after the final refinement cycle was 0.20 and -0.23 e/Å^3. The complete crystallographic data set was deposited at the Cambridge Crystallographic Data Center (CCDC deposit 953028).

The unit cell parameters of monoclinic crystals of pyrimidinamine **10b** ($C_{13}H_{10}N_6O$, *M* 266.27), space group $P2_1/n$: *a* 8.1949(4), *b* 10.5929(5), *c* 14.0631(7) Å; β 104.350(3)°; *V* 1182.7(1) Å^3; *Z* 4; d_{calc} 1.495 g/cm^3; μ 0.103 mm^{-1}; *F*(000) 552. We used a monocrystal of compound **10b** with linear dimensions 0.11×0.14×0.31 mm. A set of 11449 reflections was recorded (θ_{max} 26.65°, sphere segment $-10 \le h \le 10$, $-13 \le k \le 13$, $-17 \le l \le 17$), of which 2480 were independent (R_{int} 0.0632). A correction for absorption was introduced using the multiscanning method with the SADABS program (T_{min}/T_{max} = 0.7541/0.9887). The positions of the hydrogen atoms at the carbon atoms were calculated geometrically and refined using the rider model, while the positions of the hydrogen atoms at the N(6) atom were found objectively from the Fourier difference map and refined isotropically. A total of 1497 reflections with $I > 2\sigma(I)$ were used in the refinement (201 refined parameters, 7.44 reflections per parameter). We used the weighting scheme $\omega = 1/[\sigma^2(F_o^2) + (0.0524P)^2 + 0.061P]$, where $P = (F_o^2 + 2F_c^2)/3$. The final probability factors $R_1(F)$ 0.0509, $wR_2(F^2)$ 0.1003 for the reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.1021, $wR_2(F^2)$ 0.1196, *GOOF* 1.003 for all the independent reflections. The residual electron density from the Fourier difference map after the final refinement cycle was 0.17 and -0.24 e/Å^3. The complete crystallographic data set was deposited at the Cambridge Crystallographic Data Center (CCDC deposit 971133).

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