ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 7, pp. 1066–1073. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © A.V. Bentya, R.I. Vas'kevich, A.V. Turov, E.B. Rusanov, M.V. Vovk, V.I. Staninets, 2011, published in Zhurnal Organicheskoi Khimii, 2011, Vol. 47, No. 7, pp. 1049–1056.

Synthesis of New Imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one Derivatives by Iodocyclization of 6-Alkenyl(alkynyl)-aminopyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones

A. V. Bentya[a], R. I. Vas'kevich[a], A. V. Turov[b], E. B. Rusanov[a], M. V. Vovk[a], and V. I. Staninets[a]

[a] *Institute of Organic Chemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 5, Kiev, 02660 Ukraine*
e-mail: bentya@gmail.com

[b] *Taras Shevchenko Kiev National University, Kiev, Ukraine*

Received May 4, 2010

Abstract—6-Allyl(diallyl, prop-2-yn-1-yl)amino-1-R-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones reacted with iodine to give angularly fused 8-iodomethyl-7,8-dihydro-1-R-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones which were treated with sodium acetate to obtain 8-methylidene-1-R-7,8-dihydroimidazo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidin-4(6*H*)-ones as a result of elimination of hydrogen iodide. 8-Methylidene-1-R-7,8-dihydro-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones were converted into 8-methyl-1-R-imidazo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidin-4(5*H*)-ones on heating to the melting point. 8-Methylidene-1-phenyl-7,8-dihydroimidazo-[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one underwent isomerization into linearly fused 6-methyl-1-phenyl-1,8-dihydro-4*H*-imidazo[1,2-*a*]pyrazolo[3,4-*d*]pyrimidin-4-one on heating in sulfuric acid.

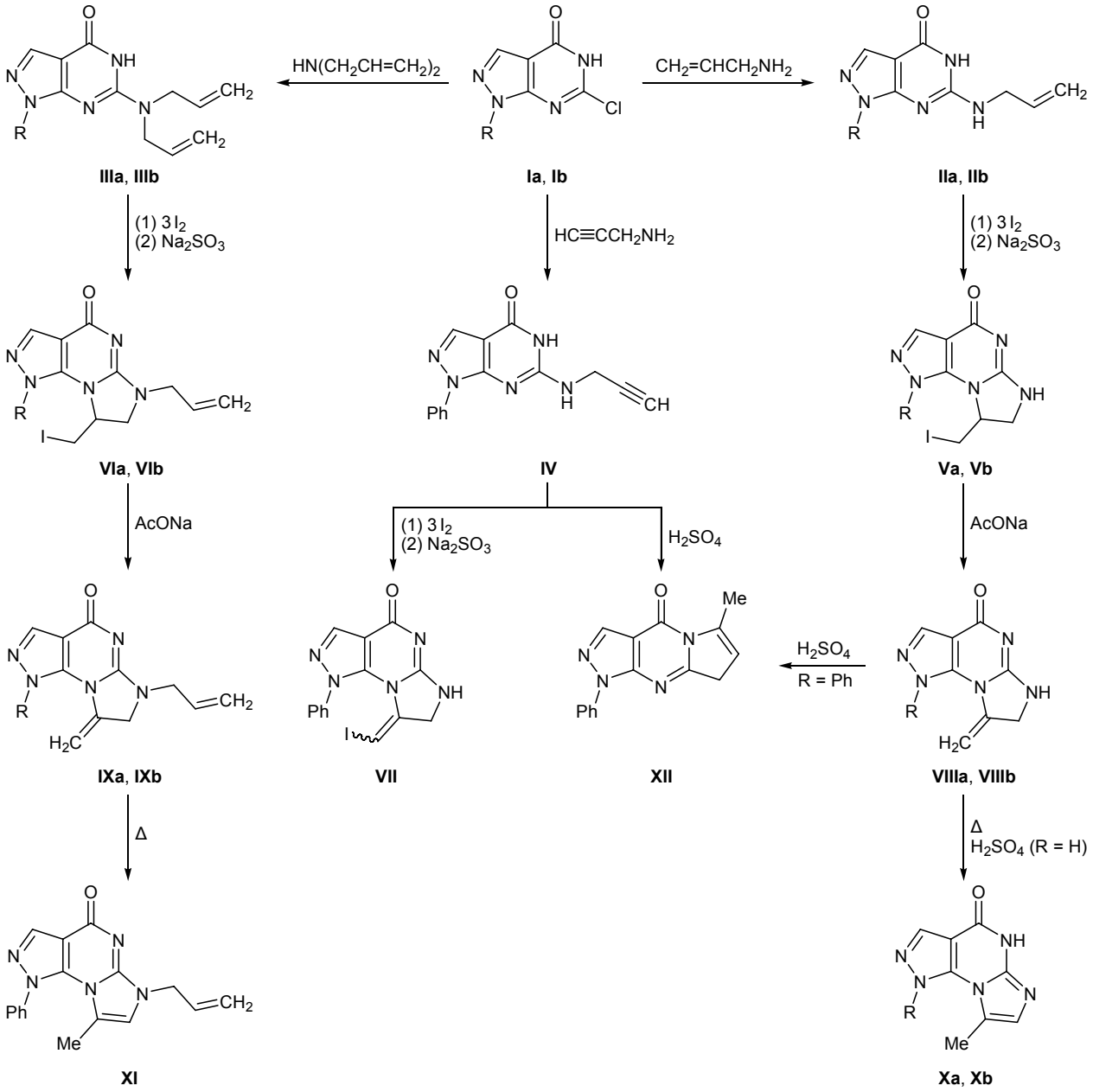
DOI: 10.1134/S1070428011070165

We previously showed [1, 2] that cyclization of 6-allyl(prop-2-yn-1-yl)sulfanylpyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones by the action of iodine or sulfuric acid provides a convenient method for the synthesis of 4*H*-pyrazolo[4,3-*e*]thiazolo[3,2-*a*]pyrimidin-4-one derivatives. Taking into account pronounced pharmacological effect of their bioisosters (in particular, imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidines are efficient phosphodiesterase inhibitors [3–6]), it seemed important to develop new preparatively simple procedures for the synthesis of such compounds. Known procedures [3, 7] generally include a number of steps and utilize difficultly accessible reagents. Furthermore, compounds having functional substituents in the imidazole ring cannot be obtained by the known methods, whereas the presence of such substituents is necessary for subsequent modifications with pharmacophoric fragments.

A promising synthetic approach to the desired compounds may be that based on electrophilic cyclization of pyrazolo[3,4-*d*]pyrimidines having allylamino or prop-2-yn-1-ylamino group in the 6-position. In the present work we used 6-chloropyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **Ia** and **Ib** as initial compounds to develop a convenient procedure for the synthesis of 6-allylamino-, 6-diallylamino-, and 6-(prop-2-yn-1-ylamino)-1-R-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones **II**–**IV** and studied in detail their cyclization by the action of iodine, as well as some interesting transformations of the cyclization products (Scheme 1).

The presence in molecules **II**–**IV** of two nucleophilic centers (N^5 and N^7) could give rise to formation of both angularly and linearly fused cyclization products. However, reactions of **II**–**IV** with 3 equiv of iodine in acetic acid at room temperature and subsequent treatment with sodium sulfite resulted in the formation of only angular 8-iodomethyl-substituted 1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones **Va**, **Vb**, **VIa**, **VIb**, and **VII**. Pyrazolopyrimidines **IIIa** and **IIIb** having two allyl groups on the exocyclic nitrogen atom reacted only at one allyl fragment. 6-Allyl derivatives **VIa** and **VIb** thus obtained were used as reference compounds for the determination of the position of hydrogen atom in compounds **Va**, **Vb**, and **VII** containing a guanidine fragment. The structure of compounds **Va**, **Vb**, **VIa**, **VIb**, and **VII** was

Scheme 1.



R = H (a), Ph (b).

confirmed by their IR and ^{1}H and ^{13}C NMR spectra. The IR spectra of these compounds displayed absorption bands due to carbonyl stretching vibrations in the region 1660–1600 cm^{-1}, which is consistent with their angular structure implying the presence of conjugated O=C–N= bond sequence in the pyrimidine ring. The carbonyl carbon atom resonated in the ^{13}C NMR spectra at δ_C 164–166 ppm [8].

Treatment of compounds **Va**, **Vb**, **VIa**, and **VIb** with an equimolar amount of sodium acetate in DMSO at 60°C led to the formation of 8-methylidene derivatives **VIIIa**, **VIIIb**, **IXa**, and **IXb** as a result of elimination of hydrogen iodide. Compound **VIIIb** characteristically showed in the ^{1}H NMR spectrum a large difference in the positions of signals from olefinic protons, one of which was displaced strongly upfield (δ 3.50 ppm) due to deshielding effect of the benzene ring on N^1 oriented orthogonally to the exocyclic double bond plane. Analogous shifts of olefinic proton signals were observed by us previously [1], and angu-

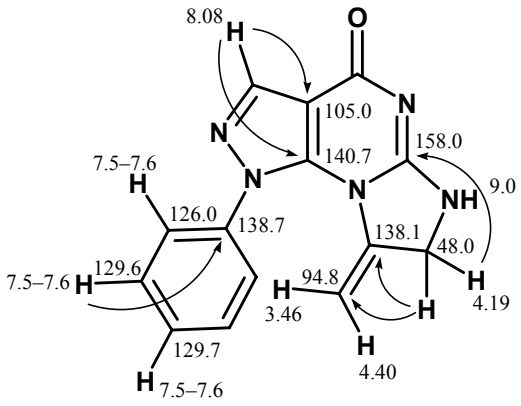


Fig. 1. Correlations in the HMBC spectrum of 8-methylidene-1-phenyl-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidin-4(6*H*)-one compound **VIIIb**.

lar structure of the corresponding cyclization product was proved by X-ray analysis. The positions of the carbonyl absorption band in the IR spectrum and of the C^4 signal in the ^{13}C NMR spectrum were almost similar. Reliable assignment of carbon signals in the ^{13}C NMR spectrum of **VIIIb** was made on the basis of heteronuclear ^1H–^{13}C correlations (HMQS and HMBC; see table and Fig. 1).

Heating of compounds **VIIIa** and **VIIIb** above their melting points (360 and 285°C, respectively) promoted 1,3-prototropic shifts in the allyl fragment in the imidazole ring and in the guanidine fragment of the imidazopyrimidine system, which resulted in the formation of isomeric 8-methyl-1R-imidazo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidin-4(5*H*)-ones **Xa** and **Xb**. The isomerization of compound **VIIIa** also occurred at room temperature in concentrated sulfuric acid. In the IR spectra of **Xa** and **Xb**, the carbonyl absorption band was observed at higher frequencies (1690–1685 cm^{-1}), and the carbonyl carbon signal in the ^{13}C NMR spectrum was displaced upfield by 8–10 ppm.

Cross peaks in the HMQC and HMBC spectra of 8-methylidene-1-phenyl-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo-[4,3-*e*]pyrimidin-4(6*H*)-one (**VIIIb**)

δ, ppm	δ_C, ppm	
	HMQC	HMBC
8.08	138.75	140.67, 105.05
7.55	129.73, 129.62, 126.03	138.75, 129.73, 129.61, 126.03
4.40	94.84	–
4.17	46.35	158.02, 138.14, 94.84
3.46	94.89	–

Compound **IXb** at 275°C was converted into imidazopyrazolopyrimidine **XI** via migration of the exocyclic double bond into the imidazole ring. The position of the carbonyl absorption band in the IR spectrum of **XI** did not differ considerably from that observed in the spectrum of **IXb**; it was located at 1615 cm^{-1}. The carbonyl carbon signal appeared in the ^{13}C NMR spectrum of **XI** at δ_C 163 ppm. Comparison of the IR and ^1H and ^{13}C NMR spectra of compound **XI** with those of **Xa** and **Xb** ensures fairly reliable interpretation of their structures.

Unlike unsubstituted analog **VIIIa**, compound **VIIIb** having a phenyl group on the nitrogen atom in the pyrazole ring underwent isomerization to linearly fused tricyclic structure **XII** in sulfuric acid at room temperature. The same product was also obtained by electrophilic cyclization of 6-(prop-2-yn-1-ylamino)-substituted pyrazolopyrimidine **IVb** by the action of concentrated sulfuric acid at 55°C. Compound **XII** displayed in the IR spectrum absorption band at 1710 cm^{-1} due to stretching vibrations of the carbonyl group. The chemical shift of the carbonyl carbon atom was equal to δ_C 155 ppm.

The structure of **XII** was unambiguously determined by X-ray analysis (Fig. 2). We have found no crystallographic data for representatives of this tricyclic system. Compounds containing particular fragments of such system were studied, e.g., in [9, 10]. The bond lengths and bond angles in the tricyclic fragment clearly indicate delocalization of electron density therein. The tricyclic skeleton is almost planar, the average deviation of atoms from the mean-square plane is as small as 0.023 Å, and the phenyl ring (C^9–C^{14}) is turned through a dihedral angle of 29° with respect to that plane. Molecules **XII** in crystal (Fig. 3) are linked to infinite chains along the *z* crystallographic axis by hydrogen bonds N^5–$H^{5n}\cdots O^{1'}$ with the following parameters: N^5–H^5 0.957(18), $N^5\cdots O^1$ 2.7375(16) Å, $\angle N^5H^5O^{1'}$ 162.7(15)° (the primed number corresponds to the oxygen atom in the neighboring molecule, which is related to the initial atoms through the symmetry transformation x, $-y + 1.5$, $z - 0.5$).

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 instrument. The ^1H NMR spectra were measured on a Varian VXR-300 spectrometer (300 MHz) using tetramethylsilane as internal reference. The ^{13}C NMR spectra were obtained on a Bruker Avance DRX-500

spectrometer (125.75 MHz), and the HMQC and HMBC spectra of compound **VIIIb** were recorded on a Varian Mercury-400 instrument (400 MHz for ^{1}H) from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectra of **VIIIa**, **IXa**, **IXb**, and **Xa** were obtained on an Agilent 1100/DAD/HSD/VLG119562 instrument.

The X-ray diffraction data for compound **XII** were acquired from a 0.08×0.20×0.41-mm single crystal at room temperature on a Bruker Smart Apex II diffractometer (λMoK_α irradiation, graphite monochromator, θ_{max} = 28.27°, spherical segment $-17 \le h \le 17$, $-9 \le k \le 9$, $-18 \le l \le 17$). Monoclinic crystal system, space group $P2_1/c$; unit cell parameters: a = 13.2138(6), b = 7.0193(3), c = 13.9798(6) Å; β = 112.473(2)°; V = 1198.18(9)Å^3; Z = 4; d_{calc} = 1.245 g/cm^3; μ = 0.082 mm^{-1}; F(000) = 884; $C_{14}H_{11}N_5O$; M 265.28. Total of 12369 reflections were measured, 2971 of which were independent (merging factor R = 0.0454). A correction for absorption was introduced using SADABS program (ratio of the minimal and maximal corrections T_{min}/T_{max} = 0.722666). The structure was solved by the direct method and was refined by the least-squares procedure in full-matrix anisotropic approximation using SHELXS97 and SHELXL97 software packages [11, 12]. Hydrogen atoms were visualized objectively, and their positions were refined in isotropic approximation. The refinement procedure involved 1996 reflections with $I > 2\sigma(I)$ (225 refined parameters, 8.87 reflections per parameter), and the weight scheme $\omega = 1/[\sigma^2(Fo^2) + (0.0551R)^2 + 0.0471P]$ was used, where $R = (Fo^2 + 2Fc^2)/3$ [ratio of the maximal (average) shift to the error in the last iteration 0.019 (0.001)]. The final divergence factors were $R_1(F)$ = 0.0436, $wR_2(F^2)$ = 0.0963 for reflections with $I > 2\sigma(I)$ and $R_1(F)$ = 0.0751, $wR_2(F^2)$ = 0.1101 for all reflections; goodness of fit 1.007. The residual electron density from the Fourier difference series after the last iteration was 0.15 and –0.25 e/Å^3. The X-ray diffraction data for compound **XII** were deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 771233).

6-Allyl(diallyl, prop-2-yn-1-yl)amino-1-R-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones IIa, IIb, IIIa, IIIb, and IV (*general procedure*). A mixture of 10 mmol of 6-chloropyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **Ia** or **Ib** and 40 mmol of prop-2-en-1-amine, *N*-(prop-2-en-1-yl)prop-2-en-1-amine, or prop-2-yn-1-amine in 15 ml of ethanol was heated for 4 h at 90–100°C in a sealed ampule. The mixture was cooled, and the precipitate was filtered off, washed with ethanol, and dried in air.

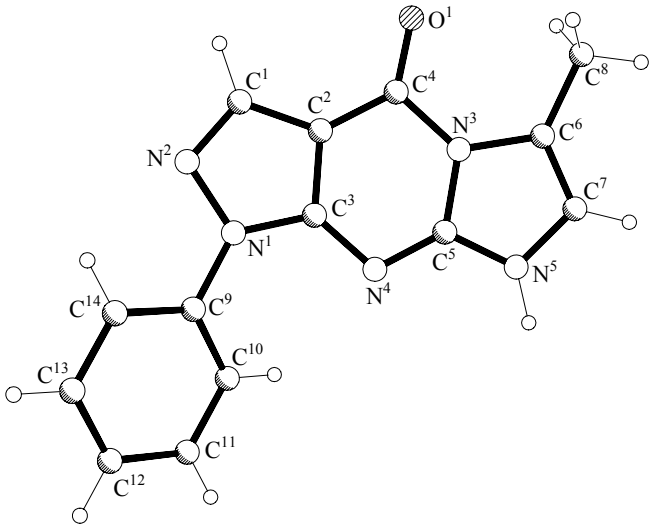


Fig. 2. Structure of the molecule of 6-methyl-1-phenyl-1,8-dihydro-4*H*-imidazo[1,2-*a*]pyrazolo[3,4-*d*]pyrimidin-4-one (**XII**) according to the X-ray diffraction data. Principal bond lengths (Å) and bond angles (deg): C^1–N^2 1.307(2), C^1–C^2 1.410(2), C^2–C^3 1.398(2), C^3–N^1 1.3685(18), N^1–N^2 1.3877(17), C^2–C^4 1.410(2), C^4–O^1 1.2306(16), C^4–N^3 1.4130(18), C^5–N^3 1.3906(17), C^5–N^4 1.3236(17), C^3–N^4 1.3468(17), C^6–N^3 1.4176(18), C^6–C^7 1.332(2), C^7–N^5 1.3802(19), C^5–N^5 1.3398(17); $C^2C^4N^3$ 111.03(12), $C^5N^3C^4$ 122.48(12), $N^4C^5N^3$ 127.10(12), $C^5N^4C^3$ 110.68(12), $N^4C^3C^2$ 127.55(13), $C^3C^2C^4$ 121.09(13).

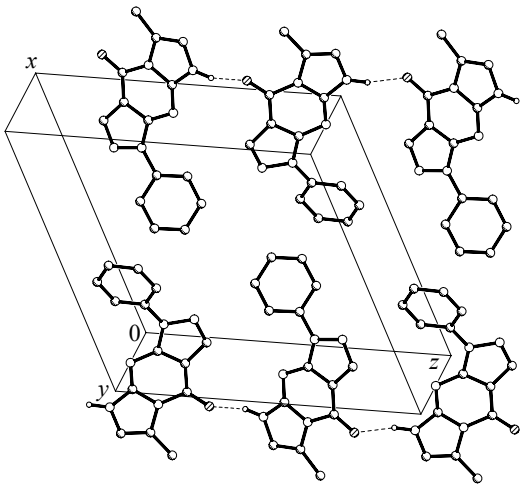


Fig. 3. A fragment of crystal packing of compound **XII**. Hydrogen-bonded chains of molecules along the z crystallographic axis are shown; hydrogen atoms (except for N^5–H) are not shown.

Compounds **IIb**, **IIIb**, and **IV** were additionally purified by recrystallization from ethanol.

6-(Prop-2-en-1-ylamino)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IIa). Yield 1.61 g (84%), mp 295–297°C. IR spectrum, ν, cm^{-1}: 3090 (NH), 1680 (C=O), 1600, 1520, 1370, 1300, 1130, 1080,

1010, 940, 830, 780, 720. ^{1}H NMR spectrum, δ, ppm: 3.93 t (2H, CH_2, J = 4.8 Hz), 5.12 d (1H, =CH, J = 10.2 Hz), 5.21 d (1H, =CH, J = 17.1 Hz), 5.86–5.99 m (1H, =CH), 6.54–6.63 m (1H, NH), 7.74 s (3-H), 10.42 s (1H, NH), 12.90 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 42.42 (CH_2), 99.39 (C^{3a}), 115.38 (=CH_2), 134.56 (C^3, =CH), 153.37 (C^{7a}) 155.88 (C^6), 157.89 (C^4). Found, %: C 50.44; H 4.86; N 36.39. $C_8H_9N_5O$. Calculated, %: C 50.26; H 4.74; N 36.63.

1-Phenyl-6-(prop-2-en-1-ylamino)-1*H*-pyrazolo-[3,4-*d*]pyrimidin-4(5*H*)-one (IIb). Yield 2.38 g (89%), mp 211–213°C (from ethanol). IR spectrum, ν, cm^{-1}: 3480, 3400, 3250, 3150 (NH), 1690 (C=O), 1620, 1590, 1550, 1500, 1400, 1290, 1110, 1060, 990, 960, 920, 830, 780, 750, 710. ^{1}H NMR spectrum, δ, ppm: 4.00 t (2H, CH_2, J = 5.4 Hz), 5.15 d (1H, =CH, J = 10.5 Hz), 5.27 d (1H, =CH, J = 17.1 Hz), 5.88–6.01 m (1H, =CH), 6.82–6.94 m (1H, NH), 7.30 t (1H, H_{arom}, J = 7.5 Hz), 7.51 t (2H, H_{arom}, J = 7.8 Hz), 8.04 s (3-H), 8.13 d (2H, H_{arom}, J = 7.8 Hz), 10.77 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 42.87 (CH_2), 101.17 (C^{3a}), 115.81 (=CH_2), 120.19 (2C, C_{arom}), 126.08 (C_{arom}), 128.73 (2C, C_{arom}), 134.42 (=CH), 135.83 (C^3), 139.00 (C_{arom}), 153.73 (C^{7a}), 154.24 (C^6), 157.58 (C^4). Found, %: C 62.84; H 4.87; N 26.18. $C_{14}H_{13}N_5O$. Calculated, %: C 62.91; H 4.90; N 26.20.

6-Bis(prop-2-en-1-yl)amino-1*H*-pyrazolo[3,4-*d*]-pyrimidin-4(5*H*)-one (IIIa). Yield 1.80 g (78%), mp 242–244°C. IR spectrum, ν, cm^{-1}: 3190, 3120 (NH), 1690 (C=O), 1600, 1410, 1320, 1290, 1260, 1070, 1010, 930, 770, 720. ^{1}H NMR spectrum, δ, ppm: 4.09–4.23 m (4H, CH_2), 5.11–5.24 m (4H, CH_2), 5.76–5.93 m (2H, CH), 7.80 s (3-H), 10.54 br.s (1H, NH), 12.94 br.s (1H, NH). Found, %: C 57.02; H 5.61; N 30.17. $C_{11}H_{13}N_5O$. Calculated, %: C 57.13; H 5.67; N 30.28.

6-Bis(prop-2-en-1-yl)amino-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (IIIb). Yield 2.70 g (88%), mp 190–192°C (from ethanol). IR spectrum, ν, cm^{-1}: 1710 (C=O), 1580, 1500, 1390, 1310, 1260, 1120, 960, 910. ^{1}H NMR spectrum, δ, ppm: 4.18–4.26 m (4H, CH_2), 5.18–5.26 m (4H, CH_2), 5.82–5.97 m (2H, CH), 7.31 t (1H, H_{arom}, J = 7.2 Hz), 7.52 t (2H, H_{arom}, J = 7.5 Hz), 8.07 s (3-H), 8.13 d (2H, H_{arom}, J = 8.1 Hz), 10.90 s (1H, NH). Found, %: C 66.33; H 5.46; N 22.64. $C_{17}H_{17}N_5O$. Calculated, %: C 66.43; H 5.58; N 22.79.

1-Phenyl-6-(prop-2-yn-1ylamino)-1*H*-pyrazolo-[3,4-*d*]pyrimidin-4(5*H*)-one (IV). Yield 2.23 g (84%), mp 242–244°C (from ethanol). IR spectrum, ν, cm^{-1}: 3460, 3280 (NH), 1690 (C=O), 1610, 1590, 1550, 1500, 1400, 1300, 1110, 1070, 980, 860, 780, 760, 720. ^{1}H NMR spectrum, δ, ppm: 3.20–3.25 m (1H, ≡CH), 4.11–4.20 m (2H, CH_2), 7.05–7.13 m (1H, NH), 7.33 t (1H, H_{arom}, J = 7.5 Hz), 7.52 t (2H, H_{arom}, J = 7.8 Hz), 8.08 s (3-H), 8.19 d (2H, H_{arom}, J = 7.8 Hz), 10.98 s (1H, NH). Found, %: C 63.22; H 4.06; N 26.39. $C_{14}H_{11}N_5O$. Calculated, %: C 63.39; H 4.18; N 26.40.

8-Iodomethyl-1-R-7,8-dihydroimidazo[1,2-*a*]-pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones Va and Vb and 6-allyl-8-iodomethyl-1-R-7,8-dihydroimidazo-[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones VIa and VIb (*general procedure*). A solution of 1.52 g (6 mmol) of iodine in 150 ml of acetic acid was added at room temperature to a suspension of 2 mmol of 6-allyl(diallyl)aminopyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one **IIa**, **IIb**, **IIIa**, or **IIIb** in 10 ml of acetic acid, and the mixture was stirred for 24 h. The solution was evaporated to dryness, 30 ml of acetonitrile was added to the residue (in the reactions with **IIa**, **IIIa**) or the salt-like precipitate was filtered off, washed with diethyl ether, and dissolved in 30 ml of acetonitrile (in the reactions with **IIb** and **IIIb**). The solution was treated under stirring with a 5% solution of sodium sulfite until brown color disappeared, the mixture was evaporated to 2/3 of the initial volume, and the precipitate was filtered off, washed with distilled water, and dried in air.

8-Iodomethyl-7,8-dihydro-1*H*-imidazo[1,2-*a*]-pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (Va). Yield 0.52 g (82%), mp 327–329°C. IR spectrum, ν, cm^{-1}: 3290 (NH), 1600 (C=O), 1500, 1460, 1340, 1270, 1180, 1120, 1020, 980, 850, 780. ^{1}H NMR spectrum, δ, ppm: 3.32–3.38 m (1H, CH), 3.71–3.74 m (1H, CH), 3.85–3.91 m (1H, CH), 3.95–4.00 m (1H, CH), 4.60–4.70 m (1H, CH), 8.19 s (3-H), 9.46–11.94 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 10.04 (CH_2I), 47.23 (C^7), 55.40 (C^8), 102.34 (C^{3a}), 128.21 (C^3), 148.29 (C^{9a}), 158.03 (C^{5a}), 165.85 (C^4). Found, %: C 30.21; H 2.46; I 39.96; N 22.03. $C_8H_8IN_5O$. Calculated, %: C 30.30; H 2.54; I 40.02; N 22.09.

8-Iodomethyl-1-phenyl-7,8-dihydro-1*H*-imidazo-[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (Vb). Yield 0.61 g (78%), mp 220–222°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 1580, 1420, 1330, 1280, 1230, 1170, 1050, 1030, 990, 960, 930, 780, 760. ^{1}H NMR spectrum, δ, ppm: 2.58–2.64 m (1H, CH), 2.77–2.81 m (1H, CH), 3.25–3.29 m (1H, CH), 3.79–3.86 m (1H, CH), 4.45–4.54 m (1H, CH), 7.59–7.77 m (5H, H_{arom}),

7.99 s (3-H), 8.26–9.15 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 7.50 (CH_2I), 46.35 (C^7), 56.59 (C^8), 103.06 (C^{3a}), 126.36 (2C, C_{arom}), 129.46 (2C, C_{arom}), 129.70 (C_{arom}), 137.26 (C^3, C_{arom}), 141.32 (C^{9a}), 157.25 (C^{5a}), 165.42 (C^4). Found, %: C 42.67; H 3.05; I 32.11; N 17.73. $C_{14}H_{12}IN_5O$. Calculated, %: C 42.77; H 3.08; I 32.28; N 17.81.

8-Iodomethyl-6-(prop-2-en-1-yl)-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (VIa). Yield 0.51 g (71%), mp 158–160°C. IR spectrum, ν, cm^{-1}: 3340, 2930 (NH), 1640 (C=O), 1590, 1530, 1510, 1440, 1410, 1370, 1330, 1270, 1180, 1080, 940, 780. ^{1}H NMR spectrum, δ, ppm: 3.33–3.38 m (1H, CH), 3.73–3.77 m (1H, CH), 3.84–3.90 m (1H, CH), 3.93–4.12 m (3H, CH), 4.59–4.66 m (1H, CH), 5.24 d (1H, =CH, *J* = 10.2 Hz), 5.34 d (1H, =CH, *J* = 17.1 Hz), 5.77–5.90 m (1H, CH), 8.18 s (3-H), 13.20 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 10.17 (CH_2I), 45.99 (CH_2), 51.04 (C^7), 52.98 (C^8), 102.76 (C^{3a}), 117.93 (=CH_2), 132.28 (C^3, =CH), 141.36 (C^{9a}), 156.55 (C^{5a}), 166.87 (C^4). Found, %: C 36.78; H 3.28; I 35.43; N 19.54. $C_{11}H_{12}IN_5O$. Calculated, %: C 36.99; H 3.39; I 35.53; N 19.61.

8-Iodomethyl-1-phenyl-6-(prop-2-en-1-yl)-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (VIb). Yield 0.81 g (93%), mp 235–237°C. IR spectrum, ν, cm^{-1}: 1660 (C=O), 1620, 1580, 1540, 1450, 1400, 1320, 1280, 1080, 980, 940, 780, 760, 740, 720. ^{1}H NMR spectrum, δ, ppm: 2.57–2.61 m (1H, CH), 2.80–2.84 m (1H, CH), 3.24–3.27 m (1H, CH), 3.81–3.87 m (1H, CH), 4.04 d (2H, CH_2, *J* = 5.4 Hz), 4.44–4.49 m (1H, CH), 5.25 d (1H, =CH, *J* = 10.2 Hz), 5.33 d (1H, =CH, *J* = 17.1 Hz), 5.77–5.91 m (1H, CH), 7.59–7.75 m (5H, H_{arom}), 8.00 s (3-H). ^{13}C NMR spectrum, δ_C, ppm: 7.49 (CH_2I), 46.39 (CH_2), 50.49 (C^7), 54.53 (C^8), 103.05 (C^{3a}), 118.38 (=CH_2), 126.25 (2C, C_{arom}), 129.46 (2C, C_{arom}), 129.79 (C_{arom}), 131.55 (=CH), 137.14 (C_{arom}), 137.27 (C^3), 141.36 (C^{9a}), 154.96 (C^{5a}), 164.87 (C^4). Found, %: C 47.01; H 3.66; I 29.16; N 16.12. $C_{17}H_{16}IN_5O$. Calculated, %: C 47.13; H 3.72; I 29.29; N 16.16.

8-Iodomethylidene-1-phenyl-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (VII). A solution of 1.52 g (6 mmol) of iodine in 150 ml of acetic acid was added at room temperature to a suspension of 0.53 g (2 mmol) of 6-(prop-2-yn-1-ylamino)pyrazolo[3,4-*d*]pyrimidin-4(*5H*)-one (**IV**) in 10 ml of acetic acid, and the mixture was stirred for 24 h. The salt-like precipitate was filtered off, washed with hexane, and dissolved in 30 ml of acetonitrile, and the solution was treated with a 5% solution of sodium sulfite until brown color disappeared. The mixture was evaporated to 2/3 of the initial volume, and the precipitate was filtered off, washed with water, dried in air, and transferred into 20 ml of acetic acid. The undissolved material was filtered off, the filtrate was evaporated, 20 ml of hexane was added to the residue, and the precipitate was filtered off and dried in air. Yield 0.65 g (83%), mp 199–201°C. IR spectrum, ν, cm^{-1}: 3430, 3020, 2810 (NH), 1670 (C=O), 1600, 1410, 1380, 1330, 1240, 1180. 1080, 970, 820, 780, 760, 740. ^{1}H NMR spectrum, δ, ppm: 4.12–4.17 m (2H, CH_2), 4.56–4.59 m (1H, =CHI), 7.51–7.61 m (5H, H_{arom}), 8.10 s (3-H), 8.82–9.94 br.s (1H, NH). ^{13}C NMR spectrum (CF_3COOD), δ_C, ppm: 52.56 (C^7), 64.61 (=CHI), 102.86 (C^{3a}), 125.73 (2C, C_{arom}), 130.32 (2C, C_{arom}), 131.72 (C^{9a}), 132.35 (C_{arom}), 136.16 (C^8), 139.38 (C^3, C_{arom}), 154.97 (C^{5a}), 156.17 (C^4). Found, %: C 43.25; H 2.72; I 32.75; N 18.08. $C_{14}H_{10}IN_5O$. Calculated, %: C 42.99; H 2.58; I 32.44; N 17.90.

8-Methylidene-1-R-7,8-dihydroimidazo[1,2-*a*]-pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones VIIIa and VIIIb and 6-allyl-8-methylidene-1-R-7,8-dihydro-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-ones IXa and IXb (*general procedure*). A mixture of 2 mmol of compound **Va**, **Vb**, **VIa**, or **VIb** and 0.25 g (3 mmol) of sodium acetate in 15 ml of dimethyl sulfoxide was stirred for 1h at 60°C. The mixture was evaporated under reduced pressure (2 mm, oil pump; in the reactions with **Va** and **VIa**) or cooled (in the reactions with **Vb** and **VIb**), 20 ml of water was added, and the precipitate was filtered off, washed in succession with ethanol and diethyl ether, and dried.

8-Methylidene-7,8-dihydro-1*H*-imidazo[1,2-*a*]-pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (VIIIa). Yield 0.28 g (74%), mp >360°C. IR spectrum, ν, cm^{-1}: 3270, 3130, 3080, 2910 (NH), 1640 (C=O), 1600, 1500, 1400, 1380, 1360, 1310, 1260, 1240, 1180, 850, 780. ^{1}H NMR spectrum, δ, ppm: 4.41 m (2H, CH_2), 4.73 m (1H, =CH), 5.60 m (1H, =CH), 8.31 s (3-H), 8.51–9.53 br.s (1H, NH), 12.97–13.92 br.s (1H, NH). Mass spectrum: *m*/*z* 190 $[M + 1]^+$. Found, %: C 50.63; H 3.58; N 36.99. $C_8H_7N_5O$. Calculated, %: C 50.79; H 3.73; N 37.02. *M* 189.18.

8-Methylidene-1-phenyl-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (VIIIb). Yield 0.41 g (77%), mp 325–328°C. IR spectrum, ν, cm^{-1}: 3100, 3040, 2800 (NH), 1660 (C=O), 1620, 1590, 1540, 1490, 1410, 1360, 1320, 1230, 1140, 960, 870, 780, 760. ^{1}H NMR spectrum, δ, ppm:

3.50 m (1H, =CH), 4.21 m (2H, CH_2), 4.42 m (1H, =CH), 7.47–7.65 m (5H, H_{arom}), 8.09 s (3-H), 9.02 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 45.72 (C^7), 93.81 (=CH_2), 104.25 (C^{3a}), 125.11 (2C, C_{arom}), 128.67 (C_{arom}), 128.77 (2C, C_{arom}), 137.44 (C_{arom}), 137.80 (C^3), 138.81 (C^{9a}), 139.88 (C^8), 157.06 (C^{5a}), 164.64 (C^4). Found, %: C 63.14; H 4.08; N 26.35. $C_{14}H_{11}N_5O$. Calculated, %: C 63.39; H 4.18; N 26.40.

8-Methylidene-6-(prop-2-en-1-yl)-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (IXa). Yield 0.26 g (57%), mp 244–246°C. IR spectrum, ν, cm^{-1}: 3110, 2900, 2820, 1660 (C=O), 1600, 1510, 1430, 1360, 1330, 1270, 1160, 1090, 990, 940, 830, 790. ^1H NMR spectrum, δ, ppm: 4.09 d (2H, CH_2, J = 5.7 Hz), 4.40 m (2H, CH_2), 4.80 m (1H, =CH), 5.23–5.32 m (2H, =CH_2), 5.64 m (1H, =CH), 5.81–5.94 m (1H, CH), 8.32 s (3-H), 13.48 s (1H, NH). Mass spectrum: m/z 230 $[M + 1]^+$. Found, %: C 57.55; H 4.71; N 30.38. $C_{11}H_{11}N_5O$. Calculated, %: C 57.63; H 4.84; N 30.55. M 229.24.

8-Methylidene-1-phenyl-6-(prop-2-en-1-yl)-7,8-dihydro-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (IXb). Yield 0.47 g (77%), mp 246–248°C. IR spectrum, ν, cm^{-1}: 1660 (C=O), 1610, 1560, 1520, 1410, 1350, 1310, 1280, 1240, 1170, 1130, 1070, 1000, 980, 940, 880, 780, 770. ^1H NMR spectrum, δ, ppm: 3.51–3.56 m (1H, =CH), 4.12 d (2H, CH_2, J = 5.4 Hz), 4.23 m (2H, CH_2), 4.49–4.53 m (1H, =CH), 5.24–5.34 m (2H, =CH_2), 5.78–5.94 m (1H, =CH), 7.47–7.64 m (5H, H_{arom}), 8.11 s (3-H). Mass spectrum: m/z 306 $[M + 1]^+$. Found, %: C 66.56; H 4.88; N 22.87. $C_{17}H_{15}N_5O$. Calculated, %: C 66.87; H 4.95; N 22.94. M 305.34.

8-Methyl-1R-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(5*H*)-ones Xa and Xb (*general procedure*). *a*. Compound **VIIIa** or **VIIIb**, 1 mmol, was heated for 5 min on a sand bath at 360°C (**VIIIa**) or 285°C (**VIIIb**). The resulting material was cooled and treated with 5 ml of diethyl ether, and the precipitate was filtered off. Compound **Xb** was purified by recrystallization from EtOH–DMSO.

b. A solution of 0.27 g (1 mmol) of compound **VIIIa** in 10 ml of sulfuric acid was left to stand for 8 h at room temperature. It was then poured onto ice and neutralized to pH 7 with 25% aqueous ammonia, and the precipitate was filtered off, washed with water, and dried.

8-Methyl-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(5*H*)-one (Xa). Yield 0.16 g (85%) (*a*), 0.14 g (74%) (*b*); mp >360°C. IR spectrum, ν, cm^{-1}: 3100, 1685, 1590, 1420, 1390, 1260, 1210, 1140, 930, 850, 800, 760, 710. ^1H NMR spectrum, δ, ppm: 2.56 s (3H, CH_3), 6.72 s (7-H), 8.60 s (3-H), 11.50–12.38 br.s (1H, NH), 13.22–14.15 br.s (1H, NH). Mass spectrum: m/z 190 $[M + 1]^+$. Found, %: C 50.68; H 3.67; N 36.95. $C_8H_7N_5O$. Calculated, %: C 50.79; H 3.73; N 37.02. M 189.18.

8-Methyl-1-phenyl-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(5*H*)-one (Xb). Yield 0.21 g (79%) (*a*), mp 336–338°C (from EtOH–DMSO). IR spectrum, ν, cm^{-1}: 2750 (NH), 1690 (C=O), 1630, 1590, 1550, 1500, 1450, 1410, 1380, 1140, 960, 770, 760, 700. ^1H NMR spectrum, δ, ppm: 1.36 s (3H, CH_3), 6.66 s (7-H), (1H, H_{arom}), 7.58–7.70 m (5H, H_{arom}), 8.28 s (3-H), 12.24 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 10.99 (CH_3), 104.21 (C^{3a}), 119.93 (C^{9a}), 126.85 (C^7), 127.88 (2C, C_{arom}), 129.56 (2C, C_{arom}), 130.40 (C_{arom}), 137.87 (C^3), 139.92 (C^8), 140.83 (C_{arom}), 144.10 (C^{5a}), 156.39 (C^4). Found, %: C 63.23; H 4.11; N 26.32. $C_{14}H_{11}N_5O$. Calculated, %: C 63.39; H 4.18; N 26.40.

8-Methyl-1-phenyl-6-(prop-2-en-1-yl)-1*H*-imidazo[1,2-*a*]pyrazolo[4,3-*e*]pyrimidin-4(6*H*)-one (XI). Compound **IXb**, 0.31 g (1 mmol), was heated for 5 min on a sand bath at 275°C, cooled to room temperature, and treated with 5 ml of diethyl ether, and the precipitate was filtered off and recrystallized from ethanol. Yield 0.28 g (91%), mp 307–309°C (from EtOH). IR spectrum, ν, cm^{-1}: 1615 (C=O), 1560, 1490, 1420, 1250, 1120, 1050, 1010, 980, 940, 770, 740, 700. ^1H NMR spectrum, δ, ppm: 1.39 s (3H, CH_3), 4.56 d (2H, CH_2, J = 5.4 Hz), 5.14–5.26 m (2H, =CH_2), 5.90–6.05 m (1H, =CH), 7.02 s (7-H), 7.60–7.68 m (5H, H_{arom}), 8.15 s (3-H). ^{13}C NMR spectrum, δ_C, ppm: 11.42 (CH_3), 46.26 (CH_2), 106.73 (C^{3a}), 115.76 (C^7), 117.61 (=CH_2), 117.94 (C^8), 127.75 (2C, C_{arom}), 129.39 (2C, C_{arom}), 130.08 (C_{arom}), 132.07 (C^3), 137.11 (=CH), 140.11 (C_{arom}), 140.27 (C^{9a}), 148.05 (C^{5a}), 163.07 (C^4). Found, %: C 66.78; H 4.83; N 22.85. $C_{17}H_{15}N_5O$. Calculated, %: C 66.87; H 4.95; N 22.94.

6-Methyl-1-phenyl-1,8-dihydro-4*H*-imidazo[1,2-*a*]pyrazolo[3,4-*d*]pyrimidin-4-one (XII). *a*. A solution of 0.27 g (1 mmol) of compound **VIIIa** in 10 ml of concentrated sulfuric acid was kept for 6 h at room temperature. It was then poured onto ice and neutralized to pH 7 with 25% aqueous ammonia, and the precipitate was filtered off, washed with water, and dried.

b. A solution of 0.27 g (1 mmol) of compound **IV** in 10 ml of concentrated sulfuric acid was heated for 6 h

at 55°C. The mixture was then treated as described above in *a*. Yield 0.21 g (78%) (*a*), 0.23 g (87%) (*b*); mp 349–351°C (from DMSO). IR spectrum, ν, cm^{-1}: 3100, 2980, 2810 (NH), 1710 (C=O), 1610, 1540, 1460, 1400, 1250, 1210, 1150, 1100, 1060, 980, 910, 820, 790, 760, 700. ^{1}H NMR spectrum, δ, ppm: 2.63 s (3H, CH_3), 7.10 s (7-H), 7.33 t (1H, H_{arom}, J = 7.8 Hz), 7.54 t (2H, H_{arom}, J = 7.8 Hz), 8.17 d (2H, H_{arom}, J = 8.4 Hz), 8.23 s (3-H), 12.00–12.69 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.28 (CH_3), 101.29 (C^{3a}), 114.00 (C^7), 120.90 (C^6), 121.03 (2C, C_{arom}), 126.37 (C_{arom}), 129.67 (2C, C_{arom}), 137.07 (C^3), 139.84 (C_{arom}), 149.28 (C^{8a}), 153.97 (C^{9a}), 155.67 (C^4). Found, %: C 63.29; H 4.17; N 26.37. $C_{14}H_{11}N_5O$. Calculated, %: C 63.39; H 4.18; N 26.40.

REFERENCES

1. Bentya, A.V., Vas'kevich, R.I., Bol'but, A.V., Vovk, M.V., Staninets, V.I., Turov, A.V., and Rusanov, E.B., *Russ. J. Org. Chem*., 2008, vol. 44, p. 1362.
2. Bentya, A.V., Vas'kevich, R.I., and Staninets, V.I., *Ukr. Khim. Zh*., 2008, vol. 74, no. 12, p. 94.
3. Xia, Y., Chackalamannil, S., Czarniecki, M., Tsai, H., Vaccaro, H., Cleven, R., Cook, J., Fawzi, A., Watkins, R., and Zhang, H., *J. Med. Chem*., 1997, vol. 40, p. 4372.
4. Beavo, J.A., *Physiol. Rev*., 1995, vol. 75, p. 725.
5. Syberts, E.J., Czarniecki, M., and Ahn, H.-S., *Curr. Pharm. Des*., 1995, vol. 1, p. 373.
6. Syberts, E.J. and Ahn, H.-S., *Annu. Rep. Med. Chem*., 1996, vol. 31, p. 61.
7. Jiang, M.X-W., Warshakoon, N.C., and Miller, M.J., *J. Org. Chem*., 2005, vol. 70, p. 2824.
8. Shawali, A.S. and Gomha, S.M., *Tetrahedron*, 2002, vol. 58, p. 8559.
9. Suwinska, K., Golankiewicz, B., and Zielenkiewicz, W., *Acta Crystallogr., Sect. C*, 2001, vol. 57, p. 767.
10. Hong-Qing Wang, Zhao-Jie Liu, and Ming-Wu Ding, *Phosphorus, Sulfur Silicon Relat. Elem*., 2004, vol. 179, p. 2039.
11. Sheldrick, G.M., *SHELXS97. Program for the Solution of Crystal Structure*, Göttingen, Germany: Univ. of Göttingen, 1997.
12. Sheldrick, G.M., *SHELXL97. Program for the Refinement of Crystal Structures*, Göttingen, Germany: Univ. of Göttingen, 1997.