ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 3, pp. 410–416. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © D.V. Kryl'skii, Kh.S. Shikhaliev, A.S. Chuvashlev, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 3, pp. 416–422.

Three-Component Condensations with 5-Amino-4-phenylpyrazole

D. V. Kryl'skii, Kh. S. Shikhaliev, and A. S. Chuvashlev

Voronezh State University, Universitetskaya pl. 1, Voronezh, 394006 Russia
e-mail: alextsh@yandex.ru

Received November 19, 2008

Abstract—Three-component condensation of 3-methyl(or methoxymethyl)-4-phenyl-1*H*-pyrazol-5-amine with triethyl orthoformate and carbonyl compounds or nitriles containing an activated methylene group (cyclohexane-1,3-diones, acetoacetanilides, benzoylacetone, ethyl cyanoacetate, malononitrile, 1*H*-benzimidazol-2-ylacetonitrile) gave substituted pyrazolopyrimidines and pyrazoloquinazolines.

DOI: 10.1134/S107042801003019X

Heterocyclic compounds containing a pyrazole ring attract interest due to broad spectrum of their biological activity. Fused systems incorporating a pyrazole fragment are commonly synthesized from 3(5)-aminopyrazoles that are convenient building blocks in the preparation of pyrazolopyrimidines, pyrazolopyridines, and pyrazolotriazines [1, 2].

Synthetic approaches to fused pyrazole derivatives are based mainly on reactions of 3(5)-aminopyrazoles with various cyclizing agents. Examples of two-component cyclizations were reported in [1–7]. Three-component condensations with participation of aromatic aldehydes, cyclic diketones, and 3(5)-aminopyrazoles having no substituent in the 4-position were also described [8, 9]. In this case, the chemoselectivity problem arises. Komykhov et al. [10] reported on three-component condensation of *N*-aryl-3-aminopyrazole-4-carboxamides with aldehydes and *N*-arylacetoacetamides.

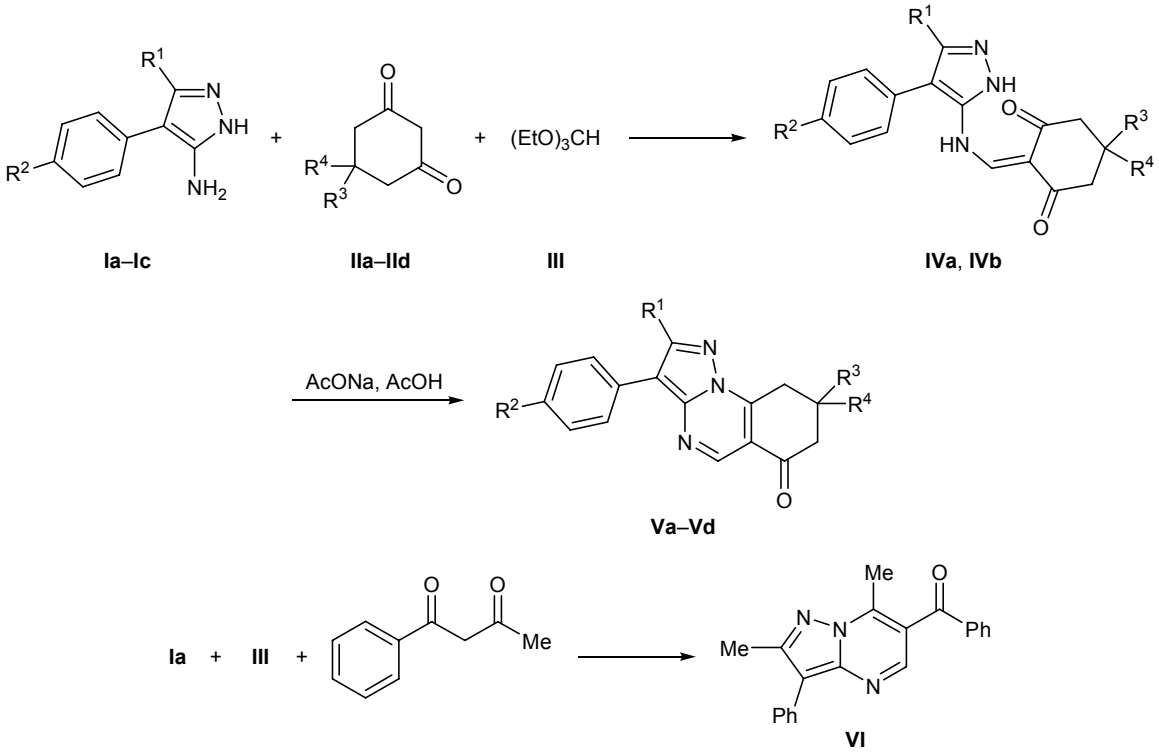
In the present work we examined three-component condensations of 3-substituted 4-phenyl-1*H*-pyrazol-5-amines with triethyl orthoformate and compounds possessing an activated methylene group (cyclic and linear dicarbonyl compounds and nitriles). Analogous reactions of hetarylguanidines were described in [11, 12].

By heating equimolar mixtures of aminopyrazoles **I** and cyclohexanediones **II** in boiling triethyl orthoformate **III** we obtained substituted 8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-ones **Va**–**Vd** (Scheme 1). The reaction involved intermediate formation of linear pyrazolylaminomethylidene derivatives **IV** which were isolated in some cases as individual substances (compounds **IVa**, **IVb**). In most cases, the crystalline product was a mixture of compounds **IV** and **V**, from which less soluble 5,5-R^3,R^4-2-{[(3-R^1-4-phenyl-1*H*-pyrazol-5-yl)amino]methylidene}cyclohexane-1,3-diones **IV** were isolated by recrystallization from a nonpolar solvent (xylene). Compounds **V** were isolated by heating mixtures **IV**/**V** in glacial acetic acid in the presence of anhydrous sodium acetate. Compounds **IV** were light yellow crystalline substances, and pyrazoloquinazolines **V** were light yellow substances with a greenish tint. The reaction of pyrazole **Ia** with triethyl orthoformate and benzoylacetone as dicarbonyl component gave in one step 2,7-dimethyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-6-yl(phenyl)methanone (**VI**).

Barbituric acid derivatives and 6-methyl-2*H*-pyran-2,4(3*H*)-dione reacted with compounds **Ia** and **Ic** and triethyl orthoformate (**III**) to give linear condensation products **VII** and **VIII** which failed to undergo intramolecular cyclization under analogous conditions (Scheme 2).

Compounds **IVa** and **IVb** characteristically displayed in the ^{1}H NMR spectra doublet signals from the CH= (δ 8.6–8.8 ppm) and NH protons (δ 12.6–12.9 ppm). Analogous pattern of signal splitting was observed previously in the spectra of linear products obtained by three-component condensation of hetarylguanidines with cyclohexanediones and ortho ester [1]. The mass spectrum of **IVa** contained a strong peak (I_{rel} 90%) from the molecular ion (*m*/*z* 323) and frag-

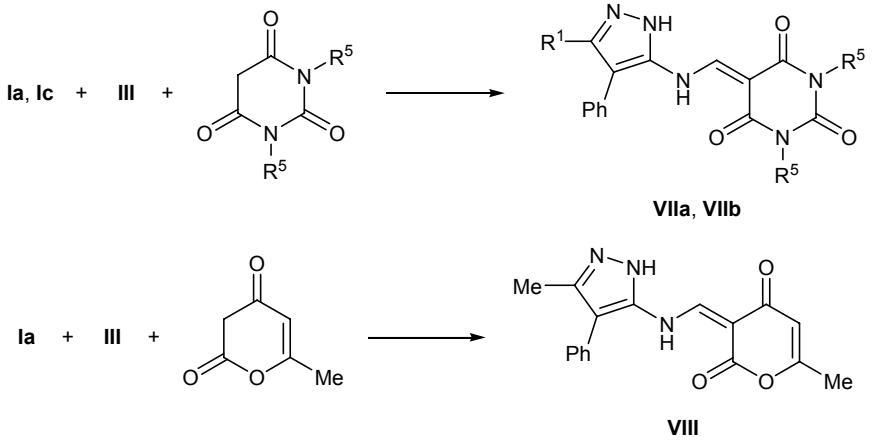
Scheme 1.



I, R^1 = Me, R^2 = H (**a**), F (**b**); R^1 = $MeOCH_2$, R^2 = H (**c**); **II**, R^3 = R^4 = Me (**a**); R^3 = H, R^4 = 2-furyl (**b**), 4-$MeOC_6H_4$ (**c**), 4-ClC_6H_4 (**d**); **IV**, R^1 = R^3 = R^4 = Me, R^2 = H (**a**); R^1 = Me, R^2 = R^3 = H, R^4 = 2-furyl (**b**); **V**, R^1 = R^3 = R^4 = Me, R^2 = H (**a**); R^1 = Me, R^2 = R^3 = H, R^4 = 2-furyl (**b**); R^1 = Me, R^2 = F, R^3 = H, R^4 = 4-$MeOC_6H_4$ (**c**); R^1 = $MeOCH_2$, R^2 = R^3 = H, R^4 = 4-ClC_6H_4 (**d**).

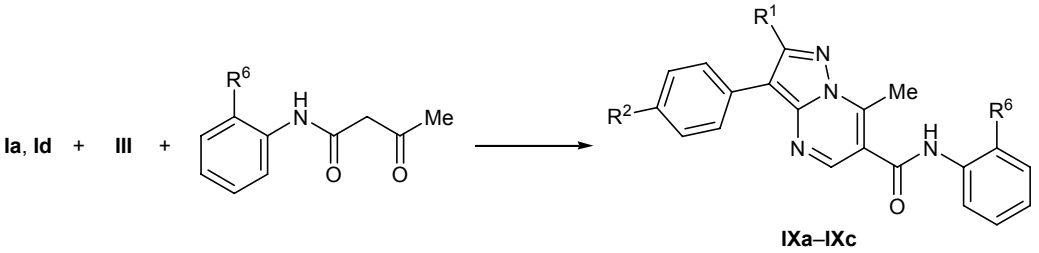
ment ion peaks with *m*/*z* 308, 282, 267, 252, 239, 224, etc. The base peak was that with *m*/*z* 184; it corresponds to methine derivative of aminopyrazole **Ia** at the amino group. In the aliphatic region of the ^{1}H NMR spectrum of **IVb** we observed a singlet at δ 2.30 ppm from the methyl group and a multiplet in the region δ 2.60–2.80 ppm from protons in the cyclohexanedione fragment. Two protons in the furan ring resonated at δ 6.06 and 6.28 ppm, and signal from the third proton in the furan ring was overlapped by aromatic multiplet at δ 7.26–7.52 ppm. The ^{1}H NMR spectra of compounds **Va**–**Vd** lacked doublet signals at δ 8.6–8.8 ppm, which are typical of CH= proton in **IV**, and no downfield signals assignable to NH protons were present

Scheme 2.



VII, R^1 = $MeOCH_2$, R^5 = H (**a**); R^1 = R^5 = Me (**b**).

Scheme 3.



I, R^1 = Me, R^2 = H (**a**), Cl (**d**); **IX**, R^1 = Me, R^2 = H, R^6 = Me (**a**), F_3C (**b**), MeO (**c**).

(δ 12.6–12.9 ppm). Instead, a singlet appeared at δ 8.7–8.9 ppm due to proton in the fused pyrimidine ring (5-H). In the ^{1}H NMR spectrum of **VIIa** and **VIIb**, the doublet signal from the endocyclic NH proton was located in a stronger field (δ 11.9–12.0 ppm).

The reaction of aminopyrazoles **Ia** and **Id** with acetoacetanilides and triethyl orthoformate afforded 2-R^1-7-methyl-*N*,3-diphenylpyrazolo[1,5-*a*]pyrimidine-6-carboxamides **IX**a–**IXc** (Scheme 3). Presumably, the first step of the process is formation of ethoxymethylidene derivative at the activated methylene group of acetoacetanilide. Its subsequent reaction at the amino group in aminopyrazole **I** is accompanied by elimination of ethanol molecule, follwed by closure of pyrimidine ring. Compounds **IX**a–**IXc** were isolated as yellow crystalline substances which are soluble in dimethylformamide and poorly soluble in most other organic solvents.

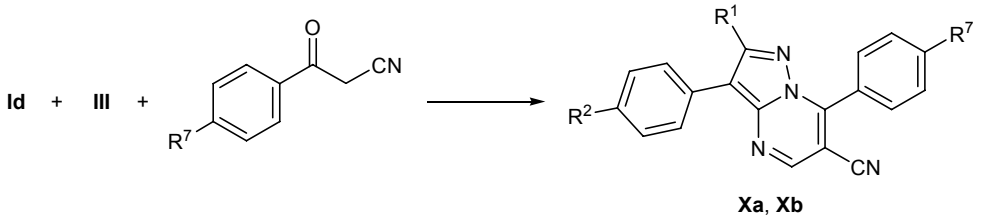
When aroylacetonitriles were used as carbonyl component with an activated methylene group, the condensation products were 3-aryl-2-R^1-7-phenylpyrazolo[1,5-*a*]pyrimidine-6-carbonitriles **Xa** and **Xb** (Scheme 4). The mass spectrum of compound **Xa** contained a strong peak from the molecular ion, *m*/*z* 344 (I_{rel} 85%). Other nitriles with an activated methylene group, namely ethyl cyanoacetate, malononitrile, and 1*H*-benzimidazol-2-ylacetonitrile, were involved in three-component condensation with aminopyrazole **Ia** and triethyl orthoformate (**III**) (Scheme 5). The reactions were carried out by heating the reactants under reflux in excess ortho ester **III** over a period of 15–30 min; the products were crystalline compounds **XI**, **XII**, and **XIV**.

Compound **XI** displayed in the ^{1}H NMR spectrum a set of signals typical of ethoxy group; splitting of the NH signal into two slightly broadened singlets at δ 8.42 and 8.53 ppm indicated imino structure **B** of this compound. By contrast, compound **XII** is likely to exist as the corresponding amino tautomer, as follows from the presence of a one-proton singlet at δ 8.31 ppm (5-H) and slightly broadened singlet from two NH_2 protons at δ 8.94 ppm. By heating 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carbonitrile (**XII**) in formamide for 10 h we obtained 8-methyl-7-phenylpyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidin-4-amine (**XIII**). Unlike compound **XII**, the ^{1}H NMR spectrum of **XIII** contained an additional signal at δ 9.14 ppm due to proton on C^2. Compound **XIV** gave rise to strong molecular ion peak in the mass spectrum, *m*/*z* 340 (I_{rel} 90 %), while no IR absorption band was observed at 2200 cm^{-1}, in keeping with its cyclic structure.

EXPERIMENTAL

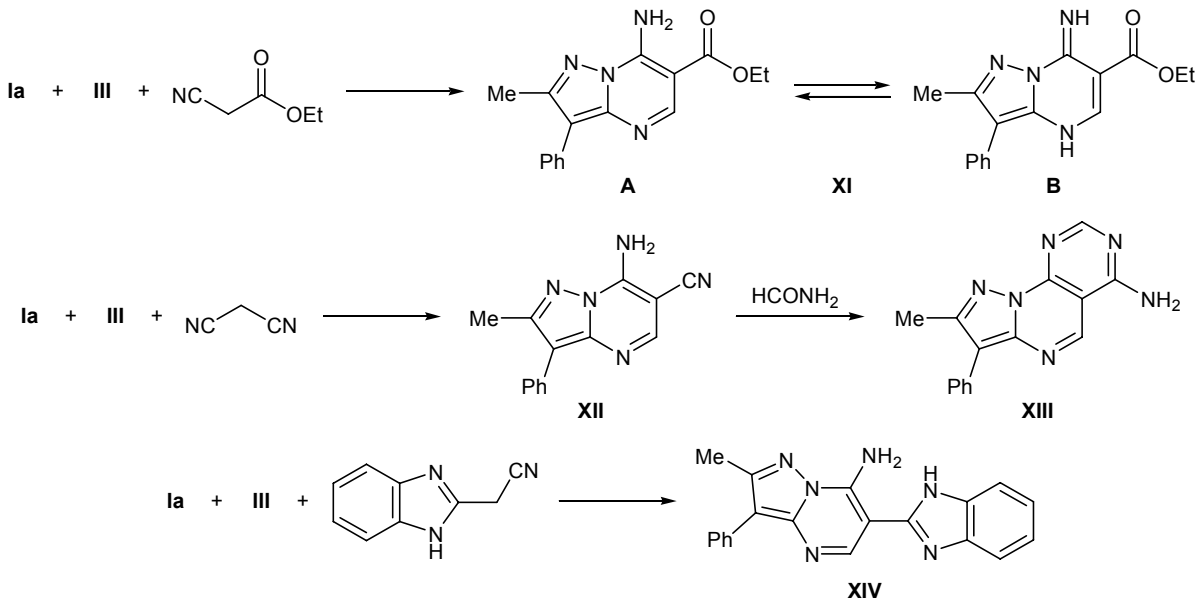
The progress of reactions was monitored, and the purity of the products was checked, by TLC on Silufol UV-254 plates. The ^{1}H NMR spectra were recorded on a Bruker AC-300 (300 MHz) spectrometer from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV)

Scheme 4.



X, R^1 = Me, R^2 = Cl, R^7 = H (**a**), F (**b**).

Scheme 5.



were obtained on an LKB 9000 instrument. The IR spectra were measured in KBr on a Specord 75IR spectrometer.

Initial 3-substituted 4-phenyl-1*H*-pyrazol-5-amines were synthesized according to the procedure reported in [13].

5,5-Dimethyl-2-[(3-methyl-4-phenyl-1*H*-pyrazol-5-ylamino)methylidene]cyclohexane-1,3-dione (IVa). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia**, 1.44 g (0.01 mol) of 5,5-dimethylcyclohexane-1,3-dione (**IIa**, dimedone), and 2 ml of triethyl orthoformate (**III**) was heated for 15 min under reflux. The yellowish precipitate was filtered off, washed with propan-2-ol, and recrystallized from xylene. Yield 2.20 g (68%), mp 244–245°C. ^{1}H NMR spectrum, δ, ppm: 1.03 s (6H, CH_3), 2.22 s (3H, CH_3), 2.28 s (4H, CH_2), 7.30–7.56 m (5H, H_{arom}), 8.68 d (1H, =CH, J = 12 Hz), 12.60 s (1H, 1′-H), 12.81 d (1H, 5′-NH, J = 12 Hz). Mass spectrum: m/z 323 (I_{rel} 90%) $[M]^+$. Found, %: C 70.42; H 6.58; N 12.73. $C_{19}H_{21}N_3O_2$. Calculated, %: C 70.57; H 6.55; N 12.99. M 323.40.

5-(2-Furyl)-2-[(3-methyl-4-phenyl-1*H*-pyrazol-5-ylamino)methylidene]cyclohexane-1,3-dione (IVb) was synthesized in a similar way from 1.73 g (0.01 mol) of aminopyrazole **Ia** and 1.78 g (0.01 mol) of diketone **IIb**. Yield 2.56 g (71%), mp 236–238°C. ^{1}H NMR spectrum, δ, ppm: 2.30 s (3H, CH_3), 2.60–2.80 m (5H, CH, CH_2), 6.06 d (1H, C_4H_3O, J = 4.6 Hz), 6.28 s (1H, C_4H_3O), 7.28–7.52 m (6H, H_{arom}, C_4H_3O), 8.70 d (1H, =CH–, J = 12 Hz), 12.67 s (1H, 1′-H), 12.84 d (1H, 5′-NH, J = 12 Hz). Found, %: C 69.90; H 5.35; N 11.76. $C_{21}H_{19}N_3O_3$. Calculated, %: C 69.79; H 5.30; N 11.63.

2,8,8-Trimethyl-3-phenyl-8,9-dihydropyrazolo-[1,5-*a*]quinazolin-6(7*H*)-one (Va). Compound **IVa**, 1.6 g (5 mmol), was ground with 1.5 g of anhydrous sodium acetate, 5 ml of glacial acetic acid was added, and the mixture was heated for 30 min under reflux. The mixture was poured into 100 ml of cold water, and the precipitate was filtered off, washed with water, dried, and recrystallized from toluene. Yield 0.93 g (61%), mp 195–196°C. ^{1}H NMR spectrum, δ, ppm: 1.21 s (6H, CH_3), 2.58 s (2H, CH_2), 2.64 s (3H, CH_3), 3.36 s (2H, CH_2), 7.31 t (1H, H_{arom}, J = 7.5 Hz), 7.45 t (2H, H_{arom}, J = 7.5 Hz), 7.70 d (2H, H_{arom}, J = 7.5 Hz), 8.78 s (1H, 5-H). Found, %: C 74.62; H 6.35; N 13.70. $C_{19}H_{19}N_3O$. Calculated, %: C 74.73; H 6.27; N 13.76.

8-(2-Furyl)-2-methyl-3-phenyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one (Vb) was synthesized in a similar way from 1.8 g (5 mmol) of compound **IVb**. Yield 1.00 g (58%), mp 196–198°C. ^{1}H NMR spectrum, δ, ppm: 2.33 s (3H, CH_3), 2.65–2.88 m (5H, CH, CH_2), 6.10 d (1H, C_4H_3O, J = 4.6 Hz), 6.32 s (1H, C_4H_3O), 7.34–7.64 m (6H, H_{arom}, C_4H_3O), 8.95 s (1H, 5-H). Found, %: C 73.60; H 5.05; N 12.36. $C_{21}H_{17}N_3O_2$. Calculated, %: C 73.45; H 4.99; N 12.24.

3-(4-Fluorophenyl)-8-(4-methoxyphenyl)-2-methyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one (Vc). A mixture of 1.91 g (0.01 mol) of aminopyrazole **Ib**, 2.18 g (0.01 mol) of diketone **IIc**, and 4 ml of triethyl orthoformate (**III**) was heated for

45 min under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from toluene. Yield 2.81 g (70%), mp 252–253°C. ^{1}H NMR spectrum, δ, ppm: 2.43–2.67 m (5H, CH, CH_2), 3.43 s (3H, OCH_3), 7.20–7.64 m (8H, H_{arom}), 9.06 s (1H, 5-H). Found, %: C 71.70; H 5.10; N 10.39. $C_{24}H_{20}FN_3O_2$. Calculated, %: C 71.81; H 5.02; N 10.47.

8-(4-Chlorophenyl)-2-methoxymethyl-3-phenyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one (Vd) was synthesized in a similar way from 2.03 g (0.01 mol) of aminopyrazole **Ic** and 2.22 g (0.01 mol) of diketone **IId**. Yield 2.79 g (67%), mp 240–241°C. ^{1}H NMR spectrum, δ, ppm: 2.50–2.71 m (5H, CH, CH_2), 3.41 s (3H, OCH_3), 4.62 s (2H, OCH_2), 7.31–7.82 m (9H, H_{arom}), 8.91 s (1H, 5-H). Found, %: C 68.77; H 4.91; N 10.19. $C_{24}H_{20}ClN_3O_2$. Calculated, %: C 68.98; H 4.82; N 10.06.

2,7-Dimethyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-6-yl(phenyl)methanone (VI). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia**, 1.62 g (0.01 mol) of benzoylacetone, and 2 ml of triethyl orthoformate (**III**) was heated for 1 h under reflux. The precipitate was filtered off, washed with propan-2-ol, and recrystallized from dioxane. Yield 1.99 g (61%), mp 205–207°C. ^{1}H NMR spectrum, δ, ppm: 2.50 s (3H, CH_3), 2.65 s (3H, CH_3), 7.23–7.70 m (10H, H_{arom}), 8.12 s (1H, 5-H). Found, %: C 76.96; H 5.35; N 12.76. $C_{21}H_{17}N_3O$. Calculated, %: C 77.04; H 5.23; N 12.83.

5-[(3-Methoxymethyl-4-phenyl-1*H*-pyrazol-5-ylamino)methylidene]hexahydropyrimidine-2,4,6-trione (VIIa). A mixture of 2.03 g (0.01 mol) of aminopyrazole **Ic**, 1.28 g (0.01 mol) of barbituric acid, and 2 ml of triethyl orthoformate (**III**) was heated for 1 h under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from DMF. Yield 1.84 g (54%), mp >300°C. ^{1}H NMR spectrum, δ, ppm: 3.32 s (3H, OCH_3), 4.41 s (2H, OCH_2), 7.30–7.60 m (5H, H_{arom}), 8.68 d (1H, =CH, J = 12 Hz), 10.80 s and 10.96 s (1H each, 1-H, 3-H), 11.98 d (1H, 5′-NH, J = 12 Hz), 13.22 s (1H, 1′-H). Found, %: C 56.56; H 4.36; N 20.57. $C_{16}H_{15}N_5O_4$. Calculated, %: C 56.30; H 4.43; N 20.52.

1,3-Dimethyl-5-[(3-methyl-4-phenyl-1*H*-pyrazol-5-ylamino)methylidene]hexahydropyrimidine-2,4,6-trione (VIIb) was synthesized in a similar way from 1.73 g (0.01 mol) of aminopyrazole **Ia** and 1.56 g (0.01 mol) of 1,3-dimethylbarbituric acid. Yield 1.76 g (52%), mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 3.22 s (3H, CH_3), 3.24 s (3H, CH_3), 7.30–7.56 m (5H, H_{arom}), 8.80 d (1H, =CH, J = 12 Hz), 11.95 d (1H, 5′-NH, J = 12 Hz), 12.70 s (1H, 1′-H). Found, %: C 60.23; H 5.13; N 20.55. $C_{17}H_{17}N_5O_3$. Calculated, %: C 60.17; H 5.05; N 20.64.

6-Methyl-3-[(3-methyl-4-phenyl-1*H*-pyrazol-5-ylamino)methylidene]-3,4-dihydro-2*H*-pyran-2,4-dione (VIII) was synthesized in a similar way from 1.73 g (0.01 mol) of aminopyrazole **Ia** and 1.26 g (0.01 mol) of 6-methyl-3,4-dihydro-2*H*-pyran-2,4-dione. Yield 1.88 g (61%), mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, CH_3), 2.27 s (3H, CH_3), 5.22 s (1H, =CH), 7.24–7.57 m (5H, H_{arom}), 8.80 d (1H, =CH, J = 12 Hz), 11.65 d (1H, 5′-NH, J = 12 Hz), 12.78 s (1H, 1′-H). Found, %: C 66.12; H 4.94; N 13.65. $C_{17}H_{15}N_3O_3$. Calculated, %: C 66.01; H 4.89; N 13.58.

2,7-Dimethyl-*N*-(2-methylphenyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carboxamide (IXa). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia**, 1.91 g (0.01 mol) of *N*-(2-methylphenyl)-3-oxobutanamide, and 2 ml of triethyl orthoformate (**III**) was heated for 1 h under reflux. The mixture was cooled, and the yellow precipitate was filtered off, washed with propan-2-ol, and recrystallized from DMF. Yield 2.31 g (65%), mp 199–200°C. ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 2.51 s (3H, CH_3), 2.68 s (3H, CH_3), 7.01–7.70 m (9H, H_{arom}), 8.70 s (1H, 5-H), 9.90 s (1H, NH). Found, %: C 74.26; H 5.55; N 15.76. $C_{22}H_{20}N_4O$. Calculated, %: C 74.14; H 5.66; N 15.72.

2,7-Dimethyl-3-phenyl-*N*-[2-(trifluoromethyl)-phenyl]pyrazolo[1,5-*a*]pyrimidine-6-carboxamide (IXb) was synthesized in a similar way from 1.73 g (0.01 mol) of aminopyrazole **Ia** and 2.45 g (0.01 mol) of 3-oxo-*N*-[2-(trifluoromethyl)phenyl]butanamide. Yield 1.97 g (48%), mp 186–188°C. ^{1}H NMR spectrum, δ, ppm: 2.66 s (3H, CH_3), 2.99 s (3H, CH_3), 7.21–7.80 m (9H, H_{arom}), 8.67 s (1H, 5-H), 10.21 s (1H, NH). Found, %: C 64.32; H 4.24; N 13.61. $C_{22}H_{17}F_3N_4O$. Calculated, %: C 64.39; H 4.18; N 13.65.

3-(4-Chlorophenyl)-*N*-(2-methoxyphenyl)-2,7-dimethylpyrazolo[1,5-*a*]pyrimidine-6-carboxamide (IXc) was synthesized in a similar way from 2.07 g (0.01 mol) of aminopyrazole **Id** and 2.07 g (0.01 mol) of *N*-(2-methoxyphenyl)-3-oxobutanamide. Yield 2.27 g (56%), mp 220–222°C. ^{1}H NMR spectrum, δ, ppm: 2.61 s (3H, CH_3), 2.94 s (3H, CH_3), 3.82 s (3H, OCH_3), 6.92–8.00 m (8H, H_{arom}), 8.68 s (1H, 5-H), 9.85 s (1H, NH). Found, %: C 65.03; H 4.64; N 13.66. $C_{22}H_{19}ClN_4O_2$. Calculated, %: C 64.95; H 4.71; N 13.77.

3-(4-Chlorophenyl)-2-methyl-7-phenylpyrazolo-[1,5-*a*]pyrimidine-6-carbonitrile (Xa). A mixture of

2.07 g (0.01 mol) of aminopyrazole **Id**, 1.45 g (0.01 mol) of benzoylacetonitrile, and 2 ml of triethyl orthoformate (**III**) was heated for 1 h under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from DMF. Yield 2.47 g (72%), mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.58 s (3H, CH_3), 7.46–7.95 m (9H, H_{arom}), 8.84 s (1H, 5-H). Mass spectrum: *m*/*z* 344 (I_{rel} 85%) $[M]^+$. Found, %: C 69.53; H 3.68; N 16.41. $C_{20}H_{13}ClN_4$. Calculated, %: C 69.67; H 3.80; N 16.25. *M* 344.81.

3-(4-Chlorophenyl)-7-(4-fluorophenyl)-2-methylpyrazolo[1,5-*a*]pyrimidine-6-carbonitrile (Xb) was synthesized in a similar way from 2.07 g (0.01 mol) of aminopyrazole **Id** and 1.63 g (0.01 mol) of 4-fluorobenzoylacetonitrile. Yield 2.31 g (64%), mp 248–250°C. ^{1}H NMR spectrum, δ, ppm: 2.55 s (3H, CH_3), 7.54–7.88 m (8H, H_{arom}), 8.90 s (1H, 5-H). Found, %: C 66.35; H 3.38; N 15.40. $C_{20}H_{12}ClFN_4$. Calculated, %: C 66.21; H 3.33; N 15.44.

Ethyl 7-imino-2-methyl-3-phenyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-6-carboxylate (XI). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia,** 1.35 g (0.012 mol) of ethyl cyanoacetate, and 2 ml of triethyl orthoformate was heated for 30 min under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from dioxane. Yield 2.01 g (68%), mp 192–193°C. ^{1}H NMR spectrum, δ, ppm: 1.42 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.1 Hz), 2.60 s (3H, CH_3), 4.38 q (2H, OCH_2, *J* = 7.1 Hz), 7.26 t (1H, H_{arom}, *J* = 7.6 Hz), 7.41 t (2H, H_{arom}, *J* = 7.6 Hz), 7.68 d (2H, H_{arom}, *J* = 7.6 Hz), 8.42 s and 8.53 s (1H each, NH), 8.60 s (1H, 5-H). Found, %: C 64.75; H 5.48; N 18.70. $C_{16}H_{16}N_4O_2$. Calculated, %: C 64.85; H 5.44; N 18.91.

7-Amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-6-carbonitrile (XII). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia**, 0.66 g (0.01 mol) of malononitrile, and 2 ml of triethyl orthoformate was heated for 20 min under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from DMF. Yield 2.04 g (82%), mp 242–243°C. ^{1}H NMR spectrum, δ, ppm: 2.56 s (3H, CH_3), 7.30 t (1H, H_{arom}, *J* = 7.6 Hz), 7.46 t (2H, H_{arom}, *J* = 7.6 Hz), 7.71 d (2H, H_{arom}, *J* = 7.6 Hz), 8.31 s (1H, 5-H), 8.94 s (2H, NH_2). Found, %: C 67.67; H 4.58; N 28.17. $C_{14}H_{11}N_5$. Calculated, %: C 67.46; H 4.45; N 28.09.

8-Methyl-7-phenylpyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidin-4-amine (XIII). A mixture of 2.49 g (0.01 mol) of compound **XII** and 5 ml of formamide was heated for 10 h under reflux. The mixture was cooled, and the precipitate was filtered off and recrystallized from DMF. Yield 1.21 g (44%), mp 206–208°C. ^{1}H NMR spectrum, δ, ppm: 2.61 s (3H, CH_3), 7.26 t (1H, H_{arom}, *J* = 7.6 Hz), 7.42 t (2H, H_{arom}, *J* = 7.6 Hz), 7.68 d (2H, H_{arom}, *J* = 7.6 Hz), 8.10 br.s. (2H, NH_2), 8.50 s (1H, CH), 9.14 s (1H, CH). Found, %: C 65.44; H 4.48; N 30.37. $C_{15}H_{12}N_6$. Calculated, %: C 65.21; H 4.38; N 30.42.

6-(1*H*-Benzimidazol-2-yl)-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-7-amine (XIV). A mixture of 1.73 g (0.01 mol) of aminopyrazole **Ia**, 1.57 g (0.01 mol) of 1*H*-benzimidazol-2-ylacetonitrile, and 3 ml of triethyl orthoformate was heated for 30 min under reflux. The mixture was cooled, and the precipitate was filtered off, washed with propan-2-ol, and recrystallized from DMF. Yield 2.11 g (62%), mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.62 s (3H, CH_3), 7.21–7.78 m (9H, H_{arom}), 8.35 br.s (2H, NH_2), 8.55 s (1H, NH), 8.91 s (1H, CH). Mass spectrum: *m*/*z* 340 (I_{rel} 90%) $[M]^+$. Found, %: C 70.61; H 4.65; N 24.71. $C_{20}H_{16}N_6$. Calculated, %: C 70.57; H 4.74; N 24.69. *M* 340.39.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 08-03-99022r_ofi).

REFERENCES

1. Gavrin, L.K., Lee, A., Provencher, B.A., Massefski, W.W., Huhn, S.D., Ciszewski, G.M., Cole, D.C., and McKew, J.C., *J. Org. Chem*., 2007, vol. 72, p. 1043.
2. Dalinger, I.L., Vatsadse, I.A., and Shevelev, S.A., *J. Comb. Chem*., 2005, vol. 7, p. 236.
3. Sadek, K.U., Selim, M.A., and El-Maghraby, M.A., *J. Chem. Eng. Data*, 1985, vol. 30, p. 514.
4. Kryl'skii, D.V., Shikhaliev, Kh.S., and Didenko, V.V., *Azotsoderzhashchie geterotsikly* (Nitrogen-Containing Heterocycles), Kartsev, V.G., Ed., Moscow: IBS, 2006, vol. 2, p. 158.
5. Yamashkin, S.A., Kucherenko, N.Ya., and Yurovskaya, M.A., *Khim. Geterotsikl. Soedin*., 1997, p. 579.
6. Nam, N.L., Sorokin, V.I., and Grandberg, I.I., *Azotsoderzhashchie geterotsikly: sintez, svoistva, primenenie* (Nitrogen-Containing Heterocycles: Synthesis, Properties, and Application), Astrakhan: Astrakhan. Gos. Ped. Univ., 2000, p. 31.
7. Petrova, O.V., Sobenina, L.N., Demenev, A.P., Mikhaleva, A.I., and Ushakov, I.A., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1471.

8. Chebanov, V.A., Saraev, V.E., Desenko, S.M., Chernenko, V.N., Shishkina, S.V., Shishkin, O.V., Kobzar, K.M., and Kappe, C.O., *Org. Lett*., 2007, vol. 9, p. 1691.
9. Drizin, I., Holladay, M.W., Yi, L., Zhang, H.Q., Gopalakrishnan, S., Gopalakrishnan, M., Whiteaker, K.L., Buckner, S.A., Sullivan, J.P., and Carrol, W.A., *Bioorg. Med. Chem. Lett*., 2002, p. 1481.
10. Komykhov, S.A., Petrova, M.G., Borovskoi, V.A., Musatov, V.I., and Desenko, S.M., *Azotsoderzhashchie geterotsikly* (Nitrogen-Containing Heterocycles), Kartsev, V.G., Ed., Moscow: IBS, 2006, vol. 2, p. 143.
11. Kryl'skii, D.V., Potapov, A.Yu., Krysin, M.Yu., Trefilova, I.N., and Shikhaliev, Kh.S., *Khim. Geterotsikl. Soedin*., 2006, p. 1080.
12. Kryl'skii, D.V., Shikhaliev, Kh.S., and Potapov, A.Yu., *Izv. Vyssh. Uchebn. Zaved., Ser. Khim. khim. Tekhnol*., 2005, vol. 48, p. 61.
13. Gilligan, P.J., Baldauf, C., Cocuzza, A., Chidester, D., Zaczek, R., Fitzgerald L.W., McElroy. J., Smith, M.F., Shen, H.-S.L., Saye, J.A., Christ, D., Trainor, G., Robertson, D.W., and Hartig, P., *Bioorg. Med. Chem*., 2000, vol. 8, p. 181.