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Synthesis of New 1-(3,4-Dimethylphenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one Derivatives

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Abstract—New substituted pyrazolo[3,4-*d*]pyrimidin-4-ones have been synthesized as a result of a series of transformations including hydrolysis of ethyl 5-amino-1*H*-pyrazole-4-carboxylates, cyclization of the carboxylic acids thus obtained to pyrazolo[3,4-*d*][1,3]oxazin-4(1*H*)-ones, and treatment of the latter with substituted anilines. The final pyrazolo[3,4-*d*]pyrimidin-4-one derivatives can also be synthesized from 5-(arylamido)-1*H*-pyrazole-4-carboxylic acids in the presence of a catalytic amount of anhydrous zinc(II) chloride.

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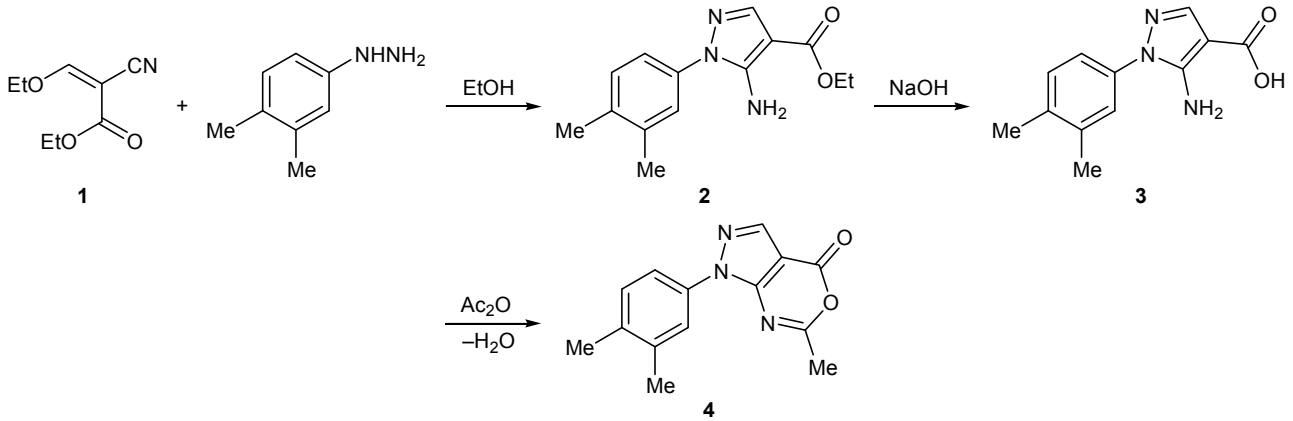
Pyrazolo[3,4-*d*]pyrimidines are conjugated heterocyclic compounds consisting of fused pyrazole and pyrimidine rings, and they may be regarded as structural analogs of purines [1]. Historically, pyrazolo[3,4-*d*]pyrimidines were planned to be used as adenosine receptor antagonists [2]. According to recently published data, compounds containing a pyrazolo[3,4-*d*]pyrimidine ring system exhibit various biological activities, in particular antimicrobial [3, 4], antiviral [5–8], antiallergic [9], antihypotensive [10, 11], antitumor [12], and anti-inflammatory [13, 14]. Therefore, it seemed reasonable to synthesize previously unknown 1-(3,4-dimethylphenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one derivatives with the goal of estimating their biological activity. The syntheses were carried out according to the approach developed by us previously [15, 16].

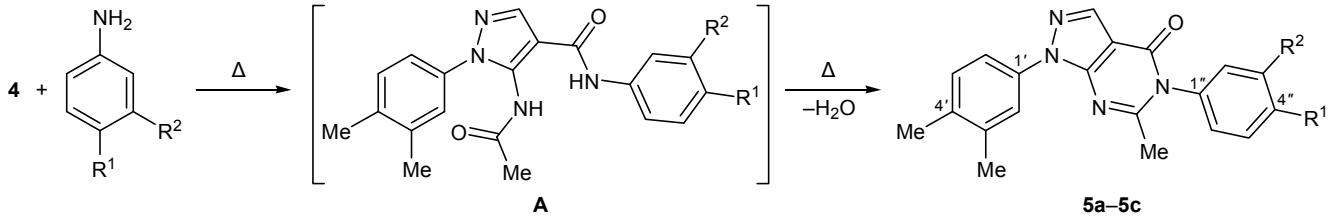
Initially, ethyl 2-cyano-2-ethoxyprop-2-enoate (**1**) was prepared by heating a mixture of triethyl orthoformate, acetic anhydride, and ethyl cyanoacetate with simultaneous removal of liberated ethyl acetate and ethanol by distillation [14]. Oxonitrile **1** was heated with (3,4-dimethylphenyl)hydrazine in boiling ethanol to give pyrazole-4-carboxylate **2** (Scheme 1). (3,4-Dimethylphenyl)hydrazine was prepared in turn from 3,4-dimethylaniline which was converted into diazonium salt, and the latter was reduced with sodium sulfite in water [17].

Ester **2** was hydrolyzed with aqueous sodium hydroxide to the corresponding acid **3** which underwent

Scheme 1.



Scheme 2.



R^1 = F, R^2 = Cl (**a**); R^1 = R^2 = Me (**b**); R^1 = EtO, R^2 = H (**c**).

cyclization on heating in boiling acetic anhydride. Substituted pyrazolo[3,4-*d*][1,3]oxazin-4(1*H*)-one **4** thus obtained is a very reactive compound capable of reacting with various nucleophiles (substituted anilines, primary and secondary amines, alcohols, and thiols) under fairly mild conditions.

Pyrazolooxazinone **4** was brought into reactions with substituted anilines at 100°C (1 h) in an inert atmosphere. As a result, we isolated 1,5-diaryl-6-methyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-ones **5a**–**5c** (Scheme 2). ^{1}H NMR monitoring of the reaction of **4** with 3-chloro-4-fluoroaniline showed that the reaction proceeds in two steps. In the first step, opening of the oxazine ring in **4** gives 5-acetamido-*N*,1-diaryl-1*H*-pyrazole-4-carboxamide **A** which then undergoes cyclization to pyrazolo[3,4-*d*]pyrimidin-4-one **5a** with elimination of water molecule.

Apart from transformations of the ester group, pyrazole-4-carboxylate **2** is also capable of reacting through the amino group. The acylation of **2** with 2-furoyl chloride in boiling 1,4-dioxane in the absence of HCl acceptor afforded amido ester **6** (Scheme 3). The hydrolysis of **6** with aqueous sodium hydroxide at 50°C selectively involved the ester group to produce pyrazolecarboxylic acid **7**, and heating of the latter with excess acetic anhydride resulted in cyclization to furyl-substituted pyrazolooxazinone **8**.

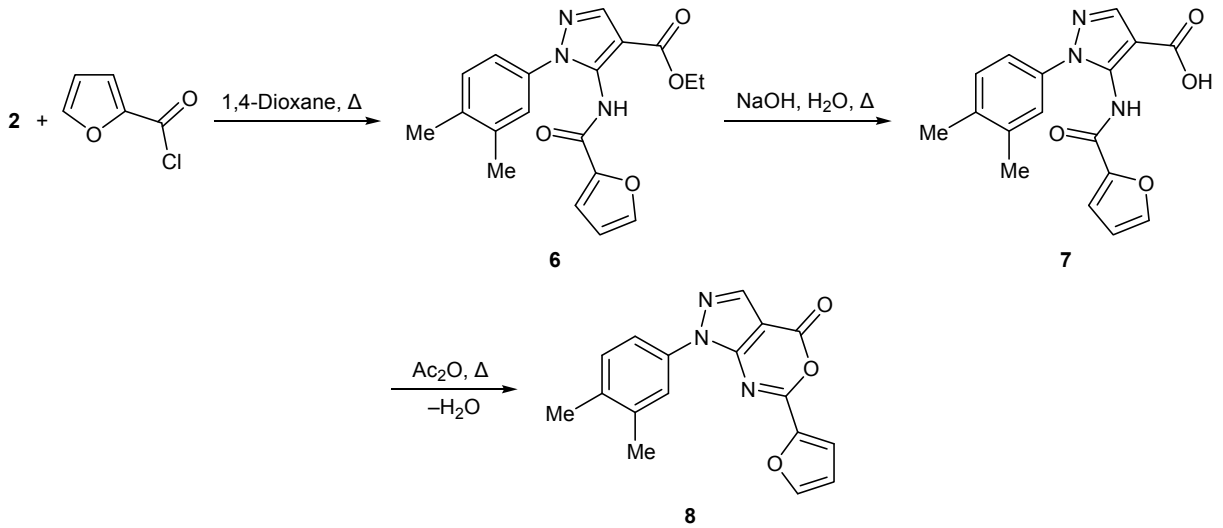
Compound **8** reacted with substituted anilines at 100–120°C to produce *N*-phenyl-1-aryl-5-[(arylcarbonyl)amino]-1*H*-pyrazole-4-carboxamides **9a**–**9e** which did not undergo cyclization to pyrazolo[3,4-*d*]-pyrimidine derivatives like **5** under these conditions. Cyclization of **9a**, **9b**, and **9d** to pyrazolopyrimidines **10a**–**10c** was achieved by heating to 240°C in the presence of a catalytic amount of anhydrous zinc(II) chloride (Scheme 4).

EXPERIMENTAL

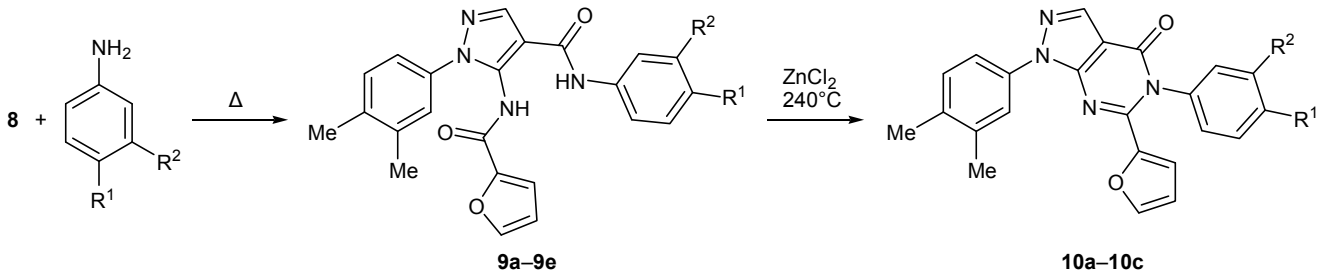
Commercial organic reagents (Aldrich) were used. The solvents were purified according to standard procedures [17]. Acids, salts, and bases of chemically pure grade were used without additional purification.

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer at 500.13 and 125.76 MHz, respectively, from solutions in DMSO-d_6

Scheme 3.



Scheme 4.



9a–9e **10a–10c**

9, $R^1 = R^2 =$ Me (**a**); $R^2 =$ H, $R^1 =$ Me (**b**), EtO (**c**), EtOC(O) (**d**), MeOC(O) (**e**); **10**, $R^1 = R^2 =$ Me (**a**); $R^2 =$ H, $R^1 =$ Me (**b**), EtOC(O) (**c**).

or $CDCl_3$ (for compound **2**) using tetramethylsilane as internal standard. HPLC/MS analyses were obtained on a Thermo Scientific LTQ XL instrument equipped with a heated electrospray ionization (HESI) probe; Thermo Scientific Hypersil Gold C18 column, 200× 2.1 mm, grain size 1.9 μm; isocratic elution, flow rate 70 μL/min; eluents: 0.1% HCOOH in water (A) or 0.1% HCOOH in acetonitrile (B); elution program: 0–30 min, 35% A, 65% B; sample volume 1.0 μL.

GC/MS analyses were obtained on an Agilent 7890A chromatograph coupled with an Agilent 5975C quadrupole mass-selective detector; HP-5MC column, 30 m×0.25 mm, film thickness 0.25 μm; oven temperature programming from 40 to 280°C (10 min) at a rate of 10 deg/min; injector temperature 260°C, interface temperature 280°C; split ratio 1/10; carrier gas helium, flow rate 1.0 mL/min; electron impact, 70 eV.

The progress of reactions was monitored by TLC on Silufol UV 254 plates using toluene–acetone (4:1) as eluent. The melting points were measured with a Mettler FP5 melting point apparatus.

Ester **1** was synthesized as described in [17].

Ethyl 5-amino-1-(3,4-dimethylphenyl)-1*H*-pyrazole-4-carboxylate (2). 3,4-Dimethylaniline, 89.8 g (0.74 mol), was added to 225 mL of concentrated aqueous HCl cooled to 0°C, the mixture was stirred for 15 min, 560 mL of water was added, the mixture was cooled to –5°C, and a 16.8% aqueous solution of sodium nitrite was added until positive starch–iodine test. The mixture was heated to 70–75°C and added with stirring to 1200 mL of a 45.2% aqueous solution of sodium sulfite. After 30 min, 28.5 mL of concentrated aqueous HCl was added to the resulting solution, and the precipitate was filtered off and dissolved in 220 mL of water. The solution was treated with 10% aqueous sodium hydroxide, and the oily material was extracted with methylene chloride (3×100 mL). The combined extracts were dried for 24 h over calcined magnesium sulfate, the drying agent was filtered off, the filtrate was evaporated under atmospheric pressure, and the residue was kept under reduced pressure (15 mm) for 1 h to remove traces of the solvent. The dark brown material (3,4-dimethylphenylhydrazine), 79.76 g, was dissolved in 100 mL of ethanol, and the solution was added over a period of 15 min to a mixture of 69.0 g (0.41 mol) of ester **1** and 100 mL of ethanol. Ethanol, 150 mL, was distilled off from the mixture, the residue was cooled to 0°C, and the precipitate was filtered off, washed with cold ethanol (3× 30 mL), dried, and recrystallized from 100 mL of ethyl acetate. Yield 73.6 g (62%), yellow powder, mp 92°C, R_f 0.64. ^{1}H NMR spectrum, δ, ppm: 1.30 t (3H, CH_3, J = 8.0 Hz), 2.23 s (3H, CH_3), 2.37 s (3H, CH_3), 4.24 d (2H, CH_2, J = 7.5 Hz), 6.22 s (1H, NH), 7.52–7.62 m (3H, H_{arom}), 7.81 s (1H, 3-H). Found, %: C 64.92; H 6.62; N 16.09. $C_{14}H_{17}N_3O_2$. Calculated, %: C 64.85; H 6.61; N 16.20.

5-Amino-1-(3,4-dimethylphenyl)-1*H*-pyrazole-4-carboxylic acid (3). A mixture of 20.0 g (0.08 mol) of ester **2**, 9.6 g (0.24 mol) of sodium hydroxide, and 100 mL of water was refluxed until it became homogeneous (~2 h). The mixture was cooled to 20°C and filtered, the filtrate was acidified to pH 3 with concentrated aqueous HCl, and the precipitate was filtered off, washed with cold water (3×30 mL), and dried first for 1 h at 50°C (15 mm) and then in a vacuum desiccator over P_2O_5. Yield 15.24 g (93%), white powder, mp 225°C, R_f 0.2. ^{1}H NMR spectrum, δ, ppm: 2.25 s (3H, CH_3), 2.39 s (3H, CH_3), 5.52–5.56 m (1H, H_{arom}), 6.45–6.50 m (1H, H_{arom}), 6.22 s (1H, NH), 7.55–7.61 m (1H, H_{arom}), 7.67 s (1H, 3-H). Found, %: C 62.40; H 5.70; N 18.12. $C_{12}H_{13}N_3O_2$. Calculated, %: C 62.33; H 5.67; N 18.17.

1-(3,4-Dimethylphenyl)-6-methylpyrazolo[3,4-*d*]-[1,3]oxazin-4(1*H*)-one (4). A mixture of 15.24 g (74 mmol) of acid **3** and 100 mL of freshly distilled

acetic anhydride was refluxed for 3 h with stirring. The mixture was cooled to 20°C, and the precipitate was filtered off, washed with cold propan-2-ol (3×30 mL), and dried for 1 h at 50°C (15 mm). Yield 11.56 g (83%), white powder, mp 113°C, R_f 0.77. ^{1}H NMR spectrum, δ, ppm: 2.15 s (3H, CH_3), 2.23 s (3H, CH_3), 2.47 s (3H, CH_3), 5.39 s (1H, NH), 7.52–7.65 m (3H, H_{arom}), 8.15 s (1H, 3-H). Found, %: C 65.82; H 5.16; N 16.49. $C_{14}H_{13}N_3O_2$. Calculated, %: C 65.87; H 5.13; N 16.46.

5-(3-Chloro-4-fluorophenyl)-1-(3,4-dimethylphenyl)-6-methyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]-pyrimidin-4-one (5a). A mixture of 1 g (5 mmol) of compound **4** and 1.45 g (10 mmol) of 3-chloro-4-fluoroaniline was stirred for 1 h at 100°C under argon, 5 mL of propan-2-ol was added, and the mixture was cooled to 20°C. The precipitate was filtered off, washed with cold propan-2-ol (3×10 mL), and dried for 1 h at 50°C (15 mm). Yield 0.94 g (61%), gray powder, mp 123–125°C, R_f 0.71. ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, CH_3), 2.29 s (3H, CH_3), 2.33 s (3H, 6-CH_3), 7.34 d (1H, H_{arom}, J = 8.0 Hz), 7.54–7.56 m (1H, H_{arom}), 7.66 t (1H, H_{arom}, J = 9.0 Hz), 7.78 d (1H, H_{arom}, J = 8.0 Hz), 7.81 s (1H, H_{arom}), 7.86 d.d (1H, H_{arom}, J = 7.0, 2.0 Hz), 8.33 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (3-CH_3), 19.68 (4-CH_3), 24.77 (6-CH_3), 105.16 (C^{3a}), 117.78 ($C^{3''}$), 117.95, 119.29, 120.24, 122.85, 129.50, 130.11 ($C^{1''}$), 131.12, 134.60, 135.58 ($C^{1'}$), 136.04, 137.38 (C^3), 150.47 (C^{7a}), 157.56 (C^6), 158.44 ($C^{4''}$), 158.66 (C^4). Mass spectrum: m/z 383 $[M + H]^+$. Found, %: C 62.82; H 4.23; Cl 9.23; N 14.60. $C_{20}H_{16}ClFN_4O$. Calculated, %: C 62.75; H 4.21; Cl 9.26; N 14.64. M 382.83.

Compounds **5b** and **5c** were synthesized in a similar way.

1,5-Bis(3,4-dimethylphenyl)-6-methyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (5b). Yield 56%, gray powder, mp 117–119°C. ^{1}H NMR spectrum, δ, ppm: 2.22 s (3H, CH_3), 2.28 s (3H, CH_3), 2.29 s (3H, CH_3), 2.32 s (3H, CH_3), 2.40 (3H, 6-CH_3), 7.18 s (1H, H_{arom}), 7.12 d (1H, H_{arom}, J = 8 Hz), 7.33 d.d (2H, H_{arom}, J = 8.0, 4.0 Hz), 7.79 d (1H, H_{arom}, J = 8.0 Hz), 7.82 s (1H, H_{arom}), 8.30 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (CH_3), 19.14 (CH_3), 19.41 (CH_3), 19.68 (CH_3), 24.76 (6-CH_3), 105.31 (C^{3a}), 117.55, 119.28, 122.84, 125.58, 129.02, 130.06, 130.52, 135.20, 135.44, 135.96, 136.15 (C^3), 137.36, 137.82 (C^{7a}), 150.51 (C^6), 159.01 (C^4). Mass spectrum: m/z 359 $[M + H]^+$. Found, %: C 73.76; H 6.20; N 15.59. $C_{22}H_{22}N_4O$. Calculated, %: C73.72; H 6.19; N 15.63. M 358.45.

5-(4-Ethoxyphenyl)-1-(3,4-dimethylphenyl)-6-methyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (5c). Yield 60%, dark gray powder, mp 105–107°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, J = 7.0 Hz), 2.17 s (3H, CH_3), 2.29 s (3H, CH_3), 2.32 s (3H, 6-CH_3), 4.10 q (2H, CH_2, J = 7.0 Hz), 7.08 d (2H, H_{arom}, J = 8.0 Hz), 7.33 t (3H, H_{arom}, J = 7.0 Hz), 7.80 t (2H, H_{arom}, J = 9.0 Hz), 8.30 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 14.68 (CH$_2$**C**H$_3$), 19.03 (3-CH_3), 19.68 (4-CH_3), 24.76 (6-CH_3), 63.43 (OCH_2), 105.31 (C^{3a}), 115.18, 119.26, 122.82, 126.10, 129.57, 129.95, 130.07, 135.44, 135.98, 136.17 (C^3), 137.32 (C^{7a}), 150.51 (C^6), 158.71 (C^3), 159.37 (C^4). Mass spectrum (EI), m/z (I_{rel}, %): 376 (3), 375 (25), 374 (100), 373 (11), 360 (6), 359 (23), 346 (6), 345 (16), 332 (2), 331 (7), 303 (1), 288 (1), 238 (4), 237 (11), 223 (2), 222 (2), 210 (2), 173 (2), 162 (3), 133 (5), 105 (4), 103 (2), 93 (2), 91 (2), 79 (2), 77 (4), 65 (4), 64 (2), 39 (1). Mass spectrum (HESI): m/z 375 $[M + H]^+$. Found, %: C 70.61; H 5.94; N 14.93. $C_{22}H_{22}N_4O_2$. Calculated, %: C 70.57; H 5.92; N 14.96. M 374.48.

Ethyl 1-(3,4-dimethylphenyl)-5-[(furan-2-ylcarbonyl)amino]-1*H*-pyrazole-4-carboxylate (6). A mixture of 23.1 g (0.09 mol) of ester **2**, 13.95 g (0.11 mol) of 2-furoyl chloride, and 50 mL of anhydrous 1,4-dioxane was refluxed for 10 h with stirring under nitrogen. The mixture was cooled, and the precipitate was filtered off, washed with cold ethanol (3×10 mL), and dried for 1 h at 50°C under reduced pressure (15 mm). Yield 23.21 g (74%), white powder, mp 112–114°C, R_f 0.43. ^{1}H NMR spectrum, δ, ppm: 1.30 t (3H, CH_3, J = 8 Hz), 2.23 s (3H, CH_3), 2.47 s (3H, CH_3), 4.24 q (2H, OCH_2, J = 8.0 Hz), 6.71 d.d (1H, 4-H_{Fu}, J = 1.2, 3.3 Hz), 7.11 d (1H, H_{arom}, J = 7.5 Hz), 7.34 d (1H, H_{arom}, J = 7.5 Hz), 7.46 d (1H, H_{arom}, J = 7.5 Hz), 7.59 s (1H, H_{arom}), 7.81 s (1H, 3-H), 7.95 s (1H, H_{arom}), 10.47 br.s (1H, NH). Found, %: C 64.61; H 5.42; N 11.86. $C_{19}H_{19}N_3O_4$. Calculated, %: C 64.58; H 5.42; N 11.89.

1-(3,4-Dimethylphenyl)-5-[(furan-2-ylcarbonyl)-amino]-1*H*-pyrazole-4-carboxylic acid (7). A mixture of 23.0 g (0.065 mol) of ester **6** and 5.2 g (0.13 mol) of sodium hydroxide in 50 mL of water was heated for 5 h at 50°C with vigorous stirring. The mixture was cooled and filtered, the filtrate was acidified to pH 2–3 with 10% aqueous HCl, and the precipitate was filtered off, washed with water (3×30 mL), and dried for 3 h at 50°C under reduced pressure (15 mm). Yield 16.9 g (80%), white powder, mp 196–199°C, R_f 0.1. ^{1}H NMR

spectrum, δ, ppm: 2.25 s (3H, CH_3), 2.48 s (3H, CH_3), 6.51 d.d (1H, 4-H_{Fu}, J = 1.2, 3.3 Hz), 7.15 d (1H, H_{arom}, J = 7.5 Hz), 7.27 d (1H, H_{arom}, J = 7.5 Hz), 7.48 d (1H, H_{arom}, J = 7.5 Hz), 7.51 s (1H, H_{arom}), 7.79 s (1H, 3-H), 7.93 s (1H, H_{arom}), 10.47 br.s (1H, NH), 11.95 br.s (1H, OH). Found, %: C 62.73; H 4.66; N 12.89. $C_{17}H_{15}N_3O_4$. Calculated, %: C 62.76; H 4.65; N 12.92.

1-(3,4-Dimethylphenyl)-6-(furan-2-yl)pyrazolo-[3,4-*d*][1,3]oxazin-4(1*H*)-one (8). A mixture of 16.5 g (0.065 mol) of acid **7** and 50 mL of acetic anhydride was refluxed for 2 h with vigorous stirring. The mixture was cooled to 20°C, and the precipitate was filtered off, washed with cold ethanol (3×30 mL), and dried for 1 h at 50°C under reduced pressure (15 mm). Yield 15.8 g (89%), white crystals, mp 173–176°C, R_f 0.85. ^{1}H NMR spectrum, δ, ppm: 2.24 s (3H, CH_3), 2.47 s (3H, CH_3), 6.74 d.d (1H, 4-H_{Fu}, J = 1.3, 3.4 Hz), 7.12–7.16 m (2H, H_{arom}), 7.46 d (1H, H_{arom}, J = 7.5 Hz), 7.59 s (1H, H_{arom}, 3-H), 7.97 d (1H, H_{arom}, J = 7.5 Hz), 8.15 s (1H, H_{arom}). Found, %: C 66.47; H 4.24; N 13.64. $C_{17}H_{13}N_3O_3$. Calculated, %: C 66.44; H 4.26; N 13.67.

***N*,1-Bis(3,4-dimethylphenyl)-5-[(furan-2-ylcarbonyl)amino]-1*H*-pyrazole-4-carboxamide (9a).** A mixture of 1.0 g (3 mmol) of compound **8** and 0.40 g (0.34 mL, 3.6 mmol) of freshly distilled 3,4-dimethylaniline was stirred for 1 h at 100–120°C. The mixture was cooled to 20°C, 10 mL of ethanol was added, and the mixture was refluxed for 5 min and cooled to 0°C. The precipitate was filtered off, washed with ethanol (3×10 mL), and dried for 1 h at 50°C under reduced pressure (15 mm). Yield 1.17 g (92%), gray powder, mp 210–215°C, R_f 0.28. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H, CH_3), 2.32 s (3H, CH_3), 2.37 s (3H, CH_3), 2.41 s (3H, CH_3), 5.55 d (1H, H_{arom}, J = 4.5 Hz), 6.49 d.d (1H, 4-H_{Fu}, J = 1.2, 3.3 Hz), 7.23 d.d (1H, H_{arom}, J = 8.0, 1.5 Hz), 7.28 s (1H, H_{arom}), 7.34 d.d (2H, H_{arom}, J = 13.0, 8.0 Hz), 7.78 s (1H, H_{arom}), 7.89 s (1H, H_{arom}), 7.97 s (1H, H_{arom}), 8.12 s (1H, 3-H), 10.12 s (1H, NH), 10.47 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (3′-CH_3), 19.14 (3″-CH_3), 19.37 (4″-CH_3), 19.47 (4′-CH_3), 112.37 (Fu), 112.81 (Fu), 117.12, 119.32, 121.34, 124.67, 125.73, 130.14, 130.63, 134.26, 135.43, 136.14, 136.97, 139.27, 139.75 (C^5), 140.14 (C^3), 146.32 (Fu), 146.79 (C^4), 148.07 (Fu), 157.32 (Fu**C**=O), 164.93 (4-C=O). Mass spectrum: m/z 429 $[M + H]^+$. Found, %: C 70.11; H 5.67; N 13.04. $C_{25}H_{24}N_4O_3$. Calculated, %: C 70.08; H 5.65; N 13.08. M 428.50.

Compounds **9b–9e** were synthesized in a similar way.

1-(3,4-Dimethylphenyl)-5-[(furan-2-ylcarbonyl)-amino]-*N*-(4-methylphenyl)-1*H*-pyrazole-4-carboxamide (9b). Yield 89%, gray powder, mp 200–203°C. ^{1}H NMR spectrum, δ, ppm: 2.30 s (3H, CH_3), 2.35 s (3H, CH_3), 2.41 s (3H, CH_3), 5.59 d (1H, H_{arom}, J = 3.5 Hz), 6.38 q (1H, H_{arom}, J = 1.5 Hz), 7.32 d (2H, H_{arom}, J = 8.0 Hz), 7.37 t (3H, H_{arom}, J = 9.0 Hz), 7.89 m (2H, H_{arom}), 7.95 s (1H, H_{arom}), 8.37 s (1H, 3-H), 10.17 s (1H, NH), 10.55 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (3′-CH_3), 19.42 (4′-CH_3), 21.13 (4″-CH_3), 111.93 (Fu), 112.24 (Fu), 117.03, 121.47, 123.52, 125.71, 129.19, 131.56, 133.49, 134.93, 135.81, 136.61, 138.14 (C^5), 139.04 (C^3), 144.93 (Fu), 147.12 (C^4), 148.27 (Fu), 159.17 (Fu**C**=O), 165.12 (4-C=O). Mass spectrum: m/z 415 $[M + H]^+$. Found, %: C 69.59; H 5.31; N 13.50. $C_{24}H_{22}N_4O_3$. Calculated, %: C 69.55; H 5.35; N 13.52. M 414.47.

***N*-(3,4-Dimethylphenyl)-1-(4-ethoxyphenyl)-5-[(furan-2-ylcarbonyl)amino]-1*H*-pyrazole-4-carboxamide (9c).** Yield 88%, dark gray powder, mp 210–213°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, J = 7.0 Hz), 2.33 s (3H, CH_3), 2.36 s (3H, CH_3), 4.23 q (2H, CH_2, J = 7.0 Hz), 5.68 d (1H, H_{arom}, J = 6.5 Hz), 6.52 t (1H, H_{arom}, J = 2.0 Hz), 7.11 d (2H, H_{arom}, J = 9.0 Hz), 7.35 t (4H, H_{arom}, J = 9.0 Hz), 7.89 s (1H, H_{arom}), 7.92 s (1H, H_{arom}), 8.37 s (1H, 3-H), 10.22 s (1H, NH), 10,61 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.27 (**C**H$_3$CH$_2$), 19.01 (3′-CH_3), 19.42 (4′-CH_3), 60.50 (CH_2O), 112.24 (Fu), 112.41 (Fu), 115.85, 119.21, 120.92, 124.92, 130.16, 130.23, 135.84, 136.74, 137.03 (C^5), 137.39 (C^3), 139.25, 143.49 (Fu), 146.39 (Fu), 146.59 (C^4), 148.96, 157.14 (Fu**C**=O), 165.41 (4-C=O). Mass spectrum: m/z 445 $[M + H]^+$. Found, %: C 67.59; H 5.45; N 12.57. $C_{25}H_{24}N_4O_4$. Calculated, %: C 67.55; H 5.44; N 12.60. M 444.49.

Ethyl 4-({1-(3,4-dimethylphenyl)-5-[(furan-2-ylcarbonyl)amino]-1*H*-pyrazole-4-carbonyl}amino)-benzoate (9d). Yield 94%, white powder, mp 180–183°C. ^{1}H NMR spectrum, δ, ppm: 1.32 t (3H, C**H**$_3$CH$_2$, J = 7.0 Hz), 2.24 s (6H, CH_3), 4.29 q (2H, OCH_2, J = 7.0 Hz), 6.70 d.d (1H, 4-H_{Fu}, J = 1.2, 3.3 Hz), 7.27–7.32 m (4H, H_{arom}), 7.86 d (2H, H_{arom}, J = 9.0 Hz), 7.92 s (1H, 3-H), 7.95 d (2H, H_{arom}, J = 3.0 Hz), 8.41 s (1H, H_{arom}), 10.25 s (1H, NH), 10.37 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.27 (CH$_2$**C**H$_3$), 19.01 and 19.42 (3′-CH_3, 4′-CH_3), 60.50

(OCH_2), 112.34 (Fu), 112.94 (Fu), 115.84, 119.22, 120.92, 124.06, 124.93, 129.90, 130.16, 135.84, 136.74, 137.03 (C^5), 137.40 (C^3), 139.25, 143.49 (Fu), 146.39 (Fu), 146.54 (C^4), 157.17 (4″-C=O), 160.29 (Fu**C**=O), 165.41 (4-C=O). Mass spectrum: *m*/*z* 473 $[M + H]^+$. Found, %: C 66.12; H 5.10; N 11.83. $C_{26}H_{24}N_4O_5$. Calculated, %: C 66.09; H 5.12; N 11.86. *M* 472.50.

Methyl 4-({1-(3,4-dimethylphenyl)-5-[(furan-2-ylcarbonyl)amino]-1*H*-pyrazole-4-carbonyl}amino)-benzoate (9e). Yield 91%, white powder, mp 208–210°C. ^{1}H NMR spectrum, δ, ppm: 2.24 s (6H, CH_3), 3.83 s (3H, OCH_3), 6.70 d.d (1H, 4-H_{Fu}, *J* = 1.2, 3.3 Hz), 7.24–7.28 m (4H, H_{arom}), 7.36 s (1H, H_{arom}), 7.86 d (2H, H_{arom}, *J* = 9.0 Hz), 7.94 d (3H, *J* = 9.0 Hz), 8.40 s (1H), 10.26 (1H, NH), 10.40 (1H, NH). ^{13}C NMR spectrum, δ, ppm: 19.01 (4′-CH_3), 19.42 (3′-CH_3), 51.94 (OCH_3), 112.34 (Fu), 112.94 (Fu), 115.84, 119.22, 120.92, 124.06, 124.93, 129.90, 130.23, 135.84, 136.74, 137.03 (C^5), 137.41 (C^3), 139.25, 143.49 (Fu), 146.39 (Fu), 146.54 (C^4), 157.17 (4″-C=O), 160.29 (Fu**C**=O), 165.41 (4-C=O) Mass spectrum: *m*/*z* 459 $[M + H]^+$. Found, %: C 65.52; H 4.86; N 12.19. $C_{25}H_{22}N_4O_5$. Calculated, %: C 65.49; H 4.84; N 12.22. *M* 458.48.

1,5-Bis(3,4-dimethylphenyl)-6-(furan-2-yl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (10a). A mixture of 1.0 g (2.3 mmol) of compound **9a** and 5 mg (0.037 mmol) of calcined zinc(II) chloride was heated at 220–240°C until water no longer evolved (~30 min). The mixture was cooled, 10 mL of ethanol was added, and the mixture was refluxed for 5 min. The dark brown solution was cooled to 0°C, and the precipitate was filtered off, washed with ethanol (3×10 mL), and dried for 1 h at 50°C under reduced pressure (15 mm). Yield 0.73 g (78%), gray powder, mp 190–193°C, R_f 0.49. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 2.31 s (3H, CH_3), 2.34 s (3H, CH_3), 2.35 s (3H, CH_3), 5.55 d (1H, H_{arom}, *J* = 4.5 Hz), 6.48 d.d (1H, 4-H_{Fu}, *J* = 1.2, 3.3 Hz), 7.15 d.d (1H, H_{arom}, *J* = 8.0, 1.5 Hz), 7.22 s (1H, H_{arom}), 7.35 d.d (2H, H_{arom}, *J* = 13.0, 8.0 Hz), 7.88 s (1H, H_{arom}), 7.89 s (1H, H_{arom}), 7.92 s (1H, H_{arom}), 8.36 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (CH_3), 19.27 (CH_3), 19.37 (CH_3), 19.74 (CH_3), 105.02 (C^4), 112.36 (Fu), 112.82 (Fu), 117.83, 119.07, 122.72, 126.35, 129.73, 130.12, 130.47, 134.47, 134.86, 135.46, 136.20, 137.37, 137.81 (C^3), 137.97 (C^{7a}), 146.63 (Fu), 148.02 (Fu), 150.49 (C^6), 157.47 (C^4). Mass spectrum (EI), *m*/*z* (I_{rel}, %): 412 (4), 411 (28), 410 (100) $[M]^+$, 409 (12), 394 (12), 393 (40), 382 (8), 381 (5), 379 (1), 367 (7), 357 (7), 356 (26), 341 (4), 289 (3), 198 (9), 183 (2), 169 (2), 155 (1), 128 (1), 118 (1), 105 (1), 103 (10), 95 (7), 91 (2), 79 (12), 77 (12), 53 (1), 39 (1). Mass spectrum (HESI): *m*/*z* 411 $[M + H]^+$. Found, %: C 70.11; H 5.69; N 13.04. $C_{25}H_{22}N_4O_2$. Calculated, %: C 70.08; H 5.65; N 13.08. *M* 410.63.

Compounds **10b** and **10c** were synthesized in a similar way.

1-(3,4-Dimethylphenyl)-6-(furan-2-yl)-5-(4-methylphenyl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]-pyrimidin-4-one (10b). Yield 79%, gray powder, mp 230–235°C. ^{1}H NMR spectrum, δ, ppm: 2.31 s (3H, CH_3), 2.34 s (3H, CH_3), 2.43 s (3H, CH_3), 5.58 d (1H, H_{Fu}, *J* = 3.5 Hz), 6.48 d.d (1H, 4-H_{Fu}, *J* = 1.2, 3.3 Hz), 7.32 d (3H, H_{arom}, *J* = 8.0 Hz), 7.37 t (3H, H_{arom}, *J* = 9.0 Hz), 7.88 m (2H, H_{arom}), 7.91 s (1H, H_{arom}), 8.37 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 19.03 (3′-CH_3), 19.74 (4′-CH_3), 20.93 (4″-CH_3), 105.07 (C^{3a}), 112.23 (Fu), 112.52 (Fu), 117.74, 119.09, 122.73, 128.97, 130.09, 130.14, 134.79, 135.48, 136.22, 137.38, 139.18 (C^3), 144.75, 146.61 (Fu), 148.06 (Fu), 150.50 (C^6), 160.37 (C^4). Mass spectrum: *m*/*z* 397 $[M + H]^+$. Found, %: C 69.59; H 5.37; N 13.49. $C_{24}H_{20}N_4O_3$. Calculated, %: C 69.55; H 5.35; N 13.52. *M* 396.45.

1-(3,4-Dimethylphenyl)-5-(4-ethoxyphenyl)-6-(furan-2-yl)-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (10c). Yield 71%, dark gray powder, mp 245–249°C. ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, C**H**$_3$CH$_2$, *J* = 7 Hz), 2.31 s (3H, CH_3), 2.35 s (3H, CH_3), 4.11 q (2H, CH_2, *J* = 7.0 Hz), 5.60 d (1H, H_{arom}, *J* = 6.5 Hz), 6.50 d.d (1H, 4-H_{Fu}, *J* = 1.2, 3.3 Hz), 7.10 d (2H, H_{arom}, *J* = 9.0 Hz), 7.35 t (3H, H_{arom}, *J* = 9.0 Hz), 7.88 s (1H, H_{arom}), 7.90 s (1H, H_{arom}), 7.92 s (1H, H_{arom}), 8.37 s (1H, 3-H). Mass spectrum: *m*/*z* 427 $[M + H]^+$. Found, %: C 67.58; H 5.46; N 12.57. $C_{25}H_{22}N_4O_3$. Calculated, %: C 67.55; H 5.44; N 12.60. *M* 426.48.

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