DOI 10.1007/s10593-017-2165-y

Chemistry of Heterocyclic Compounds **2017**, *53*(9), 1026–1032

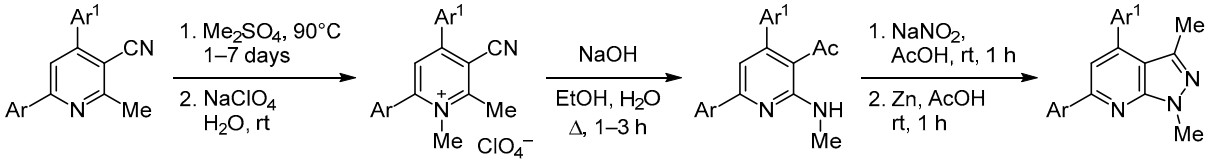
A simple synthesis of 1*H*-pyrazolo[3,4-*b*]pyridines

Ekaterina E. Sizova[1], Evgenii V. Arshinov[1], Yana A. Kotsareva[1], Larisa V. Glizdinskaya[1], Galina P. Sagitullina[1]*

[1] *F. M. Dostoevskii Omsk State University, 55a Mir Ave., Omsk 644077, Russia; e-mail: sagitullina@chemomsu.ru*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2017, *53*(9), 1026–1032

Submitted June 16, 2017
Accepted August 7, 2017



Ar = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-BrC_6H_4; Ar^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4

3-Acetyl-4,6-diaryl-2-methylaminopyridines were synthesized *via* rearrangement of quaternary 4,6-diaryl-3-cyano-2-methylpyridinium salts. Annulation of the pyrazole ring of pyrazolo[3,4-*b*]pyridines was achieved by *N*-nitrosation of the methylamino group of the pyridine and reduction of *N*-nitroso group to the hydrazine group with simultaneous intramolecular closure of the pyrazole ring.

Keywords: 3-acetyl-4,6-diaryl-2-methylaminopyridines, 4,6-diaryl-2-methylpyridine-3-carbonitriles, 1*H*-pyrazolo[3,4-*b*]pyridines, quaternary pyridinium salts, Dimroth rearrangement.

1*H*-Pyrazolo[3,4-*b*]pyridines exhibit a wide range of biological activity, in particular antimicrobial,[1a,b] antibacterial,[1c] antimalarial,[1d] antiviral,[1e] antitumor,[1f,g] and anti-leishmaniasis[1h] activity.

The inhibitory activity of pyrazolo[3,4-*b*]pyridines against the inflammatory cytokines IL-6 has been revealed, they are considered promising agents for the treatment of rheumatoid arthritis. Pyrazolo[3,4-*b*]pyridines are orexin receptor antagonists and can be used to treat insomnia. They exhibit the properties of inhibitors of glycogen synthase (GSK-3) involved in the phosphorylation of Tau protein, the consequence of which is Alzheimer's disease.[2]

Drugs based on 1*H*-pyrazolium[3,4-*b*]pyridines, cartazolate, tracazolate, and etazolate are used to treat diseases of the nervous system, while riociguat is employed as an effective tool in the treatment of pulmonary hypertension (Fig. 1).[3]

The main routes for the formation of the bicyclic structure of pyrazolo[3,4-*b*]pyridines are the reactions of annulation of the pyridine moiety to a pyrazole ring and annulation of the pyrazole moiety to a pyridine ring.[4]

An original two-component one-pot synthesis of 5-arylpyrazolo[3,4-*b*]pyridines *via* the reaction of 3-formylindoles with 5-aminopyrazoles in the presence of a Lewis acid has been published. The formation of pyrazolo[3,4-*b*]-pyridines undergoes the stages of imine formation, intramolecular alkylation of the pyrazole ring with an indolinium cation, and aromatization of the desired product accompanied by C–N bond cleavage of the indole pyrrole ring.[5a]

The three-component one-pot Hantzsch synthesis, the reaction of 1-phenyl-2-(phenylsulfonyl)ethanone, an aromatic aldehyde, and 3-amino-5-phenylpyrazole yielded

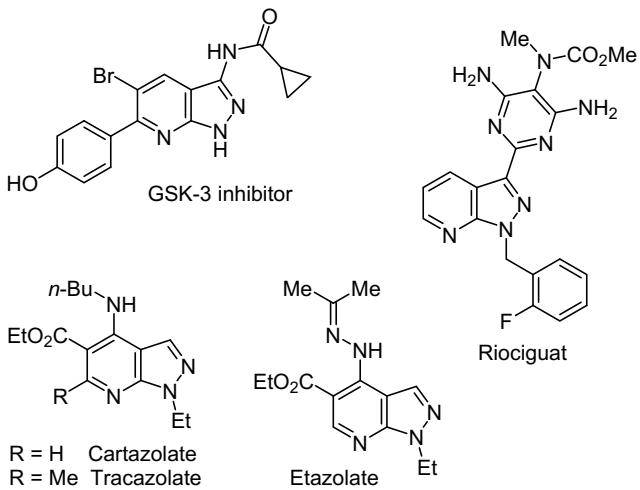
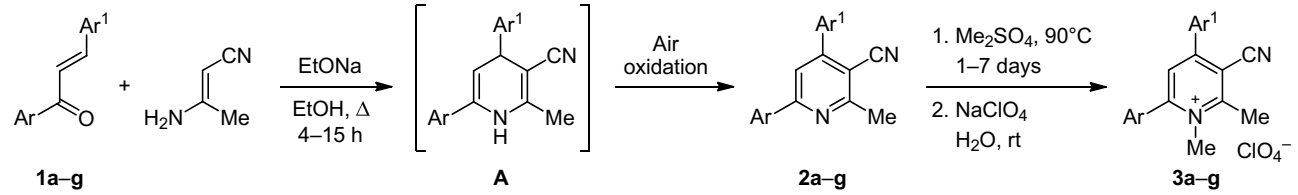


Figure 1. Biologically active derivatives of 1*H*-pyrazolo[3,4-*b*]-pyridines.

Scheme 1



a Ar = Ar[1] = Ph; **b** Ar = Ar[1] = 4-MeC$_6$H$_4$; **c** Ar = Ar[1] = 4-MeOC$_6$H$_4$; **d** Ar = Ph, Ar[1] = 4-ClC$_6$H$_4$;
e Ar = 4-MeOC$_6$H$_4$, Ar[1] = Ph; **f** Ar = Ph, Ar[1] = 4-MeOC$_6$H$_4$; **g** Ar = 4-BrC$_6$H$_4$, Ar[1] = 4-MeOC$_6$H$_4$

4-aryl-3,6-diphenylpyrazolo-1*H*-[3,4-*b*]pyridines. Aromatization of the 1,4-dihydropyridone moiety of pyrazolo[3,4-*b*]-pyridine takes place by elimination of a phenylsulfinic acid molecule.[5b]

In the same manner, pyrazolo[3,4-*b*]pyridines with the carboxyl group at position 6 and the nitro group at position 5 of the pyridine ring were obtained.[5c,d]

In 2017, a new method for the synthesis of functionally substituted pyrazolo[3,4-*b*]pyridines by cyclocondensation of 4-acyl-1*H*-pyrrole-2,3-dione with 3-methyl-1-phenyl-1*H*-pyrazole-5-amine was published. 4-Acylpyrrole-2,3-dione serves as the Michael acceptor, whereas 5-aminopyrazole serves as the donor in the Michael reaction. After cyclization of the Michael adduct with the participation of the amino group of pyrazole and the acyl group of 4-acyl-pyrrole-2,3-dione, a tricyclic molecule is formed in which cleavage of the C–N bond of the pyrrole-2,3-dione ring takes place with the formation of pyrazolo[3,4-*b*]pyridine.[5e]

The known methods for synthesizing 3-amino-1*H*-pyrazolo[3,4-*b*]pyridines by annulaling the pyrazole moiety to pyridine ring are based on the interaction of 2-halo-, 2-methoxy-, and 2-methylsulfanylpyridine-3-carbonitriles with hydrazine.[4]

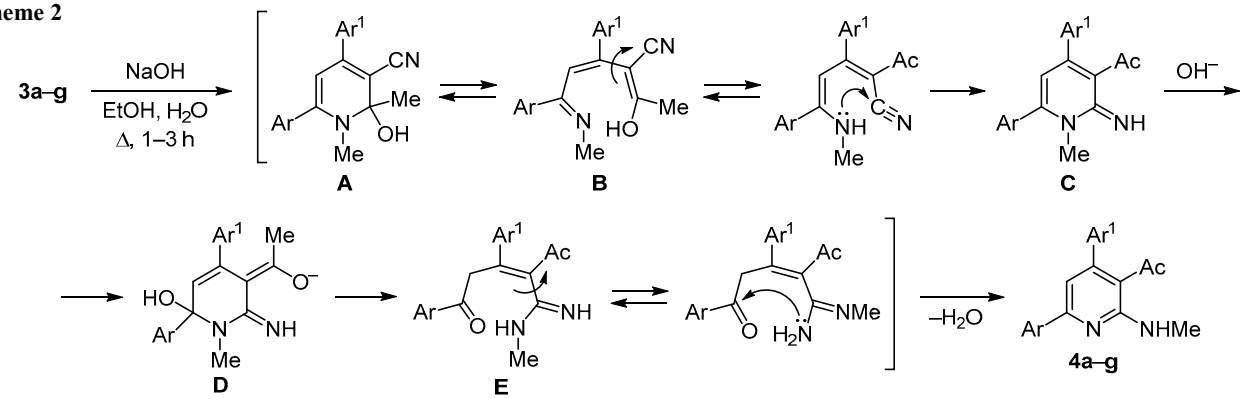
In this paper, we employ a novel method of annulaling the pyrazole moiety to pyridine ring to access 1*H*-pyrazolo[3,4-*b*]-pyridines.

The initial Hantzsch 4,6-diarylpyridine-3-carbonitriles **2a**–**g** were synthesized in a single step by the interaction of chalcones **1a**–**g** with 3-aminocrotononitrile. Intermediate 1,4-dihydropyridines **A** are oxidized by atmospheric oxygen. Quaternary pyridinium salts **3a**–**g** were obtained by alkylation of pyridines **2a**–**g** with dimethyl sulfate (Scheme 1).

For the synthesis of pyridines **4a**–**g**, a double rearrangement of quaternary 3-cyanopyridinium salts **3a**–**g** was used, the final stage being the Dimroth rearrangement.[6] The rearrangement of salts **3a**–**g** into 3-acetyl-4,6-diaryl-2-methylaminopyridines **4a**–**g** was carried out by heating with aqueous-alcoholic alkali (Scheme 2). In the first stage of the reaction, the hydroxide ion attacks position 2 of pyridinium salt **3a**–**g** to form the pseudo base **A**, a neutral analog of the anionic σ-complex. After cleavage of the C–N bond of the pyridine ring and rotation of the C(3)–C(4) bond of the open form **B**, the cyano group reacts with the electron-deficient carbon atom to form a new C–N bond of the cyclic amidine **C**. The Dimroth rearrangement proceeds *via* the addition of hydroxide ion at position 6 of the amidine **C**, which leads to the formation of an anionic σ-complex **D**, in which the polarized C–N bond breaks. The rotation of the C(2)–C(3) bond in the formed open form **E** provides a spatial convergence of the carbonyl group and the primary amino group, their interaction completing the formation of the pyridine ring of compounds **4ag**. As a result of the Dimroth rearrangement the endocyclic and exocyclic nitrogen atoms change places (Scheme 2).[6]

Annulation of the pyrazole ring of pyrazolo[3,4-*b*]-pyridines **6a**–**g** was carried out by *N*-nitrosation of the secondary amino group of pyridines **4a**–**g** followed by reduction of the *N*-nitroso group in compounds **5a**–**g** to the hydrazine group with concurrent intramolecular closure of the pyrazole ring with the participation of the acetyl group

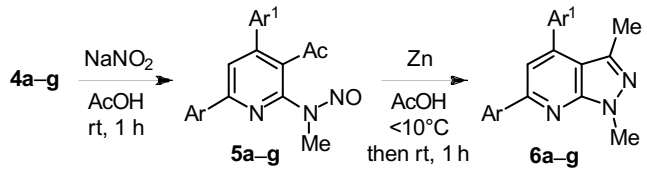
Scheme 2



a Ar = Ar[1] = Ph; **b** Ar = Ar[1] = 4-MeC$_6$H$_4$; **c** Ar = Ar[1] = 4-MeOC$_6$H$_4$; **d** Ar = Ph, Ar[1] = 4-ClC$_6$H$_4$;
e Ar = 4-MeOC$_6$H$_4$, Ar[1] = Ph; **f** Ar = Ph, Ar[1] = 4-MeOC$_6$H$_4$; **g** Ar = 4-BrC$_6$H$_4$, Ar[1] = 4-MeOC$_6$H$_4$

(Scheme 3). Both reaction steps are carried out at room temperature.

Scheme 3



a Ar = Ar^1 = Ph; **b** Ar = Ar^1 = 4-MeC_6H_4; **c** Ar = Ar^1 = 4-$MeOC_6H_4$; **d** Ar = Ph, Ar^1 = 4-ClC_6H_4; **e** Ar = 4-$MeOC_6H_4$, Ar^1 = Ph; **f** Ar = Ph, Ar^1 = 4-$MeOC_6H_4$; **g** Ar = 4-BrC_6H_4, Ar^1 = 4-$MeOC_6H_4$

To conclude, a simple and effective synthesis of 1*H*-pyrazolo[3,4-*b*]pyridines has been developed. The double rearrangement of the quaternary 4,6-diaryl-3-cyano-2-methylpyridinium salts is completed by the Dimroth rearrangement of the pyridine ring to form 3-acetyl-4,6-diaryl-2-methylaminopyridines. Annulation of the pyrazole ring of pyrazolo[3,4-*b*]pyridines is carried out by *N*-nitrosation of 3-acetyl-4,6-diaryl-2-methylaminopyridines with sodium nitrite in acetic acid and reduction of *N*-nitrosopyridine with zinc dust in acetic acid to 2-hydrazinopyridine with simultaneous intramolecular reaction of hydrazine and acetyl groups.

Experimental

IR spectra were registered on a Simex FT-801 spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance DRX-400 spectrometer (400 and 100 MHz, respectively) in DMSO-d_6 (compounds **3a**–**g**) and in $CDCl_3$ (remaining compounds). Chemical shifts were assigned relative to the signal of the solvent (DMSO-d_6: 2.50 ppm for ^{1}H nuclei, 39.5 ppm for ^{13}C nuclei; $CDCl_3$: 7.26 ppm for ^{1}H nuclei, 77.0 ppm for ^{13}C nuclei). ^{13}C NMR spectra were recorded with *J*-modulation. Elemental analysis was performed on a PerkinElmer 2400 Series II CHN-analyzer. Melting points were determined on a Boetius heating bench. Monitoring of the reaction progress and assessment of the purity of synthesized compounds was done by TLC on Silufol UV-254 plates.

3-Aminocrotononitrile supplied by Fluka was used. Chalcones **1a**–**g** were obtained according to published methods.[7] Synthesis of compound **2a** was performed according to a published method.[8a]

Synthesis of 4,6-diaryl-2-methylpyridine-3-carbonitriles 2a–g (General method). 3-Aminocrotononitrile (8.21 g, 100 mmol) and chalcone **1a**–**g** (100 mmol) were added to a solution of Na (2.00 g, 87 mmol) in absolute EtOH (75 ml). The reaction mixture was heated under reflux for 4–15 h (TLC control), then stirred at room temperature for 8–12 h. The formed crystals were filtered off, washed with EtOH.

2-Methyl-4,6-diphenylpyridine-3-carbonitrile (2a). Yield 19.44 g (72%), colorless crystals, mp 118–119°C (EtOH) (mp 116°C (EtOH);[8a,e] mp 117.5–118°C (EtOH)[8b]).

2-Methyl-4,6-bis(4-methylphenyl)pyridine-3-carbonitrile (2b). Yield 19.69 g (66%), colorless crystals, mp 192–193°C (AcOH). IR spectrum, ν, cm^{-1}: 2215, 1587, 1540, 1384, 818. ^{1}H NMR spectrum, δ, ppm: 2.45 (3H, s) and 2.48 (3H, s, ArC<u>H</u>$_3$, Ar^1C<u>H</u>$_3$); 2.93 (3H, s, 2-CH_3); 7.31–7.35 (2H, m, H-3,5 Ar^1); 7.35–7.39 (2H, m, H-3,5 Ar); 7.55–7.58 (2H, m, H-2,6 Ar^1); 7.66 (1H, s, H-5); 7.99–8.03 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 21.3; 21.4; 24.4; 105.4; 117.4; 117.6; 127.4 (2C); 128.4 (2C); 129.7 (4C); 133.8; 135.1; 140.1; 140.6; 153.8; 159.1; 162.7. Found, %: C 84.49; H 6.02; N 9.40. $C_{21}H_{18}N_2$. Calculated, %: C 84.53; H 6.08; N 9.39.

4,6-Bis(4-methoxyphenyl)-2-methylpyridine-3-carbonitrile (2c). Yield 20.48 g (62%), colorless crystals, mp 173–174°C (THF) (mp 172–173°C (EtOH)[8c]).

4-(4-Chlorophenyl)-2-methyl-6-phenylpyridine-3-carbonitrile (2d). Yield 20.12 g (66%), colorless crystals, mp 177–178°C (AcOH) (mp 178–178.5°C (EtOH)[8d]). IR spectrum, ν, cm^{-1}: 2215, 1581, 1537, 1094, 833. ^{1}H NMR spectrum, δ, ppm: 2.92 (3H, s, 2-CH_3); 7.48–7.54 (5H, m, H-3,5 Ar^1, H-3,4,5 Ph); 7.56–7.60 (2H, m, H-2,6 Ar^1); 7.64 (1H, s, H-5); 8.05–8.10 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 24.1; 105.6; 117.0; 117.7; 127.5 (2C); 129.0 (2C); 129.3 (2C); 129.8 (2C); 130.5; 134.9; 136.3; 137.6; 152.6; 159.4; 162.9. Found, %: C 74.90; H 4.35; N 9.14. $C_{19}H_{13}ClN_2$. Calculated, %: C 74.88; H 4.30; N 9.19.

6-(4-Methoxyphenyl)-2-methyl-4-phenylpyridine-3-carbonitrile (2e). Yield 20.43 g (68%), colorless crystals, mp 145–146°C (AcOH) (mp 138.5–139 °C (EtOH)[8d]). IR spectrum, ν, cm^{-1}: 2216, 1585, 1538, 1254, 1031, 820. ^{1}H NMR spectrum, δ, ppm: 2.90 (3H, s, 2-CH_3); 3.88 (3H, s, OCH_3); 6.99–7.04 (2H, m, H-3,5 Ar); 7.50–7.57 (3H, m, H-3,4,5 Ph); 7.60–7.65 (3H, m, H-5, H-2,6 Ph); 8.03–8.09 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 24.4; 55.4; 104.9; 114.4 (2C); 117.0; 117.4; 128.4 (2C); 129.0 (4C); 129.8; 130.3; 136.8; 153.7; 158.8; 161.6; 162.7. Found, %: C 80.06; H 5.41; N 9.40. $C_{20}H_{16}N_2O$. Calculated, %: C 79.98; H 5.37; N 9.33.

4-(4-Methoxyphenyl)-2-methyl-6-phenylpyridine-3-carbonitrile (2f). Yield 22.53 g (75%), colorless crystals, mp 159–160°C (AcOH) (mp 157°C (EtOH)[8e]). IR spectrum, ν, cm^{-1}: 2215, 1584, 1539, 1248, 1028, 830. ^{1}H NMR spectrum, δ, ppm: 2.91 (3H, s, 2-CH_3); 3.89 (3H, s, OCH_3); 7.03–7.09 (2H, m, H-3,5 Ar^1); 7.45–7.53 (3H, m, H-3,4,5 Ph); 7.59–7.62 (2H, m, H-2,6 Ar^1); 7.65 (1H, s, H-5); 8.04–8.11 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 24.4; 55.4; 105.5; 114.5 (2C); 117.6; 117.7; 127.4 (2C); 128.8; 128.9 (2C); 129.9 (2C); 130.2; 137.9; 153.5; 159.1; 161.1; 162.8. Found, %: C 79.96; H 5.35; N 9.36. $C_{20}H_{16}N_2O$. Calculated, %: C 79.98; H 5.37; N 9.33.

6-(4-Bromophenyl)-4-(4-methoxyphenyl)-2-methylpyridine-3-carbonitrile (2g). Yield 35.25 g (93%), colorless crystals, mp 225–226°C (EtOAc). IR spectrum, ν, cm^{-1}: 2214, 1584, 1538, 1254, 1183, 1027, 825. ^{1}H NMR spectrum, δ, ppm: 2.89 (3H, s, 2-CH_3); 3.89 (3H, s, OCH_3); 7.03–7.09 (2H, m, H-3,5 Ar^1); 7.57–7.66 (5H, m, H-5, H-3,5 Ar, H-2,6 Ar^1); 7.92–7.99 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 24.4; 55.4; 105.9; 114.5 (2C); 117.3; 117.4; 124.9; 128.6; 128.9 (2C); 129.9 (2C); 132.1 (2C); 136.7; 153.7; 157.8; 161.1; 162.9. Found, %: C 63.40; H 4.02; N 7.40. $C_{20}H_{15}BrN_2O$. Calculated, %: C 63.34; H 3.99; N 7.39.

Synthesis of quaternary 4,6-diaryl-3-cyano-2-methylpyridinium 3a–g (General method). A mixture of nitrile **2a–g** (5.0 mmol) and freshly distilled Me_2SO_4 (2.4 ml, 25.0 mmol) was heated at 90°C (reaction time shown below). After cooling, the reaction mixture was washed with Et_2O (3×10 ml), and the diethyl ether wash decanted. The residue was dissolved in the minimum amount of water, and a saturated aqueous $NaClO_4$ (0.64 g, 5.3 mmol) added. The precipitated perchlorate salt was filtered off, dried, and purified by recrystallization from EtOH.

3-Cyano-1,2-dimethyl-4,6-diphenylpyridinium perchlorate (3a). Reaction time 24 h. Yield 1.50 g (78%), colorless crystals, mp 221–223°C. ^{1}H NMR spectrum, δ, ppm: 3.13 (3H, s, 2-CH_3); 4.00 (3H, s, 1-CH_3); 7.63–7.76 (8H, m, H 4-Ph, H-3,4,5 6-Ph); 7.87–7.94 (2H, m, H-2,6 6-Ph); 8.23 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.0; 44.8; 111.7; 115.0; 128.0; 129.7 (4C); 129.7 (2C); 129.8 (2C); 132.2; 132.5; 132.6; 133.8; 158.1; 158.9; 162.2. Found, %: C 62.40; H 4.51; N 7.35. $C_{20}H_{17}ClN_2O_4$. Calculated, %: C 62.42; H 4.45; N 7.28.

3-Cyano-1,2-dimethyl-4,6-bis(4-methylphenyl)pyridinium perchlorate (3b). Reaction time 48 h. Yield 1.65 g (80%), colorless crystals, mp 202–204°C. ^{1}H NMR spectrum, δ, ppm: 2.43 (3H, s) and 2.44 (3H, s, Ar^{1}C$\underline{H}_3$, Ar^{1}C$\underline{H}_3$); 3.10 (3H, s, 2-CH_3); 4.03 (3H, s, 1-CH_3); 7.45–7.52 (4H, m, H-3,5 Ar^1, H-3,5 Ar); 7.59–7.64 (2H, m, H-2,6 Ar^1); 7.79–7.85 (2H, m, H-2,6 Ar); 8.16 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 21.5 (2C); 22.0; 44.8; 110.9; 115.3; 127.6; 129.7; 129.8 (4C); 130.2 (2C); 130.4 (2C); 130.9; 142.4; 143.2; 157.7; 158.9; 162.2. Found, %: C 64.08; H 5.13; N 6.82. $C_{22}H_{21}ClN_2O_4$. Calculated, %: C 64.00; H 5.13; N 6.78.

3-Cyano-4,6-bis(4-methoxyphenyl)-1,2-dimethylpyridinium perchlorate (3c). Reaction time 168 h. Yield 2.14 g (96%), colorless crystals, mp 212–213°C. ^{1}H NMR spectrum, δ, ppm: 3.08 (3H, s, 2-CH_3); 3.87 (6H, s, 2OCH_3); 4.03 (3H, s, 1-CH_3); 7.19–7.27 (4H, m, H-3,5 Ar, H-3,5 Ar^1); 7.65–7.73 (2H, m, H-2,6 Ar^1); 7.89–7.96 (2H, m, H-2,6 Ar); 8.13 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.0; 44.7; 56.1; 56.2; 109.9; 115.2 (2C); 115.4 (2C); 115.6; 124.6; 125.7; 127.2; 131.9 (4C); 156.9; 158.5; 162.1; 162.3; 163.1. Found, %: C 59.47; H 4.79; N 6.35. $C_{22}H_{21}ClN_2O_6$. Calculated, %: C 59.40; H 4.76; N 6.30.

4-(4-Chlorophenyl)-3-cyano-1,2-dimethyl-6-phenylpyridinium perchlorate (3d). Reaction time 96 h. Yield 1.61 g (77%), colorless crystals, mp 240–242°C. ^{1}H NMR spectrum, δ, ppm: 3.12 (3H, s, 2-CH_3); 4.05 (3H, s, 1-CH_3); 7.69–7.73 (5H, m, H-3,4,5 Ph, H-3,5 Ar^1); 7.74–7.78 (2H, m, H-2,6 Ar^1); 7.90–7.97 (2H, m, H-2,6 Ph); 8.28 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.1; 44.9; 111.6; 114.9; 128.1; 129.7 (4C); 129.9 (2C); 131.7 (2C); 132.2; 132.4; 132.5; 137.8; 156.8; 159.0; 162.2. Found, %: C 57.39; H 3.81; N 6.73. $C_{20}H_{16}Cl_2N_2O_4$. Calculated, %: C 57.30; H 3.85; N 6.68.

3-Cyano-6-(4-methoxyphenyl)-1,2-dimethyl-4-phenylpyridinium perchlorate (3e). Reaction time 168 h. Yield 1.68 g (81%), colorless crystals, mp 193–194°C. ^{1}H NMR spectrum, δ, ppm: 3.10 (3H, s, 2-CH_3); 3.87 (3H, s, OCH_3); 4.08 (3H, s, 1-CH_3); 7.19–7.28 (2H, m, H-3,5 Ar); 7.62–7.75 (5H, m, H Ph); 7.85–7.92 (2H, m, H-2,6 Ar); 8.19 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.1; 45.0; 56.2; 110.9; 115.1; 115.2 (2C); 124.5; 128.0; 129.7 (2C); 129.8 (2C); 132.0 (2C); 132.5; 133.9; 157.5; 159.1; 162.1; 162.4. Found, %: C 60.88; H 4.65; N 6.80. $C_{21}H_{19}ClN_2O_5$. Calculated, %: C 60.80; H 4.62; N 6.75.

3-Cyano-4-(4-methoxyphenyl)-1,2-dimethyl-6-phenylpyridinium perchlorate (3f). Reaction time 96 h. Yield 1.83 g (88%), colorless crystals, mp 232–233°C. ^{1}H NMR spectrum, δ, ppm: 3.09 (3H, s, 2-CH_3); 3.88 (3H, s, OCH_3); 3.99 (3H, s, 1-CH_3); 7.19–7.24 (2H, m, H-3,5 Ar^1); 7.66–7.73 (5H, m, H-3,4,5 Ph, H-2,6 Ar^1); 7.93–7.97 (2H, m, H-2,6 Ph); 8.19 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.0; 44.6; 56.2; 110.5; 115.4 (2C); 115.5; 125.5; 127.2; 129.7 (4C); 132.0 (2C); 132.1; 132.6; 157.3; 158.3; 162.2; 163.2. Found, %: C 60.84; H 4.60; N 6.78. $C_{21}H_{19}ClN_2O_5$. Calculated, %: C 60.80; H 4.62; N 6.75.

6-(4-Bromophenyl)-3-cyano-4-(4-methoxyphenyl)-1,2-dimethylpyridinium perchlorate (3g). Reaction time 24 h. Yield 2.20 g (89%), colorless crystals, mp 204–205°C. ^{1}H NMR spectrum, δ, ppm: 3.09 (3H, s, 2-CH_3); 3.88 (3H, s, OCH_3); 3.99 (3H, s, 1-CH_3); 7.20–7.25 (2H, m, H-3,5 Ar^1); 7.62–7.68 (2H, m, H-3,5 Ar); 7.86–7.97 (4H, m, H-2,6 Ar, H-2,6 Ar^1); 8.20 (1H, s, H-5). ^{13}C NMR spectrum, δ, ppm: 22.0; 44.6; 56.2; 110.6; 115.1; 115.4 (2C); 125.5; 126.0; 127.3; 131.7; 131.8 (2C); 132.0 (2C); 132.7 (2C); 157.2; 157.3; 162.2; 163.3. Found, %: C 50.99; H 3.63; N 5.74. $C_{21}H_{18}BrClN_2O_5$. Calculated, %: C 51.09; H 3.67; N 5.67.

Synthesis of 3-acetylpyridines 4a–g (General method). 10% Aqueous NaOH solution (1.8 ml, 5 mmol) was added to a suspension of the quaternary pyridinium salt **3a–g** (1 mmol) in EtOH (4 ml). The reaction mixture acquires an intense burgundy color, which disappears after heating under reflux for 1–3 h (control by TLC). The mixture was diluted with water, neutralized with 50% aqueous AcOH, and cooled. The precipitated crystals were filtered off and recrystallized from EtOH.

1-[2-(Methylamino)-4,6-diphenylpyridin-3-yl]ethanone (4a). Yield 0.26 g (87%), light-yellow crystals, mp 127–128°C. IR spectrum, ν, cm^{-1}: 3395, 1646, 1573, 1550, 1271, 763. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.82 (3H, s, $COCH_3$); 3.21 (3H, d, *J* = 4.7, NHC$\underline{H}_3$); 7.04 (1H, s, H-5); 7.41–7.54 (8H, m, H 4-Ph, H-3,4,5 6-Ph); 7.87 (1H, br. s, N$\underline{H}$CH$_3$); 8.12–8.21 (2H, m, H-2,6 6-Ph). ^{13}C NMR spectrum, δ, ppm: 28.2; 32.2; 110.2; 114.2; 127.3 (2C); 128.6 (2C); 128.7 (2C); 128.8; 128.9 (2C); 129.6; 138.9; 141.4; 153.3; 157.5; 157.9; 203.9. Found, %: C 79.51; H 5.91; N 9.32. $C_{20}H_{18}N_2O$. Calculated, %: C 79.44; H 6.00; N 9.26.

1-[2-(Methylamino)-4,6-bis(4-methylphenyl)pyridin-3-yl]-ethanone (4b). Yield 0.28 g (85%), yellow crystals, mp 139–140°C. IR spectrum, ν, cm^{-1}: 3380, 1635, 1546, 1233, 1181, 822. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 (3H, s, $COCH_3$); 2.41 (3H, s) and 2.43 (3H, s, Ar$\underline{CH}_3$, Ar^{1}C$\underline{H}_3$); 3.17 (3H, d, *J* = 4.7, NHC$\underline{H}_3$); 6.98 (1H, s, H-5); 7.23–7.32 (6H, m, H-3,5 Ar, H Ar^1); 7.85 (1H, br. s, N$\underline{H}$CH$_3$); 8.00–8.05 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 21.3; 21.4; 28.2; 32.2; 109.9; 114.0; 127.1 (2C); 128.6 (2C); 129.3 (2C); 129.5 (2C); 136.2; 138.5; 138.9; 139.7; 153.4;

157.5; 157.8; 204.0. Found, %: C 80.05; H 6.70; N 8.52. $C_{22}H_{22}N_2O$. Calculated, %: C 79.97; H 6.71; N 8.48.

1-[4,6-Bis(4-methoxyphenyl)-2-(methylamino)pyridin-3-yl]-ethanone (4c). Yield 0.32 g (89%), light-yellow crystals, mp 106–107°C. IR spectrum, ν, cm^{-1}: 3380, 1635, 1546, 1242, 1233, 1181, 1032, 825. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.81 (3H, s, $COCH_3$); 3.16 (3H, d, *J* = 4.7, $NHCH_3$); 3.87 (6H, s, $2OCH_3$); 6.93 (1H, s, H-5); 6.95–7.01 (4H, m, H-3,5 Ar, H-3,5 Ar^1); 7.30–7.35 (2H, m, H-2,6 Ar^1); 7.84 (1H, br. s, $NHCH_3$); 8.07–8.12 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 28.1; 32.1; 55.4 (2C); 109.4; 113.8; 113.9 (2C); 114.3 (2C); 128.6 (2C); 129.9 (2C); 131.6; 133.8; 153.0; 157.4; 157.5; 160.4; 161.0; 203.8. Found, %: C 72.87; H 6.06; N 7.79. $C_{22}H_{22}N_2O_3$. Calculated, %: C 72.91; H 6.12; N 7.73.

1-[(4-(4-Chlorophenyl)-2-(methylamino)-6-phenylpyridin-3-yl]ethanone (4d). Yield 0.27 g (79%), yellow crystals, mp 109–110°C. IR spectrum, ν, cm^{-1}: 3350, 1635, 1543, 1246, 1086, 1007, 778. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.82 (3H, s, $COCH_3$); 3.17 (3H, d, *J* = 4.7, $NHCH_3$); 6.95 (1H, s, H-5); 7.33–7.38 (2H, m, H-2,6 Ar^1); 7.42–7.50 (5H, m, H-3,5 Ar^1, H-3,4,5 Ph); 7.87 (1H, br. s, $NHCH_3$); 8.09–8.15 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 28.2; 32.4; 110.0; 113.9; 127.2 (2C); 128.6 (2C); 129.2 (2C); 129.7; 129.9 (2C); 135.2; 138.7; 139.8; 152.0; 157.5; 158.1; 203.4. Found, %: C 71.27; H 5.06; N 8.22. $C_{20}H_{17}ClN_2O$. Calculated, %: C 71.32; H 5.09; N 8.32.

1-[6-(4-Methoxyphenyl)-2-(methylamino)-4-phenylpyridin-3-yl]ethanone (4e). Yield 0.25 g (75%), yellow crystals, mp 104–105°C. IR spectrum, ν, cm^{-1}: 3382, 1628, 1545, 1251, 1177, 1026, 831, 772, 712. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.77 (3H, s, $COCH_3$); 3.17 (3H, d, *J* = 4.7, $NHCH_3$); 3.87 (3H, s, OCH_3); 6.94 (1H, s, H-5); 6.95–7.00 (2H, m, H-3,5 Ar); 7.38–7.48 (5H, m, H Ph); 7.96 (1H, br. s, $NHCH_3$); 8.08–8.13 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 28.2; 32.2; 55.4; 109.5; 113.4; 113.9 (2C); 128.6 (2C); 128.7 (2C); 128.8; 128.8 (2C); 131.5; 141.6; 153.4; 157.5; 157.6; 161.1; 203.6. Found, %: C 75.81; H 5.99; N 8.41. $C_{21}H_{20}N_2O_2$. Calculated, %: C 75.88; H 6.06; N 8.43.

1-[4-(4-Methoxyphenyl)-2-(methylamino)-6-phenylpyridin-3-yl]ethanone (4f). Yield 0.27 g (80%), yellow crystals, mp 118–119°C. IR spectrum, ν, cm^{-1}: 3386, 1631, 1542, 1232, 1029, 835. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.82 (3H, s, $COCH_3$); 3.17 (3H, d, *J* = 4.7, $NHCH_3$); 3.87 (3H, s, OCH_3); 6.96–7.02 (3H, m, H-5, H-3,5 Ar^1); 7.31–7.37 (2H, m, H-2,6 Ar^1); 7.40–7.49 (3H, m, H-3,4,5 Ph); 7.76 (1H, br. s, $NHCH_3$); 8.10–8.15 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 28.2; 32.1; 55.4; 110.1; 114.3 (2C); 114.4; 127.2 (2C); 128.5 (2C); 129.5; 129.9 (2C); 133.5; 139.0; 152.9; 157.4; 157.7; 160.4; 204.2. Found, %: C 75.94; H 6.09; N 8.37. $C_{21}H_{20}N_2O_2$. Calculated, %: C 75.88; H 6.06; N 8.43.

1-[6-(4-Bromophenyl)-4-(4-methoxyphenyl)-2-(methylamino)pyridin-3-yl]ethanone (4g). Yield 0.39 g (95%), yellow crystals, mp 153–154°C. IR spectrum, ν, cm^{-1}: 3380, 1634, 1545, 1248, 1030, 816. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.81 (3H, s, $COCH_3$); 3.14 (3H, d, *J* = 4.7, $NHCH_3$); 3.87 (3H, s, OCH_3); 6.96 (1H, s, H-5); 6.97–7.01 (2H, m, H-3,5 Ar^1); 7.30–7.34 (2H, m, H-2,6 Ar^1); 7.55–7.60 (2H, m, H-3,5 Ar); 7.72 (1H, br. s, $NHCH_3$); 7.97–8.02 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 28.2; 32.1; 55.4; 109.8; 114.4 (2C); 114.7; 124.0; 128.7 (2C); 129.9 (2C); 131.7 (2C); 133.3; 137.9; 153.0; 156.4; 157.3; 160.5; 204.2. Found, %: C 61.37; H 4.69; N 6.79. $C_{21}H_{19}BrN_2O_2$. Calculated, %: C 61.32; H 4.66; N 6.81.

Synthesis of *N*-nitrosoaminopyridines 5a–g (General method). $NaNO_2$ (0.21 g, 3 mmol) was added in portions at room temperature to a solution or suspension of *N*-methylaminopyridine **4a**–**g** (2 mmol) in AcOH (8 ml). When the addition was complete, the reaction mixture was stirred for 1 h, diluted with water, and the formed precipitate filtered off and recrystallized from EtOH.

1-{2-[Methyl(nitroso)amino]-4,6-diphenylpyridin-3-yl}-ethanone (5a). Yield 0.57 g (86%), light-yellow crystals, mp 136–137°C. IR spectrum, ν, cm^{-1}: 1702, 1591, 1470, 1201, 1117, 977. ^{1}H NMR spectrum, δ, ppm: 2.04 (3H, s, $COCH_3$); 3.69 (3H, s, NCH_3); 7.39–7.44 (2H, m, H-2,6 4-Ph); 7.45–7.54 (6H, m, H-3,4,5 4-Ph, H-3,4,5 6-Ph); 7.70 (1H, s, H-5); 8.05–8.10 (2H, m, H-2,6 6-Ph). ^{13}C NMR spectrum, δ, ppm: 30.5; 31.9; 119.5; 127.0 (2C); 127.9; 128.5 (2C); 128.9 (4C); 129.2; 130.1; 137.3; 137.4; 150.1; 150.2; 155.7; 202.3. Found, %: C 72.59; H 5.24; N 12.68. $C_{20}H_{17}N_3O_2$. Calculated, %: C 72.49; H 5.17; N 12.68.

1-{2-[Methyl(nitroso)amino]-4,6-bis(4-methylphenyl)-pyridin-3-yl}ethanone (5b). Yield 0.69 g (96%), colorless crystals, mp 163–164°C. IR spectrum, ν, cm^{-1}: 1698, 1591, 1461, 1201, 1185, 1111, 823. ^{1}H NMR spectrum, δ, ppm: 2.05 (3H, s, $COCH_3$); 2.43 (6H, s, $ArCH_3$, Ar^1CH_3); 3.67 (3H, s, NCH_3); 7.27–7.34 (6H, m, H-3,5 Ar, H Ar^1); 7.66 (1H, s, H-5); 7.94–7.99 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 21.2; 21.3; 30.5; 31.9; 119.2; 126.9 (2C); 127.7; 128.4 (2C); 129.6 (2C); 129.7 (2C); 134.6; 134.6; 139.2; 140.3; 150.1; 150.2; 155.7; 202.6. Found, %: C 73.59; H 5.87; N 11.62. $C_{22}H_{21}N_3O_2$. Calculated, %: C 73.52; H 5.89; N 11.69.

1-{4,6-Bis(4-methoxyphenyl)-2-[methyl(nitroso)amino]-pyridin-3-yl}ethanone (5c). Yield 0.72 g (92%), colorless crystals, mp 166–167°C. IR spectrum, ν, cm^{-1}: 1704, 1592, 1463, 1258, 1175, 1027, 837. ^{1}H NMR spectrum, δ, ppm: 2.05 (3H, s, $COCH_3$); 3.66 (3H, s, NCH_3); 3.87 (3H, s, Ar^1OCH_3); 3.88 (3H, s, $ArOCH_3$); 6.96–7.04 (4H, m, H-3,5 Ar, H-3,5 Ar^1); 7.31–7.37 (2H, m, H-2,6 Ar^1); 7.60 (1H, s, H-5); 8.00–8.05 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 30.5; 31.9; 55.3; 55.4; 114.3 (2C); 114.4 (2C); 118.7; 127.3; 128.4 (2C); 129.7; 129.8 (2C); 130.0; 149.9; 150.1; 155.3; 160.4; 161.3; 202.8. Found, %: C 67.50; H 5.47; N 10.66. $C_{22}H_{21}N_3O_4$.Calculated, %: C 67.51; H 5.41; N 10.74.

1-{4-(4-Chlorophenyl)-2-[methyl(nitroso)amino]-6-phenylpyridin-3-yl}ethanone (5d). Yield 0.70 g (95%), colorless crystals, mp 194–195 °C. IR spectrum, ν, cm^{-1}: 1696, 1593, 1464, 1212, 1070, 720. ^{1}H NMR spectrum, δ, ppm: 2.07 (3H, s, $COCH_3$); 3.68 (3H, s, NCH_3); 7.34–7.38 (2H, m, H-2,6 Ar^1); 7.45–7.49 (2H, m, H-3,5 Ar^1); 7.50–7.54 (3H, m, H-3,4,5 Ph); 7.65 (1H, s, H-5); 8.05–8.09 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 30.3; 32.0; 119.2; 127.0 (2C); 127.6; 129.0 (2C); 129.2 (2C); 129.9 (2C); 130.2; 135.6; 135.8; 137.1; 149.0; 150.3;

155.9; 201.8. Found, %: C 65.58; H 4.37; N 11.48. $C_{20}H_{16}ClN_3O_2$. Calculated, %: C 65.67; H 4.41; N 11.49.

1-{6-(4-Methoxyphenyl)-2-[methyl(nitroso)amino]-4-phenylpyridin-3-yl}ethanone (5e). Yield 0.70 g (97%), colorless crystals, mp 177–178°C. IR spectrum, ν, cm^{-1}: 1691, 1592, 1519, 1459, 1246, 1203, 1179, 1027, 839. ^{1}H NMR spectrum, δ, ppm: 2.02 (3H, s, $COCH_3$); 3.67 (3H, s, NCH_3); 3.88 (3H, s, OCH_3); 6.98–7.05 (2H, m, H-3,5 Ar); 7.38–7.44 (2H, m, H-2,6 Ph); 7.45–7.51 (3H, m, H-3,4,5 Ph); 7.62 (1H, s, H-5); 7.98–8.08 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 30.5; 31.9; 55.4; 114.3 (2C); 118.6; 127.3; 128.4 (2C); 128.5 (2C); 128.9 (2C); 129.1; 129.9; 137.6; 149.9; 150.2; 155.4; 161.3; 202.4. Found, %: C 69.76; H 5.28; N 11.58. $C_{21}H_{19}N_3O_3$. Calculated, %: C 69.79; H 5.30; N 11.63.

1-{4-(4-Methoxyphenyl)-2-[methyl(nitroso)amino]-6-phenylpyridin-3-yl}ethanone (5f). Yield 0.68 g (94%), colorless crystals, mp 164–165°C. IR spectrum, ν, cm^{-1}: 1697, 1593, 1514, 1465, 1238, 1199, 1182, 1034, 973, 843. ^{1}H NMR spectrum, δ, ppm: 2.06 (3H, s, $COCH_3$); 3.67 (3H, s, NCH_3); 3.87 (3H, s, OCH_3); 6.97–7.03 (2H, m, H-3,5 Ar^1); 7.33–7.38 (2H, m, H-2,6 Ar^1); 7.45–7.54 (3H, m, H-3,4,5 Ph); 7.68 (1H, s, H-5); 8.03–8.11 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 30.5; 31.9; 55.4; 114.4 (2C); 119.6; 127.0 (2C); 127.9; 128.9 (2C); 129.5; 129.8 (2C); 130.0; 137.4; 150.0; 150.2; 155.6; 160.4; 202.7. Found, %: C 69.72; H 5.26; N 11.65. $C_{21}H_{19}N_3O_3$. Calculated, %: C 69.79; H 5.30; N 11.63.

1-{6-(4-Bromophenyl)-4-(4-methoxyphenyl)-2-[methyl-(nitroso)amino]pyridin-3-yl}ethanone (5g). Yield 0.86 g (98%), colorless crystals, mp 174–175°C. IR spectrum, ν, cm^{-1}: 1690, 1591, 1466, 1254, 1062, 982, 841. ^{1}H NMR spectrum, δ, ppm: 2.05 (3H, s, $COCH_3$); 3.65 (3H, s, NCH_3); 3.87 (3H, s, OCH_3); 6.97–7.04 (2H, m, H-3,5 Ar^1); 7.31–7.37 (2H, m, H-2,6 Ar^1); 7.61–7.64 (2H, m, H-3,5 Ar); 7.65 (1H, s, H-5); 7.91–7.98 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 30.5; 31.8; 55.4; 114.5 (2C); 119.4; 124.6; 128.2; 128.5 (2C); 129.3; 129.8 (2C); 132.1 (2C); 136.3; 150.2; 150.4; 154.4; 160.5; 202.5. Found, %: C 57.30; H 4.17; N 9.58. $C_{21}H_{18}BrN_3O_3$.Calculated, %: C 57.29; H 4.12; N 9.54.

Synthesis of 4,6-diaryl-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]-pyridines 6a–g (General method). Zinc dust (0.65 g, 10 mmol) was added in portions to a stirred solution of nitrosoaminopyridine **5a–g** (2 mmol) in AcOH (8 ml), keeping the temperature below 10°C. The mixture was then stirred at room temperature for 1 h, filtered, and the inorganic precipitate washed with hot AcOH. The filtrate was diluted with cold water and neutralized with aqueous NH_3. The crystalline pyrazolopyridine **6a–g** was filtered off, and purified by recrystallization from EtOH.

1,3-Dimethyl-4,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (6a). Yield 0.48 g (80%), colorless crystals, mp 97–98°C. IR spectrum, ν, cm^{-1}: 1582, 1561, 1348, 1151, 775. ^{1}H NMR spectrum, δ, ppm: 2.27 (3H, s, 3-CH_3); 4.18 (3H, s, NCH_3); 7.42–7.57 (9H, m, H-5, H 4-Ph, H-3,4,5 6-Ph); 8.14–8.20 (2H, m, H-2,6 6-Ph). ^{13}C NMR spectrum, δ, ppm: 15.2; 33.6; 111.8; 114.4; 127.5 (2C); 128.3 (2C); 128.6; 128.8 (2C); 129.0 (2C); 129.3; 138.1; 139.5; 140.2; 146.4; 152.1; 156.3. Found, %: C 80.15; H 5.72; N 13.97. $C_{20}H_{17}N_3$. Calculated, %: C 80.24; H 5.72; N 14.04.

1,3-Dimethyl-4,6-bis(4-methylphenyl)-1*H*-pyrazolo-[3,4-*b*]pyridine (6b). Yield 0.52 g (80%), colorless crystals, mp 134–135°C. IR spectrum, ν, cm^{-1}: 1581, 1563, 1344, 1185, 817. ^{1}H NMR spectrum, δ, ppm: 2.29 (3H, s, 3-CH_3); 2.42 (3H, s, $Ar^1C\underline{H}_3$); 2.46 (3H, s, $ArC\underline{H}_3$); 4.17 (3H, s, NCH_3); 7.28–7.34 (4H, m, H-3,5 Ar, H-3,5 Ar^1); 7.40–7.45 (3H, m, H-5, H-2,6 Ar^1); 8.04–8.08 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 15.3; 21.3 (2C); 33.5; 111.7; 114.2; 127.4 (2C); 129.0 (4C); 129.5 (2C); 135.3; 136.7; 138.5; 139.3; 140.2; 146.3; 152.1; 156.3. Found, %: C 80.78; H 6.41; N 12.80. $C_{22}H_{21}N_3$. Calculated, %: C 80.70; H 6.46; N 12.83.

4,6-Bis(4-methoxyphenyl)-1,3-dimethyl-1*H*-pyrazolo-[3,4-*b*]pyridine (6c). Yield 0.56 g (78%), colorless crystals, mp 137–138°C. IR spectrum, ν, cm^{-1}: 1585, 1563, 1466, 1241, 1177, 1029, 822. ^{1}H NMR spectrum, δ, ppm: 2.29 (3H, s, 3-CH_3); 3.88 (3H, s, $Ar^1OC\underline{H}_3$); 3.90 (3H, s, $ArOC\underline{H}_3$); 4.15 (3H, s, NCH_3); 6.99–7.06 (4H, m, H-3,5 Ar, H-3,5 Ar^1); 7.37 (3H, s, H-5); 7.43–7.49 (2H, m, H-2,6 Ar^1); 8.10–8.15 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 15.4; 33.5; 55.4 (2C); 111.5; 113.7 (2C); 113.8; 114.1 (2C); 128.8 (2C); 130.3 (2C); 130.6; 132.1; 140.2; 146.0; 152.2; 156.0; 160.1; 160.7. Found, %: C 73.58; H 5.80; N 11.71. $C_{22}H_{21}N_3O_2$. Calculated, %: C 73.52; H 5.89; N 11.69.

4-(4-Chlorophenyl)-1,3-dimethyl-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (6d). Yield 0.55 g (83%), colorless crystals, mp 135–136°C. IR spectrum, ν, cm^{-1}: 1583, 1562, 1497, 1348, 1162, 1090, 820. ^{1}H NMR spectrum, δ, ppm: 2.27 (3H, s, 3-CH_3); 4.17 (3H, s, NCH_3); 7.42 (3H, s, H-5); 7.44–7.53 (7H, m, H Ar^1, H-3,4,5 Ph); 8.13–8.17 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 15.3; 33.6; 111.6; 114.3; 127.5 (2C); 128.6 (2C); 128.8 (2C); 129.4; 130.3 (2C); 134.9; 136.5; 139.3; 139.9; 144.9; 152.1; 156.4. Found, %: C 71.89; H 4.85; N 12.55. $C_{20}H_{16}ClN_3$. Calculated, %: C 71.96; H 4.83; N 12.59.

6-(4-Methoxyphenyl)-1,3-dimethyl-4-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (6e). Yield 0.54 g (82%), colorless crystals, mp 98–99°C. IR spectrum, ν, cm^{-1}: 1583, 1561, 1344, 1238, 1167, 1035, 826. ^{1}H NMR spectrum, δ, ppm: 2.25 (3H, s, 3-CH_3); 3.88 (3H, s, OCH_3); 4.16 (3H, s, NCH_3); 6.99–7.06 (2H, m, H-3,5 Ar); 7.40 (3H, s, H-5); 7.47–7.56 (5H, m, H Ph); 8.09–8.17 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 15.2; 33.5; 55.4; 111.4; 113.8; 114.1 (2C); 128.3 (2C); 128.5; 128.8 (2C); 129.0 (2C); 132.0; 138.2; 140.2; 146.2; 152.1; 156.0; 160.8. Found, %: C 76.60; H 5.79; N 12.80. $C_{21}H_{19}N_3O$. Calculated, %: C 76.57; H 5.81; N 12.76.

4-(4-Methoxyphenyl)-1,3-dimethyl-6-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (6f). Yield 0.61 g (92%), colorless crystals, mp 123–124°C. IR spectrum, ν, cm^{-1}: 1583, 1562, 1514, 1250, 1176, 1031, 834, 773. ^{1}H NMR spectrum, δ, ppm: 2.31 (3H, s, 3-CH_3); 3.90 (3H, s, OCH_3); 4.17 (3H, s, NCH_3); 7.02–7.08 (2H, m, H-3,5 Ar^1); 7.41–7.54 (6H, m, H-5, H-2,6 Ar^1, H-3,4,5 Ph); 8.13–8.19 (2H, m, H-2,6 Ph). ^{13}C NMR spectrum, δ, ppm: 15.4; 33.5; 55.4; 111.9; 113.8 (2C); 114.4; 127.5 (2C); 128.7 (2C); 129.2; 130.3 (2C); 130.4; 139.5; 140.2; 146.2; 152.2; 156.3; 160.1. Found, %:

C 76.62; H 5.85; N 12.71. $C_{21}H_{19}N_3O$. Calculated, %: C 76.57; H 5.81; N 12.76.

6-(4-Bromophenyl)-4-(4-methoxyphenyl)-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine (6g). Yield 0.66 g (81%), colorless crystals, mp 126–127°C. IR spectrum, ν, cm^{-1}: 1582, 1562, 1247, 1174, 1050, 828. ^{1}H NMR spectrum, δ, ppm: 2.30 (3H, s, 3-CH_3); 3.90 (3H, s, OCH_3); 4.15 (3H, s, NCH_3); 6.99–7.08 (2H, m, H-3,5 Ar[1]); 7.38 (3H, s, H-5); 7.42–7.49 (2H, m, H-3,5 Ar); 7.57–7.66 (2H, m, H-2,6 Ar[1]); 8.00–8.07 (2H, m, H-2,6 Ar). ^{13}C NMR spectrum, δ, ppm: 15.4; 33.5; 55.4; 112.1; 113.8 (2C); 114.0; 123.7; 129.0 (2C); 130.2; 130.3 (2C); 131.9 (2C); 138.4; 140.3; 146.4; 152.1; 154.9; 160.2. Found, %: C 61.63; H 4.51; N 10.35. $C_{21}H_{18}BrN_3O$. Calculated, %: C 61.78; H 4.44; N 10.29.

The work was supported by the Russian Foundation for Basic Research and the Ministry of Education of the Omsk Region (grant 16-43-550144p_a).

References

1. (a) Goda, F. E.; Abdel-Aziz, A. A.-M.; Attef, O. A. *Bioorg. Med. Chem*. **2004**, *12*, 1845. (b) El-Borai, M. A.; Rizk, H. F.; Beltagy, D. M.; El-Deeb, I. Y. *Eur. J. Med. Chem*. **2013**, *66*, 415. (c) Samar, C.; Ismail, A.; Helmi, T.; Khiari, J.; Bassem, J. *J. Bacteriol. Parasitol*. **2017**, *8*, 310. (d) Menezes, C. M. S.; Sant'Anna, C. M. R.; Rodrigues, C. R.; Barreiro, E. J. *J. Mol. Struct.: THEOCHEM* **2002**, *579*, 31. (e) Bernardino, A. M. R.; de Azevedo, A. R.; da Silva Pinheiro, L. C.; Borges, J. C.; Carvalho, V. L.; Miranda, M. D.; de Meneses, M. D. F.; Nascimento, M.; Ferreira, D.; Rebello, M. A.; da Silva, V. A. G. G.; de Frugulhetti, I. C. P. P. *Med. Chem. Res*. **2007**, *16*, 352. (f) Lin, R.; Connolly, P. J.; Lu, Y.; Chiu, G.; Li, S.; Yu, Y.; Huang, S.; Li, X.; Emanuel, S. L.; Middleton, S. A.; Gruninger, R. H.; Adams, M.; Fuentes-Pesquera, A. R.; Greenberger, L. M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4297. (g) Huang, S.; Lin, R.; Yu, Y.; Lu, Y.; Connolly, P. J.; Chiu, G.; Li, S.; Emanuel, S. L.; Middleton, S. A. *Bioorg. Med. Chem. Lett*. **2007**, *17,* 1243. (h) de Mello, H.; Echevarria, A.; Bernardino, A. M.; Canto-Cavalheiro, M.; Leon, L. L. *J. Med. Chem*. **2004**, *47*, 5427.
2. (a) Bharate, S. B.; Mahajan, T. R.; Gole, Y. R.; Nambiar, M.; Matan, T. T.; Kulkarni-Almeida, A.; Balachandran, S.; Junjappa, H.; Balakrishnan, A.; Vishwakarma, R. A. *Bioorg. Med. Chem*. **2008**, *16*, 7167. (b) Roecker, A. J.; Cox, C. D.; Coleman, P. J. *J. Med. Chem*. **2016**, *59*, 504. (c) Witherington, J.; Bordas, V.; Gaiba, A.; Garton, N. S.; Naylor, A.; Rawlings, A. D.; Slingsby, B. P.; Smith, D. G.; Takle, A. K.; Ward, R. W. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3055. (d) Qin, J.; Zhou, W.; Huang, X.; Dhondi, P.; Palani, A.; Aslanian, R.; Zhu, Z.; Greenlee, W.; Cohen-Williams, M.; Jones, N.; Hyde, L.; Zhang, L. *ACS Med. Chem. Lett*. **2011**, *2*, 471.
3. (a) Lavrard, H.; Popowycz, F. *Eur. J. Org. Chem.* **2017**, 600. (b) Follmann, M.; Griebenow, N.; Hahn, M. G.; Hartung, I.; Mais, F.-J.; Mittendorf, J.; Schäfer, M.; Schirok, H.; Stasch, J.-P.; Stoll, F.; Straub, A. *Angew. Chem.*, *Int. Ed*. **2013**, *52*, 9442. (c) Garnock-Jones, K. P. *Drugs* **2014**, *74,* 2065.
4. (a) Dodiya, D. K.; Trivedi, A. R.; Kataria, V. B.; Shah, V. H. *Curr. Org. Chem*. **2012**, *16*, 400. (b) Schirok, H.; Griebenow, N.; Fürstner, C.; Dilmac, A. M. *Tetrahedron* **2015**, *71*, 5597. (c) Behnke, D.; Cotesta, S.; Hintermann, S.; Fendt, M.; Gee, C. E.; Jacobson, L. H.; Laue, G.; Meyer, A.; Wagner, T.; Badiger, S.; Chaudhari, V.; Chebrolu, M.; Pandit, C.; Hoyer, D.; Betschart, C. *Bioor. Med. Chem. Lett.* **2015**, *25*, 5555.
5. (a) Lee, S.; Park, S. B. *Org. Lett*. **2009***, 11,* 5214. (b) Saleh, T. S.; Eldebss, T. M. A.; Albishri, H. M. *Ultrason. Sonochem*. **2012**, *19*, 49. (c) El-borai, M. A.; Rizk, H. F.; Abd-Aal, M. F.; El-Deeb, I. Y. *Eur. J. Med. Chem*. **2012**, *48*, 92. (d) Gunasekaran, P.; Prasanna, P.; Perumal, S. *Tetrahedron Lett.* **2014**, *55,* 329. (e) Dubovtsev, A. Yu.; Dmitriev, M. V.; Silaichev, P. S.; Antonov, D. I.; Maslivets, A. N. *Synthesis* **2017**, *49*, 2223.
6. (a) El Ashry, E. S. H.; El Kilany, Y.; Rashed, N.; Assafir, H. *Adv. Heterocycl. Chem*. **1999**, *75*, 79. (b) Brown, D. J.; Harper, J. S. *J. Chem. Soc*. **1965**, 5542. (c) Kost, A. N.; Sagitullin, R. S.; Gromov, S. P. *Chem. Heterocycl. Compd.* **1979**, *15*, 87. [*Khim. Geterotsikl. Soedin.* **1979**, 98.] (d) Gromov, S. P.; Kost, A. N.; Sagitullin, R. S. *Zh. Org. Khim.* **1978**, *14*, 1316. (e) Sagitullina, G. P.; Glizdinskaya, L. V.; Oleinikova, S. I.; Atavin, E. G.; Sagitullin, R. S. *Russ. J. Org. Chem.* **2005**, *41*, 1367. [*Zh. Org. Khim.* **2005**, *41*, 1395.] (f) Sagitullina, G. P.; Lisitskaya, L. A.; Vorontsova, M. A.; Sagitullin, R. S. *Mendeleev Commun.* **2007**, *17*, 192.
7. (a) Lee, G. S.; Kammermeier, T.; Kaiser, A.; Eibler, E.; Wiegrebe, W. *Arch. Pharm.* **1991**, *324*, 177. (b) Yang, J.-X; Tao, X.-T.; Yuan, C. X.; Yan, Y. X.; Wang, L.; Liu, Z.; Ren, Y.; Jiang, M. H. *J. Am. Chem. Soc.* **2005**, *127*, 3278. (c) Szmant, H. H.; Basso, A. J. *J. Am. Chem. Soc.* **1952**, *74*, 4397. (d) Bai, X.-G.; Xu, C.-L.; Zhao, S.-S.; He, H.-W.; Wang, Y.-C.; Wang, J.-X. *Molecules* **2014**, *19*, 17256.
8. (a) Treibs, W.; Beger, J. *Justus Liebigs Ann. Chem.* **1962**, *652*, 192. (b) Robinson, J. M.; Brent, L. W.; Chau, C.; Floyd, K. A.; Gillham, S. L.; McMahan, T. L.; Magda, D. J.; Motycka, T. J.; Pack, M. J.; Roberts, A. L.; Seally, L. A.; Simpson, S. L.; Smith, R. R.; Zalesny, K. N. *J. Org. Chem.* **1992**, *57*, 7352. (c) Matsui, M.; Oji, A.; Hiramatsu, K.; Shibata, K.; Muramatsu, H. *J. Chem. Soc.*, *Perkin Trans. 2* **1992**, 201. (d) Shibata, K.; Urano, K.; Matsui, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2199. (e) Meyer, E. V. *J. Prakt. Chem.* **1908**, *78*, 497.