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Application of Nickel Complexes with 1,3-Dicarbonyl Compounds for Synthesis of Fused 4-Aminopyridine-Based Systems

R. N. Vydzhak[a], S. Ya. Panchishin[a], and V. S. Brovarets[a,*]

[a] *V.P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry of the National Academy of Sciences of Ukraine, Kiev, 02094 Ukraine*
**e-mail: brovarets@bpci.kiev.ua*

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Abstract—A potential of using nickel complexes with 1,3-dicarbonyl compounds for the transformation of heterocyclic aminonitriles into fused systems with a 4-aminopyridine core was evaluated. A possibility of introducing acidophobic groups into the molecules of fused compounds was shown.

Keywords: nickel complexes with 1,3-dicarbonyl compounds, oxadiazolo[3,4-*b*]pyridines, triazolo[4,5-*b*]-pyridines, pyrazolo[3,4-*b*]pyridines

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Over the past decades, much attention has been given to the development and improvement of synthetic approaches to the preparation of azoloazines. Among such fused nitrogen-containing heterocycles, an important place belongs to 4-aminopyridine derivatives, which are promising scaffolds for the search for biologically active compounds.

The literature data include the following approaches to the synthesis of such compounds:

– reduction of nitro derivatives of azolopyridines, however, this method is practically not used due to the low availability of nitro derivatives [1–4];

– substitution of a halogen atom or alkoxyl group for an amino group; the main disadvantage of this approach is low availability of the corresponding halo- and alkoxyazolopyridines [5–7];

– substitution of the halogen atom with the azido group followed by reduction to the amino group [8, 9];

– annulation of the azole fragment to the substituted 4-aminopyridine; this method is not often used, since it requires the preparation of specifically substituted 4-aminopyridines [10–12];

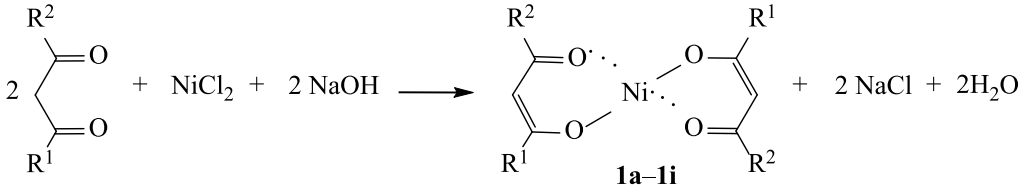
– raction of heterocyclic aminonitriles with carbonyl compounds in the presence of Lewis acids ($ZnCl_2$, $AlCl_3$, $SnCl_4$) is more often than others used to obtain azolopyridines [13–19], however, the yield of final products, as a rule, does not exceed 50%; significant restrictions are imposed on the presence functional groups in the molecules of the starting reagents;

– addition of carbonyl compounds to the nitrile group of cyanoazoles in the presence of bases with further transformation of intermediate products into azolopyridine derivatives [20–24]. Alkali metal alcoholates, potassium carbonate, amines or complexes of 1,3-dicarbonyl compounds with transition metals are used as bases.

On the other hand, nickel acetylacetonate has been known to add cyanogen [25] and other electrophilic heterocyclic nitriles under mild conditions [24]. It is also an effective catalyst for the preparation of Michael adducts of acetylacetone with unsaturated compounds. The yields of the final products are always significantly higher than in traditional syntheses using strong bases [26].

The aim of this work is to evaluate the possibility of using nickel complexes with 1,3-dicarbonyl compounds for annulation of the pyridine ring to azole systems, as well as to compare the results obtained with the known data on the construction of such fused systems. The following compounds were used as the model: 4-amino-1,2,5-oxadiazole-3-carbonitrile (the reaction with acetylacetone nickel complex has been described in [24]), 5-amino-1-benzyl-1*H*-1,2,3-triazole-4-carbonitrile (similar in the acceptor properties of the nitrile group to the nitrile group of oxadiazole) and 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile (annelated derivatives have

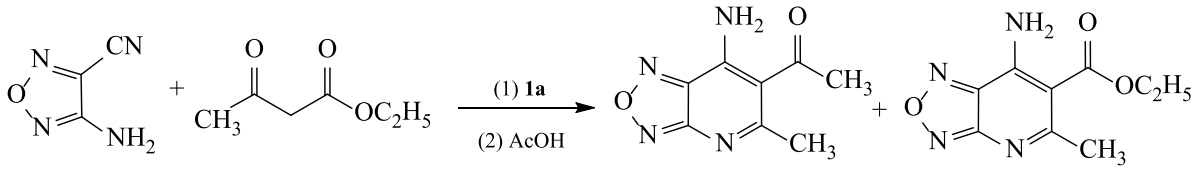
Scheme 1.



1a–1i

$R^1 = CH_3$, $R^2 = CH_3$ (**a**), OCH_3 (**b**), OC_2H_5 (**c**), $OCH_2C_6H_5$ (**d**), $OC(CH_3)_3$ (**e**), $OCH_2CH_2OCH_3$ (**f**); $R^1 = C_2H_5$, $R^2 = OC_2H_5$ (**g**); R^1 = cyclopropyl, $R^2 = OC_2H_5$ (**h**); $R^1 = CHF_2$, $R^2 = OC_2H_5$ (**i**).

Scheme 2.



2 **5a** (8%) **5c** (85%)

been described in [17, 18], and the acceptor properties of the nitrile group differ from those for the nitrile group of oxadiazole), as well as nickel complexes with acetylacetone and commercially available acetoacetic acid esters.

Nickel complexes with 1,3-dicarbonyl compounds were prepared by mixing nickel chloride, the corresponding dicarbonyl compound, and sodium hydroxide in aqueous ethanol (Scheme 1). The resulting precipitate was filtered off, and dissolved in methylene chloride. The insoluble solid was separated, the solvent was removed in vacuum, and compounds **1a**–**1i** were purified by crystallization from aqueous ethanol in the hydrate form, which easily lose water upon heating to 90–100°C in vacuum.

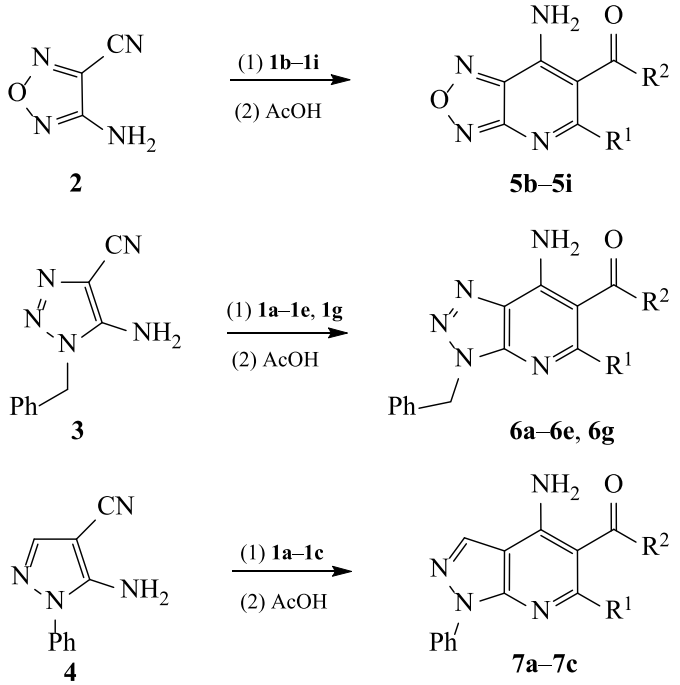
As described in [24], when using nickel acetylacetonate **1a** as a catalyst for the addition of acetoacetic acid ethyl ester to 4-amino-1,2,5-oxadiazole-3-carbonitrile **2**, the process proceeded rather quickly at first, but with time the reaction slows down and stops. Therefore, it is necessary to constantly monitor the reaction progress and add new portions of the nickel complex **1a**. After the solvent evaporation and treatment of the reaction mixture with acetic acid in ethanol, compounds **5a** (8%) and **5c** (85%) were isolated by column chromatography (Scheme 2). The formation of a mixture of compounds **5a** and **5c** is explained by the addition of both acetoacetic ester and acetylacetone, which is part of the nickel complex, to the cyano group. Therefore, we decided to use nickel complexes with the dicarbonyl compound that needs to be reacted. To accelerate the process, we carried out the addition of heterocyclic aminonitriles **2**–**4** directly to nickel complexes at a 2 : 1 ratio.

The addition of oxadiazole **2** to compounds **1a**–**1i** occurred in methylene chloride at a temperature of 35–40°C for 30–40 min. No addition of nickel complexes to cyanotriazole **3** and cyanopyrazole **4** was observed. The reaction with triazole **3** occured in boiling dichloroethane, and in the case of pyrazole **4**, the reaction was performed upon heating in chlorobenzene at 100–110°C (Scheme 3).

The ability of the nitrile group to attach nickel complexes with 1,3-dicarbonyl compounds strongly depends on the acceptor properties of the heterocyclic fragment: the more pronounced are the acceptor properties, the easier is the attachment process. The presence of an electron-withdrawing group in the nickel complex reduces its reactivity: the addition of compound **1i** to oxadiazole **2** occurs upon reflux in dichloroethane. The adducts of heterocyclic aminonitriles and complexes **1a**–**1i** were not isolated in the individual state. They were treated with acetic acid in ethanol to obtain fused derivatives **5**–**7**.

The transformation of cyanofurazan **2** into oxadiazolo[3,4-*b*]pyridines **5b**–**5i** proceeds rapidly. These compounds were isolated in high yields in pure form by crystallization. The conversion of cyanotriazole **3** to triazolo[4,5-*b*]pyridines **6** was accompanied by slight resinification. Compounds **6a**–**6c** were isolated by crystallization; compounds **6d**, **6e**, and **6g** were isolated using column chromatography on silica gel. The synthesis of pyrazolo[3,4-*b*]pyridines **7** was accompanied

Scheme 3.



$R^1 = CH_3$, $R^2 = CH_3$ (**a**), OCH_3 (**b**), OC_2H_5 (**c**), $OCH_2C_6H_5$ (**d**), $OC(CH_3)_3$ (**e**), $OCH_2CH_2OCH_3$ (**f**); $R^1 = C_2H_5$, $R^2 = OC_2H_5$ (**g**); R^1 = cyclopropyl, $R^2 = OC_2H_5$ (**h**); $R^1 = CHF_2$, $R^2 = OC_2H_5$ (**i**).

by significant resinification of the reaction mixture; therefore, compounds **7a**–**7c** can be purified only by chromatography. This approach is convenient for the preparation of compounds **5** and **6**, while derivatives **7** are easier to obtain by reacting cyanopyrazole **4** with dicarbonyl compounds in the presence of $SnCl_4$, as described in [17, 18].

Composition of compounds **5**–**7** was confirmed by elemental analysis data, and structure was proved using IR, ^{1}H and ^{13}C NMR spectroscopy. The IR spectra of compounds **5b**–**5i** contain absorption bands of stretching vibrations of the C=O group, as well as stretching and bending vibrations of the NH_2 group. The IR spectra of compounds **6** in the range of 1700–1580 cm^{-1} contain three characteristic absorption bands of almost the same intensity, as well as bands of stretching vibrations of the amino group. The ^{1}H and ^{13}C NMR spectra of the synthesized compounds contain signals of all the hydrogen and carbon atoms, respectively.

The proposed approach for the annulation of 4-aminopyridine moiety to heterocyclic aminonitriles can be an alternative in comparison with the existing synthetic methods. Advantages of this method are simplicity and possibility of introducing labile functional groups into the molecules of fused systems. One of the disadvantages of the proposed method is the strong effect of the nature of the heterocyclic fragment on the ability of nickel complexes to be attached to the nitrile group.

EXPERIMENTAL

IR spectra were recorded on a Vertex 70 spectrometer from KBr pellets. ^{1}H and ^{13}C NMR spectra were registered on a Bruker AVANCE DRX-500 instrument (500 and 125 MHz, respectively) from DMSO-d_6 solution relative to internal HMDS. Elemental analysis was carried out in the Analytical Laboratory of the V.P. Kuhar Institute of Bioorganic Chemistry and Petrochemistry of the National Academy of Sciences of Ukraine. Melting points were determined on a Fischer Johns apparatus.

4-Amino-1,2,5-oxadiazole-3-carbonitrile [27], 5-amino-1-benzyl-1*H*-1,2,3-triazole-4-carbonitrile [28] and 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile [29] were obtained according to the appropriate methods.

General procedure for the preparation of nickel complexes with 1,3-dicarbonyl compounds 1a–1i. To a solution of 4.76 g (0.02 mol) of nickel(II) chloride hexahydrate in 50 mL of water were added 50 mL of ethanol and 0.05 mol of a dicarbonyl compound. Next, a solution of 1.6 g (0.04 mol) of sodium hydroxide in 20 mL of water was added With stirring and cooling to

0–5°C over 15 min. The mixture was stirred for 2 h, and then the precipitate was filtered off, washed with water, dried in air, and then dissolved in methylene chloride. The resulting solution was filtered and evaporated in vacuum. The residue was crystallized from aqueous ethanol, and then dried in vacuum (1 mmHg) at 90–100°C for 2 h. The characteristics of compound **1a** are given in [24].

Complex 1b. Yield 4.92 g (85.1%). Found, %: C 41.05; H 4.82. $C_{10}H_{14}NiO_6$. Calculated, %: C 41.57; H 4.88.

Complex 1c. Yield 5.11 g (80.6%). Found, %: C 44.96; H 5.83. $C_{12}H_{18}NiO_6$. Calculated, %: C 45.47; H 5.72.

Complex 1d. Yield 7.27 g (82.4%). Found, %: C 59.37; H 5.11. $C_{22}H_{22}NiO_6$. Calculated, %: C 59.90; H 5.03.

Complex 1e. Yield 5.08 g (68.1%). Found, %: C 51.09; H 6.93. $C_{16}H_{26}NiO_6$. Calculated, %: C 51.51; H 7.02.

Complex 1f. Yield 4.96 g (65.8%). Found, %: C 44.16; H 5.72. $C_{14}H_{22}NiO_8$. Calculated, %: C 44.60; H 5.88.

Complex 1g. Yield 5.32 g (77.1%). Found, %: C 48.35; H 6.39. $C_{14}H_{22}NiO_6$. Calculated, %: C 48.74; H 6.43.

Complex 1h. Yield 5.24 g (71.0%). Found, %: C 51.79; H 5.94. $C_{16}H_{22}NiO_6$. Calculated, %: C 52.07; H 6.01.

Complex 1i. Yield 5.09 g (65.4%). Found, %: C 36.59; H 3.69. $C_{12}H_{14}F_4NiO_6$. Calculated, %: C 37.06; H 3.63.

1-(7-Amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridin-6-yl)ethanone (5a) and ethyl 7-amino-5-methyl[1,2, 5]oxadiazolo[3,4-*b*]pyridine-6-carboxylate (5c). To a solution of 5.5 g (0.05 mol) of compound **2** in 150 mL of methylene chloride were added 9.75 g (0.075 mol) of ethyl acetoacetate and 0.39 g (0.0015 mol) of nickel complex **1a**. The mixture was stirred at 35–40°C. After 6 h, 0.13 g of complex **1a** was added, and after 4 h, 0.13 g of complex **1a** was added, and stirring was continued for another 12 h. The solvent was evaporated in vacuum, 150 mL of ethanol and 10 mL of acetic acid were added to the residue. The resulting mixture was refluxed for 2 h, and then the solvent was evaporated in vacuum. 50 mL of water was added to the residue, the precipitate was filtered off and washed with water. The resulting mixture of the reaction products was separated by column chromatography on silica gel (eluent—chloroform–ethyl acetate, 75 : 15 with a methanol gradient from 5 to 8%). Compounds **5a** (0.77 g, 8%) and **5c** (9.44 g, 85%) were isolated.

1-(7-Amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridin-6-yl)ethanone (5a). Pale yellow crystals, mp 194–196°C (ethanol) (mp 197–198°C [24]). IR spectrum, ν, cm^{-1}: 3277, 3142, 1650, 1622, 1597, 1541, 1508, 1449, 1378, 1358, 1308, 1258, 1189, 1088, 1030. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.55 s (3H, CH_3), 8.30 br. s (2H, NH_2). Found, %: C 49.75; H 4.12; N 28.82. $C_8H_8N_4O_2$. Calculated, %: C 50.00; H 4.20; N 29.15.

Ethyl 7-amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridine-6-carboxylate (5c). Colorless crystals, mp 178–179°C (ethanol) (mp 179–180°C [24]). IR spectrum, ν, cm^{-1}: 3349, 3270, 3174, 2991, 1677, 1623, 1515, 1443, 1381, 1361, 1276, 1203, 1098, 1078, 1030, 1004. ^{1}H NMR spectrum, δ, ppm: 1.33 t (3H, $OCH_2\underline{CH_3}$, $^3J_{HH}$ = 7.1 Hz), 2.61 s (3H, CH_3), 4.35 q (2H, $O\underline{CH_2}CH_3$, $^3J_{HH}$ = 7.1 Hz), 8.57 br. s (2H, NH_2). Found, %: C 48.90; H 4.77; N 24.97. $C_9H_{10}N_4O_3$. Calculated, %: C 48.65; H 4.54; N 25.21.

Compound **5c** was also obtained from 0.55 g (0.005 mol) of compound **2** and 0.79 g (0.0025 mol) of nickel complex **1c**. Yield 1.03 g (92.8%). The mixing test of the samples of compound **5c** obtained by different methods did not give melting point depression. Their spectral data are identical.

Methyl 7-amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridine-6-carboxylate (5b). To a solution of 1.1 g (0.01 mol) of compound **2** in 50 mL of methylylene chloride were added 1.44 g (0.005 mol) of nickel complex **1b** and two drops of acetoacetic acid methyl ester. The mixture was stirred for 30 min at 35–40°C, then the solvent was evaporated in vacuum. To the residue were added 20 mL of ethanol and 3 mL of acetic acid. The resulting mixture was boiled for 1 h, then ethanol was partially evaporated in vacuum, and 30 mL of water was added to the residue. The precipitate was filtered off, washed with water, and compound **5b** was purified by crystallization. Yield 1.91 g (91.8%), mp 193–194°C (ethanol–water, 2 : 1). IR spectrum, ν, cm^{-1}: 3349, 3270, 3174, 2991, 1677, 1623, 1515, 1443, 1381, 1361, 1276, 1203, 1098, 1078, 1030, 1004. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 3.86 s (3H, OCH_3), 8.67 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 28.0, 52.5, 102.6, 140.3, 145.9, 158.4, 167.3, 170.2. Found, %: C 46.31; H 3.82; N 27.10. $C_8H_8N_4O_3$. Calculated, %: C46.16; H 3.87; N 26.91.

Benzyl 7-amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridine-6-carboxylate (5d) was prepared similarly from 0.55 g (0.005 mol) of compound **2** and 1.11 g (0.0025 mol) of nickel complex **1d**. Yield 1.25 g (88%), mp 159–161°C (ethanol–water, 3 : 1). IR spectrum, ν, cm^{-1}: 3348, 3270, 3178, 3035, 1679, 1626, 1601, 1513, 1438, 1385, 1362, 1307, 1271, 1202, 1077. ^1H NMR spectrum, δ, ppm: 2.60 s (3H, CH_3), 5.37 s (2H, CH_2), 7.34–7.48 m (5H, C_6H_5), 8.52 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 28.3, 67.1, 102.5, 128.6, 128.9, 130.0, 136.2, 140.3, 146.4, 158.5, 166.9, 170.1. Found, %: C 58.96; H 4.32; N 20.01. $C_{14}H_{12}N_4O_3$. Calculated, %: C59.15; H 4.25; N 19.71.

***tert*-Butyl 7-amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]-pyridine-6-carboxylate (5e)** was prepared similarly from 0.55 g (0.005 mol) of compound **2** and 0.94 g (0.0025 mol) of nickel complex **1e**. Yield 1.03 g (82%), mp 174–175°C (ethanol–water, 1 : 1). IR spectrum, ν, cm^{-1}: 3378, 3278, 3182, 3145, 2978, 1683, 1624, 1514, 1442, 1371, 1295, 1252, 1206, 1163, 1103, 1082, 1031. ^1H NMR spectrum, δ, ppm: 1.58 s [9H, $C(CH_3)_3$], 2.63 s (3H, CH_3), 8.55 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 28.4, 28.8, 83.0, 103.8, 140.3, 146.2, 158.3, 166.6, 170.1. Found, %: C 52.64; H 5.80; N 22.11. $C_{11}H_{14}N_4O_3$. Calculated, %: C 52.79; H 5.64; N 22.39.

2-Methoxyethyl 7-amino-5-methyl[1,2,5]oxadiazolo[3,4-*b*]pyridine-6-carboxylate (5f) was prepared similarly from 0.55 g (0.005 mol) of compound **2** and 0.95 g (0.0025 mol) of nickel complex **1f**. Yield 0.98 g (78%), mp 126–128°C (benzene–ethanol, 4 : 1). IR spectrum, ν, cm^{-1}: 3372, 3276, 3206, 2998, 2939, 2841, 1679, 1641, 1599, 1538, 1516, 1449, 1381, 1287, 1201, 1108, 1073, 1019. ^1H NMR spectrum, δ, ppm: 2.50 s (3H, CH_3), 3.32 s (3H, OCH_3), 3.65–3.69 m (2H, $OCH_2\underline{CH_2}OCH_3$), 4.41–4.45 m (2H, $O\underline{CH_2}CH_2OCH_3$), 8.90 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 27.9, 58.4, 64.0, 69.8, 102.5, 140.2, 146.1, 158.4, 166.6, 170.2. Found, %: C 46.83; H 4.72; N 22.43. $C_{10}H_{12}N_4O_4$. Calculated, %: C 46.62; H 4.80; N 22.21.

Ethyl 7-amino-5-ethyl[1,2,5]oxadiazolo[3,4-*b*]-pyridine-6-carboxylate (5g) was prepared similarly from 0.55 g (0.005 mol) of compound **2** and 0.87 g (0.0025 mol) of nickel complex **1g**. Yield 1.07 g (90.7%), mp 150–151°C (ethanol–water, 3 : 1). IR spectrum, ν, cm^{-1}: 3373, 3020, 2991, 2970, 1688, 1638, 1598, 1504, 1445, 1382, 1284, 1248, 1206, 1110, 1016. ^1H NMR spectrum, δ, ppm: 1.19 t (3H, $CH_2\underline{CH_3}$, $^3J_{HH}$ = 7.4 Hz), 1.32 t (3H, $OCH_2\underline{CH_3}$, $^3J_{HH}$ = 7.1 Hz), 2.93 q (2H, $\underline{CH_2}CH_3$, $^3J_{HH}$ = 7.4 Hz), 4.36 q (2H, $O\underline{CH_2}CH_3$, $^3J_{HH}$ = 7.1 Hz), 8.45 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 13.1, 14.3, 32.3, 61.6, 103.4, 140.2, 145.4, 158.7, 167.0, 173.9. Found, %: C 51.05; H 5.22; N 23.53. $C_{10}H_{12}N_4O_4$. Calculated, %: C 50.84; H 5.12; N 23.72.

Ethyl 7-amino-5-cyclopropyl[1,2,5]oxadiazolo[3,4-*b*]pyridine-6-carboxylate (5h) was prepared similarly from 0.55 g (0.005 mol) of compound **2** and 0.93 g (0.0025 mol) of nickel complex **1h**. Yield 1.04 g (83.9%), mp 158–160°C (ethanol–water, 3 : 1). IR spectrum, ν, cm^{-1}: 3378, 3275, 3184, 2992, 1681, 1627, 1597, 1535, 1505, 1450, 1400, 1270, 1205, 1092, 1011. ^1H NMR spectrum, δ, ppm: 0.97–1.04 m (2H, cyclopropyl), 1.12–1.18 m (2H, cyclopropyl), 1.32 t (3H, $OCH_2\underline{CH_3}$, $^3J_{HH}$ = 7.1 Hz), 2.37–2.46 m (1H, cyclopropyl), 4.37 q (2H, $O\underline{CH_2}CH_3$, $^3J_{HH}$ = 7.1 Hz), 8.31 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 12.3, 14.4, 17.5, 61.8, 104.9, 140.1, 144.2, 158.9, 167.1, 173.3. Found, %: C 53.01; H 4.99; N 22.83. $C_{11}H_{12}N_4O_4$. Calculated, %: C 53.22; H 4.87; N 22.57.

Ethyl 7-amino-5-(difluoromethyl)[1,2,5]oxadiazolo[3,4-*b*]pyridine-6-carboxylate (5i). 0.97 g (0.0025 mol) of nickel complex **1c** and two drops of ethyl 4,4-difluoro-3-oxobutanoate were added to a solution of 0.55 g (0.005 mol) of compound **2** in 20 mL of dichloroethane. The mixture was refluxed for 8 h. Compound **5i** was isolated similarly to compound **5b**. Yield 0.97 g (75.2%), mp 119–120°C (benzene–ethanol, 1 : 1). IR spectrum, ν, cm^{-1}: 3395, 3273, 1685, 1607, 1518, 1408, 1381, 1288, 1208, 1133, 1094, 1066, 1018. ^1H NMR spectrum, δ, ppm: 1.33 t (3H, $OCH_2C\underline{H_3}$, $^3J_{HH}$ = 7.2 Hz), 4.38 q (2H, $OC\underline{H_2}CH_3$, $^3J_{HH}$ = 7.2 Hz), 7.30 t (1H, $C\underline{H}F_2$, $^2J_{HF}$ = 53.6 Hz), 9.15 d (2H, NH_2). Found, %: C 41.61; H 3.26; N 21.43. $C_9H_8F_2N_4O_3$. Calculated, %: C 41.87; H 3.12; N 21.70.

1-(7-Amino-3-benzyl-5-methyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridin-6-yl)ethanone (6a). To a solution of 0.50 g (0.0025 mol) of compound **3** in 15 mL of dichloroethane were added 0.32 g (0.0013 mol) of nickel complex **1a** and two drops of acetylacetone. The mixture was refluxed for 16 h; compound **6a** was isolated similarly to compound **5b**. Yield 0.51 g (72.5%), mp 158–160°C (ethanol). IR spectrum, ν, cm^{-1}: 3419, 3293, 3234, 3186, 1629, 1581, 1486, 1448, 1419, 1342, 1273, 1222, 1109. ^1H NMR spectrum, δ, ppm: 2.51 s (3H, CH_3), 2.54 s (3H, CH_3), 5.76 s (2H, CH_2), 7.27–7.37 m (5H, C_6H_5), 7.71 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 25.9, 32.7, 49.5, 114.9, 127.2, 128.1, 128.4, 129.2, 136.7, 145.8,

146.1, 159.3, 203.9. Found, %: C 63.81; H 5.49; N 25.07. $C_{15}H_{15}N_5O$. Calculated, %: C 64.04; H 5.37; N 24.89.

Methyl 7-amino-3-benzyl-5-methyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridine-6-carboxylate (6b) was prepared similarly from 0.50 g (0.0025 mol) of compound **3** and 0.41 g (0.0013 mol) of nickel complex **1b**. Yield 0.51 g (72.5%), mp 167–169°C (methanol). IR spectrum, ν, cm^{-1}: 3397, 3279, 3229, 3177, 1678, 1638, 1583, 1428, 1385, 1364, 1339, 1277, 1249, 1102, 1071. ^{1}H NMR spectrum, δ, ppm: 2.61 s (3H, CH_3), 3.85 s (3H, OCH_3), 5.75 s (2H, $CH_2C_6H_5$), 7.27–7.38 m (5H, C_6H_5), 7.92 br. s (2H, NH_2). Found, %: C 60.88; H 5.17; N 23.30. $C_{15}H_{15}N_5O_2$. Calculated, %: C 60.60; H 5.09; N 23.55.

Ethyl 7-amino-3-benzyl-5-methyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridine-6-carboxylate (6c) was prepared similarly from 0.50 g (0.0025 mol) of compound **3** and 0.36 g (0.0013 mol) of nickel complex **1c**. Yield 0.52 g (66.7%), mp 125–127°C (ethanol). IR spectrum, ν, cm^{-1}: 3427, 3296, 3244, 3192, 1694, 1640, 1583, 1477, 1364, 1314, 1276, 1245, 1104, 1082, 1017. ^{1}H NMR spectrum, δ, ppm: 1.33 t (3H, $OCH_2C\underline{H}_3$, $^3J_{HH}$ = 7.1 Hz), 2.64 s (3H, CH_3), 4.35 q (2H, $OC\underline{H}_2CH_3$, $^3J_{HH}$ = 7.1 Hz), 5.76 s (2H, $C\underline{H}_2C_6H_5$), 7.28–7.37 m (5H, C_6H_5), 7.92 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.5, 27.4, 49.5, 61.2, 103.3, 127.1, 128.1, 128.4, 129.2, 136.6, 145.9, 148.7, 162.4, 168.2. Found, %: C 61.58; H 5.67; N 22.64. $C_{16}H_{17}N_5O_2$. Calculated, %: C 61.72; H 5.50; N 22.49.

Benzyl 7-amino-3-benzyl-5-methyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridine-6-carboxylate (6d) was prepared similarly from 0.50 g (0.0025 mol) of compound **3** and 0.56 g (0.0013 mol) of nickel complex **1d**. Compound **6d** was isolated by column chromatography (hexane–ethyl acetate, 3 : 1). Yield 0.76 g (81.7%), mp 134–135°C (hexane–ethyl acetate, 1:1). IR spectrum, ν, cm^{-1}: 3395, 3279, 3232, 3182, 1673, 1631, 1584, 1492, 1422, 1381, 1336, 1275, 1237, 1104. ^{1}H NMR spectrum, δ, ppm: 2.76 s (3H, CH_3), 5.36 s (2H, $CH_2C_6H_5$), 5.72 s (2H, $CH_2C_6H_5$), 7.23–7.45 m (10H, C_6H_5), 7.85 br. s (2H, NH_2). Found, %: C 67.82; H 5.21; N 18.49. $C_{21}H_{19}N_5O_2$. Calculated, %: C 67.55; H 5.13; N 18.75.

***tert*-Butyl 7-amino-3-benzyl-5-methyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridine-6-carboxylate (6e)** was prepared similarly from 0.50 g (0.0025 mol) of compound **3** and 0.47 g (0.0013 mol) of nickel complex **1e**. Compound **6e** was isolated by column chromatography (hexane–ethyl acetate, 4 : 1). Yield 0.47 g (55.3%), mp 177–179°C (hexane–ethyl acetate, 2 : 1). IR spectrum, ν, cm^{-1}: 3413, 3285, 3238, 3186,1681, 1631, 1588, 1389, 1366, 1340, 1306, 1282, 1253, 1164,1112.^{1}H NMR spectrum, δ, ppm: 1.60 s [9H, $C(CH_3)_3$], 2.68 s (3H, CH_3), 5.71 s (2H, $C\underline{H}_2C_6H_5$), 7.27–7.37 m (5H, C_6H_5), 7.87 br. s (2H, NH_2). Found, %: C 63.91; H 6.35; N 20.48. $C_{18}H_{21}N_5O_2$. Calculated, %: C 63.70; H 6.24; N 20.63.

Ethyl 7-amino-3-benzyl-5-ethyl-3*H*[1,2,3]triazolo[4,5-*b*]pyridine-6-carboxylate (6g) was prepared similarly from 0.50 g (0.0025 mol) of compound **3** and 0.36 g (0.0013 mol) of nickel complex **1g**. Compound **6g** was isolated by column chromatography (hexane–ethyl acetate, 7 : 2). Yield 0.52 g (64.2%), mp 151–152°C (ethanol). IR spectrum, ν, cm^{-1}: 3392, 3275, 3229, 3179,1669, 1632, 1583, 1478, 1443, 1375, 1334, 1248, 1097, 1069. ^{1}H NMR spectrum, δ, ppm: 1,20 t (3H, $CH_2\underline{CH}_3$, $^3J_{HH}$ = 7.4 Hz), 1.31 t (3H, $OCH_2\underline{CH}_3$, $^3J_{HH}$ = 7.1 Hz), 2.92 q (2H, $\underline{CH}_2CH_3$, $^3J_{HH}$ = 7.4 Hz), 4.33 q (2H, $O\underline{CH}_2CH_3$, $^3J_{HH}$ = 7.1 Hz), 5.74 s (2H, $C\underline{H}_2C_6H_5$), 7.26–7.37 m (5H, C_6H_5), 7.75 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.2, 14.4, 31.6, 49.6, 61.3, 103.7, 126.8, 128.2, 128.4, 129.1, 136.5, 146.0, 148.1, 166.3, 168.1. Found, %: C 62.59; H 6.01; N 21.28. $C_{17}H_{19}N_5O_2$. Calculated, %: C 62.76; H 5.89; N 21.52.

1-(4-Amino-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)ethanone (7a). To a solution of 0.46 g (0.0025 mol) of compound **3** in 15 mL of chlorobenzene were added 0.32 g (0.0013 mol) of nickel complex **1a** and two drops of acetylacetone. The resulting mixture was stirred at 100–110°C for 30 h. Compound **7a** was isolated by column chromatography (hexane–ethyl acetate, 5 : 2). Yield 0.27 g (40.6%), mp 196–198°C (ethanol) (mp 166–168°C [18]). ^{1}H NMR spectrum, δ, ppm: 2.54 s (3H, CH_3), 2.58 s (3H, CH_3), 7.29–7.32 m ($1H_{ar}$), 7.50–7.54 m ($2H_{Ar}$), 7.62 br. s (2H, NH_2), 8.24–8.28 m ($2H_{Ar}$), 8.48 s (1H, C^3H). Found, %: C 67.91; H 5.45; N 20.67. $C_{15}H_{14}N_4O$. Calculated, %: C 67.65; H 5.30; N 21.04.

Methyl 4-amino-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (7b) was prepared similarly from 0.46 g (0.0025 mol) of compound **4** and 0.41 g (0.0013 mol) of nickel complex **1b**. Compound **7b** was isolated by column chromatography (hexane–ethyl acetate, 3 : 1). Yield 0.15 g (21.3%), mp 128–129°C (methanol) (mp 125–126°C [17]). ^{1}H NMR spectrum, δ, ppm: 2.66 s (3H, CH_3), 3.85 s (3H, OCH_3), 7.26–7.30 m ($1H_{Ar}$), 7.51–7.55 m ($2H_{Ar}$), 7.70 br. s (2H, NH_2), 8.24–8.28 m ($2H_{Ar}$), 8.50 s (1H, C^3H). Found, %: C 63.59; H 5.11; N 20.14. $C_{15}H_{14}N_4O_2$. Calculated, %: C 63.82; H 5.00; N 19.85.

Ethyl 4-amino-6-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (7c) was prepared similarly from 0.46 g (0.0025 mol) of compound **4** and 0.41 g (0.0013 mol) of nickel complex **1c**. Compound **6d** was isolated by column chromatography (hexane–ethyl acetate, 3 : 1). Yield 0.23 g (31.1%), mp 130–131°C (ethanol) (mp 130–132°C [18]). ^{1}H NMR spectrum, δ, ppm: 1.33 t (3H, $OCH_2C\underline{H}_3$, $^3J_{HH}$ = 7.2 Hz), 2.66 s (3H, CH_3), 4.34 q (2H, $OC\underline{H}_2CH_3$, $^3J_{HH}$ = 7.2 Hz), 7.26–7.30 m ($1H_{Ar}$), 7.51–7.55 m ($2H_{Ar}$), 7.76 br. s (2H, NH_2), 8.23–8.27 m ($2H_{Ar}$), 8.51 s (1H, C^3H). Found, %: C 65.14; H 5.59; N 19.17. $C_{16}H_{14}N_4O_2$. Calculated, %: C 64.85; H 5.44; N 18.91.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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