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# Synthesis of 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one and its derivatives

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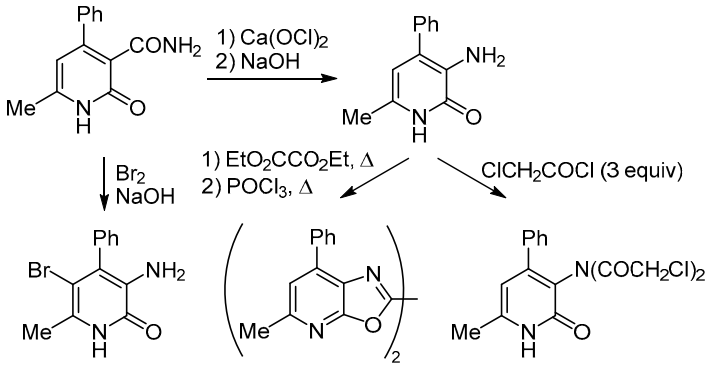



A reaction of 2-cyanoacetamide with benzylideneacetone in DMSO containing potassium *tert*-butoxide was used to synthesize 3-cyano-6-methyl-4-phenylpyridin-2(1*H*)-one, which was converted by acidic hydrolysis to 6-methyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carboxamide. A Hofmann reaction of this compound in the presence of sodium hypobromite led to 3-amino-5-bromo-6-methyl-4-phenylpyridin-2(1*H*)-one, while its treatment with calcium hypochlorite produced 5-methyl-7-phenyloxazolo[5,4-*b*]pyridin-2(1*H*)-one. The latter compound was converted by heating with alkali to 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one, which gave azomethine in a reaction with benzaldehyde, while *N*-acylated derivatives were obtained in reactions with acyl halides. The heating of $N^1$,$N^2$-bis(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)oxalylamide in the presence of $POCl_3$ allowed to obtain 5,5'-dimethyl-7,7'-diphenyl-2,2'-bis-(oxazolo[5,4-*b*]pyridine).

**Keywords**: 3-aminopyridin-2(1*H*)-one, oxazolo[5,4-*b*]pyridin-2(1*H*)-one, Hofmann reaction, intramolecular cyclization.

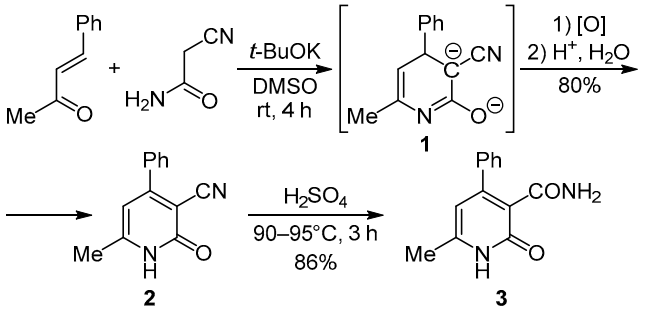
Aminopyridin-2(1*H*)-ones are commonly employed as molecular scaffolds for the synthesis of biologically active compounds,[1–3] including drugs that have been approved for clinical use, such as amrinone.[4] The presence of an amino acid motif incorporated in the structure of 3-aminopyridin-2(1*H*)-ones presents opportunities for their use as building blocks in the synthesis of peptidomimetics.[5–7]

We have previously developed a method for the preparation of pyridin-2(1*H*)-ones and -thiones functionalized at position 3, based on an intramolecular cyclization of *N*-(3-oxoalkyl)- and *N*-(3-oxoalkenyl)amides and thioamides.[8–13] This approach was used for the preparation of insufficiently studied 4-aryl-substituted 3-aminopyridin-2(1*H*)-ones.[14–16] Some of these compounds are luminophores, show antiradical activity,[15] and may present interest as specific intracellular probes for detecting the generation of reactive oxygen species. Previously reported method[14] for the preparation of 4-aryl-substituted 3-aminopyridin-2-(1*H*)-ones had some drawbacks due to scaling of starting *N*-(3-oxoalkenyl)chloroacetamide synthesis, which required a large volume of solvent. For this reason, we studied the possibility of an alternative approach to the synthesis of 4-aryl-substituted 3-aminopyridin-2(1*H*)-ones, based on Hofmann reaction of the appropriate amides.

It is known that 3-cyano-3,4-dihydropyridin-2(1*H*)-ones, which are accessible by condensation of α,β-unsaturated ketones and cyanoacetamide in alkaline medium, are capable of oxidation by air oxygen to 3-cyanopyridin-2(1*H*)-ones.[17] This method was used for the synthesis of 6-methyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile (**2**)

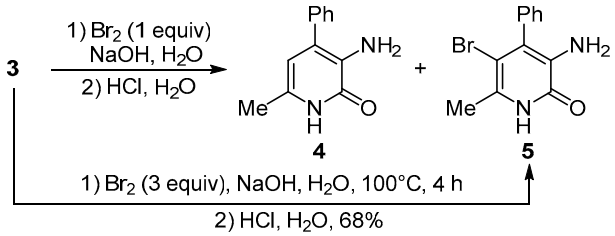
which was obtained as a result of oxidation of the dianion **1**, formed as the intermediate in condensation of benzylideneacetone with 2-cyanoacetamide in the presence of potassium *tert*-butoxide in DMSO, in 80% yield (Scheme 1). The attempts to change potassium *tert*-butoxide with sodium hydroxide or ethoxide led to decreasing the yield of compound **2** to 35 and 51%, respectively. Acidic hydrolysis of nitrile **2** in concentrated sulfuric acid produced 6-methyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carboxamide **3** in 86% yield.

**Scheme 1**




The reaction of amide **3** with 1 equiv of sodium hypobromite that was obtained *in situ* from elemental bromine and sodium hydroxide resulted in a product mixture consisting of 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one (**4**) and its brominated derivative **5** (Scheme 2). When the amount of sodium hypobromite was increased to 3 equiv, the main product of the reaction, which was isolated in 68% yield, was identified as 3-amino-5-bromo-6-methyl-4-phenylpyridin-2(1*H*)-one (**5**).

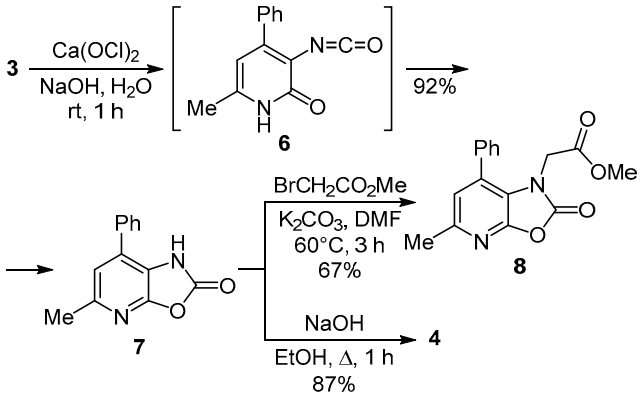
**Scheme 2**




Performing the Hofmann reaction with calcium hypochlorite containing 2 equiv of active chlorine relative to the amount of amide **3** produced 5-methyl-7-phenyloxazolo[5,4-*b*]pyridin-2(1*H*)-one (**7**) (92% yield) as a result of intramolecular cyclization of the isocyanate intermediate **6** (Scheme 3). Analogous transformations of 4-alkyl-substituted 2-oxo-1,2-dihydropyridine-3-carboxamides in the presence of sodium hypochlorite have been previously reported in the literature.[18,19] It is important to note that oxazolo[5,4-*b*]pyridin-2(1*H*)-ones are also of interest. Modulators of calcium channel activity have been recently found among compounds of this series.[20] They are used for the treatment of type 2 diabetes[21] and also exhibited analgetic activity.[22]

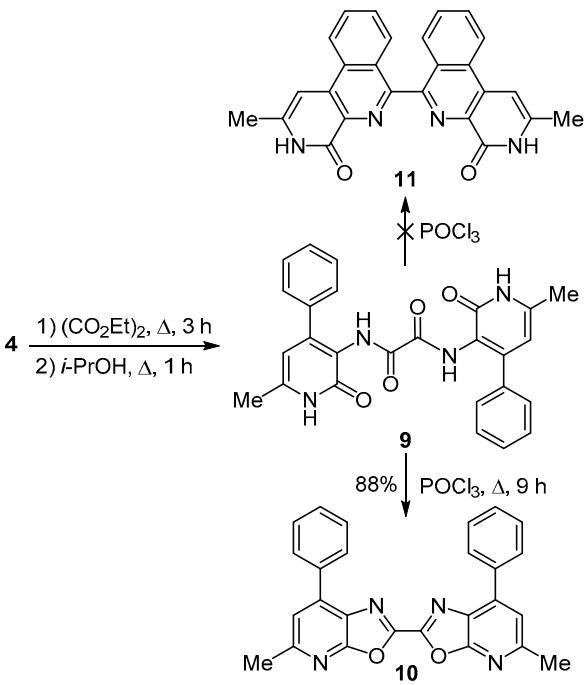
A reaction of compound **7** with methyl bromoacetate in dimethylformamide in the presence of potassium carbonate was used to prepare methyl (5-methyl-2-oxo-7-phenyl[1,3]-oxazolo[5,4-*b*]pyridin-1(2*H*)-yl)acetate (**8**) in 67% yield (Scheme 3). Oxazolo[5,4-*b*]pyridin-2(1*H*)-one **7** was converted to 3-aminopyridin-2(1*H*)-one **4** (87% yield) by heating with an alcoholic sodium hydroxide solution.

**Scheme 3**

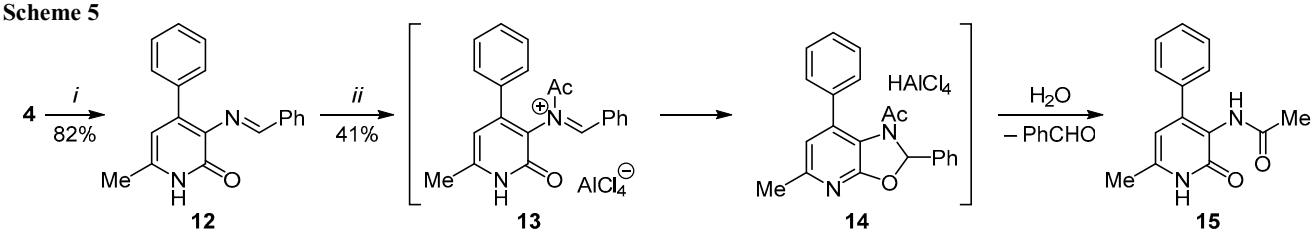



It is known that *N*-acylated 3-amino-4-arylquinolines can participate in Bischler–Napieralski reaction with the formation of dibenzo[*c*,*f*][1,7]naphthyridines.[23,24] We studied the applicability of this reaction for amide **9**, which was obtained by heating of compound **4** with ethyl oxalate according to a literature procedure.[14] The Bischler–Napieralski reaction in our case was expected to produce 2,2'-dimethyl-6,6'-bis(dibenzo[*c*][1,7]naphthyridine)-4,4'(3*H*,3'*H*)-dione (**11**). However, the heating of compound **9** with phosphorus oxychloride led to 5,5'-dimethyl-7,7'-diphenyl-2,2'-bis-(oxazolo[5,4-*b*]pyridine) (**10**) in 88% yield (Scheme 4).

**Scheme 4**



**Scheme 5**

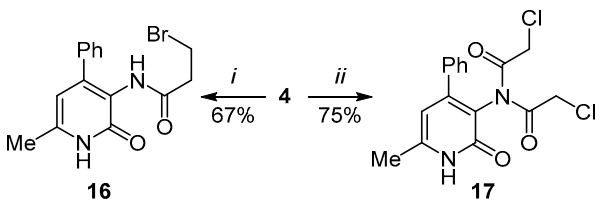



*i*: PhCHO, $HCO_2H$, *i*-PrOH, Δ, 5 h; *ii*: AcCl, $AlCl_3$, $CH_2Cl_2$, rt, 1 day

The formation of isoquinoline system may be also achieved by amidoalkylation,[25] which in several cases occurred under milder conditions[26–30] than the Bischler–Napieralski reaction. We used the reaction of compound **4** with benzaldehyde in isopropanol to obtain the azomethine **12** in 82% yield. Further treatment of this azomethine with acetyl chloride gave *N*-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)acetamide (**15**) (Scheme 5). Apparently, the acyliminium salt **13** that was formed by acylation of azomethine **12** also cyclized to the oxazole derivative **14**, which hydrolyzed during the work-up of reaction mixture, producing the acetamide **15**.

The acylation of 3-aminopyridin-2(1*H*)-one **4** with 2 equiv of chloroacetyl chloride led to the respective chloroacetamide.[14] Analogously, the use of 3-bromopropanoyl chloride in dichloromethane in the presence of pyridine gave amide **16** (Scheme 6). When the amount of chloroacetyl chloride was increased to 3 equiv, imide **17** was unexpectedly obtained as the main reaction product in 75% yield.

**Scheme 6**




*i*: $BrCH_2CH_2COCl$ (2 equiv), Py, $CH_2Cl_2$, rt, 15 h
*ii*: $ClCH_2COCl$ (3 equiv), Py, $CH_2Cl_2$, rt, 15 h

The structures of all synthesized compounds were established by IR spectroscopy, $^1H$ and $^{13}C$ spectroscopy, as well as elemental analysis data.

Thus, we have found a new approach to the synthesis of 5-methyl-7-phenyloxazolo[5,4-*b*]pyridin-2(1*H*)-one, 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one and its brominated derivative by relying on Hofmann reaction of 6-methyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carboxamide, which was obtained in two stages from readily available starting materials – benzylideneacetone and 2-cyanoacetamide. The proposed method allow to obtain 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one on preparative scale in four steps with the overall yield of 55%, exceeding the yield of a previously reported method on the basis of 1-phenylbutane-1,3-dione and chloroacetamide (42% yield). Starting from 3-amino-6-methyl-4-phenylpyridin-2(1*H*)-one, previously unknown *N*-acylated derivatives and 5,5'-dimethyl-7,7'-diphenyl-2,2'-bis(oxazolo[5,4-*b*]pyridine) were obtained.

## Experimental

IR spectra were recorded on an FT-801 FT-IR spectrometer in KBr pellets. $^1H$ and $^{13}C$ NMR spectra were acquired on a Bruker DRX-400 instrument (400 and 100 MHz, respectively), with TMS as internal standard. $^{13}C$ NMR spectra were acquired in *J*-modulation mode. Elemental analysis was performed on a Carlo Erba 1106 CHN-analyzer. Melting points were determined on a Kofler bench. The reaction progress and purity of the obtained compounds were controlled by TLC on Sorbfil UV-254 plates, with visualization under UV light. The products were purified by silica gel column chromatography.

**6-Methyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile (2)**. Method I. Potassium *tert*-butoxide (61.5 g, 0.548 mol) was added to a cooled solution of benzylideneacetone (20.0 g, 0.137 mol) and 2-cyanoacetamide (12.6 g, 0.150 mol) in DMSO (200 ml). Cooling was stopped after 30 min and the reaction mixture was stirred at room temperature for 4 h with barbotation of dry air through it. Then the reaction mixture was poured into water (1 l) and neutralized by 2 N HCl solution. The precipitate formed was filtered off, washed with water, and recrystallized from EtOH. Yield 23.0 g (80%), white crystals, mp 274–275°C (mp 274–275°C[31]). IR spectrum, ν, $cm^{-1}$: 1669, 2234, 3069, 3156. $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 1.81 (3H, s, $CH_3$); 6.31 (1H, s, H-5); 7.51–7.59 (5H, m, H Ph); 12.60 (1H, br. s, NH). $^{13}C$ NMR spectrum, δ, ppm (DMSO-$d_6$): 18.7 ($CH_3$); 97.7 (C-3); 107.0 (C-5); 117.1 (CN); 128.4, 129.2 (C-2,3,5,6 Ph); 134.4 (C-4 Ph); 136.5 (C-1 Ph); 141.1 (C-4); 152.6 (C-6); 163.2 (C-2).

Method II. Solid sodium hydroxide (1.6 g, 0.04 mol) was added to a cooled solution of benzylideneacetone (1.46 g, 0.010 mol) and 2-cyanoacetamide (0.92 g, 0.011 mol) in DMSO (10 ml). Cooling was stopped after 30 min, and the reaction mixture was stirred at room temperature for 18 h while barbotating with air, then transferred to a beaker containing water (50 ml) and neutralized with 2 N HCl solution. The precipitate that formed was filtered off, washed with water, and recrystallized from EtOH. Yield 0.73 g (35%).

Method III. Sodium ethoxide solution was prepared by from metallic sodium (0.24 mg, 10 mmol) and anhydrous ethanol (10 ml). 2-Cyanoacetamide (0.92 g, 11 mmol) was added to the sodium ethoxide solution and the mixture was vigorously stirred for 15 min, then treated by dropwise

addition of a solution of benzylideneacetone (1.46 g, 10 mmol) in anhydrous ethanol (5 ml). The reaction mixture was refluxed for 8 h, cooled, and poured into water (100 ml), then neutralized with 2 N solution of HCl. The precipitate that formed was filtered off, washed with water, and crystallized from ethanol. Yield 1.07 g (51%).

**6-Methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-carboxamide (3)**. Nitrile **2** (21.0 g, 0.10 mol) was dissolved in concentrated $H_2SO_4$ (30 ml) and heated to 90–95°C for 3 h. After cooling, the reaction mixture was poured onto ice (100 g) and neutralized with aqueous ammonia. The solid that formed was filtered off, washed with water, and recrystallized from EtOH. Yield 19.6 g (86%), mp 255–257°C (mp 253–255°C[31]). IR spectrum, ν, $cm^{-1}$: 1658, 1677, 3313, 3436. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.20 (3H, s, $CH_3$); 6.01 (1H, s, H-5); 7.15 (1H, s, $CONH_2$); 7.36–7.41 (5H, m, H Ph); 7.70 (1H, s, $CONH_2$); 11.94 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm (DMSO-$d_6$): 18.4 ($CH_3$); 106.5 (C-5); 122.9 (C-3); 127.5, 128.1 (C-2,3,5,6 Ph); 128.2 (C-4 Ph); 139.0 (C-1 Ph); 145.4 (C-4); 150.8 (C-6); 161.3 (C-2); 167.3 (3-$CONH_2$).

**3-Amino-5-bromo-6-methyl-4-phenylpyridin-2(1*H*)-one (5)**. Ice (5 g) and elemental bromine (0.16 ml, 3 mmol) were added to a solution of NaOH (240 mg, 6 mmol) in water (2 ml). The mixture was stirred until it became homogeneous, then amide **3** (228 mg, 1 mmol) was added. The resulting mixture was heated to 100°C for 4 h, then cooled on ice bath and acidified with 6 N solution of HCl to pH ~3, stirred at room temperature for additional 30 min, then neutralized with a saturated $NaHCO_3$ solution (pH ~7–8). The precipitate was filtered off, washed with water, and recrystallized from EtOH. Yield 190 mg (68%), decomp. temp. 191–192°C. IR spectrum, ν, $cm^{-1}$: 1617, 1646, 3349, 3456. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): 2.23 (3H, s, $CH_3$); 4.36 (2H, s, $NH_2$); 7.18 (2H, d, $^3J$ = 7.0, H-2,6 Ph); 7.38 (1H, t, $^3J$ = 7.4, H-4 Ph); 7.47 (2H, t, $^3J$ = 7.4, H-3,5 Ph); 11.87 (1H, br. s, NH). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 18.9 ($CH_3$); 100.7 (C-5); 124.7 (C-3); 127.7 (C-4 Ph); 128.7, 129.1 (C-2,3,5,6 Ph); 133.5 (C-1 Ph, C-4); 136.8 (C-6); 156.9 (C-2). Found, %: C 51.49; H 3.81; N 10.16. $C_{12}H_{11}BrN_2O$. Calculated, %: C 51.63; H 3.97; N 10.04.

**5-Methyl-7-phenyl[1,3]oxazolo[5,4-*b*]pyridin-2(1*H*)-one (7)**. Calcium hypochlorite (2.53 g, 56% content of active chlorine, 0.2 mol $Cl_2$) was added to a suspension of amide **3** (2.28 g, 0.1 mol) in 2 N NaOH solution (40 ml). The mixture was vigorously stirred at room temperature for 1 h and then neutralized. The precipitate was filtered off, washed with water, then recrystallized from $CHCl_3$. Yield 2.08 g (92%), white crystals, decomp. temp. 225–228°C. IR spectrum, ν, $cm^{-1}$ :1642, 1798, 3122 (br.). $^1$H NMR spectrum (acetone-$d_6$), δ, ppm: 2.43 (3H, s, $CH_3$); 7.12 (1H, s, H-6); 7.43–7.48 (3H, m, H-2,4,6 Ph); 7.60–7.62 (2H, m, H-3,5 Ph); 10.61 (1H, br. s, NH). $^{13}$C NMR spectrum (acetone-$d_6$), δ, ppm: 22.7 ($CH_3$); 118.2 (C-6); 119.04 (C-7a); 127.9, 129.1 (C-2,3,4,5,6 Ph); 131.4 (C-1 Ph); 134.7 (C-7); 149.9 (C-5); 152.7 (C-3a); 153.2 (C-2). Found, %: C 68.89; H 4.53; N 12.52. $C_{13}H_{10}N_2O_2$. Calculated, %: C 69.02; H 4.46; N 12.38.

**3-Amino-6-methyl-4-phenylpyridin-2(1*H*)-one (4)**. Solid sodium hydroxide (160 mg, 4 mmol) was added to a suspension of oxazolone **7** (226 mg, 1 mmol) in ethanol (2 ml), and the mixture was refluxed for 1 h, then poured into water (10 ml) and neutralized. The precipitate that formed was filtered off. Yield 174 mg (87%), white crystals, mp 194–195°C (ethanol) (mp 194–195°C[14]).

**Methyl (5-methyl-2-oxo-7-phenyl[1,3]oxazolo[5,4-*b*]-pyridin-1(2*H*)-yl)acetate (8)**. Dry potassium carbonate (5.52 g, 0.4 mol) and methyl bromoacetate (0.95 ml, 0.1 mol) were added to a solution of oxazolone **7** (2.25 g, 0.1 mol) in anhydrous DMF (10 ml). The reaction mixture was heated for 3 h at 60°C, then poured into water, neutralized, extracted with chloroform, and purified by column chromatography using chloroform as eluent. Yield 2.00 g (67%), white crystals, mp 92–93°C. IR spectrum, ν, $cm^{-1}$: 1635, 1742, 1796. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.56 (3H, s, $CH_3$); 3.52 (3H, s, $OCH_3$); 4.24 (2H, s, $NCH_2CO$); 6.89 (1H, s, H-6); 7.29 (2H, dd, $^3J$ = 7.4, $^4J$ = 1.5, H-2,6 Ph); 7.44–7.50 (3H, m, H-3,4,5 Ph). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 23.5 ($CH_3$); 44.1 ($OCH_3$); 52.4 ($N\underline{C}H_2CO$); 119.1 (C-7a); 121.2 (C-6); 128.5, 128.6 (C-2,3,5,6 Ph); 129.2 (C-4 Ph); 133.2 (C-1 Ph); 134.0 (C-7); 150.3 (C-5); 151.4 (C-3a); 153.2 (C-2); 167.0 ($CH_2\underline{C}O_2CH_3$). Found, %: C 64.31; H 4.85; N 9.28. $C_{16}H_{14}N_2O_4$. Calculated, %: C 64.42; H 4.73; N 9.39.

**5,5'-Dimethyl-7,7'-diphenyl-2,2'-bis(oxazolo[5,4-*b*]pyridine) (10)**. A mixture of oxalylamide **9**[14] (0.227 g, 0.5 mmol) and phosphorus oxychloride (1.0 ml) was heated for 9 h at 100°C. The solvent was removed by evaporation, the residue was treated with ice water. The precipitate that formed was filtered off and recrystallized from a 2-PrOH–DMF mixture. Yield 0.185 g (88%), white powder, mp 263–265°C (2-PrOH). IR spectrum, ν, $cm^{-1}$: 1608, 1675. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): 2.71 (6H, s, 5,5'-$CH_3$); 7.59 (2H, d, $^3J$ = 7.3, H-4,4' Ph); 7.66 (4H, t, $^3J$ = 7.3, H-3,3',5,5' Ph); 7.86 (2H, s, H-6,6'); 8.26 (2H, d, $^3J$ = 7.3, H-2,2',6,6' Ph). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 24.2 (5,5'-$CH_3$); 119.4 (C-6,6'); 127.6 (C-7a,7a'); 128.9, 129.0 (C-2,2',3,3',5,5',6,6' Ph); 130.1 (C-4,4' Ph); 133.6 (C-1,1' Ph); 141.0 (C-7,7'); 150.2 (C-5,5'); 157.6 (C-3a,3a'); 159.4 (C-2,2'). Found, %: C 74.44; H 4.50; N 13.52. $C_{26}H_{18}N_4O_2$. Calculated, %: C 74.63; H 4.34; N 13.39.

**3-(Benzylideneamino)-6-methyl-4-phenylpyridin-2(1*H*)-one (12)**. A mixture of compound **4** (200 mg, 1 mmol), benzaldehyde (160 mg, 1.5 mmol), and a catalytic amount of formic acid in isopropanol (5 ml) was refluxed for 5 h. After cooling, the crystals that precipitated were filtered off and washed with cold isopropanol, then with hexane. Yield 236 mg (82%), yellow crystals, mp 208–209°C (isopropanol). IR spectrum, ν, $cm^{-1}$: 1525, 1636, 3352, 3450. $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.41 (3H, s, $CH_3$); 6.25 (1H, s, H-5); 7.35–7.40 (5H, m, H 4-Ph); 7.48–7.53 (3H, m, H-3,4,5 Ph); 7.75 (2H, dd, $^3J$ = 7.1, $^4J$ = 2.4, H-2,6 Ph); 9.35 (1H, s, N=CH); 13.18 (1H, br. s, NH). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 18.7 ($CH_3$); 108.7 (C-5); 121.6 (C-3); 127.5, 128.0 (C-4 Ph); 128.4 (C-2,3,5,6 Ph); 128.6, 130.0 (C-2,3,5,6 Ph); 130.6 (C-4 Ph); 131.0 (C-1 Ph); 131.7 (C-1 Ph); 140.8 (C-4);

146.3 (C-6); 161.2 (C-2); 162.6 (N=CH). Found, %: C 79.52; H 5.87; N 9.91. $C_{19}H_{16}N_2O$. Calculated, %: C 79.14; H 5.79; N 9.72.

***N*-(6-Methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)-acetamide (15)**. A solution of azomethine **12** (200 mg, 0.69 mmol) in anhydrous dichloromethane (5 ml) was cooled and treated with aluminum chloride (93 mg, 0.69 mmol). After maintaining for 45 min, the reaction mixture was cooled and treated by dropwise addition of acetyl chloride (0.059 ml, 0.83 mmol) solution in dichloromethane (1 ml). The reaction mixture was stirred at room temperature for 1 day, then quenched with water (10 ml) and extracted with ethyl acetate. The product was purified by column chromatography, while using 1:1 benzene–isopropanol mixture as eluent. Yield 95 mg (41%), pale-yellow crystals, mp 159°C. IR spectrum, ν, $cm^{-1}$: 1631, 1696, 3479 (br). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 1.75 (3H, s, 6-$CH_3$); 2.20 (3H, s, $COCH_3$); 5.96 (1H, s, H-5); 7.33–7.38 (5H, m, H Ph); 8.64 (1H, br. s, N<u>H</u>CO<u>C</u>H$_3$); 11.63 (1H, br. s, 1-NH). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 18.3 ($CH_3$); 22.5 (CO<u>C</u>H$_3$); 106.3 (C-5); 121.5 (C-3); 127.6, 128.1 (C-2,3,5,6 Ph); 129.0 (C-4 Ph); 137.7 (C-1 Ph); 143.1 (C-4); 149.2 (C-6); 160.8 (C-2); 169.0 (NH<u>C</u>O<u>C</u>H$_3$). Found, %: C 69.29; H 5.94; N 11.38. $C_{14}H_{14}N_2O_2$. Calculated, %: C 69.41; H 5.82; N 11.56.

**3-Bromo-*N*-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)propanamide (16)**. Pyridine (0.081 ml, 1 mmol) was added to a solution of compound **4** (100 mg, 0.5 mmol) in dichloromethane (3 ml), the mixture was cooled to 5°C and treated by dropwise addition of 3-bromopropanoyl chloride (0.1 ml, 1 mmol). The reaction mixture was stirred at room temperature for 15 h. The solvent was removed by evaporation, the residue was treated with ice water. The precipitate that formed was filtered off, washed with distilled water, and recrystallized from a 1:1 mixture of 2-propanol–hexane. Yield 111 mg (67%), white crystals, mp 186–188°C. IR spectrum, ν, $cm^{-1}$: 1632, 1651, 1675, 3224, 3283. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.20 (3H, s, $CH_3$); 2.57–2.60 (1H, m) and 2.71–2.74 (1H, m, COC<u>H</u>$_2$CH$_2$Br); 3.49–3.51 (1H, m) and 3.64–3.67 (1H, m, COCH$_2$C<u>H</u>$_2$Br); 6.00 (1H, s, H-5); 7.31–7.41 (5H, m, H Ph); 8.98 (1H, s, N<u>H</u>COCH$_2$); 11.78 (1H, s, 1-NH). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 18.2 ($CH_3$); 28.4 (CO<u>C</u>H$_2$CH$_2$Br); 40.3 (COCH$_2$<u>C</u>H$_2$Br); 105.4 (C-5); 121.0 (C-3); 127.6 (C-4 Ph); 127.9, 128.0 (C-2,3,5,6 Ph); 137.4 (C-1 Ph); 142.8 (C-4); 148.6 (C-6); 160.6 (C-2); 168.5 (NH<u>C</u>OCH$_2$). Found, %: C 53.89; H 4.39; N 8.20. $C_{15}H_{15}BrN_2O_2$. Calculated, %: C 53.75; H 4.51; N 8.36.

**2-Chloro-*N*-(2-chloroacetyl)-*N*-(6-methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)acetamide (17)**. Pyridine (0.243 ml, 3 mmol) was added to a solution of compound **4** (200 mg, 1 mmol) in dichloromethane (6 ml), the resulting mixture was cooled to 5°C and treated by dropwise addition of chloroacetyl chloride (1 ml, 3 mmol). The reaction mixture was stirred at room temperature for 15 h. The solvent was removed by evaporation, the residue was treated with ice water. The precipitate was filtered off, washed with distilled water, and recrystallized from 50% ethanol. Yield 208 mg (75%), white crystals, mp 192–194°C. IR spectrum, ν, $cm^{-1}$: 1633, 1648, 1732, 3305. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): 2.42 (3H, s, $CH_3$); 4.34 (2H, d, $^2J_{AB}$ = 8.0) and 4.36 (2H, d, $^2J_{AB}$ = 8.0, 2$CH_2$); 6.23 (1H, s, H-5); 7.24–7.28 (2H, m, H-2,6 Ph); 7.42–7.46 (3H, m, H-3,4,5 Ph); 13.50 (1H, br. s, NH). $^{13}$C NMR spectrum (DMSO-$d_6$), δ, ppm: 19.3 ($CH_3$); 45.2 (N(CO<u>C</u>H$_2$Cl)$_2$); 108.7 (C-5); 120.4 (C-3); 127.1, 129.4 (C-2,3,5,6 Ph); 130.0 (C-4); 135.2 (C-1 Ph); 147.8 (C-4); 154.3 (C-6); 161.9 (C-2); 169.0 (N(<u>C</u>OCH$_2$Cl)$_2$). Found, %: C 54.29; H 4.12; N 8.06. $C_{16}H_{14}Cl_2N_2O_3$. Calculated, %: C 54.41; H 4.00; N 7.93.

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