Synthesis of *N*,*N*-disubstituted (*Z*)-*O*-methylnicotinamide oximes

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A number of (*Z*)-*N,N*-dialkyl- and (*Z*)-*N*-acyl-*N*-alkyl-*O*-methylnicotinamide oximes was synthesized. Their configuration was confirmed by the NOESY experiment. Evaluation of fungicidal activity of compounds obtained was performed.

Key words: pyridines substituted at position 3, *N*,*O*-substituted amide oximes, *E*,*Z*-isomerism, *O*-alkylation, *N*-acylation, fungicides, ^{1}H NMR spectroscopy.

Pyridine derivatives substituted at position 3 possess various biological activity.[1—3] In particular, it is known that the nitrogen atom of the pyridine ring can form strong complexes with the iron atom in the gems of different oxydases interfering with their work.[4] The action of 2′,4′-dichloro-2-(3-pyridyl)acetophenone *O*-methyloxime (pyrifenox) is based on this principle, which is used in agriculture as an efficient systemic fungicide.[5]

Possibilities of structural modification of analogs of fungicide antibiotic strobilurin, which inhibit bc_1-cytochrome oxydase complex of the respiratory chain, are under intensive study.[6] The residue of α-substituted methyl (*E*)-β-methoxyacrylate or groups isosteric to it serve as a toxophoric element in the strobilurin analogs. It was shown that methoxymethylene group can be exchanged with methoxyimine one, as well as methoxycarbonyl group with some heterocycles without affecting activity of the compounds. At the same time, the *trans*- or *anti*-arrangement of the methoxycarbonyl (or heterocycle replacing it) and the methoxy group at the double bond remains important.[6]

Earlier, we have synthesized nicotinamides possessing fungicidal activity.[7] We also synthesized a number of new *N*,*N*-dialkyl- (**1a**,**b**) and *N*-acyl-*N*-alkyl-substituted (*Z*)-*O*-methylnicotinamide oximes (**2a**—**g**) in order to study how activity of the nicotinic acid derivatives depends on their structure, as well as to obtain strobilurin analogs with the pyridine ring in the toxophoric residue. To choose substituents, we were guided by the structures of known strobilurin analogs, in particular, synthetic methyl (*Z*)-2-[((*E*)-cinnamoyl)(methyl)amino]-3-methoxyacrylate[8] and antibiotics cyrmenins,[9] which also contain β-acrylate toxophore bound to the acylamino group.

There is only scarce information on the synthesis of *N*-acylamide oximes in the literature. Only their preparation by the reaction of *N*-hydroxycarboximidoyl chlorides with primary amides in the presence of a base is described.[10] We found no information on *N*-acylated *N*,*O*-dialkylamide oximes. It is known that acylation of unsubstituted amide oximes with acid anhydrides and acyl chlorides furnishes *O*-acylamide oximes, whereas *N*-acylamide oximes are unstable and are formed as intermediates in the synthesis of 1,2,4-oxadiazoles.[11]

In the present work, we showed that *N*,*O*-dialkyl-*N*-acylamide oximes are stable enough, they can be isolated and characterized. We confirmed the *Z*-configuration of the compounds obtained and performed preliminary evaluation of their fungicidal properties.

For the synthesis of the target compounds, we used a sequence of transformations given in Scheme 1.

The reaction of pyridine-3-carboximidoyl chloride hydrochloride (**3**) with primary and secondary amines leads to amide oximes **4a**—**d**, whose methylation with dimethyl sulfate in the presence of sodium methoxide in anhydrous DMF converts them to amide oximes **1a**—**d**. Acylation of compounds **1c**,**d** with acyl chlorides gave (*Z*)-*N*-acyl-*N*-alkyl-*O*-methylnicotinamide oximes (**2a**—**g**).

Carrying out the reaction of compound **3** with equimolar amounts of primary amines and triethylamine as an HCl acceptor led to the formation of products **4c**,**d** in ~50% yields, whereas the use of an excess of only primary amine allows one to increase the yield to 78% for **4c** and 74% for **4d**. It is known[12] that the reaction of amines and hydroxyimidoyl chlorides proceeds through nitrile oxides, whose dimerization leads to the side formation of furoxans, therefore, the use of an excess of amine, apparently, allows one to decrease contribution of this reaction.

No formation of products was observed when acylation of amide oximes **1c**,**d** was performed with acyl chlorides in the presence of catalytic amounts of DMAP and triethylamine as an HCl acceptor, and only addition of the molar excess of DMAP allowed us to obtain acyl derivatives **2a**—**g**.

The reaction of hydroxyimidoyl chlorides with amines is a stereoselective process, which leads to the formation

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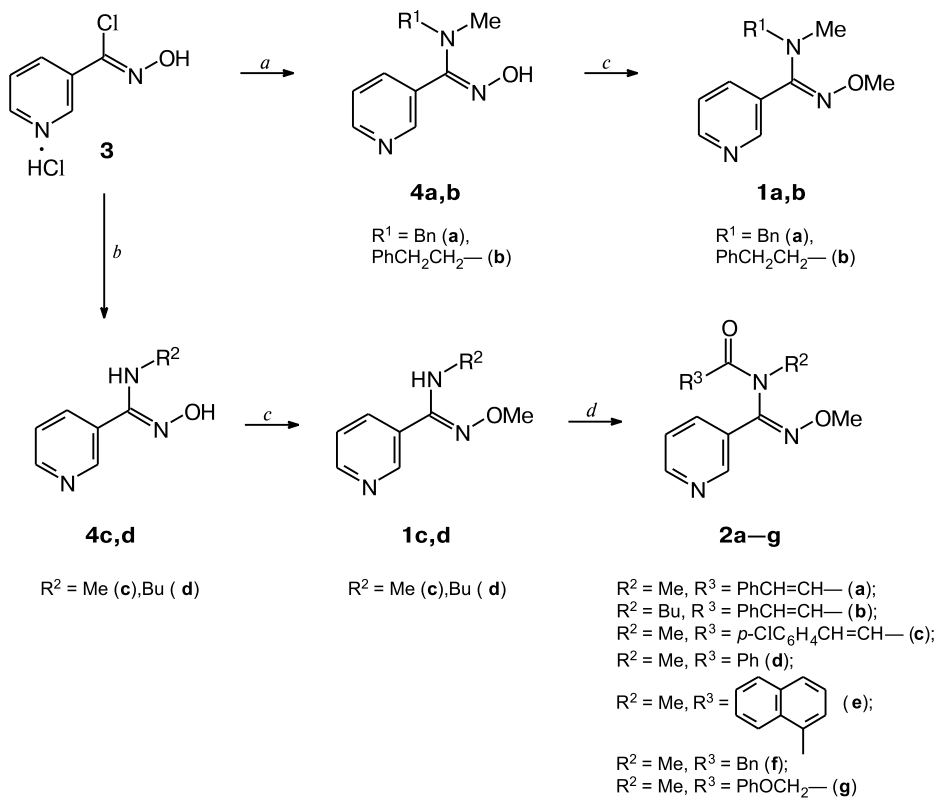
Scheme 1



Reagents and conditions: *a*. R^1MeNH, MeOH, 0 °C; *b*. R^2NH_2, MeOH, 0 °C; *c*. MeONa, Me_2SO_4, DMF, 0—5 °C; *d*. R^3COCl, DMAP, $CHCl_3$, reflux.

of *Z*-isomers of amide oximes.[13] In the case of *N*-monosubstituted amide oximes, their *Z*-isomers are stable and have no tendency to isomerization to the *E*-form.[11] We assumed that in the steps of *O*-methylation or *N*-acylation, molecular configuration can be retained, therefore, we expected to obtain *Z*-isomers of the target amide oximes with arrangement of the methoxy group and pyridine ring on the opposite sides with respect to the double bond.

To confirm the structure of the synthesized compounds, a two-dimensional correlation spectrum for the Overhauser effect (the NOESY experiment) was recorded for amide oxime **2d**, which showed that the protons of the NMe group interact with the second and fourth protons of the pyridine ring and *ortho*-protons of the phenyl ring. The protons of the OMe group interact with the *ortho*-protons of the phenyl ring, but have no interaction with the protons of the pyridine ring and the NMe group (Fig. 1). The data obtained confirm *Z*-configuration of the compound.

Fungicidal properties of several compounds (**1a** and **2a—c,f**) were preliminary evaluated in the *in vitro* experiments[14] in the six sequences against three phytopathogenic fungi: *Rhizoctonia solani* Kühn, *Fusarium moniliforme* Sheldon, and *Helminthosporium sativum* Pammel, King et Bakke. Values of the fungi mycelia radial growth suppression by the compounds in the concentration 30 mg L^{-1} compared to the untreated control sample with the confidence intervals at the confidence probability $P = 0.95$ are given in Table 1. It is seen from Table 1 that some of the amide oximes obtained possess high fungicidal activity and deserve to be studied further.

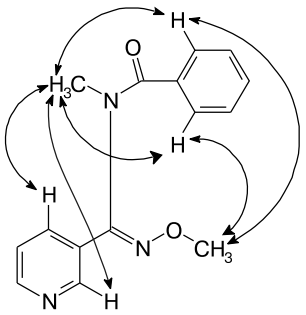


Fig. 1. Interaction of protons in compound **2d** in the NOESY experiment.

Table 1. Fungi mycelia radial growth suppression *in vitro* by compounds **1a** and **2a—c,f** in the concentration 30 mg L^{-1} compared to the untreated control sample

Compound	Fungi mycelia radial growth suppression compared to the control sample (%)		
	Rhizoctonia solani	*Fusarium moniliforme*	*Helminthosporium sativum*
1a	37±6	17±2	48±6
2a	39±7	66±5	86±5
2b	68±4	32±3	22±4
2c	62±6	62±2	81±3
2f	25±6	32±3	6±3
Standard*	70±2	60±1	69±2

* Commercial fungicide spiroxamine (8-*tert*-butyl-1,4-dioxaspiro[4.5]decan-2-ylmethyl(ethyl)(propyl)amine) was used as a standard.

Experimental

^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer (300 MHz) in $CDCl_3$ and $(CD_3)_2SO$ with Me_4Si as an internal standard. Two-dimensional correlation spectrum for the Overhauser effect was obtained on a Bruker DRX-500 spectrometer in $(CD_3)_2SO$. Reaction progress and purity of the compounds obtained were performed by TLC on Sorbfil PTSKh-AF-V-UF plates (visualization was performed in the UV light or by treatment with the modified Dragendorf or Erlich reagent).[15]

The starting **(*E*)-3-(4-chlorophenyl)propenoyl chloride** was synthesized from commercially available (*E*)-3-(4-chlorophenyl)-propionic acid (Acros Organics) and thionyl chloride.[16]

Pyridine-3-carboxaldoxime was obtained from commercially available pyridine-3-carboxaldehyde (Acros Organics) and $NH_2OH \cdot HCl$.[17]

***N*-Hydroxypyridine-3-carboximidoyl chloride hydrochloride (3).** A solution of pyridine-3-carboxaldoxime (10.1 g, 0.074 mol) in MeOH (100 mL) was cooled to 5 °C and, keep cooling, chlorine gas was passed through it over 15 min so as the temperature was kept below 10 °C. The solvent was evaporated *in vacuo* to obtain hydrochloride **3** (14.2 g, 99%), m.p. 148—150 °C. Found (%): C, 37.28; H, 3.17; N, 14.45. $C_6H_5ClN_2O \cdot HCl$. Calculated (%): C, 37.33; H, 3.13; N, 14.51. ^{1}H NMR ($(CD_3)_2SO$), δ: 7.86—7.93 (m, 1 H, 5-CH, py); 8.58 (d, 1 H, 4-CH, py, J = 7.9 Hz); 8.87 (d, 1 H, 6-CH, py, J = 4.7 Hz); 9.45 (s, 1 H, 2-CH, py); 13.11 (s, 1 H, OH).

(*Z*)-*N*-Methylnicotinamide oxime (4c). A solution of hydrochloride **3** (1.65 g, 8.55 mmol) in MeOH (10 mL) was added dropwise to a solution of $MeNH_2$ in MeOH (7 *M*, 4 mL) at 0—5 °C, which was stirred at this temperature for 8 h. The solvent was evaporated *in vacuo*, the residue was diluted with water (15 mL) and extracted with $CHCl_3$ (3×10 mL). The extract was dried with $MgSO_4$. The solvent was evaporated *in vacuo*, the residue was subjected to column chromatography on silica gel (eluent: $CHCl_3$—MeOH (10 : 1)) to obtain amide oxime **4c** (1.05 g, 79%), m.p. 108—110 °C. Found (%): C, 55.56; H, 6.03; N, 27.73. $C_7H_9N_3O$. Calculated (%): C, 55.62; H, 6.00; N, 27.80. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.59 (d, 3 H, Me, J = 6.6 Hz); 5.91 (q, 1 H, NH, J = 6.6 Hz); 7.41—7.49 (m, 1 H, 5-CH, py); 7.83 (d, 1 H, 4-CH, py, J = 8.3 Hz); 8.61 (d, 1 H, 6-CH, py, J = 4.2 Hz); 8.62 (s, 1 H, 2-CH, py); 9.81 (s, 1 H, OH).

(*Z*)-*N*-(*n*-Butyl)nicotinamide oxime (4d). A solution of hydrochloride **3** (3 g, 0.016 mol) in MeOH (25 mL) was added dropwise to a solution of *n*-butylamine (4.65 mL, 0.048 mol) in MeOH (50 mL) at 0—5 °C, which was stirred at this temperature for 6 h. The solvent was evaporated *in vacuo*, the residue was diluted with water (30 mL) and extracted with $CHCl_3$ (3×20 mL). The extract was dried with $MgSO_4$. The solvent was evaporated *in vacuo*, the residue was subjected to column chromatography on silica gel (eluent: $CHCl_3$—MeOH (10 : 1)) to obtain amide oxime **4d** (2.2 g, 74%), oil. Found (%): C, 62.22; H, 7.90; N, 21.69. $C_{10}H_{15}N_3O$. Calculated (%): C, 62.15; H, 7.82; N, 21.74. ^{1}H NMR ($CDCl_3$), δ: 0.84 (t, 3 H, $CH_2CH_2CH_2Me$, J = 5.9 Hz); 1.20—1.35 (m, 2 H, $CH_2CH_2CH_2Me$); 1.35—1.47 (m, 2 H, $CH_2CH_2CH_2Me$); 2.95—3.02 (m, 2 H, $CH_2CH_2CH_2Me$); 5.32 (br.s, 1 H, NH); 7.30—7.37 (m, 1 H, 5-CH, py); 7.79 (d, 1 H, 4-CH, py, J = 9.1 Hz); 8.65 (d, 1 H, 6-CH, py, J = 5.0 Hz); 8.72 (s, 1 H, 2-CH, py); 9.10 (br.s, 1 H, OH).

Compounds **4a,b** were obtained similarly.

(*Z*)-*N*-Benzyl-*N*-methylnicotinamide oxime (4a). The yield was 80%, m.p. 126—128 °C. Found (%): C, 69.80; H, 6.35; N, 17.33. $C_{14}H_{15}N_3O$. Calculated (%): C, 69.69; H, 6.27; N, 17.41. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.60 (s, 3 H, Me); 4.07 (s, 2 H, CH_2); 7.18—7.28 (m, 3 H, CH, Ph); 7.29—7.37 (m, 2 H, CH, Ph); 7.43—7.51 (m, 1 H, 5-CH, py); 7.81 (d, 1 H, 4-CH, py, J = 9.4 Hz); 8.56 (s, 1 H, 2-CH, py); 8.58 (d, 1 H, 6-CH, py, J = 6.2 Hz); 9.39 (s, 1 H, OH).

(*Z*)-*N*-Methyl-*N*-(2-phenethyl)nicotinamide oxime (4b). The yield was 82%, oil. Found (%): C, 70.65; H, 6.80; N, 16.38. $C_{15}H_{17}N_3O$. Calculated (%): C, 70.56; H, 6.71; N, 16.46. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.68 (t, 2 H, CH_2CH_2Ph, J = 5.7 Hz); 2.75 (s, 3 H, NMe); 3.06 (t, 2 H, CH_2CH_2Ph, J = 5.7 Hz); 6.98 (d, 2 H, CH, Ph, J = 8.6 Hz); 7.10—7.27 (m, 3 H, 2 CH, Ph, 5-CH, py); 7.35—7.47 (m, 2 CH, CH, Ph, 4-CH, py); 8.30 (s, 1 H, 2-CH, py); 8.32 (d, 1 H, 6-CH, py, J = 5.7 Hz); 9.55 (s, 1 H, OH).

(*Z*)-*N*,*O*-Dimethylnicotinamide oxime (1c). Amide oxime **4c** (1.03 g, 6.8 mmol) was added to a solution of MeONa (0.37 g, 6.8 mmol) in DMF (15 mL). After it was completely dissolved, the mixture was cooled to 0 °C, followed by addition of Me_2SO_4 (0.65 mL, 6.8 mmol) at 0—5 °C and stirring for 6 h at this temperature. The solvent was evaporated *in vacuo*, the residue was diluted with water (30 mL) and extracted with diethyl ether (3×15 mL). The extract was dried with $MgSO_4$, the solvent was evaporated *in vacuo*, the residue was recrystallized from isopropanol to obtain compound **1c** (0.54 g, 48%), m.p. 83—85 °C. Found (%): C, 58.11; H, 6.69; N, 25.46. $C_8H_{11}N_3O$. Calculated (%): C, 58.17; H, 6.71; N, 25.44. ^{1}H NMR ($CDCl_3$), δ: 2.72 (d, 3 H, NHMe, J = 5.6 Hz); 3.85 (s, 3 H, OMe); 5.21 (br.s, 1 H, NH); 7.29—7.36 (m, 1 H, 5-CH, py); 7.76 (d, 1 H, 4-CH, py, J = 10.0 Hz); 8.62 (d, 1 H, 6-CH, py, J = 4.8 Hz); 8.71 (s, 1 H, 2-CH, py).

Compounds **1a**,**b**,**d** were obtained similarly.

(*Z*)-*N*-Benzyl-*N*,*O*-dimethylnicotinamide oxime (1a) was isolated by column chromatography on silica gel (eluent: $CHCl_3$—MeOH (10 : 1)). The yield was 18%, oil. Found (%): C, 70.49; H, 6.80; N, 16.38. $C_{15}H_{17}N_3O$. Calculated (%): C, 70.56; H, 6.71; N, 16.46. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.65 (s, 3 H, NMe); 3.53 (s, 3 H, OMe); 4.11 (s, 2 H, CH_2); 7.20 (d, 2 H, CH,

Ph, J = 6.9 Hz); 7.25—7.37 (m, 3 H, CH, Ph); 7.45—7.51 (m, 1 H, 5-CH, py); 7.74 (d, 1 H, 4-CH, py, J = 7.8 Hz); 8.50 (s, 1 H, 2-CH, py); 8.59 (d, 1 H, 6-CH, py, J = 4.7 Hz).

(*Z*)-*N*,*O*-Dimethyl-*N*-(2-phenethyl)nicotinamide oxime (1b) was isolated by column chromatography on silica gel (eluent: EtOAc—hexane (3 : 1)). The yield was 28%, oil. Found (%): C, 71.40; H, 7.02; N, 15.58. $C_{16}H_{19}N_3O$. Calculated (%): C, 71.35; H, 7.11; N, 15.60. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.71 (t, 2 H, CH_2CH_2Ph, J = 5.6 Hz); 2.78 (s, 3 H, NMe); 3.08 (t, 2 H, CH_2CH_2Ph, J = 5.6 Hz); 3.51 (s, 3 H, OMe); 6.99 (d, 2 H, CH, Ph, J = 9.0 Hz); 7.16—7.27 (m, 3 H, 2 CH, Ph, 5-CH, py); 7.37—7.48 (m, 2 H, CH, Ph, 4-CH, py); 8.26 (s, 1 H, 2-CH, py); 8.58 (d, 1 H, 6-CH, py, J = 4.7 Hz).

(*Z*)-*N*-(*n*-Butyl)-*O*-methylnicotinamide oxime (1d) was isolated by column chromatography on silica gel (eluent: EtOAc). The yield was 68%, oil. Found (%): C, 63.81; H, 8.31; N, 20.33. $C_{11}H_{17}N_3O$. Calculated (%): C, 63.74; H, 8.27; N, 20.27. ^{1}H NMR ($(CD_3)_2SO$), δ: 0.73 (t, 3 H, $CH_2CH_2CH_2Me$, J = 6.7 Hz); 1.10—1.23 (m, 2 H, $CH_2CH_2CH_2Me$); 1.25—1.37 (m, 2 H, $CH_2CH_2CH_2Me$); 2.86—2.93 (q, 2 H, $CH_2CH_2CH_2Me$, J = 6.6 Hz); 3.72 (s, 3 H, OMe); 6.03 (t, 1 H, NH, J = 6.7 Hz); 7.42—7.48 (m, 1 H, 5-CH, py); 7.81 (d, 1 H, 4-CH, py, J = 8.9 Hz); 8.58 (s, 1 H, 2-CH, py); 8.62 (d, 1 H, 6-CH, py, J = 5.6 Hz).

(*E*)-*N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methylcinnamamide (2a). A solution of cinnamoyl chloride (0.168 g, 1 mmol) in $CHCl_3$ (5 mL) was added to a solution of compound **1c** (0.138 g, 0.84 mmol) and DMAP (0.122 g, 1 mmol) in $CHCl_3$ (25 mL). The mixture was refluxed for 6 h, cooled, washed with water (20 mL), and dried with $MgSO_4$. The solvent was evaporated *in vacuo*, the residue was subjected to column chromatography on silica gel (eluent: EtOAc—hexane (5 : 1)) to obtain compound **7a** (0.051 g, 24%), oil. Found (%): C, 69.20; H, 5.76; N, 14.30. $C_{17}H_{17}N_3O_2$. Calculated (%): C, 69.14; H, 5.80; N, 14.23. ^{1}H NMR ($(CD_3)_2SO$), δ: 3.14 (s, 3 H, NMe); 3.95 (s, 3 H, OMe); 6.52 (d, 1 H, PhCH=CH, J = 19.0 Hz); 6.91 (d, 1 H, PhCH=CH, J = 19.0 Hz); 7.25—7.35 (m, 3 H, CH, Ph); 7.52—7.65 (m, 2 H, CH, Ph); 7.66—7.72 (m, 1 H, 5-CH, py), 8.28 (d, 1 H, 4-CH, py, J = 9.3 Hz); 8.79 (d, 1 H, 6-CH, py, J = 5.0 Hz); 9.04 (s, 1 H, 2-CH, py).

Compounds **2b—g** were obtained similarly.

(*E*)-*N*-Butyl-*N*-[(*Z*)-methoxyimino-3-pyridylmethyl]cinnamamide (2b) was isolated by column chromatography on silica gel (eluent: EtOAc—hexane (1 : 1)). The yield was 18%, m.p. 43—45 °C. Found (%): C, 71.23; H, 6.91; N, 12.51. $C_{20}H_{23}N_3O_2$. Calculated (%): C, 71.19; H, 6.87; N, 12.45. ^{1}H NMR ($(CD_3)_2SO$), δ: 0,89 (t, 3 H, $CH_2CH_2CH_2Me$, J = 8.2 Hz); 1.17—1.30 (m, 2 H, $CH_2CH_2CH_2Me$); 1.34—1.49 (m, 2 H, $CH_2CH_2CH_2Me$); 3.43 (t, 2 H, $CH_2CH_2CH_2Me$, J = 8.5 Hz); 3.85 (s, 3 H, OMe); 6.51 (d, 1 H, PhCH=CH, J = 18.0 Hz); 6.85 (d, 1 H, PhCH=CH, J = 18.0 Hz); 7.35—7.42 (m, 3 H, CH, Ph); 7.50—7.62 (m, 2 H, CH, Ph); 7.65—7.71 (m, 1 H, 5-CH, py); 8.06 (d, 1 H, 4-CH, py, J = 9.0 Hz); 8.67 (d, 1 H, 6-CH, py, J = 4.9 Hz); 8.86 (s, 1 H, 2-CH, py).

(*E*)-*N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methyl-3-(4-chlorophenyl)propenamide (2c) was isolated by column chromatography on silica gel (eluent: EtOAc—hexane (5 : 1)). The yield was 25%, m.p. 79—81 °C. Found (%): C, 62.00; H, 4.83; N, 10.78. $C_{17}H_{16}ClN_3O_2$. Calculated (%): C, 61.92; H, 4.89; N, 10.75. ^{1}H NMR ($(CD_3)_2SO$), δ: 3.06 (s, 3 H, NMe); 3.80 (s, 3 H, OMe); 6.55 (d, 1 H, PhCH=CH, J = 20.0 Hz); 6.91 (d, 1 H, PhCH=CH, J = 20.0 Hz); 7.50—7.68 (A_2B_2-system, 4 H, C_6H_4, J = 7.8 Hz); 7.51—7.57 (m, 1 H, 5-CH, py); 8.12 (d, 1 H, 4-CH, py, J = 7.0 Hz); 8.67 (d, 1 H, 6-CH, py, J = 4.1 Hz); 8.93 (s, 1 H, 2-CH, py).

***N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methylbenzamide (2d)** was isolated by column chromatography on silica gel (eluent: EtOAc). The yield was 31%, m.p. 65—67 °C. Found (%): C, 66.83; H, 5.55; N, 15.52. $C_{15}H_{15}N_3O_2$. Calculated (%): C, 66.90; H, 5.61; N, 15.60. ^{1}H NMR ($(CD_3)_2SO$), δ: 3.23 (s, 3 H, NMe); 3.59 (s, 3 H, OMe); 7.30—7.35 (m, 2 H, CH, Ph); 7.37—7.42 (m, 3 H, CH, Ph); 7.43—7.47 (m, 1 H, 5-CH, py); 7.98 (d, 1 H, 4-CH, py, J = 9.3 Hz); 8.57 (d, 1 H, 6-CH, py, J = 5.2 Hz); 8.77 (s, 1 H, 2-CH, py).

***N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methylnaphthalene-1-carboxamide (2e)** was isolated by column chromatography on silica gel (eluent: EtOAc). The yield was 33%, m.p. 88—90 °C. Found (%): C, 71.39; H, 5.31; N, 13.20. $C_{19}H_{17}N_3O_2$. Calculated (%): C, 71.46; H, 5.37; N, 13.16. ^{1}H NMR ($(CD_3)_2SO$), δ: 3.28 (s, 3 H, NMe); 3.45 (s, 3 H, OMe); 7.21 (t, 1 H, CH, naphthyl, J = 7.4 Hz); 7.38—7.45 (m, 2 H, CH, naphthyl); 7.46—7.53 (m, 2 H, naphthyl, J = 9.2 Hz); 7.72 (d, 1 H, CH, naphthyl, J = 9.4 Hz); 7.75—7.79 (m, 1 H, 5-CH, py); 7.81—7.87 (m, 2 H, CH, naphthyl, 4-CH, py); 8.32 (d, 1 H, 6-CH, py, J = 6.0 Hz); 8.50 (s, 1 H, 2-CH, py).

***N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methylphenylacetamide (2f)** was isolated by column chromatography on silica gel (eluent: EtOAc). The yield was 17%, oil. Found (%): C, 67.78; H, 5.96; N, 14.89. $C_{16}H_{17}N_3O_2$. Calculated (%): C, 67.83; H, 6.05; N, 14.83. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.98 (s, 3 H, NMe); 3.80 (s, 2 H, CH_2); 3.92 (s, 3 H, OMe); 7.17—7.22 (m, 2 H, CH, Ph); 7.23 (m, 3 H, CH, Ph); 7.45—7.49 (m, 1 H, 5-CH, py); 7.87 (d, 1 H, 4-CH, py, J = 7.4 Hz); 8.62 (d, 1 H, 6-CH, py, J = 3.9 Hz); 8.70 (s, 1 H, 2-CH, py).

***N*-[(*Z*)-Methoxyimino-3-pyridylmethyl]-*N*-methylphenoxyacetamide (2g)** was isolated by column chromatography on silica gel (eluent: EtOAc). The yield was 42%, oil. Found (%): C, 64.22; H, 5.83; N, 13.95. $C_{16}H_{17}N_3O_3$. Calculated (%): C, 64.20; H, 5.72; N, 14.04. ^{1}H NMR ($(CD_3)_2SO$), δ: 2.99 (s, 3 H, NMe); 3.80 (s, 3 H, OMe); 4.90 (s, 2 H, CH_2); 6.78 (d, 2 H, CH, Ph, J = 8.9 Hz); 6.93 (t, 1 H, CH, Ph, J = 7.4 Hz); 7.24 (t, 2 H, CH, Ph, J = 9.2 Hz); 7.51—7.56 (m, 1 H, 5-CH, py); 8.04 (d, 1 H, 4-CH, py, J = 11.0 Hz); 8.66 (d, 1 H, 6-CH, py, J = 5.2 Hz); 8.87 (s, 1 H, 2-CH, py).

References

1. V. G. Granik, *Osnovy meditsinskoi khimii* [*Basics of Medicinal Chemistry*], Vuzovskaya kniga, Moscow, 2001, 384 pp. (in Russian).
2. A. Kleemann, J. Engel, *Pharmazeutische Wirkstoffe: Synthesen, Patente, Anwendungen*, Thieme, Stuttgart—New York, 1982.
3. M. D. Mashkovskii, *Lekarstvennye sredstva* [*Medicines*], Meditsina, Moscow, 1998, Parts 1, 2.
4. N. N. Mel´nikov, *Pestitsidy. Khimiya, tekhnologiya, primenenie* [*Pesticides. Chemistry, Technology, Application*], Khimiya, Moscow, 1987, 712 pp. (in Russian).
5. *The Pesticide Manual*, 12th ed., Ed. C. D. S. Tomlin, British Crop Protection Council Publications, Hardback, 2000, 1250 pp.
6. H. Sauter, W. Steglich, T. Anke, *Angew. Chem., Int. Ed.*, 1999, **38**, 1328.

7. RF Pat. 2341525; *Chem. Abstrs*, 2009, **150**, 56187.
8. EP Pat. 178808; *Chem. Abstrs*, 1986, **105**, 37476.
9. T. Leibold, F. Sasse, H. Reichenbach, G. Hoefle, *Eur. J. Org. Chem.*, 2004, **2004**, 431.
10. O. Exner, N. Motekov, *Coll. Czech. Chem. Commun.*, 1982, **47**, 814.
11. I. A. Poplavskaya, R. G. Kurmangalieva, *Khimiya amidoksimov* [*Chemistry of Amide Oximes*], Nauka, Alma-Ata, 1989, 141 pp. (in Russian).
12. P. Quadrelli, A. G. Invernizzi, M. Falzoni, P. Caramella, *Tetrahedron*, 1997, **53**, 1787.
13. O. Exner, V. Jehlička, A. Dondoni, A. C. Boicelli, *J. Chem. Soc., Perkin Trans. 2*, 1974, 567.
14. *Metodicheskie rekomendatsii po ispytaniyu khimicheskikh veshchestv na fungitsidnuyu aktivnost´* [*Methodical Recommendations for Testing Chemical Compounds for Fungicidal Activity*], NPO Zashchita rastenii, VNII KhSZR, Cherkassy, 1990, 68 pp. (in Russian).
15. M. Šaršúnová, V. Schwarz, Č. Michalec, *Chromatografia na tenkych vrstách vo farmácii a v klinickej biochémii* [*Thin-layer Chromatography in Pharmacy and Clinical Biochemistry*], Vydatel´stvo Osteva, Bratislava, Czechoslovakia, 1977.
16. *Organicum. Organisch-chemisches Grundprakticum. 18, durchgesehene Auflage*, VEB Deutscher Verlag der Wissenschaften, Berlin, 1990.
17. G. Goto, K. Kawakita, T. Okutani, T. Miki, *Chem. Pharm. Bull.*, 1986, **34**, 3202.

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