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Synthesis and Fungicidal Activity of Substituted *N*-(Alkoxy)-1-(3-pyridinyl)methanonimines

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Abstract—A number of new substituted *N*-(alkoxy)-1-phenyl- and *N*-(alkoxy)-1-cyclohexyl-1-(3-pyridinyl)-methanonymines were prepared by reacting the corresponding *N*-hydroxyl derivatives with benzyl chloride under phase transfer catalysis in a 10% NaOH–benzene system, as well as with 1-bromohexane and bromocyclohexane in DMF in the presence of NaH. The fungicidal activity of the obtained compounds was studied in vitro towards phytopathogenic fungi *Venturia inaequalis*, *Rhizoctonia solani*, *Fusarium oxysporum*, *F. moniliforme*, and *Helminthosporium sativum*.

Keywords: pyridine, *O*-alkylation, ketoximes, fungicidal activity

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Fungicides based on triazole, imidazole and pyridine derivatives are capable of using a heterocycle to coordinate the iron atom in the C14-demethylase heme, the CYP51 enzyme from the P450 monooxygenase group, disrupting its work. Demethylase blocking leads to cessation of the synthesis of ergosterol, an essential component of the cell membranes of fungi [1], and the accumulation of its toxic precursors. Among the sterol biosynthesis inhibitors, β-picoline **1** derivatives [2] have been the first discovered in the mid-1960s. Demethylase inhibitors have become the largest, most widely used and most commercially successful group of fungicides. However, from the beginning of the 1990s to the mid-2000s, new compounds of this class did not appear. Interest in the search for new representatives of this series resumed after the release of pyrisoxazole **2** [3, 4], a broad-spectrum fungicide against asco-, basidio- and deuteromycetes (Scheme 1).

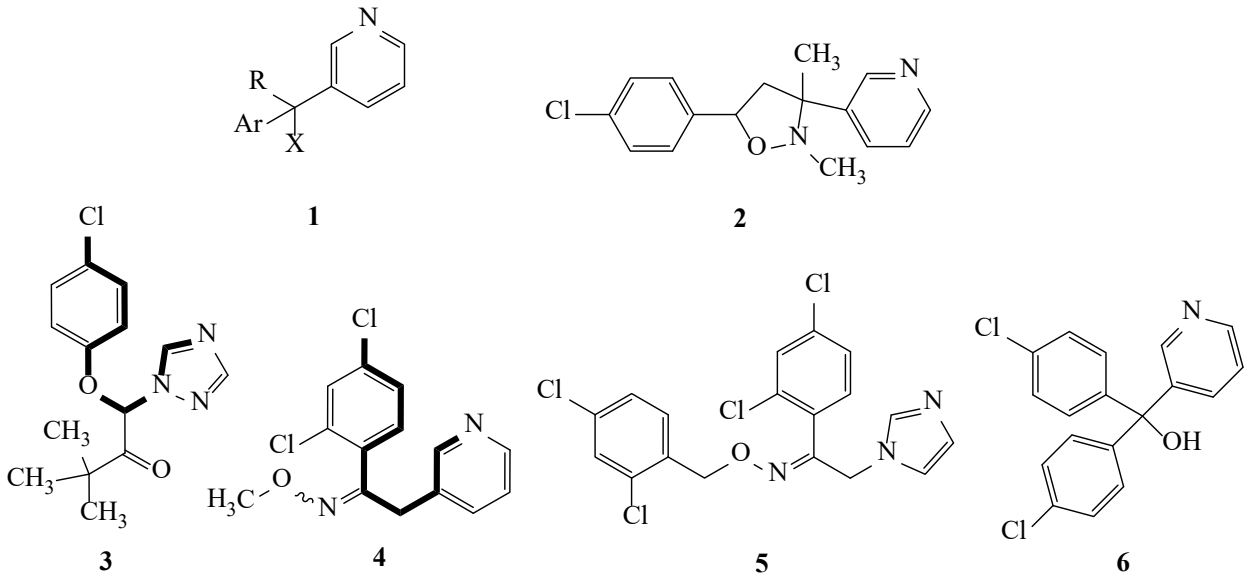
Comparison of the structure of many compounds with such an activity mechanism revealed the similarity of structural elements in triadimefon **3** and pyrifenox **4** (Scheme 1) [5], in particular, the presence of a diatomic chain separating the heterocyclic and phenyl nuclei. The molecule of oxyconazole **5**, a medical antifungal drug, is constructed in a similar way [6]. At the same time, C14-demethylase inhibitors of a different structure are known, such as parinol 6 [7], in which molecule only one carbon atom binds the ring.

We synthesized a number of new substituted *N*-(alkoxy)-1-phenyl- and *N*-(alkoxy)-1-cyclohexyl-1-(3-pyridinyl)methanonimines **7a–7l**, which are close in structure to pyrifenox and parinol, and examined their fungicidal properties.

To obtain the target compounds **7a**–**7l**, oximes **9a**–**9d** were obtained by treating the corresponding ketone with hydroxylamine hydrochloride and NaOH, which was added to the neutral reaction, in aqueous ethanol (Scheme 2) [8, 9]. The neutral medium turned out to be optimal when ketones **8a**–**8d** were oximated. The basicity of pyridine for the accepting of HCl was insufficient; an excess of alkali also led to a decrease in the yield of the product.

Further, oximes **9a**–**9d** were alkylated with benzyl chloride, 1-bromohexane or bromocyclohexane (Scheme 2). The reactions with benzyl chloride proceeded smoothly in a two-phase system (10% NaOH–benzene) using 5 mol% of benzyltriethylammonium chloride (TEBAC) as a phase transfer catalyst. Despite the high alkylating activity of benzyl chloride, in none of the experiments we were able to achieve complete conversion of the starting oxime. Along with the target *O*-(benzyloxy)imines, the products of alkylation at the pyridine and hydroxyimine nitrogen atoms were also obtained. In the case of benzyloxime **7b** synthesis, isomeric nitrone was predominantly formed. The highest conversion of the starting oxime **9b** was observed in this series.

Scheme 1.

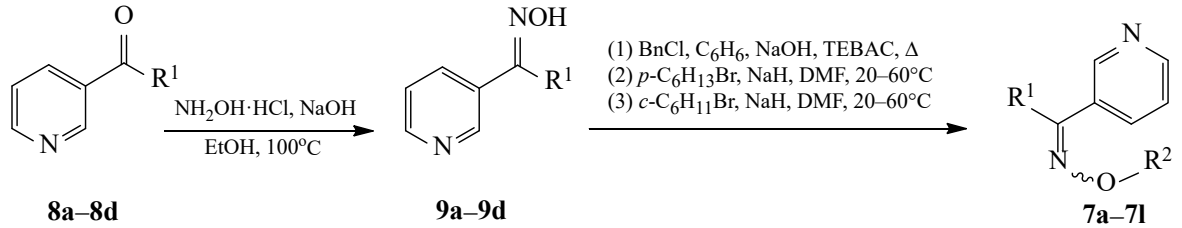


When using weaker alkylating agents (1-bromohexane and bromocyclohexane), the reaction proceeded under more severe conditions, and the use of NaH in DMF was required for deprotonation of oximes. In the reaction with bromocyclohexane, the conversion of the starting oximes was significantly lower than with benzylation, and significant amounts of olefin, the product of the elimination of HBr from alkyl bromide, were formed. It was possible to separate the unreacted oxime from the target compound by repeatedly washing the reaction mixture with a 15% KOH solution. Purification of the target reaction products was carried out by flash chromatography on a dry column [10] filled with silica gel.

All the obtained oximes were mixtures of *E*- and *Z*-isomers in different ratios, clearly distinguished by the doubled proton signal at position 4 of the pyridine ring in ^{1}H NMR spectra, with the predominance of the *E*-form (55–85%). This proton in the spectra was manifested by a doublet signal with a characteristic constant of spin-spin coupling (7.5–8.1 Hz). The isomeric composition of the mixtures was established based on the ratio of signal intensities. In the case of *Z*-isomers, the proton in the position 4 of the pyridine ring was deshielded by an approximate oxygen atom, shifting its signal to a weak field. Similarly, in the case of (*Z*)-*O*-benzyl derivatives **7a**–**7d**, the protons of the CH_2O group were deshielded by the electron-deficient pyridine nucleus.

The obtained compounds **7a**–**7l** were tested for fungicidal activity in vitro on a solid nutrient medium on five phytopathogenic fungi belonging to the classes of

Scheme 2.



8a–**8d** **9a**–**9d** **7a**–**7l**

R^1 = 4-FC_6H_4 (**8a**, **9a**), 4-ClC_6H_4 (**8b**, **9b**), 4-BrC_6H_4 (**8c**, **9c**), *c*-C_6H_{11} (**8d**, **9d**); R^1 = 4-FC_6H_4, R^2 = $PhCH_2$ (**7a**); R^1 = 4-ClC_6H_4, R^2 = $PhCH_2$ (**7b**); R^1 = 4-BrC_6H_4, R^2 = $PhCH_2$ (**7c**); R^1 = *c*-C_6H_{11}, R^2 = $PhCH_2$ (**7d**); R^1 = 4-FC_6H_4, R^2 = *p*-C_6H_{13} (**7e**); R^1 = 4-ClC_6H_4, R^2 = *p*-C_6H_{13} (**7f**); R^1 = 4-BrC_6H_4, R^2 = *p*-C_6H_{13} (**7g**); R^1 = *c*-C_6H_{11}, R^2 = *p*-C_6H_{13} (**7h**); R^1 = 4-FC_6H_4, R^2 = *c*-C_6H_{11} (**7i**); R^1 = 4-ClC_6H_4, R^2 = *c*-C_6H_{11} (**7j**); R^1 = 4-BrC_6H_4, R^2 = *c*-C_6H_{11} (**7k**); R^1 = R^2 = *c*-C_6H_{11} (**7l**).

Inhibition of in vitro radial growth of fungal mycelium by compounds **7a**–**7l** (c = 30 mg/mL)

Compound	Inhibition of radial growth of fungal mycelium relative to the control±standard deviation, %					
	V. inaequalis	*R. solani*	*F. oxysporum*	*F. moniliforme*	*H. sativum*	*S. sclerotiorum*
7a	50±1	56±3	34±2	52±3	74±2	17±2
7b	39±3	45±3	33±2	41±4	59±2	16±2
7c	30±3	51±3	23±1	44±4	43±3	10±1
7d	51±2	54±4	32±2	57±3	65±2	18±2
7e	54±2	43±2	29±1	58±2	52±2	20±2
7f	54±2	12±5	17±1	45±5	37±5	4±1
7g	43±3	29±4	12±1	36±4	36±5	11±1
7h	86±1	63±2	33±1	67±2	74±3	17±1
7i	54±3	60±2	24±1	60±2	52±3	22±1
7j	30±5	43±4	33±2	51±3	55±4	16±1
7k	34±5	38±5	25±1	47±3	48±4	16±1
7l	57±1	43±5	23±1	60±3	24±5	16±2
Triadimefon	60±5	54±4	72±5	85±7	60±5	67±6

asco-, basidio- and deuteromycetes: *Venturia inaequalis* (Cooke) Winter, *Rhizoctonia solani* Kühn, *Fusarium oxysporum* Schlecht, *Fusarium moniliforme* Sheldon и *Helminthosporium sativum* Pammel, King et Bakke from the collection of the All-Russian Research Institute of Plant Protection Chemicals (Moscow). An analysis of biological test data (see Table) shows that *V. inaequalis*, *R. solani*, and *F. moniliforme* turned out to be the most sensitive to the tested compounds, and *S. sclerotiorum* the least. All the obtained compounds suppressed fungal growth; however, in most cases, fungitoxicity inferior to triadimefon. *N*-(Benzyloxy)imines **7a**–**7d** and *N*-(hexyloxy)-imine **7h** showed the greatest activity. The high activity of compound **7h** was somewhat unexpected, since it is known [11] that the presence of a halogen atom in the structure is important for CYP51 cytochrome oxidase ligands. Considering that the main field of application of C14-demethylase inhibitors is the fight against obligate pathogens of powdery mildew (*Erysiphe graminis*) and rust (*Puccinia recondita*) and the optional causative agent of septoria (*Septoria tritici*) crops [12], it is advisable to study the obtained compounds *in planta* against relevant pathogens.

In conclusion, new substituted *N*-(alkoxy)-1-phenyl- and *N*-(alkoxy)-1-cyclohexyl-1-(3-pyridinyl)methanonimines were synthesized, similar in structure to the known CYP51 enzyme inhibitors pyrifenox, parinol and oxyconazole used as agricultural and medical fungicides. All the obtained compounds inhibited in vitro the growth of fungi of different taxonomic classes, in some cases exceeding the activity of the commercial fungicide triadimefon, which also inhibits CYP51. The resulting compounds can be recommended for the second stage of screening studies in planta.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker AM300 (300 MHz) instrument from DMSO-d_6 solutions.

***N*-Hydroxy-1-(4-fluorophenyl)-1-(3-pyridinyl)-methanimine (9a).** A solution of 0.695 g (10 mmol) of hydroxylamine hydrochloride in 1 mL of water was added to a solution of 1.010 g (5 mmol) of 4-fluorophenyl-(3-pyridinyl)methanone **8a** in 15 mL of ethanol. The mixture was heated in a water bath for 1 h, then cooled to room temperature. A solution of 0.400 g (10 mmol) of NaOH in 1 mL of water was added. Carbon dioxide was passed through the solution, adjusting pH ~ 7. The precipitate was filtered off, heated with 5 mL of ethanol to a boil. Then, 5 mL of tetrahydrofuran was added, the resulting mixture was cooled to room temperature and filtered. The organic extract was evaporated to dryness, and the residue

was recrystallized from ethanol. Yield 1.027 g (95.1%), mp 154–156°C (mp 155–156°C [9]).

Compounds **9b**–**9d** were prepared similarly.

***N*-Hydroxy-1-(4-chlorophenyl)-1-(3-pyridinyl)-methanimine (9b).** Yield 1.100 g (94.6%), mp 152–153°C (mp 151°C [9]).

***N*-Hydroxy-1-(4-bromophenyl)-1-(3-pyridinyl)-methanimine (9c).** Yield 0.630 g (46.1%), mp 159–161°C (mp 159–161°C [9]).

***N*-Hydroxy-1-cyclohexyl-1-(3-pyridinyl)methanimine (9d).** Yield 0.911 g (89.3%), mp 174–175°C (mp 173–175°C [9]).

***N*-(Benzyloxy)-1-(4-fluorophenyl)-1-(3-pyridinyl)-methanimine (7a).** A solution of 0.300 g (2.37 mmol) of benzyl chloride and 0.230 g (0.1 mmol) of benzyltriethylammonium chloride in 4.2 mL of benzene was added to a solution of 0.432 g (2 mmol) of oxime **9a** in a 10% aqueous solution of NaOH (3.08 g, 77 mmol) in 28 mL of water. The biphasic system was vigorously stirred at reflux for 8.5 h, monitoring the reaction progress using TLC. After the reaction completed, the mixture was cooled to room temperature. The organic layer was separated, and the solvent was distilled off. The residue was separated by flash chromatography on silica gel 5/40, eluent CH_2Cl_2–ethyl acetate, 1 : 1. Yield 0.348 g (56.9%, *E* : *Z* = 75 : 25), oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.18 s (2H, OCH_2, *E*-isomer), 5.28 s (2H, OCH_2, *Z*-isomer), 7.27–7.48 m (10H, 5-CH_{Py}, Ph, FC_6H_4), 7.66 d (1H, 4-CH_{Py}, *J* = 8.1, *E*-isomer), 7.74 d (1H, 4-CH_{Py}, *J* = 8.1, *Z*-isomer), 8.59 s (1H, 2-CH_{Py}), 8.64 m (1H, 6-CH_{Py}). Found, %: C 74.35; H 4.50; N 9.10. $C_{19}H_{15}FN_2O$. Calculated, %: C 74.50; H 4.94; N 9.14.

Compounds **7b**–**7d** were prepared similarly.

***N*-(Benzyloxy)-1-(4-chlorophenyl)-1-(3-pyridinyl)-methanimine (7b).** Yield 0.44 g (68.2%, *E* : *Z* = 56 : 44), reddish brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.19 s (2H, OCH_2, *E*-isomer), 5.30 s (2H, OCH_2, *Z*-isomer), 7.20–7.50 m (10H, 5-CH_{Py}, Ph, ClC_6H_4), 7.65 d (1H, 4-CH_{Py}, *J* = 8.1, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, *J* = 8.1, *Z*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.65 s (1H, 6-CH_{Py}, *J* = 8.0). Found, %: C 70.67; H 4.71; N 8.67. $C_{19}H_{15}ClN_2O$. Calculated, %: C 70.70; H 4.60; N 8.58.

***N*-(Benzyloxy)-1-(4-bromophenyl)-1-(3-pyridinyl)-methanimine (7c).** Yield 0.458 g (62.4%, *E* : *Z* = 67 : 33), reddish brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.20 s (2H, OCH_2, *E*-isomer), 5.29 s (2H, OCH_2, *Z*-isomer), 7.28–7.50 m (10H, 5-CH_{Py}, Ph, BrC_6H_4), 7.65 d (1H, 4-CH_{Py}, *J* = 8.1, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, *J* = 8.1, *Z*-isomer), 8.59 s (1H, 2-CH_{Py}), 8.65 m (1H, 6-CH_{Py}). Found, %: C 62.11; H 4.15; N 7.65. $C_{19}H_{15}BrN_2O$. Calculated, %: C 62.04; H 4.12; N 7.53.

***N*-(Benzyloxy)-1-cyclohexyl-1-(3-pyridinyl)methanimine (7d).** Yield 0.429 g (62.4%, *E* : *Z* = 55 : 45), reddish brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.06–1.81 m (11H, *c*-C_6H_{11}), 5.05 s (2H, OCH_2, *E*-isomer), 5.19 s (2H, OCH_2, *Z*-isomer), 7.22–7.44 m (6H, 5-CH_{Py}, Ph), 7.64 d (1H, 4-CH_{Py}, *J* = 7.6, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, *J* = 7.6, *Z*-isomer), 8.55 s (1H, 2-CH_{Py}), 8.62 d (1H, 6-CH_{Py}, *J* = 5.0). Found, %: C 77.50; H 7.57; N 9.40. $C_{19}H_{22}N_2O$. Calculated, %: C 77.52; H 7.53; N 9.52.

***N*-(Hexyloxy)-1-(4-fluorophenyl)-1-(3-pyridinyl)-methanimine (7e).** To a solution of 0.432 g (2 mmol) of oxime **9a** in 7 mL of absolute DMF was added under cooling with an ice bath 0.120 g (3 mmol) of 60% suspension of NaH under argon atmosphere. The mixture was stirred for 30 min, and then 0.34 mL (2.5 mmol) of 1-bromohexane was added. The resulting mixture was stirred for 24 h at room temperature, then 2.5 h at 60°C. The reaction mixture was poured into ice water (50 mL). The aqueous phase was extracted with diethyl ether, and the organic layer was washed 3 times with water, 4 times with a 15% KOH solution and dried with Na_2SO_4. The solvent was distilled off. An admixture of olefin and DMF was distilled off in vacuum of 1 Torr. The product was purified by flash chromatography on silica gel 5/40, eluent CH_2Cl_2–ethyl acetate. Yield 0.546 g (91%, *E* : *Z* = 57 : 43), yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.80 t [3H, C*H*$_3$(CH$_2$)$_5$, *J* = 0.5], 1.20–1.35 m [6H, $CH_3(CH_2)_3CH_2CH_2O$], 1.35–1.50 m (2H, $C_4H_9CH_2CH_2O$), 4.10 t (2H, $C_5H_{11}CH_2O$, *J* = 3.0), 7.20–7.50 m (5H, 5-CH_{Py}, FC_6H_4), 7.65 d (1H, 4-CH_{Py}, *J* = 8.1, *Z*-isomer) 7.73 d (1H, 4-CH_{Py}, *J* = 8.1, *E*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.61 d (1H, 6-CH_{Py}, *J* = 5.0). Found, %: C 71.90; H 7.01; N 9.25. $C_{18}H_{21}FN_2O$. Calculated, %: C 71.98; H 7.05; N 9.33.

Compounds **7e**–**7l** were prepared similarly.

***N*-(Hexyloxy)-1-(4-chlorophenyl)-1-(3-pyridinyl)-methanimine (7f).** Eluent – hexane–acetone. Yield 0.208 g (32.7%, *E* : *Z* = 71 : 29), yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.90 t [3H, C$\underline{H}_3$(CH$_2$)$_5$O, *J* = 1.0], 1.20–1.45 m [6H, $CH_3(CH_2)_3CH_2CH_2O$], 1.60–1.80 m (2H, $C_4H_9CH_2CH_2O$), 4.0 t (2H, $C_5H_{11}\underline{CH}_2O$, *J* = 3.5), 7.25–7.50 m (5H, 5-CH_{Py}, ClC_6H_4), 7.65 d (1H, 4-CH_{Py}, *J* = 7.5, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, *J* = 7.5, *Z*-isomer),

8.57 s (1H, 2-CH_{Py}) 8.65 d (1H, 6-CH_{Py}, J = 5.0). Found, %: C 68.15; H 6.76; N 8.75. $C_{18}H_{21}ClN_2O$. Calculated, %: C 68.24; H 6.68; N 8.84.

***N*-(Hexyloxy)-1-(4-bromophenyl)-1-(3-pyridinyl)-methanimine (7g).** Yield 0.356 g (51.3%, E : Z = 67 : 33), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 0.80 t [3H, $CH_3(CH_2)_5O$, J = 1.0], 1.20–1.40 m (6H, $C_4H_9CH_2CH_2O$), 1.70–1.90 m (2H, $C_4H_9CH_2CH_2O$), 4.20 t (2H, $C_5H_{11}CH_2O$, J = 4.0), 7.25–7.50 m (5H, 5-CH_{Py}, BrC_6H_4), 7.65 d (1H, 4-CH_{Py}, J = 7.5, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, J = 7.5, *Z*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.65 d (1H, 6-CH_{Py}, J = 5.0). Found, %: C 59.80; H 5.96; N 7.66. $C_{18}H_{21}BrN_2O$. Calculated, %: C 59.84; H 5.86; N 7.75.

***N*-(Hexyloxy)-1-cyclohexyl-1-(3-pyridinyl)methanimine (7h).** Yield 0.450 g (78.2%, E : Z = 75 : 25), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 0.75–0.90 m [8H, $CH_3(CH_2)_4CH_2$], 1.10–1.40 m (11H, *c*-C_6H_{11}), 1.50 t [3H, $CH_3(CH_2)_5O$, J = 2.0], 3.90 t (2H, $C_5H_{11}\underline{CH_2}O$, J = 3.5), 7.40 t (1H, 5-CH_{Py}, J = 3.0), 7.62 d (1H, 4-CH_{Py}, J = 8.0, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, J = 8.0, *Z*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.65 d (1H, 6-CH_{Py}, J = 5.0). Found, %: C 74.90; H 9.83; N 9.62. $C_{18}H_{28}N_2O$. Calculated, %: C 74.96; H 9.78; N 9.71.

***N*-(Cyclohexyloxy)-1-(4-fluorophenyl)-1-(3-pyridinyl)methanimine (7i).** Yield 0.139 g (23.4%, E : Z = 60 : 40), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.15–1.60 m and 1.70–1.90 m [10H, $(CH_2)_5$)], 4.12–4.27 m (1H, CHO), 7.25–7.50 m (5H, 5-CH_{Py}, FC_6H_4), 7.60 d (1H, 4-CH_{Py}, J = 7.6, *E*-isomer), 7.72 d (1H, 4-CH_{Py}, J = 7.6, *Z*-isomer), 8.58 s (1H, 2-CH_{Py}), 8.64 d (1H, 6-CH_{Py}, J = 4.0). Found, %: C 72.34; H 6.48; N 9.30. $C_{18}H_{19}FN_2O$. Calculated, %: C 72.46; H 6.42; N 9.39.

***N*-(Cyclohexyloxy)-1-(4-chlorophenyl)-1-(3-pyridinyl)methanimine (7j).** Yield 0.160 g (25.4%, E : Z = 85 : 15), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.10–1.90 m [10H, $(CH_2)_5$], 4.10–4.25 m (1H, CHO), 7.30–7.45 m (4H, ClC_6H_4), 7.50 t (1H, 5-CH_{Py}, J = 3.0), 7.64 d (1H, 4-CH_{Py}, J = 8.0, *E*-isomer), 7.73 d (1H, 4-CH_{Py}, J = 8.0, *Z*-isomer), 8.56 s (1H, 2-CH_{Py}), 8.62 d (1H, 6-CH_{Py}, J = 4.0). Found, %: C 68.61; H 6.10; N 8.79. $C_{18}H_{19}ClN_2O$. Calculated, %: C 68.67; H 6.08; N 8.90.

***N*-(Cyclohexyloxy)-1-(4-bromophenyl)-1-(3-pyridinyl)methanimine (7k).** Yield 0.175 g (24.4%, E : Z = 67 : 33), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.16–1.57 m and 1.73–1.94 m [10H, $(CH_2)_5$], 4.15–4.29 m (1H, CHO), 7.20–7.50 m (5H, 5-CH_{Py}, BrC_6H_4), 7.66 d (1H, 4-CH_{Py}, J = 8.0, *E*-isomer), 7.74 d (1H, 4-CH_{Py}, J = 8.0, *Z*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.65 d (1H, 6-CH_{Py}, J = 5.0). Found, %: C 60.09; H 5.39; N 7.69. $C_{18}H_{19}BrN_2O$. Calculated, %: C 60.18; H 5.33; N 7.80.

***N*-(Cyclohexyloxy)-1-cyclohexyl-1-(3-pyridinyl)-methanimine (7l).** Yield 0.102 g (17.9%, E : Z = 67 : 33), yellow oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.02–2.05 m and 4.00–4.25 m (22H, *c*-C_6H_{11}), 7.37–7.50 m (1H, 5-CH_{Py}), 7.65 d (1H, 4-CH_{Py}, J = 7.6, *E*-isomer), 7.70 d (1H, 4-CH_{Py}, J = 7.6, *Z*-isomer), 8.57 s (1H, 2-CH_{Py}), 8.65 m (1H, 6-CH_{Py}). Found, %: C 75.32; H 9.19; N 9.68. $C_{18}H_{26}N_2O$. Calculated, %: C 75.48; H 9.15; N 9.78.

Screening of *in vitro* biological activity. Before the study, mushrooms were grown on sucrose-potato agar in Petri dishes at 25±0.5°C for 10 days. The nutrient medium was prepared from filtered through a filter potato broth (200 g/L chopped potatoes), sucrose (20 g/L) and agar (10 g/L). After preparation, the medium was autoclaved at 120°C for 20 min.

Solutions of test compounds in acetone were prepared at a concentration of 3 mg/mL. The resulting solutions were added to molten potato-sucrose agar at 50°C at the rate of 1 mL per 100 mL of agar. Medium containing 30 mg/L of the test substance was obtained, which under aseptic conditions was poured into 15 mL into Petri dishes with an inner diameter of 10 cm. The final concentration of acetone in all the media was 1%. As a control, a medium containing only acetone was used. The surface of agar chilled and hardened at room temperature was inoculated with slices of mycelium fungi. Three colonies of mushrooms were sown per cup; in total, six replicates were used for each experiment. After incubation of the fungi in a thermostat at 25±0.5°C for 72 h, the diameter of the colonies of microorganisms was measured. The inhibition of mycelial growth was calculated in % relative to the untreated control and its standard deviation. As a reference substance, the commercial fungicide triadimefon **3** [3,3-dimethyl-1-(1,2,4-triazol-1-yl)-1-(4-chlorophenoxy)butan-2-one] containing 98% of active substances (ZAO Shchelkovo Agrochem) was used. The test results are presented in the table.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Kuck, K.H. and Vors, J.-P., *Modern Crop Protection Compounds*, Krämer, W. and Schirmer, U., Eds., Weinheim: Wiley-VCH, 2007, p. 605.

2. USA Patent 3396224, 1965; *C. A*., 1968, vol. 39, p. 1724.
3. Chen, F., Han, P., Liu, P., Si, N., Liu, J., and Liu, X., *Sci. Rep*., 2014, vol. 4, p. 6473. https://doi.org/10.1038/srep064773
4. EP Patent 1035122, 1999; *C. A*., 2000, vol. 12, p. 963.
5. Dorn, F., Pfiffner, A., and Schlageter, M., *Synthesis and Chemistry of Agrochemicals II*, Baker, D., Washington: Am. Chem. Soc., 1991, p. 506.
6. Griffin, R. and Tracy, T., *Foye's Principles of Medicinal Chemistry*, Williams, D.A. and Lemke, Th.L., Eds., Philadelphia: Lippincott Williams anf Wilkins, 2002, p. 891.
7. Shimanskaya, M.V. and Leitis, L.Ya., *Chem. Heterocycl. Compd*., 1989, vol. 25, no. 5, p. 477. https://doi.org/10.1007/BF00482487
8. EP Patent 221601, 1985; *C. A*., 1987, vol. 27, p. 1374.
9. RU Patent 2617413, 2015; *Byull. Izobret.*, 2017, no. 12.
10. Sharp, J.T., Gosney, I., and Rowley, A.G., *Practical Organic Chemistry. A Student Handbook of Techniques*. London; New York: Chapman and Hall, 1989.
11. Jeshke, P., *Pest Manag. Sci*., 2010, vol. 66, no. 1, p. 10.
12. Oliver, R. and Hewitt, H.G., *Fungicides in Plant Protection*, Boston: CABI, 2012.