



Synthesis and study of the fungicidal activity of substituted 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-imidazoles, 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles and 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles

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Abstract

In vitro tests of substituted 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-imidazoles, 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles and 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles showed high fungicidal activity against six common fungal phytopathogens: *Sclerotinia sclerotiorum*, *Fusarium oxysporum*, *Fusarium moniliforme*, *Bipolaris sorokiniana*, *Rhizoctonia solani* and *Venturia inaequalis*. The target compounds were derived by cyclization of substituted benzylphenylketones or dibenzylketones with 3-chloro-1,2-propanediol followed by alkylation of the derived 4-chloromethyl-1,3-dioxolanes of sodium salts of imidazole or 1,2,4-triazole.

Keywords: alkylation, 1,3-dioxolane, gradient flash chromatography, imidazole, fungicidal activity, ketalization, ketals, 1,2,4-triazole.

INTRODUCTION

The overwhelming majority of systemic fungicides and antimycotics used are 1-substituted 1,2,4-triazoles and imidazoles [1-3]. The mechanism of action ofazole fungicides and antimycotics is well studied: these preparations inhibit the biosynthesis of ergosterol (a component of the cell membrane of many fungi) at the stage of oxidative demethylation of lanosterol, which involves P-450 cytochrome oxidase. Azole fungicides inhibit cytochrome oxidase, forming a donor-acceptor bond between the nitrogen atom of the heterocycle and the heme iron atom in the catalytic site [4]. Azole preparations are systemic, have low consumption rates, are low in toxicity, have a wide range of action, and surpass other classes of fungicides on these parameters. The foregoing stimulated the search for new effective fungicides and antimycotics in the series of substituted 1,2,4-triazoles and imidazoles.

The earlier synthesized 2,2-disubstituted 1-[(1,3-dioxolan-4-yl)methyl]-1*H*-imidazoles and 1-[(1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles demonstrated a wide range of biological activities: antimycobacterial [5], growth-regulating [6,7], antiradical [8], antibacterial [9], cytotoxic [10], as well as pronounced fungicidal [11-20] and antimycotic [19, 20].

In the syntheses of substituted 1-[(1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles by alkylation of the 1,2,4-triazole sodium salt with substituted 4-chloromethyl-1,3-dioxolanes, minor alkylation by-products were also prepared: 4-[(1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles. We studied and compared the fungicidal activities of 1-[(1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles and 4-[(1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles.

MATERIALS AND METHODS

¹H NMR spectra were recorded on Bruker AM-300 instrument (300.13 MHz). IR spectra were recorded on a Specord M-80 instrument (Nujol). The course of reaction was monitored and the purity of the compounds was checked by TLC (Silufol UV-254).

The target compounds were tested for fungicidal activity *in vitro* according to the procedure of [21] on six common fungal

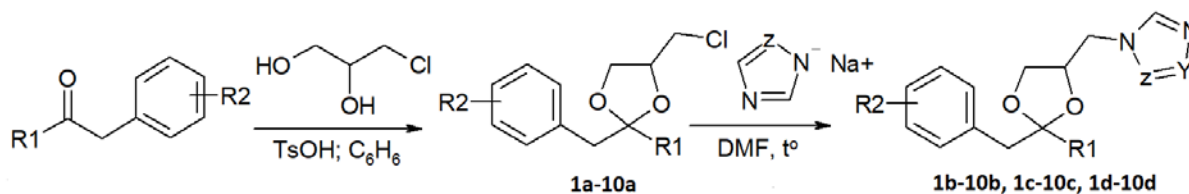
phytopathogens: *Sclerotinia sclerotiorum* (*S.s.*) – causative agent of white rot, *Fusarium oxysporum* (*F.o.*), *Fusarium moniliforme* (*F.m.*) – causative agent of Fusarium wilt, *Bipolaris sorokiniana* (*B.s.*) – causative agent of helminthosporium root rot, *Rhizoctonia solani* (*R.s.*) – causative agent of brown rot – *Rhizoctonia* rot and *Venturia inaequalis* (*V.i.*) – causative agent of apple scab. Effect of compounds on the radial growth of mycelium was studied at a concentration of 30 mg/l. Solutions of the test substances were prepared in acetone, their aliquots were added to the molten sterile potato-sucrose agar, and the resulting media were poured into aseptic conditions in Petri dishes, in which case a final concentration of acetone in all media, including test medium, did not exceed 1%. Pieces of fungus mycelium were placed on the consolidated nutrient medium, thermostated in the dark at 25±0.5°C, and the radial growth was measured after 72 h. The experiment was repeated three times. The percent of mycelial growth inhibition (I) was calculated by Abbott:

$$I = \frac{D_c - D_t}{D_c} \cdot 100\%$$

D_c – is the diameter of the fungus colonies in the test medium (control), D_t – is the diameter of the fungal colonies in the medium with the test substance.

As the reference substances, the well-known 1,2,4-triazole fungicide triadimefon and 1,3-dioxolane-containing fungicide spiroxamine were used.

We synthesized the target compounds according to **Scheme 1**. Intermediate substituted 4-chloromethyl-1,3-dioxolanes **1a–10a** were obtained with 65–99% yields by condensation of ketones with 3-chloro-1,2-propanediol in benzene catalyzed by *p*-toluenesulfonic acid with azeotropic removal of water. The target compounds **1b–10b** were derived with 15–89% yields by alkylation of sodium salts of imidazole with substituted 4-chloromethyl-1,3-dioxolanes **1a–10a** with boiling in DMF for 8 h. The target compounds were purified from the by-products ofazole's alkylation using gradient flash chromatography.



Scheme 1.

Alkylation of the sodium salt of 1,2,4-triazole with 4-chloromethyl-1,3-dioxolanes **1a–10a** derived the mixtures of 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles **1c–10c** and 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles **1d–10d**, which were separated from each other and from polyalkylation and blending products by gradient flash chromatography as well.

Sodium salts of imidazole and 1,2,4-triazole were prepared in quantitative yield by the reaction of sodium isopropylate with azoles in isopropanol [22].

Compounds **1a–10a**, **1b–10b** and **1c–10c** were synthesized earlier and described in [5, 8, 20].

Procedure for purification and separation of 1,2,4-triazole alkylation products by gradient flash chromatography.

4.0 g of the technical product of alkylation of the sodium salt of 1,2,4-triazole with substituted 4-chloromethyl-1,3-dioxolane **4a**, consisting of products **4c** and **4d**, as well as the products of asphaltization and polyalkylation, were dissolved in 15 ml of 7:3 hexane-acetone mixture and applied to the chromatographic column. The column was a 70 mm diameter glass filter filled with 90 g of Acros 35/70 silica gel. Gradient elution was carried out with a mixture of hexane-acetone: 100 ml (10:1), 100 ml (10:3), 100 ml (7:3). Fractions with $R_f = 0.62$ (in a chloroform-methanol (10:1) system) were collected, combined, and the solvent was evaporated in vacuum; 2.08 g (51 %) of the 1-[(2-(4-chlorophenyl)-2-[(4-chlorophenyl)methyl]-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazole (**4c**) were derived.

A filter with silica gel containing the other isomer was dried from the previous eluent and eluted with 200 ml of a chloroform-methanol (10:1) system, collecting fractions with $R_f = 0.15$ (in a chloroform-methanol (10:1) system), fractions were combined and the solvent was evaporated in vacuum; 1.15 g (26%) of the 4-[(2-(4-chlorophenyl)-2-[(4-chlorophenyl)methyl]-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole (**4d**) were derived, m.p. 150-151°C. NMR^{1H} (CDCl₃, δ, ppm, *J*/Hz): 3.05 (s, 2H, *n*-ClPhCH₂); 3.55-3.79 (m, 2H, CH₂O); 3.84-4.04 (m, 2H, CH₂N); 4.29 (q, 1H, CHO, ³*J*=5.4); 6.97, 6.99 (both d, no 1H, C^{2,6}H, C₆H₄ClCH₂, ³*J*=8.1); 7.13-7.33 (m, 6H, C^{2,6}H, C₆H₄Cl, C^{3,5}H, C₆H₄ClCH₂, C^{3,5}H, C₆H₄Cl); 8.06 (s, 0.5H; CH triaz.); 8.55 (s, 1.5H; CH triaz.). IR (Nujol, v/sm⁻¹): 1279 (β CH triaz.); 1245, 1172, 1084 (COCOC); 784 (C-Cl).

Similar procedure was used to isolate substituted 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles **1d–3d**, **5d–10d**:

4-[(2-benzyl-2-phenyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole (1d), yield 22%, semisolid. NMR^{1H} (CDCl₃, δ, ppm, *J*/Hz): 2.08 (s, 2H, PhCH₂CH₂); 2.54 (s, 2H, PhCH₂CH₂); 3.46 (d, 0.3H, CH₂O, ³*J*=7.1); 3.61–3.85 (m, 0.70H, CH₂O); 4.08–4.76 (m, 4H, CH₂O + CHO + CH₂N); 7.39–7.58 (m, 4H aryl.); 7.58–7.72 (m, 2H, aryl.); 7.83–8.06 (m, 4H, aryl.); 8.50 (s, 1H, CH triaz.). IR (Nujol, v/sm⁻¹): 1288 (β CH triaz.); 1245, 1220, 1195, 1175, 1078, (COCOC).

4-[(2-[(4-chlorophenyl)methyl]-2-(4-methylphenyl)-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole oxalate (2d), yield 4%, m.p. 219-225 (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 2.27 (d, 3H CH₃); 3.09 (s, 2H, *n*-ClPhCH₂); 3.46-3.73 (m, 2H,

CH₂O); 3.97-4.14 (m, 2H, CH₂N); 4.56 (q, 1H, CHO, ³*J*=8.1); 7.01 (d.d, 2H, C^{3,5}H, C₆H₄CH₃, ³*J*=8.6, ²*J*=9.0); 7.09 (d.d, 2H, C^{2,6}H, *n*-ClPhCH₂, ³*J*=8.2, ²*J*=9.0); 7.13-7.25 (m, 4H, C^{2,6}H, C₆H₄CH₃, C^{3,5}H, *n*-ClPhCH₂); 8.04 (s, 0.71H; CH triaz.); 8.54 (s, 1.29H; CH triaz.). IR (Nujol, v/sm⁻¹): 1280 (β CH triaz.); 1245, 1220, 1190, 1170, 1085 (COCOC); 784 (C-Cl).

4-[(2-[(4-chlorophenyl)methyl]-2-(4-fluorophenyl)-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole oxalate (3d), yield 9%, m.p. 209-215 (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 3.10 (s, 2H, CH₂Ar); 3.52 (d.d, 0.36H; CH₂O, ³*J*=6.1, ²*J*=8.6); 3.71 (d, 1.36H, CH₂O, ³*J*=6.1); 3.83-4.03 (m, 1H, CH₂O + CH₂N); 4.07-4.37 (m, 2.36H, CH₂O+CHO+CHN); 7.02 (d, 2H, C^{2,6}H 4-CIBz; ³*J*=7.3); 7.06-7.17 (m, 2H; C^{2,6}H 4-FPh); 7.17-7.37 (m, 4H; C^{3,5}H 4-CIBz; C^{3,5}H 4-FPh); 8.04 (s, 0.64H; CH triaz.); 8.54 (s, 1.36H; CH triaz.). IR (Nujol, v/sm⁻¹): 1280 (β CH triaz.); 1245, 1190, 1160, 1080, (COCOC), 792 (C-Cl).

4-[(2-[(4-bromophenyl)-2-[(4-chlorophenyl)methyl]-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole oxalate (5d), yield 10%, m.p. 141-145 (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 3.09 (s, 2H, CH₂Ar); 3.51 (d.d, 0.4H^B, CH₂O, ³*J*=7.2, ²*J*=8.8); 3.63-3.79 (m, 1.6H, CH₂O+CH₂N); 3.86-4.05 (m, 2H, CH₂N+CHO); 4.08-4.37 (m, 1H, CHO); 7.02 (d, 2H, C^{2,6}C₆H₄Cl, ³*J*=8.2); 7.14 (d, 2H, C^{2,6}C₆H₄Br, ³*J*=8.8); 7.23 (d, 2H, C^{3,5}C₆H₄Cl, ³*J*=8.2); 7.47 (d, 2H, C^{3,5}C₆H₄Br, ³*J*=8.8); 8.43 (s, 0.8H, CH triaz.); 8.55 (s, 1.2H, CH triaz.). IR (Nujol, v/sm⁻¹): 1279 (β CH triaz.); 1240, 1192, 1175, 1085 (COCOC); 782 (C-Cl).

4-[(2-[(4-chlorophenyl)methyl]-2-[4-(hexylsulfanyl)phenyl]-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole (6d), yield 9%, m.p. 68-70°C. NMR^{1H} (CDCl₃, δ, ppm, *J*/Hz): 0.85 (t, 3H, CH₃, ³*J*=5.9); 1.19-1.31 (m, 4H, CH₂CH₂CH₃); 1.32-1.45 (m, 2H, CH₂CH₂CH₂CH₃); 1.54 (q, 2H, CH₂CH₂CH₂CH₂CH₃, ³*J*=7.4); 2.92 (t, 2H, SCH₂, ³*J*=6.6); 3.10 (s, 1H, CH₂Ar); 3.70 (d, 1H, CH₂O, ³*J*=5.9); 3.95 (d.d, 1H, CH₂O, ³*J*=7.4, ²*J*=14.7); 4.04-4.43 (m, 3H, CH₂N+CHO); 7.04 (d, 2H, C^{2,6}H, PhCH₂, ³*J*=8.1); 7.11-7.38 (m, 6H aryl.); 8.35 (s, 1H, CH triaz.); 8.47 (s, 1H, CH triaz.). IR (Nujol, v/sm⁻¹): 1274 (β CH triaz.); 1245, 1220, 1195, 1170, 1082 (COCOC); 782 (C-Cl); 688 (CS).

4-[(2,2-dibenzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole oxalate (7d), yield 5%, m.p. 203-208 (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 2.73-2.89 (m, 4H, (CH₂Ph)₂); 3.48 (d.d, 1H, CH₂O, ³*J*=8.0, ²*J*=8.7); 3.70 (d.d, 1H, CH₂O, ³*J*=6.6, ²*J*=8.7); 3.91 (d, 1H, CH₂N, ³*J*=7.2); 4.07 (d, 1H, CH₂N, ³*J*=7.2); 4.37 (q, 1H, CHO, ³*J*=5.3); 7.10-7.33 (m, 10H aryl.); 8.33 (s, 1H, CH triaz.); 8.43 (s, 1H, CH triaz.). IR (Nujol, v/sm⁻¹): 1270 (β CH triaz.); 1245, 1220, 1195, 1130, 1085 (COCOC).

4-[(2-benzyl-2-[(4-chlorophenyl)methyl]-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole oxalate (8d), yield 8%, m.p. 85-87°C, (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 2.50 (s, 2H, CH₂Ph); 2.83 (s, 2H, CH₂PhCl); 3.30-3.42 (m, 2H, CH₂O); 3.77-4.09 (m, 3H, CH₂N+CHO); 7.11-7.40 (m, 9H, aryl.); 8.32 (s, 1H, CH triaz.); 8.42 (s, 1H, CH triaz.). IR (Nujol, v/sm⁻¹): 1272 (β CH triaz.); 1240, 1221, 1190, 1136, 1080 (COCOC).

4-[(2-[(4-chlorophenyl)methyl]-2-(4-fluorophenyl)methyl]-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazole (9d), yield 12%, m.p. 238-245°C, (decomp.). NMR^{1H} (DMSO-d₆, δ, ppm, *J*/Hz): 2.84 (s, 2H, CH₂C₆H₄F); 3.72 (s, 2H,

CH₂C₆H₄Cl); 3.97-4.09 (m, 4H, CH₂O+CH₂N); 4.16-4.30 (m, 1H, CHO); 6.99-7.42 (m, 8H, aryl.); 7.94 (s, 1H, CH triaz.); 8.40 (s, 1H, CH triaz.). IR (Nujol, v/cm⁻¹): 1274 (β CH triaz.); 1245, 1220, 1205, 1146, 1085 (COCOC); 788 (C-Cl).

4-({2,2-bis[(4-chlorophenyl)methyl]-1,3-dioxolan-4-yl)methyl}-4H-1,2,4-triazole (10d), yield 7%, semisolid. NMR¹H (CDCl₃, δ, ppm, J/Hz): 3.73 (c, 4H, (CH₂Ar)₂); 3.90-4.15 (m, 3H, CH₂O+CH₂N); 4.15-4.35 (m, 2H, CH₂N+CHO); 7.30 (d, 4H, C^{3,5}; C^{3,5}H, 4-CIBz, ³J=8.5); 7.37 (d, 4H, C^{2,6}H, C^{2,6}H, 4CIBz, ³J=8.5); 8.32 (s, 1.8H, CH triaz.); 8.44 (s, 0.2H, CH triaz.). IR (Nujol, v/cm⁻¹): 1274 (β CH triaz.); 1245, 1220, 1200, 1146, 1088, (COCOC); 788 (C-Cl).

To analyze the relationship of the structure of synthesized compounds with their fungicidal activity, logPow of

synthesized compounds was calculated [23]. The calculated lipophilicity index corresponded to the values determined experimentally [24] for the studied series of compounds.

The structure of synthesized compounds is given in

Table 1.

RESULTS AND DISCUSSION

The content of the products of 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1H-1,2,4-triazoles **1c-10c** in the technical product of alkylation of 1,2,4-triazole was 57 to 94%, while the content of the products of 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4H-1,2,4-triazoles **1d-10d** was 5–26%.

Table 1. Structure of substituted 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1H-imidazoles, 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1H-1,2,4-triazoles and 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4H-1,2,4-triazoles

N ₂	R1	R2	X	Z	N ₂	R1	R2	X	Z
1b	C ₆ H ₅	H	CH	CH	6b	4-(C ₆ H ₁₃ S)C ₆ H ₄	Cl	CH	CH
1c	C ₆ H ₅	H	N	CH	6c	4-(C ₆ H ₁₃ S)C ₆ H ₄	Cl	N	CH
1d	C ₆ H ₅	H	CH	N	6d	4-(C ₆ H ₁₃ S)C ₆ H ₄	Cl	CH	N
2c	4-CH ₃ C ₆ H ₄	Cl	CH	CH	7b	CH ₂ C ₆ H ₅	H	CH	CH
2b	4-CH ₃ C ₆ H ₄	Cl	N	CH	7c	CH ₂ C ₆ H ₅	H	N	CH
2d	4-CH ₃ C ₆ H ₄	Cl	CH	N	7d	CH ₂ C ₆ H ₅	H	CH	N
3b	4-FC ₆ H ₄	Cl	CH	CH	8b	CH ₂ C ₆ H ₅	Cl	CH	CH
3c	4-FC ₆ H ₄	Cl	N	CH	8c	CH ₂ C ₆ H ₅	Cl	N	CH
3d	4-FC ₆ H ₄	Cl	CH	N	8d	CH ₂ C ₆ H ₅	Cl	CH	N
4b	4-ClC ₆ H ₄	Cl	CH	CH	9b	CH ₂ C ₆ H ₄ F	Cl	CH	CH
4c	4-ClC ₆ H ₄	Cl	N	CH	9c	CH ₂ C ₆ H ₄ F	Cl	N	CH
4d	4-ClC ₆ H ₄	Cl	CH	N	9d	CH ₂ C ₆ H ₄ F	Cl	CH	N
4b	4-BrC ₆ H ₄	Cl	CH	CH	10b	CH ₂ C ₆ H ₄ Cl	Cl	CH	CH
5c	4-BrC ₆ H ₄	Cl	N	CH	10c	CH ₂ C ₆ H ₄ Cl	Cl	N	CH
5d	4-BrC ₆ H ₄	Cl	CH	N	10d	CH ₂ C ₆ H ₄ Cl	Cl	CH	N

Table 2. Inhibition (I) of mycelial growth of phytopathogenic fungi under the action of test compounds.

Compound	I, %						logP _{ow}
	V.i.	R.s.	F.o.	F.m.	B.s.	S.s.	
1b	30	53	29	45	16	10	3.90±0,57
1c	42	67	38	51	16	14	3.25±0,69
1d	16	27	13	28	5	3	3.25±0,69
2b	54	99	72	89	-	66	4.96±0,58
2c	65	96	79	74	79	57	4.30±0,70
2d	15	35	25	53	44	17	4.30±0,69
3b	64	90	79	83	67	72	4.55±0,64
3c	54	73	73	81	80	43	3.90±0,75
3d	14	27	22	30	0	12	3.89±0,73
4b	63	100	85	88	95	74	5.09±0,59
4c	68	83	75	70	71	53	4.44±0,70
4d	31	66	68	62	72	33	4.44±0,70
5b	50	87	79	81	71	69	5.27±0,64
5c	38	72	70	72	60	36	4.62±0,75
5d	16	53	43	53	49	20	4.61±0,73
6b	32	46	28	61	49	22	7.64±0,61
6c	14	22	34	44	34	15	6.99±0,72
6d	21	47	32	65	16	9	6.98±0,71
7b	45	44	46	70	72	45	3.66±0,42
7c	26	43	21	48	41	20	3.01±0,57
7d	19	21	15	35	23	20	3.01±0,64
8b	62	65	69	83	84	44	4.26±0,43
8c	45	44	47	60	60	25	3.61±0,48
8d	23	24	18	41	32	21	3.60±0,64
9b	48	80	60	78	78	58	4.31±0,51
9c	52	67	69	70	70	48	3.66±0,64
9d	21	25	22	38	35	21	3.66±0,67
10b	16	18	31	44	27	17	4.85±0,44
10c	48	81	52	63	64	37	4.20±0,59
10d	20	28	8	35	2	8	4.20±0,65
triadimefon	58	40	82	89	54	57	
spiroxamine	81	70	16	59	70	59	

The target compounds were tested for fungicidal activity on six phytopathogenic fungi. The test results are shown in **Table 2**. Analysis of the results of fungicidal activity showed that displacement of the aryl fragment to one methylene group from the 1,3-dioxolane ring does not increase the activity in comparison with the diaryl derivatives described earlier [11], while the benzylphenyl derivatives show a fungitoxicity higher than the dibenzyl derivatives. The compounds with logP values in the range of 3.5–5.5 and with halogen atoms, both in the aryl and benzyl rings, exhibited the highest fungitoxicity. When replacing the 4-halogenaryl substituent with 4-hexylthiophenyl in compound **6b**, **6c**, **6d**, the fungicidal activity decreased.

Fungitoxicity of minor 4-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-4*H*-1,2,4-triazoles **1d-10d** had lower values than that of isomers of 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles **1c-10c**.

CONCLUSIONS

In general, substituted 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-imidazoles, 1-[(2-benzyl-1,3-dioxolan-4-yl)methyl]-1*H*-1,2,4-triazoles showed fungicidal activity exceeding the activity of the reference substances (triadimefon and spiroxamine). Therefore, the search for new fungitoxic compounds of this series is promising.

REFERENCES

- [1] Spampinato C., Leonardi D., *BioMed Research International*. 2013, № 204237.
- [2] Zhang L., Peng X.-M., Damu G.L.V., Geng R.-X., Zhou C.-H., *Medicinal Research Reviews*. 2014, 34, 340–437.
- [3] The Pesticide Manual: A World Compendium. In: MacBean C. (Eds.), British Crop Production Council, Surrey, 16th edn., 2012.
- [4] Vanden Bossche H., Koymans L., Moereels H., *Pharmacology and Therapeutics*. 1995, 67, 79–100.
- [5] Talismanov V.S., Popkov S.V., Zykova S.S., Karmanova O.G., *Journal of Pharmaceutical Sciences and Research*. 2018, 10, 950–955.
- [6] Talismanov V.S., Popkov S.V., Polivanov R.V., Starygin V.A., Spiridonov Yu.Ya., Mirovova O.Yu., Kalashnikova E.A., *Uspekhi v Khimii I Khimicheskoy Tekhnologii*. 2006, 20, 94–99.
- [7] Talismanov V.S., Polivanov R.V., Popkov S.V., *Uspekhi v Khimii I Khimicheskoy Tekhnologii*. 2005, 19, 31–36.
- [8] Talismanov V.S., Popkov S.V., Zykova S.S., Karmanova O.G., *Journal of Pharmaceutical Sciences and Research*. 2018, 10, 1267–1271.
- [9] Talismanov V.S., Popkov S.V., Zykova S.S., Karmanova O.G., *Journal of Pharmaceutical Sciences and Research*. 2018, 10, 328–332.
- [10] Talismanov V.S., Popkov S.V., Zykova S.S., Karmanova O.G., Bondarenko S.A. *Journal of Pharmaceutical Sciences and Research*. 2018, 10, 152–155.
- [11] Talismanov V.S., Popkov S.V., *Russian Chemical Bulletin*. 2007, 56, 975–979.
- [12] Talismanov V.S., Popkov S.V., *Izvestiya Vuzov. Khimiya I Khimicheskaya Tekhnologiya*. 2007, 7, 98–102.
- [13] Talismanov V.S., Popkov S.V., Arkhipova O.N., *Khimicheskaya promyshlennost segodnya*. 2007, 5, 32–35.
- [14] Talismanov V.S., Popkov S.V., Karmanova O.G., Zykova S.S., *Journal of Pharmaceutical Sciences and Research*. 2017, 9, 1985–1988.
- [15] Popkov S.V., Talismanov V.S., (2008) Patent RU 2326878.
- [16] Talismanov V.S., Popkov S.V., *Agrokimiya*. 2007, 5, 53–57.
- [17] Panasyuk A.A., Talismanov V.S., Popkov S.V., *Uspekhi v Khimii I Khimicheskoy Tekhnologii*. 2005, 20, 91–94.
- [18] Talismanov V.S., Popkov S.V., Polivanov R.V., *Izvestiya Vuzov. Khimiya I Khimicheskaya Tekhnologiya*. 2007, 7, 102–104.
- [19] Talismanov V.S., Popkov S.V., Panasyuk A.A., *Uspekhi v Khimii I Khimicheskoy Tekhnologii*. 2008, 22, 101–104.
- [20] Talismanov V.S., Popkov S.V., Zykova S.S., Karmanova O.G., Tsaplin G.V., *Journal of Pharmaceutical Sciences and Research*. 2018, 10, 1625–1628.
- [21] Metodicheskie rekomendatsii po opredeleniyu fungitsidnoi aktivnosti novykh soedinenii [Methodological Recommendations for Estimation of the Fungicidal Activities of Novel Compounds], NIITEKhim, Cherkassy, 1984, 32 pp.
- [22] Karachev D.A., Popkov S.V., *Chemistry of Heterocyclic Compounds*. 2005, 41, 987–993.
- [23] ACD/Labs 2017.2.1 (File Version C40E41, Build 99535, 14 Feb 2018)
- [24] Talismanov V.S., Popkov S.V., Karmanova O.G., Zykova S.S., Chernobrovkina A.P., *Journal of Pharmaceutical Sciences and Research*. 2017, 9, 2372–2375.