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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Synthesis and Herbicidal and Antioxidant Activity of a Series of Hetero- and Carbocyclic Derivatives of Monochloroacetic Acid

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Abstract—Monochloroacetic acid esters and amides containing carbo- and heterocycles and heterocyclic esters and amides derived from commercial aryloxyacetyl chlorides were synthesized. The structures of the compounds were confirmed by ^{1}H and ^{13}C spectroscopy. The herbicidal activity of the substances was studied with respect to mono- and dicotyledonous plants. The relative antioxidant activity of the compounds was studied by recording the luminol-dependent chemiluminescence. The experimental data, on the whole, confirm that the development of herbicides containing acetal and *gem*-dichlorocyclopropane fragments is appropriate and promising.

Keywords: amines, monochloroacetic acid esters and amines, cyclic acetal and *gem*-dichlorocyclopropane fragments, herbicidal and antioxidant activity

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Monochloroacetic acid derivatives, primarily aryloxyacetic acid esters and amines, exhibit high herbicidal activity and are widely used as chemical means for plant protection [1, 2]. Therefore, synthesis of new hetero- and carbocyclic derivatives of monochloroacetic acid and evaluation of their herbicidal and biological activity is a topical problem.

As shown previously [3], the presence of cyclic acetal and *gem*-dichlorocyclopropane fragments in the structure of the molecules enhances their biological activity and the ability to control the plant growth [3].

In this study, we prepared monochloroacetic acid esters and amides containing 1,3-dioxolane and *gem*-dichlorocyclopropane fragments and evaluated their biological and herbicidal activity.

EXPERIMENTAL

Chromatographic analysis of reaction products was performed with an HRGS 5300 Mega Series Carlo Erba chromatograph equipped with a flame ionization detector. The analysis conditions were as follows: carrier gas helium, flow rate 30 mL min^{-1}, column length 25 m, column temperature 50–280°C with programmed heating at a rate of 8 deg min^{-1}, detector temperature 250°C, and vaporizer temperature 300°C. Analysis by gas chromatography–mass spectrometry was performed with Fisons (DB 560 50-m quartz capillary column) and Focus devices using a Finnigan DSQII mass-spectrometric detector (ion source temperature 200°C, direct inlet temperature 50–270°C, heating rate 10 deg min^{-1}, Thermo TR-5MS 50 m × 0.25 mm column, helium flow rate 0.7 mL min^{-1}). The mass spectra were recorded with electron impact ionization. The NMR spectra were taken with a Bruker Avance-500 spectrometer (^{1}H 500.13 MHz) in $CDCl_3$.

We used freshly distilled acetonitrile, dimethyl sulfoxide, and pyridine solvents (all chemically pure grade, OOO Tekhresurs, Russia), monochloroacetyl chloride (Sigma–Aldrich), freshly calcined K_2CO_3 and $MgSO_4$ (both pure grade, OOO Steklopribor, Russia), 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane as a heterocyclic alcohol, and its monochloroacetic acid ester (**1**), prepared as described in [4].

Synthesis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl morpholin-4-ylacetate (2), (2,2-dimethyl-1,3-dioxolan-4-yl)methyl piperazin-1-ylacetate (3), (2,2-dimethyl-1,3-dioxolan-4-yl)methyl *N,N*-diethylglycinate (4), and bis[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl] 2,2'-(piperazine-1,4-diyl)diacetate (5) *(general procedure).* To a mixture of 20 mL of acetonitrile and 0.15 mol (20.7 g) of K_2CO_3, we added 0.1 mol of an amine: morpholine (8.7 g), piperazine (8.6 g), or diethylamine (7.3 g). The mixture was refluxed for 2 h. Then, 0.12 mol (20.8 g) of compound **1** was added, and the mixture was refluxed for 7 h. The resulting mixture was filtered while hot, and the filtrate was evaporated and vacuum-distilled.

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl morpholin-4-ylacetate (2). Yield 37%, T_b = 160°C (2 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 s (3H, C^7H_3), 1.39 s (3H, C^6H_3), 2.52 s (4H, $C^{3'}H_2$, $C^{3''}H_2$), 3.20 s (2H, $C^{10}H_2$), 3.75 s (4H, $C^{2'}H_2$, $C^{2''}H_2$), 3.70–3.74 m (1H, C^4H_1), 4.14 d (1H, C^5H_a, ^2J = 2.8), 4.26 d (1H, C^5H_b, ^2J = 2.8). ^{13}C NMR spectrum, δ_C, ppm: 25.23 (C^7), 26.57 (C^6), 53.14 ($C^{3'}$ + $C^{3''}$), 59.21 ($C^{10}H_2$), 64.52 (C^8H_2), 64.71 (C^5H_2), 66.10 ($C^{2'}$ + $C^{2''}$), 73.72 (C^4H_1) 109.77 (C^2), 169.77 (C^9). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 259 (1), 193 (50), 101 (24), 77 (24), 72 (14), 57 (20), 43 (100).

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl piperazin-1-ylacetate (3). Yield 31%, T_m = 135–137°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.32 s (3H, C^7H_3), 1.38 s (3H, C^6H_3), 2.31 s (1H, NH), 2.53 s (4H, $C^{2'}H_2$, $C^{2''}H_2$), 3.11 s (4H, $2CH_2$), 3.20 s (2H, $C^{10}H_2$), 3.72 m (1H, C^4H_1), 4.02 d (2H, C^8H_2, ^2J = 4.1), 4.15-4.25 d.d (2H, C^5H_2, ^2J = 7.8, ^3J = 4.6). ^{13}C NMR spectrum, δ_C, ppm: 25.41 (C^7), 26.35 (C^6), 46.91 ($C^{3'}$ + $C^{3''}$), 55.74 ($C^{2'}$ + $C^{2''}$), 56.22 (C^{10}), 64.10 (C^8), 64.46 (C^5), 73.70 (C^4), 107.97 (C^2), 173.01 (C^9).

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl *N,N*-diethylglycinate (4). Yield 58%, T_b = 142°C (5 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 t (6H, $2C^{13}H_3$, ^2J = 7.2), 1.31 s (3H, C^7H_3), 1.39 s (3H, C^6H_3), 2.61 q (4H, $2C^{11}H_2$, ^2J = 7.1), 3.32 s (2H, $C^{10}H_2$), 3.71 m (1H, C^4H_1), 4.05 d (1H, C^5H_b, ^2J = 6.0), 4.15 d.d (2H, C^8H_2, ^2J = 4.3, ^3J = 7.1), 4.29 d (1H, C^5H_a, ^2J = 6.0). ^{13}C NMR spectrum, δ_C, ppm: 12.08 ($2C^{12}$), 25.31 (C^7), 26.65 (C^6), 47.66 ($2C^{11}$), 53.73 (C^{10}), 64.58 (C^8), 65.80 (C^5), 73.50 (C^4), 109.82 (C^2), 171.12 (C^9). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 245 (2), 230 (6.5), 86 (100), 43 (10).

Bis[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl] 2,2'-(piperazine-1,4-diyl)diacetate (5). Yield 57%, T_m = 152–154°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 s (6H, $2C^7H_3$), 1.39 s (6H, C^6H_3), 2.52 s (4H, $C^{1'}H_2$, $C^{1''}H_2$), 3.20 s (4H, $2C^{10}H_2$), 3.75 s (4H, $C^{2'}H_2$, $C^{2''}H_2$), 3.71 m (1H, C^4H_1), 4.14 d (1H, C^5H_a, ^2J = 2.8), 4.27 d (1H, C^5H_b, ^2J = 2.8). ^{13}C NMR spectrum, δ_C, ppm: 25.73 ($2C^7H_3$), 26.94 ($2C^6H_3$), 52.45 ($C^{2'}$ + $C^{2''}$, $C^{1'}$ + $C^{1''}$), 58.59 (C^{10}), 64.69 (C^8), 65.80 (C^4), 73.49 (C^5), 109.22 (C^2), 170.15 (C^9).

Synthesis of methyl piperazin-1-ylacetate (6) and dimethyl 2,2'-(piperazine-1,4-diyl)diacetate (7) *(general procedure).* A three-necked flask equipped with a reflux condenser, a thermometer, and a mechanical stirrer was charged with 0.03 mol (2.58 g) of piperazine, 15 mL of DMSO, and 0.01 mol (2.08 g) of methyl monochloroacetate. The mixture was stirred for the required time at 70–75°C. After the reaction completion, the mixture was washed with a 20% NaOH solution and extracted with ether. The upper organic layer was washed with water to neutral reaction and dried over anhydrous potassium carbonate. The solvent was evaporated on a rotary evaporator, and the residue was distilled under reduced pressure in a nitrogen flow.

Methyl piperazin-1-ylacetate (6). Yield 48%, T_m = 122–124°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.51 s (1H, NH), 2.63 s (8H, C^4H_2, $C^{4'}H_2$, C^5H_2, $C^{5'}H_2$), 3.36 s (2H, C^1H_2), 3.69 s (3H, C^3H_3). ^{13}C NMR spectrum, δ_C, ppm: 47.01 (C^5 + $C^{5'}$), 52.13 (C^3), 54.10 (C^1), 57.32 (C^4 + $C^{4'}$), 176.71 (C^2). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 158 (8), 116 (20), 99 (100), 88 (8), 70 (18), 56 (34).

Dimethyl 2,2'-(piperazin-1,4-diyl)diacetate (7). Yield 70%, T_m = 134–136°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.65 s (8H, C^4H_2, $C^{4'}H_2$, C^5H_2, $C^{5'}H_2$), 3.25 s (4H, $2C^1H_2$), 3.71 s (6H, $2C^3H_3$). ^{13}C NMR spectrum, δ_C, ppm: 51.73 ($2C^3$), 52.76 (C^4 + $C^{4'}$, C^5 + $C^{5'}$), 59.33 ($2C^1$), 170.65 ($2C^2$). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 230 (10), 171 (100), 98 (58), 80 (8) 70 (12), 56 (28).

Synthesis of (2,2-dimethyl-1,3-dioxolan-4-yl) methyl *N*-benzyl-*N*-[(2,2-dichlorocyclopropyl)methyl]glycinate (8) and methyl *N*-benzyl-*N*-[(2,2-dichlorocyclopropyl)methyl]glycinate (9) *(general procedure).* To a mixture of 20 mL of acetonitrile and 0.15 mol (20.7 g) of K_2CO_3, we added 0.1 mol (23 g) of *N*-benzyl-1-(2,2-dichlorocyclopropyl)methanamine and 0.12 mol (24.9 g) of (2,2-dimethyl-1,3-dioxolan-4-yl) methyl chloroacetate (**1**) or 0.12 mol (12.9 g) of methyl chloroacetate. The mixture was stirred under microwave

heating for 1 h, after which it was filtered while hot, and the filtrate was evaporated and vacuum-distilled.

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl *N*-benzyl-*N*-[(2,2-dichlorocyclopropyl)methyl]glycinate (8). Yield 78%, T_b = 270°C (3 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.18 t (1H, C$^{1'}$H$_a$, ^2J = 7.5), 1.36 s (3H, C^{7}H$_3$), 1.39 s (3H, C^{6}H$_3$), 1.68 t (1H, C$^{1'}$H$_b$, ^2J = 2.8), 1.78–1.84 m (1H, C$^{3'}$H$_1$), 2.95 d (2H, C^{11}H$_2$, ^2J = 7.3), 3.45 s (2H, C^{10}H$_2$), 3.62 m (1H, C^{4}H$_1$), 3.71 d (2H, C^{12}H$_2$, ^2J = 7.3), 4.01 d.d (2H, C^{8}H$_2$, ^2J = 6.9, ^3J = 5.6), 4.15 d.d (2H, C^{5}H$_2$, ^2J = 4.9, ^3J = 5.6), 7.13–7.65 (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 24.63 (C$^{3'}$), 25.31 (C^7), 26.01 (C^6), 26.58 (C$^{2'}$), 56.74 (C^{12}), 60.29 (C$^{1'}$), 61.31 (C^{10}), 64.18 (C^5), 64.26 (C^8), 66.10 (C^{11}), 73.71 (C^4), 107.94 (C^2), 127.11–130.37 (Ph), 140.21 (C^{Ph}), 170.46 (C^9).

Methyl *N*-benzyl-*N*-[(2,2-dichlorocyclopropyl)methyl]glycinate (9). Yield 88%, T_b = 182°C (2 mmHg). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 t (1H, C^{1}H$_a$, ^2J = 7.5), 1.66 t (1H, C^{1}H$_b$, ^2J = 2.8), 1.79–1.85 m (1H, C^{3}H$_1$), 2.95 d (2H, C^{4}H$_2$, ^2J = 7.3), 3.45 s (2H, C^{6}H$_2$), 3.65 s (3H, C^{8}H$_3$), 3.91 s (2H, C^{5}H$_2$), 7.15–7.65 (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 25.22 (C^3), 29.23 (C^1), 51.23 (C^8), 53.46 (C^4), 57.96 (C^6), 60.75 (C^5), 127.20–129.27 (Ph), 138.52 (C^2), 171.51 (C^7). Mass spectrum, *m*/*e* (I_{rel}, %): [M]$^+$ not observed, 242/244/246 (28/20/3), 91 (100), 65 (10).

Synthesis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl phenoxyacetate (10) and (2,2-dimethyl-1,3-dioxolan-4-yl)methyl (2,4-dichlorophenoxy)acetate (11) *(general procedure).* A mixture of 0.03 mol (3.96 g) of 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane, 0.03 mol of phenoxyacetyl (5.1 g) or 2,4-dichlorophenoxyacetyl (7.17 g) chloride, and 0.03 mol (2.37 g) of freshly distilled pyridine was stirred for 9 h. The oil that formed was left to crystallize for 24 h with cooling and intermittent trituration with a glass rod. Then, a mixture of 15 g of ice and 10 mL of 1 M HCl was added, and the resulting mixture was stirred until a suspension was formed. The crude product was filtered off, washed with ice-cold water, dried with freshly calcined $MgSO_4$ and the residue was vacuum-distilled.

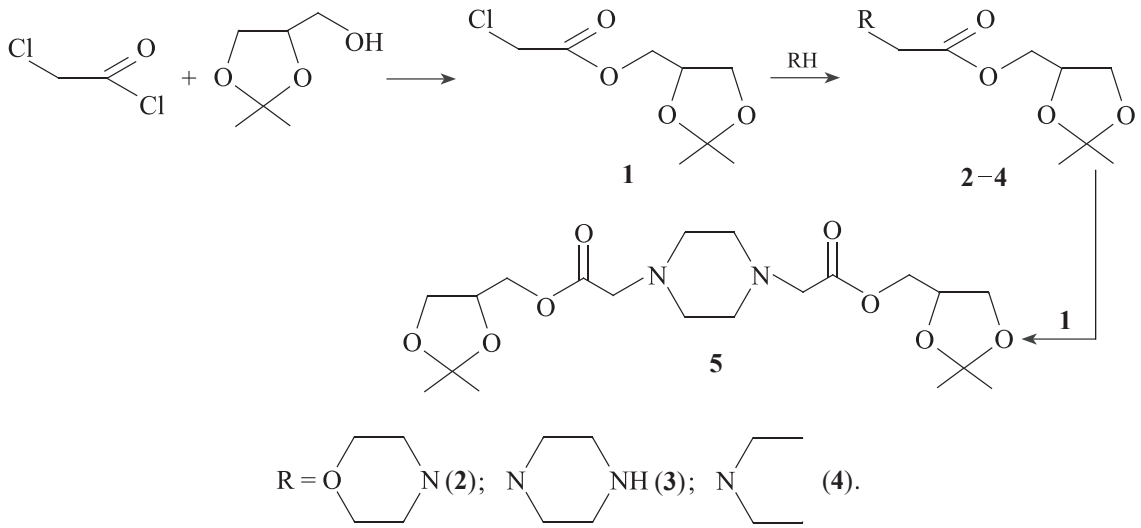
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl phenoxyacetate (10). Yield 67%, T_b = 180°C (4 mmHg). ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 1.20 s (3H, C^{7}H$_3$), 1.50 s (3H, C^{6}H$_3$), 3.65 m (1H, C^{4}H$_1$), 3.95 d.d (2H, C^{5}H$_2$, ^2J = 6.9, ^3J = 5.6), 4.20 d.d (2H, C^{8}H$_2$, ^2J = 4.9, ^3J = 5.6), 4.60 s (2H, C^{10}H$_2$), 6.80–7.40 (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$, δ_C, ppm): 25.24 (C^7), 26.61 (C^6), 63.14 (C^8), 65.45 (C^4), 69.77 (C^{10}), 71.12 (C^5), 109.88 (C^2), 114.56–129.60 (5C, Ph), 157.64 (C^{Ph}), 168.79 (C^9). Mass spectrum, *m*/*e* (I_{rel}, %): [M]$^+$ 266 (18), 251 (68), 117 (17), 107 (100), 101 (32), 79 (14), 77 (50), 72 (12), 59 (10), 51 (9).

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl (2,4-dichlorophenyl)acetate (11). Yield 33%, T_b = 215°C (3 mmHg). ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 1.34 s (3H, C^{7}H$_3$), 1.42 s (3H, C^{6}H$_3$), 3.72 m (1H, C^{4}H$_1$), 4.19 d.d (2H, C^{5}H$_2$, ^2J = 7.2, ^3J = 5.7), 4.25 d (2H, C^{8}H$_2$, ^2J = 5.9), 4.75 s (2H, C^{10}H$_2$), 6.75–7.45 (3H, Ph). ^{13}C NMR spectrum ($CDCl_3$, δ_C, ppm): 25.25 (C^7), 26.62 (C^6), 63.13 (C^8), 66.02 (C^5), 66.26 (C^{10}), 73.22 (C^4), 109.99 (C^2), 114.70–130.36 (Ph), 152.25 (C^{Ph}), 167.88 (C^9). Mass spectrum, *m*/*e* (I_{rel}, %): M$^+$ not observed, 334/336/338 (10/6/2), 319/321/323 (100/72/8), 175/177/179 (66/38/8), 145/147/149 (14/9/2), 133/135/137 (14/8/2), 109/111/113 (14/8/2), 101 (44), 73 (28), 57 (14), 43 (96).

Synthesis of 1-[(2,2-dichlorocyclopropyl)methyl]-4-(phenoxyacetyl)piperazine (12), *N*-[(2,2-dichlorocyclopropyl)methyl]-*N*-(1,3-dioxolan-4-ylmethyl)-2-phenoxyacetamide (13), and *N*-[(2,2-dichlorocyclopropyl)methyl]-2-phenoxy-*N*-(tetrahydrofuran-2-ylmethyl)acetamide (14) *(general procedure).* To a mixture of 0.02 mol of appropriate amine (4.18 g of [(2,2-dichlorocyclopropyl)methyl]piperazine, 5.21 g of [(2,2-dichlorocyclopropyl)methyl](1,3-dioxolan-4-ylmethyl)amine, or 5.08 g of [(2,2-dichlorocyclopropyl)methyl](tetrahydrofuran-2-ylmethyl)amine) and 0.02 mol (1.58 g) of freshly distilled pyridine, we added with stirring and cooling to 0°C 0.02 mol (3.41 g) of phenoxyacetyl chloride. The mixture was heated at 35°C with continuous stirring for 1 h and left overnight, after which it was washed with ice-cold water to neutral reaction. The precipitated flakes were filtered off on a Büchner funnel, washed with water, separated, and dried in air.

1-[(2,2-Dichlorocyclopropyl)methyl]-4-(phenoxyacetyl)piperazine (12). Yield 31%, T_m = 142–144°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 1.12 t (2H, C^{1}H$_2$, ^2J = 6.8), 1.76 m (1H, C^{3}H$_1$), 2.57 d.d (4H, C^{5}H$_2$, C$^{5'}$H$_2$, ^2J = 6.8, ^3J = 5.4), 2.66 d.d (4H, C^{6}H$_2$, C$^{6'}$H$_2$, ^2J = 5.4, ^3J = 6.8), 4.59 s (2H, C^{8}H$_2$), 6.85–7.35 (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$, δ_C, м. д.): 25.12 (C^1), 28.04 (C^3), 41.89 (C^5), 45.17 (C$^{5'}$), 52.31 (C^4), 57.61 (C^6 + C$^{6'}$), 60.61 (C^1), 67.60 (C^8), 114.54–129.60 (Ph),

Scheme 1.



157.71 (C^{Ph}), 166.38 (C^7). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 355 (1), 342/344/346 (2/1/0.5), 307/309/311 (18/6.5/0.5), 233/235/237 (26/1/0.5), 205/207/209 (4.5/50/10), 178/180/182 (100/36/5), 123/125/127 (14/10/6.5), 107/109/111 (24/1.5/8), 85/87/89 (4/26/10), 77 (52), 54/56/58 (8/46/4), 42/44 (30/36).

***N*-[(2,2-Dichlorocyclopropyl)methyl]-*N*-(1,3-dioxolan-4-ylmethyl)-2-phenoxyacetamide (13).** Yield 53%, T_m = 138–140°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65 t (2H, C^1H_2, ^2J = 7.5), 1.95 m (1H, C^3H_2), 3.11 d (2H, C^6H_2, ^2J = 5.7), 3.25 d (2H, C^4H_2, ^2J = 7), 3.75 d (2H, $C^{5'}H_2$, ^2J = 7.3), 4.10 d.d (1H, $C^{4'}H_1$, ^2J = 4.5, ^3J = 7.0), 4.35 d (2H, $C^{2'}H_2$, ^2J = 2.1), 4.59 s (2H, C^8H_2), 6.85–7.35 (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 25.34 (C^1), 25.70 (C^3), 29.35 (C^4), 29.92 (C^6), 47.38 (C^2), 51.13 (C^8), 60.52 ($C^{5'}$), 77.72 ($C^{4'}$), 94.80 ($C^{2'}$), 114.58–129.62 (Ph), 157.99 (C^{Ph}), 168.85 (C^7). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ not observed, 274/276/278 (25/20/5), 152/154/156 (5/3/0.8), 123/125/127 (9/6/1), 107 (76), 84 (55), 73 (100), 43 (27).

***N*-[(2,2-Dichlorocyclopropyl)methyl]-2-phenoxy-*N*-(tetrahydrofuran-2-ylmethyl)acetamide (14).** Yield 53%, T_m = 133–135°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 m (2H, $C^{3'}H_2$), 1.65 d (1H, $C^{1'}H_1$, ^2J = 7.5), 1.95 d (2H, C^4H_2, ^2J = 5.7), 2.05 m (1H, C^3H_1), 3.55 d (2H, $C^{2'}H_2$, ^2J = 7.3), 3.60 d (2H, C^6H_2, ^2J = 7.3), 3.75 d (2H, $C^{5'}H_2$, ^2J = 6.7), 4.10 d (1H, $C^{4'}H_1$, ^2J = 4.5), 4.85 s (2H, C^8H_2), 6.85–7.35 (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 25.34 (C^1), 25.70 ($C^{3'}$), 29.35 (C^3), 29.92 (C^4), 47.38 (C^6), 51.13 (C^2), 60.52 (C^8), 67.72 ($C^{2'}$), 76.80 ($C^{4'}$), 114.58–129.62 (Ph), 157.99 (C^{Ph}), 168.85 (C^7). Mass spectrum, *m*/*e* (I_{rel}, %): $[M]^+$ 358 (0.3), 322/324 (1/0.4), 274/276/278 (25/20/5), 152/154/156 (5/3/0.8), 123/125/127 (9/6/1), 107 (76), 84 (55), 71 (100), 43 (27).

RESULTS AND DISCUSSION

The reaction of monochloroacetyl chloride with an alcohol, (2,2-dimethyl-1,3-dioxolan-4-yl)carbinol (isopropylidene derivative of glycerol), gave ester **1** in quantitative yield [4]. Its reactions with secondary amines yielded the corresponding amino acid esters **2–4**. In deep steps of piperazine alkylation at a 3–5-fold excess of ester **1**, dimer **5** was obtained along with monosubstituted compound **3** (Scheme 1).

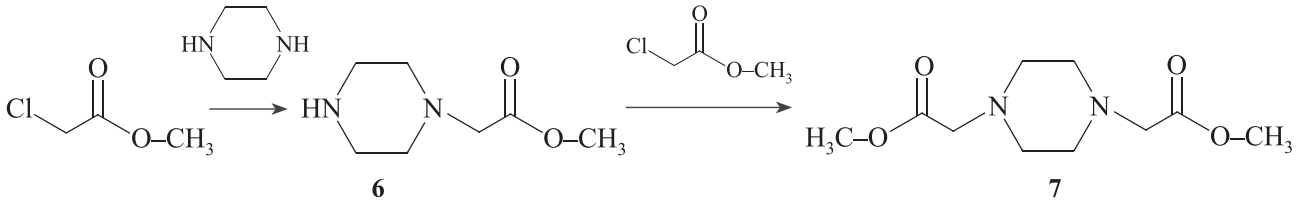
To compare the herbicidal activity of "simple" alkyl and cyclic acetal esters, we prepared from commercial methyl chloroacetate piperazine derivatives **6** and **7** (product yield 47 and 57%, respectively), which are "simpler" analogs of compounds **3** and **5** (Scheme 2).

By the reaction of chloroacetic acid esters with the previously described secondary amine [5], we prepared amino acid esters **8** and **9** in more than 90% yield (Scheme 3).

From chlorides of commercial aryloxyacetic acids, we prepared heterocyclic esters **10** and **11** in 75–85% yield (Scheme 4).

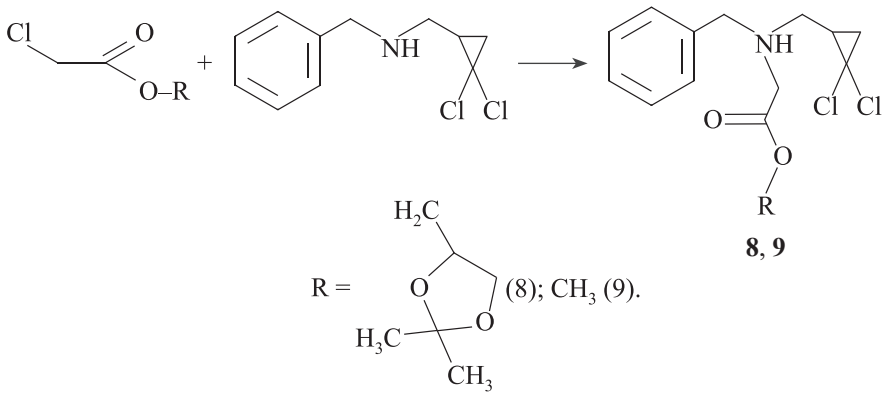
By the reaction of phenoxyacetyl chloride with secondary amines containing heterocyclic and *gem*-

Scheme 2.



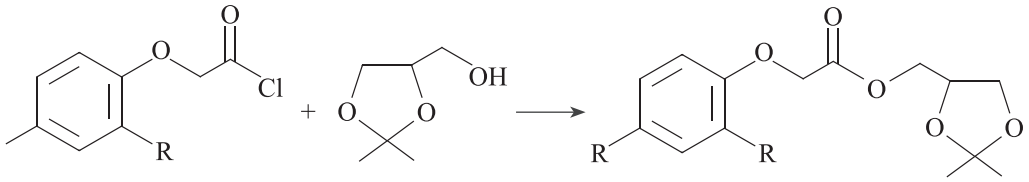
6 **7**

Scheme 3.



8, **9**

Scheme 4.



R = H (**10**),
R = Cl (**11**).

dichlorocyclopropane fragments, we prepared the corresponding amines **12–14** in 30–60% yield (Scheme 5).

According to the results of testing monochloroacetic acid derivatives, compounds **2**, **11**, **12**, and **14** showed biological activity. Therefore, these compounds were studied in more detail. We determined the herbicidal and growth-stimulating activity of compounds **2**, **11**, **12**, and **14** on wheat and pea sprouts by the procedure described previously [6, 7].

The performance of the compounds (Table 1) was determined after 3-day exposure relative to a reference, Octapon extra (C^8), octyl 2,4-dichlorophenoxyacetate (reg. no. 068(116)-03-605). The dosage of 100 mg L^{-1} increases the efficiency of inhibiting the wheat sprout length and weight. Compound **11** inhibits to the greatest extent the growth of dicotyledonous plants (wheat), whereas the piperazine detivative containing the *gem*-dichlorocyclopropane fragment (**12**) exerts the strongest inhibiting effect on monocotyledonous plants (pea). Compounds **2** and **14** are moderately active with respect to both wheat and pea.

Morpoline derivative **2** containing the dioxolane fragment inhibited the pea sprout weight to an approximately the same extent as the reference agent did. The presence of the *gem*-dichlorocyclopropyl fragment in phenoxyacetamides **12** and **14** influences insignificantly the sprout length for both di- and monocotyledonous plants.

Compounds **2** and **12** showed the best results. They may be of interest from the viewpoint of the development of new polyfunctional chemical agents for plant protection [8, 9]. We evaluated the effect of these compounds on the in vitro free-radical oxidation in model

Scheme 5.

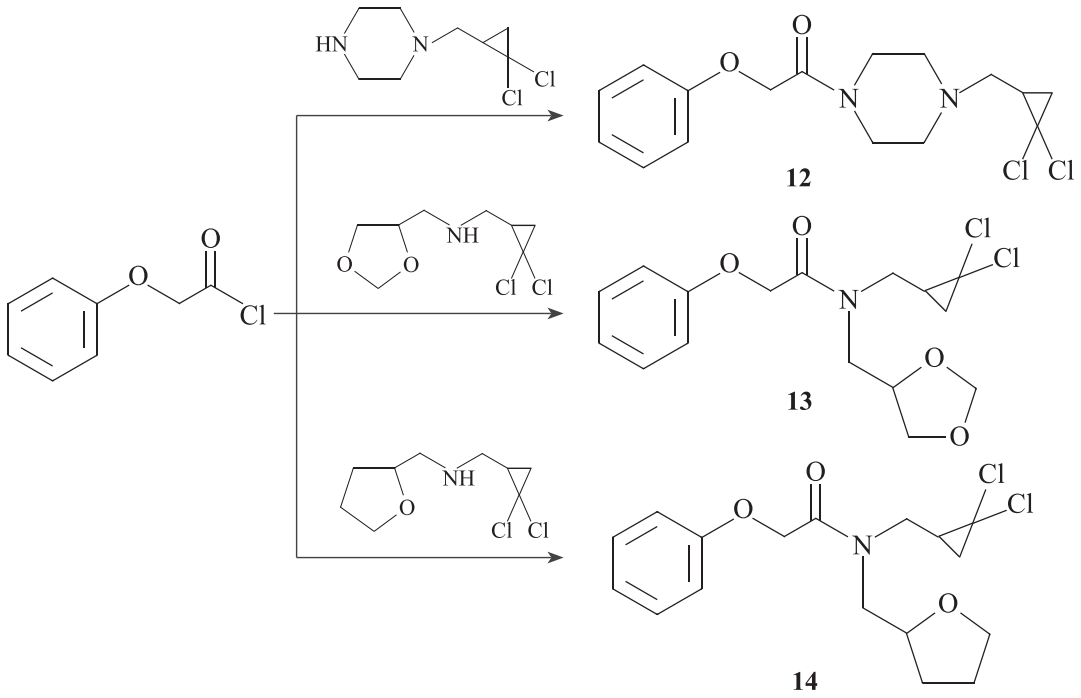


Table 1. Herbicidal activity of compounds (T = 24–25°C)

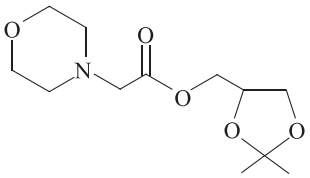
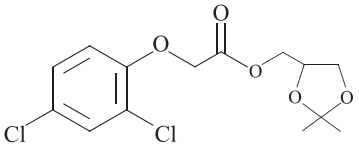
Compound	Dosage, mg L^{-1}	Mean sprout length, mm	Length inhibition, %	Mean sprout weight, g	Weight inhibition, %
		Wheat			
Control	–	69.7	–	14.1	–
Reference compound	50	12.8	81.6	9.6	31.9
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl morpholin-4-ylacetate (**2**)	50	71.5	+2.6	13.5	4.0
	100	54.8	21.4	11.4	4.3
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl (2,4-dichlorophenoxy)acetate (**11**)	50	11.5	83.5	9.9	29.8
	100	10.0	85.6	8.7	38.3

Table 1. (Contd.)

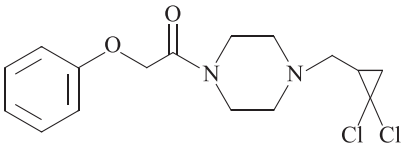
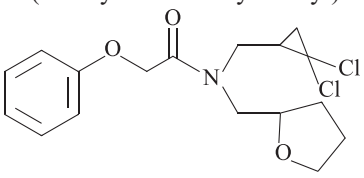
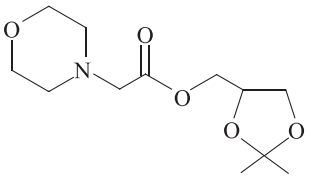
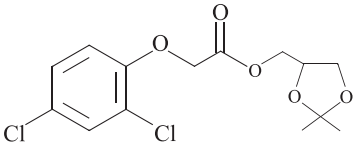
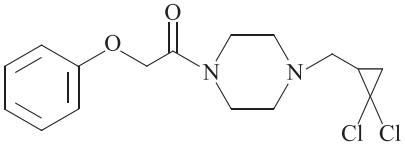
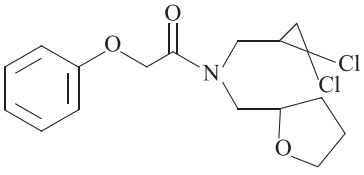
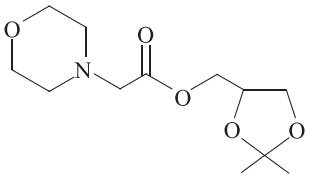
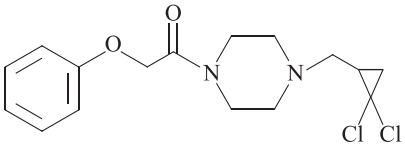
Compound	Dosage, mg L^{-1}	Mean sprout length, mm	Length inhibition, %	Mean sprout weight, g	Weight inhibition, %
1-[(2,2-Dichlorocyclopropyl)methyl]-4-(phenoxyacetyl)piperazine (**12**)	50	73.7	31.8	13.2	25.4
	100	36.8	65.9	10.9	38.4
N-[(2,2-Dichlorocyclopropyl)methyl]-2-phenoxy-*N*-(tetrahydrofuran-2-ylmethyl)acetamide (**14**)	50	65.9	39.0	13.3	24.9
	100	51.3	52.5	10.7	39.5
		Pea			
Control	–	18.4	–	72.1	–
Reference compound	5	13.0	29.3	60.0	16.8
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl morpholin-4-ylacetate (**2**)	5	18.4	0	63.5	11.9
					
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl (2,4-dichlorophenoxy)acetate (**11**)	5	7.0	62.0	65.6	9.0
					
1-[(2,2-Dichlorocyclopropyl)methyl]-4-(phenoxyacetyl)piperazine (**12**)	5	36.7	34.3	6.9	72.2
					
N-[(2,2-Dichlorocyclopropyl)methyl]-2-phenoxy-*N*-(tetrahydrofuran-2-ylmethyl)acetamide (**14**)	5	45.9	17.9	28.8	16.1
					

Table 2. Variation of the light sum and maximal chemiluminescence intensity in model systems generating active oxygen species and simulating peroxide oxidation of lipids in the presence of compounds **2** and **12**

Compound	Model of active oxygen species		Model of peroxide oxidation of lipids	
	S (light sum), %	I_{max} (maximal luminance), %	*S* (light sum), %	I_{max} (maximal luminance), %
Control (no antioxidant)	100	100	100	100
Reference (5-hydroxy-6-methyluracil)	5	7	44	49
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl morpholin-4-ylacetate (**2**) 	45	65	113	132
1-[(2,2-Dichlorocyclopropyl)methyl]-4-(phenoxyacetyl)piperazine (**12**) 	53	66	109	116

systems generating active oxygen species and in systems simulating the peroxide oxidation of lipids. The antioxidant activity was studied in dimethyl sulfoxide solution by measuring the chemiluminescence as described in [10, 11]. Control experiments were performed without antioxidant. For comparison, we used as a reference an inhibitor of free-radical oxidation in biological systems, 5-hydroxy-6-methyluracil [12, 13]. The main characteristics of the chemiluminescence were the light sum (*S*) and maximal flash intensity (I_{max}) [14]. Reagents **2** and **12** exhibit insignificant anitioxidant effect (Table 2) in a model system of active oxygen species and prooxidant effect in peroxide oxidation of lipids.

Importance of searching for compounds exhibiting not only antioxidant [15, 16] but also prooxidant properties [17] was noted in the literature. Different directions of the action of **2** and **12** show that it is promising to search for new bioactive agents among compounds related to the carbo- and heterocycles studied.

CONCLUSIONS

Biological tests of the synthesized compounds revealed among them the compounds exhibiting herbicidal, antimicrobial, and antioxidant activity, giving grounds to recommend these compounds for further studies to find fields of their efficient use.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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