

Synthesis and Herbicidal Activity of Some Substituted 1,3-Dioxacycloalkanes and *gem*-Dichlorocyclopropanes

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Abstract—Starting from ethylene glycol and *cis*-butene-1,4-diol, 1,3-dioxacycloalkanes derivatives with carbo- and heterocyclic fragments were obtained and characterized by mass spectrometry and NMR. Studying the herbicidal activity of the obtained compounds on monocotyledonous and dicotyledonous plants confirm the feasibility and prospects of creating herbicides combining in their structure cycloacetal and *gem*-dichlorocyclopropane fragments.

Keywords: acetalization, cyclic acetals, ethers, herbicidal activity

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Some substituted cyclic acetals and *gem*-dichlorocyclopropanes have herbicidal and growth-stimulating activity and can be considered as promising chemical plant protection agents [1–3]. In continuation of these researches, we synthesized a number of compounds in the molecules of which both cycloacetal and *gem*-dichlorocyclopropane fragments are present, and their herbicidal activity was determined.

2-Vinyl-2-ethyl-1,3-dioxolane **1** and 4-hydroxymethyl-2,2-dimethyl-1,3-dioxolane **2**, obtained by a known method [4], were used in the synthesis of compounds **3** and **5** with *gem*-dichlorocyclopropyl substituent in position 2 or 4, respectively (Scheme 1). Dichlorocarbenation proceeded with quantitative yield. With alkylation of hydroxymethylketal **2** with allyl chloride, the yield of allyloxy derivative **4** was 70%.

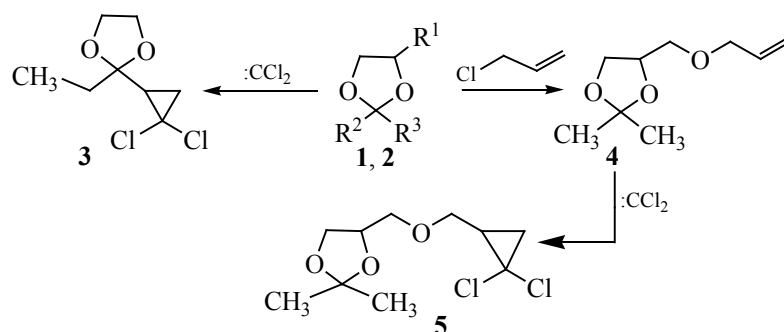
Dioxepines **6**, **7** were obtained by condensation of *cis*-butene-1,4-diol according to a known procedure [4]. Their dichlorocarbenation led to bicyclic compounds **8**, **9** with a yield of more than 80%. Since compounds with high biological activity were previously obtained based on hydroxyalkyl-*gem*-dichlorocyclopropanes, we carried

out deacetalization of compounds **8**, **9** to cyclopropane derivative **10**, exhaustive *O*-alkylation of which gave dibenzyloxy derivative **11** (Scheme 2).

The structure of the obtained compounds was proved by ¹H, ¹³C NMR spectroscopy and chromatomass spectrometry. The physico-chemical constants of the compounds correspond to the literature data [4, 5].

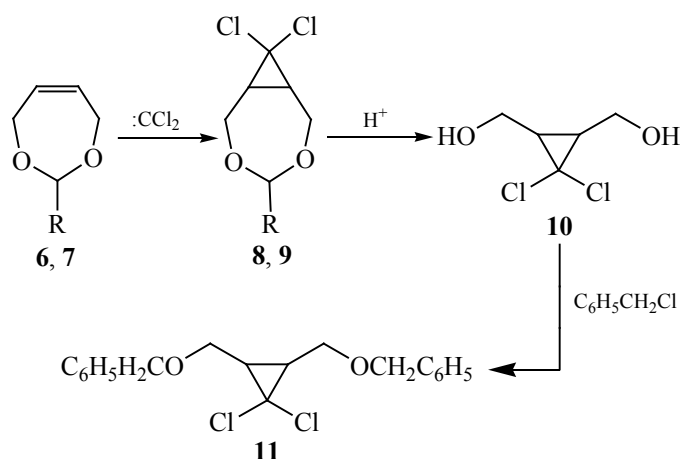
The herbicidal and growth-stimulating activity of compounds **3**, **5**, **8**, **9**, **11** (Table 1) on wheat and pea seedlings was determined according to the previously described method [5]. The best herbicidal activity among the studied series of compounds **3**, **5**, **8**, **9**, **11** was shown by compounds **5** (inhibition of an increase in the mass of seedlings was also noted) and **11**, slightly inferior to the standard Octapon extra (a herbicide based on low-volatile esters of 2,4-dichlorophenoxyacetic acid). Compound **5** exhibited inhibitory activity in relation to both the length and the mass of seedlings of dicotyledonous plants (peas). The most active inhibitor of pea seedling growth was 4-isopropyl-8,8-dichloro-3,5-dioxabicyclooctane **9**, the herbicidal activity of which is 2 times higher than that of the standard Octapon extra.

Scheme 1.



$R^1 = H$, $R^2 = C_2H_5$, $R^3 = CH=CH_2$ (**1**); $R^1 = CH_2OH$, $R^2 = R^3 = CH_3$ (**2**).

Scheme 2.



$R = H$ (**6**, **8**), $i-C_3H_7$ (**7**, **9**).

Compounds **3**, **5**, **8**, and **9** have a growth-stimulating effect on the length and weight of wheat seedlings, and compound **9** has a positive effect on both weight and length of seedlings of a monocotyledonous culture. In relation to dicotyledonous plants, the studied compounds did not show growth-stimulating activity.

The obtained experimental data show that the synthesized compounds, which contain cycloacetal and *gem*-dichlorocyclopropane fragments, exhibit herbicidal activity with respect to mono- and dicotyledonous crops, which is close to the reference drug, which confirms the prospects of their practical use.

EXPERIMENTAL

Reaction products analysis and recording of mass spectra of compounds was carried out on a hardware-software complex Chromatek-Kristall 5000M (Khromatek, Russia) with a NIST 2012 database. Analysis conditions: capillary quartz column, 30 m, analysis duration—20 min, ion source temperature—260°C, transition line temperature—300°C, scanning range 30–300 Da, pressure—37–43 mTorr, carrier gas—helium, heating rate—20 deg/min. The electron impact ionization method was used to obtain mass spectra of the compounds. 1H and ^{13}C NMR spectra were recorded on a

Table 1. Herbicidal and growth-stimulating activity of compounds **3**, **5**, **8**, **9**, **11** at 24–25°C

Compound	Dose, mg/L	Average seedling length, mm	Inhibition of seedling length, %	Average weight of seedlings, g	Mass inhibition, %
Wheat					
Control	–	33.5	–	12.3	–
11	50	30.9	7.8	12.0	2.4
	100	25.7	23.3	11.0	10.6
8	50	34.2	3	11.0	10.6
	100	33.2	0.9	11.5	6.5
9	50	34.4	2.4	12.5	1.6
	100	28.2	15.8	10.8	12.2
3	50	34.2	2.1	11.7	4.9
	100	30.3	9.6	11.5	6.5
5	50	35.1	4.8	11.6	5.7
	100	23.5	29.9	9.9	19.5
Reference standard	50	21.4	35.1	11.5	6.5
	100	15.3	54.3	9.2	25.2
Peas					
Control	–	29.7	–	21.6	–
11	5	23.2	21.9	16.1	25.3
	10	22.6	23.9	13.9	35.6
8	5	24.4	17.8	20.4	5.5
	10	19.2	35.5	15.5	28.2
9	5	22.5	24.2	17.0	92.1
	10	19.8	33.3	16.5	23.6
3	5	25.7	13.5	19.7	8.8
	10	23.6	20.5	21.4	0.9
5	5	18.9	36.4	17.1	20.8
	10	17.5	41.1	16.8	22.2
Reference standard	5	13.5	54.5	11.0	49.1
	10	12.0	59.6	9.1	57.9

Bruker AM-500 spectrometer with operating frequencies of 500 and 125 MHz, respectively; the solvent—CDCl₃.

We used freshly distilled solvents benzene (chemically pure) and chloroform (chemically pure) produced by OOO Bashhimprodukt, as well as commercial reagents: ethylene glycol, *cis*-butene-1,4-diol, allyl chloride, isobutyraldehyde, acetone, ethyl vinyl ketone, paraform (Sigma-Aldrich), freshly calcined desiccants: potassium carbonate (pure) and calcium chloride (pure) produced by OOO Steklopribor.

2-Ethyl-2-vinyl-1,3-dioxolane **1**, 4-hydroxymethyl-2,2-dimethyl-1,3-dioxolane **2** and 4-[(allyloxy)methyl]-2,2-dimethyl-1,3-dioxolane **4** were obtained according to

previously described methods [4–7]. The NMR spectrum of compound **4** is given in [8]. 4,7-Dihydro-1,3-dioxepine **7** and 2-isopropyl-4,7-dihydro-1,3-dioxepine **9** were obtained by the previously described methods; NMR data for compounds **7**, **9** are given in the works [4, 9–11].

General synthesis procedure. A mixture of compound **1**, **4**, **6**, or **7** (0.05 mol), 150 mL of chloroform, 160 g of a 50% NaOH solution was stirred at 5–7°C until complete conversion of the starting compound (control by GLC). At the reaction completion, the mixture was washed with water until neutral, dried with calcium chloride, filtered, and evaporated. The reaction products were isolated by vacuum distillation.

2-(2,2-Dichlorocyclopropyl)-2-ethyl-1,3-dioxolane (3). Yield 90%, colorless liquid, bp 40°C (4 mmHg). ¹H NMR spectrum, δ , ppm: 0.87 t (3H, CH₃, *J* 7.0), 1.37 d (2H, CH^A, *J* 8.0), 1.45 t (2H, CH^B, *J* 7.0), 1.60–1.66 m (2H, CH₂), 1.72 t (1H, CH, *J* 7.0), 3.95 d (2H, CH^A, *J* 7.0), 4.04 t (2H, CH^B, *J* 6.4). ¹³C NMR spectrum, δ_C , ppm: 9.45 (CH₃), 27.49 (CH₂), 30.11 (CH₂), 39.56 (CH), 66.49 (C), 69.29 (CH₂), 109.00 (C). Mass spectrum, *m/z* (*I*_{rel}, %): 211 (5), 213 (3), 215 (2) [*M*]⁺, 109 (15), 111 (7), 113 (5), 123 (30), 125 (18), 127 (7), 73 (100).

2,2-Dimethyl-4-[(2,2-dichlorocyclopropyl)methoxymethyl]-1,3-dioxolane (5). Yield 70%, colorless liquid, bp 74–76°C (8 mmHg). ¹H NMR spectrum, δ , ppm: 0.95–1.04 m (1H, CH), 1.37 t (3H, CH₃, *J* 7.0), 1.43 t (3H, CH₃, *J* 6.8), 1.62 t (1H, CH^A, *J* 5.3), 1.68 d (1H, CH^B, *J* 5.4), 3.45 t (1H, CH^A, *J* 11.0), 3.57 d (1H, CH^B, *J* 11.2), 3.61 t (1H, CH^A, *J* 9.0), 3.69 d (1H, CH^B, *J* 8.9), 3.84 d (1H, CH^A, *J* 6.0), 4.02 t (1H, CH^B, *J* 6.7), 4.33–4.38 m (1H, CH). ¹³C NMR spectrum, δ_C , ppm: 24.52 (CH₂), 25.46 (CH₃), 27.34 (CH₃), 28.49 (CH), 61.03 (C), 67.83 (CH₂), 68.58 (CH₂), 69.42 (CH₂), 69.78 (CH), 108.96 (C). Mass spectrum, *m/z* (*I*_{rel}, %): 225, 227, 229 (≤ 3) [*M*]⁺, 219 (40), 221 (15), 145 (45), 115 (30), 117 (8), 101 (100), 89 (60), 91 (35), 43 (80).

6,6-Dichloro-3,5-dioxabicyclooctane (8). Yield 90%, colorless liquid, bp 119°C (3 mmHg). ¹H NMR spectrum, δ , ppm: 2.23 m (2H, CH), 3.70 m (2H, OCH), 4.50 m (2H, OCH), 4.60 d (1H, OCHO, *J* 7.0), 5.05 d (1H, OCHO, *J* 7.0). ¹³C NMR spectrum, δ_C , ppm: 35.3 (CH₂), 66.7 (CCl₂), 70.0 (CH₂), 101.7 (C).

4-Isopropyl-8,8-dichloro-3,5-dioxabicyclooctane (9). Yield 98%, colorless liquid, bp 103°C (3 mmHg). ¹H NMR spectrum, δ , ppm: 0.85 d (6H, CH₃, *J* 10.1), 1.70–1.76 m (1H, CH), 2.15–2.20 m (2H, CH), 4.05 d (2H, CH^A, *J* 3.6, 8.4), 4.55 d (2H, CH^B, *J* 4.0, 9.0), 5.02 s (1H, CH). ¹³C NMR spectrum, δ_C , ppm: 17.36 (2CH₃), 32.03 (CH), 34.93 (2CH), 65.65 (2CH₂), 66.26 (C), 108.24 (CH). Mass spectrum, *m/z* (*I*_{rel}, %): 188 (20), 190 (7), 77 (100), 75 (35), 109 (45), 111 (17), 51 (80), 53 (30).

2,3-Bis(benzyloxymethyl)-1,1-dichlorocyclopropane (11) was obtained according to the previously described procedure [10]. Yield 86%, light-yellow liquid, bp 101°C (3 mmHg). ¹H NMR spectrum, δ , ppm: 2.07 t (2H, CH, *J* 10.5), 4.10 d (2H, CH^A, *J* 10.0), 4.52 t (2H, CH^B, *J* 10.2), 7.05–7.70 m (10H, Ph). ¹³C NMR spectrum, δ_C , ppm: 32.05 (2CH), 63.44 (C), 65.74 (2CH₂), 72.93 (2CH₂), 128.41–141.18 m (Ph). Mass spectrum, *m/z* (*I*_{rel},

%): 352 (8), 354 (5), 356 (1), 274 (32), 276 (18), 278 (8), 91 (100), 77 (32).

Evaluation of the herbicidal activity of the obtained compounds was carried out in laboratory conditions. Seedlings of sowing peas and spring wheat were placed in Petri dishes with aqueous emulsions of compounds with a concentration of active substances of 5 and 10 mg/L for peas and 50 and 100 mg/L for wheat. Octapone extra herbicide was used as a reference standard. Petri dishes were kept in a thermostat for 3 days at 24–25°C, after which the length was measured and the weight of the seedlings was determined. The degree of inhibition of growth and mass of shoots was determined in % with respect to the control—the variant without chemical preparations. The experiments were repeated three times.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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