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Synthesis of Potential Biologically Active Compounds Based on Aryloxy- and Arylaminopropanehydrazides

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Abstract—New derivatives of a number of aryloxy and arylaminopropanehydrazides were synthesized. Their heterocyclization under the action of carbon disulfide and potassium hydroxide and subsequent alkylation of the resulting 2-thioxo-1,3,4-oxadiazole ring, the corresponding S-substituted products were obtained. The reaction of the starting hydrazides with arylaldehydes and pentane-2,4-dione afforded their *N*′-arylidene and *N*′-(4-oxopentan-2-ylidene) derivatives. In preliminary laboratory tests, the synthesized compounds showed a pronounced stimulating effect on plant growth. Their activity was 44–95% compared with heteroauxin.

Keywords: aryloxyhydrazides, arylaminohydrazides, *N*′-arylidene(4-oxopentane-2-ylidene)-2-aryloxy(amino)-propanehydrazides, 1,3,4-oxadiazole-2(3*H*)-thione, plant growth stimulators

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Most pharmaceutical preparations that mimic biologically active natural substances consist of heterocyclic scaffolds. Hydrazides and their derivatives, in particular hydrazones, are often used as starting compounds to obtain new heterocyclic structures. Hydrazine derivatives occupy a special place in the chemotherapy of tuberculosis [1]. Isonicotinic acid hydrazide (isoniazid) has been used in medical practice for more than half a century and has not lost its significance to this day. On its basis, ftivazide, saluside, metazide and other modified analogs with improved pharmacological properties have been obtained. In medical practice, antidepressants iproniazid and nialamide (monoamine oxidase inhibitors) are widely used [1]. Studies of new hydrazine derivatives are ongoing, among which compounds with antimicrobial [2–5], anti-tuberculosis [6], anti-inflammatory [7], antimalarial [8], antitumor [9], anticonvulsant [10] and antidepressant [11] activities have been revealed. In agriculture, some hydrazide derivatives are used, in particular, herbicides (benquinox, saijunmao, phenoxyaryl hydrazides of nicotinic acid) [12]. Compounds with growth-stimulating activity have been found [13–15].

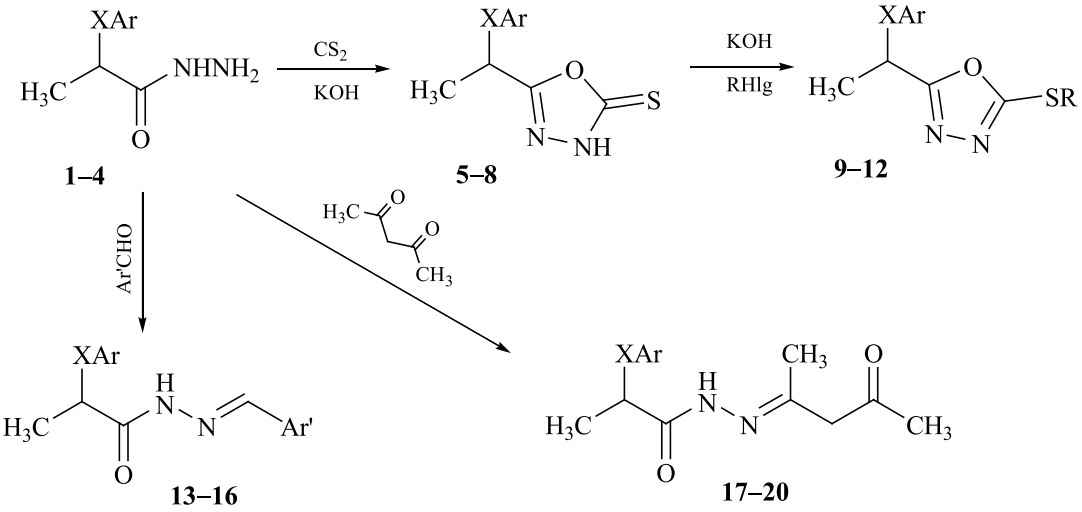
In order to obtain new potential biologically active compounds, we carried out the reaction of 2-aryloxy- and 2-(arylamino)propanehydrazides **1–4** with carbon disulfide and KOH in an anhydrous ethanol medium. As a result, heterocyclization of the hydrazide fragment took place with the formation of 1,3,4-oxadiazole-2-thione derivatives **5–8** (Scheme 1, Table 1).

The ^{13}C NMR spectra of compounds **5–8** contain signals from the sp^2-hybridized carbon atom C=S at 177.9 ppm, which indicates the thionic structure. In the ^{13}C NMR spectra of the alkylation products **9–12**, these signals disappear and new ones appear, corresponding to methylene groups at the S atom. This indicates that the reaction is proceeding at the exocyclic sulfur atom of the heterocycle.

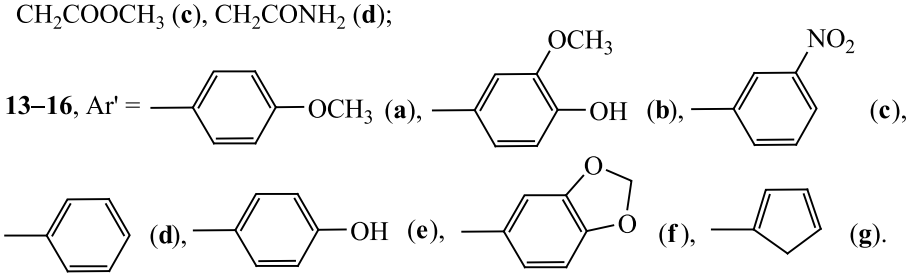
The reaction of starting hydrazides **1–4** with various arylaldehydes in the presence of hydrochloric acid at room temperature led to the formation of *N*′-arylidene-2-aryloxy(amino)propanehydrazides **13–16** (Scheme 1). Hydrazides **1–4** reacted with pentane-2,4-dione in acetic acid in the presence of a catalytic amount of DMF at room temperature to yield *N*′-(4-oxopentan-2-ylidene)-2-aryloxy(amino)propanehydrazides **17–20** (Scheme 1).

Due to the hindered rotation around the C=N double bond (or due to inversion at the nitrogen atom), molecules of compounds **13–20** can exist as *E*- and *Z*-isomer forms. The NMR spectra of compounds **13–16** show two sets of signals corresponding to the *E*- and *Z*-isomers, with

Scheme 1.



XAr = OC_6H_5 (**1**, **5**, **9**, **13**, **17**), OC_6H_3-3,4-Cl_2 (**2**, **6**, **10**, **14**, **18**), NHC_6H_4-4-Cl (**3**, **7**, **11**, **15**, **19**), NHC_6H_3-3,4-Cl_2 (**4**, **8**, **12**, **16**, **20**); **9**–**12**, R = $CH_3C(O)CH(CO)CH_3$ (**a**), $(CH_2)_2OC_6H_5$ (**b**), CH_2COOCH_3 (**c**), CH_2CONH_2 (**d**);



an intensity ratio from 1 : 1 to 7 : 3. In the latter case, the spatially more favorable *E*-form prevails. In the ^1H and ^{13}C NMR spectra of compounds **17–19**, the signals of two isomers practically coincide, and only in the NMR spectra of compound **20** the chemical shifts of signals with an intensity ratio of 1 : 1 corresponding to *E*- and *Z*-isomers differ only slightly.

During laboratory vegetation tests, almost all of the compounds obtained showed a stimulating effect on plant growth. The experiments were carried out on seeds and seedlings of common beans (*Phaseolus vulgaris L.*). The effect of aqueous suspensions of compounds **1–14** at concentrations of 25 and 50 mg/L on seed viability, germination, and seedling growth was studied. These data were compared with a similar effect of heteroauxin solutions of the same concentrations. Activity of the compounds ranged from 44 to 95% compared to heteroauxin (see Table). Substances that showed activity above 70% in the test (**5**, **7**, **11b**, **11c**, **11d**, **14a**, **14b**, **15d**, **15f**, **16a**, **16b**, **16d**) were selected for further research.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded at 30°C on a Varian Mercury-300 NMR spectrometer (300 and 75 MHz, respectively) in a mixture of DMSO-d_6–CCl_4 (3 : 1); TMS was used as an internal standard. The reactions progress and the purity of the obtained compounds were monitored by TLC on Silufol UV-254 plates; an acetone–hexane 2:1 mixture was used as an eluent. Elemental analysis was performed on a Eurovector EA3000 CHNS analyzer. Melting points were determined by the capillary method and were uncorrected.

General procedure for the synthesis of compounds 5–8. To a mixture of 10 mmol of compound **1–4** and 10 mmol of KOH were added 10 mL of absolute ethanol and 20 mmol of carbon disulfide. The resulting mixture was stirred for 8–10 h at 75–80°C and then evaporated. To the residue was added 20–30 mL of water, acidified with hydrochloric acid to pH = 4. The precipitate was filtered off, washed with water, and dried.

Table 1. Physico-chemical characteristics and plant growth stimulating activity of compounds **5–20**

Comp. no.	Yield, %	mp, °C	Calculated, %			Formula	Found, %			Activity[a], %	
			C	H	N		C	H	N	50 mg/L	25 mg/L
5	94	80–82	54.04	4.54	12.60	$C_{10}H_{10}N_2O_2S$	54.11	4.40	12.33	74	51.4
6	84	Масло	41.25	2.77	9.62	$C_{10}H_8Cl_2N_2O_2S$	41.14	2.66	9.41	–	79
7	80	162–164	46.97	3.94	16.43	$C_{10}H_{10}ClN_3OS$	46.88	3.89	16.17	76.3	81.1
8	81	108–110	41.39	3.13	14.48	$C_{10}H_9Cl_2N_3OS$	41.44	3.20	14.62		
9a	65	108–110	56.24	5.03	8.74	$C_{15}H_{16}N_2O_4S$	56.14	5.12	8.55		
9b	63	62–63	63.14	5.30	8.18	$C_{18}H_{18}N_2O_3S$	63.01	5.22	7.88	–	51.3
10c	72	Масло	42.99	3.33	7.71	$C_{13}H_{12}Cl_2N_2O_4S$	42.85	3.28	7.55		
10d	75	120–122	41.39	3.18	12.07	$C_{12}H_{11}Cl_2N_3O_3S$	41.44	3.22	12.28	–	44.9
11b	92	112–114	57.52	4.83	11.18	$C_{18}H_{18}ClN_3O_2S$	57.40	4.75	11.32	88.1	56.2
11c	90	85–86	47.64	4.31	12.82	$C_{13}H_{14}ClN_3O_3S$	47.71	4.40	12.70	73.0	59.1
11d	83	120–122	46.08	4.19	17.91	$C_{12}H_{13}ClN_4O_2S$	46.00	4.05	17.73	59.9	74.9
12c	68	128–130	43.11	3.62	11.60	$C_{13}H_{13}Cl_2N_3O_3S$	43.20	3.69	11.80		
12d	71	133–135	41.51	3.48	16.14	$C_{12}H_{12}Cl_2N_4O_2S$	41.42	3.44	15.90	–	62.0
13a	95	147–149	68.44	6.08	9.39	$C_{17}H_{18}N_2O_3$	68.52	6.13	9.51	43.8	65.6
13b	90	194–196	64.96	5.77	8.91	$C_{17}H_{18}N_2O_4$	64.88	5.71	8.73	56.6	44.5
13c	96	166–168	61.34	4.83	13.41	$C_{16}H_{15}N_3O_4$	61.21	4.73	13.20	67.2	64.2
14a	91	169–171	55.60	4.39	7.63	$C_{17}H_{16}Cl_2N_2O_3$	55.49	4.28	7.37	62.2	82.0
14b	87	83–84	53.14	4.46	7.29	$C_{17}H_{17}Cl_2N_2O_4$	53.01	4.38	7.05	63.5	76.0
14c	75	88–89	50.28	3.43	10.99	$C_{16}H_{13}Cl_2N_3O_4$	50.17	3.33	10.74		
15d	82	218–220	63.68	5.34	13.92	$C_{16}H_{16}ClN_3O$	63.78	5.42	13.80	53.7	75.1
15e	77	223–225	60.48	5.08	13.22	$C_{16}H_{16}ClN_3O_2$	60.55	5.17	13.47	–	51.3
15f	75	205–207	59.05	4.66	12.15	$C_{17}H_{16}ClN_3O_3$	59.00	4.59	11.89	56.9	77.6
15g	79	198–200	57.64	4.84	14.40	$C_{14}H_{14}ClN_3O_2$	57.49	4.75	14.21	61.2	66.1
16a	76	187–189	55.75	4.68	11.47	$C_{17}H_{17}Cl_2N_3O_2$	55.64	4.60	11.27	81.0	76.0
16b	83	216–218	53.28	4.73	10.96	$C_{17}H_{17}Cl_2N_3O_3$	53.12	4.80	10.71	94.8	70.7
16d	83	168–170	57.16	4.50	12.50	$C_{16}H_{15}Cl_2N_3O$	57.25	4.59	12.29	71.1	87.2
17	62	152–154	64.11	6.92	10.68	$C_{14}H_{18}N_2O_3$	64.01	6.83	10.49		
18	65	161–163	50.77	4.87	8.46	$C_{14}H_{16}Cl_2N_2O_3$	50.67	4.79	8.28		
19	62	133–135	56.85	6.13	14.21	$C_{14}H_{18}ClN_3O_2$	56.99	6.20	14.45		
20	63	136–138	50.92	5.19	12.73	$C_{14}H_{17}Cl_2N_3O_2$	50.79	5.11	12.62		

[a] Compared to heteroauxin, the activity of which was taken as 100%.

5-(1-Phenoxyethyl)-1,3,4-oxadiazole-2(3*H*)-thione (5). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.72 d (3H, CH_3, *J* = 6.6), 5.52 q (1H, OCH, *J* = 6.6), 6.94–7.33 m (5H, C_6H_5), 14.30 s (1H, NH).

5-[1-(3,4-Dichlorophenoxy)ethyl]-1,3,4-oxadiazole-2(3*H*)-thione (6). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.75 d (3H, CH_3, *J* = 6.5), 5.56 q (1H, OCH, *J* = 6.5), 7.21–7.39 m (3H, C_6H_3), 14.36 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.5, 68.5, 117.7, 124.3, 126.7, 127.5, 129.3, 151.0, 160.7, 177.9.

5-[1-(4-Chlorophenylamino)ethyl]-1,3,4-oxadiazole-2(3*H*)-thione (7). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.58 d (3H, CH_3, *J* = 6.8), 4.62 d. q (1H, NCH, J_1 = 6.8, J_2 = 8.2), 6.22 d (1H, NHCH, *J* = 8.2), 6.60–7.05 m (4H, C_6H_4), 11.10 br. s (1H, NH).

5-[1-(3,4-Dichlorophenylamino)ethyl]-1,3,4-oxadiazole-2(3*H*)-thione (8). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.60 d (3H, CH_3, *J* = 6.8), 4.63 d. q (1H, NCH, J_1 = 6.8, J_2 = 8.2), 6.45 d (1H, NHCH, *J* = 8.2), 6.58–7.15 m (3H, C_6H_3), 7.20–8.50 br. s (2H, 2NH). ^{13}C NMR spectrum, δ_C, ppm: 18.1, 44.3, 112.4, 113.8, 118.5, 129.9, 131.6, 146.3, 163.5, 177.9.

General procedure for the synthesis of compounds 9a, 10c, 10d, 11c, 11d, 12c, 12d. To 10 mmol of the potassium salt of compound **5–8** was added 10 mL of DMF, and then 11 mmol of the corresponding alkyl halide was slowly added with stirring at 0°C. The resulting mixture was stirred for 30 min at 0°C, then at room temperature for 3 h. The next day the reaction mixture

was stirred at 65–70°C for 12 h, and then evaporated. The precipitate was treated with water, filtered off and dried.

3-[5-(1-Phenoxyethyl)-1,3,4-oxadiazol-2-ylsulfanyl]pentane-2,4-dione (9a). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.77 d (3H, CH_3, *J* = 6.6), 2.39 s (6H, $2CH_3$), 5.66 q (1H, OCH, *J* = 6.6), 6.88–7.28 m (5H, C_6H_5), 10.40 s (0.6H, OH-enol).

Methyl 2-{5-[1-(3,4-dichlorophenoxy)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}acetate (10c). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 d (3H, CH_3, *J* = 6.6), 3.74 s (3H, OCH_3), 4.12 s (2H, SCH_2), 5.72 q (1H, OCH, *J* = 6.6), 7.21–7.40 m (3H, C_6H_3). ^{13}C NMR spectrum, δ_C, ppm: 18.0, 33.3, 52.2, 68.4, 117.6, 124.2, 126.6, 127.4, 128.3, 129.3, 151.0, 163.5, 165.3, 166.9.

2-{5-[1-(3,4-Dichlorophenoxy)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}acetamide (10d). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.79 d (3H, CH_3, *J* = 6.6), 3.99 s (2H, SCH_2), 5.69 q (1H, OCH, *J* = 6.6), 7.10 br. s and 7.57 br. s (2H, NH_2), 7.20–7.38 m (3H, C_6H_3). ^{13}C NMR spectrum, δ_C, ppm: 18.1, 35.9, 68.4, 117.7, 124.3, 126.6, 127.4, 128.3, 129.3, 151.1, 164.5, 165.0, 167.0.

Methyl 2-{5-[1-(4-chlorophenylamino)ethyl]1,3,4-oxadiazol-2-ylsulfanyl}acetate (11c). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.61 d (3H, CH_3, *J* = 6.8), 3.70 s (3H, OCH_3), 4.07 s (2H, SCH_2), 4.77 d. q (1H, NCH, J_1 = 6.8, J_2 = 8.2), 6.18 d (1H, NHCH, *J* = 8.2), 6.60–7.04 m (4H, C_6H_4).

2-{5-[1-(4-Chlorophenylamino)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}acetamide (11d). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.61 d (3H, CH_3, *J* = 6.8), 3.97 s (2H, SCH_2), 4.77 d. q (1H, NCH, J_1 = 6.8, J_2 = 8.2), 6.20 d (1H, NHCH, *J* = 8.2), 6.60–7.04 m (4H, C_6H_4), 7.08 br. s and 7.57 br. s (2H, NH_2).

1,3,4-Methyl 2-{5-[1-(3,4-dichlorophenylamino)ethyl]-oxadiazol-2-ylsulfanyl}acetate (12c). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.61 d (3H, CH_3, *J* = 6.9), 3.71 s (3H, OCH_3), 4.08 s (2H, SCH_2), 4.79 d. q (1H, NCH, J_1 = 6.9, J_2 = 8.1), 6.46 d (1H, NHCH, *J* = 8.1), 6.57–7.16 m (3H, C_6H_3). ^{13}C NMR spectrum, δ_C, ppm: 18.5, 33.3, 44.2, 52.1, 112.2, 113.7, 118.3, 129.8, 131.5, 146.4, 162.3, 167.0, 168.1.

2-{5-[1-(3,4-Dichlorophenylamino)ethyl]1,3,4-oxadiazol-2-ylsulfanyl}acetamide (12d). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.61 d (3H, CH_3, *J* = 6.9), 3.96 s (2H, SCH_2), 4.79 d. q (1H, NCH, J_1 = 6.9, J_2 = 8.2), 6.47 d (1H, NHCH, *J* = 8.2), 6.56–7.17 m (3H, C_6H_3), 7.08 br. s and 7.56 br. s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 18.6, 35.8, 44.2, 112.3, 113.7, 118.3, 129.9, 131.5, 146.5, 163.4, 167.2, 167.7.

General procedure for the synthesis of compounds 9b, 10b, 11b, 12b. To a mixture of 10 mmol of the potassium salt of compound **5–8** and 10 mL of DMF was added 10 mmol of (2-bromoethoxy)benzene. The reaction mixture was stirred at 70–75°C for 8–10 h. The solution was evaporated; the precipitate was washed with water, filtered off and dried.

2-(1-Phenoxyethyl)-5-[(2-phenoxyethyl)sulfanyl]-1,3,4-oxadiazole (9b). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.78 d (3H, CH_3, *J* = 6.6), 3.63 t (2H, SCH_2, *J* = 6.8), 4.52 t (2H, OCH_2, *J* = 6.8), 5.65 q (1H, OCH, *J* = 6.6), 6.82–7.32 m (10H, C_6H_5).

***N*-(1-{5-[(2-Phenoxyethyl)sulfanyl]1,3,4-oxadiazol-2-yl}ethyl)-4-chloroaniline (11b).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.62 d (3H, CH_3, *J* = 6.8), 3.58 t (2H, SCH_2, *J* = 6.8), 4.28 t (2H, OCH_2, *J* = 6.8), 4.78 d. q (1H, NCH, J_1 = 6.8, J_2 = 8.2), 6.17 d (1H, NHCH, *J* = 8.2), 6.60–7.32 m (9H, C_6H_5 + C_6H_4).

General procedure for the synthesis of compounds 13–16. To 10 mmol of compound **1–4** were added 15 mL of water, 15 mL of 36% hydrochloric acid, and 12 mmol of the corresponding aldehyde. The mixture was stirred at room temperature for 6 h and left overnight. The next day, 10–15 mL of water was added; the precipitate was filtered off and dried.

***N′*-(4-Methoxybenzylidene)-2-phenoxypropanehydrazide (13a).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.58 d (1.2H, CH_3, *J* = 6.6), 1.60 d (1.8H, CH_3, *J* = 6.6), 4.71 q (0.4H, OCH, *J* = 6.6), 5.56 q (0.6H, OCH, *J* = 6.6), 6.76–7.63 m (9H, C_6H_5 + C_6H_4), 7.94 s (0.6H, CH), 8.27 s (0.4H, CH), 11.08 s (0.4H, NHCO), 11.31 s (0.6H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.5, 18.3, 54.6, 69.1, 73.4, 113.5, 113.6, 114.2, 115.0, 119.9, 120.7, 126.5, 126.7, 127.9, 128.3, 128.7, 128.9, 143.4, 147.5, 157.0, 157.5, 160.4, 166.7, 171.3.

***N′*-(4-Hydroxy-3-methoxybenzylidene)-2-phenoxypropanehydrazide (13b).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.58 d (1.5H, CH_3, *J* = 6.6), 1.60 d (1.5H, CH_3, *J* = 6.6), 3.83 s (1.5H, OCH_3), 3.85 s (1.5H, OCH_3), 4.72 q (0.5H, OCH, *J* = 6.6), 5.57 q (0.5H, OCH, *J* = 6.6), 6.75–7.28 m (8H, C_6H_5 + C_6H_3), 7.89 s (0.5H, CH), 8.19 s (0.5H, CH), 8.95 s (0.5H, OH), 8.96 s (0.5H, OH), 11.05 s (0.5H, NHCO), 11.24 s (0.5H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.4, 18.4, 55.26, 55.28, 69.1, 73.3, 108.7, 109.3, 114.2,114.9, 115.0, 115.1, 120.0, 120.8,

121.1, 122.0, 125.2, 125.3, 128.7, 128.9, 144.2, 147.6, 147.7, 148.5, 148.8, 149.0, 157.1, 157.5, 166.8, 171.2.

***N′*-(3-Nitrobenzylidene)-2-phenoxypropanehydrazide (13c).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.60 d (1.5H, CH_3, *J* = 6.6), 1.62 d (1.5H, CH_3, *J* = 6.6), 4.77 q (0.5H, OCH, *J* = 6.6), 5.60 q (0.5H, OCH, *J* = 6.6), 6.78–8.47 m (9H, C_6H_5 + C_6H_4), 8.13 s (0.5H, CH), 8.49 s (0.5H, CH), 11.54 s (0.5H, NHCO), 11.71 s (0.5H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.4, 18.2, 69.2, 73.5, 114.3, 115.1, 120.1, 120.9, 121.2, 123.4, 123.5, 128.7, 128.9, 129.4, 129.5, 131.9, 132.4, 135.8, 136.2, 141.1, 145.1, 148.0, 148.1, 157.0, 157.4, 167.4, 171.7.

2-(3,4-Dichlorophenoxy)-*N′*-(4-methoxybenzylidene)propanehydrazide (14a). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65 d (0.9H, CH_3, *J* = 6.6), 1.69 d (2.1H, CH_3, *J* = 6.6), 3.80 s (3H, OCH_3), 4.80 q (0.3H, *J* = 6.6), 5.58 q (0.7H, OCH, *J* = 6.6), 6.78–7.65 m (7H, C_6H_3 + C_6H_4), 7.95 s (0.7H, CH=N), 8.25 s (0.3H, CH=N), 11.27 s (0.3H, NHCO), 11.42 s (0.7H, NHCO).

***N′*-(4-Hydroxy-3-methoxybenzylidene)-2-(3,4-dichlorophenoxy)propanehydrazide (14b).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.63 d (1.2H, CH_3, *J* = 6.6), 1.68 d (1.8H, CH_3, *J* = 6.6), 3.82 s (1.8H, OCH_3), 3.85 s (1.2H, OCH_3), 4.85 q (0.4H, OCH, *J* = 6.6), 5.58 q (0.6H, OCH, *J* = 6.6), 6.75–7.40 m (6H, $2C_6H_3$), 7.90 s (0.6H, CH=N), 8.20 s (0.4H, CH=N), 9.00 s (1H, OH), 11.27 s (0.4H, NHCO), 11.42 s (0.6H, NHCO).

2-(3,4-Dichlorophenoxy)-*N′*-(3-nitrobenzylidene)propanehydrazide (14c). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65 d (1.2H, CH_3, *J* = 6.6), 1.70 d (1.8H, CH_3, *J* = 6.6), 4.80 q (0.4H, OCH, *J* = 6.6), 5.62 q (0.6H, OCH, *J* = 6.6), 6.80–8.70 m (8H, C_6H_3, C_6H_4, CH=N), 11.58 s (0.4H, NHCO), 11.80 s (0.6H, NHCO).

***N′*-Benzylidene-2-(4-chlorophenylamino)propanehydrazide (15d).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.43 d (3H, CH_3, *J* = 6.8), 3.90 m (0.3H, NCH), 4.88 m (0.7H, NCH), 5.52 d (0.7H, NHCH, *J* = 8.2), 5.73 d (0.3H, NHCH, *J* = 8.2), 6.55–7.70 m (9H, C_6H_5 + C_6H_4), 8.01 s (0.7H, CH=N), 8.28 s (0.3H, CH=N), 11.15 s (0.3H, NHCO), 11.36 (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.7, 18.5, 47.9, 51.9, 113.7, 113.9, 120.1, 120.5, 126.48, 126.51, 126.8, 128.0, 128.1, 128.2, 129.1, 129.2, 134.1, 134.2, 143.5, 146.0, 146.1, 147.0, 169.8, 174.6.

***N′*-(4-Hydroxybenzylidene)-2-(4-chlorophenylamino)propanehydrazide (15e).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.41 d (3H, CH_3, *J* = 6.8), 3.89 m (0.4H, NCH), 4.86 m (0.6H, NCH), 5.50 br. s (1H, NHCH), 6.55–7.52 m (8H, C_6H_4), 7.90 s (0.6H, CH=N), 8.24 s (0.4H, CH=N), 9.44 br. s (1H, OH), 10.91 s (0.4H, NHCO), 11.09 s (0.6H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.6, 18.5, 47.8, 51.8, 113.7, 113.9, 115.25, 115.31, 120.0, 120.4, 124.9, 128.0, 128.1, 128.13, 128.4, 144.0, 146.0, 146.1, 147.4, 159.1, 159.3, 169.3, 174.1.

***N′*-(Benzo[*d*][1,3]dioxol-5-ylmethylidene)-2-(4-chlorophenylamino)propanehydrazide (15f).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.41 d (3H, CH_3, *J* = 6.8), 3.90 m (0.3H, NCH), 4.86 m (0.7H, NCH), 5.50 br. s (0.7H, NHCH), 5.71 br. s (0.3H, NHCH), 6.01 s (2H, OCH_2O), 6.57–7.28 m (7H, C_6H_3 + C_6H_4), 7.91 s (0.7H, CH=N), 8.28 s (0.3H, CH=N), 11.05 s (0.3H, NHCO), 11.22 s (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.6, 18.5, 47.8, 51.9, 100.9, 104.8, 105.1, 107.6, 107.7, 113.7, 113.9, 120.0, 120.4, 122.6, 122.8, 128.10, 128.15, 128.5, 128.6, 143.3, 145.9, 146.1, 146.7, 147.7, 147.8, 148.6, 148.7, 169.6, 174.4.

***N′*-(Furan-2-ylmethylidene)-2-(4-chlorophenylamino)propanehydrazide (15g).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.40 d. d and 1.41 d. d (3H, CH_3, *J* = 6.8), 3.89 m (0.3H, NCH), 4.85 m (0.7H, NCH), 5.50 d (0.7H, NHCH, *J* = 8.2), 5.72 d (0.3H, NHCH, *J* = 8.2), 6.47–7.60 m (7H, 3H-furan + C_6H_4), 7.90 s (0.7H, CH=N), 8.26 s (0.3H, CH=N), 11.15 s (0.3H, NHCO), 11.30 s (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.6, 18.4, 47.7, 51.9, 111.27, 111.34, 111.50, 111.53, 113.7, 113.8, 120.0, 120.4, 128.07, 128.10, 133.3, 137.1, 143.5, 143.7, 145.9, 146.0, 149.4, 149.6, 169.8, 174.5.

2-(3,4-Dichlorophenylamino)-*N′*-(4-methoxybenzylidene)propanehydrazide (16a). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 d (0.9H, CH_3, *J* = 6.8), 1.43 d (2.1H, CH_3, *J* = 6.8), 3.82 s (0.9H, OCH_3), 3.83 s (2.1H, OCH_3), 3.92 m (0.3H, NCH), 4.86 m (0.7H, NCH), 5.91 br. s (0.7H, NHCH), 6.05 br. s (0.3H, NHCH), 6.50–7.65 m (7H, C_6H_3 + C_6H_4), 7.95 s (0.7H, CH=N), 8.20 s (0.3H, CH=N), 11.06 s (0.3H, NHCO), 11.22 s (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.4, 18.3, 47.6, 51.4, 54.59, 54.61, 112.1, 112.4, 113.5, 113.6, 117.4, 117.5, 126.6, 126.7, 127.9, 128.2, 129.7, 129.8, 131.4, 143.4, 146.8, 147.3, 160.4, 160.5, 168.9, 173.8.

***N′*-(4-Hydroxy-3-methoxybenzylidene)2-(3,4-dichlorophenylamino)propanehydrazide (16b).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 d (0.9H, CH_3, *J* = 6.8), 1.43 d (2.1H, CH_3, *J* = 6.8), 3.86 s (0.9H, OCH_3), 3.87 s (2.1H, OCH_3), 3.91 q (0.3H, *J* = 6.8, NCH), 4.87 q (0.7H, *J* = 6.8, NCH), 5.98 br. s (1H, NHCH), 6.50–7.32 m (6H, C_6H_3 + C_6H_3), 7.88 s (0.7H, CH=N), 8.12 s (0.3H,

CH=N), 8.93 br. s (1H, OH), 11.01 s (0.3H, NHCO), 11.15 s (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.4, 18.4, 47.6, 51.5, 55.3, 108.8, 109.5, 112.3, 112.5, 113.5, 113.7, 114.9, 115.2, 117.5, 117.9, 121.1, 122.1, 125.3, 129.8, 129.9, 131.5, 144.3, 147.2, 147.4, 147.6, 147.7, 147.8, 148.8, 149.0, 169.1, 173.8.

***N′*-Benzylidene-2-(3,4-dichlorophenylamino)propanehydrazide (16d).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 d (0.9H, CH_3, *J* = 6.8), 1.43 d (2.1H, CH_3, *J* = 6.8), 3.92 q (0.3H, NCH, *J* = 6.8), 4.88 q (0.7H, NCH, *J* = 6.8), 5.93 br. s (0.7H, NHCH), 6.07 br. s (0.3H, NHCH), 6.50–7.98 m (8H, C_6H_5 + C_6H_3), 7.98 s (0.7H, CH=N), 8.26 s (0.3H, CH=N), 11.21 s (0.3H, NHCO), 11.38 s (0.7H, NHCO). ^{13}C NMR spectrum, δ_C, ppm: 17.5, 18.3, 47.7, 51.5, 112.1, 112.4, 113.6, 113.7, 117.5, 126.5, 126.8, 127.6, 128.0, 128.1, 128.4, 129.08, 129.12, 129.2, 129.7, 129.8, 131.4,131.7, 134.0,134.2, 143.6, 147.0, 147.2, 147.3, 169.3, 174.1.

General procedure for the synthesis of compounds 17–20. 10 mmol of pentane-2,4-dione and 3 drops of DMF were added to a solution of 10 mmol of hydrazide **1–4** in 10 mL of acetic acid at 0°C. The reaction mixture was stirred for 6 h at 80°C, and then left overnight. The next day, 20–30 mL of ice water was added. The formed precipitate was filtered off, washed with water, and dried.

***N′*-(4-Oxopentan-2-ylidene)-2-phenoxypropanehydrazide (17).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50 d (3H, CH_3, *J* = 6.6), 1.80 s (3H, N=CCH_3), 2.08 s (3H, $COCH_3$), 2.80 d and 2.86 d (2H, CH_2, *J* = 18.4), 5.38 q (1H, OCH, *J* = 6.6), 6.22 s (1H, NHCO), 6.73–7.28 m (5H, C_6H_5).

2-(3,4-Dichlorophenoxy)-*N′*-(4-oxopentan-2-ylidene)propanehydrazide (18). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.47 d (3H, CH_3, *J* = 6.6), 1.79 s (3H, N=CCH_3), 2.08 s (3H, $COCH_3$), 2.80 d and 2.86 d (2H, CH_2, *J* = 18.4), 5.35 q (1H, OCH, *J* = 6.6), 6.20 s (1H, NHCO), 6.62–7.21 m (3H, C_6H_3).

***N′*-(4-Oxopentan-2-ylidene)-2-(4-chlorophenylamino)propanehydrazide (19).** ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.32 d (3H, OCH, *J* = 6.7), 1.75 s (3H, N=CCH_3), 2.06 s (3H, $COCH_3$), 2.79 d and 2.86 d (2H, CH_2, *J* = 18.5), 4.65 m (1H, NCH), 5.42 br. s (1H, NH), 5.92 br. s (1H, NHCO), 6.48–7.05 m (4H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 15.7, 17.1, 26.1, 49.2, 51.5, 90.4, 113.5, 113.7, 119.9, 128.0, 146.0, 153.6, 170.8.

2-(3,4-Dichlorophenylamino)-*N′*-(4-oxopentan-2-ylidene)propanehydrazide (20). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 d (1.5H, CH_3, *J* = 6.7), 1.34 s (1.5H, CH_3), 1.76 s (1.5H, N=CCH_3), 1.78 s (1.5H, N=CCH_3), 2.07 s (3H, $COCH_3$), 2.80 d and 2.88 d (2H, CH_2, *J* = 18.4), 4.63 d. q (0.5H, NCH, J_1 = 8.7, J_2 = 6.7), 4.67 d. q (0.5H, NCH, J_1 = 8.7, J_2 = 6.7), 5.84 d (1H, NHCH, *J* = 8.7), 5.95 s (0.5H, NHCO), 6.00 s (0.5H, NHCO), 6.47–7.15 m (3H, C_6H_3). ^{13}C NMR spectrum, δ_C, ppm: 15.7, 16.9, 17.5, 25.7, 26.0, 49.1, 49.3, 51.6, 90.5, 112.1, 113.4, 113.7, 129.66, 129.70, 131.36, 131.4, 147.2, 147.3, 153.8, 153.9, 170.4, 170.8.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: Novaya Volna, 2019.
2. Masunari, A. and Tavaris, L.C., *Bioorg. Med. Chem*., 2007, vol. 15, p. 4229. https://doi.org/10.1016/j.bmc.2007.03.068
3. Loncle, C., Brunel, J., Vidal, N., Dherbomez, M., and Letourneux, Y., *Eur. J. Med. Chem.*, 2004, vol. 39, p. 1067. https://doi.org/10.1016/j.ejmech.2004.07.005
4. Küçükgüzel, S.G., Mazi, A., Sahin, F., Öztürk, S., and Stables, J.P., *Eur. J. Med. Chem*., 2003, vol. 38, p. 1005. https://doi.org/10.1016/j.ejmech.2003.08.004
5. Vicini, P., Zani, F., Cozzini, P., and Doytchinova, I., *Eur. J. Med. Chem*., 2002, vol. 37, p. 553. https://doi.org/10.1016/S0223-5234(02)01378-8
6. Bijev, A., *Lett. Drug Des. Discovery*, 2006, vol. 3, p. 506.
7. Todeschini, A.R., Miranda, A.L., Silva, C.M., Parrini, S.C., and Barreiro, E.J., *Eur. J. Med. Chem*., 1998, vol. 33, p. 189. https://doi.org/10.1016/S0223-5234(98)80008-1
8. Gemma, S., Kukreja, G., Fattorusso, C., Persico, M., Romano, M., Altarelli, M., Savini, L., Campiani, G., Fattorusso, E., and Basilico, N., *Bioorg. Med. Chem. Lett*., 2006, vol. 16, p. 5384. https://doi.org/10.1016/j.bmcl.2006.07.060
9. Gürsoy, E., and Ulusoy-Güzeldemirci, N., *Eur. J. Med. Chem*., 2007, vol. 42, p. 320. https://doi.org/10.1016/j.ejmech.2006.10.012
10. Ragavendran, J., Sriram, D., Patel, S., Reddy, I., Bharathwajan, N., Stables, J., and Yogeeswari, P., *Eur. J. Med. Chem*., 2007, vol. 42, p. 146. https://doi.org/10.1016/j.ejmech.2006.08.010
11. Ergenç, N., Günay, N.S., and Demirdamar, R., *Eur. J. Med. Chem.*, 1998, vol. 33, p. 143.

https://doi.org/10.1016/S0223-5234(98)80039-1
12. http://www.alanwood.net/pesticides/class_pesticides.html.
13. Gomktsyan, T.A., Karapetyan, A.V., Abrahamyan, L.G., and Yengoyan, A.P., *Khim. Zh. Arm*., 2012, vol. 65, no. 3, p. 342.
14. Yengoyan, A.P., Gomktsyan, T.A., Karapetyan, A.V., and Shainova, R.S., *Khim. Zh. Arm*., 2017, vol. 70, nos. 1–2, p. 199.
15. Pivazyan, V.A., Ghazaryan, E.A., Azaryan, Zh.A., and Yengoyan, A.P., *Russ. J. Gen. Chem.*, 2019, vol. 89, no. 10, p. 2010. https://doi.org/10.1134/S1070363219100050
16. Shainova, R.S., Gomktsyan, T.A., Karapetyan, A.V., and Yengoyan, A.P., *J. Chem. Res.*, 2019, vol. 43, nos. 9–10, p. 352. https://doi.org/10.1177/1747519819866402