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Synthesis and bioactivity of benzohydrazide derivatives

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ABSTRACT

N'-[4-(Hydroxyimino)-cyclohexa-2,5-dien-1-ylidene]-benzohydrazides have been synthesized by reaction of 4-(hydroxyimino)-cyclohexa-2,5-dien-1-one with different benzohydrazides in one stage. N'-(4-[(Aroyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-benzohydrazides were obtained in reaction of 4-[(aroyloxy)imino]cyclohexa-2,5-dien-1-ones with corresponding benzohydrazides in one step too. Biological activities of the synthesized compounds were studied. N'-[4-{[(4-nitrobenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene]benzo-hydrazide showed high insecticidal activity against house fly and rice weevil. 3,4-Dichloro-*N*'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide and N'-{4-[(benzoyloxy)imino]-cyclohexa-2,5-dien-1-ylidene}-2-bromobenzohydrazide showed excellent anti-nematode activity: decrease in gall formation on the cucumber roots was 93 and 91%, respectively.

Keywords: *benzohydrazide; 4-(hydroxyimino)-cyclohexa-2,5-dien-1-one; N'-[4-(Hydroxyimino)-cyclohexa-2,5-dien-1-ylidene]-benzohydrazides; 4-[(aroyloxy)imino]cyclohexa-2,5-dien-1-one; insecticide; nematicide; fungicide.*

1. INTRODUCTION

Benzoyl hydrazide, benzoyl hydrazones, and their derivatives are intensively studied in some research fields because of their high bioactivity [1, 2], chelating ability [3], and high reaction ability [3–5]. They are resource-rich compounds in organic chemistry and show high physiologic activity [3–5]. Some benzohydrazide derivatives show activity against prostate cancer [4]. Hydrazones have a wide field of biological properties including antibacterial, anti-fungal, anti-tubercular [1], antioxidant [2, 6–8], photoprotective [7, 9], anticancer [7, 9, 10], and anti-inflammatory activity [1, 11].

3,4,5-Trihydroxybenzohydrazones showed excellent results as urease inhibitors [5]. Benzofuranhydrazones showed a different extent antioxidant activity in ORAC, DPPH, and FRAP assays, photoprotective properties with satisfactory in vitro SPF, and antiproliferative effects on Colo-38 melanoma and erythroleukemia K562 human cells [6]. Some benzoyl hydrazone derivatives exhibited good results against *E.histolytica* [12]. Naphthyl-N-acylhydrazone derivatives were characterized as p38α MAPK inhibitors and showed in vivo anti-inflammatory action using animal models [9]. 4-Hydroxybenzhydrazide derivatives have high bioactivity and can be used as inhibitors of laccase from *Trametes versicolor*. [13].

Hydrazones and acid hydrazide are used in biological as well as analytical chemistry [14, 15]. 2-Hydroxy-N′-((thiophene-2-yl)methylene)-benzohydrazide was found to be a good corrosion inhibitor [3].

In light of the significance of hydrazine for pharmaceuticals and agrochemicals, to find new ways in synthesis of hydrazine derivatives and novel types of hydrazine structures is a hot topic [1, 4, 6, 7, 11, 14].

In the synthesis of new bioactive compounds, benzohydrazide can be regarded as a potential pharmacophore or as a lead compound. Some new bioactive benzohydrazide derivatives were synthesized in the reaction of benzohydrazide with 2-carbaldehyde [4]. 3,4,5-Trihydroxybenzohydrazones were obtained from methyl 3,4,5-trihydroxybenzoate by refluxing with hydrazine hydrate [5]. 2-Hydroxy-N′-((thiophene-2-yl)methylene)-benzohydrazide was synthesized by ultrasonication [3]. The benzoyl hydrazone derivatives were obtained by the combination of two pharmacophores, the N-dimethylaminoethoxy tail and different substituted aldehydes [12]. New 4-(4-hydroxyphenyl)semicarbazide derivatives were obtained in the reaction of 1-(4-hydroxyphenyl)ureas with hydrazine hydrate [16]. N-acylhydrazines can be obtained by a multi-step procedure using catalysts [17]. However, these methods require multi-step reactions, long reaction time, and sometimes difficult post-processing. Multi-component reactions play an important role in synthetic organic chemistry because they effectively combine three and more reactants in a one-stage synthesis without separating any intermediates [18, 19].

Benzoylhydrazones can be synthesized in one stage on the basis of a quinoid system. 1,4-Benzoquinone monoimines [20, 21], their reduced forms and O-ethers of quinone oximes [22] are good synthons for the synthesis of new biologically active derivatives [23–26].

It is noted that some hydrazones are used as herbicides, insecticides, nematicides, rodenticides, and plant growth regulators [27–29]. But there are not many publications on this subject. Therefore, the purpose of this work is to synthesize new aroylhydrazones from 4-(hydroxyimino)cyclohexa-2,5-dien-1-one in one stage and to study the insecticidal, anti-nematode, and fungicidal activities of the result products.

2. MATERIALS AND METHODS

2.1. General experimental details.

The ^{1}H NMR spectra were measured on a Varian VXR-300 spectrometer (300 MHz) using tetramethylsilane as internal standard and aceton-d6 as a solvent. The IR spectra were recorded in KBr on a UR-20 spectrometer. The purity of the initial compounds and reaction products was tested by TLC on Silufol UV-254 plates; samples were applied from solutions in acetone, and ethanol–chloroform (1:10) were used as eluents; spots were visualized under UV light.

The melting points of compounds were determined in open capillary tubes and were uncorrected.

N'-[4-(Hydroxyimino)-cyclohexa-2,5-dien-1-ylidene]-benzohydrazides 3a–d (general procedure). 4-(Hydroxyimino)-cyclohexa-2,5-dien-1-one **1**, 0.05 mol, was dissolved in 150 mL of methanol. 600 mL of water and equimolar quantity of corresponding muriatic benzohydrazide **2**, 0.05 mol, were added. The reaction mixture was stirred during 1.5 h, the separated precipitate was filtered off and dried.

N'-[4-(Hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide (3a). Yield 72 %; m.p. 194–195ºC. NMR ^{1}H (δ, ppm): 7.15 (d, 2H, H^{2,6}, *J* 9 Hz), 7.22 (d, 2H, H^{3,5}, *J* 9 Hz), 7.43–7.99 (m, 5H, Ph), 9.89 (s, 1H, NH), 10.76 (s, 1H, OH). Anal. Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; N, 17.42%. Found: C, 63.56; N, 17.78%.

4-Chloro-N'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide (3b). Yield 61 %, m.p. 152–153ºC. NMR ^{1}H (δ, ppm): 7.16 (d, 2H, H^{2,6}, *J* 9 Hz), 7.21 (d, 2H, H^{3,5}, *J* 9 Hz), 7.62 (d, 2H, 4-ClC_6H_4, H$^{3',5'}$, *J* 9 Hz), 8.04 (d, 2H, 4-ClC_6H_4, H$^{2',6'}$, *J* 9 Hz), 9.78 (s, 1H, NH), 10.72 (s, 1H, OH). Anal. Calcd. for $C_{13}H_{10}ClN_3O_2$: C, 56.64; Cl, 12.86; N, 15.24%. Found: C, 57.02; Cl, 13.06; N, 14.61%.

3,4-Dichloro-N'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide (3c). Yield 69 %, m.p. 191–192ºC. NMR ^{1}H (δ, ppm): 7.14 (d, 2H, H^{2,6}, *J* 9 Hz), 7.23 (d, 2H, H^{3,5}, *J* 9 Hz), 7.80 (d, 1H, 3,4-diClC_6H_3, H$^{2'}$, *J* 2.4 Hz), 7.83 (d, 1H, 3,4-diClC_6H_3, H$^{5'}$, *J* 9 Hz), 8.08 (k, 1H, 3,4-diClC_6H_3, H$^{5'}$, *J* 2.4, 9 Hz), 9.69 (s, 1H, NH), 10.85 (s, 1H, OH). Anal. Calcd. for $C_{13}H_9Cl_2N_3O_2$: C, 50.35; Cl, 22.86; N, 13.55%. Found: C, 50.88; Cl, 22.54; N, 13.78%.

2-Bromo-N'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide (3d). Yield 82 %, m.p. 194–195ºC. NMR ^{1}H (δ, ppm): 7.15 (d, 2H, H^{2,6}, *J* 9 Hz), 7.21 (d, 2H, H^{3,5}, *J* 9 Hz), 7.38–7.98 (m, 4H, 2-BrC_6H_4), 9.62 (s, 1H, NH), 10.01 (s, 1H, OH). Anal. Calcd. for $C_{13}H_{10}BrN_3O_2$: C, 48.77; Br, 24.96; N, 13.13%. Found: C, 49.05; Br, 25.15; N, 12.89%.

N'-(4-[(Aroyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-benzohydrazides 5a–h, (general procedure). 4-[(Aroyloxy)-imino]cyclohexa-2,5-dien-1-one **4**, 0.01 mol, was dissolved in 20 mL of ethanol. 60 mL of water and equimolar quantity of corresponding benzohydrazide **2**, 0.01 mol, were added. The reaction mixture was stirred during 2 h, the separated precipitate was filtered off, dried, and recrystallized from ethanol.

N'-(4-[(benzoyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-2-chlorobenzohydrazide (***5a).*** Yield 85 %; m.p. 210ºC (decomp.). NMR ^{1}H (δ, ppm): 7.11 (d, 2H, H^{2,6}, *J* 9 Hz), 7.21 (d, 2H, H^{3,5}, *J* 9 Hz), 7.67–8.13 (m, 5H, Ph), 7.52–8.91 (m, 4H, 2-ClC_6H_4), 10.44 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{14}ClN_3O_3$: C, 63.25; Cl, 9.33; N, 11.06%. Found: C, 62.98; Cl, 9.58; N, 11.25%.

N'-(4-[(benzoyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-2-hydroxybenzohydrazide (***5b).*** Yield 69 %; m.p. 215ºC (decomp.). NMR ^{1}H (δ, ppm): 7.10 (d, 2H, H^{2,6}, *J* 9 Hz), 7.22 (d, 2H, H^{3,5}, *J* 9 Hz), 7.67–8.13 (m, 5H, Ph), 7.04–7.51 (m, 4H, 2-OHC_6H_4), 8.76 (s, 1H, NH), 10.35 (s, 1H, OH). Anal. Calcd. for $C_{20}H_{15}N_3O_4$: C, 66.48; N, 11.63%. Found: C, 66.27; N, 11.42%.

N'-(4-[(benzoyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-2-bromobenzohydrazide (***5c).*** Yield 81 %; m.p. 195ºC (decomp.). NMR ^{1}H (δ, ppm): 7.11 (d, 2H, H^{2,6}, *J* 9 Hz), 7.20 (d, 2H, H^{3,5}, *J* 9 Hz), 7.66–8.14 (m, 5H, Ph), 7.39–7.97 (m, 4H, 2-BrC_6H_4), 8.34 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{14}BrN_3O_3$: C, 56.62; Br, 18.83; N, 9.90%. Found: C, 56.78; Br, 19.05; N, 9.78%.

N'-(4-{[(4-fluorobenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene)benzohydrazide (***5d).*** Yield 74 %; m.p. 205ºC (decomp.). NMR ^{1}H (δ, ppm): 7.10 (d, 2H, H^{2,6}, *J* 9 Hz), 7.21 (d, 2H, H^{3,5}, *J* 9 Hz), 7.31 (d, 2H, 4-FC_6H_4, H$^{3',5'}$, *J* 9 Hz), 7.45–7.99 (m, 5H, Ph), 8.22 (d, 2H, 4-FC_6H_4, H$^{2',6'}$, *J* 9 Hz), 9.85 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{14}FN_3O_3$: C, 66.11; N, 11.56%. Found: C, 66.26; N, 11.68%.

2-Chloro-N'-(4-[(4-fluorobenzoyloxy)imino]cyclohexa-2,5-dien-1-ylidene)benzohydrazide (***5e).*** Yield 79 %; m.p. 203ºC (decomp.). NMR ^{1}H (δ, ppm): 7.12 (d, 2H, H^{2,6}, *J* 9 Hz), 7.20 (d, 2H, H^{3,5}, *J* 9 Hz), 7.30 (d, 2H, 4-FC_6H_4, H$^{3',5'}$, *J* 9 Hz), 7.52–7.91 (m, 4H, 2-ClC_6H_4), 8.21 (d, 2H, 4-FC_6H_4, H$^{2',6'}$, *J* 9 Hz), 10.44 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{13}ClFN_3O_3$: C, 60.39; N, 10.56%. Found: C, 60.46; N, 10.42%.

N'-(4--{[(4-fluorobenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene)pyridine-4-carbohydrazide (***5f).*** Yield 65 %; m.p. 208ºC (decomp.). NMR ^{1}H (δ, ppm): 7.11 (d, 2H, H^{2,6}, *J* 9 Hz), 7.21 (d, 2H, H^{3,5}, *J* 9 Hz), 7.31 (d, 2H, 4-FC_6H_4, H$^{3',5'}$, *J* 9 Hz), 8.08 (d, 2H, 4-C_6H_4N, H$^{3',5'}$, *J* 6 Hz), 8.23 (d, 2H, 4-FC_6H_4, H$^{2',6'}$, *J* 9 Hz), 8.89 (d, 2H, 4-C_6H_4N, H$^{2',6'}$, *J* 6 Hz), 9.85 (s, 1H, NH). Anal. Calcd. for $C_{19}H_{13}FN_4O_3$: C, 62.64; N, 15.38%. Found: C, 62.49; N, 15.49%.

N'-(4-{[(4-methylbenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene)benzohydrazide (***5g).*** Yield 83 %; m.p. 198ºC (decomp.). NMR ^{1}H (δ, ppm): 7.11 (d, 2H, H^{2,6}, *J* 9 Hz), 7.22 (d, 2H, H^{3,5}, *J* 9 Hz), 7.31 (d, 2H, 4-MeC_6H_4, H$^{3',5'}$, *J* 9 Hz), 7.45–7.99 (m, 5H, Ph), 8.09 (d, 2H, 4-MeC_6H_4, H$^{2',6'}$, *J* 9 Hz), 9.85 (s, 1H, NH). Anal. Calcd. for $C_{21}H_{17}N_3O_3$: C, 70.18; N, 11.69%. Found: C, 70.26; N, 11.55%.

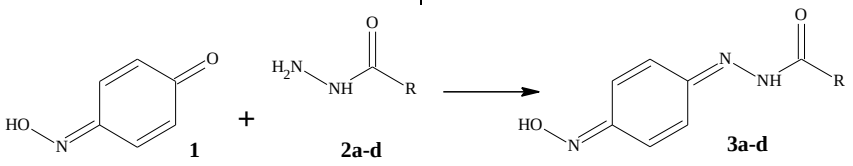
N'-(4-{[(4-nitrobenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene)benzohydrazide (***5h).*** Yield 71 %; m.p. 206ºC (decomp.). NMR ^{1}H (δ, ppm): 7.09 (d, 2H, H^{2,6}, *J* 9 Hz), 7.19 (d, 2H, H^{3,5}, *J* 9 Hz), 8.43 (d, 2H, 4-$NO_2C_6H_4$, H$^{3',5'}$, *J* 9 Hz), 7.44–8.00 (m, 5H, Ph), 8.51 (d, 2H, 4-$NO_2C_6H_4$, H$^{2',6'}$, *J* 9 Hz), 9.79 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{14}N_4O_5$: C, 61.54; N, 14.35%. Found: C, 61.72; N, 14.18%.

2.2. Biological studies.

Biological studies were carried out in the biological testing laboratory of the Kiev Research Institute Sinteko OJSC, Ukraine.

3. RESULTS

N'-[4-(Hydroxyimino)-cyclohexa-2,5-dien-1-ylidene]-benzohydrazides **3a–d** were synthesized in the result of one-stage reaction of 4-(hydroxyimino)-cyclohexa-2,5-dien-1-one **1** with benzohydrazides **2a-d** in aqueous-alcoholic solution (Scheme 1).

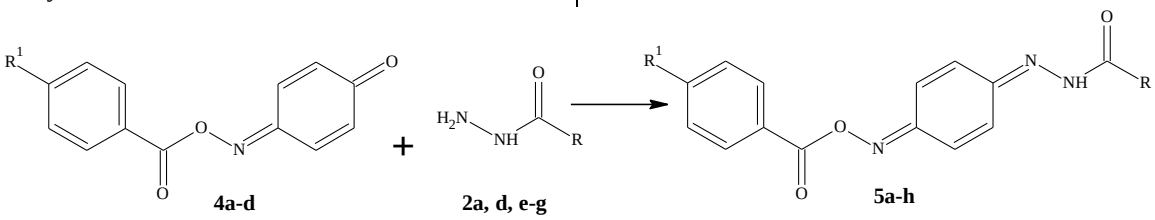


1 **2a-d** **3a-d**

2, 3: R=Ph (a), 4-ClC_6H_4 (b), 3,4-diClC_6H_3 (c), 2-BrC_6H_4 (d)

Scheme 1. Reaction of 4-(hydroxyimino)cyclohexa-2,5-dien-1-one **1** with benzohydrazides **2a-d**

N'-(4-[(Aroyloxy)imino]cyclohexa-2,5-dien-1-ylidene)-benzohydrazides **5a–h** were obtained by reaction of 4-[(aroyloxy)imino]cyclohexa-2,5-dien-1-ones **4a–d** with corresponding benzohydrazides **2a, d, e-g** in aqueous-alcoholic solution (Scheme 2).



4a-d **2a, d, e-g** **5a-h**

2: R=Ph (a), 2-BrC_6H_4 (d), 2-ClC_6H_4 (e), 2-OHC_6H_3 (f), 4-C_5H_4N (g); **4**: R^1=H (a), F (b), Me (c), NO_2 (d);
5: R^1=H, R=2-ClC_6H_4 (a), R^1=H, R=2-OHC_6H_4 (b), R^1=H, R=2-BrC_6H_4 (c), R^1=F, R=Ph (d), R^1=H, R=2-ClC_6H_4 (e), R^1=F, R=4-C_5H_4N (f), R^1=Me, R=Ph (g), R^1=NO_2, R=Ph (h).

Scheme 2. Reaction of 4-[(aroyloxy)imino]cyclohexa-2,5-dien-1-ones **4a–d** with benzohydrazides **2a, d, e-g**

Flies, rice weevils, arachnoidal mites and aphids are all harmful pests. The house flies can spread bacteria, disease-causing organisms, diseases such as food poisoning and dysentery. They eat and oviposit on garbage, manure, and carrion and after contaminate human foods by landing on them. The use of pesticides is usually not the best means of managing fly problems, but chemical control can be a useful component of an integrated fly management program.

The rice weevil is also known as *Sitophilus Oryzae*. Rice weevils are usually found in processing plants and grain storage. They infest wheat, rye, oats, rice, barley, and corn. Sometimes, they are also found in beans, sunflower seeds, and dried corn. Rice weevils are the most destructive pests of stored grain.

Arachnoidal mite is also called *Tetranychus atlanticus McGregor*. It is polyphage, which damages vegetable (in open and protected ground), technical and decorative crops, fruit, berry, and flower. Arachnoidal mite severely damages strawberries. Chemical protection against mites is an important link in the integrated plant protection system, and it still remains effective factor in increasing crop yields.

The black aphid is a main pest of a bean, celery crops, and sugar beet. Large numbers of aphids promote stunting of the plants. The aphid damages to pods and flowers, which may not develop properly.

Gall formation on plant roots is most often due to exposure to nematodes of the genus *Meloydogyne*. Nematodes cause huge damage to agriculture. The biggest losses are among tomatoes, cucumbers and various decorative crops. Sick plants wither in hot weather, have poor harvests, and suffer from secondary diseases.

Thus, it is important to develop new effective insecticides, acaricides, and nematicides.

The test results for the insecticidal and anti-nematode activities of compounds **3a–d**, **5a–h** are presented in Table 1. The concentrations of these compounds were equal 0.5% in tests on flies and bugs, 0.1% in tests on mites, 0.01% in tests on aphids, and 80 mg/kg in tests on nematodes with soil application.

At the use of high concentration, one compound **5h** showed excellent insecticidal activity: the death rate of flies and rice weevils was 100% (see in Table 1). However, with a decrease in the concentration of compounds to 0.05%, insect death did not exceed 42%.

Table 1. The test results for the insecticidal and anti-nematode activities of compounds **3a–d**, **5a–h**

Compound number	The death rate of insects and mites, %				Decrease in gall formation on the cucumber roots, %
	House fly	Rice weevil	Arachnoidal mite	Black beet aphid	
3a	0	19	0	0	62
3b	5	15	10	0	19
3c	5	41	0	0	93
3d	25	53	31	0	89
5a	0	41	7	0	45
5b	35	17	0	0	62
5c	0	0	0	0	91
5d	0	9	27	0	–
5e	5	15	9	0	–

Compound number	The death rate of insects and mites, %				Decrease in gall formation on the cucumber roots, %
	House fly	Rice weevil	Arachnoidal mite	Black beet aphid	
5f	0	0	10	0	72
5g	0	15	27	13	–
5h	100	100	21	35	–

It is worth noting that the death rates of arachnoidal mites and black beet aphids were only 21 and 35%, respectively. Insects and mites are systematically close organisms, both are arthropods, but morphological, physiological and anatomical differences exist between these two groups. So, a good insecticide may not have any action on mites.

Compound **3d** showed significant insecticidal activity against rice weevil. The death rate of test objects was 53%.

Compounds **3c, 3d**, **5c**, and **5f** showed high anti-nematode activity. The decrease in gall formation on the cucumber roots was 93, 89, 91, and 72% under the action of benzohydrazides **3c, 3d**, **5c**, and **5f**, respectively.

Many of the most common plant diseases depend on microorganisms. From two up to thirteen species of microbial phytopathogens parasitize on one type of plant. For example, *Xanthomonas malvacearum* can cause cotton gummosis, *Fusarium moniliforme* can produce pink corn mold and Fusarium stems of rice. The fungus *Penicillium cyclopium* affects grains and cereal products. *Venturia inaequalis* is a fungus, which causes the apple scab disease. *Aspergillus niger* is a haploid filamentous fungus, which causes aspergillosis. Therefore, the study of the fungicidal activity of synthesized compounds is relevant.

New compounds were tested for bactericidal activity against eight objects. We studied the effects of the new compounds on 1 type of bacteria, *Xanthomonas malvacearum*; 4 types of fungi on a solid medium, *Fusarium moniliforme*, *Penicillium cyclopium*, *Venturia Inaequalis*, *Aspergillus niger*; and 3 types of fungi on green plants, late blight of tomatoes (*Phytophthora infestans*), gray rot of beans (*Botrytis cinerea*), and cucumber powdery mildew (*Oidium erysiphoides*).

The test results for the fungicidal activity of the compounds **3a–d**, **5a–h** are shown in Table 2.

Benzohydrazides **3d** and **5g** showed good results. Under the action of these compounds, the growth and development of *Venturia Inaequalis* colonies were inhibited by 52%. Under the action of benzohydrazide **5g**, the growth of *Fusarium moniliforme* was reduced by 56%**.**

Unfortunately, all of the compounds studied showed low herbicidal activity: Inhibition of the fungi growth and development on green plants was low.

Table 2. The test results for the fungicidal activity of compounds **3a–d**, **5a–h**

Compound number	Inhibition of growth and development,% Colonies of bacteria and fungi, concentration of 0.003%					Green plant diseases Concentration of 0.1%		Concentration of 0.05%
	Xanthomonas malvacearum	*Fusarium moniliforme*	*Penicillium cyclopium*	*Venturia Inaegualis*	*Aspergillius niger*	*Phytophthora infestans*	*Botrytis cinerea*	*Oidium erysiphoides*
3a	28	17	13	35	33	30	0	12
3b	14	20	34	57	23	0	0	0
3c	21	24	30	0	11	0	0	0
3d	35	20	34	52	5	0	0	17
5a	7	28	30	19	17	0	0	0
5b	0	32	30	42	5	0	0	0
5c	35	32	26	28	11	15	13	0
5d	14	24	13	23	11	0	23	0
5e	28	40	43	38	41	14	0	25
5f	14	20	13	14	35	22	9	13
5g	21	56	26	52	17	18	35	16
5h	21	0	0	38	23	0	0	0

4. CONCLUSIONS

Thus, new benzohydrazide derivatives were synthesized in the result of reaction of benzohydrazides with 4-(hydroxyimino)-cyclohexa-2,5-dien-1-one and 4-[(aroyloxy)imino]cyclohexa-2,5-dien-1-ones in one step in aqueous-alcoholic solution. N'-[4-{[(4-nitrobenzoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene]benzo-hydrazide showed high insecticidal activity against house fly and rice weevil. 3,4-Dichloro-*N*'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide and N'-{4-[(benzoyloxy)imino]-cyclohexa-2,5-dien-1-ylidene}-2-bromobenzohydrazide showed excellent anti-nematode activity: decrease in gall formation on the cucumber roots was 93 and 91%, respectively. Inhibition of growth and development of colonies of *Venturia Inaegualis* was 52% under action of 2-bromo-*N*'-[4-(hydroxyimino)cyclohexa-2,5-dien-1-ylidene]benzohydrazide and *N*'-[4-{[(4-methylben-zoyl)oxy]imino}cyclohexa-2,5-dien-1-ylidene]benzohydrazide.

5. REFERENCES

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