Turk J Chem
35 (2011) , 99 – 108.

doi:10.3906/kim-0908-177

Synthesis and biological activity of 5-substituted-2-amino-1,3,4-oxadiazole derivatives

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Received 12.08.2009

Electrical energy offers numerous benefits for performing synthesis, including increased reaction rates, enhanced yields, and cleaner chemistries. 5-Substituted-2-amino-1,3,4-oxadiazoles were synthesized directly from the semicarbazone at a platinum electrode under controlled potential electrolysis in an undivided cell assembly in acetonitrile. The compounds were screened for antibacterial and antifungal activity against *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pellicularia salmonicolor*, and *Macrophomina phaseolina*.

Key Words: Antibacterial, antifungal, controlled potential, electrolysis, platinum electrode

Introduction

Recent trends and advances in the technology for the development of ecofriendly synthetic methods in chemical research have great importance and are urgently needed for society. At present, organic synthesis involving electrochemical techniques under suitable solvents and electrolytes are basic requirements, as multistep conventional synthesis produces a considerably large amount of environmentally unfavorable wastes, mainly due to a series of complex isolation procedures involving expensive and toxic solvents after each step. Electrochemical oxidation has various merits. These reactions do not require oxidizing reagents and can be performed at room temperature. Application of electricity as a nonconventional energy source for activation of reactants in suitable solvents has now gained popularity over the usual homogeneous and heterogeneous reactions. It provides chemical processes with special attributes, such as enhanced reaction rate, higher yield of pure products, better selectivity, and several ecofriendly advantages. Electroorganic synthesis of 5-substituted-2-amino-1,3,4-oxadiazole is an important step in this direction.

Various 1,3,4-oxadiazoles have been reported to have a broad spectrum of biological activity, including antimicrobial,[1–3] antifungal,[4,5] antiinflammatory,[6] and hypotensive activity.[7] During hit-to-lead efforts

following a recent high-throughput screening campaign, we initiated a program that required the synthesis of a series of 5-substituted-2-amino-1,3,4-oxadiazoles **4**. Literature syntheses of these oxadiazoles[8−14] include bromine oxidation of a semicarbazide derivative and the cyclodesulfurization of acylthiosemicarbazide derivatives in a solution using I_2/NaOH or 1,3-dicyclohexylcarbodimide (DCC),[15−20] as well as mercury(II) acetate ($Hg(OAc)_2$) or yellow mercury(II) oxide HgO,[21−23] and they produce undesirable mercury byproducts that must be removed and properly disposed of after the reaction is completed. These aforementioned solution phase methods, while successful, were deemed not readily amenable to high-throughput synthesis, and thus did not meet our needs. A solution-phase dehydrative synthesis from 1,2-diacylhydrazines and several solid-phase methods were also considered.[24,25] Evans[26] synthesized a similar cyclized product with one-pot preparation using resin-bound reagents.

Experimental

General procedure

Melting points were recorded from an open capillary and were uncorrected. The IR spectra, in KBr, were recorded on a Shimadzu 8201 PC IR spectrophotometer. ^{1}H-NMR (300, 300 MHz) and ^{13}C-NMR (75, 300 MHz) spectra were measured at room temperature on Bruker DRX 300 FT spectrometer instruments with TMS and $CDCl_3$ or C_6D_6 as internal standards. Carbon multiplities were assigned by DEPT techniques. Microanalyses were carried out in an Elementar Vario EL III. The purity of the compounds was confirmed by TLC on silica gel-coated glass plates.

Synthesis of semicarbazone 3

Semicarbazide hydrochloride (9.0 mmol) **2** and sodium acetate (12.2 mmol) were dissolved in water (10 mL), and then aldehyde (4.16 mmol) **1** was added with continuous stirring. The mixture was left overnight, which gave semicarbazone **3**.

Preparative-scale controlled potential electrolysis

Thoroughly mixed semicarbazone (18.0 mmol) **3** and lithium perchlorate (3.0 mmol) in acetonitrile acid (200 mL) were taken in a 250 mL 3-electrode cell assembly with a platinum plate (1.0 cm × 1.0 cm) as working, as well as a counter electrode and saturated calomel electrode (SCE) as a reference electrode. Preparative-scale controlled potential electrolysis[27−32] was performed (25 °C) at the corresponding oxidation potential and completed in 3-5 h. The current potential data were recorded with a potentiostat (Table 1). A magnetic stirrer was used for the diffusion of the product from the electrode and the proper mixing of the reaction mixture. The products were extracted from the acetic acid solution with chloroform by the simple solvent extraction, and the extracted chloroform layer was left overnight to evaporate the extract. Purification by silica gel chromatography afforded **4** in excellent yield. Analytical and spectral data were obtained from all compounds.

Table 1. Synthesis of 5-substituted-2-amino-1,3,4-oxadiazole derivatives.

Entry	R	Time (h)	Product	Applied Potential (V)	Current (A)	Yield (%)
1	2-Cl,5-$(NO_2)C_6H_3$	3	**4a**	1.85	0.16	78
2	2,3-$Cl_2C_6H_3$	5	**4b**	1.90	0.18	82
3	2-$CH_3C_6H_4$	4	**4c**	1.60	0.15	91
4	9-Anthryl	3	**4d**	1.65	0.14	86
5	3-OEt,4-$(OH)C_6H_3$	4	**4e**	1.65	0.16	89
6	2-F, 6-$ClC_6H_3CH_2$	5	**4f**	1.85	0.19	75
7	C_6H_4CH=CBr	5	**4g**	1.95	0.17	74
8	3,5-$(OMe)_2$, 4-$(OH)C_6H_2$	5	**4h**	1.70	0.16	90
9	4-$Et_2NC_6H_4$	3	**4i**	1.60	0.15	89
10	2-$(HOOC)C_6H_4$	4	**4j**	1.85	0.18	78
11	3,5-Cl_2, 2-OHC_6H_2	3	**4k**	2.00	0.11	83
12	2,5-$F_2C_6H_3$	5	**4l**	2.10	0.16	75
13	3,5-$F_2C_6H_3$	5	**4m**	2.20	0.17	78

2-amino-5-(2-chloro-5-nitrophenyl)-1,3,4-oxadiazole (4a)

Dark yellow needles; mp 80-82 °C; IR υ_{max}/cm^{-1} 750, 815, 1032 (C-O-C), 1560, 1618 (C=N-N=C), 1660, 3035, 3341; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25-7.69 (dd, J = 2.6, 5.6 Hz, 3H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 113.3, 122.2, 123.1, 138.2, 139.8, 148.3, 149.6, 156.7, 171.5. MS (ESI) m/z 241.60 (M+H), found: 241.22. Analysis Calc. for $C_8H_5N_4O_3Cl$ (241.60): C, 42.47; H, 2.21; N, 24.77; Cl, 15.70%, found: C, 42.21; H, 2.09; N, 24.48; Cl, 15.40%.

2-amino-5-(2,3-dichlorophenyl)-1,3,4-oxadiazole (4b)

Brownish needles; mp 85-86 °C; IR υ_{max}/cm^{-1} 600, 655, 775, 1020 (C-O-C), 1603 (C=N-N=C), 3045, 3360; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.94-7.14 (dd, J = 2.6, 5.6 Hz, 4H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 128.5, 128.7, 131.7, 133.5, 135.0, 143.0, 157, 163.2, 171.4. MS (ESI) m/z 231.048 (M+H), found: 230.542. Analysis Calc. for $C_8H_5N_3OCl_2$ (231.048): C, 41.73; H, 2.17; N, 18.26; Cl, 30.86%, found: C, 41.15; H, 2.08; N, 18.17; Cl, 30.54%.

2-amino-5-(2-methylphenyl)-1,3,4-oxadiazole (4c)

Brownish needles; mp 71-72 °C; IR υ_{max}/cm^{-1} 765, 1060 (C-O-C), 1609 (C=N-N=C), 2927, 2965, 3444; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.9 (s, 3H, CH_3), 6.52-7.14 (dd, J =2.6, 5.6 Hz, 4H, Ph), 7.75(s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 126.5, 126.6, 126.8, 129.1, 136.6, 138.6, 141.3, 149.9, 171.6. MS (ESI) m/z 175.191 (M+H), found: 174.324. Analysis Calc. for $C_9H_9N_3O$ (175.191): C, 61.71; H, 5.14; N, 24.00%, found: C, 61.56; H, 5.06; N, 23.89%.

2-amino-5-(9-anthryl)-1,3,4-oxadiazole (4d)

Light brown needles; mp 84-86 °C; IR υ_{max}/cm^{-1} 775, 1055 (C-O-C), 1612 (C=N-N=C), 3045, 3330; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25-7.69 (dd, J = 2.6, 5.6 Hz, 9H, Ar), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 125.3, 128.3, 131.5, 139.2, 139.5, 149.5, 171.5. MS (ESI) m/z 262.284 (M+H), found: 2671.746. Analysis Calc. for $C_{16}H_{11}N_3O$ (262.284): C, 73.56; H, 4.21; N, 16.09%, found: C, 73.23; H, 4.05; N, 15.89%.

2-amino-5-(3-ethoxy-4-hydroxyphenyl)-1,3,4-oxadiazole (4e)

Pale yellow needles; mp 78-80 °C; IR υ_{max}/cm^{-1} 750, 790, 1055 (C-O-C), 1200-1275, 1611 (C=N-N=C), 2810, 2865, 2927, 3330, 3444; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.4 (t, J = 5 Hz, 3H, CH_3), 3.2 (q, J =7.2 Hz, 2H,CH_2), 5.68 (s, 1H, OH), 6.52-7.14 (dd, J = 2.6, 5.6 Hz, 3H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.1, 67.4, 115.5, 120.0, 134.9, 138.5, 139.6, 145.4, 147.1, 149.5, 171.7. MS (ESI) m/z 222.217 (M+H), found: 221.116. Analysis Calc. for $C_{10}H_{11}N_3O_3$ (222.217): C, 58.53; H, 5.36; N, 20.48%, found: C, 58.32; H, 5.15; N, 20.22%.

2-amino-5-(6-chloro-2-fluorophenyl)-1,3,4-oxadiazole (4f)

Yellow needles; mp 81-83 °C; IR υ_{max}/cm^{-1} 745, 810, 1035 (C-O-C), 1220, 1618 (C=N-N=C), 3050, 3360; ^{1}H-NMR (200 MHz; $CDCl_3$/TMS) δ 6.94-7.04 (dd, J =2.6, 5.6 Hz, 4H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (300 MHz; $CDCl_3$/TMS) δ 113.4, 124.1, 126.5, 128.8, 134.0, 138.6, 149.8, 162.5, 172.0. MS (ESI) m/z 228.628 (M+H), found: 227.068. Analysis Calc. for $C_9H_7N_3OFCl$ (228.628): C, 47.57; H, 3.08; N, 18.50; F, 8.27; Cl, 15.63%, found: C, 47.32; H, 2.95; N, 18.19; F, 8.11; Cl, 15.52%.

2-amino-5-(α-bromocinnamyl)-1,3,4-oxadiazole (4g)

Dark yellow crystal; mp 82-84 °C; IR υ_{max}/cm^{-1} 580, 695, 1025 (C-O-C), 1609 (C=N-N=C), 1670, 2855, 3030, 3033, 3336; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.52 (d, J = 16.8 Hz, 1H, Ph*CH*=CBr), 6.94-7.14 (dd, J =2.6, 5.6 Hz, 5H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 126.5, 126.6, 128.2, 128.7, 137.6, 138.6, 149.0, 171.5. MS (ESI) m/z 254.175 (M+H), found: 253.425. Analysis Calc. for $C_{10}H_7N_3OBr$ (254.175): C, 45.11; H, 3.01; N, 15.48; Br, 29.66%, found: C, 44.89; H, 2.98; N, 15.27; Br, 29.43%.

2-amino-5-(3,5-dimethoxy-4-hydroxyphenyl)-1,3,4-oxadiazole (4h)

Dark brownish crystal; mp 83-85 °C; IR υ_{max}/cm^{-1} 752, 810, 1028 (C-O-C), 1602 (C=N-N=C), 2856, 2870, 2927, 3335, 3444; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.10-3.73 (s, 6H, OCH_3), 6.09 (s, 1H, OH), 6.52-7.14 (dd, J =2.6, 5.6 Hz, 2H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75MHz, $CDCl_3$) δ 46.7, 54.1, 108.0, 120.8, 126.8, 135.6, 138.3, 148.2, 149.6, 173.4. MS (ESI) m/z 238.224 (M+H), found: 237.232. Analysis Calc. for $C_{10}H_{11}N_3O_4$ (238.224): C, 50.42; H, 5.04; N, 17.64%, found: C, 50.12; H, 4.73; N, 17.35%.

2-amino-5-(4-*N,N*-diethylaminophenyl)-1,3,4-oxadiazole (4i)

Black needles; mp 79-81 °C; IR υ_{max}/cm^{-1} 850, 1032 (C-O-C), 1610 (C=N-N=C), 2870, 3030, 3334; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.38 (t, J = 7.2 Hz, 6H, CH_3), 3.12 (q, J =7.2 Hz, 4H, CH_2), 6.94-7.14 (dd, J = 2.6, 5.6 Hz, 4H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.7, 14.2, 116.2, 116.3, 128.5, 128.9, 131.1, 138.6, 146.5, 149.5, 172.5. MS (ESI) m/z 233.285 (M+H), found: 232.557. Analysis Calc. for $C_{12}H_{16}N_4O$ (233.285): C, 62.06; H, 6.89; N, 24.13%, found: C, 61.80; H, 6.70; N, 24.00%.

2-amino-5-(2-carboxyphenyl)-1,3,4-oxadiazole (4j)

Pale yellow needles; mp 81-83 °C; IR υ_{max}/cm^{-1} 690, 750, 810, 890, 1021 (C-O-C), 1654 (C=N-N=C), 1715, 2750, 3035, 3341; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25-7.69 (dd, J = 2.6, 5.6 Hz, 4H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 127.1, 129.6, 129.8, 132.5, 133.2, 142.8, 167.0, 171.9, 172.6. MS (ESI) m/z 206.173 (M+H), found: 205.221. Analysis Calc. for $C_9H_7N_3O_3$(206.173): C, 47.05; H, 2.91; N, 20.38%, found: C, 46.80; H, 2.70; N, 20.03%.

2-amino-5-(3,5-dichloro-2-hydroxyphenyl)-1,3,4-oxadiazole (4k)

Brown needles; mp 83-85 °C; IR υ_{max}/cm^{-1} 600, 655, 775, 1026 (C-O-C), 1070, 1633 (C=N-N=C), 3045, 3360, 3640; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.70 (s, 1H, OH), 6.8-7.30 (dd, J = 2.6, 5.6 Hz, 2H, Ph), 7.72 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 117.8, 123.2, 126.5, 128.6, 128.9, 153.3, 167.2, 171.6. MS (ESI) m/z 247.046 (M+H), found: 246.372. Analysis Calc. for $C_8H_5N_3O_2Cl_2$ (247.046): C, 39.06; H, 2.04; N, 17.08; Cl, 28.82%, found: C, 38.62; H, 1.94; N, 16.75; Cl, 28.56%.

2-amino-5-(2,5-difluorophenyl)-1,3,4-oxadiazole (4l)

Yellow needles; mp 77-79 °C; IR υ_{max}/cm^{-1} 815, 830, 850, 1035 (C-O-C), 1260, 1665 (C=N-N=C), 3050, 3360; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.94-7.04 (dd, J = 2.6, 5.6 Hz, 3H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz $CDCl_3$) δ 113.3, 113.5, 123.1, 127.2, 138.5, 147.6, 149.2, 149.5, 171.8. MS (ESI) m/z 198.148 (M+H), found: 197.235. Analysis Calc. for $C_8H_7N_3OF_2$(198.148): C, 48.24; H, 3.51; N, 21.10; F, 19.09%, found: C, 48.07; H, 3.38; N, 21.00; F, 18.90%.

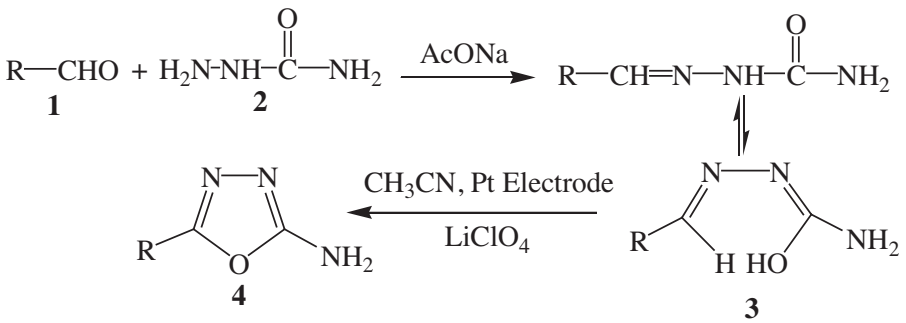
2-amino-5-(3,5-difluorophenyl)-1,3,4-oxadiazole (4m)

Yellow needles; mp 77-79 °C; IR υ_{max}/cm^{-1} 815, 830, 850, 1022 (C-O-C), 1260, 1652 (C=N-N=C), 3050, 3360; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.94-7.04 (dd, J = 2.6, 5.6 Hz, 3H, Ph), 7.75 (s, 2H, NH_2); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 113.3, 113.5, 123.3, 127.5, 138.5, 147.6, 149.2, 149.5, 171.6. MS (ESI) m/z 198.164 (M+H), found: 197.352. Analysis Calc. for $C_8H_7N_3OF_2$(198.164): C, 48.24; H, 3.51; N, 21.10; F, 19.09%, found: C, 48.07; H, 3.38; N, 21.00; F, 18.90%.

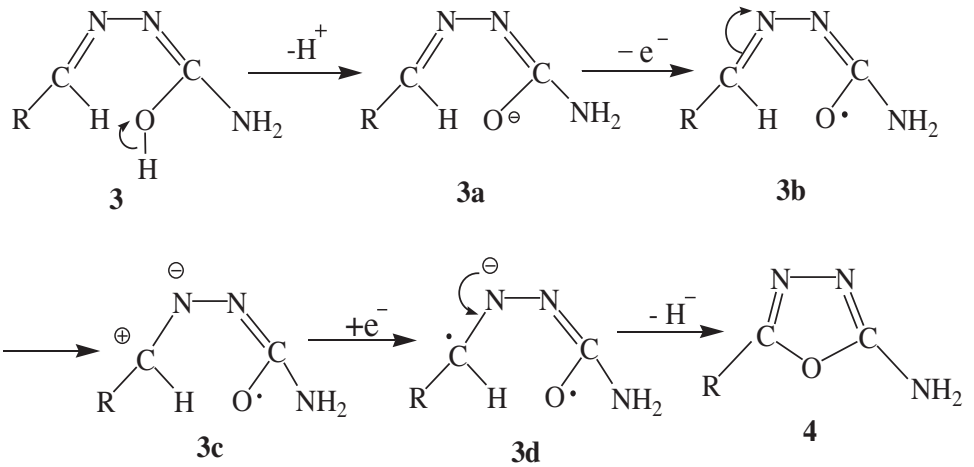
Results and discussion

Our objective was to find a new environmentally benign general synthetic method for the preparation of 1,3,4-oxadiazoles, in which the use of the aforementioned reagents could be minimized in both amount and number. Keeping that objective in mind, we synthesized some 5-substituted-2-amino-1,3,4-oxadiazoles **4** by electrooxidative cyclization of semicarbazone **3** at the platinum electrode. This electrochemical cyclization gave the oxadiazoles (Scheme 1) without the requirement of any hazardous reagents. We used acetonitrile as a solvent and lithium perchlorate ($LiClO_4$) as an electrolyte, which can be handled very easily, without major precautions.

Compounds **4b**, **4c**, and **4j** are not new and have been previously reported.[33–35] Compounds **4a**, **4f**, **4l**, and **4m** are commercially available. The present study proposes a new methodology for obtaining these compounds.



Scheme 1. Synthesis of 5-substituted-2-1,3,4-oxadiazols 4.



Scheme 2. Mechanistic proposal.

2-Amino-5-substituted-1,3,4-oxadiazoles were synthesized in excellent yields using the synthetic route outlined in Scheme 1. IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectral data are in agreement with the proposed structures of all synthesized compounds. Lack of ^{1}H NMR resonances observed with NH and NH_2 functions in the ^{1}H-NMR spectrum of **4a-m** proved that ring closure starting from **3** resulted in the formation of a

2-amino-1,3,4-oxadiazole ring. This was further substantiated by the ^{13}C-NMR data of **4**, which showed peaks at δ 170-173 and 145-150 due to the C_2 and C_5 of oxadiazole, respectively. The IR spectrum showed 1600-1620 cm^{-1} for (C=N-N=C) and 1063-1073 cm^{-1} for (C-O-C) in compounds **4a-m**, which confirmed the synthesis of 1,3,4-oxadiazoles.

Compounds **4a-m** were screened for their antibacterial activity against *Staphylococcus aureus* and *Klebsiella pneumoniae* by comparing them with standard streptomycin, and antifungal activity against *Pellicularia salmonicolor* and *Macrophomina phaseolina* was compared with the standard fungicide griseofulvin. It is interesting to observe that the maximum compounds had excellent antifungal and antibacterial activity.

The antimicrobial activity of the compounds varied upon the type and position of the substituents at 5-substituted-2-amino-1,3,4-oxadiazole moiety. It can be concluded from the antimicrobial screening results that when 5-substituted-2-amino-1,3,4-oxadiazoles were substituted with aryl halide, the antimicrobial activity was altered to an appreciable extent.

Biological activity

All of the synthesized compounds were tested for antimicrobial activity with the experimental method of Benson.[36,37] Whatman No. 1 filter paper disks, 6 mm in diameter, were placed in a petri dish and autoclaved. The test compounds, in measured quantities (1.0 and 0.5 mg), were dissolved in 5 mL of dimethylformamide to produce 200 ppm and 100 ppm solutions, respectively. The filter paper disks were allowed to dry, and the amount of substance per disk was taken as 500 and 250 μg. The bacterial (24 h) and fungal (48 h) cultures from the slants were diluted with sterile water and mixed thoroughly to prepare a clear homogeneous suspension. These suspensions were uniformly spread on solidified agar (nutrient and potato dextrose agar) medium. The filter paper disks prepared from the dimethylformamide medium were carefully placed over the spread cultures and incubated at 37 °C for 24 h for bacteria and at 28-30 °C for 48 h for fungi. Paper disks treated with dimethylformamide alone served as the control. After the incubation period, the plates were examined for inhibition zones. The diameters of the inhibition zones (including the diameter of the disk) were measured. All determinations were made in triplicate for each of the compounds and the average value was taken. The compounds were assayed for antimicrobial activity against registered bacterial isolates.

Compounds **4a-m** (Table 2) were screened for their antifungal activity against *Pellicularia salmonicolor* and *Macrophomina phaseolina* along with the standard fungicide griseofulvin. The disk diffusion method[36,37] was followed for screening the compounds at 3 concentrations (25, 50, and 100 μg disk^{-1}). Their antibacterial activity (Table 3) was also evaluated according to the disk diffusion method at 3 different concentrations against *Staphylococcus aureus* and *Klebsiella pneumoniae* by comparing them with the standard streptomycin.

It is obvious from Table 2 that compound **4g** had a higher antifungal activity than the standard griseofulvin for both *Pellicularia salmonicolor* and *Macrophomina phaseolina*. Compounds **4a**, **b**, **f**, and **k** were slightly less active than the standard, while **4c**, **e**, **g**, **h**, **i**, **l**, and **m** had moderate activity. Compounds **4d** and **4j** were much less active or had negligible activity. It is evident from Table 3 that compound **4g** had higher antibacterial activity than the standard streptomycin for both *Staphylococcus aureus* and *Klebsiella pneumoniae*. Compounds **4a**, **b**, **f**, **k**, and **l** were slightly less active than the standard, while **4d**, **e**, **i**, and **j** had moderate activity.

It is interesting to observe that all **4a-m** compounds with antifungal activity were also antibacterial.

Table 2. Antifungal activity of compounds **4a-m**.

	Diameter of zone of growth inhibition (mm)					
	Pellicularia salmonicolor ($\mu g\ disk^{-1}$)			*Macrophomina phaseolina* ($\mu g\ disk^{-1}$)		
Compound	25	50	100	25	50	100
4a	2	5	8	2	4	9
4b	4	6	10	3	6	9
4c	1	4	6	2	4	7
4d	-	-	2	-	-	2
4e	2	4	7	2	3	6
4f	2	5	9	3	5	10
4g	3	7	11	4	8	11
4h	2	5	7	1	3	5
4i	3	6	7	1	4	6
4j	-	2	4	-	2	4
4k	2	4	8	3	6	9
4l	1	3	6	2	4	6
4m	2	4	7	1	3	6
Griseofulvin	-	6	10	3	7	11

Table 3. Antibacterial activity of compounds **4a-m**.

	Diameter of zone of growth inhibition (mm)					
	Pellicularia salmonicolor ($\mu g\ disk^{-1}$)			*Macrophomina phaseolina* ($\mu g\ disk^{-1}$)		
Compound	25	50	100	25	50	100
4a	4	7	11	3	6	10
4b	3	6	10	2	6	8
4c	3	5	8	1	4	6
4d	-	-	4	-	-	3
4e	1	3	6	3	5	7
4f	3	6	9	4	7	9
4g	5	8	12	5	9	13
4h	2	4	7	2	5	8
4i	1	3	5	2	4	7
4j	-	2	6	-	2	5
4k	2	6	9	3	7	10
4l	3	5	8	3	6	9
4m	1	4	7	2	4	8
Streptomycin	2	7	11	2	7	10

Conclusion

It is evident from the electrochemical method that the electroorganic synthesis of 1,3,4-oxadiazole derivatives is an example of electrochemical cyclization by electrooxidation of semicarbazone. It provides a good method for the synthesis of oxadiazoles with antimicrobial activity in excellent yields. In the present electrolytic method, electrolysis was carried out at ordinary temperatures and no hazardous chemicals were used. Therefore, the method is environmentally benign and a great contribution to the field of green chemistry.

Acknowledgements

The author thanks the University Grant Commission, New Delhi, for the financial assistance, and SAIF (Sophisticated Analytical Instrumentation Facility), a division of CDRI Lucknow, India, for providing microanalyses and spectra.

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