ANODIC SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF NOVEL 2-AMINO-5-SUBSTITUTED-1,3,4-OXADIAZOLES

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ABSTRACT

Synthesis of 2-amino-5-substituted-1,3,4-oxadiazoles through the electrochemical oxidation of semicarbazone was carried out at platinum anode at room temperature under controlled potential electrolysis in an undivided cell assembly. The electrolysis were carried out in the non aqueous medium acetic acid and lithium perchlorate was used as a supporting electrolyte. The antimicrobial activities of the compounds have been studied by screening the compounds against two gram negative organisms *Klebsiella pneumoniae*, *Escherichia coli*, and two gram positive organisms *Bacillus subtilis* and *Streptococcus aureus* and antifungal activity against *Aspergillus niger* and *Crysosporium pannical* and results have been compared with the standard antibacterial Streptomycin and antifungal Griseofulvin.

Keywords: Semicarbazone, Oxadiazoles, Electrolysis, Antimicrobial studies

INTRODUCTION

1,3,4-oxadiazole is a versatile lead molecule for designing potential bioactive agents. The 1,3,4-oxadiazole derivatives have been found to exhibit diverse biological activities such as hypotensive¹ anti-microbial²⁻⁴, anti-HIV²⁻⁴, anti-fungal⁵⁻⁶ anti-inflammatory⁷ antimitotic activity⁸ and muscle relaxant⁹.

It have been found in the literature study that the methods for synthesis of oxadiazole **1** include bromine oxidation of semicarbazide derivative and the cyclodesulfurization of acylthiosemicarbazide derivatives in the solution using $I_2/NaOH$ or 1,3-dicyclohexylcarbodiimide (DCC)¹⁰⁻¹³ as well as mercury(II) acetate ($Hg(OAc)_2$) or yellow mercury(II) oxide HgO ¹⁴⁻¹⁶. Evans¹⁷ synthesized oxadiazole derivatives by rapid parallel synthesis in efficient one-pot preparation using resin-bound reagents. All these methods are usually carried out in various different synthetic steps and require the heating at higher temperature. The handling of these reagents is not only difficult but also very hazardous to environment. The each stage of the reaction including extraction and purification of the products from the mixture requires great precautions.

These reports including our earlier work¹⁸⁻²³ prompted us to synthesize 2-amino-5-substituted-1,3,4-oxadiazole derivatives through the electrochemical oxidation of semicarbazone **4** in the hope of getting potent biodynamic agents and evaluate their antimicrobial activity.

EXPERIMENTAL

Analysis and measurements

The reagents used for the preparation of oxadiazoles were of Merck products. Spectroscopic grade solvents were used for spectral measurements. The carbon, hydrogen and nitrogen contents in each sample were performed at RSIC, CDRI Lucknow. The IR spectra were recorded on a Perkin-Elmer 783 spectrophotometer KBr pellets. 1H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 300 (300MHz) FT spectrometer in $CDCl_3$ using TMS as internal reference. Chemical shifts are reported in ppm downfield from TMS as internal reference. Elemental analyses were carried out in the Elementar VarioEL III instrument. Melting points were determined on a VEB Wagetchink Rapio PHMK05 instrument and are uncorrected. Water used was doubly distilled.

General procedure for the synthesis of compounds (1a-1n)

Semicarbazide hydrochloride **3** (9.0 mmol) and sodium acetate (12.2 mmol) was dissolved in water (10 mL) and then aldehyde **2** (4.16 mmol) was added with continuous stirring. The mixture was left overnight, which gives semicarbazone **4**. Now semicarbazone **4** (12.25 mmol), lithium perchlorate (1.3 mmol) and acetic acid (200 mL) was taken in the reaction cell assembly with platinum plate as working as well as counter electrode and saturated calomel electrode as reference electrode. Controlled potential electrolysis²⁴⁻³¹ were performed at their corresponding oxidation potentials at room temperature, tabulated as Table 1. The product was extracted from the acetic acid solution to chloroform by the simple solvent extraction technique. 4-6 Fmol⁻¹ of electricity was passed for the electrolysis, which is very small in comparison to energy used in other conventional methods.

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

Entry	R	Time [h]	Product	Applied Potential [V]	Current [A]	Yield [%]
1	3-MeC ₆ H ₄	3	1a	1.60	0.15	90
2	3-C ₆ H ₄ COC ₆ H ₄	4	1b	1.90	0.18	85
3	5-Br, 2-OHC ₆ H ₃	4	1c	2.00	0.17	75
4	3-(4-Me ₂ CC ₆ H ₄ O) C ₆ H ₄	3	1d	1.75	0.19	92
5	4-(COOH)C ₆ H ₄	5	1e	2.10	0.20	70
6	10-Cl Anthryl	4	1f	1.95	0.15	88
7	5-Cl, 2-(NO ₂)C ₆ H ₃	5	1g	2.20	0.17	80
8	5-Cl, 2-OHC ₆ H ₃	5	1h	1.80	0.18	83
9	4-(CN)C ₆ H ₄	4	1i	1.80	0.19	78
10	3,5-Br ₂ C ₆ H ₃	4	1j	1.65	0.18	81
11	3,5-(Me ₂ C) ₂ 4-OHC ₆ H ₂	3	1k	1.60	0.11	86
12	2,4-Cl ₂ C ₆ H ₃	5	1l	1.95	0.18	82
13	2,3-F ₂ C ₆ H ₃	5	1m	2.10	0.21	79
14	2,6-F ₂ C ₆ H ₃	5	1n	2.20	0.20	78

The spectral data of compounds, **1a-1n** is given below.

2-amino-5-methylphenyl-1,3,4-oxadiazole (1a) Light brown needles, m. p. 74-75 °C; IR cm⁻¹ 3444, 3045, 3010, 2965, 2927, 1602 (C=N-N=C), 1265, 1069 (C-O-C), 960, 765; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH₂), 6.52-7.24 (m, J= 2.6 and 5.6 Hz, 4H), 1.12 (s, 3H, CH₃); ^{13}C NMR (75 MHz, $CDCl_3$)

178.2, 149.9, 138.6, 141.3, 136.5, 129, 127.8, 126.5, 20.6; *m/z* (ES-MS) 173.0, Mol. Formula $C_9H_7N_3O$, Mol. Wt.: 173.2, Calculated C, 62.42; H, 4.04; N, 24.27, found C, 62.12; H, 4.00; N, 23.86.

2-amino-5-(3-benzoyloxy)phenyl-1,3,4-oxadiazole (1b) Pale yellow needles, *m. p.* 72-74 °C; IR cm^{-1} 3350, 3045, 1755, 1617 (C=N-N=C), 1269, 1065 (C-O-C), 910, 860; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 7.25-7.69 (m, *J* = 2.6 and 5.6 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 172, 149.5, 137.1, 136.3, 132.9, 131.3, 130.2, 128.7, 128.1, 128.0, 127.8; *m/z* (ES-MS) 264.8, Mol. Formula $C_{15}H_{11}N_3O_2$, Mol. Wt.: 265.3, Calculated C, 67.92; H, 4.14; N, 15.84, found C, 67.45; H, 4.03; N, 15.44.

2-amino-5-(5-bromo-4-hydroxy)phenyl-1,3,4-oxadiazole (1c) Black needles, *m. p.* 85-87 °C; IR cm^{-1} 3440, 3360, 3045, 1604 (C=N-N=C), 1267, 1070 (C-O-C), 980, 890, 755, 655; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 7.25-7.69 (m, *J* = 2.6 and 5.6 Hz, 4H), 6.09 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) 158.9, 147.2, 141.2, 136.4, 134.2, 129.7, 123.9, 123.7; *m/z* (ES-MS) 265.2, Mol. Formula $C_{10}H_8N_3OBr$, Mol. Wt.: 266.1, Calculated C, 45.11; H, 3.02; N, 15.79; Br, 30.07, found C, 44.85; H, 2.75; N, 15.39; Br, 29.65.

2-amino-5-(3-(4-*tert*-butyl phenoxy)phenyl-1,3,4-oxadiazole (1d) Yellow needles, *m. p.* 85-87 °C; IR cm^{-1} 3444, 3360, 2860, 1608 (C=N-N=C), 1270, 1265, 1072 (C-O-C), 1130, 749.5; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.52-7.14 (m, *J* = 2.6 and 5.6 Hz, 8H), 1.3 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 172.4, 167, 147.5, 140.2, 138.9, 137.5, 132.6, 128.5, 128.2, 128.1, 128.4, 122.8, 118.6, 114.6, 42.1, 20.6; *m/z* (ES-MS) 308.1, Mol. Formula $C_{18}H_{19}N_3O_2$, Mol. Wt.: 308.5, Calculated C, 69.90; H, 6.14; N, 13.59, found C, 69.12; H, 5.88; N, 13.36.

2-amino-5-(4-carboxy)phenyl-1,3,4-oxadiazole (1e) Brown needles, *m. p.* 87-89 °C; IR cm^{-1} 3360, 3300, 3060, 1715, 1612 (C=N-N=C), 1280, 1275, 1065 (C-O-C), 962; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.52-7.24 (m, *J* = 2.6 and 5.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.6, 144.9, 141.5, 141.2, 129.9, 129.5, 129.3; *m/z* (ES-MS) 204.6, Mol. Formula $C_8H_7N_3O_3$, Mol. Wt.: 205.2, Calculated C, 52.68; H, 3.41; N, 20.48, found C, 51.82; H, 3.22; N, 20.00.

2-amino-5-(10-chloro)anthryl-1,3,4-oxadiazole (1f) Brown needles, *m. p.* 93-95 °C; IR cm^{-1} 3330, 3030, 1670, 1607 (C=N-N=C), 1267, 1068 (C-O-C), 780; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 7.25-7.69 (m, *J* = 2.6 and 5.6 Hz, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.4, 149.5, 139.2, 131.5, 128.3, 125.3; *m/z* (ES-MS) 295.0, Mol. Formula $C_{16}H_9N_3OCl$, Mol. Wt.: 295.7, Calculated C, 64.95; H, 3.38; N, 14.20; Cl, 12.00, found C, 64.12; H, 3.11; N, 14.05; Cl, 11.66.

2-amino-5-(5-chloro-2-nitro)phenyl-1,3,4-oxadiazole (1g) Dark yellowish needles, *m. p.* 71-73 °C; IR cm^{-1} 3341, 3035, 1614 (C=N-N=C), 1580, 1273, 1071 (C-O-C), 860, 735; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 7.25-7.69 (m, *J* = 2.6 and 5.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.3, 148.3, 147.1, 146.8, 140.8, 136.8, 130.4, 121.2; *m/z* (ES-MS) 239.7, Mol. Formula $C_8H_5N_3O_3Cl$, Mol. Wt.: 240.6, Calculated C, 39.90; H, 2.07; N, 23.27; Cl, 14.75, found C, 39.45; H, 1.95; N, 22.95; Cl, 14.52.

2-amino-5-(5-chloro-2-hydroxy)phenyl-1,3,4-oxadiazole (1h) Yellow needles, *m. p.* 78-80 °C; IR cm^{-1} 3440, 3261, 3045, 1611 (C=N-N=C), 1276, 1073 (C-O-C), 1050, 760; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.46-7.70 (m, *J* = 2.6 and 5.6 Hz, 3H), 6.09 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) 171.9, 166.2, 151.3, 128.7, 128.5, 128, 116.8; *m/z* (ES-MS) 211.2, Mol. Formula $C_{10}H_7N_3OCl$, Mol. Wt.: 211.6, Calculated C, 56.71; H, 3.78; N, 19.84; Cl, 16.77, found C, 55.82; H, 3.48; N, 19.65; Cl, 16.55.

2-amino-5-(4-cyano)phenyl-1,3,4-oxadiazole (4i) Yellow crystals, *m. p.* 69-71 °C; IR cm^{-1} 3330, 3060, 2230, 1620 (C=N-N=C), 1265, 1064 (C-O-C), 960; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.54-7.52 (m, *J* = 2.6 and 5.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 171.9, 166.1, 145.8, 132.5, 128.6, 128.5, 125, 111; *m/z* (ES-MS) 185.4, Mol. Formula $C_8H_6N_4O$, Mol. Wt.: 186.2, Calculated C, 58.06; H, 3.22; N, 30.10, found C, 57.55; H, 3.10; N, 29.76.

2-amino-5-(3,5-dibromo-2-hydroxy)phenyl-1,3,4-oxadiazole (1j) Black needles, *m. p.* 88-89 °C; IR cm^{-1} 3440, 3360, 3045, 1610 (C=N-N=C), 1266, 1071 (C-O-C), 980, 890, 755, 655; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 7.25-7.69 (m, *J* = 2.6 and 5.6 Hz, 2H), 6.09 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) 158.9, 147.5, 141.6, 136.2, 134.2, 129.9, 124, 123.7; *m/z* (ES-MS) 344.3, Mol. Formula $C_{10}H_7N_3OBr_2$, Mol. Wt.: 344.9, Calculated C, 34.78; H, 2.02; N, 12.17; Br, 46.37, found C, 34.10; H, 1.88; N, 12.03; Br, 46.11.

2-amino-5-(3,5-di-*tert*-butyl-4-hydroxy)phenyl-1,3,4-oxadiazole (1k) Brownish crystals, *m. p.* 83-85 °C; IR cm^{-1} 3444, 3360, 2860, 1605 (C=N-N=C), 1273, 1063 (C-O-C), 1130, 749.5; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.52-7.14 (m, *J* = 2.6 and 5.6 Hz, 3H), 1.3 (s, 18H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 172.4, 167, 147.5, 137.5, 132.6, 128.5, 140.2, 138.9, 42.1, 20.6; *m/z* (ES-MS) 288.6, Mol. Formula $C_{16}H_{23}N_3O_2$, Mol. Wt.: 289.4, Calculated C, 66.43; H, 7.95; N, 14.53, found C, 65.88; H, 7.56; N, 14.36.

2-amino-5-(2,4-dichloro)phenyl-1,3,4-oxadiazole (1l) Pale yellow needles, *m. p.* 89-91 °C; IR cm^{-1} 3360, 3045, 1608 (C=N-N=C), 1267, 1069 (C-O-C), 775, 655, 600; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.94-7.04 (m, *J* = 2.6 and 5.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 164.5, 157, 143, 135, 133.5, 131.7, 128.7, 128.5; *m/z* (ES-MS) 229.7, Mol. Formula $C_8H_5N_3OCl_2$, Mol. Wt.: 230.0, Calculated C, 41.92; H, 2.18; N, 18.34; Cl, 30.56, found C, 41.25; H, 2.03; N, 18.17; Cl, 30.27.

2-amino-5-(2,3-difluoro)phenyl-1,3,4-oxadiazole (1m) Dark brownish needles, *m. p.* 80-82 °C; IR cm^{-1} 3360, 3050, 1611 (C=N-N=C), 1269, 1064 (C-O-C), 935, 765; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.94-7.04 (m, *J* = 2.6 and 5.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 164.5, 162.5, 142.5, 140.6, 122.2, 111.0, 109.7, 100.1; *m/z* (ES-MS) 196.6, Mol. Formula $C_8H_5N_3F_2O$, Mol. Wt.: 197.1, Calculated C, 48.73; H, 2.53; N, 21.31; F, 19.28, found C, 48.12; H, 2.45; N, 21.18; F, 19.03.

2-amino-5-(2,6-difluoro)phenyl-1,3,4-oxadiazole (1n) Dark brownish needles, *m. p.* 82-83 °C; IR cm^{-1} 3360, 3055, 1601 (C=N-N=C), 1273, 1068 (C-O-C), 950, 790; 1H NMR (400 MHz, $CDCl_3$) 7.75 (s, 2H, NH_2), 6.94-7.04 (m, *J* = 2.6 and 5.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 165, 162.7, 142.5, 141.0, 122.2, 111.5, 109.7, 100.2; *m/z* (ES-MS) 196.4, Mol. Formula $C_8H_5N_3F_2O$, Mol. Wt.: 197.1, Calculated C, 48.73; H, 2.53; N, 21.31; F, 19.28, found C, 48.20; H, 2.35; N, 21.10; F, 19.05.

Biological Activity

All the title compounds were tested for their antimicrobial activity by adopting the experimental method of Benson³². Whatman No.1 filter paper discs of 6 mm diameter, placed in a Petri dish, were autoclaved. The test compounds in measured quantities (1.0 mg, 0.5 mg) were dissolved in 5 mL of dimethylformamide to produce 200 ppm and 100 ppm solutions, respectively. The filter paper discs were allowed to dry and the amount of the substance per disc 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 discs prepared from dimethylformamide medium were carefully placed over the spreaded cultures and incubated at 37 °C for 24 h for bacteria and at 28-30 °C for 48 h for fungi. Paper discs treated with dimethylformamide alone served as control. After the incubation period the plates were examined for inhibition zones. The diameters of inhibition zones (including the diameter of the disc) were measured. All determinations were made in triplicate for each of the compounds and the average value was taken.

RESULTS AND DISCUSSION

The organic synthesis involving electrochemical techniques under suitable solvents and electrolytes are the basic requirements. The solution phase methods, while successful, were deemed not readily amenable to high throughput synthesis, and thus did not meet our needs. Considering the importance of 1,3,4-oxadiazoles and methods of preparation, 2-amino-5-substituted-1,3,4-oxadiazoles were synthesized by electrooxidative cyclization of semicarbazone as an environmentally benign synthetic method in which aforementioned troublesome were removed and minimized. The electroorganic synthesis of 1,3,4-oxadiazole derivatives **1** is electrochemical cyclization by electrooxidation of semicarbazone **4**. The electrochemical oxidation has various merits. The electrooxidation does not require oxidizing reagents and can be performed at room temperature. Electricity provides chemical processes with special attributes, such as enhanced reaction rate, higher yield of pure products, better selectivity and several ecofriendly advantages.

This electrochemical cyclization gives the oxadiazoles (Scheme1). Acetic acid was used as a solvent and lithium perchlorate as an electrolyte.

Scheme 1: Synthesis of oxadiazoles 2-amino-5-substituted-1,3,4-oxadiazoles. Reagents and conditions: (a) sodium acetate; (b) CH_3COOH , LiClO_4 ; 25°C .

Scheme 2. Mechanistic proposal.

Novel 2-amino-5-substituted-1,3,4-oxadiazoles have been synthesized in excellent yields using the synthetic route outlined in Scheme 1. IR, ^1H NMR, ^{13}C NMR and mass spectral data are in agreement with the proposed structures of all synthesized compounds. Lack of ^1H NMR resonances observed with NH and NH_2 functions in the ^1H NMR spectrum of **1a-n** proved that ring closure starting from **4** resulted in the formation of 2-amino-1,3,4-oxadiazole ring. This was further substantiated by the ^{13}C NMR data of **1** which showed the peaks at δ 170-173 and 145-150 due to C_2 and C_5 of oxadiazole respectively. The IR spectrum shows $1600\text{--}1620\text{ cm}^{-1}$ for $(\text{C}=\text{N}-\text{N}=\text{C})$ and $1063\text{--}1073\text{ cm}^{-1}$ for $(\text{C}-\text{O}-\text{C})$ in the compounds **1a-1n** which confirmed the synthesis of 1,3,4-oxadiazoles.

Antibacterial Activity

The antibacterial activity of compounds **1a-1n** was studied against the growth of *Klebsiella pneumoniae*, *Escherichia coli*, (Gram-negative) and *Bacillus subtilis*, *Streptococcus aureus* (Gram-positive) organisms at the two concentrations (25 and 50 ppm) taking Streptomycin as the standard (Table 2). The majority of the compounds exhibited significant (good) antibacterial activity against *E. coli*, *K. pneumoniae*, *B. subtilis* and *S. aureus* as compared to Streptomycin. The screening results of antibacterial activity revealed that compounds **1c** and **1j** exhibited approximately similar activity to the standard Streptomycin. Compounds **1f**, **1g**, **1h**, **1i** and **1l** exhibited slightly less antibacterial activity. Remaining compounds exhibited weak antibacterial activity against all bacterial strains used for our evaluation.

Antifungal Activity

The compounds **1a-1n** were screened for their antifungal activity against *Aspergillus niger* and *C. pannical* species along with the standard fungicide Griseofulvins **1a-1n** (Table 3). The disc diffusion method was followed for screening the compounds at three concentrations (10, 100 and 1000 ppm). The screening results revealed that all the compounds displayed good antifungal activity against *A. niger* and *C. pannical*. However, compounds **1c** and **1j** showed equal antifungal activity when compared with the Griseofulvins.

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.

Table 2. Antibacterial activity of compounds **1a-1n**

Compound	Zone of inhibition (mm)							
	<i>E. coli</i>		<i>K. pneumoniae</i>		<i>B. subtilis</i>		<i>S. aureus</i>	
	25 ppm	50 ppm	25 ppm	50 ppm	25 ppm	50 ppm	25 ppm	50 ppm
1a	8	14	11	17	10	15	12	15
1b	10	15	10	16	12	18	13	17
1c	17	22	18	21	18	23	16	22
1d	12	17	9	13	12	15	11	15
1e	10	15	9	14	12	16	13	16
1f	16	20	17	21	15	20	14	19
1g	17	21	14	20	16	20	16	20
1h	14	19	16	19	15	18	17	20
1i	15	18	14	18	13	17	17	19
1j	18	22	18	23	17	22	18	23
1k	12	15	12	16	10	14	13	17
1l	17	20	16	20	18	21	15	19
1m	14	18	13	17	14	18	12	16
1n	15	18	12	16	13	18	13	17
Streptomycin	20	23	19	24	19	24	19	23
Control (DMF)	0	0	0	0	0	0	0	0

Table 3. Antifungal activity of the compounds **1a-1n***

Compound	<i>A. niger</i>			<i>C. pannical</i>		
	10 ppm	100 ppm	1000 ppm	10 ppm	100 ppm	1000 ppm
1a	19	42	73	19	41	74
1b	18	42	72	21	45	77
1c	44	58	98	45	57	98
1d	20	44	72	22	43	75
1e	17	36	63	18	37	65
1f	38	56	97	40	51	96
1g	40	53	96	42	53	97
1h	41	51	96	39	54	96
1i	21	44	70	20	43	68
1j	46	59	98	46	58	98
1k	26	45	71	23	46	75
1l	42	55	95	41	55	97
1m	33	45	88	21	39	84
1n	32	46	87	22	42	85
Griseofulvin	66	86	100	65	83	100
Control (DMF)	0	0	0	0	0	0

*Average inhibition of fungal growth (%) at stated concentration (mg/liter⁻¹)

CONCLUSION

In conclusion we have developed a convenient method for the synthesis of novel 2-amino-5-substituted-1,3,4-oxadiazole derivatives in excellent yields which is not so easy to achieve by chemical methods. These compounds exhibited significant activity against the growth of bacterial and fungal strain. 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 is evident 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.

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