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Electrochemical oxidation of aldehyde-*N*-arylhydrazones into symmetrical-2,5-disubstituted-1,3,4-oxadiazoles

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Abstract A convenient, efficient and one-pot synthesis of chemically and pharmaceutically interesting symmetrical-2,5-disubstituted-1,3,4-oxadiazoles is reported. The protocol involves anodic oxidation of aldehyde-*N*-arylhydrazones in anhyd. MeCN–$LiClO_4$. Constant potential electrolysis carried out in an undivided cell and platinum electrodes leads to the formation of the corresponding oxadiazoles under ambient condition and the mechanism was deduced from voltammetry studies. The reaction proceeded smoothly with high atom economy.

Keywords Aldehyde-*N*-arylhydrazones · Controlled potential electrolysis · Cyclic voltammetry · Electrochemical oxidation · 1,3,4-Oxadiazoles · Green chemistry

Introduction

Heterocycles form by far the largest of the classical divisions of organic chemistry and are of immense importance biologically, industrially, and indeed to the functioning of any developed human society. *N*-containing heterocycles, especially five-membered rings, are of great interest as they are found in natural products [1] and frequently used in medicinal chemistry [2]. Amongst these heterocycles, the 1,3,4-oxadiazole motif is of particular value in material science [3], agrochemistry [4], and in pharmaceutical chemistry, as it has been used by medicinal chemists for many years as a bioisosteric replacement of acid, ester and amide functionalities in compounds exhibiting a wide range of biological activities (Fig. 1) [5–10].

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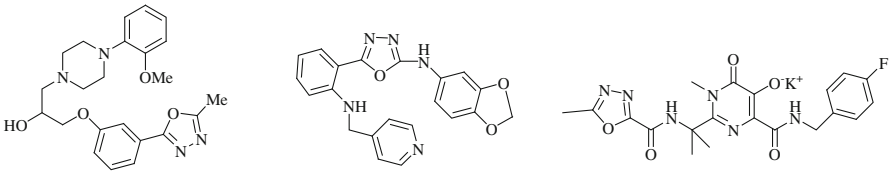


Fig. 1 Pharmaceuticals containing the 1,3,4-oxadiazole motif

Symmetrical-2,5-disubstituted-1,3,4-oxadiazoles have been synthesized by traditional methodology via several approaches [11–22], three of the more popular being the cyclization of diarylhydrazines [11], cyclization of arylthiosemicarbazides [12], and oxidation of arylhydrazones [13–15]. However, prolonged reaction time, extended reaction period, at elevated temperature, and harsh reagents, e.g., BF_3–OEt_2 [16], 1,1,1,3,3,3-hexamethydisilazane [17], triflic anhydride [18], phosphorus pentoxide [19], polyphosphoric acid [20], thionyl chloride [21–23], phosphorus oxychloride [24–26], and sulfuric acid [27–29], are usually encountered. These liquid reagents not only make the reaction systems corrosive but also cause severe environmental problems because of their difficult separation and recovery after reactions.

Recently, chemists have reported some greener approaches using polymer-supported Burgess reagent [30–33], silica sulfuric acid [34, 35], and solid supported Nafion NR50 [36] as dehydrants to the synthesis of 2,5-disubstituted-1,3,4-oxadiazoles, which could efficiently avoid the corrosion and pollution caused by other liquid homogeneous reagents because of the easy separation. Most of these processes have some disadvantages such as use of expensive reagents, harsh experimental conditions, long reaction times, and tedious work-up procedures that generate large amounts of toxic waste. Hence the development of a synthetic protocol that is nature friendly, simple, efficient, and cost-effective remains an ever-challenging objective.

Among the most interesting and innovative chemical technologies, the electrochemical method provides a powerful means for the small-scale production of a number of value-added and high purity compounds. Electroorganic reactions [37–39] have found wide application in industrial processes [40] and are of increasing interest with regard to the synthesis of complex molecules [41–44]. The major advantages of electrochemical methods include mild reaction conditions, the use of inexpensive electricity as a source of reduction equivalents, and high selectivity, resulting from the possibility to precisely tune the electrochemical potential at an electrode. Furthermore, in some cases, electrochemical reactions can afford unexpected products that are difficult to prepare using chemical methods.

The principles of green chemistry dictate that chemical transformations should be designed to minimize (1) required energy input, either mechanical or thermal, and (2) the use of harmful organic solvents. Electrochemistry can be considered as a green methodology in organic synthesis [38, 45–47], due to its non-polluting reagent,

the electron. A wide variety of reactions can be performed in all areas of organic chemistry [48–50], but electrochemistry is more adapted to small-scale synthesis of pharmaceutical [51] and other high-value, low-volume specialty products [52].

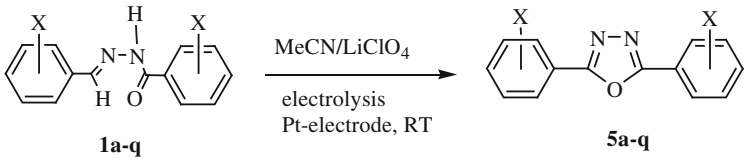
Results and discussion

Recently, we have reported a highly effective electrochemical technique for the oxidative conversion of semicarbazones and arylthiosemicarbazones to several useful heterocyclic compounds [53–56]. In continuation of our research applying the electrochemical method as a useful and efficient alternative for the synthesis of heterocyclic compounds, here we wish to report the electrochemical cyclization of aldehyde-*N*-arylhydrazone **1a–q** into corresponding symmetrical-2,5-disubstituted-1,3,4-oxadiazoles **5a–q** under mild conditions by combined electrolysis (Scheme 1).

Chiba and Okimoto [57] reported the synthesis of 1,3,4-oxadiazoles in low yield using methanol and sodium acetate as solvent and electrolyte, respectively. The low yield was attributed to the formation of acetate ion during the reaction which could react with the radical cation of the species to simultaneously suppress the ionization cyclization. However, in the present study, we have used lithium perchlorate as supporting electrolyte which is inert and gives a good yield of product without formation of any by-products at the platinum electrode.

Having these preliminary observations in hand, we have synthesized a series of aldehyde-*N*-arylhydrazones **1a–q** in order to generalize the scope of their oxidative cyclization. These substrates are easily accessible in high yields and purity from aroyl hydrazides and aldehydes.

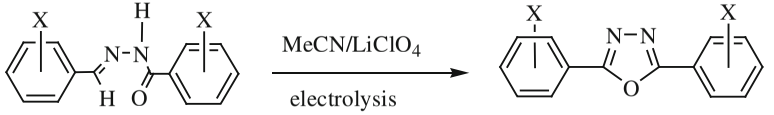
In all cases, the conversion of the substrate **1a–q** to desired oxadiazoles **5a–q** was completed within 3–4 h. Chromatographic analysis of the crude mixture indicated the presence of the desired 1,3,4-oxadiazole as the major product usually with excellent purity. The structures of the isolated oxidation products as oxadiazole derivatives **5a–q** were determined on the basis of their spectral analysis. The results obtained are summarized in Table 1.



X
H, *p*-Me, *p*-Cl, *p*-OMe, *m*-NO_2, *p*-F, *m*-Cl, *o*-OMe, *m, p*-$(OMe)_2$, *p*-OH, *p*-NO_2, *p*-NH_2, *m*-Br, *o*-OH, *o, p*-dichloro, *1*-Naphthol, *2*-Naphthol

Scheme 1 One-pot synthesis of symmetrical-2,5-disubstituted-1,3,4-oxadiazoles **5a–q** *N*′-benzylidene-*N*-benzhydrazide **1a** was chosen as a model substrate, in order to test the effectiveness of the process. We found that placing **1a** in pure MeCN at room temperature in the presence of $LiClO_4$ resulted in the formation of the desired 2,5-diphenyl-1,3,4-oxadiazole **5a** with complete consumption of the starting material in few hours. No significant by–products were detected by ^{1}H and ^{13}C NMR spectroscopy

Table 1 Electroorganic synthesis of symmetrical-2,5-disubstituted-1,3,4-oxadiazole **5a–q** and their physical parameters



1a-q **5a-q**

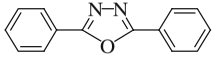
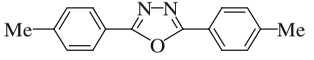
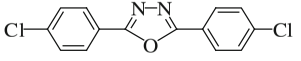
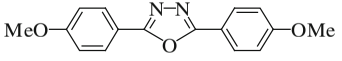
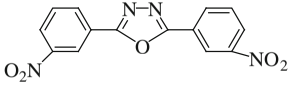
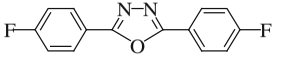
Entry	Conversion[a]	X	Time[b] (h)	Anode potential[c] (V vs. SCE)	Current (A)	Product[d] **5**
1	1a → 5a	H	3	2.0	0.61	
2	1b → 5b	*p*-Me	3	1.9	0.40	
3	1c → 5c	*p*-Cl	3	2.1	0.55	
4	1d → 5d	*p*-OMe	3	2.0	0.61	
5	1e → 5e	*m*-NO_2	4	1.7	0.36	
6	1f → 5f	*p*-F	3	2.1	0.56	

Table 1 continued

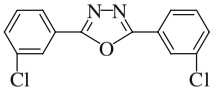
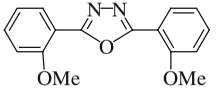
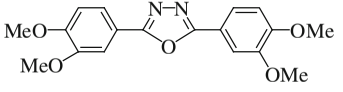
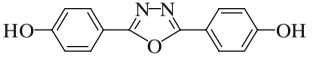
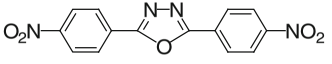
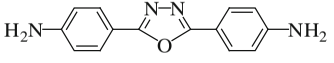
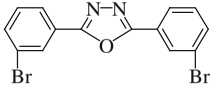
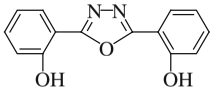
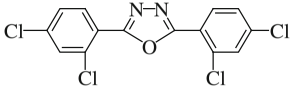
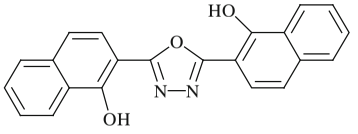
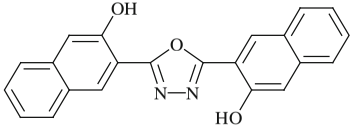
Entry	Conversion[a]	X	Time[b] (h)	Anode potential[c] (V vs. SCE)	Current (A)	Product[d] **5**
7	1g → 5g	*m*-Cl	4	2.0	0.58	
8	1 h → 5 h	*o*-OMe	4	1.7	0.42	
9	1i → 5i	*m*, *p*-$(OMe)_2$	3	1.8	0.44	
10	1j → 5j	*p*-OH	3	1.9	0.50	
11	1 k → 5 k	*p*-NO_2	3	2.2	0.65	
12	1 l → 5 l	*p*-NH_2	3	1.8	0.48	
13	1 m → 5 m	*m*-Br	3	1.8	0.42	

Table 1 continued

Entry	Conversion[a]	X	Time[b] (h)	Anode potential[c] (V vs. SCE)	Current (A)	Product[d] **5**
14	1n → 5n	*o*-OH	3	1.7	0.48	
15	1o → 5o	*o*, *p*-Dichloro	3	2.1	0.59	
16	1p–5p	*1*-Naphthol	4	2.0	0.50	
17	1q–5q	*2*-Naphthol	3	1.9	0.48	

[a] Prepared according to Scheme 1

[b] Reaction time at r.t.

[c] Applied potential of the substrates

[d] All compounds gave satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR, and EIMS) data

Cyclic voltammetry of **1a**

The cyclic voltammogram of 0.1 M substrate **1a** (scan rate: 0.01 V s^{-1}; $t = 25 \pm 1$ °C) exhibits two anodic peaks potential first at 0.90 V and the second at 2.0 V without any reduction peak potential which proves the transformation of **1a** to **5a** and within a two-electron oxidation process (Fig. 2).

Proposed reaction mechanism

In the proposed mechanism (Scheme 2), the aldehyde-*N*-arylhydrazone **1a–q**, undergoes electron oxidation to provide the radical cation intermediate **3**. Subsequent electron oxidation of **3** provides intermediate **4** which furnishes the corresponding oxadiazoles after intramolecular cyclization and deprotonation steps resulting in the formation of oxadiazoles **5a–q** in 61–93 % yields.

In the process of our study regarding variation of the nature of aldehyde moiety participating in the formation of oxadiazoles **5a–q**, we have observed that the best results were obtained with hydrazones derived from aromatic aldehydes possessing electron-donating groups, although the presence of an electron-withdrawing group on the aromatic ring decreased the yield. This is probably due to the fact that radical cation intermediates **4** having electron–donating substituents are better stabilized in comparison to that having electron-withdrawing substituents.

Experimental

Apparatus and reagents

Cyclic voltammetry was performed using ALSCH instruments electrochemical analyzer Model 600A with a traditional three-electrode system. Cyclic voltammetry

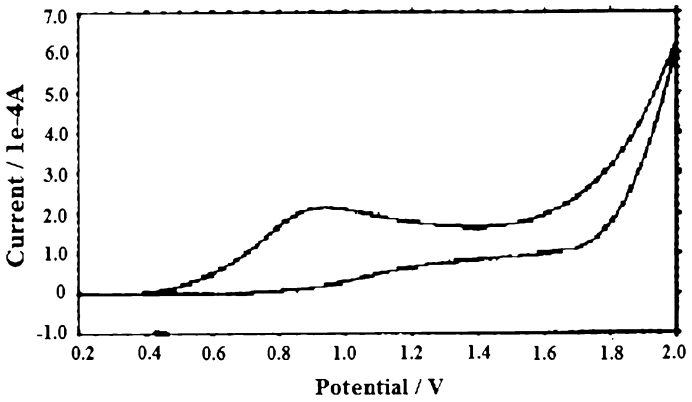
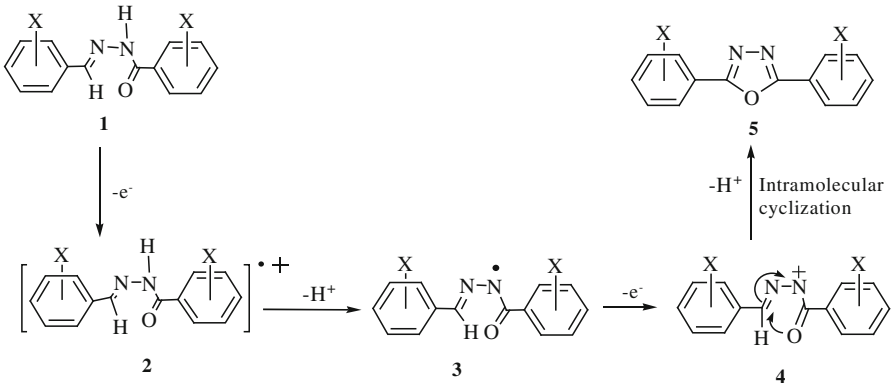


Fig. 2 Cyclic voltammogram of 0.1 M solution of aldehyde-*N*-arylhydrazones **1a** in 0.1 M ($LiClO_4$–MeCN) on a platinum electrode (area 2.5 mm^2) at a scan rate of 0.01 V s^{-1}, auxiliary electrode; platinum mesh, reference electrode; SCE, $t = 25 \pm 1$ °C



Scheme 2 Proposed mechanism for the synthesis of symmetrical-2,5-disubstituted-1,3,4-oxadiazoles **5a–q**

of substrate **1a** were recorded using MeCN as solvent and $LiClO_4$ as supporting electrolyte at 25 °C. All experiments were carried out in a conventional electrochemical cell, the electrode system containing a platinum electrode working as well as the auxiliary electrode, and a saturated calomel electrode (SCE) as reference electrode. The potential of the working electrode was measured versus SCE as reference electrode at a scan rate of 0.01 V s^{-1}.

Melting points were obtained using a capillary melting point apparatus (Mel-Temp®) and are uncorrected. IR spectra were registered with a Shimadzu 8201 PC spectrometer in KBr pellets. ^1H and ^{13}C NMR spectra were recorded with a Bruker DRX 400 (400 MHz) spectrometer in $CDCl_3$. Chemical shifts are reported in ppm downfield from Me_4Si as internal reference. Mass spectra were obtained directly with a Shimadzu GCMS-QP5050A (EI) spectrometer.

Chemicals used in reaction were reagent-grade, from Merck and Fluka. These chemicals were used without further purification. Water used for the experiment was double-distilled.

General procedure for the synthesis of aldehyde-*N*-arylhydrazones **1a–q**

A mixture of 3 mmol of aroyl hydrazines and 3 mmol of aryl aldehydes was refluxed in 40 mL of ethanol for 7 h. Then, the reaction mixture was cooled to r.t., and the precipitates were collected by filtration and recrystallized from ethanol to give the pure aldehyde-*N*-arylhydrazones **1a–q**. The structures of the products **1a–q** were confirmed from their spectral data and comparison of melting points with literature values [58].

Characterization data of representative compound **1a**

Melting point 207–208 °C [14]. IR (KBr) ν: 3,236 (N–H), 1,667 (C=O), 1,640 (C=N), 1,472 (C=C aromatic), 3,060 (C–H aromatic) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 10.5 (bs, 1H), 8.8 (s, 1H) 7.29–7.96 (m, 10H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ 127.2, 128.5, 129.0, 130.7, 131.1, 132.0, 133.4, 154.6, 170.1. EIMS (*m*/*z*): 224(M^+).

Controlled potential electrolysis (CPE)

Preparative-scale [59] electrolysis were carried out in a 250-mL three-electrode cell assembly with a platinum plate (flattened sheet of dimension 1.0 × 1.0 cm), working as well as the auxiliary electrode, and SCE [53–56, 60] as reference electrode. Electrooxidation of the substrates were as follows: a solution of substrate **1a–q** (10 mmol) and powdered $LiClO_4$ (5 mmol) in MeCN (100 mL) was electrolyzed in an undivided cell equipped with a magnetic stirrer under constant potential electrolysis indicated in Table 1. After the electrolysis was finished, the MeCN was evaporated using the rotator evaporator, extracted with $CHCl_3$, and after removal of the solvent, the residue was purified by EtOH and recrystallization from small amounts of EtOH. The structures of the synthesized products **5a–q** were clearly determined on the basis of their IR, ^{1}H NMR, ^{13}C NMR, and MS spectra. The results obtained are summarized in Tables 1 and 2.

Characterization data of representative compounds (**5a–q**)

*2,5-Bis-(phenyl)-1,3,4-oxadiazole (**5a**)*

IR (KBr) ν: 1,066 (C–O–C), 1614 (C=N), 1,465 (C=C aromatic), 3,045 (C–H aromatic) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.58 (m, 6H), 8.14–8.16

Table 2 Physical and yield data of synthesized compound **5a–q**

Compound	Empirical formula	Melting point (°C)	Yield (%)
5a	$C_{14}H_{10}N_2O$	135–137 (137–138) [61]	77
5b	$C_{16}H_{14}N_2O$	175–177 (175) [62]	86
5c	$C_{14}H_8N_2OCl_2$	239–240 (241–242) [62]	69
5d	$C_{16}H_{14}N_2O_3$	159–161 (160) [63]	90
5e	$C_{14}H_8N_4O_5$	135–137 (136–138) [64]	63
5f	$C_{14}H_8N_2OF_2$	200–202 (200) [63]	65
5g	$C_{14}H_8N_2OCl_2$	156–158 (154–156) [16]	69
5h	$C_{16}H_{14}N_2O_3$	99–101 (98–99) [62]	90
5i	$C_{18}H_{18}N_2O_5$	176–179 (179–181) [61]	93
5j	$C_{14}H_{10}N_2O_3$	349–351 (350) [62]	81
5k	$C_{14}H_8N_4O_5$	314–316 (314) [62]	61
5l	$C_{14}H_{12}N_4O$	254–256 (253–254) [16]	83
5m	$C_{14}H_8N_2OBr_2$	199–202 (200–201) [62]	74
5n	$C_{14}H_{10}N_2O_3$	119–122 (121) [62]	78
5o	$C_{14}H_6N_2OCl_4$	194–197 (194–195) [64]	67
5p	$C_{22}H_{14}N_2O_3$	198–200	78
5q	$C_{22}H_{14}N_2O_3$	199–201	82

(m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.9, 126.9, 129.0, 131.7, 164.6. EIMS (*m/z*): 222 [M^+].

*2,5-Bis-(p-methylphenyl)-1,3,4-oxadiazole (**5b**)*

IR (KBr) ν: 1,075 (C–O–C), 1,617 (C=N), 1475 (C=C aromatic), 3,035 (C–H aromatic), 3,010 (C–H methyl), 985, 890, 755 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 6H), 7.32 (d, 4H), 8.01(d, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 121.2, 126.7, 129.6, 142.0, 164.4. EIMS (*m/z*): 250 [M^+].

*2,5-Bis-(p-chlorophenyl)-1,3,4-oxadiazole (**5c**)*

IR (KBr) ν: 1,065 (C–O–C), 1,605 (C=N), 1462 (C=C aromatic), 3,052 (C–H aromatic), 689 (C–Cl), 960, 865, 750 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, 4H), 8.00 (d, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.0, 128.1, 129.4, 138.0, 167.8. EIMS (*m/z*): 290 [M^+].

*2,5-Bis-(p-methoxyphenyl)-1,3,4-oxadiazole (**5d**)*

IR (KBr) ν: 1,076 (C–O–C), 1,640 (C=N), 1472 (C=C aromatic), 3,060 (C–H aromatic), 2,815 (O–CH_3), 980, 810, 765 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 6H), 7.01–7.03 (m, 4H), 8.04–8.06 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.5, 114.5, 116.5, 128.6, 162.2, 164.1. EIMS (*m/z*): 282 (M^+).

*2,5-Bis-(m-nitrophenyl)-1,3,4-oxadiazole (**5e**)*

IR (KBr) ν: 1,080 (C–O–C), 1,622 (C=N), 1,456 (C=C aromatic), 3,059 (C–H aromatic), 1,550 (N=O), 915, 870, 775 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–8.61 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.0, 123.5, 129.8, 133.0, 137.3, 148.7, 163.6, 172.7. EIMS (*m/z*): 312 [M^+].

*2,5-Bis-(p-fluorophenyl)-1,3,4-oxadiazole (**5f**)*

IR (KBr) ν: 1058 (C–O–C), 1622 (C=N), 1465 (C=C aromatic), 3048 (C–H aromatic), 830 (C–F), 984, 832, 765 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99–7.15 (m, 4H), 7.96–8.16 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.0, 128.5, 132.1, 162.1, 167.8, 172.6. EIMS (*m/z*): 258 [M^+].

*2,5-Bis-(m-chlorophenyl)-1,3,4-oxadiazole (**5g**)*

IR (KBr) ν: 1,065 (C–O–C), 1612 (C=N), 1,462 (C=C aromatic), 3,052 (C–H aromatic), 690 (C–Cl), 985, 830, 758 (substituted benzene) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.60 (m, 6H), 7.89–7.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.1, 127.4, 128.8, 130.3, 134.2, 137.8, 167.2, 171.4. EIMS (*m/z*): 293 [M^+].

*2,5-Bis-(o-methoxyphenyl)-1,3,4-oxadiazole (**5h**)*

IR (KBr) ν: 1,056 (C–O–C), 1,617 (C=N), 1,465 (C=C aromatic), 3,049 (C–H aromatic), 2,815 (O-CH_3), 965, 892, 750 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.95 (s, 6H), 7.03–7.07 (m, 4H), 7.45–7.49 (m, 2H), 7.97–7.99 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 114.5, 121.2, 122.0, 128.0, 129.4, 160.4, 167.4, 172.7. EIMS (*m*/*z*): 282 [M^+].

*2,5-Bis-(m,p-dimethoxyphenyl)-1,3,4-oxadiazole (**5i**)*

IR (KBr) ν: 1,050 (C–O–C), 1,621 (C=N), 1,459 (C=C aromatic), 3,045 (C–H aromatic), 2,810 (O–CH_3), 978, 866, 751 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.95 (s, 6H), 3.98 (s, 6H), 6.96 (d, 2H), 7.63–7.68 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.0, 56.2, 109.5, 111.1, 116.6, 120.3, 149.4, 151.9, 164.2. EIMS (*m*/*z*): 342 [M^+].

*2,5-Bis-(p-hydroxyphenyl)-1,3,4-oxadiazole (**5j**)*

IR (KBr) ν: 1,046 (C–O–C), 1,606 (C=N), 1,465 (C=C aromatic), 3,052 (C–H aromatic), 3,594 (O–H), 967, 885, 785 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.95 (d, 4H), 7.91 (d, 4H), 10.27 (s, 2H, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.2, 116.1, 128.4, 160.6, 163.5. EIMS (*m*/*z*): 254 [M^+].

*2,5-Bis-(p-nitrophenyl)-1,3,4-oxadiazole (**5k**)*

IR (KBr) ν: 1,057 (C–O–C), 1610 (C=N), 1,463 (C=C aromatic), 3,056 (C–H aromatic), 1,555 (N=O), 974, 872, 790 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, 4H), 8.56 (d, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.4, 126.9, 129.3, 149.3, 162.6. EIMS (*m*/*z*): 312 [M^+].

*2,5-Bis-(p-aminophenyl)-1,3,4-oxadiazole (**5l**)*

IR (KBr) ν: 1,062 (C–O–C), 1,618 (C=N), 1,468 (C=C aromatic), 3,058 (C–H aromatic), 3,416 (N–H), 985, 890, 755 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.61–6.66 (m, 4H), 7.85–7.87 (m, 4H), 7.16 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 115.5, 126.4, 127.7, 146.6, 164.3, 171.5. EIMS (*m*/*z*): 252 [M^+].

*2,5-Bis-(m-bromophenyl)-1,3,4-oxadiazole (**5m**)*

IR (KBr) ν: 1056 (C–O–C), 1621 (C=N), 1461 (C=C aromatic), 3032 (C–H aromatic), 736 (C–Br), 985, 890, 755 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, 2H), 7.54 (br s, 2H), 7.35 (t, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.5, 126.0, 130.2, 131.1, 131.7, 138.6, 162.5, 172.8. EIMS (*m*/*z*): 380 [M^+].

*2,5-Bis-(o-hydroxyphenyl)-1,3,4-oxadiazole (**5n**)*

IR (KBr) ν: 1,035 (C–O–C), 1,609 (C=N), 1,449 (C=C aromatic), 3,018 (C–H aromatic), 983, 891, 753 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, 2H), 7.44–7.51 (m, 4H), 7.94 (d, 2H), 10.91 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.1, 121.5, 123.6, 128.3, 129.8, 155.7, 167.2, 172.6. EIMS (*m*/*z*): 254 [M^+].

*2,5-Bis-(o,p-dichlorophenyl)-1,3,4-oxadiazole (**5o**)*

IR (KBr) ν: 1,066 (C–O–C), 1,611 (C=N), 1,465 (C=C aromatic), 3,054 (C–H aromatic), 695 (C–Cl), 985, 890, 757 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (dd, 2H), 7.44 (d, 2H), 7.89 (d, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.9, 127.4, 130.8, 131.6, 133.5, 138.0, 162.3. EIMS (*m*/*z*): 357 [M^+].

*2,5-Bis-(naphthalen-1-ol)-1,3,4-oxadiazole (**5p**)*

IR (KBr) ν: 1,059 (C–O–C), 1,606 (C=N), 1,469 (C=C aromatic), 3,057 (C–H aromatic), 690 (C–Cl), 980, 895, 760 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.4 (s, 2H), 7.34–8.09 (m, 6H), 8.45 (d, $J = 7.7$ Hz, 2H), 7.46 (d, $J = 8.6$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.7, 121.1, 121.4, 124.2, 124.9, 126.1, 126.4, 127.6, 134.7, 150.1, 168.2. EIMS (*m*/*z*): 354 [M^+].

*2,5-Bis-(naphthalen-2-ol)-1,3,4-oxadiazole (**5q**)*

IR (KBr) ν: 1,064 (C–O–C), 1,609 (C=N), 1,474 (C=C aromatic), 3,045 (C–H aromatic), 696 (C–Cl), 976, 890, 765 (substituted benzene) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.4 (s, 2H), 7.03–7.94 (m, 10H), 7.89 (d, $J = 7.7$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 109.8, 123.6, 125.5, 126.3, 126.4, 124.9, 127.7, 129.4, 128.3, 134.6, 151.8, 169.8. EIMS (*m*/*z*): 354 [M^+].

Conclusion

In summary, we have developed a convenient and efficient one-pot electrochemical synthesis of 2,5-disubstituted-1,3,4-oxadiazole derivatives at ambient temperature. The novelty of this methodology can be summarized as follows:

(1) We first synthesized a series of 2,5-disubstituted-1,3,4-oxadiazole derivatives in good to excellent yield by utilizing inexpensive reagents, simple equipment, and undivided cell.
(2) In our study, we have used lithium perchlorate as supporting electrolyte which is inert and gives good yield of product without formation of any by-product at the platinum electrode.

Further expansion of the scope and application of this methodology for the synthesis of bioactive compounds is currently underway and will be reported in due course.

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