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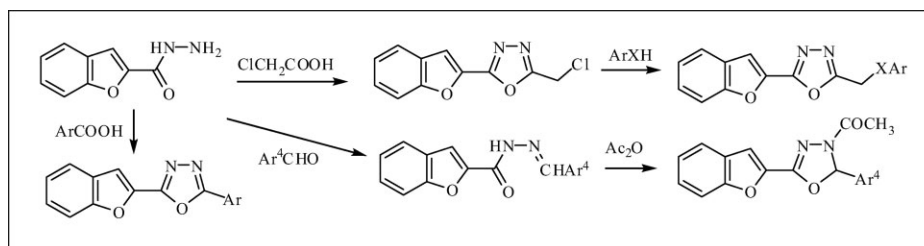
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In this study, the synthesis of series of 2-benzo[*b*]furan-substituted 1,3,4-oxadiazole derivatives using readily available 2-benzo[*b*]furan carboxylic acid hydrazide as starting material has been investigated.

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INTRODUCTION

1,3,4-Oxadiazoles are five-membered aromatic heterocycles with great utility in synthetic, medicinal, and material chemistry [1–4]. The widespread use of 1,3,4-oxadiazoles as a scaffold in medicinal chemistry establishes this moiety as an important bioactive class of heterocycles. These molecules are also utilized as pharmacophores because of their favorable metabolic profile and ability to engage in hydrogen bonding. In particular, marketed antihypertensive agents, such as tiodazosin [5] and nesapidil [6], and antibiotics, such as furamizole [7], contain the oxadiazole nucleus. They are also useful as HIV integrase inhibitors and angiogenesis inhibitors [7,8]. 2,5-Disubstituted 1,3,4-oxadiazoles have also attracted significant interest because of their applications in organic light-emitting diodes, photoluminescence, polymers, and material science [9,10].

Several methods have been reported in the literature for the synthesis of 1,3,4-oxadiazoles. Most of these protocols are multistep in nature and generally involve the cyclization of diacylhydrazides or acylthiosemicarbazides and the oxidation of acylhydrozones [11] with a variety of reagents such as thionyl chloride, phosphorus oxychloride, or sulfuric acid, usually under harsh reaction conditions. Recently, a few efficient examples have been reported for the synthesis of 1,3,4-oxadiazoles by treatment of readily available carboxylic acids with acid hydrazides under acid conditions [12]. 1,3,4-Oxadiazoles by condensation of acid hydrazide and triethyl orthoalkanoates under microwave irradiations have also been reported. This green protocol was catalyzed efficiently by solid-supported Nafion_NR50 [13].

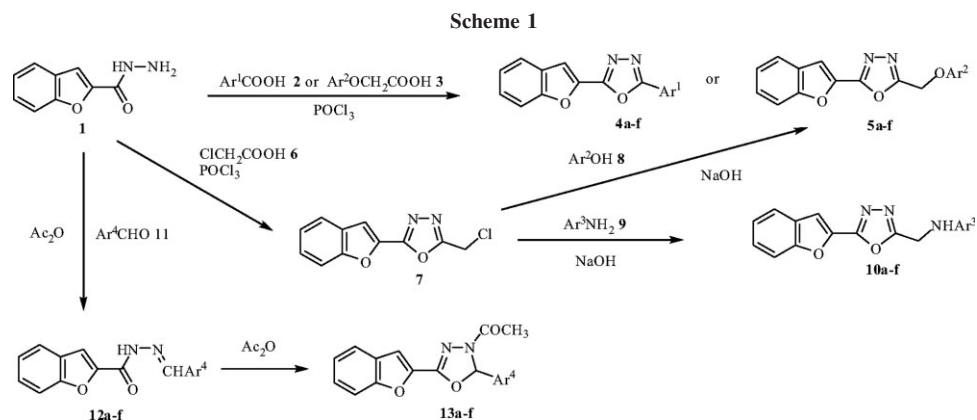
2-Substituted benzo[*b*]furans [14,15] are widely distributed in nature and have a range of biological activities [16], for example, as insulin-sensitivity enhancers [17], inhibitors of tubulin polymerase [18], antagonists of the A1 adenosine receptor [19], inhibitors of testosterone 5R-reductase [20], and inhibitors of 5-lipoxygenase [21]. Recently, of particular interest is BPAP, which enhances impulse propagation mediated by the release of catecholamines and serotonin in the brain and so may slow progression of Parkinson's and Alzheimer's disease [22].

In previous reports, we demonstrated the use of 2-benzo[*b*]furan carboxylic acid and 2-benzo[*b*]furan carboxylic acid hydrazide as versatile building blocks for the synthesis of functionalized heterocycles [23]. We now report the investigations on the use of 2-benzo[*b*]furan carboxylic acid hydrazide (**1**) for the synthesis of 2,5-disubstituted 1,3,4-oxadiazole derivatives **4a–f**, **5a–f**, **10a–f**, and **13a–f** (Schemes 1).

RESULTS AND DISCUSSION

Scheme 1 outlines the synthetic sequences used in our laboratories for the preparation of the key intermediate **1** and its derivatives 1,3,4-oxadiazoles **4**, **5**, **10**, and **13**.

Synthesis of 2-aryl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles 4a–f and 2-aryloxymethyl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles 5a–f. Treatment of 2-benzofuroyl hydrazine (**1**) with 1 equiv of substituted benzoic acids (**2a–f**) in the presence of POCl₃ under reflux for 6 h produced 2,5-diaryl-substituted 1,3,4-oxadiazoles (**4a–f**) in high yields. However, the reaction of compound



1 with aryloxyacetic acids (**3a–f**) need catalytic amounts of pyridine in reflux POCl₃ and longer time (8 h) to give the corresponding 1,3,4-oxadiazoles (**5a–f**) in higher yields (method A) (entries 7–12, Table 1).

Synthesis of 2-chloromethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazole (7) and its utilization for the synthesis of 2-aryloxymethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazoles (5a–f) and 2-arylaminomethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazoles (10a–f). The reaction of acylhydrazine (1) with 2-chloroacetic acid in xylene in

the presence of POCl₃ under reflux for 8 h gave compound 7 in 89% yield. Treatment of 7 with 1.1 equiv of substituted phenylamines (**9a–f**) gave 2-arylamino-methyl-5-(2-benzo[b]furan)-1,3,4-oxadiazoles (**10a–f**) (entries 13–18, Table 1), which cannot be synthesized by cyclization reaction of corresponding acids and acylhydrazines, and the reaction gave high yields. In examining the reactivity of 2-chloromethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazole (7), the reaction of 7 with aryl-substituted phenols (**8**) was carried out in the

Table 1
Physical and analytical data of compounds.^a

Entry	Compd.	Aryl	Yield ^b (%)	Molecular formula	Analysis (%) calcd./found		
					C	H	N
1	4a	C ₆ H ₅	81	C ₁₆ H ₁₀ N ₂ O ₂	73.27/73.05	3.84/3.92	10.68/10.51
2	4b	4-CH ₃ OC ₆ H ₄	75	C ₁₇ H ₁₂ N ₂ O ₃	69.86/69.64	4.14/4.10	9.58/9.45
3	4c	2-ClC ₆ H ₄	81	C ₁₆ H ₉ ClN ₂ O ₂	64.77/64.49	3.06/3.18	9.44/9.38
4	4d	4-ClC ₆ H ₄	73	C ₁₆ H ₉ ClN ₂ O ₂	64.77/64.95	3.06/3.13	9.44/9.25
5	4e	2-NO ₂ C ₆ H ₄	83	C ₁₆ H ₉ N ₃ O ₄	62.54/62.40	2.95/3.05	13.68/13.56
6	4f	4-NO ₂ C ₆ H ₄	78	C ₁₆ H ₉ N ₃ O ₄	62.54/62.74	2.95/2.86	13.68/13.49
7	5a	C ₆ H ₅ OCH ₂	65(88)	C ₁₇ H ₁₂ N ₂ O ₃	69.86/69.98	4.14/4.20	9.58/9.68
8	5b	4-ClC ₆ H ₄ OCH ₂	68(93)	C ₁₇ H ₁₁ ClN ₂ O ₃	62.49/62.31	3.39/3.48	8.57/8.68
9	5c	2-CH ₃ C ₆ H ₄ OCH ₂	72(96)	C ₁₈ H ₁₄ N ₂ O ₃	70.58/70.80	4.61/4.53	9.15/9.04
10	5d	4-CH ₃ C ₆ H ₄ OCH ₂	60(77)	C ₁₈ H ₁₄ N ₂ O ₃	70.58/70.35	4.61/4.69	9.15/9.26
11	5e	4-CH ₃ OC ₆ H ₄ OCH ₂	63(88)	C ₁₈ H ₁₄ N ₂ O ₄	67.17/67.07	4.45/4.38	8.58/8.69
12	5f	2-NO ₂ C ₆ H ₄ OCH ₂	60(83)	C ₁₇ H ₁₁ N ₃ O ₅	60.54/60.68	3.29/3.35	12.46/12.39
13	10a	C ₆ H ₅	78	C ₁₈ H ₁₆ N ₃ O ₂	70.09/70.28	4.50/4.41	14.42/14.55
14	10b	4-CH ₃ C ₆ H ₄	86	C ₁₈ H ₁₅ N ₃ O ₂	70.81/71.01	4.95/4.90	13.76/14.68
15	10c	4-CH ₃ OC ₆ H ₄	80	C ₁₈ H ₁₅ N ₃ O ₃	67.28/67.42	4.71/4.67	13.08/13.17
16	10d	4-ClC ₆ H ₄	75	C ₁₇ H ₁₂ ClN ₃ O ₂	62.68/62.56	3.71/3.78	12.90/11.78
17	10e	2-NO ₂ C ₆ H ₄	76	C ₁₇ H ₁₂ N ₄ O ₄	60.71/60.48	3.60/3.72	16.66/16.84
18	10f	4-NO ₂ C ₆ H ₄	81	C ₁₇ H ₁₂ N ₄ O ₄	60.71/60.98	3.60/3.72	16.66/16.84
19	13a	C ₆ H ₅	70(78)	C ₁₈ H ₁₄ N ₂ O ₃	70.58/70.76	4.61/4.55	9.15/9.06
20	13b	4-CH ₃ OC ₆ H ₄	72(80)	C ₁₉ H ₁₆ N ₂ O ₄	67.85/68.02	4.79/4.70	8.33/8.42
21	13c	2-ClC ₆ H ₄	60(67)	C ₁₈ H ₁₃ ClN ₂ O ₃	63.44/63.62	3.85/3.92	8.22/8.08
22	13d	4-ClC ₆ H ₄	62(75)	C ₁₈ H ₁₃ ClN ₂ O ₃	63.44/63.19	3.85/3.91	8.22/8.31
23	13e	3-NO ₂ C ₆ H ₄	65(78)	C ₁₈ H ₁₃ N ₃ O ₅	61.54/61.73	3.73/3.90	11.96/12.08
24	13f	4-NO ₂ C ₆ H ₄	65(79)	C ₁₈ H ₁₃ N ₃ O ₅	61.54/61.32	3.73/3.81	11.96/11.77

The values in parenthesis indicate the yields of method B for compounds **5** and **13**.

^a Isolated yield.

^b Yields of method A for compounds **5** and **13**.

presence of NaOH powder under reflux ethanol condition. Compounds **5a–f** could also be obtained in good yields (method B) (entries 7–12, Table 1).

One-pot synthesis of 3-acetyl-2-aryl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazolines (13a–f). First, the synthesis of 1,3,4-oxadiazoles **13a–f** were investigated through a two-step pathway. Treatment of **1** with aromatic aldehydes (**11a–f**) in the presence of catalytic amounts of Ac₂O under refluxing ethanol for 6 h gave 2-benzo[*b*]furoyl hydrazones **12a–f**, which upon treatment in refluxing Ac₂O afforded 1,3,4-oxadiazolines **13a–f** in moderate total yields (entries 19–24, Table 1).

The ability of Ac₂O to promote both steps led us to investigate the one-pot synthesis of oxadiazolines **13a–f** starting from the same substrates. When acylhydrazine (**1**) and aromatic aldehydes (**11a–f**) were stirred in Ac₂O under reflux, the corresponding oxadiazolines **13a–f** were obtained in good yields after 2 h (entries 19–24, Table 1). It could be seen from Table 1 that the one-pot method was a more efficient way than the two-step procedures for the preparation of compounds **13a–f**.

In conclusion, the synthesis of series of 2-benzo[*b*]furan-substituted 1,3,4-oxadiazole derivatives using readily available 2-benzo[*b*]furan carboxylic acid hydrazide as starting material has been investigated. These processes are highly efficient with good yields and use cheap and easily available aldehydes and acids.

EXPERIMENTAL

All reagents were obtained commercially and used without further purification. Melting points were determined on an XT-4 electrothermal micromelting point apparatus and uncorrected. IR spectra were recorded using KBr pellets on Nicolet AVATAR 36 FTIR spectrophotometer. For compounds **4a–f** and **5a–f**, NMR spectra were recorded on an Avanci-D2X-200 instrument using CDCl₃ as solvent and TMS as internal standard. For compounds **7**, **10a–f**, and **13a–f**, NMR spectra were recorded at 400 (¹H) and 100 (¹³C) MHz, respectively, on a Varian Mercury plus-400 instrument using CDCl₃ as solvent and TMS as internal standard.

General procedure for the synthesis of 2-aryl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles (4a–f). The mixture of 2-benzo[*b*]furan carboxylic acid hydrazide (**1**) (1 mmol), substituted benzoic acids (**2a–f**) (1 mmol), and POCl₃ (5 mL) was stirred under reflux condition for 6 h. The excess of POCl₃ was evaporated under reduced pressure. The residue was poured into ice water (50 mL). Then the precipitate was filtered and washed with aqueous solution of NaOH (1%) and subsequently with water. The solid was recrystallized from EtOH to give the products 2-aryl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles (**4a–f**).

4a: m.p. 170–172°C; IR (KBr): 1633, 1579, 1506, 1210, 1058 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.00–8.14 (m, 10H, Ar-H); ¹³C NMR (75 Hz, CDCl₃): δ = 164.5, 159.8, 158.4, 144.1, 129.8, 128.1, 127.7, 127.1, 124.8, 124.6, 122.9, 121.2, 116.9, 110.4.

4b: m.p. 153–155°C; IR (KBr): 1639, 1580, 1501, 1209, 1052 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.00–8.14 (m,

9H, Ar-H), 3.80 (s, 3H, OCH₃); ¹³C NMR (75 Hz, CDCl₃): δ = 164.5, 161.2, 159.2, 144.5, 130.0, 128.2, 127.6, 126.9, 124.9, 124.2, 123.0, 116.3, 112.6, 110.7, 57.9.

4c: m.p. 126–128°C; IR (KBr): 1640, 1577, 1511, 1202, 1056 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.15–7.81 (m, 9H, Ar-H); ¹³C NMR (75 Hz, CDCl₃): δ = 164.7, 158.6, 156.4, 144.3, 139.8, 132.8, 129.5, 128.2, 127.7, 127.4, 124.9, 124.2, 122.9, 122.2, 116.7, 110.1.

4d: m.p. 177–179°C; IR (KBr): 1638, 1582, 1505, 1209, 1052 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.00–7.84 (m, 9H, Ar-H); ¹³C NMR (75 Hz, CDCl₃): δ = 164.5, 158.3, 156.4, 144.4, 136.8, 130.3, 127.6, 127.2, 124.5, 124.3, 122.3, 120.4, 116.4, 110.2.

4e: m.p. 140–142°C; IR (KBr): 1640, 1577, 1511, 1202, 1056 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.16–8.14 (m, 9H, Ar-H); ¹³C NMR (75 Hz, CDCl₃): δ = 164.8, 160.5, 158.6, 155.3, 147.3, 140.2, 130.8, 129.7, 128.4, 127.4, 124.6, 124.0, 122.8, 122.5, 116.9, 110.4.

4f: Yield 78%, m.p. 257–259°C; IR (KBr): 1638, 1582, 1505, 1209, 1052 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.16–8.46 (m, 9H, Ar-H); ¹³C NMR (75 Hz, CDCl₃): δ = 164.7, 158.8, 155.3, 147.5, 136.2, 135.2, 131.8, 129.3, 128.6, 124.9, 124.3, 122.3, 116.6, 110.6.

General procedure for the synthesis of 2-aryl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles (5a–f).

Method A. The mixture of 2-benzo[*b*]furan carboxylic acid hydrazide (**1**) (1 mmol), substituted aryloxyacetic acids (**3a–f**) (1 mmol), pyridine (0.1 mL), and POCl₃ (5 mL) were stirred under reflux condition for 8 h. The excess of POCl₃ was evaporated under reduced pressure. The residue was poured into ice water (50 mL). Then the precipitate was filtered and washed with aqueous solution of NaOH (1%) and subsequently with water. The solid was recrystallized from EtOH to give the products 2-aryloxymethyl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles (**5a–f**).

Method B. The mixture of 2-chloromethyl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazole (**7**) (1 mmol), substituted phenols (**8**) (1.1 mmol), and NaOH (1.1 mmol) in 10 mL ethanol were stirred at 80°C for 12 h. The mixture was poured into ice water (50 mL). Then the precipitate was filtered and washed with water (3 × 10 mL). The solid was recrystallized from EtOH to give the product 2-aryloxymethyl-5-(2-benzo[*b*]furan)-1,3,4-oxadiazoles (**5a–f**).

5a: m.p. 184–186°C, IR (KBr): 1640, 1577, 1511, 1202, 1056 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.01–7.76 (m, 10H, Ar-H), 5.37 (s, 2H, CH₂); ¹³C NMR (75 Hz, CDCl₃): δ = 164.4, 161.2, 158.3, 157.8, 154.6, 129.8, 128.0, 127.7, 124.3, 122.8, 120.3, 114.0, 112.3, 110.5, 72.6.

5b: m.p. 130–132°C, IR (KBr): 1638, 1580, 1489, 1214, 1048 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.10–7.91 (m, 9H, Ar-H), 5.37 (s, 2H, CH₂); ¹³C NMR (75 Hz, CDCl₃): δ = 164.6, 161.3, 158.3, 156.6, 154.8, 131.4, 130.9, 127.5, 126.5, 124.8, 123.2, 122.5, 114.1, 112.6, 110.3, 72.6.

5c: m.p. 187–189°C; IR (KBr): 1651, 1564, 1512, 1214, 1056 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 6.88–7.92 (m, 9H, Ar-H), 5.37 (s, 2H, CH₂), 2.36 (s, 3H, CH₃); ¹³C NMR (75 Hz, CDCl₃): δ = 164.3, 161.5, 158.6, 156.3, 154.1, 131.3, 131.4, 130.1, 127.7, 124.7, 124.8, 123.0, 122.1, 121.7, 112.6, 110.2, 72.9, 22.1.

5d: m.p. 137–139°C; IR (KBr): 1650, 1569, 1520, 1214, 1059 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 6.94–7.92 (m, 9H,

Ar-H), 5.36 (s, 2H, CH₂), 2.35 (s, 3H, CH₃); ¹³C NMR (75 Hz, CDCl₃): δ = 164.8, 160.4, 158.9, 156.9, 157.4, 131.1, 130.8, 128.1, 127.5, 124.0, 122.3, 120.8, 111.9, 110.3, 72.5, 22.2.

5e: m.p. 141–142°C; IR (KBr) 1639, 1567, 1501, 1208, 1052 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 6.84–7.73 (m, 9H, Ar-H), 5.37 (s, 2H, CH₂), 3.77 (s, 3H, CH₃O); ¹³C NMR (75 Hz, CDCl₃): 161.9, 160.3, 157.8, 156.9, 155.0, 154.0, 130.7, 128.8, 127.1, 126.0, 118.5, 115.7, 112.2, 111.2, 58.9, 56.1.

5f: m.p. 192–194°C; IR (KBr): 1652, 1580, 1508, 1206, 1056 cm⁻¹; ¹H NMR (200 Hz, CDCl₃): δ = 7.02–8.21 (m, 9H, Ar-H), 5.37 (s, 2H, CH₂); ¹³C NMR (75 Hz, CDCl₃): δ = 164.9, 160.9, 158.8, 156.0, 155.8, 145.8, 132.3, 130.2, 127.3, 124.2, 124.0, 122.8, 121.1, 114.4, 112.2, 110.5, 70.7.

Synthesis of 2-chloromethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazole (7). The mixture of 2-benzo[b]furan carboxylic acid hydrazide (**1**) (10 mmol), 2-chloroacetic acid (**6**) (11 mmol), xylene (10 mL), and POCl₃ (5 mL) were stirred under reflux for 8 h. The excess of POCl₃ and solvent were evaporated under reduced pressure. The residue was poured into ice water (50 mL). Then the precipitate was filtered and washed with aqueous solution of NaOH (1%) and subsequently with water. The solid was recrystallized from EtOH to give the product 2-chloromethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazole (**7**).

Yield 89%, m.p. 149–151°C; IR (KBr): 3024, 1638, 1574 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.71 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.63 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.58 (s, 1H, Ar-H), 7.47 (t, *J* = 8.0 Hz, Ar-H), 7.34 (t, *J* = 8.0 Hz, Ar-H), 4.82 (s, 2H, CH₂).

General procedure for the synthesis of 2-arylamino-methyl-5-(2-benzo[b]furan)-1,3,4-oxadiazoles (10a–f). The mixture of 2-chloromethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazole (**7**) (1 mmol), arylamines (**9**) (1.1 mmol), and NaOH (1.1 mmol) in 10 mL ethanol were stirred at 80°C for 12 h. The mixture was poured into ice water (50 mL). Then the precipitate was filtered and washed with water (3 × 10 mL). The solid was recrystallized from EtOH to give the product 2-aryloxymethyl-5-(2-benzo[b]furan)-1,3,4-oxadiazoles (**10a–f**).

10a: m.p. 204–205°C; IR (KBr): 3334, 1579, 1642, 1203, 1060 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.63 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.57 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.74–7.40 (m, 2H, Ar-H), 7.34–7.23 (m, 1H, Ar-H), 7.21–6.85 (m, 5H, Ar-H), 4.30 (s, 1H, NH); ¹³C NMR (100 Hz, CDCl₃): δ = 163.9, 158.0, 154.9, 146.5, 140.8, 128.7, 128.2, 126.8, 126.9, 124.5, 123.0, 115.2, 111.8, 109.5, 38.8.

10b: m.p. 150–151°C; IR (KBr): 3384, 1558, 1644, 1206, 1171 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.65 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.58 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.46–7.40 (m, 2H, Ar-H), 7.33–7.25 (m, 1H, Ar-H), 7.01 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.68 (d, 2H, *J* = 8.0 Hz, Ar-H), 4.35 (s, 2H, NH); 4.31 (s, 1H, NH), 2.23 (s, 3H, CH₃); ¹³C NMR (100 Hz, CDCl₃): δ = 164.6, 158.3, 155.6, 143.9, 140.3, 129.9, 128.3, 127.1, 127.1, 124.0, 122.3, 113.4, 110.3, 39.4, 20.3.

10c: m.p. 128–130°C; IR (KBr): 3304, 1557, 1641, 1241, 1173 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.64 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.54 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.45–7.39 (m, 2H, Ar-H), 7.31–7.28 (m, 1H, Ar-H), 6.72 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.69 (d, 2H, *J* = 8.0 Hz, Ar-H), 4.32 (s, 1H, NH), 3.77 (s, 3H, CH₃O); ¹³C NMR (100 Hz, CDCl₃): δ = 164.9, 159.3, 155.8, 154.8, 140.9, 136.7, 128.5, 127.9, 124.8, 123.0, 116.0, 113.9, 113.0, 110.8, 40.4, 23.6.

10d: m.p. 169–171°C; IR (KBr): 3352, 1511, 1640, 1170, 1089 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.69 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.65 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.62–7.52 (m, 2H, Ar-H), 7.50–7.34 (m, 1H, Ar-H), 7.32–7.14 (m, 2H, Ar-H), 6.73–6.66 (m, 2H, Ar-H), 4.68 (s, 2H, CH₂), 4.33 (s, 1H, NH); ¹³C NMR (100 Hz, CDCl₃): δ = 164.1, 158.5, 155.7, 144.8, 140.2, 129.3, 127.3, 127.1, 124.1, 123.9, 122.4, 114.4, 112.1, 110.5, 39.2.

10e: m.p. 200–202°C; IR (KBr): 3347, 1569, 1650, 1206, 1196 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 8.24–7.75 (m, 2H, Ar-H), 7.68 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.67 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.63–7.52 (m, 2H, Ar-H), 7.51–7.35 (m, 1H, Ar-H), 7.20–6.98 (m, 2H, Ar-H), 4.68 (s, 2H, CH₂), 4.43 (s, 1H, NH); ¹³C NMR (100 Hz, CDCl₃): δ = 163.4, 158.1, 154.9, 141.1, 138.4, 134.8, 132.9, 128.0, 123.8, 123.0, 122.6, 121.0, 117.6, 113.9, 111.7, 111.1, 39.8.

10f: m.p. 142–144°C; IR (KBr): 3351, 1571, 1652, 1210, 1200 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 8.27–8.05 (m, 2H, Ar-H), 7.68 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.67 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.63–7.52 (m, 2H, Ar-H), 7.51–7.35 (m, 1H, Ar-H), 7.05–6.95 (m, 2H, Ar-H), 4.67 (s, 2H, CH₂), 4.43 (s, 1H, NH); ¹³C NMR (100 Hz, CDCl₃): δ = 165.0, 158.8, 156.2, 154.6, 142.1, 137.5, 128.0, 124.5, 124.4, 123.0, 122.2, 114.8, 112.9, 111.1, 44.8.

General procedure for one-pot synthesis of 3-acetyl-2-aryl-5-(2-benzo[b]furan)-1,3,4-oxadiazolines (13a–f). The mixture of 2-benzo[b]furan carboxylic acid hydrazide (**1**) (1 mmol), aromatic aldehydes (**11a–f**) (1 mmol), and Ac₂O (5 mL) were stirred under reflux condition for 2 h. The excess of Ac₂O was evaporated under reduced pressure. The residue was recrystallized from benzene to give the product 2-aryl-5-(2-benzo[b]furan)-3-acetyl-1,3,4-oxadiazoline (**13a–f**).

13a: m.p. 150–151°C; IR (KBr): 1671, 1588, 1260, 1073 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.66 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.59 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.52 (s, 1H, Ar-H), 7.49 (t, 1H, 8.0 Hz, Ar-H), 7.45 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.29–7.43 (m, 5H, Ar-H), 7.13 (s, 1H, oxadiazoline-H), 2.42 (s, 3H, COCH₃); ¹³C NMR (100 Hz, CDCl₃): δ = 167.9, 155.8, 149.1, 141.1, 135.8, 130.1, 128.8, 127.1, 127.0, 126.6, 123.9, 122.2, 111.9, 111.2, 92.7, 21.6.

13b: m.p. 153–155°C; IR (KBr): 1693, 1636, 1277, 1083 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.66 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.57 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.51 (s, 1H, Ar-H), 7.47 (t, 1H, *J* = 8.8 Hz, Ar-H), 7.44 (t, 1H, *J* = 8.8 Hz, Ar-H), 6.80 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.34 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.10 (s, 1H, oxadiazoline-H), 2.40 (s, 3H, COCH₃), 3.73 (s, 3H, OCH₃); ¹³C NMR (100 Hz, CDCl₃): δ = 167.8, 155.7, 148.7, 140.8, 135.8, 131.0, 128.4, 127.0, 126.7, 126.4, 123.7, 122.1, 111.7, 111.0, 92.3, 21.3.

13c: m.p. 192–194°C; IR (KBr): 1681, 1623, 1280, 1063 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.65 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.60 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.50 (s, 1H, Ar-H), 7.48 (t, 1H, *J* = 8.8 Hz, Ar-H), 7.48 (t, 1H, *J* = 8.8 Hz, Ar-H), 7.17–7.40 (m, 5H, Ar-H), 7.16 (s, 1H, oxadiazoline-H), 2.45 (s, 3H, COCH₃); ¹³C NMR (100 Hz, CDCl₃): δ = 167.9, 155.8, 149.3, 141.3, 136.3, 130.2, 128.4, 128.0, 126.9, 126.5, 123.6, 122.5, 111.6, 111.4, 92.9, 21.8.

13d: m.p. 118–120°C; IR (KBr): 1688, 1612, 1272, 1075 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): δ = 7.69 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.59 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.54 (s, 1H, Ar-H), 7.49 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.47 (t, 1H, *J* = 8.8 Hz,

Ar-H), 7.23 (d, 2H, $J = 8.0$ Hz, Ar-H), 7.47 (d, 2H, $J = 8.0$ Hz, Ar-H), 7.15 (s, 1H, oxadiazoline-H), 2.43 (s, 3H, COCH₃); ¹³C NMR (100 Hz, CDCl₃): $\delta = 167.9, 155.9, 149.0, 141.1, 136.2, 130.4, 129.1, 127.9, 126.8, 126.1, 123.9, 122.2, 111.7, 111.1, 92.7, 21.6$.

13e: m.p. 158–160°C; IR (KBr): 1719, 1635, 1280, 1088 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): $\delta = 8.20$ (s, 1H, Ar-H), 8.34–7.75 (m, 3H, Ar-H), 7.69 (d, 1H, $J = 8.0$ Hz, Ar-H), 7.59 (d, 1H, $J = 8.0$ Hz, Ar-H), 7.56 (s, 1H, Ar-H), 7.51 (t, 1H, $J = 8.8$ Hz, Ar-H), 7.46 (t, 1H, $J = 8.8$ Hz, Ar-H), 7.16 (s, 1H, oxadiazoline-H), 2.43 (s, 3H, COCH₃); ¹³C NMR (100 Hz, CDCl₃): $\delta = 167.9, 155.8, 149.2, 141.0, 136.0, 130.0, 129.1, 127.1, 127.0, 126.8, 124.2, 122.0, 111.8, 111.1, 92.5, 21.6$.

13f: m.p. 144–146°C; IR (KBr): 1721, 1630, 1287, 1093 cm⁻¹; ¹H NMR (400 Hz, CDCl₃): $\delta = 8.28$ (d, 2H, $J = 8.0$ Hz, Ar-H), 7.68 (d, 1H, $J = 8.0$ Hz, Ar-H), 7.60 (d, 1H, $J = 8.0$ Hz, Ar-H), 7.55 (s, 1H, Ar-H), 7.50 (t, 1H, $J = 8.8$ Hz, Ar-H), 7.45 (t, 1H, $J = 8.8$ Hz, Ar-H), 7.55 (d, 2H, $J = 8.0$ Hz, Ar-H), 7.15 (s, 1H, oxadiazoline-H), 2.44 (s, 3H, COCH₃); ¹³C NMR (100 Hz, CDCl₃): $\delta = 167.9, 155.8, 149.2, 140.8, 136.2, 132.1, 128.8, 127.3, 126.5, 126.9, 123.9, 122.1, 111.6, 111.0, 92.5, 21.5$.

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