



## One-Pot Synthesis of 2-Arylbenzoxazoles Using Cu(OTf)<sub>2</sub>-Catalyzed Condensation and Oxidative Tandem Reaction

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An efficient one-pot condensation and oxidative tandem process has been developed for the synthesis of 2-arylbenzoxazoles derivatives from 2-aminophenols and substituted aldehydes in presence of the catalytic amounts Cu(OTf)<sub>2</sub>. Reactions were conducted with short reaction times, ligands free, high conversion, high functional group tolerability and straight forward procedure under reflux conditions in air. This protocol provides a straight-forward approach to synthesize 2-arylbenzoxazoles.

**Key Words:** Tandem process, 2-Arylbenzoxazoles, Cu(OTf)<sub>2</sub>-catalyzed.

### INTRODUCTION

2-Arylbenzoxazoles are an important class of compounds with a variety of biological activities, such as antimicrobial, antitumor and antiviral properties<sup>1</sup>. The applications of 2-arylbenzoxazoles as photo chromic agents<sup>2</sup> and laser dyes<sup>3</sup> in material sciences were also reported. Although several synthetic routes to 2-arylbenzoxazoles have been developed<sup>4</sup>, but these methods have some limitations such as multistep procedures, harsh conditions and poor selectivity. Recently, other alternative route to 2-arylbenzoxazoles through one-step intramolecular cross-coupling have been reported but special precursors should be prepared<sup>5</sup>. Accordingly, new approaches allowing for the selective assembly of different 2-arylbenzoxazoles skeletons with diverse substitution patterns catalyzed by simple, efficient, inexpensive and ligand-free catalysts from facile precursors is still needed.

During the past decades, tandem processes involve multiple chemical transformations in a single-pot has undergone great development<sup>6</sup>. Especially, utilizing a single catalyst that could promotes multiple transformation in a selective manner attracted greater attention. This innovative strategy result in a reduced number of operations, giving significant time-cost benefits as well as preventing side product formation and loss of starting material<sup>7</sup>. As a part of continuing efforts towards the transition-metal-catalyzed reaction in our group, herein, we wish to report a highly efficient tandem reaction for the synthesis of 2-arylbenzoxazoles start from the facile 2-aminophenols and substituted aldehydes using Cu(OTf)<sub>2</sub> as single catalyst. This

one-pot transformation involves the condensation of above start material and subsequent the oxidative cyclization of phenolic schiff bases resulting 2-arylbenzoxazoles compounds.

### EXPERIMENTAL

Melting points were uncorrected. NMR spectra were in CDCl<sub>3</sub> (<sup>1</sup>H at 500 MHz and <sup>13</sup>C at 125 MHz). Column chromatography was performed on silica gel (300-400 mesh). Unless otherwise noted, all reagents were obtained commercially and used without further purification.

**Synthesis:** A 10 mL round bottom flask was charged with 2-amino-phenol (**1**) (1 mmol), the substituted aldehyde (**2**) (1 mmol), Cu(OTf)<sub>2</sub> (10 mol %), followed by 2 mL chlorobenzene. The reaction mixture was stirred at reflux and monitored periodically by TLC. Upon completion, the chlorobenzene was removed under reduced pressure by an aspirator and then the residue was purified by silica gel column chromatography (EtOAc/hexane) to afford 2-arylbenzoxazoles (**3aa-3cg**). The structures of all the products were unambiguously established on the basis of their spectral analysis.

### Characterization data

**2-Phenylbenzo[d]oxazole (3aa):** White solid; yield: 90 %; m.p.: 101.7-103.5 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.35-7.39 (m, 2H), 7.53-7.55 (m, 3H), 7.57-7.61 (m, 1H), 7.77-7.82 (m, 1H), 8.27-8.29 (m, 2H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 110.59, 120.04, 124.58, 125.11, 127.21, 127.64, 128.91, 131.52, 142.14, 150.79, 163.06 ppm; *m/z* (MS): 196.05 [M + H]<sup>+</sup>.

**2-(4-Methylphenyl)benzo[d]oxazole (3ab):** Colourless solid; yield: 87 %; m.p.: 110.2–111.7 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.42 (s, 3H), 7.30–7.34 (m, 4H), 7.55–7.57 (m, 1H), 7.77–7.78 (m, 1H), 8.15 (d,  $J$  = 8.1 Hz, 2H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.61, 110.48, 119.85, 124.46, 124.85, 127.60, 129.62, 142.00, 142.23, 150.71, 163.28 ppm;  $m/z$  (MS): 210.34  $[\text{M} + \text{H}]^+$ .

**2-(4-Methoxyphenyl)benzo[d]oxazole (3ac):** Colourless solid; yield: 91 %; m.p.: 101.2–102.5 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.88 (s, 3H), 7.01–7.03 (m, 2H), 7.30–7.32 (m, 2H), 7.54–7.55 (m, 1H), 7.73 (dd,  $J$  = 5.5, 2.2 Hz, 1H), 8.18–8.20 (m, 2H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 54.88, 109.83, 113.86, 119.12, 119.27, 123.87, 124.04, 128.88, 141.84, 150.21, 161.86, 162.66 ppm;  $m/z$  (MS): 226.1  $[\text{M} + \text{H}]^+$ .

**4-(Benzo[d]oxazol-2-yl)-2-methoxyphenol (3ad):** Pink solid; yield: 93 %; m.p.: 158.7–159.6 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 4.01 (s, 3H), 6.25 (br, s, 1H), 7.36 (d,  $J$  = 8.3 Hz, 1H), 7.32–7.36 (m, 2H), 7.55–7.57 (m, 1H), 7.74–7.78 (m, 2H), 7.82 (dd,  $J$  = 8.4, 1.7 Hz, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 56.22, 109.91, 110.35, 114.87, 119.36, 119.58, 121.93, 142.23, 124.45, 124.64, 146.90, 149.10, 150.72, 163.25 ppm;  $m/z$  (MS): 242.01  $[\text{M} + \text{H}]^+$ .

**4-(Benzo[d]oxazol-2-yl)-N,N-dimethylaniline (3ae):** White solid; yield: 79 %; m.p.: 182.3–183.7 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.09 (s, 6H), 6.79 (d,  $J$  = 8.5 Hz, 2H), 7.28–7.34 (m, 2H), 7.54 (d,  $J$  = 7.8 Hz, 1H), 7.72 (d,  $J$  = 7.5 Hz, 1H), 8.14 (d,  $J$  = 8.7 Hz, 2H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 40.11, 110.09, 111.59, 119.12, 123.88, 124.14, 129.09, 142.64, 150.60, 152.42, 164.21 ppm;  $m/z$  (MS): 239.07  $[\text{M} + \text{H}]^+$ .

**2-(Benzo[d]oxazol-2-yl)phenol (3af):** White solid; yield: 86 %; m.p.: 123.1–124 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.03 (t,  $J$  = 7.3 Hz, 1H), 7.15 (d,  $J$  = 8.2 Hz, 1H), 7.40–7.41 (m, 2H), 7.46 (t,  $J$  = 7.4 Hz, 1H), 7.61–7.63 (m, 1H), 7.74–7.75 (m, 1H), 8.05 (d,  $J$  = 7.6 Hz, 1H), 11.49 (s, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 110.10, 116.91, 118.73, 119.01, 124.46, 124.83, 126.60, 133.01, 139.57, 148.66, 158.27, 162.42 ppm;  $m/z$  (MS): 212.09  $[\text{M} + \text{H}]^+$ .

**2-(4-Bromophenyl)benzo[d]oxazole (3ag):** White solid; yield: 81 %; m.p. 157.3–157.8 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.37–7.38 (m, 2H), 7.56–7.59 (m, 1H), 7.67–7.69 (m, 2H), 7.78–7.79 (m, 1H), 8.12–14 (m, 2H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 110.61, 120.13, 124.46, 124.75, 125.37, 126.22, 129.02, 132.23, 142.07, 150.80, 162.15 ppm;  $m/z$  (MS): 273.91  $[\text{M} + \text{H}]^+$ .

**4-(Benzo[d]oxazol-2-yl)benzonitril (3ah):** White solid; yield: 75 %; m.p.: 207.4–209.3 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.41–7.42 (m, 2H), 7.62–63 (m, 1H), 7.83–7.83 (m, 3H), 8.36–8.38 (m, 2H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 110.85, 114.80, 118.10, 120.59, 125.11, 126.14, 127.98, 131.18, 132.66, 141.93, 150.95, 160.94 ppm;  $m/z$  (MS): 221.13  $[\text{M} + \text{H}]^+$ .

**2-(Pyridin-2-yl)benzo[d]oxazole (3ai):** White solid; yield: 71 %; m.p.: 114.6–115.7 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.36–7.48 (m, 3H), 7.68 (d,  $J$  = 7.7 Hz, 1H), 7.84 (d,  $J$  = 7.3 Hz, 1H), 7.90 (t,  $J$  = 7.7 Hz, 1H), 8.38 (d,  $J$  = 7.9 Hz, 1H), 8.83 (d,  $J$  = 4.6 Hz, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 111.23, 120.66, 123.46, 124.92, 125.53, 126.03,

137.06, 141.82, 146.15, 150.31, 151.31, 161.48 ppm;  $m/z$  (MS): 197.05  $[\text{M} + \text{H}]^+$ .

**2-(Thiophenyl)benzoxazole (3aj):** White solid; yield: 67 %; m.p. 108.9–111.2 °C;  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ ):  $\delta$  = 7.20–7.22 (m, 2H), 7.35–7.37 (m, 2H), 7.56–7.59 (m, 2H), 7.75–7.76 (m, 1H), 7.93–7.94 (m, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 110.41, 119.83, 124.71, 125.06, 128.23, 129.70, 129.93, 130.21, 142.05, 150.47, 159.06 ppm;  $m/z$  (MS): 202.53  $[\text{M} + \text{H}]^+$ .

**2-(Naphthalen-2-yl)benzo[d]oxazole (3ak):** White solid; yield 85 %; m.p. 115.3–116.7 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.43 (dd,  $J$  = 5.8, 3.2 Hz, 2H), 7.61–7.64 (m, 2H), 7.67–7.68 (m, 1H) 7.75 (t,  $J$  = 7.7 Hz, 1H), 7.92–7.97 (m, 2H), 8.05 (d,  $J$  = 8.1 Hz, 1H), 8.47 (d,  $J$  = 7.3 Hz, 1H), 9.53 (d,  $J$  = 7.3 Hz, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 110.52, 120.32, 123.68, 124.51, 124.94, 125.29, 126.36, 126.47, 127.91, 128.68, 129.34, 130.8, 132.31, 134.02, 142.39, 150.24, 162.85 ppm;  $m/z$  (MS): 246.21  $[\text{M} + \text{H}]^+$ .

**2-(Benzo[d][1,3]dioxol-5-yl)benzo[d]oxazole (3al):** Pink solid; yield: 74 %; m.p.: 150.5–152.3 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.02 (d,  $J$  = 3.2 Hz, 2H), 6.91 (dd,  $J$  = 8.0 Hz,  $J$  = 3.2 Hz, 1H), 7.29–7.32 (m, 2H), 7.52–7.53 (m, 1H), 7.68 (s, 1H), 7.73–7.74 (m, 1H), 8.81 (d,  $J$  = 6.9 Hz, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 101.72, 107.66, 108.65, 110.35, 119.70, 121.17, 122.76, 124.44, 124.70, 142.23, 148.19, 150.53, 150.68, 162.82 ppm;  $m/z$  (MS): 240.15  $[\text{M} + \text{H}]^+$ .

**6-Methyl-2-phenylbenzo[d]oxazole (3ba):** Pale yellow solid; yield: 92 %; m.p.: 90.4–91.3 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.50 (s, 3H), 7.17 (dd,  $J$  = 8.1, 0.83, 1H), 7.37–7.38 (m, 1H), 7.50–7.53 (m, 3H), 7.67–7.65 (d,  $J$  = 8.1, 1H), 8.23–8.26 (m, 2H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.78, 110.75, 119.35, 125.80, 127.38, 127.47, 128.85, 131.25, 135.55, 139.95, 151.07, 162.56 ppm;  $m/z$  (MS): 210.06  $[\text{M} + \text{H}]^+$ .

**6-Nitro-2-phenylbenzo[d]oxazole (3ca):** Yellow solid; yield: 86 %; m.p.: 237.5–238.7 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.55–7.65 (m, 3H), 7.84 (d,  $J$  = 8.8, 1H), 8.28–8.34 (m, 3H), 8.49 (d,  $J$  = 2.0, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 107.20, 119.79, 120.82, 125.99, 128.25, 129.18, 132.85, 145.18, 147.43, 149.92, 167.43 ppm;  $m/z$  (MS): 241.14  $[\text{M} + \text{H}]^+$ .

**6-Methyl-2-(*p*-tolyl)benzo[d]oxazole (3bb):** Pale Yellow solid; yield: 88 %; m.p.: 105.2–106.4 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.42 (s, 3H), 2.50 (s, 3H), 7.15 (dd,  $J$  = 0.7, 8.11, H), 7.30–7.35 (m, 3H), 7.63 (d,  $J$  = 8.1, 1H), 8.12 (d,  $J$  = 8.2, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.59, 21.76, 110.67, 119.17, 124.61, 125.67, 127.43, 129.58, 135.27, 140.00, 141.73, 150.99, 162.82 ppm;  $m/z$  (MS): 240.32  $[\text{M} + \text{H}]^+$ .

**6-Nitro-2-(*p*-tolyl)benzo[d]oxazole (3cb):** Yellow solid; yield: 83 %; m.p.: 160.2–161.9 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.47 (s, 3H), 7.36 (d,  $J$  = 8.0, 2H), 7.80 (d,  $J$  = 8.8, 2H), 8.15 (d,  $J$  = 8.2, 2H), 8.30 (dd,  $J$  = 8.8, 2.1, 1H), 8.45 (d,  $J$  = 2.1, 1H) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.75, 107.06, 119.52, 120.76, 123.19, 128.22, 129.91, 143.77, 144.98, 147.58, 149.83, 167.69 ppm;  $m/z$  (MS): 271.29  $[\text{M} + \text{H}]^+$ .

**2-(4-Bromophenyl)-6-methylbenzo[d]oxazole (3bg):** White solid; yield: 86 %; m.p.: 157.5–158.9 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.51 (s, 3H), 7.17–7.19 (m, 1H), 7.38–7.39 (m, 1H), 7.63–7.67 (m, 3H), 8.08–8.11 (m, 2H) ppm;  $^{13}\text{C}$  NMR

(100 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.80, 110.78, 119.44, 125.92, 126.01, 126.32, 128.85, 132.18, 135.91, 139.85, 151.08, 161.66. ppm;  $m/z$  (MS): 288.12 [M + H]<sup>+</sup>.

### 2-(4-Bromophenyl)-6-nitrobenzo[d]oxazole (3cg):

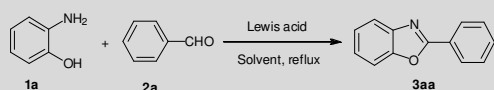
White solid; yield: 78 %; m.p.: 175.8-177.3 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.71-7.74 (m, 2H), 7.86 (d,  $J$  = 8.8 Hz, 2H), 8.14-8.17 (m, 2H), 8.34 (dd,  $J$  = 8.8, 2.1 Hz, 1H), 8.50 (d,  $J$  = 2.0 Hz, 1H) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 107.27, 119.95, 120.98, 124.91, 127.90, 129.56, 132.59, 145.36, 147.27, 149.92, 166.53 ppm;  $m/z$  (MS): 318.88 [M + H]<sup>+</sup>.

## RESULTS AND DISCUSSION

Initially, 2-aminophenols (**1a**) (1 mmol) was treated with benzaldehyde (**2a**) (1 mmol) in the presence of 10 mol % of InCl<sub>3</sub> in chlorobenzene after reflux for 4 h and the desired product (**3aa**) was isolated in 76 % (Table-1, entry 1). With other Lewis acids such as FeCl<sub>3</sub>, ZnCl<sub>2</sub>, CuSO<sub>4</sub> and Cu(NO<sub>3</sub>)<sub>2</sub>, similar results were obtained after 18-24 h (Table-1, entries 2-5), but CuCl resulted with low yield (Table-1, entry 6) which might due to its low oxidizability. Remarkably, trifluoromethanesulfonic salts such as AgOTf and Zn(OTf)<sub>2</sub> gave benzoxazole (**3aa**) in good yields (Table-1, entries 7 and 8), especially Cu(OTf)<sub>2</sub> obtain an excellent yield of 90 % (Table-1, entry 9). However, the yield decreased when the amount of Cu(OTf)<sub>2</sub> was 5 mol % (Table-1, entry 10 vs. 9), while there was no prominent difference when the catalytic amount of Cu(OTf)<sub>2</sub> was increased from 10 mol % to 15 mol % (Table-1, entry 11 vs. 9).

TABLE-1

### OPTIMIZATION OF REACTION CONDITIONS<sup>a</sup>



Entry	Catalyst	Mol (%)	Solvents	Time (h)	Yield (%) <sup>b</sup>
1	InCl <sub>3</sub>	10	PhCl	4	76
2	ZnCl <sub>2</sub>	10	PhCl	18	80
3	FeCl <sub>3</sub>	10	PhCl	18	82
4	CuSO <sub>4</sub>	10	PhCl	24	85
5	Cu(NO <sub>3</sub> ) <sub>2</sub>	10	PhCl	24	83
6	CuCl	10	PhCl	18	25
7	AgOTf	10	PhCl	4	87
8	Zn(OTf) <sub>2</sub>	10	PhCl	4	85
9	Cu(OTf) <sub>2</sub>	10	PhCl	4	90
10	Cu(OTf) <sub>2</sub>	5	PhCl	12	82
11	Cu(OTf) <sub>2</sub>	15	PhCl	4	89
12	Cu(OTf) <sub>2</sub>	10	Toluene	18	50
13	Cu(OTf) <sub>2</sub>	10	THF	4	77
14	Cu(OTf) <sub>2</sub>	10	CH <sub>3</sub> CN	4	82
15	Cu(OTf) <sub>2</sub>	10	DMSO	24	Trace
16	Cu(OTf) <sub>2</sub>	10	CH <sub>3</sub> NO <sub>2</sub>	18	27
17	Cu(OTf) <sub>2</sub>	10	DME	4	76

<sup>a</sup>Reaction conditions: 2-aminophenol (1.0 mmol), benzaldehyde (1.0 mmol) and catalyst in solvent (2 mL) at reflux;

<sup>b</sup>Isolated yields.

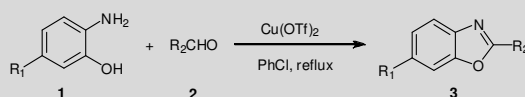
To further improve the efficiency of this synthetic approach, a screening of the suitable solvents for the desired reaction was established. As shown in Table-1, other conven-

tional solvents such as toluene, THF, CH<sub>3</sub>CN, DMSO, CH<sub>3</sub>NO<sub>2</sub> and DME (Table-1, entries 12-17) were also screened. Among these solvents, THF, CH<sub>3</sub>CH and DME were also able to facilitate the reaction with common yields (Table-1, entries 13, 14, 17). However, the use of toluene and CH<sub>3</sub>NO<sub>2</sub> obviously increased the reaction time from 4 to 18 h with low yields (Table-1, entries 12 and 16 vs. 9). Unexpectedly, the use of DMSO only obtained trace yield although reacted for 24 h (Table-1, entry 15). The results showed that all various factors of solvents, such as polarity, boiling point and pH *etc.* might influence the reaction yields and time. However, the detailed mechanism is still unclear. In brief, chlorobenzene was proved to be the best partner for the Cu(OTf)<sub>2</sub> comparing reaction time and yields with other solvents. So the reaction conditions were then finally established as shown in entry 9 (Table-1).

With the optimal conditions in hand, we examined the scope of this reaction. As shown in Table-2, the reaction proceeds smoothly at suitable temperature in good to excellent yields. Among the substituted aldehydes examined, (**2d**) gave the most desirable result, providing the (**3ad**) with an excellent yield (Table-2, entry 4). Other benzaldehydes with electron-donating groups at the aryl ring also reacted smoothly affording good yields (Table-2, entries 2 and 3) except (**2e**) obtain a tolerable yield of 79 % (Table-2, entry 5). Substrates (**2g**) and (**2h**) possessing electron withdrawing group at the aryl ring were also successfully employed in the reaction to give the 2-arylbenzoxazoles (**3ag**) and (**3ah**) with 81 and 75 % yields, respectively (Table-2, entries 7 and 8). The results showed that the reaction yield decreased to some extent when the electro-withdrawing power of the substituent in the substituted benzaldehydes increases. Interestingly, although steric hindrance of (**2f**) might hampered the reaction, benzoxazoles **3af** was obtained in good yield (Table-2, entry 6). This might owe to the promotion effects of the hydrogen bond in reaction as well as the electron-donating effect of hydroxyl group. In this reaction conditions, heterocyclic aldehydes (**2i** and **2j**) could also be used for efficient preparation of various 2-heterocyclic substituted benzoxazoles (**3ai** and **3aj**) with comparing yields of 71 and 67 %, respectively (Table-2, entries 9 and 10). Moreover, this reaction conditions is not only limited to above common aldehydes, other special aldehydes such as (**2k**) and (**2l**) could also obtain (**3ak**) and (**3al**) with satisfied yields, respectively (Table-2, entries 11 and 12). On the other hand, 2-aminophenols with electron-donating or electron-drawing group (methyl or nitro group) were also used to examine the generality of this reaction conditions. Both of them could react to different aldehydes with satisfied yields of substituted 2-arylbenzoxazoles (Table-2, entries 13-18). When react to the same aldehyde, the general order of products yields was: 2-amino-5-methylphenol > 2-aminophenol > 2-amino-5-nitrophenol (Table-2, entries 1 vs. 13 vs. 14, 2 vs. 15 vs. 16, 7 vs. 17 vs. 18). Just as the effects to the reaction by substituted groups in aryl ring of aldehydes, electron-drawing groups in 2-aminophenol also decreased the reaction yields contrary with that of the electron-donating group.

## Conclusion

In conclusion, we have reported a highly efficient and green protocol for one-pot synthesis of 2-arylbenzoxazoles

TABLE-2  
 Cu(OTf)<sub>2</sub>-CATALYZED FACILE SYNTHESIS OF 2-ARYLBENZOXAZOLES<sup>a</sup>


Entry	2-Amino-phenol	Aldehydes	Products	Yield (%) <sup>b</sup>
1	<b>1a</b> : R <sub>1</sub> = H	<b>2a</b> : R <sub>2</sub> = Ph	<b>3aa</b>	90
2	<b>1a</b> : R <sub>1</sub> = H	<b>2b</b> : R <sub>2</sub> = 4-MeC <sub>6</sub> H <sub>4</sub>	<b>3ab</b>	87
3	<b>1a</b> : R <sub>1</sub> = H	<b>2c</b> : R <sub>2</sub> = 4-MeOC <sub>6</sub> H <sub>4</sub>	<b>3ac</b>	91
4	<b>1a</b> : R <sub>1</sub> = H	<b>2d</b> : R <sub>2</sub> = 3-OH-4-OMeC <sub>6</sub> H <sub>4</sub>	<b>3ad</b>	93
5	<b>1a</b> : R <sub>1</sub> = H	<b>2e</b> : R <sub>2</sub> = 4-(NMe <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	<b>3ae</b>	79
6	<b>1a</b> : R <sub>1</sub> = H	<b>2f</b> : R <sub>2</sub> = 2-OHC <sub>6</sub> H <sub>4</sub>	<b>3af</b>	86
7	<b>1a</b> : R <sub>1</sub> = H	<b>2g</b> : R <sub>2</sub> = 4-BrC <sub>6</sub> H <sub>4</sub>	<b>3ag</b>	81
8	<b>1a</b> : R <sub>1</sub> = H	<b>2h</b> : R <sub>2</sub> = 4-CNC <sub>6</sub> H <sub>4</sub>	<b>3ah</b>	75
9	<b>1a</b> : R <sub>1</sub> = H	<b>2i</b> : R <sub>2</sub> = 2- pyridine	<b>3ai</b>	71
10	<b>1a</b> : R <sub>1</sub> = H	<b>2j</b> : R <sub>2</sub> = 2- thienyl	<b>3aj</b>	67
11	<b>1a</b> : R <sub>1</sub> = H	<b>2k</b> : R <sub>2</sub> = 2-naphthyl	<b>3ak</b>	85
12	<b>1a</b> : R <sub>1</sub> = H	<b>2l</b> : R <sub>2</sub> = Piperonyl	<b>3al</b>	74
13	<b>1b</b> : R <sub>1</sub> = CH <sub>3</sub>	<b>2a</b> : R <sub>2</sub> = Ph	<b>3ba</b>	92
14	<b>1c</b> : R <sub>1</sub> = NO <sub>2</sub>	<b>2a</b> : R <sub>2</sub> = Ph	<b>3ca</b>	86
15	<b>1b</b> : R <sub>1</sub> = CH <sub>3</sub>	<b>2b</b> : R <sub>2</sub> = 4-MeC <sub>6</sub> H <sub>4</sub>	<b>3bb</b>	88
16	<b>1c</b> : R <sub>1</sub> = NO <sub>2</sub>	<b>2b</b> : R <sub>2</sub> = 4-MeC <sub>6</sub> H <sub>4</sub>	<b>3cb</b>	83
17	<b>1b</b> : R <sub>1</sub> = CH <sub>3</sub>	<b>2g</b> : R <sub>2</sub> = 4-BrC <sub>6</sub> H <sub>4</sub>	<b>3bg</b>	86
18	<b>1c</b> : R <sub>1</sub> = NO <sub>2</sub>	<b>2g</b> : R <sub>2</sub> = 4-BrC <sub>6</sub> H <sub>4</sub>	<b>3cg</b>	78

<sup>a</sup>Reaction conditions: 2-aminophenol (1 mmol), benzaldehyde (1 mmol) and Cu(OTf)<sub>2</sub> (10 Mol %) in chlorobenzene (2 mL) at reflux;<sup>b</sup>Isolated yields.

derivatives starting from substituted 2-aminophenols and substituted benzaldehydes. This newly developed procedure offers several advantages such as broad application scope, good to excellent yields, mild reaction conditions, facile precursors, simple operation and environmental friendliness. The present study provided a useful supplement for the synthesis of 2-arylbenzoxazoles.

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