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Copper-catalyzed synthesis of 2-arylbenzoxazoles from *o*-aminophenol derivatives with arylmethyl chlorides

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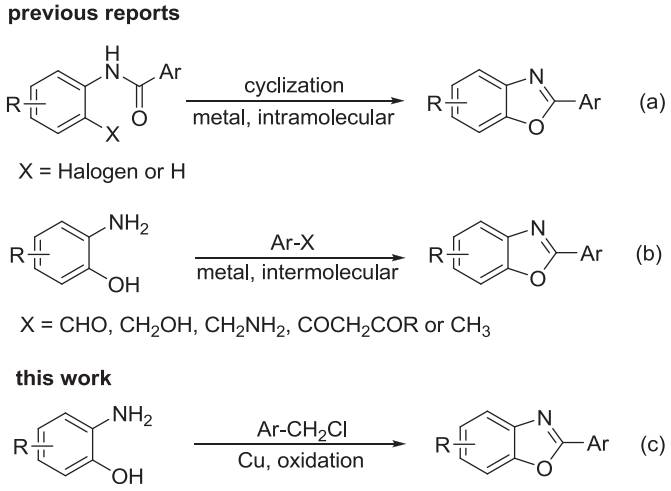
ABSTRACT

A facile and efficient synthesis of 2-arylbenzoxazoles via copper-catalyzed tandem condensation/oxidative reaction of *o*-aminophenol derivatives with arylmethyl chlorides was developed. Note that this reaction utilized arylmethyl chlorides as a new type of simple and cheap acyl sources and KNO_3 as a readily available and low-cost benign oxidant.

1. Introduction

Benzoxazole backbone is a ubiquitous structural unit in biologically active natural products, functional materials, alkaloids, and particularly pharmaceuticals compounds due to its high biological activities, such as antitumor, antimicrobial, and antiviral properties.[1] The most primitive synthetic route is condensation of *o*-aminophenol with carboxylic acids, which suffered from using a strong acid as the raw material and the hash reaction conditions.[2] Therefore, many efforts have been devoted to the development of economical and environment-friendly routes to benzoxazole derivatives.[3]

In recent years, two transition metal-promoted synthetic processes have emerged as popular protocols for the construction of the benzoxazole ring: one is the transition metal-catalyzed intramolecular cyclization of *ortho*-haloanilides or their analogs derivatives, and great progress has been achieved in the groups of Glorius and others (Scheme 1a);[4] the other is transition metal-catalyzed intermolecular condensation/oxidative reaction of *o*-aminophenol with an acyl source such as aromatic aldehyde,[5] benzylic alcohol,[6] benzylic amine[7] and 1,3- diketones[8] in the presence of an oxidant (Scheme 1b). Recently, Wang group reported an elegant procedure to aryl-substituted benzoxazoles from



Scheme 1. Synthetic strategies for the construction of benzoxazole skeleton.

o-aminophenol with toluene derivatives as the acyl source and solvent under argon atmosphere,[9] albeit this catalytic system may not be suitable for the toluene derivatives with a melting point. On the other hand, arylmethyl chloride derivatives as a family of inexpensive organic intermediates can be oxidized to aldehydes by the oxidants,[10] thereby serving as new and potential acyl sources, which would be an important complement to abovementioned

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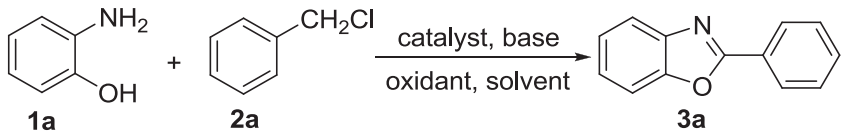
methods. Inspired by these previous reports, we envisioned a new, simple, and efficient synthesis of benzoxazole derivatives by tandem condensation/oxidative reaction of *o*-aminophenol derivatives with arylmethyl chlorides under air (Scheme 1c).

2. Results and discussion

In our initial investigation, we performed the model reaction of *o*-aminophenol (**1a**) with benzyl chloride (**2a**) in the presence of KNO_3 as oxidant and $Cu(OAc)_2$ as catalyst in toluene at 140 °C under air, and the desired product could be obtained in 25% isolated yield (Table 1, entry 1). However, base effect is remarkable in this reaction. For example, when the bases such as K_2CO_3, $KHCO_3$, $NaHCO_3$ and KF were added to the above catalytic system, only trace amount of desired product was detected in the presence of K_2CO_3, $NaHCO_3$ and KF; to the contrary, $KHCO_3$ as the best base could afford the product in 66% yield (Table 1, entries 2–5). Increasing the loading of KNO_3 to 4.0 equiv or decreasing the reaction temperature to 120 °C did not improve the catalytic process (Table 1, entries 6 and 7). Then, some other solvents (e.g., 1,4-dioxane, DMSO, xylene, DMF, bromobenzene and chlorobenzene) were evaluated, and to our surprise, the reaction in chlorobenzene could give an up to 77% yield (Table 1, entries 8–13). Using DDQ and BQ as the oxidant or performing the reaction under an oxygen atmosphere did not generate the product in higher yields (Table 1, entries 14–16). Finally, some commercially available copper catalysts such as $Cu(OTf)_2$, $CuCl_2$ and $CuBr_2$ were also screened, and unfortunately, all of them did not exhibit higher catalytic activity (Table 1, entries 17–19). In addition, the desired product was not detected at all under the copper-free conditions (Table 1, entry 20).

Table 1
Optimization of the reaction conditions[a]



1a + **2a** → **3a**

Entry	Catalyst	Base	Oxidant	Solvent	Yield (%)[b]
1	$Cu(OAc)_2$	—	KNO_3	Toluene	25
2	$Cu(OAc)_2$	K_2CO_3	KNO_3	Toluene	<5
3	$Cu(OAc)_2$	$KHCO_3$	KNO_3	Toluene	66
4	$Cu(OAc)_2$	$NaHCO_3$	KNO_3	Toluene	<5
5	$Cu(OAc)_2$	KF	KNO_3	Toluene	<5
6[c]	$Cu(OAc)_2$	$KHCO_3$	KNO_3	Toluene	65
7[d]	$Cu(OAc)_2$	$KHCO_3$	KNO_3	Toluene	30
8	$Cu(OAc)_2$	$KHCO_3$	KNO_3	Dioxane	11
9	$Cu(OAc)_2$	$KHCO_3$	KNO_3	DMSO	10
10	$Cu(OAc)_2$	$KHCO_3$	KNO_3	Xylene	23
11	$Cu(OAc)_2$	$KHCO_3$	KNO_3	DMF	18
12	$Cu(OAc)_2$	$KHCO_3$	KNO_3	PhBr	43
13	**$Cu(OAc)_2$**	**$KHCO_3$**	**KNO_3**	**PhCl**	**77**
14	$Cu(OAc)_2$	$KHCO_3$	DDQ	PhCl	<5
15	$Cu(OAc)_2$	$KHCO_3$	BQ	PhCl	<5
16	$Cu(OAc)_2$	$KHCO_3$	O_2	PhCl	53
17	$Cu(OTF)_2$	$KHCO_3$	KNO_3	PhCl	57
18	$CuCl_2$	$KHCO_3$	KNO_3	PhCl	36
19	$CuBr_2$	$KHCO_3$	KNO_3	PhCl	34
20	—	$KHCO_3$	KNO_3	PhCl	<5

Bold represents the optimal conditions.
[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.8 mmol), oxidant (3.0 equiv), base (2.0 equiv), catalyst (20 mol %) in solvent (1.0 mL) at 140 °C for 20 h under air.
[b] Isolated yield.
[c] KNO_3 (4 equiv).
[d] At 120 °C.

With these optimized reaction condition in hand, we first explored the reaction scope of arylmethyl chlorides, and the results were summarized in Table 2. The substrates bearing an electron-donating group such as Me and OMe could give the corresponding products in moderate to good yields (Table 2, entries 2–5). Steric effect had an evident influence and the reaction of 2-methylbenzyl chloride (**2b**) only afforded the product in a relatively lower yield of 65% owing to *ortho*-methyl group in the benzene ring (Table 2, entry 2). Notably, the oxidant-sensitive vinyl group could be well tolerated and the product was obtained in a satisfying yield of 55% (Table 2, entry 6). However, electron-withdrawing groups (e.g., COOMe, Br, Cl, F and CN) substituted benzyl chloride derivatives generated the desired products in relative lower yields than those of substrates bearing electron-donating groups (Table 2, entries 7–11). Exceptionally, the reaction of 4-bromobenzyl chloride could lead to the product in up to 83% yield (Table 2, entry 8). Moreover, other aromatic arylmethyl chloride like 1-(chloromethyl)naphthalene (**2l**) also afforded the desired product in a good yield of 82% (Table 2, entry 12).

To further establish the scope of this reaction, some substituted *o*-aminophenol derivatives were then screened (Table 3). Under the optimized reaction conditions, *o*-aminophenol possessing a methyl group at *meta*- or *para*-position gave the corresponding desired products in yields of 71% and 80%, respectively (Table 3, entries 1 and 2). 2-Amino-4-methoxyphenol (**1d**) and 3-amino-2-naphthol (**1e**) could also give the corresponding products in moderate yields after prolonged reaction time (Table 3, entries 3 and 4). The electron-poor substrate **1f** was also tolerated and gave the product in a moderate yield of 46% in the presence of $FeCl_2$ as an additive (Table 3, entry 5). Finally, this reaction could also be applied to the synthesis of benzothiazole and benzimidazole rings, and gratifyingly, the desired products could be obtained in yields of 60% and 85%, respectively (Scheme 2).

Mechanistic studies were explored to obtain a deeper insight into the reaction process. The reaction of benzyl chloride (**2a**) with *o*-aminophenol in the presence of KNO_3 under copper-free conditions resulted in the production of benzaldehyde in 73% yield (Scheme 3a). Taking benzaldehyde (0.6 mmol) instead of benzyl chloride under optimized conditions without $KHCO_3$ could afford the product (**3a**) in 70% yield (Scheme 3b). The results reveals that

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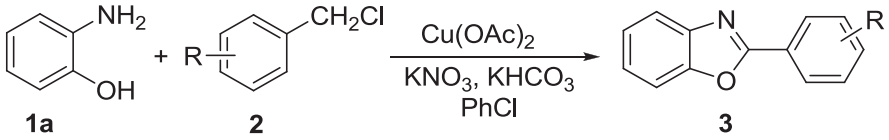
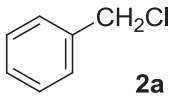
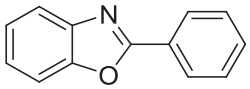
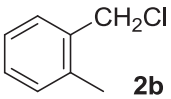
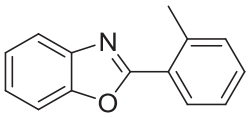
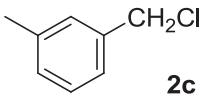
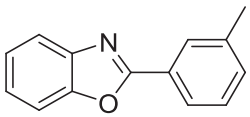
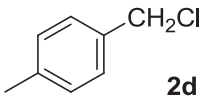
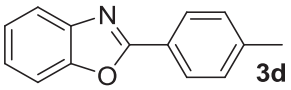
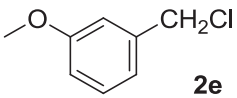
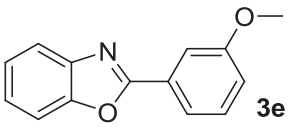
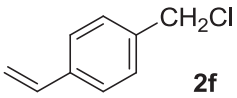
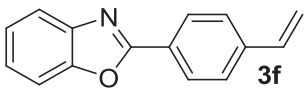
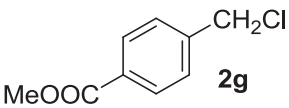
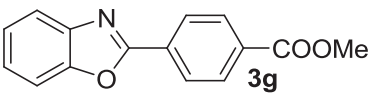
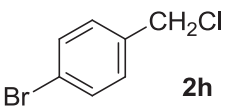
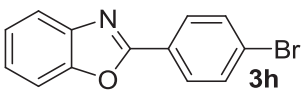
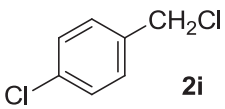
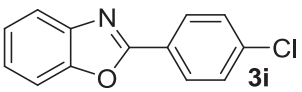
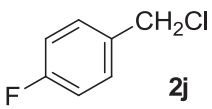
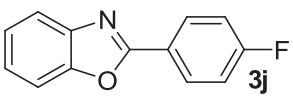
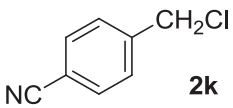
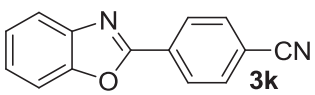
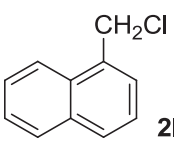
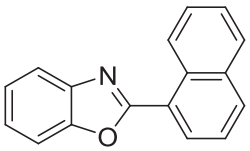
Table 2
Scope of arylmethyl chlorides[a]



1a 2 3

Entry	Arylmethyl chloride	Product	Yield (%)[b]
1	 2a	 3a	77
2	 2b	 3b	65
3	 2c	 3c	81
4	 2d	 3d	78
5	 2e	 3e	82
6	 2f	 3f	55
7	 2g	 3g	54
8	 2h	 3h	83
9	 2i	 3i	61
10	 2j	 3j	53
11	 2k	 3k	52
12	 2l	 3l	82

[a] Reaction conditions: **1a** (0.4 mmol), **2** (0.8 mmol), $Cu(OAc)_2$ (20 mol %), KNO_3 (3.0 equiv) and $KHCO_3$ (2.0 equiv) in PhCl (1.0 mL) at 140 °C for 20 h under air.
[b] Isolated yield.

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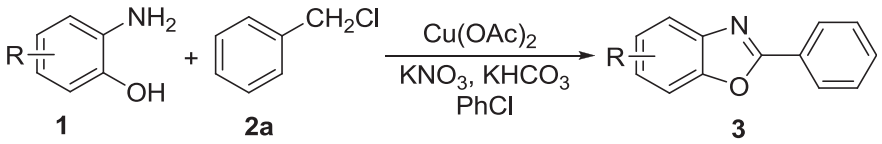
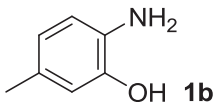
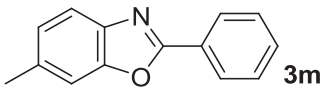
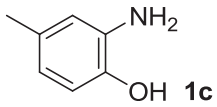
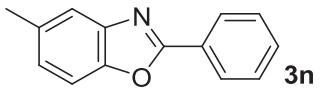
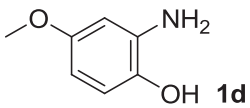
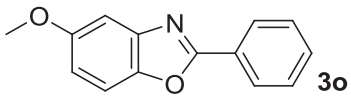
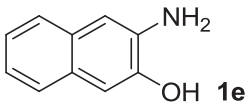
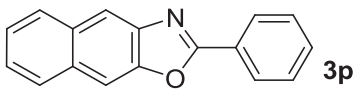
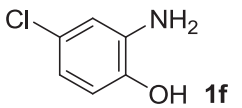
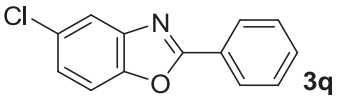
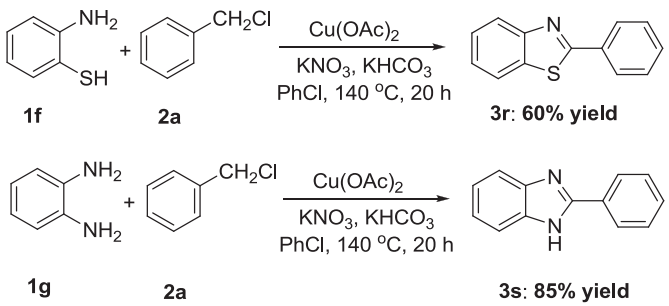
Table 3
Scope of *o*-aminophenol derivatives[a]



Entry	*o*-Aminophenol	Product	Yield (%)[b]
1			71
2			80
3[c]			51
4[c]			50
5[d]			46

[a] Reaction conditions: **1** (0.4 mmol), **2a** (0.8 mmol), $Cu(OAc)_2$ (20 mol %), KNO_3 (3.0 equiv) and $KHCO_3$ (2.0 equiv) in PhCl (1.0 mL) at 140 °C for 20 h under air.
[b] Isolated yield.
[c] For 30 h.
[d] $FeCl_2$ (10 mol %) as an additive.



Scheme 2. Construction of benzothiazole and benzoimidazole via the condensation/oxidative reaction.

the catalytic system is effective for the reaction of aldehydes with *o*-aminophenols, and the generation of aldehyde in the presence of KNO_3 is the key step in the reaction progress. In addition, only trace amount of benzoxazole (**3a**) was observed under copper-free conditions, accompanied by the generation of an imine (**A**) and a dihydrobenzoxazole (**B**) in yields of 15% and 45%, respectively (Scheme 3c). The existence of imine (**A**) and dihydrobenzoxazole (**B**) reveals that the condensation still takes place without the assistance of the catalyst and copper plays a key role for oxidizing dehydrogenative step form dihydrobenzoxazole to benzoxazole (**3a**).

Reaction conditions: (a): **2a** (0.8 mmol), KNO_3 (0.8 mmol), and $KHCO_3$ (0.8 mmol) in PhCl (1.0 mL) at 140 °C for 20 h under air. (b): Benzaldehyde (0.56 mmol) instead of benzyl chloride, and KNO_3 (0.4 mmol) under optimized conditions without $KHCO_3$. (c): Under optimized conditions in the absence of Cu catalyst.

On the basis of the above-mentioned results and the previous reports,[5–7,9] a tentative mechanism to account for this transformation is illustrated in Scheme 4. Firstly, benzyl chloride (**2a**) is oxidized to benzaldehyde in the presence of KNO_3, accompanied by the generation of KCl, CO_2 and H_2O. Then, an intermediate imine **A** is generated from the condensation of *o*-aminophenol (**1a**) with benzaldehyde, which rapidly reaches equilibrium with another cyclic intermediate dihydrobenzoxazole **B**. Finally, the oxidation of the intermediate **B** affords 2-phenylbenzoxazole (**3a**) as the desired product via the second oxidative process with the assistance of $Cu(OAc)_2$.

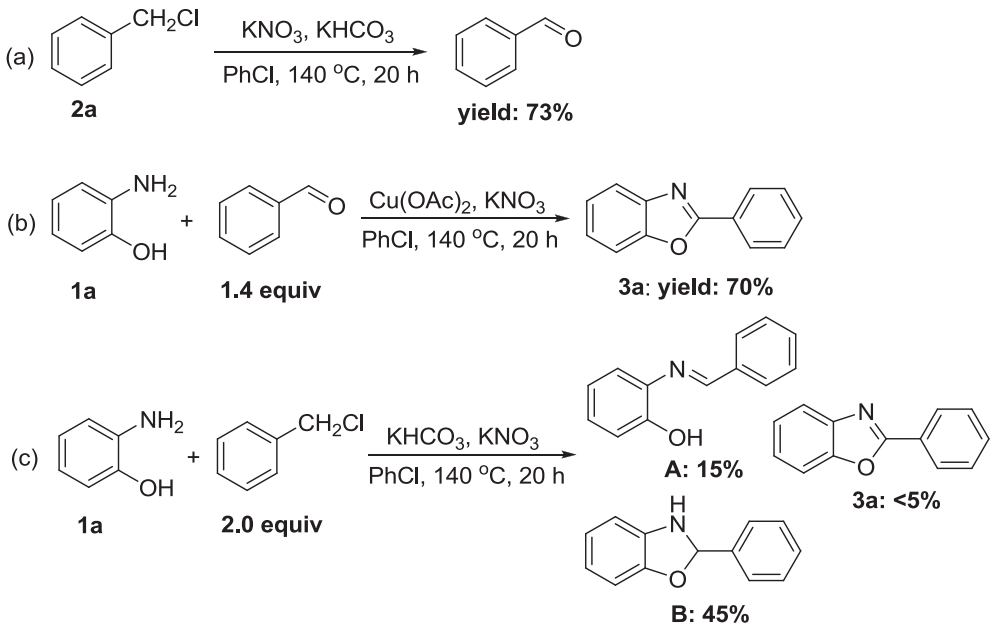
3. Conclusions

In summary, we have developed a new approach for the synthesis of 2-arylbenzoxazoles from substituted *o*-aminophenol and arylmethyl chlorides as the starting materials. This tandem condensation/oxidative reaction could proceed under air utilizing arylmethyl chlorides as a new and commercially available acyl source. KNO_3 could be employed as low-cost and moderate inorganic oxidant in this reaction, and various functional groups even the oxidant-sensitive vinyl group were well tolerated. In addition, this reaction can also be applied to the synthesis of benzimidazoles and benzothiazoles.

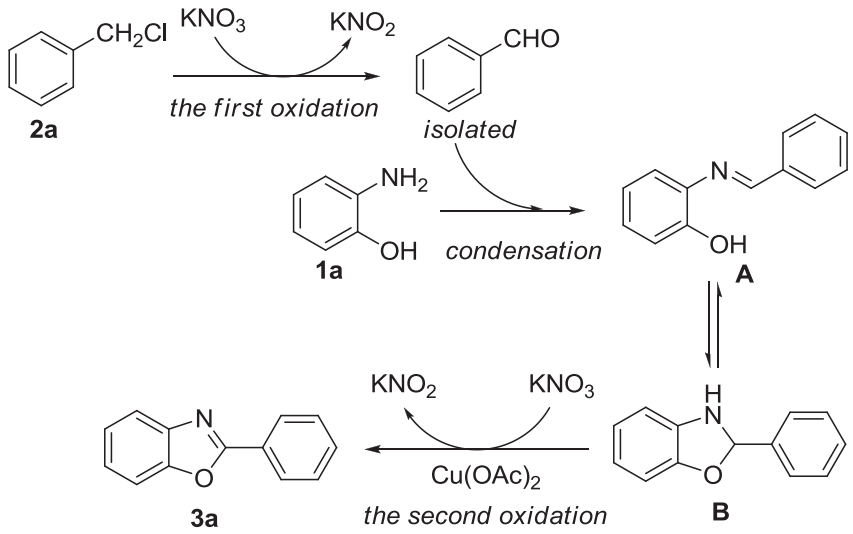
4. Experimental

4.1. General information

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ or DMSO-d_6 as the solvent and TMS as an internal standard. Melting points were measured using a WC-1 microscopic apparatus and are uncorrected. Mass spectra were



Scheme 3. Controlled experiments.



Scheme 4. Plausible mechanism.

measured on an LC-MSD-Trap-XCT instrument. High resolution mass spectra were ensured on a MALDI-FTMS. Dichloromethane, ethyl acetate and hexane were used for column chromatography without further purification. Other solvents were purified according to the standard methods. Reagents were obtained from commercial sources and used without further purification.

4.2. General procedure for copper-catalyzed synthesis of 2-arylbenzoxazoles from *o*-aminophenol derivatives with arylmethyl chlorides

To a solution of *o*-aminophenol (0.4 mmol) in PhCl (1.0 mL), arylmethyl chloride (0.8 mmol), $Cu(OAc)_2$ (0.08 mmol), $KHCO_3$ (0.8 mmol), and KNO_3 (1.2 mmol) were added. The resulting mixture was heated at 140 °C for 20 h under air unless otherwise noted. After the reaction was complete and cooling to room temperature, the mixture was added into H_2O (25 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent in vacuo, the residue was purified by column chromatography (ethyl acetate/hexane) to afford the pure product.

*4.2.1. 2-Phenylbenzo[d]oxazole (**3a**).* White solid (60 mg, 77%), mp 79–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.34–7.39 (m, 2H), 7.52–7.61 (m, 4H), 7.77–7.81 (m, 1H), 8.26–8.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=110.6, 120.0, 124.6, 125.1, 127.2, 127.6, 128.9, 131.6, 142.1, 150.8, 163.1; HRMS-ESI (*m*/*z*): calcd for $C_{13}H_{10}NO$ $[M+H]^+$ 196.0757, found 196.0752.

*4.2.2. 2-o-Tolylbenzo[d]oxazole (**3b**).* White solid (54 mg, 65%), mp 64–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.81 (s, 3H), 7.31–7.42 (m, 5H), 7.55–7.60 (m, 1H), 7.78–7.82 (m, 1H), 8.16–8.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=23.5, 111.8, 121.5, 125.7, 126.3, 127.4, 127.6, 131.3, 132.2, 133.1, 140.2, 143.5, 151.6, 164.7; HRMS-ESI (*m*/*z*): calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0913, found 210.0909.

*4.2.3. 2-m-Tolylbenzo[d]oxazole (**3c**).* White solid (68 mg, 81%), mp 79–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.43 (s, 3H),

7.31–7.35 (m, 3H), 7.37–7.41 (m, 1H), 7.53–7.57 (m, 1H), 7.74–7.78 (m, 1H), 8.04 (d, J=7.7 Hz, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=22.7, 111.9, 121.3, 125.8, 126.1, 126.3, 128.3, 129.5, 130.1, 133.7, 140.0, 143.4, 152.0, 164.6; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0913, found 210.0909.

*4.2.4. 2-p-Tolylbenzo[d]oxazole (**3d**).* White solid (65 mg, 78%), mp 116–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.43 (s, 3H), 7.31–7.36 (m, 4H), 7.54–7.57 (m, 1H), 7.74–7.78 (m, 1H), 8.14 (d, J=8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=22.9, 111.8, 121.1, 125.7, 125.8, 126.2, 128, 9, 130.9, 143.4, 143.5, 152.0, 164.6; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0913, found 210.0910.

*4.2.5. 2-(3-Methoxyphenyl)benzo[d]oxazole (**3e**).* White solid (74 mg, 82%), mp 72–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=3.86 (s, 3H), 7.03 (dd, J=1.8, 8.3 Hz, 1H), 7.29–7.34 (m, 2H), 7.35–7.39 (m, 1H), 7.52–7.54 (m, 1H), 7.75–7.77 (m, 2H), 7.81 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=56.7, 111.9, 113.2, 119.5, 121.3, 121.4, 125.9, 126.4, 129.6, 131.3, 143.4, 152.0, 161.2, 164.2; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO_2$ $[M+H]^+$ 226.0863, found 226.0857.

*4.2.6. 2-(4-Vinylphenyl)benzo[d]oxazole (**3f**).* White solid (49 mg, 55%), mp 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=5.36 (d, J=10.9 Hz, 1H), 5.86 (d, J=17.6 Hz, 1H), 6.71–6.78 (dd, J=10.9, 17.6 Hz, 1H), 7.32–7.35 (m, 2H), 7.52–7.56 (m, 3H), 7.75–7.77 (m, 1H), 8.19 (d, J=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.6, 115.0, 119.0, 123.6, 124.1, 125.3, 125.7, 126.9, 135.1, 139.6, 141.2, 149.8, 161.9; HRMS-ESI (m/z): calcd for $C_{15}H_{12}NO$ $[M+H]^+$ 222.0913, found 222.0910.

*4.2.7. Methyl 4-(benzo[d]oxazol-2-yl)benzoate (**3g**).* White solid (55 mg, 54%), mp 197–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=3.96 (s, 3H), 7.36–7.41 (m, 2H), 7.58–7.61 (m, 1H), 7.79–7.81 (m, 1H), 8.17–8.19 (m, 2H), 8.33 (d, J=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=51.4, 109.8, 119.4, 123.9, 124.7, 126.5, 129.1, 130.0, 131.5, 141.0, 149.9, 160.9, 165.3; HRMS-ESI (m/z): calcd for $C_{15}H_{12}NO_3$ $[M+H]^+$ 254.0812, found 254.0802.

*4.2.8. 2-(4-Bromophenyl)benzo[d]oxazole (**3h**).* White solid (91 mg, 83%), mp 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.35–7.37 (m, 2H), 7.56–7.58 (m, 1H), 7.67 (d, J=8.5 Hz, 2H), 7.75–7.78 (m, 1H), 8.12 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.7, 119.1, 123.8, 124.4, 125.1, 125.2, 128.0, 131.2, 141.0, 149.8, 161.1; HRMS-ESI (m/z): calcd for $C_{13}H_9BrNO$ $[M+H]^+$ 273.9862, found 273.9853.

*4.2.9. 2-(4-Chlorophenyl)benzo[d]oxazole (**3i**).* White solid (56 mg, 61%), mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.31–7.33 (m, 2H), 7.42–7.44 (m, 2H), 7.50–7.52 (m, 1H), 7.72–7.75 (m, 1H), 8.11–8.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.6, 119.1, 123.7, 124.3, 124.6, 127.8, 128.2, 136.7, 141.0, 149.7, 161.0; HRMS-ESI (m/z): calcd for $C_{13}H_9ClNO$ $[M+H]^+$ 230.0367, found 230.0361.

*4.2.10. 2-(4-Fluorophenyl)benzo[d]oxazole (**3j**).* White solid (46 mg, 53%), mp 94–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.12–7.16 (m, 2H), 7.27–7.33 (m, 2H), 7.49–7.51 (m, 1H), 7.71–7.74 (m, 1H), 7.17–7.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.5, 115.1 (d, J=22.1 Hz), 119.0, 122.4 (d, J=3.2 Hz), 123.6, 124.1, 128.8 (d, J=8.8 Hz), 141.0, 149.7, 161.0, 163.7 (d, J=251.1 Hz); HRMS-ESI (m/z): calcd for $C_{13}H_9FNO$ $[M+H]^+$ 214.0663, found 214.0655.

*4.2.11. 4-(Benzo[d]oxazol-2-yl)benzonitrile (**3k**).* Light yellow solid (46 mg, 52%), mp 202–204 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.38–7.44 (m, 2H), 7.60–7.62 (m, 1H), 7.81 (d, J=8.4 Hz, 3H), 8.35 (d, J=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.9, 113.8, 117.2, 119.6, 124.1, 125.2, 127.0, 130.1, 131.7, 140.9, 149.9, 159.9; HRMS-ESI (m/z): calcd for $C_{14}H_9N_2O$ $[M+H]^+$ 221.0709, found 221.0704.

*4.2.12. 2-(Naphthalen-1-yl)benzo[d]oxazole (**3l**).* White solid (80 mg, 82%), mp 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.36–7.38 (m, 2H), 7.54–7.62 (m, 3H), 7.67–7.71 (m, 1H), 7.86–7.91 (m, 2H), 7.99 (d, J=8.2 Hz, 1H), 8.40 (d, J=7.2 Hz, 1H), 9.46 (d, J=8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=109.5, 119.3, 122.5, 123.5, 123.9, 124.3, 125.3, 125.4, 126.9, 127.7, 128.3, 129.7, 131.3, 132.9, 141.3, 149.1, 161.8; HRMS-ESI (m/z): calcd for $C_{17}H_{12}NO$ $[M+H]^+$ 246.0913, found 246.0907.

*4.2.13. 6-Methyl-2-phenylbenzo[d]oxazole (**3m**).* White solid (59 mg, 71%), mp 93–95 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.50 (s, 3H), 7.16 (d, J=8.1 Hz, 1H), 7.37 (s, 1H), 7.50–7.52 (m, 3H), 7.64 (d, J=8.1 Hz, 1H), 8.22–8.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=20.8, 109.8, 118.4, 124.8, 126.4, 126.5, 127.9, 130.3, 134.6, 139.0, 150.1, 161.6; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0913, found 210.0909.

*4.2.14. 5-Methyl-2-phenylbenzo[d]oxazole (**3n**).* White solid (67 mg, 80%), mp 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.47 (s, 3H), 7.13–7.15 (m, 1H), 7.43 (d, J=8.3 Hz, 1H), 7.50–7.51 (m, 3H), 7.55 (s, 1H), 8.22–8.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=20.5, 108.9, 119.0, 125.2, 126.4, 126.6, 127.9, 130.4, 133.4, 141.4, 148.0, 162.1; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0913, found 210.0910.

*4.2.15. 5-Methoxy-2-phenylbenzo[d]oxazole (**3o**).* White solid (46 mg, 51%), mp 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=3.86 (s, 3H), 6.94 (dd, J=2.6, 8.9 Hz, 1H), 7.26 (d, J=2.3 Hz, 1H), 7.45 (d, J=8.9 Hz, 1H), 7.50–7.52 (m, 3H), 8.21–8.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=54.9, 101.9, 109.7, 112.7, 126.3, 126.5, 127.9, 130.4, 142.0, 144.5, 156.4, 162.8; HRMS-ESI (m/z): calcd for $C_{14}H_{12}NO_2$ $[M+H]^+$ 226.0863, found 226.0857.

*4.2.16. 2-Phenylnaphtho[2,3-d]oxazole (**3p**).* White solid (49 mg, 50%), mp 201–203 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.41–7.46 (m, 2H), 7.50–7.52 (m, 3H), 7.89–7.91 (m, 2H), 7.94–7.97 (m, 1H), 8.16 (s, 1H), 8.29–8.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=105.3, 116.4, 123.6, 124.4, 126.1, 126.9, 127.2, 127.5, 127.9, 130.6, 130.8, 131.0, 141.2, 148.8, 164.0; HRMS-ESI (m/z): calcd for $C_{17}H_{12}NO$ $[M+H]^+$ 246.0913, found 246.0906.

*4.2.17. 5-chloro-2-phenylbenzo[d]oxazole (**3q**).* White solid (42 mg, 46%), mp 99–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.26–7.29 (m, 1H), 7.43–7.54 (m, 4H), 7.71 (d, J=1.1 Hz, 1H), 8.18–8.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=110.2, 119.0, 124.3, 125.7, 126.7, 127.9, 129.0, 130.9, 142.3, 148.3, 163.3; HRMS-ESI (m/z): calcd for $C_{13}H_9ClNO$ $[M+H]^+$ 230.0367, found 230.0361.

*4.2.18. 2-Phenylbenzo[d]thiazole (**3r**).* Light yellow solid (51 mg, 60%), mp 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=7.36 (t, J=7.6 Hz, 1H), 7.46–7.49 (m, 4H), 7.87 (d, J=8.0 Hz, 1H), 8.06–8.09 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ=120.6, 122.3, 124.2, 125.3, 126.6, 128.0, 130.0, 132.7, 134.1, 153.2, 167.1; HRMS-ESI (m/z): calcd for $C_{13}H_{10}NS$ $[M+H]^+$ 212.0528, found 212.0523.

*4.2.19. 2-Phenyl-1H-benzo[d]imidazole (**3s**).* White solid (66 mg, 85%), mp 288–290 °C; ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ=7.23–7.25 (m, 2H), 7.49–7.65 (m, 5H), 8.25 (d, J=7.5 Hz, 2H), 12.97 (broad s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6, 25 °C): δ=121.6,

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126.0, 128.4, 129.3, 129.7, 150.8; HRMS-ESI (m/z): calcd for $C_{13}H_{11}N_2$ $[M+H]^+$ 195.0917, found 195.0912.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.11.040.

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