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Base-Promoted Formal Arylation of Benzo[*d*]oxazoles with Acyl Chloride

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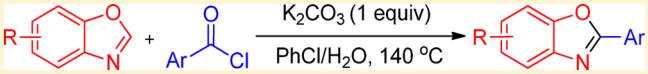
Supporting Information

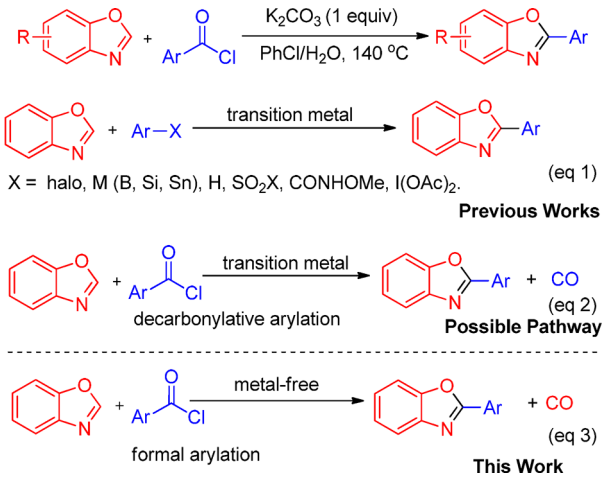
ABSTRACT: A base-promoted formal arylation of benzo[*d*]-oxazoles with acyl chloride was achieved in moderate to good yields. This reaction was triggered by the *N*-acylation of oxazole to form an iminium intermediate. Then, the addition of H_2O to the iminium formed the hemiacetal intermediate. After the sequential ring-opening, extrusion of CO, the ring closure, the dehydration delivered the formal arylation product. In comparison with the transition-metal-catalyzed methodology, it represents an alternative arylation method leading to 2-arylbenzooxazole.



INTRODUCTION

The frameworks of 2-arylbenzooxazole are widely found in pharmaceuticals, organic dyes, and natural products.[1] The direct arylation of benzooxazole C−H bond was the most straightforward method to construct this structure because prefunctionalization is not required.[2] As such, the use of $PhSO_2X$,[3] aryl boron,[4] aryl silicon,[5] aryl tin,[6] phenol derivatives,[7] and aryl halide[8] as arylation reagents in such transformations was well developed (Scheme 1, eq 1).

Scheme 1. Arylation of Benzooxazole



Meanwhile, other arylation regents were also well developed. For example, in 2012, we described a palladium-catalyzed direct arylation of benzooxazole with $ArI(OAc)_2$.[9] Su reported the palladium-catalyzed direct arylation of benzooxazole by simple unactivated arene.[10] Wang demonstrated the palladium-catalyzed deamidative arylation of azoles with arylamides.[11] The iron-catalyzed arylation of oxazole by aldehyde was reported by Li.[12] However, a transition metal was required for all of the aforementioned transformations.

Recently, the carboxylic acid derivatives were widely used as the arylating reagent via the transition-metal-catalyzed decarboxylation[13] or decarbonylation.[14] We envisioned that arylation of the benzooxazole C−H bond could be achieved by the transition-metal-catalyzed decarbonylative coupling of acyl chloride (Scheme 1, eq 2).[15] With this in mind, we found an unexpected transition-metal-free base-promoted formal arylation of benzooxazole stemmed from its inherent property by acyl chloride proceeding through a ring-opening and closure pathway (Scheme 1, eq 3). Although 2-arylbenzooxazole could be facile prepared from the annulation of 2-hydroxyphenylamine and benzoic acid,[16] from the functional group transformation point of view, this formal arylation procedure represents an alternative arylation method leading to 2-aryl benzooxazole. Herein, we report our study on it.

RESULTS AND DISCUSSION

Initially, in light of our recent work on the copper(II)-catalyzed *ortho*-functionalization of 2-arylpyridines with acyl chlorides,[17] we envisioned developing the copper-catalyzed decarbonylation of acyl chloride by in situ formation of anhydride in the presence of base and H_2O. Indeed, heating the combination of benzooxazole, benzoyl chloride (2 equiv), $CuCl_2$ (0.2 equiv), and K_2CO_3 (1 equiv) in H_2O (0.4 mL) at 140 °C afforded the arylation product in 23% yield. To our surprise, the arylation product was isolated in a slightly higher yield of 31% in the absence of $CuCl_2$ (table 1, entry 1). Further studies revealed the employment of cosolvent also delivered the yield in the absence of any transition metal. In $PhCl/H_2O$ (1/1), the arylation product was isolated in 31% yield in the presence of 1 equiv of K_2CO_3 (Table 1, entry 3). To our delight, the yield

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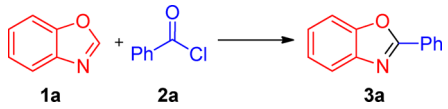
Table 1. Selected Results for Screening the Optimized Reaction Conditions[a]



1a 2a 3a

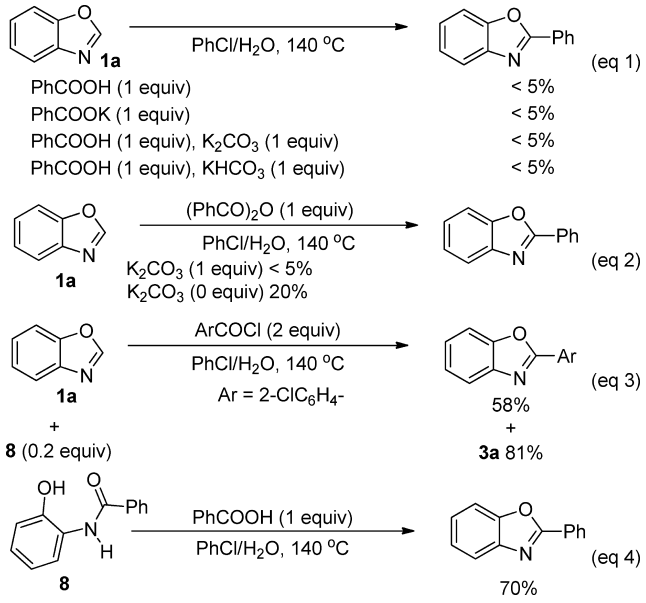
entry	base	solvent	yield(%)
1	K_2CO_3	H_2O	31
2	K_2CO_3	CH_3CN/H_2O = 1:1 (0.6 mL)	24
3	K_2CO_3	PhCl/H_2O = 1:1 (0.6 mL)	31
4	K_2CO_3	PhCl/H_2O = 3:1 (0.4 mL)	82 (41)[b]
5	K_3PO_4	PhCl/H_2O = 3:1 (0.4 mL)	71
6	Na_2CO_3	PhCl/H_2O = 3:1 (0.4 mL)	36
7	$NaHCO_3$	PhCl/H_2O = 3:1 (0.4 mL)	61
8	*t*-BuOK	PhCl/H_2O = 3:1 (0.4 mL)	43
9	NaOAc	PhCl/H_2O = 3:1 (0.4 mL)	49
10	KOH	PhCl/H_2O = 3:1 (0.4 mL)	50

[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), K_2CO_3 (1.0 equiv), air, 140 °C, 12 h, sealed tube. [b]N_2.

dramatically increased to 82% by adjusting the ratio of PhCl and H_2O to 3:1 (table 1, entry 4). A 41% yield was obtained under N_2. Under this cosolvent, replacing K_2CO_3 with other bases, such as K_3PO_4, Na_2CO_3, $NaHCO_3$, *t*-BuOK, NaOAc, and KOH, resulted in low efficiency (Table 1, entries 5−10).

More experiments were conducted to gain some insight into this unexpected reaction. Replacing acyl chloride with benzoic acid, the arylation product was isolated in less than 5% yield either in the presence or the absence of K_2CO_3 (1 equiv) and $KHCO_3$ (1 equiv) (Scheme 2, eq 1). Benzoic potassium also

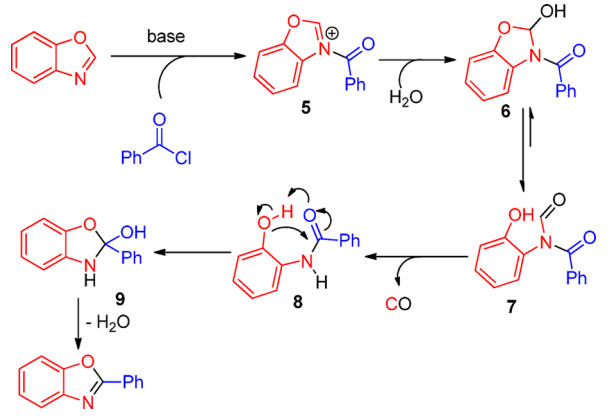
Scheme 2. Mechanism Study



failed to deliver the arylation product. To our surprise, in the presence and absence of K_2CO_3, benzoic anhydride only delivered the arylation product in <5% and 20% yields, respectively (Scheme 2, eq 2). These results ruled out the possibility of benzoic acid and anhydride as the intermediate in this transformation. Further study revealed compound **8** was detected during this reaction. When 0.2 equiv of compound **8** was subjected to the standard reaction system of 2-ClC_6H_4COCl and benzooxazole, 2-phenylbenzooxazole was isolated in 81% yield (Scheme 2, eq 3). Under the standard procedure, the extrusion of CO was detected by phosphomolybdic acid strip and none of CO was detected in the reaction of eq 4 in Scheme 2 (for details, see the Supporting Information). In the presence of 0.2 mL of Hg(0), **3a** was isolated in a comparable 70% yield under the standard procedure, ruling out the possibility of trace of transition metal as the true catalyst.

Based on these experimental results, we believed the reaction proceeded through a sequential ring-opening and closure pathway, as illustrated in Scheme 3. First, in the presence of

Scheme 3. Proposed Mechanism



base, the *N*-acylation of benzooxazole takes place to form the iminium species **5**.[18] The poor reactivity of benzoic acid in this procedure is at least partly due to its poor ability in this acylating step. Then, the hemiacetal intermediate **6** is formed by the nucleophilic attack of H_2O to the iminium **5**. Second, the equilibrium reaction between aldehyde and hemiacetal facilitates the ring-opening of intermediate **6** to form intermediate **7**. Then, the formed intermediate **7** produces intermediate **8** by the loss of CO.[19] Third, the cyclization of intermediate **8** forms the hemiacetal intermediate **9**. Finally, the dehydration of intermediate **9** delivers the formal arylation product.

Next, we examined the substrate scope of acyl chlorides in this arylation reaction. As shown in Figure 1, acyl chlorides substituted with a series of functional groups at the phenyl ring, such as chloro, fluoro, as well as trifluoromethyl, afforded satisfactory yields (**3d−i**, Figure 1). Either electron-rich or electron-poor substrates readily reacted with benzo[*d*]oxazole in good to excellent yields. For some substrates with electron-withdrawing substituents, prolonged reaction time was required. In particular, the electron-poor *m*-trifluoromethylbenzoyl delivered the arylation product in 91% yield (**3h**, Figure 1). The steric hindrance had little effect on the reaction. For example, **3f** was isolated in 80% yield. Notably, cyclohexanecarbonyl chloride also took part in this reaction with moderate yield (**3j**, Figure 1).

Next, we conducted the reaction of benzo[*d*]oxazole and 4-trifluoromethylbenzoyl chloride on a 6 mmol scale with elongated time (20 h). To our delight, **3i** was isolated in a comparable 84% (1.319 g) yield.

Encouraged by these promising results, various benzo[*d*]-oxazole derivatives were tested. To our delight, different functional groups including 5-methyl, 5-chloro, 6-methyl, and 5-*tert*-butyl were well tolerated (**4a−g**, Figure 2). Satisfyingly,

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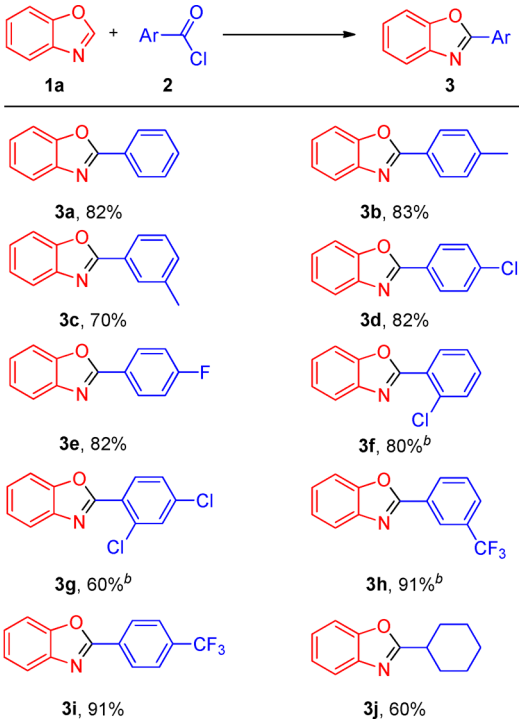

Figure 1. Arylation of benzo[*d*]oxazole with acyl chlorides. (a) Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), K_2CO_3 (1.0 equiv), solvent (0.4 mL, PhCl/H_2O = 3/1), air, 140 °C, 12 h, sealed tube. (b) 24 h.

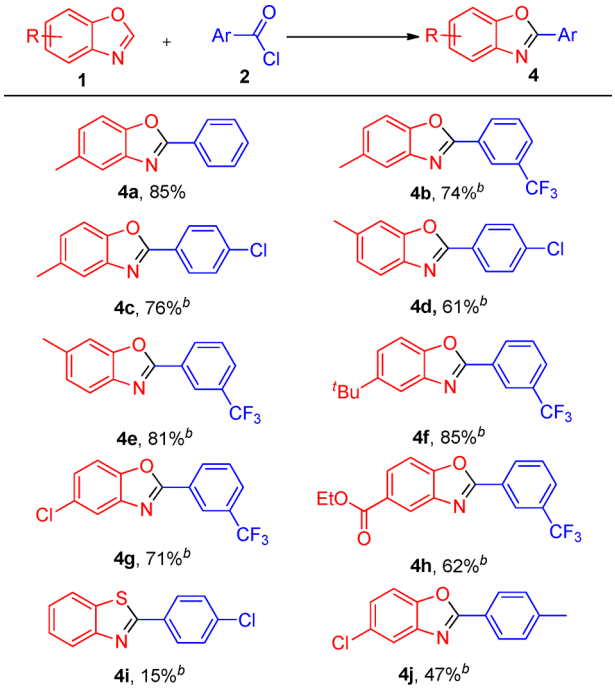

Figure 2. Arylation of benzo[*d*]oxazole derivatives with acyl chlorides. (a) Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), K_2CO_3 (1.0 equiv), solvent (0.4 mL, PhCl/H_2O = 3/1), air, 140 °C, 12 h, sealed tube. (b) 24 h.

the electron-withdrawing substituents such as ethyloxycarbonyl also tolerated well to afford the arylation products in moderate yield (**4h**, Figure 2). Significantly, benzothiazole also took part in the formal arylation under the standard procedure in low yield (**4i**, Figure 2).

CONCLUSION

In conclusion, we have developed a base-promoted protocol of formal benzooxazole 2-arylation using aryl chloride as the coupling partner. *N*-acylated product of oxazole served as the intermediate in this transformation. Then, the sequential addition of H_2O, ring-opening, extrusion of CO, ring closure, and dehydration delivered the formal arylation product. It represents an alternative arylation method leading to 2-aryl benzooxazole.

EXPERIMENTAL SECTION

General Information. Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 or 300 MHz spectrometer (^{1}H 500 or 300 MHz, ^{13}C 125 or 75 MHz) using $CDCl_3$ as the solvent at room temperature. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) or 7.26 ppm in $CDCl_3$ as an internal standard. ^{13}C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm). Chemical shifts are given in δ relative to TMS, and the coupling constants J are given in Hz. Column chromatography was performed using EM silica gel 60 (300−400 mesh).

General Procedure. Under air atmosphere, a sealed reaction tube was charged with benzo[*d*]oxazole (0.2 mmol), acyl chloride (0.4 mmol), K_2CO_3 (0.2 mmol), and PhCl/H_2O = 3/1 (0.4 mL). The mixture was kept stirring under air at 140 °C for 12 h. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether−ethyl acetate as eluent to give the desired product.

2-Phenylbenzo[*d*]oxazole (3a).[3d] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (31.9 mg, 82% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.28−8.26 (m, 2H), 7.79−7.78 (m, 1H), 7.60−7.58 (m, 1H), 7.54−7.53 (m, 3H), 7.38−7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.0, 150.8, 142.1, 131.5, 128.9, 127.6, 127.2, 125.1, 124.6, 120.0, 110.6.

2-(*p*-Tolyl)benzo[*d*]oxazole (3b).[3d] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (34.6 mg, 83% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.15 (d, J = 8.2 Hz, 2H), 7.77−7.75 (m, 1H), 7.57−7.55 (m, 1H), 7.34−7.32 (m, 4H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.3, 150.7, 142.2, 142.0, 129.6, 127.6, 124.8, 124.5, 124.4, 119.8, 110.5, 21.6.

2-(*m*-Tolyl)benzo[*d*]oxazole (3c).[20] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (29.1 mg, 70% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.10 (s, 1H), 8.06 (d, J = 7.6 Hz, 1H), 7.79−7.76 (m, 1H), 7.59−7.57 (m, 1H), 7.44−7.39 (m, 1H), 7.37−7.33 (m, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.2, 150.7, 142.1, 138.7, 132.3, 128.8, 128.2, 127.0, 125.0, 124.7, 124.5, 119.9, 110.5, 21.3.

2-(4-Chlorophenyl)benzo[*d*]oxazole (3d).[21] Flash column chromatography on silica gel (ethyl acetate/ petroleum ether, 1:20) gave the product (37.8 mg, 82% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.19 (d, J = 8.7 Hz, 2H), 7.78−7.75 (m, 1H), 7.58−7.56 (m, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.38−7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.0, 150.7, 142.0, 137.7, 129.2, 128.8, 125.6, 125.3, 124.7, 120.1, 110.6.

2-(4-Fluorophenyl)benzo[*d*]oxazole (3e).[3d] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (35 mg, 82% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27−8.23 (m, 2H), 7.79−7.74 (m, 1H), 7.58−7.54 (m, 1H), 7.38−7.32 (m, 2H), 7.24−7.18 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8 (d, J_{C-F} = 251.1 Hz), 162.1, 150.8, 142.0,

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129.8 (d, J_{C-F} = 8.9 Hz), 125.1, 124.6, 123.5 (d, J_{C-F} = 3.1 Hz,) 120.0, 116.1 (d, J_{C-F} = 22.0 Hz,) 110.5.

2-(2-Chlorophenyl)benzo[*d*]oxazole (3f).[21] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (36.8 mg, 80% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (dd, J_1 = 7.5, J_2 = 2.0 Hz, 1H), 7.86−7.85 (m, 1H), 7.63−7.61 (m, 1H), 7.58−7.56 (m, 1H), 7.47−7.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.9, 150.6, 141.6, 133.5, 131.9, 131.8, 131.4, 126.9, 126.3, 125.5, 124.6, 120.5, 110.7.

2-(2,4-Dichlorophenyl)benzo[*d*]oxazole (3g).[21] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (31.7 mg, 60% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 6.7 Hz,1H), 7.62−7.59 (m, 2H), 7.42−7.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.1, 150.5, 141.6, 137.5, 134.3, 132.5, 131.3, 127.4, 125.8, 124.8, 124.7, 120.6, 110.8.

2-(3-(Trifluoromethyl)phenyl)benzo[*d*]oxazole (3h).[20] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gave the product (48.0 mg, 91% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.53 (s, 1H), 8.43 (d, J = 7.8 Hz, 1H), 7.80−7.77 (m, 2H), 7.66 (t, J = 7.8 Hz, 1H), 7.62−7.60 (m, 1H), 7.41−7.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.5, 150.8, 141.9, 131.6 (q, J_{C-F} = 32.7 Hz,), 130.6, 129.5, 128.1, 127.9 (q, J_{C-F} = 3.5 Hz), 125.7, 124.9, 124.5 (q, J_{C-F} = 3.9 Hz), 123.7 (q, J_{C-F} = 271.0 Hz), 120.3, 110.8.

2-(4-(Trifluoromethyl)phenyl)benzo[*d*]oxazole (3i).[3c] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gave the product (48.0 mg, 91% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.38 (d, J = 8.1 Hz, 2H), 7.82−7.78 (m, 3H), 7.64−7.60 (m, 1H), 7.44−7.39 (m, 2H);^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 150.8, 141.8, 132.9 (q, J_{C-F} = 32.8 Hz), 130.3, 127.7, 125.8 (q, J_{C-F} = 3.75 Hz), 124.8, 123.7 (q, J_{C-F} = 270.8 Hz), 120.3, 110.7.

2-Cyclohexylbenzo[*d*]oxazole (3j).[23] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (24.1 mg, 60% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.66 (m, 1H), 7.48−7.45 (m, 1H), 7.27 (dd, J_1 = 6.0 Hz, J_2 = 3.2 Hz, 2H), 3.00−2.89 (m, 1H), 2.18−2.13 (m, 2H), 1.89−1.84 (m, 2H), 1.76−1.64 (m, 3H), 1.49−1.25 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 150.5, 141.2, 124.3, 123.9, 119.5, 110.2, 37.9, 30.4, 25.7, 25.6.

5-Methyl-2-phenylbenzo[*d*]oxazole (4a).[3c] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (35.7 mg, 85% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.26−8.24 (m, 2H), 7.56 (s, 1H), 7.52−7.51 (m, 3H), 7.45 (d, J = 8.3 Hz, 1H), 7.16 (d, J = 8.2 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 163.1, 149.0, 142.3, 134.3, 131.3, 128.8, 127.5, 127.3, 126.2, 119.9, 109.9, 21.5.

5-Methyl-2-(3-(trifluoromethyl)phenyl)benzo[*d*]oxazole (4b). Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (41.2 mg, 74% yield) as a white solid: mp 116−117 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.50 (s, 1H), 8.40 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.7 Hz, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.56 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.5, 149.1, 142.1, 134.8, 131.6 (q, J_{C-F} = 32.6 Hz), 130.5, 129.4, 128.2, 127.7 (q, J_{C-F} = 3.5 Hz), 126.8, 124.4 (q, J_{C-F} = 3.8 Hz), 123.7 (q, J_{C-F} = 270.9 Hz), 120.1, 110.1, 21.5; IR (prism, cm^{-1}): 1713, 1345, 1223, 1114, 804; MS(EI) 277 (M^+); HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{15}H_{11}F_3NO$ 278.0787, found 278.0788.

2-(4-Chlorophenyl)-5-methylbenzo[*d*]oxazole (4c).[21] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (37.0 mg, 76% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.16 (d, J = 8.6 Hz, 2H), 7.54 (s, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.3 Hz, 1H), 7.16 (d, J = 8.3 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.1, 148.9, 142.1, 137.5, 134.5, 129.1, 128.7, 126.4, 125.8, 119.9, 109.9, 21.5.

2-(4-Chlorophenyl)-6-methylbenzo[*d*]oxazole (4d).[22] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (29.5 mg, 61% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.7 Hz, 2H), 7.35 (s, 1H), 7.16 (d, J = 8.15 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.5, 151.0, 139.8, 137.4, 135.8, 129.2, 128.6, 125.9, 125.8, 119.4, 110.7, 21.8.

6-Methyl-2-(3-(trifluoromethyl)phenyl)benzo[*d*]oxazole (4e). Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (44.9 mg, 81% yield) as a white solid: mp 84−85 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.50 (s, 1H), 8.40 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.66−7.62 (m, 2H), 7.39 (s, 1H), 7.19 (d, J = 8.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.0, 151.1, 139.7, 136.2, 131.6 (q, J_{C-F} = 32.5 Hz), 130.4, 129.5, 128.2, 127.6(q, J_{C-F} = 3.6 Hz), 126.2, 124.4 (q, J_{C-F} = 3.6 Hz), 123.7 (q, J_{C-F} = 270.8 Hz), 119.6, 110.8, 21.8; IR (prism, cm^{-1}): 1708, 1363, 1223, 1123, 808; MS(EI) 277 (M^+); HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{15}H_{11}F_3NO$ $(M + H)^+$ 278.0787, found 278.0787.

5-*tert*-Butyl-2-(3-(trifluoromethyl)phenyl)benzo[*d*]oxazole (4f). Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (54.2 mg, 85% yield) as a white solid: mp 113−114 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.52 (s, 1H), 8.42 (d, J = 7.8 Hz, 1H), 7.82 (s, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.51 (d, J = 8.6 Hz, 1H), 7.45 (m, J = 8.6 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.6, 148.8, 148.5, 141.8, 131.6 (q, J_{C-F} = 32.6 Hz), 130.5, 129.5, 128.2, 127.7 (q, J_{C-F} = 3.5 Hz) 124.4 (q, J_{C-F} = 3.6 Hz), 124.1 (q, J_{C-F} = 270.6 Hz), 116.8, 109.9, 35.0, 31.7; IR (prism, cm^{-1}): 1708, 1363, 1223, 1131, 810; MS(EI) 319 (M^+); HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{17}F_3NO$ $(M + H)^+$ 320.1257, found 320.1258.

5-Chloro-2-(3-(trifluoromethyl)phenyl)benzo[*d*]oxazole (4g).[3d] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (42.2 mg, 71% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.48 (s, 1H), 8.39 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.75 (s, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.52−7.51 (m, 1H), 7.36−7.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.8, 149.3, 143.0, 131.7 (q, J_{C-F} = 33.1 Hz), 130.7, 130.4, 129.6, 128.3 (q, J_{C-F} = 3.8 Hz), 127.6, 126.0, 124.6 (q, J_{C-F} = 3.9 Hz), 123.6 (q, J_{C-F} = 271.0 Hz), 120.3, 111.5.

Ethyl 2-(3-(Trifluoromethyl)phenyl)benzo[*d*]oxazole-5-carboxylate (4h). Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gave the product (41.6 mg, 62% yield) as a white solid: mp 109−110 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.51 (s, 1H), 8.48 (s, 1H), 8.42 (d, J = 7.9 Hz, 1H), 8.14 (dd, J_1 = 8.6 Hz, J_2 = 1.6 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.67 (t, J = 7.8 Hz, 1H), 7.62 (d, J = 8.6 Hz, 1H), 4.42 (q, J_1 = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.0, 162.7, 153.6, 141.9, 131.7 (q, J_{C-F} = 32.0 Hz), 130.8, 129.6, 128.3 (q, J_{C-F} = 3.6 Hz), 127.8, 127.5, 124.6 (q, J_{C-F} = 4.4 Hz), 123.4 (q, J_{C-F} = 271.0 Hz), 122.2, 110.5, 61.3, 14.3; IR (prism, cm^{-1}) 1709, 1365, 1223, 1119, 812; MS(EI) 335 (M^+); HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{17}H_{13}F_3NO_3$ $(M + H)^+$ 336.0842, found 336.0857.

2-(4-Chlorophenyl)benzo[*d*]thiazole (4i).[24] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (7.5 mg, 15% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, J = 8.1 Hz, 1H), 8.02 (d, J = 8.6 Hz, 2H), 7.90 (d, J = 7.9 Hz, 1H), 7.53−7.45 (m, 3H), 7.40 (t, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 154.1, 137.0, 135.0, 132.1, 129.3, 128.7, 126.5, 125.4. 123.3, 121.6.

5-Chloro-2-*p*-tolylbenzo[*d*]oxazole (4j).[3c] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (22.7 mg, 47% yield) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 2.0 Hz, 1H), 7.45 (d, J = 8.6 Hz, 1H), 7.32−7.27 (m, 3H), 2.43(s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 149.2, 143.3, 142.5, 129.9, 129.6, 127.7, 125.0, 123.9, 119.7, 110.1, 21.6.

Procedure for the Synthesis of 3i on Gram Scale. Under air atmosphere, a flask was charged with benzo[*d*]oxazole (0.715 g, 6 mmol), 4-trifluoromethylbenzoyl chloride (2.503 g, 12 mmol), K_2CO_3 (0.829 g, 6 mmol), and PhCl/H_2O = 3/1 (12 mL). The mixture was kept stirring under air at 140 °C for 20 h. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography

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on silica gel with petroleum ether/ethyl acetate as eluent to give **3i** (1.319 g, 84%).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **3aa**−**aj** and **3ba**−**ia**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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