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Copper-Catalyzed Synthesis of Benzoxazoles via a Regioselective C−H Functionalization/C−O Bond Formation under an Air Atmosphere

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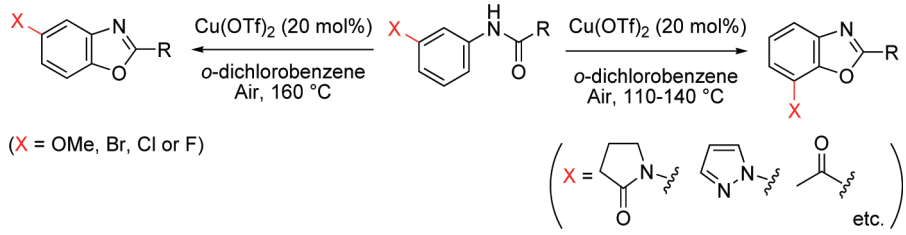

An efficient method for the synthesis of functionalized benzoxazoles is described that involves a copper(II)-catalyzed regioselective C−H functionalization/C−O bond formation protocol. The use of dichlorobenzene as a solvent at 160 °C allows the use of air as the terminal oxidant in the catalytic synthesis of benzoxazoles in a process that has high functional group tolerance. The presence of a directing group at the meta position markedly improves the reaction efficacy and a variety of 7-substituted benzoxazoles are selectively produced under mild reaction conditions. The mechanism of the reaction is also discussed in this report.

Introduction

Benzoxazoles are an important class of heterocyclic compounds that have many applications in medicinal chemistry. For example, benzoxazole derivatives have been characterized as estrogen receptor agonists,[1] 5-HT_3 receptor agonists,[2] melatonin receptor agonists,[3] HIV-1 reverse transcriptase inhibitors,[4] amyloidogenesis inhibitors,[5] Rho kinase inhibitors,[6] and anti-tumor agents.[7] In addition to their use in medicinal chemistry, benzoxazoles are recognized as an important scaffold in fluorescent probes such as anion and metal cation sensors.[8] Because of these and other applications, much attention has been paid to the development of efficient methods for the preparation of benzoxazoles.

A number of methods for the synthesis of benzoxazoles have been reported. Among these, two classical approaches that start from 2-aminophenol precursors have often been applied for the elaboration of the benzoxazole moiety. The first approach involves a condensation reaction of the 2-aminophenols with acid chlorides in the presence of strong acid under heat or microwave irradiation.[9] The second involves the reaction of the 2-aminophenols with aldehydes in the presence of a stoicheometric or catalytic amount of an oxidant.[10] Recently, several

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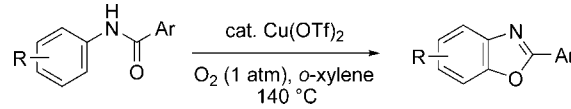
groups reported transition-metal-catalyzed C−N and/or C−O coupling approaches for the synthesis of benzoxazoles using halogenated arene precusors. For example, Glorius reported the copper-catalyzed domino C−N/C−O bond forming reaction between 1,2-dihaloarenes and primary amides.[11] Batey and Bolm reported copper-[12] or iron-catalyzed[13] intramolecular O-arylation of 2-haloanilides for the synthesis of benzoxazoles. Although these approaches provide an efficient access to functionalized benzoxazoles, development of new and effective synthetic approaches with high atom economy is still desired.

In recent years, transition metal-catalyzed C−H functionalization/C−heteroatom bond formation has emerged as a powerful method for the direct conversion of arenes and alkanes into functionalized products.[14] An intramolecular version of this process has been successfully applied to the direct construction of benzo-fused heterocyclic compounds from simple precusors. In 2005, pioneering work by the Buchwald group[15a] afforded efficient synthetic approaches to functionalized carbazoles by palladium-catalyzed aromatic C−H activation followed by intramolecular C−N bond formations.[15] Subsequently, Yu and Inamoto expanded the scope of the palladium-catalyzed C−H functionalization/C−heteroatom bond forming reaction to include a variety of substrates thereby providing straightforward access to other classes of benzo-fused heterocycles such as indazoles,[16] indolines,[17] oxindoles,[18] benzothiazoles,[19] and benzothiophenes.[20] More recently, Buchwald has reported the use of a novel $Cu(OAc)_2/O_2$ catalytic system for C−H functionalization/C−N bond formation for the synthesis of benzimidazoles.[21] In a recent report, we also described a related $Cu(OTf)_2/O_2$ catalytic system for intramolecular oxidative C−O coupling of anilides in the synthesis of 2-arylbenzoxazoles (Scheme 1).[22,23] In this paper, we report a detailed investigation of the scope and limitations of the intramolecular C−O coupling process under an air atmosphere. We also disclose the results of directing group assisted regiocontrolled C−H functionalization/C−O bond formation for the efficient construction of 7-substituted benzoxazoles.

SCHEME 1. Copper-Catalyzed Intramolecular Oxidative C−O Coupling



Results and Discussion

Substrate Scope and Limitation. In our earlier work, a number of 2-arylbenzoxazoles were successfully synthesized from benzanilides utilizing 20 mol % of $Cu(OTf)_2$ and 1 atm of O_2 gas as terminal oxidant in *o*-xylene at 140 °C (method A). In a subsequent exploration, it became apparent that the reactions in *o*-dichlorobenzene (*o*-DCB) at 160 °C under an atmosphere of air gave superior results in most cases (method B).

Table 1 summarizes the scope and limitation of the oxidative C−O coupling reaction. Reactions of benzanilide **1a** and *p*-halogen-substituted derivatives **1b** and **1c** gave the corresponding benzoxazoles in good yield (entries 1−3). The reactions of substrates with a halogen or methoxy substituent at the meta position proceeded regioselectively at the less sterically hindered 6-position of the anilide to produce the corresponding 5-substituted benzoxazoles **2d**−**f**,**i** (entries 4−6 and 9). The *m*-halogen-substituted substrates **1d** and **1e** showed lower reactivities than the corresponding *p*-halogen-substituted substrates **1b** and **1c** (entries 2−5). Reaction of a substrate with the strongly electron-withdrawing nitro group did not proceed at all, even at elevated temperature (entry 7). Similarly, the electron-deficient 4-pyridinyl derivative **1h** failed to react and starting material was recovered (entry 8). On the other hand, substrates with an electron-donating alkoxy group at the 3- or 4-position gave the corresponding benzoxazoles in high yield (entries 9 and 10). The strong dependence of the reaction efficacy on the electronic nature of the arene ring indicates the involvement of an electrophilic aromatic substitution process in the cyclization reactions (see the later mechanistic discussion). The use of method B provided an increase in yield for the reactions of sterically demanding ortho-substituted substrates **1m** and **1n** (entries 13 and 14).

In contrast to the syntheses of 2-arylbenzoxazoles, the developed procedures were not effective for the preparation of simple 2-alkylbenzoxazoles. For example, the reaction of pivalanilide **1o** gave the desired product in only 19% yield. Cyclohexane-substituted substrate **1p** gave no desired product and instead the aromatized product **2a** was formed as a major product.

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TABLE 1. Scope of the Copper-Catalyzed Oxidative Cyclization[a]

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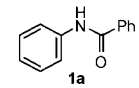
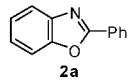
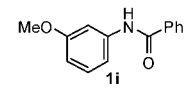
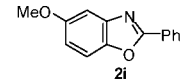
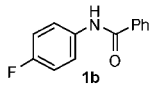
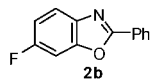
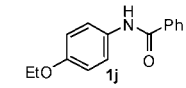
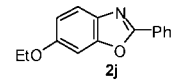
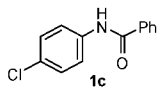
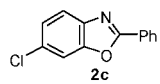
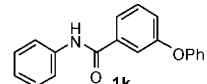
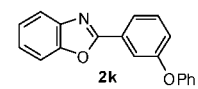
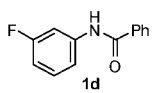
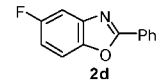
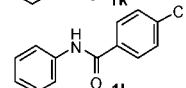
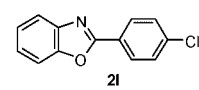
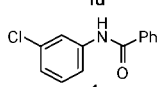
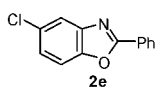
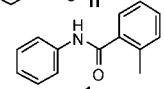
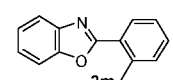
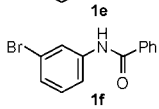
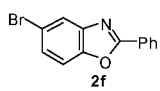
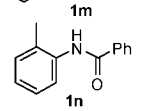
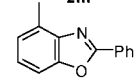
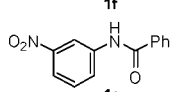
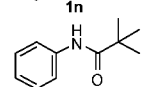
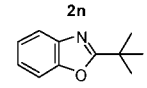
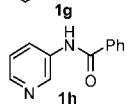
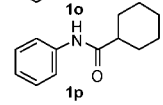
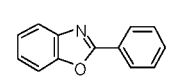
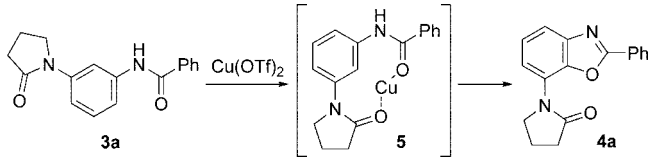
1	 1a	 2a	81	89	9	 1i	 2i	93	91
2	 1b	 2b	80	82	10	 1j	 2j	91	90
3	 1c	 2c	76	76	11	 1k	 2k	64	79
4	 1d	 2d	N.T.[b]	61	12	 1l	 2l	78	88
5	 1e	 2e	30	54	13	 1m	 2m	42	55
6	 1f	 2f	19	28	14	 1n	 2n	51	76
7	 1g	-	-	-	15	 1o	 2o	22	19
8	 1h	-	-	-	16	 1p	 2a	33	N.T.[b]

[a] Reaction conditions: method A: $Cu(OTf)_2$ (20 mol %), *o*-xylene, O_2 (1 atm), 140 °C, 28 h; method B: $Cu(OTf)_2$ (20 mol %), *o*-DCB, air (1 atm), 160 °C, 28 h. [b] Not tested.

SCHEME 2. Directed Cyclization of 3a



A Directed Cyclization Approach to 7-Substituted Benzoxazoles. Next, we focused our attention on the regioselectivity of the C−H functionalization/cyclization.[24] As discussed above, cyclization of *m*-halogen- or *m*-methoxy-substituted substrates cyclized at a less sterically hindered site. In contrast, *m*-pyrrolidinone-substituted substrate **3a** cyclized exclusively at the more sterically hindered 2 position to afford 7-substituted benzoxazole **4a** (Scheme 2). This regioselectivity can be ascribed to the formation of the doubly coordinated intermediate **5**. In addition to regiocontrol, the presence of the pyrrolidinone directing group at the meta position seems to improve the reaction efficacy (Table 2). The cyclization of **3a** proceeds under an atmosphere of air at 110 °C without significant drop in yield (entry 2). The use of *o*-DCB as a solvent at 110 °C gave the best result (entry 3). When the catalyst loading was lowered to 10 mol %, the yield of **4a** dropped to 73% yield.

(24) For intramolecular hydroarylation of alkenes by directed aromatic C−H functionalization/C−C bond formation, see: (a) Harada, H.; Thalji, R. K.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2008**, *73*, 6772. (b) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2005**, *70*, 6775. (c) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 9692.

TABLE 2. Optimization of Directed Cyclization of 3a[a]

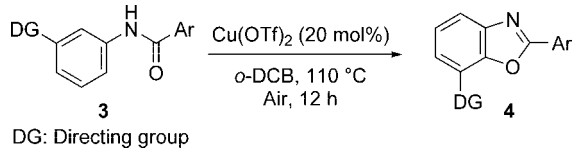
entry	$Cu(OTf)_2$ (mol %)	solvent	temp (°C)	gas (1 atm)	yield of **4a** (%)
1	20	*o*-xylene	140	O_2	82[b]
2	20	*o*-xylene	110	air	72
3	20	*o*-DCB	110	air	89
4	10	*o*-DCB	110	air	73

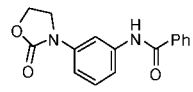
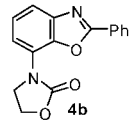
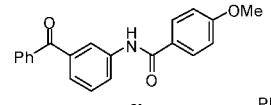
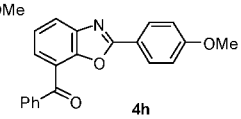
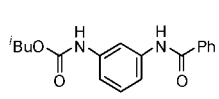
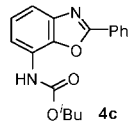
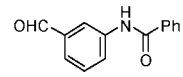
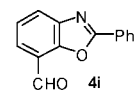
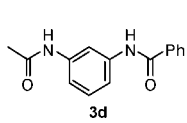
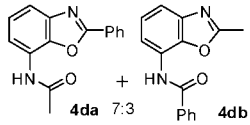
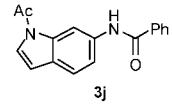
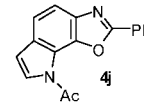
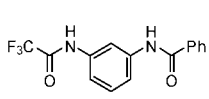
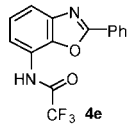
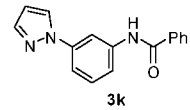
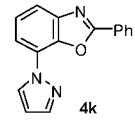
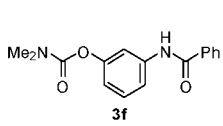
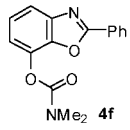
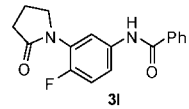
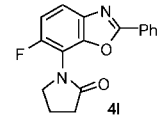
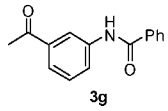
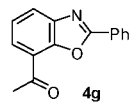
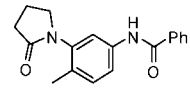
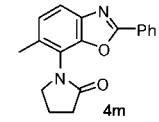
[a] Reaction run with 0.25 mmol substrate for 12 h. [b] Reaction time = 28 h.

The relatively mild conditions as well as the high yield of the directed cyclization of **3a** encouraged us to extend this methodology to the synthesis of a series of 7-substituted benzoxazoles. To our knowledge, there are no reports on the systematic evaluation of directed cyclization by aromatic C−H functionalization/C−heteroatom bond formation. As shown in Table 3, a broad range of functional groups can be utilized as directing group in the directed C−O coupling reactions.

The reaction of oxazolidinone-substituted substrates **3b** gave the desired 7-substituted benzoxazole **4b** in good yield (entry 1). A similar result was obtained with the acyclic carbamate-substituted substrate **3c** (entry 2). The reaction of the *m*-acetamide-substituted substrate **3d** gave a mixture of 2-phenylbenzoxazole **4da** and 2-methylbenzoxazole **4db** in 7:3 ratio, suggesting that the *N*-benzoyl group is more prone to cyclize as compared to the *N*-acetyl group (entry 3). In contrast, the *m*-trifluoroacetamide-substituted substrate **3e** cyclized exclusively at the *N*-benzoyl group to produce the corresponding 7-substituted 2-phenylbenzoxazole **4e** (entry 4). The reaction of phenyl dimethylcarbamate derivative **3f** gave the desired

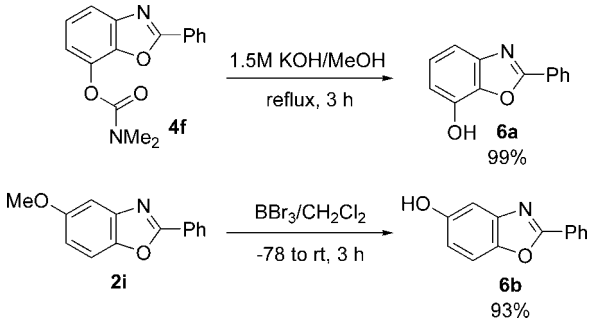
TABLE 3. Scope of Directed Cyclization[a]



entry	substrate	product	yield (%)	entry	substrate	product	yield (%)
1	 **3b**	 **4b**	82	7	 **3h**	 **4h**	80
2	 **3c**	 **4c**	82	8	 **3i**	 **4i**	74[b]
3	 **3d**	 **4da** 7:3 **4db**	70	9	 **3j**	 **4j**	90
4	 **3e**	 **4e**	58	10	 **3k**	 **4k**	44[c] 92[d]
5	 **3f**	 **4f**	64	11	 **3l**	 **4l**	69
6	 **3g**	 **4g**	78	12	 **3m**	 **4m**	40

[a] Reaction conditions: $Cu(OTf)_2$ (20 mol %), *o*-DCB, air, 110 °C, 12 h. [b] Reaction conducted at 140 °C. [c] Reaction conducted at 130 °C; 6-chlorinated **4k** was obtained (39% yield) as byproduct. [d] Reaction conducted at 125 °C in chlorobenzene.

SCHEME 3. Synthesis of 5- and 7-Hydroxybenzoxazoles



7-substituted product **4f** in moderate yield (entry 5). This product can be readily converted to 7-hydroxybenzoxazole **6a** by treatment with KOH in MeOH. On the other hand, the 5-hydroxy-substituted regioisomer **6b** can be obtained by deprotection of **2i** with BBr_3 (Scheme 3). The results described above demonstrate that ortho- and meta-substituted anilides can be converted to two different regioisomeric benzoxazoles respectively by changing the nature of the protecting groups of the intended substituent. Benzamides with electron-withdrawing directing groups such as acetyl, benzoyl, and formyl (**3g**−**i**) are good substrates for the directed cyclization providing the corresponding 7-substituted products in 74−80% yields (entries 6−8). An *N*-acetyl group on indole also served as directing group to afford the tricyclic product **4j** in high yield (entry 9). Interestingly, the reaction of pyrazole-substituted substrate **3k** in *o*-DCB at 130 °C afforded the desired product **4k** (44% yield) and 6-chlorinated compound **4k** as a byproduct (39% yield) (entry 10).[25] When the reaction was conducted in chlorobenzene at 125 °C, **4k** was obtained in 92% yield and no chlorinated byproduct was observed. Although the mechanism for the formation of the chlorinated byproduct is uncertain, *o*-DCB would be a source of Cl required for formation of the 6-chlorinated byproduct in the reaction of the pyrazole-substituted substrate **3k**. Introduction of substituents into the ortho position of the pyrrolidinone directing group did not affect regioselectivity of the cyclization (entry 11 and 12). However, the methyl-substituted substrate showed lower reactivity as compared with **3b** or ***3l***. One might predict this result because the steric bulk of the methyl substituent of **3m** would direct the

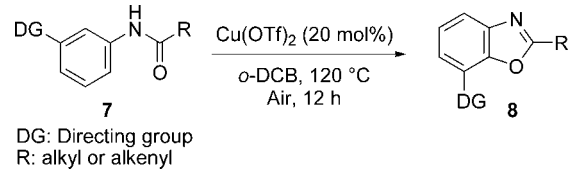
(25) Reaction of **3k** in *o*-DCB at 110 °C resulted in incomplete reaction and **4k** was obtained in 24% yield with a trace amount of chlorinated byproduct. The formation of chlorinated byproduct was not observed for the reaction of other substrates.

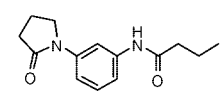
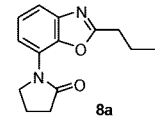
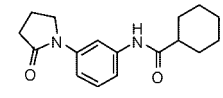
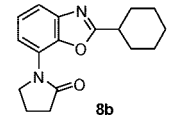
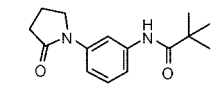
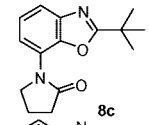
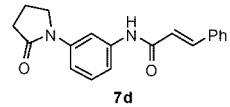
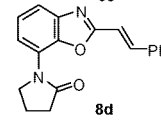
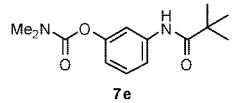
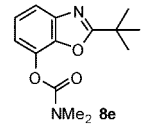
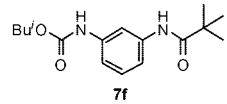
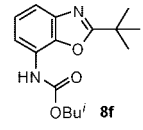
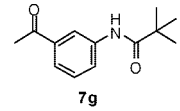
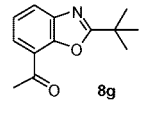
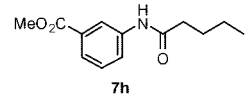
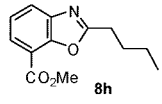
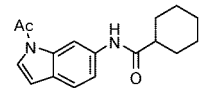
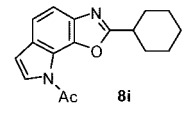
pyrrolidinone carbonyl group away from the plane of the aromatic ring, thus disturbing effective formation of a doubly coordinated intermediate such as **5**.

Directed Cyclizations toward 2-Alkyl- and 2-Alkenylbenzoxazoles. The successful formation of 7-substituted 2-arylbenzoxazoles under relatively mild conditions led us to reexamine the synthesis of 7-substituted 2-alkylbenzoxazoles by means of directed cyclization. Although copper-catalyzed cyclizations of simple alkyl-substituted anilides were unsuccessful (Table 1, entries 15 and 16), the use of the directed cyclization approach resulted in successful formation of 2-alkyl-substituted benzoxazoles. Although the yields are generally lower than the directed cyclizations of benzanilides (Table 3), a variety of 7-substituted 2-alkyl- and 2-alkenylbenzoxazoles can be synthesized in synthetically acceptable yields (Table 4). The prrolidinone-substituted substrates **7a**−**c** provided the corresponding 2-alkylbenzoxazoles in moderate to good yields (entries 1−3). Cinnamoylanilide **7d** provided **8d** without isomerization of olefin geometry (entry 4). Other directing groups were also effective for the directed cyclizations of alkyl-substituted substrates. These reactions demonstrate that the directed intramolecular C−O coupling reaction should be a useful methodology for generating medicinally important 7-substituted benzoxazoles and their derivatives.[1b,3,26]

Mechanistic Consideration. During our studies of the scope of the reaction, we had noticed that electron-rich anilides showed higher reactivities than electron-deficient anilides. This was confirmed by the time dependence curve for the oxidative coupling reactions of unsubstituted anilide **1a** and anilides with either an electron-donating methoxy substitution (**1i**) or an electron-withdrawing chloro substitution (**1e**) (Figure 1). This result is consistent with the findings of Buchwald et al., who observed that more electron-rich benzamidines reacted faster than electron-deficient benzamidines in the copper-catalyzed oxidative synthesis of benzimidazoles.[21] Furthermore, an electron-withdrawing halogen substituent at the meta position resulted in lower relativities as compared to *p*-halogen-substituted substrates with a halogen reactivity order of F > Cl > Br (Table 1). These observations suggest the involvement of an electrophilic aromatic substitution process in the reaction. In conjunction with the observed regioselectivity in the directed cyclizations, we currently believe an electrophilic metalation process is involved in the oxidative C−O coupling reaction (Scheme 4).[27] In this model, initial coordination of benzanilide to $Cu(OTf)_2$ would lead to directed ortho metalation by electrophilic aromatic substitution at the Cu center. The presence of a directing group at the meta position of the anilide would promote this process by the formation of doubly coordinated intermediate. The formation of a six-membered metallacycle and subsequent reductive elimination affords benzoxazole and a reduced copper species that is then reoxidized by molecular oxygen to complete the catalytic cycle. A different mechanism, which involves electrophilic aromatic substitution at the amide oxygen with concurrent leaving of the reduced copper species, seems unlikely, since favorable geometry of copper coordination for such a process would be hard to align in the doubly coordinated intermediate of directed cyclizations. Although there is no clear evidence for the formation of an ortho-metalated intermediate, experimental observations do not contradict the electrophilic metalation mechanism.

TABLE 4. Synthesis of 2-Alkyl-/2-Alkenylbenzoxazoles[a]



entry	substrate	product	yield (%)
1	 **7a**	 **8a**	58
2	 **7b**	 **8b**	76
3	 **7c**	 **8c**	83
4	 **7d**	 **8d**	60
5	 **7e**	 **8e**	46[b]
6	 **7f**	 **8f**	63
7	 **7g**	 **8g**	76
8	 **7h**	 **8h**	43
9	 **7i**	 **8i**	50

[a] Reaction conditions: $Cu(OTf)_2$ (20 mol %), *o*-DCB, air 120 °C, 12 h. [b] Reaction conducted at 130 °C.

(26) (a) Terasaka, T.; Tsuji, K.; Kato, T.; Nakanishi, I.; Kinoshita, T.; Kato, Y.; Kuno, M.; Inoue, T.; Tanaka, K.; Nakamura, K. *J. Med. Chem.* **2005**, *48*, 4750. (b) Harikrishnan, L. S.; Kamau, M. G.; Herpin, T. F.; Morton, G. C.; Liu, Y.; Cooper, C. B.; Salvati, M. E.; Qiao, J. X.; Wang, T. C.; Adam, L. P.; Taylor, D. S.; Chen, A. Y. A.; Yin, X.; Seethala, R.; Peterson, T. L.; Nirschl, D. S.; Miller, A. V.; Weigelt, C. A.; Appiah, K. K.; O'Connell, J. C.; Lawrence, M. R. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2640.

(27) We have reported in our previous communication that no kinetic isotope effect was observed in an intramolecular competition experiment using ortho deuterium labeled substrate (see ref 22). This suggests that a hydrogen abstraction step is not involved in the rate determining step and other metalation mechanisms such as σ-bond metathesis might be eliminated. Intramolecular isotope effects are sometimes observed in palladium-catalyzed C−H functionalizations, see: (a) Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 12084. (b) Shi, Z.; Li, B.; Wan, X.; Cheng, J.; Fang, Z.; Cao, B.; Qin, C.; Wang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 5554. (c) Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581.

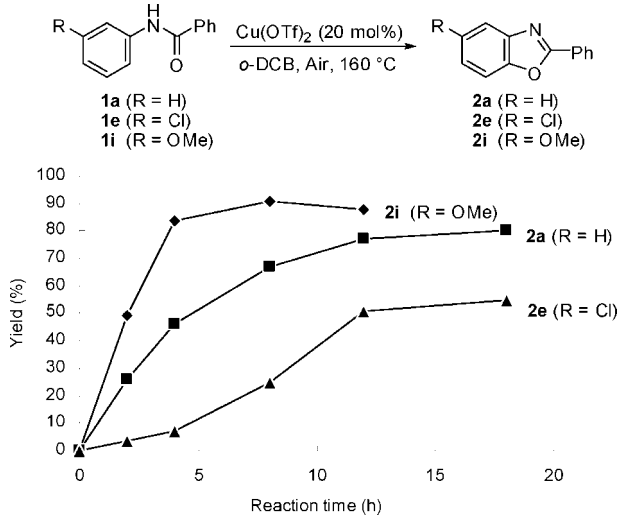
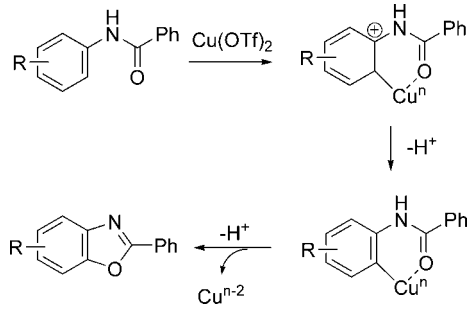


FIGURE 1. Time-dependent production of **2a**, **2e**, and **2i**.

SCHEME 4. Plausible Mechanism of Oxidative Cyclization



Conclusion

A variety of benzoxazoles have been obtained by the copper-catalyzed intramolecular oxidative C−O coupling of anilides that are synthesized from readily available anilines. This study has proven that O_2 gas can be successfully replaced with atmospheric air without affecting the efficiency of the reaction. Furthermore, the optimized directed cyclization conditions are mild enough to allow for the use of a range of directing groups and functional groups providing a variety of 7-substituted benzoxazoles. The directed cyclization approach should provide opportunities for further derivatization since many directing groups used in the present study can be converted into other functionalities after copper-catalyzed reactions. Overall, we believe that the described chemistry will give access to differently substituted benzoxazole skeletons in a simple and straightforward way.

Experimental Section

General Procedure for the Synthesis of Benzoxazoles under O_2 (Method A). To a dried Schlenk tube was added the anilide (0.25 mmol) and $Cu(OTf)_2$ (0.05 mmol). The tube and its contents were then purged under oxygen and *o*-xylene (0.5 mL) was added via syringe. The reaction mixture was then heated with stirring at 140 °C for 28 h under an oxygen atmosphere (balloon). After cooling to room temperature, a small amount of methanol was added to dissolve insoluble materials and the mixture was purified by preparative TLC.

General Procedure for the Synthesis of Benzoxazoles under Air (Method B). To a dried Schlenk tube was added the anilide (0.25 mmol), $Cu(OTf)_2$ (0.05 mmol), and *o*-dichlorobenzene (0.5 mL). The reaction mixture was then heated with stirring at 160 °C for 28 h under atmospheric air (balloon). After cooling to room temperature, a small amount of methanol was added to dissolve insoluble materials and the mixture was purified by preparative TLC.

2-Phenylbenzoxazole (2a). According to the general procedures described above with benzanilide **1a**, the product **2a** was obtained by preparative TLC (EtOAc−hexane 1:9) as a white solid (method A: 39.5 mg, 81%; method B: 43.3 mg, 89%). Mp 102−103 °C (lit.[12a] mp 101−102 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, 2H, J = 2.2 Hz, J = 5.6 Hz), 7.69 (m, 1H), 7.43−7.57 (m, 4H), 7.25−7.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 150.7, 142.1, 131.5, 128.9, 127.6, 127.1, 125.1, 124.6, 120.0, 110.6; MS (EI) *m*/*z* 195 (M^+).

General Procedure for the Directed Cyclization. To a dried Schlenk tube was added the anilide (0.25 mmol), $Cu(OTf)_2$ (0.05 mmol), and *o*-dichlorobenzene (0.5 mL). The reaction mixture was then heated with stirring at 110 °C for 12 h under atmospheric air (balloon). After cooling to room temperature, a small amount of methanol was added to dissolve insoluble materials and the mixture was purified by preparative TLC.

3-(2-Phenylbenzoxazol-7-yl)oxazolidin-2-one (4b). According to the general procedure described above with anilide **3b**, the product **4b** was obtained by preparative TLC (EtOAc−hexane 2:1) as a white solid (57.4 mg, 82%). Mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25−8.20 (m, 2H), 7.73 (d, 1H, J = 8.4 Hz), 7.62 (d, 1H, J = 8.0 Hz), 7.60−7.50 (m, 3H), 7.38 (t, 1H, J = 8.0 Hz), 4.65−4.50 (m, 2H), 4.82−4.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 155.6, 143.6, 142.6, 131.9, 129.0, 127.7, 126.6, 125.1, 122.4, 118.7, 117.2, 62.3, 46.5; HRMS (EI), *m*/*z* calcd for $C_{16}H_{12}N_2O_3$ (M^+) 280.0848, found 280.0855.

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Supporting Information Available: Full experimental details of the preparation and characterization of the starting materials and characterization data for all known products and for all new compounds (including copies of ^{1}H and ^{13}C NMR spectra). This material is available free of charge via the Internet at http://pubs.acs.org.

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