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Copper-Catalyzed Intramolecular C−N Bond Formation: A Straightforward Synthesis of Benzimidazole Derivatives in Water

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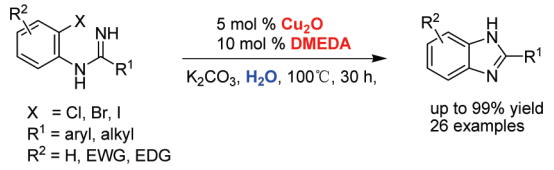

A straightforward, efficient, and more sustainable copper-catalyzed method has been developed for intramolecular *N*-arylation providing the benzimidazole ring system. With Cu_2O (5 mol %) as the catalyst, DMEDA (10 mol %) as the ligand, and K_2CO_3 as the base, this protocol was applied to synthesize a small library of benzimidazoles in high yields. Remarkably, the reaction was exclusively carried out in water, rendering the methodology highly valuable from both environmental and economical points of view.

Benzimidazoles are frequently found in a diverse array of compounds, including biologically and therapeutically active agents or natural products[1] and functional materials.[2] Therefore, the construction of these heterocycles has received much attention. The classical method for the synthesis of benzimidazoles is via the condensation of benzene-1,2-diamines with either carboxylic acid derivatives under strong acid/high temperature conditions or aldehydes under oxidative conditions.[3] Although these transformations are widely used in the preparation of benzimidazoles, there remain many drawbacks to overcome such as the use of highly toxic reagents, strong acids and, in some cases, harsh reaction conditions.[3]

Given the importance of these heterocycles in drug synthesis, the design and development of more milder, novel, and sustainable processes for the assembly of the benzimidazole ring system is imperative. One of the methods employed for the synthesis of nitrogen heterocycles is the transition-metal-catalyzed carbon−nitrogen cross-coupling reaction.[4] Although significant progress in the palladium-[5] and nickel-catalyzed[6] C−N bond formation have been made under mild conditions, the high cost of palladium and the required especially designed ligands, as well as the high toxicity of nickel catalysts, led to a need to explore the use of inexpensive and more sustainable metals for such coupling reactions. Therefore, the development of an environmentally benign and cheaper copper-[7] or iron-mediated[8] catalysis for carbon−carbon or carbon−heteroatom cross-coupling reactions has become an important goal. Additionally, organic reactions in water have recently attracted much attention because water is the most economical, safest, and environmentally friendly medium.[9]

The transition-metal-catalyzed C−N cross-coupling methodologies for the synthesis of benzimidazole derivatives

(1) (a) Baudy, R. B.; Fletcher, H., III; Yardley, J. P.; Zaleska, M. M.; Bramlett, D. R.; Tasse, R. P.; Kowal, D. M.; Katz, A. H.; Moyer, J. A.; Abou-Gharbia, M. *J. Med. Chem.* **2001**, *44*, 1516. (b) Boiami, M.; Gonzalez, M. *Mini-Rev. Med. Chem.* **2005**, *5*, 409. (c) Kataoka, M.; Tatsuta, M.; Yasoshima, K.; Yura, T.; Urbahns, K.; Kiba, A.; Yamamoto, N.; Gupta, J. B.; Hashimoto, K. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 805. (d) Ragno, G.; Risoli, A.; Ioele, G.; De Luca, M. *Chem. Pharm. Bull.* **2006**, *54*, 802. (e) Sabat, M.; Vanrens, J. C. L. M. J.; Brugel, T. A.; Maier, J.; Golebiowski, A.; De, B.; Easwaran, V.; Hsieh, L. C.; Walter, R. L.; Mekel, M. J.; Evdokimov, A.; Janusz, M. J. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5973. (f) Figueiras, A.; Sarraguça, J. M. G.; Carvalho, R. A.; Pais, A. A. C. C.; Veiga, F. J. B. *Pharm. Res.* **2007**, *24*, 377.

(2) (a) Asensio, J. A.; Gomez-Romero, P. *Fuel Cells* **2005**, *5*, 336. (b) Schwartz, G.; Fehse, K.; Pfeiffer, M.; Walzer, K.; Leo, K. *Appl. Phys. Lett.* **2006**, *89*, 083509.

(3) (a) Grimmett, M. R. *Imidazole and Benzimidazole Synthesis, Best Synthetic Methods*; Meth-Cohn, O., Ed.; Academic: London, 1997. (b) Yang, D.; Fokas, D.; Yu, J.; Li, L.; Baldino, C. M. *Synthesis* **2005**, *47* and references therein. (c) Ebenezer, W. J.; Hutchings, M.; Jones, K.; Lambert, D. A.; Watt, I. *Tetrahedron Lett.* **2007**, *48*, 1641.

(4) For examples: (a) Zou, B. L.; Yuan, Q. L.; Ma, D. W. *Angew. Chem.* **2007**, *119*, 2652. *Angew. Chem., Int. Ed.* **2007**, *46*, 2598. (b) Zheng, N.; Anderson, K. W.; Huang, X. H.; Nguyen, H. N.; Buchwald, S. L. *Angew. Chem.* **2007**, *119*, 7653. (g) *Angew. Chem., Int. Ed.* **2007**, *46*, 7509. (c) Willis, M. C.; Brace, G. N.; Holmes, I. P. *Angew. Chem., Int. Ed.* **2005**, *44*, 403. (d) Barluenga, J.; Jiménez-Aquino, A.; Aznar, F.; Valdés, C. *J. Am. Chem. Soc.* **2009**, *131*, 4031. (e) Tan, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 3767.

(5) For reviews on Pd-catalyzed aminations of aryl halides, see: (a) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 133. (b) Zapf, A.; Beller, M.; Riermeier, T. H. *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, p 231.

(6) Selected examples: (a) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054. (b) Bricout, H.; Carpentier, J.-F.; Mortreux, A. *Tetrahedron* **1998**, *54*, 1073. (c) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029and references therein. (d) Omar-Amrani, R.; Thomas, A.; Brenner, E.; Schneider, R.; Fort, Y. *Org. Lett.* **2003**, *5*, 2311. (e) Matsubara, K.; Ueno, K.; Koga, Y.; Hara, K. *J. Org. Chem.* **2007**, *72*, 5069. (f) Chen, C.; Yang, L.-M. *J. Org. Chem.* **2007**, *72*, 6324.

(7) For recent reviews on copper-catalyzed cross couplings, see: (a) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727. (b) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428. (c) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400. (d) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337. (e) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450. (f) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (g) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954 and references cited therein.

(8) For reviews, see: (a) Bolm, C.; Legros, J.; Paih, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Fürstner, A.; Martin, R. *Chem. Lett.* **2005**, 624. (c) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500. (d) Plietker, B. *Iron Catalysis in Organic Chemistry: Reactions and Applications*; Wiley-VCH: Weinheim, 2008; p 147. (e) Czaplik, W. M.; Mayer, M.; Cvengroš, J.; von Wangelin, A. J. *ChemSusChem* **2009**, *2*, 396 and references therein.

(9) (a) *Organic Synthesis in Water*; Grieca, P. A., Ed.; Blackie A & P: London, 1998. (b) Lindström, U. M. *Chem. Rev.* **2002**, *102*, 2741. (c) Kobayahi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209. (d) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095. (e) Blackmond, D. G.; Armstrong, A.; Coomber, V.; Wells, A. *Angew. Chem.* **2007**, *119*, 3872. *Angew. Chem., Int. Ed.* **2007**, *46*, 3798.

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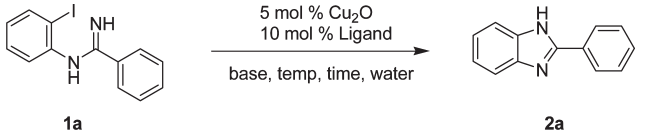
TABLE 1. Optimization of Copper-Catalyzed Intramolecular C−N Cross-Coupling of Benzamidine 1a in Water[a]



1a **2a**

entry	catalyst	ligand	base	temp (°C)	time (h)	yield[b] (%)
1[c]			K_2CO_3	100	30	19
2[c]		L2	K_2CO_3	100	30	22
3	Cu_2O		K_2CO_3	100	30	83
4[d]	CuI	L1	K_2CO_3	100	30	81
5[d]	CuBr	L1	K_2CO_3	100	30	65
6[d]	CuCl	L1	K_2CO_3	100	30	67
7	Cu_2O	L1	K_2CO_3	100	24	84 (71)[e]
8	Cu_2O	L1	K_2CO_3	110	24	86
9	Cu_2O	L1	K_2CO_3	100	30	91
10	Cu_2O	L2	K_2CO_3	100	30	98(88)[f]
11	Cu_2O	L3	K_2CO_3	100	30	82
12	Cu_2O	L4	K_2CO_3	100	30	94
13	Cu_2O	L5	K_2CO_3	100	30	91
14	Cu_2O	L2	Cs_2CO_3	100	30	94
15	Cu_2O	L2	NEt_3	100	30	94
16	Cu_2O	L2	$K_3PO_4 \cdot 3H_2O$	100	30	91

[a]Reaction conditions: 1.0 equiv of **1a** (1.0 mmol), 2.0 equiv of base, 5 mol % of Cu_2O, 10 mol % of ligand, water (1.5 mL). [b]Yield of isolated product after chromatography. [c]Decomposition product of **1a** was also isolated from the reaction mixture in ca. 70% yield. [d]10 mol % of the catalyst was used. [e]3 mol % of Cu_2O and 6 mol % of ligand were used. [f]80 °C for 48 h.

have also been reported. For example, Brain[10] reported the first palladium-catalyzed *N*-arylation of (*o*-bromophenyl)-amidines to give benzimidazoles in toluene. Batey[11] demonstrated an intramolecular aryl guanidinylation to form biologically relevant 2-aminobenzimidazoles using both palladium and copper catalysts in DME. Palladium- or copper-catalyzed cascade aryl amination/condensation processes of *o*-haloacetanilides have been developed for the synthesis of 1,2-disubstituted benzimidazoles in *t*-BuOH or DMSO by Ma[4a] and Buchwald,[4b] respectively. Buchwald[12] also pioneered studies to construct a benzimidazole core structure through an efficient copper^{II}-catalyzed C−H functionalization/C−N bond-forming approach in DMSO. Shortly afterward, Yang and Shi[13] developed a straightforward method for the synthesis of benzimidazoles via Pd^{II}-catalyzed C−H activation with $Cu(OAc)_2/O_2$ as a co-oxidant in NMP. More recently, the regiospecific reaction of 1,2-dihaloarenes with *N*-substituted amidines or guanidines was conducted in NMP to synthesize benzimidazoles with low to moderate yields under the high-temperature conditions.[14] Nevertheless, the aforementioned method[15] implied the use of toxic and hazardous organic solvents and, in some cases, the requirement of additives, high temperature or excess oxidative reagents. Herein, we report

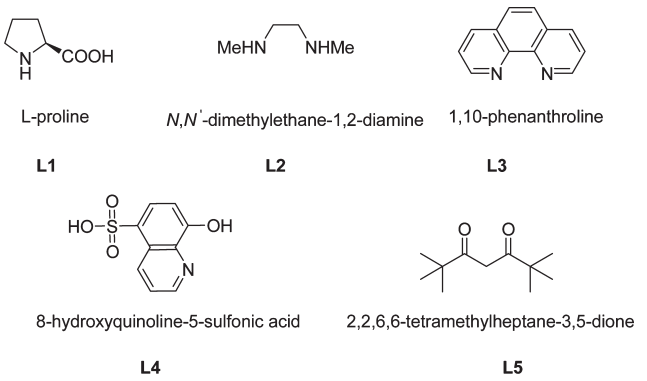


FIGURE 1. Selected ligands used in copper-catalyzed intramolecular *N*-arylation of **1a** in water.

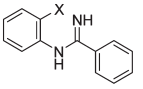
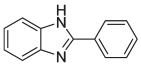
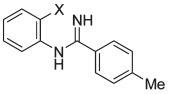
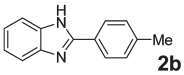
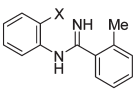
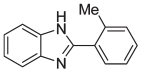
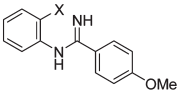
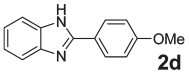
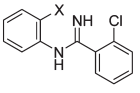
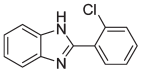
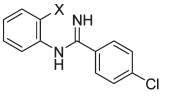
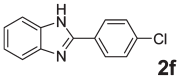
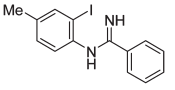
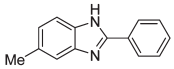
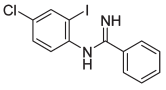
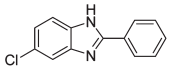
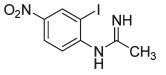
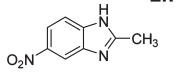
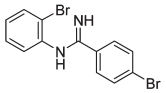
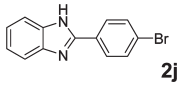
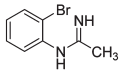
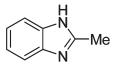
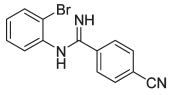
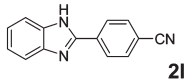
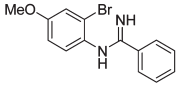
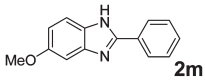
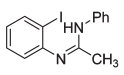
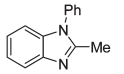
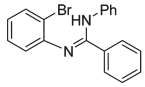
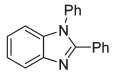
a practical, cheap, and efficient copper-catalyzed intramolecular *N*-arylation of (*o*-haloaryl)amidines to afford synthetically valuable benzimidazole derivatives with environmentally benign water as the solvent.[16]

N-(2-Iodophenyl)benzamidine (**1a**) derived from the addition of 2-iodobenzenamine to benzonitrile was selected as a model substrate for a copper-catalyzed intramolecular *N*-arylation reaction in aqueous media. After an initial screen of various copper catalysts (5 mol %), we found that the use of Cu_2O gave the best yield (84%) with potassium carbonate as the base in water at 100 °C (entries 4−7, Table 1). To optimize other reaction conditions, we then examined different ligands, bases, reaction time and temperature using 5 mol % of Cu_2O as the catalyst. Some results from that study are summarized in Table 1. At first, the blank experiment (without the copper catalyst) of **1a** was examined in water at 100 °C for 30 h, we were surprised to find that **1a** showed very low conversion into the corresponding benzimidazole (ca. 20%) and mainly the formation of decomposition products (ca. 70%) (entries 1 and 2, Table 1). The use of Cu_2O as the catalyst could efficiently promote this transformation giving 83% yield; more importantly, it could suppress the formation of undesired decomposition products, confirming that these results attributed predominantly to the copper-catalyzed arylation reaction (entries 1−3, Table 1). Compared to the ligand-free cross-coupling reaction, the use of 10 mol % of L-proline slightly shortened the reaction time (24 h vs 30 h, entries 3 and 7, Table 1). We then carried out a set of experiments to reveal the crucial role of the reaction temperature (entries 7−9, Table 1). Although at higher temperature, the transformation gave comparable yield to the reaction at 100 °C (86% vs 84%, entries 7 and 8, Table 1). In order to increase the yield of **2a**, we then investigated the effect of various bidentate ligands (L-proline, DMEDA, 1,10-phenanthroline, 8-hydroxyquinoline-5-sulfonic acid and TMHD, Figure 1) on the reaction (entries 9−13, Table 1). Cu_2O(DMEDA) was found to be a very effective catalyst for this cross-coupling reaction with the best yield (entry 10, Table 1). Finally, other bases such as Cs_2CO_3, Et_3N, and $K_3PO_4 \cdot 3H_2O$ were examined; K_2CO_3 provided better results (entries 10, 14−16, Table 1).

(10) (a) Brain, C. T.; Brunton, S. A. *Tetrahedron Lett.* **2002**, *43*, 1893. (b) Brain, C. T.; Brunton, S. A. *J. Org. Chem.* **2003**, *68*, 6814.
(11) Evindar, G.; Batey, R. A. *Org. Lett.* **2003**, *5*, 133.
(12) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932.
(13) Xiao, Q.; Wang, W.-H.; Liu, G.; Meng, F.-K.; Chen, J.-H.; Yang, Z.; Shi, Z.-J. *Chem.—Eur. J.* **2009**, *15*, 7292.
(14) (a) Deng, X.; Mani, N. S. *Eur. J. Org. Chem.* **2010**, 680. (b) Deng, X.; McAllister, H.; Mani, N. S. *J. Org. Chem.* **2009**, *74*, 5742.
(15) Other recent examples, see: (a) Lv, X.; Bao, W. *J. Org. Chem.* **2009**, *74*, 5618. (b) Saha, P.; Ramana, T.; Purkait, N.; Ali, M. A.; Paul, R.; Punniyamurthy, T. *J. Org. Chem.* **2009**, *74*, 8719. (c) Kumar, S.; Ila, H.; Junjappa, H. *J. Org. Chem.* **2009**, *74*, 7046.

(16) Selected examples on copper-catalyzed intermolecular aminations of aryl halides in neatly aqueous media, see: (a) Lu, Z.; Twieg, R. J. *Tetrahedron Lett.* **2005**, *46*, 2997. (b) Wang, F.; Fu, H.; Jiang, Y.; Zhao, Y. *Green Chem.* **2008**, *10*, 452. (c) Wang, Y.; Wu, Z.; Wang, L.; Li, Z.; Zhou, X. *Chem.—Eur. J.* **2009**, *15*, 8971. (d) Liang, L.; Li, Z.; Zhou, X. *Org. Lett.* **2009**, *11*, 3294. (e) Li, X.; Yang, D.; Jiang, Y.; Fu, H. *Green Chem.* **2010**, *12*, 1097.

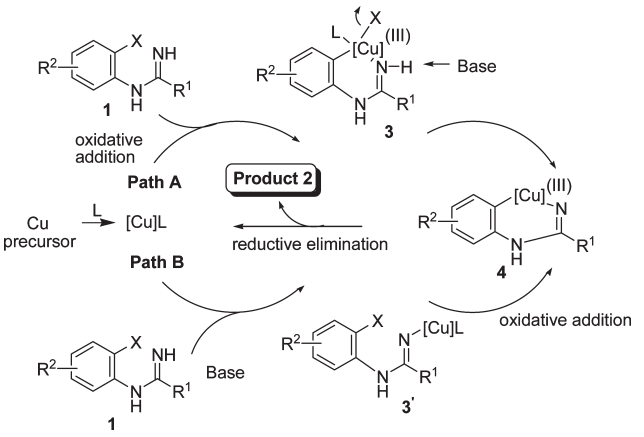
TABLE 2. Copper-Catalyzed Synthesis of Benzimidazole Derivatives[a]

entry	substrate	product		yield[b] (%)
1		 **2a**	X = I	98
2			X = Br	92
3			X = Cl	0 (100)
4		 **2b**	X = I	88
5			X = Br	82
6			X = Cl	0 (30)
7		 **2c**	X = I	87
8			X = Br	94
9			X = Cl	23 (25)
10		 **2d**	X = I	99.6
11			X = Br	78
12			X = Cl	0 (60)
13		 **2e**	X = I	99
14			X = Br	98
15			X = Cl	0 (20)
16		 **2f**	X = I	88
17			X = Br	62
18[c]		 **2g**		98
19[d]		 **2h**		73
20		 **2i**		99
21		 **2j**		81
22		 **2k**		78
23		 **2l**		56
24[e]		 **2m**		86
25		 **2n**		99
26		 **2o**		38

[a]Reaction conditions: 1.0 equiv of *N*-(2-haloaryl)benzamidine (1.0 mmol), 2.0 equiv of K_2CO_3, 5 mol % of Cu_2O, 10 mol % of DMEDA, water (1.5 mL), 100 °C, 30 h. [b]Yield of isolated product after chromatography; the values in parentheses are isolated yields of the corresponding decomposition products. [c]Two tautomers were observed in 60:1 ratios by GC. [d]Two tautomers were observed in 100:1 ratios by GC. [e]Two tautomers were observed in 1:5 ratios by GC.

With the optimized reaction conditions in hand, we then explored the scope and generality of the present process (Table 2). As shown in Table 2, this method is efficient for the synthesis of a number of benzimidazoles 2 in good to excellent yields. The nature of the ortho-substituted halogen on the aniline moiety was very important to the reaction outcome. (*o*-Iodoaryl)amidines or (*o*-bromoaryl) amidines can smoothly be converted to the desired products in high to

SCHEME 1. Proposed Mechanism for the Intramolecular N-Arylation of Amidines Using a Copper Catalyst



excellent yields, however, the use of aryl chlorides to effect such transformations afforded inferior results than their iodo or bromo analogues. No desired products were obtained for all the selected *o*-chloro-substituted substrates in Table 2 (with the exception of entry 9) that probably attributed to their poorer tendency to undergo oxidative addition to transition metal complexes (entries 3, 6, and 12, Table 2). For aryl iodides or bromides, a variety of substituents on the benzonitrile moiety, such as Me, OMe, Cl, Br, or CN, can be used. It is worth noting that C-Br or C-Cl compatible with reaction conditions are particularly appealing, since these substituents offer great opportunity for further synthetic manipulations (entries 13, 14, 16, 17, 19, and 21, Table 2). The steric hindrance of ortho substituents on the nitrile moiety seemed not to hamper the reaction, and the benzimidazoles could be obtained in excellent yields (entries 7, 8, 13, and 14, Table 2). In addition, 2-alkylbenzimidazoles can also be obtained in good yields (entries 20, 22, and 25, Table 2).

Regarding the aniline moiety, several functional groups including halogens and electron-donating (Me and OMe, entries 18 and 24) or electron-withdrawing (NO_2, entry 20) substituents were tolerated well; the electronic nature of the aromatic motifs did not seem to affect the efficiency of this transformation. It is important to note that for the use of *p*-methyl or chloro substrates, two tautomers were observed in above 50:1 ratios by GC that may arise from the migration of C=N group (entries 18 and 19, Table 2).[17] Interestingly, when *p*-nitro substrate was used, only one tautomer was isolated in excellent yield (entry 20, Table 2). In comparison, two tautomers of the product were isolated in 1:5 ratios when the MeO group was introduced into the para position of the *N*-aryl ring of the amidine (entry 24, Table 2). The tautomeric ratios were probably dependent on the electronic effect of substituents on the aniline moiety.[18] The desired products **2n** and **2o** from *N*′-phenylated alkyl or aryl amidine substrates could also be obtained in moderate to good yields (entries 25 and 26, Table 2).

A proposed reaction mechanism of the intramolecular C−N bond formation of amidines to benzimidazole derivatives was shown in Scheme 1. This transformation presumably occurred through a coordination of the imine function group of amidine to the Cu(I) center followed by an intramolecular oxidative addition of aryl halide **1** to Cu(I), affording an intermediate complex **3**. The resulting complex **3** reacted with base to form Cu−N bond and afforded an intermediate complex **4**, which preceded the formation of the coupling product **2** and regeneration of the catalytic copper species (path A, Scheme 1).[7g] However, an alternative pathway via nucleophilic substitution in the first step[19] then followed by oxidative addition could not be completely ruled out (path B).

In summary, we have successfully developed a straightforward, efficient, and more sustainable copper-catalyzed method for intramolecular *N*-arylation providing the benzimidazole ring system, a valuable framework with interesting therapeutic properties. The present protocol uses Cu_2O in combination with a simple diamine derivative (DMEDA) as the catalyst under mild reaction conditions; furthermore, the use of a water as the solvent will render the methodology described herein economically and environmentally advantageous and of remarkable practical value for industrial applications.

Experimental Section

General Procedures for Copper-Catalyzed Intramolecular C−N Bond-Forming Reaction of (*o*-Halophenyl)benzamidine. A 10 mL Schlenk tube equipped with a magnetic stirring bar was charged with (*o*-haloaryl)benzamidine substrates (1.0 mmol, 1.0 equiv), Cu_2O (0.05 mmol, 7.2 mg), DMEDA (0.1 mmol, 8.8 mg), and K_2CO_3 (276 mg, 2.0 mmol, 2.0 equiv), and then 1.5 mL of H_2O was added via syringe at room temperature. The tube was sealed and put into a preheated oil bath at 100 °C for 30 h. The reaction mixture was cooled to room temperature, quenched with water (3 mL), and diluted with ethyl acetate (5 mL). The layers were separated, and the aqueous layer was extracted with (2 × 5 mL) ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel (H), eluting with 5−10% ethyl acetate/petroleum ether.

Product Characterization of Representative Examples. 2-Phenyl-1*H*-benzo[d]imidazole (2a): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.92 (s, 0.19H), 8.20 (d, 2H, J = 7.6 Hz), 7.68 (d, 1H, J = 6.8 Hz), 7.58−7.48 (m, 4H), 7.23 (d, 2H, J = 6.8 Hz). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 151.6, 144.2, 135.3, 130.6, 130.3, 129.4, 126.9, 123.0, 122.2, 119.3, 111.8; HRMS-ESI (m/z) $[M + Na]^+$ calcd for $C_{13}H_{10}N_2Na$ 217.0742, found 217.0745.

2-(4-Bromophenyl)-1*H*-benzo[d]imidazole (2g): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 13.01 (s, 0.17H), 8.14 (d, 2H, J = 8.8 Hz), 7.78 (d, 2H, J = 8.8 Hz), 7.69 (d, 1H, J = 7.6 Hz), 7.56 (d, 1H, J = 7.2 Hz), 7.26−7.22 (m, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 150.6, 144.2, 135.5, 132.5, 129.8, 128.8, 123.7, 123.3, 122.4, 119.4, 111.9; HRMS-ESI (m/z) $[M + Na]^+$ calcd for $C_{13}H_9BrN_2Na$ 294.9847, found 294.9845.

Acknowledgment. We are grateful to the funds supported by the Fundamental Research Funds for the Central Universities (DL10BB07, DL09BB34) and by a Grant-in-Aid for Young Teachers from Northeast Forestry University.

Supporting Information Available: Experimental procedures and spectral data for the compounds. This material is available free of charge via the Internet http://pubs.acs.org.

(17) 5-Substituted benzoimidazoles were confirmed as major tautomers by NMR and GC experiment with the standard samples.

(18) Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2003**, 3025.

(19) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120.