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Selective C-O Coupling Reaction of N-Methoxy Arylamides and Arylboronic Acids Catalyzed by Copper Salt

Ying Wang, Huilin Xie, Kunming Liu *, Jinhui Li * and Jin-Biao Liu *

Jiangxi Provincial Key Laboratory of Functional Molecular Materials Chemistry, Jiangxi University of Science and Technology, 86 Hongqi Road, Ganzhou 341000, China

* Correspondence: liukunming@jxust.edu.cn (K.L.); jinhuili@jxust.edu.cn (J.L.); liujinbiao@jxust.edu.cn (J.-B.L.)

Abstract: Herein, we report a copper-catalyzed C-O cross-coupling of N-methoxy amides and arylboronic acids for the synthesis of aryl-N-methoxy arylimides. The fully selective O-arylation of the N-methoxy amides is found to be greatly prompted by the inexpensive and commercially available CuI. The reaction conditions tolerate a variety of functional groups and promote different reactivities depending on the electronic and steric properties of the distorted substrates.

Keywords: copper catalyzed; N-methoxy amides; selective C-O cross-coupling; aryl-N-methoxy arylimides

1. Introduction

The transition-metal-catalyzed cross-coupling of amides has emerged as a powerful tool for the construction of carbon–carbon and carbon–heteroatom bonds, enabling the broad application of traditionally inert amides in the synthesis of pharmaceutical agents, natural products, agrochemicals and functional materials [1–4]. Palladium-catalyzed Buchwald–Hartwig couplings [5], as well as copper-catalyzed Ullmann couplings [6] and Goldberg couplings [7], employ aryl halides as the arylating reagents of the amides. Nevertheless, high temperatures, stoichiometric amounts of basic additives and specific halide substrates are required in such reactions, thereby limiting the further application of these methodologies [8–10].

In 1998, Chan and Lam reported the first example of the N/O-arylation of amides using aryl boronic acids as the substrate [11]. Due to their environmental benefits, functional group tolerance and commercial availability, arylboronic acids have been successfully utilized as arylating reagents for the direct cross-coupling of amides in recent years [12–14]. The palladium- and nickel-catalyzed Suzuki–Miyaura coupling of amides via N–C(O) acyl cleavage are representative approaches for C-arylation (Scheme 1a) [15–17]. To date, significant progress has been reported in the use of amide derivatives, including N-acetyl-amides [18], N-acylsuccinimides [19], N, N-di-Boc amides [20], and N-acyl-pyrroles [21] as cross-coupling partners. Copper-mediated Chan–Lam reactions are an efficient protocol for the N-arylation of amides [22–25], and encouraging results have been obtained for both amides and boronic acid substrates over the past decades (Scheme 1b). In addition to amides, O-protected hydroxamic acids have also been used as an amide source. In 2008, the Liebeskind group [26] reported the C-N cross-coupling of O-acetyl hydroxamic acids with arylboronic acids which was promoted by stoichiometric copper. A novel mechanochemical synthesis of N-aryl amides from O-pivaloyl hydroxamic acids and arylboronic acids in the presence of stoichiometric copper has also been developed by the Vilela and Lloyd groups [27]. Although N-arylation exhibits a high amenability to O-protected hydroxamic acids, the methods for selective O-arylation are noticeably lacking. Thus, the development of new amide precursors that are compatible with various reaction pathways is required to fully exploit the potential of the amides in cross-coupling reactions.

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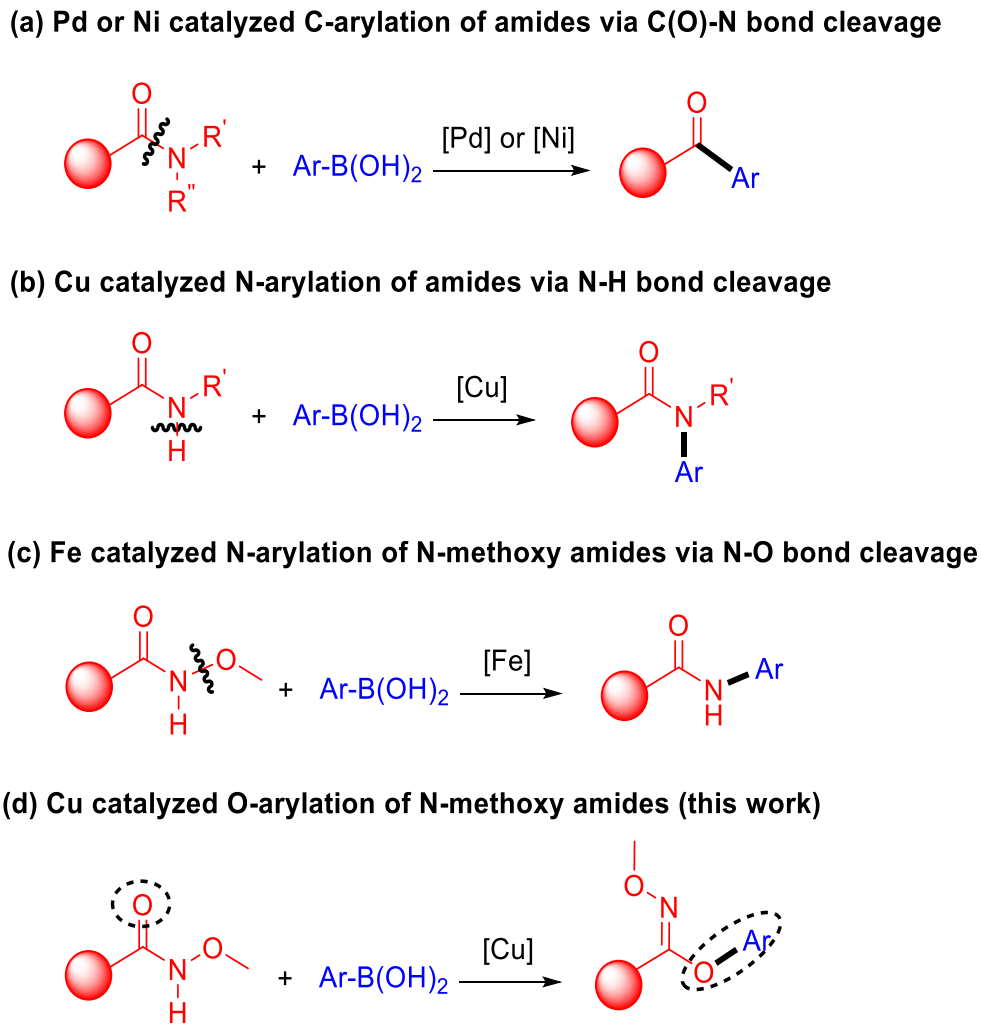


Scheme 1. (**a**) Pd or Ni catalyzed C-arylation; (**b**) Cu catalyzed N-arylation; (**c**) Fe catalyzed N-arylation; (**d**) Cu catalyzed O-arylation (this work).

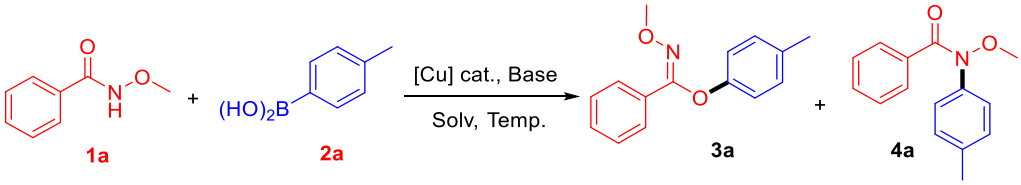
In 2021, our group [28] developed an efficient iron-catalyzed synthesis of N-aryl amides from N-methoxy amides and arylboronic acids (Scheme 1c). In the presence of an Fe catalyst, N-methoxy amides were converted into methyloxonio amides via 1, 2-H migration and subsequent C-N construction steps. Based on our experience in amide bond conversion [29–31] and inspired by the structural features of N-methoxy amides [32,33], we questioned whether the amide group that is linked to a methoxy substituent could be strategically employed to accomplish C-O cross-coupling in the form of hydroxamic acid. To our delight, a selective C-O coupling of N-methoxy amides with arylboronic acids occurred in the presence of a copper salt (Scheme 1d).

2. Results and Discussion

We first examined the cross-coupling reaction of *N*-methoxybenzamide (**1a**) with *p*-tolylboronic acid (**2a**) under a variety of conditions. The selected optimization results are shown in Table 1. We were delighted to find that the desired *p*-tolyl (E)-N-methoxybenzimidate **3a** was obtained with a promising 28% yield using $Cu(OAc)_2 \cdot H_2O$ (20 mol%) and K_2CO_3 (2 equiv.) in dichloroethane (DCE) at 130 °C, whereas the N-arylation product **4a** was obtained a 6% yield (Entry 1, Table 1). As we were encouraged by this preliminary result, various bases were tested. $Na_3PO_4 \cdot 12H_2O$ appeared to be the best base for the coupling reaction since **3a** was obtained in lower yields using the common bases such as K_2CO_3, Et_3N, KOH, Cs_2CO_3, *t*-BuOK, and Na_2CO_3 under otherwise identical

conditions (Entries 2–9, Table 1). Interestingly, we found that the solvent choice had a major impact on the reaction. THF, acetone, EtOH, DMF, 1, 4-dioxane, DMSO, and MeCN had a deleterious effect on the cross-coupling, while EA, toluene, and Et_2O provided less satisfactory results than DCE did (Entries 10–19, Table 1). Further studies were focused on the reaction temperature (Entries 20–24, Table 1). When the temperature was elevated to 130 °C, the yield of **3a** was improved to 48%, while **4a** was obtained in a yield of less than 5%. Unfortunately, higher temperatures did not lead to substantially higher yields due to the inevitable decomposition of *p*-tolylboronic acid. With the optimal conditions in hand, other copper salt catalysts including CuI, CuBr, and CuCl were also explored (Entries 25–27, Table 1). Encouragingly, **3a** was obtained selectively in a 70% yield in the presence of CuI. Finally, the optimal reaction conditions for the selective C-O coupling of N-methoxyarylimides with arylboronic acids were found to be 20 mol% CuI and two equiv. $Na_3PO_4{\cdot}12H_2O$ in DCE at 130 °C.

Table 1. Optimization of the reaction conditions [a].

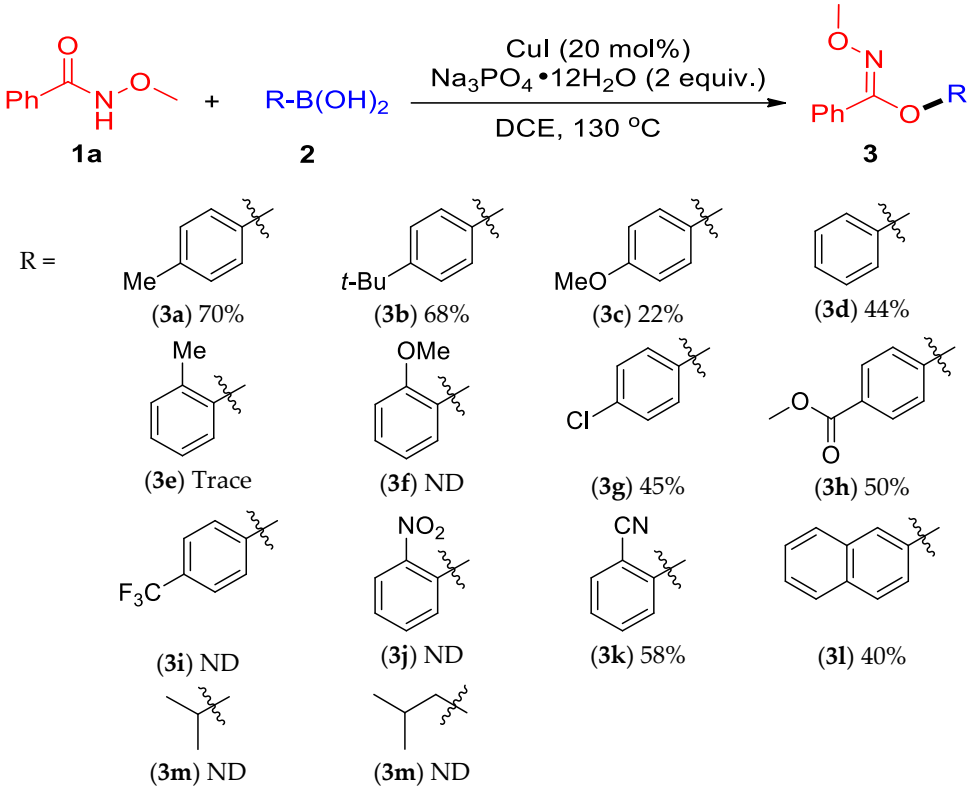


Entry	[Cu]	Base (equiv)	Solv.	Temp. (°C)	Yield of 3a [b] (%)	Yield of 4a [b] (%)
1	$Cu(OAc)_2{\cdot}H_2O$	K_2CO_3	DCE	80	28	6
2	$Cu(OAc)_2{\cdot}H_2O$	-	DCE	RT	<5	9
3	$Cu(OAc)_2{\cdot}H_2O$	K_2CO_3	DCE	RT	30	19
4	$Cu(OAc)_2{\cdot}H_2O$	Et_3N	DCE	RT	<5	12
5	$Cu(OAc)_2{\cdot}H_2O$	KOH	DCE	RT	18	11
6	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	DCE	RT	19	30
7	$Cu(OAc)_2{\cdot}H_2O$	*t*-BuOK	DCE	RT	11	33
8	$Cu(OAc)_2{\cdot}H_2O$	Na_2CO_3	DCE	RT	8	31
9	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	RT	34	29
10	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	THF	RT	0	0
11	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	acetone	RT	<5	<5
12	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	EA	RT	22	<5
13	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	EtOH	RT	0	<5
14	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	Toluene	RT	32	25
15	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DMF	RT	0	0
16	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	1,4-dioxane	RT	0	0
17	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DMSO	RT	0	0
18	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	Et_2O	RT	31	9
19	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	MeCN	RT	<5	<5
20	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	40	18	<5
21	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	80	28	<5
22	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	120	41	<5
23	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	130	48	<5
24	$Cu(OAc)_2{\cdot}H_2O$	$Na_3PO_4{\cdot}12H_2O$	DCE	140	30	0
25	**CuI**	**$Na_3PO_4{\cdot}12H_2O$**	**DCE**	**130**	**70**	**0**
26	$CuCl_2$	$Na_3PO_4{\cdot}12H_2O$	DCE	130	38	16
27	CuBr	$Na_3PO_4{\cdot}12H_2O$	DCE	130	37	0

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (0.2 equiv), base (0.4 mmol), solvent (2.0 mL), air, 24 h. [b] Isolated yield based on **1a**.

The evaluation of the C-O cross-coupling strategy was first examined by screening a range of electronically and sterically distorted boronic acids under the optimized conditions (Scheme 2). The reaction tolerates a wide range of arylboronic acids bearing sensitive functional groups, such as aryl halide (**2g**), ester (**2h**) and nitriles (**2k**), which act as synthetic handles for further functionalization. Aromatic boronic acids bearing moderate electron-donating (**2a**, **2b**) and electron-withdrawing (**2g**, **2h**, **2k**) groups produced products in satisfactory yields, while the strong electronic effect in the arylboronic acids (**2c**, **2i**, **2j**) were detrimental to the reaction. An ortho-substituted electron-withdrawing group (**2j**) is more

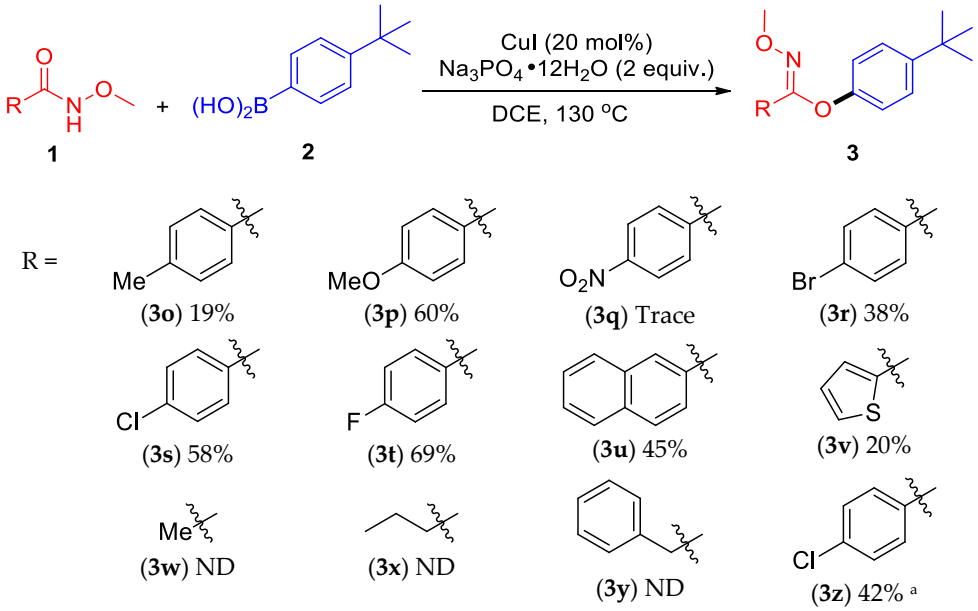
beneficial to the C-O coupling of boric acid substrates than the electron-donating group is (**2e**, **2f**). When the R group was a 2-naphthyl group, N-aryl amide **2l** could also be prepared in a 40% yield. However, alkylboronic acids (**2m**, **2n**) were inert in this cross-coupling, which may be due to their tendency to undergo *β*-H elimination.



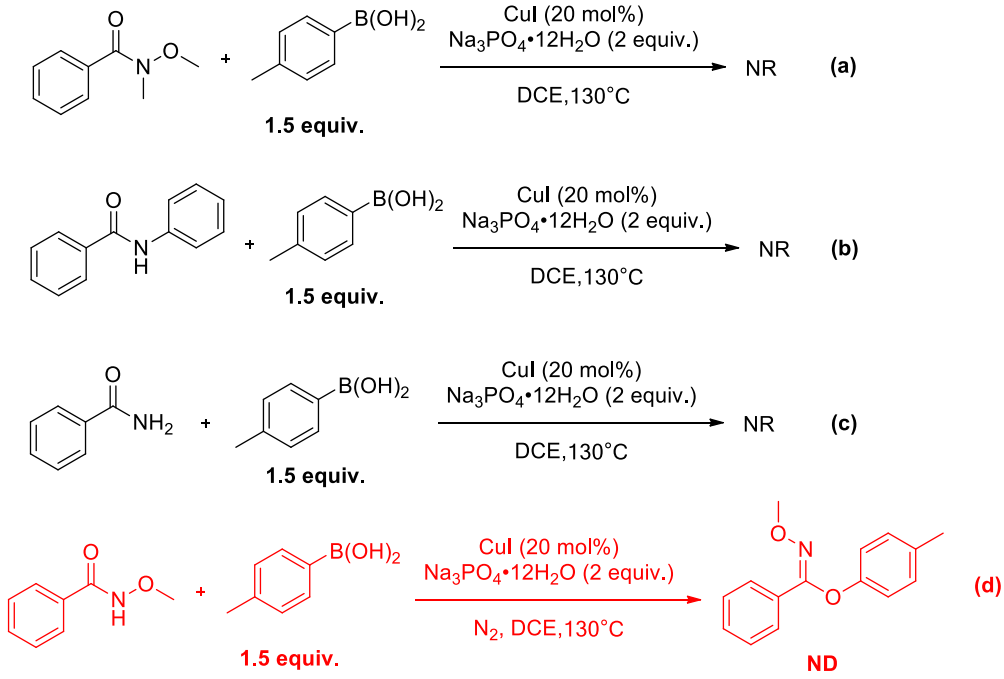
Scheme 2. Boronic acid scope in copper-catalyzed C-O coupling of N-methoxy amides [a,b]. [a] Reaction conditions: **1** (0.2 mmol), **2** (1.5 equiv.), CuI (0.2 equiv.), $Na_3PO_4 \cdot 12H_2O$ (2 equiv.), DCE (2.0 mL), air, 130 °C, 24 h. [b] Isolated yield based on **1a**. ND = Not Detected.

Subsequently, the reaction scope with respect to the N-methoxy amide component was examined (Scheme 3). Electron-rich N-methoxy amides bearing a *p*-methoxy group (**1p**) or electron-deficient N-methoxy amides bearing halides (**1r–1t**, **1z**) smoothly gave their corresponding C-O coupling products in moderate-to-good yields (38–69%). Of note, the ideal leaving groups, -Br (**1r**) and -Cl (**1s**), which are commonly used in Suzuki–Miyaura couplings were preserved, displaying the high selectivity of the C-O cross-coupling reaction. Nevertheless, the reaction was incompatible with an N-methoxy amide bearing a strong electron-donating substituent (-NO_2, **1q**). Sterically hindered (**1u**) and heterocyclic (**1v**) N-methoxy amides showed a moderate tolerance under the optimized conditions. Unfortunately, the attempts to explore the alkylated substrates (**1w, 1x, 1y**) failed, implying that the reaction was very sensitive to the alkyl groups of the N-methoxy amides.

To gain an insight into the reaction mechanism, a number of control experiments were carried out. When N-methoxy-N-methylbenzamide was utilized as the starting material, the desired O-arylation product was not formed (Scheme 4a). Similarly, N-phenylbenzamide and benzamide were inert under these copper-catalyzed C-O coupling conditions (Scheme 4b,c). Taken together, these findings suggest that the N-methoxy group increased the electron cloud density on the carbonyl oxygen atom, facilitating the tautomerization of the N-methoxy amides to the O-protected hydroxamic acids, thus changing the coupling reaction site from the nitrogen atom to the oxygen atom. Furthermore, we conducted an experiment under an N_2 atmosphere instead of in air, and the expected product was not obtained, indicating that oxygen is required for this reaction to occur (Scheme 4d).



Scheme 3. N-methoxy amides scope in copper-catalyzed C-O cross-coupling [b,c]. [a] The boronic acid component is *p*-tolylboronic acid. [b] Reaction conditions: **1** (0.2 mmol), **2** (1.5 equiv.), CuI (0.2 equiv.), $Na_3PO_4 \cdot 12H_2O$ (2 equiv.), DCE (2.0 mL), air, 130 °C, 24 h. [c] Isolated yield based on **1a**. ND = Not Detected.



Scheme 4. Control experiments of the copper-catalyzed C-O coupling reaction.

In light of the above results and the previous research [34–37], a plausible reaction mechanism has been proposed (Figure 1). Cu(I) is firstly oxidized into a Cu(II) species **B**, which then undergoes transmetalation with arylboronic acid **2** to form aryl-Cu(II) intermediate **C**. Subsequently, N-methoxy amide **1** undergoes H-migration and anion exchange with **C** to generate Cu(II) complex **D** under the alkaline conditions. The oxidation of **D** results in the formation of Cu(III) complex **E**, which is followed by a reductive elimination to regenerate the Cu(I) catalyst and produce the desired product **3**.

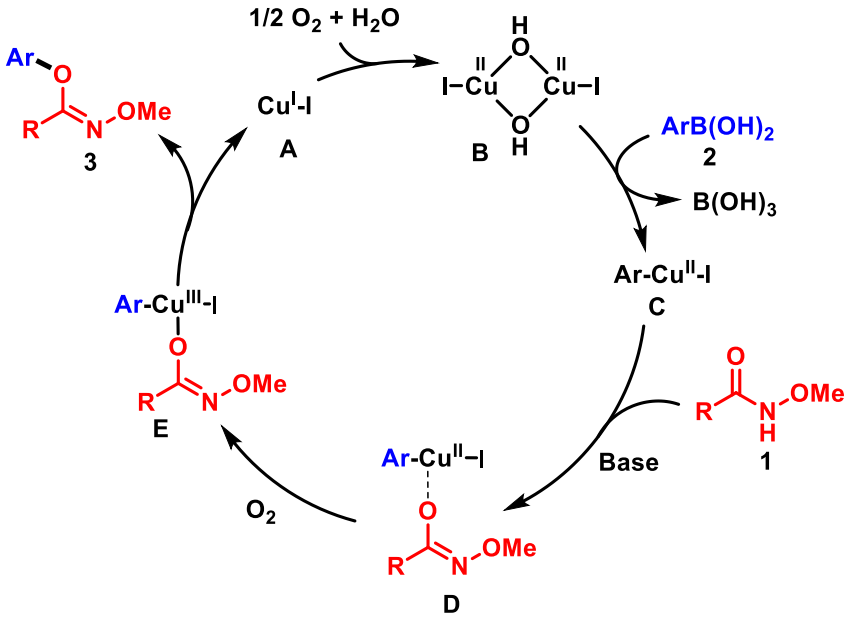


Figure 1. Plausible mechanism of the copper-catalyzed C-O coupling reaction.

3. Materials and Methods

3.1. General Information

Unless otherwise noted, all of the reagents were purchased from Shanghai Aladdin Bio-Chem Technology Co., Ltd. (Shanghai, China) and used without purification. Purification of products was conducted by flash chromatography on silica gel (200–300 mesh). Nuclear magnetic resonance (NMR) spectra were measured on a Bruker Avance III 400 (Bruker, Billerica, MA, USA). The ^{1}H-NMR (400 MHz) chemical shifts were obtained relative to $CDCl_3$ as the internal reference ($CDCl_3$: δ 7.26 ppm). The ^{13}C-NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ 77.16 ppm). Chemical shifts are reported in ppm using tetramethylsilane as internal standard (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet). HR-MS data were obtained on a VG ZAB-HS mass spectrometer, Bruker Apex IV FTMS spectrometer.

3.2. General Procedure for the Copper-Catalyzed C-O Coupling of N-Methoxy Amides

N-methoxy amide **1** (0.2 mmol), arylboronic acid **2** (0.3 mmol), CuI (20 mmol%), $Na_3PO_4{\cdot}12H_2O$ (0.4 mmol) and dichloroethane (DCE, 2.0 mL) were added to a sealed tube. Then, the mixture was stirred at 130 °C in the air for 24 h. After the disappearance of the substrate as indicated by the TLC, the mixture was concentrated in vacuo, and the resulting crude product was purified by column chromatography to afford the products **3**.

3.3. Characterization Data for Products **3a**–**3v**

The following characterization data are shown in the Supplementary Materials.

(*E*)-*p*-tolyl N-methoxybenzimidate (**3a**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.4 Hz, 2H), 7.23 (dd, J = 15.7, 7.9 Hz, 3H), 6.95 (d, J = 8.3 Hz, 2H), 6.77 (d, J = 8.3 Hz, 2H), 3.83 (s, 3H), 2.17 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.18, 150.81, 132.18, 130.23, 130.19, 130.07, 128.52, 126.85, 115.75, 62.88, 20.62. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_2$ 242.1181; Found: 242.1182.

(*E*)-4-(tert-butyl)phenyl N-methoxybenzimidate (**3b**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79–7.77 (m, 2H), 7.41–7.37 (m, 2H), 7.36 (s, 1H), 7.32–7.29 (m, 2H), 6.94–6.91 (m, 2H), 3.97 (s, 3H), 1.31 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.90, 150.69, 145.44, 130.21, 128.50, 126.79, 126.43, 115.15, 62.88, 34.21, 31.48. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{22}NO_2$ 284.1651; Found: 284.1647.

(*E*)-4-Methoxyphenyl N-methoxybenzimidate (**3c**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65–7.60 (m, 2H), 7.31–7.22 (m, 3H), 6.84–6.79 (m, 2H), 6.73–6.68 (m, 2H), 3.86 (s, 3H),

3.66 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 155.20, 151.11, 149.18, 130.19, 130.13, 128.49, 126.96, 117.04, 114.62, 62.85, 55.62. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_3$ 258.1130; Found: 258.1128.

(*E*)-Phenyl N-methoxybenzimidate (**3d**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.5 Hz, 2H), 7.30–7.22 (m, 3H), 7.18 (t, J = 7.7 Hz, 2H), 6.93 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 3.84 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 155.26, 150.50, 130.29, 130.06, 129.60, 128.54, 126.77, 122.78, 115.89, 62.89. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}NO_2$ 228.1025; Found: 228.1020.

(*E*)-4-Chlorophenyl N-methoxybenzimidate (**3g**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.76–7.73 (m, 2H), 7.43–7.35 (m, 3H), 7.27–7.23 (m, 2H), 6.95–6.91 (m, 2H), 3.95 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.89, 150.12, 130.47, 129.70, 129.53, 128.61, 127.80, 126.64, 117.18, 62.94. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}NO_2Cl$ 262.0635; Found: 262.0632.

(*E*)-Methyl 4-((methoxyimino)(phenyl)methoxy)benzoate (**3h**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.9 Hz, 2H), 7.68–7.64 (m, 2H), 7.33–7.25 (m, 3H), 6.92 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.51, 158.88, 149.64, 131.69, 130.62, 129.50, 128.69, 126.51, 124.73, 115.51, 63.02, 52.09. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_4$ 286.1079; Found: 286.1080.

(*E*)-3-Cyanophenyl N-methoxybenzimidate (**3k**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.76–7.71 (m, 2H), 7.44–7.32 (m, 5H), 7.24–7.19 (m, 2H), 3.91 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 155.38, 149.25, 130.78, 130.57, 129.24, 128.75, 126.55, 126.44, 120.57, 119.11, 118.21, 113.49, 63.06. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_2O_2$ 253.0977; Found: 253.0977.

(*E*)-Naphthalen-2-yl N-methoxybenzimidate (**3l**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78–7.67 (m, 4H), 7.59 (d, J = 8.2 Hz, 1H), 7.36–7.23 (m, 5H), 7.22–7.15 (m, 2H), 3.86 (d, J = 4.6 Hz, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.08, 150.55, 134.16, 130.37, 130.00, 129.92, 129.84, 128.60, 127.74, 127.08, 126.77, 126.62, 124.55, 117.48, 110.85, 62.96. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_2$ 278.1181; Found: 278.1178.

(*E*)-4-(tert-butyl)phenyl N-methoxy-4-methylbenzimidate (**3o**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2 Hz, 2H), 7.25 (dt, J = 3.9, 2.4 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.89–6.85 (m, 2H), 3.92 (s, 3H), 2.32 (s, 3H), 1.27 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.97, 150.86, 145.34, 140.45, 129.26, 127.31, 126.75, 126.42, 115.14, 62.81, 34.21, 31.49, 21.45. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{24}NO_2$ 298.1807; Found: 298.1807.

(*E*)-4-(tert-butyl)phenyl N, 4-dimethoxybenzimidate (**3p**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.68–7.65 (m, 2H), 7.27–7.24 (m, 2H), 6.89 (s, 1H), 6.86 (s, 1H), 6.84 (s, 1H), 6.82 (s, 1H), 3.90 (s, 3H), 3.77 (s, 3H), 1.27 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.24, 152.98, 150.68, 145.33, 128.39, 126.42, 122.50, 115.14, 113.95, 62.73, 55.31, 34.21, 31.49. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{24}NO_3$ 314.1756; Found: 314.1757.

(*E*)-4-(tert-butyl)phenyl 4-bromo-N-methoxybenzimidate (**3r**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62–7.59 (m, 2H), 7.47–7.44 (m, 2H), 7.28–7.25 (m, 2H), 6.87–6.84 (m, 2H), 3.92 (s, 3H), 1.27 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.68, 149.89, 145.69, 131.76, 129.23, 128.27, 126.52, 124.67, 115.07, 63.01, 34.24, 31.47. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}NO_2Br$ 362.0756; Found: 362.0759.

(*E*)-4-(tert-butyl)phenyl 4-chloro-N-methoxybenzimidate (**3s**)**.** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69–7.65 (m, 2H), 7.31–7.25 (m, 4H), 6.87–6.84 (m, 2H), 3.92 (s, 3H), 1.27 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.69, 149.81, 145.68, 136.28, 128.81, 128.76, 128.06, 126.51, 115.07, 62.99, 34.24, 31.47. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}NO_2Cl$ 318.1261; Found: 318.1260.

(*E*)-4-(tert-butyl)phenyl 4-fluoro-N-methoxybenzimidate (**3t**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.74–7.70 (m, 2H), 7.28–7.25 (m, 2H), 7.03–6.98 (m, 2H), 6.88–6.85 (m, 2H), 3.91 (s, 3H), 1.27 (s, 9H).^{13}C-NMR (101 MHz, $CDCl_3$) δ 165.24, 162.75, 151.31, 145.62, 128.84, 126.49, 126.37, 115.66, 115.11, 62.89, 34.23, 31.47. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}NO_2F$ 302.1556; Found: 302.1554.

(*E*)-4-(tert-butyl)phenyl N-methoxy-2-naphthimidate (**3u**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 1.1 Hz, 1H), 7.92 (dd, J = 8.7, 1.7 Hz, 1H), 7.81–7.78 (m, 3H), 7.50–7.42 (m, 2H), 7.29–7.25 (m, 2H), 6.96–6.92 (m, 2H), 3.97 (s, 3H), 1.27 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$)

δ 153.09, 150.85, 145.46, 134.16, 132.94, 128.73, 128.32, 127.73, 127.66, 127.12, 126.94, 126.48, 123.55, 115.11, 62.98, 34.23, 31.49. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO_2$ 334.1807; Found: 334.1812.

(*E*)-4-(tert-butyl)phenyl N-methoxythiophene-2-carbimidate (**3v**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 4H), 6.96–6.90 (m, 3H), 3.90 (d, J = 1.4 Hz, 3H), 1.28 (d, J = 1.4 Hz, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.91, 147.76, 145.75, 132.93, 128.62, 128.08, 127.30, 126.43, 115.15, 62.91, 34.24, 31.48.

(*E*)-*p*-tolyl 4-chloro-N-methoxybenzimidate (**3z**). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H), 2.20 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.89, 149.90, 136.28, 132.44, 130.14, 128.82, 128.66, 128.10, 115.63, 63.02, 20.64. HR-MS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}NO_2Cl$ 276.0791; Found: 276.0797.

4. Conclusions

In conclusion, we have described a copper-salt-catalyzed selective C-O cross-coupling of N-methoxy amides and arylboronic acids for the synthesis of aryl-N-methoxy arylimides in moderate yields. The optimal parameters were obtained by systematically exploring the reaction conditions such as the types of catalyst and base, the applicable temperature range, and the choice of solvents. A wide range of N-methoxy amides as well as arylboronic acids can serve as viable substrates, with various functional groups being tolerated. The most obvious finding to emerge from this study is that the type of copper salt greatly affects the reaction site of the N-methoxy amides. These findings enhance our understanding of the use of N-methoxy amides, and they will serve as a foundation for the future studies on the reaction mechanism.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal12101278/s1. The experimental procedures and characterization (^{1}H- and ^{13}C-NMR, and HR-MS) for all of the products are provided in the supporting information.

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