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Copper-Catalyzed Amidation of 2-Phenylpyridine with Oxygen as the Terminal Oxidant

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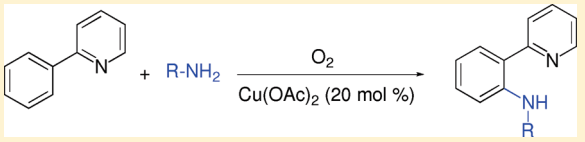
Supporting Information

ABSTRACT: The $Cu(OAc)_2$-catalyzed, O_2-mediated amidation of 2-phenylpyridine via C−H bond activation is reported. A variety of nitrogen reagents including sulfonamides, carboxamides, and anilines participate in the reaction in moderate to good yields.



Transition metal-catalyzed C−H functionalization to produce C−C and C−X (X = halide, N, O, S, etc.) bonds has emerged as a valuable protocol in contemporary organic synthesis, providing both economic and environmental benefits.[1] The C−H functionalization strategy offers numerous opportunities to streamline chemical synthesis, as it circumvents the need for prefunctionalization of the coupling partners which is required for other complementary metal-catalyzed cross-coupling reactions.[2] Among the C−H functionalization strategies of particular importance is C−N[3] bond formation because of the ubiquitous presence of the amine functionality in pharmaceuticals, specialty chemicals, and biologically important compounds.[4]

Following the pioneering report by Buchwald and co-workers[4b] on Pd-catalyzed intramolecular C−H amidation, there has been a surge of activity in this area with several key *N*-containing structural motifs being constructed from readily accessible starting materials.[5] Apart from the intramolecular version of the reaction, there have also been some reports on palladium-catalyzed intermolecular amination reactions.[6] Besides palladium, other metals which have been used recently to achieve catalytic arene C−H amination include rhodium,[7] ruthenium,[8] and platinum.[9]

Concern regarding the high cost and toxicity of heavy metal catalysts has stimulated efforts to achieve Cu-promoted C−N bond forming processes.[10] In this respect, Yu[11] reported the Cu-mediated functionalization of 2-phenylpyridine with several nucleophiles; the acetoxylation and chlorinations were catalytic in copper but the *N*-functionalization with toluenesulfonamide was stoichiometric. Chatani et al.[12] demonstrated similarly the Cu-promoted (stoichiometric) amination of 2-arylpyridines with substituted anilines in low to moderate yields. Li and co-workers recently demonstrated a copper-catalyzed amidation of 2-arylpyridine derivatives and 1-methylindoles using CuBr with *tert*-butyl peroxide serving as the stoichiometric oxidant.[13] The reaction proceeded in good to excellent yields for secondary-amide coupling partners under solvent-free conditions, but primary amides gave only low yields. Along similar lines, Su et al. reported a $Cu(OAc)_2/KOBu^t/TEMPO/O_2$ system for the intermolecular amination of *acidic* aryl C−H bonds with primary amines.[14]

We are seeking new catalytic amination reactions using inexpensive and readily available *N*-reagents and catalysts. In this respect we recently reported the Cu(I)-catalyzed intermolecular amination of benzylic C−H bonds using anhydrous Chloramine-T,[15] as well as the intramolecular amination[16] of sulfamates and carbamates. In keeping with our interest in copper-catalyzed amination reactions, we turned our attention to the development of a simple and efficient catalytic system for the amination of aromatic C−H bonds. In particular we were interested in employing primary sulfonamides and carboxamides as the *N*-reagents since the amidated products can be converted conveniently to the corresponding aryl amines. Also of interest was the identity of the Cu-containing intermediates and the factors controlling the efficiency of the catalyst turnover. Herein we report a simple and efficient $Cu(OAc)_2$-catalyzed amidation of 2-phenylpyridine using molecular oxygen as the terminal oxidant. A variety of primary *N*-reagents, including sulfonamides, carboxamides, and anilines, participate in the reaction, providing the desired amination products in moderate to good yields.

In light of the initial report on copper-mediated amidation of 2-phenylpyridine by Yu et al.,[11] we began our investigation by carrying out an extensive screening of variables to identify conditions for achieving the catalytic amidation of 2-phenylpyridine with *p*-toluenesulfonamide (eq 1 and Table 1) under aerobic conditions. It is worth noting that preliminary studies pointed toward the need for moderately high temperatures for achieving catalytic turnover and the prospect of using molecular oxygen as the terminal oxidant. It was observed that the reaction proceeded with negligible product formation (as detected by TLC and further confirmed by NMR studies) in aromatic hydrocarbon solvents (toluene and xylenes) and was accompanied by the appearance of a considerable amount of a red copper-containing precipitate (entries 2−4).[17] Analysis of this complex by

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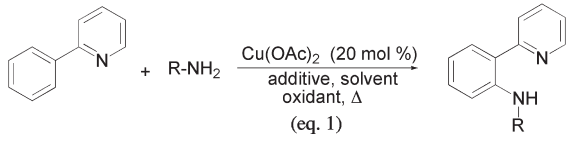
Table 1. Amidation of 2-Phenylpyridine with *p*-Toluenesulfonamide[a]

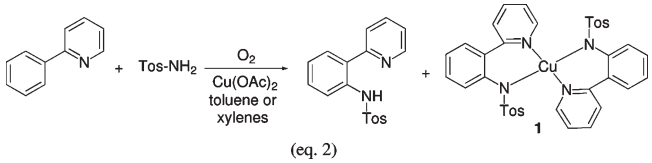
entry	solvent	additive (mol %)	oxidant	T (°C)	yield (%)[b,c]
1	DCE		$PhI(OAc)_2$	100	0
2	toluene		O_2	110	<5% + **1** (48%)
3	xylenes		O_2	130	<10% + **1** (45%)
4	xylenes	PPh_3 (40)	O_2	130	**1** (47%)
5	CH_3CN		O_2	80	25
6	DMF		O_2	140	28
7	DMSO		O_2	160	22
8	NMP		O_2	160	32
9	chlorobenzene		O_2	140	18
10	*o*-dichlorobenzene		O_2	140	40
11	*o*-dichlorobenzene		O_2	160	39
12	*o*-dichlorobenzene	DMSO (2.5 vol %)	O_2	160	25
13	anisole		O_2	140	61
14	anisole	DMSO (2.5 vol %)	O_2	140	51
15	anisole		O_2	160	51
16	anisole	DMSO (2.5 vol %)	O_2	160	79 (65)
17	anisole	pyridine (40)	O_2	160	63
18	anisole	PPh_3 (40)	O_2	160	(48)
19	anisole	1-methylimidazole (40)	O_2	160	<5
20	anisole	TMEDA (20)	O_2	160	44
21	anisole	2,2′-bipyridine (20)	O_2	160	29
22	anisole	DMSO (2.5 vol %)	air	160	58
23[d]	anisole	DMSO (2.5 vol %)	none	160	27

[a] Reaction conditions: 2-phenylpyridine (0.054 g, 0.35 mmol), *p*-toluenesulfonamide (0.12 g, 0.70 mmol), $Cu(OAc)_2$ (0.070 mmol, 20 mol %) in solvent (ca. 2 mL), 48 h. [b] Yield determined by ^1H NMR analysis with 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yields given in parentheses. [d] Reaction carried out under argon atmosphere.

ESI-MS indicated its composition to be $[(2\text{-NTs-Ph-pyridine})_2Cu]$, indicative of the known square-planar compound **1** (eq 2).[18] Importantly, this result shows that C−H *N*-functionalization had occurred. However, we were unable to efficiently liberate the sulfonamidated phenyl pyridine from **1** and it was found to be ineffective in catalyzing the amidation of 2-phenylpyridine with $TsNH_2$ (anisole, 160 °C). We conclude, therefore, that complex **1** is a "dead-end" species, limiting the catalytic turnover. In several polar solvents such as CH_3CN, DMF, DMSO, and NMP, sulfonamidated product **3aa** was formed, but only in stoichiometric quantity relative to $Cu(OAc)_2$, while complex **1** was detected in small quantities (entries 5−8).



(eq. 1)



(eq. 2)

Reactions conducted in more polar aromatic solvents gave modest catalytic turnover numbers (TON), ca. 1.2−2.0 (entries 10−12) for 1,2-dichlorobenzene and 2.5 for anisole (entry 14 and 15). Gratifyingly, the reaction yield increased to 79% when DMSO (2.5 vol %) was added to the reaction in anisole (entry 16). Other potentially coordinating additives, namely, pyridine, PPh_3, 1-methylimidazole, TMEDA, 2,2′-bipyridine, etc., gave poorer yields (Table 1, entries 17−21). It is worth pointing out that the reaction can be carried out in air at the expense of a slightly lower yield (58%, entry 22) and, additionally, it does not require dry solvents. The crucial role of O_2 in rendering the reaction catalytic by recycling the copper catalyst is strongly suggested by the observation that the reaction proceeds only stoichiometrically under an inert atmosphere (TON = 1.3, entry 23).

A survey of the activity of other copper salts revealed $Cu(O_2CPh)_2$ and $Cu(O_2CCF_3)_2$ also to be effective catalysts for the amidation reaction (Table 2). In general the organic carboxylate salts were found to be the most effective in promoting the amidation reaction. With the cupric halide salts like $CuCl_2$, only trace amounts of the amidated product could be detected by TLC, while the main organic product (∼20%) from the reaction was the *o*-chlorinated 2-phenylpyridine.[11] Similarly, the copper salts of dianions, e.g. $CuSO_4$, were found to effect the amidation only stoichiometrically, which may be attributable to the high lattice energy of these salts and, hence, their low solubility in the reaction medium. The Cu(I) salts were found to be ineffective possibly due to their diminished Lewis acidity.

After reaction optimization, we next explored the scope of the reaction with a range of readily available aminating agents as summarized in Table 3. Sulfonamides, carboxamides, and

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Table 2. Amidation of 2-Phenylpyridine with *p*-Toluenesulfonamide—Catalyst Variation[a]

entry	[Cu]	catalyst loading (mol %)	yield (%)[b,c]
1	$Cu(OAc)_2$	20	79 (65)
2	$Cu(O_2CCF_3)_2$	20	54
3	$Cu(OTf)_2$	20	36
4	$Cu(acac)_2$	20	40
5	$Cu(OTs)_2$	20	39
6	$Cu(OBz)_2$	20	(54)
7	$CuSO_4$	20	21
8	$CuCO_3 \cdot Cu(OH)_2$	10	21
9	$CuCl_2$	20	<5
10	CuI	20	<5

[a] A mixture of 2-phenylpyridine (0.054 g, 0.35 mmol), *p*-toluenesulfonamide (0.12 g, 0.70 mmol), CuZ_n (0.07 mmol), and DMSO (0.05 mL) in anisole (ca. 2 mL) was heated at 160 °C for 48 h under an oxygen atmosphere. [b] Yield determined by ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yields given in parentheses.

Table 3. Amidation of 2-Phenylpyridine−Amidating Agent Variation[a]

Entry	Reactant	Amide	Product	Yield (%)[b]
1	**1a**	**2a**	**3aa**	65
2	**1a**	**2b**	**3ab**	49
3	**1a**	**2c**	**3ac**	26
4	**1a**	**2d**	**3ad**	52
5	**1a**	**2e**	**3ae**	66
6	**1a**	**2f**	**3af**	46
7	**1a**	**2g**	**3ag**	38

[a] Reaction conditions: 2-phenylpyridine (1 equiv), amide or aniline (2 equiv), $Cu(OAc)_2$ (20 mol %), and DMSO (0.05 mL) in anisole (ca. 2 mL), 160 °C, 48 h, 1 atm of O_2. [b] Isolated.

anilines were found to serve as effective *N*-reagents, providing moderate to good yields of the corresponding amidated derivatives. It is noteworthy that the electron-deficient reagents, 4-nitrobenzene sulfonamide ($NosNH_2$) and 4-nitroaniline, exhibited lower amidation efficiencies, indicating that the electronic nature of the *N*-reagent is important to the reaction efficiency.

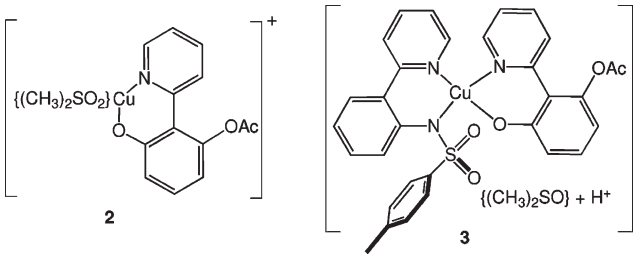
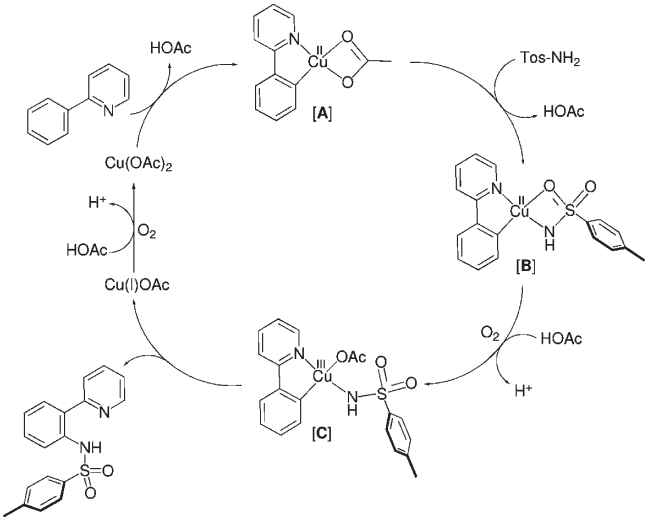


Figure 1. Cu-containing ESI-MS ions detected.

Scheme 1. Proposed Pathway for the $Cu(OAc)_2$-Catalyzed Amidation



With the intent of understanding the fate of the $Cu(OAc)_2$ at the end of the catalytic reaction, we isolated the copper-containing species from the catalysis reaction using silica gel chromatography (10% CH_3OH/90% CH_2Cl_2). ESI mass analysis of the copper-containing fraction revealed the presence of two major copper-containing ions with m/z 385/387 and 693/695, which could be assigned to copper species **2** (m/z 385/387) and **3** ($[\mathbf{3} + H^+]$, m/z 693/695); **2** is probably a fragment derived from **3** (Figure 1). The incorporation of DMSO and Me_2SO_2 in these complex ions suggests that coordination of the additive DMSO is important to its facilitation of the catalytic reaction. The detection of **2** and **3** also points toward a competing *o*-acetoxylation of 2-phenylpyridine[11] during the reaction. This is consistent with the observation that we always recovered less starting material from the reactions than expected on the basis of the product yield. Furthermore, during the course of our early attempts to enhance the yields by increasing the catalyst loading we observed that the yields decreased with increased catalyst loading.

Although there have been several reports of copper-mediated amidation, the mechanistic aspects are still not well understood. A plausible catalytic pathway for the $Cu(OAc)_2$-catalyzed amidation of 2-phenylpyridine is outlined in Scheme 1. The first step involves coordination of the substrate to $Cu(OAc)_2$ followed by C−H activation to generate intermediate **A**. The C−H activation step may proceed through a single electron transfer pathway as previously suggested[11] or by electrophilic aromatic substitution. Subsequently, the intermediate **A** combines with the amide

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partner to produce **B**. The intermediate **B** could undergo a *one-electron* oxidation to give the Cu(III)-intermediate **C**, which can undergo C−N reductive elimination to release the *o*-amidated 2-phenylpyridine. Aerobic oxidation of the Cu(I)OAc can reform the active catalyst to restart the catalytic cycle. It should be pointed out that C−O reductive elimination from intermediate **C** would produce the detected *o*-acetoxylated complex **3**.

In summary, a simple and efficient copper-catalyzed amidation of 2-phenylpyridine has been developed employing molecular oxygen as the terminal oxidant. A variety of *N*-reagents including sulfonamides, carboxamides, and anilines have been found to participate in the reaction with varying efficiency. Use of anisole as solvent and DMSO as an additive enables catalytic turnover, with oxygen putatively involved in inducing elimination of the product from the copper center and in regenerating the active catalyst.

EXPERIMENTAL SECTION

General Procedures. All manipulations were carried out with Schlenk tube techniques under oxygen atmosphere (balloon). The copper salts, anisole, 2-phenylpyridine, and the *N*-reagents were obtained from commercial sources and used without any further purification. $Cu(PhCO_2)_2$[19] and $Cu(OTs)_2$[20] were synthesized by literature methods. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a 300 MHz NMR spectrometer. ^1H NMR peaks are labeled as singlet (s), doublet (d), triplet (t), and multiplet (m). Mass spectra were acquired on a quadrupole MS instrument in the ESI(+) mode for low resolution spectra and in the ESI(−) mode for high resolution analysis respectively. The ^1H NMR yields were determined with 1,3,5-trimethoxybenzene as an internal standard.

General Procedure for the $Cu(OAc)_2$-Catalyzed Amidation of 2-Phenylpyridine. To an oven-dried Schlenk tube under an O_2 atmosphere was sequentially added $Cu(OAc)_2$ (0.014 mmol) and the *N*-reagent (1.39 mmol), followed by a solution of 2-phenylpyridine (0.70 mmol) and DMSO (0.05 mL) in anisole (ca. 2 mL). The reaction vessel was immersed in an oil bath preheated to 160 °C and allowed to stir for the stipulated period of time. After this the reaction mixture was allowed to cool to room temperature, diluted with ethyl acetate (ca. 5 mL), and filtered through a pad of silica. The silica pad was washed with ethyl acetate (ca. 3 × 5 mL) and then finally with dichloromethane (ca. 10 mL). The combined organic washings were concentrated under vacuum to yield the crude product, which was purified by silica gel column chromatography [diethyl ether/hexane (4:6)] to obtain the spectroscopically pure compounds. The ^1H NMR yields were determined with 1,3,5-trimethoxybenzene as the internal standard. NMR and MS spectral properties determined for known products were identical with those reported (referenced below). New compounds were also characterized by HR-MS and their purity assessed by ^1H NMR (see the SI).

***N*-(2-Pyridylphenyl)-4-methylbenzenesulfonamide (3aa).**[11] The product was obtained as a pale yellow solid (0.15 g, 65% yield). R_f (3:2 ethyl ether/hexane) 0.39; ^1H NMR ($CDCl_3$, 300 MHz) δ 12.06 (br, 1H), 8.53 (d, $^3J_{HH}$ = 4.8 Hz, 1H), 7.61 (d, $^3J_{HH}$ = 8 Hz, 2H), 7.44 (d, $^3J_{HH}$ = 8 Hz, 1H), 7.33−7.23 (m, 4H), 7.16 (t, $^3J_{HH}$ = 4.8 Hz, 1H), 7.07 (t, $^3J_{HH}$ = 7.8 Hz, 1H), 6.88 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 157.2, 147.5, 143.1, 137.6, 137.0, 136.6, 130.3, 129.3, 128.7, 127.4, 126.9, 124.8, 123.6, 122.4, 122.2, 21.6; LRMS (ESI) 325 [$(M + H)^+$], 347 [$(M + Na)^+$].

***N*-(2-Pyridylphenyl)-4-methoxybenzenesulfonamide (3ab).** The product was obtained as an off-white solid (0.12 g, 49% yield). R_f (3:2 ethyl ether/hexane) 0.26; ^1H NMR ($CDCl_3$, 300 MHz) δ 12.05 (br, 1H), 8.60 (d, $^3J_{HH}$ = 4.2 Hz, 1H), 7.72−7.68 (m, 1H), 7.76−7.69 (m, 2H), 7.52 (dd, 6.3 and 1.8 Hz, 1H), 7.42−7.31 (m, 4H), 7.25 (t, $^3J_{HH}$ = 6.2 Hz, 1H), 7.16 (t, $^3J_{HH}$ = 6.6 Hz, 1H), 6.63 (d, $^3J_{HH}$ = 9.0 Hz, 1H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 162.5, 147.3, 137.6, 130.2, 129.3, 129.3, 128.8, 128.5, 124.7, 123.6, 122.3, 122.1, 114.1, 114.3, 114.7, 113.7, 55.5; HRMS (ESI) calcd for $C_{18}H_{16}N_2O_3S$ (M − H) requires *m*/*z* 339.0809, found *m*/*z* 339.0791.

***N*-(2-Pyridylphenyl)-4-nitrobenzenesulfonamide (3ac).**[21] The product was obtained as a bright yellow solid (0.064 g, 26% yield). R_f (3:2 ethyl ether/hexane) 0.40; ^1H NMR ($CDCl_3$, 300 MHz) δ 12.44 (br, 1H), 8.61 (d, $^3J_{HH}$ = 4.2 Hz, 1H), 7.98 (d, $^3J_{HH}$ = 8.1 Hz, 2H), 7.74−7.68 (m, 2H), 7.61 (d, $^3J_{HH}$ = 6.6 Hz, 2H), 7.55 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.43−7.37 (m, 2H), 7.29 (t, $^3J_{HH}$ = 6.0 Hz, 1H), 7.23 (t, $^3J_{HH}$ = 7.8 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 156.6, 147.4, 144.9, 137.8, 135.8, 130.5, 128.6, 127.9, 125.7, 124.2, 123.6, 122.4, 122.2; LRMS (ESI) 356 [$(M + H)^+$], 378 [$(M + Na)^+$].

***N*-(2-Pyridylphenyl)methylsulfonamide (3ad).** The product was obtained as a pale yellow solid (0.099 g, 52% yield). R_f (3:2 ethyl ether/hexane) 0.28; ^1H NMR ($CDCl_3$, 300 MHz) δ 12.33 (br, 1H), 8.63 (d, $^3J_{HH}$ = 4.2 Hz, 1H), 7.89−7.74 (m, 4H), 7.42 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 7.31 (t, $^3J_{HH}$ = 5.4 Hz, 1H), 7.22 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 2.88 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 157.4, 147.7, 138.2, 137.7, 130.8, 129.0, 125.6, 124.2, 122.5, 122.4, 121.1, 39.7; HRMS (ESI) calcd for $C_{12}H_{12}N_2O_2S$ (M − H) requires *m*/*z* 247.0547, found *m*/*z* 247.0540.

***N*-(2-Pyridylphenyl)-2,2,2-trifluoroacetamide (3ae).**[6b] The product was obtained as a white solid (0.12 g, 66% yield). R_f (3:2 ethyl ether/hexane) 0.55; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.64 (d, $^3J_{HH}$ = 6.0 Hz, 1H), 8.58 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 7.93−7.87 (m, 2H), 7.83 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 7.50 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 7.36 (t, $^3J_{HH}$ = 6.9 Hz, 1H), 7.33 (d, $^3J_{HH}$ = 7.5 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 157.2, 155.2 (q, *J* = 36.6 Hz), 147.2, 138.3, 136.1, 130.6, 128.5, 125.4, 125.2, 122.6, 122.4, 122.0, 116.3 (q, *J* = 287 Hz); LRMS (ESI) 267 [$(M + H)^+$], 289 [$(M + Na)^+$].

***N*-(2-Pyridylphenyl)benzamide (3af).**[22] The product was obtained as a pale yellow solid (0.088 g, 46% yield). R_f (3:2 ethyl ether/hexane) 0.64; ^1H NMR ($CDCl_3$, 300 MHz) δ 13.33 (br, 1H), 8.81 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 8.69 (d, $^3J_{HH}$ = 4.2 Hz, 1H), 8.05 (d, $^3J_{HH}$ = 7.8 Hz, 2H), 7.89−7.79 (m, 2H), 7.74 (d, $^3J_{HH}$ = 7.5 Hz, 1H), 7.55−7.46 (m, 4H), 7.30 (t, $^3J_{HH}$ = 6.9 Hz, 1H), 7.22 (t, $^3J_{HH}$ = 8.7 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 165.7, 158.4, 147.4, 138.2, 138.0, 135.9, 131.7, 130.4, 128.9, 128.7, 127.5, 125.7, 123.7, 123.2, 122.2, 122.1; LRMS (ESI) 275 [$(M + H)^+$], 297 [$(M + Na)^+$].

***N*-(2-Pyridylphenyl)-4-nitroaniline (3ag).** The product was obtained as a yellow solid (0.076 g, 38% yield). R_f (3:2 ethyl ether/hexane) 0.45; ^1H NMR ($CDCl_3$, 300 MHz) δ 10.89 (br, 1H), 8.66 (d, $^3J_{HH}$ = 4.5 Hz, 1H), 8.11 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 7.82 (dt, 7.5 and 1.8 Hz, 1H), 7.74−7.66 (m, 2H), 7.60 (dd, 8.4 and 1.2 Hz, 1H), 7.39 (dt, 8.1 and 1.8 Hz, 1H), 7.31−7.25 (m, 1H), 7.15 (dt, 8.7 and 1.2 Hz, 1H), 7.11 (d, $^3J_{HH}$ = 9.0 Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 158.3, 149.6, 147.8, 139.9, 139.5, 137.8, 130.4, 129.9, 126.3, 123.2, 123.0, 122.1, 120.2, 115.2, 110.2; HRMS (ESI) calcd for $C_{17}H_{13}N_3O_2$ (M − H) requires *m*/*z* 290.0935, found *m*/*z* 290.0924.

Isolation of [*N*-(2-Pyridylphenyl)-4-methylbenzenesulfonamido]$_2$Cu(II)[18] (1). To an oven−dried Schlenk tube was added 2-phenylpyridine (0.155 g, 1.00 mmol), *p*-toluenesulfonamide (0.17 g, 1.00 mmol), and $Cu(OAc)_2$ (0.091 g, 0.50 mmol) in xylenes (ca. 5 mL) and the reaction mixture was stirred at 140 °C for 12 h under an oxygen atmosphere. The reaction mixture was cooled to room temperature and filtered. The copper **1** complex was collected as a red precipitate, washed with diethyl ether (ca. 2 × 5 mL), and dried under vacuum (0.18 g, 50%). LRMS (ESI) 710 [$(^{63}Cu - M + H)^+$], 732 [$(^{63}Cu - M + Na)^+$].

ASSOCIATED CONTENT

Supporting Information. Characterization data for all the new compounds reported (^1H and ^{13}C NMR spectra, HR

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ESI-MS). This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169. (b) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242–3272. (c) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (d) Mori, A.; Sugie, A. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 548–561. (e) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041–4047.

(2) Diederich, F.; Stang, P. J., Eds. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley VCH: Weinheim, Germany, 1998, .

(3) (a) Thansandote, P.; Lautens, M. *Chem.—Eur. J.* **2009**, *15*, 5874–5883. (b) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061–5074. (c) Armstrong, A.; Collins, J. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2282–2285.

(4) (a) Struff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586–14587. (b) Tsang, W. C. P.; Zheng, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 14560–14561. (c) Davies, H. M. L.; Long, M. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 3518–3520. (d) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905–2920.

(5) (a) Tan, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 3676–3677. (b) Miura, T.; Ito, Y.; Murakami, M. *Chem. Lett.* **2009**, *38*, 328–329. (c) Tsang, W. C. P.; Munday, R. H.; Brasche, G.; Zheng, N.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7603–7610. (d) Inamoto, K.; Saito, T.; Hiroya, K.; Doi, T. *Synlett* **2008**, *20*, 3157–3162. (e) Jordan-Hore, J. A.; Johansson, C. C. C.; Gulias, M.; Beck, E. M.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 16184–16186. (f) Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14058–14059. (g) Li, J.-J.; Mei, T.-S.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 6452–6455. (h) Inamoto, K.; Saito, T.; Katsuno, M.; Sakamoto, T.; Hiroya, K. *Org. Lett.* **2007**, *9*, 2931–2934.

(6) (a) Ng, K.-H.; Chan, A. S. C.; Yu, W.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 12862–12864. (b) Thu, Y.-H.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048–9049.

(7) Chiba, S.; Hattori, G.; Narasaka, K. *Chem. Lett.* **2007**, *36*, 52–53.

(8) Shou, W. G.; Li, J.; Guo, T.; Lin, Z.; Jia, G. *Organometallics* **2009**, *28*, 6874–6854.

(9) Yamamoto, M.; Matsubara, S. *Chem. Lett.* **2007**, *36*, 172–173.

(10) (a) Zhang, M. *Appl. Organomet. Chem.* **2010**, *24*, 269–284. (b) Kawano, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2010**, *132*, 6900–6901. (c) Wang, Q.; Schreiber, S. L. *Org. Lett.* **2009**, *11*, 5178–5180. (d) Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.* **2009**, *11*, 1607–1610. (e) Miyasaka, M.; Hirano, K.; Satoh, T.; Kowalczyk, R.; Bolm, C.; Miura, M. *Org. Lett.* **2011**, *13*, 359–361.

(11) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790–6791.

(12) Uemara, T.; Imoto, S.; Chatani, N. *Chem. Lett.* **2006**, *35*, 842–843.

(13) Shuai, Q.; Deng, G.; Chua, Z.; Bohle, D. S.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 632–636.

(14) Zhao, H.; Wang, M.; Su, W.; Hong, M. *Adv. Synth. Catal.* **2010**, *352*, 1301–1306.

(15) (a) Barman, D. N.; Nicholas, K. M. *Tetrahedron Lett.* **2010**, *51*, 1815–1818. (b) Bhuyan, R.; Nicholas, K. M. *Org. Lett.* **2007**, *9*, 3957–3959.

(16) Barman, D. N.; Nicholas, K. M. *Eur. J. Org. Chem.* **2011**, 908–911.

(17) The yield of the copper complex **1** was 45−48% with respect to $Cu(OAc)_2$.

(18) Otter, C. A.; Couchman, S. M.; Jeffery, J. C.; Mann, K. L. V.; Psillakis, E.; Ward, M. D. *Inorg. Chim. Acta* **1998**, *278*, 178–184.

(19) Deveruex, M.; O'Shea, D.; O'Connor, M.; Grehan, H.; Connor, G.; McCann, M.; Rosair, G.; Lyng, F.; Kellett, A.; Walsh, M.; Egan, D.; Thati, B. *Polyhedron* **2007**, *26*, 4073–4084.

(20) Deleersnyder, K.; Mehdi, H.; Horváth, I.; Binnemans, K.; Parac-Vogt, T. *Tetrahedron* **2007**, *63*, 9063–9070.

(21) Furuya, T.; Benitez, D.; Tkatchouk, E.; Strom, A. E.; Tang, P.; Goddard, W. A., III; Ritter, T. *J. Am. Chem. Soc.* **2010**, *132*, 3793–3807.

(22) Yamashita, Y.; Hayashi, T.; Masumura, M. *Chem. Lett.* **1980**, 1133–1136.