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Mild and efficient copper-catalyzed *N*-arylation of alkylamines and N–H heterocycles using an oxime-phosphine oxide ligand

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Abstract—A mild and efficient copper-catalyzed system for *N*-arylation of alkylamines and N–H heterocycles with aryl iodides using a novel, readily prepared and highly stable oxime-functionalized phosphine oxide ligand was developed. The coupling reactions could even be performed in solvent-free conditions with moderate to good yields.

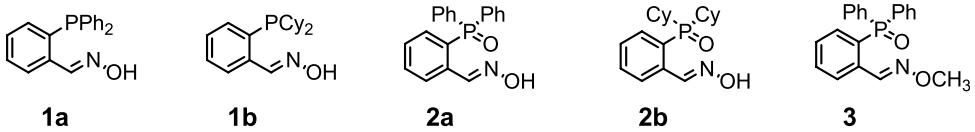
1. Introduction

Recently, copper-catalyzed Ullmann-type C(aryl)–N bond formation under mild conditions has become a focus of research to include a wide range of subsrates.[1–3] By using certain copper precatalysts and ligands, successful *N*-arylation of anilines,[4,5] amides,[6] amino acid,[7] amino alcohols,[8] hydrazides,[9] oxazolidinones[10] and various N–H heterocycles[6a,11] with aryl halides as arylating reagents was reported. However, only limited papers have contributed to *N*-arylation of alkylamines (not chelating substrates) and just several ligands were found to be effective in these transformation.[12] Therefore, to find more efficient ligands and expand the scope of the substrates are desirable.

In copper-mediated cross-coupling systems, the most used ligands were those containing nitrogen and/or oxygen bidentated with copper, while phosphines were mainly used in palladium-mediated systems.[13] Only recently, several phosphine ligands have been reported in Cu-catalyzed reactions of arylamines with aryl halides.[5] However, no efficient phosphine ligands for copper have been described for cross coupling of alkylamines with aryl halides to the best of our knowledge. In our initial studies, we attempted to find a highly efficient phosphine to achieve this coupling and have designed two oxime-functionalized phosphines (Fig. 1, **1a** and **1b**).[14] To our disappointment, neither of them were satisfying. We then tried using their oxides (**2a** and **2b**) as ligands considering that they have potential chelating ability to copper.[15] After a series of experiments, we found that both of **2a** and **2b** were effective supporting ligands and demonstrated excellent stability. Herein, we report a new class of oxime-phosphine oxide ligands (**2**) for copper-catalyzed *N*-arylation of alkylamines and N–H heterocycles under mild conditions.

2. Results and discussion

The synthesis of various phosphines and phosphine oxides was depicted in Scheme 1. Ligand **1a** was conveniently synthesized from commercially available **4** in one step. **2a** was readily prepared by oxidizing **1a**. Both **1a** and **2a** were obtained by recrystallization rather than using complex column chromatography. Similarly, ligand **1b** was readily prepared from 2-(dicyclohexylphosphino)benzaldehyde (**5**) which was prepared according to the literature.[16] Further



1a **1b** **2a** **2b** **3**

Figure 1.

Keywords: *N*-arylation; Oxime-phosphine oxide; Aryl iodides; Copper; Catalysis.
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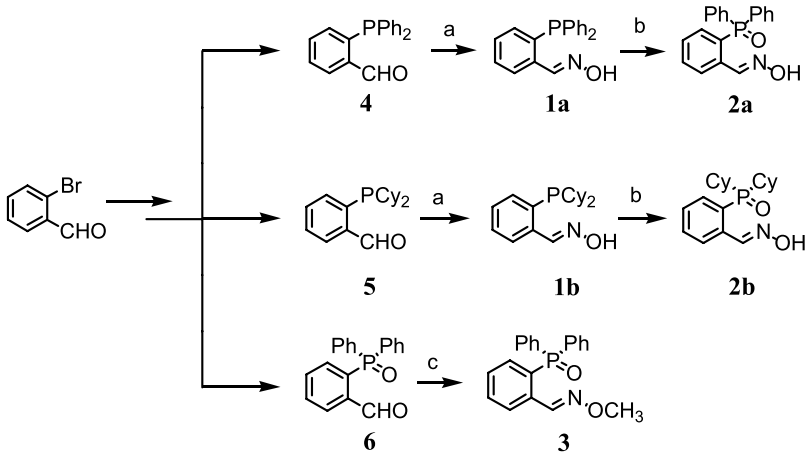
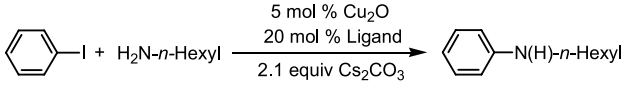


Scheme 1. Synthesis of the ligands. Reaction conditions: (a) H_2N–OH·HCl, $NaHCO_3$, H_2O, EtOH; (b) H_2O_2, CH_2Cl_2; (c) H_2N–OCH_3·HCl, $NaHCO_3$, H_2O, EtOH.

oxidizing **1b** gave **2b**. As a comparison, ligand **3** was also synthesized.

In our initial screening experiments, iodobenzene and *n*-hexylamine were used as model substrates to examine the above ligands (Table 1). Neither **1a** nor **1b** were efficient when the reactions were performed at 60 °C (entries 1 and 2). To our delight, both of their oxides (**2a** and **2b**) were highly effective giving the coupling product in high yields under the same conditions (entries 3 and 4). Moreover, the use of **1a** could only give a 78% conversion of the iodobenzene and 42% yield after 24 h at an elevated temperature of 90 °C (entry 1 in paretheses). These results showed that the phosphine oxides were remarkablely superior to the corresponding phosphines. Additionally, ligand **3** was not effective at all for the reaction (entry 5). Apparently, both the moieties of P═O and oxime were critical. **2a** was slightly better in result and more available than **2b**, so we chose for further study.

Table 1. Screening of the ligands[a]



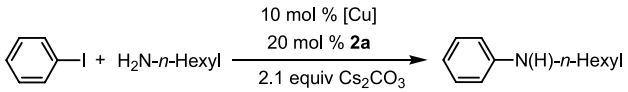
Entry	Ligand	Conversion, %[b]	Yield, %[b]
1	**1a**	0 (78)[c]	0 (42)[c]
2	**1b**	0	0
3	**2a**	95	92
4	**2b**	92	88
5	**3**	0	0

[a] Reaction conditions: 1.0 mmol PhI, 1.2 mmol *n*-hexylamine, 0.05 mmol Cu_2O, 0.2 mmol ligand, 2.1 mmol Cs_2CO_3, 0.2 mL CH_3CN, 60 °C, 18 h.
[b] GC yield.
[c] 24 h, 90 °C.

Preliminary results showed that the use of Cs_2CO_3 was important to the effectiveness, while K_3PO_4, K_2CO_3 or KOH only gave poor results.[17,18] Among the copper sources investigated, air and light stable Cu_2O was optimal (Table 2). CuBr, CuI, CuCN and Cu power only provided inferior results, while the use of CuO resulted in bad yield. A brief survey for solvent influence showed that the model reaction could be conducted with comparable efficiency in a wide range of solvents including CH_3CN, dioxane, DMF, toluene or even crude CH_3OH; while pyridine, THF or DMSO were less efficient. Hence, CH_3CN with lower polarity and boiling point was chosen for subsequent experiments.

The scope of the copper-catalyzed *N*-arylation of different amines was explored generally by using 5 mol% Cu_2O, 20 mol% **2a** and 2.1 equiv Cs_2CO_3 in CH_3CN. The results of aryl iodides with primary amines are detailed in Table 3. As we can see, various primary amines including *n*-hexylamine, *sec*-butylamine, *iso*-butylamine, cyclopentylamine were coupled successfully (entries 1–5). The reaction of iodobenzene with benzylamine resulted in an excellent yield of 95% with 1 mol% Cu_2O, the best result reported so far (entry 6). Both electron-donating and electron-withdrawing group, such as methoxy, cyano, nitro, trifluoromethyl were tolerated on the aryl iodide component (entries 8–13). Compared with the previous reported results, the couplings of both 3-iodobenzonitrile and 1-iodo-3-nitrobenzene with benzylamine were more effective (entries 12 and 13).[12b]

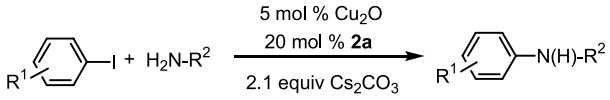
Table 2. Optimization studies[a]

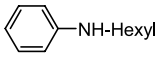
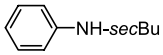
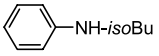
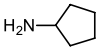
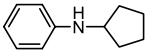
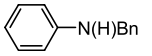
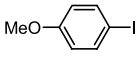
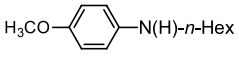
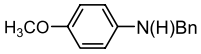
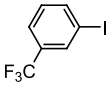
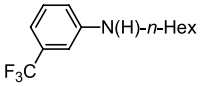
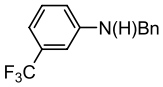
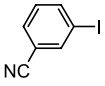
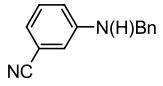
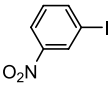
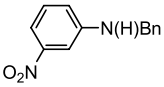
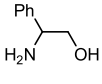
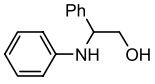


Entry	[Cu]	Solvent	Conversion, %[b]	Yield, %[b]
1	Cu_2O	CH_3CN	95	92[c]
2	Cu_2O	Dioxane	95	92
3	Cu_2O	DMF	93	91
4	Cu_2O	Toluene	92	90
5	Cu_2O	CH_3OH	96	89
6	Cu_2O	Pyridine	84	77
7	Cu_2O	DMSO	77	70
8	Cu_2O	THF	82	74
9	CuO	CH_3CN	20	18
10	CuBr	CH_3CN	95	83[d]
11	CuI	CH_3CN	95	83[d]
12	CuCN	CH_3CN	91	81[d]
13	Cu Power	CH_3CN	76	70[d]

[a] Reaction conditions: 1.0 mmol PhI, 1.2 mmol *n*-hexylamine, 10 mol% [Cu], 20 mmol% **2a**, 2.1 mmol Cs_2CO_3, 0.2 mL solvent, 60 °C, 18 h.
[b] GC yield.
[c] Using 5 mol% [Cu], nearly identical result could be obtained.
[d] Using 5 mol% [Cu].

Table 3. Coupling of aryl iodides with primary amines[a]



Entry	ArI	Amine	Product	Yield, %[b]
1		H_2N-*n*-Hexyl		88
2				85[c]
3		NH_2-*sec*-Bu		65
4		NH_2-*i*-Bu		80
5				88[d]
6		H_2NBn		95[e]
7				85[c]
8		H_2N-*n*-Hexyl		78[f]
9		H_2NBn		90
10		H_2N-*n*-Hexyl		76
11		H_2NBn		91
12		H_2NBn 1.5 equiv		85[d,g]
13		H_2NBn 1.5 equiv		87[d,g]
14				91

[a] Reaction conditions: 1.0 mmol ArI, 1.2 mmol amine, 0.05 mmol Cu_2O, 0.2 mmol **2a**, 2.1 mmol Cs_2CO_3, 0.6 mL CH_3CN, 80 °C, 18 h.
[b] Isolated yield.
[c] 60 °C.
[d] 90 °C.
[e] 1 mol% Cu_2O was used.
[f] $PhCH_3$ as solvent.
[g] 24 h.

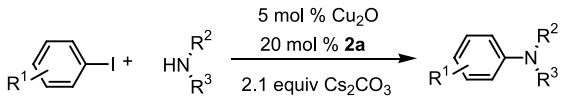
Moreover, aminoalcohol could also be transformed to the desired product in high yield (entry 14). Notably, diarylation products were minimal in all reactions.

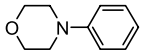
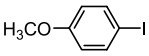
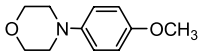
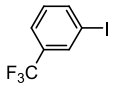
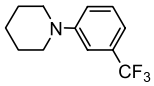
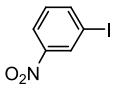
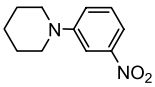
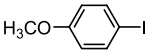
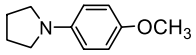
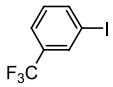
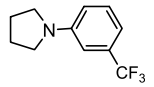
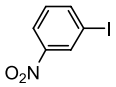
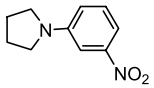
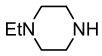
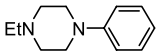
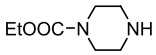
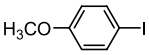
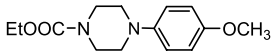
The optimized reaction condition was also used to examine the couplings of cyclic secondary amines with aryl iodides (Table 4). Morpholine was shown to be a good substrate to give the desired product in high yield, the best result to date (entry 1). Other cyclic secondary amines such as piperidine, pyrrolidine, *N*-ethylpiperazine and ethyl 1-piperazine-carboxylate could also be coupled successfully with aryl iodides (entries 2–9). In general, secondary amines gave the corresponding arylated products in slightly lower yields.

The practical benefits of these copper-catalyzed amination methodology were briefly noted. On one hand, although the reactions were moderately sensitive to oxygen and have to be performed under an inert atmosphere, neither glove-box techniques nor further purification of the commercially available reagents were essential. On the other hand, the key ligand **2a** could be obtained readily from commercial available materials and it was stable and not hydroscopic. Furthermore, we found that this newly developed protocol could also be applied to the coupling of N–H heterocycles with aryl iodides in mild conditions (Table 5).

As seen in Table 5, several *N*-heterocycles could be effectively transformed to the desired products. The arylation of pyrazole was carried out smoothly using various aryl iodides (entries 1–4). It is noteworthy that the reaction of pyrazole with iodobenzene could even be performed at rt (entry 2). Imidazole was transformed to

Table 4. Coupling of aryl iodides with cyclic secondary amines[a]



Entry	Amine	ArI	Product	Yield, %[b]
1				85
2				70[c]
3				70[d]
4				68[d]
5				65[d]
6				72[d]
7				73[d]
8				72
9				60[e]

[a] Reaction conditions: 1.0 mmol ArI, 1.2 mmol amine, 0.05 mmol Cu_2O, 0.2 mmol **2a**, 2.1 mmol Cs_2CO_3, 0.6 mL CH_3CN, 80 °C, 18 h.
[b] Isolated yield.
[c] $PhCH_3$ as solvent.
[d] 90 °C, 1.5 equiv amines.
[e] 24 h, 90 °C.

the desired product with high yield (entry 5). The arylation of benzimidazole and indole also proved to be successful under the general conditions (entries 6 and 7).

The use of such stable, readily available and efficient ligand as well as mild reaction condition made this protocol attractive. Furthermore, as seen in Table 6, different amine could be coupled with aryl iodides successfully in the solvent-free condition with moderate to good yields. This enhanced the attractiveness for practical utility.[12a,19]

3. Conclusion

In summary, we have developed a mild and efficient copper-catalyzed system for *N*-arylation of alkylamines and N–H heterocycles with aryl iodides using a novel, readily prepared and highly stable oxime-functionalized phosphine oxide ligand. The reaction could even be performed in solvent-free conditions. Although this method is restricted to the coupling of aryl iodides, the readily available ligand with excellent stability and high efficiency makes this protocol of potentially practical utility in many cases. Further studies to expand the application of this method to other catalytic reactions are currently underway.

4. Experimental

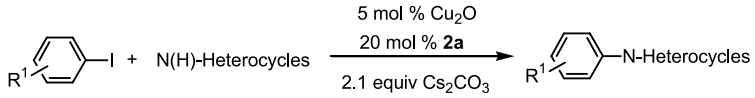
4.1. Materials and methods

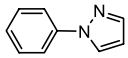
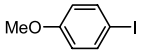
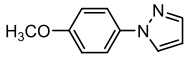
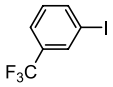
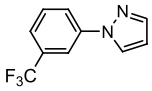
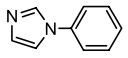
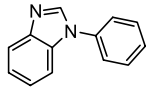
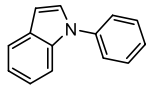
Melting points were measured on a Yazawa micro melting point apparatus (uncorrected). ^1H, ^{31}P and ^{13}C NMR spectra were measured on a Bruker DRX-400 NMR spectrometer (400 MHz) with TMS as an internal reference. $CDCl_3$ was used as the solvent for all NMR spectra unless otherwise stated. High-resolution mass spectra (HRMS) were recorded on a Mariner 5303 (Applied Biosystems, USA). All products were characterized by ^1H NMR and HRMS and compared with the previously reported data.[11,12a,b,c] All reactions were carried out under an argon atmosphere. Column chromatography purifications were performed using silica gel. All solvents were dried and degassed by standard methods and all starting materials were commercially available. Petroleum ether refers to the boiling range 60–90 °C. When solvent gradient was used, the increase of polarity was made gradually from petroleum ether to mixtures of petroleum ether/ethyl acetate until the isolation of the product.

4.2. Synthesis of ligands

4.2.1. 2-(Diphenylphosphino)-benzaldoxime (1a). An

Table 5. Coupling of aryl iodides with various *N*-heterocycles[a]

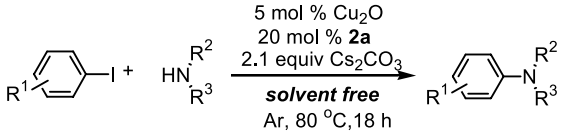


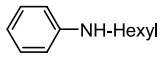
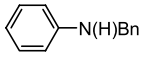
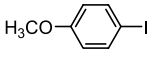
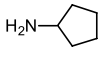
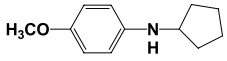
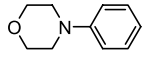
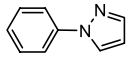
Entry	Amine	ArI	Product	Yield, %[b]
1				94
2				65[c]
3				95
4				81
5				92
6				60
7				64

[a] Reaction conditions: 1.0 mmol ArI, 1.2 mmol amine, 0.05 mmol Cu_2O, 0.2 mmol **2a**, 2.1 mmol Cs_2CO_3, 0.6 mL CH_3CN, 80 °C, 18 h.
[b] Isolated yield.
[c] Performed at rt.

aqueous solution (20 mL) containing hydroxylamine hydrochloride (938.0 mg, 13.5 mmol) was prepared and $NaHCO_3$ (1.51 g, 18 mmol) was added under stirring. 2-(Diphenylphosphino)benzaldehyde (**4**) (3.34 g, 9 mmol) was dissolved in EtOH (50 mL) in reflux and the above aqueous solution was added dropwise. After the reaction mixture was refluxed continuously for 2 h, the mixture was cooled to rt with stirring. The white solid was filtered (1.8 g) and the filtrate was concentrated, exacted with Et_2O, washed with H_2O, dried (Na_2SO_4). The solution was concentrated to give the product (0.8 g). The two portions weighed 2.6 g of crude product (95%). The crude product could be used directly in the next step without further purifications, or can be recrystallized from ethanol to give the product **1a** as a white solid in 83% yield. Mp 176–177 °C. ^{1}H NMR δ 8.81 (d, 1H, J=4.4 Hz), 7.81–7.84 (m, 1H), 7.67(s, 1H), 7.23–7.38 (m, 12H), 6.90–6.93 (m, 1H). ^{31}P NMR δ −13.4. ^{13}C NMR δ 149.3, 149.1, 136.8, 136.6, 136.2, 136.0, 135.9,

Table 6. Solvent-free Cu-catalyzed amination of aryl iodides[a]



Entry	ArI	Amine	Product	Yield, %[b]
1		H_2N-*n*-Hexyl		78
2		H_2NBn		87
3				64[c]
4				62[c]
5				70

[a] Reaction conditions: 1.0 mmol ArI, 1.2 mmol amine, 0.05 mmol Cu_2O, 0.2 mmol **2a**, 2.1 mmol Cs_2CO_3, 80 °C, 18 h.
[b] Isolated yield.
[c] Performed 24 h at 90 °C.

134.2, 133.9, 133.9, 130.0, 129.2, 129.1, 128.9, 128.8, 126.7. HRMS (APCI) calcd for $C_{19}H_{17}NOP$ ($M+H^+$): 306.1042, found: 306.1050.

4.2.2. 2-(Diphenylphosphinyl)-benzaldoxime (2a). Compound (**1a**) (2.60 g, 8.5 mmol) was dissolved in CH_2Cl_2 (50 mL) and 30% H_2O_2 (4 mL) was added at rt. The mixture was stirred for 2 h and large amount of white solid precipitated. The solid was filtered and washed with water then recrystallized from MeOH to give the product as a white solid (1.7 g, 70%). Mp 203–206 °C. ^1H NMR (400 MHz, DMSO-d^6) δ 11.43 (s, 1H), 8.74 (s, 1H), 8.01–8.03 (m, 1H), 7.43–7.66 (m, 12H), 7.01–7.07 (m, 1H). ^{31}P NMR δ 30.5. ^{13}C NMR δ 146.3, 136.6, 133.0, 132.9, 132.3, 131.8, 131.5, 131.4, 131.0, 130.0, 129.0, 128.9, 128.7, 126.3, 126.2. HRMS (APCI) calcd for $C_{19}H_{17}NO_2P$ ($M+HP^+$): 322.0991, found: 322.1021.

4.2.3. 2-(Diphenylphosphinyl)benzaldehyde *O*-methyloxime (3). An aqueous solution (10 mL) containing methoxylamine hydrochloride (45.0 mg, 0.54 mmol) was prepared and $NaHCO_3$ (53.0 mg, 0.63 mmol) was added with stirring. Compound **6** (138.0 mg, 0.45 mmol) was dissolved in ethanol (10 mL) and the above aqueous solution was added dropwise. The reaction mixture was refluxed continuously for 1 h, The reaction mixture was concentrated, extracted with ethyl acetate, washed with H_2O, brine and dried (Na_2SO_4). The solution was concentrated to give a crude product which was purified by column chromatograph on silica gel to afford a white solid 0.12 g (80%). Mp 123–125 °C. ^1H NMR (400 MHz, DMSO-d^6) δ 8.83 (s, 1H), 7.99–8.01 (m, 1H), 7.48–7.68 (m, 12H), 7.04–7.10 (m, 1H), 3.81 (s, 3H). ^{31}P NMR δ 30.5 ^{13}C NMR δ 147.5, 136.9, 133.6, 133.5, 133.0, 132.2, 132.1, 128.9, 128.8, 127.6, 127.5, 62.1. HRMS (APCI) calcd for $C_{20}H_{19}NO_2$ ($M+H^+$): 336.1148, found: 336.1134.

4.2.4. 2-(Dicyclohexylphosphino)-benzaldoxime (1b). 2-(Dicyclohexylphosphino)-benzaldehyde (1.0 g, 3.3 mmol) was dissolved in deoxygenated ethanol and the solution was transferred to a flask including 30 mL of deoxygenated ethanol flushed by nitrogen. Hydroxylamine hydrochloride (1.39 mg, 20 mmol) was dissolved in deoxygenated H_2O (40 mL) and $NaHCO_3$ (2.5 g, 30 mmol) was added under stirring. The aqueous solution was added dropwise to the 2-(dicyclohexylphosphino)-benzaldehyde solution, and the reaction mixture was stirred for 1 h. The resulting mixture was extracted with Et_2O and dried over Na_2SO_4, concentrated, and purified by flash chromatograph on a short silica gel column with N_2 pressure (100% petroleum ether) to give the product as a white solid (390 mg, 37%). Mp 116–118 °C. ^1H NMR δ 9.16–9.18 (m, 1H), 8.05 (s, 1H), 7.85–7.86 (m, 1H), 7.48–7.50 (m, 1H), 7.33–7.39 (m, 3H), 0.97–1.97 (m, 22H). ^{31}P NMR δ −15.9. ^{13}C NMR δ 150.7, 150.4, 135.1, 133.0, 128.9, 126.3, 33.4, 33.3, 30.5, 30.3, 28.9, 27.4, 27.2, 27.1, 26.4. HRMS (APCI) calcd for $C_{19}H_{29}NO$ ($M+H^+$): 318.1981, found: 318.1988.

4.2.5. 2-(Dicyclohexylphosphinyl)-benzaldoxime (2b). To a solution of 2-(dicyclohexylphosphino)-benzaldoxime (159 mg, 0.5 mmol) in CH_2Cl_2 (20 mL), H_2O_2 (1.0 ml) was added under rt. The mixture was stirred for 1 h. The organic layer was separated and washed with water, dried (Na_2SO_4), concentrated to give the product as a white solid. Mp 199–202 °C. ^1H NMR δ 9.29 (s, 1H), 7.98–8.00 (m, 1H), 7.45–7.51 (m, 3H), 1.13–2.15 (m, 22H). ^{31}P NMR δ 53.1. ^{13}C NMR δ 149.9, 131.9, 131.5, 128.8, 128.2, 36.7, 36.0, 26.5, 25.8, 25.1. HRMS (APCI) calcd for $C_{19}H_{29}NO_2$ ($M+H^+$): 334.1930, found: 334.1918.

4.3. General procedure for copper-catalyzed *N*-arylation of various amines

Cu_2O (7.4 mg, 0.05 mmol), ligand (0.2 mmol), Cs_2CO_3 (685.0 mg, 2.1 mmol) and aryl iodides (if solid, 1.0 mmol) were weighed in air and transferred into a dried Schlenk tube. The tube was evacuated and back filled with argon (3 cycles). Freshly distilled CH_3CN, aryl iodides (if liquid, 1.0 mmol) and amines (1.2 mmol) were injected to the tube successively by micro-syringe at rt. The tube was sealed and stirred in an oil bath (preheated to reaction temperature) for the required timeperiod. The reaction mixture was cooled to rt, ethyl acetate (3 mL), H_2O (3 mL) and tetradecane (100 μL, GC standard) were added. The organic layer was analyzed by GC and separated. The aqueous layer was further extracted by ethyl acetate (10 mL×4). The combined organic layers were washed with brine, dried (Na_2SO_4). Then the solution was concentrated to give a residue, which was purified by column chromatograph on silica gel. The characterization of the products is listed following.

4.3.1. *N*-Hexylaniline (Table 3, entry 1). A liquid (155.0 mg, 88% yield). ^1H NMR: δ 7.21–7.25 (m, 2 H), 6.73–6.77 (m, 1 H), 6.66 (d, 2 H, J=7.6 Hz), 3.36 (s, 1H), 3.15 (t, 2H, J=7.2 Hz), 1.63–1.70 (m, 2H), 1.33–1.49 (m, 6H), 0.97 (t, 3H, J=6.8 Hz). HRMS (APCI) calcd for $C_{12}H_{20}N$ ($M+H^+$): 178.1590, found: 178.1580.

4.3.2. *N*-(*sec*-Butyl)aniline (Table 3, entry 3). A liquid (97.0 mg, 65% yield). ^1H NMR: δ 7.13–7.17 (m, 2H), 6.63–7.67 (m, 1H), 6.57 (d, 2H, J=8 Hz), 3.36–3.43 (m, 2H), 1.55–1.63 (m, 1H), 1.43–1.50 (m, 1H), 1.14–1.17 (m, 3H), 0.93–0.97 (m, 2H). HRMS (APCI) calcd for $C_{10}H_{16}N$ ($M+H^+$): 150.1277, found: 150.1272.

4.3.3. *N*-(*iso*-Butyl)aniline (Table 3, entry 4). A liquid (119.0 mg, 80% yield). ^1H NMR: δ 7.14–7.18 (m, 2H), 6.67–6.69 (m, 1H), 6.60 (d, 2H, J=8 Hz), 3.74 (br, 1H), 2.92 (d, 2H, J=6.8 Hz), 1.85–1.90 (m, 1H), 0.97 (d, 6H, J=6.8 Hz). HRMS (APCI) calcd for $C_{10}H_{16}N$ ($M+H^+$): 150.1277, found: 150.1285.

4.3.4. *N*-Cyclopentylaniline (Table 3, entry 5). A liquid (142.0 mg, 88% yield). ^1H NMR: δ 7.13–7.20 (m,2H), 6.65–6.68 (m,1H), 6.58–6.60 (m, 2H), 3.74–3.80 (m, 1H), 3.61 (s, 1H), 1.98–2.02 (m, 2H), 1.67–1.73 (m, 2H), 1.59–1.62 (m, 2H), 1.43–1.47 (m, 2H). HRMS (APCI) calcd for $C_{11}H_{16}N$ ($M+H^+$): 162.1277, found: 162.1283.

4.3.5. *N*-(Phenyl)benzylamine (Table 3, entry 6). A white solid (174.0 mg, 95% yield). ^1H NMR: δ 7.34–7.38 (m, 4H), 7.25–7.29 (m, 1H), 7.16–7.19 (m, 2H), 6.72–6.74 (m, 1H), 6.64–6.70 (m, 2H), 4.33 (s, 2H), 4.25 (br, 1H). HRMS (APCI) calcd for $C_{13}H_{14}N$ ($M+H^+$): 184.1121, found: 184.1119.

4.3.6. 4-Methoxy-*N*-hexylaniline (**Table 3**, entry 8). A liquid (162.0 mg, 78% yield). ^{1}H NMR: δ 6.77 (d, 2H, J=8.8 Hz), 6.57 (d, 2H, J=8.8 Hz), 3.73 (s, 3H), 3.22 (br, 1H), 3.03–3.06 (m, 2H), 1.57–1.61 (m, 2H), 1.31–1.40 (m, 6H), 0.89 (t, 3H, J=6.4 Hz). HRMS (APCI) calcd for $C_{13}H_{22}NO$ (M+H$^+$): 208.1696, found: 208.1680.

4.3.7. *N*-(4-Methoxyphenyl)benzylamine (**Table 3**, entry 9). A solid (192.0 mg, 90% yield). ^{1}H NMR: δ 7.28–7.40 (m, 5H), 6.78–6.80 (m, 1H), 6.62 (d, 2H, J=8.6 Hz), 4.29 (s, 2H), 3.75 (s, 3H). HRMS (APCI) calcd for $C_{14}H_{16}NO$ (M+H$^+$): 214.1226, found: 214.1207.

4.3.8. 3-Trifluoromethyl-*N*-hexylaniline (**Table 3**, entry 10). A liquid (186.0 mg, 76% yield). ^{1}H NMR: δ 7.20–7.24 (m, 1H), 6.89–6.90 (d, 1H, J=7.6 Hz), 6.78 (s, 1Hz), 6.71 (d, 1H, J=8.0 Hz), 3.68 (br, 1H), 3.10 (t, 2H, J=7.2 Hz), 1.57–1.63 (m, 2H), 1.32–1.41 (m, 6H), 0.90 (t, 3H, J=6.4 Hz). HRMS (APCI) calcd for $C_8H_{19}N_3O_2F_3$ (M+H$^+$): 246.1424, found: 246.1441.

4.3.9. *N*-(3-Trifluoromethylphenyl)benzylamine (**Table 3**, entry 11). A liquid (228.0 mg, 91% yield). ^{1}H NMR: δ 7.18–7.33 (m, 6Hz), 6.92 (d, 1H, J=7.6 Hz), 6.82 (s, 1H), 6.71 (d, 1H, J=8.0 Hz), 4.30 (s, 2H), 4.15 (br, 1H). HRMS (APCI) calcd for $C_9H_{13}N_3O_2F_3$ (M+H$^+$): 252.0954, found: 252.0967.

4.3.10. *N*-(3-Cyanophenyl)benzylamine (**Table 3**, entry 12). A white solid (176.0 mg, 85% yield). ^{1}H NMR: δ 7.30–7.38 (m, 5H), 7.20–7.26 (m, 1H), 6.99 (d, 1H, J=7.2 Hz), 6.82–6.84 (m, 2H), 4.64 (br, 1H), 4.34 (s, 2H). HRMS (APCI) calcd for $C_{14}H_{13}N_2$ (M+H$^+$): 209.1073, found: 209.1064.

4.3.11. *N*-(3-Nitrophenyl)benzylamine (**Table 3**, entry 13). An orange solid (198.0 mg, 87% yield). ^{1}H NMR: δ 7.55 (d, 1H, J=7.6 Hz), 7.46 (s, 1H), 7.26–7.38 (m, 6H), 6.90 (d, 1H, J=7.6 Hz), 4.39 (s, 2H). HRMS (APCI) calcd for $C_{13}H_{13}N_2O_2$ (M+H$^+$): 229.0972, found: 229.0959.

4.3.12. 2-Phenyl-2-(phenylamino)ethanol (**Table 3**, entry 16). A colorless liquid (193.0 mg, 91% yield). ^{1}H NMR: δ 7.25–7.38 (m, 5H), 7.08–7.12 (m, 2H), 6.66–6.69 (m, 1H), 6.56 (d, 2H, J=8.0 Hz), 4.49–4.52 (m, 2H), 3.92–3.95 (m, 1H), 3.73–3.77 (m, 1H), 1.77 (br, 1H). HRMS (APCI) calcd for $C_{14}H_{16}NO$ (M+H$^+$): 214.1226, found: 214.1209.

4.3.13. *N*-(Phenyl)morpholine (**Table 4**, entry 1). A white solid (138.0 mg, 85% yield). ^{1}H NMR: δ 7.25–7.30 (m, 2H), 6.87–6.94 (m, 3H), 3.87 (t, 4H, J=4.0 Hz), 3.16 (t, 4H, J=4.0 Hz). HRMS (APCI) calcd for $C_{10}H_{14}NO$ (M+H$^+$): 164.1070, found: 164.1080.

4.3.14. *N*-(4-Methoxyphenyl)morpholine (**Table 4**, entry 2). A liquid (135.0 mg, 70% yield). ^{1}H NMR: δ 6.76–6.83 (m, 4H), 3.78 (t, 4H, J=5.2Hz), 3.69 (s, 3H), 2.97 (t, 4H, J=4.8Hz). HRMS (APCI) calcd for $C_{11}H_{16}NO_2$ (M+H$^+$): 194.1176, found: 194.1165.

4.3.15. *N*-(3-Trifluoromethylphenyl)piperidine (**Table 4**, entry 3). A liquid (160.0 mg, 70% yield). ^{1}H NMR: δ 7.29–7.33 (m, 2H), 7.01–7.11 (m, 2H), 3.19–3.21 (m, 2H), 1.68–1.74 (m, 2H), 1.57–1.62 (m, 1H). HRMS (APCI) calcd for $C_{12}H_{15}NF_3$ (M+H$^+$): 230.1151, found: 230.1132.

4.3.16. *N*-(3-Nitrophenyl)piperidine (**Table 4**, entry 4). A liquid (140.0 mg, 68% yield). ^{1}H NMR: δ 7.70 (s, 1H), 7.55–7.60 (m, 1H), 7.22–7.36 (m, 1H), 7.17–7.19 (m, 1H), 3.25–3.27 (m, 4H), 1.70–1.74 (m, 4H), 1.62–1.63 (m, 2H). HRMS (APCI) calcd for $C_{11}H_{15}NO_2$ (M+H$^+$): 207.1128, found: 207.1112.

4.3.17. *N*-(4-Methoxyphenyl)pyrrolidine (**Table 4**, entry 5). A liquid (115.0 mg, 65% yield). ^{1}H NMR: δ 6.85 (d, 2H, J=8.8 Hz), 6.54 (d, 2H, J=7.6 Hz), 3.76 (s, 3H), 3.23 (s, 4H), 1.97–2.00 (m, 4H). HRMS (APCI) calcd for $C_{11}H_{16}NO$ (M+H$^+$): 178.1226, found: 178.1216.

4.3.18. *N*-(3-Trifluoromethylphenyl)pyrrolidine (**Table 4**, entry 6). A solid (155.0 mg, 72% yield). ^{1}H NMR: δ 7.26–7.30 (m, 1H), 6.87 (d, 1H, J=8.0 Hz), 6.73 (s, 1H), 6.67 (d, 1H, J=8.0 Hz), 3.27–3.31 (m, 4H), 2.02 (m, 4H). HRMS (APCI) calcd for $C_{11}H_{13}NF_3$ (M+H$^+$): 216.0995, found: 216.0979.

4.3.19. *N*-(3-Nitrophenyl)pyrrolidine (**Table 4**, entry 7). An orange solid (140.0 mg, 73% yield). ^{1}H NMR: δ 7.52 (d, 1H, J=8.0 Hz), 7.40 (s, 1H), 7.31–7.35 (m, 1H), 6.91 (d, 1H, J=8.0 Hz), 3.36–3.37 (m, 4H), 2.07–2.09 (m, 4H). HRMS (APCI) calcd for $C_{10}H_{13}N_2O_2$ (M+H$^+$): 193.0972, found: 193.0959.

4.3.20. *N*-Phenyl-*N*-(ethyl)piperazine (**Table 4**, entry 8). A solid (136.0 mg, 72% yield). ^{1}H NMR: δ 7.25–7.29 (m, 2H), 6.93–6.95 (m, 1H), 6.84–6.87 (m, 1H), 3.22–3.24 (m, 4H), 2.61–2.63 (m, 4H), 2.45–2.51 (m, 2H), 1.12–1.15 (m, 3H). HRMS (APCI) calcd for $C_{12}H_{19}N_2$ (M+H$^+$): 191.1543, found: 191.1534.

4.3.21. Ethyl *N*-(4-Methoxyphenyl)piperazinecarboxylate (**Table 4**, entry 9).. A solid (158.0 mg, 60% yield). ^{1}H NMR: δ 6.83–6.92 (m, 4H), 4.14–4.19 (m, 2H), 3.76–3.77 (m, 3H), 3.63 (s, 4H), 3.02 (s, 4H), 1.28 (t, 3H, J=7.2 Hz). HRMS (APCI) calcd for $C_{14}H_{21}N_2O_3$ (M+H$^+$): 265.1547, found: 265.1531.

4.3.22. *N*-(Phenyl)pyrozole (**Table 5**, entry 1). A liquid (134.0 mg, 94% yield). ^{1}H NMR: δ 7.88 (d, 1H, J=2.4 Hz), 7.66–7.71 (m, 3H), 7.39–7.43 (m, 2H), 7.23–7.27 (m, 1H), 6.42–6.43 (m, 1H). HRMS (APCI) calcd for $C_9H_9N_2$ (M+H$^+$): 145.0760, found: 145.0751.

4.3.23. *N*-(4-Methoxyphenyl)pyrozole (**Table 5**, entry 3). A liquid (165.0 mg, 95% yield). ^{1}H NMR: δ 7.83 (d, 1H, J=4.0 Hz), 7.70 (s, 1H), 7.58–7.60 (m, 2H), 6.96–6.98 (m, 2H), 6.44 (s, 1H), 3.84 (s, 3H). HRMS (APCI) calcd for $C_{10}H_{11}N_2O$(M+H$^+$): 175.0866, found: 175.0856.

4.3.24. *N*-(3-Trifluoromethylphenyl)pyrozole (**Table 5**, entry 4). A liquid (172.0 mg, 81% yield). ^{1}H NMR: δ 7.74–7.89 (m, 4H), 7.51–7.57 (m, 2H), 6.48–6.49 (m, 1H). HRMS (APCI) calcd for $C_{10}H_8NF_3$ (M+H$^+$): 213.0634, found: 213.0610.

4.3.25. *N*-(Phenyl)imidazole (**Table 5**, entry 5). A liquid (132.0 mg, 92% yield). ^{1}H NMR: δ 7.86 (m, 1H), 7.46–7.50

(m, 2H), 7.35–7.39 (m, 3H), 7.28 (s, 1H), 7.21 (s, 1H). HRMS (APCI) calcd for $C_9H_9N_2$ ($M+H^+$): 145.0760, found:145.0773.

4.3.26. *N*-(Phenyl)benzimidazole (Table 5, entry 6). A solid (125.0 mg, 64% yield). ^{1}H NMR: δ 8.07 (s, 1H), 7.87–7.89 (m, 1H), 7.46–7.50 (m, 3H), 7.36–7.41 (m, 3H), 7.24–7.31 (m, 2H). HRMS (APCI) calcd for $C_{13}H_{11}N_2$ ($M+H^+$): 195.0917, found: 195.0895.

4.3.27. *N*-(Phenyl)indole (Table 5, entry 7). A solid (116.0 mg, 60% yield). ^{1}H NMR: δ 7.67–7.69 (m, 1H), 7.55 (d, 1H, $J=7.6$ Hz), 7.44–7.47 (m, 4H), 7.28–7.33 (m, 2H), 7.14–7.22 (m, 2H), 7.67 (d, 1H, $J=3.6$ Hz). HRMS (APCI) calcd for $C_{14}H_{12}N$ ($M+H^+$): 194.0964, found: 194.0975.

4.3.28. *N*-Cyclopentyl-4-methoxyaniline (Table 6, entry 3). A liquid (122.0 mg, 64% yield). ^{1}H NMR: δ 6.75–6.78 (m, 2H), 6.56–6.58 (m, 2H), 3.69–3.73 (m, 3H), 3.38 (s, 1H). HRMS (APCI) calcd for $C_{12}H_{18}NO$ ($M+H^+$): 192.1383, found: 194.1364.

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