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Nano copper(I) oxide/zinc oxide catalyzed *N*-arylation of nitrogen-containing heterocycles with aryl halides and arylboronic acids in air

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The synergistic effect of zinc and copper in Cu_2O/ZnO nanoflake as a heterogeneous catalyst for the *N*-arylation of heterocycles with aryl halides and arylboronic acids in the absence of additional ligand in air were demonstrated. The catalyst was characterized by powder X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), BET surface area measurement, and FT-IR spectroscopy.

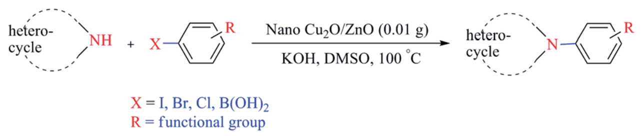
Introduction

N-aryl heterocycles, are ubiquitous in biochemical, biological, and medicinal structures and functions,[1] and have been exploited as precursors of versatile *N*-heterocyclic carbenes,[2] and efficient ligands for synthesis of transition-metal catalysts[3] or ionic liquids.[4] Traditionally, these compounds have usually been prepared by Ullmann-type coupling reactions. However, these reactions were conducted under harsh conditions, including high temperature (around 200 °C) for extended periods of time, stoichiometric amount of copper reagents, and selective halide substrate, which is problematic for industrial use due to high cost and waste disposal. To overcome these drawbacks, great progresses have been made recently to develop new catalytic systems. In some instances catalytic amounts of copper agent and arylboronic acids in place of aryl halides have been employed, but this protocol is not general due to the relative instability of boronic acids and the tedious purification procedure.[5] Buchwald[1b,6] and Hartwig[1d,7] independently reported the applicability of Pd catalysts for *N*-arylation of amines with aryl halides. However, industrial use of these procedures is problematic in many cases due to their air and moisture sensitivity, as well as the higher costs of palladium catalysts and the ligands. Thus, Cu-based catalysts have continued to provide the most effective system for the *N*-arylation of nitrogen-containing heterocycles. Indeed, Buchwald[8] and Taillefer[9] reported, respectively, that copper-catalyzed cross-coupling of *N*–H heterocycles with aryl halides could be improved with the addition of diamines or oxime/imine derivatives as additives. Other groups have also utilized various ligands, such as β-diketones,[10] 1,2-diamines,[8b,11] phenanthrolines,[12] bipyridines,[13] α-aminoacids,[14] phosphines,[15] Schiff bases,[9a] ethylene glycol,[16] diethyl salicylamide,[17] per-6-amino-β-cyclodextrin,[18] 1,1,1-tris(hydroxymethyl)ethane,[19] thiophenecarboxylate,[20] pyridine *N*-oxides,[21] phosphorus dendrimers,[22] and tricarbene.[23] These ligands play an important role in controlling the concentration of active catalytic species, but they may contaminate the final product.[24] Using a catalyst in the absence of any additional ligands could be a good alternative to avoid the inconvenience of ligand removal from the reaction mixture.

In recent years, several CuI/Cu_2O-catalyzed ‘ligand-free’ catalytic systems have emerged.[9c,25] However, these catalytic systems often require excess substrates[25a,b,j] or high catalyst loadings.[25c–f] Although there are some reports on the amination of aryl halides with amines promoted by Cu(II) salts without using organic ligands, they often suffer from one or more limitations,[26] such as high reaction temperature and/or prolonged reaction time.[26e–h] In addition, some of these methods require large amounts of catalyst, which raised the cost of the reaction[26a–d] and some of the catalyst are air sensitive.[26h] Thus, a need to develop a ligand-free, environmentally friendly, less expensive and easily separable catalytic system for such coupling reactions is substantial.

Herein, for the first time, we report the efficient catalytic activity of Cu_2O/ZnO nanoparticles toward the *N*-arylation of various *N*-heterocycles with aryl halides and arylboronic acid under ‘ligand-free’ conditions (Scheme 1).

In comparison with the current methods of the C–N bond formation, our approach has several distinguishing features that are worth mentioning: (i) the coupling yield is excellent,



Scheme 1 Synthesis of *N*-aryl heterocycles in air catalyzed by Cu_2O/ZnO nanoflake.

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and the reaction tolerates both electron-donating and electron-withdrawing substituents in *ortho*-, *meta*-, or *para*-positions of the aryl halide. (ii) The approach offers experimental simplicity and can be performed without the need for protection from air or moisture; (iii) this procedure can be performed in the absence of any additional ligand at lower cost, safely and is environmentally benign on a large, or industrial scale. Furthermore, this approach is not only efficient for aryl halides but also it is convenient for arylboronic acids.

Results and discussion

Characterization of Cu_2O/ZnO nanoflake

The Cu_2O/ZnO nanoflake catalyst was prepared by a simple method from cheap and commercial sources. The preparation process involved combing of the zinc oxide (ZnO) and the copper sulfate ($CuSO_4$) as copper source, centrifuged and washed with deionized water and absolute ethanol to dispose of free Cu^{2+} ions, and finally reducing by hydrazine hydrate ($N_2H_4 \cdot H_2O$).

In order to evaluate the Cu and Zn contents of the catalyst, it was treated with concentrated HCl to digest the metal complex and then analyzed by inductively coupled plasma (ICP) analysis. The results revealed that the contents of Cu and Zn were 47.01% (w/w) and 21.77% (w/w) respectively (see Experimental section for details).

The FT-IR spectrum of the catalyst in the region of 400–950 cm^{-1} is shown in Fig. 1. The peak at 624 cm^{-1} corresponds to the Cu–O bond,[27] and a weak absorption at about 455 cm^{-1} is attributed to the characteristic absorption band of Zn–O.[28]

The crystal structure and composition of the obtained sample were analyzed by X-ray diffraction. Fig. 2 displays the XRD pattern of the sample. The XRD pattern of the Cu_2O/ZnO nanoflake can be indexed with five Cu_2O diffraction peaks at 29.5° (110), 36.4° (111), 42.3° (200), 61.6° (220), 73.8° (311) and six ZnO diffraction peaks at 31.8° (100), 34.5° (002), 36.4° (101), 47.8° (102), 56.7° (110), 63.0° (103) (JCPDS 78-2076 and 89-1397), which suggests the presence of Cu_2O and ZnO phases in the sample. Considering the overlapping of a ZnO (101) diffraction peak with a Cu_2O (111) diffraction peak, the Cu_2O (200) diffraction peak was selected to calculate the average grain size of Cu_2O by using the Scherrer formula. The average grain size of Cu_2O along the (200) direction and ZnO along the (002) direction in a Cu_2O/ZnO nanoflake is about 21 nm and 30 nm respectively.

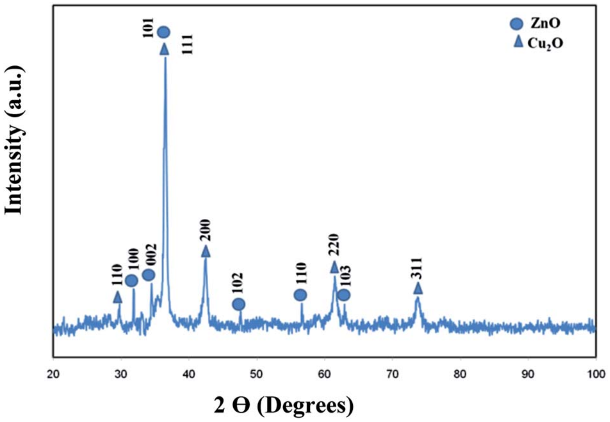


Fig. 2 The XRD pattern of Cu_2O/ZnO nanoflake.

The scanning electron micrograph (SEM) of the synthesized Cu_2O/ZnO particles is shown in Fig. 3. It demonstrates that a well defined and discrete Cu_2O/ZnO nanoflake has been formed. The size and morphology of Cu_2O/ZnO nanoparticles analyzed by TEM is represented in Fig. 4. This image reveals that the product consists of flake particles with the average size of 32 nm.

The data obtained by BET measurements of nano Cu_2O/ZnO powder are shown in Table 1. The BET surface area of nano Cu_2O/ZnO powder was found to be 14.74 $m^2\ g^{-1}$, whereas the BJH adsorption surface area of pores was 13.08 $m^2\ g^{-1}$. The single point total pore volume was found to be 0.07 $cm^3\ g^{-1}$, and the cumulative adsorption pore volume was 0.06 $cm^3\ g^{-1}$. The pore size distribution was found to be 2.41 nm and the mean pore diameter was 19.54 nm.

Catalytic activity of the nano Cu_2O/ZnO for *N*-arylation of nitrogen heterocycles

In order to establish the optimum conditions, for our initial screening experiment, the catalytic activity of a few zinc and

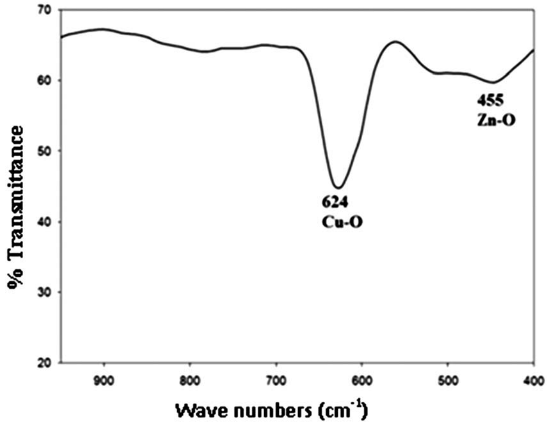


Fig. 1 FT-IR spectrum of Cu_2O/ZnO nanoflake.

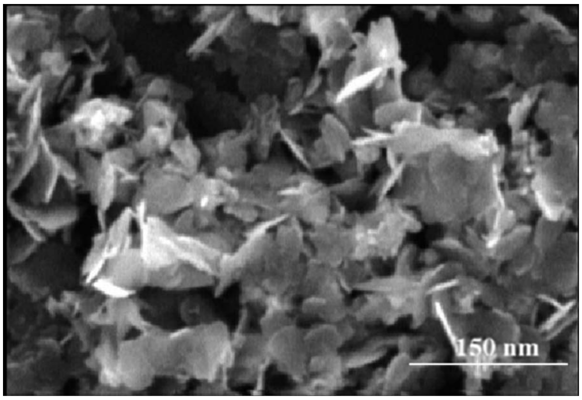


Fig. 3 The SEM image of Cu_2O/ZnO nanoflake.

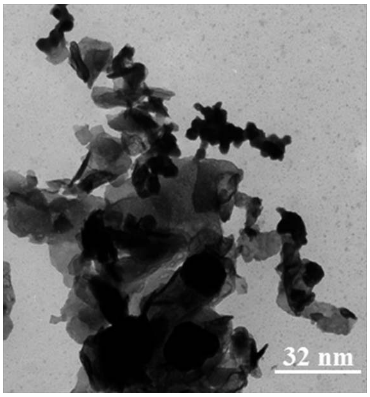


Fig. 4 TEM image of Cu_2O/ZnO nanoflake.

Table 1 Results of BET surface area measurements for Cu_2O/ZnO nanoflake

Surface area	BET surface area (m^2 g^{-1})	14.74
	BJH adsorption cumulative surface area of pores (m^2 g^{-1})	13.08
Pore volume	Single point adsorption total pore volume of pores (cm^3 g^{-1})	0.07
	BJH adsorption cumulative volume of pores (cm^3 g^{-1})	0.06
Pore size	Mean pore diameter (nm)	19.54
	Pore size distribution (nm)	2.41

copper metal oxides were examined in a model reaction between imidazole (**1a**) and iodobenzene (**2a**) in DMSO at 100 °C (Table 2). Nano Cu_2O/ZnO was found to be the most effective catalyst in terms of reaction rate, and isolated yield of the corresponding products without observing any other products (Table 2, entry 1). Both nano and bulk Cu_2O afforded the desired products in 60 and 48% yields, respectively (Table 2, entries 2 and 4). However, no product was formed when the reaction was run in the presences of nano or bulk ZnO individually (Table 2, entries 3 and 5). This may be because of increasing the reactivity of Cu_2O after interacting with ZnO. With respect to the catalyst loading, 0.010 g of nano Cu_2O/ZnO was found to be optimal. When 0.005 g of nano Cu_2O/ZnO was used, the reaction did not go to completion, and good yield of the product was obtained as the reaction time prolonged (Table 2, entry 6). However, no significant improvement was observed with 0.020 g and 0.040 g of nano Cu_2O/ZnO (Table 2, entries 7 and 8). In addition, performing the experiment in the absence of nano Cu_2O/ZnO did not lead to any product even after 48 h (Table 2, entry 9). In addition, we further investigated the *N*-arylation reaction between imidazole (**1a**) and iodobenzene (**2a**) by adding some nitrogen-containing ligands such as 1,10-phenanthroline and ethylenediamine (Table 2, entries 10 and 11). However, surprisingly it was found that the effect of the ligand is negligible as compared to the reactions without additional ligand.

Encouraged by this result, then we examined the effect of different solvents and bases on the coupling reaction (Table 3). Among the solvents used, DMSO was found to be the best one for such reaction (Table 3, entry 1), while other solvents such as DMF, PEG, and MeCN gave comparatively lower yields (Table 3, entries 2–4). Toluene and water did not afford any product (Table 3, entries 5 and 6). For a variety of bases (*e.g.*, KOH,

Table 2 Investigation of a few zinc and copper metal oxides in *N*-arylation of imidazole with iodobenzene[a]

Entry	Catalyst (g)	Time (h)	Yield[b] (%)
1	Nano Cu_2O/ZnO (0.01)	2	95
2	Nano Cu_2O[c] (0.01)	24	60
3	Nano ZnO[c] (0.01)	24	0
4	Bulky Cu_2O[d] (0.01)	24	48
5	Bulky ZnO[d] (0.01)	24	0
6	Nano Cu_2O/ZnO (0.005)	3	70
7	Nano Cu_2O/ZnO (0.02)	2	95
8	Nano Cu_2O/ZnO(0.04)	2	95
9	None	48	0
10	Nano Cu_2O/ZnO (0.01)[e]	2	95
11	Nano Cu_2O/ZnO (0.01)[f]	2	95

[a] *Reaction conditions*: imidazole (1.2 mmol), iodobenzene (1 mmol), KOH (2 mmol), and catalyst (0.010 g, 7.3×10^{-2} mmol Cu) in DMSO (2 mL) at 100 °C. [b] Isolated yield. [c] Nano Cu_2O and ZnO individually, were prepared according to the Experimental section. [d] Cu_2O and ZnO were purchased from Merck. [e] 1,10-Phenanthroline (7.3×10^{-2} mmol) as ligand. [f] Ethylenediamine (7.3×10^{-2} mmol) as ligand.

Table 3 The optimization of solvent and base[a]

Entry	Solvent/base	Time (h)	Yield[b] (%)
1	DMSO/KOH	2	95
2	DMF/KOH	4	40
3	PEG (300)/KOH	4	35
4	Acetonitrile/KOH	4	20
5	H_2O/KOH	4	0
6	Toluene/KOH	4	0
7	DMSO/Cs_2CO_3	4	45
8	DMSO/K_2CO_3	4	35
9	DMSO/K_3PO_4	4	30
10	DMSO/NaOAc	4	10
11	DMSO/NEt_3	4	0

[a] *Reaction conditions*: imidazole (1.2 mmol), iodobenzene (1 mmol), base (2 mmol), and Cu_2O/ZnO nanoflake (0.010 g) in solvent (2 mL) at 100 °C. [b] Isolated yield.

Table 4 The optimization of temperature[a]

Entry	Temperature (°C)	Time (h)	Yield[b] (%)
1	25	6	0
2	50	6	30
3	80	6	45
4	100	2	95
5	120	2	96

[a] *Reaction conditions*: imidazole (1.2 mmol), iodobenzene (1 mmol), KOH (2 mmol), and Cu_2O/ZnO nanoflake (0.010 g) in DMSO (2 mL). [b] Isolated yield.

Table 5 *N*-Arylation of imidazole with aryl halide or arylboronic acid[a]

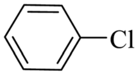
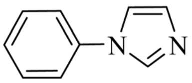
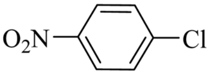
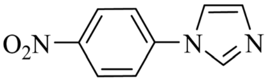
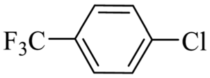
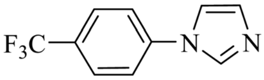
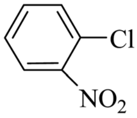
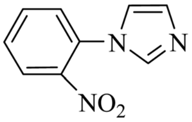
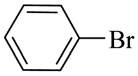
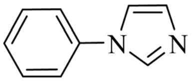
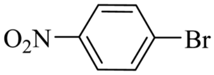
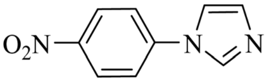
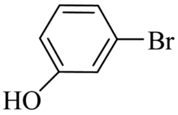
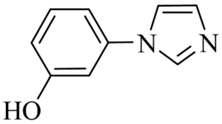
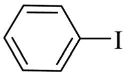
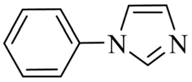
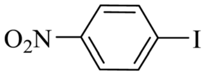
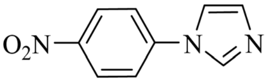
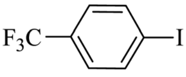
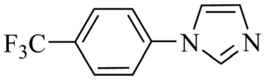
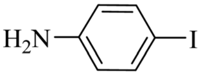
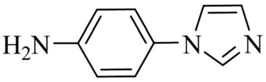
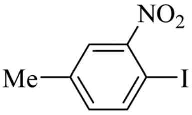
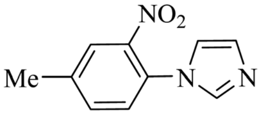
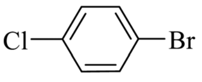
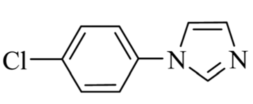
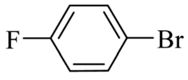
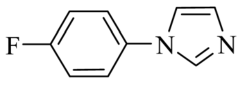
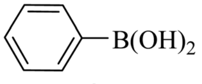
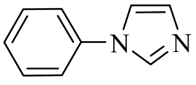
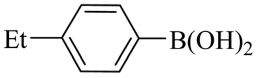
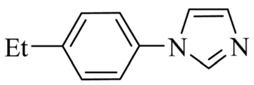
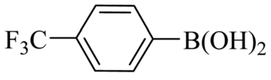
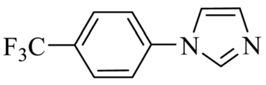
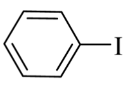
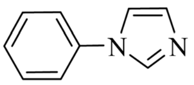
Entry	ArX	Product	Time (h)	Yield[b] (%)	Ref.
1	 **2a**	 **3a**	15	90	25*c*
2	 **2b**	 **3b**	3	90	25*c*
3	 **2c**	 **3c**	4.25	90	33
4	 **2d**	 **3d**	3	85	34
5	 **2e**	 **3a**	10	90	25*c*
6	 **2f**	 **3b**	2	95	25*c*
7	 **2g**	 **3e**	3	90	35
8	 **2h**	 **3a**	2	95	25*c*
9	 **2i**	 **3b**	1.25	95	25*c*
10	 **2j**	 **3c**	4.66	92	33
11	 **2k**	 **3f**	15	90	25*c*
12	 **2l**	 **3g**	4.83	90	36

Table 5 (*Contd.*)

Entry	ArX	Product	Time (h)	Yield^b (%)	Ref.
13	 **2m**	 **3h**	6	80	33
14	 **2n**	 **3i**	4.66	90	33
15	 **2o**	 **3a**	1.25	95	25*c*
16	 **2p**	 **3j**	1.33	90	37
17	 **2q**	 **3c**	2.25	90	33
18^c	 **2h**	 **3a**	3.5	95	25*c*

^{a} *Reaction conditions*: imidazole (1.2 mmol), aryl halide or arylboronic acid (1 mmol), KOH (2 mmol), and catalyst (0.010 g) in DMSO (2 mL) at 100 °C. ^{b} Isolated yield. ^{c} Large scale test.

K_2CO_3, K_3PO_4, Cs_2CO_3, NaOAc, and NEt_3), KOH was selected as the best one for this reaction in DMSO (Table 3, entry 1). NEt_3 as an organic base was ineffective (Table 3, entry 11) and moderate yield was afforded by using Cs_2CO_3 (Table 3, entry 7) and poor result was observed by using NaOAc (Table 3, entry 10).

Furthermore, during our optimization studies, the effect of temperature utilizing nano Cu_2O/ZnO (0.010 g), was also examined and it was found that the reaction temperature exerts great impact on this reaction (Table 4). Finally, the optimized reaction conditions were found to be 0.010 g of nano Cu_2O/ZnO, KOH (as the base) and DMSO (as a solvent) at 100 °C.

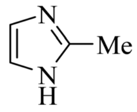
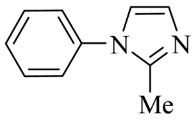
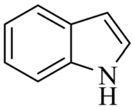
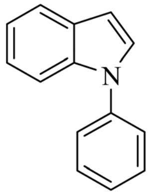
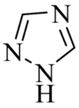
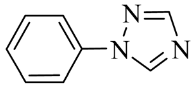
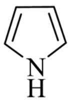
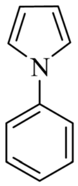
With the optimized reaction conditions in hand, a variety of substituted aryl halides derivatives were chosen as the substrates in this cross-coupling reaction. As shown in Table 5, the coupling reactions were performed well for all the substrates examined, and the desired products were isolated in moderate to excellent yields. Notably, the present catalyst system could facilitate the *N*-arylation of imidazole with *ortho*-substituted aryl iodide and chloride. For example, the reaction of imidazole with 2-nitrochlorobenzene and 4-methyl-2-nitroiodobenzene, afforded the corresponding coupling products in 85 and 90% yields, respectively (Table 5, entries 4 and 12). Generally, the Ullmann-type condensations are sensitive to steric hindrance near the halogen atom, and only a few examples concerning with the copper-catalyzed arylation of imidazole with sterically hindered aryl halides were found in the literatures.[8c] The reaction with bromobenzene (**2e**) relative to iodobenzene (**2h**) was slower with a lower conversion of starting materials, even after extending the reaction time (Table 5, entry 5). Coupling reaction of imidazole **1** with chlorobenzene (**2a**) was also investigated, and the chloride showed lower reactivity compared with bromide and iodide (Table 5, entry 1). Independently on the aryl halide used the reactions were never accompanied by the formation of biaryl homocoupling by products.

To our delight, our system could promote almost exclusively the selective *N*-arylation of 4-iodoaniline to afford the corresponding *N*-arylimidazole (**3f**) in high yield, avoiding the competition from the formation of diarylamine (Table 5, entry 11). It is noteworthy that the reaction was highly chemoselective, for example, reaction between 1-bromo-4-chlorobenzene, 1-bromo-4-fluorobenzene and imidazole gave 1-(4-chlorophenyl)-1*H*-imidazole and 1-(4-fluorophenyl)-1*H*-imidazole as the only products respectively (Table 5, entries 13 and 14). To explore further the applicability of nano Cu_2O/ZnO catalyst for C–N coupling reactions, we tested the *N*-arylation of imidazole with various arylboronic acids bearing electron-donating and withdrawing groups; and the desired products were isolated in high yields (Table 5, entries 15–17). To check the feasibility of this procedure on a preparative scale, we carried out the *N*-arylation of imidazole (**1a**) with iodobenzene (**2a**) on a 50 mmol scale in the presence of nano Cu_2O/ZnO catalyst. As expected, the reaction proceeded similarly to the experiment on a smaller scale, except that a slight increase in the reaction time was observed (3.5 h) (Table 5, entry 18).

The catalytic activity of nano Cu_2O/ZnO in *N*-arylation reactions of other nitrogen-containing heterocycles was also investigated. 2-Methyl-1*H*-imidazole, indole, 1*H*-1,2,4-triazole, and pyrrole, underwent coupling with iodobenzene under the optimized experimental conditions and provided their corresponding products in 50–85% yield (Table 6, entries 1–4).

In order to show the merit of this catalytic method, we compared our obtained results with similar data published by other groups which used other catalysts. For this purpose, the reactions of imidazole and iodobenzene were chosen as a model reaction and comparison was carried out on the basis of reaction conditions, time, and percentage yields (Table 7).

Table 6 *N*-Arylation of various nitrogen heterocycles[a]

Entry	Amine	Product	Time (h)	Yield[b] (%)	Ref.
1	 **1b**	 **3j**	12	75	18
2	 **1c**	 **3k**	5	50[c]	25*c*
3	 **1d**	 **3l**	3	85	25*c*
4	 **1f**	 **3m**	5	80	25*c*

[a] *Reaction conditions*: Het-NH (1.2 mmol), iodobenzene (1 mmol), KOH (2 mmol), and catalyst (0.010 g) in DMSO (2 mL) at 100 °C. [b] Isolated yield. [c] The yield was not improved event after 12 h.

Table 7 Comparison of activity of different copper catalysts in the *N*-arylation reaction of iodobenzene and imidazole

Entry	Catalyst, ligand	Reaction conditions	Time (h)/yield (%)	Ref.
1	$Cu(OAc)_2 \cdot H_2O$ (1 mol%)	DMF, 110 °C	24/98	26*g*
2	Cu(0) (2 equiv.)	MeCN, reflux	12/95	25*f*
3	Cu_2O (0.05 mol%), 4,7-dimethoxy-1,10-phenanthroline (0.075 mol%)	Butyronitrile, Ar or N_2, 110 °C	24–48/95	8*c*
4	MnF_2 (30 mol%), CuI (10 mol%), *trans*-1,2-diaminocyclohexane (20 mol%)	H_2O, 100 °C	24/63	29
5	$Cu(OAc)_2 \cdot H_2O$ (20 mol%), hippuric acid (20 mol%)	DMF, Ar, 140 °C	30/87	30
6	Silica tethered copper complexes (5 mol%)	Toluene, N_2, 100–135 °C	8/89	31
7	Cu_2O (10 mol%), ninhydrin (20 mol%)	DMSO, Ar, 90 °C	24/92	32
8	CuI (0.05 mmol), tetrazole-1-acetic (0.1 mmol)	DMSO, 110 °C	12/84	38
9	Nano Cu_2O/ZnO (0.010 g)	DMSO, 100 °C	2/95	This study

Conclusions

In conclusion, for the first time, we have demonstrated the application of Cu_2O/ZnO nanoflake for 'ligand free' *N*-arylation of various *N*-heterocycles from differently substituted aryl halides (X = I, Br, Cl) and arylboronic acids. The low cost and readily available Cu and Zn salts, mild reaction conditions, and the operational simplicity render this transformation as an attractive alternative for the assembly of *N*-arylated products and make it viable for use both in laboratory research and in larger industrial scales.

Experimental section

NMR spectra were recorded on a Bruker Avance DPX-250 (^1H NMR 250 MHz and ^{13}C NMR 62.9 MHz) in pure deuterated solvents with tetramethylsilane (TMS) as internal standards. Scanning electron micrographs were obtained by SEM instrumentation (SEM, XL-30 FEG SEM, Philips, at 20 kV). A transmission electron microscopy TEM was also used for TEM (Philips CM10) image. Spectroscopic methods including X-ray diffraction (XRD, D8, Advance, Bruker, axs) and FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) were employed for characterization of the heterogeneous catalyst. Surface area measurements were conducted according to the Brunauer–Emmett–Teller (BET) gas (nitrogen) adsorption method. The porous structural parameter used in this paper was taken from Barret–Joyner–Halenda (BJH) data. Metal contents were obtained by an ICP analyzer (Varian, vista-pro). Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instrument at 70 or 20 eV. Melting points determined in open capillary tubes in a Büchi-535 circulating oil melting point apparatus. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel PolyGram SILG/UV254 plates or by a Shimadzu Gas Chromatograph (GC-10A) instrument with a flame ionization detector using a column of 15% carbowax 20 M chromosorb-w acid washed 60–80 mesh. Column chromatography was carried out on short columns of silica gel 60 (70–230 mesh) in glass columns (2–3 cm diameter) using 15–30 grams of silica gel per one gram of crude mixture. Chemical materials were purchased from Fluka, Aldrich, Alfa Aesar, and Merck Companies.

General procedure for the synthesis of Cu_2O/ZnO nanoflake

$CuSO_4$ (1 g, 6.26 mmol), was dissolved in 50 mL distilled water to obtain a certain concentration solutions. Commercially ZnO (0.51 g, 6.26 mmol) was then dispersed in the above solution and sonicated to obtain a uniform suspension. The suspension was vigorously stirred at room temperature for 50 min to ensure enough Cu^{2+} ion adsorbed on the surface of ZnO. After stirring, in order to dispose of free Cu^{2+} ions, the mixtures were centrifuged and washed by deionized water and absolute ethanol alternately for three times. Then the mixture was added into 30 mL deionized water to obtain suspension. The suspension was subsequently heated to 70 °C in a water bath for 5 min under stirring. Then 1 mol L^{-1} $N_2H_4 \cdot H_2O$ was slowly added into the suspension until lots of red-brown precipitates were produced. After constant temperature water bath for 30 min under stirring, products were collected by filtration, washed with deionized water and absolute ethanol several times, and finally dried in air at 60 °C for 3 h. According to the ICP analysis, the Cu and Zn content in the catalyst was determined to be 47% (w/w) and 21.77% (w/w) respectively. Therefore, each gram of catalyst includes 7.3 mmol of copper and 3.3 mmol of zinc.

General procedure for the synthesis of nano Cu_2O

$CuSO_4$ (1 g, 6.26 mmol) was dissolved in 50 mL distilled water to obtain a solutions. After stirring, the solution was subsequently heated to 70 °C in a water bath for 5 min under stirring. Then 1 mol L^{-1} $N_2H_4 \cdot H_2O$ was slowly added into the suspension until lots of red-brown precipitates were produced. After constant temperature water bath for 30 min under stirring, products were collected by filtration, washed with deionized water and absolute ethanol several times, and finally dried in air at 60 °C for 3 h.

General procedure for the synthesis of nano ZnO

First, $Zn(OAc)_2 \cdot 2H_2O$ (as Zn^{2+} source, 1 g) and PEG 2000 (0.30 g) were dissolved in water (140 mL) and then by drop wise addition of NH_4OH (1.5 mL, 25%) at reflux condition after 6 h, $Zn(OH)_4{}^{2-}$ were formed. With the presence of a water-soluble linear polymer (PEG 2000), ZnO crystals form at the interface between substrate and solution by the dehydration of $Zn(OH)_4{}^{2-}$. After that, the product was centrifuged and washed with deionized water and absolute ethanol. Then 90 mL deionized water was added and the mixture was refluxed for 8 h. It was cooled by cold water, centrifuged and washed. Finally, the nano-rods ZnO powders are dried at 100 °C in an oven to give 0.65 g powder.

General procedure for the catalytic *N*-arylation of nitrogen-containing heterocycles with aryl halides and arylboronic acid

To a mixture of imidazole (1.2 mmol), Cu_2O/ZnO nanoflake (0.01 g), KOH (2 mmol), in DMSO (2 mL), aryl halide or arylboronic acid (1 mmol) was added and stirred at 100 °C until complete consumption of starting material as monitored by TLC. The reaction mixture was centrifuged to separate the catalyst. After that ethyl acetate was poured into the mixture, and then washed with water. The organic layer was separated, dried over Na_2SO_4 and the solvent was removed under reduced pressure to get the crude product. The crude product was purified by column chromatography (hexane/ethyl acetate, 70/30) to afford the pure product. The known compounds were characterized by comparison of their physical and spectroscopic data with the already described in the literature.[18,25c,33–37]

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