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Novel CuO Nanoparticle Catalyzed C–N Cross Coupling of Amines with Iodobenzene

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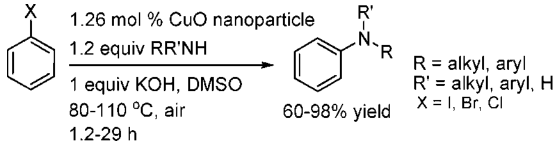
ABSTRACT



CuO nanoparticles catalyze the C–N cross coupling of amines with iodobenzene in excellent yields. The reaction is simple and efficient and operates under air with ligand free conditions. The catalyst is recyclable without loss of activity.

The formation of C−N bonds by cross coupling reactions represents a powerful means for the preparation of numerous compounds in biological, pharmaceutical, and material sciences.[1] The traditional methods employed for C−N bond formation, however, often require stoichiometric amounts of copper reagents, which, on scale-up, leads to the problem of waste disposal.[2] To overcome these drawbacks, considerable attention has been recently focused to develop catalytic systems for this purpose.[3] From an industrial standpoint, these reactions are attractive because the cost and environmental impact (E-factor) of the process can be reduced.[4] In 1983 Migita and co-workers first reported the cross coupling of tributyltin amide with aryl bromide catalyzed by $PdCl_2\{P(o\text{-}C_6H_4Me)_3\}_2$.[5] Palladium complexes bearing sterically hindered phosphine ligands[6] and copper complexes having electron-rich ligands such as diamines,[7] ethylene glycol,[8a] *N*,*N*-diethylsalicylamide,[8b] 1,10-phenanthroline,[9] *N*-oxime,[10] thiophencarboxylate,[11] amino acids,[12] and 1,3-dicarbonyl compounds[13] have been subsequently studied as catalysts for amination of aryl halides. Herein, we report that CuO nanoparticles (Aldrich: particle size 33 nm and surface area 29 m^2/g) catalyze efficiently the C−N cross coupling of amines with iodobenzene in excellent yields. The reactions

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(11) Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.

(12) (a) Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164. (b) Pan, X.; Cai, Q.; Ma, D. *Org. Lett.* **2004**, *6*, 1809. (c) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* **1998**, *120*, 12459.

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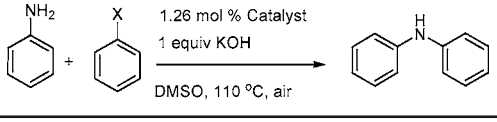
are effective at 110 °C in DMSO in the presence of KOH under air. The catalyst is cheap, air stable, and recyclable without loss of activity.

For high catalytic activity, colloidal metal nanoparticles have been widely used in organic synthesis.[14] The reaction of aniline with iodobenzene was first studied as standard substrate with CuO nanoparticles as catalyst (Table 1). We were pleased to find that the reaction occurred to afford diphenylamine in 95% yield when it was stirred for 2 h at 110 °C in the presence of 1.26 mol % of CuO nanoparticles and 1 equiv of KOH in DMSO under air. Copper(II) salts such as $CuSO_4{\cdot}5H_2O$, $Cu(OAc)_2{\cdot}H_2O$, and CuO were inferior to CuO nanoparticles affording diphenylamine in low yield. Among the solvents studied, DMSO, toluene, dioxane, and DMF, the former provided the best result. Likewise, the reaction with KOH was more effective in comparison to that with K_2CO_3. When iodobenzene was replaced by bromo- and chlorobenzene, the reactions were moderately effective providing diphenylamine in 80% and 60% yield, respectively.

Table 1. Reaction of Aniline with Aryl Halides

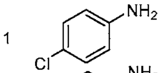
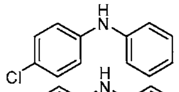
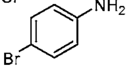
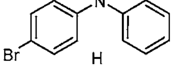
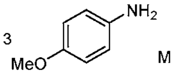
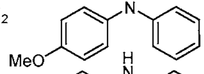
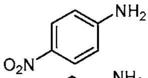
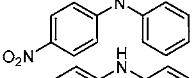
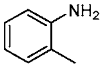
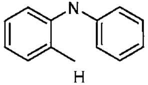
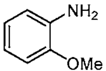
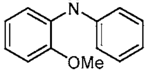
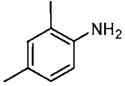
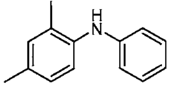


catalyst	X	solvent	base	temp (°C)	time (h)	yield (%)[a,b]
$CuSO_4{\cdot}5H_2O$	I	DMSO	KOH	110	10	46
$Cu(OAc)_2{\cdot}H_2O$		DMSO	KOH	110	10	33
CuO		DMSO	KOH	110	10	35
CuO nanoparticles		toluene	KOH	110	8	30
		DMF	KOH	110	10	10
		dioxane	KOH	110	8	0
		DMSO	KOH	110	2	95
		DMSO	KOH	90	8	15
		DMSO	KOH	rt	8	0
		DMSO	K_2CO_3	rt	8	0
	Br	DMSO	KOH	110	10	80
	Cl	DMSO	KOH	110	18	60

[a] Aniline (1.2 mmol), catalyst (1.26 mol %), iodobenzene (1 mmol), base (1 mmol), and solvent (1 mL) were stirred at appropriate time and temperature. [b] Isolated yield.

To study the scope of the procedure, the reaction of other amines was next studied. Substituted anilines, 4-chloro-, 4-bromo-, 4-methoxy-, and 4-nitroaniline, underwent reaction with iodobenzene in 70−94% yield (Table 2, entries 1−4). Similar reactivity was observed with 2-methyl-, 2-methoxy-, and 2,4-dimethylaniline (Table 2, entries 5−7). Anilines having electron-donating groups showed greater reactivity in comparison to those with electron-withdrawing groups.

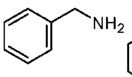
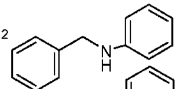
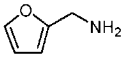
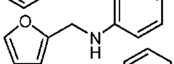
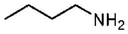
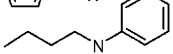
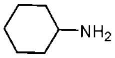
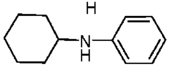
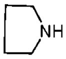
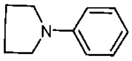
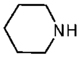
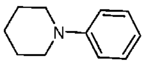
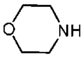
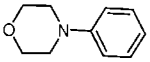
Table 2. Reaction of Aryl Amines with Iodobenzene

entry	substrate	product	time (h)	yield (%)[a,b]
1			4	92
2			3.8	83
3			1.5	94
4			10	70
5			1.6	96
6			1.7	98
7			5	92

[a] Substrate (2.5 mmol), CuO nanoparticles (1.26 mol %), iodobenzene (2 mmol), and KOH (2 mmol) were stirred at 110 °C in DMSO (2 mL) under air. [b] Isolated yield.

These reaction conditions were also suitable for the cross coupling of alkyl amines and *N*-heterocyclic compounds with iodobenzene. Benzylamine, furfurylamine, *n*-butylamine, cyclohexylamine, pyrrolidine, piperidine, and morpholine underwent reaction with 85−93% yield (Table 3). A similar result was obtained with pyrrole, indole, imidazole, 2-methylimidazole, and benzimidazole (Table 4). Imidazole derivatives required longer reaction time with an additional 1.24 mol % of catalyst to complete the reaction.

Table 3. Reaction of Alkyl Amines with Iodobenzene

entry	substrate	product	temp (°C)	time(h)	yield(%)[a,b]
1			110	4	90
2			110	17	85
3			80	13	91
4			110	6.2	93
5			85	8	93
6			110	7	90
7			110	6.5	89

[a] Substrate (1.2 mmol), CuO nanoparticles (1.26 mol %), iodobenzene (1 mmol), and KOH (1 mmol) were stirred in DMSO (1 mL) under air. [b] Isolated yield.

Finally, the reaction of aniline was studied with substituted iodobenzenes (Table 5). 1-Iodo-4-nitrobenzene underwent

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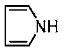
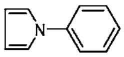
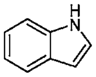
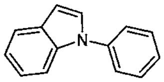
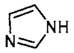
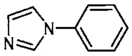
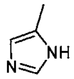
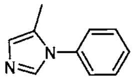
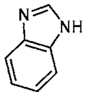
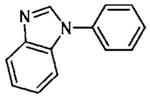
[14] (a) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *J. Am. Chem. Soc.* **2002**, *124*, 11858. (b) Weddle, K. S.; Aikin, J. D.; Finke, R. G. *J. Am. Chem. Soc.* **1998**, *120*, 5653. (c) Johnson, B. F. G. *Coord. Chem. Rev.* **1999**, *190*, 1269. (d) Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 165. (e) Zhao, M.; Crooks, R. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 364. (f) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215.

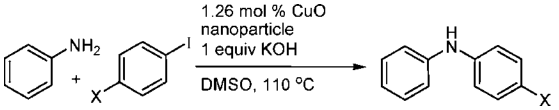
Table 4. Reaction of Heterocyclic Compounds with Iodobenzene

entry	substrate	product	time(h)	yield(%)[a,b]
1			2.5	93
2			3.5	94
3			24	91[c]
4			27	96[c]
5			29	98[c]

[a] Substrate (1.2 mmol), CuO nanoparticles (1.26 mol %), iodobenzene (1 mmol), and KOH (1 mmol) were stirred in DMSO (1 mL) at 110 °C under air. [b] Isolated yield. [c] 2.5 mol % of catalyst was used.

reaction in 1.2 h with 93% yield. Iodobenzene and 4-iodoanisole were relatively less reactive providing the corresponding cross coupled products in 75% and 22% yield, respectively. These studies suggest that the reaction may occur via oxidative addition followed by reductive elimination (Scheme 1). Stabilization of CuO nanoparticles by DMSO and amine may lead to an active cluster **b** which may undergo oxidative addition with aryl halide to give intermediate **c** where the positive charge developed may be shared among the CuO nanoparticles present in the surface of the cluster. The intermediate **c** may transform to **a** by reductive elimination providing the C−N cross coupled product followed by removal of hydrogen halide with base. It is a heterogeneous process and the catalyst is recyclable without loss of activity (Table 6). After completion of the reaction of aniline with iodobenzene, the catalyst was recovered by centrifugation and reused for the fresh reaction of aniline with iodobenzene and no loss of activity was observed.

Table 5. Reaction of Aniline with Substituted Iodobenzenes



entry	X	time (h)	product (yield, %)[a,b]
1	H	1.2	75
2	MeO	1.2	22
3	NO_2	1.2	93

[a] Aniline (1.2 mmol), CuO nanoparticles (1.26 mol %), aryl iodide (1 mmol), and KOH (1 mmol) were stirred in DMSO (1 mL) at 110 °C under air. [b] Isolated yield.

Scheme 1. Proposed Catalytic Cycle

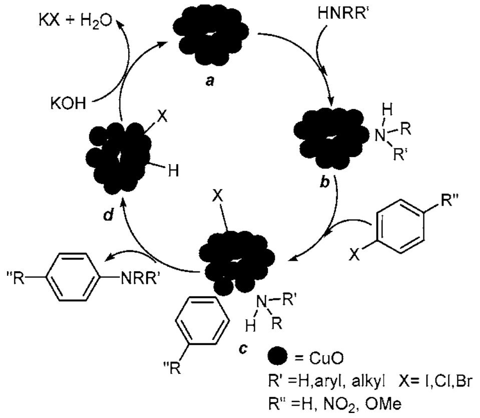
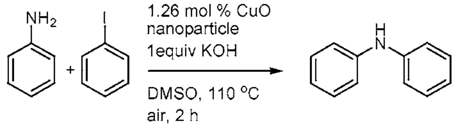


Table 6. Recyclability of the CuO Nanoparticles



run	recoverability (%)	product (%)
1[a]	95	95
2[b]	89	93
3[b]	81	91

[a] Aniline (1.2 mmol), CuO nanoparticles (1.26 mol %), iodobenzene (1 mmol), KOH (1 mmol), and DMSO (1 mL) were stirred at 110 °C for 2 h under air. [b] Recovered used.

In conclusion, recyclable CuO nanoparticles catalyze the C−N cross coupling of amines with iodobenzene in high yields. The reaction is simple and efficient and involves cheap air stable catalyst. Further investigation of this catalytic system is currently underway in our laboratory.

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Supporting Information Available: Experimental procedure, data, and NMR (^{1}H and ^{13}C) spectra of all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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