CuO Nanoparticles Catalyzed C−N, C−O, and C−S Cross-Coupling Reactions: Scope and Mechanism

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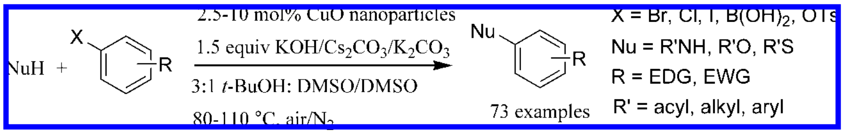

CuO nanoparticles have been studied for C−N, C−O, and C−S bond formations via cross-coupling reactions of nitrogen, oxygen, and sulfur nucleophiles with aryl halides. Amides, amines, imidazoles, phenols, alcohols and thiols undergo reactions with aryl iodides in the presence of a base such as KOH, Cs_2CO_3, and K_2CO_3 at moderate temperature. The procedure is simple, general, ligand-free, and efficient to afford the cross-coupled products in high yield.

Introduction

The formation of C−N, C−O, and C−S bonds is prevalent in numerous compounds that are of biological, pharmaceutical, and material interest (Figure 1).[1] One of the most common synthetic methods for their preparation is the copper-assisted classic Ullmann reaction. However, these reactions often require harsh conditions such as high temperature (>200 °C) and stoichiometric or greater amount of copper reagent, which on scale-up leads to problem of waste disposal.[2] To overcome these limitations, much attention has been recently focused to develop catalytic systems to reduce the environmental impact (E-factor) of the processes.[3,4] Palladium[5−7] and copper[8−11] complexes containing electron-rich ligands have been studied considerably for the cross-coupling of nitrogen, oxygen, and sulfur nucleophiles with aryl halides. Subsequently, few studies have focused on the use of iron-[12] and nickel-based[13] catalytic systems for this purpose. Most of the systems involve a homogeneous process, and the ligand chelated with the metal plays a crucial role in the catalysis.

Nanomaterials containing high surface area and reactive morphologies have been studied as effective catalysts for organic synthesis.[8k,11k,14] Furthermore, the nanomaterial catalyzed reactions provide the advantages of high atom efficiency, simplified isolation of product, and easy recovery and recyclability of the catalysts. In preliminary communication, we reported the catalysis of CuO nanoparticles for the cross-coupling reactions of amines[8k] and thiols[11k] with iodobenzene. The reactions were simple, general, and ligand-free, and the CuO nanoparticles were recyclable. These features led us to further study the scope of

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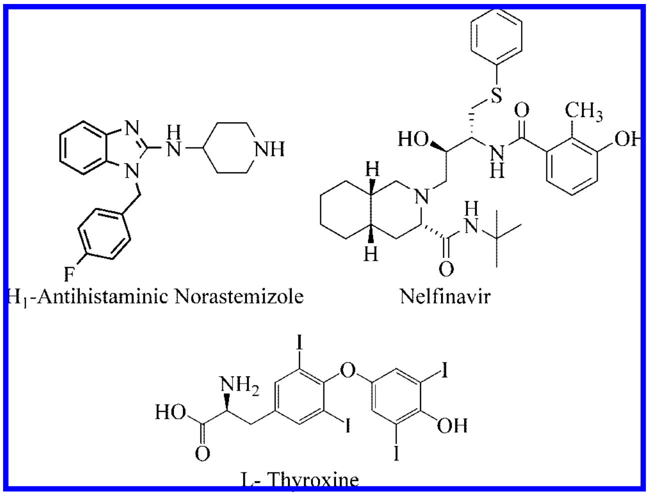


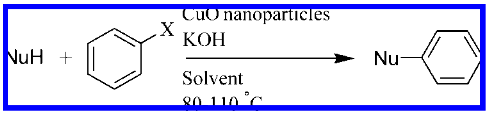
FIGURE 1. Examples for biologically active compounds.

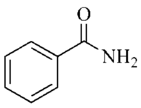
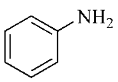
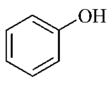
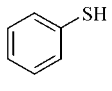
the CuO nanoparticles for the catalysis of the C−N, C−O, and C−S cross-coupling reactions. Here we report the reactions of amides, amines, imidazoles, phenols, alcohols, and thiols with aryl iodides. The reactions of bromobenzene, chlorobenzene, phenyl tosylate, and phenylboronic acid are also studied, but those are found to be inferior to that of aryl iodides, leading to the cross-coupled products in lower yield.

Results and Discussion

The cross-coupling reactions of benzamide, aniline, phenol, and thiophenol with aryl halides and their analogues were studied as model substrates (Table 1). We were pleased to find that the reactions occurred to afford the corresponding cross-coupled products in high yield. The C−N cross-coupling reactions were effective under air, and the C−S and C−O cross-couplings provided the best results in nitrogen atmosphere.[15] Iodobenzene exhibited greater reactivity compared to that of phenylboronic acid and bromobenzene. Under these conditions, chlorobenzene and phenyl tosylate were less reactive, affording the cross-coupled products in <5% yield. The C−N cross-coupling reactions were effective in a 1:3 mixture of DMSO/*t*-BuOH, while DMSO was found to be the solvent of choice for the C−O and C−S cross-coupling reactions. The reactions were free from the formation of homocoupled biaryl compound, and the controlled experiments without CuO nanoparticles showed no reaction.

TABLE 1. Reactions of Benzamide, Aniline, Phenol and Thiophenol with Aryl Halides, Phenyl Tosylate, and Phenylboronic Acid



entry	NuH	X	time (h)	product (yield, %)
1[a]		I	24	74
		Br	24	nr
		Cl	24	nr
		OTs	24	nr
		B(OH)$_2$	24	15
2[a]		I	18	88
		Br	18	nr
		Cl	18	nr
		OTs	18	nr
		B(OH)$_2$	18	31
3[b]		I	15	93
		Br	15	40
		Cl	15	nr
		OTs	15	nr
		B(OH)$_2$	15	13
4[c]		I	10	95
		Br	10	37
		Cl	10	<5
		OTs	10	nr
		B(OH)$_2$	10	16

[a] CuO nanoparticles (5 mol %), amide/aniline (1.2 mmol), aryl halide/phenylboronic acid/phenyl tosylate (1 mmol), and KOH (1.5 mmol) were stirred at 110 °C in a 1:3 mixture of dry DMSO:*t*-BuOH under air. [b] CuO nanoparticles (2.5 mol %), phenol (1 mmol), aryl halide/phenylboronic acid/phenyl tosylate (1.2 mmol), and KOH (1.5 mmol) were stirred at 110 °C in dry DMSO (1 mL) under N_2 atmosphere. [c] CuO nanoparticles (2.5 mol %), thiol (1 mmol), aryl halide/phenylboronic acid/phenyl tosylate (1.2 mmol), and KOH (1.5 mmol) were stirred at 80 °C in dry DMSO (1 mL) under N_2 atmosphere.

Reactions of Amides, Amines and Imidazoles. The C−N cross-coupling reactions of benzamide, *p*-toluenesulfonamide, oxazolidinone, and hexanoamide with aryl iodides were investigated (Table 2). The reactions with iodobenzene occurred to give the cross-coupled products in 45−88% yield, whereas 4-nitro-1-iodobenzene showed greater reactivity compared to that of 4-methoxy-1-iodobenzene. These reactions could be performed in the presence of either K_2CO_3 or Cs_2CO_3 as a base in moderate to good yield. Reactions of substituted aryl iodides with amines and imidazoles were further studied (Table 3).

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TABLE 2. CuO Nanoparticles Catalyzed Amidation of Aryl Iodides

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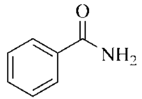
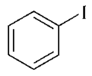
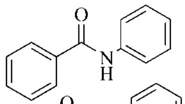
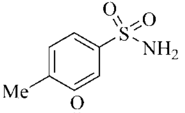
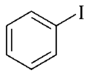
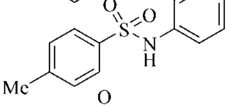
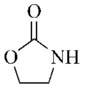
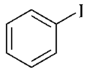
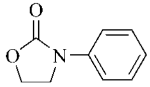
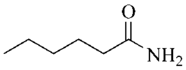
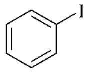
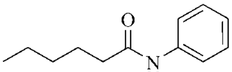
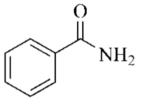
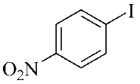
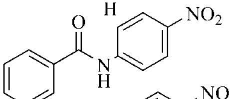
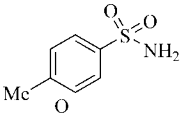
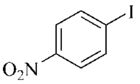
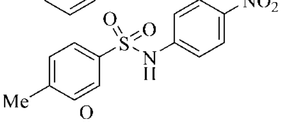
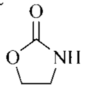
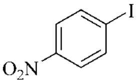
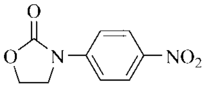
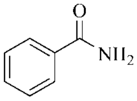
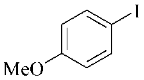
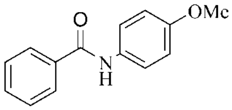
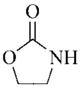
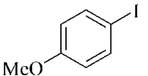
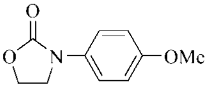
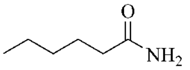
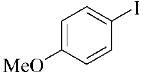
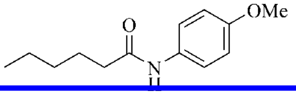
1			24		74
2			24		45
3			24		67
4			18		88
5			15		68[b]
6			21		54
7			6		60[c]
8			30		25[d]
9			36		54[c,d]
10			30		54[d]

[a] CuO nanoparticles (5 mol %), amide (1.2 mmol), aryl iodide (1 mmol), and KOH (1.5 mmol) were stirred at 110 °C in a 1:3 mixture of dry DMSO/*t*-BuOH (1 mL). [b] Cs_2CO_3 (1.5 mmol) used. [c] K_2CO_3 (1.5 mmol) used. [d] CuO nanoparticles (10 mol %) used.

Imidazole, 2-methylimidazole, benzimidazole, and aniline underwent reactions with up to 89% yield. The reactions were clean, and no byproduct was observed.

Reactions of Phenols, Naphthols, and Alcohols. Next, the C–O cross-coupling reactions of the hydroxy compounds with aryl iodides were studied. Phenols having 2-*t*-Bu, 2-Me, 2-OMe, 3-Me, 3-NO_2, 4-*t*-Bu, 4-Me, 4-OMe, 4-NO_2, 2,4-di-*t*-Bu, and 2,4-di-Me groups, 1-naphthol, 2-naphthol, and 1-decanol with iodobenzene underwent reaction to give the corresponding C–O cross-coupled products in high yield (Table 4). These hydroxy compounds with bromobenzene were further investigated by increasing the catalyst to 5 mol % and the temperature to 120 °C to give the C–O cross-coupled products in moderate yield. The substrate having an electron-donating group showed greater reactivity compared to those with electron-withdrawing groups. Under these reaction conditions, polyhydroxy compounds, pentaerythritol, and triethanolamine with iodobenzene provided the corresponding polyaryl ether in excellent yield (eqs 1 and 2). To study the effect of substituent, phenol with aryl iodides having 3-NO_2, 4-NO_2, 4-Me, 2- OMe, 4-OMe, and 2,4-di-Me substituents were further examined (Table 5). As above, the

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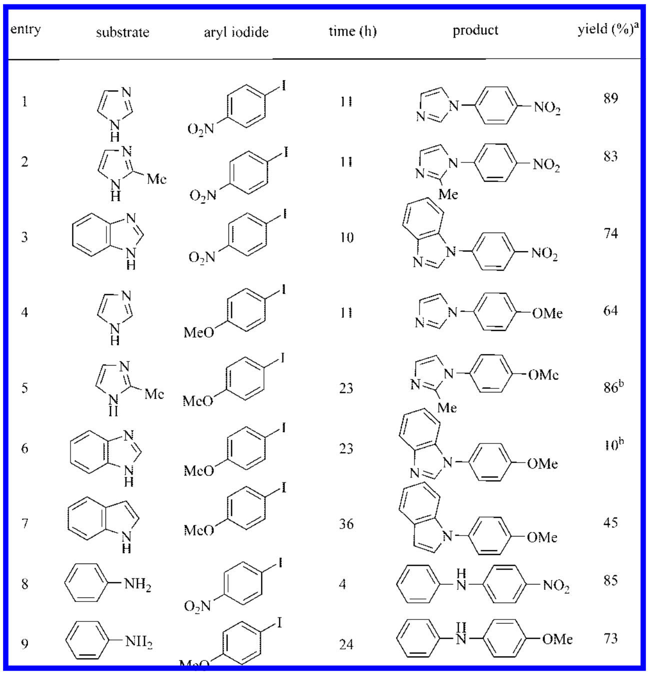
(9) For N-arylation of amides, imidazoles, and N-heterocycles, see: (a) Kiyomori, A.; Marcoux, J.-F.; Buchwald, S. L. *Tetrahedron Lett.* **1999**, *40*, 2657. (b) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727. (c) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578. (d) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Eur. J. Org. Chem.* **2004**, 695. (e) Pan, X.; Cai, Q.; Ma, D. *Org. Lett.* **2004**, *6*, 1809. (f) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421. (g) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120. (h) Hosseinzadeh, R.; Tajbakhsh, M.; Mohadjerani, M.; Mehdinejad, H. *Synlett* **2004**, 1517. (i) Guo, X.; Rao, H.; Fu, H.; Jiang, Y.; Zhao, Y. *Adv. Synth. Catal.* **2006**, *348*, 2197. (j) Deng, W.; Wang, Y.-F.; Zou, Y.; Liu, L.; Guo, Q.-X. *Tetrahedron Lett.* **2004**, *45*, 2311. (k) Cristau, H,-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Chem. Eur. J.* **2004**, *10*, 5607. (l) Moriwaki, K.; Satoh, K.; Takada, M.; Ishino, Y.; Ohno, T. *Tetrahedron Lett.* **2005**, *46*, 7559. (m) Huang, Y.-Z.; Gao, J.; Ma, H.; Miao, H.; Xu, J. *Tetrahedron Lett.* **2008**, *49*, 948. (n) Ma, H.-C.; Jiang, X.-Z. *J. Org. Chem.* **2007**, *72*, 8943. (o) Mao, J.; Guo, J.; Song, H.; Ji, S.-J. *Tetrahedron* **2008**, *64*, 1383. (p) Altman, R. A.; Koval, E. D.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 6190. (q) Verma, A. K.; Singh, J.; Sankar, V. K.; Chaudhary, R.; Chandra, R. *Tetrahedron Lett.* **2007**, *48*, 4207. (r) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 2779.

(10) For C-O couplings, see: (a) Marcoux, J.-F.; Doye, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 10539. (b) Wolter, M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 973. (c) Altman, R. A.; Shafir, A.; Choi, A.; Lichtor, P. A.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 284. (d) Buck, E.; Song, Z. J.; Tschaen, D.; Dormer, P. G.; Volante, R. P.; Reider, P. J. *Org. Lett.* **2002**, *4*, 1623. (e) Lv, X.; Bao, W. *J. Org. Chem.* **2007**, *72*, 3863. (f) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5*, 3799. (g) Cristau, H.-J.; Cellier, P. P.; Hamada, S.; Spindler, J.-F.; Taillefer, M. *Org. Lett.* **2004**, *6*, 913. (h) Ouali, A.; Spindler, J.-F.; Cristau, H.-J.; Taillefer, M. *Adv. Synth. Catal.* **2006**, *348*, 499. (i) Palomo, C.; Oiarbide, M.; Lopez, R.; Gomez-Bengoa, E. *Chem. Commun.* **1998**, 2091. (j) Fagan, P. J.; Hauptman, E.; Shapiro, R.; Casalnuovo, A. *J. Am. Chem. Soc.* **2000**, *122*, 5043. (k) Benyahya, S.; Monnier, F.; Taillefer, M.; Wong Chi Man, M.; Bied, C.; Ouazzani, F. *Adv. Synth. Catal.* **2008**, *350*, 2205.

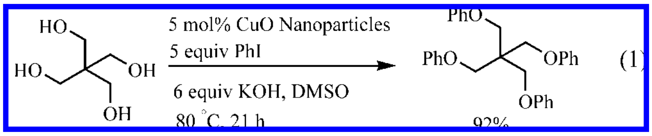
TABLE 3. CuO Nanoparticles Catalyzed Reactions of Imidazoles, Indole, and Aniline with Aryl Iodides



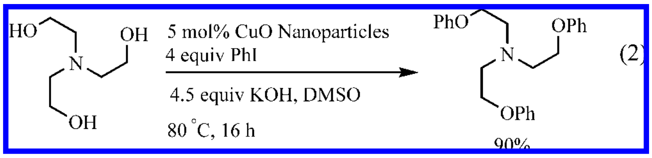
entry	substrate	aryl iodide	time (h)	product	yield (%)[a]
1			11		89
2			11		83
3			10		74
4			11		64
5			23		86[b]
6			23		10[b]
7			36		45
8			4		85
9			24		73

[a] CuO nanoparticles (5 mol %), substrate (1.2 mmol), aryl iodide (1 mmol), and KOH (1.5 mmol) were stirred at 110 °C in a 1:3 mixture of dry DMSO/*t*-BuOH (1 mL). [b] CuO nanoparticles (10 mol %) used.

reactions occurred to afford the C−O cross-coupled products in 70−98% yield.

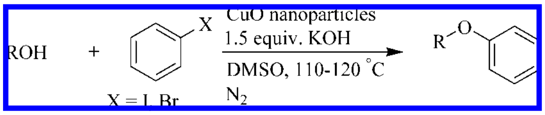


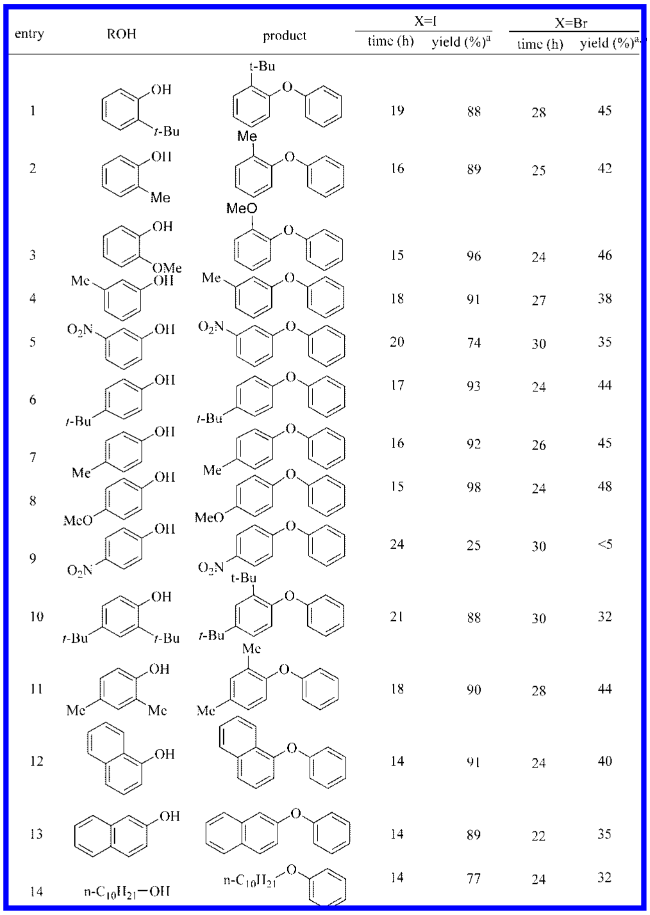
(1)



(2)

TABLE 4. CuO Nanoparticles Catalyzed C−O Cross-Coupling of Substituted Phenols, 1-Naphthol, 2-Naphthol, and Decanol with Iodo- and Bromobenzene





entry	ROH	product	X=I		X=Br	
			time (h)	yield (%)[a]	time (h)	yield (%)[a,b]
1			19	88	28	45
2			16	89	25	42
3			15	96	24	46
4			18	91	27	38
5			20	74	30	35
6			17	93	24	44
7			16	92	26	45
8			15	98	24	48
9			24	25	30	<5
10			21	88	30	32
11			18	90	28	44
12			14	91	24	40
13			14	89	22	35
14	$n\text{-}C_{10}H_{21}{-}OH$		14	77	24	32

[a] CuO nanoparticles (2.5 mol %), ROH (1 mmol), iodobenzene (1.2 mmol), and KOH (1.5 mmol) were stirred at 110 °C in dry DMSO (1 mL) under N_2 atmosphere. [b] CuO nanoparticles (5 mol %), bromobenzene (1.2 mmol), and temperature of 120 °C were used.

Reactions of Thiols. Finally, the C−S cross-coupling reactions of thiols with aryl iodides were studied (Table 6). Thiophenol and 4-methylthiophenol were investigated as representative examples with aryl iodides having 3-NO_2, 4-NO_2, 4-Br, 4-Me, 4-OMe, and 2,4-di-Me substituents. The reactions occurred efficiently to afford the C−S cross-coupled products with up to 96% yield. Under these conditions, thiophenol with 1-naphthyl iodide showed moderate reactivity, leading to the cross-coupled product in 38% yield.

Mechanism. The enhanced reactivity of the aryl iodide having an electron-withdrawing group compared to that with an electron-donating group suggests that the reactions occur via oxidative addition followed by a reductive elimination process. The reactions are heterogeneous, and no leaching of the metal species is involved.[4i,16] To reveal that, the CuO nanoparticles were stirred at 110 °C for 24 h in DMSO in the presence as

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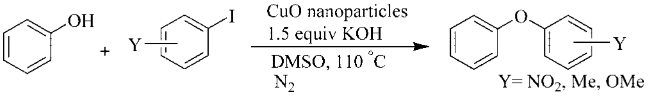
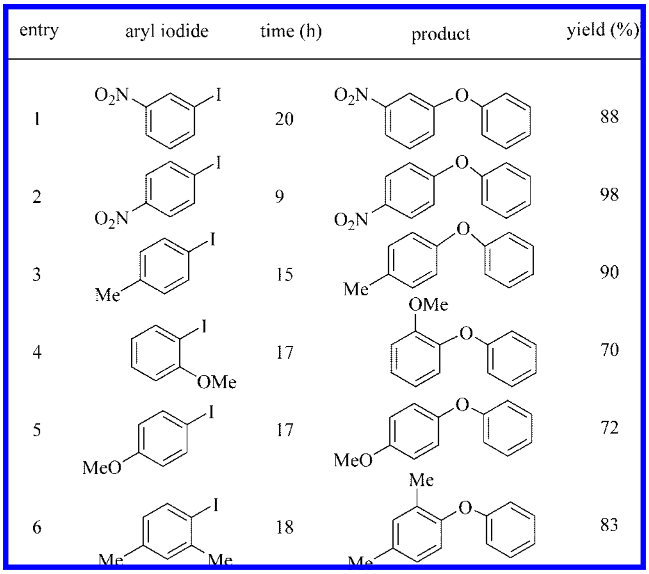
(11) For C-S couplings, see: (a) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803. (b) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517. (c) Wu, Y.-J.; He, H. *Synlett* **2003**, 1789. (d) Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 5005. (e) Deng, W.; Zou, Y.; Wang, Y.-F.; Liu, L.; Guo, Q.-X. *Synlett* **2004**, 1254. (f) Palomo, C.; Oiarbide, M.; Lopez, R.; Gomez-Bengoa, E. *Tetrahedron Lett.* **2000**, *41*, 1283. (g) Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2002**, *4*, 4309. (h) Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019. (i) Zhu, D.; Xu, L.; Wu, F.; Wan, B. *Tetrahedron Lett.* **2006**, *47*, 5781. (j) Sperotto, E.; van Klink, G. P. M.; de Vries, J. G.; van Koten, G. *J. Org. Chem.* **2008**, *73*, 5625. (k) Rout, L.; Sen, T. K.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 5583. (l) Rout, L.; Saha, P.; Jammi, S.; Punniyamurthy, T. *Eur. J. Org. Chem.* **2008**, 640.

(12) (a) Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 8862. (b) Correa, A.; Elmore, S.; Bolm, C. *Chem. Eur. J.* **2008**, *14*, 3527. (c) Correa, A.; Carril, M.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2880. (d) Bistri, O.; Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 586. (e) Bonnamour, J.; Bolm, C. *Org. Lett.* **2008**, *10*, 2665.

(13) For C-N couplings, see: (a) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054. (b) Brenner, E.; Fort, Y. *Tetrahedron Lett.* **1998**, *39*, 5359. (c) Lipshutz, B. H.; Ueda, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 4492. (d) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029. For C-S coupling see: (e) Cristau, H. J.; Chabaud, B.; Chene, A.; Christol, H. *Synthesis* **1981**, 892. (f) Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 6895. (g) Takagi, K. *Chem. Lett.* **1987**, 2221. (h) Jammi, S.; Barua, P.; Rout, L.; Saha, P.; Punniyamurthy, T. *Tetrahedron Lett.* **2008**, *49*, 1484.

TABLE 5. CuO Nanoparticles Catalyzed C−O Cross-Coupling of Phenol with Substituted Aryl Iodides

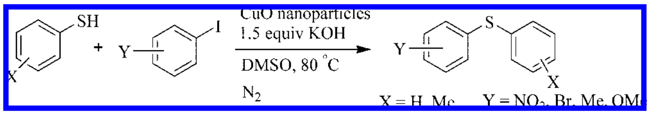


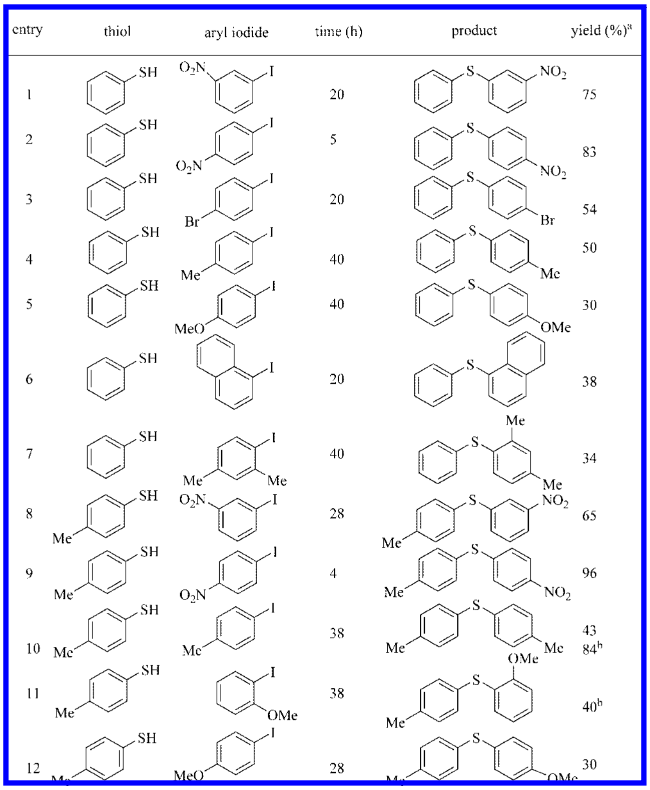


entry	aryl iodide	time (h)	product	yield (%)
1		20		88
2		9		98
3		15		90
4		17		70
5		17		72
6		18		83

[a] CuO nanoparticles (2.5 mol %), phenol (1 mmol), aryl iodide (1.2 mmol), and KOH (1.5 mmol) were stirred at 110 °C in dry DMSO (1 mL) under N_2 atmosphere.

TABLE 6. CuO Nanoparticles Catalyzed C−S Cross-Coupling of Thiols with Aryl Iodides





entry	thiol	aryl iodide	time (h)	product	yield (%)[a]
1			20		75
2			5		83
3			20		54
4			40		50
5			40		30
6			20		38
7			40		34
8			28		65
9			4		96
10			38		43 84[b]
11			38		40[b]
12			28		30

[a] CuO nanoparticles (2.5 mol %), thiol (1 mmol), aryl iodide (1.2 mmol), and KOH (1.5 mmol) were stirred at 80 °C in dry DMSO (1 mL) under N_2 atmosphere. [b] Catalyst (5 mol %) used.

well as in the absence of KOH. The catalyst was then separated by centrifugation, and the solutions were independently studied at 110 °C for the C−O cross-coupling reaction of phenol with iodobenzene in the presence of KOH under nitrogen atmosphere. Both experiments showed no reaction, and the starting materials were recovered intact. In addition, the TEM analysis of the CuO nanoparticles, before and after the reaction, showed identical particle shape and size (Figure 2). Likewise, the powder X-ray diffraction analysis exhibited identical peaks for both the fresh and recovered CuO nanoparticles (Figure 3).[17] These experimental results clearly suggest that the reaction involves a heterogeneous process and the catalysis may occur on the surface of the CuO nanoparticles. Thus, the DMSO-stabilized CuO nanoparticles ***a*** may undergo reaction with aryl halide to give intermediate ***b*** where the excess positive charge generated could be shared among the CuO nanoparticles present on the surface of the cluster (Scheme 1). The latter ***b*** may then undergo reaction with nucleophile to give intermediate ***c*** that can complete the catalytic cycle by reductive elimination of the cross-coupled product.

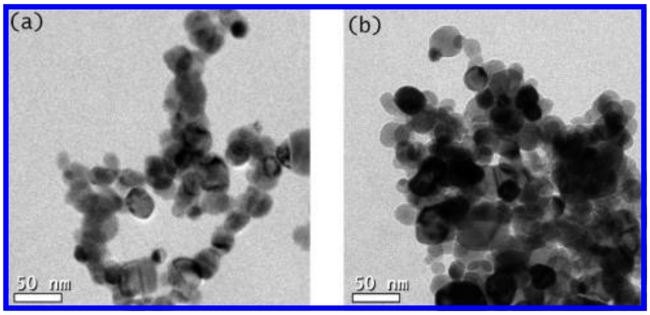


FIGURE 2. TEM images of (a) fresh CuO nanoparticles and (b) CuO nanoparticles after the third catalytic cycle.

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(14) (a) Bönnemann, H.; Richards, R. M. *Eur. J. Inorg. Chem.* **2001**, 2455. (b) Pachón, L. D.; Thathagar, M. B.; Hartl, F.; Rothenberg, G. *Phys. Chem. Chem. Phys.* **2006**, *8*, 151. (c) Su, F.-Z.; Liu, Y.-M.; Wang, L.-C.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Angew. Chem., Int. Ed.* **2008**, *47*, 334. (d) Uozumi, Y.; Nakao, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 194. (e) Hou, Z.; Theyssen, N.; Brinkmann, A.; Leitner, W. *Angew. Chem., Int. Ed.* **2005**, *44*, 1346. (f) Karimi, B.; Abedi, S.; Clark, J. H.; Budarin, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 4776. (g) Mori, K.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 10657. (h) Cassol, C. C.; Umpierre, A. P.; Machado, G.; Wolke, S. I.; Dupont, J. *J. Am. Chem. Soc.* **2005**, *127*, 3298. (i) Rocaboy, C.; Gladysz, J. A. *Org. Lett.* **2002**, *4*, 1993. (j) Proch, S.; Mei, Y.; Villanueva, J. M. R.; Lu, Y.; Karpov, A.; Ballauff, M.; Kempe, R. *Adv. Synth. Catal.* **2008**, *350*, 493. (k) Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385. (l) Li, J.-H.; Tang, B.-X.; Tao, L.-M.; Xie, Y.-X.; Liang, Y.; Zhang, M.-B. *J. Org. Chem.* **2006**, *71*, 7488. (m) Zhu, Y.; Peng, S. C.; Emi, A.; Su, Z.; Monalisa;Kemp, R. A. *Adv. Synth. Catal* **2007**, *349*, 1917. (n) Son, S. U.; Jang, Y.; Park, J.; Na, H. B.; Park, H. M.; Yun, H. J.; Lee, J.; Hyeon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5026. (o) Thathagar, M. B.; Kooyman, P. J.; Boerleider, R.; Jansen, E.; Elsevier, C. J.; Rothenberg, G. *Adv. Synth. Catal.* **2005**, *347*, 1965. (p) Tang, B.-X.; Wang, F.; Li, J.-H.; Xie, Y.-X.; Zhang, M.-B. *J. Org. Chem.* **2007**, *72*, 6294. (q) Chung, M.-K.; Schlaf, M. *J. Am. Chem. Soc.* **2004**, *126*, 7386. (r) Cho, J. K.; Najman, R.; Dean, T. W.; Ichihara, O.; Muller, C.; Bradley, M. *J. Am. Chem. Soc.* **2006**, *128*, 6276. (s) Tamura, M.; Fujihara, H. *J. Am. Chem. Soc.* **2003**, *125*, 15742.

(15) The C-S and C-O cross-coupling reactions under air provided disulfide and quinone, respectively, as byproducts.

(16) (a) Pachón, L. D.; Rothenberg, G. *Appl. Organomet. Chem.* **2008**, *22*, 288. (b) Gaikwad, A. V.; Holuigue, A.; Thathagar, M. B.; ten Elshof, J. E.; Rothenberg, G. *Chem. Eur. J.* **2007**, *13*, 6908.

(17) Wang, W.; Zhan, Y.; Wang, G. *Chem. Commun.* **2001**, 727.

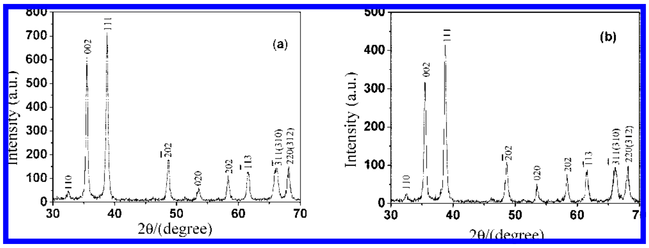


FIGURE 3. Powder X-ray diffraction patterns of (a) fresh CuO nanoparticles and (b) CuO nanoparticles after the third catalytic cycle.

SCHEME 1. Proposed Mechanism for CuO Nanoparticles Catalyzed Cross-Coupling Reactions

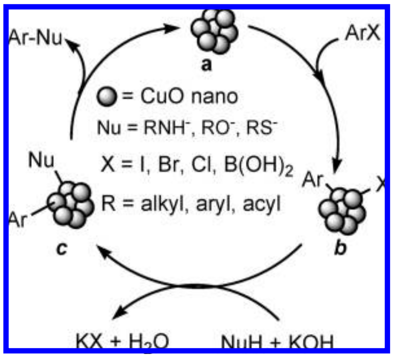
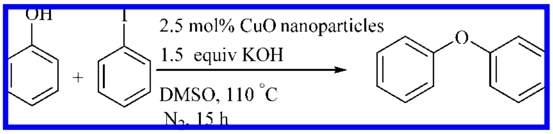


TABLE 7. Recyclability of the CuO Nanoparticles



run	catalyst recoverability (%)	product (conversion, %)[c]
1[a]	98	97
2[b]	98	97
3[b]	97	95

[a] CuO nanoparticles (2.5 mol %), phenol (1 mmol), iodobenzene (1.2 mmol), and KOH (1.5 mmol) were stirred for 15 h at 110 °C in dry DMSO (1 mL) under N_2 atmosphere. [b] Recovered catalyst used. [c] Determined from ^{1}H NMR.

Recyclability Experiments. The CuO nanoparticles are recyclable without loss of activity (Table 7). After completion of the C−O cross-coupling of phenol with iodobenzene, the reaction mixture was treated with water and EtOAc. The CuO nanoparticles were recovered from the aqueous solution by centrifugation. It was reused for the fresh C−O cross-coupling of phenol with iodobenzene for three runs, and no loss of activity was observed providing the cross-coupled product in high yield.

Conclusions

A simple, general, and efficient procedure is described for the cross-coupling of nitrogen, oxygen, and sulfur nucleophiles with aryl iodides using CuO nanoparticles under ligand-free conditions. The catalyst is recyclable, and a variety of substrates undergo reaction in high yield.

Experimental Section

General Procedure for C−N Cross-Coupling Reactions. Nitrogen nucleophile (1.2 mmol), aryl iodide (1 mmol), CuO nanoparticles (5 mol %), and KOH (1.5 mmol) were stirred at 110 °C in a 1:3 mixture of dry DMSO/*t*-BuOH (1 mL). The progress of the reaction was monitored by TLC using EtOAc and hexane as eluent. After completion, the reaction mixture was treated with EtOAc (10 mL) and water (3 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic solution was washed with brine (3 × 5 mL) and water (1 × 5 mL). Drying (Na_2SO_4) and evaporation of the solvent provided a residue, which was purified on short pad of silica gel using EtOAc and hexane as eluent.

***N*-Phenylbenzamide.** (Table 2, entry 1).[12b] Colorless solid; yield 74%; mp 163 °C (lit.[18] 162−163 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, $J = 7.2$ Hz, 2H), 7.78 (s, 1H), 7.61 (d, $J = 8.0$ Hz, 2H), 7.52 (d, $J = 7.6$ Hz, 1H), 7.47 (t, $J = 8.0$ Hz, 2H), 7.36 (t, $J = 8.0$ Hz, 2H), 7.14 (t, $J = 7.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 138.1, 135.2, 132.0, 129.3, 129.0, 127.2, 124.8, 120.5; FT-IR (KBr) 3310, 2995, 1659, 1604, 1533, 1420, 1315, 1233, 1185, 1090, 1023 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.23; H, 5.65; N, 7.06.

General Procedure for C−O and C−S Cross-Coupling Reactions. Oxygen or sulfur nucleophile (1 mmol), aryl iodide (1.2 mmol), CuO nanoparticles (2.5 mol %), and KOH (1.5 mmol) were stirred at 80−110 °C in dry DMSO (1 mL) under N_2 atmosphere. Monitoring of the reaction, workup procedure, and purification of the C−O and C−S cross-coupled products were performed as described for the C−N cross-coupling reactions.

1,1′-Oxy-bis-benzene. (Table 1, entry 3).[8c] Colorless liquid; yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 4H), 7.12−7.08 (m, 2H), 7.00 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 129.9, 123.4, 119.1; FT-IR (neat) 3038, 2910, 2864, 1583, 1484, 1456, 1254, 1216, 1161, 1138, 1017 cm^{-1}. Anal. Calcd for $C_{12}H_{10}O$: C, 84.68; H, 5.92. Found: C, 84.66; H, 5.93.

1-[(4-Methylphenyl)thio]-3-nitrobenzene. (Table 6, entry 8). Yellow liquid; yield 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.95 (m, 2H), 7.43−7.38 (m, 3H), 7.29−7.22 (m, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 139.4, 134.3, 133.5, 132.6, 130.9, 129.7, 122.9, 122.4, 120.6, 21.5; FT-IR (neat) 3087, 2924, 2857, 1599, 1528, 1489, 1459, 1347, 1270, 1124, 1015 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_2S$: C, 63.65; H, 4.52; N, 5.71; S, 13.07. Found: C, 63.73; H, 4.55; N, 5.76; S, 13.10.

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

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