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Copper Oxide Nanoparticle-Catalyzed Coupling of Diaryl Diselenide with Aryl Halides under Ligand-Free Conditions

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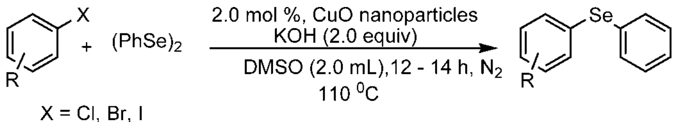
ABSTRACT



A new, efficient and ligand-free cross-coupling reaction of aryl halides and diaryl diselenides using a catalytic amount of nanocrystalline CuO as a recyclable catalyst with KOH as the base in DMSO at 110 °C is reported. This protocol has been utilized for the synthesis of a variety of aryl selenides in excellent yields from the readily available aryl halides and diaryl diselenides.

Diaryl selenides play an importent role in organic chemistry, acting as versatile reagents in organic synthesis[1] and catalysis.[2] The biological and medicinal properties of selenium and organo selenium compounds are also increasingly appreciated, mainly due to their antioxidant, antitumor, antimicrobial, anticancer, and antiviral properties.[3]

Traditional methods for the formation of a C−Se bond require photochemical or harsh reaction conditions such as the use of polar and toxic solvents like HMPA and high reaction temperatures,[4] reaction of aryl halide and benzeneselenate anion in liquid ammonia under UV light, reaction of sodium selenide with arenediazonium salts, etc.[5] In general, to avoid handling unstable reagents such as selenols because of their instability against air and/or moisture and foul-smelling nature, diphenyl diselenides are used as starting materials. Cristau and co-workers were the first to show that aryl selenides can be obtained by cross-coupling of aryl halides and sodium benzeneselenolate using Ni(II)-based catalysts.[6] Several Copper, and palladium-based catalysts in combination with various ligands are generally employed for this coupling reaction.[7] Recently Engman reported the synthesis of diaryl selenides in the presence of a copper(I)-

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(1) (a) Krief, A.; Hevesi, L. *Organoselenium Chemistry I*; Springer: Berlin, 1988. (b) Comasseto, J. V.; Ling, L. W.; Petragnani, N.; Stefani, H. A. *Synthesis* **1997**, 373. (c) *Organoselenium Chemistry: A Practical Approach*; Back, T. G., Ed.; Oxford University Press: Oxford, UK, 1999. (d) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 835.

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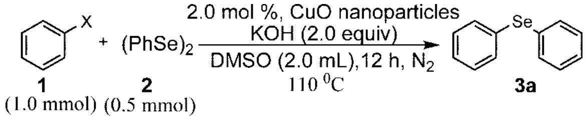
catalyst, 2,2′-bipyridyl and magnesium under microwave heating.[8] Most of these metal-catalyzed reactions involve specially designed ligands or well-defined catalysts/reagents, which may increase the cost and limit the scope of applications. It is desirable to find novel catalytic procedures especially in the absence of any ligand for an efficient access to such highly useful organic products.

In general, nanoscale heterogeneous catalysts offer higher surface area and low-coordinated sites, which are responsible for the higher catalytic activity.[9] However, till now, the investigation of nanoparticles as catalysts has been rare. In this regard, we envisaged the application of readily available and inexpensive copper oxide nano particles as a catalyst. Recently, it has been employed as a heterogeneous catalyst for various organic transformations.[10] This inspired us to focus on the aspect of copper oxide nano particle catalysis for the formation of aryl-selenium bonds. The copper based catalysts are also attractive both from economic and industrial points of view as compared to palladium.

Herein, we wish to report the catalysis by copper oxide nanoparticles for the formation of aryl-selenium bonds in a very efficient manner. In a preliminary reaction, iodobenzene **1** was treated with diphenyl diselenide **2** in the presence of 2 mol % of CuO nano particles and KOH (2.0 equiv) in DMSO (2.0 mL) for 12 h, the corresponding diaryl selenide **3a** was obtained in 94% yield (Scheme 1). To the best of our knowledge, this is the first CuO nano particles-catalyzed coupling of aryl halides with diphenyl diselenide to form diaryl selenide.

Scheme 1. CuO Nanoparticles Catalyzed C−Se Coupling Reaction



To optimize the reaction conditions, first we tried the dependence of the Se-arylation of iodobenzene **1** with diphenyl diselenide **2** on the nature of the base. KOH and Cs_2CO_3 provided the arylated compound **3a** in moderate to excellent yields (Table 1, entries 2, and 4) where as other bases such as K_3P0_4, KO^{t}Bu, and NaOMe gave trace amounts of diaryl selenide (Table 1 entries 1, 3, 7−9, and 12). Solvents other than DMSO, such as DMF, and toluene were less effective. Of the bases tested, KOH gave the best results with DMSO as the solvent.[11]

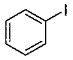
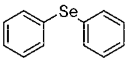
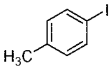
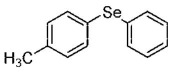
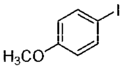
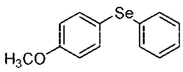
Table 1. Nano CuO Oxide-Catalyzed Cross-Coupling of Diphenyl Diselenide with Iodobenzene[a]

entry	base	solvent	temp (°C)	yield[b] (%)
1	K_3PO_4	DMSO	110	26
2	Cs_2CO_3	DMSO	110	71
3	KO^{t}Bu	DMSO	110	trace
4	KOH	DMSO	110	94
5	KOH	DMSO	80	76
6	KOH	DMSO	rt	25
7	KOH	PhMe	110	trace
8	KOH	DMF	110	trace
9	NaOMe	DMSO	110	trace
10	Cs_2CO_3	PhMe	110	0
11	KO^{t}Bu	PhMe	110	0
12	Cs_2CO3	DMF	110	trace
13	KOH	Water	110	0
14	none	DMSO	110	0

[a] Reaction conditions: Iodobenzene (1.0 mmol), diphenyl diselenide (0.5 mmol), CuO (2.0 mol %), base (2.0 equiv), solvent (2.0 mL), 110 °C, 12 h, under a nitrogen atmosphere. [b] Isolated yield.

Next, we investigated the effect of different combinations of various metal nano oxides on the diaryl selenide formation with KOH in DMSO at 110 °C using different substituted aryl iodides (Table 2). However, their catalytic activities were much lower than CuO nano particles. The yields were highly dependent upon the reaction temparatures and the base.

Table 2. Evaluation of Different Catalyst for the Formation of Diphenyl Selenide[a]

entry	aryl halides	diaryl selenide	catalyst	time (h)	yield[b](%)
1			nano-Fe_2O_3	24	69
2			nano-Bi_2O_3	24	71
3			nano-In_2O_3	24	70
4			nano-NiO	24	72
5			nano-ZnO	24	65
6			nano-CuO	12	94
7			nano-Fe_2O_3	24	64
8			nano-Bi_2O_3	24	67
9			nano-In_2O_3	24	63
10			nano-NiO	24	70
11			nano-ZnO	24	64
12			nano-CuO	12	89
13			nano-Fe_2O_3	24	0
14			nano-Bi_2O_3	24	25
15			nano-In_2O_3	24	0
16			nano-NiO	24	60
17			nano-ZnO	24	30
18			nano-CuO	14	82

[a] Reaction conditions: Iodobenzene (1.0 mmol), diphenyl diselenide (0.5 mmol), catalyst (2.0 mol %), KOH (2.0 equiv), DMSO (2.0 mL), 110 °C, under a nitrogen atmosphere. [b] Isolated yield.

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(8) Kumar, S.; Engman, L. *J. Org. Chem.* **2006**, *71*, 5400.

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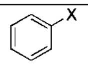
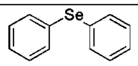
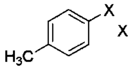
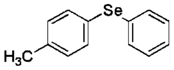
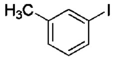
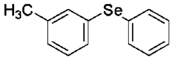
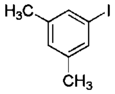
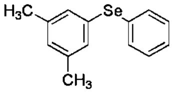
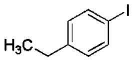
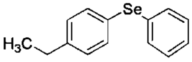
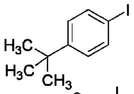
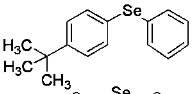
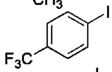
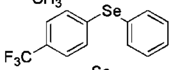
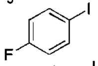
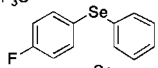
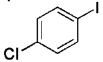
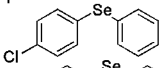
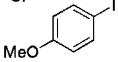
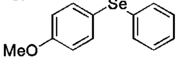
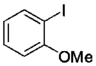
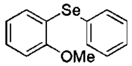
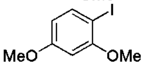
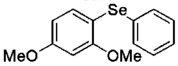
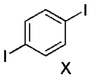
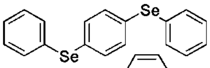
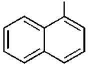
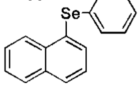
To explore the scope of this novel transformation, a coupling reaction of diphenyl diselenide with various substituted aryl halides was evaluated (Table 3). In general, all reactions were very clean, and the diaryl selenides were obtained in high yields under the optimized conditions. This protocol efficiently coupled diphenyl diselenide with electron-rich and electron-neutral and electron-deficient aryl iodides (Table 3, entries 1−18). Sterically demanding ortho substituents did not hamper the arylation reaction and the corresponding diaryl selenides were obtained in good yield (Table 3, entries 14, 15). Furthermore, iodobenzene was a more reactive substrate than chlorobenzene or bromobenzene (Table 3, entries 1, 2, 3). Consequently, cross-coupling reactions with chloro substituted aryl iodides proceeded exclusively at the iodo group. Unfortunately, all attempts to couple aliphatic dimethyl diselenide with aryl halides were not successful. To check for recyclability, the catalyst was centrifuged from the reaction mixture and dried in vacuo. It could then be reused for further catalytic reactions. The yields of diaryl selenides after two to three recycles were almost same without loss of catalytic activity (Table 4).

Table 3. CuO-Nanoparticle-Catalyzed Cross-Coupling of Iodobenzene with Diphenyl Diselenide[a]

entry	aryl halide		product		time (h)	yield[b](%)
1 2 3		X = I Br Cl		3a	12 12 12	94 65 10
4 5		X = I Br		3b	12 12	89 59
6				3c	12	88
7				3d	12	86
8				3e	12	86
9				3f	12	85
10				3g	12	89
11				3h	12	89
12				3i	12	88
13				3j	14	84
14				3k	14	86
15				3l	14	83
16				3m	12	82
17 18		X = I Br		3n	12 12	87 54

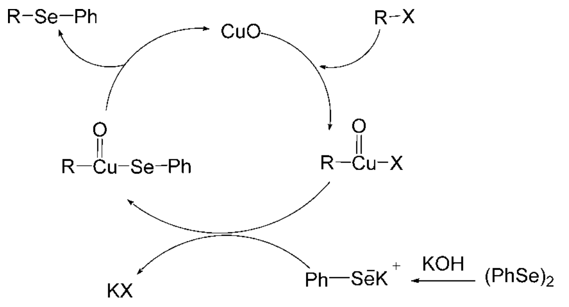
[a] Reaction condition: Diphenyl diselenide (0.5 mmol), iodobenzene (1.0 mmol), CuO nanoparticles (2.0 mol %), KOH (2.0 equiv) and DMSO (2.0 mL) were stirred under a nitrogen atmosphere, 110 °C. [b] Yield of the isolated product.

Table 4. Recycling of CuO Nanoparticles

recycles	yield (%)	catalyst recovery (%)
1	94	93
2	91	91
3	90	89

A plausible mechanism for the CuO nano particle catalyzed C−Se cross-coupling of arylhalides and diphenyl diselenide is illustrated in Scheme 2.

Scheme 2. Plausible Reaction Pathway for the CuO-Nanoparticle-Catalyzed C−Se Cross-Coupling of aryl halides with Diphenyl Diselenide in the Presence of KOH



In conclusion, we have developed a nanocrystalline CuO-catalyzed coupling of aryl halides with diphenyl diselenide to form diaryl selenide under ligand-free conditions in excellent yields. This new coupling reaction underlines the potential of using nanocrystalline CuO as a very user-friendly, inexpensive, and efficient catalyst for the coupling of carbon-heteroatom. The catalyst can be easily recovered and reused. We are in the process of expanding the substrate scope of the reaction.

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Supporting Information Available: Detailed experimental procedures and copies of analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) In this reaction, DMSO may also be acting as a reducing agent required in the reaction by producing dimsyl ion in the presence of KOH as suggested by one of the reviewers. Hunter, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5765.