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CuO nanoparticles: an efficient and recyclable catalyst for cross-coupling reactions of organic diselenides with aryl boronic acids

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ABSTRACT

We present here an efficient and ligand-free cross-coupling reaction of organic diselenides with aryl boronic acids using a catalytic amount of CuO nanoparticles in DMSO at 100 °C under air atmosphere. This is a general cross-coupling reaction and was performed with organic diselenides and aryl boronic acids bearing electron-withdrawing and electron-donating groups affording the corresponding selenides in good to excellent yields. The CuO nanoparticles can be easily recovered and utilized for further catalytic reactions.

Organoselenium compounds have become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions,[1] are used in asymmetric catalysis[2] and as drug candidates.[3] Many classes of organoselenium compounds have been prepared and studied to date, among them aryl- and vinyl selenides are certainly the most applied compounds in organic synthesis.[4]

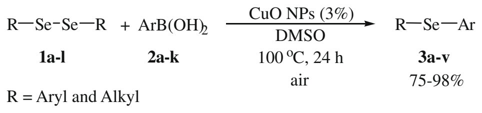
A large number of methodologies have been reported to prepare these compounds; however, the reaction often needs long time, harsh reaction conditions, and sometimes generates the products in moderate yields.[5] In recent years, a copper-catalyzed reaction of diaryl diselenides with aryl halides or aryl boronic acids has become a versatile tool for the synthesis of symmetrical or unsymmetrical diaryl selenides.[6] Generally these copper-catalyzed reactions involve particularly specific ligands, which may increase the cost and limit the scope of applications. Furthermore, Rao and co-workers described an efficient and ligand-free cross-coupling reaction of aryl halides and diaryl diselenides using a catalytic amount of CuO nanoparticles (CuO NPs) as a recyclable catalyst.[7]

The application of metal nanoparticles for organic reactions has attracted immense attention in recent years.[8] Since the turn of the millennium, interest in metal nanoparticles catalysis has considerably increased because this class of catalysts appears as one of the most promising solutions toward efficient reactions under mild and environmentally benign conditions in the context of *Green Chemistry*.[9]

Metal nanoparticles catalysis offers high catalytic efficiency due to their larger surface area and low-coordinated sites, which maximizes the reaction rates and minimizes consumption of the catalyst.[10] Additionally, the copper nanoparticle-catalyzed reactions provide the advantages of high atom efficiency, simplified isolation of product, and easy recovery and recyclability of the catalysts.[7,11]

To the best of our knowledge, no copper nanoparticle-catalyzed coupling reactions of organic diselenides with arylboronic acids have been described to form organic selenides. Our continuing interest in the C–Y (Y = Se, Te) bond formation under copper catalysis[12] prompted us to explore in detail a general procedure to obtain organic selenides by copper oxide nanoparticles (CuO NPs)-catalyzed coupling reactions of diselenides with aryl boronic acids (Scheme 1).

Our initial studies have focused on the development of an optimum set of reaction conditions. In this approach, diphenyl diselenide **1a** and 4-methoxyphenyl boronic acid **2a** were used as model substrates. Thus, a mixture of diselenide **1a**, boronic acid **2a,** and CuO NPs as a catalyst was reacted under air atmosphere for 24 h, applying different solvents, amount of substrates, or catalyst, and the results are summarized in Table 1.



$$\underset{\mathbf{1a\text{-}l}}{R{-}Se{-}Se{-}R} + \underset{\mathbf{2a\text{-}k}}{ArB(OH)_2} \xrightarrow[\substack{100\,^{\circ}C,\ 24\ h \\ air}]{\text{CuO NPs (3\%)} \\ \text{DMSO}} \underset{\substack{\mathbf{3a\text{-}v} \\ 75\text{-}98\%}}{R{-}Se{-}Ar}$$

Scheme 1.

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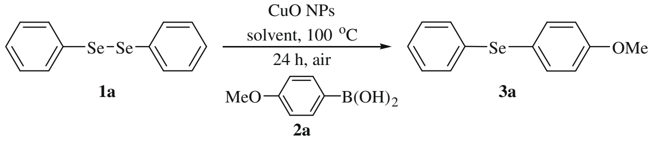
Table 1
Optimization of reaction conditions



Entry	CuO NPs[a] (mol %)	Boronic acid **2a** (equiv)	Solvent	Yield **3a**[b] (%)
1	1	1.0	DMSO	76
2	5	1.0	DMSO	80
3	5	1.2	DMSO	85
4	5	1.5	DMSO	98
5	3	1.5	DMSO	97
6	1	1.5	DMSO	84
7	3	1.5	DMSO/H_2O	78
8	3	1.5	1,4-Dioxane	65
9	3	1.5	DMF	86
10[c]	3	1.5	CH_3CN	—
11	3	1.5	Toluene	—

[a] CuO nanopowder was purchased from Aldrich®, with an average of 30–40 nm as shown in technical information.
[b] Yields are given for isolated products.
[c] Reaction was performed at 80 °C.

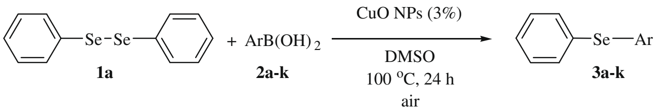
We observed that this cross-coupling reaction required the use of an excess of organoboron reagent (1.5 equiv) (Table 1; entry 4). In this way, the use of 1.0 or 1.2 equiv of boronic acid afforded lower yields than the use of 1.5 equiv (Table 1; entries 1–3 vs 4). The use of catalyst in an amount of 5 mol % yielded 98% of compound **3a** and fortunately, when the catalyst loading was reduced from 5 mol % to 3 mol %, excellent yield of product **3a** was obtained (Table 1; entry 5). Finally, we observed that the influence of the solvent was important for the coupling success. When 1,4 dioxane, DMF, and a mixture of DMSO/H_2O were used, the desired product was obtained in moderate to good yields (Table 1; entries 7–9), while no cross-coupling was observed with other solvents such as toluene and CH_3CN (Table 1; entries 10 and 11).

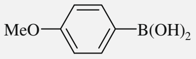
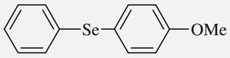
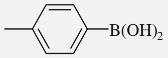
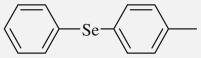
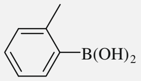
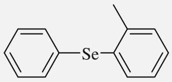
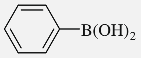
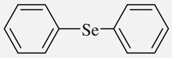
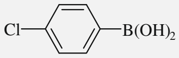
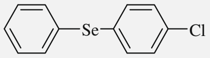
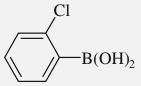
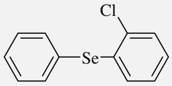
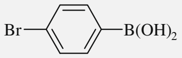
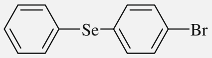
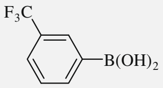
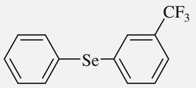
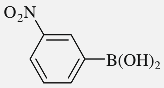
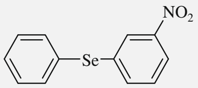
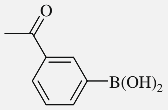
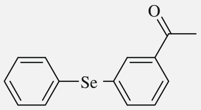
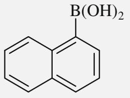
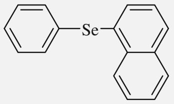
Careful analysis of the optimized reactions revealed that the optimum conditions for this coupling reaction were found to be the use of CuO NPs (3 mol %) as a catalytic system, diphenyl diselenide **1a** (0.25 mmol), and 4-methoxyphenyl boronic acid **2a** (1.5 equiv), utilizing DMSO as a solvent. The heterogeneous reaction mixture was stirred for 24 h at 100 °C under air atmosphere affording the desired diaryl selenide **3a** in 97% yield.[13]

In order to demonstrate the efficiency of this protocol, we explored the generality of our methodology by reacting other aryl boronic acids **2b–k** with diphenyl diselenide **1a** (Table 2). The results reported in Table 2 show that the reaction worked well for a variety of aryl boronic acids. A closer inspection of the results revealed that the reaction is not sensitive to electronic effects of the substituents attached to the aromatic ring. Aryl boronic acids bearing both electron-donating (Table 2; entries 1–3) and electron-withdrawing groups (Table 2; entries 5–10) gave excellent yields of the desired products. Differentiation in the reactivity between bromine and boron atoms of boronic acid can be seen by coupling of 4-bromophenyl boronic acid **2g** with diphenyl diselenide **1a**. In this case, only the coupling product **3g** was obtained in 97% yield, without by-products (Table 2; entry 7). In our case, the bromine substituent was not affected. A decrease in the yield of cross-coupling was obtained when we used a hindered boronic acid **2k**, furnishing the corresponding products in 78% yield (Table 2; entry 11).

In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with other organic diselenides was also investigated (Table 3). 4-Methoxyphenyl boronic acid **2a** was coupled efficiently with a variety of organic disele-

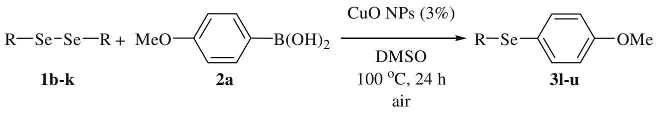
Table 2
Coupling products using diphenyl diselenide **1a** and aryl boronic acids **2a–k**

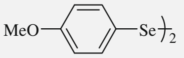
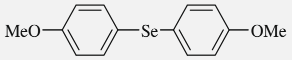
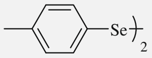
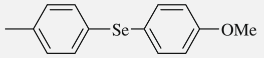
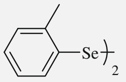
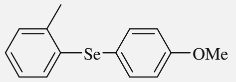
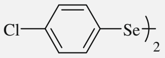
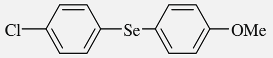
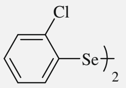
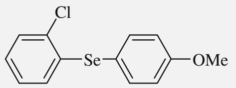
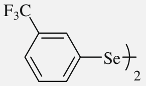
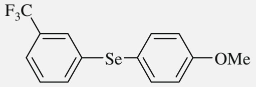
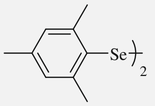
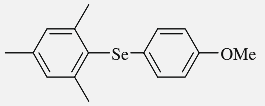
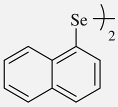
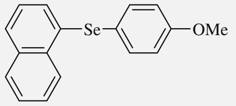
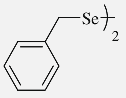
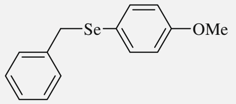
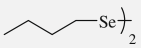
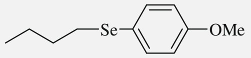
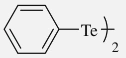
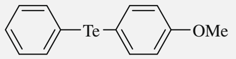


Entry	$R^2B(OH)_2$	Product yield[b] (%)
1	 **2a**	 **3a** (97%)
2	 **2b**	 **3b** (93%)
3	 **2c**	 **3c** (90%)
4	 **2d**	 **3d** (94%)
5	 **2e**	 **3e** (96%)
6	 **2f**	 **3f** (94%)
7	 **2g**	 **3g** (97%)
8	 **2h**	 **3h** (94%)
9	 **2i**	 **3i** (98%)
10	 **2j**	 **3j** (95%)
11	 **2k**	 **3k** (78%)

[a] Reactions performed in the presence of **1a** (0.25 mmol), aryl boronic acid (1.5 equiv), and 3 mol % of CuO NPs and DMSO (0.5 mL).
[b] Yields are given for isolated products.

Table 3
Coupling products using compounds **1b–l** and 4-methoxyphenyl boronic acid **2a**[a]

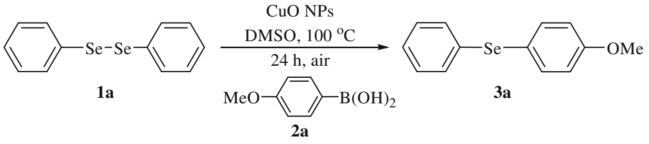


Entry	R–Se–Se–R	Product yield[b] (%)
1	 **1b**	 **3l** (84%)
2	 **1c**	 **3m** (87%)
3	 **1d**	 **3n** (85%)
4	 **1e**	 **3o** (95%)
5	 **1f**	 **3p** (93%)
6	 **1g**	 **3q** (95%)
7	 **1h**	 **3r** (79%)
8	 **1i**	 **3s** (82%)
9	 **1j**	 **3t** (91%)
10	 **1k**	 **3u** (75%)
11	 **1l**	 **3v** (94%)

[a] Reactions performed in the presence of diorganoyl diselenide (0.25 mmol), 4-methoxyphenyl boronic acid **2a** (1.5 equiv), and 3 mol % of CuO NPs and DMSO (0.5 mL).

[b] Yields are given for isolated products.

Table 4
Recycling of CuO NPs



Run	Catalyst recovery (%)	Yield **3a**[c] (%)
1[a]	95	97
2[b]	92	92
3[b]	88	89
4[b]	85	83

[a] Reaction performed in the presence of **1a** (0.5 mmol), aryl boronic acid (1.5 equiv), 3 mol % of CuO NPs, and DMSO (1 mL).

[b] Recovered catalyst used.

[c] Yields are given for isolated products.

nides **1b–k**. The results revealed that the reaction is sensitive to the electronic effect of an aromatic ring attached to the diaryl diselenide. For example, diaryl diselenides bearing electron-donating groups gave lower yields than the diselenides bearing electron-withdrawing groups (Table 3; entries 1–3 vs 4–6).

We have found that steric effects had a little influence on the coupling reaction, and diselenides containing mesityl and naphthyl groups gave lower yields of the desired products (Table 3; entries 7 and 8). Notably, when dibenzyl diselenide **1j** and dibutyl diselenide **1k** were used, the corresponding products **3t** and **3u** were obtained in excellent and good yields, respectively (Table 3; entries 9 and 10). Diphenyl ditelluride **1l** was also efficiently coupled in these conditions and diaryl telluride **3v** was formed in excellent yield (Table 3; entry 11).

To check the recyclability of the catalyst, it was separated from the reaction mixture. After completion of the C–Se cross-coupling, the reaction mixture was treated with water and ethyl acetate. The catalyst was recovered from the aqueous solution by centrifugation, dried under vacuum, and reused for further catalytic reactions.[14] The catalyst maintained its good level of activity even after being recycled four times as shown in Table 4.

In conclusion, we have explored in detail efficient and ligand-free cross-coupling reactions of organic diselenides with aryl boronic acids using a catalytic amount of CuO nanoparticles in DMSO at 100 °C under air atmosphere. This cross-coupling reaction is general and affords the corresponding products in good to excellent yields. The catalyst can be easily recovered and utilized for further catalytic reactions. Studies toward the mechanism insight of this reaction and the combination of others reaction partners are in progress in our laboratory.

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13. *General procedure for the cross-coupling reaction*: To a round-bottomed flask containing organic diselenide (0.25 mmol), aryl boronic acid (1.5 equiv), and CuO NPs (3 mol %) was added DMSO (0.5 mL). The reaction mixture was allowed to stir at 100 °C for 24 h. After this time, the solution was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with water (3 × 20 mL). The organic phase was separated, dried over MgSO$_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent. Selected spectral and analytical data for *4-methoxyphenyl-phenyl-selenide* **3a**:[6a] yield: 0.128 g (97%). ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.50 (d, J = 8.4 Hz, 2H), 7.33–7.31 (m, 2H), 7.21–7.16 (m, 3H), 6.84 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 159.7, 136.5, 133.2, 130.9, 129.1, 126.4, 119.9, 115.1, 55.2.
14. *Recycling of catalyst*: To a round-bottomed flask containing organic diselenide (0.5 mmol), aryl boronic acid (1.5 equiv), CuO, and NPs (3 mol %) was added DMSO (1.0 mL). The reaction mixture was allowed to stir at 100 °C for 24 h. After this time, the reaction mixture was allowed to cool, and a 1:1 mixture of ethyl acetate/water (2.0 mL) was added and CuO NPs were removed by centrifugation. After each cycle, the catalyst was recovered by simple centrifugation, washed with deionized water and ethyl acetate, and then dryed in vacuo. The recovered CuO NPs were used directly in the next cycle.