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CuS/Fe: a novel and highly efficient catalyst system for coupling reaction of aryl halides with diaryl diselenides

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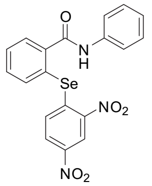
ABSTRACT

The CuS catalyzed coupling reactions of aryl halides and diaryl diselenides were accelerated by the addition of Fe powder in only 3–12 h with good to excellent yields. SEM–EDX indicated that the in situ iron oxides as support against catalyst agglomeration accelerated the reaction. This catalyst system was also demonstrated recyclable without significant loss of catalytic activity.

1. Introduction

During the past decade, a lot of efforts have been directed toward the development of organoselenium compounds for their potential as drug candidates.[1] The examples include human breast cancer cell growth inhibitor **1**;[2] Urdpase (uridine phosphorylase) inhibitor **2** for treatment of various human solid tumors;[3] a possible lead compound for antitumor agent **3**;[4] potent inhibitor of 5-LOX (lipoxygenases) **4**;[5] and RAR (retinoic acid receptors, 10 times more potent than its sulfur analogue) agonist **5**.[6] In addition, many chiral and achiral organoselenium compounds also exert catalytic role in organic synthesis.[7]



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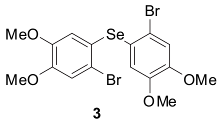

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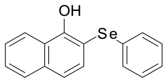

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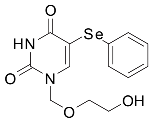

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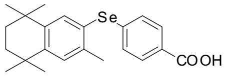

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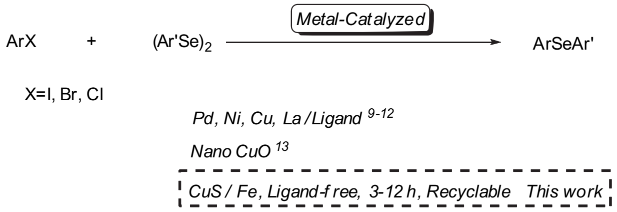
Practical methods for the synthesis aryl selenides involved harsh reaction conditions such as the use of polar and toxic solvent like HMPA and high reaction temperature.[8] The direct syntheses by transition metal-catalyzed (Pd,[9] Ni,[10] Cu,[11] and La[12]) coupling reactions of aryl donors with diaryl diselenides have become versatile tools. However, these metal-catalyzed reactions involve the addition of ligands, well-defined catalysts, and long reaction times, which may increase the cost and limit the scope of applications. Thus, it is desirable to explore novel catalytic procedures for an efficient route to such highly useful organic products. Nano CuO was employed on the basis of this strategy.[13] These processes were demonstrated as efficient protocols for the synthesis of organoselenium. For the practical purpose, it is worthwhile to develop a general, simple, and economical catalyst system for the coupling of aryl halides with diaryl diselenides.



In the previous studies, our and other groups have reported that copper-catalyzed S-arylation of diaryl disulfides with aryl halides.[11,14] Based on the bond energy that the C–Se bond (243 kJ/mol) is weaker than the C–S bond (272 kJ/mol), we considered our catalyst systems for C–S coupling should be more efficient for preparing the organic selenides. Herein, we would like to release it.

2. Results and discussion

Our initial studies focused on the development of an optimum set of reaction condition. In this approach, diphenyl diselenide and

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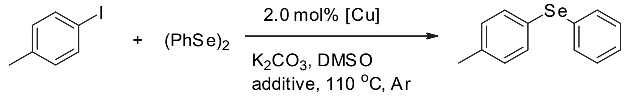
4-methyl-iodobenzene were used as model substrates. These studies showed that the desired aryl selenide formed in 88% yield with 2 mol % CuI as catalyst, K_2CO_3 as base, and DMSO as solvent at 110 °C in 15 h (Table 1, entry 1). However, the formation of the aryl selenide product under the standard conditions also produced undesired symmetrical diphenyl selenide in a 3% yield. Cu or CuS as catalyst occurred to higher conversion but also along with the byproduct observation. To our delight, the reaction was dramatically accelerated by the addition of Fe powder and the aryl selenide formed in 99% yield without side product. Further careful monitoring indicated that the reaction was able to complete only in 6 h (Table 1, entry 6). Control experiments showed that Mg powder as reductant formed lower yield product, $FeCl_3$ and $FeCl_2$ as co-catalyst resulted in much low conversion and the sole Fe and FeS as catalyst demonstrated no catalyst effect (Table 1, entries 7–10). The Cu_2S as catalyst shows similar activity as CuS (Table 1, entry 11), but without the addition of Fe, the yield was decreased (Table 1, entry 12). It was noted that the polar donor solvent DMF was slightly inferior to DMSO and weak polar solvent dioxane only gave trace desired product.

To investigate the role of Fe powder, the prepared CuS and recovered CuS were characterized by scanning electron microscopic scanning (SEM) and energy dispersive X-ray spectroscopy, respectively (Fig. 1). The prepared CuS was flake by the SEM and the

Table 1
Optimum of reaction conditions[a]

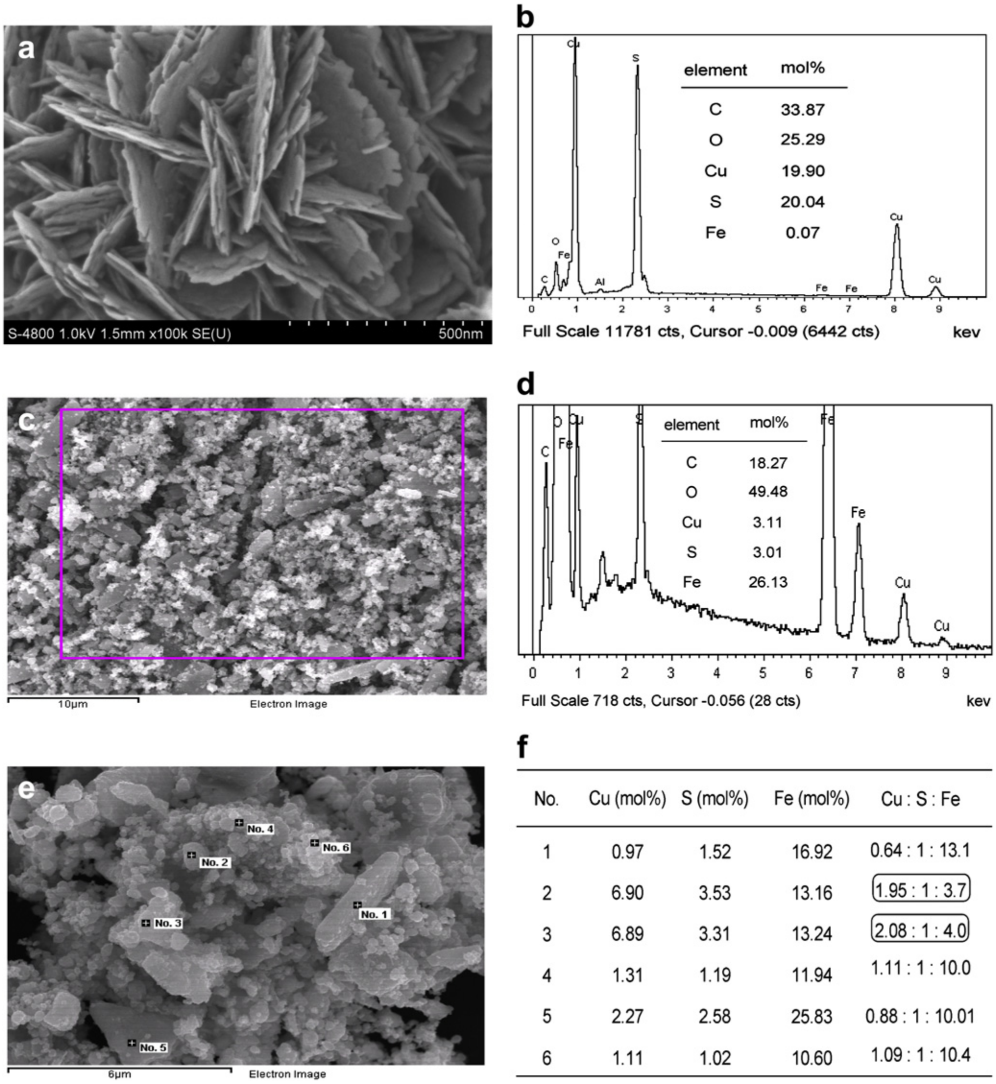


Entry	[Cu]	Time (h)	Additive	Yield[b] (%)
1	CuI	15		88 (3)
2	Cu	15		93 (3)
3	CuS	15		94 (2)
4	CuS	15	Fe	99 (0)
5	CuS	15	Mg	89 (2)
6	CuS	6	Fe	99 (0)
7	CuS	6	$FeCl_3$	30
8	CuS	6	$FeCl_2$	45
9		6	Fe	Trace
10		6	FeS	Trace
11	Cu_2S	6	Fe	99 (0)
12	Cu_2S	6		73
13	CuS	6	Fe	30[c]

[a] Reaction conditions: 1-iodo-4-methylbenzene (0.6 mmol), diphenyl diselenide (0.3 mmol), [Cu] (0.012 mmol), additive (0.36 mmol), K_2CO_3 (0.6 mmol), and DMSO (1 mL) stirred at 110 °C under Ar.

[b] GC yield (little symmetrical selenide was observed).

[c] Without addition of K_2CO_3.



b

element	mol%
C	33.87
O	25.29
Cu	19.90
S	20.04
Fe	0.07

d

element	mol%
C	18.27
O	49.48
Cu	3.11
S	3.01
Fe	26.13

f

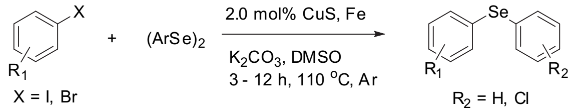
No.	Cu (mol%)	S (mol%)	Fe (mol%)	Cu : S : Fe
1	0.97	1.52	16.92	0.64 : 1 : 13.1
2	6.90	3.53	13.16	1.95 : 1 : 3.7
3	6.89	3.31	13.24	2.08 : 1 : 4.0
4	1.31	1.19	11.94	1.11 : 1 : 10.0
5	2.27	2.58	25.83	0.88 : 1 : 10.01
6	1.11	1.02	10.60	1.09 : 1 : 10.4

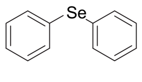
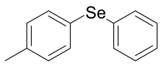
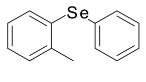
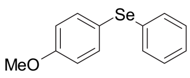
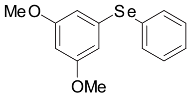
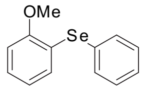
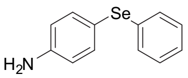
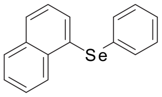
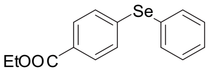
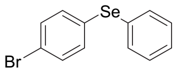
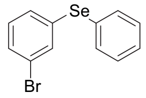
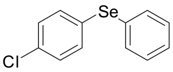
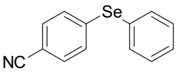
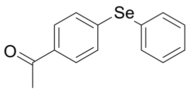
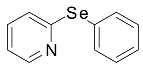
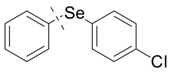
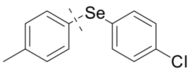
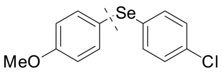
Fig. 1. SEM–EDX analyzed the catalyst: (a) SEM of CuS before reaction, (b) EDX of CuS before reaction, (c) SEM of surface CuS/Fe after reaction, (d) EDX of region CuS/Fe after reaction, (e) SEM of point CuS/Fe after reaction and (f) EDX of point CuS/Fe after reaction.

elemental composition was regular 1:1 ratio of Cu and S by the EDX. After the reaction, the region EDX showed that the ratio of Cu and S is also about 1:1, but the concentration of Fe increased dramatically (Fig. 1c and d). It is presumable that CuS was reductive to Cu_2S based on the redox potential of Cu^{2+}/Fe. From the random points of SEM, we observed that the 2:1 ratio of Cu and S appeared (Fig. 1e and f), which indicated the formation of Cu_2S. Besides, based on the fact that the Fe powder binded to magneton as its magnet before the stirring but most divorced after the reaction, we speculated that the Fe powder not only reduced CuS to form the real catalyst Cu_2S but also in situ generated Fe_xO_y by the oxidation of DMSO. In the course of redox reaction, the in situ formation of Fe_xO_y as support dispersed the in situ Cu_2S against agglomeration to accelerate the reaction.

To demonstrate the scope of this novel transformation, we studied the electronic and steric effects of attached groups at the aryl halides and diphenyl diselenides moiety. In general, this protocol efficiently coupled diphenyl diselenide with electron-rich, electron-neutral, and electron-deficient aryl iodides. Substrates with electron-withdrawing groups were more reactive than those with electron-donating groups. It took only 3 h for electron-withdrawing substituents (Table 2, **2i**, **2j**, **2k**, and **2l**). Sterically *ortho* substituents did not hamper the arylation reaction (Table 2, **2c**, **2f**, and **2h**). Furthermore, methyl, methoxy, chloro, bromo, ester, and cyano groups were well tolerated to afford the corresponding cross-coupled products in excellent yield. Aryl iodide with a free amino group was well tolerant without the need of a protecting group (Table 2, **2g**). We also observed that iodobenzene was more reactive. Consequently, cross-coupling reactions with chloro or bromo substituted aryl iodides showed an interesting chemoselectivity to proceed exclusively at the iodo group (Table 2, **2j**, **2k**, **2l**). In fact, by prolonging the reaction time, electron-deficient bromobenzene could also be efficiently transformed in 12 h under the optimized conditions. Heterocycle 2-bromopyridine was efficiently transformed to corresponding aryl selenide in 93% yield (Table 2, **2o**). At last, when 4-chloro diphenyl diselenides were used, the corresponding products were obtained in excellent to good yield (Table 2, **2l′**, **2p**, and **2q**).

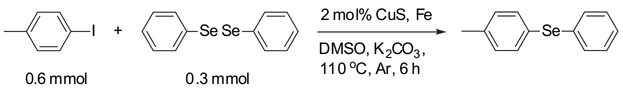
Table 2
Couplings of aryl halides with diaryl diselenides[a]



 **2a**, 6 h, 99%	 **2b**, 6 h, 99%	 **2c**, 6 h, 99%
 **2d**, 6 h, 94%	 **2e**, 6 h, 90%	 **2f**, 6 h, 90%
 **2g**, 6 h, 82%	 **2h**, 6 h, 98%	 **2i**, 3 h, 91%
 **2j**, 3 h, 98%	 **2k**, 3 h, 98%	 **2l**, X = I, 3 h, 91% X = Br, 12 h, 28%
 **2m**, X = I, 3 h, 98% X = Br, 12 h, 96%	 **2n**, X = Br, 12 h, 99%	 **2o**, X = Br, 12 h, 99%
 **2l′**, 6 h, 90%	 **2p**, 6 h, 92%	 **2q** 6 h, 84%

[a] Reaction conditions: 1-iodo-4-methylbenzene (0.6 mmol), diaryl diselenide (0.3 mmol), CuS (0.012 mmol), Fe powder (0.36 mmol), K_2CO_3 (0.6 mmol) and DMSO (1 mL) stirred at 110 °C for 3–12 h under argon. Isolated yields.

Table 3
Recyclability experiments of the CuS[a]



Entry	Recycle	GC yield (%)
1	Run 1	99
2	Run 2	98
3	Run 3	93
4	Run 4	87

[a] Reaction conditions: After the first run, a drop of resulting mixture was removed and treated with H_2O (1 mL) and ethyl acetate (0.2 mL). The organic layer was detected by GC. Then to the tube was added fresh Fe powder (20.2 mg, 0.36 mmol), diselenide (0.3 mmol), aryl halide (0.6 mmol) and reacted at 110 °C for 6 h under argon. The catalyst was used four times.

The recyclability of catalyst was also checked. After the first run, a drop of reaction mixture was removed for GC analysis and to the remaining mixture was added new raw materials for further catalytic reactions. It was found that the catalyst could be reused for the fresh cross-coupling reaction without significant loss of catalytic activity (Table 3). This novel and efficient system is valuable in large scale synthesis of aryl selenides considering the economical cost of the catalyst.

3. Conclusion

In conclusion, we have explored a highly efficient and ligand-free CuS/Fe catalyzed cross-coupling reaction of aryl halides with diaryl diselenides. In this catalytic process, the addition of Fe played an important role not only reduced CuS to form the real catalyst Cu_2S but also in situ generated Fe_xO_y as support against catalyst agglomeration to accelerate the reaction. By this new protocol, aryl halides reacted with diaryl diselenides at 110 °C for 3–12 h giving corresponding aryl organoselenium with good to excellent yields. In addition, this novel CuS/Fe system showed widely functional-group-tolerant and well chemoselective. At last, this catalyst system was also demonstrated recyclable without significant loss of catalytic activity. We believe this simple and effective catalyst system may find application in the synthesis of the related organoselenium compounds.

4. Experimental

4.1. General information

All reagents were obtained from commercial source (>99%) and used without further purification. The reactions were carried out under argon atmosphere. Gas chromatography analyses were performed with an FID detector. All products were isolated by column chromatography on silica gel (200–300 mesh) using petroleum ether (60–90 °C) and ethyl acetate as eluate. Compounds described in the literature were characterized by comparison of their ^1H NMR, ^{13}C NMR spectra and MS to the reported data. ^1H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ and chemical shifts were reported in parts per million relative to TMS.

4.2. Experimental procedure for all compounds

4.2.1. The preparation of copper sulfide. CuS can be prepared by slowly adding the solution of $CuSO_4$ to the aqueous solution of Na_2S. The precipitated CuS was produced by filtration and washing sequentially with H_2O, EtOH, EtOAc and drying in vacuo for 24 h. The block CuS was ground up into fine powder prior to use.

4.2.2. General procedure for the coupling of aryl halides with diaryl diselenides. A flame-dried test tube with a magnetic stirring bar was charged with CuS (1.3 mg, 0.012 mmol), Fe powder (20.2 mg, 0.36 mmol), K_2CO_3 (82.8 mg, 0.6 mmol), diselenide (0.3 mmol), aryl halide (0.6 mmol), and DMSO (1 mL) under argon. The mixture reacted at the indicated temperature for 3–12 h and cooled to room temperature. The resulting mixture was extracted with ethyl acetate (3×25 mL). The combined organic layers were dried over Na_2SO_4 and then were concentrated under vacuum. The residue was purified by column chromatography on silica gel with an eluent of petroleum ether and ethyl acetate. All the physical data of the known compounds were in agreement with those reported in the literatures (see: Supplementary data).

4.2.3. The SEM–EDX experiments for recovered CuS. Following the general procedure, the resulting mixture was treated with H_2O (10 mL) and ethyl acetate (3×5 mL). The catalyst was recovered from the solution by centrifugation and then was dried under vaccum. The brown solid was collected and then characterized by SEM–EDX.

4.2.4. Recyclability experiments of the CuS. Following the general procedure, after the first run completion, a drop of resulting mixture was removed and treated with H_2O (1 mL) and ethyl acetate (0.2 mL). The organic layer was detected by GC. Then to the tube was added fresh Fe powder (20.2 mg, 0.36 mmol), diselenide (0.3 mmol), aryl halide (0.6 mmol) and reacted at 110 °C for 6 h under argon. This process was repeated and the catalyst was used four times.

Acknowledgements

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Supplementary data

Experimental procedures and characterization of the products. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.09.061.

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