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Copper-catalyzed Stereoselective Synthesis of Vinyl Selenides under Ligand-free Conditions

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A mild and efficient protocol for the stereoselective synthesis of vinyl selenides catalyzed by CuO nanoparticles as recyclable catalyst under ligand-free conditions is reported. This methodology results in the synthesis of a variety of vinyl selenides in excellent yields with retention of stereochemistry.

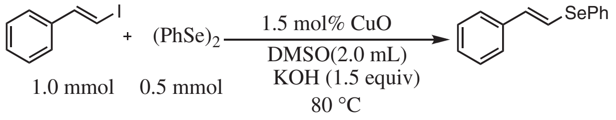
Organoselenium compounds have received considerable attention due to their wide utility in organic synthesis and various biological activities especially anticancer, and antioxidant properties.[1] Amongst the organoselenium compounds, vinyl selenides have acequired high significance as intermediates in the preparation of carbonyl compounds and in the synthesis of stereoselectively functionalized alkenes.[2] This led to the development of various processes for vinyl selenides. Though traditional methods such as the Wittig olefination,[2c] selenide ion displacement of vinyl halides[3] etc.[4] are generally satisfactory, stereoselective outcome has always been a limitation. To overcome this limitation various approaches have been developed.[5,6] Recently Bao and co-workers developed a protocol for the synthesis of vinyl selenides by using copper iodide as a catalyst in the presence of zinc metal in ionic liquid and L-proline as a ligand for 24 h.[3d] Ranu and co-workers reported the nano-copper-catalyzed synthesis of vinyl selenides in the presence of zinc metal as additive in water.[7]

However, most of these metal-catalyzed reactions involve expensive and moisture-sensitive catalysts/reagents with ligands/additives at higher temperatures causing major problems in purification of the product and separation of the metal catalyst. These problems are of environmental and economic concern in large scale synthesis. Thus, it is desirable to develop an inexpensive, environmentally benign, and recyclable catalytic system for an efficient access to such highly useful vinyl selenides under ligand-free conditions and if possible at temperatures lower than 100 °C.

Recently, heterogeneous catalysts have become attractive both from economic and industrial points of view as compared to homogeneous catalysts. In general, nanoscale heterogeneous catalysts offer higher surface area responsible for higher catalytic activity.[8] Furthermore, heterogeneous catalysts have also the advantage of high atom efficiency, easy product purification, and reusability of the catalyst.

Encouraged by the intense research activity in the field of selenium chemistry and in continuation of our interest in copper-catalyzed coupling of arylhalides with diselenide,[9] we report herein the CuO nanoparticles-catalyzed synthesis of vinyl selenides under ligand-free conditions (Scheme 1). However, to the best of our knowledge, this is the first example of the synthesis of vinyl selenides in the absence of any ligand or co-metal catalyst.

The coupling reaction of *trans*-β-iodostyrenes with diphenyl diselenide was used as a model reaction to optimize reaction conditions including bases, solvents, catalysts, and temperature. Among the bases examined, KOH (Table 1, Entry 5) was found to be the best for coupling providing the highest yield. Other bases, such as Cs_2CO_3 and K_3PO_4 (Table 1, Entries 1 and 6) gave trace yields. The influence of solvents on the reaction was also investigated. DMSO as a solvent gave the best yield of the product in comparison with other solvents (Table 1, Entry 5).



Scheme 1. CuO nanoparticles-catalyzed synthesis of vinyl selenides.

Table 1. Cross coupling of diphenyl diselenide with *trans*-β-iodostyrene[a]

Entry	Base	Solvent	Yield[b]/%
1	K_3PO_4	DMSO	trace
2	KOH	DMF	79
3	KOH	DMSO	10[c]
4	KOH	DMSO	81[d]
5	KOH	DMSO	97
6	Cs_2CO_3	PhMe	trace
8	K_3PO_4	DMF	trace
9	K_3PO_4	PhMe	0
10	KOH	PhMe	0
11	KOH	Water	0
12	none	DMSO	17
13	KOH	DMSO	25[e]

[a]Reaction conditions: *trans*-β-iodostyrene (1.0 mmol), diphenyl diselenide (0.5 mmol), CuO (1.5 mol %), base (1.5 equiv), solvent (2.0 mL), 80 °C, 4 h. [b]Isolated yield. [c]At rt. [d]At 50 °C. [e]Absence of catalyst.

The reaction temperature was investigated by using 1.5 mol % of CuO as the catalyst and 1.5 equiv of KOH as the base in DMSO. The yield of the target product was greatly improved as the reaction temperature was increased, and higher yields were provided at 80 °C (Table 1, Entry 5). The coupling efficiency was evidently decreased in the absence of base (Table 1, Entry 12), and only a trace amount of the product was observed without addition of the catalyst (Table 1, Entry 13). Several metal oxides were also tested (compare Table 2), and CuO was observed to be the most effective catalyst (Table 2, Entry 6).[10]

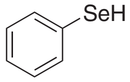
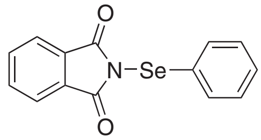
We have also made a study of the cross coupling with various nucleophiles under these conditions (Table 3). In general, selenols are avoided because of their instability in air and/or moisture and foul-smelling nature. *N*-(Phenylseleno)-

Table 2. Effect of different catalysts for the synthesis of vinyl selenides[a]

Entry	Catalyst	Yield[b]/%
1	nano-ZnO	31
2	nano-Bi_2O_3	29
3	nano-In_2O_3	35
4	nano-Sb_2O_3	24
5	nano-Co_3O_4	26
6	**nano-CuO**	**98**
7	nano-Fe_2O_3	33
8	nano-NiO	46

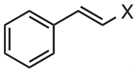
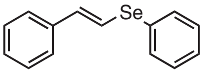
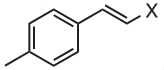
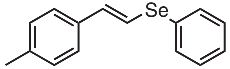
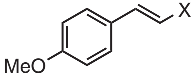
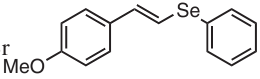
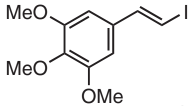
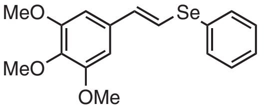
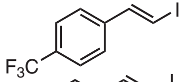
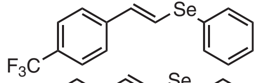
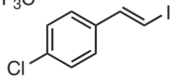
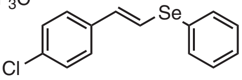
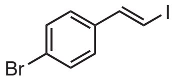
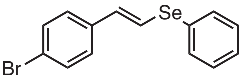
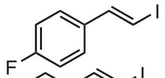
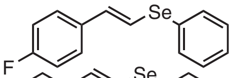
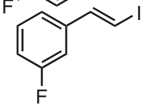
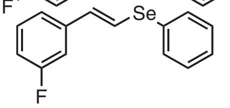
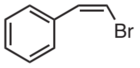
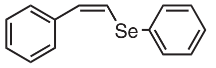
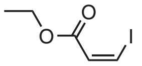
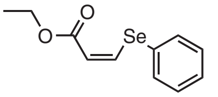
[a]Reaction conditions: *trans*-β-iodostyrene (1.0 mmol), diphenyl diselenide (0.5 mmol), catalyst (1.5 mol %), KOH (1.5 equiv), DMSO (2.0 mL) at 80 °C. [b]Isolated yield.

Table 3. Effect of different nucleophiles for the synthesis of vinyl selenides[a]

Entry	Nucleophiles	Yields[c]/%
1		79
2	$(PhSe)_2$	98[b]
3		95

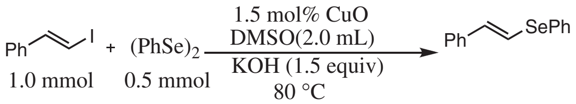
[a]Reaction conditions: nucleophiles (1.0 mmol), CuO (1.5 mol %), KOH (1.5 equiv), DMSO (2.0 mL) at 80 °C. [b]Diphenyl diselenide (0.5 mmol). [c]Isolated yield.

Table 4. Nano CuO-catalyzed cross coupling of various *trans*-β-halostyrene and *cis*-β-halostyrene with diphenyl diselenide[a]

Entry	Halides		Product	Yield[b]/%
1		X = I		98
2		Br		61
3		Cl		0
4		X = I		96
5		Br		45
6		X = I		95
7		Br		41
8				89
9				92
10				90
11				93
12				93
13				90
14				56
15				81

[a]Reaction conditions: *trans*-β-iodostyrene or *cis*-β-halostyrene (1.0 mmol), diphenyl diselenide (0.5 mmol), CuO (1.5 mol %), KOH (1.5 equiv), DMSO (2.0 mL) at 80 °C. [b]Isolated yield.

Table 5. Recycling of CuO nanoparticles



Recycles	Yield/%	Catalyst recovery/%
1	98	96
2	95	93
3	91	90
4	91	90

phthalimide was more expensive compared to diphenyl diselenide. Among these nucleophiles, diphenyl diselenide appeared to be the best choice for cross coupling.

To explore the scope of this novel transformation, we first examined the cross coupling of diphenyl diselenide with different *trans*-β-iodostyrenes (Table 4).[11] In general, all reactions were very clean, and the vinyl selenides were obtained in high yields under the optimized conditions. This protocol efficiently coupled *trans*-β-iodostyrene having electron-rich, electron-neutral, and electron-poor functionalities with diphenyl diselenide (Table 4, Entries 1, 4, 6, and 8–13). Encouraged by these results, we tested the coupling of several *trans*-β-bromostyrenes with diphenyl diselenide under the same conditions. The reaction of *trans*-β-bromostyrenes with diphenyl diselenide proceeded smoothly to afford the desired product in reasonable yield (Table 4, Entry 2). However, low yields were observed in the coupling of substituted *trans*-β-bromostyrene and *cis*-β-bromostyrene (Table 4, Entries 5, 7, and 14). Furthermore, the stereochemistry of the vinyl selenides was retained in all the cases. This protocol was also applied for the cross coupling of β-alkoxycarbonyl-substituted vinyl iodide with diphenyl diselenide and the corresponding vinyl selenide was obtained in excellent yield (Table 4, Entry 15).

In addition, the recyclability of the catalyst was checked using the coupling of *trans*-β-iodostyrene with vinyl selenide as the model reaction. After the reaction was complete, the reaction mixture was allowed to cool, and a 1:1 mixture of ethyl acetate/water (2.0 mL) was added and CuO was removed by centrifugation. After each cycle, the catalyst was recovered by simple centrifugation, washed with deionized water followed by acetone and then dried in vacuo. The recovered CuO was used directly in the next cycle (Table 5). TEM images of the catalyst indicated no change before and after the reaction, which confirms the heterogeneous nature of the catalyst (Figures 1a and 1b). This indicates that the catalysis may be occurring on the surface of CuO nanoparticles.[12]

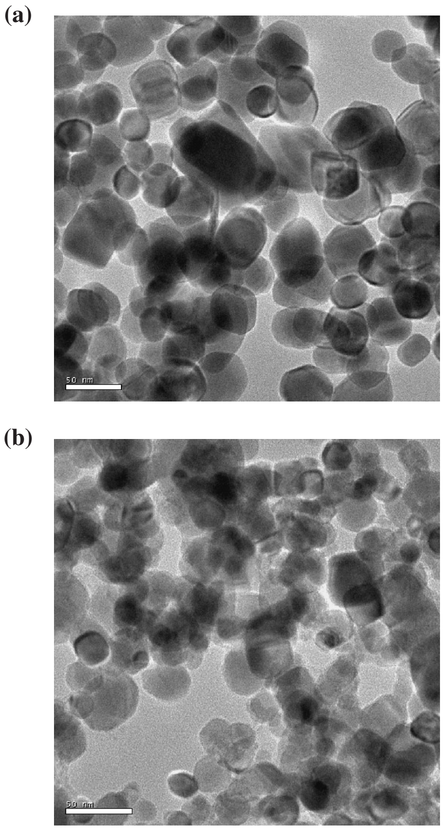
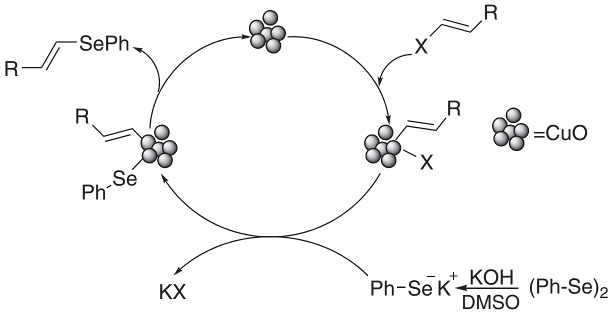


Figure 1. TEM images of the catalyst (a) before and (b) after the reaction.



Scheme 2. A plausible mechanism for the CuO nanoparticle-catalyzed cross coupling of vinyl halides and diphenyl diselenide in the presence of DMSO and KOH.

A plausible mechanism for the CuO nanoparticle-catalyzed cross coupling of vinyl halides and diphenyl diselenide is illustrated in Scheme 2.[13]

In conclusion, CuO acts as an active, moisture stable, inexpensive, and nontoxic catalyst for the stereoselective synthesis of vinyl selenides under ligand-free conditions in excellent yields. This method precludes the use of external ligands and provides, in most cases, the desired vinyl selenides in high yields. The catalyst was simply recovered and reused without significant loss of catalytic activity.

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10 All catalysts including CuO nanoparticles were purchased from Sigma Aldrich.

11 To a stirred solution of diphenyl diselenide (0.5 mmol) and *trans*-β-iodostyrene (1.0 mmol) in DMSO (2.0 mL) was added CuO nanoparticles (1.5 mol %) followed by KOH (1.5 equiv) and stirred at 80 degrees for 4 h. The progress of the reaction was monitored by TLC. After the reaction was complete, the reaction mixture was allowed to cool, and a 1:1 mixture of ethyl acetate/water (2.0 mL) was added and CuO was removed by centrifugation. The organic layer was washed and separated, the aqueous layer was further washed with another 10-mL portion of ethyl acetate, and the combined organic extracts were dried with anhydrous Na_2SO_4. The solvent and volatiles were completely removed under vacuum to give the crude product, which was subjected to column chromatographic separation to give analytically pure product (98%) as yellow oil.

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13 In this reaction, DMSO may be acting as a reducing agent required in the reaction by producing dimsyl ion in the presence of KOH. Ref: D. H. Hunter, D. J. Cram, *J. Am. Chem. Soc.* **1966**, *88*, 5765.