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A convenient synthetic route for alkynylselenides from alkynyl bromides and diaryl diselenides employing copper(I)/imidazole as novel catalyst system

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ABSTRACT

A mild, convenient, and effective strategy is developed for the synthesis of alkynyl selenides from alkynyl bromides and respective diselenides using CuI/imidazole as a novel catalyst system with Mg as additive. The procedure affords the title compounds in moderate to good yield (51–89%). The main advantages of the protocol include the use of inexpensive copper catalyst, a novel Cu(I)/imidazole combination, and good yield of the products.

1. Introduction

Organic chalcogens as structural motifs are commonly found in a variety of molecules of biological/pharmaceutical[1] and material[2] interest. Among them, alkynyl chalcogenides are interesting class of compounds having a variety of uses in organic synthesis.[3] For example, alkynylselenides have been useful precursors in hydroamination,[4] hydrohalogenation,[5] hydrosulfonation,[6] hydrostannylation,[7] hydrozirconation,[8] and hydroboration[9] reactions. They have also been used for the preparation of selenocarboxylic esters, which are useful acyl transfering agents.[10]

The commonly used method for the synthesis of alkynyl selenides involves metal-assisted cross coupling with either Mg or Cu salts.[5,7,11] However, delicate reaction conditions and stoichiometric amount of toxic metal salts leave scope for modifications of these protocols. In this regard, oxidative dehydrogenation of alkynes through iodobenzene diacetate is a useful proposition, but the scope of the protocol has to be evaluated for substituted phenylselenides.[12]

The recent past has witnessed emergence of copper-catalyzed coupling reactions as principal method of forming aromatic carbon–heteroatom bonds.[13] Copper catalysts have been preferred to other organometallic compounds due to obvious advantage of their being inexpensive and providing clean reactions. We had previously reported preparation of alkynyl selenides using stoichiometric amount of copper(I),[11b,c] and realized that reducing amount of copper to catalytic scale for preparation of alkynyl selenides would be a significant development.

In this context, we disclose a mild and inexpensive methodology for the synthesis of alkynyl selenides from alkynyl bromides and respective diselenides using copper salt/imidazole as a novel catalyst system. Recently, CuI has been utilized for preparation of alkynyl selenides from phenylacetylene in the presence of DMSO as oxidant.[14] We decided to apply the above methodology in a reaction between phenylacetylene bromide **1a** with diphenyl diselenide **2a** (1 equiv), CuI (10 mol %) and K_2CO_3 (2 equiv) in DMSO. However, the methodology did not work in our system and within 10 min, a precipitation of **2a** and no product were observed even after 7 h of reaction.

In another reaction, **1a** was reacted with **2a** (1 equiv) in the presence of CuI (10 mol %), Mg (2 equiv), in DMF at 120 °C for 24 h, unfortunately the product phenylethynyl selenide **3a** was obtained in only 25% yield, the rest being acetylene dimer and the starting material. Recently, Beller reported a novel and efficient Cu(I)–imidazole catalyst–ligand combination in cyanation reactions.[15] Inspired by their results, we decided to incorporate copper–imidazole system in our case. Emulating the above methodology, compounds **1a** and **2a** (1 equiv) were reacted with CuI (10 mol %), imidazole (10 mol %), and Mg (2 equiv) as additive. Much to our gratification, it brought about 83% yield of **3a** in 48 h.

In order to optimize the above protocol, different Cu(I) catalysts, ligands, additives, and solvents were screened in the above reaction. For example, in one set of reactions, different copper catalysts were tested (Table 1, entry 1–3) and CuI provided maximum yield of the product (entry 1). The catalyst loadings were also analyzed. It was observed that using 20 and 5 mol % of the catalyst, the desired product was obtained with 79% and 69% of yield, respectively (entries 4 and 5). However, 10 mol % CuI seemed to provide optimum yield of **3a** (entry 1).

Furthermore, Zn was tried in place of Mg, but was less effective (entry 6). Moreover, reaction did not proceed in absence of either imidazole or Cu(I) (entry 7), and only traces of **3a** formed in absence of Mg (entry 8).

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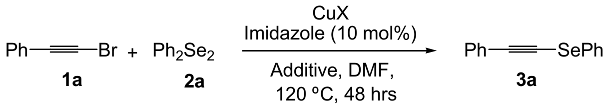
Table 1
Effect of catalyst and additive in coupling of alkynyl bromide and diphenyl diselenide[a]



Entry	CuX_3	Additive	Yield[b,c] (%)
1	CuI (10 mol %)	Mg	83
2	CuCl (10 mol %)	Mg	67
3	Cu(OAc) (10 mol %)	Mg	51[d]
4	CuI (20 mol %)	Mg	79
5	CuI (5 mol %)	Mg	69
6	CuI (10 mol %)	Zn	56[e]
7[f]	—	Mg	—
8	CuI (10 mol %)	—	—

[a] Reactions were run on a 1.1 mmol scale of **1a** in DMF (5 mL) with 0.55 mmol of **2a**, catalyst, 10 mol % of imidazole and additive (2.2 mmol) at 120 °C for 48 h.
[b] Isolated yields.
[c] Yields are based on acetylene **1a**.
[d] Dimeric product along with unidentifiable side products observed.
[e] Unidentifiable mixture of side products observed.
[f] Neither CuI or imidazole was used in the reaction, only starting material remained unreacted.

In another set of experiments, comparisons were made among PPh_3, TMEDA, and imidazole, and 10 mol % imidazole proved to be the most effective ligand for preparation of **3a** (Table 2, entry 4). It is thus surprising that, despite being so effective, imidazole had remained untapped as ligand in copper catalyst systems.

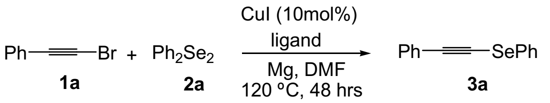
Similarly, a survey of solvents was conducted and DMF was found to be the solvent of choice (Table 3, entry 1). It is worth noting that DMSO and DMF–H_2O combination was less effective than DMF for the reaction. This implied a different mechanism in operation than the ones postulated in literature.[14]

Finally, we found that the reaction of **1a** with **2a** (1 equiv), in the presence of CuI (10 mol %), imidazole (10 mol %) in DMF at 120 °C for 48 h provided optimum yield of the product.[16]

After having achieved optimum conditions for preparation of alkynyl selenides, we decided to explore the scope of this reaction. Different alkynyl bromides and diarylselenides were reacted under the devised protocol and the results are delineated in Table 4. As clear from the table, the reactions proceeded to provide moderate to good yield of the products with varied substrates.

Finally, the scope of the reaction was also extended on diphenyl tellurides. In one reaction, compound **1a** was reacted with diphenyl telluride (**4a**) using the optimized conditions. Gratifyingly, the resulting product **5a** was obtained in 65% yield (Scheme 1).

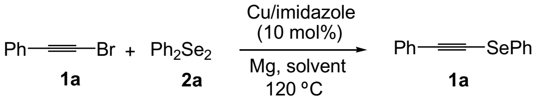
Table 2
Effect of ligands on copper-catalyzed coupling of bromophenylacetylene and diphenyl diselenide[a]



Entry	Ligand	mol %	Yield[b,c] (%)
1	Ph_3P	20	83
2	TMEDA	10	67
3	Imidazole	20	51[d]
4	Imidazole	10	79

[a] Reactions were run on a 1.1 mmol scale of **1a** in dry DMF (5 mL) with 0.55 mmol of **2a**, 10 mol % of CuI, ligand and Mg turnings (2.2 mmol) at 120 °C for 48 h.
[b] Isolated yields.
[c] Yields are based on acetylene **1a**.
[d] Rest being unreacted **1a**.

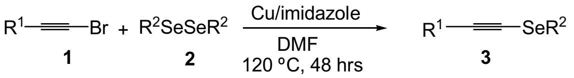
Table 3
Effect of solvent on copper-catalyzed coupling of bromophenylacetylene and diphenyl diselenide[a]

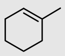


Entry	Solvent	Time (h)	Yield[b,c] (%)
1	DMF	48	83
2	DMSO	48	67
3	DCM	48	59[d]
4	THF	48	53[d]
5	DMF/H_2O	48	21[e]

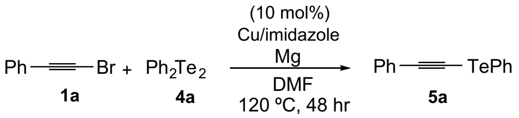
[a] Reactions were run on a 1.1 mmol scale of 1a in solvent (5 mL) with 0.55 mmol of **2a**,10 mol % of CuI, 10 mol % of imidazole, and Mg turnings (2.2 mmol) at 120 °C for 48 h.
[b] Isolated yields.
[c] Yields are based on acetylene **1a**.
[d] Unidentifiable side products observed.
[e] Diphenyl diselenide precipitated and most of **1a** remained unreacted.

Table 4
Copper-catalyzed coupling of bromoacetylene derivatives with diselenides[a]



Entry	R^1	R^2	Product	Yield[b,c] (%)
1	Ph	Ph	**3a**	83
2	p-ClC_6H_4	Ph	**3b**	67
3	p-MeC_6H_4	Ph	**3c**	79
4		Ph	**3d**	68
5	Ph	p-MeC_6H_4	**3e**	86
6	Ph	p-$CF_3C_6H_4$	**3f**	57
7	Ph	p-$MeOC_6H_4$	**3g**	81

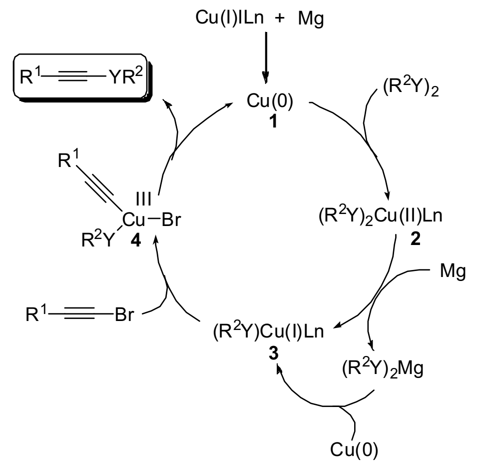
[a] Reactions were run on a 1.1 mmol scale of **1** in DMF (5 mL) with 0.55 mmol of 2,10 mol % of CuI, 10 mol % of imidazole, and Mg turnings (2.2 mmol) at 120 °C for 48 h.
[b] Isolated yields.
[c] Yields are based on acetylene **1a**.



Scheme 1. Copper-catalyzed coupling of bromophenylacetylene with diphenyl ditelluride.

On the basis of the Taniguchi and Onami[17] and Engman and Kumar[18] results, we proposed a possible mechanistic pathway for the synthesis of alkynyl chalcogenide as outlined in Scheme 2. When, CuI was employed as the promoter, the reaction process was considered as follows. Firstly, CuI was reduced to Cu(0) **1**, the oxidative addition of Cu(0) to $(R^2Y)_2$ furnished $(R^2Y)_2$Cu(II) **2**. Subsequently, the copper complex is reduced by magnesium to (R^2Y)Cu(I) **3** which is the activate species. The insertion of (R^2Y)Cu(I) species to alkynyl bromide produced a copper(III) species. Finally, reductive elimination of the alkynylchalcogenylcopper(III) intermediate **4** could undergo to form the desired alkynyl chalcogenide and Cu(I) species leading to a new catalytic cycle.

In conclusion, we have successfully demonstrated a convenient methodology for the synthesis of alkynyl chalcogenides in very good yield with modifications over the existing methodologies.



Scheme 2. Plausible reaction mechanism for the copper-catalyzed synthesis of the alkynyl chalcogenide.

This is the first report of Cu–imidazole combination as catalyst for organochalcogen compounds. Extension of this methodology to diversified substrates to broaden the scope of this novel catalyst combination will be reported in due course.

Acknowledgements

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16. *General procedure for the synthesis of substituted alkynyl selenides (Table 4).* Substituted alkynyl bromide (1.1 mmol) and diphenyl diselenide (0.55 mmol) were added to a 50 mL two-necked round-bottomed flask under argon containing CuI (209 mg, 0.11 mmol), imidazole (149 mg, 0.11 mmol), and magnesium turnings (53 mg, 2.2. mmol) in DMF (5 mL) with continuous stirring. The reaction mixture was heated in an oil bath at 120 °C for 48 h. After the reaction, the resulting mixture was cooled to room temperature, added 10–15 mL of DCM, and filtered. The filtrate was washed with brine (3 × 5 mL), water (3 × 5 mL), and was dried over $MgSO_4$. Solvent was evaporated under reduced pressure and the crude product was purified through a pad of silica with only hexane, providing the colorless viscous oil. The known compounds were identified by comparison of their spectral data with those reported and the new compounds were properly characterized by their IR, ^1H NMR, and ^{13}C NMR spectroscopic data and mass analysis.
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