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Glycerol as a promoting medium for cross-coupling reactions of diaryl diselenides with vinyl bromides

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ABSTRACT

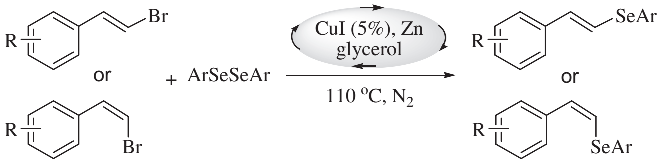
We described herein the use of glycerol as a novel solvent in the cross-coupling reaction of diaryl diselenides with vinyl bromides catalyzed by CuI. This cross-coupling reaction was performed with diaryl diselenides and (*Z*)- or (*E*)-vinyl bromides bearing electron-withdrawing and electron-donating groups, affording the corresponding vinyl selenides in good to excellent yields. The mixture glycerol/catalyst can be directly reused for further cross-coupling reactions.

The versatility and utility of organochalcogen compounds in organic synthesis are well documented through the publication of a number of reviews[1] and books.[2] Organochalcogen compounds are attractive synthetic targets because of their selective reactions,[1] their use in asymmetric catalysis,[3] natural products synthesis[4], and also due to their interesting biological activities.[5] Due to their usefulness in organic reactions, vinyl selenides and tellurides are certainly the most applied compounds in organochalcogen chemistry. A large number of synthetic methods have been reported to prepare these compounds and they follow two main categories: (a) use of the organochalcogen as an electrophile and (b) use of nucleophilic organochalcogen species.[1,2] Alternatively, in recent years, copper-catalyzed protocols have become a versatile tool for the synthesis of vinyl selenides or tellurides.[6] Unfortunately, the majority of synthetic approaches to obtain vinyl chalcogenides have some disadvantages, such as, harsh reaction conditions, expensive reagents, and the use of toxic organic solvents.

In this context, the choice of the solvent is a crucial step in a chemical reaction. The development of green solvents from renewable resources has gained much interest recently because of the extensive uses of solvents in almost all of the chemical industries and the predicted disappearance of fossil oil.[7] The wanted characteristics for a green solvent include no flammability, high availability, obtainability from renewable sources, and biodegradability.[8] With the increase in biodiesel production world-wide, the market saturation of glycerol, a co-product of biodiesel production, is inevitable.[9] The use of glycerol as a sustainable solvent for green chemistry was recently related by Gu and Jèrôme.[10] These include Pd-catalyzed Heck and Suzuki cross-couplings, base- and acid- promoted condensations, catalytic hydrogenation, and asymmetrical reduction.[10]

The peculiar physical and chemical properties of glycerol, such as polarity, low toxicity, biodegradability, high boiling point, and ready availability from renewable feedstocks,[11] prompted us to extend its use as a green solvent in organic synthesis. In this sense and due to our interest on green protocols correlated to the organochalcogen chemistry,[12] we describe herein the use of glycerol as a green solvent in the copper-catalyzed coupling reaction of diaryl diselenides with vinyl bromides (Scheme 1).

To identify the optimum reaction conditions, we first investigated the reaction of (*E*)-β-bromostyrene **1a** (0.6 mmol) with diphenyldiselenide **2a** (0.3 mmol) in glycerol under nitrogen atmosphere at 110 °C using different copper salts. From the variety of copper salts examined [CuI, CuCl, CuCN, CuO, $CuCl_2$ and $Cu(OAc)_2$], CuI gave the best result and using 5 mol % of this catalyst, the desired product **3a** was obtained in 43% yield. Fortunately, the addition of zinc dust (0.6 mmol) as an additive to the reaction mixture could afford the corresponding product **3a** in 95% yield after 4 h. In other experiments, the catalyst loading was varied from 1 to 10 mol % and 5 mol % of CuI gave better results. When, in the



Scheme 1. Synthesis of vinyl selenides using glycerol.

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separate control experiment, the catalyst was fully absent in the reaction mixture, zinc alone could not promote this reaction and no product **3a** was detected. Thus, it was evident that in this reaction, the use of both the copper catalyst (CuI) and zinc gave the best result.

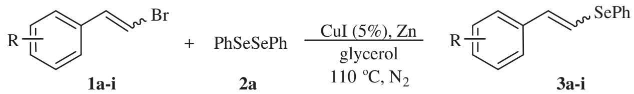
In an optimized reaction, (*E*)-β-bromostyrene **1a** (0.6 mmol), diphenyl diselenide **2a**, CuI (5 mol %), and zinc dust (0.6 mmol) were dissolved in glycerol (1.5 mL) and reacted under nitrogen at 110 °C during 4 h, yielding **3a** in 95% yield (Table 1, entry 1).[13]

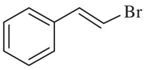
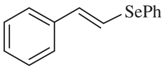
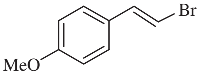
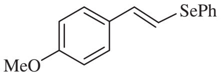
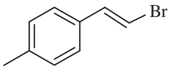
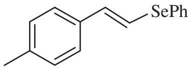
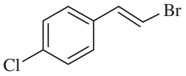
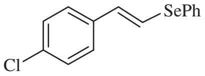
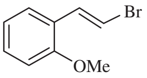
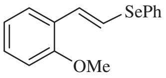
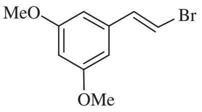
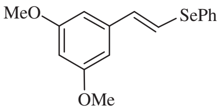
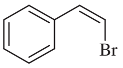
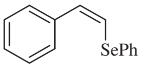
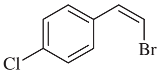
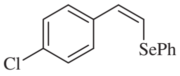
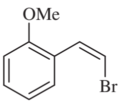
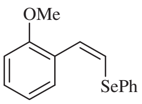
In order to demonstrate the efficiency of this protocol, we explored the generality of our methodology reacting other vinyl bromides **1b–i** with diphenyl diselenide **2a** (Table 1). A closer inspection of the results showed in Table 1 revealed that the reaction worked well with a sort of substituted vinyl bromides, affording excellent yields of the desired products. In a general way, the (*E*)-vinyl bromides **1a–f** afforded the respective (*E*)-vinyl selenides 3a–f with good selectivity, maintaining the (*E*):(*Z*) ratio of the starting halides (Table 1, entries 1–6). In contrast, the selectivity for the (*Z*)-vinyl selenides **3g–i**, slightly decreased when compared with the starting (*Z*)-vinyl bromides **1g–i** (Table 1, entries 7–9). In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with other diselenides was also investigated (Table 2). (*E*)-β-Bromostyrene **1a** (*E*:*Z* ratio = 93:7) was coupled efficiently with a variety of aryl diselenides (**2b–g**). For all the examples tested, the respective (*E*)-vinyl selenides **3j–o** were selectively obtained in very good yields using the optimized conditions (Table 2, entries 1–6). (*E*)-β-(Naphthyl)seleno styrene **3o** was obtained exclusively in 86% yield after stirring a mixture of **1a** and di(2-naphthyl) diselenide **2g** at 110 °C for 5 h (Table 2, entry 6).

Studies regarding the preparation and reactivity of zinc selenolate species generated 'on water',[14] in ionic liquid,[15] and in the presence of other solvents[16] were recently described. Due to the polarity of glycerol (three-OH groups), we believe that a nucleophilic species like PhSeZnSePh could be involved, similar to that described by Santi et al. for the reaction in the presence of water.[14a] Our glycerol-based method was also successfully applied in the

Table 1

Coupling products using vinyl bromides **1a–i** and diphenyl diselenide **2a**

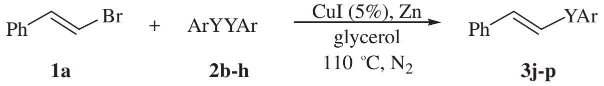


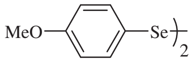
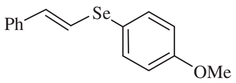
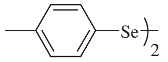
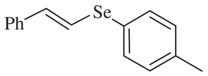
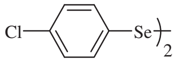
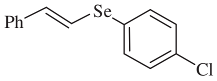
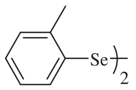
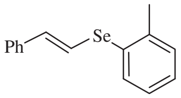
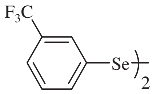
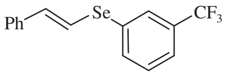
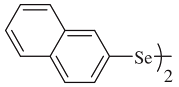
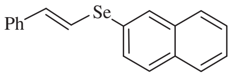
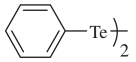
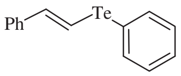
Entry	Vinyl bromide ratio (*E*:*Z*)	Time (h)	Product	Yield (%)[a,b]	Ratio (*E*:*Z*)
1	 **1a** (93:7)	4	 **3a**	95	90:10
2	 **1b** (100:0)	4	 **3b**	90	100:0
3	 **1c** (87:13)	4	 **3c**	93	92:8
4	 **1d** (97:3)	4	 **3d**	85	90:10
5	 **1e** (99:1)	6	 **3e**	90	91:9
6	 **1f** (99:1)	24	 **3f**	75	99:1
7	 **1g** (2:98)	4	 **3g**	86	8:92
8	 **1h** (4:96)	4	 **3h**	75	15:85
9	 **1i** (2:98)	3	 **3i**	88	19:81

[a] Reactions performed in the presence of vinyl bromide **1a–i** (0.6 mmol), diphenyl diselenide (0.3 mmol), Zn dust (0.6 mmol), and 5 mol % of CuI in glycerol (1.5 mL).

[b] Yields are given for isolated products.

Table 2
Coupling products using (*E*)-β-bromostyrene **1a** and diaryl dichalcogenides **2b–h**



Entry	Diaryl dichalcogenide	Time (h)	Product	Yield (%)[a,b]	Ratio (*E*:*Z*)
1	 **2b**	24	 **3j**	68	90:10
2	 **2c**	4	 **3k**	90	90:10
3	 **2d**	5	 **3l**	86	88:12
4	 **2e**	6	 **3m**	96	92:8
5	 **2f**	10	 **3n**	85	93:7
6	 **2g**	5	 **3o**	86	100:0
7	 **2h**	20	 **3p**	85	100:0

[a] Reactions performed in the presence of (*E*)-β-bromostyrene **1a** (0.6 mmol; *E*:*Z* ratio = 93:7), diaryl dichalcogenide (0.3 mmol), Zn dust (0.6 mmol), and 5 mol % of CuI in glycerol (1.5 mL).

[b] Yields are given for isolated products.

synthesis of (*E*)-styryl telluride **3p**, which was obtained exclusively in 85% yield after stirring a mixture of **1a** and diphenyl ditelluride **2h** for 20 h (Table 2, entry 7).

A reuse study of the catalyst/glycerol mixture was carried out for the reaction showed in Figure 1. After the consumption of starting materials, the reaction mixture was diluted with hexanes and the product was isolated. After complete removal of residual hexanes, the remaining CuI/Zn/glycerol mixture was directly reused for further reactions. It was observed that a good level of efficiency was maintained even after being reused four times (Fig. 1). The product **3a** was obtained in 95%, 93%, 92%, 86%, and 72% yields after successive cycles.

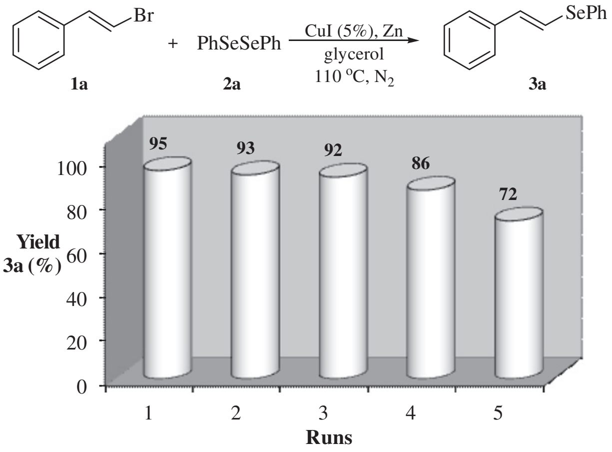


Figure 1. Reuse of CuI/Zn/glycerol.

In summary, glycerol/CuI/Zn has proved to be an efficient and recyclable catalytic system for the copper-catalyzed cross-coupling reactions of vinyl bromides with diaryl diselenides. The reactions proceed easily using this green protocol and the desired products were obtained in good to excellent yields. The glycerol/CuI/Zn can be easily recovered and utilized for further cross-coupling reactions.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.10.107.

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13. *General procedure for the cross-coupling reaction*: To a round-bottomed flask, under nitrogen atmosphere, containing CuI (0.03 mmol; 5 mol %) and Zn dust (0.6 mmol) was added glycerol (1.5 mL). The reaction mixture was stirred for 30 min at 110 °C and cooled to room temperature. After that, diaryl dichalcogenide (0.3 mmol) and vinyl bromide (0.6 mmol) were added and the reaction mixture was allowed to stir at 110 °C for the time indicated in the Tables 1 and 2. After this time, the solution was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with NH_4Cl saturated aqueous (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/hexanes as the eluent. Selected spectral data for *(E)-1-Methoxy-4-(2-phenylselanylvinyl)-benzene* **3b**:[6a] yield: 0.156 g (90%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.43 (m, 2H), 7.24–7.19 (m, 5H), 6.94 (d, J = 15.6 Hz, 1H), 6.82–6.76 (m, 3H), 3.72 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.5, 136.0, 132.1 (2C), 130.9, 130.0, 129.4 (2C), 127.5 (2C), 127.2, 116.0, 114.2 (2C), 55.4. MS m/z (%) 290 (M^+, 13), 210 (100), 195 (16), 165 (24), 132 (12), 89 (32), 77 (29).
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