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Cyclization of Homopropargyl Chalcogenides by Copper(II) Salts: Selective Synthesis of 2,3-Dihydroselenophenes, 3-Arylselenophenes, and 3-Haloselenophenes/thiophenes

Ricardo F. Schumacher, Alisson R. Rosário, Marlon R. Leite, and Gilson Zeni*[a]

Abstract: Copper(II) halide mediated cyclization of homopropargyl chalcogenides gave three types of chalcogenophene derivatives. Selective product formation was achieved by controlling solvent, temperature, and atmosphere. By using $CuBr_2$ and 1,2-dichloroethane at room temperature under ambient atmosphere, 4-bromo dihydroselenophene derivatives were obtained, whereas $CuBr_2$ and 1,2-dichloroethane at reflux gave selectively 2-substituted selenophenes. When 1,2-dichloroethane was replaced by dimethylacetamide, 3-halo-selenophenes were obtained exclusively. The versatility of chalcogenophenes was also studied by reaction of 3-haloselenophenes with terminal alkynes under Sonogashira conditions affording the cross-coupled products. In addition, the reaction of 3-haloselenophenes with boronic acids gave the corresponding Suzuki-type products in good yields.

Keywords: copper · cyclization · heterocycles · selenium heterocycles · synthetic methods

Introduction

The interest in organochalcogen compounds has increased considerably in the last decade, because incorporation of a chalcogen atom in a carbon chain modifies characteristics such as reactivity, physical properties, and pharmacological and toxicological profiles.[1] Besides the pharmacological properties, the presence of chalcogen atom in a potentially bioactive molecule can dramatically increase the native biological activity of the substrate.[2] This is mainly attributed to the fact that the chalcogen atom can serve as hydrogen-bond acceptor or electron donor that alters the chemical characteristics of an enzyme active site.[3] From the synthetic point of view, organochalcogen compounds are often chosen as ideal substrates in organic synthesis because they have an adequately polarized carbon–chalcogen bond which is susceptible to both nucleophilic and electrophilic attack with high chemo- and regioselectivity.[4] This property leads to broad applications in organic synthesis, since it allows the introduction of new functionalities. Among these applications, a major advance is the use of organochalcogen compounds as substrates in transition metal catalyzed cross-coupling reactions,[5] in transmetalation reactions,[6] and more recently in cyclization reactions.[7] Metal-catalyzed cyclization of unsaturated substrates containing heteroatoms such as nitrogen and oxygen is a widely used method for the synthesis of N and O heterocycles.[8] Cyclizations of unsaturated substrate containing a chalcogen heteroatom, catalyzed by copper salts, are practically absent from the above cited references, but some have appeared recently.[9] Among the chalcogen heterocycles, chalcogenophenes play important roles in science and technology, mainly as semiconductors applicable in high-performance, air-stable thin-film transistors,[10] and recently they have also attracted considerable attention as pharmacologically active agents.[11] Traditional methods for the synthesis of chalcogenophenes require harsh reaction conditions, strong bases, high temperature, and often the use of toxic polar solvents such as hexamethylphosphoramide (HMPA), and thus their large-scale applications in industry are limited.[12] Consequently, the preparation of chalcogenophenes by protocols that are more attractive to both academia and industry is a subject of great interest. Furthermore, we envisioned examining the versatility of the homopropargyl selenides **1** in the preparation of 4-halo-2,3-dihydroselenophenes **2**, selenophenes **3** and 3-haloselenophenes **4** by using CuX_2 as halogenating/cycling agent (Figure 1).

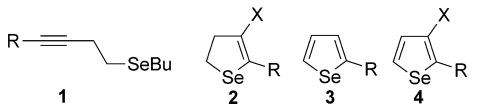

Figure 1. Alkynyl selenide **1** and selenophene derivatives **2**, **3**, and **4**.

Results and Discussion

We first turned our attention to cyclization of homopropargyl selenides **1**[13] to synthesize 4-halo-2,3-dihydroselenophenes **2**. For this purpose, we systematically evaluated the

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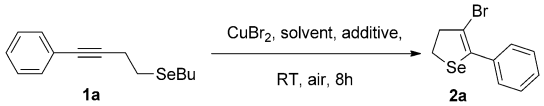
Table 1. Influence of reaction conditions on the formation of 4-bromo-2,3-dihydroselenophene (**2a**).[a]

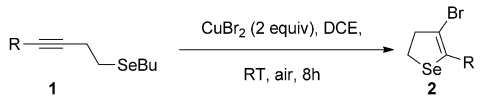


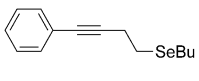
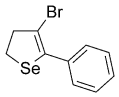
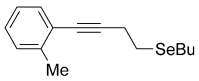
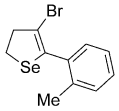
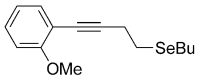
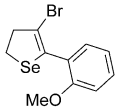
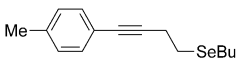
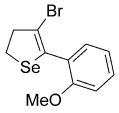
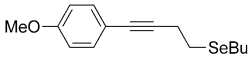
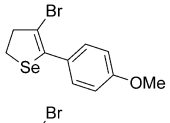
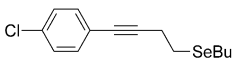
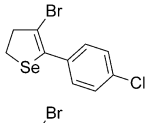
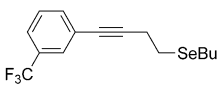
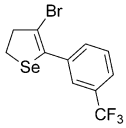
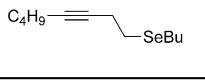
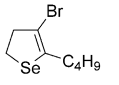
	Copper [equiv]	Solvent	Additive	Yield [%]
1	2	MeCN	–	40
2	2	acetone	–	8
3	2	toluene	–	–
4	2	DMF	–	20
5	2	THF	–	25
6	2	EtOH	–	32
7	2	DMA	–	50
8	2	CH_2Cl_2	–	50
9	2	DCE	–	72
10	1	DCE	–	38
11	0.1	DCE	–	7
12	3	DCE	–	70
13	4	DCE	–	50
14	2	DCE	LiBr[b]	42
15	2	DCE	NaBr[b]	50
16	2	DCE	Bu_4NBr[b]	65

[a] Reactions were performed with **1a** (0.5 mmol), $CuBr_2$, and solvent (4 mL) at room temperature under air for 8 h. [b] Two equivalents of additive were used.

role of solvents, temperature, additives, and the amount of copper by subjecting homopropargyl selenide **1a** to a copper(II)-catalyzed cyclization process (Table 1). In a preliminary experiment we treated homopropargyl selenide **1a** (0.5 mmol) with $CuBr_2$ (2 equiv) in MeCN at room temperature under air. After 8 h, the cyclization reaction provided only 40% yield of isolated 4-bromo-2,3-dihydroselenophene **2a** (Table 1, entry 1). Replacing the solvent MeCN by acetone resulted in a lower yield, and in the case of toluene the cyclized product was not obtained (Table 1, entries 2 and 3). The cyclization reaction was then carried out in DMF, THF, and ethanol as solvents, and the yields of isolated products were not better than 32% (Table 1, entries 4–6). The yields are rather low and could not significantly be improved by changing the solvent to dimethylacetamide (DMA) and dichloromethane (Table 1, entries 7 and 8). Among the solvents tested, 1,2-dichloroethane (DCE) provided the best yield, and product **2a** was obtained in 72% yield (Table 1, entry 9). Assuming that $CuBr_2$ acts not only as a triple-bond activator, but also as a bromine source and as oxidizing agent for Cu^0,[9a] use of less than 2.0 equiv of $CuBr_2$ would hamper the cyclization reaction. To test our hypothesis the reaction was carried out with 1.0 and 0.1 equivalents of $CuBr_2$. As predicted, under these conditions the cyclized product was obtained in poor yields (Table 1, entries 10 and 11). These results are in agreement with other studies[14] suggesting that Cu^0, formed in the reaction medium, can be oxidized by Cu^{II} to produce Cu^{I}, which justifies the need for two equivalents of $CuBr_2$ for this reaction (for mechanistic proposal, see Supporting Information). Moreover, we found that more than 2 equiv of $CuBr_2$ had no positive effect on the yield (Table 1, entries 12 and 13). It was demonstrated that certain soluble halide salts play an important roles in taking copper halides into solution.[15] These halide salts are thought to increase metal solubility and stability and to prevent aggregation of the metal. We thus screened additives using $CuBr_2$ (2 equiv) as copper source and 1,2-dichloroethane as solvent at room temperature. However, under these experimental conditions with LiBr, NaBr, or Bu_4NBr as additive, the yield of the target product was not improved (Table 1, entries 14–16). Finally, the optimal reaction conditions were determined as follows: substrate **1a** (0.5 mmol) and $CuBr_2$ (2 equiv) were stirred in 1,2-dichloroethane (2 mL) at room temperature under air for 8 h (Table 1, entry 9). On the basis of these results, we performed a systematic study by applying these conditions to several substituted homopropargyl selenides **1** to test the tolerance of functional groups and their effects on the conversion (Table 2).

Table 2. Cyclization reactions of homopropargyl selenides **1a–h** mediated by $CuBr_2$.[a]



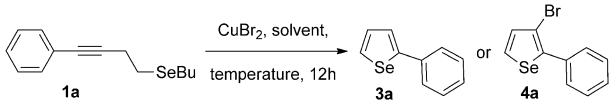
	Alkynyl selenide **1**		Product **2**		Yield [%]
1		**1a**		**2a**	72
2		**1b**		**2b**	60
3		**1c**		**2c**	55
4		**1d**		**2d**	56
5		**1e**		**2e**	62
6		**1f**		**2f**	60
7		**1g**		**2g**	57
8		**1h**		**2h**	51

[a] Reactions were performed with **1** (0.5 mmol), $CuBr_2$ (2 equiv), and 1,2-dichloroethane (2 mL) at room temperature under air for 8 h.

On the one hand, these conditions were applicable to both electron-donating (Table 2, entries 2–5) and electron-withdrawing substituents (Table 2, entries 6 and 7) on the aryl ring of homopropargyl selenides **1b–g**. Besides, the reaction yield does not seem to be strongly influenced by the steric effect of the substituent, since *ortho*-substituted aromatic rings were compatible with the reaction conditions, and the corresponding 2,3-dihydroselenophenes **2b**,**c** were obtained in very similar yields (Table 2, entries 2 and 3). On the other hand, only 51% yield of product **2h** was obtained for the cyclization between homopropargyl selenide **1h** having an alkyl group directly attached to the triple bond, where it may exert negative effects (Table 2, entry 8). *o*-Alkynylanisoles could undergo cyclization reaction in the presence of transition metal to afford benzofuran derivatives.[16] Regarding selenium versus oxygen cyclization, we did not obtain any amount of benzo[*b*]furan derivative, and the unique product obtained during the course of this cyclization was selenophene derivative **2c** (Table 2, entry 3). This high selectivity can be attributed to the electronic effect (the relative nucleophilicity of the selenium atom, the cationic nature of the intermediate) and the resistance of the methoxyl group to demethylation and ring closure.[17]

Aromatic halo heterocycles are versatile reagents in organic synthesis.[18] In particular, heterocycles such as halochalcogenophenes are useful precursors for the synthesis of a variety of more highly functionalized heterocyclic systems.[12] The most promising application of halochalcogenophenes is copper/palladium-catalyzed cross-coupling reactions.[11] For example, palladium-catalyzed cross-coupling of halo-chalcogenophenes with terminal alkynes has been widely used in the synthesis of chalcogenophenes with pharmacological activity, such as furans, thiophenes, selenophenes, and tellurophenes.[19] Other applications of halochalcogenophenes include palladium-catalyzed coupling reactions with organoboron compounds to give alkyl, aryl and heteroaryl substituents at different positions of the chalcogenophene.[20] Although a variety of reagents are effective in performing the oxidation/aromatization of dihydroheterocycles, some methods suffer from low chemical yields, strongly oxidative conditions, unwieldy workup, or side-product formation. Despite the disadvantages to this approach, recently Chen and co-workers reported a powerful strategy for the oxidation of 2,5-dihydroheterocycles using a bromine source and obtained good results in aromatization.[21] In this approach, dihydroheterocycles were used as starting materials for aromatization. To avoid multistep reactions, we envisioned that the **3** and **4** (Figure 1) could be obtained by a one-pot cyclization/aromatization sequence of homopropargyl selenides, under similar conditions to those used for the preparation of **2a** in Table 1, entry 9. For this purpose, we treated, under ambient atmosphere, homopropargyl selenide **1a** (0.25 mmol) with $CuBr_2$ (2 equiv) in refluxing 1,2-dichloroethane (2 mL). The 3-bromo-2-phenylselenophene **4a** (7% yield) was obtained besides dehalogenated selenophene **3a**, derived from cyclization/aromatization without incorporation of the bromine atom (Table 3, entry 1). This result is significant since we obtained a further class of chalcogenophenes by using similar reaction conditions. With this result in hand, we studied the behavior of the cyclization/oxidation reaction by varying solvents, temperature, and amount of copper(II) bromide (Table 3, entries 2–7). When the reaction was carried out in toluene, **4a** was obtained in 42% yield, along with 20% yield of **3a** (Table 3, entry 2). When the reaction was performed with 4 equiv of $CuBr_2$ in 1,2-dichloroethane the desired selenophene **4a** was obtained in 60% yield with complete absence of **3a** (Table 3, entry 3). No remarkable increase in the yield of the product was observed on keeping 4 equiv of $CuBr_2$ and changing the solvent from 1,2-dichloroethane to toluene or DMF (Table 3, entries 4–6). The use of dimethylacetamide as solvent with 4 equiv of $CuBr_2$ at 100°C was superior to other conditions tested (Table 3, entry 7) that either promoted the formation of 3-bromoselenophene **4a** in the best yield or avoided the formation of **3a**. Under the reaction conditions shown in Table 3, homopropargyl selenides **1a** and 2 equiv of $CuBr_2$ under ambient atmosphere in 1,2-dichloroethane at reflux gave preferably selenophene **3a**, whereas using 4 equiv of $CuBr_2$ in dimethylacetamide at 100°C gave exclusively the 3-bromoselenophene **4a**.

Table 3. Influence of reaction conditions on the preparation of selenophenes **3a** and **4a**.[a]

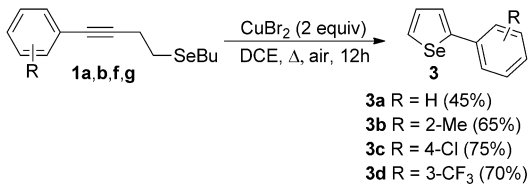


	$CuBr_2$ [equiv]	Solvent	Yield of **3a**:**4a** [%]
1	2	DCE	45:7
2	2	toluene[b]	20:42
3	4	DCE	–:60
4	4	toluene[b]	–:58
5	2	DMF[b]	–:50
6	4	DMF[b]	–:65
7	4	DMA[b]	–:86

[a] Reactions were performed with **1a** (0.5 mmol) and solvent (4 mL) at reflux temperature under air. [b] A temperature of 100°C was used.

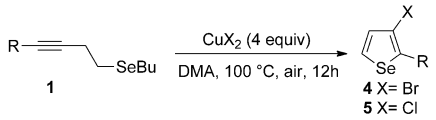
We systematically applied the conditions of entries 1 and 7 in Table 3 to other substituted homopropargyl selenides **1** to test the tolerance for functional groups and their effects on the conversion. For preparation of selenophenes **3**, aryl groups having neutral and electron-donating substituents gave the worst yields of 45 and 65% compared to the substituent having electron-withdrawing groups which afforded the cyclized products in 75 and 70% yield (Scheme 1).

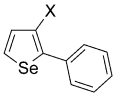
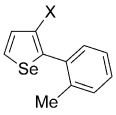
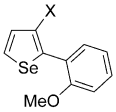
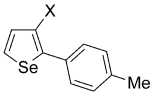
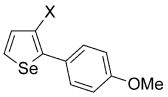
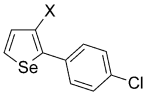
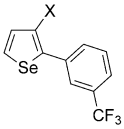
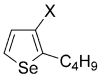
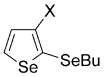
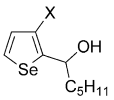
Beside the synthesis of 2-substituted selenophenes **3**, a series of 3-halo 2-substituted selenophenes **4** and **5** was also prepared (Table 4). For the preparation of 3-bromo-selenophene **4**, we observed that the reaction yield does not seem to be strongly influenced by the electronic effect of the substituent, since different aryl groups having neutral, electron-withdrawing, and electron-donating groups in the aromatic rings were compatible with the reaction conditions, and yielded the corresponding selenophenes **4a–g** without any



Scheme 1. Synthesis of 2-arylselenophenes **3**.

Table 4. Synthesis of 3-bromoselenophenes **4a–j**[a] and 3-chlorochalcogenophenes **5a–j**.[b]

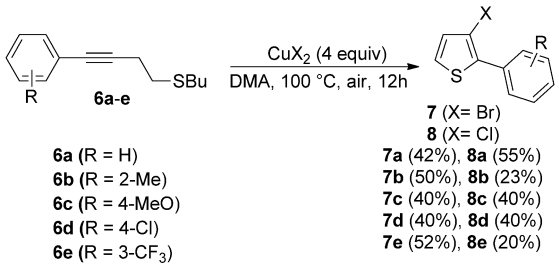


	Alkynyl selenide **1**	Product **4** or **5**		Yield [%]
1	**1a**		**4a** **5a**	86 67
2	**1b**		**4b** **5b**	30 41
3	**1c**		**4c** **5c**	53 52
4	**1d**		**4d** **5d**	78 68
5	**1e**		**4e** **5e**	60 48
6	**1f**		**4f** **5f**	85 77
7	**1g**		**4g** **5g**	69 66
8	**1h**		**4h** **5h**	63 56
9	**1i**		**4i** **5i**	42 35
10	**1j**		**4j** **5j**	53 60

[a] Conditions for synthesis of **4a–j**: alkyne **1** (0.5 mmol) and $CuBr_2$ (4 equiv) in dimethylacetamide (4 mL) at 100 °C for 12 h.

major byproducts and in very similar yields (Table 4, entries 1–7). However, a moderate yield of product **4b** was obtained for cyclization with homopropargyl selenide **1b** having a methyl group at the *ortho* position, that is, the steric hindrance of the *o*-methyl group appears to exert a significant negative effect (Table 4, entry 2). When the reaction was carried out with homopropargyl selenide **1h** having an alkyl group directly bonded to the alkyne, a decrease in the yield was observed, and cyclized 3-bromo-4-butyl-selenophene **4h** was obtained in 63% yield (Table 3, entry 8). The use of propargyl alcohol **1j** or alkyl selenide substituted **1i** as substrate was also tested, and cyclization gave the desired cyclized 3-bromoselenophenes in moderate yields (Table 4, entries 9 and 10). Our methodology could be readily adapted to the preparation of 3-chloroselenophenes **5** simply by replacing $CuBr_2$ with $CuCl_2$ (Table 4). This result is significant, particularly when the different reactivity of the halogens for further functionalization is considered.

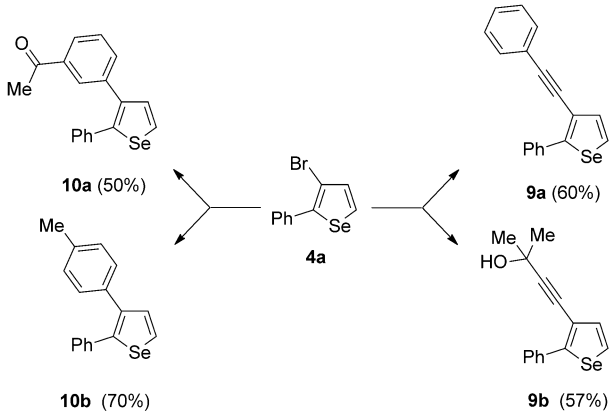
Thiophenes are useful substrates found in numerous natural products and biologically active molecules.[21] In this context, we also investigated the behavior of homopropargyl sulfides **6** containing differently substituted aromatic rings. The synthesis of 3-bromo- and 3-chlorothiophenes **7** and **8** was also feasible employing $CuBr_2$ and $CuCl_2$, respectively, in dimethylacetamide at 100 °C under air (Scheme 2). The



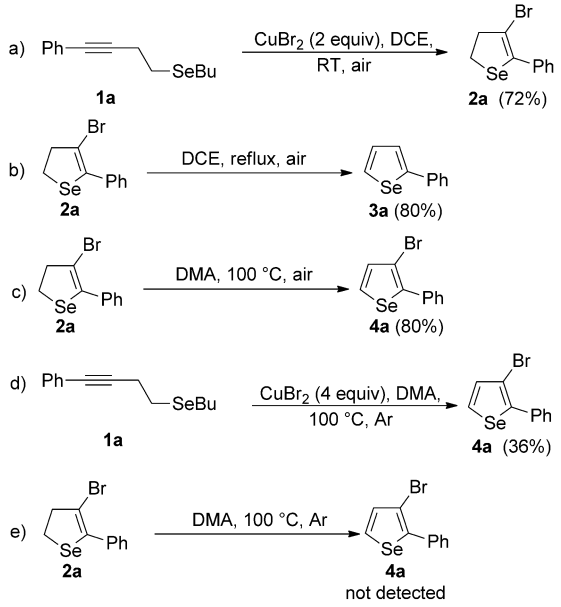
Scheme 2. Synthesis of 3-halothiophenes **7** and **8**.

cyclization reaction tolerated neutral, electron-donating, and electron-withdrawing groups and gave the expected products in moderate yields. Although the yields are lower than those of selenophenes under the same conditions, this may be acceptable considering the higher nucleophilicity of selenium compared to sulfur and that a halogenated aromatic heterocycle is generated from an acyclic substrate in a simple and easily handled protocol.

To complete our investigation and to show the versatility and the synthetic value of our methodology, we tested the reactivity of 3-bromoselenophene **4a** toward Sonogashira- and Suzuki-type cross-coupling reactions. Thus, the reaction of **4a** with terminal alkynes in the presence of a cooperative Pd/Cu system as catalyst in Et_3N afforded the 3-alkynylselenophenes **9a** (from phenylacetylene) and **9b** (from 2-methyl-3-butyn-2-ol) in 60 and 57% yield of isolated product, respectively. In addition, the reaction of **4a** with *m*-acetylphenyl boronic acid and *p*-methylphenyl boronic acid gave the corresponding Suzuki-type products **10a** and **10b** in 50 and 70% yield, respectively (Scheme 3).



Scheme 3. Suzuki- and Sonogashira-type cross-coupling reactions of 3-bromo-selenophene **4a**. a) $[Pd(PPh_3)_4]$ (5 mol%), K_3PO_4 aq, $ArB(OH)_2$, toluene/dioxane, 90°C. b) $[PdCl_2(PPh_3)_2]$ (5 mol%), CuI (10 mol%), alkyne, Et_3N, 80°C.



Scheme 4. Experiments on mechanism elucidation.

To demonstrate the influence of air as a non-unique but essential oxidant in the formation of the selenophene ring, as well as to obtain evidence for the reaction mechanism, we carried out the experiments depicted in Scheme 4. 1) As demonstrated in Table 2 (entry 1), homopropargyl selenide **1a** reacted with $CuBr_2$ in 1,2-dichloroethane at room temperature under air to give **2a** in 72% yield (Scheme 4a). 2) When dichloromethane was heated to reflux under air in the presence of substrate **2a** and in the absence of $CuBr_2$, selenophene **3a** was obtained in 80% yield (Scheme 4b). This indicates that substrate **2a** is the key intermediate in the reaction of homopropargyl selenide **1** with $CuBr_2$ to form product **3**. When the solvent was changed to dimethylacetamide, **4a** was obtained in 80% yield (Scheme 4c). This suggests that dimethylacetamide is also essential for the cyclization mediated by $CuBr_2$. 4) The experiments depicted in Scheme 4d and e were conducted with homopropargyl selenide **1a** and dihydroselenophene **2a** under our optimized conditions to obtain 3-bromoselenophenes **3**, but argon atmosphere was used instead of air. Under these conditions, propargyl selenide **1a** in the presence of $CuBr_2$ gave a mixture of 2,3-dihydroselenophene **2a** as major product and the expected product **3a** in 36% yield (Scheme 4d). In the absence of $CuBr_2$ no product **3a** was obtained and dihydroselenophene **2a** was completely recovered. These reactions show that 1) room temperature is essential to formation of 4-halo-2,3-dihydroselenophenes; 2) the formation of selenophenes **3** depends on the solvent and temperature; 3) temperature and air are crucial to the formation of 3-halo-selenophenes **4**; and 4) 4-halo-2,3-dihydroselenophene **2** seems to be a common intermediate to the formation of both selenophenes **3** and 3-haloselenophenes **4**.

Conclusion

We have developed an alternative and selective method for the synthesis of chalcogenophene derivatives by intramolecular 5-*endo-dig* cyclization of homopropargyl chalcogenides. This study introduced copper(II) salts as halogenating/cyclizing agent for the selective preparation of 4-halodihydroselenophenes **2**, 2-substituted selenophenes **3**, and 3-halochalcogenophenes **4**, **5**, **7**, and **8**. These results are significant since, using similar reaction conditions, we obtained four classes of chalcogenophene derivatives. The reactions were carried out under air, which is considered an economic protocol. Unfortunately, under these cyclization reactions alkynyl sulfides could not be used to generate 2,3-dihydrothiophenes, since they proved to unreactive under the presented conditions. The presence of a halogen substituent in the selenophene structure allowed further structural elaboration through conversion of the halogen group to other substituents. For example, employing compound **4a** as substrate under Suzuki and Sonogashira coupling conditions afforded the corresponding products through C–C bond formation in moderate to good yields. Another feature of this protocol is that the reactions were carried with copper salts, which are readily available commercially, inexpensive, and relatively nontoxic.

Experimental Section

General procedure for CuX_2-promoted synthesis of 5-substituted-2,3-dihydroselenophenes 2: Two equivalents of $CuBr_2$ were added to a solution of 0.5 mmol of the appropriate alkynyl selenide **1** in 4 mL of DCE. The reaction mixture was allowed to stir at room temperature for the desired time. The reaction was quenched with saturated aqueous NH_4Cl/NH_4OH (20 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous Mg_2SO_4 and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel with hexane as the eluent. Representative data for 4-bromo-5-phenyl-2,3-dihydroselenophene **(2a):** Yield: 0.103 g (72%); ^1H NMR ($CDCl_3$, 400 MHz): $\delta=7.57$–7.48 (m, 2H), 7.40–7.29 (m, 3H), 3.43–3.32 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=135.0$, 130.9,

128.7, 128.5, 128.2, 105.0, 47.0, 22.2; MS: *m/z* (%): 287 (33), 128 (100), 115 (31), 102 (12), 89 (16), 208 (12); elemental analysis (%) calcd for $C_{10}H_9BrSe$: C 41.70, H 3.15; found: C 41.85, H 3.22.

General procedure for CuX_2-promoted synthesis of 2-substituted-selenophenes 3: Two equivalents of $CuBr_2$ were added to a solution of 0.5 mmol of the appropriate alkynyl selenide **1** in 4 mL of DCE. The reaction mixture was allowed to stir at reflux temperature for the desired time. The reaction was quenched with saturated aqueous NH_4Cl/NH_4OH (20 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous Mg_2SO_4 and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel with hexane as eluent. Representative data for 2-phenylselenophene **(3a)**: Yield: 0.046 g (45%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.91 (dd, J = 5.4, 1.0 Hz, 1H), 7.60–7.52 (m, 2H), 7.45 (dd, J = 3.6, 1.0 Hz, 1H), 7.40–7.25 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 150.7, 136.3, 130.5, 129.9, 128.8, 127.5, 126.3, 125.1 ppm; MS: *m/z* (%): 208 (64), 128 (100), 115 (23), 102 (21), 51 (12).

General procedure for CuX_2-promoted synthesis of 3-halo 2-substituted selenophenes 4 and 5: Four equivalents of CuX_2 were added to a solution of 0.5 mmol of the appropriate alkynyl selenide **1** in 4 mL of DMA. The reaction mixture was allowed to stir at 100 °C for the desired time. The reaction was quenched with saturated aqueous NH_4Cl/NH_4OH (20 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous Mg_2SO_4 and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel with hexane as the eluent. Representative data for 3-bromo-2-phenylselenophene **(4a):** Yield: 0.122 g (86%); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.91 (d, J = 5.86 Hz, 1H), 7.63–7.57 (m, 2H), 7.46–7.34 ppm (m, 3H), 7.30 (d, J = 5.86 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 142.9, 134.6, 134.3, 129.9, 129.2, 128.4, 128.1, 107.9 ppm; MS: *m/z* (%): 285 (77), 206 (26), 126 (34), 115 (100), 103 (11), 89 (10); elemental analysis (%) calcd for $C_{10}H_7BrSe$: C 41.99, H 2.47; found: C 42.12, H 2.55.

General procedure for CuX_2-promoted synthesis of 3-halo 2-substituted thiophenes 7 and 8: Four equivalents of CuX_2 were added to a solution of 0.5 mmol of the appropriate alkynyl sulfide **6** in 4 mL of DMA. The reaction mixture was allowed to stir at 100 °C for the desired time. The reaction was quenched with saturated aqueous NH_4Cl/NH_4OH (20 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous Mg_2SO_4 and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel with hexane as eluent. Representative data for 3-bromo-2-phenylthiophene **(7a)**: Yield: 0.025 g (42%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.67–7.62 (m, 2H), 7.47–7.36 (m, 3H), 7.28–7.23 (m, 1H), 7.06–7.03 ppm (d, J = 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 138.2, 132.8, 131.6, 129.0, 128.4, 128.2, 124.9, 107.5 ppm; MS: *m/z* (%): 239 (91), 159 (15), 115 (100), 79 (14); elemental analysis (%) calcd for $C_{10}H_7BrS$: C 50.23, H 2.95; found: C 50.44, H 3.02.

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