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Diorganyl Dichalcogenides-Promoted Nucleophilic Closure of 1,4-Diyn-3-ols: Synthesis of 2-Benzoyl Chalcogenophenes

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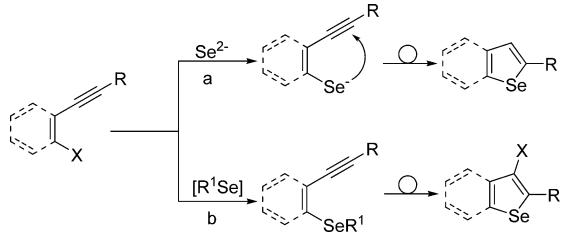
Supporting Information

ABSTRACT: We report here the preparation of chalcogenophene derivatives via cyclization reactions of diynols promoted by diorganyl dichalcogenides and a halogen source. Different chalcogenophenes, such as 4-halo-selenophenes, 4-butylselenyl-selenophenes, halo-thiophenes, and 4-methylthio-thiophenes, were selectively prepared in good yields from the same starting materials. The results revealed that the halogen source had a significant effect on the proportion of 4-bromo-selenophenes and 4-butylselenyl-selenophenes. The best yields of 4-iodo-selenophenes were obtained with iodine as a halogen source, while the use of NBS gave exclusively the 4-butylselenyl-selenophenes. The experiments also revealed that the cyclization reaction to form 4-halo-thiophene derivatives can also be controlled changing the ratios of reagents. The 4-iodo-thiophenes were exclusively obtained by using dimethyl disulfide (2.0 equiv) and iodine (1.5 equiv), while the 4-bromo-thiophenes were obtained when the reaction was carried out with a 1.5 molar ratio of dimethyl disulfide and a halogen source. In addition, the reaction of diynols with an excess of dimethyl disulfide in the presence of NBS gave the 4-methylthio-thiophenes as sole products. We also studied the application of chalcogenophenes obtained as starting materials in the Suzuki, Sonogashira, and Ullmann cross-coupling reactions.

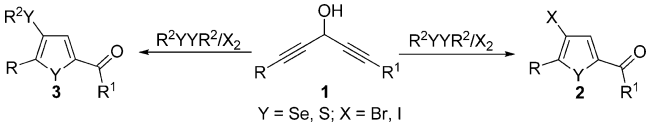
INTRODUCTION

Chalcogen-heterocycles have attracted much attention in both academia and industry due to their applications in a wide range of electronic and optoelectronic devices.[1] In particular, chalcogenophenes have been widely used as organic light emitting diodes (OLEDs),[2] organic field effect transistors (OFETs),[3] organic solar cells (OSC),[4] and photorefractive holography.[5] In addition to the progress in materials science, chalcogenophenes have been reported to have pharmacological activities.[6] They are used, among others, for their hepatoprotective,[7] anticonvulsant,[8] antioxidant,[9] antidepressant,[10] anticancer,[11] antitumor,[12] and antiviral properties.[13] In view of their pharmacological activities and applications in material science, considerable efforts have been made to develop new methodologies for the direct preparation of chalcogenophenes.[14] Two main general approaches to the synthesis of chalcogenophenes have been reported to date: (1) Addition of either electrophilic or nucleophilic chalcogen reagents to appropriate acyclic precursors followed by an intramolecular cyclization (Scheme 1, pathway a).[15] Usually, the chalcogenation reactions of a substrate occur with high regio- and stereoselectivity,[16] affording the intermediate with a proper structural arrangement, which allows the direct chalcogen cyclization step. (2) Preparation of a suitable organochalcogen substrate followed by a transition-metal-catalyzed cyclization or electrophilic cyclization reaction (Scheme 1, pathway b).[17] The cyclization of organochalcogen substrates consists of the activation of the reactive center, usually an unsaturated carbon−carbon bond, through a transition metal or electrophilic source with subsequent nucleophilic chalcogen cyclization.[18] The advantage of this latest method is that the intermediate formed is suitable to undergo further transformations, in special palladium cross-coupling reactions.[19] Although highly efficient approaches to synthesize chalcogenophenes have been developed, we reasoned that further improvement is still possible. Toward this end, we proposed that the reaction of diynols **1** with diorganyl dichalcogenides and halogens could be a suitable approach to the synthesis of chalcogenophenes **2** and **3** (Scheme 2). The innovative features of this reaction are the preparation of different chalcogenophene derivatives from the same starting materials and the use of diorganyl dichalcoge-

Scheme 1



Scheme 2



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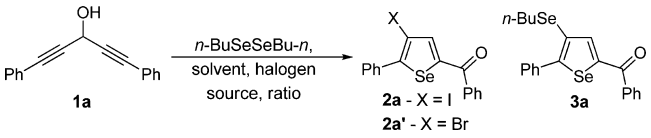
nides and a halogen source not only as the cyclizing agent but also to incorporate new functionalities in the chalcogenophene ring. In addition, the use of this strategy avoids the previous preparation of organoselenium substrates or unstable and air-sensitive selenolate anions.

RESULTS AND DISCUSSION

The desired symmetrical diynols were prepared in high yields by treatment of ethyl formate with alkynyl lithium.[20] The corresponding unsymmetrical diynols were synthesized by the reaction of alkynyl aldehydes with alkynyl lithium according to earlier reported procedures.[21] The conditions for the cyclization were optimized beginning with the reaction of diynol **1a** with di-*n*-butyl diselenide (0.5 equiv) and NBS (1.0 equiv) in dichloromethane. The progress of the reaction was monitored using TLC, which indicated the consumption of the starting material after 15 min in an open atmosphere at room temperature and the appearance of two spots. After the GC/MS analysis, the products were identified as a 67:33 mixture of 4-bromo-selenophene **2a′** and 4-butylselenyl-selenophene **3a**, respectively (Table 1, entry 1). The results revealed that the molar ratios of the reagents had great effect on the proportion of 4-bromo-selenophene **2a′** and 4-butylselenyl-selenophene **3a**. The use of di-*n*-butyl diselenide (1.5 equiv) and NBS (1.5 equiv) significantly improved the reaction leading to the exclusive formation of 4-butylselenyl-selenophene **3a** in 96% yield (Table 1, entry 3). The experiments revealed that the cyclization reaction can be also controlled to exclusively form 4-iodo-selenophene **2a** or 4-butylselenyl-selenophene **3a**, by changing the halogen source. The complete consumption of **1a** was obtained using bromine as halogen source, at room temperature within 15 min, which exclusively afforded **3a** in 90% yield (Table 1, entry 4). On the other hand, under identical conditions, the change in halogen source to iodine gave the 4-iodo-selenophene **2a** in 91% yield as the sole product (Table 1, entry 5). Of the reactions to obtain the 4-iodo-selenophene **2a** using different solvents, the best results were obtained with dichloromethane and dichloroethane (Table 1, entries 5−10). This model reaction was also carried out under an inert atmosphere of argon, which did not further improve the yield of 4-iodo-selenophene **2a** (Table 1, entry 11). We also optimized the molar ratios of the reagents. When 0.3 mmol of diynol **1a** was used the maximum yield of 4-iodo-selenophene **2a** (96%) could be achieved in a 1.5 molar ratio of di-*n*-butyl diselenide and iodine (Table 1, entries 12−14). During the course of the optimization, the reaction, monitored by TLC, showed that diynol **1a** was completely consumed after 1.5 h; however, the aqueous workup after this reaction time afforded the 4-iodo-selenophene **2a** in poor yield (Table 1, entry 15). The target reaction became rapid giving the highest yield with the addition of ethanol (1.0 mL) after 15 min (Table 1, entry 16). On the basis of the above-mentioned results, although the exact structures of intermediates in the cyclization of diynol **1a** are unknown, we propose a reduction of the carbon−carbon triple bond via the electrophilic addition of BuSeI, obtained in situ via reaction of di-*n*-butyl diselenide and iodine, giving the *E*-vinyl selenide **a**[22] (Scheme 3). The alkyne coordination to the additional BuSeI leads to the seleniranium intermediate **b** and iodide species.[23] The subsequent selenium nucleophilic intramolecular *anti* attack at the activated triple bond affords the dihydroselenophene **c**, via a selective intramolecular 5-*exo*-dig cyclization.[24] The 1,3-migration of the hydroxyl, via allylic cation **d**,[17a] gives the O,Se-ketal **e**, which affords the 4-iodo-selenophenes **2** after elimination of butylselenolate (Scheme 3). The butylselenolate anion delivered to the reaction medium could attack the carbonyl group of ketone at the 2-position of the selenophene to afford the Se-ketals. However, under these aerobic conditions, the selenolate ion was rapidly oxidized to diselenide avoiding the formation of byproducts.

Table 1. Effect of Different Reaction Parameters on Cyclization of Diynol 1a[a]



entry	solvent	*n*-BuSeSeBu-*n* (equiv)	halogen source (equiv)	yield (%)[b] 2a	3a
1[c,d]	DCM	0.5	NBS (1.0)	–	–
2	DCM	1.5	NBS (3.0)	23	77
3	DCM	1.5	NBS (1.5)	–	96
4	DCM	1.5	Br_2 (1.5)	–	90
5	DCM	1.2	I_2 (1.2)	91	–
6	DCE	1.2	I_2 (1.2)	91	–
7	MeCN	1.2	I_2 (1.2)	51	–
8	THF	1.2	I_2 (1.2)	80	–
9	hexane	1.2	I_2 (1.2)	–	–
10	acetone	1.2	I_2 (1.2)	–	–
11[e]	DCM	1.2	I_2 (1.2)	90	–
12	DCM	1.1	I_2 (1.1)	80	–
13	DCM	1.5	I_2 (1.5)	96	–
14	DCM	1.5	I_2 (1.0)	93	–
15	DCM	1.5	I_2 (1.5)	20[f]	–
16	DCM	1.5	I_2 (1.5)	98[g]	–

[a]The reaction was performed by the addition of a halogen source to a solution of di-*n*-butyl diselenide in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added. [b]Yields shown are of isolated products. [c]A 67:33 mixture of selenophenes **2a′**:**3a** was obtained. The formation of **2a′** could involve the bromonium ion in the second step of the cyclization. [d]When the reaction was run with a catalytic amount of NBS di-*n*-butyl diselenide and diynol **1a** were recovered. [e]The reaction was carried out under an inert atmosphere of argon. [f]Water was added after 1.5 h at room temperature. [g]Ethanol was added after 15 min at room temperature.

While the formation of the 4-iodo-selenophenes **2** may be attributed to the formation of vinylic selenides **a** as an intermediate, the formation of vinylic selenide **f** probably is the crucial step for the formation of 4-butylselenyl-selenophenes **3** (Scheme 4). The analysis of the products led us to infer that the reaction with BuSeI gave the vinylic selenide **a**, while the reaction with BuSeBr gave the vinylic selenide **f**. Consequently, we concluded that the regiospecific anti-addition of the selenium electrophile to the triple bond of propargylic alcohols **1** involves the direct effect of the halogen atom. Extensive work on the addition of selenium electrophilic species to alkynes has disclosed that the halogen species, the solvent, and the presence of an oxygen atom at the propargyl position of the substrates are important structural factors that affect the regiochemical preference.[25] Due to their very high reactivity to give the cyclized products, our efforts to isolate and identify the intermediates failed. However, on the basis of the assigned

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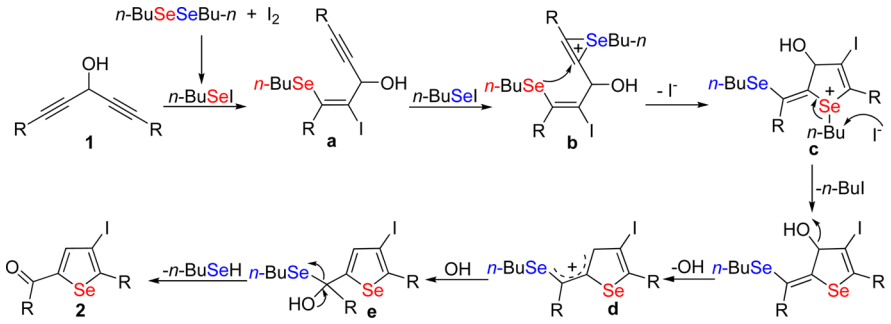
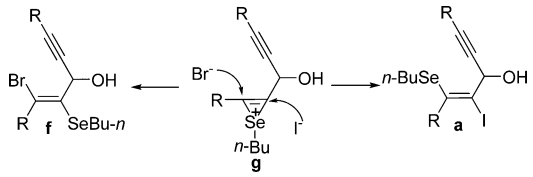
Scheme 3



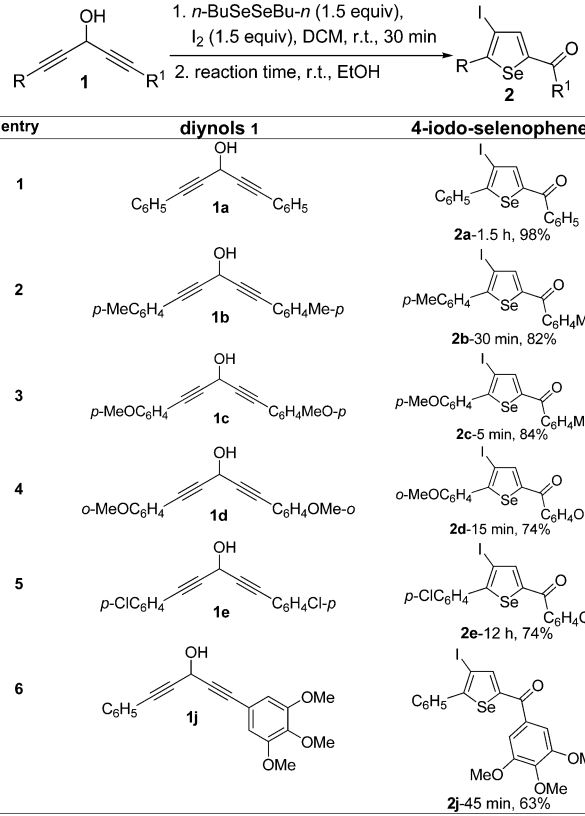
Scheme 4



structures for the 4-butylselenyl-selenophenes **3**, the mechanism for the formation of vinylic selenide **f** may be rationalized via the initial formation of the seleniranium ion **g**,[26] which was formed by the reaction of the electrophilic selenium reagents with acetylenes. The steric hindrance of the seleniranium ion **g** in association with the smaller size of bromine directs the nucleophilic attack of the bromide ion at carbon 1, while the larger iodide anion attacks the distal carbon of the triple bond (Scheme 4). From the vinylic selenide **f**, we propose the following mechanism for the formation of 4-butylselenyl-selenophenes **3**: (1) the carbon−carbon triple bond of **f** reacts with BuSeBr generating an seleniranium intermediate **h**; (2) the intramolecular nucleophilic attack of the selenium atom at the activated triple bond forms dihydroselenophene **i**; (3) dihydroselenophene **i** undergoes 1,3-migration of the hydroxyl group followed by HBr elimination to generate 4-butylselenyl-selenophenes **3** (Scheme 5).

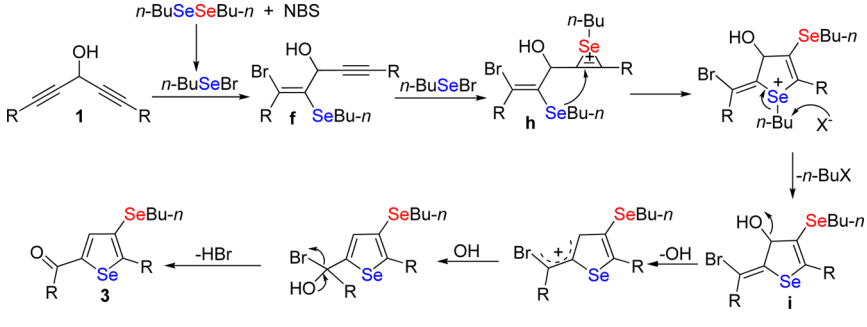
On the basis of the optimized reaction conditions shown in Table 1, we concluded that the best yield of 4-iodo-selenophene **2a** was obtained using the diynol **1a** (0.3 mmol) in combination with di-*n*-butyl diselenide and iodine in the ratio of 1.5 equiv, in dichloromethane (3 mL) with addition of ethanol, after 1.5 h at room temperature (Table 1, entry 16). In the next series of experiments, we studied the applicability of these reaction conditions to other diynols **1a−f** and the results are shown in Table 2. First, symmetrical diynols **1a−d** were subjected to the title reaction. The reactions with aryl groups

Table 2. Synthesis of 4-Iodo-selenophene 2[a]



[a]The reaction was carried out by the addition of iodine (1.5 equiv) to a solution of di-*n*-butyl diselenide (1.5 equiv) in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added; the reactions were run at room temperature for the indicated time, and ethanol was added.

Scheme 5



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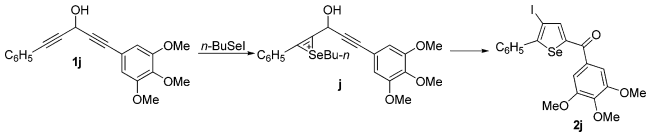
directly bonded to an alkyne, bearing either neutral or electron-rich substituents, proceeded efficiently to afford the 4-iodo-selenophenes **2a–d** in good yields and in short reaction times (Table 2, entries 1–4). The introduction of an electron-deficient substituent on the aryl group gave the selenophene **2e** in 74% yield, but a longer reaction time was needed for completion of the reaction, indicating an electron-deficient substituent on the aryl group has a pronounced effect (Table 2, entry 5). The cyclization of unsymmetrical diynol **1j** proceeds regioselectively with the exclusive formation of **2j** in 63% yields (Table 2, entry 6). The sterically bulky trimethoxybenzene present in the alkyne might contribute to the exclusive formation of the intermediate **j**, which is the key intermediate to the 4-iodo-selenophene **2j** (Scheme 6). This result supports

Scheme 6

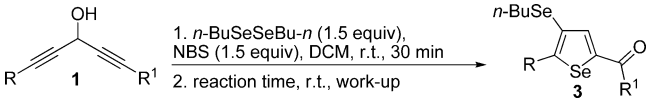


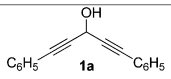
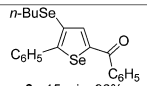
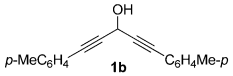
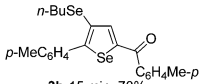
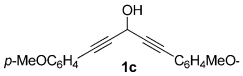
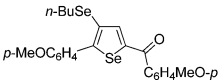
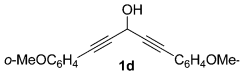
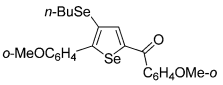
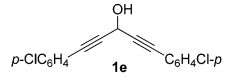
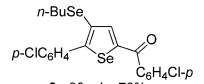
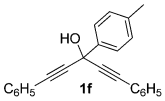
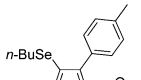
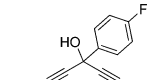
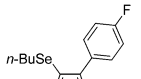
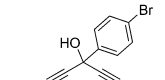
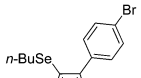
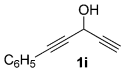
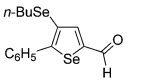
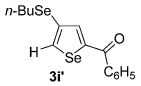
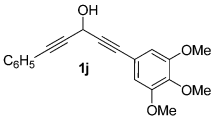
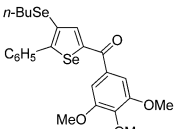
our statement that a sterically bulky group has a significant influence on the regioselectivity of this cyclization. The structure of selenophene **2j** agrees with HRMS as well as ^{1}H and ^{13}C NMR spectra as listed in the Experimental Section. In addition, the crystal structure shown in Figure S1 (Supporting Information, CCDC 1029272) confirms the exact positions of the benzene and the trimethoxybenzene groups on the selenophene ring.

As shown in Table 1 (entry 3), when diynol **1a** reacted with NBS instead of iodine and di-*n*-butyl diselenide in the ratio of 1.5:1.5, in dichloromethane (3 mL), the 4-butylselenyl-selenophene **3a** was exclusive obtained in 96% yield. In order to explore the general effectiveness of our method a number of diynols **1** were subjected to these conditions and the results are summarized in Table 3. Although the reaction with symmetrical diynol **1a** having a neutral phenyl group at the end of the alkyne resulted in the formation of the 4-butylselenyl-selenophene **3a** in high yield, other symmetrical diynols **1b–1e** with *p*-MeC_6H_4, *p*-$MeOC_6H_4$, *o*-MeC_6H_4, *p*-ClC_6H_4 groups at the end of the alkyne also gave the 4-butylselenyl-selenophenes **3b–3e** in good yields (Table 3, entries 1–5). In contrast, when we extended the optimized conditions to tertiary diynols **1f–h** only moderated yields of the 4-butylselenyl-selenophenes **3f–3h** were obtained (Table 3, entries 6–8). In these examples, the starting materials were consumed in a short time, but even after the reaction time was extended and reflux temperatures were used, the yields were not improved. In these cases, side products were observed which could not be identified. The cyclization of unsymmetrical diynols **1i** and **1j** resulted in the formation of 4-butylselenyl-selenophenes **3i** and **3j** in 80% and 68% yields, respectively, in the absence of regioisomers (Table 3, entries 9 and 10). This regioselectivity could be explained by the nucleophilicity of the bromine ion, which would guide the preferential attack to strong stabilizing seleniranium **k** promoted by the π bonds from the aromatic ring next to the alkyne (Scheme 7).

The significant importance of thiophenes as units often observed in biologically active compounds[27] prompted us to apply the sequential cyclization reaction to the preparation of 4-halothiophene derivatives **4** and **5** (Table 4). Initially, diynol **1a** was submitted to the reaction with dimethyl disulfide and

Table 3. Synthesis of 4-Butylselenyl-Selenophenes 3[a]



entry	diynols 1	4-butylselenyl-selenophenes 3
1		 **3a**-15 min, 96%
2		 **3b**-15 min, 78%
3		 **3c**-5 min, 75%
4		 **3d**-15 min, 72%
5		 **3e**-30 min, 70%
6		 **3f**-12 h, 48%
7		 **3g**-12 h, 44%
8		 **3h**-12 h, 49%
9		 **3i**-30 min, 80%  **3i'** not observed
10		 **3j**-15 min, 68%

[a]The reaction was carried out by the addition of NBS (1.5 equiv) to a solution of di-*n*-butyl diselenide (1.5 equiv) in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added; the reactions were run at room temperature for the indicated time, and $Na_2S_2O_3$ (aq) was added.

iodine in the ratio of 1.5:1.5, in dichloromethane (3 mL) at room temperature, under aerobic conditions, with workup after 1.5 h. The desired product 4-iodo-thiophene **4a** was obtained in a moderated yield (Table 4, entry 1). It was found that the use of a stoichiometric amount or a slight excess of iodide gave the

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Scheme 7

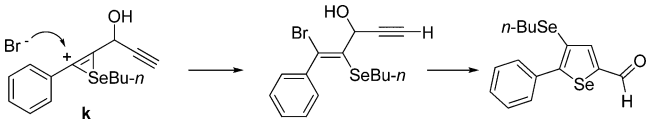
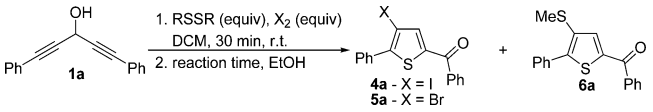


Table 4. Effect of Different Reaction Parameters on Cyclization of Diynol 1a[a]



entry	RSSR (equiv)	R	X_2 (equiv)	reaction time (h)	yield (%) **4a**
1	1.5	Me	I_2 (1.5)	1.5	55
2	2.0	Me	I_2 (2.0)	1.5	58
3	3.0	Me	I_2 (1.5)	1.0	73
4	3.0	Et	I_2 (1.5)	1.0	68
5	1.5	Me	Br_2 (1.5)	0.5	82[b]
6	2.0	Me	Br_2 (2.0)	0.5	78[b]
7	3.0	Me	Br_2 (1.5)	0.5	48[b]
8	1.5	Me	NBS (1.5)	1.5	–[c]

[a]The reaction was performed by the addition of a halogen source to a solution of dialkyl disulfides in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min, the diynol **1** (0.3 mmol) was added; the reactions were run at room temperature for the indicated time, and ethanol was added. [b]4-Bromo-thiophene **5a** was obtained. [c]A 1:2 mixture of thiophenes **5a**:**6a** was obtained.

addition product of iodine to the alkyne. This reduction of the triple bond by iodine suggests that, in a competition reaction between iodine and electrophilic sulfur species, the diynol **1a** preferentially reacts with iodine (Table 4, entries 1–2). In this way, the further increase in the amount of dimethyl disulfide to 3 equiv led to a good yield of **4a** (Table 4, entry 3). The use of diethyl disulfide instead of dimethyl disulfide did not improve the yield of **4a** (Table 4, entry 4). The effect of bromine as the halogen source to the preparation of 4-bromo-thiophene derivative **5a** was also examined. For instance, the cyclization reaction of diynol **1a** with a stoichiometric amount of bromine and dimethyl disulfide (1.5 equiv), in dichloromethane (3 mL) at room temperature, with workup, after 0.5 h, gave the target 4-bromo-thiophene **5** in 82% yield (Table 4, entry 5). Additional experiments were carried out changing the temperature, solvents, and molar ratio between bromine and dimethyl disulfide but were ineffective to improve the yield of **5a**. In addition, when the halogen source was changed to NBS (1.5 equiv) a 2:1 mixture of 3-methylsulfide-thiophene **6a** and 4-bromo-thiophene **5a** was obtained (Table 4, entry 8).

Therefore, the optimal reaction conditions for the formation of 4-iodo-thiophene derivatives **4** are the addition of iodine (1.5 equiv) to a solution of dimethyl disulfide (3.0 equiv) in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere and after 15 min the addition of diynol **1** (0.3 mmol). These conditions were then applied to other diynols **1a–g** to explore the substrate generality, and the results are presented in Table 5. We started our experiments studying the influence of aryl groups bonded to the alkyne (Table 5, entries 1–4). For phenyl and aryl substitution with electron-donating groups, the 4-iodo-thiophenes were obtained in moderate to good yields in short reaction times (Table 5, entries 1–4). However, the aryl-substituted diynol bearing an electron-deficient group showed lower activity than those containing electron-donating groups (Table 5, entry 5). When tertiary diynol **1g** was subjected to the same conditions, the yield was moderate (Table 5, entry 6). Even under different conditions, such as increasing the reaction time, temperature, and amount of iodine, only decomposition of the starting materials to unidentified products was observed. The screening of the conditions summarized in Table 4 showed that 4-bromo-thiophene was also obtained selectively by the addition of bromine (1.5 equiv) to a solution of dimethyl disulfide (3.0 equiv) in CH_2Cl_2 (3 mL), at room temperature under an air atmosphere. After 15 min, the diynol **1a** (0.3 mmol) was added and the reaction was run for 30 min, giving the 4-bromo-thiophene **5a** in 82% yield. Under these optimized conditions, we performed the reactions using other diynols **1** (Table 5). While activated aryl diynols **1a–c** were cyclized to afford the expected 4-bromo-thiophenes **5a–c** in good yields (Table 5, entries 7–9), the electron-deficient aryl group gave a poor result (Table 5, entry 10). These results indicated that the reactions for the formation of 4-halo-thiophenes **4** and **5** seem to be sensitive to electronic effects due to the substituents on the aromatic ring directly bonded to the triple bond. The aryl substituent containing an electron donating group increases the electron density of the carbon–carbon triple bond which makes it more reactive toward coordination to the selenium atom to form the seleniranium ion. The optimized reaction conditions were also applicable to tertiary diynols, such as **1f** and **1g**, giving the corresponding 4-bromo-thiophenes **5e** and **5f** in 62% and 65% yields, respectively (Table 5, entries 11 and 12).

On the basis of the experimental conditions shown in Table 4, entry 8, the reaction of diynol **1a** with a stoichiometric amount of dimethyl disulfide and NBS gave a 2:1 mixture of 3-methylsulfide-thiophene **6a** and 3-bromo-thiophene **5a**. In order to improve the yield and selectivity of the 3-methylsulfide-thiophene **6a**, the addition of MeSBr to diynol **1a** was examined under different conditions (Table 6). The reaction is clearly affected by varying temperatures and the amount of dimethyl disulfide. After several attempts, the best yield of 3-methylsulfide-thiophene **6a** was obtained using 5 equiv of dimethyl disulfide at 75 °C in dichloromethane (Table 6, entry 5).

Under the optimized reaction conditions found in Table 6, diynols **1** gave 4-methylthio-thiophenes **6** in good yields (Table 7, entries 1–5). The reactions with diynols **1a** and **1b**, which have neutral and electron-rich aryl groups on the alkyne, proceeded extremely quickly to complete conversion, but the reaction with diynol **1e**, with an electron-poor aryl group, required 3 h for formation of 4-methylthio-thiophene **6d** in 79% yield (Table 6, entry 3). The reaction with tertiary diynols **1f** and **1g** afforded the desired products in good yields but required 12 h for the conversion of the starting materials (Table 6, entries 4 and 5).

The rich reactivity of the carbon–halogen bond makes these halo-chalcogenophene derivatives extremely versatile substrates in several well-known transformations, especially in palladium cross-coupling reactions. In order to demonstrate the synthetic utility of the halo-selenophenes and halo-thiophenes, we studied the reactivity of these compounds toward Suzuki, Sonogashira, and Ullmann cross-coupling reactions. In Scheme 8, the 4-iodo-selenophene **2a** and 4-iodo-thiophene **4a** were applied as substrates under the Suzuki cross-coupling conditions affording 4-methoxyphenyl-selenophene **7a** and 4-methoxyphenyl-thiophene **7b** in 95% and 86% yield, respectively. We then examined the possibility of using 4-

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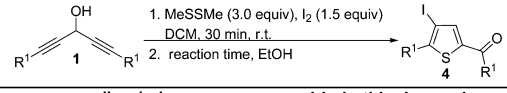
Table 5. Synthesis of 4-Iodo-thiophenes 4 and 4-Bromo-thiophenes 5



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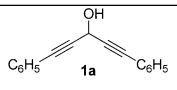
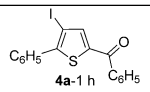
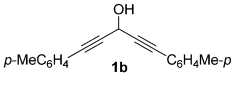
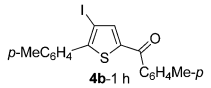
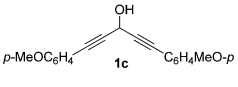
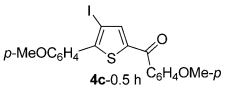
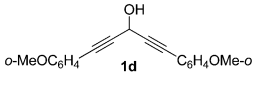
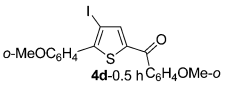
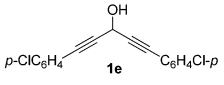
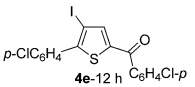
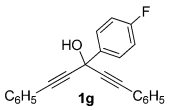
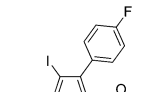
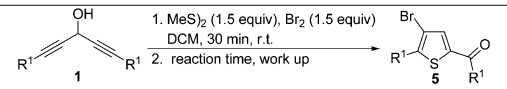
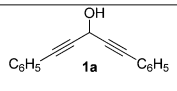
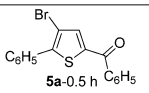
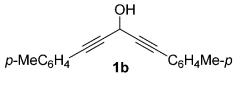
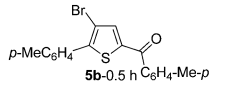
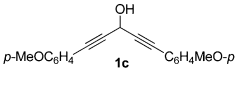
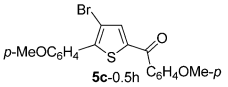
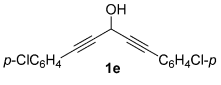
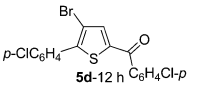
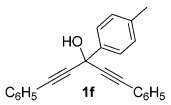
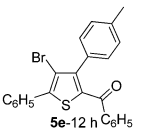
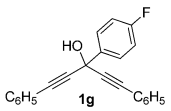
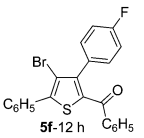
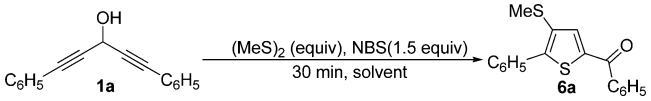
1			73
2			57
3			55
4			53
5			41
6			48



entry	diynols 1	4-bromo-thiophenes 5	yield (%)[b]
7			82
8			67
9			60
10			54
11			62
12			65

[a]The reaction was performed by the addition of iodide (1.5 equiv) to a solution of dimethyl disulfide (3.0 equiv) in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added; the reactions were run at room temperature for the times indicated, and ethanol was added. [b]The reaction was performed by the addition of bromine (1.5) to a solution of dimethyl disulfide (1.5 equiv) in CH_2Cl_2 (3 mL), at 0 °C, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added; the reactions were run at room temperature for the times indicated, and water was added.

Table 6. Effect of Different Reaction Parameters on Cyclization of Diynol 1a[a]



entry	solvent	reaction time (h)	temp (°C)	$(MeS)_2$ (equiv)	yield (%) **6a**
1	DCM	1.5	rt	3.0	80
2	DCM	3.0	0	3.0	70
3	DCM	0.5	39	3.0	80
4	DCM	0.5	39	5.0	91
5	DCE	0.5	75	5.0	94

[a]The reaction was performed by the addition of NBS (1.5 equiv) to a solution of dimethyl disulfide in CH_2Cl_2 (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added, and the reactions were run at 75 °C for 30 min.

iodo-selenophene **2a** as a substrate in the Sonogashira cross-coupling reaction. Thus, the reactions of 4-iodo-chalcogenophenes **2a** and **4a** with terminal alkynes catalyzed by palladium and copper allowed the preparation of 4-alkynyl-chalcogenophenes **8a−d** in good yields (Scheme 9). Further reactions of chalcogenophenes **2a** and **4a** with benzenethiol under Ullmann conditions gave 4-phenylthio-chalcogenophenes **9a** and **9b** in 83% and 73% yield, respectively (Scheme 10).

CONCLUSION

In summary, we developed a methodology to synthesize 4-substituted chalcogenophenes via cyclization of diynols promoted by diorganyl dichalcogenides and a halogen source. The protocol provides facile access to five classes of different chalcogenophenes, among them 4-halo-selenophenes, 4-butylselenyl-selenophenes, halo-thiophenes, and 4-methylthio-thiophenes, which were selectively prepared in good yields from the same starting materials. The optimization studies showed that the cyclization reaction proceeds under aerobic conditions, at room temperature and in the absence of additives. The optimized reaction conditions could be applied to symmetrical and unsymmetrical diynols having a wide range of functional groups, including electron-rich and -poor substrates. The experiments revealed that the selectivity in the cyclization was controlled by changing the halogen source and the ratio of reagents. The analyses of products and mechanistic studies

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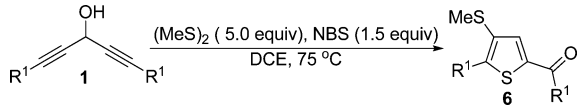
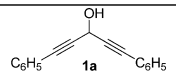
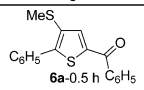
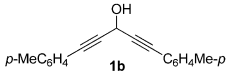
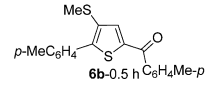
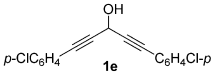
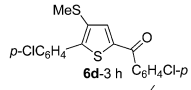
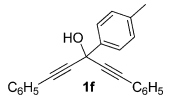
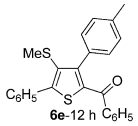
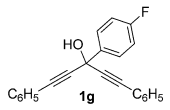
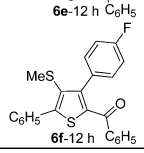
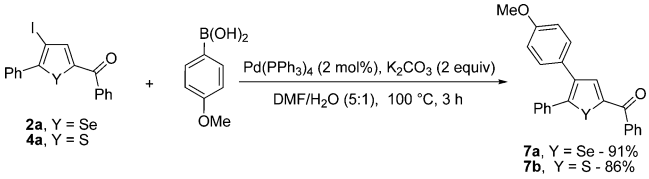
Table 7. Synthesis of 4-Methylthio-thiophenes 6



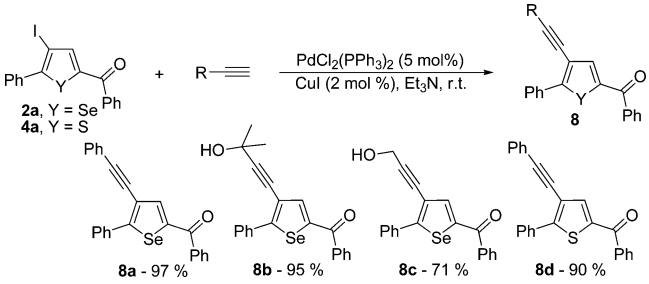
entry	diynols 1	4-methylthio-thiophenes 6	yield (%)[a]
1			94
2			80
3			79
4			77
5			65

[a]The reaction was performed by the addition of NBS (1.5 equiv) to a solution of dimethyl disulfide (5.0 equiv) in DCE (3 mL), at room temperature, under an air atmosphere. After 30 min the diynol **1** (0.3 mmol) was added. The reactions were run at 75 °C for the time indicated.

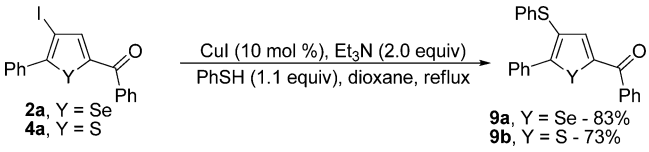
Scheme 8



Scheme 9



Scheme 10



indicate that the first step of this cyclization, which involves the reduction of alkynes by organochalcogen electrophilic addition, gives the key intermediates that guide the selectivity of the transformation. We also demonstrated the possibility of introducing different functionalities at the C-4 of the chalcogenophene ring via palladium catalyzed cross-coupling reactions.

EXPERIMENTAL SECTION

Materials and Methods. Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained on a NMR spectrometer at 400 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in hertz, and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained on a 400 NMR spectrometer at 100 MHz. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Abbreviations denoting the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), quart. (quartet), quint. (quintet), sext. (sextet), dd (double doublet), and m (multiplet). High-resolution mass spectra were recorded on a mass spectrometer using electrospray ionization (ESI). Column chromatography was performed using Silica Gel (230−400 mesh). Thin layer chromatography (TLC) was performed using Gel GF254, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light or stained with iodine vapor, or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. The following solvents were dried and purified by distillation from the reagents indicated: tetrahydrofuran from sodium with a benzophenone ketyl indicator. All other solvents were ACS or HPLC grade unless otherwise noted. Air- and moisture-sensitive reactions were conducted in flame-dried or oven-dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry nitrogen or argon. Reagents and solvents were handled using standard syringe techniques.

General Procedure for the I_2/(n-BuSe)$_2$ Cyclization. To a Schlenck tube, under an ambient atmosphere, containing CH_2Cl_2 (4 mL) were added (n-BuSe)$_2$ (1.5 equiv) and iodine (1.5 equiv), and the reaction mixture was stirred for 30 min at room temperature. After this time, the appropriate diynol **1** (0.30 mmol) was added. After consumption of starting material, the reaction was quenched with EtOH 95% (1 mL) and stirred for 15 min. The reaction was diluted with dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_3$ (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/acetate (98:2).

*(4-Iodo-5-phenylselenophen-2-yl)(phenyl)methanone (**2a**).* Obtained as a yellow solid. Yield: 0.128 g (98%); mp 108−110 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ (ppm) 7.88−7.83 (m, 3H), 7.65−7.40 (m, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.0, 157.0, 150.3, 145.7, 137.0, 135.9, 132.4, 129.2, 129.1, 129.0, 128.6, 128.5, 80.1. MS (EI, 70 eV; m/z (relative intensity)): 438 (39), 361 (27), 311 (04), 231 (10), 105 (72), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{17}H_{11}IOSe$ (M + H$^+$): 438.9098, found: 438.9102.

*(4-Iodo-5-(p-tolyl)selenophen-2-yl)(p-tolyl)methanone (**2b**).* Obtained as a yellow solid. Yield: 0.114 g (82%); mp 110−112 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ (ppm) 7.84 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.33−7.22 (m, 4H), 2.45 (s, 3H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ (ppm) 187.7, 156.6, 150.1, 145.5, 143.3, 139.4, 134.2, 133.0, 129.3, 129.2, 128.9, 97.5, 79.7, 21.6, 21.3. MS (EI, 70 eV; m/z (relative intensity)): 466 (83), 375 (22), 139 (41), 119 (99), 91 (100). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}IOSe$ (M + H$^+$): 466.9411, found: 466.9416.

*(4-Iodo-5-(4-methoxyphenyl)selenophen-2-yl)(4-methoxyphenyl)methanone (**2c**).* Obtained as a yellow solid. Yield: 0.125 g (84%); mp 123−125 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.89 (d, J = 8.8 Hz, 2H), 7.83 (s, 1H), 7.55 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.0, 163.3, 160.3, 156.0, 150.0, 145.1, 131.5, 130.4, 129.5, 128.3, 114.0, 113.9, 79.4, 55.5, 55.4. MS (EI, 70 eV; m/z (relative intensity)): 498 (42), 371 (02), 291 (07), 235 (04), 135 (100), 77 (31). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}IO_3Se$ (M + H$^+$): 498.9309, found: 498.9313.

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*(4-Iodo-5-(2-methoxyphenyl)selenophen-2-yl)(2-methoxyphenyl)methanone (**2d**).* Obtained as a yellow solid. Yield: 0.110 g (74%); mp 109−111 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.63 (s, 1H), 7.48−7.38 (m, 4H), 7.05−6.96 (m, 4H), 3.84 (s, 3H), 3.83 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.1, 157.1, 156.1, 153.6, 151.4, 145.3, 131.9, 131.4, 130.8, 129.2, 127.9, 125.2, 120.4, 120.3, 111.8, 111.5, 83.0, 55.8, 55.6. MS (EI, 70 eV; *m*/*z* (relative intensity)): 412 (63), 335 (57), 306 (35), 226 (32), 105 (96), 77 (100). HRMS (ESI-TOF) *m*/*z* calcd for $C_{19}H_{15}IO_3Se$ (M + H^+): 498.9309, found: 498.9315.

*(4-Chlorophenyl)(5-(4-chlorophenyl)-4-iodoselenophen-2-yl)-methanone (**2e**).* Obtained as a yellow solid. Yield: 0.112 g (74%); mp 135−137 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.83−7.79 (m, 3H), 7.53−7.48 (m, 4H), 7.41 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.6, 155.4, 150.2, 145.6, 139.1, 135.5, 135.0, 134.2, 130.5, 130.3, 128.93, 128.90, 80.6. MS (EI, 70 eV; *m*/*z* (relative intensity)): 506 (53), 395 (28), 316 (09), 240 (14), 160 (42), 139 (100), 111 (86), 75 (35). HRMS (ESI-TOF) *m*/*z* calcd for $C_{17}H_9Cl_2IOSe$ (M + H^+): 506.8319, found: 506.8325.

*(4-Iodo-5-phenylselenophen-2-yl)(3,4,5-trimethoxyphenyl)-methanone (**2j**).* Obtained as a yellow solid. Yield: 0.100 g (63%); mp 165−167 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.92 (s, 1H), 7.60−7.57 (m, 2H), 7.44−7.42 (m, 3H), 7.14 (s, 2H), 3.95 (s, 3H), 3.92 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.6, 156.3, 153.0, 149.8, 145.3, 142.2, 135.7, 131.9, 129.1, 128.9, 128.5, 106.8, 79.9, 60.8, 56.3. MS (EI, 70 eV; *m*/*z* (relative intensity)): 528 (38), 485 (05), 401 (02), 361 (03), 321 (04), 207 (100), 195 (14), 126 (20). HRMS (ESI-TOF) *m*/*z* calcd for $C_{20}H_{17}IO_4Se$ (M + H^+): 528.9415, found: 528.9419.

General Procedure for the NBS/(*n*-BuSe)$_2$ Cyclization. To a Schlenck tube, under ambient atmosphere, containing CH_2Cl_2 (4 mL) were added (*n*-BuSe)$_2$ (1.5 equiv) and NBS (1.5 equiv), and the reaction mixture was stirred for 30 min at room temperature. After this time, the appropriate diynol **1** (0.30 mmol) was added and the reaction mixture was stirred for a determined time. Afterward, the mixture was diluted with dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_3$ (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/acetate (99:1).

*(4-(Butylselanyl)-5-phenylselenophen-2-yl)(phenyl)methanone (**3a**).* Obtained as a yellow oil. Yield: 0.129 g (96%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.88−7.86 (m, 3H), 7.62−7.58 (m, 3H), 7.53−7.50 (m, 2H), 7.46−7.38 (m, 3H), 2.71 (t, *J* = 7.3 Hz, 2H), 1.52 (quint., *J* = 7.3 Hz, 2H), 1.27 (sext., *J* = 7.3 Hz, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.7, 157.9, 148.0, 143.4, 137.4, 135.8, 132.3, 129.2, 129.1, 128.8, 128.5, 128.4, 123.1, 32.1, 28.9, 22.7, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 448 (06), 392 (02), 206 (02), 126 (08), 105 (100), 77 (39). HRMS (ESI-TOF) *m*/*z* calcd for $C_{21}H_{20}OSe_2$ (M + H^+): 448.9923, found: 448.9929.

*(4-(Butylselanyl)-5-(p-tolyl)selenophen-2-yl)(p-tolyl)methanone (**3b**).* Obtained as a yellow oil. Yield: 0.111 g (78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.86 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 2.71 (t, *J* = 7.3 Hz, 2H), 2.44 (s, 3H), 2.38 (s, 3H), 1.53 (quint., *J* = 7.3 Hz, 2H), 1.28 (sext., *J* = 7.3 Hz, 2H), 0.81 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.3, 157.7, 147.8, 143.0, 142.9, 138.9, 134.8, 132.9, 129.3, 129.1, 129.08, 129.05, 122.6, 32.1, 28.8, 22.6, 21.5, 21.2, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 476 (09), 281 (12), 207 (69), 119 (100), 91 (40). HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{24}OSe_2$ (M + H^+): 477.0236, found: 477.0241.

*(4-(Butylselanyl)-5-(4-methoxyphenyl)selenophen-2-yl)(4-methoxyphenyl)methanone (**3c**).* Obtained as a yellow oil. Yield: 0.114 g (75%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.89 (d, *J* = 8.7 Hz, 2H), 7.85 (s, 1H), 7.55 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 2.72 (t, *J* = 7.3 Hz, 2H), 1.54 (quint., *J* = 7.3 Hz, 2H), 1.29 (sext., *J* = 7.3 Hz, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.3, 163.1, 160.1, 157.4, 147.6, 142.8, 131.5, 130.6, 130.2, 128.4, 122.1, 113.9, 113.8, 55.5, 53.3, 32.1, 28.9, 22.7, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 508 (10), 281 (06), 135 (100), 77 (13), 57 (02). HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{24}O_3Se_2$ (M + H^+): 509.0134, found: 509.0139.

*(4-(Butylselanyl)-5-(2-methoxyphenyl)selenophen-2-yl)(2-methoxyphenyl)methanone (**3d**).* Obtained as a yellow oil. Yield: 0.110 g (72%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.67 (s, 1H), 7.47−7.35 (m, 4H), 7.05−6.95 (m, 4H), 3.83 (s, 6H), 2.63 (t, *J* = 7.3 Hz, 2H), 1.48 (quint., *J* = 7.3 Hz, 2H), 1.23 (sext., *J* = 7.3 Hz, 2H), 0.79 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.8, 157.0, 156.3, 153.9, 149.4, 142.8, 131.7, 131.4, 130.4, 129.2, 128.4, 125.5, 124.8, 120.3, 120.2, 111.7, 111.1, 55.7, 55.4, 32.1, 28.3, 22.7, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 508 (07), 135 (100), 92 (05), 77 (20), 57 (01). HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{24}O_3Se_2$ (M + H^+): 509.0134, found: 509.0142.

*(4-(Butylselanyl)-5-(4-chlorophenyl)selenophen-2-yl)(4-chlorophenyl)methanone (**3e**).* Obtained as a yellow oil. Yield: 0.108 g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.85−7.80 (m, 3H), 7.55−7.39 (m, 6H), 2.72 (t, *J* = 7.3 Hz, 2H), 1.52 (quint., *J* = 7.3 Hz, 2H), 1.29 (sext., *J* = 7.3 Hz, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.2, 156.5, 147.9, 143.2, 138.8, 135.6, 135.1, 134.1, 132.8, 130.5, 130.4, 128.8, 128.7, 123.7, 32.1, 29.1, 22.6, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 516 (10), 460 (01), 281 (12), 139 (100), 111 (33). HRMS (ESI-TOF) *m*/*z* calcd for $C_{21}H_{18}Cl_2OSe_2$ (M + H^+): 516.9143, found: 516.9151.

*(4-(Butylselanyl)-5-phenyl-3-(p-tolyl)selenophen-2-yl)(phenyl)-methanone (**3f**).* Obtained as a yellow oil. Yield: 0.077 g (48%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.65−7.61 (m, 2H), 7.56−7.54 (m, 2H), 7.45−7.39 (m, 3H), 7.29−7.24 (m, 1H), 7.14−7.10 (m, 4H), 6.95−6.90 (m, 2H), 2.20 (s, 3H), 2.07 (t, *J* = 7.2 Hz, 2H), 1.11 (quint, *J* = 7.2 Hz, 2H), 0.94 (sex, *J* = 7.2 Hz, 2H), 0.61 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 191.8, 156.4, 151.9, 143.8, 137.8, 137.4, 136.6, 134.8, 131.6, 130.6, 129.9, 129.4, 128.6, 128.3, 128.0, 127.6, 125.0, 31.5, 28.3, 22.3, 21.1, 13.2. MS (EI, 70 eV; *m*/*z* (relative intensity)): 538 (10), 481 (02), 401 (03), 281 (07), 105 (100), 77 (44). HRMS (ESI-TOF) *m*/*z* calcd for $C_{28}H_{26}OSe_2$ (M + H^+): 539.0392, found: 539.0395.

*(4-(Butylselanyl)-3-(4-fluorophenyl)-5-phenylselenophen-2-yl)-(phenyl)methanone (**3g**).* Obtained as a yellow oil. Yield: 0.072 g (44%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.64−7.61 (m, 2H), 7.56−7.53 (m, 2H), 7.46−7.38 (m, 3H), 7.32−7.29 (m, 1H), 7.22−7.14 (m, 4H), 6.83−6.78 (m, 2H), 2.06 (t, *J* = 7.2 Hz, 2H), 1.10 (quint., *J* = 7.2 Hz, 2H), 0.95 (sext., *J* = 7.2 Hz, 2H), 0.61 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 191.5, 162.2 (d, *J* (C−F) = 248.0 Hz), 157.0, 150.4, 144.4, 137.6, 136.4, 133.7 (d, *J* (C−F) = 2.9 Hz), 132.4 (d, *J* (C−F) = 8.0 Hz), 132.0, 129.8, 129.3, 128.7, 128.3, 127.7, 124.8, 114.3 (d, *J* (C−F) = 21.3 Hz), 31.5, 28.4, 22.3, 13.2. MS (EI, 70 eV; *m*/*z* (relative intensity)): 542 (10), 485 (03), 405 (03), 300 (02), 105 (100), 77 (45). HRMS (ESI-TOF) *m*/*z* calcd for $C_{27}H_{23}FOSe_2$ (M + H^+): 543.0142, found: 543.0148.

*(3-(4-Bromophenyl)-4-(butylselanyl)-5-phenylselenophen-2-yl)-(phenyl)methanone (**3h**).* Obtained as a yellow oil. Yield: 0.088 g (49%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.63−7.61 (m, 2H), 7.57−7.54 (m, 2H), 7.45−7.41 (m, 3H), 7.37−7.33 (m, 1H); 7.27−7.24 (m, 2H), 7.20−7.16 (m, 2H), 7.12−7.01 (m, 2H), 2.08 (t, *J* = 7.3 Hz, 2H), 1.11 (quint., *J* = 7.3 Hz, 2H), 0.96 (sext., *J* = 7.3 Hz, 2H), 0.63 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 191.4, 157.3, 150.4, 144.4, 137.7, 136.7, 136.4, 132.3, 132.1, 130.5, 129.9, 129.3, 128.8, 128.4, 127.8, 124.6, 122.1, 31.6, 28.6, 22.3, 13.2. MS (EI, 70 eV; *m*/*z* (relative intensity)): 600 (04), 545 (02), 465 (02), 387 (01), 105 (100), 77 (38). HRMS (ESI-TOF) *m*/*z* calcd for $C_{27}H_{23}BrOSe_2$ (M + H^+): 602.9341, found: 602.9349.

*4-(Butylselanyl)-5-phenylselenophene-2-carbaldehyde (**3i**).* Obtained as a yellow oil. Yield: 0.089 g (80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.76 (s, 1H), 8.02 (s, 1H), 7.59−7.55 (m, 2H), 7.45−7.39 (m, 3H), 2.77 (t, *J* = 7.3 Hz, 2H), 1.55 (quint., *J* = 7.3 Hz, 2H), 1.31 (sext., *J* = 7.3 Hz, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 183.6, 158.2, 147.7, 145.4, 135.7, 129.2, 129.1, 128.5, 123.6, 32.1, 28.9, 22.7, 13.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 372 (48), 316 (22), 286 (23), 208 (84), 126 (100), 57

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(36). HRMS (ESI-TOF) m/z calcd for $C_{15}H_{16}OSe_2$ (M + H^+): 372.9610, found: 372.9613.

*(4-(Butylselanyl)-5-phenylselenophen-2-yl)(3,4,5-trimethoxyphenyl)methanone (**3j**).* Obtained as a yellow oil. Yield: 0.110 g (68%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.94 (s, 1H), 7.61−7.58 (m, 2H), 7.46−7.40 (m, 3H), 7.16 (s, 2H), 3.95 (s, 3H), 3.92 (s, 6H), 2.74 (t, J = 7.3 Hz, 2H), 1.54 (quint., J = 7.3 Hz, 2H), 1.29 (sext., J = 7.3 Hz, 2H), 0.81 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.5, 157.5, 153.1, 147.7, 142.9, 142.2, 135.8, 132.6, 129.2, 128.8, 128.5, 123.2, 107.0, 60.9, 56.4, 32.1, 28.9, 22.6, 13.4. MS (EI, 70 eV; m/z (relative intensity)): 538(23), 478 (03), 321 (06), 195 (100), 152 (08), 124 (05). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{26}O_4Se_2$ (M + H^+): 539.0240, found: 539.0246.

General Procedure for the I_2/$(MeS)_2$ Cyclization. To a Schlenck tube, under ambient atmosphere, containing CH_2Cl_2 (4 mL) were added $(MeS)_2$ (3.0 equiv) and iodine(1.5 equiv), and the reaction mixture was stirred for 30 min at room temperature. After this time, the appropriate diynol **1** (0.30 mmol) was added. After consumption of starting material, the reaction was quenched with EtOH 95% (1 mL) and stirred for 15 min. The reaction was diluted with dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_3$ (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/acetate (98:2).

*(4-Iodo-5-phenylthiophen-2-yl)(phenyl)methanone (**4a**).* Obtained as a yellow solid. Yield: 0.085 g (73%); mp 105−107 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.89−7.86 (m, 2H), 7.67−7.60 (m, 4H), 4.29−4.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.8, 150.9, 143.5, 143.2, 137.3, 133.4, 132.5, 129.4, 129.2, 129.0, 128.6, 128.5, 78.6. MS (EI, 70 eV; m/z (relative intensity)): 390 (97), 313 (56), 263 (09), 158 (60), 105 (78), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{17}H_{11}IOS$ (M + H^+): 390.9654, found: 390.9659.

*(4-Iodo-5-(p-tolyl)thiophen-2-yl)(p-tolyl)methanone (**4b**).* Obtained as a yellow solid. Yield: 0.071 g (57%); mp 120−122 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.79 (d, J = 8.1 Hz, 2H), 7.64 (s, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.32−7.25 (m, 4H), 2.45 (s, 3H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.6, 150.9, 143.4 (2C), 142.9, 139.6, 134.8, 130.7, 129.4, 129.3, 129.2, 129.1, 78.3, 21.6, 21.3. MS (EI, 70 eV; m/z (relative intensity)): 418 (92), 327 (28), 291 (09), 172 (25), 119 (100), 91 (87). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}IOS$ (M + H^+): 418.9967, found: 418.9971.

*(4-Iodo-5-(4-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl)methanone (**4c**).* Obtained as a yellow solid. Yield: 0.074 g (55%); mp 135−137 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.90 (d, J = 8.8 Hz, 2H), 7.63 (s, 1H), 7.60 (d, J = 8.8 Hz, 2H), 7.02−6.98 (m, 4H), 3.90 (s, 3H), 3.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 185.5, 163.3, 160.5, 150.4, 143.2, 142.5, 131.5, 130.6, 130.0, 125.9, 114.1, 113.9, 78.0, 55.5, 55.4. MS (EI, 70 eV; m/z (relative intensity)): 450 (93), 433 (19), 323 (11), 151 (27), 135 (100), 77 (54). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}IO_3S$ (M + H^+): 450.9865, found: 450.9869.

*(4-Iodo-5-(2-methoxyphenyl)thiophen-2-yl)(2-methoxyphenyl)methanone (**4d**).* Obtained as a brown solid. Yield: 0.072 g (53%); mp 101−103 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.49−7.34 (m, 5H), 7.05−6.95 (m, 4H), 3.84 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.9, 157.1, 156.8, 148.8, 145.0, 142.5, 132.0, 131.9, 131.1, 129.2, 128.2, 122.6, 120.4, 120.3, 111.8, 111.5. 82.0, 55.8, 55.6. MS (EI, 70 eV; m/z (relative intensity)): 450 (93), 433 (19), 323 (11), 151 (27), 135 (100), 77 (54). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}IO_3S$ (M + H^+): 450.9865, found: 450.9868.

*(4-Chlorophenyl)(5-(4-chlorophenyl)-4-iodothiophen-2-yl)methanone (**4e**).* Obtained as a yellow solid. Yield: 0.056 g (41%); mp 139−141 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.82 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 185.4, 149.8, 143.3, 143.0, 139.2, 135.8, 135.5, 131.7, 130.5, 130.4, 128.97, 128.95, 79.1. MS (EI, 70 eV; m/z (relative intensity)):458 (63) 347 (32), 192 (21), 139 (100), 111 (78), 75 (33). HRMS (ESI-TOF) m/z calcd for $C_{17}H_9Cl_2IOS$ (M + H^+): 458.8874, found: 458.8877.

*(3-(4-Fluorophenyl)-4-iodo-5-phenylthiophen-2-yl)(phenyl)methanone (**4f**).* Obtained as a yellow oil. Yield: 0.070 g (48%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.66−7.64 (m, 2H), 7.60−7.58 (m, 2H), 7.49−7.44 (m, 3H), 7.38−7.34 (m, 1H), 7.24−7.16 (m, 4H), 6.92−6.86 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 189.0, 162.4 (d, J = 248.0 Hz), 148.6, 147.9, 138.3, 137.2, 134.2, 132.6 (d, J (C−F) = 2.9 Hz), 132.4, 132.38 (d, J (C−F) = 8.0 Hz), 129.8, 129.3, 128.6, 127.9, 114.8 (d, J (C−F) = 21.3 Hz), 87.9. MS (EI, 70 eV; m/z (relative intensity)): 484 (70), 407 (18), 280 (09), 178 (11), 105 (75), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{23}H_{14}FIOS$ (M + H^+): 484.9872, found: 484.9875.

General Procedure for the Br_2/$(MeS)_2$ Cyclization. To a solution of $(MeS)_2$ (1.5 equiv) in CH_2Cl_2 (3 mL), at 0 °C, was added gradually Br_2 (1.1 equiv) in CH_2Cl_2 (2 mL). After 30 min at this temperature the diynol **1** (0.3 mmol) was added and the ice bath was removed allowing the reaction to react at room temperature for the desired time. After this, the mixture was diluted with dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_3$ (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/acetate (98:2).

*(4-Bromo-5-phenylthiophen-2-yl)(phenyl)methanone (**5a**).* Obtained as a yellow solid. Yield: 0.084 g (82%); mp 72−74 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.87 (d, J = 8.6 Hz, 2H), 7.71−7.69 (m, 2H), 7.63−7.58 (m, 2H), 7.53−7.43 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.8, 147.0, 141.4, 138.2, 137.2, 132.6, 132.0, 129.3, 129.0, 128.9, 128.7, 128.5, 108.0. MS (EI, 70 eV; m/z (relative intensity)): 344 (52), 267 (37), 234 (04), 158 (79), 105 (80), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{17}H_{11}BrOS$ (M + H^+): 342.9792, found: 342.9798.

*(4-Bromo-5-(p-tolyl)thiophen-2-yl)(p-tolyl)methanone (**5b**).* Obtained as a yellow solid. Yield: 0.074 g (67%); mp: 114−116 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.79 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 7.55 (s, 1H), 7.33−7.26 (m, 4H), 2.45 (s, 3H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.6, 147.0, 143.4, 141.2, 139.6, 138.0, 134.6, 133.4, 129.4, 129.3, 129.2, 128.8, 107.6, 21.6, 21.3. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}BrOS$ (M + H^+): 371.0105, found: 371.0109.

*(4-Bromo-5-(4-methoxyphenyl)thiophen-2-yl)(4-methoxyphenyl)methanone (**5c**).* Obtained as a yellow solid. Yield: 0.072 g (60%); mp 138−140 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.90 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 8.9 Hz, 2H), 7.55 (s, 1H), 7.02−6.92 (m, 4H), 2.89 (s, 3H), 3.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 185.4, 163.3, 160.5, 146.4, 140.9, 137.5, 131.5, 130.3, 129.9, 124.5, 114.2, 113.9, 107.2, 55.5, 55.3. MS (EI, 70 eV; m/z (relative intensity)): 404 (36), 323 (03), 188 (12), 135 (100), 77 (23). HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}BrO_3S$ (M + H^+): 403.0004, found: 403.0010.

*(4-Bromo-5-(4-chlorophenyl)thiophen-2-yl)(4-chlorophenyl)methanone (**5d**).* Obtained as a yellow solid. Yield: 0.066 g (54%); mp 140−142 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.83 (d, J = 8.7 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.55 (s, 1H), 7.51 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 185.5, 145.9, 141.3, 139.3, 138.1, 135.8, 135.5, 130.5, 130.4, 130.2, 129.1, 129.0, 108.5. MS (EI, 70 eV; m/z (relative intensity)): 412 (62), 301 (32), 192 (37), 139 (100), 75 (37). HRMS (ESI-TOF) m/z calcd for $C_{17}H_9BrCl_2OS$ (M + H^+): 410.9013, found: 410.9017.

*(4-Bromo-5-phenyl-3-(p-tolyl)thiophen-2-yl)(phenyl)methanone (**5e**).* Obtained as a yellow oil. Yield: 0.080 g (62%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.80−7.75 (m, 2H), 7.66−7.63 (m, 2H), 7.54−7.48 (m, 3H), 7.39−7.35 (m, 1H), 7.24−7.17 (m, 4H), 7.05−7.02 (m, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 189.2, 146.7, 143.9, 138.0, 137.4, 137.2, 132.8, 132.1, 132.0, 130.4, 129.5, 129.4, 129.2, 128.7, 128.5, 127.8, 111.8, 21.2. MS (EI, 70 eV; m/z (relative intensity)): 433 (54), 419 (25), 353 (06), 276 (19), 247 (22), 176 (28), 105 (62), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{17}BrOS$ (M + H^+): 433.0262, found: 433.0265.

*(4-Bromo-3-(4-fluorophenyl)-5-phenylthiophen-2-yl)(phenyl)methanone (**5f**).* Obtained as a yellow oil. Yield: 0.085 g (65%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.76−7.70 (m, 2H), 7.59−7.57

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(m, 2H), 7.50−7.43 (m, 3H); 7.38−7.33 (m, 1H), 7.28−7.17 (m, 4H), 6.90−6.85 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.9, 162.5 (d, J (C−F) = 248.0 Hz) 145.4, 144.3, 137.5, 137.2, 132.5, 132.4, 132.3 (d, J (C−F) = 8.8 Hz), 130.8 (d, J (C−F) = 3.6 Hz), 129.4 129.3 (2C), 128.7, 127.9, 114.8 (d, J (C−F) = 22.0 Hz), 111.6. MS (EI, 70 eV; m/z (relative intensity)): 438 (65), 359 (25), 280 (38), 252 (24), 179 (39), 105 (79), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{23}H_{14}BrFOS$ (M + H$^+$): 437.0011, found: 437.0019.

General Procedure for the NBS/$(MeS)_2$ Cyclization. To a Schlenck tube, under ambient atmosphere, containing DCE (4 mL) were added $(MeS)_2$ (5.0 equiv) and NBS (1.5 equiv). The reaction mixture was stirred for 30 min at room temperature and then warmed to 75 °C. After that, the appropriate diynol **1** (0.30 mmol) was added in one portion. After consumption of the starting material, the mixture was diluted with dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_3$ (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/acetate (95:5).

*(4-(Methylthio)-5-phenylthiophen-2-yl)(phenyl)methanone (**6a**).* Obtained as a yellow oil. Yield: 0.088 g (95%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.90−7.87 (m, 2H), 7.70−7.68 (m, 2H), 7.62 (s, 1H), 7.59−7.57 (m, 1H), 7.52−7.39 (m, 5H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.3, 148.2, 140.8, 137.8, 136.9, 132.8, 132.3, 131.1, 129.0, 128.93. 128.91, 128.6, 128.5, 18.5. MS (EI, 70 eV; m/z (relative intensity)): 310 (100), 233 (28), 190 (05), 158 (17), 105 (78), 77 (62). HRMS (ESI-TOF) m/z calcd for $C_{18}H_{14}OS_2$ (M + H$^+$): 311.0564, found: 311.0571.

*(4-(Methylthio)-5-(p-tolyl)thiophen-2-yl)(p-tolyl)methanone (**6b**).* Obtained as a red solid. Yield: 0.081 g (80%); mp 90−92 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.80 (d, J = 8.2 Hz, 2H), 7.60 (s, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 2.44 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.0, 148.1, 143.1, 140.6, 139.0, 136.7, 135.1, 130.5, 130.0, 129.3, 129.2, 129.1, 128.8, 21.5, 21.3, 18.5. MS (EI, 70 eV; m/z (relative intensity)): 338 (60), 281 (14), 247 (16), 119 (100), 91 (56). HRMS (ESI-TOF) m/z calcd for $C_{20}H_{18}OS_2$ (M + H$^+$): 339.0877, found: 339.0880.

*(4-Chlorophenyl)(5-(4-chlorophenyl)-4-(methylthio)thiophen-2-yl)methanone (**6d**).* Obtained as an orange solid. Yield: 0.090 g (79%); mp 111−113 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.83 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.57 (s, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm) 185.9, 146.7, 140.6, 138.9, 136.7, 135.9, 135.1, 131.1 (2C), 130.4, 130.1, 128.8, 18.5. MS (EI, 70 eV; m/z (relative intensity)): 378 (67), 267 (27), 192 (12), 139 (100), 111 (62) 75 (22). HRMS (ESI-TOF) m/z calcd for $C_{18}H_{12}Cl_2OS_2$ (M + H$^+$): 378.9785, found: 378.9788.

*(4-(Methylthio)-5-phenyl-3-(p-tolyl)thiophen-2-yl)(phenyl)-methanone (**6e**).* Obtained as a yellow oil. Yield: 0.092 g (77%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.77−7.74 (m, 2H), 7.60−7.57 (m, 2H), 7.48−7.40 (m, 3H), 7.32−7.28 (m, 1H), 7.18−7.13 (m, 4H), 6.99−6.96 (m, 2H), 2.24 (s, 3H), 1.77 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 189.9, 149.8, 149.4, 137.8, 137.5, 137.0, 133.5, 131.9, 130.5, 130.3, 129.6, 129.4, 128.9, 128.5, 128.3, 127.7, 21.1, 18.8. MS (EI, 70 eV; m/z (relative intensity)): 401 (100), 391 (15), 310 (12), 234 (15), 119 (73), 91 (67). HRMS (ESI-TOF) m/z calcd for $C_{25}H_{20}OS_2$ (M + H$^+$): 401.1034, found: 401.1037.

*(3-(4-Fluorophenyl)-4-(methylthio)-5-phenylthiophen-2-yl)-(phenyl)methanone (**6f**).* Obtained as a yellow solid. Yield: 0.079 g (65%); mp 104−106 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.76−7.72 (m, 2H), 7.60−7.57 (m, 2H), 7.49−7.40 (m, 3H), 7.36−7.32 (m, 1H), 7.29−7.24 (m, 2H), 7.22−7.17 (m, 2H), 6.90−6.84 (m, 2H), 1.75 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 189.7, 162.3 (d, J = 248.0 Hz), 150.3, 148.1, 137.6, 137.4, 133.2, 132.2 (d, J (C−F) = 8.8 Hz), 131.2 (d, J (C−F) = 3.6 Hz), 130.3, 129.6, 129.4, 129.0, 128.5, 127.8, 114.6 (d, J (C−F) = 21.3 Hz), 18.8. MS (EI, 70 eV; m/z (relative intensity)): 405 (79), 389 (27), 309 (08), 234 (14), 123 (100), 95 (49). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{17}FOS_2$ (M + H$^+$): 405.0783, found: 405.0785.

General Procedure for the Suzuki Coupling Reaction. A solution of 4-iodo-chalcogenophene (0.5 mmol) in DMF/H_2O (5:1, 5 mL) was added to a mixture of $Pd(PPh_3)_4$ (2 mol %) and K_2CO_3 (2 equiv). After that, the boronic acid (1.5 equiv) in DMF (0.5 mL) was added dropwise, and the reaction mixture was stirred under reflux temperature for 3 h. The organic phase was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography (hexane/ethyl acetate, 98:2).

*(4-(4-Methoxyphenyl)-5-phenylselenophen-2-yl)(phenyl)-methanone (**7a**).* Obtained as a yellow solid. Yield: 0.190 g (91%); mp 145−147 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.90−7.87 (m, 3H), 7.58−7.54 (m, 1H), 7.50−7.46 (m, 2H), 7.32−7.24 (m, 5H), 7.14 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 189.1, 158.9, 153.9, 147.4, 141.0 (2C), 137.8, 135.8, 132.0, 130.3, 129.2, 129.1, 129.08, 128.6, 128.4, 128.2, 114.0, 55.2. MS (EI, 70 eV; m/z (relative intensity)): 418 (61), 341 (17), 189 (15), 165 (16), 105 (86), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{18}O_2Se$ (M + H$^+$): 419.0550, found: 419.0558.

*(4-(4-Methoxyphenyl)-5-phenylthiophen-2-yl)(phenyl)-methanone (**7b**).* Obtained as a yellow solid. Yield: 0.160 g (86%); mp 113−115 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.92−7.90 (m, 2H), 7.64 (s, 1H), 7.59−7.55 (m, 1H), 7.51−7.47 (m, 2H), 7.37−7.33 (m, 2H), 7.30−7.27 (m, 3H), 7.17 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.9, 159.0, 146.9, 140.9, 138.8, 138.0, 137.6, 133.4, 132.1, 130.1, 129.1, 129.0, 128.6, 128.5, 128.4, 127.9, 113.9, 55.2. MS (EI, 70 eV; m/z (relative intensity)): 370 (100), 293 (24), 221 (13), 105 (72), 77 (75). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{18}O_2S$ (M + H$^+$): 371.1106, found: 371.1109.

General Procedure for the Sonogashira Coupling Reaction. The 4-iodo-chalcogenophene (0.5 mmol) was added to a Schlenk tube containing $PdCl_2(PPh_3)_2$ (0.0175 g, 5 mol %) and Et_3N (5 mL). To the resulting solution was added CuI (0.0019 g, 2 mol %). The reaction mixture was stirred for 15 min at room temperature, and a solution of the terminal alkyne (1.5 mmol) in Et_3N (1 mL) was added dropwise. The reaction mixture was stirred at room temperature. Subsequently, the mixture was diluted with CH_2Cl_2 (20 mL) and washed with brine (3 × 20 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated under vacuum. The residue was purified by flash chromatography (silica gel, EtOAc−hexane).

*Phenyl(5-phenyl-4-(phenylethynyl)selenophen-2-yl)methanone (**8a**).* Obtained as a yellow solid. Yield: 0.200 g (97%); mp 86−88 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.93−7.86 (m, 5H), 7.59−7.55 (m, 1H), 7.51−7.47 (m, 2H), 7.46−7.37 (m, 5H), 7.30−7.28 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.6, 161.1, 146.9, 141.3, 137.3, 135.2, 132.2, 131.4, 129.2, 129.1, 128.7, 128.5, 128.4 (3C), 122.9, 121.0, 90.7, 85.9. MS (EI, 70 eV; m/z (relative intensity)): 412 (50), 335 (30), 306 (21), 226 (14), 105 (70), 77 (100). HRMS (ESI-TOF) m/z calcd for $C_{25}H_{16}OSe$ (M + H$^+$): 413.0445, found: 413.0449.

*(4-(3-Hydroxy-3-methylbut-1-yn-1-yl)-5-phenylselenophen-2-yl)-(phenyl)methanone (**8b**).* Obtained as a brown solid. Yield: 0.187 g (95%); mp 130−132 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.84−7.80 (m, 5H), 7.60−7.55 (m, 1H), 7.50−7.46 (m, 2H), 7.43−7.38 (m, 3H), 2.36 (s, 1H), 1.55 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.7, 161.4, 146.7, 141.5, 137.1, 134.9, 132.3, 129.3, 129.1, 128.6, 128.5, 128.2, 120.4, 95.1, 78.4, 65.5, 31.1. MS (EI, 70 eV; m/z (relative intensity)): 394 (04), 376 (25), 336 (06), 259 (09), 105 (100), 77 (90). HRMS (ESI-TOF) m/z calcd for $C_{22}H_{18}O_2Se$ (M + H$^+$): 395.0550, found: 395.0557.

*(4-(3-Hydroxyprop-1-yn-1-yl)-5-phenylselenophen-2-yl)(phenyl)-methanone (**8c**).* Obtained as a brown solid. Yield: 0.130 g (71%); mp 168−170 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.84−7.80 (m, 5H), 7.61−7.57 (m, 1H), 7.51−7.47 (m, 2H), 7.45−7.39 (m, 3H), 4.42 (s, 2H), 1.85 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.7, 161.8, 147.0, 141.7, 137.1, 134.9, 132.4, 129.1, 128.8, 128.5, 128.3, 120.2, 88.6, 81.8, 51.5. MS (EI, 70 eV; m/z (relative intensity)): 366 (30), 348 (09), 289 (08), 152 (38), 105 (100), 77 (75). HRMS (ESI-TOF) m/z calcd for $C_{20}H_{14}O_2Se$ (M + H$^+$): 367.0237, found: 367.0241.

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*Phenyl(5-phenyl-4-(phenylethynyl)thiophen-2-yl)methanone (**8d**).* Obtained as a yellow solid. Yield: 0.164 g (90%); mp 98−100 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.00−7.97 (m, 2H), 7.91−7.88 (m, 2H), 7.69 (s, 1H), 7.61−7.57 (m, 1H), 7.52−7.37 (m, 7H), 7.32−7.30 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 187.6, 153.6, 140.8, 138.9, 137.7, 133.0, 132.5, 131.5, 129.5, 129.2, 128.8, 128.6, 128.5, 128.1, 122.9, 118.9, 92.0, 84.4. MS (EI, 70 eV; *m*/*z* (relative intensity)): 364 (100), 287 (61), 258 (27), 215 (36), 105 (63), 77 (75). HRMS (ESI-TOF) *m*/*z* calcd for $C_{25}H_{16}OS$ (M + H^+): 365.1000, found: 365.1006.

General Procedure for the Copper-Catalyzed Coupling Reaction of 2a and 4a with Thiols. To a Schlenck tube, under argon, containing the appropriate 4-iodo-chalcogenophene (0.5 mmol) in dry dioxane (3 mL) was added the appropriate thiol (0.6 mmol). After this Et_3N (1 mmol) was added dropwise, followed by CuI (0.0095 g, 10 mol %), and the reaction mixture was stirred at reflux temperature for 12 h. After that, the solution was cooled to room temperature, diluted with dichloromethane (20 mL), and washed with saturated aqueous NH_4Cl (3 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum.

*Phenyl(5-phenyl-4-(phenylthio)selenophen-2-yl)methanone (**9a**).* Obtained as a yellow solid. Yield: 0.174 g (83%); mp 74−76 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.79−7.77 (m, 3H), 7.61−7.57 (m, 2H), 7.54−7.45 (m, 1H), 7.43−7.36 (m, 5H), 7.23−7.18 (m, 2H), 7.15−7.10 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 188.4, 160.6, 147.6, 143.2, 137.2, 136.9, 134.5, 132.3, 129.1 (3C), 128.5, 128.4, 128.0 (2C), 127.6, 126.1. MS (EI, 70 eV; *m*/*z* (relative intensity)): 420 (61), 343 (23), 126 (22), 105 (100), 77 (75). HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{16}OSSe$ (M + H^+): 421.0165, found: 421.0170.

*Phenyl(5-phenyl-4-(phenylthio)thiophen-2-yl)methanone (**9b**).* Obtained as an orange solid. Yield: 0.136 g (73%); mp 63−65 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.84−7.81 (m, 2H), 7.68−7.64 (m, 2H), 7.56−7.52 (m, 2H), 7.46−7.36 (m, 5H), 7.24−7.11 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm). MS (EI, 70 eV; *m*/*z* (relative intensity)): 372 (53), 295 (10), 234 (21), 158 (12), 105 (100), 77 (42). HRMS (ESI-TOF) *m*/*z* calcd for $C_{23}H_{16}OS_2$ (M + H^+): 373.0721, found: 373.0723.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02334.

Text and figures giving spectroscopic data for all new compounds; X-ray results (CCDC 1029272) (PDF)
Crystallographic data for **2j** (CIF)

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Notes

The authors declare no competing financial interest.

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