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Electrophilic Cyclization of (*Z*)-Selenoenynes: Synthesis and Reactivity of 3-Iodoselenophenes

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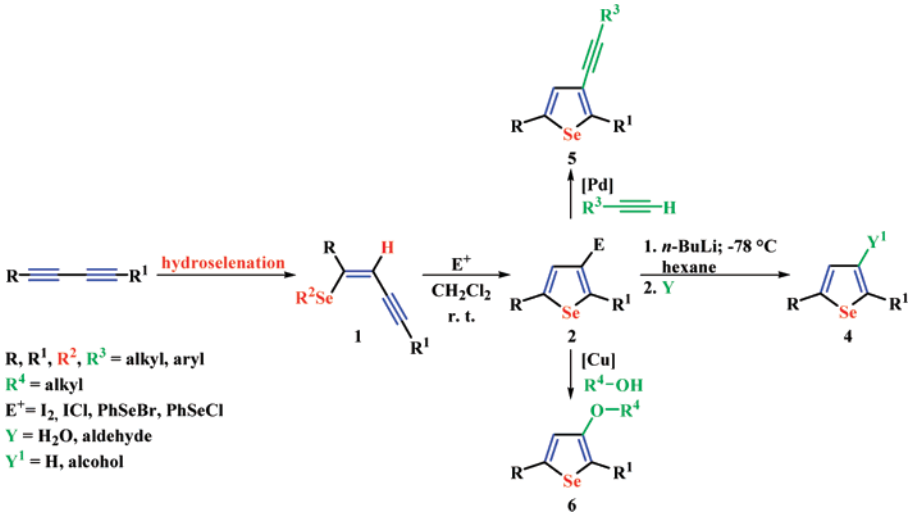

We present here our results of the electrophilic cyclization reaction of (*Z*)-selenoenynes with different electrophiles such as I_2, ICl, PhSeBr, and PhSeCl. The cyclization reaction proceeded cleanly under mild reaction conditions, and 3-substituted selenophenes were formed in moderate to excellent yields. We observed that the nature of solvent and structure of (*Z*)-selenoenyne were important to the cyclization reaction. In addition, the obtained 3-iodoselenophenes were readily transformed to more complex products using a metal−halogen exchange reaction with *n*-BuLi and trapping the intermediate formed with aldehydes, furnishing the desired secondary alcohols in good yields. Conversely, using the palladium or copper catalyzed cross-coupling reactions with terminal alkynes or alkyl alcohols, we were able to convert 3-iodoselenophene to Sonogashira or Ullmann type products, respectively, in good yields.

Introduction

Chalcogenide compounds have found such wide utility because their effects on an extraordinary number of very different reactions, including many carbon−carbon bond formations,[1] under relatively mild reaction conditions. In addition, they have become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions,[2] use in a wide variety of functional groups, thus avoiding protection group chemistry, and useful biological activities.[3] The selenium group can be introduced in an organic substrate via both nucleophile and electrophile reagents. After being introduced in an organic substrate, the organoselenium group can easily be removed by selenoxide *syn* elimination[4] and [2,3] sigmatropic rearrangement.[5] Conversely, the carbon−selenium bond can also be

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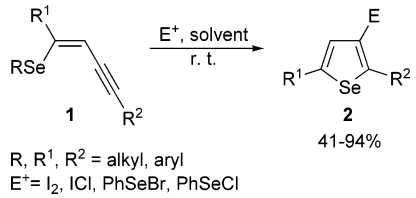
replaced by a carbon−hydrogen,[6] carbon−halogen,[7] carbon−lithium,[8] or carbon−carbon bond.[9]

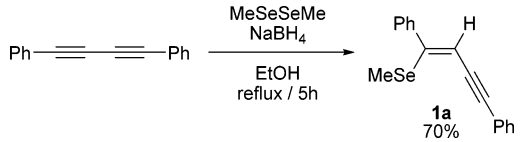
Among chalcogenides, the chalcogenophene derivatives play an important role in organic synthesis because of their excellent electrical properties and environmental stability. Chalcogenophene oligomers are compounds of current interest because many of them show photoenhanced biological activities,[10] and alpha-type of chalcogenophene oligomers such as 5,2′:5′,2″-terthiophene produce crystalline, electroconductive polythiophenes in electrochemical polymerizations.[11] Thus, a wide variety of oligomers and related chalcogen compounds including mixed thiophene−pyrrole oligomers have been synthesized mainly with the expectation of obtaining excellent precursor compounds for molecular devices and electroconductive polymers. In addition, chalcogenophenes are widely studied agents with a diverse array of biological effects. These include potent antitumor and antiviral activity, as well as efficacy as a maturation inducing agent.[12]

In the context of heterocycles, electrophilic cyclization of unsaturated compounds has proved to be an efficient method for one-step construction of a substituted heterocyclic unit.[13] Important heterocycles such as indoles, [13a,b] benzo[*b*]furans,[13c,d] benzo[*b*]thiophenes,[13e,f] benzo[*b*]selenophenes,[13g] thiophenes,[13h] furans,[13i] and pyrroles,[13j] among others,[13k−v] have been accessed using this protocol. This reaction is believed to proceed through an intramolecular, stepwise mechanism involving a cationic intermediate.[13b,g,r]

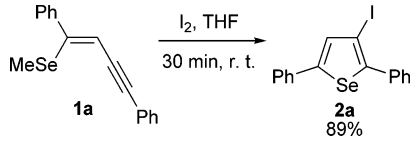
SCHEME 1



SCHEME 2



SCHEME 3



Haloheterocycles, in particular halochalcogenophenes, are important derivatives that provide an opportunity for further functionalization.[14] In particular, iodo- and bromoselenophenes are useful as substrates in a variety of C−C,[14a−b] C−N,[14c] and C−S[14d] bond forming reactions. However, to the best of our knowledge, there is no protocol describing the preparation of 3-haloselenophenes, using selenoenynes as substrate, via electrophilic cyclization. Our continuing interest in the synthesis and applications of chalcogenophenes in organic synthesis[14] prompted us to examine the electrophilic cyclization of (*Z*)-selenoenynes **1** to obtain 3-substituted selenophenes **2** (Scheme 1). Studies defining the scope and limitations of this reaction led us to a good understanding of this process.

Results and Discussion

The starting (*Z*)-1-(methylseleno)-1,4-diphenylbut-1-en-3-yne **1a** was readily available by using the process of hydroselenation of alkynes.[15] Treatment of 1,3-diphenylbutadiyne with methaneselenolate anion, generated from dimethyl diselenide and $NaBH_4$ in ethanol, under reflux, gave the corresponding (*Z*)-selenoenyne **1a** as the only isomer in 70% yield (Scheme 2).

Since our initial studies have focused on the development of an optimum set of the electrophilic cyclization conditions, the reaction of (*Z*)-selenoenyne **1a** with iodine was chosen as a model system for this process. We have found that the reaction of (*Z*)-selenoenyne **1a** with I_2 in THF as the solvent at room temperature yielded the desired product 2,5-diphenyl-3-iodoselenophene **2a** in 89% yield, after 30 min (Scheme 3).

Regarding the influence of the solvent, better results were achieved using CH_2Cl_2, which furnished the desired product

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(13) (a) Barluenga, J.; Trincado, M.; Rubio, E.; Gonzalez, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2406. (b) Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 62. (c)Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 10292. (d) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Moro, L. *Synlett* **1999**, 1432. (e) Yue, D.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 1905. (f) Hessian, K. O.; Flynn, B. L. *Org. Lett.* **2003**, *5*, 4377. (g) Kesharwani, T.; Worlikar, S. A.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 2307. (h) Flynn, B. L.; Flynn, G. P.; Hamel, E.; Jung, M. K. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2341. (i) Sniady, A.; Wheeler, K. A.; Dembinski, R. *Org. Lett.* **2005**, *7*, 1769. (j) Knight, D. W.; Redfern, A. L.; Gilmore, J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 622. (k) Huang, Q.; Hunter, J. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 3437. (l) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936. (m) Yue, D.; Della Ca, N.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1581. (n) Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 1432. (o) Yao, T.; Campo, M. A.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 3511. (p) Zhou, C.; Dubrovsky, A. V.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 1626. (q) Waldo, J. P.; Larock, R. C. *Org. Lett.* **2005**, *7*, 5203. (r) Arcadi, A.; Cacchi, S.; Giuseppe, S. D.; Fabrizi, G.; Marinelli, F. *Org. Lett.* **2002**, *4*, 2409. (s) Dabdoub, M. J.; Dabdoub, V. B.; Pereira, M. A. *J. Org. Chem.* **1996**, *61*, 9503. (t) Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron* **2001**, *57*, 2857. (u) Peng, A.; Ding, Y. *J. Am. Chem. Soc.* **2003**, *125*, 15006. (v) Djuardi, E.; McNelis, E. *Tetrahedron Lett.* **1999**, *40*, 7193.

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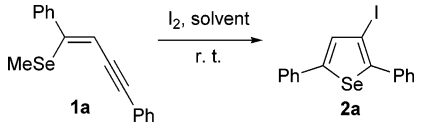
(15) Dabdoub, M. J.; Baroni, A. C. M.; Lenardão, E. J.; Gianeti, T. R.; Hurtado, G. R. *Tetrahedron* **2001**, *57*, 4271.

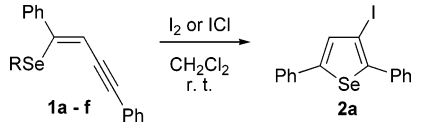
TABLE 1. Study of the Solvent Effect on Selenoenyne Cyclization Reactions[a]



entry	solvent	time (min)	yield **2a**[b] (%)
1	THF	30	89
2	CH_2Cl_2	5	90
3	Et_2O	30	85
4	MeOH	45	79
5	MeCN	30	87
6	hexane	60	82

[a] Reactions performed in the presence of **1a** (0.50 mmol), I_2 (0.55 mmol). [b] Yields of **2a** are given for isolated products.

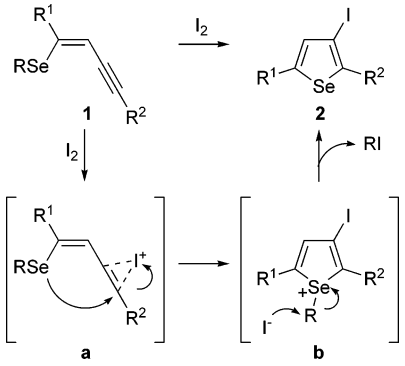
TABLE 2. Influence of the Group Bonded to a Selenium Atom[a]



entry	(*Z*)-selenoenyne (**1a**−**f**)	time (min)	yield **2a**[b] (%)
1	**1a** (R = Me)	5	90 (89)
2	**1b** (R = Et)	5	90 (89)
3	**1c** (R = *n*-Bu)	5	93 (90)[c]
4	**1d** (R = *t*-Bu)	30	88 (88)
5	**1e** (R = Bn)	10	88 (87)
6	**1f** (R = Ph)	48 h[d]	−

[a] Reactions performed in the presence of (*Z*)-selenoenyne (0.50 mmol), I_2, or ICl (0.55 mmol) in CH_2Cl_2 (10 mL). [b] Yields in parentheses correspond to reactions performed with ICl as eletrophile. [c] Reaction performed at 5 mmol scale gave the same result. [d] (*Z*)-Selenoenyne **1f** was recovered in 96% yield.

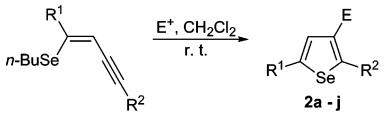
SCHEME 4

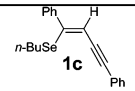
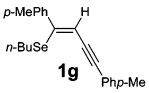
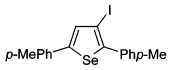
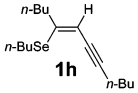
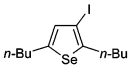
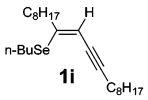
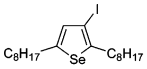
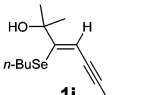
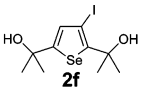
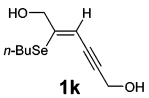
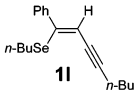
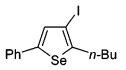
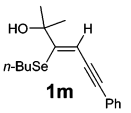
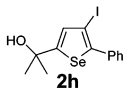
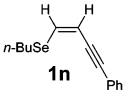
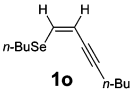


2a in 90% yield, after a very short reaction time (Table 1, entry 2). When THF, Et_2O, MeOH, hexane, and MeCN were used as solvent, good yields were also obtained; however these reactions proceeded more slowly.

We believe that the mechanism of theses cyclization reactions involve the following: (i) coordination of the carbon−carbon triple bond to the I_2 to generate an iodonium intermediate **a**, (ii) anti attack of the selenium atom on the activated iodonium intermediate to produce the salt **b**, and (iii) facile removal of the alkyl group by the iodide anion present in the reaction mixture to generate the 3-iodoselenophene product and one molecule of RI (Scheme 4). Only selenophene derivatives have

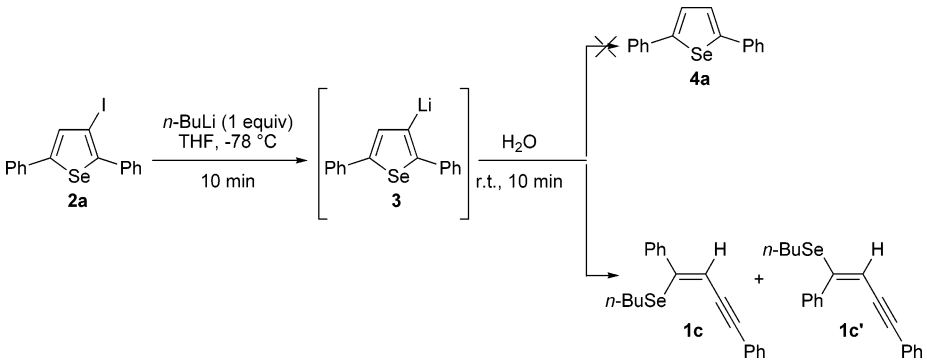
TABLE 3. Scope and Generality of the Electrophilic Cyclization of (*Z*)-Selenoenynes[a]



Entry	Selenoenyne	E^+	Time (min.)	Product	Yield (%)
1	 **1c**	I_2	5	 **2a**	93
2	**1c**	ICl	5		90
3	**1c**	PhSeBr	10	 **2b**	80
4	**1c**	PhSeCl	15		76
5	 **1g**	I_2	5	 **2c**	94
6		ICl	10		93
7	 **1h**	I_2	15	 **2d**	90
8		ICl	15		89
9	 **1i**	I_2	15	 **2e**	88
10		ICl	15		88
11	 **1j**	I_2	5	 **2f**	43
12		ICl	5		41
13	 **1k**	I_2	5	complex mixture	-
14		ICl	5	complex mixture	-
15	 **1l**	I_2	10	 **2g**	90
16		ICl	15		89
17	 **1m**	I_2	5	 **2h**	57
18		ICl	5		56
19	 **1n**	I_2	15	 **2i**	82
20		ICl	15		80
21	 **1o**	I_2	20	 **2j**	81
22		ICl	20		81

[a] Reactions performed in the presence of (*Z*)-selenoenyne (0.50 mmol), E^+ (0.55 mmol) in CH_2Cl_2 (10 mL).

SCHEME 5



been obtained from this process. No other cyclized product has ever been observed to arise by this process.

Since the accomplishment of this reaction probably is dependent on the nature of the group directly linked to the selenium atom, we decided to explore this influence using different aryl and alkyl groups, and the results are shown in Table 2. Inspection of Table 2 shows that the cyclization reactions of (*Z*)-selenoenynes containing different groups bonded at selenium atom, using I_2 or ICl, as an electrophile source, in CH_2Cl_2, at room temperature, afforded 2,5-diphenyl-3-iodoselenophene **2a** in good yields.

A closer inspection of these results revealed that methyl, ethyl, and *n*-butyl groups bonded at selenium atom resulted in the formation of products in high yields after very short reaction times (Table 1, entries 1−3). The selenoenynes having a *tert*-butyl or benzyl groups also gave the product **2a** in good yield, however with higher reaction times (Table 1, entries 4−5). Nonetheless, performing the reaction with selenoenyne **1f**, which has a phenyl group bonded at the selenium atom, the desired product was not observed, even under a long reaction time (Table 1, entry 6). These results demonstrated that the efficiency of the selenophene formation could significantly depend on the steric effects and that this cyclization reaction occurs only with selenoenynes having a Se−Csp^3 bond.

Thus, the careful analysis of the optimized reactions revealed that the optimum condition for this electrophilic cyclization reaction was the combination of 1.0 equiv of (*Z*)-selenoenyne, 1.1 equiv of electrophile source, and CH_2Cl_2 as the solvent, at room temperature. To demonstrate the efficiency of this reaction, we explored the generality of our method extending the conditions to other selenoenynes, and these results are summarized in Table 3.

Inspection of Table 3 shows that, in general, all of the reactions proceeded smoothly with good yields. Most importantly, the cyclization turned out to be general with respect to a diverse array of functionality and electrophile sources. Satisfactorily, all electrophile sources tested were effective. Our experiments also showed that the reaction with selenoenynes having aryl, aryl substituted, alkyl, and propargyl groups gave the selenophene derivatives in good yields, although the yield was lower for the selenoenynes with a hydroxyl function at the propargyl position (Table 3, entries 11, 12, 17, and 18). Finally, it is worth mentioning that, through our methodology, it was possible to prepare highly functionalized selenophenes, using as substrate not only symmetrical (Table 3, entries 1−12) but also unsymmetrical selenoenynes (Table 3, entries 15−22).

The selenophenes obtained by electrophilic cyclization appear highly promising as intermediates for the preparation of more highly substituted selenophenes. To further prove the utility of our methodology, we have carried out the halogen−lithium exchange reaction of our product **2a** with *n*-butyllithium. Metal−halogen exchange reactions have great importance in synthetic organic chemistry, particularly with respect to the formation of new C−C bonds.[16] In addition, the development of the synthetic methodology to prepare 3-substituted heterocycle derivatives has attracted much attention. Previously, Gronowitz showed that 3-lithiothiophene derivatives can be prepared by metal−halogen exchange of 3-bromothiophenes with *n*-butyllithium.[17] The reaction of 3-lithiothiophene reagents with electrophiles has been widely used; however the utility of these reactions is limited owing to the lack of regiospecificity, as well as decomposition of the thiophene ring at room temperature.[18] Analogous to the well-known metal−halogen exchange reactions, which lead to a lithium intermediate, we extended this finding to obtain an intermediate 2,5-diphenyl-3-lithioselenophene **3**. Nonetheless, performing the reaction of **2a**, in THF, with addition of 1 equiv of *n*-BuLi at −78 °C gave unsatisfactory results, and a mixture of (*Z*)- and (*E*)-selenoenynes **1c** and **1c′** in 71% yield in a proportion of 4:1 respectively was obtained instead of the desired product **4a** (Scheme 5).

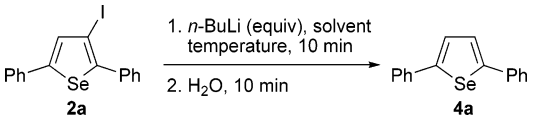
Based on the disappointing results above we initiated our investigations exploring the best experimental conditions for this halogen−metal exchange reaction (Table 4). At first, the reaction was carried out using different amounts of *n*-butyllithium from 1 to 0.8 equiv, in THF (Table 1, entries 1−3). Unfortunately, this condition was not effective giving again only a mixture of (*Z*)- and (*E*)-selenoenynes **1c** and **1c′**. However, it was gratifying to discover that simply changing the solvent from THF to hexane had a dramatic effect, giving the 2,5-diphenylselenophene **4a** in 85% yield (Table 4, entry 4). Using hexane as a solvent we also observed that the yield of compound **4a** was greatly enhanced by decreasing the amount of lithium reagent from 1.0 to 0.8 equiv (Table 4, entries 4−6). We also

(16) (a) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1. (b) Knochel, P.; Dohle, W.; Gommerman, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4302. (c) Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300. (d) Rogers, H. R.; Houk, J. *J. Am. Chem. Soc.* **1982**, *104*, 522. (e) Rieke, R. D.; Lee, J.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J. R. *J. Org. Chem.* **2000**, *65*, 5428. (f) Slocum, D. W.; Carroll, A.; Dietzel, P.; Eilerman, S.; Culver, J. P.; McClure, B.; Brown, S.; Holman, R. W. *Tetrahedron Lett.* **2006**, *47*, 865. (g) Oshima, K.; Inoue, A.; Kitagawa, K.; Shinokubo, H. *J. Org. Chem.* **2001**, *66*, 4333.

(17) (a) Gronowitz, S.; Hakansson, R. *Arkiv. Kemi*. **1959**, *17*, 73. (b) Gronowitz, S. In *Organic Sulphur Chemistry-Structure, Mechanism, and Synthesis*; Sterling, C. J. M., Ed.; Butterworths: London, 1975; p 203.

(18) (a) Ritter, S. K.; Noftle, R. E. *Chem. Mater*. **1992**, *4*, 872. (b) Frohlich, H.; Kalt, W. *J. Org. Chem.* **1990**, *55*, 2993. (c) Gronowitz, S. *Adv. Heterocycl. Chem.* **1963**, *1*, 75.

TABLE 4. Optimization of Halogen−Metal Exchange Reaction[a]



entry	*n*-BuLi (equiv)	solvent	*T* (°C)	**4a** (%)	**1c**−**1c′** (%)
1	1.0	THF	−78	−	71
2	0.9	THF	−78	−	70
3	0.8	THF	−78	−	71
4	1.0	hexane	−78	85	−
5	0.9	hexane	−78	88	−
6	0.8	hexane	−78	97	−
7	0.8	hexane	0	35	54
8	0.8	hexane	rt	17	68

[a] Reaction performed at 0.25 mmol scale.

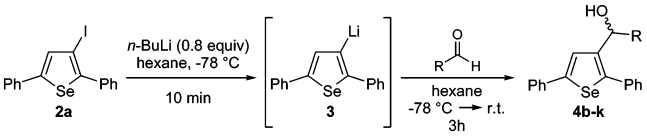
found that the reaction is highly affected by the temperature, and unsatisfactory results were obtained in the reactions when the temperature was increased from −78 °C to room temperature (Table 4, entries 7 and 8).

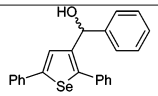
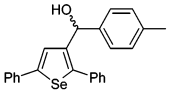
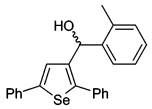
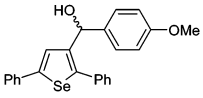
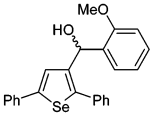
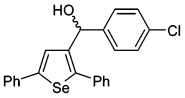
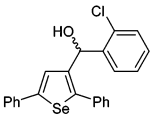
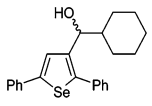
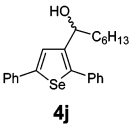
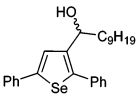
Thus, careful analysis of the optimized reactions revealed that the general synthetic procedure for the reaction is as follows: *n*-butyllithium (0.2 mmol) is added to a solution of 2,5-diphenyl-3-iodoselenophene **2a** (0.25 mmol) and hexane (2 mL), at −78 °C. The resulting solution is stirred for 10 min at −78 °C and allowed to stir at room temperature. After that, water is added and the product is then isolated. In further experiments, we examined the scope of this procedure trapping the intermediate 2,5-diphenyl-3-lithioselenophene **3** with several aldehydes, and these results are shown in Table 5.

Our first investigations focused on the influence of aryl or alkyl groups in the reactivity of aldehyde. Satisfactorily, all aldehydes were found to be effective, although moderated yields were observed for aliphatic aldehydes. Next, aromatic aldehydes having different substituents were tested. As shown in Table 5, bulky aromatic aldehydes afforded the alcohols **4** in good yield (Table 5, entries 3, 5, and 7). Our experiments showed that the reaction with aromatic aldehyde having neutral (entry 1), electron-donating (entries 2−5), or electron-withdrawing (entries 6 and 7) substituents also gave the desired alcohols **4** in good yields.

We believe that this approach to selenophenes should prove quite useful in synthesis, particularly when one considers that there are many ways to transform the resulting halogen and selenium functionalities into other substituents. For instance, the resulting selenophene iodides should be particularly useful intermediates in many transition metal catalyzed processes, such as Sonogashira,[19] Suzuki,[20] Stille,[21] Heck,[22] and Ullmann[23] cross-couplings. In view of this, the potential of 3-iodoselenophene derivatives as precursors for increasing molecular complexity via palladium and copper catalyzed reactions has

TABLE 5. Reactions of Intermediate 2,5-Diphenyl-3-lithioselenophene 3 with Aldehydes[a]

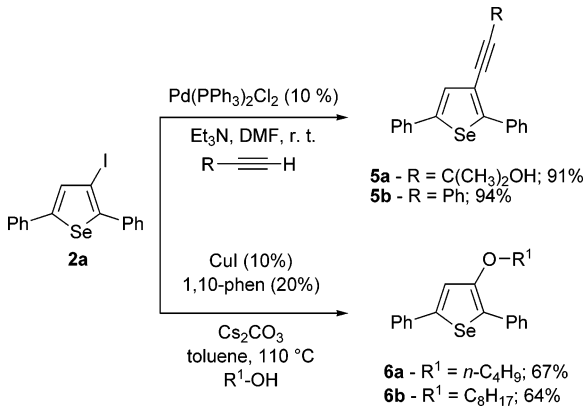


Entry	R	Product	Yield (%)
1		 **4b**	82
2		 **4c**	86
3		 **4d**	87
4		 **4e**	70
5		 **4f**	68
6		 **4g**	74
7		 **4h**	64
8		 **4i**	67
9	C_6H_{13}	 **4j**	62
10	C_9H_{19}	 **4k**	71

[a] Reactions are performed with **2a** (0.25 mmol), aldehyde (0.30 mmol) in hexane (2.5 mL).

(19) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467.
(20) Suzuki, A. *Pure Appl. Chem.* **1985**, *57*, 1749.
(21) Scott, W. J.; Peña, M. R.; Sward, K.; Stoessel, S. J.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2302.
(22) Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259.
(23) (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382. (b) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 2779. (c) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578. (d) Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684. (e) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727.

SCHEME 6



been briefly investigated (Scheme 6). For example, compound **2a** which underwent Sonogashira cross-coupling with different alkynes gave the corresponding 3-alkynylselenophenes **5a** and **5b** in 91% and 94% yields respectively. These reactions constitute an interesting alternative route to preparing alkynyl compounds functionalized in high yields. In addition, the reactions of **2a** with alcohols in dry toluene, using a catalytic system of CuI/1,10-phenanthroline and Cs_2CO_3 as base, afforded the resultant ethers **6a** and **6b** in good isolated yields.

Conclusion

In summary, we have demonstrated the electrophilic cyclization reaction of (*Z*)-selenoenynes with different electrophilic sources under exceptionally mild conditions and established a route to obtain 3-substituted selenophenes in good to excellent yields. We observed that the reaction was sensitive to the nature of solvent and the structure of (*Z*)-selenoenynes. The selenophenes obtained by electrophilic cyclization appear highly promising as intermediates for the preparation of more highly substituted selenophenes. For instance, 3-iodoselenophene was treated under metal−halogen exchange conditions with *n*-BuLi, and trapping the intermediates with aldehydes provided the corresponding secondary alcohols in good yields. Conversely, using the palladium or copper catalyzed cross-coupling reactions with terminal alkynes or alkyl alcohols we were able to convert 3-iodoselenophene to Sonogashira or Ullmann type products, respectively, in good yields. We believe that this approach to selenophene should prove quite useful in synthesis, particularly when one considers that there are many ways to transform the resulting halogen and selenium functionalities into other substituents.

Experimental Section

General Procedure for the Preparation of the (*Z*)-Selenoenynes 1a,b and 1d−f. To a solution of 1,4-diphenyl-1,3-butadiyne (1.010 g; 5.0 mmol) and appropriate diorganoyldiselenide (2.5 mmol) in 95% ethanol (50 mL) under a nitrogen atmosphere was added $NaBH_4$ (0.472 g; 12.5 mmol), at room temperature, under vigorous stirring. Gas evolution was observed during addition. The reaction mixture was stirred under reflux for 5 h and then allowed to reach room temperature. Afterward, the mixture was diluted with ethyl acetate (20 mL) and washed with brine (2 × 30 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.

(*Z*)-1-(Methylseleno)-1,4-diphenylbut-1-en-3-yne (1a). Yield: 1.039 g (70%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.55−7.30 (m, 10H), 6.17 (s, 1H), 1.95 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.58, 139.41, 131.37, 128.46, 128.45, 128.30, 128.29, 128.21, 123.44, 110.08, 96.98, 88.07, 7.05. MS (relative intensity) *m*/*z*: 297 (100), 203 (65), 173 (35), 96 (21), 77 (15), 47 (21). HRMS calcd for $C_{17}H_{14}Se$: 298.0261. Found: 298.0266.

(*Z*)-1-(Ethylseleno)-1,4-diphenylbut-1-en-3-yne (1b). Yield: 1.104 g (71%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.54−7.30 (m, 10H), 6.22 (s, 1H), 2.59 (q, J = 7.50 Hz, 2H), 1.26 (t, J = 7.50 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.63, 140.03, 131.37, 128.42, 128.38, 128.27, 128.17, 128.13, 123.49, 111.25, 96.85, 88.32, 20.49, 15.56. MS (relative intensity) *m*/*z*: 312 (100), 204 (75), 127 (62), 106 (39), 102 (45), 77 (16). HRMS calcd for $C_{18}H_{16}Se$: 312.0417. Found: 312.0422.

(*Z*)-1-(*tert*-Butylseleno)-1,4-diphenylbut-1-en-3-yne (1d). Yield: 1.084 g (64%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.67−7.62 (m, 2H), 7.54−7.49 (m, 2H), 7.39−7.31 (m, 6H), 6.56 (s, 1H), 1.36 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.02, 142.72, 131.54, 128.31, 128.30, 128.25, 128.20, 128.19, 123.63, 118.68, 95.85, 89.87, 46.48, 32.93. MS (relative intensity) *m*/*z*: 339 (100), 283 (65), 204 (54), 127 (25), 77 (23), 56 (13), 42 (18). HRMS calcd for $C_{20}H_{20}Se$: 340.0730. Found: 340.0735.

(*Z*)-1-(Benzylseleno)-1,4-diphenylbut-1-en-3-yne (1e). Yield: 1.268 g (68%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.52−7.12 (m, 15H), 6.23 (s, 1H), 3.87 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.64, 140.05, 138.35, 131.40, 128.92, 128.55, 128.46, 128.33, 128.29, 128.27, 128.26, 126.77, 123.38, 111.61, 97.26, 88.29, 30.57. MS (relative intensity) *m*/*z*: 374 (100), 283 (63), 204 (50), 127 (20), 91 (53), 77 (17). HRMS calcd for $C_{23}H_{18}Se$: 374.0573. Found: 374.0577.

(*Z*)-1-(Phenylseleno)-1,4-diphenyl-but-1-en-3-yne[15] (1f). Yield: 1.220 g (68%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50−7.40 (m, 4H), 7.38−7.22 (m, 5H), 7.19 (m, 3H), 7.07 (m, 3H), 6.40 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.10, 139.40, 133.20, 133.00, 131.40, 129.90, 128.30, 128.20, 127.90, 126.90, 123.20, 112.60, 97.60, 88.30. MS (relative intensity) *m*/*z*: 359 (100), 282 (39), 203 (82), 156 (72), 126 (42), 101 (35), 77 (31). HRMS calcd for $C_{22}H_{16}Se$: 360.0417. Found: 360.0410.

General Procedure for the Preparation of the (*Z*)-Selenoenynes 1c and 1 g−m. To a suspension of elemental selenium (0.395 g; 5 mmol) in dry THF (25 mL), under argon and with magnetic stirring, was added *n*-butyllithium (2.0 mL of a 2.5 M solution in hexane; 5 mmol). A yellow solution was formed. To this solution was added the appropriate diyne (5 mmol) in deoxygenated ethanol (25 mL). The mixture was then heated at reflux for 24 h. After this time, the mixture was cooled to room temperature and diluted with ethyl acetate (60 mL) and washed with saturated aq NH_4Cl (30 mL) and water (3 × 30 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent. **(*Z*)-1-(*n*-Butylseleno)-1,4-diphenyl-but-1-en-3-yne (1c).**[24] Yield: 1.135 g (67%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53−7.45 (m, 4H), 7.38−7.30 (m, 6H), 6.21 (s, 1H), 2.58 (t, J = 7.44 Hz, 2H), 1.53 (quint, J = 7.44 Hz, 2H), 1.28 (sex, J = 7.44 Hz, 2H), 0.78 (t, J = 7.44 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.90, 140.09, 131.39, 128.43, 128.37, 128.28, 128.21, 128.16, 123.56, 111.15, 96.77, 88.39, 32.47, 26.55, 22.72, 13.47. MS (relative intensity) *m*/*z*: 339 (100), 283 (65), 204 (54), 127 (25), 77 (23), 56 (13), 42 (18). HRMS calcd for $C_{20}H_{20}Se$: 340.0730. Found: 340.0735.

(*Z*)-1-(*n*-Butylseleno)-1,4-bis-(*p*-methylphenyl)-but-1-en-3-yne (1g). Yield: 1.266 g (69%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42−7.36 (m, 4H), 7.17−7.12 (m, 4H), 6.19 (s, 1H), 2.60 (t, J = 7.44 Hz, 2H), 2.36−2.35 (m, 6H), 1.54 (quint, J = 7.44 Hz, 2H), 1.29 (sex, J = 7.44 Hz, 2H), 0.79 (t, J = 7.44 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.30, 138.37, 138.22, 137.26, 131.24, 129.05, 129.04, 128.08, 120.52, 110.72, 96.78, 87.94, 32.41, 26.55,

(24) Zeni, G.; Stracke, M. P.; Nogueira, C. W.; Braga, A. L.; Menezes, P. H.; Stefani, H. A. *Org. Lett.* **2004**, *6*, 1135.

22.73, 21.50, 21.19, 13.48. MS (relative intensity) *m*/*z*: 368 (100), 311 (44), 232 (37), 141 (63), 136 (29), 91 (78), 57 (22), 43 (19). HRMS calcd for $C_{22}H_{24}Se$: 368.1043. Found: 368.1047.

(*Z*)-5-(*n*-Butylseleno)-dodec-5-en-7-yne (1h). Yield: 0.956 g (64%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.76−5.74 (m, 1H), 2.81 (t, J = 7.44 Hz, 2H), 2.39−2.30 (m, 4H), 1.70−1.29 (m, 12H), 0.94−0.89 (m, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.41, 108.66, 96.29, 78.41, 37.45, 32.58, 31.21, 30.84, 24.04, 24.03, 23.03, 22.00, 21.96, 19.40, 13.84, 13.57. MS (relative intensity) *m*/*z*: 299 (100), 242 (15), 163 (75), 136 (25), 106 (45), 56 (19). HRMS calcd for $C_{16}H_{28}Se$: 300.1356. Found: 300.1361.

(*Z*)-9-(*n*-Butylseleno)-icos-9-en-11-yne (1i). Yield: 1.274 g (62%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.74 (s, 1H), 2.81 (t, J = 7.44 Hz, 2H), 2.38−2.29 (m, 4H), 1.70−1.28 (m, 28H), 0.94−0.86 (m, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.56, 108.50, 96.39, 78.43, 37.72, 32.56, 31.83, 29.37, 29.36, 29.21, 29.19, 29.13, 29.09, 28.94, 28.91, 28.78, 24.01, 23.05, 22.64, 22.63, 19.73, 14.08, 14.07, 13.59. MS (relative intensity) *m*/*z*: 411 (100), 354 (11), 275 (87), 261 (15), 247 (21), 233 (17), 219 (11), 136 (51), 112 (52), 56 (31), 42 (24). HRMS calcd for $C_{24}H_{44}Se$: 412.2608. Found: 412.2613.

(*Z*)-3-(*n*-Butylseleno)-2,7-dimethyl-oct-3-en-5-yne-2,7-diol (1j). Yield: 1.060 g (70%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.35 (s, 1H), 3.04 (t, J = 7.50 Hz, 2H), 2.53−2.45 (m, 2H), 1.74−1.33 (m, 16H), 0.92 (t, J = 7.50 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 154.42, 112.19, 100.72, 80.11, 74.54, 65.55, 32.34, 31.21, 28.98, 28.20, 22.96, 13.57. MS (relative intensity) *m*/*z*: 267 (100), 210 (23), 136 (78), 131 (56), 56 (21), 42 (23). HRMS calcd for $C_{14}H_{24}O_2Se$: 304.0942. Found: 304.0948.

(*Z*)-2-(*n*-Butylseleno)-hex-2-en-4-yne-1,6-diol (1k).[24] Yield: 0.852 g (69%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.16 (s, 1H), 4.44 (s, 2H), 4.30 (s, 2H), 2.92 (t, J = 7.50 Hz, 2H), 2.75 (m, 2H), 1.67 (quint, J = 7.50 Hz, 2H), 1.42 (sex, J = 7.50 Hz, 2H), 0.93 (t, J = 7.50 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.26, 109.08, 94.54, 82.81, 66.07, 51.51, 32.54, 24.36, 22.87, 13.51. MS (relative intensity) *m*/*z*: 230 (40), 212(15), 191 (34), 112 (100), 94 (22), 76 (31). HRMS calcd for $C_{10}H_{16}O_2Se$: 248.0365. Found: 248.0378.

(*Z*)-1-(*n*-Butylseleno)-1-phenyl-oct-1-en-3-yne (1l).[24] Yield: 1.052 g (66%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47−7.45 (m, 2H), 7.35−7.25 (m, 3H), 5.97 (s, 1H), 2.88 (t, J = 7.44 Hz, 2H), 2.40 (t, J = 7.44 Hz, 2H), 1.69 (quint, J = 7.44 Hz, 2H), 1.54 (quint, J = 7.44 Hz, 2H), 1.48−1.32 (m, 4H), 0.95−0.90 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.54, 131.20, 128.19, 127.87, 123.68, 107.90, 95.01, 87.56, 37.75, 32.54, 31.27, 24.39, 23.01, 22.02, 13.87, 13.59. MS (relative intensity) *m*/*z*: 319 (100), 213 (76), 184 (48), 127 (10), 102 (29), 77 (38), 57 (47), 43 (32). HRMS calcd for $C_{18}H_{24}Se$: 320.1043. Found: 320.1048.

(*Z*)-3-(*n*-Butylseleno)-2-methyl-6-phenyl-hex-3-en-5-yn-2-ol (1m).[24] Yield: 1.011 g (63%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48−7.45 (m, 2H), 7.34−7.32 (m, 3H), 6.55 (s, 1H), 3.12 (t, J = 7.60 Hz, 2H), 2.32 (s, 1H), 1.70 (quint, J = 7.60 Hz, 2H), 1.51−1.36 (m, 8H), 0.89 (t, J = 7.60 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.00, 131.27, 128.35, 128.34, 123.31, 112.49, 96.19, 87.57, 74.54, 32.42, 29.09, 28.55, 22.96, 13.55. MS (relative intensity) *m*/*z*: 304 (21), 265 (44), 186 (100), 168 (75), 77 (11). HRMS calcd for $C_{17}H_{22}OSe$: 322.0858. Found: 322.0877.

(*Z*)-1-(*n*-Butylseleno)-4-phenyl-but-1-en-3-yne (1n). Powdered NaOH (0.220 g, 5.5 mmol) was added to a two-neck round bottomed flask equipped with a reflux condenser, containing a solution of 2-hydroxy-2-methyl-6-phenyl-3,5-hexadiyne (0.830 g; 5.0 mmol) in dry toluene (10 mL) under an argon atmosphere. The mixture was slowly heated to reach reflux temperature; at this time the reaction mixture became dark brown and was refluxed until all the starting material was transformed. The solution of the 1-phenyl-1,3-butadiyne obtained was cooled to room temperature, and then a solution of dibutyldiselenide (0.680 g; 2.5 mmol) in 95% ethanol (50 mL) was added. $NaBH_4$ (0.472 g; 12.5 mmol) was added under vigorous stirring (gas evolution was observed during this addition). The reaction mixture was stirred under reflux for 4 h, allowed to reach room temperature, diluted with ethyl acetate (60 mL), and washed with brine (3 × 30 mL) and water (3 × 30 mL). After the organic phase was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel using hexane as the eluent. Yield: 0.841 g (64%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48−7.47 (m, 2H), 7.31−7.29 (m, 3H), 6.95 (d, J = 9.76 Hz, 1H), 6.12 (d, J = 9.76 Hz, 1H), 2.83 (t, J = 7.44 Hz, 2H), 1.74 (quint, J = 7.44 Hz, 2H), 1.44 (sex, J = 7.44 Hz, 2H), 0.93 (t, J = 7.44 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.90, 131.35, 128.23, 128.12, 123.34, 109.15, 96.77, 87.04, 33.07, 26.43, 22.73, 13.53. MS (relative intensity) *m*/*z*: 263 (100), 206 (31), 127 (76), 136 (71), 77 (34), 56 (31), 42 (13). HRMS calcd for $C_{14}H_{16}Se$: 264.0417. Found: 264.0422.

(*Z*)-1-(*n*-Butylseleno)-oct-1-en-3-yne (1o). The same procedure as that for **1n** was followed. Yield: 0.802 g (66%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.74 (d, J = 9.46 Hz, 1H), 5.90 (dt, J = 9.46, 2.17 Hz, 1H), 2.77 (t, J = 7.44 Hz, 2H), 2.37 (td, J = 2.17, 7.44 Hz, 2H), 1.72 (quint, J = 7.44 Hz, 2H), 1.58−1.38 (m, 6H), 0.94−0.91 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 134.33, 109.89, 98.23, 78.14, 33.08, 30.76, 26.04, 22.74, 21.90, 19.37, 13.58, 13.52. MS (relative intensity) *m*/*z*: 243 (100), 186 (52), 136 (58), 107 (79), 56 (35), 42 (21). HRMS calcd for $C_{12}H_{20}Se$: 244.0730. Found: 244.0724.

General Procedure for the Iodocyclizations. To a solution of 0.50 mmol of the appropriate (*Z*)-selenoenyne in 3 mL of CH_2Cl_2 was added gradually 1.1 equiv of I_2 or ICl dissolved in 7 mL of CH_2Cl_2. The reaction mixture was allowed to stir at room temperature for the time shown in Table 3. Excess I_2 or ICl was removed by washing with saturated aq $Na_2S_2O_3$. The product was then extracted by CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

2,5-Diphenyl-3-iodoselenophene (2a). Yield: 0.189 g (93%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.62−7.30 (m, 11H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.27, 146.01, 136.33, 134.97, 134.59, 129.27, 129.01, 128.41, 128.34, 128.19, 126.00, 80.23. MS (relative intensity) *m*/*z*: 409 (12), 283 (100), 206 (55), 129 (25), 126 (31), 77 (16). HRMS calcd for $C_{16}H_{11}ISe$: 409.9070. Found: 409.9074

2,5-Bis(*p*-methylphenyl)-3-iodoselenophene (2c). Yield: 0.205 g (94%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.51−7.39 (m, 5H), 7.25−7.16 (m, 4H), 2.39−2.36 (m, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 151.07, 145.56, 138.29, 138.16, 133.97, 133.51, 132.30, 129.67, 129.55, 129.13, 125.87, 79.90, 21.32, 21.20. MS (relative intensity) *m*/*z*: 437 (100), 311 (58), 220 (25), 126 (12), 129 (77), 91 (53). HRMS calcd for $C_{18}H_{15}ISe$: 437.9383. Found: 437.9388.

2,5-Bis(*n*-butyl)-3-iodoselenophene (2d). Yield: 0.166 g (90%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.77 (s, 1H), 2.83−2.70 (m, 4H), 1.69−1.29 (m, 8H), 0.98−0.89 (m, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 151.36, 146.90, 79.63, 34.83, 34.18, 33.98, 32.15, 22.17, 22.07, 13.89, 13.79. MS (relative intensity) *m*/*z*: 369 (23), 243 (100), 228 (39), 214 (40), 200 (31), 186 (44), 129 (56), 126 (67), 57 (13), 43 (11). HRMS calcd for $C_{12}H_{19}ISe$: 369.9696. Found: 369.9701.

2,5-Bis(*n*-octyl)-3-iodoselenophene (2e). Yield: 0.212 g (88%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.77 (s, 1H), 2.81−2.69 (m, 4H), 1.66−1.53 (m, 4H), 1.43−1.41 (m, 20H), 0.91−0.85 (m, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 151.44, 146.96, 133.40, 79.61, 35.12, 32.49, 32.11, 31.85, 31.84, 29.33, 29.32, 29.18, 29.17, 29.05, 29.04, 29.01, 22.65, 22.64, 14.10, 14.09. MS (relative intensity) *m*/*z*: 481 (26), 355 (100), 340 (37), 326 (41), 312 (29), 298 (54), 284 (32), 270 (39), 259 (28), 256 (53), 229 (43), 126 (75), 96 (34), 57 (18), 43 (13). HRMS calcd for $C_{20}H_{35}ISe$: 482.0948. Found: 482.0953.

2,5-Bis[(α-hydroxy-α,α-dimethyl)methyl]-3-iodoselenophene (2f). Yield: 0.080 g (43%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.00 (s, 1H), 2.33 (s, 2H), 1.73 (s, 6H), 1.61 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.59, 155.95, 134.53, 74.30, 72.44,

71.90, 32.07, 29.68. MS (relative intensity) *m*/*z*: 373 (100), 356 (73), 338 (55), 211 (23), 157 (39), 126 (14), 45 (11). HRMS calcd for $C_{10}H_{15}IO_2Se$: 373.9282. Found: 373.9286.

2-(*n*-Butyl)-3-iodo-5-phenylselenophene (2g). Yield: 0.175 g (90%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.56−7.51 (m, 2H), 7.43−7.33 (m, 3H), 6.98 (s, 1H), 2.85 (t, J = 7.06 Hz, 2H), 1.56 (quint, J = 7.06 Hz, 2H), 1.42 (sex, J = 7.06 Hz, 2H), 0.95 (t, J = 7.06, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 154.32, 144.16, 136.74, 135.76, 129.30, 128.23, 127.97, 78.54, 34.20, 32.13, 22.11, 13.79. MS (relative intensity) *m*/*z*: 389 (23), 263 (100), 206 (39), 129 (64), 77 (29), 57 (54), 43 (19). HRMS calcd for $C_{14}H_{15}ISe$: 389.9383. Found: 389.9387.

2-Phenyl-3-iodo-5-(α-hydroxy-α,α-dimethyl)methyl-3-iodoselenophene (2h). Yield: 0.111 g (57%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.55−7.50 (m, 2H), 7.41−7.36 (m, 3H), 7.08 (s, 1H), 2.29 (s, 1H), 1.65 (s, 6H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 163.04, 145.42, 136.55, 132.93, 129.25, 128.33, 128.17, 78.54, 72.71. MS (relative intensity) *m*/*z*: 391 (13), 374 (100), 332 (71), 265 (54), 205 (38), 129 (41), 77 (29), 58 (12), 43 (16). HRMS calcd for $C_{13}H_{13}IOSe$: 391.9176. Found: 391.9179.

2-phenyl-3-iodoselenophene (2i). Yield: 0.136 g (82%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.90 (d, J = 5.74 Hz, 1H), 7.57−7.54 (m, 2H), 7.43−7.35 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.00, 139.19, 136.35, 131.99, 129.41, 128.35, 128.27, 79.68. MS (relative intensity) *m*/*z*: 333 (21), 205 (100), 129 (72), 126 (47), 77 (21). HRMS calcd for $C_{10}H_7ISe$: 333.8757. Found: 333.8761.

2-(*n*-butyl)-3-iodoselenophene (2j). Yield: 0.127 g (81%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75 (d, J = 5.74 Hz, 1H), 7.18 (d, J = 5.74 Hz, 1H), 2.95 (t, J = 7.06 Hz, 2H), 1.81 (quint, J = 7.06 Hz, 2H), 1.57 (sex, J = 7.06 Hz, 2H), 1.08 (t, J = 7.06, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.63, 137.21, 129.11, 80.85, 34.59, 32.09, 22.19, 13.87. MS (relative intensity) *m*/*z*: 185 (100), 128 (78), 115 (25), 56 (32), 42 (12). HRMS calcd for $C_8H_{11}ISe$: 313.9071. Found: 313.9076.

General Procedure for the PhSeBr and PhSeCl cyclizations. To a solution of (*Z*)-selenoenyne **1c** (0.169 g; 0.5 mmol) in 3 mL of CH_2Cl_2 was added gradually 1.1 equiv of PhSeBr or PhSeCl dissolved in 7 mL of CH_2Cl_2. The reaction mixture was allowed to stir at room temperature for the time shown in Table 3. The reaction mixture was washed with 40 mL of water and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel using hexane as the eluent.

2,5-Diphenyl-3-(selenophenyl)-selenophene (2b). Yield: 0.175 g (80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56−7.54 (m, 2H), 7.49−7.47 (m, 2H), 7.40−7.19 (m, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.44, 135.90, 135.52, 132.43, 131.03, 129.32, 129.24, 128.95, 128.33, 128.24, 128.13, 127.94, 127.86, 126.67, 126.05, 122.164. MS (relative intensity) *m*/*z*: 439 (100), 284 (46), 207 (58), 156 (75), 129 (37), 77 (21). HRMS calcd for $C_{22}H_{16}Se_2$: 439.9582. Found: 439.9585.

2,5-Diphenylselenophene (4a)[14b] by Reaction of 2a with *n*-BuLi in Hexane. To a two-neck round-bottomed flask, under argon, containing a solution of **2a** (0.102 g; 0.25 mmol) in hexane (2 mL) at − 78 °C was added *n*-BuLi (0.08 mL of a 2.5 M solution in hexane, 0.20 mmol) in one portion. The reaction mixture was stirred for 10 min and allowed to stir at room temperature. Then water (2 mL) was added, and the reaction mixture was diluted with hexane (20 mL) and washed with brine (3 × 20 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel using hexane as the eluent. Yield: 0.055 g (97%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59−7.57 (m, 4H), 7.46 (s, 2H), 7.40−7.36 (m, 4H), 7.31−7.26 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 149.83, 136.33, 128.92, 127.60, 126.21, 126.06. MS (relative intensity) *m*/*z*: 283 (100), 205 (79), 128 (51), 115 (13), 77 (32). HRMS calcd for $C_{16}H_{12}Se$: 284.0104. Found: 284.0110.

General Procedure for the Reactions of Intermediate 2,5-Diphenyl-3-lithioselenophene (3) with Aldehydes. To a two-neck round-bottomed flask, under argon, containing a solution of **2a** (0.102 g; 0.25 mmol) in hexane (2 mL) at − 78 °C was added *n*-BuLi (0.08 mL of a 2.5 M solution in hexane, 0.20 mmol) in one portion. The reaction mixture was stirred for 10 min, and then a solution of appropriated aldehyde (0.3 mmol) in hexane (1 mL) at −78 °C was added. The reaction mixture was allowed to stir at room temperature for 3 h. After this time, the mixture was diluted with ethyl acetate (20 mL) and washed with saturated aq NH_4Cl (20 mL) and water (3 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

(2,5-Diphenyl-selenophen-3-yl)-phenyl-methanol (4b). Yield: 0.064 g (82%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51−7.25 (m, 16H), 5.88 (s, 1H), 2.28 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.47, 145.97, 143.28, 142.38, 136.02, 135.31, 129.49, 128.84, 128.66, 128.42, 128.03, 127.69, 127.36, 126.15, 126.07, 125.92, 70.64. MS (relative intensity) *m*/*z*: 371 (100), 294 (15), 281 (21), 205 (52), 128 (34), 115 (21), 91 (42), 77 (23). HRMS calcd for $C_{23}H_{18}OSe$: 390.0523. Found: 390.0528.

(2,5-Diphenyl-selenophen-3-yl)-*p*-tolyl-methanol (4c). Yield: 0.069 g (86%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51−7.46 (m, 5H), 7.41−7.21 (m, 8H), 7.14 (d, J = 7.9 Hz, 2H), 5.84 (s, 1H), 2.33 (m, 4H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 149.35, 145.68, 142.56, 140.49, 136.99, 136.07, 135.36, 129.47, 129.10, 128.80, 128.60, 127.95, 127.63, 126.12, 126.05, 125.82, 70.55, 21.06. MS (relative intensity) *m*/*z*: 385 (100), 281 (32), 205 (44), 128 (62), 115 (17), 104 (23), 91 (29), 77 (21). HRMS calcd for $C_{24}H_{20}OSe$: 404.0679. Found: 404.0682.

(2,5-Diphenyl-selenophen-3-yl)-*o*-tolyl-methanol (4d). Yield: 0.070 g (87%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.54−7.12 (m, 15H), 5.86 (s, 1H), 2.32 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.07, 141.52, 141.13, 136.03, 135.45, 135.34, 134.41, 130.47, 130.31, 129.28, 128.81, 128.69, 127.64, 127.06, 126.39, 126.24, 126.04, 125.08, 70.68, 19.03. MS (relative intensity) *m*/*z*: 385 (100), 281 (39), 205 (41), 128 (77), 115 (19), 104 (29), 91 (32), 77 (35). HRMS calcd for $C_{24}H_{20}OSe$: 404.0679. Found: 404.0684.

(2,5-Diphenyl-selenophen-3-yl)-(*p*-methoxy-phenyl)-methanol (4e). Yield: 0.059 g (70%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.54−7.25 (m, 13H), 6.91−6.85 (m, 2H), 5.83 (s, 1H), 3.79 (s, 3H), 2.27 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.85, 149.37, 145.56, 142.61, 136.05, 135.54, 135.33, 129.45, 128.84, 128.62, 127.96, 127.67, 127.50, 126.05, 125.96, 113.80, 70.38, 55.24. MS (relative intensity) *m*/*z*: 401 (100), 370 (19), 281 (45), 205 (32), 128 (82), 120 (54), 77 (28). HRMS calcd for $C_{24}H_{20}O_2Se$: 420.0628. Found: 420.0633.

(2,5-Diphenyl-selenophen-3-yl)-(*o*-methoxy-phenyl)-methanol (4f). Yield: 0.057 g (68%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.60−7.23 (m, 13H), 6.98−6.86 (m, 2H), 6.09 (s, 1H), 3.77 (s, 3H), 3.19 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.74, 148.85, 145.70, 140.94, 136.26, 135.73, 131.64, 129.37, 128.81, 128.73, 128.47, 128.43, 127.68, 127.53, 126.62, 126.04, 120.82, 110.56, 67.58, 55.29. MS (relative intensity) *m*/*z*: 401 (100), 370 (17), 281 (38), 205 (40), 128 (77), 120 (47), 77 (31). HRMS calcd for $C_{24}H_{20}O_2Se$: 420.0628. Found: 420.0631.

(2,5-Diphenyl-selenophen-3-yl)-(*p*-chlorophenyl)-methanol (4g). Yield: 0.063 g (74%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.51−7.22 (m, 15H), 5.83 (s, 1H), 2.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.79, 146.16, 143.27, 141.95, 135.83, 135.11, 133.06, 129.40, 128.87, 128.72, 128.49, 128.14, 127.54, 127.24, 126.02, 125.55, 73.94. MS (relative intensity) *m*/*z*: 369 (100), 356 (21), 281 (35), 205 (49), 128 (72), 124 (38), 115 (23), 77 (39). HRMS calcd for $C_{23}H_{17}ClOSe$: 424.0133. Found: 424.0140.

(2,5-Diphenyl-selenophen-3-yl)-(*o*-chlorophenyl)-methanol (4h). Yield: 0.054 g (64%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.56−7.17 (m, 15H), 6.07 (s, 1H), 2.47 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.17, 147.30, 140.79, 140.02, 136.02, 135.46, 132.68,

129.68, 129.29, 128.83, 128.72, 128.61, 127.98, 127.67, 127.43, 127.03, 126.04, 125.96, 68.39. MS (relative intensity) *m*/*z*: 369 (100), 356 (34), 281 (42), 205 (27), 128 (79), 124 (30), 115 (12), 77 (28). HRMS calcd for $C_{23}H_{17}ClOSe$: 424.0133. Found: 424.0139.

(2,5-Diphenyl-selenophen-3-yl)-cyclohexyl-methanol (4i). Yield: 0.053 g (67%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.59−7.55 (m, 3H), 7.46−7.25 (m, 8H), 4.34 (d, J = 8.82 Hz, 1H), 2.15 (s, 1H), 1.86−0.63 (m, 11H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.39, 145.86, 142.56, 136.19, 135.58, 129.69, 128.89, 128.49, 127.76, 127.64, 126.05, 124.85, 73.77, 44.62, 29.66, 26.29, 25.87. MS (relative intensity) *m*/*z*: 377 (100), 281 (72), 205 (61), 128 (64), 96 (45), 82 (23), 77 (34). HRMS calcd for $C_{23}H_{24}OSe$: 396.0992. Found: 396.0998.

1-(2,5-Diphenyl-selenophen-3-yl)-heptan-1-ol (4j). Yield: 0.049 g (62%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.64−7.55 (m, 3H), 7.46−7.26 (m, 8H), 4.72 (t, J = 7.48 Hz, 1H), 1.96−1.70 (m, 3H), 1.42−1.23(m, 8H), 0.91−0.82 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.55, 145.08, 143.67, 136.20, 135.51, 129.56, 128.89, 128.55, 127.81, 127.67, 126.06, 124.82, 69.16, 38.23, 31.71, 29.08, 25.94, 22.57, 14.03. MS (relative intensity) *m*/*z*: 379 (100), 364 (53), 350 (23), 336 (45), 322 (41), 281 (52), 205 (73), 128 (72), 98 (88), 77 (35). HRMS calcd for $C_{23}H_{26}OSe$: 398.1149. Found: 398.1151.

1-(2,5-Diphenyl-selenophen-3-yl)-decan-1-ol (4k). Yield: 0.062 g (71%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.63 (s, 1H), 7.58−7.54 (m, 2H), 7.45−7.24 (m, 8H), 4.74−4.67 (m, 1H), 2.01−1.69 (m, 3H), 1.40−1.20 (m, 14H), 0.87 (t, J = 6.76 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.51, 145.03, 143.67, 136.17, 135.49, 129.54, 128.87, 128.53, 127.78, 127.64, 126.02, 124.82, 69.12, 38.19, 31.85, 29.49, 29.48, 29.39, 29.26, 25.95, 22.63, 14.08. MS (relative intensity) *m*/*z*: 421 (100), 406 (29), 392 (32), 378 (39), 364 (41), 350 (36), 336 (26), 281 (63), 205 (77), 128 (65), 140 (86), 77 (31). HRMS calcd for $C_{26}H_{32}OSe$: 440.1618. Found: 440.1616.

General Procedure for the Palladium-Catalyzed Coupling Reaction of 2a with Alkynes. To a Schlenck tube, under argon, containing a solution of 2,5-diphenyl-3-iodoselenophene **2a** (0.204 g; 0.50 mmol) in DMF (2.5 mL) was added to $Pd(PPh_3)_2Cl_2$ (0.035 g, 0.05 mmol). The resulting solution was stirred for 5 min at room temperature. After this time, appropriate alkyne (1.5 mmol) dissolved in 1 mL of Et_3N was then added dropwise, and the reaction mixture was allowed to stir at room temperature for 12 h. After this, the mixture was diluted with dichloromethane (20 mL) and washed with brine (3 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

4-(2,5-Diphenyl-selenophen-3-yl)-2-methyl-but-3-yn-2-ol (5a). Yield: 0.166 g (91%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83−7.81 (m, 2H), 7.54−7.50 (m, 3H), 7.42−7.29 (m, 6H), 2.11 (s, 1H), 1.60 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.79, 147.42, 135.50, 135.41, 129.59, 128.95, 128.45, 128.12, 128.05, 127.97, 125.99, 119.94, 94.66, 79.44, 65.67, 31.20. MS (relative intensity) *m*/*z*: 347 (100), 305 (77), 281 (61), 128 (50), 77 (21). HRMS calcd for $C_{21}H_{18}OSe$: 366.0523. Found: 366.0529.

2,5-Diphenyl-3-(phenylethynyl)-selenophene (5b). Yield: 0.180 g (94%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92−7.89 (m, 2H), 7.61 (s, 1H), 7.58−7.56 (m, 2H), 7.49−7.29 (m, 11H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.76, 147.47, 135.71, 135.50, 131.41, 129.61, 129.00, 128.59, 128.36, 128.16, 128.15, 128.14, 128.00, 126.08, 123.37, 120.57, 90.34, 86.86. MS (relative intensity) *m*/*z*: 383 (100), 306 (56), 282 (77), 204 (38), 128 (51), 101 (19), 77 (28). HRMS calcd for $C_{24}H_{16}Se$: 384.0417. Found: 384.0411.

General Procedure for the Copper-Catalyzed Coupling Reaction of 2a with Alcohols. To a Schlenck tube, under argon, containing a mixture of CuI (0.0095 g; 0.05 mmol) in dry toluene (1.5 mL) was added 1,10-phenanthroline (0.018 g, 0.1 mmol). The resulting solution was stirred for 30 min at room temperature. After this 2,5-diphenyl-3-iodoselenophene **2a** (0.204 g; 0.50 mmol) was added, and the resulting solution was stirred for additional 15 min at room temperature. Afterward, Cs_2CO_3 (0.325 g; 1.0 mmol) and appropriate alcohol (1.5 mmol) were added. The mixture was then heated at 110 °C for 12 h. After this the solution was cooled to room temperature, diluted with dichloromethane (20 mL), and washed with saturated aq NH_4Cl (3 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

2,5-Diphenyl-3-butoxy-selenophene (6a). Yield: 0.119 g (67%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73−7.71 (m, 2H), 7.57−7.26 (m, 9H), 4.08 (t, J = 7.44 Hz, 2H), 1.79 (quint, J = 7.44 Hz, 2H), 1.49 (sex, J = 7.44 Hz, 2H), 0.96 (t, J = 7.44 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.69, 144.76, 136.04, 135.07, 128.89, 128.47, 127.78, 127.53, 126.36, 126.02, 125.42, 118.10, 71.69, 31.83, 19.24, 13.83. MS (relative intensity) *m*/*z*: 355 (100), 341 (39), 327 (27), 313 (25), 283 (60), 206 (52), 129 (28), 77 (11), 73 (9), 57 (16), 43 (17). HRMS calcd for $C_{20}H_{20}OSe$: 356.0679. Found: 356.0682.

2,5-Diphenyl-3-octyloxy-selenophene (6b). Yield: 0.131 g (64%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.73−7.71 (m, 2H), 7.55−7.53 (m, 2H), 7.45 (s, 1H), 7.38−7.27 (m, 6H), 4.07 (t, J = 7.44 Hz, 2H), 1.63−1.53 (m, 2H), 1.38−1.18 (m, 10H), 0.89−0.87 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.69, 144.74, 136.04, 135.07, 128.89, 128.46, 127.77, 127.55, 126.36, 126.01, 125.41, 118.11, 72.01, 31.76, 29.74, 29.26, 29.20, 26.00, 22.64, 14.09. MS (relative intensity) *m*/*z*: 411 (100), 397 (19), 383 (21), 369 (23), 355 (29), 341 (18), 327 (16), 283 (52), 206 (33), 129 (61), 77 (30), 57 (21), 43 (12). HRMS calcd for $C_{24}H_{28}OSe$: 412.1305. Found: 412.1309.

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Supporting Information Available: Experimental procedures, additional experimental details for the preparation of all compounds, and ^{1}H and ^{13}C NMR spectra for all reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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