Catalytic Chalcogenylation under Greener Conditions: A Solvent-Free Sulfur- and Seleno-functionalization of Olefins via I_2/DMSO Oxidant System

André A. Vieira,[‡] Juliano B. Azeredo,[†] Marcelo Godoi,[§] Claudio Santi,[∥] Eufrânio N. da Silva Júnior,[⊥] and Antonio L. Braga*,[†]

[†]Departamento de Química, Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil

[‡]Instituto de Química, Departamento de Química Orgânica, Universidade Federal da Bahia, Campus de Ondina, Salvador, 40170-290, Brazil

[§]Escola de Química e Alimentos, Universidade Federal do Rio Grande — Campus Santo Antônio da Patrulha, RS, Brazil

[∥]Dipartimento di Scienze Farmaceutiche, Università di Perugia, Via del Liceo 1, 06134, Perugia, Italy

[⊥]Universidade Federal de Minas Gerais, Instituto de Ciências Exatas, Departamento de Química, Av. Antônio Carlos, 6627 - Belo Horizonte, MG — Brazil

S Supporting Information

ABSTRACT: Herein, we report a solvent- and metal-free methodology for the alkoxy-chalcogenylation of styrenes, using molecular iodine as a catalyst, DMSO as a stoichiometric oxidant, and different nucleophiles under microwave irradiation. This eco-friendly approach afforded the desired products in good to excellent yields in only 10 min. In addition, using the same protocol, we carried out the cyclization reaction of relevant molecules, such as lapachol derivatives.

INTRODUCTION

Organoselenium compounds continue to be extensively studied due to their recognized biological activities.[1] The antioxidant properties and mimetic activity of some enzymes are well-established, making these compounds interesting synthetic targets.[2] Particularly relevant is the fact that organoselenium compounds have been widely used as versatile reagents in organic synthesis, playing an important role in a wide range of transformations.[3]

In this regard, the electrophilic addition of sulfur or selenium species (RYX, where X = a halide or other anion) to double bonds with the formation of a thiiranium or a seleniranium intermediate that rapidly reacts with a number of nucleophiles is one of the most common methodologies for the formation of new C—S or C—Se bonds.[4] In this context, alkoxy-chalcogenylation processes have been reported and several electrophilic selenium or sulfur reagents have been employed for this purpose.[5] The electrophilic selenium species either are commercially available (for instance, chloride, bromide, and N-phenylselenophthalimide[6]) or can be conveniently prepared through the reaction of diorganoyl diselenides with stoichiometric amounts of halogens.[7] However, in this kind of transformation, the halide anion generated in the reaction medium can give rise to undesirable side processes due to the nucleophilicity of the halide anions.

Alternatively, electrophilic selenium species can also be generated in situ through the oxidation of diorganoyl diselenides with several oxidants, such as ammonium persulfate,[8] hypervalent iodine species,[9] and metallic inorganic reagents, such as KNO_3,[10] $CuSO_4$,[11] $Ce(NH_4)_2(NO_2)_6$,[12] and $Mn(OAc)_2$.[13] Similarly, the electrophilic sulfur species is also well-established in relation to the oxysulfenylation of alkenes through the use of several sulfenylation agents, such as sulfenamides,[14] sulfenate esters,[15] disulfides,[16] sulfenyl halides,[17] sulfonium salts,[18] and, more recently, sulfonyl hydrazides.[19]

Although several methodologies have been reported for reactions involving the addition of an electrophilic chalcogenide specie to alkenes, all of these methods have some particular disadvantages, such as long reaction times and the use of large amounts of metals and/or solvents. Thus, the development of a new environmentally friendly approach for alkoxy-selenylation and related reactions remains an important challenge in organic synthesis.

In this context, molecular iodine (I_2) has emerged as a convenient catalyst in several organic transformations, because it is a nontoxic, nonmetallic, and low-cost reagent.[20] We recently reported a protocol that involves the use of a stoichiometric amount of DMSO in the presence of a catalytic loading of molecular iodine to generate in situ RYI.[21] Using this methodology, the preparation of 3-selenyl- and sulfenyl-indoles under solvent-free conditions can be easily carried out.[22] As a continuation of this project, herein, we describe a new and fast method for the alkoxy-chalcogenylation of olefins in the absence of solvent, under microwave irradiation (Scheme 1).

Scheme 1. Molecular Iodine-Catalyzed Alkoxy-selenylation of Olefins under Solvent-Free Conditions
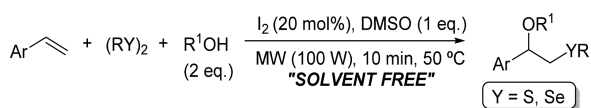
RESULTS AND DISCUSSION

The reaction conditions were optimized for styrene **1a** and diphenyl diselenide **2a** in the presence of dimethyl sulfoxide (DMSO), methanol, and iodine as the catalyst (Table 1). When

Table 1. Optimization of Microwave Parameters[a]

entry	MW (W)	T (°C)	time (min)	yield (%)[b]
1	100	50	3	55
2	100	50	5	78
3	100	50	10	96 (94)[c]
4	100	80	10	89
5	100	40	10	80
6	150	50	10	86
7	50	50	10	74
8		50	10 h	76[d]
9		r.t	24 h	80[e,c]

[a]Reaction conditions: styrene **1a** (0.5 mmol), (PhSe)₂, **2a** (0.25 mmol). [b]Conversion yields. [c]Isolated yield. [d]Conventional heating. [e]Reaction performed at room temperature without microwave irradiation.

the reaction was carried out for 3 min, the desired product was obtained in only 55% yield (entry 1). However, a significant improvement in the yield of the product **3a** was achieved when the reaction time was increased to 5 min (entry 2). Notably, carrying out the reaction for 10 min afforded the desired product in almost quantitative yield (entry 3).

In the next step, we evaluated the effect of temperature on the reaction system (entries 3−5). Screening of this parameter revealed that 50 °C was the best choice, affording the product **3a** in 96% yield.

The influence of the radiation power of the microwave equipment was also studied, using different levels of power. However, employing either 50 or 150 W provided the desired product **3a** in lower yields (entries 6 and 7). Thus, 100 W was selected as the irradiation power for all subsequent experiments.

Additionally, the reaction was tested under conventional heating using a preheated oil bath. Under these conditions, the reaction provided acceptable yield but required a very long reaction time (entry 8). Similarly, the reaction was performed at room temperature for 24 h, providing the desired product in 80% yield (entry 9).

In a second step of the investigation, we considered the influence of several reaction parameters, including the oxidant, the methanol loading, and the catalyst (Table 2). First, we examined the influence of the nucleophile loading, carrying out the reaction with different amounts of methanol, and a significant improvement in the chemical yield was observed when the amount of methanol was increased from 1.0 to 2.0 (entries 1−3). Thus, 2 equiv of methanol were found to be the most appropriate, affording the desired product in very high yield.

Table 2. Optimization of Reaction Conditions[a]

| entry	MeOH (equiv)	oxidant (equiv)	I₂ (mol %)	yield (%)[b]
1	1.0	DMSO (1)	20	79
2	1.5	DMSO (1)	20	86
3	2.0	DMSO (1)	20	96 (94)[c]
4	2.0	TBHP (1)	20	90
5	2.0	H₂O₂ (1)	20	77
6	2.0	air	20	56
7	2.0	DMSO (2)	20	93
8	2.0	DMSO (1.5)	20	87
9	2.0	DMSO (1)	10	85
10	2.0	DMSO (1)	5	56
11	2.0	DMSO (1)		

[a]Reaction conditions: styrene **1a** (0.5 mmol), (PhSe)₂ **2a** (0.25 mmol). [b]Conversion yields. [c]Isolated yield.

The effect of the oxidant was then studied (entries 3−8). In this regard, a number of oxidants (DMSO, TBHP, H₂O₂, and air) were evaluated, and DMSO provided the best results when used in stoichiometric excess (entry 3). A slight decrease in the yield was observed on increasing the DMSO loading to 1.5 and 2.0 equiv (entries 7 and 8).

Concerning the amount of catalyst (iodine), it was observed that the best results were obtained using 20 mol % (entry 3), since a decrease in the yield was observed when the iodine loading decreased (entries 9 and 10). Moreover, we observed that the catalyst has a substantial influence on this reaction, because no product formation was observed in the absence of iodine (entry 11).

In order to demonstrate the synthetic utility of this methodology, a scale-up reaction of 10 mmol was carried out under the optimized conditions (Scheme 2). Thereby, the reaction between styrene **1a** and diphenyl diselenide **2a** provided the product **3a** in 81% yield after 1 h of reaction time.

Scheme 2. Scale-Up Reaction between 1a and 2a
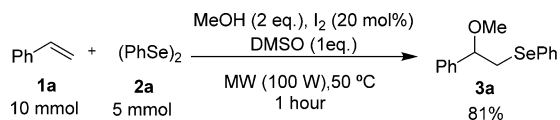
More importantly, the formation of the undesirable side product derived from the competition between the iodide nucleophile formed in the reaction medium and the nucleophile used was not observed. This is probably a consequence of the low concentration of iodide formed, since it is continuously oxidized by the DMSO to iodine, as shown in the plausible reaction pathway in Scheme 6.

After the determination of the optimized conditions, the scope and limitations of the proposed protocol were further investigated. First, a variety of diorganyl diselenides were reacted with methanol in order to prepare different β-methoxy-selenides (Table 3).

Electronic effects seem to have a significant influence on the reaction course. In general, diaryl diselenides with electron-releasing groups gave the products (**3e−f**) in better yields than those with electron-withdrawing groups, with the exception of *para*-chlorophenyl diselenide, which afforded the product **3d** in

Table 3. Synthesis of β-Methoxy-selenides 3a–l[a,b,c]
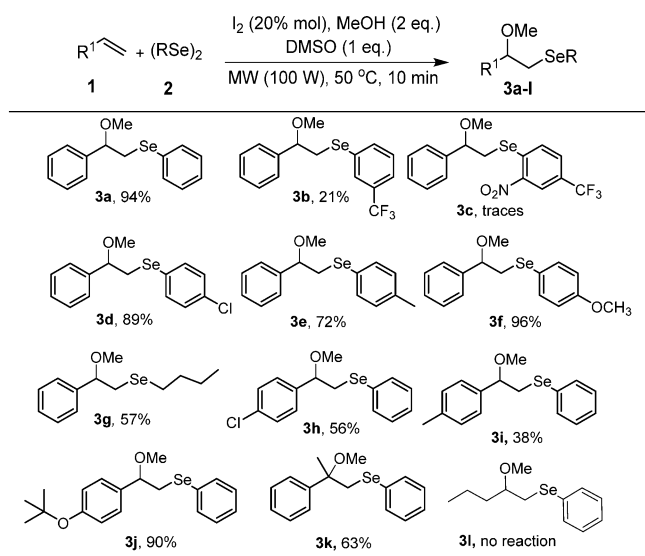
*a*Reaction conditions: styrene (0.5 mmol), diorganoyl diselenide (0.25 mmol), I₂ (20 mol %), MeOH (2 equiv), and DMSO (1 equiv), MW (100 W), 10 min, 50 °C. *b*Isolated yields. *c*Determined by CG–MS.

Table 4. Synthesis of Compounds 3m–u Using the Styrene 1a, Diphenyl Diselenide 2a, and Different Nucleophile Species[a,b,c]

*a*Reaction conditions: styrene (0.5 mmol), diphenyl diselenide (0.25 mmol), I₂ (20 mol %), Nu (2 equiv), and DMSO (1 equiv), MW (100 W), 10 min, 50 °C. *b*Isolated yields. *c*Determined by CG–MS.

we turned our attention to their preparation applying our protocol (Table 5). In general, all the reactions proceeded

Table 5. Synthesis of Compounds 5a–f Using the Styrene 1a, Diorganoyl Dichalcogenides, and Different Nucleophiles[a,b]

*a*Reaction conditions: styrene (0.5 mmol), diorganoyl dichalcogenides (0.25 mmol), I₂ (20 mol %), R³-OH (2 equiv), and DMSO (1 equiv), MW (100 W), 10 min, 50 °C. *b*Isolated yields.
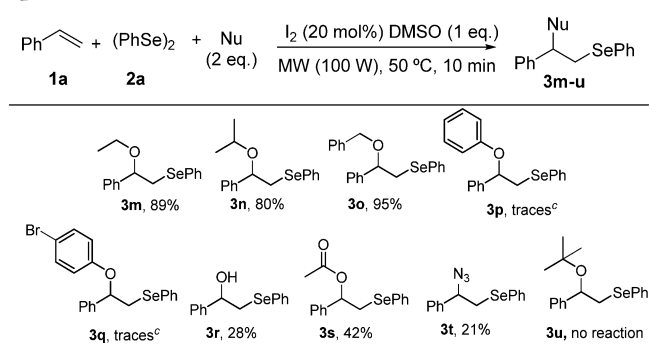
89% yield. Notably, when we employed *para*-methoxyphenyl diselenide as a selenium source, the corresponding product **3f** was achieved in 96% yield, suggesting that aromatic diselenides with electron-donating groups are favored substrates for this transformation.

Moreover, the reaction was also effective when a less reactive organoyl diselenide, such as dibutyl diselenide, was employed, giving the respective product in satisfactory yield.

The reactions of various styrenes with diphenyl diselenide were also examined under optimized conditions. *Para*-substituted styrenes were suitable substrates, affording the expected products (**3h–j**) in reasonable yields. It is noteworthy that, when we employed 4-*tert*-butoxystyrene, the respective product **3j** was achieved in 90% yield. Furthermore, the protocol was also applicable to α-methylstyrene, affording the desired product **3k** in good yield. However, when 1-pentene was employed as substrate in the optimized conditions, the corresponding methoxy-selenilation product **3l** was not obtained.
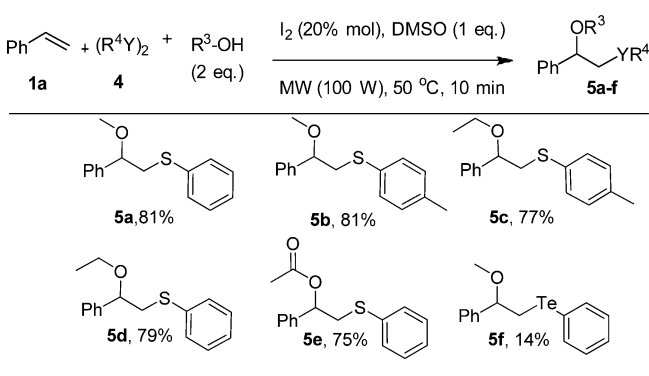
In the next step, we evaluated the effect of several nucleophiles on the reaction (Table 4). The influence of the nucleophilic species was investigated initially by evaluating different alcohols (**3m–q**). Ethanol and *iso*-propanol proved to be very good nucleophiles for this transformation, affording the corresponding products (**3m–n**) in very high yields. However, when *tert*-butanol was used as nucleophile, there was no formation of the corresponding product **3u**. Notably, when we employed a benzylic alcohol as the nucleophile source, the respective product **3o** was achieved in 95% yield. In contrast, the protocol was not efficient for phenol derivatives since only trace levels of the corresponding products were observed. However, other nucleophiles, such as acetic acid and water, afforded the corresponding products in moderate yields (**3q–s**). In addition, our protocol was also useful for the preparation of a selenium azide derivative (**3t**), which was obtained in reasonable yield using sodium azide as the nucleophile source.

Encouraged by these results and considering the particular relevance of the functionalization of olefins with sulfur atoms,[23]

smoothly, allowing the preparation of sulfur derivatives in very good yields (**5a–e**). For instance, when we employed *p*-toluyl disulfide as a sulfur source, the respective product **5b** was obtained in 81% yield.

Similarly, ethanol proves to be an effective alcohol in the alkoxy-sulfenylation reaction. When *p*-tolyl disulfide and diphenyl disulfide were used, the corresponding products **5c** and **5d** were obtained in 77% and 79% yield, respectively. Acetic acid also showed good activity as a nucleophile with diphenyl disulfide, furnishing the product **5e** in good yield.

In addition, the reaction of methoxy-tellurenylation was also performed using the same methodology. However, diphenyl ditelluride was less reactive than its selenium and sulfur analogues under the same reaction conditions, providing the respective product **5f** in lower yield.

The well-known functionalization of alkenes reaction with electrophilic reagents of selenium via the cyclization reaction has attracted considerable attention in organic synthesis.[24] Therefore, in order to extend the scope of the present methodology, we attempted to extend our protocol to unsaturated substrates containing internal nucleophiles. Using

the reagent 4-penten-1-ol **6** as a substrate, we observed the formation of a seleno tetrahydrofuran derivative **6a** in 81% yield via the *5-exo-trig* pathway.[25] Similarly, when 4-pentenoic acid **7** was employed as substrate, the corresponding seleno-lactone **7a** was achieved in excellent yield (95%) (Scheme 3).

Scheme 3. Seleno-cyclofunctionalization of Olefins Containing an Internal Nucleophile
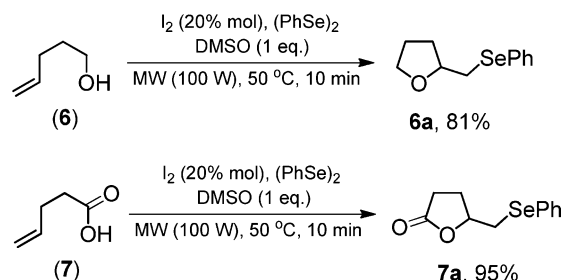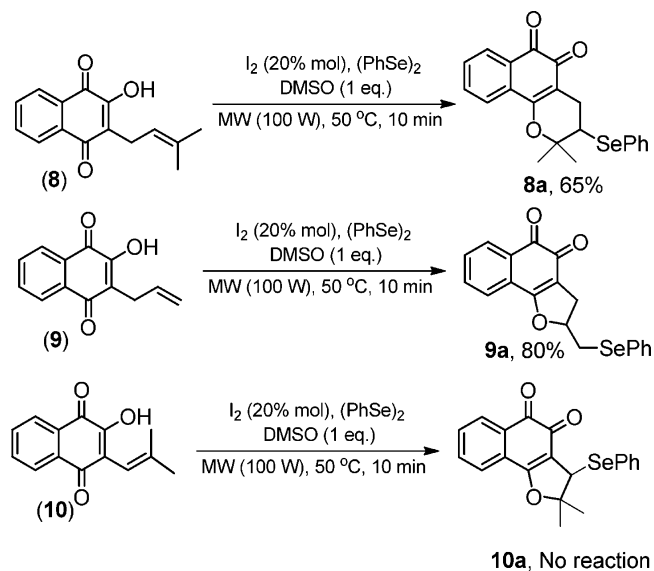
Recently, Jacob and co-workers described quinoidal compounds containing selenium or tellurium as multifunctional redox agents. These compounds present important activity against cancer cell lines with low cytotoxity in normal cell lines.[26] Lapachol, a naturally occurring naphthoquinone, is important due to its biological activities, for instance, trypanocidal,[27] leishmanicidal,[28] and antitumoral.[29−31] Based on the potential activity of lapachol, a quinonoid compound containing an unsaturated system with an internal nucleophile, in this study, we also selected some lapachol derivatives for the application of the methodology described herein.

Lapachol **8**, C-allyl lawsone **9**, and nor-lapachol **10** were employed as substrates for the seleno-functionalization. Using compound **8**, the respective 3-selenophenyl-β-lapachone **8a** was obtained in good yield (65%) in a *6-endo-trig* fashion (Scheme 4).

The chemical shifts of the hydrogens belonging to the pyranic ring of 3-phenylselanyl-β-lapachone **8a** appear among δ 2.6−3.4. The diastereotopic methyl groups showed chemical shifts at δ 1.68 and 1.54 as singlets and are in accordance with previously reported compounds.[31] The others signals corresponding to the aromatic rings are totally in accordance with those expected for **8a**. Compound **9a** presented chemical shifts among δ 2.9−3.4 related to methylenic hydrogens. A multiplet signal (methynic H-2) was observed at δ 5.2−5.3. In a similar way, the signals corresponding to the aromatic rings are consistent.

As observed with other electrophiles, two pathways (β- or α-cyclizations) are possible in the reaction with lapachol **8**. Initially, the selenonium ion was formed and the carbon atom with a partial positive charge was better stabilized. The C−Se bond was weakened and suffered an internal nucleophilic attack, β-cyclization occurred, and the preferential kinetic product was formed under the pre-established conditions. In general, β-lapachone derivatives are preferentially formed in reactions without heating and in a shorter reaction time compared with α-lapachone derivatives (thermodynamic product) (Scheme 5).

**Scheme 5. Pathways for the Formation of β- or α-Lapachone Analogues from Lapachol (8)**
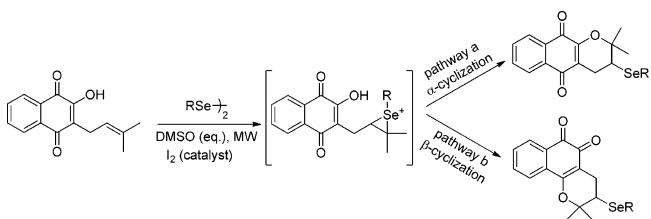
When this chalcogenylation method was applied to the C-allyl lawsone **9**, the selenium product **9a** was obtained in excellent yield (80%) (Scheme 4).

Finally, nor-lapachol **10**, the inferior homologue of lapachol (**8**), was synthesized by Hooker oxidation[32] and used under the same reaction conditions, but no reaction was observed.

On the basis of previous reports,[33] a plausible reaction pathway for the chalcogen functionalization of styrenes is illustrated in Scheme 6. First, the electrophilic species in the

Scheme 4. Seleno-cyclofunctionalization of Lapachol Derivatives

Scheme 6. Plausible Reaction Pathway
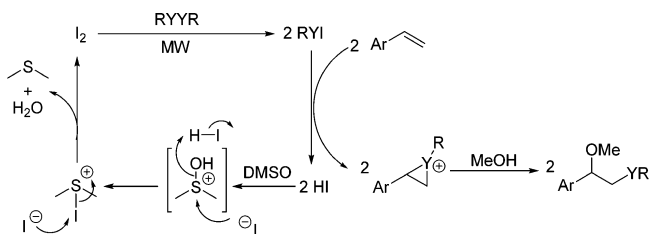
form of RYI (Y = S, Se) would be generated through the reaction of diorganyl dichalcogenide with the catalyst. Next, the RYI undergoes nucleophilic attack of the double bond of styrene, leading to the formation of the intermediate chalcogeniranium ion. Subsequently, this intermediate undergoes attack by the nucleophile to furnish the desired β-methoxy-selenide with the concomitant formation of HI. Two equivalents of HI would then react with DMSO, affording an intermediate of the protonated sulfur species, which is rapidly converted to the iodine-dimethyl sulfide adduct.[34] Finally, the iododimethylsulfonium iodide species is converted to water and dimethyl sulfide, and the catalyst is regenerated in the reaction

medium, completing the cycle. It is important to mention that, in this process, the amount of iodide anions in the reaction medium is low, since they are continuously converted to I_2 by reaction with DMSO. This is important in order to avoid nucleophilic competition of the iodide with the nucleophile.

◾ CONCLUSIONS

In conclusion, we have developed a fast and sustainable approach for the alkoxy-selenylation of styrenes, employing an oxidant catalytic system composed of I_2/DMSO. This new regioselectivity method afforded the desired products in good to excellent yields in only 10 min, in solvent- and metal-free reaction media. Another important advance associated with this methodology is the applicability of different nucleophiles, such as alcohols, carboxylic acid, azide, and water, which allows the preparation of β-substituted aryl selenides with different functionalities. Furthermore, the present methodology was satisfactorily applied to the reaction of the styrene with diorganoyl disulfides. One important advantage of this method is the fact that the side product derived from the competition between the iodide generated in the reaction medium and the nucleophile used was not observed. We also extended our protocol to the seleno-cyclofunctionalization reactions, using a nucleophile containing olefins. In this regard, lapachol and C-allyl-lawsone selenium derivatives, which are compounds with potential biological activity, were prepared in good yields.

◾ EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ at 400 and 200 MHz or at 100 and 50 MHz, respectively. Chemical shifts (δ) are reported (ppm) relative to the TMS (^{1}H NMR) and the solvent (^{13}C NMR). APPI-Q-TOFMS measurements were taken on a mass spectrometer equipped with an automatic syringe pump for sample injection. Infrared spectra were recorded on a commercial Fourier transformer spectrometer. The styrenes were obtained from commercial sources and used without further purification. All reactions were performed in 10 mL sealed glass tubes in a commercially available microwave monomode CEM reactor with IR monitoring and a noninvasive pressure transducer. The yields are based on isolated compounds after purification.

General Procedure for the Synthesis of the Aryl Chalcogenides. The styrene (0.5 mmol), diorganyl chalcogenide (0.25 mmol), iodine (20% mol), respective nucleophile (2 equiv), and DMSO (1 equiv) were placed in a dry microwave glass tube. The tube was sealed and placed into a CEM Discover microwave apparatus. Initially, an irradiation power of 100 W was applied. After the temperature reached 50 °C, the instrument was automatically adjusted to maintain a constant temperature. After 10 min, the reaction was quenched with a solution of sodium thiosulfate 10% and the aqueous layer was extracted with ethyl acetate. The organic phase was dried over MgSO$_4$ and filtered, and the solvent was completely removed under vacuum to give the crude product. Purification was carried out by flash chromatography with a mixture of hexane/ethyl acetate (96:4), affording the desired product.

Characterization. *(2-Methoxy-2-phenylethyl)(phenyl)selane (Compound 3a).* 0.1363 g, Yield: 94%, yellow oil,[35] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.49−7.44 (m, 2H); 7.38−7.19 (m, 8H); 4.34 (dd, J^1 = 4.0 Hz; J^2 = 8.4 Hz, 1H); 3.32 (dd, J^1 = 8.4 Hz, J^2 = 12.0 Hz, 1H); 3.23 (s, 3H); 3.09 (dd, J^1 = 4.0 Hz, J^2 = 12.0 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 140.8; 132.5; 130.6; 128.9; 128.4; 127.9; 126.7; 126.6; 83.1; 56.9; 35.3. IR (film): 3057, 3026, 2980, 2929, 2819, 1578, 1477, 1436, 1105, 1090, 1022, 765, 736, 701, 691 cm^{-1}.

(2-Methoxy-2-phenylethyl)(3-(trifluoromethyl)phenyl)selane (Compound 3b). 0.0376 g, yield 21%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.49−7.44 (m, 2H); 7.38−7.19 (m, 8H); 4.34 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.32 (dd, J^1 = 8.0 Hz, J^2 = 11.0 Hz, 1H); 3.23 (s, 3H); 3.09 (dd, J^1 =4.0 Hz, J^2 = 11.1 Hz 1H). ^{13}C NMR (CDCl$_3$, 50

MHz) δ: = 140.5; 135.5; 132.0; 131.5 (q, J = 32.2 Hz); 129.1; 128.8 (q, J = 3.84 Hz), 128.3; 126.0, 126.4 (q, J = 272 Hz); 123.4 (q. J 3.84 Hz); 83.2; 57.0; 35.4. (APPI+) *m/z*: calculated for C$_{16}$H$_{15}$F$_3$OSe [M]$^+$: 360.0240; found 360.0234. IR (film): 3061, 3028, 2985, 2933, 2822, 1579, 1492, 1453, 1421, 1321, 1270, 1166, 1127, 796, 695 cm^{-1}.

(4-Chlorophenyl)(2-methoxy-2-phenylethyl)selane (Compound 3d). 0.1444 g, yield 89%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.38 (d, J = 8.0 Hz, 2H); 7.33−7.29 (m, 5H); 7.18 (d, J = 8.0 Hz, 2H); 4.33 (dd, 1H, J^1 = 4.0 Hz; J^2 = 8.0 Hz); 3.32 (dd, J^1 = 8.0 Hz; J^2 = 11.4 Hz, 1H); 3.24 (s, 3H); 3.07 (dd, 1H, J^1 = 4.0 Hz, J^2 = 12.0 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 140.7; 134.0; 133.0; 129.1; 128.9; 128.5; 128.1; 126.6; 83.1; 57.0; 35.7. IR (film): 3028, 2983, 2930, 2821, 1473, 1453, 1386, 1106, 1089, 1010, 814, 766, 729, 701 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{15}$H$_{15}$ClOSe [M]$^+$: 325.9977; found 325.9970.

(2-Methoxy-2-phenylethyl)(p-tolyl)selane (Compound 3e). 0.1094 g, yield 72%. [1]NMR (CDCl$_3$, 200 MHz) δ: = 7.43 (d, J = 8,0 Hz, 2H); 7.38−7.29 (m, 5H); 7.09 (d, J = 8.0 Hz, 2H); 4.37 (1H, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.33 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.28 (s, 3H); 3.10 (dd, J^1 = 4.0 Hz, J^2 = 12.0 Hz, 1H); 2.35 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: 140.8; 136.8; 133.0; 129.7; 128.4; 127.9; 126.6; 83.0; 56.9; 35.6; 21.0. IR (film): 3060, 3026, 2978, 2963, 2819, 1489, 1453, 1352, 1106, 1089, 1016, 803, 766, 701 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{16}$H$_{18}$OSe [M]$^+$: 306.0523; found: 306.0518.

(2-Methoxy-2-phenylethyl)(4-methoxyphenyl)selane (Compound 3f). 0.1535 g, yield 96%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: 7.46 (d, J = 8.0 Hz, 2H); 7.37−7.29 (m, 5H); 6.81 (d, J = 8.0 Hz, 2H); 4.31 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.80 (s, 3H), 3.31−3.20 (m, 1H); 3.25 (s, 3H); 3.02 (dd, 1H, J^1 = 4.0 Hz; J^2 = 12.0 Hz). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: 159.1; 140.8; 135.5; 128.4; 127.9; 126.6; 114.6; 83.0; 56.9; 55.2; 36.3. IR (film): 3060, 3026, 2998, 2932, 2833, 2820, 1590, 1571, 1490, 1454, 1284, 1247, 1173, 1071, 1030, 1006, 824, 766, 702 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{16}$H$_{18}$O$_2$Se [M]$^+$: 322.0472; found 322.0468.

Butyl(2-methoxy-2-phenylethyl)selane (Compound 3g). 0.0769 g, yield: 57%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.34 (m, 5H); 4.33 (dd, J^1 = 6.0 Hz; J^2 = 8.0 Hz, 1H); 3.26 (s, 3H); 2.98 (dd, J^1 = 12.0 Hz; J^2 = 8.0 Hz, 1H); 2.75 (dd, 1H, J^1 = 6.0 Hz, 12.0 Hz, 1H); 2.49 (t, J = 7.3 Hz, 2H); 1.60 (m, 2H); 1.42−1.27 (m, 2H); 0.89 (t, J = 7.38 Hz, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: 141.3; 128.4; 127.9; 126.6; 84.5; 56.8; 32.6; 30.9; 24.5; 22.9; 13.5. IR (film): 2954, 2925, 2869, 2856, 2818, 1463, 1453, 1106, 1090, 1070, 955, 765, 701 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{13}$H$_{20}$OSe [M]$^+$: 272.0679; found: 272.0679.

(2-(4-Chlorophenyl)-2-methoxyethyl)(phenyl)selane (Compound 3h). 0.0908 g, yield: 56%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.47−7.41 (m, 2H); 7.32−7.20 (m, 8H); 4.30 (dd, J^1 = 6.0 Hz; J^2 = 8.0 Hz, 1H); 3.28 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.22 (s, 3H); 3.05 (dd, J^1 =6.0 Hz, J^2 = 12.0 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 139.3; 133.7, 132.6; 130.3; 128.9; 128.6; 128.0; 126.9; 82.5; 56.9; 35.0. IR (film): 3054, 2983, 2929, 2819, 1595, 1578, 1488, 1436, 1099, 1088, 827, 736, 690 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{15}$H$_{15}$ClOSe [M]$^+$: 325.9977; found: 325.9967.

(2-Methoxy-2-(p-tolyl)ethyl)(phenyl)selane (Compound 3i). 0.0577 g, yield 38%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.64−7.59 (m, 2H); 7.37−7.31 (m, 8H); 4.46 (dd, J^1 = 4.8 Hz; J^2 = 8.0 Hz, 1H); 3.47 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.37 (s, 3H); 3.23 (dd, J^1 = 4.8 Hz, J^2 = 12.0 Hz, 1H); 2.48 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 137.8; 137.7; 132.4; 130.6; 129.2; 128.9; 126.7; 126.5; 82.8; 56.8; 35.3; 21.1. IR (film): 2975, 2929, 2818, 1604, 1578, 1504, 1477, 1365, 1236, 1161, 1105, 897, 736, 691 cm^{-1}. HRMS (APPI+) *m/z*: calculated for C$_{16}$H$_{18}$OSe [M]$^+$: 306.0518; found: 306.0523

(2-(4-tert-Butoxyphenyl)-2-methoxyethyl)(phenyl)selane (Compound 3j). 0.1629 g, yield 90%. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.47 (d, J = 7.0 Hz, 2H); 7.25−7.18 (m, 5H); 6.96 (d, J = 7.0 Hz, 2H); 4.32 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.32 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.23 (s, 3H); 3.09 (dd, J^1 = 4.0 Hz, J^2 =12.0 Hz, 1H); 1.34 (s, 9H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 155.2; 135.5; 132.5; 130.7; 128.9; 127.1; 126.7; 124.0; 82.7; 56.9; 35.4; 28.8. IR (film): 2981, 2928, 2818, 1578, 1511, 1477, 1436, 1102, 1022, 818, 736, 691 cm^{-1}.

HRMS (APPI+) m/z: calculated for $C_{19}H_{23}O_2Se$ [M − H]$^+$: 363.0859; found: 363.0862.

(2-Methoxy-2-phenylpropyl)(phenyl)selane (Compound 3k). 0.0957 g, Yield 63%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.44−7.24 (m, 8H); 7.19−7.16 (m, 2H); AB system (J = 12.0 Hz); 3.12 (s, 3H); 1.72 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 143.6; 132.6; 131.3; 128.8; 128.2; 127.3; 126.6; 126.2; 78.9; 50.9; 42.2; 23.1. IR (film): 3055, 2977, 2931, 2822, 1578, 1476, 1444, 1436, 1369, 1072, 1022, 764, 737, 701, 691 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{16}H_{18}OSe$ [M]$^+$: 306.0518; found: 306.0514.

(2-Ethoxy-2-phenylethyl)(phenyl)selane (Compound 3m). 0.1352 g, yield 89%, yellow oil.[36] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.50−7.49 (m, 2H); 7.35−7.23 (m, 8H); 4.47 (dd, J^1 = 5.0 Hz; J^2 = 8.0 Hz, 1H); 3.43−3.32 (m, 3H); 3.10 (dd, J^1 = 5.0 Hz, J^2 = 12.0 Hz, 1H); 1.19 (t, J = 7.0 Hz, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 141.6; 132.5; 130.8; 128.9; 128.4; 127.9; 126.7; 126.5; 81.3; 64.6; 35.5; 15.2. IR (film): 3057, 3026, 2971, 2926, 2865, 1578, 1490, 1477, 1454, 1436, 1115, 1091, 1022, 763, 735, 701 cm^{-1}.

(2-Isopropoxy-2-phenylethyl)(phenyl)selane (Compound 3n). 0.1272 g, yield 80%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.50−7.47 (m, 2H); 7.35−7.22 (m, 8H); 4.59 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.51 (m, 1H); 3.30 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.08 (dd, J^1 = 4.0 Hz, J^2 = 12.0 Hz, 1H); 1.17 (d, J = 6.0 Hz, 3H); 1.09 (d, J = 6.0 Hz, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 142.4; 132.2; 131.0; 128.9; 128.4; 127.8; 126.6; 126.5; 78.7; 69.7; 35.9; 23.3; 21.3. IR (film): 3057, 3026, 2968, 2928, 2876, 1578, 1491, 1462, 1452, 1436, 1120, 1084, 1022, 763, 735, 701 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{17}H_{20}OSe$ [M]$^+$: 320.0679; found: 320.0678.

(2-(Benzyloxy)-2-phenylethyl)(phenyl)selane (Compound 3o). 0.1738 g, yield 95%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.49−7.44 (m, 2H), 7.38−7.19 (m, 8H), 4.34 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.32 (dd, J^1 = 8.0 Hz, J^2 = 11.5 Hz, 1H); 3.23 (s, 3H); 3.09 (dd, J^1 = 4.0 Hz, J^2 = 11.5 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 140.9; 137.9; 133.0; 132.4; 130.8; 129.7; 128.9; 128.5; 128.3; 128.3; 128.1; 127.8; 127.6; 126.8; 126.7; 80.7; 70.8; 66.6; 35.5. IR (film): 3059, 3028, 2930, 2862, 1720, 1578, 1494, 1477, 1453, 1436, 13.46, 1270, 1095, 1072, 1022, 735, 700 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{21}H_{20}Se$ [M]$^+$: 368.0679; found: 368.0673.

1-Phenyl-2-(phenylselanyl)ethanol (Compound 3r). 0.0386 g, yield 28%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.57−7.52 (m, 2H); 7.35−7.25 (m, 8H); 4.77 (dd, J^1 = 4.0 Hz; J^2 = 8.4 Hz, 1H); 3.30 (dd, J^1 = 4.0 Hz, J^2 = 13.0 Hz, 1H); 3.11 (dd, J^1 = 8.4 Hz, J^2 = 13.0 Hz, 1H); 2.81 (s, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 142.5; 133.1; 129.2; 128.5; 127.9; 127.4; 125.8; 72.2; 38.4. IR (film): 3451(OH), 3057, 3027, 2926, 2851, 2358, 2336, 1578, 1491, 1443, 1193, 1084, 1022, 765, 700 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{14}H_{14}OSe$ [M]: 278.0205; found: 278.0206.

1-Phenyl-2-(phenylselanyl)ethyl acetate (Compound 3s). 0.0667 g, yield 42%, yellow oil.[16a] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.46−7.39 (m, 2H); 7.24−7.17 (m, 8H); 5.88 (dd, J^1 = 4.0 Hz; J^2 = 6.0 Hz, 1H); 3.32 (dd, J^1 = 6.0 Hz, J^2 = 12.0 Hz, 1H); 3.16 (dd, J^1 = 4.0 Hz, J^2 = 12.0 Hz 1H); 1.95 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 170.0; 139.3; 133.0; 129.1; 128.5; 128.3; 127.2; 126.5; 75.2; 33.3; 21.0. IR (film): 3058, 3029, 2998, 2928, 2851, 1737, 1578, 1493, 1477, 1453, 1436, 1370, 1236, 1021, 762, 737, 699 cm^{-1}.

(2-Azido-2-phenylethyl)(phenyl)selane (Compound 3t). 0.0316 g, 21%, yellow oil.[37] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.52−7.48 (m, 2H); 7.37−7.24 (m, 8H); 4.62 (t, J = 7.0 Hz, 1H); 3.23 (d, J^1 = 4.0 Hz, J^2 =12.0 Hz 1H); 3.20 (dd, J^1 = 4.0 Hz, J^2 = 12.0 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 138.7; 133.3; 129.3; 128.9; 128.7; 127.5; 126.8; 66.0; 34.0. IR (film): 3059, 3028, 2926, 2101, 1578, 1492, 1476, 1453, 1436, 1248, 1209, 1022, 737, 700 cm^{-1}.

(2-Methoxy-2-phenylethyl)(phenyl)sulfane (Compound 5a). 0.0988 g, 81%, colorless oil.[38] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.38−7.25 (m, 10H); 4.30 (dd, J^1 = 4.0 Hz; J^1 = 8.0 Hz, 1H); 3.32 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.25 (s, 3H); 3.13 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = ^{13}C NMR (CDCl$_3$, 50 MHz) δ = 140.4; 136.5; 129.3; 128.9; 128.5; 128.1; 126.7; 126.0; 82.4; 57.0; 41.5. IR (film): 3059, 3027, 2924, 2853, 2821, 1742, 1582, 1480, 1454, 1438, 1239, 1106, 1090, 1025, 738, 699, 692 cm^{-1}.

(2-Methoxy-2-phenylethyl)(p-tolyl)sulfane (Compound 5b). 0.1044 g, yield 74%, colorless oil.[38] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.38−7.25 (m, 7H); 7.10 (d, J^1 = 8.0 Hz, 2H); 4.28 (dd, J^1 = 4.0 Hz; J^2 = 8.0 Hz, 1H); 3.29−3.26 (m, 1H); 3.26 (s, 3H); 3.10 (dd, J^1 = 8.0 Hz; J^2 = 12.0 Hz, 1H); 2.33 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 140.5; 136.2; 132.6; 130.1; 129.6; 128.5; 128.0; 126.7; 82.4; 57.0; 42.2; 21.0. IR (film): 3058, 3023, 2981, 2922, 2866, 2820, 1492, 1453, 1352, 1106, 1098, 1091, 804, 699 cm^{-1}.

(2-Ethoxy-2-phenylethyl)(p-tolyl)sulfane (Compound 5c). 0.1048 g , yield 77%, colorless oil.[19] ^{1}H NMR (CDCl$_3$, 400 MHz) δ: = 7.37−7.02 (m, 9H); 4.38 (dd, J^1 = 5.08 Hz, J^2 = 3.03 Hz, 1H); 3.48−3.27 (m, 3H); 3.08 (dd, J^1 = 5.08; J^2 = 8.21 Hz, 1H); 2.31 (s, 3H); 1.18 (t, J = 7.31 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ: = 141.3; 136.0; 133.3; 130.0; 129.6; 128.3; 127;9; 126.6; 80.6; 64.6; 42.2; 20.9; 15.2.

(2-Ethoxy-2-phenylethyl)(phenyl)sulfane (Compound 5d). 0.1015 g, yield 79%, colorless oil.[19] ^{1}H NMR (CDCl$_3$, 400 MHz) δ: = 7.33−7.14 (m, 10H); 4.40 (dd, J^1 = 5.08 Hz; J^2 = 2.74 Hz, 1H); 3.42−3.30 (m, 3H); 3.11 (dd, J^1 = 5.08 Hz; J^2 = 8.21 Hz, 1H); 1.17 (t, J = 7.03 Hz, 3H).^{13}C NMR (CDCl$_3$, 100 MHz) δ: = 141.2; 136.7; 132.8; 129.2; 128.7; 128.5; 127.9; 126.6; 80.6; 64.6; 41.6; 15.2.

(2-Ethoxy-2-phenylethyl)(p-tolyl)sulfane (Compound 5d). 0.1048 g, yield 77%, colorless oil.[19] ^{1}H NMR (CDCl$_3$, 400 MHz) δ: = 7.37−7.02 (m, 9H); 4.38 (dd, J^1 = 5.08 Hz, J^2 = 3.03 Hz, 1H); 3.48−3.27 (m, 3H); 3.08 (dd, J^1 = 5.08; J^2 = 8.21 Hz, 1H); 2.31 (s, 3H); 1.18 (t, J = 7.31 Hz, 3H). ^{13}C NMR (CDCl$_3$, 100 MHz) δ: = 141.3; 136.0; 133.3; 130.0; 129.6; 128.3; 127;9; 126.6; 80.6; 64.6; 42.2; 20.9; 15.2.

1-Phenyl-2-(phenylthio)ethyl Acetate (Compound 5e). 0.102 g, yield 75%, colorless oil.[16a] ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.40−7.18 (m, 10H); 5.88 (dd, J^1 = 6.0 Hz; J^2 = 8.0 Hz, 1H); 3.42 (dd, J^1 = 8.0 Hz, J^2 = 12.0 Hz, 1H); 3.23 (dd, J^1 = 6.0 Hz, J^2 = 12.0 Hz, 1H); 2.01 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 170.0; 139.0; 135.6; 130.1; 129.0; 128.5; 128.4; 126.6; 76.4; 74.6; 40.1; 21.0. IR (film): 3058, 3029, 2923, 1742, 1582, 1493, 1480, 1438, 1370, 1238, 1230, 1024, 739, 697 cm^{-1}.

(2-Methoxy-2-phenylethyl)(phenyl)tellane (Compound 5f). 0.0237 g, yield 14%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 7.6 (d, 2H, J = 8.0, 2H); 7.38−7.11 (m, 8H); 4.44 (dd, J^1 = 6.0 Hz; J^2 = 9.0 Hz, 1H); 3.43 (dd, J^1 = 9.0 Hz, J^2 = 12.0 Hz, 1H); 3.24 (s, 3H); 3.10 (dd, J^1 = 6.0, J^2 = 12.0, 1H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 141.8; 138.2; 129.1; 128.7; 128.5; 128.0; 127.4; 126.4; 84.2; 57.0; 17.4. IR (film): 3060, 3025, 2979, 2924, 2851, 2819, 1574, 1491, 1473, 1453, 1432, 1221, 1100, 1018, 763, 731, 700 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{15}H_{16}OTe$ [M]$^+$: 342.0263; found: 342.0253.

2-((Phenylselanyl)methyl)tetrahydrofuran (Compound 6a). 0.0972 g, yield 81%, yellow oil.[39] ^{1}H NMR (400 MHz, CDCl$_3$) δ: = 7.53−7.51 (m, 2H); 7.27−7.20 (m, 3H); 4.09 (qui, J = 6.9 Hz, 1H), 3.93−3.88 (m, 1H); 3.79−3.73 (m, 1H); 3.12 (dd, J^1 = 5.8 Hz ; J^2 = 12.0 Hz, 1H); 2.97 (dd, J^1 = 6.9 Hz, J^2 = 12.0 Hz, 1H); 2.10−2.02 (m, 1H); 1.96−1.88 (m, 2H); 1.66−1.67 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ: = 132.4; 130.2; 128.9; 126.7; 78.2; 68.3; 32.9; 31.4; 25.9.

Dihydro-[(phenylseleno)methyl]-2(3H)-furanone (Compound 7a). 0.1243 g, yield 95%, yellow oil.[39] ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.6−7.5 (m, 2H), 7.30−7.25 (m, 3H), 4.68−4.41 (m, 1H), 3.27 (dd, J^1 = 4.9; J^2 = 12.8 Hz, 1H), 3.01 (dd, J^1 = 7.8; J^2 = 12.8 Hz, 1H), 2.63−2.35 (m, 3H), 1.99−1.89 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ: 176.5; 133.0; 129.2; 128.7; 127.5; 79.2; 31.7; 28.6; 27.5.

2,2-Dimethyl-3-(phenylselanyl)-3,4-dihydro-2H-benzo[h]-chromene-5,6-dione (Compound 8a). 0,1296 g, 65%, yellow oil. ^{1}H NMR (CDCl$_3$, 200 MHz) δ: = 8.06 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.69−7.47 (m, 5H), 7.28 (d, J = 4.0, 2H), 3.41 (dd, J^1 = 5.6 Hz, J^2 = 9.6 Hz, 1H), 3.10 (dd, J^1 = 5.6 Hz, J^2 = 18.0 Hz, 1H), 2.73 (dd, J = 9.6, J = 18.0, 1H), 1.68 (s, 3H), 1.54 (s, 3H). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 179.4, 178.0, 161.4, 135.1, 134.8, 132.1, 130.8, 130.1, 129.3, 128.7, 128.5, 128.3, 124.1, 112.5, 82.9, 45.7, 27.7, 25.3, 23.2. IR (film): 2974, 2927, 2851, 1693, 1658, 1611, 1590, 1572, 1454, 1370, 1286, 1264, 1227, 1154, 1111, 1091, 777, 746 cm^{-1}. HRMS (APPI+) m/z: calculated for $C_{21}H_{19}O_3Se$ [M + H]$^+$: 399.0495; found: 399.0493.

2-((Phenylselanyl)methyl)-2,3-dihydronaphtho[1,2-b]furan-4,5-dione (Compound 9a). 0,1484 g, 80%, yellow oil.^{1}H NMR (CDCl$_3$,

200 MHz) δ: = 8.04 (d, J = 8.0, 1H), 7.61−7.54 (m, 4H), 7.44 (d, J = 8.0, 1H), 7.29−7.24 (m, 1H), 5.29 (m, 1H), 3.74 (dd, 1H, J = 8.0, J = 16.0), 3.27−3.17 (m, 2H), 2.96 (dd, 1H, J^1 = 8.0 Hz, J^2 = 16.0 Hz). ^{13}C NMR (CDCl$_3$, 50 MHz) δ: = 180.9, 175.2, 169.3, 134.4, 133.4, 131.8, 130.5, 129.3, 129.2, 128.6, 127.6, 127.2, 124.5, 114.9, 86.6, 40.8, 32.3, 32.1. IR (film): 3045, 2982, 2959, 2922, 2854, 1697, 1646, 1613, 1587, 1572, 1489, 1405, 1246, 1146, 1080, 891, 734 cm^{-1}. HRMS (APPI+) m/z: calculated for C$_{19}$H$_{15}$O$_3$Se [M + H]$^+$: 371.0182; found: 371.0187.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: 55 48 3721 6427. Tel: 55 48 37216427. E-mail: braga. antonio@ufsc.br (A.L.B.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) (a) Klayman, D. L.; Günter, H. H. *Organoselenium Compounds: Their Chemistry and Biology*; Wiley: New York, 1973. (b) Dias, G.; De Almeida, R. M.; Moraes, T.; Sudati, H. J.; Dobrachinski, F.; Pavin, S.; Soares, F. A. A.; Nogueira, C. W.; Barbosa, N. B. V. *Physiol. Behav.* 2014, *124*, 116. (c) Gai, B. M.; Bortolatto, C. F.; Brüning, C. A.; Zborowski, V. A.; Stein, A. L.; Zeni, G.; Nogueira, C. W. *Neuropharmacology* 2014, *79*, 580. (d) Hort, M. A.; Straliotto, M. R.; Netto, P. M.; da Rocha, J. B. T.; de Bem, A. F.; Ribeiro-do-Valle, R. M. *J. Cardiovasc. Pharmacol.* 2011, *58*, 91. (e) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* 2004, *104*, 6255. (f) Tiekink, E. R. T. *Dalton Trans.* 2011, *41*, 6390.

(2) (a) Nascimento, V.; Alberto, E. E.; Tondo, D. W.; Dambrowski, D.; Detty, M. R.; Nome, F.; Braga, A. L. *J. Am. Chem. Soc.* 2012, *134*, 138. (b) Sarma, B. K.; Mugesh, G. *J. Am. Chem. Soc.* 2005, *127*, 11477. (c) Roy, G.; Nethaji, M.; Mugesh, G. *J. Am. Chem. Soc.* 2004, *126*, 2712. (d) Flohé, L.; Günzler, E. A.; Schock, H. H. *FEBS Lett.* 1979, *32*, 132. (e) Shamberger, R. J. *Biochemistry of Selenium*; Plenum Press: New York, 1983. (f) Mugesh, G.; Du Mont, W. W.; Sies, H. *Chem. Rev.* 2001, *101*, 2125.

(3) (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Organic Chemistry Series; Pergamon: Oxford, U.K., 1986. (b) Freudendahl, D. M.; Santoro, S.; Shahzad, S. A.; Santi, C.; Wirth, T. *Angew. Chem., Int. Ed.* 2009, *48*, 8409. (c) Derek, W. J.; Risto, L. *Selenium and Tellurium Chemistry: From Small Molecules to Biomolecules and Materials*; Springer-Verlag: Berlin, 2011. (d) Godoi, M.; Paixão, M. W.; Braga, A. L. *Dalton Trans.* 2011, *40*, 11347. (e) Reich, H. J. *J. Org. Chem.* 1975, *40*, 2570. (f) Sharpless, K. B.; Laurer, R. F. *J. Am. Chem. Soc.* 1972, *94*, 7154.

(4) (a) Back, T. G. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley: New York, 1987; Chapter 1. (b) Back, T. G. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; Wiley: Chichester, U.K., 1987; Vol. 2, Chapter 3. (c) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Organic Chemistry Series; Pergamon Press: Oxford, U.K., 1986; Chapters 7 and 8.

(d) Schmid, G. H.; Garratt, D. G. In *The Chemistry of Double-bonded Functional Groups. Supplement A*; Patai, S., Ed.; Wiley: New York, 1977; Chapter 9.

(5) (a) Tiecco, M.; Lorenzo, T.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* 1988, *44*, 2261. (b) Tiecco, M.; Lorenzo, T.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron Lett.* 1989, *30*, 1417. (c) Toriil, S.; Uneyama, K.; Ono, M. *Tetrahedron Lett.* 1980, *21*, 2741. (d) Back, T. G.; Moussa, Z.; Parvez, M. *J. Org. Chem.* 2002, *67*, 499. (e) Back, T. G.; Nan, S. *J. Chem. Soc., Perkin Trans. 1* 1998, 3123. (f) Back, T. G.; Moussa, Z. *Org. Lett.* 2000, *19*, 3007. (g) Zhao, L.; Li, Z.; Wirth, T. *Eur. J. Org. Chem.* 2011, 7080.

(6) Nicolaou, K. C.; Petatis, N. A.; Claremon, D. A. *Tetrahedron* 1985, *41*, 4835.

(7) Santi, C.; Tidei, C. Addition Reactions with Formation of Carbon−Sulfur and Carbon Selenium Bonds. In *Comprehensive Organic Synthesis*, 2nd ed.; Knochel, P., Molander, G. A., Eds.; Elsevier: Oxford, U.K., 2014; Vol. 7, pp 605−637.

(8) (a) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D. *Tetrahedron Lett.* 1989, *30*, 1417. (b) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *J. Chem. Soc., Chem. Commun.* 1993, *7*, 637.

(9) Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Synth. Commun.* 1998, *28*, 1769.

(10) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* 1988, *44*, 2273.

(11) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Marini, F. *J. Chem. Soc., Perkin Trans. 1* 1993, *17*, 1989.

(12) Bosman, C.; D'Annibale, A.; Resta, S.; Trogolo, C. *Tetrahedron Lett.* 1994, *35*, 6525.

(13) Lee, D. H.; Kim, Y. H. *Synlett* 1995, *4*, 349.

(14) (a) Brownbridge, P. *J. Chem. Soc., Chem. Commun.* 1987, *17*, 1280. (b) López-Tudanca, P. L.; Jones, K.; Brownbridge, P. *Tetrahedron Lett.* 1991, *32*, 2261. (c) Wang, H.; Huang, D.; Cheng, D.; Li, L.; Shi, Y. *Org. Lett.* 2011, *13*, 1650. (d) Denmark, S. E.; Kornfilt, D. J. P.; Vogler, T. *J. Am. Chem. Soc.* 2011, *133*, 15308. (e) Guan, H.; Wang, H.; Huang, D.; Shi, Y. *Tetrahedron* 2012, *68*, 2728.

(15) (a) Furukawa, N.; Morishita, T.; Akasaka, T.; Oae, S. *Tetrahedron Lett.* 1979, *20*, 3973. (b) Morishita, T.; Furukawa, N.; Oae, S. *Tetrahedron* 1981, *37*, 2539. (c) Ito, Y.; Ogawa, T. *Tetrahedron Lett.* 1987, *28*, 2723. (d) Ramesh, S.; Franck, R. W. *J. Chem. Soc., Chem. Commun.* 1989, *14*, 960.

(16) (a) Taniguchi, N. *J. Org. Chem.* 2006, *71*, 7874. (b) Movassagh, B.; Navidi, M. *Tetrahedron Lett.* 2008, *49*, 6712. (c) Muangkaew, C.; Katrun, P.; Kanchanarugee, P.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Jaipetch, T.; Kuhakarn, C. *Tetrahedron* 2013, *69*, 8847.

(17) (a) Nicolaou, K. C.; Lysenk, Z. *J. Chem. Soc., Chem. Commun.* 1977, *9*, 293. (b) Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* 1979, *101*, 3884. (c) Young, R. N.; Coombs, W.; Guindon, Y.; Rokach, J. *Tetrahedron Lett.* 1981, *22*, 4933. (d) Aoki, T.; Konoike, T.; Itana, H.; Tsuji, T.; Yoshioka, M.; Nagata, W. *Tetrahedron* 1983, *39*, 2515. (e) Huckstep, M. R.; Taylor, R. J. K. *Tetrahedron Lett.* 1986, *27*, 5919. (f) Tuladhar, S. M.; Fallis, A. G. *Tetrahedron Lett.* 1987, *28*, 523. (g) Arjona, O.; de la Pradilla, R. F.; Pérez, R. A.; Plumet, J.; Viso, A. *Tetrahedron Lett.* 1987, *28*, 5549. (h) Tuladhar, S. M.; Fallis, A. G. *Can. J. Chem.* 1987, *65*, 1833. (i) Preuss, R.; Schmidt, R. R. *Synthesis* 1988, *9*, 694.

(18) (a) Trost, B. M.; Shibata, T.; Martin, S. J. *J. Am. Chem. Soc.* 1982, *104*, 3228. (b) O'Malley, G. J.; Cava, M. P. *Tetrahedron Lett.* 1985, *26*, 6159.

(19) Yang, F.; Wang, F.; Wang, T.; Wanga, Y.; Tian, S. *Chem. Commun.* 2014, *50*, 2111.

(20) (a) Ramalinga, K.; Vijayalakshmi, P.; Kaimal, T. N. B. *Tetrahedron Lett.* 2002, *43*, 879. (b) Liu, J.; Li, P.; Chenb, W.; Wang, L. *Chem. Commun.* 2012, *48*, 10052. (c) Wang, X.; Chen, F. *Tetrahedron* 2011, *67*, 4547. (d) Gabriele, E.; Singh, F. V.; Freudendahl, D. M.; Wirth, T. *Tetrahedron* 2012, *68*, 10573.

(21) Ge, W.; Wey, Y. *Green Chem.* 2012, *14*, 2066.

(22) Azeredo, J. B.; Godoi, M.; Martins, G. M.; Silveira, C. C.; Braga, A. L. *J. Org. Chem.* 2014, *79*, 4125.

(23) Rayner, C. M. In *Organosulfur Chemistry: Synthetic Aspects*; Page, P., Ed.; Academic Press: London, 1995; p 89.

(24) (a) Santi, C.; Santoro, S. Eletrophilic Selenium Reagents. In *Organoselenium Chemistry*; Wirth, T., Ed.; Wiley-VCH: Weinheim, Germany, 2011; pp 1−51. (b) Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. *Synlett* **2003**, *5*, 655. (c) Aprile, C.; Gruttadauria, M.; Amato, M. E.; Anna, F. D.; Meo, P. L.; Riela, S.; Noto, R. *Tetrahedron* **2003**, *59*, 2241. (d) Petragnani, N.; Stefani, H. A.; Valduga, C. J. *Tetrahedron* **2001**, *57*, 1411. (e) Denmark, S. E.; Edwards, M. G. *J. Org. Chem.* **2006**, *71*, 7293. (f) Clive, D. L. J.; Chittattu, G.; Wong, C. K. *Can. J. Chem.* **1987**, *55*, 3894.

(25) (a) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, *18*, 734. (b) Gilmore, K.; Alabugin, I. V. *Chem. Rev.* **2011**, *111*, 6513.

(26) Jamier, V.; Ba, L. A.; Jacob, C. *Chem.—Eur. J.* **2010**, *16*, 10920.

(27) Pinto, A. V.; Neves Pinto, C.; Pinto, M. C. F. R.; Santa Rita, R. M.; Pezzella, C.; de Castro, S. L.; de Castro, S. L. *Arzneim. Forsch.* **1997**, *47*, 74.

(28) Lima, N. M. F.; Correia, C. S.; Leon, L. L.; Machado, G. M. C.; Madeira, M. F.; Santana, A. E. G.; Goulart, M. O. F. *Mem. Inst. Oswaldo Cruz* **2004**, *99*, 757.

(29) Rao, K. V.; McBride, T. J.; Oleson, J. J. *Cancer Res.* **1968**, *28*, 1952.

(30) Fiorito, S.; Epifano, F.; Bruyère, C.; Mathieu, V.; Kiss, R.; Genovese, S. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 454.

(31) (a) Sunassee, S. N.; Veale, C. G. L.; Shunmoogam-Gounden, N.; Osoniyi, O.; Hendricks, D. T.; Caira, M. R.; la Mare, J.; Edkins, A. L.; Pinto, A. V.; da Silva Júnior, E. N.; Davies-Coleman, M. T. *Eur. J. Med. Chem.* **2013**, *62*, 98. (b) da Silva Júnior, E. N.; Guimarães, T. T.; Menna-Barreto, R. F. S.; Pinto, M. C. F. R.; de Simone, C. A.; Pessoa, C.; Cavalcanti, B. C.; Sabino, J. R.; Andrade, C. K. Z.; Goulart, M. O. F.; de Castro, S. L.; Pinto, A. V. *Bioorg. Med. Chem.* **2010**, *18*, 3224. (c) Sun, J. S.; Geiser, A. H.; Frydman, B. *Tetrahedron Lett.* **1998**, *39*, 8221.

(32) Fieser, L. F.; Fieser, M. *J. Am. Chem. Soc.* **1948**, *70*, 3215.

(33) Hiller, F. W.; Krueger, J. H. *Inorg. Chem.* **1967**, *6*, 528.

(34) (a) Tamres, M.; Bhat, S. N. *J. Am. Chem. Soc.* **1972**, *94*, 2577. (b) Lo, S. J.; Tamres, M. *Can. J. Chem.* **1983**, *61*, 1933.

(35) Zhang, W.; Yu, H.; Gao, Y.; Meng, J.; Matsuura, T. *Chem. Commun.* **2003**, 498.

(36) Tiecco, M.; Chianelli, D.; Tingoli, M.; Testaferri, L.; Bartolli, D. *Tetrahedron* **1986**, *42*, 4897.

(37) Tingoli, M.; Diana, R.; Panunzi, B. *Tetrahedron Lett.* **2006**, *47*, 7529.

(38) Solladié-Cavallo, A.; Adib, A. *Tetrahedron* **1992**, *48*, 2453.

(39) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D.; Balducci, R. *J. Org. Chem.* **1990**, *55*, 429.