JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

Synthesis of 4-Selanyl- and 4-Tellanyl-1*H*-isochromen-1-ones Promoted by Diorganyl Dichalcogenides and Oxone

Helen A. Goulart, José S. S. Neto, Angelita M. Barcellos, Krigor B. Silva, Maiara C. de Moraes, Raquel G. Jacob, Eder J. Lenardão, Thiago Barcellos, and Gelson Perin*

Cite This: https://doi.org/10.1021/acs.joc.1c00271 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A new method was developed for the synthesis of 4-chalcogenyl-1*H*-isochromen-1-ones through the 6-*endo*-*dig* electrophilic cyclization of 2-alkynylaryl esters and diorganyl dichalcogenides under ultrasound irradiation. The reactions were performed under mild conditions, using Oxone as a green oxidant to promote the cleavage of the chalcogen−chalcogen bond in diorganyl diselenides and ditellurides to generate electrophilic species *in situ*. A total of 25 compounds were selectively obtained after 30−70 min, in good to excellent yields (74−95%). This procedure was extended to prepare 5*H*-selenopheno[3,2-*c*]isochromen-5-ones. Additionally, for the first time, the 4-chalcogenyl-1*H*-isochromen-1-ones were used as substrates in the thionation reaction, using Lawesson's reagent and microwave irradiation under solvent-free conditions, obtaining the thio derivatives in yields of up to 99% in only 15 min.

INTRODUCTION

1*H*-2-Benzopyran-1-ones or 1*H*-isochromen-1-ones are benzannulated analogues of the six-membered oxygen heterocycle *α*-pyrone (2*H*-pyran-2-one) (Figure 1). The 1*H*-isochromen-1-one core occurs in nature as a secondary metabolite of plants and lower microorganisms or as a component of some insect pheromones and venoms.[1] As a structural subunit in natural products, this class of compounds exhibits remarkable bioactivities and structural diversity (Figure 1); for example, they show therapeutic applications such as anticancer, antibacterial, antidiabetic, fungicidal, and anti-inflammatory.[1,2]

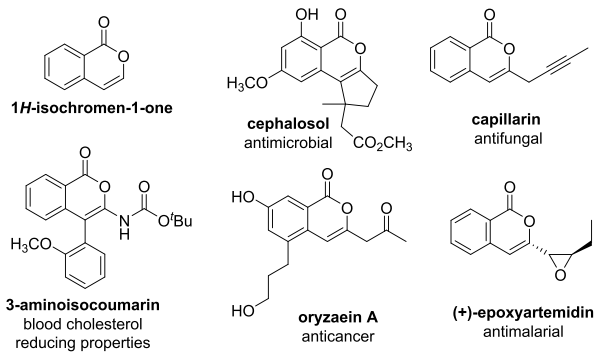


Figure 1. Examples of biologically active compounds with the isochromen-1-one scaffold.

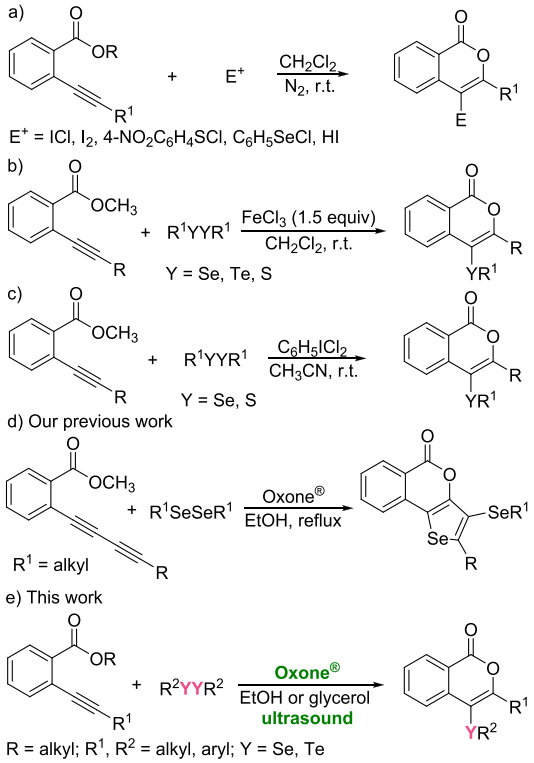
Nowadays, connecting the pharmacological potential of several heterocyclic compounds with organochalcogens is a growing field of research.[3] Several reports describe that the insertion of an organoselenium or organosulfur moiety in a heterocycle can potentialize its biological activities. As has already been recognized, molecules containing chalcogen show antioxidant, antinociceptive, antidepressant, anticancer, antibacterial, and antifungal properties.[4] In this sense, some new protocols were developed to prepare chalcogen-substituted 1*H*-isochromen-1-ones.[5] In 2003, Yao and Larock[6] reported the synthesis of a variety of substituted isochromen-1-ones in excellent yields by the reaction of 2-(1-alkynyl)benzoates with ICl, I_2, PhSeCl, 4-$NO_2C_6H_4SCl$, and HI (Scheme 1a). Later, the regioselective synthesis of 1*H*-isochromen-1-ones by the iron(III)/diorganyl dichalcogenide-mediated cyclization of 2-alkynylaryl esters was described (Scheme 1b).[7] More recently, a metal-free protocol to the formation *in situ* of RSCl/ArSeCl and their application in the intramolecular cyclization of 2-(1-alkynyl)benzoates was described (Scheme 1c).[8]

Searching for an environmentally benign oxidizing agent, potassium peroxymonosulfate, marketed as Oxone, has emerged as an excellent alternative due to its low cost, stability, water solubility, simplicity in handling, and low toxicity. Oxone is a triple salt ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$)

Special Issue: Enabling Techniques for Organic Synthesis

Received: February 3, 2021

Scheme 1. Methods for the Synthesis of Chalcogen-1*H*-isochromen-1-ones



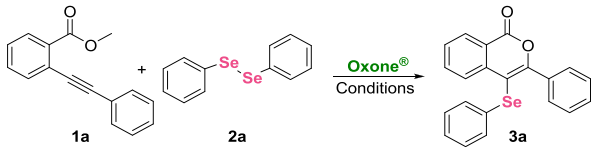
containing about 50% of active oxidant/mole, which is the anion peroxymonosulfate (HSO_5^-).[9] In view of the good performance of Oxone, it has been used in a great number of green organic transformations, especially cyclization ones.[10] A successful example is the cyclization of 2-alkynylbenzoic acid in water for the synthesis of isocoumarin.[11] Over the past few years, our group has strived toward developing safer, cleaner, and less expensive procedures applying Oxone to prepare organochalcogen compounds.[12] For instance, the diselenide/Oxone system was used to prepare 4-organoselanyl-1*H*-pyrazoles,[13] 5-methylselanyl-4,5-dihydroisoxazoles,[14] and 4-(chalcogenyl)isoquinoline *N*-oxides.[15] This strategy was successfully used by us in the synthesis of 5*H*-selenopheno-[3,2-*c*]isochromen-5-ones through a double intramolecular cyclization of methyl 2-(organyl-1,3-diynyl)benzoate (Scheme 1d).[16]

Another way to make organic synthesis greener is by using ultrasonic irradiation (US) as an alternative energy source. The ultrasound is a well-established tool used to promote reactions through a specific activation based on acoustic cavitation. This physical phenomenon can modify the course of reactions, improving yields and increasing the selectivity in a shorter reaction time than the conventional procedures.[17] In this sense, and in continuation to our interest in green procedures correlated with organochalcogen chemistry, herein we describe an alternative method for the preparation of 4-chalcogenyl-1*H*-isochromen-1-ones. Our new proposal involves the US-promoted 6-*endo*-*dig* electrophilic cyclization of 2-alkynylaryl esters and diorganyl dichalcogenides using Oxone as a green oxidant (Scheme 1e).

RESULTS AND DISCUSSION

We started our investigation by searching for the best reaction conditions for the preparation of 3-phenyl-4-(phenylselanyl)-1*H*-isochromen-1-one **3a**, with methyl 2-(phenylethynyl)-benzoate **1a** (0.250 mmol) and diphenyl diselenide **2a** as model substrates in the presence of Oxone. Thus, in a first experiment, a mixture of **1a** (0.250 mmol), **2a** (0.125 mmol), and Oxone (0.250 mmol) in ethanol (2.0 mL) was stirred at room temperature for 24 h in a conventional system (magnetic stirrer), affording the desired product **3a** in 30% yield (Table 1, entry 1).

Table 1. Optimization Studies to Prepare 3-Phenyl-4-(phenylselanyl)-1*H*-isochromen-1-one 3a[a]



no.	2a (mmol)	Oxone (mmol)	time (h)	amplitude (%)	solvent	yield[b] (%)
1	0.125	0.250	24	*c*	EtOH	30
2	0.125	0.250	3.0	*d*	EtOH	77
3	0.125	0.250	1.0	60	EtOH	71
4	0.150	0.250	0.5	60	EtOH	95
5	0.170	0.250	0.5	60	EtOH	93
6	0.200	0.250	0.5	60	EtOH	93
7	0.250	0.250	0.5	60	EtOH	96
8	0.150	0.250	1.5	60	EtOH/H_2O	72
9	0.150	0.250	1.5	60	PEG-400	69
10	0.150	0.250	1.5	60	glycerol	60
11	0.150	0.250	1.5	60	H_2O	NR
12	0.150	0.250	1.5	60	DCM	NR
13	0.150	0.250	1.5	60	CH_3CN	50
14	0.150	0.250	1.5	60	DMF	traces
15	0.150	0.250	1.5	60	AcOEt	16
16	0.150	0.250	1.5	60	THF	10
17	0.150	0.375	0.5	60	EtOH	92
18	0.150	0.187	1.0	60	EtOH	93
19	0.150	0.250	0.5	80	EtOH	91
20	0.150	0.250	1.25	40	EtOH	93

[a]Reactions were performed using a mixture of **1a** (0.250 mmol), **2a**, and Oxone in 2.0 mL of solvent under US. [b]Yields obtained after column chromatography. [c]Reaction performed under magnetic stirring at room temperature. [d]Reaction performed under conventional heating (oil bath at 78 °C) and magnetic stirring. NR = no reaction.

Aiming to improve the reaction yield and to reduce the reaction time, the reaction was performed at 78 °C (refluxing ethanol). After 3 h, the expected product **3a** was obtained in 77% yield (Table 1, entry 2). To achieve the product **3a** in an acceptable yield and in shorter reaction time, we decided to change our initial strategy by performing the reaction under ultrasonic irradiation (US) at an amplitude of 60% and a frequency of 20 kHz (Cole-Parmer model CPX 130 ultrasonic processor). To our delight, when the reaction was sonicated for 1 h (monitored by thin layer chromatography (TLC)), a similar yield of **3a** was obtained (71%), proving that the efficient energy transfer by the US can significantly reduce the reaction time (Table 1, entry 3). Inspired by this outcome, the

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

following additional experiments were conducted using US at 60% of amplitude. First, we studied the effect of the amount of diphenyl diselenide **2a** in the reaction (Table 1, entries 4−7). Fortunately, using a 20% excess of **2a** (0.150 mmol), the product **3a** was obtained in 95% yield after only 0.5 h of sonication (Table 1, entry 4). However, larger amounts of **2a** (0.170, 0.200, and 0.250 mmol) were not effective in increasing the reaction yield, giving the product **3a** in 93%, 93%, and 96% yield, respectively (Table 1, entries 5−7).

Next, a study about the influence of the solvent in the reaction was performed, and the reaction was tested in polar protic and aprotic solvents (Table 1, entries 8−16). In the reactions using a mixture of ethanol/water (1:1), polyethylene glycol-400 (PEG-400), glycerol, acetonitrile, ethyl acetate and tetrahydrofuran, the product **3a** was obtained in lower yields compared to the reaction in ethanol (Table 1, entry 4 vs 8−10, 13, 15, and 16). No reaction was observed when water or dichloromethane was used as solvent, while only trace amounts of isochromen-1-one **3a** were observed using dimethylformamide; in all cases, the starting materials were recovered (Table 1, entries 11−12 and 14). The use of larger (0.375 mmol) or smaller amounts (0.187 mmol) of Oxone, did not alter the reaction performance, giving the product **3a** in 92% and 93% yield after 0.5 and 1.0 h of sonication, respectively (Table 1, entries 17 and 18). Finally, a study was carried out to evaluate the effect of the amplitude of the US in the reaction (Table 1, entries 19 and 20). We observed that by increasing the amplitude to 80% there was no significant change in both the reaction time (0.5 h) and the yield of product **3a** (Table 1, entry 19). However, by reducing the amplitude to 40%, a longer reaction time (1.25 h) was required for the consumption of the starting materials, while the yield of **3a** did not change significantly (Table 1, entry 20). Based on the results depicted on Table 1, the best reaction conditions to prepare **3a** were defined as the sonication (60% of amplitude) of a mixture of 0.250 mmol of 2-alkynylaryl ester **1a**, 0.150 mmol of diphenyl diselenide **2a** ,and 0.250 mmol of Oxone in 2.0 mL of ethanol as the solvent (Table 1, entry 4).

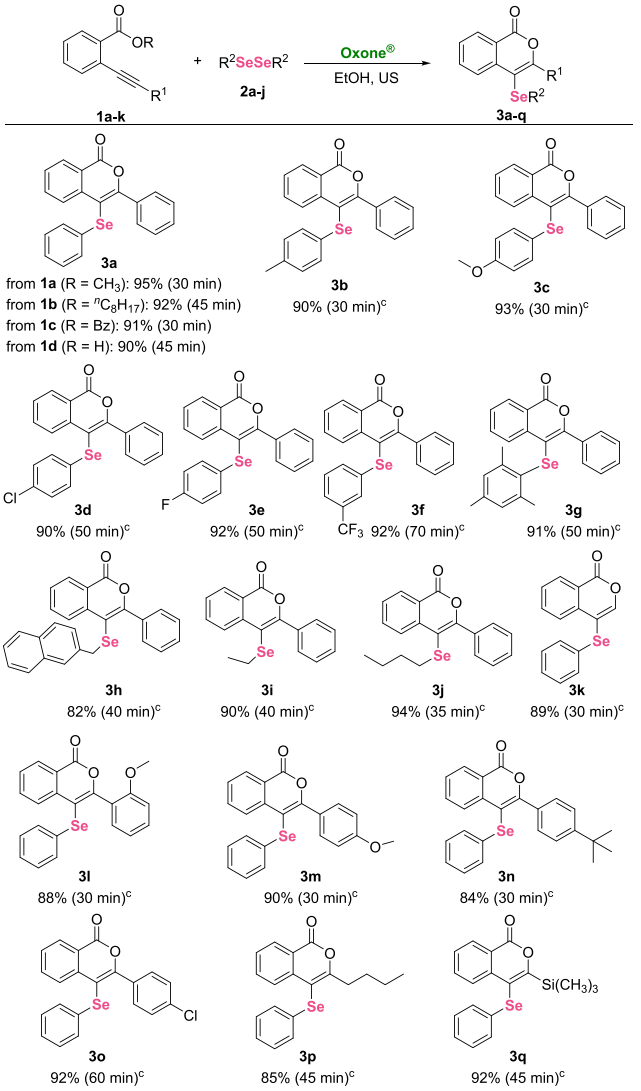
Under the optimized conditions, a series of isochromen-1-ones **3** were prepared by this newly established approach. We examined the generality and limitations of this method with a variety of diorganyl dichalcogenides **2** and 2-alkynylaryl esters **1** (Schemes 2−4).

Initially, we have checked the possibility of performing these reactions with other alkoxy groups in the ester **1** (R = $^{n}C_8H_{17}$ and $C_6H_5CH_2$) and with carboxylic acid. When octyl 2-(phenylethynyl)benzoate **1b** was used, product **3a** was obtained in 92% yield, requiring more time for the consumption of the starting materials (45 min) compared to the reaction using methyl 2-(phenylethynyl)benzoate **1a**. Benzyl 2-alkynylbenzoate **1c** and 2-(phenylethynyl)benzoic acid **1d** were good substrates for the reaction, affording **3a** in 91% and 90% yield, after 30 and 45 min of sonication, respectively (Scheme 2). The electrophilic cyclization of 2-(phenylethynyl)benzoic acid **1d** was already described, and a mixture of five- and six-membered ring products was obtained.[10a,18] To our satisfaction, our novel protocol proved to be highly regioselective also for this substrate, providing only the six-membered product.

Next, we turned our attention to investigate the scope of diorganyl diselenides **2** in the reaction with methyl 2-(phenylethynyl)benzoate **1a** and Oxone in ethanol. Diaryl diselenides substituted at the *para*-position with electron-donating groups **2b** (R^2 = 4-$CH_3C_6H_4$) and **2c** (R^2 = 4-$CH_3OC_6H_4$) were suitable substrates for the reaction, and the respective products **3b** and **3c** were obtained in 90% and 93% yield after 30 min (Scheme 2). The presence of electron-withdrawing substituents decreased the reactivity of the diaryl diselenide **2**, and longer reaction times were necessary for the consumption of the starting materials compared to the electron-donating ones. Thus, diaryl diselenides **2d** (R^2 = 4-ClC_6H_4), **2e** (R^2 = 4-FC_6H_4), and **2f** (R^2 = 3-$CF_3C_6H_4$) afforded **3d**, **3e**, and **3f** in 90%, 92%, and 92% yield, respectively, after reaction times of 50−70 min (Scheme 2).

When the bulky dimesityl diselenide **2g** was used, the corresponding product **3g** was obtained in 91% yield after 50 min of reaction (Scheme 2). The reactions were conducted satisfactorily with alkyl diselenides such as bis(2-naphthylmethyl) diselenide **2h**, diethyl diselenide **2i**, and dibutyl diselenide **2j**, affording the respective products **3h**, **3i**, and **3j** in

Scheme 2. Scope of the Reaction to Synthesize 4-(Organylselanyl)-1*H*-isochromen-1-ones 3a−q[a,b]



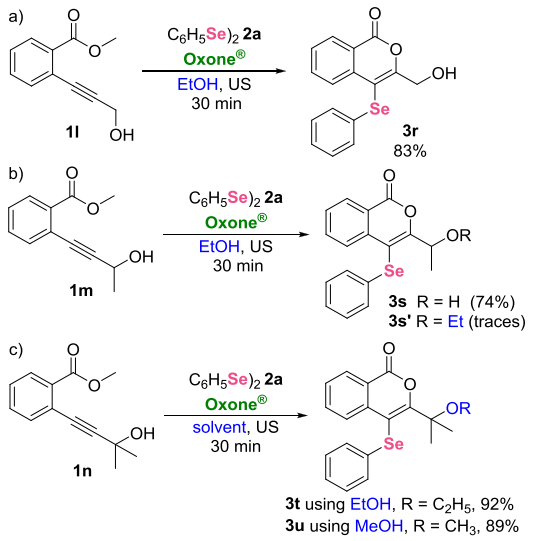
[a]Reactions were performed using a mixture of **1** (0.250 mmol), **2** (0.150 mmol), and Oxone (0.250 mmol) in 2.0 mL of EtOH under ultrasonic irradiation. [b]Yields are of pure products, after column chromatography. [c]The leaving group in **1** is R = CH_3 (**1a**).

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

82%, 90%, and 94% yield, respectively, after 35−40 min of reaction (Scheme 2).

The effect of the substituent R^1 in the pendant 2-alkynyl group of the arylester **1** was investigated in the reaction with diphenyl diselenide **2a** (Schemes 2 and 3). When methyl 2-

Scheme 3. Synthesis of 4-(Organylselanyl)-1*H*-isochromen-1-ones 3r−u



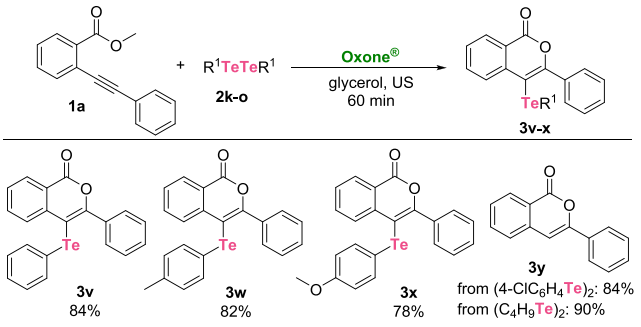
ethynylbenzoate **1e** (R^1 = H) reacted with **2a** under the optimal conditions, the isochromen-1-one **3k** was obtained in 89% yield after 30 min. There is no remarkable electronic effect caused by the presence of electron-donating substituents at the *ortho*- or *para*-position of the aromatic ring in the methyl 2-(arylethynyl)benzoate **1**. Thus, compounds **3l** (R^1 = 2-$CH_3OC_6H_4$) and **3m** (R^1 = 4-$CH_3OC_6H_4$) were obtained in 88% and 90% yield, respectively, by the reaction of **1f** and **1g** with **2a** (Scheme 2). The use of substrate **1f**, substituted with an *o*-methoxy group, could favor the *O*-cyclization reaction, leading to the benzofuran derivative. However, our method was selective to the formation exclusively of the isochromen-1-one **3l**. When methyl 2-[4-(^{t} butyl)phenylethynyl]benzoate **1h** (R^1 = 4-$^tC_4H_9C_6H_4$) reacted with **2a** under the optimal conditions, the expected isochromen-1-one **3n** was obtained in 84% yield after 30 min of sonication. The presence of an electron-withdrawing substituent, however, reduced the reactivity of the substrate **1**, and the 2-alkynylaryl ester **1i** (R^1 = 4-ClC_6H_4) required 60 min to be cyclized to the expected isochromen-1-one **3o**, in 92% yield. Furthermore, alkynes **1j** (R^1 = $^nC_4H_9$) and **1k** (R^1 = $Si(CH_3)_3$) were suitable substrates for the reaction, and the respective products **3p** and **3q** were obtained in 85% and 92% yield, respectively, after 45 min (Scheme 2). The usefulness of this US-promoted protocol in preparative synthesis was demonstrated in a reaction using 3.0 mmol (0.711 g) of methyl 2-(phenylethynyl)benzoate (**1a**) and 1.8 mmol (0.565 g) of diphenyl diselenide (**2a**), affording 1.021 g of pure **3a** (yield 90%) after 30 min of sonication.

Next, we evaluated the influence of the presence of a hydroxyl substituent in the 2-alkynyl group in the esters **1l−n**, in the reaction with diphenyl diselenide **2a** (Scheme 3). Methyl 2-(3-hydroxyprop-1-yn-1-yl)benzoate **1l** reacted with diselenide **2a** under the optimized conditions to produce the corresponding product **3r** in 83% yield (Scheme 3a). When methyl 2-(3-hydroxybut-1-yn-1-yl)benzoate **1m** was used as substrate in the reaction with **2a**, the expected isochromen-1-one **3s** (R = H) was isolated in 74% yield. In this case, a second, unexpected product was detected in trace amounts, which was characterized as **3s′** (R = C_2H_5), as indicated by GC/MS analysis (Scheme 3b).

Interested in this result, we look for a strategy to selectively obtain the product with the alkoxy group in the structure. For that, methyl 2-(3-hydroxy-3-methylbut-1-yn-1-yl)benzoate **1n** was used as substrate in the reaction with **2a** under the optimal conditions, using ethanol as solvent. To our satisfaction, the ether **3t** (R = C_2H_5) was selectively obtained in 92% yield (Scheme 3c). This can be explained by the formation of the alkynyl carbocation intermediate, from the elimination of a water molecule, followed by the nucleophilic attack by the alcohol solvent.[19] The elimination of water from the propargyl alcohol is favored in the acidic medium of the reaction, due to the presence of Oxone (pH = 1). This hypothesis was proved by changing the reaction solvent for methanol, giving, after 30 min, the product containing the methyl ether derivative **3u** in 89% yield (Scheme 3c).

In the sequence, we turned our attention on the reaction between 2-alkynylaryl ester **1a** and diphenyl ditelluride (**2k**) under the optimal conditions defined for the analogue diselenides. Unfortunately, no reaction occurred after 60 min of sonication, and the starting materials were recovered at the end of the reaction. Recently, some of us[20] have observed that the use of glycerol as a solvent favors the achievement of high temperatures under ultrasonic irradiation. Thus, we wonder if this solvent could make possible the formation of products using the recalcitrant ditelluride as chalcogen source. Fortunately, when the reaction was repeated using glycerol (2.0 mL) as solvent instead ethanol, the expected tellurium-substituted product **3v** was obtained in 84% yield after 60 min (Scheme 4). Generally, electrophilic species of tellurium are

Scheme 4. Synthesis of 4-(Organyltellanyl)-1*H*-isochromen-1-ones 3v−x and 3-Phenyl-1*H*-isochromen-1-one 3y



unstable in open air and decompose more easily in the reaction medium, thus requiring inert atmosphere. The high yield obtained of **3v** indicates that our protocol is suitable also to electrophilic cyclization involving electrophilic tellurium species, without the need for special apparatus and inert atmosphere. The same reaction conditions were then extended to other substituted diaryl ditellurides (**2l−n**) and to dibutyl ditelluride (**2o**) (Scheme 4). Diaryl ditellurides substituted with electron-donating groups **2l** (R^1 = 4-$CH_3C_6H_4$) and **2m** (R^1 = 4-$CH_3OC_6H_4$) were good substrates for the reaction, and the respective products **3w** and **3x** were obtained in 82% and 78% yield, respectively. On the other hand, the electron-deficient diaryl ditelluride **2n** (R^1 = 4-ClC_6H_4) and dibutyl

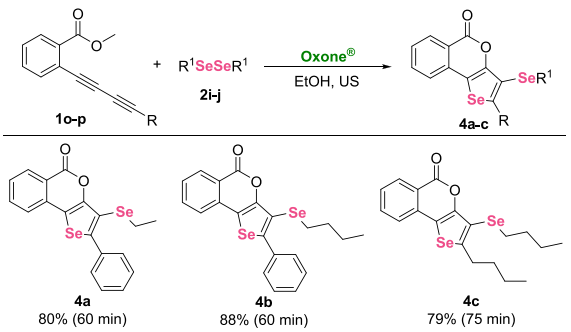
https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

ditelluride **2o** ($R^1 = C_4H_9$) were not reactive under the optimal conditions, and the expected tellurium-containing products could not be prepared. In both reactions, the obtained product was 3-phenyl-1*H*-isochromen-1-one **3y**, formed from the loss of the respective organotellurium groups after the cyclization (Scheme 4).

After, we try to expand the scope of products to sulfur-containing compounds in their structure. We examined the reaction between 2-alkynylaryl ester **1a**, diphenyl disulfide **2p** and Oxone using ethanol or glycerol as a solvent for the reactions. Unfortunately, in both cases the desired product **3z** was not obtained, even after 2 h of sonication, and the starting material **1a** was recovered. This lack of reactivity of disulfide could be attributed, at least in part, to the stronger S−S bond compared to the Se−Se and Te−Te ones, making the formation of the electrophilic species of sulfur more difficult.

Additionally, considering the great importance presented by selenophenes in chemistry, material field, and their promising biological activities,[21] we decided to extend our protocol to the synthesis of isochromenones fused to selenophenes **4** (Scheme 5). For that, methyl 2-(phenylbuta-1,3-diyn-1-yl)benzoate **1o** and methyl 2-(octa-1,3-diyn-1-yl)benzoate **1p** were used as substrates in the reaction with **2i** and **2j**. To our satisfaction, the double intramolecular cyclization reactions were successful, and the expected products **4a−c** were obtained in 80%, 88%, and 79% yield, respectively, after reaction times of 60−75 min (Scheme 5).

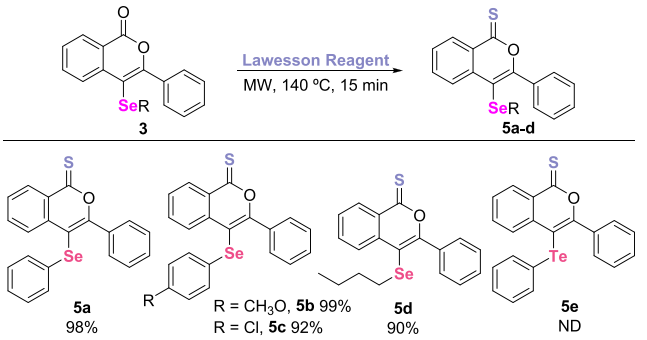
Scheme 5. Synthesis of 5*H*-Selenopheno[3,2-*c*]isochromen-5-ones 4a−c[a,b]



[a]Reactions were performed using a mixture of **1** (0.250 mmol), **2** (0.30 mmol), and Oxone (0.50 mmol) in 2.0 mL of EtOH under ultrasonic irradiation. [b]Yields are of pure products, after column chromatography.

Finally, we studied the synthetic potential of isochromen-1-ones **3** using them as substrates in thionation reactions. The conventional procedures reported in the literature for the thionation involve refluxing a mixture of the substrate and a large excess of 2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiadiphosphetane (the Lawesson's reagent) in dry toluene or benzene for several hours under inert atmosphere.[22] As mentioned before, our research group has invested in the development of green methods for obtaining organochalcogen compounds. Along this line, we decided to investigate the use of ultrasound irradiation as an energy source in the thionation reaction. For this, we initially tested the reaction between compound **3a** (0.250 mmol) and the Lawesson's reagent (0.130 mmol), using ethanol (2.0 mL) as solvent and US at an amplitude of 60% and a frequency of 20 kHz. Unfortunately, after 1 h of sonication, the expected 1*H*-isochromene-1-thione **5a** was not detected, and the starting substrate **3a** was recovered (Scheme 6).

Scheme 6. Synthesis of 1*H*-Isochromene-1-thiones 5



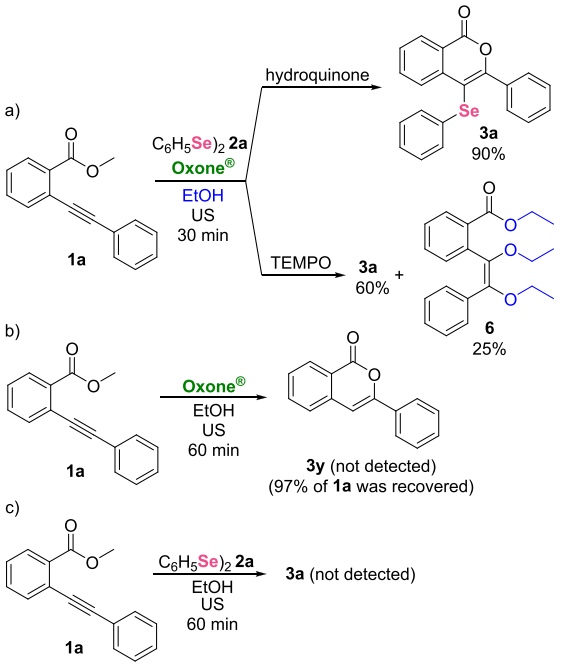
Seeking to obtain the desired products in acceptable yields, through clean reaction conditions and short reaction times, we have adapted a procedure previously described by Saeed and Ashraf that uses microwave irradiation to perform the thionation of 3-aryl-1*H*-isochromene-1-ones.[23] Thus, a mixture of **3a** (0.250 mmol) and Lawesson's reagent (0.130 mmol) was irradiated in a microwave reactor at 140 °C, using an irradiation power of 200 W (100 psi) under solvent-free conditions. After 15 min (monitored by TLC), the desired product **5a** was obtained in 98% yield (Scheme 6). For the first time, we have demonstrated the synthesis of this highly functionalized 3-organyl-4-(organylselanyl)-1*H*-isochromene-1-thione **5**. Motivated by this result, we evaluated the reactivity of a variety of 4-(organylselanyl)-1*H*-isochromen-1-ones **3**. In general, our method proved to be efficient, affording the corresponding selenylated isochromenethiones **5a−d** in excellent yields (90−99%) in only 15 min. However, when 4-(phenyltellanyl)-1*H*-isochromen-1-one **3v** was employed, the expected product **5e** was not detected, and the starting material was recovered (Scheme 6).

To achieve substantial support to elucidate the mechanism of the synthesis of 4-chalcogenyl-1*H*-isochromen-1-ones **3**, some control experiments were conducted (Scheme 7). The reaction between 2-alkynylaryl ester **1a** and diphenyl diselenide **2a** was performed using the standard conditions but in the presence of 3 equiv of the radical inhibitors hydroquinone and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) (Scheme 7a). After 30 min of reaction, the isochromen-1-one **3a** was isolated in 90% and 60% yield using hydroquinone and TEMPO, respectively. The lower yield of product **3a** in the reaction using TEMPO is attributed to the parallel formation of the product **6** (identified by 2D NMR spectroscopy; for more details, see the Supporting Information), formed by the transesterification reaction and the addition of the solvent to the triple bond in **1a**. These findings suggest that the present transformation is not going through a radical pathway.

Moreover, when the reaction was performed in the absence of diphenyl diselenide **2a**, the cyclization product **3y** was not detected, even after 60 min of reaction (Scheme 7b). This result demonstrates that the C−Se bond formation does not occur after the ring closure step and that **3y** is not an intermediate in this reaction. Finally, the reaction was carried out in the absence of Oxone, and after 60 min, no product was formed (as indicated by GC/MS analysis), indicating the need of using this oxidant in the reaction medium (Scheme 7c).

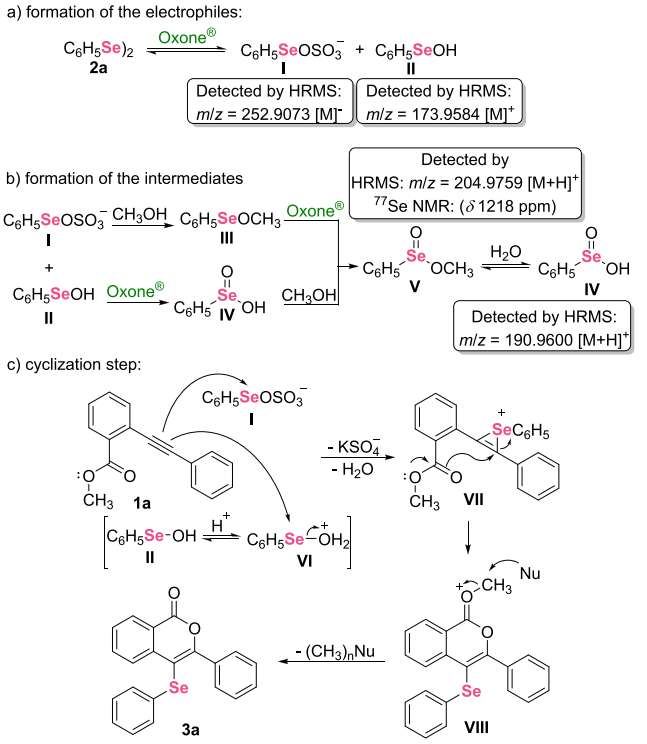
https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 7. Control Experiments



Next, we seek to identify the possible reactive intermediates generated by the reaction of diphenyl diselenide **2a** with Oxone through high-resolution mass spectrometry (HRMS) analysis. For this, a mixture of diselenide **2a** (0.150 mmol) and Oxone (0.250 mmol) was solubilized in EtOH and maintained at room temperature under constant stirring. After 1 h, an aliquot of the reaction mixture (0.05 mL) was diluted in MeOH (2 mL) and filtered. The filtrate was immediately injected in an APCI ionization source and analyzed in positive and negative modes. The HRMS spectrum recorded under negative mode revealed the ion at *m/z* 252.9073, of low intensity. Through the analysis of the exact mass, isotopic pattern, and product ions from the fragmentation (MS^2), the elemental formula $C_6H_5O_4SSe$ **I** can be inferred (Scheme 8a), which refers to the proposed intermediate arising from the oxidation of diselenide **2a** by Oxone (Figures S108 and S109). Also, the ion at *m/z* 268.9022 was observed. The exact mass analysis, as well as the isotopic pattern and fragmentation, allow us to infer that it refers to the elemental formula $C_6H_5O_5SSe$, which corresponds to the oxidized adduct of intermediate **I**, which it is believed to be generated in the ionization source. However, its presence contributes to the intermediate **I** assignment (Figures S108 and S109). Under positive mode, the ions at *m/z* 173.9584, 190.9600, and 204.9759 were recorded with higher intensity (Figures S110 and S111). The ion at *m/z* 173.9584 is attributed to the formula C_6H_6OSe $[M]^+$, corresponding to the proposed intermediate benzeneseleninic acid (**II**). The ion at *m/z* 190.9600 is attributed to the benzeneseleninic acid (**IV**) ($C_6H_6O_2Se$ $[M + H]^+$). Finally, the ion at *m/z* 204.9759 was indicated as the methyl ester of seleninic acid (**V**). This intermediate was previously described by us,[13] which was detected in the ^{77}Se NMR experiments (δ 1218 ppm). During our HRMS mechanistic studies, no peaks related to the intermediates **VII** and **VIII** were observed. Thus, based on our results and in the literature,[13,16] a reasonable mechanism is proposed, as outlined in Scheme 8.

Scheme 8. Possible Reaction Mechanism



At first, the diselenide **2a** reacts with Oxone to afford two electrophilic selenium species, $C_6H_5SeOSO_3^-$ (**I**) and C_6H_5SeOH (**II**) (Scheme 8). The electrophiles **I** and **II**, in the presence of solvent and Oxone, can be transformed into benzeneseleninic acid **IV** and methylbenzeneseleninate **V** (when R = CH_3). The species **II** can react with H^+ from the reaction medium, leading to $C_6H_5SeOH_2^+$ **VI**. The intermediates **I** and **VI** are most probably the active electrophiles in the reaction with substrate **1a**. Following, the 2-alkynylaryl ester **1a** interacts with the electrophilic species **I** or **VI**, affording the seleniranium intermediate **VII** and releasing the sulfate anion (KSO_4^-) and water (H_2O) to the medium. Then an intramolecular attack by the double bond of the carbonyl group occurs, forming the cation isochromen-1-one intermediate **VIII**, by a 6-*endo-dig* electrophilic cyclization. In the last step, a displacement of the methyl group from **VIII** by a nucleophile present in the reaction medium affords the expected isochromen-1-one **3a**.

CONCLUSIONS

In conclusion, a simple and general metal-free approach to prepare 4-chalcogenyl-1*H*-isochromen-1-ones **3** through of the 6-*endo-dig* electrophilic cyclization between 2-alkynylaryl esters **1** and diorganyl dichalcogenides **2** promoted by Oxone was developed. The protocol using ultrasound irradiation is versatile and was efficiently applied to several 2-alkynylaryl esters **1** and diorganyl dichalcogenides **2**, obtaining the products **3** with high regioselectivity and yields that varied from good to excellent (74−95%). In addition, the synthetic potential of this class of compounds was demonstrated, and their respective isochromenethione analogues **5** were obtained through the thionation reaction using Lawesson's reagent and microwave irradiation under solvent-free conditions.

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

EXPERIMENTAL SECTION

General Information. The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) using UV light as visualization agent and the mixture between 5% of vanillin in 10% of H_2SO_4 under heating conditions as developing agents. Column chromatography was performed using Merck silica gel (pore size 60 Å, 230−400 mesh). Low-resolution mass spectra (MS) were measured on a Shimadzu GC-MS-QP2010 mass spectrometer. High-resolution mass spectra (HRMS) were recorded in positive-ion mode (APCI/ESI) using a Q-TOF spectrometer. Hydrogen nuclear magnetic resonance (^{1}H NMR) and carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained on Bruker Avance III HD spectrometer at 400 at 100 MHz, respectively. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts (δ) are reported in ppm, referenced to tetramethylsilane (TMS) as the internal reference for ^{1}H NMR and the solvent peak of $CDCl_3$ for ^{13}C NMR. Coupling constants (J) are reported in hertz. The ^{77}Se NMR chemical shifts are reported in ppm relative to the internal standard $C_6H_5SeSeC_6H_5$ (δ 463 ppm). The ^{125}Te NMR chemical shifts are reported in ppm relative to the internal standard $C_6H_5TeTeC_6H_5$ (δ 422 ppm). Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), dd (double doublet), td (triple doublet), and m (multiplet). Ultrasonic waves were generated by a Cole Parmer CPX 130 operating with an amplitude of 60% and a maximum power of 130 W at 20 kHz. The temperature of the reactions under US was monitored with an Incoterm digital infrared thermometer. Microwave reactions were conducted using a CEM Discover focused microwave oven, operating at 2.45 GHz with a power of 200 W, in a glass vessel (10 mL) sealed with Teflon cap, under magnetic stirring. Melting point (mp) values were measured in a Marte PFD III instrument with a 0.1 °C precision. Oxone was purchased from Sigma-Aldrich.

Procedure for the Synthesis of Methyl 2-(Organylethynyl)-benzoate Derivatives 1. Compounds **1a**−**x** were prepared according to a published procedure.[24] Unpublished compounds **1h**, **1l**, **1m**, and **1n** were obtained using the same procedure.

*Methyl 2-(4-tert-Butylphenylethynyl)benzoate (**1h**).* Purified by column chromatography (hexane/ethyl acetate = 97:3); yield 2.629 g (90%); brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.96 (dd, J = 7.9 and 1.1 Hz, 1H); 7.63 (dd, J = 7.9 and 1.1 Hz, 1H); 7.52−7.46 (m, 3H); 7.39−7.36 (m, 3H); 3.96 (s, 3H); 1.33 (s, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 166.8, 151.8, 133.9, 131.8, 131.6, 131.4, 130.4, 127.7, 125.3, 123.9, 120.3, 94.5, 87.6, 52.1, 34.8, 31.1. MS (rel int, %) m/z: 292 (59.9), 277 (100.0), 202 (15.5), 109 (11.2). HRMS (APCI-QTOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}O_2$ 293.1542; found: 293.1543.

*Methyl 2-(3-Hydroxyprop-1-yn-1-yl)benzoate (**1l**).* Purified by column chromatography (hexane/ethyl acetate = 80:20); yield 1.521 g (80%); brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.90 (dd, J = 7.7 and 1.2 Hz, 1H); 7.52 (dd, J = 7.7 and 1.2 Hz, 1H); 7.43 (td, J = 7.7 and 1.2 Hz, 1H); 7.34 (td, J = 7.7 and 1.2 Hz, 1H); 4.55 (s, 2H); 3.90 (s, 3H); 3.47 (br s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 166.5, 134.1, 131.7, 131.4, 130.1, 127.8, 123.3, 92.9, 83.7, 52.1, 51.3. MS (rel int, %) m/z: 190 (38.1), 147 (100.0), 101 (37.7), 77 (55.5). HRMS (APCI-QTOF) m/z: [M + Na]$^+$ calcd for $C_{11}H_{10}O_3Na$ 213.0528; found: 213.0524.

*Methyl 2-(3-Hydroxybut-1-yn-1-yl)benzoate (**1m**).* Purified by column chromatography (hexane/ethyl acetate = 80:20); yield 1.673 g (82%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.89 (dd, J = 7.8 and 1.0 Hz, 1H); 7.50 (dd, J = 7.8 and 1.0 Hz, 1H); 7.41 (td, J = 7.8 and 1.0 Hz, 1H); 7.32 (td, J = 7.8 and 1.0 Hz, 1H); 4.83 (q, J = 6.6 Hz, 1H); 3.98 (br s, 1H); 3.89 (s, 3H); 1.58 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 166.5, 133.8, 131.5, 131.3, 130.0, 127.6, 123.1, 96.4, 82.0, 58.3, 51.9, 23.9. MS (rel int, %) m/z: 204 (38.1), 187 (33.2), 147 (100.0), 101 (33.2), 77 (15.5). HRMS (APCI-QTOF) m/z: [M + Na]$^+$ calcd for $C_{12}H_{12}O_3Na$ 227.0684; found: 227.0674.

*Methyl 2-(3-Hydroxy-3-methylbut-1-yn-1-yl)benzoate (**1n**).* Purified by column chromatography (hexane/ethyl acetate = 75:25); yield 1.309 g (60%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.91 (dd, J = 7.8 and 1.2 Hz, 1H); 7.51 (dd, J = 7.8 and 1.2 Hz, 1H); 7.44 (td, J = 7.8 and 1.2 Hz, 1H); 7.34 (td, J = 7.8 and 1.2 Hz, 1H); 3.91 (s, 3H); 2.85 (br s, 1H); 1.64 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 166.7, 133.9, 131.9, 131.6, 130.3, 127.8, 123.2, 99.0, 80.8, 65.6, 52.1, 31.2. MS (rel int, %) m/z: 218 (0.5), 203 (30.4), 171 (100.0), 129 (35.2). HRMS (APCI-QTOF) m/z: [M + Na]$^+$ calcd for $C_{13}H_{14}O_3Na$ 241.0841; found: 241.0832.

Procedure for the Synthesis of 3-Organyl-4-(organylchalcogenyl)-1*H*-isochromen-1-ones 3a−y. To a 10.0 mL glass tube were added the appropriate methyl 2-(organylethynyl)benzoate **1** (0.25 mmol), diorganyl dichalcogenide **2** (0.15 mmol, 1.2 equiv), Oxone (0.25 mmol, 0.077 g, 1 equiv), and solvent (2.0 mL). The amplitude of the ultrasound waves was fixed at 60%. Then the reaction mixture was sonicated for the time required to consume the starting material **1**. The progress of the reaction was monitored by TLC. After that, the resulting solution was received in water (10.0 mL), and the product was extracted with ethyl acetate (3 × 10.0 mL). The organic layer was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography using silica gel and hexane/ethyl acetate as eluent to afford **3a**−**y**.

Preparation of 3a in Gram Scale. To a 20.0 mL glass tube were added the methyl 2-(phenylethynyl)benzoate **1a** (3.0 mmol, 0.711 g), diphenyl diselenide **2a** (1.8 mmol, 0.565 g, 1.2 equiv), Oxone (3.0 mmol, 0.921 g, 1 equiv), and ethanol (8.0 mL). The amplitude of the ultrasound waves was fixed at 60%. Then the reaction mixture was sonicated for 30 min. After that, the resulting solution was received in water (30.0 mL), and the product was extracted with ethyl acetate (3 × 30.0 mL). The organic layer was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography using silica gel and hexane/ethyl acetate (95:5) as eluent to afford 1.021 g of pure **3a** (yield 90%).

*3-Phenyl-4-(phenylselanyl)-1H-isochromen-1-one (**3a**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.090 g (95%); white solid, mp 134−136 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.27 (dd, J = 7.9 and 1.0 Hz, 1H); 7.98−7.95 (m, 1H); 7.63−7.56 (m, 3H); 7.46−7.42 (m, 1H); 7.36−7.28 (m, 3H); 7.12−7.06 (m, 5H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 159.5, 138.4, 135.3, 134.0, 131.8, 130.1, 129.7, 129.6, 129.5, 128.8, 128.7, 128.2, 127.8, 126.4, 120.8, 104.7. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 295.5. MS (rel int, %) m/z: 378 (24.8), 193 (14.7), 105 (100.0), 77 (19.2).

*3-Phenyl-4-(4-tolylselanyl)-1H-isochromen-1-one (**3b**[7]).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.088 g (90%); white solid, mp 170−173 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.26 (dd, J = 7.9 and 1.0 Hz, 1H); 8.00−7.96 (m, 1H); 7.63−7.57 (m, 3H); 7.45−7.41 (m, 1H); 7.37−7.29 (m, 3H); 7.02−6.99 (m, 2H); 6.92−6.89 (m, 2H); 2.17 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 159.3, 138.5, 136.4, 135.3, 134.0, 130.2, 130.0, 129.7, 129.6, 129.0, 128.6, 128.3, 127.9, 127.7, 120.8, 105.0, 20.9. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 288.6. MS (rel int, %) m/z: 392 (18.2), 287 (10.8), 105 (100.0), 77 (18.8).

*4-(4-Methoxyphenylselanyl)-3-phenyl-1H-isochromen-1-one (**3c**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.095 g (93%); white solid, mp 94−97 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.24 (dd, J = 7.9 and 1.1 Hz, 1H); 8.04−8.01 (m, 1H); 7.64−7.60 (m, 1H); 7.58−7.56 (m, 2H); 7.43−7.39 (m, 1H); 7.36−7.30 (m, 3H); 7.05−7.01 (m, 2H); 6.64−6.60 (m, 2H); 3.62 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 158.9, 158.8, 138.4, 135.2, 134.0, 131.4, 130.0, 129.8, 129.6, 128.5, 128.2, 127.7, 121.3, 120.8, 115.1, 105.9, 55.2. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 279.8. MS (rel int, %) m/z: 408 (27.4), 223 (37.9), 105 (100.0), 77 (28.1). HRMS (APCI-QTOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{17}O_3Se$ 409.0343; found: 409.0338.

*4-(4-Chlorophenylselanyl)-3-phenyl-1H-isochromen-1-one (**3d**[7]).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.093 g (90%); white solid, mp 139−142 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.28 (dd, J = 7.9 and 1.0 Hz, 1H); 7.93−7.90 (m, 1H); 7.65−7.61 (m, 1H); 7.56−7.53 (m, 2H); 7.48−

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

7.44 (m, 1H); 7.37−7.30 (m, 3H); 7.07−7.01 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.5, 159.7, 138.1, 135.4, 133.8, 132.6, 130.2, 130.1, 129.9, 129.8, 129.6, 128.8, 128.0, 127.8, 120.8, 104.6. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 295.9. MS (rel int, %) *m/z*: 412 (9.9), 304 (4.2), 105 (100.0), 77 (23.8).

*4-(4-Fluorophenylselanyl)-3-phenyl-1H-isochromen-1-one (**3e**[7]).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.091 g (92%); white solid, mp 137−140 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.35 (dd, *J* = 7.8 and 1.0 Hz, 1H); 8.07−8.04 (m, 1H); 7.75−7.70 (m, 1H); 7.65−7.62 (m, 2H); 7.56−7.53 (m, 1H); 7.45−7.39 (m, 3H); 7.18−7.13 (m, 2H); 6.91−6.85 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9 (d, $^1J_{C-F}$ = 245.0 Hz), 161.6, 159.4, 138.2, 135.3, 133.9, 131.2 (d, $^3J_{C-F}$ 7.8 Hz), 130.1, 129.8, 129.7, 128.7, 128.0, 127.8, 125.9 (d, $^4J_{C-F}$ 3.3 Hz), 120.8, 116.6 (d, $^2J_{C-F}$ = 21.8 Hz), 105.3. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 289.7. MS (rel int, %) *m/z*: 396 (20.1), 288 (10.6), 105 (100.0), 77 (21.7).

*3-Phenyl-4-[3-(trifluoromethyl)phenylselanyl]-1H-isochromen-1-one (**3f**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.103 g (92%); white solid, mp 81−83 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.37 (dd, *J* = 7.9 and 0.7 Hz, 1H); 8.02−7.98 (m, 1H); 7.75−7.70 (m, 1H); 7.64−7.59 (m, 2H); 7.58−7.52 (m, 1H); 7.47−7.37 (m, 5H); 7.31−7.24 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.4, 160.0, 137.9, 135.5, 133.7, 132.9, 132.0, 131.6 (q, $^2J_{C-F}$ = 32.3 Hz), 130.3, 129.9, 129.8, 129.5, 128.9, 127.9, 127.8, 125.6 (q, $^3J_{C-F}$ = 3.8 Hz), 123.5 (q, $^1J_{C-F}$ = 271.3 Hz), 123.3 (q, $^4J_{C-F}$ = 3.6 Hz), 120.8, 104.3. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 305.1. MS (rel int, %) *m/z*: 446 (36.2), 338 (25.1), 105 (100.0), 77 (33.1). HRMS (APCI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{14}F_3O_2Se$ 447.0111; found: 447.0104.

*4-(Mesitylselanyl)-3-phenyl-1H-isochromen-1-one (**3g**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.096 g (91%); white solid, mp 110−113 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.23 (dd, *J* = 7.8 and 0.9 Hz, 1H); 7.76−7.73 (m, 1H); 7.57−7.53 (m, 1H); 7.42−7.36 (m, 3H); 7.35−7.28 (m, 3H); 6.62 (s, 2H); 2.09 (s, 6H); 2.07 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9, 156.1, 141.0, 138.5, 137.7, 134.8, 134.1, 129.8, 129.7, 129.6, 129.0, 128.3, 128.0, 127.7, 127.2, 120.6, 107.3, 23.6, 20.7. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 210.3. MS (rel int, %) *m/z*: 420 (28.7), 105 (100.0), 77 (19.8). HRMS (APCI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{21}O_2Se$ 421.0707; found: 421.0700.

*4-(Naphthalen-2-ylmethylselanyl)-3-phenyl-1H-isochromen-1-one (**3h**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.091 g (82%); white solid, mp 98−101 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.25 (dd, *J* = 7.7 and 0.8 Hz, 1H); 8.17−8.14 (m, 1H); 7.72−7.64 (m, 2H); 7.48−7.43 (m, 3H); 7.36−7.32 (m, 2H); 7.28−7.22 (m, 1H); 7.13−7.11 (m, 4H); 7.06−7.04 (m, 1H); 6.88−6.85 (m, 1H); 3.80 (s, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 159.3, 138.8, 135.2, 134.8, 133.8, 133.0, 132.3, 129.9, 129.8, 129.5, 128.4, 128.1, 128.0, 127.5, 127.4, 127.3, 127.2, 126.8, 126.2, 125.9, 120.5, 104.8, 32.4. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 251.5. MS (rel int, %) *m/z*: 442 (3.3), 141 (100.0), 105 (2.9). HRMS (APCI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{19}O_2Se$ 443.0550; found: 443.0547.

*4-(Ethylselanyl)-3-phenyl-1H-isochromen-1-one (**3i**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.074 g (90%); yellow solid, mp 120−123 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.36 (dd, *J* = 7.8 and 0.7 Hz, 1H); 8.26−8.23 (m, 1H); 7.85−7.80 (m, 1H); 7.71−7.67 (m, 2H); 7.58−7.54 (m, 1H); 7.46−7.43 (m, 3H); 2.56 (q, *J* = 7.4 Hz, 2H); 1.17 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9, 158.0, 139.0, 135.1, 134.3, 130.1, 129.7, 128.4, 128.1, 127.7, 120.7, 104.8, 22.3, 15.0. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 189.6. MS (rel int, %) *m/z*: 330 (40.9), 193 (100.0), 105 (17.3), 77 (37.0).

*4-(n-Butylselanyl)-3-phenyl-1H-isochromen-1-one (**3j**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.084 g (94%); yellow solid, mp 62−64 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.30−8.26 (m, 1H); 8.20−8.17 (m, 1H); 7.77−7.73 (m, 1H); 7.65−7.60 (m, 2H); 7.51−7.46 (m, 1H); 7.40−7.36 (m, 3H); 2.47 (t, *J* = 7.3 Hz, 2H); 1.32 (quint, *J* = 7.3 Hz, 2H); 1.09 (sext, *J* = 7.3 Hz, 2H); 0.66 (t, *J* = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9, 157.9, 139.0, 135.1, 134.3, 130.1, 129.7, 128.4, 128.1, 127.7, 120.7, 105.1, 31.5, 28.7, 22.5, 13.4. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 156.8. MS (rel int, %) *m/z*: 358 (48.1), 193 (100.0), 105 (69.1), 77 (47.5).

*4-(Phenylselanyl)-1H-isochromen-1-one (**3k**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.067 g (89%); white solid, mp 111−113 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.30 (dd, *J* = 7.9 and 1.0 Hz, 1H); 7.82−7.79 (m, 1H); 7.76 (s, 1H); 7.72−7.67 (m, 1H); 7.54−7.50 (m, 1H); 7.36−7.32 (m, 2H); 7.23−7.18 (m, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.5, 149.8, 136.9, 135.2, 130.2, 130.0, 129.9, 129.4, 129.1, 127.1, 127.0, 121.8, 107.7. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 286.1. MS (rel int, %) *m/z*: 302 (61.4), 165 (72.5), 105 (100.0), 77 (36.5). HRMS (APCI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{11}O_2Se$ 302.9924; found: 302.9921.

*3-(2-Methoxyphenyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3l**).*[5c] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.090 g (88%); white solid, mp 109−111 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.35 (dd, *J* = 7.9 and 1.0 Hz, 1H); 7.97−7.95 (m, 1H); 7.69−7.64 (m, 1H); 7.53−7.49 (m, 1H); 7.43−7.38 (m, 1H); 7.37−7.35 (m, 1H); 7.21−7.18 (m, 2H); 7.15−7.10 (m, 3H); 7.0−6.96 (m, 1H); 6.93−6.90 (m, 1H); 3.71 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.2, 157.2, 157.1, 138.1, 135.1, 131.6, 131.4, 130.8, 129.7, 129.4, 129.1, 128.5, 127.8, 126.3, 123.7, 121.1, 120.0, 110.8, 107.5, 55.3. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 296.7. MS (rel int, %) *m/z*: 408 (34.9), 300 (67.8), 135 (100.0), 77 (46.6).

*3-(4-Methoxyphenyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3m**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.092 g (90%); white solid, mp 155−158 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.34 (dd, *J* = 8.3 and 1.2 Hz, 1H); 8.04−8.0 (m, 1H); 7.70−7.63 (m, 3H); 7.52−7.48 (m, 1H); 7.21−7.13 (m, 5H); 6.92−6.88 (m, 2H); 3.83 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.8, 161.0, 159.5, 138.7, 135.3, 132.0, 131.3, 129.6, 129.5, 128.6, 128.4, 128.1, 126.34, 126.27, 120.6, 113.1, 103.7, 55.3. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 297.0. MS (rel int, %) *m/z*: 408 (31.1), 300 (91.9), 135 (100.0), 77 (21.0).

*3-(4-tert-Butylphenyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3n**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.091 g (84%); brown solid, mp 51−53 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.37−8.33 (m, 1H); 8.04−8.01 (m, 1H); 7.70−7.66 (m, 1H); 7.65−7.61 (m, 2H); 7.53−7.48 (m, 1H); 7.43−7.39 (m, 2H); 7.22−7.14 (m, 5H); 1.33 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.8, 159.6, 153.5, 138.5, 135.3, 132.0, 131.0, 129.6, 129.5, 128.7, 128.5, 128.2, 126.4, 124.7, 120.8, 104.1, 34.8, 31.2. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 294.1. MS (rel int, %) *m/z*: 434 (32.8), 326 (30.7), 161 (100.0), 77 (9.2). HRMS (APCI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{23}O_2Se$ 435.0863; found: 435.0858.

*3-(4-Chlorophenyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3o**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.095 g (92%); white solid, mp 105−108 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.27−8.23 (m, 1H); 8.0−7.94 (m, 1H); 7.63−7.58 (m, 1H); 7.52−7.50 (m, 2H); 7.45−7.41 (m, 1H); 7.27−7.24 (m, 2H); 7.10−7.05 (m, 5H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MH) δ (ppm) = 161.4, 158.2, 138.2, 136.2, 135.4, 132.3, 131.5, 131.0, 129.7, 129.5, 128.9, 128.7, 128.2, 128.0, 126.6, 120.7, 105.1. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 295.0. MS (rel int, %) *m/z*: 412 (25.5), 304 (16.1), 139 (100.0), 111 (14.7).

*3-n-Butyl-4-(phenylselanyl)-1H-isochromen-1-one (**3p**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.076 g (85%); yellow solid, mp 51−54 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31−8.27 (m, 1H); 7.96−7.93 (m, 1H); 7.68−7.63 (m, 1H); 7.49−7.44 (m, 1H); 7.26−7.15 (m, 5H); 3.04 (t, *J* = 7.4 Hz, 2H); 1.69 (quint, *J* = 7.4 Hz, 2H); 1.38 (sext, *J* = 7.4 Hz, 2H); 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 163.8, 162.1, 138.4, 135.2, 131.3, 129.6, 129.4, 128.8, 128.0, 127.3, 126.4,

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

120.4, 104.2, 34.4, 30.1, 22.3, 13.7. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 264.0. MS (rel int, %) m/z: 358 (98.3), 274 (84.9), 159 (86.6), 57 (100.0).

*4-(Phenylselanyl)-3-(trimethylsilyl)-1H-isochromen-1-one (**3q**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.086 g (92%); yellow solid, mp 108−110 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31−8.28 (m, 1H); 7.80−7.77 (m, 1H); 7.63−7.59 (m, 1H); 7.50−7.46 (m, 1H); 7.19−7.12 (m, 5H); 0.42 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 170.2, 162.6, 136.8, 134.9, 131.7, 129.3, 129.0, 128.0, 126.9, 126.2, 121.9, 116.3, −0.5. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 271.1. MS (rel int, %) m/z: 374 (13.3), 359 (11.5), 217 (22.2), 73 (100.0). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}O_2SeSi$ 375.0320; found: 375.0312.

*3-(Hydroxymethyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3r**).* Purified by column chromatography (hexane/ethyl acetate = 80:20); yield 0.069 g (83%); brown oil. We noticed that this product is quite unstable. After purification, the solvent was quickly removed under vacuum and the NMR spectra were collected. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.32−8.29 (m, 1H); 8.03−8.0 (m, 1H); 7.73−7.69 (m, 1H); 7.55−7.50 (m, 1H); 7.31−7.28 (m, 2H); 7.23−7.18 (m, 3H); 4.95 (s, 2H); 2.69 (br s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.4, 159.3, 137.6, 135.5, 129.8, 129.7, 129.6, 129.5, 129.0, 127.7, 127.0, 121.0, 105.7, 62.6. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 252.7. MS (rel int, %) m/z: 332 (87.4), 273 (48.7), 165 (100.0), 77 (36.2). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{13}O_3Se$ 333.0030; found: 333.0030.

*3-(1-Hydroxyethyl)-4-(phenylselanyl)-1H-isochromen-1-one (**3s**).* Purified by column chromatography (hexane/ethyl acetate = 80:20); yield 0.064 g (74%); yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31 (dd, J = 7.9 and 1.0 Hz, 1H); 8.03−8.0 (m, 1H); 7.73−7.69 (m, 1H); 7.54−7.50 (m, 1H); 7.29−7.26 (m, 2H); 7.23−7.18 (m, 3H); 5.67−5.61 (m, 1H); 2.48 (br s, 1H); 1.51 (d, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.7, 161.4, 137.8, 135.4, 130.6, 129.8, 129.6, 129.2, 128.8, 127.8, 126.8, 121.0, 103.8, 67.8, 21.8. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 249.9. MS (rel int, %) m/z: 346 (51.8), 273 (29.2), 193 (67.6), 147 (100.0), 77 (37.8). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}O_3Se$ 347.0186; found: 347.0181.

*3-(2-Ethoxypropan-2-yl)-4-(phenylselanyl)-1H-isochromen-1-one (**3t**).* Purified by column chromatography (hexane/ethyl acetate = 90:10); yield 0.089 g (92%); yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.69−7.66 (m, 1H); 7.44−7.40 (m, 1H); 7.36−7.32 (m, 1H); 7.24−7.15 (m, 6H); 4.20 (q, J = 7.1 Hz, 2H); 2.25 (s, 3H); 2.18 (s, 3H); 1.20 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 195.3, 167.8, 154.3, 140.2, 131.7, 131.4, 130.7, 130.6, 130.4, 129.01, 128.99, 128.5, 126.5, 124.6, 61.4, 26.5, 23.5, 13.9. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 357.3. MS (rel int, %) m/z: 388 (2.6), 231 (100.0), 149 (74.2), 77 (18.2). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{21}O_3Se$ 389.0656; found: 389.0652.

*3-(2-Methoxypropan-2-yl)-4-(phenylselanyl)-1H-isochromen-1-one (**3u**).* Purified by column chromatography (hexane/ethyl acetate = 90:10); yield 0.083 g (89%); yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.68−7.65 (m, 1H); 7.43−7.39 (m, 1H); 7.36−7.32 (m, 1H); 7.23−7.19 (m, 3H); 7.17−7.13 (m, 3H); 3.62 (s, 3H); 2.25 (s, 3H); 2.17 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 195.1, 168.2, 154.0, 140.1, 131.2, 131.1, 130.7, 130.6, 130.4, 129.0, 128.9, 128.3, 126.5, 124.6, 52.2, 26.3, 23.3. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 357.8. MS (rel int, %) m/z: 374 (3.0), 217 (100.0), 163 (59.1), 77 (19.7). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}O_3Se$ 375.0499; found: 375.0494.

*3-Phenyl-4-(phenyltellanyl)-1H-isochromen-1-one (**3v**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.090 g (84%); white solid, mp 135−137 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31 (dd, J = 7.9 and 1.1 Hz, 1H); 8.10−8.05 (m, 1H); 7.67−7.63 (m, 1H); 7.56−7.52 (m, 2H); 7.49−7.45 (m, 1H); 7.43−7.33 (m, 5H); 7.16−7.06 (m, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.1, 161.3, 139.7, 136.3, 135.4, 135.0, 132.7, 130.0, 129.9, 129.64, 129.6, 128.7, 127.7, 127.5, 120.5, 115.5, 93.7. $^{125}Te\{^1H\}$ NMR ($CDCl_3$, 127 MHz) δ (ppm) = 508.5. MS (rel int, %) m/z: 429 (M^+ + 1, 0.1), 312 (7.6), 91 (100.0).

*3-Phenyl-4-(4-tolyltellanyl)-1H-isochromen-1-one (**3w**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.091 g (82%); yellow solid, mp 114−117 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31 (dd, J = 7.9 and 1.0 Hz, 1H); 8.13−8.10 (m, 1H); 7.70−7.66 (m, 1H); 7.56−7.53 (m, 2H); 7.51−7.47 (m, 1H); 7.43−7.37 (m, 3H); 7.29−7.25 (m, 2H); 6.95−6.91 (m, 2H); 2.26 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.1, 161.1, 139.8, 137.6, 136.3, 135.5, 135.3, 132.8, 130.5, 129.94, 129.9, 129.6, 128.6, 127.7, 120.4, 111.1, 93.8, 21.0. $^{125}Te\{^1H\}$ NMR ($CDCl_3$, 127 MHz) δ (ppm) = 497.9. MS (rel int, %) m/z: 442 (40.8), 312 (62.0), 105 (100.0), 77 (45.1). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}O_2Te$ 443.0291; found: 443.0286.

*4-(4-Methoxyphenyltellanyl)-3-phenyl-1H-isochromen-1-one (**3x**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.089 g (78%); yellow solid, mp 130−132 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31 (dd, J = 7.8 and 0.8 Hz, 1H); 8.17−8.14 (m, 1H); 7.73−7.69 (m, 1H); 7.55−7.52 (m, 2H); 7.51−7.48 (m, 1H); 7.45−7.39 (m, 3H); 7.36−7.32 (m, 2H); 6.68−6.65 (m, 2H); 3.72 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.2, 160.7, 159.7, 139.9, 138.1, 136.3, 135.3, 132.7, 130.0, 129.9, 129.6, 128.6, 127.7, 120.5, 115.5, 104.0, 94.3, 55.1. $^{125}Te\{^1H\}$ NMR ($CDCl_3$, 127 MHz) δ (ppm) = 491.9. MS (rel int, %) m/z: 458 (36.5), 328 (100.0), 105 (92.2), 77 (67.1). HRMS (APCI-QTOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}O_3Te$; 459.0240, found: 459.0239.

*3-Phenyl-1H-isochromen-1-one (**3y**).*[7] Purified by column chromatography (hexane/ethyl acetate = 95:5); yield from $(4\text{-}ClC_6H_4Te)_2$: 0.047 g (84%) and yield from $(C_4H_9Te)_2$: 0.050 g (90%);[7] white solid, mp 87−90 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.31−8.28 (m, 1H); 7.89−7.85 (m, 2H); 7.73−7.69 (m, 1H); 7.51−7.40 (m, 5H); 6.94 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.3, 153.6, 137.5, 134.8, 131.9, 129.9, 129.6, 128.8, 128.1, 125.9, 125.2, 120.5, 101.8. MS (rel int, %) m/z: 222 (100.0), 194 (79.1), 105 (27.0), 77 (46.0).

Procedure for the Synthesis of 4a−c. To a 10.0 mL glass tube were added the appropriate 1,3-diyne **1o−p** (0.25 mmol), dialkyl diselenide **2** (0.300 mmol, 2.4 equiv), Oxone (0.500 mmol, 0.154 g, 2.0 equiv), and solvent (2.0 mL). The amplitude of the ultrasound waves was fixed at 60%. Then the reaction mixture was sonicated for the time required to consume the starting material **1**. The progress of the reaction was monitored by gas chromatography. After that, the resulting solution was received in water (10.0 mL), and the product was extracted with ethyl acetate (3 × 10.0 mL). The organic layer was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography using silica gel and hexane/ethyl acetate as eluent to afford **4a−c**.

*3-(Ethylselanyl)-2-phenyl-5H-selenopheno[3,2-c]isochromen-5-one (**4a**).*[16] Purified by column chromatography (hexane/ethyl acetate = 96:4); yield 0.087 g (80%); yellow solid, mp 155−158 °C (lit.[16] 155−157 °C). ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.39−8.35 (m, 1H); 7.74 (td, J = 7.7 and 1.1 Hz, 1H); 7.62−7.58 (m, 2H); 7.52−7.42 (m, 5H); 2.93 (q, J = 7.5 Hz, 2H); 1.29 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.8, 152.5, 148.7, 135.6, 135.33, 135.26, 130.9, 129.6, 128.9, 128.5, 128.0, 123.6, 119.2, 117.9, 113.9, 21.9, 15.4. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 536.8, 227.1. MS (rel int, %) m/z: 434 (100.0), 406 (29.7), 326 (61.7), 297 (54.4), 207 (27.9).

*3-(Butylselanyl)-2-phenyl-5H-selenopheno[3,2-c]isochromen-5-one (**4b**).*[16] Purified by column chromatography (hexane/ethyl acetate = 96:4); yield 0.102 g (88%); yellow solid, mp 80−82 °C (lit.[16] 80−82 °C). ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.37−834 (m, 1H); 7.74 (td, J = 7.7 and 1.3 Hz, 1H); 7.62−7.58 (m, 2H); 7.52−7.41 (m, 5H); 2.89 (t, J = 7.4 Hz, 2H); 1.52 (quint, J = 7.4 Hz, 2H); 1.28 (sext, J = 7.4 Hz, 2H); 0.79 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.8, 152.5, 148.6, 135.6, 135.3, 135.2, 130.9, 129.6, 128.9, 128.4, 128.0, 123.6, 119.2, 117.9, 114.2, 32.1, 28.1, 22.6, 13.4. $^{77}Se\{^1H\}$ NMR ($CDCl_3$, 76 MHz) δ (ppm) = 536.2, 194.9. MS (rel int, %) m/z: 462 (79.0), 406 (89.6), 326 (100.0), 189 (72.6), 89 (25.5).

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

*2-Butyl-3-(butylselanyl)-5H-selenopheno[3,2-c]isochromen-5-one (**4c**).*[16] Purified by column chromatography (hexane/ethyl acetate = 96:4); yield 0.087 g (79%); yellow solid, mp 60−63 °C (lit.[16] 60−62 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.32−8.28 (m, 1H); 7.68 (td, J = 7.9 and 1.3 Hz, 1H); 7.45−7.41 (m, 1H); 7.38−7.35 (m, 1H); 3.11 (t, J = 7.6 Hz, 2H); 2.91 (t, J = 7.4 Hz, 2H); 1.69 (quint, J = 7.3 Hz, 2H); 1.60 (quint, J = 7.3 Hz, 2H); 1.50−1.36 (m, 4H); 0.98 (t, J = 7.3 Hz, 3H); 0.88 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.0, 154.5, 152.0, 135.5, 135.1, 130.7, 127.4, 123.1, 118.1, 115.4, 114.4, 34.4, 32.8, 32.4, 28.0, 22.6, 22.2, 13.8, 13.5. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 521.8, 168.7. MS (rel int, %) m/z: 442 (70.6), 385 (43.4), 343 (62.3), 305 (37.4), 263 (100.0).

Procedure for the Synthesis of 1*H*-isochromene-1-thione 5a−d. Compounds **5** were prepared according to a published procedure, with minor changes.[23] In a 10 mL glass vial equipped with small magnetic stirring bar was added the mixture of Lawesson's reagent (0.13 mmol, 0.053 g, 1.04 equiv) and the respective **3** (0.25 mmol). Then the reaction mixture was irradiated in a focused microwave reactor (CEM) at 140 °C (temperature was measured with an IR sensor on the outer surface of the reaction vial) for 15 min, using an irradiation power of 200 W and pressure of 100 psi (the ramp temperature rate was 40 s). The progress of the reaction was monitored by TLC. The reaction mixture was received in water (10.0 mL), and the product was extracted with ethyl acetate (3x 10.0 mL). The organic layer was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography using silica gel and hexane/ethyl acetate as eluent to afford **5a−d**.

*3-Phenyl-4-(phenylselanyl)-1H-isochromene-1-thione (**5a**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.097 g (98%); yellow solid, mp 140−142 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.79−8.74 (m, 1H); 8.08−8.04 (m, 1H); 7.71−7.66 (m, 3H); 7.51−7.39 (m, 4H); 7.19−7.14 (m, 5H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 199.9, 161.9, 135.6, 133.6, 133.1, 133.0, 131.5, 130.34, 130.3, 129.9, 129.5, 129.1, 128.4, 127.9, 126.7, 108.1. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 295.3. MS (rel int, %) m/z: 394 (63.4), 237 (100.0), 105 (60.4), 77 (57.8). HRMS (APCI-QTOF) m/z: $[M]^+$ calcd for $C_{21}H_{14}OSSe$ 393.9931; found: 393.9932.

*4-(4-Methoxyphenylselanyl)-3-phenyl-1H-isochromene-1-thione (**5b**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.105 g (99%); yellow solid, mp 111−113 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.76−8.71 (m, 1H); 8.16−8.12 (m, 1H); 7.73−7.68 (m, 3H); 7.49−7.40 (m, 4H); 7.11 (d, J = 8.6 Hz, 2H); 6.70 (d, J = 8.6 Hz, 2H); 3.70 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 199.9, 161.3, 159.0, 135.4, 133.6, 133.04, 133.0, 131.8, 130.25, 130.2, 130.0, 129.3, 128.4, 127.8, 121.0, 115.1, 109.4, 55.2. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 282.5. MS (rel int, %) m/z: 424 (18.3), 165 (30.5), 105 (100.0), 77 (42.6). HRMS (APCI-QTOF) m/z: $[M]^+$ calcd for $C_{22}H_{16}O_2SSe$ 424.0036; found: 424.0032.

*4-(4-Chlorophenylselanyl)-3-phenyl-1H-isochromene-1-thione (**5c**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.098 g (92%); yellow solid, mp 123−125 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.78−8.75 (m, 1H); 8.03−8.0 (m, 1H); 7.74−7.70 (m, 1H); 7.68−7.65 (m, 2H); 7.54−7.50 (m, 1H); 7.47−7.40 (m, 3H); 7.16−7.08 (m, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 199.7, 162.0, 135.7, 133.4, 133.2, 132.8, 132.6, 130.5, 130.3, 129.8, 129.7, 129.6, 128.2, 128.0, 107.9. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 295.3. MS (rel int, %) m/z: 428 (32.2), 237 (100), 165 (56.8), 105 (97.5). HRMS (APCI-QTOF) m/z: $[M]^+$ calcd for $C_{21}H_{13}ClOSSe$ 427.9541; found: 427.9556.

*4-(n-Butylselanyl)-3-phenyl-1H-isochromene-1-thione (**5d**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.084 g (90%); yellow solid, mp 66−68 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.80−8.77 (m, 1H); 8.29−8.26 (m, 1H); 7.85−7.81 (m, 1H); 7.75−7.73 (m, 2H); 7.57−7.52 (m, 1H); 7.48−7.45 (m, 3H); 2.56 (t, J = 7.2 Hz, 2H); 1.40 (quint, J = 7.2 Hz, 2H); 1.17 (sext, J = 7.2 Hz, 2H); 0.74 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 200.1, 160.6, 135.4, 133.9, 133.6, 133.2, 130.3, 130.1, 130.0, 129.3, 128.4, 127.8, 125.4, 31.6, 29.0, 22.5, 13.4. ^{77}Se{^{1}H} NMR ($CDCl_3$, 76 MHz) δ (ppm) = 164.1. MS (rel int, %) m/z: 374 (25.1), 165 (33.1), 105 (100.0), 77 (72.7). HRMS (APCI-QTOF) m/z: $[M]^+$ calcd for $C_{19}H_{18}OSSe$ 374.0244; found: 374.0260.

*Ethyl 2-(1,2-Diethoxy-2-phenylvinyl)benzoate (**6**).* Purified by column chromatography (hexane/ethyl acetate = 95:5); yield 0.021 g (25%); white solid, mp 70−73 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 8.05−8.02 (m, 2H); 7.75−7.72 (m, 1H); 7.41−7.37 (m, 3H); 7.35−7.32 (m, 1H); 7.31−7.26 (m, 2H); 4.30 (q, J = 7.2 Hz, 2H); 3.47−3.41 (m, 4H); 1.34 (t, J = 7.2 Hz, 3H); 1.19 (t, J = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) = 193.9, 169.7, 135.7, 135.4, 132.7, 132.3, 129.8, 129.7, 128.6, 128.4, 128.2, 127.9, 102.0, 61.2, 58.4, 14.9, 14.0. MS (rel int, %) m/z: 311 (M^+-C_2H_5, 5.3), 251 (68.1), 149 (100.0), 105 (19.4), 77 (20.6). HRMS (APCI-QTOF) m/z: $[M\text{-}C_2H_5]^+$ calcd for $C_{21}H_{24}O_4$ 311.1283; found: 311.1282.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00271.

Copies of ^{1}H, ^{13}C{^{1}H}, ^{77}Se{^{1}H}, and ^{125}Te{^{1}H} spectra of all the synthesized compounds (PDF)

FAIR data, including the primary NMR FID files, for compounds **3a−y**, **4a−c**, **5a−d**, and **6** (ZIP)

■ AUTHOR INFORMATION

Corresponding Author

Gelson Perin − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil;* orcid.org/0000-0003-0359-0811; Email: gelson_perin@ufpel.edu.br

Authors

Helen A. Goulart − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil*

José S. S. Neto − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil*

Angelita M. Barcellos − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil*

Krigor B. Silva − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil*

Maiara C. de Moraes − *Laboratory of Biotechnology of Natural and Synthetic Products, Universidade de Caxias do Sul, 95070-560 Caxias do Sul, RS, Brazil*

Raquel G. Jacob − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil*

Eder J. Lenardão − *Laboratório de Síntese Orgânica Limpa − LASOL, CCQFA, Universidade Federal de Pelotas − UFPel, 96010-900 Pelotas, RS, Brazil;* orcid.org/0000-0001-7920-3289

Thiago Barcellos − *Laboratory of Biotechnology of Natural and Synthetic Products, Universidade de Caxias do Sul, 95070-560 Caxias do Sul, RS, Brazil;* orcid.org/0000-0001-9872-4602

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00271

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001. FAPERGS (PqG 19/2551-0001867-3), CNPq and FINEP are acknowledged for financial support. CNPq is also acknowledged for Fellowships to R.G.J., E.J.L., and G.P.

■ REFERENCES

(1) (a) Pal, S.; Chatare, V.; Pal, M. Isocoumarin and Its Derivatives: An Overview on Their Synthesis and Applications. *Curr. Org. Chem.* **2011**, *15*, 782−800. (b) Saddiqa, A.; Usman, M.; Çakmak, O. Isocoumarins and 3,4-Dihydroisocoumarins, Amazing Natural Products: a Review. *Turk. J. Chem.* **2017**, *41*, 153−178. (c) Saikia, P.; Gogoi, S. Isocoumarins: General Aspects and Recent Advances in Their Synthesis. *Adv. Synth. Catal.* **2018**, *360*, 2063−2075.

(2) (a) Saeed, A. Isocoumarins, Miraculous Natural Products Blessed with Diverse Pharmacological Activities. *Eur. J. Med. Chem.* **2016**, *116*, 290−317. (b) Hussain, H.; Green, I. R. A Patent Review of Two Fruitful Decades (1997−2016) of Isocoumarin Research. *Expert Opin. Ther. Pat.* **2017**, *27*, 1267−1275.

(3) (a) Ninomiya, M.; Garud, D. R.; Koketsu, M. Biologically Significant Selenium-Containing Heterocycles. *Coord. Chem. Rev.* **2011**, *255*, 2968−2990. (b) Ruberte, A. C.; Sanmartin, C.; Aydillo, C.; Sharma, A. K.; Plano, D. Development and Therapeutic Potential of Selenazo Compounds. *J. Med. Chem.* **2020**, *63*, 1473−1489. (c) Banerjee, B.; Koketsu, M. Recent developments in the synthesis of biologically relevant selenium-containing scaffolds. *Coord. Chem. Rev.* **2017**, *339*, 104−127. (d) Ranu, B. C.; Banerjee, B. *Organoselenium Chemistry*; De Gruyter GmbH: Berlin, 2020. DOI: 10.1515/9783110625110. (e) Penteado, F.; Peglow, T. J.; Silva, M. S.; Perin, G.; Lenardão, E. J. Greening the synthesis of selenium-containing heterocycles: Recent efforts and advances. *Curr. Opin. Green Sustain. Chem.* **2020**, *26*, 100372.

(4) (a) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. Organoselenium and Organotellurium Compounds: Toxicology and Pharmacology. *Chem. Rev.* **2004**, *104*, 6255−6286. (b) Santi, C. *Organoselenium Chemistry: Between Synthesis and Biochemistry*; Santi, C., Ed.; Bentham Science Publishers, 2014. DOI: 10.2174/9781608058389114010 1. (c) Lenardão, E. J.; Santi, C.; Sancineto, L. *New Frontiers in Organoselenium Compounds*; Springer International Publishing: Cham, Switzerland, 2018. DOI: 10.1007/978-3-319-92405-2.

(5) (a) Neto, J. S. S.; Back, D. F.; Zeni, G. Nucleophilic Cyclization of *o*-Alkynylbenzamides Promoted by Iron(III) Chloride and Diorganyl Dichalcogenides: Synthesis of 4-Organochalcogenyl-1*H*-isochromen-1-imines. *Eur. J. Org. Chem.* **2015**, *2015*, 1583−1590. (b) Wilkins, L. C.; Günther, B. A. R.; Walther, M.; Lawson, J. R.; Wirth, T.; Melen, R. L. Contrasting Frustrated Lewis Pair Reactivity with Selenium and Boron-Based Lewis Acids. *Angew. Chem., Int. Ed.* **2016**, *55*, 11292−11295. (c) Mehta, S.; Waldo, J. P.; Larock, R. C. Competition Studies in Alkyne Electrophilic Cyclization Reactions. *J. Org. Chem.* **2009**, *74*, 1141−1147. (d) Jin, G.-Q.; Gao, W.-X.; Zhou, Y.-B.; Liu, M.-C.; Wu, H.-Y. Synthesis of selenated isochromenones by $AgNO_3$-catalyzed three-component reaction of alkynylaryl esters, selenium powder and $ArB(OH)_2$. *RSC Adv.* **2020**, *10*, 30439−30442.

(6) Yao, T.; Larock, R. C. Synthesis of Isocoumarins and α-Pyrones via Electrophilic Cyclization. *J. Org. Chem.* **2003**, *68*, 5936−5942.

(7) Sperança, A.; Godoi, B.; Pinton, S.; Back, D. F.; Menezes, P. H.; Zeni, G. Regioselective Synthesis of Isochromenones by Iron(III)/PhSeSePh-Mediated Cyclization of 2-Alkynylaryl Esters. *J. Org. Chem.* **2011**, *76*, 6789−6797.

(8) Xing, L.; Zhang, Y.; Li, B.; Du, Y. *In Situ* Formation of RSCl/ArSeCl and Their Application to the Synthesis of 4-Chalcogenylisocumarins/Pyrones from *o*-(1-Alkynyl)benzoates and (*Z*)-2-Alken-4-ynoates. *Org. Lett.* **2019**, *21*, 3620−3624.

(9) Hussain, H.; Green, I. R.; Ahmed, I. Journey Describing Applications of Oxone in Synthetic Chemistry. *Chem. Rev.* **2013**, *113*, 3329−3371.

(10) (a) Zheng, Y.; Liu, M.; Qiu, G.; Xie, W.; Wu, J. Synthesis of 3-(Bromomethylene)isobenzofuran-1(3*H*)-ones through Regioselective 5-*Exo*-*Dig* Bromocyclization of 2-Alkynylbenzoic Acids. *Tetrahedron* **2019**, *75*, 1663−1668. (b) Uyanik, M.; Kato, T.; Sahara, N.; Katade, O.; Ishihara, K. High-Performance Ammonium Hypoiodite/Oxone Catalysis for Enantioselective Oxidative Dearomatization of Arenols. *ACS Catal.* **2019**, *9*, 11619−11626. (c) Uyanik, M.; Sahara, N.; Katade, O.; Ishihara, K. Chemoselective Oxidative Spiroetherification and Spiroamination of Arenols Using I^+/Oxone Catalysis. *Org. Lett.* **2020**, *22*, 560−564. (d) Wang, Y.-C.; Liu, J.-B.; Zhou, H.; Xie, W.; Rojsitthisak, P.; Qiu, G. *Ortho*-Hydroxylative Ipso-Cyclization of *N*-Arylpropiolamide. *J. Org. Chem.* **2020**, *85*, 1906−1914.

(11) Wang, Y.-H.; Qiu, G.; Zhou, H.; Xie, W.; Liu, J.-B. Regioselective Cyclization of 2-Alkynylbenzoic Acid in Water for the Synthesis of Isocoumarin. *Tetrahedron* **2019**, *75*, 3850−3855.

(12) (a) Perin, G.; Santoni, P.; Barcellos, A. M.; Nobre, P. C.; Jacob, R. G.; Lenardão, E. J.; Santi, C. Selenomethoxylation of Alkenes Promoted by Oxone®. *Eur. J. Org. Chem.* **2018**, *2018*, 1224−1229. (b) Perin, G.; Araujo, D. R.; Nobre, P. C.; Lenardão, E. J.; Jacob, R. G.; Silva, M. S.; Roehrs, J. A. Ultrasound-promoted Synthesis of 2-Organoselanyl-naphthalenes Using Oxone® in Aqueous Medium as an Oxidizing Agent. *PeerJ* **2018**, *6*, No. e4706. (c) Perin, G.; Duarte, L. F. B.; Neto, J. S. S.; Silva, M. S.; Alves, D. Alternative Metal-Free Synthesis of Diorganoyl Selenides and Tellurides Mediated by Oxone®. *Synlett* **2018**, *29*, 1479−1484. (d) Perin, G.; Soares, L. K.; Hellwig, P. S.; Silva, M. S.; Neto, J. S. S.; Roehrs, J. A.; Barcellos, T.; Lenardão, E. J. Synthesis of 2,3-Bis-Organochalcogenyl-benzo[*b*]-chalcogenophenes Promoted by Oxone®. *New J. Chem.* **2019**, *43*, 6323−6331.

(13) Perin, G.; Nobre, P. C.; Mailahn, D. H.; Silva, M. S.; Barcellos, T.; Jacob, R. G.; Lenardão, E. J.; Santi, C.; Roehrs, J. A. Synthesis of 4-Organoselanyl-1*H*-pyrazoles: Oxone®-Mediated Electrophilic Cyclization of α,β-Alkynyl Hydrazones by Using Diorganyl Diselenides. *Synthesis* **2019**, *51*, 2293−2304.

(14) Araujo, D. R.; Lima, Y. R.; Barcellos, A. M.; Silva, M. S.; Jacob, R. G.; Lenardão, E. J.; Bagnoli, L.; Santi, C.; Perin, G. Ultrasound-Promoted Radical Synthesis of 5-Methylselanyl-4,5-dihydroisoxazoles. *Eur. J. Org. Chem.* **2020**, *2020*, 586−592.

(15) Araujo, D. R.; Goulart, H. A.; Barcellos, A. M.; Cargnelutti, R.; Lenardão, E. J.; Perin, G. Oxone-Promoted Synthesis of 4-(Chalcogenyl)isoquinoline-*N*-oxides from Alkynylbenzaldoximes and Diorganyl Dichalcogenides. *J. Org. Chem.* **2021**, *86*, 1721−1729.

(16) Goulart, H. A.; Neto, J. S. S.; Barcellos, A. M.; Barcellos, T.; Silva, M. S.; Alves, D.; Jacob, R. G.; Lenardão, E. J.; Perin, G. Synthesis of 5*H*-Selenopheno[3,2-*c*]isochromen-5-ones Promoted by Dialkyl Diselenides and Oxone®. *Adv. Synth. Catal.* **2019**, *361*, 3403−3411.

(17) (a) Grieser, F.; Choi, P.-K.; Enomoto, N.; Harada, H.; Okitsu, K.; Yasui, K. *Sonochemistry and the Acoustic Bubble*; Elsevier: New York, 2015. (b) Mojtahedi, M. M.; Abaee, M. S. In *Ultrasound Applications in Synthetic Organic Chemistry*; Chen, D., Sharma, S. K., Mudhoo, A., Eds.; CRC Press: New York, 2012; pp 281−322. (c) Banerjee, B. Recent developments on ultrasound assisted catalyst-free organic synthesis. *Ultrason. Sonochem.* **2017**, *35*, 1−14. (d) Banerjee, B. Recent developments on ultrasound-assisted one-pot multicomponent synthesis of biologically relevant heterocycles. *Ultrason. Sonochem.* **2017**, *35*, 15−35. (e) Banerjee, B. Recent Developments on Ultrasound-Assisted Synthesis of Bioactive *N*-Heterocycles at Ambient Temperature. *Aust. J. Chem.* **2017**, *70*, 872−888.

(18) Mancuso, R.; Pomelli, C. C.; Malafronte, F.; Maner, A.; Marino, N.; Chiappe, C.; Gabriele, B. Divergent Syntheses of Iodinated Isobenzofuranones and Isochromenones by Iodolactonization of 2-Alkynylbenzoic Acids in Ionic Liquids. *Org. Biomol. Chem.* **2017**, *15*, 4831−4841.

(19) Sanz, R.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. Metal-Free Catalytic Nucleophilic Substitution of Propargylic

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX

Alcohols. *Eur. J. Org. Chem.* **2006**, *2006*, 1383−1386. (b) Lukyanov, S. M.; Koblik, A. V.; Muradyan, L. A. Alkynylcarbenium Ions and Related Unsaturated Cations. *Russ. Chem. Rev.* **1998**, *67*, 817−856.
(20) Soares, L. K.; Barcellos, A. M.; Neto, J. S. S.; Alves, D.; Lenardão, E. J.; Rosati, O.; Santi, C.; Perin, G. Dichalcogenides/Oxone®-Mediated Cyclization of (*Z*)-Chalcogenoenynes under Ultrasound Irradiation. *Chemistry Select* **2020**, *5*, 9813−9819.
(21) (a) Mahmoud, A. B. A.; Kirsch, G.; Peagle, E. Biologically Active Selenophenes and Benzo[*b*]selenophenes. *Curr. Org. Synth.* **2017**, *14*, 1091−1101. (b) Tavadyan, L. A.; Manukyan, Z. H.; Harutyunyan, L. H.; Musayelyan, M. V.; Sahakyan, A. D.; Tonikyan, H. G. Antioxidant Properties of Selenophene, Thiophene and Their Aminocarbonitrile Derivatives. *Antioxidants* **2017**, *6*, 22. (c) Elsherbini, M.; Hamama, W. S.; Zoorob, H. H. An Easy Synthetic Approach to Construct Some Ebselen Analogues and Benzo[*b*]selenophene Derivatives: Their Antioxidant and Cytotoxic Assessment. *J. Heterocycl. Chem.* **2018**, *55*, 1645−1650. (d) Hellwig, P. S.; Peglow, T. J.; Penteado, F.; Bagnoli, L.; Perin, G.; Lenardão, E. J. Recent Advances in the Synthesis of Selenophenes and Their Derivatives. *Molecules* **2020**, *25*, 5907.
(22) (a) Manivel, P.; Roopan, S. M.; Kumar, D. P.; Khan, F. N. Isocoumarin Thioanalogues as Potential Antibacterial Agents. *Phosphorus, Sulfur Silicon Relat. Elem.* **2009**, *184*, 2576−2582. (b) Manivel, P.; Sharma, A.; Maiyalagan, T.; Rajeswari, M. R.; Khan, F. N. Synthesis and Antiproliferative Activity of Some 1*H*-Isochromen-1-ones and Their Thio Analogues. *Phosphorus, Sulfur Silicon Relat. Elem.* **2010**, *185*, 387−393. (c) Delgado Espinosa, Z. Y.; Saeed, A.; Mahmood, S.; Echeverria, G. A.; Piro, O. E.; Erben, M. F. The Effect of Chalcogen Substitution on the Structure and Spectroscopy of 4,7-Dimethyl-2*H*-chromen-2-one/thione Analogues. *New J. Chem.* **2017**, *41*, 5770−5783.
(23) Saeed, A.; Ashraf, Z. Synthesis of Some 3-Aryl-1*H*-isochromene-1-thiones. *J. Heterocycl. Chem.* **2008**, *45*, 679−682.
(24) Gianni, J.; Pirovano, V.; Abbiati, G. Silver Triflate/*p*-TSA co-catalysed Synthesis of 3-Substituted Isocoumarins from 2-Alkynylbenzoates. *Org. Biomol. Chem.* **2018**, *16*, 3213−3219.

https://doi.org/10.1021/acs.joc.1c00271
J. Org. Chem. XXXX, XXX, XXX−XXX