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## Accepted Article

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Promoted by Dialkyl Diselenides and Oxone®

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# Synthesis of 5*H*-Selenopheno[3,2-*c*]isochromen-5-ones Promoted by Dialkyl Diselenides and Oxone<sup>®</sup>

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**Abstract.** We describe here for the first time the synthesis of isochromenones fused to selenophenes. 5*H*-Selenopheno[3,2-*c*]isochromen-5-ones were obtained through a double intramolecular cyclization of methyl 2-(organyl-1,3-diynyl)benzoate promoted by electrophilic species of selenium generated *in situ* by the reaction of dialkyl diselenides with Oxone<sup>®</sup>, using ethanol as solvent.

The reactions were conducted satisfactorily under mild conditions, using a range of 1,3-diynes and dialkyl diselenides as substrates. A total of sixteen unprecedented 5*H*-selenopheno[3,2-*c*]isochromen-5-ones were selectively obtained in moderate to good yields (40-86%) under reflux in an open flask and in short reaction times (1.0-2.5 h).

**Keywords:** electrophilic cyclization; dialkyl diselenides; heterocycles; isochromenones; Oxone<sup>®</sup>; selenophenes.

## Introduction

Organochalcogen compounds are considered an important class of molecules in organic synthesis, due to their special structural characteristics and unique reactivity. These compounds have been applied as versatile synthetic intermediates in the synthesis of different target molecules,<sup>[1]</sup> allowing selective transformations,<sup>[2]</sup> and as catalysts in asymmetric synthesis.<sup>[3]</sup> They also have shown interesting biological activities, including antiparasitic,<sup>[4]</sup> antioxidant,<sup>[5]</sup> anticholinesterase,<sup>[6]</sup> antinociceptive<sup>[7]</sup> and anxiolytic effects.<sup>[8]</sup>

In particular, selenophenes are an interesting class of bioactive compounds, presenting anticonvulsant,<sup>[9]</sup> antioxidant,<sup>[10]</sup> hepatoprotective,<sup>[11]</sup> antinociceptive<sup>[12]</sup> and antitumor<sup>[13]</sup> activities. Besides that, these compounds are used to obtain new materials, like semiconductors<sup>[14]</sup> and solar cells.<sup>[15]</sup> Regarding the preparation of selenophenes, the most efficient methods reported in the literature involve the addition of either nucleophilic or electrophilic selenium species to appropriate acyclic precursors containing the  $\pi$ -system, followed by an intramolecular cyclization.<sup>[16]</sup>

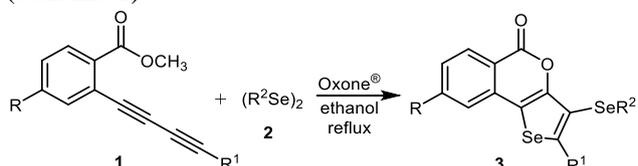
On the other hand, isochromenones represent an important class of naturally occurring lactones. A large number of these compounds are found in nature as component of insect pheromones and venoms, and as part of the structure of secondary metabolites of plants, bacteria and fungi.<sup>[17]</sup> The reasons for the

interest in isochromenone derivatives are due to the variety of pharmacological activities reported for these compounds, including antifungal,<sup>[18]</sup> antimalarial,<sup>[19]</sup> antibacterial,<sup>[20]</sup> anticancer,<sup>[21]</sup> anti-inflammatory,<sup>[22]</sup> and antioxidant<sup>[23]</sup> ones.

These aspects have stimulated the studies towards the synthesis of isochromenone derivatives.<sup>[24]</sup> The traditional approaches include transition-metal-catalyzed reactions<sup>[24c]</sup> and intramolecular electrophilic cyclizations.<sup>[25]</sup> However, there are few protocols describing the synthesis of isochromenones decorated with organochalcogen groups.<sup>[26]</sup> In 2003, Yao and Larock<sup>[26a]</sup> described the synthesis of selenium- and sulfur-containing isochromenones *via* the electrophilic cyclization of 2-alkynylaryl esters with PhSeCl and 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>SeCl in DCM at room temperature. In 2011, Zeni and co-workers<sup>[26b]</sup> reported a FeCl<sub>3</sub>-mediated cyclization of 2-alkynylaryl esters in the presence of diorganyl dichalcogenides in DCM at room temperature to prepare 4-chalcogen-substituted isochromenones. In 2012, Zhou and co-workers<sup>[26c]</sup> reported the synthesis of sulfur-containing isochromenones by the FeCl<sub>3</sub>-promoted intermolecular sulfoesterification of 2-alkynylaryl esters with diorganyl disulfides in DCE at 80 °C.

In parallel, the use of Oxone<sup>®</sup> as an oxidant in organic synthesis has been widely explored because of its low cost, stability, water solubility and low toxicity.<sup>[27]</sup> Oxone<sup>®</sup> is commercially available as a triple salt (2KHSO<sub>5</sub>.KHSO<sub>4</sub>.K<sub>2</sub>SO<sub>4</sub>) and contains about 50% of active oxidant per mol (anion

peroxymonosulfate,  $\text{HSO}_5^-$ ).<sup>[27]</sup> Recently, we and others have explored the combination of Oxone<sup>®</sup> with organoselenium chemistry. Oxone<sup>®</sup> was used in the reaction of selenomethoxylation of alkenes,<sup>[28]</sup> in the carbocyclization of alkynols to obtain 2-organoselanyl-naphthalenes,<sup>[29]</sup> in the synthesis of diorganyl selenides and tellurides,<sup>[30]</sup> in the oxidation of vinyl selenides to selenones<sup>[31]</sup> and in the arylselenylation of imidazo[2,1-*b*]thiazoles, imidazo[1,2-*a*]pyridines and 1*H*-pyrazoles.<sup>[32]</sup> Considering the importance of selenophenes and isochromenone derivatives, and our interest in the synthesis of organochalcogen compounds, we describe herein the first synthesis of isochromenones fused to selenophenes. The developed protocol involves a simple, practical, and selective tandem cyclization of 1,3-diynes **1** with dialkyl diselenides **2** to obtain 5*H*-selenopheno[3,2-*c*]isochromen-5-ones **3**. The electrophilic species of selenium (ES) was generated *in situ*, through the reaction of dialkyl diselenides with Oxone<sup>®</sup> using ethanol as the solvent (Scheme 1).



**Scheme 1.** Synthesis of 5*H*-selenopheno[3,2-*c*]isochromen-5-ones **3**.

## Results and Discussion

Methyl 2-(phenylbuta-1,3-diyne-1-yl)benzoate **1a** (0.25 mmol) and dibutyl diselenide **2a** were chosen as standard starting materials to perform the optimization studies in the reaction with Oxone<sup>®</sup> under argon atmosphere (Table 1). We examined the effect of the nature of the solvent, the amounts of diselenide and Oxone<sup>®</sup> and the temperature.

In our first experiment, 1,3-diyne **1a** (0.25 mmol) and Oxone<sup>®</sup> (1.0 mmol) were added to a solution of dibutyl diselenide **2a** (0.44 mmol) in 3.0 mL of ethanol. The resulting yellowish mixture was stirred at reflux for 12 h to deliver the desired product **3a** in 85% yield (Table 1, entry 1). Aiming to improve the reaction yield and reduce the time, the reaction was performed under ultrasonic irradiation (US) at 60% of amplitude and, unfortunately, the expected product **3a** was obtained in only 20% yield after 1 h (Table 1, entry 2). By setting the conventional heating method (oil bath), a range of solvents were tested, such as AcOEt,  $\text{CH}_3\text{CN}$ , DMF, 1,4-dioxane and DCM, as well as, green solvents like glycerol and PEG-400 (Table 1, entries 3-9).

In the reactions using AcOEt,  $\text{CH}_3\text{CN}$ , 1,4-dioxane and PEG-400, the isochromenone **3a** was obtained in lower yields compared to the reaction performed in ethanol (Table 1, entry 1 vs 3, 4, 6 and 9). When the reaction was carried out using DMF, a complex mixture of products was obtained (Table 1, entry 5).

No product **3a** was obtained in the reactions using DCM and glycerol as solvent, as indicated by GC/MS analysis, and the starting materials were recovered (Table 1, entries 7-8).

To our satisfaction, the expected product **3a** could be isolated in 82% yield under refluxing ethanol in only 2.5 h (Table 1, entry 1 vs 10). The effect of using different quantities of Oxone<sup>®</sup> was evaluated and a little influence was observed when larger amounts were used (1.25, 0.75 and 0.69 mmol), with the corresponding product **3a** being isolated in 83%, 82% and 86% yields, respectively (Table 1, entries 11-13). However, the yields have decreased when the amount of Oxone<sup>®</sup> was reduced to 0.63 and 0.50 mmol, and **3a** was obtained in 77% and 69% yields, respectively (Table 1, entries 14-15). A similar behavior was observed regarding the amounts of dibutyl diselenide **2a**, with the better result (82% yield) being obtained using 0.38 mmol (1.5 equiv) (Table 1, entries 16-18).

**Table 1.** Optimization of the conditions to prepare **3a**.<sup>[a]</sup>

#	<b>2a</b> (mmol)	Oxone <sup>®</sup> (mmol)	Solvent	T (°C)	Time (h)	Yield (%) <sup>[b]</sup>
1	0.44	1.0	EtOH	78	12	85
2	0.44	1.0	EtOH	-	1	20 <sup>c</sup>
3	0.44	1.0	AcOEt	77	12	70
4	0.44	1.0	$\text{CH}_3\text{CN}$	82	12	65
5	0.44	1.0	DMF	153	12	— <sup>[d]</sup>
6	0.44	1.0	1,4-dioxane	101	12	30
7	0.44	1.0	DCM	40	12	nr <sup>[e]</sup>
8	0.44	1.0	glycerol	100	12	nr <sup>[e]</sup>
9	0.44	1.0	PEG-400	100	12	20
10	0.44	1.0	EtOH	78	2.5	82
11	0.44	1.25	EtOH	78	2.5	83
12	0.44	0.75	EtOH	78	2.5	82
13	0.44	0.69	EtOH	78	2.5	86
14	0.44	0.63	EtOH	78	2.5	77
15	0.44	0.50	EtOH	78	2.5	69
16	0.50	0.69	EtOH	78	2.5	82
17	0.38	0.69	EtOH	78	2.5	82
18	0.25	0.69	EtOH	78	2.5	35
19	0.38	0.69	EtOH	50	12	75
20	0.38	0.69	EtOH	25	12	14
21	0.38	0.69	EtOH	78	2.5	80 <sup>[f]</sup>
22	0.38	0.69	EtOH	78	2.5	86 <sup>[g]</sup>

<sup>[a]</sup> A mixture of 1,3-diyne **1a** (0.25 mmol), Oxone<sup>®</sup> and dibutyl diselenide **2a** in the solvent (3.0 mL) under argon atmosphere was stirred at the temperature and time indicated; <sup>[b]</sup> Yields after purification by column chromatography; <sup>[c]</sup> Reaction performed under ultrasonic irradiation (US) at 60% of amplitude; <sup>[d]</sup> A complex mixture of products was obtained; <sup>[e]</sup> The product was not formed and the starting material was recovered; <sup>[f]</sup> Oxone<sup>®</sup> was added to a solution of dibutyl diselenide **2a** in ethanol (3.0 mL) at room temperature, under argon atmosphere. After 15 min, 1,3-diyne **1a** (0.25 mmol) was added. The resulting mixture was refluxed for 2.5 h; <sup>[g]</sup> Reaction performed under air atmosphere. nr = no reaction.

Next, we investigated the possibility of performing the reaction at lower temperatures, i.e., 50 °C and

25 °C. The expected product **3a** was obtained, however in lower yields, of 75% and 14%, respectively (Table 1, entries 19-20). Additionally, in an attempt to improve the yield of **3a**, we performed two steps, one-pot experiment. Firstly, Oxone® was added to a solution of dibutyl diselenide **2a** in ethanol and the mixture was stirred at room temperature for 15 min to generate the electrophilic selenium species. Following, the 1,3-diyne **1a** was added and the reaction mixture was refluxed for 2.5 h, affording the desired product **3a** in 80% yield (Table 1, entry 21). Finally, the reaction was carried out under an air atmosphere (open flask) and a similar yield of **3a** was obtained (Table 1, entry 22 vs 17).

Thus, from the results presented on Table 1, the best reaction conditions to prepare compound **3a** involve the stirring of a mixture of 1,3-diyne **1a** (0.25 mmol), Oxone® (0.69 mmol) and diselenide **2a** (0.38 mmol) in refluxing EtOH (3.0 mL) for 2.5 h in an open flask (Table 1, entry 22).

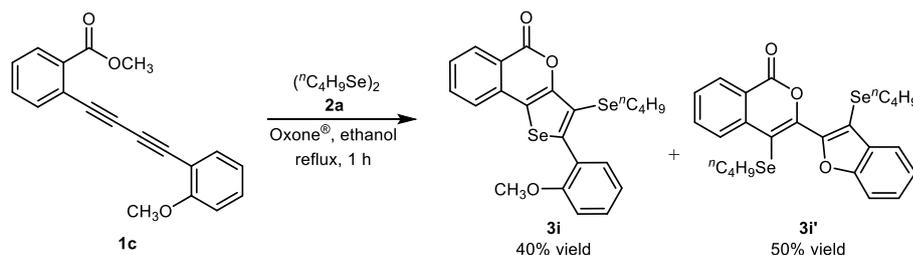
### Scope of the Reaction

With the optimal conditions in hand, we decided to explore the scope and limitations of the reaction using different 1,3-diyne **1** and various dialkyl dichalcogenides **2** (Table 2). Besides dibutyl diselenide **2a**, our protocol was suitable to dialkyl diselenides **2b** ( $R^2 = C_2H_5$ ) and **2c** ( $R^2 = nC_8H_{17}$ ), which reacted with **1a** to give the expected isochromenones **3b** and **3c** in 77% and 82% yields, respectively (Table 2, compounds **3b** and **3c**). No product was observed starting from dibenzyl diselenide **2d** or bis(2-naphthylmethyl) diselenide **2e**, even after 3 h of reaction, as indicated by GC/MS analysis and the starting materials were recovered (Table 2, compounds **3d** and **3e**). No product was observed when diphenyl diselenide was used as substrate in the reaction with **1a**, and a complex mixture was obtained in the end of the reaction. Also, we examined the reaction between 1,3-diyne **1a** and dibutyl telluride or dimethyl disulfide. Unfortunately, in both cases the desired products **3f** and **3g** were not obtained, even after 3 h of reaction (Table 2).

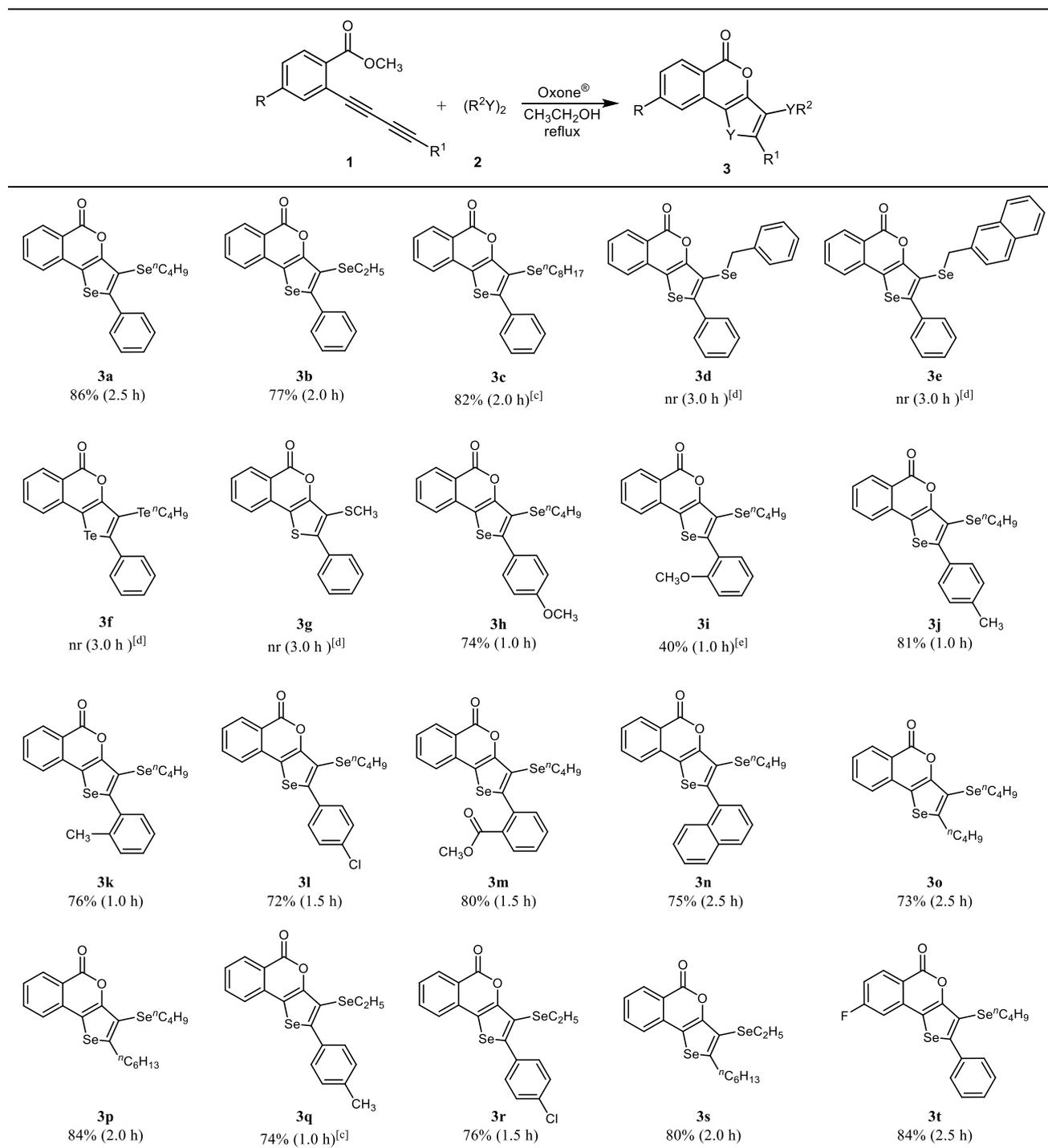
Regarding the 1,3-diyne counterpart **1**, both electron-releasing and electron-withdrawing groups in the pendent phenyl ring of **1** were tolerated in the reaction with dibutyl diselenide **2a**. There is no a remarkable electronic effect caused by the introduction of substituents in the *para*-position, and

compounds **3h** ( $R^1 = 4-CH_3OC_6H_4$ ), **3j** ( $R^1 = 4-CH_3C_6H_4$ ) and **3l** ( $R^1 = 4-ClC_6H_4$ ) were isolated in 74%, 81% and 72% yields, respectively (Table 2, compounds **3h**, **3j** and **3l**). Surprisingly, when 1,3-diyne **1c** ( $R^1 = 2-CH_3OC_6H_4$ ) was used as substrate in the reaction with **2a**, the expected 5*H*-selenopheno[3,2-*c*]isochromen-5-one **3i** was isolated in only 40% yield (Table 2, compound **3i**). This can be explained by two competing reactions of the intermediate **8c** formed in the first step of the reaction (see Scheme 7, for the reaction mechanism): the intramolecular *Se*-cyclization and the *O*-cyclization. As a consequence, the benzofuran derivative **3i'** was formed in 50% yield as a co-product of the reaction (Scheme 2).<sup>[25a]</sup> The steric hindered *ortho*-substituted diynes **1e** ( $R^1 = 2-CH_3C_6H_4$ ), **1g** ( $R^1 = 2-CH_3OCOC_6H_4$ ) and **1h** ( $R^1 = 1-naphthyl$ ) satisfactorily reacted with **2a** to afford the respective products **3k**, **3m** and **3n** in 76%, 80% and 75% yields, respectively (Table 2, compounds **3k**, **3m** and **3n**). Interestingly, when using the dimer **1g**, the double intramolecular *O*-cyclization product was not formed. Alkyl-substituted 1,3-diyne **1i** and **1j** were good substrates for the reaction with **2a**, giving the respective products **3o** and **3p** in 73% and 84% yield, under the optimal conditions (Table 2, compounds **3o** and **3p**). The scope of products was extended further by the reaction of diethyl diselenide **2b** ( $R^2 = C_2H_5$ ) with 1,3-diyne **1d**, **1f** and **1j**. In all cases the reaction proceeded smoothly, giving the corresponding isochromenones **3q**, **3r** and **3s** in 74%, 76% and 80% yields, respectively (Table 2, compounds **3q**, **3r** and **3s**). Finally, the 1,3-diyne tri-substituted on the ring of the ester group **1k** was investigated in the reaction with dibutyl diselenide **2a**, giving the expected product **3t** in 84% yield after 2.5 h.

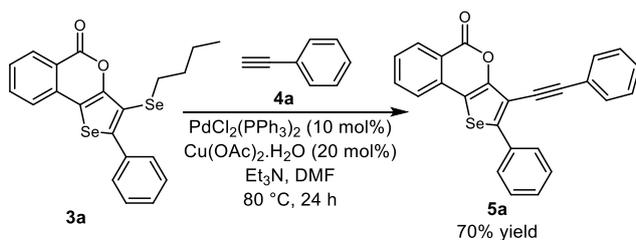
The synthetic potential of this new class of compounds was demonstrated using 5*H*-selenopheno[3,2-*c*]isochromen-5-one **3a**, which was subjected to a Sonogashira-type cross-coupling reaction.<sup>[33]</sup> The reaction of **3a** (0.25 mmol) with phenylacetylene **4a** (1.0 mmol) in the presence of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (10 mol%), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (20 mol%), and Et<sub>3</sub>N (0.25 mmol) in DMF (3.0 mL) for 24 h at 80 °C gave the product **5a** in 70% yield (Scheme 3).



**Scheme 2.** Selenocyclization competition reaction.

**Table 2.** Scope of the reaction to prepare compounds **3**.<sup>[a,b]</sup>

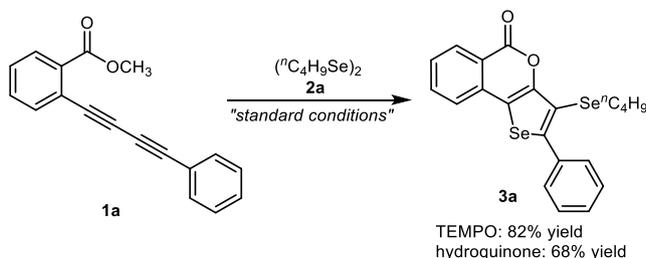
<sup>[a]</sup> A mixture of 1,3-diyne **1a-k** (0.25 mmol), Oxone<sup>®</sup> (0.69 mmol) and diorganyl dichalcogenides **2** (0.38 mmol) in EtOH (3.0 mL) was stirred under air atmosphere and reflux. The progress of the reaction was monitored by gas chromatography. <sup>[b]</sup> Yields after purification by column chromatography. <sup>[c]</sup> Products **3c** and **3q** are quite unstable. After purification, the solvent was quickly removed under vacuum and the NMR spectra were collected. <sup>[d]</sup> No product was detected and the starting materials were recovered. <sup>[e]</sup> Benzofuran **3i'** (50% yield) was isolated as a co-product. nr = no reaction.



**Scheme 3.** Sonogashira cross-coupling reaction.

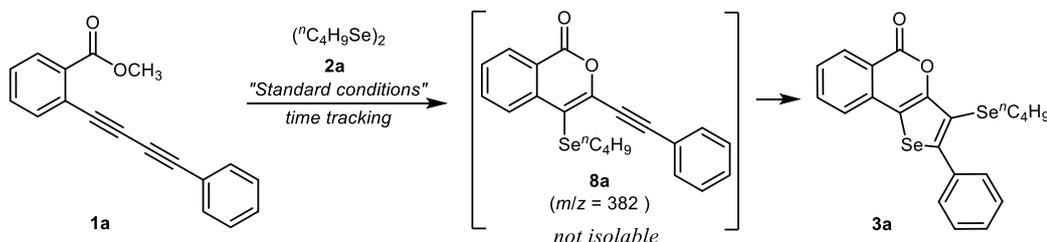
### Mechanism Discussion

After the synthesis of compounds **3**, we performed a series of control experiments to collect evidences to understand the mechanism of this process. Firstly, the reaction was conducted in the presence of 2 equiv of the radical inhibitors 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) and benzene-1,4-diol (hydroquinone). In these experiments, the product **3a** was formed in 82% yield using TEMPO and in 68% yield using hydroquinone. These findings suggest that a radical pathway is not involved in the reaction (Scheme 4).



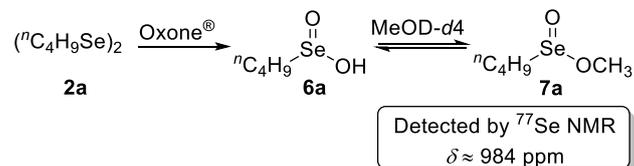
**Scheme 4.** Reactions in the presence of 2 equiv of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) or benzene-1,4-diol (hydroquinone).

Turning our attention to the identity of the active electrophilic selenium species involved in the reaction, we have collected the  $^{77}\text{Se}$  NMR spectrum of the reaction between Oxone<sup>®</sup> and dibutyl diselenide **2a** in an NMR tube, using MeOD-*d*4 as the solvent. It was observed a signal at 984 ppm (Figure S59), which is due to methyl butane-1-seleninate **7a**,<sup>34</sup> formed from the reaction between <sup>n</sup>butylseleninic acid **6a** and MeOD-*d*4 (Scheme 5).<sup>34</sup>



**Scheme 6.** Formation of the mono-cyclized intermediate **8a**.

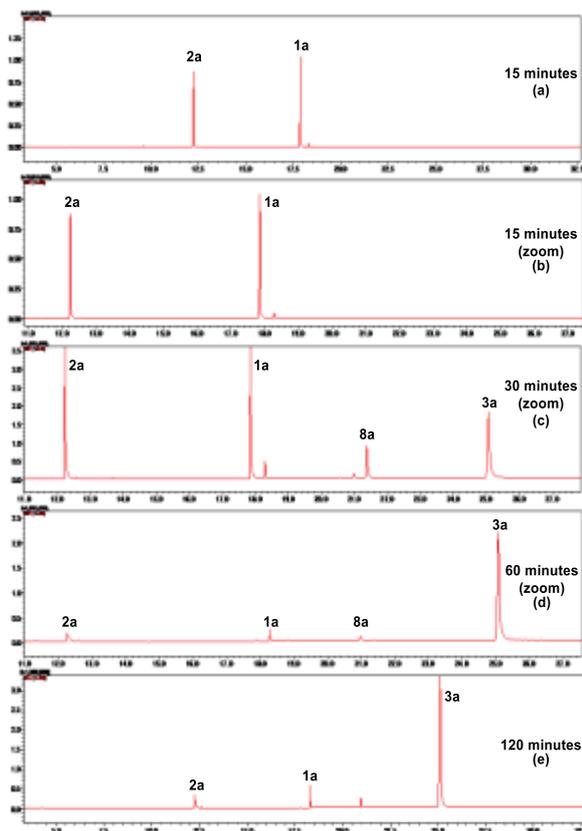
The formation of <sup>n</sup>butylseleninic acid **6a** is a result of the overoxidation of dibutyl diselenide **2a** by Oxone<sup>®</sup> and it could pass by the intermediates  $^n\text{C}_4\text{H}_9\text{SeOSO}_3^-$  (**I**) and  $^n\text{C}_4\text{H}_9\text{SeOH}$  (**II**) (See Scheme 7 for a plausible mechanism).



**Scheme 5.** Formation of methyl butane-1-seleninate **7a**.

All attempts to isolate the intermediate 4-<sup>n</sup>butylselenanyl isochromen-1-one intermediate **8a**, formed in the first step of the reaction between the 1,3-diyne **1a** and diselenide **2a**, were unsuccessful, once compound **8a** was inseparable from the product **3a** (Scheme 6). To obtain more information to support a plausible mechanism for the reaction of **1a** with **2a** in the presence of Oxone<sup>®</sup>, the reaction was monitored by GC/MS. Aliquots of the reaction mixture were collected, pre-treated by a “micro work-up” and injected into the GC/MS spectrometer. This experiment was carried out under the optimal conditions and the aliquots were collected at 15, 30, 60 and 120 min (Figure 1). After 15 min of reaction, only starting materials **1a** and **2a** were present [Figures 1(a) and 1(b)]. After 30 min, we observed a partial consumption of the starting materials, with the appearance of a peak at 21.38 min, which mass and fragmentation correspond to the intermediate **8a** [Figure 1(c)]. At this stage of the reaction, the amount of the product **3a** is around the triple of **8a**, indicating that the formation of **3a** from **8a** is fast [Figure 1(c)]. After 60 min, product **3a** is the major component of the mixture [Figure 1(d)], and after 120 min the starting materials **1a** and **2a** were almost totally consumed [Figure 1(e)].

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**Figure 1.** GC/MS studies monitoring a time reaction for product formation. Chromatogram of the mixture at (a): 15 min. (b): 15 min (zoom). (c): 30 min (zoom). (d): 60 min (zoom). (e): 120 min.

Based on the control experiments and in the literature,<sup>34-36</sup> a plausible mechanism for the reaction of **1a** with **2a** promoted by Oxone<sup>®</sup> is presented in Scheme 7. Firstly, dibutyl diselenide **2a** reacts with Oxone<sup>®</sup> to form two intermediates: <sup>124</sup>C<sub>4</sub>H<sub>9</sub>SeOSO<sub>3</sub><sup>-</sup> (**I**) and <sup>124</sup>C<sub>4</sub>H<sub>9</sub>SeOH (**II**) (Scheme 7, *path a*).<sup>35</sup> The species (**II**) can react with H<sup>+</sup> through the reaction medium, leading to <sup>124</sup>C<sub>4</sub>H<sub>9</sub>SeOH<sub>2</sub><sup>+</sup> (**V**). The intermediates **I** and **V** are most probably the active electrophiles in the reaction with substrate **1a**.<sup>36</sup> The reaction of **1a** with **I** and **V** leading to the cyclic intermediate **VI**, releasing HSO<sub>4</sub><sup>-</sup> and H<sub>2</sub>O to the medium. The displacement of the methyl group from **VI** by a nucleophile (HSO<sub>4</sub><sup>-</sup> from previous step and SO<sub>4</sub><sup>2-</sup> of Oxone<sup>®</sup>), affords the intermediate **8a**. Following, **8a** reacts in the same way with **I** and **V** to give the fused-selenophene cation intermediate **VII**. The displacement of the <sup>124</sup>butyl group from the selenium cation affords the expected product **3a**.

## Conclusion

In resume, 5*H*-selenopheno[3,2-*c*]isochromen-5-ones were prepared for the first time, by the reaction between methyl 2-(organylbuta-1,3-diyne-1-yl)benzoates and dialkyl diselenides using Oxone<sup>®</sup> as oxidant. This method involves a selective, sequential

intramolecular cyclization of 1,3-diynes promoted by electrophilic species of organoselenium, generated *in situ* by the oxidative cleavage of the Se-Se bond of dialkyl diselenides by Oxone<sup>®</sup>. The protocol is versatile and was successfully applied to dialkyl diselenides with open chains containing 2, 4 and 8 carbon atoms and a range of 1,3-diynes. Control experiments, GC/MS and <sup>77</sup>Se NMR analysis gave insights on the reaction intermediates involved in the reaction mechanism.

## Experimental Section

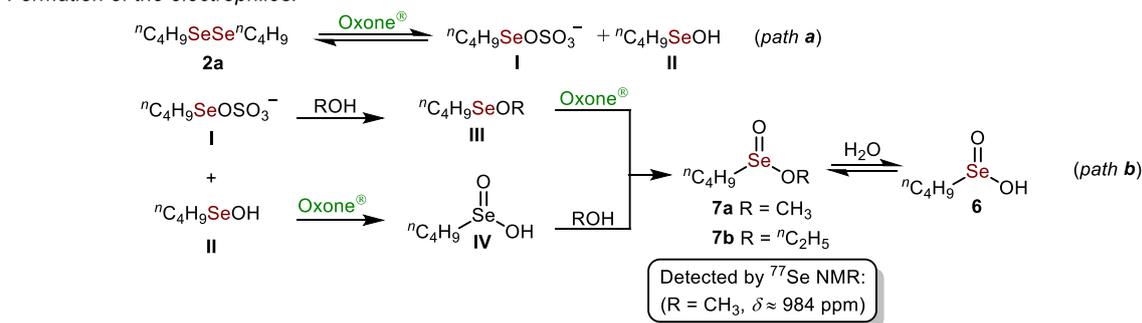
### Materials and methods

The reactions were monitored by gas chromatography or TLC carried out on Merck silica gel (60 F<sub>254</sub>) by using UV light as visualization agent and the mixture between 5% of vanillin in 10% of H<sub>2</sub>SO<sub>4</sub> under heating conditions as developing agents. Merck silica gel (particle size 0.040-0.063 mm) was used to flash chromatography. High-resolution mass spectra (HRMS) were recorded in positive ion mode (ESI) using a Q-TOF spectrometer. Low-resolution mass spectra (MS) were measured on a Shimadzu GC-MS-QP2010 mass spectrometer. Hydrogen nuclear magnetic resonance spectra (<sup>1</sup>H NMR) were obtained at 400 MHz spectrometer. The spectra were recorded in CDCl<sub>3</sub> solutions. The chemical shifts ( $\delta$ ) are reported in ppm, referenced to tetramethylsilane (TMS) as the internal pattern. Coupling constants (*J*) are reported in Hertz. Carbon-13 nuclear magnetic resonance spectra (<sup>13</sup>C NMR) were obtained at 100 MHz spectrometer. 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), ddd (double double doublet), td (triple doublet) and m (multiplet). Melting point (m.p.) values were measured in a Marte PFD III instrument with a 0.1 °C precision. Oxone<sup>®</sup> was purchased from Sigma-Aldrich. Compounds **1a-k** were prepared according to a procedure described in SI.

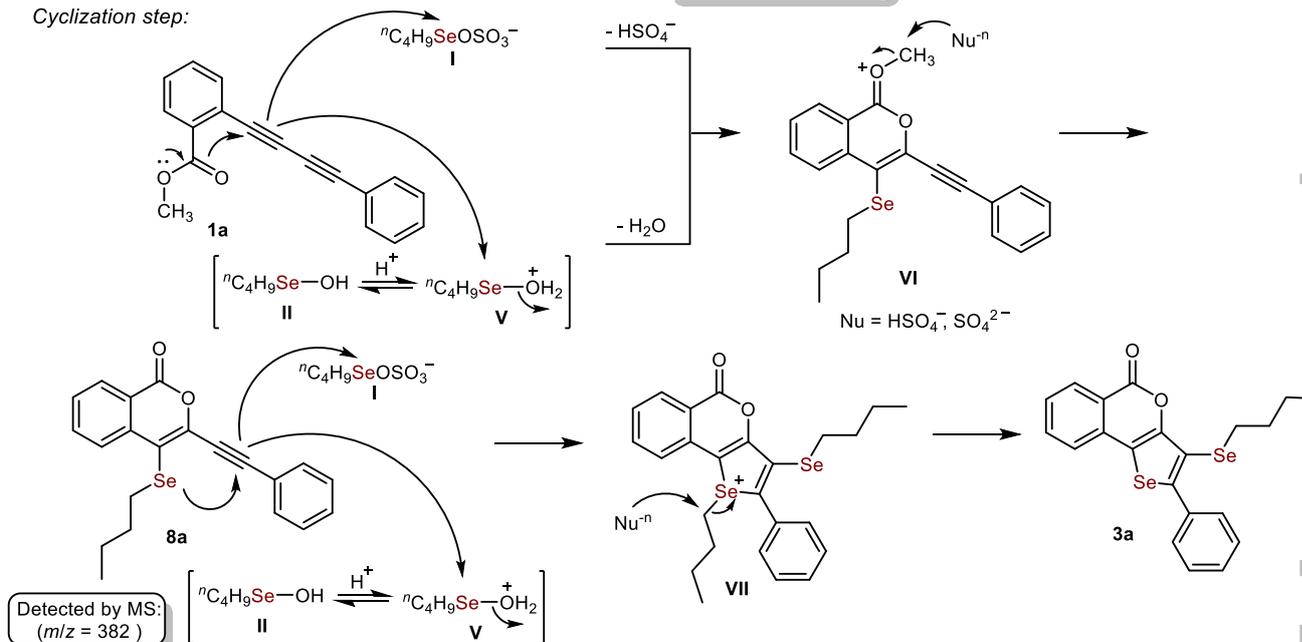
### General procedure for the synthesis of **3**

To a 25.0 mL two-neck round-bottomed flask containing a solution of the appropriate dialkyl diselenide **2a-c** (0.38 mmol) in ethanol (3.0 mL), 1,3-diyne **1a-k** (0.25 mmol) and Oxone<sup>®</sup> (0.69 mmol, 0.211 g) were added under air atmosphere. The resulting mixture was refluxed for the time indicated in Table 2. The progress of the reaction was monitored by gas chromatography. After this time, the resulting solution was received in water (10.0 mL) and the aqueous phase was extracted with ethyl acetate (3x 10.0 mL). The organic layer was separated, dried with MgSO<sub>4</sub> and concentrated under vacuum. The residue was purified by column chromatography using silica gel 60Å (0.060-0.200 mm) and hexane/ethyl acetate (96:04) as eluent to afford **3** (40-86% yield).

Formation of the electrophiles:



Cyclization step:



Scheme 7. Proposed mechanism for the synthesis of **3a**.

### 3-(*n*-Butylselanyl)-2-phenyl-5*H*-selenopheno[3,2-

**c]isochromen-5-one (3a):** Yield: 0.099 g (86%); yellow solid, m.p: 80-82 °C.  ${}^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.34 (ddd,  $J = 8.0, 1.3$  and  $0.6$  Hz, 1H); 7.74-7.70 (m, 1H); 7.60-7.58 (m, 2H); 7.50-7.48 (m, 1H); 7.47-7.41 (m, 4H); 2.89 (t,  $J = 7.4$  Hz, 2H); 1.52 (quint,  $J = 7.4$  Hz, 2H); 1.27 (sext,  $J = 7.4$  Hz, 2H); 0.79 (t,  $J = 7.4$  Hz, 3H).  ${}^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.7, 152.5, 148.5, 135.5, 135.3, 135.2, 130.8, 129.6, 128.8, 128.4, 127.9, 123.5, 119.1, 117.9, 114.1, 32.1, 28.0, 22.5, 13.4. MS (rel. int., %)  $m/z$ : 462 (43.0), 406 (47.8), 326 (51.3), 281 (27.9), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for C<sub>21</sub>H<sub>18</sub>O<sub>2</sub>Se<sub>2</sub> [M+H]<sup>+</sup>: 462.9716, found: 462.9710.

### 3-(Ethylselanyl)-2-phenyl-5*H*-selenopheno[3,2-

**c]isochromen-5-one (3b):** Yield: 0.084 g (77%); yellow solid, m.p: 155-157 °C.  ${}^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.34 (ddd,  $J = 8.0, 1.3$  and  $0.6$  Hz, 1H); 7.74-7.70 (m, 1H); 7.60-7.57 (m, 2H); 7.50-7.41 (m, 5H); 2.92 (q,  $J = 7.5$  Hz, 2H); 1.28 (t,  $J = 7.5$  Hz, 3H).  ${}^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.7, 152.5, 148.6, 135.5, 135.2, 135.1, 130.8, 129.6, 128.9, 128.4, 128.0, 123.5, 119.1, 117.9, 113.9, 21.8, 15.4. MS (rel. int., %)  $m/z$ : 434 (100.0), 406 (29.0), 326 (56.3), 297 (46.8), 207 (47.6). HRMS

(ESI-QTOF) Calculated mass for C<sub>19</sub>H<sub>14</sub>O<sub>2</sub>Se<sub>2</sub> [M+H]<sup>+</sup>: 434.9403, found: 434.9407.

### 3-(*n*-Octylselanyl)-2-phenyl-5*H*-selenopheno[3,2-

**c]isochromen-5-one (3c):** Yield: 0.106 g (82%); yellow oil.  ${}^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.37-8.33 (m, 1H); 7.74-7.70 (m, 1H); 7.61-7.57 (m, 2H); 7.51-7.48 (m, 1H); 7.47-7.41 (m, 4H); 2.88 (t,  $J = 7.4$  Hz, 2H); 1.52 (quint,  $J = 7.4$  Hz, 2H); 1.27-1.15 (m, 10H); 0.83 (t,  $J = 7.2$  Hz, 3H).  ${}^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.7, 152.5, 148.6, 135.6, 135.3, 135.2, 130.8, 129.6, 128.8, 128.4, 127.9, 123.5, 119.1, 117.9, 114.1, 31.7, 30.0, 29.4, 29.0, 28.9, 28.4, 22.6, 14.0. MS (rel. int., %)  $m/z$ : 518 (17.2), 406 (32.8), 326 (25.5), 281 (40.8), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for C<sub>25</sub>H<sub>26</sub>O<sub>2</sub>Se<sub>2</sub> [M+H]<sup>+</sup>: 519.0341, found: 519.0341.

### 3-(*n*-Butylselanyl)-2-(4-methoxyphenyl)-5*H*-

**selenopheno[3,2-c]isochromen-5-one (3h):** Yield: 0.091 g (74%); yellow solid, m.p: 95-98 °C.  ${}^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.36-8.33 (m, 1H); 7.71 (td,  $J = 7.8$  and  $1.3$  Hz, 1H); 7.54 (d,  $J = 8.8$  Hz, 2H); 7.49-7.42 (m, 2H); 6.97 (d,  $J = 8.8$  Hz, 2H); 3.87 (s, 3H); 2.89 (t,  $J = 7.4$  Hz, 2H); 1.52 (quint,  $J = 7.4$  Hz, 2H); 1.28 (sext,  $J = 7.4$  Hz, 2H); 0.80 (t,  $J = 7.4$  Hz, 3H).  ${}^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.8, 160.1, 152.5, 148.7, 135.4, 135.2, 130.9, 130.8, 128.0, 127.8, 123.5, 119.1, 117.2, 113.8, 113.3, 55.3,

32.1, 28.0, 22.6, 13.4. MS (rel. int., %)  $m/z$ : 492 (38.9), 434 (23.1), 356 (50.4), 281 (36.3), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{22}H_{20}O_3Se_2$   $[M+H]^+$ : 492.9821, found: 492.9828.

**3-(<sup>n</sup>Butylselanyl)-2-(2-methoxyphenyl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3i):** Yield: 0.049 g (40%); yellow solid, m.p: 86-89 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.31-8.27 (m, 1H); 7.67-7.62 (m, 1H); 7.43-7.31 (m, 4H); 6.99-6.91 (m, 2H); 3.78 (s, 3H); 2.80 (t,  $J = 7.4$  Hz, 2H); 1.43 (quint,  $J = 7.4$  Hz, 2H); 1.18 (sext,  $J = 7.4$  Hz, 2H); 0.72 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 162.0, 156.6, 152.0, 144.1, 135.6, 135.1, 131.7, 130.8, 130.6, 127.8, 124.3, 123.5, 120.3, 119.1, 118.3, 116.5, 111.0, 55.5, 32.2, 27.3, 22.6, 13.5. MS (rel. int., %)  $m/z$ : 492 (46.9), 434 (12.6), 356 (59.8), 281 (32.9), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{22}H_{20}O_3Se_2$   $[M+H]^+$ : 492.9821, found: 492.9824.

**3-(<sup>n</sup>Butylselanyl)-4-(3-<sup>n</sup>butylselanylbenzofuran-2-yl)-1H-isochromen-1-one (3i')**: Yield: 0.067 g (50%); yellow oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.41-8.38 (m, 1H); 8.28-8.26 (m, 1H); 7.89-7.84 (m, 1H); 7.74-7.72 (m, 1H); 7.65-7.61 (m, 1H); 7.57-7.54 (m, 1H); 7.44-7.40 (m, 1H); 7.38-7.34 (m, 1H); 2.84 (t,  $J = 7.4$  Hz, 2H); 2.63 (t,  $J = 7.4$  Hz, 2H); 1.61-1.54 (m, 2H); 1.49-1.42 (m, 2H); 1.37-1.27 (m, 2H); 1.23-1.14 (m, 2H); 0.80 (t,  $J = 7.4$  Hz, 3H); 0.74 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.2, 154.6, 150.5, 148.0, 137.9, 135.2, 130.3, 130.0, 129.4, 128.7, 126.3, 123.5, 121.7, 121.6, 111.8, 111.1, 109.2, 32.5, 31.8, 29.3, 28.3, 22.6, 22.5, 13.4, 13.3. MS (rel. int., %)  $m/z$ : 534 (15.2), 397 (16.8), 340 (100.0), 207 (34.5). HRMS (ESI-QTOF) Calculated mass for  $C_{25}H_{26}O_3Se_2$   $[M+H]^+$ : 535.0291, found: 535.0292.

**3-(<sup>n</sup>Butylselanyl)-2-(4-tolyl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3j):** Yield: 0.096 g (81%); yellow solid, m.p: 102-104 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.37-8.34 (m, 1H); 7.75-7.70 (m, 1H); 7.51-7.44 (m, 4H); 7.27-7.24 (m, 2H); 2.90 (t,  $J = 7.4$  Hz, 2H); 2.41 (s, 3H); 1.53 (quint,  $J = 7.4$  Hz, 2H); 1.28 (sext,  $J = 7.4$  Hz, 2H); 0.80 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.8, 152.5, 148.9, 139.0, 135.4, 135.2, 132.7, 130.8, 129.5, 129.2, 127.9, 123.5, 119.2, 117.5, 113.8, 32.1, 28.1, 22.6, 21.3, 13.5. MS (rel. int., %)  $m/z$ : 476 (71.1), 420 (66.8), 340 (88.6), 281 (42.8), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{22}H_{20}O_2Se_2$   $[M+H]^+$ : 476.9872, found: 476.9874.

**3-(<sup>n</sup>Butylselanyl)-2-(2-tolyl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3k):** Yield: 0.090 g (76%); yellow solid, m.p: 119-121 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.37 (ddd,  $J = 8.0, 1.4$  and  $0.6$  Hz, 1H); 7.75-7.71 (m, 1H); 7.52-7.44 (m, 2H); 7.37-7.25 (m, 4H); 2.85 (t,  $J = 7.4$  Hz, 2H); 2.28 (s, 3H); 1.52 (quint,  $J = 7.4$  Hz, 2H); 1.27 (sext,  $J = 7.4$  Hz, 2H); 0.81 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.8, 151.9, 147.7, 137.1, 135.4, 135.2, 135.0, 130.8, 130.5, 130.2, 129.2, 127.9, 125.4, 123.5, 119.2, 118.4, 116.1, 32.3, 27.4, 22.6, 20.4, 13.4. MS (rel. int., %)  $m/z$ : 476 (100.0), 420 (79.9), 340 (42.4), 281 (26.5), 207 (46.9). HRMS (ESI-QTOF) Calculated mass for  $C_{22}H_{20}O_2Se_2$   $[M+H]^+$ : 476.9872, found: 476.9876.

**3-(<sup>n</sup>Butylselanyl)-2-(4-chlorophenyl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3l):** Yield: 0.089 g (72%); yellow solid, m.p: 84-87 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.34 (ddd,  $J = 8.0, 1.2$  and  $0.5$  Hz, 1H); 7.75-7.71 (m, 1H); 7.54-7.51 (m, 2H); 7.50-7.45 (m, 2H); 7.43-7.39 (m, 2H); 2.90 (t,  $J = 7.4$  Hz, 2H); 1.52 (quint,  $J = 7.4$  Hz, 2H); 1.28 (sext,  $J = 7.4$  Hz, 2H); 0.80 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.6, 152.4, 146.9, 135.2, 135.1, 135.0, 134.0, 130.83, 130.8, 128.7, 128.1, 123.5, 119.2, 118.1, 114.7, 32.1, 28.2, 22.5, 13.4. MS (rel. int., %)  $m/z$ : 496 (17.4), 440 (24.5), 360 (24.1), 281 (36.0), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{21}H_{17}ClO_2Se_2$   $[M+H]^+$ : 496.9326, found: 496.9324.

**Methyl 2-(3-butylselanyl-5-oxo-5H-selenopheno[3,2-*c*]isochromen-2-yl)benzoate (3m):** Yield: 0.104 g (80%); yellow oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.38-8.35 (m, 1H); 8.03-8.00 (m, 1H); 7.75-7.70 (m, 1H); 7.61-7.56 (m, 1H); 7.54-7.48 (m, 2H); 7.46-7.40 (m, 2H); 3.76 (s, 3H); 2.80 (t,  $J = 7.3$  Hz, 2H); 1.48 (quint,  $J = 7.3$  Hz, 2H); 1.29-1.21 (m, 2H); 0.79 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 166.9, 161.8, 151.8, 147.9, 136.2, 135.4, 135.2, 132.1, 131.4, 131.2, 130.8, 130.4, 129.0, 127.9, 123.5, 119.2, 118.3, 116.0, 52.3, 32.2, 27.6, 22.5, 13.4. MS (rel. int., %)  $m/z$ : 520 (8.3), 383 (100.0), 168 (12.9), 41 (41.4). HRMS (ESI-QTOF) Calculated mass for  $C_{23}H_{20}O_4Se_2$   $[M+H]^+$ : 520.9769, found: 520.9753.

**3-(<sup>n</sup>Butylselanyl)-2-(naphthalen-1-yl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3n):** Yield: 0.096 g (75%); yellow solid, m.p: 142-144 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.41-8.38 (m, 1H); 7.96-7.90 (m, 2H); 7.84-7.80 (m, 1H); 7.73 (td,  $J = 7.7$  and  $1.3$  Hz, 1H); 7.55-7.45 (m, 6H); 2.79 (t,  $J = 7.4$  Hz, 2H); 1.44 (quint,  $J = 7.4$  Hz, 2H); 1.16 (sext,  $J = 7.4$  Hz, 2H); 0.73 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 161.8, 151.9, 146.0, 135.4, 135.2, 133.4, 133.0, 131.9, 130.9, 129.6, 128.6, 128.3, 128.1, 126.6, 126.3, 125.7, 124.9, 123.6, 119.2, 118.9, 117.4, 32.2, 27.5, 22.5, 13.4. MS (rel. int., %)  $m/z$ : 512 (31.9), 453 (28.4), 376 (15.7), 281 (42.1), 207 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{25}H_{20}O_2Se_2$   $[M+H]^+$ : 512.9872, found: 512.9872.

**2-<sup>n</sup>Butyl-3-(<sup>n</sup>butylselanyl)-5H-selenopheno[3,2-*c*]isochromen-5-one (3o):** Yield: 0.081 g (73%); yellow solid, m.p: 60-62 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.31 (ddd,  $J = 8.0, 1.2$  and  $0.6$  Hz, 1H); 7.71-7.66 (m, 1H); 7.46-7.42 (m, 1H); 7.39-7.36 (m, 1H); 3.11 (t,  $J = 7.6$  Hz, 2H); 2.92 (t,  $J = 7.4$  Hz, 2H); 1.73-1.57 (m, 4H); 1.51-1.37 (m, 4H); 0.98 (t,  $J = 7.3$  Hz, 3H); 0.88 (t,  $J = 7.4$  Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  (ppm) = 162.0, 154.4, 152.1, 135.6, 135.1, 130.8, 127.5, 123.1, 119.0, 115.4, 114.6, 34.4, 32.8, 32.4, 28.0, 22.7, 22.2, 13.8, 13.5. MS (rel. int., %)  $m/z$ : 442 (76.0), 385 (45.6), 343 (61.4), 305 (36.7), 263 (100.0). HRMS (ESI-QTOF) Calculated mass for  $C_{19}H_{22}O_2Se_2$   $[M+H]^+$ : 443.0029, found: 443.0026.

**3-(<sup>n</sup>Butylselanyl)-2-<sup>n</sup>hexyl-5H-selenopheno[3,2-*c*]isochromen-5-one (3p):** Yield: 0.099 g (84%); yellow oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  (ppm) = 8.34-8.30 (m, 1H); 7.73-7.65 (m, 1H); 7.47-7.42 (m, 1H); 7.40-7.37 (m, 1H); 3.11 (t,  $J = 7.6$  Hz, 2H); 2.92 (t,  $J = 7.4$  Hz, 2H); 1.74-1.66 (m, 2H); 1.64-1.57 (m, 2H); 1.46-1.38 (m, 4H);

1.36-1.31 (m, 4H); 0.93-0.86 (m, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 162.0, 154.5, 152.1, 135.6, 135.1, 130.8, 127.5, 123.2, 118.9, 115.4, 114.5, 33.1, 32.4, 32.3, 31.5, 28.7, 28.0, 22.7, 22.5, 14.0, 13.5. MS (rel. int., %)  $m/z$ : 470 (52.3), 413 (30.0), 343 (43.3), 263 (100.0). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{21}\text{H}_{26}\text{O}_2\text{Se}_2$   $[\text{M}+\text{H}]^+$ : 471.0340, found: 471.0315.

**3-(Ethylselenanyl)-2-(4-tolyl)-5H-selenopheno[3,2-c]isochromen-5-one (3q)**: Yield: 0.083 g (74%); yellow solid, m.p: 129-131 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm) = 8.36 (ddd,  $J$  = 8.0, 1.3 and 0.6 Hz, 1H); 7.75-7.71 (m, 1H); 7.51-7.45 (m, 4H); 7.27-7.25 (m, 2H); 2.93 (q,  $J$  = 7.4 Hz, 2H); 2.42 (s, 3H); 1.29 (t,  $J$  = 7.4 Hz, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 161.9, 152.5, 149.0, 139.1, 135.4, 135.2, 132.7, 130.9, 129.5, 129.2, 127.9, 123.5, 119.2, 117.6, 113.5, 21.9, 21.4, 15.4. MS (rel. int., %)  $m/z$ : 448 (15.0), 281 (24.5), 207 (56.7), 44 (100.0). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{20}\text{H}_{16}\text{O}_2\text{Se}_2$   $[\text{M}+\text{H}]^+$ : 448.9559, found: 448.9561.

**2-(4-Chlorophenyl)-3-(ethylselenanyl)-5H-selenopheno[3,2-c]isochromen-5-one (3r)**: Yield: 0.089 g (76%); yellow solid, m.p: 133-135 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm) = 8.35 (ddd,  $J$  = 8.0, 1.3 and 0.5 Hz, 1H); 7.75-7.71 (m, 1H); 7.54-7.51 (m, 2H); 7.50-7.43 (m, 2H); 7.42-7.40 (m, 2H); 2.93 (q,  $J$  = 7.5 Hz, 2H); 1.28 (t,  $J$  = 7.5 Hz, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 161.6, 152.4, 147.0, 135.3, 135.1, 135.0, 134.0, 130.8, 128.7, 128.2, 123.6, 119.2, 118.1, 114.4, 22.0, 15.4. MS (rel. int., %)  $m/z$ : 468 (100.0), 440 (32.2), 281 (26.9), 207 (65.8). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{19}\text{H}_{13}\text{ClO}_2\text{Se}_2$   $[\text{M}+\text{H}]^+$ : 468.9013, found: 468.9015.

**3-(Ethylselenanyl)-2-hexyl-5H-selenopheno[3,2-c]isochromen-5-one (3s)**: Yield: 0.088 g (80%); yellow oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm) = 8.32-8.29 (m, 1H); 7.71-7.67 (m, 1H); 7.46-7.42 (m, 1H); 7.39-7.36 (m, 1H); 3.10 (t,  $J$  = 7.5 Hz, 2H); 2.92 (q,  $J$  = 7.5 Hz, 2H); 1.70 (quint,  $J$  = 7.2 Hz, 2H); 1.40-1.30 (m, 9H); 0.92-0.88 (m, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 162.0, 154.8, 152.0, 135.5, 135.1, 130.7, 127.4, 123.1, 118.8, 115.4, 114.1, 33.0, 32.2, 31.5, 28.7, 22.5, 21.7, 15.7, 14.0. MS (rel. int., %)  $m/z$ : 442 (42.8), 290 (35.5), 263 (100.0), 41 (59.5). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{19}\text{H}_{22}\text{O}_2\text{Se}_2$   $[\text{M}+\text{H}]^+$ : 443.0027, found: 443.0015.

**3-(*n*-Butylselenanyl)-8-fluoro-2-phenyl-5H-selenopheno[3,2-c]isochromen-5-one (3t)**: Yield: 0.101 g (84%); yellow solid, m.p: 103-105 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm) = 8.41-8.37 (m, 1H); 7.61-7.58 (m, 2H); 7.49-7.44 (m, 3H); 7.21-7.16 (m, 1H); 7.13-7.10 (m, 1H); 2.89 (t,  $J$  = 7.4 Hz, 2H); 1.52 (quint,  $J$  = 7.4 Hz, 2H); 1.32-1.29 (m, 2H); 0.79 (t,  $J$  = 7.4 Hz, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 166.90 (d,  $J$  = 256.0 Hz), 160.9, 153.5, 149.7, 137.9 (d,  $J$  = 10.9 Hz), 135.4, 134.3 (d,  $J$  = 10.5 Hz), 129.6, 129.1, 128.5, 117.0 (d,  $J$  = 2.7 Hz), 116.1 (d,  $J$  = 23.0 Hz), 115.6 (d,  $J$  = 2.1 Hz), 114.3, 109.5 (d,  $J$  = 23.3 Hz), 32.1, 28.1, 22.6, 13.4. MS (rel. int., %)  $m/z$ : 480 (60.9), 424 (77.4), 344 (84.1), 41 (100.0). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{21}\text{H}_{17}\text{FO}_2\text{Se}_2$   $[\text{M}+\text{H}]^+$ : 480.9620, found: 480.9613.

### General procedure for the synthesis of 5a

Compound **5a** was prepared according to a published procedure.<sup>[34]</sup> A mixture of **3a** (0.25 mmol, 0.116 g),  $\text{PdCl}_2(\text{PPh}_3)_2$  (0.025 mmol, 0.0175 g), phenylacetylene **4a** (1.0 mmol, 0.102 g) and triethylamine (0.25 mmol, 0.025 g) were dissolved in DMF (3.0 mL). After this, the  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (0.05 mmol, 0.010 g) was added. The resulting mixture was stirred for 24 h at 80 °C. After the reaction was cooled to ambient temperature, the crude reaction mixture was received in a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (10.0 mL) and the product was extracted with ethyl acetate (3x 10.0 mL). The organic layer was separated, dried with  $\text{MgSO}_4$  and concentrated under vacuum. The residue was purified by column chromatography using silica gel 60Å (0.060-0.200 mm) and hexane/ethyl acetate (90:10) as eluent to afford **5a** as an orange solid (0.075 g, 70% yield).

### 2-Phenyl-3-(phenylethynyl)-5H-selenopheno[3,2-c]isochromen-5-one (5a)

**5a**: Yield: 0.075 g (70%); orange solid, m.p: 192-195 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  (ppm) = 8.27-8.23 (m, 1H); 7.85-7.81 (m, 2H); 7.65-7.61 (m, 1H); 7.48-7.46 (m, 2H); 7.41-7.32 (m, 5H); 7.29-7.26 (m, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  (ppm) = 161.5, 151.1, 150.4, 135.2, 134.9, 134.8, 131.7, 130.9, 129.3, 128.8, 128.6, 128.3, 128.1, 128.0, 123.3, 122.7, 119.3, 116.4, 112.4, 94.9, 82.4. MS (rel. int., %)  $m/z$ : 426 (100.0), 318 (23.1), 289 (43.5), 202 (41.7). HRMS (ESI-QTOF) Calculated mass for  $\text{C}_{25}\text{H}_{14}\text{O}_2\text{Se}$   $[\text{M}+\text{H}]^+$ : 427.0237, found: 427.0239.

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Synthesis of 5*H*-Selenopheno[3,2-*c*]isochromen-5-one Promoted by Dialkyl Diselenides and Oxone<sup>®</sup>*Adv. Synth. Catal.* **Year**, *Volume*, Page – Page

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