The Free Internet Journal
for Organic Chemistry

Paper

Archive for
Organic Chemistry

Arkivoc **2020**, part __, 0-0
to be inserted by editorial office

Ultrasound and Oxone® promoting regioselective selenofunctionalization of chromone

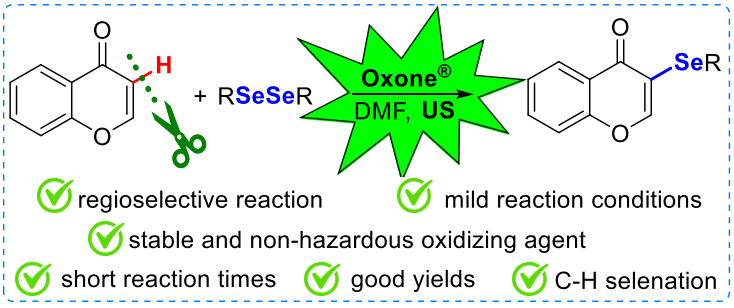
Daniela R. Araujo, Yanka R. Lima, Angelita M. Barcellos, Raquel G. Jacob, Márcio S. Silva, and Gelson Perin*

Address: Laboratório de Síntese Orgânica Limpa – LASOL, Federal University of Pelotas – UFPel, P.O. Box 354, 96010-900, Pelotas – RS, Brazil
Email: gelson_perin@ufpel.edu.br

Received mm-dd-yyyy **Accepted** mm-dd-yyyy **Published on line** mm-dd-yyyy
Dates to be inserted by editorial office

Abstract

Selective, simple and green synthetic procedures constitute an important goal in organic synthesis. In this sense, we describe the synthesis of 3-(organylselanyl)-4*H*-chromen-4-ones by regioselective selenofunctionalization of the chromone core using diorganyl diselenides. These reactions were efficiently conducted under mild conditions, employing Oxone® as stable and non-hazardous oxidizing agent in the presence of ultrasound in short reaction times. By this efficient approach, new eight compounds were obtained in moderate to excellent yields.



Keywords: Chromone, organochalcogen, Oxone®, selenium, ultrasound

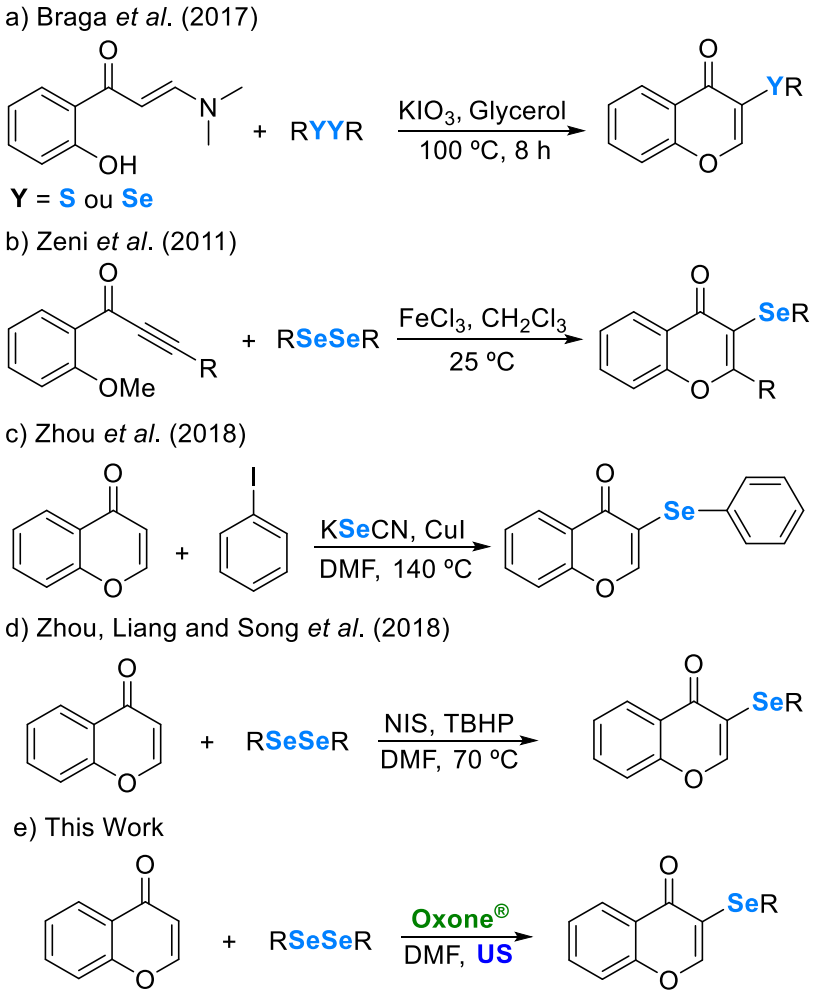
Introduction

Organochalcogen compounds have been widely study by the scientific community based on their antioxidant activity related to biological properties which are well described in the literature.[1] In the last decades there has been a growing interest in the synthesis of these compounds, specifically organoselenium compounds, due to their promising biological applications, such as antifungal,[2] antibacterial[3] and antiviral.[4] Indeed, selenium is recognized as an essential micronutrient of particular interest because of its ability to participate in crucial redox reactions that are particularly implicated in antioxidant,[5] chemopreventive[6] or apoptotic activities.[7] In addition, the chemical modification of natural compounds is of utmost strategic importance, to those considering increasing or improving the biological activities already present in a natural way, for example, the selenium-containing citronellol derivatives causing the potentiation of the antioxidant activity of this natural compound,[8] the insertion of selenium into structures of sugars[9] and the selenofunctionalization of a flavonoid, chrysin, enhancing the antioxidant and anticancer activities.[10]

Another class of compounds, which play an important role in the design and discovery of new pharmacologically active compounds, are heterocyclic compounds, among which are flavonoids.[11] Flavonoids are natural polyphenolic phytochemicals that can be found in many fruits and vegetables and are usually present in the human diet.[10] Specifically, chromones are of synthetic interest, not only due of their natural occurrence, which makes them ubiquitous in nature, but also because of their amphoteric nature and low mammalian toxicity.[12] Molecules containing the chromone core have a wide range of biological activities including tyrosine and protein kinase C inhibitors,[13] anticancer agents[14] and antimalarial.[15] Many of these biological actions are attributed to the ability to transfer electrons, activate antioxidant enzymes,[16] reduce α-tocopherol radicals,[17] chelate metal catalysts[18] and inhibit oxidases.[19] Few methods are found to obtain chromones containing an organochalcogen moiety, for example, Braga et al.[20] described the cyclization of enaminones with diorganyl dichalcogenides (Scheme 1a), in 2011 Zeni et al.[21] reported the intramolecular cyclization reactions using $FeCl_3$/RSeSeR as cyclizing agent to prepare these chromone derivatives (Scheme 1b). More recently, its core has been functionalized by KSeCN via copper catalysis (Scheme 1c)[22] or direct NIS and TBHP-induced C-H functionalization employing diselenides as starting materials (Scheme 1d) .[23]

In parallel, our research group studied the application of Oxone® as an oxidizing agent in some organochalcogen compound transformations.[24] More specifically, we demonstrated its application in the carbocyclization of alkynols for the synthesis of 2-organoselanyl naphthalenes,[25] to prepare 1*H*-pyrazole[26] and in the synthesis of isochromenones fused to selenophenes.[27] Our interest in Oxone® is due to its advantages as being non-toxic, easy to handle white solid, and it has low cost.[28]

Additionally, in order to minimize the energy used in the chemical processes, several procedures were described using ultrasound irradiation.[29] The use of ultrasound in organic synthesis is linked to the phenomenon of acoustic cavitation and it was used in the synthesis of selanylindoles,[30] selanylimidazopyridines,[31] alkali metals diselenides[32] and in the functionalization of chrysin,[33] for example. Therefore, based on what was previously mentioned, the aim of this work was to combine of these two moieties by regioselective selenofunctionalization of the chromone core **1** using diorganyl diselenides **2** and Oxone® as oxidizing agent to obtaining the 3-(organylselanyl)-4*H*-chromen-4-ones **3** (Scheme 1e).



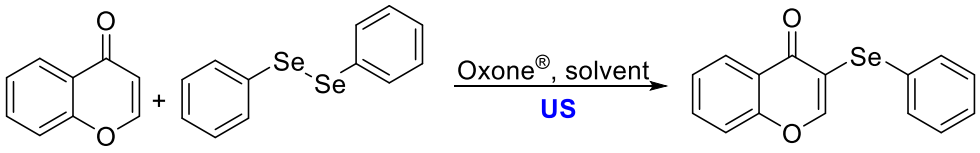
Scheme 1

Results and Discussion

Initially, in order to obtain the desired product 3-(phenylselanyl)-4*H*-chromen-4-one (**3a**), first a test was performed through the use of 0.250 mmol chromone **1**, 0.125 mmol diselenide **2a**, 0.250 mmol Oxone® and dimethylformamide (DMF, 2.0 mL) as solvent in a conventional system using 50 ºC temperature. After 24 h, the total consumption of the starting materials was observed (monitored by TLC), and the desired product **3a** was isolated in 76% yield (Table 1, entry 1). To our satisfaction, this condition promoted the regioselective selenofunctionalization in the position 3 of chromone core, by verification using 2D NMR techniques (See Support Information). In order to shorten the reaction time and possibly increase the yield of the desired product by using an alternative energy source, the ultrasound probe was applied. A test using the same quantities of the reagents was performed. In this test with ultrasound, fortunately a decrease in reaction time occurred from 24 h to 0.8 h giving the compound **3a** in 86% yield (Table 1, entry 2). Encouraged by this result, a comparative study was carried out to check the influence of different stoichiometric amounts of diselenides **2a** and Oxone®, as well as the best reaction solvent for this synthesis (Table 1, entry 3-12). In order to increase the reaction yield, a reaction was performed using excess reagent **2a**, however no significant increase in

reaction yield occurred (Table 1, entry 3). To verify the importance of Oxone®, two reactions were performed with distinct amounts. In the first one, a small excess was used and in the second one, a decrease in the amount was used. However, in both cases, satisfactory results were not observed (Table 1, entries 4 and 5). Aditionally, without Oxone® the formation of the product **3a** did not occur, proving the necessity of using this reagent (Table 1, entry 6). After that, the solvent variation study was carried out. When testing EtOH and MeOH, a complex mixture of products was observed and the desired **3a** product was obtained in 68 and 56% yield, respectively (Table 1, entries 7 and 8). Furthermore, using acetonitrile as solvent, the product was obtained in 74% yield (Table 1, entry 9). When the reaction in water was performed, only traces of the product **3a** were observed (Table 1, entry 10). This result can be explained by the lower solubility of the starting materials in polar solvents. The use of alternative green solvents such as glycerol and polyethylene glycol-400 (PEG-400) was evaluated, however the results were not satisfactory (Table 1, entries 11 and 12). Finally, based on the results depicted in Table 1, the best reaction condition was defined as the sonication of a mixture of 0.250 mmol of chromone **1a**, 0.125 mmol of diphenyl diselenide (**2a**) and 0.250 mmol of Oxone® in DMF as the solvent (2.0 mL) (Table 1, entry 2).

Table 1. Optimization of the reaction conditions[a]



1 **2a** **3a**

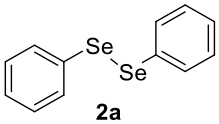
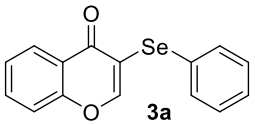
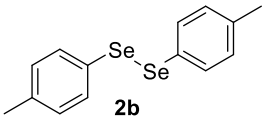
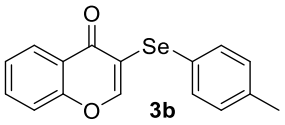
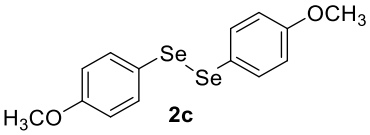
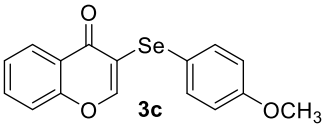
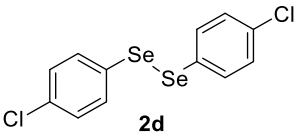
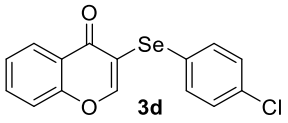
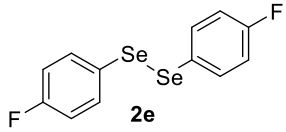
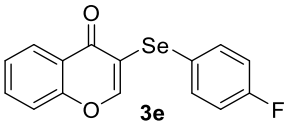
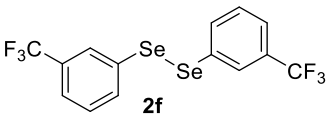
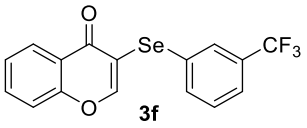
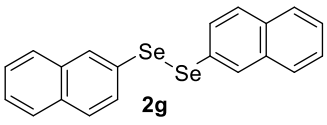
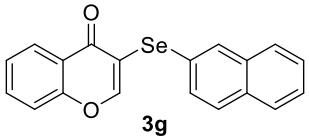
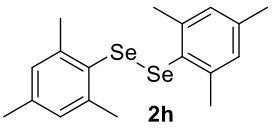
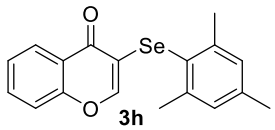
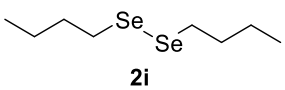
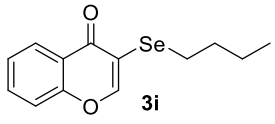
Entry	**2a** (mmol)	Oxone® (mmol)	Time (hours)	Solvent	Yield (%)[c]
1[b]	0.125	0.250	24	DMF	76
2	0.125	0.250	0.8	DMF	86
3	0.250	0.250	0.8	DMF	85
4	0.125	0.300	0.8	DMF	80
5	0.125	0.125	1.5	DMF	41
6	0.125	-	1.0	DMF	NR
7	0.125	0.250	1.0	EtOH	68
8	0.125	0.250	1.5	MeOH	56
9	0.125	0.250	1.5	MeCN	74
10	0.125	0.250	2.0	H_2O	Traces
11	0.125	0.250	1.4	Glycerol	59
12	0.125	0.250	1.5	PEG-400	47

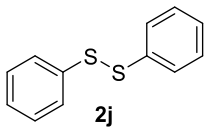
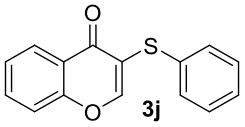
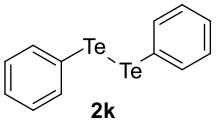
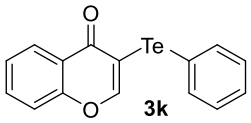
[a]A mixture of **1** (0.250 mmol), **2a**, Oxone® and the solvent (2.0 mL) in a glass tube was sonicated for the time indicated in the Table and 60% amplitude was used in the ultrasound. [b]Reaction under conventional heating of 50 °C. [c]Isolated yields after column chromatography. NR: no reaction.

Once the best conditions were determined, the method was extended to different substrates, in order to evaluate its generality and robustness in the synthesis of different 3-(organoselanyl)-4*H*-chromen-4-ones **3** (Table 2). The effect of electron-withdrawing groups (EWG) and electron-donor ones (EDG) attached to the aromatic ring of the diaryl diselenide **2** was evaluated in the reaction with chromone **1** (Table 2, entries 1-6). In general, there was no significant difference in yield when diaryl diselenides containing electron-deficient and

electron-rich were used, leading to the formation of all desired products in good yields. For example, when diaryl diselenides attached in *para* position with electron donor groups **2b** (R = 4-CH_3) and **2c** (R = 4-CH_3O) were used, the respective products **3b** and **3c** were obtained in 78% and 80% yields after 0.6 and 0.7 h, respectively (Table 2, entries 2 and 3). Similarly, good yields and short reaction times were obtained when the reaction proceeded with diaryl diselenides electron-deficient **2d** (R = 4-Cl) and **2e** (R = 4-F). The respective products were isolated in 87% and 72% yields, both after just 0.5 hour (Table 2, entries 4 and 5).

Table 2. Synthesis of 3-(organochalcogenyl)-4*H*-chromen-4-ones **3a**-**k**[a]

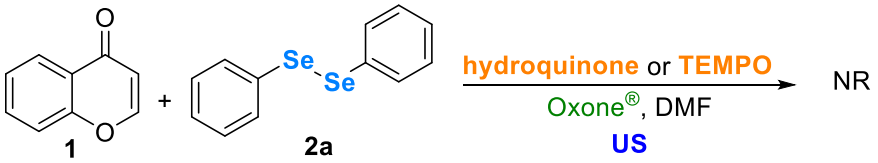
Entry	Dichalcogenide **2**	Product **3**	Time (h)	Yield[b] (%)
1	 **2a**	 **3a**	0.8	86
2	 **2b**	 **3b**	0.6	78
3	 **2c**	 **3c**	0.7	80
4	 **2d**	 **3d**	0.5	87
5	 **2e**	 **3e**	0.5	72
6	 **2f**	 **3f**	0.6	82
7	 **2g**	 **3g**	0.5	74
8	 **2h**	 **3h**	0.5	82
9	 **2i**	 **3i**	2.0	NR

10	 **2j**	 **3j**	2.0	NR
11	 **2k**	 **3k**	2.0	NR

[a]A mixture of chromone **1** (0.250 mmol), **2** (0.125 mmol), Oxone® and the DMF (2.0 mL) in a glass tube was sonicated for the time indicated in the Table and 60% amplitude was used in the ultrasound. [b] Isolated yields after column chromatography. NR: no reaction.

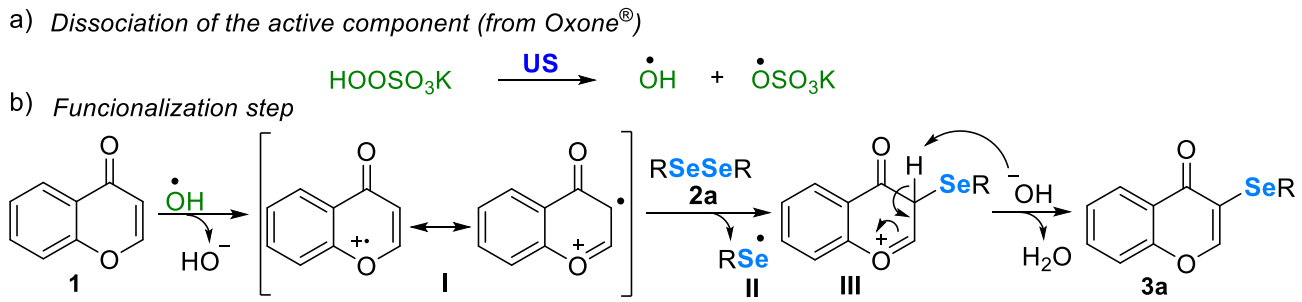
Still, when a diaryl diselenide strong electron-deficient **2f** (R = 3-CF_3) was used, the product **3f** was obtained after 0.6 hours in 82% yield (Table 2, entry 6). The voluminous groups 2-naphthyl diselenide (**2g**) and dimesityl diselenide **2h** were also suitable substrates for the reaction, affording the expected product **3g** and **3h** in 74% and 82% yields after 0.5 hours, respectively (Table 2, entries 7 and 8). When we tried to apply the method to alkyl-substituted dibutyl diselenide **2i**, unfortunately the desired product **3i** was not obtained even after 2 h of reaction, and only the presence of starting materials was observed (monitored by TLC) (Table 2, entry 9). Finally, the substrate scope was extended to other dichalcogenides using diphenyl disulfide (**2j**) and diphenyl ditelluride (**2k**), but only oxidation products of the starting materials were observed, not forming the desired products **3j** and **3k** (Table 2, entries 10 and 11).

To propose a reaction mechanism for this synthesis, control experiments were carried out. The formation of radical intermediates was verified, by performed the best reaction condition under sonication in the presence of two radical scavengers. When 3.0 equivalents of hydroquinone or 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) were used, the product **3a** was not observed, even 2 h of reaction (Scheme 2). With the results obtained in these tests, it was suggested that the reaction mechanism occurred radically.



Scheme 2

Based on the literature[23,34,35] and in our own results, the plausible mechanism for the formation of 3-(organoselanyl)-4*H*-chromen-4-one **3** were proposed (Scheme 3). The first step is the formation of $HO^{\bullet}$ and $SO_4^{\bullet}$ from the US-promoted dissociation of Oxone®. The second step, a single electron transfer (SET) from **1** to hydroxyl radical form the intermediate **I**. Then, the formation of the selenide radical **II** and the selenylated flavone cation **III** occur from the reaction of intermediate **I** with the diselenide **2a**. Finally, the deprotonation of intermediate **III** provided the product **3** (Scheme 3a).



Scheme 3

Conclusions

Through the obtained results we demonstrate the regioselective selenofunctionalization of the chromone using diselenides, Oxone® and DMF as solvent. To form the 3-(organylselanyl)-4*H*-chromen-4-ones, the reaction was carried out in the presence of ultrasound, which caused short reaction times and good yields. The method allowed the use of several diaryl diselenides, providing new eight compounds in a regioselective way under mild conditions.

Experimental Section

General. The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) by using UV light as visualizing agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Baker silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. Hydrogen nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 400 MHz. Spectra were recorded in DMSO solutions. Chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the external reference. Coupling constant (*J*) are reported in Hertz. Abbreviations to denote the multiplicity of a signal are s (singlet), d (doublet), dd (doublet of doublet) and m (multiplet). Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 100 MHz. Chemical shifts are reported in ppm, referenced to the solvent peak of DMSO. Low-resolution mass spectra (MS) were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer. The HRMS analyses were performed in a Bruker micrOTOF-QII spectrometer equipped with an APCI source operating in positive mode. The samples were solubilized in acetonitrile and analyzed by direct infusion. The ultrasound-promoted reactions were performed using a Cole Parmer-ultrasonic processor Model CPX 130, with a maxim power of 130 W, operating at amplitude of 60% and a frequency of 20 kHz. The temperature of the reaction under US was monitored using an Incoterm digital infrared thermometer Model Infraterm (Brazil). Melting point (mp) values were measured in a Marte PFD III instrument with a 0.1 °C precision. Oxone® was purchased from Sigma Aldrich.

General procedure for synthesis of 3-(phenylselanyl)-4*H*-chromen-4-ones 3. To a 10 mL round-bottomed glass vial, the chromone **1** (0.250 mmol), diselenide **2a**-**i** (0.125 mmol), Oxone® (0.077 g; 0.250 mmol) and DMF (2.0 mL) were added. The US probe was placed in the reaction vial, which was sonicated (20 KHz, 60% of sonic amplitude) for the time indicated in Table 2. The reaction progress was monitored by TLC in order to evaluate the starting materials consumption. After that, the reaction mixture was extracted with ethyl acetate

(3x 15.0 mL), the organic phase was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was isolated by column chromatography using silica gel 60Å (0.060-0.200 mm-Across) and using a mixture of hexane and ethyl acetate (90:10).

3-(Phenylselanyl)-4*H*-chromen-4-one (3a).[20] Yield: 0.065 g (86%); white solid, m.p: 65-66 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.56 (s, 1H); 8.05 (dd, *J* 8.0, 1.7 Hz, 1H); 7.84-7.80 (m, 1H); 7.65 (d, *J* 8.0 Hz, 1H); 7.53-7.49 (m, 1H); 7.47-7.44 (m, 2H); 7.31-7.25 (m, 3H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.1, 159.2, 155.9, 134.5, 131.2, 129.5, 127.2, 126.0, 125.5, 122.7, 118.5, 114.8. MS (rel. int., %) *m*/*z*: 302 (M^+, 100.0), 182 (91.5), 165 (21.8), 102 (92.9), 77 (61.9), 51 (59.7).

3-(4-Tolylselanyl)-4*H*-chromen-4-one (3b).[20] Yield: 0.062 g (78%); white solid, m.p: 87-88 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.47 (s, 1H); 8.05 (d, *J* 8.4 Hz, 1H); 7.85-7.81 (m, 1H); 7.66 (d, *J* 8.4 Hz, 1H); 7.54-7.51 (m, 1H); 7.39 (d, *J* 7.9 Hz, 2H); 7.12 (d, *J* 7.9 Hz, 2 H); 2.26 (s, 3H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.1, 158.2, 155.9, 137.1, 134.5, 132.1, 130.2, 126.0, 125.4, 125.1, 122.6, 118.5, 115.6, 20.6. MS (rel. int., %) *m*/*z*: 316 (M^+, 91.2), 235 (100.0), 196 (50.0), 115 (54.6), 91 (30.6), 65 (21.9).

3-[(4-Methoxyphenyl)selanyl]-4*H*-chromen-4-one (3c).[20] Yield: 0.066 g (80%); white solid, m.p: 93-94 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.25 (s, 1H); 8.04 (dd, *J* 8.3, 1.7 Hz, 1H); 7.82-7.80 (m, 1H); 7.63 (d, *J* 8.3 Hz, 1H); 7.53-7.49 (m, 3H); 6.93-6.90 (m, 2H); 3.74 (s, 3H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.1, 159.4, 156.6, 155.8, 135.2, 134.5, 125.9, 125.3, 122.4, 118.4, 117.6, 116.9, 115.3, 55.2. MS (rel. int., %) *m*/*z*: 331 (M^+, 90.6), 251 (100.0), 212 (26.9), 132 (39.3), 92 (48.2), 63 (66.8).

3-[(4-Chlorophenyl)selanyl)-4*H*-chromen-4-one (3d).[20] Yield: 0.073 g (87%); white solid, m.p: 117-118 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.70 (s, 1H); 8.06 (d, *J* 8.2 Hz, 1H); 7.87-7.83 (m, 1H); 7.69 (d, *J* 8.2 Hz, 1H); 7.56-7.52 (m, 1H); 7.46 (d, *J* 8.6 Hz, 2H); 7.33 (d, *J* 8.6 Hz, 2H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 173.9, 159.9, 155.9, 134.6, 132.6, 131.9, 129.3, 128.6, 126.1, 125.5, 122.8, 118.5, 114.3. MS (rel. int., %) *m*/*z*: 336 (M^+, 28.6), 255 (35.3), 155 (9.2), 120 (42.1), 92 (100.0), 50 (53.3).

3-[(4-Fluorophenyl)selanyl)-4*H*-chromen-4-one (3e).[20] Yield: 0.058 g (72%); white solid, m.p: 83-84 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.55 (s, 1H); 8.05 (d, *J* 8.0 Hz, 1H); 7.85-7.81 (m, 1H); 7.66 (d, *J* 8.0 Hz, 1H); 7.56-7.52 (m, 3H); 7.17-7.13 (m, 2H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.0, 161.8 (d, *J* 243.2 Hz), 158.7, 155.9, 134.5, 134.2 (d, *J* 7.9 Hz), 126.0, 125.4, 124.0 (d, *J* 3.4 Hz), 122.7, 118.5, 116.5 (d, *J* 21.8 Hz), 115.3. MS (rel. int., %) *m*/*z*: 320 (M^+, 27.0), 239 (31.1), 200 (29.6), 120 (100.0), 92 (54.0), 75 (21.1).

3-{[3-(Trifluormethyl)phenyl]selanyl}-4*H*-chromen-4-one (3f).[20] Yield: 0.076 g (82%); white solid, m.p: 112-113 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.82 (s, 1H); 8.08-8.06 (m, 1H); 7.88-7.84 (m, 1H); 7.80 (s, 1H); 7.72-7.69 (m, 2H); 7.60-7.47 (m, 3H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.0, 160.7, 156.0, 134.7, 134.4, 131.8, 130.2, 129.8 (q, *J* 31.7 Hz), 126.7 (q, *J* 3.9 Hz), 126.2, 125.5, 123.8 (q, *J* 271.1 Hz), 123.6 (q, *J* 3.9 Hz), 122.9, 118.6, 113.6. MS (rel. int., %) *m*/*z*: 370 (M^+,10.4), 249 (30.2), 220 (3.9), 120 (100.0), 92 (71.7), 63 (26.8).

3-(Naphthalen-2-ylselanyl)-4*H*-chromen-4-one (3g).[20] Yield: 0.065 g (74%); white solid, m.p: 68-69 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.32 (s, 1H); 8.24 (d, *J* 8.2 Hz, 1H); 8.06 (dd, *J* 7.6, 1.2 Hz, 1H); 7.98-7.96 (m, 1H); 7.92 (d, *J* 8.2 Hz, 1H); 7.84-7.79 (m, 1H); 7.72 (dd, *J* 7.6, 1.2 Hz, 1H); 7.52 (m, 4H) 7.44-7.40 (m, 1H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.2, 158.0, 155.9, 134.6, 133.7, 132.7, 131.8, 128.8, 128.7, 127.3, 127.2, 126.5, 126.3, 126.0, 125.4, 122.5, 118.5, 115.1, 109.5. MS (rel. int., %) *m*/*z*: 352 (M^+, 57.6), 270 (100.0), 253 (18.6), 152 (60.1), 126 (21.7), 77 (17.6).

3-(Mesitylselanyl)-4*H*-chromen-4-one (3h). Yield: 0.071 g (82%); yellowish solid, m.p: 110-111 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) = 8.05 (dd, *J* 8.0, 1.7 Hz, 1H); 7.83-7.78 (m, 1H); 7.59 (d, *J* 8.0 Hz, 1H); 7.53-7.49 (m, 1H); 7.43 (s, 1H); 7.05 (s, 2H); 2.45 (s, 6H); 2.26 (s, 3H). ^{13}C-{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm) = 174.6, 155.8, 151.6, 143.2, 139.1, 134.4, 129.0, 125.8, 125.1, 123.6, 121.7, 118.4, 117.1, 23.6, 20.6. MS (rel. int., %)

m/z: 344 (M^+, 8.0), 263 (49.4), 235 (17.4), 192 (5.4), 119 (100.0), 77 (43.1). HRMS (APCI-QTOF) calculated mass for $C_{18}H_{17}O_2Se$ $[M+H]^+$: 345.0394, found: 345.0388.

Acknowledgements

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. and G.P. Prof. Thiago Barcellos from University of Caxias do Sul is acknowledged for providing the HRMS analysis.

Supplementary Material

General procedure for synthesis of 3-(organylselanyl)-4*H*-chromen-4-ones and selected spectra can be found in the online version.

References

1. Lenardão, E. J.; Santi, C.; Sancineto, L. *New Frontiers in Organoselenium Compounds*. Springer International Publishing: Cham, Switzerland, 2018.
2. Venturini, T. P.; Chassot, F.; Loreto, E. S.; Keller, J. T.; Azevedo, M. I.; Zeni, G.; Santurio, J. M.; Alves, S. H. *Med. Mycol.* **2016**, *54*, 550-555. https://doi.org/10.1093/mmy/myv120
3. Sancineto, L.; Piccioni, M.; De Marco, S.; Pagiotti, R.; Nascimento, V.; Braga, A. L.; Santi, C.; Pietrella, D. *BMC Microbiol*. **2016**, *16*, 220-229. https://doi.org/10.1186/s12866-016-0837-x
4. Rossato, L.; Loreto, E. S.; Venturini, T. P.; Azevedo, M. I.; Al-Hatmi, A. M. S.; Santurio, J. M.; Alves, S. H. *Mycoses* **2019**, *62*, 508-512. https://doi.org/10.1111/myc.12905
5. Rahmanto, A. S.; Davies, M. J. *IUBMB Life* **2012**, *64*, 863-871. https://doi.org/10.1002/iub.1084
6. Janakiram, N. B.; Mohammed, A.; Ravillah, D.; Choi, C. I.; Zhang, Y.; Desai, D.; Amin, S.; Rao, C. V. *Oncol. Rep.* **2013**, *30*, 952-960. https://doi.org/10.3892/or.2013.2483
7. Sanmartín, C.; Plano, D.; Palop, J. A. *Mini Rev. Med. Chem.* **2008**, *8*, 1020-1031. https://doi.org/10.2174/138955708785740625
8. Victoria, F. N.; Anversa, R.; Penteado, F.; Castro, M.; Lenardão, E. J.; Savegnago, L. *Eur. J. Pharmacol.* **2014**, *742*, 131-138. https://doi.org/10.1016/j.ejphar.2014.09.005
9. Vargas, J. P.; Pinto, L. M.; Savegnago, L.; Ludtke, D.S. *J. Braz. Chem. Soc*. **2015**, *26*, 810-815. https://doi.org/10.5935/0103-5053.20150021
10. Keri, R. S.; Budagumpi, S.; Pai, R. K.; Balakrishna, R. G. *Eur. J. Med. Chem.* **2014**, *78*, 340-374.

https://doi.org/10.1016/j.ejmech.2014.03.047
11. Fonseca, S. F.; Lima, D. B.; Alves, D.; Jacob, R. G.; Perin, G.; Lenardão, E. J.; Savegnago, L. *New J. Chem.* **2015**, *39*, 3043-3050. https://doi.org/10.1039/c4nj02329c
12. Khadem, S.; Marles, R. J. *Molecules* **2012**, *17*, 191-206. https://doi.org/10.3390/molecules17010191
13. Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev*. **2003**, *103*, 893-930. https://doi.org/10.1021/cr020033s
14. Duan, Y.-d.; Jiang, Y.-y.; Guo, F.-x.; Chen, L.-x.; Xu, L.-l.; Zhang, W.; Liu, B. *Fitoterapia* **2019**, *135*, 114-129. https://doi.org/10.1016/j.fitote.2019.04.012
15. Bathini, P. K.; Yerrabelly, H.; Yerrabelly, J. R. *Arkivoc*, **2018**, (*iii)*, 212-228. https://doi.org/10.24820/ark.5550190.p010.348
16. Elliott, A. J.; Scheiber, S. A.; Thomas, C.; Pardini, R. S. *Biochem. Pharmacol*. **1992**, *44*, 1603-1608. https://doi.org/10.1016/0006-2952(92)90478-2
17. Hirano, R.; Sasamoto, W.; Matsumoto, A.; Itakura, H.; Igarashi, O.; Kondo, K. J. *Nutr. Sci. Vitaminol*. **2001**, *47*, 357-362. https://doi.org/10.3177/jnsv.47.357
18. Ferrali, M.; Signorini, C.; Caciotti, B.; Sugherini, L.; Ciccoli, L.; Giachetti, D.; Comporti, M. *FEBS Lett*. **1997**, *416*, 123-129. https://doi.org/10.1016/S0014-5793(97)01182-4
19. Cos, P.; Ying, L.; Calomme, M.; Hu, J. P.; Cimanga, K.; Van Poel, B.; Pieters, L.; Vlietinck, A. J.; Vanden Berghe, D. *J. Nat. Prod*. **1998**, *61*, 71-76. https://doi.org/10.1021/np970237h
20. Rafique, J.; Saba, S.; Schneider, A. R.; Franco, M. S.; Silva, S. M.; Braga, A. L. *ACS Omega* **2017**, *2*, 2280-2290. https://doi.org/10.1021/acsomega.7b00445
21. Godoi, B.; Sperança, A.; Bruning, C. A.; Back, D. F.; Menezes, P. H.; Nogueira, C. W.; Zeni, G. *Adv. Synth. Catal*. **2011**, *353*, 2042-2050. https://doi.org/10.1002/adcs.201100189
22. Zhu, J.; Xu, B.; Yu, J.; Ren, Y.; Wang, J.; Xie, P.; Pittman, C. U.; Zhou, A. *Org. Biomol. Chem*. **2018**, *16*, 5999-6005. https://doi.org/10.1039/C8OB01398E
23. Ding, C.; Yu, Y.; Yu, Q.; Xie, Z.; Zhou, Y.; Zhou, J.; Liang, G.; Song, Z. *ChemCatChem* **2018**, *10*, 5397-5401. https://doi.org/10.1002/cctc.201801548
24. Perin, G.; Santoni, P.; Barcellos, A. M.; Nobre, P. C.; Jacob, R. G.; Lenardão, E. J.; Santi, C. *Eur. J. Org. Chem.* **2018**, *10*, 1224-1229. https://doi.org/10.1002/ejoc.201701775
25. Perin, G.; Araujo, D. R.; Nobre, P. C.; Lenardão, E. J.; Jacob, R. G.; Silva, M. S.; Roehrs, J. A. *PeerJ* **2018**, *6*, e4706. https://doi.org/10.7717/peerj.4706
26. 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* **2019**, *51*, 2293-2304.

https://doi.org/10.1055/s-0037-1611747
27. Goulart, H. G.; Neto, J. S. S.; Barcellos, A. M.; Barcellos, T.; Silva, M.; Alves, D.; Jacob, R. G.; Lenardao, E.; Perin, G. *Adv. Synth. Catal.* **2019**, *14*, 3403-3411. https://doi.org/10.1002/adsc.201900288
28. Hussain, H.; Green, I. R.; Ahmed, I. *Chem. Rev.* **2013**, *113*, 3329-3371. https://doi.org/10.1021/cr3004373
29. Penteado, F.; Monti, B.; Sancineto, L.; Perin, G.; Jacob, R. G.; Santi, C.; Lenardão, E. J. *Asian J. Org. Chem.* **2018**, *7*, 2368-2385. https://doi.org/10.1002/ajoc.201800477
30. Vieira, B. M.; Thurow, S.; Brito, J. S.; Perin, G.; Alves, D.; Jacob, R. G.; Santi, C.; Lenardão, E. J. *Ultrason. Sonochem*. **2015**, *27*, 192-199. https://doi.org/10.1016/j.ultsonch.2015.05.012
31. Vieira, B. M.; Padilha, N.; Nascimento, N. M.; Perin, G.; Alves, D.; Schumacher, R. F.; Lenardao, E. J. *Arkivoc* **2019**, (*ii)*, 6-23. https://doi.org/10.24820/ark.5550190.p010.972
32. Krasowska, D.; Begini, F.; Santi, C.; Mangiavacchi, F.; Drabowicz, J.; Sancineto, L. *Arkivoc* **2019**, (*ii)*, 24-37. https://doi.org/10.24820/ark.5550190.p010.981
33. Fonseca, S. F.; Padilha, N. B.; Thurow, S.; Rohers, J. A.; Savegnago, L.; Souza, M. N.; Fronza, M. G.; Collares, T.; Buss, J.; Seixas, F. K.; Alves, D.; Lenardão, E. J. *Ultrason. Sonochem*. **2017**, *39*, 827-836. https://doi.org/10.1016/j.ultsonch.2017.06.007
34. Soumia, F.; Petrier, C. *Ultrason. Sonochem*. **2016**, *32*, 343-347. https://doi.org/10.1016/j.ultsonch.2016.03.032
35. Araujo, D. R.; Lima, Y. L.; Barcellos, A. M.; Silva, M. S.; Jacob, R. G.; Lenardão, E. J.; Bagnoli, L.; Santi, C.; Perin, G. *Eur. J. Org. Chem*. **2020**, 586-592. https://doi.org/10.1002/ejoc.201901611