Synthesis, characterization and antioxidant activity of organoselenium and organotellurium compounds derivatives of chrysin

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General Information:

The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) by using UV light, iodine vapor and 5% vanillin in 10% H_2SO_4 and heat as developing agents. ¹H NMR and ¹³C NMR spectra were recorded with a Bruker DPX 300 and 75 (300 and 75 MHz respectively) instrument using CDCl₃ as solvent and calibrated using tetramethylsilane as internal standard. Coupling constants (*J*) are reported in Hertz.

High-resolution mass spectra (HRMS) were obtained for all compounds on a LTQ Orbitrap Discovery mass spectrometer (Thermo Fisher Scientific). This hybrid system meets the LTQ XL linear ion trap mass spectrometer and an Orbitrap mass analyzer. The experiments were performed via direct infusion of sample (flow: 10 µL/min) in the positive-ion mode using electrospray ionization. Elemental composition calculations for comparison were executed using the specific tool included in the Qual Browser module of Xcalibur (Thermo Fisher Scientific, release 2.0.7) software. Mass spectra (MS) were measured on a Shimadzu GCMSQP2010 mass spectrometer. Melting point (mp) values were measured in a Marte PFD III instrument with a 0.1 °C precision.

General procedure for the synthesis of organochalcogens compounds derivatives from chrysin:

In a 25 mL two necked round-bottomed flask, equipped with a reflux condenser containing a solution of diorganyl dichalcogenide **3** (0.5 mmol) in ethanol (15 mL) under N₂ atmosphere, sodium borohydride (0.047g, 1.25 mmol) was added at room temperature under vigorous stirring. Gas evolution was observed during addition. The reaction mixture was stirred under N₂ until it became colorless. Then, the 7-bromoethoxy chrysin **2** (0.361g, 1.0 mmol) was added and the resultant mixture was refluxed (during 1.5 – 6.0 h, see Table 1) until all the starting material was transformed (followed by TLC). After that, the reaction mixture was cooled at room temperature, diluted with ethyl acetate (15 mL) and washed with water (3x 15 mL). The organic phase was separated, dried over anhydrous MgSO₄ and concentrated under vacuum. The crude products were purified by column chromatography on silica gel using initially hexanes as an eluent to remove the remaining diorganyl dichalcogenide and then a mixture of hexanes/ethyl acetate (2/8) was used to afford the desired products **4a-k**. The spectral data and physical properties of all synthesized compounds are presented below.

4.1.2.1 5-hydroxy-2-phenyl-7-(2-(phenylselanyl)ethoxy)-4H-chromen-4-one (4a)



Yield: 0.377 g (86%); white solid; mp 155 – 156 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.69 (s, 1H); 7.86–7.83 (m, 2H); 7.59–7.50 (m, 5H); 7.31–7.29 (m, 3H); 6.63 (s, 1H); 6.38 (d, J = 2.1 Hz, 1H); 6.26 (d, J = 2.1 Hz, 1H); 4.24 (t, J = 7.2 Hz, 2H); 3.23 (t, J = 7.2 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.2, 163.8, 162.0, 157.6, 133.2, 131.8, 131.1, 129.2, 129.0, 127.5, 126.2, 105.7, 98.5, 92.9, 67.9, 25.5. MS (relative intensity) m/z: 439 (M+1, 3); 438 (M⁺, 10); 281 (5); 254 (22); 185 (100); 157 (69); 77 (27). HRMS: calculated to C₂₃H₁₈O₄Se⁺ [M+H] 439.0443, found 439.0434.

4.1.2.2 5-hydroxy-2-phenyl-7-(2-(o-tolylselanyl)ethoxy)-4H-chromen-4-one (4b)



Yield: 0.321 g (71%); light yellow solid; mp 123.9 – 127.4 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.87–7.84 (m, 2H); 7.53–7.50 (m, 4H); 7.26–7.10 (m, 3H); 6.64 (s, 1H); 6.40 (d, *J* = 2.2 Hz, 1H); 6.28 (d, *J* = 2.2 Hz, 1H); 4.23 (t, *J* = 7.2 Hz, 2H); 3.21 (t, *J* = 7.2 Hz, 2H); 2.45 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 182.4, 164.2, 163.9, 162.1, 157.6, 139.9, 132.3, 131.8, 131.2, 130.2, 129.8, 129.0, 127.4, 126.7, 126.2, 105.8, 98.6, 93.0, 67.7, 24.4, 22.5. MS (relative intensity) m/z: 452 (M⁺, 7); 281 (6); 254 (28); 236 (7); 199 (90); 185 (7); 171 (65); 91 (88); 77 (11); 57 (100). HRMS: calculated to C₂₄H₂₁O₄Se⁺ [M+H] 453.0600, found 453.0615.

4.1.2.3 5-hydroxy-7-(2-((2-methoxyphenyl)selanyl)ethoxy)-2-phenyl-4*H*-chromen-4-one **(4c)**



Yield: 0.378 g (81%); grey solid; mp 132.9 – 135.6 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.65 (s, 1H); 7.85–7.82 (m, 2H); 7.51–7.44 (m, 4H); 7.25 (ddd, J = 8.1, 7.4 and 1.6 Hz, 1H); 6.91 – 6.85 (m, 2H); 6.61 (s, 1H); 6.40 (d, J = 2.2 Hz, 1H); 6.27 (d, J = 2.2 Hz, 1H); 4.26 (t, J = 7.3 Hz, 2H); 3.88 (s, 3H); 3.23 (t, J = 7.3 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.9, 164.3, 163.9, 162.2, 158.3, 157.7, 132.4, 131.7, 131.2, 128.9,

128.5, 128.6, 126.2, 121.4, 117.9, 110.8, 105.8, 105.7, 98.6, 93.1, 68.1, 55.8, 22.9. MS (relative intensity) m/z: 468 (M⁺, 6); 281 (5); 254 (9); 236 (7); 215 (44); 187 (32); 107 (33); 77 (11); 57 (100). HRMS: calculated to $C_{24}H_{21}O_5Se^+$ [M+H] 469.0549, found 469.0562.

4.1.2.4 5-hydroxy-7-(2-(mesitylselanyl)ethoxy)-2-phenyl-4H-chromen-4-one (4d)



Yield: 0.289g (60%); white/pink solid; mp 135.7–138.4 °C. ¹H NMR (300 MHz, CDCl₃) $\overline{0}$ 12.70 (s, 1H); 7.86–7.84 (m, 2H); 7.53–7.52 (m, 3H); 6.95 (s, 2H); 6.63 (s, 1H); 6.35 (d, J = 2.2 Hz, 1H); 6.23 (d, J = 2.2 Hz, 1H); 4.12 (t, J = 7.0 Hz, 2H); 2.99 (t, J = 7.0 Hz, 2H); 2.55 (s, 6H); 2.26 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) $\overline{0}$ 182.3, 164.9, 164.2, 163.9, 162.1, 157.6, 143.1, 138.6, 131.8, 131.2, 129.0, 128.6, 126.4, 126.2, 105.8, 105.7, 98.4, 93.0, 67.9, 25.2, 24.5, 20.9. MS (relative intensity) m/z: 480 (M⁺, 6); 361 (1); 281 (12); 254 (35); 227 (60); 199 (100); 119 (98); 77 (10). HRMS: calculated to C₂₆H₂₅O₄Se⁺ [M+H] 481.0913, found 481.0918.

4.1.2.5 7-(2-((4-fluorophenyl)selanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (4e)



Yield: 0.282g (62%); white solid; mp 171.1–173.7 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.87–7.84 (m, 2H); 7.59–7.53 (m, 5H); 7.07-6.97 (m, 2H); 6.64 (s, 1H); 6.36 (d, *J* = 2.2 Hz, 1H); 6.26 (d, *J* = 2.2 Hz, 1H); 4.23 (t, *J* = 7.1 Hz, 2H); 3.18 (t, *J* = 7.1 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.4, 164.3, 163.9, 162.6 (d, ¹*J*_{C-F} = 247.9 Hz), 162.1, 157.6, 136.0 (d, ³*J*_{C-F} = 8.0 Hz), 131.8, 131.1, 129.0, 126.2, 123.2 (d, ⁴*J*_{C-F} = 3.4 Hz), 116.4 (d, ²*J*_{C-F} = 21.5 Hz), 105.8 (2C), 98.5, 92.9, 67.8, 26.4. MS (relative intensity) m/z: 456 (M⁺, 12); 254 (27); 225 (13); 203 (100); 77 (11). HRMS: calculated to C₂₃H₁₈FO₄Se⁺ [M+H] 457.0349, found 457.0366.

4.1.2.6 5-hydroxy-2-phenyl-7-(2-((3-(trifluoromethyl)phenyl)selanyl)ethoxy)-4*H*-chromen-4-one **(4f)**



Yield: 0.289g (57%); white solid; mp 154.1–157.7 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.87–7.44 (m, 3H); 7.74 (d, *J* = 7.7 Hz, 1H); 7.55–7.50 (m, 4H); 7.41 (t, *J* = 7.7 Hz, 1H); 6.64 (s, 1H); 6.39 (d, *J* = 2.2 Hz, 1H); 6.27 (d, *J* = 2.2 Hz, 1H); 4.29 (t, *J* = 6.8 Hz, 2H); 3.30 (t, *J* = 6.8 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.4, 164.9, 164.0, 163.9, 162.1, 157.6, 136.0 (q, ^{*4*}*J*_{*C*-*F*} = 1.26 Hz), 131.8, 131.4 (q, ²*J*_{*C*-*F*} = 32.5 Hz), 131.1, 130.4, 129.5 (q, ³*J*_{*C*-*F*} = 3.80 Hz), 129.0, 126.2, 124.1 (q, ³*J*_{*C*-*F*} = 3.77 Hz), 123.5 (q, ¹*J*_{*C*-*F*</sup> = 272.7 Hz) 105.8, 105.7, 98.4, 93.0, 67.8, 25.9. MS (relative intensity) m/z: 506 (M⁺, 17); 281 (5); 253 (100); 225 (87); 145 (14); 77 (12); 69 (36). HRMS: calculated to C₂₄H₁₈F₃O₄Se⁺ [M+H] 507.0317, found 507.0326.}

4.1.2.77-(2-(benzylselanyl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (4g)



Yield: 0.336g (74%); green solid; mp 115.4–118.2 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.71 (s, 1H); 7.87–7.84 (m, 2H); 7.52–7.50 (m, 3H); 7.32–7.25 (m, 5H); 6.63 (s, 1H); 6.41 (d, *J* = 2.2 Hz, 1H); 6.28 (d, *J* = 2.2 Hz, 1H); 4.13 (t, *J* = 7.0 Hz, 2H); 3.89 (t, *J* = 6.7 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.2, 163.8, 162.1, 157.6, 138.8, 131.8, 131.1, 129.0, 128.8, 128.6, 126.9, 126.2, 105.7, 105.7, 98.5, 93.0, 68.7, 27.7, 21.4. MS (relative intensity) m/z: 452 (M⁺, 1); 285 (6); 255 (9); 171 (11); 77 (5); 69 (75); 55 (100). HRMS: calculated to C₂₄H₂₁O₄Se⁺ [M + H] 453.0605, found 453.0603.

4.1.2.87-(2-(butylselanyl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (4h)



Yield: 0.404g (96%); yellow solid; mp 85.9–87.8 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.88–7.85 (m, 2H); 7.53–7.50 (m, 3H); 6.64 (s, 1H); 6.47 (d, *J* = 2.2 Hz, 1H); 6.33 (d, *J* = 2.2 Hz, 1H); 4.25 (t, *J* = 7.2 Hz, 2H); 2.91 (t, *J* = 7.2 Hz, 2H); 2.69 (t, *J* = 7.4 Hz, 2H); 1.69 (qui, *J* = 7.5 Hz, 2H); 1.44 (sex, *J* = 7.5 Hz, 2H); 0.94 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.3, 163.9, 162.1, 157.7, 131.8, 131.2, 129.0, 126.2, 105.8, 105.2, 98.5, 93.0, 68.9, 32.7, 24.5, 22.9, 21.3, 13.5. MS (relative intensity) m/z: 418 (M⁺, 5); 361 (18); 254 (31); 165 (100); 77 (9). HRMS: calculated to C₂₁H₂₃O₄Se⁺ [M+H] 419.0756, found 419.0758.

4.1.2.97-(2-(butyltellanyl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (4i)



Yield: 0.327g (70%); yellow solid; mp 79.5–81.4 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.87 – 7.84 (m, 2H); 7.53 – 7.50 (m, 3H); 6.64 (s, 1H); 6.46 (d, *J* = 2.2 Hz, 1H); 6.32 (d, *J* = 2.2 Hz, 1H); 4.32 (t, *J* = 7.6 Hz, 2H); 2.96 (t, *J* = 7.6 Hz, 2H); 2.75 (t, *J* = 7.0 Hz, 2H); 1.77 (qui, *J* = 7.0 Hz, 2H); 1.40 (sex, *J* = 7.0 Hz, 2H); 0.93 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.2, 163.8, 162.1, 157.6, 131.8, 131.1, 129.0, 126.2, 105.7, 105.7, 98.6, 93.0, 70.8, 34.3, 25.0, 13.4, 3.6. MS (relative intensity) m/z: 468 (M⁺, 3); 411 (19); 254 (100); 215 (8); 187 (11); 77 (9); 57 (93). HRMS: calculated to C₂₁H₂₃O₄Te⁺ [M+H] 469.0653, found 469.0554.

4.1.2.10 5-hydroxy-2-phenyl-7-(2-(phenyltellanyl)ethoxy)-4H-chromen-4-one (4)



Yield: 0.407 g (87%); yellow solid; mp 128–129 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.69 (s, 1H); 7.86–7.79 (m, 4H); 7.53–7.50 (m, 3H); 7.33–7.21 (m, 3H); 6.63 (s, 1H); 6.37 (d, J = 2.2 Hz, 1H); 6.26 (d, J = 2.2 Hz, 1H); 4.34 (t, J = 7.6 Hz, 2H); 3.19 (t, J = 7.6= Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.1, 163.8, 162.0, 157.7, 138.8, 131.8, 131.1, 129.3, 129.0, 128.1, 126.2, 105.7, 105.6, 98.6, 93.0, 69.9, 5.9. MS (relative intensity) m/z: 488 (M⁺, 5); 330 (100); 254 (35); 207 (46); 77 (81). HRMS: calculated to C₂₃H₁₉O₄Te⁺ [M+H] 488.0267, found 488.0274.

4.1.2.11 7-(2-((4-chlorophenyl)tellanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one **(4k)**



Yield: 0.297g (57%); yellow solid; mp 140.3–143 °C. ¹H NMR (300 MHz, CDCl₃) δ 12.70 (s, 1H); 7.87–7.84 (m, 2H); 7.71 (d, *J* = 8.4 Hz, 2H); 7.53–7.51 (m, 3H); 7.20 (d, *J* = 8.4 Hz, 2H); 6.64 (s, 1H); 6.38–6.37 (d, *J* = 2.4 Hz, 2H); 6.27–6.26 (d, *J* = 2.1 Hz, 2H); 4.34 (t, *J* = 7.5 Hz, 2H); 3.19 (t, *J* = 7.5 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 182.3, 164.9, 164.0, 163.9, 162.1, 157.6, 140.2, 134.8, 131.8, 131.1, 129.6, 129.0, 126.2, 108.1, 105.8, 98.5, 93.1, 69.7, 6.5. MS (relative intensity) m/z: 522 (M⁺, 6); 364 (100); 281 (6); 254 (32); 241 (41); 237 (19); 111 (19); 77 (12). HRMS: calculated to C₂₃H₁₈ClO₄Te⁺ [M+H] 522.9950, found 522.9766.

HRMS of Compounds 4a-k



High Resolution Mass Spectrum (ESI-FTMS) of compound 4a. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4b. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4c. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4d. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4e. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4f. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4g. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4h. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4i. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4j. (Superior: Experimental and Inferior Calculated).



High Resolution Mass Spectrum (ESI-FTMS) of compound 4k. (Superior: Experimental and Inferior Calculated).

¹H and ¹³C NMR Spectra of compounds 4a-k.



¹H NMR (300 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(phenylselanyl)ethoxy)-4H-chromen-4-one (**4a**)



¹³C NMR (75 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(phenylselanyl)ethoxy)-4H-chromen-4-one (**4a**).



¹H NMR (300 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(*o*-tolylselanyl)ethoxy)-4*H*-chromen-4-one (**4b**).



 ^{13}C NMR (75 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(o-tolylselanyl)ethoxy)-4H-chromen-4-one (**4b**).



¹H NMR (300 MHz, $CDCl_3$) spectrum of 5-hydroxy-7-(2-((2-methoxyphenyl)selanyl)ethoxy)-2-phenyl-4*H*-chromen-4-one (**4c**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 5-hydroxy-7-(2-((2 methoxyphenyl)selanyl)ethoxy)-2-phenyl-4*H*-chromen-4-one (**4c**).



 1 H NMR (300 MHz, CDCl₃) spectrum of 5-hydroxy-7-(2-(mesitylselanyl)ethoxy)-2-phenyl-4*H*-chromen-4-one (**4d**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 5-hydroxy-7-(2-(mesitylselanyl)ethoxy)-2-phenyl-4*H*-chromen-4-one (**4d**).



¹H NMR (300 MHz, CDCl₃) spectrum of 7-(2-((4-fluorophenyl)selanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4e**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 7-(2-((4-fluorophenyl)selanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4e**).



¹H NMR (300 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-((3-(trifluoromethyl)phenyl)selanyl)ethoxy)-4*H*-chromen-4-one (**4f**).



(trifluoromethyl)phenyl)selanyl)ethoxy)-4*H*-chromen-4-one (**4f**).



¹H NMR (300 MHz, CDCl₃) spectrum of 7-(2-(benzylselanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4g**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 7-(2-(benzylselanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4g**).



¹H NMR (300 MHz, CDCl₃) spectrum of 7-(2-(butylselanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4h**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 7-(2-(butylselanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4h**).



¹H NMR (300 MHz, CDCl₃) spectrum of 7-(2-(butyltellanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4i**).



¹³C NMR (75 MHz, CDCl₃) spectrum of 7-(2-(butyltellanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4i**).



¹H NMR (300 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(phenyltellanyl)ethoxy)-4H-chromen-4-one (**4j**)



¹³C NMR (75 MHz, CDCl₃) spectrum of 5-hydroxy-2-phenyl-7-(2-(phenyltellanyl)ethoxy)-4*H*-chromen-4-one (**4j**).



¹H NMR (300 MHz, CDCl₃) spectrum of **7-(2-((4-chlorophenyl)tellanyl)ethoxy)-5-hydroxy-2-phenyl-4***H***-chromen-4-one (4k)**.



¹³C NMR (75 MHz, CDCl₃) spectrum of 7-(2-((4-chlorophenyl)tellanyl)ethoxy)-5-hydroxy-2-phenyl-4*H*-chromen-4-one (**4k**).