

Polyethylene Glycol-400/H₃PO₂: An Eco-Friendly Reductive System for the Synthesis of Selanylesters

G. Perin,* M. B. Silveira, A. M. Barcellos, R. G. Jacob and D. Alves*

Laboratório de Síntese Orgânica Limpa - LASOL - Universidade Federal de Pelotas - UFPel

Box 354, 96010-900, Pelotas - RS – Brazil; Tel: +55 (53) 3275-7533.

e-mail: gelson_perin@ufpel.edu.br and diego.alves@ufpel.edu.br

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General Information

The reactions were monitored by thin layer chromatography (TLC) was performed using Merck silica gel (60 F₂₅₄), 0.25 mm thickness. For visualization, TLC plates were either placed under UV light, or stained with iodine vapor, or and 5% vanillin in 10% H₂SO₄ and heat. Column chromatography was performed using Merck Silica Gel (230-400 mesh). High resolution mass spectra (HRMS) were recorded on a Bruker Micro TOF-QII spectrometer 10416. Low-resolution mass spectra (MS) were measured on a Shimadzu GC-MS-QP2010 mass spectrometer. NMR spectra were recorded with Bruker DPX (¹H NMR = 300 and 400 MHz; ¹³C NMR = 75 and 100 MHz) instruments using CDCl₃ as solvent and calibrated using tetramethylsilane (TMS) as internal standard. Coupling constants (*J*) are reported in Hertz and chemical shift (δ) in ppm. The reagents (4-bromobenzoyl chloride, trimethylacetyl chloride, hypophosphorous acid solution, 50 wt.% in H₂O and PEG-400) were purchased from Sigma-Aldrich.

General Procedure for the Synthesis of selenoesters 3a-l

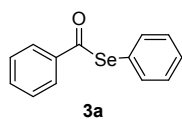
To a 10.0 mL round-bottomed flask containing a solution of diorganyl diselenide **1a-f** (0.6 mmol) in PEG-400 (3.0 mL) under N₂ atmosphere, was added H₃PO₂ 50 wt% in H₂O (0.5 mL). The resulting solution was stirred for 0.5 hour at room temperature, when its color changes from yellow to colorless. After this time, the corresponding acyl chloride **2a-g** (1.0 mmol) was added and the mixture was stirred at room temperature for the time indicated in Table 2. The reactions were monitored by TLC until total disappearance of the starting materials. After that, the reaction mixture was received in water (50.0 mL), extracted with ethyl acetate (3x 15.0 mL), dried over MgSO₄, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using hexane as the eluent. All the compounds were properly characterized by melting point, MS, ¹H NMR and ¹³C NMR.

General procedure for the reuse of PEG-400

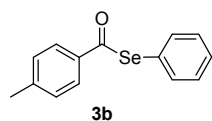
The aforementioned procedure was used with diphenyl diselenide **1a** (0.60 mmol), H₃PO₂ 50 wt% in H₂O (0.5 mL), benzoyl chloride **2a** (1.0 mmol) and PEG-400 (3.0 mL). After

the reaction was complete, the reaction mixture was washed with a mixture of hexane/ethyl acetate (90:10) (3x 15.0 mL) and the upper organic phases were separated from PEG-400. The product was isolated according procedure above. The resulting PEG-400 phase was dried under vacuum and reused for further reactions without previous purification. For the best performance of recycling experiments, it was necessary the addition of 0.5 mL of H₃PO₂ in each successive runs.

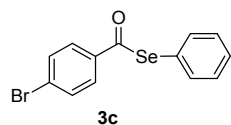
Compound Characterization



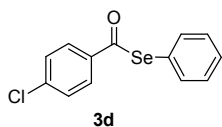
Se-phenyl benzoselenoate **3a**: Yield: 0.231 g (88%); yellow solid; mp 38-40 °C (37-38 °C).¹ ¹H NMR (CDCl₃, 300 MHz) δ = 7.90-7.93 (m, 2H), 7.55-7.60 (m, 3H), 7.38-7.47 (m, 5H). ¹³C NMR (CDCl₃, 75 MHz) δ = 193.201, 138.39, 136.23, 133.79, 129.27, 129.96, 128.84, 127.23, 125.69. MS *m/z* (rel. int. %): 262 (M⁺, 1.4), 157 (3.8), 105 (100.0), 77 (54.4).



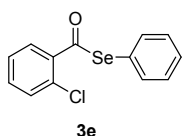
Se-phenyl 4-methylbenzoselenoate **3b**: Yield: 0.204 g (74%); white solid; mp 96-98 °C (97-98°C).² ¹H NMR (CDCl₃, 300 MHz) δ = 7.82 (d, *J* = 8.1 Hz, 2H), 7.55-7.61 (m, 2H), 7.38-7.43 (m, 3H), 7.25 (d, *J* = 8.1 Hz, 2H), 2.39 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ = 192.64, 144.83, 136.28, 135.89, 129.52, 129.24, 128.89, 127.37, 125.83, 21.70. MS *m/z* (rel. int. %): 276 (M⁺, 0.4), 157 (2.7), 119 (100.0), 91 (46.8), 77 (5.8).



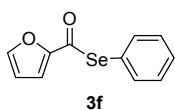
Se-phenyl 4-bromobenzoselenoate **3c**: Yield: 0.275 g (81%); white solid; mp 95-98 °C. ¹H NMR (CDCl₃, 300 MHz) δ = 7.77 (d, *J* = 8.7 Hz, 2H), 7.61 (d, *J* = 8.7 Hz, 2H), 7.54-7.60 (m, 2H), 7.38-7.45 (m, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ = 192.41, 137.20, 136.20, 132.17, 129.39, 129.18, 128.92, 128.64, 125.34. MS *m/z* (rel. int. %): 340 (M⁺, 2.0), 183 (100.0), 157 (35.5), 76 (25.8).³



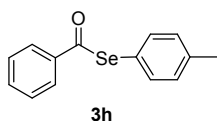
Se-phenyl 4-chlorobenzoselenoate **3d**: Yield: 0.222 g (75%); white solid; mp 83-85 °C (85-87 °C).² ¹H NMR (CDCl₃, 300 MHz) δ = 7.85 (d, *J* = 8.8 Hz, 2H), 7.55-7.59 (m, 2H), 7.39-7.46 (m, 5H). ¹³C NMR (CDCl₃, 75 MHz) δ = 192.17, 140.21, 136.77, 136.21, 129.39, 129.19, 129.17, 128.56, 125.38. MS *m/z* (rel. int. %): 296 (M⁺, 1.8), 156 (5.7), 139 (100.0), 111 (37.6), 77 (10.4).



Se-phenyl 2-chlorobenzoselenoate **3e**: Yield: 0.210 g (71%); white solid; mp 59-62 °C (59 °C).¹ ¹H NMR (CDCl₃, 300 MHz) δ = 7.72-7.75 (m, 1H), 7.57-7.63 (m, 2H), 7.32-7.46 (m, 6H). ¹³C NMR (CDCl₃, 75 MHz) δ = 193.14, 138.39, 135.85, 132.55, 131.02, 130.01, 129.42, 129.17, 128.91, 126.77, 126.54. MS *m/z* (rel. int. %): 296 (M⁺, 0.7), 157 (5.5), 141 (32.3), 139 (100), 113 (10.9), 111 (33.5), 77 (9.8), 75 (16.9).

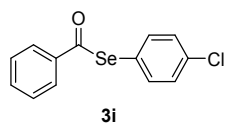


Se-phenyl furan-2-carboselenoate **3f**: Yield: 0.204 g (81%); pale yellow solid; mp 59-62 °C (61-63 °C).^{2,4} ¹H NMR (CDCl₃, 400 MHz) δ = 7.47-7.50 (m, 3H), 7.29-7.30 (m, 3H), 7.08-7.09 (m, 1H), 6.43-6.45 (m, 1H). ¹³C NMR (CDCl₃, 100 MHz) δ = 180.57, 151.58, 146.54, 136.20, 129.23, 129.01, 124.66, 115.17, 112.71. MS *m/z* (rel. int. %): 252 (M⁺, 7.0), 157 (4.3), 95 (100.0), 77 (8.5), 67 (6.4).

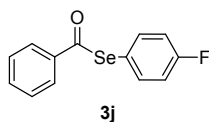


Se-(*p*-tolyl) benzoselenoate **3h**: Yield: 0.166 g (60%); yellow solid; mp 72-74 °C (72-73 °C).⁵ ¹H NMR (CDCl₃, 400 MHz) δ = 7.91 (d, *J* = 8.4 Hz, 2H), 7.53-7.58 (m, 1H), 7.40-7.47 (m, 4H), 7.20 (d, *J* = 8.4 Hz, 2H), 2.36 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ = 193.54, 139.07, 138.56,

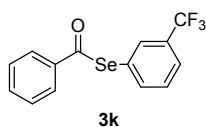
136.18, 133.67, 130.14, 128.80, 127.21, 122.16, 21.24. MS m/z (rel. int. %): 276 (M^+ , 2.0), 171 (2.7), 105 (100.0), 91 (10.1), 77 (43.3).



Se-(4-chlorophenyl) benzoselenoate **3i**: Yield: 0.269 g (91%); pale yellow solid; mp 82-84 °C (84-85 °C).¹ ^1H NMR (CDCl_3 , 400 MHz) δ = 7.79 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.33-7.40 (m, 4H), 7.26 (d, J = 8.4 Hz, 2H). ^{13}C NMR (CDCl_3 , 100 MHz) δ = 192.54, 138.18, 137.49, 135.46, 133.97, 129.50, 128.93, 127.29, 123.95. MS m/z (rel. int. %): 296 (M^+ , 0.3), 191 (2.2), 112 (0.8), 105 (100.0), 77 (51.0).



Se-(4-fluorophenyl) benzoselenoate **3j**: Yield: 0.260 g (93%); yellow solid; mp 52-54 °C (51 °C).⁶ ^1H NMR (CDCl_3 , 400 MHz) δ = 7.84 (d, J = 7.5 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.47 (dd, J = 8,7 and 5,4 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.03 (t, J = 8.7 Hz, 2H). ^{13}C NMR (CDCl_3 , 100 MHz) δ = 193.15, 163.44 (d, J = 249.3 Hz), 138.35, 138.32 (d, J = 8.3 Hz), 133.97, 128.97, 127.34, 120,60 (d, J = 3.4 Hz), 116,65 (d, J = 21.7 Hz). MS m/z (rel. int. %): 280 (M^+ , 0.6), 174 (4.0), 154 (0.6), 105 (100.0), 77 (54.7).

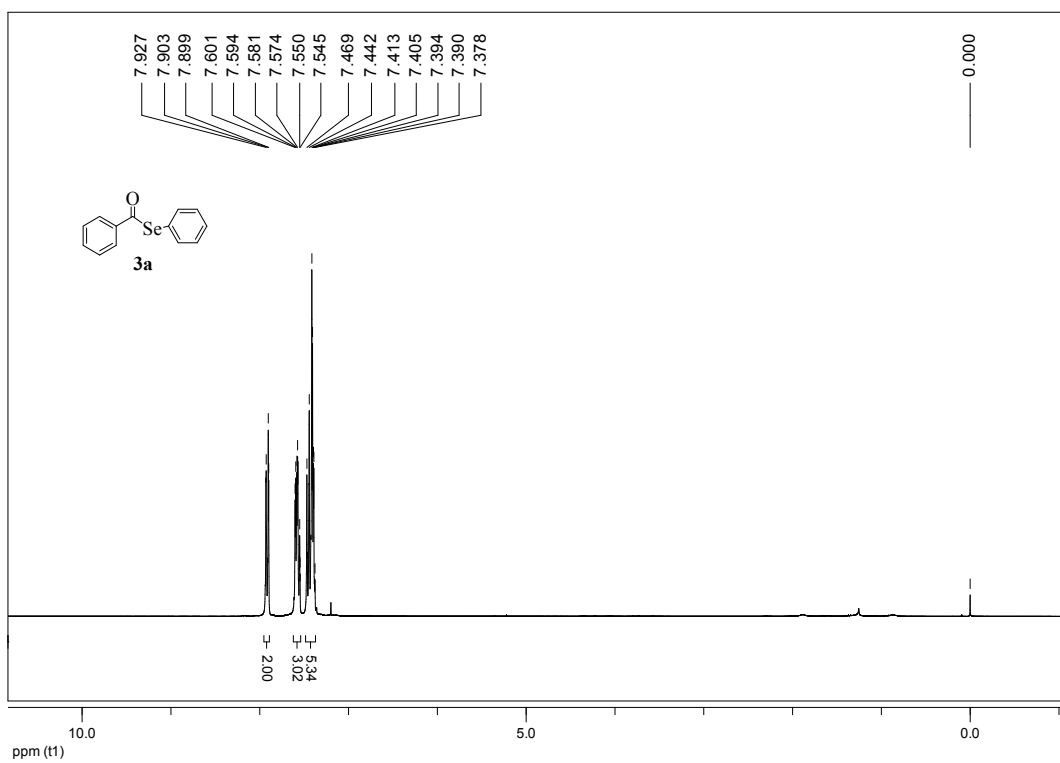


Se-(3-(trifluoromethyl)phenyl) benzoselenoate **3k**: Yield: 0.317 g (96%); white solid; mp 51-53 °C. ^1H NMR (CDCl_3 , 400 MHz) δ = 7.76-7.83 (m, 2H), 7.79 (s, 1H) 7.67-7.71 (m, 1H), 7.53-7.61 (m, 2H), 7.40-7.47 (m, 3H). ^{13}C NMR (CDCl_3 , 100 MHz) δ = 192.00, 139.66, 138.19, 134.18, 132.91 (d, J = 3.7 Hz), 131.66 (d, J = 32.7 Hz), 129.56, 129.07, 127.43, 126.93, 125.80 (d, J = 3.8 Hz), 123.70 (d, J = 272,8 Hz). MS m/z (rel. int. %): 330 (M^+ , 0.1), 225 (3.4), 156 (0.8), 105 (100.0), 77 (53.2). HRMS-ESI m/z calcd for $\text{C}_{14}\text{H}_9\text{F}_3\text{OSe}+\text{H}^+$ 330,9849, found 330,9838.

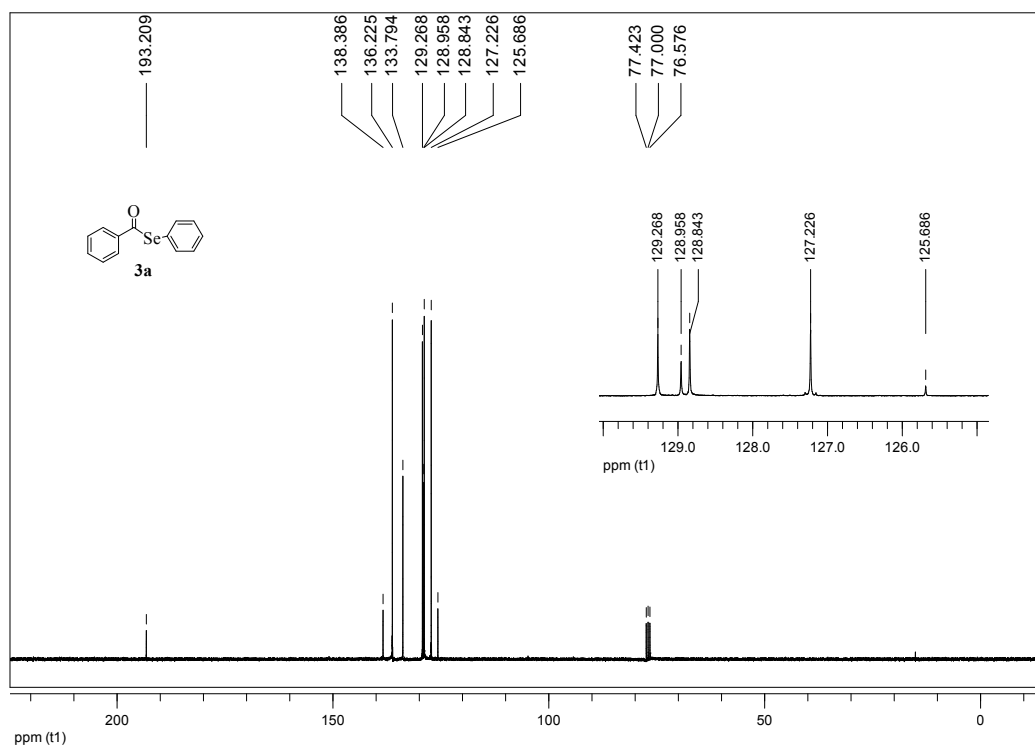
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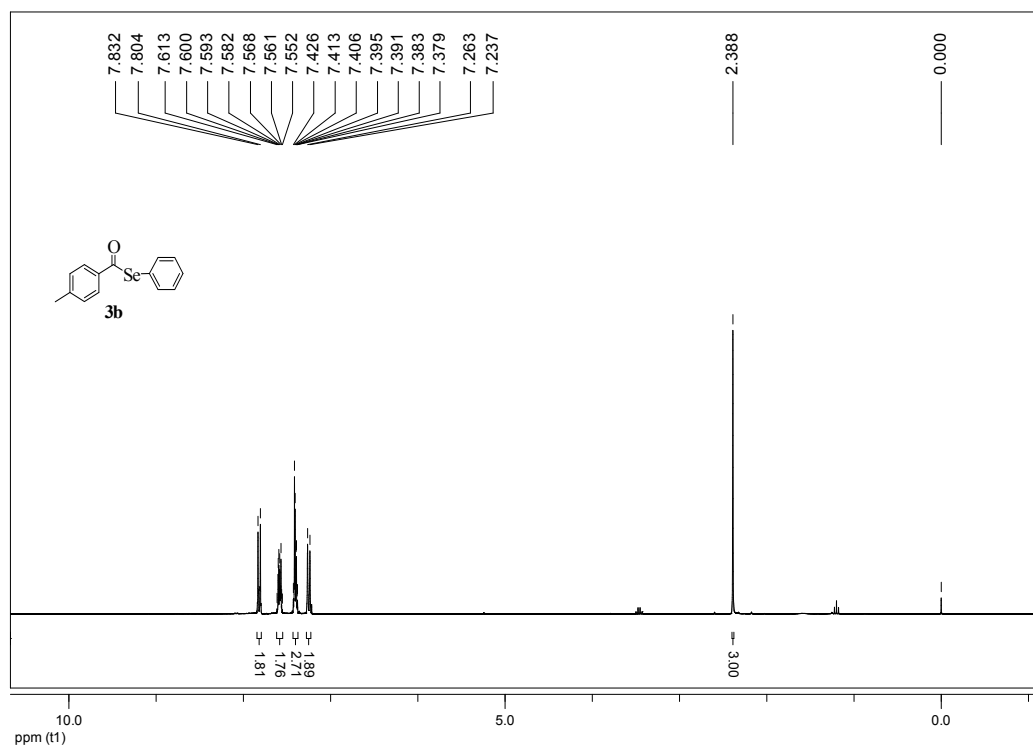
SELECTED SPECTRA



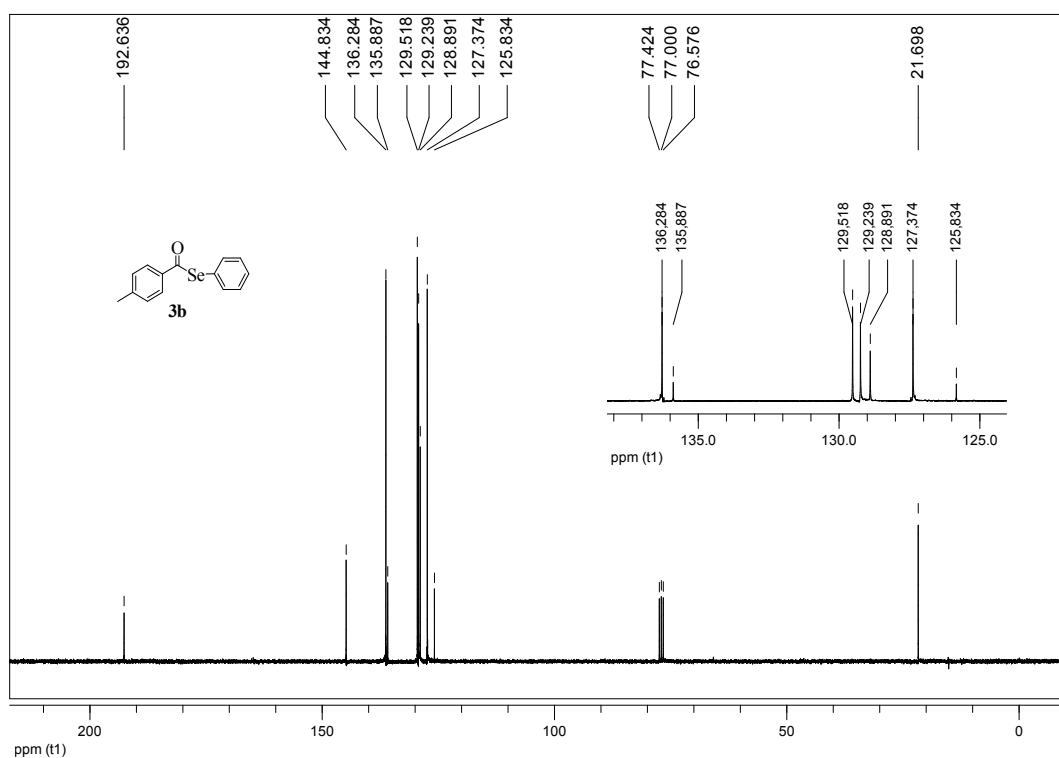
¹H NMR (300 MHz, CDCl₃) spectrum of *Se-phenyl benzoselenoate 3a*



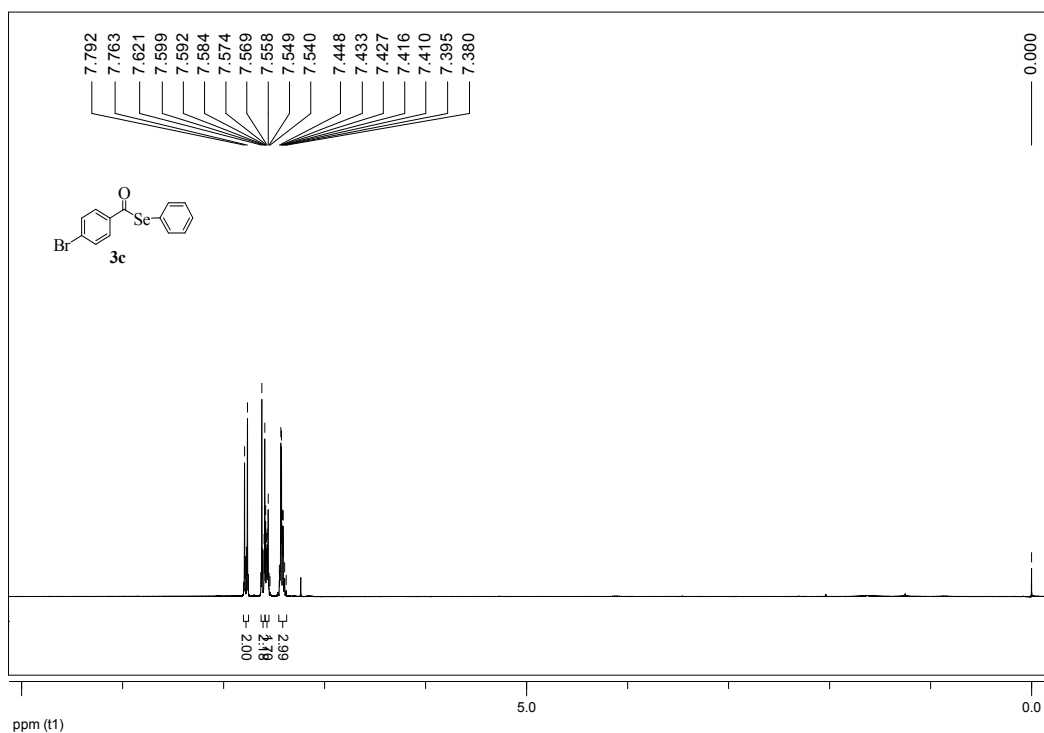
¹³C NMR (75 MHz, CDCl₃) spectrum of *Se-phenyl benzoselenoate 3a*



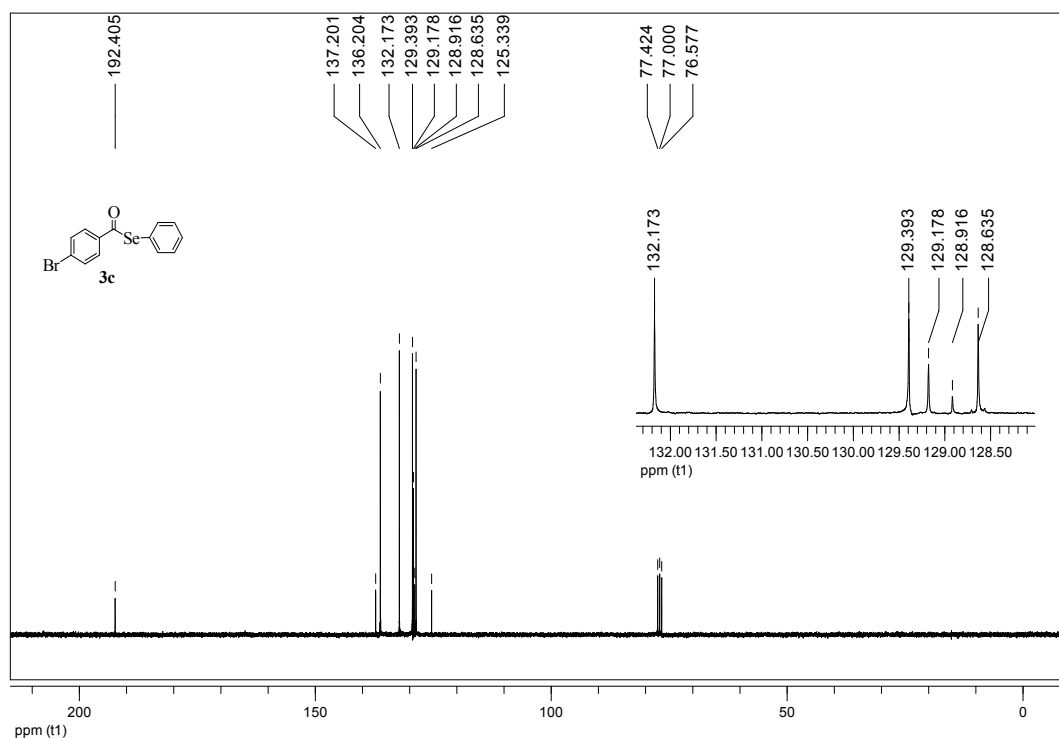
¹H NMR (300 MHz, CDCl₃) spectrum of *Se-phenyl 4-methylbenzoselenoate 3b*



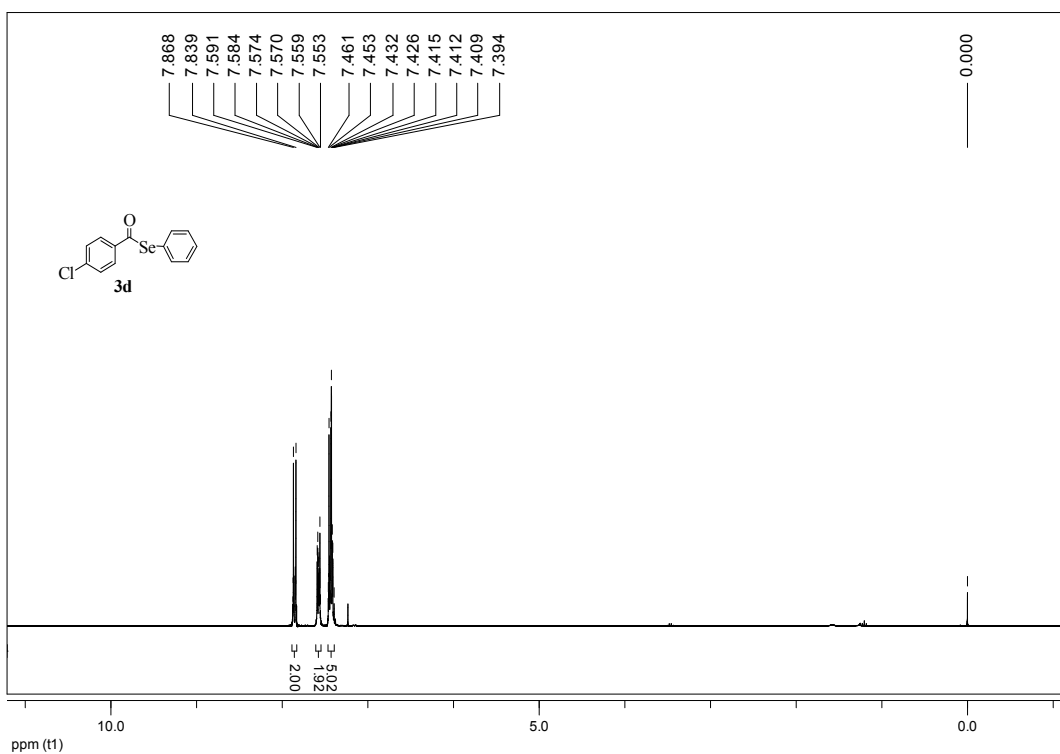
¹³C NMR (75 MHz, CDCl₃) spectrum of *Se-phenyl 4-methylbenzoselenoate 3b*



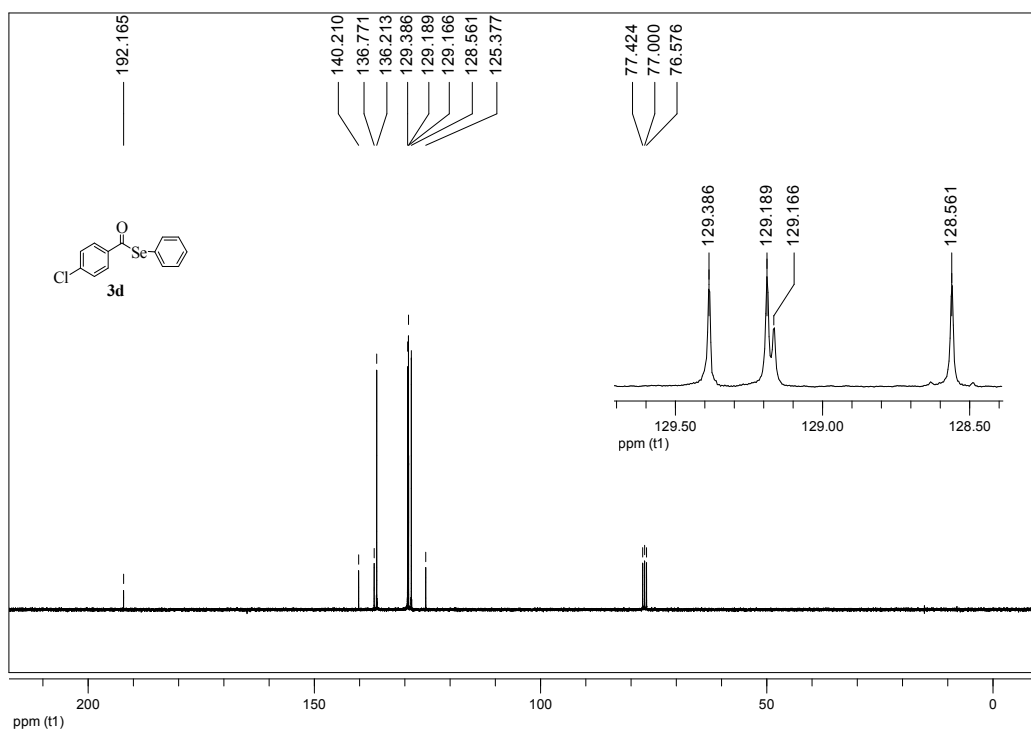
¹H NMR (300 MHz, CDCl₃) spectrum of *Se-phenyl 4-bromobenzoselenoate 3c*



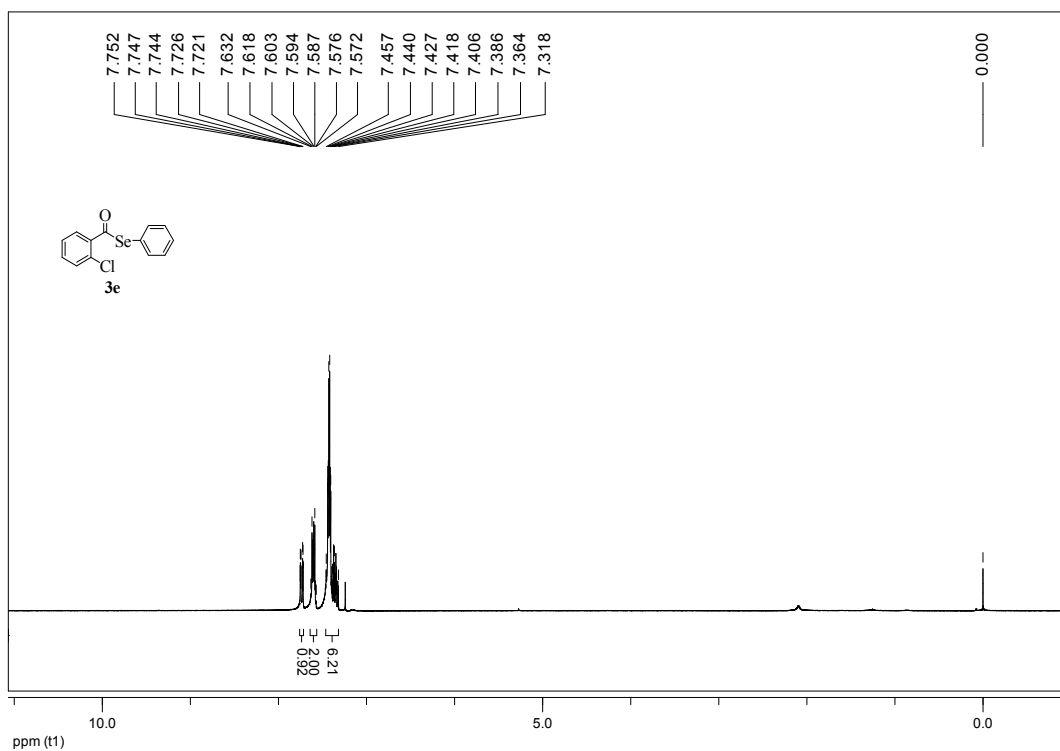
¹³C NMR (75 MHz, CDCl₃) spectrum of *Se-phenyl 4-bromobenzoselenoate 3c*



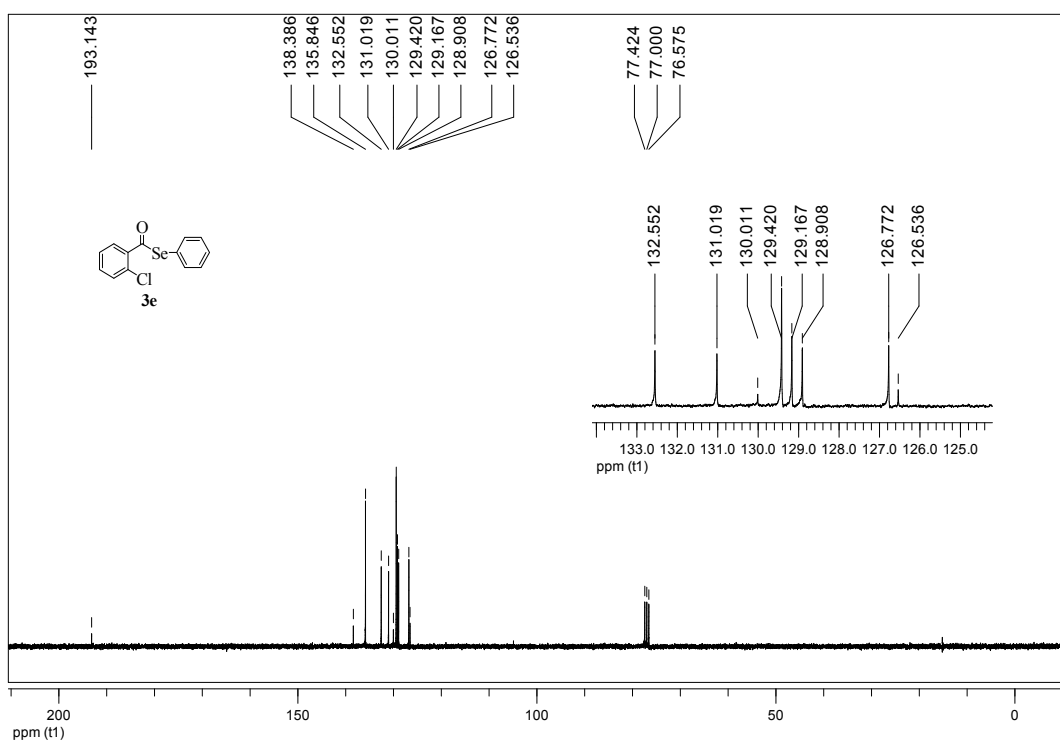
¹H NMR (300 MHz, CDCl₃) spectrum of *Se-phenyl 4-chlorobenzoselenoate 3d*



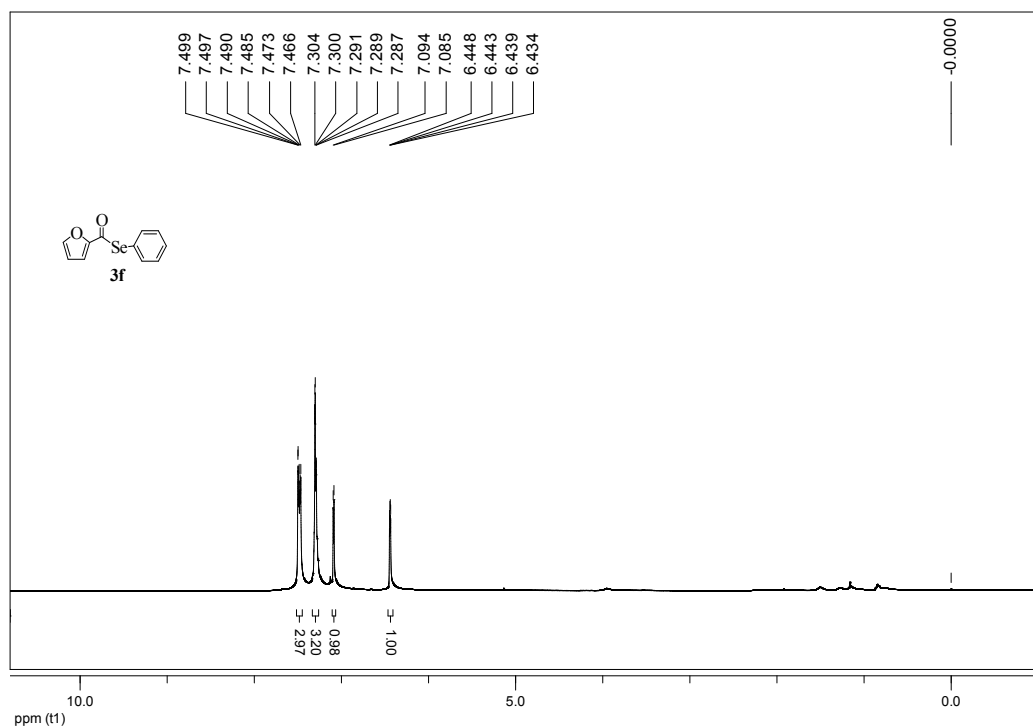
¹³C NMR (75 MHz, CDCl₃) spectrum of *Se-phenyl 4-chlorobenzoselenoate 3d*



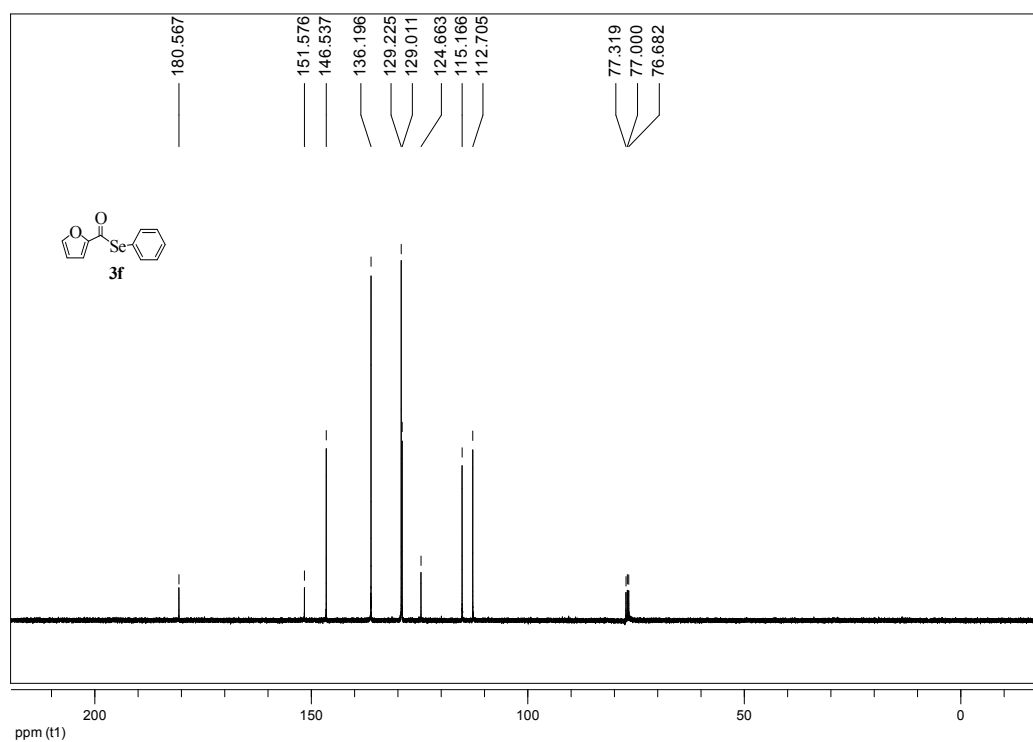
¹H NMR (300 MHz, CDCl₃) spectrum of *Se-phenyl 2-chlorobenzoselenoate 3e*



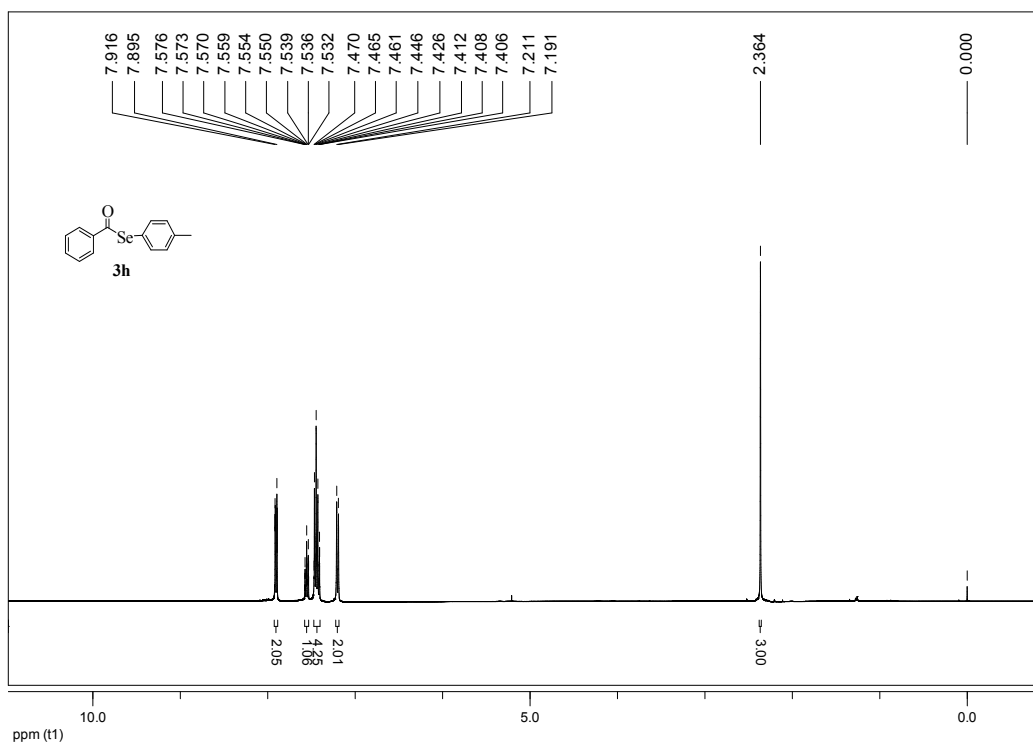
¹³C NMR (75 MHz, CDCl₃) spectrum of *Se-phenyl 2-chlorobenzoselenoate 3e*



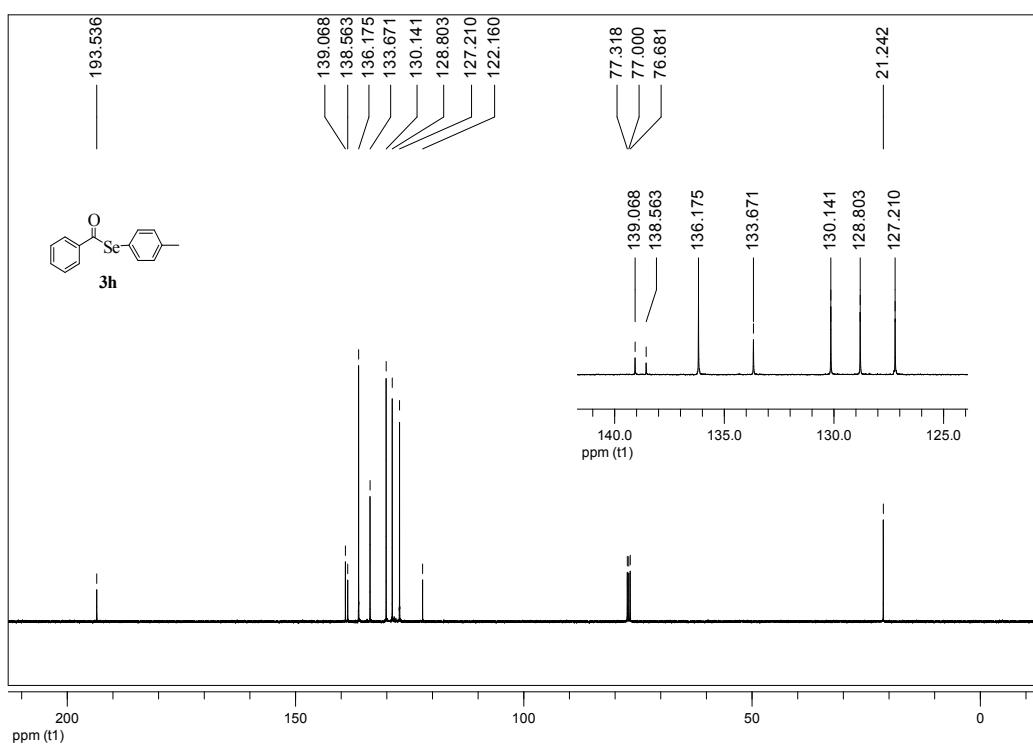
^1H NMR (400 MHz, CDCl_3) spectrum of *Se-phenyl furan-2-carboselenoate 3f*



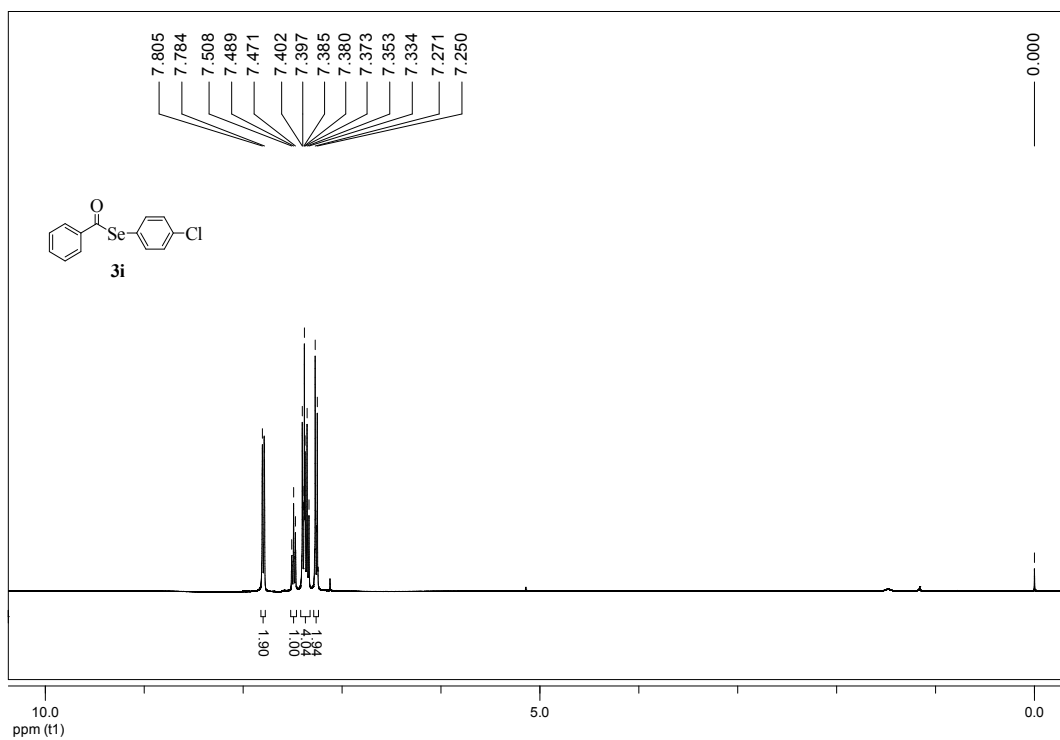
^{13}C NMR (100 MHz, CDCl_3) spectrum of *Se-phenyl furan-2-carboselenoate 3f*



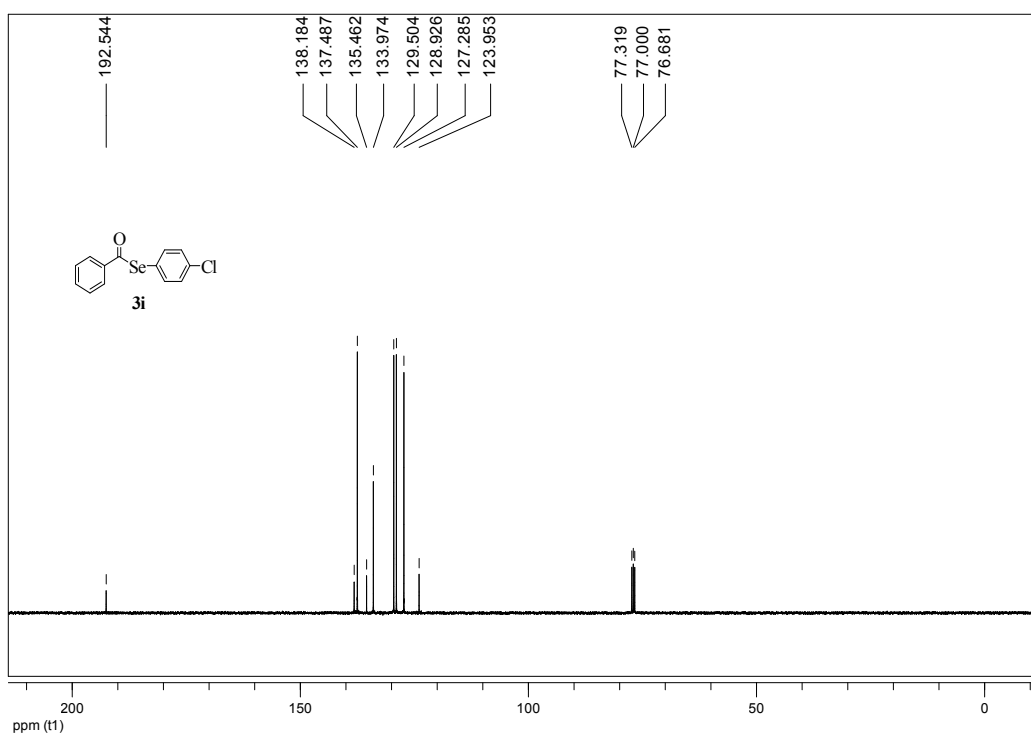
¹H NMR (400 MHz, CDCl₃) spectrum of *Se*-(*p*-tolyl) benzoselenoate **3h**



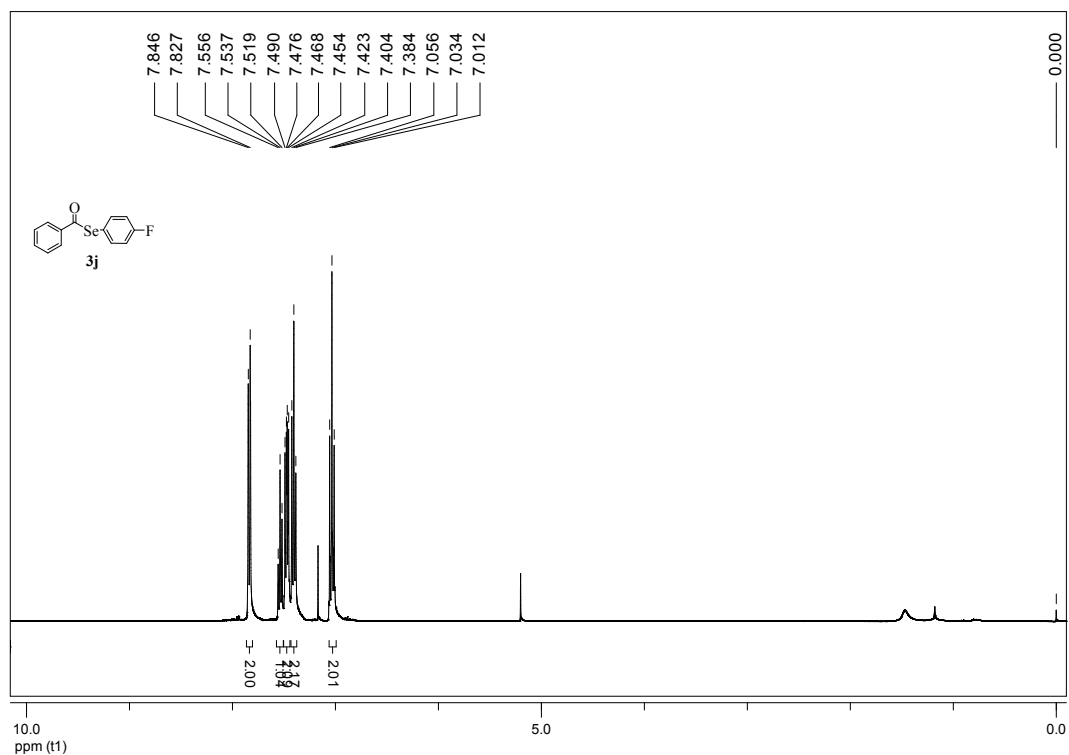
¹³C NMR (100 MHz, CDCl₃) spectrum of *Se*-(*p*-tolyl) benzoselenoate **3h**



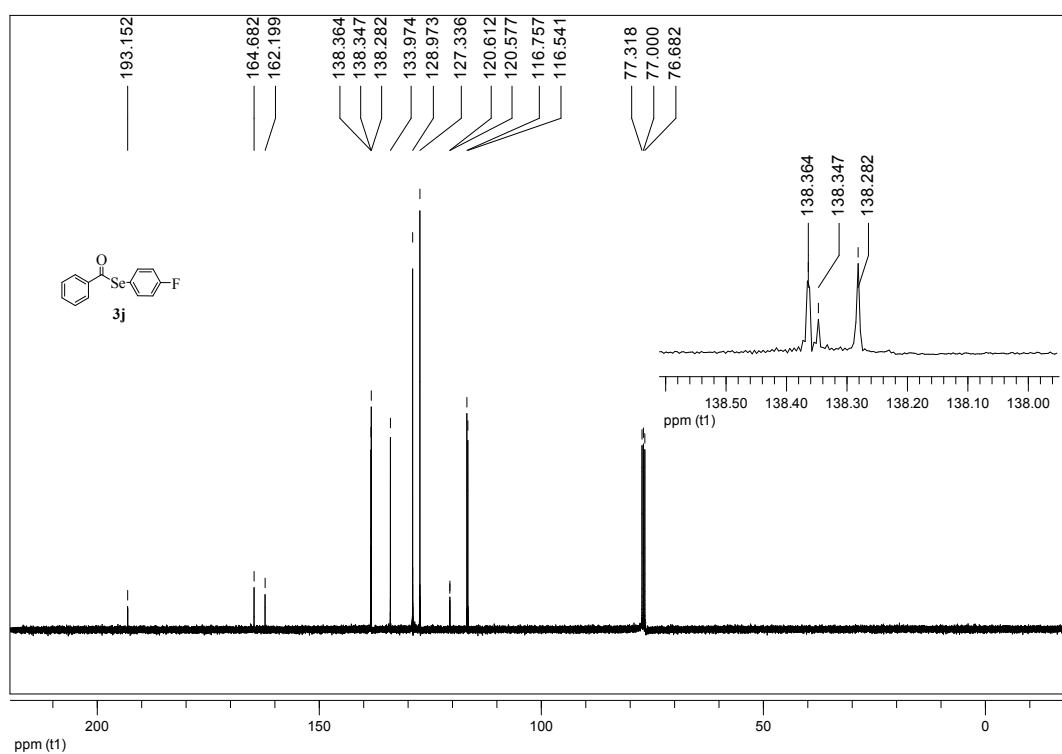
¹H NMR (400 MHz, CDCl₃) spectrum of *Se*-(4-chlorophenyl) benzoselenoate **3i**



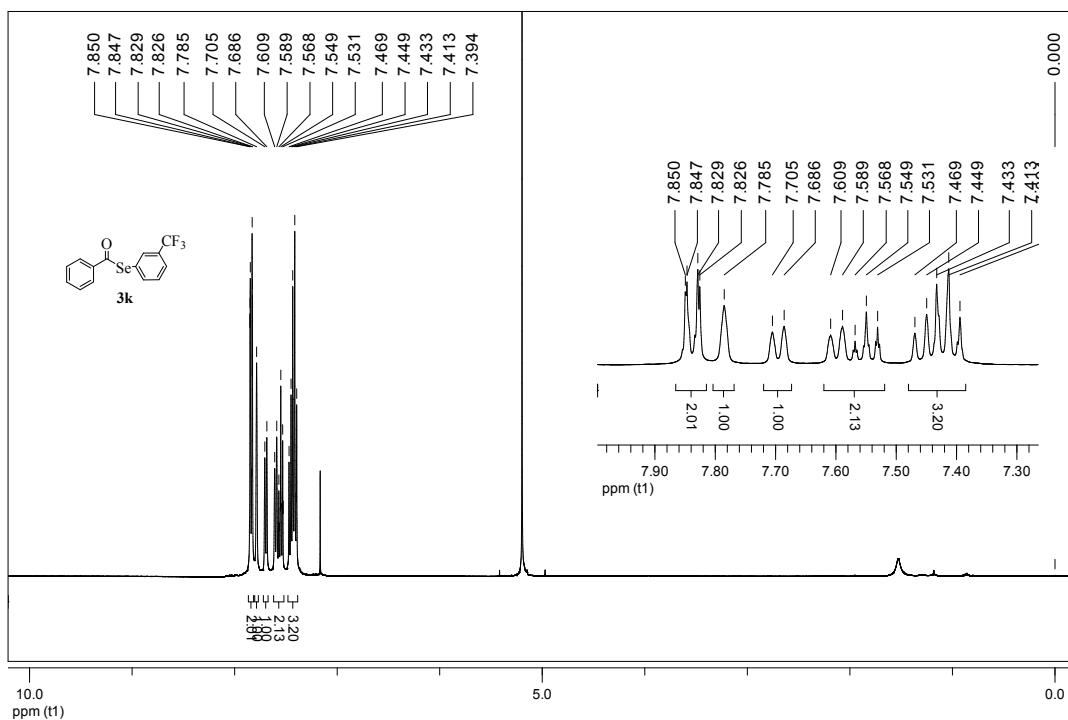
¹³C NMR (100 MHz, CDCl₃) spectrum of *Se*-(4-chlorophenyl) benzoselenoate **3i**



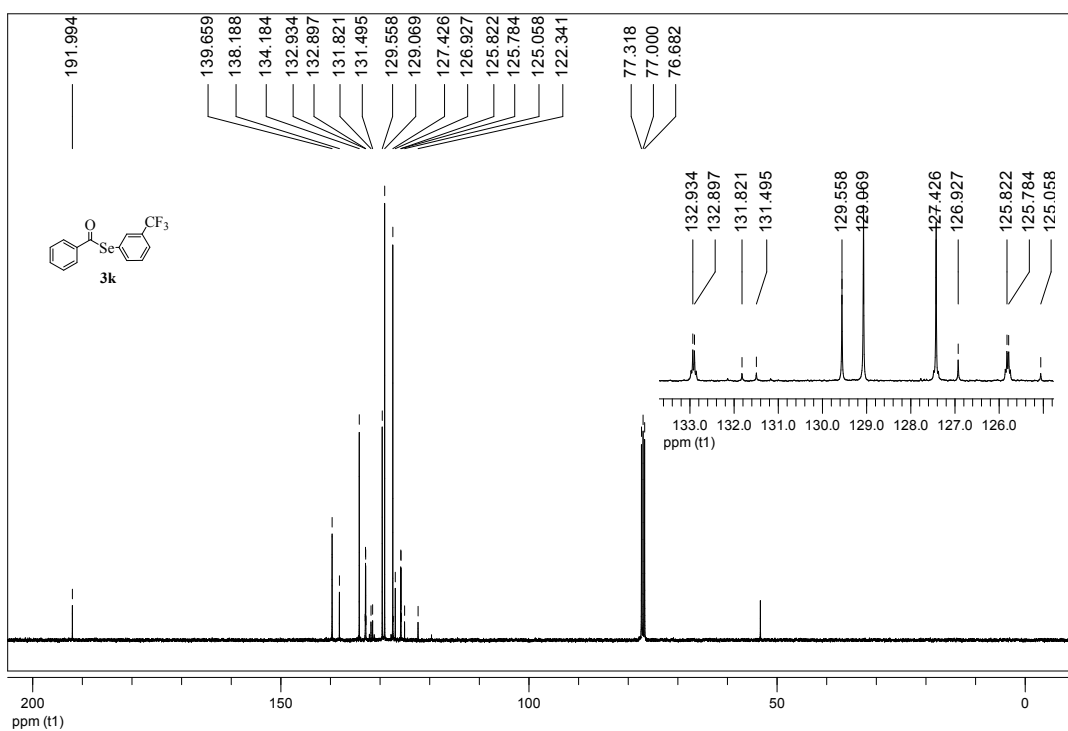
¹H NMR (400 MHz, CDCl₃) spectrum of *Se*-(4-fluorophenyl) benzoselenoate **3j**



¹³C NMR (100 MHz, CDCl₃) spectrum of *Se*-(4-fluorophenyl) benzoselenoate **3j**



¹H NMR (400 MHz, CDCl₃) spectrum of *Se*-(3-(trifluoromethyl)phenyl) benzoselenoate **3k**



¹³C NMR (100 MHz, CDCl₃) spectrum of *Se*-(3-(trifluoromethyl)phenyl) benzoselenoate **3k**