

Supplementary Information

One Pot Synthesis of Selenocysteine Containing Peptoid Libraries by Ugi Multicomponent Reactions in Water

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Procedure for synthesis of **2a** and **2b**

At 0 °C, to 15 mmol of diselenoacetal **1** (prepared by a procedure similar to that reported by Krief et al.)¹¹ in 100 ml ethanol, 40 mmol NaBH₄ are slowly added in portions during 30 min until the solution turns clear or slightly yellow. The mixture is warmed to 25 °C for 30 min and recooled to 0 °C, whereupon 28 mmol of electrophile (MeI or BnBr) are added. The solution is stirred at room temperature for 2 h (MeI) or heated to 58 °C for 4 h (BnBr). The reaction mixture is filtered, the solvent evaporated, the residue dissolved in water, and extracted with diethylether. The organic layer is dried over Na₂SO₄ and the solvent is evaporated. The residue is chromatographed on silica gel (petrol ether : ethyl acetate = 10 : 1 or 20 : 1) to yield 89% and 84% of **2a** and **2b**, respectively.

Procedure for microwave assisted selenopeptoid syntheses:

Microwave reactions were performed in single-mode Emrys Synthesizer (Personal Chemistry) operating at 2.45 GHz with continuous microwave irradiation (0 to 300 W) in a pressure resistant glass tube (10 mL) sealed with Teflon septa and aluminium crimp provided with magnetic stirring bar. Temperature is measured with an IR sensor on the outer surface of the process vial and was set to 160 °C. The software regulates the microwave output power so as to maintain the selected temperature. “Fixed hold time” options allows the time countdown to start when the target temperature is reached, i.e. the initial time taken to reach the target temperature is not included in the heating time. Three levels of absorption are available (“Normal”, “High” and “Very High” sample/solvent absorption). In case of high ionic content or with water, “High” or “Very High” absorption level presetting is recommended as in such cases energy is applied at a lower rate to the reaction mixture in order to maintain a well-controlled rate of temperature increase.

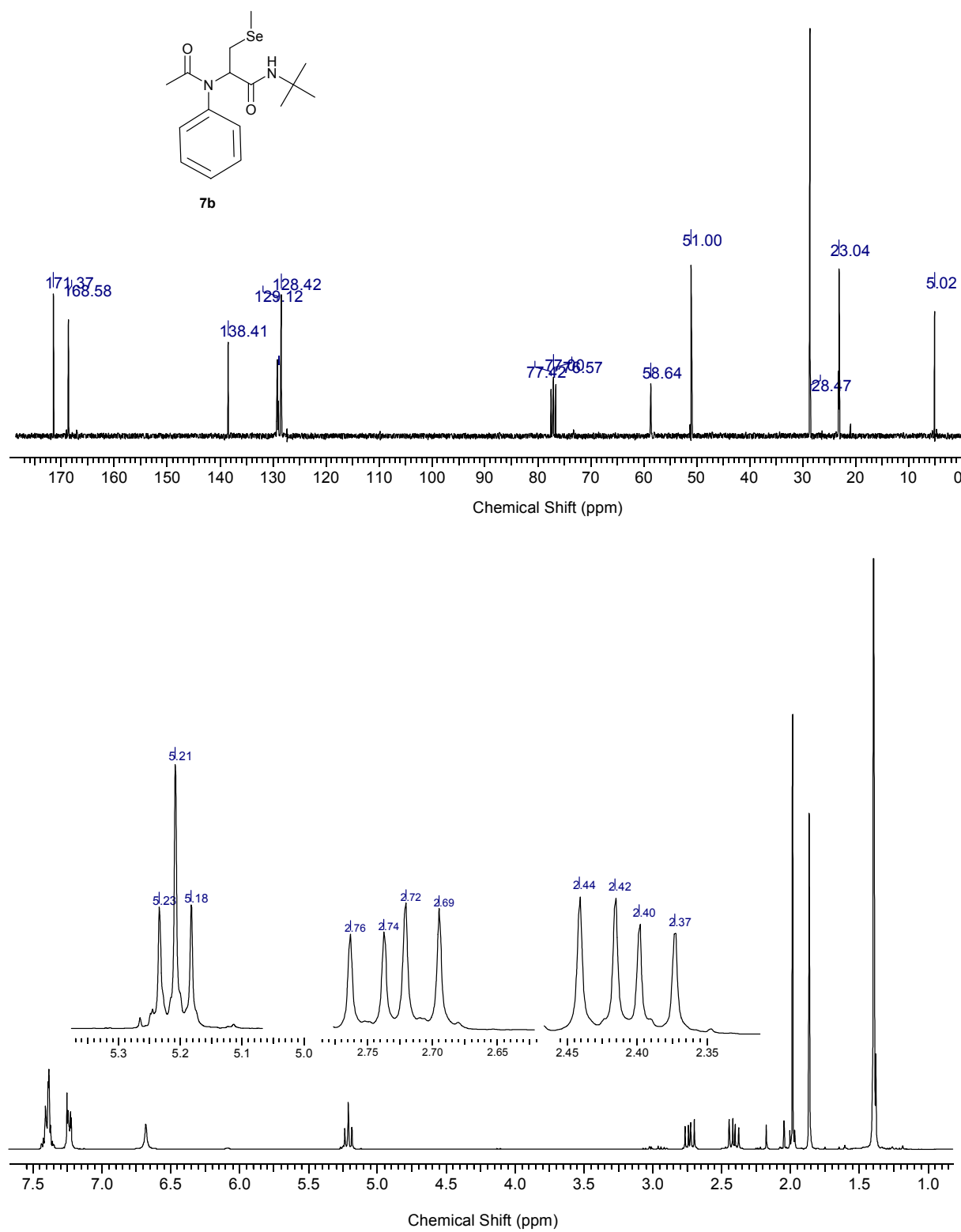
Typically, in a closed 10 ml vessel 1 mmol selenenylaldehyde **3a** or **3c**, 1 mmol amine, 0.5 mmol carboxylic acid, and 0.5 mmol isonitrile in 6 mL CHCl₃ are heated in the *Emrys optimizer* microwave oven (“High” absorption setting) at 160 °C for 30 min (fixed hold time). After removal of the solvent, the residue is chromatographed on silica gel, usually with petrol ether : ethyl acetate (ca. 3:1).

Peptoid **7b**: TLC petrol ether : ethyl acetate = 4:1, R_f 0.28, purified by column chromatography on silica gel of mesh 0.04-0.06 with petrol ether : ethyl acetate = 2.5:1. ¹H-NMR (CDCl₃, 300 MHz): 7.41 – 7.37 (m, 3H), 7.24 – 7.19 (m, 2H), 5.20 (t, *J*₁ = 7.6 Hz, *J*₂ = 15.3 Hz, 1H), 2.72 (dd, *J*₁ = 7.6 Hz, *J*₂ = 15.8 Hz, 1H), 2.42 (dd, *J*₁ = 7.6 Hz, *J*₂ = 15.8 Hz, 1H), 1.98 (s, 3H), 1.86 (s, 3H), 1.38 (s, 9H) ppm. ¹³C-NMR (CDCl₃, 75.5 MHz): 171.69 (s), 168.83 (s), 138.60 (s), 129.35 (d, 2C), 129.16 (d), 128.65 (d, 2C), 58.82 (d), 51.24 (s), 28.71 (q, 3C), 23.36 (t), 23.25 (q), 5.25 (q) ppm.

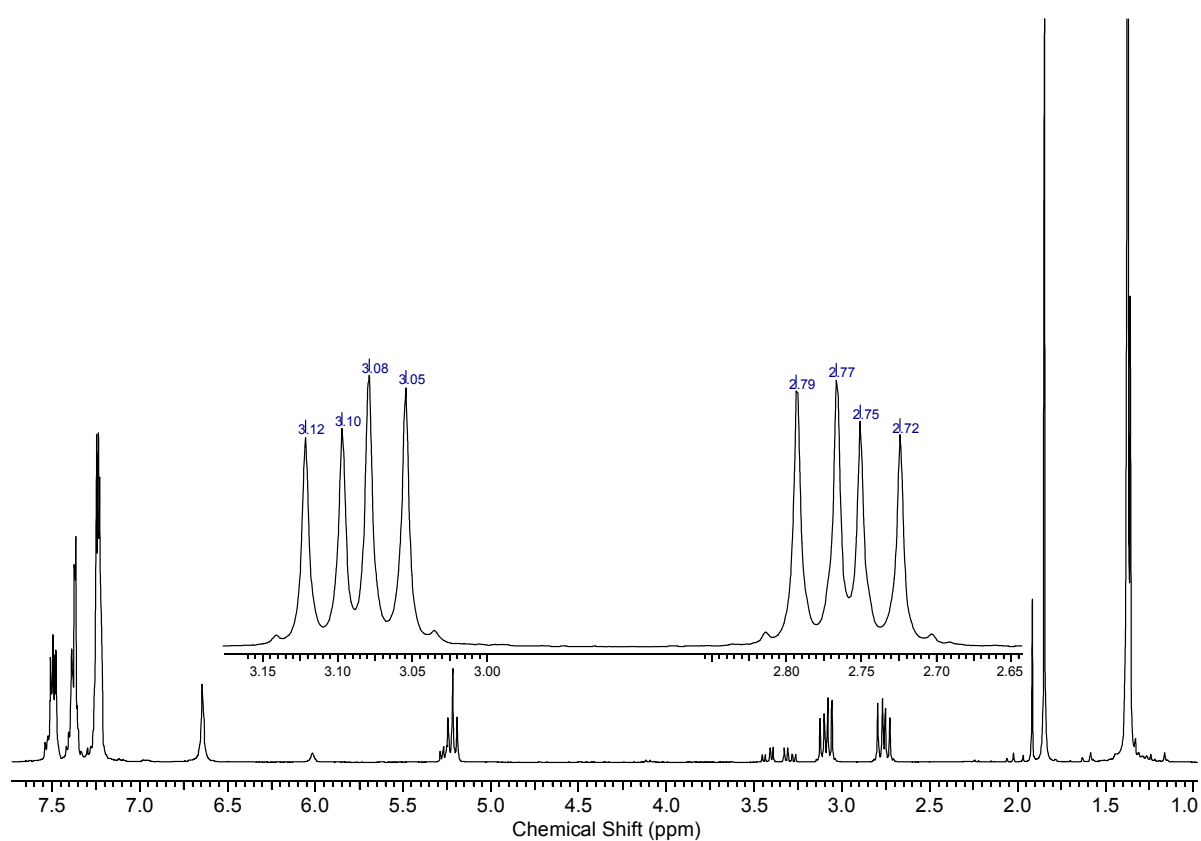
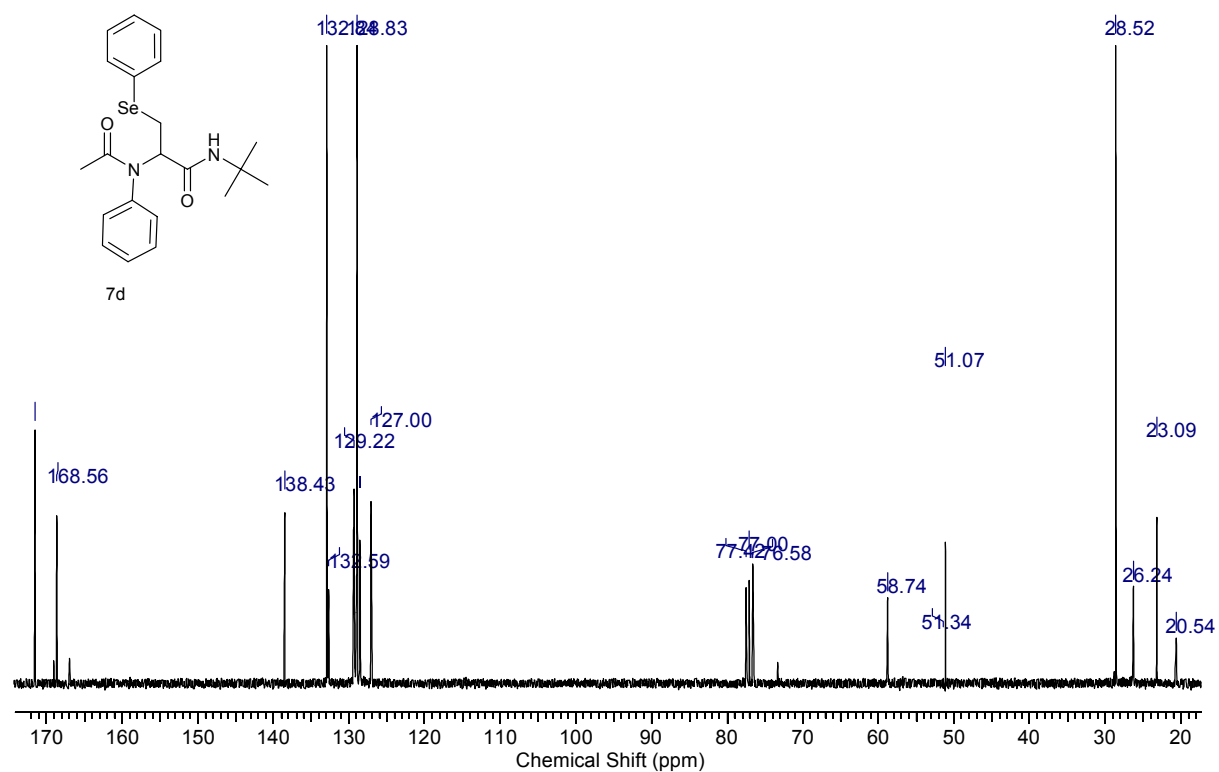
Peptoid **7d**: TLC petrol ether : ethyl acetate = 4:1, R_f 0.32, purified by column chromatography on silica gel of mesh 0.04-0.06 with petrol ether : ethyl acetate ¹H-NMR (CDCl₃, 300 MHz): 7.60 – 7.20 (m, 2H), 7.41 – 7.37 (m, 3H), 7.24 – 7.20 (m, 5H), 6.62 (br s, 1H), 5.20 (t, *J*₁ = 7.6 Hz, *J*₂ = 15.4 Hz, 1H), 3.07 (dd, *J*₁ = 7.3 Hz, *J*₂ = 12.8 Hz, 1H), 2.74 (dd, (*J*₁ = 7.3 Hz, *J*₂ = 12.8 Hz, 1H), 1.82 (s, 3H), 1.38 (s, 9H) ppm. ¹³C-NMR (CDCl₃, 75.5 MHz): 171.78 (s), 168.84 (s), 138.63 (s), 133.13 (d, 2C), 129.50 (s), 129.44 (d, 2C), 129.04 (d, 2C), 128.72 (d, 2C), 127.24 (d, 2C), 58.94 (d), 51.32 (s), 28.73 (q, 3C), 26.44 (t), 23.32 (q) ppm.

Peptoid **7e**: TLC petrol ether : ethyl acetate = 2.5:1, R_f 0.35, purified by column chromatography on silica gel with petrol ether : ethyl acetate = 2.5:1. ¹H-NMR (CDCl₃, 300 MHz): 7.56 – 7.48 (m, 3H), 7.45 – 7.24 (m, 7H), 5.35 – 5.25 (m, 2H), 4.32 – 4.20 (m, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.86 (dd, *J*₁ = 18.1 Hz, *J*₂ = 4.9 Hz, 1H), 3.76 (dd, *J*₁ = 17.9 Hz, *J*₂ = 5.3 Hz, 1H), 3.48 (dd, *J*₁ = 17.9 Hz, *J*₂ = 4.4 Hz, 1H), 3.14 (dd, *J*₁ = 12.8 Hz, *J*₂ = 7.3 Hz, 1H), 2.80 (dd, *J*₁ = 12.8 Hz, *J*₂ = 8.1 Hz, 1H), 1.40 (s, 9H), 1.29 (t, *J*₁ = 7.1 Hz, 3H) ppm. ¹³C-NMR (CDCl₃, 75.5 MHz): 170.55 (s), 169.70 (s), 169.38 (s), 155.54 (s), 136.29 (s), 133.44 (d, 2C), 129.37 (d, 2C), 129.14 (d, 4C), 128.87 (s), 127.54 (d, 2C), 79.72 (s), 61.49 (t), 58.92 (d), 43.80 (t), 41.33 (t), 28.34 (q, 3C), 25.82 (t), 14.25 (q) ppm.

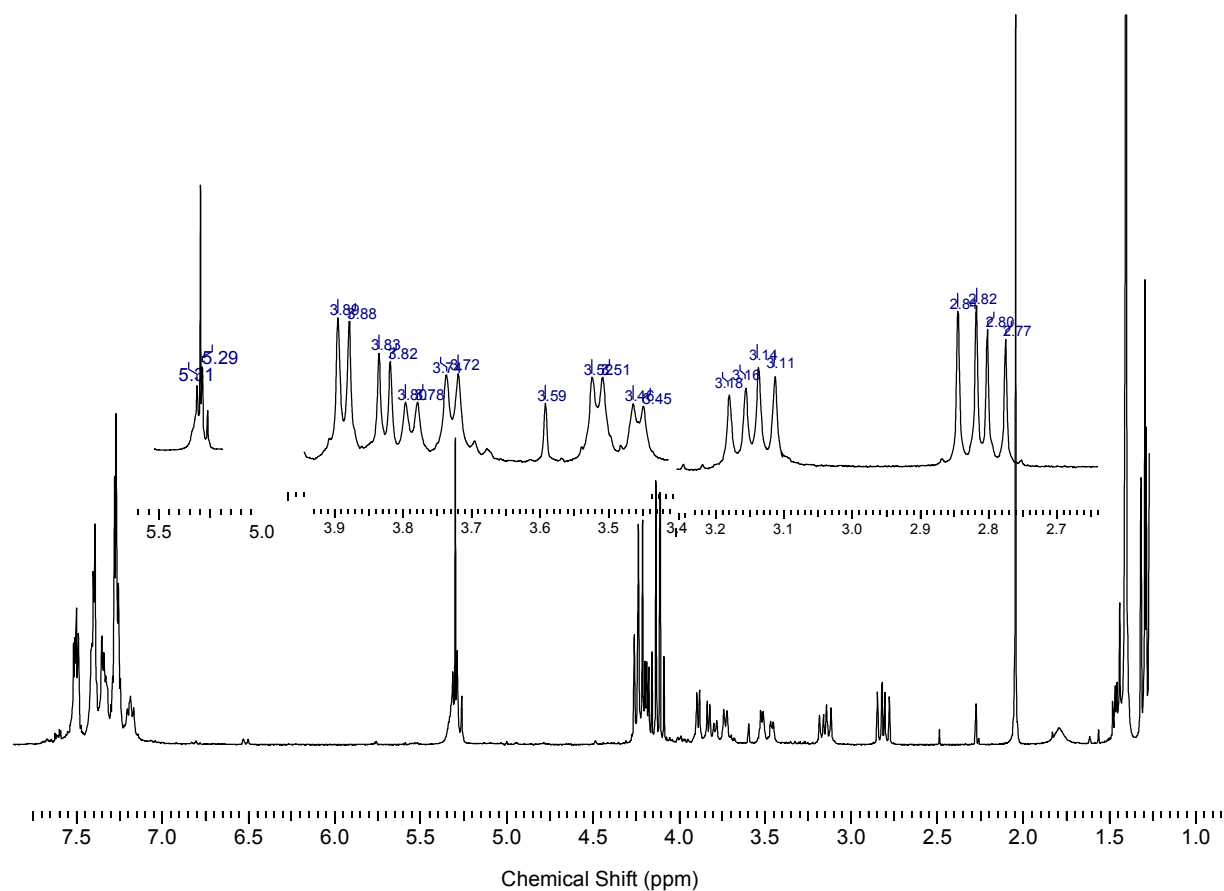
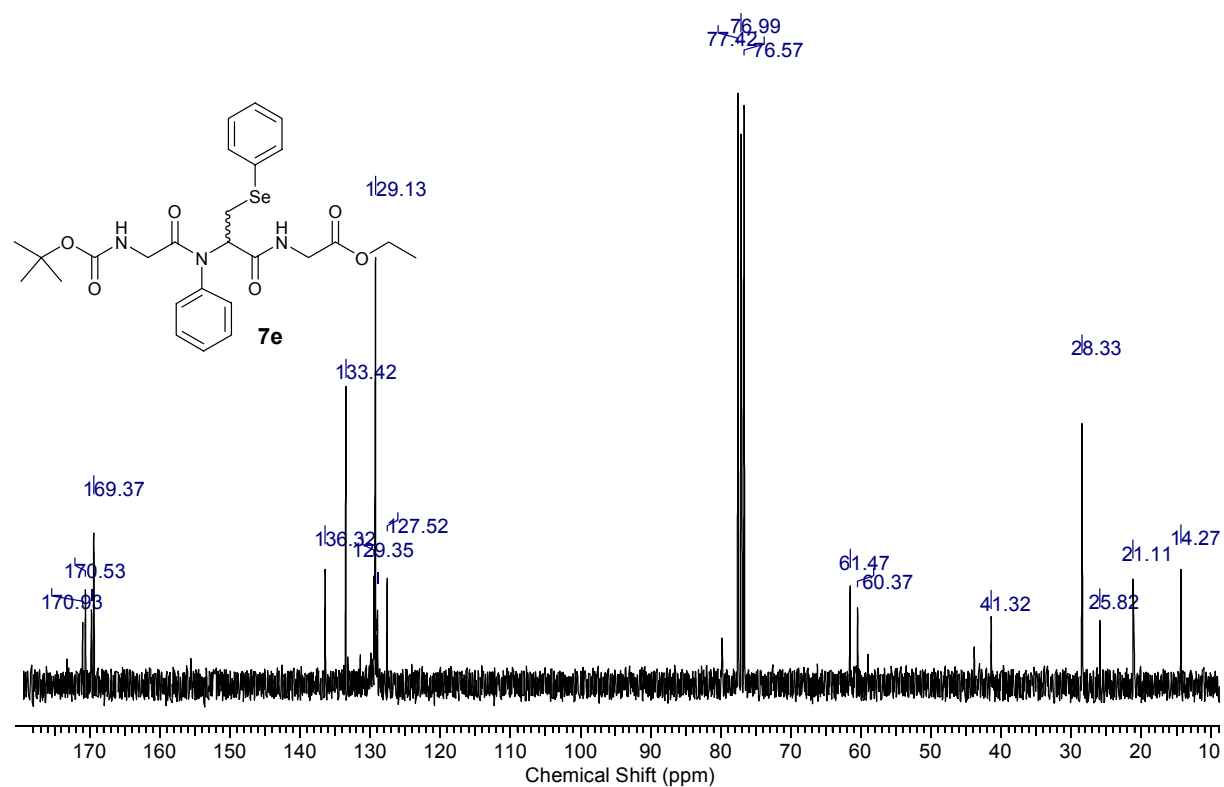
Peptoid **7h**: TLC petrol ether : ethyl acetate = 4:1, R_f 0.30, purified by column chromatography on silica gel with petrol ether : ethyl acetate = 2.5:1. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): 7.44 – 7.24 (m, 9H), 6.84-6.60 (br t, $J_1 = 5.49$ Hz, $J_2 = 10.60$ Hz, 1H), 5.44-5.37 (t, $J_1 = 5.13$ Hz, $J_2 = 9.88$ Hz, 1H), 5.24-5.17 (t, $J_1 = 8.05$ Hz, $J_2 = 15.73$ Hz, 1H), 5.10 (s, 2H), 3.74-3.64 (br q, $J_1 = 5.13$ Hz, $J_2 = 17.56$ Hz, 1H), 3.52-8.42 (br q, $J_1 = 4.75$ Hz, $J_2 = 17.56$ Hz, 1H), 3.34-3.24 (dd, $J_1 = 6.95$ Hz, $J_2 = 13.17$ Hz, 2H), 2.84-2.76 (q, $J_1 = 7.68$ Hz, $J_2 = 12.81$ Hz, 1H), 2.52-2.43 (q, $J_1 = 8.05$ Hz, $J_2 = 12.81$ Hz, 1H), 2.40-2.34 (t, $J_1 = 7.32$ Hz, $J_2 = 14.60$ Hz, 2H), 1.80 (s, 3H), 1.74-1.52 (m, 6H), 1.40 (s, 9H) ppm. $^{13}\text{C-NMR}$ (CDCl_3 , 75.5 MHz): 173.20 (s), 169.70 (s), 169.18 (s), 156.16 (s), 135.76 (s), 128.36 (d, 2C), 128.02 (d), 127.90 (d, 2C), 80.46 (s), 66.11 (t), 52.35 (d), 44.55 (t), 39.51 (t), 34.05 (t), 28.87 (t), 28.29 (q, 3C), 27.06 (t), 26.29 (t), 24.44 (t), 5.18 (q) ppm.



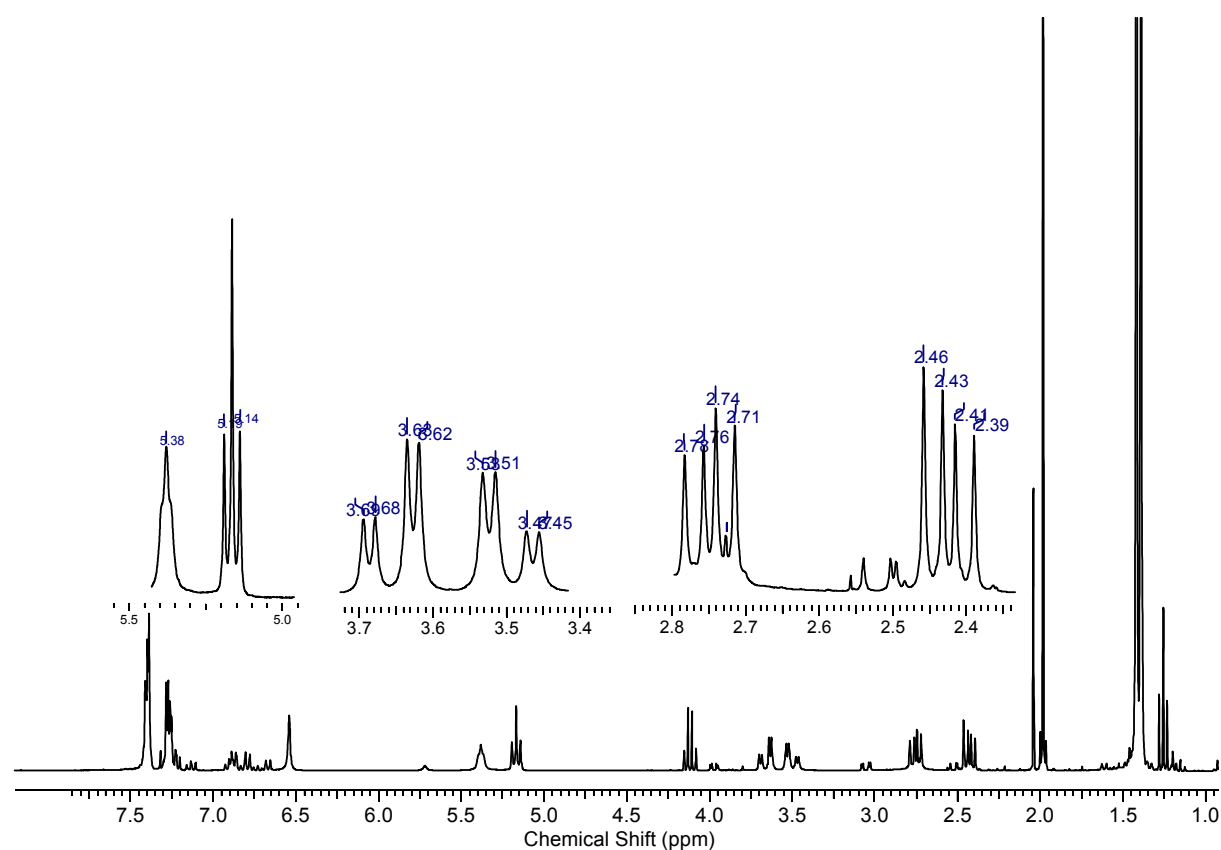
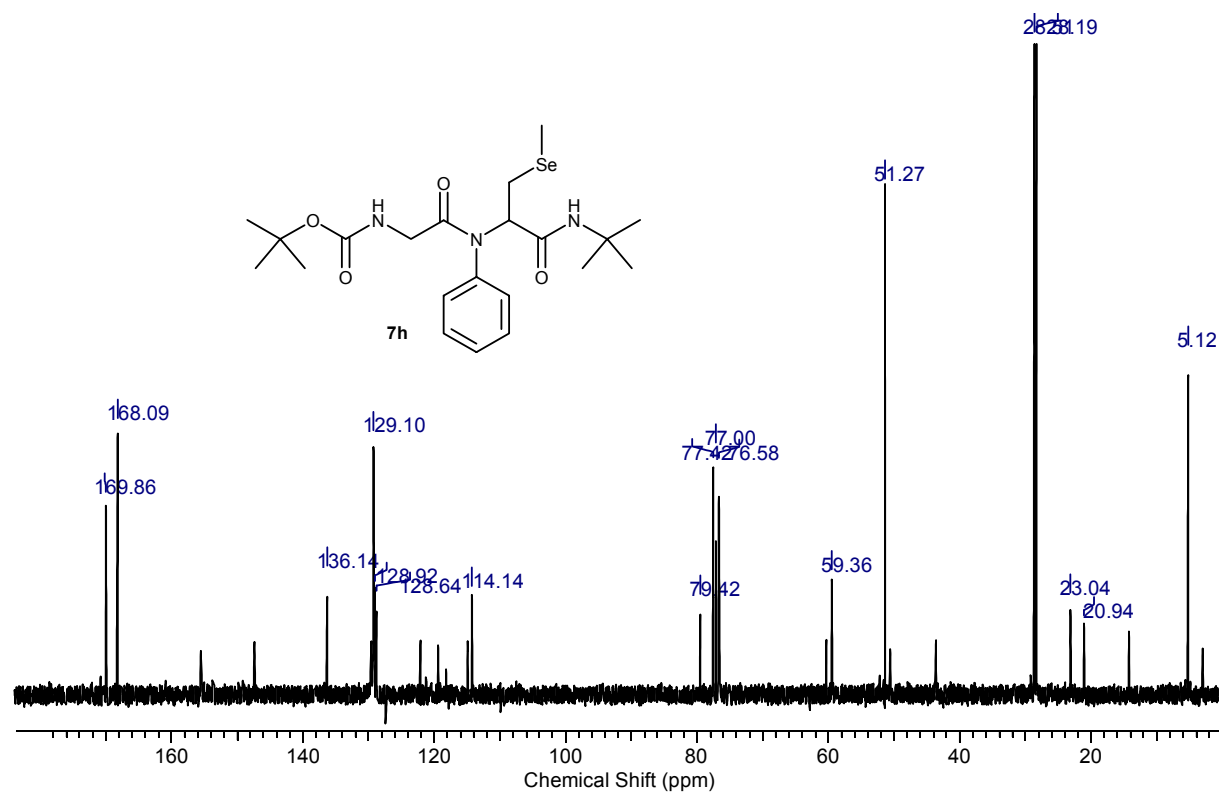
¹H and ¹³C NMR spectra for selenocystein peptoid **7b**



¹H and ¹³C NMR spectra for selenocystein peptoid **7d**



^1H and ^{13}C NMR spectra for selenocystein peptoid **7e**



^1H and ^{13}C NMR spectra for selenocystein peptoid **7h**