Aerobic, Diselenide-Catalyzed Redox Dehydration: Amides and Peptides.

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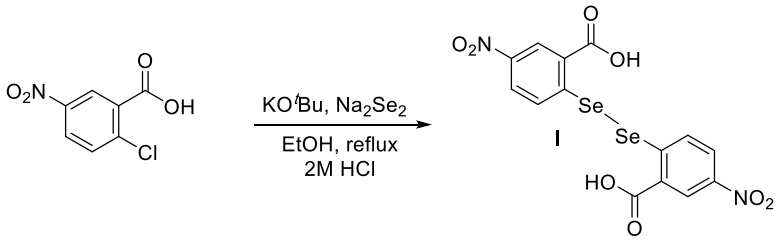
GENERAL INFORMATION:

All solvents were purchased from Fisher Scientific and dried using a JC Mayer solvent drying system. Unless otherwise noted, all commercially available reagents and substrates were used directly as received. Ultra-High Purity dry air was purchased from nexAir LLC. Thin layer chromatography was performed on Merck silica gel plates and visualized by UV light /phosphomolybdic acid /ninhydrin. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker 600, Varian INOVA 600, INOVA 500 and INOVA 400 spectrometers. In the spectra, the residual protic solvent absorbances were treated as internal reference signals ($CDCl_3$: ^{1}H-7.26 ppm and ^{13}C- 77.16 ppm; DMSO-d_6: ^{1}H-2.50 ppm and ^{13}C-39.52). GC optimization studies were performed on a HP 6850 series GC system. UV-Vis studies were performed on a Cary® 50 UV-Vis Spectrophotometer. IR spectra were recorded on a Nicolet *i*S10 FT-IR spectrometer and the absorption peaks were reported in cm^{-1}. All racemization studies were performed on an Agilent 1100 series HPLC system with chiral AS-RH stationary phase. The purification of the products was performed on a Biotage flash chromatography system using silica gel flash cartridges. A Thomas capillary melting point apparatus was used to determine the melting points (uncorrected). High resolution mass spectra were obtained from the Emory University Mass Spec Facility Inc. X-ray crystal structure data was obtained from Dr. John Bacsa of the Emory University X-ray Crystallography Center. 8-(4-Chlorophenylsulfonamido)-4-(3-(pyridin-3-yl)propyl)octanoic acid was obtained from Novartis (as a gift to the Emory University Center for C-H Functionalization).

Synthesis of 6,6'-Diselanediylbis(3-nitrobenzoic acid) (I)[1]

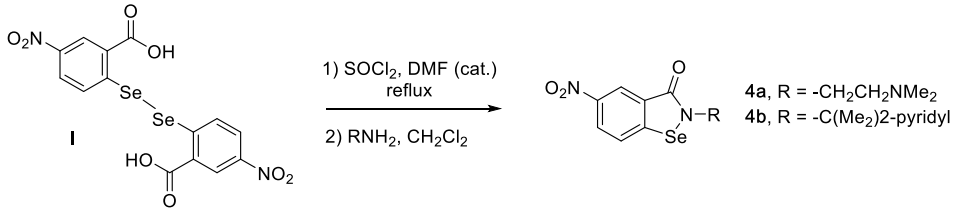


Preparation of Na_2Se_2:[2] Selenium powder (7.9 g, 100.0 mmol) was added to an aqueous solution (50 mL) of NaOH (4.0 g, 100.0 mmol) and hexadecyltrimethyl ammonium bromide (36 mg, 0.1 mmol). Then, to the above solution, $NaBH_4$ (475 mg, 12.5 mmol) with NaOH (400 mg, 10.0 mmol) in 10 mL of water (cooled in an ice bath) was added dropwise at room temperature under a nitrogen atmosphere with stirring. The mixture was stirred for 1 h at room temperature, then raised to 90 °C and stirred at that temperature for 1 h to complete the reaction. A brownish red aqueous solution of Na_2Se_2 was obtained.

Then, to a stirred solution of 2-chloro-5-nitrobenzoic acid (19.15 g, 95.0 mmol) in EtOH (120 mL) was added a solution of KO^{t}Bu (10.66 g, 95.0 mmol) in EtOH (60 mL) *via* addition funnel at room temperature. After that, the Na_2Se_2 solution was added dropwise through an addition funnel and refluxed overnight. The reaction mixture was filtered while hot and concentrated to remove EtOH. The resulting slurry was acidified slowly with 2M aqueous HCl followed by filtration to give the pure acid **I** as yellow solid (19.2 g, 82% yield). Mp = > 280 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.64 (d, J = 2.7 Hz, 1H), 8.21 (dd, J = 8.8, 2.6 Hz, 1H), 7.86 (d, J = 8.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.8, 146.6, 143.4, 131.7, 131.5, 127.1, 125.9. IR (neat, cm^{-1}): 3305, 1597. HRMS (-APCL) Calcd. for $C_{14}H_7N_2O_8Se_2$ [M-H]$^-$: 490.8538. Found: 490.8536.

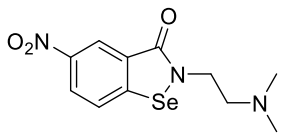
Synthesis of the Benzoisoselenazolones 4a and 4b:

*General Synthetic Route for **4a, 4b***:



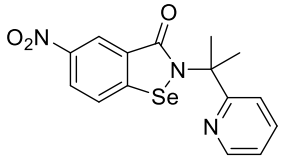
A solution of 6,6'-diselanediylbis(3-nitrobenzoic acid) **I** (2.04 mmol) in thionyl chloride (15 mL) and catalytic amount of DMF (0.2 ml) was stirred at reflux (90 °C) for 3 h. The solvents were evaporated under vacuum and the crude product dissolved in dry CH_2Cl_2 (10 mL) was added dropwise to a stirred solution of the corresponding amine (10.20 mmol) in dry CH_2Cl_2 (5 mL) at room temperature. After completion of the reaction as monitored by silica gel TLC, the reaction mixture was neutralized with an aqueous ammonia solution, diluted with water and extracted into CH_2Cl_2 (2 x 100 mL). The combined CH_2Cl_2 layers were washed with aqueous sat'd. NaCl (100 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by SiO_2 flash column chromatography eluting with ethyl acetate/hexanes.

2-(2-(Dimethylamino)ethyl)-5-nitrobenzo[*d*][1,2]selenazol-3(2*H*)-one (4a)



Prepared according to the general procedure from **I** (1.00 g, 2.04 mmol), thionyl chloride (15 mL), DMF (0.2 mL) and N,N-dimethylethylenediamine (0.67 mL, 6.12 mmol), **4a** was obtained as a pale yellow solid (1.04 g, 81% yield). Mp = 223 – 225 °C. ^{1}H NMR (399 MHz, chloroform-*d*) δ 8.86 (d, *J* =0.8 Hz, 1H), 8.34 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 3.98 (t, *J* = 5.4 Hz, 2H), 2.68 (t, *J* = 5.4 Hz, 2H), 2.41 (s, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 166.3, 152.2, 146.6, 128.7, 125.2, 124.3, 123.3, 57.3, 44.3, 41.2. IR (neat, cm^{-1}): 1615, 1596. HRMS (ESI) Calcd. for $C_{11}H_{14}N_3O_3Se$ $(M+H)^+$: 316.0195, Found: 316.0193.

5-Nitro-2-(2-(pyridin-2-yl)propan-2-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (4b)



Prepared according to the general procedure from **I** (0.20 g, 0.41 mmol), thionyl chloride (3 mL), DMF (40 μL) and 2-(pyridin-2-yl)propan-2-amine[3] (0.17 g, 1.23 mmol), **4b** was obtained as a pale yellow solid (0.18 g, 62% yield). Mp = 198 – 200 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.76 (d, *J* = 2.3 Hz, 1H), 8.60 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.43 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.71(dt, *J* = 7.8, 1.8 Hz, 1H), 7.45 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.24 – 7.20 (m, 1H), 2.07 (s, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 165.0, 163.0, 149.0, 146.8, 145.3, 136.6, 130.2, 125.8, 124.3, 124.1, 122.3, 119.7, 64.2, 28.3. IR (neat, cm^{-1}): 1590, 1510. HRMS (ESI) Calcd. for $C_{15}H_{14}N_3O_3Se$ $(M+H)^+$: 364.0195, Found: 364.0195.

Formation of *p*-toluic benzylamide using benzoisoselenazolones (4) in the presence of $CuI_2(NMI)_4$:

A 12 mL test tube was charged with a 4 Å molecular sieves (50 mg), activated in a microwave oven for 3 min twice and kept under reduced pressure for 5 min. Then, *p*-toluic acid (50 mg, 0.37 mmol), benzoisoselenazolone **4** (0.0185 mmol), $CuI_2(NMI)_4$[4] (24 mg, 0.037 mmol) and 1,3,5-tri-*tert*-butylbenzene (90.5 mg, 0.37 mmol, GC internal standard) were added followed by dry acetonitrile (1.9 mL, 0.2M, moisture content <25 ppm). Triethylphosphite (95 μL, 0.55 mmol) and benzylamine (48 μL, 0.44 mmol) were added sequentially at 30 °C and the reaction mixture was stirred for 8 h at the same temperature under dry air atmosphere (balloon). The reaction was monitored periodically by GC.

Table S1

	yield of *p*-toluic benzylamide (%)[a]	
time (h)	**4a**	**4b**
0	0	0
2	61	58
4	82	81
6	89	87
8	93	92

a: GC corrected yield with internal standard (1,3,5-tri-*tert*-butylbenzene). Column: Agilent HP-5, length – 30 m, diameter 0.32 mm, film 0.25 μm. Method: Initial temp: 70 °C (0 min), ramp: 20 °C/min to maximum 300 °C (7 min wait time, total time 19.0 min).

Formation of *p*-toluic benzylamide using benzoisoselenazolones (4) in the absence of $CuI_2(NMI)_4$:

A 12 mL test tube was charged with a 4 Å molecular sieves (50 mg), activated in a microwave oven for 3 min twice and kept under reduced pressure for 5 min. Then, *p*-toluic acid (50 mg, 0.37 mmol), benzoisoselenazolone **4** (0.0185 mmol) and 1,3,5-tri-*tert*-butylbenzene (90.5 mg, 0.37 mmol, GC internal standard) were added followed by dry acetonitrile (1.9 mL, 0.2M, moisture content <25 ppm). Triethylphosphite (95 μL, 0.55 mmol) and benzylamine (48 μL, 0.44 mmol) were added sequentially at 30 °C and the reaction mixture was stirred for 8 h at the same temperature under dry air atmosphere (balloon). The reaction was monitored by GC.

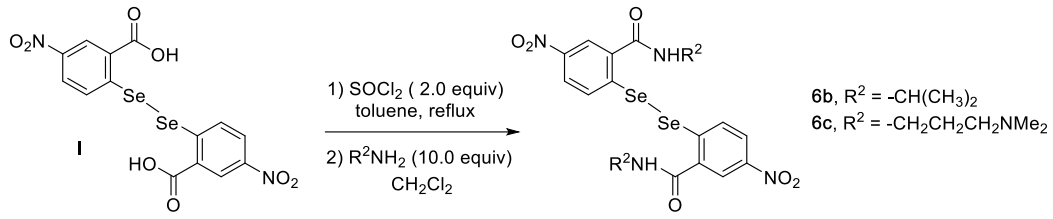
Table S2

	yield of *p*-toluic benzylamide (%)[a]	
time (h)	**4a**	**4b**
0	0	0
2	64	63
4	83	80
6	89	88
8	94	92

a: GC corrected yield with internal standard (1,3,5-tri-*tert*-butylbenzene). Column: Agilent HP-5, length – 30 m, diameter 0.32 mm, film 0.25 μm. Method: Initial temp: 70 °C (0 min), ramp: 20 °C/min to maximum 300 °C (7 min wait time, total time 19.0 min).

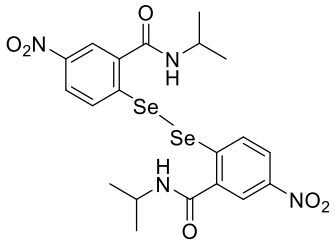
Synthesis of Diselenides:

*General Synthetic Route for **6b, 6c***:



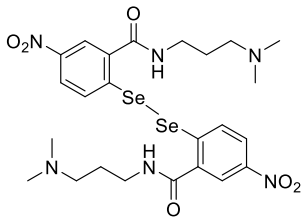
A solution of 6,6'-diselanediylbis(3-nitrobenzoic acid) **I** (0.551 mmol) and thionyl chloride (1.102 mmol) in toluene (5 mL) was refluxed under N_2 until the diselenide had dissolved completely. Then, volatiles were evaporated under vacuum to give the crude product. The crude product in dry CH_2Cl_2 (5 mL) was added dropwise over a period of 30 min to a stirred solution of the corresponding amine (5.51 mmol) in dry CH_2Cl_2 (5 mL) at room temperature. After completion of the reaction as monitored by silica gel TLC (2-5% MeOH in CH_2Cl_2), the reaction mixture was neutralized with aqueous ammonia solution, diluted with water and extracted into CH_2Cl_2 (2 x 100 mL). The combined CH_2Cl_2 layers were washed with aqueous sat'd. NaCl (100 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by SiO_2 flash column chromatography eluting with 2-5% MeOH in CH_2Cl_2.

6,6'-Diselanediylbis(*N*-isopropyl-3-nitrobenzamide) (6b)



Prepared according to the general procedure from **I** (100 mg, 0.203 mmol), thionyl chloride (30 mL, 0.406 mmol) and isopropylamine (0.17 mL, 2.03 mmol). The crude product was purified by SiO_2 flash column chromatography eluting with 2% MeOH in CH_2Cl_2 to give **6b** as a pale yellow solid (60 mg, 52% yield). Mp = 278 – 280 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (d, J = 7.6 Hz, 2H), 8.73 (d, J = 2.5 Hz, 2H), 8.20 (dd, J = 8.8, 2.4 Hz, 2H), 7.87 (d, J = 8.9 Hz, 2H), 4.20 – 4.04 (m, 2H), 1.21 (d, J = 6.6 Hz, 12H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 146.6, 142.5, 133.9, 131.8, 126.1, 123.1, 42.3, 22.5. IR (neat, cm^{-1}): 3321, 1616, 1332. HRMS (ESI) Calcd. for $C_{20}H_{21}N_4O_6Se_2$ $(M-H)^+$: 572.9797, Found: 572.9797.

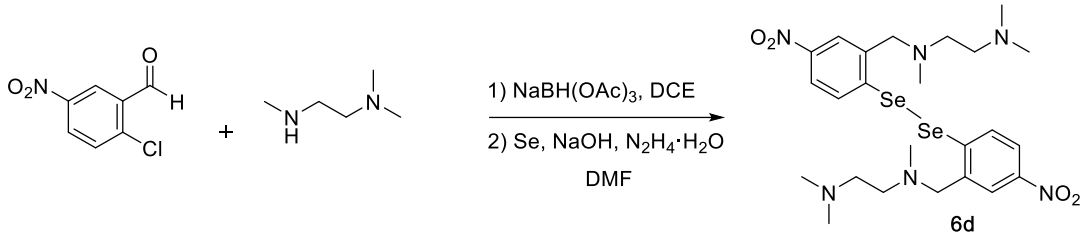
6,6'-Diselanediylbis(*N*-(3-(dimethylamino)propyl)-3-nitrobenzamide) (6c)



Prepared according to the general procedure from **I** (100 mg, 0.203 mmol), thionyl chloride (30 mL, 0.406 mmol) and 3-(dimethylamino)-1-propylamine (0.25 mL, 2.03 mmol). The crude product was

purified by SiO_2 flash column chromatography eluting with 5% MeOH in CH_2Cl_2 to give **6c** as a pale yellow solid (58 mg, 43% yield). Mp = 206 – 208 °C. ^{1}H NMR (399 MHz, chloroform-*d*) δ 10.31 (brs, 2H), 8.40 – 8.36 (m, 2H), 8.02 (d, *J* = 1.3 Hz, 4H), 3.64 (q, *J* = 5.4 Hz, 4H), 2.63 (t, *J* = 5.4 Hz, 4H), 2.41 (s, 12H), 1.81 (p, *J* = 5.9 Hz, 4H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 165.6, 146.3, 143.3, 133.0, 132.2, 125.0, 121.5, 60.1, 45.2, 42.1, 23.7. IR (neat, cm^{-1}): 3314, 1615. HRMS (ESI) Calcd. for $C_{24}H_{31}N_6O_6Se_2$ $(M-H)^+$: 659.0641, Found: 659.0641.

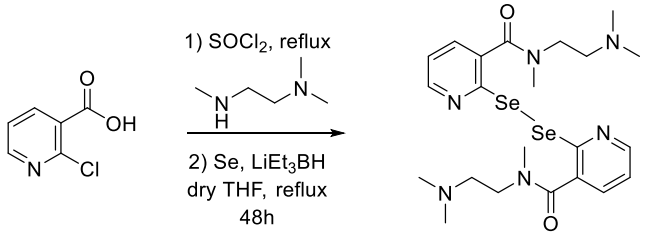
Synthesis of *N*^{1},*N*$^{1'}$-((diselanediylbis(5-nitro-2,1-phenylene))bis(methylene))bis(*N*^{1},*N*^{2},*N*^{2}-trimethylethane-1,2-diamine) (6d)



To a mixture of N,N,N'-trimethylethylenediamine (0.14 mL, 1.06 mmol) and 2-chloro-5-nitrobenzaldehyde (200 mg, 1.06 mmol) in 1,2-dichloroethane (4 mL) was added sodium triacetoxyborohydride (314 mg, 1.48 mmol) portion-wise. The mixture was stirred at rt under a N_2 atmosphere for 16 h. The reaction mixture was quenched with 1 N NaOH, and the product was extracted into ethyl acetate. The ethyl acetate extract was washed with brine, dried over Na_2SO_4 and concentrated to give the crude halo amine.

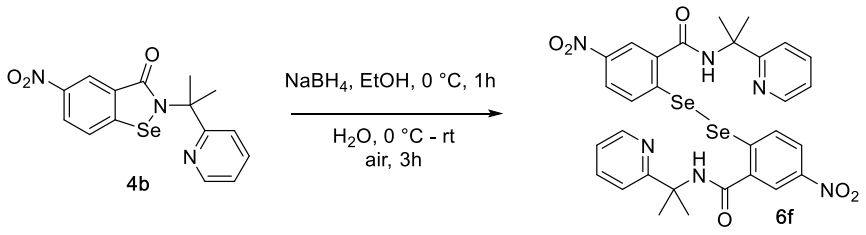
To a rapidly stirred solution of sodium hydroxide (64 mg, 1.59 mmol) and selenium powder (82 mg, 1.06 mmol) in dimethylformamide (5 mL) was added 100% hydrazine hydrate (81 μL, 1.06 mmol) dropwise at room temperature. The mixture was allowed to stir for an additional two hours. The crude halo amine (287 mg, 1.06 mmol) was added dropwise to the reaction mixture and refluxed for 4 hours. The reaction was quenched by adding water and the product was extracted into ethyl acetate. The ethyl acetate extract was washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by SiO_2 flash column chromatography eluting with 5% aqueous NH_4OH in CH_3CN to obtain compound **6d** as a yellow oil (204 mg, 61% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.01 (d, *J* = 2.5 Hz, 2H), 7.93 (dd, *J* = 8.7, 2.5 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 4H), 2.64 (t, *J* = 7.3 Hz, 4H), 2.52 (t, *J* = 7.3 Hz, 4H), 2.30 (s, 6H), 2.24 (s, 12H). ^{13}C NMR (75 MHz, chloroform-*d*) δ 146.3, 143.4, 140.4, 131.7, 122.9, 122.8, 63.0, 56.9, 54.4, 45.8, 41.1. IR (neat, cm^{-1}): 1513, 1336. HRMS (ESI) Calcd. for $C_{24}H_{37}N_6O_4Se_2$ $(M+H)^+$: 633.1201, Found: 633.1208.

2,2'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-*N*-methylnicotinamide) (6e)



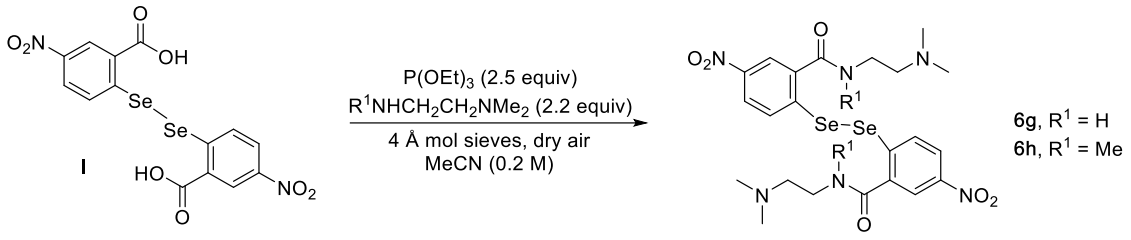
Into a flame-dried round-bottomed flask, 2-chloronicotinic acid (1.0 g, 6.35 mmol) and $SOCl_2$ (4.6 mL, 63.5 mmol) were charged under an argon atmosphere and the solution was refluxed overnight. The excess $SOCl_2$ was removed under reduced pressure to provide the crude acid chloride. This acid chloride in dry THF (3.0 mL) was added to a mixture of N,N,N'-trimethylethylenediamine (0.697 mL, 6.82 mmol) and trimethylamine (0.69 g, 6.82 mmol) in THF (10 mL) at 0 °C under an argon atmosphere. The reaction mixture was stirred at room temperature until the acid chloride was completely consumed (a small portion of the reaction mixture was quenched with methanol and monitored by silica gel TLC). After completion of the reaction, water (5 mL) was added to the reaction mixture, which as extracted with CH_2Cl_2 (2 x 10 mL). The combined CH_2Cl_2 layer was washed with aqueous sat'd $NaHCO_3$ (5 mL) and brine solution. The CH_2Cl_2 layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to provide the crude amide that was taken directly into the next reaction. In a dry, round-bottomed flask (100 mL), selenium (0.602 g, 7.62 mmol) and dry THF (10 mL) were charged under and argon atmosphere, then a 1M solution of lithium triethylborohydride in dry THF (7.62 mL, 7.62 mmol) was added at room temperature. The reaction mixture was heated to 90 °C and stirred for 1 h under an argon atmosphere. The reaction mixture was cooled to 50 °C and the crude amide in dry THF (5 mL) was added. Then, the reaction mixture was again heated to 90 °C and stirred for 16 h. After cooling to the room temperature, water (20 mL) was added to precipitate the unreacted selenium metal, which was filtered through a small plug of Celite and washed with CH_2Cl_2 (30 mL). Two layers were separated, and the CH_2Cl_2 layer was washed with aqueous sat'd. $NaHCO_3$ (15 mL) solution. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum to provide the crude product. Purification of the crude product by flash column chromatography using SiO_2 and 5% MeOH in CH_2Cl_2 provided **6e** as a creamy white solid (1.7 g, 47% yield). Mp = 174 – 176 °C. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.8 Hz, 2H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.09 (dd, *J* = 7.5, 4.8 Hz, 2H), 3.72 – 1.99 (m, 26H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 168.6, 151.7, 150.5, 134.2, 133.1, 121.0, 45.7 (only one aliphatic peak was resolved). IR (neat, cm^{-1}): 1605, 1382. HRMS (ESI) Calcd. for $C_{22}H_{33}N_6O_2Se_2$ $(M+H)^+$: 573.0995, Found: 573.0994.

Synthesis of 6,6'-diselanediylbis(3-nitro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide) (6f)



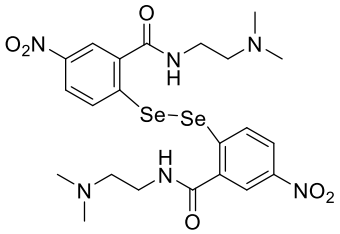
To a solution of **4b** (30 mg, 0.083 mmol) in ethanol (1 mL) was added sodium borohydride (3 mg, 0.083 mmol) at 0 ºC. After 1 h water (0.2 mL) was added. The reaction mixture was allowed to warm to room temperature. After stirring for 3 h in air, the product was extracted with dichloromethane (10 mL) three times. The combined organic layers were washed with brine (10 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting compound was recrystallized from ethyl acetate to provide **6f** (21 mg, 71% yield) as a yellow solid. Mp = 214 – 216 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 9.47 (s, 2H), 8.60 (ddd, *J* = 4.9, 1.8 Hz, 2H), 8.58 (d, *J* = 2.3 Hz, 2H), 8.09 (dd, *J* = 8.8, 2.3 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.82 (td, *J* = 7.7, 1.8 Hz, 2H), 7.50 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.30 (ddd, *J* = 7.4, 4.8, 1.2 Hz, 2H), 1.94 (s, 12H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 165.4, 163.6, 147.6, 146.5, 142.5, 137.7, 135.2, 132.1, 125.3, 122.4, 121.8, 119.5, 57.3, 27.3. IR (neat, cm^{-1}): 3314, 1649, 1342. HRMS (ESI) Calcd. for $C_{18}H_{33}N_8O_{13}Se_2$ $(M+H)^+$: 729.0492, Found: 729.0484.

*General Synthetic Route for **6g, 6h***:



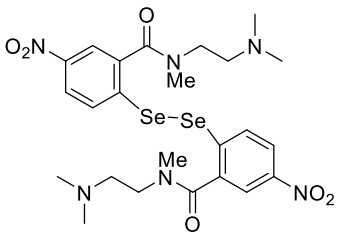
An oven dried round-bottomed flask was charged with a 4 Å molecular sieves (275 mg) that were previously activated in a microwave oven for 3 min and dried under reduced pressure for 5 min. Then, 6,6'-diselanediylbis(3-nitrobenzoic acid) (0.551 mmol) was added followed by dry acetonitrile (2.75 mL, 0.2M). Triethylphosphite (1.377 mmol) was added to the reaction mixture followed after 5 min by the corresponding amine (1.212 mmol). The reaction mixture was stirred for 24 h at the room temperature under a dry air atmosphere (balloon). The reaction mixture was concentrated and purified by flash chromatography (SiO_2, eluted with MeOH in CH_2Cl_2) to obtain the pure compound.

6,6'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-3-nitrobenzamide) (6g)



A mixture of **I** (1.0 g, 2.04 mmol) and 4 Å molecular sieves (1.0 g) in dry CH_3CN (10 mL, 0.2M) was treated with $P(OEt)_3$ (0.88 mL, 5.10 mmol), followed by N,N-dimethylethylenediamine (0.50 mL, 4.50 mmol) according to the general procedure. The reaction was stirred for 28 h under dry air and purified by flash column chromatography using SiO_2 and 5% MeOH in CH_2Cl_2 to give **6g** as a pale yellow solid (920 mg, 72% yield). Mp = 230 – 232 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.35 (d, *J* = 2.3 Hz, 2H), 8.02 (dd, *J* = 8.8, 2.3 Hz, 2H), 7.96 (d, *J* = 8.9 Hz, 2H), 7.12 (s, 2H), 3.53 (q, *J* = 5.4 Hz, 4H), 2.54 (t, *J* = 5.9 Hz, 4H), 2.26 (s, 12H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 166.2, 146.4, 142.9, 133.3, 132.2, 125.5, 121.7, 57.3, 45.1, 37.6. IR (neat, cm^{-1}): 3305, 1616, 1597. HRMS (ESI) Calcd. for $C_{22}H_{29}N_6O_6Se_2$ $(M+H)^+$: 633.0473, Found: 633.0476.

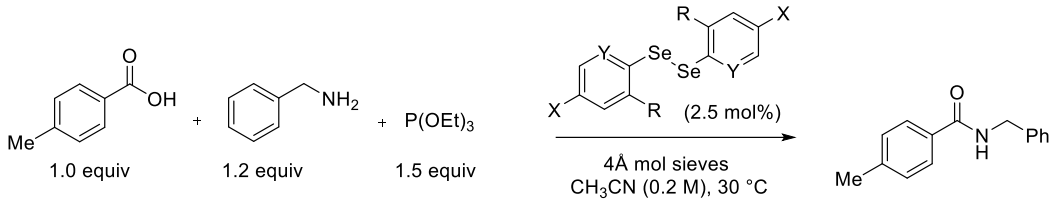
6,6'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-*N*-methyl-3-nitrobenzamide) (6h)

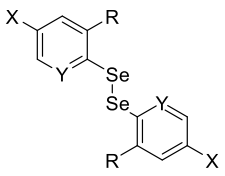


A mixture of **I** (1.0 g, 2.04 mmol) and 4 Å molecular sieves (1.0 g) in dry CH_3CN (10 mL, 0.2M) was treated with $P(OEt)_3$ (0.88 mL, 5.10 mmol), followed by N,N,N'-trimethylethylenediamine (0.58 mL,

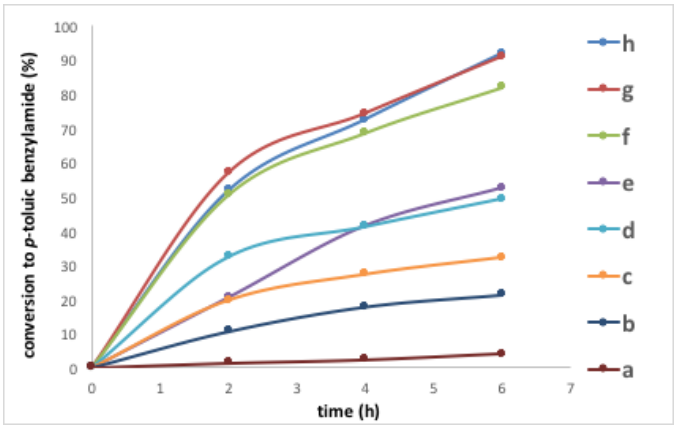
4.50 mmol) according to the general procedure. The reaction was stirred for 24 h under dry air and purified by flash column chromatography using SiO_2 and 5% MeOH in CH_2Cl_2 to give **6g** as a pale yellow semi-solid (980 mg, 73% yield). ^{1}H NMR (400 MHz, DMSO-d_6, 85 °C) δ 8.12 (dd, J = 8.6, 2.5 Hz, 2H), 8.09 (d, J = 2.4 Hz, 2H), 8.01 (d, J = 8.6 Hz, 2H), 3.41 (t, J = 6.5 Hz, 4H), 2.96 (s, 6H), 2.45 (t, J = 6.5 Hz, 4H), 2.09 (s, 12H). ^{13}C NMR (126 MHz, DMSO-d_6, 85 °C) δ 167.6, 147.1, 139.0, 138.2, 133.4, 124.8, 122.0, 56.7, 45.6 (only two aliphatic peaks were resolved). IR (neat, cm^{-1}): 1614, 1515. HRMS (ESI) Calcd. for $C_{24}H_{32}N_6O_6Se_2$ $(M+H)^+$: 661.0786, Found: 661.0789.

Screening of Diselenides:





#	R	X	Y
6a	H	H	CH
6b	CONH*i*Pr	NO_2	CH
6c	$CONH(CH_2)_3NMe_2$	NO_2	CH
6d	$CH_2NMe(CH_2)_2NMe_2$	NO_2	CH
6e	$CONMe(CH_2)_2NMe_2$	H	N
6f	$CONHC(Me_2)$2-pyridyl	NO_2	CH
6g	$CONH(CH_2)_2NMe_2$	NO_2	CH
6h	$CONMe(CH_2)_2NMe_2$	NO_2	CH



Procedure:

A 12 mL test tube was charged with a 4 Å molecular sieves (50 mg), activated in a microwave oven for 3 min twice and kept under reduced pressure for 5 min. Then, *p*-toluic acid (50 mg, 0.37 mmol), diselenide **6** (0.0092 mmol), and 1,3,5-tri-*tert*-butylbenzene (90.5 mg, 0.37 mmol, GC internal standard) were added and followed by dry acetonitrile (1.9 mL, 0.2M, moisture content <25ppm). Triethylphosphite (95 µL, 0.55 mmol) and benzylamine (48 µL, 0.44 mmol) were added sequentially at 30 °C and the reaction mixture was stirred for 8 h at the same temperature under dry air atmosphere (balloon). The reaction was monitored by GC. The conversion rate curves for the different diselenides are presented in the manuscript.

Table S3

entry	diselenide **6**	time (h)	yield (%)[a]
1	**6a**	6	4
2	**6b**	6	21
3	**6c**	6	32
4	**6d**	6	49
5	**6e**	6	52
6	**6f**	6	82
7	**6g**	6	91
8	**6h**	6	92, 90[b]

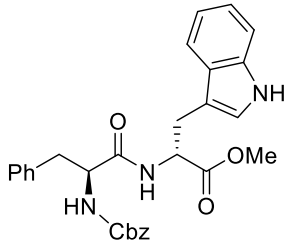
a: GC corrected yield with internal standard (1,3,5-tri-*tert*-butylbenzene). Column: Agilent HP-5, length – 30 m, diameter 0.32 mm, film 0.25 μm. Method: Initial temp: 70 °C (0 min), ramp: 20 °C/min to maximum 300 °C (7 min wait time, total time 19.0 min). *b*: isolated yield.

Substrate Scope:

General Experimental Procedure for Amide Bond Formation:

A 12 mL test tube was charged with 4 Å molecular sieves (100 mg) previously activated in a microwave oven for 3 min and dried under reduced pressure for 5 min. Then the carboxylic acid (0.367 mmol) and diselenide **6g** or **6h** (0.009 mmol) were added followed by dry acetonitrile or DMF (1.8 mL, 0.2M, moisture content <25 ppm). Triethyl phosphite (0.550 mmol) and amine (0.403 – 0.440 mmol) or amine·HCl with DIPEA (0.385 – 0.422 mmol) were added sequentially. The reaction mixture was stirred for 6 - 24 h at 30 - 50 °C under a dry air atmosphere (balloon). Upon complete conversion of carboxylic acid as monitored by TLC (EtOAc in hexanes or MeOH in CH_2Cl_2), the reaction mixture was filtered and the molecular sieves thoroughly washed with CH_2Cl_2. The combined filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel with ethyl acetate in hexanes) to obtain the pure amide product.

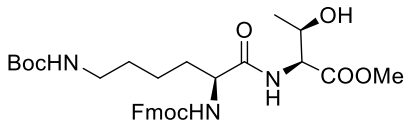
Methyl ((benzyloxy)carbonyl)-*L*-phenylalanyl-*D*-tryptophanate (entry 1)[5]



A mixture of *L*-Cbz-Phe-OH (1.0 g, 3.34 mmol), diselenide **6g** (60 mg, 0.084 mmol) and 4 Å molecular sieves (1.0 g) in dry CH_3CN (17 mL, 0.2M) was treated with $P(OEt)_3$ (0.86 mL, 5.01 mmol) followed by *D*-tryptophan methyl ester hydrochloride (1.02 g, 4.008 mmol) and DIPEA (0.66 mL, 3.84 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexane to give the pure

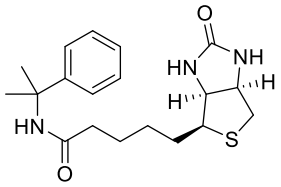
amide **1** as a white solid (1.60 g, 96% yield). Mp = 129 – 130 °C. ^{1}H NMR (399 MHz, chloroform-*d*) δ 8.01 (s, 1H), 7.41 – 7.34 (m, 1H), 7.34 – 7.18 (m, 9H), 7.16 – 7.07 (m, 3H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.78 (s, 1H), 6.37 (d, *J* = 7.7 Hz, 1H), 5.24 (d, *J* = 8.4 Hz, 1H), 5.03 - 4.93 (m, 2H), 4.86 – 4.80 (m, 1H), 4.42 (d, *J* = 7.9 Hz, 1H), 3.61 (s, 3H), 3.21 (d, *J* = 5.5 Hz, 2H), 3.00 (d, *J* = 6.2 Hz, 2H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 171.7, 170.3, 155.8, 136.3, 136.0, 129.4, 128.6, 128.5, 128.2, 128.0, 127.4, 127.0, 122.9, 122.3, 119.7, 118.4, 111.3, 109.6, 66.9, 56.0, 52.9, 52.4, 38.4, 27.6. IR (neat, cm^{-1}): 3353, 3267, 1616. HRMS (ESI) Calcd for $C_{29}H_{29}N_3O_5Na$ [M+Na]+: 522.1999. Found: 522.1999.

Methyl *N*^{2}-(((9*H*-fluoren-9-yl)methoxy)carbonyl)-*N*^{6}-(*tert*-butoxycarbonyl)-*L*-lysyl-*L*-threoninate (entry 2)



A mixture of N_α-FMOC-N_ε-*t*-Boc-*L*-lysine (1.0 g, 2.134 mmol), diselenide **6g** (33.6 mg, 0.053 mmol) and 4 Å molecular sieves (1.0 g) in dry CH_3CN (10.7 mL, 0.2M) was treated with $P(OEt)_3$ (0.55 mL, 3.20 mmol), followed by H-Thr-OMe·HCl (434 mg, 2.56 mmol) and DIPEA (0.41 mL, 2.348 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 55% EtOAc in hexane to give the pure amide **2** as a white solid (1.01 g, 81% yield). Mp = 75 – 77 °C. ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.23 (m, 2H), 7.11 (brs, 1H), 5.79 (s, 1H), 4.81 (s, 1H), 4.57 (dd, *J* = 8.8, 2.0 Hz, 1H), 4.37 – 4.24 (m, 4H), 4.16 (t, *J* = 7 Hz, 1H), 3.72 (s, 3H), 3.19 – 2.93 (m, 3H), 1.95 – 1.63 (m, 3H), 1.58 – 1.32 (m, 12H), 1.17 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 172.5, 171.3, 156.2, 143.8, 143.6, 141.2, 127.7, 127.0, 125.1, 119.9, 79.2, 67.9, 67.1, 57.5, 54.6, 52.6, 47.0, 39.9, 32.2, 29.4, 28.4, 22.2, 20.0. IR (neat, cm^{-1}): 3308 (broad), 1684. HRMS (ESI) Calcd for $C_{31}H_{42}N_3O_8$ [M+H]$^{+}$: 584.2966. Found: 584.2975.

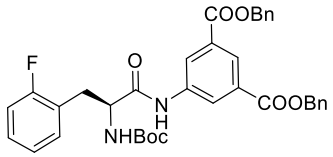
5-((3a*S*,4*S*,6a*R*)-2-Oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)-*N*-(2-phenylpropan-2-yl)pentanamide (entry 3)



A mixture of (+)-biotin (50 mg, 0.205 mmol), diselenide **6h** (3 mg, 0.0051 mmol) and 4 Å molecular sieves (100 mg) in dry DMF (1.0 mL, 0.2M) was treated with $P(OEt)_3$ (53 μL, 0.307 mmol), followed by 2-phenylpropan-2-amine (32 μL, 0.225 mmol) according to the general procedure. The coupling reaction was stirred for 18 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 10% MeOH in CH_2Cl_2 to give the pure amide **4** as a yellow crystalline solid (64 mg, 87% yield). Mp = 120 – 122 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.37 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 5.99 (s, 1H), 5.94 (s, 1H), 5.21 (s, 1H), 4.46 (dd, *J* = 7.7, 5.0 Hz, 1H), 4.25 (dd, *J* = 8.1, 4.7 Hz, 1H), 3.12 (td, *J* = 7.4, 4.6 Hz, 1H), 2.86 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.66 (d, *J* = 12.8 Hz, 1H), 2.18 (t, *J* = 7.4 Hz, 2H), 1.81 – 1.58 (m, 10H), 1.48 – 1.35 (m, 2H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 172.0, 163.5, 147.0, 128.3, 126.6, 124.8, 61.8, 60.1, 55.7, 55.4,

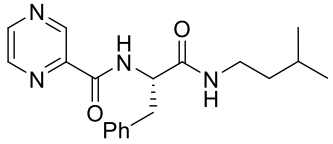
40.5, 36.7, 29.2, 29.1, 28.2, 28.1, 25.6. IR (neat, cm^{-1}): 3207, 3061, 1696, 1644. HRMS (ESI) Calcd. for $C_{19}H_{28}N_3O_2S$ $(M+H)^+$: 362.1902, Found: 362.1892.

Dibenzyl (*S*)-5-(2-((*tert*-butoxycarbonyl)amino)-3-(2-fluorophenyl)propanamido)isophthalate (entry 4)[6]



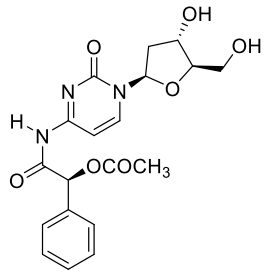
A mixture of N-Boc-2-fluoro-*L*-phenylalanine (50 mg, 0.176 mmol), diselenide **6h** (3 mg, 0.0044 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (0.9 mL, 0.2M) was treated with $P(OEt)_3$ (42 μL, 0.265 mmol), followed by dibenzyl 5-aminoisophthalate (70 mg, 0.194 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexane to give the pure amide **5** as a white solid (76 mg, 69% yield). Mp = 176 – 178 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.46 (s, 1H), 8.49 (s, 2H), 8.21 (s, 1H), 7.48 (dd, *J* = 8.0, 1.8 Hz, 4H), 7.45 – 7.34 (m, 7H), 7.32 – 7.27 (m, 1H), 7.25 – 7.19 (m, 2H), 7.15 – 7.04 (m, 2H), 5.38 (s, 4H), 4.35 (q, *J* = 8.0 Hz, 1H), 3.06 (dd, *J* = 13.9, 6.1 Hz, 2H), 2.90 (dd, *J* = 13.9, 9.2 Hz, 2H), 1.31 (s, 9H).^{13}C NMR (151 MHz, DMSO-d_6) δ 170.9, 164.6, 161.5 (d, *J* = 245.0 Hz), 155.1, 139.7, 135.8, 131.6, 130.6, 128.6, 128.3, 128.2, 124.4, 124.2, 124.1, 115.0 (d, *J* = 21.5 Hz), 78.3, 66.7, 55.0, 30.8, 28.1. IR (neat, cm^{-1}): 3315 (broad), 1718, 1667, 1223, 1163.

(*S*)-*N*-(1-(Isopentylamino)-1-oxo-3-phenylpropan-2-yl)pyrazine-2-carboxamide (entry 5)[7]



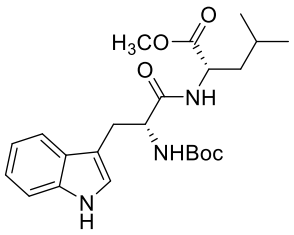
A mixture of (pyrazine-2-carbonyl)-*L*-phenylalanine[8-9] (50 mg, 0.184 mmol), diselenide **6h** (3 mg, 0.0046 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (0.9 mL, 0.2M) was treated with $P(OEt)_3$ (47 μL, 0.276 mmol), followed by isopentylamine (24 μL, 0.202 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 40% EtOAc in hexane to give the pure amide **6** as a white solid (52 mg, 78% yield). Mp = 99 - 100 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 9.38 (d, *J* = 1.4 Hz, 1H), 8.78 (d, *J* = 2.5 Hz, 1H), 8.57 (dd, *J* = 2.4, 1.5 Hz, 1H), 8.44 (d, *J* = 8.3 Hz, 1H), 7.36 – 7.24 (m, 5H), 5.57 (s, 1H), 4.76 (td, *J* = 8.4, 6.1 Hz, 1H), 3.32 – 3.12 (m, 4H), 1.48 -1.40 (m, 1H), 1.28 – 1.19 (m, 2H), 0.86 (d, *J* = 2.7 Hz, 3H), 0.85 (d, *J* = 2.7 Hz, 3H).^{13}C NMR (151 MHz, chloroform-*d*) δ 169.9, 162.9, 147.5, 144.3, 144.0, 142.8, 136.6, 129.3, 128.8, 127.1, 55.1, 38.7, 38.1, 37.9, 25.6, 22.3. IR (neat, cm^{-1}): 3328, 3315, 1659, 1646. HRMS (ESI) Calcd. for $C_{19}H_{24}N_4O_2Na$ $(M+Na)^+$: 363.1797, Found: 363.1786.

(*S*)-2-((1-((2*R*,4*S*,5*R*)-4-Hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)amino)-2-oxo-1-phenylethyl acetate (entry 6)



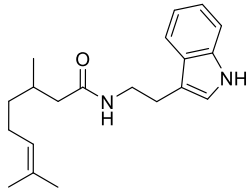
A mixture of (*S*)-(+)-*O*-acetylmandelic acid (50 mg, 0.257 mmol), diselenide **6h** (3 mg, 0.0045 mmol) and 4 Å molecular sieves (100 mg) in dry DMF (1.3 mL, 0.2M) was treated with $P(OEt)_3$ (66 μL, 0.385 mmol), followed by 2'-deoxycytidine monohydrochloride (75 mg, 0.283 mmol) and DIPEA (48 μL, 0.270 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 55 °C and purified by flash column chromatography using SiO_2 and 4% MeOH in CH_2Cl_2 to give the pure amide **7** as a white solid (72 mg, 69% yield). Mp = 190 – 192 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.37 (s, 1H), 8.34 (d, *J* = 7.3 Hz, 1H), 7.62 – 7.50 (m, 2H), 7.49 – 7.35 (m, 3H), 7.21 – 6.95 (m, 1H), 6.05 (d, *J* = 14.1 Hz, 2H), 5.24 (brs, 1H), 5.02 (brs, 1H), 4.18 (brs, 1H), 3.85 (brs, 1H), 3.65 – 3.50 (m, 2H), 2.35 – 2.23 (m, 1H), 2.14 (s, 3H), 2.02 – 1.92 (m, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 170.0, 169.2, 161.9, 154.1, 145.5, 133.9, 129.2, 128.7, 127.7, 95.0, 88.0, 86.3, 75.0, 69.7, 60.8, 40.9, 20.4. IR (neat, cm^{-1}): 3348, 1741, 1723, 1632, 1483. HRMS (ESI) Calcd. for $C_{19}H_{22}N_3O_7$ $(M+H)^+$: 404.1452, Found: 404.1451.

Methyl (*tert*-butoxycarbonyl)-*D*-tryptophyl-*L*-leucinate (entry 7)



A mixture of Boc-*D*-trp-OH (50 mg, 0.164 mmol), diselenide **6h** (3 mg, 0.0041 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (0.8 mL, 0.2M) was treated with $P(OEt)_3$ (42 μL, 0.246 mmol), followed by *L*-leucine methyl ester hydrochloride (33 mg, 0.180 mmol) and DIPEA (32 μL, 0.742mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexane to give the pure amide **8** as a thick yellow oil (62 mg, 88% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.28 (s, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.09 (s, 1H), 6.24 (d, *J* = 8.1 Hz, 1H), 5.16 (s, 1H), 4.52 (s, 2H), 3.67 (s, 3H), 3.39 – 3.28 (m, 1H), 3.22 (dd, *J* = 14.9, 7.2 Hz, 1H), 1.58 – 1.30 (m, 12H), 0.83 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 173.1, 171.6, 155.5, 136.2, 127.5, 123.1, 122.3, 119.8, 118.8, 111.2, 110.5, 80.2, 55.2, 52.2, 50.7, 41.2, 28.3, 24.5, 22.7, 21.8. IR (neat, cm^{-1}): 3315, 2957, 1726, 1709, 1658. HRMS (ESI) Calcd. for $C_{23}H_{34}N_3O_5$ $(M+H)^+$: 432.2504, Found: 432.2504.

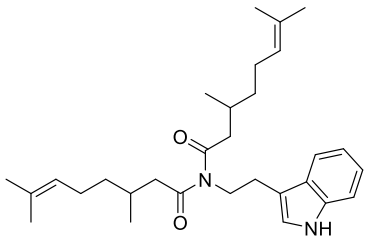
***N*-(2-(1*H*-Indol-3-yl)ethyl)-3,7-dimethyloct-6-enamide (entry 8)**



A mixture of citronellic acid (50 mg, 0.294 mmol), diselenide **6h** (5 mg, 0.0074 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (1.5 mL, 0.2M) was treated with $P(OEt)_3$ (76 μL, 0.385 mmol), followed by tryptamine (52 mg, 0.323 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 10% and 20% EtOAc in hexane to give **9** (74 mg, 81% yield) and **9'** (6 mg, 8% yield), respectively, as thick oils.

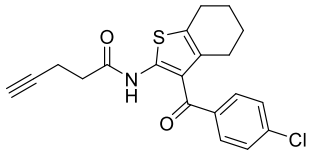
For compound **9** : ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.43 (s, 1H), 7.61(d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 8.2 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 5.60 (t, *J* = 5.9 Hz, 1H), 5.07 (t, *J* = 7.3 Hz, 1H), 3.61 (q, *J* = 6.5 Hz, 2H), 2.97 (t, *J* = 6.8 Hz, 2H), 2.14 (dd, *J* = 13.4, 5.6 Hz, 1H), 2.07 – 1.89 (m, 3H), 1.85 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.67 (s, 3H), 1.59 (s, 3H), 1.38 - 1.28 (m, 1H), 1.20 – 1.10 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 172.6, 136.4, 131.5, 127.3, 124.3, 122.1, 122.1, 119.4, 118.7, 112.8, 111.3, 44.6, 39.6, 36.9, 30.4, 25.7, 25.5, 25.4, 19.5, 17.7. IR (neat, cm^{-1}): 3403, 3279, 1641. HRMS (ESI) Calcd. for $C_{20}H_{29}N_2O$ $(M+H)^+$: 313.2274, Found: 313.2269.

For compound **8'**:



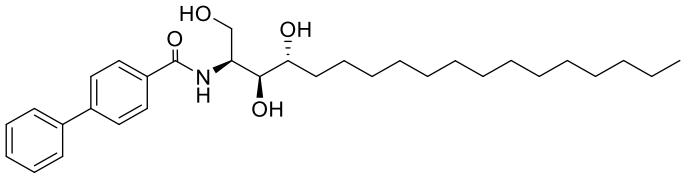
^{1}H NMR (600 MHz, chloroform-*d*) δ 8.00 (s, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.2 Hz, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 5.07 (t, *J* = 7.2 Hz, 2H), 4.03 – 3.84 (m, 2H), 3.03 (t, *J* = 7.5 Hz, 2H), 2.58 (ddd, *J* = 16.2, 5.5, 3.4 Hz, 2H), 2.39 (ddd, *J* = 16.2, 8.0, 2.3 Hz, 2H), 2.06 – 1.88 (m, 6H), 1.67 (s, 6H), 1.59 (s, 6H), 1.34 – 1.25 (m, 2H), 1.17 – 1.10 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 176.0, 136.3, 131.4, 127.3, 124.4, 122.3, 119.7, 118.6, 112.6, 111.3, 45.2, 45.1, 36.9, 29.7, 29.6, 25.7, 25.5, 25.2, 19.7, 17.7. IR (neat, cm^{-1}): 2959, 2922, 1696. HRMS (ESI) Calcd. for $C_{30}H_{45}N_2O_2$ $(M+H)^+$: 465.3476, Found: 465.3477.

***N*-(3-(4-Chlorobenzoyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)pent-4-ynamide (entry 9)**



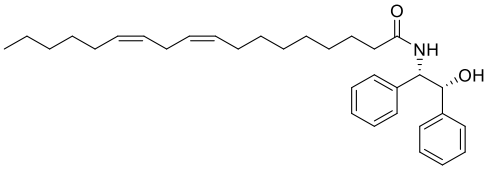
A mixture of 4-pentynoic acid (50 mg, 0.510 mmol), diselenide **6h** (3 mg, 0.012 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (2.5 mL, 0.2M) was treated with $P(OEt)_3$ (131 μL, 0.765 mmol), followed by (2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophen-3-yl)(4-chlorophenyl)methanone (163 mg, 0.561 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 20% ethyl acetate in hexane to give the pure amide **10** as a yellow oil (148 mg, 78% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 11.37 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 2.73 – 2.69 (m, 2H), 2.69 (t, *J* = 6.4 Hz, 2H), 2.65-2.61 (m, 2H), 2.01 (t, *J* = 2.6 Hz, 2H), 1.93 (t, *J* = 6.4 Hz, 2H), 1.81 – 1.75 (m, 2H), 1.57 – 1.51 (m, 2H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 193.5, 168.5, 148.3, 139.0, 137.9, 129.7, 129.5, 128.6, 128.2, 121.0, 82.1, 69.7, 35.7, 27.6, 24.3, 22.9, 22.8, 14.5. IR (neat, cm^{-1}): 3302, 2361, 2337, 1684, 1551. HRMS (ESI) Calcd. for $C_{20}H_{19}NO_2ClS$ $(M+H)^+$: 372.0819, Found: 372.0818.

_N_-((2_S_,3_S_,4_R_)-1,3,4-Trihydroxyoctadecan-2-yl)-[1,1'-biphenyl]-4-carboxamide (entry 10)



A mixture of biphenyl-4-carboxylic acid (50 mg, 0.252 mmol), diselenide **6h** (4 mg, 0.0063 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (1.3 mL, 0.2M) was treated with $P(OEt)_3$ (65 μL, 0.385 mmol), followed by phytosphingosine (75 mg, 0.283 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 55 °C and purified by flash column chromatography using SiO_2 and 10% MeOH in CH_2Cl_2 to give the pure amide **11** as a white solid (102 mg, 82% yield). Mp = 163 – 165 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.01 (d, *J* = 8.7 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.75(d, *J* = 8.4 Hz, 2H), 7.73 – 7.69 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.37 (m, 1H), 4.71 (d, *J* = 5.3 Hz, 1H), 4.52 (t, *J* = 5.7 Hz, 1H), 4.35 (d, *J* = 6.7 Hz, 1H), 4.14 (dtd, *J* = 8.7, 6.5, 4.3 Hz, 1H), 3.71 – 3.65 (m, 1H), 3.59 (dt, *J* = 10.9, 6.4 Hz, 1H), 3.52 (q, *J* = 5.7 Hz, 1H), 3.40 (dtd, *J* = 9.2, 6.3, 2.4 Hz, 1H), 1.58 – 1.51 (m, 1H), 1.39 (s, 1H), 1.31 – 1.10 (m, 27H), 0.83 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.1, 143.0, 139.7, 134.2, 129.5, 128.4, 127.3, 126.8, 74.9, 71.3, 60.8, 53.7, 32.3, 31.8, 29.6, 29.6, 29.5, 29.5, 29.5, 29.2, 25.7, 22.6, 14.4. IR (neat, cm^{-1}): 3334 (broad), 1619, 1541. HRMS (ESI) Calcd. for $C_{31}H_{48}NO_4$ $(M+H)^+$: 498.3578, Found: 498.3569.

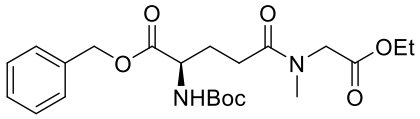
(9_Z_,12_Z_)-_N_-((1_S_,2_R_)-2-Hydroxy-1,2-diphenylethyl)octadeca-9,12-dienamide (entry 11)



A mixture of linoleic acid (50 mg, 0.178 mmol), diselenide **6h** (3 mg, 0.0045 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (890 μL, 0.2M) was treated with $P(OEt)_3$ (46 μL, 0.267 mmol), followed by (1*R*,2*S*)-2-amino-1,2-diphenylethan-1-ol (42 mg, 0.196 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 25% ethyl acetate in hexane to give the pure amide **12** as a

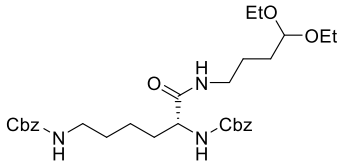
white solid (53 mg, 63% yield). Mp = 110 – 112 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.26 – 7.18 (m, 6H), 7.05-6.99 (m, 4H), 6.17 (d, *J* = 8.0 Hz, 1H), 5.50 – 5.24 (m, 5H), 5.07 (t, *J* = 4.3 Hz, 1H), 3.06 (d, *J* = 4.8 Hz, 1H), 2.77 (t, *J* = 6.9 Hz, 2H), 2.21 (t, *J* = 7.6 Hz, 2H), 2.10 – 1.95 (m, 4H), 1.46 – 1.22 (m, 15H), 10.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 173.3, 139.7, 137.2, 130.2, 130.0, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 126.6, 59.3, 36.8, 31.5, 29.6, 29.4, 29.3, 29.2, 29.1, 27.2, 25.7, 25.6, 22.6, 14.1. IR (neat, cm^{-1}): 3313, 1640, 1540. HRMS (ESI) Calcd. for $C_{32}H_{46}NO_2$ $(M+H)^+$: 476.3523, Found: 476.3517.

Benzyl *N*^{2}-(*tert*-butoxycarbonyl)-*N*^{5}-(2-ethoxy-2-oxoethyl)-*N*^{5}-methyl-*D*-glutaminate (entry 12)



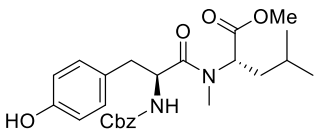
A mixture of Boc-*D*-glu(OBzl)-OH (50 mg, 0.148 mmol), diselenide **6h** (3 mg, 0.0037 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (750 μL, 0.2M) was treated with $P(OEt)_3$ (38 μL, 0.222 mmol), followed by sarcocine ethyl ester hydrochloride (25 mg, 0.163 mmol) and DIPEA (28 μL, 0.163 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 25% ethyl acetate in hexane to give the pure amide **13** as a thick oil (60 mg, 92% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.58 – 7.27 (m, 4H), 5.40 (d, *J* = 8.5 Hz, 0.8H), 5.33 (d, *J* = 8.5 Hz, 0.2H), 5.18 - 5.07 (m, 2H), 4.78 (td, *J* = 8.9, 3.8 Hz, 0.8H), 4.59 (td, *J* = 8.9, 3.8 Hz, 0.2H), 4.41 – 4.08 (m, 3H), 3.86 (d, *J* = 17.3 Hz, 1H), 3.16 (s, 2.4H), 2.96 (s, 0.6H), 2.62 – 2.36 (m, 2H), 2.21 – 2.08 (m, 1H), 1.81 – 1.63 (m, 2H), 1.42 (s, 7H), 1.41 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 0.6H), 1.25 (t, *J* = 7. 1 Hz, 2.4H).^{13}C NMR (151 MHz, chloroform-*d*) δ 172.8, 172.5, 168.8, 168.7, 155.6, 135.9, 128.5, 128.2, 128.2, 79.7, 66.4, 66.4, 61.7, 61.3, 60.4, 51.3, 49.7, 49.3, 49.2, 36.4, 35.0, 29.7, 29.5, 29.5, 28.5, 28.3, 28.3, 28.2, 28.1, 21.0, 14.2, 14.1, 14.1. IR (neat, cm^{-1}): 3403 (broad), 1733, 1706, 1647. HRMS (ESI) Calcd. for $C_{22}H_{33}N_2O_7$ $(M+H)^+$: 437.2282, Found: 437.2285.

Dibenzyl (6-((4,4-diethoxybutyl)amino)-6-oxohexane-1,5-diyl)(*R*)-dicarbamate (entry 13)



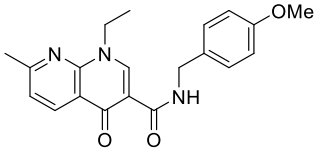
A mixture of $N_α$,$N_ε$-di-*Z*-*L*-lysine (50 mg, 0.120 mmol), diselenide **6h** (2 mg, 0.003 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (600 μL, 0.2M) was treated with $P(OEt)_3$ (31 μL, 0.180 mmol), followed by 4-aminobutyraldehyde diethyl acetal (21.4 mg, 0.132 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 20% ethyl acetate in hexane to give the pure amide **14** as a white solid (56 mg, 83% yield). Mp = 108 – 110 °C. ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.27 (m, 10H), 6.40 – 6.30 (m, 1H), 5.57 (d, *J* = 7.9 Hz, 1H), 5.17 – 5.00 (m, 4H), 4.98 – 4.90 (m, 1H), 4.46 (t, *J* = 5.2 Hz, 1H), 4.15 - 4.00 (m, 1H), 3.62 (dqd, *J* = 9.0, 7.0, 1.9 Hz, 2H), 3.47 (dq, *J* = 9.4, 7.0 Hz, 2H), 3.30 - 3.20 (m, 2H), 3.20 – 3.10 (m, 2H), 1.90 – 1.73 (m, 2H), 1.70 – 1.43 (m, 6H), 1.35 (p, *J* = 7.1 Hz, 2H), 1.18 (td, *J* = 7.1, 1.2 Hz, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 171.5, 156.7, 156.3, 136.6, 136.2, 128.5, 128.5, 128.4, 128.2, 128.1, 102.6, 67.1, 66.7, 61.5, 61.4, 54.9, 40.2, 39.3, 32.0, 30.9, 29.4, 24.4, 22.3, 15.3. IR (neat, cm^{-1}): 3294, 1690, 1680, 1641, 1533. HRMS (ESI) Calcd. for $C_{30}H_{43}N_3O_7Na$ $(M+Na)^+$: 580.2993, Found: 580.2995.

Methyl *N*-(((benzyloxy)carbonyl)-*L*-tyrosyl)-*N*-methyl-*L*-leucinate (entry 14)



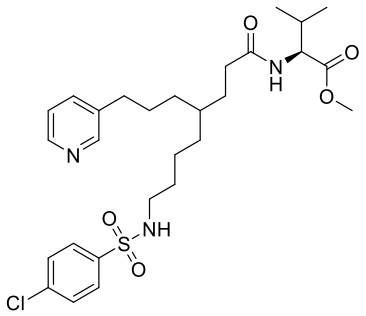
A mixture of N-carbobenzoxy-*L*-tyrosine (50 mg, 0.158 mmol), diselenide **6h** (3 mg, 0.0039 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (0.8 mL, 0.2M) was treated with $P(OEt)_3$ (38 μL, 0.222 mmol), followed by N-methyl methyl-*L*-leucinate hydrochloride (25 mg, 0.163 mmol) and DIPEA (28 μL, 0.163 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 40% EtOAc in hexane to give the pure amide **15** as a thick oil (46 mg, 63% yield). ^{1}H NMR (399 MHz, chloroform-*d*) δ 7.39 – 7.28 (m, 5H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 8.7 Hz, 2H), 5.90 (brs, 1H), 5.60 (d, *J* = 8.8 Hz, 1H), 5.28 (dd, *J* = 10.4, 5.3 Hz, 1H), 5.14 – 4.96 (m, 2H), 4.88 (dd, *J* = 15.1, 6.5 Hz, 1H), 3.69 (s, 3H), 3.03 (dd, *J* = 13.9, 6.8 Hz, 1H), 2.86 (s, 3H), 2.84 (dd, *J* = 13.9, 5.3 Hz, 1H), 1.79 – 1.62 (m, 2H), 1.50 – 1.35 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 172.3, 171.9, 155.8, 155.0, 136.3, 130.7, 130.6, 128.5, 128.1, 127.9, 127.4, 115.4, 115.4, 66.9, 54.7, 52.3, 52.2, 37.9, 37.1, 31.1, 29.7, 24.8, 23.2, 21.4. IR (neat, cm^{-1}): 3297, 1734, 1700, 1635. HRMS (ESI) Calcd. for $C_{25}H_{33}N_2O_6$ $(M+H)^+$: 457.2333, Found: 457.2328.

1-Ethyl-*N*-(4-methoxybenzyl)-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxamide (entry 15)



A mixture of nalidixic acid (50 mg, 0.215 mmol), diselenide **6h** (4 mg, 0.0054 mmol) and 4 Å molecular sieves (100 mg) in dry CH_3CN (1.1 mL, 0.2M) was treated with $P(OEt)_3$ (55 μL, 0.323 mmol), followed by 4-methoxybenzylamine (31 μL, 0.237 mmol) according to the general procedure. The coupling reaction was stirred for 28 h under dry air at 55 °C and purified by flash column chromatography using SiO_2 and 5% MeOH in CH_2Cl_2 to give the pure amide **16** as a white solid (51 mg, 68% yield). Mp = 188 – 190 °C. ^{1}H NMR (600 MHz, chloroform-*d*) δ 10.23 (t, *J* = 6.5 Hz, 1H), 8.93 (s, 1H), 8.62 (d, *J* = 8.1 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.61 (d, *J* = 5.7 Hz, 2H), 4.55 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 2.69 (s, 3H), 1.50 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 176.9, 164.6, 163.2, 158.7, 148.5, 147.4, 136.3, 131.0, 129.0, 121.2, 120.3, 114.0, 112.9, 55.3, 46.8, 42.8, 25.2, 15.2. IR (neat, cm^{-1}): 3180 (broad), 1658, 1604. HRMS (ESI) Calcd. for $C_{20}H_{22}N_3O_3$ $(M+H)^+$: 352.1656, Found: 352.1654.

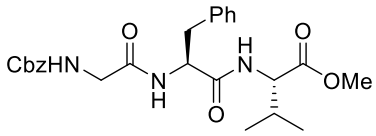
Methyl (8-((4-chlorophenyl)sulfonamido)-4-(3-(pyridin-3-yl)propyl)octanoyl)-*L*-valinate (entry 16)



A mixture of 8-(4-chlorophenylsulfonamido)-4-(3-(pyridin-3-yl)propyl)octanoic acid (30 mg, 0.066 mmol), diselenide **6h** (1 mg, 0.00165 mmol) and 4 Å molecular sieves (60 mg) in dry CH_3CN (0.3 mL, 0.2M) was treated with $P(OEt)_3$ (17 μL, 0.099 mmol), followed by L-valine methyl ester hydrochloride (12 mg, 0.073 mmol) and DIPEA (13 μL, 0.073 mmol) according to the general procedure. The coupling reaction was stirred for 16 h under dry air at 30 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexane to give the pure amide **17** as a white solid (34 mg, 92% yield). (It is a 1:1 mixture of diastereomers) ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.36 (brs, 2H), 7.76 – 7.69 (m, 2H), 7.51 – 7.44 (m, 3H), 7.14 (2xd, *J* = 4.9 Hz, 1H), 6.02 (2xd, *J* = 8.5 Hz, 1H), 5.13 (2xt, *J* = 6.1 Hz, 1H), 4.49 (2xdd, *J* = 5.3, 8.5 Hz, 1H), 3.66 (2xs, 3H), 2.95 – 2.80 (m, 2H), 2.51 (t, *J* = 7.6 Hz, 2H), 2.17 – 2.03 (m, 3H), 1.59 – 1.45 (m, 4H), 1.42 – 1.31 (m, 2H), 1.21 – 1.08 (m, 7H), 0.88 – 0.81 (m, 6H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 173.1, 173.1, 173.0, 172.8, 149.8, 147.2, 138.9, 138.8, 137.7, 135.9, 129.3, 128.5, 123.4, 57.0, 56.9, 52.2, 52.2, 43.0, 36.7, 36.5, 33.7, 33.6, 33.2, 33.2, 32.9, 32.8, 32.4, 32.3, 31.2, 29.7, 29.5, 28.9, 28.9, 28.0, 23.3, 23.2, 19.0, 19.0, 17.9, 17.9. IR (neat, cm^{-1}): 3328 (broad), 1740, 1649, 1157. HRMS (ESI) Calcd. for $C_{30}H_{32}N_9OS$ $(M+H)^+$: 566.2445, Found: 566.2443.

Optimized procedure for the synthesis of racemization sensitive peptides:

Methyl ((benzyloxy)carbonyl)glycyl-*L*-phenylalanyl-*L*-valinate (**entry 17**)[10-11]



A 12 mL test tube was charged with 4 Å molecular sieves (140 mg) previously activated in a microwave oven for 3 min and dried under reduced pressure for 5 min. Then, Z-Gly-L-Phe-OH (100 mg, 0.281 mmol), L-Val-OMe•HCl (56 mg, 0.337 mmol), anhydrous $CuCl_2$ (37.7 mg, 0.281 mmol), and diselenide **6g** (5 mg, 0.007 mmol) were added along with dry acetonitrile (1.4 mL, 0.2M, moisture content <25 ppm). The reaction mixture was cooled to 0 °C, DIPEA (39.9 mg, 0309 mmol) and triethylphosphite (69.9 mg, 0.421 mmol) were added sequentially at 0 °C. The reaction mixture was allowed slowly to rise in temperature to 23 °C and stirred for 18 h under a dry air atmosphere (balloon) at 23 °C. The reaction mixture was filtered, washed with CH_2Cl_2 (20 ml), and concentrated under reduced pressure to give the crude product **18**. The diastereomeric ratio of the crude product determined as 98:2 through HPLC using chiral OJ-RH stationary phase. The crude product was purified by silica gel flash column chromatography using ethyl acetate and hexanes as mobile phase to give pure tripeptide **18** in 68% yield (89 mg, 0.190 mmol) as a white solid. The spectroscopic data are consistent with those reported in literature.

HPLC conditions: Column: Chiral AS-RH (0.46 X 15 cm); λ = 254 nm; Flow rate: 0.7 mL/min; Mobile phase: 30 – 40 % CH_3CN in H_2O for 10 min, 40 – 45 % CH_3CN in H_2O for 5 min, 45 – 50 % CH_3CN in H_2O for 10 min; major isomer Ret. Time = 20.8 min, minor isomer Ret. Time = 21.8 min.

Optimization:

Table S4

entry	reagents and conditions	*dr*
1	Followed general procedure	60:40
2	DIPEA and triethylphosphite were added at 0 °C and stirred at 23 °C	70:30
3	1.0 equiv of anhydrous $CuCl_2$ was added, then DIPEA and triethylphosphite were added at 0 °C and stirred at 23 °C	98:2

Experimental procedure for UV-vis studies:

A 2.5 mL solution of 0.04 mM diselenide **6h** in CH_3CN was placed in a UV cuvette with a screw cap in the absence of air and its UV absorption spectrum was measured. (**Figure 1**)

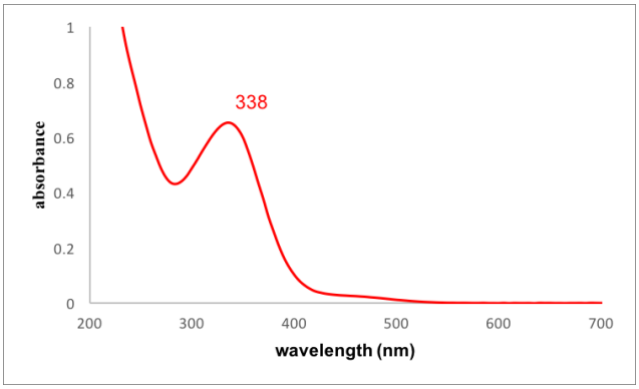


Figure S1: UV absorption spectrum of **6h** (0.04mM in CH_3CN)

50 µL of 2mM $P(OEt)_3$ and 100 µL of 2mM toluic acid were added into the same cuvette in the absence of air. It was monitored over 30 cycles for every half minute. Almost complete transformation of **6h** into a new product took place within 15 minutes. (**Figure 2**)

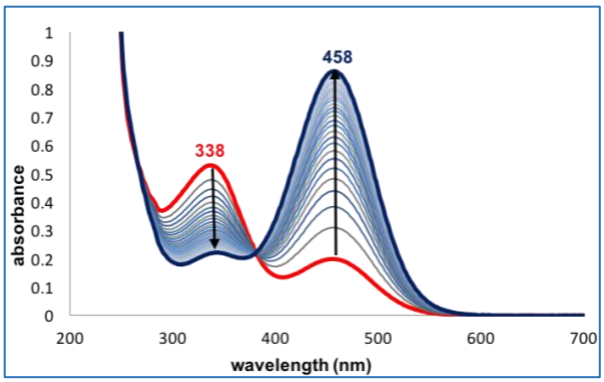


Figure S2: transformation of **6h** (0.04 mM in CH_3CN) into selenide **5h** within 15 min

After that, the solution was exposed to dry air through a balloon and the regeneration of **6h** was monitored over a period of 15 hours. (**Figure 3**)

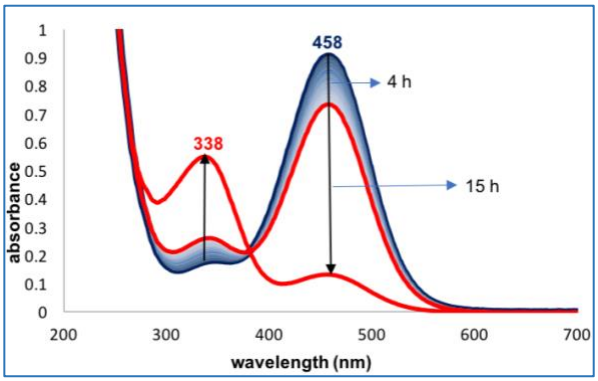
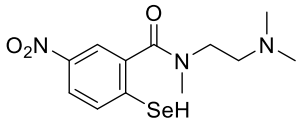
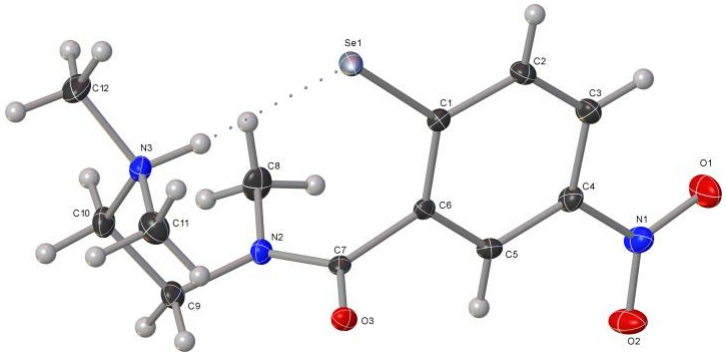


Figure S3: regeneration of **6h** under air over 15 h

Structure determination of *N*-(2-(dimethylamino)ethyl)-2-hydroseleno-*N*-methyl-5-nitrobenzamide (5h)



To a solution of **6h** (24 mg, 0.036 mmol) in CD_3CN (0.5 mL) in an NMR tube was added $P(OEt)_3$ (6 μL, 0.036 mmol) and toluic acid (5 mg, 0.036 mmol) under an argon atmosphere. After standing at room temperature for 24 hours orange reddish crystals of **5h** formed. These crystals were collected by filtration and analyzed by X-ray crystallography. CCDC 1577749 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre. In **5h** the tertiary amidic moiety ortho to the selenium is almost fully orthogonal to the aromatic ring (N2-C7-C6-C1 torsion angle = 90.31°)



Experimental. Single red prism-shaped crystals of **5h** were chosen from the sample as supplied. A suitable crystal (0.23×0.16×0.07 mm^3) was selected and mounted on a loop with paratone oil on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was cooled to T = 100(2) K during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) structure solution program using the Intrinsic Phasing solution method and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with version 2014/7 of **ShelXL-2014** (Sheldrick, 2015) using Least Squares minimisation.

Crystal Data. $C_{14}H_{20}N_4O_3Se$, M_r = 371.30, monoclinic, $P2_1/n$ (No. 14), a = 6.0940(3) Å, b = 12.4007(6) Å, c = 22.2062(9) Å, β = 94.542(4)°, $\alpha = \gamma$ = 90°, V = 1672.85(13) $Å^3$, T = 100(2) K, Z = 4, Z' = 1, $\mu(MoK_\alpha)$ = 2.262 mm^{-1}, 15838 reflections measured, 5096 unique (R_{int} = 0.0492) which were used in all calculations. The final wR_2 was 0.0795 (all data) and R_1 was 0.0357 (I > 2σ(I)).

Compound	**5h**
Formula	$C_{14}H_{20}N_4O_3Se$
$D_{calc.}$/ g cm^{-3}	1.474
μ/mm^{-1}	2.262
Formula Weight	371.30
Colour	red
Shape	prism
Size/mm^3	0.23×0.16×0.07
T/K	100(2)
Crystal System	monoclinic
Space Group	$P2_1/n$
a/Å	6.0940(3)
b/Å	12.4007(6)
c/Å	22.2062(9)
α/°	90
β/°	94.542(4)
γ/°	90
V/Å^3	1672.85(13)
Z	4
Z'	1
Wavelength/Å	0.71073
Radiation type	MoK_α
Θ_{min}/°	2.467
Θ_{max}/°	30.508
Measured Refl.	15838
Independent Refl.	5096
Reflections with I > 2σ(I)	3990
R_{int}	0.0492
Parameters	207
Restraints	46
Largest Peak	0.808
Deepest Hole	-0.544
GooF	1.060
wR_2 (all data)	0.0795
wR_2	0.0758
R_1 (all data)	0.0536
R_1	0.0357

Reflection Statistics

Total reflections (after filtering)	16276	Unique reflections	5096
Completeness	0.997	Mean I/σ	12.42
hkl_{max} collected	(8, 17, 26)	hkl_{min} collected	(-8, -17, -31)
hkl_{max} used	(8, 17, 31)	hkl_{min} used	(-8, 0, 0)
Lim d_{max} collected	100.0	Lim d_{min} collected	0.36
d_{max} used	8.26	d_{min} used	0.7
Friedel pairs	2613	Friedel pairs merged	1
Inconsistent equivalents	1	R_{int}	0.0492
R_{sigma}	0.0608	Intensity transformed	0
Omitted reflections	0	Omitted by user (OMIT hkl)	0
Multiplicity	(7258, 3513, 616, 36)	Maximum multiplicity	12
Removed systematic absences	438	Filtered off (Shel/OMIT)	0

Table S5: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **5h**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
Se1	4744.1(3)	1125.5(2)	5466.6(2)	14.77(6)
O3	5213(2)	3753.1(11)	4745.7(6)	13.3(3)
O1	7936(3)	4752.1(13)	7649.2(7)	27.5(4)
O2	6959(3)	5867.2(12)	6932.9(7)	27.3(4)
N2	1807(2)	3590.0(13)	5087.0(7)	12.7(3)
N3	1215(3)	1694.1(14)	4276.0(7)	14.7(3)
N1	7218(3)	4943.0(14)	7126.7(8)	18.3(4)
C6	5019(3)	3382.2(15)	5788.7(8)	10.5(3)
C2	6614(3)	2155.9(16)	6540.9(9)	15.1(4)
C1	5502(3)	2315.3(15)	5966.0(8)	11.5(3)
C7	4028(3)	3593.9(14)	5159.3(8)	10.2(3)
C4	6640(3)	4045.3(15)	6729.9(8)	14.1(4)
C5	5575(3)	4245.5(16)	6166.2(8)	11.9(3)
C10	-394(3)	2605.9(16)	4287.2(9)	17.0(4)
C11	2831(3)	1829.9(18)	3816.8(9)	20.9(4)
C3	7171(3)	3006.9(16)	6922.9(9)	16.0(4)
C9	676(3)	3669.0(16)	4484.5(9)	15.7(4)
C12	-17(4)	661.4(18)	4187.8(11)	24.6(5)
C8	444(3)	3340.5(19)	5579.1(9)	19.4(4)
N4	2667(4)	2888(2)	7775.7(12)	52.1(7)
C14	2143(4)	1143(2)	7136.6(13)	40.4(6)
C13	2449(4)	2124(3)	7495.4(13)	39.3(6)

Table S6: Anisotropic Displacement Parameters (×10^4) **5h**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \ldots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Se1	18.92(9)	8.61(10)	15.93(10)	-1.53(7)	-4.08(6)	0.74(7)
O3	12.7(6)	13.8(7)	13.8(6)	1.4(5)	2.8(4)	0.3(5)
O1	44.9(10)	21.6(9)	14.5(7)	-3.3(6)	-7.6(7)	-3.1(7)
O2	50.4(10)	12.9(8)	18.2(8)	-0.4(6)	-0.6(7)	-5.6(7)
N2	10.2(6)	13.7(8)	14.0(7)	-0.3(6)	0.0(5)	0.2(5)
N3	13.6(7)	13.4(9)	16.3(8)	0.0(6)	-2.8(6)	-1.4(6)
N1	26.3(9)	14.0(9)	14.6(8)	-2.2(6)	0.9(7)	-3.4(7)
C6	8.3(7)	11.4(9)	11.9(7)	1.0(6)	1.8(6)	-1.4(6)
C2	17.3(9)	12.6(10)	15.2(9)	2.4(7)	-0.9(7)	1.1(7)
C1	11.5(8)	11.0(9)	12.3(8)	-0.5(7)	1.6(6)	-0.6(6)
C7	12.0(7)	5.1(8)	13.1(7)	-0.6(6)	0.0(5)	0.9(5)
C4	17.6(9)	12.1(10)	12.6(8)	-3.5(7)	0.8(7)	-2.3(7)
C5	12.9(8)	10.1(9)	13.1(8)	1.1(7)	3.3(7)	0.0(6)
C10	12.3(8)	17.2(11)	20.9(10)	-2.0(8)	-3.5(7)	1.1(7)
C11	23.7(10)	22.8(12)	16.1(9)	-1.7(8)	1.4(8)	2.1(8)
C3	19.5(9)	16.9(10)	11.4(9)	1.6(7)	-0.5(7)	-1.8(7)
C9	12.8(8)	14.4(10)	19.3(10)	0.6(7)	-2.9(7)	2.6(6)
C12	26.3(11)	12.8(11)	33.1(12)	0.1(9)	-7.1(9)	-4.9(8)
C8	12.0(8)	27.6(12)	19.4(10)	-2.0(8)	6.0(7)	-1.5(8)
N4	33.6(12)	76.7(17)	45.2(13)	-13.8(12)	-2.6(10)	1.0(11)
C14	30.1(11)	53.6(14)	37.6(12)	1(1)	3.3(9)	-2.1(10)
C13	33.5(9)	48(1)	35.9(9)	-0.9(8)	0.4(7)	0.6(7)

Table S7: Bond Lengths in Å for **5h**.

Atom	Atom	Length/Å
Se1	C1	1.8813(18)
O3	C7	1.229(2)
O1	N1	1.230(2)
O2	N1	1.230(2)
N2	C7	1.350(2)
N2	C9	1.459(2)
N2	C8	1.457(3)
N3	C10	1.498(2)
N3	C11	1.482(3)
N3	C12	1.489(3)
N1	C4	1.446(2)
C6	C1	1.405(3)
C6	C7	1.501(2)
C6	C5	1.385(3)
C2	C1	1.411(2)
C2	C3	1.379(3)
C4	C5	1.386(2)
C4	C3	1.387(3)
C10	C9	1.520(3)
N4	C13	1.136(4)
C14	C13	1.457(4)

Table S8: Bond Angles in ° for **5h**.

Atom	Atom	Atom	Angle/°
C7	N2	C9	120.33(17)
C7	N2	C8	122.49(16)
C8	N2	C9	116.49(15)
C11	N3	C10	113.40(16)
C11	N3	C12	111.26(17)
C12	N3	C10	109.10(15)
O1	N1	C4	118.55(17)
O2	N1	O1	122.39(17)
O2	N1	C4	119.05(16)
C1	C6	C7	119.05(16)
C5	C6	C1	121.49(16)
C5	C6	C7	119.30(17)
C3	C2	C1	121.76(18)
C6	C1	Se1	122.48(13)
C6	C1	C2	117.42(16)
C2	C1	Se1	120.09(14)
O3	C7	N2	123.71(16)
O3	C7	C6	120.48(16)
N2	C7	C6	115.81(16)
C5	C4	N1	119.12(17)
C5	C4	C3	121.76(17)
C3	C4	N1	119.12(16)
C6	C5	C4	118.86(18)
N3	C10	C9	113.12(14)
C2	C3	C4	118.70(17)
N2	C9	C10	111.52(16)
N4	C13	C14	179.4(3)

Table S9: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **5h**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
H2	6980	1458	6666	18
H5	5239	4947	6043	14
H10A	-1503	2425	4561	20
H10B	-1131	2693	3887	20
H11A	2066	1893	3424	31
H11B	3791	1215	3825	31
H11C	3684	2470	3904	31
H3A	7888	2887	7302	19
H9A	1723	3876	4198	19
H9B	-442	4226	4483	19
H12A	-1018	585	4498	37
H12B	1002	70	4210	37
H12C	-828	664	3799	37
H8A	384	2573	5633	29
H8B	-1016	3614	5484	29
H8C	1066	3670	5945	29
H14A	2414	1295	6725	61
H14B	662	889	7153	61
H14C	3154	601	7295	61
H3	2050(40)	1660(20)	4656(7)	36(7)

Crystallography Citations

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Rigaku Corporation, Oxford, UK.

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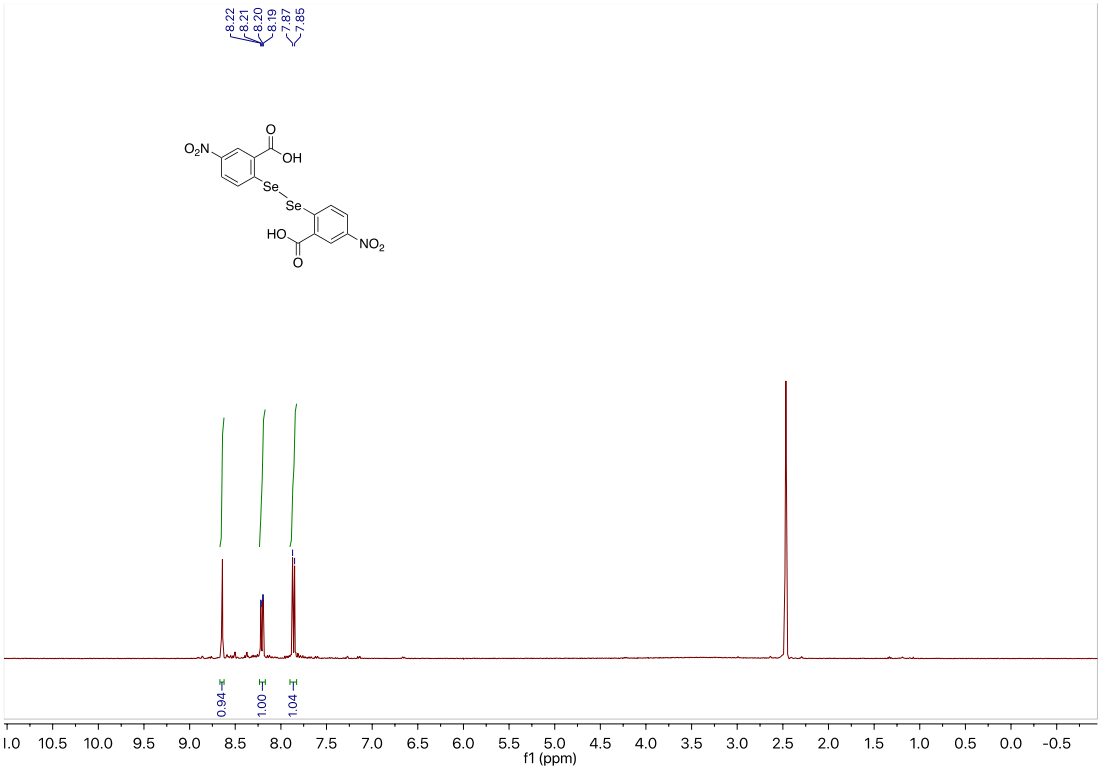
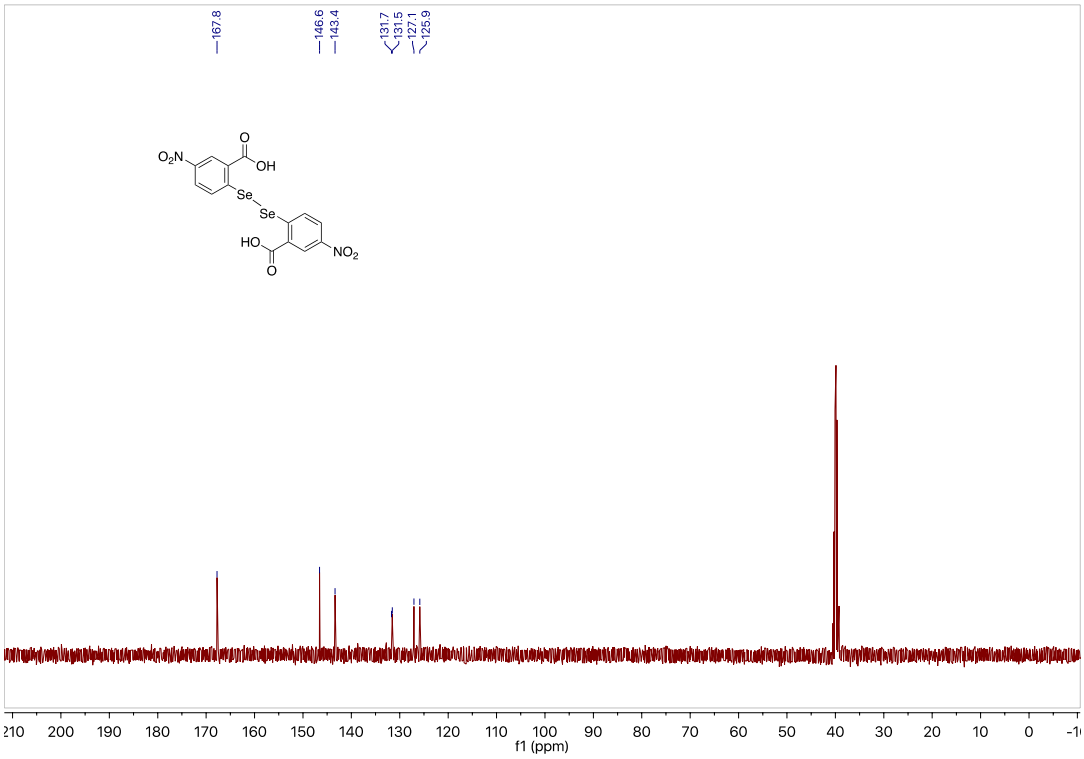
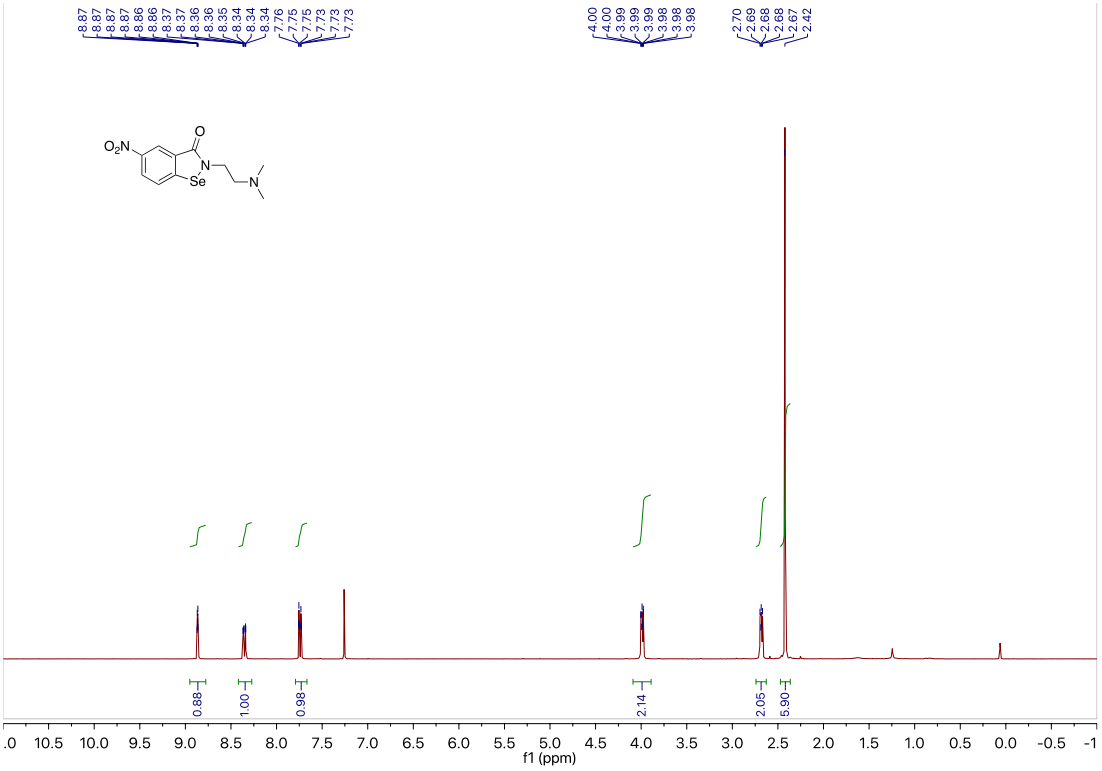
Scans of ^{1}H and ^{13}C NMR of new compounds

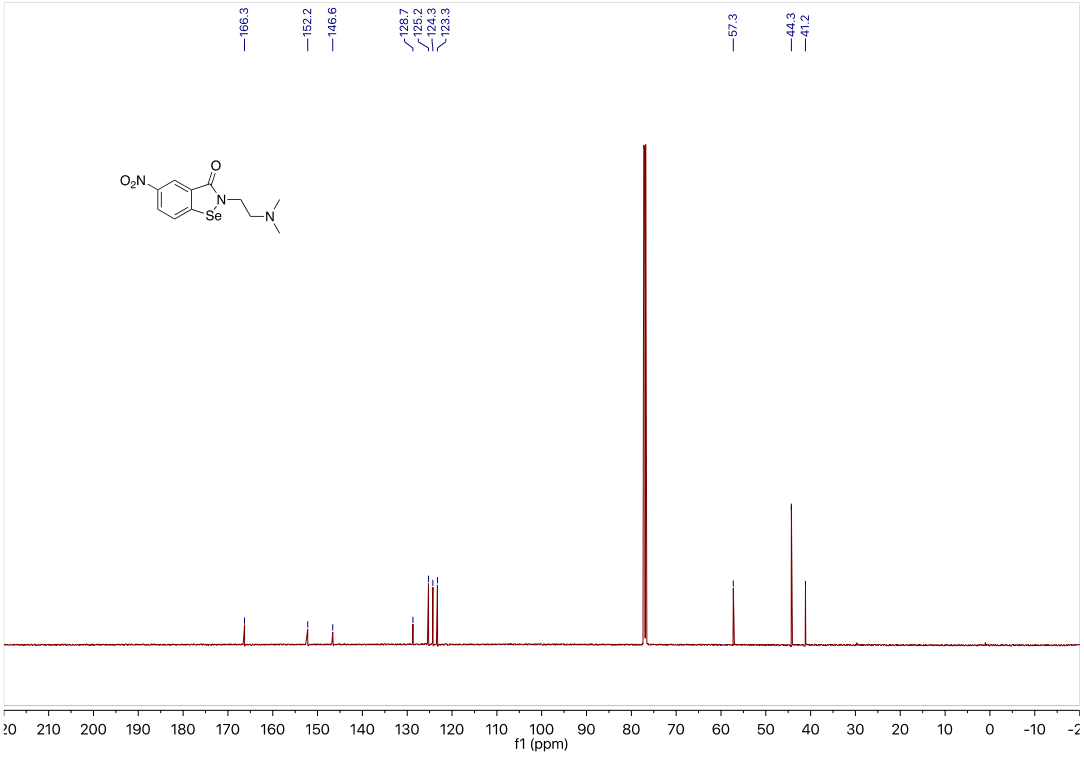
6,6'-Diselanediylbis(3-nitrobenzoic acid) (**I**)



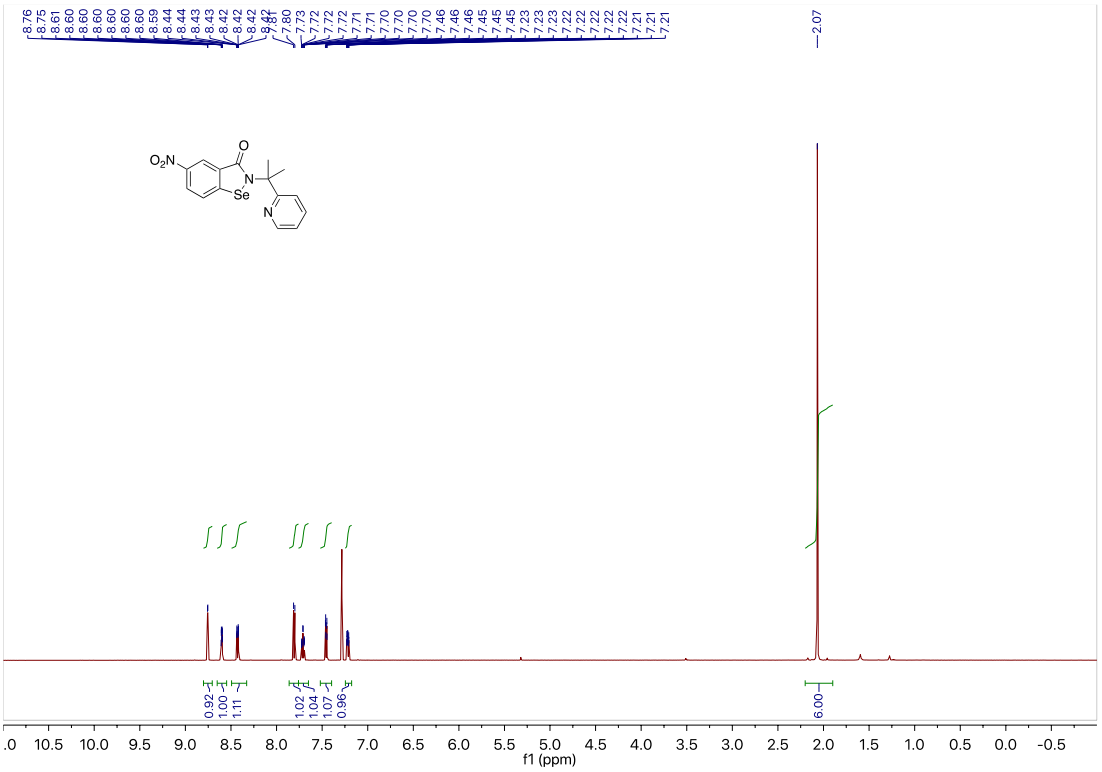


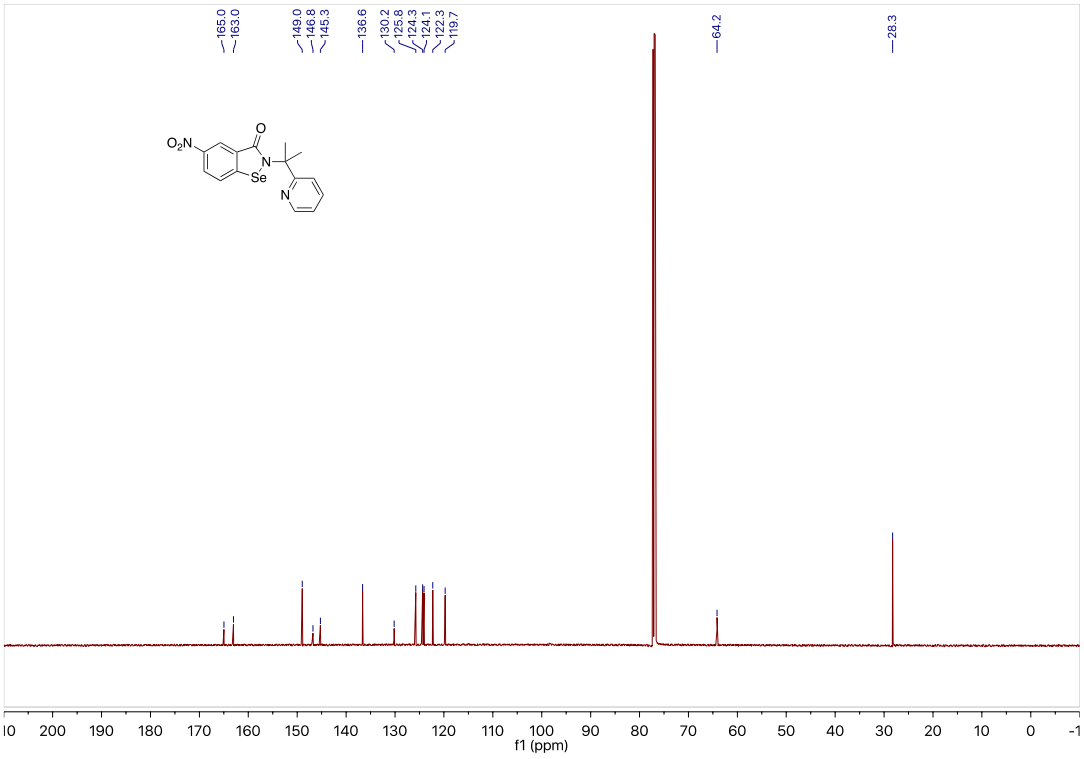
2-(2-(Dimethylamino)ethyl)-5-nitrobenzo[*d*][1,2]selenazol-3(2*H*)-one (**4a**)



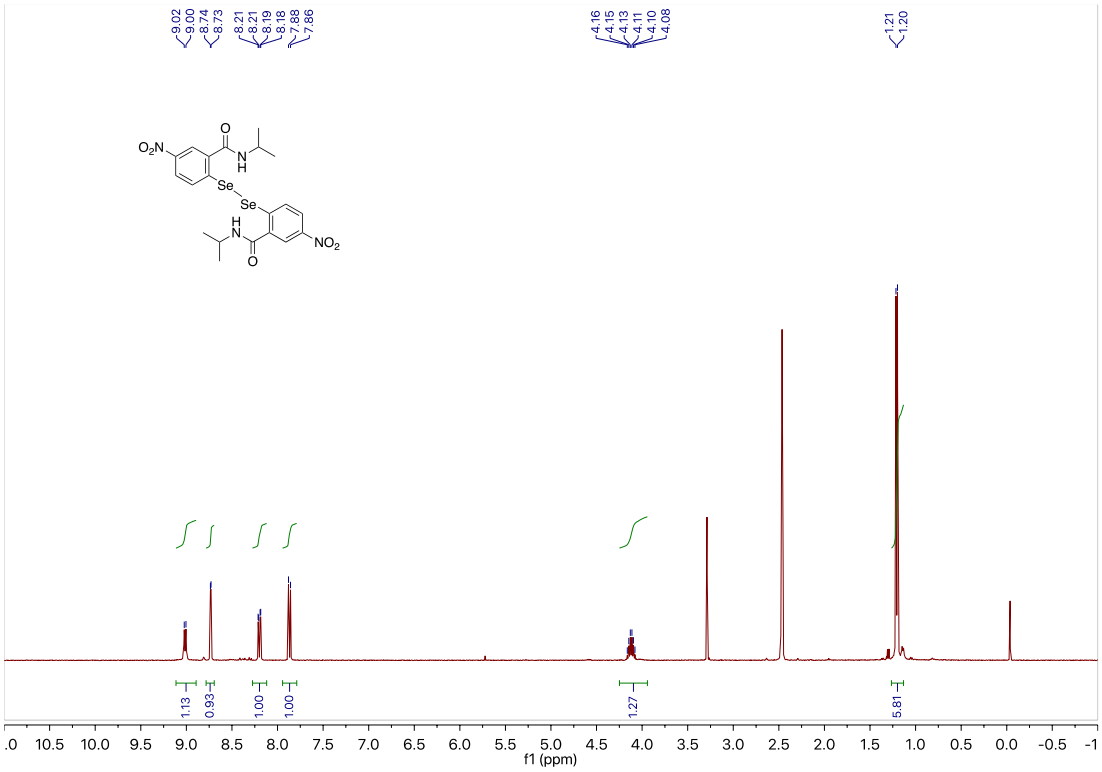


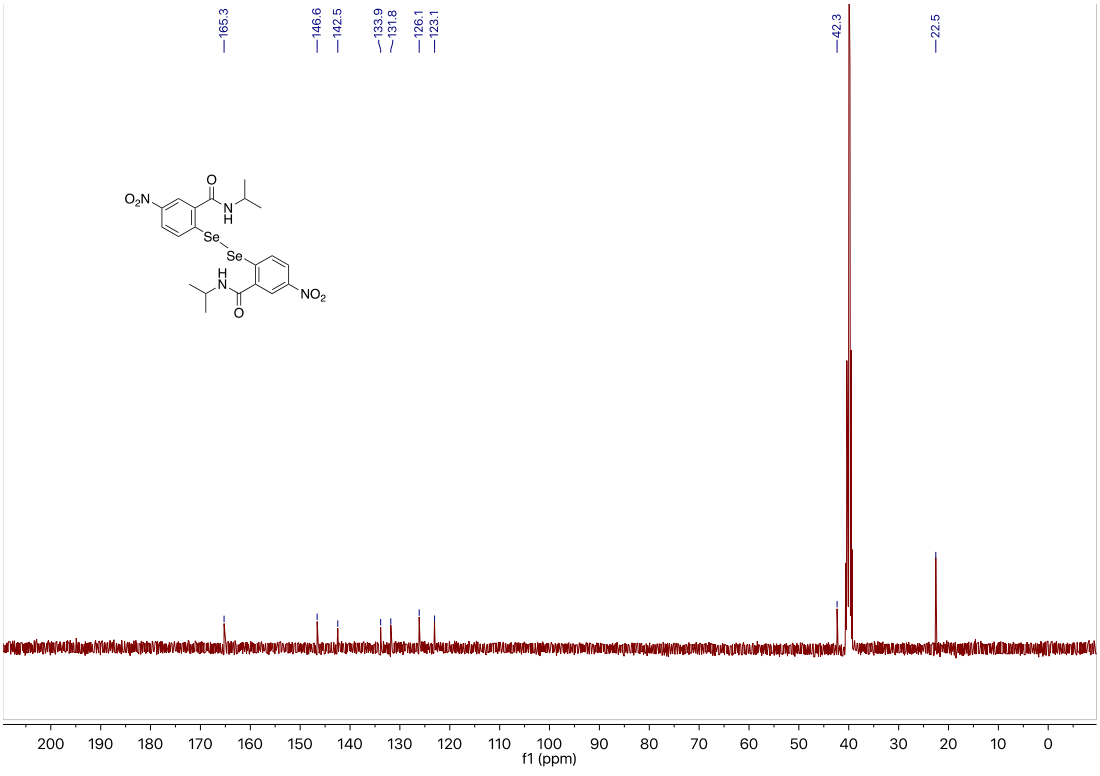
5-Nitro-2-(2-(pyridin-2-yl)propan-2-yl)benzo[*d*][1,2]selenazol-3(2*H*)-one (**4b**)



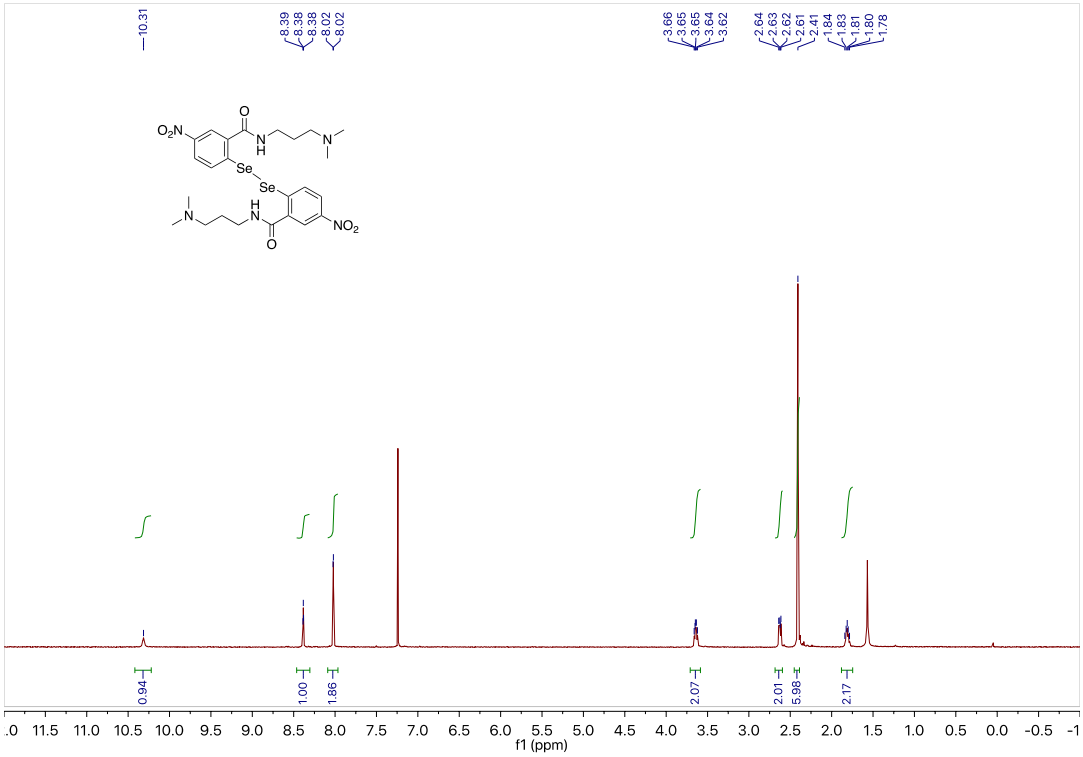


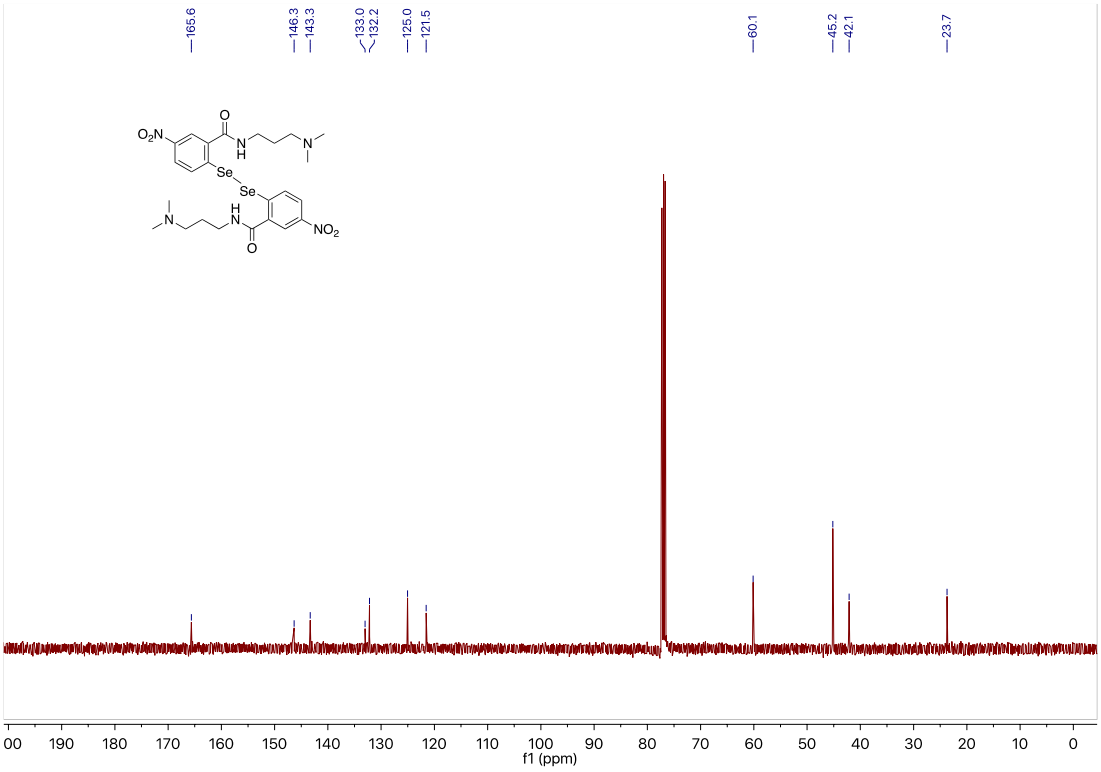
6,6'-Diselanediylbis(*N*-isopropyl-3-nitrobenzamide) (**6b**)



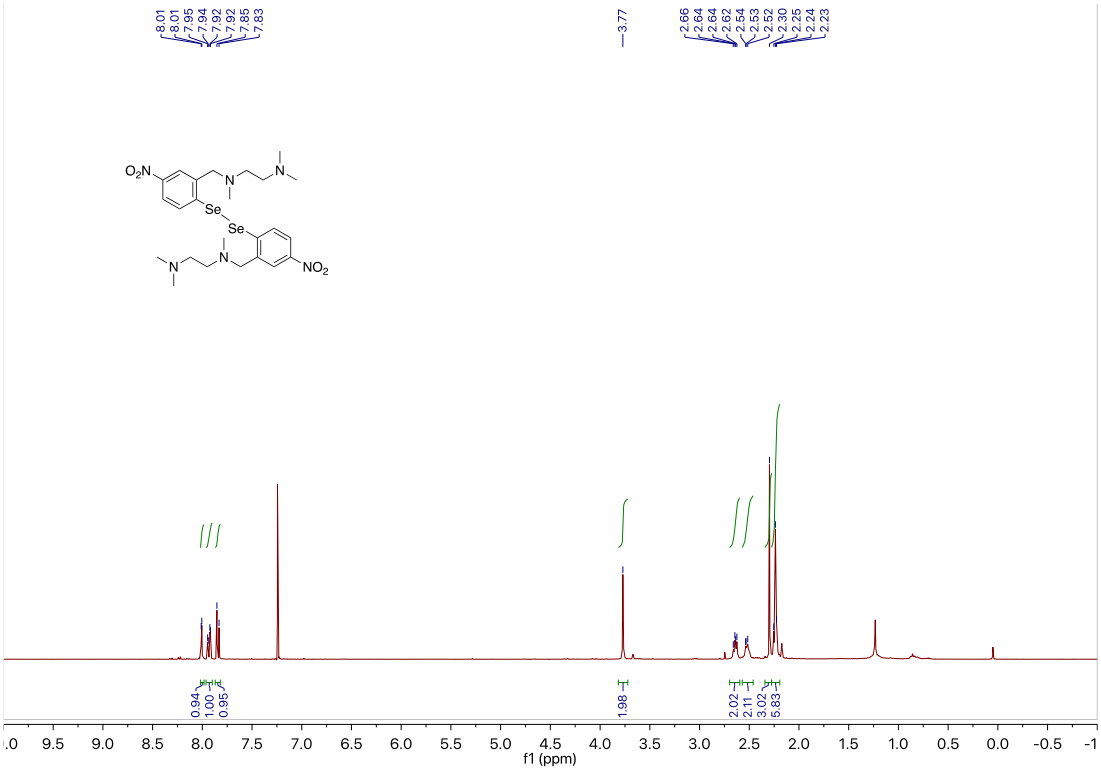


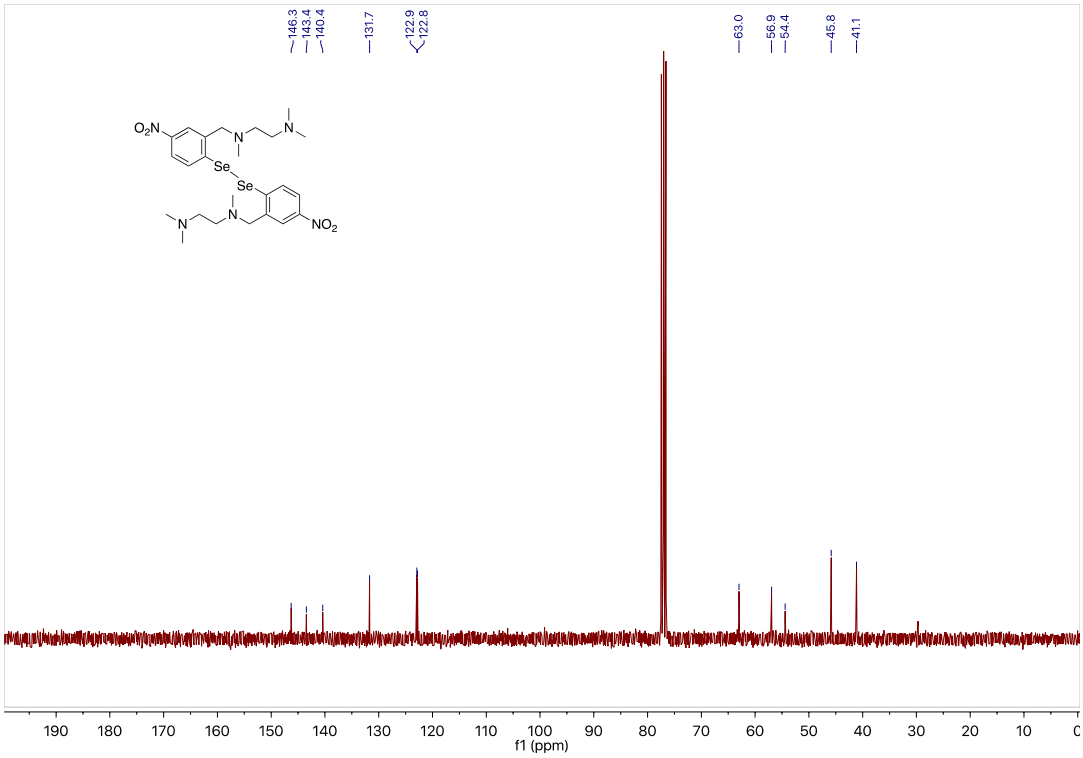
6,6'-Diselanediylbis(*N*-(3-(dimethylamino)propyl)-3-nitrobenzamide) (**6c**)



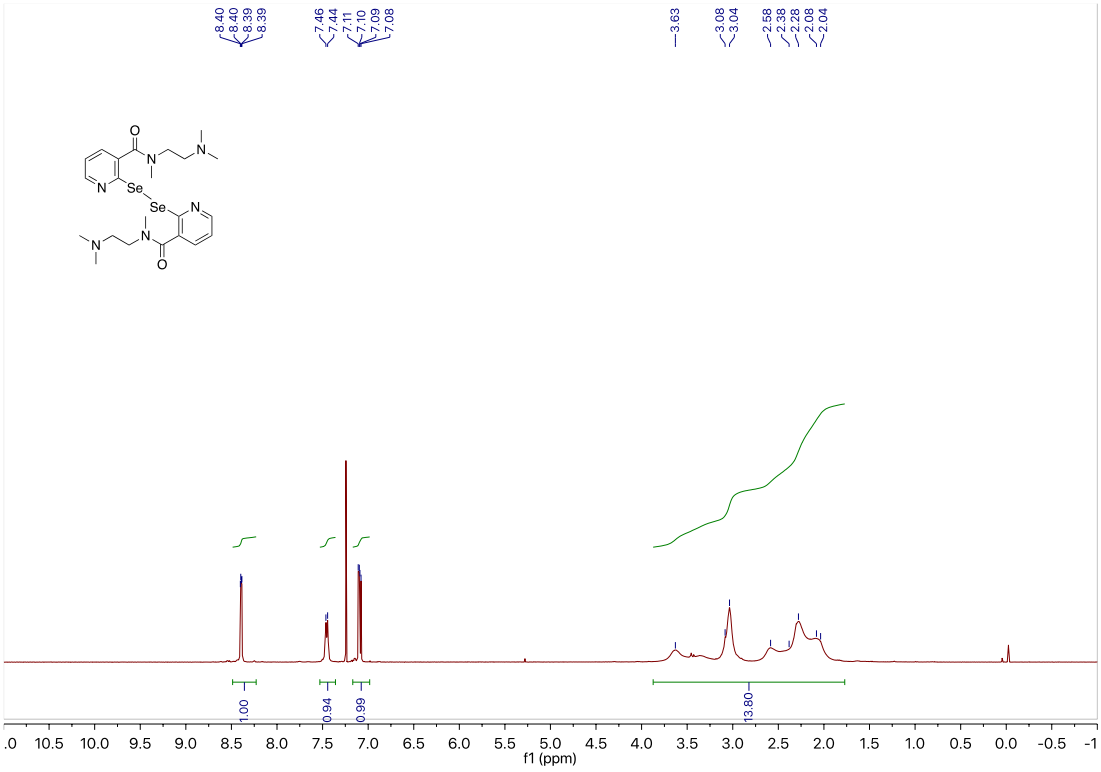


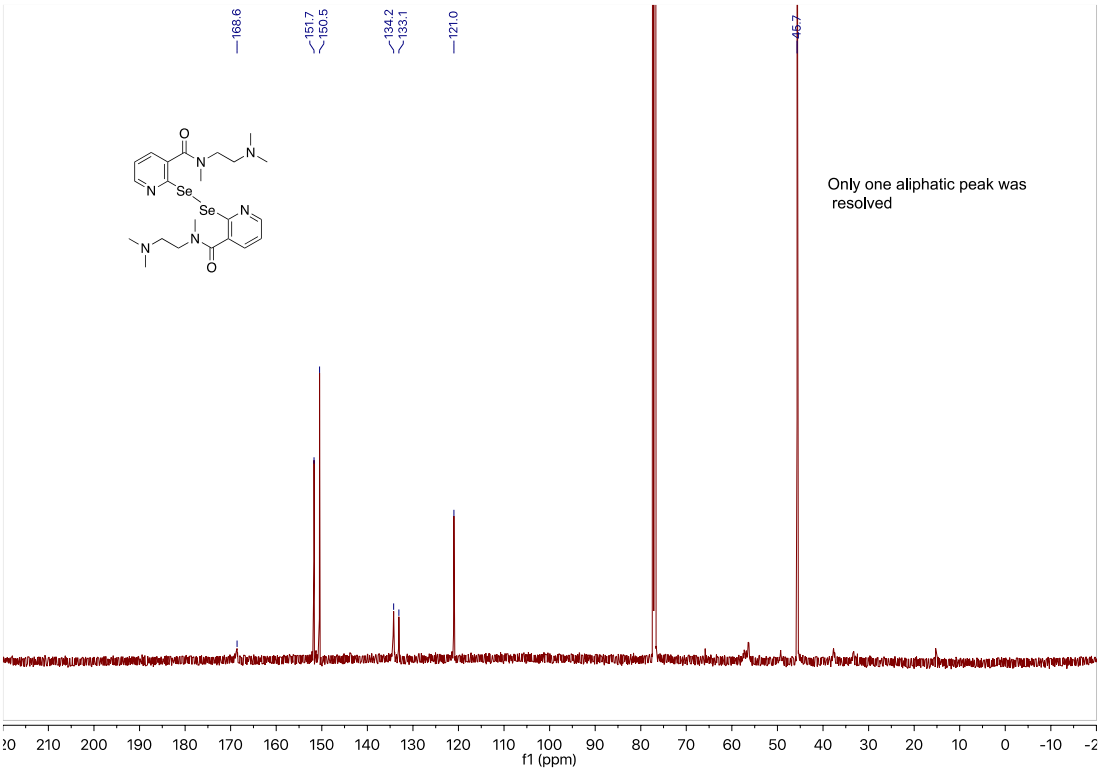
N[1],*N*[1']-((diselanediylbis(5-nitro-2,1-phenylene))bis(methylene))bis(*N*[1],*N*[2],*N*[2]-trimethylethane-1,2-diamine) (**6d**)



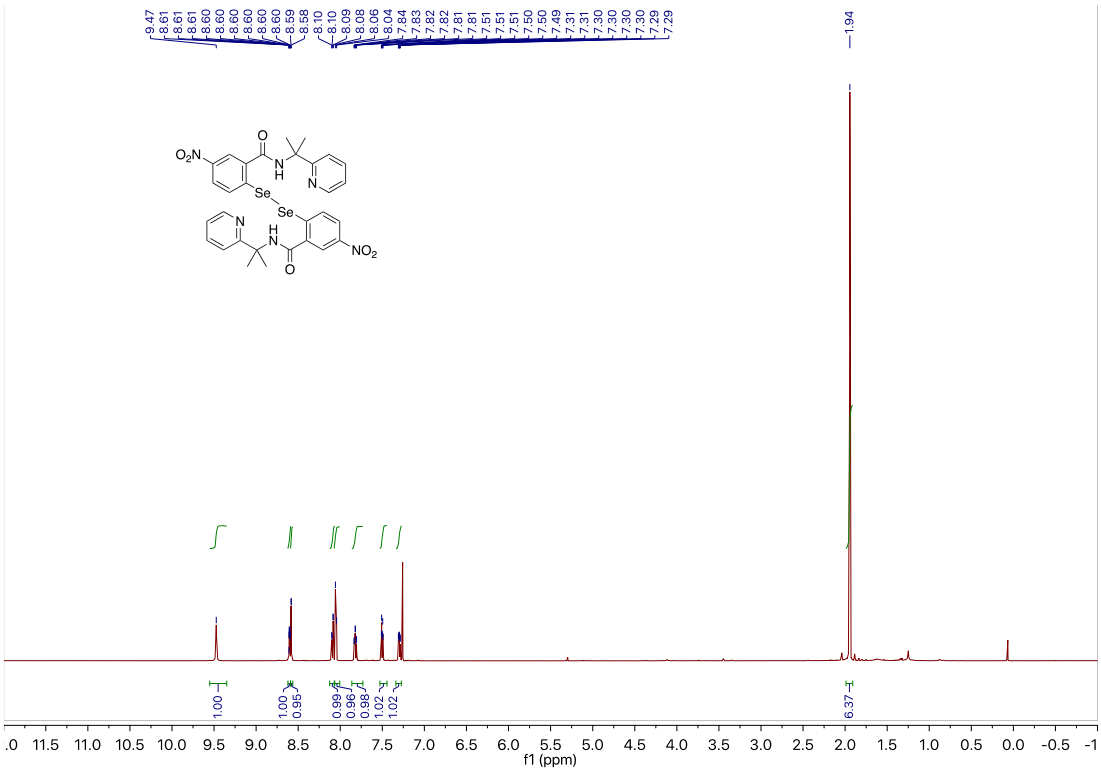


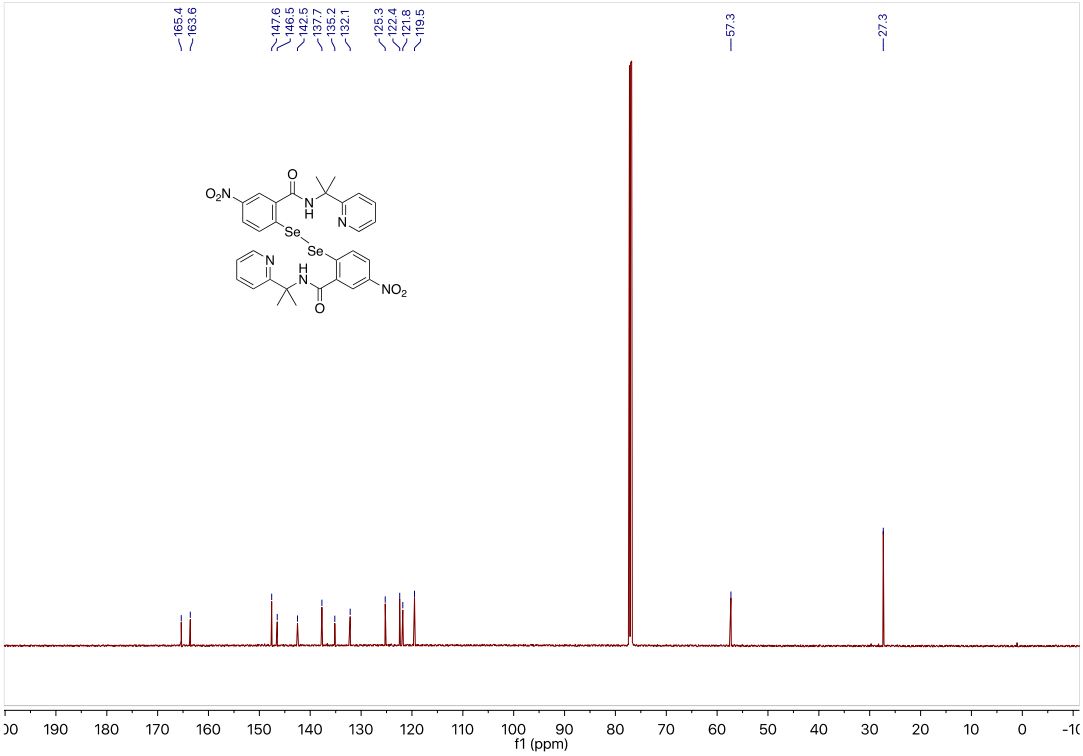
2,2'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-*N*-methylnicotinamide) (**6e)**



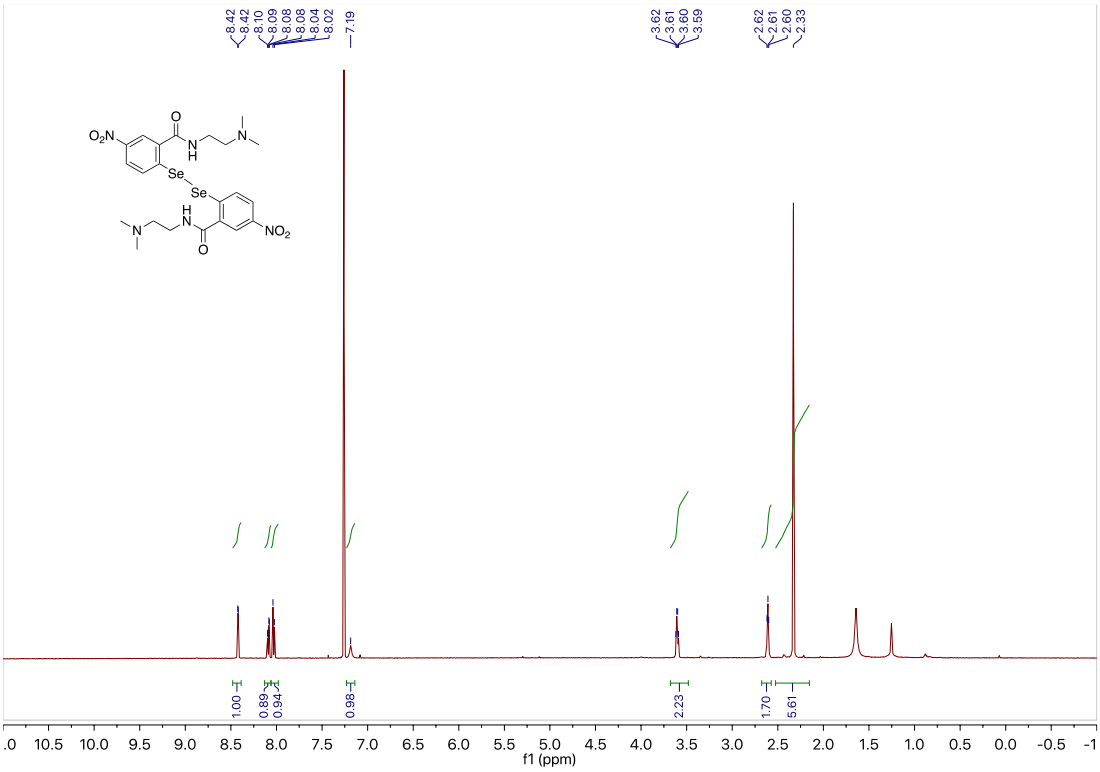


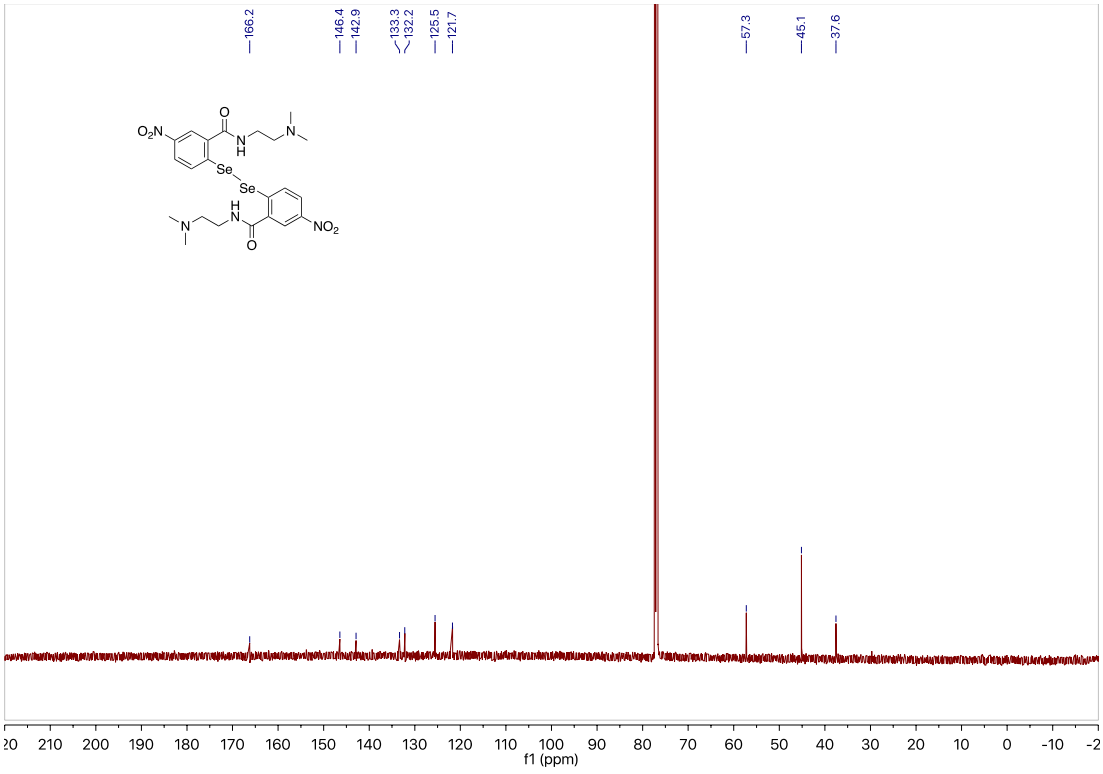
6,6'-diselanediylbis(3-nitro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide) (**6f**)



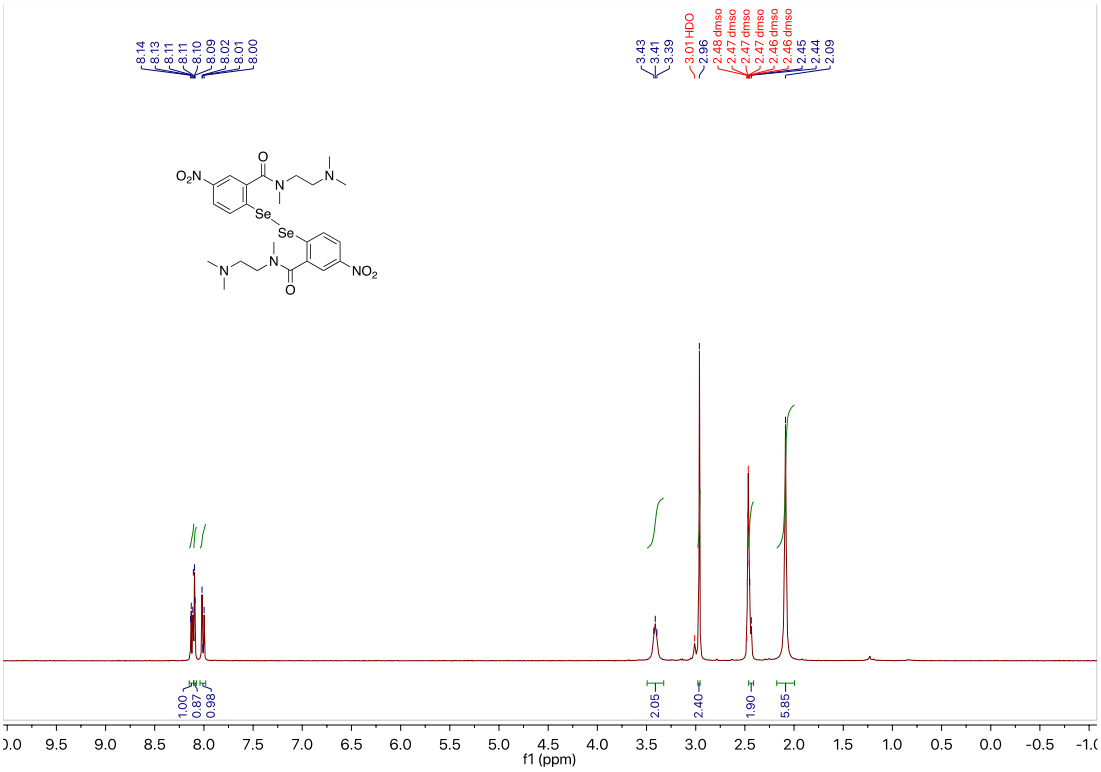


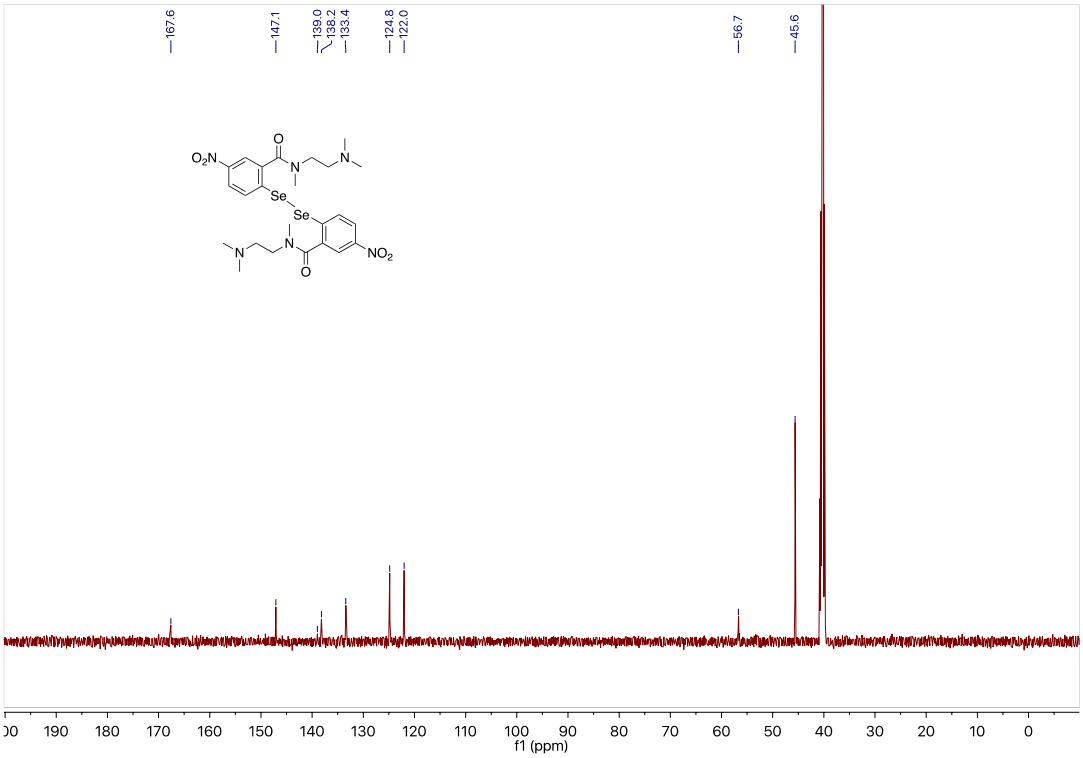
6,6'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-3-nitrobenzamide) (**6g**)



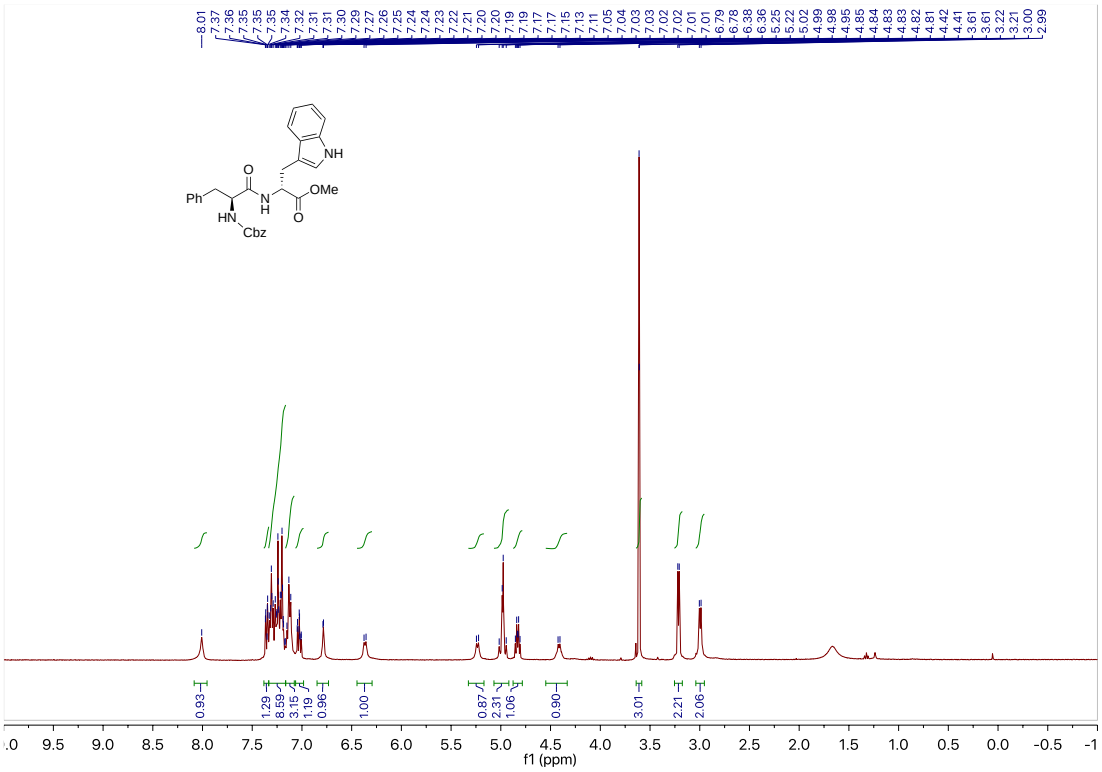


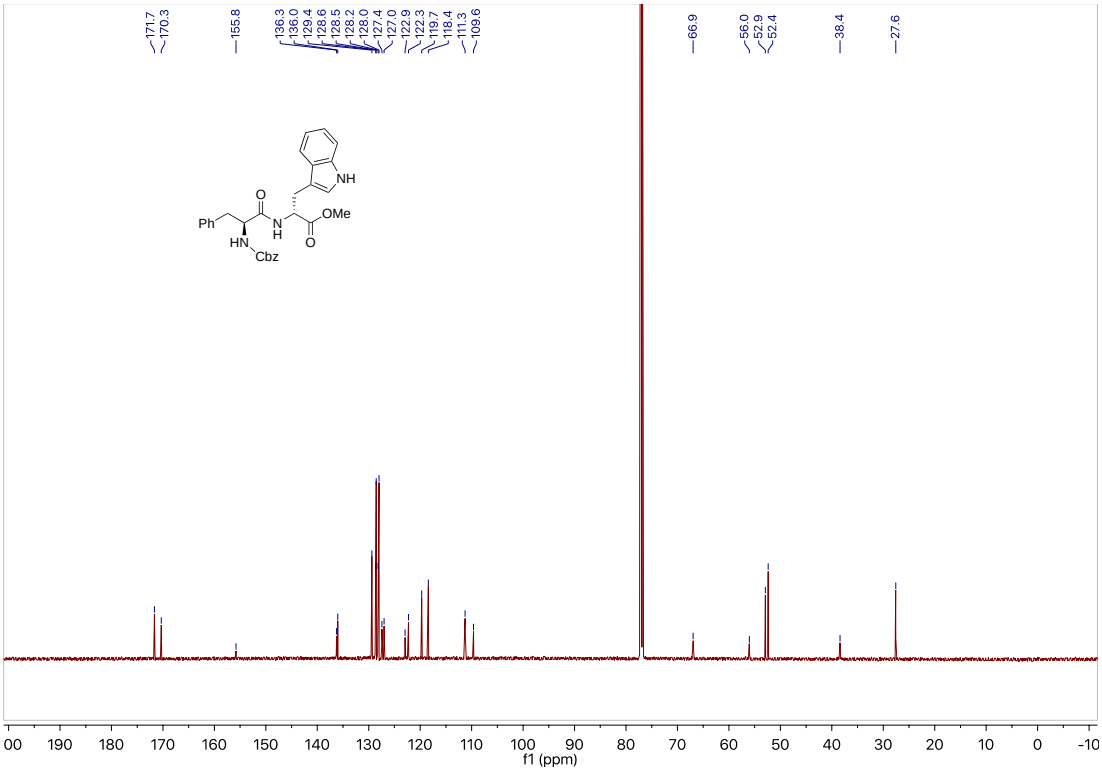
6,6'-Diselanediylbis(*N*-(2-(dimethylamino)ethyl)-*N*-methyl-3-nitrobenzamide) (**6h**)



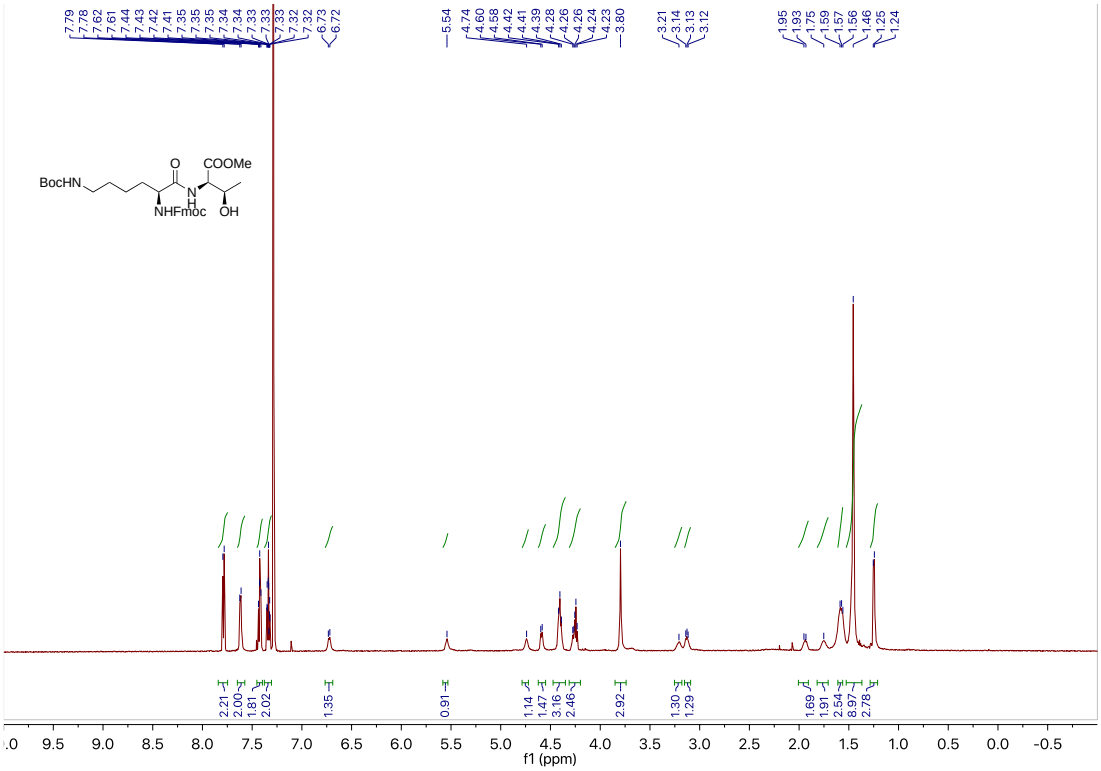


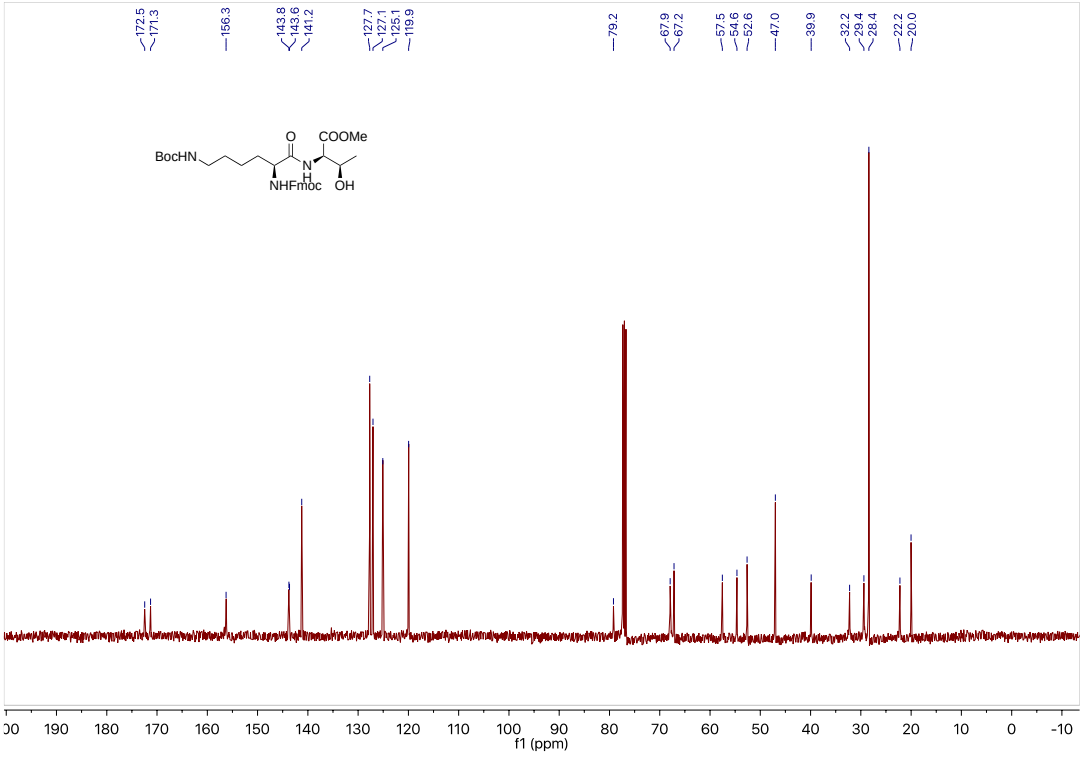
Methyl ((benzyloxy)carbonyl)-*L*-phenylalanyl-*D*-tryptophanate (Table 1, entry **1**)



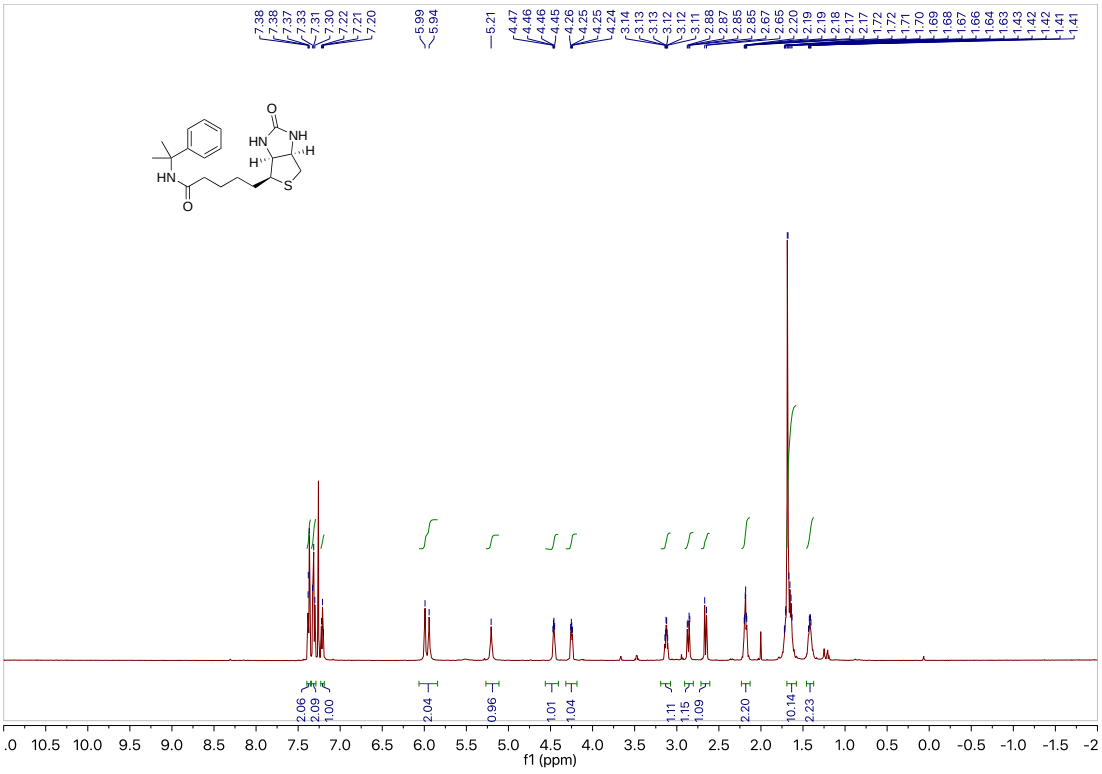


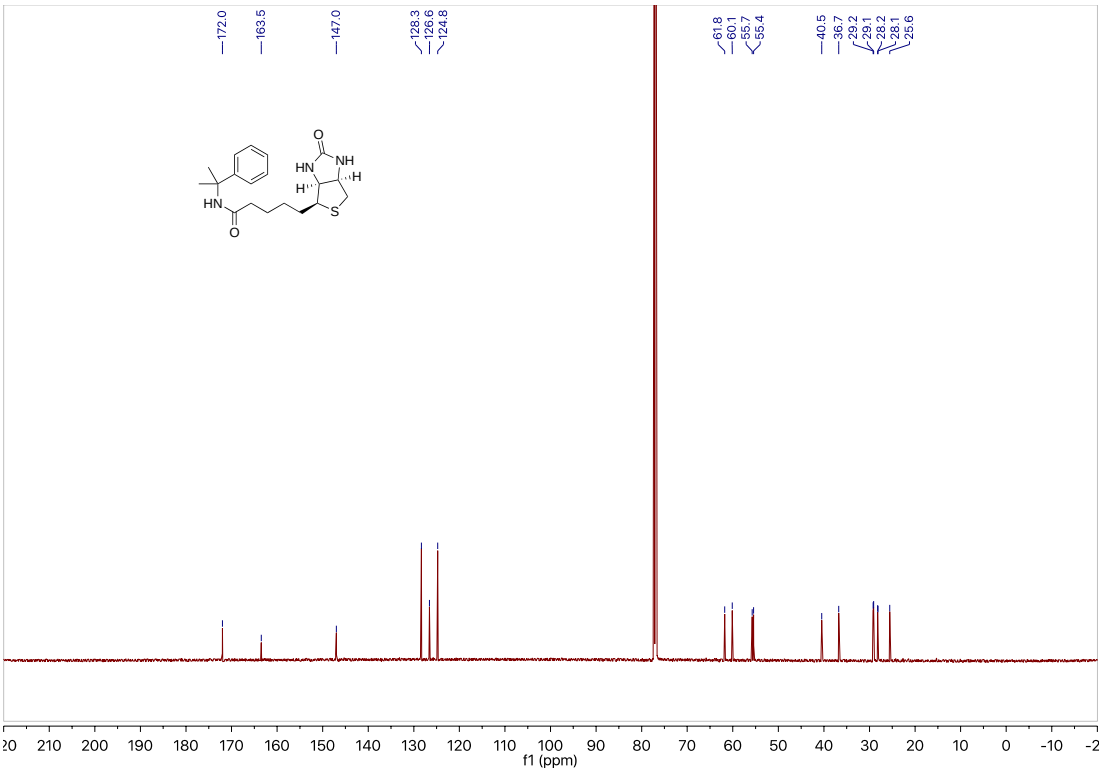
Methyl N^2-(((9*H*-fluoren-9-yl)methoxy)carbonyl)-N^6-(*tert*-butoxycarbonyl)-*L*-lysyl-*L*-threoninate (Table 1, entry **2**)



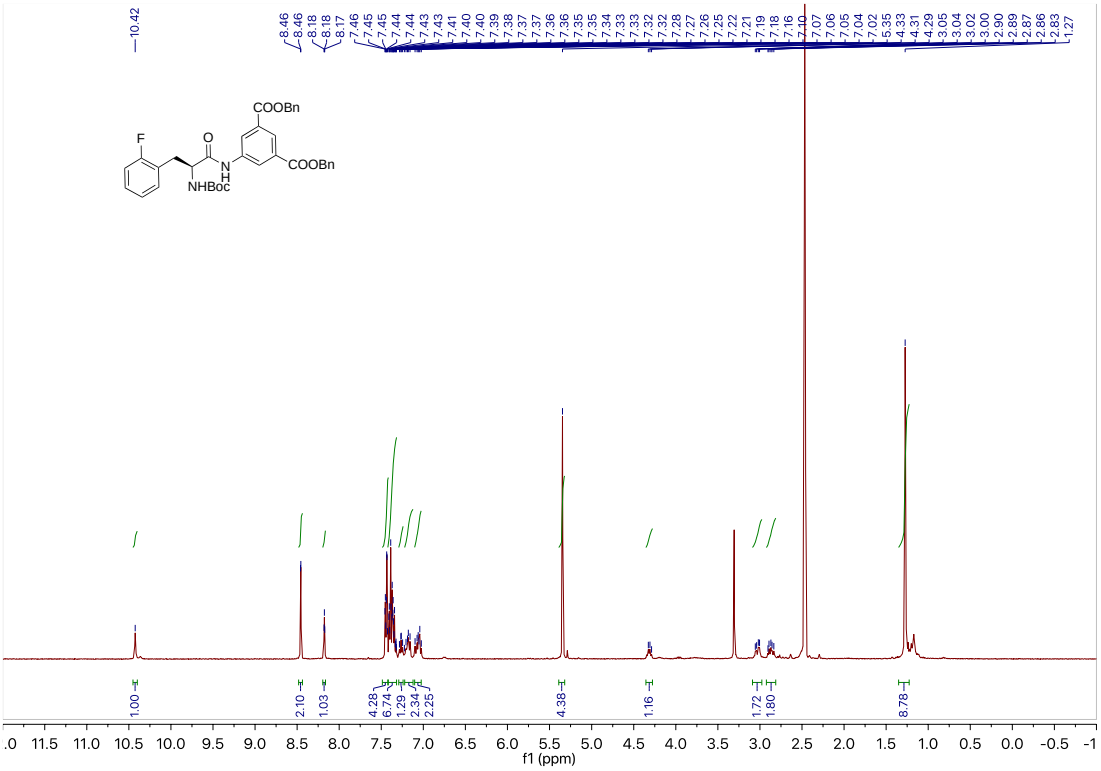


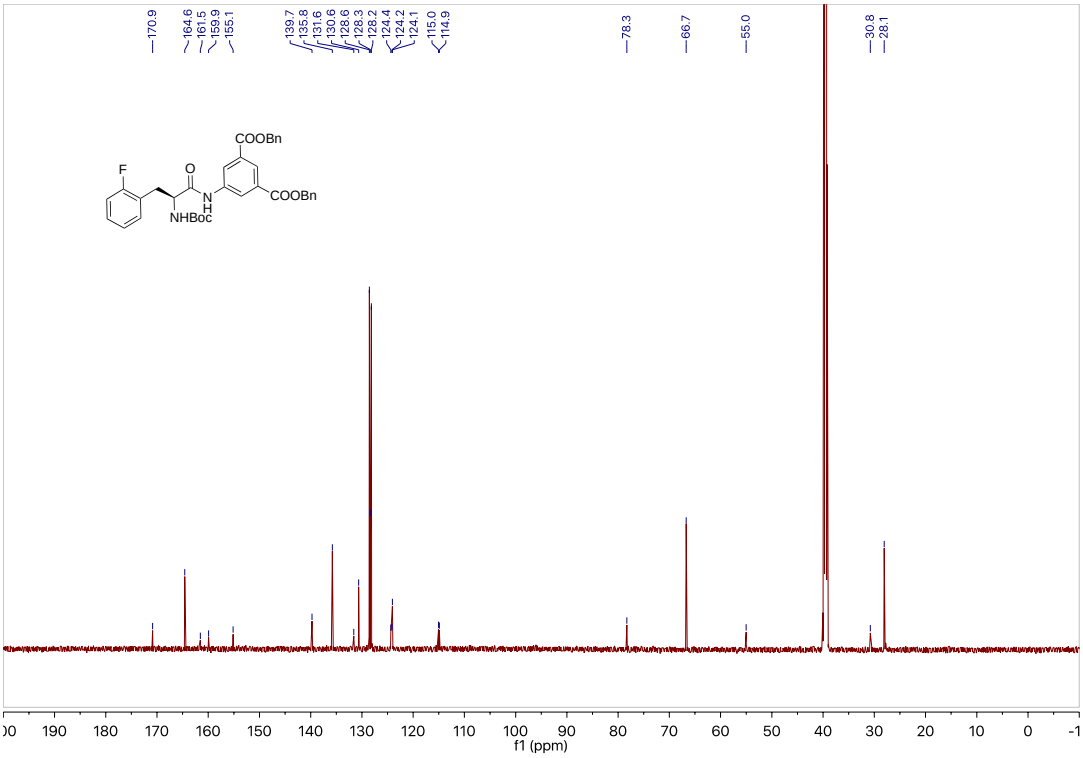
5-((3a*S*,4*S*,6a*R*)-2-Oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)-*N*-(2-phenylpropan-2-yl)pentanamide (Table 1, entry **3**)



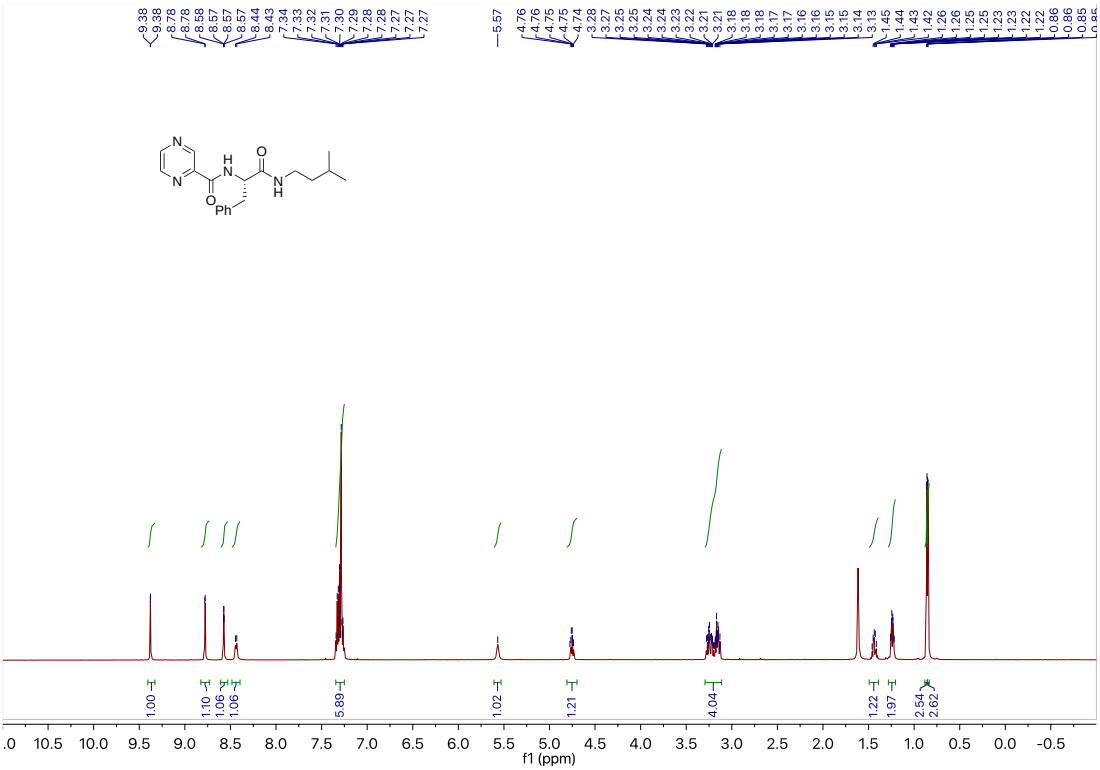


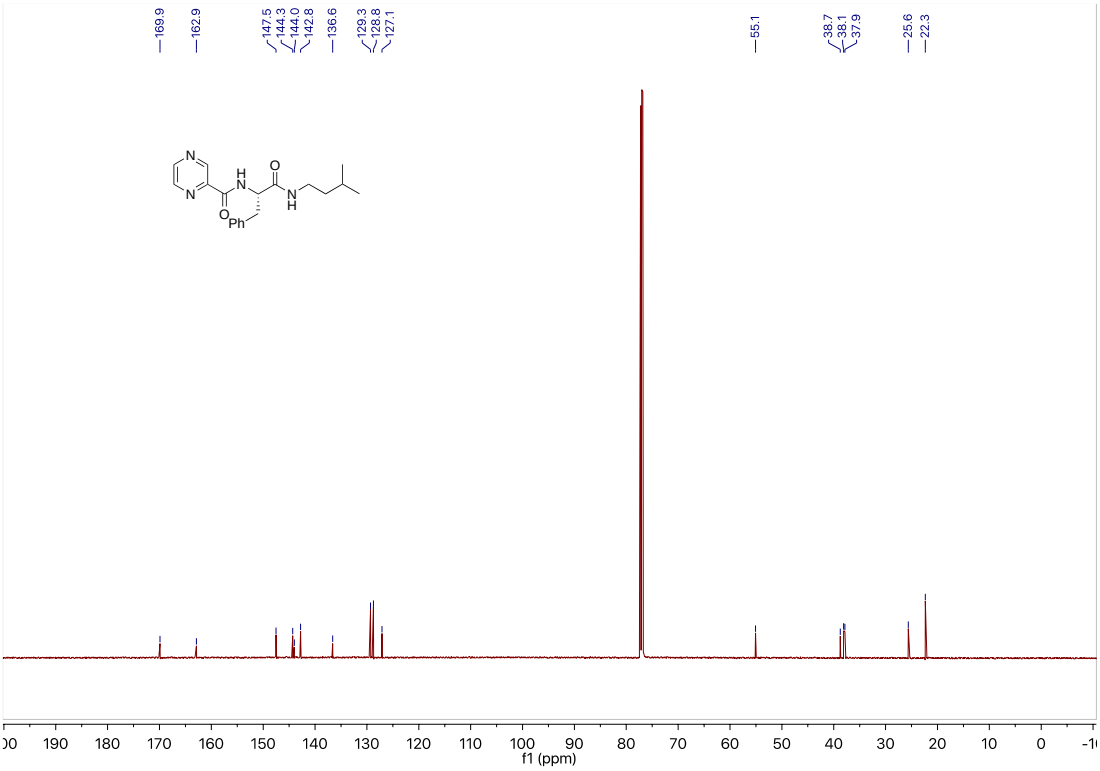
Dibenzyl (*S*)-5-(2-((*tert*-butoxycarbonyl)amino)-3-(2-fluorophenyl)propanamido)isophthalate (Table 1, entry **4**)



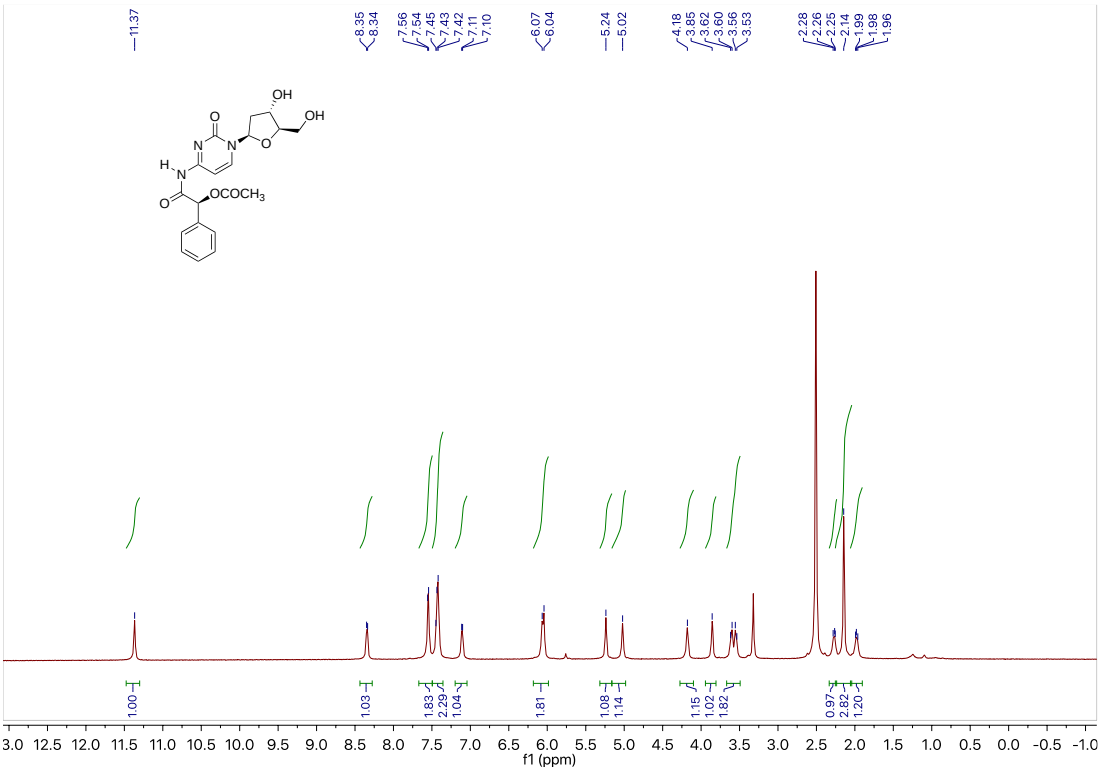


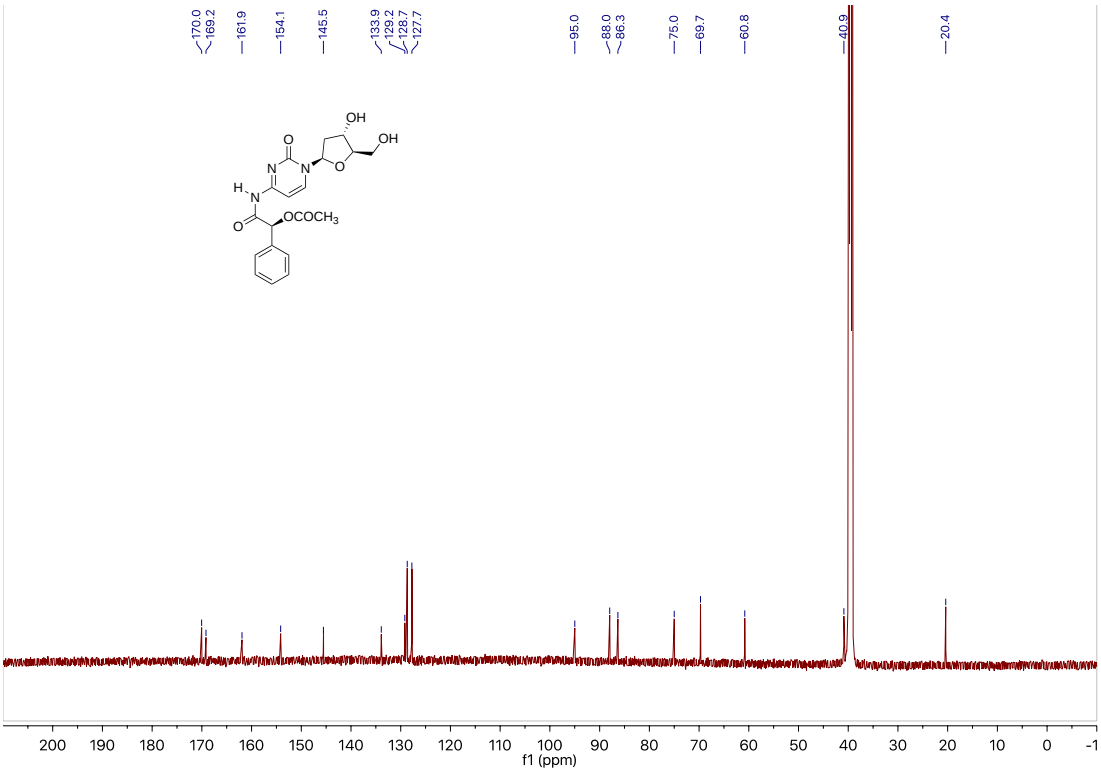
(*S*)-*N*-(1-(Isopentylamino)-1-oxo-3-phenylpropan-2-yl)pyrazine-2-carboxamide (Table 1, entry **5**)



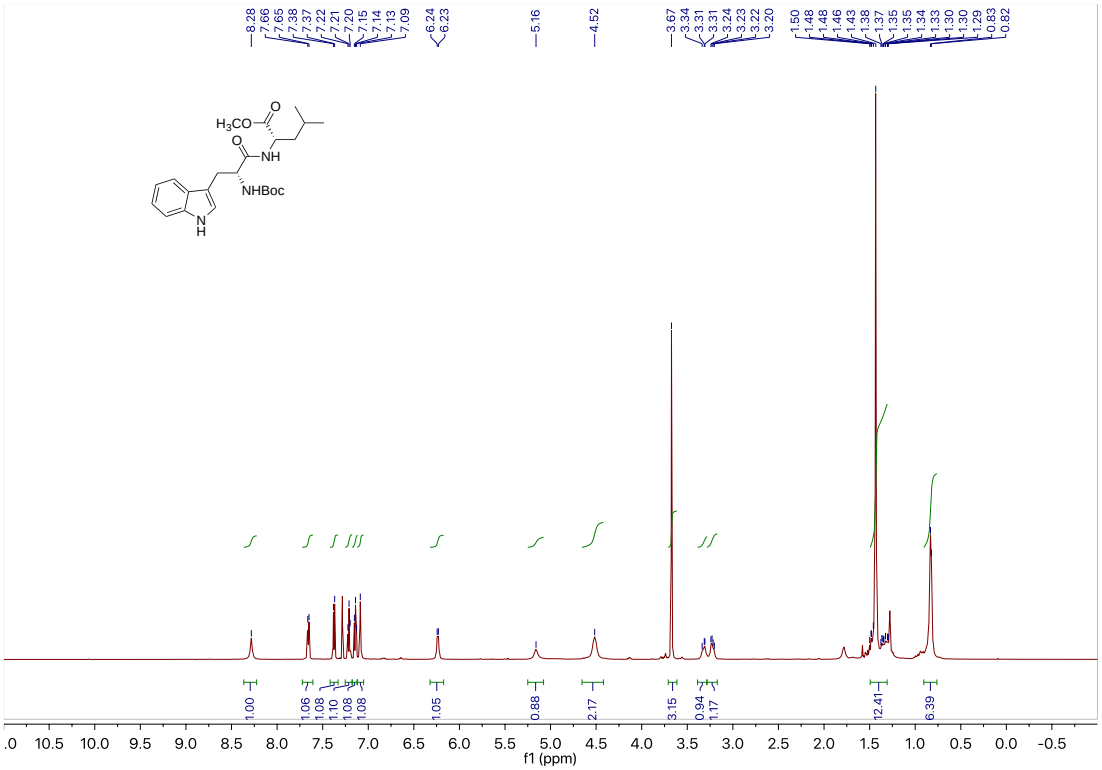


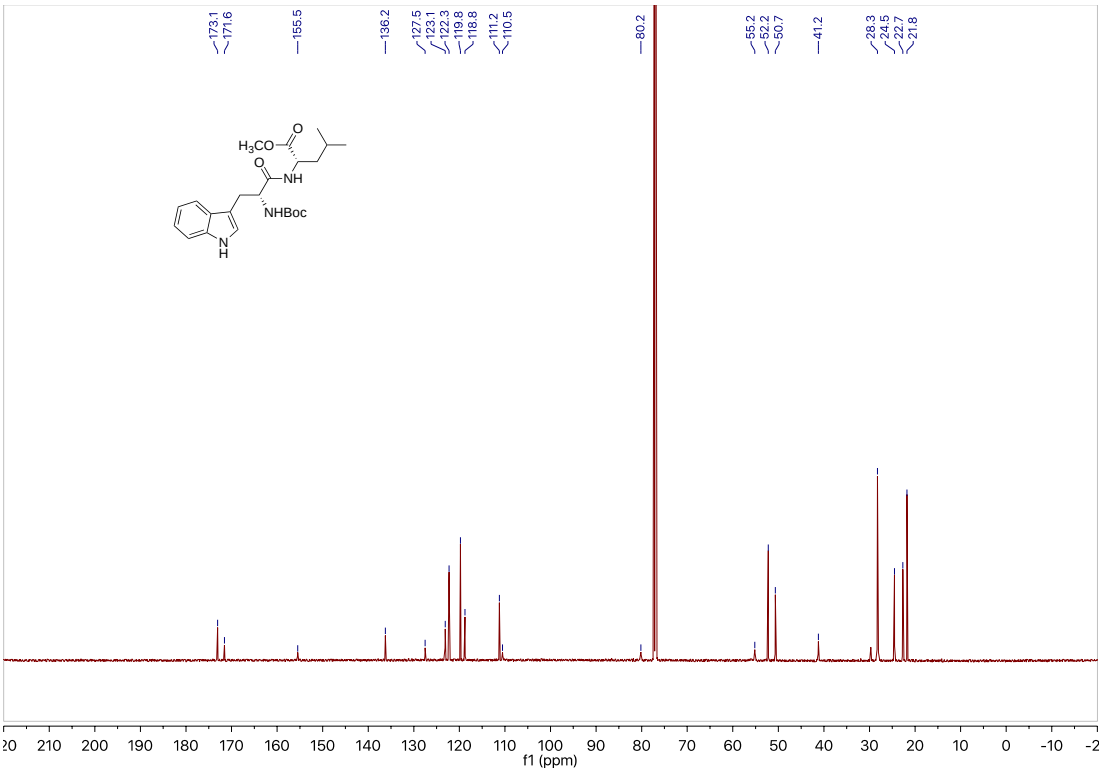
(*S*)-2-((1-((2*R*,4*S*,5*R*)-4-Hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)amino)-2-oxo-1-phenylethyl acetate (Table 1, entry **6**)



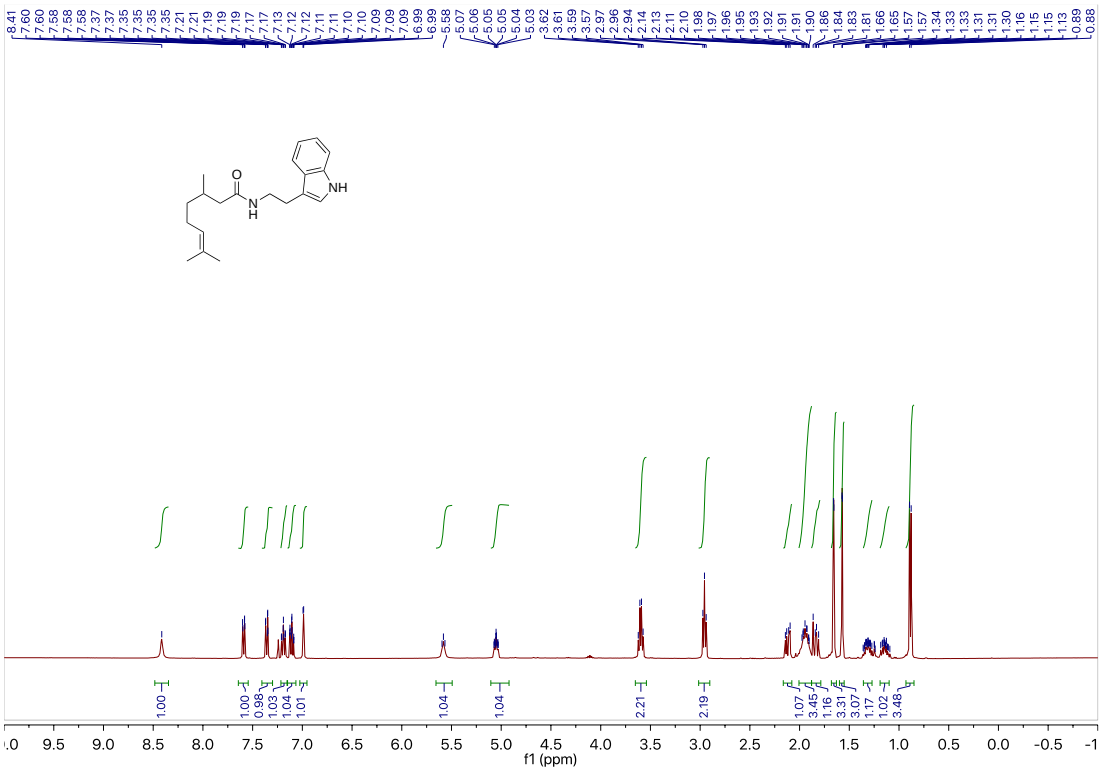


Methyl (*tert*-butoxycarbonyl)-*D*-tryptophyl-*L*-leucinate (Table 1, entry **7**)





N-(2-(1*H*-Indol-3-yl)ethyl)-3,7-dimethyloct-6-enamide (Table 1, entry **8**)



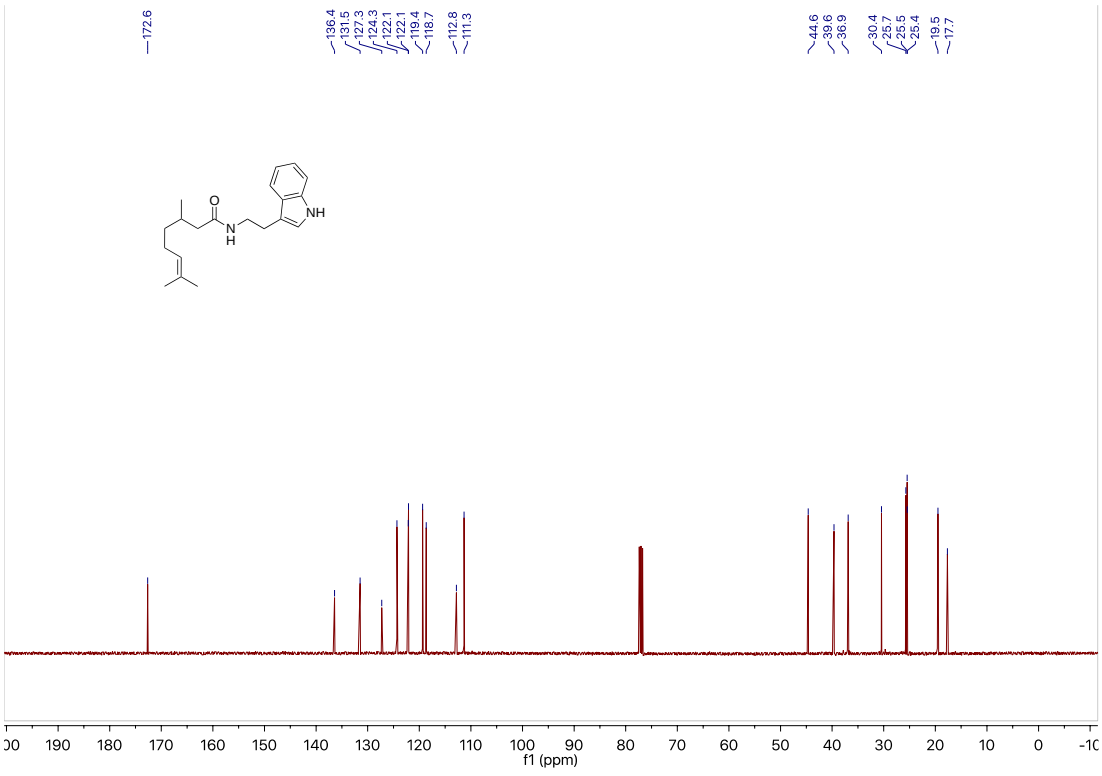
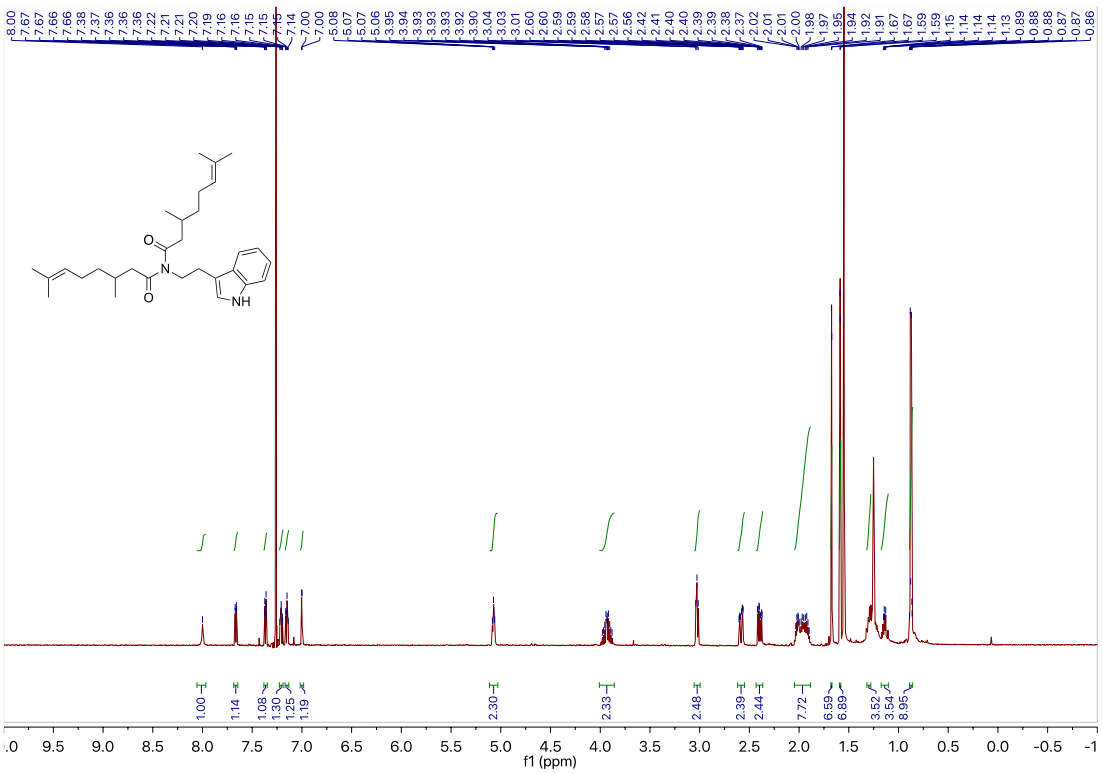
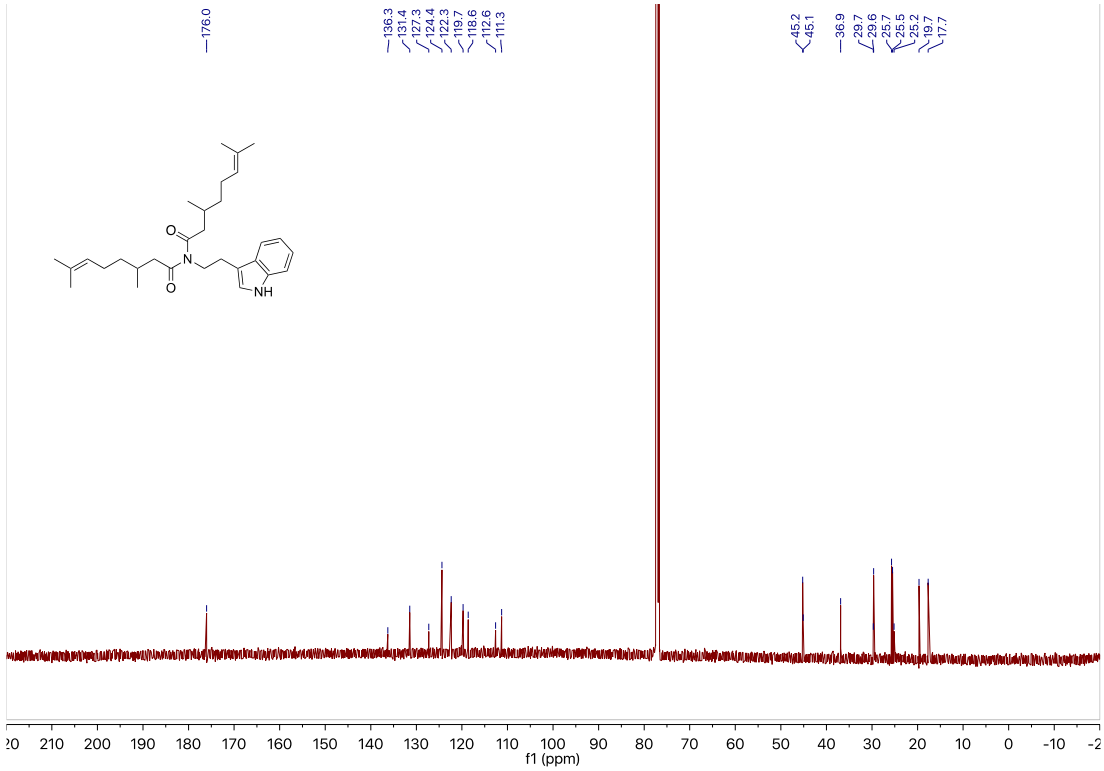
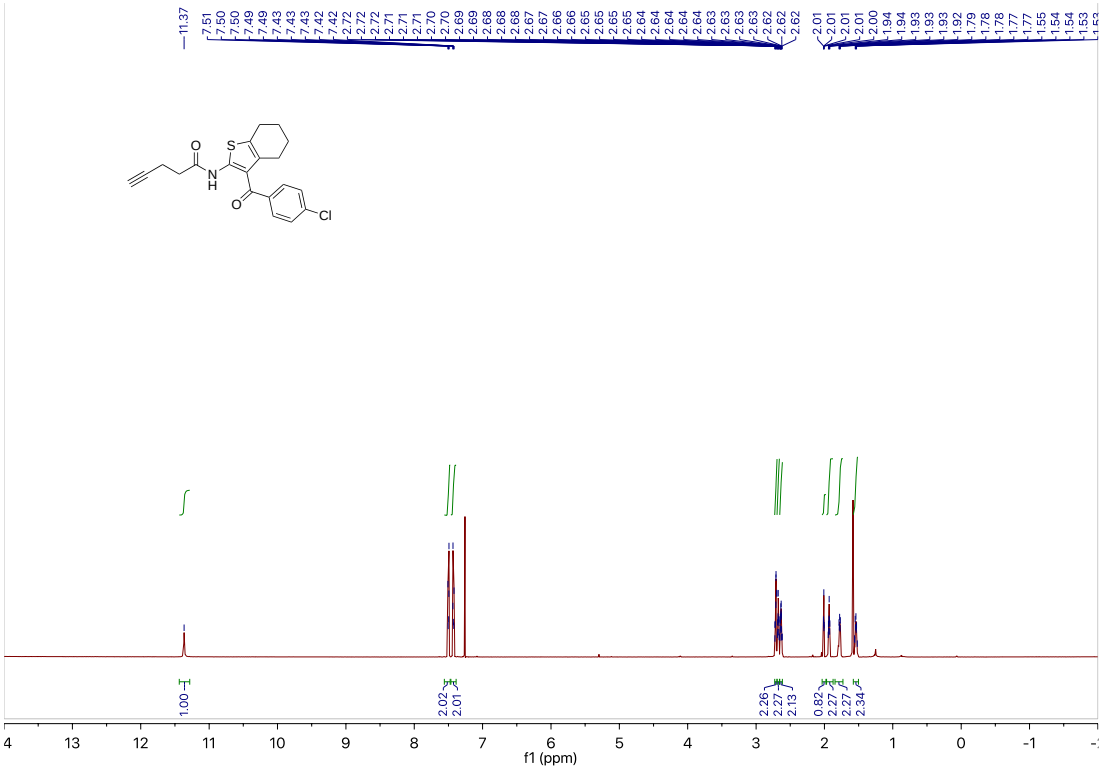


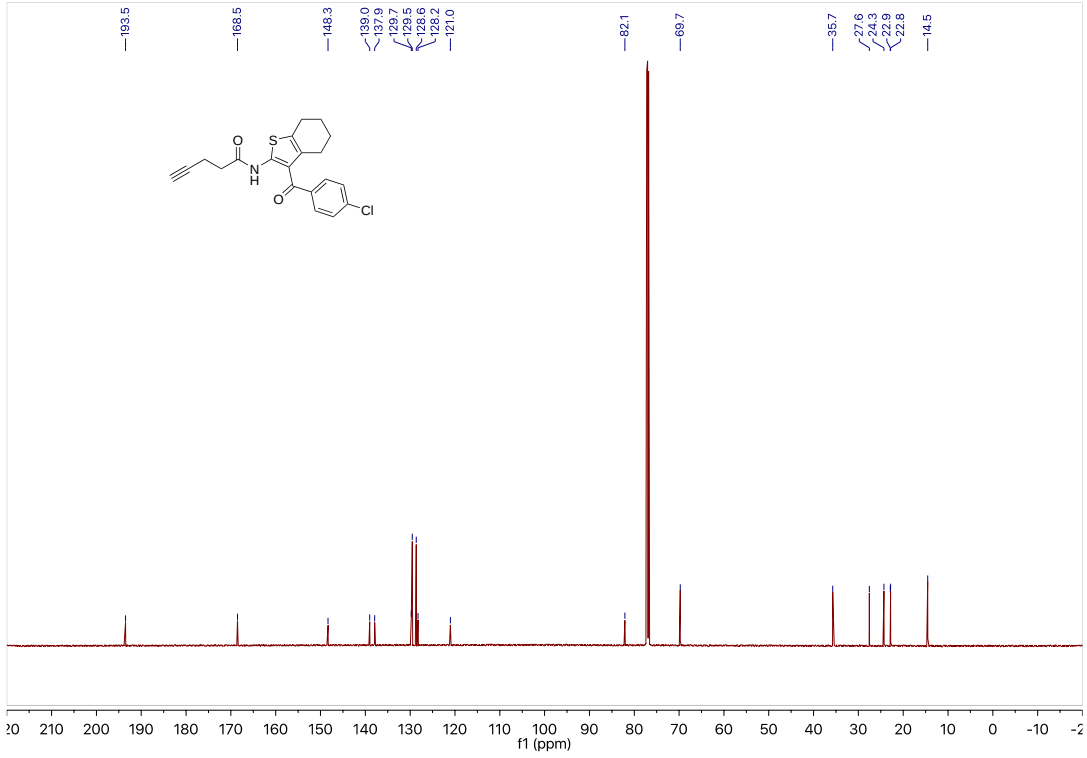
Table 1, entry **8'**:



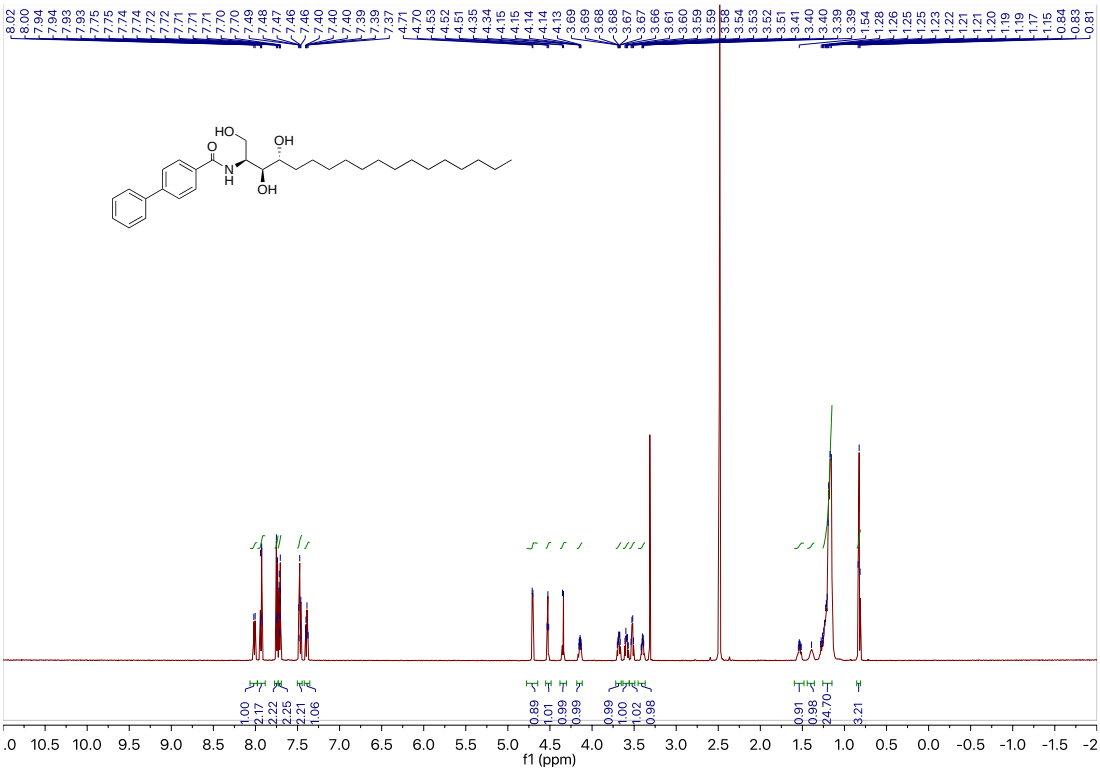


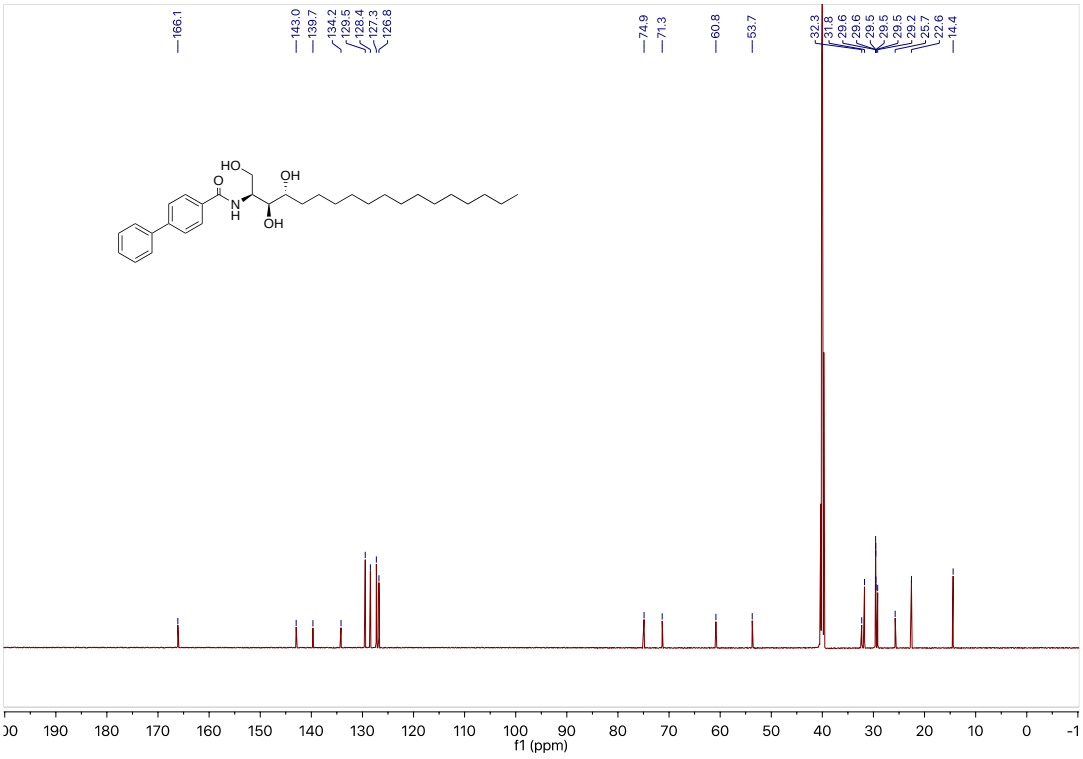
N-(3-(4-Chlorobenzoyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)pent-4-ynamide (Table 1, entry **9**)



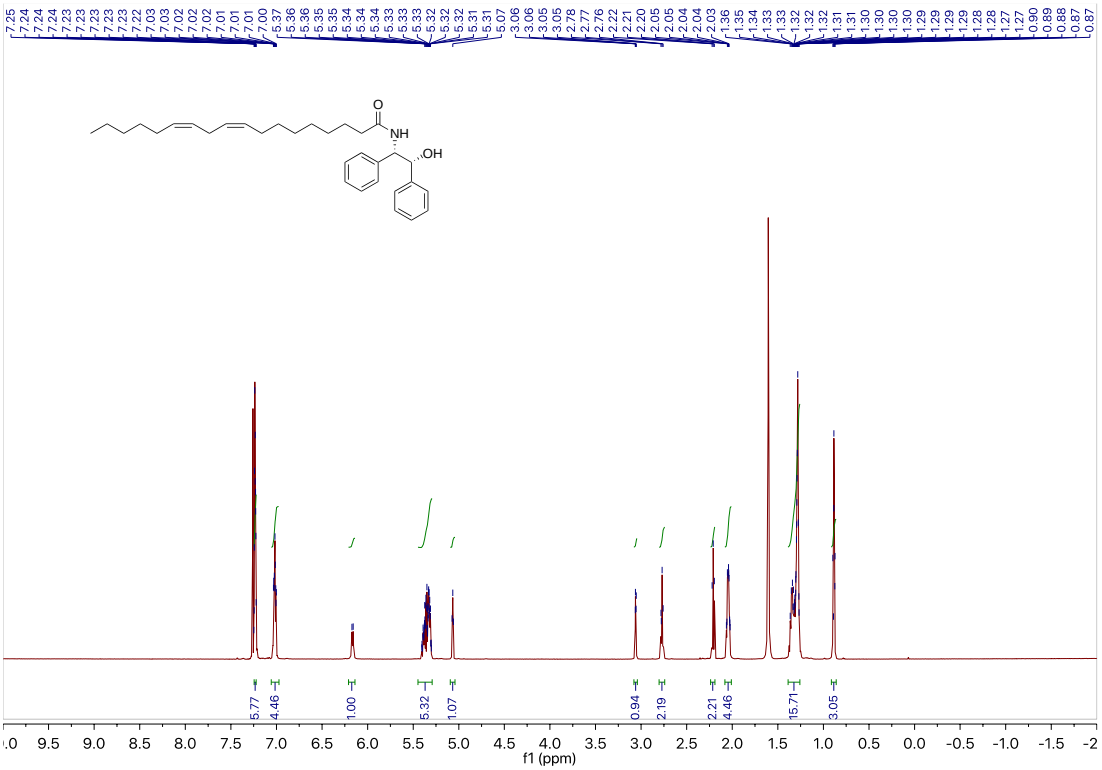


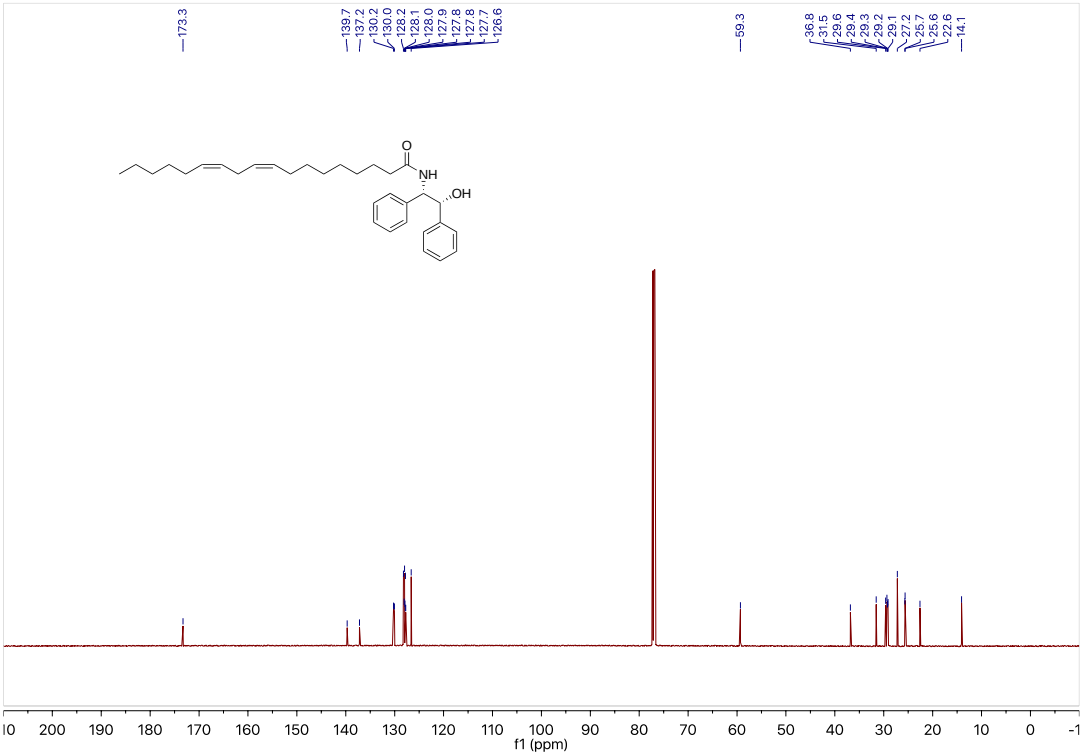
N-((2*S*,3*S*,4*R*)-1,3,4-Trihydroxyoctadecan-2-yl)-[1,1'-biphenyl]-4-carboxamide (Table 1, entry **10**)



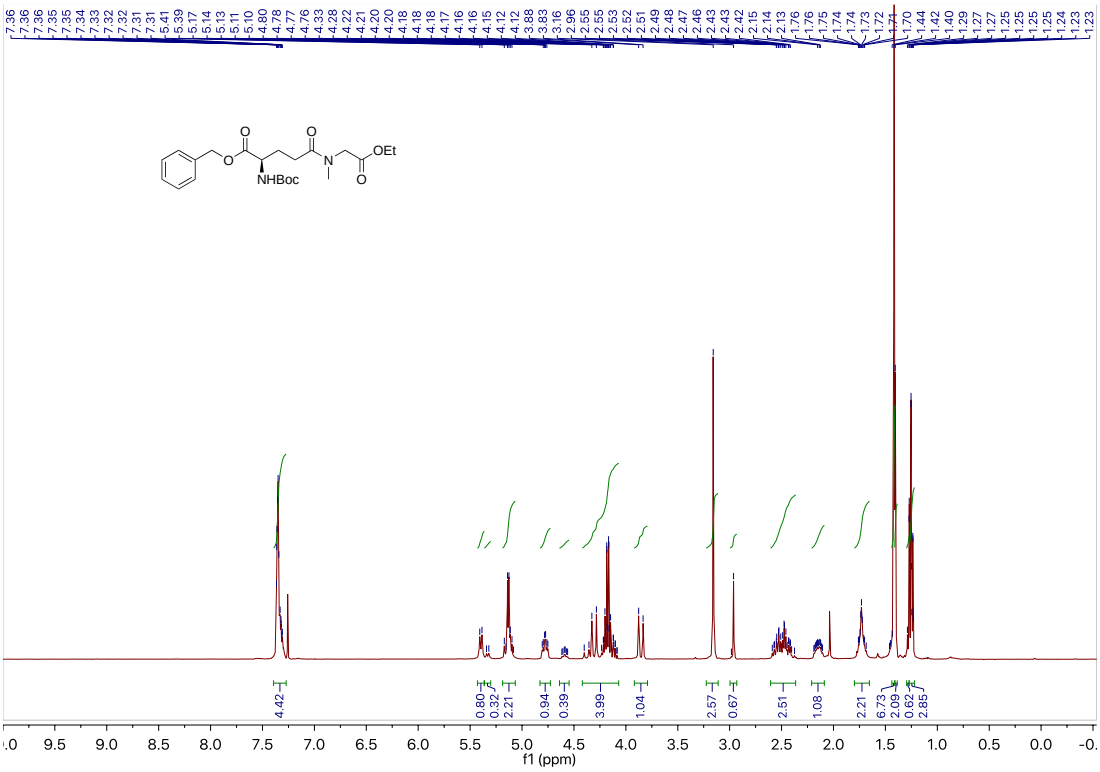


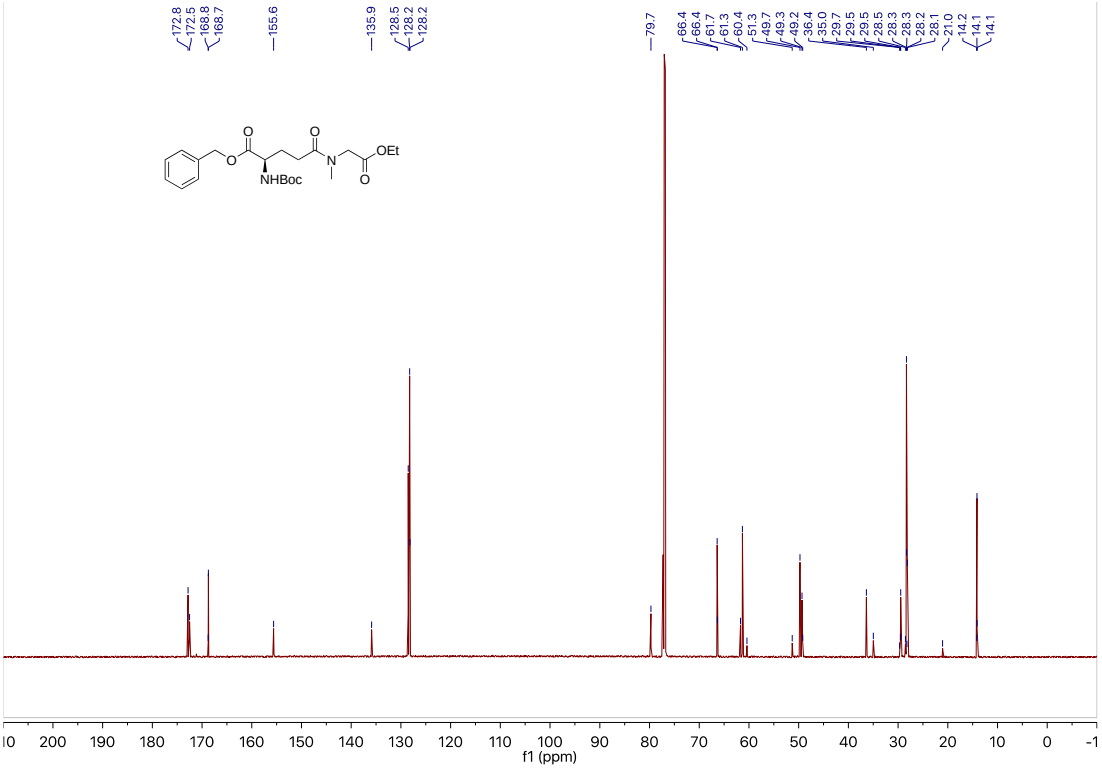
9*Z*,12*Z*)-*N*-((1*S*,2*R*)-2-Hydroxy-1,2-diphenylethyl)octadeca-9,12-dienamide (Table 1, entry **11**)



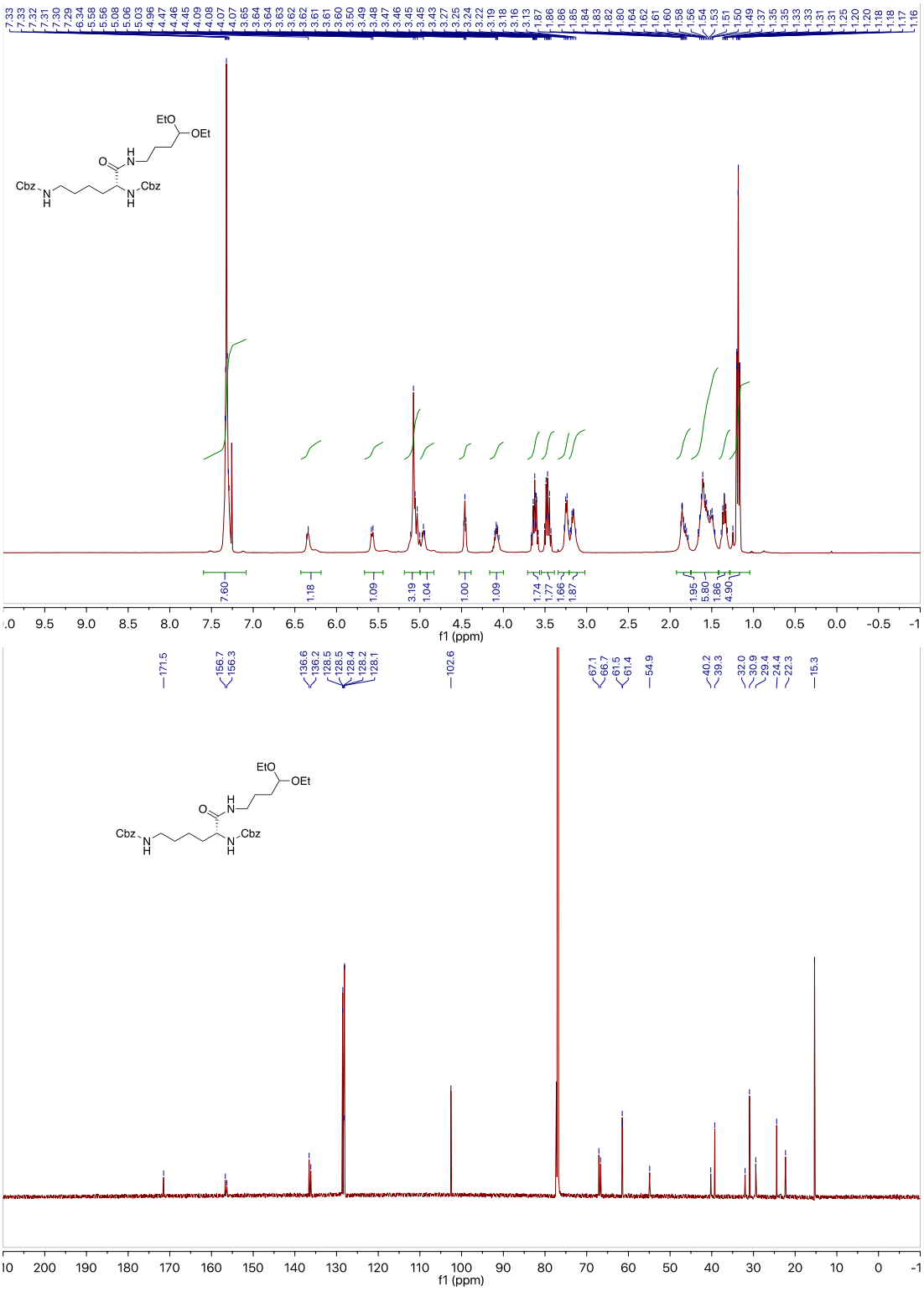


Benzyl N^2-(*tert*-butoxycarbonyl)-N^5-(2-ethoxy-2-oxoethyl)-N^5-methyl-*D*-glutaminate (Table 1, entry **12**)

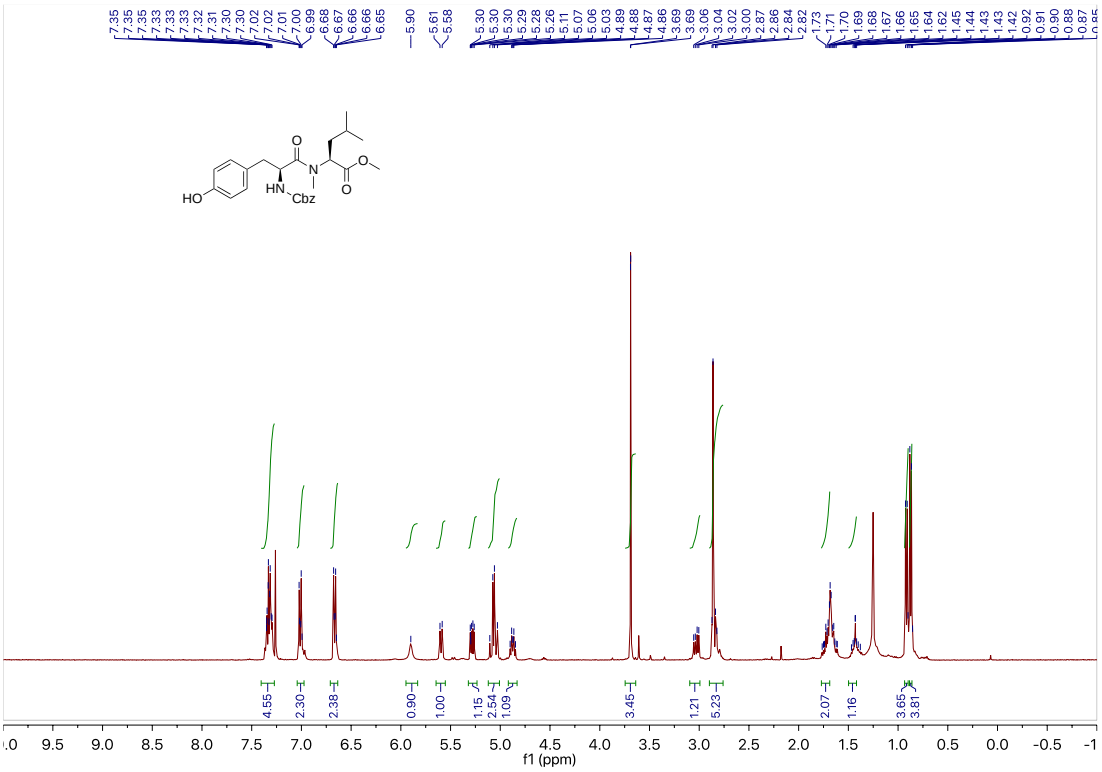


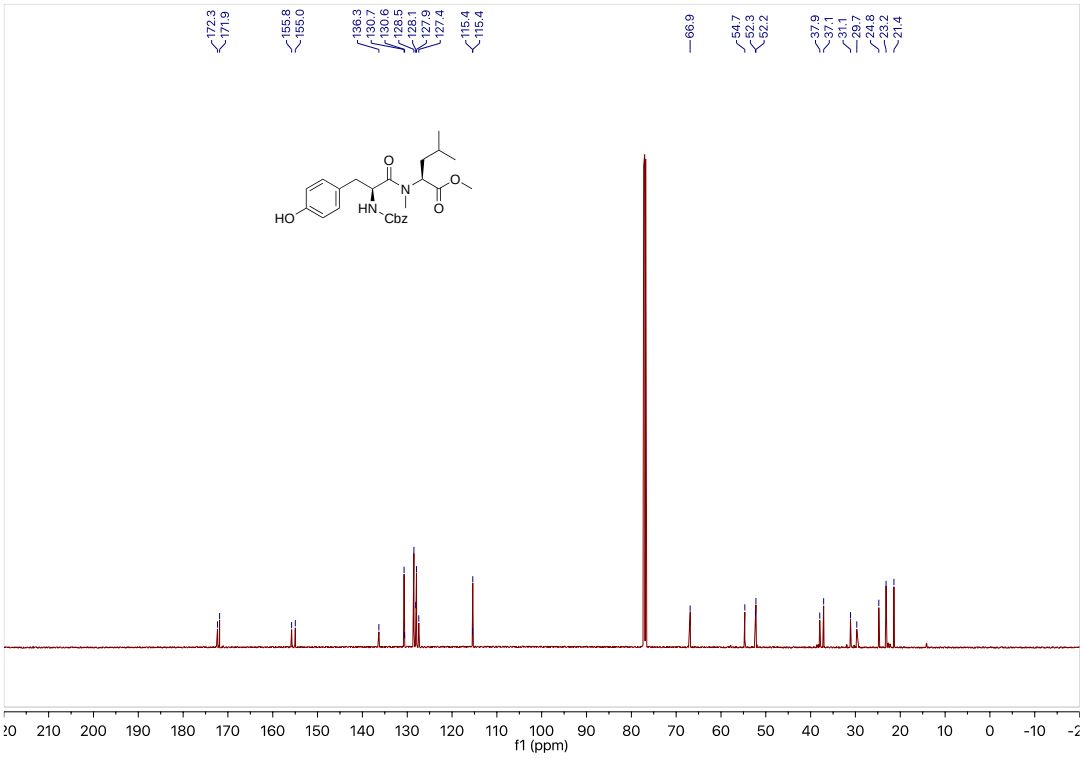


Dibenzyl (6-((4,4-diethoxybutyl)amino)-6-oxohexane-1,5-diyl)(*R*)-dicarbamate (Table 1, entry **13**)

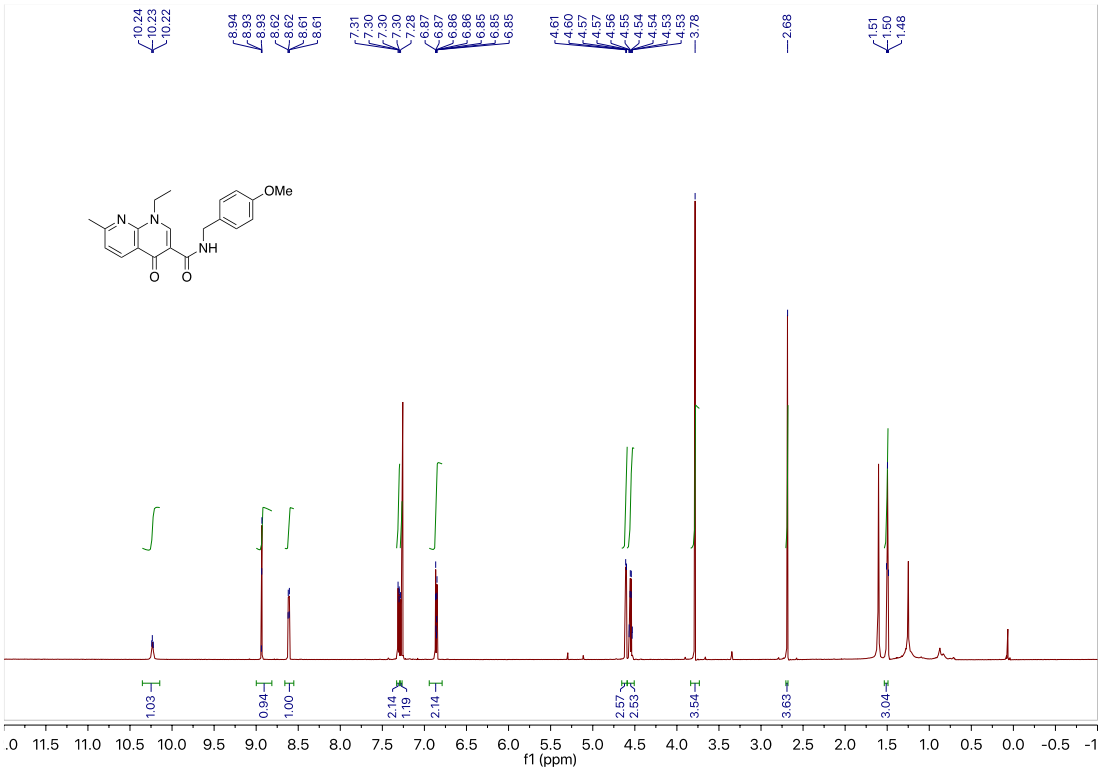


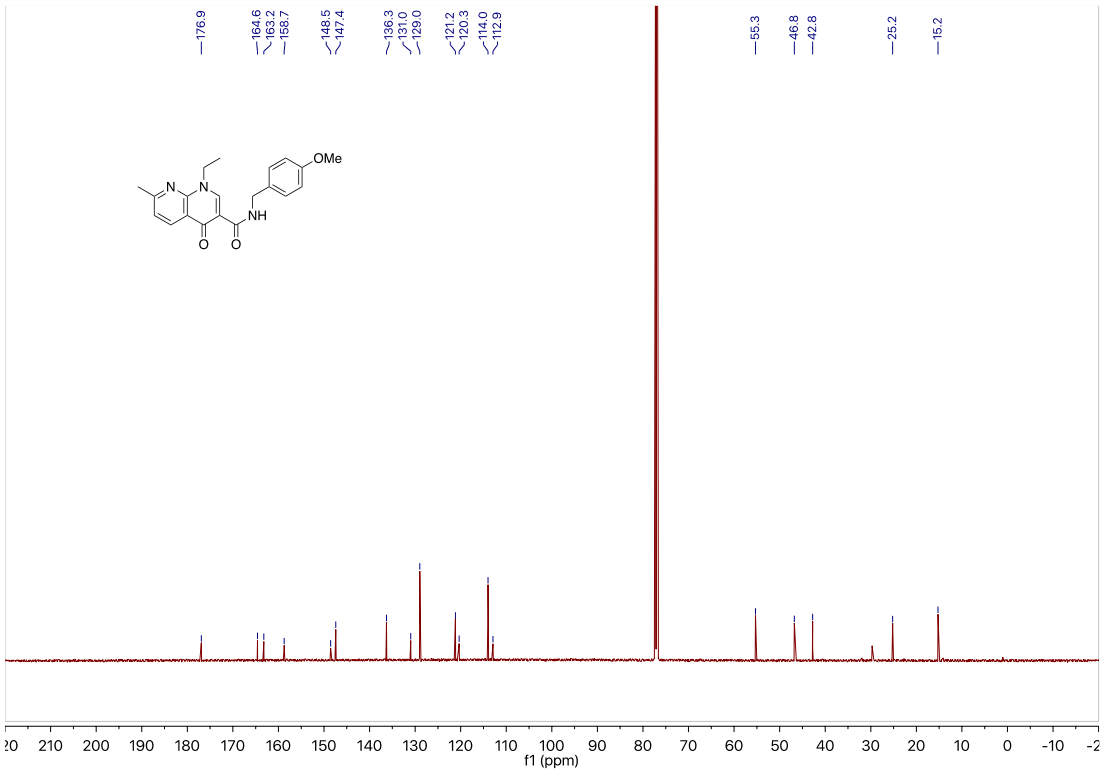
Methyl *N*-(((benzyloxy)carbonyl)-*L*-tyrosyl)-*N*-methyl-*L*-leucinate (Table 1, entry **14**)





1-Ethyl-*N*-(4-methoxybenzyl)-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxamide (Table 1, entry **15**)





Methyl (8-((4-chlorophenyl)sulfonamido)-4-(3-(pyridin-3-yl)propyl)octanoyl)-*L*-valinate (Table 1, entry **16**)