Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Backbone thioamide directed macrocyclisation: lactam stapling of peptides

Ameer B. Taresh and Craig A. Hutton*

School of Chemistry and Bio21 Molecular Science and Biotechnology Institute,

The University of Melbourne, Victoria, Australia, 3010.

Supporting Information

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General Information

Reactions requiring anhydrous conditions were carried out under an atmosphere of dry nitrogen or argon in flame- or oven-dried glassware. Anhydrous dichloromethane, tetrahydrofuran and dimethylformamide were obtained from solvent dispensing system where the solvent was dried by passage through two columns of neutral alumina. Most reagents were commercially available reagent grade chemicals and were used without further purification.

Analytical thin layer chromatography (TLC) was performed with aluminium-backed plates precoated with silica gel 60 F254 (0.2 mm), and chromatograms were visualised using was short- and long-wave UV light. Compounds were then stained with phosphomolybdic acid dip [phosphomolybdic acid (5 g), absolute ethanol (100 ml)]. Column chromatography was performed using silica gel (230–400 mesh); eluting solvents are reported as %volume/volume mixtures.

Analytical and preparative reversed-phase HPLC (RP-HPLC) were performed using an Agilent 1200 series LC System. Analytical HPLC employed a Discovery C18 column (4.6 × 150 mm column, 5 μm particle size, flow rate of 1 mL min^{-1}). Preparative RP-HPLC employed a Phenomenex C18 column (21.2 × 150 mm, 5 μm particle size, flow rate 6 mL min $^{-}$1). The mobile phase consisted of eluents A (0.1% TFA in water) and B (0.1% TFA in acetonitrile). The results were analyzed on Agilent ChemStation version B.01.03 software.

^{1}H NMR spectra were recorded using an Agilent 500 (500 MHz) or a Varian Unity Inova 400 (400 MHz). Spectra were obtained in $CDCl_3$ (7.26) or d_6 DMSO (2.50). The spectra are reported as: parts per million (ppm) downfield shift, relative to the residual solvent peak; relative integral, multiplicity (s = singlet, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq doublet of quartets, m = multiplet) and coupling constant (*J* in Hz). ^{13}C NMR spectra were recorded using an Agilent 500 (125 MHz) or a Varian Unity Inova 400 (101 MHz). Chemical shifts (δ) are reported in parts

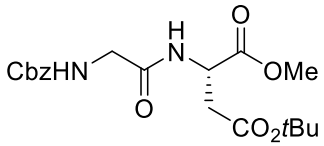
per million (ppm) relative to the internal standard of the solvent peak; $CDCl_3$ (77.16), and DMSO (39.52). Mass spectra were obtained using an MSFP OrbiTRAP infusion Mass Spectrometer.

Experimental Procedures

General procedure A: Peptide couplings in solution phase

To a solution of an *N*-protected amino acid (1.0 mmol) and an amino acid ester (1.0 mmol) in DMF (10 mL) at 0 °C was added EDC.Cl (1.1 mmol), HOBt (1.1 mmol) and DIEA (2.2 mmol), and stirred for 15 min. The reaction mixture was then stirred at room temperature overnight. The mixture was diluted with EtOAc (30 mL) and water (10 mL). The aqueous layer was extracted with EtOAc (2 × 20 mL) and the combined organic extracts were washed with aqueous HCl (30 mL, 1N), saturated aqueous $NaHCO_3$ (30 mL), brine (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (5% MeOH/DCM) to afford the desired peptide.

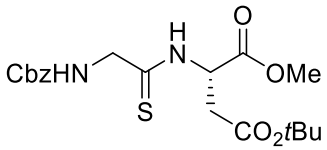
Cbz-Gly-Asp(OtBu)-OMe (S1)



Dipeptide **S1** was prepared from H-Asp(OtBu)-OMe hydrochloride (316 mg, 1.32 mmol) and Cbz-Gly (276 mg, 1.32 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S1** (435 mg, 92%) as colourless crystals; R_f 0.33 (10% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.26 (m, 5H), 6.95 (d, *J*=8.1 Hz, 1H), 5.46 (m, 1H), 5.12 (s, 2H), 4.83 (dt, *J*=8.6, 4.5 Hz, 1H), 4.01–3.83 (m, 2H), 3.73 (s, 3H), 2.93 (dd, *J*=17.0, 4.5 Hz, 1H), 2.72 (dd, *J*=17.2, 4.5 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.0, 169, 136.1, 128.5, 128.2, 128.1, 82.0,

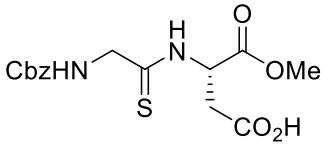
67.2, 52.7, 48.6, 44.4, 37.3, 28.0. MS (ESI) *m/z* 395 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{19}H_{27}N_2O_7$ 395.1813, found 395.1813.

Cbz-Gly$^{[S]}$-Asp(O*t*Bu)-OMe (S2)



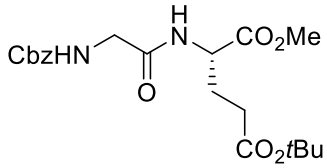
To a solution of the dipeptide **S2** (193 mg, 0.49 mmol) in toluene (5 mL) was added Lawesson's reagent (238 mg, 0.59 mmol). The reaction mixture was heated at 60 °C for 2 h. The solvent was evaporated under reduced pressure. Purification of the residue by column chromatography (50% EtOAc/Hex) gave the title compound **S2** (165 mg, 82%) as a light yellow oil; R_f 0.50 (50% EtOAc/Hex).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.40–7.27 (m, 5H), 5.57 (s, 1H), 5.42 (dd, *J*=10.1, 6.2 Hz, 1H), 5.18–5.09 (m, 2H), 4.31 (dd, *J*=17.3, 6.1 Hz, 1H), 4.22 (dd, *J*=17.3, 6.0 Hz, 1H), 3.76 (s, 3H), 3.0 –2.91 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.4, 170.2, 169.8, 156.6, 135.70, 128.6, 128.3, 128.1, 82.2, 67.4, 53.7, 52.9, 52.1, 35.97, 27.9. MS (ESI) *m/z* 411 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{19}H_{27}N_2O_6S$ 411.1584, found 411.1584.

Cbz-Gly$^{[S]}$-Asp-OMe (5)



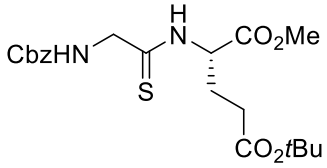
To a solution of **S2** (100 mg, 0.24 mmol) in DCM (2 mL) at 0 °C was added TFA (2 mL) and the solution was stirred for 1 h. The solvent and TFA were evaporated to afford the title compound **5** (84 mg) as colourless oil which was used without further purification. MS (ESI) *m/z* 355 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{15}H_{19}N_2O_6S$ 355.0958, found 355.0959.

Cbz-Gly-Glu(tBu)-OMe (S3)



Dipeptide **S3** was prepared from Glu(OtBu)-OMe hydrochloride (254 mg, 1.0 mmol) and Cbz-Gly-OH (209 mg, 1.0 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S3** (392 mg, 96%) as colourless crystals; R_f 0.34 (10% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.20 (m, 5H), 6.79 (d, *J*=7.5 Hz, 1H), 5.41 (m, 1H), 5.13 (s, 2H), 4.60 (m, 1H), 3.99–3.84 (m, 2H), 3.74 (s, 3H), 2.39–2.20 (m, 2H), 2.14 (m, 1H), 1.95 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 169.0, 156.5, 136.1, 128.5, 128.2, 128.0, 81.0, 67.2, 52.5, 51.8, 44.3, 31.3, 28.0, 27.1. MS (ESI) *m/z* 409 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{20}H_{29}N_2O_7$ 409.1969, found 409.1969.

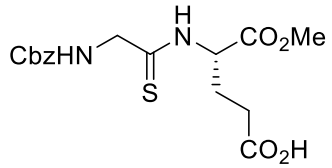
Cbz-Gly$^{[S]}$-Glu(tBu)-OMe (S4)



To a solution of the dipeptide **S3** (204 mg, 0.5 mmol) in toluene (5 mL) was added Lawesson's reagent (243 mg, 0.6 mmol). The reaction mixture was heated at 60 °C for 2 h. The solvent was evaporated under reduced pressure. Purification of the residue by column chromatography (50% EtOAc/hexane) gave the title compound **S4** (180 mg, 85%) as a light yellow oil; R_f 0.45 (50% EtOAc/hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.47–7.21 (m, 5H), 5.59 (m, 1H), 5.15 (s, 2H), 5.10 (m, 1H), 4.34–4.18 (m, 2H), 3.75 (s, 3H), 2.43–2.30 (m, 2H), 2.26 (m, 1H), 2.11 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 172.4, 171.0, 156.7, 136.0, 128.5, 128.2, 128.1, 81.3, 67.4, 57.2, 52.7, 51.9, 31.3, 28.0,

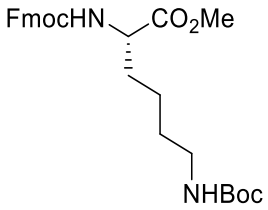
26.0. MS (ESI) *m/z* 409 [$(M+H)^+$,100%]. HRMS (ESI, $[M+H]^+$ calcd. for $C_{20}H_{29}N_2O_6S$ 425.1741, found 425.1741.

Cbz-Gly[S]-Glu-OMe (8)



To a solution of **S4** (100 mg, 0.24 mmol) in DCM (2 mL) was added TFA (2 mL) and the solution was stirred for 1 h at room temperature. The solvents were evaporated to afford the title compound **8** (85 mg) as colourless oil which was used without further purification. MS (ESI) *m/z* 369 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{16}H_{21}N_2O_6S$ 369.1115, found 369.1113.

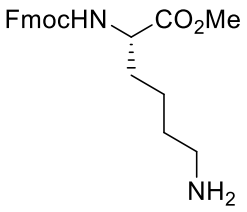
Fmoc-Lys(Boc)-OMe (S5)



To a suspension of Fmoc-Lys(Boc)-OH (937 mg, 2.0 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol) in DMF (20 mL) at 0 °C was added methyl iodide (187 µL, 3.0 mmol). The reaction mixture was stirred at room temperature for 16 h. The mixture was diluted with EtOAc (25 mL) and water (10 mL). The aqueous layer was extracted with EtOAc (2 × 25 mL) and the combined organic extracts were washed with water (30 mL), brine (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (30% EtOAc/hexanes) to give the title compound **S5** as a white solid (917 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J*=7.5 Hz, 2H), 7.65–7.56 (m, 2H), 7.40 (t, *J*=7.5 Hz, 2H), 7.32 (dd, *J*=8.1, 6.6 Hz, 2H), 5.37 (d, *J*=8.3 Hz, 1H), 4.55 (s,

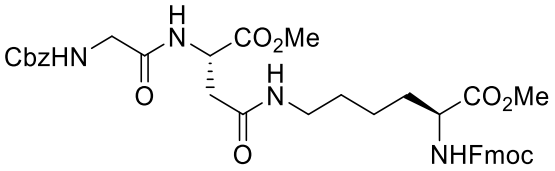
1H), 4.47–4.31 (m, 3H), 4.23 (t, *J*=7.0 Hz, 1H), 3.75 (s, 3H), 3.11 (q, *J*=6.6 Hz, 2H), 1.86 (m, 1H), 1.71 (m, 1H), 1.53–1.32 (m, 13H);^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 156.1, 156.0, 143.9, 143.8, 141.3, 127.7, 127.1, 125.1, 120.0, 120.0, 67.0, 53.7, 52.4, 47.2, 40.0, 32.1, 29.6, 28.4, 22.4. MS (ESI) *m/z* 483 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{27}H_{35}N_2O_6$ 483.2490, found 483.2487.

Fmoc-Lys-OMe (6)



To a solution of **S5** (200 mg, 0.4 mmol) in DCM (3.0 mL) at 0 °C, was added TFA (1.0 mL). The mixture was stirred for 1 h at room temperature. The solution was brought to pH 8.0 by adding saturated aqueous $NaHCO_3$. The aqueous layer was extracted with DCM (3 × 10 mL) and the combined organic extracts were dried with Na_2SO_4. The solvent was evaporated under reduced pressure to give **6** as colourless oil (155 mg), which was used in the next step without purification. MS (ESI) *m/z* 383 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{22}H_{27}N_2O_4$ 383.1965, found 383.1962.

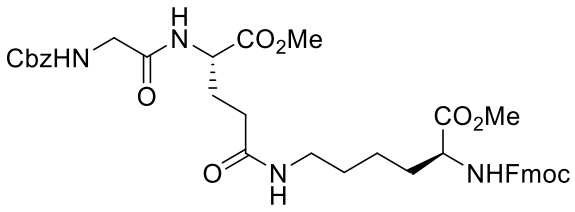
Cbz-Gly-Asp(Fmoc-Lys-OMe)-OMe (7)



To a solution of **5** (35 mg, 0.1 mmol) in dichloromethane (3.0 mL) was added Ag_2CO_3 (41 mg, 0.15 mmol) and **6** (77 mg, 0.2 mmol) and the mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue purified by column chromatography (10% MeOH/DCM) to give the compound **7** (59 mg, 84%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, *J*=7.8 Hz, 1H),

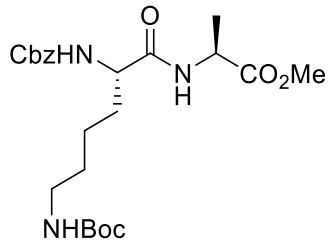
7.94–7.83 (m, 3H), 7.74 (d, *J*=7.7 Hz, 1H), 7.69 (dd, *J*=7.5, 2.6 Hz, 2H), 7.45 (t, *J*=6.2 Hz, 1H), 7.40 (t, *J*=7.4 Hz, 2H), 7.37 – 7.21 (m, 7H), 5.01 (s, 2H), 4.60 (m, 1H), 4.34–4.24 (m, 2H), 4.20 (m, 1H), 3.97 (m, 1H), 3.66–3.53 (m, 2H), 3.60 (s, 3H), 3.57 (s, 3H), 3.06–2.93 (m, 2H), 2.60–2.49 (m, 2H), 1.75–1.51 (m, 2H), 1.47–1.18 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.4, 172.1, 169.5, 169.0, 156.9, 156.6, 144.2, 141.2, 137.5, 128.8, 128.2, 128.1, 127.5, 125.7, 120.6, 66.1, 65.9, 54.3, 52.3, 49.2, 47.1, 43.7, 38.7, 37.4, 30.8, 29.0, 23.4. MS (ESI) *m/z* 703 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$ calcd. for $C_{37}H_{43}N_4O_{10}$ 703.2974, found 703.2977.

Cbz-Gly-Glu(Fmoc-Lys-OMe)-OMe (9)



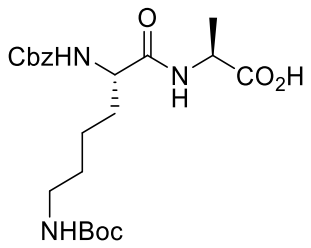
To a solution of **8** (37 mg, 0.1 mmol) in DCM (3.0 mL) was added Ag_2CO_3 (41 mg, 0.15 mmol) and **6** (77 mg, 0.2 mmol) and the mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue purified by column chromatography (10% MeOH/DCM) to give the compound **9** (34 mg, 47%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (d, *J*=7.4 Hz, 1H), 7.88 (d, *J*=7.5 Hz, 2H), 7.80–7.72 (m, 2H), 7.70 (dd, *J*=7.5, 2.4 Hz, 2H), 7.40 (m, 3H), 7.36–7.21 (m, 7H), 5.01 (s, 2H), 4.29 (m, 1H), 4.25– 4.16 (m, 2H), 4.0 –3.97 (m, 2H), 3.6 –3.62 (m, 2H), 3.60 (s, 3H), 3.59 (s, 3H), 3.04–2.93 (m, 2H), 2.17–2.00 (m, 2H), 1.92 (m, 1H), 1.78 (m, 1H), 1.71–1.50 (m, 2H), 1.43–1.13 (m, 4H).^{13}C NMR (101 MHz, DMSO-d_6) δ 173.4, 172.7, 171.3, 169.7, 156.9, 156.6, 144.2, 141.2, 137.5, 128.8, 128.2, 128.1, 128.1, 127.5, 125.7, 120.6, 66.1, 65.9, 54.3, 52.3, 52.0, 47.1, 43.6, 38.7, 31.9, 30.8, 29.1, 27.4, 23.4. MS (ESI) *m/z* 717 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$ calcd. for $C_{38}H_{45}N_4O_{10}$ 717.3130, found 717.3136.

Cbz-Lys(Boc)-Ala-OMe (S6)



Dipeptide **S6** was prepared from Cbz-Lys(Boc)-OH **11a** (380 mg, 1.0 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S6** (442 mg, 95%) as a white solid; R_f 0.34 (10% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 6.62 (d, *J*=7.5 Hz, 1H), 5.50 (d, *J*=7.8 Hz, 1H), 5.10 (s, 2H), 4.69 (m, 1H), 4.55 (m, 1H), 4.17 (m, 1H), 3.74 (s, 3H), 3.20–2.99 (m, 2H), 1.86 (m, 1H), 1.65 (m, 1H), 1.53–1.46 (m, 2H), 1.45–1.37 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 171.4, 156.2, 136.2, 128.5, 128.2, 128.1, 79.1, 67.0, 54.6, 52.5, 48.0, 39.7, 32.1, 29.5, 28.4, 22.2, 18.1.MS (ESI) *m/z* 466 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{23}H_{36}N_3O_7$ 466.2548, found 466.2548.

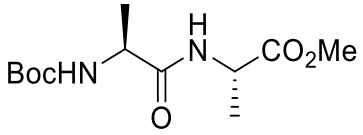
Cbz-Lys(Boc)-Ala-OH (11b)



To a solution of **S6** (100 mg, 0.22 mmol) in a mixture of MeOH/H_2O (1:1, 5 mL) cooled to 0 °C, was added LiOH.H_2O (28 mg, 0.66 mmol). The mixture was stirred for 10 min at 0 °C and 2 h at room temperature. The solution was concentrated and was diluted with water (10 mL) then acidified to pH 4 with aqueous HCl (1 M). The solution was extracted with EtOAc (3 ×10 mL) and washed with water (20 mL), brine (20 mL) and dried with Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude acid **11b** as colourless oil (90 mg), which was used in the next step without further purification.

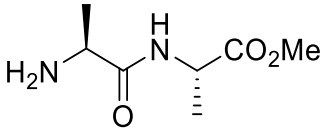
MS (ESI) *m/z* 452 [(M+H)$^+$,100%]; HRMS (ESI, [M+H] $^+$) calcd. for $C_{22}H_{34}N_3O_7$ 452.2391, found 452.2390.

Boc-Ala-Ala-OMe (S7)



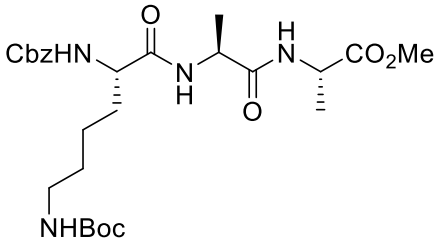
Dipeptide **S7** was prepared from Boc-Ala-OH (189 mg, 1.0 mmol) and H-Ala-OMe (140 mg, 1.0 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S7** (252 mg, 92%) as a white solid; R_f 0.34 (50% EtOAc/Hex). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (d, *J*=7.5 Hz, 1H), 5.11–4.84 (m, 1H), 4.57 (p, *J*=7.2 Hz, 1H), 4.27–4.02 (m, 1H), 3.75 (s, 3H), 1.45 (s, 9H), 1.40 (d, *J*=7.1 Hz, 3H), 1.36 (d, *J*=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 172.2, 52.4, 49.9, 48.0, 28.3, 18.3. MS (ESI) *m/z* 275 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$ calcd. for $C_{12}H_{23}N_2O_5$ 275.1601, found 275.1601.

H-Ala-Ala-OMe (S8)



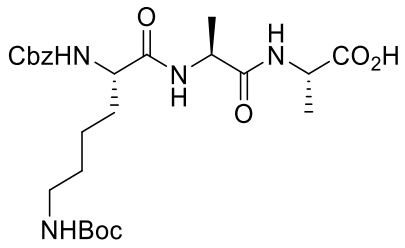
To a solution of **S7** (200 mg, 0.73 mmol) in DCM (1.5 mL) at 0 °C, was added TFA (0.5 mL). The mixture was stirred for 1 h at room temperature. The solvent was evaporated under reduced pressure to give **S8** trifluoroacetate salt as colourless oil (205 mg), which was used in the next step without purification. MS (ESI) *m/z* 383 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$ calcd. for $C_7H_{15}N_2O_3$ 175.1077, found 175.1075.

Cbz-Lys(Boc)-Ala-Ala-OMe (S9)



Tripeptide **S9** was prepared from Cbz-Lys(Boc)-OH **11a** (278 mg, 0.73 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S9** (341 mg, 87%) as a white solid; R_f 0.3 (10% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.24 (m, 5H), 6.87 (d, *J*=8.0 Hz, 1H), 6.77 (d, 1H), 5.79–5.67 (m, 1H), 5.09 (s, 2H), 4.75 (t, *J*=5.9 Hz, 1H), 4.52 (h, *J*=7.7 Hz, 2H), 4.23–4.09 (m, 1H), 3.73 (s, 3H), 3.18–2.98 (m, 2H), 1.90–1.62 (m, 3H), 1.4 (s, 9H), 1.51–1.34 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 171.7, 171.5, 156.4, 136.1, 128.5, 128.2, 128.1, 79.2, 67.1, 54.9, 52.5, 48.8, 48.1, 39.5, 31.8, 29.5, 28.4, 22.2, 18.1. MS (ESI) *m/z* 537 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{26}H_{41}N_4O_8$ 537.2919, found 537.2922.

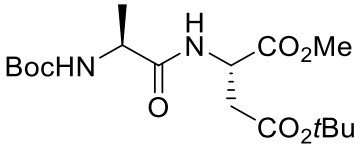
Cbz-Lys(Boc)-Ala-Ala-OH (11c)



To a solution of **S9** (118 mg, 0.22 mmol) in a mixture of MeOH/H_2O (1:1, 5 mL) cooled to 0 °C, was added LiOH.H_2O (28 mg, 0.66 mmol). The mixture was stirred for 10 min at 0 °C and 2 h at room temperature. The solution was concentrated and was diluted with water (10 mL) then acidified to pH 4 with aqueous HCl (1 M). The solution was extracted with EtOAc (3 ×10 mL) and washed with water (20 mL), brine (20 mL) and dried with Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude acid **11c** as colourless oil (105 mg) which was used in the next step without further purification.

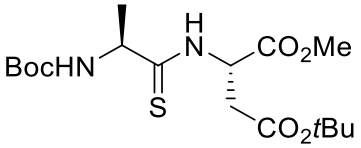
MS (ESI) *m/z* 536 [(M+H)$^+$,100%]; HRMS (ESI, [M+H] $^+$) calcd. for $C_{26}H_{40}N_4O_8$ 536.2846, found 536.2844.

Boc-Ala-Asp(*t*Bu)-OMe (S10)



Dipeptide **S10** was prepared from Boc-Ala-OH (189 mg, 1.0 mmol) and H-Asp(tBu)-OMe hydrochloride (**94**) (240 mg, 1.0 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **S10** (356 mg, 95%) as a white solid; R_f 0.38 (10% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, *J*=8.3 Hz, 1H), 5.05 (s, 1H), 4.78 (dt, *J*=8.7, 4.6 Hz, 1H), 4.26–4.07 (m, 1H), 3.73 (s, 3H), 2.92 (dd, *J*=17.0, 4.6 Hz, 1H), 2.70 (dd, *J*=17.0, 4.6 Hz, 1H), 1.43 (s, 9H), 1.42 (s, 9H), 1.36 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 171.1, 170.0, 81.8, 52.6, 48.6, 37.3, 28.3, 28.0, 18.6. MS (ESI) *m/z* 375 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{17}H_{31}N_2O_7$ 375.2126, found 375.2126.

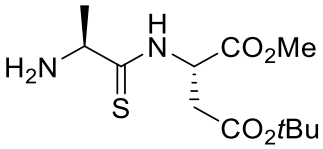
Boc-Ala$^{[S]}$-Asp(*t*Bu)-OMe (S11)



To a solution of the dipeptide **S10** (337 mg, 0.9 mmol) in toluene (10 mL) was added Lawesson's reagent (437 mg, 1.08 mmol). The reaction mixture was heated at 60 °C for 2 h. The solvent was evaporated under reduced pressure. Purification of the residue by column chromatography (50% EtOAc/Hex) gave the title compound **S11** (288 mg, 82%) as a light yellow oil; R_f 0.47 (50% EtOAc/Hex. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J*=7.8 Hz, 1H), 5.38 (dt, *J*=8.1, 4.2 Hz, 1H), 5.20 (s, 1H), 4.46 (m, 1H), 3.78 (s,

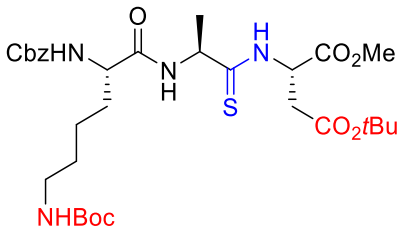
3H), 3.07–2.94 (m, 2H), 1.46 (d, *J*=6.9 Hz, 3H), 1.44 (s, 9H), 1.43 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 205.4, 170.2, 170.0, 154.9, 82.2, 53.7, 52.8, 35.9, 28.3, 28.0, 21.9. MS (ESI) *m/z* 391 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{17}H_{31}N_2O_6S$ 391.1897, found 391.1899.

H-Ala[S]-Asp(*t*Bu)-OMe (10)



To a solution of **S11** (234 mg, 0.6 mmol) in DCM (9.0 mL) at 0 °C, was added TFA (1.0 mL). The mixture was stirred for 1 h at room temperature. The solution was brought to pH 8.0 by adding saturated aqueous $NaHCO_3$. The aqueous layer was extracted with DCM (3 × 15 mL) and the combined organic extracts were dried with Na_2SO_4. The solvent was evaporated under reduced pressure to give **10** as a yellow oil (144 mg) which was used in the next step without purification. MS (ESI) *m/z* 291 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{12}H_{23}N_2O_4S$ 291.1373, found 291.1372.

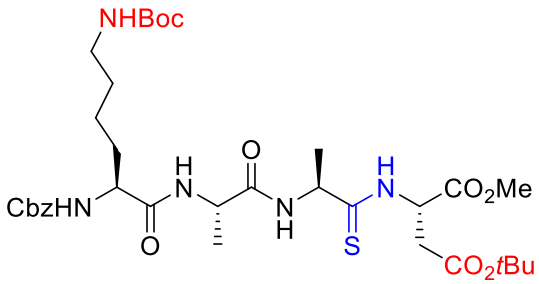
Cbz-Lys(Boc)- Ala[S]-Asp(tBu)-OMe (12a)



Tripeptide **12a** was prepared from Cbz-Lys(Boc)-OH **11a** (19 mg, 0.05 mmol) and amine **10** (15 mg, 0.05 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **12a** (27 mg, 83%) as a white solid; R_f 0.35 (5% MeOH/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J*=9.4 Hz, 1H), 7.4 –7.27 (m, 5H), 7.12 (d, *J*=7.4 Hz, 1H), 5.60 (s, 1H), 5.39 (m, 1H), 5.15–5.07 (m, 2H), 4.78 (m, 1H), 4.67 (s, 1H), 4.19 (m, 1H), 3.76 (s, 3H), 3.19–3.05 (m, 2H), 3.00 (dd, *J*=17.2,

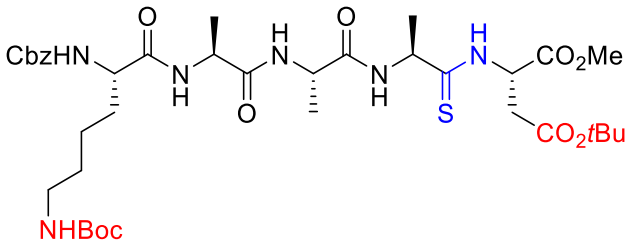
4.4 Hz, 1H), 2.93 (dd, *J*=17.1, 4.3 Hz, 1H), 1.96–1.76 (m, 2H), 1.75–1.60 (m, 2H), 1.51–1.45 (m, 5H), 1.43 (s, 9H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.9, 171.9, 171.6, 171.1, 170.2, 170.1, 170.0, 156.3, 136.2, 128.5, 128.1, 82.2, 81.9, 79.2, 67.1, 54.8, 54.7, 53.9, 52.8, 48.9, 48.7, 37.3, 36.0, 29.5, 28.4, 28.0, 22.4, 22.0. MS (ESI) *m/z* 291 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{31}H_{49}N_4O_9S$ 653.3215, found 653.3217.

Cbz-Lys(Boc)-Ala-Ala[S]-Asp(tBu)-OMe (12b)



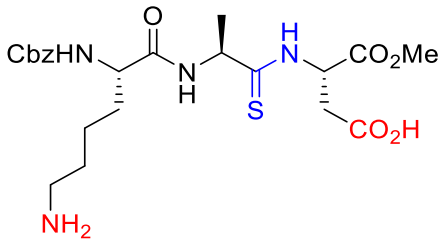
Tetrapeptide **12b** was prepared from Cbz-Lys(Boc)-Ala-OH **11b** (90 mg, 0.2 mmol) and amine **10** (58 mg, 0.2 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **12b** (116 mg, 80%) as a white solid; R_f 0.31 (5% MeOH/DCM). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (d, *J*=7.7 Hz, 1H), 8.05 (d, *J*=7.6 Hz, 1H), 8.00 (d, *J*=7.4 Hz, 1H), 7.44–7.24 (m, 5H), 6.74 (t, *J*=5.8 Hz, 1H), 5.25 (m, 1H), 5.01 (s, 2H), 4.70 (m, 1H), 4.28 (m, 1H), 3.95 (m, 1H), 3.63 (s, 3H), 2.95–2.82 (m, 2H), 2.82–2.70 (m, 2H), 1.70–1.44 (m, 2H), 1.38 (s, 9H), 1.36 (s, 9H), 1.26 (d, *J*=6.9 Hz, 3H), 1.36–1.08 (m, 2H), 1.21 (d, *J*=7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 206.9, 172.2, 171.7, 170.1, 168.9, 156.4, 156.0, 137.5, 128.8, 128.2, 128.1, 81.3, 77.8, 65.8, 55.0, 54.4, 54.1, 52.8, 48.3, 36.4, 32.1, 29.7, 28.7, 28.1, 23.3, 21.8, 18.4. MS (ESI) *m/z* 724 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{34}H_{54}N_5O_{10}S$ 724.3586, found 724.3589.

Cbz-Lys(Boc)-Ala-Ala-Ala[S]-Asp(tBu)-OMe (12c)



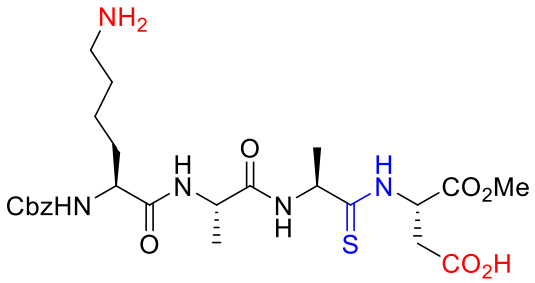
Pentapeptide thioamide **12c** was prepared from Cbz-Lys(Boc)-Ala-Ala-OH **11c** (52 mg, 0.1 mmol) and amine **10** (29 mg, 0.1 mmol) according to General Procedure A. Purification by column chromatography gave the title compound **12c** (61 mg, 76%) as a white solid; R_f 0.3 (5% MeOH/DCM). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (d, *J*=7.5 Hz, 1H), 8.10–7.90 (m, 3H), 7.45–7.23 (m, 6H), 6.74 (t, *J*=5.8 Hz, 1H), 5.25 (m, 1H), 5.01 (s, 2H), 4.69 (m, 1H), 4.33–4.20 (m, 2H), 3.94 (m, 1H), 3.63 (s, 3H), 2.91–2.82 (m, 2H), 2.84–2.72 (m, 2H), 1.63–1.45 (m, 2H), 1.38 (s, 9H), 1.36 (s, 9H), 1.42-125(m, 6H), 1.27 (d, *J*=6.8 Hz, 3H), 1.22 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 206.9, 172.3, 172.1, 171.6, 170.1, 168.9, 156.4, 137.5, 128.8, 128.2, 128.1, 81.3, 77.8, 65.8, 55.0, 54.4, 54.1, 52.8, 48.4, 36.4, 32.0, 29.6, 28.7, 28.1, 23.3, 21.8, 18.7, 18.3. MS (ESI) *m/z* 795 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{37}H_{59}N_6O_{11}S$ 795.3957, found 795.3960.

Cbz-Lys-Ala[S]-Asp-OMe (13a)



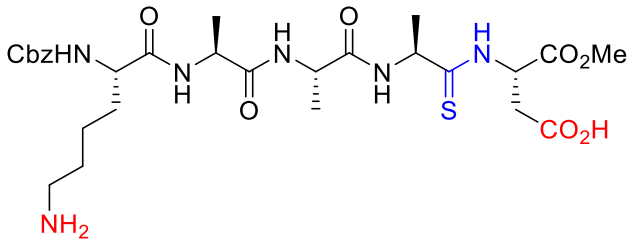
To a solution of **12a** (25 mg, 0.038 mmol) in DCM (1 mL) was added TFA (1 mL) and the solution was stirred for 1 h. The solvent and TFA were evaporated to afford the title compound **13a** (16 mg) as colourless oil which was used without further purification. MS (ESI) *m/z* 496 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{22}H_{33}N_4O_7S$ 497.5865, found 497.5863.

Cbz-Lys-Ala-Ala[S]-Asp-OMe (13b)



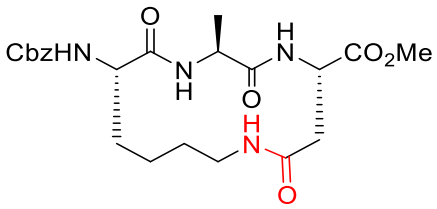
To a solution of **12b** (100 mg, 0.14 mmol) in DCM (1 mL) was added TFA (1 mL) and the solution was stirred for 1 h. The solvent and TFA were evaporated to afford the title compound **13b** (60 mg) as colourless oil which was used without further purification. MS (ESI) *m/z* 568 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{25}H_{38}N_5O_8S$ 568.2436, found 568.2433.

Cbz-Lys-Ala-Ala-Ala[S]-Asp-OMe (13c)



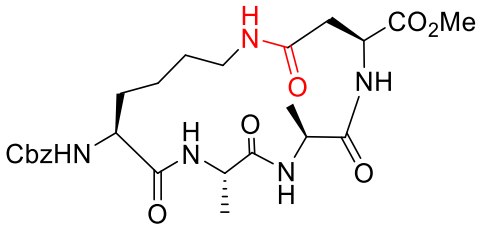
To a solution of **12c** (50 mg, 0.063 mmol) in DCM (1 mL) was added TFA (1 mL) and the solution was stirred for 1 h. The solvent and TFA were evaporated to afford the title compound **13c** (40 mg) as colourless oil which was used without further purification. MS (ESI) *m/z* 639 [(M+H)$^+$,100%]; HRMS (ESI, [M+H]$^+$) calcd. for $C_{28}H_{43}N_6O_9S$ 639.2807, found 639.2805.

Cbz-(cyclo-1,3)-[Lys-Ala-Asp]-OMe (14a)



To a solution of **13a** (16 mg, 0.032 mmol) in DCM (10 mL) was added Ag_2CO_3 (11 mg, 0.039 mmol) and the mixture was stirred at room temperature for 6 h. The solvent was evaporated and the residue purified by column chromatography (10% MeOH /DCM) to give the stapled peptide **14a** (11 mg, 76%) as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.38 (d, J=8.4 Hz, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.59 (t, J=5.7 Hz, 1H), 7.39–7.28 (m, 6H), 5.04–4.93 (m, 2H), 4.53 (m, 1H), 4.43 (m, 1H), 3.94 (m, 1H), 3.61 (s, 3H), 3.29–3.13 (m, 2H), 2.56–2.51 (m, 2H), 1.56–1.39 (m, 2H), 1.31–1.20 (m, 2H), 1.19–1.02 (m, 5H). MS (ESI) *m/z* 463 [(M+H)$^+$,100%]; HRMS (ESI, [M+H] $^+$) calcd. for $C_{22}H_{31}N_4O_7$ 463.5105, found 463.5103.

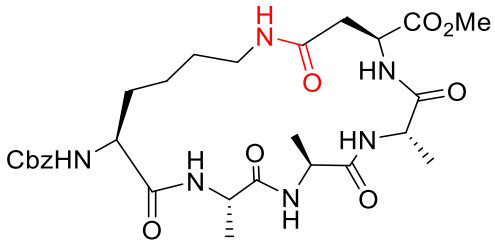
Cbz-(cyclo-1,4)-[Lys-Ala-Ala-Asp]-OMe (14b)



To a solution of **13b** (50 mg, 0.088 mmol) in DCM (10 mL) was added Ag_2CO_3 (30 mg, 0.11 mmol) and the mixture was stirred at room temperature for 6 h. The solvent was evaporated and the residue purified by column chromatography (10% MeOH /DCM) to give the stapled peptide **14b** (38 mg, 81%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.19 (d, J=7.7 Hz, 1H), 8.02 (d, J=8.3 Hz, 1H), 7.73 (t, J=5.5 Hz, 1H), 7.56 (d, J=6.7 Hz, 1H), 7.40–7.24 (m, 6H), 4.99 (s, 2H), 4.66 (m, 1H), 4.25–4.11 (m, 2H), 3.97 (m, 1H), 3.61 (s, 3H), 3.12–2.89 (m, 2H), 2.48–2.39 (m, 2H), 1.46 (m, 2H), 1.34–1.11 (m, 10H).^{13}C

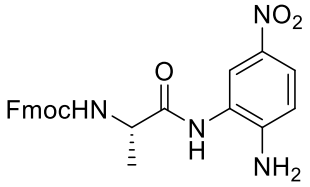
NMR (101 MHz, DMSO-d_6) δ 172.5, 172.0, 171.6, 169.0, 137.5, 128.8, 128.2, 128.2, 65.8, 54.7, 52.6, 49.6, 49.5, 48.9, 38.8, 38.1, 32.3, 29.2, 22.4, 18.6, 17.9. MS (ESI) *m/z* 534 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{25}H_{36}N_5O_8$ 534.2558, found 534.2559.

Cbz-(cyclo-1,5)-[Lys-Ala-Ala-Ala-Asp]-OMe (14c)



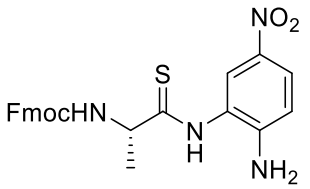
To a solution of **13c** (40 mg, 0.063 mmol) in DCM (10 mL) was added Ag_2CO_3 (21 mg, 0.076 mmol) and the mixture was stirred at room temperature for 6 h. The solvent was evaporated and the residue purified by column chromatography (10% MeOH /DCM) to give the stapled peptide **14c** (31 mg, 82%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (d, *J*=8.1 Hz, 1H), 8.17 (d, *J*=5.4 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.46 (t, *J*=5.7 Hz, 1H), 7.39 (d, *J*=7.5 Hz, 1H), 7.32 (m, 5H), 7.26 (d, *J*=7.2 Hz, 1H), 4.98 (s, 2H), 4.53 (m, 1H), 4.22–4.10 (m, 2H), 3.99 (m, 1H), 3.91 (m, 1H), 3.60 (s, 3H), 3.23 (m, 1H), 2.81 (m, 1H), 2.44–2.39 (m, 2H), 1.50–1.35 (m, 4H), 1.24–1.11 (m, 11H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 206.9, 172.3, 172.1, 171.6, 170.1, 168.9, 156.4, 137.5, 128.8, 128.2, 128.1, 81.3, 77.8, 65.8, 55.0, 54.4, 54.1, 52.8, 48.4, 36.4, 32.0, 29.6, 28.7, 28.1, 23.3, 21.8, 18.7, 18.3. MS (ESI) *m/z* 605 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{28}H_{41}N_6O_9$ 605.2930, found 605.2934.

Fmoc-Ala-2-amino-5-nitroanilide (S12)



A solution of Fmoc-Ala-OH (1.56 g, 5.0 mmol) in dry tetrahydrofuran (50 mL) was cooled to –20 °C, then N-methylmorpholine (NMM) (1.1 mL, 10 mmol) and isobutyl chloroformate (IBCF) (0.714 mL, 5.5 mmol) were added dropwise and the mixture stirred for 15 min under Ar. 1,2-Diamino-4-nitrobenzene (0.842 g, 5.5 mmol) was added and the mixture was stirred at –20 °C for 2 h, then at room temperature overnight under Ar. The solvent was removed under reduced pressure, and the residue was dissolved in DMF (20 mL). Upon addition of brine (100 mL) into the crude mixture, a yellow solid precipitated. The precipitate was filtered and rinsed with cold water. The crude mixture was purified by flash chromatography (5% methanol/dichloromethane) to give the title compound **S12** as a yellow solid (2.054 g, 92%); R_f 0.45 (5% MeOH/DCM). ^{1}H NMR (400 MHz, DMSO) δ 9.35 (s, 1H), 8.16 (d, *J*=2.7 Hz, 1H), 7.91–7.80 (m, 3H), 7.77–7.67 (m, 3H), 7.40 (t, *J*=7.5 Hz, 2H), 7.32 (t, *J*=7.4 Hz, 2H), 6.75 (d, *J*=9.1 Hz, 1H), 6.42 (brs, 2H), 4.35–4.27 (m, 2H), 4.26–4.16 (m, 2H), 1.32 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.6, 156.5, 149.9, 144.3, 144.2, 141.2, 135.9, 128.1, 127.5, 125.8, 125.7, 123.6, 122.3, 121.6, 120.6, 114.0, 66.2, 51.1, 47.1, 18.1. MS (ESI) *m/z* 447 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$) calcd. for $C_{24}H_{23}N_4O_5$ 447.1663, found 447.1667.

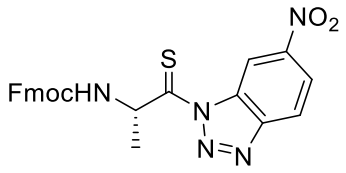
Fmoc-Ala$^{[S]}$-2-amino-5-nitroanilide (S13)



To a solution of phosphorus pentasulfide (311 mg, 0.7 mmol) in dry tetrahydrofuran (10 mL) was added anhydrous sodium carbonate (74 mg, 0.7 mmol) and the mixture was stirred at room temperature for 1 h under argon. The reaction was cooled to 0 °C and the amide **S12** (447 mg, 1.0 mmol) was added. The mixture was stirred at room temperature for 3 h. The mixture was filtered through a pad of Celite, and the solvent evaporated under reduced pressure. The residue was dissolved in ethyl acetate (25 mL), and

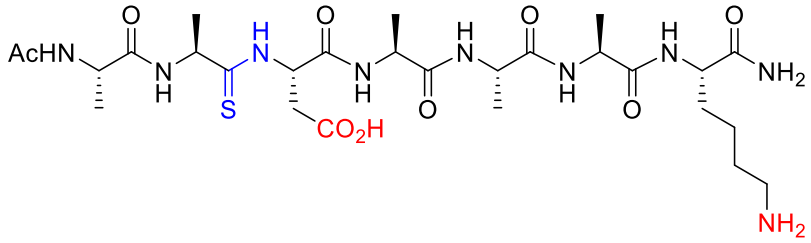
washed with aqueous sodium hydrogen carbonate solution (2 × 15 mL, 5% w/v) and brine (20 mL). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (50% ethyl acetate / hexane) to give the title compound **S13** as a yellow solid (379 mg, 82%); R_f 0.34 (50% ethyl acetate / hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.23 (s, 1H), 7.97–7.91 (m, 2H), 7.90–7.88 (m, 2H), 7.87 (s, 1H), 7.74 (d, *J*=7.5 Hz, 1H), 7.71 (d, *J*=7.5 Hz, 1H), 7.45–7.36 (m, 2H), 7.35–7.27 (m, 2H), 6.77 (d, *J*=9.1 Hz, 1H), 6.37 (brs, 2H), 4.51 (m, 1H), 4.30 (m, 1H), 4.27–4.15 (m, 2H), 1.43 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 208.7, 156.6, 151.1, 144.3, 141.2, 144,1, 135.7, 128.1, 127.6, 125.8, 125.7, 125.4, 125.2, 122.9, 120.6, 114.3, 66.3, 57.4, 47.1, 20.7. MS (ESI) *m/z* 463 [$(M+H)^+$,100%]; HRMS (ESI, $[M+H]^+$ calcd. for $C_{24}H_{23}N_4O_4S$ 463.1435, found 463.1433.

Fmoc-Ala$^{[S]}$-6-nitrobenzotriazolide (16)



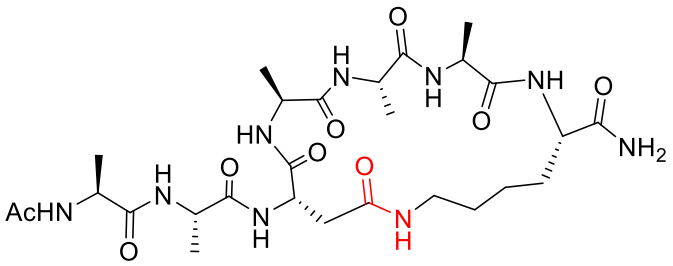
Thioamide **S13** (93 mg, 0.2 mmol) was dissolved in 95% glacial acetic acid (2.0 mL), and cooled to 0 °C. Sodium nitrite (21 mg, 0.3 mmol) was added and the mixture was stirred at 0 °C for 30 min. The reaction was quenched with ice-water (10 mL), and the precipitated product was filtered and washed with cold water (3 x 10 mL). The solid was dried to give nitrobenzotriazolide **16** as a light orange solid (84 mg) which was used without purification.

Ac-Ala-Ala[S]-Asp-Ala-Ala-Ala-Lys-NH_2 (19)



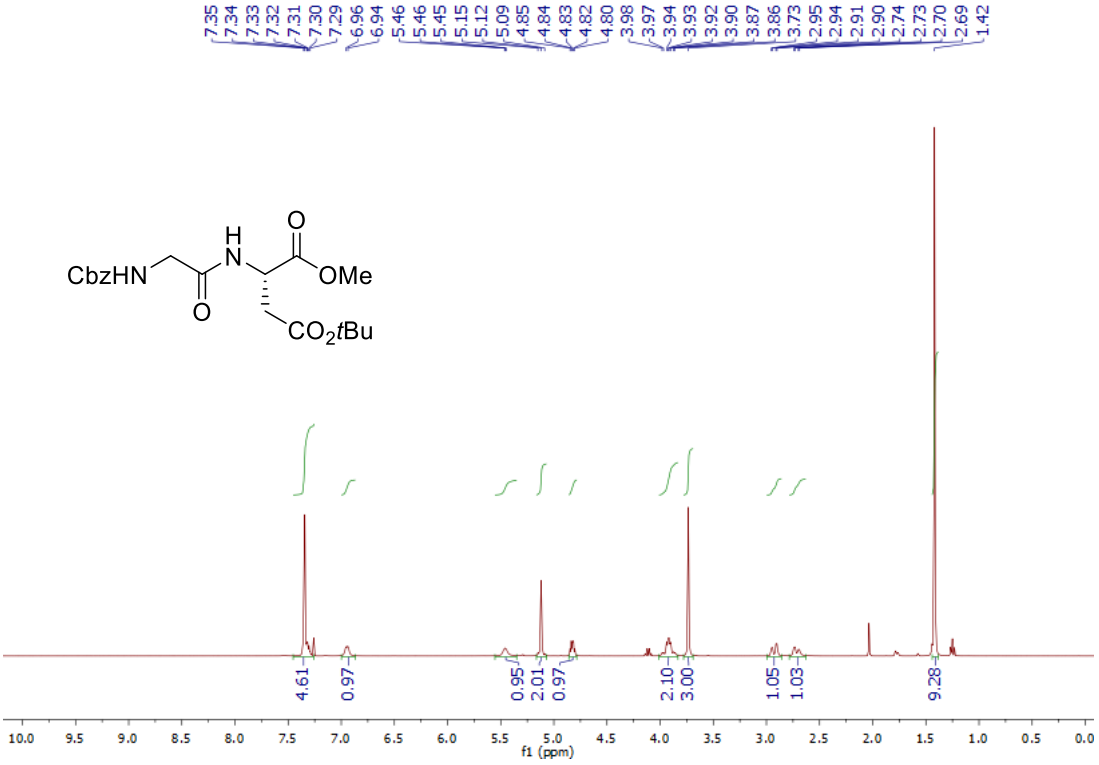
Heptapeptide thioamide **19** was synthesised using standard Fmoc SPPS coupling methods on Sieber amide resin (100-200 mesh, 0.51 mmol/g loading) in a 12 mL fritted syringe. The resin was swelled in DMF (6 mL) for 1 h, then the solvent was drained. Solid phase synthesis was performed on 0.05 mmol scale using 4 equiv. of Fmoc-amino acid (0.2 mmol) activated using 2 equiv. of HATU in the presence of DIPEA (4 equiv.). The coupling reactions were stirred for 1 h at room temperature. Fmoc removal was performed using 20% v/v piperidine in DMF (2 x 5 min). The peptides were elongated up to the thioamide position. Before thioamide coupling, the resin was washed with dry DCM (2 x 5 mL), then Fmoc-Ala-thiobenzotriazolide **16** (0.15 mmol. 1.5 equivalents) and DIPEA (0.15 mmol,1.5 equivalents) in dry DCM (5 mL) were added and the reaction was stirred for 1 h. Removal of the Fmoc protecting group, followed by coupling with *N*-Ac-Ala completed the SPPS steps. Peptide thioamide on resin **18** was treated with TFA in DCM (50%) for 30 min. The solvent was drained and this process was repeated a further 2 times. The solvent was evaporated and the crude peptide thioamide **19** (34 mg) was used in the next step without purification. MS (ESI) *m/z* 674 [$(M+H)^+$,100%]. HRMS (ESI, $[M+H]^+$) calcd. for $C_{27}H_{48}N_9O_9S$ 674.3290, found 674.3293.

Ac-Ala-Ala-(cyclo-3,7)-[Asp-Ala-Ala-Ala-Lys]-NH_2 (20)

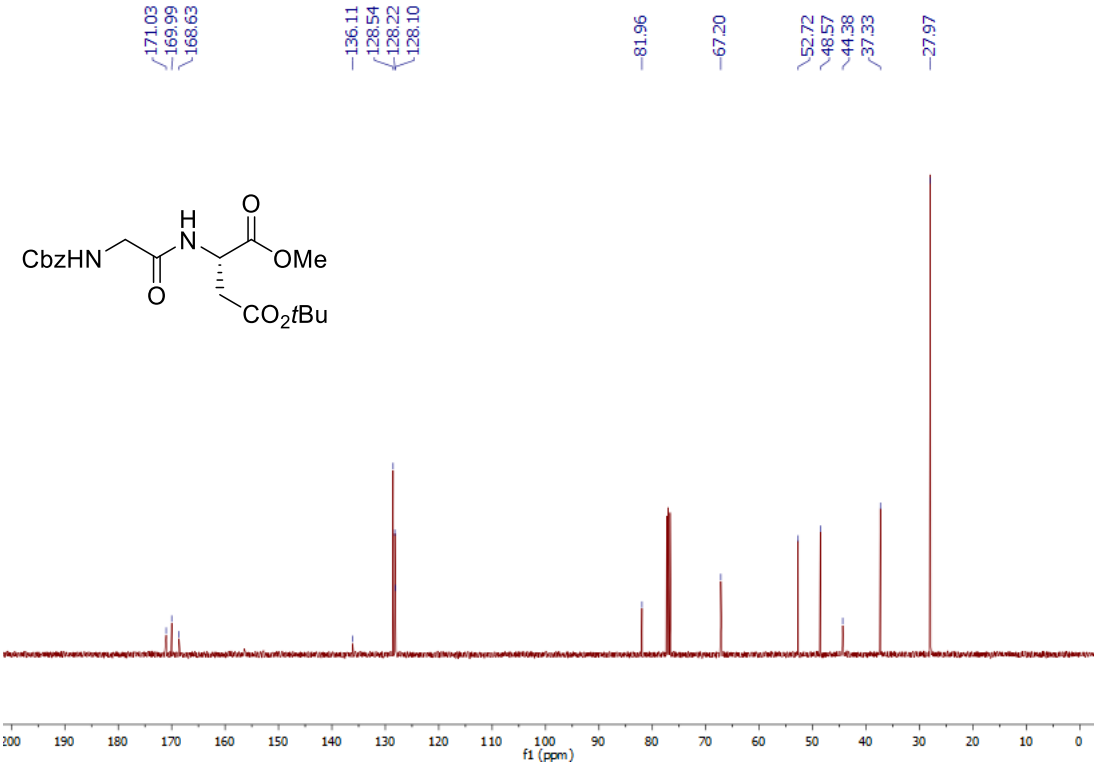


To a solution of crude peptide thioamide **19** (34 mg) in DCM/CH_3CN (1:1, 5 mL) was added Ag_2CO_3 (17 mg, 0.06 mmol) and the mixture was stirred at room temperature for 6 h. The solvent was evaporated and the residue was purified by HPLC to give the product **20** (4.0 mg) as a white solid. MS (ESI) *m/z* 640 [$(M+H)^+$,100%]. HRMS (ESI, $[M+H]^+$) calcd. for $C_{27}H_{44}N_9O_9$ 640.3413, found 640.3417.

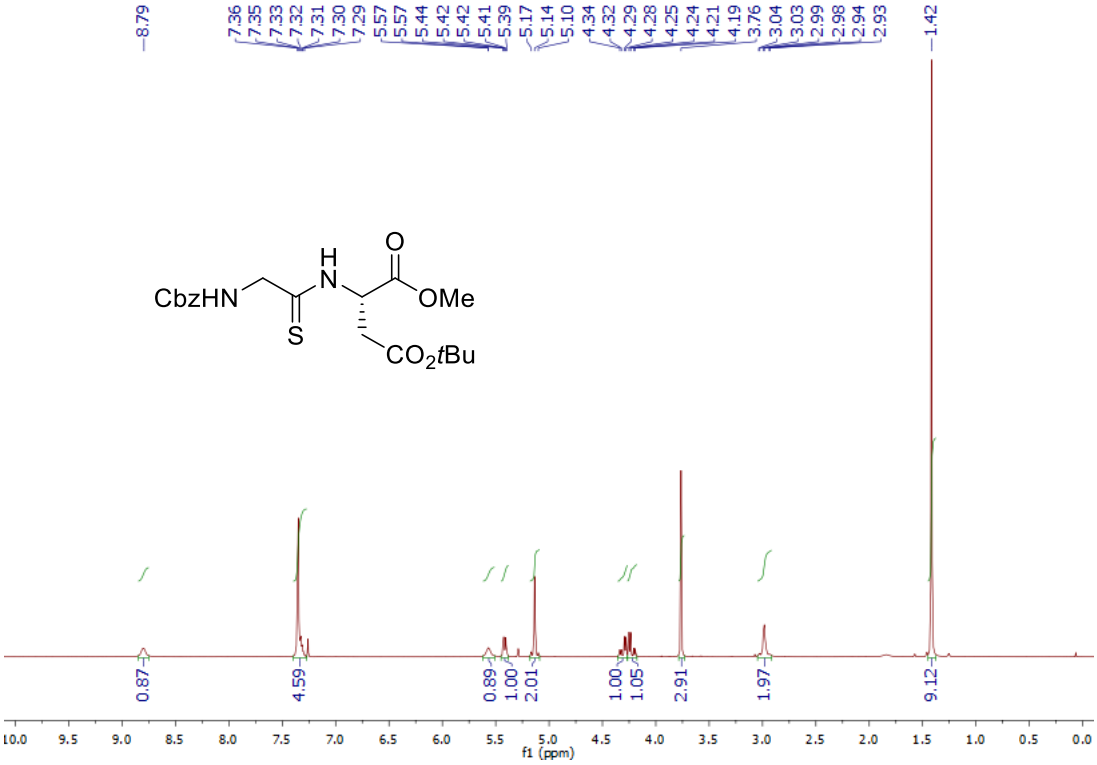
^{1}H NMR of **S1** in $CDCl_3$, 400 MHz



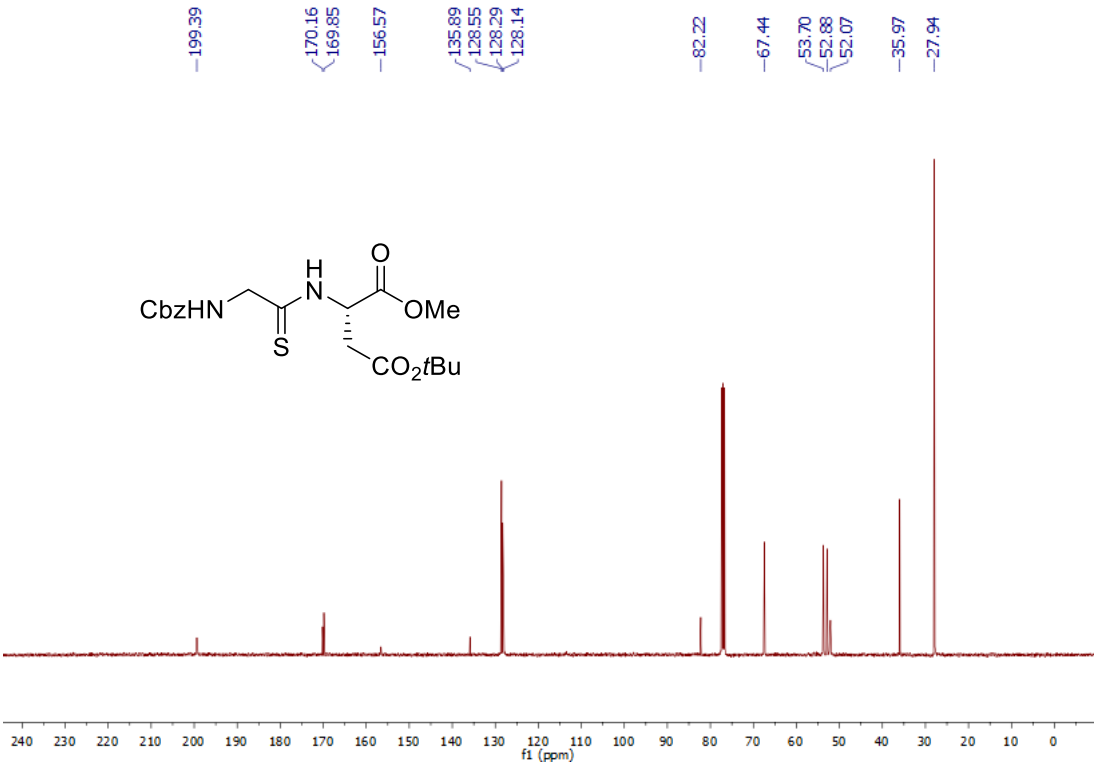
^{13}C NMR of **S1** in $CDCl_3$, 101 MHz



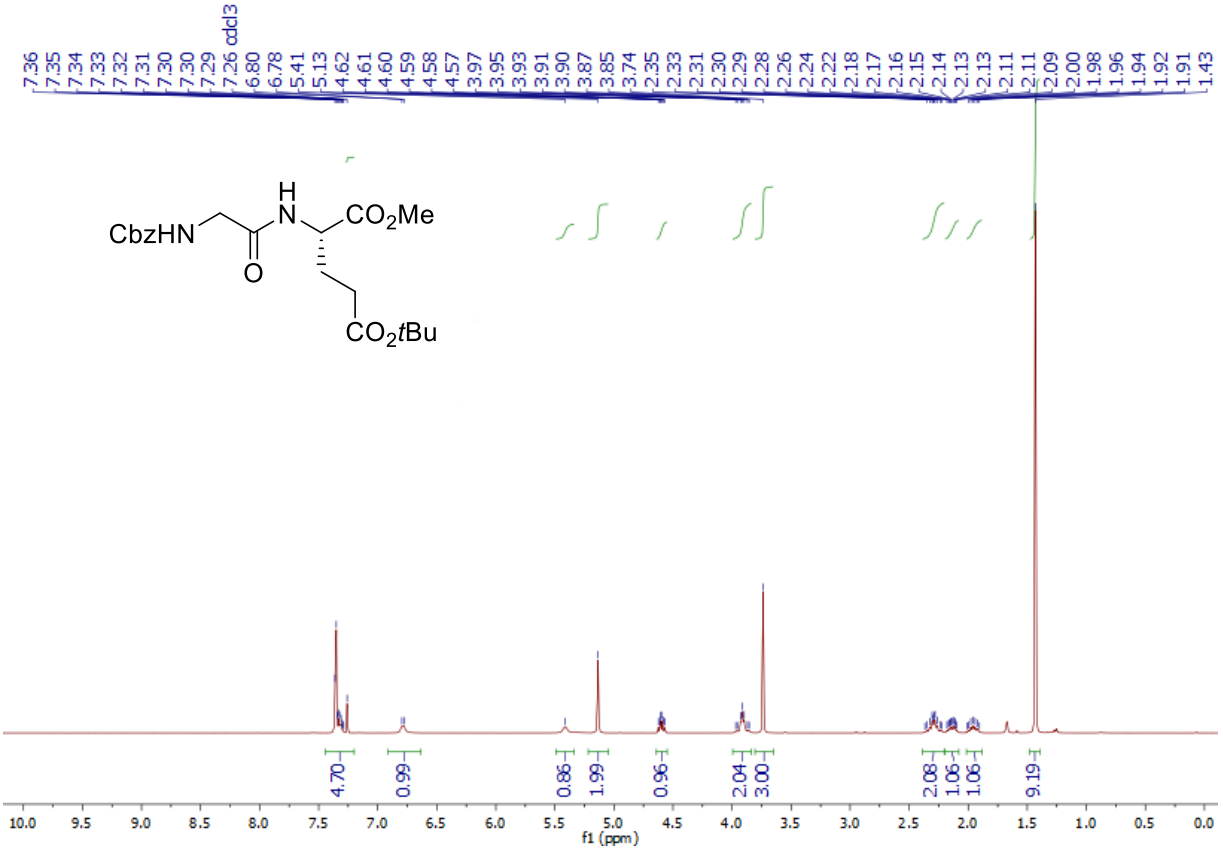
^{1}H NMR for **S2** in $CDCl_3$, 400 MHz



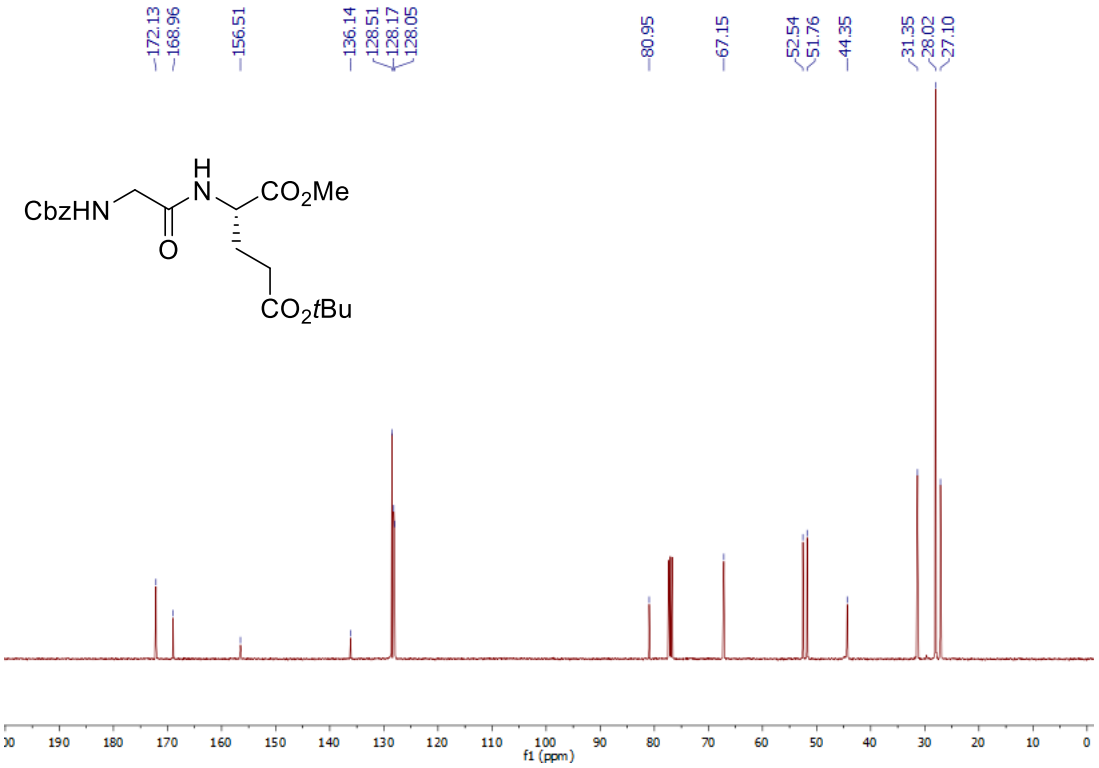
^{13}C NMR for **S2** in $CDCl_3$, 101 MHz



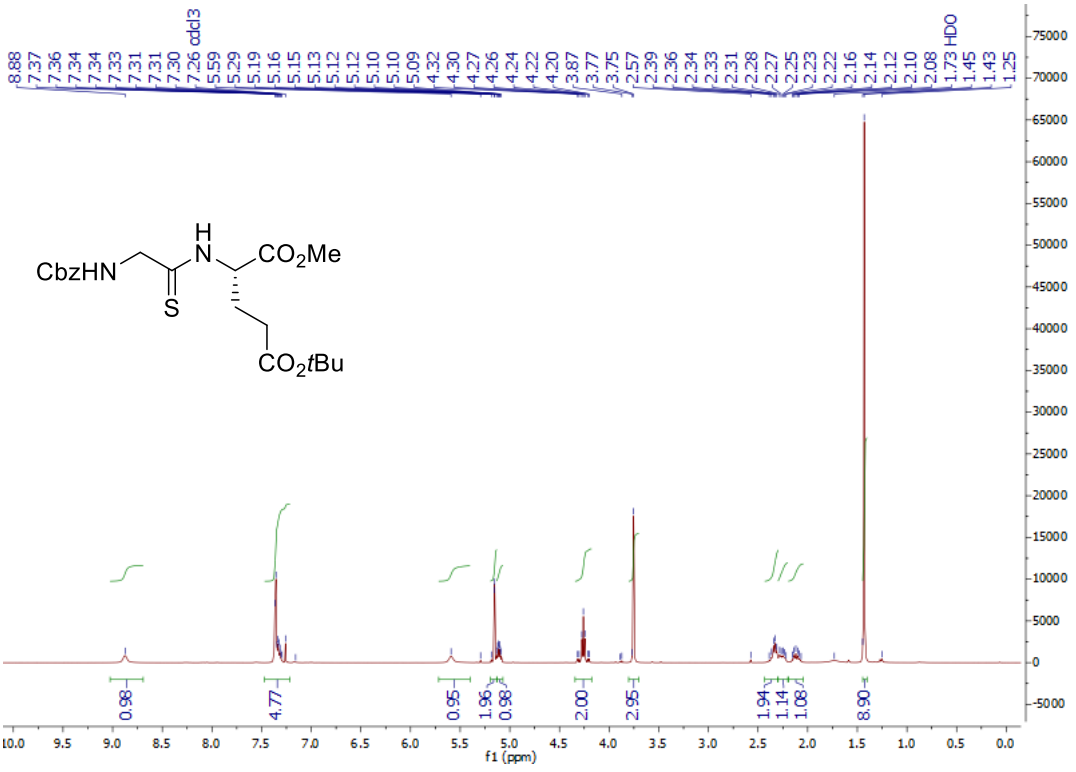
^{1}H NMR of **S3** in $CDCl_3$, 400 MHz



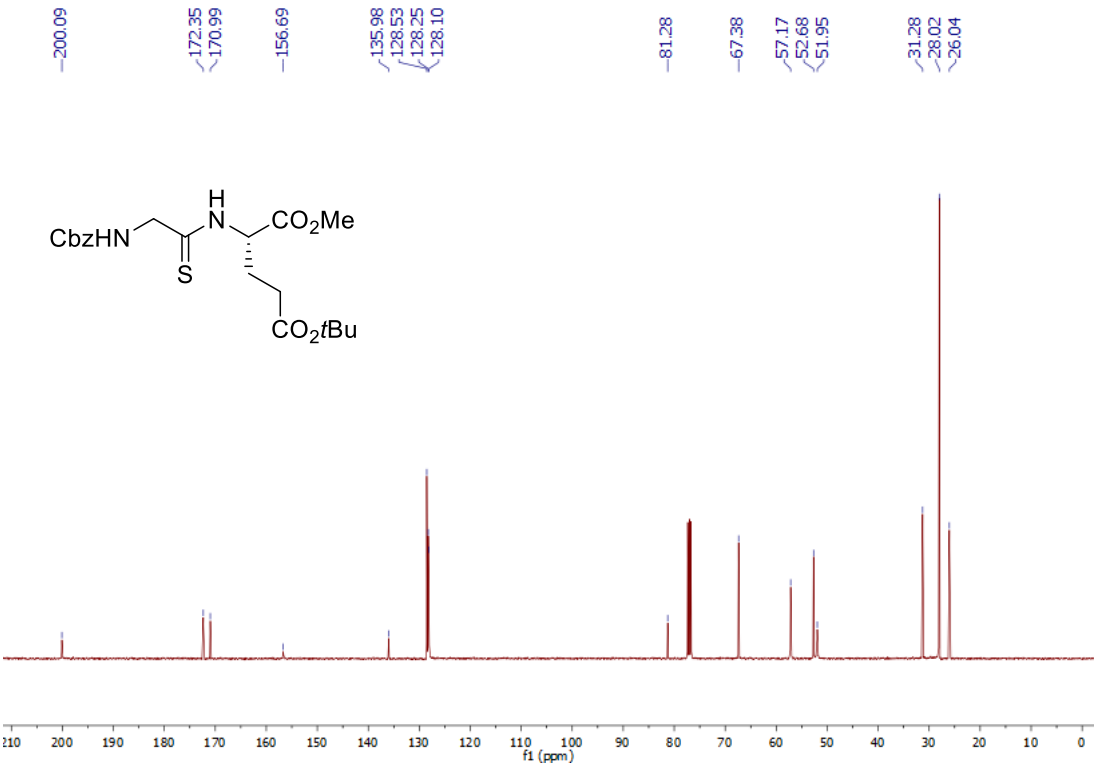
^{13}C NMR of **S3** in $CDCl_3$, 101 MHz



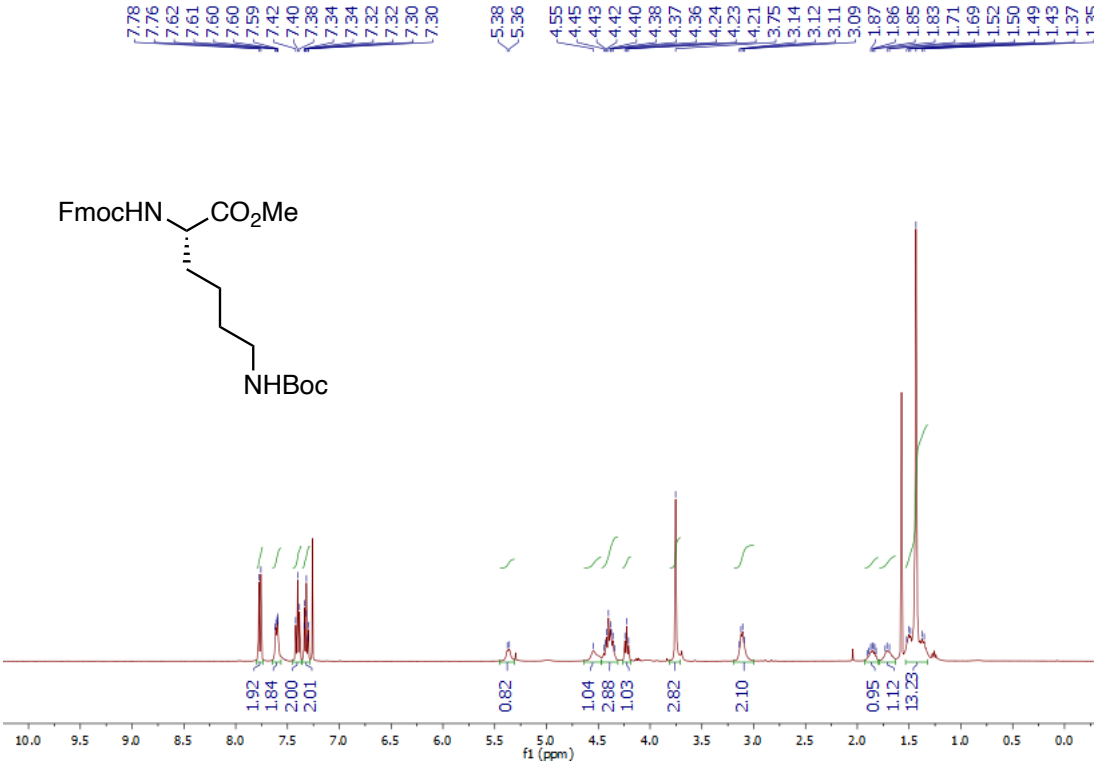
^{1}H NMR of **S4** in $CDCl_3$, 400 MHz



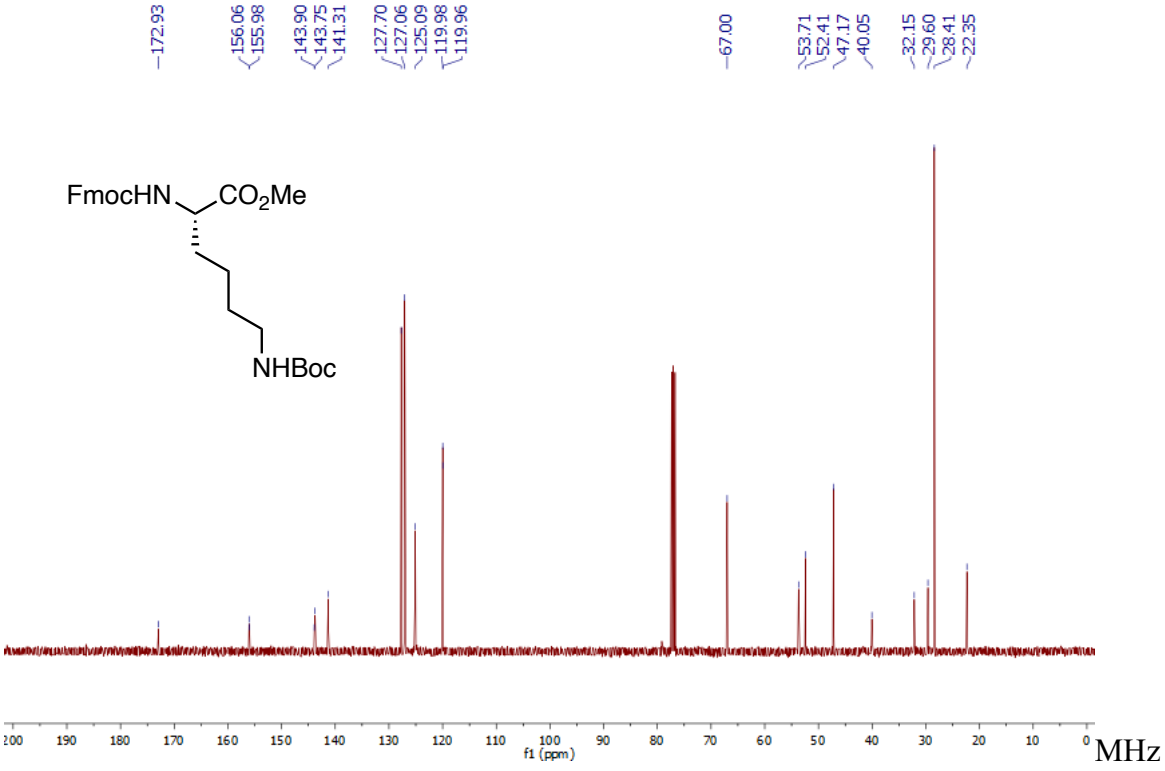
^{13}C NMR for **S4** in $CDCl_3$, 101 MHz



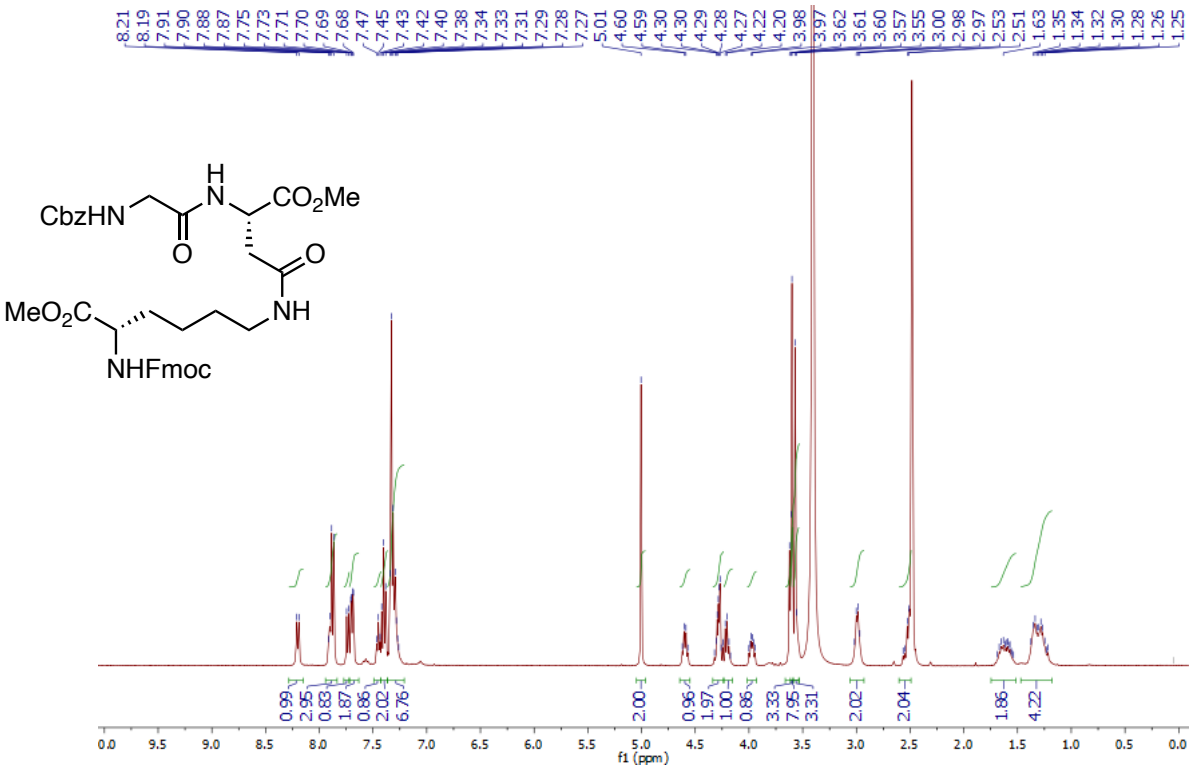
^{1}H NMR of **S5** in $CDCl_3$, 400 MHz



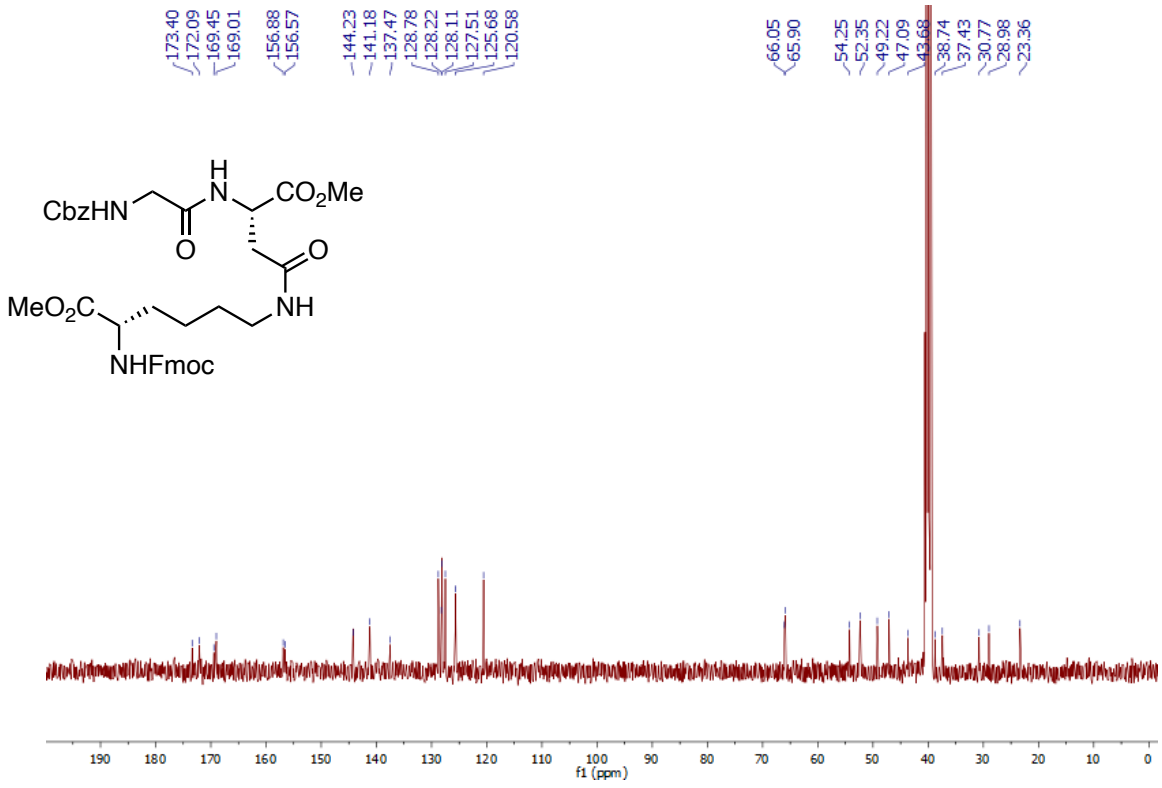
^{13}C NMR of **S5** in $CDCl_3$, 101 MHz



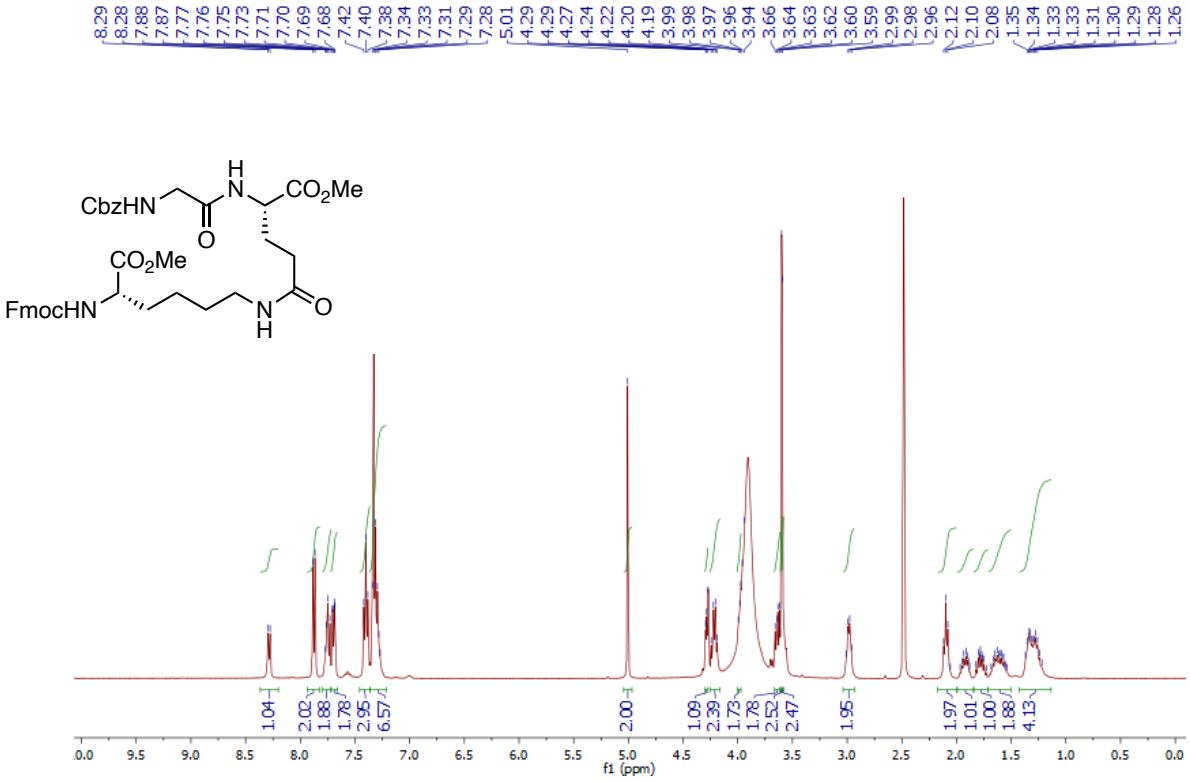
^{1}H NMR for **7** in $CDCl_3$, 400 MHz



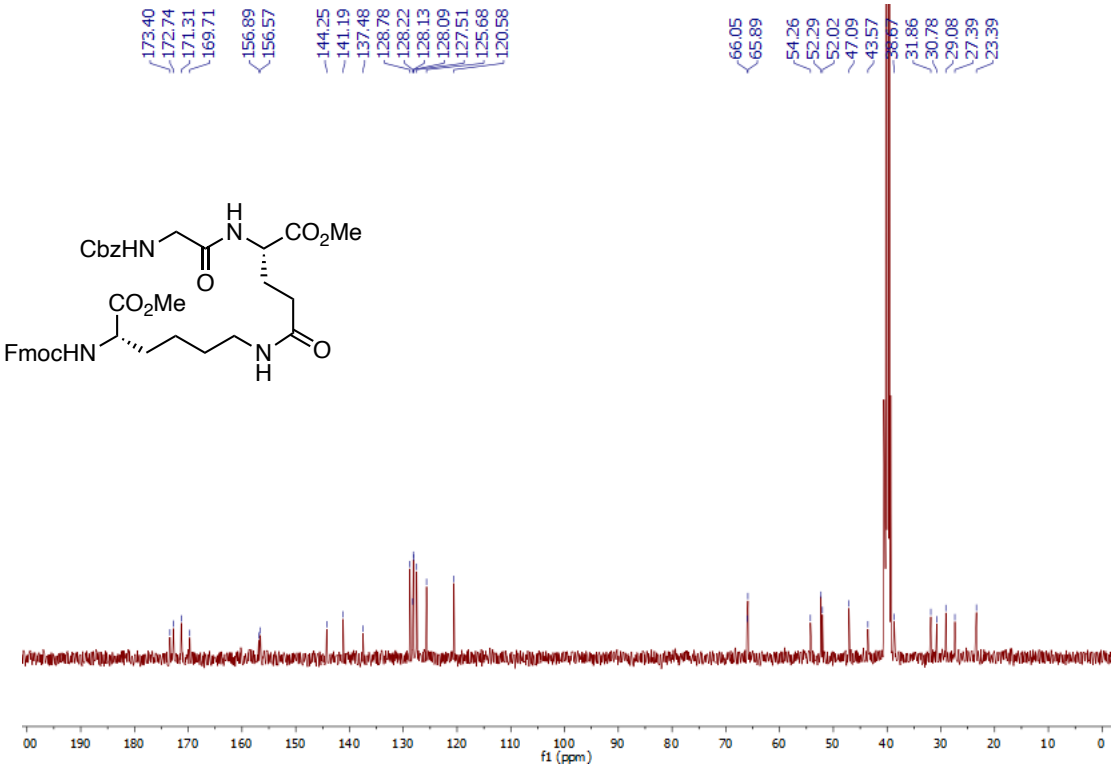
^{13}C NMR for **7** in $CDCl_3$, 101 MHz



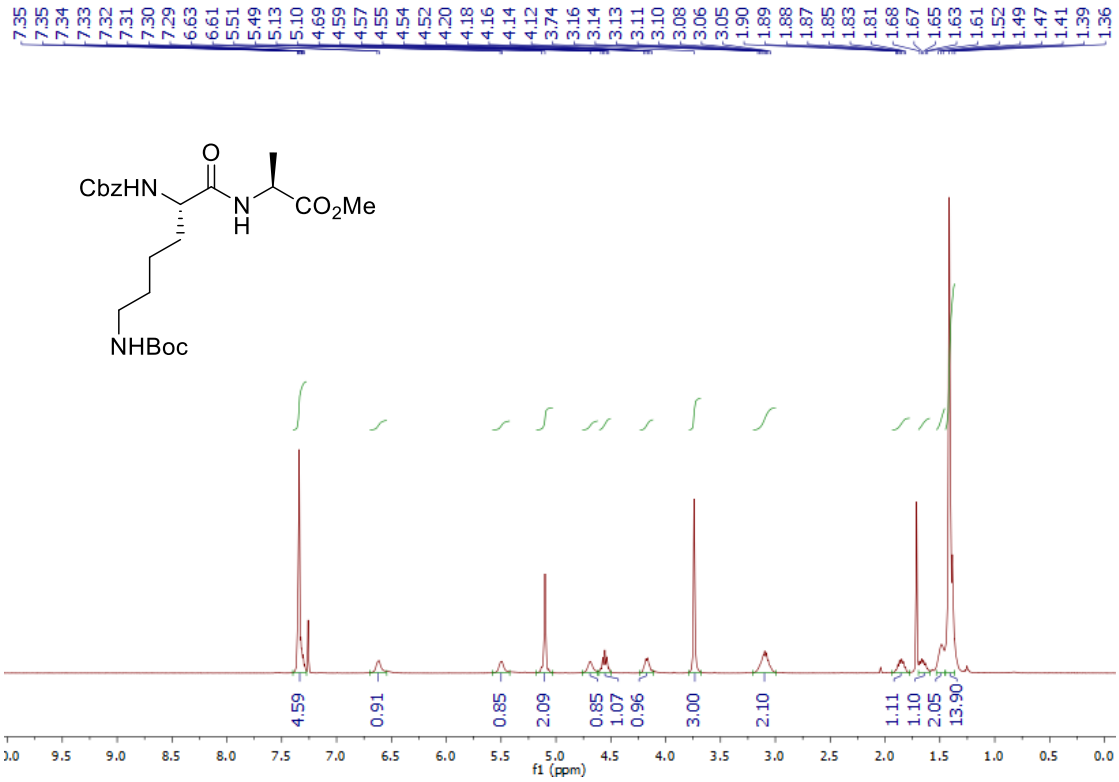
^{1}H NMR of **9** in DMSO-d6, 400 MHz



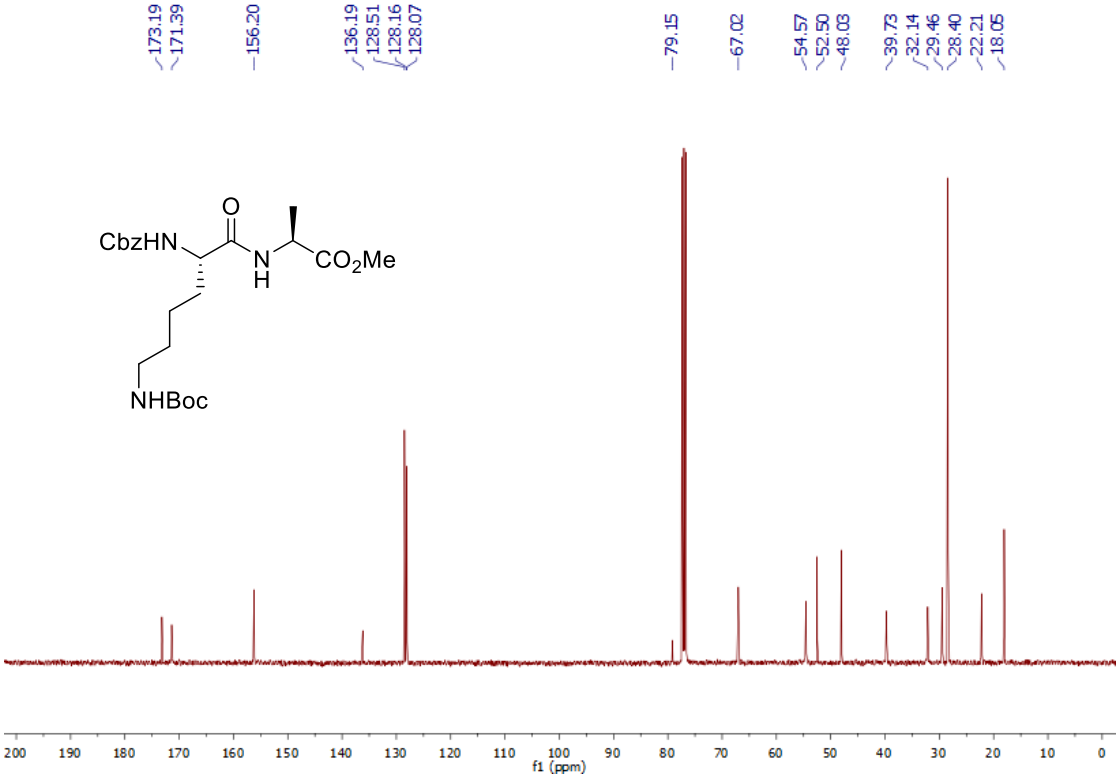
^{13}C NMR of **9** in DMSO-*d6*, 101 MHz



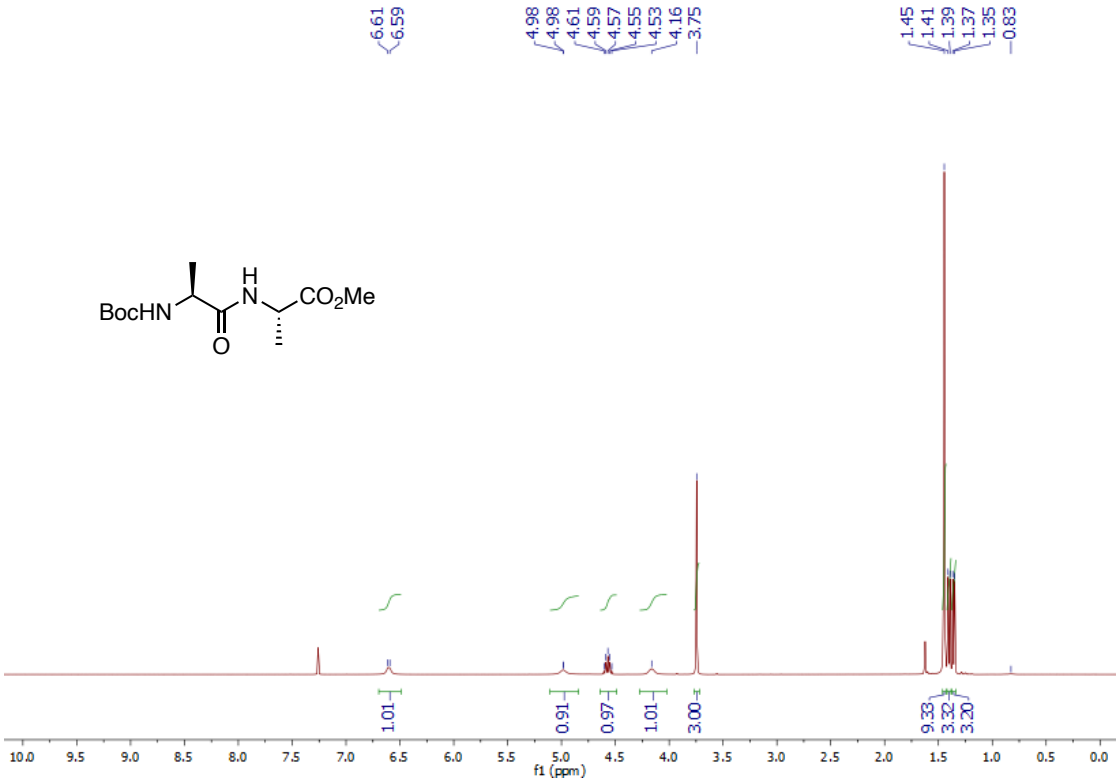
^{1}HNMR of **S6** in $CDCl_3$, 400 MHz



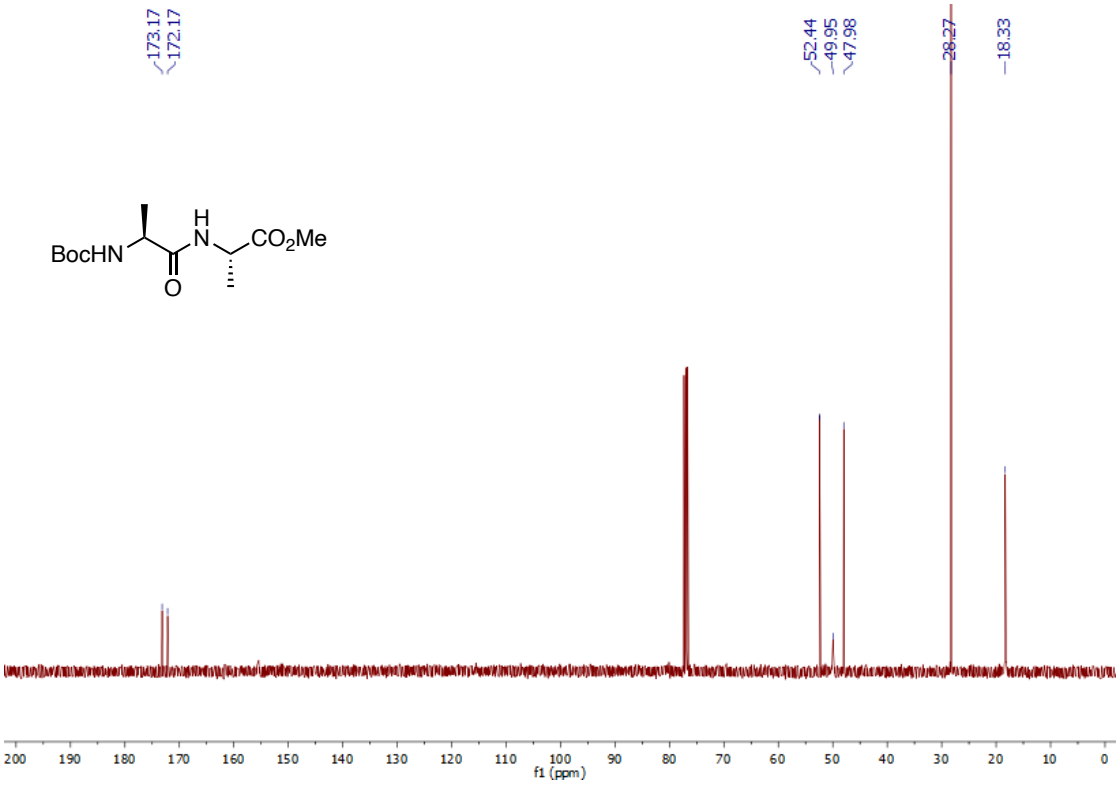
^{13}C NMR for **S6** in $CDCl_3$, 101 MHz



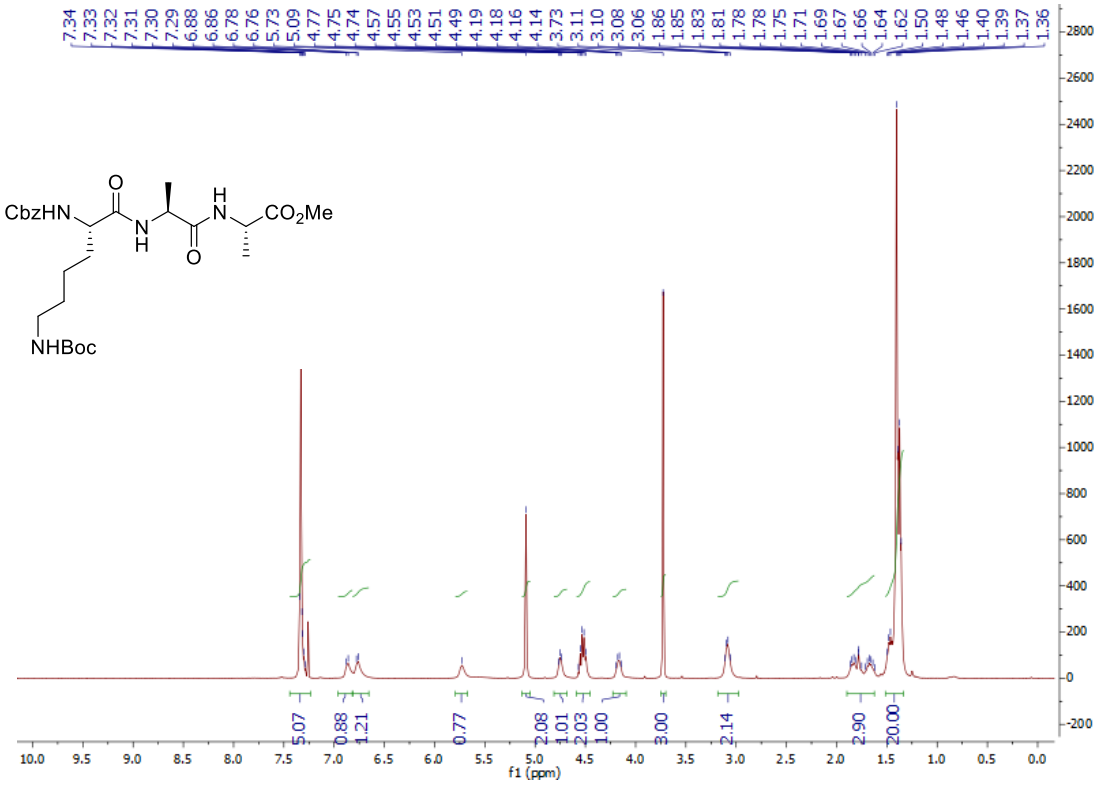
^{1}H NMR of **S7** in $CDCl_3$, 400 MHz



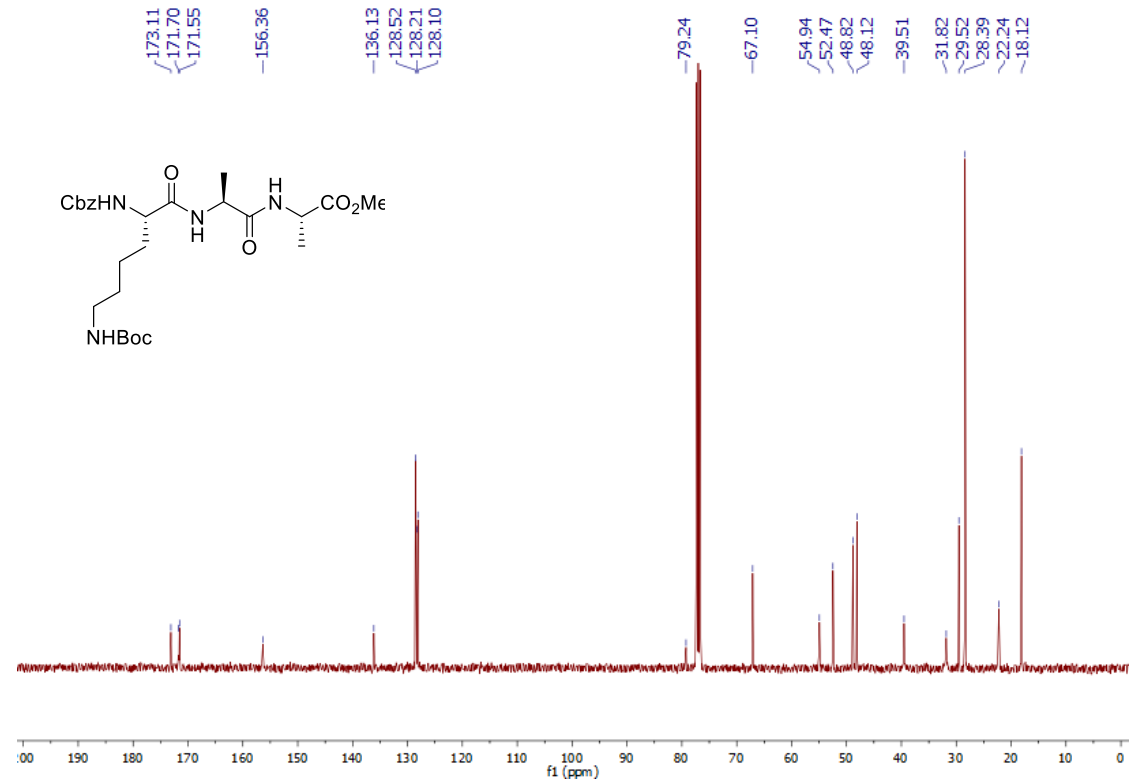
^{13}CNMR for **S7** in $CDCl_3$, 101 MHz



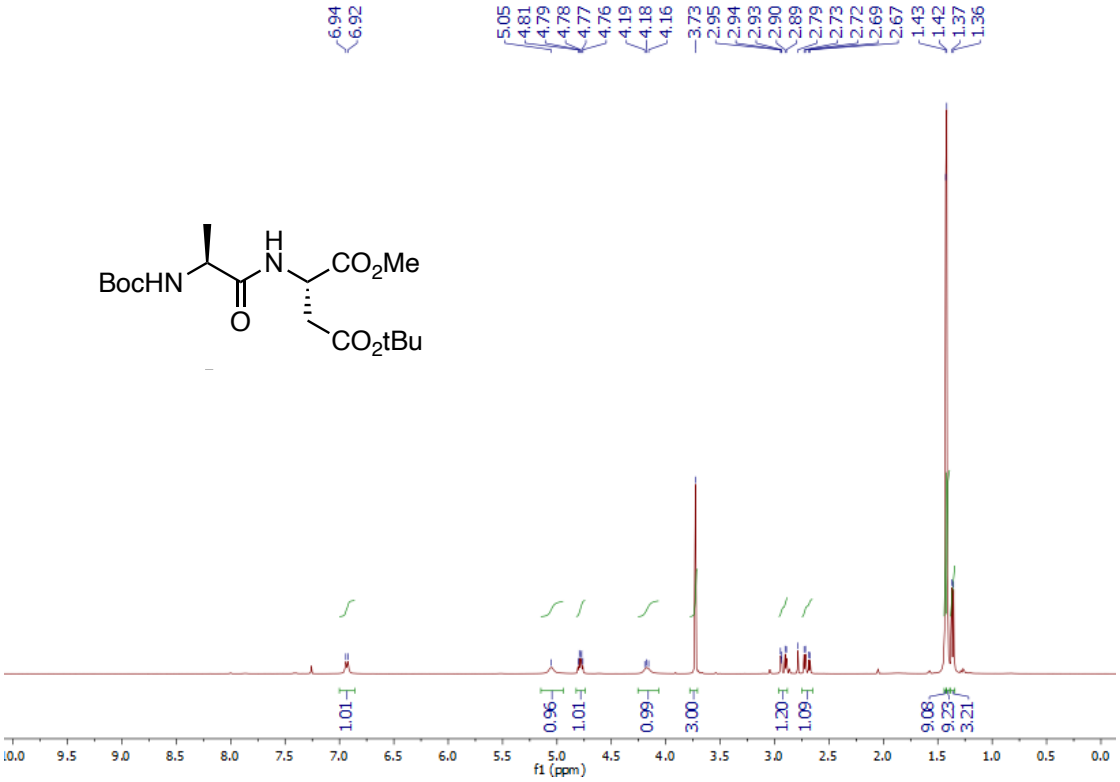
^{1}H NMR of **S9** in $CDCl_3$, 400 MHz



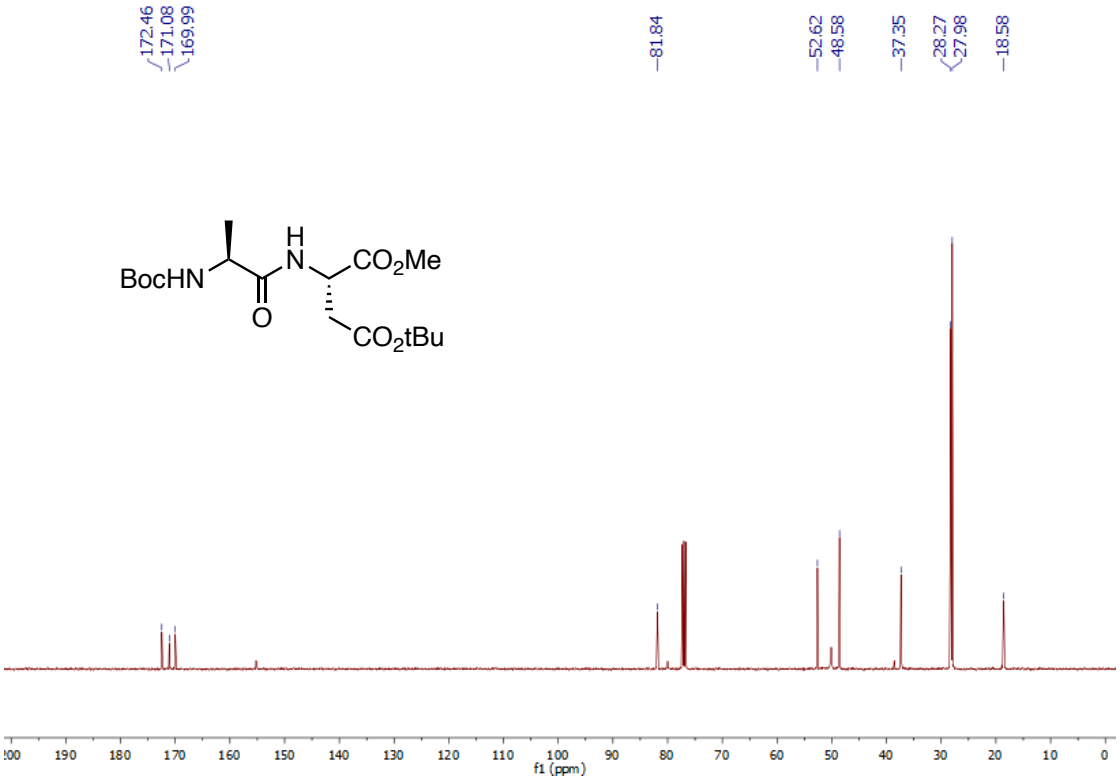
^{13}C NMR of **S9** in $CDCl_3$, 400 MHz



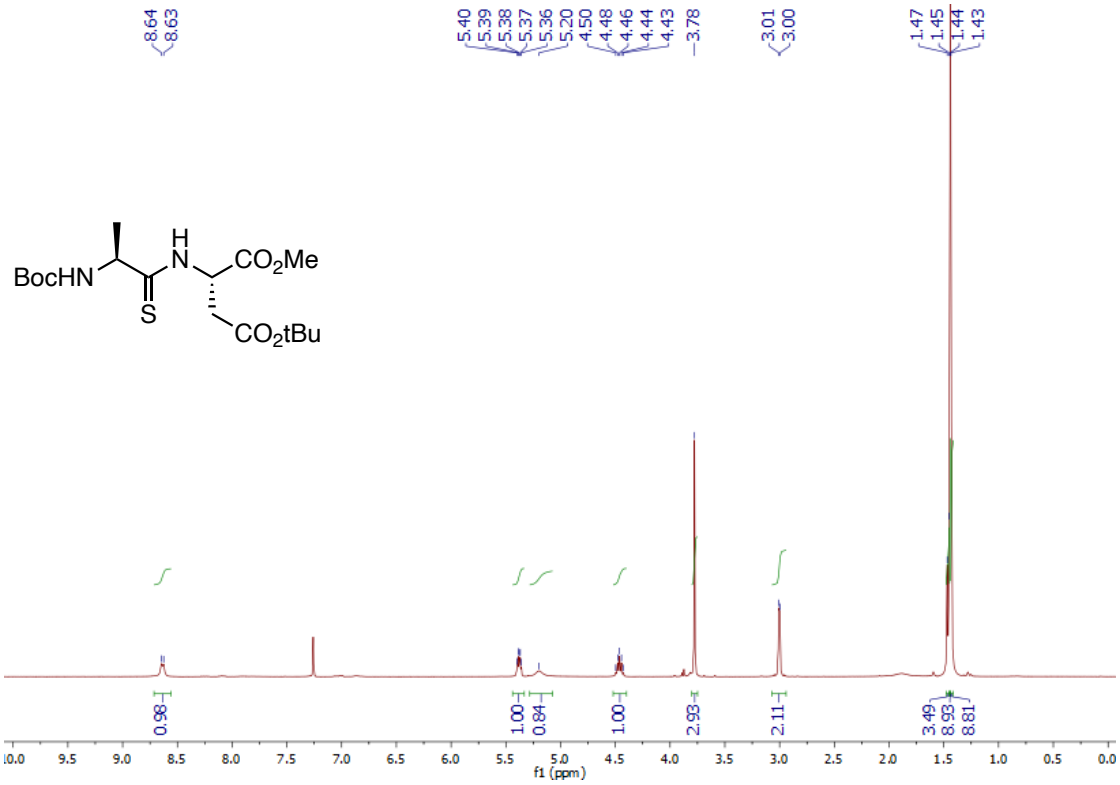
^{1}H NMR of **S10** in $CDCl_3$, 400 MHz



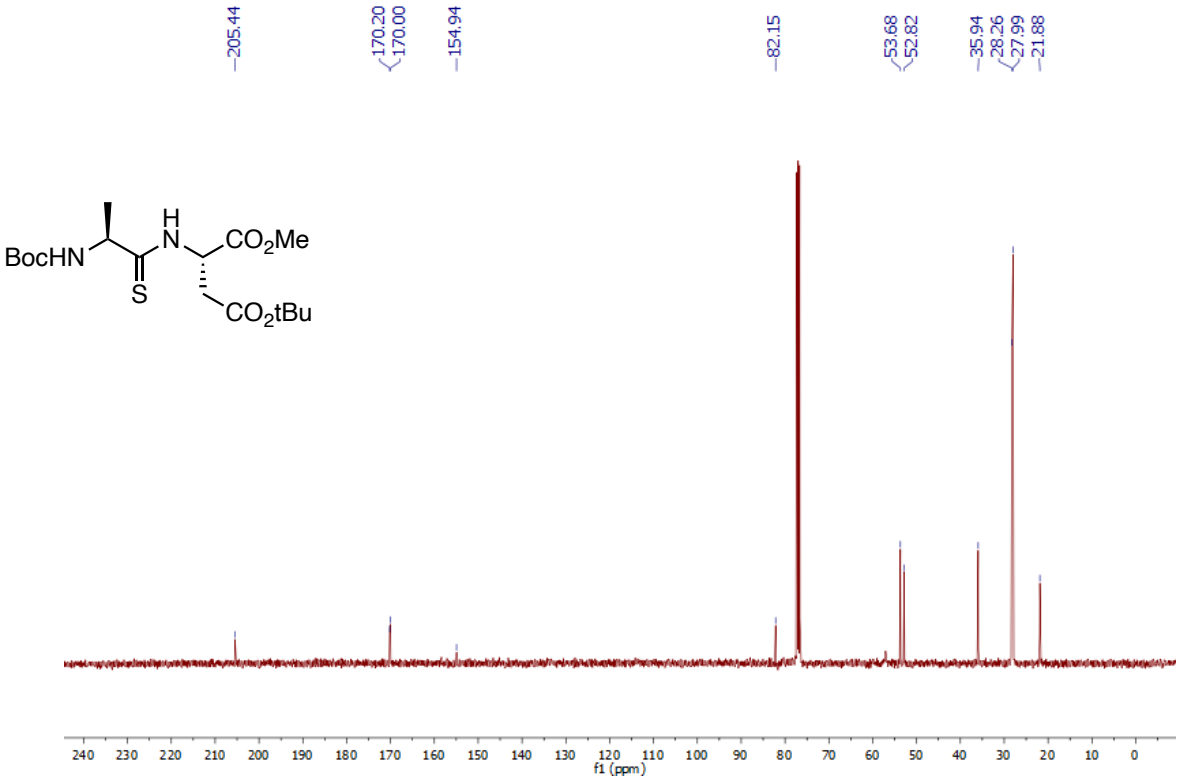
^{13}C NMR of **S10** in $CDCl_3$, 101 MHz



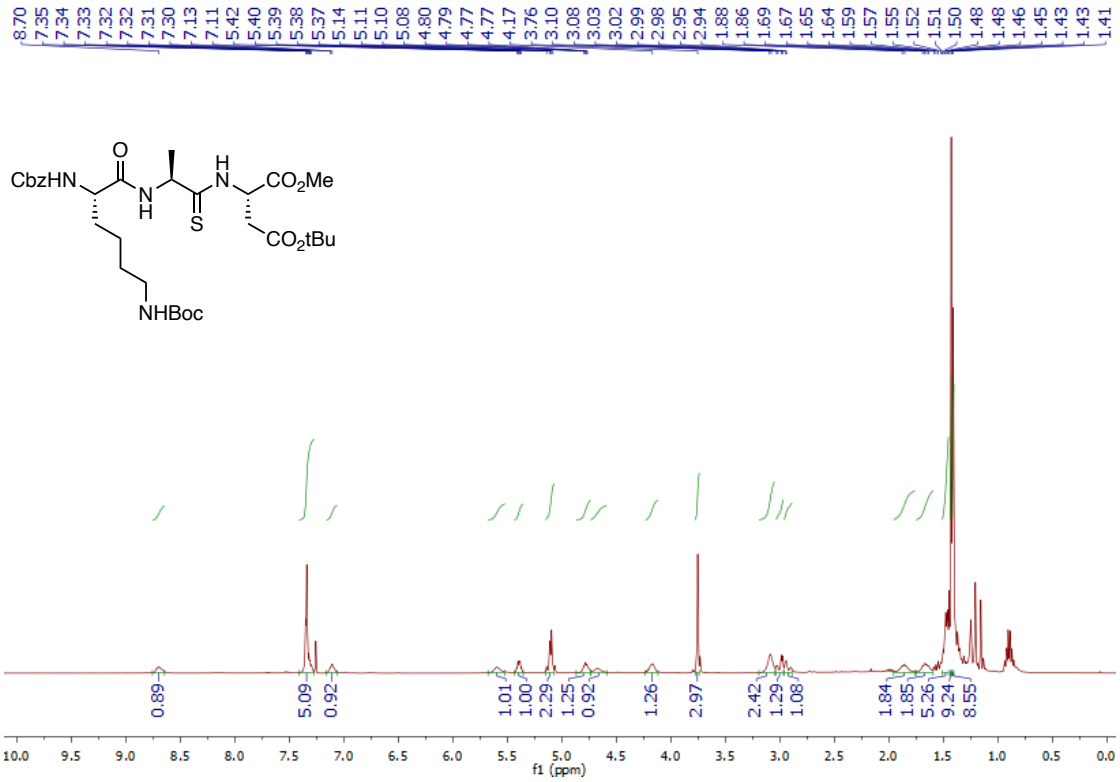
^{1}H NMR of **S11** in $CDCl_3$, 400 MHz



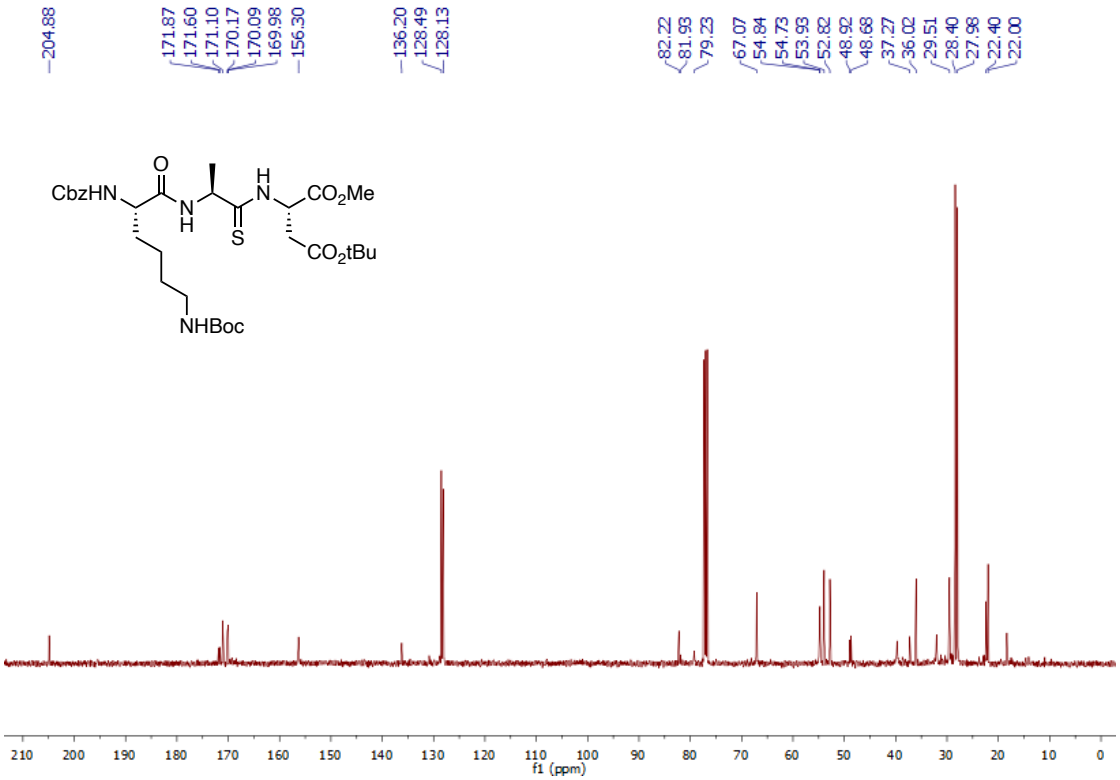
^{13}C NMR of **S11** in $CDCl_3$, 101 MHz



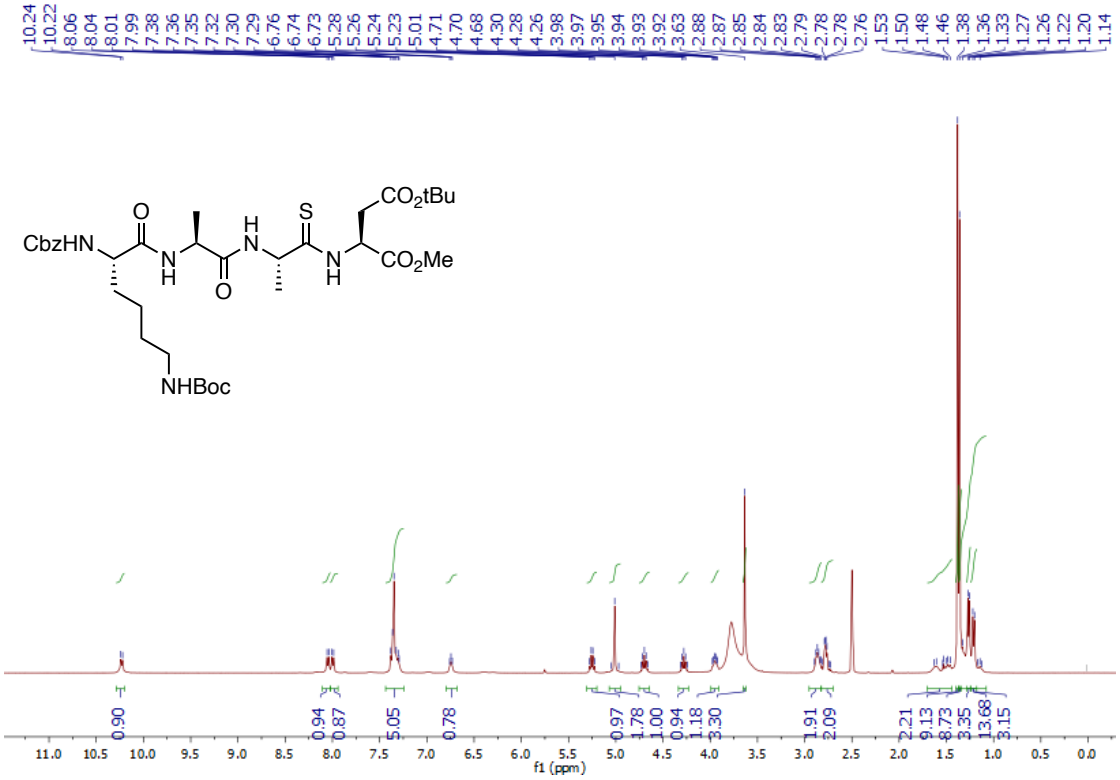
^{1}H NMR of **12a** in $CDCl_3$, 400 MHz



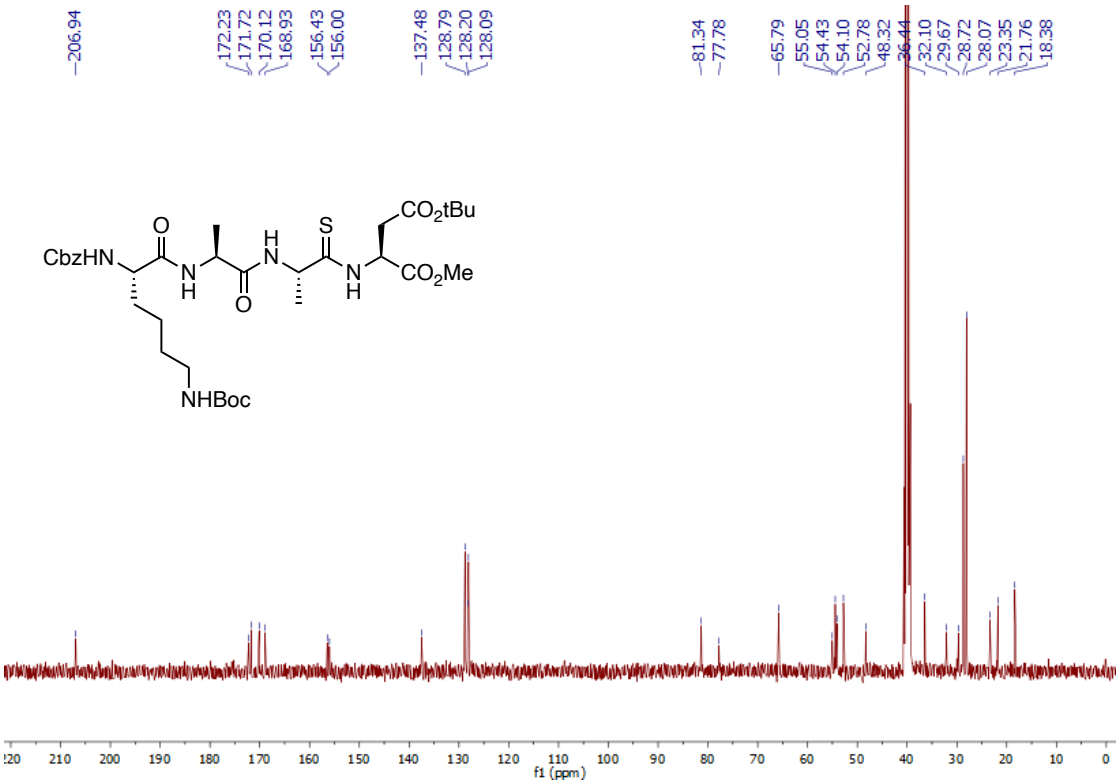
^{13}C NMR of **12a** in $CDCl_3$, 101 MHz



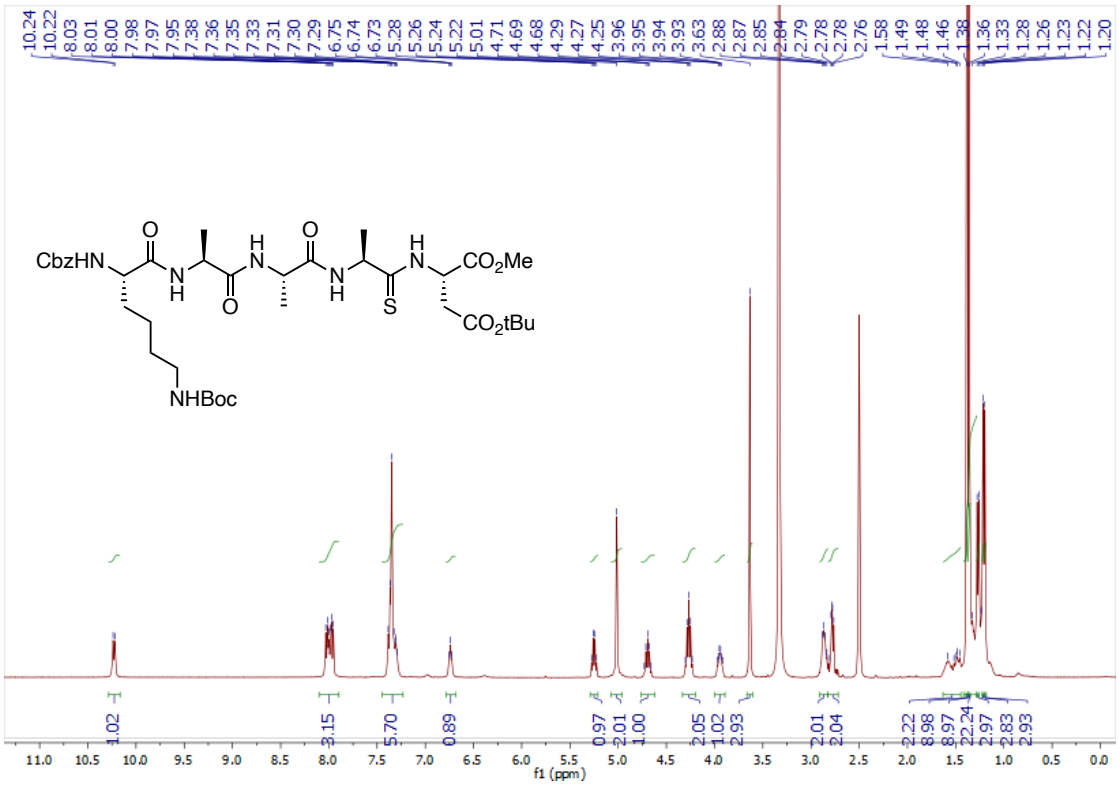
^{1}H NMR of **12b** in DMSO-*d6*, 400 MHz



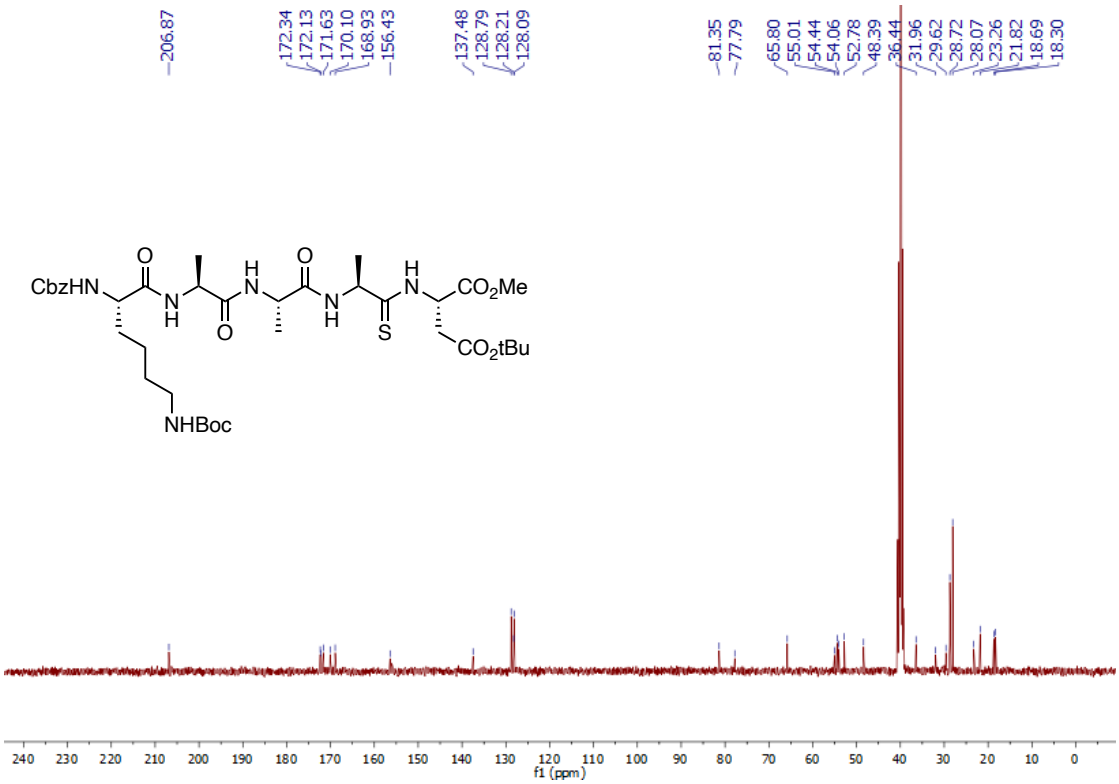
^{13}C NMR for **12b** in DMSO-*d6*, 101 MHz



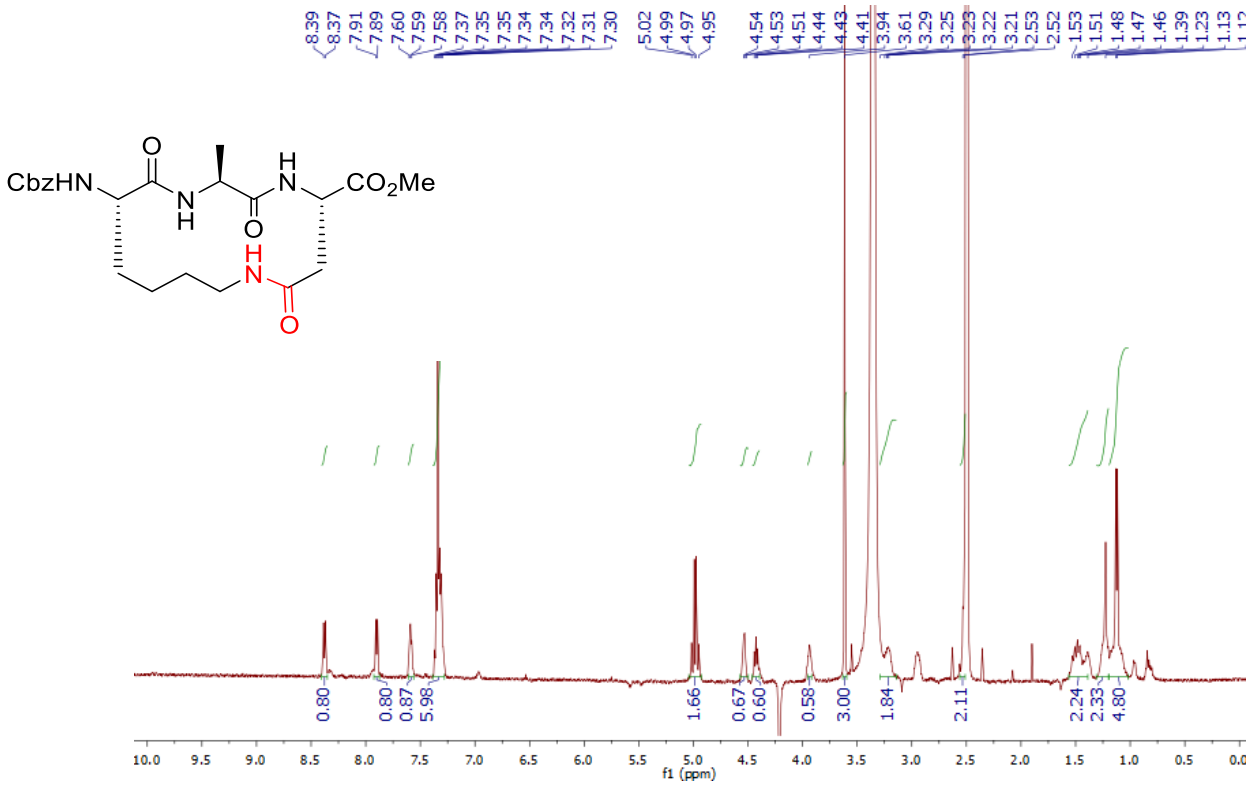
^{1}H NMR of **12c** in DMSO-*d6*, 400 MHz



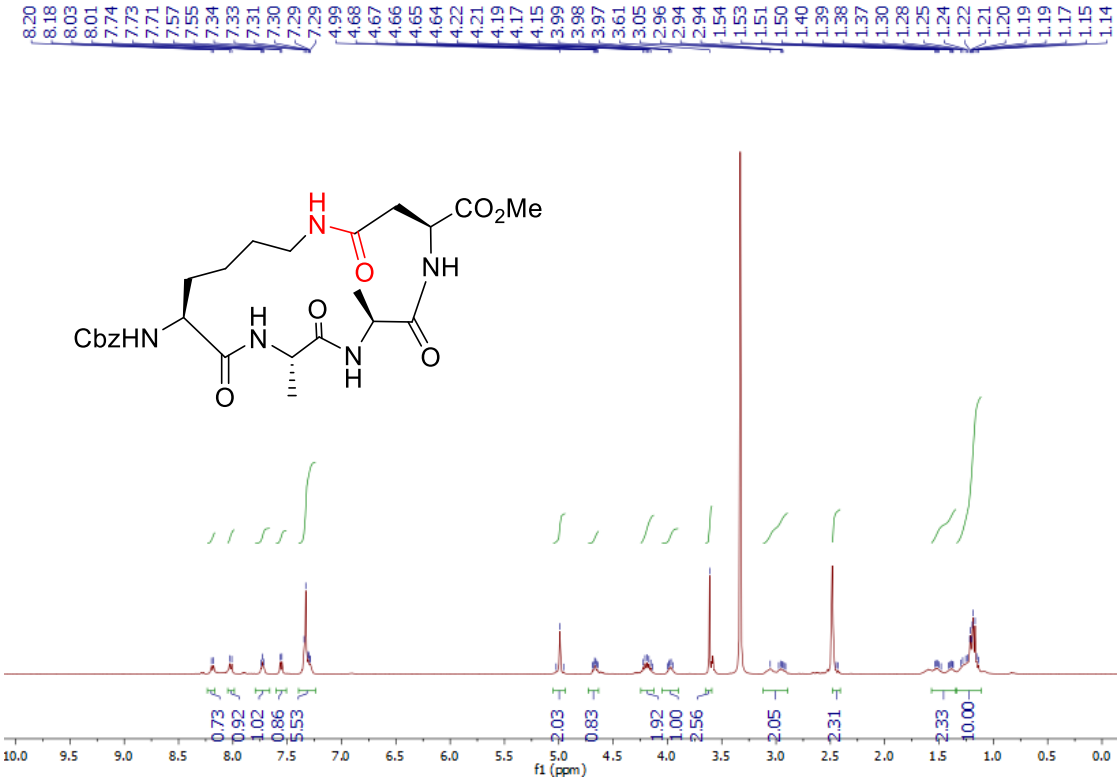
^{13}C NMR of **12c** in DMSO-*d6*, 101 MHz



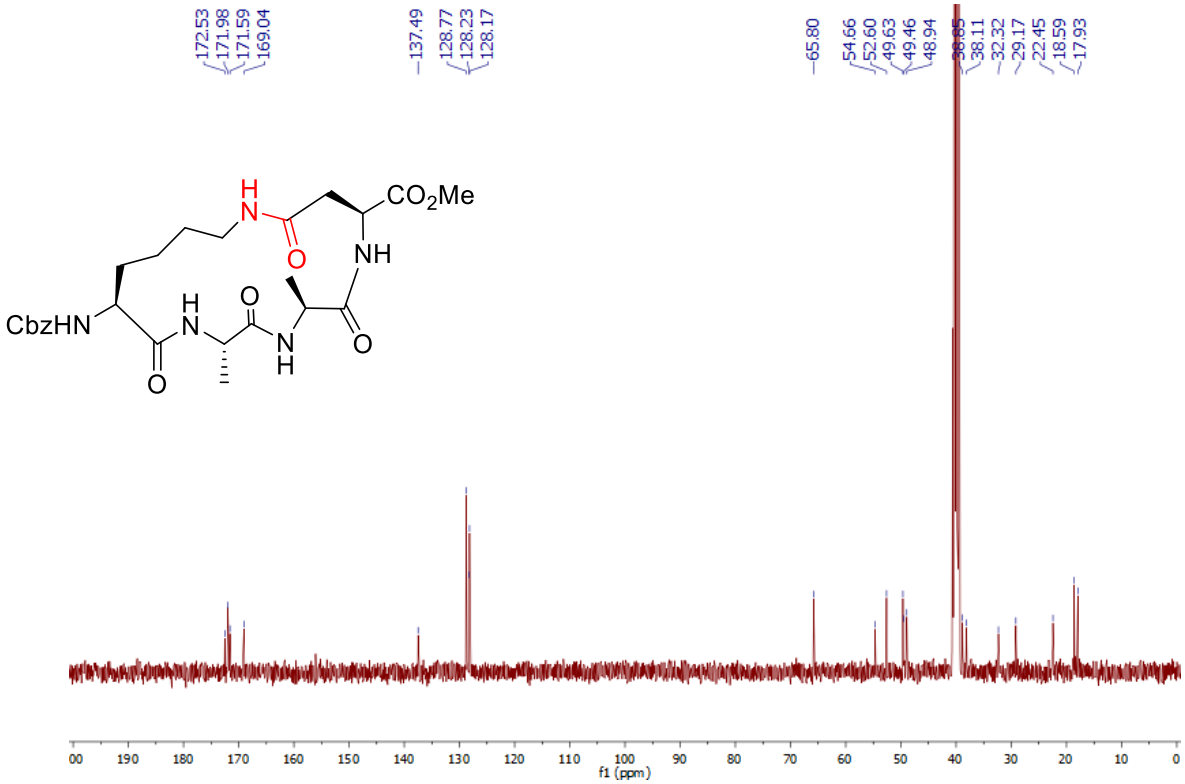
^{1}H NMR of **14a** in DMSO-*d6*, 400 MHz



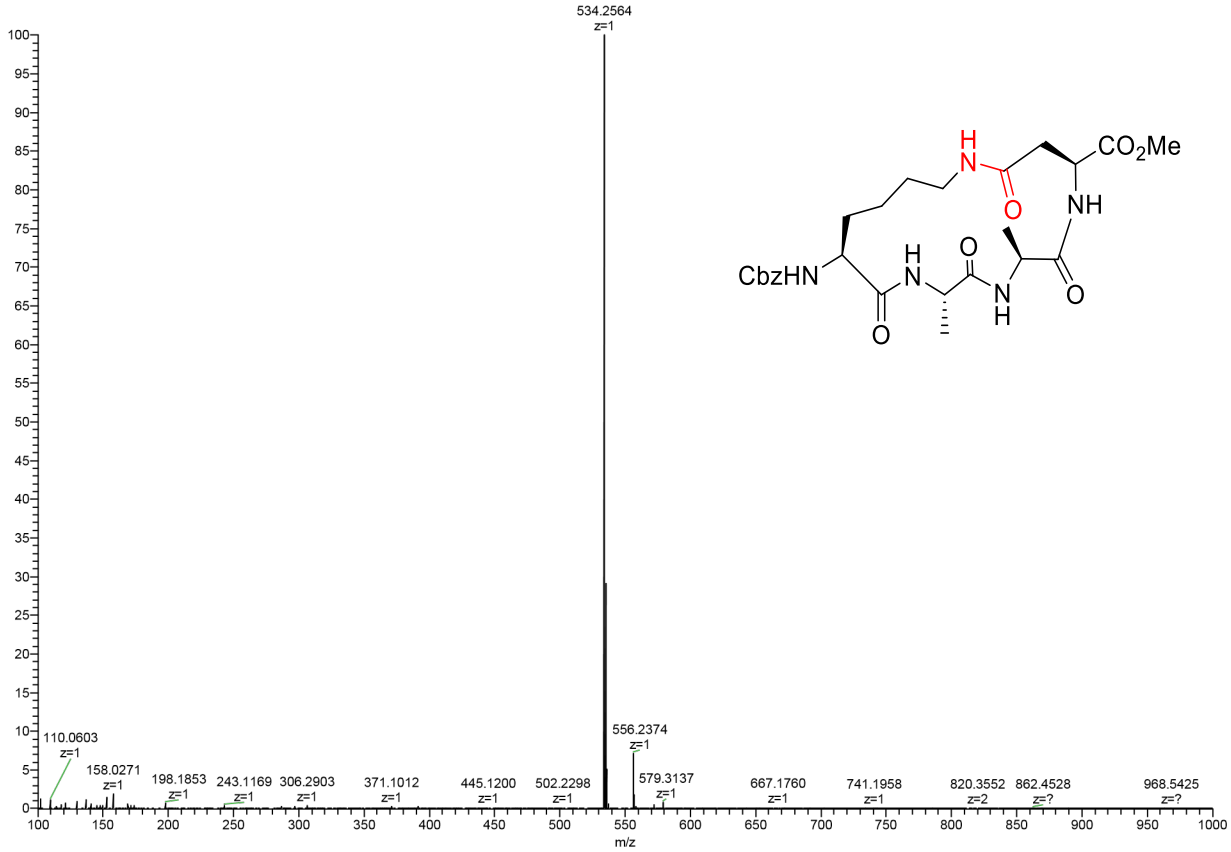
^{1}H NMR of **14b** in DMSO-*d6*, 400 MHz



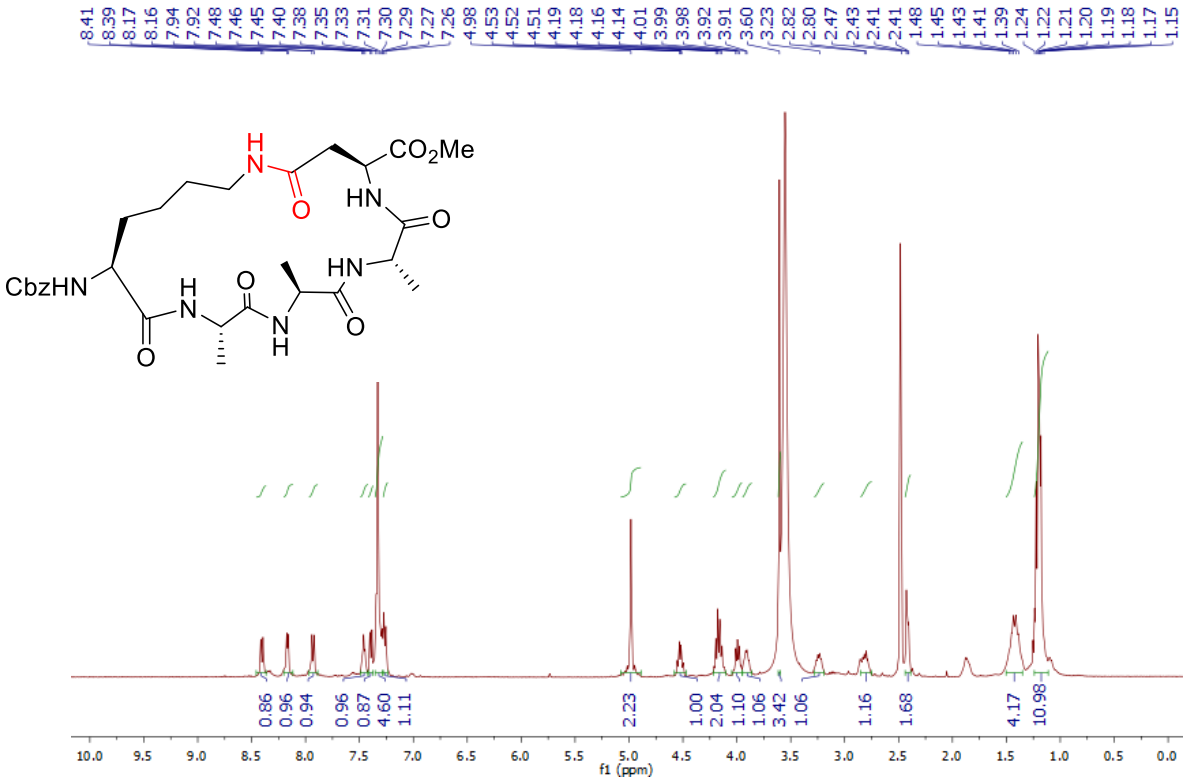
^{13}C NMR of **14b** in DMSO-*d6*, 101 MHz



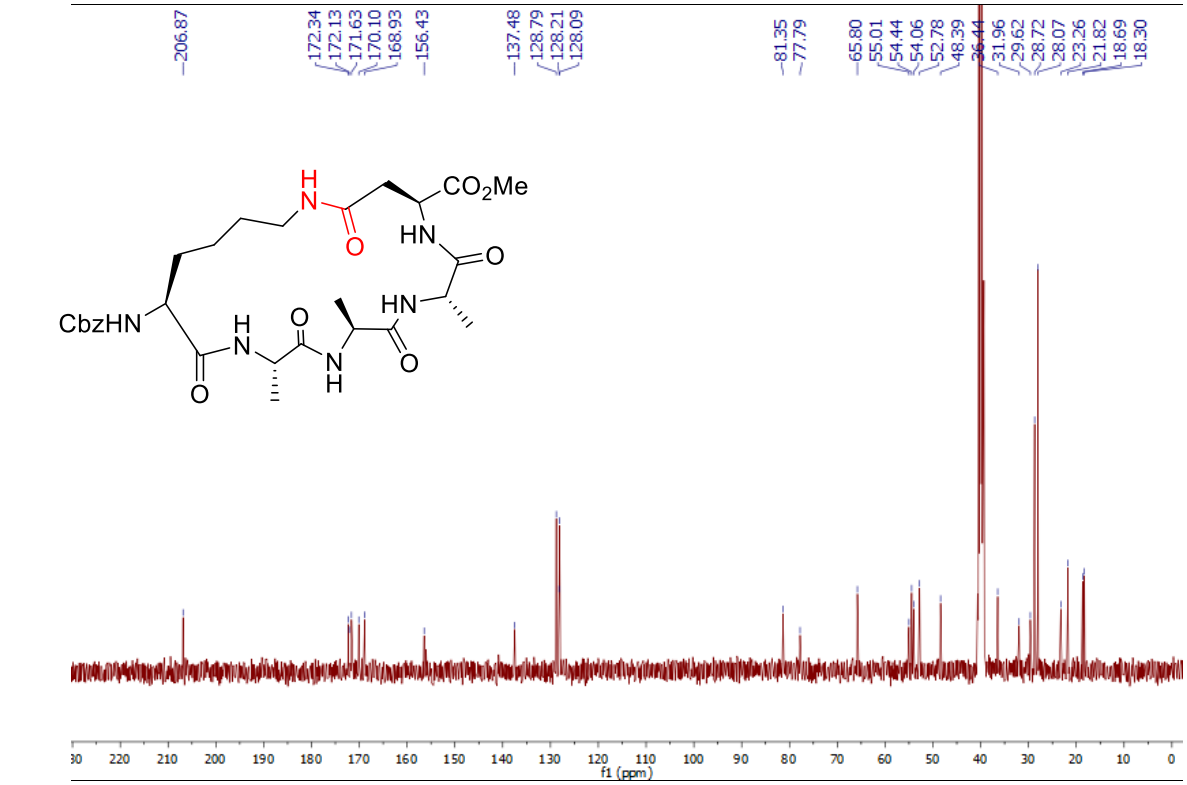
Mass spectrum of **14b**



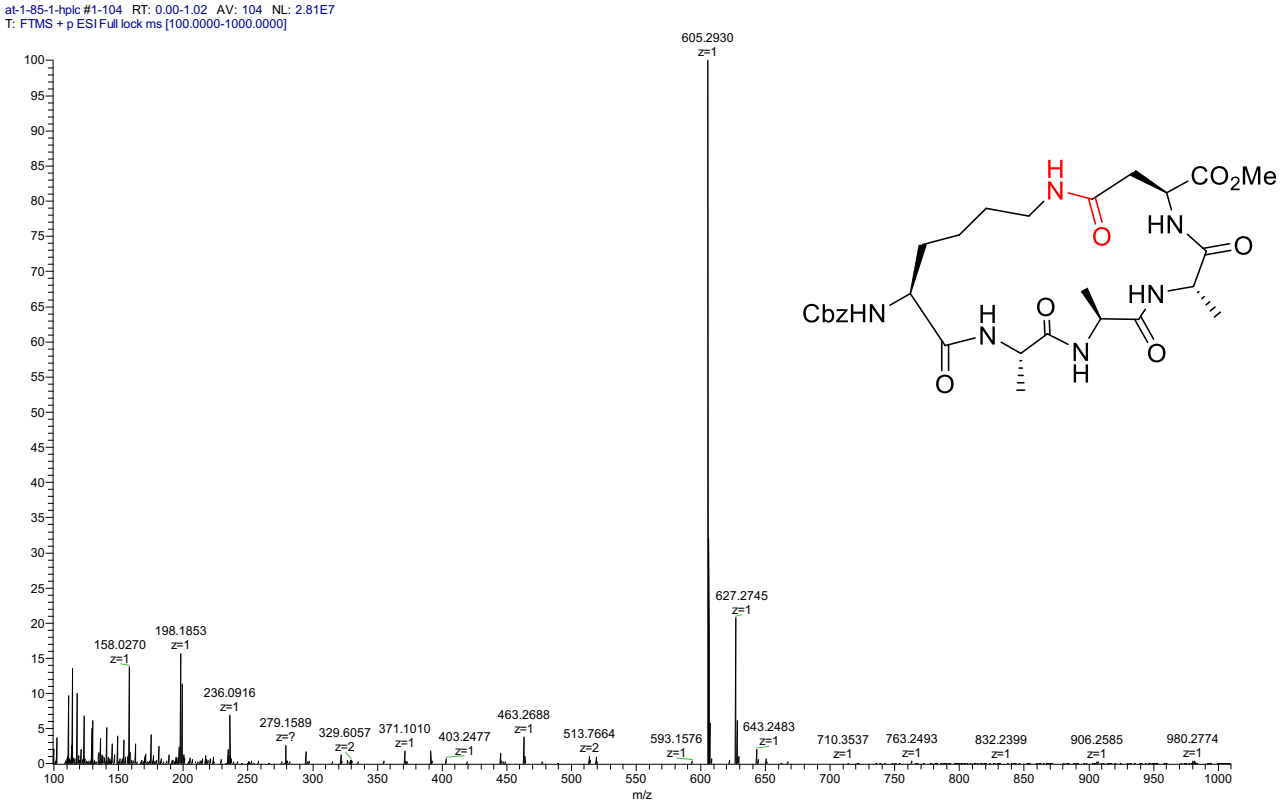
^{1}H NMR of **14c** in DMSO-*d6*, 400 MHz



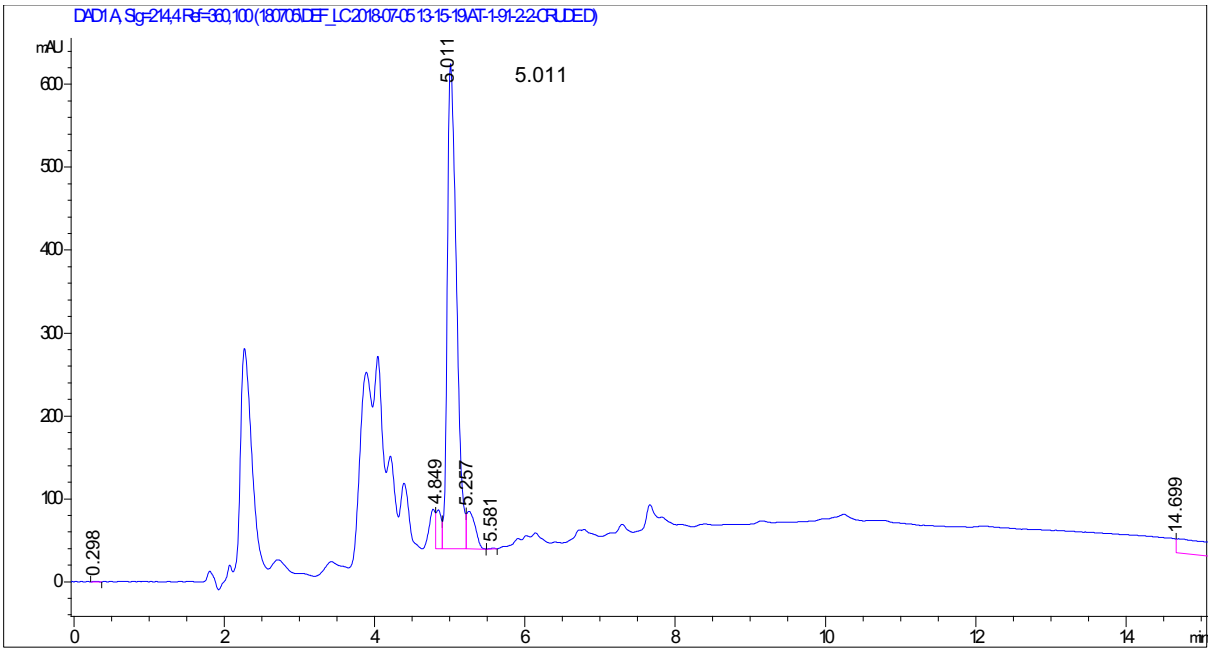
^{13}C NMR of **14c** in DMSO-*d6*, 101 MHz



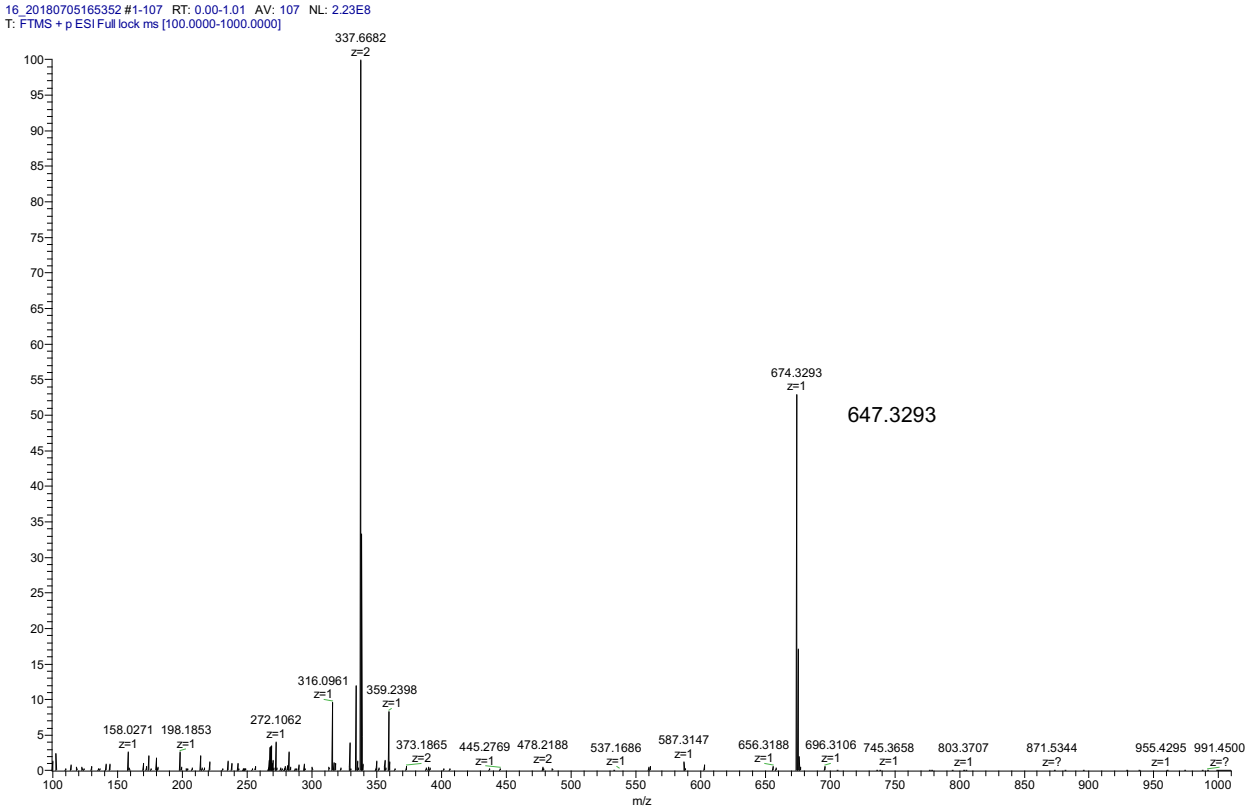
Mass spectrum of **14c**



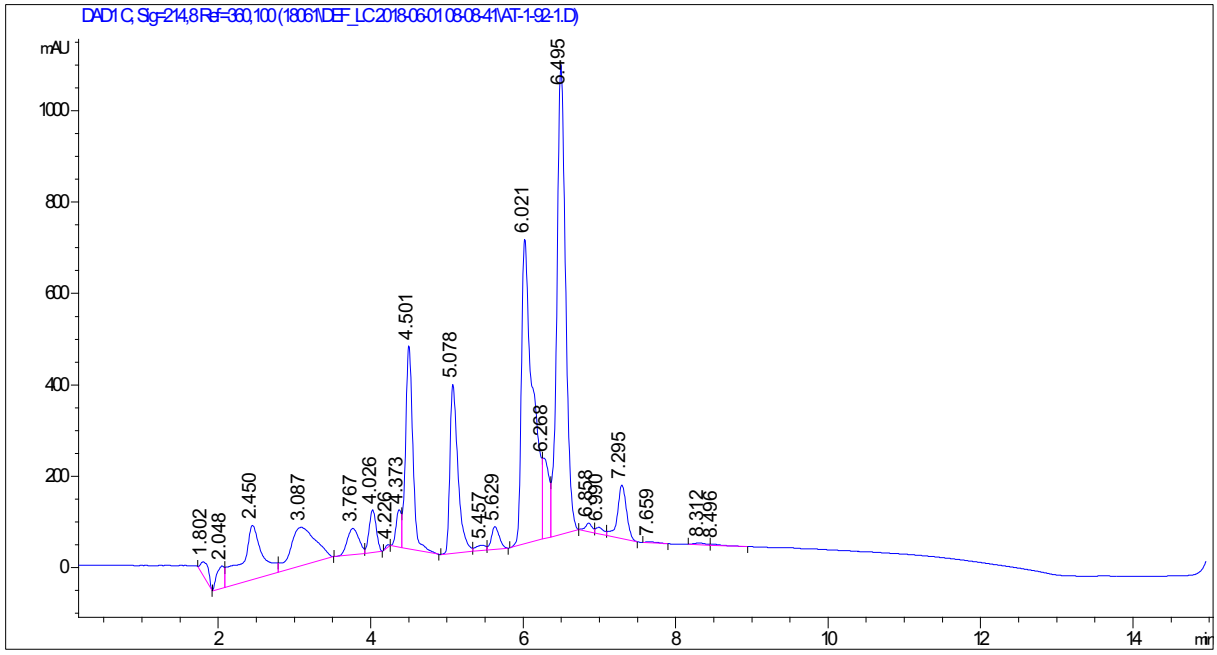
HPLC trace of crude peptide thioamide **19**



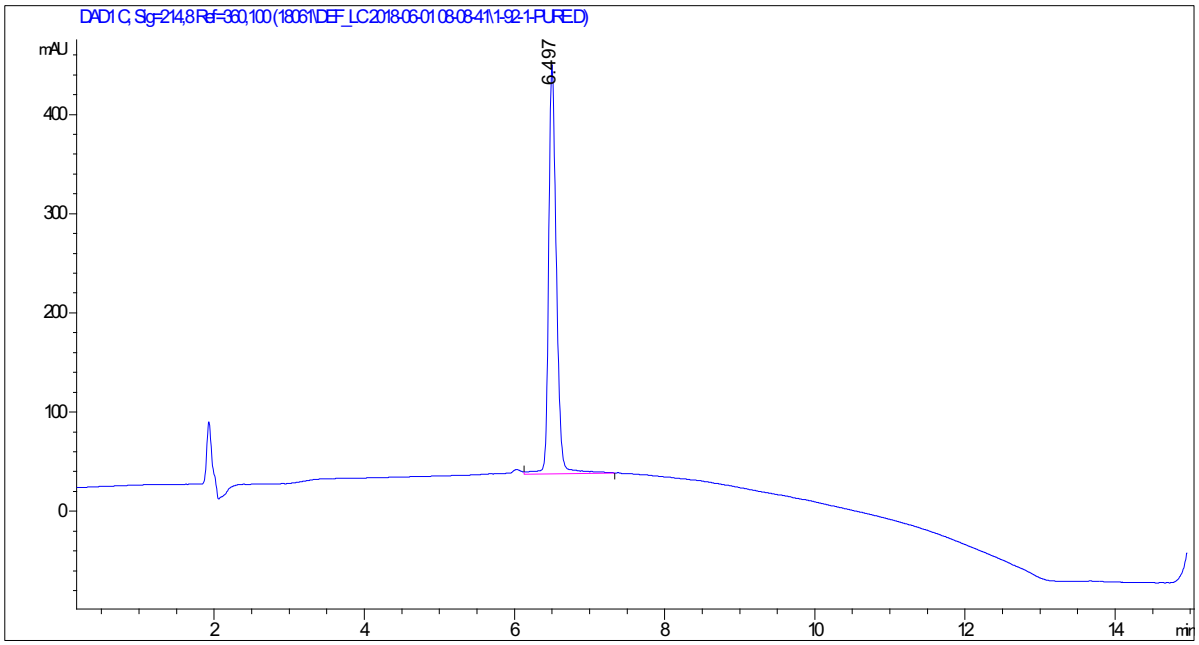
Mass spectrum of crude peptide thioamide **19**



HPLC trace of the crude cyclised peptide **20**



HPLC trace of purified cyclised peptide **20**



Mass spectrum of **20**