SUPPORTING INFORMATION

The Greening of Peptide Synthesis.

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A dataset of the spectra recorded during the course of this project can be downloaded from:

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General experimental procedures

Instrumentation

All experiments were carried out under an atmosphere of N_2. Analytical TLC was performed on aluminum backed plates pre-coated (0.25 mm) with Merck KGaA silica Gel 60 F_{254}. Compounds were visualized by exposure to UV light and stained using potassium permanganate solution ($KMnO_4$) followed by heating. Flash column chromatography was performed using Flurochem Silica Gel LC60A (40-60 μM). All solvent mixtures are reported as v/v solutions. All reagents were purchased from either Sigma Aldrich or Fluorochem and were used as received unless otherwise stated. Propylene carbonate and DMF were reagent grade (99%) and were used without additional purification. PE refers to the fraction of petroleum ether boiling between 40 and 60 °C. All amino acid derivatives have *S*-configuration unless stated otherwise.

^{1}H- and ^{13}C-NMR spectra were obtained using a JEOL ECS 400 MHz spectrometer at ambient temperature (unless specified otherwise). Both ^{1}H and ^{13}C spectra were referenced to the residual protic solvent ($CHCl_3$ = 7.26 ppm, CH_3OH = 4.78 ppm, $(CH_3)_2SO$ = 2.50 ppm). Coupling constants are reported using the following notation or combination of: s = singlet, br= broad, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, sept = septet, oct = octet, non = nonet, m = multiplet). Assignment of signals in ^{1}H and ^{13}C spectra were performed using ^{1}H-^{1}H COSY, DEPT-135 and ^{1}H-^{13}C HSQC, where appropriate.

High resolution mass spectra (HRMS) were recorded using ESI, on a Bruker micrOTOF MS in tandem with an Agilent series 1200 LC system. All IR data was obtained using a Perkin Elmer Spectrum Two FT-IR spectrometer. Optical rotations were obtained using a Jasco DIB370 digital polarimeter, all concentrations are given in g/100 mL. Melting points were determined with a Stuart SMP3 melting point apparatus and are uncorrected.

Chiral normal phase HPLC was performed using a Daicel Chiralcel OD column (4.6 × 250 mm × 5 μm) fitted with a Chiralpak 1A (5 μm) guard column (4 × 10 mm) and monitored using a DAD on an Agilent Infinity 1220 LC system equipped with Agilent OpenLab software. Flow rate: 0.7 mL min^{-1}, 97:3 Hexane: i-PrOH, detection at 210 and 254 nm.

Bradykinin samples were analysed on the Bruker microTOF mass spectrometer in tandem with an Agilent series 1200 LC system with an additional diode array detector. Chromatography was carried out at 40 ^{o}C on a Waters Sunfire C18 column (3.5 μm packing, 2.1 mm x 100 mm) with a solvent flow rate of 0.2 mL min^{-1} and UV detection at 214 nm. A dual solvent system was employed:

Solvent A: MeCN + 0.1% formic acid

Solvent B: water + 0.1% formic acid

The solvent system was varied following the sequence: 10% A / 90% B for 5 minutes, then ramp to 50% A / 50% B over the next 10 minutes, hold at 50% A / 50% B for 5 minutes then ramp back to 10% A / 90% B. The times given in Figure 1 and page 94-96 of the supplementary information are delayed by 5 minutes due to the time taken for the solvent to pass through the pumps, column, mass spectrometer and UV-vis detector.

Microwave reactions were carried out in a G10 microwave vial equipped with a rare Earth stirrer bar, using an Anton Paar Monowave 300 microwave reactor. The temperature was held at 70 °C (monitored using a ruby thermometer) for the duration of the reaction.

Characterizing data for compounds 5-11

Boc-Ala-Phe-OBn **5a**[S1]

Boc-Ala-OH (324 mg, 1.71 mmol) and HCl.H-Phe-OBn (500 mg, 1.71 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (35:65, EtOAc:PE) to give Boc-Ala-Phe-OBn **5a** as a white crystalline solid (682 mg, 93%). R_F = 0.34 (40:60, EtOAc:PE); mp 95.6-96.3 °C; $[\alpha]_D^{23}$ -27.7 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3347 (m), 3063 (w), 3029 (w), 2928 (m), 2852 (w), 1735 (w), 1684 (w) 1666 (w) and 1521 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36-7.31 (m, 3H, ArH), 7.29-7.24 (m, 2H, ArH), 7.26-7.21 (m, 3H, ArH), 7.04-6.97 (m, 2H, ArH), 6.72 (d *J* 7.7 Hz, 1H, Phe-NH), 5.16-5.10 (m, 1H, Ala-NH), 5.13 (d *J* 12.1 Hz, 1H, OCH_2Ph), 5.07 (d *J* 12.1 Hz, 1H, OCH_2Ph), 4.88 (dt, *J* 7.7, 5.9 1H, Phe-NCH), 4.11 (br, 1H, Ala-NCH), 3.13 (dd *J* 13.9, 6.1 Hz, 1H, CH_2Ph), 3.08 (dd *J* 13.9, 6.1 Hz, 1H, CH_2Ph), 1.41 (s, 9H, $C(CH_3)_3$), 1.29 (d *J* 6.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C=O), 171.2 (C=O), 155.6 (NC=O), 135.7 (ArC), 135.1 (ArC), 129.5 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 127.2 (ArCH), 80.2 (CMe_3), 67.4 (OCH_2Ph), 53.3 (Phe-NCH), 50.3 (Ala-NCH), 38.0 (CH_2Ph), 28.4 ($C(CH_3)_3$), 18.5 (CH_3); MS (ESI) m/z 449 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{24}H_{30}N_2O_5Na$ 449.2048 $(M+Na)^+$, found 449.2047 (0.6 ppm error).

Boc-(R)-Ala-Phe-OBn **5a'**

Boc-(*R*)-Ala-OH (164 mg, 0.87 mmol) and HCl.H-Phe-OBn (250 mg, 0.87 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (40:60, EtOAc:PE) to give Boc-(R)-Ala-Phe-OBn **5a'** as an off-white solid (323 mg, 87%). R_F = 0.38, (40:60, EtOAc:PE); mp 75.4-76.2 °C; $[\alpha]_D^{23}$ 6.5 (*c* 1.0 in MeOH); IR (Neat) ν_{max}3294 (m), 3066 (w), 3030 (w), 2977 (m), 2930 (m), 1717 (m), 1687 (m) and 1648 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.32 (m, 3H, ArH), 7.32-7.27 (m, 2H, ArH), 7.25-7.16 (m, 3H, ArH), 7.06-6.98 (m, 2H, ArH), 6.80 (br, 1H, Phe-NH), 5.15 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.11 (br, 1H, Ala-NH), 5.08 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.90 (dt *J* 7.7, 6.2 Hz, 1H, Phe-NCH), 4.20 (br, 1H,

Ala-NCH), 3.13 (dd *J* 13.9, 6.0 Hz, 1H, CH_2Ph), 3.07 (dd *J* 13.9, 6.0 Hz, 1H, CH_2Ph), 1.42 (s, 9H, $C(CH_3)_3$), 1.27 (d *J* 7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C=O), 171.3 (C=O), 155.6 (NC=O), 135.7 (ArC), 135.2 (ArC), 129.4 (ArCH), 128.8 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 127.2 (ArCH), 80.3 (CMe_3), 67.4 (OCH_2Ph), 53.2 (Phe-NCH), 50.1 (Ala-NCH), 38.0 (CH_2Ph), 28.4 ($C(CH_3)_3$), 18.5 (CH_3); MS (ESI) m/z 449 [$(M+Na)^+$, 20], 427 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{24}H_{31}N_2O_5$ 427.2155 $(M+H)^+$, found 427.2227 (-0.3 ppm error).

Boc-Leu-Phe-OBn **5b**[S2]

Boc-Leu-OH (100 mg, 0.43 mmol) and $HCl.H_2N$-Phe-OBn (110 mg, 0.43 mmol) and were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (40:60, EtOAc:PE) to give Boc-Leu-Phe-OBn **5b** as a white powder (162 mg, 80%). R_F = 0.42 (30:70, EtOAc:PE); mp 100.8-102.1 °C (lit.[S2] 103–105 °C); $[\alpha]_D^{23}$ -27.4 (*c* 1.0 in MeOH) [lit.[S2] -33.8 (*c* 1.0 in MeOH)]; IR (Neat) ν_{max} 3339 (m), 3064 (w), 3034 (w), 2956 (w), 2935 (w), 2879 (w), 1731 (s), 1679 (m), 1665 (s) and 1518 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.34 (m, 3H, ArH), 7.29-7.26 (m, 2H, ArH), 7.22-7.19 (m, 3H, ArH), 7.03-7.01 (m, 2H, ArH), 6.53 (d *J* 7.6 Hz, 1H, Phe-NH), 5.15 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.10 (d *J* 12.0 Hz, 1H, OCH_2Ph), 4.88 (dt *J* 7.7, 6.0 Hz, 1H, Phe-NCH), 4.86 (br, 1H, Leu-NH), 4.08 (br, 1H, Leu-NCH), 3.14 (dd *J* 14.0, 6.4 Hz, 1H, CH_2Ph), 3.09 (dd *J* 14.0, 6.4 Hz, 1H, CH_2Ph), 1.68-1.58 (m, 2H, CH_2CHMe_2), 1.43 (s, 9H, $C(CH_3)_3$), 1.45-1.35 (m, 1H, $CH(Me)_2$), 0.90 (d *J* 6.4 Hz, 3H, $CH(CH_3)_2$), 0.89 (d *J* = 6.4 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C=O), 171.2 (C=O), 155.6 (NC=O), 135.7 (ArC), 135.1 (ArC), 129.5 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 127.2 (ArCH), 80.1 (CMe_3), 67.4 (OCH_2Ph), 53.3 (Phe-NCH), 53.2 (Leu-NCH), 41.4 (CH_2CHMe_2), 38.0 (CH_2Ph), 28.4 ($C(CH_3)_3$), 24.8 ($CHMe_2$), 23.0 ($CH(CH_3)_2$), 22.0 ($CH(CH_3)_2$); MS (ESI) m/z 491 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{27}H_{37}N_2O_5$ 469.2697 $(M+H)^+$, found 469.2691 (1.2 ppm error).

Boc-(*R*)-Leu-Phe-OBn **5b'**[S3]

Boc-(*R*)-Leu-OH (100 mg, 0.43 mmol) and HCl.H_2N-Phe-OBn (110 mg, 0.43 mmol) and were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (20:80-30:70, EtOAc:PE) to give Boc-(R)-Leu-Phe-OBn **5b'** as a white powder (187 mg, 92%). R_F = 0.48 (30:70, EtOAc:PE); mp 96.2-97.4 °C (lit.[S3] 97 °C); $[\alpha]_D^{23}$ +4.8 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3334 (m), 3064 (w), 3031 (w), 2961 (w), 1739 (m), 1726 (m), 1686 (m), 1652 (s) and 1519 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.34 (m, 3H, ArH), 7.31-7.28 (m, 2H, ArH), 7.22-7.19 (m, 3H, ArH), 7.04-7.00 (m, 2H, ArH), 6.61 (d *J* 6.4 Hz, 1H, Phe-NH), 5.17 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.10 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.89 (dt, *J* 7.9, 6.0 Hz, 1H, Phe-NCH), 4.78 (d *J* 6.8 Hz, 1H, Leu-NH), 4.17-4.05 (m, 1H, Leu-NCH), 3.13 (dd *J* 14.0, 6.0 Hz, 1H, CH_2Ph), 3.08 (dd, *J* 14.0, 6.4 Hz, 1H, CH_2Ph), 1.65-1.50 (m, 2H, CH_2CHMe$_2$), 1.42 (s, 9H, C(CH_3)$_3$), 1.41-1.30 (m, 1H, CH_2C*H*Me$_2$), 0.88 (d *J* 6.0 Hz, 6H, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C=O), 171.3 (C=O), 155.7 (NC=O), 135.7 (ArC), 135.1 (ArC), 129.4 (ArCH), 128.8 (ArCH,), 128.7 (ArCH,), 128.6 (ArCH), 127.2 (ArCH), 80.2 (O*C*Me$_3$), 67.4 (OCH_2Ph), 53.2 (Phe-NCH), 53.1 (Leu-NCH), 41.3 (*C*H_2CHMe$_2$), 38.0 (CH_2Ph), 28.4 (C(*C*H_3)$_3$), 24.8 (*C*HMe$_2$), 23.0 (CH(*C*H_3)$_2$), 21.9 (CH(*C*H_3)$_2$); MS (ESI) m/z 491 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{27}H_{37}N_2O_5$ 469.2697 $(M+H)^+$, found 469.2694 (0.2 ppm error).

Boc-Met-Val-OBn **5c**[S4]

Boc-Met-OH (374 mg, 1.5 mmol) and H_2N-Val-OBn (569 mg, 1.5 mmol) and were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (30:70, EtOAc:PE) to give Boc-Met-Val-OBn **5c** as a clear oil (603 mg, 91%). R_F = 0.33 (30:70, EtOAc); $[\alpha]_D^{23}$ -25.1 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3314.7 (w), 2968 (w), 2932 (w), 1739 (m), 1658 (s) and 1521 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.29 (m, 5H, ArH), 6.72 (d *J* 8.2 Hz, 1H, Val-NH), 5.23 (br, 1H, Met-NH), 5.19 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.12 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.56 (dd *J* 8.8, 4.7 Hz, 1H, Val-NCH), 4.31 (dt, *J* 7.3, 7.1 Hz, 1H,

Met-NCH), 2.58 (t *J* 7.2 Hz, 2H, CH_2CH_2SMe), 2.21 (dsep, *J* 7.0, 4.6 Hz, 1H, $CHMe_2$), 2.09 (s, 3H, SCH_3), 2.03 (dt, *J* 14.0, 7.1 Hz, 1H, CH_2CH_2SMe), 1.95 (dt *J* 14.0, 7.1 Hz, 1H, CH_2CH_2SMe), 1.43 (s, 9H, $C(CH_3)_3$), 0.91 (d, *J* 7.0 Hz, 3H, $CH(CH_3)_2$), 0.86 (d *J* 7.0 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6 (C=O), 171.5 (C=O), 155.6 (NC=O), 135.4 (ArC), 128.7 (Ar-CH), 128.6 (Ar-CH), 128.5 (Ar-CH), 80.2 (CMe_3), 67.2 (OCH_2Ph), 57.3 (Val-NCH), 53.3 (Met-NCH), 31.3 (CH_2SMe), 31.2 ($CHMe_2$), 30.2 (CH_2CH_2SMe), 28.4 ($C(CH_3)_3$), 19.1 ($CH(CH_3)_2$), 17.6 ($CH(CH_3)_2$), 15.2 (CH_2SCH_3); MS (ESI) m/z 477 [$(M+K)^+$, 15], 461 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{22}H_{34}N_2NaO_5S$ 461.2086 $(M+Na)^+$, found 461.2081 (-2.2 ppm error).

Boc-Asp(OBn)-Val-OBn **5d**[S5]

Boc-Asp(OBn)-OH (808 mg, 2.5 mmol) and H_2N-Val-OBn *para*-toluenesulfonate (949 mg, 2.5 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (25:75, EtOAc:PE) to give Boc-Asp(OBn)-Val-OBn **5d** as a pale yellow oil (897 mg, 70%). R_F = 0.29 (25:75, EtOAc:PE); $[\alpha]_D^{23}$ -28.4 (*c* 1.0 in MeOH) [lit.[S5] -33.3 (*c* 1.07 in MeOH)]; IR (Neat) ν_{max} 3332 (w), 3033 (w), 2967 (w), 2934 (w), 1734 (s), 1679 (s) and 1517 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.29 (m, 10H, ArH), 7.07 (d *J* 8.9 Hz, 1H, NH), 5.75 (d *J* 8.2 Hz, 1H, NH), 5.19 (d *J* 12.0, 1H, OCH_2Ph), 5.17-5.08 (m, 3H, 3×OCH_2Ph) 4.61-4.50 (m, 2H, 2×NCH), 3.03 (dd *J* 17.2, 4.7 Hz, 1H, CH_2CO_2) 2.71 (dd *J* 17.2, 4.7 Hz, 1H, CH_2CO_2), 2.26-2.12 (m, 1H, $CHMe_2$), 1.45 (s, 9H, $C(CH_3)_3$), 0.91 (d *J* 6.9 Hz, 1H, $CH(CH_3)_2$), 0.86 (d *J* 6.9 Hz, 1H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1 (C=O), 171.4 (C=O), 170.8 (C=O), 155.8 (NC=O), 13.5 (CAr), 135.4 (CAr), 128.7 (ArCH), 128.6 (ArCH), 128.5 (ArCH), 128.4 (ArCH), 128.3 (ArCH), 80.6 (CMe_3), 67.1 (OCH_2Ph), 67.0 (OCH_2Ph), 57.5 (Val-NCH), 50.7 (Asp(OBn)-NCH), 36.0 (CH_2CO_2), 31.3 ($CHMe_2$), 28.4 ($C(CH_3)_3$), 19.1 ($CH(CH_3)_2$), 17.6 ($CH(CH_3)_2$); MS (ESI) m/z 535 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{28}H_{36}N_2NaO_7$ 535.2429 $(M+Na)^+$, found 535.2417 (-0.1 ppm error).

Boc-Aib-Leu-OBn **5e**[S6]

Boc-Aib-OH (508 mg, 2.5 mmol) and H_2N-(*S*)-Leu-OBn *p*-toluenesulfonate (934 mg, 2.5 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (30:70, EtOAc:PE) to give Boc-Aib-Leu-OBn **5e** as a white powder (794 mg, 78%). R_F = 0.25 (25:75, EtOAc:PE); mp 93.8-94.5 °C; $[\alpha]_D^{23}$ -16.3 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3308 (m), 2953 (m), 2869 (w), 1720 (m), 1685 (s), 1659 (s), 1534 (m) and 1507 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39-7.29 (m, 5H, ArH), 6.88 (br, 1H, NH), 5.16 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.11 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.89 (br, 1H, NH), 4.66-4.60 (m, 1H, NCH), 1.72-1.56 (m, 3H, CH_2CHMe_2), 1.49 (s, 3H, $C(CH_3)_2$), 1.45 (s, 3H, $C(CH_3)_2$), 1.42 (s, 9H, $C(CH_3)_3$), 0.91 (d *J* 6.6 Hz, 3H, $CH(CH_3)_2$), 0.89 (d *J* 6.6 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5 (C=O), 173.0 (C=O), 154.7 (NC=O), 135.6 (ArC), 128.7 (ArCH), 128.5 (ArCH), 128.3 (ArCH), 77.4 ($OCMe_3$), 67.1 (OCH_2Ph), 56.9 ($NCMe_2$), 50.9 (NCH), 41.7 (CH_2CHMe_2), 28.4 ($C(CH_3)_3$), 26.3 (CH_2CHMe_2), 24.8 ($C(CH_3)_2$), 23.0 ($CH(CH_3)_2$), 21.9 ($CH(CH_3)_2$); MS (ESI) m/z 429 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{22}H_{34}N_2NaO_5$ 429.2365 $(M+Na)^+$, found 429.2373 (-2.7 ppm error).

TFA.H-Ala-Phe-OBn **6a**[S7]

Boc-Ala-Phe-OBn (340 mg, 0.8 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Ala-Phe-OBn **6a** as an off white solid (351 mg, 99%). Mp 180.7-181.3 °C; $[\alpha]_D^{23}$ -8.1 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3333 (m), 3165 (w), 3031 (w), 2938 (w), 1725 (s), 1660 (s), 1547 (m) and 1523 (m) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 7.40-7.15 (m, 10H, ArH), 5.16 (d *J* 12.1 Hz, 1H, OCH_2Ph), 5.11 (d *J* 12.1 Hz, 1H, OCH_2Ph), 4.76 (dd, *J* 8.9, 5.8 1H, Phe-NCH), 3.86 (q *J* 6.8 Hz, 1H, Ala-NCH), 3.20 (dd *J* 14.1, 5.9 Hz, 1H, CH_2Ph), 2.98 (dd *J* 14.1, 5.9 Hz, 1H, CH_2Ph), 1.42 (d *J* 6.9 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, CD_3OD): δ = 172.4 (C=O), 171.1 (C=O), 137.9 (ArC), 136.9 (ArC), 130.2 (ArCH), 129.6 (ArCH), 129.6 (ArCH), 129.6 (ArCH), 129.5 (ArCH), 128.0 (ArCH), 68.2 (OCH_2Ph), 55.6 (Phe-NCH), 50.0 (Ala-NCH), 38.1

(CH_2Ph), 17.6 (CH_3); MS (ESI) m/z 349 [$(M+Na)^+$, 50], 327 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{19}H_{23}N_2O_3$ 327.1709 $(M\text{-}CF_3CO_2^-)^+$, found 327.1695 (2.3 ppm error).

TFA.H-Leu-Phe-OBn **6b**[S8]

Boc-Leu-Phe-OBn (600 mg, 1.28 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Leu-Phe-OBn **6b** as an off white solid (1.33 g, 99%). Mp 172.7-173.5 °C; IR (Neat) ν_{max} 2960 (w), 2485 (w), 1731 (s), 1723 (s), 1679 (m), 1674 (s), 1665 (s) and 1518 (s) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 7.35-7.30 (m, 3H, ArH), 7.29-7.23 (m, 4H, ArH), 7.22-7.16 (m, 3H, ArH), 5.12 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.08 (d *J* 12.0 Hz, 1H, OCH_2Ph), 4.74 (dd *J* 8.8, 6.0 Hz, 1H, Phe-NCH), 4.59 (br, 1H, NH), 3.77 (dd *J* 8.8, 6.0 Hz, 1H, Leu-NCH), 3.18 (dd *J* 14.0, 6.4 Hz, 1H, CH_2Ph), 3.01 (dd *J* 14.0, 8.8 Hz, 1H, CH_2Ph), 1.73-1.53 (m, 2H, CH_2CHMe_2), 0.91 (d *J* 6.4 Hz, 3H, $CH(CH_3)_2$), 0.90 (d *J* 6.4 Hz, 3H, $CH(CH_3)_3$); ^{13}C NMR (100 MHz, CD_3OD): δ = 172.3 (C=O), 170.9 (C=O), 137.9 (ArC), 136.9 (ArC), 130.2 (ArCH), 129.6 (ArCH), 129.6 (ArCH), 129.6 (ArCH), 129.5 (ArCH), 128.0 (ArCH), 68.2 (OCH_2Ph), 55.7 (Phe-NCH), 52.7 (Leu-NCH), 41.7 (CH_2CHMe_2), 38.0 (CH_2Ph), 25.2 ($CH(Me)_2$), 23.2 ($CH(CH_3)_2$), 21.8 ($CH(CH_3)_2$); MS (ESI) m/z 391 [$(M+Na)^+$, 35], 369 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{22}H_{29}N_2O_3$ 369.2173 $(M\text{-}CF_3CO_2^-)^+$, found 369.2173 (0.3 ppm error).

TFA.H-Met-Val-OBn **6c**

Boc-Met-Val-OBn (603 mg, 1.37 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Met-Val-OBn **6c** as a white solid (474 mg, 80%). Mp 169.6-170.1 °C; $[\alpha]_D^{23}$ -10.0 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3344 (w), 2975 (w), 1693 (s), 1663 (s), 1544 (m) and 1518 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.74 (d *J* 7.9 Hz, 1H, NH), 8.20 (br, 3H, NH_3^+), 7.41-7.32 (m, 5H, ArH), 5.16 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.13 (d *J* 12.0 Hz, 1H, OCH_2Ph), 4.26 (dd *J* 7.5, 6.1 Hz, 1H, Val-NCH), 3.97 (t *J* 6.2 Hz, 1H, Met-NCH), 2.50-2.44 (m, 2H, CH_2SMe), 2.19-2.06 (m, 1H, $CHMe_2$), 2.01 (s, 3H, SCH_3), 2.02-1.89 (m, 2H, CH_2CH_2SMe), 0.91 (d *J* 6.8 Hz, 3H, $CH(CH_3)_2$), 0.90 (d J 6.8 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-

d_6): δ = 170.9 (C=O), 168.9 (C=O), 135.7 (ArC), 128.5 (ArCH), 128.2 (ArCH), 128.1 (ArCH), 66.2 (OCH_2Ph), 57.8 (Val-NCH), 51.4 (Met-NCH), 31.2 (CH_2CH_2SMe), 29.7 ($CHMe_2$), 28.0 (CH_2SMe), 18.9 ($CH(CH_3)_2$), 18.0 ($CH(CH_3)_2$), 14.5 (SCH_3); MS (ESI) m/z 361 [$(M+Na)^+$, 50], 339 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{17}H_{27}N_2O_3S$ 339.1742 $(M-CF_3CO_2^-)^+$, found 339.1737 (2.9 ppm error).

TFA.H-Asp(OBn)-Val-OBn **6d**[S5]

Boc-Asp(OBn)-Val-OBn (747 mg mg, 1.46 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Asp(OBn)-Val-OBn **6d** as an off-white solid (650 mg, 85%). Mp 147.8-148.4 °C; $[\alpha]_D^{23}$ -16.0 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3328 (m), 3032 (w), 2976 (w), 2884 (w), 2586 (w), 1734 (m), 1705 (s), 1661 (s), 1558 (m) and 1519 (w) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.77 (d *J* 8.2 Hz, 1H, NH), 8.34 (br, 3H, NH_3^+), 7.46-7.27 (m, 10H, ArH), 5.20-5.07 (m, 4H, 2×OC*H*$_2$Ph), 4.33-4.24 (m, 2H, 2×NCH), 2.88 (dd *J* 17.6, 3.9 Hz, 1H, CH_2CO_2Bn), 2.78 (dd *J* 17.6, 8.9 Hz, 1H, CH_2CO_2Bn) 2.11 (oct *J* 6.7 Hz, 1H, $CHMe_2$), 0.89 (d *J* 7.3 Hz, 3H, CH(C*H*$_3$)$_2$), 0.87 (d *J* 7.3 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 170.7 (C=O), 169.1 (C=O), 168.9 (C=O), 135.7 (ArC), 135.6 (ArC), 128.5 (ArCH), 128.5 (ArCH), 128.3 (ArCH), 128.3 (ArCH), 128.2 (ArCH), 66.4 (OCH_2Ph), 66.3 (OCH_2Ph), 57.8 (Val-NCH), 48.6 (Asp-NCH), 35.5 (CH_2CO_2Bn), 29.8 ($CHMe_2$), 18.9 ($CH(CH_3)_2$), 17.9 ($CH(CH_3)_2$); MS (ESI) m/z 435 [$(M+Na)^+$, 75], 413 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{23}H_{29}N_2O_5$ 413.2076 $(M-CF_3CO_2^-)^+$, found 413.2060 (3.5 ppm error).

TFA.H-Aib-Leu-OBn **6e**[S6]

Boc-Aib-Leu-OBn (100 mg, 0.25 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Aib-Leu-OBn **6e** as a yellow oil (102 mg, 97%). IR (Neat) ν_{max} 2960 (w), 1728 (m), 1661 (s) and 1530 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.59 (d *J* 8.3 Hz, 1H, NH), 8.23 (s, 3H, NH_3^+), 7.42-7.31 (m, 5H, ArH), 5.13 (d *J* 12.9 Hz, 1H, OCH_2Ph), 5.10 (d *J* 12.9 Hz, 1H, OCH_2Ph), 4.44-4.37 (m, 1H, Leu-NCH), 1.77-1.52 (m, 3H, CH_2CHMe_2), 1.48 (s,

3H, $C(CH_3)_2$), 1.45 (s, 3H, $C(CH_3)_2$), 0.90 (d *J* 6.1 Hz, 3H, $CH(CH_3)_2$), 0.83 (d *J* 6.1 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.0 (C=O), 171.9 (C=O), 135.8 (ArC), 128.5 (ArCH), 128.2 (ArCH), 127.9 (ArCH), 66.2 (OCH_2Ph), 56.4 (Aib-NC), 50.8 (Leu-NCH), 39.3 (CH_2CHMe_2), 24.4 ($CHMe_2$), 23.4 ($C(CH_3)_2$), 23.3 ($C(CH_3)_2$), 22.8 ($CH(CH_3)_2$), 20.9 ($CH(CH_3)_2$); MS (ESI) m/z 329 [$(M+Na)^+$, 50], 307 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{17}H_{27}N_2O_3$ 307.2022 $(M-CF_3CO_2^-)^+$, found 307.2008 (2.0 ppm error).

Boc-Leu-Ala-Phe-OBn **7a**

Boc-Leu-OH (185 mg, 0.8 mmol) and TFA.H_2N-Ala-Phe-OBn (352 mg, 0.8 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (35:65-60:40, EtOAc:PE) to give the Boc-Leu-Ala-Phe-OBn **7a** as a white solid (325 mg, 75%). R_F = 0.35 (60:40, EtOAc:PE); mp 143.9-144.6 °C; $[\alpha]_D^{23}$ -37.4 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3326 (m), 2955 (w), 1983 (w), 1730 (m), 1688 (m), 1639 (s) and 1523 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.29 (m, 3H, ArH), 7.29-7.22 (m, 2H, ArH), 7.21-7.13 (m, 3H, ArH), 7.04-6.91 (m, 2H, ArH), 6.65 (d *J* 7.1 Hz, Ala-NH), 6.59 (d *J* 7.0 Hz, Phe-NH), 5.14 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.06 (d *J* 12.0 Hz, 1H, OCH_2Ph), 4.90 (br, 1H, Leu-NH), 4.87 (dt *J* 7.5, 6.9 Hz, 1H, Phe-NCH), 4.46 (q *J* 7.2 Hz, 1H, Ala-NCH), 4.09 (br, 1H, Leu-NCH), 3.10 (dd *J* 14.2, 6.6 Hz, CH_2Ph), 3.05 (dd *J* 14.2, 6.6 Hz, CH_2Ph), 1.70-1.58 (m, 1H, $CHMe_2$), 1.59-1.51 (m, 2H, CH_2CHMe_2), 1.42 (s, 9H, $OC(CH_3)_3$), 1.29 (d, *J* 7.2 Hz, 3H, $NCHCH_3$), 0.90 (d J 6.6 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6 (C=O), 171.8 (C=O), 171.2 (C=O), 155.8 (NC=O), 135.7 (ArC), 135.1 (ArC), 129.3 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 127.2 (ArCH), 80.2 ($OCMe_3$), 67.4 (OCH_2Ph), 53.5 (Phe-NCH), 53.0 (Leu-NCH), 48.9 (Ala-NCH), 41.2 (CH_2CHMe_2), 37.9 (CH_2Ph), 28.4 ($OC(CH_3)_3$), 24.8 ($CH(CH_3)_2$), 23.2 ($CH(CH_3)_2$), 21.9 ($CHMe_2$), 18.3 ($NCHCH_3$); MS (ESI) m/z 562 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{30}H_{41}N_3NaO_6$ 540.3074 $(M+Na)^+$, found 562.2888 (-1.3 ppm error).

Boc-(*R*)-Leu-Ala-Phe-OBn **7a'**

Boc-(*R*)-Leu-OH (69 mg, 0.3 mmol) and TFA.H_2N-Ala-Phe-OBn (164 mg, 0.3 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (30:20:50-40:20:40, EtOAc:CH_2Cl_2:PE) to give Boc-(*R*)-Leu-Ala-Phe-OBn **7a'** as a white solid (132 mg, 82%). R_F = 0.18 (30:20:50, EtOAc:CH_2Cl_2:PE); mp 131.7-132.5 °C; $[\alpha]_D^{23}$ -9.3 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3319 (m), 3277 (m), 2930 (w), 1730 (m), 1686 (m), 1638 (s) and 1528 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.32 (m, 3H, ArH), 7.29-7.24 (m, 2H, ArH), 7.23-7.18 (m, 3H, ArH), 7.05-7.00 (m, 2H, ArH), 6.67 (br, 1H, Phe-NH), 6.60 (d *J* 7.6 Hz, 1H, Ala-NH), 5.14 (d *J* 12.3 Hz, 1H, OCH_2Ph), 5.08 (d *J* 12.3 Hz, 1H, OCH_2Ph), 4.88-4.78 (m, 2H, Leu-NH + Phe-NCH), 4.50 (q *J* 7.3 Hz, 1H, Ala-NCH), 4.06 (br, 1H, Leu-NCH), 3.12 (dd *J* 14.0, 5.1 Hz, 1H, CH_2Ph), 3.05 (dd *J* 14.0, 5.1 Hz, 1H, CH_2Ph), 1.69-1.55 (m, 3H, CH_2CHMe$_2$), 1.43 (s, 9H, C(CH_3)$_3$), 1.29 (d *J* 6.3 Hz, 3H, NCHCH_3), 0.92 (d *J* 6.2 Hz, 3H, CH(CH_3)$_2$), 0.91 (d *J* 6.2 Hz, 3H, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.5 (C=O), 171.8 (C=O), 171.2 (C=O), 155.8 (NC=O), 135.2 (ArC), 129.4 (ArC), 128.7 (ArCH), 128.7 (ArCH), 127.2 (ArCH), 80.3 ($OCMe_3$), 67.4 (OCH_2Ph), 53.5 (Phe-NCH), 53.3 (Leu-NCH), 48.8 (Ala-NCH), 41.3 (Leu-CH$_2$CHMe$_2$), 34.7 (CH_2Ph), 28.4 C(CH_3)$_3$), 24.9 (CH(CH_3)$_2$), 23.1 (CH(CH_3)$_2$), 22.0 (CHMe$_2$), 18.1 (NCHCH_3); MS (ESI) m/z 562 [(M+Na)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{30}H_{41}N_3NaO_6$ 562.2893 (M+Na)$^+$, found 562.2876 (1.9 ppm error).

Boc-Gly-Leu-Phe-OBn **7b**[S9]

Boc-Gly-OH (145 mg, 0.83 mmol) and TFA.H_2N-Leu-Phe-OBn (400 mg, 0.83 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (50:50-60:40, EtOAc:PE) to give Boc-Gly-Leu-Phe-OBn **7b** as a white powder (371 mg, 78%). R_F = 0.46 (50:50, EtOAc:PE); mp 86.1-87.4 °C; $[\alpha]_D^{23}$ -23.4 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3295 (w), 2958 (w), 1714 (s), 1640 (s) and 1546 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38-7.34 (m, 3H, ArH), 7.30-7.27 (m, 2H, ArH), 7.24-7.20 (m, 3H, ArH), 7.04-7.02 (m, 2H,

ArH), 6.57 (d, *J* 7.6 Hz, 1H, Phe-NH), 6.46 (d *J* 8.4 Hz, 1H, Leu-NH), 5.26 (t *J* 5.7 Hz, 1H, Gly-NH), 5.16 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.10 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.87 (dt *J* 8.0, 6.4 Hz, 1H, Phe-NCH), 4.50-4.40 (m, 1H, Leu-NCH), 3.76 (dd, *J* 16.8, 5.6 Hz, 1H, Gly-NCH_2), 3.67 (dd *J* 16.8, 5.2 Hz, 1H, Gly-NCH_2), 3.14 (dd *J* 14, 6.0 Hz, 1H, CH_2Ph), 3.06 (dd *J* 14.0, 6.4 Hz, 1H, CH_2Ph), 1.65-1.54 (m, 2H, CH_2CHMe_2), 1.53-1.46 (m, 1H, $CHMe_2$), 1.45 (s, 9H, $OC(CH_3)_3$), 0.87 (d *J* 6.0 Hz, 3H, $CH(CH_3)_2$), 0.86 (d *J* 6.0 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6 (C=O), 171.2 (C=O), 169.6 (C=O), 156.1 (NC=O), 135.8 (ArC), 135.1 (ArC), 129.4 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 128.6 (ArCH), 127.1 (ArCH), 77.4 ($OC(CH_3)_3$), 67.4 (OCH_2Ph), 53.3 (Phe-NCH), 51.6 (Leu-NCH), 44.3 (Gly-NCH_2), 40.1 (CH_2CHMe_2), 37.9 (CH_2Ph), 28.4 ($OC(CH_3)_3$), 24.7 (CH_2CHMe_2), 22.9 ($CH(CH_3)_2$), 22.1 ($CH(CH_3)_2$); MS (ESI) m/z 548 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{29}H_{39}N_3NaO_6$ 548.2731 $(M+Na)^+$, found 548.2719 (2.4 ppm error).

Boc-Ser(OBn)-Met-Val-OBn **7c**

Boc-Ser(OBn)-OH (313 mg, 1.1 mmol) and TFA.H_2N-Met-Val-OBn (478 mg, 1.1 mmol) were coupled according to the general coupling procedure. The residue was then purified using flash column chromatography (47.5:52.5, EtOAc:PE) to give Boc-Ser(OBn)-Met-Val-OBn **7c** as a colourless oil (537 mg, 83%). R_F = 0.46 (47.5:52.5, EtOAc:PE); $[\alpha]_D^{23}$ -26.8 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3299 (w), 2967 (w), 2930 (w), 1738 (m), 1714 (m) and 1644 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.26 (m, 10H, ArH), 7.22 (d *J* 6.9 Hz, 1H, Met-NH), 6.79 (d *J* 8.4 Hz, 1H, Val-NH), 5.38 (d *J* 6.0 Hz, 1H, Ser-NH), 5.19 (d *J* 12.4 Hz, 1H, CO_2CH_2Ph), 5.12 (d *J* 12.4 Hz, 1H, CO_2CH_2Ph) 4.63 (dt *J* 7.6, 6.8 Hz, 1H, Met-NCH), 4.56 (d *J* 11.8 Hz, 1H, CH_2OCH_2Ph), 4.51 (d *J* 11.8 Hz, 1H, CH_2OCH_2Ph), 4.56-4.51 (m, 1H, Val-NCH), 4.29 (br, 1H, Ser-NCH), 3.91 (dd *J* 9.4, 3.7 Hz, 1H, CH_2OBn), 3.57 (dd *J* 9.4, 6.0 Hz, 1H, CH_2OBn) 2.54 (t *J* 7.1 Hz, 2H, CH_2SMe), 2.24-2.13 (m, 1H, Val-$CHMe_2$), 2.06 (s, 3H, SCH_3), 2.06-1.95 (m, 2H, CH_2CH_2SMe), 1.44 (s, 9H, $OC(CH_3)_3$), 0.89 (d *J* 7.0 Hz, 3H, $CH(CH_3)_2$), 0.85 (d *J* 7.0 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5 (C=O), 170.7 (C=O), 170.5 (C=O), 155.7 (NC=O), 137.4 (ArC), 135.4

(ArC), 128.7 (ArCH), 128.6 (ArCH), 128.6 (ArCH), 128.1 (ArCH), 127.9 (ArCH), 73.6 (OCH_2Ph), 69.9 (CH_2OBn), 67.2 (OCH_2Ph), 57.5 (Val-NCH), 54.3 (Ser-NCH) 52.4 (Met-NCH), 31.1 ($CHMe_2$), 30.8 (CH_2CH_2SMe), 30.0 (CH_2SMe), 28.4 ($OC(CH_3)_2$), 19.2 ($CH(CH_3)_2$), 17.7 ($CH(CH_3)_2$), 15.0 (SCH_3); MS (ESI) m/z 638 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{32}H_{45}N_3NaO_7S$ 638.2876 $(M+Na)^+$, found 638.2870 (4.2 ppm error).

Boc-Trp-Asp(OBn)-Val-OBn **7d**

Boc-Trp-OH (231 mg, 0.76 mmol) and TFA.H_2N-Asp(OBn)-Val-OBn (400 mg, 0.76 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (50:50, EtOAc:PE) to give Boc-Trp-Asp(OBn)-Val-OBn **7d** as a pale yellow solid (363 mg, 68%). R_F = 0.32 (50:50, EtOAc:PE); mp 57.8-58.5 °C; $[\alpha]_D^{23}$ -36.2 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3320 (m), 3062 (w), 2967 (w), 2932 (w), 1729 (s) and 1646 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (s, 1H, ArNH), 7.62 (d *J* 7.5 Hz, 1H, ArH), 7.40-7.27 (m, 11H, ArH), 7.19-7.09 (m, 3H, ArH), 7.03 (d *J* 2.1 Hz, 1H, Asp-NH), 7.01 (d *J* 8.8 Hz, 1H, Val-NH), 5.18 (d *J* 11.8 Hz, 1H, OCH_2Ph), 5.10 (d *J* 11.8 Hz, 1H, OCH_2Ph), 5.06-5.01 (m, 3H, OCH_2Ph + Trp-NH), 4.80-4.72 (m, 1H, Asp-NCH), 4.46-4.39 (m, 2H, Val-NCH, Trp-NCH), 3.33 (dd *J* 14.4, 5.2 Hz, 1H, Trp-CH_2), 3.18 (dd *J* 14.7, 6.6 Hz, 1H, Trp-CH_2), 2.91 (d *J* = 16.2 Hz, 1H, CH_2CO_2Bn), 2.36 (dd *J* 17.2, 6.6 Hz, 1H, CH_2CO_2Bn), 2.11 (oct *J* 6.8 Hz, 1H, $CHMe_2$), 1.41 (s, 9H, $OC(CH_3)_3$), 0.87 (d *J* 6.7 Hz, 3H, $CH(CH_3)_2$), 0.78 (d *J* 6.7 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2 (C=O), 172.0 (C=O), 171.4 (C=O), 170.1 (C=O), 155.6 (NC=O), 136.3 (ArC), 13.6 (ArC), 135.5 (ArC), 128.7 (ArCH), 128.6 (ArCH), 128.5 (ArCH), 128.5 (ArCH), 128.4 (ArCH), 128.4 (ArCH), 127.4 (ArC), 123.2 (ArCH), 122.5 (ArCH), 119.9 (ArCH), 118.9 (ArCH), 111.4 (ArCH), 110.3 (ArC), 80.5 ($OCMe_3$) 67.1 (OCH_2Ph), 66.9 (OCH_2Ph), 57.7 (Val-NCH), 55.4 (Asp-NCH), 49.3 (Trp-NCH), 35.5 (Trp-CH_2), 31.0 ($CHMe_2$), 28.4 ($C(CH_3)_3$), 19.1 ($CH(CH_3)_2$), 17.7 ($CH(CH_3)_2$); MS (ESI) m/z 721 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{39}H_{46}N_4NaO_8$ 721.3213 $(M+Na)^+$, found 721.3208 (1.8 ppm error).

Boc-Pro-Aib-Leu-OBn **7e**

Boc-Pro-OH (357 mg, 1.66 mmol) and TFA.H_2N-Aib-Leu-OBn (700 mg, 1.66 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (2:98-5:95, MeOH:CH_2Cl_2) to give Boc-Pro-Aib-Leu-OBn **7e** as a white powder (618 mg, 73%). R_F = 0.18, (2:98, MeOH:CH_2Cl_2); mp 157.5-158.1 °C; $[\alpha]_D^{23}$ -51.9 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3382 (w), 3274 (w), 3060 (w), 2974 (w), 2871 (w), 1735 (m), 1681 (s), 1643 (s), 1549 (m), 1522 (m) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 7.40-7.22 (m, 5H, ArH), 5.17 (d *J* 12.6 Hz, 1H, CH_2Ph), 5.11 (d *J* 12.6 Hz, 1H, CH_2Ph), 4.57-4.44 (m, 1H, Leu-NCH), 4.18-4.07 (Pro-NCH), 3.54-3.33 (m, 2H, CH_2N), 2.26-2.09 (m, 1H, C*H*$_2$$CH_2CH_2N$), 2.09-1.75 (m, 3H, C*H*$_2$C*H*$_2$$CH_2N$), 1.73-1.57 (m, 3H, CH_2CHMe_2), 1.45 (s, 9H, $OC(CH_3)_3$), 1.43 (s, 3H, $C(CH_3)_2$), 1.41 (s, 3H, $C(CH_3)_2$), 0.91 (3H, d *J* 5.7 Hz, $CH(CH_3)_2$), 0.89 (3H, d *J* 4.8 Hz, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, CD_3OD, major rotomer): δ = 176.8 (C=O), 174.5 (C=O), 173.8 (C=O), 156.4 (NC=O), 137.3 (ArC), 129.5 (ArCH), 129.4 (ArCH), 129.3 (ArCH), 81.3 ($OCMe_3$), 67.7 (OCH_2Ph), 61.5 (Pro-NCH), 57.8 (Aib-NC), 52.5 (Leu-NCH), 47.9 (CH_2N), 41.5 (*C*$H_2CH_2CH_2N$), 31.3 (*C*H_2CH_2N), 28.9 ($OC(CH_3)_3$), 26.5 ($CHMe_2$), 25.7 (*C*H_2CHMe_2), 25.4 ($C(CH_3)_2$), 24.5 ($C(CH_3)_2$), 23.2 ($CH(CH_3)_2$), 22.2 ($CH(CH_3)_2$); MS (ESI) m/z 526 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{27}H_{41}N_3NaO_6$ 526.2893 $(M+Na)^+$, found 526.2893 (-0.9 ppm error).

TFA.H-Leu-Ala-Phe-OBn **8a**[S10]

Boc-Leu-Ala-Phe-OBn (260 mg, 0.48 mmol) was deprotected according to the general procedure for Boc deprotections, giving TFA.H-Leu-Ala-Phe-OBn **8a** as an off white solid (257 mg, 96%). Mp 196.0-196.5 °C; $[\alpha]_D^{23}$ -15.2 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3394 (w), 3262 (w), 2957 (m), 1732 (w), 1648 (s) and 1516 (m) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 7.32-7.12 (m, 10H, ArH), 5.10 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.06 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.65 (dd *J* 7.8, 6.2 Hz, 1H, Phe-NCH), 4.39 (q *J* 7.2 Hz, 1H, Ala-NCH), 3.86-3.78 (m, 1H, Leu-NCH), 3.10 (dd *J* 13.8, 6.1 Hz, 1H,

CH_2Ph), 2.99 (dd *J* 13.8, 6.1 Hz, 1H, CH_2Ph), 1.71-1.55 (m, 3H, Leu-C*H*$_2$C*H*Me$_2$), 1.29 (d *J* 7.2 Hz, 3H, NCHC*H*$_3$), 0.95 (d *J* 6.0 Hz, 3H, CH(C*H*$_3$)$_2$), 0.93 (d *J* 6.0 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, CD_3OD): δ = 174.3 (C=O), 172.6 (C=O), 172.5 (C=O), 137.8 (ArC), 136.9 (ArC), 130.3 (ArCH), 129.5 (ArCH), 129.5 (ArCH), 129.4 (ArCH), 127.9 (ArCH), 68.1 (OCH_2Ph), 55.4 (Phe-NCH), 52.8 (Ala-NCH), 50.0 (Leu-NCH), 41.7 (*C*H$_2$CHMe$_2$), 38.3 (CH_2Ph), 25.3 (*C*HMe$_2$), 23.1 (CH(*C*H$_3$)$_2$), 22.0 (CH(*C*H$_3$)$_2$), 18.3 (NCH*C*H$_3$); MS (ESI) m/z 462 [(M-TFA+Na)$^+$, 85], 440 [(M-TFA+H)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{25}H_{33}N_3NaO_4$ 462.2369 (M-TFA+Na)$^+$, found 462.2363 (3.2 ppm error).

TFA.H-Gly-Leu-Phe-OBn **8b**[S9]

Boc-Gly-Leu-Phe-OBn (200 mg, 0.38 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Gly-Leu-Phe-OBn **8b** as an off white solid (192 mg, 94%). Mp 185.6-186.2 °C; $[\alpha]_D^{23}$ -28.4 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3405 (w), 3277 (w), 2955 (w), 1721 (m), 1693 (m), 1641 (s) and 1528 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.34-7.29 (m, 3H, ArH), 7.27-7.23 (m, 2H, ArH), 7.22-7.18 (m, 2H, ArH), 7.17-7.13 (m, 3H, ArH), 5.10 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.06 (d *J* 12.0 Hz, 1H, OCH_2Ph), 4.65 (dd *J* 8.0, 6.4 Hz, 1H, Phe-NCH), 4.42 (dd *J* 8.0, 6.8 Hz, 1H, Leu-NCH), 3.68 (d, *J* 16.0 Hz, 1H, Gly-NCH_2), 3.62 (d, *J* 16.0 Hz, 1H, Gly-NCH_2), 3.12 (dd *J* 14.0, 6.0 Hz, 1H, CH_2Ph), 2.99 (dd *J* 14.0, 8.4 Hz, 1H, CH_2Ph), 1.62 (non *J* 6.8 Hz , 1H, $CHMe_2$), 1.53-1.42 (m, 2H, C*H*$_2$CHMe$_2$), 0.87 (d *J* 8.8, 6.4 Hz, 3H, CH(C*H*$_3$)$_2$), 0.85 (d *J* 8.8, 6.4 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.5 (C=O), 172.6 (C=O), 167.0 (C=O), 138.0 (ArC), 136.9 (ArC), 130.3 (ArCH), 129.6 (ArCH), 129.5 (ArCH), 129.4 (ArCH), 127.9 (ArCH), 68.1 (CH_2Ph), 55.5 (Phe-NCH), 53.0 (Leu-NCH), 42.2 (*C*H$_2$CHMe$_2$), 41.4 (Gly-NCH_2), 38.2 (CH_2Ph), 25.8 ($CHMe_2$), 23.4 (CH(*C*H$_3$)$_2$), 21.9 (CH(*C*H$_3$)$_2$); MS (ESI) m/z 426 [(M-TFA+H)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{24}H_{32}N_3O_4$ 426.2387 (M-TFA+H)$^+$, found 426.2374 (2.6 ppm error).

TFA.H-Ser(OBn)-Met-Val-OBn **8c**

Boc-Ser(OBn)-Met-Val-OBn (300 mg, 0.49 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Ser(OBn)-Met-Val-OBn **8c** as an off-white solid (257 mg, 84%). Mp 137.8-138.3 °C; IR (Neat) ν_{max} 3274 (w), 3035 (w), 2922 (w), 2964 (w), 1728 (m), 1671 (s), 1644 (s), 1553 (s) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.69 (d, *J* 8.1 Hz, 1H, Met-NH), 8.38 (d *J* 7.7 Hz, 1H, Val-NH), 8.18 (br, 3H, NH_3^+), 7.43-7.24 (m, 10H, ArH), 5.15 (d *J* 12.4 Hz, 1H, CO_2CH_2Ph), 5.10 (d *J* 12.4 Hz, 1H, CO_2CH_2Ph) 4.66-4.53 (m, 1H, Met-NCH), 4.53 (d *J* 7.7 Hz, 1H, OCH_2Ph), 4.49 (d *J* 7.7 Hz, 1H, OCH_2Ph), 4.20 (dd, *J* 7.9, 6.1 Hz, Val-NCH), 4.09 (dd *J* 6.3, 3.9 Hz, 1H, Ser-NCH), 3.75 (dd, *J* 10.7, 4.1 Hz, 1H, C*H*$_2$OBn), 3.67 (dd *J* 10.7, 4.1 Hz, 1H, C*H*$_2$OBn), 2.49-2.36 (m, 2H, CH_2SMe), 2.12-2.02 (m, 1H, $CHMe_2$), 2.01 (s, 3H, SCH_3), 1.97-1.72 (m, 2H, C*H*$_2$CH$_2$SMe), 0.86 (d *J* 6.8 Hz, 3H, CH(C*H*$_3$)$_2$), 0.85 (d *J* 6.8 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 171.2 (C=O), 170.9 (C=O), 166.4 (C=O), 137.6 (ArC), 135.9 (ArC), 128.5 (ArCH), 128.3 (ArCH), 128.2 (ArCH), 128.1 (ArCH), 127.8 (ArCH), 72.5 (CH_2OCH_2Ph), 68.5 (CH_2OBn), 66.0 (CO_2CH_2Ph), 57.6 (Val-NCH), 52.4 (Ser-NCH), 51.9 (Met-NCH), 32.4 (*C*H$_2$CH$_2$SMe), 29.7 ($CHMe_2$), 29.3 (CH_2SMe), 18.9 (CH(*C*H$_3$)$_2$), 18.1 (CH(*C*H$_3$)$_2$), 14.6 (SCH_3); MS (ESI) m/z 538 [(M-TFA+Na)$^+$, 70], 516 [(M-TFA+H)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{27}H_{38}N_3O_5S$ 516.2532 (M-TFA+H)$^+$, found 516.2527 (1.8 ppm error).

TFA.H-Trp-Asp(OBn)-Val-OBn **8d**

Boc-Trp-Asp(OBn)-Val-OBn (100 mg mg, 0.14 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Trp-Asp(OBn)-Val-OBn **8d** as a yellow solid (102 mg, 99%). Mp 78.7-79.4 °C; $[\alpha]_D^{23}$ -27.0 (*c* 0.5, in MeOH); IR (Neat) ν_{max} 3313 (m), 3032 (w), 2938 (w), 1693 (s), 1655 (s) and 1514 (s) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 7.67 (d *J* 7.9 Hz, 1H, ArH), 7.42-7.20 (m, 12H, ArH), 7.17-7.11 (m, 1H, ArH), 7.09-7.03 (m, 1H, ArH), 5.17 (d *J* 12.1 Hz, 1H, OCH_2Ph), 5.12 (s, 2H, OCH_2Ph), 5.09 (d *J* 12.1 Hz, 1H, OCH_2Ph), 4.91-4.86 (m, 1H, Asp-NCH), 4.34 (d *J* 5.5 Hz, 1H, Val-NCH), 4.19-4.12 (m, 1H, Trp-NCH), 3.44 (dd *J* 15.1, 5.3 Hz,

1H, Trp-CH_2), 3.18 (dd *J* 15.1, 8.7 Hz, 1H, Trp-CH_2), 2.87 (dd, *J* 16.7, 5.7 Hz, 1H, CH_2CO_2), 2.76 (dd, *J* 16.7, 7.9 Hz, 1H, CH_2CO_2), 2.14 (oct *J* 6.8 Hz, 1H, $CHMe_2$), 0.93 (d *J* 6.6 Hz, 3H, $CH(CH_3)_2$), 0.91 (d, *J* 6.6 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, CD_3OD): δ = 172.5 (C=O), 172.4 (C=O), 171.6 (C=O), 170.2 (C=O), 138.3 (ArC), 137.2 (ArC), 137.1 (ArC), 129.6 (ArCH), 129.6 (ArCH), 129.5 (ArCH), 129.4 (ArCH), 129.3 (ArCH), 128.2 (ArC), 125.7 (ArCH), 122.9 (ArCH), 120.3 (ArCH), 119.1 (ArCH), 112.6 (ArCH), 107.7 (ArC), 68.0 (OCH_2Ph), 67.8 (OCH_2Ph), 59.5 (Val-NCH), 54.7 (Trp-NCH), 51.3 (Asp-NCH), 37.1 (CH_2CO_2), 31.7 ($CHMe_2$), 28.9 (Trp-CH_2), 19.5 ($CH(CH_3)_2$), 18.5 ($CH(CH_3)_2$); MS (ESI) m/z 637 [$(M\text{-}TFA+K)^+$, 100], 621 [$(M\text{-}TFA+Na)^+$, 60], 599 [$(M\text{-}TFA+H)^+$, 80]; HRMS (ESI) m/z calculated for $C_{34}H_{38}N_4NaO_6$ 621.2689 $(M\text{-}TFA+Na)^+$, found 621.2684 (-4.0 ppm error).

TFA.H-Pro-Aib-Leu-OBn **8e**

Boc-Pro-Aib-Leu-OBn (200 mg, 0.39 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Pro-Aib-Leu-OBn **8e** as a yellow solid (200 mg, 97%). Mp105.3-106.2 °C; $[\alpha]_D^{23}$ -52.7 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3034 (w), 2957 (w), 1735 (m), 1670 (s) and 1645 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 9.50 (br, 1H, NH_2^+), 8.54 (s, 1H, $NHCMe_2$), 8.50 (br, 1H, NH_2^+), 7.90 (d *J* 7.9 Hz, 1H, N*H*CH), 7.41-7.29 (m, 5H, ArH), 5.11 (d *J* 12.5 Hz, 1H, OCH_2Ph), 5.07 (d *J* 12.5 Hz, 1H, OCH_2Ph), 4.37-4.30 (m, 1H, Leu-NCH), 4.18 (dd, *J* 8.2, 6.4 Hz, 1H, Pro-NCH), 3.25-3.13 (m, 2H, CH_2N), 2.31-2.20 (m, 1H, 1×Pro-CH_2), 1.99-1.75 (m, 3H, 3×Pro-CH_2), 1.73-1.45 (m, 3H, Leu-CH_2CHMe_2), 1.40 (s, 3H, $C(CH_3)_2$), 1.37 (s, 3H, $C(CH_3)_2$), 0.86 (d *J* 6.4 Hz, 3H, $CH(CH_3)_2$), 0.81 (d *J* 6.4 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 173.3 (C=O), 172.4 (C=O), 167.6 (C=O), 135.9 (ArC), 128.4 (ArCH), 128.1 (ArCH), 127.9 (ArCH), 65.9 (CH_2Ph), 59.1 (Pro-NCH), 54.5 (Aib-NC), 50.6 (Leu-NCH), 45.9 (CH_2N), 39.8 (CH_2CHMe_2), 29.5 ($CH_2CH_2CH_2N$), 25.0 ($C(CH_3)_2$), 24.5 ($C(CH_3)_2$), 24.1 ($CHMe_2$), 23.5 (CH_2CH_2N), 22.9 ($CH(CH_3)_2$), 21.2 ($CH(CH_3)_2$); MS (ESI) m/z 426 [$(M\text{-}TFA+Na)^+$, 40], 404

[(M-TFA+H)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{22}H_{34}N_3O_4$ 404.2549 (M-TFA+H)$^+$, found 404.2379 (-3.1 ppm error).

Boc-Gly-Leu-Ala-Phe-OBn **9a**

Boc-Gly-OH (44 mg, 0.25 mmol) and TFA.H_2N-Leu-Ala-Phe-OBn (140 mg, 0.25 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (95:5, EtOAc:PE) to give Boc-Gly-Leu-Ala-Phe-OBn **9a** as a white solid (109 mg, 72%). R_F = 0.31 (95:5, EtOAc); mp 77.6-78.2 °C; $[\alpha]_D^{23}$ -22.5 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3278 (m), 3066 (w), 2957 (m), 1742 (m), 1711 (m) and 1634 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.30 (m, 5H, 3×ArCH + Phe-NH + Leu-NH), 7.28-7.23 (m, 2H, ArCH), 7.21-7.14 (m, 4H, 3×ArCH + Ala-NH), 7.07-7.00 (m, 2H, ArCH), 5.46 (br t, 1H, Gly-NH), 5.15 (d *J* 12.4 Hz, 1H, OCH_2Ph), 5.07 (d *J* 12.4 Hz, 1H, OCH_2Ph), 4.96-4.87 (m, 1H, Phe-NCH), 4.75-4.63 (m, 1H, Ala-NCH), 4.63-4.52 (m, 1H, Leu-NCH), 3.89-3.72 (m, 2H, Gly-NCH_2), 3.13 (dd *J* 13.9, 6.0 Hz, 1H, CH_2Ph), 3.04 (dd *J* 13.9, 6.0 Hz, 1H, CH_2Ph), 1.66-1.56 (m, 1H, C*H*Me_2), 1.58-1.49 (m, 2H, C*H*$_2$CHMe_2), 1.43 (s, 9H, $OC(CH_3)_3$), 1.32 (d *J* 7.0 Hz, 3H, NCHC*H*$_3$), 0.91 (d *J* 6.0 Hz, 3H, CH(C*H*$_3$)$_2$), 0.90 (d *J* 6.0 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2 (C=O), 171.9 (C=O), 171.3 (C=O), 169.4 (C=O), 156.2 (NC=O), 136.0 (ArC), 135.2 (ArC), 129.4 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 128.6 (ArCH), 127.1 (ArCH), 80.3 (O*C*Me_3), 67.3 (OCH_2Ph), 53.5 (Phe-NCH), 51.0 (Leu-NCH), 48.9 (Ala-NCH), 44.3 (Gly-NCH_2), 41.9 (*C*H$_2$CHMe_2), 37.9 (CH_2Ph), 28.4 (C(*C*H$_3$)$_3$), 23.1 (CH(*C*H$_3$)$_2$), 22.2 (*C*H(CH$_3$)$_2$), 18.6 (NCHC*H*$_3$); MS (ESI) m/z 619 [(M+Na)$^+$, 100]; HRMS (ESI) m/z calculated for $C_{32}H_{44}N_4NaO_7$ 619.3108 (M+Na)$^+$, found 619.3088 (2.7 ppm error).

Boc-Ala-Gly-Leu-Phe-OBn **9b**

Boc-Ala-OH (35 mg, 0.19 mmol) and TFA.H_2N-Gly-Leu-Phe-OBn (100 mg, 0.19 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (80:20, EtOAc:PE) to give Boc-Ala-Gly-Leu-Phe-OBn **9b** as a white powder (101

mg, 91%). R_F = 0.49 (80:20, EtOAc:PE); mp 119.4-120.8 °C; $[\alpha]_D^{23}$ -21.8 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3287 (m), 2961 (w), 1718 (m), 1643 (s), 1564 (m) and 1510 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.34 (m, 3H, ArH), 7.30-7.27 (m, 2H, ArH), 7.24-7.20 (m, 3H, ArH), 7.06-7.04 (m, 2H, ArH), 6.79 (t *J* 6.2 Hz, 1H, Gly-NH), 6.76 (br d, 1H, Phe-NH), 6.70 (d *J* 6.3 Hz, Leu-NH), 5.16 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.09 (d *J* 12.0 Hz, 1H, OCH_2Ph), 5.08 (br, 1H, Ala-NH), 4.87 (dd *J* 14.0, 6.4 Hz, 1H, Phe-NCH), 4.43 (dt, *J* 14.0, 8.8 Hz, 1H, Leu-NCH), 4.07 (quin, *J* 6.9 Hz, 1H, Ala-NCH), 3.99 (dd *J* 14.0, 6.4 Hz, 1H, Gly-NCH_2), 3.79 (dd *J* 16.8, 5.2 Hz, 1H, Gly-NCH_2), 3.15 (dd *J* 14.0, 6.0 Hz, 1H, CH_2Ph), 3.06 (dd *J* 14.0, 6.8 Hz, 1H, CH_2Ph), 1.69-1.52 (m, 2H, CH_2CHMe_2), 1.50-1.37 (m, 1H, $CHMe_2$), 1.44 (s, 9H, $OC(CH_3)_3$), 1.32 (d *J* 6.8 Hz, 3H, $NCHCH_3$), 0.87 (d *J* 6.8 Hz, 3H, $CH(CH_3)_2$), 0.85 (d *J* 6.8 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7 (C=O), 171.8 (C=O), 171.5 (C=O), 169.0 (C=O), 155.8 (NC=O), 136.0 (ArC), 135.2 (ArC), 129.5 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 128.5 (ArCH), 127.0 (ArCH), 77.4 ($OCMe_3$), 67.4 (OCH_2Ph), 53.4 (Phe-NCH), 52.0 (Leu-NCH), 50.7 (Ala-NCH), 43.3 (Gly-NCH_2), 40.1 (CH_2CHMe_2), 37.9 (CH_2Ph), 28.5 ($OC(CH_3)_3$), 24.8 ($CHMe_2$), 22.9 ($CH(CH_3)_2$), 22.1 ($CH(CH_3)_2$), 18.3 ($NCHCH_3$); MS (ESI) m/z 619 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{32}H_{44}N_4NaO_7$ 619.3108 $(M+Na)^+$, found 619.3098 (1.0 ppm error).

Boc-Lys(Z)-Ser(OBn)-Met-Val-OBn **9c**

Boc-Lys(Z)-OH (61 mg, 0.16 mmol) and TFA.H_2N-Ser(OBn)-Met-Val-OBn (100 mg, 0.16 mmol) were coupled according to the general coupling procedure. The residue was then purified using flash column chromatography (60:40-70:30, EtOAc:PE) to give Boc-Lys(Z)-Ser(OBn)-Met-Val-OBn **9c** as a white solid (91 mg, 65%). R_F = 0.44 (70:30, EtOAc:PE); mp 75.4-75.9 °C; $[\alpha]_D^{23}$ -23.77 (*c* 1.0 in MeOH); IR (Neat) ν_{max} 3282 (w), 2930 (w), 1689 (m), 1635 (s) and 1519 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d *J* 8.3 Hz, 1H, Met-NH), 7.40-7.21 (m, 15H, ArH), 7.06-6.93 (m, 2H, Ser-NH + Val-NH), 5.64 (d *J* 3.2 Hz, 1H, Lys-NH), 5.18 (d *J* 11.8 Hz, 1H, CO_2CH_2Ph), 5.15-5.04 (m, 4H, Lys-ε-NH + 3× CO_2CH_2Ph), 4.69 (dt *J* 8.6, 5.1 Hz, 1H, Met-NCH),

4.54 (d *J* 11.7 Hz, 1H, OCH_2Ph), 4.51 (d *J* 11.7 Hz, 1H, OCH_2Ph), 4.51-4.42 (m, 2H, Val-NCH, Ser-NCH), 4.07-3.99 (m, 1H, CH_2OBn), 3.96-3.88 (m, 1H, Lys-NCH), 3.59 (dd, *J* 9.5, 4.6 Hz, 1H, CH_2OBn), 3.30-3.09 (m, 2H, CH_2NH), 2.51 (t *J* 7.5 Hz, 2H, CH_2SMe), 2.37-2.23 (m, 1H, CH_2CH_2SMe), 2.20-2.10 (m, 1H, $CHMe_2$), 2.04 (s, 3H, SCH_3), 1.97-1.79 (m, 2H, CH_2CH_2SMe + $(CH_2)_3$), 1.74-1.61 (m, 1H, $(CH_2)_3$), 1.56-1.36 (m, 4H, $(CH_2)_3$), 1.35 (s, 9H, $OC(CH_3)_3$), 0.90 (d *J* 6.9 Hz, $CH(CH_3)_2$), 0.89 (d *J* 6.6 Hz, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6 (C=O), 171.4 (C=O), 171.1 (C=O), 170.0 (C=O), 157.3 (C=O), 156.8 (NC=O), 137.3 (ArC), 136.5 (ArC), 135.7 (ArC), 128.7 (ArCH), 128.6 (ArCH), 128.4 (ArCH), 128.3 (ArCH), 128.2 (ArCH), 128.1 (ArCH), 128.0 (ArCH), 80.9 ($-OCMe_3$), 73.6 (OCH_2Ph), 69.0 (CH_2OBn), 66.9 ($2\times CO_2CH_2Ph$), 57.7 (Val-NCH), 55.9 (Lys-NCH), 54.0 (Ser-NCH), 52.7 (Met-NCH), 39.0 ($(CH_2)_4$), 31.1 ($(CH_2)_4$), 31.0 ($CHMe_2$), 30.5 ($(CH_2)_4$), 30.5 (CH_2SMe), 29.7 (CH_2CH_2SMe), 28.3 ($-OC(CH_3)_3$), 22.4 ($(CH_2)_4$), 19.1 ($CH(CH_3)_2$), 18.1 ($CH(CH_3)_2$), 15.2 (SCH_3); MS (ESI) m/z 900 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{46}H_{63}N_5NaO_{10}S$ 900.4193 $(M+Na)^+$, found 900.4188 (0.1 ppm error).

Boc-Gln(Trt)-Trp-Asp(OBn)-Val-OBn **9d**

Boc-Gln(Trt)-OH (137 mg, 0.28 mmol) and TFA.H_2N-Trp-Asp(OBn)-Val-OBn (200 mg, 0.28 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (50:50, EtOAc:PE) to give Boc-Gln(Trt)-Trp-Asp(OBn)-Val-OBn **9d** as an off white solid (166 mg, 78%). R_F = 0.23 (44:55, EtOAc:PE); mp 78.7-79.4 °C; $[\alpha]_D^{23}$ -27.4 (*c* 0.5 in MeOH); IR (Neat) ν_{max} 3301 (m), 2967 (w), 1666 (s) and 1513 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (s, 1H, NH), 7.54 (d *J* 8.0 Hz, 1H, ArH), 7.38-6.97 (m, 31H, 29×ArH + NH + Asp-NH), 6.93 (d *J* 7.1 Hz, 1H, Val-NH), 6.86 (d *J* 2.4 Hz, 1H, Trp-NH), 5.60 (d *J* 4.9 Hz, 1H, Gln-NH), 5.18 (d *J* 12.2 Hz, 1H, $-OCH_2Ph$), 5.10 (d *J* 12.2 Hz, 1H, $-OCH_2Ph$), 4.98 (s, 2H, $-OCH_2Ph$), 4.79-4.75 (m, 1H, Asp-NCH), 4.56 (dt *J* 6.3, 6.0 Hz, 1H, Trp-NCH), 4.42 (dd *J* 8.7, 4.5 Hz, 1H, Val-NCH), 3.91 (dd *J* 6.2, 6.0 Hz, 1H, Gln-NCH), 3.30 (dd *J* 15.1, 6.2 Hz, 1H, Trp-CH_2), 3.09 (dd

J 14.5, 6.2 Hz, 1H, Trp-CH_2), 2.49 (dd *J* 16.7, 4.5 Hz, 1H, Gln-CH_2CO), 2.41-2.20 (m, 3H, 1×Gln-CH_2CO, 2× CH_2CO_2Bn), 2.12 (oct *J* 6.7 Hz, 1H, $CHMe_2$), 2.05-1.83 (m, 2H, Gln-CH_2CH_2CO), 1.34 (s, 9H, OC(CH_3)$_3$), 0.85 (d *J* 6.8 Hz, 3H, CH(CH_3)$_2$), 0.82 (d *J* 6.8 Hz, 3H, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1 (C=O), 171.6 (C=O), 171.5 (C=O), 171.3 (C=O), 170.3 (C=O), 156.1 (NC=O), 144.6 (ArC), 136.2, (ArC), 136.2 (ArC), 135.7 (ArC), 128.8 (ArCH), 128.7 (ArC), 128.6 (ArCH), 128.4 (ArCH), 128.4 (ArCH), 128.1 (ArCH), 127.3 (ArCH), 127.3 (ArCH), 123.8 (ArCH), 122.3 (ArCH), 119.8 (ArCH), 118.9 (ArCH), 111.3 (ArCH), 109.6 (ArC), 80.2 ($OCMe_3$), 70.9 (CPh_3), 66.9 (OCH_2Ph), 66.7 (OCH_2Ph), 57.8 (Val-NCH), 54.6 (Gln-NCH), 54.2 (Asp-NCH), 49.4 (Trp-NCH), 35.2 (Trp-CH_2), 33.4 (CH_2CH_2CO), 31.0 ($CHMe_2$), 28.5 (CH_2CH_2CO); 28.4 (C(CH_3)$_3$), 27.1 (CH_2CO_2Bn), 19.1 (CH(CH_3)$_2$), 17.8 (CH(CH_3)$_2$); MS (ESI) m/z 1091 [$(M+Na)^+$, 100]; HRMS (ESI) m/z calculated for $C_{63}H_{68}N_6NaO_{10}$ 1091.4895 $(M+Na)^+$, found 1091.4889 (-0.7 ppm error).

Boc-Tyr(OBn)-Pro-Aib-Leu-OBn **9e**

Boc-Pro-OH (71 mg, 0.19 mmol) and TFA.H_2N-Pro-Aib-Leu-OBn (100 mg, 0.19 mmol) were coupled according to the general coupling procedure. The residue was purified using flash column chromatography (5:95, MeOH:CH_2Cl_2) to give Boc-Tyr(OBn)-Pro-Aib-Leu-OBn **9e** as a white powder (105 mg, 72%). R_F = 0.21, (4:96, MeOH:CH_2Cl_2); mp 117.0-117.8 °C; $[\alpha]_D^{23}$ -23.0 (*c* 0.5, in MeOH); IR (Neat) ν_{max} 3318 (w), 2957 (w), 1731 (m), 1682 (s), 1634 (s) and 1510 (s) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, 80°C): δ = 7.81 (s, 1H, Aib-NH), 7.47-7.27 (m, 11H, 10×ArH, + Leu-NH), 7.21-7.10 (m, 2H, ArH), 6.93-6.86 (m, 2H, ArH), 6.38 (br, 1H, Tyr-NH), 5.12 (s, 2H, OCH_2Ph), 5.07 (s, 2H, OCH_2Ph), 4.41-4.29 (m, 3H, 3×NCH), 3.70-3.59 (m, 1H, CH_2N), 3.48-3.88 (m, 1H, CH_2N), 2.96-2.68 (m, 2H, Tyr-CH_2), 2.09-1.93 (m, 2H, C$H_2CH_2CH_2N$), 1.91-1.78 (m, 1H, CH_2CH_2N), 1.66-1.49 (m, 4H, 1×CH_2CH_2N + CH_2CHMe_2), 1.41 (s, 3H, C(CH_3)$_2$), 1.36 (s, 3H, C(CH_3)$_2$), 1.31 (s, 9H, OC(CH_3)$_3$), 0.85 (d *J* 5.9 Hz, 3H, CH(CH_3)$_2$), 0.83 (d *J* 5.9 Hz, 3H,

CH(CH_3)$_2$); ^{13}C NMR (100 MHz, DMSO-d$_6$, 80°C): δ = 173.9 (C=O), 172.2 (C=O), 171.1 (C=O), 170.5 (C=O), 156.9 (NC=O), 155.2 (ArC), 137.2 (CAr), 135.9 (ArC), 130.4 (ArCH), 129.8 (ArC), 128.4 (ArCH), 128.0 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 127.6 (ArCH), 127.5 (ArCH), 114.4 (ArCH), 78.1 (-OCMe$_3$), 69.1 (OCH$_2$Ph), 65.8 (OCH$_2$Ph), 60.1 (NCH), 55.9 (NCH), 54.0 (NCH), 50.7 (NCMe$_2$), 49.9 (CH$_2$N), 39.6 (*C*H$_2$CH$_2$CH$_2$N), 35.5 (Tyr-CH$_2$), 28.7 (*C*H$_2$CHMe$_2$), 28.2 (*C*HMe$_2$), 28.1 (OC(*C*H$_3$)$_3$), 25.9 (C(*C*H$_3$)$_2$), 24.8 (CH$_2$*C*H$_2$CH$_2$N), 24.1 (OC(*C*H$_3$)$_2$), 22.5 (CH(*C*H$_3$)$_2$), 21.8 (CH(*C*H$_3$)$_2$); MS (ESI) m/z 779 [(M+Na)$^+$, 100]; HRMS (ESI) m/z calculated for C$_{43}$H$_{56}$N$_4$NaO$_8$ 779.3996 (M+Na)$^+$, found 779.4010 (-2.4 ppm error).

Boc-Leu-Ala-Phe-OH **10a**[S11]

A solution of Boc-Leu-Ala-Phe-OBn (325 mg, 0.6 mmol, 1.0 eq) in methanol (5 mL) was added to a suspension of Pd/C (10% w/w) in methanol (5 mL) under H_2 (1 Bar). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was then filtered through a short plug of celite® and concentrated *in vacuo* to give Boc-Leu-Ala-Phe-OH **10a** as an off-white solid (258 mg, 96%). Mp 82.4-83.1 °C; $[\alpha]_D^{23}$ -13.5 (*c* 1.0, in MeOH); IR (Neat) ν_{max} 3300 (m), 2958 (m), 1644 (s) and 1514 (m) cm^{-1}; ^{1}H NMR (400 MHz, CD$_3$OD): δ = 7.24-7.13 (m, 5H, ArH), 4.58 (dd *J* 7.6, 5.3 Hz, 1H, Leu-NCH), 4.33 (dt *J* 7.1, 6.8 Hz, 1H, Phe-NCH), 4.10-4.01 (m, 1H, Ala-NCH), 3.15 (dd *J* 13.9, 5.4 Hz, 1H, CH$_2$Ph), 2.97 (dd *J* 13.9, 5.4 Hz, 1H, CH$_2$Ph), 1.64 (sept, *J* 6.7 Hz, 1H, C*H*Me$_2$), 1.45 (t *J* 7.2 Hz, 2H, C*H*$_2$CHMe$_2$), 1.40 (s, 9H, OC(CH$_3$)$_3$), 1.28 (d *J* 7.1 Hz, 3H, NCHC*H*$_3$), 0.90 (d, *J* 6.7 Hz, 3H, CH(C*H*$_3$)$_2$), 0.88 (d *J* 6.7 Hz, 3H, CH(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, CD$_3$OD): δ = 175.3 (C=O), 174.5 (C=O), 174.4 (C=O), 157.9 (NC=O), 138.2 (ArC), 130.4 (ArCH), 129.4 (ArCH), 127.8 (ArCH), 80.6 (O*C*Me$_3$), 55.2 (Leu-NCH), 54.3 (Ala-NCH), 50.1 (Phe-NCH), 42.1 (*C*H$_2$CHMe$_2$), 38.4 (CH$_2$Ph), 28.7 (OC(*C*H$_3$)$_3$), 25.9 (CHMe$_2$), 23.5 (CH(*C*H$_3$)$_2$), 21.8 (CH(*C*H$_3$)$_2$), 18.4 (NCH*C*H$_3$); MS (ESI) m/z 472 [(M+Na)$^+$, 100]; HRMS (ESI) m/z calculated for C$_{23}$H$_{35}$N$_3$NaO$_6$ 472.2424 (M+Na)$^+$, found 472.2413 (1.2 ppm error).

TFA.H-Leu-Ala-Phe-OH **11a**[S12]

Acid **10a** (90 mg, 0.2 mmol) was deprotected according to the general procedure for Boc deprotections to give TFA.H-Leu-Ala-Phe-OH **11a** as a white solid (90 mg, 97%). Mp 189.6-191.4 °C; IR (Neat) ν_{max} 3265 (w), 3036 (w), 3967 (w), 2401 (w), 2344 (w), 1735 (m), 1646 (s), 1555 (w) and 1514 (w) cm^{-1}; ^1H NMR (400 MHz, TFA-d): δ = 7.20-7.09 (m, 3H, ArH), 7.07-7.00 (m, 2H, ArH), 5.01-4.85 (m, 1H, Phe-NCH), 4.65-4.48 (m, 1H, Ala-NCH), 4.28-4.12 (m, 1H, Leu-NCH), 3.23 (dd *J* 14.3, 4.3 Hz, 1H, CH_2Ph), 3.01 (dd *J* 14.3, 8.5 Hz, 1H, CH_2Ph), 1.78-1.51 (m, 3H, Leu-CH_2CHMe_2), 1.32 (d *J* 6.3 Hz, 3H, NCHCH_3), 0.87 (d *J* 6.0 Hz, 3H, CH(CH_3)$_2$), 0.85 (d *J* 6.0 Hz, 3H, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, TFA-d): δ = 178.9 (C=O), 176.0 (C=O), 172.1 (C=O), 136.6 (ArC), 131.0 (ArCH), 131.0 (ArCH), 129.9 (ArCH), 56.2 (Phe-NCH), 55.8 (Leu-NCH), 52.5 (Ala-NCH), 42.4 (CH_2CHMe_2), 39.0 (CH_2Ph), 26.5 (CH_2CHMe_2), 23.2 (CH(CH_3)$_2$), 22.2 (CH(CH_3)$_2$), 18.8 (NCHCH_3); MS (ESI) m/z 372 [$(M+Na)^+$, 20], 350 [$(M+H)^+$, 100]; HRMS (ESI) m/z calculated for $C_{18}H_{28}N_3O_4$ 350.2080 $(M+Na)^+$, found 350.2076 (-0.8 ppm error).

Solid phase synthesis of TFA.H-Leu-Ala-Phe-OH **11a**

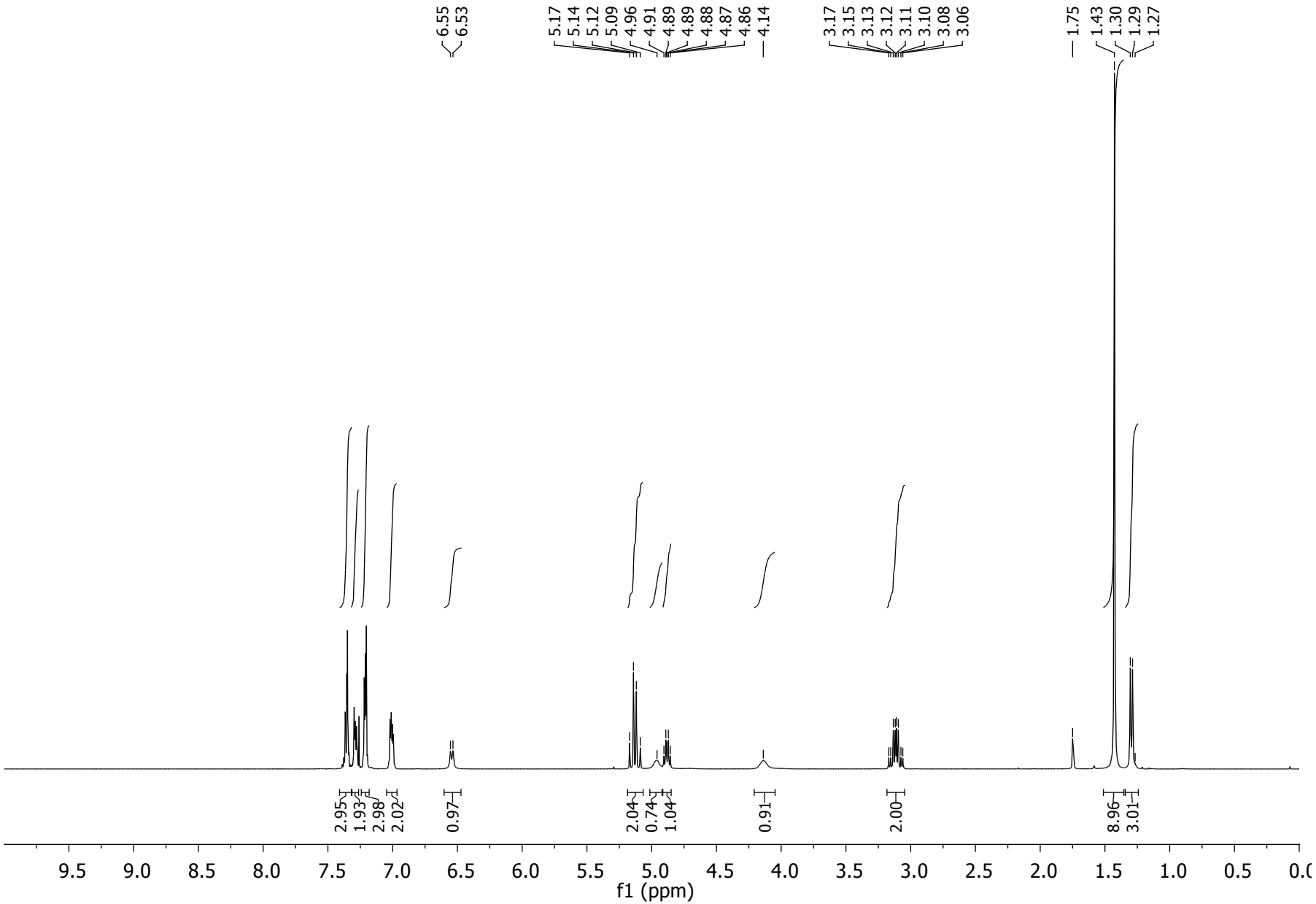
This tripeptide was prepared using the general method for solid phase synthesis starting with ChemMatrix-HMPB-Phe-H resin and adding Fmoc-amino acids in the sequence Fmoc-Ala-OH then Fmoc-Leu-OH. TFA.H-Leu-Ala-Phe-OH **11a** prepared in this way had identical analytical data to that prepared by solution phase synthesis.

Solid phase synthesis of Bradykinin

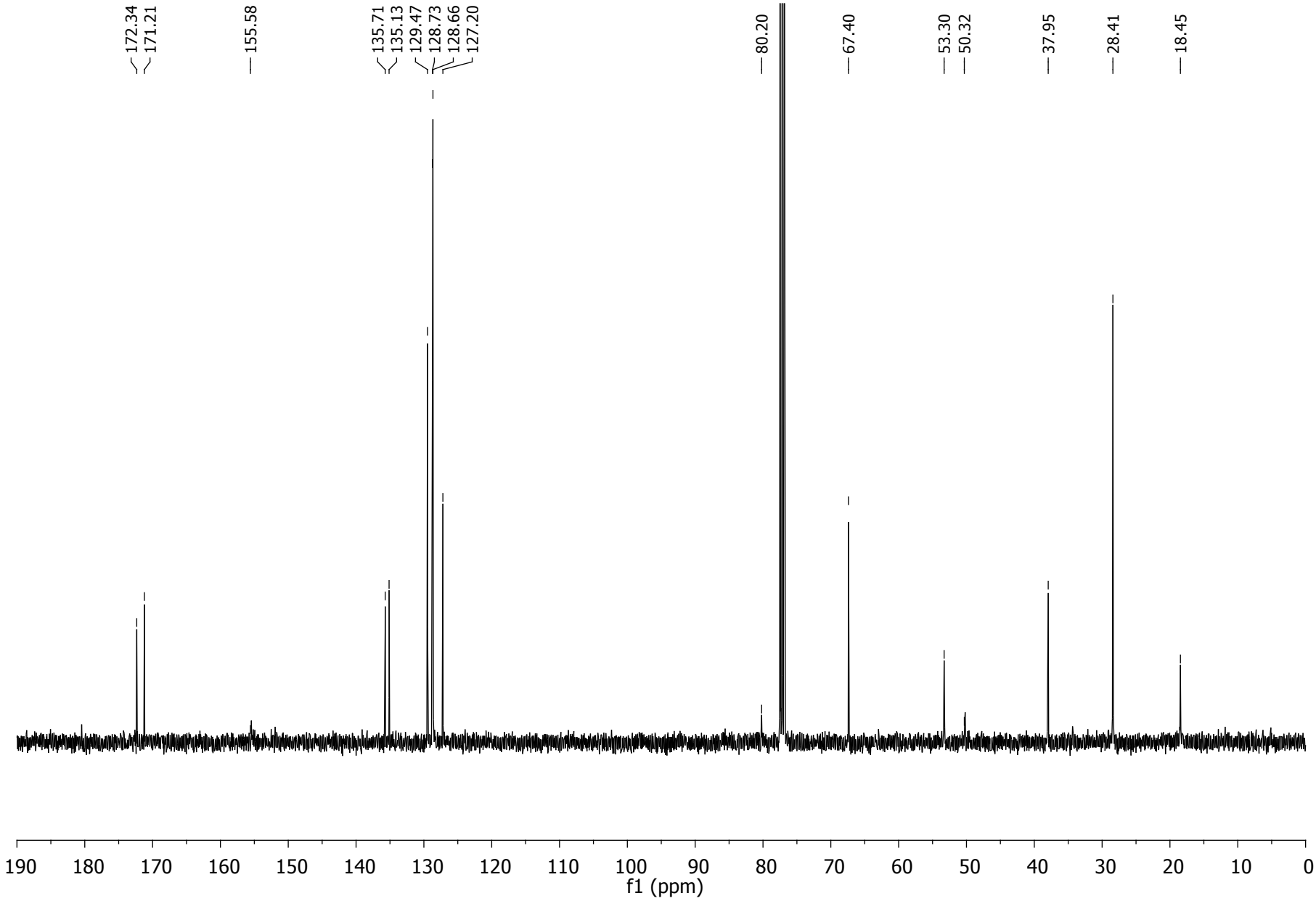
This nonapeptide was prepared using the general method for solid phase synthesis using ChemMatrix-HMPB-Arg(pbf)-H resin and adding Fmoc-amino acids in the sequence Fmoc-Phe-OH, Fmoc-Pro-OH, Fmoc-Ser(Bn)-OH, Fmoc-Phe-OH, Fmoc-Gly-OH, Fmoc-Pro-OH, Fmoc-Pro-OH and Fmoc-Arg(pbf)-OH. After each step, successful coupling or deprotection was confirmed using either the chloranil or Kaiser colormetric tests. After cleavage from the resin, the peptide was

precipitated into cold Et_2O, triturated (3×20 mL Et_2O) and lyophilized to give Bradykinin as a white powder. Reverse phase HPLC retention time 11.8 minutes. MS (ESI) m/z 1060.6 $(M+H)^+$, 710.4, 642.3, 555.3, 530.8 $(M+2H)^{2+}$; HRMS (ESI) m/z calculated for $C_{50}H_{75}N_{15}O_{11}$ 530.787976 $(M+2H)^{2+}$, found 530.786911 (-2.0 ppm error).

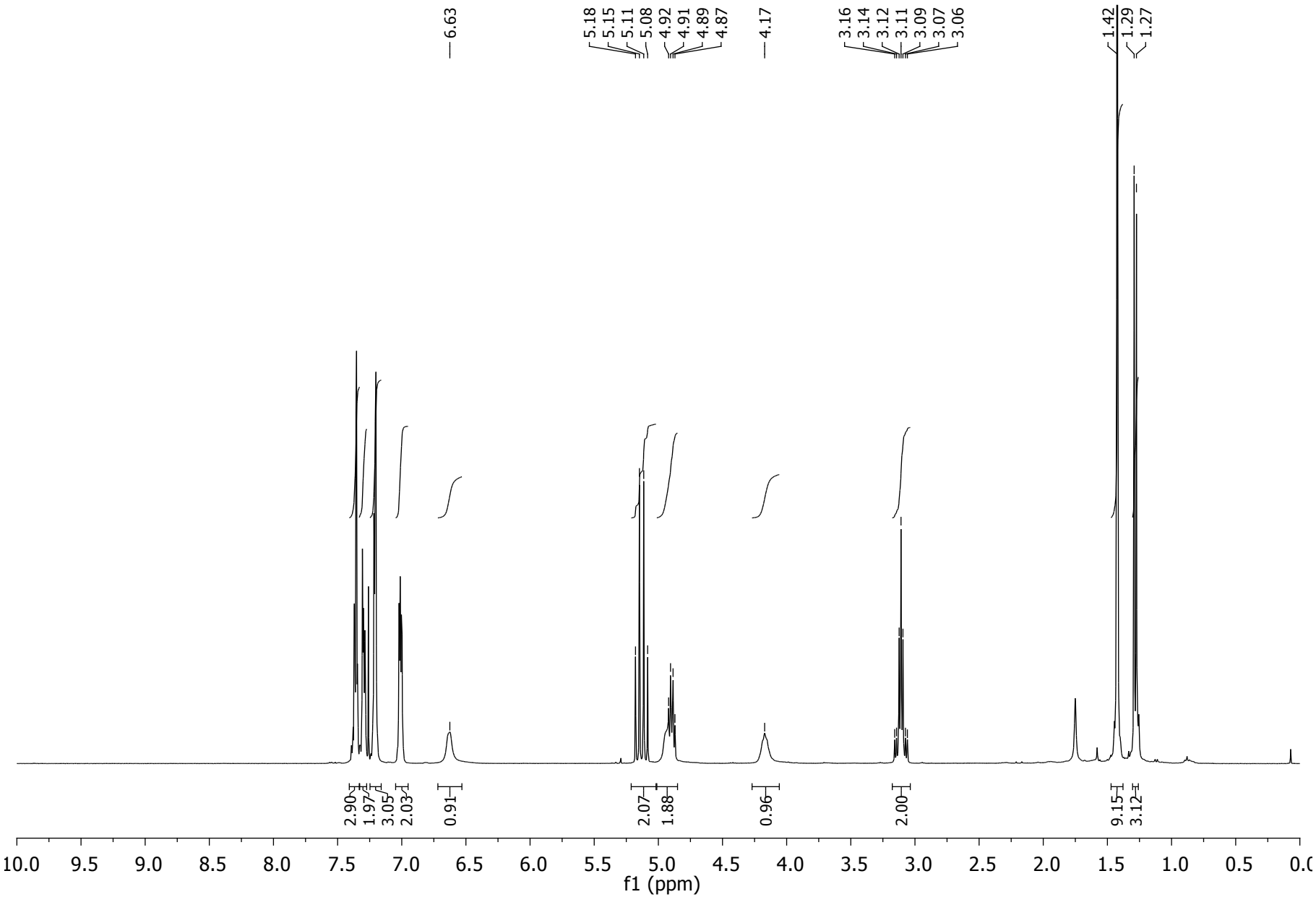
^{1}H NMR spectrum of Boc-Ala-Phe-OBn 5a



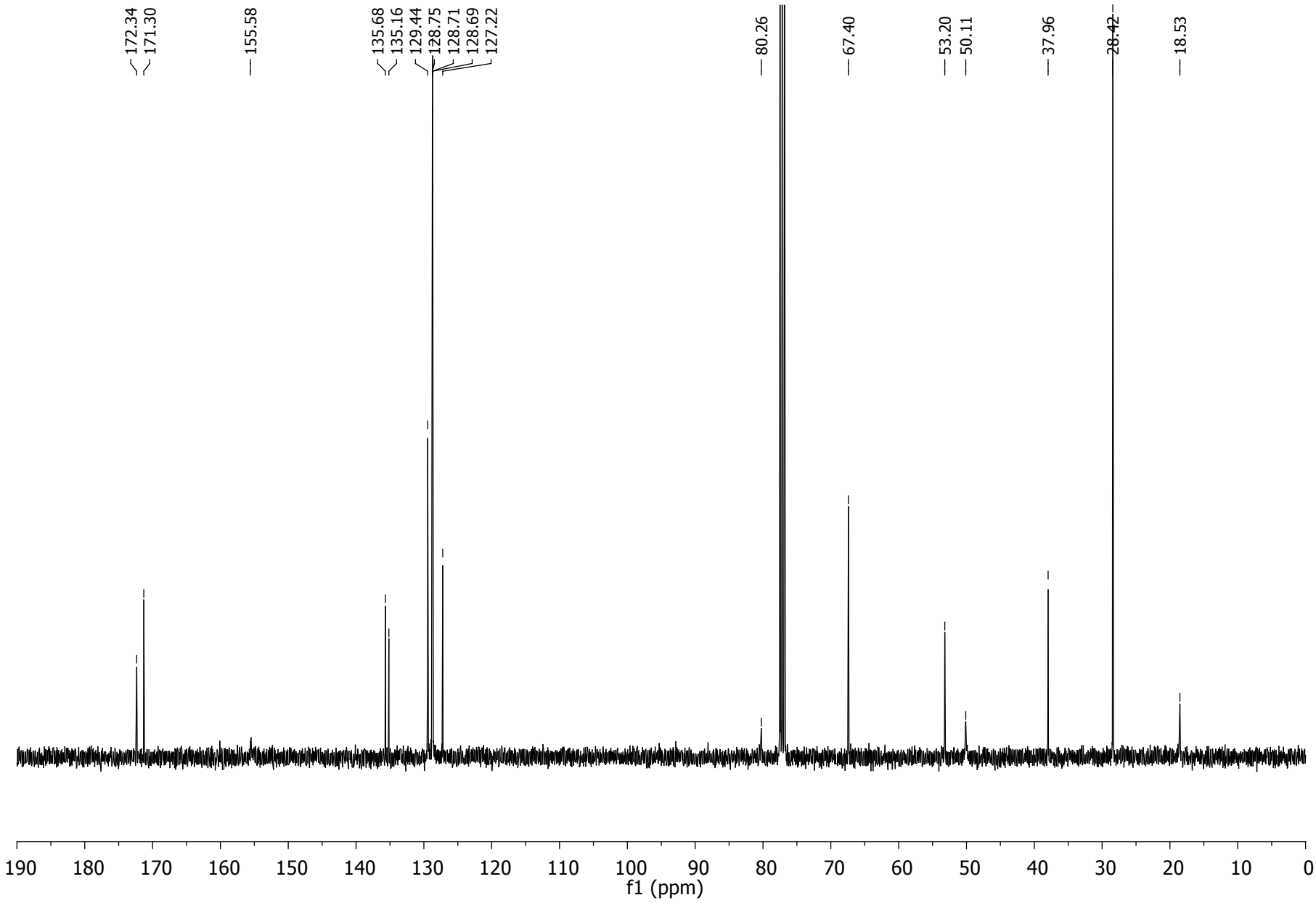
^{13}C NMR spectrum of Boc-Ala-Phe-OBn 5a



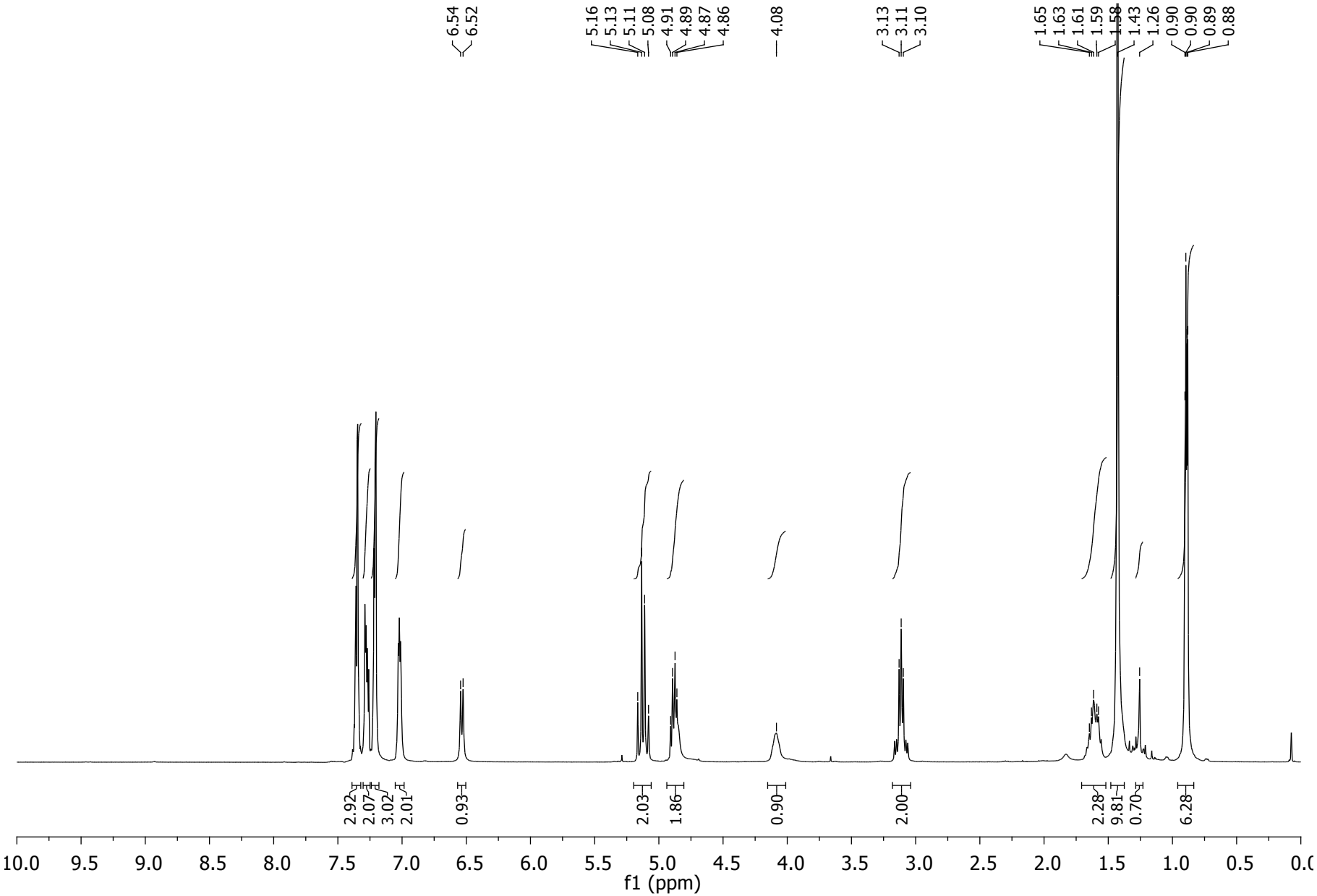
^{1}H NMR spectrum of Boc-(*R*)-Ala-Phe-OBn 5a'



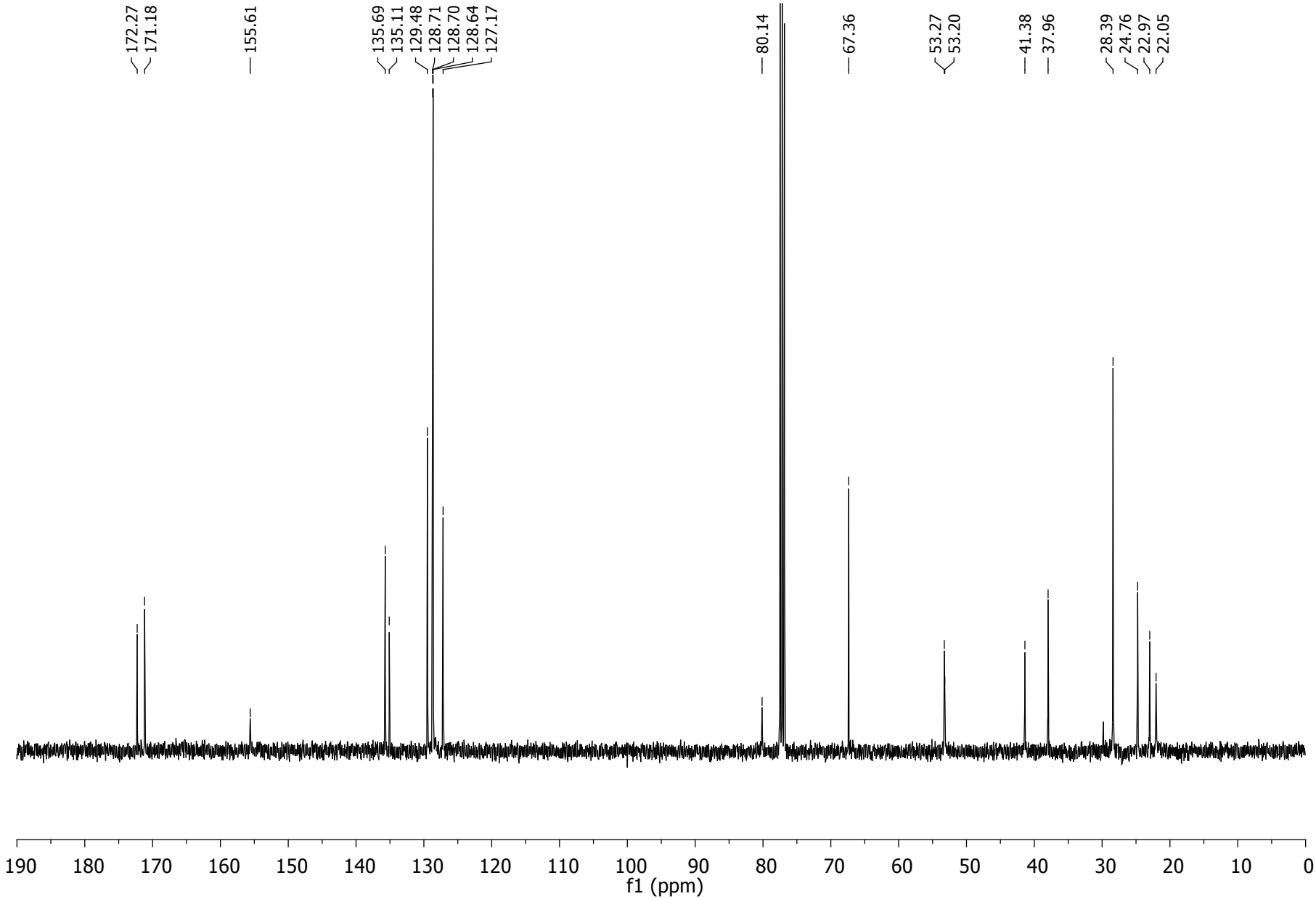
^{13}C NMR spectrum of Boc-(*R*)-Ala-Phe-OBn 5a'



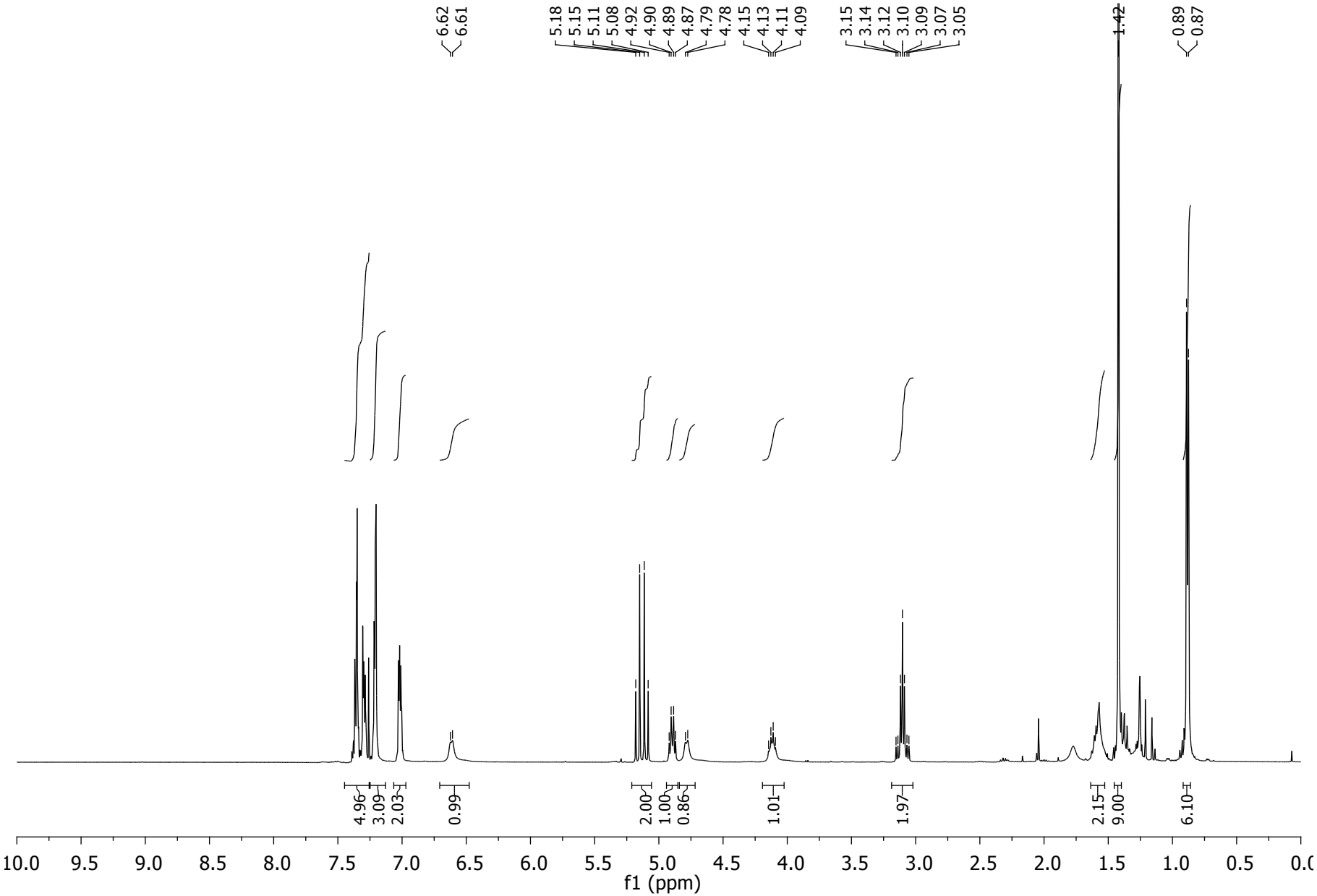
^{1}H NMR spectrum of Boc-Leu-Phe-OBn 5b



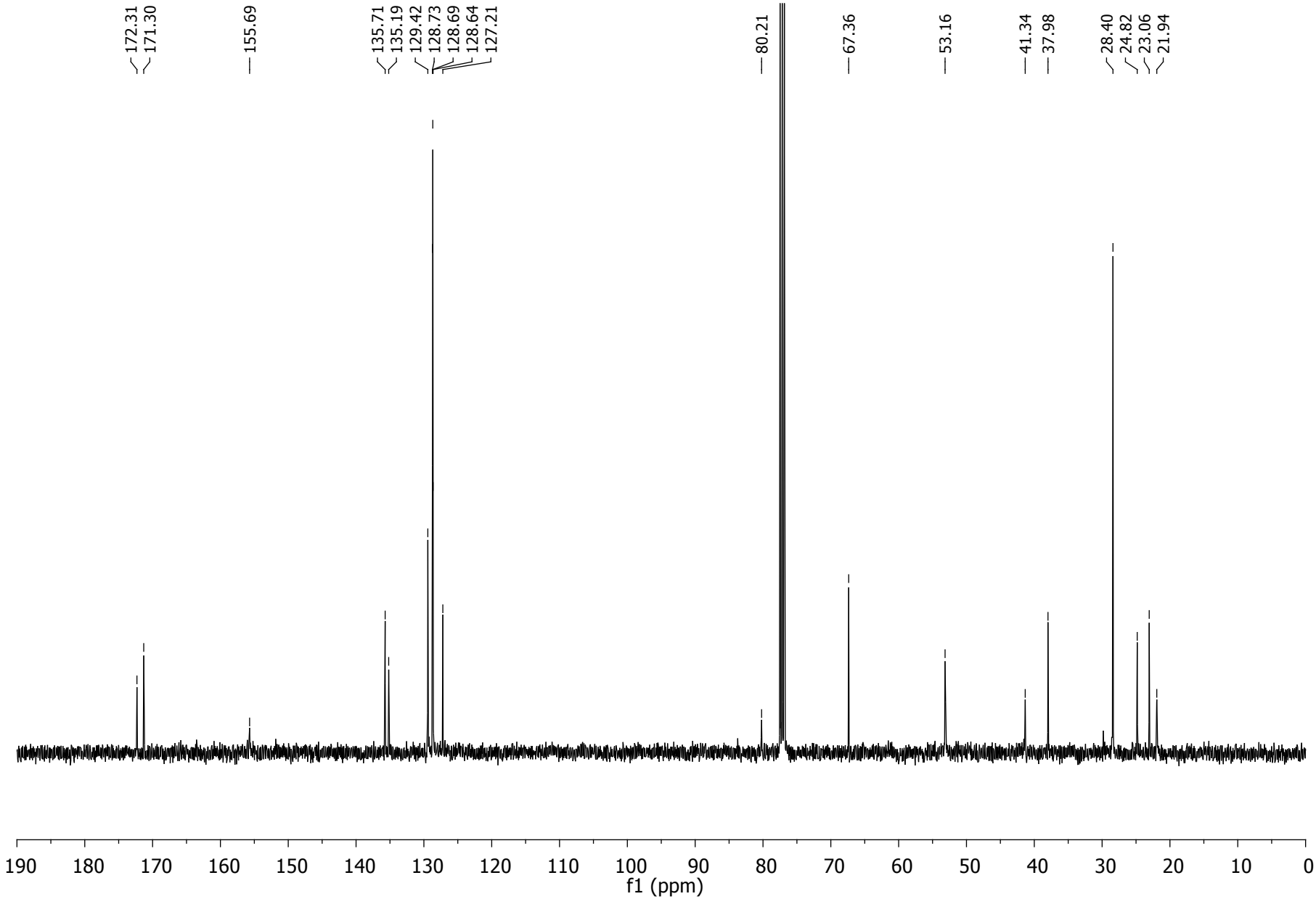
^{13}C NMR spectrum of Boc-Leu-Phe-OBn 5b



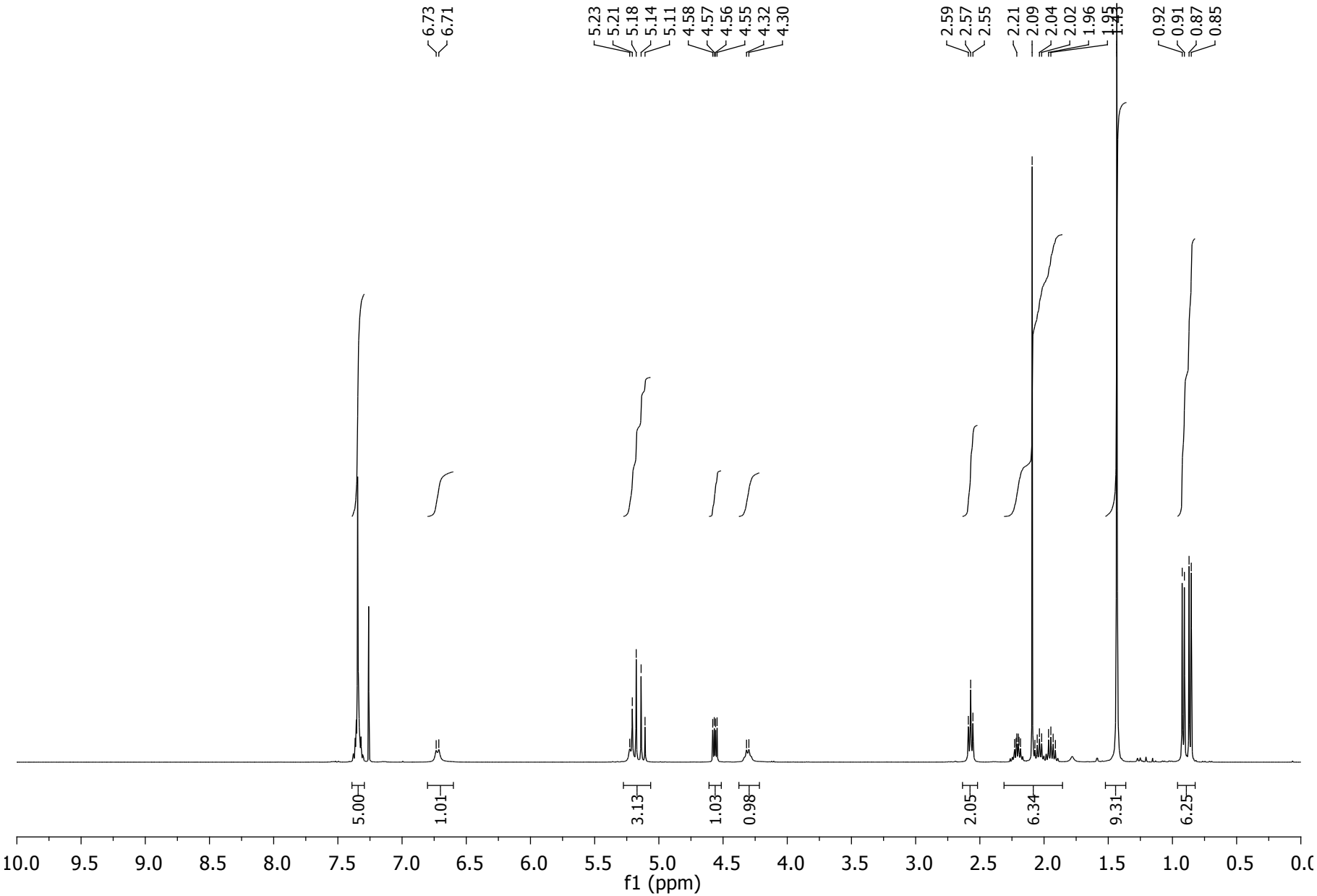
^{1}H NMR spectrum of Boc-(R)-Leu-Phe-OBn 5b'



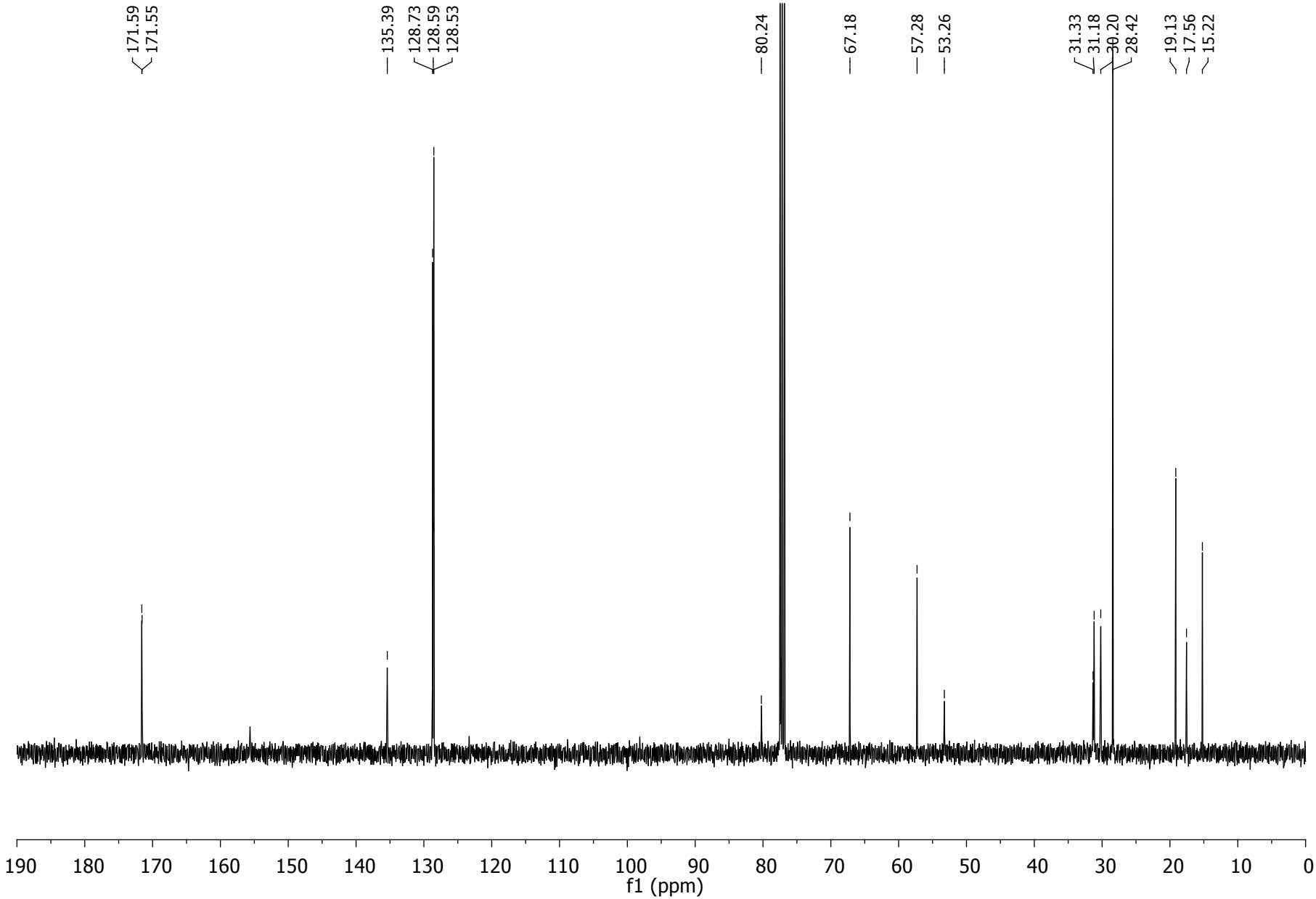
^{13}C NMR spectrum of Boc-(R)-Leu-Phe-OBn 5b'



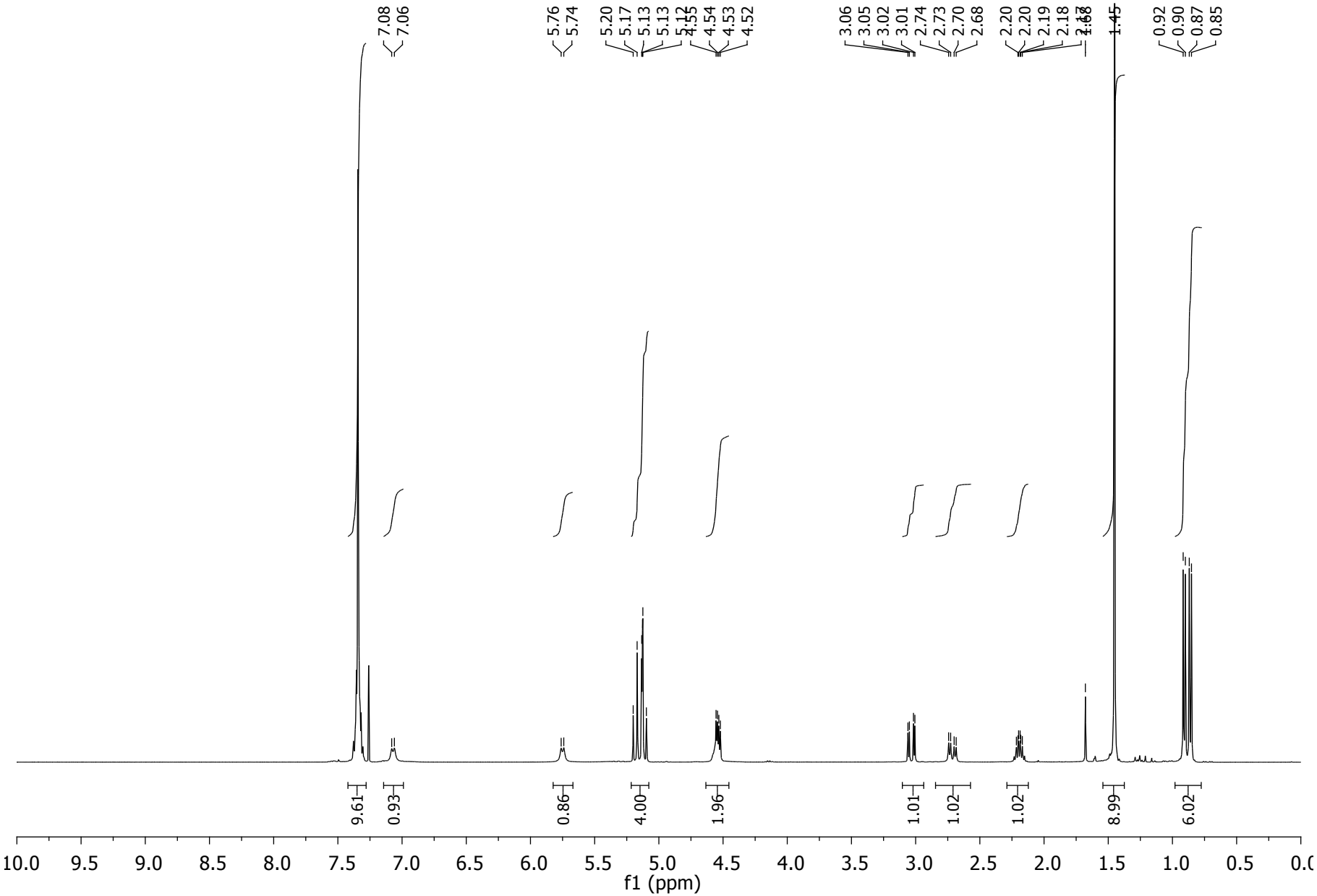
^{1}H NMR spectrum of Boc-Met-Val-OBn 5c



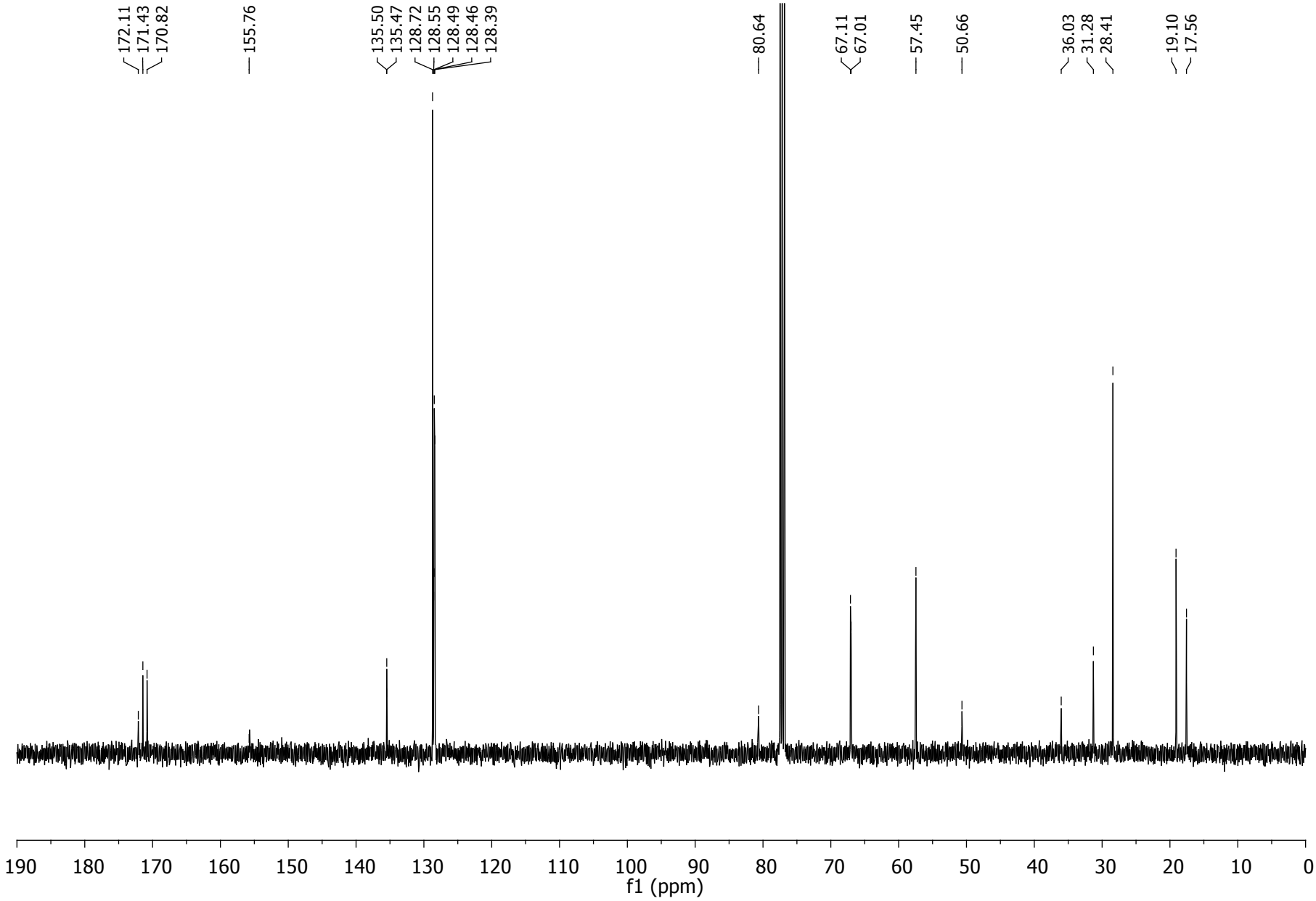
^{13}C NMR spectrum of Boc-Met-Val-OBn 5c



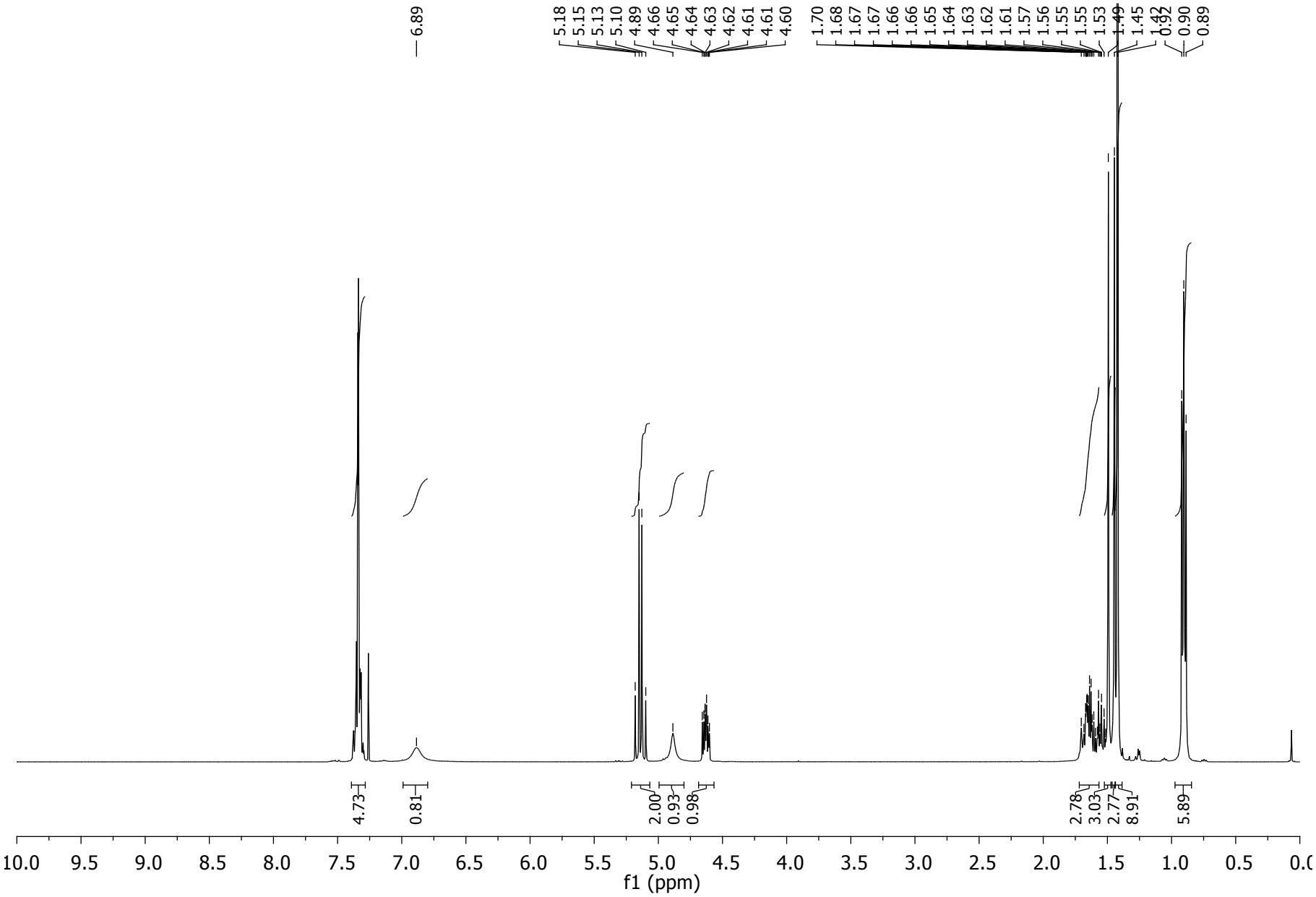
^{1}H NMR spectrum of Boc-Asp(OBn)-Val-OBn 5d



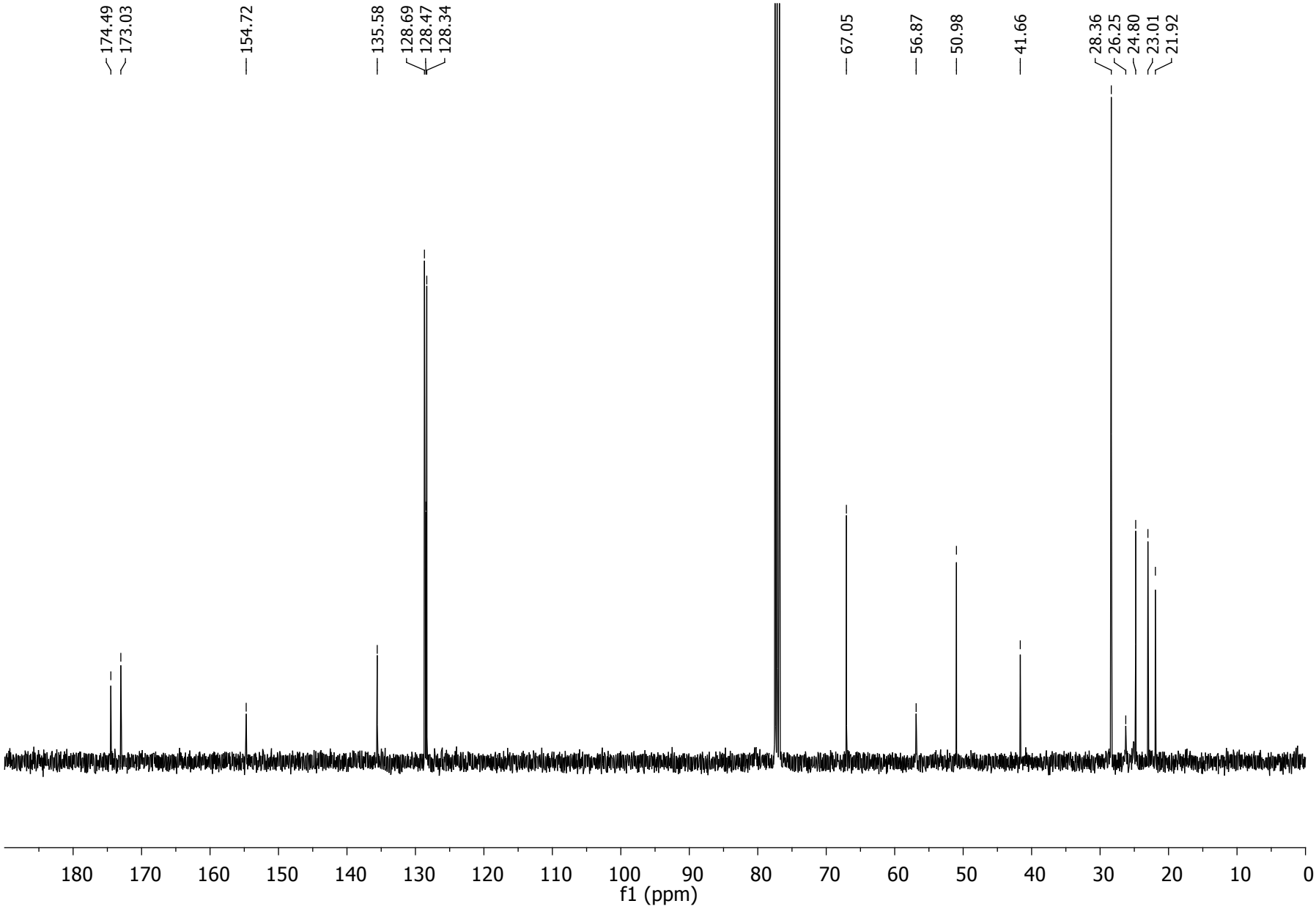
^{13}C NMR spectrum of Boc- Asp(OBn)-Val-OBn 5d



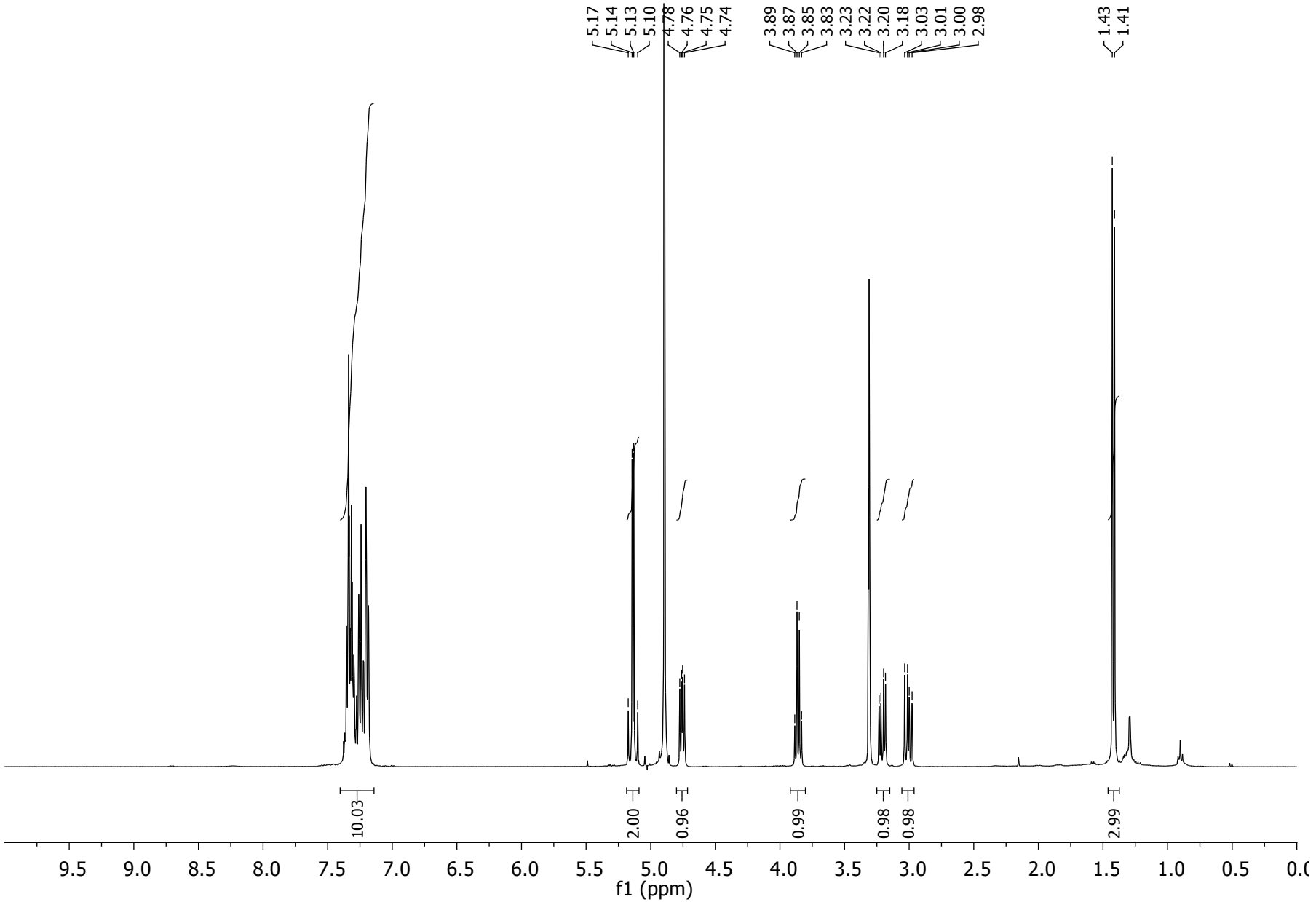
^{1}H NMR spectrum of Boc-Aib-Leu-OBn 5e



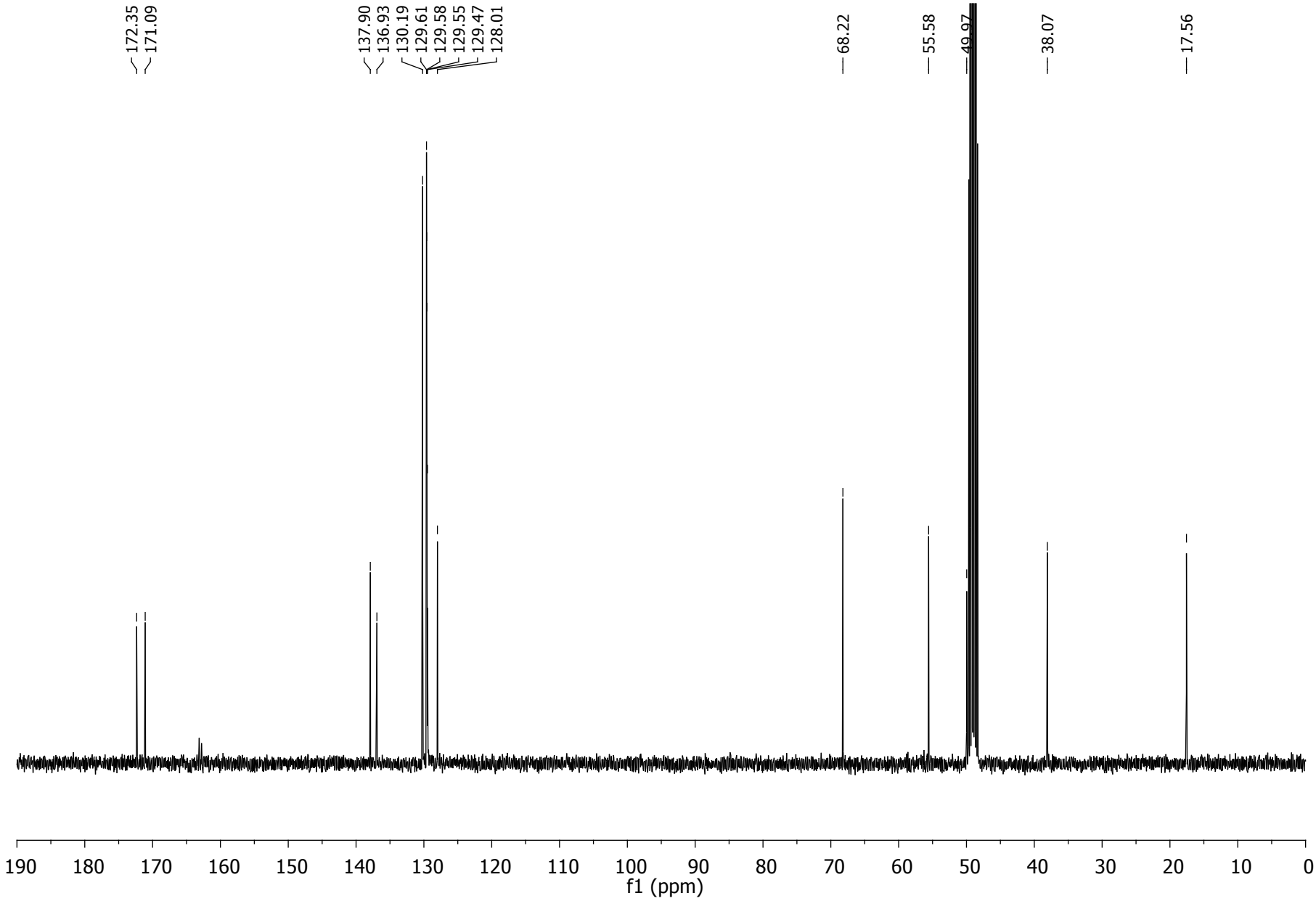
^{13}C NMR spectrum of Boc-Aib-Leu-OBn 5e



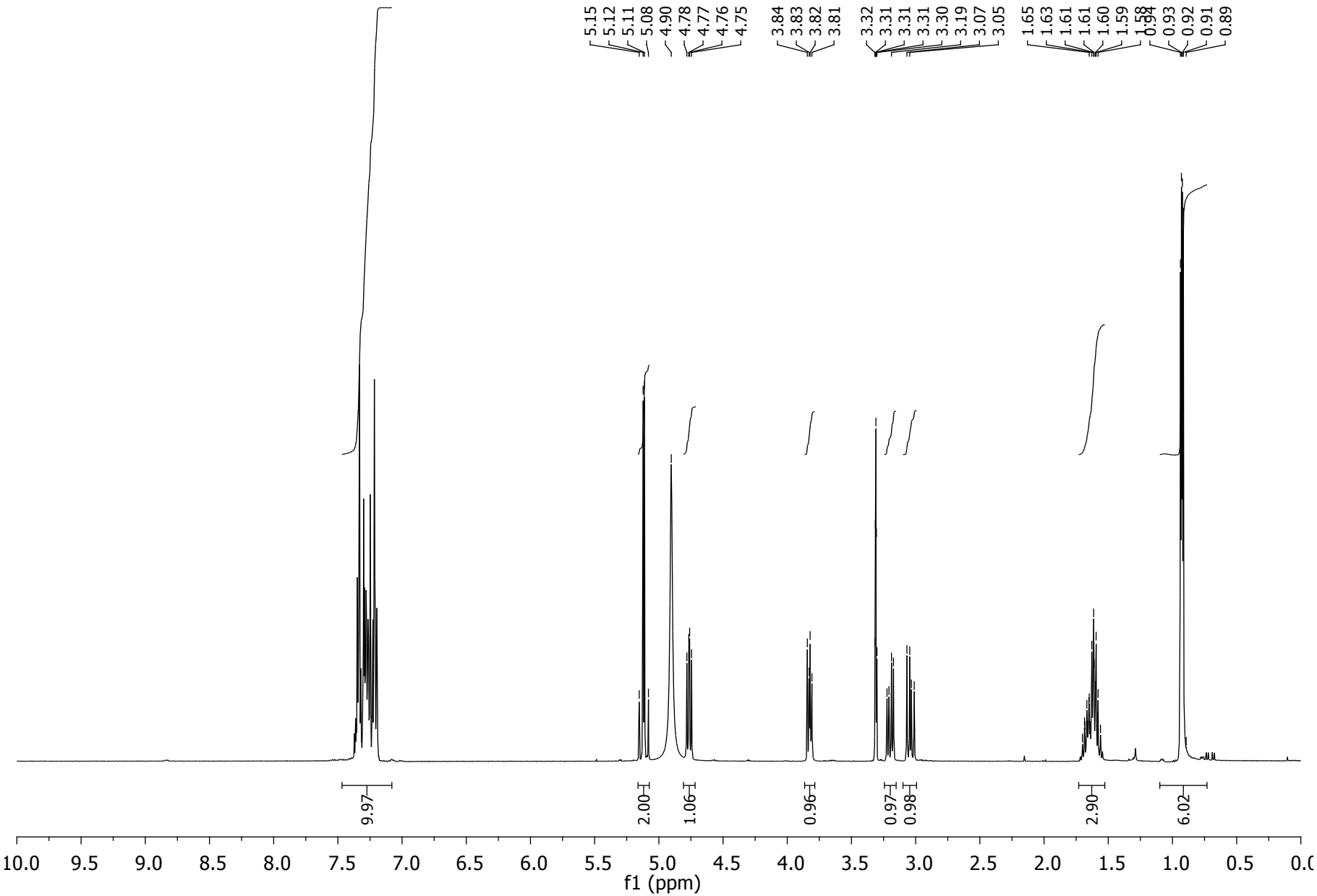
^{1}H NMR spectrum of TFA.H-Ala-Phe-OBn 6a



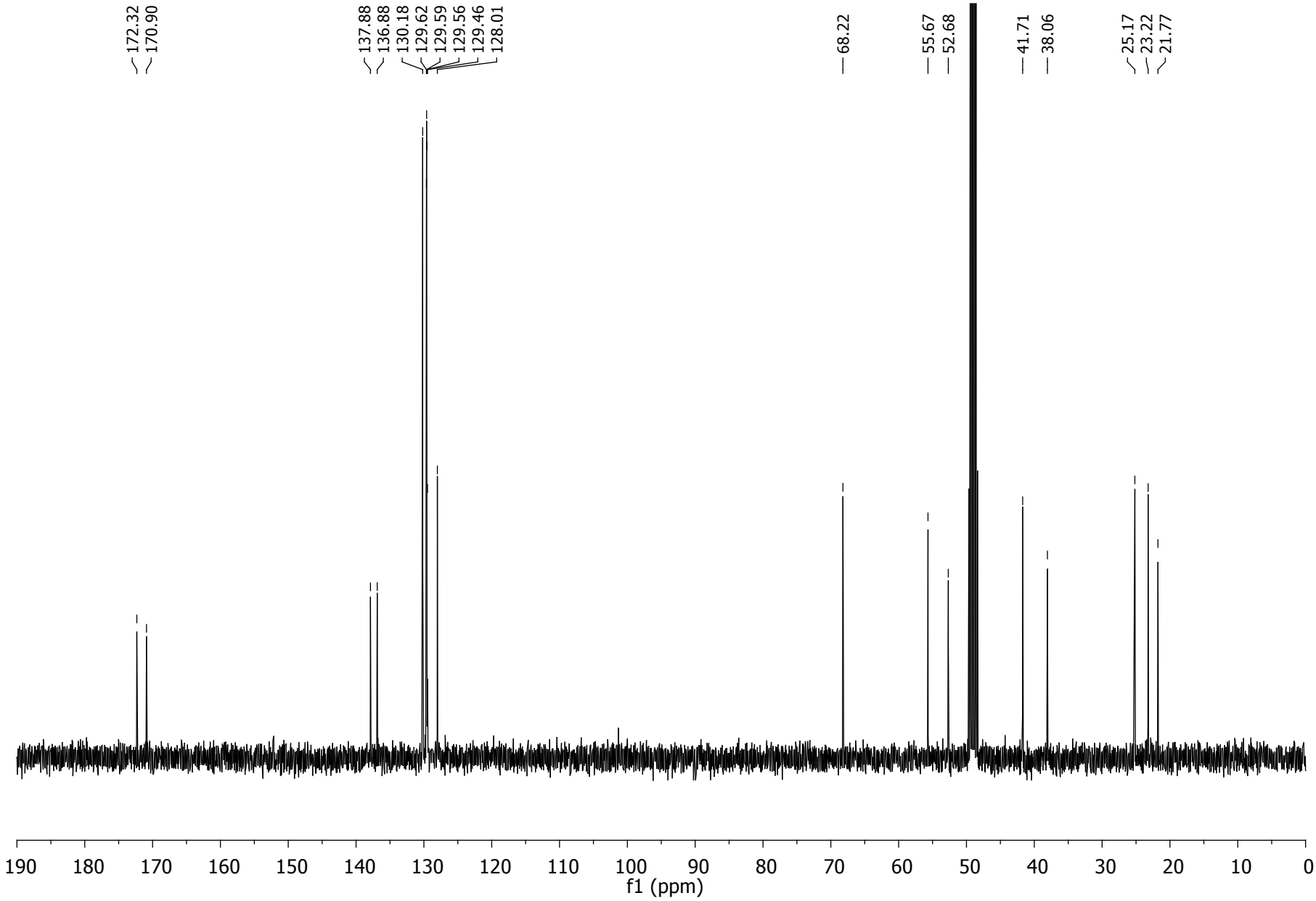
^{13}C NMR spectrum of TFA.H-Ala-Phe-OBn 6a



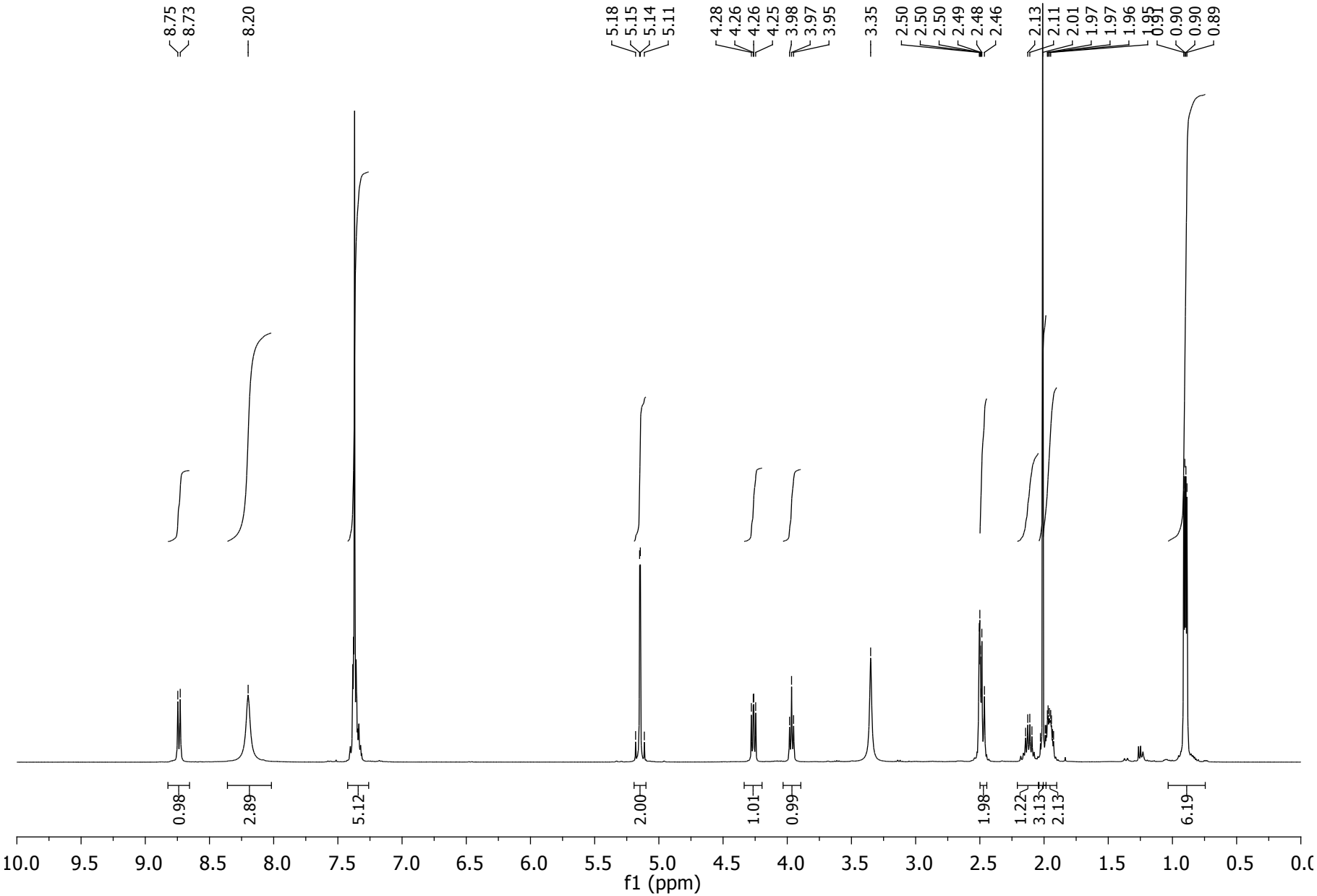
^{1}H NMR spectrum of TFA.H-Leu-Phe-OBn 6b



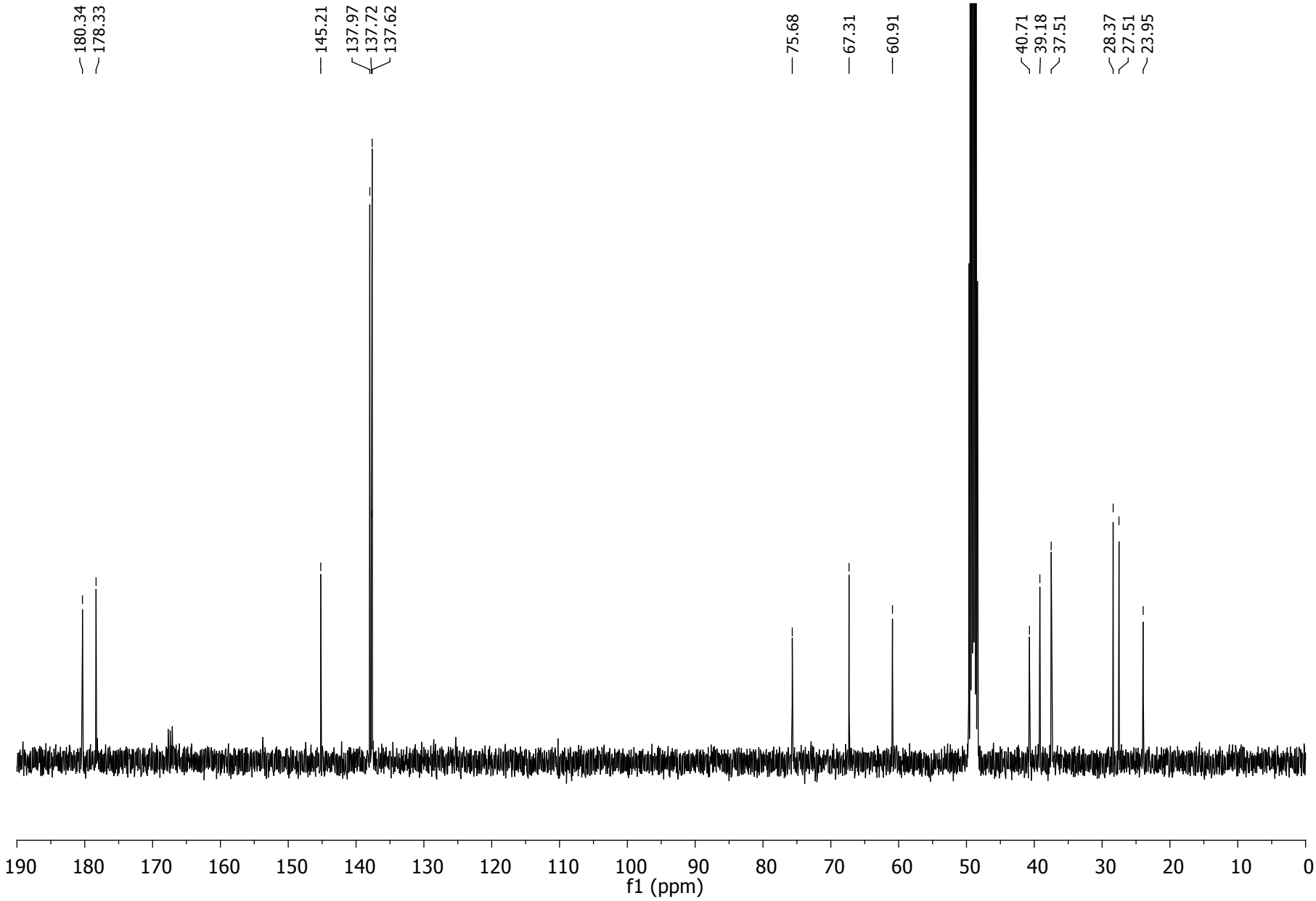
^{13}C NMR spectrum of TFA.H-Leu-Phe-OBn 6b



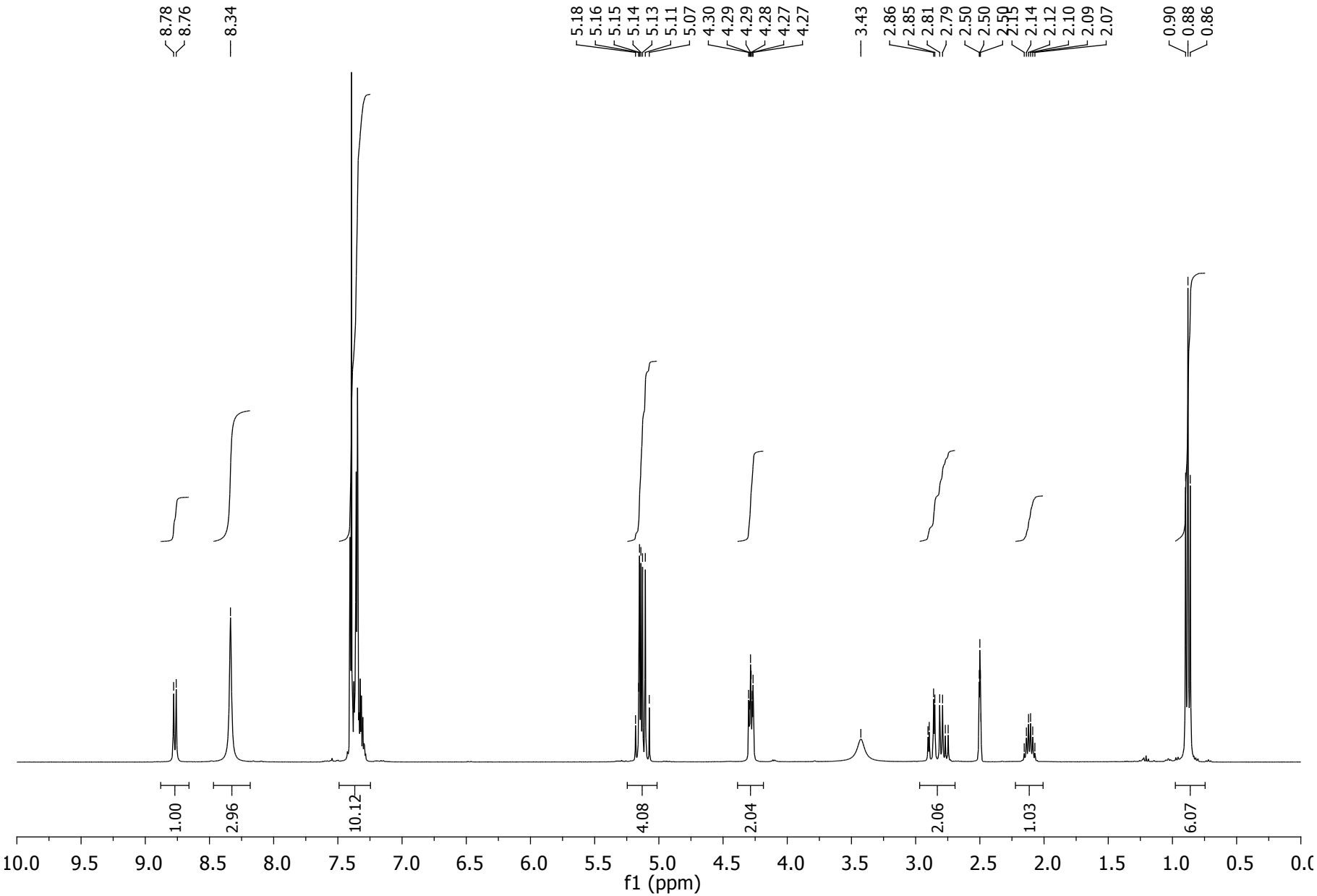
^{1}H NMR spectrum of TFA.H-Met-Val-OBn 6c



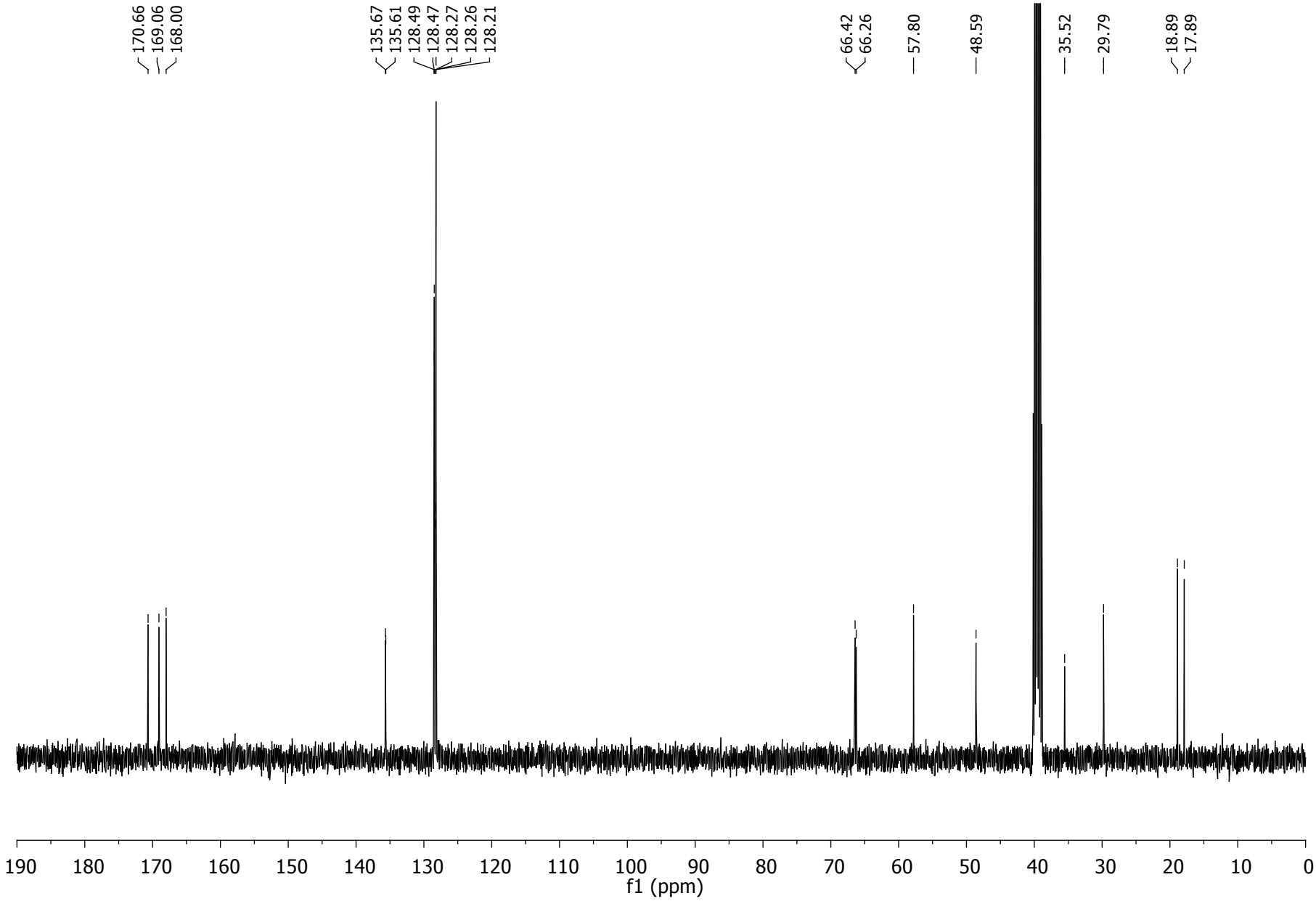
^{13}C NMR spectrum of TFA.H-Met-Val-OBn 6c



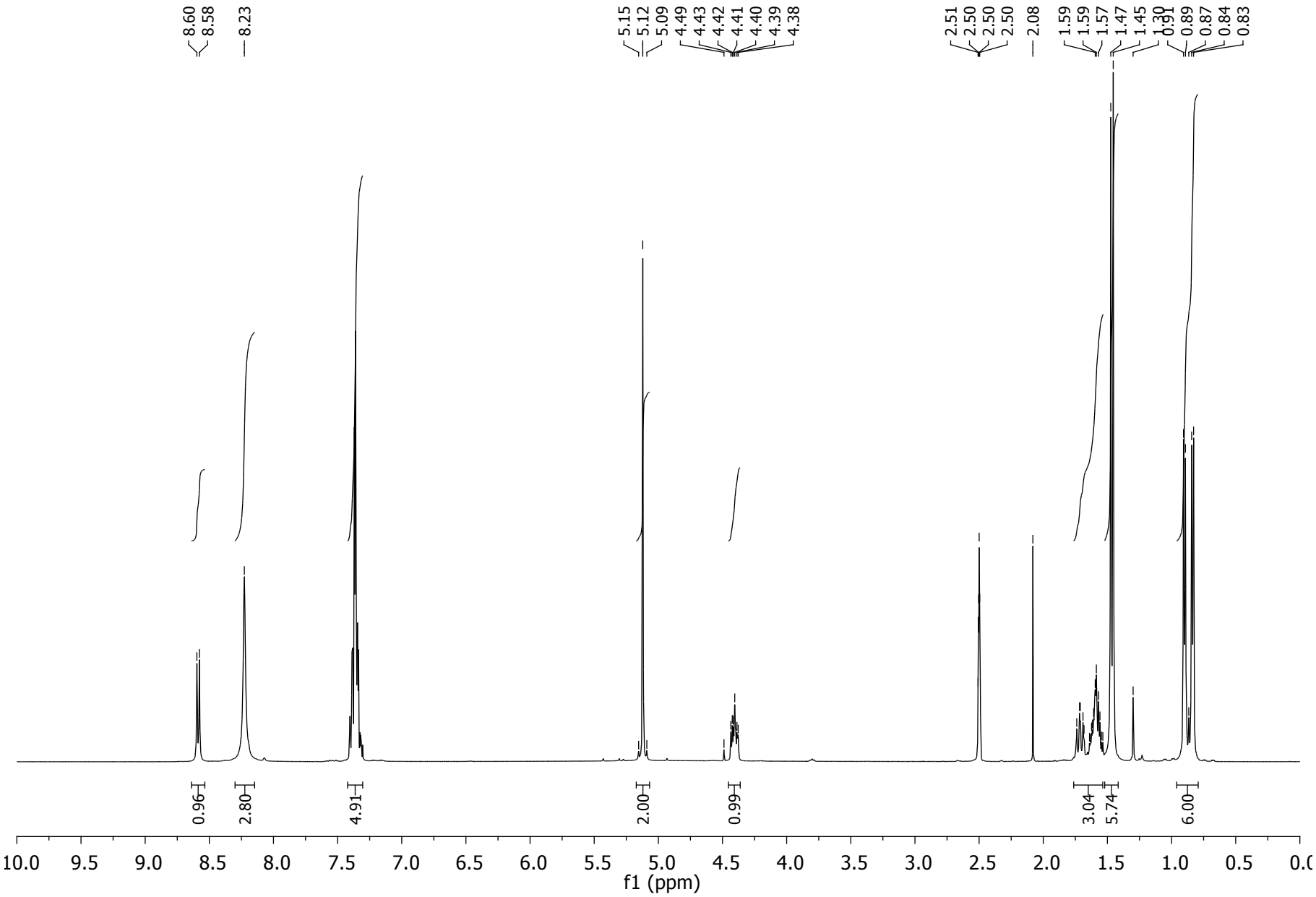
^{1}H NMR spectrum of TFA.H-Asp(OBn)-Val-OBn 6d



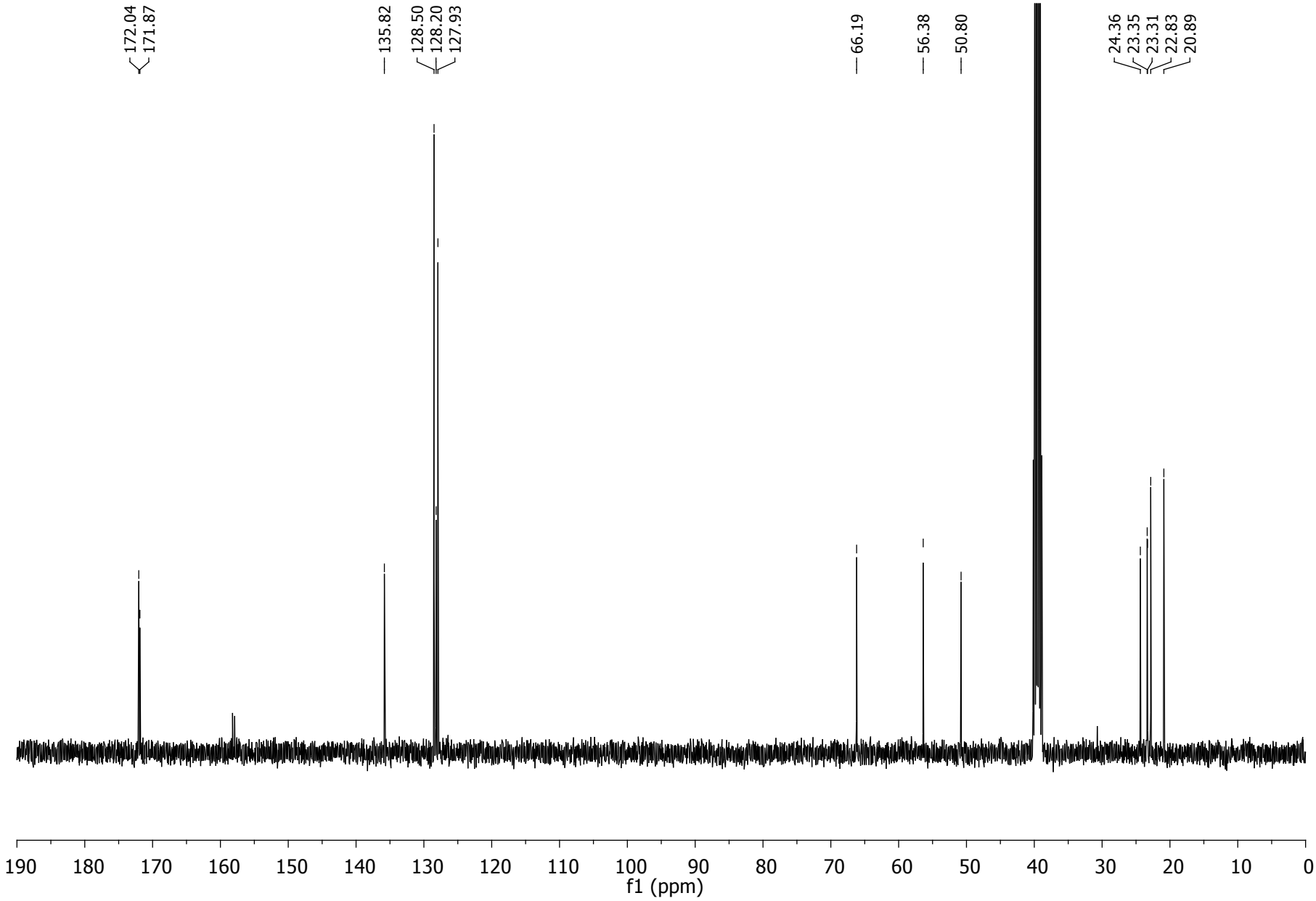
^{13}C NMR spectrum of TFA.H-Asp(OBn)-Val-OBn 6d



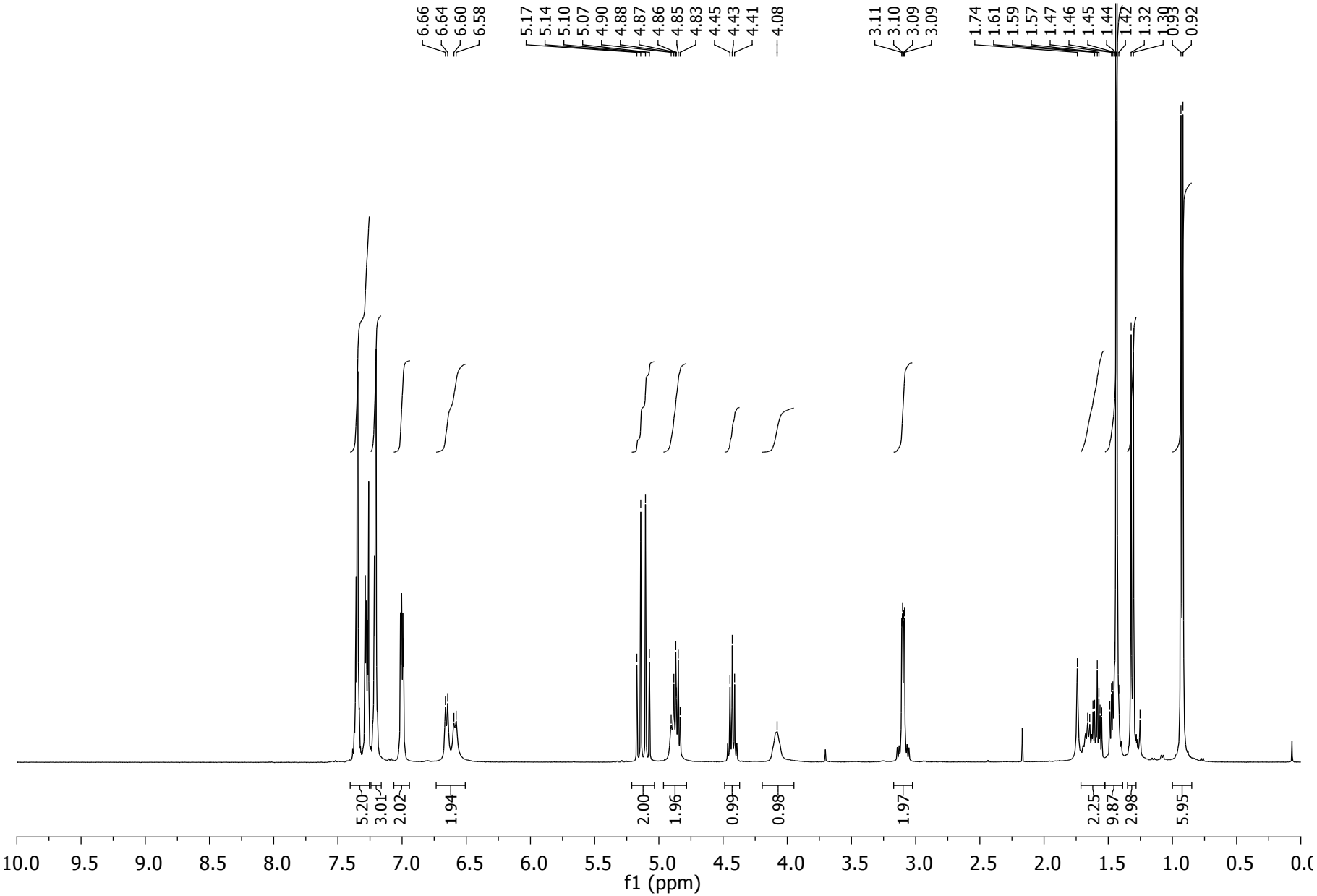
^{1}H NMR spectrum of TFA.H-Aib-Leu-OBn 6e



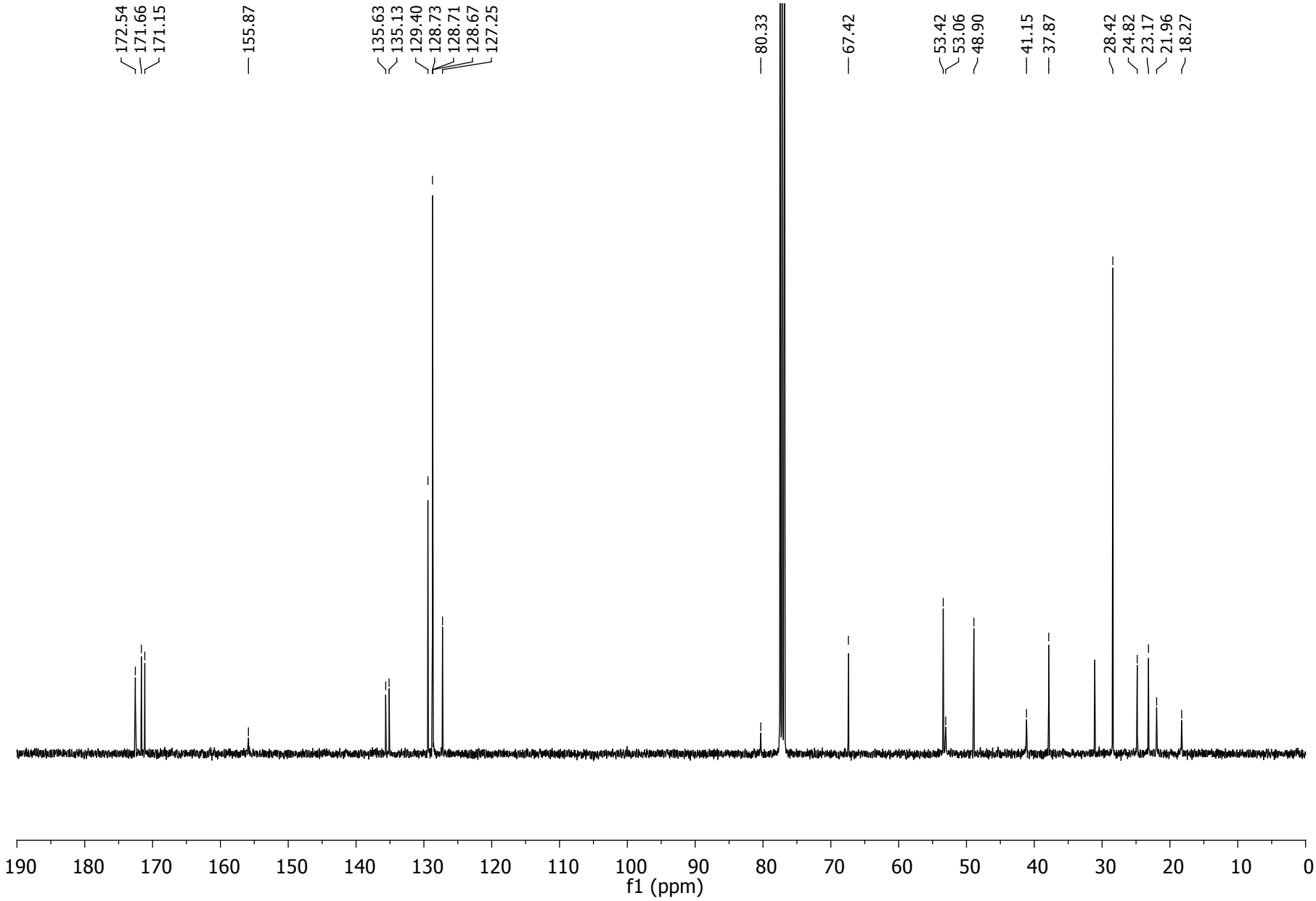
^{13}C NMR spectrum of TFA.H-Aib-Leu-OBn 6e



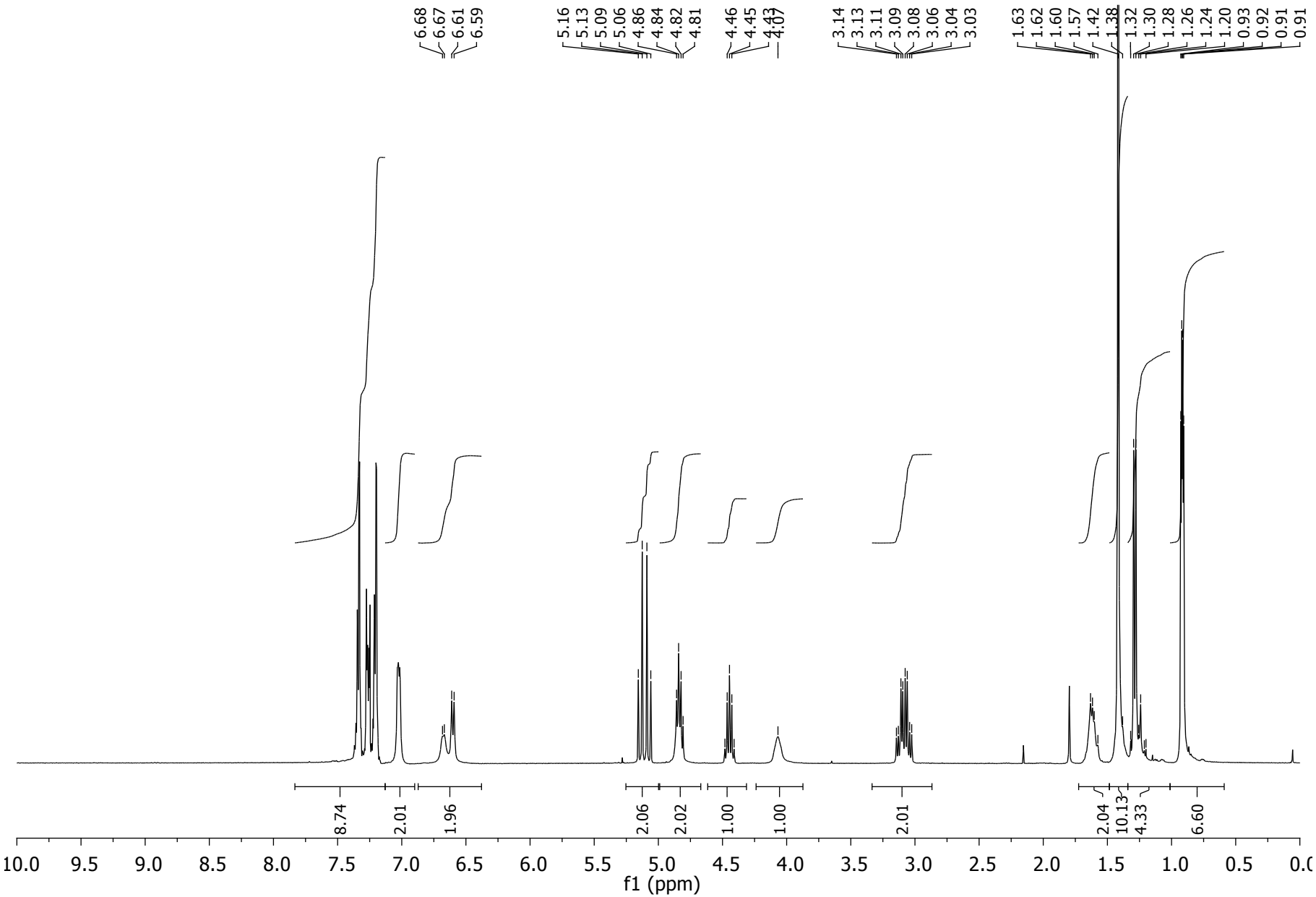
^{1}H NMR spectrum of Boc-Leu-Ala-Phe-OBn 7a



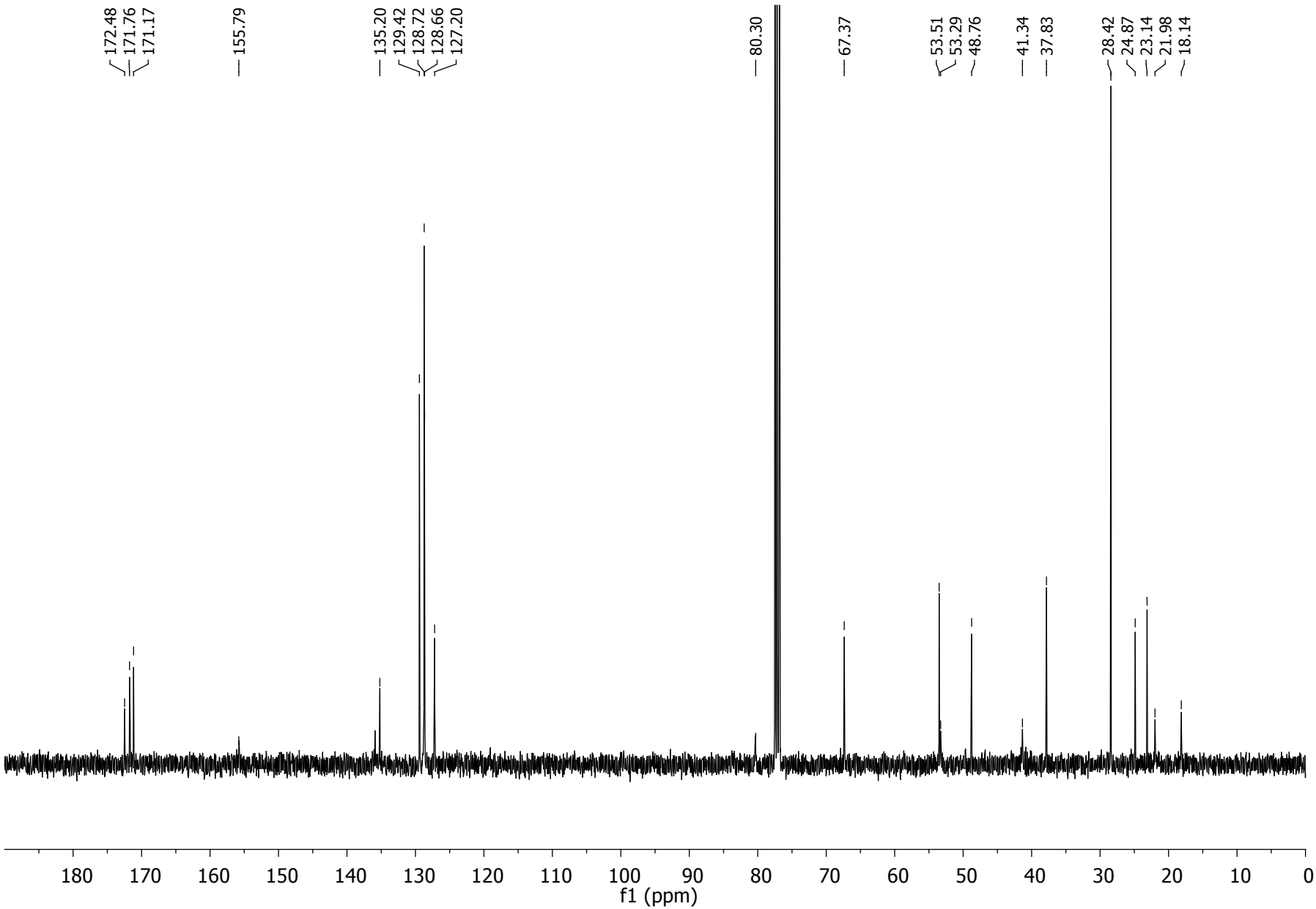
^{13}C NMR spectrum of Boc-Leu-Ala-Phe-OBn 7a



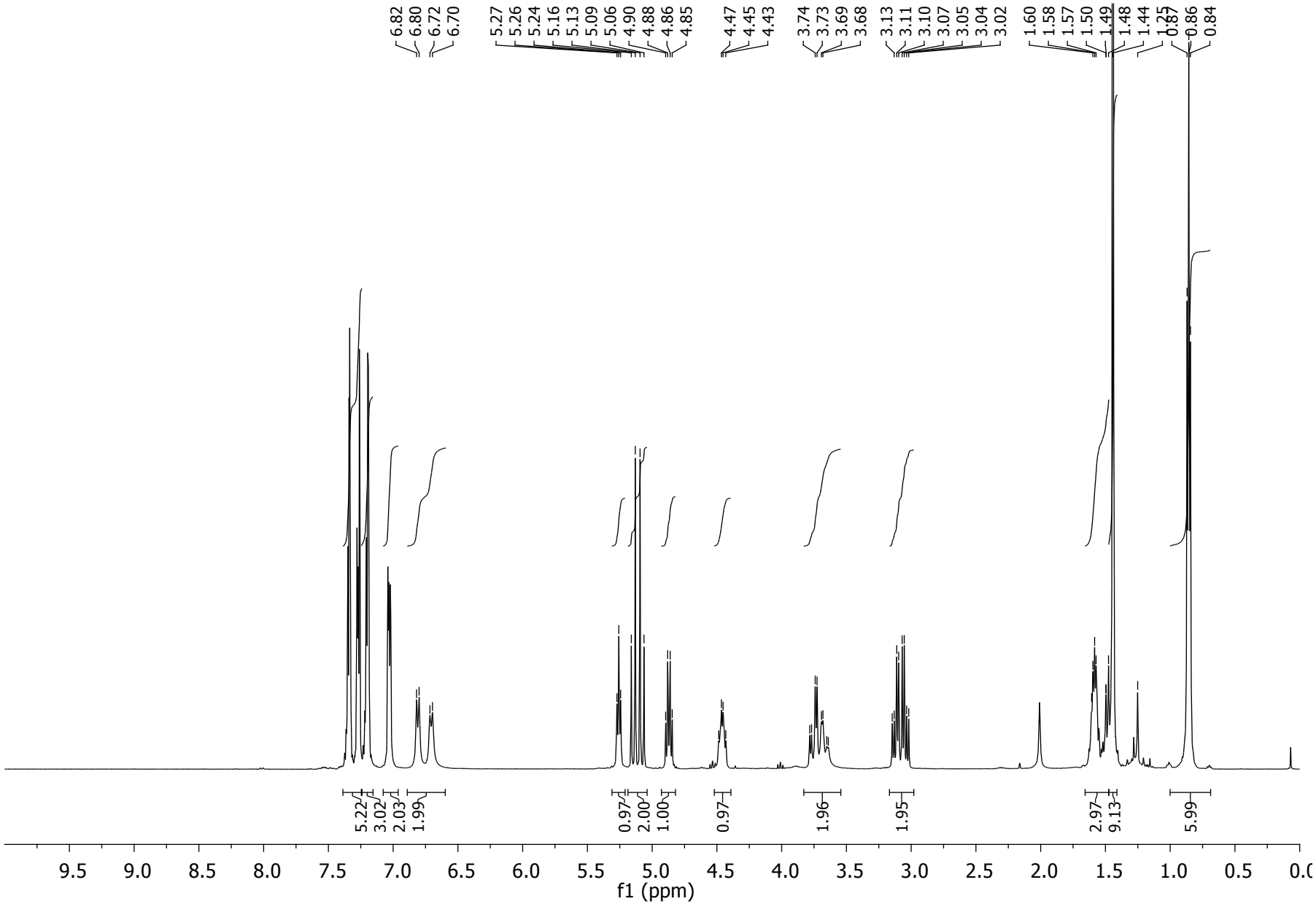
^{1}H NMR spectrum of Boc-(*R*)-Leu-Ala-Phe-OBn 7a'



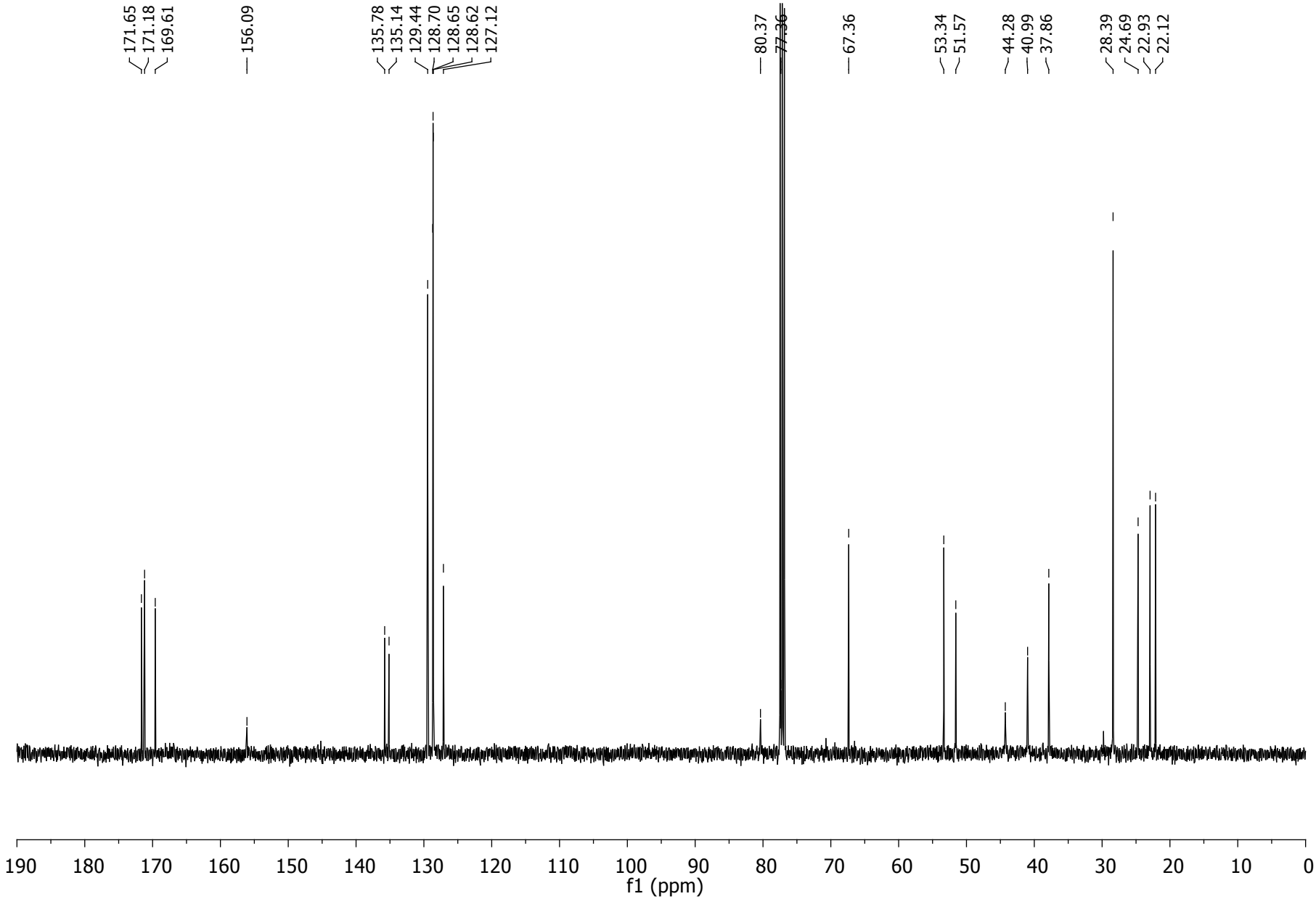
^{13}C NMR spectrum of Boc-(*R*)- Leu-Ala-Phe-OBn 7a'



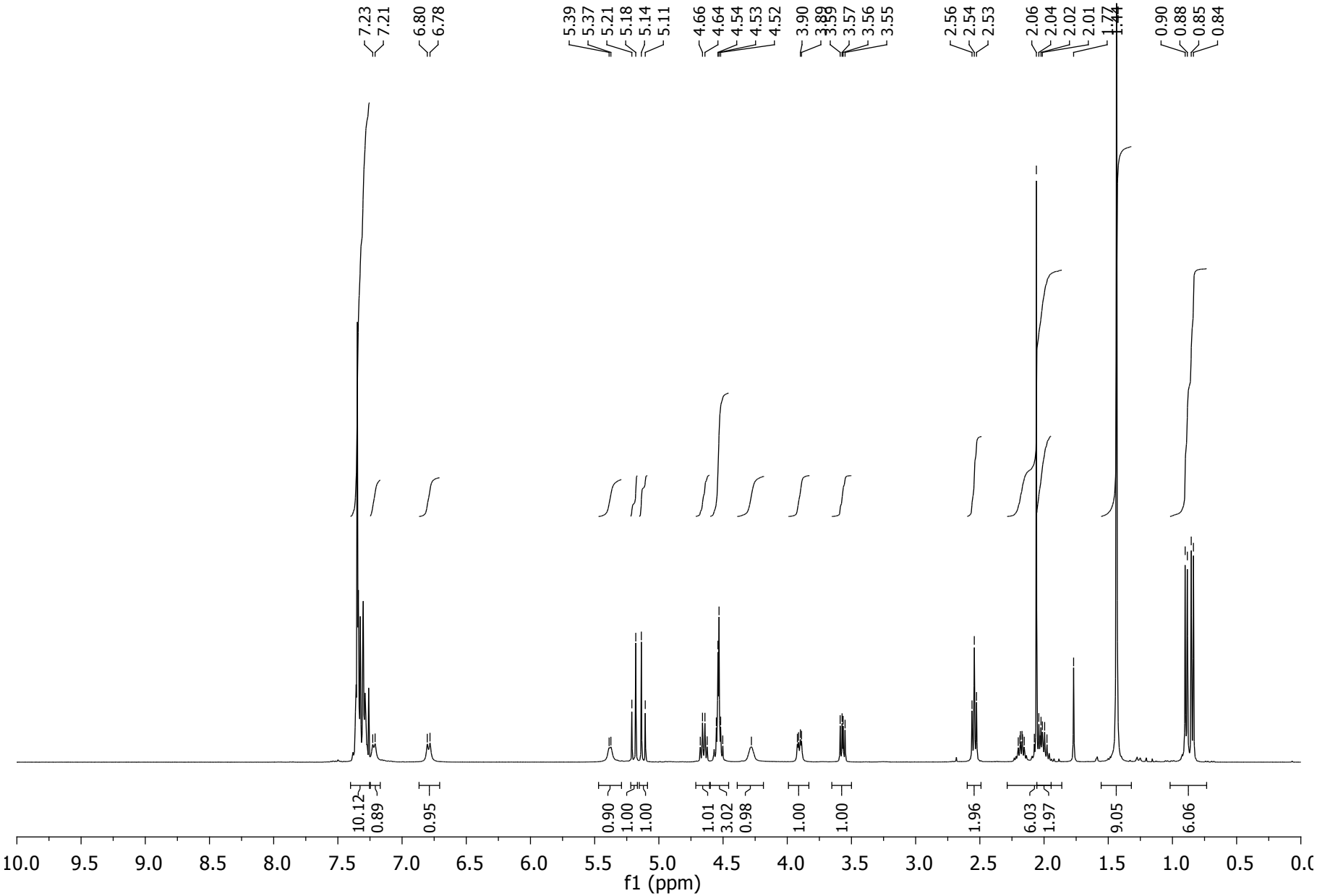
^{1}H NMR spectrum of Boc-Gly-Leu-Phe-OBn 7b



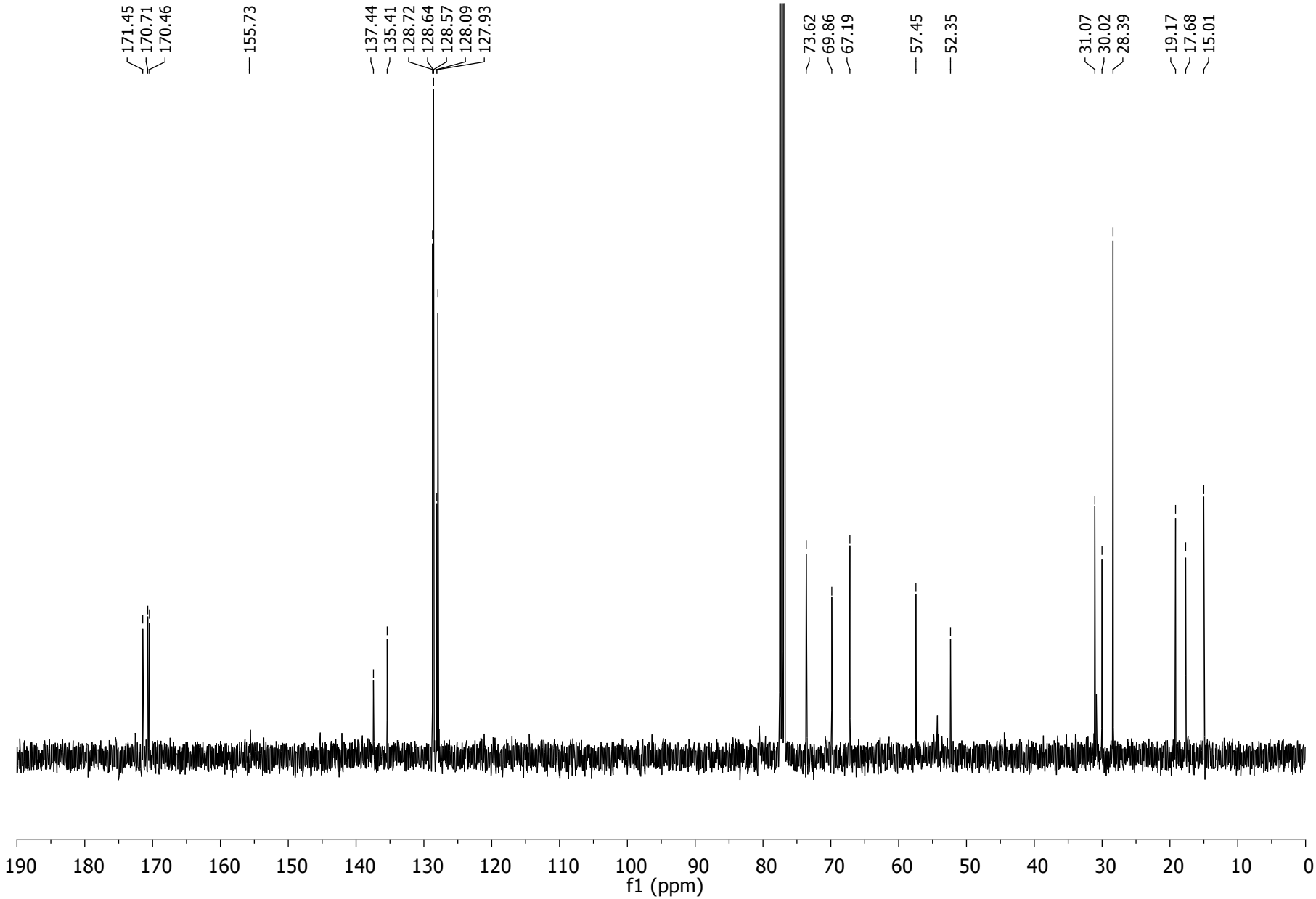
^{13}C NMR spectrum of Boc-Gly-Leu-Phe-OBn 7b



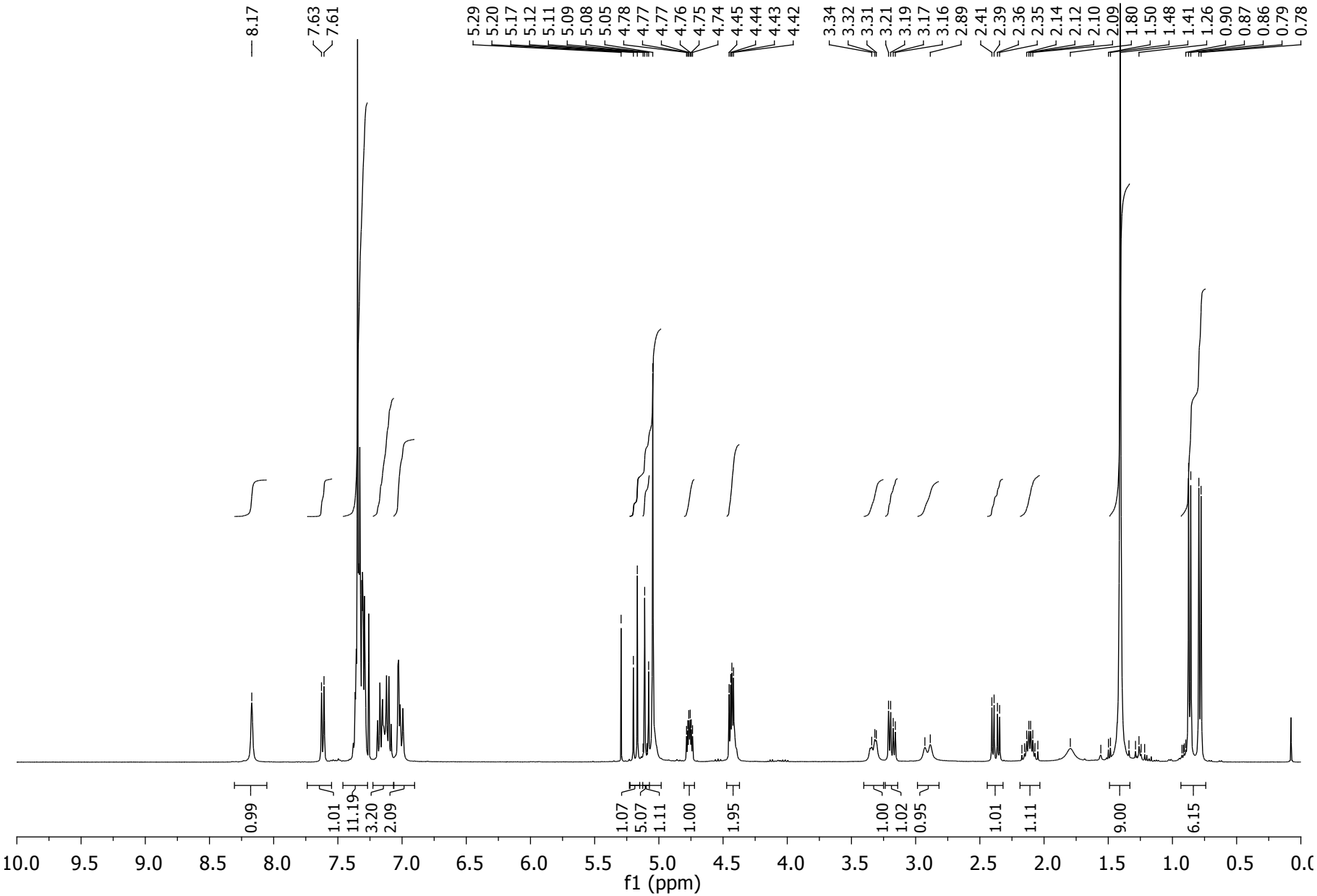
^{1}H NMR spectrum of Boc-Ser(OBn)-Met-Val-OBn 7c



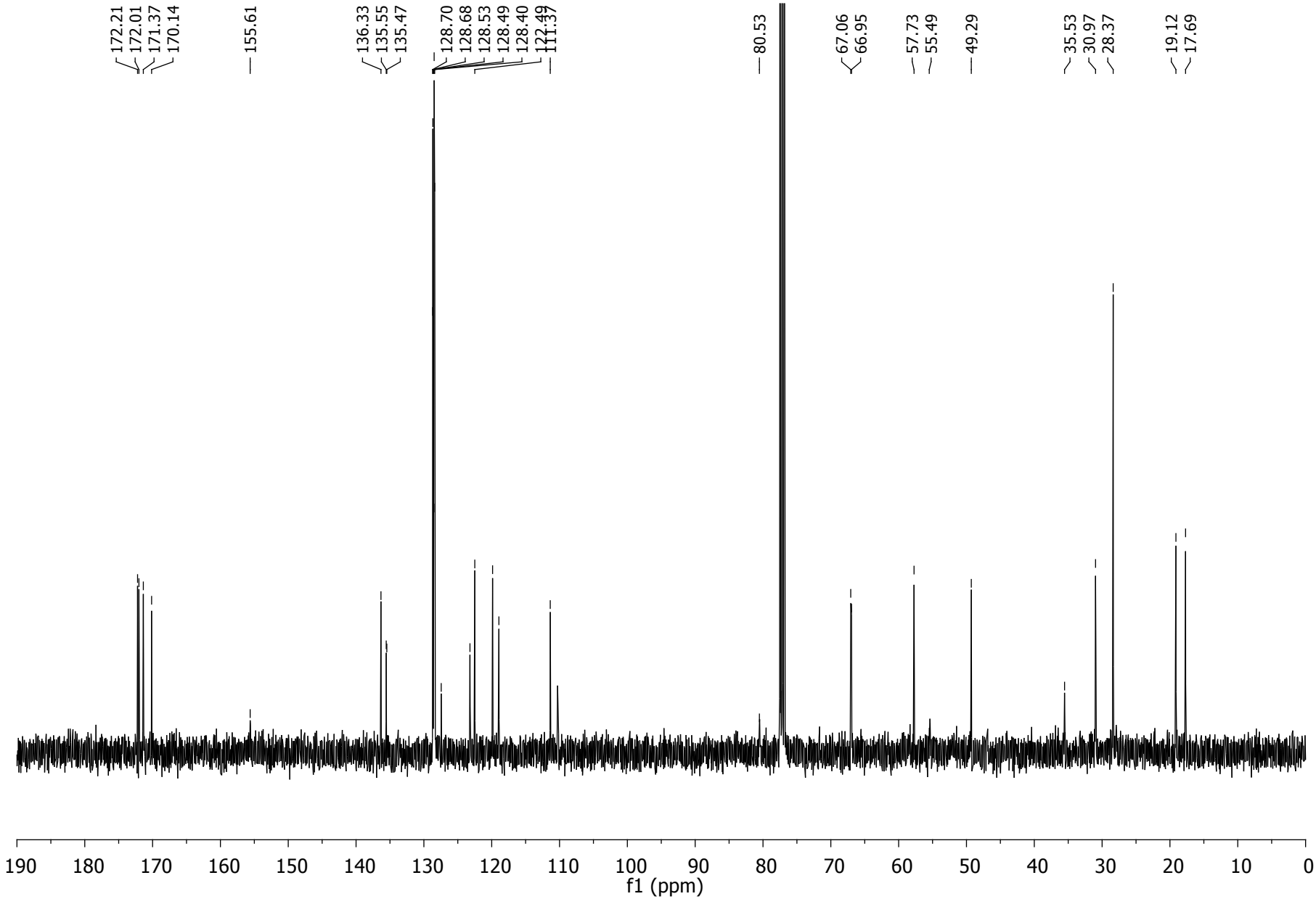
^{13}C NMR spectrum of Boc-Ser(OBn)-Met-Val-OBn 7c



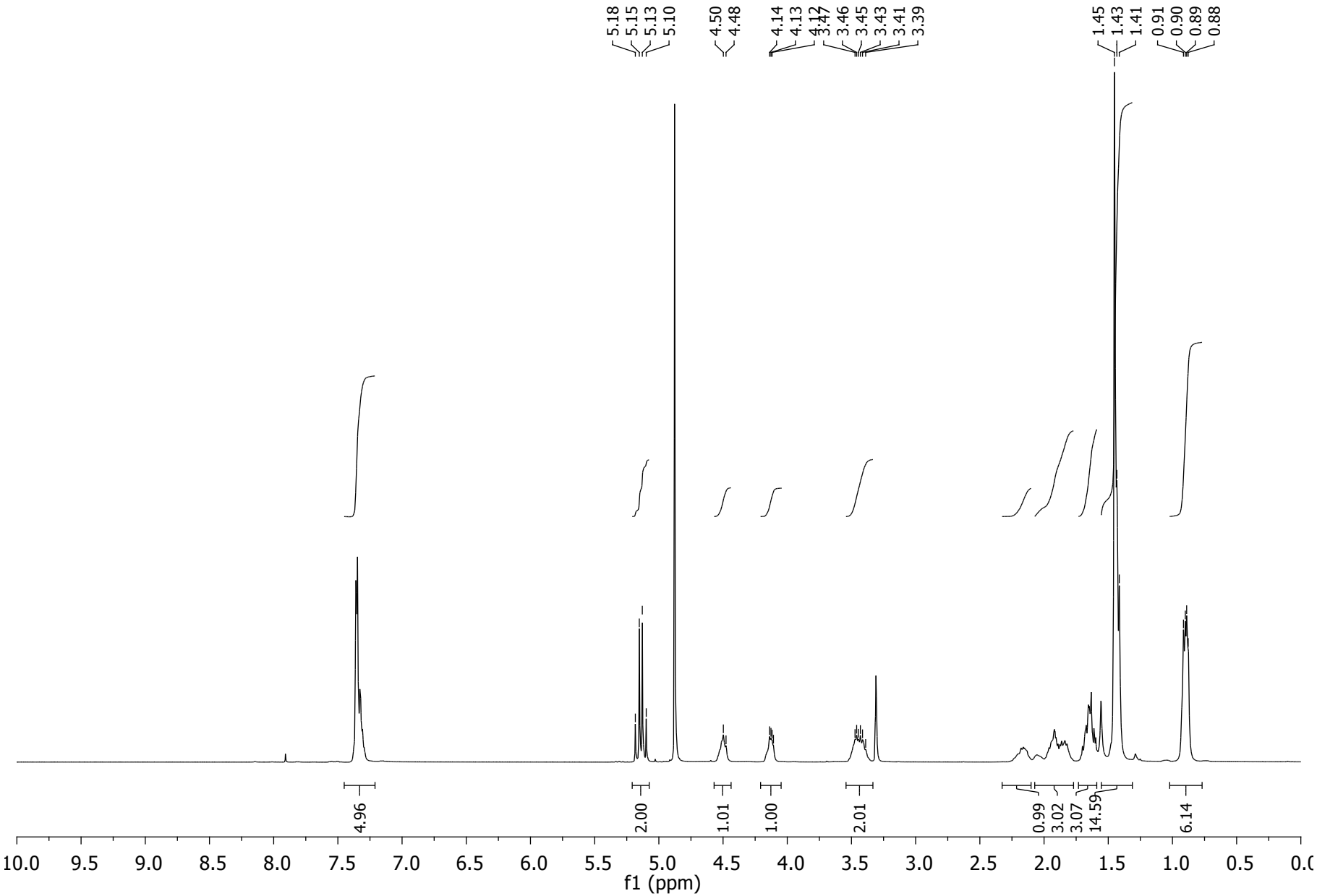
^{1}H NMR spectrum of Boc-Trp-Asp(OBn)-Val-OBn 7d



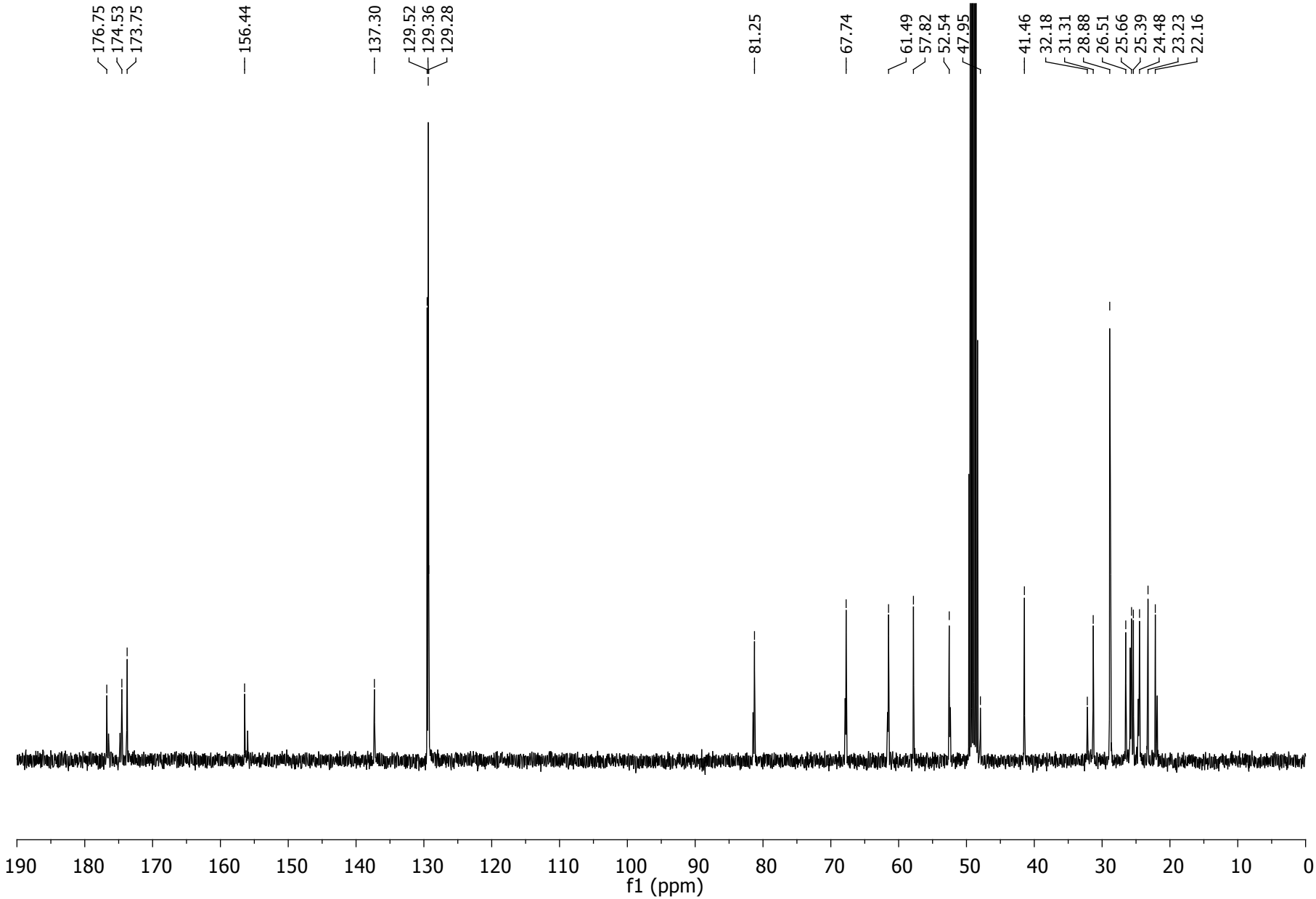
^{13}C NMR spectrum of Boc-Trp-Asp(OBn)-Val-OBn 7d



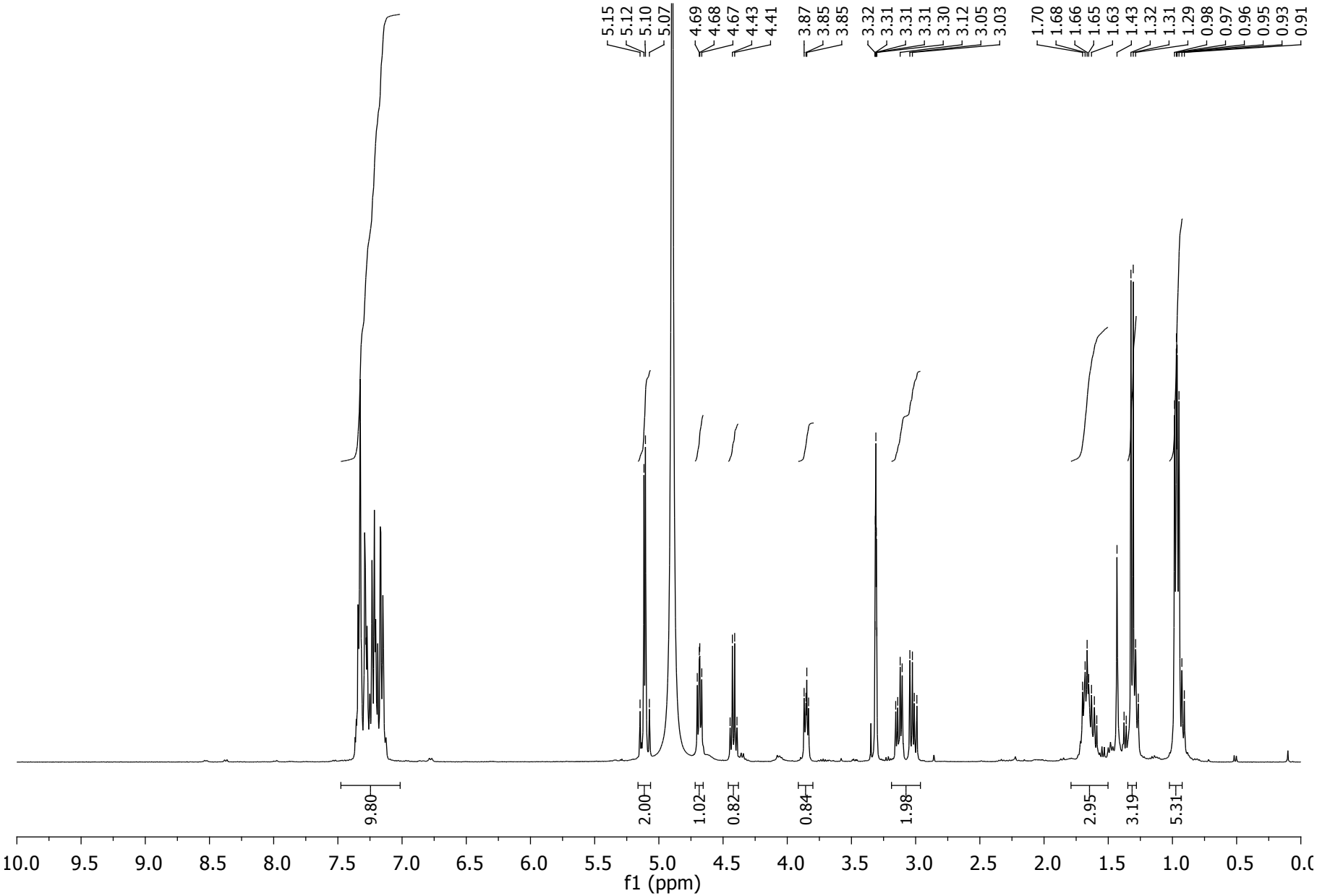
^{1}H NMR spectrum of Boc-Pro-Aib-Leu-OBn 7e



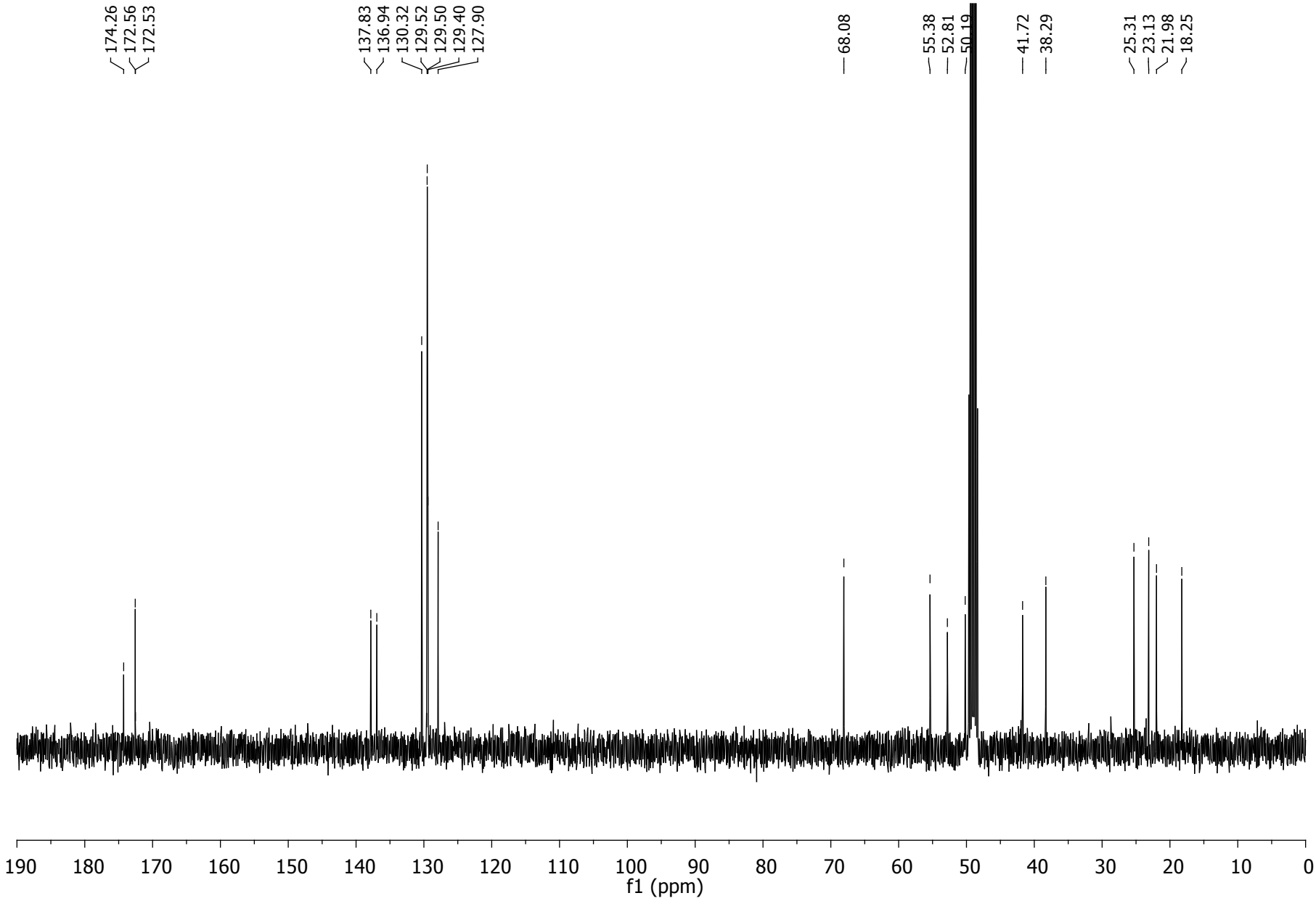
^{13}C NMR spectrum of Boc-Pro-Aib-Leu-OBn 7e



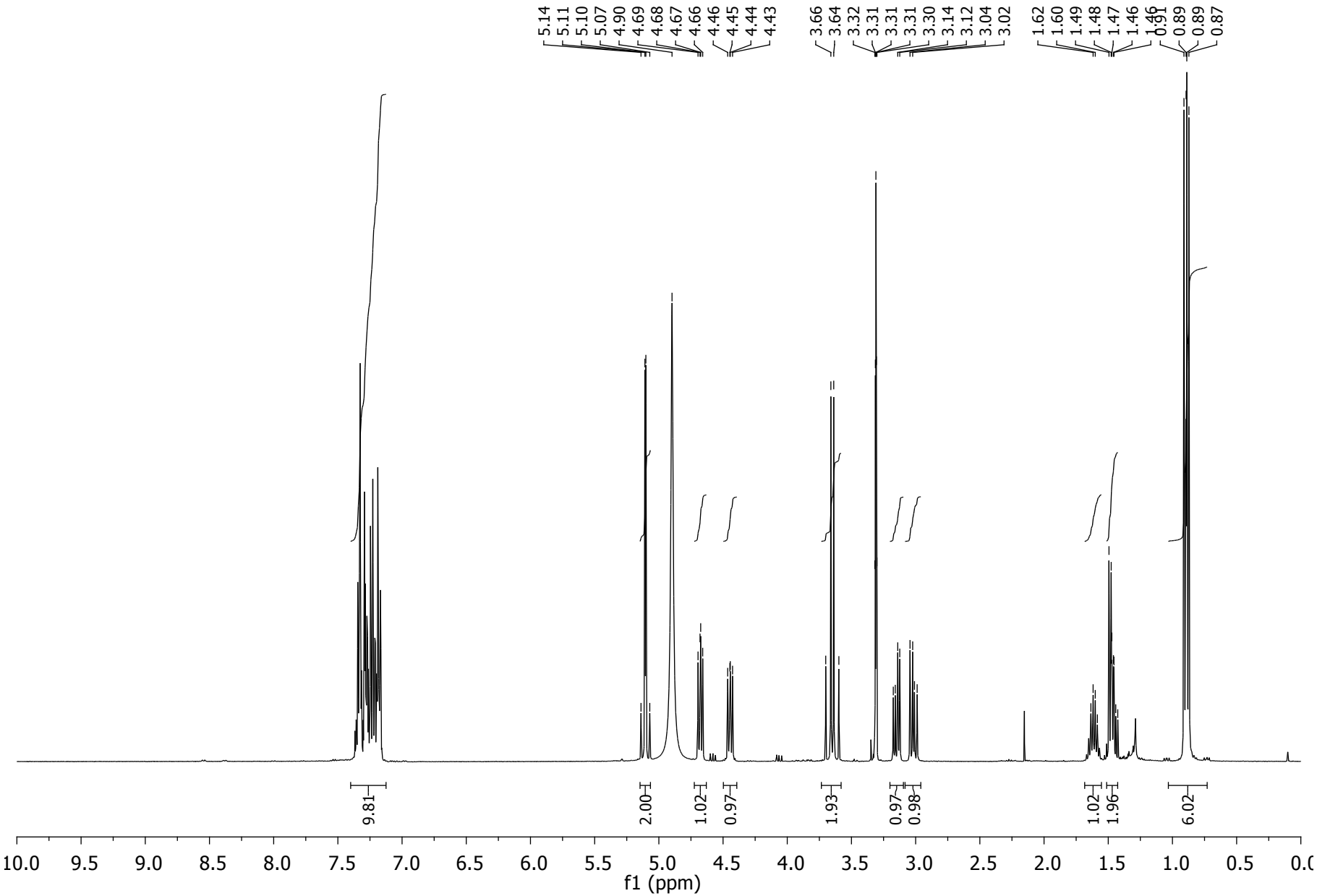
^{1}H NMR spectrum of TFA.H-Leu-Ala-Phe-OBn 8a



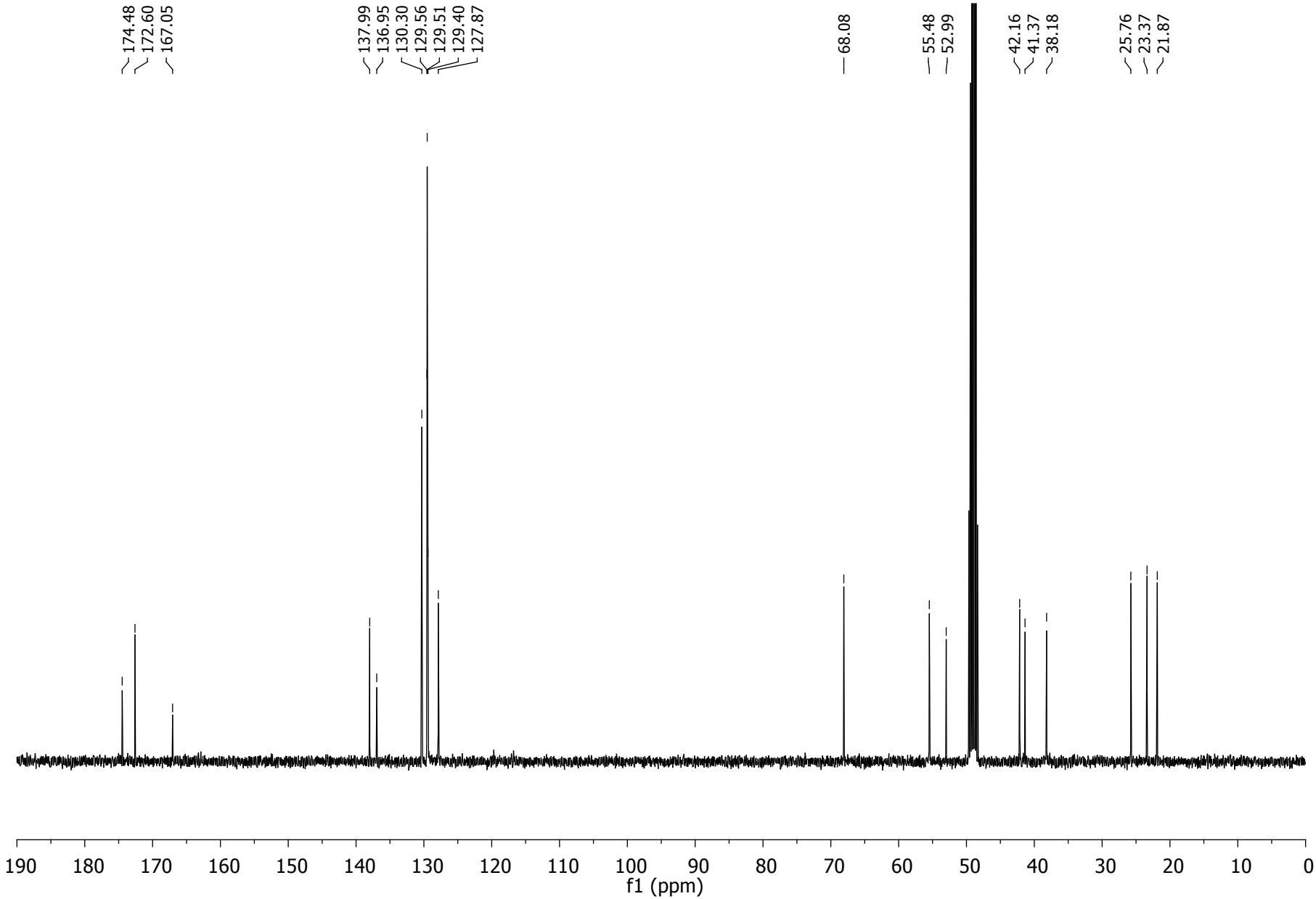
^{13}C NMR spectrum of TFA.H-Leu-Ala-Phe-OBn 8a



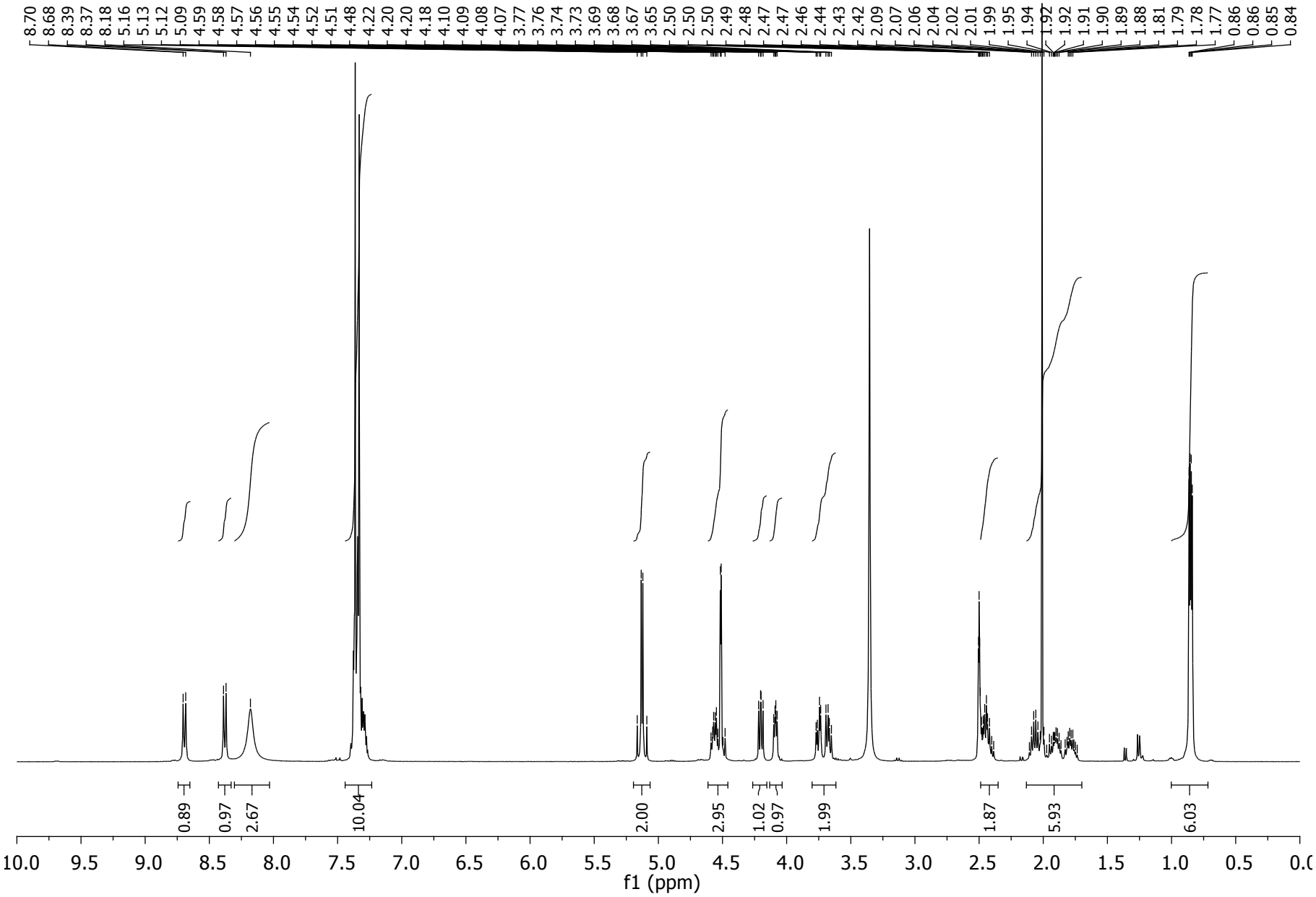
^{1}H NMR spectrum of TFA.H-Gly-Leu-Phe-OBn 8b



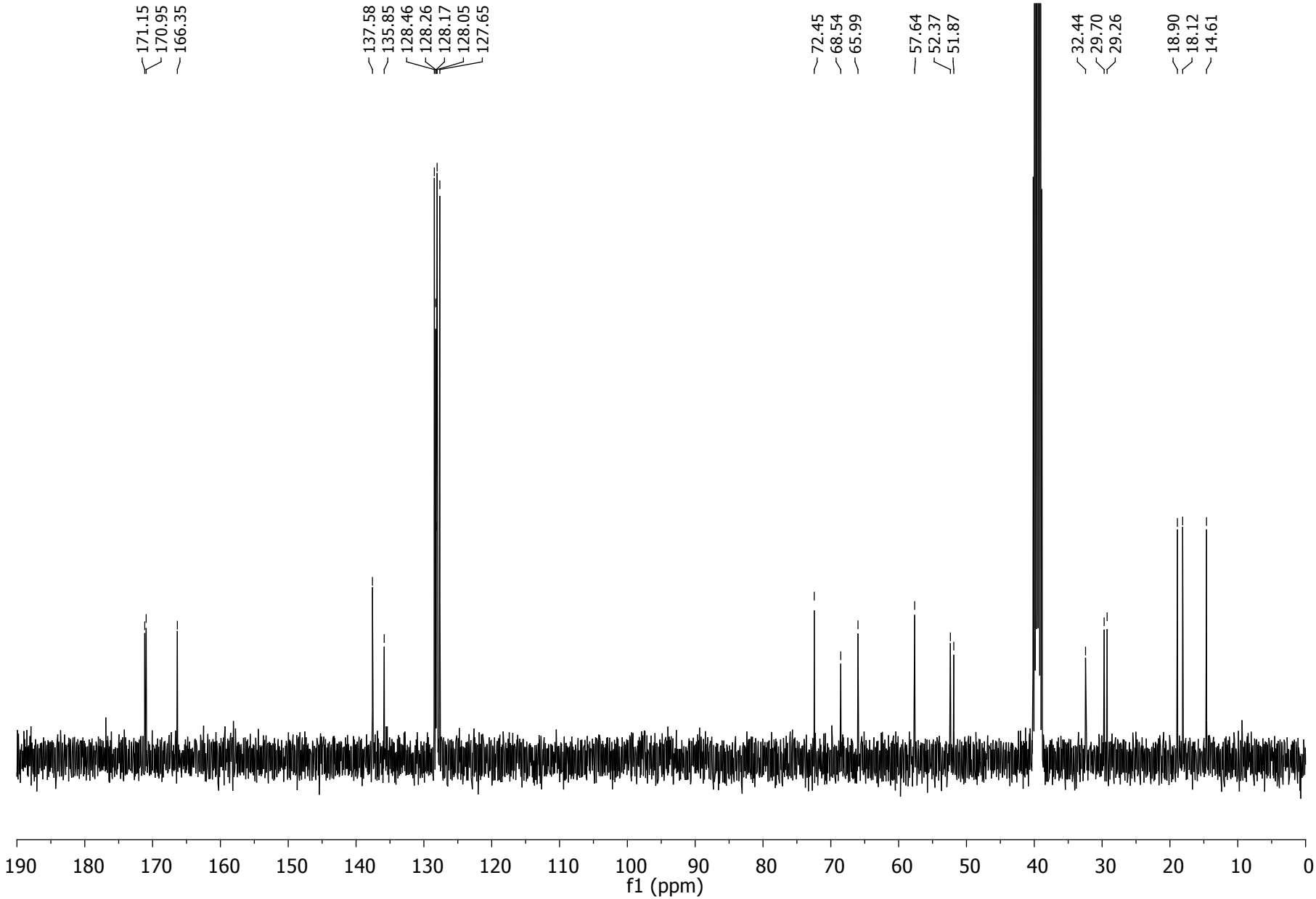
^{13}C NMR spectrum of TFA.H-Gly-Leu-Phe-OBn 8b



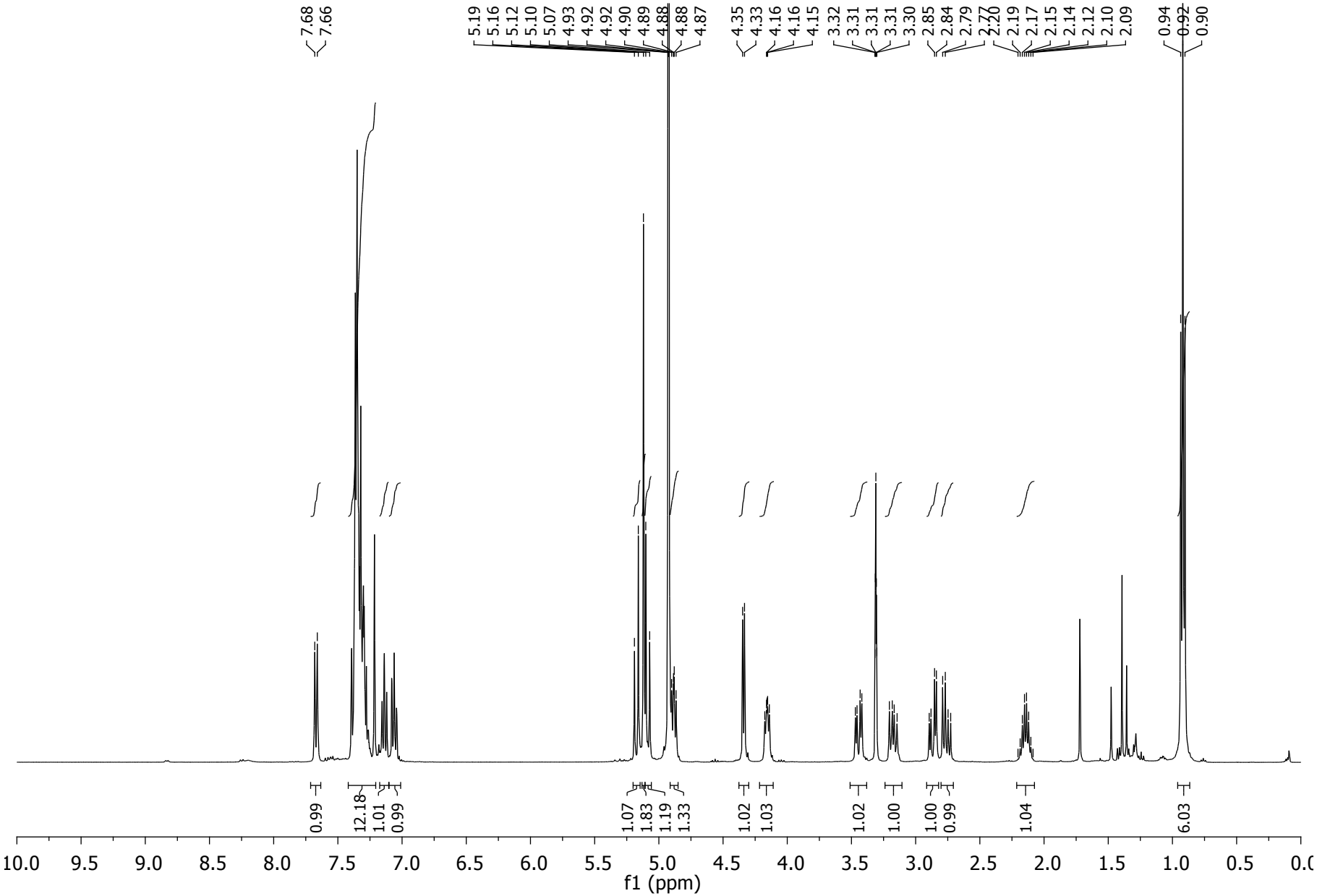
^{1}H NMR spectrum of TFA.H-Ser(OBn)-Met-Val-OBn 8c



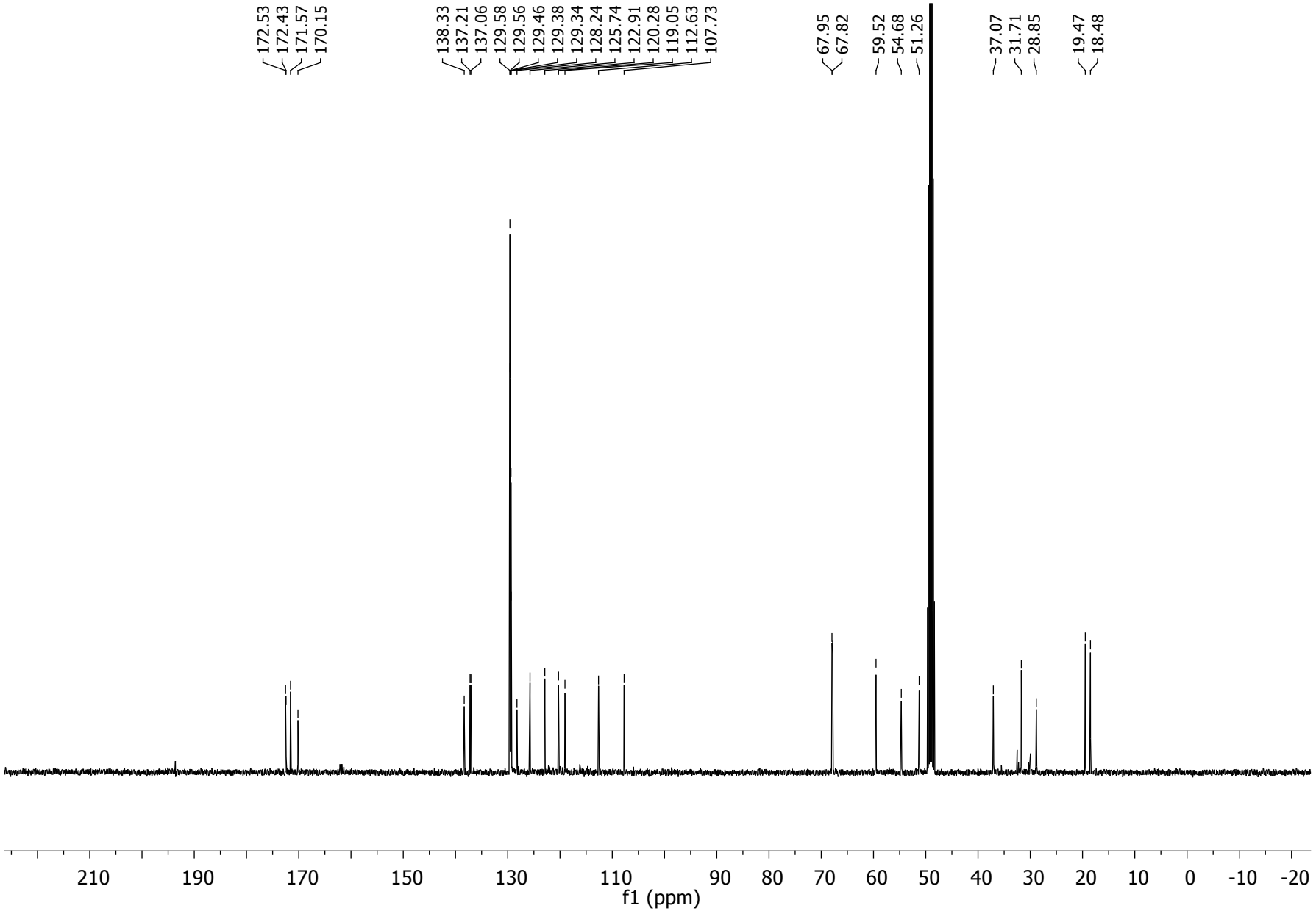
^{13}C NMR spectrum of TFA.H-Ser(OBn)-Met-Val-OBn 8c



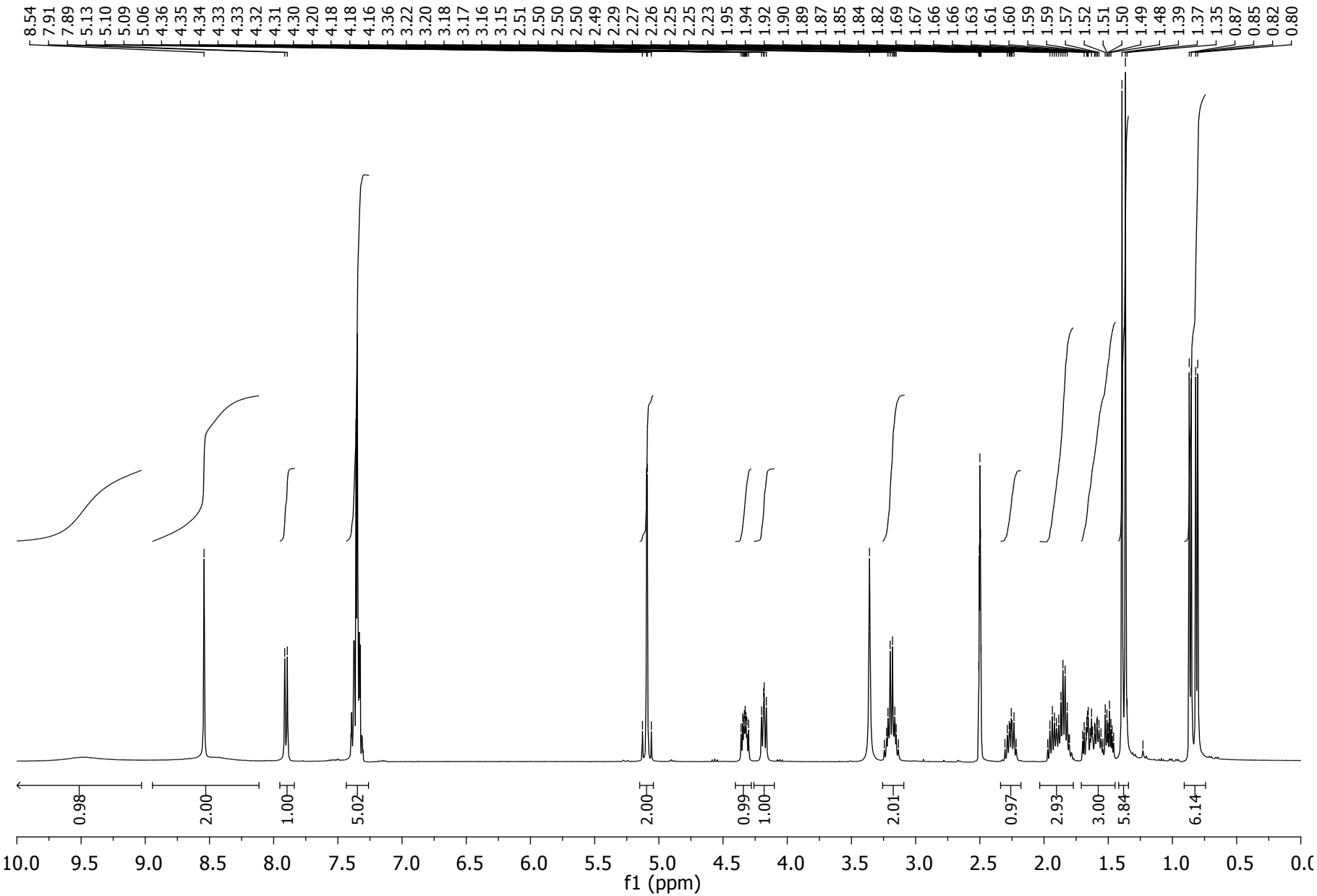
^{1}H NMR spectrum of TFA.H-Trp-Asp(OBn)-Val-OBn 8d



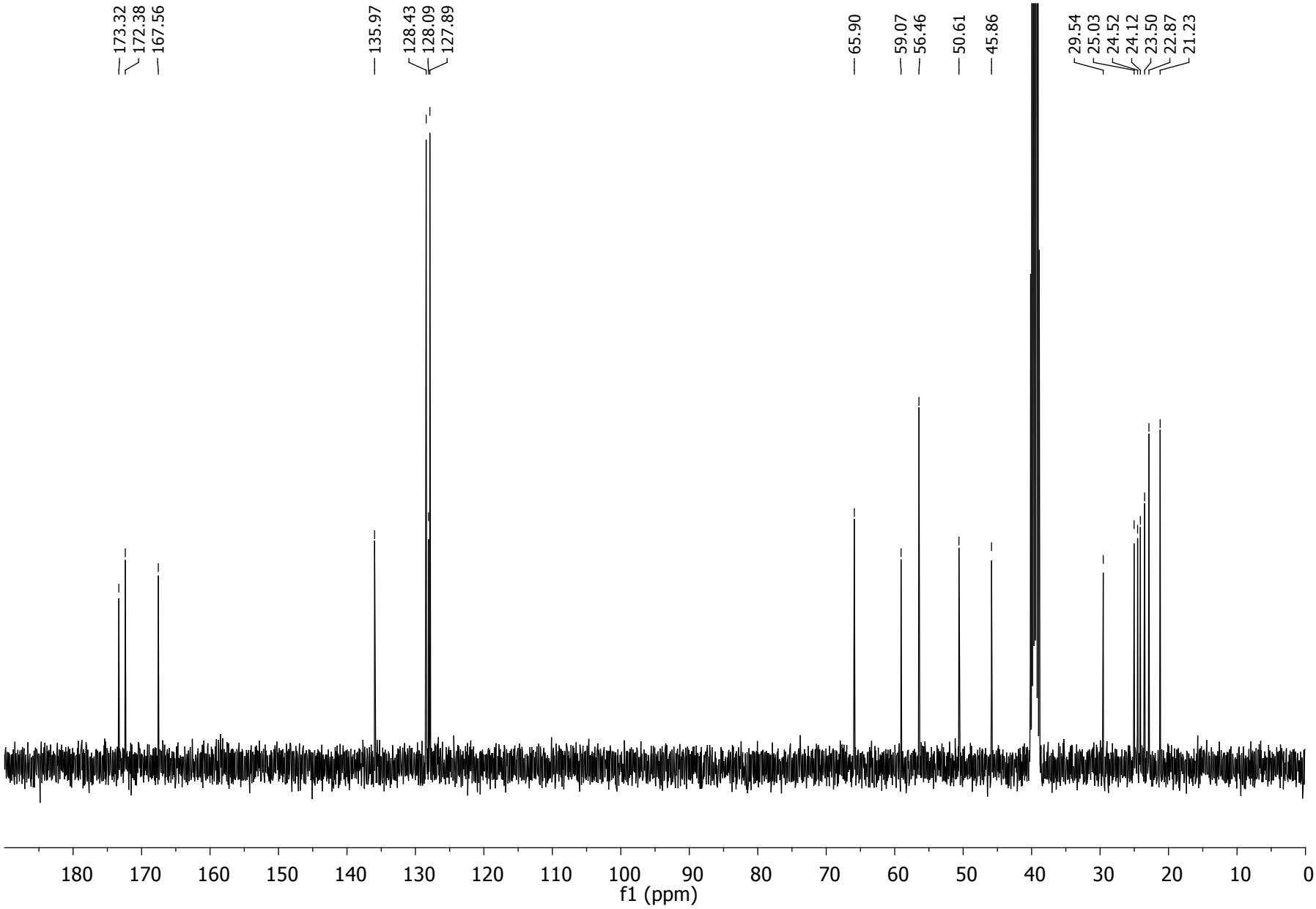
^{13}C NMR spectrum of TFA.H-Trp-Asp(OBn)-Val-OBn 8d



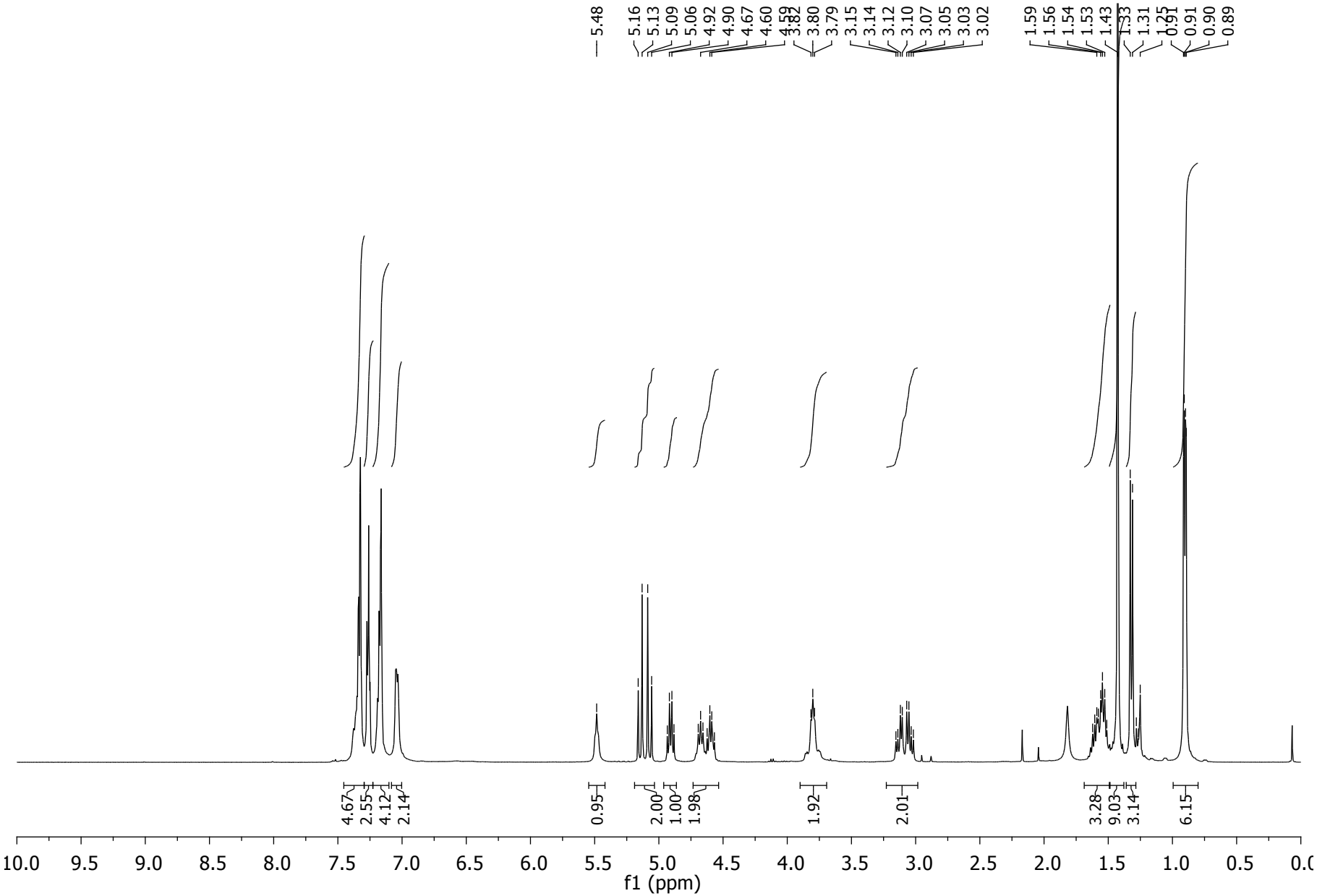
^{1}H NMR spectrum of TFA.H-Pro-Aib-Leu-OBn 8e



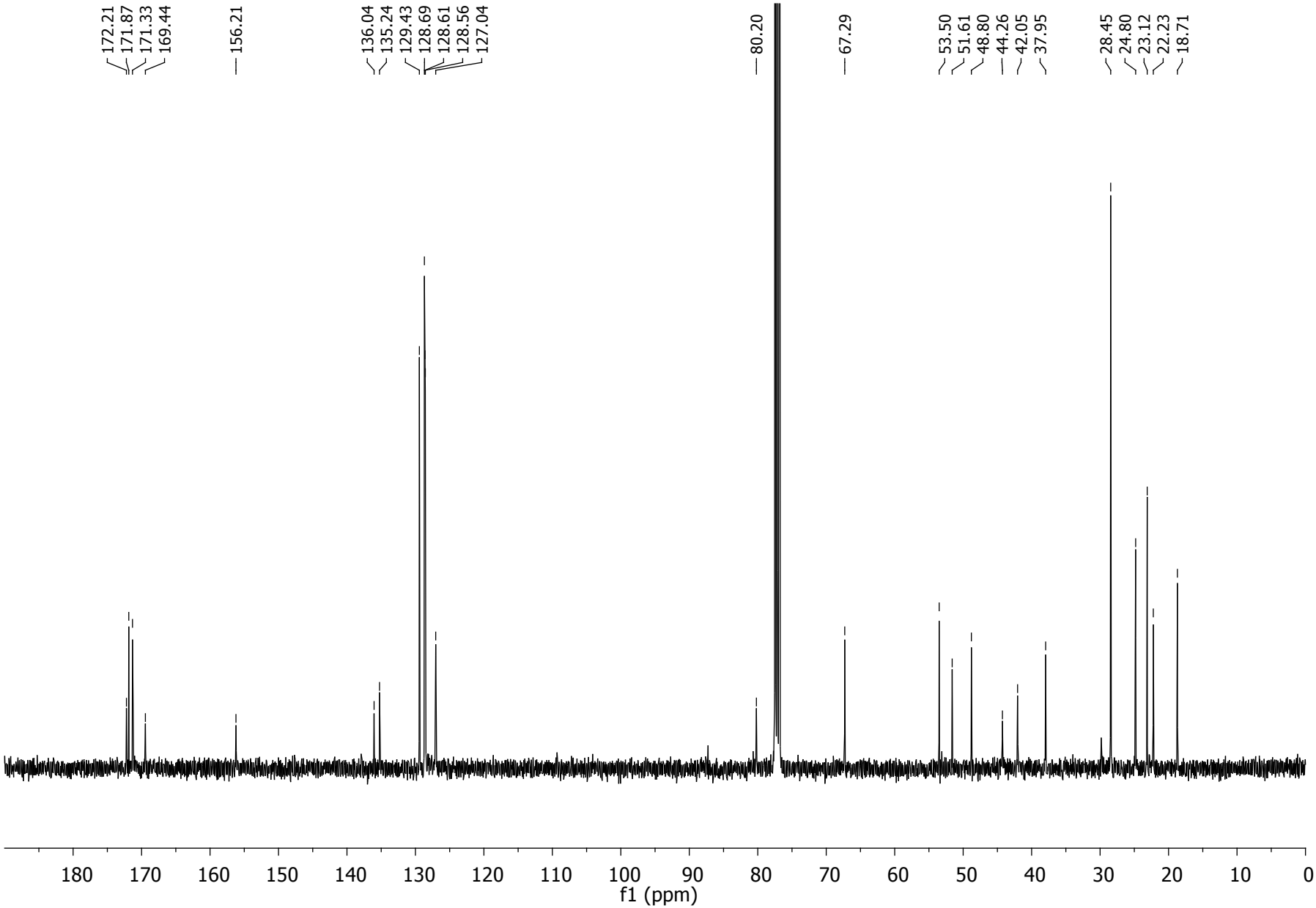
^{13}C NMR spectrum of TFA.H-Pro-Aib-Leu-OBn 8e



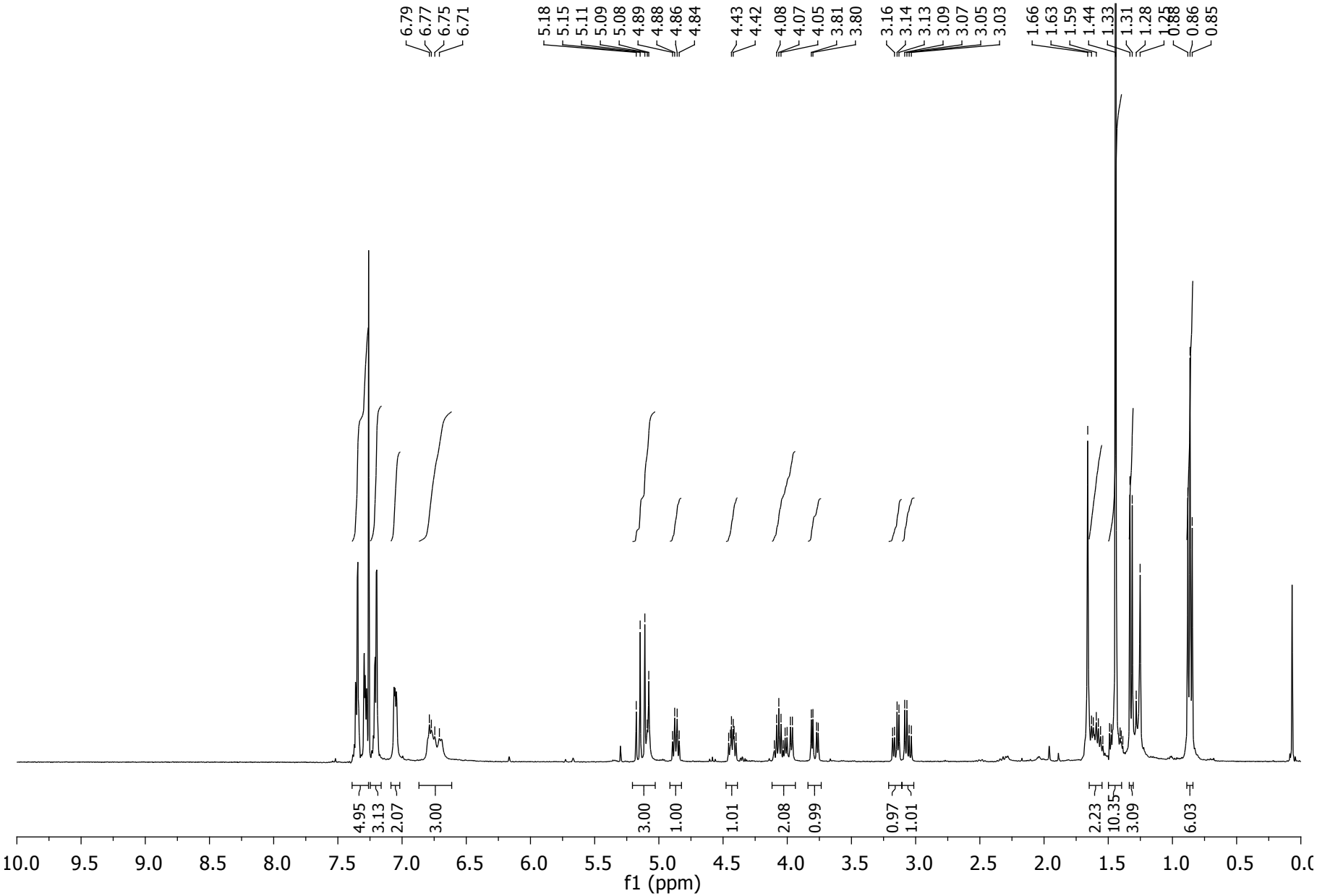
^{1}H NMR spectrum of Boc-Gly-Leu-Ala-Phe-OBn 9a



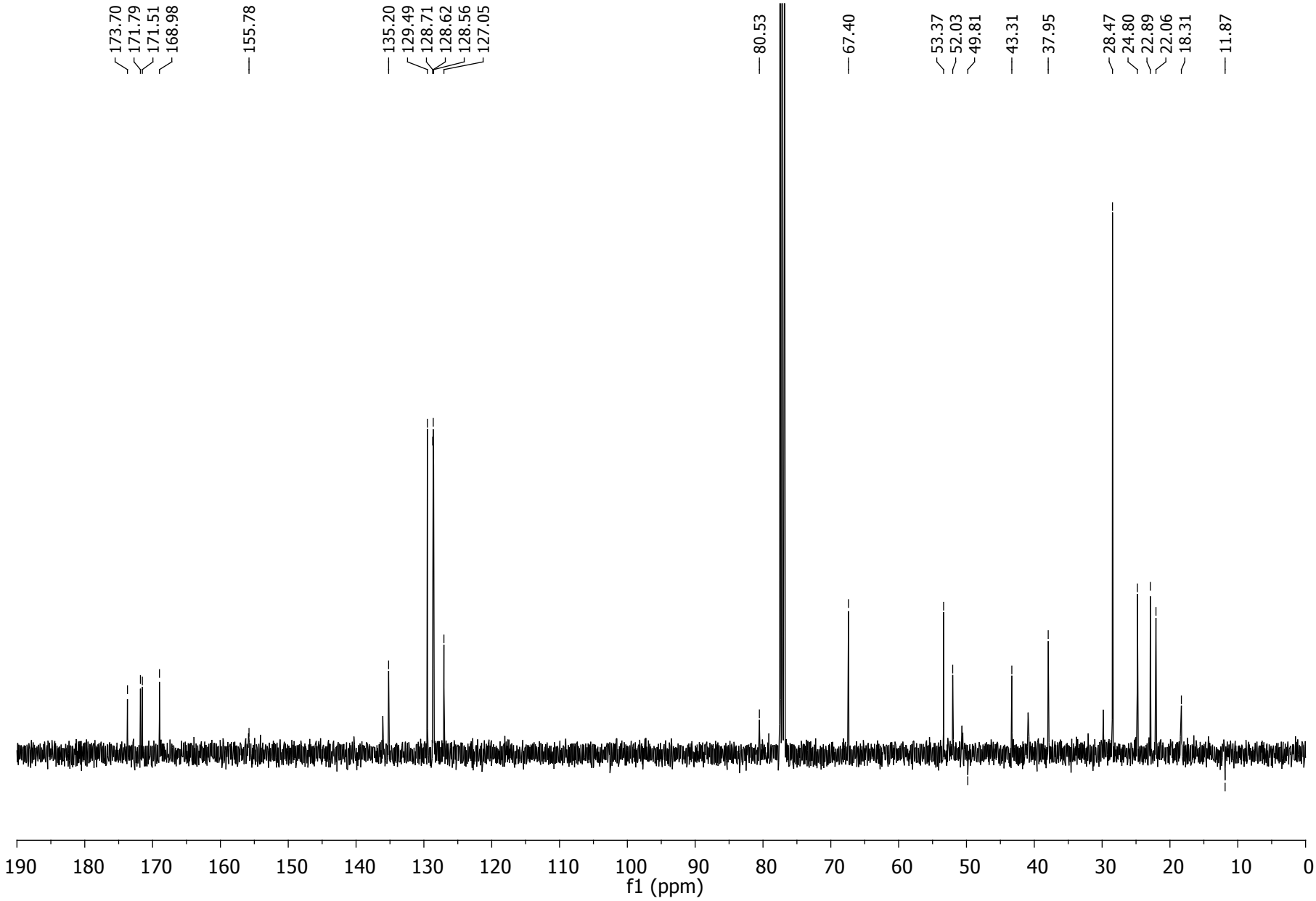
^{13}C NMR spectrum of Boc-Gly-Leu-Ala-Phe-OBn 9a



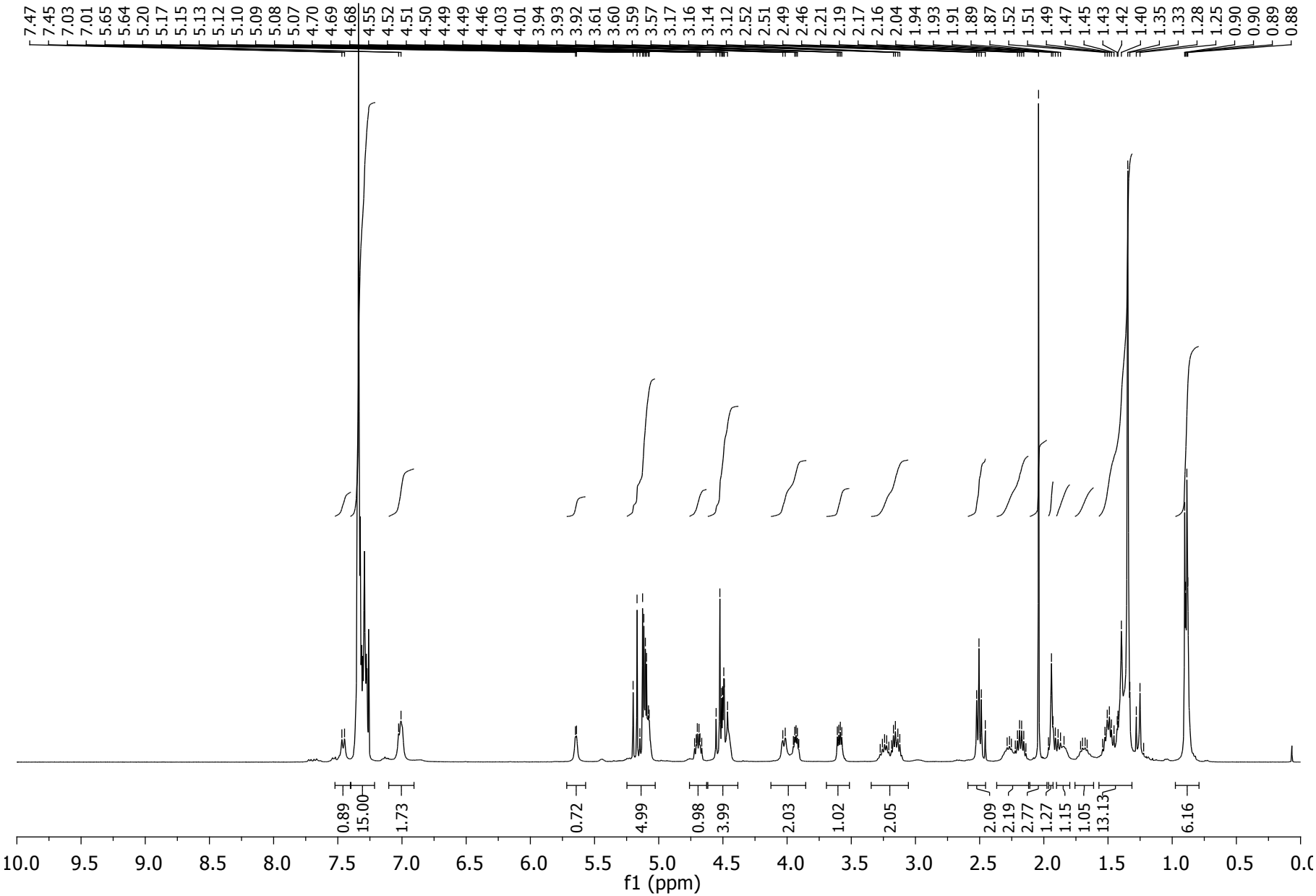
^{1}H NMR spectrum of Boc-Ala-Gly-Leu-Phe-OBn 9b



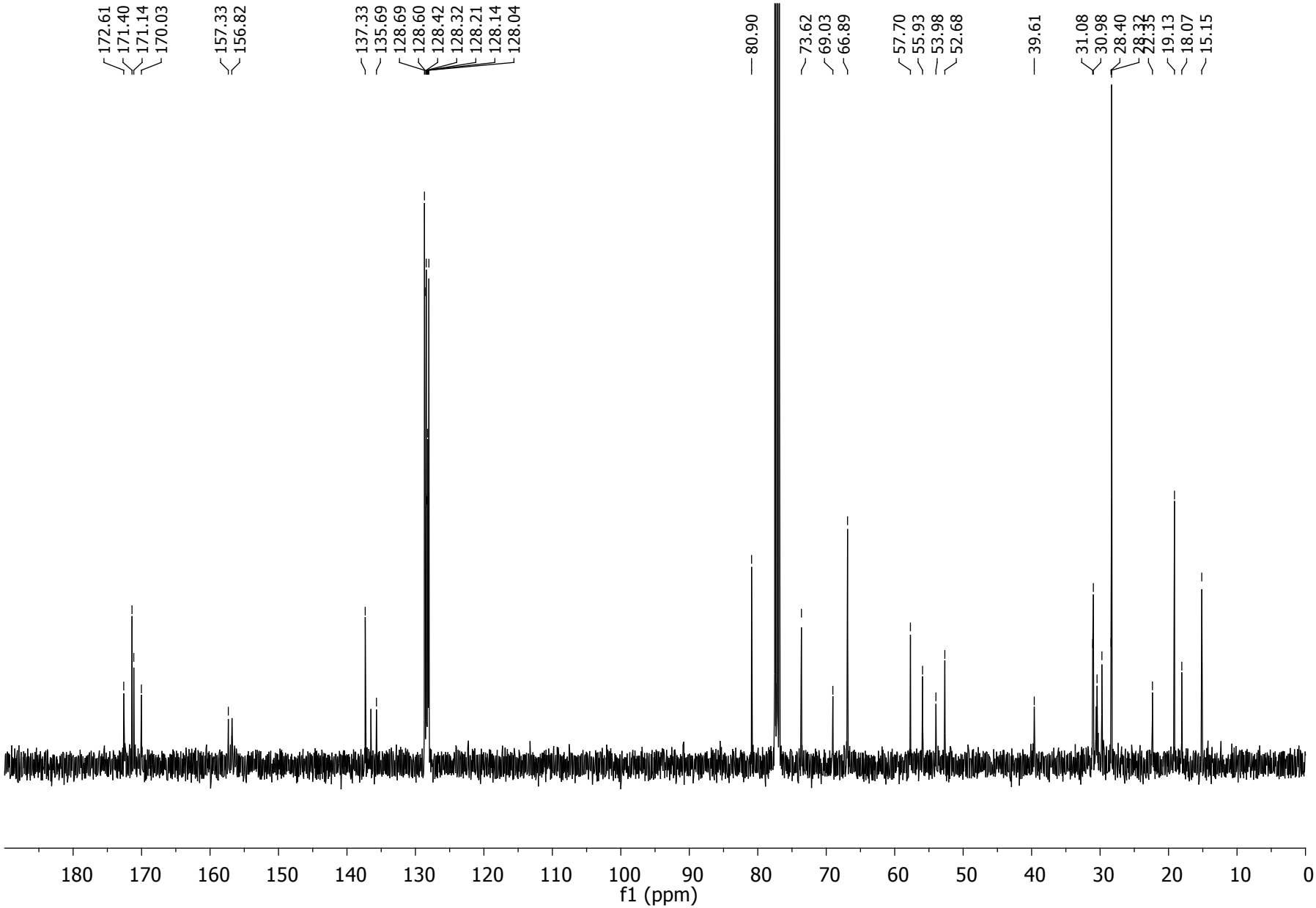
^{13}C NMR spectrum of Boc-Ala-Gly-Leu-Phe-OBn 9b



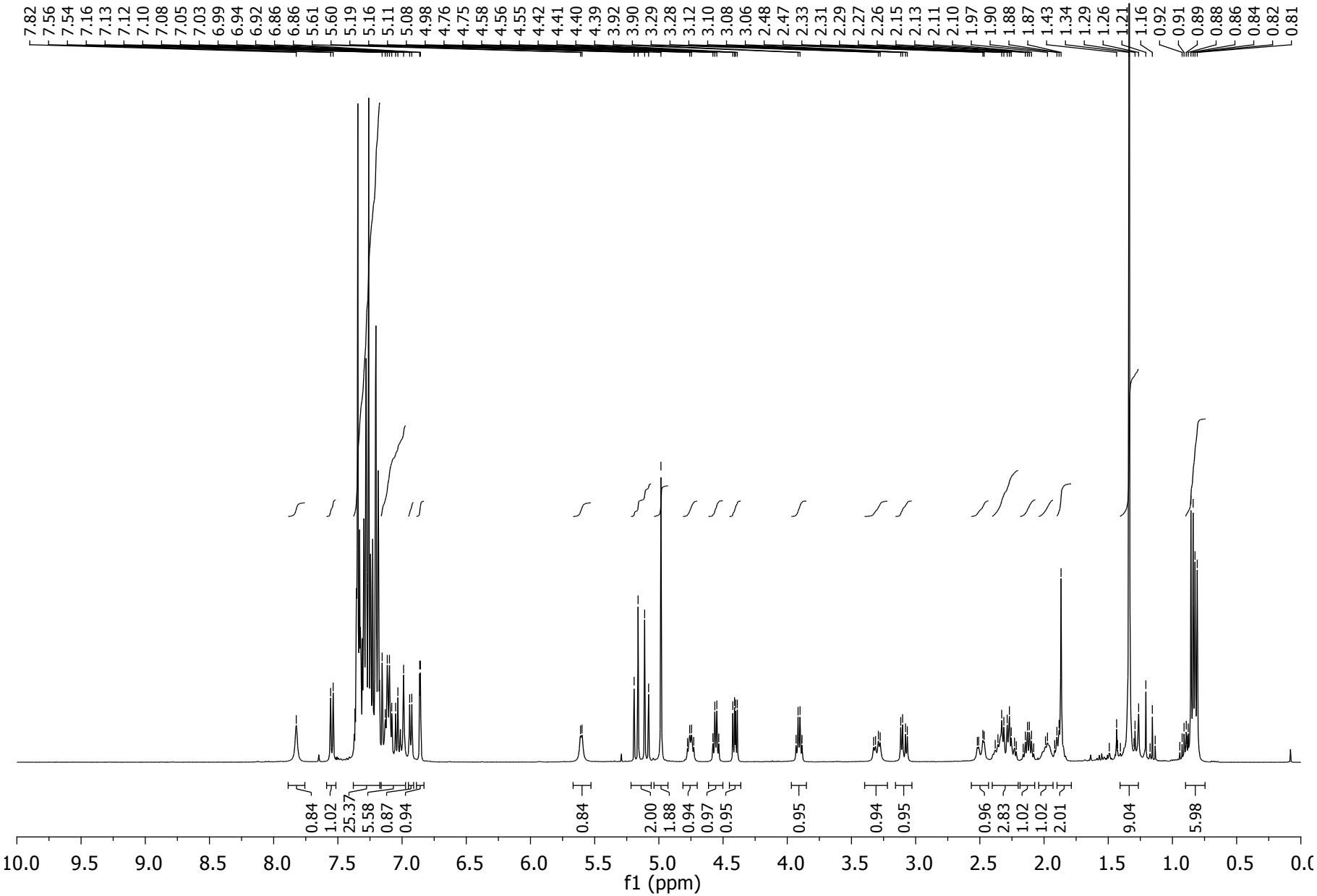
^{1}H NMR spectrum of Boc-Lys(Z)-Ser(OBn)-Met-Val-OBn 9c



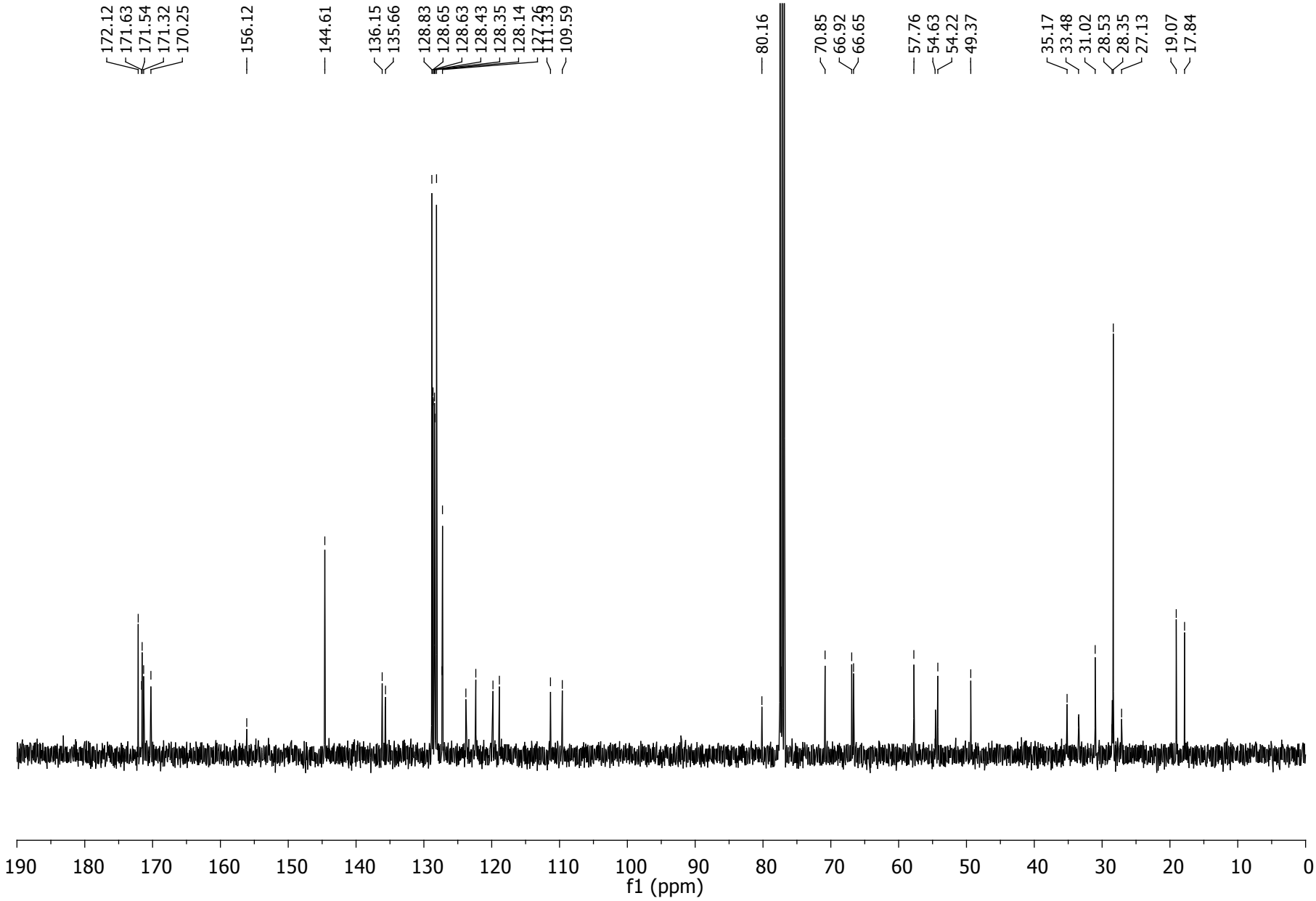
^{13}C NMR spectrum of Boc-Lys(Z)-Ser(OBn)-Met-Val-OBn 9c



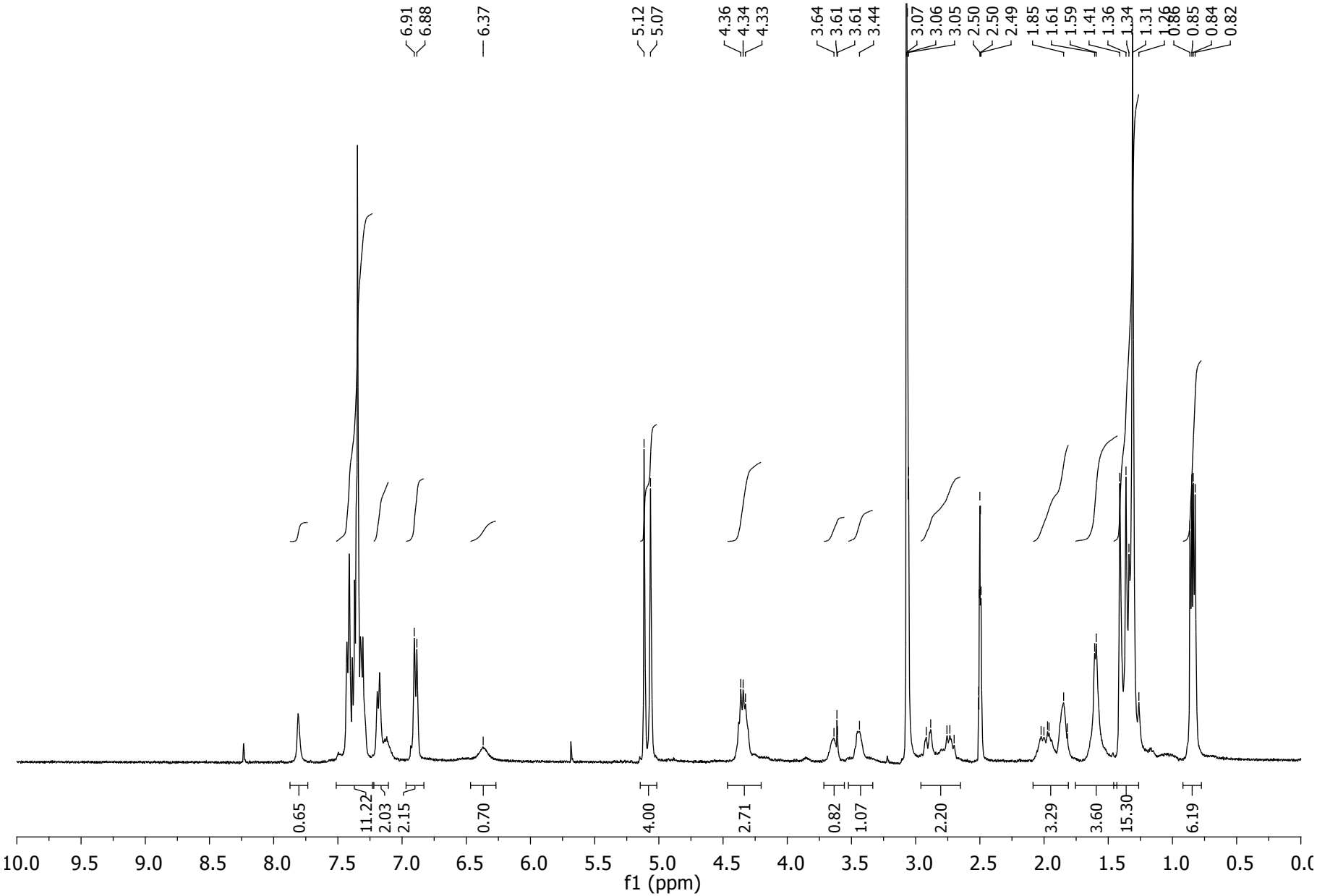
^{1}H NMR spectrum of Boc-Gln(Trt)-Trp-Asp(OBn)-Val-OBn 9d



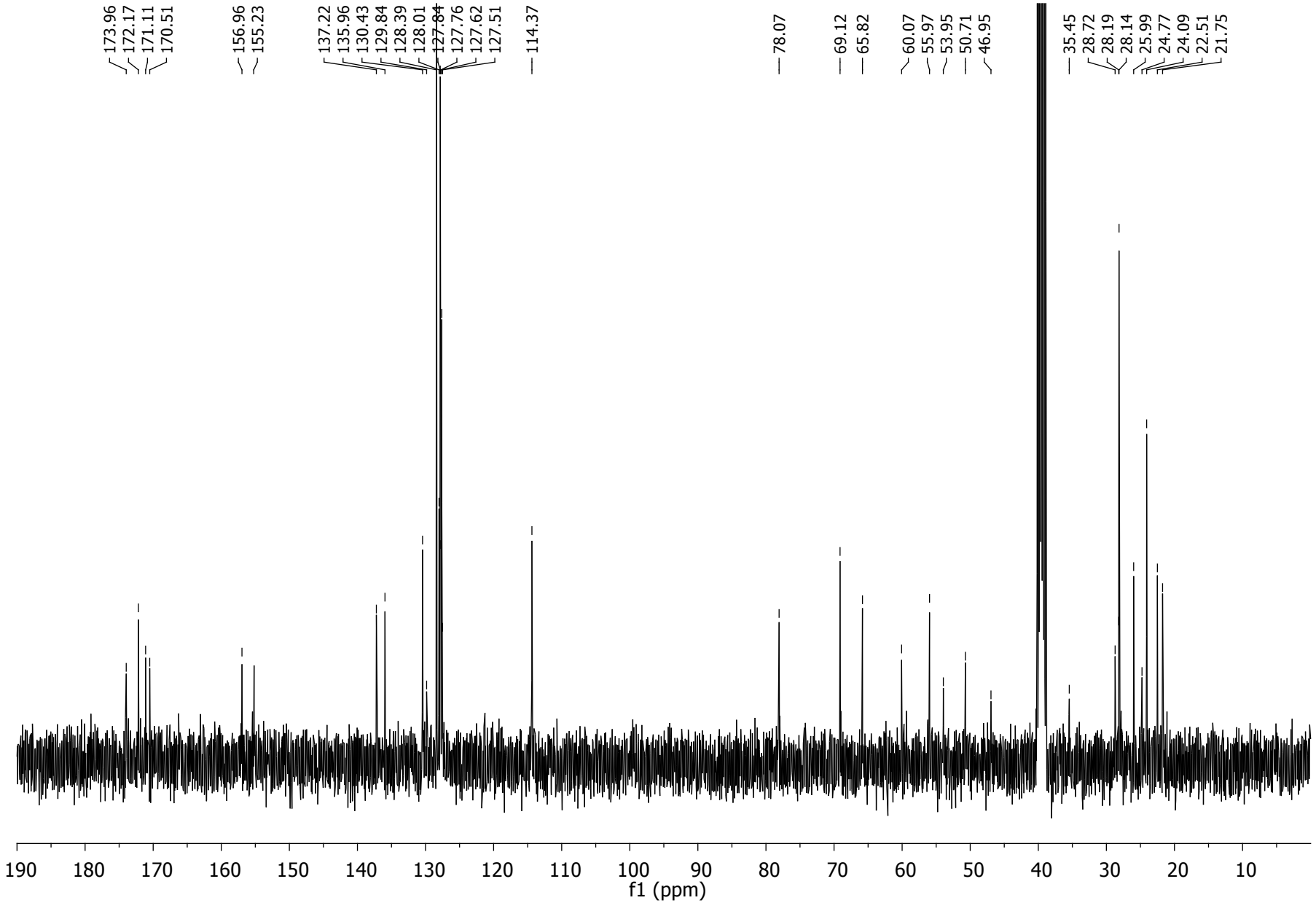
^{13}C NMR spectrum of Boc-Gln(Trt)-Trp-Asp(OBn)-Val-OBn 9d



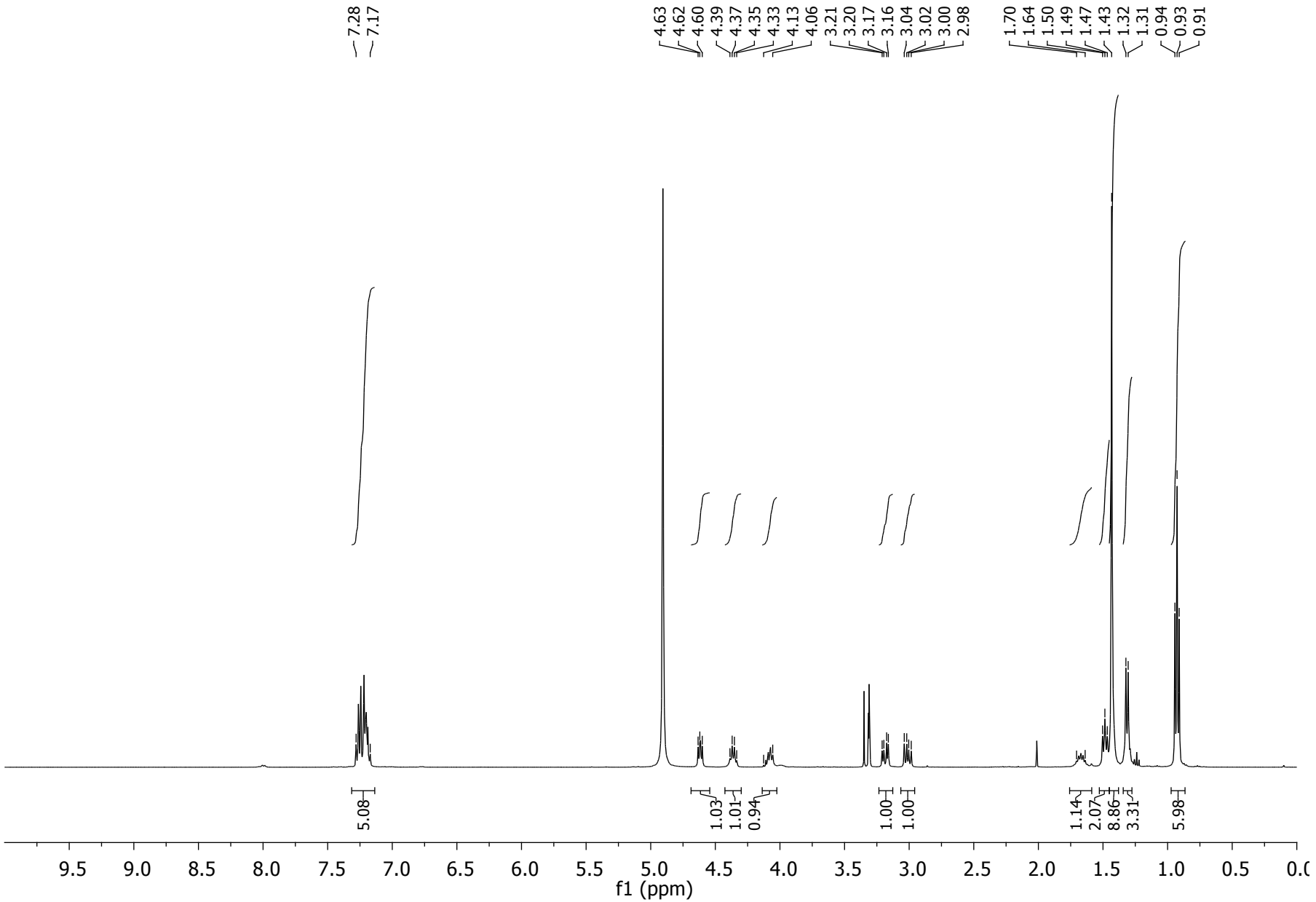
^{1}H NMR spectrum of Boc-Tyr(OBn)-Pro-Aib-Leu-OBn 9e



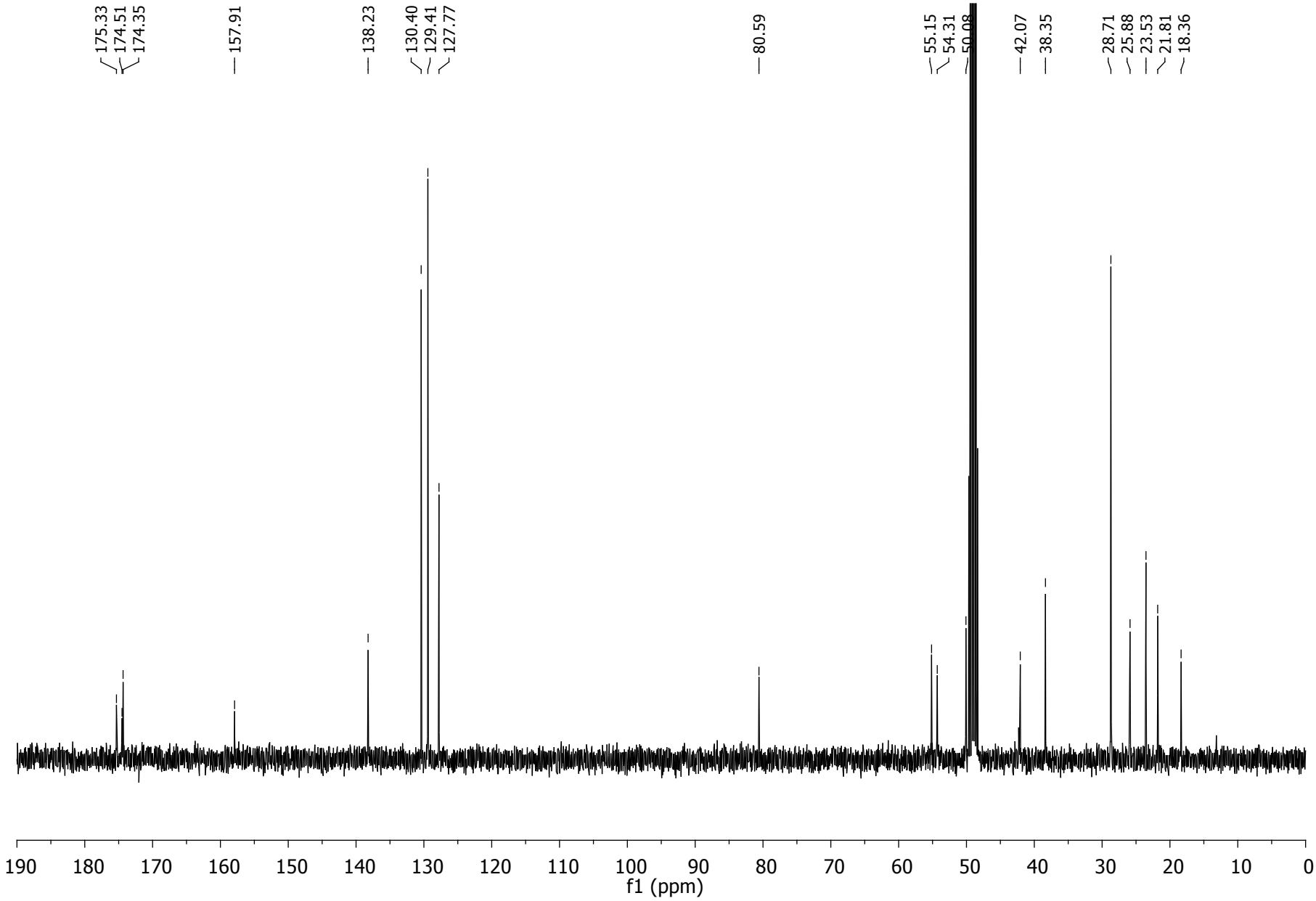
^{13}C NMR spectrum of Boc-Tyr(OBn)-Pro-Aib-Leu-OBn 9e



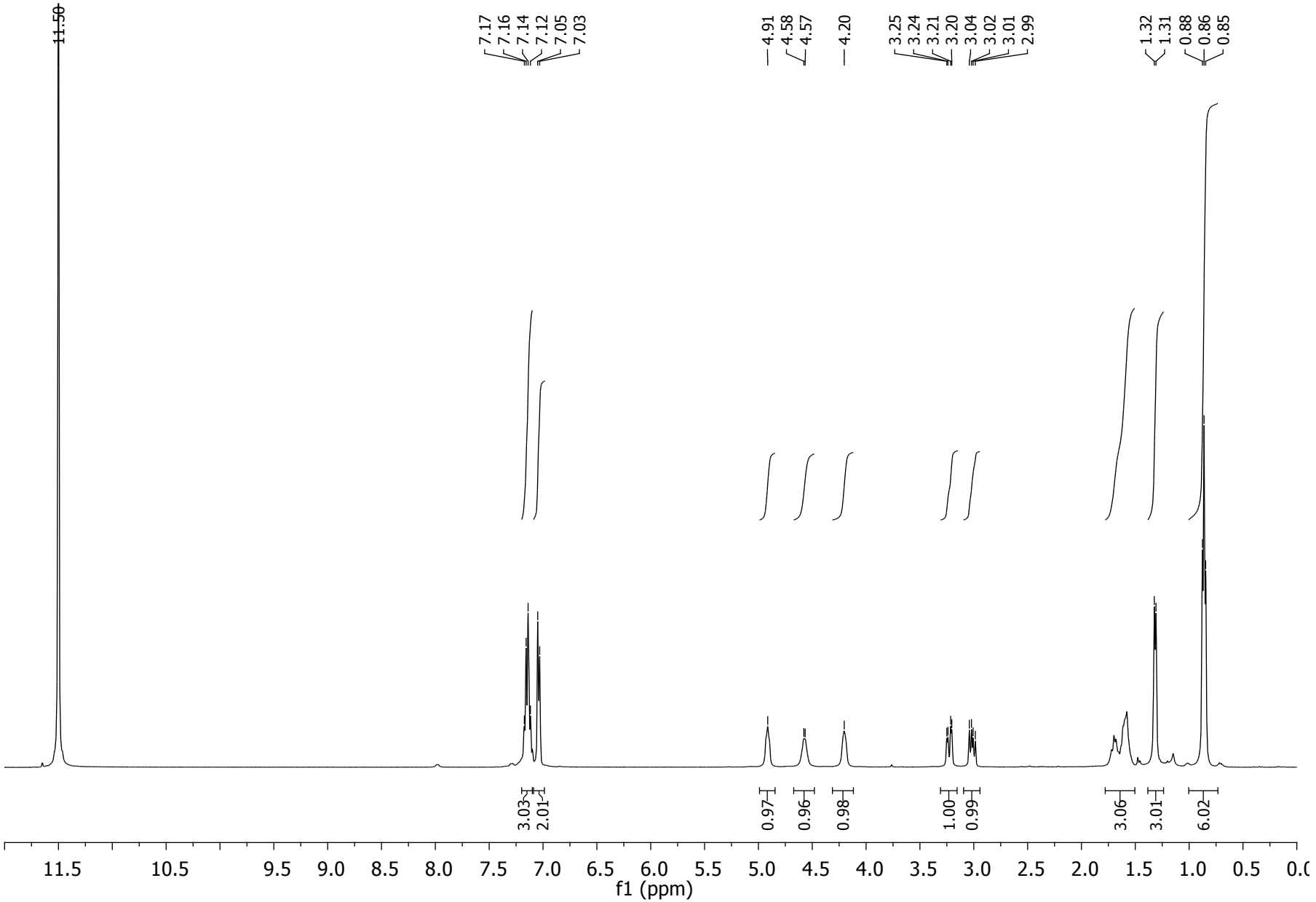
^{1}H NMR spectrum of Boc-Leu-Ala-Phe-OH 10a



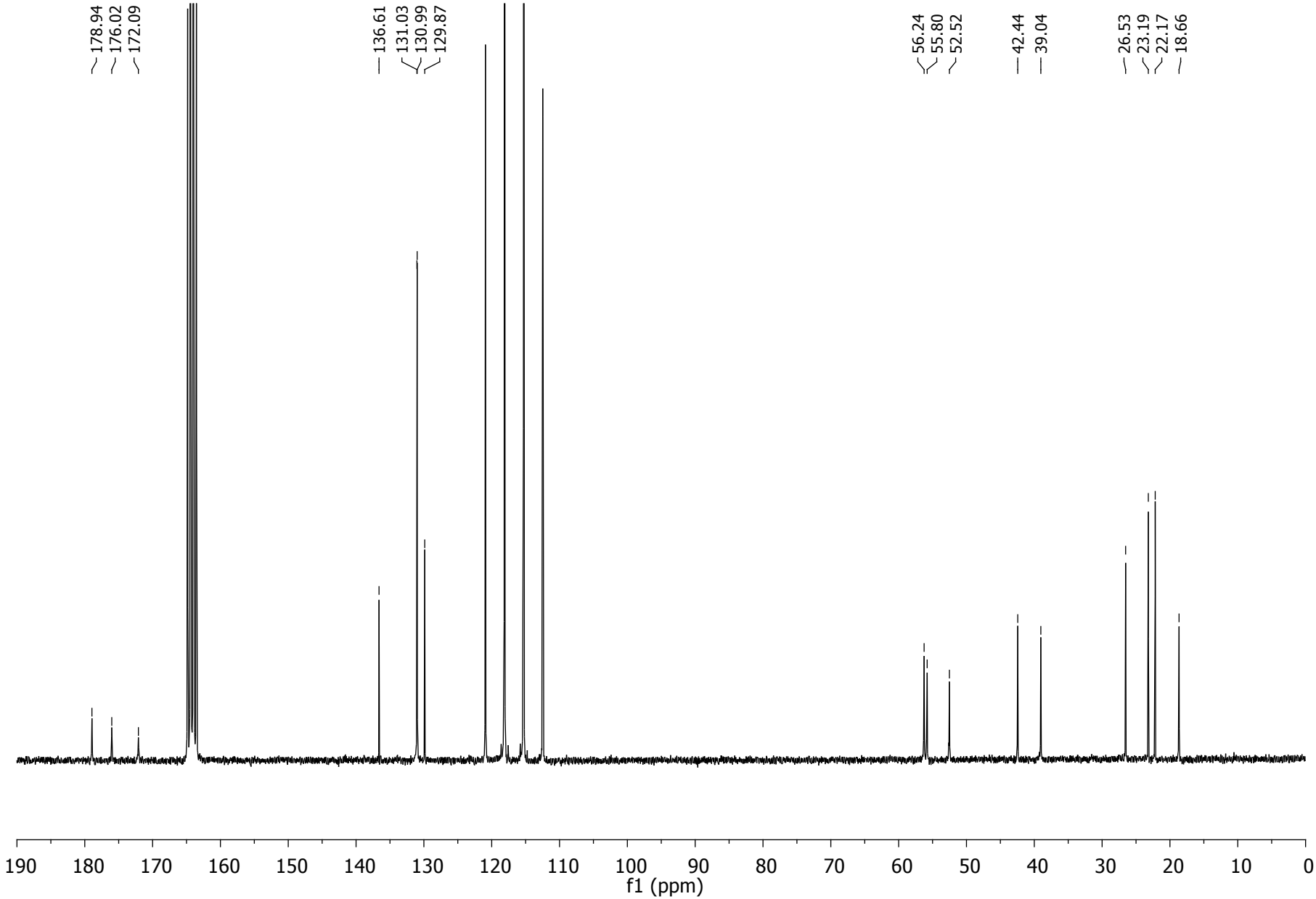
^{13}C NMR spectrum of Boc-Leu-Ala-Phe-OH 10a



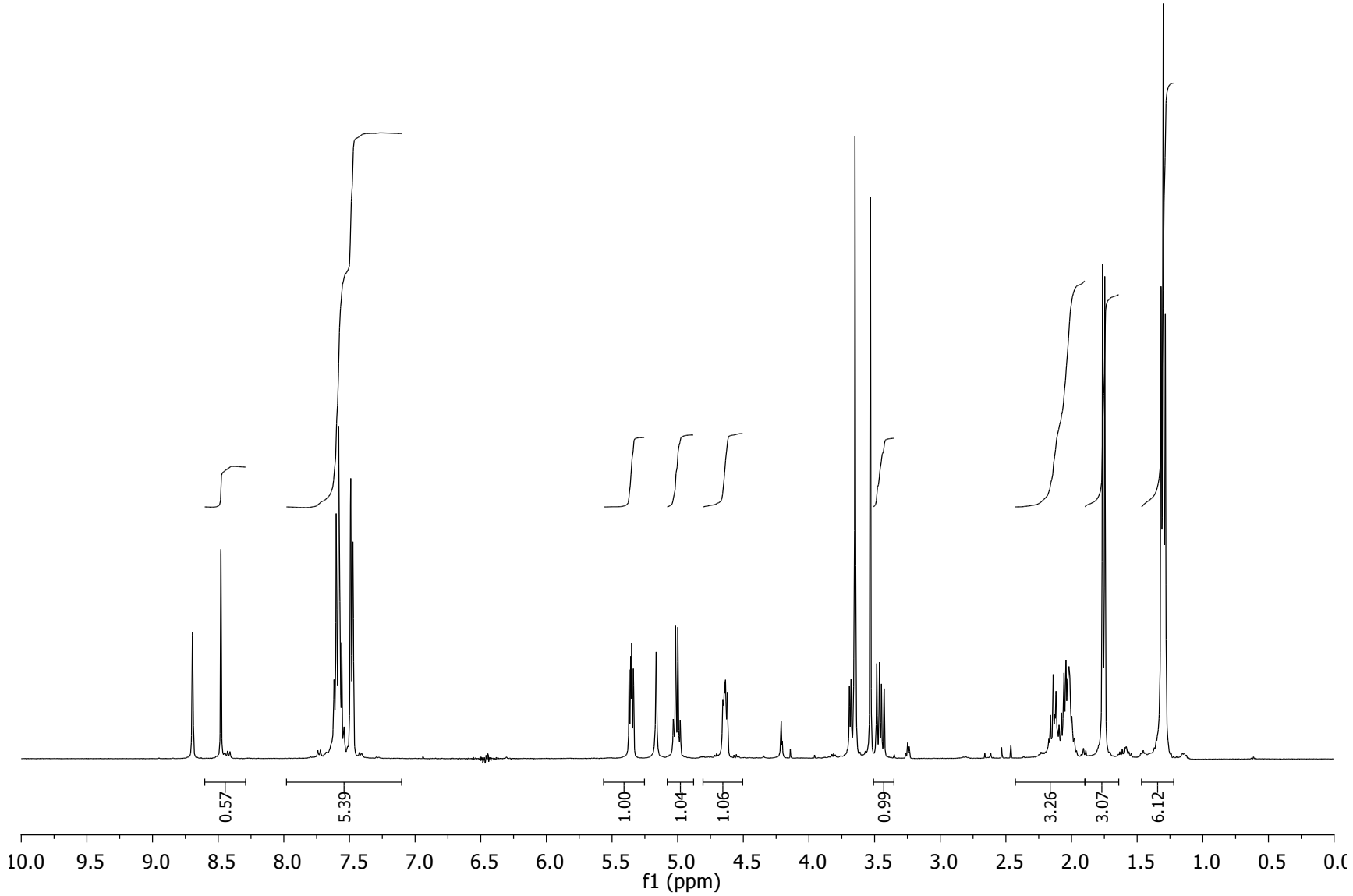
^{1}H NMR spectrum of TFA.H-Leu-Ala-Phe-OH 11a prepared by solution-phase synthesis



^{13}C NMR spectrum of TFA.H-Leu-Ala-Phe-OH 11a prepared by solution-phase synthesis

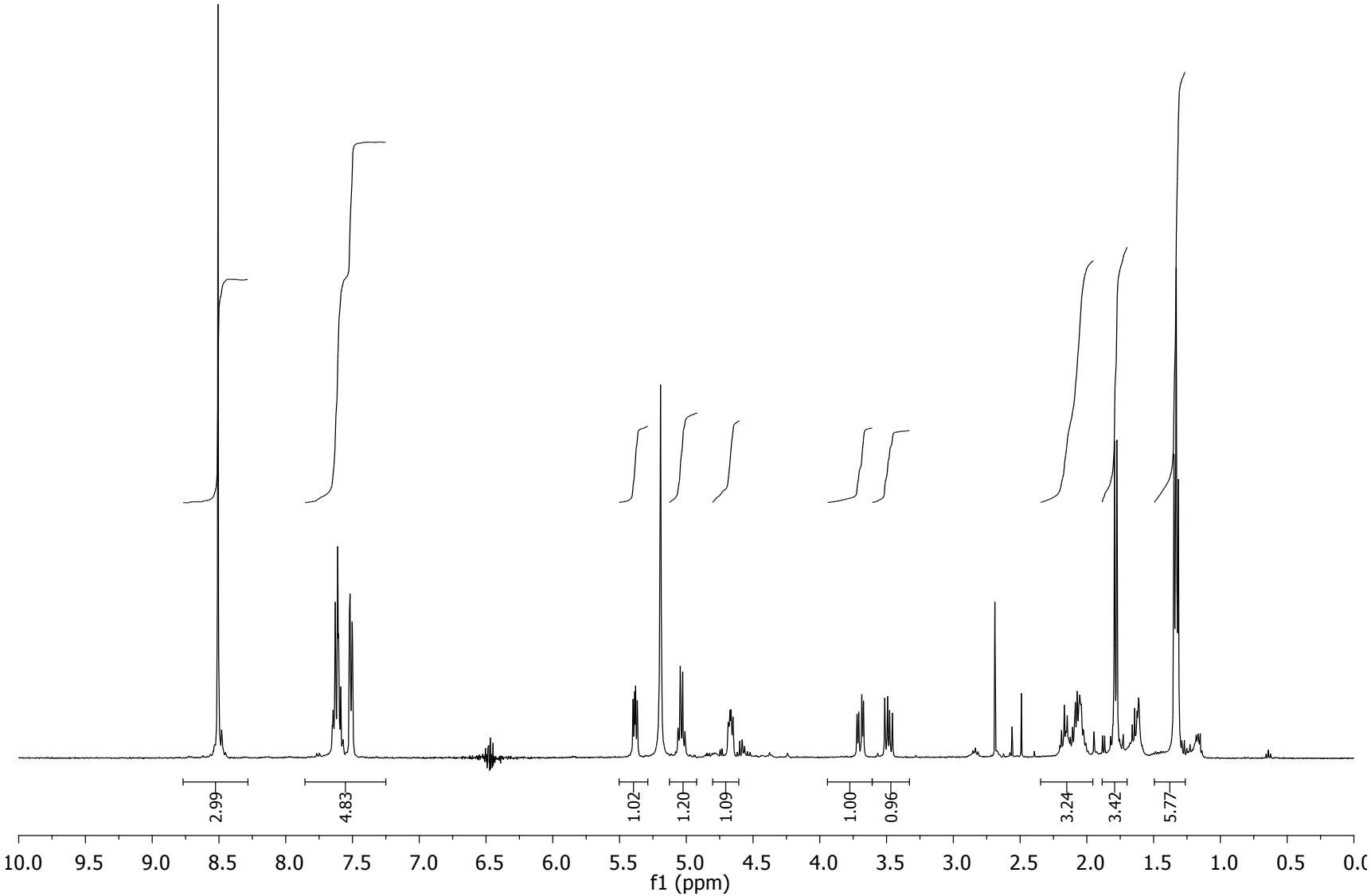


^{1}H NMR spectrum of TFA.H-Leu-Ala-Phe-OH 11a prepared by solid-phase synthesis in DMF



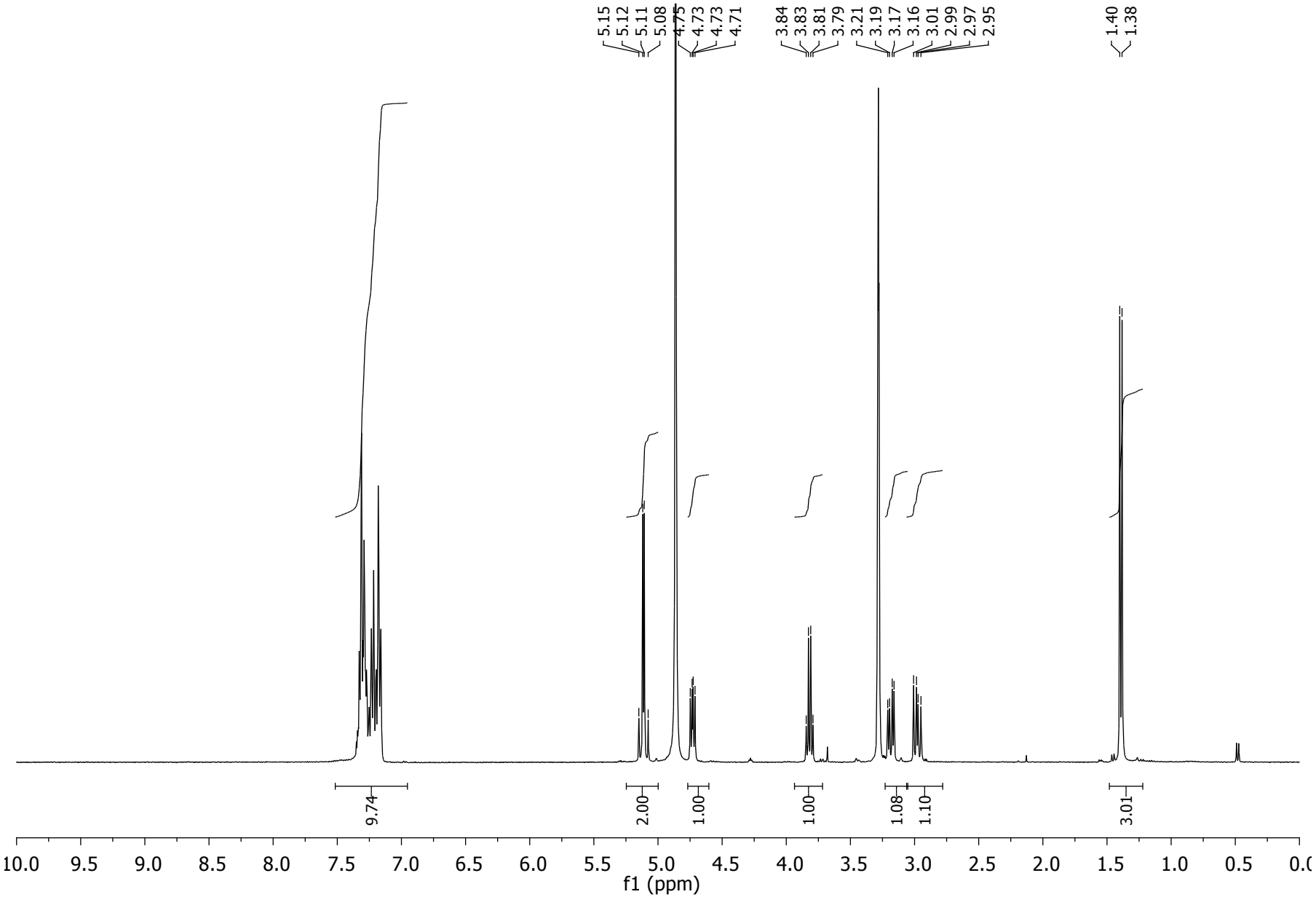
Singlets at 8.7, 3.7 and 3.5 ppm correspond to residual DMF. The singlet at 5.2 ppm corresponds to PEG from the ChemMatrix resin.

^{1}H NMR spectrum of TFA.H-Leu-Ala-Phe-OH 11a prepared by solid-phase synthesis in PC



The singlet at 5.2 ppm corresponds to PEG from the ChemMatrix resin.

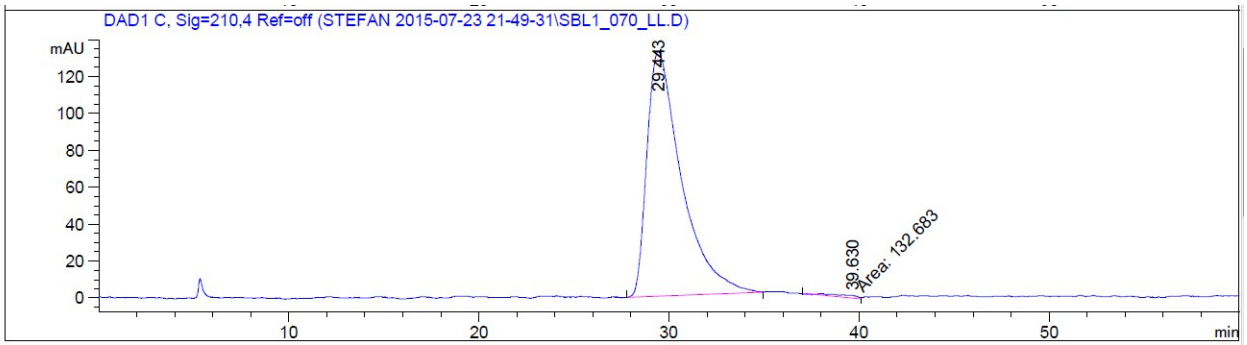
^{1}H NMR spectrum of HCl.H-Ala-Phe-OBn (in CD_3OD) prepared in PC

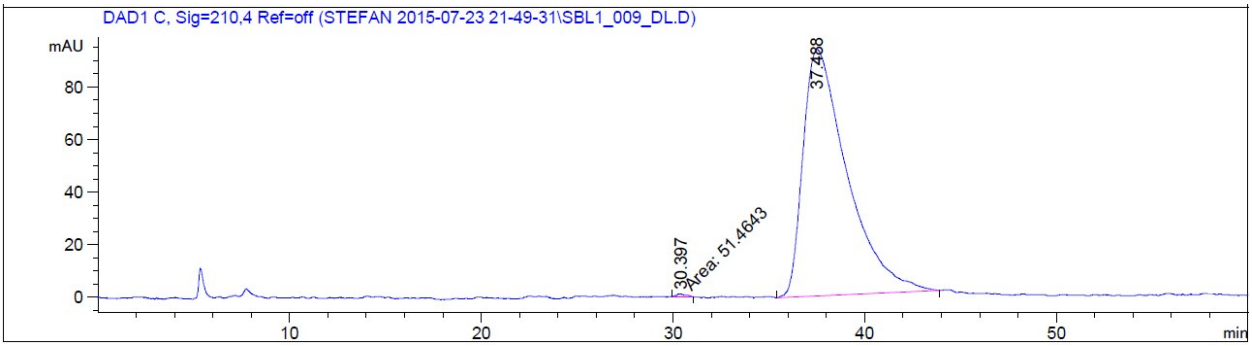


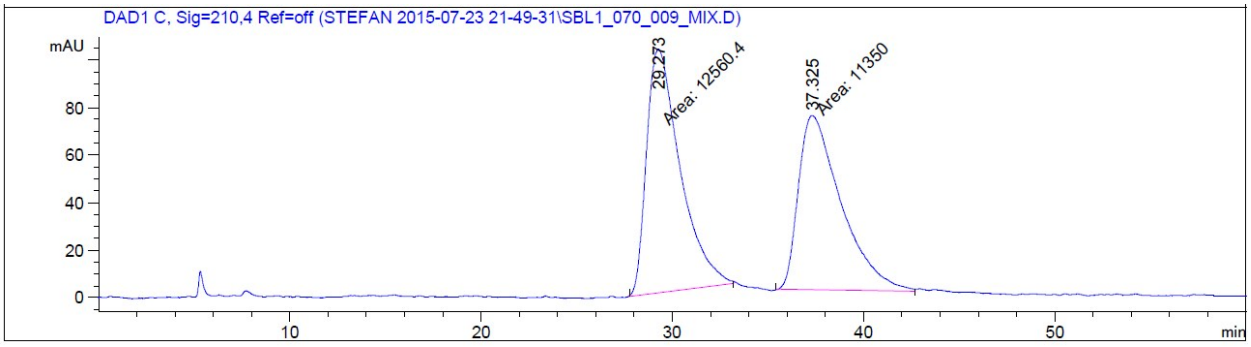
HPLC traces of diastereomeric peptides 5a and 5a'

Chromatograms from a reaction carried out at 20 °C

Top Boc-Ala-Phe-OBn **5a**
Middle: Boc-(*R*)-Ala-Phe-OBn **5a'**
Bottom: 1:1 mixture of 5a and 5a'

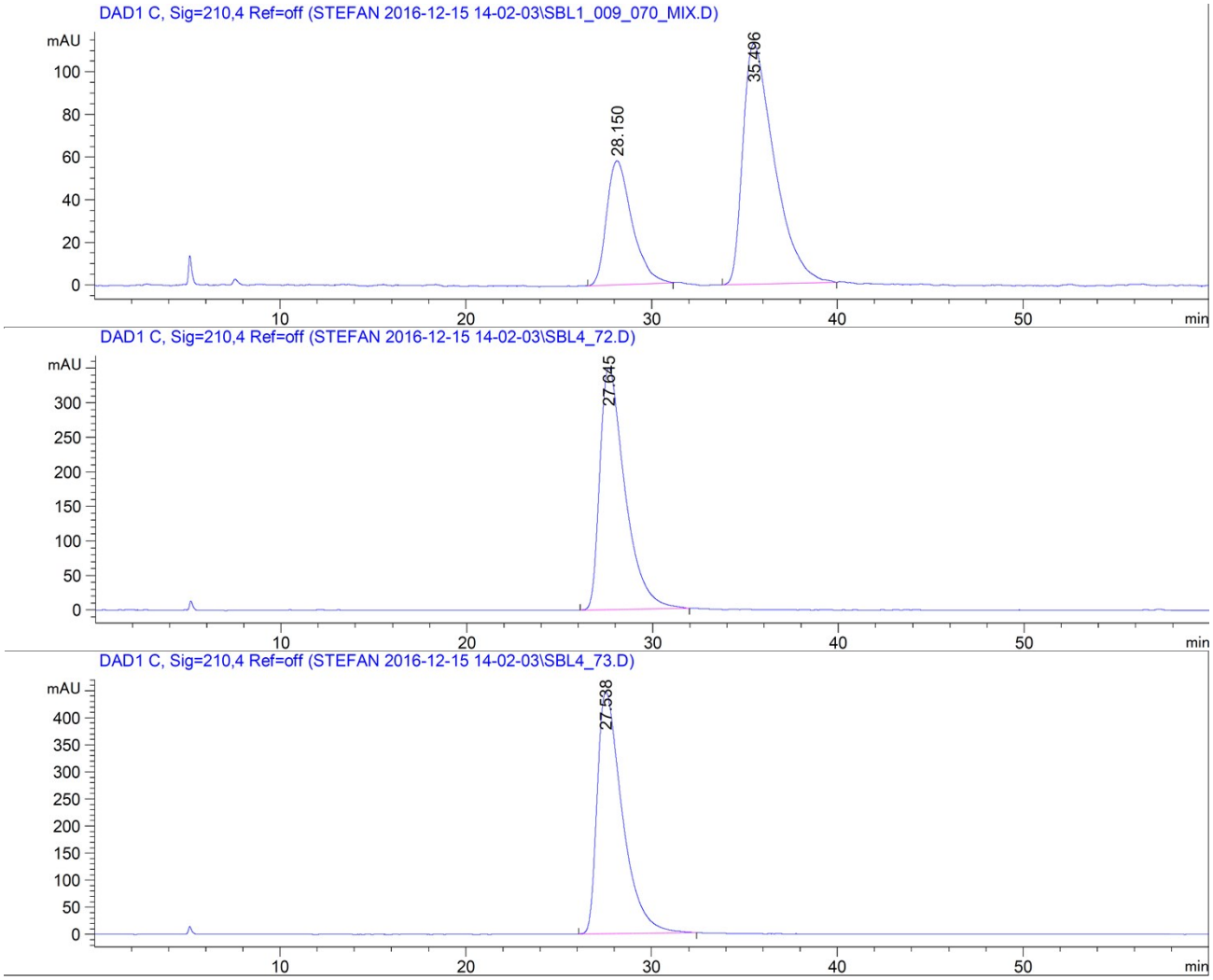






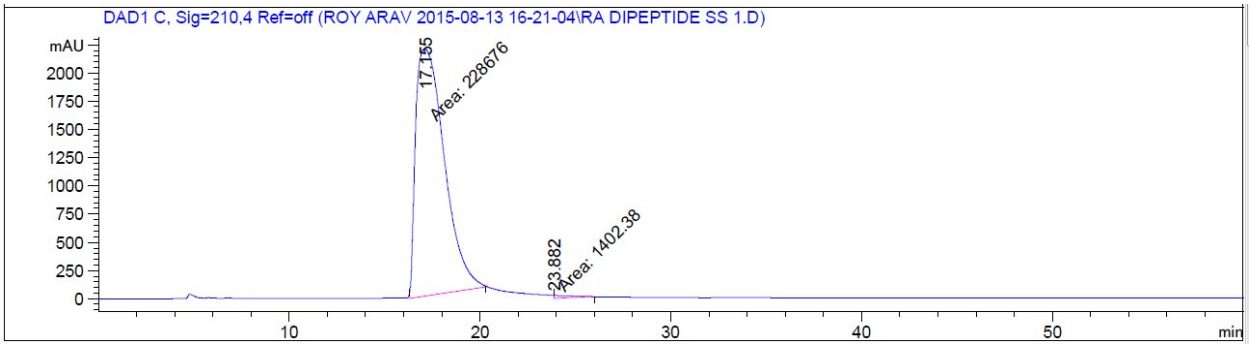
Chromatograms from a reaction carried out at 70 °C in a microwave reactor

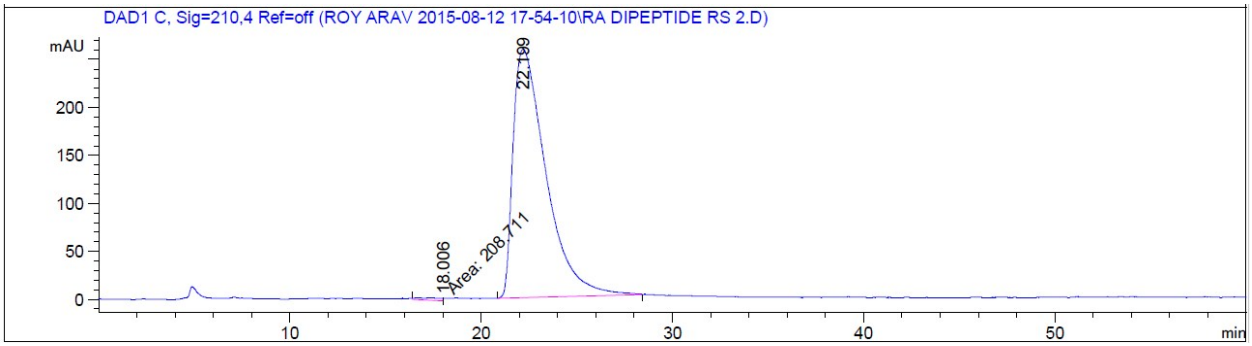
Top 1:1 mixture of **5a** and **5a'**
Middle: Boc-Ala-Phe-OBn **5a** prepared in DMF
Bottom: Boc-Ala-Phe-OBn **5a** prepared in propylene carbonate

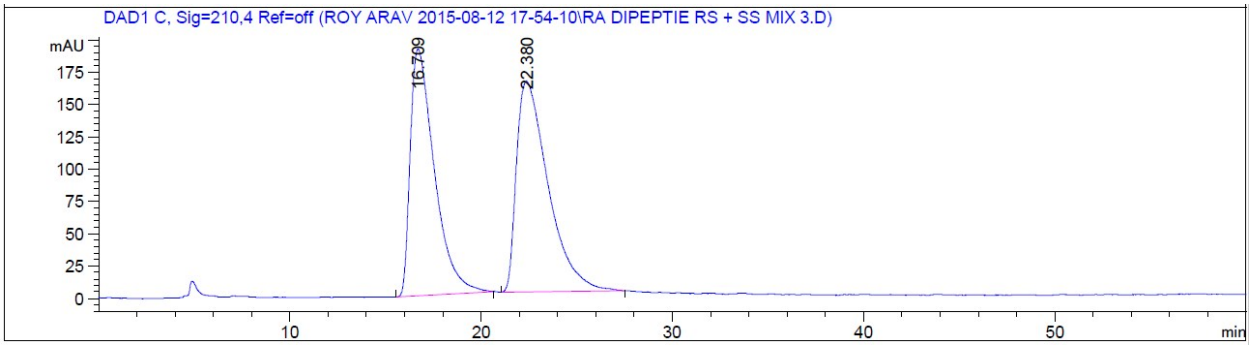


HPLC traces of diastereomeric peptides 5b and 5b'

Top Boc-Leu-Phe-OBn **5b**
Middle: Boc-(*R*)-Leu-Phe-OBn **5a'**
Bottom: 1:1 mixture of **5b** and **5b'**

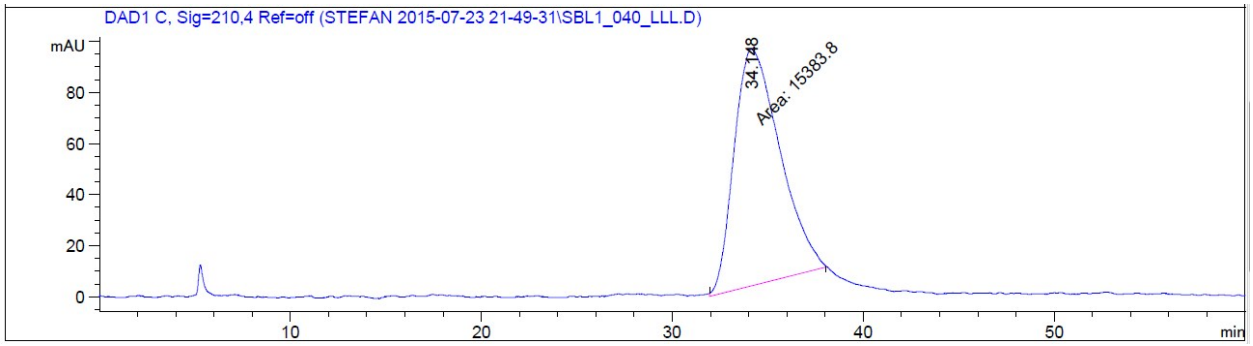


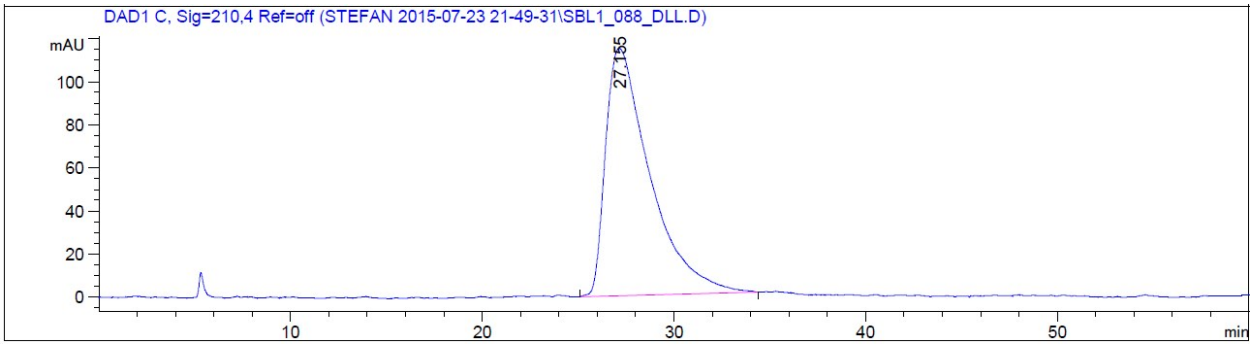


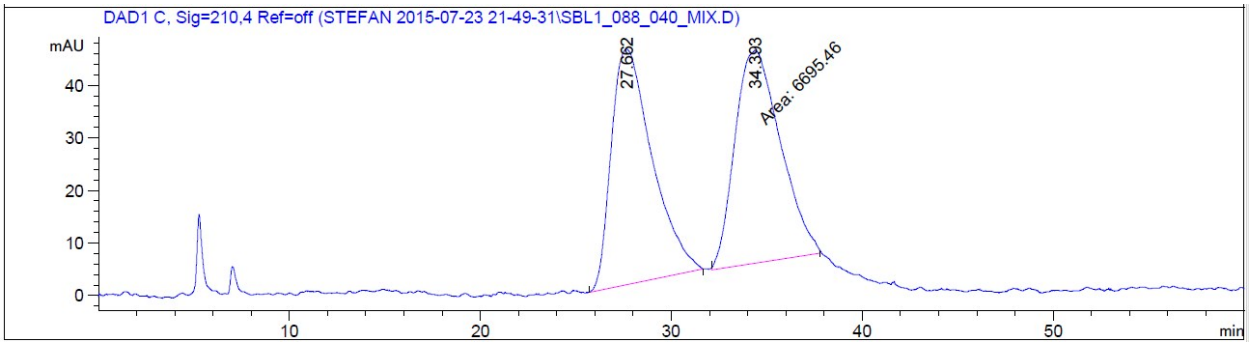


HPLC traces of diastereomeric peptides 7a and 7a'

Top Boc-Leu-Ala-Phe-OBn **7a**
Middle: Boc-(*R*)-Leu-Ala-Phe-OBn **7a'**
Bottom: 1:1 mixture of **7a** and **7a'**

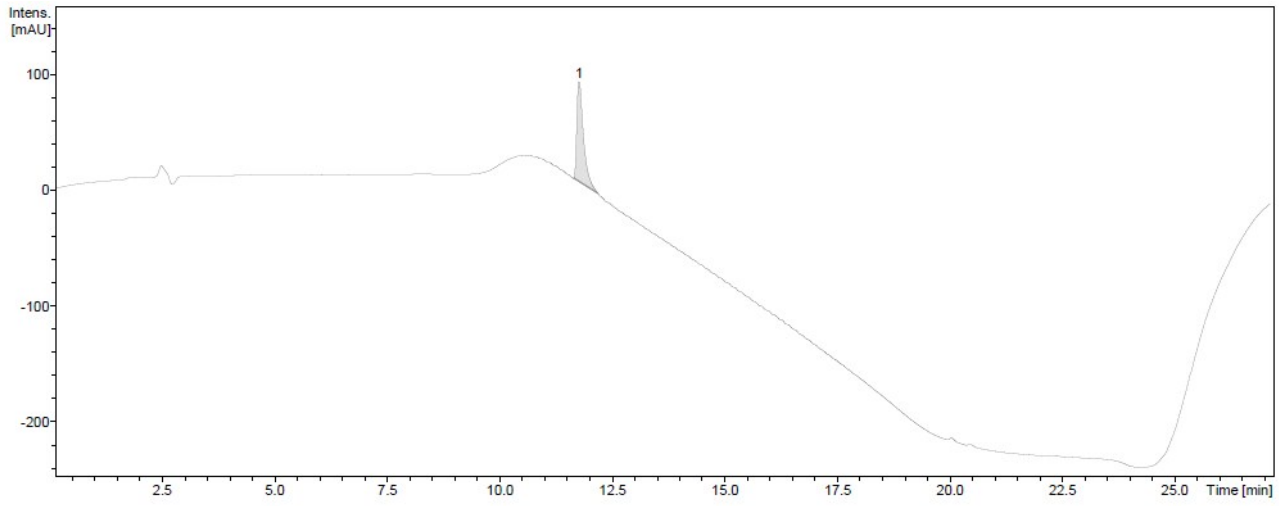






HPLC-UV-HRMS of Bradykinin

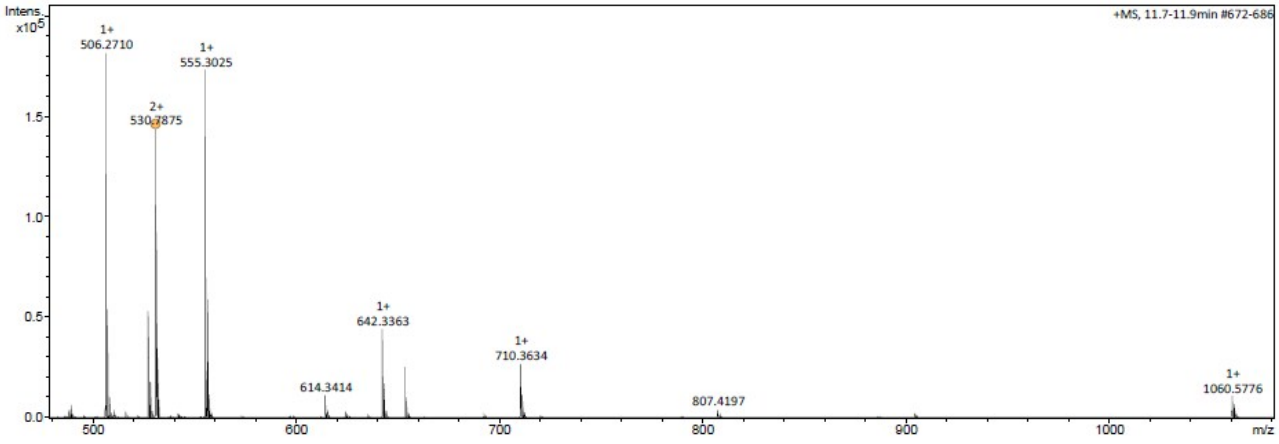
Commercial sample HPLC-UV trace



Compound Spectrum Report

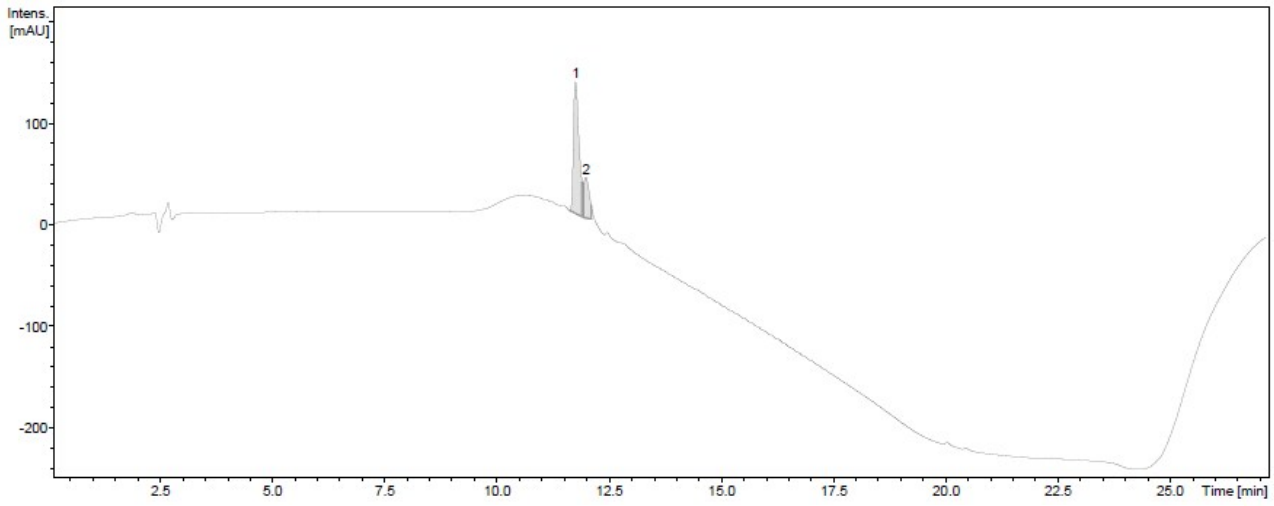
#	RT [min]	Area	I	Range [min]	Chromatogram	Max. m/z
1	11.8	863.15	93	11.7 - 12.2	UV Chromatogram, 214 nm	0.0000
2	11.8	3028746.75	542631	11.7 - 11.9	BPC +	506.2710

Commercial sample HRMS of peak at 11.8 minutes



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
530.787490	1	C50H75N15O11	530.787976	0.9	0.5	22.7	0.2

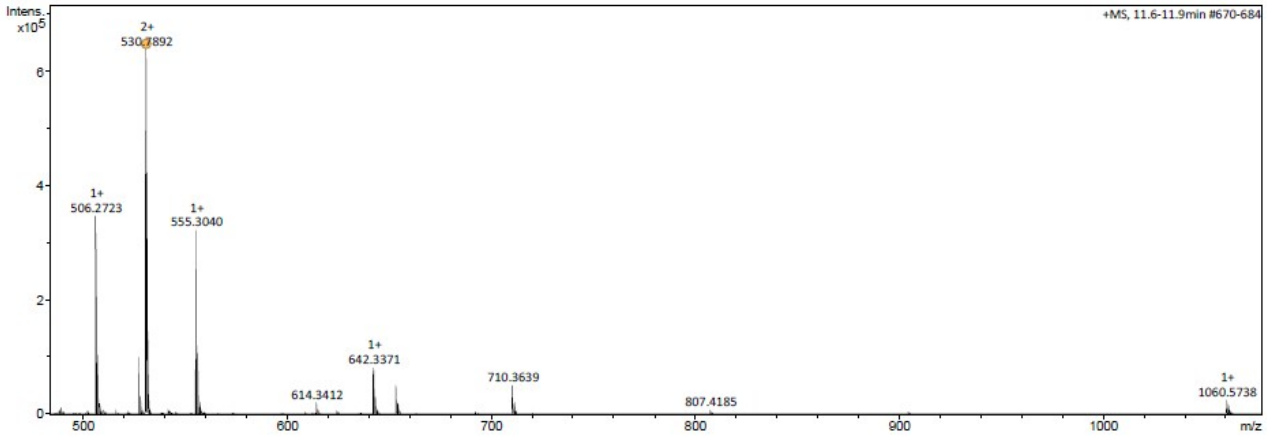
Sample prepared in DMF HPLC-UV trace



Compound Spectrum Report

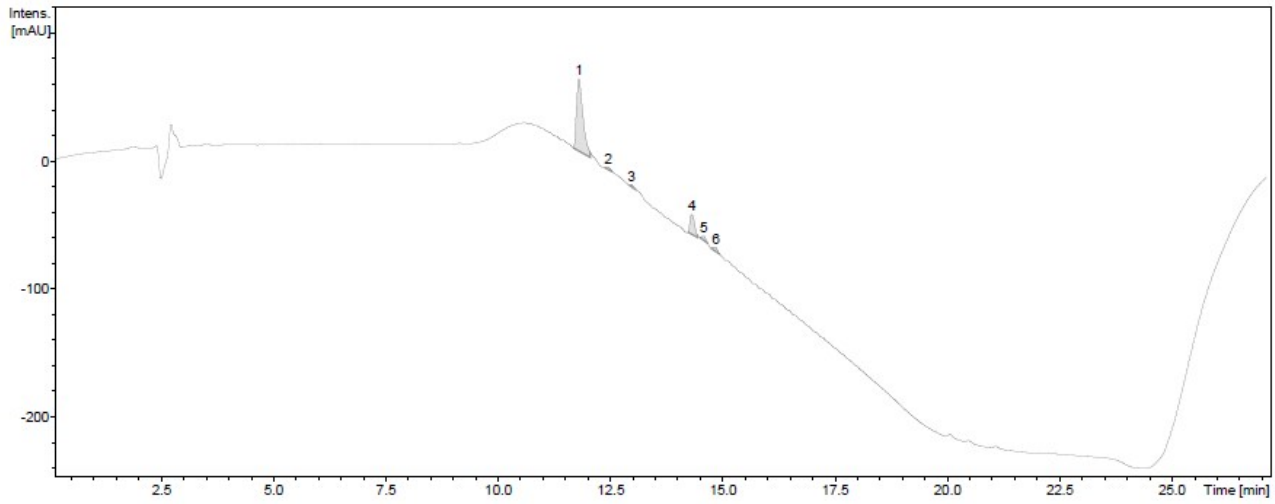
#	RT [min]	Area	I	Range [min]	Chromatogram	Max. m/z
1	11.8	1116.45	140	11.6 - 11.9	UV Chromatogram, 214 nm	0.0000
2	12.0	300.10	46	11.9 - 12.1	UV Chromatogram, 214 nm	0.0000

Sample prepared in DMF HRMS of peak at 11.8 minutes



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
530.789164	1	C50H75N15O11	530.787976	2.2	1.2	25.7	-2.1

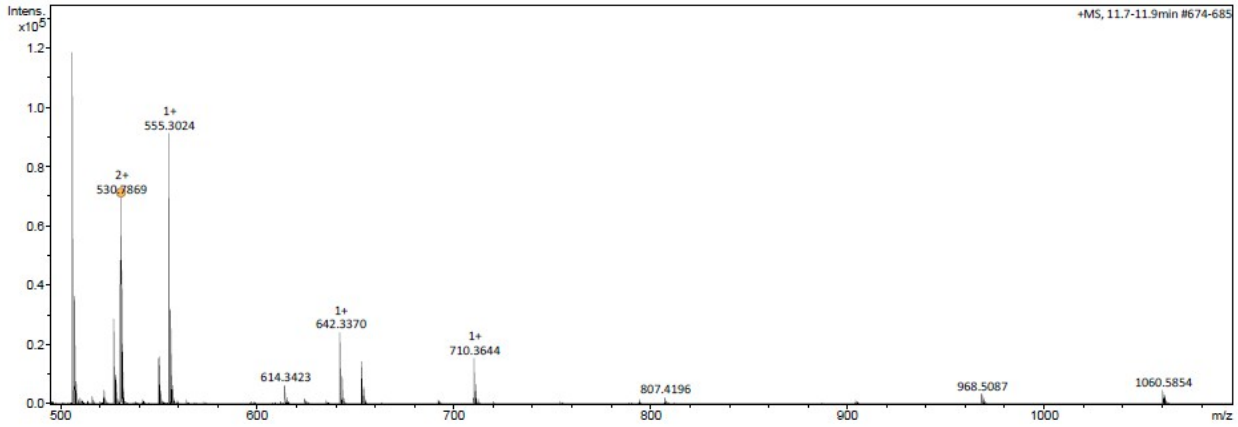
Sample prepared in propylene carbonate HPLC-UV trace



Compound Spectrum Report

#	RT [min]	Area	I	Range [min]	Chromatogram	Max. m/z
1	11.8	562.8484	63	11.7 - 12.0	UV Chromatogram, 214 nm	0.0000
2	12.4	10.7454		12.4 - 12.5	UV Chromatogram, 214 nm	0.0000
3	13.0	8.0444		12.9 - 13.1	UV Chromatogram, 214 nm	0.0000
4	14.3	111.6037		14.2 - 14.4	UV Chromatogram, 214 nm	0.0000
5	14.6	19.2939		14.5 - 14.7	UV Chromatogram, 214 nm	0.0000
6	14.8	18.9010		14.7 - 14.9	UV Chromatogram, 214 nm	0.0000

Sample prepared in propylene carbonate HRMS of peak at 11.8 minutes



Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
530.786911	1	C50H75N15O11	530.787976	-2.0	-1.1	29.4	1.3

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