Structural characterization of folded and extended conformations in peptides containing γ amino acids with proteinogenic side chains: Crystal structures of γ_n, $\alpha\gamma_n$ and γγδγ sequences.

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Synthetic Procedures

Boc–[γ^4(*R*)Val]$_2$–OMe (1): Boc–γ^4(*R*)Val–OH (2 g, 8.16 mmol) was dissolved in 30 mL of DCM (dichloromethane) and cooled in an ice salt bath while stirring. NMM (N-methylmorpholine, 0.99 mL, 8.97 mmol) and IBCF (isobutylchloroformate, 1.16 mL, 8.97 mmol) were added into the reaction mixture. After stirring the reaction mixture for about 10 min, a pre-cooled solution of HCl.H-γ^4Val-OMe (1.6 g, 8.16 mmol) was added. After 10 min, the pH of the solution was adjusted to ~8 by adding NMM and the reaction mixture was stirred overnight at room temperature. 100 mL of DCM was added to the reaction mixture and washed

successively with 10% $KHSO_4$ (potassium hydrogen sulphate) (3 × 40 mL), 20% $NaHCO_3$ (sodium hydrogen carbonate) (3 × 40 mL), Water and brine (3 × 40 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated in vacuo. The yellow oil was triturated with hexane (2 x 10 mL) to yield **1** (2.6 g, 82%) as a white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 386.28; $[M+H]^+_{obsd}$, 387.19; $[M+Na]^+_{obsd,}$ 409.18; $[M+K]^+_{obsd,}$ 425.13; MP (˚C): 119–120.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.25 (d, *J* = 9.4 Hz, 1NH), 4.42 (d, *J* = 9.8 Hz, 1NH).

Boc-[γ^4(*R*)Val]$_3$-NHMe (2): Boc–[γ^4(*R*)Val]$_2$–OH (1g, 2.7mmol) was dissolved in 20 mL of DCM (dichloromethane) and cooled in an ice salt bath while stirring. NMM (N-methylmorpholine, 0.4 mL, 3.4 mmol) and IBCF (isobutylchloroformate, 0.4 mL, 3.4 mmol) were added into the reaction mixture. After stirring the reaction mixture for about 10 min, a pre-cooled solution of HCl.H-γ^4(*R*)Val-NHMe (0.5 g, 3.2 mmol) was added. After 10 min, the pH of the solution was adjusted to ~8 by adding NMM and the reaction mixture was stirred overnight at room temperature. 60 mL of DCM was added to the reaction mixture and washed successively with 10% $KHSO_4$ (potassium hydrogen sulphate) (3 × 40 mL), 20% $NaHCO_3$ (sodium hydrogen carbonate) (3 × 40 mL), Water and brine (3 × 40 mL). The combined organic layer was dried over anhydrous sodium sulfate and evaporated in vacuo. The viscous oil was triturated with hexane (2 x 15 mL) to yield **2** (1.1g, 78%) as a white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 512.74; $[M+H]^+_{obsd}$, 513.3; $[M+Na]^+_{obsd,}$ 535.4; MP (˚C): 218.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.65 (s, 1NH), 6.95 (d, *J* = 9.5 Hz, 1NH), 5.50 (d, *J* = 9.7 Hz, 1NH), 4.32 (d, *J* = 10.5 Hz, 1NH).

Boc–γ^4(*S*)Val–γ^4(*R*)Val–OMe (3): Boc–γ^4(*S*)Val–OH (2 g, 8.16 mmol) was dissolved in 30 mL of DCM (dichloromethane) and cooled in an ice salt bath while stirring. NMM (N-methylmorpholine, 0.99 mL, 8.97 mmol) and IBCF (isobutylchloroformate, 1.16 mL, 8.97 mmol) were added into the reaction mixture. After stirring the reaction mixture for about 10 min, a pre-cooled solution of HCl.H-γ^4(R)Val-OMe (1.6 g, 8.16 mmol) was added. After 10 min, the pH of the solution was adjusted to ~8 by adding NMM and the reaction mixture was stirred overnight at room temperature. 100 mL of DCM was added to the reaction mixture and washed successively 10% $KHSO_4$ (potassium hydrogen sulphate) (3 × 40 mL), 20% $NaHCO_3$ (sodium hydrogen carbonate) (3 × 40 mL), Water and brine (3 × 40 mL). The combined organic layer was

dried over anhydrous sodium sulfate and evaporated in vacuo. The pale yellow oil was triturated with hexane (2 x 10 mL) to yield **3** (2.4 g, 75.6%) as a white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 386.28; $[M+H]^+_{obsd}$, 387.1; $[M+Na]^+_{obsd,}$ 409.1; $[M+K]^+_{obsd,}$ 425.1; MP (˚C): 117–122.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.20 (d, *J* = 9.3 Hz, 1NH), 4.40 (d, *J* = 9.5 Hz, 1NH).

Boc–[γ^4(*R*)Val]$_4$–OMe (4): Boc–[γ^4(*R*)Val]$_2$–OH (0.39 g, 1.05 mmol), obtained by alkaline hydrolysis of Boc–[γ^4(*R*)Val]$_2$–OMe and a free base H–[γ^4(*R*)Val]$_2$–OMe (0.3 g, 1.05 mmol) were coupled using HATU (0.44 g, 1.15 mmol)/HOBT (0.16 g, 1.05 mmol) as coupling agents, DCM:DMF solvent mixture followed by reaction work up as in section (i). The peptide **4** (0.5 g, 74%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 640.48; $[M+H]^+_{obsd}$, 641.53; $[M+Na]^+_{obsd,}$ 663.54; $[M+K]^+_{obsd,}$ 679.49; MP (˚C): 180 –182.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.21 (d, *J* = 9.3 Hz, 1NH), 6.86 (d, *J* = 9.4 Hz, 1NH), 5.63 (d, *J* = 9.8 Hz, 1NH), 4.345 (d, *J* = 10.5 Hz, 1NH).

Boc–[Ala-γ^4(*R*)Leu]$_2$–OMe (5): Boc–[Ala-γ^4(*R*) Leu]–OH (0.068 g, 0.156 mmol), was coupled to a free base H–[Ala-γ^4(*R*) Leu]–OMe (0.098 g, 0.156 mmol) in DCM:DMF solvent mixtures using HATU (0.6 g, 0.156 mmol)/HOBT (0.024 g, 0.156 mmol) as coupling agents followed by reaction work up as in section (i). The peptide **5** (0.11 g, 80%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 556.38; $[M+H]^+_{obsd}$, 557.29; $[M+Na]^+_{obsd}$, 579.29; $[M+K]^+_{obsd,}$ 595.27; MP (˚C): 171–173.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.75 (d, *J* = 9.2 Hz, 1NH), 6.56 (d, *J* = 9.1 Hz, 1NH), 6.17 (d, *J* = 9.0 Hz, 1NH), 4.89 (d, *J* = 9.6 Hz, 1NH).

Boc–[Aib-γ^4(*S*)Leu]$_2$–OMe (6): Boc–[Aib-γ^4(*S*) Leu]–OH (0.06 g, 0.161 mmol), was coupled to H–[Aib-γ^4(*S*) Leu]–OMe (0.066 g, 0.161 mmol) using HATU (0.061 g, 0.161 mmol)/HOBT (0 .0246 g, 0.161 mmol) as coupling agents in DCM:DMF solvent mixture followed by reaction work up as in section (i). The peptide **6** (0.1 g, 81%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 584.51; $[M+H]^+_{obsd}$, 585.45; $[M+Na]^+_{obsd,}$ 607.32; $[M+K]^+_{obsd,}$ 623.32; MP (˚C): 110–112.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.45 (d, *J* = 9.4 Hz, 1NH), 6.91 (s, 1NH), 5.80 (d, *J* = 9.1 Hz, 1NH), 4.90 (s, 1NH).

Boc–[Leu-γ^4(*R*)Leu]$_2$–OMe (7): Boc–[Leu-γ^4(*R*) Leu]–OH (0.058 g, 0.156 mmol), was coupled to a free base H–[Leu-γ^4(*R*) Leu]–OMe (0.084 g, 0.156 mmol) in DCM:DMF solvent mixtures using HATU (0.6 g, 0.156 mmol)/HOBT (0.024 g, 0.156 mmol) as coupling agents followed by reaction work up as in section (i). The peptide **7** (0.11 g, 79%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 640.48; $[M+H]^+_{obsd}$, 641.25; $[M+Na]^+_{obsd}$, 663.18; $[M+K]^+_{obsd,}$ 679.15; MP (˚C): 153–155.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.76 (d, *J* = 9.9 Hz, 1NH), 6.33 (d, *J* = 10.8 Hz, 1NH).

Boc–Leu-γ^4(*R*)Val-Val-^{D}Pro-Gly-Leu-γ^4(*R*)Val-Val–OMe (8): Boc–[Leu-γ^4(*R*)Val-Val]–OH (0.10 g, 0.156 mmol), was coupled to a free base H–[^{D}Pro-Gly-Leu-γ^4(*R*) Val-Val]–OMe (0.214 g, 0.176 mmol) in DCM:DMF solvent mixtures using HATU (0.6 g, 0.156 mmol)/HOBT (0.024 g, 0.156 mmol) as coupling agents followed by reaction work up as in section (i). The peptide **8** (0.22 g, 83%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 964.66; $[M+H]^+_{obsd}$, 964.13; $[M+Na]^+_{obsd}$, 987.12, $[M+K]^+_{obsd}$, 1003.08; MP (˚C): 205–207.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.41 (d, *J* = 9.2 Hz, 1NH), 8.39 (d, *J* = 8.9 Hz, 1NH), 8.27 (d, *J* = 9.8 Hz, 1NH), 8.21 (d, *J* = 9.5 Hz, 1NH), 8.05 (d, *J* = 9.1 Hz, 1NH), 7.68 (d, *J* = 9.1 Hz, 1NH), 7.52 (d, *J* = 8.8 Hz, 1NH), 6.77 (d, *J* = 10.7 Hz, 1NH).

Boc–[γ^4(*R*)Leu]$_2$-δ^5(*R*)Leu–γ^4(*R*)Leu-OMe (9): Boc–[γ^4(*R*) Leu]$_2$–OH (0.073 g, 0.156 mmol), was coupled to a free base H–[δ^5(R)Leu -γ^4(*R*) Leu]–OMe (0.114 g, 0.156 mmol) in DCM:DMF solvent mixtures using HATU (0.6 g, 0.156 mmol)/HOBT (0.024 g, 0.156 mmol) as coupling agents followed by reaction work up as in section (i). The peptide **9** (0.150 g, 85%) was obtained as white solid. ESI-MS [Da]: $[M^+]_{calcd}$, 710.56; $[M+H]^+_{obsd}$, 711.6; $[M+Na]^+_{obsd}$, 733.6; $[M+K]^+_{obsd}$, 749.5; MP (˚C): 162–165.

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.89 (d, *J* = 9.3 Hz, 1NH), 6.33 (d, *J* = 9.2 Hz, 1NH), 6.06 (d, *J* = 8.9 Hz, 1NH), 4.26 (d, *J* = 10.1 Hz, 1NH).

Table S1. Hydrogen bond parameters in the crystal structures of peptides**1**-**9**

Donor	Acceptor	D…A (Å)	H…A (Å)	D-H…A (º)
Boc-[γ^4(*R*)Val]$_2$-OMe 1				
Intermolecular Hydrogen bonds				
N1	O0 (x-1, y, z)	**3.02**	**2.21**	**157.5**
N2	O1 (x+1, y, z)	**3.07**	**2.25**	**150.7**
Boc-[γ^4(*R*)Val]$_3$-NHMe 2				
Intermolecular Hydrogen bonds				
N1	O0 (x-1, y, z)	**2.85**	**2.05**	**154.3**
N2	O1 (x+1, y, z)	**2.98**	**2.13**	**172.5**
N3	O2(x-1, y, z)	**2.93**	**2.08**	**173.3**
N4	O3(x+1, y, z)	**2.90**	**2.05**	**170.9**
Boc-γ^4(*S*)Val-γ^4(*R*)Val-OMe 3				
Intermolecular Hydrogen bonds				
N1	O0 (x, y+1, z)	**3.04**	**2.19**	**168.1**
N2	O1 (x, y-1, z)	**3.03**	**2.19**	**170.8**
Boc-[γ^4(*R*)Val]$_4$-OMe 4				
Intermolecular Hydrogen bonds				
N1	O0 (x-1, y, z)	**3.02**	**2.22**	**153.2**
N2	O1 (x+1, y, z)	**3.01**	**2.17**	**166.2**
N3	O2(x-1, y, z)	**3.00**	**2.16**	**165.9**
N4	O3(x+1, y, z)	**3.07**	**2.23**	**164.7**
Boc-[Ala-γ^4(*R*)Leu]$_2$-OMe 5				
Intra-Asymmetric unit Hydrogen bonds				
N3	O0′	**3.00**	**2.16**	**168.4**
N4	O1′	**2.96**	**2.14**	**159.0**
N3′	O0	**3.12**	**2.28**	**165.4**
N4′	O1	**3.00**	**2.16**	**166.4**
Intermolecular Hydrogen bonds				
N1	O3′ (x+1, y, z)	**2.90**	**2.09**	**156.0**
N2	O2′ (x+1, y, z)	**3.22**	**2.45**	**150.6**
N1′	O3 (x-1, y, z)	**2.89**	**2.07**	**156.5**
N2′	O2 (x-1, y, z)	**3.47**	**2.67**	**154.9**
Boc-[Aib-γ^4(*S*)Leu]$_2$-OMe 6				
Intramolecular Hydrogen bonds				
N3	O0	**2.95**	**2.10**	**171.9**
N4	O1	**2.90**	**2.13**	**150.0**
Intermolecular Hydrogen bonds				
N1	O2 (x, y+1, z)	**2.94**	**2.06**	**161.3**
Solvent mediated hydrogen bonds				
N2	O10	**2.88**	**2.09**	**153.5**

Donor	Acceptor	D…A (Å)	H…A (Å)	D-H…A (º)
Boc-[Leu-γ^4(*R*)Leu]$_2$-OMe 7				
Intramolecular Hydrogen bonds				
N3	O0	**2.96**	**2.11**	**173.1**
N4	O1	**2.92**	**2.07**	**170.5**
N1	O3 (x+1, y, z)	**2.92**	**2.06**	**174.5**
Solvent mediated hydrogen bonds				
N2	O1w	**2.96**	**2.16**	**156.5**
O2w	O2	**2.79**		
O1w	O2w (x+1, y, z)	**2.73**		
Boc-Leu-γ^4(*R*)Val-Val-^{D}Pro-Gly-Leu-γ^4(*R*)Val-Val-OMe 8				
Intramolecular hydrogen bonds				
N3	O6	**3.03**	**2.22**	**152.6**
N6	O3	**2.95**	**2.17**	**156.5**
N8	O1	**2.94**	**2.12**	**163.2**
Intermolecular hydrogen bonds				
N2	O7 (x+1, y, z)	**2.85**	**2.02**	**170.5**
N5	O5 (-x-1, y-1/2, -z)	**3.35**	**2.58**	**148.3**
N7	O2 (x-1, y, z)	**2.97**	**2.10**	**178.5**
Water mediated hydrogen bonds				
O1W	O4	**2.69**		
O1W	O6	**2.88**		
Boc-[γ^4(*R*)Leu]$_2$-δ^5(*R*)Leu-γ^4(*R*)Leu-OMe 9				
Intermolecular Hydrogen bonds				
N1	O0 (x+1, y, z)	**2.94**	**2.13**	**158.5**
N2	O1 (x-1, y, z)	**2.97**	**2.13**	**160.5**
N3	O2 (x+1, y, z)	**2.96**	**2.13**	**161.4**
N4	O3 (x+1, y, z)	**2.92**	**2.08**	**165.5**

X-ray structure analysis of peptides 1 to 9(Supplementary Tables S1-S4).

Table S2. Crystal data and structure refinement parameters for the peptides **1**, **2** and **3**.

Peptides	Boc-[γ^4(*R*)Val]$_2$-OMe **1**	Boc-[γ^4(*R*)Val]$_3$-NHMe **2**	Boc-γ^4(*S*)Val-γ^4(*R*)Val-OMe **3**
Empirical formula	$C_{20}H_{38}N_2O_5$	$C_{27}H_{52}N_4O_5$	$C_{20}H_{38}N_2O_5$
Crystal habit (Crystal size (mm))	Rectangular block (0.12 × 0.07 × 0.05)	Rectangular block (0.20 × 0.15 × 0.07)	Rectangular block (0.35 × 0.20 × 0.15)
Crystallizing solvent			
Crystal system (Space group)	Monoclinic($P2_1$)	Monoclinic($P2_1$)	Monoclinic($C2$)
a (Å)	5.1643(2)	5.0056(14)	28.9383(8)
b (Å)	30.0027(11)	15.829(4)	5.14190(10)
c (Å)	7.5724(3)	20.317(5)	18.4128(5)
β (°)	94.261(2)	93.452(18)	120.3230(10)
Volume (Å^3)	1170.05(8)	1606.9(7)	2364.96(10)
Z / Z´	2 / 1	2 / 1	4 / 1
Co-crystallized solvent	None	None	None
Molecular weight, Calculated density (g/cm^3)	386.52, 1.097	512.73, 1.060	386.52, 1.086
F (000)	424	564	848
Radiation	Cu K_α (1.54178 Å)	Mo K_α (0.71073 Å)	Cu K_α (1.54178 Å)
Temperature (K)	296	296	296
2θ max. (˚)	140.04	60.12	140.22
Unique reflections (Measured reflections)	2030 (6082)	8798 (14463)	2405 (6864)
Observed reflection [$\lvert F \rvert > 4\sigma(F)$]	1752	2846	2116
R_{int}	0.0049	0.0918	0.0030
Final R (%)/*w*R2 (%)	6.62 / 21.06	14.33 / 37.42	4.99 / 14.96
Goodness-of-fit on F^2 (S)	1.074	1.087	1.143
Δρ max (e.Å^{-3})/ Δρ min(e.Å^{-3})	0.63 / -0.24	0.31 / -0.28	0.23 / -0.30
No. of restraints/parameters	2 / 253	1 / 325	15 / 300
Data($\lvert F \rvert > 4\sigma(F)$)-to-parameter ratio	6.92 : 1	8.76 : 1	7.05 : 1

Table

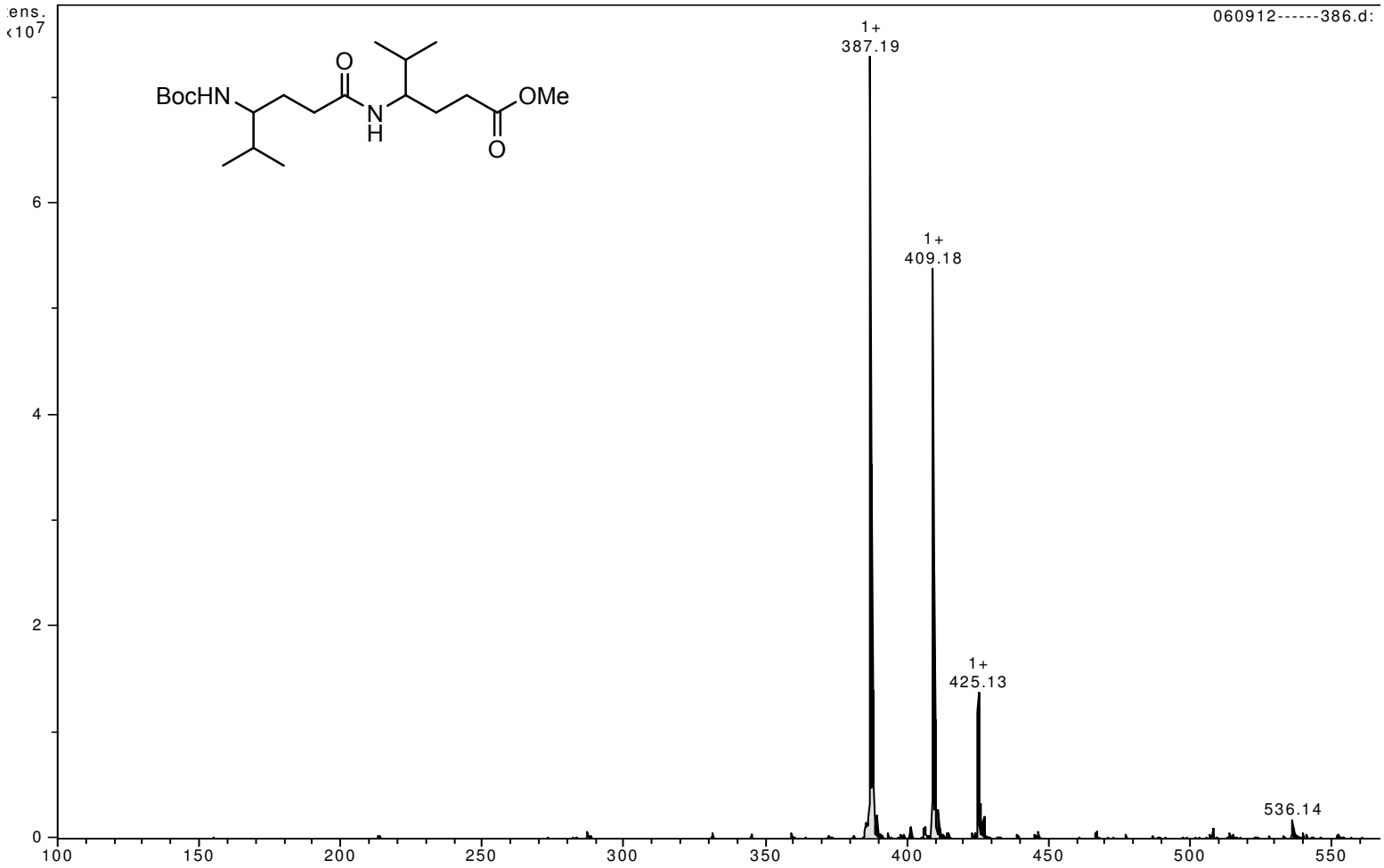
S3. Crystal data and structure refinement parameters for the peptides **4**, **5** and **6**.

Peptides	Boc-[γ^4(*R*)Val]$_4$-OMe **4**	Boc-[Ala-γ^4(*R*)Leu]$_2$-OMe **5**	Boc-[Aib-γ^4(*S*)Leu]$_2$-OMe **6**
Empirical formula	$C_{34}H_{64}N_4O_7$	$C_{28}H_{52}N_4O_7$	$C_{30}H_{56}N_4O_7 + C_3H_7NO$
Crystal habit (Crystal size (mm))	Thin plate (0.30 × 0.25 × 0.05)	Rectangular block (0.20 × 0.06 × 0.05)	Rectangular block (0.20 × 0.06 × 0.05)
Crystallizing solvent			
Crystal system (Space group)	Monoclinic($P2_1$)	Triclinic($P1$)	Triclinic($P1$)
a (Å)	5.1182(3)	8.999(4)	9.901(2)
b (Å)	50.153(3)	14.013(6)	10.527(3)
c (Å)	7.4046(4)	14.873(6)	10.553(2)
α (°)		66.19(2)	100.403(12)
β (°)	97.675(4)	75.21(3)	106.665(13)
γ (°)		73.60(2)	93.047(14)
Volume (Å^3)	1883.67(18)	1624.6(11)	1030.0(4)
Z / Z´	2 / 1	2 / 2	1 / 1
Co-crystallized solvent	None	None	Dimethylformamide (DMF)(C_3H_7NO)
Molecular weight, Calculated density (g/cm^3)	640.89, 1.130	556.74, 1.138	657.88 , 1.061
F (000)	704	608	360
Radiation	Cu K_α (1.54178 Å)	Mo K_α (0.71073 Å)	Mo K_α (0.71073 Å)
Temperature (K)	296	296	296
2θ max. (°)	138.02	61.34	60.20
Unique reflections (Measured reflections)	3271 (9533)	9095 (24067)	5851 (17289)
Observed reflection [$\lvert F \rvert > 4\sigma(F)$]	2736	1954	1991
R_{int}	0.0208	0.1991	0.0611
Final R (%)/*w*R2 (%)	9.56 / 27.40	8.01 / 22.71	8.56 / 28.75
Goodness-of-fit on F^2 (S)	1.195	0.849	0.905
Δρ max (e.Å^{-3})/ Δρ min(e.Å^{-3})	0.75 / -0.48	0.18 / -0.18	0.24 / -0.19
No. of restraints/parameters	118 / 406	6 / 767	6 / 427
Data($\lvert F \rvert > 4\sigma(F)$)-to-parameter ratio	6.74 : 1	2.55 : 1	4.66 : 1

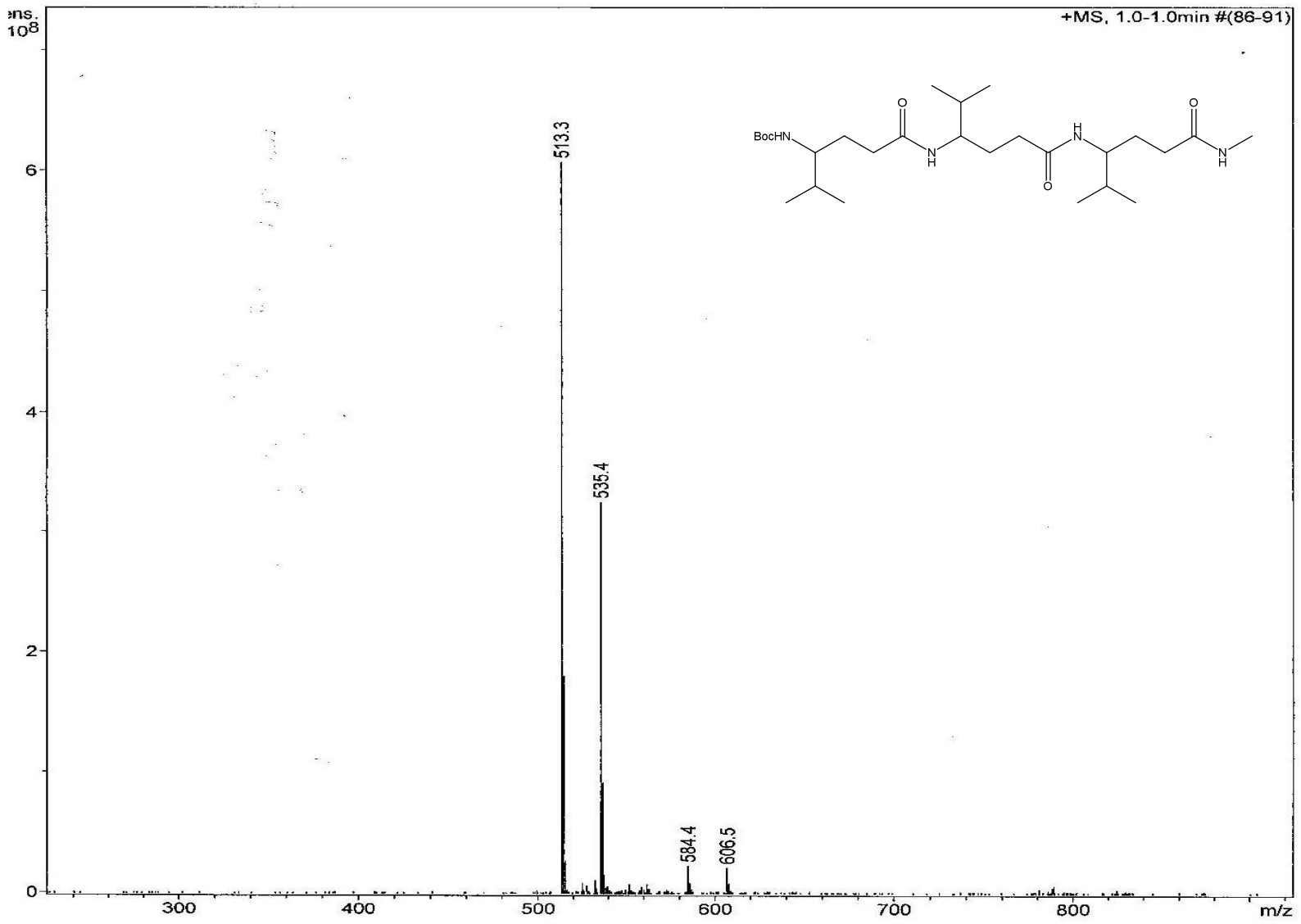
Table S4. Crystal data and structure refinement parameters for the peptides **7**, **8** and **9**.

Peptides	Boc-[Leu-γ^4(*R*)Leu]$_2$-OMe **7**	Boc-Leu-γ^4(*R*)Val-Val-^{D}Pro-Gly-Leu-γ^4(*R*)Val-Val-OMe **8**	Boc-[γ^4(*R*)Leu]$_2$-δ^5(*R*)Leu-γ^4(*R*)Leu-OMe **9**
Empirical formula	$C_{34}H_{64}N_4O_7 + 2(H_2O)$	$C_{49}H_{88}N_8O_{11} + H_2O$	$C_{39}H_{74}N_4O_7$
Crystal habit [Crystal size (mm)]	Rectangular block (0.47 × 0.34 × 0.09)	Rectangular block (0.30 × 0.10 × 0.09)	Rectangular block (0.30 × 0.10 × 0.05)
Crystallizing solvent			
Crystal system (Space group)	Monoclinic($P2_1$)	Monoclinic($P2_1$)	Triclinic($P1$)
a (Å)	10.6075(3)	9.5742(2)	5.0768(11)
b (Å)	10.7350(3)	10.8563(3)	8.924(2)
c (Å)	19.1418(6)	28.0245(7)	25.120(6)
α (°)			98.670(13)
β (°)	105.348(2)	93.811(2)	94.399(14)
γ (°)			99.374(14)
Volume (Å^3)	2101.97(11)	2906.44(12)	1104.0(4)
Z / Z´	2 / 1	2 / 1	1 / 1
Co-crystallized solvent	2O (H_2O)	O (H_2O)	None
Molecular weight, Calculated density (g/cm^3)	672.89, 1.063	981.27, 1.121	711.02, 1.069
F (000)	736	1068	392
Radiation	Mo K_α (0.71073 Å)	Cu K_α (1.54178 Å)	Mo K_α (0.71073 Å)
Temperature (K)	296	296	296
2θ max. (°)	60.10	142.90	60.28
Unique reflections (Measured reflections)	6354 (23550)	5461 (16874)	6488 (21539)
Observed reflection [$\lvert F \rvert > 4\sigma(F)$]	4338	5082	2976
R_{int}	0.0340	0.0121	0.0538
Final R (%)/*w*R2 (%)	6.00 / 18.12	5.77 / 17.62	7.01 / 23.08
Goodness-of-fit on F^2 (S)	1.095	1.128	0.994
Δρ max (e.Å^{-3})/ Δρ min(e.Å^{-3})	0.38 / -0.24	0.32 / 0.34	0.30 / -0.28
No. of restraints/parameters	5 / 520	74 / 777	12 / 535
Data($\lvert F \rvert > 4\sigma(F)$)-to-parameter ratio	8.34 : 1	6.54 : 1	5.56 : 1

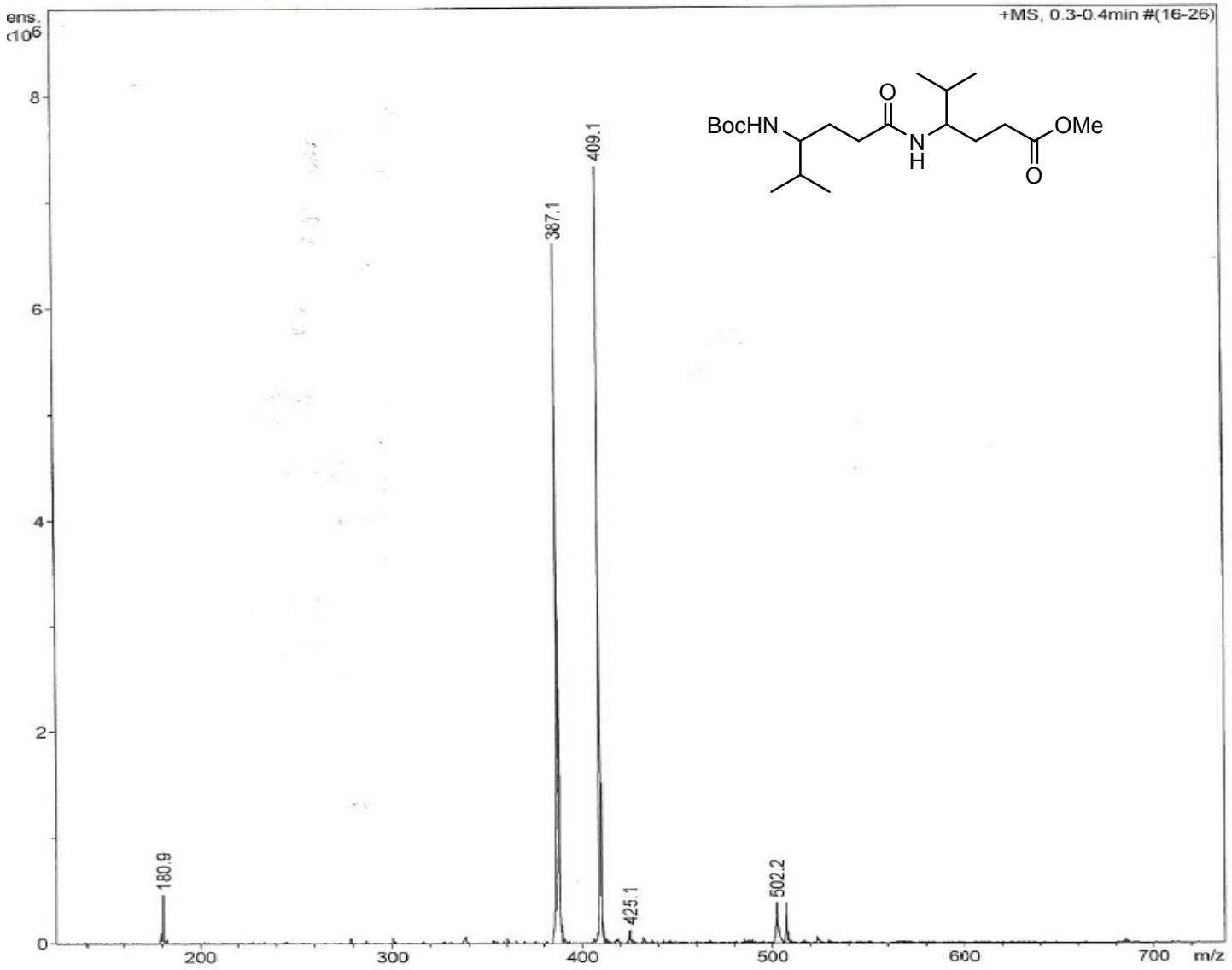
ESI-MS of peptides 1 to 9



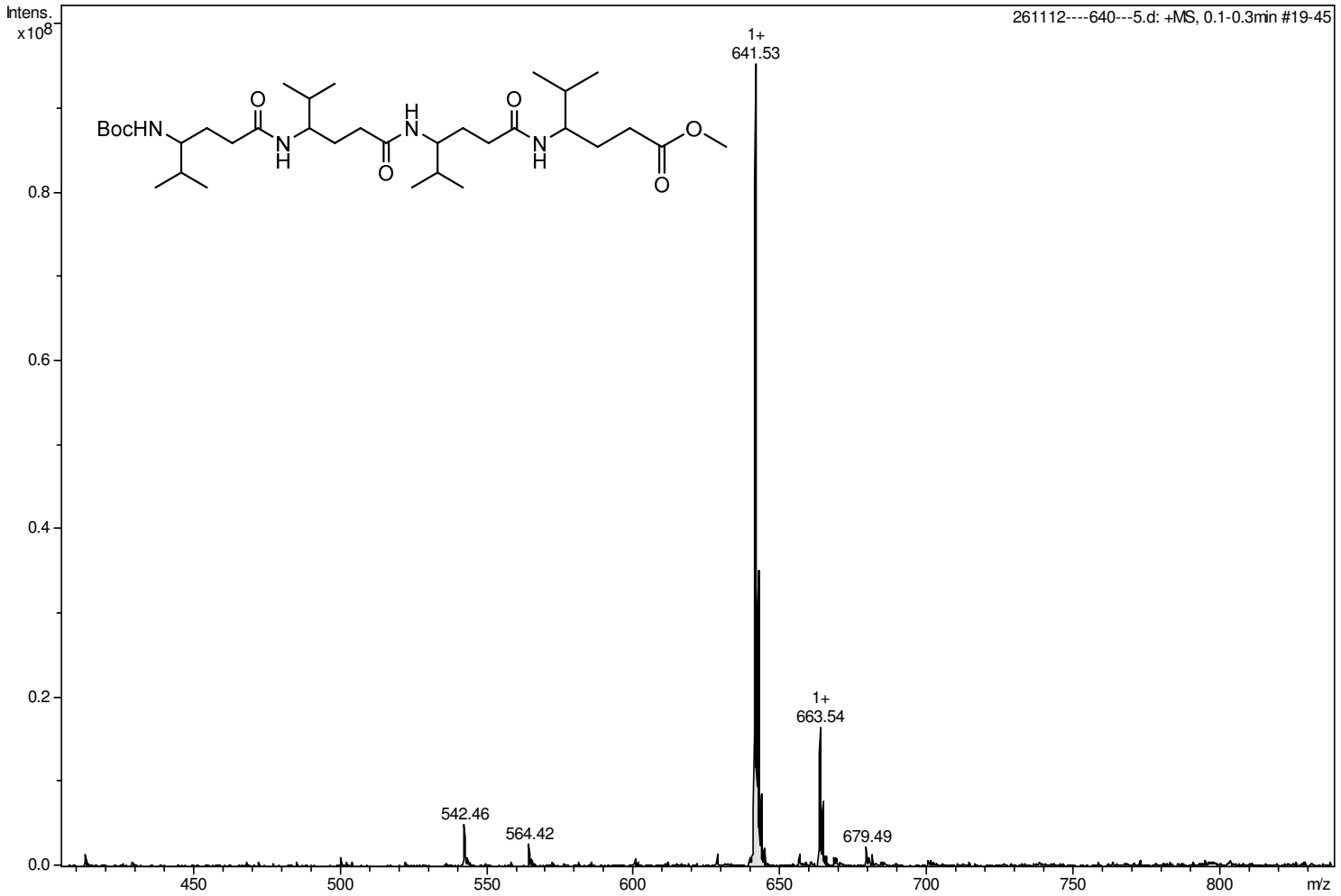
ESI-MS of Boc–[γ^4(*R*)Val]$_2$–OMe **1**



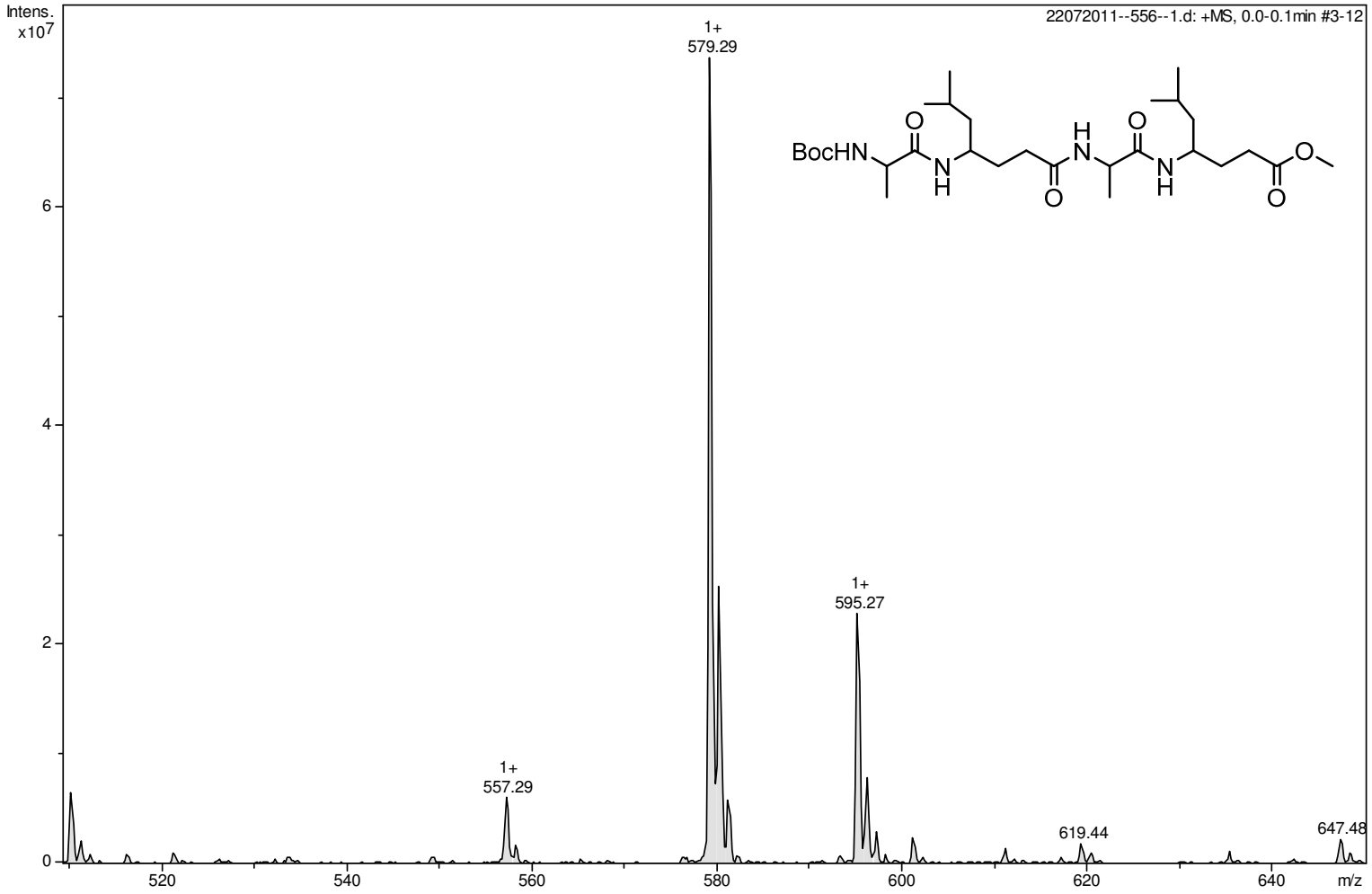
ESI-MS of Boc-[γ^4Val]$_3$-NHMe **2**



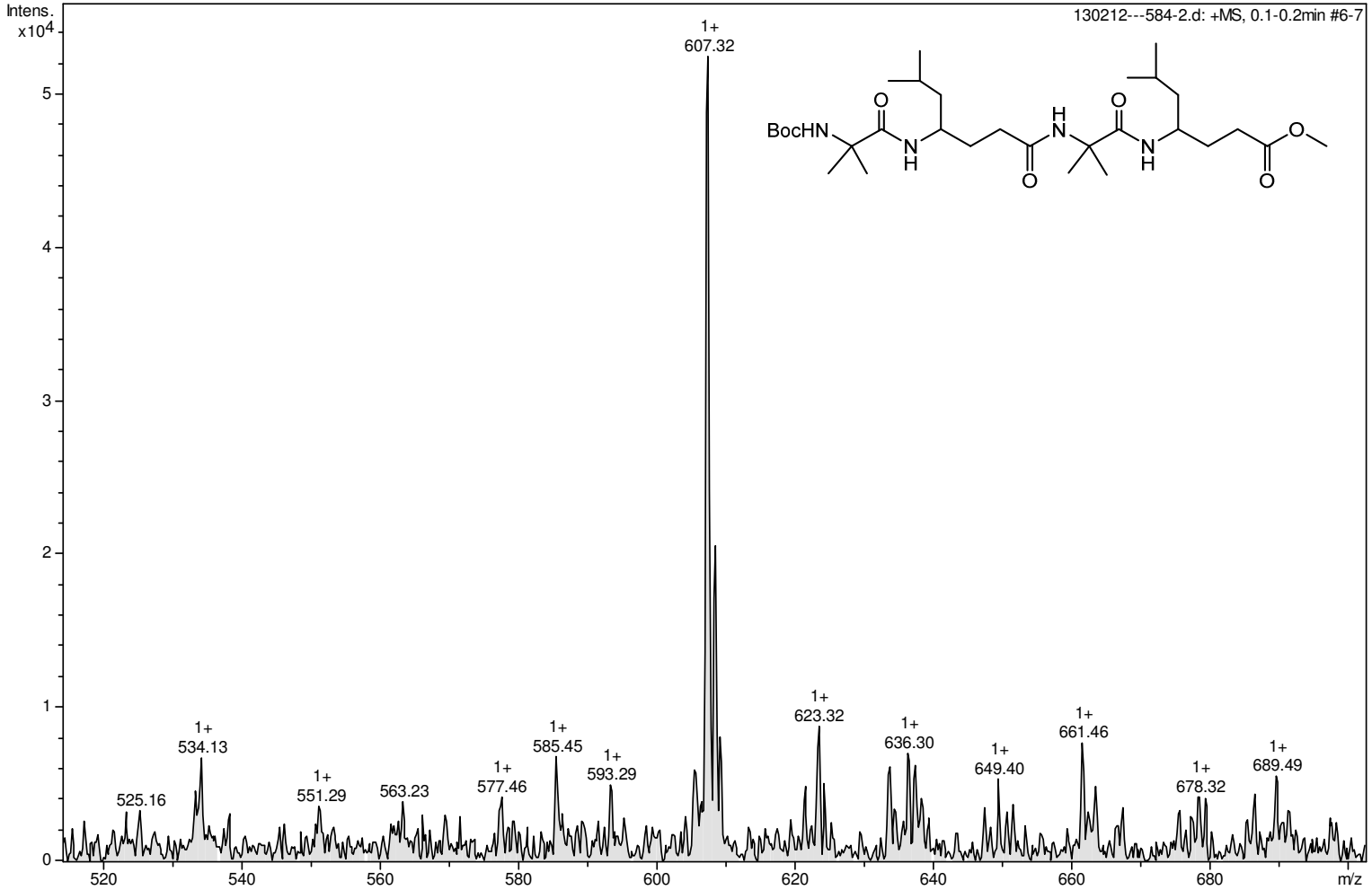
ESI-MS of Boc-γ^4(*S*)Val-γ^4(*R*)Val-OMe **3**



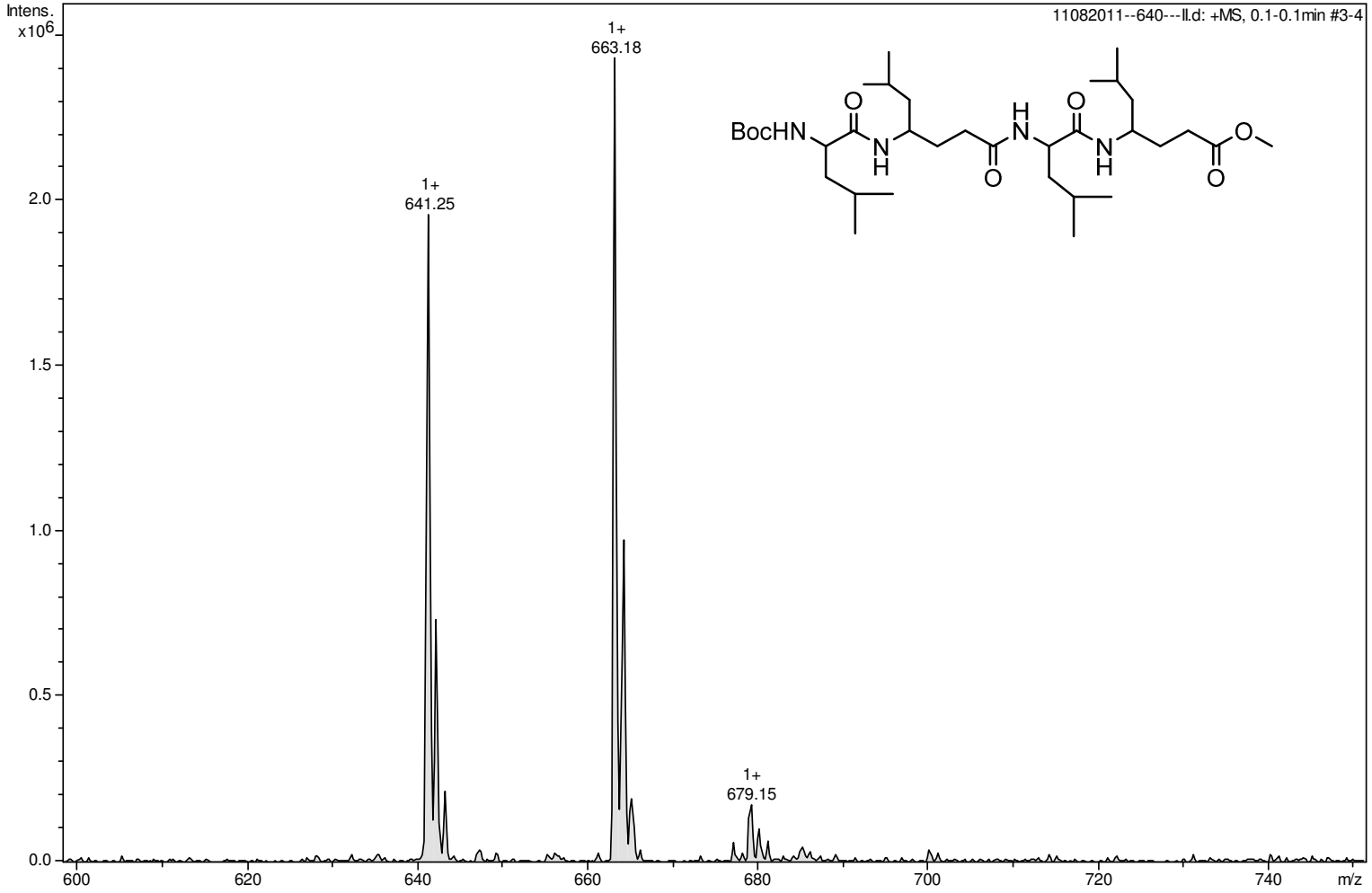
ESI-MS of Boc–[γ^4(*R*)Val]$_4$–OMe **4**



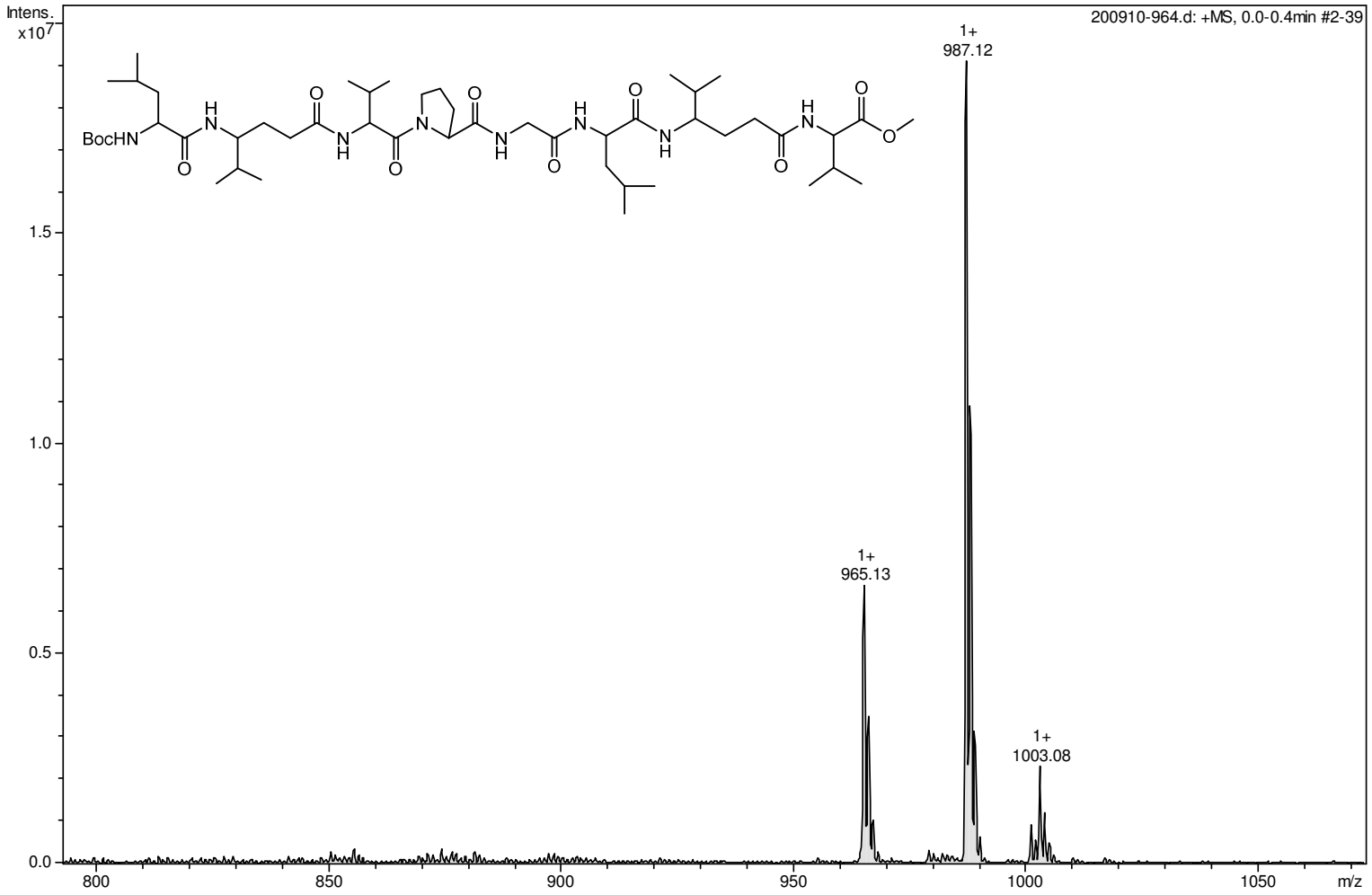
ESI-MS of Boc–[Ala-γ^4(*R*)Leu]$_2$–OMe **5**



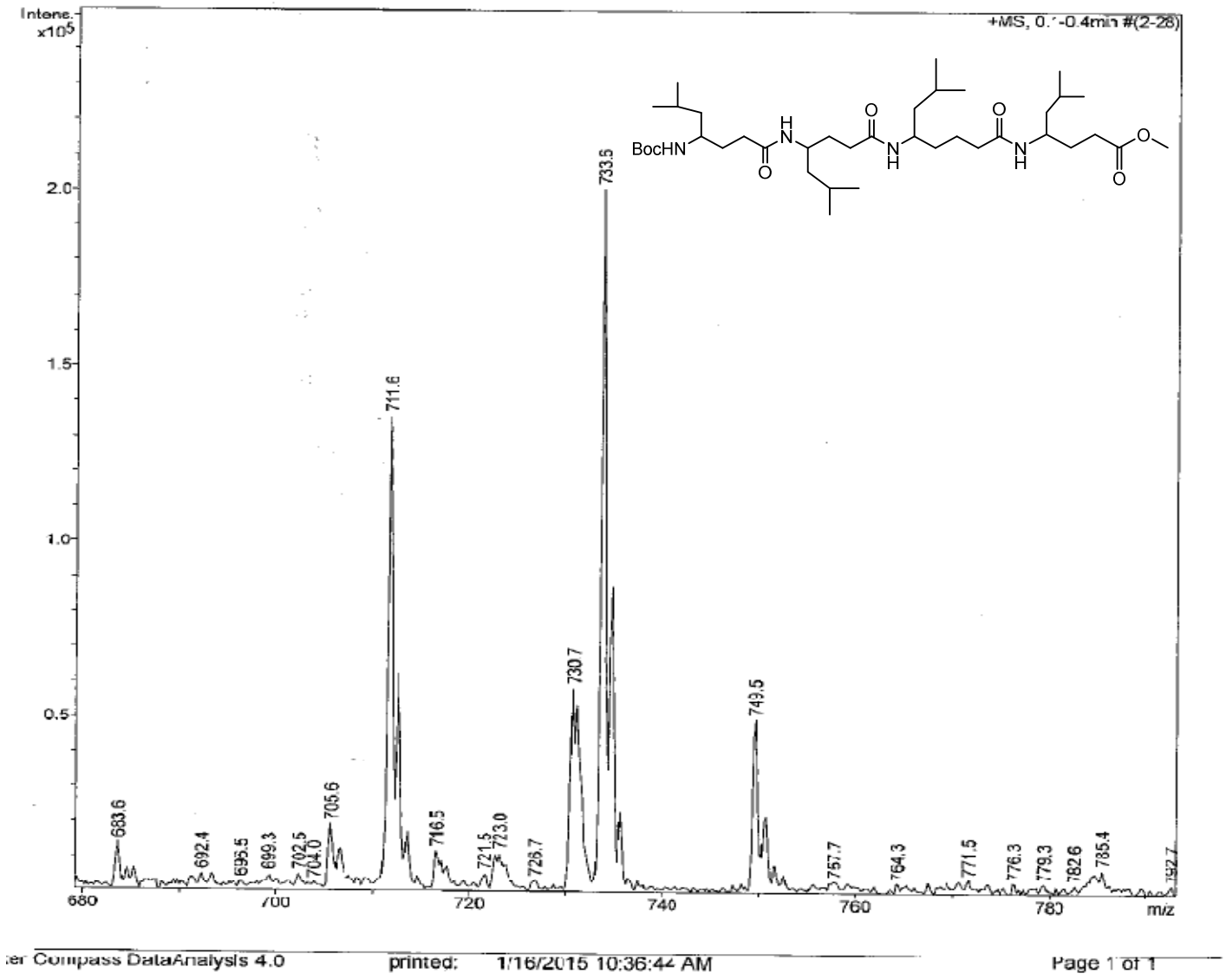
ESI-MS of Boc–[Aib-γ^4(*S*)Leu]$_2$–OMe **6**



ESI-MS of Boc–[Leu-γ^4(*R*)Leu]$_2$–OMe **7**

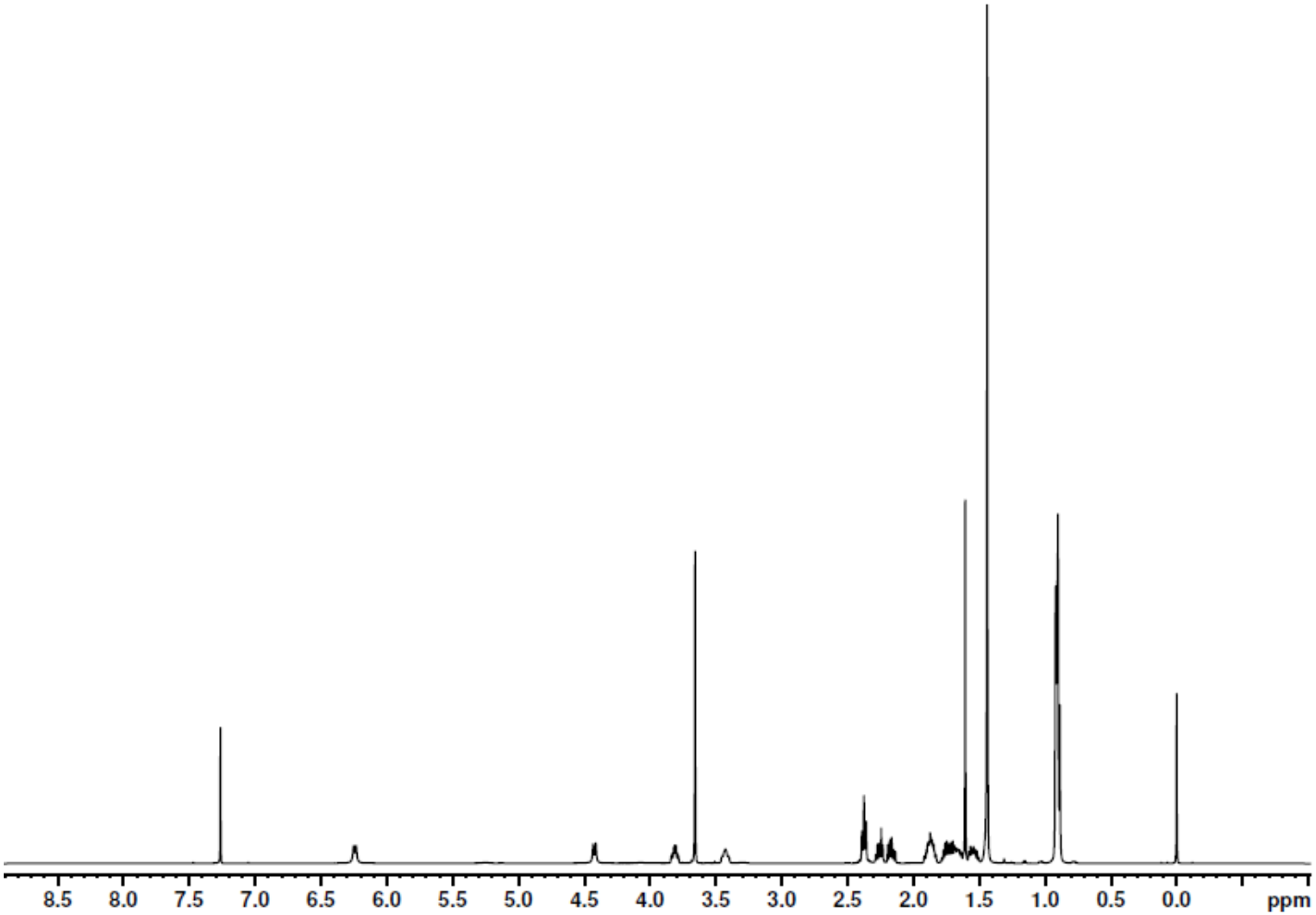


ESI-MS of Boc–Leu-γ^4(*R*)Val-Val-^{D}Pro-Gly-Leu-γ^4(*R*)Val-Val–OMe **8**

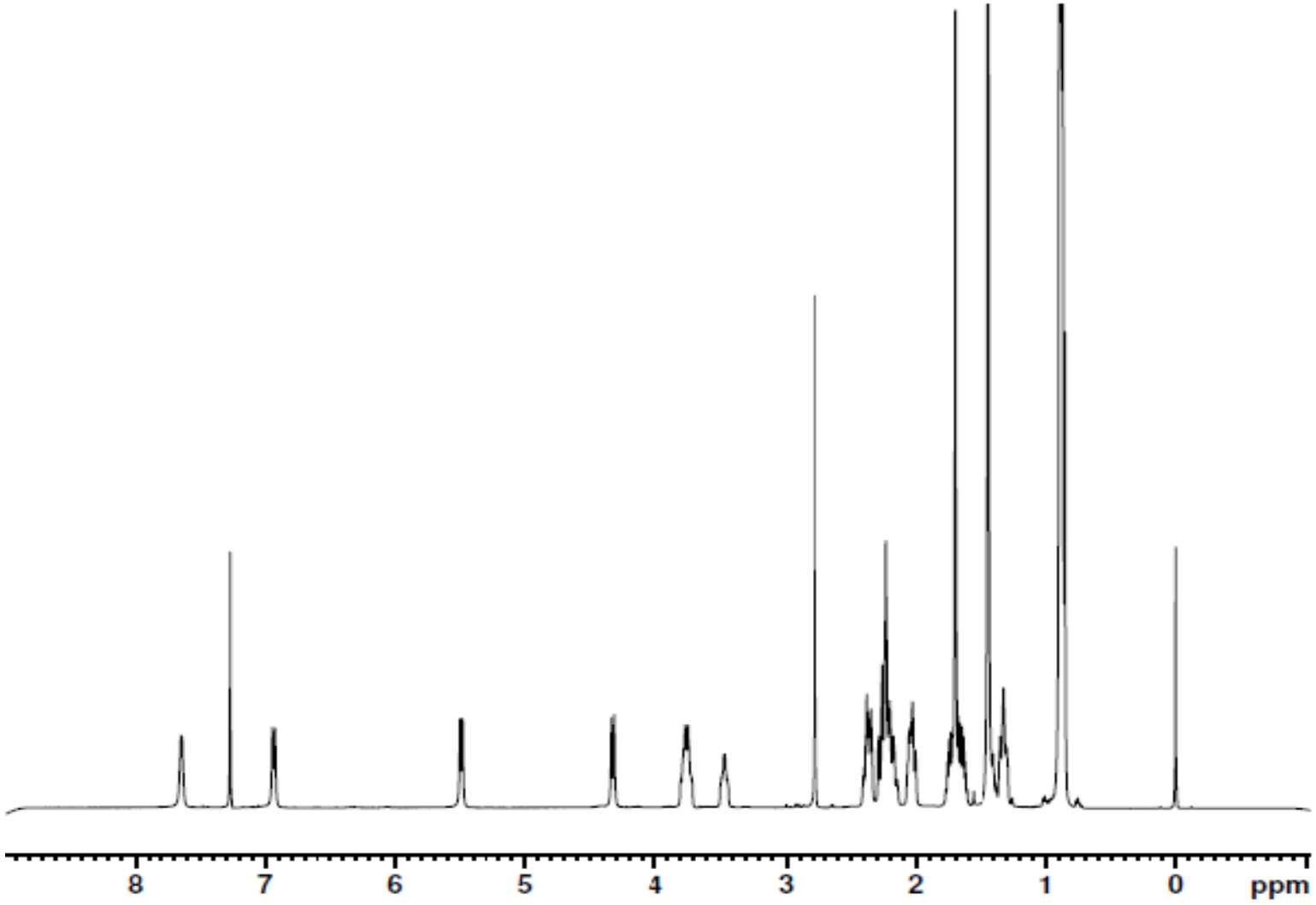


ESI-MS of Boc–[γ^4(*R*)Leu]$_2$-δ^5(*R*)Leu–γ^4(*R*)Leu-OMe **9**

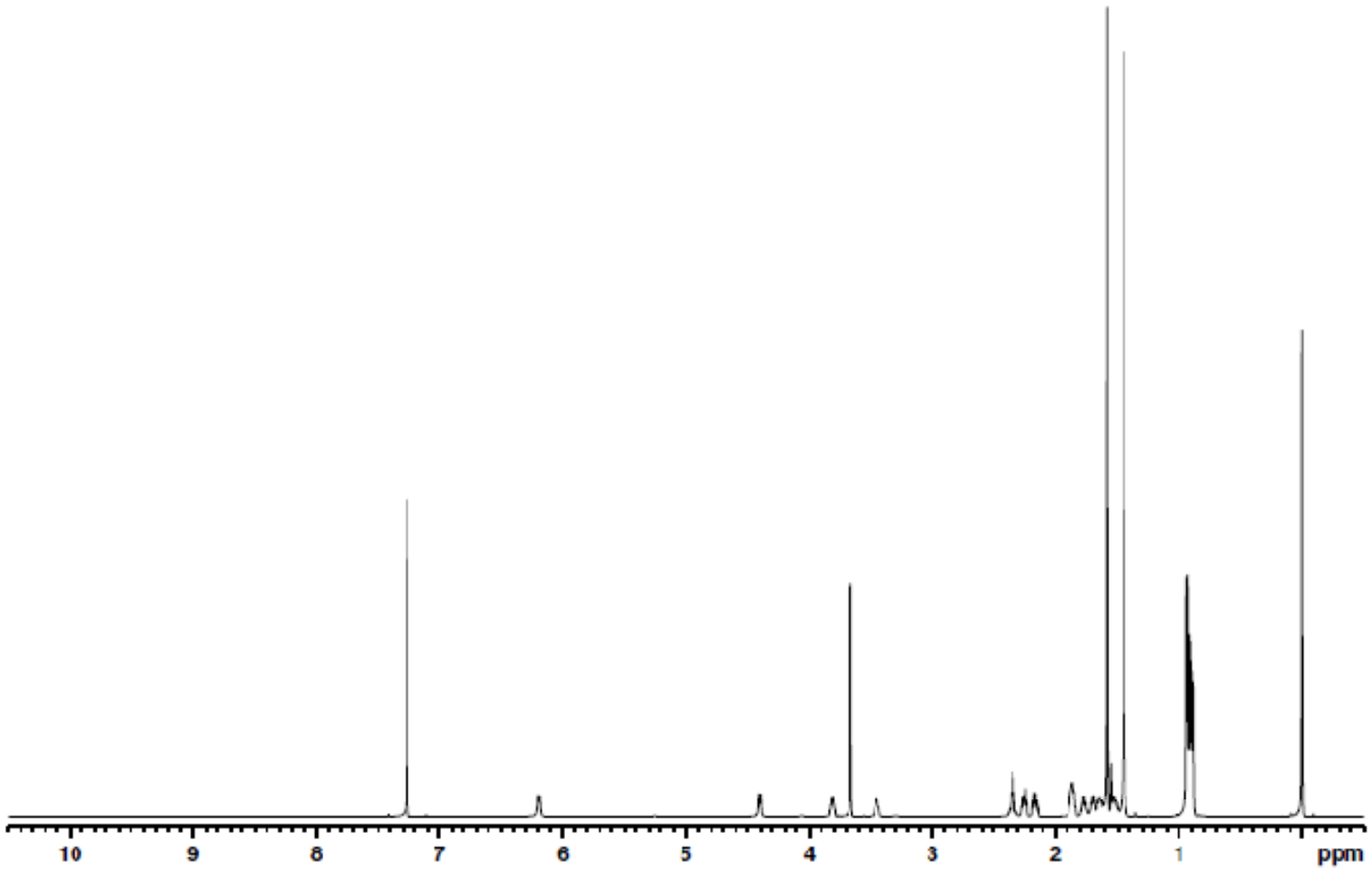
^{1}H NMR spectra of peptides 1 to 9



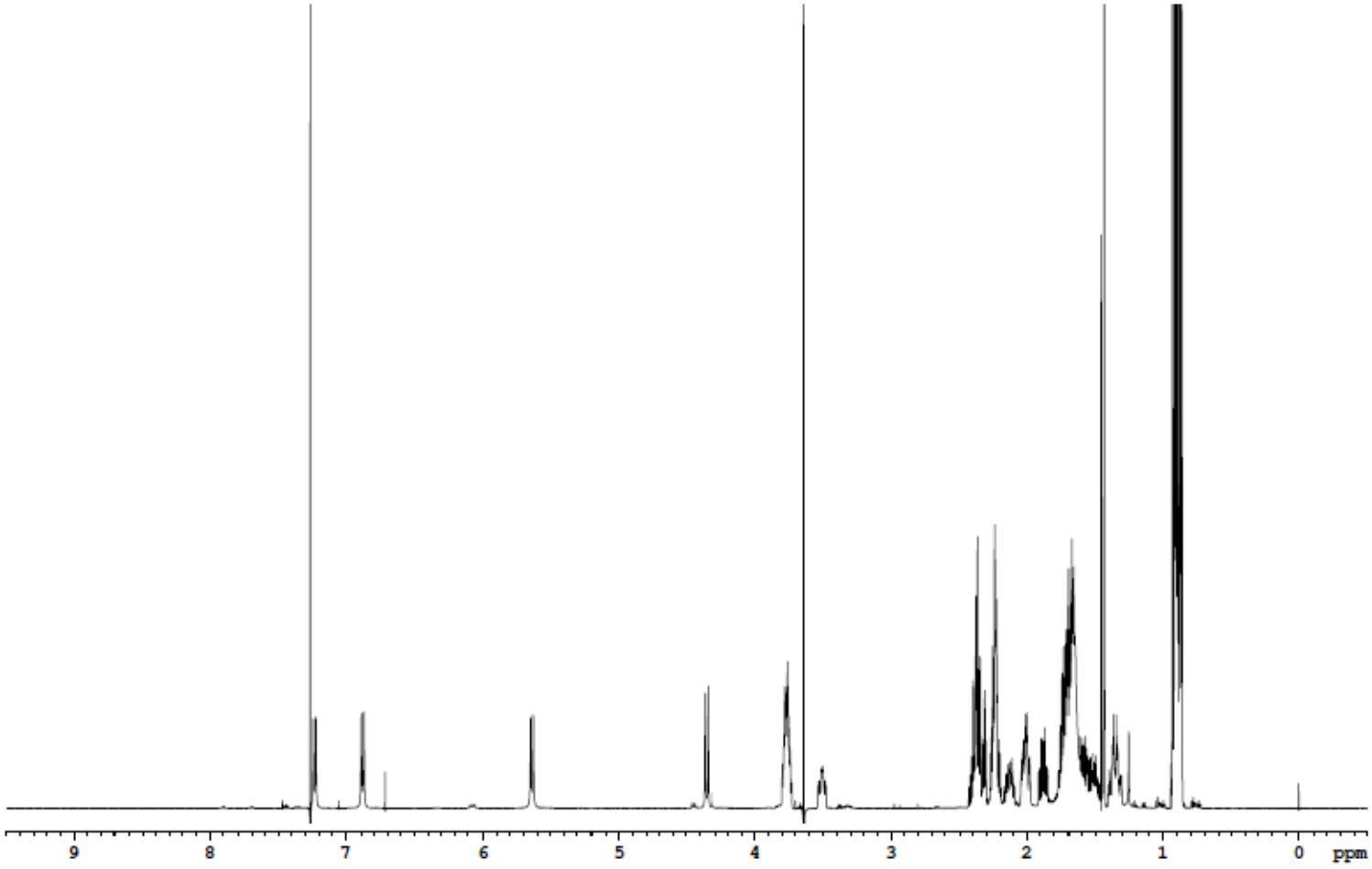
500 MHz 1D ^{1}H NMR spectrum of Boc-[γ^{4}(*R*)Val]$_2$-OMe **1** in $CDCl_3$ at 298 K.



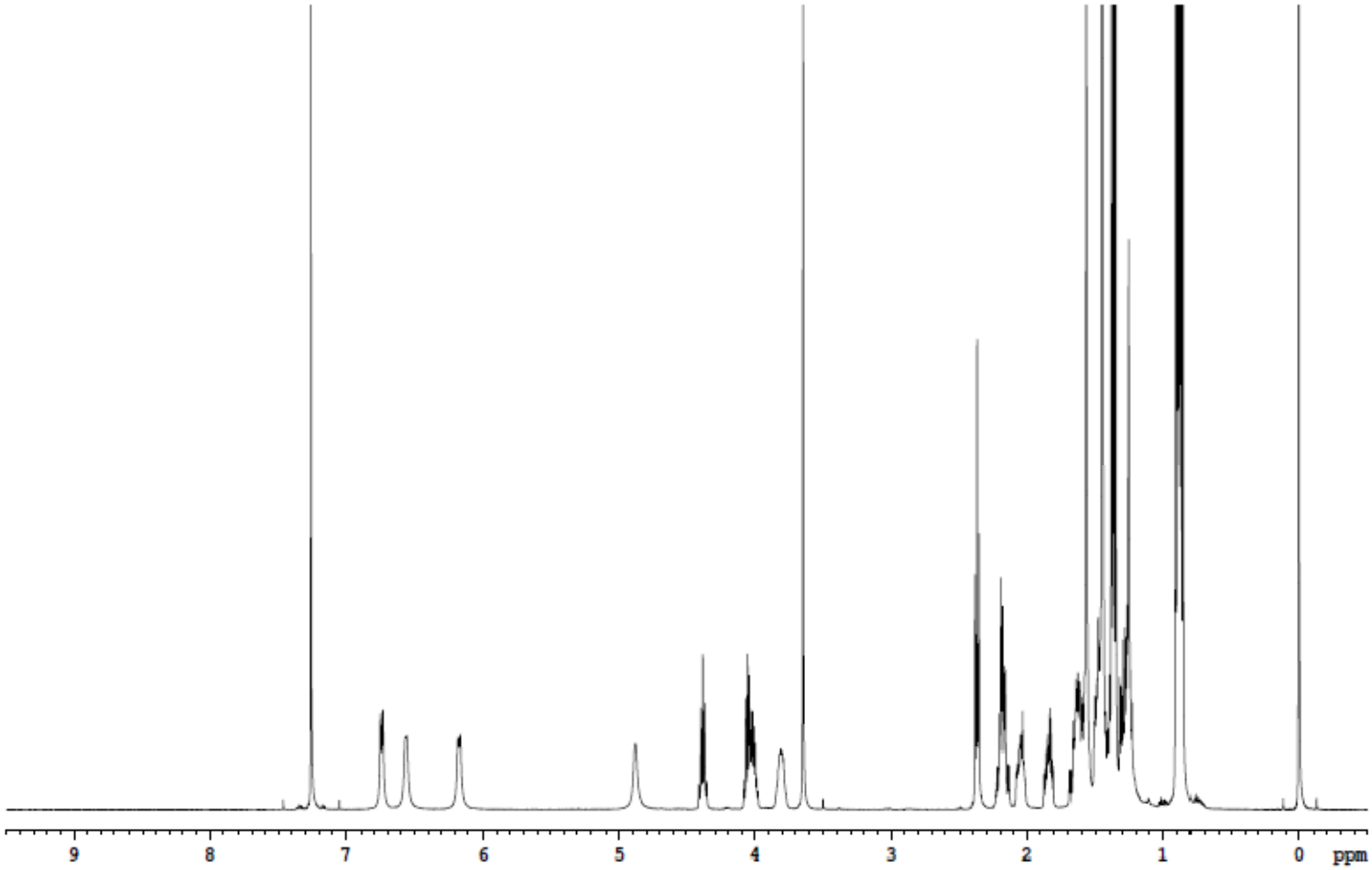
500 MHz 1D ^{1}H NMR spectrum of Boc-[γ^{4}(*R*)Val]$_{3}$-NHMe **2** in $CDCl_3$ at 298 K.



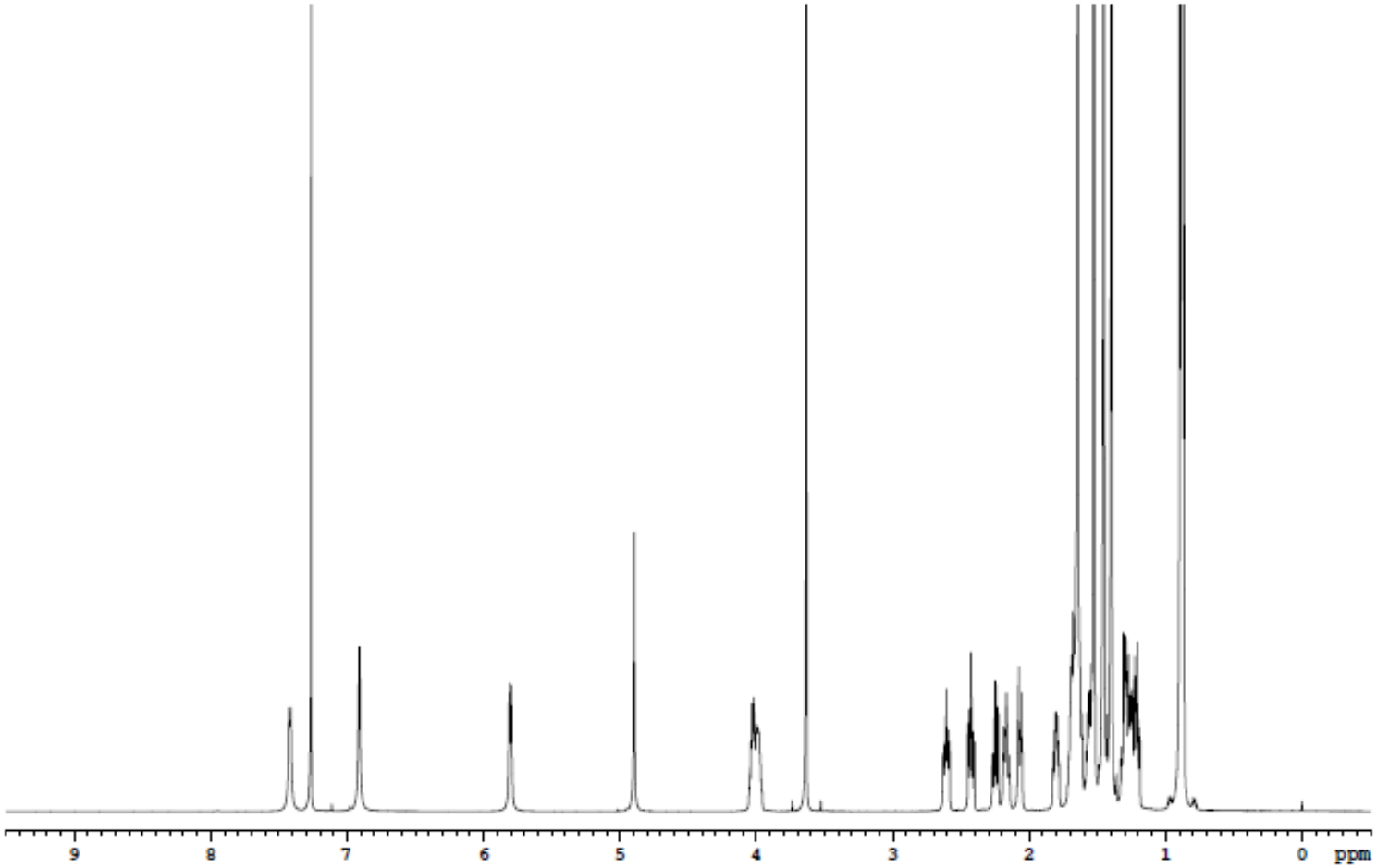
700 MHz 1D ^{1}H NMR spectrum of Boc-γ^{4}(*S*)Val-γ^{4}(*R*)Val-OMe **3** in $CDCl_3$ at 298 K.



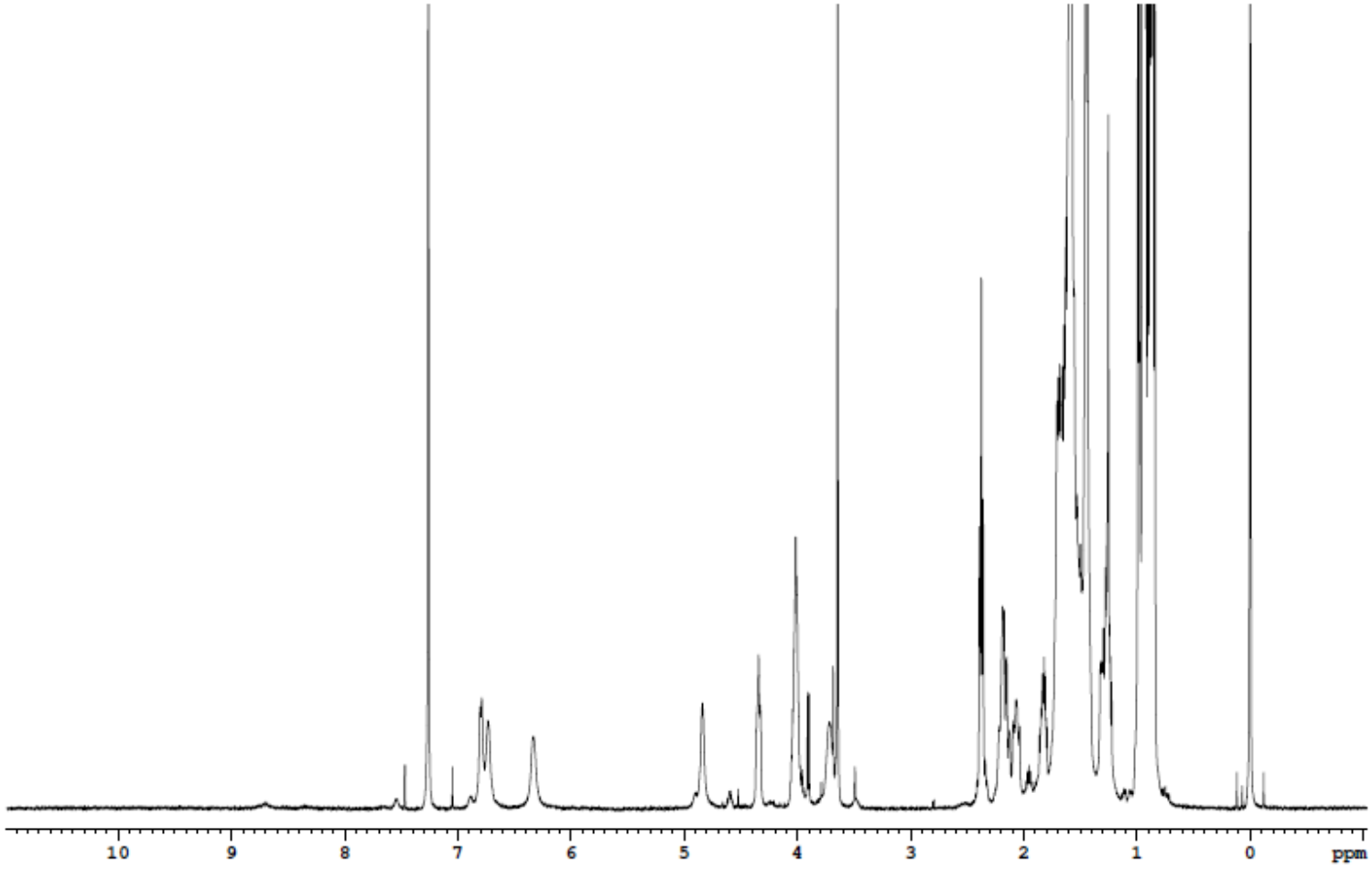
500 MHz 1D ^{1}H NMR spectrum of Boc-[γ^{4}(*R*)Val]$_{4}$-OMe **4** in $CDCl_3$ at 300 K.



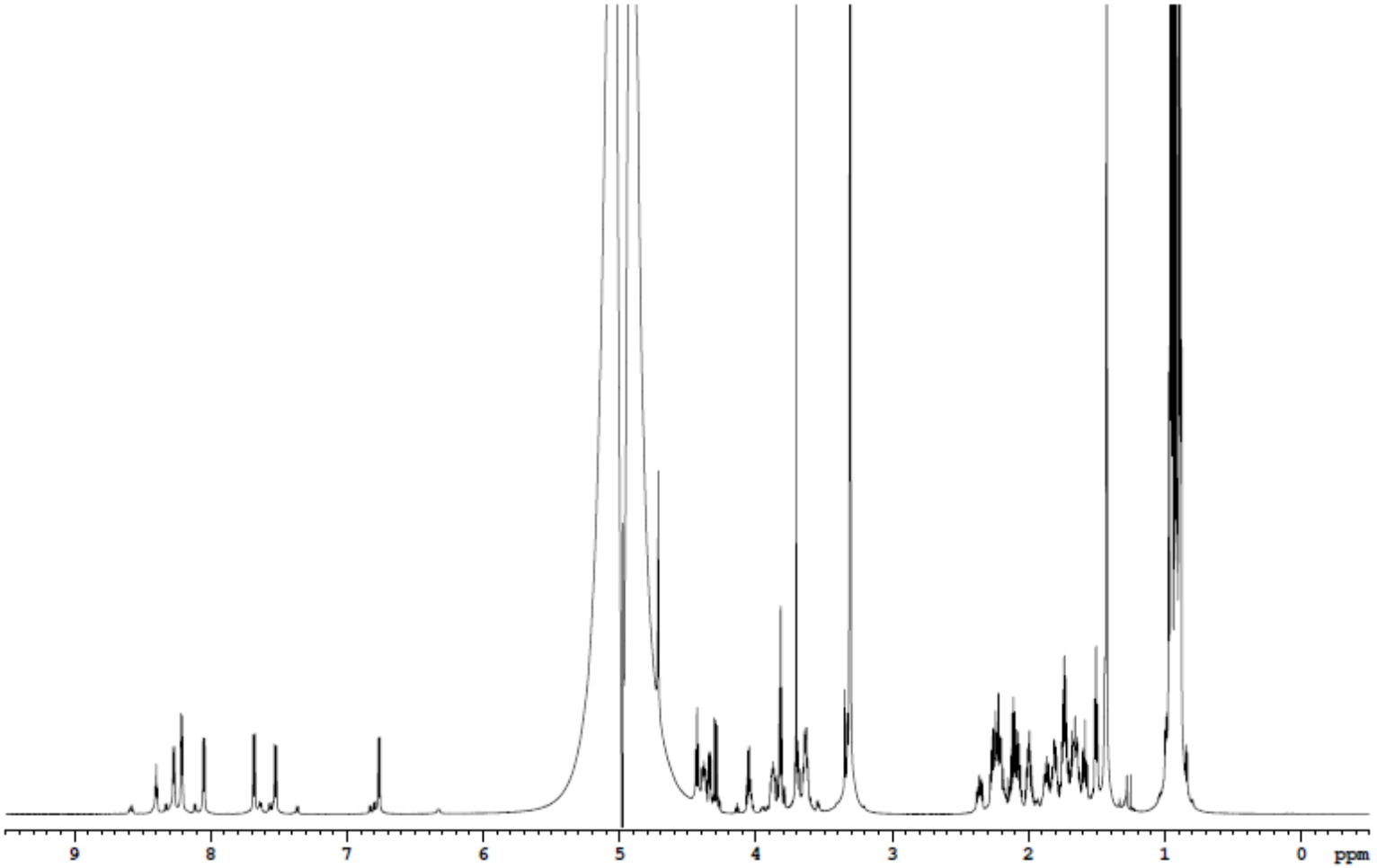
500 MHz 1D ^{1}H NMR spectrum of Boc-[Ala-γ^{4}(*R*)Leu]$_2$-OMe **5** in $CDCl_3$ at 298 K.



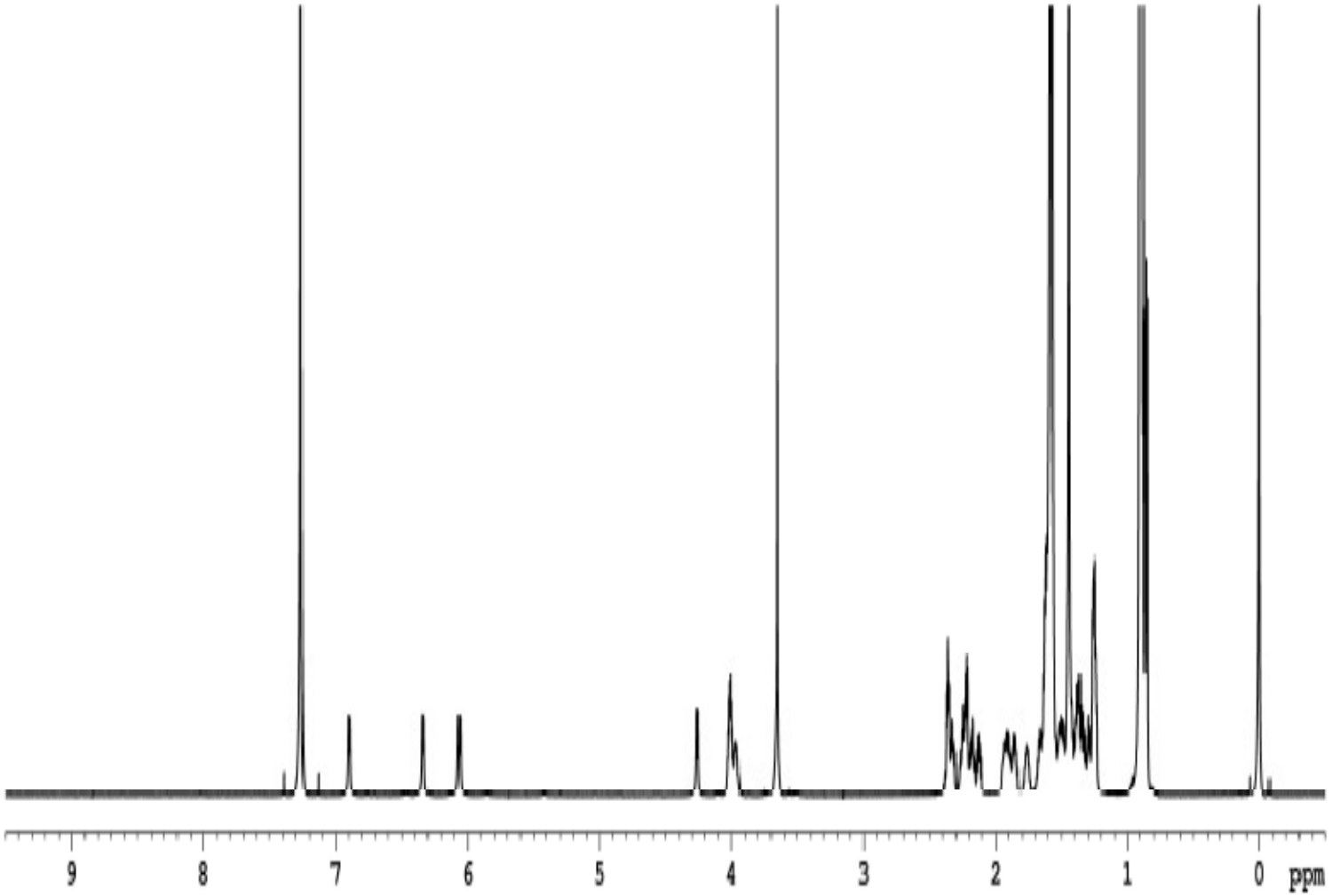
500 MHz 1D ^{1}H NMR spectrum of Boc-[Aib-γ^{4}(*S*)Leu]$_2$-OMe **6** in $CDCl_3$ at 298 K.



500 MHz 1D ^{1}H NMR spectrum of Boc-[Leu-γ^{4}(*R*)Leu]$_2$-OMe**7** in $CDCl_3$ at 298 K.



700 MHz 1D ^{1}H NMR spectrum of Boc-Leu-γ^{4}(*R*)Val-Val-^{D}Pro-Gly-Leu-γ^{4}(*R*)Val-Val-OMe **8** in CD_3OH at 288 K.



500 MHz 1D ^{1}H NMR spectrum of Boc-[γ^{4}(*R*)Leu]$_{2}$-δ^{5}(*R*)Leu-γ^{4}(*R*)Leu-OMe **9** in $CDCl_3$ at 298 K.