**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**


# Supplementary Data

## Application of Carbodiimide Mediated Lossen Rearrangement for the Synthesis of α-Ureidopeptides and peptidyl Ureas Employing *N*-Urethane α-Amino/Peptidyl Hydroxamic Acids

**N. Narendra, Gundala Chennakrishnareddy and Vommina V. Sureshbabu***

*Peptide Research Laboratory, Department of studies in Chemistry, Central College Campus, Bangalore University,Dr. B. R. Ambedkar Veedhi, Bangalore 560 001, INDIA*

E-mail: hariccb@rediffmail.com

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**General Information.** Optical rotations were determined with an automatic digital AA-10 polarimeter. TLC was performed on precoated silica gel plate. IR analysis was carried out on NaCl crystal. Analytical HPLC was performed on Zorbax C-18, 100 X 4.6 mm column; Mobile phase: CH3CN (60%) :: H2O (40%); Absorbance : 260 nm; flow rate : 1 mL/min. 1H NMR was recorded on a 400 MHz instrument with Me4Si as an internal standard. Mass spectra (MALDI-TOF) was recorded on Kratos PCKompact SEQ V1.2.2 spectrometer.

**General experimental procedure for the preparation of $N^{\alpha}$-protected amino/peptide hydroxamic acid**.

To a solution of $N^{\alpha}$-protected amino/peptide acid (1.0 mmol) dissolved in dry THF at -20 ºC, was added *N*-methylmorpholine (1.05 mmol) followed by the slow addition of ethyl chloroformate (1.1 mmol). The resulting reaction mixture was stirred at -20 ºC for 20 min. To the reaction mixture, freshly prepared hydroxylamine solution (1.0 mmol) was added and stirred at rt for 2.30-3.00 hr until the completion of the reaction (as monitored by TLC). The solvent was removed *in vacuo,* resulting products were purified by column chromatography.

Preparation of neutral hydroxylamine solution. Hydroxalamine hydrochloride dissolved (69.9 mg. 1.0 mmol) in methanol (5 mL) was added to a stirred solution of potassium hydroxide (56.1 mg, 1.0 mmol) in methanol (5 mL) at 0 ºC. The resulting reaction mixture was stirred for 15 min at 0 ºC, potassium chloride precipitates out as a solid, which was removed by filtration and the resulting filtrate, was used as such directly.

**Boc-Phe-$\psi$[NH-CO-NH]-Leu-OMe, 1b.** mp 152-154 °C; $^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.85-0.95 (m, 6H), 1.25-1.45 (m, 12H), 2.75-2.90 (m, 2H), 3.60 (s, 3H), 4.75 (m, 1H), 6.25 (m, 1H) 6.45-6.65(br, 2H), 7.20-7.45 (m, 5H), 8.20 (br, 1H); $^{13}$C NMR (DMSO-$d_6$,

100 MHz) $\delta$ 16.5, 18.2, 21.5, 28.3, 37.4, 50.3, 54.2, 63.1, 82.1, 126.5, 127.3, 128.5, 140.3, 153.1, 155.3, 171.9; HRMS m/z 430.2318 ($M + Na^+$), calcd for $C_{21}H_{33}N_3O_5$ Na 430.2318.

**Boc-Phe-$\psi$[NHCONH]-Val-OMe, 1c.** mp 141-143 °C; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.85 (d, $J$ = 6.6, 6H), 1.45 (s, 9H), 1.90-2.10 (m, 1H), 2.85-2.95 (m, 2H), 3.65 (s, 3H), 4.65 (m, 1H), 5.95 (m, 1H), 6.35-6.45 (br, 2H), 7.25-7.45 (m, 5H), 8.10 (br, 1H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$ 18.5, 23.0, 28.1, 37.3, 51.6, 55.9, 59.83, 75.9, 126.5, 127.3, 129.5, 141.3, 154.0, 156.2, 173.4; ESIMS m/z 394.3 ($M + H^+$), calcd for $C_{20}H_{31}N_3O_5H$ 394.2.

**Boc-Val-$\psi$[NH-CO-NH]-Ala-OMe, 1d.** mp 167-169 °C; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.95 (d, J = 6.9, 6H), 1.26 (d, J = 6.5, 3H), 1.40 (s, 9H), 2.10 (m, 1H), 3.62 (s, 3H), 4.70 (m, 1H), 5.3 (m, 1H), 6.54 (br, 2H), 7.55 (br, 2H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$ 18.6, 18.8, 28.6, 32.9, 52.1, 60.6, 63.0, 78.0, 155.1, 156.6, 174.5; ESIMS m/z 318.3 ($M + H^+$), calcd for $C_{14}H_{27}N_3O_5H$ 318.2.

**Boc-Val-$\psi$[NH-CO-NH]-Phe-OMe, 1e.** mp 161-163 °C; $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 0.94-0.97 (d, $J$ = 6.8, 6H), 1.43 (s, 9H), 1.67 (m, 1H), 3.10 (m, 2H), 3.66 (s, 3H), 4.7 (m, 1H)5.2 (m, 1H), 6.1 (br, 1H),7.30-7.45 (m, 5H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$ 14.5, 28.1, 32.2, 37.0, 52.5, 55.2, 54.5, 95.0, 126.4, 128.3, 129.3, 137.5, 155.2, 156.3, 172.3; ESIMS m/z 394.3 ($M + H^+$), calcd for $C_{20}H_{31}N_3O_5H$ 394.2.

**Boc-Val-$\psi$[NHCONH]-*R*-(+)-1-Phenylethylamine, 1f.** mp 141-143 °C; $^1$H NMR (DMSO-$d_6$, 200MHz) $\delta$ 0.70-0.90 (m, 6H)1.30 (d, 3H), 1.45 (s, 9H), 1.75-1.90 (m, 1H), 4.70-4.85 (m, 1H), 6.05 (br, 1H), 6.55 (br, 1H), 7.22-7.45 (m, 5H), 8.15 (br, 1H); ESIMS m/z 336.2 ($M + H^+$), calcd for $C_{18}H_{29}N_3O_3H$ 336.2.

**Boc-Ser(Bzl)-*ψ*[NH-CO-NH]-Gly-OMe, 1g.** mp 130-132 °C; $^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.35 (s, 9H), 3.45 (t, $J$ = 2H), 3.62 (s, 3H), 3.82 (d, $J$ = 6.9, 2H), 4.49 (s, 2H), 5.25 (m, 1H), 6.45-6.55 (m, 1H), 7.15 (br, 1H), 7.25-7.37 (m, 6H); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$ 28.8, 45.5, 71.3, 76.4, 77.2, 78.5, 126.6, 127.1, 128.5, 138.1, 156.3, 157.2, 171.3; ESIMS m/z 382.3 ($M + H^+$), calcd for $C_{18}H_{27}N_3O_6H$ 382.2.

**Z-Ala-*ψ*[NH-CO-NH]-Gly-OMe, 2a.** mp 142-144 °C; $^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.40 (d, J = 7.7 Hz, 3H,) 3.59 (s ,3H), 4.44 (d, J = 6.5 Hz, 2H), 5.12 (s, 2H), 5.76 (m, 1H), 7.28 (5H, m); $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$ 21.5, 41.2, 51.5, 49.8, 64.9, 127.4, 127.6, 128.5, 137.0, 155.1, 156.2, 171.5; ESIMS m/z 310.3 ($M + H^+$), calcd for $C_{14}H_{19}N_3O_5H$ 310.2.

**Z-Phg-NHOH,** mp 159-161 ºC; $^{1}$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 5.04 (s, 2H), 5.12 (d, $J$ = 8.6 Hz, 1H), 7.28-7.44 (m, 10H), 8.04 (d, $J$ = 8.6 Hz, 1H), 8.99 (s, 1H), 10.94 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 55.7, 65.5, 127.0, 127.5, 127.8, 128.1, 128.5, 136.9, 138.5, 155.6, 166.5; ESI-MS m/z 323.1 ($M + Na^+$), calcd for $C_{16}H_{16}N_2O_4Na$ 323.1.

**Z-Phg-*ψ*[NH-CO-NH]-*R*-(+)-1-Phenylethylamine, 2c.** mp 181-183 °C; $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.37 (d, J= 8.0 Hz, 3H), 4.87 (m, 1H), 5.03 (d, J= 12 Hz, 2H), 6.28-6.57 (m. 1H), 7.16-7.85 (m, 15H), 11.21 (br, 1H); ESIMS m/z 404.3 ($M + H^+$), calcd for $C_{24}H_{25}N_3O_3H$ 404.2.

**Z-Phg-*ψ*[NH-CO-NH]-*S*-(-)-1-Phenylethylamine, 2d.** mp 178-180 °C; $^{1}$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.38 (d, J= 6.8 Hz, 3H), 4.84-4.89 (m, 1H), 5.04 (d, $J$= 8.8 Hz, 2H), 6.26-6.59 (m. 1H), 7.19-7.89 (m, 15H); ESIMS m/z 404.3 ($M + H^+$), calcd for $C_{24}H_{25}N_3O_3H$ 404.2.

**Fmoc-Glu (O$^t$Bu)-NHOH,** mp 131-133 ºC; $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 1.37 (s, 9H), 1.78-1.80 (m, 2H), 2.17-2.22 (m, 2H), 3.86 (d, $J$ = 6.3 Hz 1H), 4.20-4.25 (m, 3H), 7.30-7.89 (m, 8H), 8.85 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 27.7, 31.3, 46.5, 51.5, 65.5, 79.6, 125.2, 127.0, 127.4, 127.6, 129.0, 140.6, 142.5, 155.8, 168.0, 171.5; HRMS m/z 463.1834 (M + Na$^+$), calcd for $C_{24}H_{28}N_2O_6Na$ 463.1845.

**Fmoc-Val-$\psi$[NH-CO-NH]-Leu-OBzl, 3a.** mp 179-181°C; $^1$H NMR (DMSO-$d_6$, 200 MHz): $\delta$ 0.92 (12H, m), 1.32-1.85 (4H, m), 3.1 (2H, s), 3.7-3.8 (2H, m), 4.2 (1H, t), 4.42 (2H, m), 5.1 (1H, d), 6.6-6.7 (2H, m); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): $\delta$ 18.5, 19.5, 22.0, 23.1, 24.5, 29.2, 37.2, 40.2, 47.2, 51.5, 59.0, 66.6, 120.0, 125.0, 126.5, 127.2, 128.0, 128.0, 128.4, 129.3, 137.6, 141.2, 144.0, 155.4, 156.8, 176.4; MALDI-TOF m/z 504.3 (M + Na$^+$), calcd for $C_{27}H_{35}N_3O_5Na$ 504.2.

**Z-Ala-Ile-NHOH,** mp 177-179 ºC; $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 0.75-0.90 (m,5H), 1.15(d, $J$ = 5.6 Hz, 3H), 1.42 (m,1H), 1.65 (m,1H), 1.75 (m,1H), 2.08 (s, 1H), 4.00 (m, 1H), 4.11 (m, 1H), 5.00 (s, 2H), 7.35 (m, 5H), 7.46 (d, 1H), 7.80 (d, 1H), 7.80 (d, 1H), 8.89 (br, 1H), 10.65 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 10.6, 15.1, 18.2, 24.5, 36.5, 50.0, 54.1, 65.3, 127.2, 127.5, 128.0, 137.1, 155.5, 167.2, 171.0; HRMS m/z 374.1700 (M + Na$^+$), calcd for $C_{17}H_{25}N_3O_5Na$ 374.1692.

**Z-Leu-Phe-NHOH.** mp 168-170 ºC ; $^1$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 0.87 (d, $J$ = 8.1, 6H), 1.18-1.54 (m, 2H), 2.88-3.07 (m, 3H), 4.06 (m, 1H), 4.58 (m, 1H), 5.04 (s, 2H), 6.78 (d, $J$ = 8.8 Hz, 1H), 7.18-7.32 (m, 10H), 7.64 (m, 1H), 8.67 (br, 1H), 10.50 (br, 1H) ; $^{13}$C NMR ($CDCl_3$, DMSO-$d_6$, 100 MHz) $\delta$ 21.4, 23.0, 24.1, 38.2, 41.5, 51.4, 53.3, 65.5, 126.3, 127.7, 127.8, 128.4, 129.2, 137.0, 137.4, 155.8, 167.5, 171.9 ; HRMS m/z 450.2010 (M + Na$^+$), calcd for $C_{23}H_{29}N_3O_5Na$ 450.2005.

**Z-Leu-Phe-ψ[NHCONH]-Ala-OMe, 5b.** mp 186-188 ºC; $^{1}$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 0.87 (d, $J$ = 5.6 Hz, 6H), 1.27-1.58 (m, 6H), 2.93-3.10 (m, 2H), 3.68 (s, 3H), 4.03-4.33 (m, 2H), 5.04 (s, 2H), 5.15-5.19 (m, 1H), 6.31-6.59 (br, 3H), 7.19-7.31 (br, 10H), 8.02 (br, 1H) ; $^{13}$C NMR ($CDCl_3$, DMSO-$d_6$, 100 MHz) $\delta$ 18.1, 21.5, 22.9, 24.2, 40.9, 47.9, 51.6, 53.3, 58.3, 65.5, 126.0, 127.6, 127.9, 128.2, 129.3, 136.9, 137.6, 155.7, 156.1, 171.9, 173.9. HRMS m/z 535.2544 (M + $Na^+$), calcd for $C_{27}H_{36}N_4O_6Na$ 535.2533.

**Z-Phe-Leu-NHOH,** mp 181-183 ºC; $^{1}$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 0.95 (m, 6H), 1.50 (m, 3H), 2.65-3.00 (m, 2H), 4.25 (m, 2H), 4.95 (s, 2H), 7.10-7.28 (m, 10H), 7.50 (d, 1H), 8.10 (d, 1H), 8.89 (br, 1H), 10.70 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 22.0, 24.1, 37.2, 41.9, 48.6, 56.0, 65.1, 126.0, 127.1, 127.5, 128.0, 128.2, 129.4, 137.0, 139.0, 155.6, 168.4, 171.1; HRMS m/z 450.2006 (M + $Na^+$), calcd for $C_{23}H_{29}N_3O_5Na$ 450.2005.

**Z-Phe-Leu-ψ[NHCONH]-Ile-OMe, 5c.** mp 185-187 ºC; $^{1}$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 0.89-1.09 (m, 6H), 1.12-1.45 (m, 3H), 1.50-1.77 (m, 3H), 2.40-3.07 (m, 6H), 3.66 (s, 3H), 4.31 (m, 1H), 4.89-5.10 (m, 4H), 6.21-6.45 (br, 2H), 7.18-7.27 (m, 10H), 7.90-8.02 (br, 2H) ; $^{13}$C NMR ($CDCl_3$, DMSO-$d_6$, 100MHz) $\delta$ 11.4, 15.6, 22.3, 22.4, 24.4, 24.8, 37.3, 37.6, 43.8, 51.6, 55.4, 56.2, 56.7, 65.3, 126.3, 127.5, 127.8, 128.1, 128.4, 129.3, 137.1, 138.2, 155.9, 156.5, 171.0, 173.2; HRMS m/z 577.2997 (M + $Na^+$), calcd for $C_{30}H_{42}N_4O_6Na$ 577.3002.

**Boc-Val-Leu-NHOH,** mp 167-169 ºC; $^{1}$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 0.85-0.90 (m, 12H), 1.35 (s, 9H), 1.43-1.57 (m, 3H), 1.90 (m, 1H), 3.76 (t, $J$ = 7.16 Hz, 1H), 4.23 (m, 1H), 6.76 (d, $J$ = 9.12 Hz, 1H), 7.78 (d, $J$ = 8.36 Hz, 1H), 8.84 (s, 1H), 10.65 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 16.1, 22.5, 28.0, 33.1, 44.5, 48.9, 58.2, 78.0, 156.1, 168.2, 170.5; HRMS m/z 368.2164 (M + $Na^+$), calcd for $C_{16}H_{31}N_3O_5Na$ 368.2161.

**Boc-Val-Leu-*ψ*[NHCONH]-Phe-OMe, 5d.** mp 180-182 ºC. $^{1}$H NMR ($CDCl_3$, DMSO, 200 MHz) $\delta$ 0.82-0.89 (m, 12H), 1.41 (s, 9H), 1.60-2.01 (m, 3H), 2.55 (m, 1H), 2.95-2.97 (m, 2H), 3.63 (s, 3H), 5.11-5.14 (m, 1H), 5.69-5.74 (m, 1H), 6.47-6.51 (br, 1H), 7.09-7.23 (m, 7H), 7.92-7.95 (br, 1H) ; $^{13}$C NMR (CDCl3, DMSO, 200 MHz) $\delta$ 18.2, 19.2, 22.1, 22.4, 24.1, 28.2, 30.4, 37.7, 43.5, 51.6, 53.9, 55.0, 59.8, 77.9, 126.5, 128.2, 129.2, 137.0, 155.4, 156.3, 171.5, 172.8; HRMS m/z 529.2999 (M + $Na^+$), calcd for $C_{26}H_{42}N_4O_6Na$ 529.3002.

**Boc-Val-Leu-*ψ*[NHCONH]-Val-Leu-OMe, 5e.** mp 191-192 ºC; $^{1}$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz): $\delta$ 0.82-1.00 (m, 12H), 1.24-1.70 (m, 23 H), 1.91-2.00 (m, 2H), 2.80-3.20 (m, 3H), 3.62 (s, 3H), 3.86 (m, 1H), 4.56 (m, 1H), 5.11-5.14 (m, 1H), 5.69-5.74 (m, 1H), 5.69-5.74 (m, 1H), 6.35-6.65 (br, 3H), 7.1 (br, 1H), 7.92-7.95 (br, 2H) ; $^{13}$C NMR ($CDCl_3$, DMSO, 200 MHz): $\delta$ 14.1, 17.9, 18.2, 19.4, 21.7, 22.6, 23.1, 24.4, 24.6, 24.7, 24.8, 28.5, 31.2, 40.9, 43.9, 50.5, 51.8, 55.8, 56.5, 59.9, 77.5, 155.5, 156.9, 171.0, 172.5, 173.0 ; ESIMS m/z 594.4 (M + $Na^+$), calcd for $C_{28}H_{53}N_5O_7Na$ 594.4.

**Boc-Val-Pro-NHOH,** mp 147-149 ºC; $^{1}$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 0.95 (d, $J$=8.41 Hz), 1.36 (s, 9H), 1.56-2.23 (m, 5H), 3.13 (m, 2H), 4.15 (m, 1H), 4.42 (m, 1H), 8.91 (s, 1H); $^{13}$C NMR (DMSO-$d_6$, 100MHz) $\delta$ 18.2, 24.3, 28.1, 29.3, 33.1, 42.3, 49.5, 52.7, 79.1, 155.6, 169.0, 171.1; HRMS m/z 352.1842 (M + $Na^+$), calcd for $C_{15}H_{27}N_3O_5Na$ 352.1848.

**Boc-Val-Pro-*ψ*[NHCONH]-Val-Ala-Leu-OMe, 5f.** mp 168-170 ºC ; $^{1}$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 0.80-1.05 (m, 18H), 1.32-1.45 (m, 9H), 1.50-1.71 (m, 4H)), 1.80-2.15 (m, 9H), 3.75 (s, 3H), 4.25 (m, 1H), 4.60-4.71 (m, 2H), 4.85 (m, 1H), 5.12 (m, 1H),

7.15 (d, *J*=5.6 Hz, 1H), 7.65 (d, *J*= 6.5 Hz, 1H), 8.00 (d, *J*=5.6 Hz , 1H) ; $^{13}$C NMR ($CDCl_3$, DMSO-$d_6$, 100 MHz) $\delta$ 18.4, 18.7, 19.5, 22.0, 22.8, 23.4, 24.1, 37.5, 28.2, 30.5, 32.04, 41.3, 43.8, 50.4, 52.5, 55.3, 56.7, 58.6, 78.9, 155.6, 158.7, 169.0, 171.5, 173.3, 175.6; HRMS m/z 649.3900 (M + $Na^+$), calcd for $C_{30}H_{54}N_6O_8Na$ 649.3901.

**Boc-Phe-Phg-NHOH, 4f.** mp 109-111 ºC; $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 1.31 (s, 9H), 2.67 (m, 1H), 2.93 (m, 1H), 4.31 (t, *J* = 2.4 Hz, 1H), 5.39 (d, *J* = 8.2 Hz, 1H), 7.03-7.34 (m, 10H), 8.73 (d, *J* = 8.2 Hz, 1H) ; $^{13}$C NMR (DMSO-$d_6$, 50MHz) $\delta$ 27.9, 37.2, 53.6, 56.0, 78.1, 126.1, 126.6, 127.5, 127.8, 128.1, 129.3, 138.0, 138.9, 155.5, 166.2, 171.5; HRMS m/z 436.1846 (M + $Na^+$), calcd for $C_{22}H_{27}N_3O_5Na$ 436.1848.

**Boc-Phe-Phg-ψ[NH-CO-NH]-(*R*)-(+)-Phenylethylamine, 5h.** mp 175-177 ºC; $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 1.29 (s, 9H), 1.38 (d, *J* = 8.1 Hz, 3H), 2.70-2.92 (m, 1H), 4.19 (m, 1H), 4.77 (t, *J* = 6.6 Hz, 1H), 6.37 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 8.7 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.21-7.30 (m, 15H), 8.70 (br, 1H); HRMS m/z 539.2639 (M + $Na^+$), calcd for $C_{30}H_{36}N_4O_4Na$ 539.2634.

**Boc-Phe-Phg-ψ[NH-CO-NH]-(*S*)-(-)-Phenylethylamine, 5i.** mp 167-169 ºC; $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 1.29 (s, 9H), 1.48 (d, *J* = 6.6 Hz, 3H), 2.70-2.92 (m, 1H), 4.19 (m, 1H), 4.77 (t, *J* = 6.6 Hz, 1H), 6.37 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 8.7 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.21-7.30 (m, 15H), 8.70 (d, *J* = 6.6 Hz, 1H)

**Boc-Phe-Phg-ψ[NH-CO-NH]-(*R,S*)-(±)-Phenylethylamine** $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 1.29 (s, 9H), 1.38 (d, *J* = 8.1 Hz, 3H), 1.46 (d, *J* = 6.6 Hz, 3H), 2.70-2.92 (m, 1H), 4.19 (m, 1H), 4.77 (t, *J* = 6.6 Hz, 1H), 6.37 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 8.7 Hz,

1H), 6.72 (d, *J* = 7.2 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 7.21-7.30 (m, 15H), 8.75 (d, *J*=6.5Hz, 1H);

**Boc-Phg-Phe-NHOH**, **4i.** mp 198-200 ºC. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 1.35 (s, 9H), 2.31-2.80 (m, 2H), 4.73 (m, 1H), 5.51 (d, *J*=7.8 Hz, 1H), 7.08-7.29 (m, 10H), 8.44 (d, *J*=8.2 Hz); HRMS m/z 436.1843 (M + Na$^+$), calcd for $C_{22}H_{27}N_3O_5Na$ 436.1848.

**Boc-Phg-Phe-$\psi$[NHCONH]-(*R*)-(+)-Phenylethylamine, 5j.** mp 174-176 ºC. $^1$H NMR (DMSO-$d_6$, 500 MHz) $\delta$ 1.26 (d, *J*=8.7 Hz, 3H), 1.37 (s, 9H), 2.83-2.88 (m, 1H), 2.93-2.98 (m, 1H), 4.66 (t, *J*=9.1 Hz, 1H), 5.13 (d, *J*=10.5 Hz, 1H), 5.26 (t, *J*=9.4 Hz 1H), 6.33 (d, *J*=10.2 Hz, 1H), 6.56 (d, *J*=9.38 Hz, 1H), 7.08-7.36 (m, 15H), 8.51-8.53 (d, *J*=9.0 Hz, 1H); HRMS m/z 539.2632 (M + Na$^+$), calcd for $C_{30}H_{36}N_4O_4Na$ 539.2634.

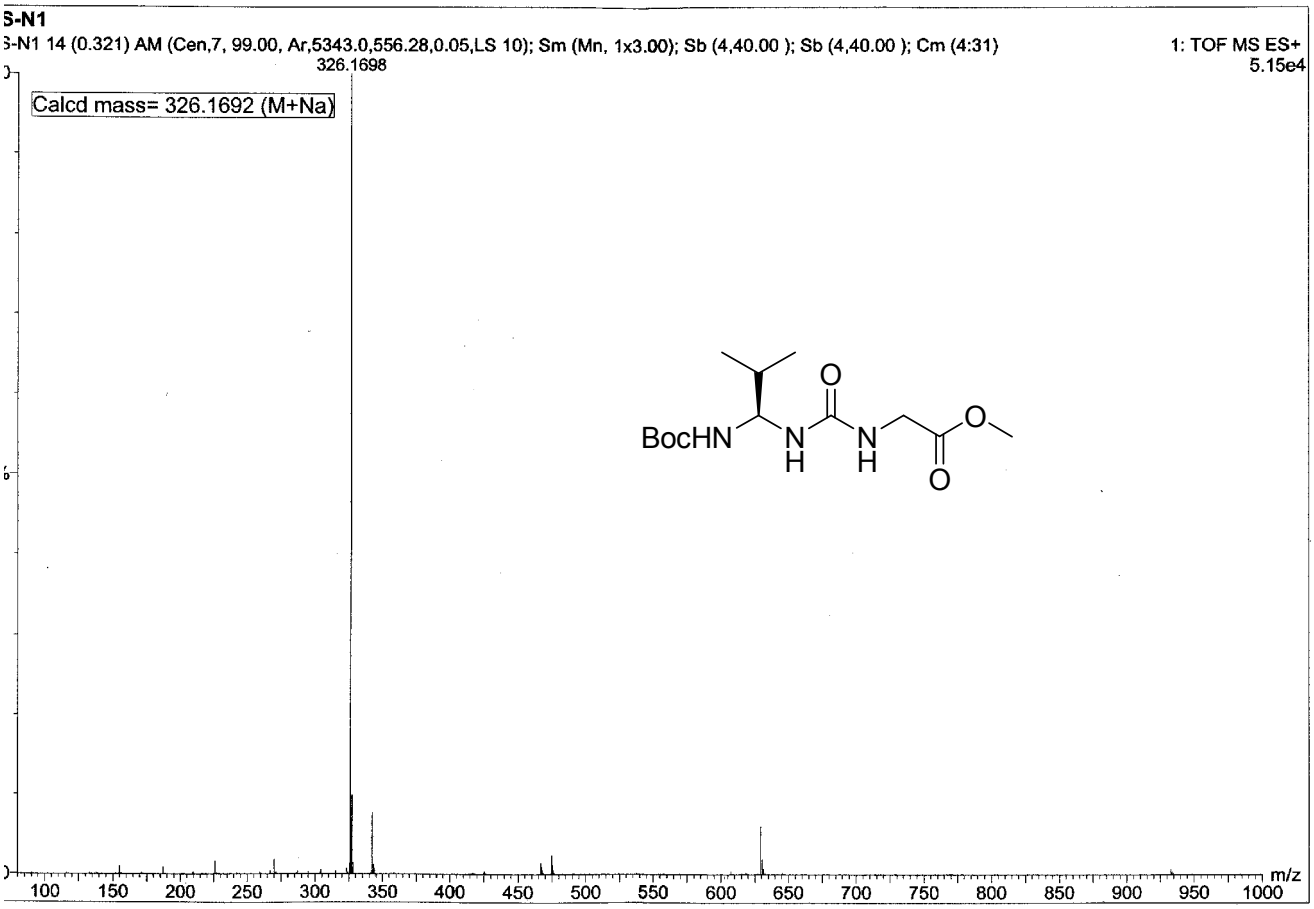
**Boc-Phg-Phe-$\psi$[NHCONH]-(*S*)-(-)-Phenylethylamine, 5k**. mp 209-211 ºC. $^1$H NMR (DMSO-$d_6$, 500 MHz) $\delta$ 1.22 (d, *J*=8.6 Hz, 3H), 1.37 (s, 9H), 2.86-2.97 (m, 1H), 4.66 (t, *J*=9.0 Hz, 1H), 5.11 (d, *J*=10.5 Hz, 1H), 5.24 (t, *J*=9.6 Hz, 1H), 6.39 (d, *J*=10.4 Hz 1H), 6.58 (d, *J*=9.8 Hz 1H), 7.07-7.33 (m, 15H), 8.55 (d, *J*=9.0 Hz 1H).

**Boc-Phg-Phe-$\psi$[NHCONH]-(*R,S*)-(±)-Phenylethylamine**. mp 180-182 ºC. $^1$H NMR (DMSO-$d_6$, 500 MHz) $\delta$ 1.22 (d, *J*=8.6 Hz, 3H), 1.26 (d, *J*=8.7 Hz, 3H), 1.37 (s, 9H), 2.82-2.97 (m, 2H), 4.62-4.70 (m, 1H), 5.10-5.15 (m, 1H), 5.20-5.28 (m, 1H), 6.35-6.39 (m, 1H), 6.55-6.60 (m, 1H), 7.05-7.36 (m, 15H), 8.55-8.59 (d, 1H);

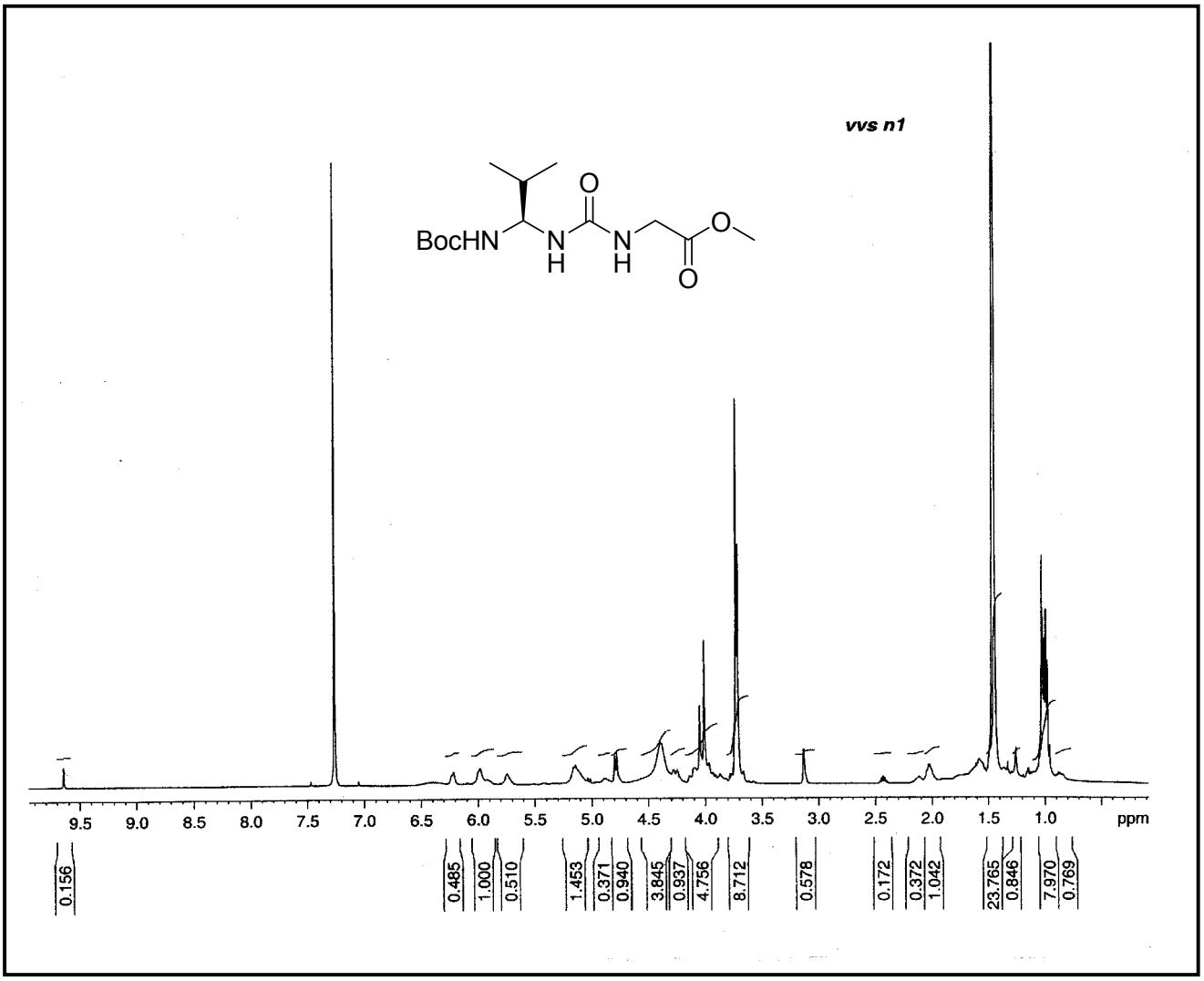
**Boc-Val-Ala-Leu-$\psi$[NH-CO-NH]-Val-Ala-Leu-OMe, 5g.** mp 205-207 ºC ; $^1$H NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 0.75-1.08 (m, 24H), 1.25-1.70 (m, 21H), 1.97 (m, 2H), 2.70-3.10 (m, 2H), 3.66 (s, 3H), 3.82 (m, 2H), 4.12 (m, 1H), 4.36-4.48 (m, 2H), 5.17-5.31 (m, 2H), 5.76-5.81 (by, 1H), 5.98-6.02 (m, 1H), 7.65-8.01 (br, 2H); $^{13}$C NMR ($CDCl_3$, DMSO-$d_6$, 100 MHz) $\delta$ 14.1, 14.7, 17.8, 18.0, 19.7, 19.9, 21.9, 22.7, 23.5, 24.9, 25.0,

28.7, 32.1, 44.0, 50.6, 51.5, 53.6, 56.2, 59.0, 95.6, 155.2, 155.37, 156.3, 157.2, 171.5, 172.6, 173.5 ; MALDI-TOF m/z 736.5 ($M + Na^+$), calcd for $C_{34}H_{63}N_7O_9Na$ 736.5.

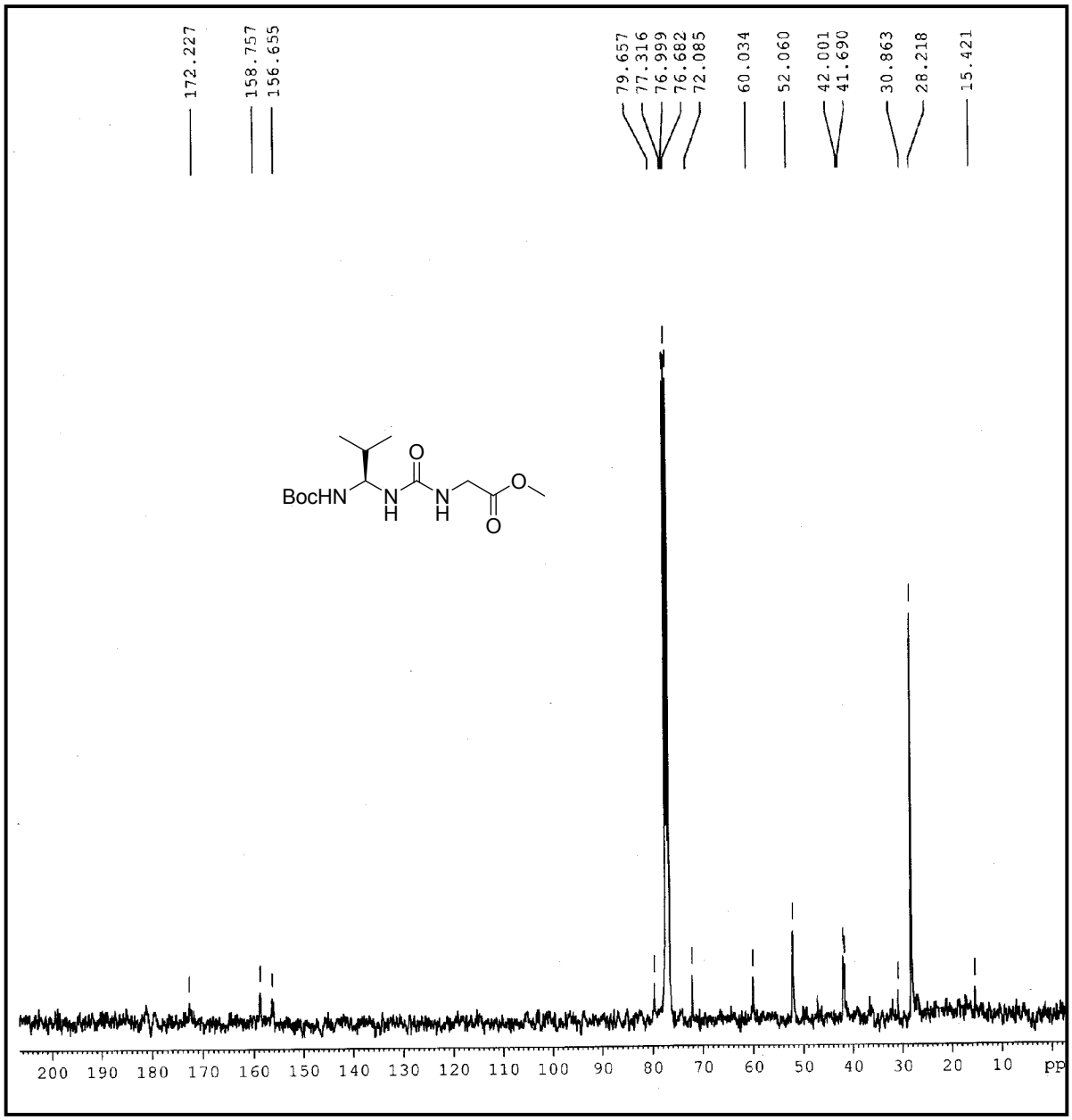
**Z-ureidoalanine derivative, 8.** $^1H$ NMR ($CDCl_3$, DMSO-$d_6$, 200 MHz) $\delta$ 1.41 (d, 3H), 3.60 (s, 3H), 4.05 (d, 2H, $J$=7.12 Hz), 4.43 (m, 1H), 4.86 (t, 1H), 5.21 (s, 2H), 5.60 (s, 2H), 7.21-7.36 (m, 5H); $^{13}C$ NMR ($CDCl_3$, DMSO-$d_6$, 100 MHz) $\delta$ 16.2, 40.4, 51.4, 50.0, 66.0, 67.5, 77.8, 66.0, 127.0, 127.6, 128.8, 141.0, 154.0, 157.5, 171.2, 174.7; ESIMS m/z 380.0 ($M + H^+$), calcd for $C_{17}H_{21}N_3O_7H$ 380.1.



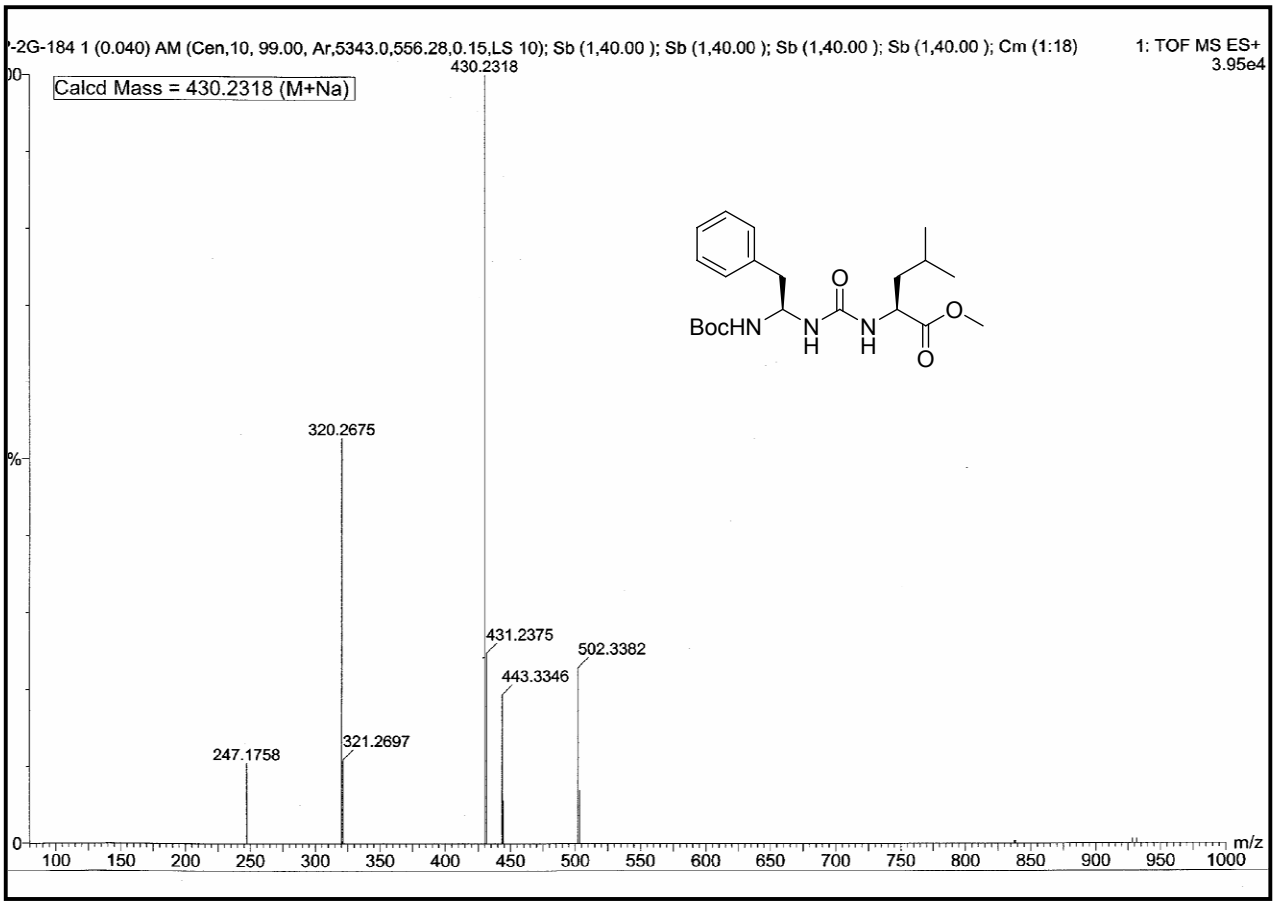

**HRMS of Boc-Val-$\psi$[NHCONH]-Gly-OMe**



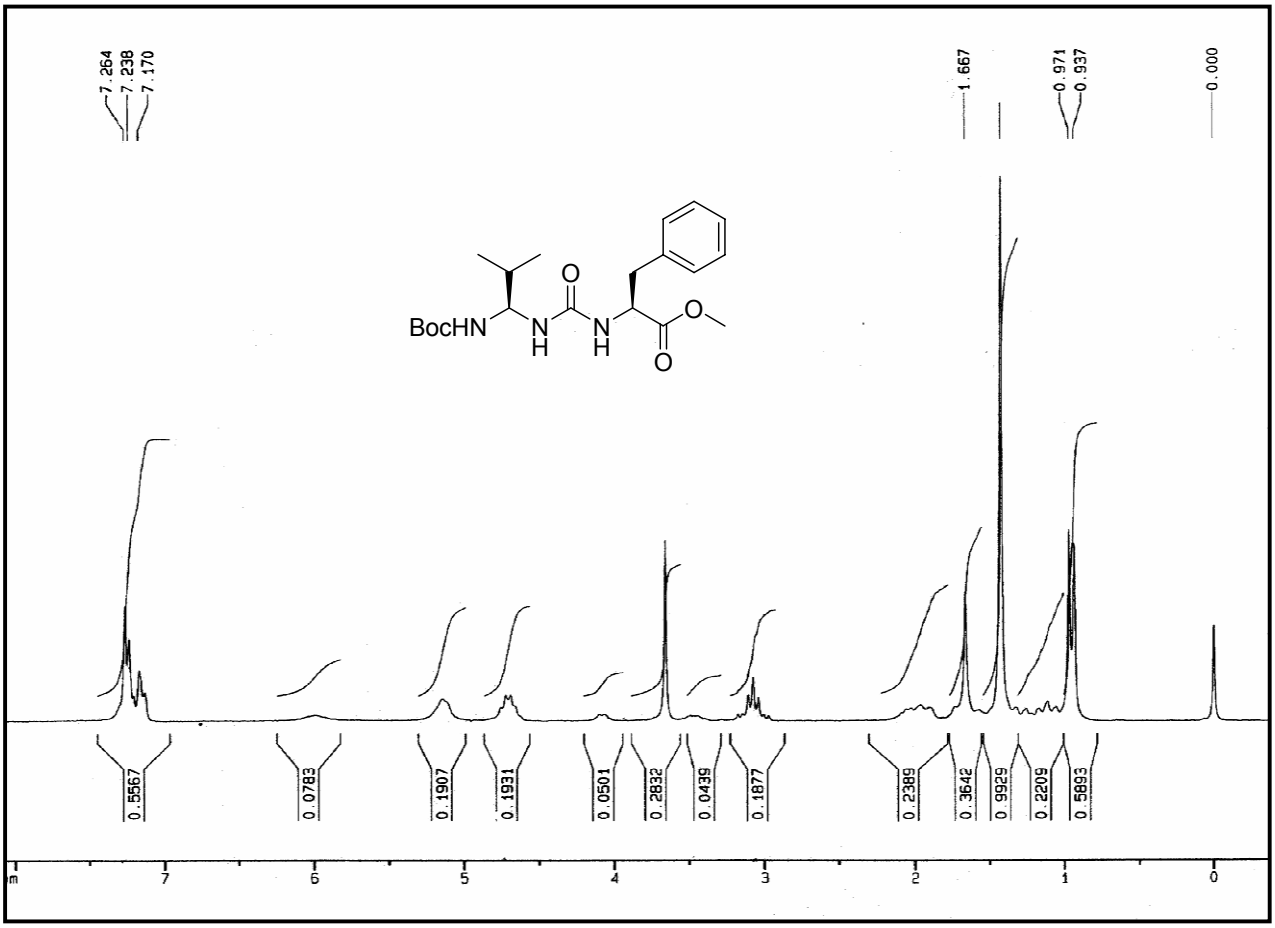

**$^{1}$H NMR of Boc-Val-$\psi$[NHCONH]-Gly-OMe**



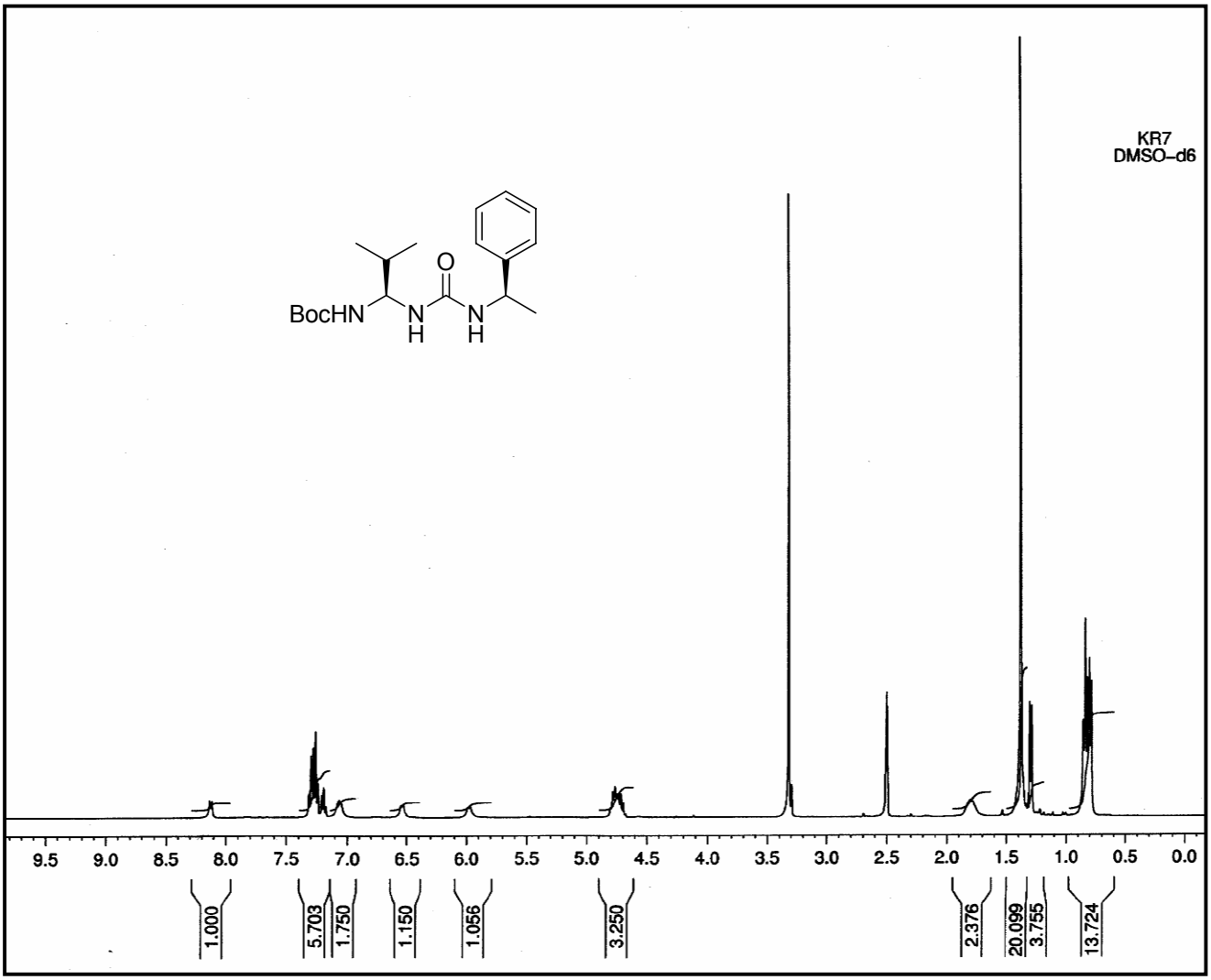

**$^{13}$C NMR of Boc-Val-$\psi$[NHCONH]-Gly-OMe**



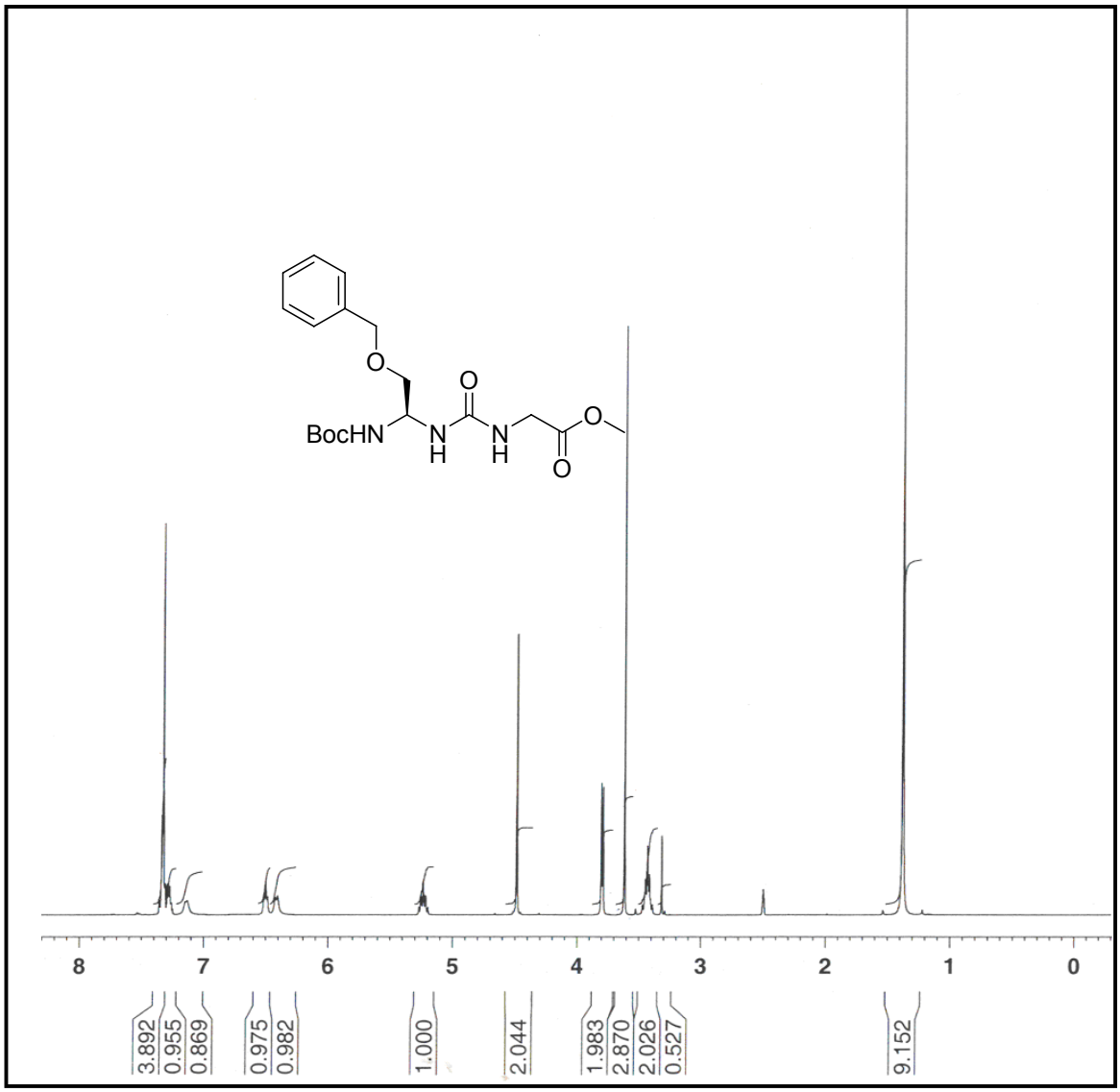

**HRMS of Boc-Phe-$\psi$[NHCONH]-Leu-OMe**



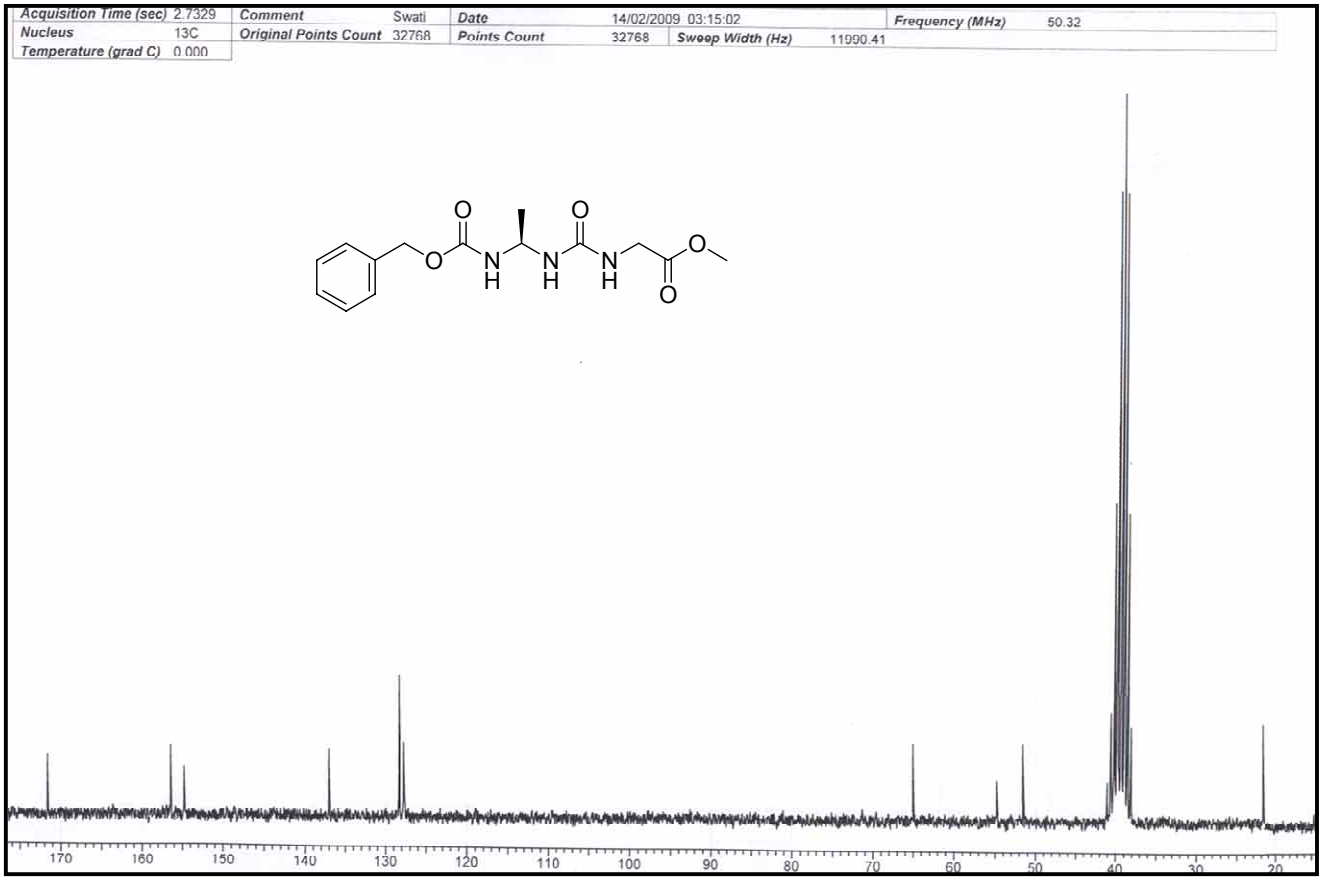

**$^1$H NMR of Boc-Val-$\psi$[NHCONH]-Phe-OMe**



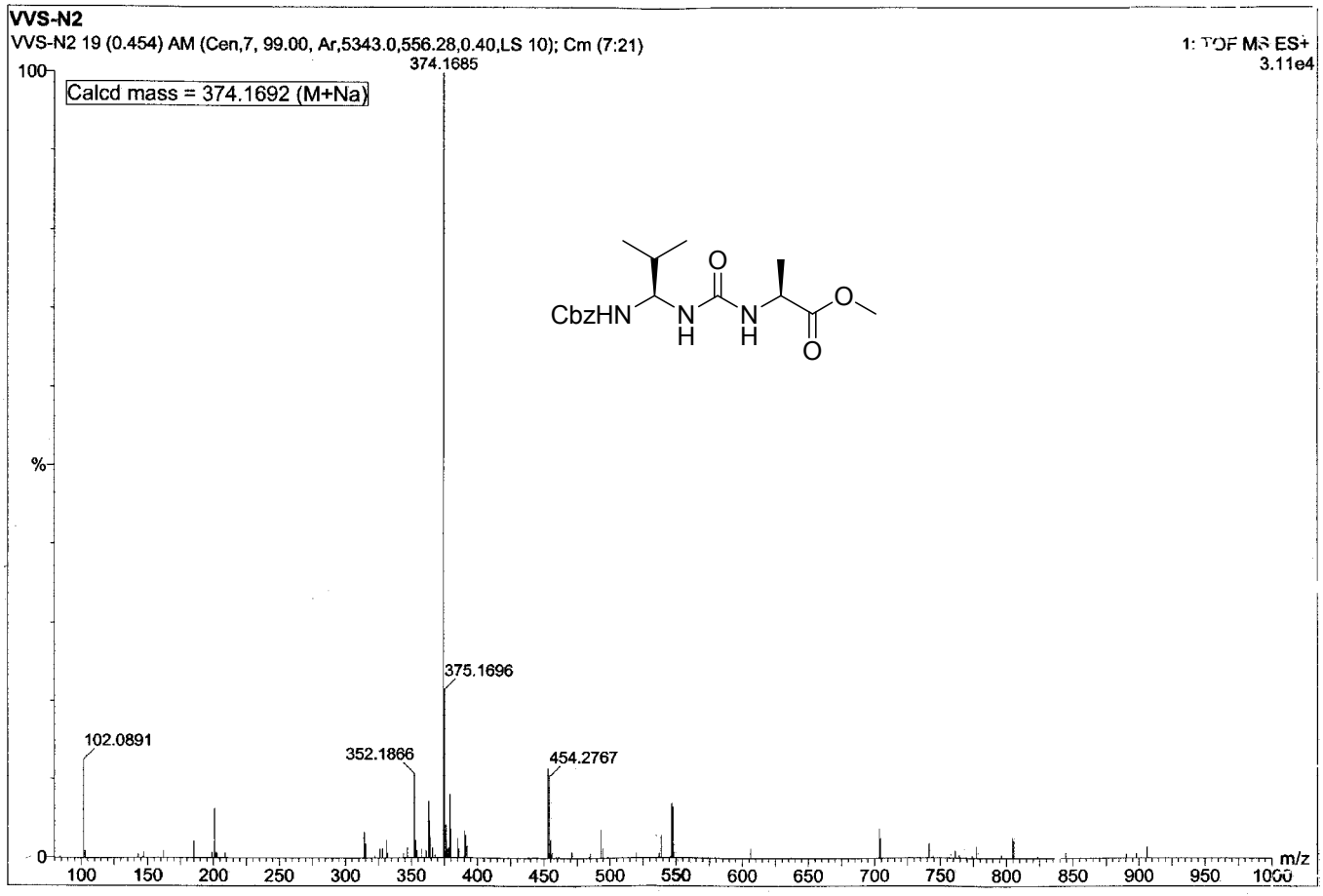

**$^1$H NMR spectra of Boc-Val- $\psi$ [NHCONH]-R-(+)-phenylethylamine**



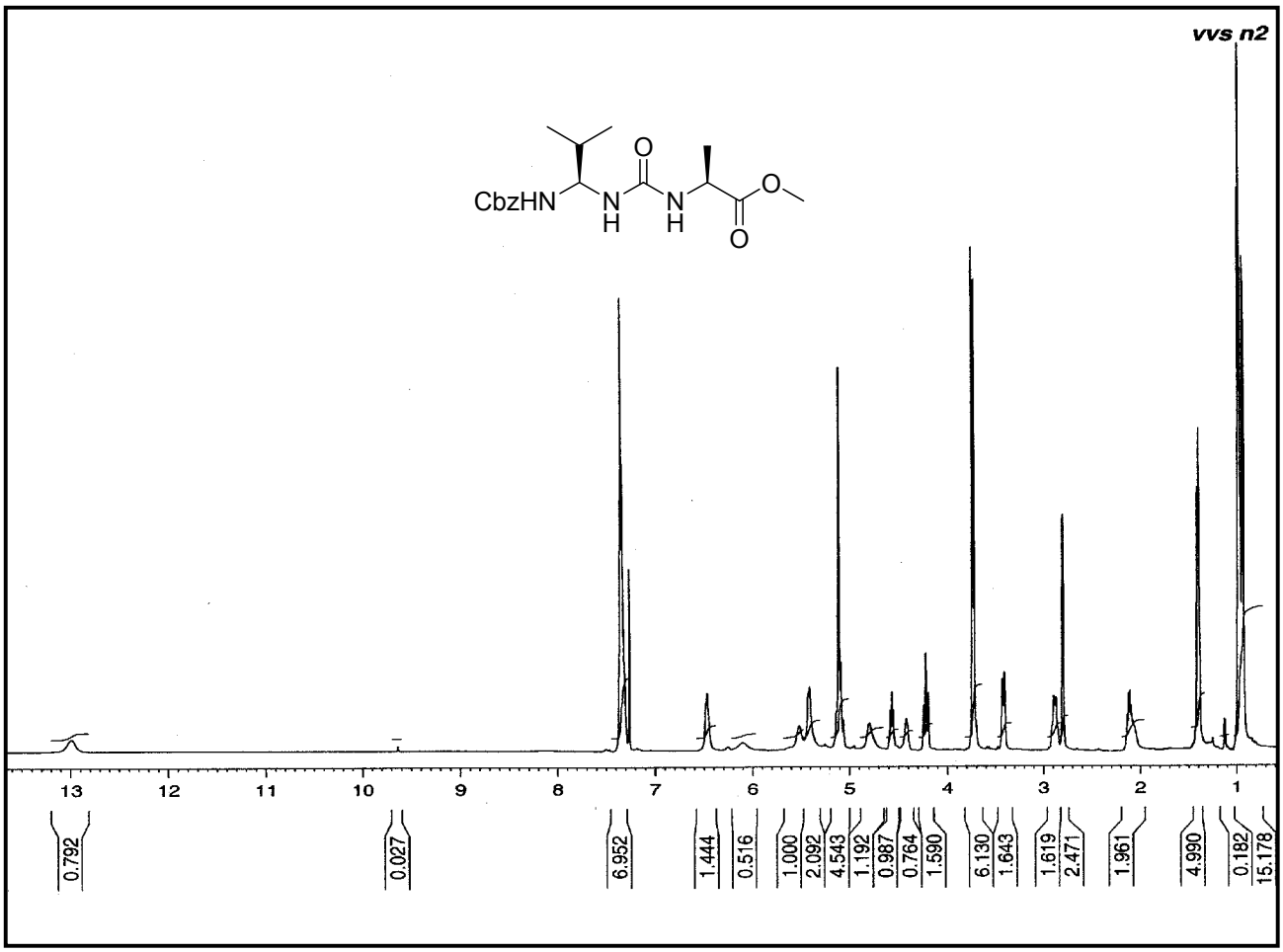

**$^{1}$H NMR of Boc-Ser(Bzl)-$\psi$[NHCONH]-Gly-OMe**



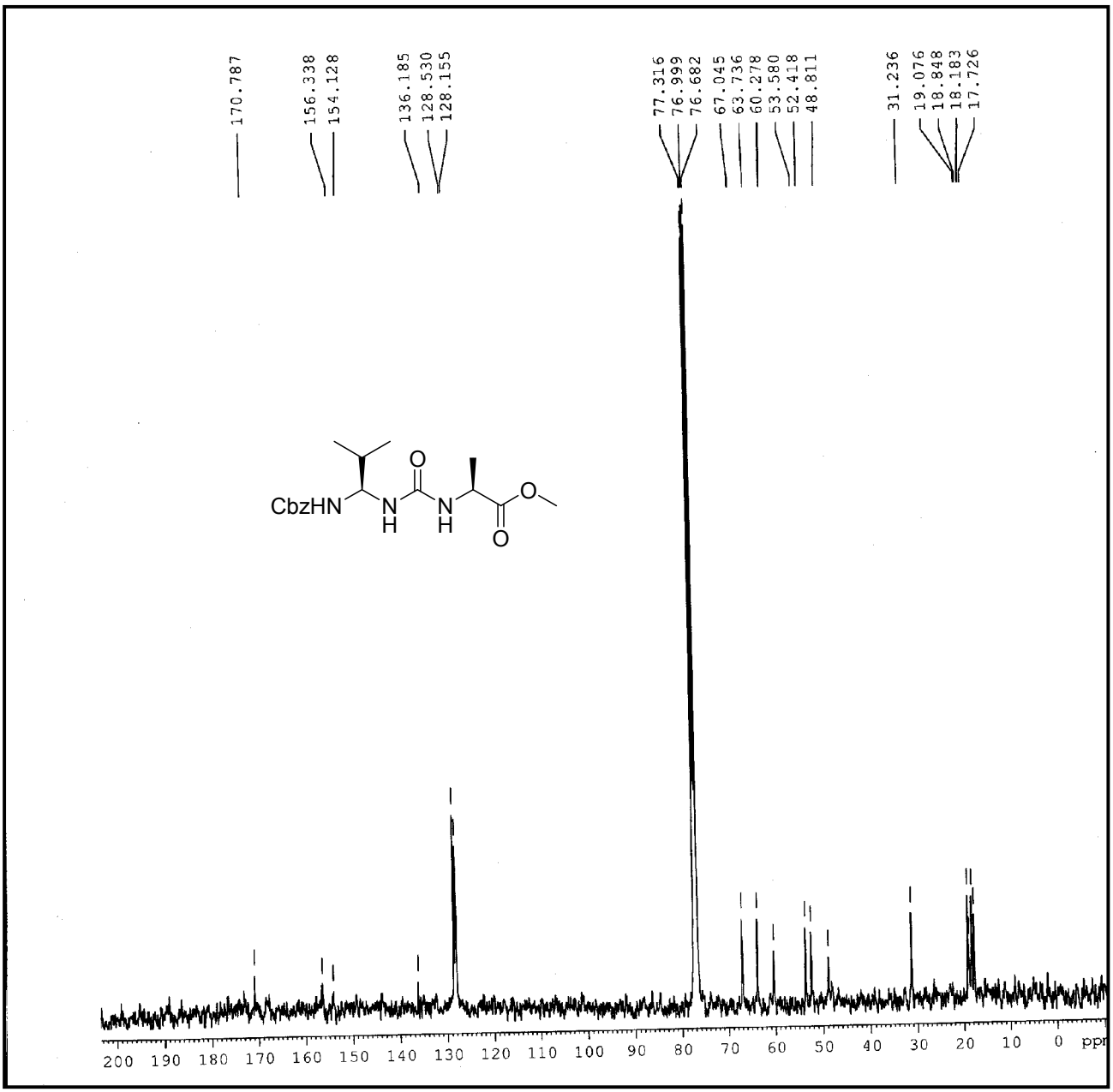

**$^{13}$C NMR spectra of Z-Ala-$\psi$[NH-CO-NH]-Gly-OMe**



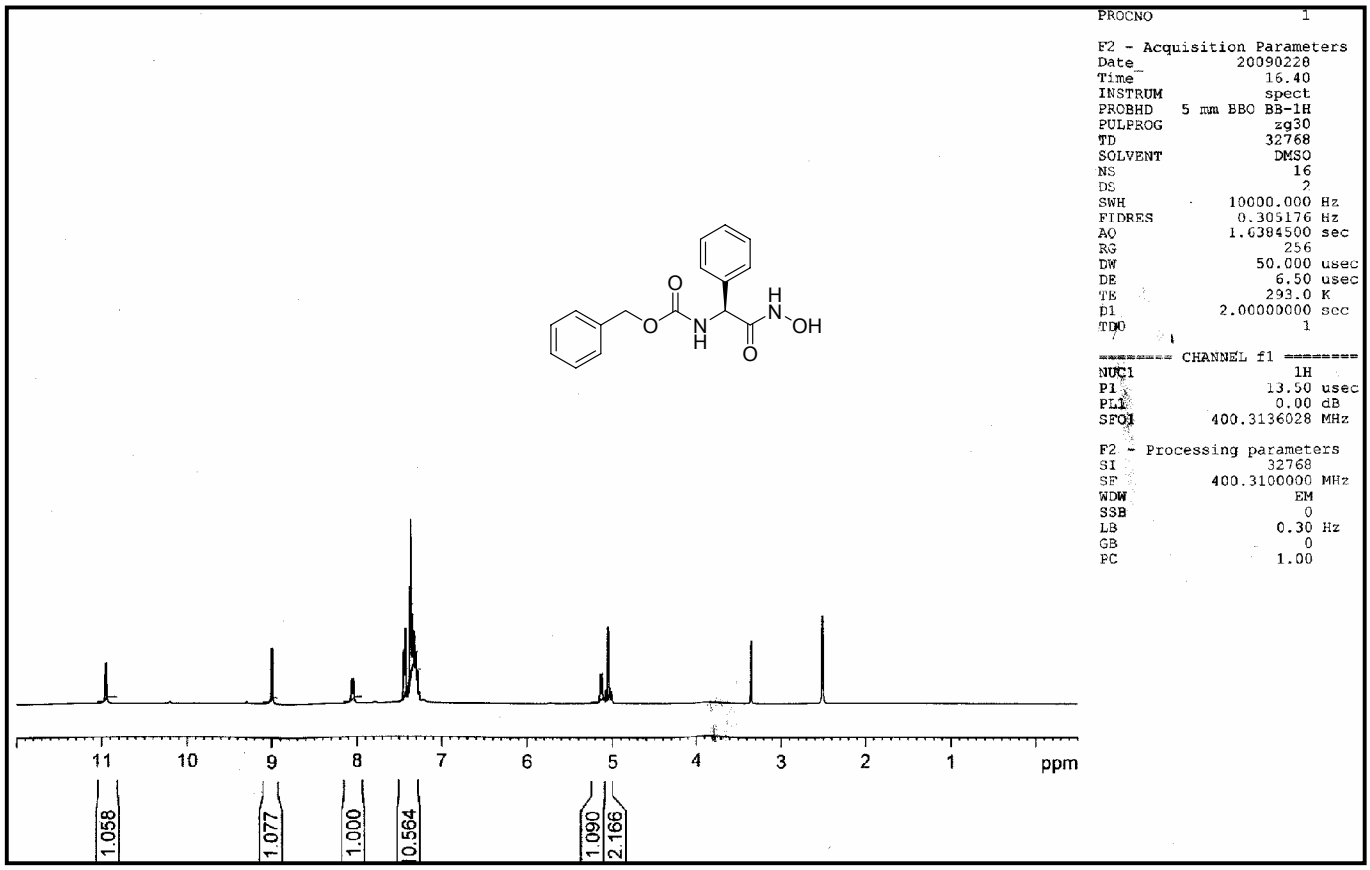

**HRMS of Z-Val- $\psi$[NHCONH]-Ala-OMe**



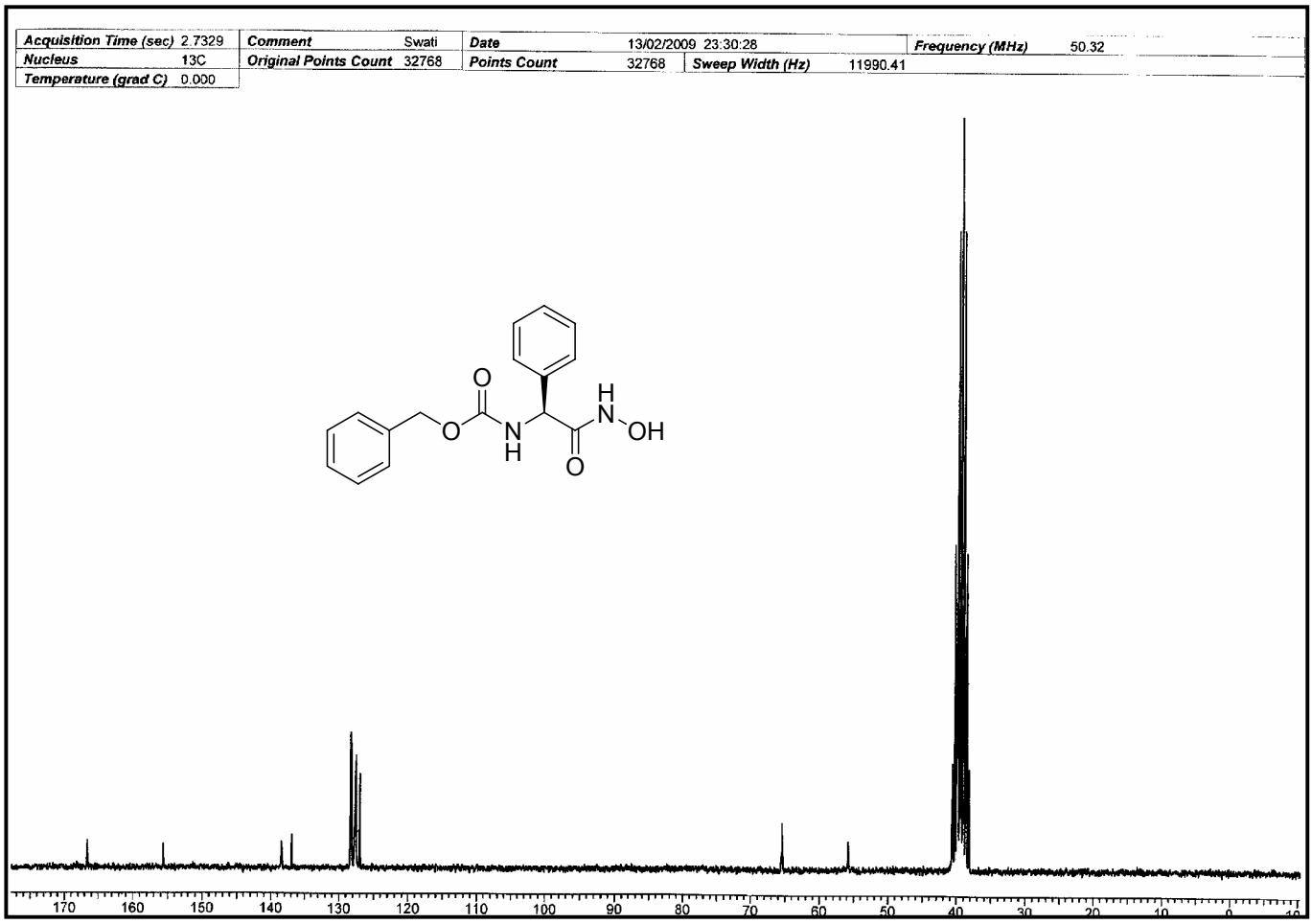

**$^{1}$H NMR of Z-Val- $\psi$[NHCONH]-Ala-OMe**



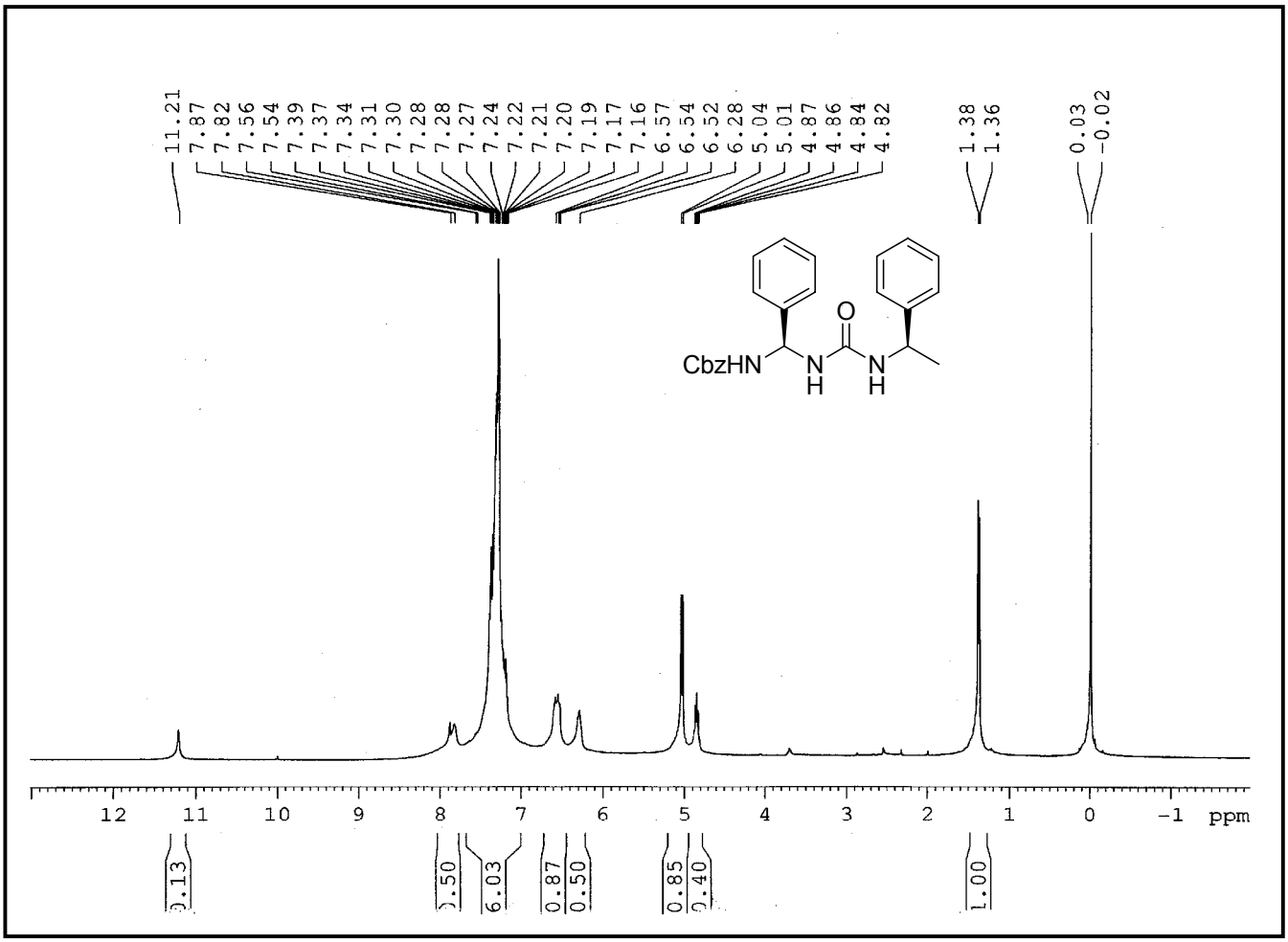

**$^{13}$C NMR spectra of Z-Val- $\psi$[NHCONH]-Ala-OMe**



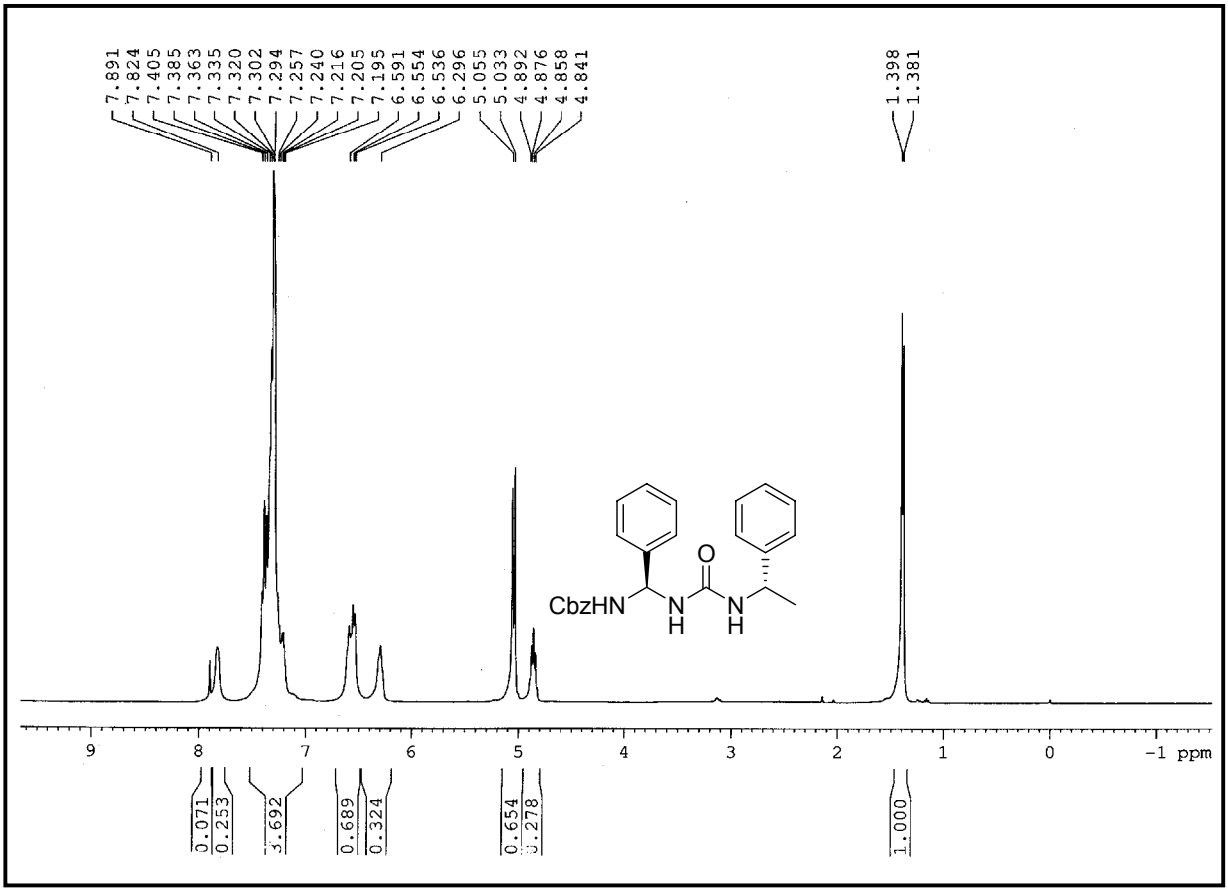

**$^{1}$H NMR spectra of Z-Phg-NHOH**



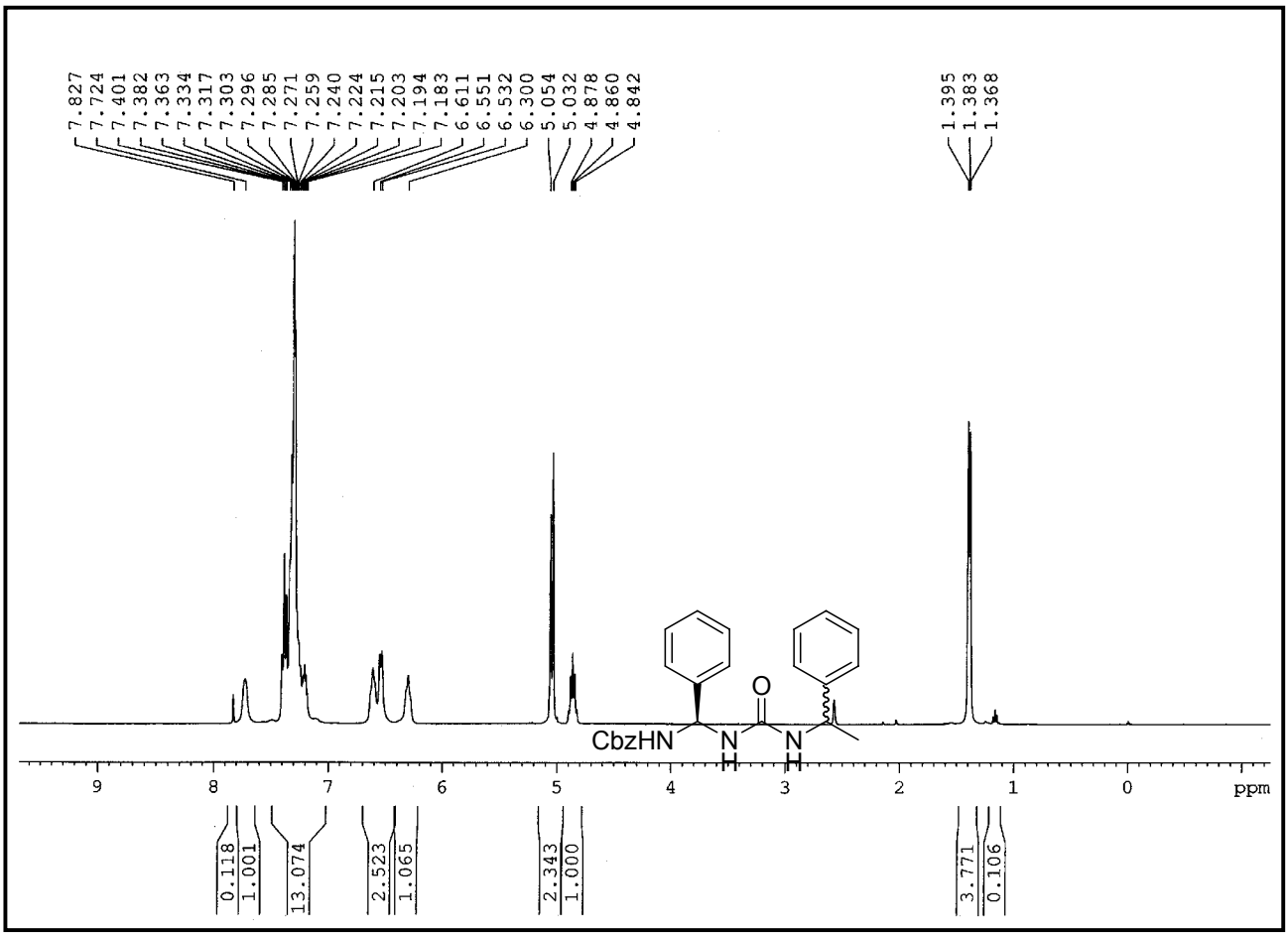

**$^{13}$C NMR spectra of Z-Phg-NHOH**



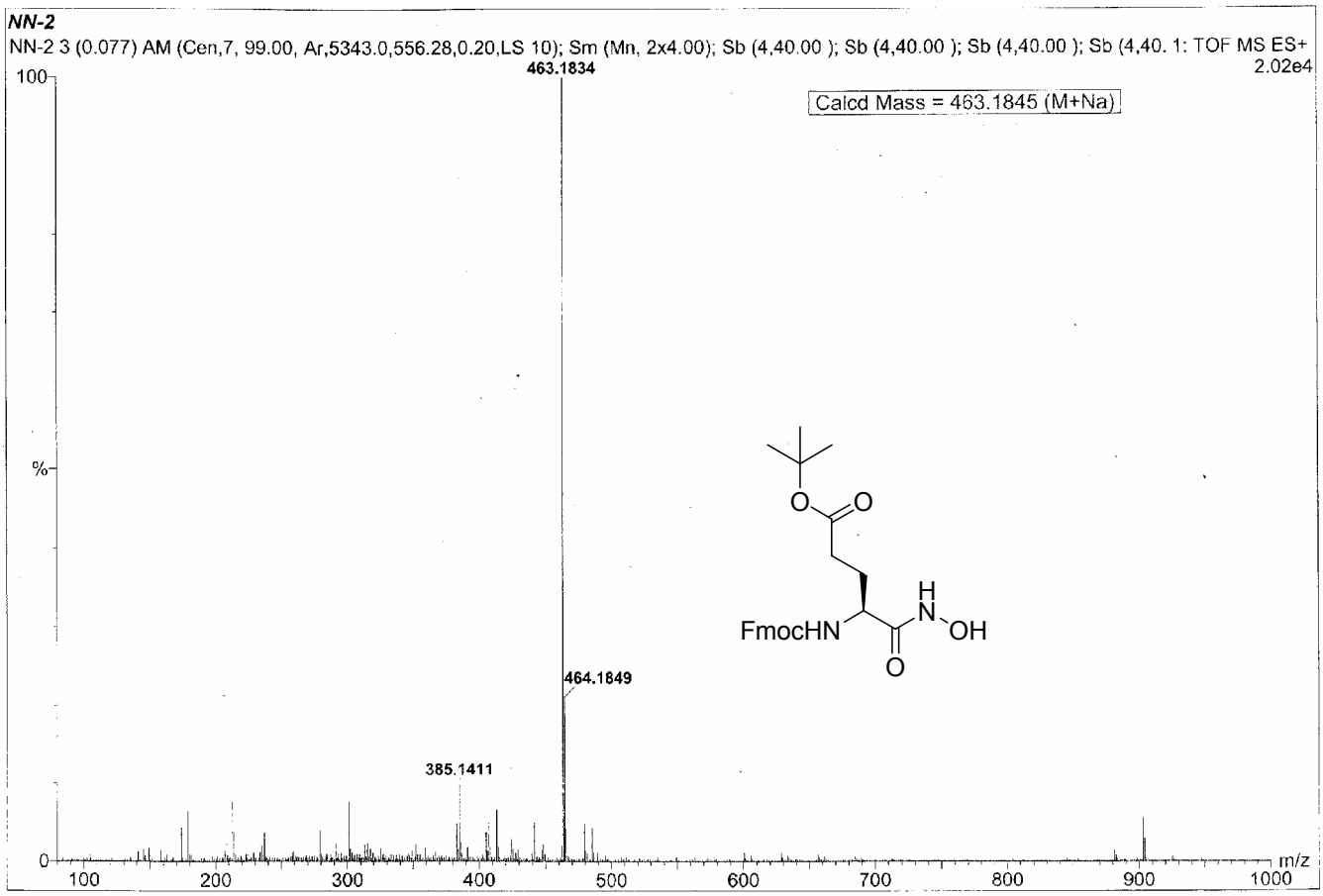

**$^{1}$H NMR spectra of Z-Phg-$\psi$ [NHCONH]-*R*-(+)-phenylethylamine**



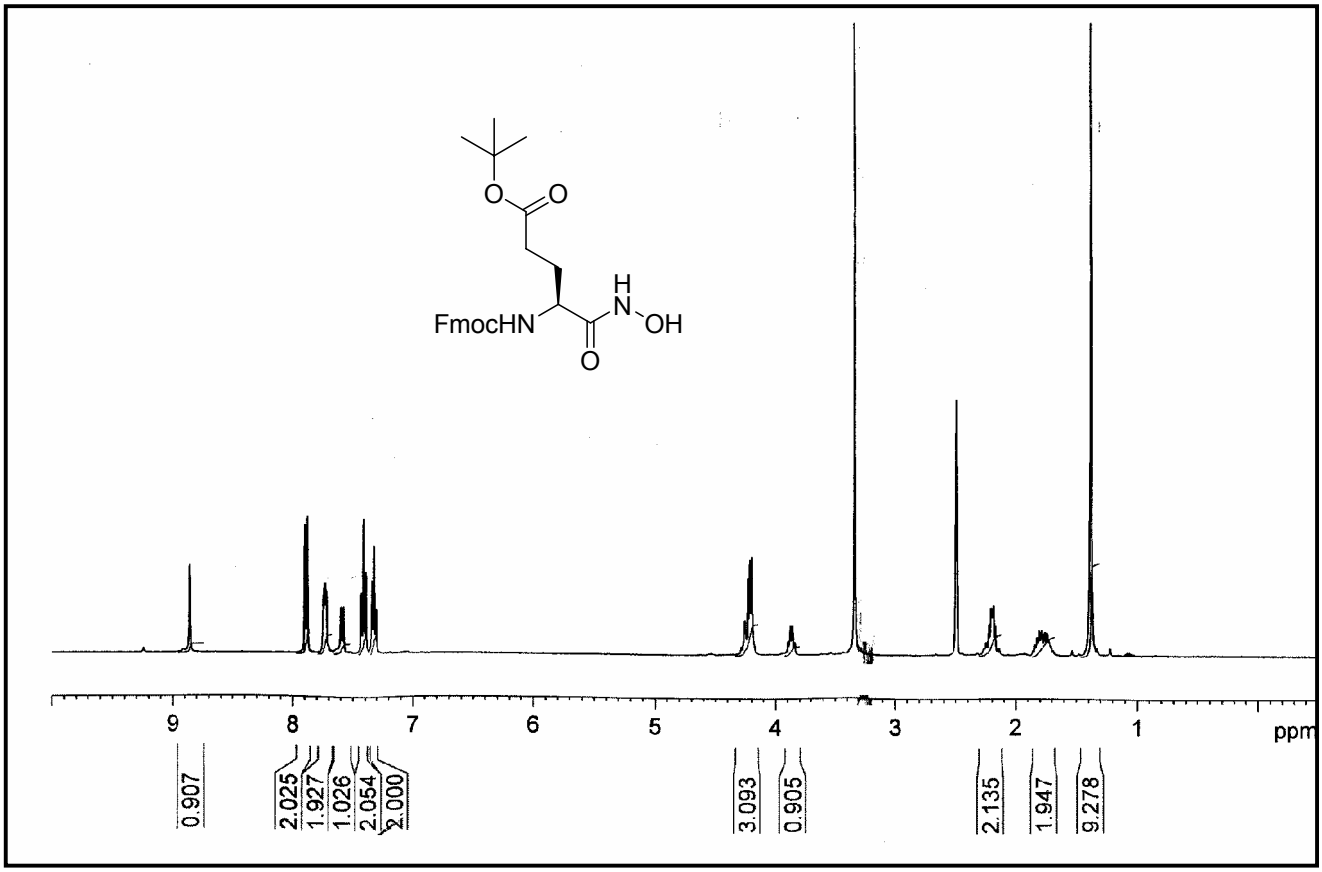

**$^{1}$H NMR spectra of Z-Phg- *ψ* [NHCONH]-*S*-(-)-phenylethylamine**



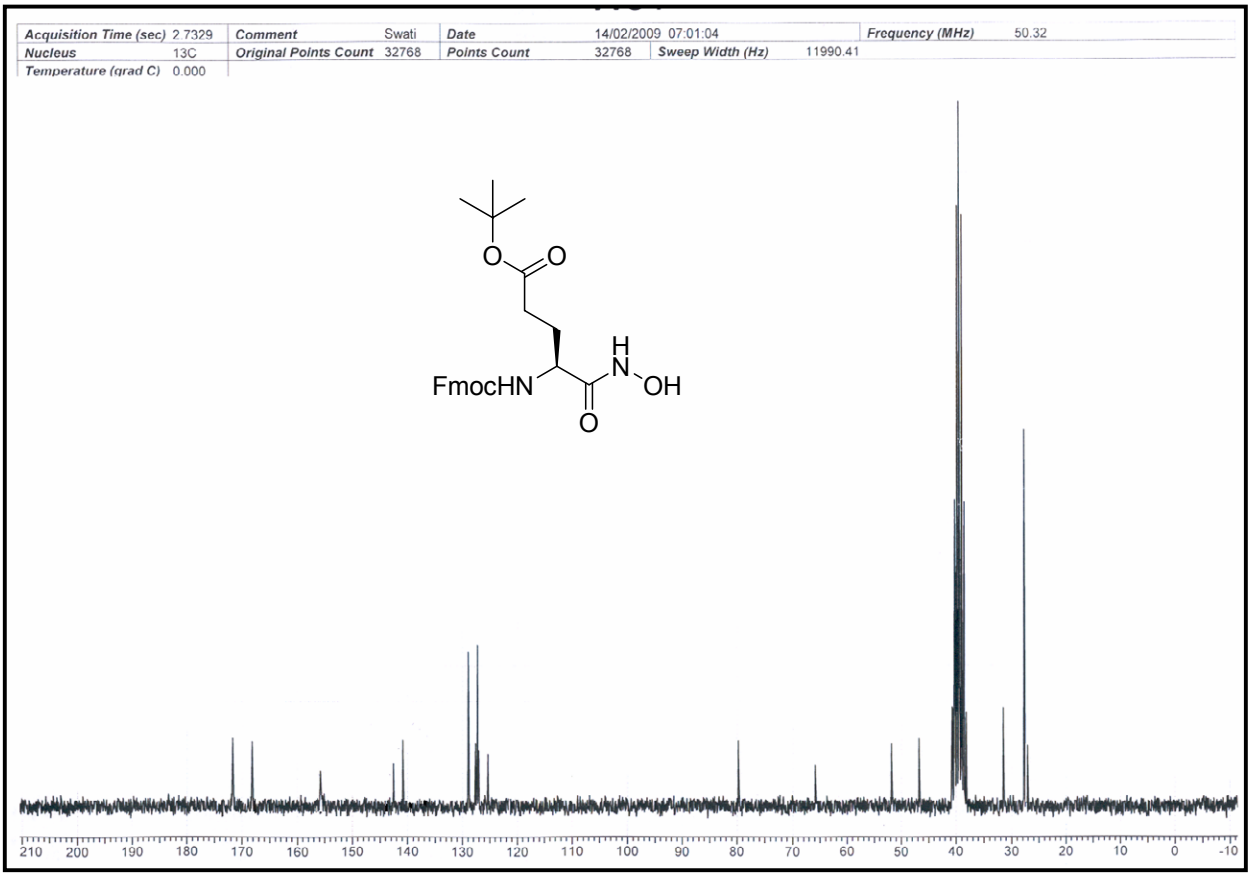

**$^{1}$H NMR spectra of Z-Phg-$\psi$[NHCONH]-R/S-(±)-Phenylethylamine**



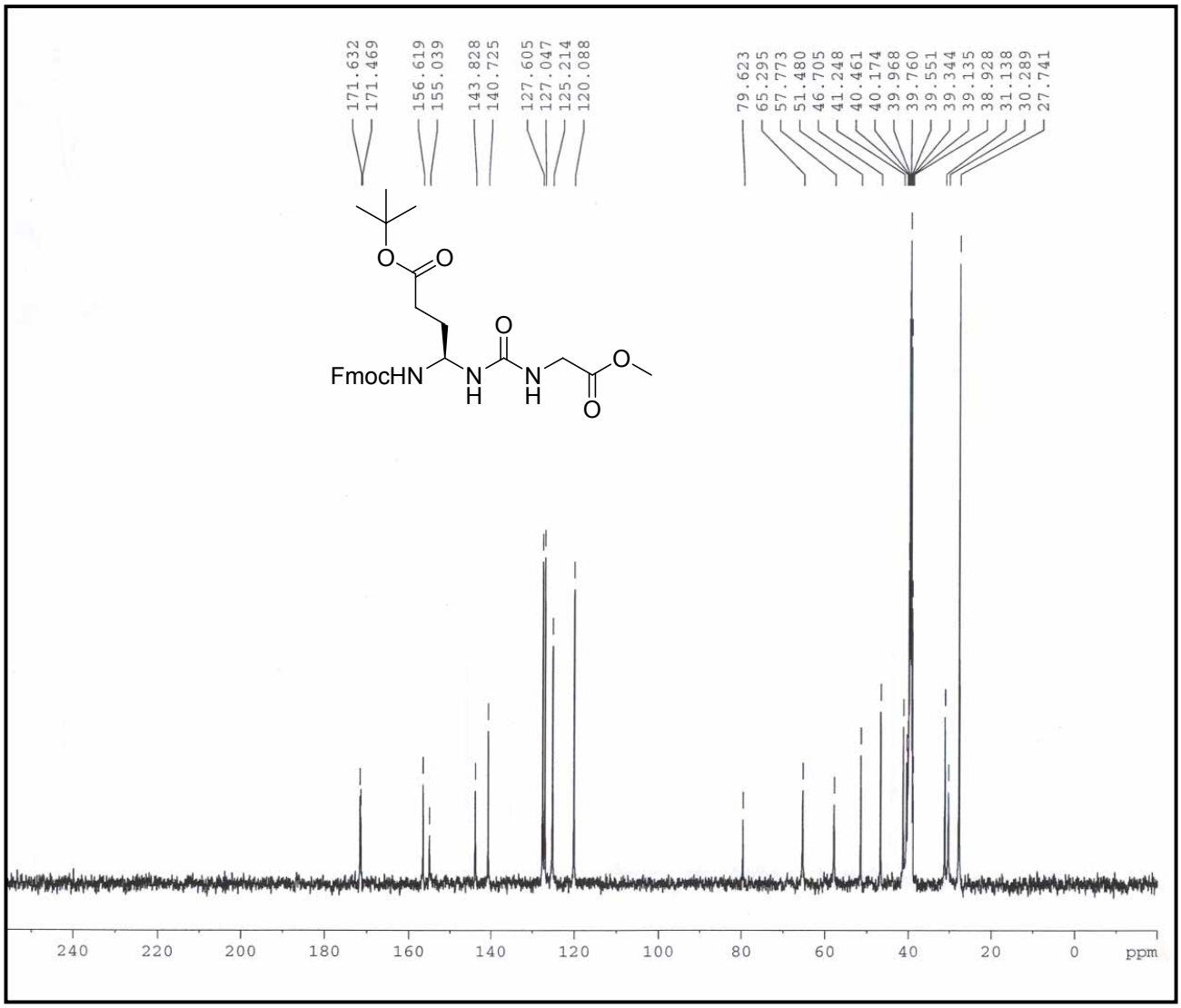

**HRMS of Fmoc-Glu(OtBu)-NHOH**



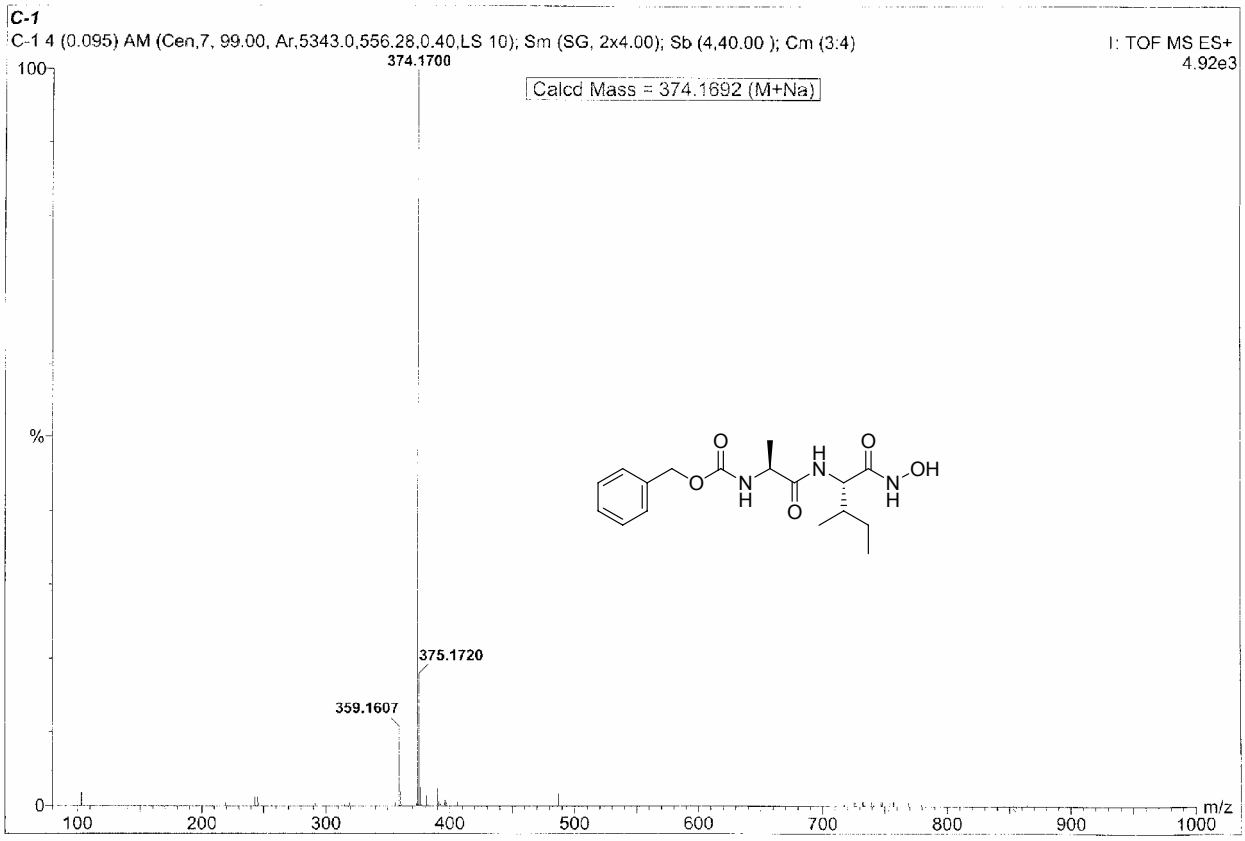

**$^{1}$H NMR of Fmoc-Glu(OtBu)-NHOH**



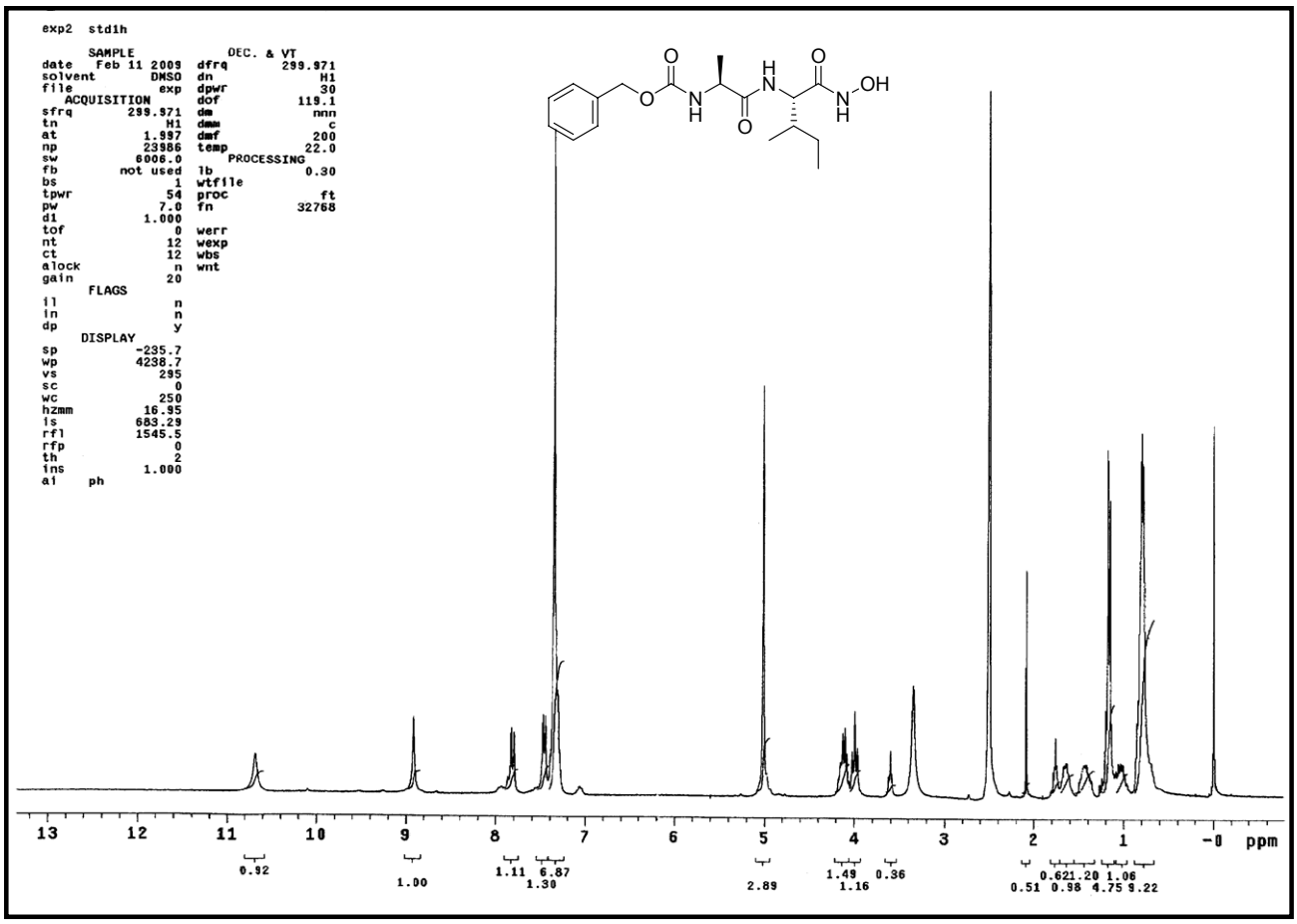

**$^{13}$C NMR spectra of Fmoc-Glu(O$^{t}$Bu)-NHOH**



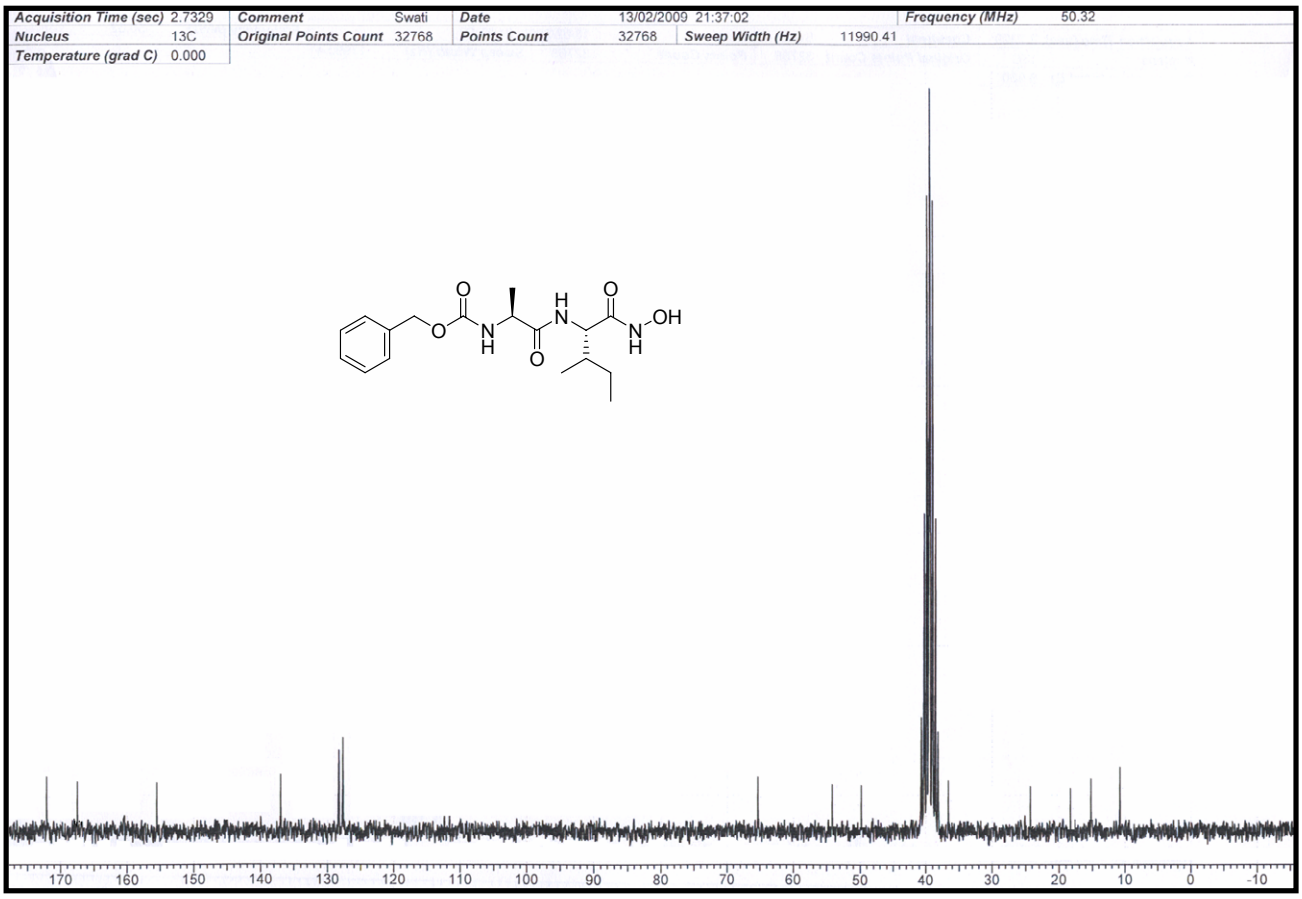

**$^{13}$C NMR spectra of Fmoc-Glu(OtBu)-$\psi$[NH-CO-NH]-Gly-OMe**



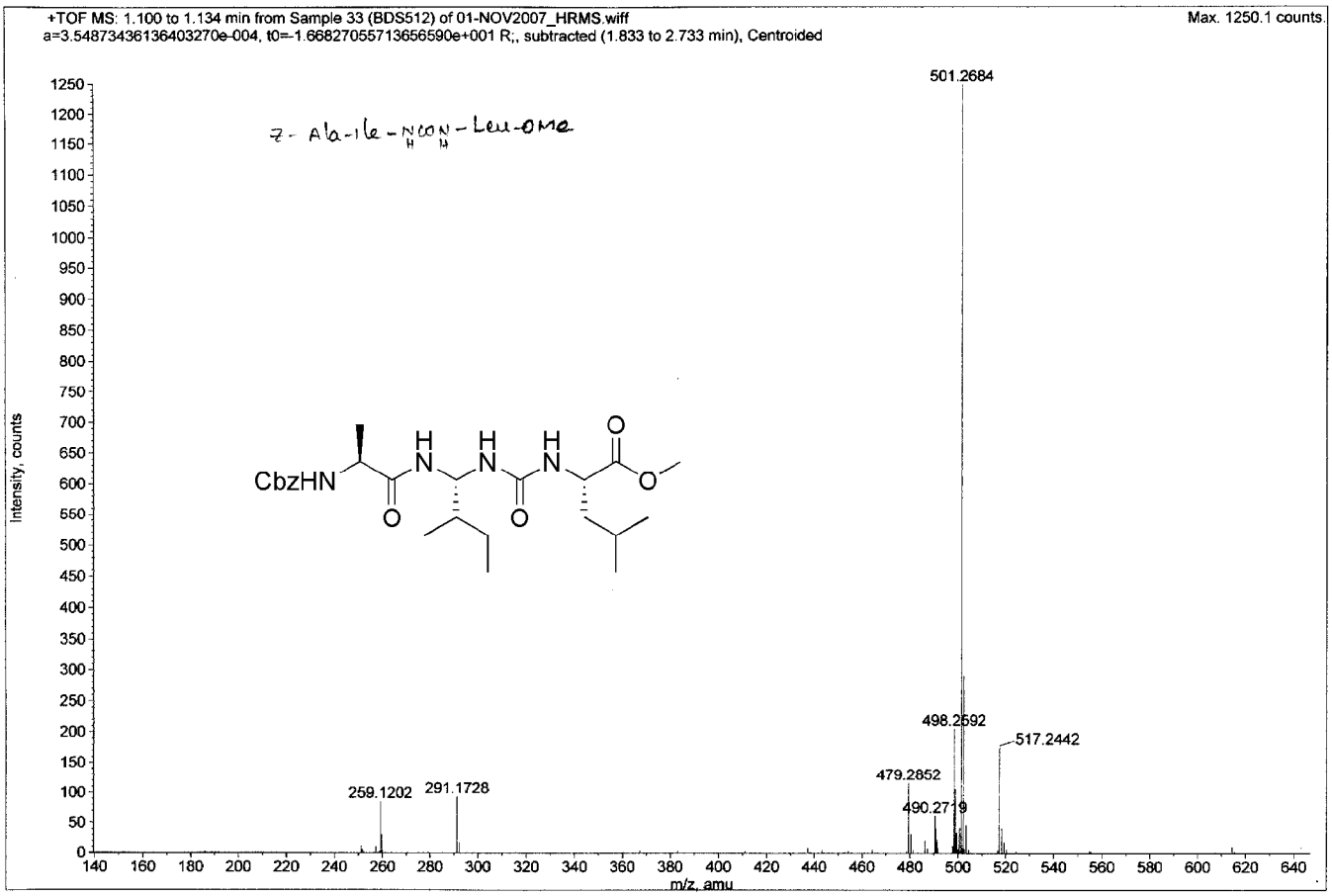

**HRMS of Z-Ala-Ile-NHOH**



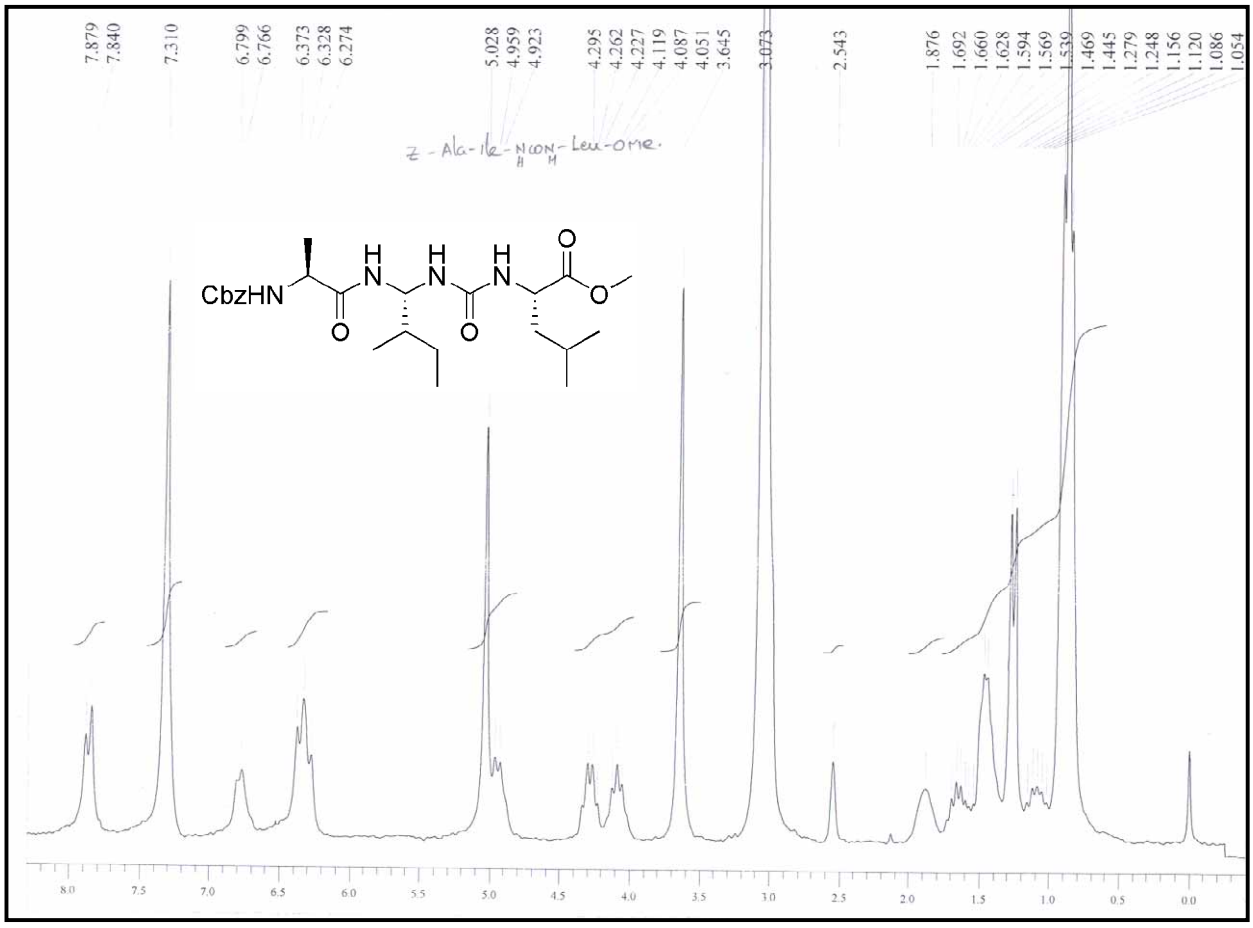

**$^{1}$H NMR spectra of Z-Ala-Ile-NHOH**



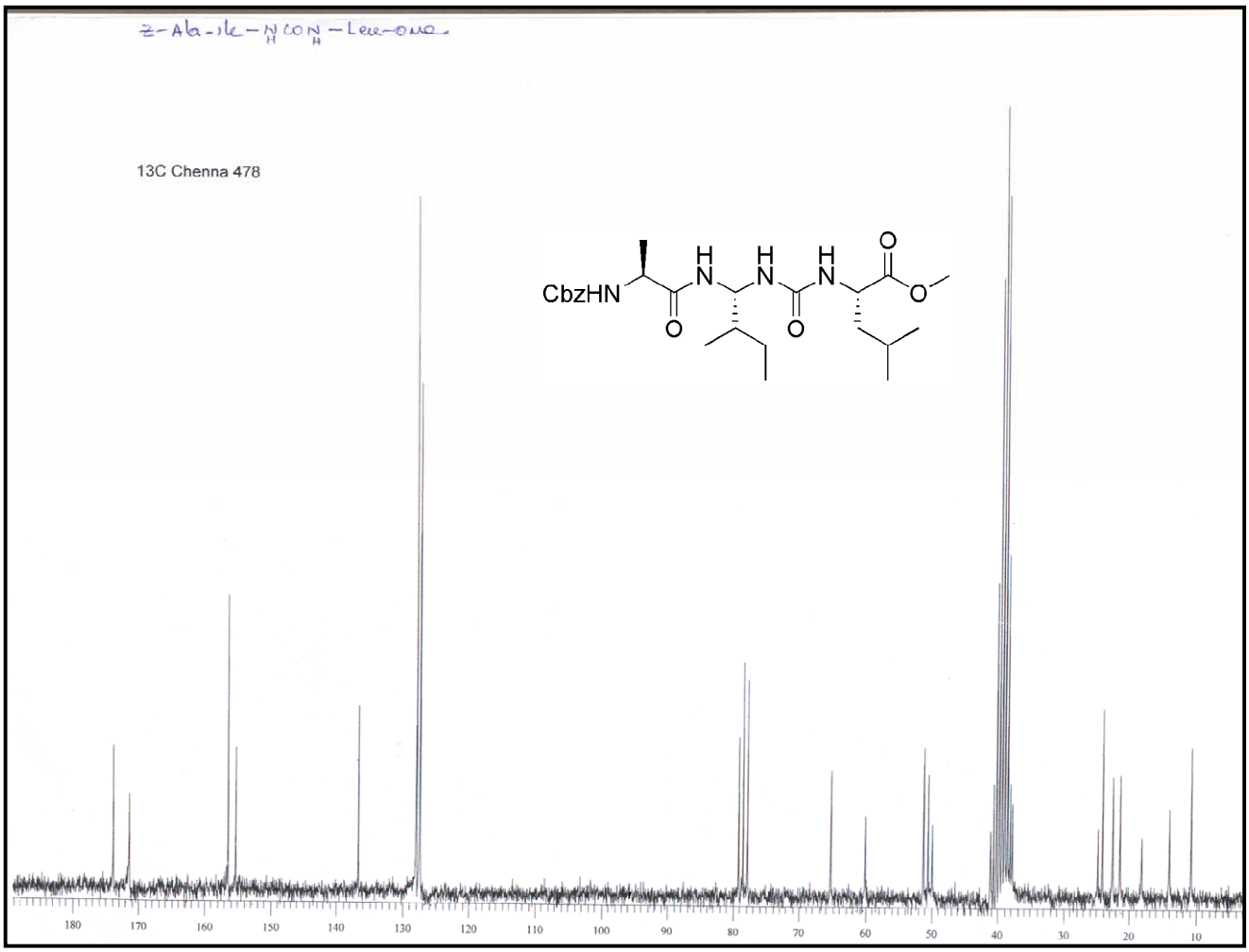

**$^{13}$C NMR spectra of Z-Ala-Ile-NHOH**



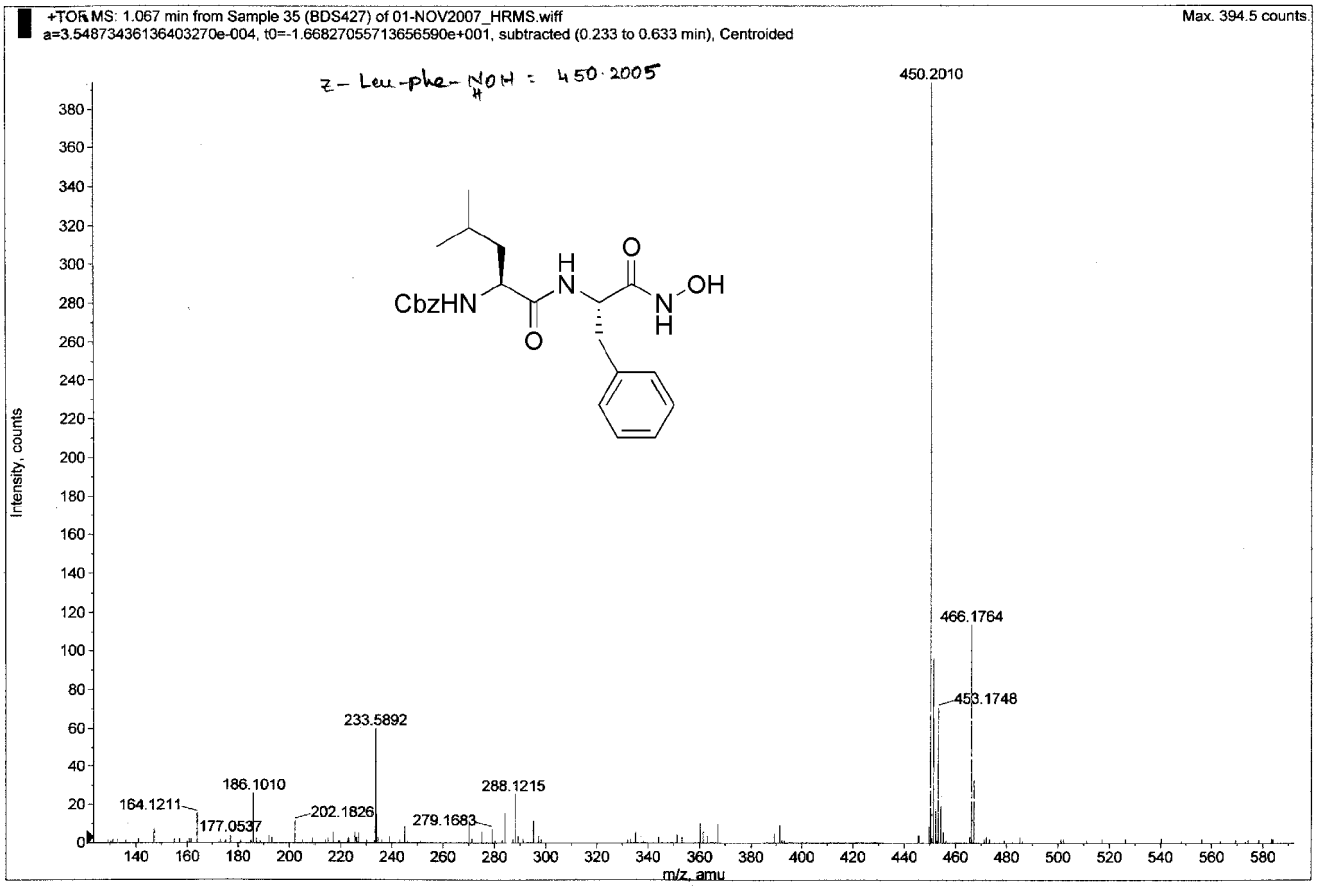

**HRMS of Z-Ala-Ile-$\psi$[NHCONH]-Leu-OMe**



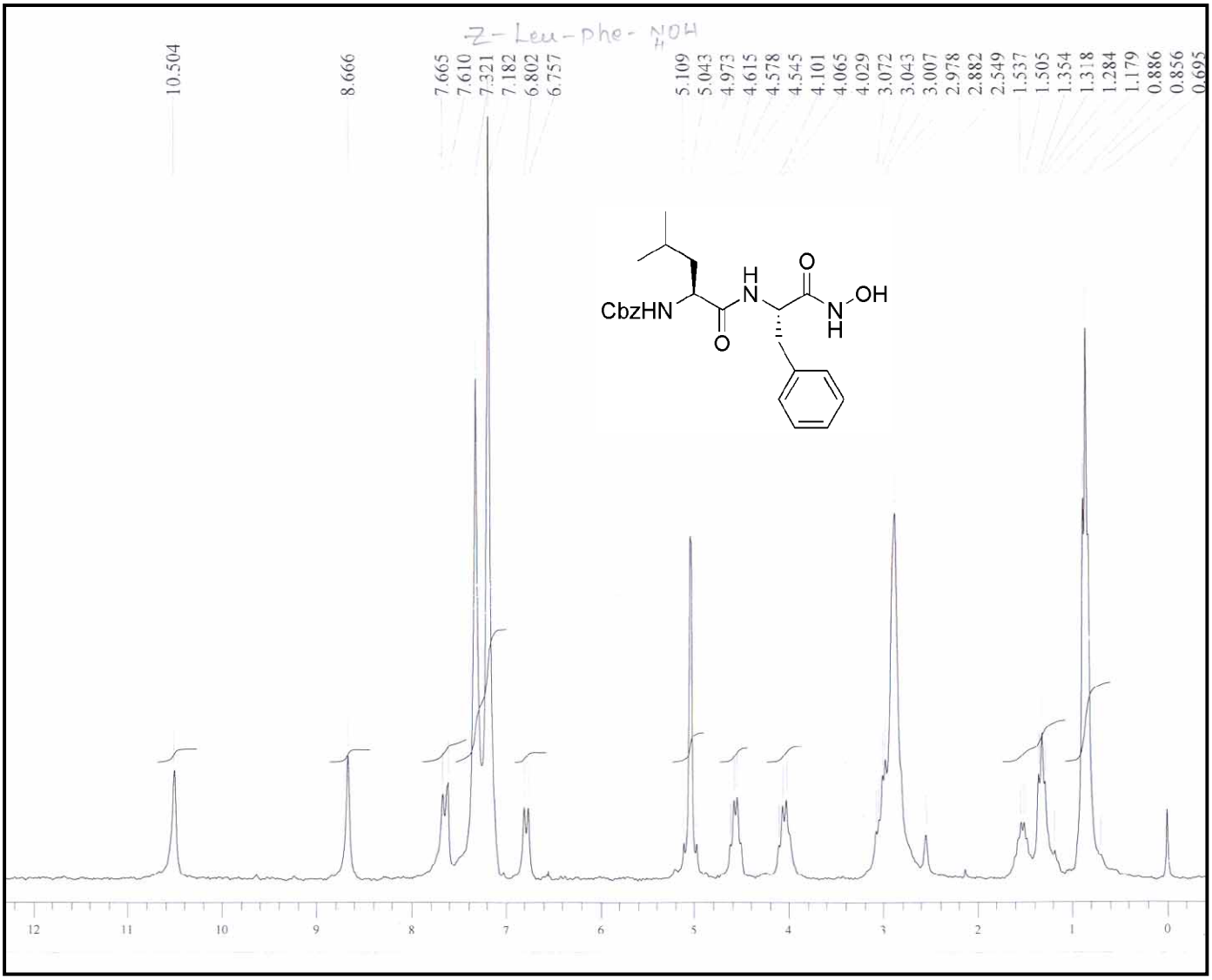

**$^{1}$H NMR spectra of Z-Ala-Ile-$\psi$[NHCONH]-Leu-OMe**



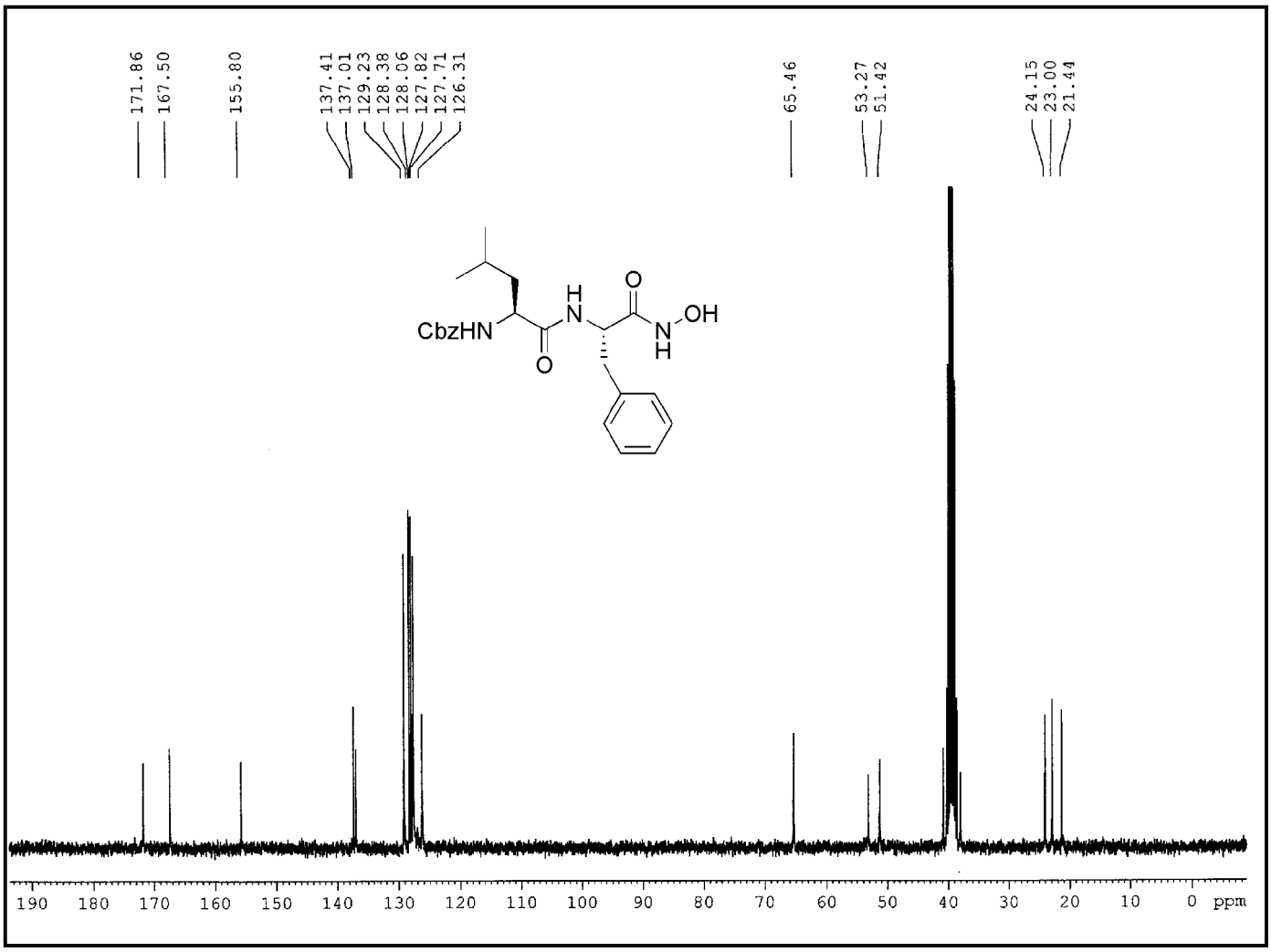

**$^{13}$C NMR spectra of Z-Ala-Ile-$\psi$[NHCONH]-Leu-OMe**




**HRMS of Z-Leu-Phe-NHOH**




**$^{1}$H NMR spectra of Z-Leu-Phe-NHOH**

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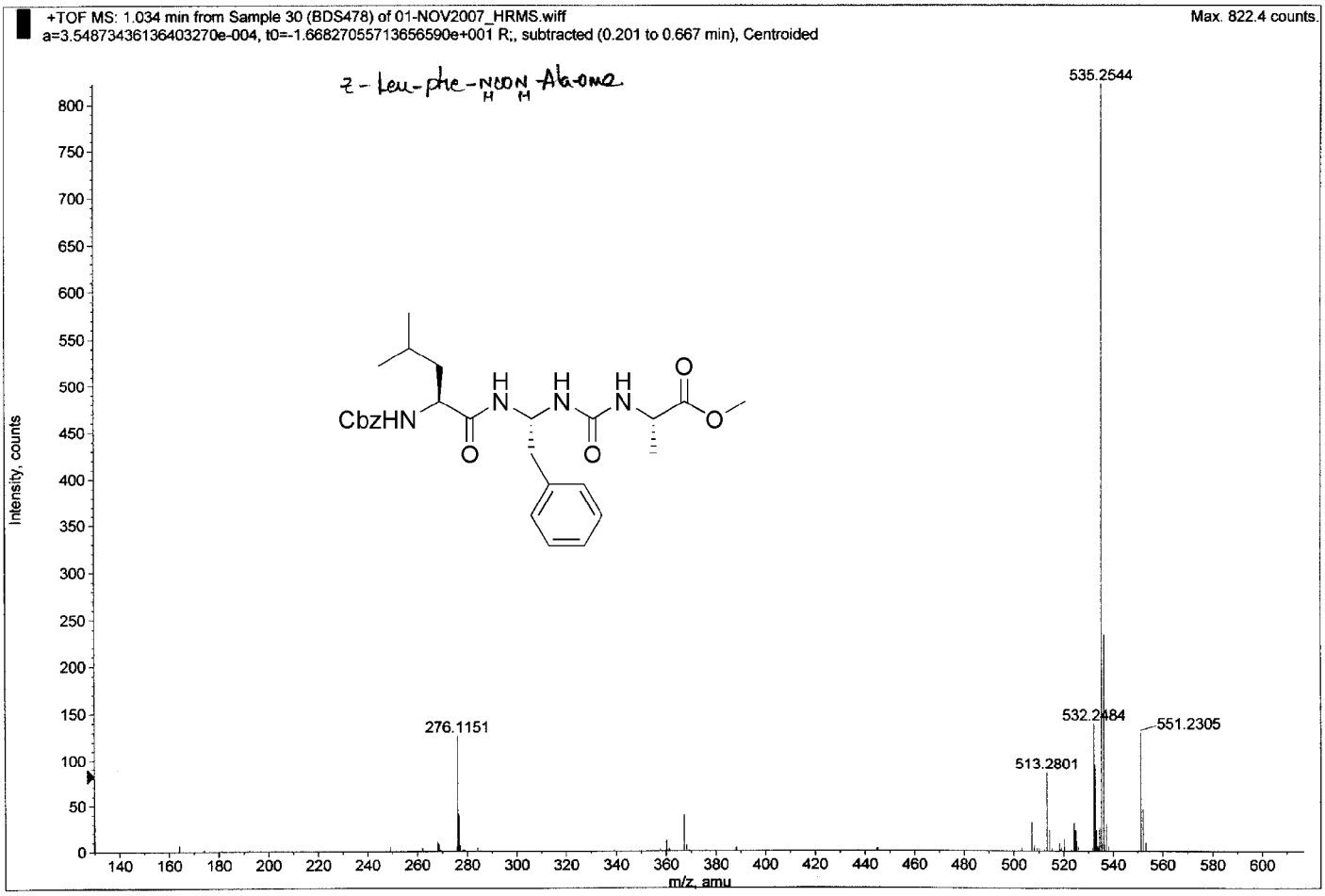
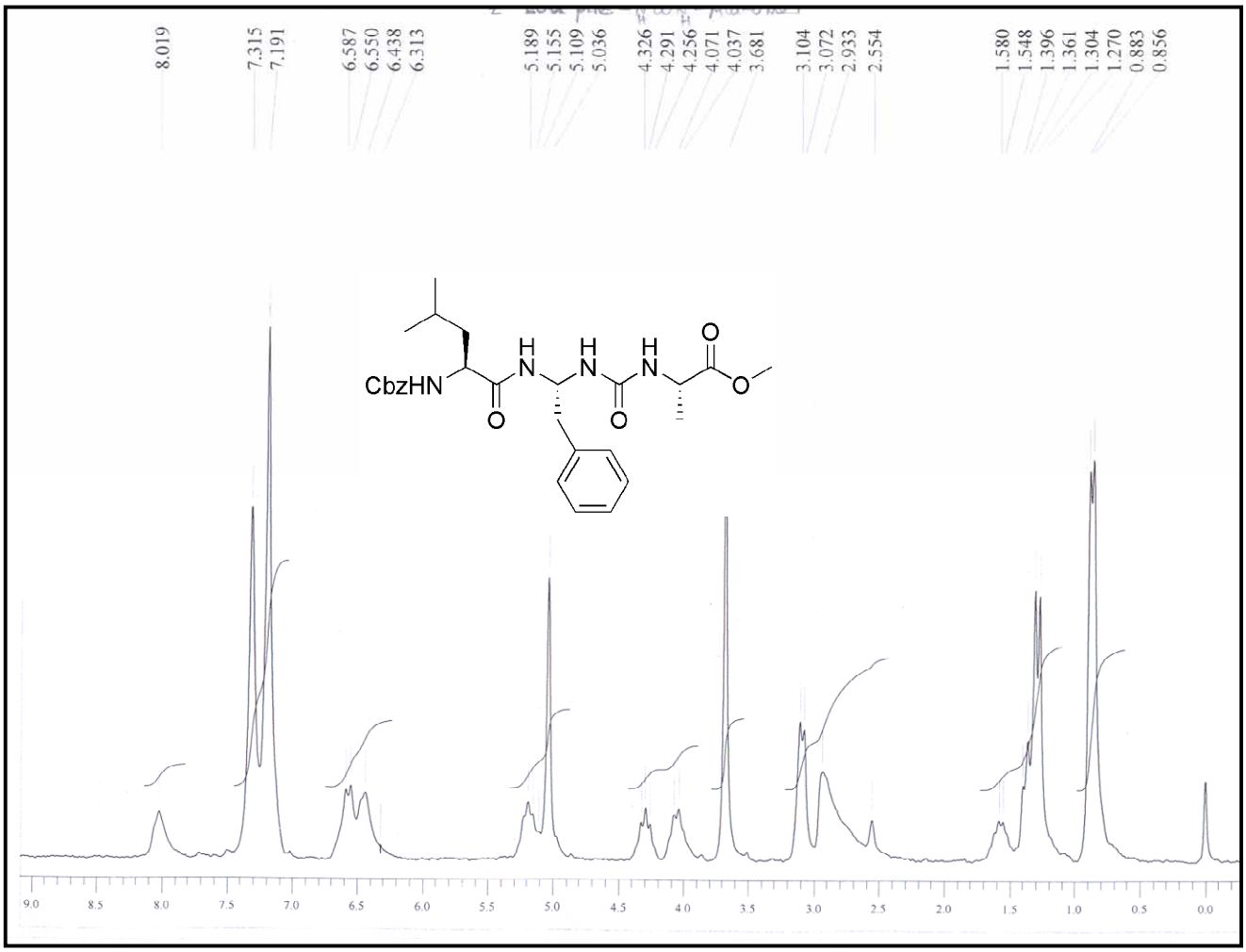
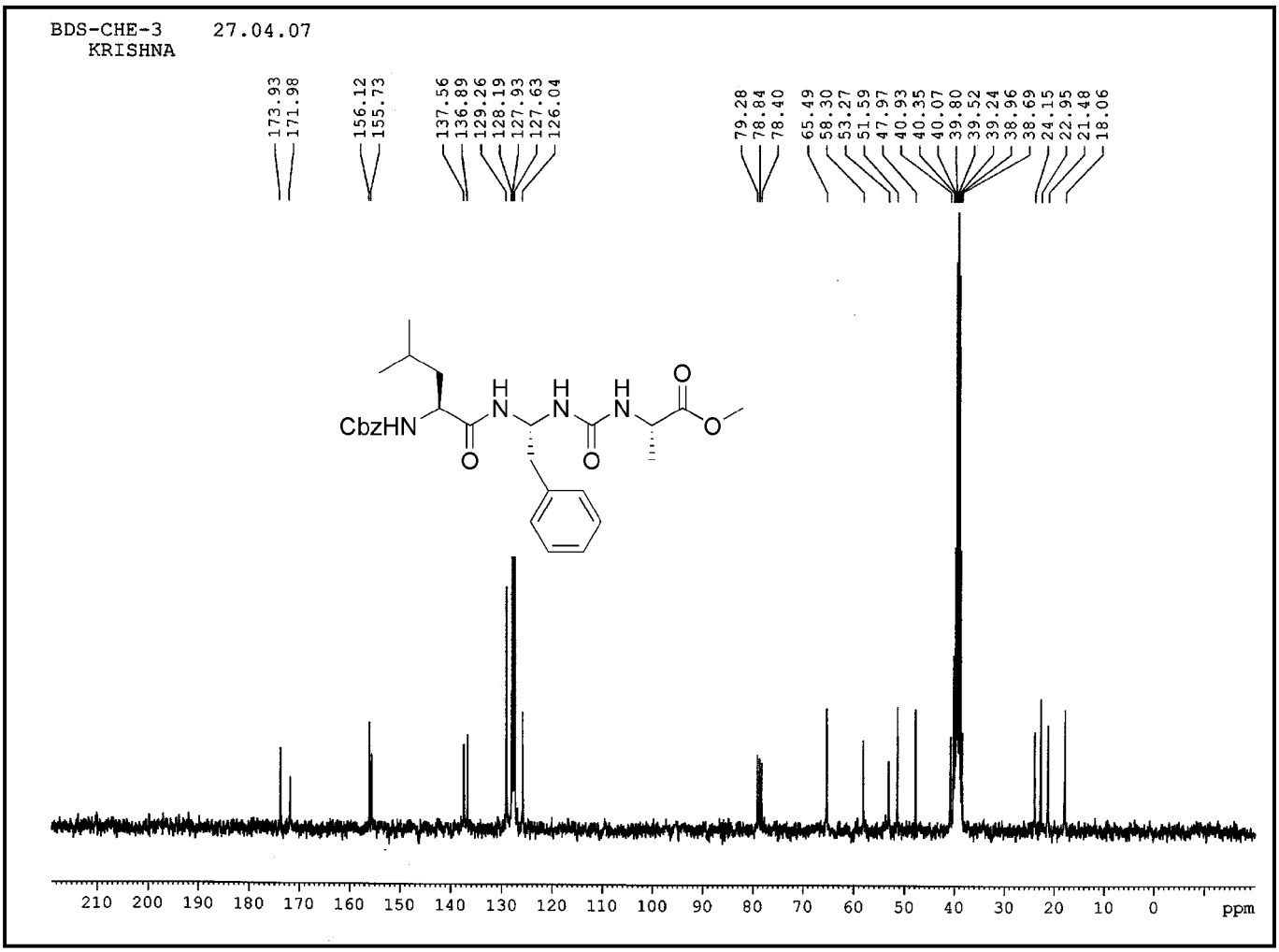


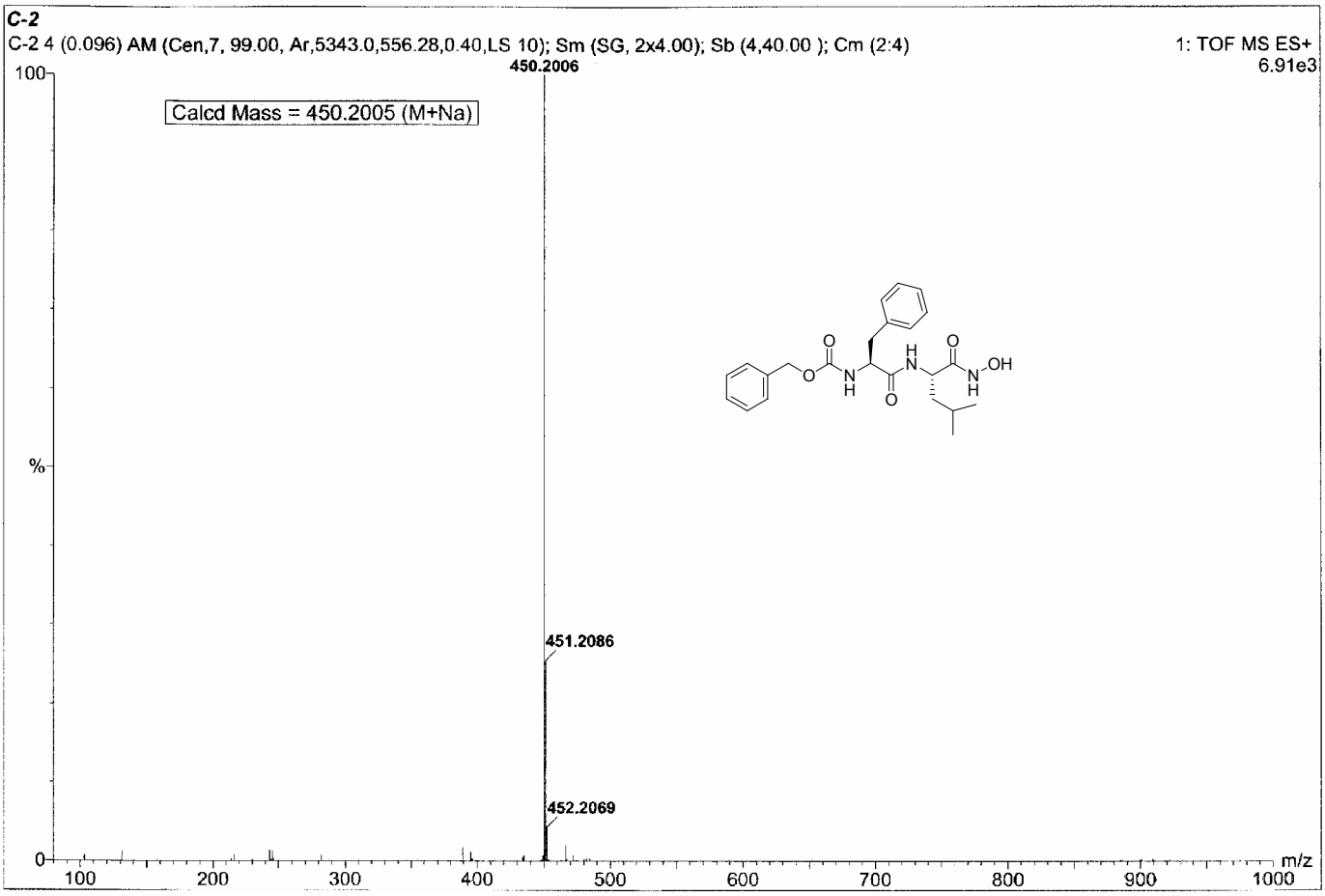

**HRMS spectra of Z-Leu-Phe-$\psi$[NHCONH]-Ala-OMe**



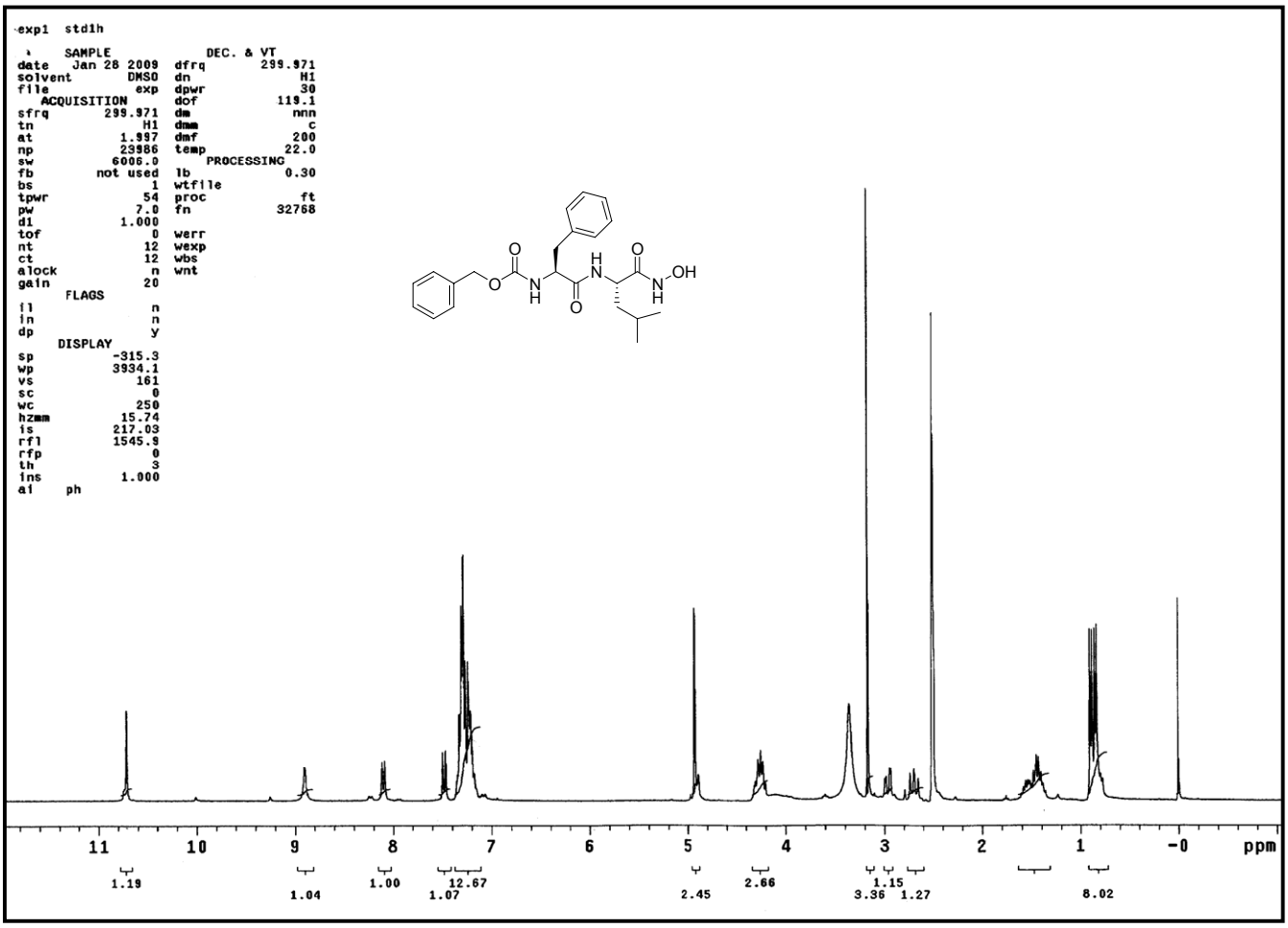

**$^{1}$H NMR spectra of Z-Leu-Phe-$\psi$[NHCONH]-Ala-OMe**



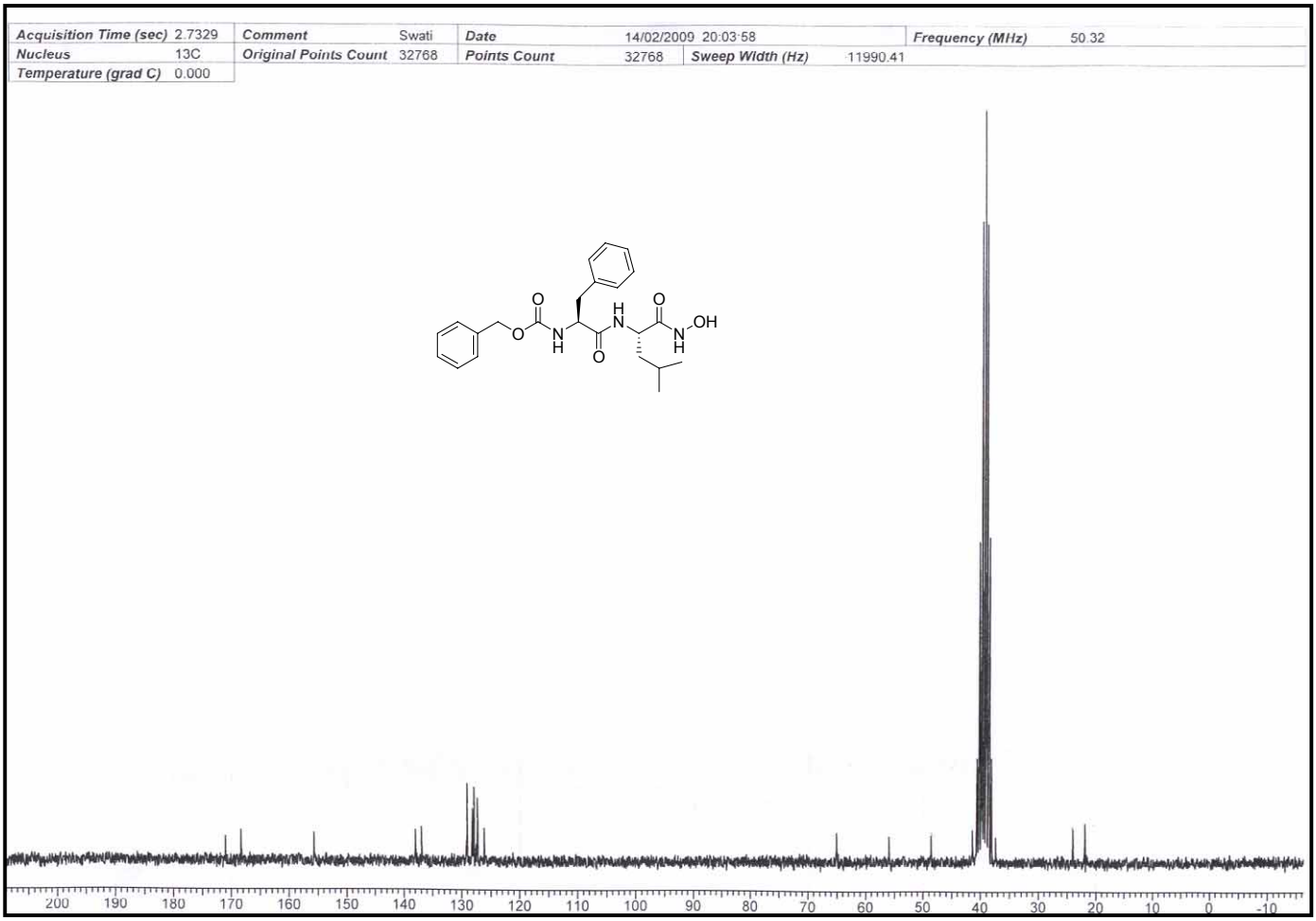

**$^{13}$C NMR spectra of Z-Leu-Phe-$\psi$[NHCONH]-Ala-OMe**



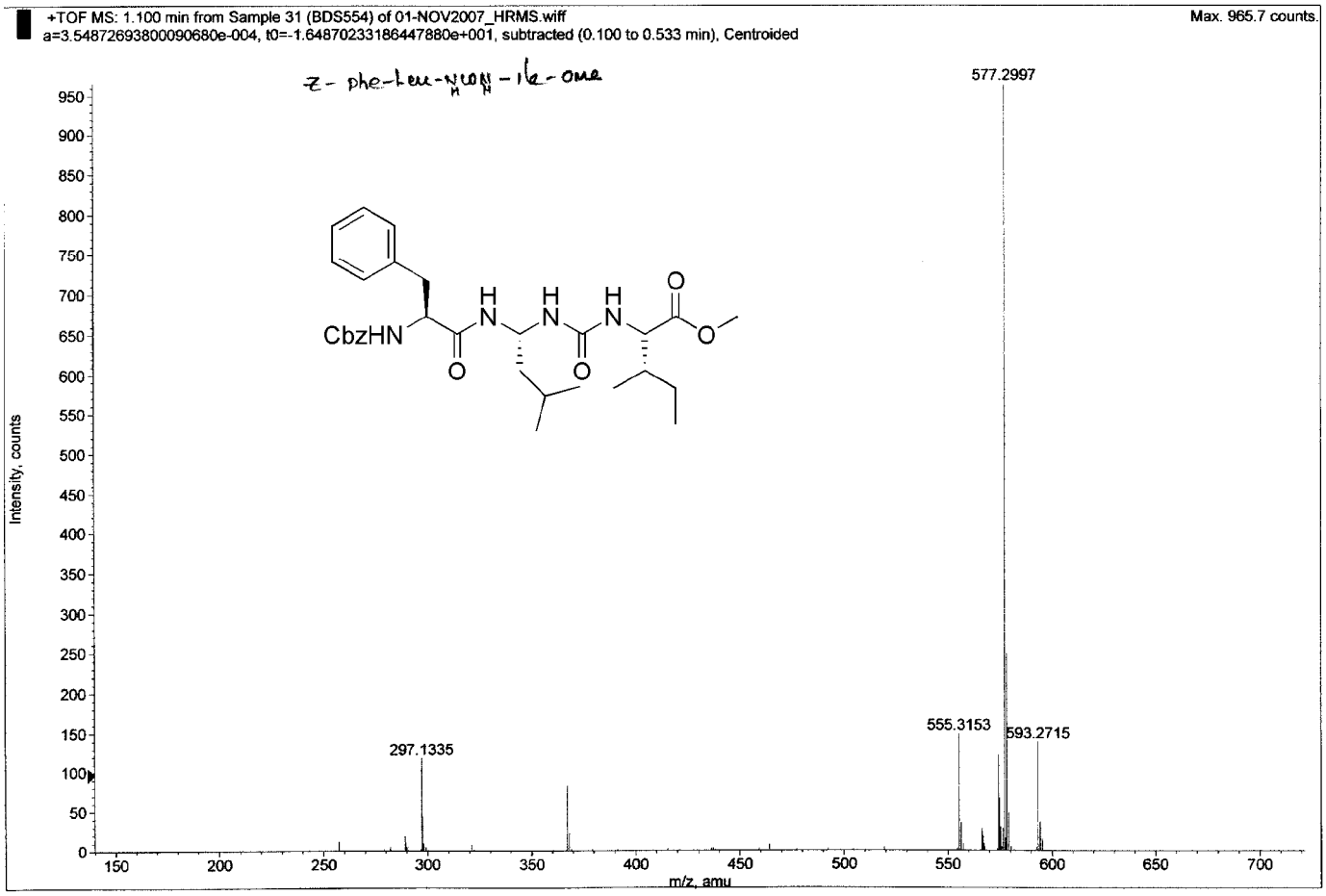

**HRMS of Z-Phe-Leu-NHOH**



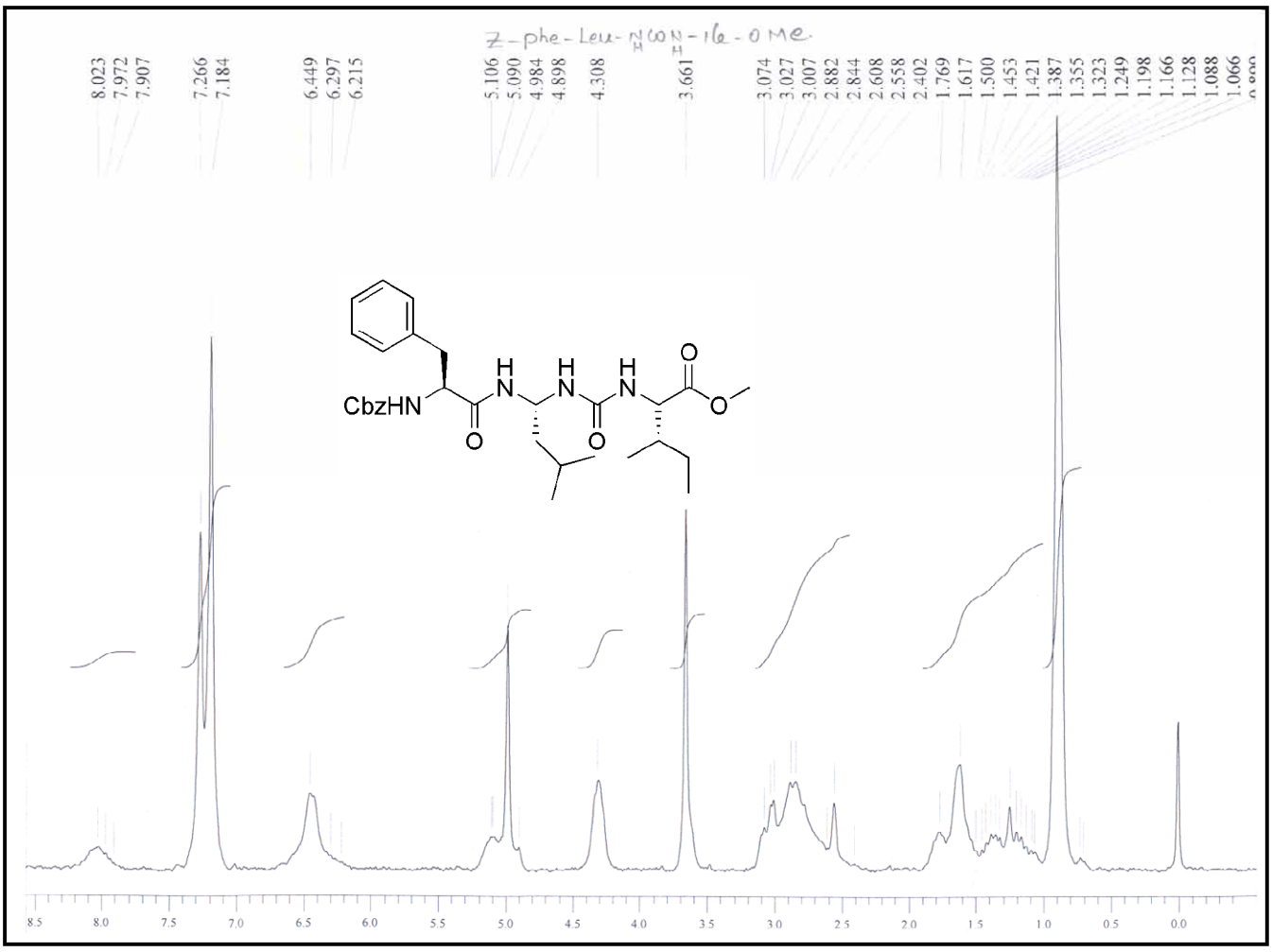

**$^{1}$H NMR spectra of Z-Phe-Leu-NHOH**



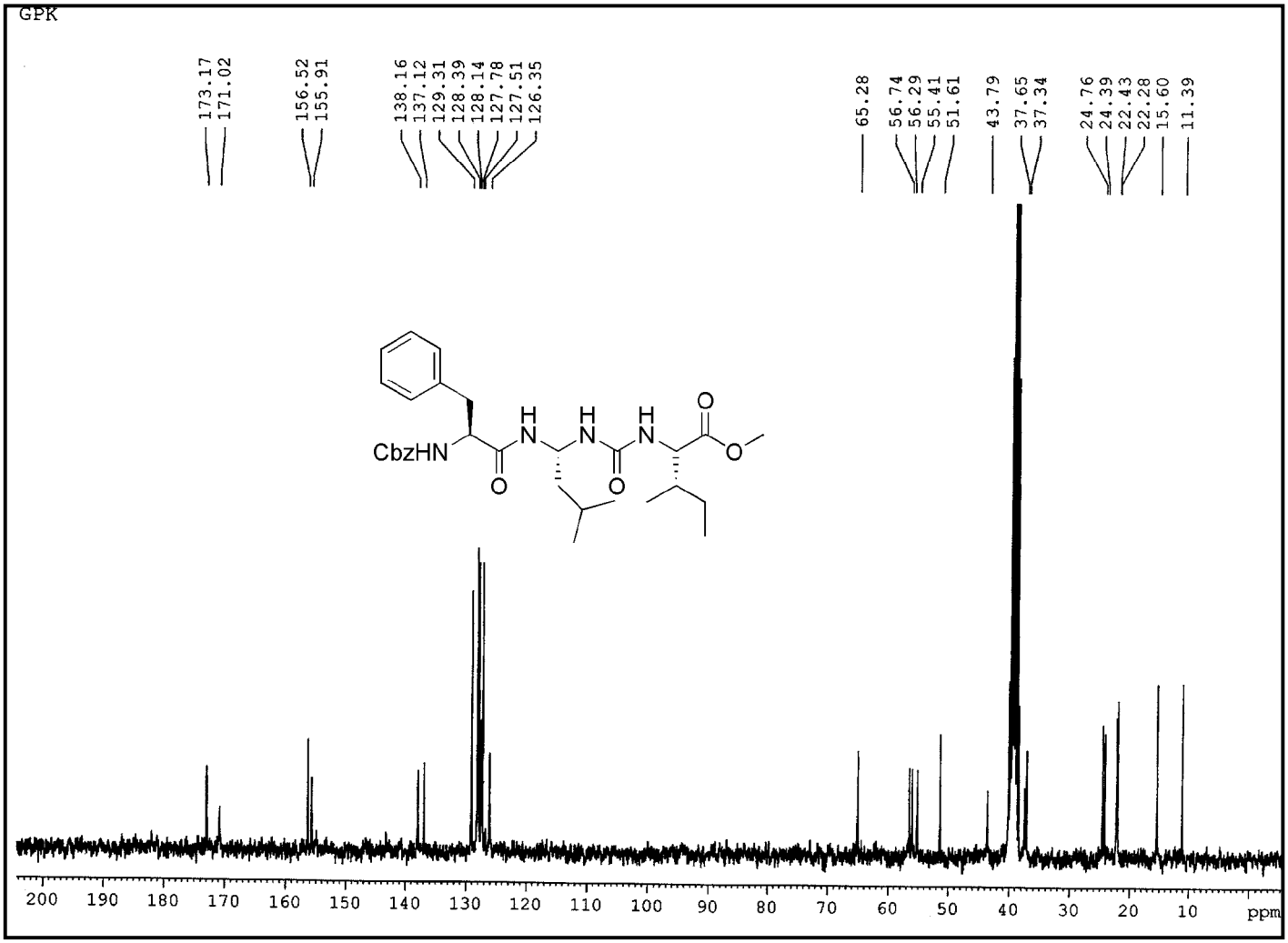

**$^{13}$C NMR spectra Z-Phe-Leu-NHOH**



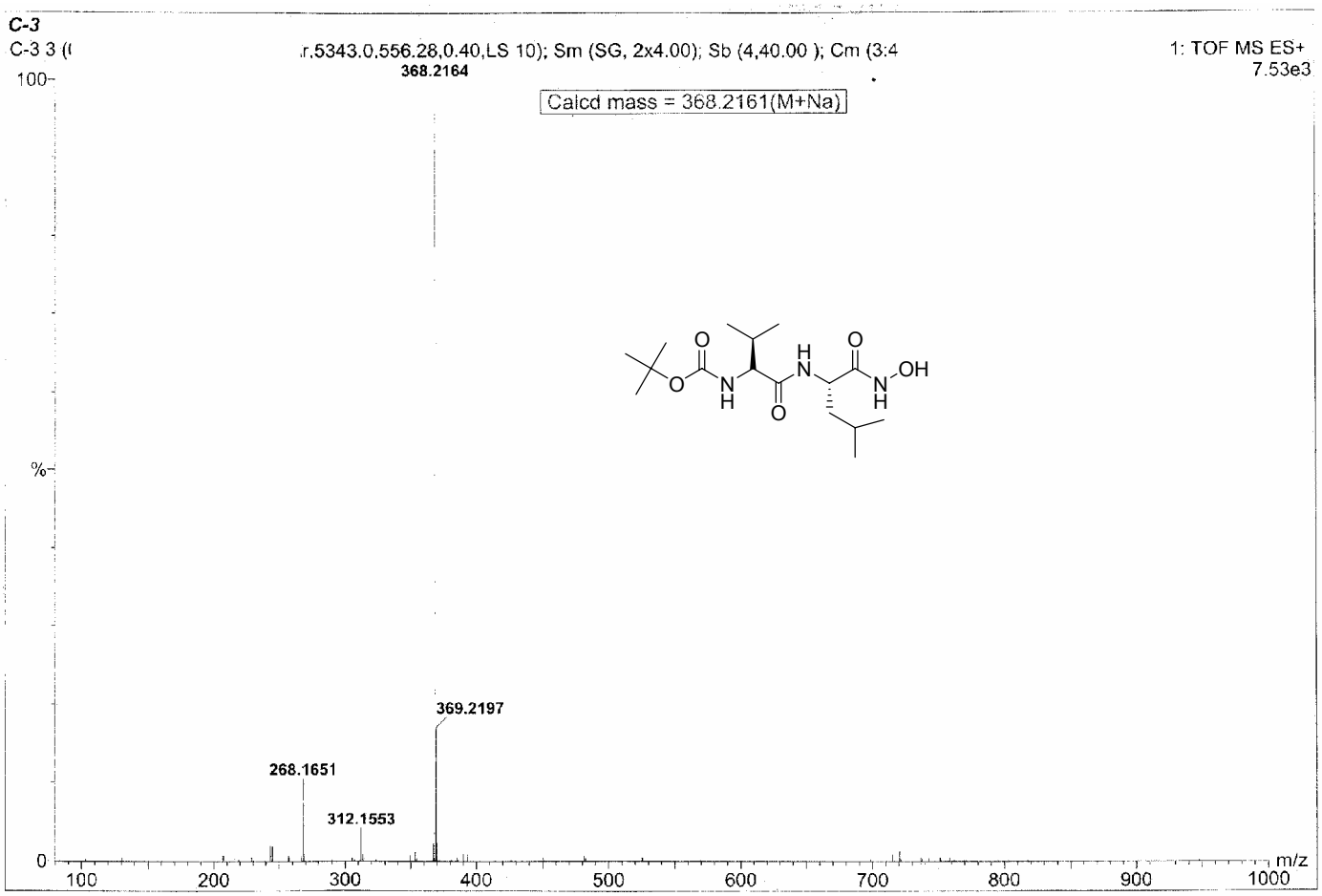

**HRMS of Z-Phe-Leu-ψ[NHCONH]-Ile-OMe**



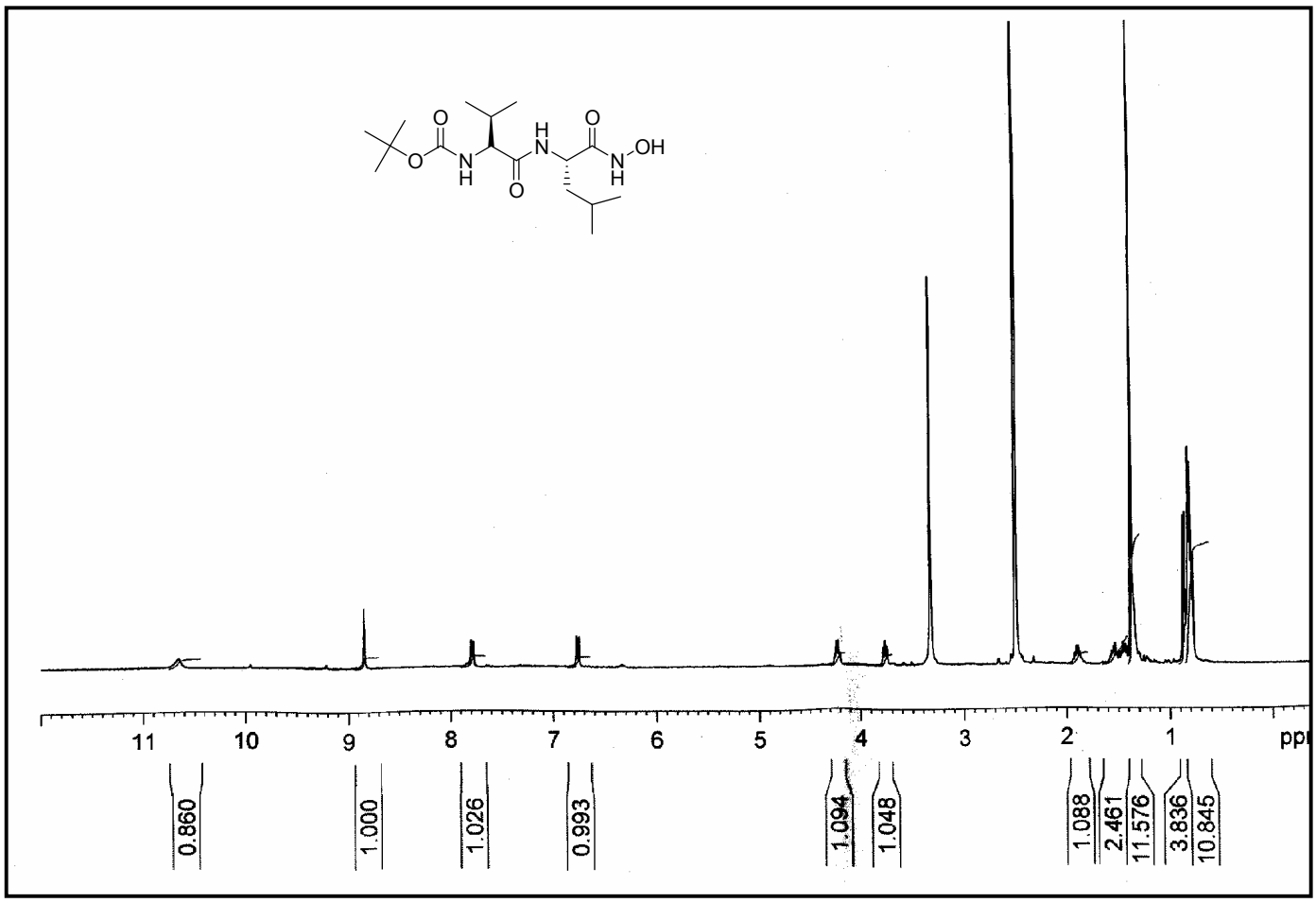

**$^{1}$H NMR spectra of Z-Phe-Leu--$\psi$[NHCONH]-Ile-OMe**



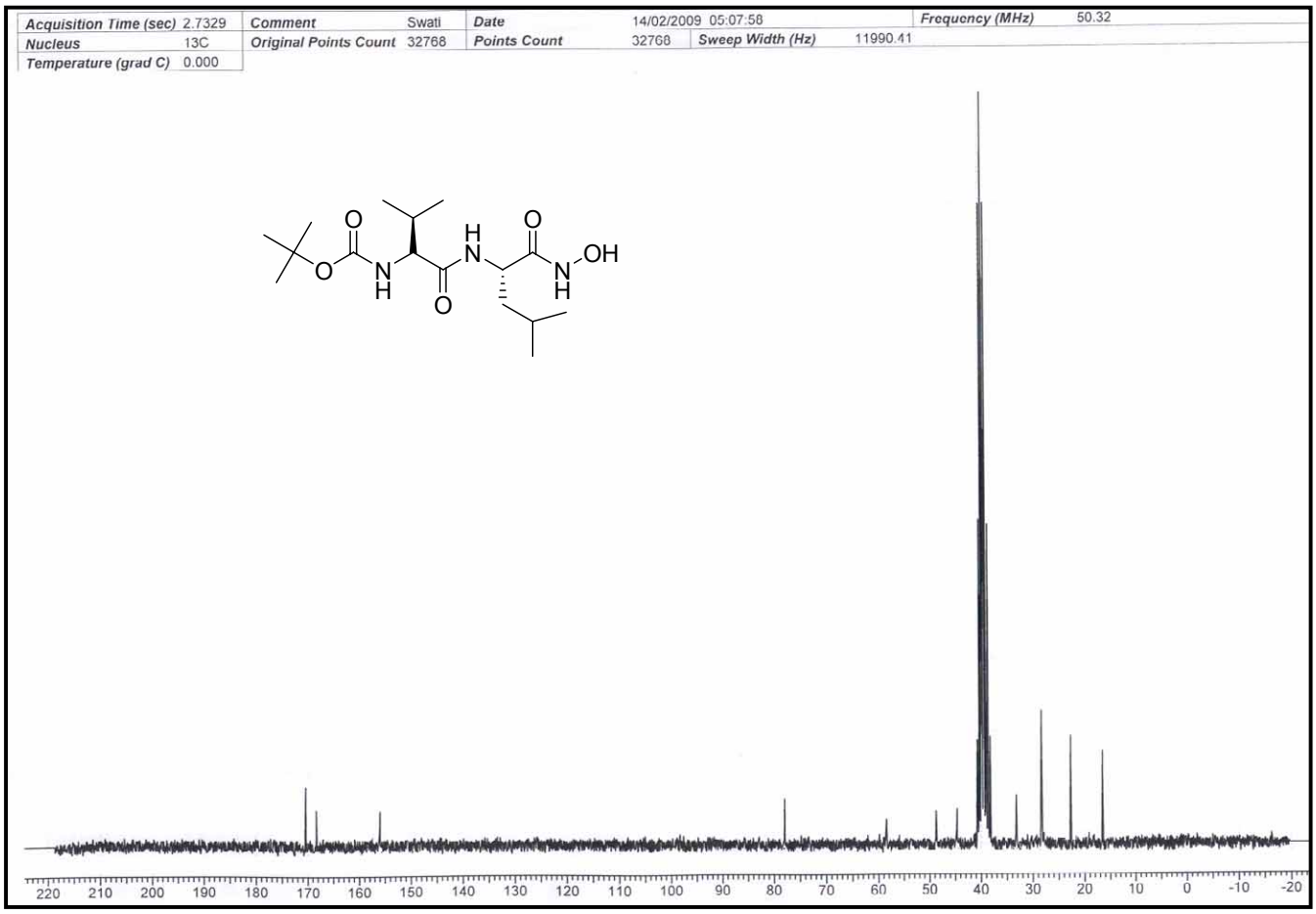

**$^{13}$C NMR spectra of Z-Phe-Leu-$\psi$[NHCONH]-Ile-OMe**



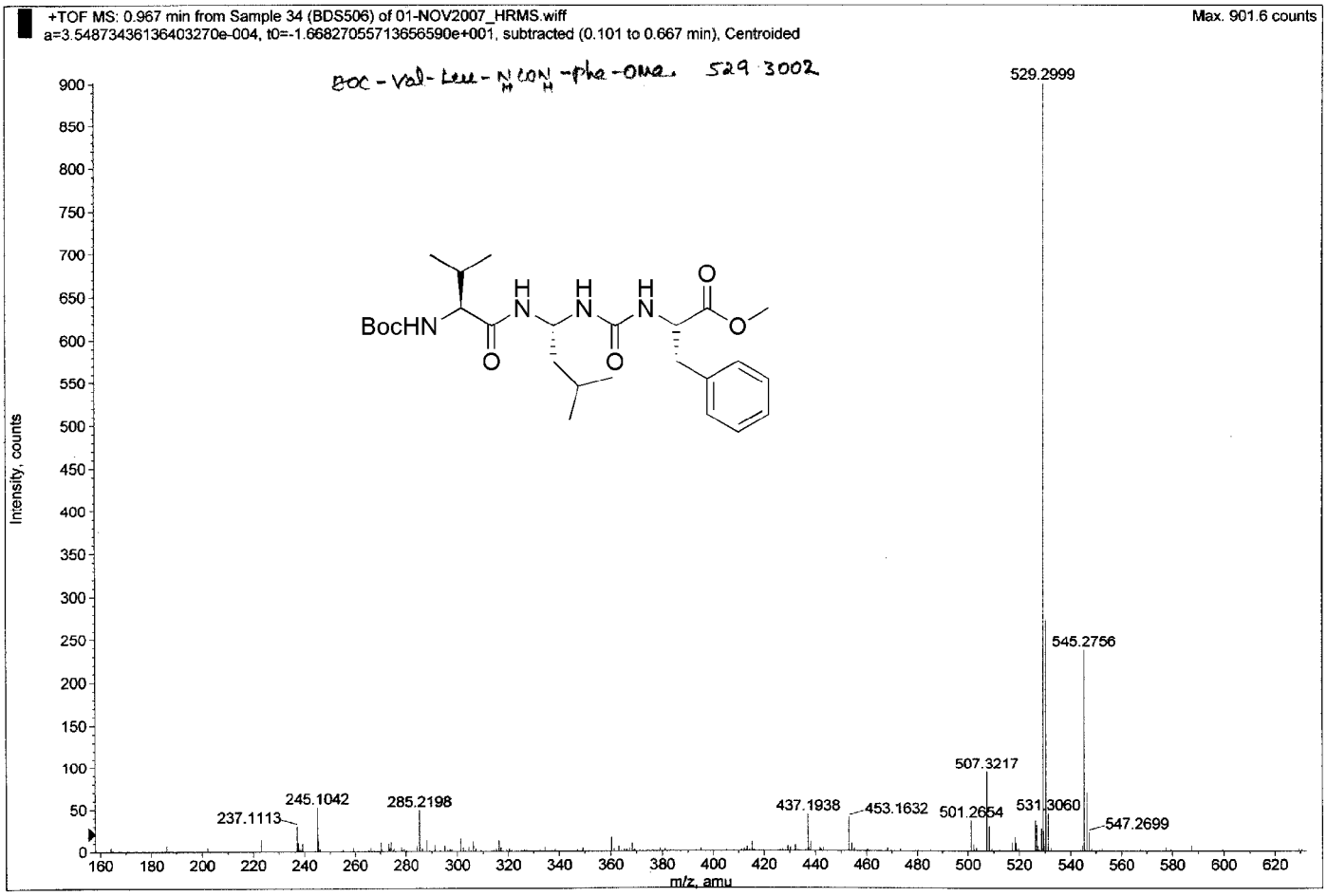

**HRMS of Boc-Val-Leu-NHOH**



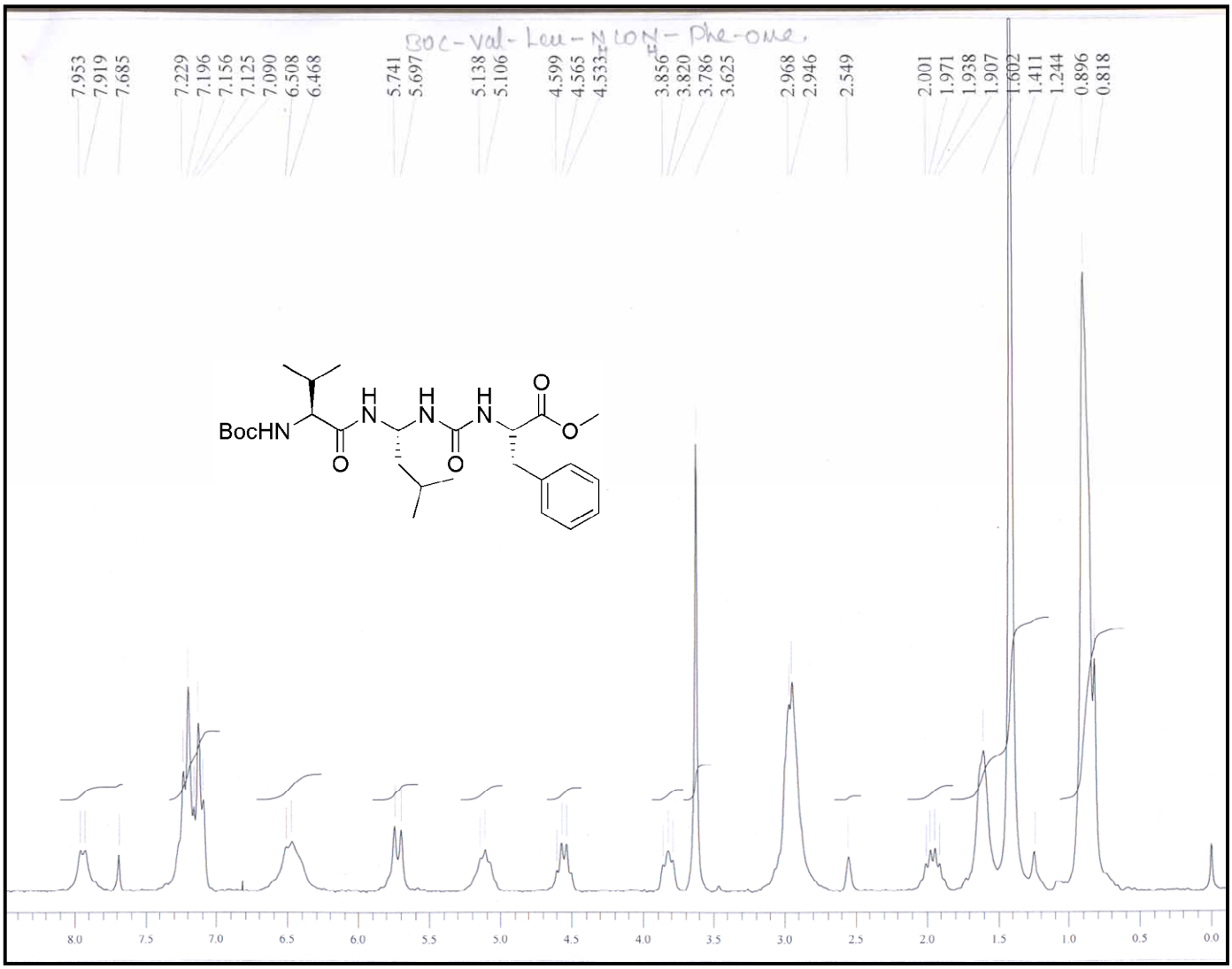

**$^{1}$H NMR spectra of Boc-Val-Leu-NHOH**



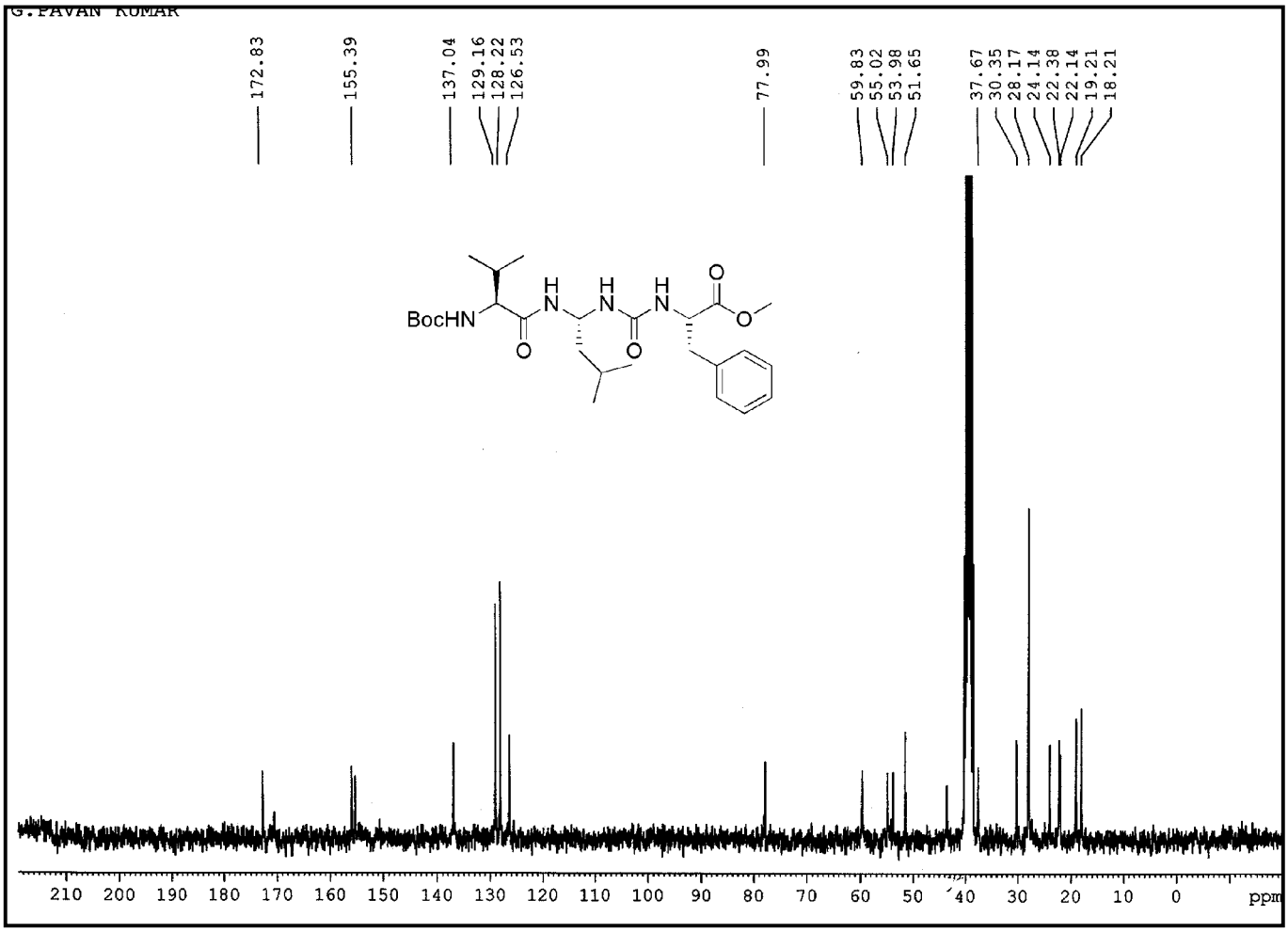

**$^{13}$C spectra of Boc-Val-Leu-NHOH**



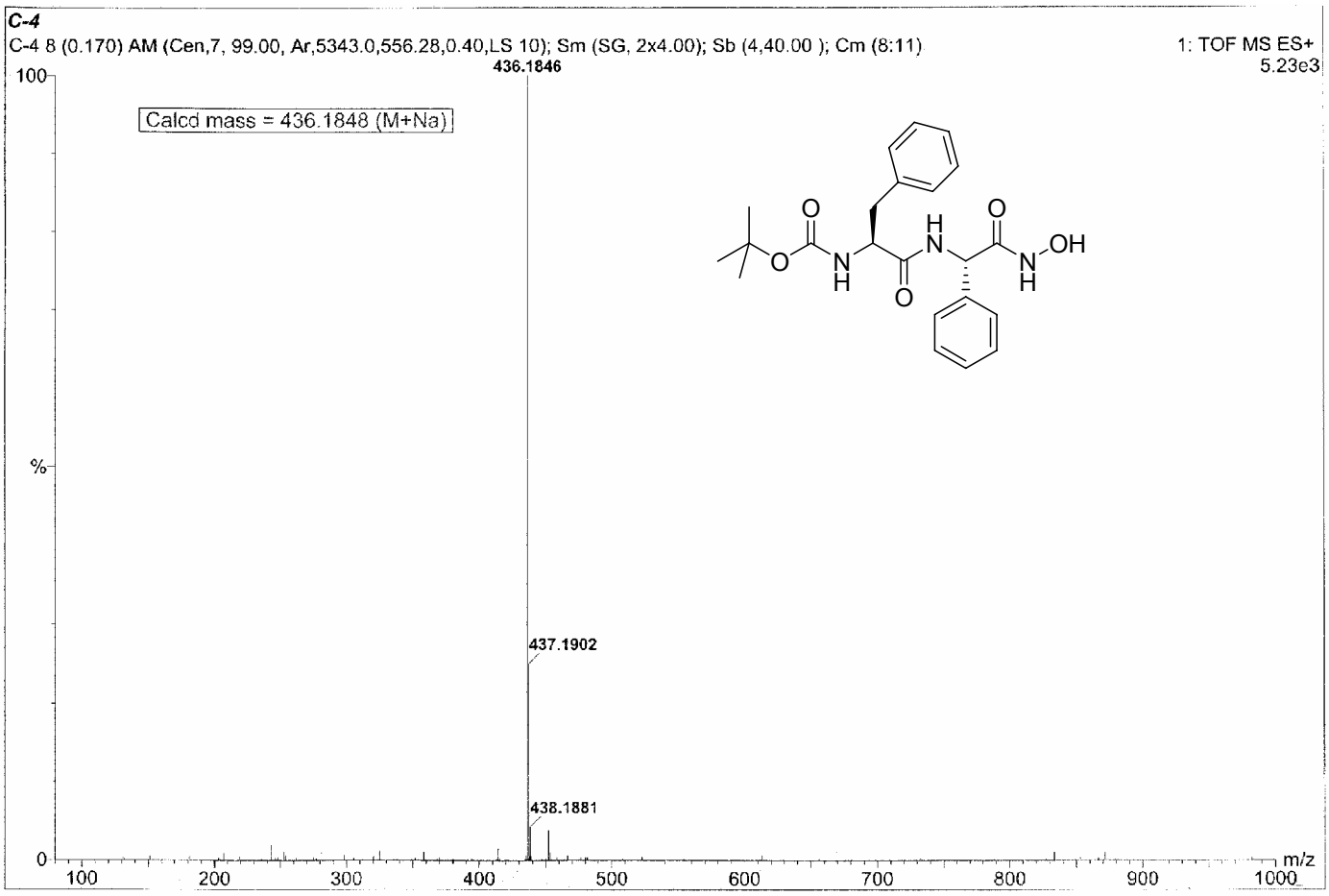

**HRMS of Boc-Val-Leu-ψ[NHCONH]-Phe-OMe**



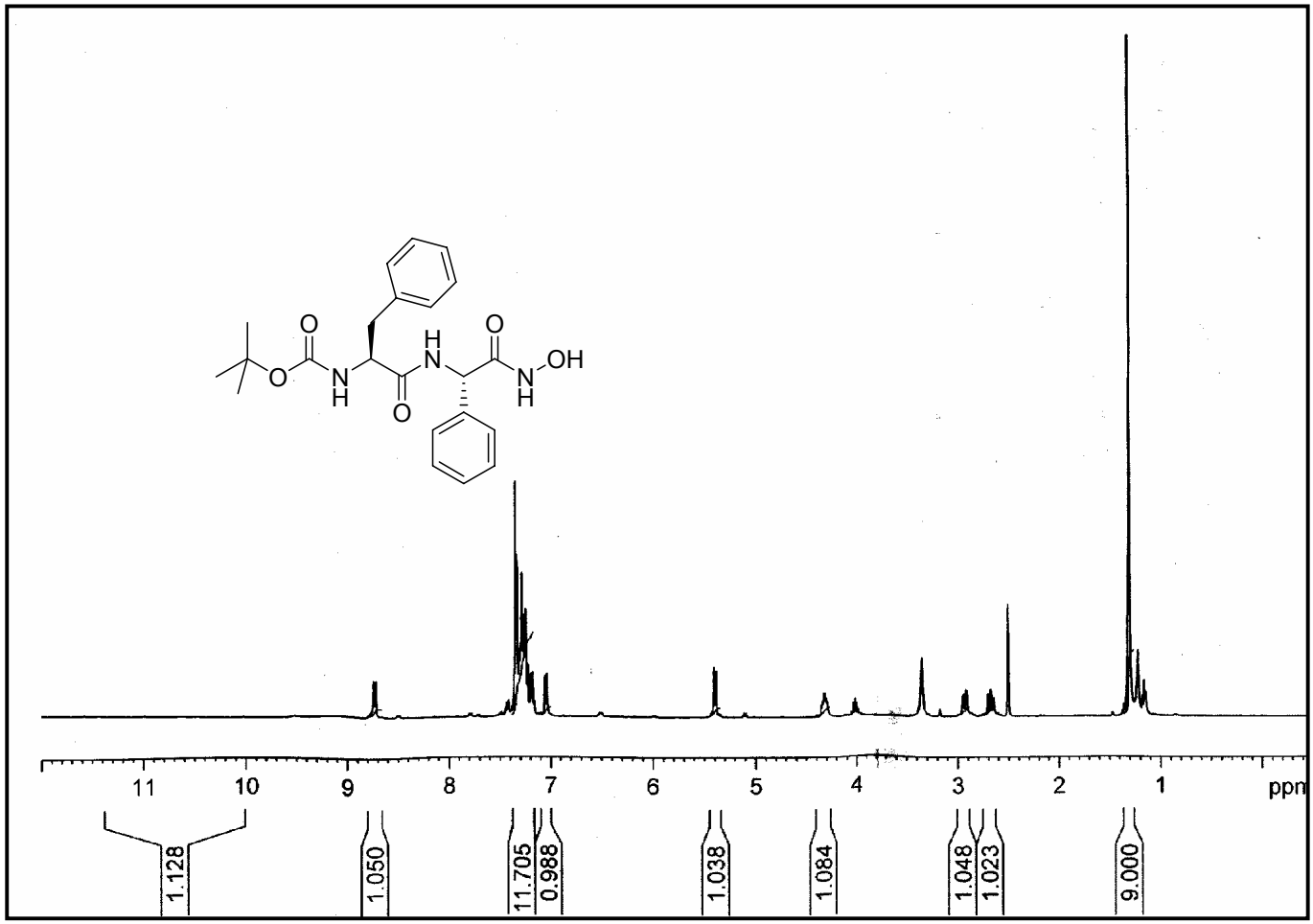

**$^{1}$H spectra of Boc-Val-Leu-$\psi$[NHCONH]-Phe-OMe**



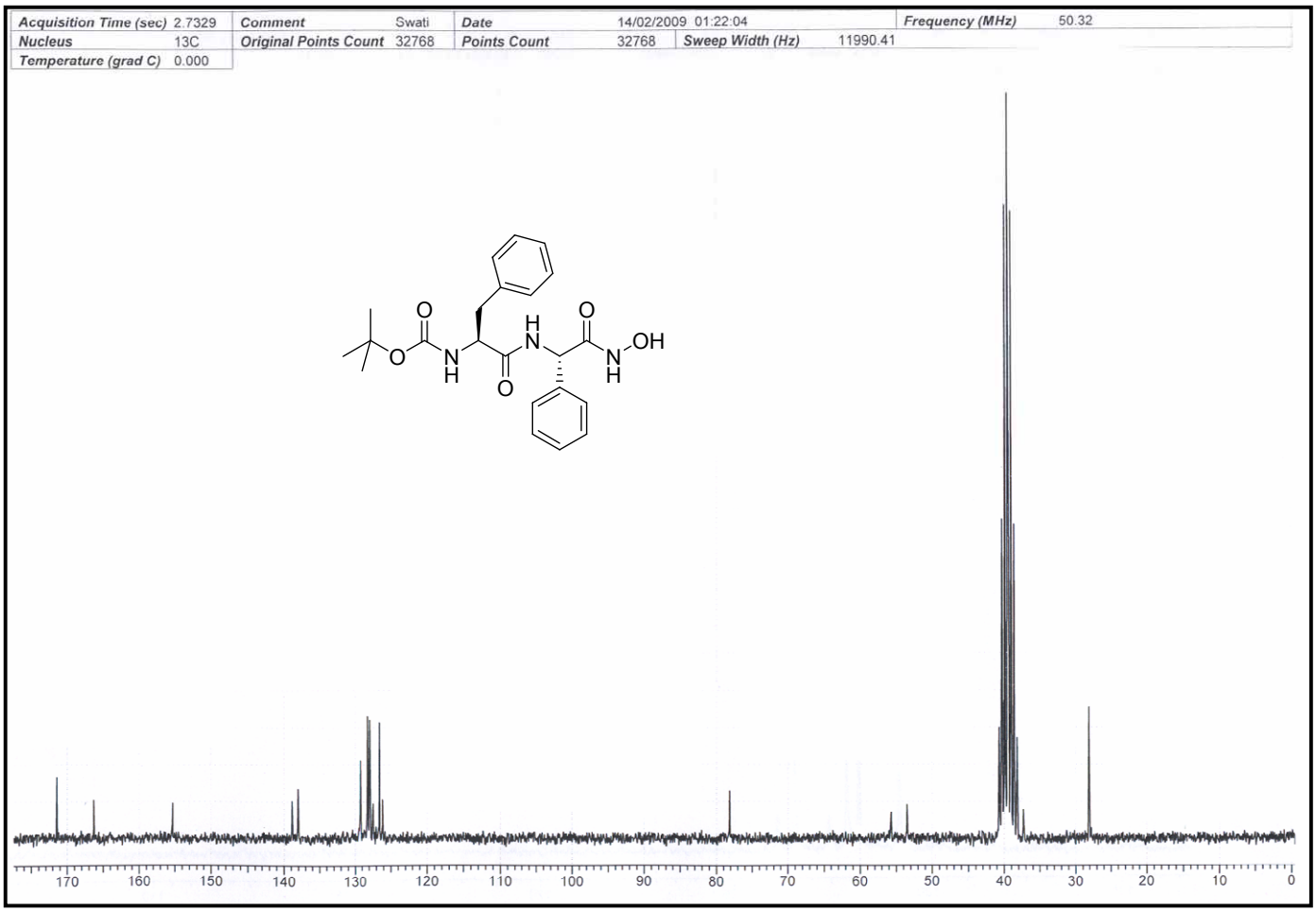

**$^{13}$C spectra of Boc-Val-Leu-$\psi$[NHCONH]-Phe-OMe**



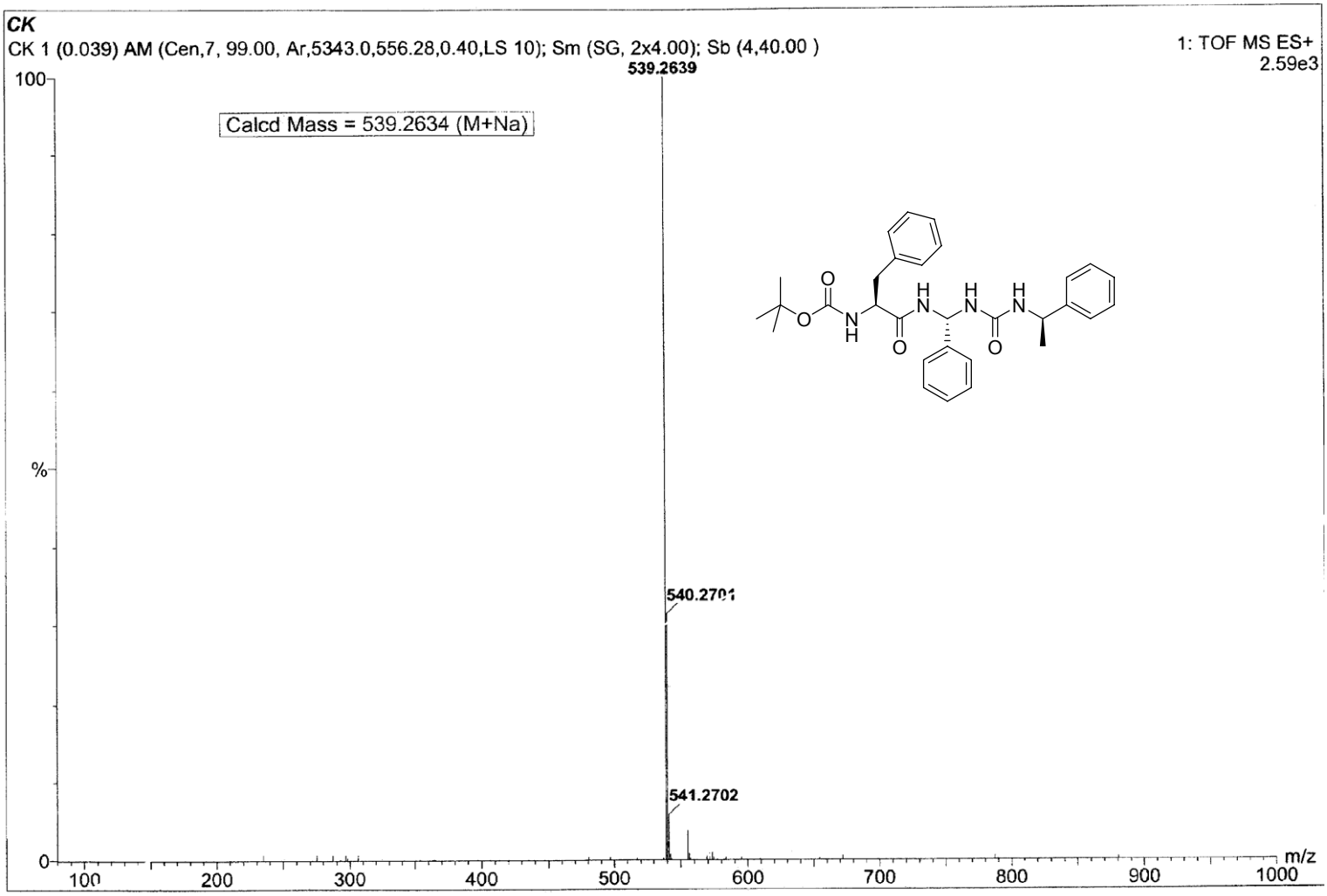

**HRMS of Boc-Phe-Phg-NHOH**



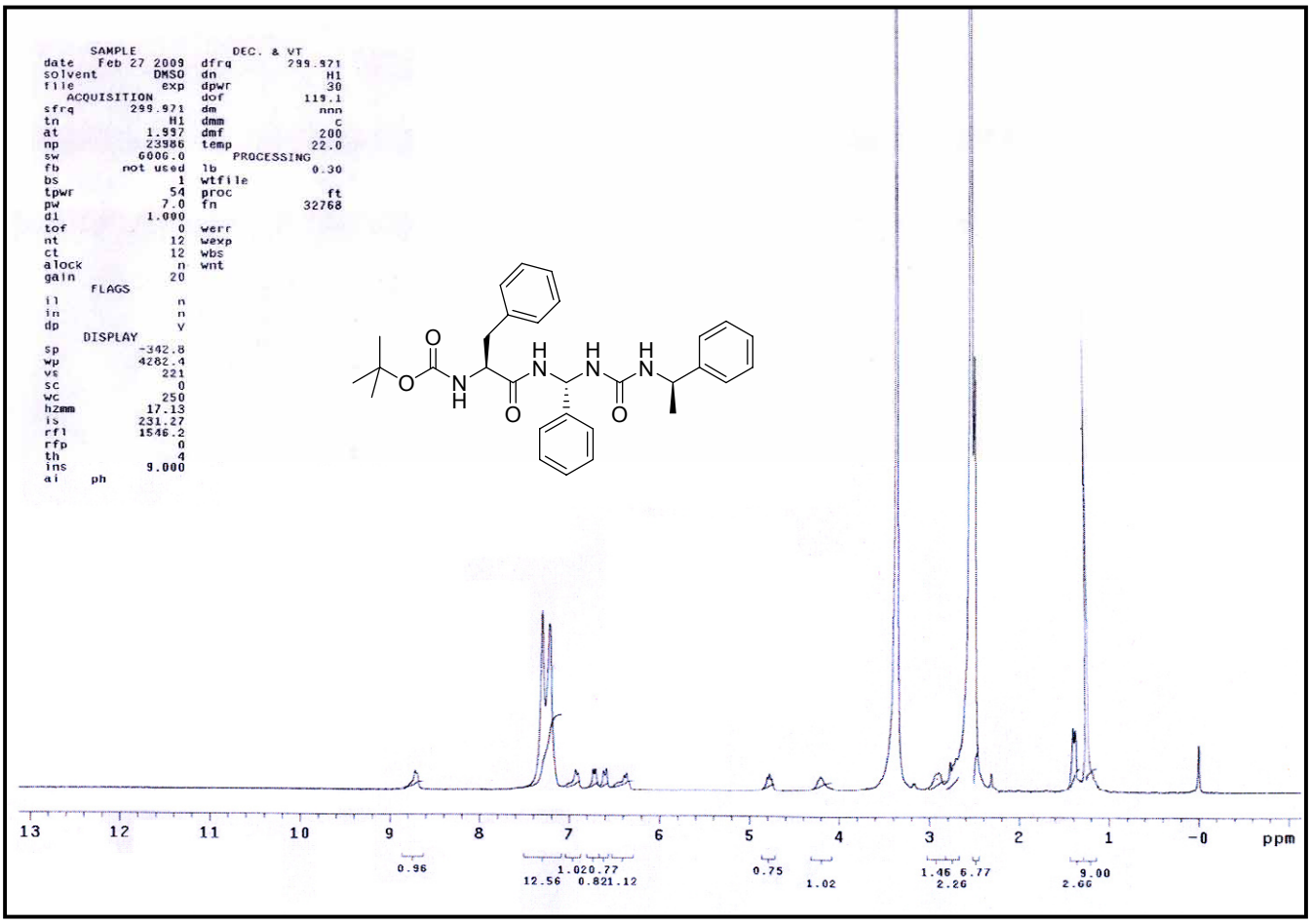

**$^{1}$H NMR spectra Boc-Phe-Phg-NHOH**



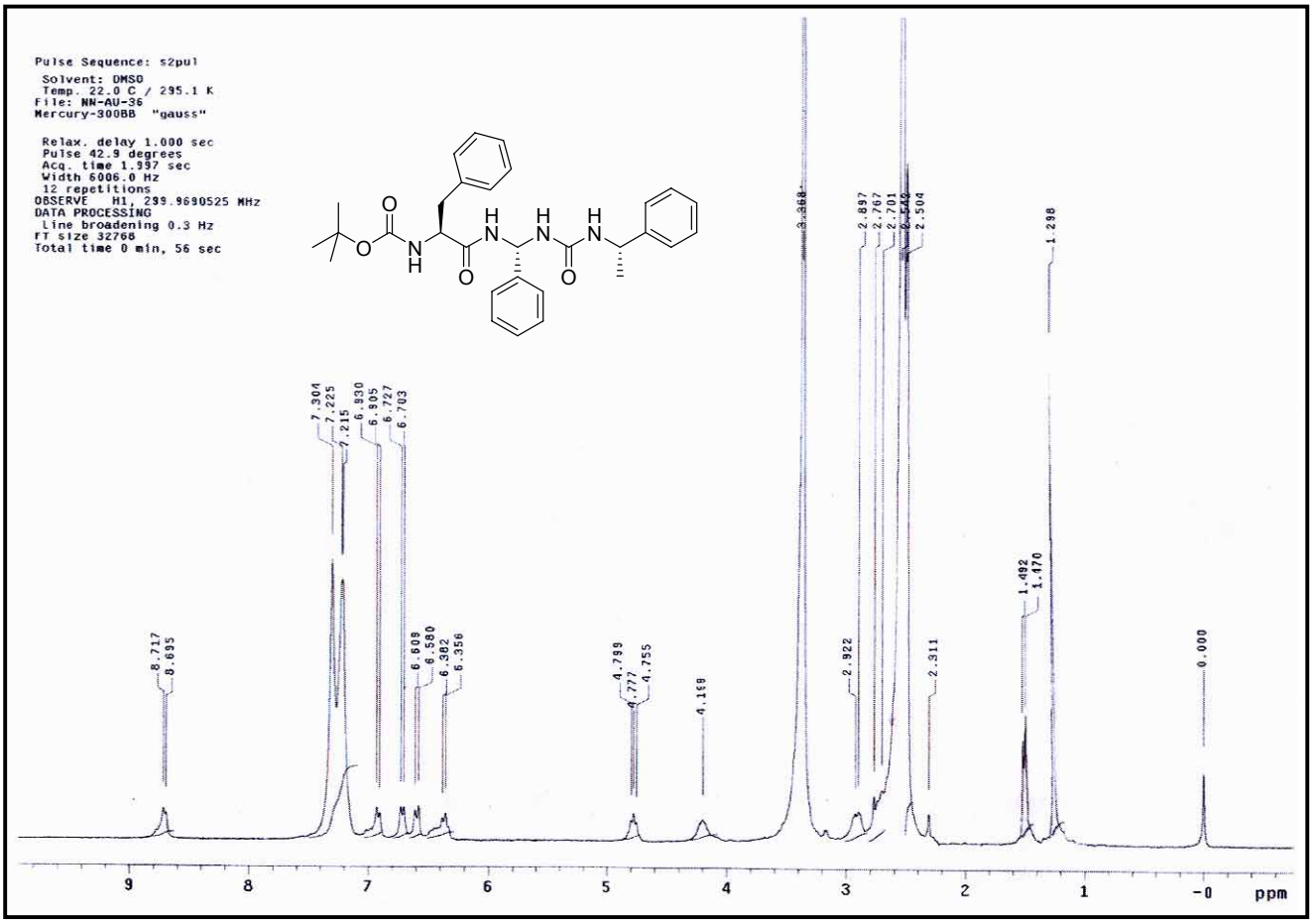

**$^{13}$C NMR spectra Boc-Phe-Phg-NHOH**



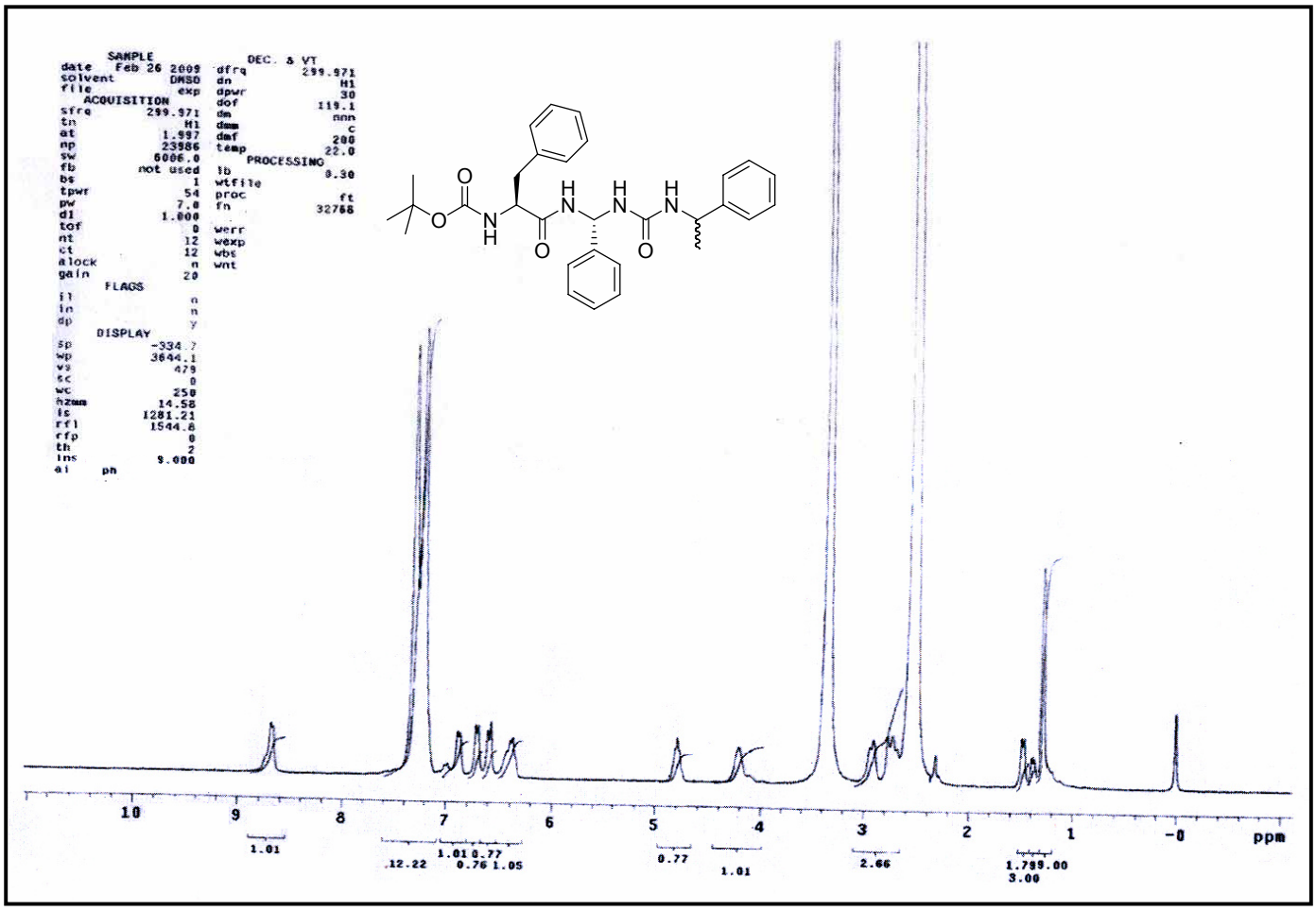

**HRMS of Boc-Phe-Phg-$\psi$[NH-CO-NH]-*R*-(+)phenylethylamine**



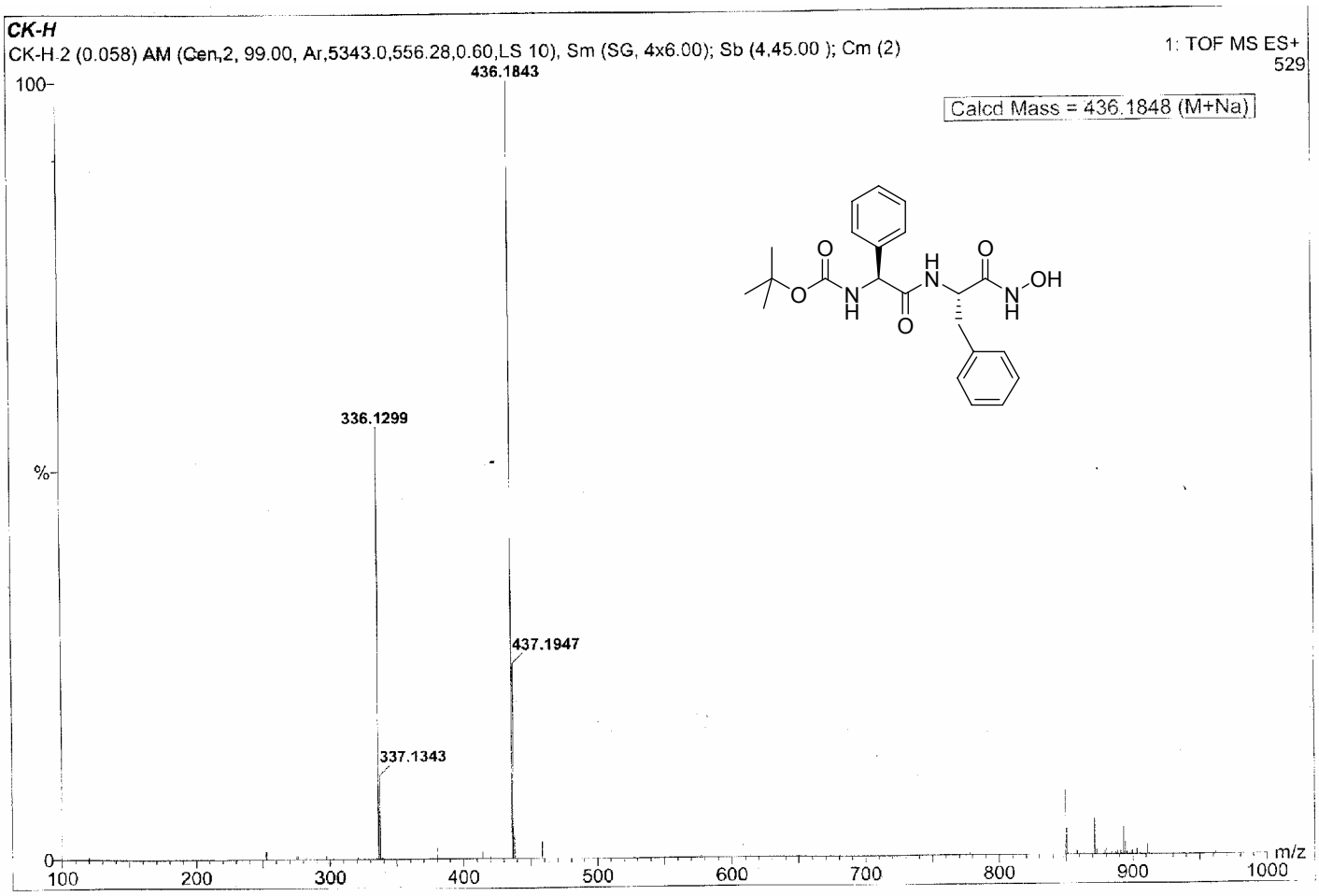

**$^{1}$H NMR Spectra of Boc-Phe-Phg-$\psi$[NH-CO-NH]- R-(+)-Phenylethylamine**



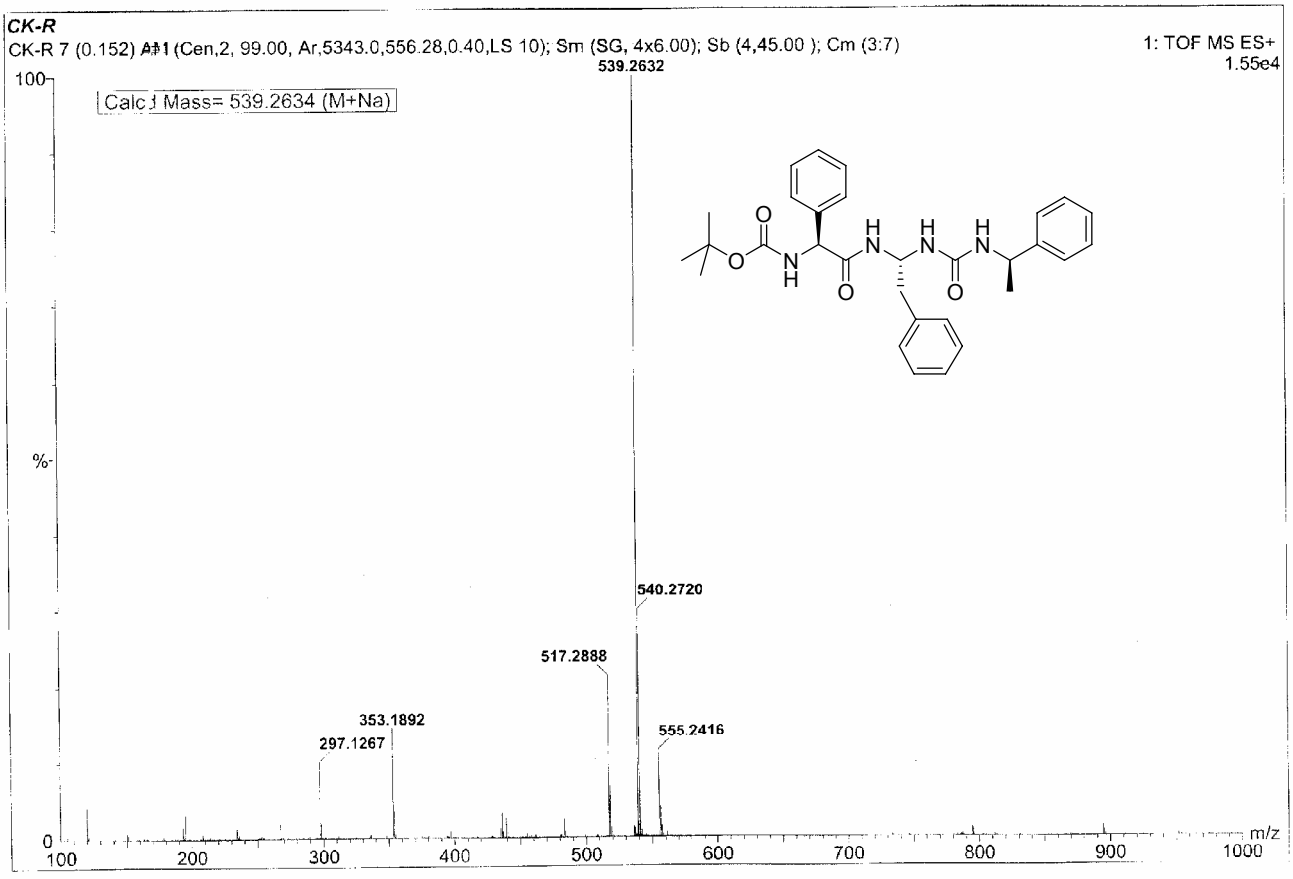

**$^1$H NMR Spectra of Boc-Phe-Phg-$\psi$[NH-CO-NH]-S-(-)-Phenylethylamine**



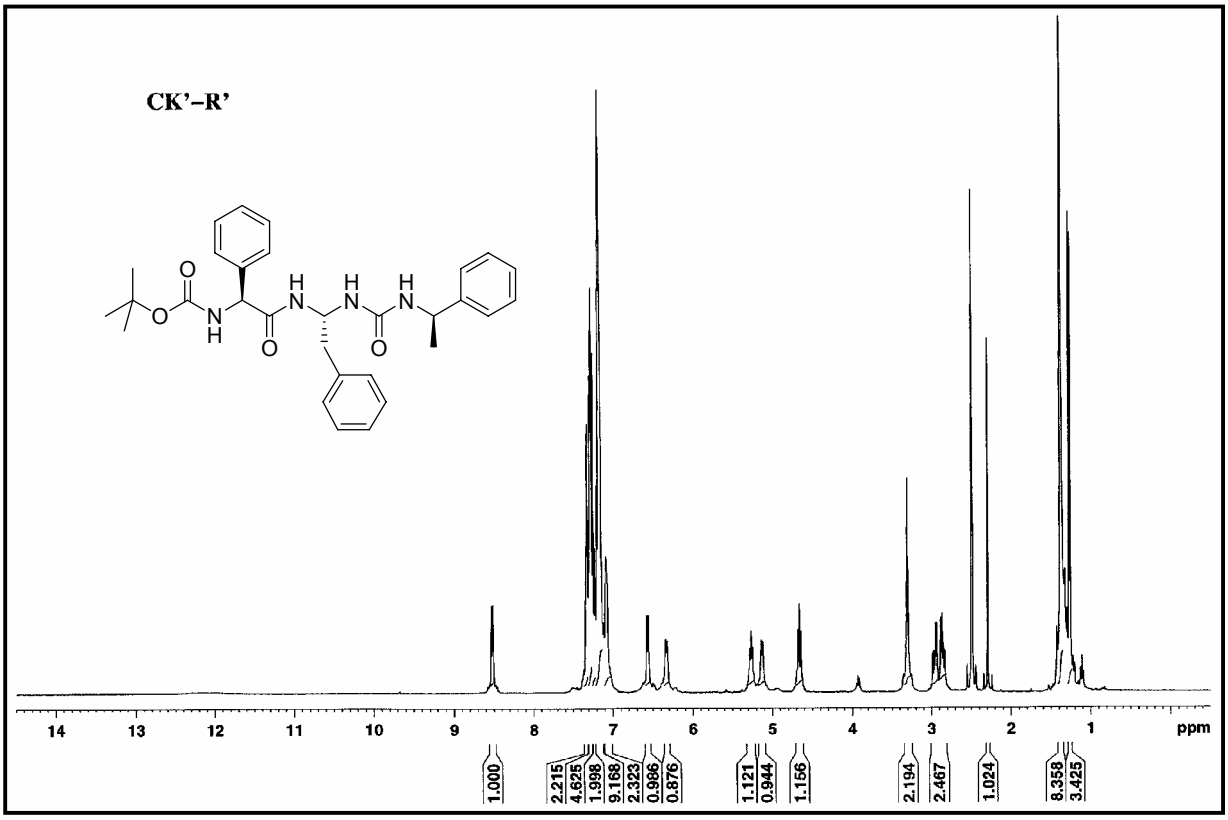

**$^1$H NMR Spectra of Boc-Phe-Phg-$\psi$[NH-CO-NH]- R/S-(±)-Phenylethylamine**



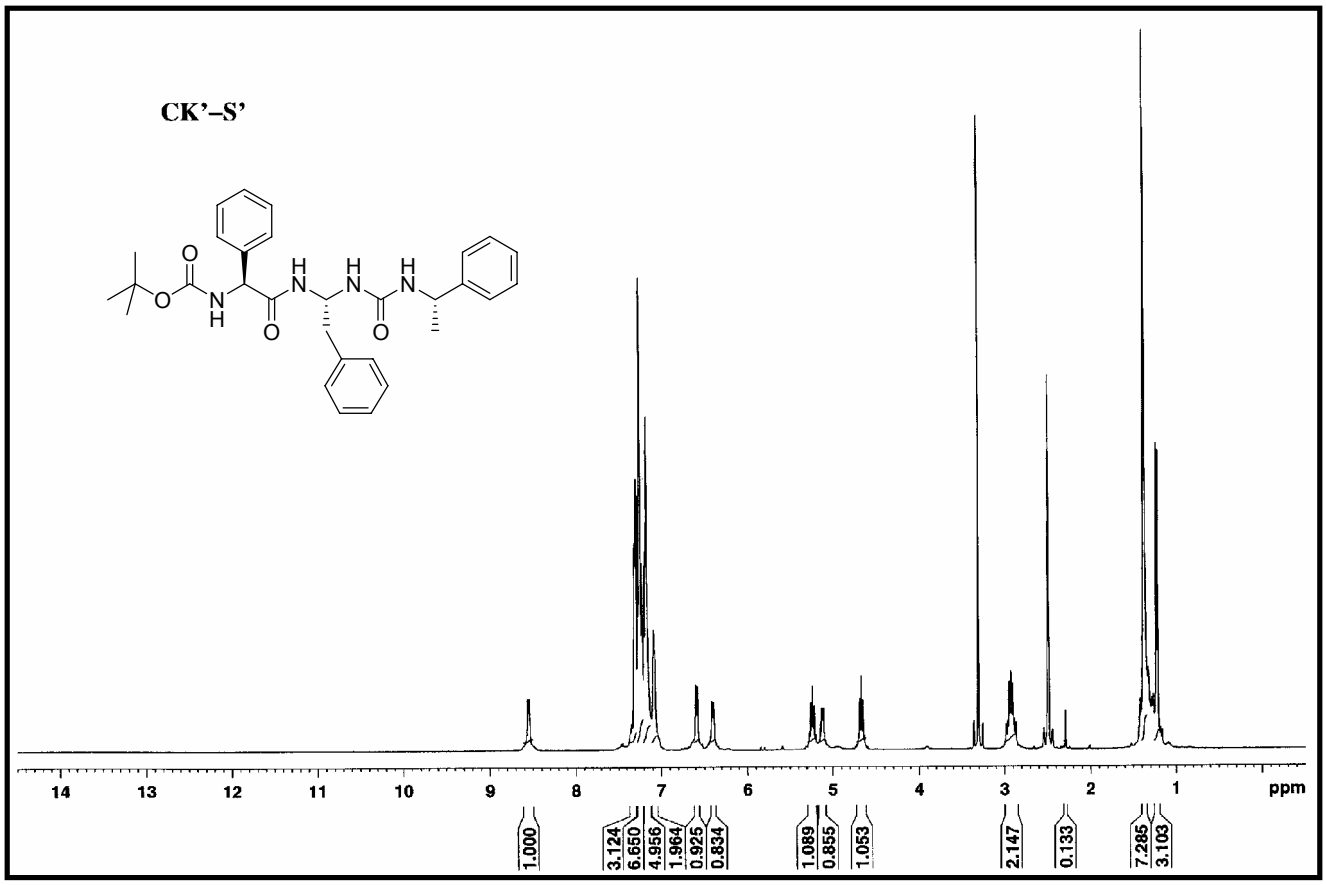

**HRMS of Boc-Phg-Phe-NHOH**



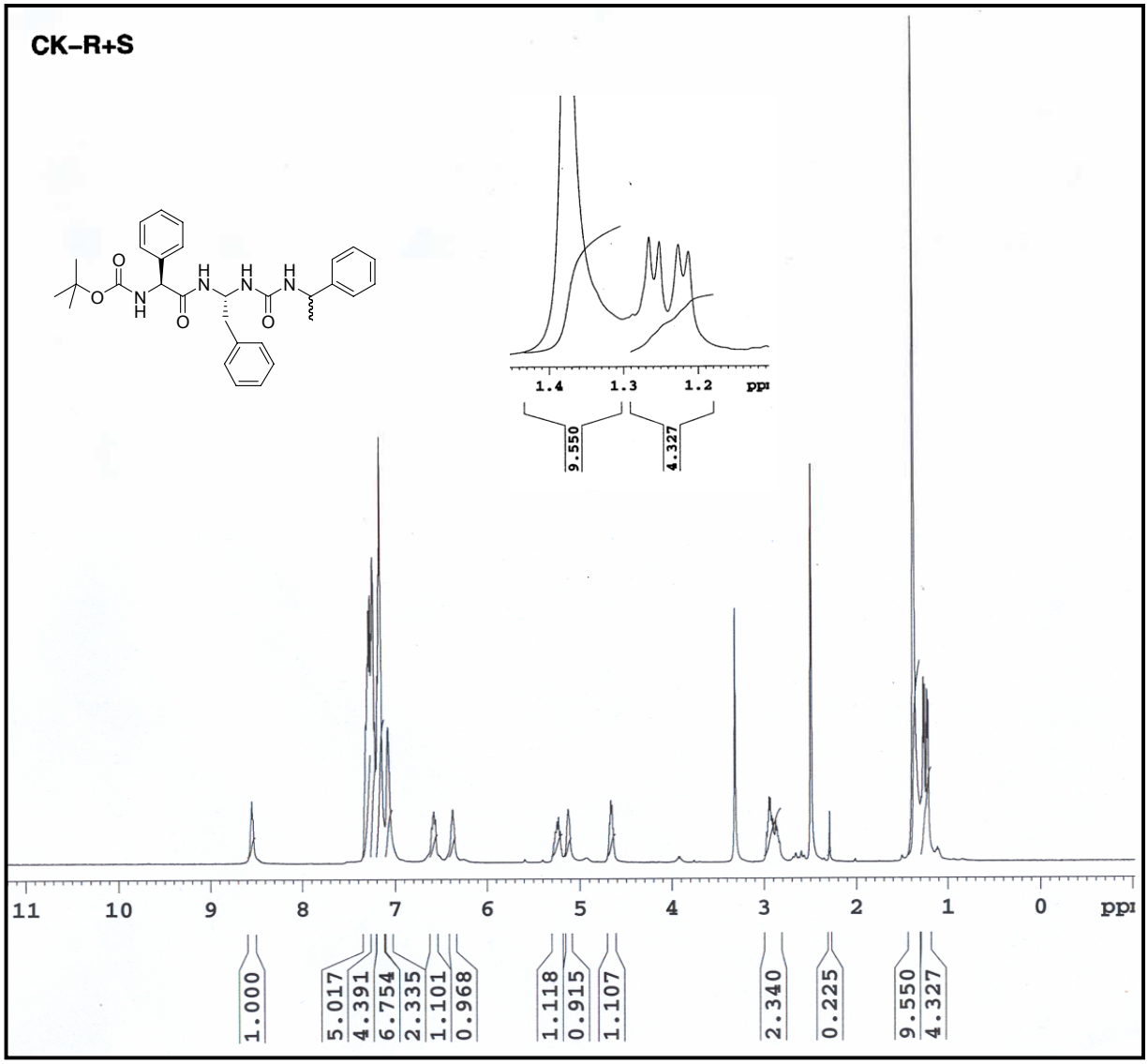

**HRMS spectra of Boc-Phg-Phe-ψ[NH-CO-NH]-R-(+)-Phenylethylamine**



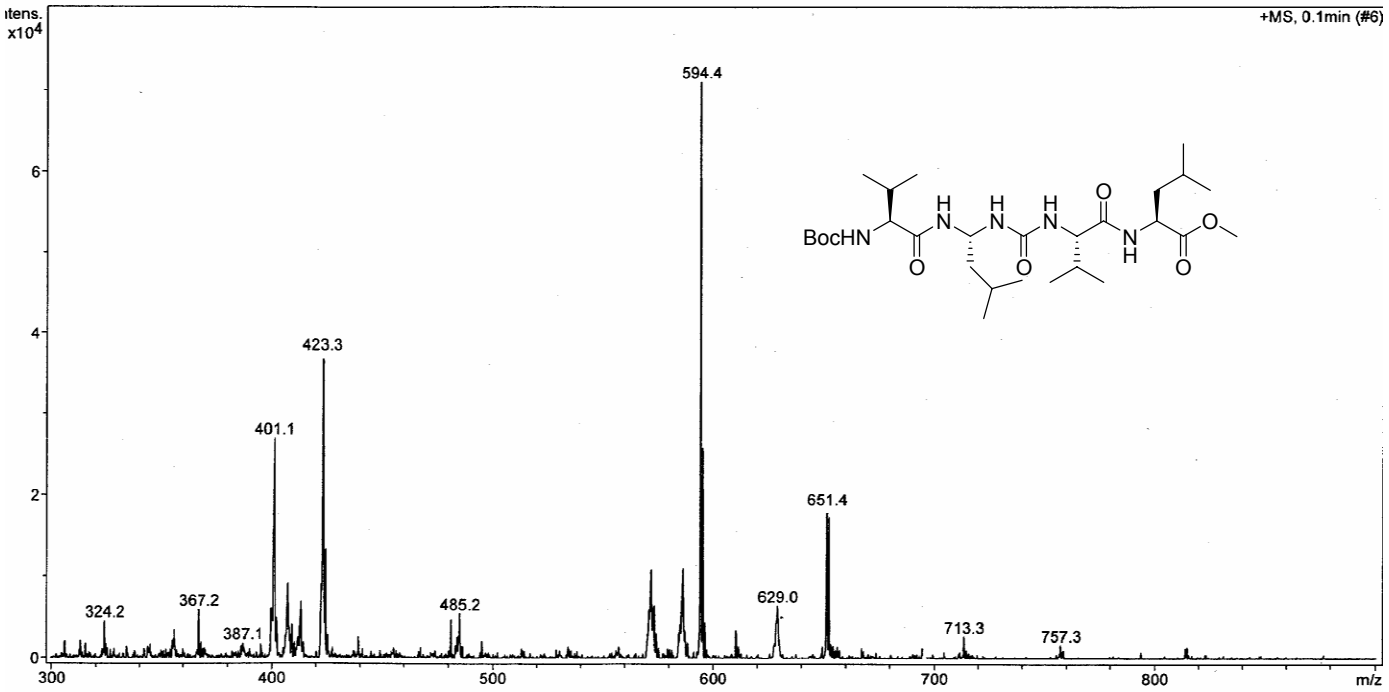

**$^{1}$H NMR spectra of Boc-Phg-Phe-$\psi$[NH-CO-NH]-R-(-)-Phenylethylamine**



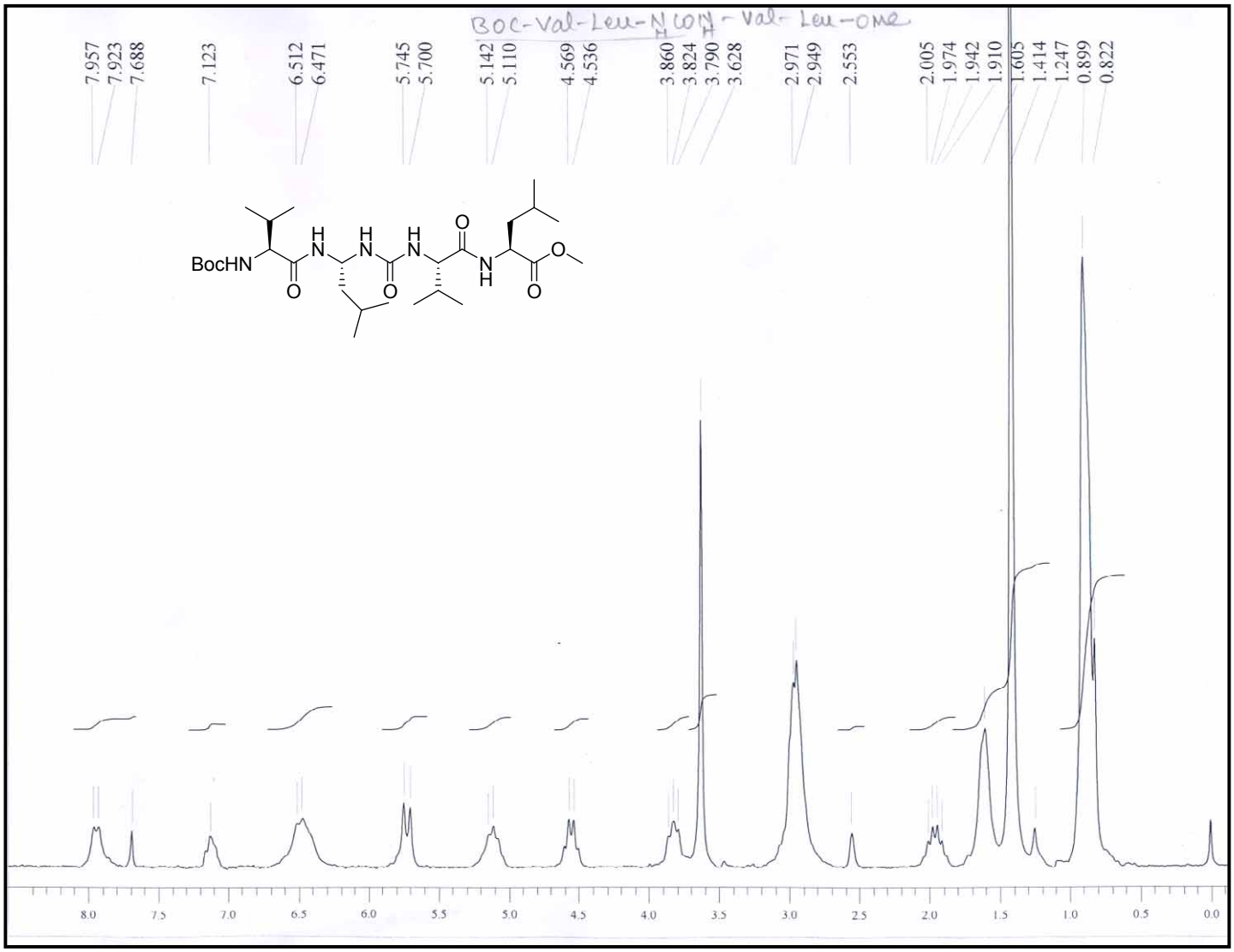

**$^{1}$H NMR spectra of Boc-Phg-Phe-$\psi$[NH-CO-NH]-S-(+)-Phenylethylamine**



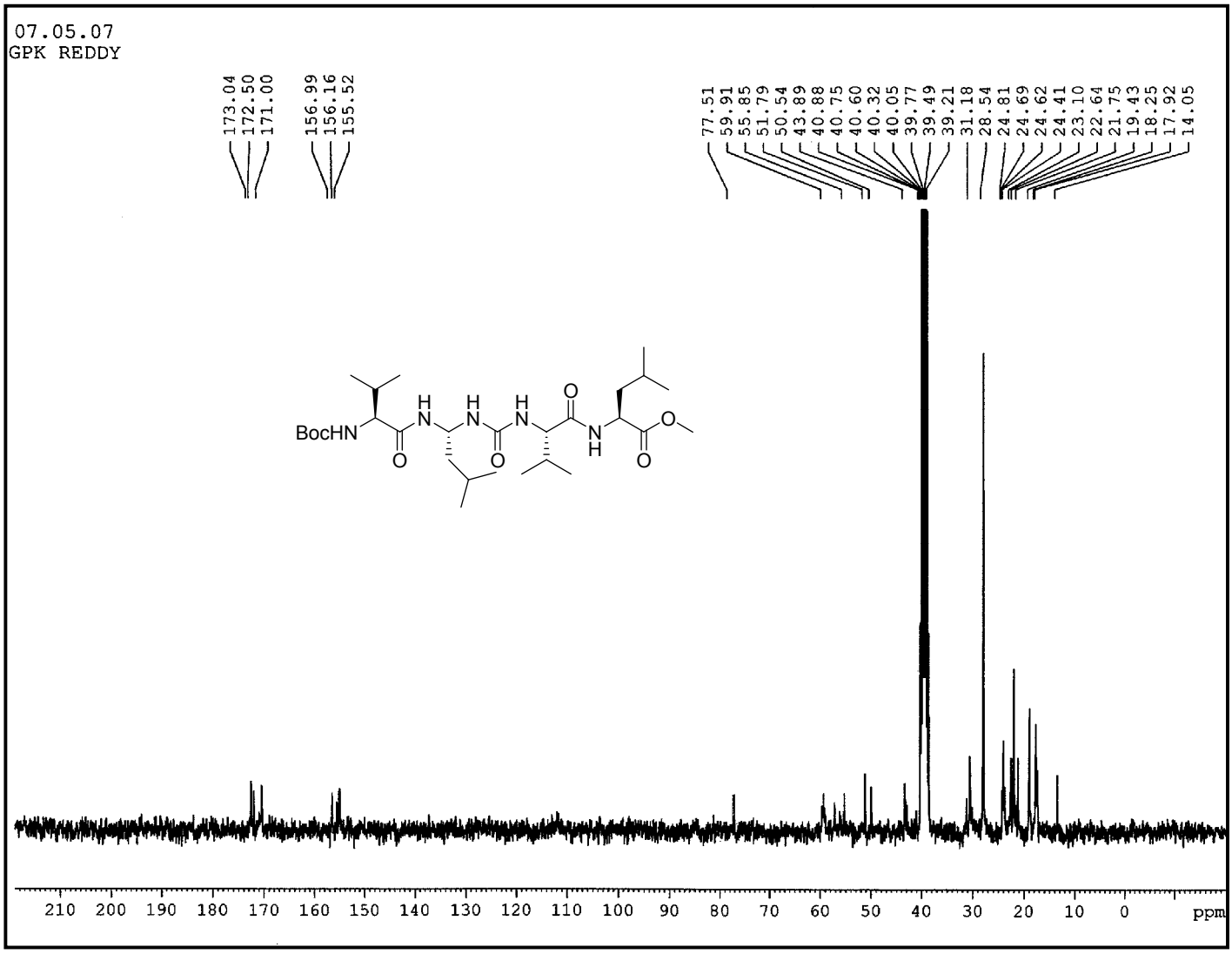

**$^{1}$H NMR Spectra of Boc- Phg-Phe-$\psi$[NH-CO-NH]- R/S-(±)-Phenylethylamine**



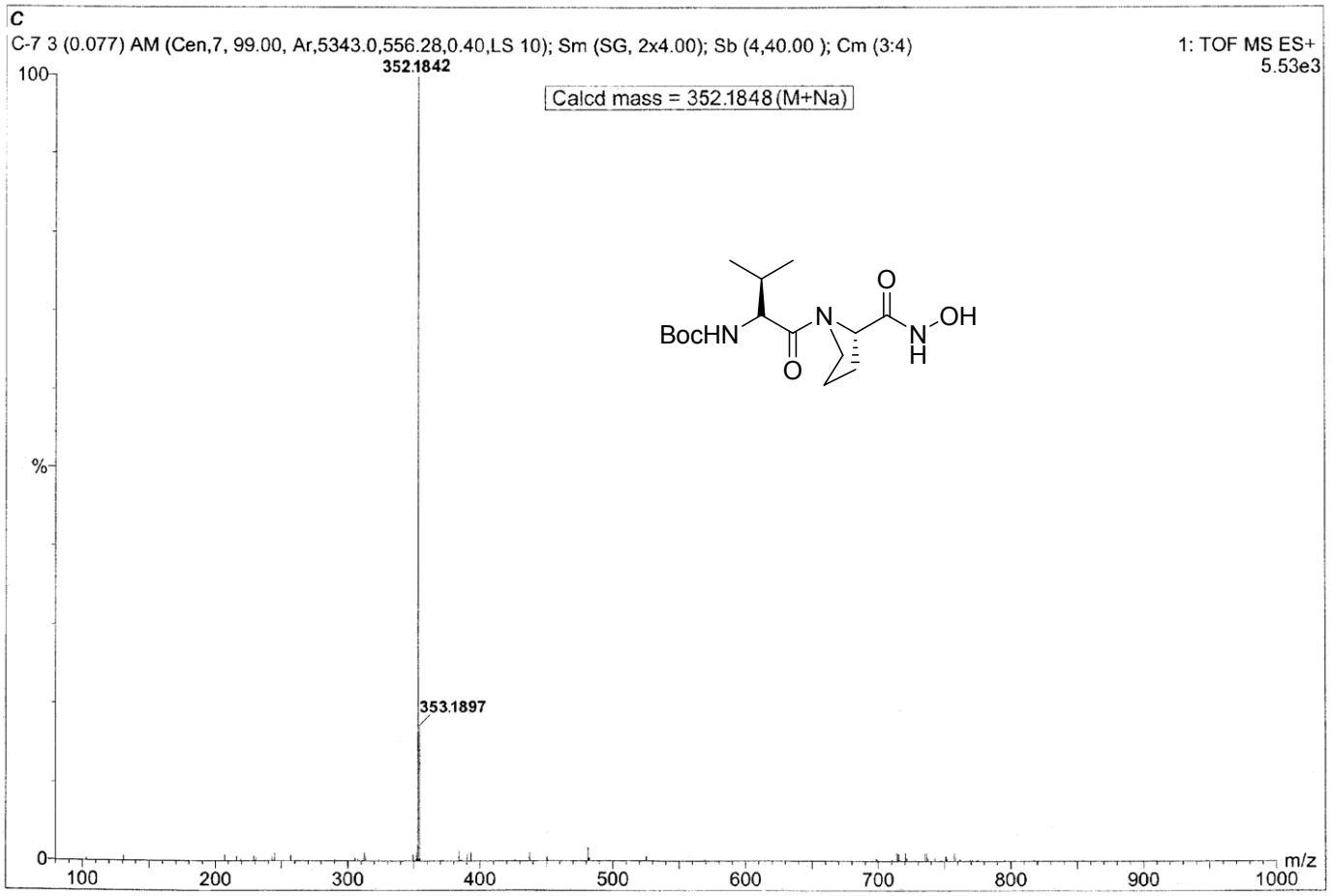

**ESIMS Spectra of Boc-Val-Leu-ψ[NHCONH]-Val-Leu-OMe**



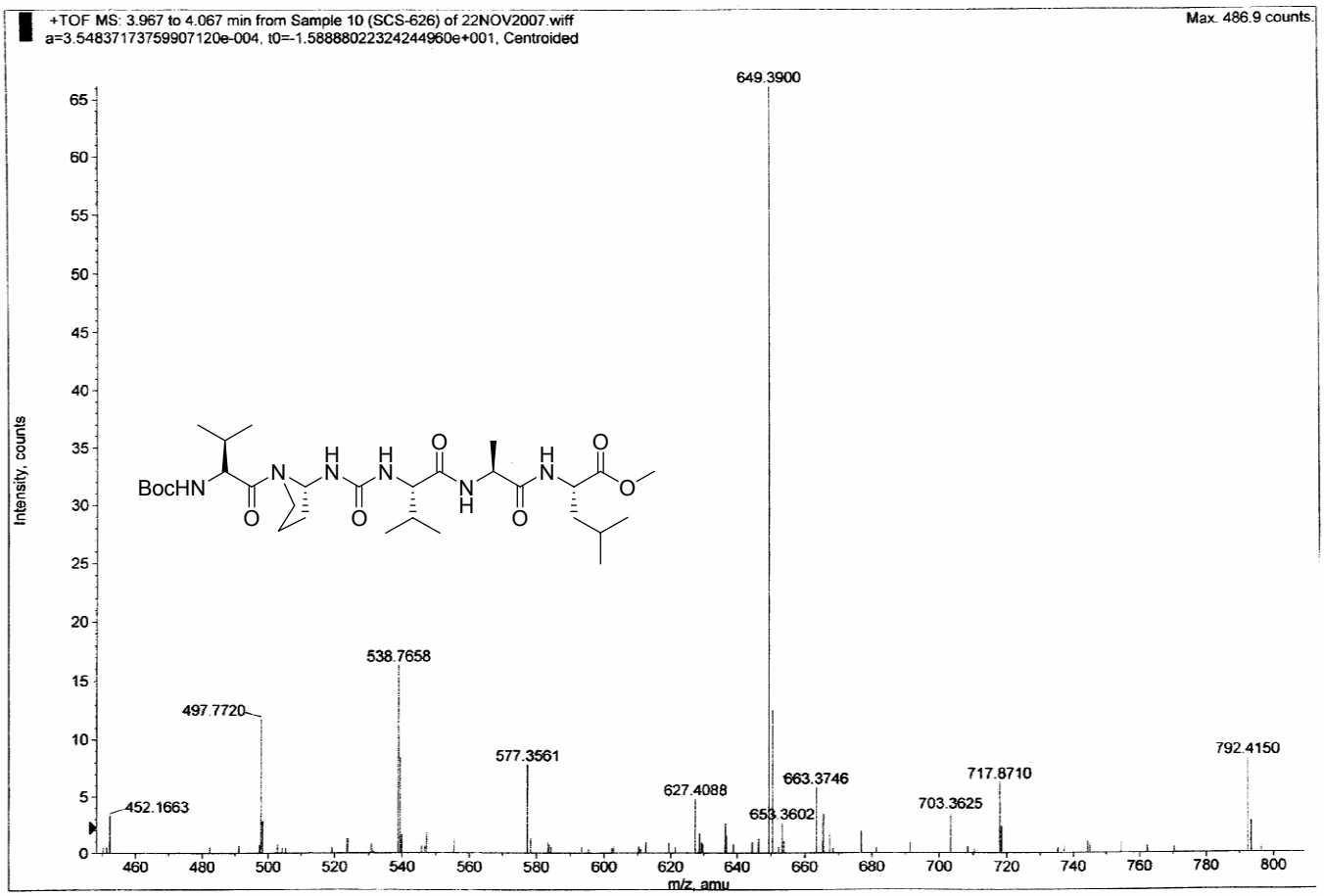

**$^{1}$H Spectra of Boc-Val-Leu-$\psi$[NHCONH]-Val-Leu-OMe**



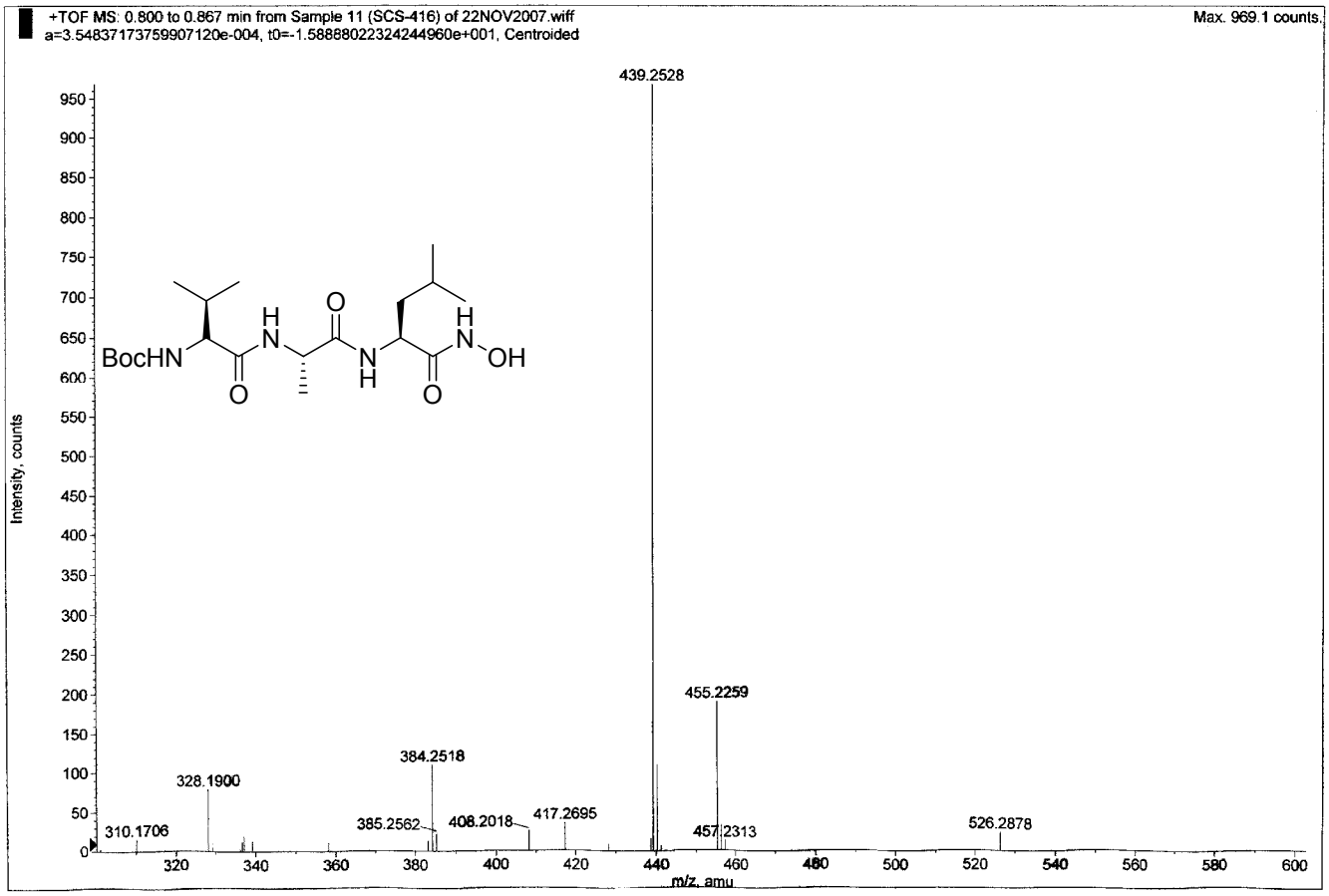

**$^{13}$C Spectra of Boc-Val-Leu-$\psi$[NHCONH]-Val-Leu-OMe**



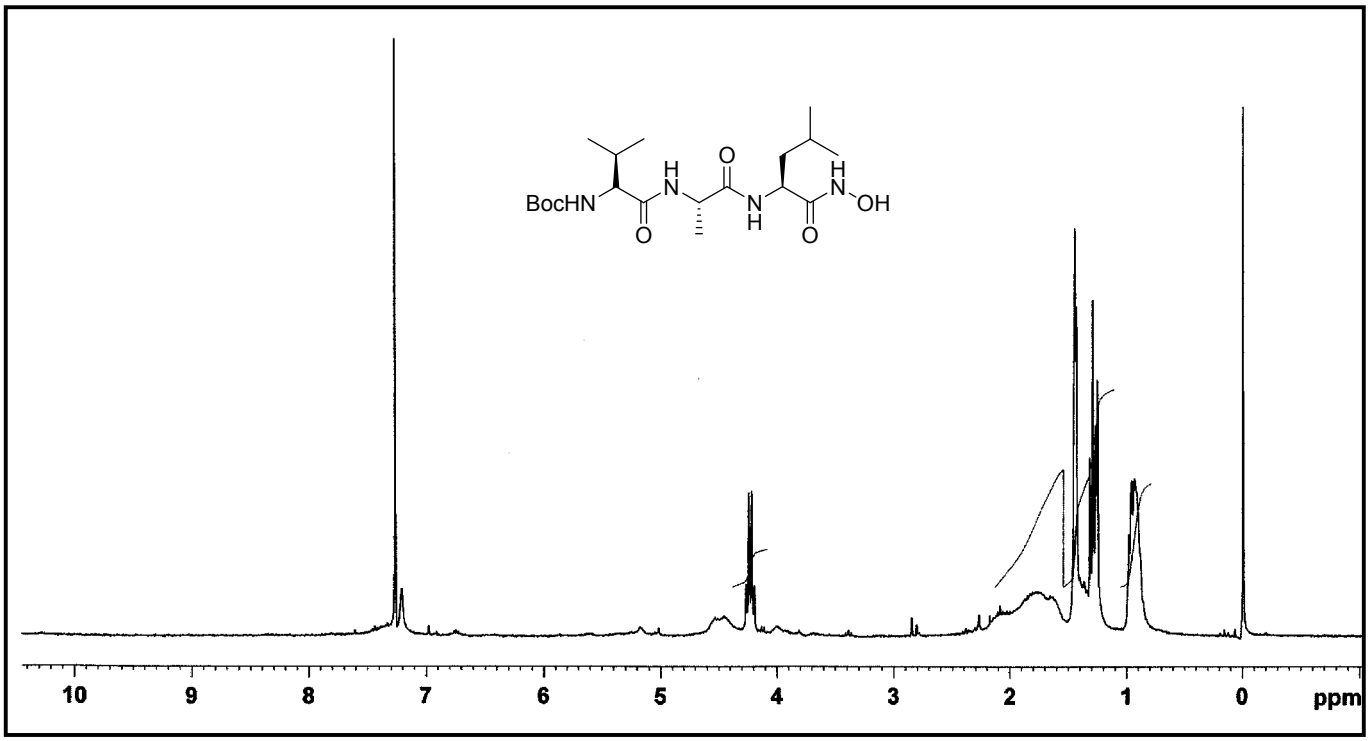

**HRMS of Boc-Val-Pro-NHOH**



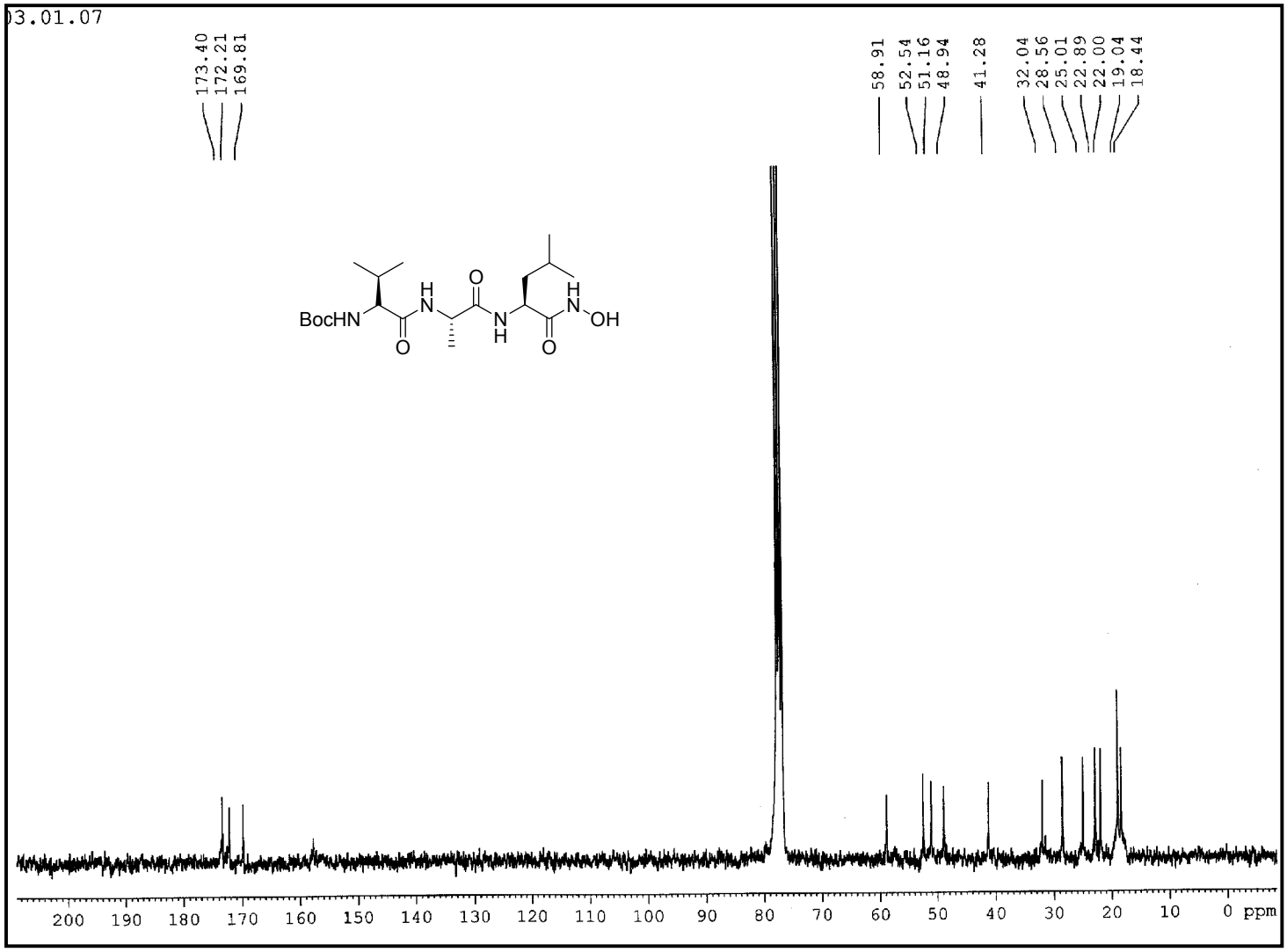

**HRMS of Boc-Val-Pro-$\psi$[NHCONH]-Val-Ala-Leu-OMe**



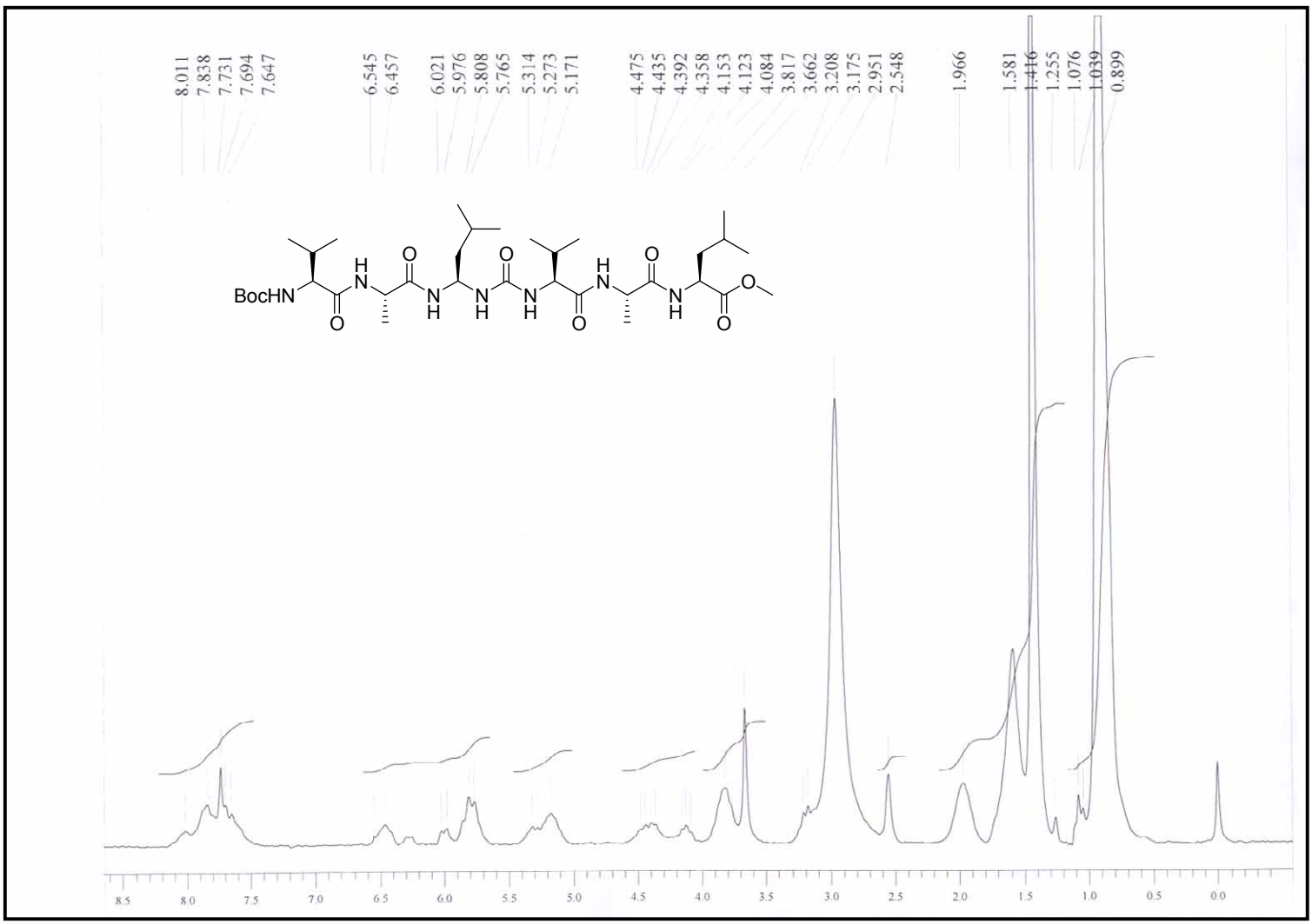

**HRMS of Boc-Val-Ala-Leu-NHOH**



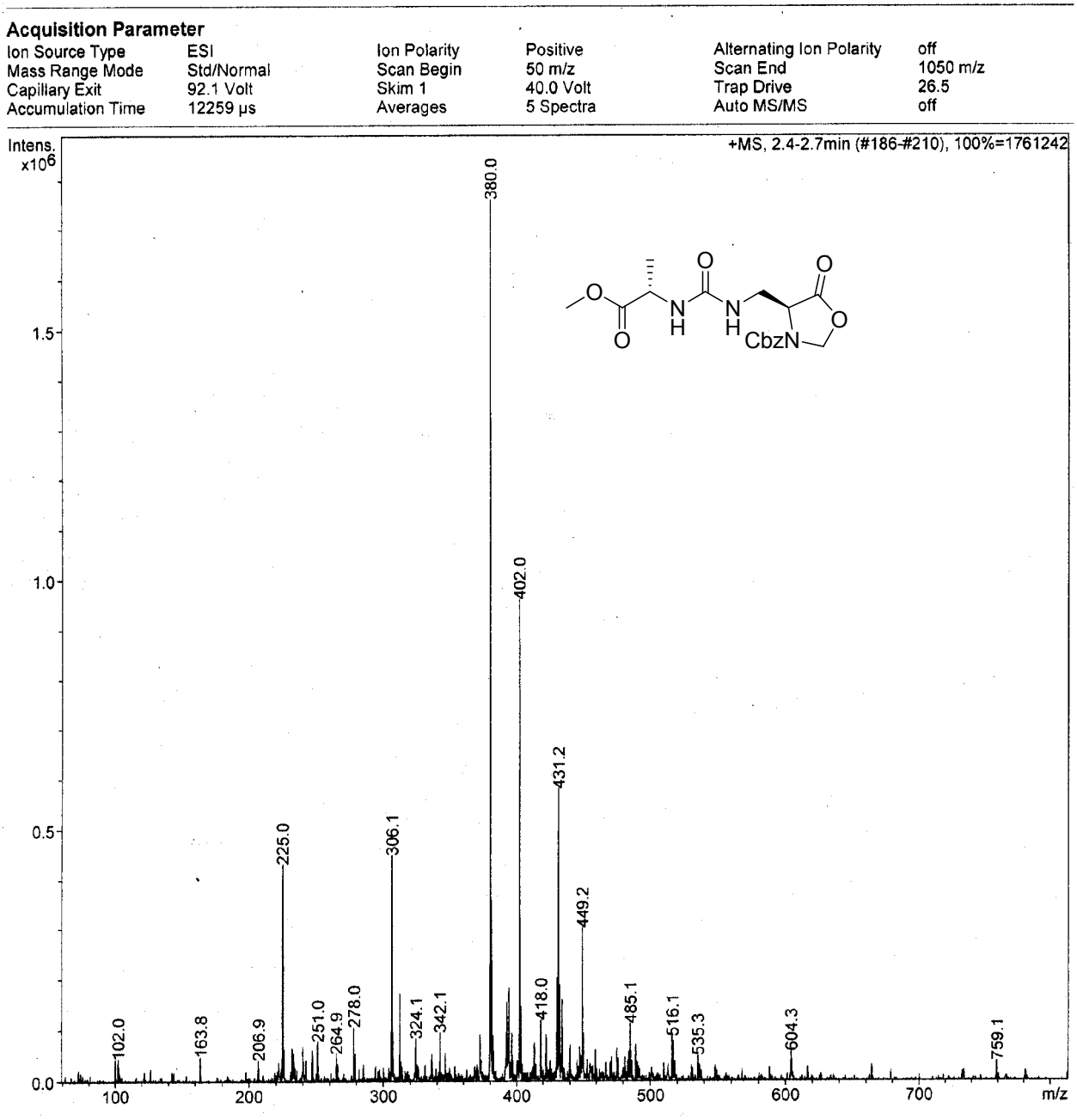

**$^{1}$H NMR of Boc-Val-Ala-Leu-NHOH**




**$^{13}$C NMR of Boc-Val-Ala-Leu-NHOH**




**$^{1}$H Spectra of Boc-Val-Ala-Leu-$\psi$[NHCONH]-Val-Ala-Leu-OMe**




**ESIMS spectrum of Z-protected ureidoalanine derivative**