Supporting Information for

Title: A Facile Synthesis and Crystallographic Analysis of *N*-Protected *β*-Amino Alcohols and Short Peptaibols

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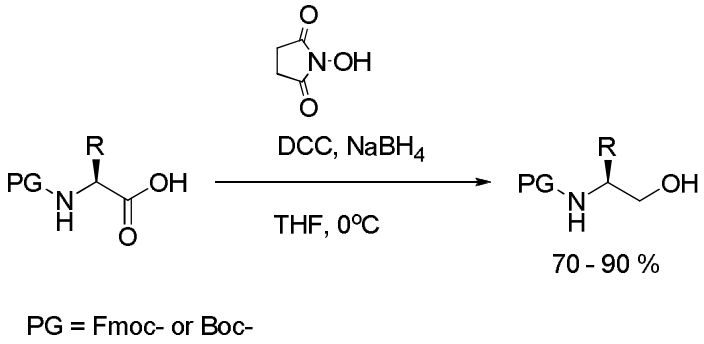
General Experimental Details

All amino acids, *N*-hydroxysuccinimide, Isobutyl Chloroformate, DiPEA, $NaBH_4$,TFA,were purchased from Aldrich.THF, EtOAc, were purchased from Merck. Di-tert-butyl dicarbonate obtained from spectrochem and used without further purification. THF and DiPEA were distilled over sodium prior to use. Column chromatography was performed on Merck silica gel (120-200 mesh). Reactions were monitored by thin-layer chromatography (TLC) using 60 F_{254} Merck precoated silica gel plates. Visualization was accomplished with UV light and phosphomolybdic acid (PMA) or ninhydrin stain followed by charring on hot-plate. Yields refer to chromatographically pure compounds unless otherwise stated. The ^{1}H spectra were recorded over Jeol 400 MHz (or 100 MHz for ^{13}C) spectrometer using residual solvents signals as an internal reference ($CDCl_3$ δ_H, 7.24 ppm, δ_c 77.0 ppm),unless otherwise stated. The chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. Specific rotations were recorded using MeOH as a solvent (Rudolph Analytical Research) at ambient temperature. Melting points were determined over Veego VMP-DS hot stage apparatus and were not corrected. Chiral HPLC was performed on Waters 600 equipped with empower software using CHIRALPAK®AD Analytical Column, which was purchased from Daicel Chemical Industries. Mass spectra obtained from MALDI TOF/TOF (Applied Biosciences) and LCMS/MS (waters). Data for X-ray structure determination were obtained with Bruker APEXII DUO diffractometer using Mo-Kα (λ = 0.71073 Å) graphite monochromated radiation.

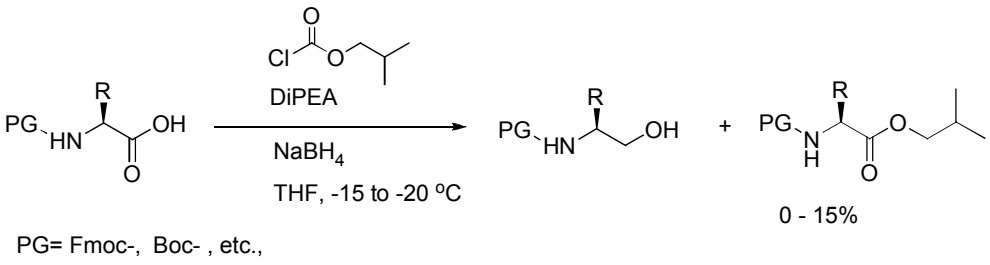
General procedure for the synthesis of Fmoc- or Boc- protected *β*-amino alcohol from *N*-hydroxysuccinimide esters:



Scheme 1

To a solution of Fmoc- or Boc-protected amino acid (2 mmol) and N-hydroxysuccinimide (0.345 g, 3 mmol) at 0 ^{o}C in THF (5 mL), was added DCC (0.413 g, 2 mmol), and reaction was stirred at this temperature for 1 h. precipitated DCU was filtered and washed with THF (3 X 2 mL), combined organic layer was cooled to ice temperature and the solution of sodium borohydride (0.152 g, 4 mmol) in water (1 mL) was added in one portion which leads to the vigorous evolution of gas. After 5 min, 5 mL of 0.5 N HCl was added to quench unreacted $NaBH_4$. Reaction mixture was extracted in EtOAc (3 X 10 mL), and combined organic layer was washed with 5% Na_2CO_3 (3 X 10 mL),brine (3 X 10 mL),dried over Na_2SO_4, and concentrated in *vacuo*. After work up procedure, Boc protected beta amino alcohols were obtained as pure product over 80-90% yield. Fmoc protected Products were purified over silica gel column chromatography to get pure beta amino alcohol over 70-90% yield.

General procedure for the synthesis of *N*-protected *β*-amino alcohol using mixed anhydride method:[1-3]

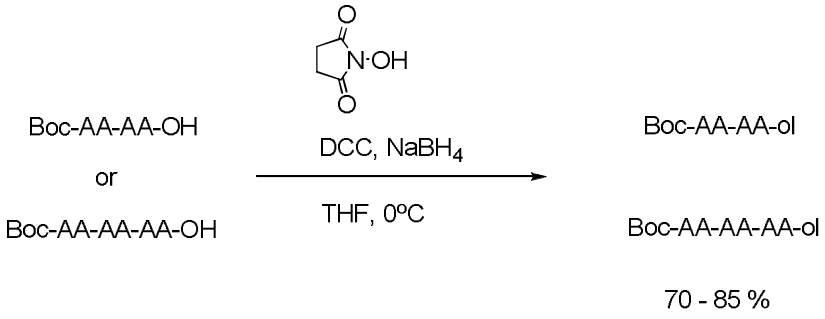


Scheme 2

Isobutyl chloroformate (0.26 mL, 2 mmol) was added dropwise to the solution of N-protected amino acid (2 mmol) and DiPEA(0.35 mL,2 mmol) at -15 to -20 ^{o}C in THF (5 mL), After 5 min. precipitate of DiPEA hydrochloride salt was filtered and washed with THF (2 X 3 mL). Combined organic layer was cooled in salt-ice temperature and the solution of sodium borohydride (0.152 g, 4 mmol) in water (1 mL) was added in one portion which leads to strong evolution of gas. After 5 min, 5 mL of 0.5 N HCl was added to quench unreacted $NaBH_4$.
The reaction mixture was extracted in EtOAc (3 X 10 mL), washed with 5% Na_2CO_3 (3 X 10 mL), brine (3 X 10 mL), dried over Na_2SO_4 and concentrated in *vacuo*.

Peptide synthesis: Dipeptide and tripeptide were synthesized by conventional solution-phase methods by using a fragment-condensation strategy. The *tert*-butyloxycarbonyl group was used for N-terminus protection, and the C-terminus was protected as a methyl ester. Deprotections were performed with trifluoroacetic acid and saponification for the N- and C-termini, respectively. Couplings were mediated by dicyclohexylcarbodiimide (DCC)/1-hydroxybenzotriazole (HOBt). The tripeptide Boc-Aib-Ala-Leu-OMe was prepared by [2+1] condensation involving an N-terminus dipeptide acid Boc-Aib-Ala-OH and H-Leu-OMe using DCC/N-Hydroxysuccinimide (HOSu). Another Tripeptide Boc-Ala-Leu-Val-OMe was prepared by [2+1] condensation involving N-terminus dipeptide acid Boc-Ala-Leu-OH and H-Val-OMe, by using DCC/N-Hydroxysuccinimide (HOSu).

General procedure for the synthesis of Boc protected dipeptide alcohol and tripeptide alcohol (Peptaibol)



Scheme 3

The previous procedure was utilized to synthesize Boc protected dipeptides and tripeptides and pentapeptide alcohols. Products were obtained in pure form after work up procedure, and were obtained over 70-90% yield.

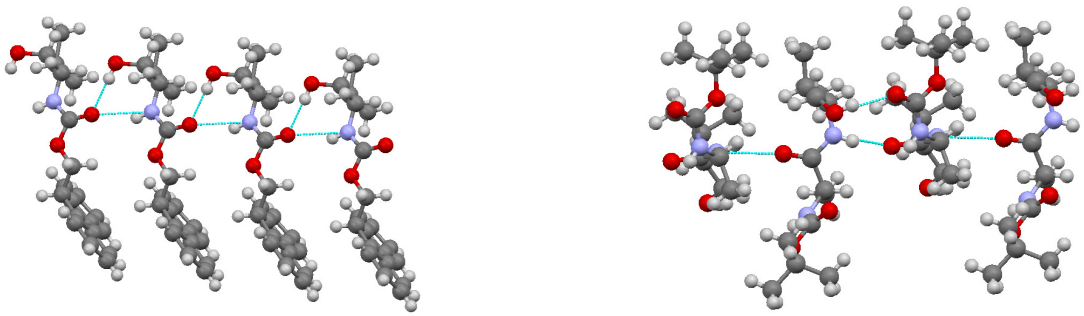
Crystal structure information Fmoc-Valol and Boc-Ala-Valol:

Crystal structure of Fmoc-Valol (3):[28] $C_{20}H_{23}N_1O_3$; A colourless crystal with approximate dimensions 0.85 x 0.50 x 0.25 mm gave a Monoclinic with space group *P2(1);a* = 4.942(4), *b* =11.622(11), *c* = 15.783(14) Å, $\alpha = 90^o$ $\beta = 93.573(14)^o$ $\gamma = 90^o$; *V* = 904.7(14)Å^3; *T* = 296 (2) K; *Z* = 2; ρ_{calcd} =1.195 Mgm^{-3}; $2\theta max$ = 56.56°; $MoK\alpha\lambda$= 0.71073 Å. Fine-focus sealed tube source with graphite monochromator. *R* = 0.410 (for 2760 reflections with $I>2\sigma(I)$); *wR* = 0.0508 which was refined against $|F^2|$ and *S* = 1.456, for 220 parameters and 4239 unique reflections. The structure was obtained by direct methods using SHELXS-97.[29] All non-hydrogen atoms were refined isotropically. The hydrogen atoms were fixed geometrically in the idealized position and refined in the final cycle of refinement as riding over the atoms to which they are bonded. μ = 0.08 mm^{-1}; Minimum/maximum residual electron density –0.161/0.107 eÅ^{-3}.

Crystal structure of Boc-Ala-Valol (16):[28] $C_{13}H_{26}N_2O_4$; A colourless crystal with approximate dimensions 0.45 x 0.35 x 0.30 mm gave orthorhombic space group *P* 21 21 21*; a* = 9.6178(4), *b* =13.321(2), *c* = 25.115(4) Å, $\alpha = \beta = \gamma = 90^o$; *V* = 3217.8(8)Å^3; *T* = 100 (2) K; *Z* = 8; ρ_{calcd} =1.133 Mgm^{-3}; $2\theta max$ = 56.76°; $MoK\alpha\lambda$= 0.71073 Å. Fine-focus sealed tube source with graphite monochromator. *R* = 0.0580 (for 5149 reflections with $I>2\sigma(I)$); *wR* = 0.1345 which was refined against $|F^2|$ and *S* = 0.851, for 357 parameters and 7971 unique reflections. The structure was obtained by direct methods using SHELXS-97.[29] All non-hydrogen atoms were refined isotropically. The hydrogen atoms were fixed geometrically in the idealized position and refined in the final cycle of refinement as riding over the atoms to which they are bonded, μ = 0.083 mm^{-1}; Minimum/maximum residual electron density –0.233/0.224 eÅ^{-3}.

TABLE 1

	Residue	ϕ	ψ	ω	$\chi 1$	$\chi 2$	$\chi 3$
3	Val-ol	-96	-68	---	-62/175	---	---
16	Ala1	-82	153	178	--	---	---
		(-75)	(153)	(168)	---	---	---
	Val-ol2	65	47	--	-48/-171		
		(-127)	(139)	---	(67/-161)		

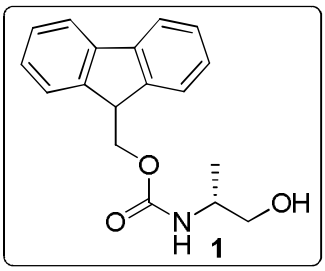


A B

Figure 1: The extended assembly of Fmoc-Valol(A) and Boc-Aal-Valol through intermolecular H-bonding.

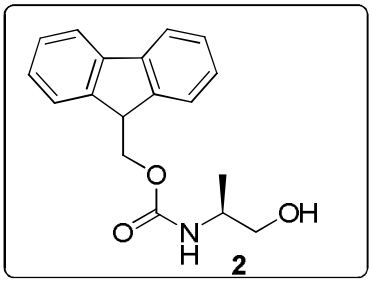
The conformation of Fmoc-Valol was studied in the crystals. The crystal structure of Fmoc-Valol is shown in Fig. 2A. The crystals were obtained after slow evaporation of ethyl acetate. The crystal structure showed that, the OH group of the alcohol is in gauche conformation with Val side chain (g+g- conformation) and the NH group. The torsional angles ϕ and ψ were found to be -96^{o} and -70^{o}, respectively. This energetically unfavorable conformation is stabilized by the intermolecular H-bonding of NH and OH groups with the urethane carbonyl of neighboring molecule. In the case of dipeptide alcohol 16, single crystals were obtained after slow evaporation of methanol solution. The crystal structure is shown in Fig. 1B. Two molecules are appeared in the asymmetric unit with relevant variation in the torsional values. The torsional variables are given in the Table 1. The dipeptide alcohol adapted irregular structure in the crystal packing. Surprisingly, energetically unfavorable *cis* Boc-urethane bond is observed in the molecule B (Fig.1B). The reason for adapting *trans* and *cis* conformations of Boc-urethane in the same molecule is unclear.

Spectroscopic Data for N-protected β-amino alcohols obtained from the N-hydroxysuccinimide method



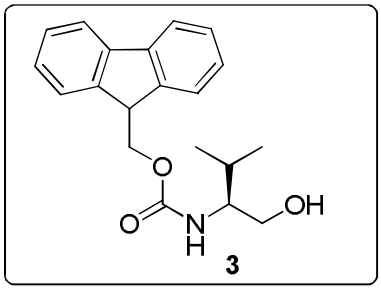
1

(R)-(9H-fluoren-9-yl)methyl 1-hydroxypropan-2-ylcarbamate (1) : white solid (0.505 g, 85%), mp 148-151 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.36 Hz, 2H), 7.58 (d, J = 7.32 Hz, 2H), 7.40 (t, J = 7.50 Hz, 2H), 7.31 (td, J = 0.85 Hz, J = 7.60 Hz, 2H), 4.94 (bs, 1H), 4.42 (d, J = 6.44 Hz, 2H), 4.22 (t, J = 6.44 Hz, 1H), 2.40 (bs, 1H), 1.18 (d, J = 6.43 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.56, 143.85, 141.29, 127.67, 127.02, 124.99, 119.94, 66.78, 48.91, 47.21, 33.87, 25.72, 24.92, 17.23; **MALDI TOF/TOF**- *m/z* calcd. for $C_{18}H_{19}NO_3$ $[M+K]^+$ 336.1002, obsrvd. 335.9430, $[\alpha]_D^{25}$ = +2 (c = 1, MeOH).



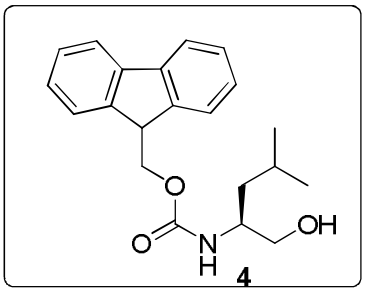
2

(S)-(9H-fluoren-9-yl)methyl 1-hydroxypropan-2-ylcarbamate (2) : white solid (0.534g, 90%); mp 150-153^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, J =7.36 Hz, 2H), 7.60 (d, J = 7.32 Hz, 2H), 7.47 (t, J = 7.52 Hz, 2H), 7.32 (td, J = 0.9 Hz, J = 7.62 Hz, 2H), 4.86 (bs, 1H), 4.43 (d, J = 6.44 Hz, 2H), 4.22 (t, 6.44 Hz, 1H), 3.83 (bs, 1H), 1.18 (d, J = 6.44 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.60, 143.86, 141.32, 127.69, 127.04, 125.01, 119.97, 66.92, 66.62, 48.94, 47.23, 17.34; **MALDI TOF/TOF**- *m/z* calcd. for $C_{18}H_{19}NO_3$ $[M+K]^+$ 336.1002, obsrvd. 335.9779, $[\alpha]_D^{25}$ = -2.0 (c = 1, MeOH).



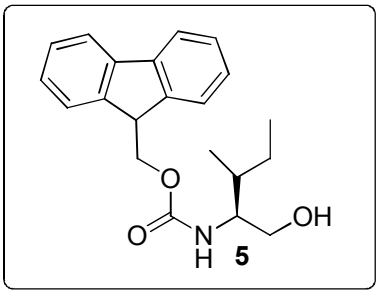
3

(S)-(9H-fluoren-9-yl)methyl 1-hydroxy-3-methylbutan-2-ylcarbamate (3) : white solid (0.520 g, 80%), mp 121-122 ºC, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.33 Hz, 2H), 7.59 (d, J = 7.30 Hz, 2H), 7.45 (t, J = 7.51 Hz, 2H), 7.32 (td, J = 0.9 Hz, J=7.62 Hz, 2H), 4.90 (bs, 1H), 4.45 (d, J = 6.44 Hz, 2H), 4.21 (t, J = 6.44 Hz, 1H), 3.66 (m, 2H), 3.46 (m, 1H), 2.04 (bs, 1H), 1.83 (m, 1H), 0.94 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.05, 143.86, 141.32, 127.65, 127.02, 124.97, 119.94, 66.54, 63.72, 58.53, 47.29, 29.15, 19.47, 18.61; **MALDI TOF/TOF**- *m/z* calcd. for $C_{20}H_{23}NO_3$ $[M+Na]^+$ 348.1576, obsrvd. 348.0117, **$[\alpha]_D^{25}$** = -13.0 (c = 1, MeOH).



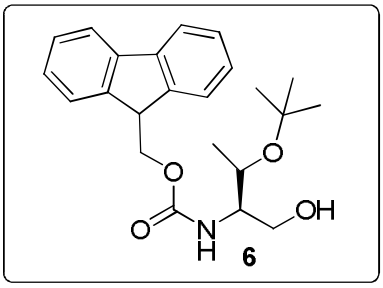
4

(S)-(9H-fluoren-9-yl)methyl 1-hydroxy-4-methylpentan-2-ylcarbamate (4): white solid (0.549 g, 81%), mp 133-135ºC, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.76 Hz, 2H), 7.59 (d, J = 7.32 Hz, 2H), 7.40 (t, J = 7.32 Hz, 2H), 7.32 (t, J = 7.32 Hz, 2H), 4.78 (bs, 1H), 4.45 (d, J = 6.88 Hz, 2H), 4.21 (t, J = 6.88 Hz, 1H), 3.85 (m, 1H), 3.58 (m, 1H), 1.63 (m, 3H), 1.32 (m,1H), 0.92 (dd, J = 2.28 Hz, J = 6.2 Hz, 6H) **;** **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.76, 143.85, 141.33, 127.67, 127.03, 125.0, 119.95, 66.47, 66.05, 51.30, 47.30, 40.34, 24.72, 23.04, 22.10; **MALDI TOF/TOF**- *m/z* calcd. for $C_{21}H_{25}NO_3$ $[M+K]^+$ 378.1472, obsrvd. 377.9655, **$[\alpha]_D^{25}$** = -20.1 (c = 1, MeOH).



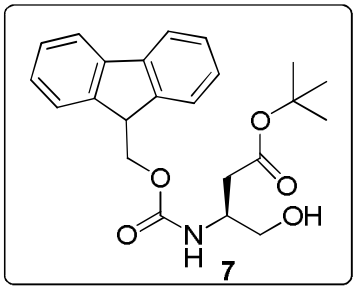
5

(9H-fluoren-9-yl)methyl (2S,3R)-1-hydroxy-3-methylpentan-2-ylcarbamate (5): white solid (0.423 g, 65%), mp 114-116 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.8 Hz, 2H), 7.60 (d, J = 7.32 Hz, 2H), 7.41 (t, J = 7.36Hz,2H), 7.32 (dt, J = 1.36 Hz, J=7.32 Hz, 2H), 4.88 (bd, J = 8.24 Hz,1H) , 4.44 (d, J = 6.4 Hz, 2H), 4.22 (t, J = 6.4 Hz, 1H), 4.12 (bs,1H), 3.68 (m,2H), 3.54 (m, 1H), 1.93 (m, 1H), 1.13 (m,2H), 0.92 (m,6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.00, 143.85, 141.32, 141.29, 127.65, 127.02, 124.98, 119.94, 66.51, 63.49, 57.36, 47.31, 35.83, 25.40, 15.48, 11.35; **MALDI TOF/TOF**- *m/z* calcd. for $C_{21}H_{25}NO_3$ $[M+K]^+$ 378.1472, obsrvd. 377.9658, **$[\alpha]_D^{25}$** = -11.7 (c = 1, MeOH).



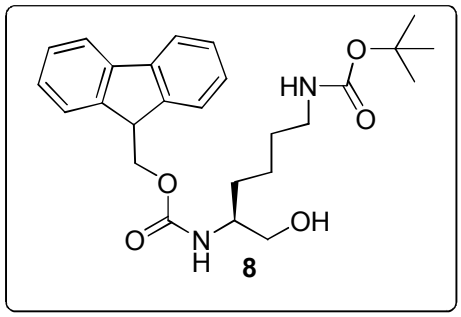
6

(9H-fluoren-9-yl) methyl (2R, 3S)-3-tert-butoxy-1-hydroxybutan-2-ylcarbamate (6): colorless oil (0.651 g, 85%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.76 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 7.32 Hz, 2H), 7.32 (t, J = 7.32 Hz, 2H), 5.28 (bd, J = 7.76 Hz,1H) , 4.41 (m,2H), 4.23 (t, J = 6.88 Hz, 1H), 3.96 (m, 1H), 3.66 (m, 3H), 2.86 (bs,1H), 1.21 (s,9H), 1.16 (d, J = 5.96 Hz, 3H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.28, 144.16, 141.56, 127.94, 127.30, 125.34, 120.23, 74.59, 67.45, 67.06, 63.96, 57.39, 47.53, 28.91, 20.36 ; **MALDI TOF/TOF**- *m/z* calcd. for $C_{23}H_{29}NO_4$ $[M+Na]^+$ 406.1994, obsrvd. 406.0422; **$[\alpha]_D^{25}$** = +6.1 (c = 1, MeOH).



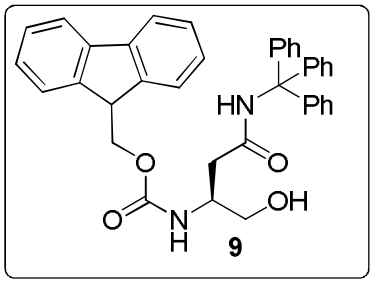
7

(S)-tert-butyl 3-(((9H-fluoren-9-yl)methoxy)carbonylamino)-4-hydroxybutanoate (7): white solid (0.730 g, 92 %), mp 93-96 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 7.32 Hz, 2H), 7.40 (t, *J* = 7.32 Hz, 2H), 7.31 (t, *J* =7.32 Hz, 2H), 5.54 (bs, 1H) , 4.40 (d, *J* =6.92,2H), 4.22 (t, *J* = 6.92 Hz, 1H), 4.03 (m,1H), 3.74 (m,2H), 2.57-2.52 (m,2H), 1.46 (s,9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.10, 156.30, 143.79, 141.28, 127.69, 127.03, 125.02, 119.96, 82.00, 67.95, 66.84, 64.53, 49.92, 47.15, 37.26, 28.00; **MALDI TOF/TOF**- *m/z* calcd. for $C_{23}H_{27}NO_5$ $[M+K]^+$ 436.1526, obsrvd. 435.9662; **$[\alpha]_D^{25}$** = -7.4 (c = 1, MeOH).



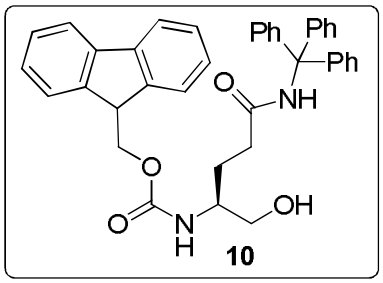
8

(S)-(9H-fluoren-9-yl)methyl6-((tert-butoxycarbonyl)amino)-1-hydroxyhexan-2-ylcarbamate (8): white solid (0.681 g, 75%), mp 136-138 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.77 Hz, 2H), 7.60 (d, *J* = 7.31 Hz, 2H), 7.41 (t, *J* = 7.32 Hz, 2H), 7.32 (t, *J* = 7.32 Hz, 2H), 5.10 (bs, 1H), 4.60 (bs, 1H), 4.40 (d, *J* = 6.90 Hz,2H), 4.21 (t, *J* = 6.90 Hz, 1H), 3.62 (bs,3H), 3.18-3.07 (m, 2H), 2.56 (bs, 1H), 1.67 (m,2H), 1.47 (m,2H), 1.43 (s,9H), 1.36 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.78, 156.53, 144.00, 141.42, 127.77, 127.15, 125.16, 120.05, 80.00, 66.69, 64.78, 53.03, 47.38, 39.61, 30.43, 30.09, 28.50, 22.60; **MALDI TOF/TOF**- *m/z* calcd. for $C_{26}H_{34}N_2O_5$ $[M+Na]^+$ 477.2399, obsrvd. 477.2375 and *m/z* calcd. for $C_{21}H_{26}N_2O_3$ $[M-Boc+H]^+$ 355.2022, obsrvd. 355.1945 , **$[\alpha]_D^{25}$** = -6.9 (c = 1, MeOH).



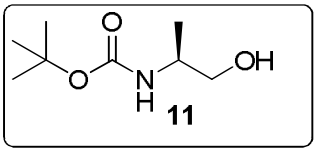
9

(S)-(9H-fluoren-9-yl)methyl 1-hydroxy-4-oxo-4-(tritylamino)butan-2-ylcarbamate (9) : white solid (1.048 g, 90%)[a], mp 155-159 ^{o}C ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74-7.17 (m, 23H), 7.03 (bs,1H), 5.77 (d, J = 7.28 Hz, 1H), 4.32 (m, 2H), 4.15 (t, J = 6.88 Hz, 1H), 3.91 (m, 1H), 3.64 (m, 2H), 3.43 (bs, 1H), 2.71 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.00, 144.07, 141.25, 128.53, 128.02, 127.70, 125.05, 119.96, 80.7, 70.95, 66.88, 49.97, 47.10, 39.50; **MALDI TOF/TOF**- *m/z* calcd. for $C_{38}H_{34}N_2O_4$ $[M+Na]^+$ 605.2416, obsrvd. 605.2652; **$[\alpha]_D^{25}$** = -12.3 (c = 1, MeOH).



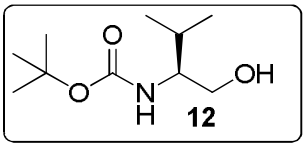
10

(S)-(9H-fluoren-9-yl)methyl 1-hydroxy-5-oxo-5-(tritylamino)pentan-2-ylcarbamate (10) : white solid (1.013 g, 85%), mp 74-77 ^{o}C ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.36 Hz, 2H), 7.56 (d, J = 7.36 Hz,2H), 7.39-7.16 (m,19H), 6.93 (s, 1H), 5.36 (d, J = 8.72 Hz, 1H), 4.50 (bs,1H), 4.37 (m, 2H), 4.17 (t, J = 6.88 Hz, 1H) , 5.53 (m,1H), 3.39 (m, 2H), 2.28 (m,2H), 1.79 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.40, 156.83, 144.54, 143.94, 141.41, 128.73, 128.06, 127.80, 127.18, 125.19, 120.08, 70.75, 66.59, 64.09, 52.76, 47.36, 33.57, 26.40; **MALDI TOF/TOF**- *m/z* calcd. for $C_{39}H_{36}N_2O_4$ $[M+Na]^+$ 619.2573, obsrvd. 619.2513; **$[\alpha]_D^{25}$** = -5.8 (c = 1, MeOH).



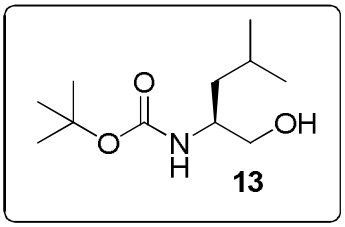
11

(*S*)-*tert*-butyl 1-hydroxypropan-2-ylcarbamate (11) : colorless oil (0.280 g, 80%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.74 (bs,1H), 3.77 (m, 1H), 3.57 (m, 2H), 1.44 (s,9H), 1.15 (d, J = 6.88 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.45, 79.72, 67.15, 48.57, 28.44, 17.39 ; **LCMS/MS** - *m/z* calcd. for $C_8H_{17}NO_3$ $[M+Na]^+$ 198.1106, obsrvd. 198.1172; **$[\alpha]_D^{25}$** = -8.5 (c = 1, MeOH).



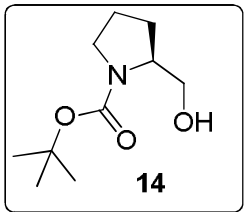
12

(*S*)-*tert*-butyl 1-hydroxy-3-methylbutan-2-ylcarbamate (12): colorless oil (0.312 g, 77 %); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.83 (bs, 1H), 3.52 (m, 2H), 3.43 (m,1H), 3.10 (bs, 1H), 1.82 (m.1H), 0.94 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.97, 79.57, 64.05, 58.04, 29.33, 28.34, 19.58, 18.53 ; **LCMS/MS** - *m/z* calcd. for $C_{10}H_{21}NO_3$ $[M+Na]^+$ 226.1419, obsrvd. 226.1481; **$[\alpha]_D^{25}$** = -17.6 (c = 1, MeOH).



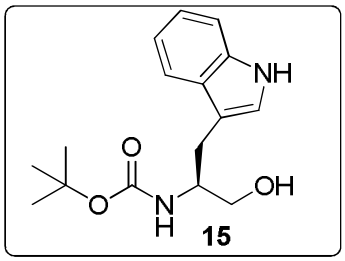
13

***(S)*-*tert*-butyl 1-hydroxy-4-methylpentan-2-ylcarbamate (13) :** colorless oil (0.369 g, 85%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.75 (bs, 1H), 3.71 (m, 1H), 3.55 (m, 2H), 2.98 (bs, 1H), 1.67 (m, 1H), 1.45 (s, 9H), 0.93 (dd, J = 1.4 Hz, J = 6.42 Hz, 6H) ;**^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.64, 79.60, 66.35, 50.97, 40.58, 28.64, 25.00, 24.86, 23.12, 22.27; **LCMS/MS** - *m/z* calcd. for $C_{11}H_{23}NO_3$ $[M+Na]^+$ 240.1576, obsrvd. 240.1544; **$[\alpha]_D^{25}$** = -23.2 (c = 1, MeOH).



14

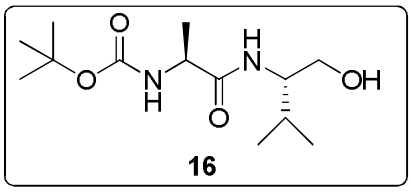
***(S)-tert*-butyl 2-(hydroxymethyl)pyrrolidine-1-carboxylate (14) :** colorless oil (0.313 g, 78%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.98 (m,1H), 3.59 (m, 2H), 3.92 (m, 2H), 2.04 (m,2H), 1.82 (m,2H), 1.47 (s, 9H)`; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.27, 80.35, 67.69, 60.21, 47,63, 30.09, 24.38, 22.03; **LCMS/MS** - *m/z* calcd. for $C_{10}H_{19}NO_3$ $[M+Na]^+$ 224.1263, obsrvd. 224.1223; **[α]** $_D^{25}$ = -45.7 (c = 1, MeOH).



15

***(S)-tert*-butyl 1-hydroxy-3-(1H-indol-3-yl)propan-2-ylcarbamate (15):** white solid (0.414 g, 75%), mp 99-103 ^oC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (bs, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.19 (t, J = 7.32 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 7.00 (d, J = 6.88 Hz, 1H), 4.92 (bs, 1H), 3.97 (m, 1H), 3.60 (m, 2H), 2.97 (d, J = 5.96 Hz, 2H), 2.78 (bs,1H), 1.42 (s, 9H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.60, 136.35, 127.73, 122.90, 122.15, 119.46, 118.93, 111.71, 111.31, 79.83, 64.85, 53.22, 28.46, 27.01; **LCMS/MS** - *m/z* calcd. for $C_{16}H_{22}N_2O_3$ $[M+K]^+$ 329.1267, obsrvd. 328.9698; **[α]** $_D^{25}$ = -22.2 (c = 1, MeOH).

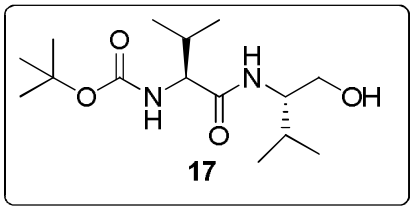
Spectroscopic Data for the Boc-protected peptaibols



16

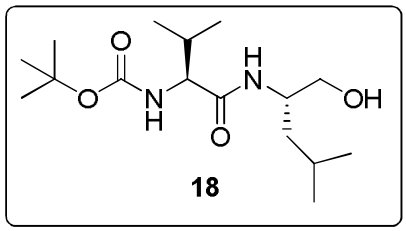
***tert*-butyl (*S*)-1-((S)-1-hydroxy-3-methylbutan-2-ylamino)-1-oxopropan-2-ylcarbamate (16):** off-white solid (0.471 g, 86%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.57 (bs, 1H), 5.14 (bs, 1H),

4.13 (m, 1H), 3.70 (m, 2H), 3.50 (m, 1H), 1.89 (m, 1H), 1.44 (s,9H), 1.37 (d, *J* = 6.88 Hz, 3H), 0.93 (m,6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.59, 155.99, 80.58, 63.76, 57.34, 50.57, 33.98, 28.36, 25.01, 19.61, 18.67; **MALDI TOF/TOF**- *m/z* calcd. for $C_{13}H_{26}N_2O_4$ $[M+Na]^+$ 297.1790, obsrvd. 297.0301; **$[\alpha]_D^{25}$** = -22.2 (c = 1, MeOH).



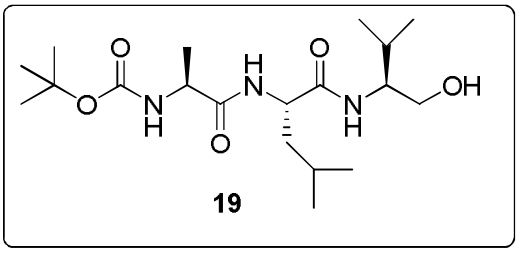
17

***tert*-butyl(*S*)-1-((*S*)-1-hydroxy-3-methylbutan-2-ylamino)-3-methyl-1-oxobutan-2-ylcarbamate (17) :** off-white solid (0.495 g, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.36 (bs, 1H), 5.12 (bs, 1H), 3.84 (m, 1H), 3.67 (m, 3H), 1.89 (m, 2H), 1.44 (s, 9H), 0.96 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.59, 155.99, 80.58, 63.76, 57.34, 50.57, 33.98, 29.01, 28.36, 25.67, 25.01, 19.60, 18.67; **MALDI TOF/TOF**- *m/z* calcd. for $C_{15}H_{30}N_2O_4$ $[M+K]^+$ 341.1843, obsrvd. 341.0229; **$[\alpha]_D^{25}$** = -34.7 (c = 1, MeOH).



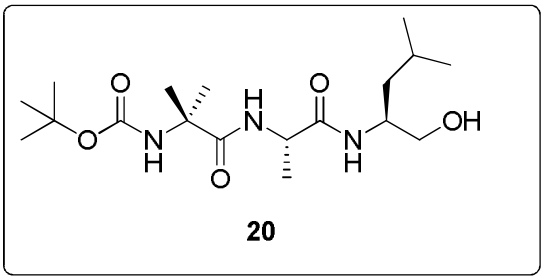
18

***tert*-butyl(*S*)-1-((*S*)-1-hydroxy-4-methylpentan-2-ylamino)-3-methyl-1-oxobutan-2-ylcarbamate (18) :** off-white solid (0.518 g, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.11 (bs,1H), 5.02 (bs,1H), 4.08 (m,1H), 3.84-3.66 (m, 2H), 3.53 (m, 1H), 2.16 (m, 1H), 1.62 (m,2H), 1.45 (s,9H), 1.35 (m, 1H), 0.93 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.27, 156.23, 80.31, 65.93, 60.71, 50.14, 39.99, 30.42, 28.34, 24.87, 23.15, 22.11, 19.43; **MALDI TOF/TOF**- *m/z* calcd. for $C_{16}H_{32}N_2O_4$ $[M+K]^+$ 355.1999, obsrvd. 355.0220; **$[\alpha]_D^{25}$** = -35.9 (c = 1, MeOH).



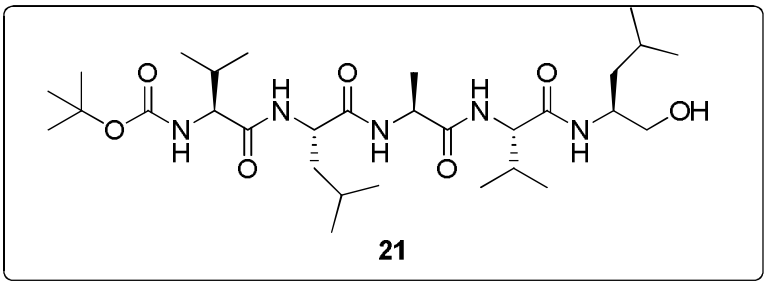
19

***tert*-butyl (*S*)-1-((*S*)-1-((*S*)-1-hydroxy-3-methylbutan-2-ylamino)-4-methyl-1-oxopentan-2-ylamino)-1-oxopropan-2-ylcarbamate (19) :** white solid (0.612 g, 79%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.69 (m,1H), 5.10 (d, J = 5.36 Hz, 1H), 4.36 (m, 1H), 4.22 (d, J = 7.36 Hz, 1H), 4.11 (m, 1H), 3.66 (m, 2H), 3.47 (m, 1H), 3.03 (bs, 1H), 1.71 (m, 4H), 1.45 (s, 9H), 1.36 (d, J = 7.08 Hz, 3H), 1.16-0.89 (m, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.35, 172.43, 156.92, 80.96, 63.86, 57.66, 49.22, 40.51, 34.01, 30.39, 28.93, 25.68, 25.02, 23.12, 19.61, 19.06, 17.85; **MALDI TOF/TOF**- *m/z* calcd. for $C_{19}H_{37}N_3O_5$ $[M+K]^+$ 426.2370, obsrvd. 426.0512; $[\alpha]_D^{25}$ = -34.59 (c = 1, MeOH).



20

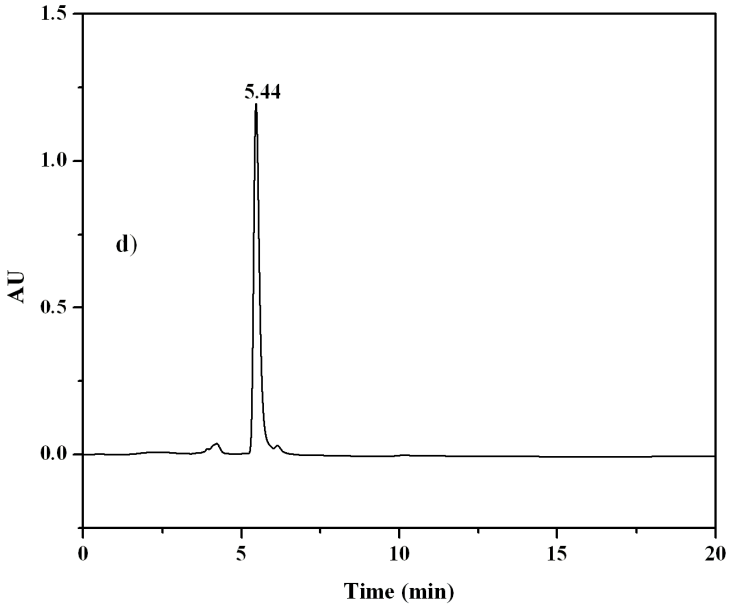
***tert*-butyl 1-((*S*)-1-((*S*)-1-hydroxy-4-methylpentan-2-ylamino)-1-oxopropan-2-ylamino)-2-methyl-1-oxopropan-2-ylcarbamate (20) :** white solid (0.567 g, 76%) ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.07 (bs, 1H), 6.57 (bd, J = 5.04 Hz, 1H), 5.10 (bs, 1H), 4.22 (m, 1H), 3.70 (m, 2H), 3.47 (m, 1H), 3.09 (bs,1H), 1.94-1.68 (m, 12H), 1.46 (s, 9H), 0.90 (m, 6H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.10, 172.58, 81.37, 65.67, 60.51, 57.01, 50.26, 39.55, 34.01, 30.39, 28.31, 25.68, 25.02, 22.27, 17.80, 14.27; **MALDI TOF/TOF**- *m/z* calcd. for $C_{18}H_{35}N_3O_5$ $[M+K]^+$ 412.2214, obsrvd. 412.0356; $[\alpha]_D^{25}$ = -13.6 (c = 1, MeOH).



21

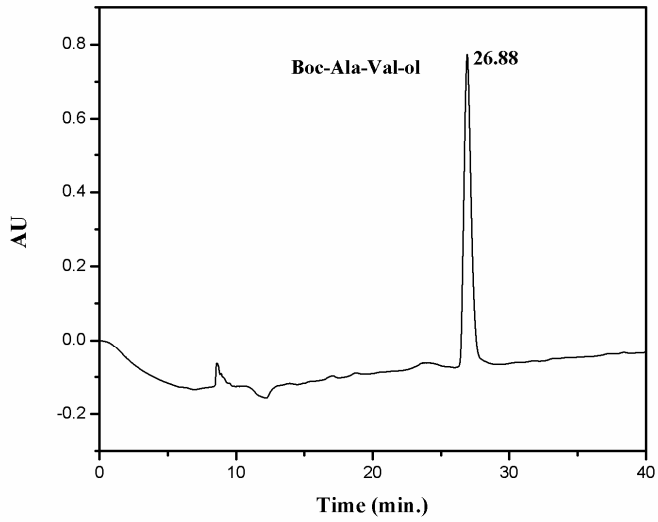
***tert*-butyl (3*S*,6*S*,9*S*,12*S*,15*S*)-15-(hydroxymethyl)-6-isobutyl-12-isopropyl-2,9,17-trimethyl-4,7,10,13-tetraoxo-5,8,11,14-tetraazaoctadecan-3-ylcarbamate:** white solid (0.032 g, 65%); **^{1}H NMR** (400 MHz, DMSO d_6) δ 7.97 (d, J = 8 Hz,1H,-NH of Ala_3), 7.79 (d, J = 8.24,1H, -NH of Leu_2), 7.57 (d, J = 8.72 Hz, 1H,-NH of Val_4), 7.46 (d, J = 8.60 Hz, 1H, -NH of Leu_5), 6.71 (d, J = 8.72 Hz,1H,-NH of Val_1), 4.60 (t, J = 5.96 Hz,1H,-OH), 4.25 (m, 2H,α CH of Leu_2 and Ala_3), 3.97 (m, 1H, α CH of Val_4), 3.68 (m, α CH of Val_1 and β CH of Leu_5), 3.22-3.09 (m, 2H, α CH_2 of Leu_5), 1.85 (m, 2H, β CH of Val_1 and Val_4), 1.52 (m, γ CH of Leu_2 and δ CH of Leu_5), 1.36 (m, 2H, β CH_2 of Leu_2),1.31 (s, 9H, ^{t}Boc of Val_1), 1.20 (m, 2H, γ CH_2 of Leu_5), 1.10 (d, J = 6.88 Hz, 3H, β CH_3 of Ala_3), 0.69-0.81(m, 24H, γ CH_3 of Val_1 and Val_4,δ CH_3 of Leu_2,ω CH_3 of Leu_5); **MALDI TOF/TOF**- *m/z* calcd. for $C_{30}H_{57}N_5O_7$ $[M+K]^+$ 638.3895, obsrvd. 638.1087 and *m/z* calcd. for $C_{30}H_{57}N_5O_7$ $[M-{}^t\text{Boc} + Na]^+$ 522.3631, obsrvd. 522.1472.

Chiral HPLC trace

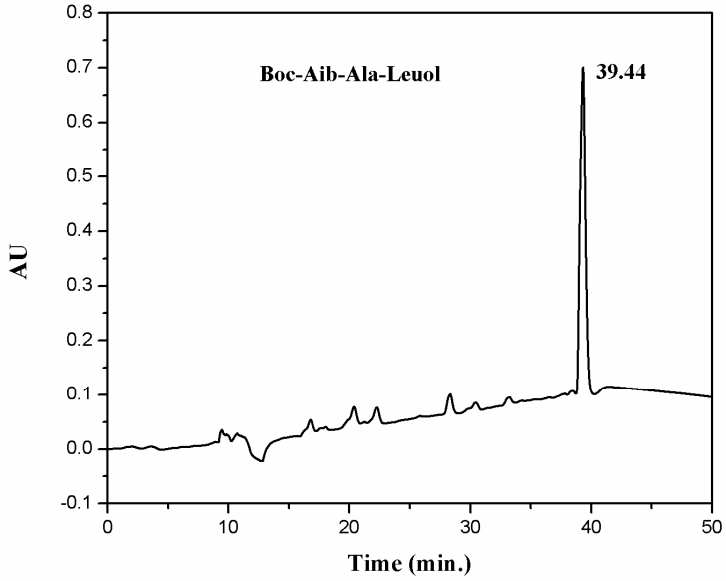


Fmoc-Ile-ol (5): The HPLC was performed on chiral pack AD column using 90% isopropanol in *n*-hexane as a solvent system at isocratic mode with the flow rate of 1 mL/ min

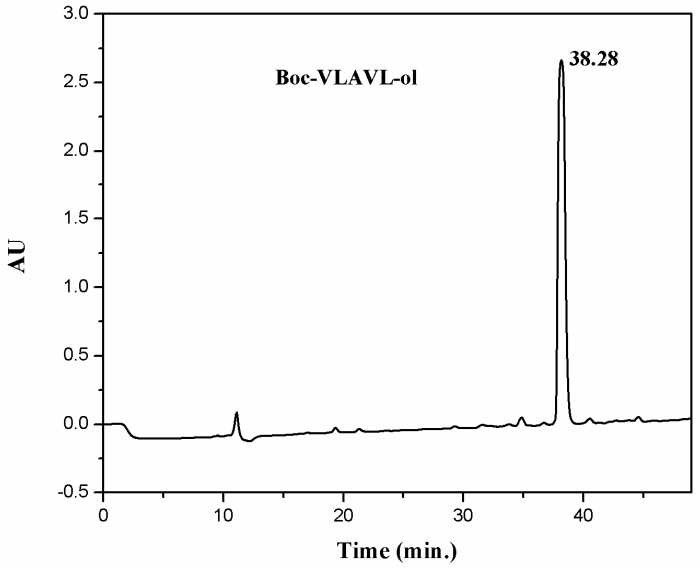
HPLC traces for short peptaibols



Boc-Ala-Valol (16): Used a HPLC gradient system equipped with a detector (220 nm) and a reversed-phase C18 column (4.6 mm × 250 mm; 5 μm). A linear gradient of 60–95% (vol/vol) solvent B in solvent A for 50 min was used. (flow rate 1 mL min − 1; solvent A: 0.1% (vol/vol) TFA in H_2O, solvent B: 0.1% (vol/vol) TFA in MeOH)

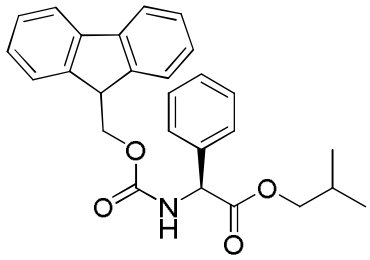


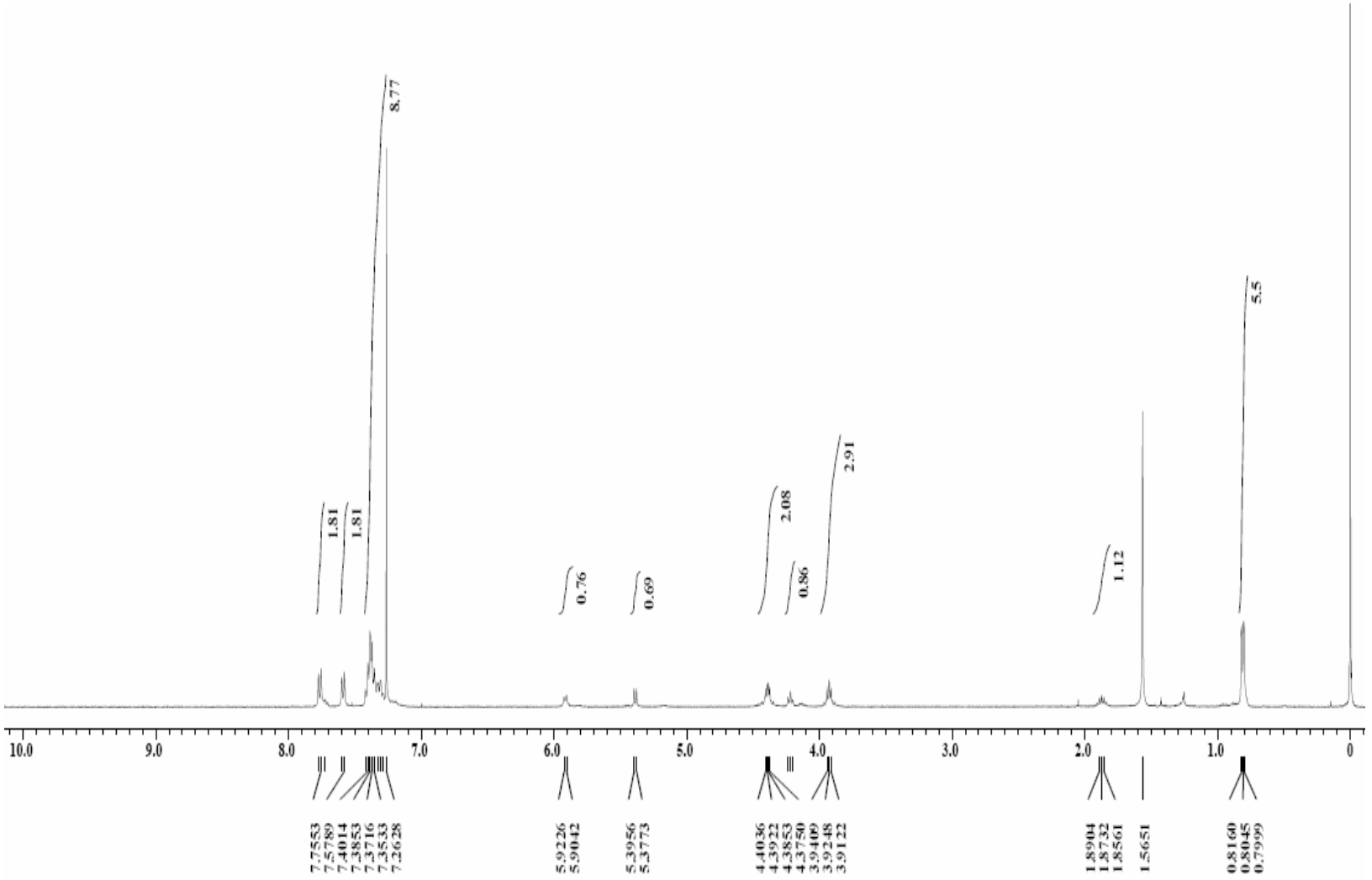
Boc-Aib-Ala-Leuol(20): Used a HPLC gradient system equipped with a detector (220 nm) and a reversed-phase C18 column (4.6 mm × 250 mm; 5 μm A linear gradient of 60–95% (vol/vol) solvent B in solvent A for 50 min was used. (flow rate 1 mL min − 1; solvent A: 0.1% (vol/vol) TFA in H_2O, solvent B: 0.1% (vol/vol) TFA in MeOH)

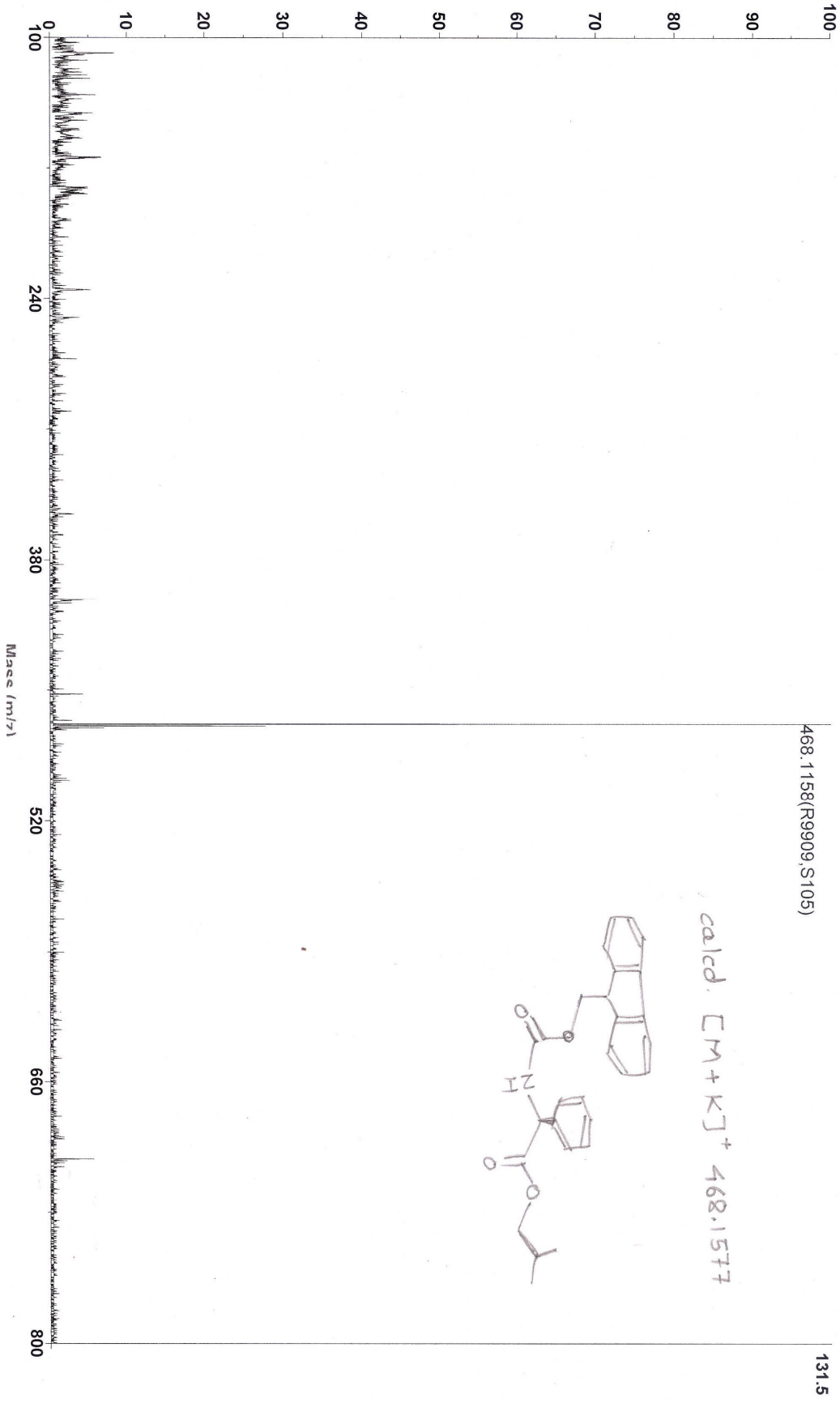


Boc-Val-Leu-Ala-Val-Leuol(21): Reverse HPLC gradient system equipped with a detector (220 nm) and a reversed-phase C18 column (4.6 mm × 250 mm; 5 μm). A linear gradient of 60–95% (vol/vol) solvent B in solvent A for 50 min was used. (flow rate 1 mL min − 1; solvent A: 0.1% (vol/vol) TFA in H_2O, solvent B: 0.1% (vol/vol) TFA in MeOH)

Copies of ^{1}H NMR, ^{13}C NMR and Mass Spectra for Products



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Mass (m/z)
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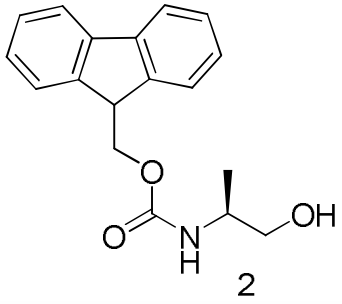
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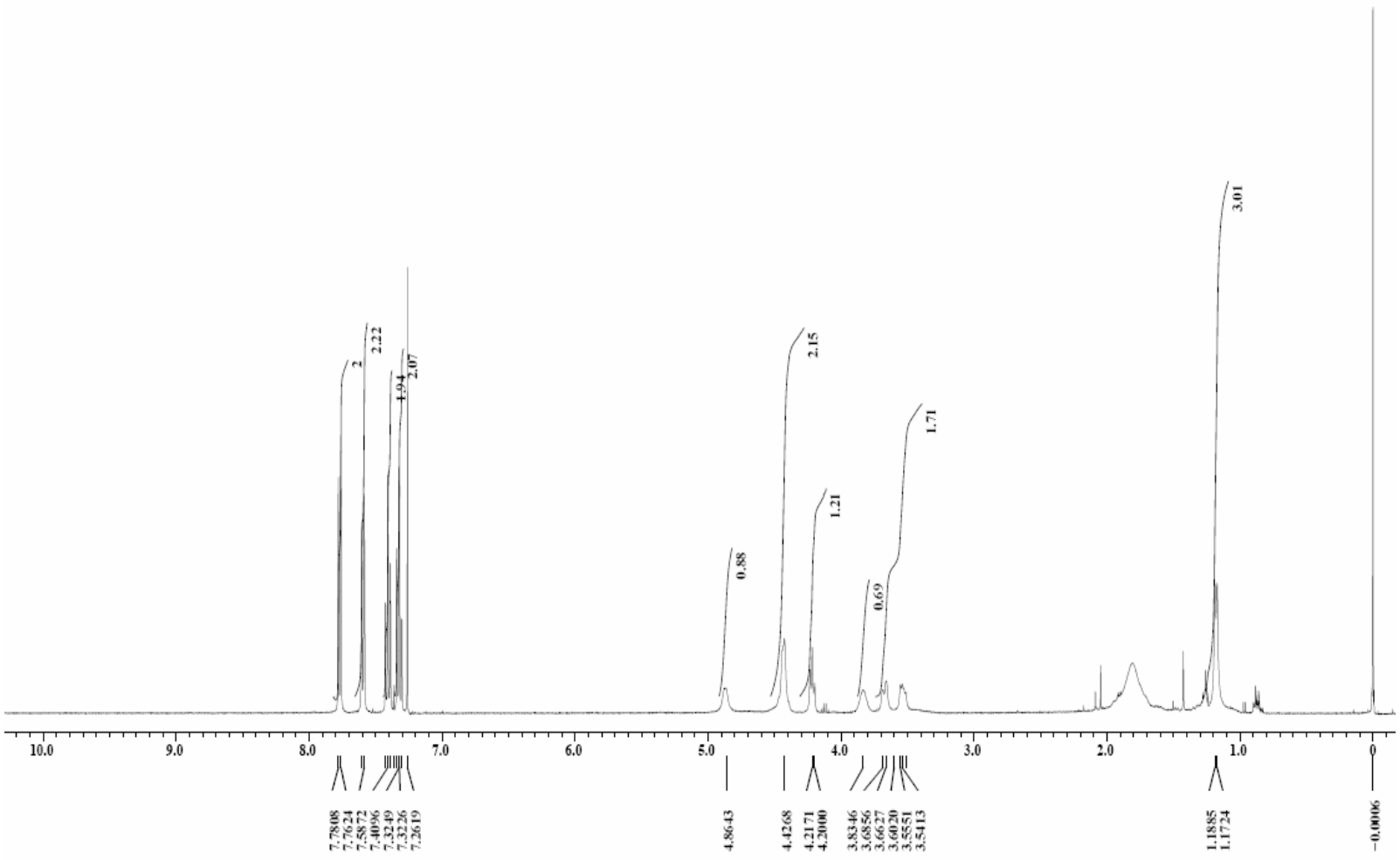
O
N
H
OH

2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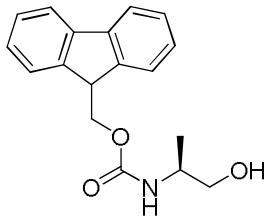
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O
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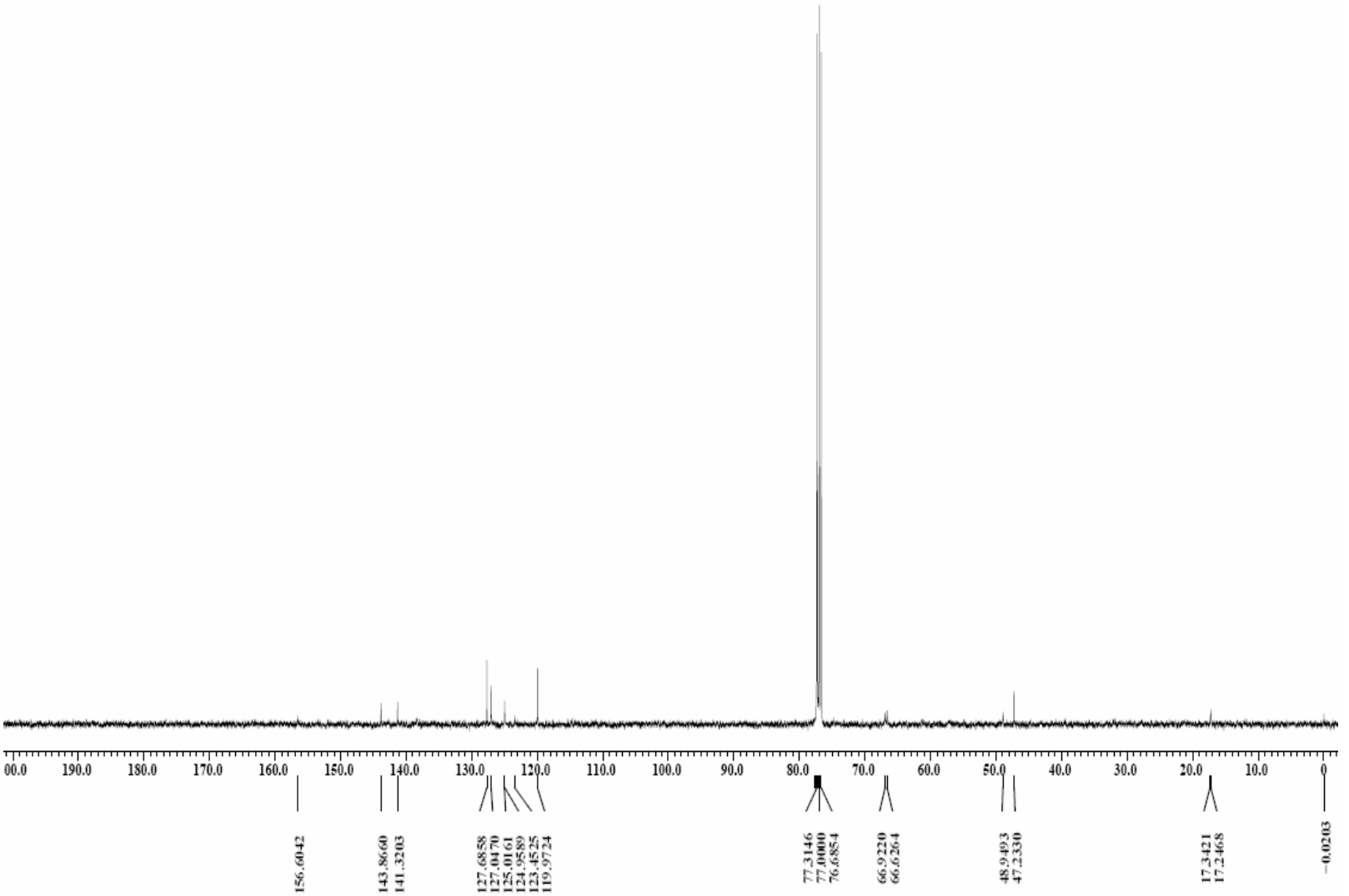
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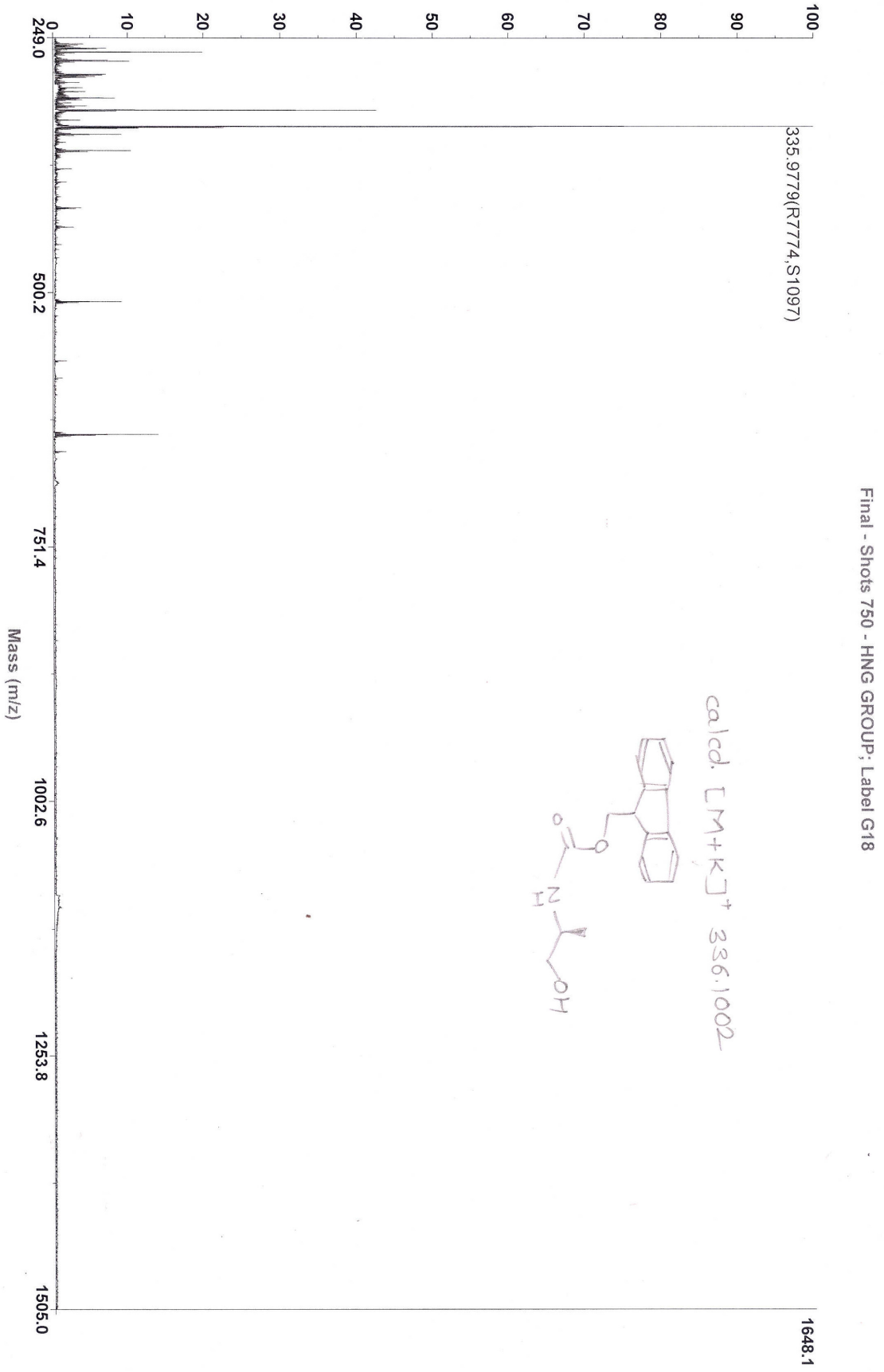
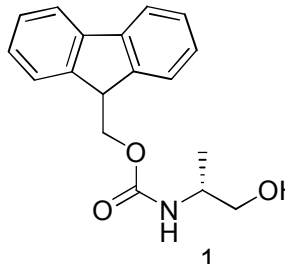
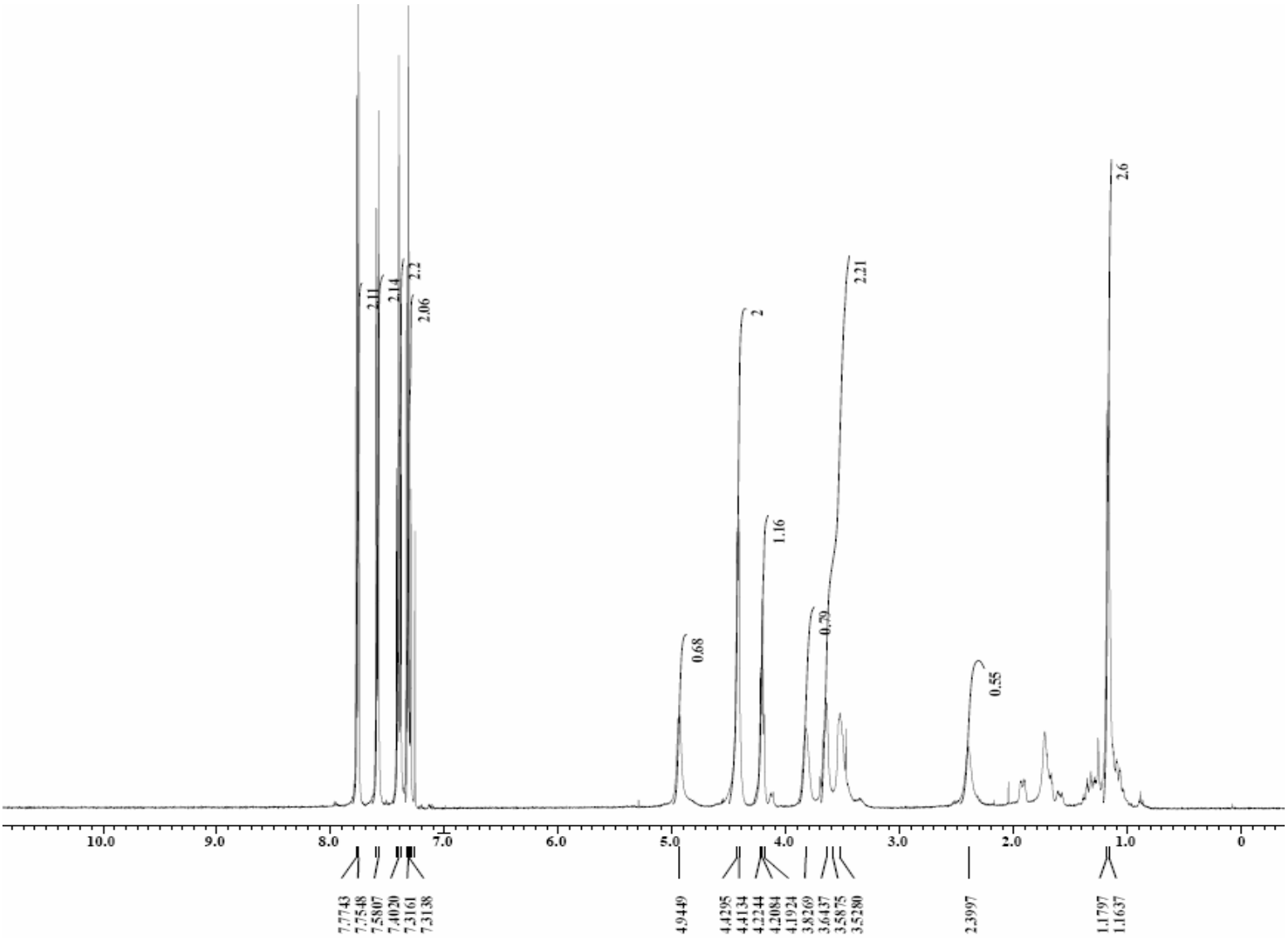
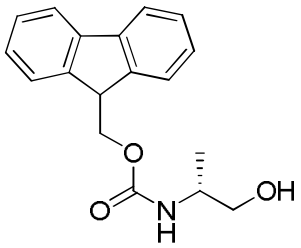

Final - Shots 750 - HNG GROUP; Label G18
335.9779(R7774,S1097)
calcd. [M+K]+ 336.1002
Mass (m/z)
249.0
500.2
751.4
1002.6
1253.8
1505.0
1648.1


O
O
N
H
OH

1


2.11
2.14
2.2
2.06
2
2.21
2.6
1.16
0.68
0.79
0.55
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7743
7.7548
7.5807
7.4020
7.3161
7.3138
4.9449
4.4295
4.4134
4.2244
4.2084
4.1924
3.8269
3.6437
3.5875
3.5280
2.3997
1.1797
1.1637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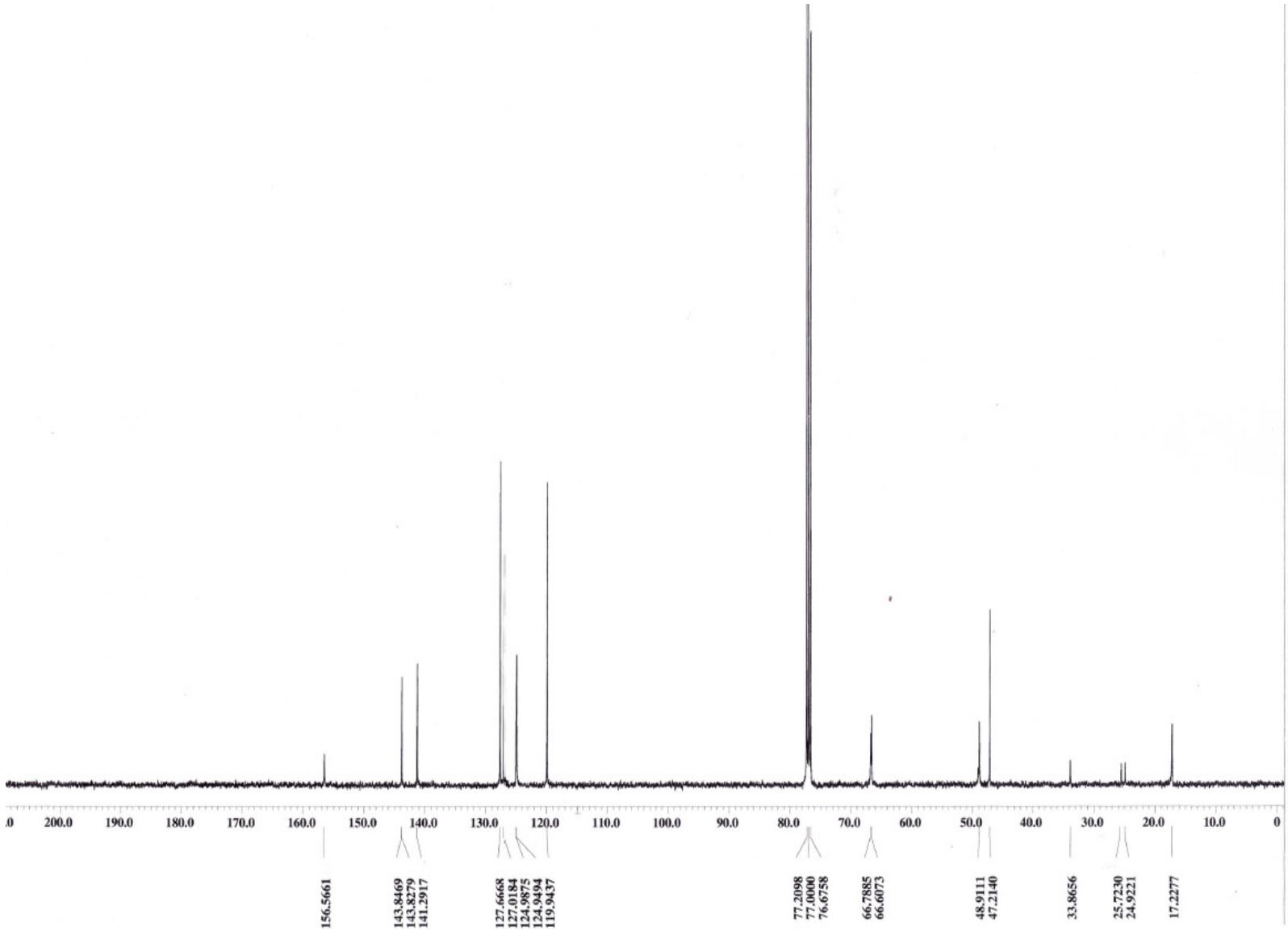
O
N
H
OH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150.0
140.0
130.0
120.0
110.0
100.0
90.0
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70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
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143.8469
143.8279
141.2917
127.6668
127.0184
124.9875
124.9494
119.9437
77.2098
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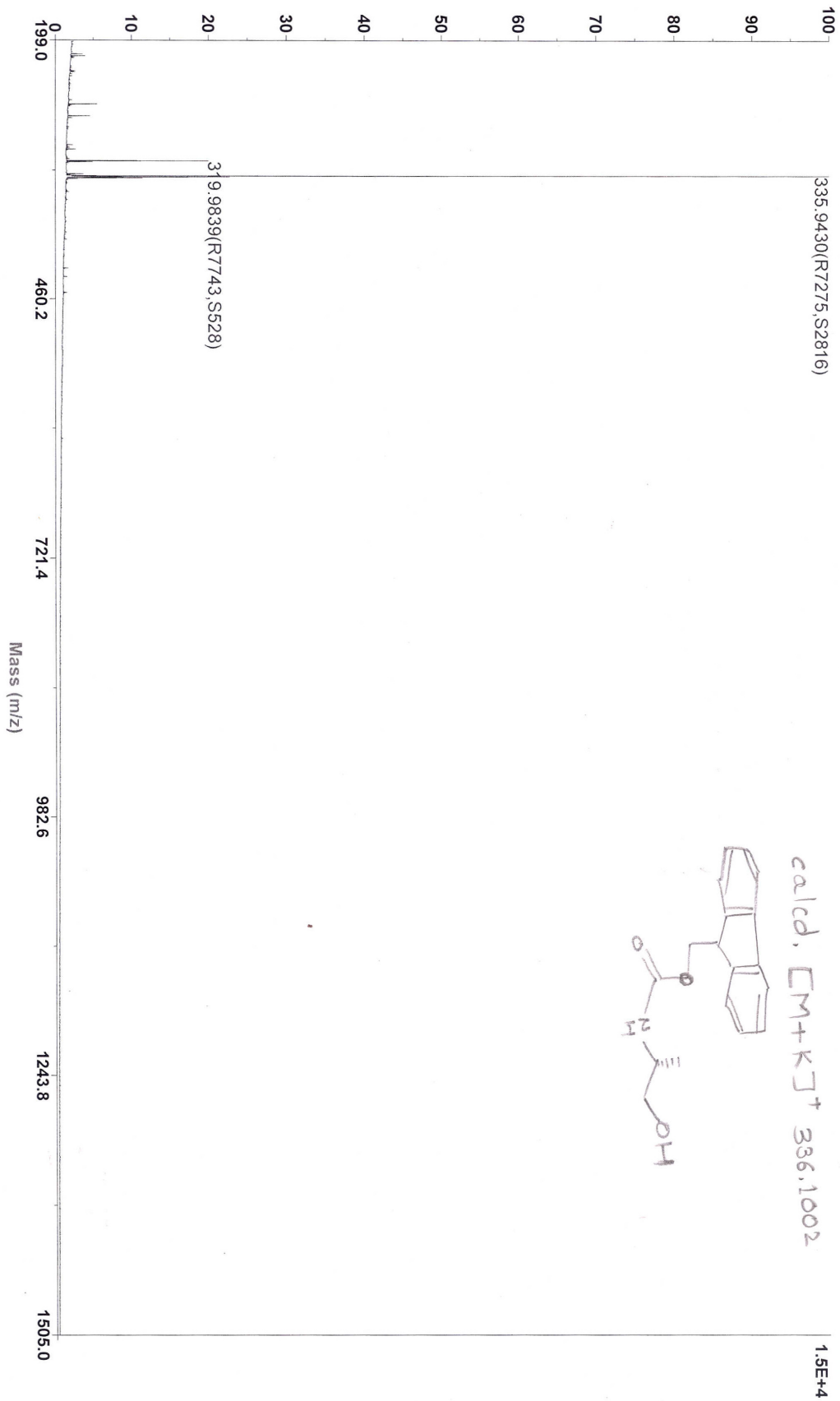
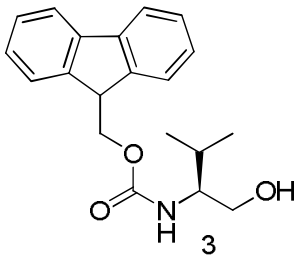
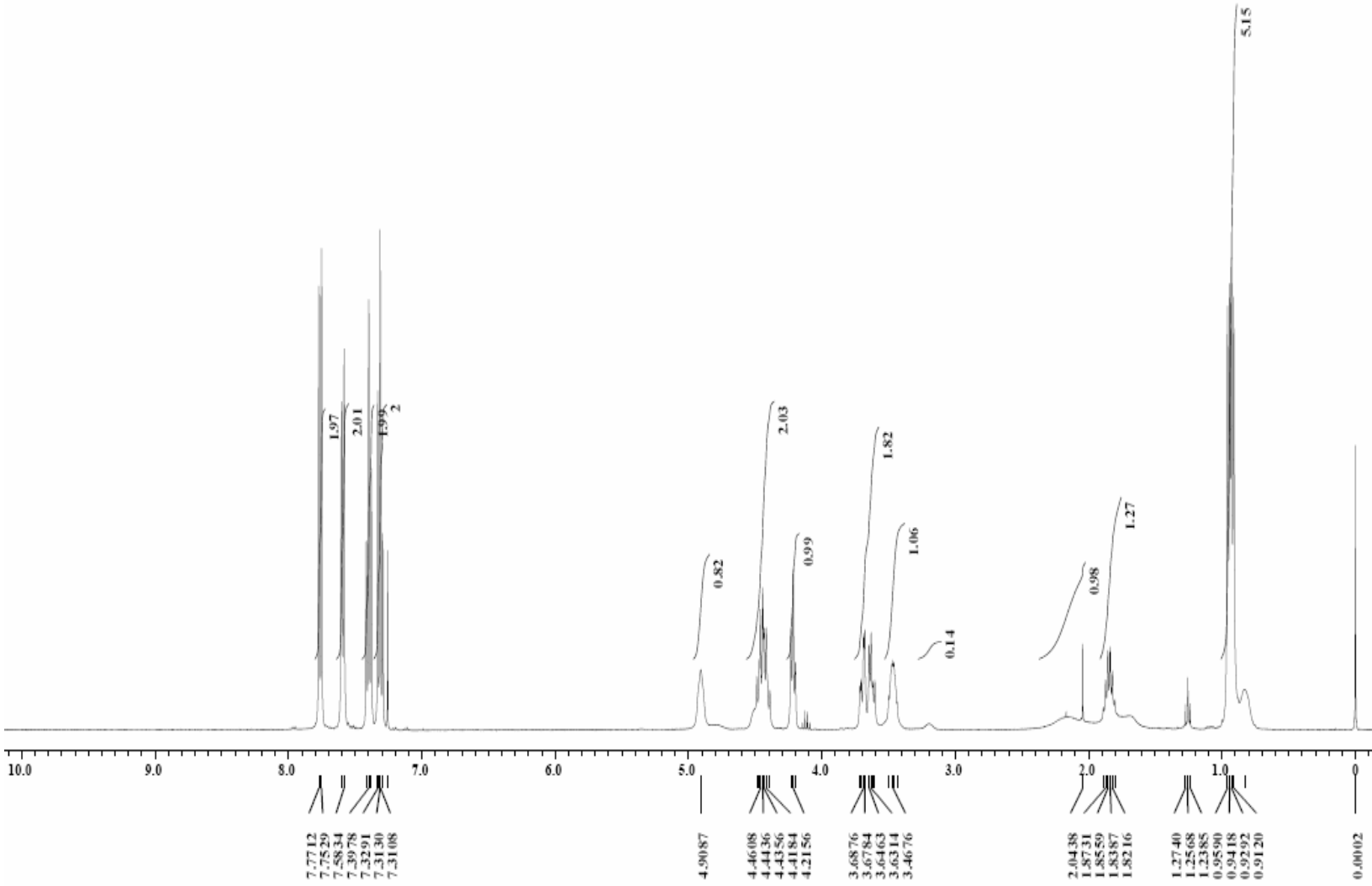
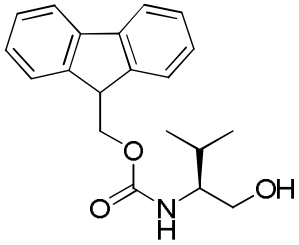
47.2140
33.8656
25.7230
24.9221
17.2277

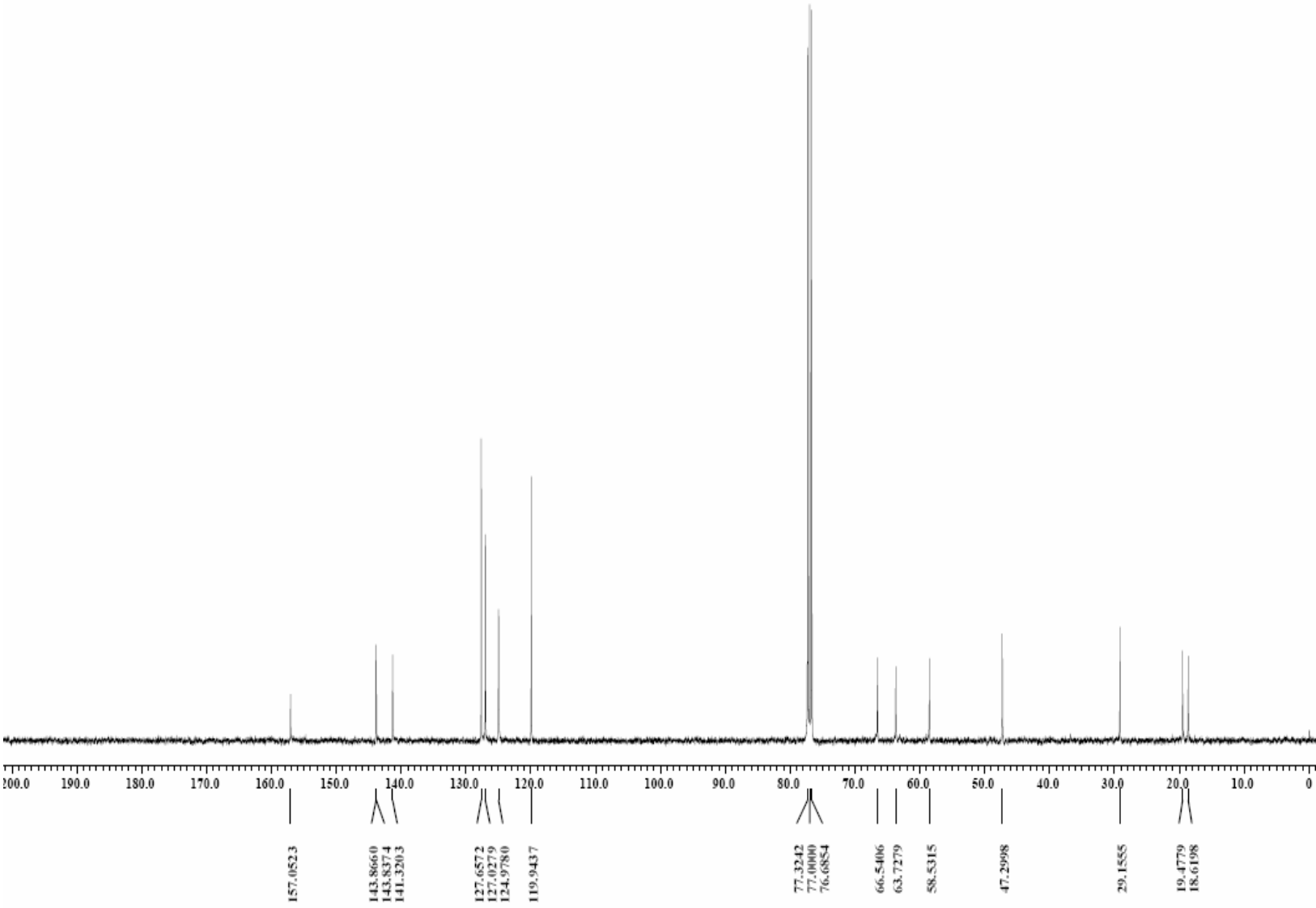

Final - Shots 750 - HNG GROUP; Label E2
335.9430(R7275,S2816)
319.9839(R7743,S528)
calcd. [M+K]+ 336.1002
Mass (m/z)
199.0
460.2
721.4
982.6
1243.8
1505.0
1.5E+4


O
O
N
H
OH

3


1.97
2.01
1.99
2
0.82
2.03
0.99
1.82
1.06
0.14
0.98
1.27
5.15
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.77 12
7.75 29
7.58 34
7.39 78
7.32 91
7.31 30
7.31 08
4.90 87
4.46 08
4.44 36
4.43 56
4.41 84
4.21 56
3.68 76
3.67 84
3.64 63
3.63 14
3.46 76
2.04 38
1.87 31
1.85 59
1.83 87
1.82 16
1.27 40
1.25 68
1.23 85
0.95 90
0.94 18
0.92 92
0.91 20
0.00 02


O
O
N
H
OH


200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
157.0523
143.8660
143.8374
141.3203
127.6572
127.0279
124.9780
119.9437
77.3242
77.0000
76.6854
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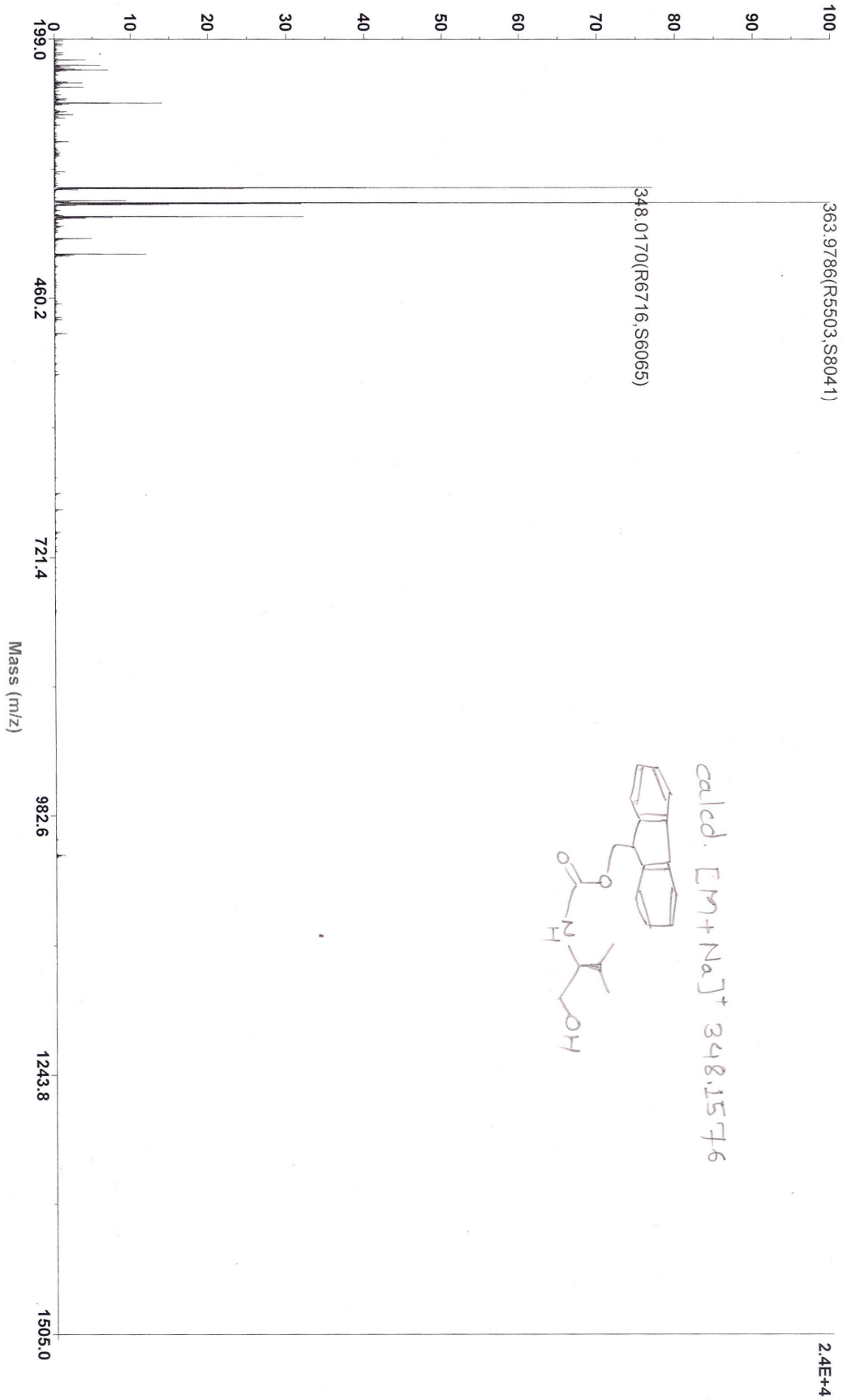
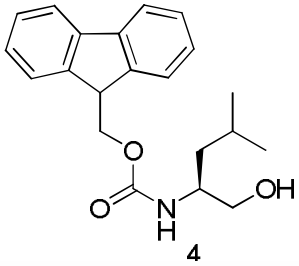
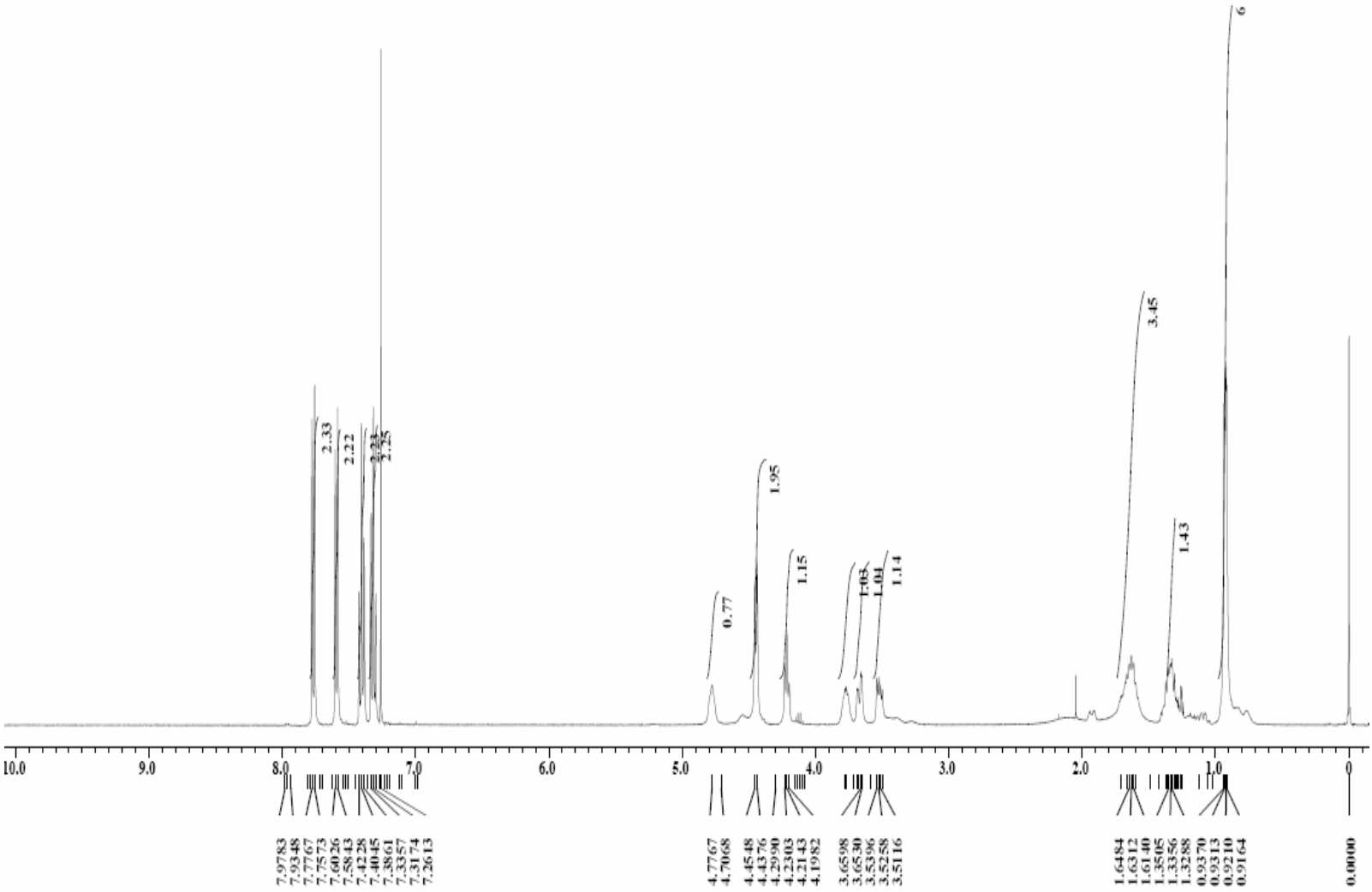
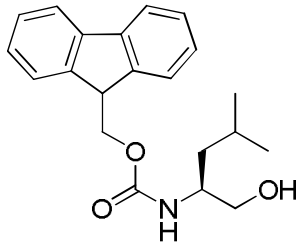
58.5315
47.2998
29.1555
19.4779
18.6198

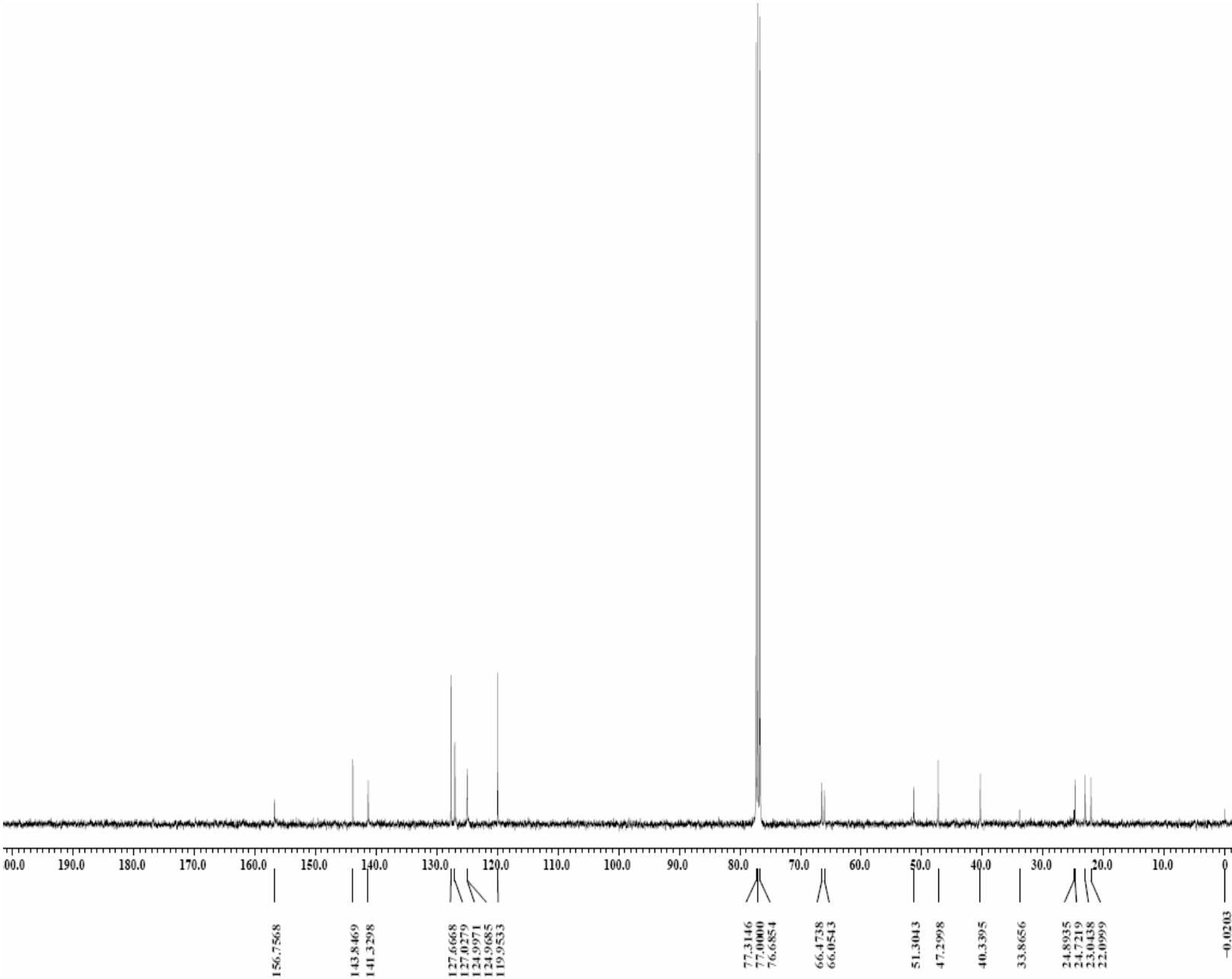

Final - Shots 750 - HNG GROUP; Label G15
363.9786(R5503,S8041)
348.0170(R6716,S6065)
calcd. [M+Na]+ 348.1576
Mass (m/z)
199.0
460.2
721.4
982.6
1243.8
1505.0
2.4E+4

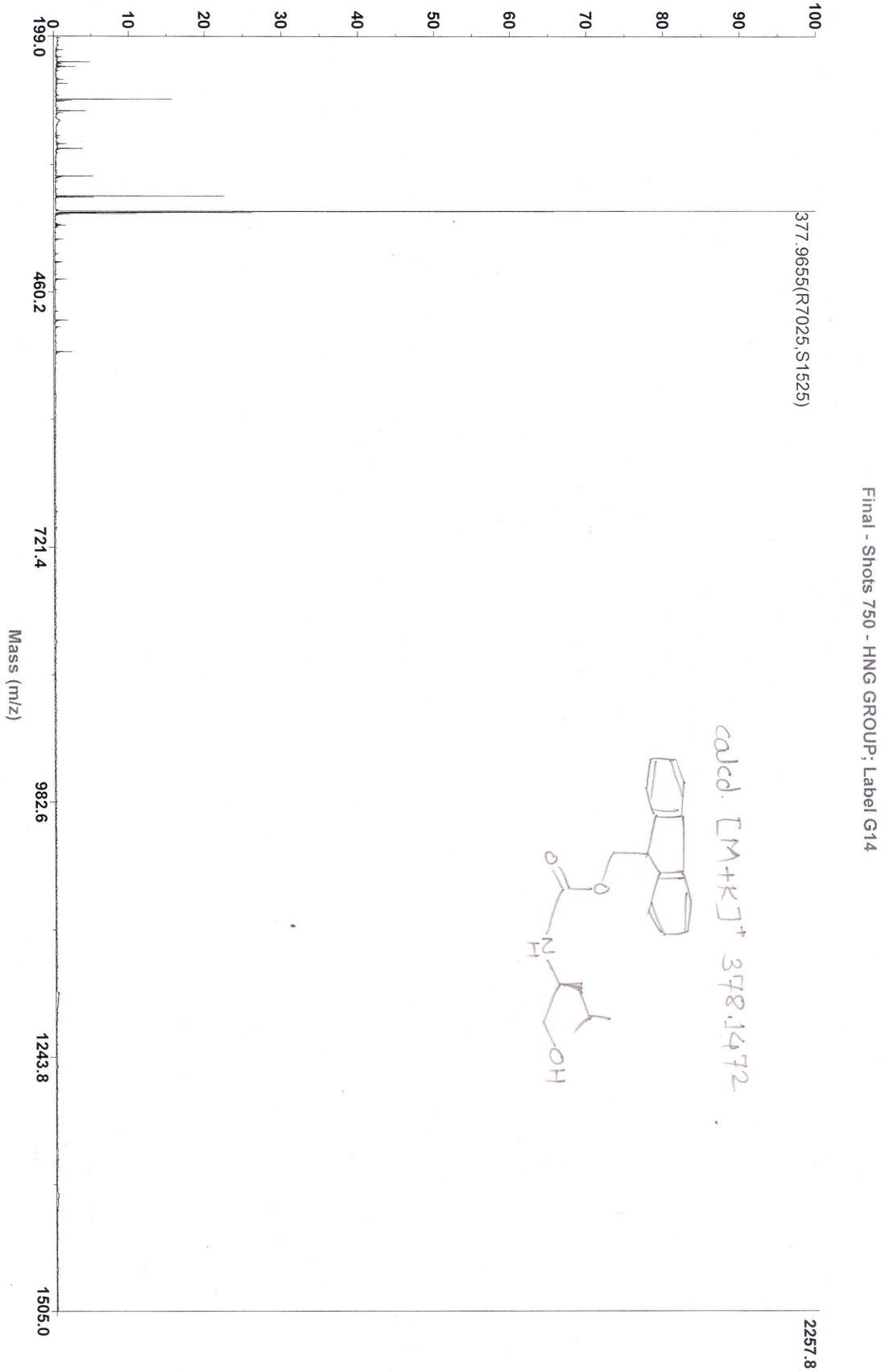

O
O
N
H
OH

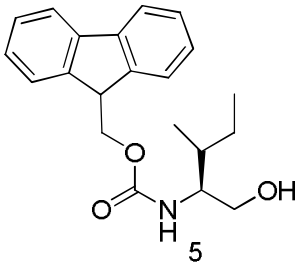
4

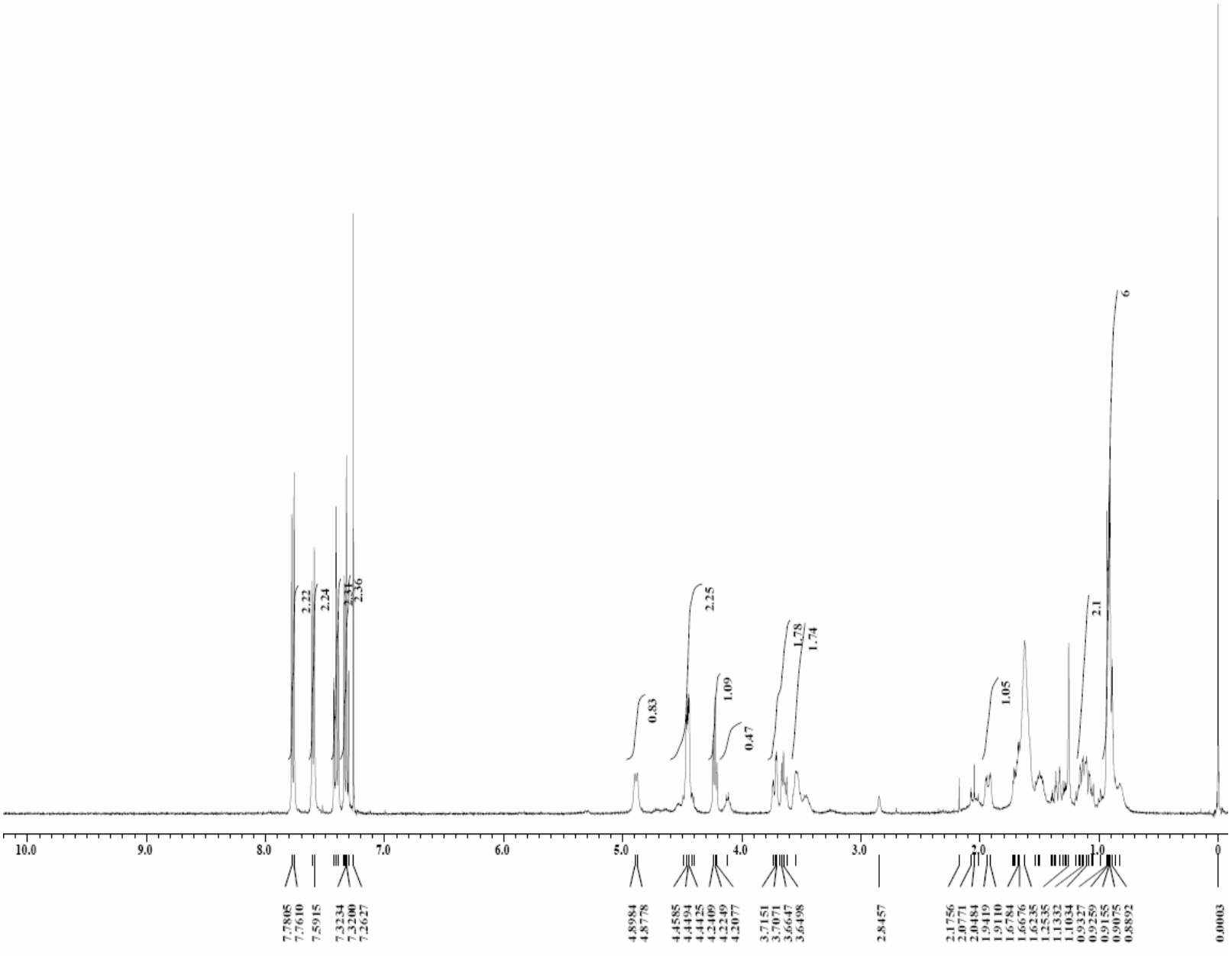

2.33
2.22
2.23
2.25
1.95
1.15
0.77
1.03
1.01
1.14
3.45
1.43
6
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.9783
7.9348
7.7767
7.7573
7.6026
7.5843
7.4228
7.4045
7.3861
7.3357
7.3174
7.2613
4.7767
4.7068
4.4548
4.4376
4.2990
4.2303
4.2143
4.1982
3.6598
3.6530
3.5396
3.5258
3.5116
1.6484
1.6312
1.6140
1.3505
1.3356
1.3288
0.9370
0.9313
0.9210
0.9164
0.0000

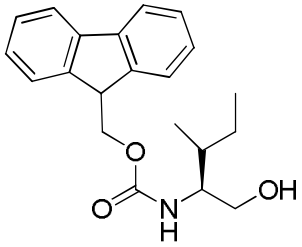

O
O
N
H
OH

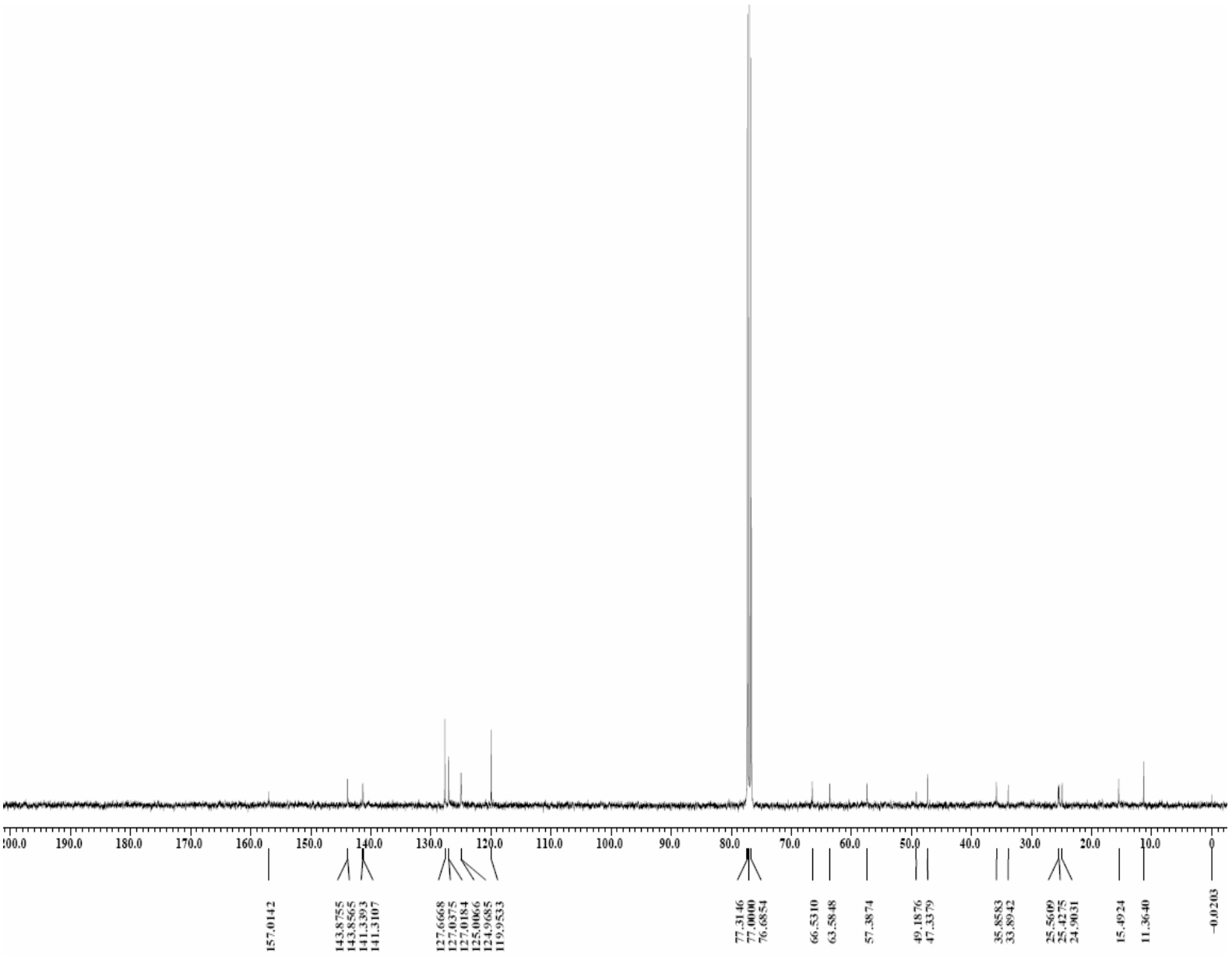

00.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.7568
143.8469
141.3298
127.6668
127.0279
124.9971
124.9685
119.9533
77.3146
77.0000
76.6854
66.4738
66.0543
51.3043
47.2998
40.3395
33.8656
24.8935
24.7219
23.0438
22.0999
-0.0203

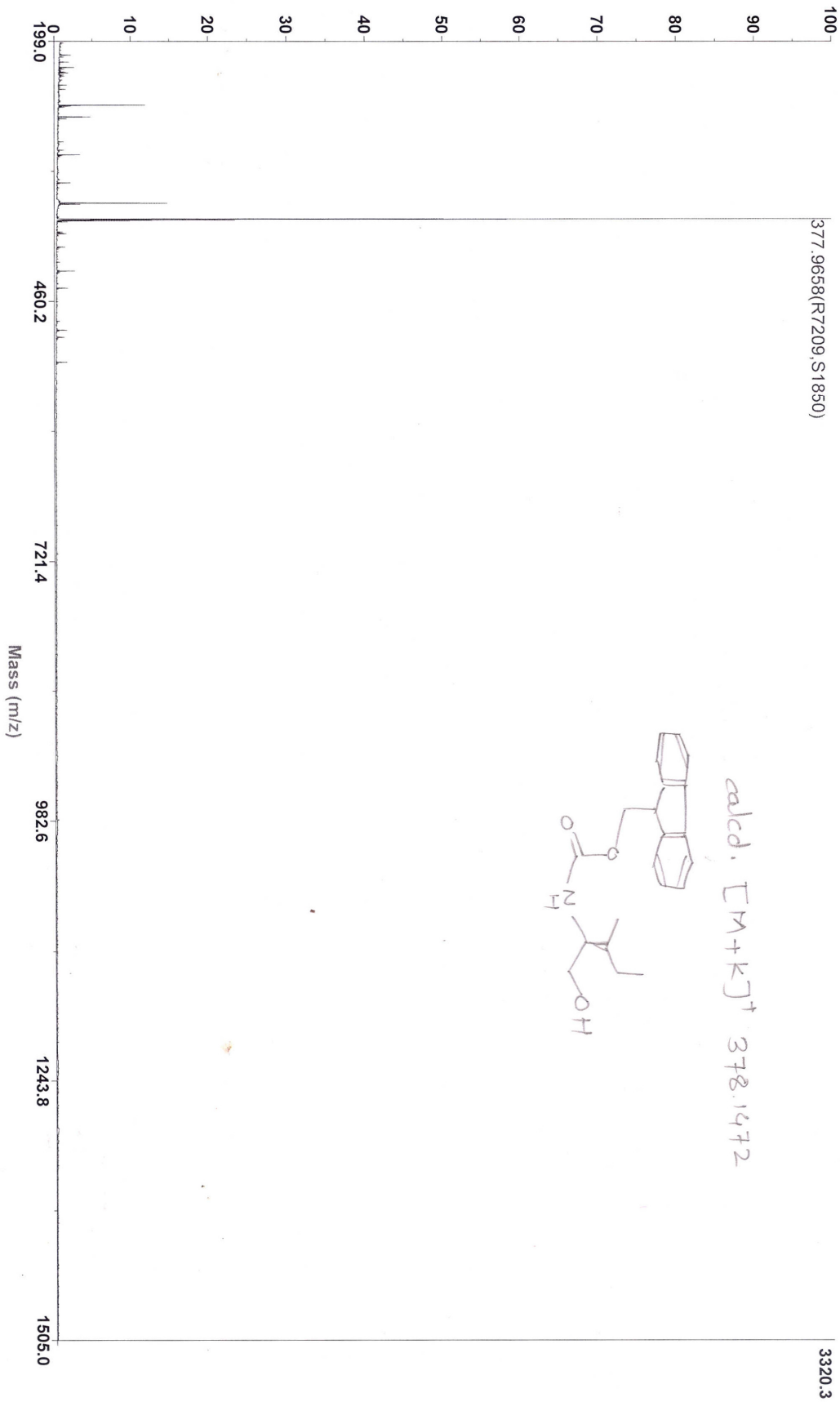

Final - Shots 750 - HNG GROUP; Label G14
377.9655(R7025,S1525)
calcd. [M+K]+ 378.1472
Mass (m/z)
199.0
460.2
721.4
982.6
1243.8
1505.0
2257.8

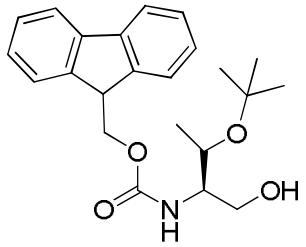

O
O
N
H
OH
5


2.22
2.24
2.31
2.36
0.83
2.25
1.09
0.47
1.78
1.74
1.05
2.1
6
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7805
7.7610
7.5915
7.3234
7.3200
7.2627
4.8984
4.8778
4.4585
4.4494
4.4425
4.2409
4.2249
4.2077
3.7151
3.7071
3.6647
3.6498
2.8457
2.1756
2.0771
2.0484
1.9419
1.9110
1.6784
1.6676
1.6235
1.2535
1.1332
1.1034
0.9327
0.9259
0.9155
0.9075
0.8892
0.0003

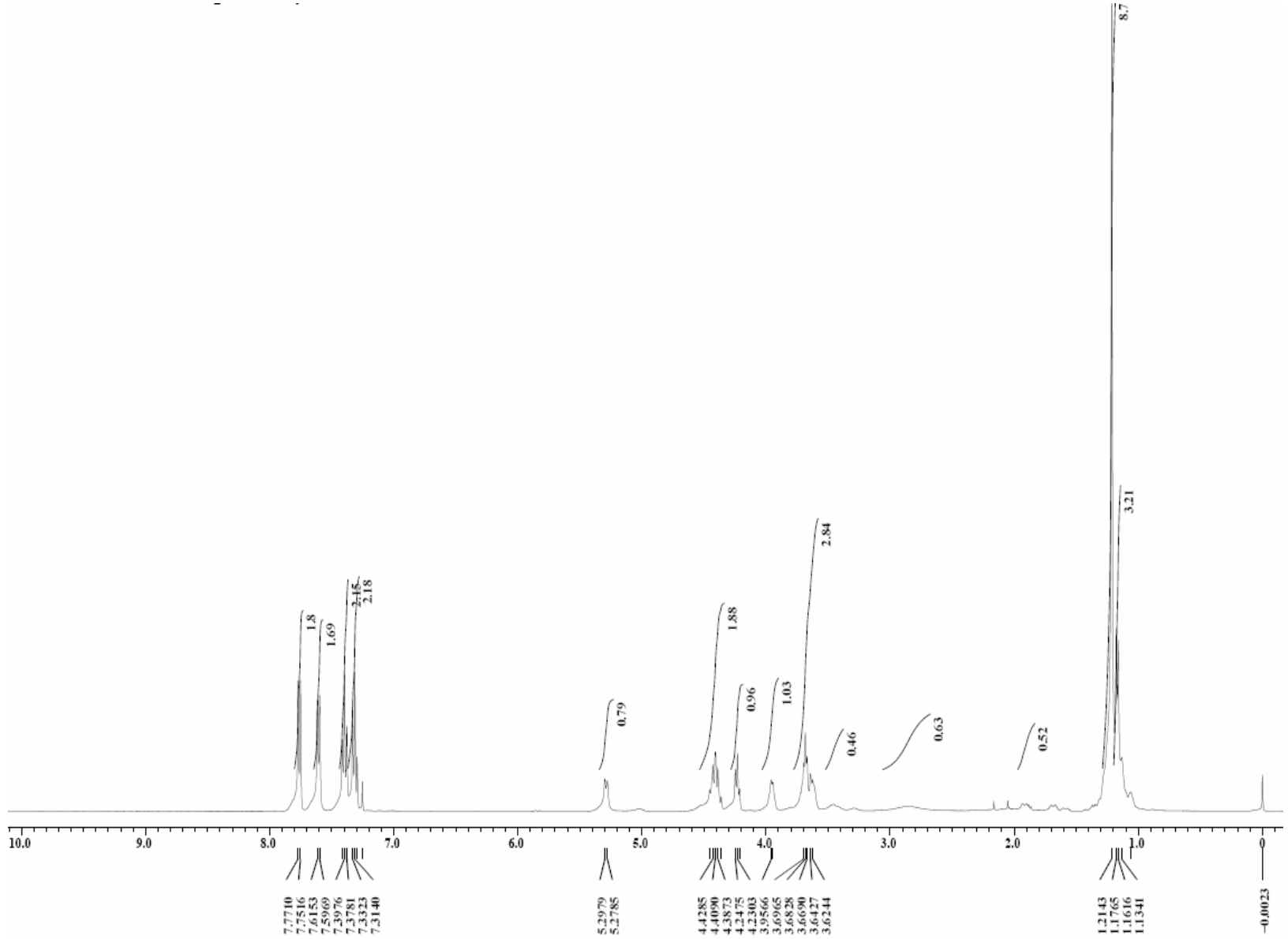

O
O
N
H
OH

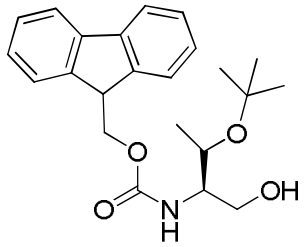

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
157.0142
143.8755
143.8565
141.3393
141.3107
127.6668
127.0375
127.0184
125.0066
124.9685
119.9533
77.3146
77.0000
76.6854
66.5310
63.5848
57.3874
49.1876
47.3379
35.8583
33.8942
25.5609
25.4275
24.9031
15.4924
11.3640
-0.0203

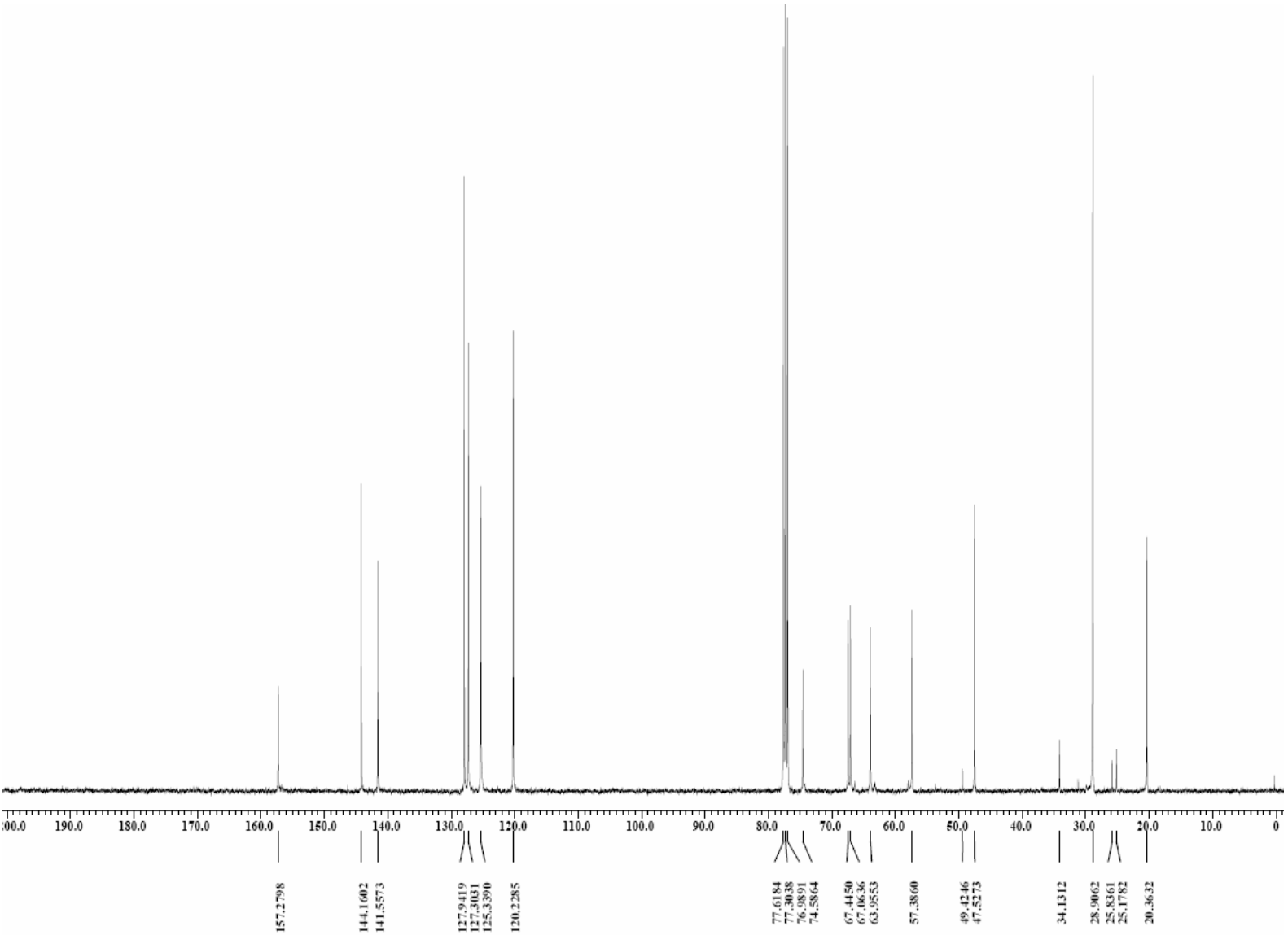

Final - Shots 750 - HNG GROUP; Label G14
377.9658(R7209,S1850)
100
90
80
70
60
50
40
30
20
10
0
199.0
460.2
721.4
982.6
1243.8
1505.0
3320.3
Mass (m/z)
calcd. [M+K]+ 378.1472
O
O
N
H
OH


O
O
O
N
H
OH

6


8.7
3.21
2.84
2.18
2.16
1.88
1.8
1.69
1.03
0.96
0.79
0.63
0.52
0.46
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7710
7.7516
7.6153
7.5969
7.3976
7.3781
7.3323
7.3140
5.2979
5.2785
4.4285
4.4090
4.3873
4.2475
4.2303
3.9566
3.6965
3.6828
3.6690
3.6427
3.6244
1.2143
1.1765
1.1616
1.1341
-0.0023


O
O
O
N
H
OH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160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
157.2798
144.1602
141.5573
127.9419
127.3031
125.3390
120.2285
77.6184
77.3038
76.9891
74.5864
67.4450
67.0636
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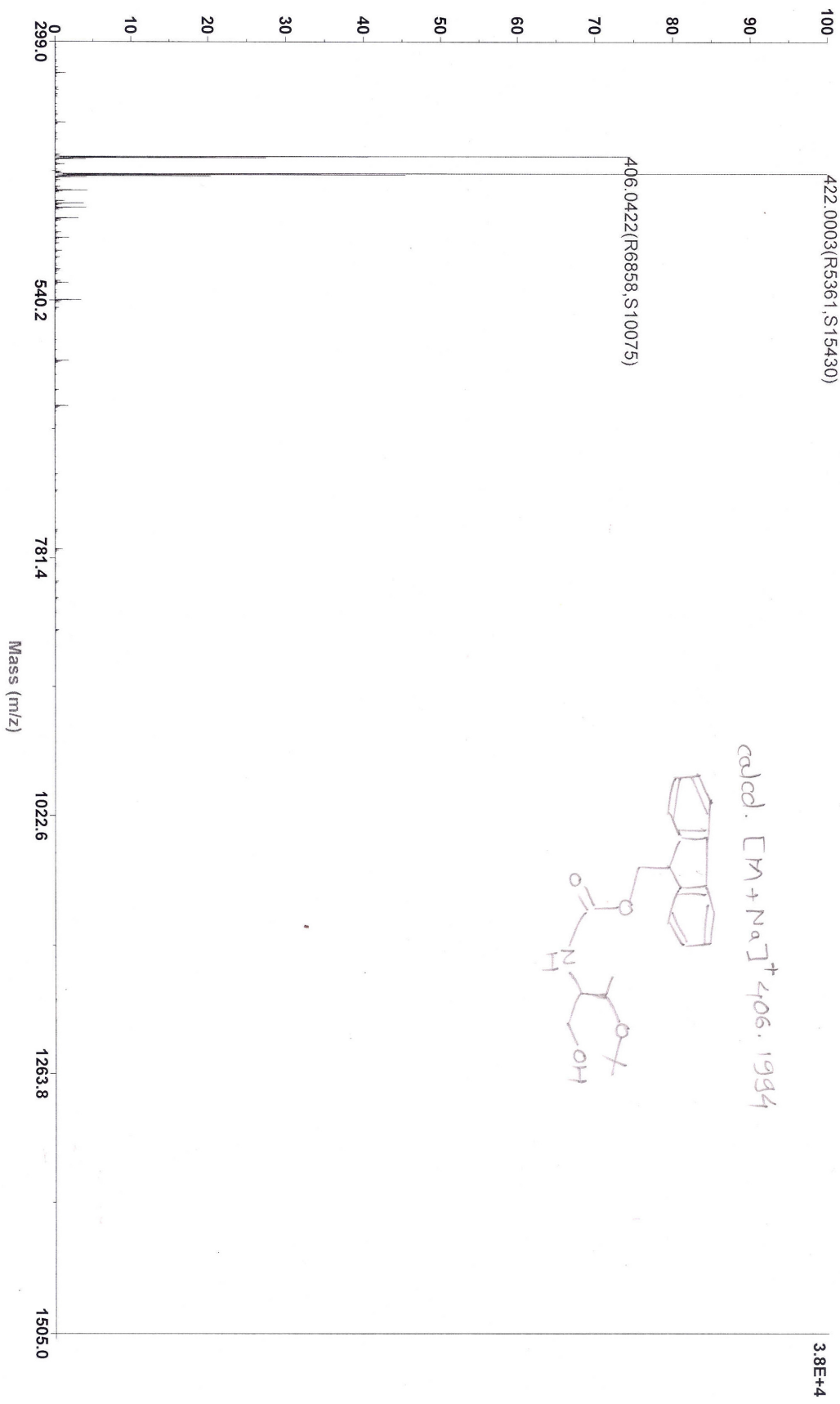
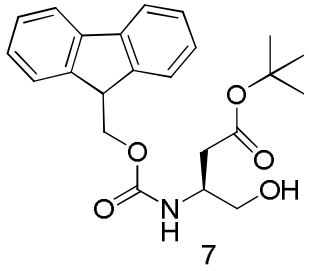
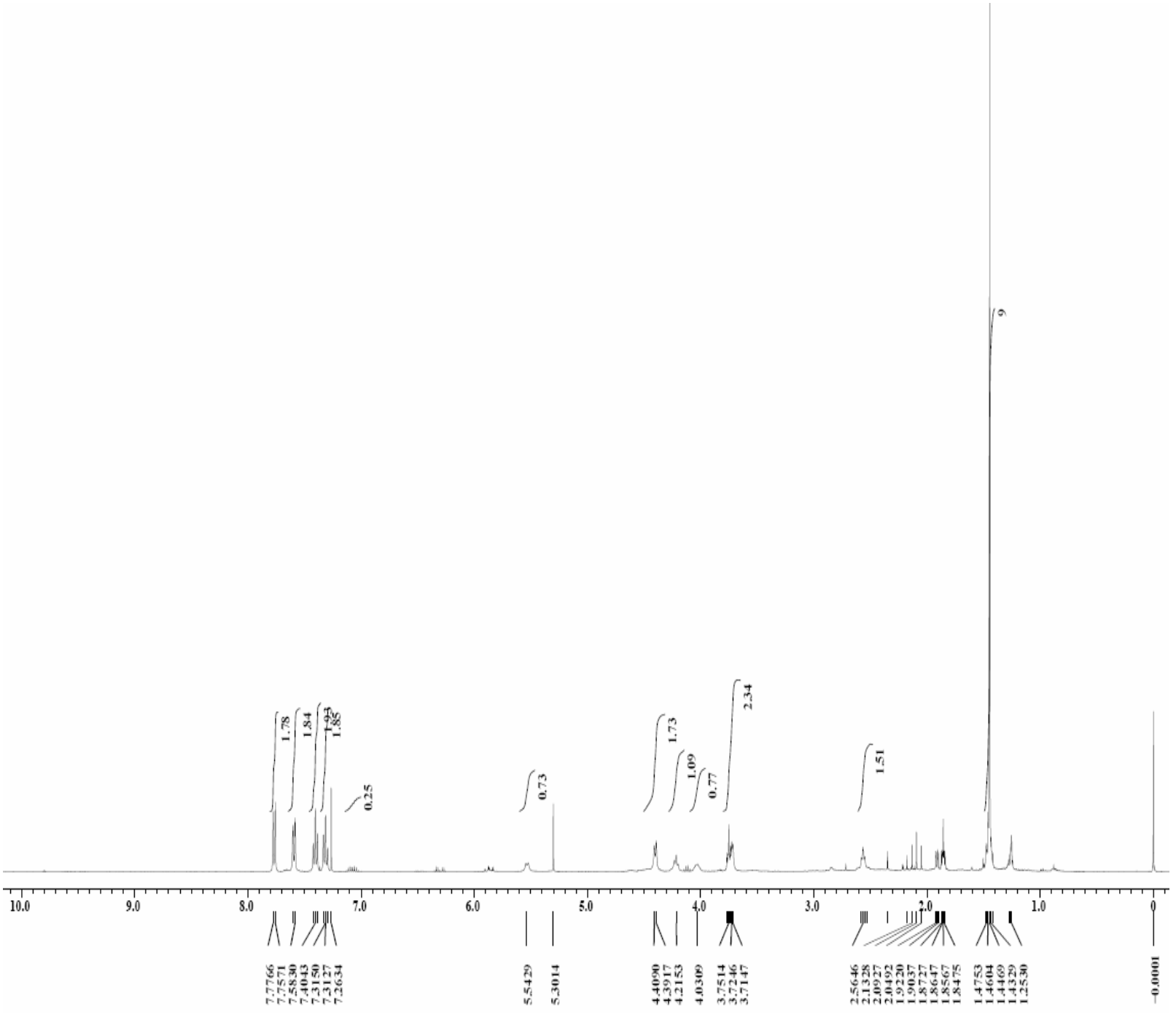
57.3860
49.4246
47.5273
34.1312
28.9062
25.8361
25.1782
20.3632


Final - Shots 750 - HNG GROUP; Label B13
422.0003(R5361,S15430)
406.0422(R6858,S10075)
calcd. [M+Na]+ 406.1994
Mass (m/z)
299.0
540.2
781.4
1022.6
1263.8
1505.0
3.8E+4


O
O
O
O
N
H
OH

7


9
2.34
1.73
1.09
0.77
1.51
1.78
1.84
1.93
1.85
0.25
0.73
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7766
7.7571
7.5830
7.4043
7.3150
7.3127
7.2634
5.5429
5.3014
4.4090
4.3917
4.2153
4.0309
3.7514
3.7246
3.7147
2.5646
2.1328
2.0927
2.0492
1.9220
1.9037
1.8727
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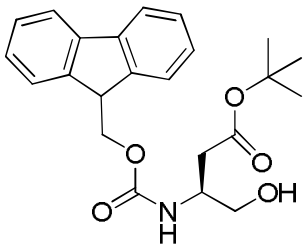
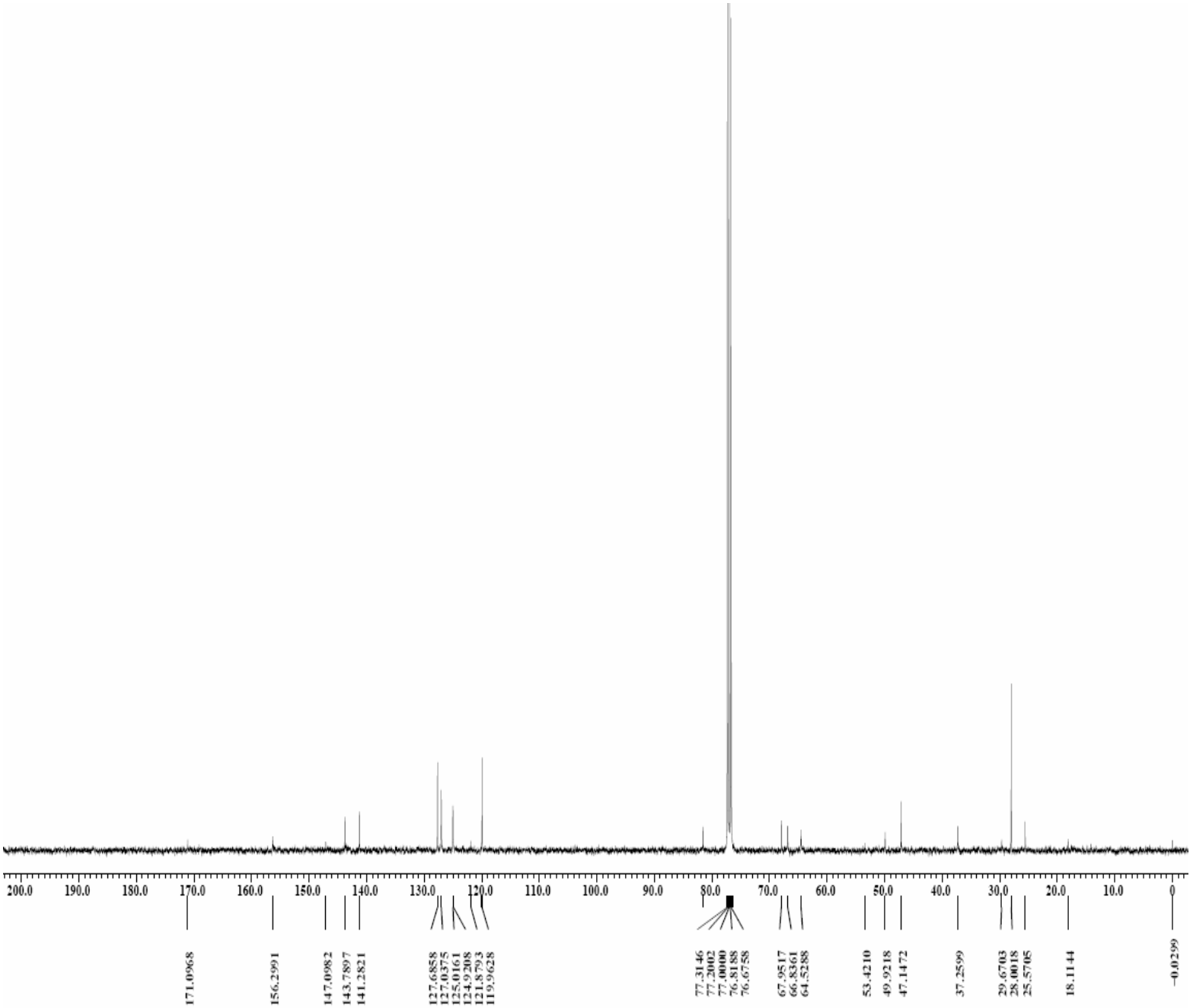
1.8567
1.8475
1.4753
1.4604
1.4469
1.4329
1.2530
-0.0001


O
O
O
O
N
H
OH


200.0
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170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
171.0968
156.2991
147.0982
143.7897
141.2821
127.6858
127.0375
125.0161
124.9208
121.8793
119.9628
77.3146
77.2042
77.0000
76.8188
76.6758
67.9517
66.8361
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49.9218
47.1472
37.2599
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28.0018
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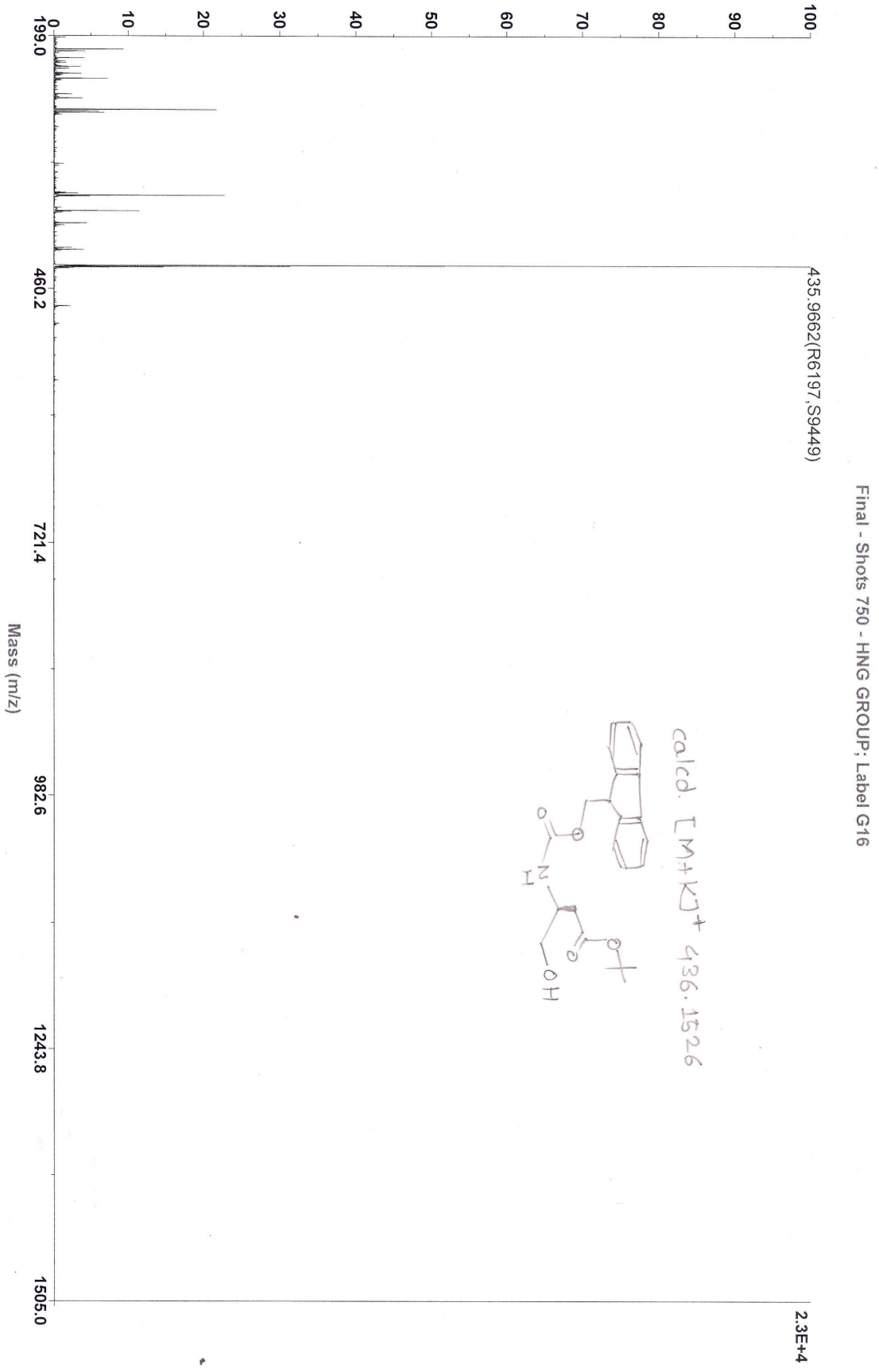
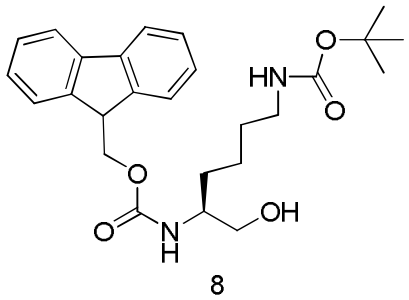
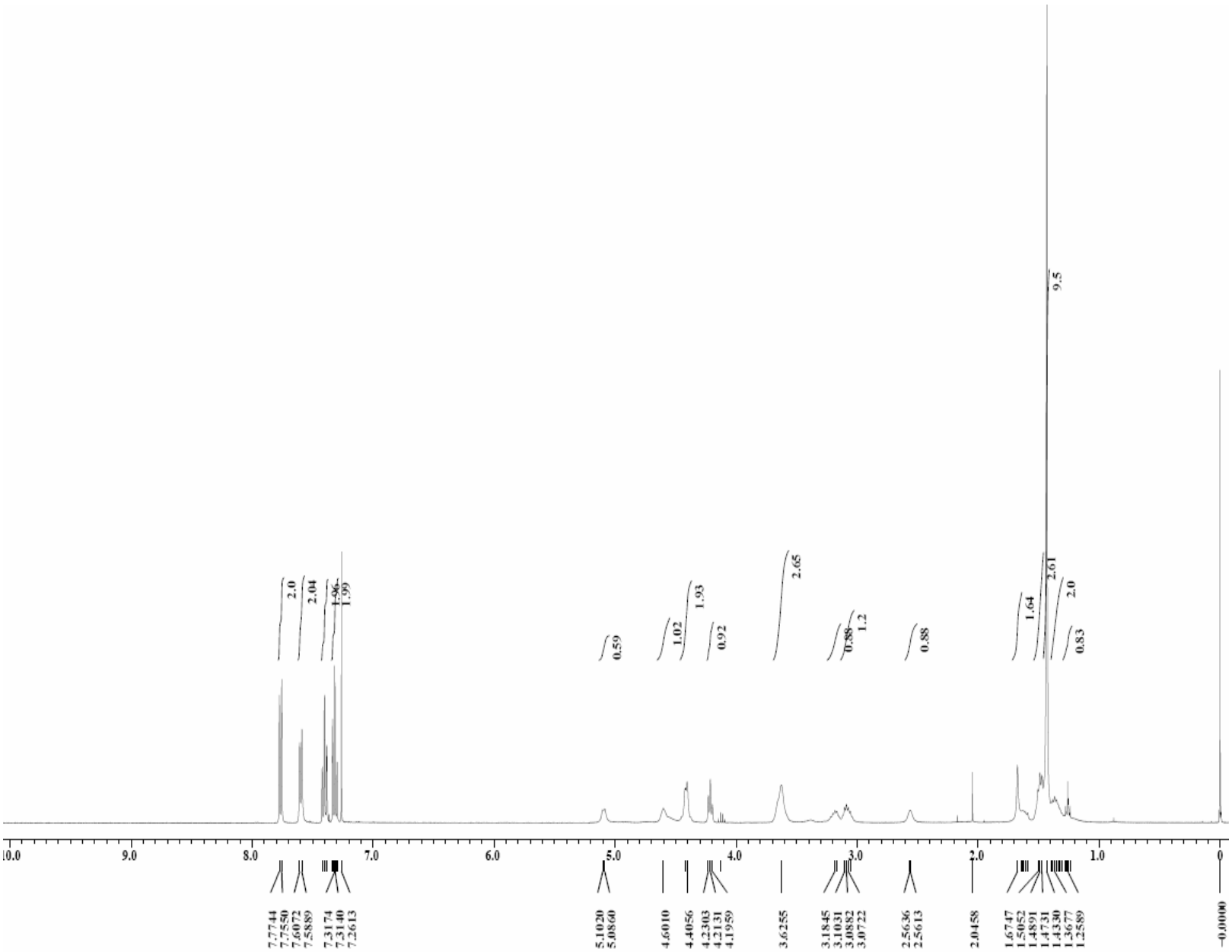
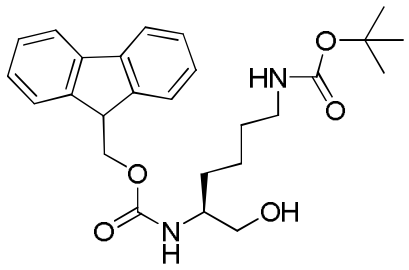
18.1144
-0.0299

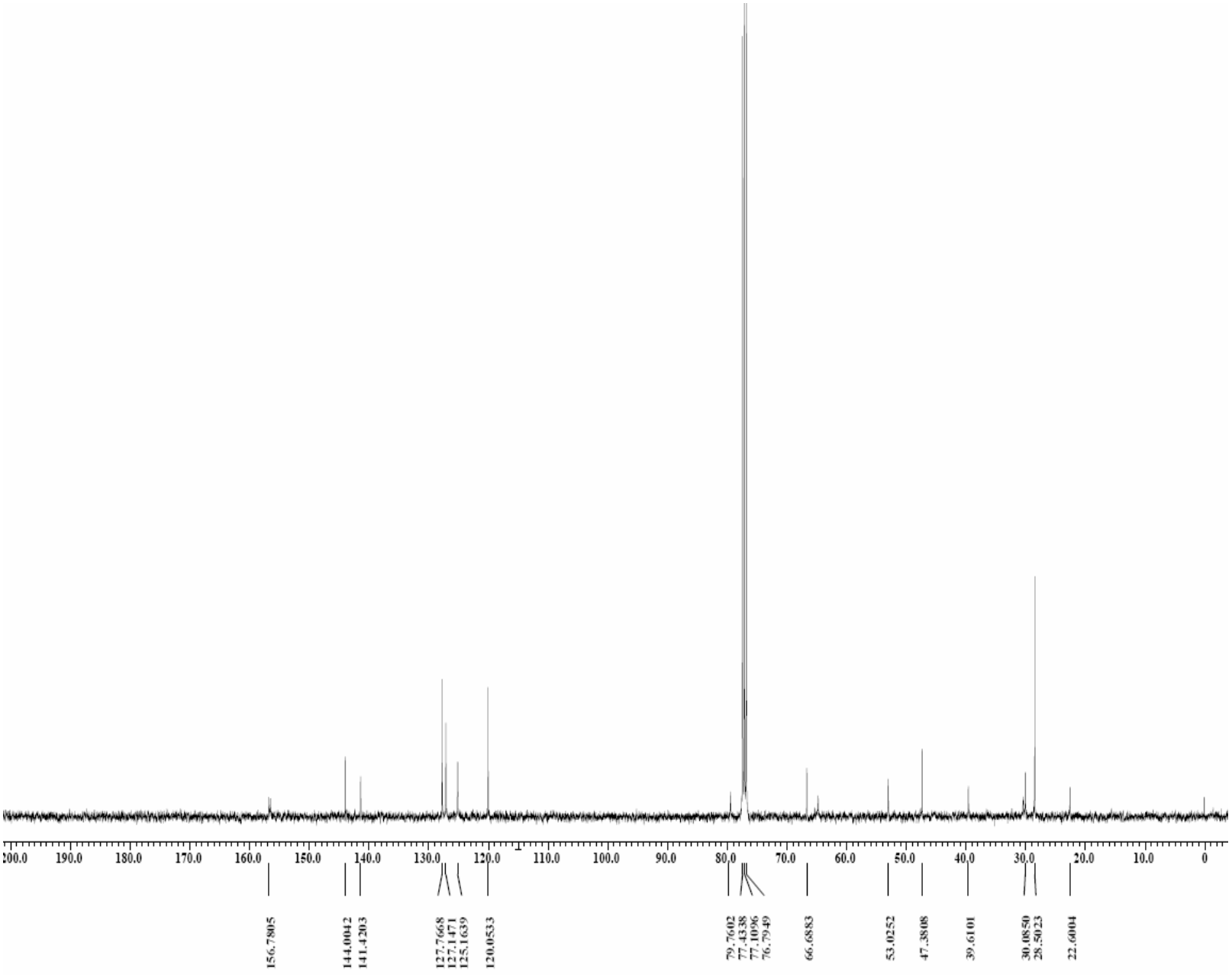

Final - Shots 750 - HNG GROUP; Label G16
435.9662(R6197,S9449)
calcd. [M+K]+ 436.1526
Mass (m/z)
199.0
460.2
721.4
982.6
1243.8
1505.0
2.3E+4

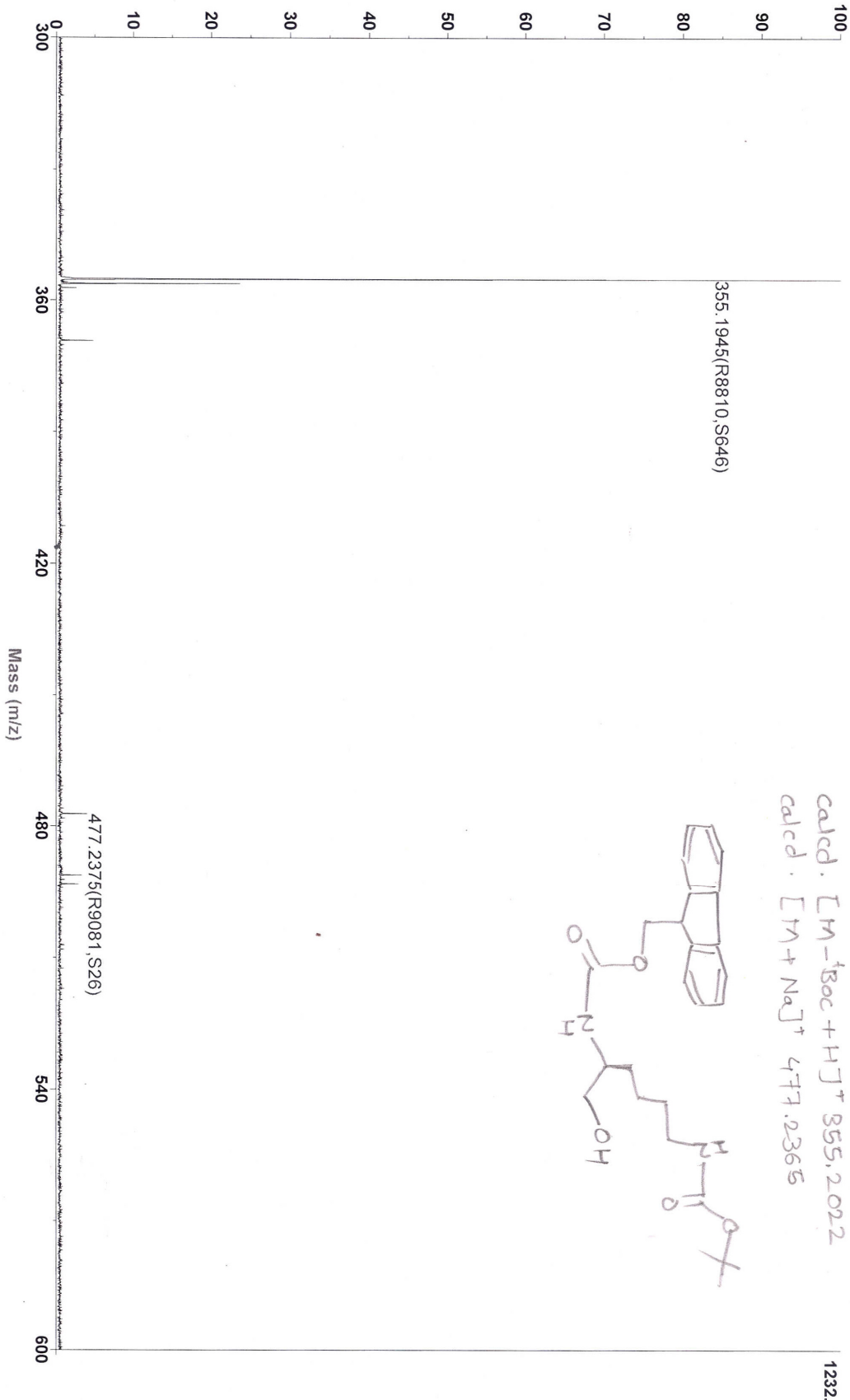

HN
O
O
O
O
N
H
OH

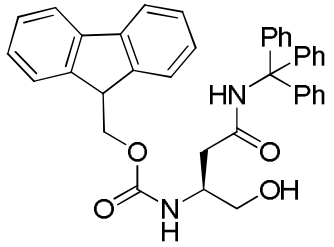
8


2.0
2.04
1.96
1.99
0.59
1.02
1.93
0.92
2.65
0.88
1.2
0.88
1.64
2.61
2.0
0.83
9.5
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7744
7.7550
7.6072
7.5889
7.3174
7.3140
7.2613
5.1020
5.0860
4.6010
4.4056
4.2303
4.2131
4.1959
3.6255
3.1845
3.1031
3.0882
3.0722
2.5636
2.5613
2.0458
1.6747
1.5052
1.4891
1.4731
1.4330
1.3677
1.2589
-0.0000

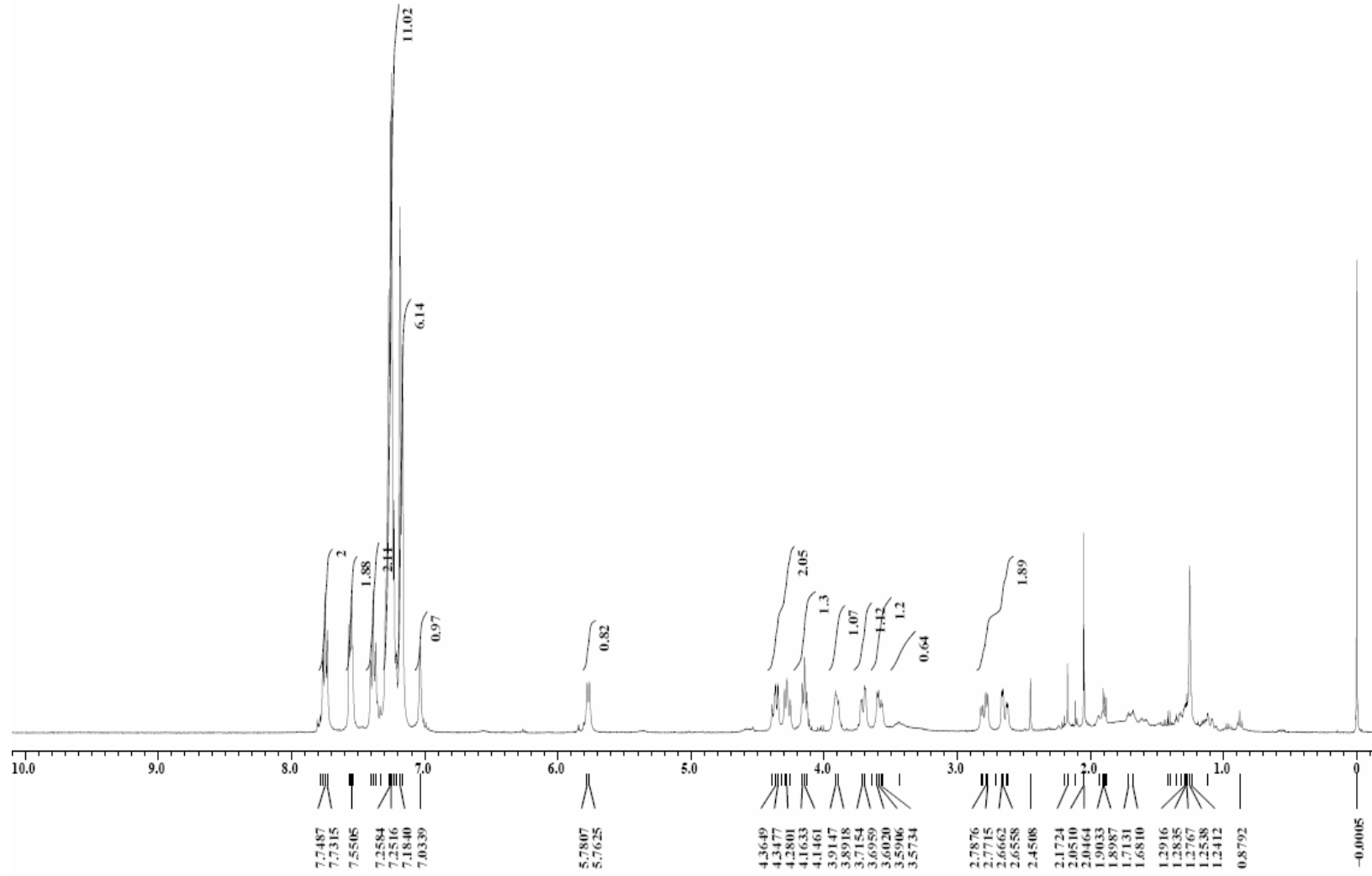

HN
O
O
O
O
N
H
OH

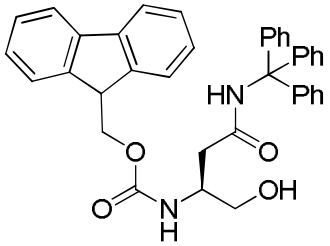

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.7805
144.0042
141.4203
127.7668
127.1471
125.1639
120.0533
79.7602
77.4338
77.1096
76.7949
66.6883
53.0252
47.3808
39.6101
30.0850
28.5023
22.6004

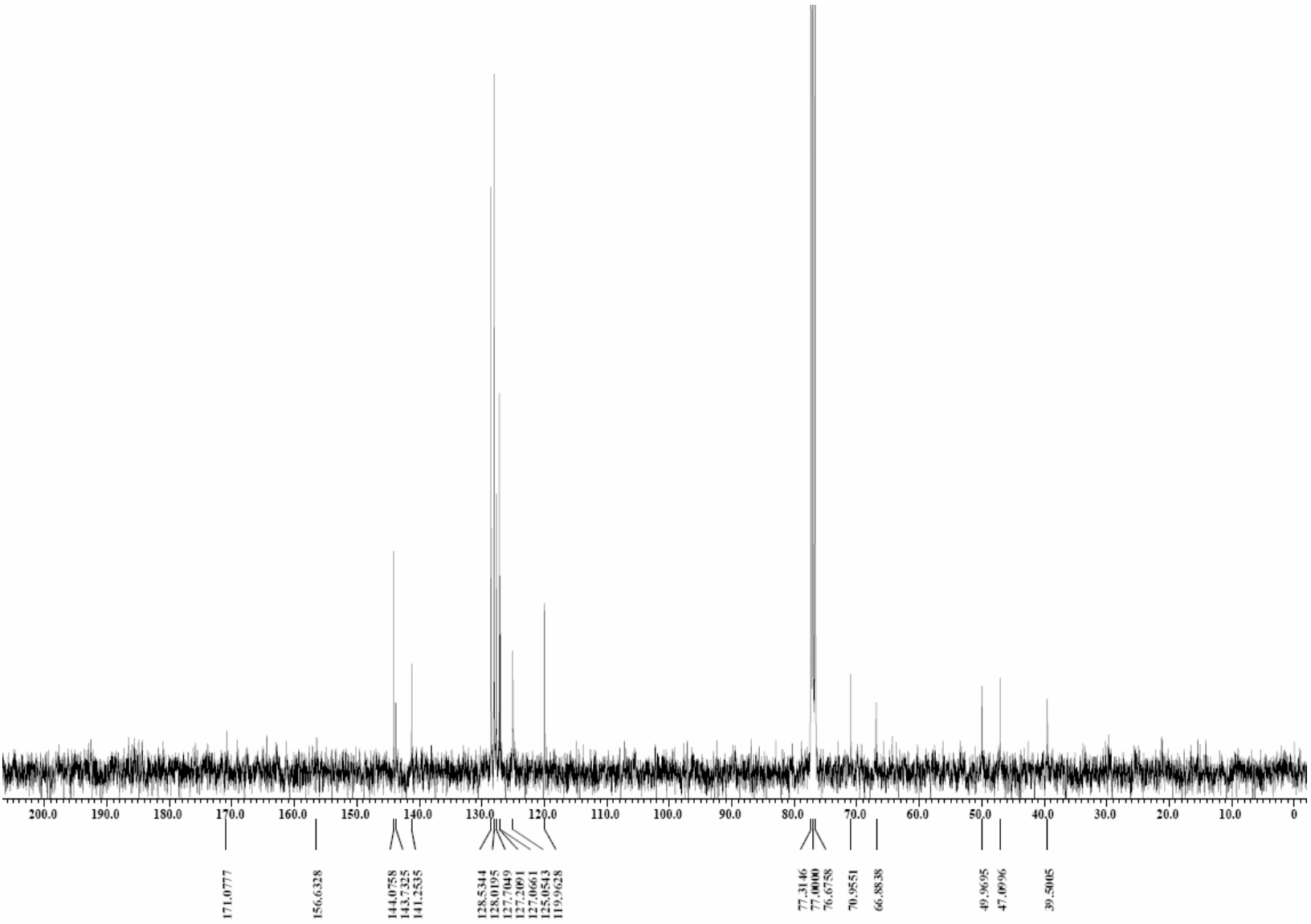

Final - Shots 500 - HNG GROUP; Label L7
Calcd. [M-tBoc+H]+ 355.2022
Calcd. [M+Na]+ 477.2365
355.1945(R8810,S646)
477.2375(R9081,S26)
Mass (m/z)
1232.9

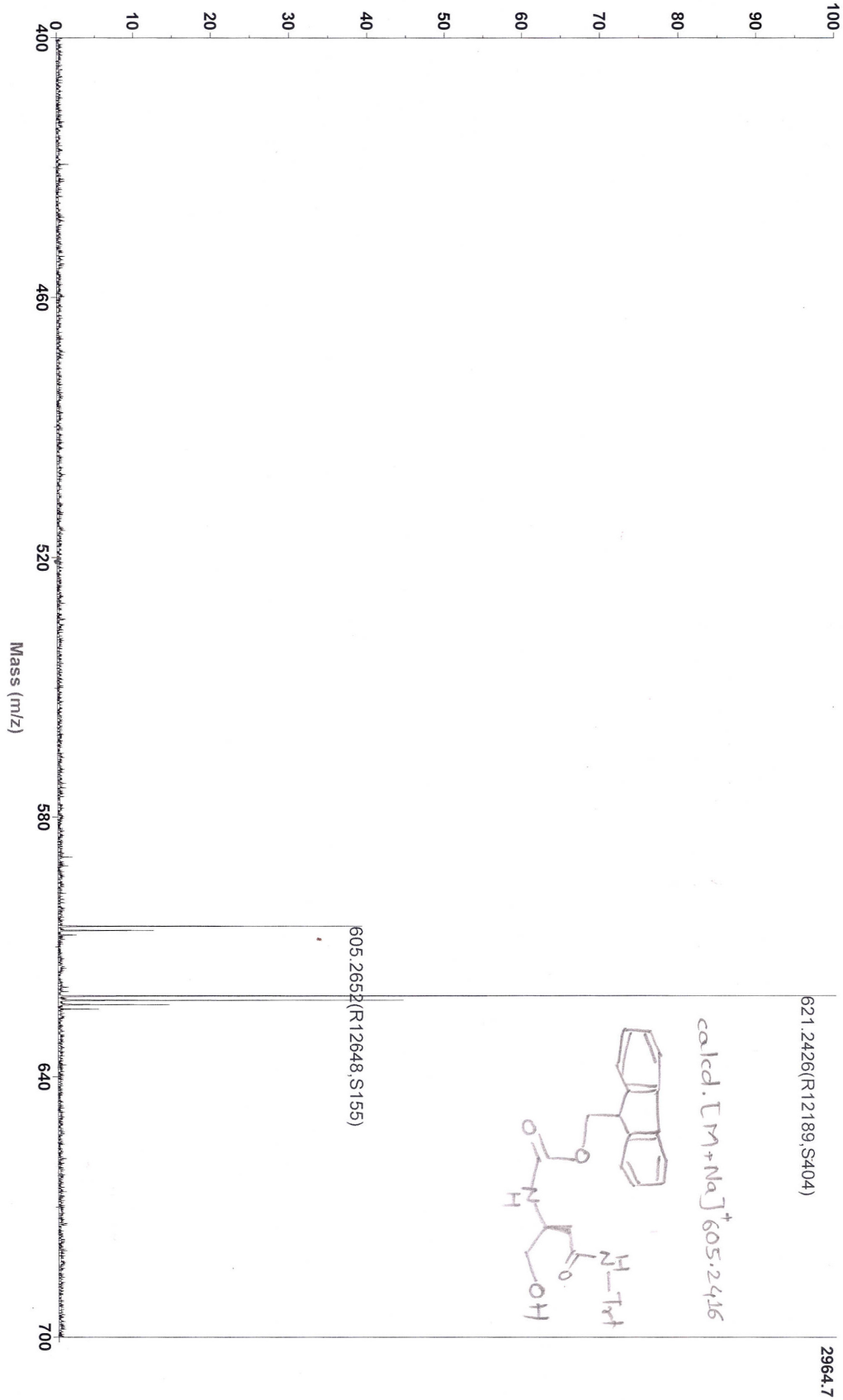

Ph
Ph
HN
Ph
O
O
O
OH
O
N
H

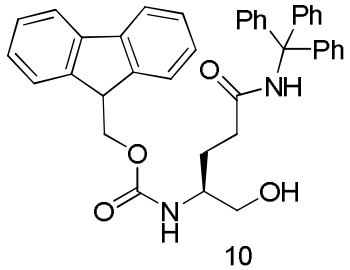
9


11.02
6.14
2
1.88
2.11
0.97
0.82
2.05
1.3
1.07
1.12
1.2
0.64
1.89
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7487
7.7315
7.5506
7.2584
7.2516
7.1840
7.0339
5.7807
5.7625
4.3649
4.3477
4.2801
4.1633
4.1461
3.9147
3.8918
3.7154
3.6959
3.6020
3.5906
3.5734
2.7876
2.7715
2.6662
2.6558
2.4508
2.1724
2.0510
2.0464
1.9033
1.8987
1.7131
1.6810
1.2916
1.2835
1.2767
1.2538
1.2412
0.8792
-0.0005

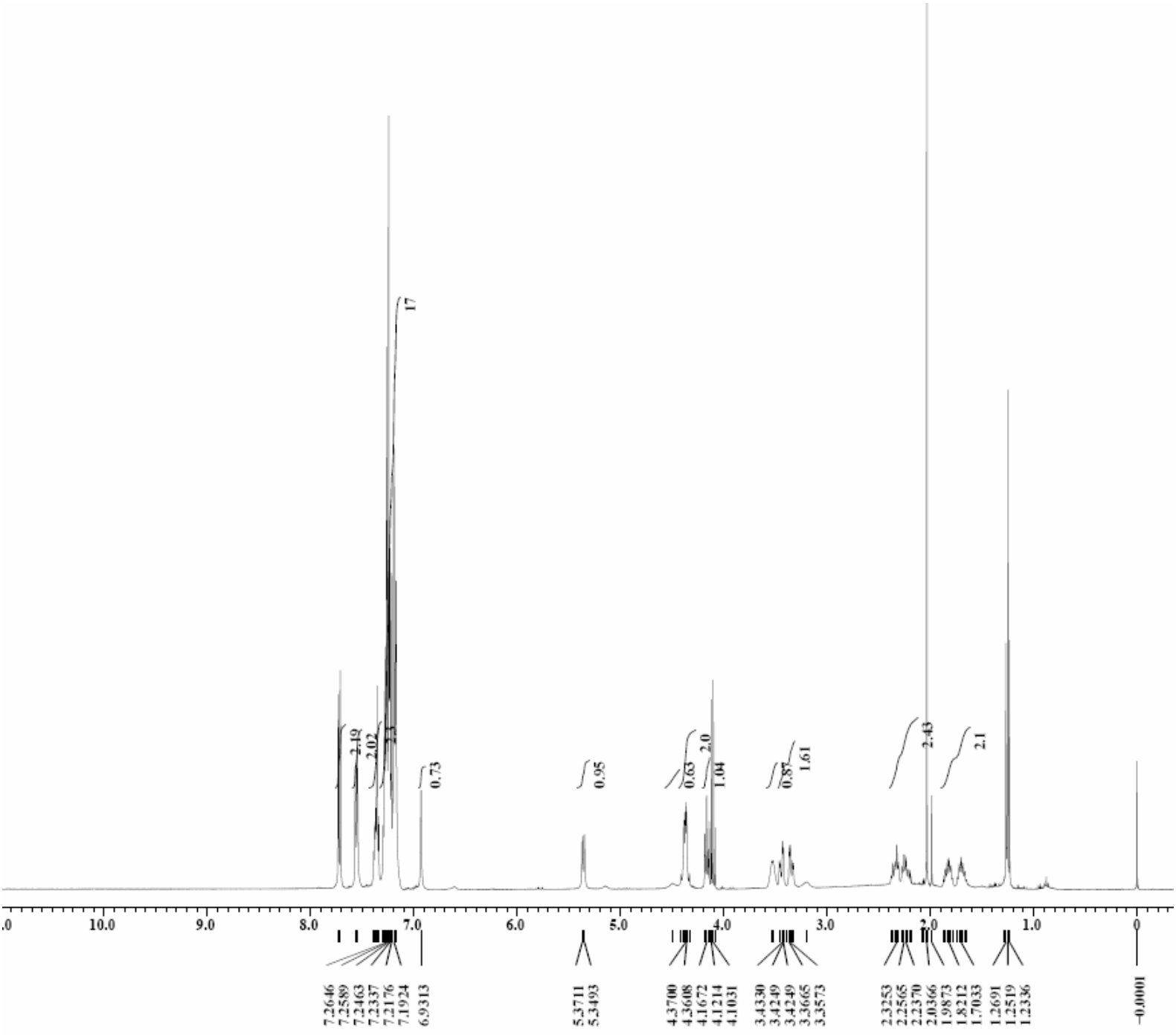

Ph
Ph
HN
Ph
O
O
O
OH
O
N
H

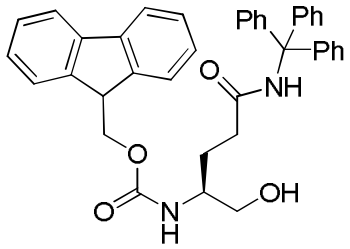

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
171.0777
156.6328
144.0758
143.7325
141.2535
128.5344
128.0195
127.7049
127.2091
127.0661
125.0543
119.9628
77.3146
77.0000
76.6758
70.9551
66.8838
49.9695
47.0996
39.5005

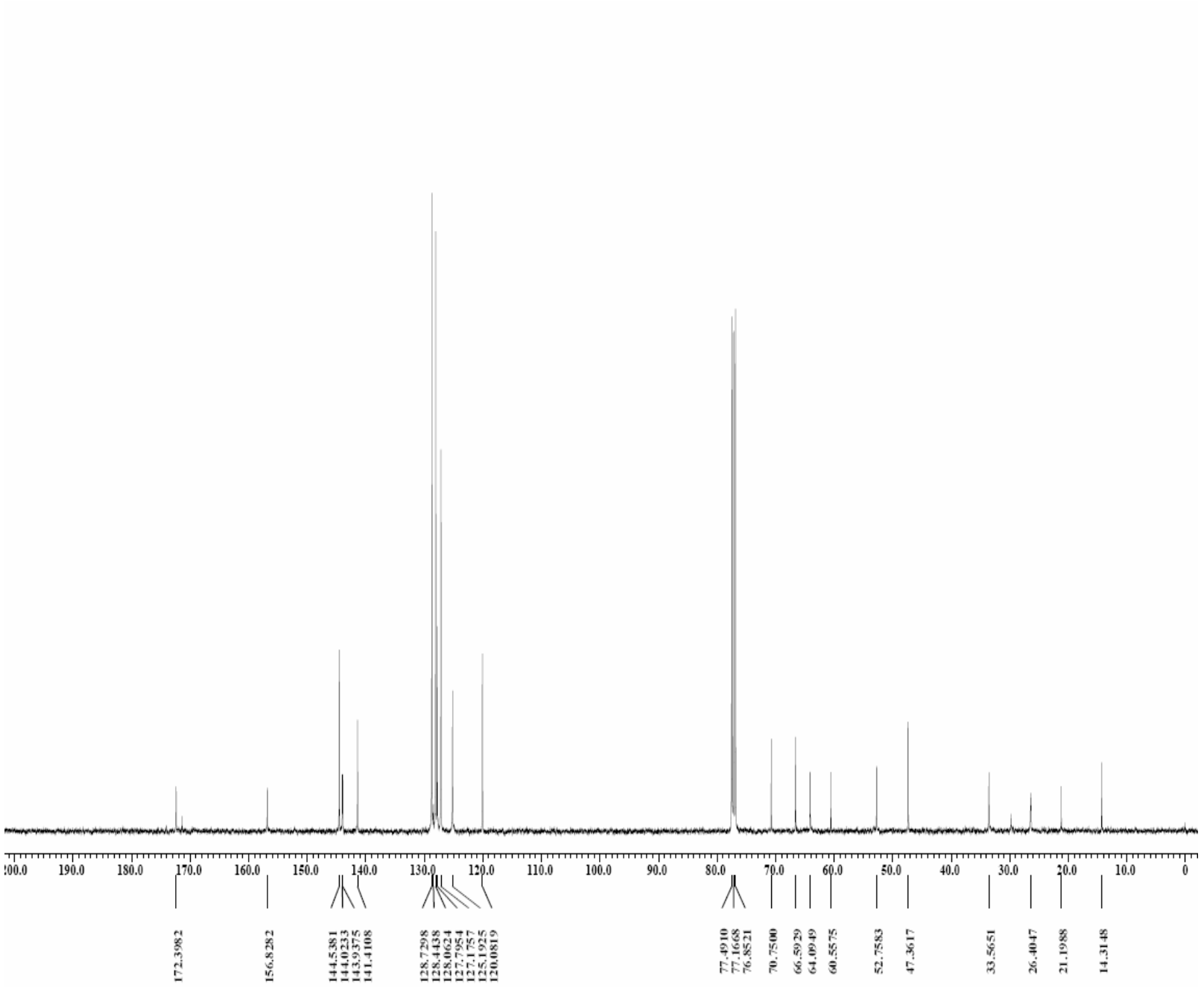

Final - Shots 50 - HNG GROUP; Label L10
621.2426(R12189,S404)
calcd. [M+Na]+ 605.2416
605.2652(R12648,S155)
2964.7
Mass (m/z)
100
90
80
70
60
50
40
30
20
10
0
400
460
520
580
640
700

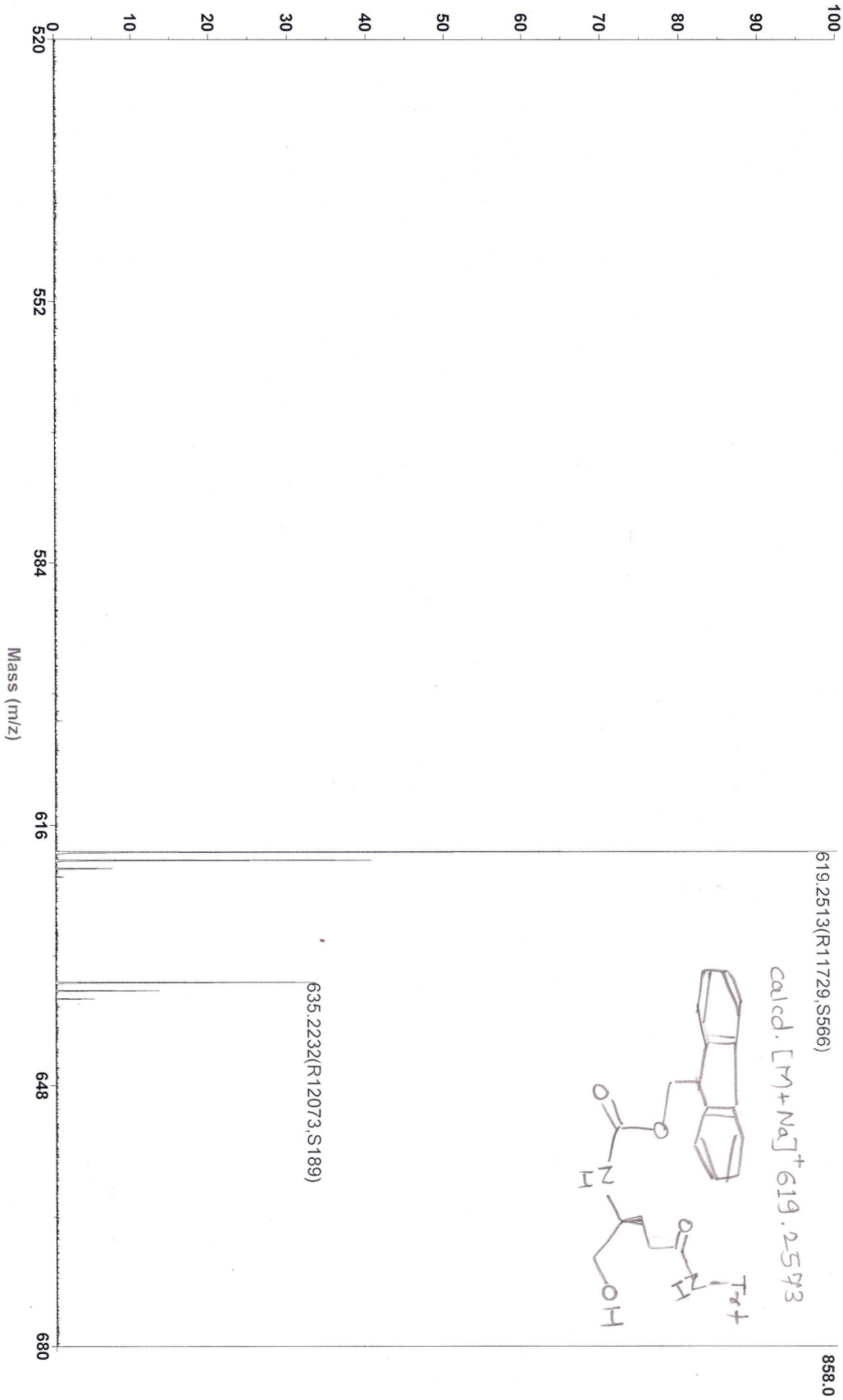

Ph
Ph
Ph
O
NH
O
O
N
H
OH

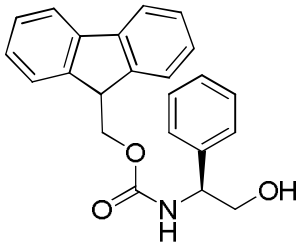
10

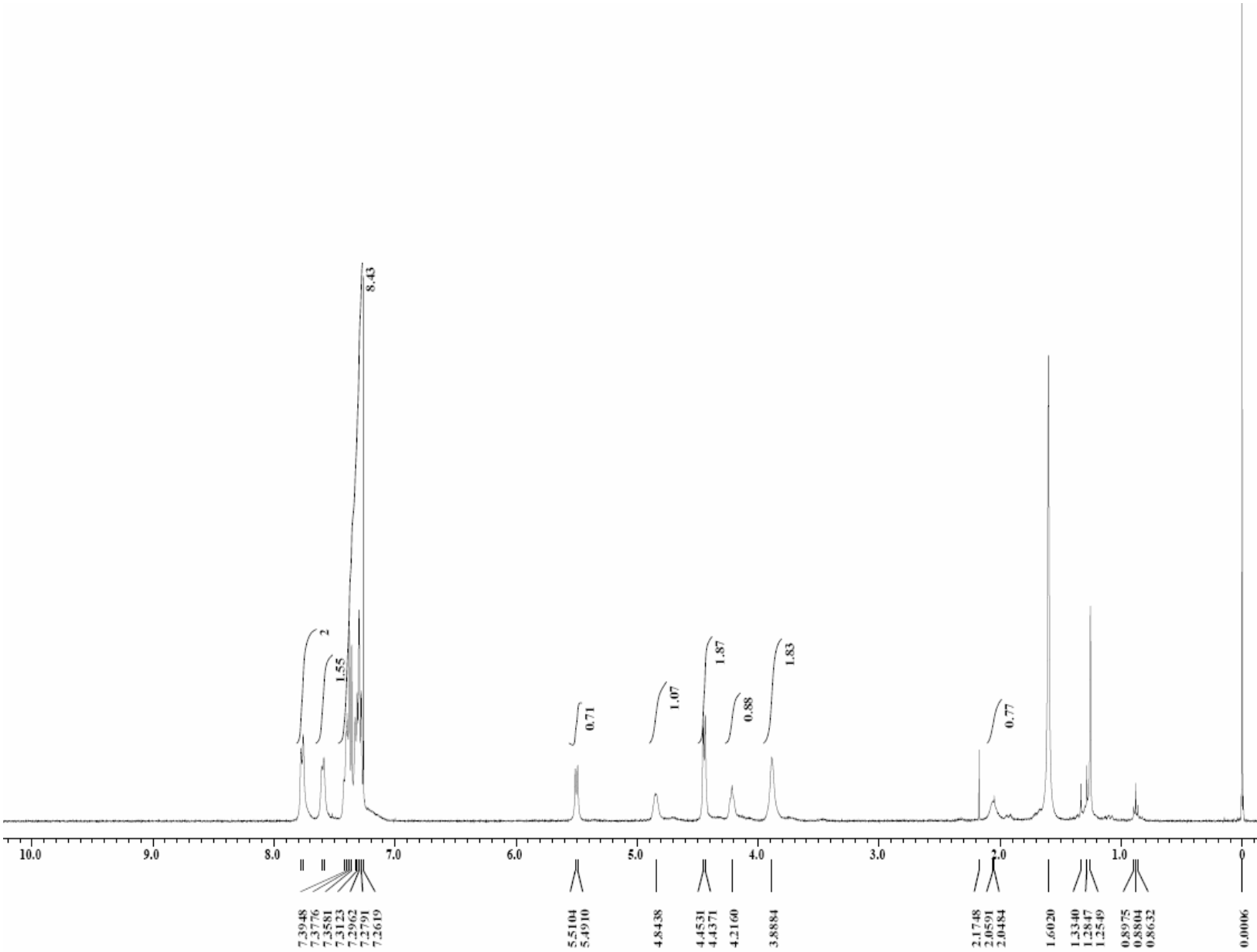

17
2.19
2.02
2.3
0.73
0.95
0.63
2.0
1.04
0.87
1.61
2.43
2.1
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2646
7.2589
7.2463
7.2337
7.2176
7.1924
6.9313
5.3711
5.3493
4.3700
4.3608
4.1672
4.1214
4.1031
3.4330
3.4249
3.4249
3.3665
3.3573
2.3253
2.2565
2.2370
2.0366
1.9873
1.8212
1.7033
1.2691
1.2519
1.2336
-0.0001

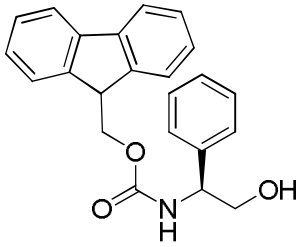

Ph
Ph
Ph
O
NH
O
O
N
H
OH

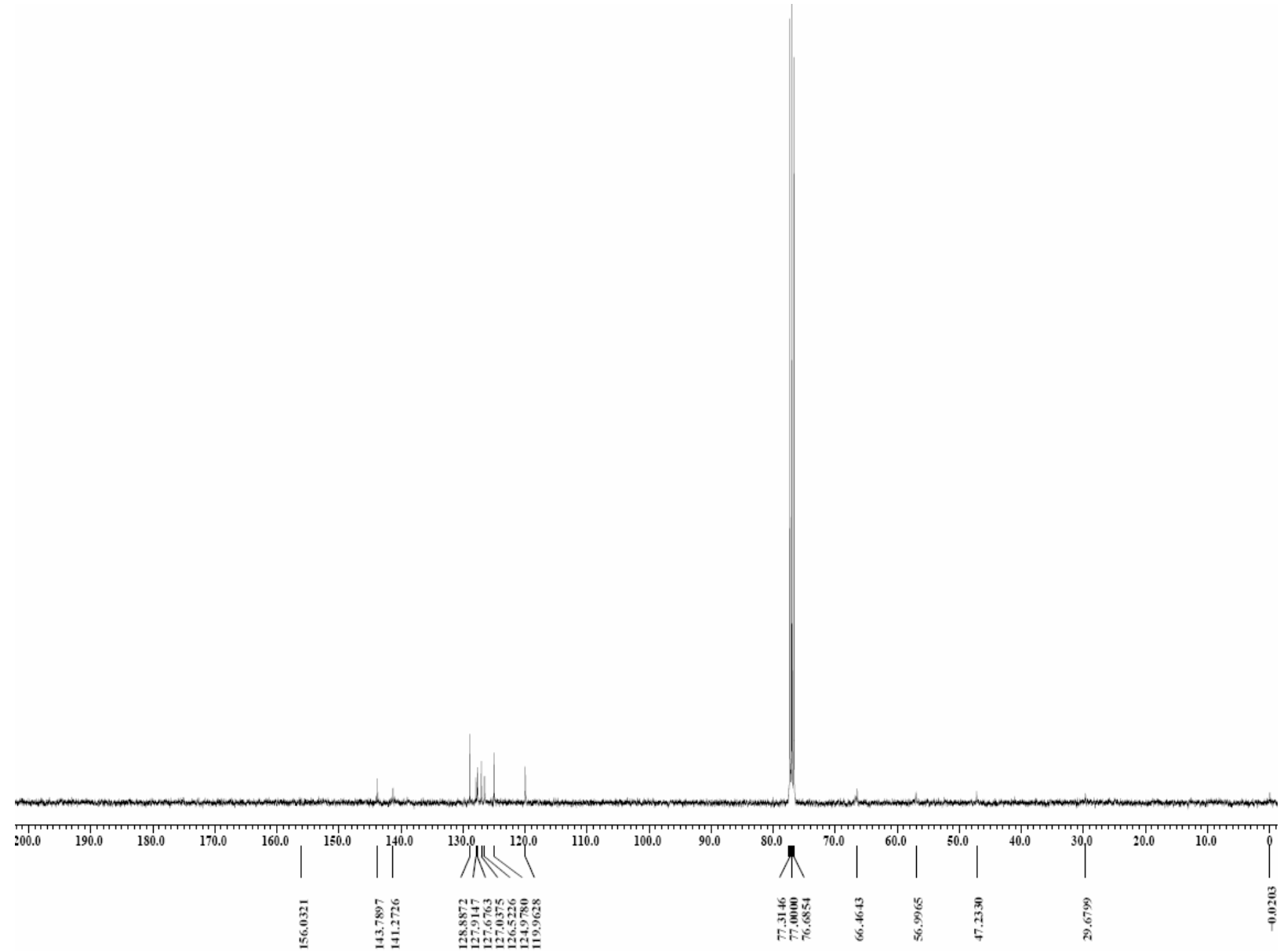

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
172.3982
156.8282
144.5381
144.0233
143.9375
141.4108
128.7298
128.4438
128.0624
127.7954
127.1757
125.1925
120.0819
77.4910
77.1668
76.8521
70.7500
66.5929
64.0949
60.5575
52.7583
47.3617
33.5651
26.4047
21.1988
14.3148

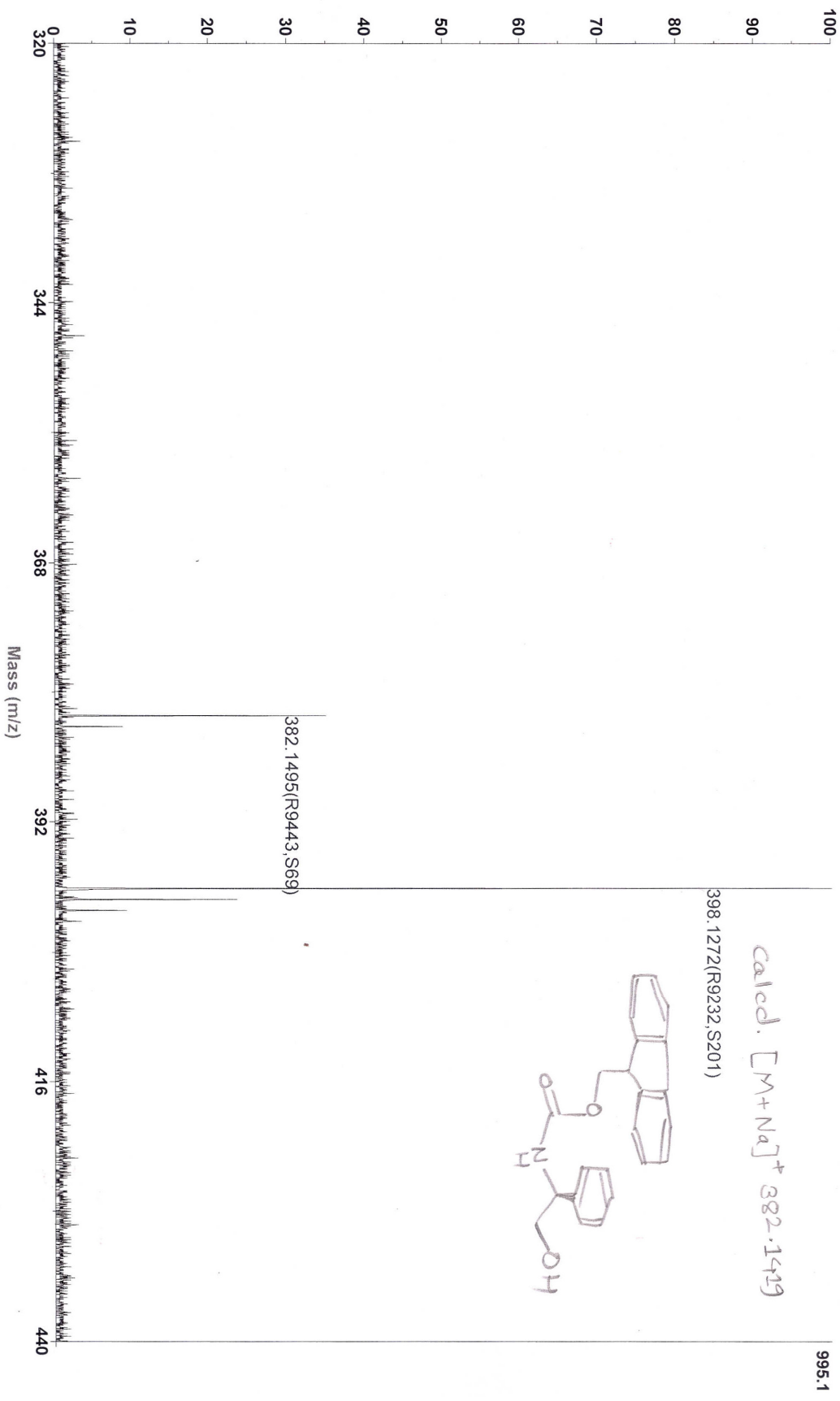

Final - Shots 500 - HNG GROUP; Label M12
619.2513(R11729,S566)
635.2232(R12073,S189)
calcd. [M+Na]+ 619.2573
Mass (m/z)
100
90
80
70
60
50
40
30
20
10
0
520
552
584
616
648
680
858.0

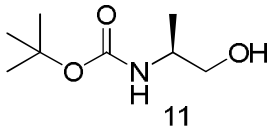

O
O
N
H
OH


8.43
2
1.55
0.71
1.07
1.87
0.88
1.83
0.77
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.3948
7.3776
7.3581
7.3123
7.2962
7.2791
7.2619
5.5104
5.4910
4.8438
4.4531
4.4371
4.2160
3.8884
2.1748
2.0591
2.0484
1.6020
1.3340
1.2847
1.2549
0.8975
0.8804
0.8632
0.0006

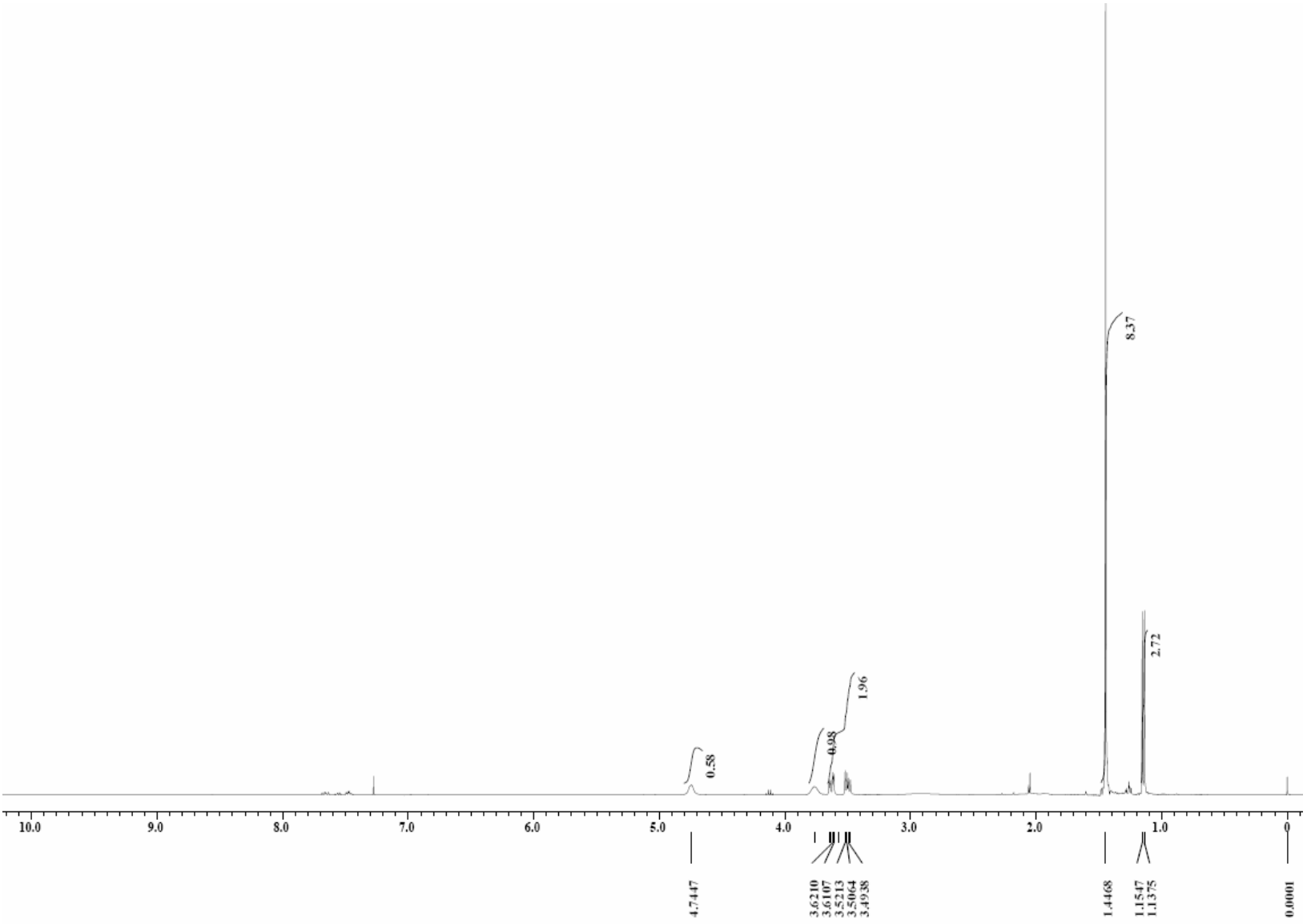

O
O
N
H
OH

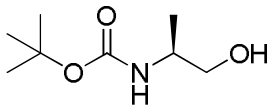

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.0321
143.7897
141.2726
128.8872
127.9147
127.6763
127.0375
126.5226
124.9780
119.9628
77.3146
77.0000
76.6854
66.4643
56.9965
47.2330
29.6799
-0.0203

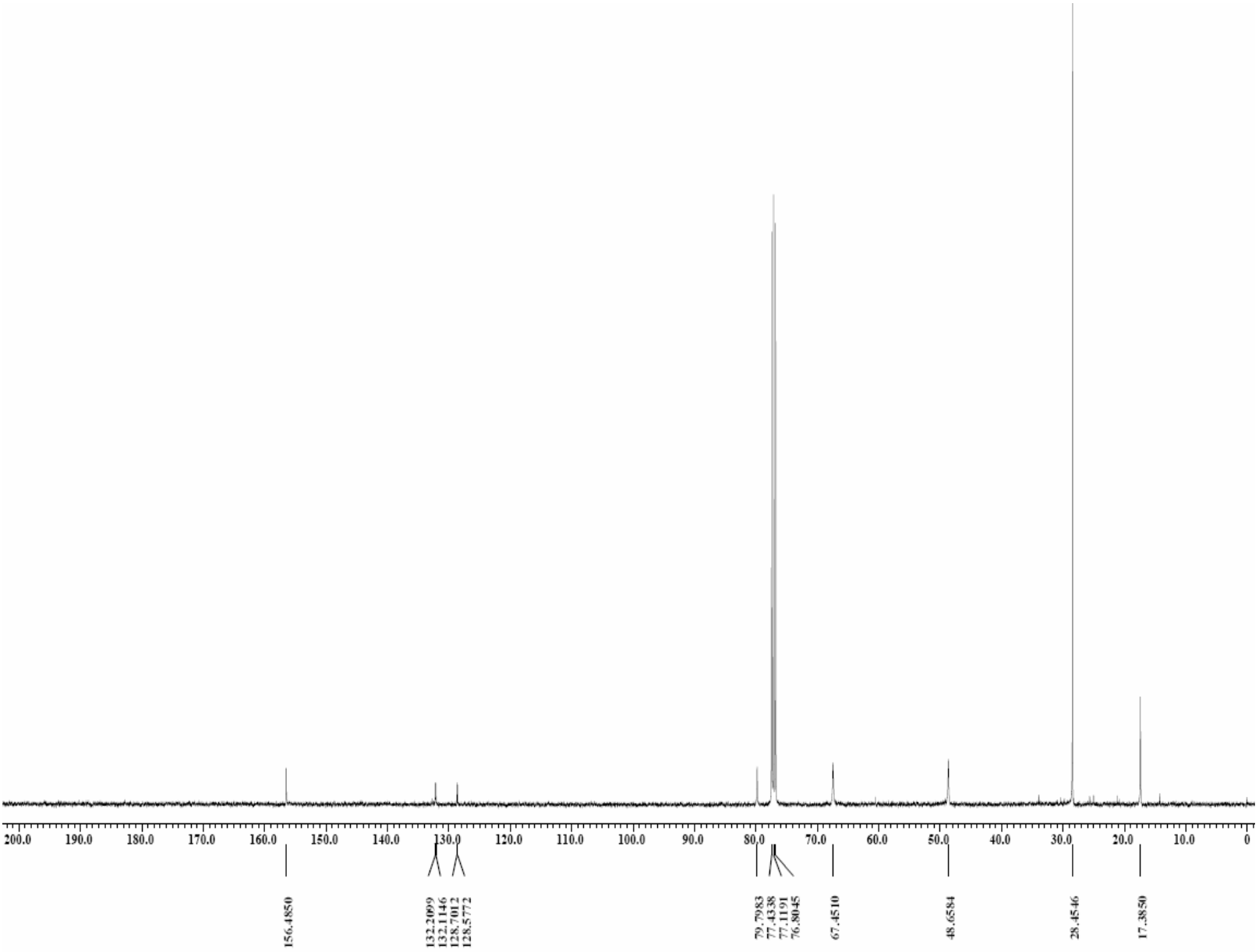

Final - Shots 80 - HNG GROUP; Label M10
100
90
80
70
60
50
40
30
20
10
0
320
344
368
392
416
440
Mass (m/z)
382.1495(R9443,S69)
398.1272(R9232,S201)
Calcd. [M+Na]+ 382.1419
995.1

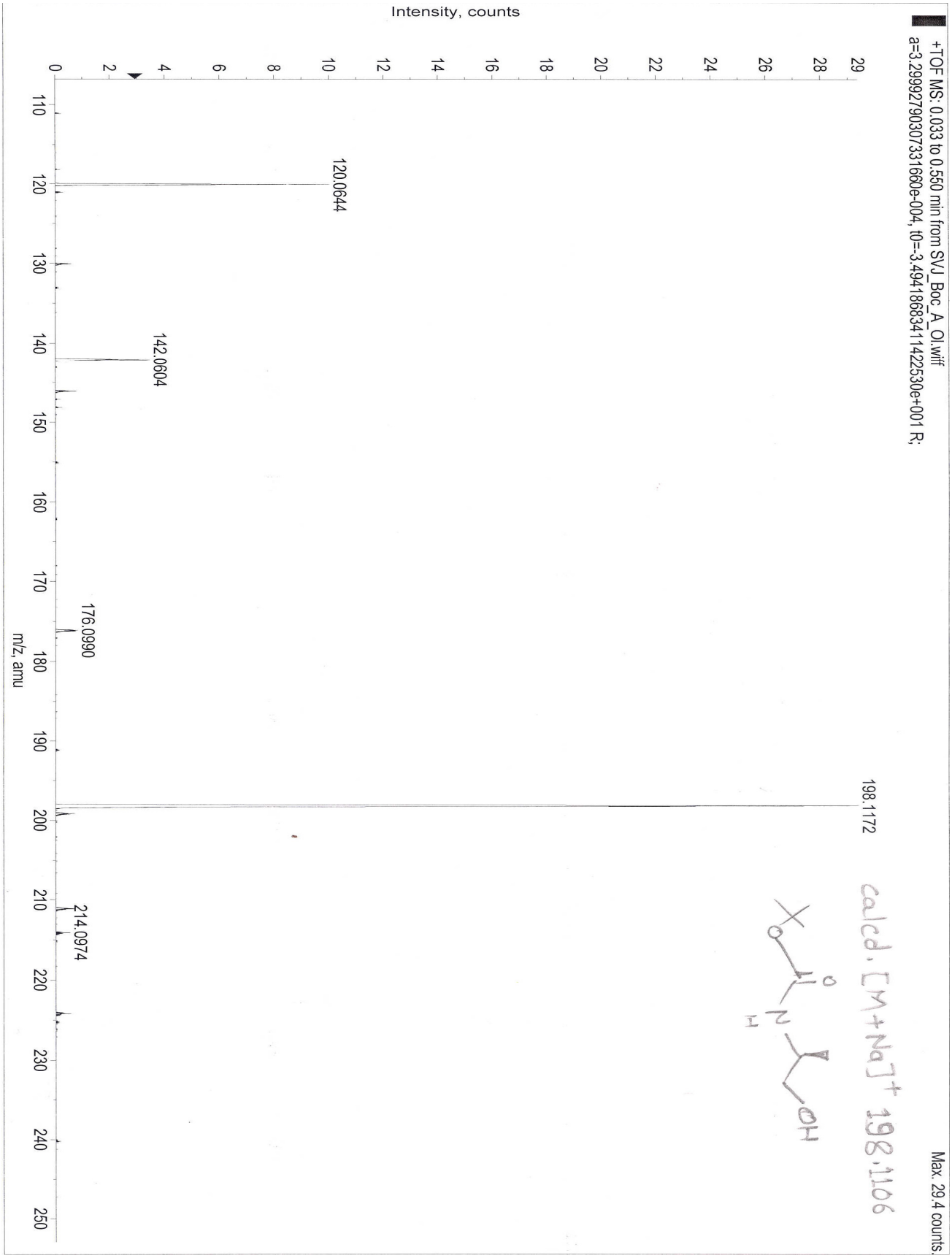

O
O
N
H
OH

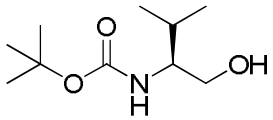
11


8.37
2.72
1.96
0.98
0.58
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
4.7447
3.6210
3.6107
3.5213
3.5064
3.4938
1.4468
1.1547
1.1375
0.0001

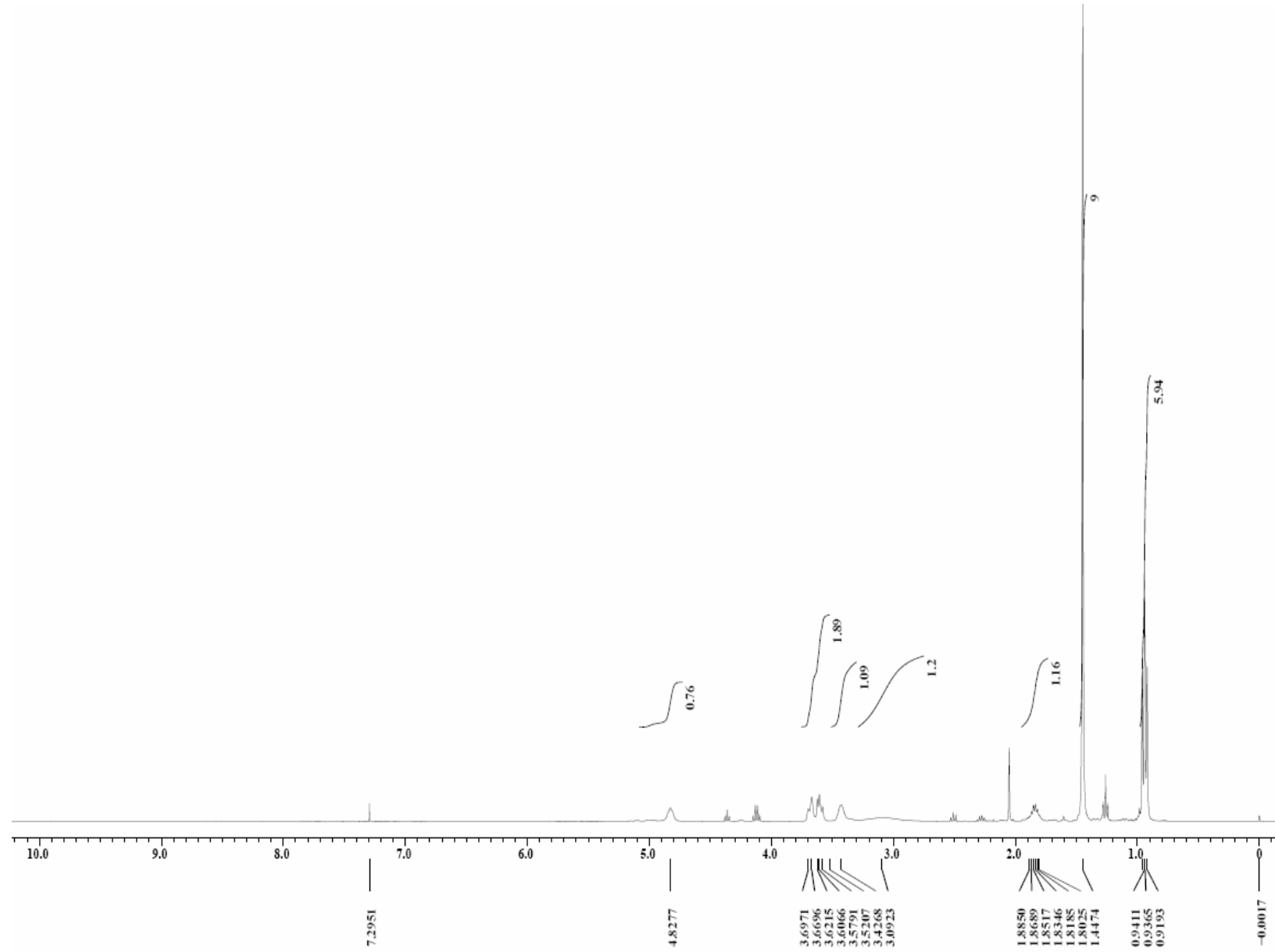

O
O
N
H
OH

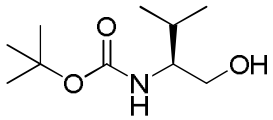

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.4850
132.2099
132.1146
128.7012
128.5772
79.7983
77.4338
77.1191
76.8045
67.4510
48.6584
28.4546
17.3850

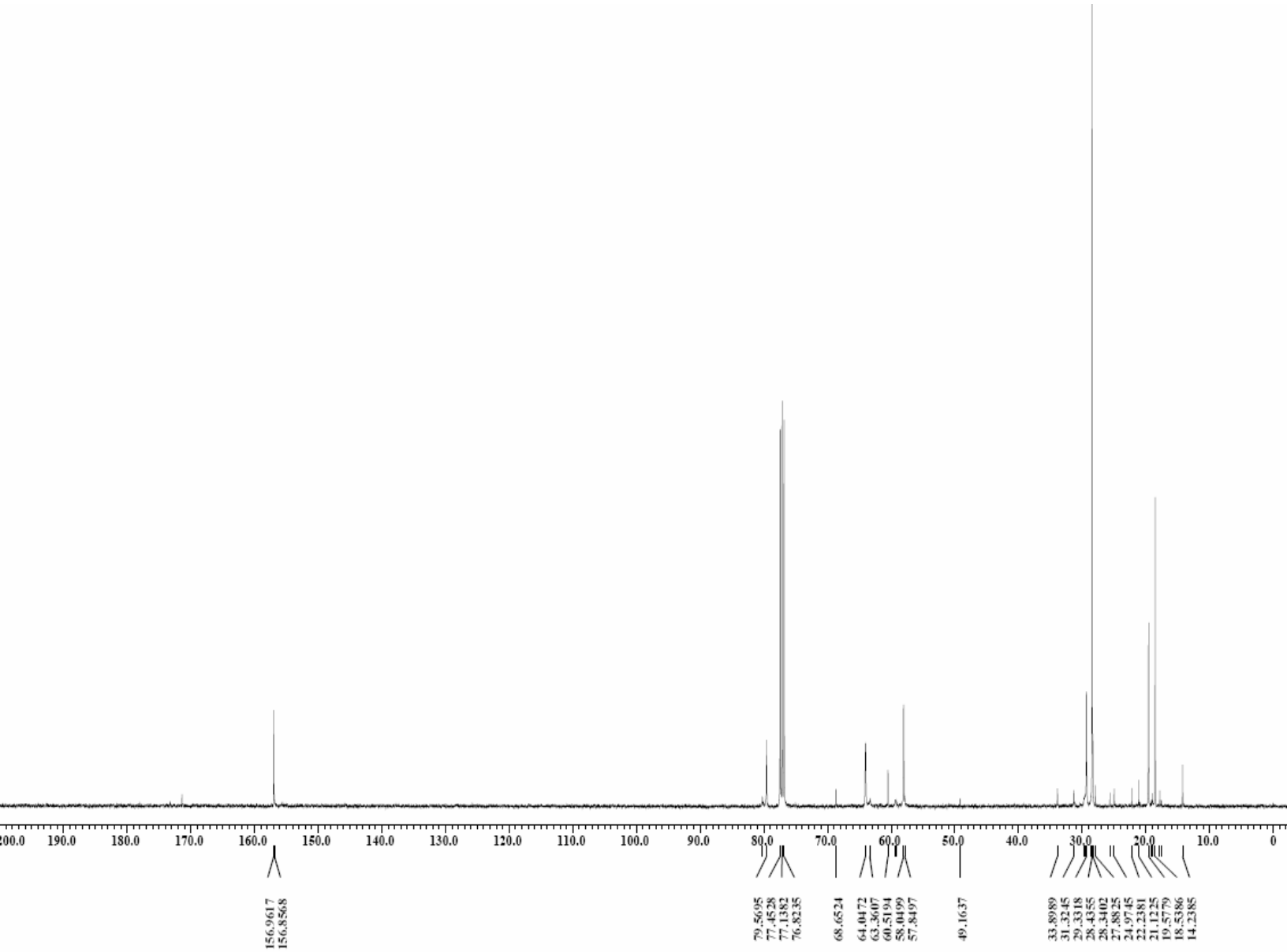

+TOF MS: 0.033 to 0.550 min from SVJ_Boc_A_OI.wiff
a=3.29992790307331680e-004, t0=-3.49418683411422530e+001 R;
Max. 29.4 counts.
Intensity, counts
m/z, amu
120.0644
142.0604
176.0990
198.1172
214.0974
calcd. [M+Na]+ 198.1106

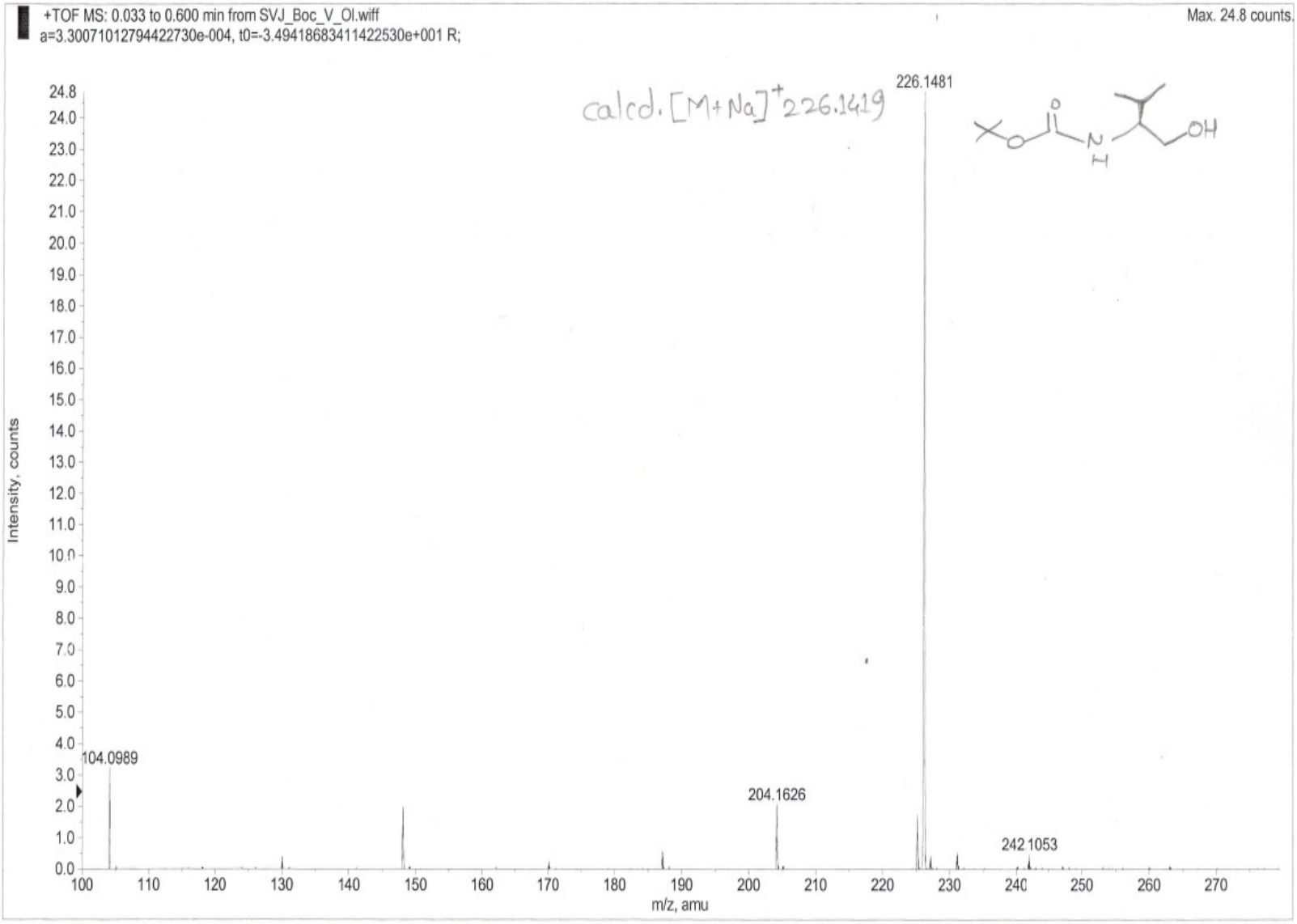

O
O
N
H
OH

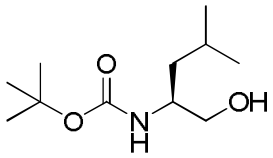
12


0.76
1.89
1.09
1.2
1.16
9
5.94
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2951
4.8277
3.6971
3.6696
3.6215
3.6066
3.5791
3.5207
3.4268
3.0923
1.8850
1.8689
1.8517
1.8346
1.8185
1.8025
1.4474
0.9411
0.9365
0.9193
-0.0017

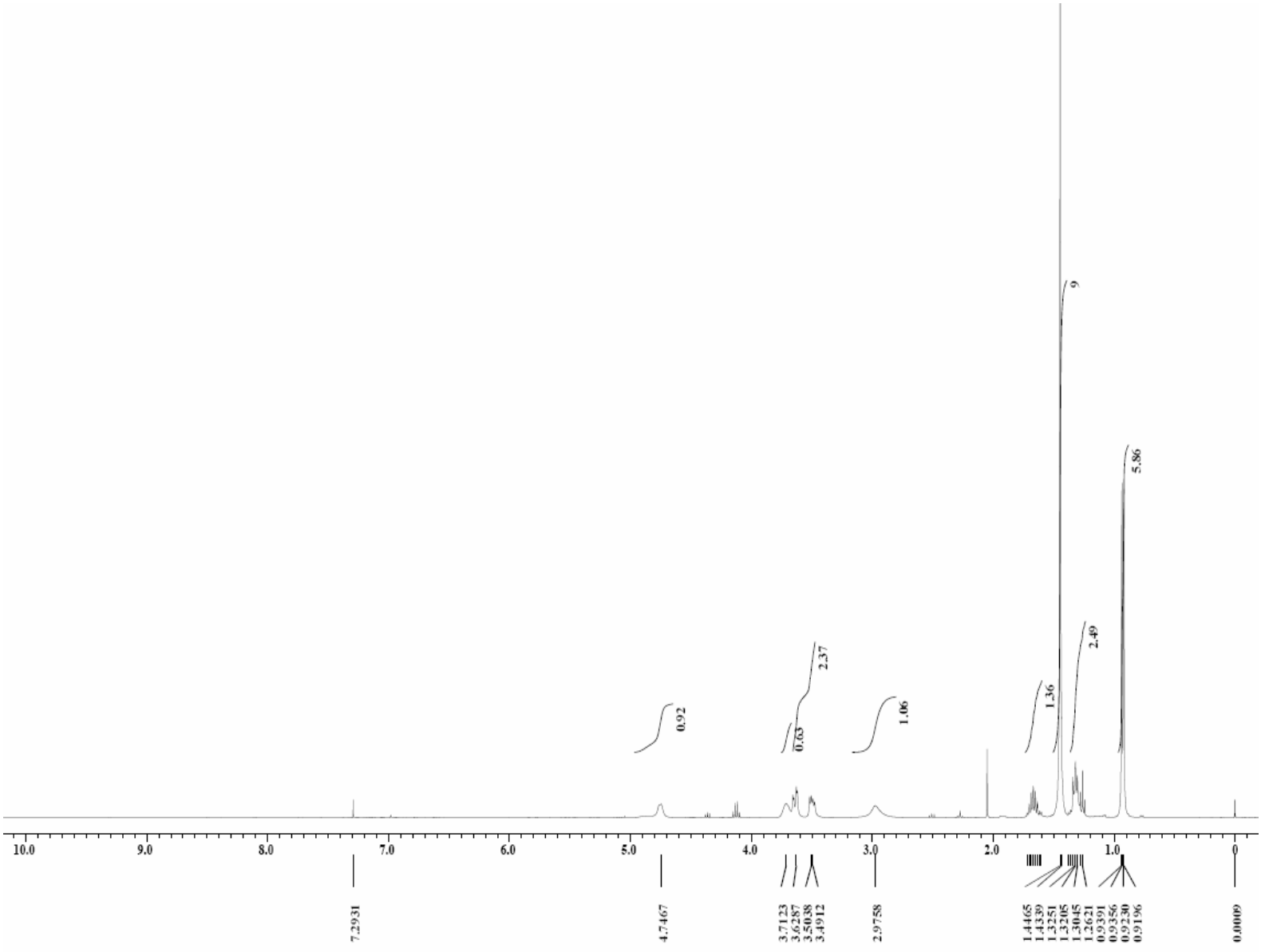

O
O
N
H
OH

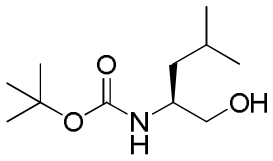

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.9617
156.8568
79.5695
77.4528
77.1382
76.8235
68.6524
64.0472
63.3607
60.5194
58.0499
57.8497
49.1637
33.8989
31.3245
29.3318
28.4355
28.3402
27.8825
24.9745
22.2381
21.1225
19.5779
18.5386
14.2385

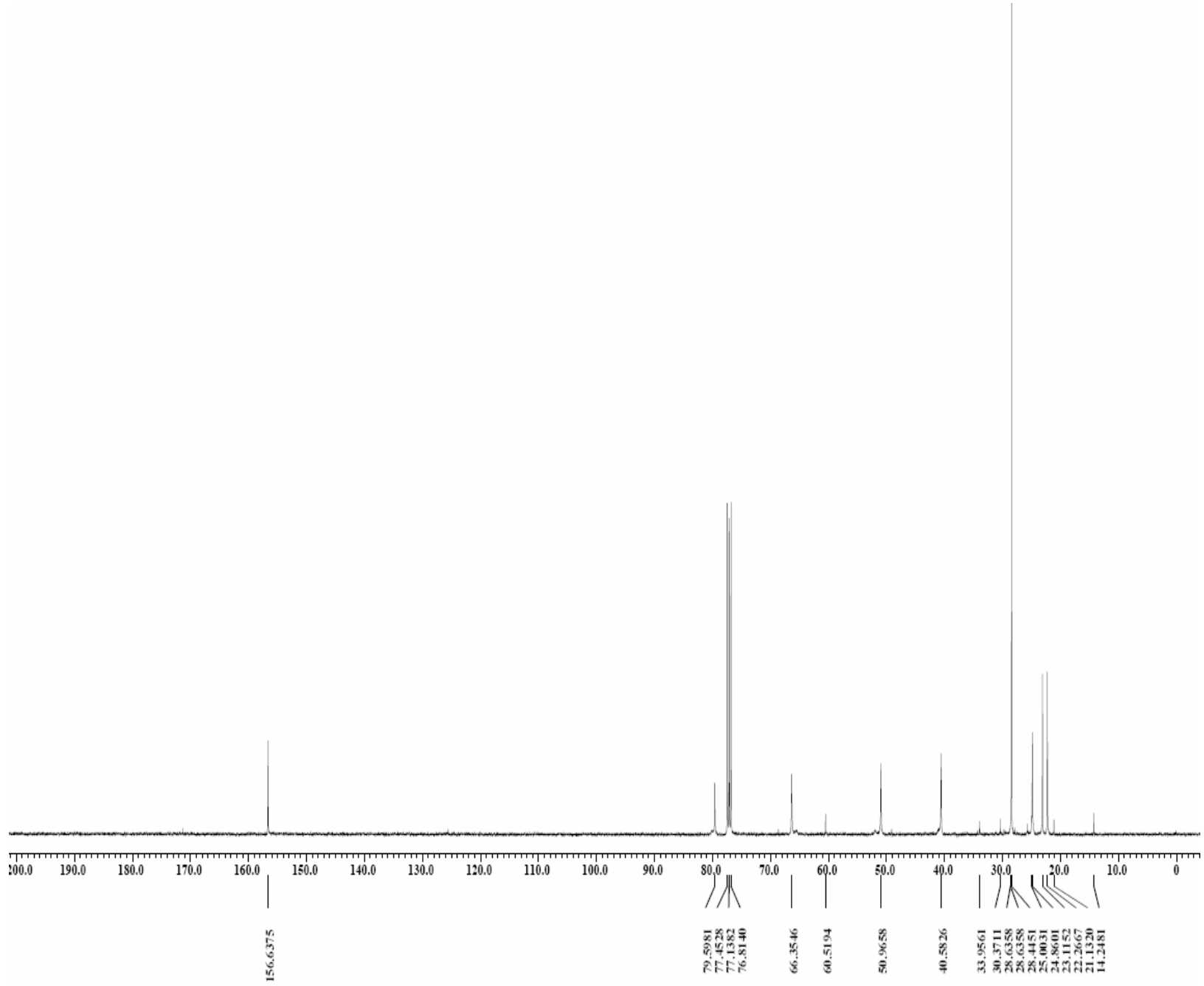

+TOF MS: 0.033 to 0.600 min from SVJ_Boc_V_OI.wiff
a=3.30071012794422730e-004, t0=-3.49418683411422530e+001 R;
Max. 24.8 counts.
calcd. [M+Na]+ 226.1419
226.1481
OH
N
H
104.0989
204.1626
242.1053
Intensity, counts
m/z, amu

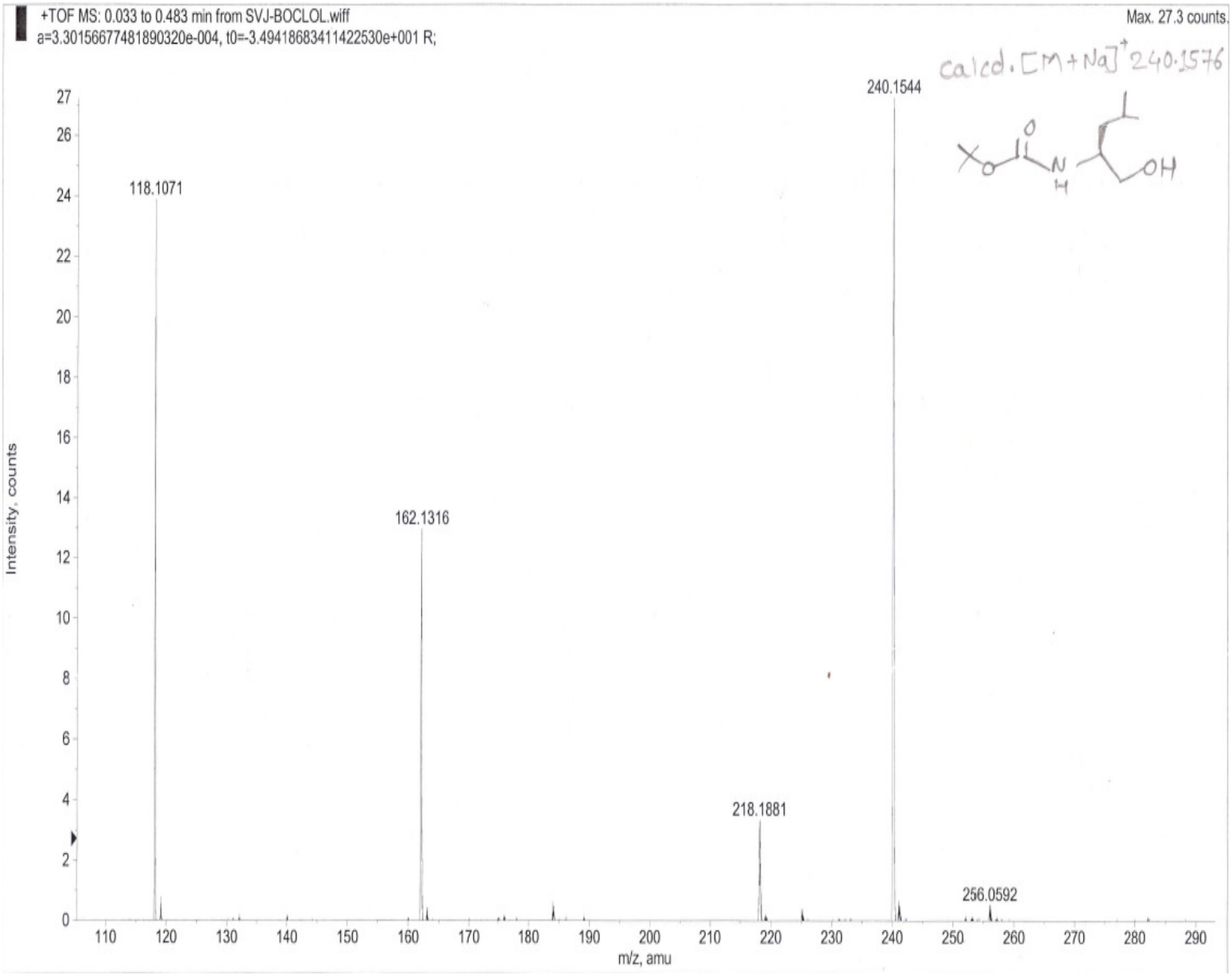

O
O
N
H
OH

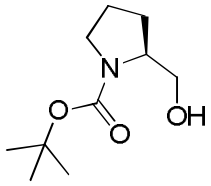
13


0.92
0.63
2.37
1.06
1.36
9
2.49
5.86
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2931
4.7467
3.7123
3.6287
3.5038
3.4912
2.9758
1.4465
1.4339
1.3251
1.3205
1.3045
1.2621
0.9391
0.9356
0.9230
0.9196
0.0000

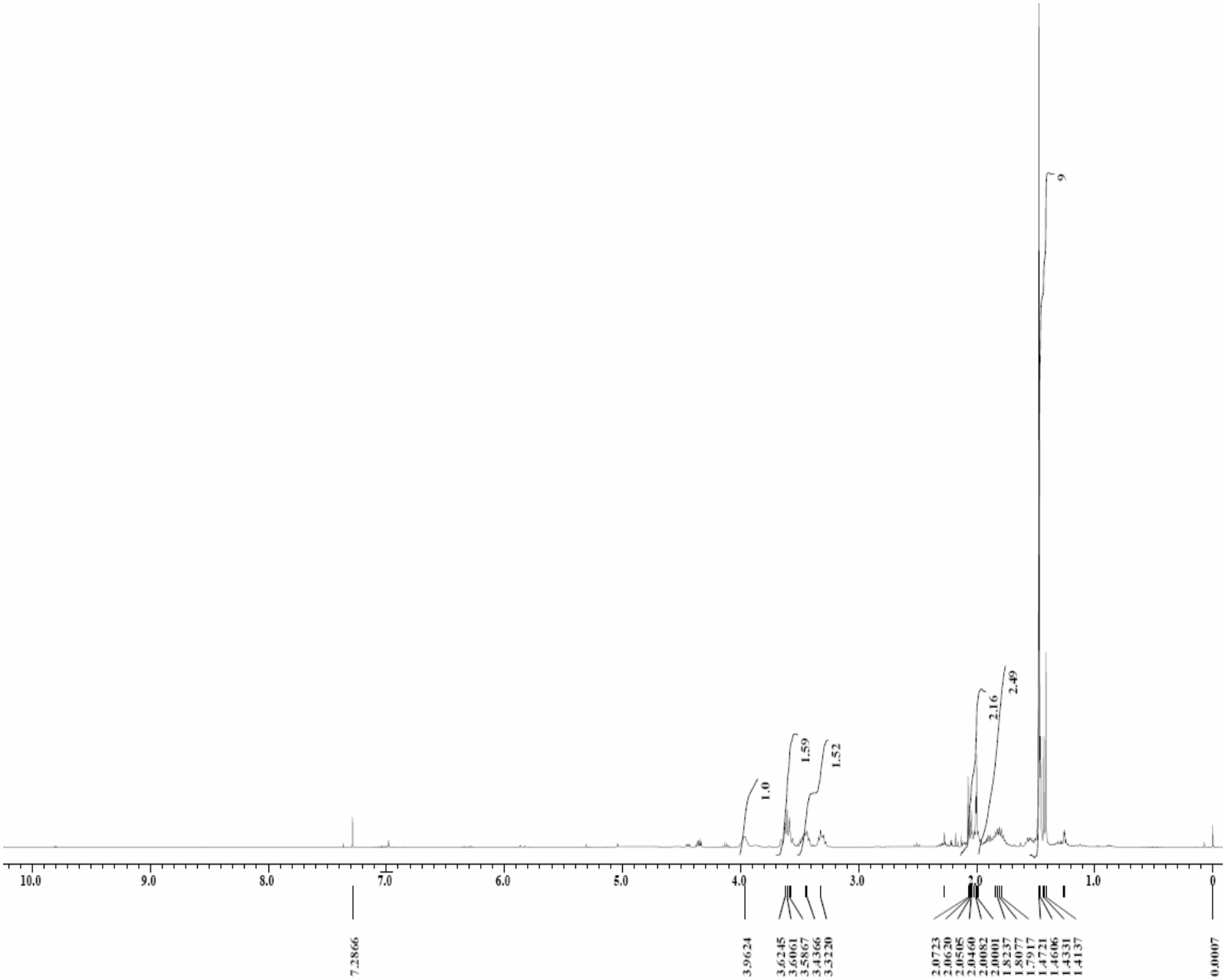

O
O
N
H
OH

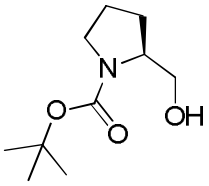

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.6375
79.5981
77.4528
77.1382
76.8140
66.3546
60.5194
50.9658
40.5826
33.9561
30.3711
28.6358
28.6358
28.4451
25.0031
24.8601
23.1152
22.2667
21.1320
14.2481

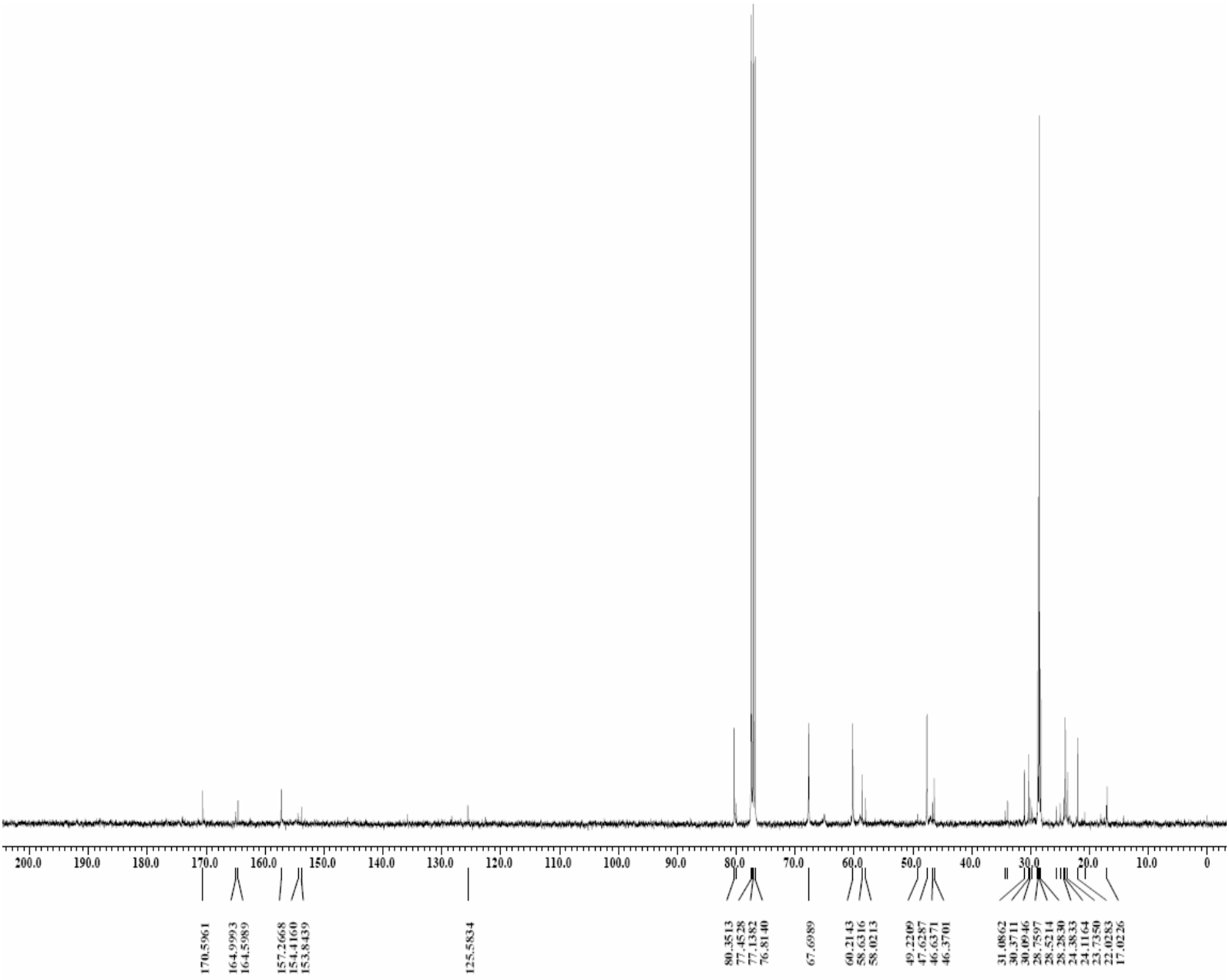

+TOF MS: 0.033 to 0.483 min from SVJ-BOCLOL.wiff
a=3.30156677481890320e-004, t0=-3.49418683411422530e+001 R;
Max. 27.3 counts.
calcd. [M+Na]+ 240.1576
240.1544
118.1071
162.1316
218.1881
256.0592
Intensity, counts
m/z, amu

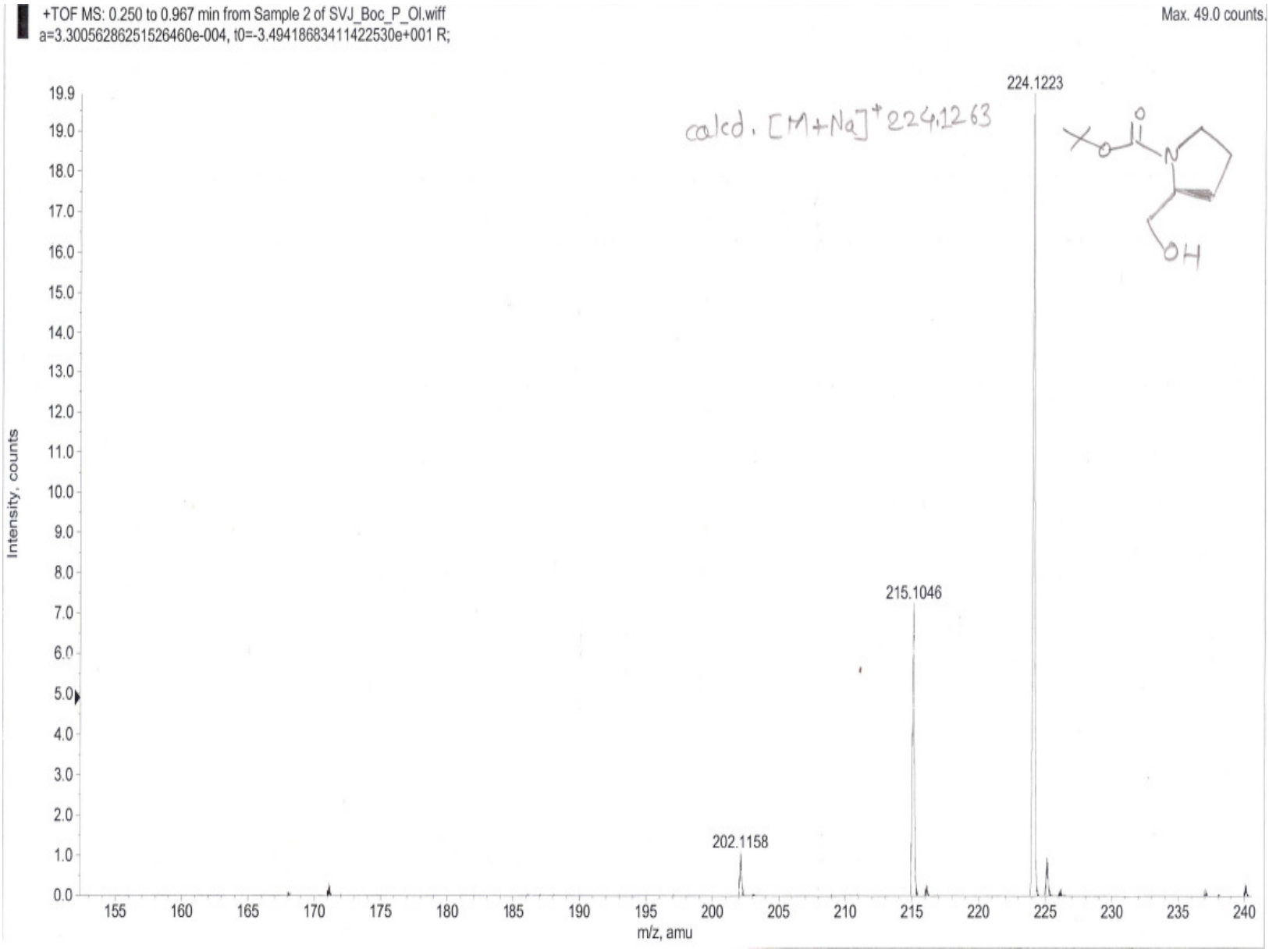

N
O
O
OH

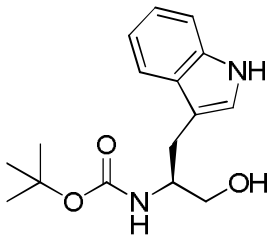
14


9
2.49
2.16
1.59
1.52
1.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2866
3.9624
3.6245
3.6061
3.5867
3.4366
3.3220
2.0723
2.0620
2.0505
2.0460
2.0082
2.0001
1.8237
1.8077
1.7917
1.4721
1.4606
1.4331
1.4137
0.0007

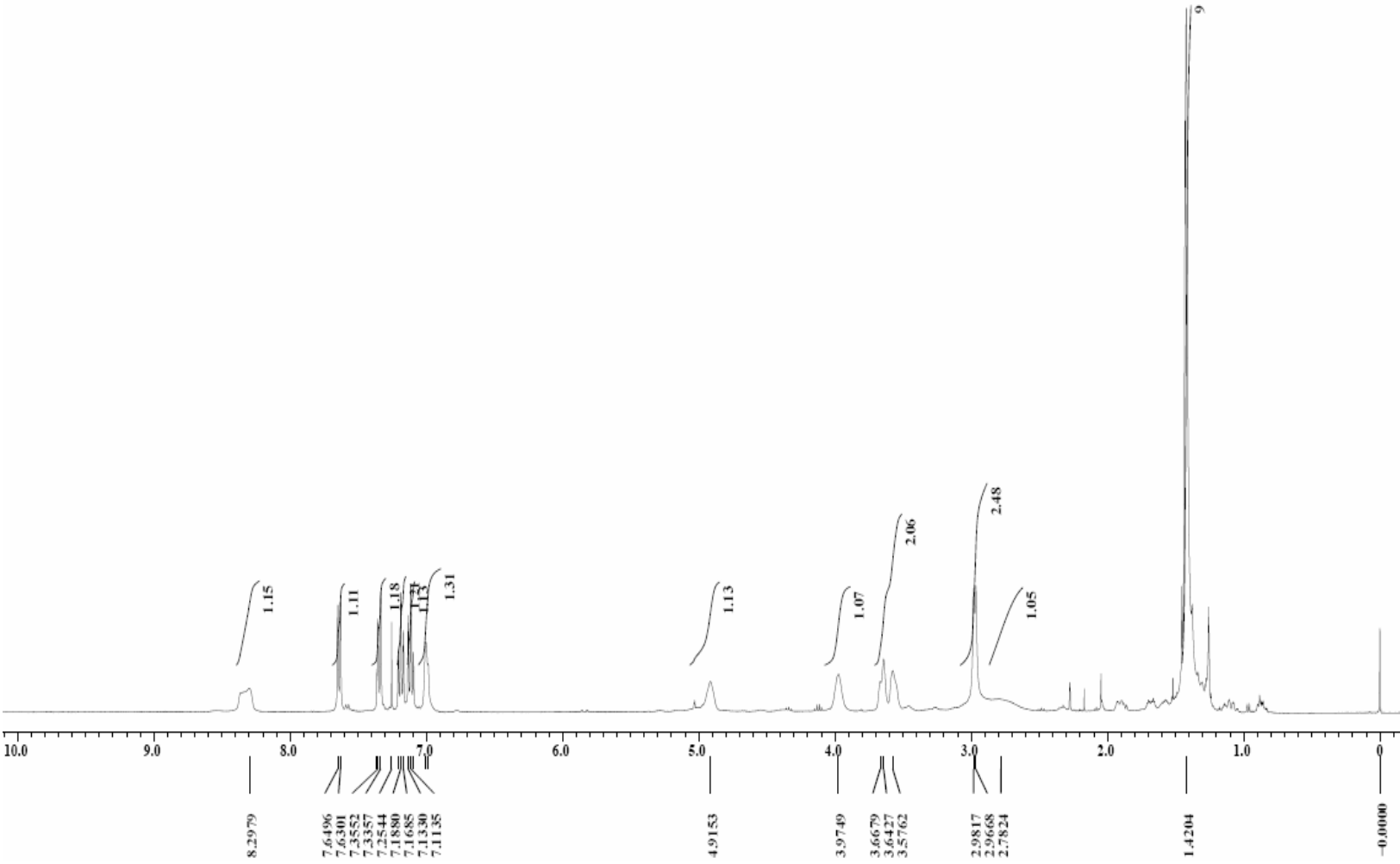

N
O
O
OH

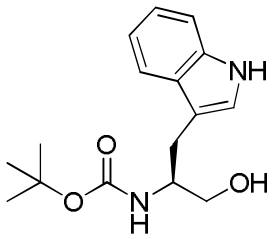

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.5961
164.9993
164.5989
157.2668
154.4160
153.8439
125.5834
80.3513
77.4528
77.1382
76.8140
67.6989
60.2143
58.6316
58.0213
49.2209
47.6287
46.6371
46.3701
31.0862
30.3711
30.0946
28.7597
28.5214
28.2830
24.3833
24.1164
23.7350
22.0283
17.0226

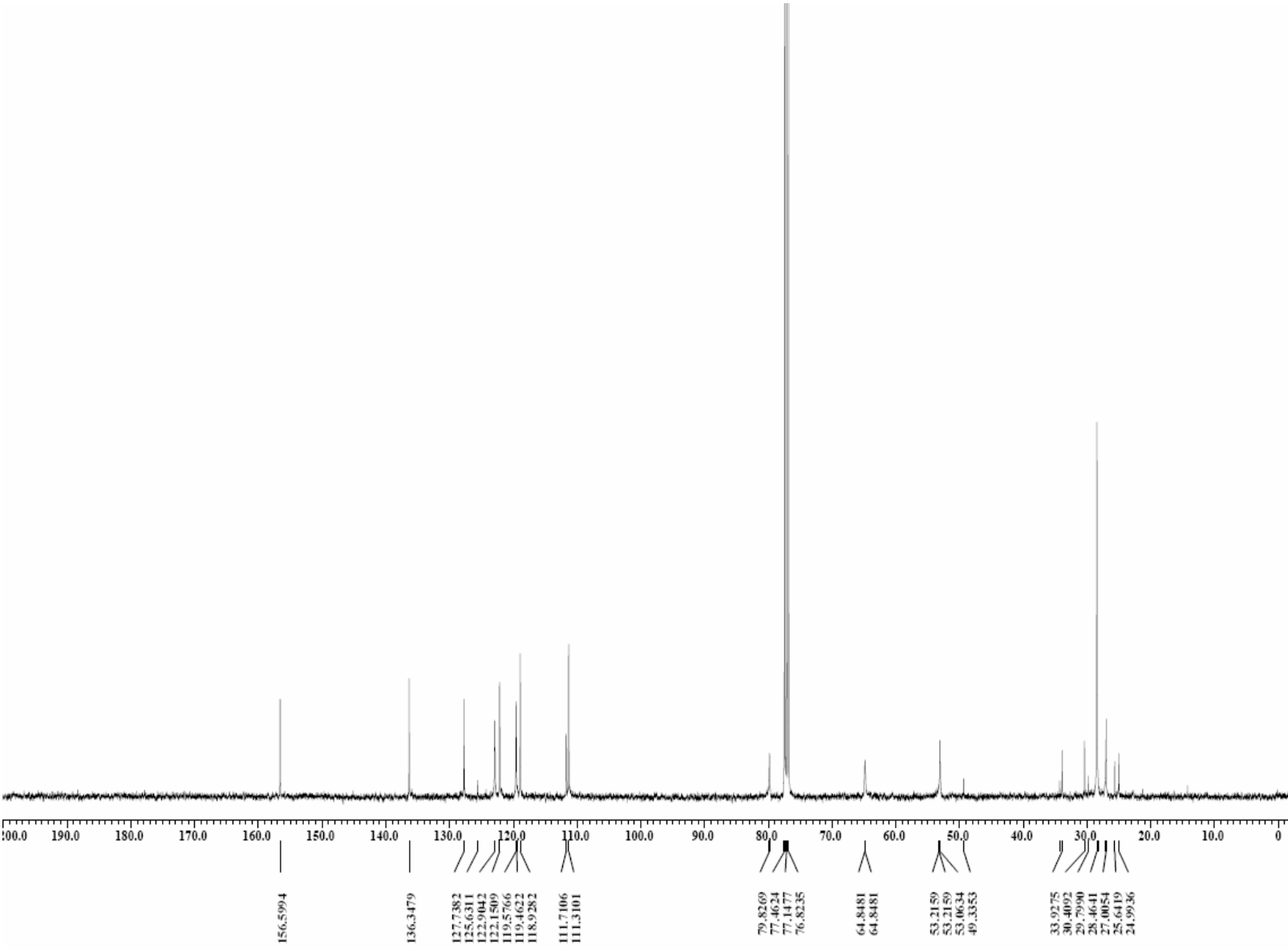

+TOF MS: 0.250 to 0.967 min from Sample 2 of SVJ_Boc_P_OI.wiff
a=3.30056286251526460e-004, t0=-3.49418683411422530e+001 R;
Max. 49.0 counts.
224.1223
calcd. [M+Na]+ 224.1263
215.1046
202.1158
OH
Intensity, counts
m/z, amu

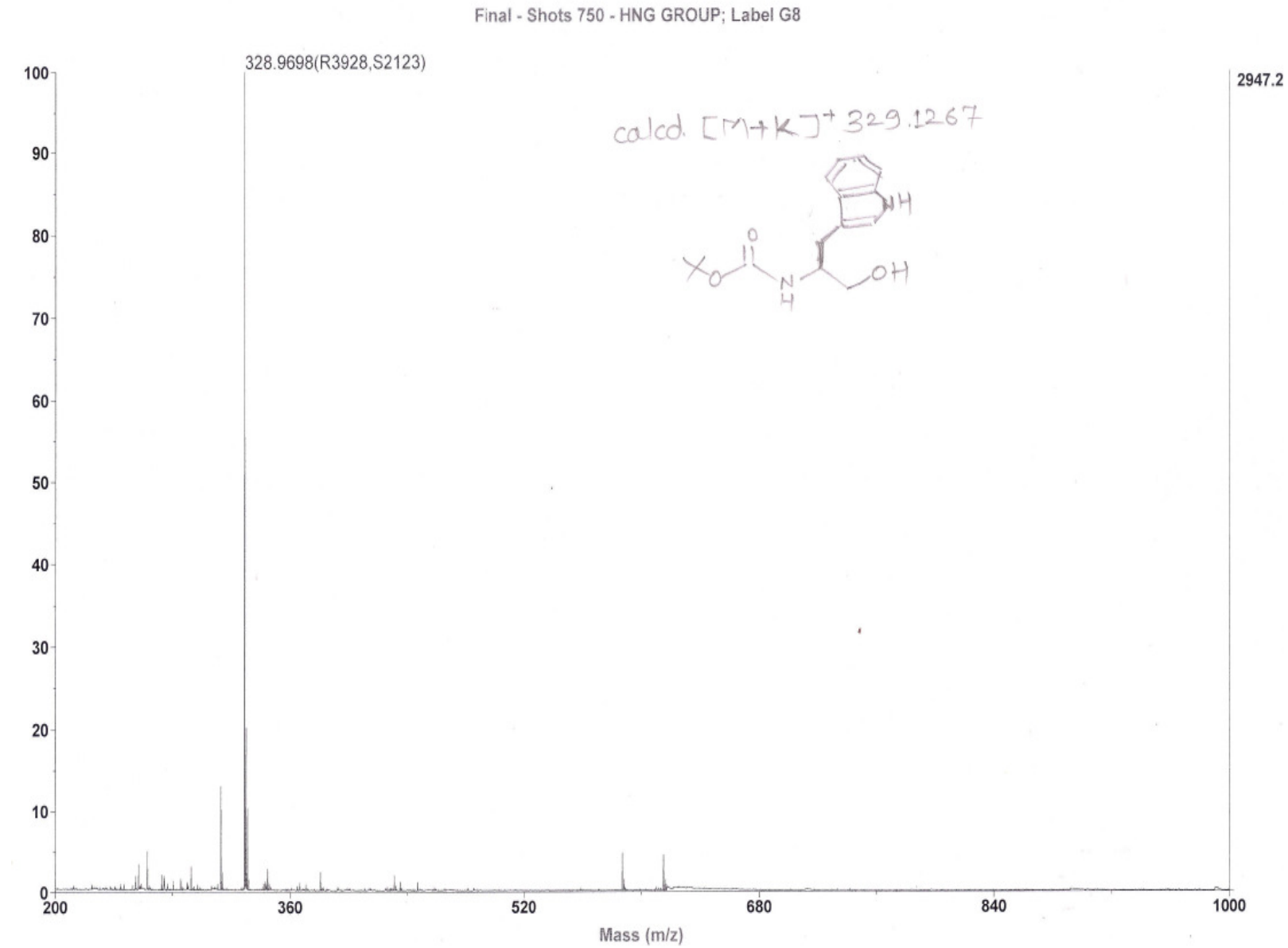

NH
O
O
N
H
OH

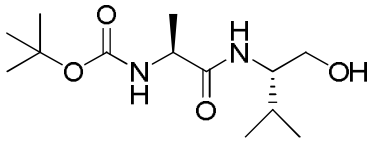
15


1.15
1.11
1.18
1.31
1.13
1.07
2.06
2.48
1.05
9
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.2979
7.6496
7.6301
7.3552
7.3357
7.2544
7.1880
7.1685
7.1330
7.1135
4.9153
3.9749
3.6679
3.6427
3.5762
2.9817
2.9668
2.7824
1.4204
-0.0000

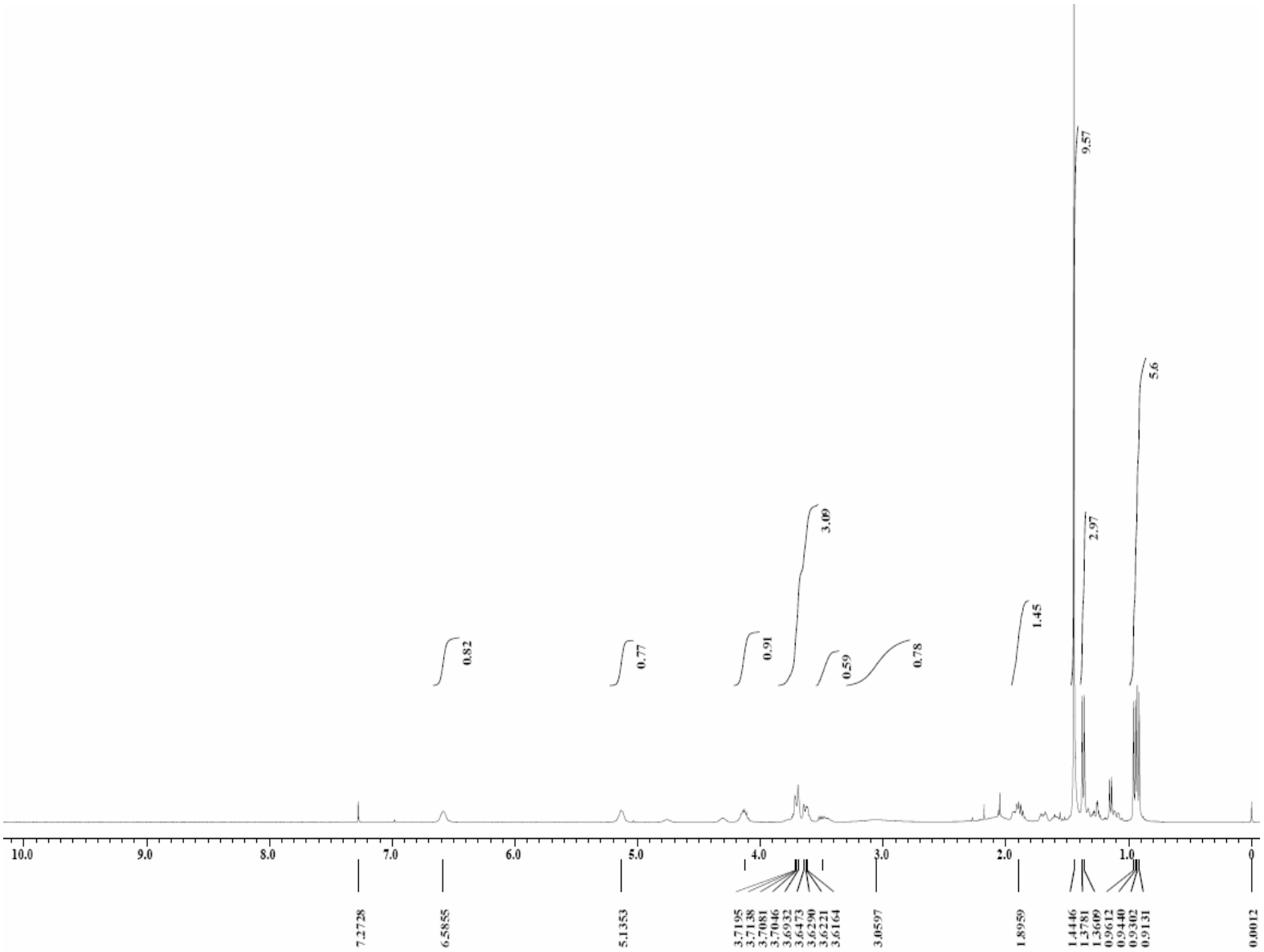

NH
O
O
N
H
OH

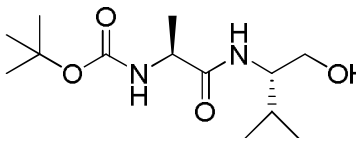

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
156.5994
136.3479
127.7382
125.6311
122.9042
122.1509
119.5766
119.4622
118.9282
111.7106
111.3101
79.8269
77.4624
77.1477
76.8235
64.8481
64.8481
53.2159
53.2159
53.0634
49.3353
33.9275
30.4092
29.7990
28.4641
27.0054
25.6419
24.9936

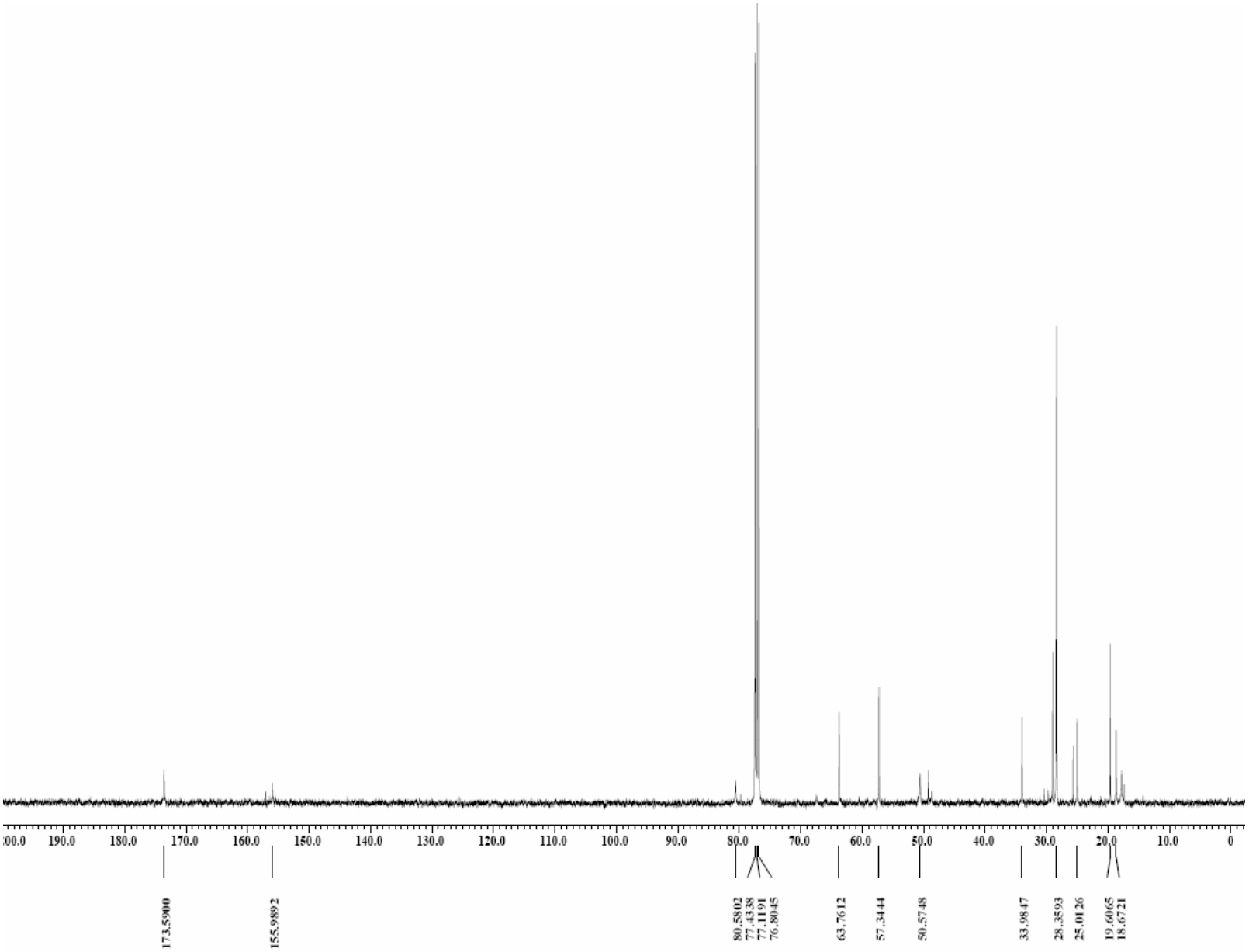

Final - Shots 750 - HNG GROUP; Label G8
328.9698(R3928,S2123)
2947.2
calcd. [M+K]+ 329.1267
NH
O
O
N
H
OH
100
90
80
70
60
50
40
30
20
10
0
200
360
520
680
840
1000
Mass (m/z)

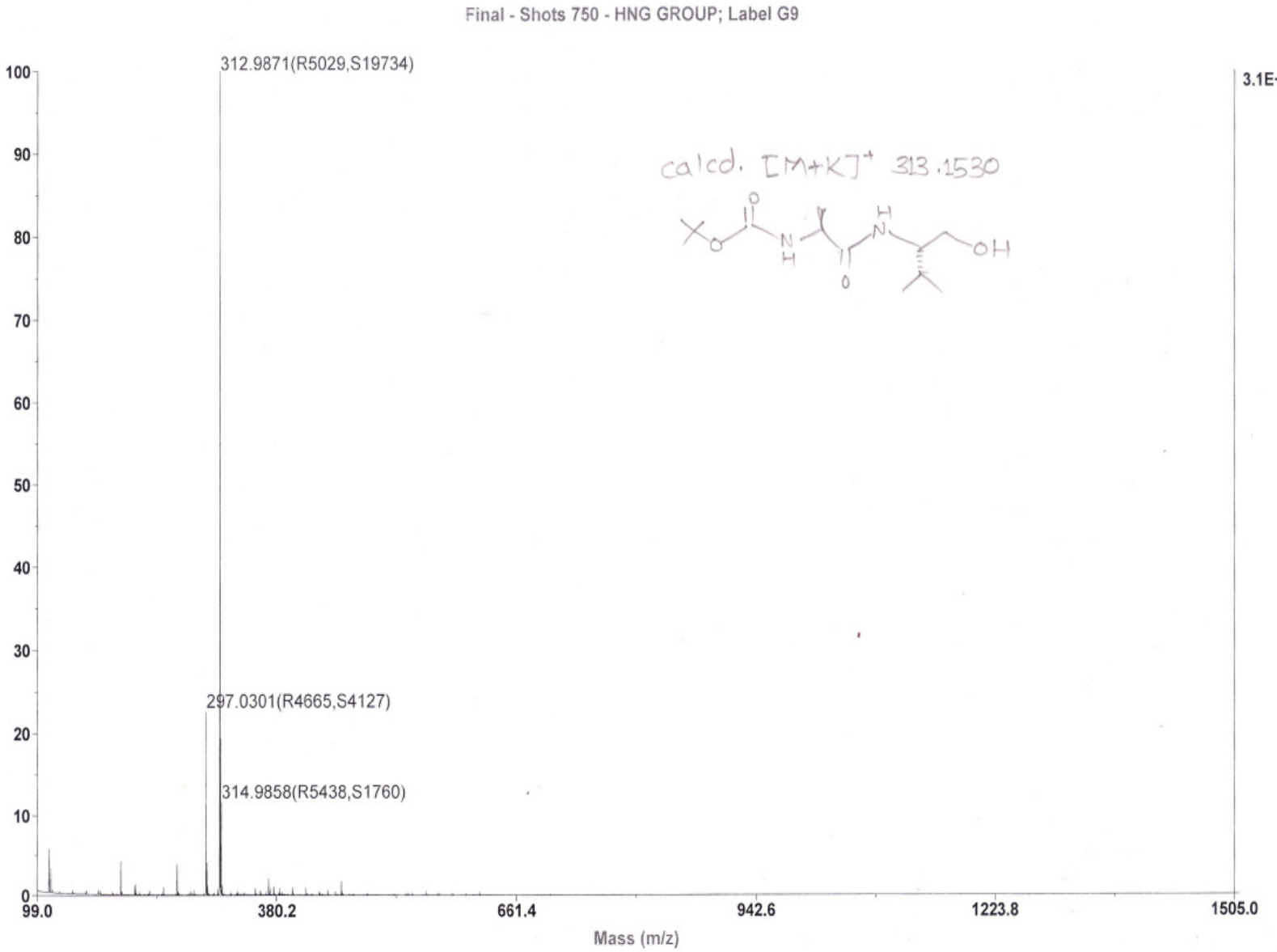


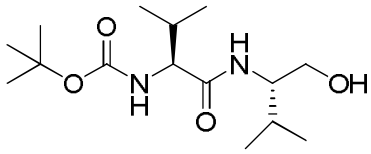
16


9.57
5.6
3.09
2.97
1.45
0.82
0.77
0.91
0.59
0.78
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2728
6.5855
5.1353
3.7195
3.7138
3.7081
3.7046
3.6932
3.6473
3.6290
3.6221
3.6164
3.0597
1.8959
1.4446
1.3781
1.3609
0.9612
0.9440
0.9302
0.9131
0.0012

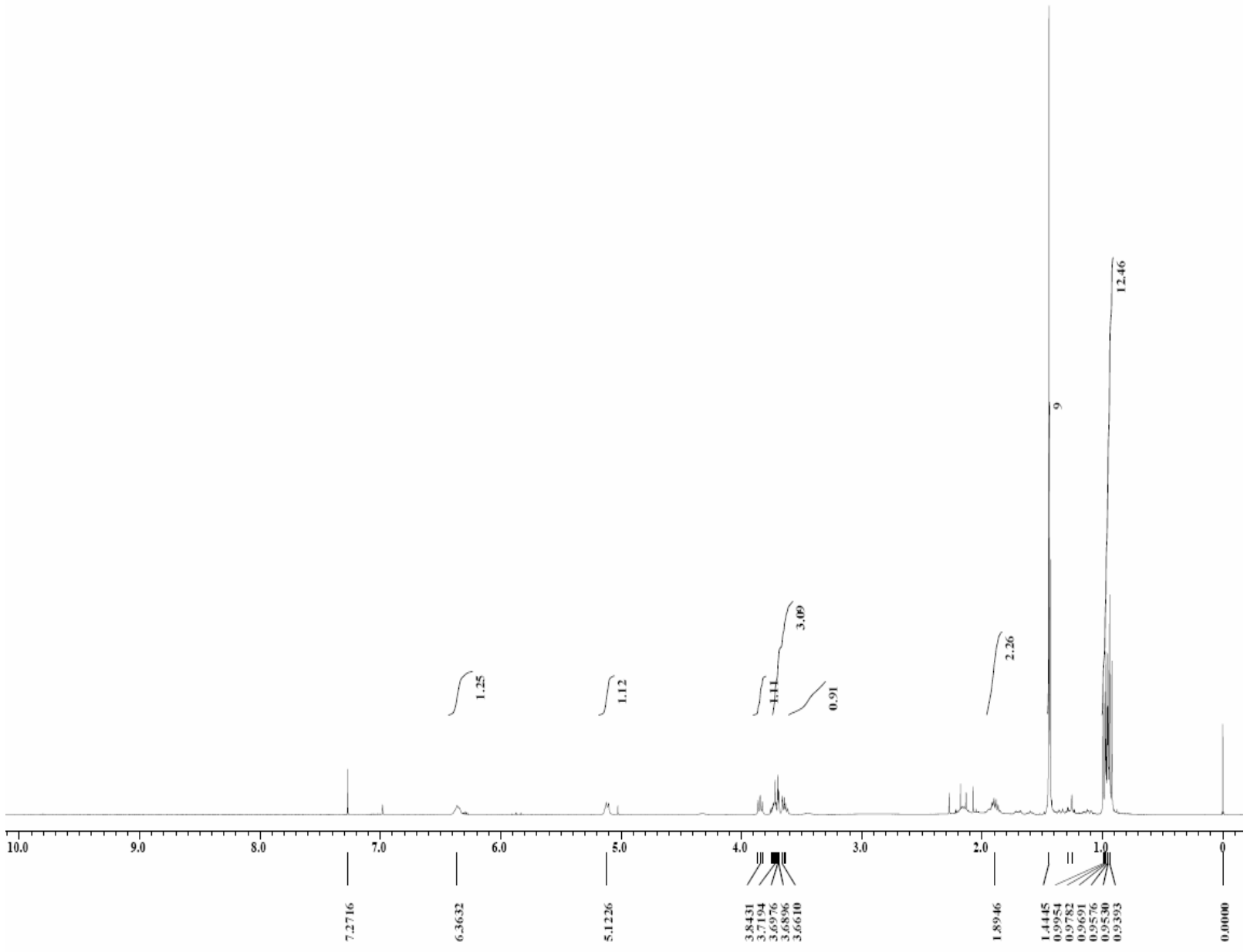


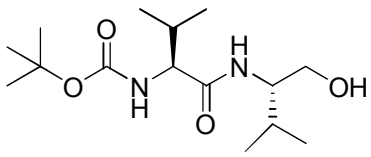

173.5900
155.9892
80.5802
77.4338
77.1191
76.8045
63.7612
57.3444
50.5748
33.9847
28.3593
25.0126
19.6065
18.6721

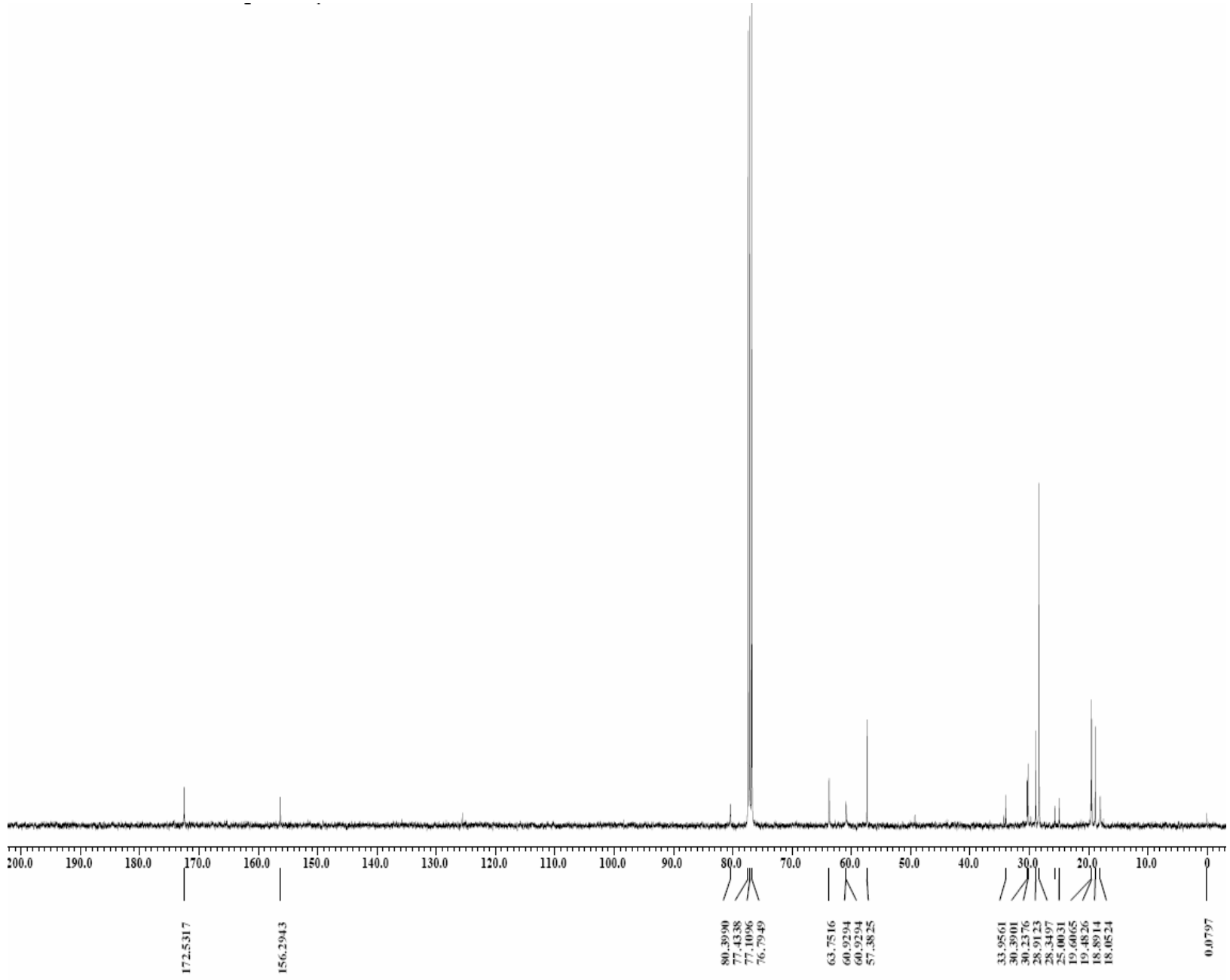

Final - Shots 750 - HNG GROUP; Label G9
312.9871(R5029,S19734)
calcd. [M+K]+ 313.1530
297.0301(R4665,S4127)
314.9858(R5438,S1760)
100
90
80
70
60
50
40
30
20
10
0
99.0
380.2
661.4
942.6
1223.8
1505.0
Mass (m/z)

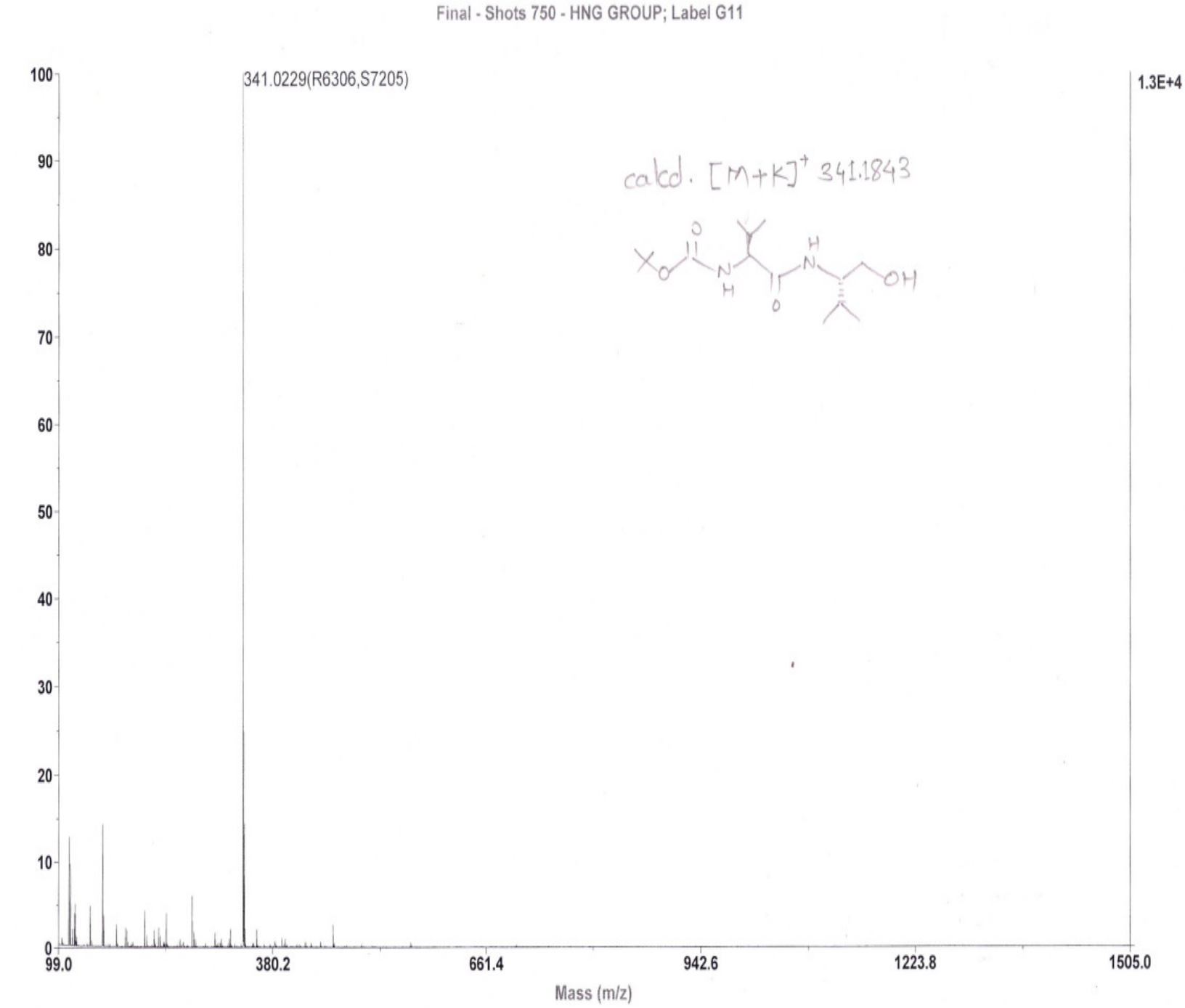


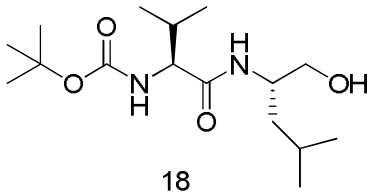
17


1.25
1.12
4.11
3.09
0.91
2.26
9
12.46
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2716
6.3632
5.1226
3.8431
3.7194
3.6976
3.6896
3.6610
1.8946
1.4445
0.9954
0.9782
0.9691
0.9576
0.9530
0.9393
0.0000

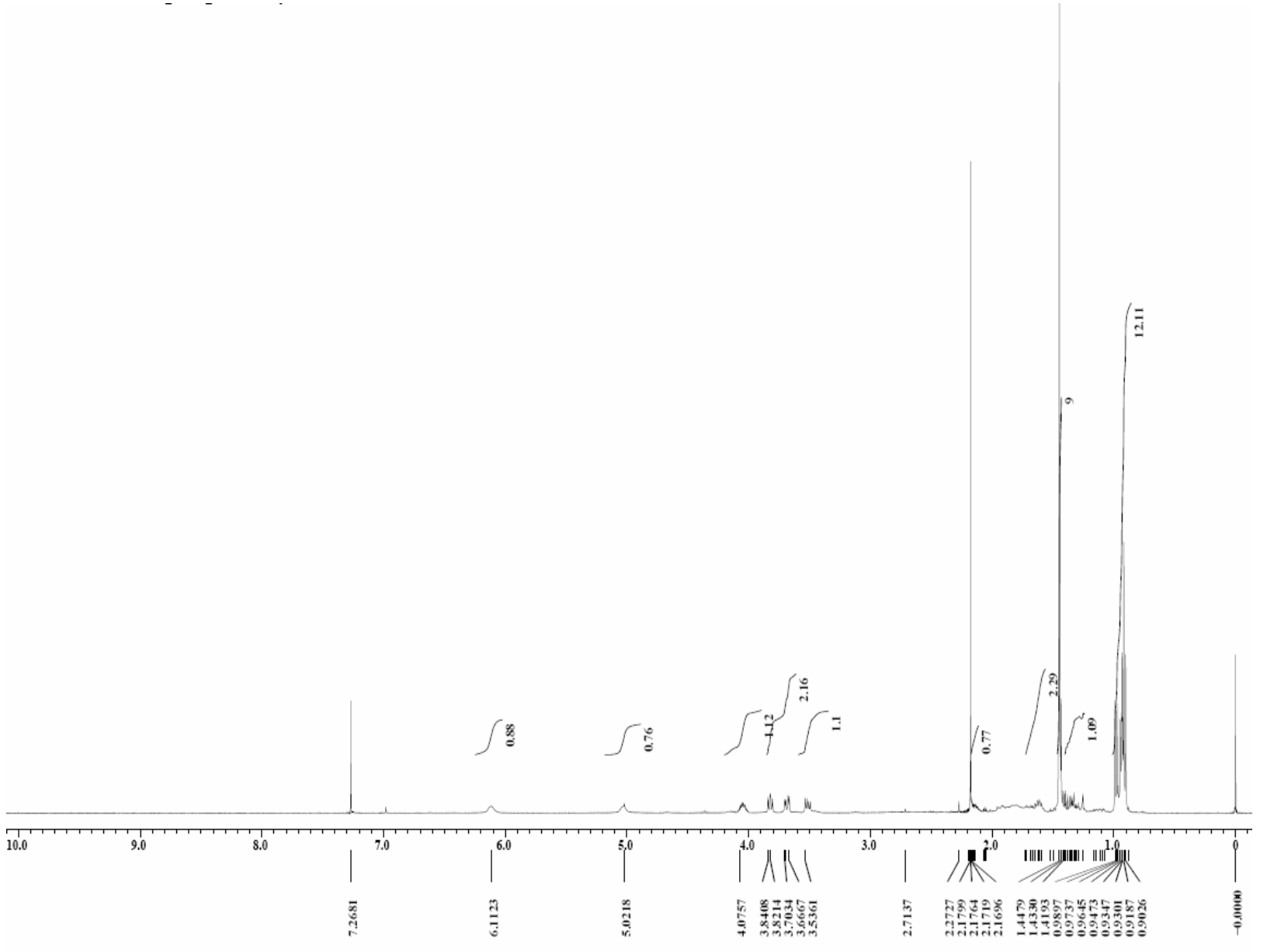

O
O
N
H
H
N
OH
O

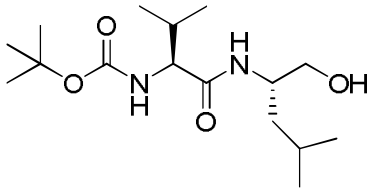

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
172.5317
156.2943
80.3990
77.4338
77.1096
76.7949
63.7516
60.9294
60.9294
57.3825
33.9561
30.3901
30.2376
28.9123
28.3497
25.0031
19.6065
19.4826
18.8914
18.4524
0.0797

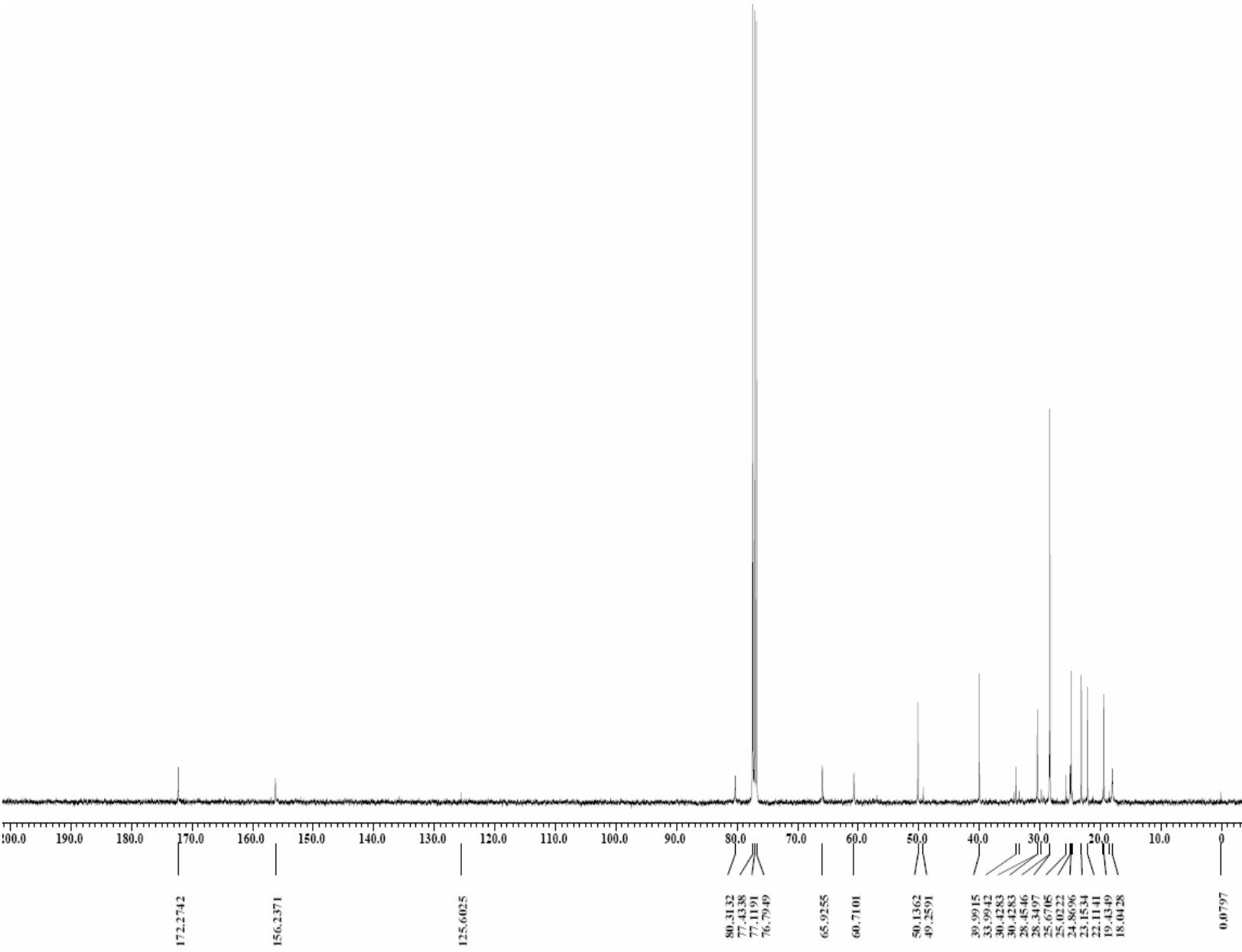

Final - Shots 750 - HNG GROUP; Label G11
341.0229(R6306,S7205)
1.3E+4
calcd. [M+K]+ 341.1843
100
90
80
70
60
50
40
30
20
10
0
99.0
380.2
661.4
942.6
1223.8
1505.0
Mass (m/z)

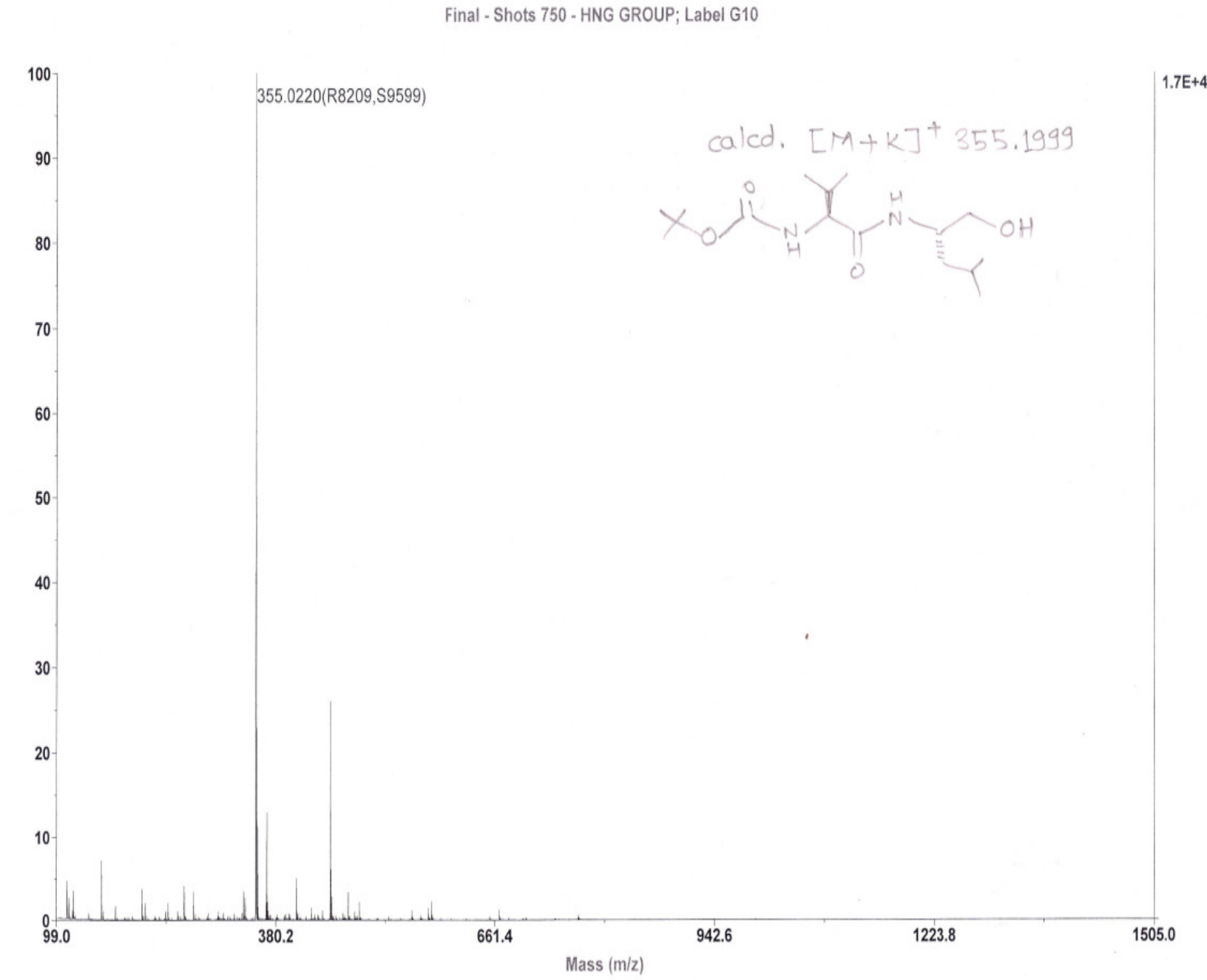

O
O
N
H
H
N
OH
O

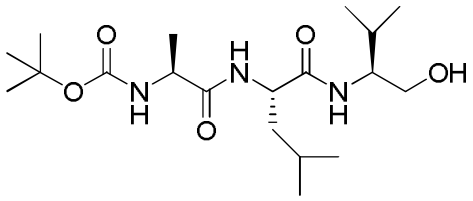
18


0.88
0.76
1.12
2.16
1.1
0.77
2.29
9
1.09
12.11
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2681
6.1123
5.0218
4.0757
3.8408
3.8214
3.7034
3.6667
3.5361
2.7137
2.2727
2.1799
2.1764
2.1719
2.1696
1.4479
1.4330
1.4193
0.9897
0.9737
0.9645
0.9473
0.9347
0.9301
0.9187
0.9026
-0.0000

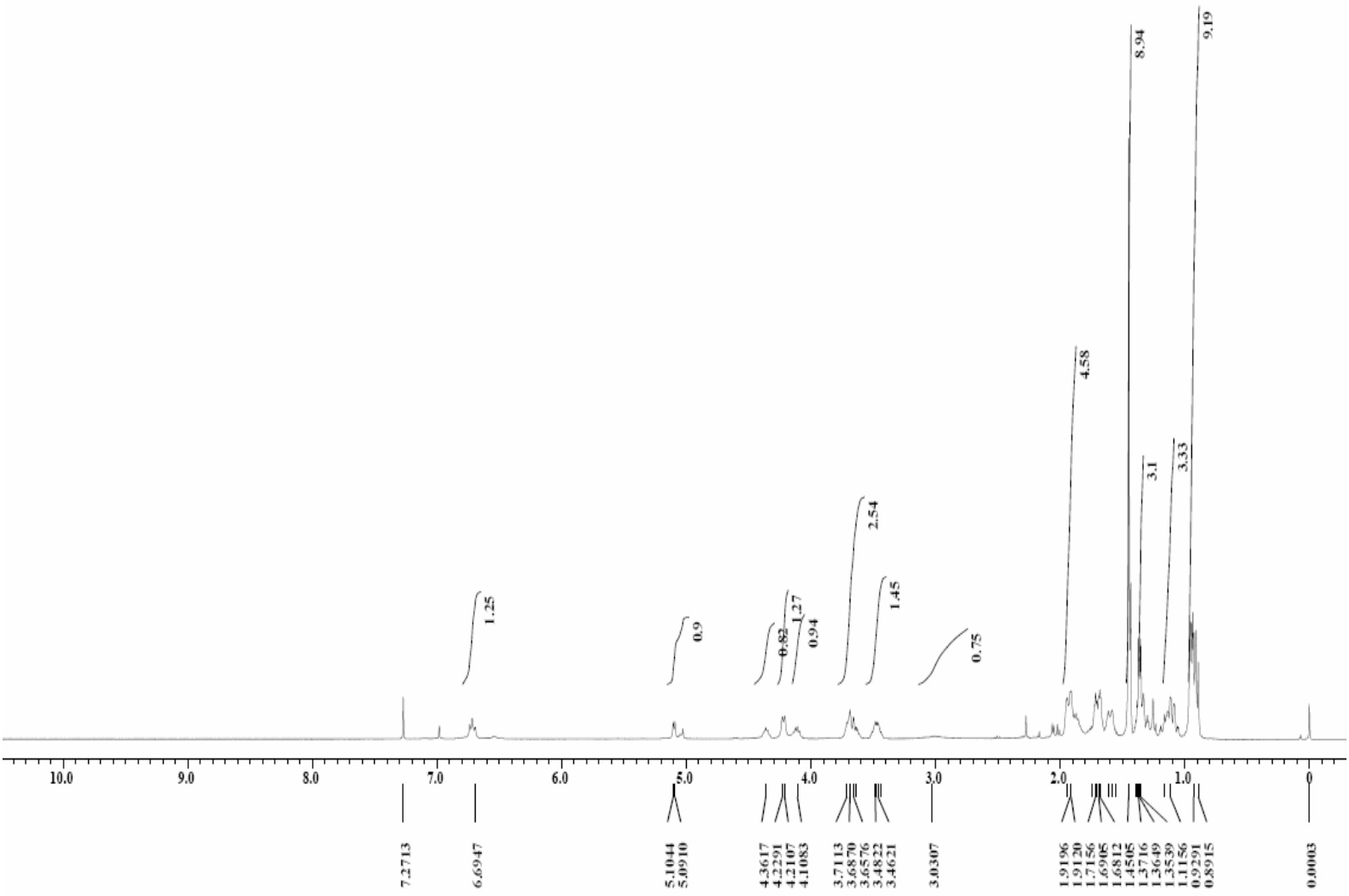

O
O
N
H
H
N
OH
O

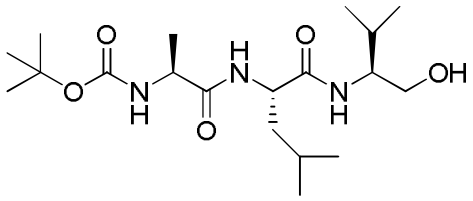

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
172.2742
156.2371
125.6025
80.3132
77.4438
77.1191
76.7949
65.9255
60.7101
50.1362
49.2591
39.9915
33.9942
30.4283
30.4283
28.4546
28.3497
25.6705
25.0222
24.8696
23.1534
22.1141
19.4349
18.0428
0.0797

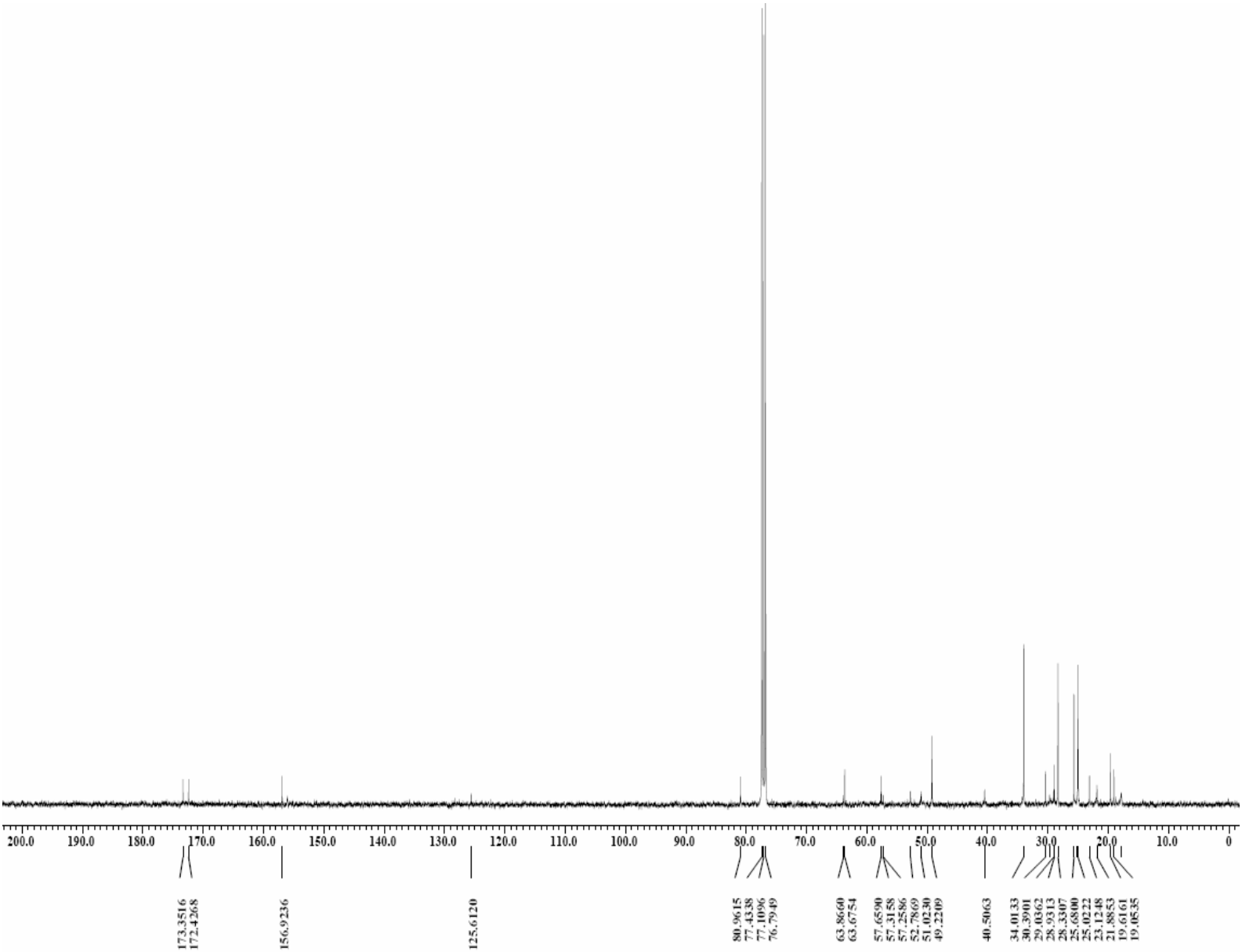

Final - Shots 750 - HNG GROUP; Label G10
355.0220(R8209,S9599)
calcd. [M+K]+ 355.1999
1.7E+4
100
90
80
70
60
50
40
30
20
10
0
99.0
380.2
661.4
942.6
1223.8
1505.0
Mass (m/z)

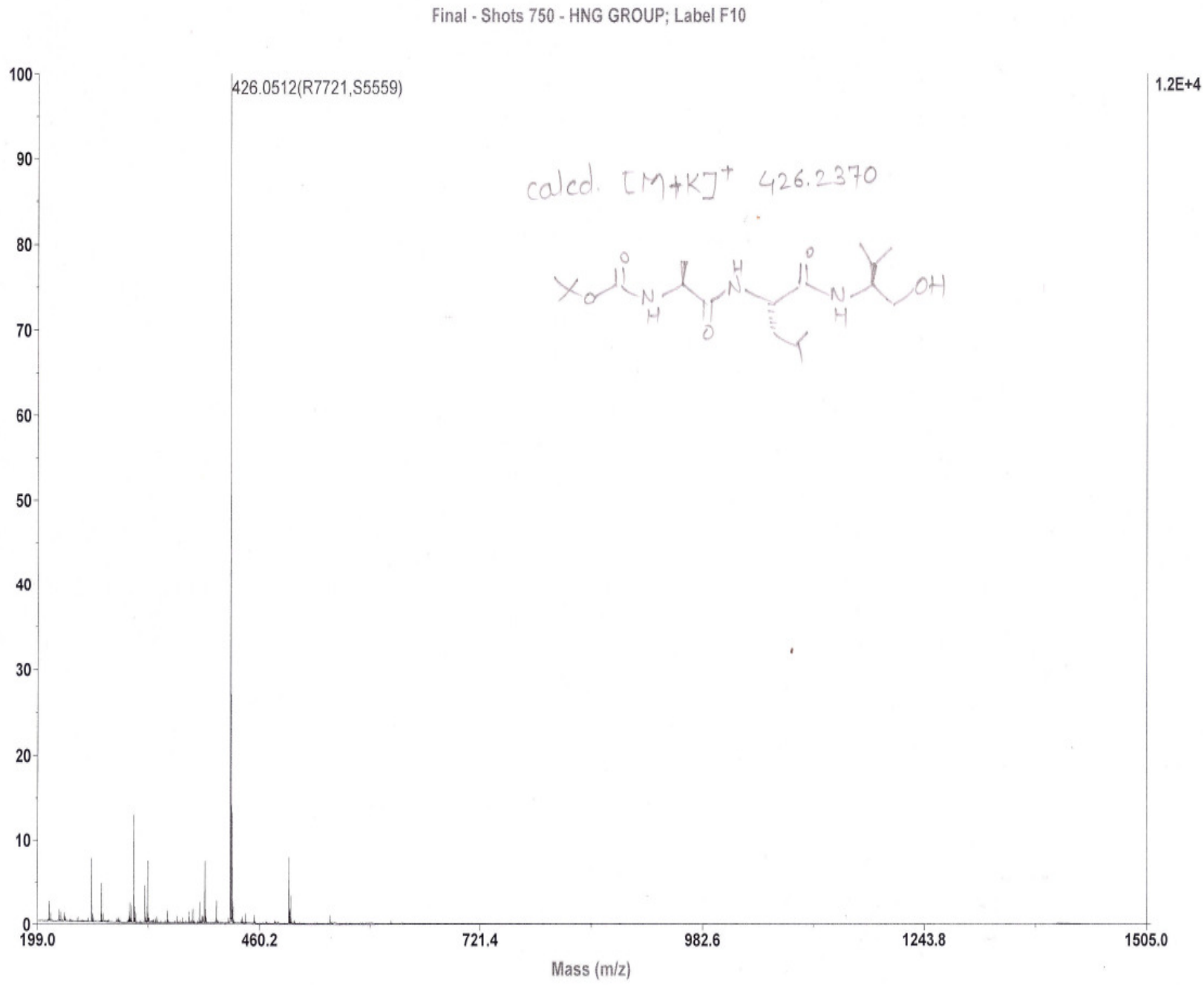


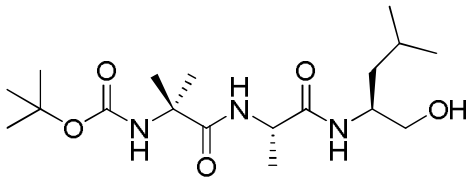
19


9.19
8.94
4.58
3.1
3.33
2.54
1.45
1.25
0.9
0.82
1.27
0.94
0.75
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2713
6.6947
5.1044
5.0910
4.3617
4.2291
4.2107
4.1083
3.7113
3.6870
3.6576
3.4822
3.4621
3.0307
1.9196
1.9120
1.7156
1.6905
1.6812
1.4508
1.3716
1.3649
1.3539
1.1156
0.9291
0.8915
0.0003

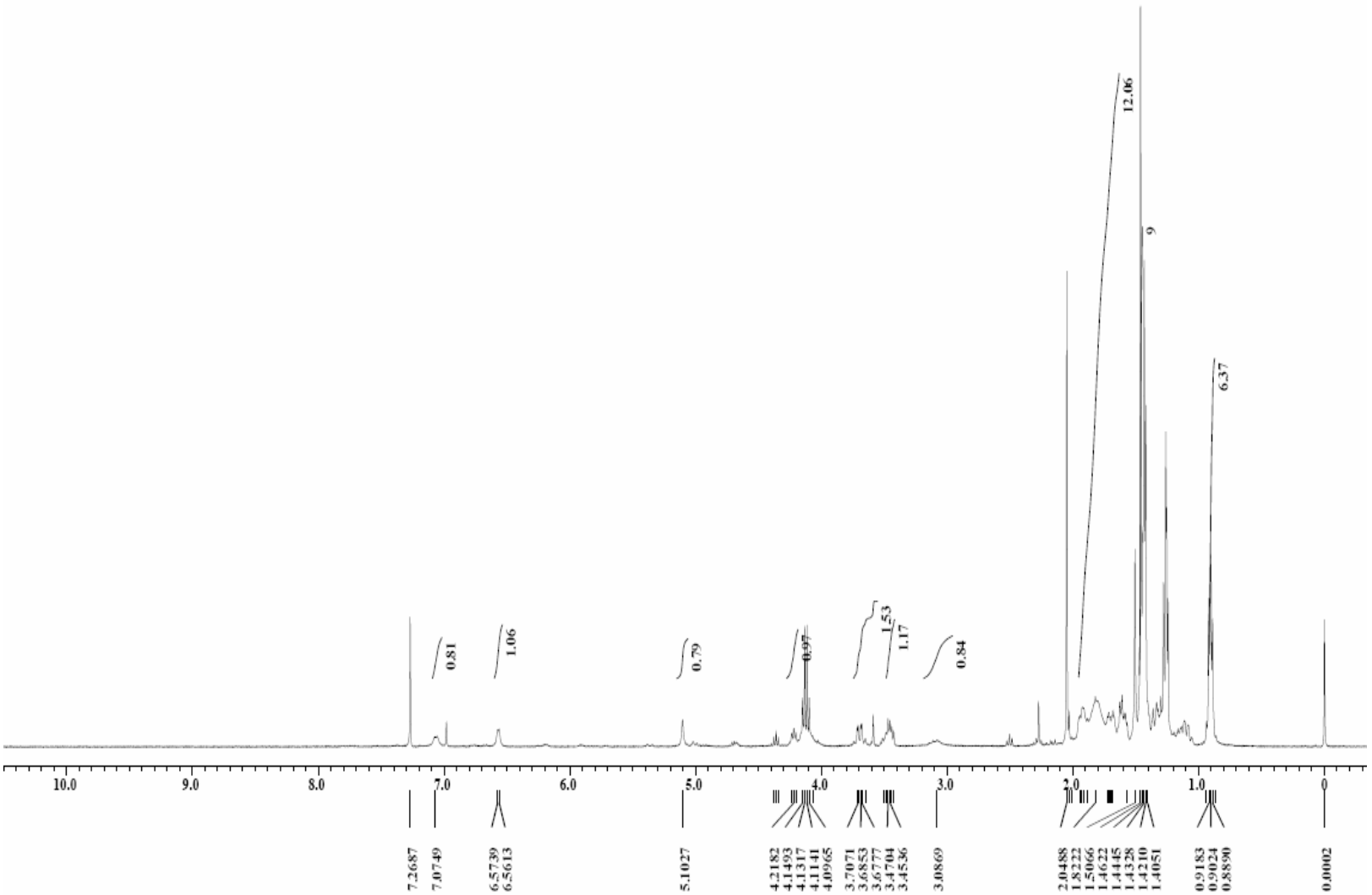

O
O
N
H
H
N
O
O
N
H
OH

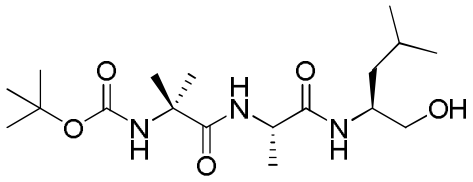

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
173.3516
172.4268
156.9236
125.6120
80.9615
77.4338
77.1096
76.7949
63.8660
63.6754
57.6590
57.3158
57.2586
52.7869
51.0230
49.2209
40.5063
34.0133
30.3901
29.0362
28.9313
28.3307
25.6800
25.0222
23.1248
21.8853
19.6161
19.0535

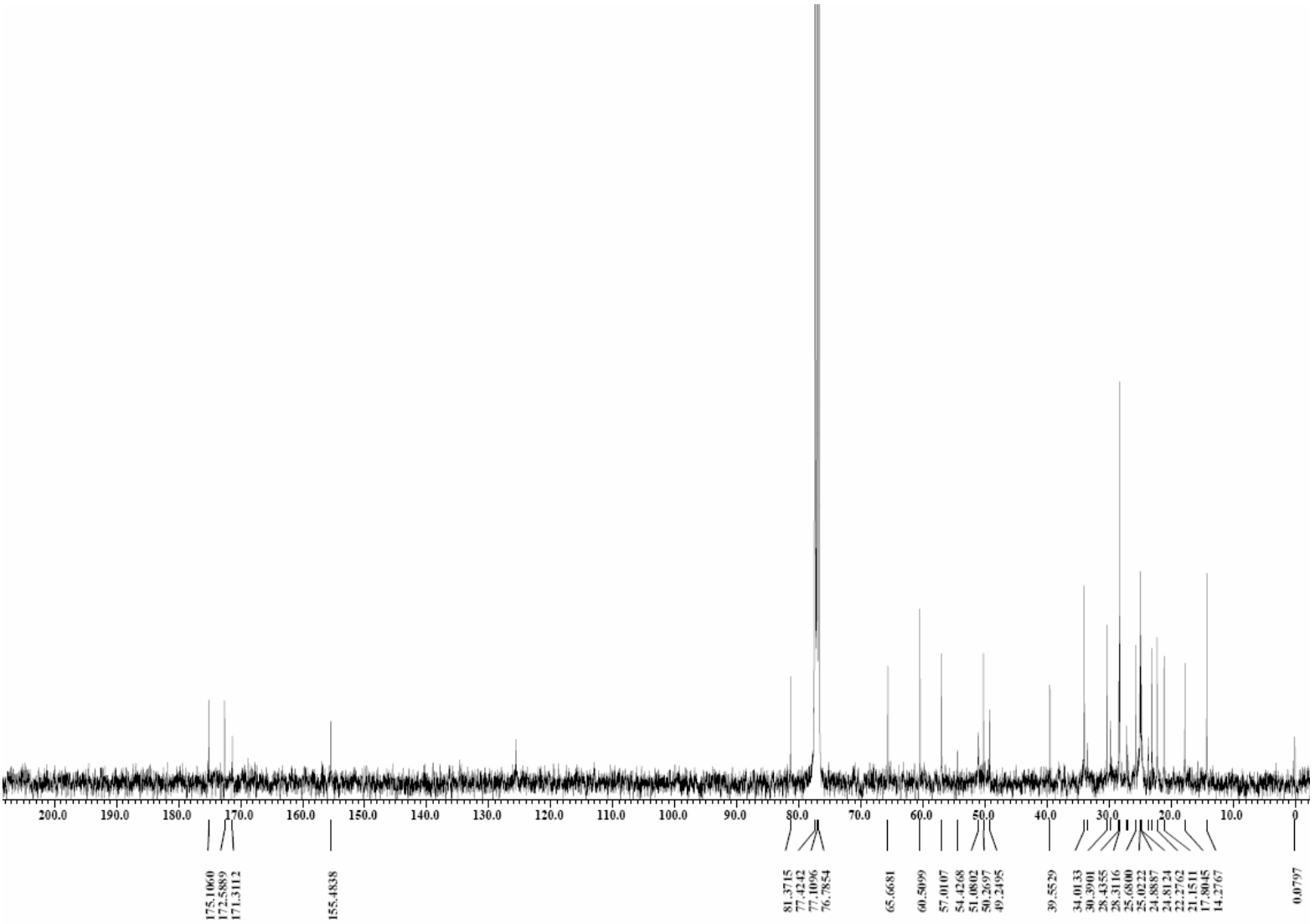

Final - Shots 750 - HNG GROUP; Label F10
426.0512(R7721,S5559)
1.2E+4
calcd. [M+K]+ 426.2370
100
90
80
70
60
50
40
30
20
10
0
199.0
460.2
721.4
982.6
1243.8
1505.0
Mass (m/z)

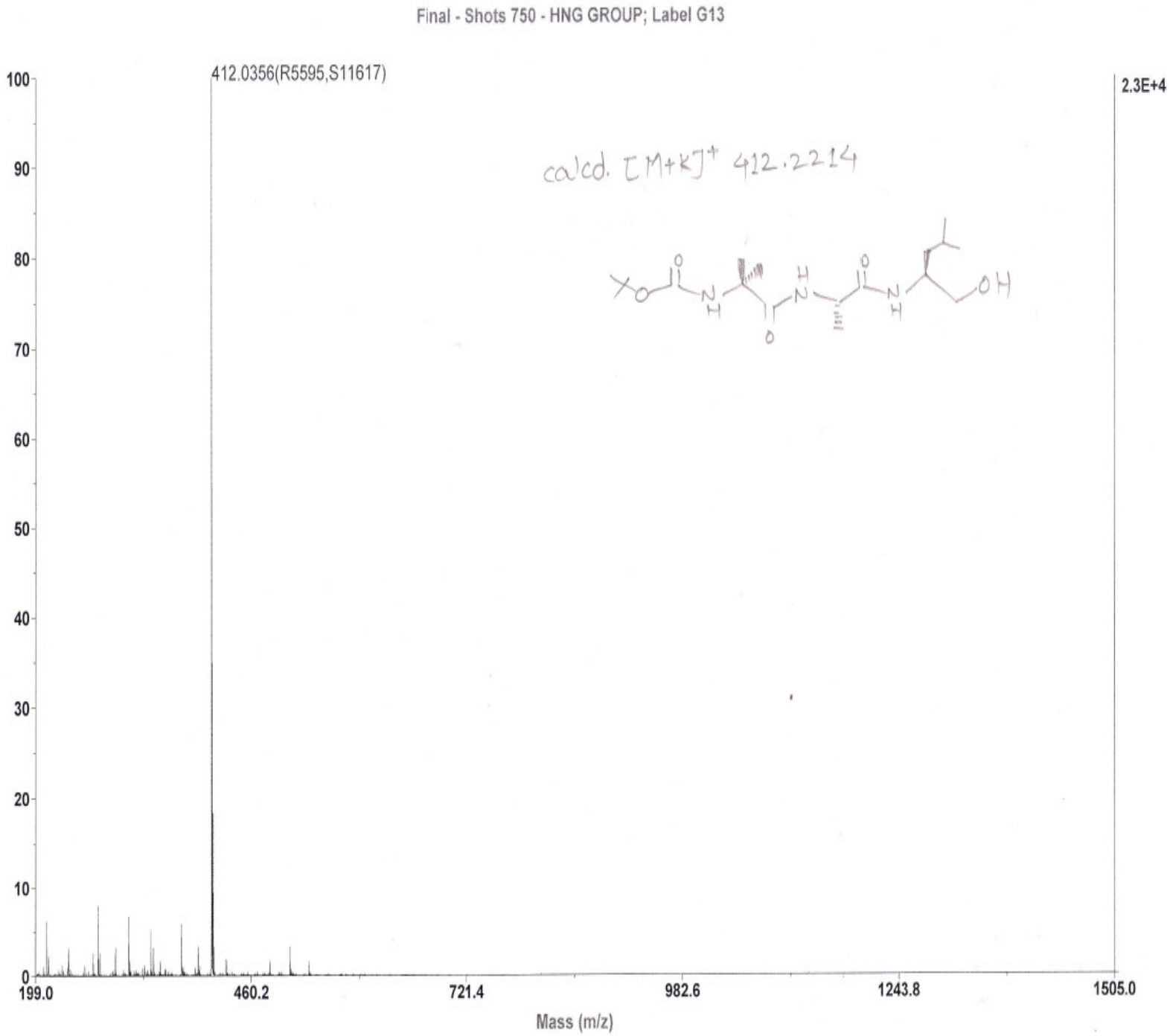


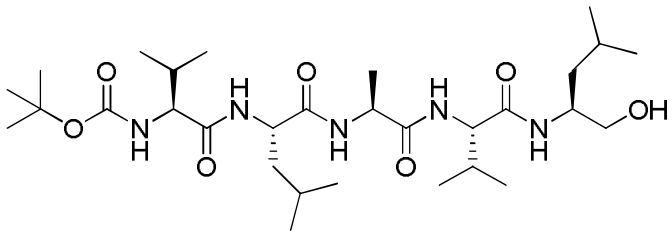
20


12.06
9
6.37
0.81
1.06
0.79
0.97
1.53
1.17
0.84
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2687
7.0749
6.5739
6.5613
5.1027
4.2182
4.1493
4.1317
4.1141
4.0965
3.7071
3.6853
3.6777
3.4704
3.4536
3.0869
2.0488
1.8222
1.5066
1.4622
1.4445
1.4338
1.4210
1.4051
0.9183
0.9024
0.8890
0.0002

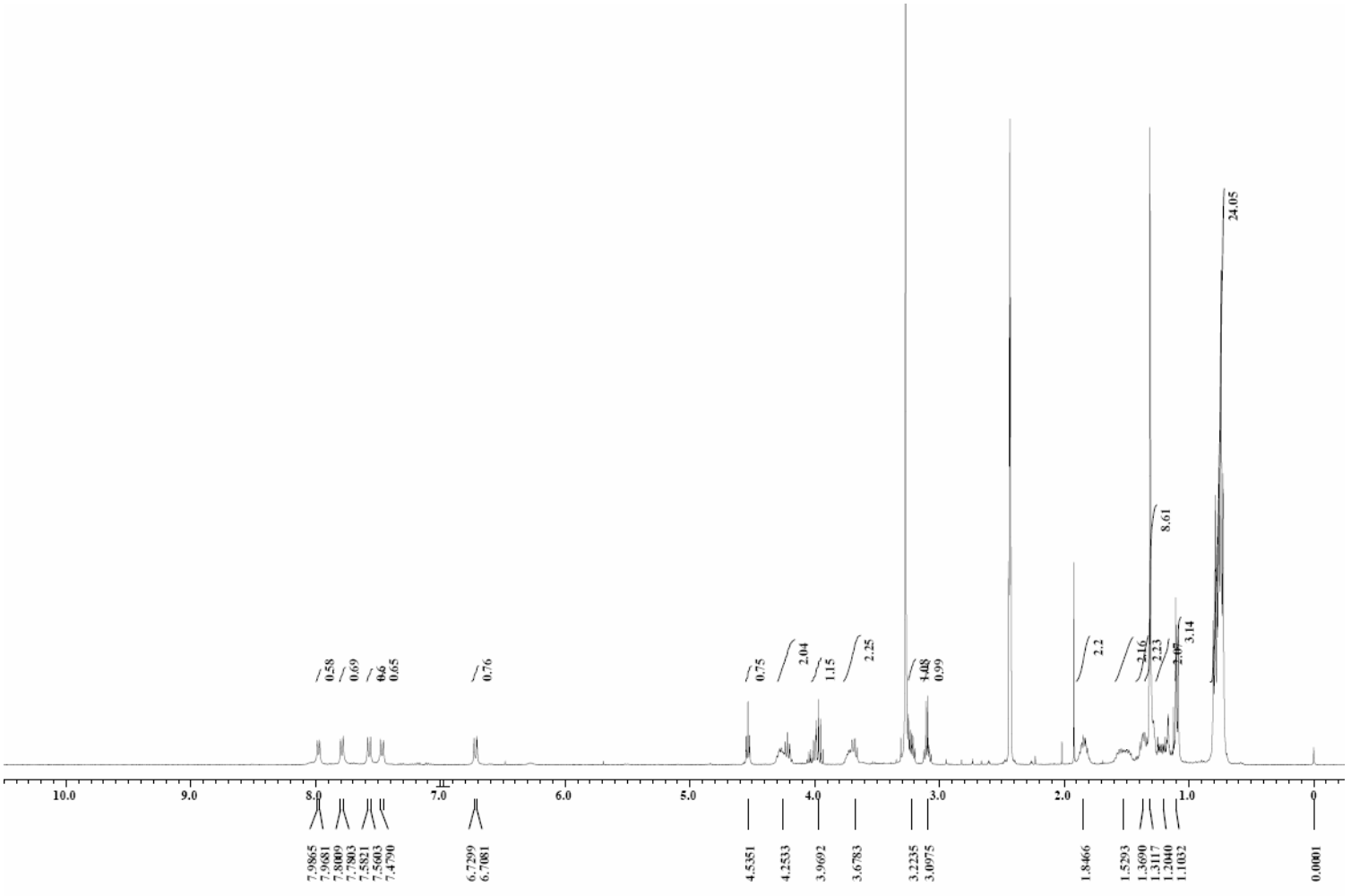

O
O
N
H
H
N
O
O
N
H
OH

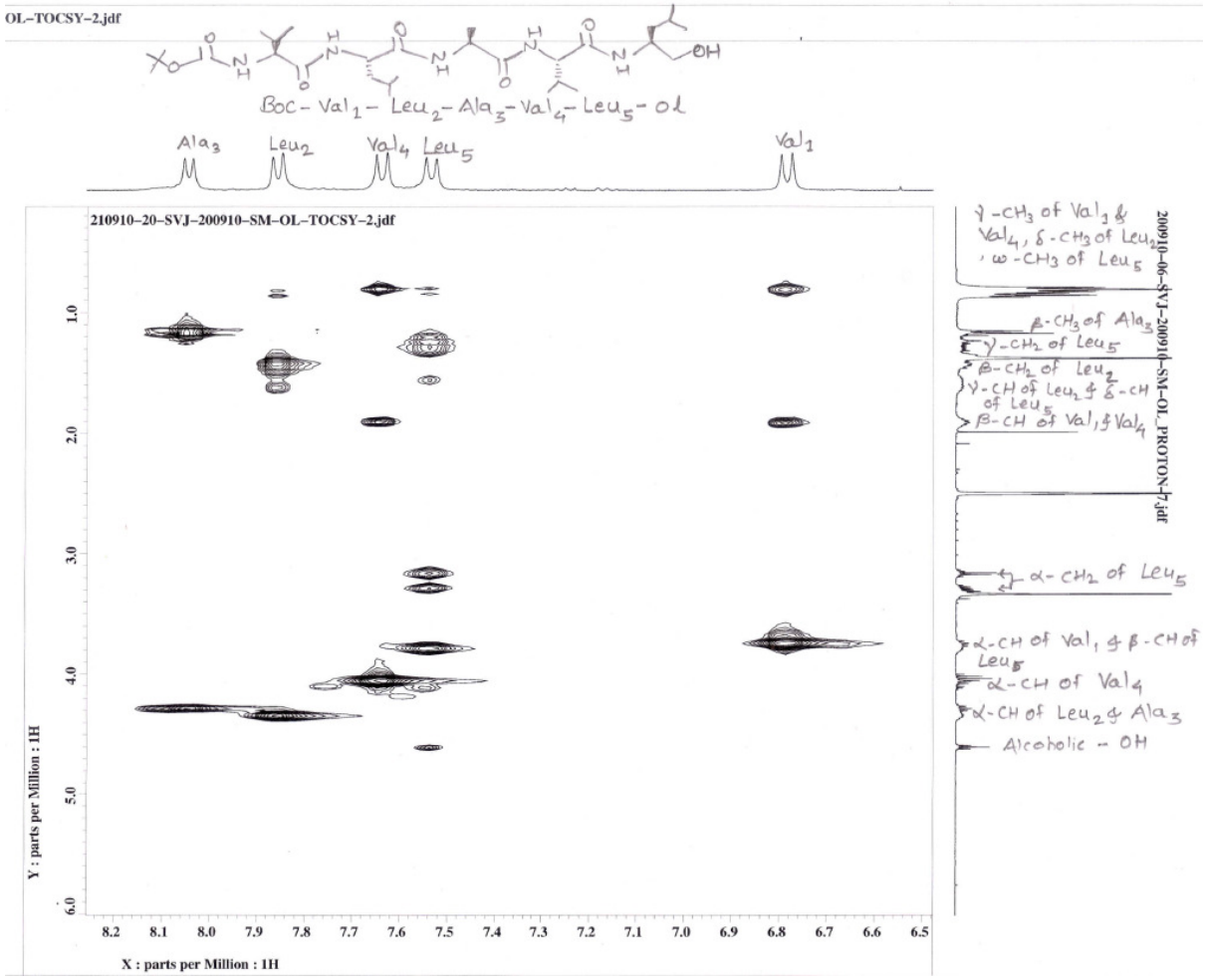

200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
175.1060
172.5889
171.3112
155.4838
81.3715
77.4242
77.1096
76.7854
65.6681
60.5099
57.0107
54.4268
51.0802
50.2697
49.2495
39.5529
34.0133
30.3901
28.4355
28.3116
25.6800
25.0222
24.8887
24.8124
22.2762
21.1511
17.3045
14.2767
0.0797

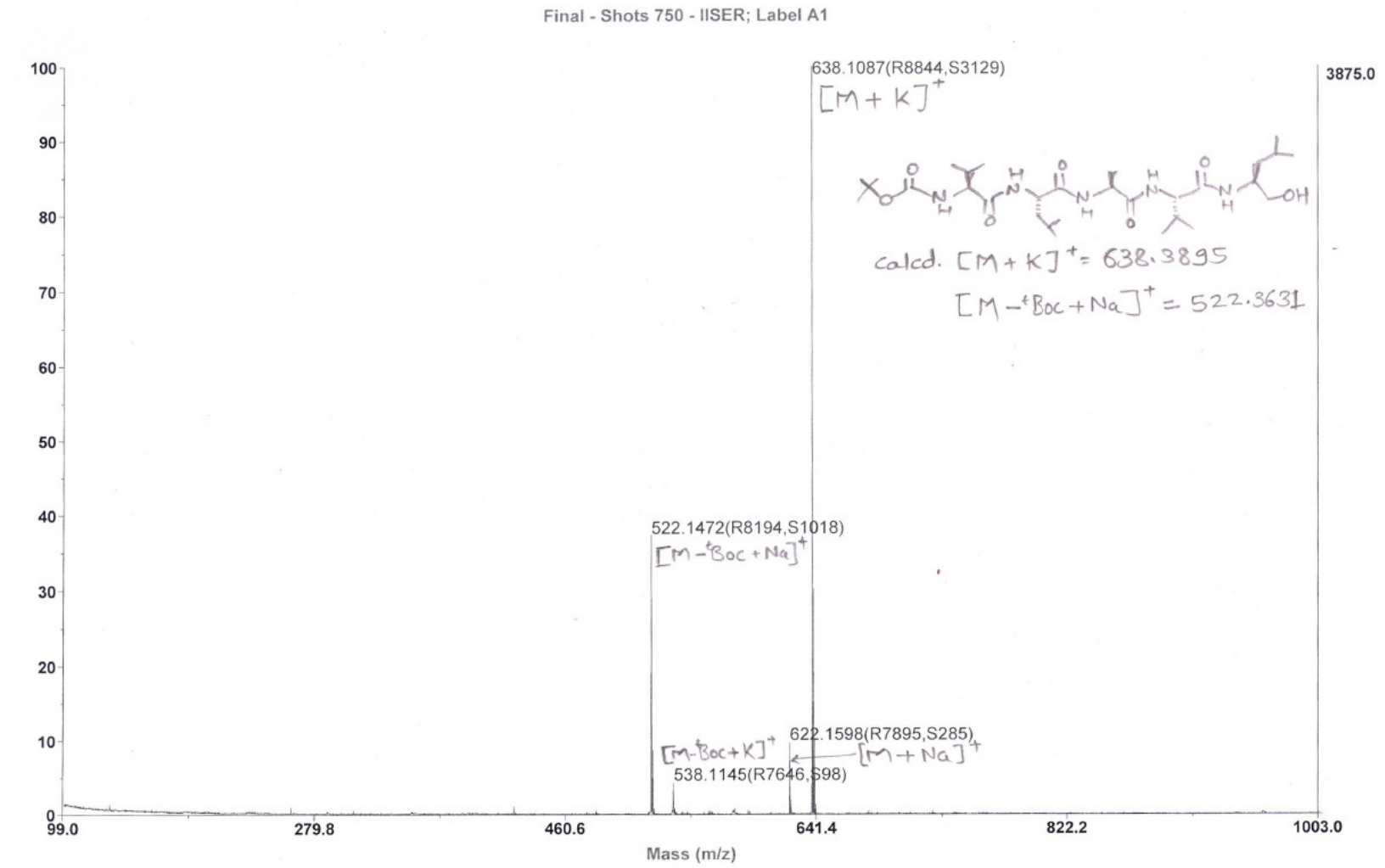

Final - Shots 750 - HNG GROUP; Label G13
412.0356(R5595,S11617)
2.3E+4
calcd. [M+K]+ 412.2214
100
90
80
70
60
50
40
30
20
10
0
199.0
460.2
721.4
982.6
1243.8
1505.0
Mass (m/z)



21


0.58
0.69
0.65
0.76
0.75
2.04
1.15
2.25
0.99
2.2
8.61
24.05
3.14
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.9865
7.9681
7.5821
7.5603
7.4790
6.7299
6.7081
4.5351
4.2533
3.9692
3.6783
3.2235
3.0975
1.8466
1.5293
1.3690
1.3117
1.2040
1.1032
0.0001


OL–TOCSY–2.jdf
Boc – Val1 – Leu2 – Ala3 – Val4 – Leu5 – ol
Ala3
Leu2
Val4
Leu5
Val1
210910–20–SVJ–200910–SM–OL–TOCSY–2.jdf
Y : parts per Million : 1H
X : parts per Million : 1H
γ-CH3 of Val1 & Val4, δ-CH3 of Leu2, ω-CH3 of Leu5
β-CH3 of Ala3
γ-CH2 of Leu5
β-CH2 of Leu2
γ-CH of Leu2 & δ-CH of Leu5
β-CH of Val1 & Val4
α-CH2 of Leu5
α-CH of Val1 & β-CH of Leu5
α-CH of Val4
α-CH of Leu2 & Ala3
Alcoholic – OH
210910–06–SVJ–200910–SM–OL–PROTON–7.jdf


Final - Shots 750 - IISER; Label A1
638.1087(R8844,S3129)
[M + K]+
3875.0
calcd. [M + K]+ = 638.3895
[M - tBoc + Na]+ = 522.3631
522.1472(R8194,S1018)
[M - tBoc + Na]+
[M-tBoc+K]+
622.1598(R7895,S285)
[M + Na]+
538.1145(R7646,S98)
100
90
80
70
60
50
40
30
20
10
0
99.0
279.8
460.6
641.4
822.2
1003.0
Mass (m/z)

References

1. M. Rodriguez, M. Llinaero, S. Doulet, A. Heitz, J. Martinez, Tetrahedron Lett. 1991, 32, 923–926.

2. G. Kokotos, Synthesis, 1990, 299-301,

3. K. Soai, S. Yokoyama, K. Mochida, Synthesis 1987, 647–648