Electronic supplementary information

Pd-catalysed oxidative carbonylation of α-amino amides to hydantoins under mild conditions

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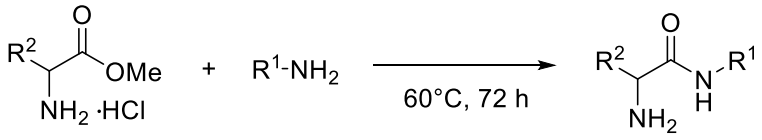
1. General information

All reagents were used as received from commercial sources without further purification. All solvents were dried over activated 4 Å molecular sieves for 24 h. All reactions were analyzed by TLC and by GC using a 30 m SE-30 capillary column. Flash column chromatography was performed on silica gel 60 (70–230 mesh). Melting points were measured with an Electrothermal apparatus and are uncorrected. Electron impact mass spectra [m/z, relative intensity (%)] were determined with a GC-MS apparatus at 70 eV ionization energy, optical purity was analyzed using Agilent CP-Chirasil 25 m column. IR spectra were run on PerkinElmer Spectrum Two spectrometer paired with a Diamond Smart Orbit accessory. Specific rotation angles were measured with polarimeter PerkinElmer 341. HRMS spectra were obtained with LTQ Orbitrap XL Thermo. Unless otherwise indicated NMR spectra were recorded on Bruker AVANCE 400 and JEOL 600MHz ECZ600R spectrometers in deuterated chloroform, using the solvent residual signals as internal reference (7.26 and 77.00 ppm, respectively for ^{1}H and ^{13}C), or deuterated dimethyl sulfoxide (2.50 and 39.52 ppm, respectively for ^{1}H and ^{13}C). Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively.

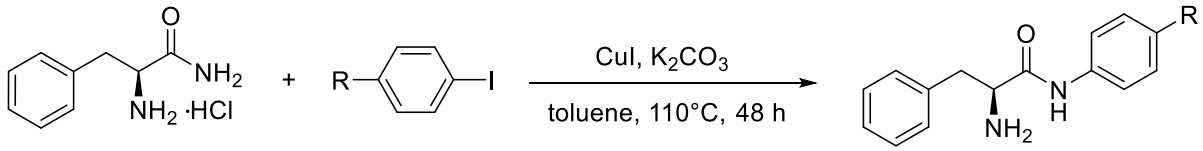
2. Experimental procedures

*2.1 General procedure for the synthesis of amino acid amides **1a-h**, **1n**, **1o**, **1q-t***



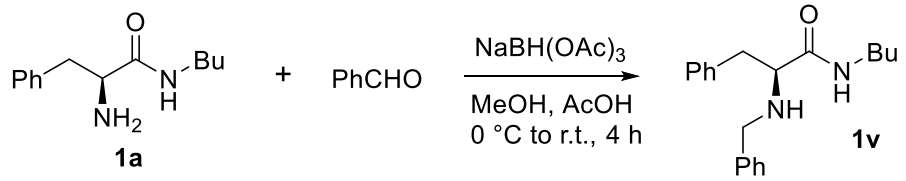
A 10 mL Schlenk tube was charged with the amino acid methyl ester hydrochloride (2 mmol) and an amine (8 mmol) under N_2. The Schlenk tube was sealed and the mixture was stirred at 60°C for 72 h. The crude mixture was transferred to a 50 mL flask and the excess of amine was removed under vacuum (in case of high-boiling amines the evaporation step was skipped). The residue was washed with brine and extracted with ethyl acetate (3x10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was then purified by silica gel column chromatography (ethyl acetate/hexane/methanol (5:10:1)) to afford the pure amino acid amide **1**.

*2.2 General procedure for the synthesis of amino acid amides **1i-k**, **1l**, **1p**[1]*



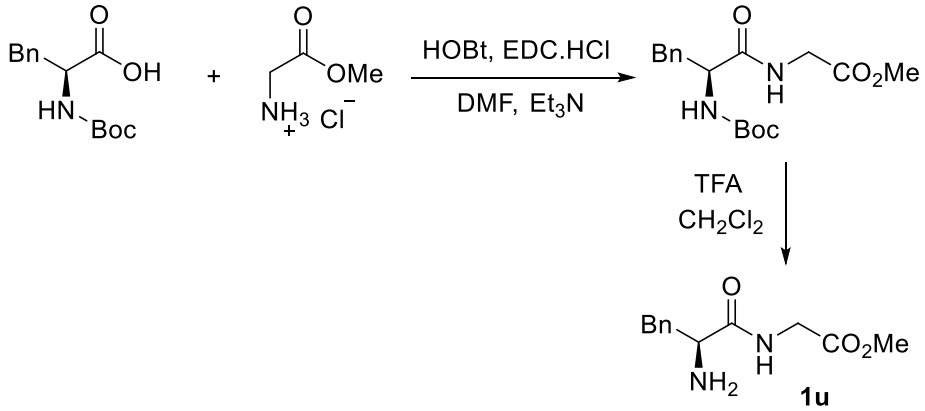
A literature procedure has been followed for the synthesis of amino acid amides **1i-k, 1l, 1p**[1]

*2.3 Synthesis of the amino acid amides **1v***



To a solution of **1a** (330 mg, 1.5 mmol) in dry MeOH (8.0 mL), benzaldehyde (0.158 mL, 1.55 mmol) and acetic acid (2 mL) were added. The reaction mixture was stirred at room temperature for 10 min and cooled to 0 °C, then $NaBH(OAc)_3$ (650 mg, 3 mmol) was added portionwise. After stirring at room temperature for additional 4 h, the solvent was evaporated, and the residue was extracted with ethyl acetate and washed with brine. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography (ethyl acetate/hexane/methanol (5:15:1)).

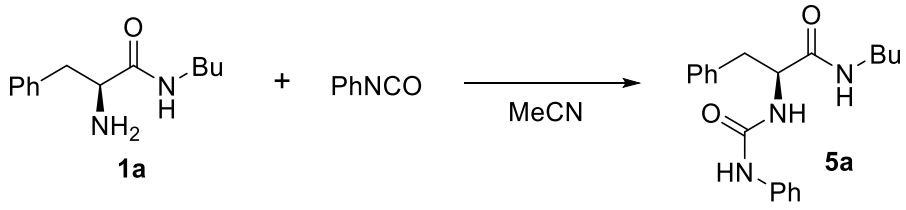
*2.4 Synthesis of methyl L-phenylalanylglycinate **1u**[2]*



N-Boc-phenylalanine (292 mg, 1.1 mmol) and HOBt (203 mg, 1.5 mmol) were dissolved in cooled at 0˚C DMF (10 mL) and maintained under stirring for 15 minutes. To the resulting solution methyl glycinate hydrochloride (125 mg, 1.0 mmol), EDC·HCl (287 mg, 1.5 mmol), and, 5 minutes later, TEA (0.67 mL, 5 mmol) were added. The reaction mixture was stirred at room temperature for 24 hours and monitored by TLC until the complete consume of methyl

glycinate. The mixture was filtered through a pad of SiO_2, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography using ethyl acetate/hexane (2:3) mixture as eluent. The obtained colourless oil (317 mg, 0.94 mmol) was dissolved in 3 mL of DCM, and TFA (0.72 mL, 9.4 mmol) was added dropwise to the solution. After stirring for 8 hours at room temperature, the excess of TFA was removed under reduced pressure, the residue was dissolved in ethyl acetate (3 mL), and potassium carbonate (414 mg, 3 mmol) was added. The solution was then filtered through a pad of SiO_2 and concentrated under vacuo. The product (219 mg, 93% yield) did not require any further purification.

*2.5 Synthesis of urea **5a** (Scheme 2b)*



In a 25 ml Schlenk tube, **1a** (66 mg, 0.3 mmol) was dissolved in dry acetonitrile (3 mL) under N_2. Phenyl isocyanate was added (0.033 mL, 0.3 mmol), and the mixture was stirred for 1h. Solvent evaporation afforded **5a** in quantitative yield, and no further purification was required.

*2.6 PdI_2/KI oxidative carbonylation of amino amide **1a***

A 45 mL stainless steel autoclave was charged with substrate **1a** (110 mg, 0.5 mmol), PdI_2 (2-5 mol%), KI (20-100%) and the solvent (5 mL). The autoclave was sealed and pressurized with CO and air, heated at 70-115 °C (oil bath) under stirring for 18 h. Then the autoclave was cooled, degassed and opened. The mixture was passed through a pad of Celite®, and the solvent was removed in vacuo affording product **3a** in quantitative yield.

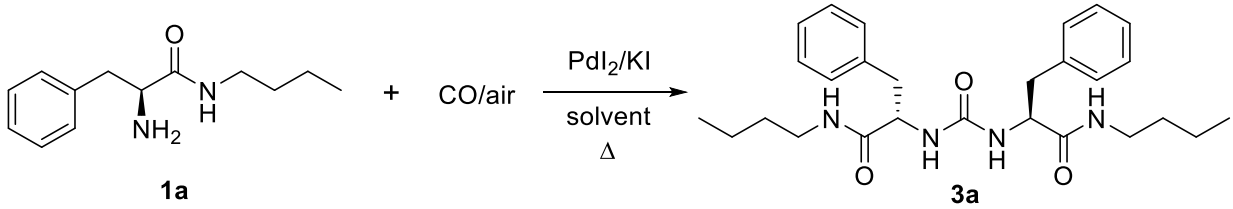


Table S1. PdI_2/KI-catalysed oxidative carbonylation of **1a**.[a]

N	**PdI_2**, mol%	**KI**, mol%	***p*(CO)**, bar	***p*(air)**, bar	**T**, °C	**Solvent**	**Yield 3a**[b]
1	2	20	16	4	115	1,4-dioxane	72%
2	2	20	16	4	100	1,4-dioxane	84%
3	2	20	16	4	80	1,4-dioxane	92%
4	2	20	4	16	80	1,4-dioxane	94%
5	5	50	4	16	80	1,4-dioxane	99%
6	5	50	8	2	80	1,4-dioxane	99%
7	5	50	8	2	70	1,4-dioxane	99%
8	5	50	8	2	70	MeCN	93%
9	5	50	8	2	70	DME	88%
10	5	100	16	4	80	DMF	94%

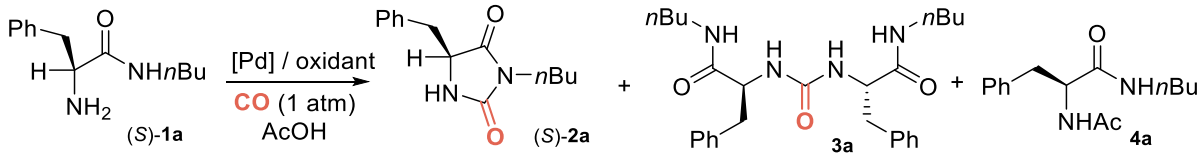
[a] Reaction conditions: **1a** (0.5 mmol), PdI_2 (2-5 mol%), KI (20-50), solvent (5 mL), CO/air (reported pressure measured at 25 °C), 45 ml autoclave, 18h. [b] Isolated yield.

*2.7 Pd-catalysed oxidative carbonylation of amino amides **1a-r** to hydantoins **2a-r***

A 25 mL Schlenk tube was charged with a solution of amino acid amide **1** (0.3 mmol) in glacial acetic acid (3 mL), palladium acetate (6.7 mg, 0.03 mmol) and TEMPO (104 mg, 0.66 mmol) under N_2. The tube was sealed and the mixture was stirred for 5 minutes at 80 °C. Then, the tube was evacuated and filled with carbon monoxide gas using a balloon (1 atm of CO). The reaction was kept at 80 °C under stirring for 2-6 h. The crude reaction mixture was cooled down to room temperature and passed through a Celite® path. Acetic acid was evaporated under reduced pressure at 60 °C and the residue was neutralized with K_2CO_3 powder (400 mg, 2.9 mmol), dissolved in ethyl acetate (5 mL) and filtered. The product was purified by silica gel column chromatography (ethyl acetate/dichloromethane (1:8)).

3. Table S2

Additional experiments for optimisation study of $Pd(OAc)_2$-catalysed carbonylation of amino amides **1a** to hydantoin **2a**.[a]

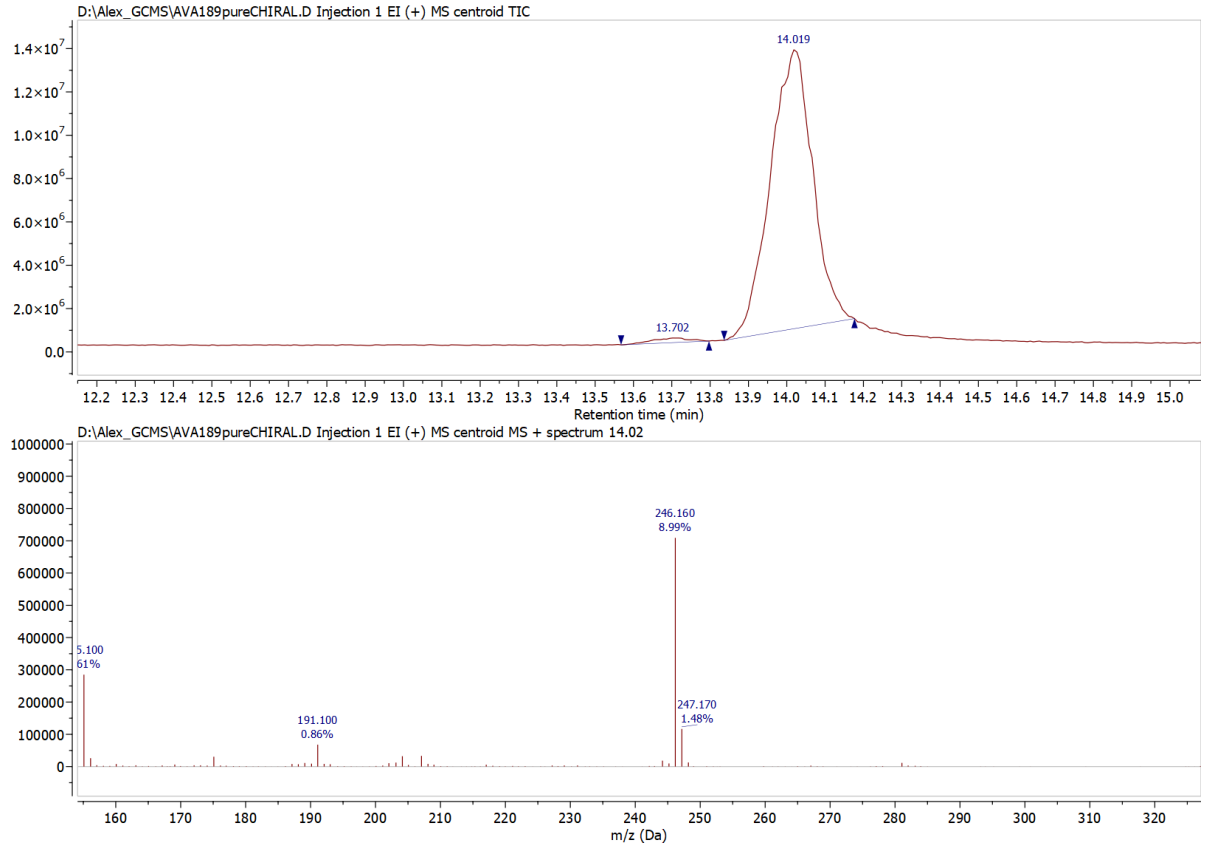


N	**T** (**ºC**)	**Oxidant** (equiv)	**co-oxidant**	**Solvent**	**Yield** (%) **2a**[b]	**Yield** (%) **3a**[b]	**Yield** (%) **4a**[b]
1	120	BQ (2)	-	AcOH	74	-	-
2	120	DDQ (2)	-	AcOH	66	-	28
3	120	AgOTf (2)	air	AcOH	62	30	-
4	120	$AgNO_3$ (2)	air	AcOH	23	27	25
5	120	$Cu(OAc)_2$ (0.5)	air	AcOH	37	-	44
6	120	BQ (2)	-	AcOH + DMF (1:1)	62	-	-
7	80	BQ (1.2)	-	AcOH + MeCN (1:1)	81	-	-
8	80	BQ (1.2)	-	AcOH + MeCN (1:10)	61	-	-
9	80	TEMPO (0.1)	$Na_2S_2O_8$ (2 eq)	AcOH	11	-	-
10	80	TEMPO (0.3)	Urea-hydrogen peroxide (3 eq)	AcOH	19	-	-
11	80	TEMPO (1.2)	-	AcOH	51	-	-

[a] Reaction conditions: **1a** (0.5 mmol), $Pd(OAc)_2$ (10 mol%), solvent (5 mL), 6h. [b] Isolated yield.

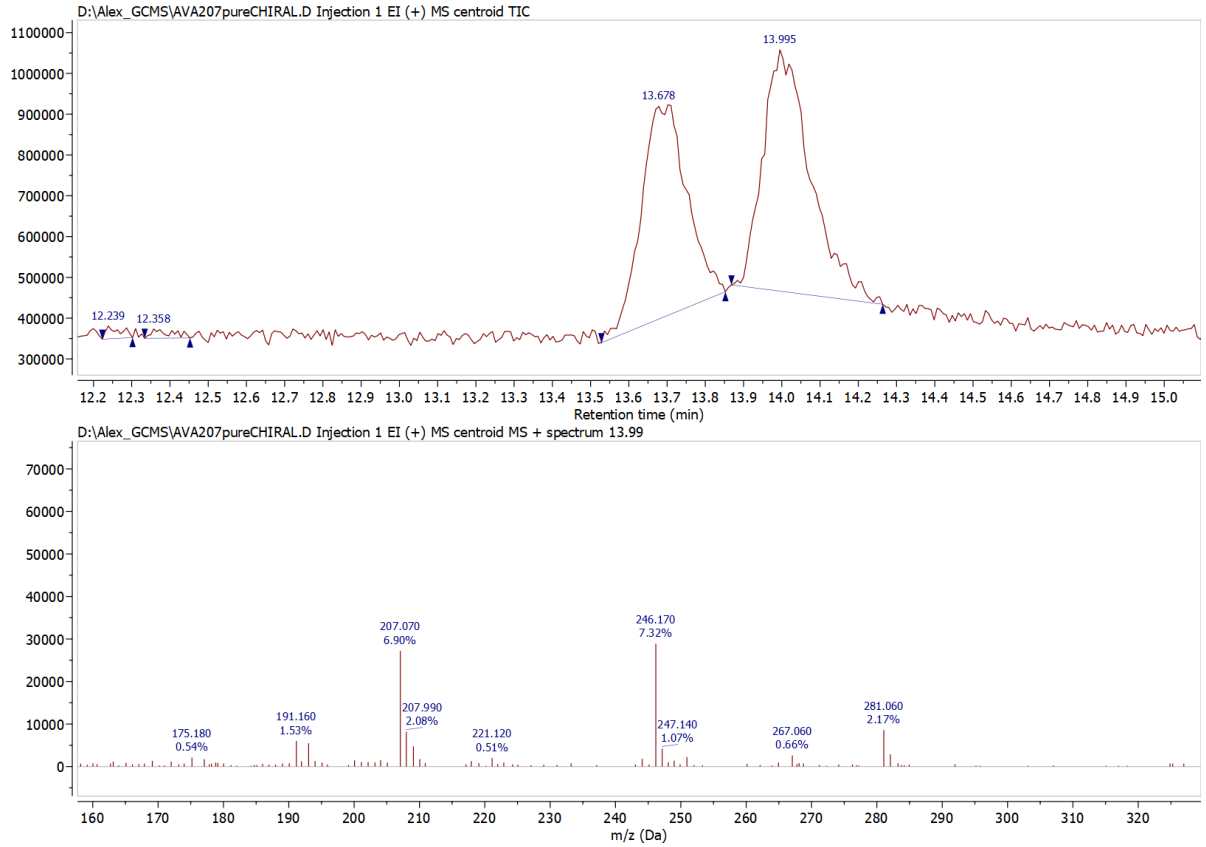
4. Figure S1

Gas chromatogram and mass spectrum of *(S)*-**2a**



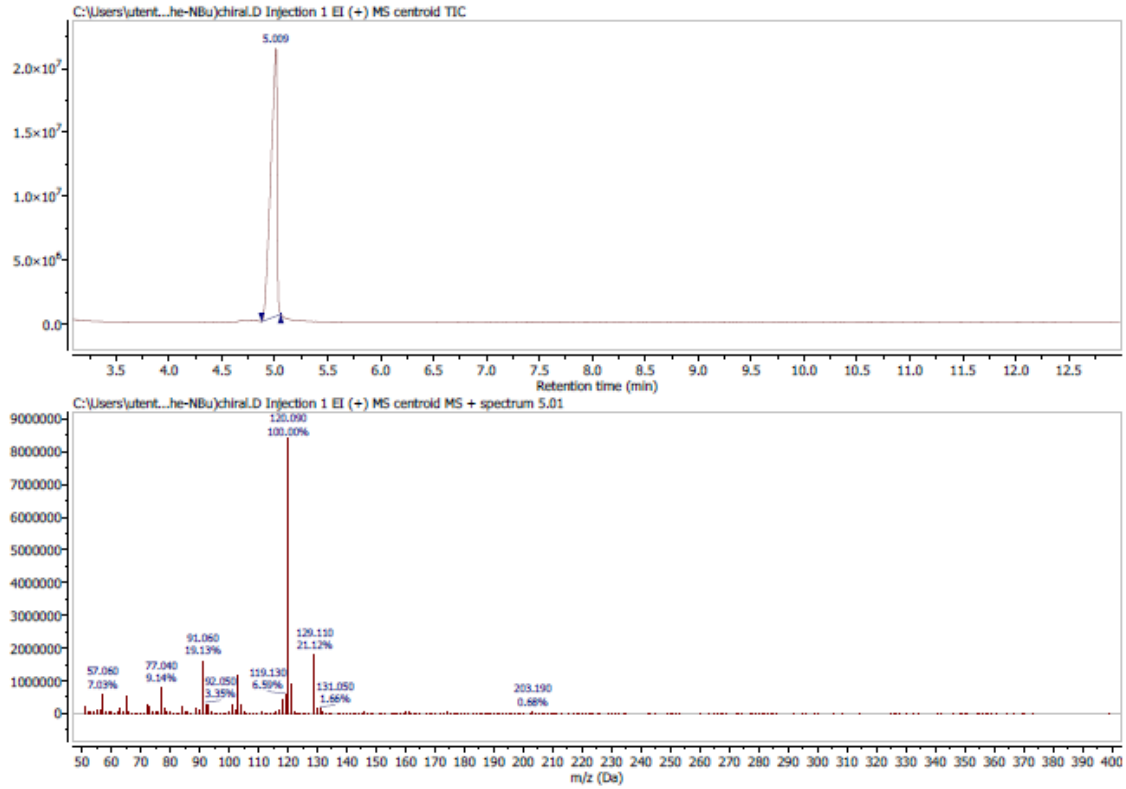
5. Figure S2

Gas chromatogram and mass spectrum of *(rac)*-**2a**

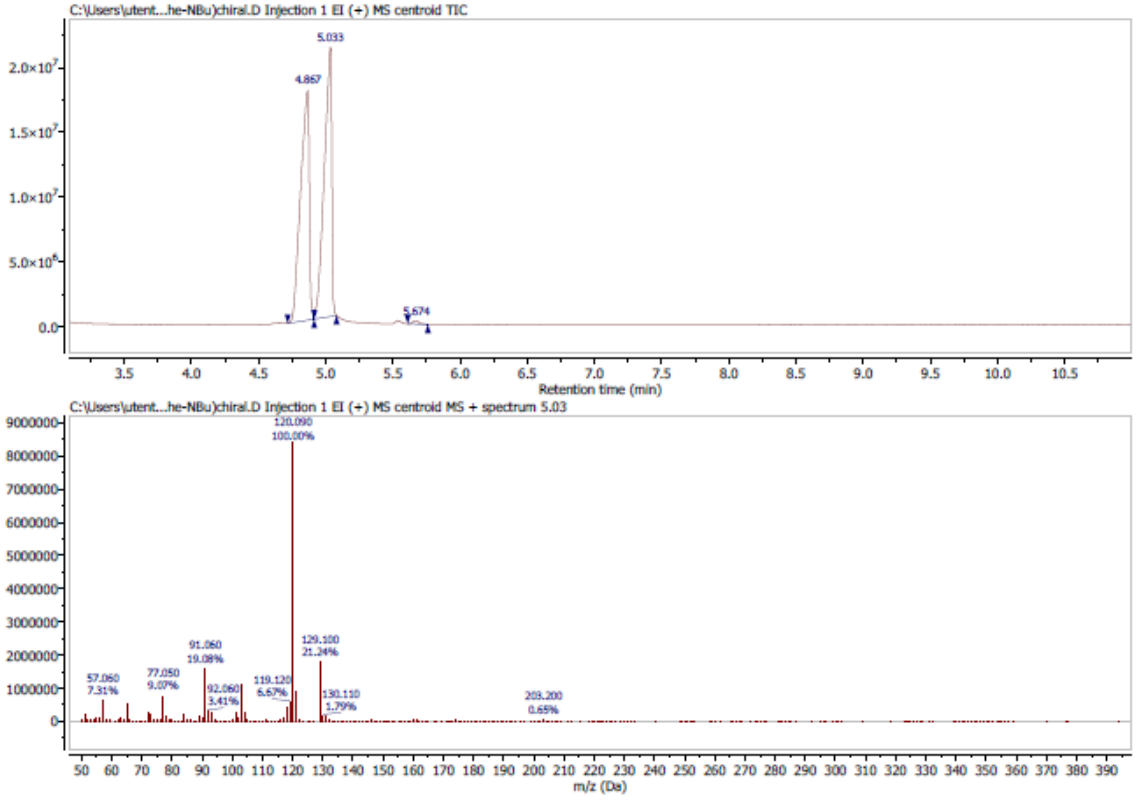


6. Enantiomeric excess of selected amino amides 1 and hydantoins 2

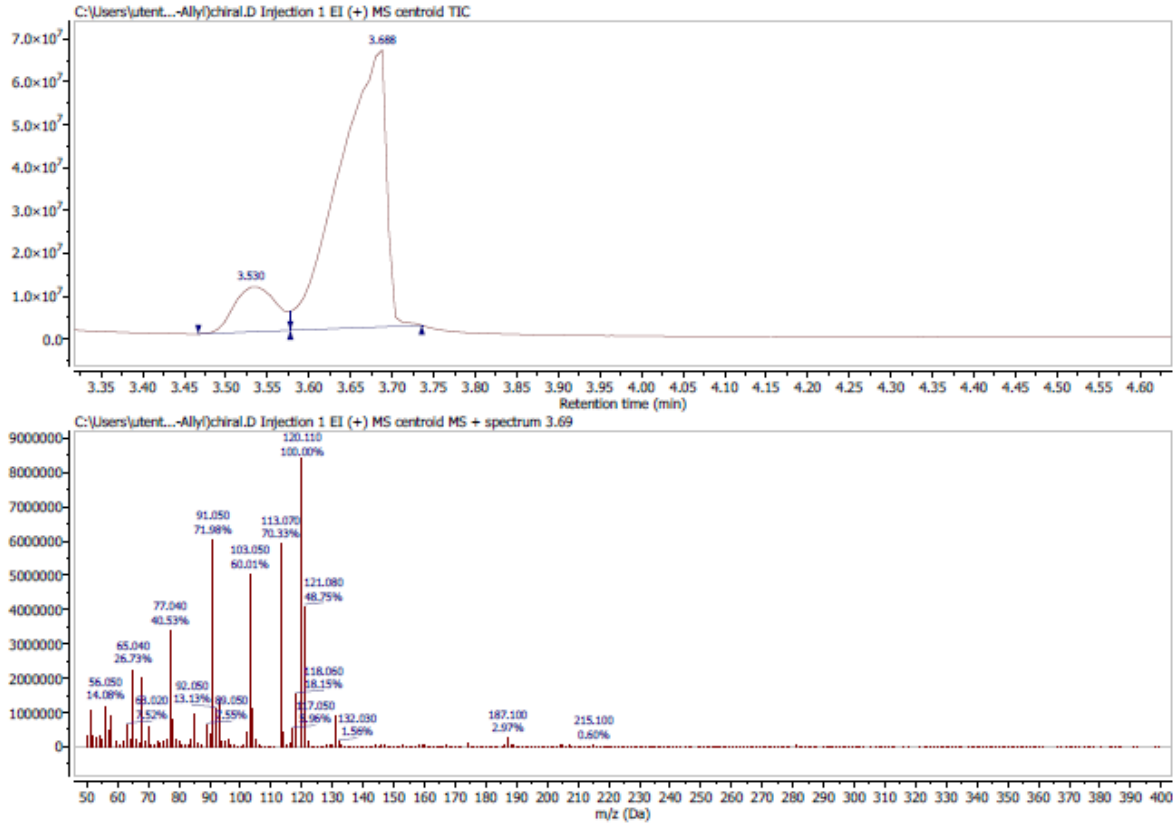
Gas chromatogram and mass spectrum of *(S)*-**1a**



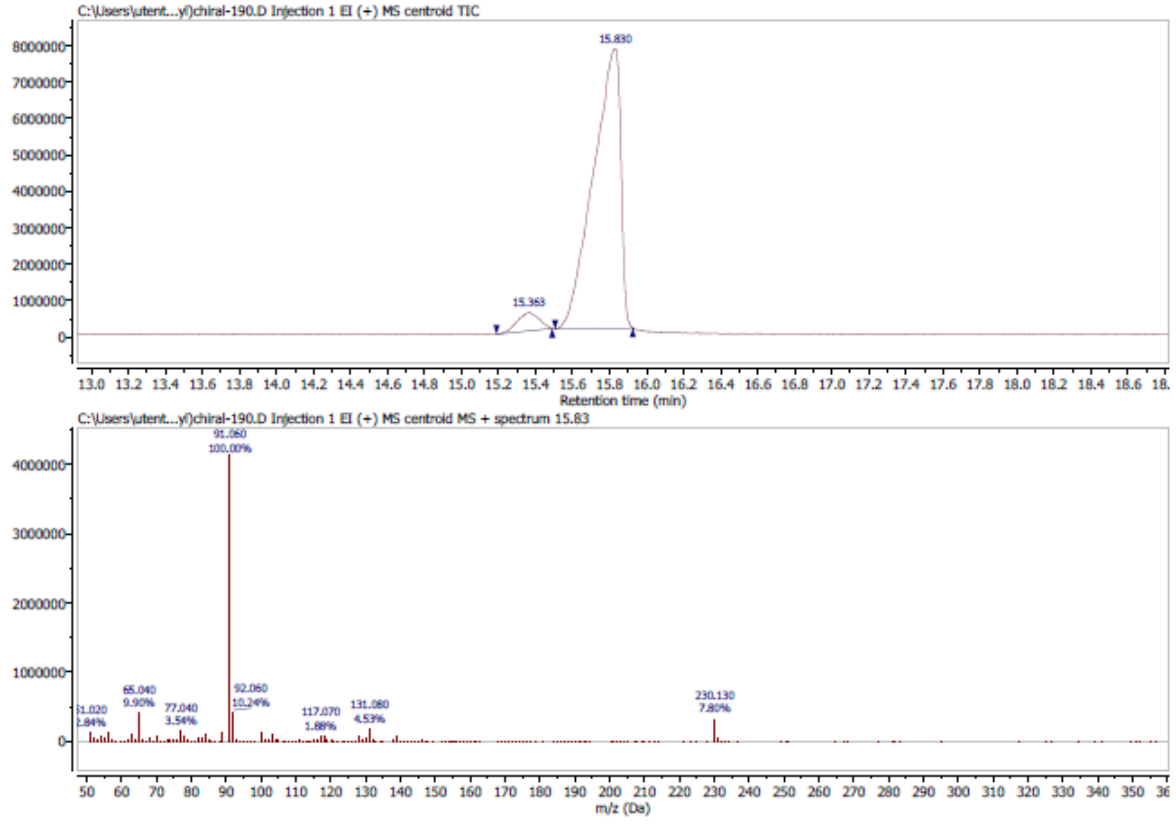
Gas chromatogram and mass spectrum of *(rac)*-**1a**



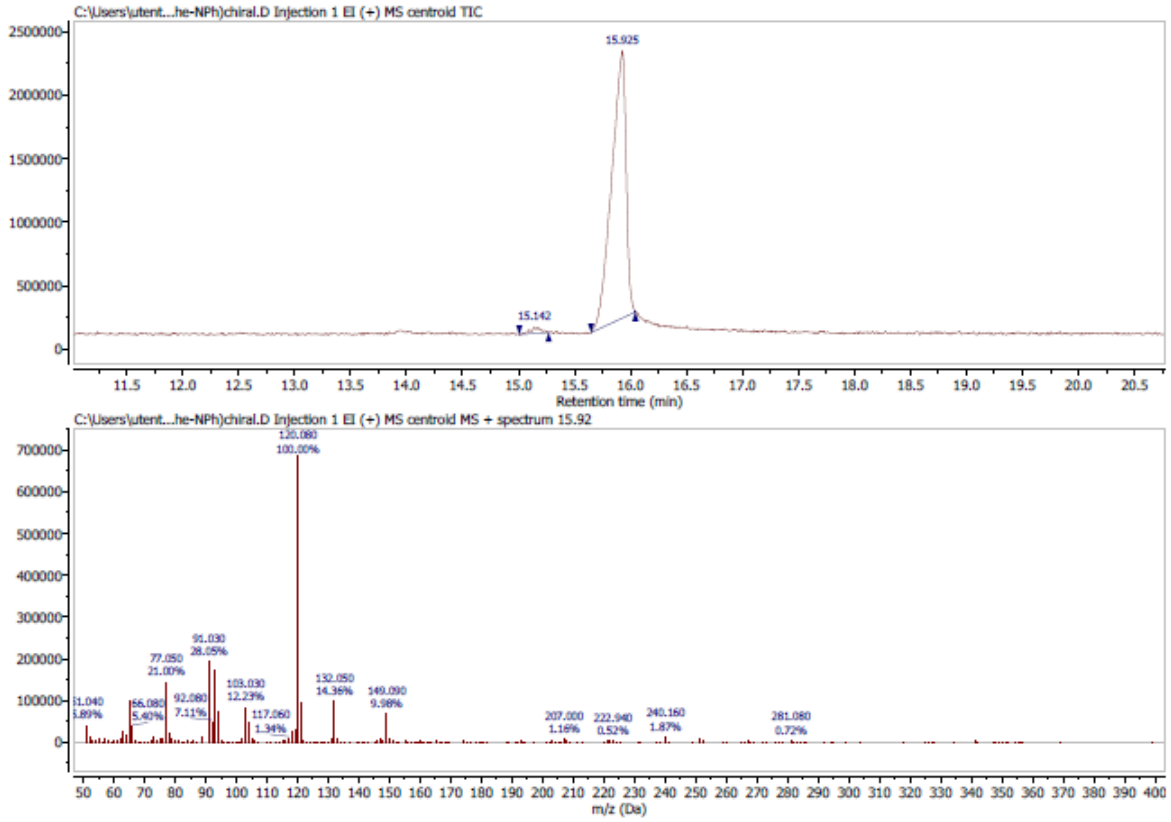
Gas chromatogram and mass spectrum of *(S)*-**1d**



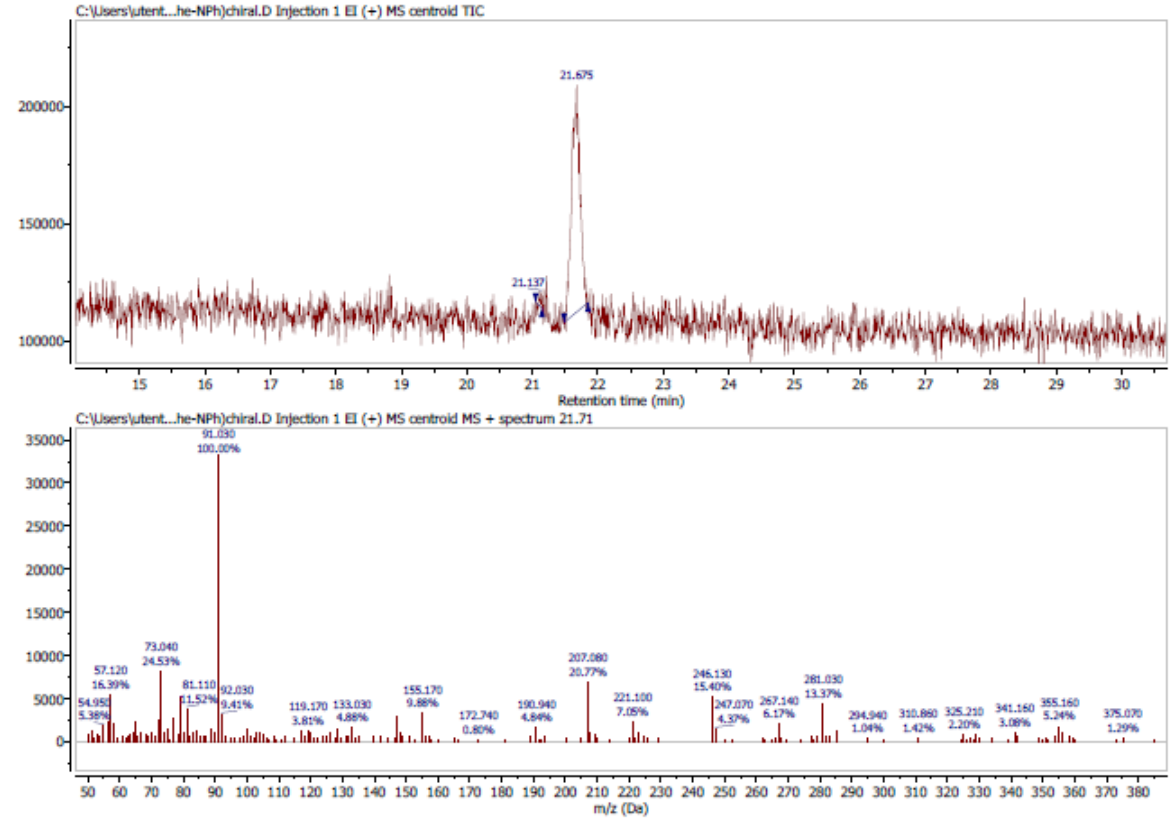
Gas chromatogram and mass spectrum of *(S)*-**2d**



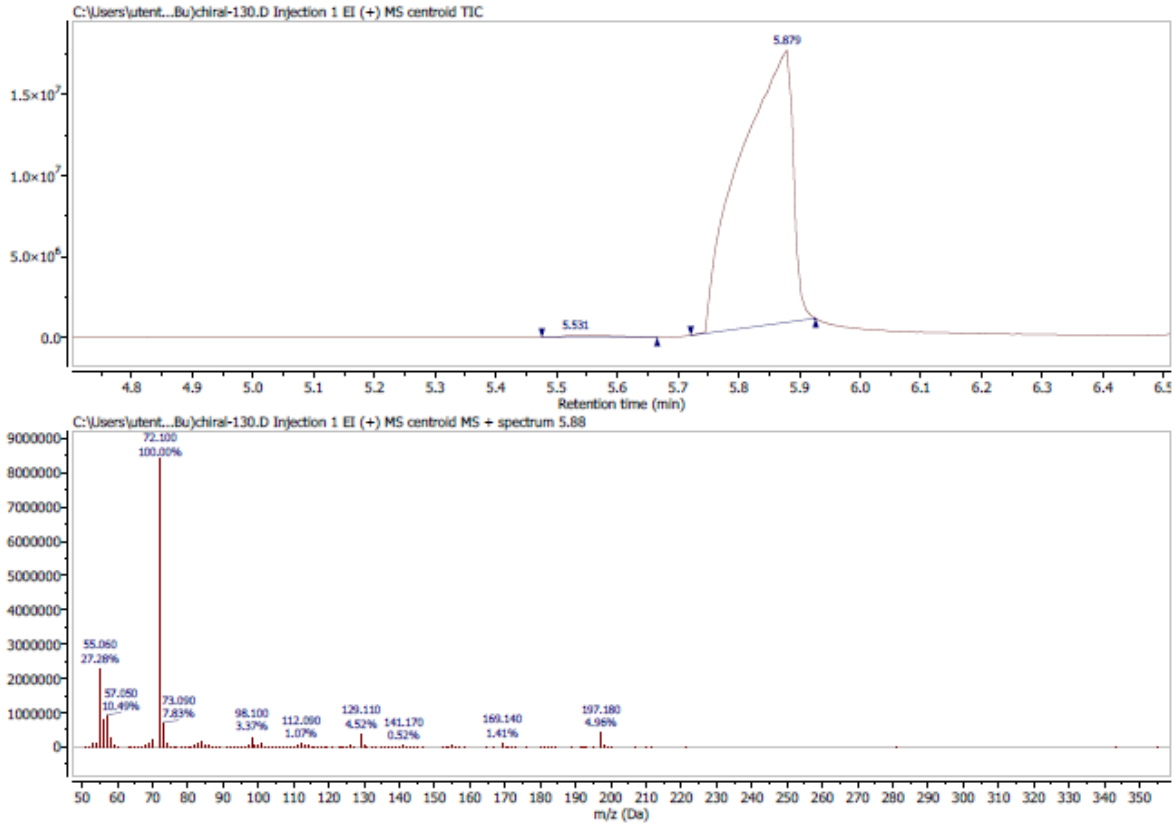
Gas chromatogram and mass spectrum of *(S)*-**1i**



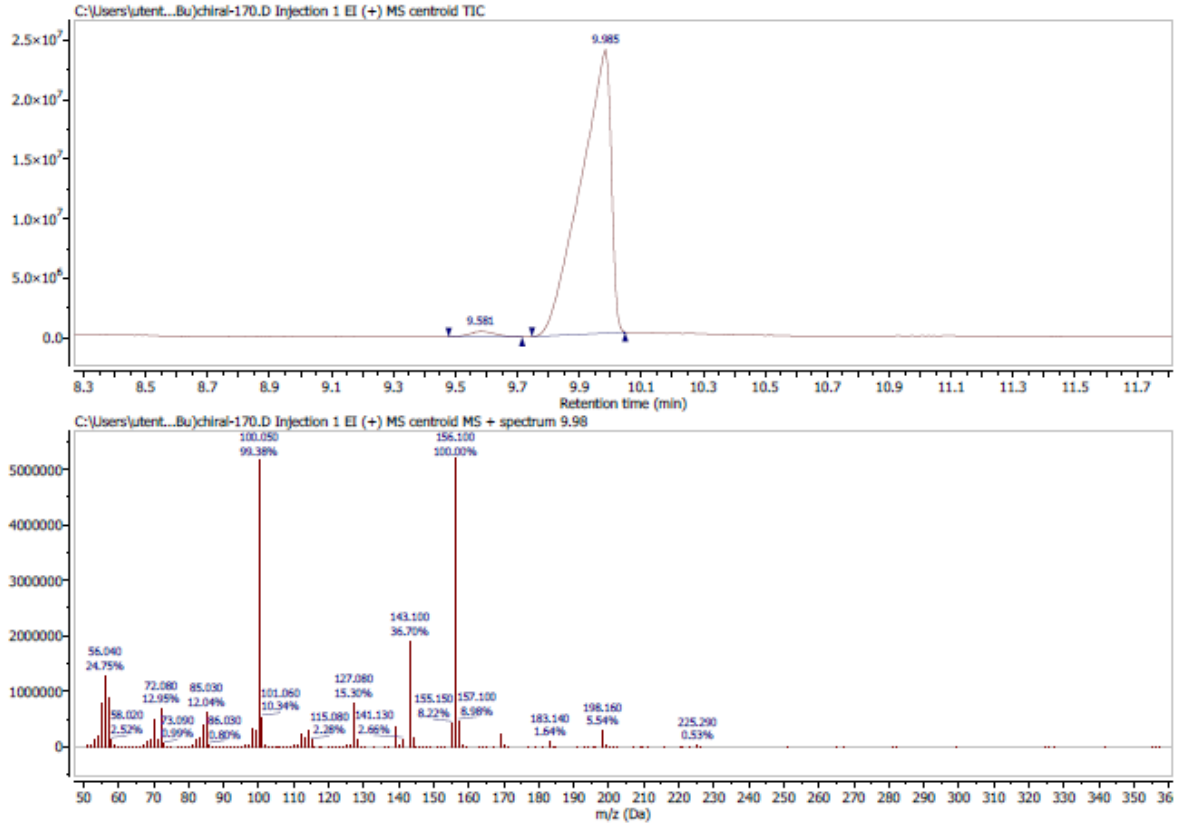
Gas chromatogram and mass spectrum of *(S)*-**2i**



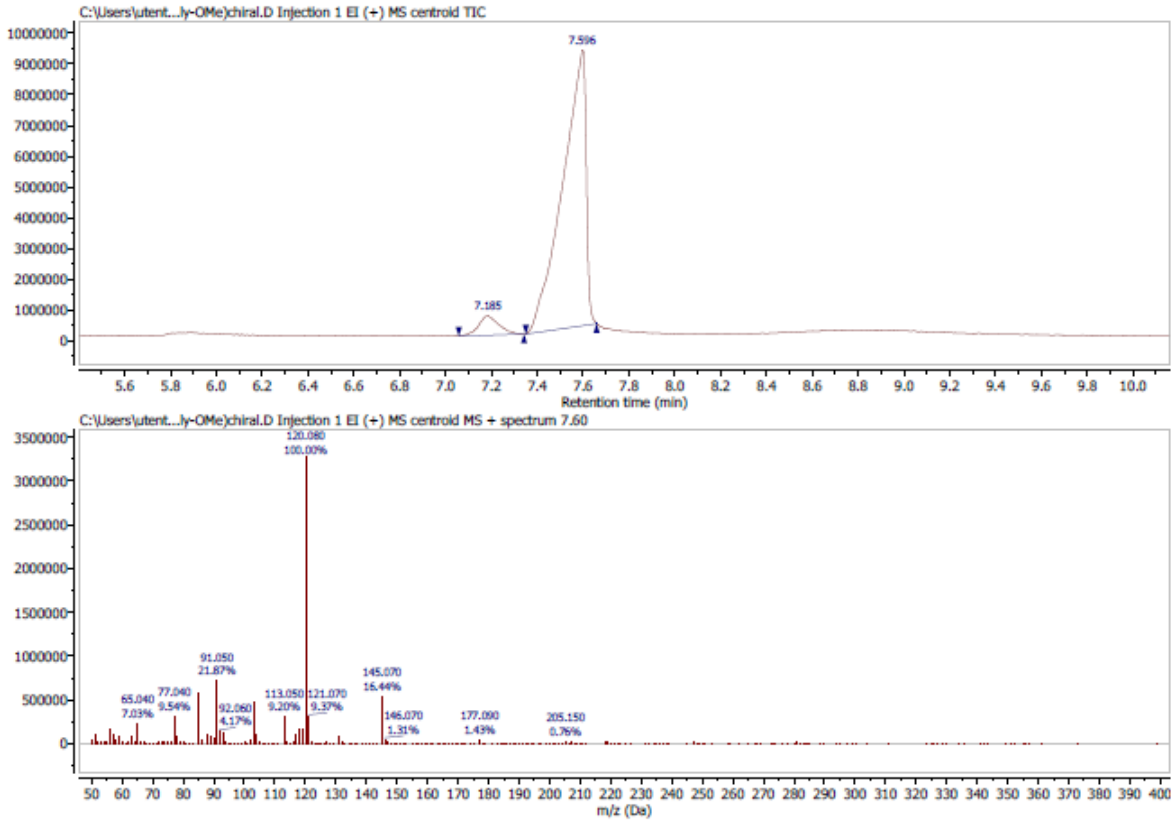
Gas chromatogram and mass spectrum of *(S)*-**1q**



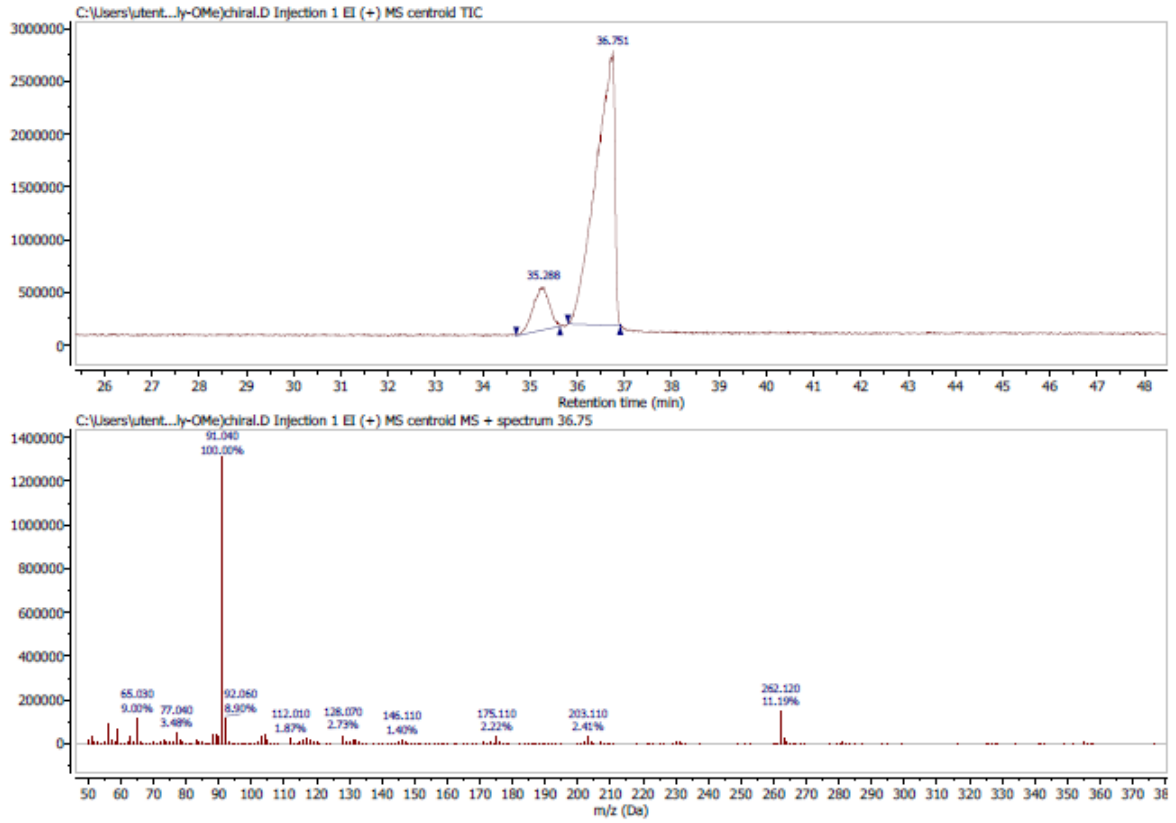
Gas chromatogram and mass spectrum of *(S)*-**2q**



Gas chromatogram and mass spectrum of *(S)*-**1u**

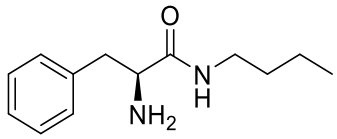


Gas chromatogram and mass spectrum of *(S)*-**2u**



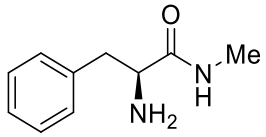
7. Characterizations

(S)-2-amino-N-butyl-3-phenylpropanamide (**1a**)[3,4]



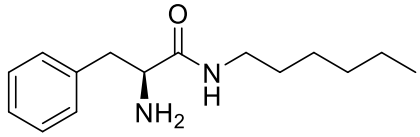
Colourless oil (414 mg, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.20 (m, 5H), 3.59 (br s, 2H), 3.25-3.22 (m, 3H), 2.70 (dd, J = 13.7, 9.1 Hz, 1H), 1.65-1.42 (m, 3H), 1.35-1.24 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 138.0, 129.3 (2C), 128.6 (2C), 126.7, 56.4, 41.1, 38.8, 31.6, 20.0, 13.7; HRMS (ESI) *m/z* calculated for $C_{13}H_{20}N_2O$ $[M+H]^+$: 221.1468, found: 221.1466; IR (ATR diamond, neat): v 3299.8, 3063.5, 3027.6, 2956.9, 2929.4, 2871.3, 2358.9, 2337.9, 1647.2, 1522.3, 1454.0, 741.7, 698.8 cm^{-1}.

(S)-2-amino-N-methyl-3-phenylpropanamide (**1b**)[5,6,11]



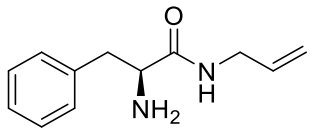
Colourless solid (328 mg, 92% yield); m.p. 58.5-60.6°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (br s, 1H), 7.30 – 7.09 (m, 5H), 3.55 (br s, 1H), 3.19 (dd, J = 13.6, 3.9 Hz, 1H), 2.73 (d, J = 5.0 Hz, 3H), 2.63 (dd, J = 13.7, 9.2 Hz, 1H), 1.57 (br s, 2H); IR (ATR diamond, neat): v 3372, 3344, 3291, 2939, 2914, 2876, 1644, 1522, 1455, 1439, 744, 698 cm^{-1}.

(S)-2-amino-N-hexyl-3-phenylpropanamide (**1c**) [4]



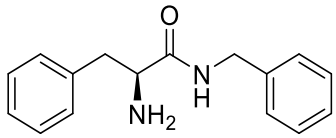
Light yellow solid (432 mg, 87% yield); m.p. 39.2-39.6°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.22 (m, 3H), 7.17 (d, J = 6.7 Hz, 2H), 5.99 (s, 1H), 4.21 (dd, J = 4.2, 1.2 Hz, 1H), 3.38 (dd, J = 7.9, 7.0 Hz, 2H), 3.22 (dd, J = 14.0, 3.9 Hz, 1H), 2.87 (dd, J = 14.0, 8.0 Hz, 1H), 1.43 (t, J = 7.1 Hz, 2H), 1.29 – 1.13 (m, 6H), 0.86 (t, J = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.2, 138.1, 129.3 (2C), 128.6 (2C), 126.7, 56.5, 41.2, 39.1, 31.5, 29.6, 26.6, 22.6, 14.0; HRMS (ESI) *m/z* calculated for $C_{15}H_{24}N_2O$ $[M+H]^+$: 249.1961, found: 249.1660; IR (ATR diamond, neat): v 3304.1, 2956.8, 2921.4, 2987.6, 1638.4, 1545.8, 1491.0, 1453.8, 744.2, 697.2 cm^{-1}.

(S)-N-allyl-2-amino-3-phenylpropanamide (**1d**) [7]



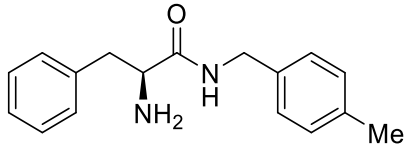
Colourless oil (384 mg, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.18 (m, 6H), 5.83 (ddt, *J* = 17.3, 10.7, 5.6 Hz, 1H), 5.21 – 5.09 (m, 2H), 3.90 (td, *J* = 5.8, 1.6 Hz, 2H), 3.64 (dd, *J* = 9.3, 4.1 Hz, 1H), 3.29 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.73 (dd, *J* = 13.7, 9.3 Hz, 1H), 1.41 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 137.9, 134.3, 129.3 (2C), 128.7 (2C), 126.8, 116.1, 56.5, 41.5, 41.1; HRMS (ESI) *m/z* calculated for $C_{12}H_{16}N_2O$ $[M+H]^+$: 205.1335, found: 205.1334**;** IR (ATR diamond, neat): *v* 3299.1, 3082.8, 3027.2, 2919.3, 1652.5, 1640.9, 1517.3, 1496.0, 1453.8, 1419.3, 1254.5, 989.9, 918.2, 743.6, 699.7 cm^{-1}.

(S)-2-amino-N-benzyl-3-phenylpropanamide (**1e**) [8]



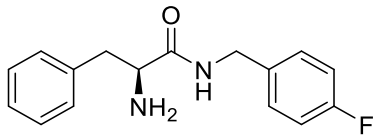
Colourless oil (437 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (t, *J* = 5.8 Hz, 1H), 7.41 – 7.22 (m, 10H), 4.47 (dd, *J* = 5.9, 4.0 Hz, 2H), 3.80 – 3.63 (m, 1H), 3.33 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.79 (dd, *J* = 13.7, 9.1 Hz, 1H), 1.61 (br s, 2H).

(S)-2-amino-N-(4-methylbenzyl)-3-phenylpropanamide (**1f**)



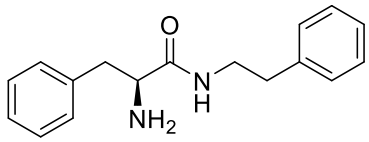
Yellow solid (488 mg, 91% yield); m.p. 70.1-71.5°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.37 – 7.09 (m, 9H), 4.41 (dd, *J* = 5.9, 2.6 Hz, 2H), 3.67 (s, 1H), 3.30 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.79 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.36 (s, 3H), 1.64 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 137.9, 137.0, 135.4, 129.4 (2C), 129.3 (2C), 128.7 (2C), 127.8 (2C), 126.8, 56.5, 42.9, 41.0, 21.1; HRMS (ESI) *m/z* calculated for $C_{17}H_{20}N_2O$ $[M+H]^+$: 269.1648, found: 269.1650; IR (ATR diamond, neat): *v* 3284.9, 3022.7, 2915.4, 2857.7, 1637.5, 1530.2, 1515.0, 1493.1, 743.3, 697.1 cm^{-1}.

(S)-2-amino-N-(4-fluorobenzyl)-3-phenylpropanamide (**1g**) [8]



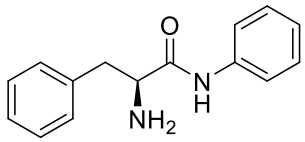
Yellow solid (501 mg, 92% yield); m.p. 59.4-60.0°C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (br s, 1H), 7.29 (t, J = 7.4 Hz, 2H), 7.26-7.21 (m, 1H), 7.20 – 7.15 (m, 4H), 6.97 (t, J = 8.6 Hz, 2H), 4.38 (qd, J = 14.8, 6.0 Hz, 2H), 3.64 (dd, J = 9.1, 4.3 Hz, 1H), 3.25 (dd, J = 13.7, 4.2 Hz, 1H), 2.75 (dd, J = 13.7, 9.0 Hz, 1H), 1.42 (br s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 174.2, 162.2 (d, $J_{C,F}$ = 245.5 Hz), 137.9, 134.3 (d, $J_{C,F}$ = 3.2 Hz), 129.5, 129.4, 128.8, 126.9, 115.52 (d, $J_{C,F}$ = 21.5 Hz), 56.5, 42.5, 41.1; HRMS (ESI) *m/z* calculated for $C_{16}H_{17}FN_2O$ $[M+H]^+$: 273.1398, found: 273.1395; IR (ATR diamond, neat): ν 3350.2, 3297.0, 3271.2, 1654.1, 1601.7, 1526.3, 1507.3, 1220.8, 723.5, 703.2 cm^{-1}.

(S)-2-amino-N-phenethyl-3-phenylpropanamide (**1h**)



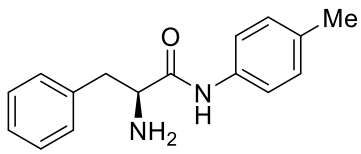
Yellow solid (494 mg, 92% yield); m.p. 58.6-60.7°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 5.9 Hz, 1H), 7.35 – 7.11 (m, 10H), 3.51 (dq, *J* = 19.9, 6.7 Hz, 3H), 3.22 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.78 (t, *J* = 7.1 Hz, 2H), 2.69 (dd, *J* = 13.6, 9.1 Hz, 1H), 1.33 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.2, 139.0, 137.9, 129.3 (2C), 128.8 (2C), 128.7 (2C), 128.5 (2C), 126.8, 126.4, 56.5, 41.1, 40.3, 35.8; HRMS (ESI) *m/z* calculated for $C_{17}H_{20}N_2O$ $[M+H]^+$: 269.1648, found: 269.1649; IR (ATR diamond, neat): *ν* 3360.5, 3331.3, 3062.4, 3026.7, 2918.8, 1644.4, 1522.9, 1494.2, 1453.8, 740.9, 695.7 cm^{-1}.

(S)-2-amino-N,3-diphenylpropanamide (**1i**) [1]



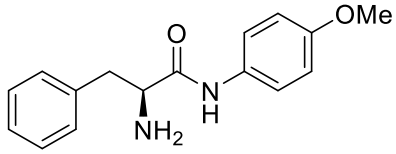
Colourless solid (374 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.44 (s, 1H), 7.66 – 7.58 (m, 2H), 7.42 – 7.23 (m, 7H), 7.13 (t, *J* = 7.4 Hz, 1H), 3.77 (dd, *J* = 9.5, 4.0 Hz, 1H), 3.41 (dd, *J* = 13.8, 3.9 Hz, 1H), 2.82 (dd, *J* = 13.8, 9.5 Hz, 1H), 1.61 (s, 2H).

(S)-2-amino-3-phenyl-N-(p-tolyl)propanamide (**1j**) [1]



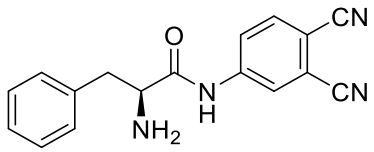
Colourless solid (532 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.37 (br s, 1H), 7.50 (m, 2H), 7.35–7.24 (m, 5H), 7.18-7.06 (m, 2H), 3.83–3.63 (m, 1H) 3.47–3.31 (dd, J = 14, 4.8 Hz, 1H), 2.88–2.73 (m ,1H), 2.35 (s, 3H), 1.56 (br s, 2H).

(S)-2-amino-3-phenyl-N-(4-methoxyphenyl)propanamide (**1k**) [9,10]



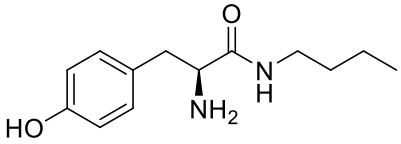
Colourless solid (516 mg, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.26 (br s, 1H), 7.55-7.52 (m, 2H), 7.25-7.04 (m, 7H), 3.38-3.35 (m, 1H), 3.23 (m, 4H), 2.82-2.76 (br s, 1H), 1.91 (br s, 2H).

(S)-2-amino-N-(3,4-dicyanophenyl)-3-phenylpropanamide (**1l**)



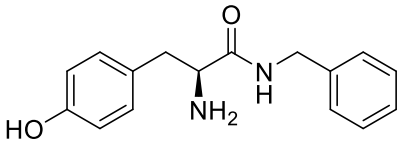
Light green oil (69 mg, 33% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.03 (br s, 1H), 8.21 (d, *J* = 2.2 Hz, 1H), 7.88 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 7.24 – 7.19 (m, 2H), 3.78 (dd, *J* = 9.3, 4.0 Hz, 1H), 3.32 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.83 (dd, *J* = 13.9, 9.2 Hz, 1H), 1.61 (br s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.5, 156.0, 142.2, 136.9, 134.6, 129.3 (2C), 129.1 (2C), 127.4, 123.4, 122.8, 117.0, 115.6, 115.3, 110.0, 56.7, 40.3; HRMS (ESI) *m/z* calculated for $C_{17}H_{14}N_4O$ $[M+H]^+$: 290.1168, found: 290.1164; IR (ATR diamond, neat): *v* 3385.8, 3265.1, 3028.3, 2923.5, 2230.9, 1693.9, 1597.3, 1568.7, 1497.2, 1407.5, 1315.3, 1253.1, 1187.7, 1098.4, 906.4, 837.9, 727.5, 699.7 cm^{-1}.

(*S*)-2-amino-*N*-butyl-3-(4-hydroxyphenyl)propanamide (**1n**) [7]



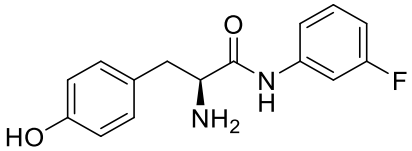
Colourless solid (455 mg, 96% yield); m.p. 140.7-141.2°C; ^{1}H NMR (600 MHz, DMSO): δ 7.71 (t, J = 5.8 Hz, 1H), 6.99 – 6.87 (m, 2H), 6.68 – 6.55 (m, 2H), 3.26 (dd, J = 7.8, 5.5 Hz, 1H), 3.05 – 2.91 (m, 2H), 2.73 (dd, J = 13.4, 5.5 Hz, 1H), 2.52 – 2.47 (m, 1H), 2.37 (d, J = 5.5 Hz, 1H), 1.35 – 1.22 (m, 2H), 1.22 – 1.08 (m, 2H), 0.80 (t, J = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 174.4, 156.3, 130.7 (2C), 129.0, 115.4 (2C), 56.9, 40.8, 38.5, 31.7, 20.0, 14.2; HRMS (ESI) *m/z* calculated for $C_{13}H_{20}N_2O_2$ $[M+H]^+$: 237.1598, found: 237.1560; IR (ATR diamond, neat): ν 3338.5, 3322.0, 3281.5, 2952.1, 2925.8, 2871.7, 2854.0, 2669.3, 2585.8, 1635.9, 1554.8, 1516.7, 1455.4, 1381.2, 1250.4, 1098.8, 996.6, 825.1, 700.0, 557.8 cm^{-1}.

(S)-2-amino-N-benzyl-3-(4-hydroxyphenyl)propanamide (**1o**) [10]



Colourless solid (496 mg, 92% yield); m.p. 144.5-145.3°C; ^{1}H NMR (600 MHz, DMSO): δ 9.25 – 9.03 (m, 1H), 8.23 (t, J = 6.1 Hz, 1H), 7.32 – 7.11 (m, 3H), 7.14 – 7.03 (m, 2H), 7.00 – 6.89 (m, 2H), 6.68 – 6.56 (m, 2H), 4.22 (ddd, J = 50.0, 15.1, 6.0 Hz, 2H), 3.34 (dd, J = 7.7, 5.8 Hz, 1H), 2.77 (dd, J = 13.4, 5.7 Hz, 1H), 2.53 (dd, J = 13.4, 7.7 Hz, 1H), 1.94 – 1.69 (m, 2H); ^{13}C NMR (151 MHz, DMSO): δ 174.9, 156.3, 140.0, 130.8 (2C), 129.1 (2C), 128.7 (2C), 127.7, 127.2, 115.5 (2C), 57.1, 42.4, 41.0; HRMS (ESI) *m/z* calculated for $C_{16}H_{18}N_2O_2$ $[M+H]^+$: 271.1441, found: 271.1440; IR (ATR diamond, neat): ν 3334.3, 3276.5, 2950.1, 2926.6, 2856.5, 2669.3, 2580.7, 1636.3, 1542.9, 1515.2, 1453.9, 1243.6, 1098.9, 998.2, 825.5, 696.7, 536.8 cm^{-1}.

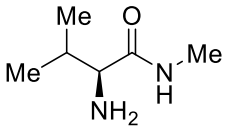
(S)-2-amino-N-(3-fluorophenyl)-3-(4-hydroxyphenyl)propanamide (**1p**)



Light yellow waxy solid (139 mg, 50% yield); ^{1}H NMR (400 MHz, CD_3OD) δ 7.51 (dt, J = 11.2, 2.2 Hz, 1H), 7.30 – 7.17 (m, 2H), 7.09 – 7.01 (m, 2H), 6.81 (tdd, J = 8.3, 2.6, 1.1 Hz, 1H), 6.77 – 6.71 (m, 2H), 4.93 (br s, 1H), 3.64 (dd, J = 7.2, 6.4 Hz, 1H), 2.99 (dd, J = 13.6, 6.4

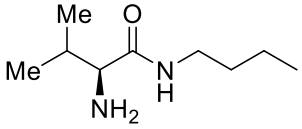
Hz, 1H), 2.86 – 2.75 (dd, *J* = 13.6, 7.2 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD): *δ* 173.9, 164.0, 161.6, 156.0, 139.8, 139.6, 130.1 (2C), 129.9, 129.8, 127.8, 115.4, 115.3, 115.1 (2C), 110.5, 110.2, 107.1, 106.8, 57.1, 47.5, 47.3, 47.1, 40.4; HRMS (ESI) *m/z* calculated for $C_{15}H_{15}FN_2O_2$ $[M+H]^+$: 274.1118, found: 258.1117; IR (ATR diamond, neat): *v* 3270.2, 3029.1, 2920.7, 2397.7, 1667.5, 1610.0, 1551.4, 1512.7, 1491.7, 1443.0, 1423.3, 1249.9, 1016.4, 954.7, 858.3, 814.4, 774.9, 678.4 cm^{-1}.

(S)-2-amino-N,3-dimethylbutanamide (**1q**) [11]



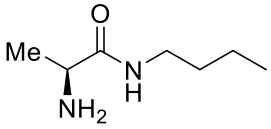
Colourless oil (234 mg, 90% yield); ^{1}H NMR (400 MHz, DMSO): *δ* 7.94 (br s, 1H), 3.78 (s, 2H), 3.05 (d, *J* = 5.4 Hz, 1H), 2.61 (d, *J* = 4.6 Hz, 3H), 1.89 (pd, *J* = 6.9, 5.4 Hz, 1H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO): *δ* 173.8, 60.0, 31.6, 25.8, 19.7, 17.9; HRMS (ESI) *m/z* calculated for $C_6H_{14}N_2O$ $[M+H]^+$: 131.1179, found: 131.1176; IR (ATR diamond, neat): *v* 3265.3, 3084.0, 2962.4, 2901.5, 2876.8, 1641.9, 1563.0, 1466.5, 1410.9, 1371.8, 1301.1, 1251.2, 1160.9, 1056.7, 977.8, 885.7, 586.7 cm^{-1}.

(S)-2-amino-N-butyl-3-methylbutanamide (**1r**)



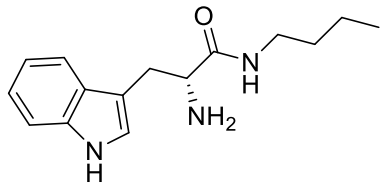
Colourless oil (320 mg, 93% yield); ^{1}H NMR (400 MHz, DMSO): *δ* 7.99 (br t, 1H), 3.92 (s, 2H), 3.20 – 2.93 (m, 3H), 1.99 – 1.80 (m, 1H), 1.45 – 1.34 (m, 2H), 1.28 (dp, *J* = 9.0, 7.0 Hz, 2H), 0.87 (dt, *J* = 7.3, 3.9 Hz, 6H), 0.82 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, DMSO): *δ* 173.0, 59.9, 38.5, 31.7, 31.6, 20.0, 19.7, 17.9, 14.1; HRMS (ESI) *m/z* calculated for $C_9H_{20}N_2O$ $[M+H]^+$: 173.1648, found: 173.1650; IR (ATR diamond, neat): *v* 3675.4, 3280.3, 3071.0, 2958.6, 2931.4, 2872.7, 1642.8, 1531.5, 1465.2, 1370.7, 1299.9, 1242.0, 1076.3, 980.0, 686.1 cm^{-1}.

(S)-2-amino-N-butylpropanamide (**1s**)



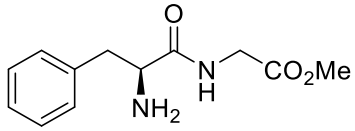
Colourless oil (252 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (t, J = 6.0 Hz, 1H), 3.47 (qt, J = 6.9, 2.6 Hz, 1H), 3.23 – 3.10 (m, 2H), 2.12 (d, J = 6.6 Hz, 2H), 1.52 – 1.35 (m, 2H), 1.35 – 1.21 (m, 5H), 0.94 – 0.77 (m, 3H**); ^{13}C** NMR (101 MHz, $CDCl_3$): δ 175.2, 50.6, 38.7, 31.6, 21.5, 20.0, 13.7; HRMS (ESI) *m/z* calculated for $C_7H_{16}N_2O$ $[M+H]^+$: 145.1335, found: 145.1336; IR (ATR diamond, neat): ν 3287.2, 3082.6, 2959.3, 2931.4, 2873.0, 1643.6, 1536.2, 1455.7, 1368.8, 1259.0, 1229.0, 1130.0, 1074.3, 956.8, 856.4, 665.4 cm^{-1}.

(R)-2-amino-N-butyl-3-(1H-indol-3-yl)propanamide (**1t**) [12]



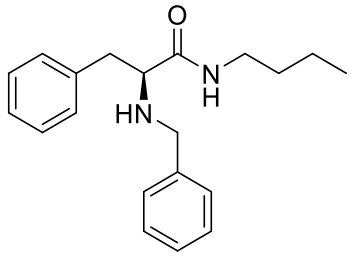
Colourless solid (471 mg, 91% yield); ^{1}H NMR (600 MHz, DMSO): δ 10.80 (s, 1H), 7.75 (d, J = 5.7 Hz, 1H), 7.52 (dd, J = 7.9, 2.8 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.10 (d, J = 2.4 Hz, 1H), 7.02 (ddd, J = 8.1, 6.9, 1.3 Hz, 1H), 6.93 (td, J = 7.4, 6.9, 1.1 Hz, 1H), 3.43 – 3.35 (m, 1H), 3.07 – 2.94 (m, 3H), 2.72 (dd, J = 14.1, 8.1 Hz, 1H), 2.08 – 1.71 (m, 2H), 1.34 – 1.24 (m, 2H), 1.22 – 1.11 (m, 2H), 0.80 (s, 3H).

Methyl L-phenylalanylglycinate (**1u**) [2]



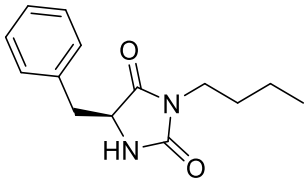
Colourless oil (221 mg, 94% yield); ^{1}H NMR (400 MHz, CD_3OD) δ 7.41 – 7.26 (m, 5H), 4.98 (br s, 1H), 4.23 (dd, J = 7.7, 6.4 Hz, 1H), 4.00 (s, 2H), 3.74 (s, 3H), 3.28 (dd, J = 14.1, 6.4 Hz, 1H), 3.13 (dd, J = 14.1, 7.8 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 170.2, 169.1, 134.2, 129.2 (2C), 128.7 (2C), 127.4, 54.3, 51.5, 40.6, 37.1.

(S)-2-(benzylamino)-N-butyl-3-phenylpropanamide (**1v**)



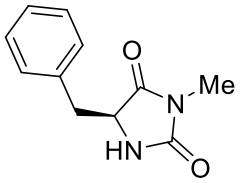
Colourless solid (395 mg, 85% yield); m.p. 58.6-61.4°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.22 (m, 7H), 7.22 – 7.16 (m, 2H), 7.14 – 7.04 (m, 2H), 3.72 (d, *J* = 13.3 Hz, 1H), 3.59 (d, *J* = 13.3 Hz, 1H), 3.51 – 3.18 (m, 5H), 2.78 (dd, *J* = 13.8, 9.2 Hz, 1H), 1.48 (ddd, *J* = 14.3, 7.6, 5.0 Hz, 2H), 1.41 – 1.25 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 138.9, 137.3, 129.1 (2C), 128.8 (2C), 128.9 (2C), 128.0 (2C), 127.3, 126.9, 63.2, 52.6, 39.2, 38.8, 31.7, 20.1, 13.8; HRMS (ESI) *m/z* calculated for $C_{20}H_{26}N_2O$ $[M+H]^+$: 311.2118, found: 311.2115; IR (ATR diamond, neat): *v* 3314.7, 3286.1, 3059.7, 3027.0, 2958.4, 2930.0, 2872.9, 1626.5, 1542.3, 1496.1, 1472.2, 1453.2, 1301.1, 1126.4, 750.1, 740.0, 695.0 cm^{-1}.

(S)-5-benzyl-3-butylimidazolidine-2,4-dione (**2a**) [13]



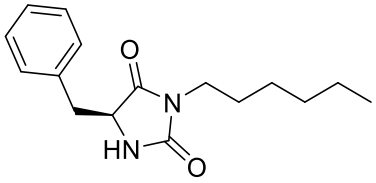
Colourless solid (62 mg, 84% yield); $[\alpha]_D^{27}$ −72.52° (c 0.3, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30-7.21 (m, 3H), 7.21-7.13 (m, 2H), 6.21 (s, 1H), 4.21 (ddd, *J* = 7.8, 3.9, 1.2 Hz, 1H), 3.47-3.29 (m, 2H), 3.21 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.89 (dd, *J* = 14.0, 7.7 Hz, 1H), 1.46-1.37 (m, 2H), 1.19-1.09 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H).

(S)-5-benzyl-3-methylimidazolidine-2,4-dione (**2b**) [14]



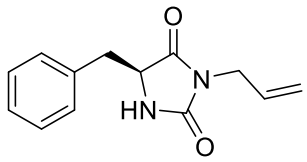
Colourless solid (56 mg, 91% yield); $[\alpha]_D^{27}$−87.75° (c 0.3, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.20 (m, 3H), 7.17 (m, 2H), 6.08 (s, 1H), 4.21 (ddd, *J* = 8.8, 3.9, 1.2 Hz, 1H), 3.25 (dd, *J* = 14.0, 3.8 Hz, 1H), 2.91 (s, 3H), 2.86 – 2.78 (m, 1H).

(S)-5-benzyl-3-hexylimidazolidine-2,4-dione (**2c**) [15]



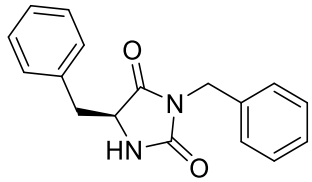
Colourless solid (58 mg, 71% yield); $[\alpha]_D^{23}$ −58.81° (c 0.3, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 – 7.22 (m, 3H), 7.17 (d, *J* = 6.7 Hz, 2H), 5.99 (s, 1H), 4.21 (dd, *J* = 4.2, 1.2 Hz, 1H), 3.38 (dd, *J* = 7.9, 7.0 Hz, 2H), 3.22 (dd, *J* = 14.0, 3.9 Hz, 1H), 2.87 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.43 (t, *J* = 7.1 Hz, 2H), 1.29 – 1.13 (m, 6H), 0.86 (t, *J* = 7.0 Hz, 3H).

(S)-3-allyl-5-benzylimidazolidine-2,4-dione (**2d**)



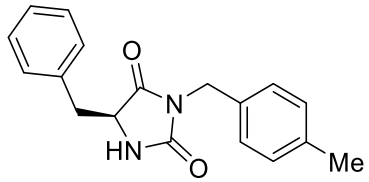
Colourless solid (39 mg, 85% yield); $[\alpha]_D^{20}$ −69.6° (c 0.3, MeOH); m.p. 94.5-95.3°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.24 (m, 3H), 7.20 (dd, *J* = 7.7, 1.8 Hz, 2H), 6.33 (s, 1H), 5.68 (ddt, *J* = 17.1, 10.2, 5.6 Hz, 1H), 5.11 (dp, *J* = 10.3, 1.3 Hz, 1H), 5.02 (dq, *J* = 17.1, 1.5 Hz, 1H), 4.28 (ddd, *J* = 7.8, 4.0, 1.3 Hz, 1H), 4.13 – 3.95 (m, 2H), 3.26 (dd, *J* = 14.0, 3.9 Hz, 1H), 2.94 (dd, *J* = 14.0, 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.8, 157.1, 135.0, 130.9, 129.5, 128.8, 127.4, 117.6, 58.4, 40.5, 37.8; HRMS (ESI) *m/z* calculated for $C_{13}H_{14}N_2O_2$ $[M+H]^+$: 231.1288, found: 231.1289; IR (ATR diamond, neat): *v* 3284.7, 2926.2, 1750.3, 1697.5, 1452.2, 1421.5, 1355.7, 1334.7, 1142.0, 1094.8, 964.5, 700.2 cm^{-1}.

(S)-3,5-dibenzylimidazolidine-2,4-dione (**2e**) [13,14,15]



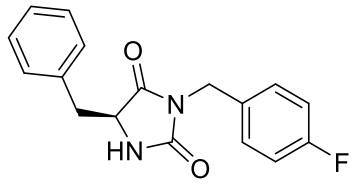
Colourless solid (76 mg, 90% yield); $[\alpha]_D^{27}$ −36.18° (c 0.3, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.07 (m, 10H), 6.43 (s, 1H), 4.63 – 4.48 (m, 2H), 4.22 (dd, *J* = 7.6, 5.3 Hz, 1H), 3.18 (dd, *J* = 14.1, 4.0 Hz, 1H), 2.89 (dd, *J* = 14.0, 7.7 Hz, 1H).

(S)-5-benzyl-3-(4-methylbenzyl)imidazolidine-2,4-dione (**2f**)



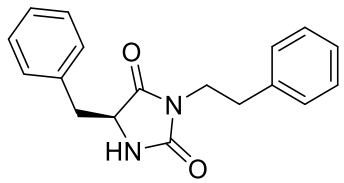
Colourless solid (78 mg, 88% yield); $[\alpha]_D^{23}$ –38.40° (c 0.3, MeOH); m.p. 125.6-127.1°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.27 (m, 3H), 7.19-7.17 (m, 4H), 7.11-7.10 (m, 2H), 5.50 (br s, 1H), 4.58 (d, *J* = 6.5 Hz, 2H), 4.25 (ddd, *J* = 8.7, 3.8, 1.2 Hz, 1H), 3.28 (dd, *J* = 13.9, 3.8 Hz, 1H), 2.85 (dd, *J* = 13.9, 8.7 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.7, 156.6, 137.6, 135.2, 132.8, 129.3 (2C), 129.2 (2C), 128.9 (2C), 128.4 (2C), 127.4, 58.4, 41.9, 37.9, 21.2; HRMS (ESI) *m/z* calculated for $C_{18}H_{18}N_2O_2$ $[M+H]^+$: 295.1441, found: 295.1442; IR (ATR diamond, neat): *v* 3240.0, 3031.0, 2922.4, 1769.6, 1707.0, 1446.7, 1349.2, 1196.8, 906.8, 725.2 cm^{-1}.

(S)-5-benzyl-3-(4-fluorobenzyl)imidazolidine-2,4-dione (**2g**) [15]



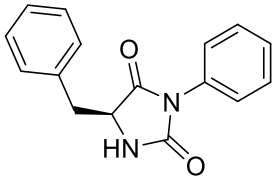
Colourless solid (80 mg, 89% yield); $[\alpha]_D^{23}$ –15.49° (c 0.4, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18-7.02 (m, 7H), 6.88-6.83 (m, 2H), 5.29 (br s, 1H), 4.43 (dd, *J* = 15.0, 11.5 Hz, 2H), 4.18 (ddt, *J* = 7.6, 4.1, 1.1 Hz, 1H), 3.11 (ddd, *J* = 14.0, 4.0, 1.3 Hz, 1H), 2.83 (ddd, *J* = 14.0, 7.5, 1.1 Hz, 1H).

(S)-5-benzyl-3-phenethylimidazolidine-2,4-dione (**2h**) [16]



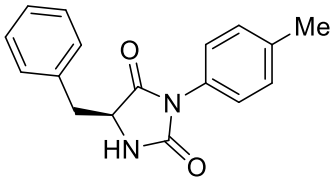
Colourless solid (75 mg, 85% yield); $[\alpha]_D^{27}$ –89.90° (c 0.3, MeOH); m.p. 126.1-126.4°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.09 (m, 10H), 5.78 (br s, 1H), 4.09 (ddd, *J* = 8.8, 3.8, 1.1 Hz, 1H), 3.66-3.52 (m, 2H), 3.13 (dd, *J* = 13.9, 3.8 Hz, 1H), 2.74-2.63 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.9, 157.0, 137.8, 135.3, 128.3 (2C), 129.0 (2C), 128.9 (2C), 128.6 (2C), 127.5, 126.7, 58.2, 38.6, 38.0, 33.8; HRMS (ESI) *m/z* calculated for $C_{18}H_{18}N_2O_2$ $[M+H]^+$: 295.1441, found: 295.1443; IR (ATR diamond, neat): *v* 3286.0, 2985.3, 1764.3, 1683.3, 1453.2, 1423.6, 1355.5, 1130.1, 749.0, 726.0, 696.4 cm^{-1}.

(S)-5-benzyl-3-phenylimidazolidine-2,4-dione (**2i**) [15,16]



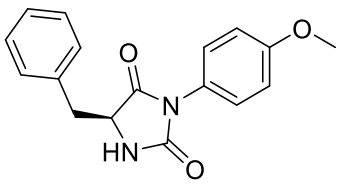
Colourless solid (68 mg, 85% yield); $[\alpha]_D^{27}$ −109.72° (c 0.3, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.08 (m, 10H), 6.55 (br s, 1H), 4.30 (ddd, *J* = 7.1, 4.0, 1.2 Hz, 1H), 3.16 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.99 (dd, *J* = 13.9, 7.0 Hz, 1H).

(S)-5-benzyl-3-(p-tolyl)imidazolidine-2,4-dione (**2j**)



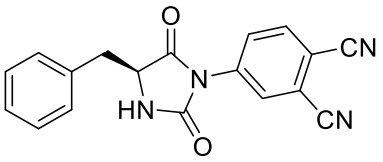
Colourless solid (78 mg, 93% yield); $[\alpha]_D^{23}$ −163.89° (c 0.3, MeOH); m.p. 124.9-127.0°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.22 (m, 7H), 7.06 (dd, *J* = 8.4, 2.0 Hz, 2H), 6.55 (d, *J* = 7.6 Hz, 1H), 4.40 (ddd, *J* = 7.1, 4.0, 1.1 Hz, 1H), 3.26 (dt, *J* = 13.9, 3.7 Hz, 1H), 3.17 – 3.01 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.3, 156.7, 138.5, 134.7, 129.8 (2C), 129.6 (2C), 128.8 (2C), 128.6, 127.5, 126.2 (2C), 58.1, 37.8, 21.2; HRMS (ESI) *m/z* calculated for $C_{17}H_{16}N_2O_2$ $[M+H]^+$: 281.1285, found: 281.1283; IR (ATR diamond, neat): *v* 3325.0, 3116.2, 2920.0, 2848.8, 1774.8, 1711.8, 1513.1, 1404.3, 1358.1, 1162.8, 818.1, 746.8, 695.4 cm^{-1}.

(S)-5-benzyl-3-(4-methoxyphenyl)imidazolidine-2,4-dione (**2k**) [15]



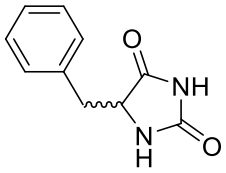
Colourless solid (76 mg, 86% yield); $[\alpha]_D^{27}$ −143.07° (c 0.3, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.30 (m, 3H), 7.27 – 7.21 (m, 2H), 7.09 – 7.03 (m, 2H), 7.00 – 6.92 (m, 2H), 6.76 (s, 1H), 4.39 (ddd, *J* = 6.8, 4.1, 1.2 Hz, 1H), 3.83 (s, 3H), 3.24 (dd, *J* = 13.9, 4.1 Hz, 1H), 3.10 (dd, *J* = 13.9, 6.7 Hz, 1H).

(S)-4-(4-benzyl-2,5-dioxoimidazolidin-1-yl)phthalonitrile (**2l**)



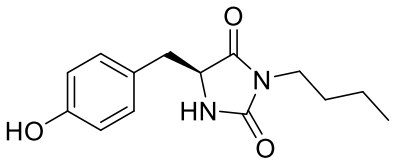
Yellow solid (10 mg, 13% yield); $[\alpha]_D^{20}$ –101.3° (c 0.1, MeOH); m.p. 165.1-167.2°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 1H), 7.89 – 7.81 (m, 2H), 7.37 – 7.28 (m, 3H), 7.21 (dt, *J* = 6.1, 1.6 Hz, 2H), 6.06 (br s, 1H), 4.48 (ddd, *J* = 7.9, 3.9, 1.2 Hz, 1H), 3.34 (dd, *J* = 14.0, 3.9 Hz, 1H), 3.05 (dd, *J* = 14.0, 7.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 181.7, 170.8, 154.0, 141.5, 136.3, 134.2, 134.1, 134.1, 129.5, 129.4 (2C), 129.2 (2C), 129.1, 128.1, 116.8, 115.0, 114.7, 114.3, 58.1, 38.1; HRMS (ESI) *m/z* calculated for $C_{18}H_{12}N_4O_2$ $[M+H]^+$: 316.3200, found: 316.3197; IR (ATR diamond, neat): *v* 3327.9, 3116.2, 3030.2, 2925.7, 2853.0, 2235.3, 1784.7, 1720.1, 1599.4, 1494.2, 1392.7, 1348.1, 1186.1, 1160.7, 1112.8, 1030.1, 907.7, 841.6, 727.7 cm^{-1}.

(rac)-5-Benzylimidazolidine-2,4-dione (**2m**) [16]



Colourless solid (43 mg, 75% yield); ^{1}H NMR (400 MHz, DMSO): δ 10.43 (s, 1H), 7.93 (s, 1H), 7.35 – 7.13 (m, 5H), 4.39 – 4.29 (m, 1H), 2.93 (dd, *J* = 5.0, 3.7 Hz, 2H); ^{13}C NMR (101 MHz, DMSO): δ 180.4, 162.4, 140.9, 135.0, 133.3, 131.9, 63.6, 41.7.

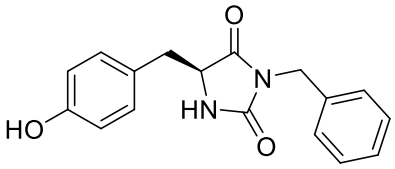
(S)-3-butyl-5-(4-hydroxybenzyl)imidazolidine-2,4-dione (**2n**)



Light yellow solid (70 mg, 89% yield); $[\alpha]_D^{23}$ –50.81° (c 0.3, MeOH); m.p. 173.5-174.2°C; ^{1}H NMR (400 MHz, DMSO): δ 9.21 (s, 1H), 8.26 – 8.03 (m, 1H), 7.07 – 6.85 (m, 2H), 6.71 – 6.53 (m, 2H), 4.27 (d, *J* = 1.1 Hz, 1H), 3.14 (d, *J* = 18.5 Hz, 2H), 2.84 (dd, *J* = 4.6, 2.2 Hz, 2H), 1.29 – 1.08 (m, 2H), 1.03 – 0.82 (m, 2H), 0.75 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO): δ 174.0, 157.1, 156.7, 131.2 (2C), 125.3, 115.2 (2C), 57.6, 37.5, 35.9, 29.9, 19.5, 14.0; HRMS (ESI) *m/z* calculated for $C_{14}H_{18}N_2O_3$ $[M+H]^+$: 263.1690, found: 262.1689; IR (ATR diamond,

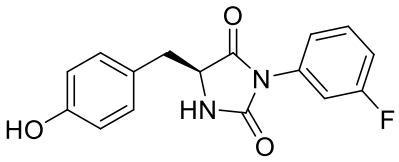
neat): *v* 3285.8, 2954.1, 2926.0, 2866.0, 1742.6, 1689.1, 1613.9, 1515.3, 1448.7, 1204.9, 1175.0, 1109.2, 1081.3, 864.0, 824.1, 766.0, 566.5 cm^{-1}.

(S)-3-benzyl-5-(4-hydroxybenzyl)imidazolidine-2,4-dione (**2o**)



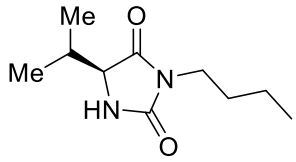
Light yellow solid (83 mg, 94% yield); $[\alpha]_D^{23}$ −19.71° (c 0.3, MeOH); m.p. 149.4-150.2°C; ^{1}H NMR (600 MHz, DMSO): δ 9.29 (s, 1H), 8.28 (s, 1H), 7.17 – 7.13 (m, 3H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.72 – 6.64 (m, 2H), 6.63 – 6.56 (m, 2H), 4.44 – 4.22 (m, 3H), 2.92 – 2.78 (m, 2H); ^{13}C NMR (151 MHz, DMSO): δ 173.9, 156.9, 156.8, 136.8, 131.5 (2C), 128.7 (2C), 127.4, 126.9 (2C), 125.4, 115.5 (2C), 58.0, 41.2, 35.7; HRMS (ESI) *m/z* calculated for $C_{17}H_{16}N_2O_3$ $[M+H]^+$: 296.1234, found: 296.1233; IR (ATR diamond, neat): *v* 3304.8, 3190.2, 3028.7, 2927.8, 1759.8, 1693.9, 1599.9, 1514.7, 1451.3, 1422.9, 1360.7, 1240.3, 1131.5, 961.9, 818.6, 755.0, 715.3, 694.9, 631.5, 569.1 cm^{-1}.

(S)-3-(3-fluorophenyl)-5-(4-hydroxybenzyl)imidazolidine-2,4-dione (**2p**)



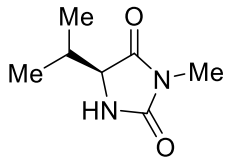
Colourless solid (60 mg, 67% yield); $[\alpha]_D^{20}$ −92.3° (c 0.2, MeOH); m.p. 150.0-151.5°C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.40 (td, *J* = 8.2, 6.3 Hz, 1H), 7.15 – 7.04 (m, 3H), 6.90 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 6.84 (dt, *J* = 9.8, 2.3 Hz, 1H), 6.79 – 6.71 (m, 2H), 4.88 (br s, 2H) 4.46 (dd, *J* = 4.5 Hz, *J* = 4.5 Hz, 1H), 3.15 – 3.01 (m, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 173.1, 163.6, 161.2, 156.5, 156.3, 133.2, 133.1, 130.8 (2C), 129.9, 129.8, 125.0, 122.2, 122.2, 114.8 (2C), 114.7, 114.5, 113.6, 113.4, 58.0, 36.0; HRMS (ESI) *m/z* calculated for $C_{16}H_{13}FN_2O_3$ $[M+H]^+$: 300.0910, found: 300.0913; IR (ATR diamond, neat): *v* 3260.9, 2426.2, 1771.9, 1599.0, 1600.4, 1514.0, 1492.1, 1422.2, 1348.8, 1238.6, 1185.9, 1166.8, 1015.1, 802.0, 781.5, 735.6 cm^{-1}.

(S)-3-butyl-5-isopropylimidazolidine-2,4-dione (**2q**)



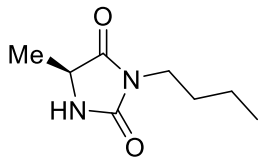
Colourless oil (52 mg, 88% yield); $[\alpha]_D^{20}$ –36.91° (c 0.3, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.71 (s, 1H), 3.93 (dd, *J* = 3.7, 1.1 Hz, 1H), 3.59 – 3.40 (m, 2H), 2.28-2.20 (m, 1H), 1.66 – 1.49 (m, 2H), 1.41 – 1.27 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.99 – 0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.7, 158.7, 62.3, 38.3, 30.2, 30.1, 20.0, 18.8, 15.9, 13.6; HRMS (ESI) *m/z* calculated for $C_{10}H_{18}N_2O_2$ $[M+H]^+$: 199.1441, found: 199.1440; IR (ATR diamond, neat): *v* 3662.0, 3283.9, 2961.3, 2934.6, 2874.9, 1770.9, 1696.4, 1449.4, 1421.1, 1353.1, 1294.6, 1200.1, 1103.5, 1042.3, 922.1, 765.2, 624.1 cm^{-1}.

(S)-5-isopropyl-3-methylimidazolidine-2,4-dione (**2r**) [17]



Colourless solid (34 mg, 72% yield); $[\alpha]_D^{20}$ –59.80° (c 0.3, MeOH); m.p. 127.1-128.6°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.68 (s, 1H), 3.95 (dd, *J* = 3.9, 1.2 Hz, 1H), 3.01 (s, 3H), 2.29-2.20 (m, 1H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.7, 158.6, 62.6, 30.2, 24.4, 18.8, 16.1; HRMS (ESI) *m/z* calculated for $C_7H_{12}N_2O_2$ $[M+H]^+$: 157.0972, found: 157.0972; IR (ATR diamond, neat): *v* 3283.6, 2966.0, 2874.7, 1745.7, 1693.8, 1470.0, 1392.2, 1355.2, 1305.7, 1280.3, 1197.4, 1143.9, 1115.1, 1100.2, 1041.6, 947.3, 832.6, 761.5, 719.9 cm^{-1}.

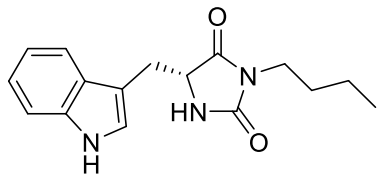
(S)-3-butyl-5-methylimidazolidine-2,4-dione (**2s**)



Colourless oil (37 mg, 73% yield); $[\alpha]_D^{20}$ –14.06° (c 0.3, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (s, 1H), 4.08 (qd, *J* = 6.9, 1.0 Hz, 1H), 3.49 (td, *J* = 7.2, 1.5 Hz, 2H), 1.67 – 1.53 (m, 2H), 1.45 (d, *J* = 7.0 Hz, 3H), 1.41 – 1.26 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.9, 158.0, 52.8, 38.4, 30.1, 19.9, 17.6, 13.6; HRMS (ESI) *m/z* calculated for $C_8H_{14}N_2O_2$ $[M+H]^+$: 171.1128, found: 171.1126; IR (ATR diamond, neat): *v* 3299.8,

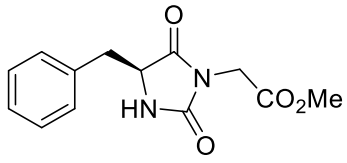
2959.1, 2935.1, 2874.0, 1771.7, 1695.0, 1449.4, 1421.2, 1370.9, 1344.4, 1321.6, 1200.9, 1133.8, 1045.4, 936.2, 772.0, 594.5 cm^{-1}.

(R)-5-((1H-indol-3-yl)methyl)-3-butylimidazolidine-2,4-dione (**2t**)



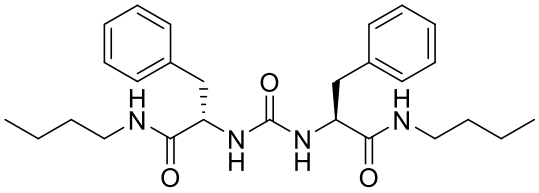
Brown solid (35 mg, 41% yield); $[\alpha]_D^{20}$ +2.6° (c 0.1, MeOH); m.p. 129.0-130.8°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.61 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.35 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.13 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.00 (d, *J* = 1.9 Hz, 1H), 6.07 (s, 1H), 4.26 (ddd, *J* = 8.1, 3.8, 1.0 Hz, 1H), 3.50 – 3.31 (m, 3H), 3.07 (dd, *J* = 14.8, 8.1 Hz, 1H), 1.40 (p, *J* = 7.4 Hz, 2H), 1.27 – 1.11 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.8, 157.8, 136.2, 127.1, 123.3, 122.4, 119.9, 118.7, 111.4, 109.3, 57.8, 38.4, 29.9, 27.9, 19.8, 13.6; HRMS (ESI) *m/z* calculated for $C_{16}H_{19}N_3O_2$ $[M+H]^+$: 286.1550, found: 286.1553; IR (ATR diamond, neat): *v* 3313.6, 2956.6, 2929.3, 2879.6, 1767.4, 1692.8, 1452.5, 1422.1, 1341.9, 1232.6, 1096.5, 739.5, 553.1 cm^{-1}.

Methyl (S)-2-(4-benzyl-2,5-dioxoimidazolidin-1-yl)acetate (**2u**)



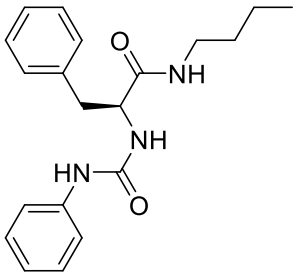
Colourless solid (30 mg, 38% yield); $[\alpha]_D^{20}$ −94.5° (c 0.2, MeOH); m.p. 132.9-135.4°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 2H), 7.34 – 7.26 (m, 1H), 7.26 – 7.18 (m, 2H), 5.96 (br s, 1H), 4.34 (ddd, *J* = 9.4, 3.8, 1.2 Hz, 1H), 4.22 (d, *J* = 1.0 Hz, 2H), 3.77 (s, 3H), 3.34 (dd, *J* = 14.0, 3.8 Hz, 1H), 2.88 (dd, *J* = 13.9, 9.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 167.4, 156.1, 135.4, 129.2 (2C), 129.0 (2C), 127.5, 58.8, 52.7, 39.2, 38.0; HRMS (ESI) *m/z* calculated for $C_{13}H_{14}N_2O_4$ $[M+H]^+$: 262.0954, found: 262.0950; IR (ATR diamond, neat): *v* 3232.1, 3108.9, 3031.5, 2954.5, 1774.6, 1716.3, 1498.8, 1455.4, 1431.9, 1344.6, 1221.7, 1157.4, 1084.9, 924.6, 729.0 cm^{-1}.

2,2'-(carbonylbis(azanediyl))bis(N-butyl-3-phenylpropanamide) (**3a**)



Colourless solid (116 mg, quant. yield); m.p. 210.5-211.7°C; ^{1}H NMR (400 MHz, DMSO): δ 7.76 (t, J = 5.6 Hz, 2H), 7.33 – 7.11 (m, 10H), 6.33 (d, J = 8.3 Hz, 2H), 4.27 (td, J = 7.8, 6.2 Hz, 2H), 3.03 (dt, J = 13.1, 6.6 Hz, 2H), 2.95 (dt, J = 12.7, 6.2 Hz, 2H), 2.85 (dd, J = 13.5, 6.2 Hz, 2H), 2.73 (dd, J = 13.6, 7.6 Hz, 2H), 1.37 – 1.24 (m, 4H), 1.24 – 1.10 (m, 4H), 0.82 (t, J = 7.2 Hz, 6H); ^{13}C NMR (101 MHz, DMSO): δ 171.8 (2C), 157.1, 138.3 (2C), 129.7 (4C), 128.4 (4C), 126.6 (2C), 54.9 (2C), 39.3 (2C), 38.5 (2C), 31.5 (2C), 19.9 (2C), 14.1 (2C); HRMS (ESI) *m/z* calculated for $C_{27}H_{38}N_4O_3$ $[M+H]^+$: 467.3017, found: 467.3014; IR (ATR diamond, neat): ν 3381.2, 3280.0, 2960.8, 2934.8, 2885.3, 1632.6, 1548.6, 1495.0, 1449.2, 1372.9, 1283.7, 1225.6, 1077.6, 1031.9, 740.2, 701.2, 615.5 cm^{-1}.

(S)-N-butyl-3-phenyl-2-(3-phenylureido)propanamide (**5a**)



Colourless solid (101 mg, quant. yield); m.p. 181.7-183.1°C; ^{1}H NMR (400 MHz, DMSO): δ 8.66 (s, 1H), 8.05 (t, J = 5.6 Hz, 1H), 7.39 – 7.15 (m, 9H), 6.89 (t, J = 7.3 Hz, 1H), 6.36 (d, J = 8.3 Hz, 1H), 4.47 (td, J = 7.8, 5.9 Hz, 1H), 3.18 – 2.91 (m, 3H), 2.84 (dd, J = 13.6, 7.5 Hz, 1H), 1.44 – 1.28 (m, 2H), 1.28 – 1.15 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO): δ 171.6, 155.0, 140.8, 138.0, 129.8 (2C), 129.1 (2C), 128.5 (2C), 126.7, 121.6, 117.9 (2C), 54.4, 39.6, 38.6, 31.6, 20.0, 14.1; HRMS (ESI) *m/z* calculated for $C_{20}H_{25}N_3O_2$ $[M+H]^+$: 340.2020, found: 340.2017; IR (ATR diamond, neat): ν 3279.3, 3089.2, 3062.7, 2957.2, 2929.4, 2870.3, 1634.0, 1544.3, 1497.3, 1440.9, 1312.2, 1225.9, 1030.9, 742.6, 691.6, 503.0 cm^{-1}.

8. References

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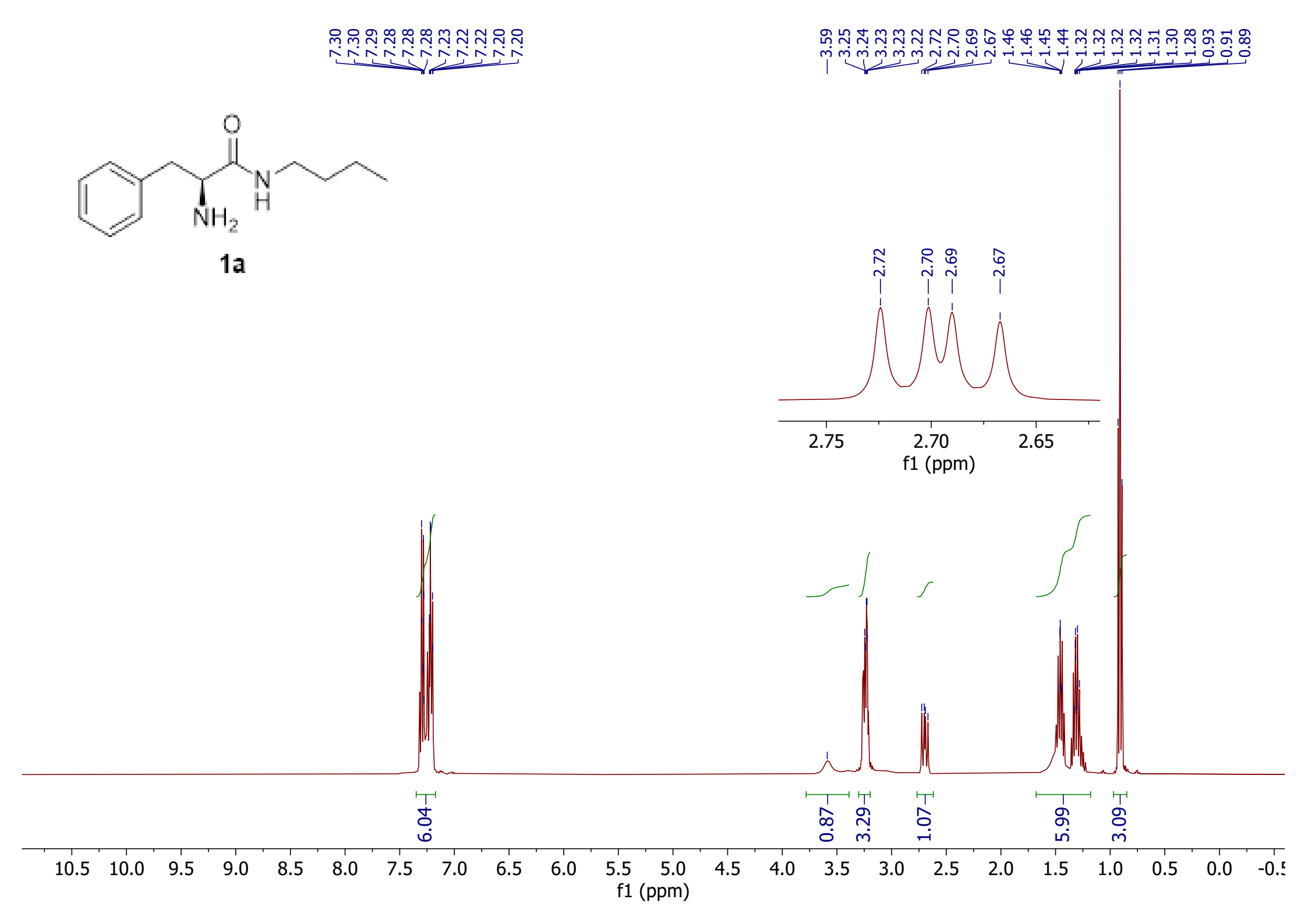
9. Copy of NMR Spectra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7.29
7.28
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7.23
7.22
7.22
7.20
7.20
3.59
3.25
3.24
3.23
3.23
3.22
2.72
2.70
2.69
2.67
1.46
1.46
1.45
1.44
1.32
1.32
1.32
1.31
1.30
1.28
0.93
0.91
0.89
O
N
H
NH2
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2.70
2.69
2.67
2.75
2.70
2.65
f1 (ppm)
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0.87
3.29
1.07
5.99
3.09
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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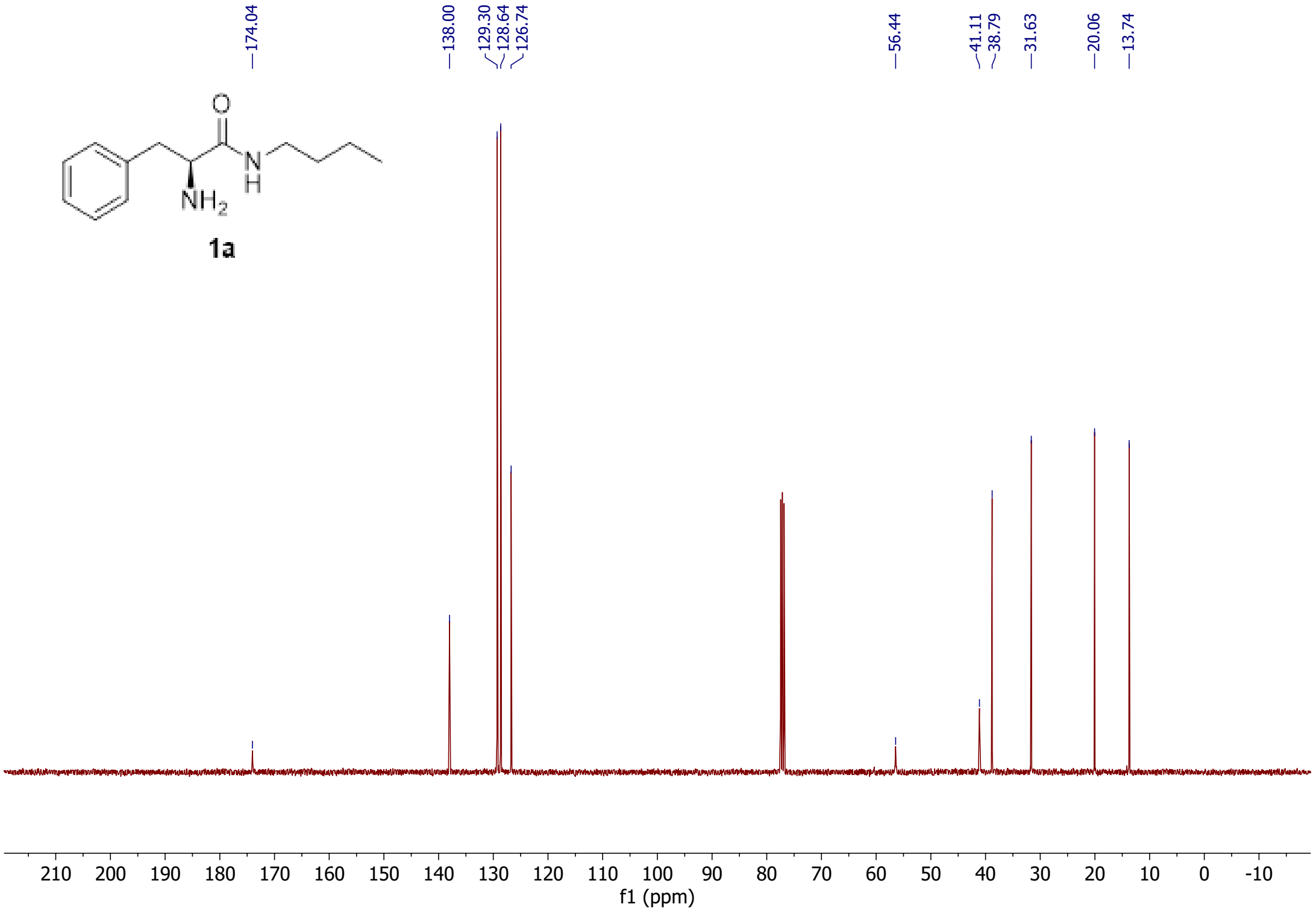
f1 (ppm)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N
H
NH2
1a
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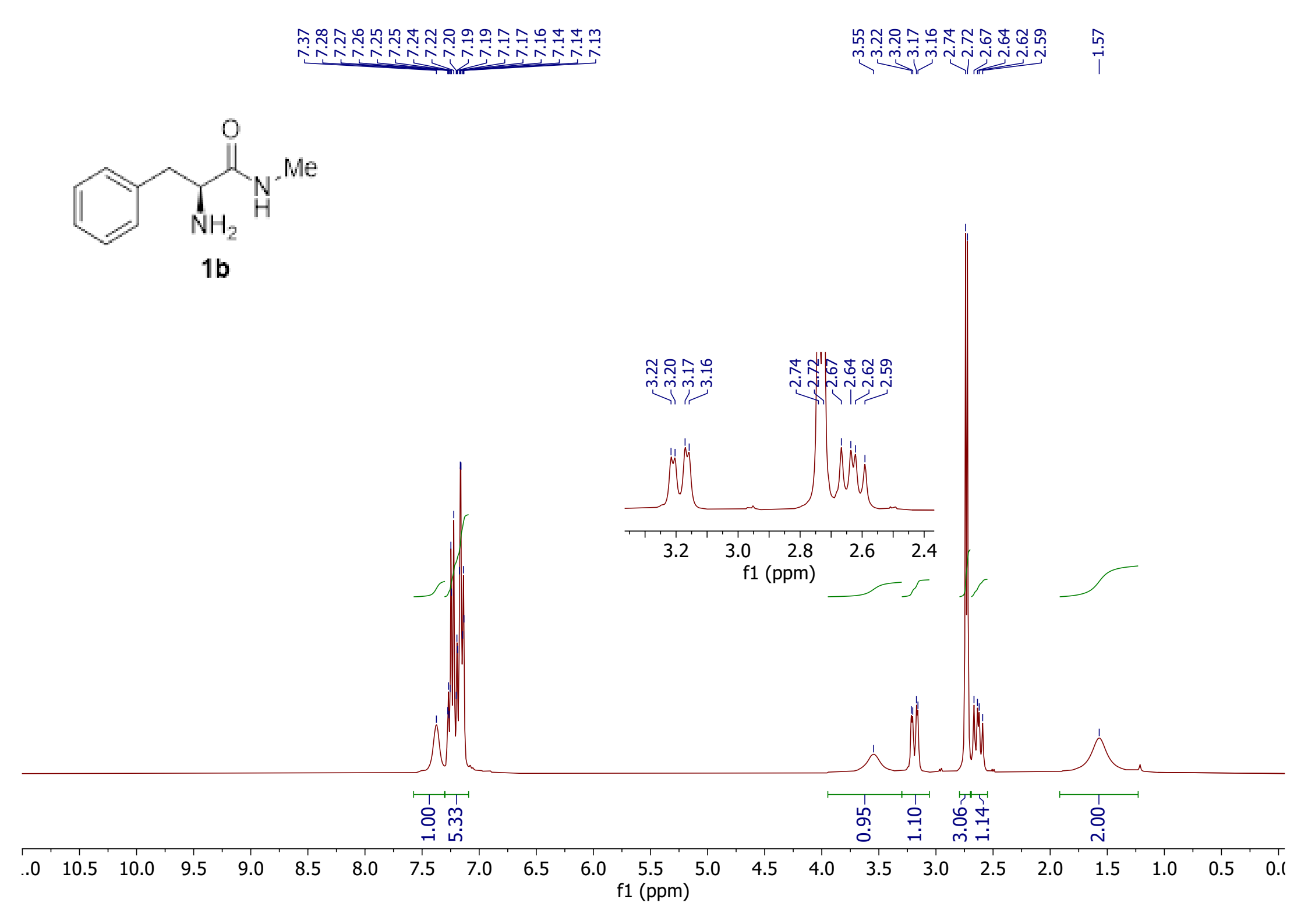
f1 (ppm)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7.16
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7.14
7.13
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Me
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H
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3.16
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2.8
2.6
2.4
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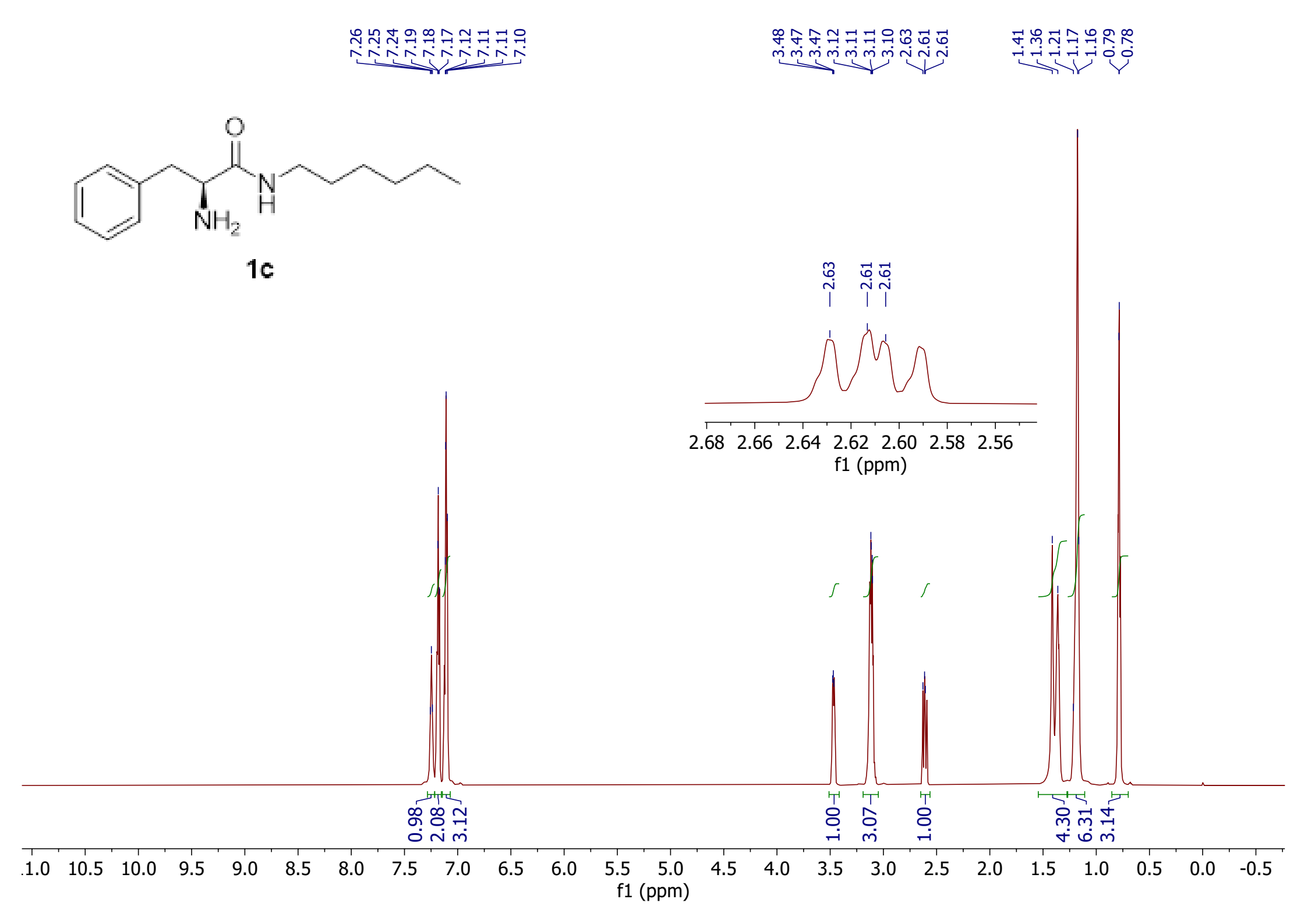
f1 (ppm)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3.11
3.10
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3.14
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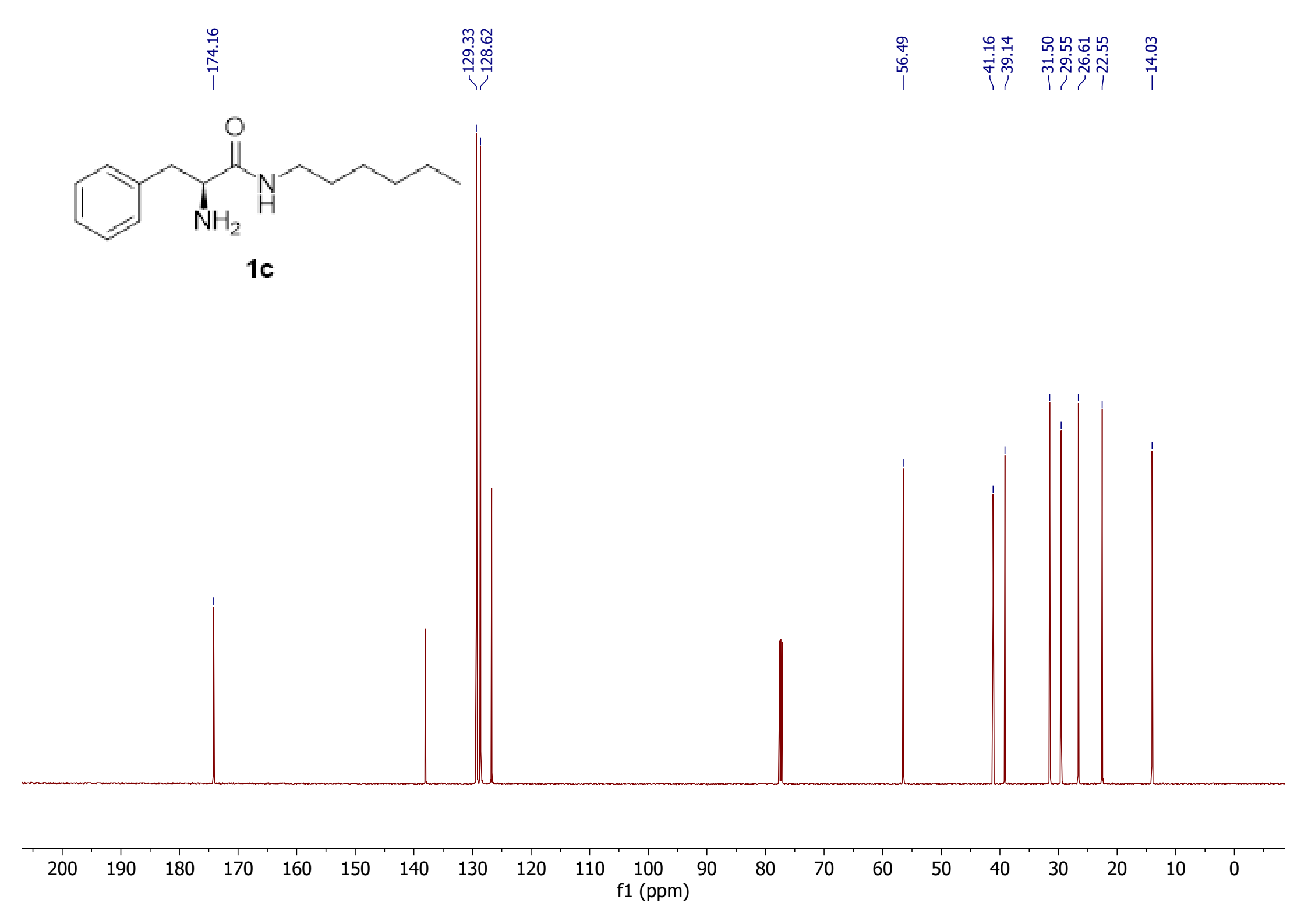
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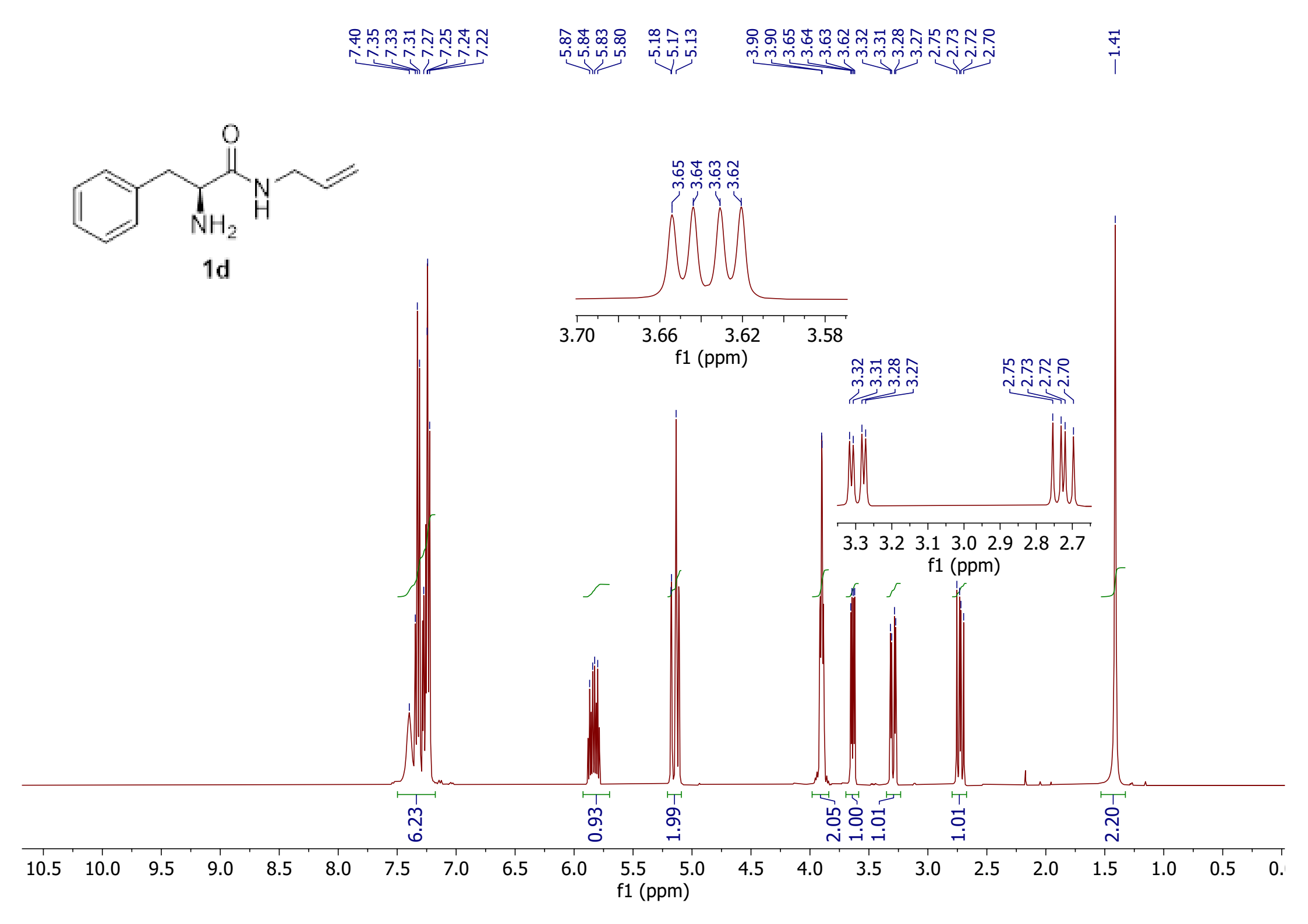
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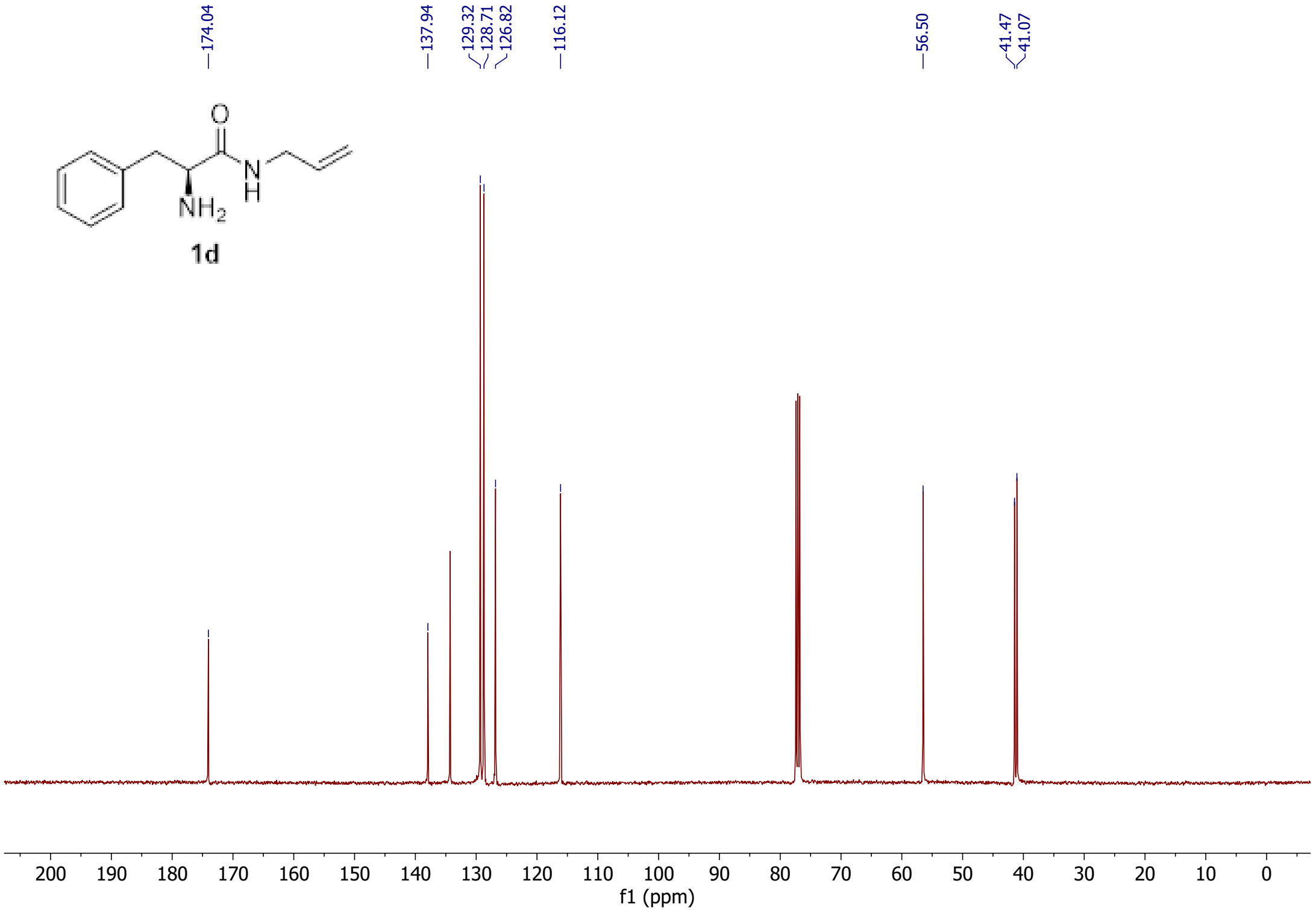
f1 (ppm)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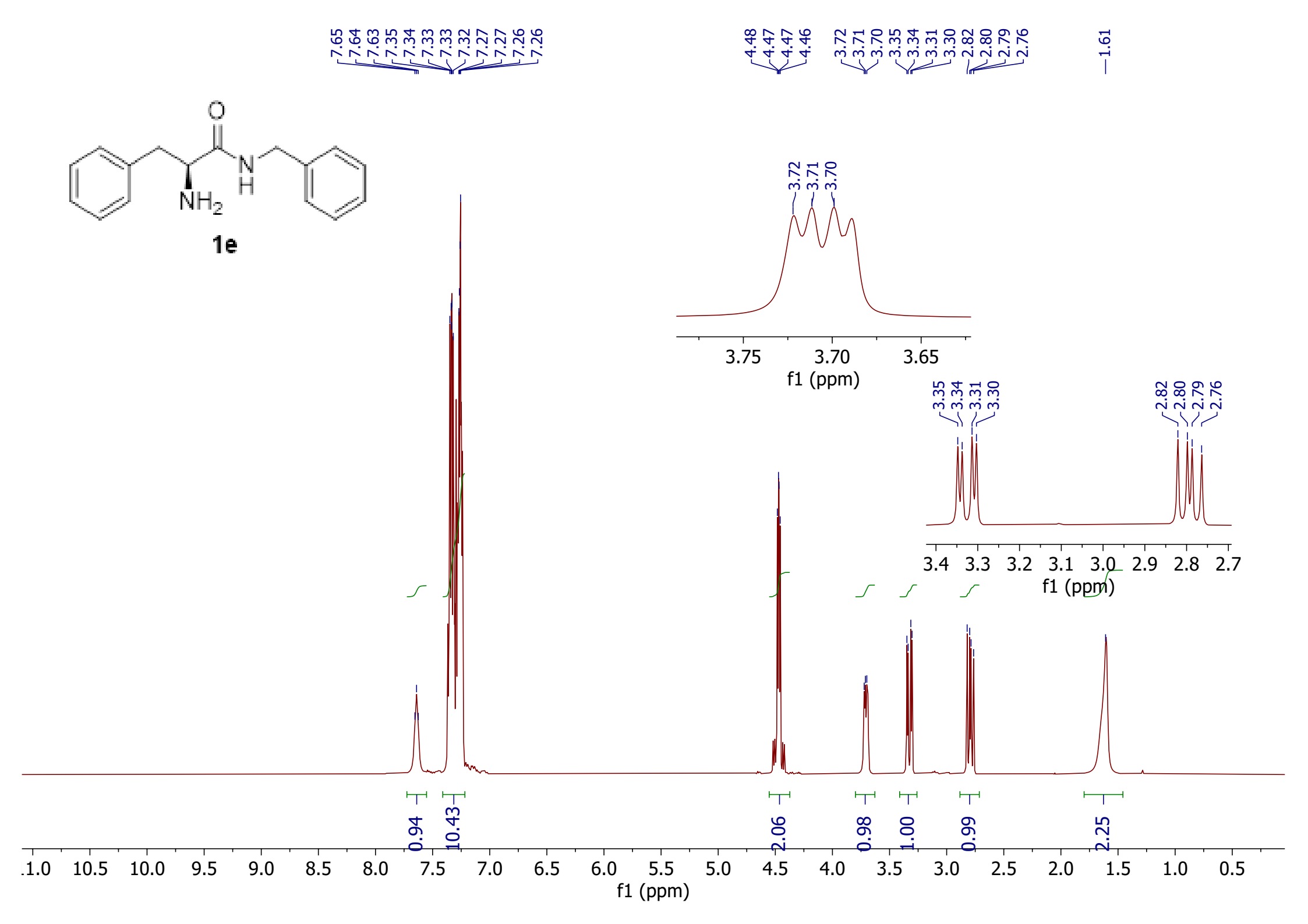
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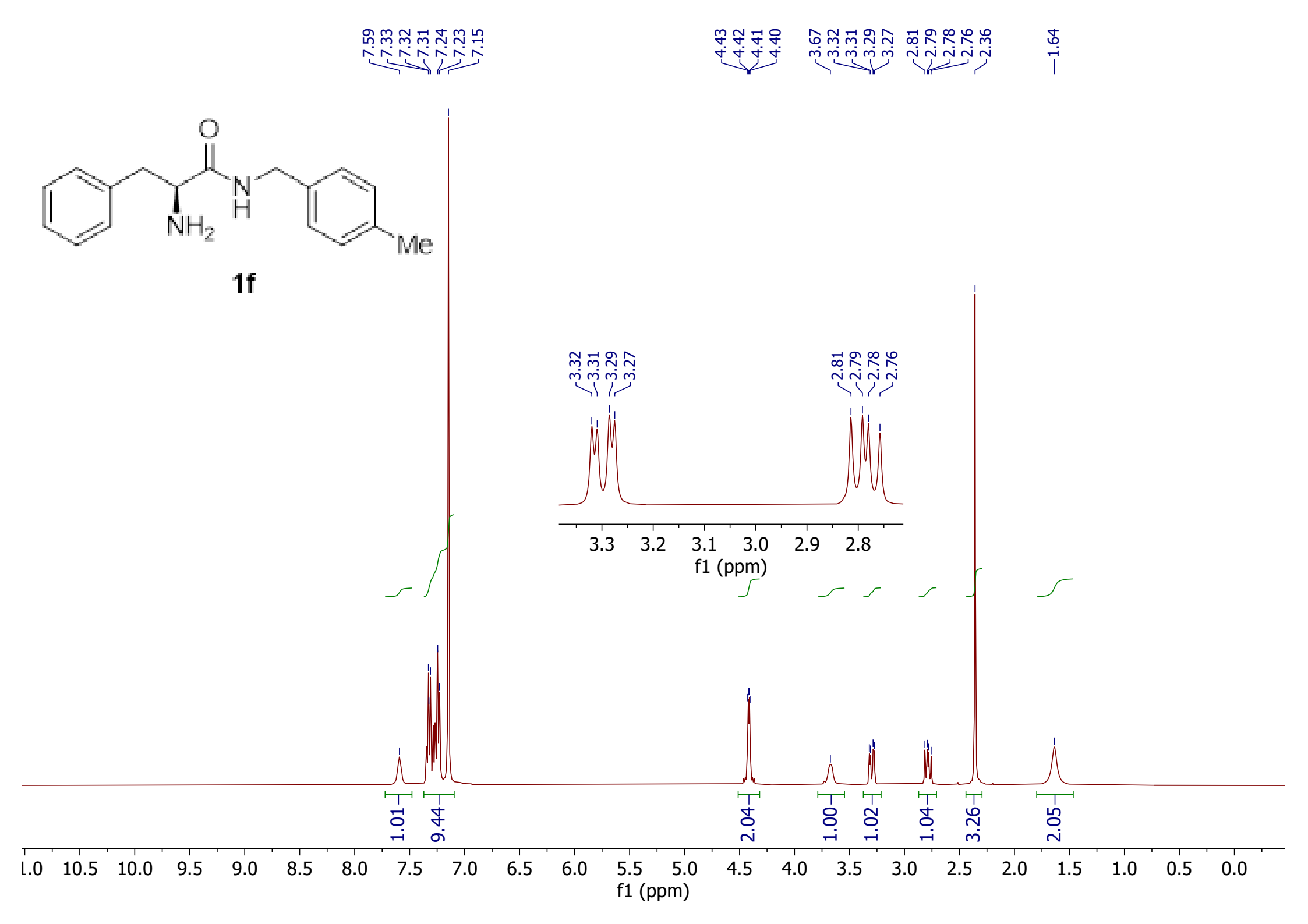
f1 (ppm)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2.78
2.76
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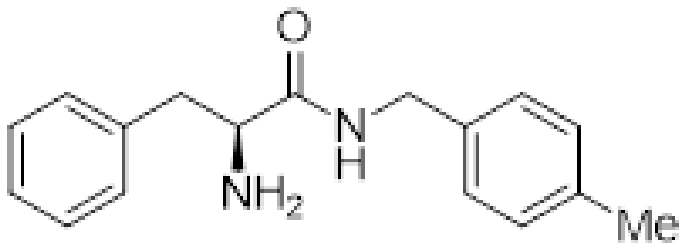
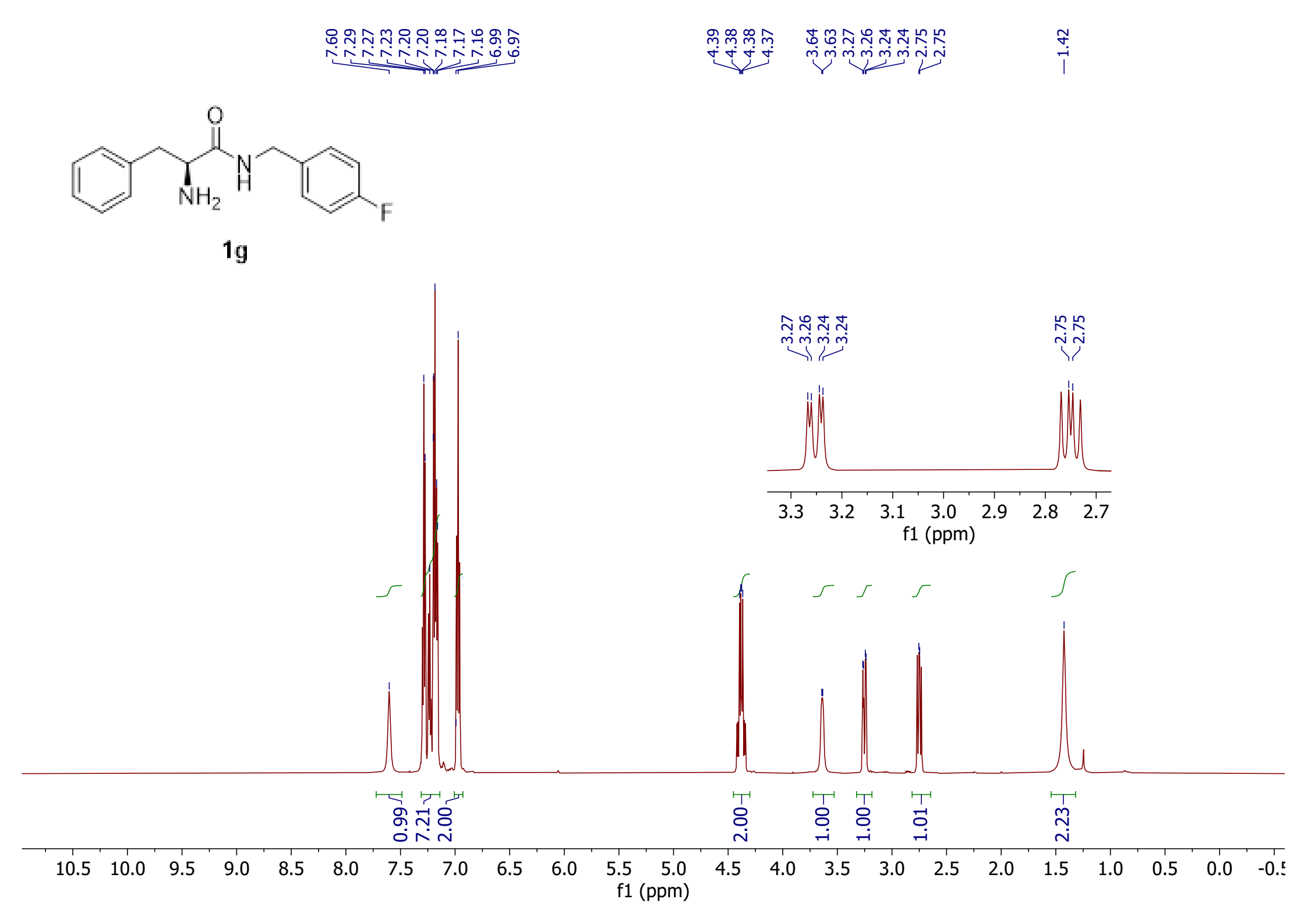
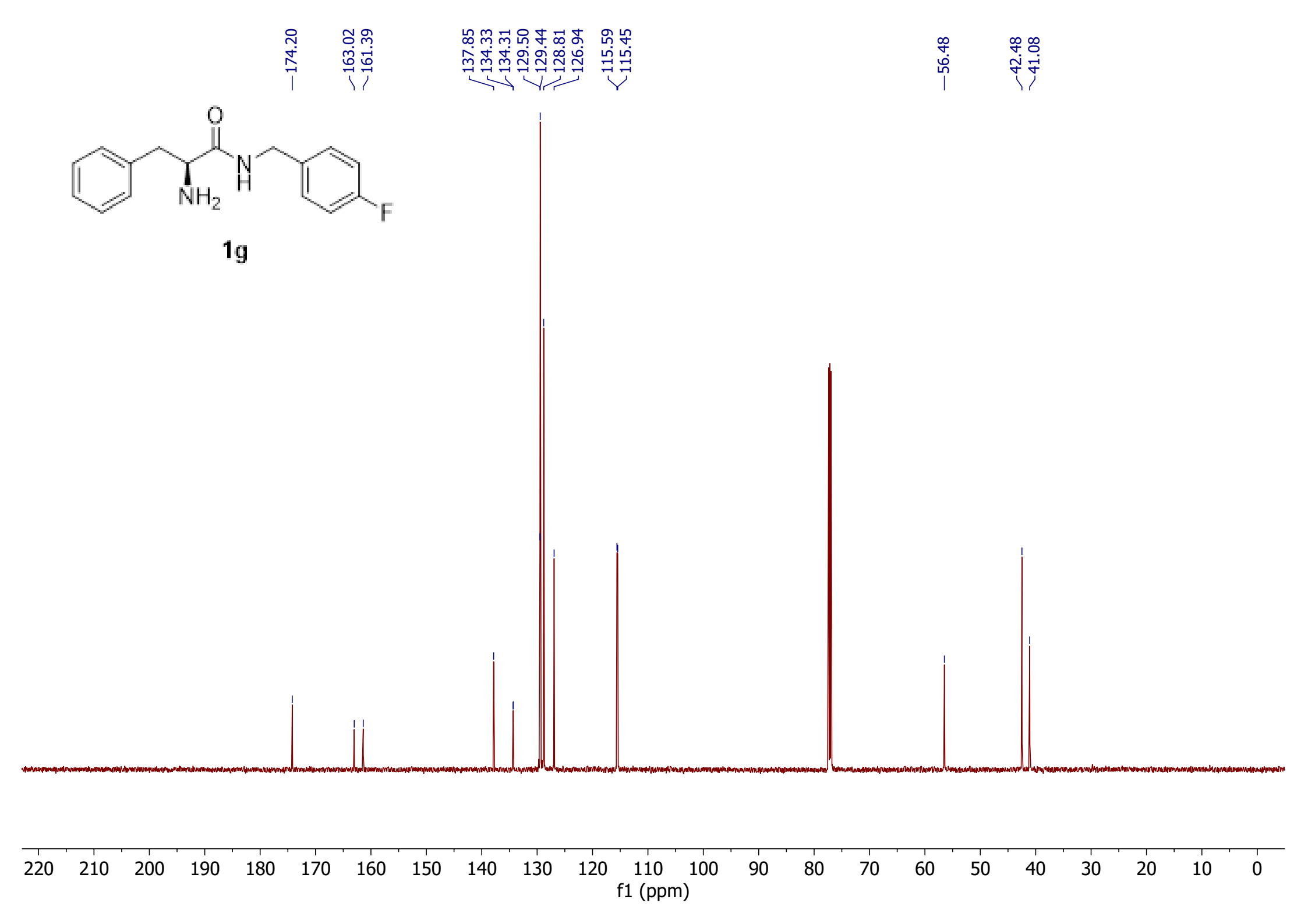
3.2
3.1
3.0
2.9
2.8
f1 (ppm)
1.01
9.44
2.04
1.00
1.02
1.04
3.26
2.05
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
N
H
NH2
Me

1f

173.97
137.90
137.02
135.39
129.38
129.31
128.71
127.75
126.81
56.48
42.94
41.05
21.10
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.60
7.29
7.27
7.23
7.20
7.20
7.18
7.17
7.16
6.99
6.97
4.39
4.38
4.38
4.37
3.64
3.63
3.27
3.26
3.24
3.24
2.75
2.75
1.42
O
N
H
NH2
F
1g
3.27
3.26
3.24
3.24
2.75
2.75
3.3
3.2
3.1
3.0
2.9
2.8
2.7
f1 (ppm)
0.99
7.21
2.00
2.00
1.00
1.00
1.01
2.23
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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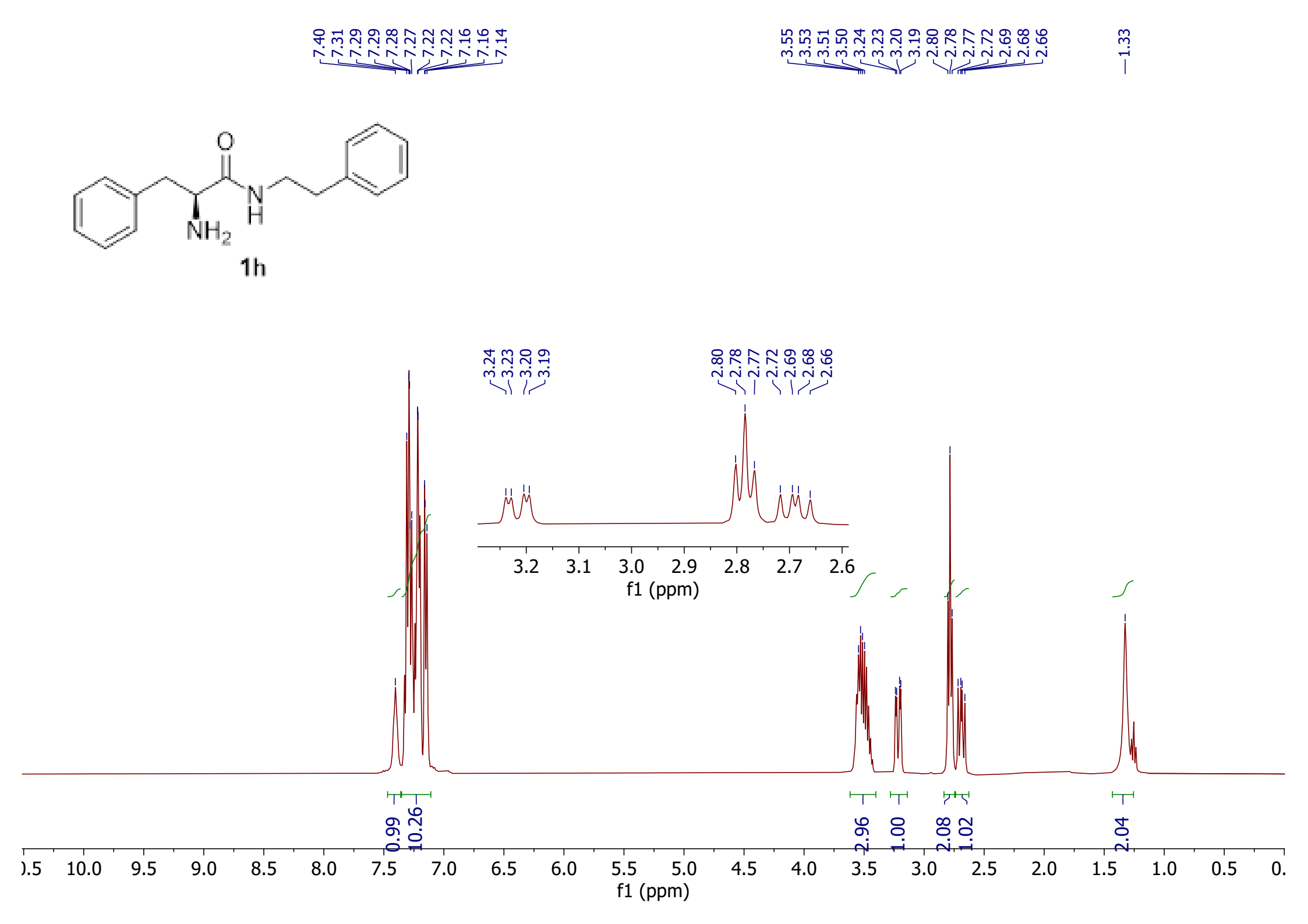
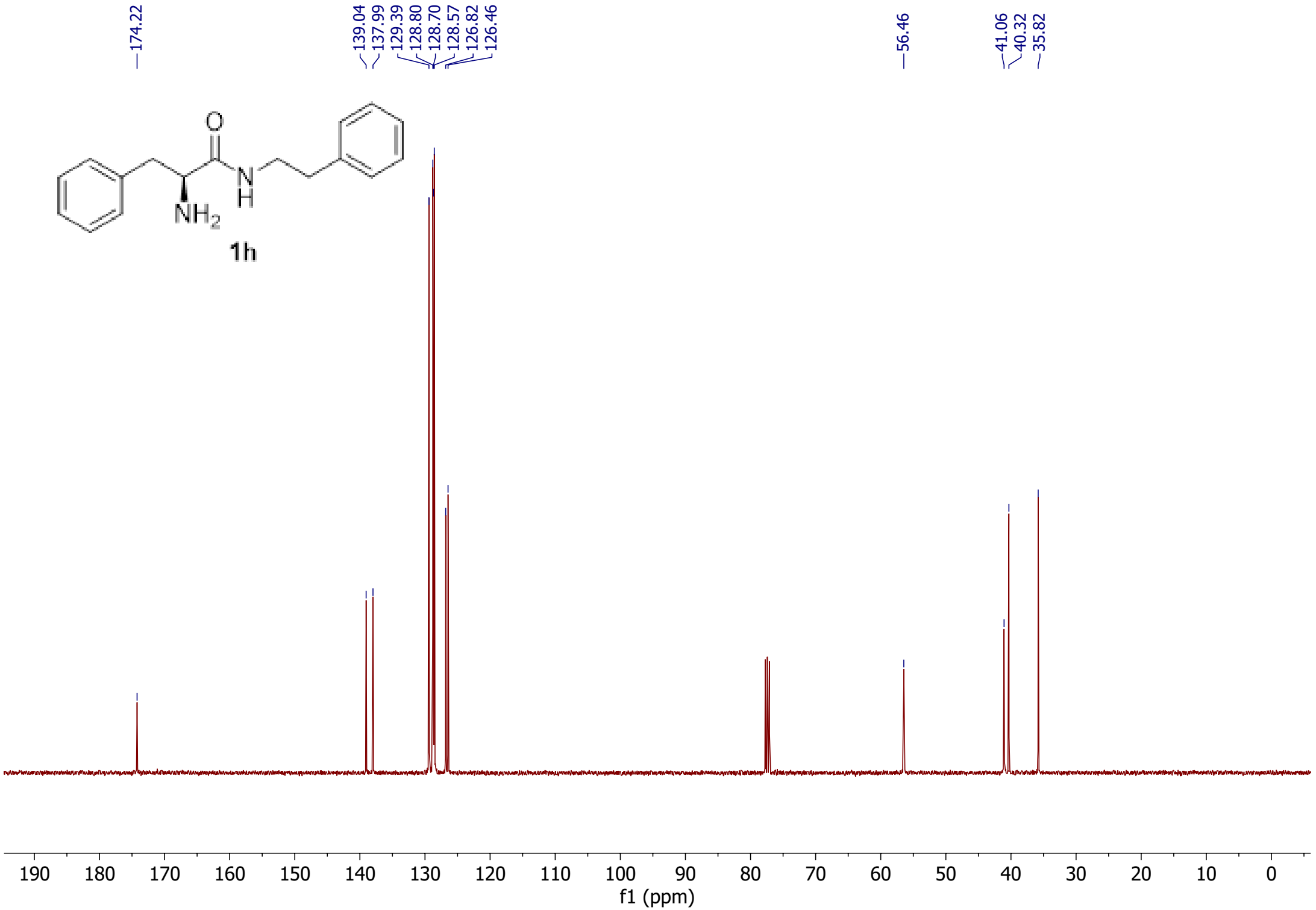
163.02
161.39
137.85
134.33
134.31
129.50
129.44
128.81
126.94
115.59
115.45
56.48
42.48
41.08
O
N
H
NH2
F
1g
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.40
7.31
7.29
7.29
7.28
7.27
7.22
7.22
7.16
7.16
7.14
3.55
3.53
3.51
3.50
3.24
3.23
3.20
3.19
2.80
2.78
2.77
2.72
2.69
2.68
2.66
1.33
O
N
H
NH2
1h
3.24
3.23
3.20
3.19
2.80
2.78
2.77
2.72
2.69
2.68
2.66
3.2
3.1
3.0
2.9
2.8
2.7
2.6
f1 (ppm)
0.99
10.26
2.96
1.00
2.08
1.02
2.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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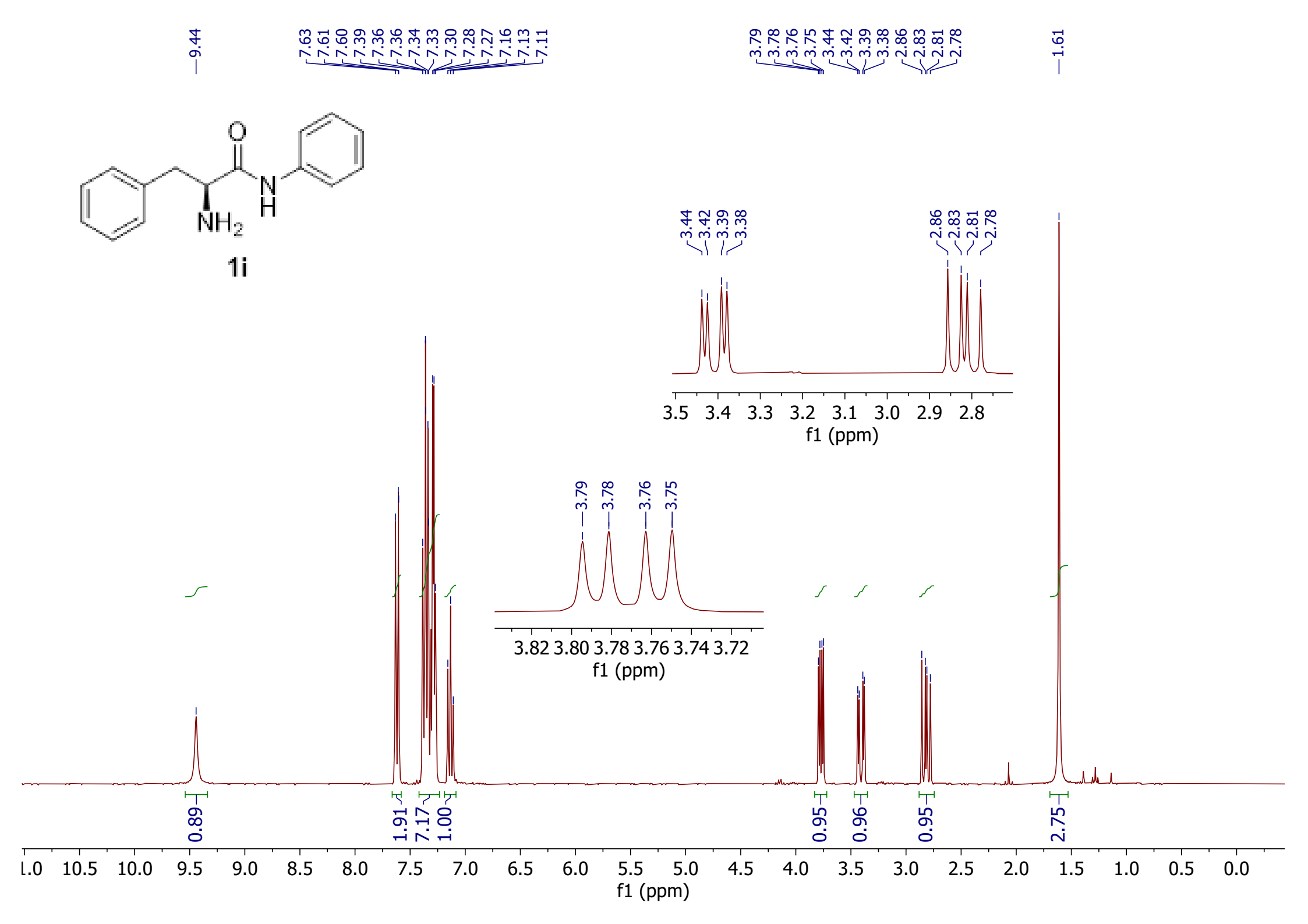
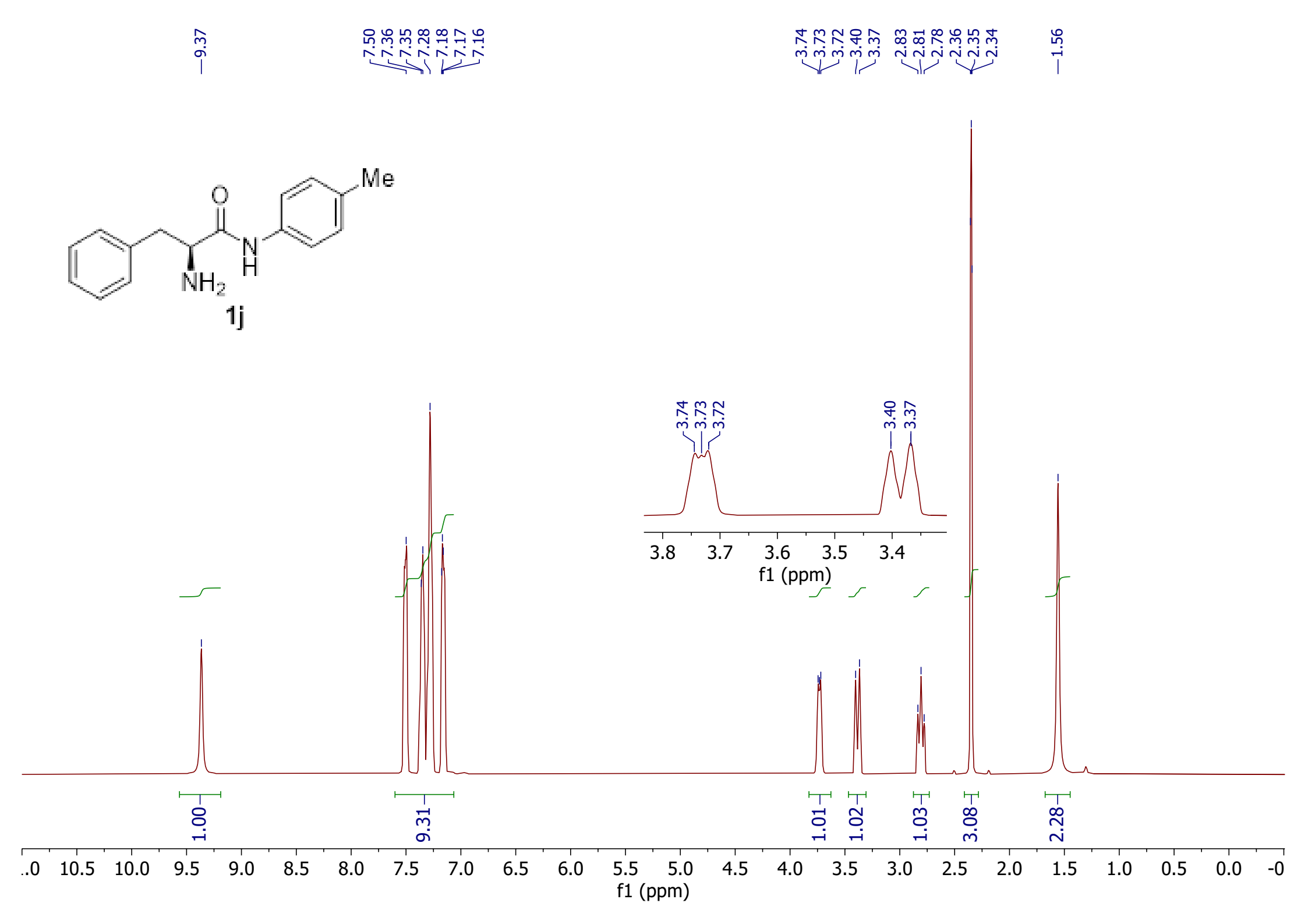
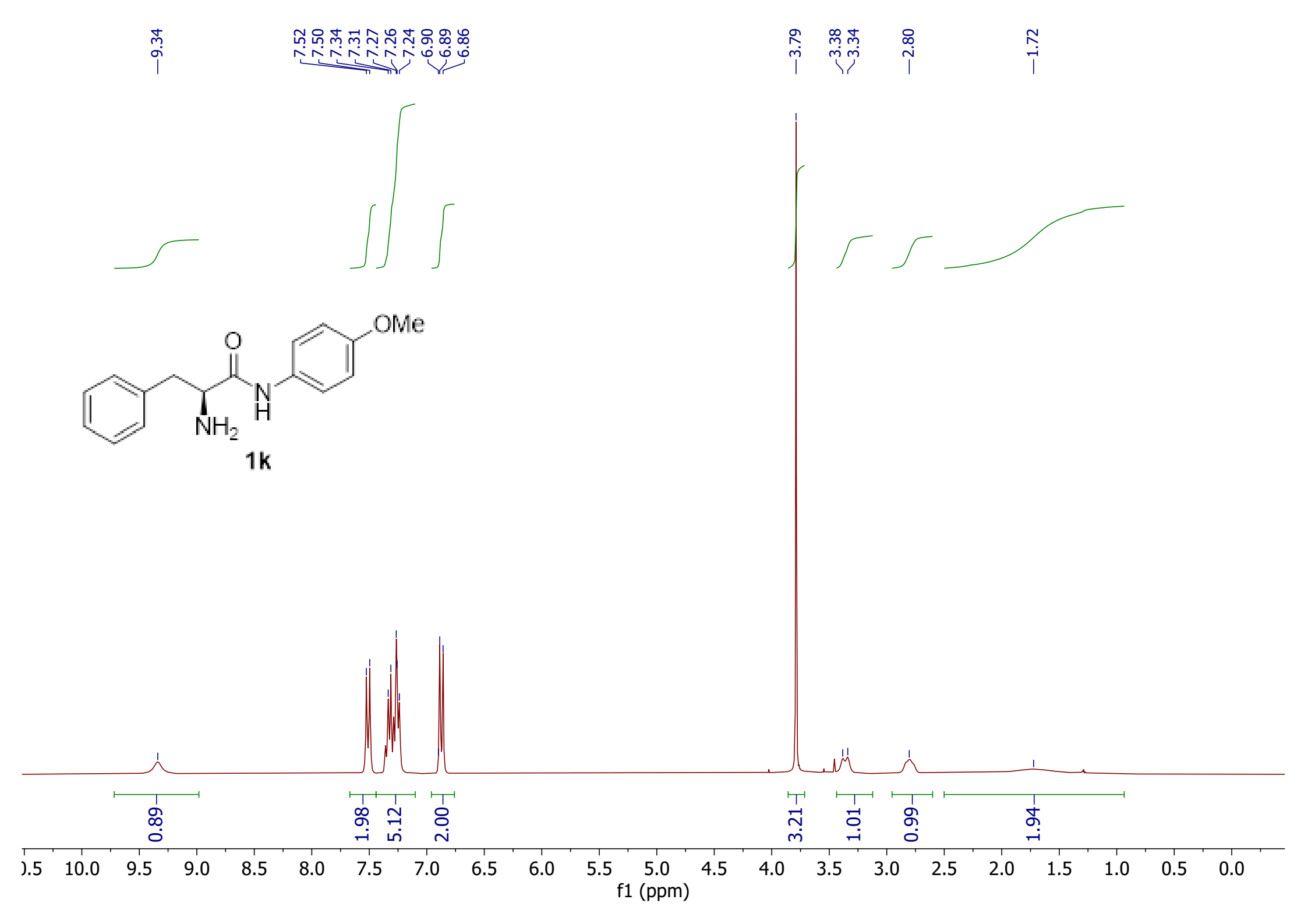
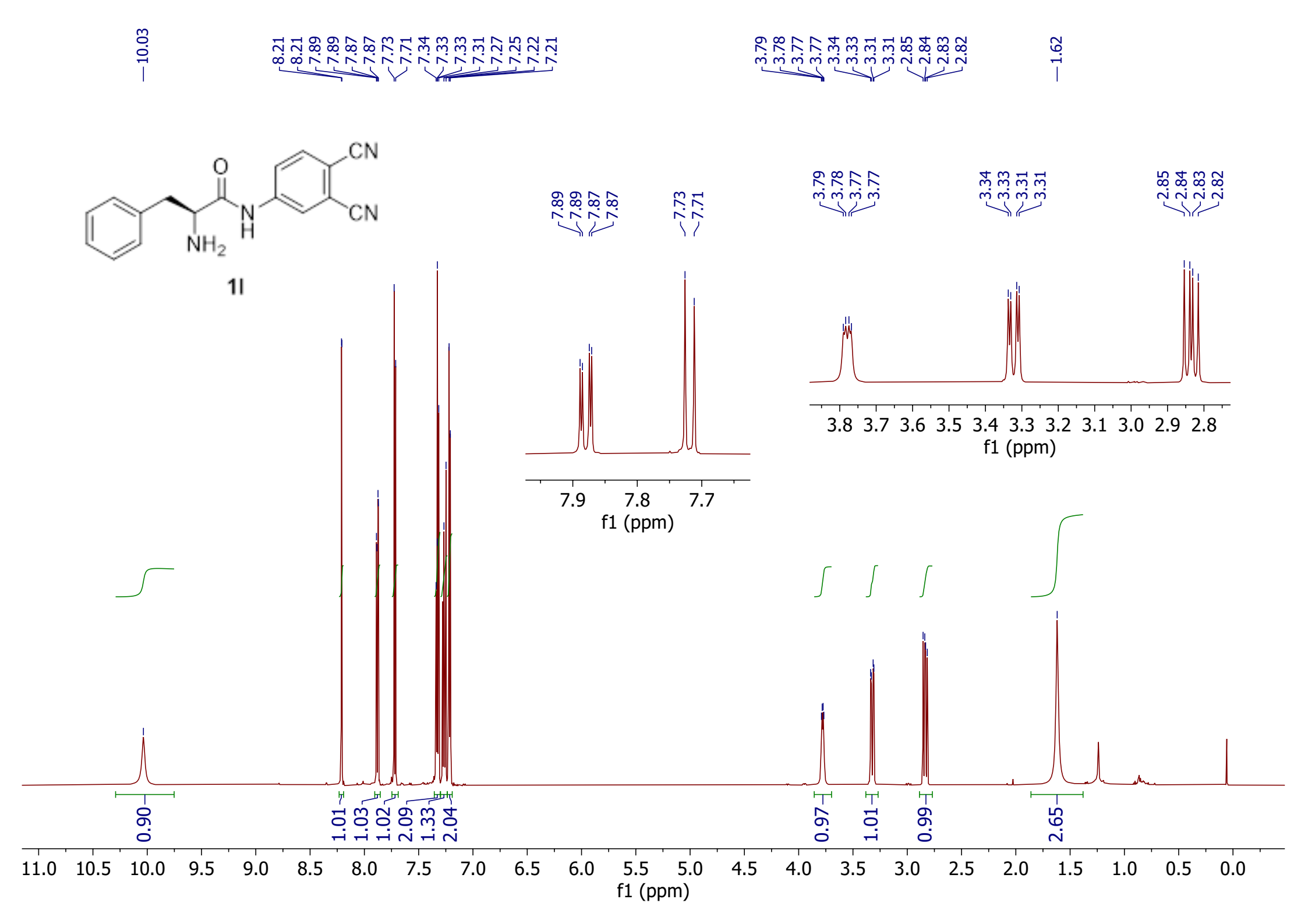
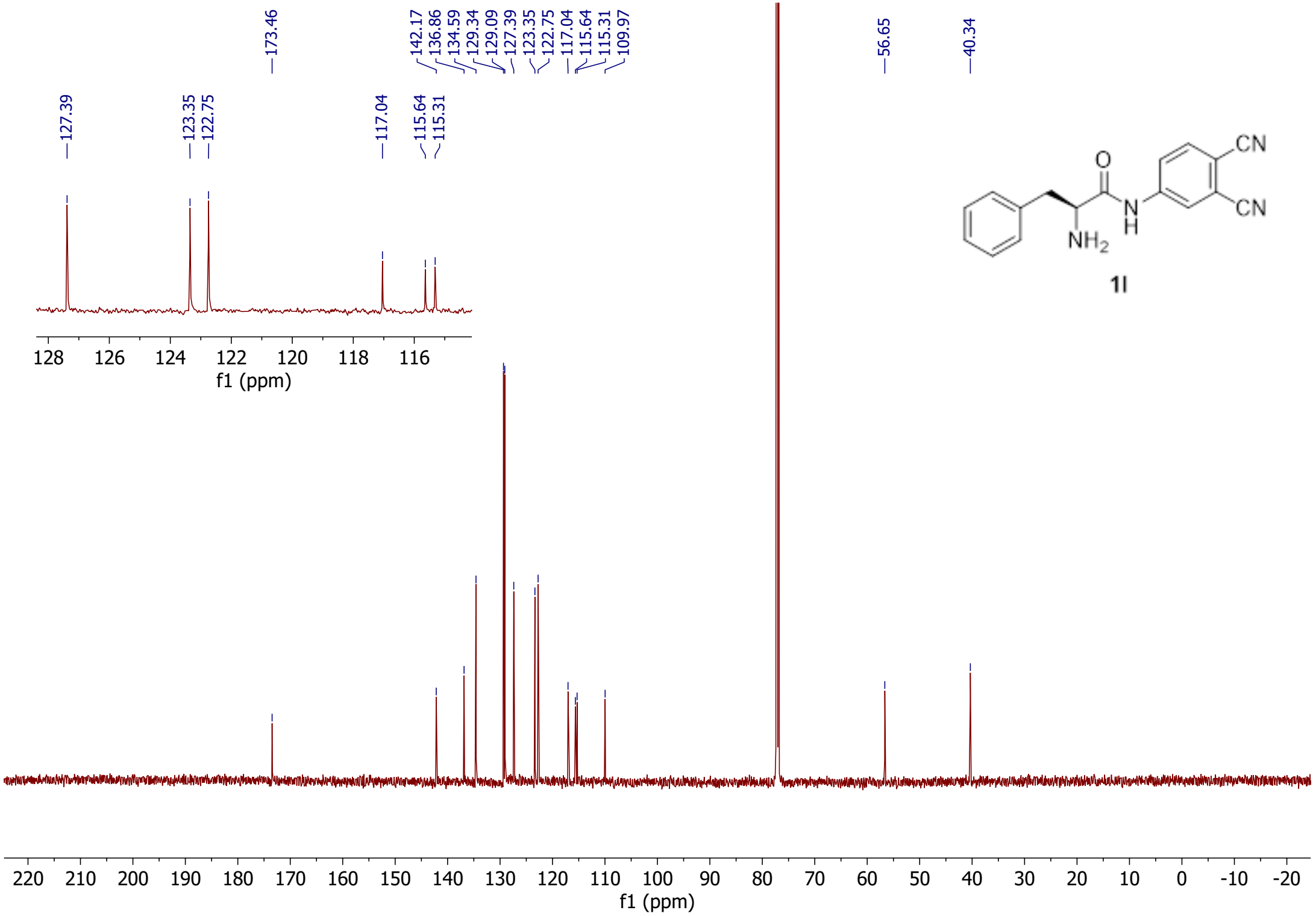
139.04
137.99
129.39
128.80
128.70
128.57
126.82
126.46
56.46
41.06
40.32
35.82
O
N
H
NH2
1h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

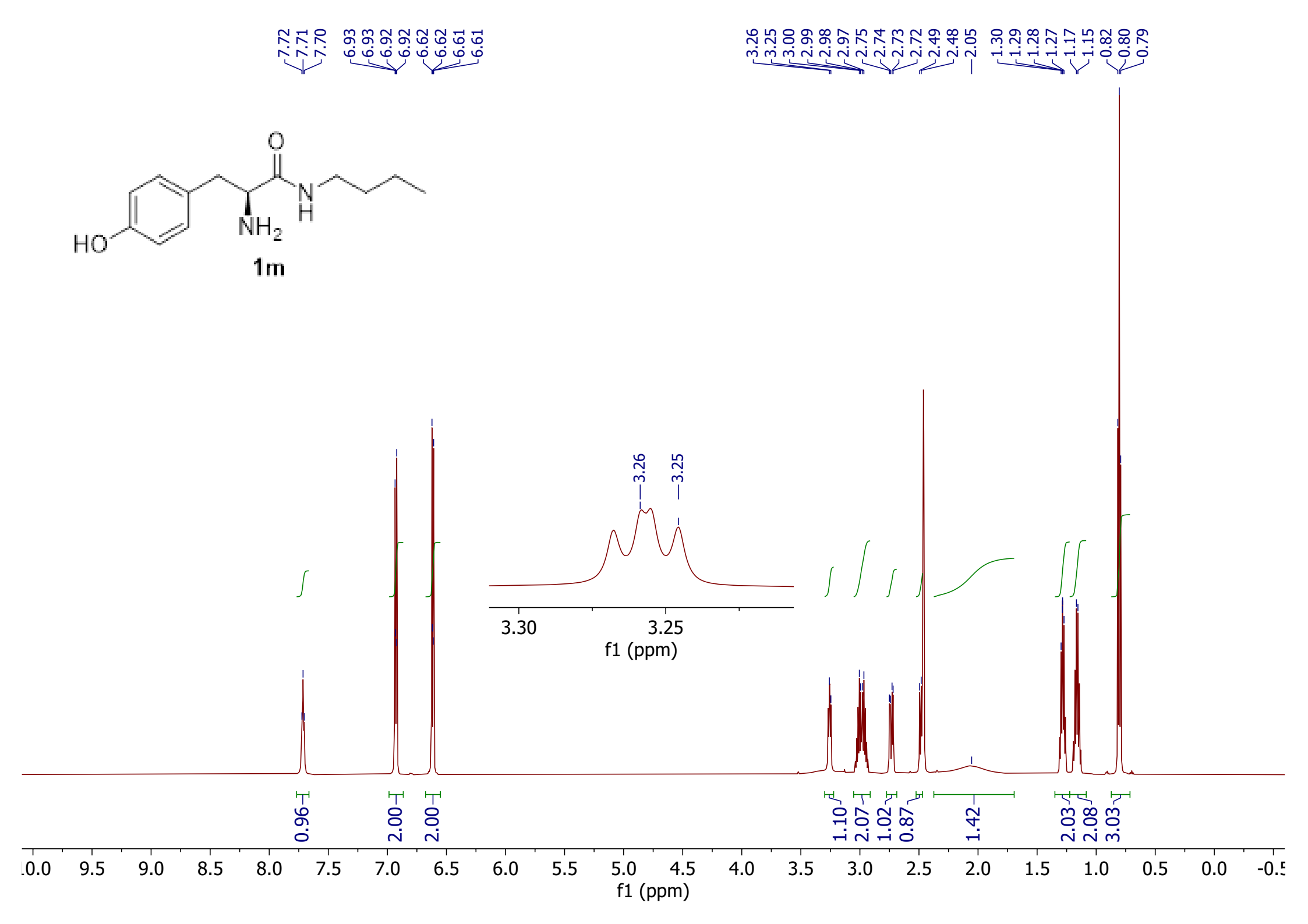

9.44
7.63
7.61
7.60
7.39
7.36
7.36
7.34
7.33
7.30
7.28
7.27
7.16
7.13
7.11
3.79
3.78
3.76
3.75
3.44
3.42
3.39
3.38
2.86
2.83
2.81
2.78
1.61
O
N
H
NH2
1i
3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)
3.82 3.80 3.78 3.76 3.74 3.72
f1 (ppm)
0.89
1.91
7.17
1.00
0.95
0.96
0.95
2.75
f1 (ppm)

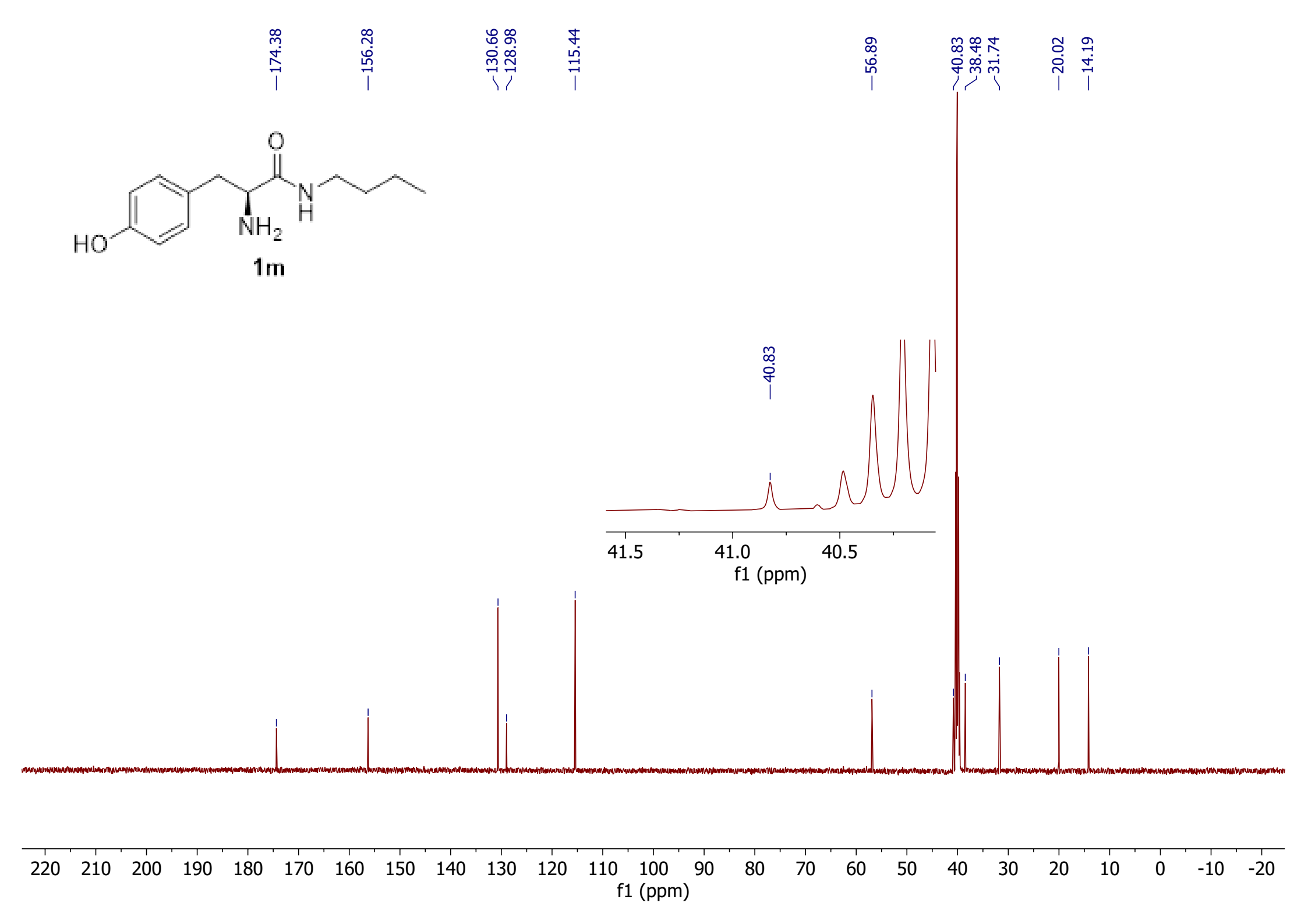

9.37
7.50
7.36
7.35
7.28
7.18
7.17
7.16
3.74
3.73
3.72
3.40
3.37
2.83
2.81
2.78
2.36
2.35
2.34
1.56
Me
O
N
H
NH2
1j
3.74
3.73
3.72
3.40
3.37
3.8
3.7
3.6
3.5
3.4
f1 (ppm)
1.00
9.31
1.01
1.02
1.03
3.08
2.28
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

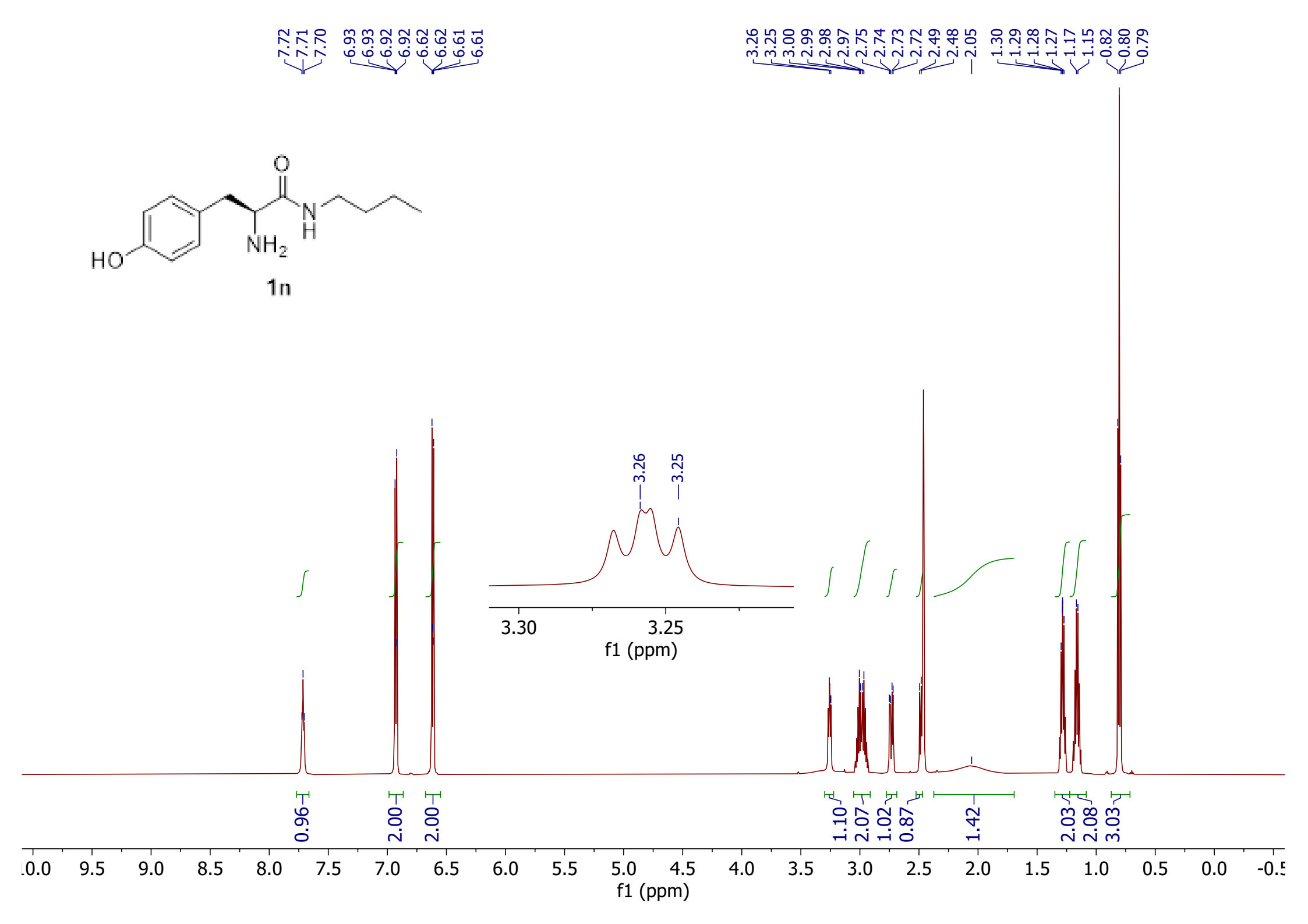

9.34
7.52
7.50
7.34
7.31
7.27
7.26
7.24
6.90
6.89
6.86
3.79
3.38
3.34
2.80
1.72
OMe
O
N
H
NH2
1k
0.89
1.98
5.12
2.00
3.21
1.01
0.99
1.94
f1 (ppm)

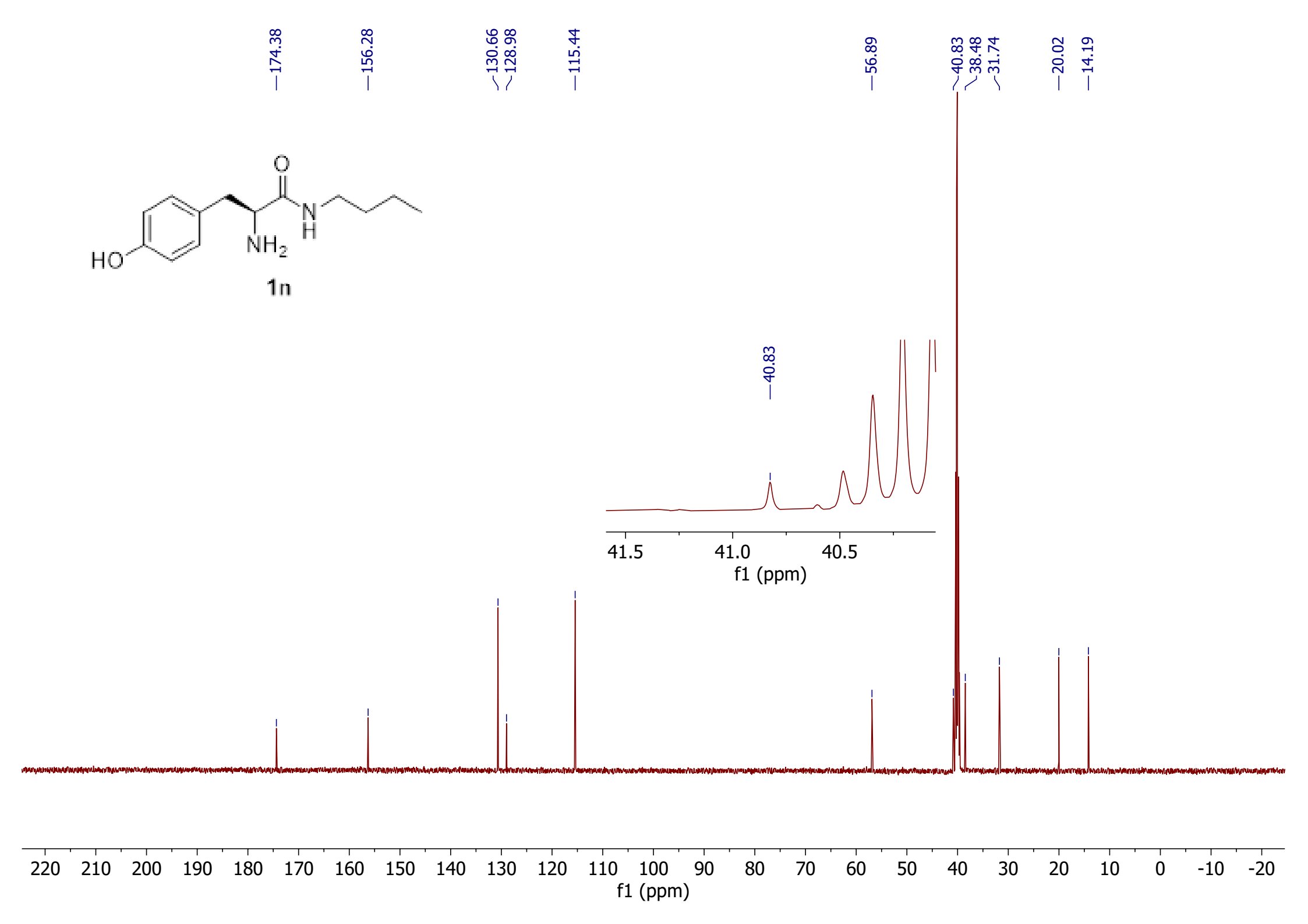

10.03
8.21
8.21
7.89
7.89
7.87
7.87
7.73
7.71
7.34
7.33
7.33
7.31
7.27
7.25
7.22
7.21
3.79
3.78
3.77
3.77
3.34
3.33
3.31
3.31
2.85
2.84
2.83
2.82
1.62
O
N
H
NH2
CN
CN
1l
f1 (ppm)
f1 (ppm)
f1 (ppm)
0.90
1.01
1.03
1.02
2.09
1.33
2.04
0.97
1.01
0.99
2.65


173.46
142.17
136.86
134.59
129.34
129.09
127.39
123.35
122.75
117.04
115.64
115.31
109.97
56.65
40.34
127.39
123.35
122.75
117.04
115.64
115.31
128
126
124
122
120
118
116
f1 (ppm)
O
N
H
NH2
CN
CN
1l
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


7.72
7.71
7.70
6.93
6.93
6.92
6.92
6.62
6.62
6.61
6.61
3.26
3.25
3.00
2.99
2.98
2.97
2.75
2.74
2.73
2.72
2.49
2.48
2.05
1.30
1.29
1.28
1.27
1.17
1.15
0.82
0.80
0.79
O
N
H
NH2
HO
1m
3.26
3.25
3.30
3.25
f1 (ppm)
0.96
2.00
2.00
1.10
2.07
1.02
0.87
1.42
2.03
2.08
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


174.38
156.28
130.66
128.98
115.44
56.89
40.83
38.48
31.74
20.02
14.19
O
N
H
NH2
HO
1m
40.83
41.5
41.0
40.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


7.72
7.71
7.70
6.93
6.93
6.92
6.92
6.62
6.62
6.61
6.61
3.26
3.25
3.00
2.99
2.98
2.97
2.75
2.74
2.73
2.72
2.49
2.48
2.05
1.30
1.29
1.28
1.27
1.17
1.15
0.82
0.80
0.79
O
N
H
NH2
HO
1n
3.26
3.25
3.30
3.25
f1 (ppm)
0.96
2.00
2.00
1.10
2.07
1.02
0.87
1.42
2.03
2.08
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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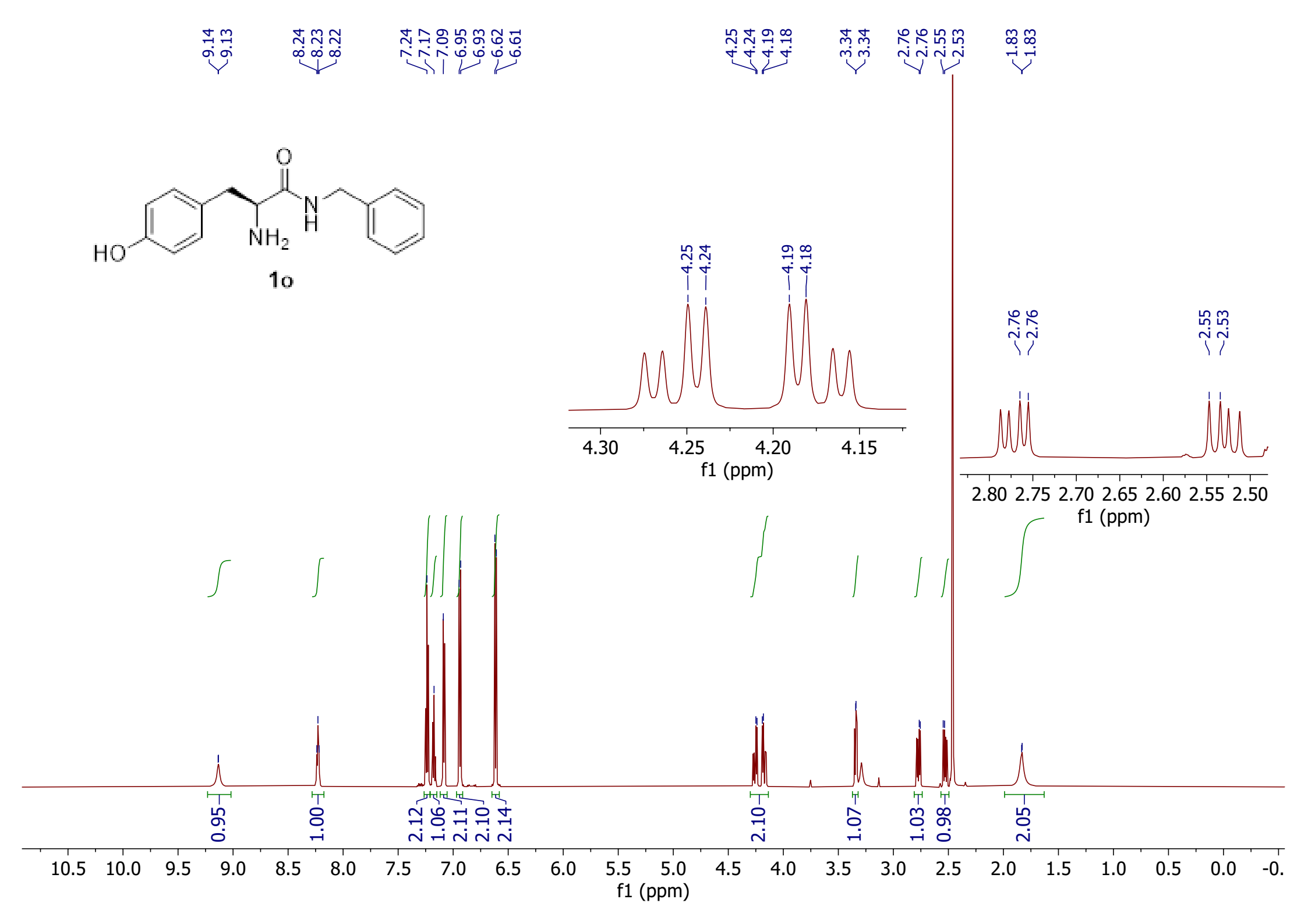
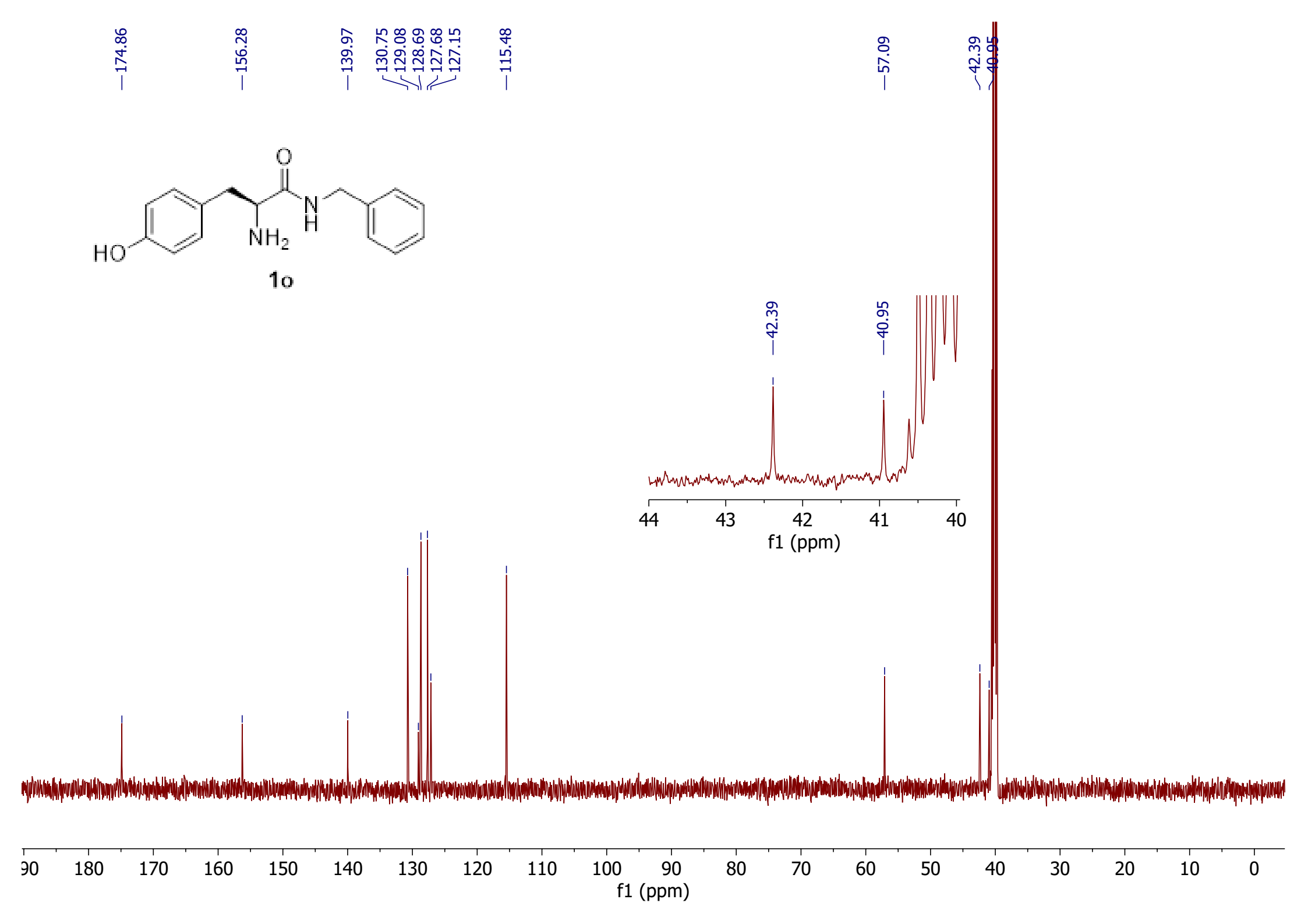
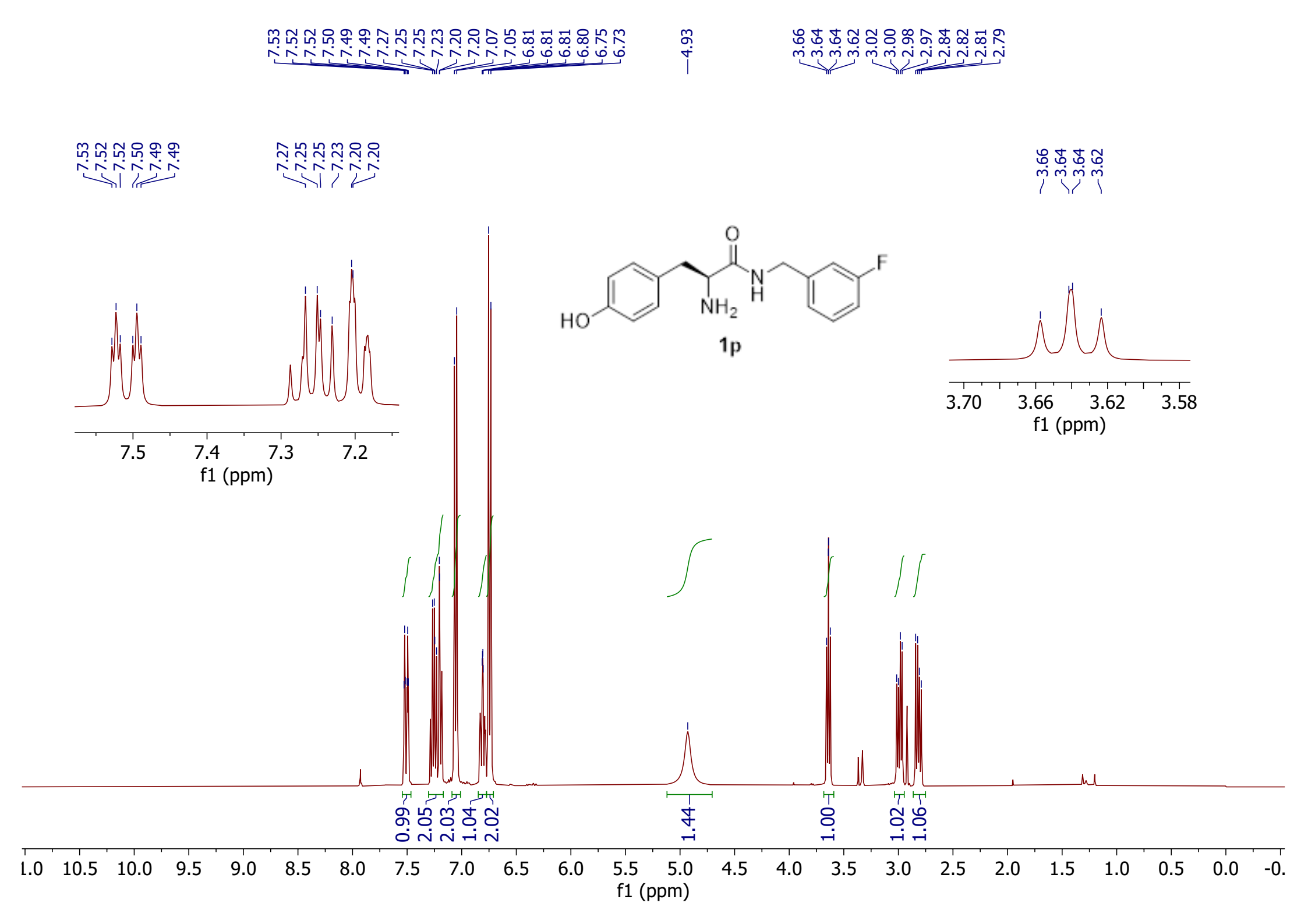
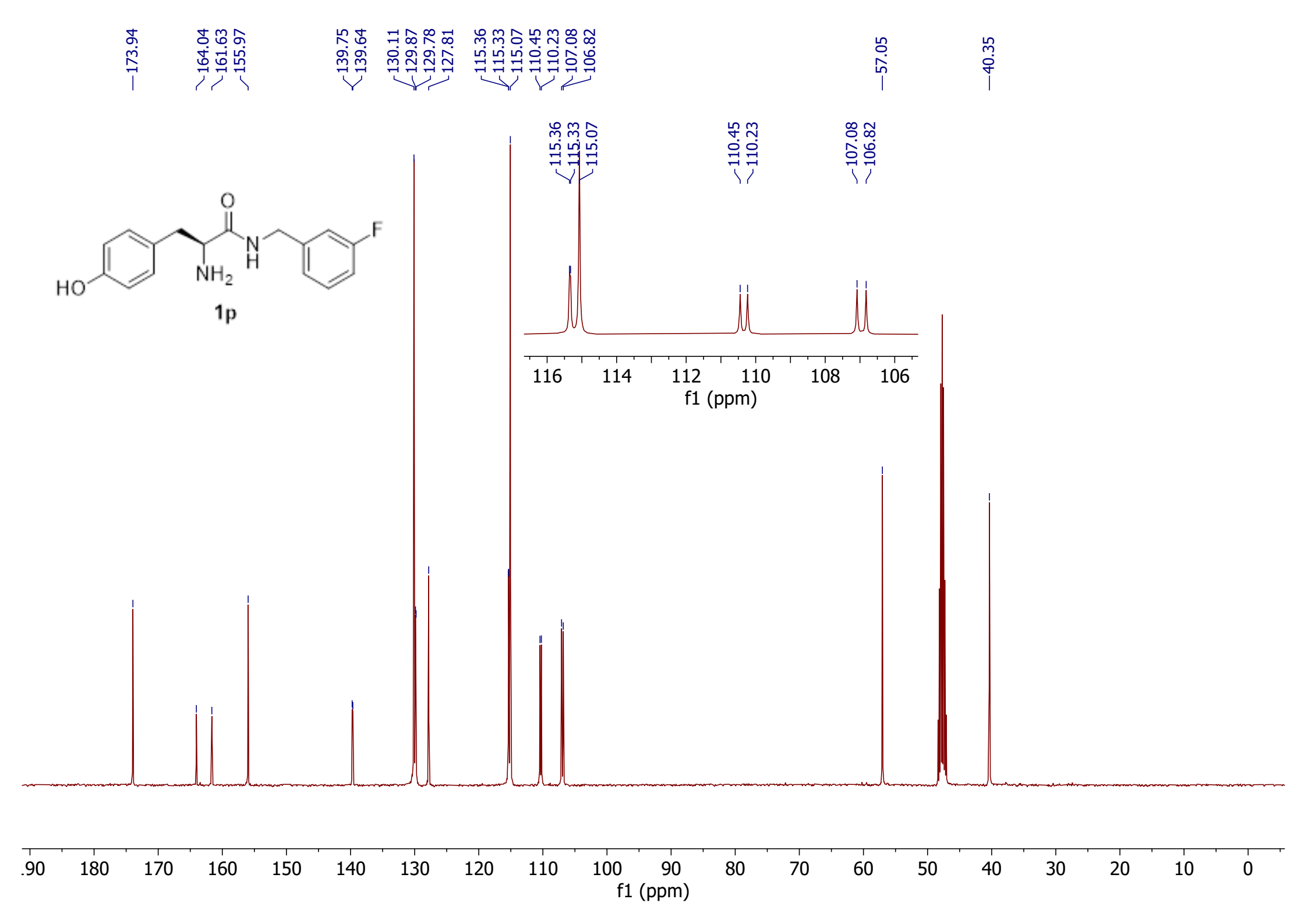
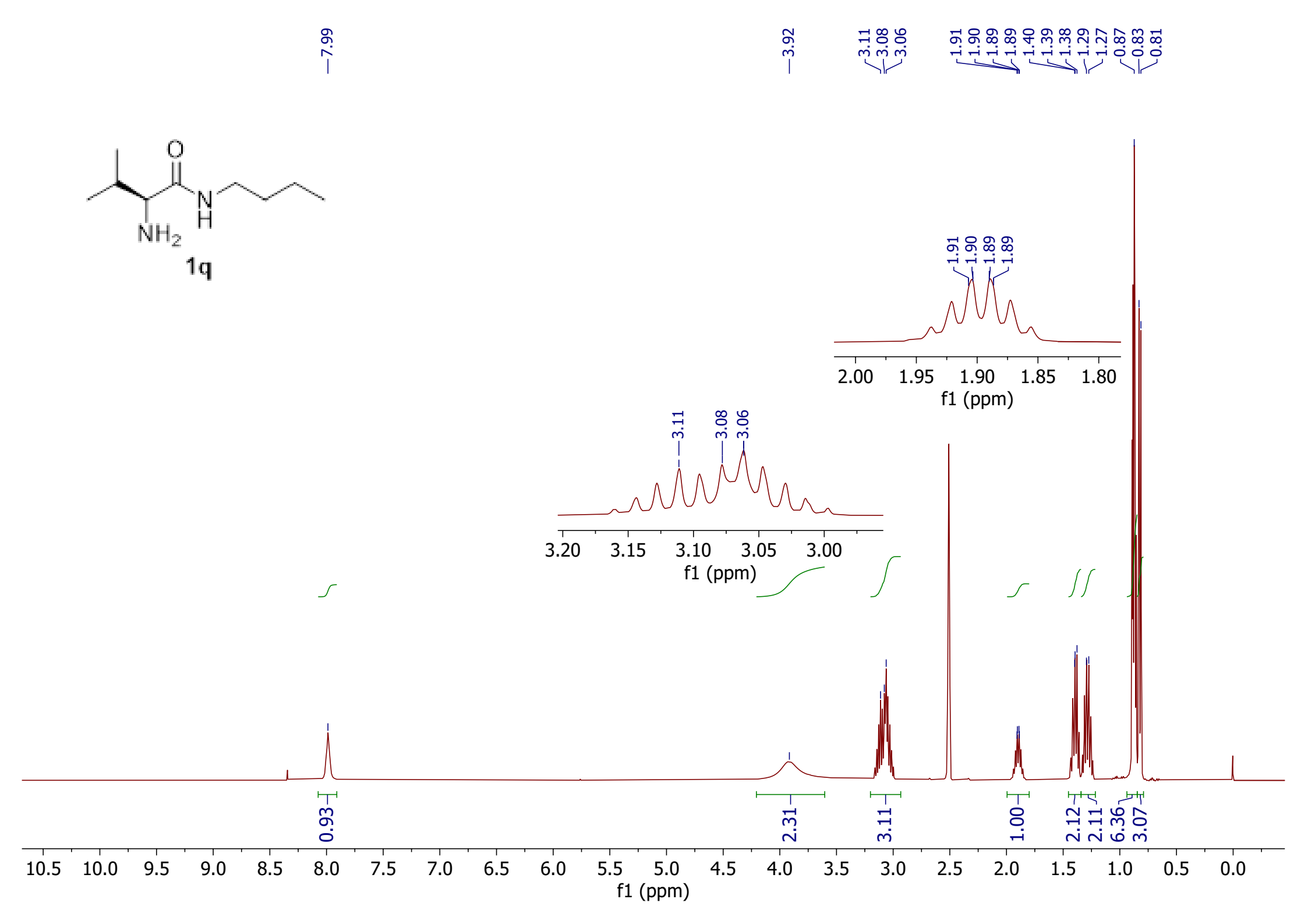
156.28
130.66
128.98
115.44
56.89
40.83
38.48
31.74
20.02
14.19
O
N
H
NH2
HO
1n
40.83
41.5
41.0
40.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

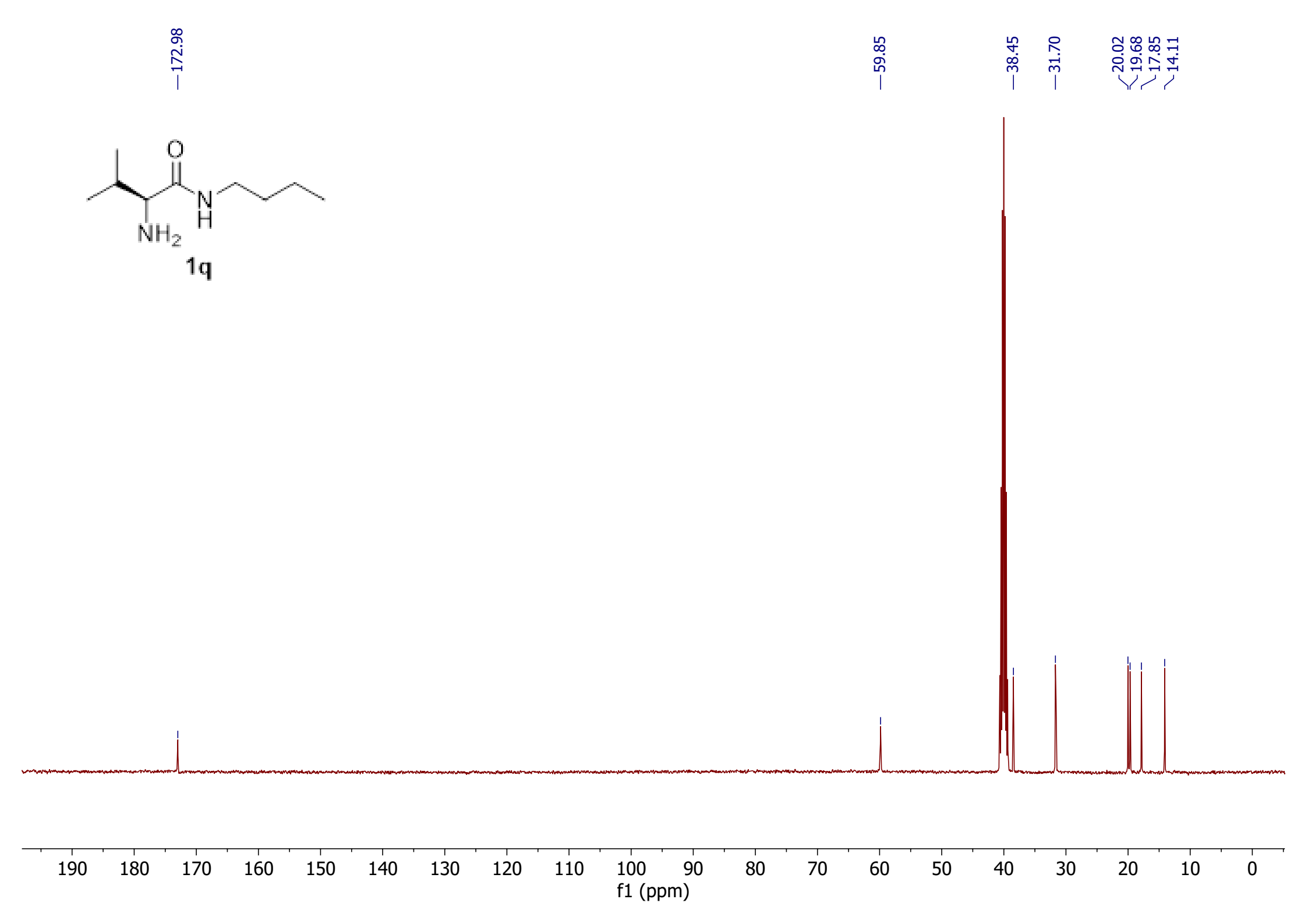

9.14
9.13
8.24
8.23
8.22
7.24
7.17
7.09
6.95
6.93
6.62
6.61
4.25
4.24
4.19
4.18
3.34
3.34
2.76
2.76
2.55
2.53
1.83
1.83
O
N
H
NH2
HO
1o
4.25
4.24
4.19
4.18
4.30
4.25
4.20
4.15
f1 (ppm)
2.76
2.76
2.55
2.53
2.80 2.75 2.70 2.65 2.60 2.55 2.50
f1 (ppm)
0.95
1.00
2.12
1.06
2.11
2.10
2.14
2.10
1.07
1.03
0.98
2.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

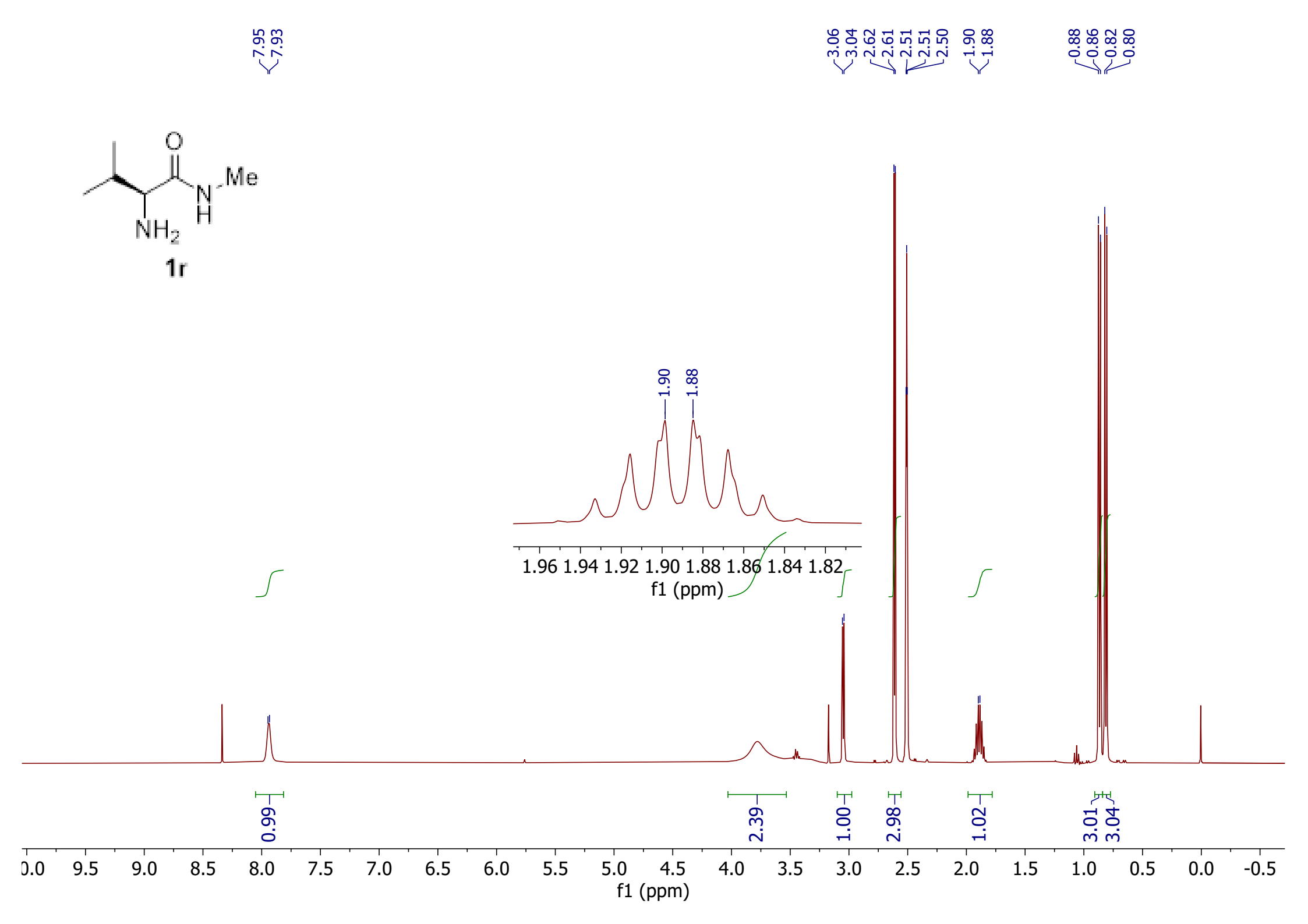

174.86
156.28
139.97
130.75
129.08
128.69
127.68
127.15
115.48
57.09
42.39
40.95
HO
NH2
O
N
H
1o
42.39
40.95
44
43
42
41
40
f1 (ppm)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

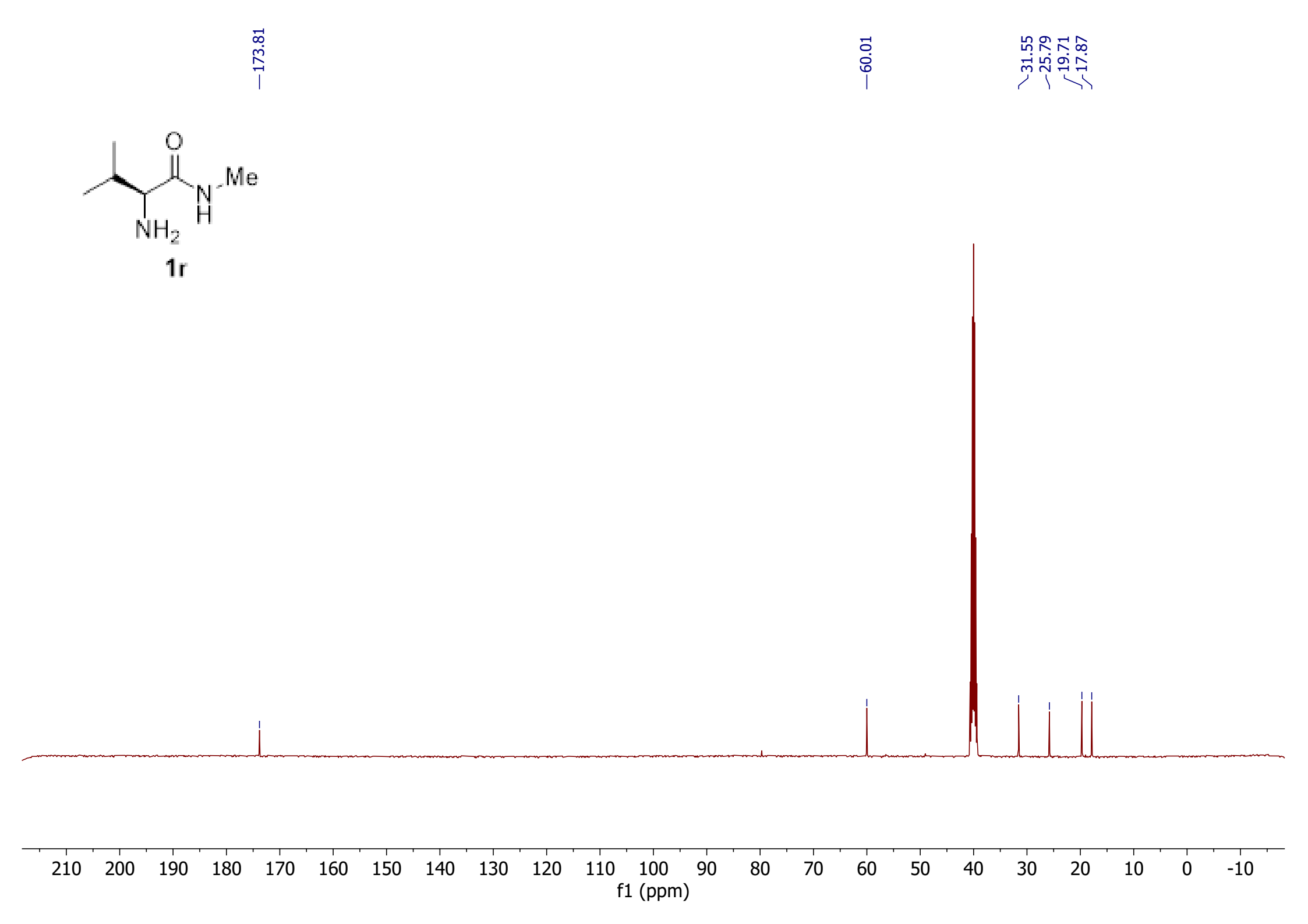

7.53 7.52 7.52 7.50 7.49 7.49 7.27 7.25 7.25 7.23 7.20 7.20 7.07 7.05 6.81 6.81 6.81 6.80 6.75 6.73
4.93
3.66 3.64 3.64 3.62 3.02 3.00 2.98 2.97 2.84 2.82 2.81 2.79
7.53 7.52 7.52 7.50 7.49 7.49
7.27 7.25 7.25 7.23 7.20 7.20
3.66 3.64 3.64 3.62
HO
NH2
O
N
H
F
1p
7.5 7.4 7.3 7.2
f1 (ppm)
3.70 3.66 3.62 3.58
f1 (ppm)
0.99 2.05 2.03 1.04 2.02
1.44
1.00
1.02 1.06
f1 (ppm)

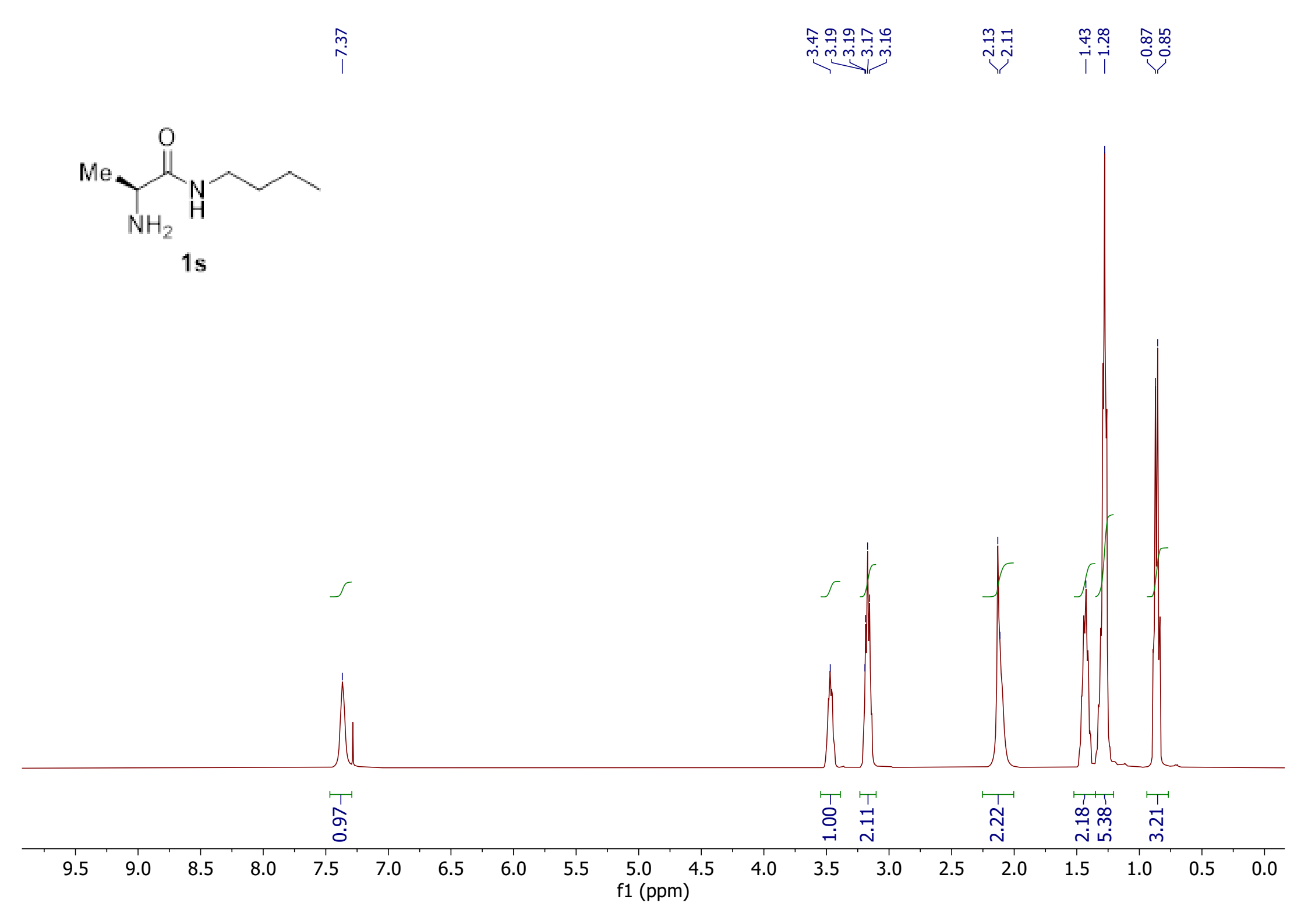

173.94
164.04
161.63
155.97
139.75
139.64
130.11
129.87
129.78
127.81
115.36
115.33
115.07
110.45
110.23
107.08
106.82
57.05
40.35
O
N
H
NH2
HO
F
1p
f1 (ppm)
f1 (ppm)

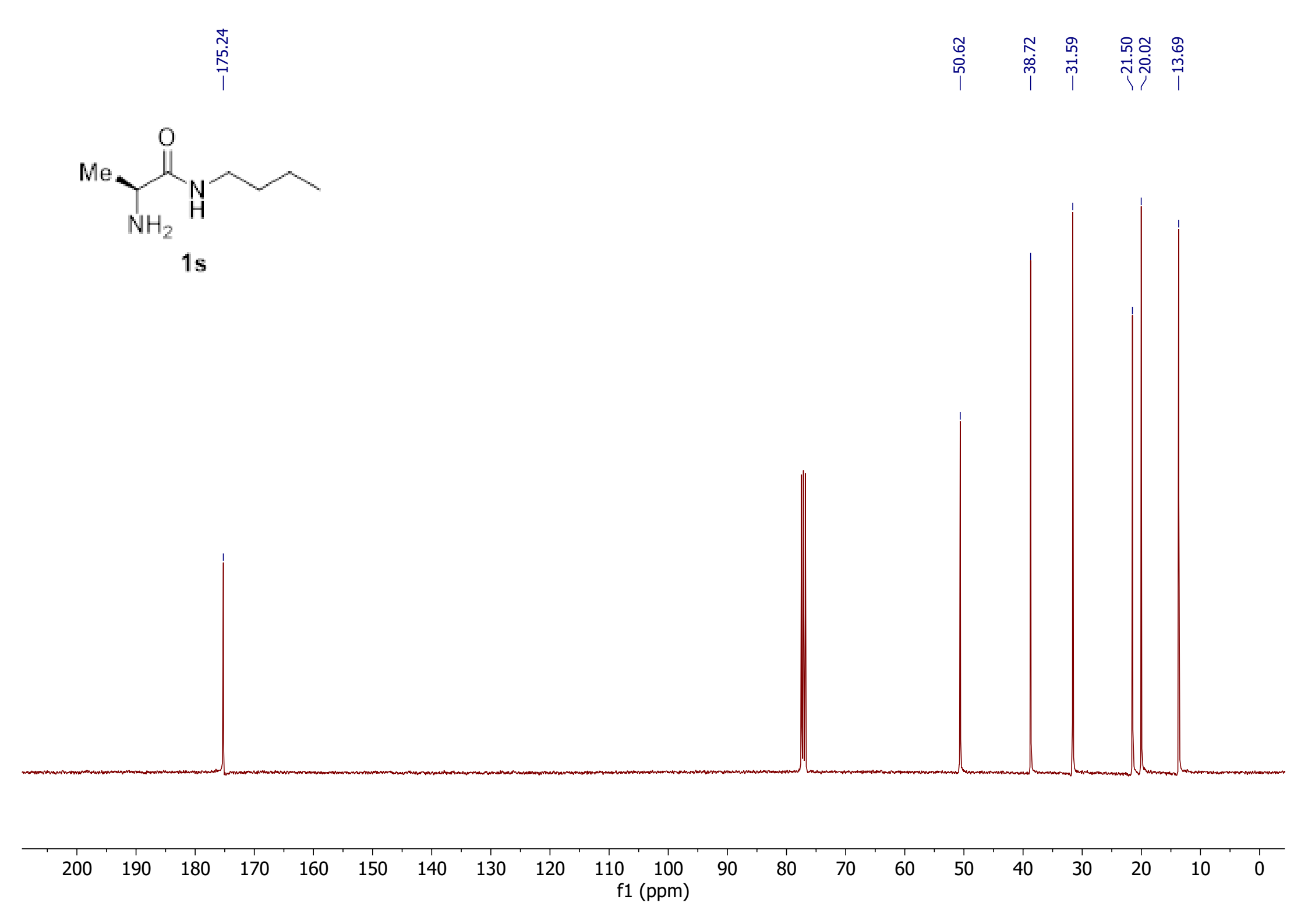

7.99
3.92
3.11
3.08
3.06
1.91
1.90
1.89
1.89
1.40
1.39
1.38
1.29
1.27
0.87
0.83
0.81
O
N
H
NH2
1q
1.91
1.90
1.89
1.89
2.00
1.95
1.90
1.85
1.80
f1 (ppm)
3.11
3.08
3.06
3.20
3.15
3.10
3.05
3.00
f1 (ppm)
0.93
2.31
3.11
1.00
2.12
2.11
6.36
3.07
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

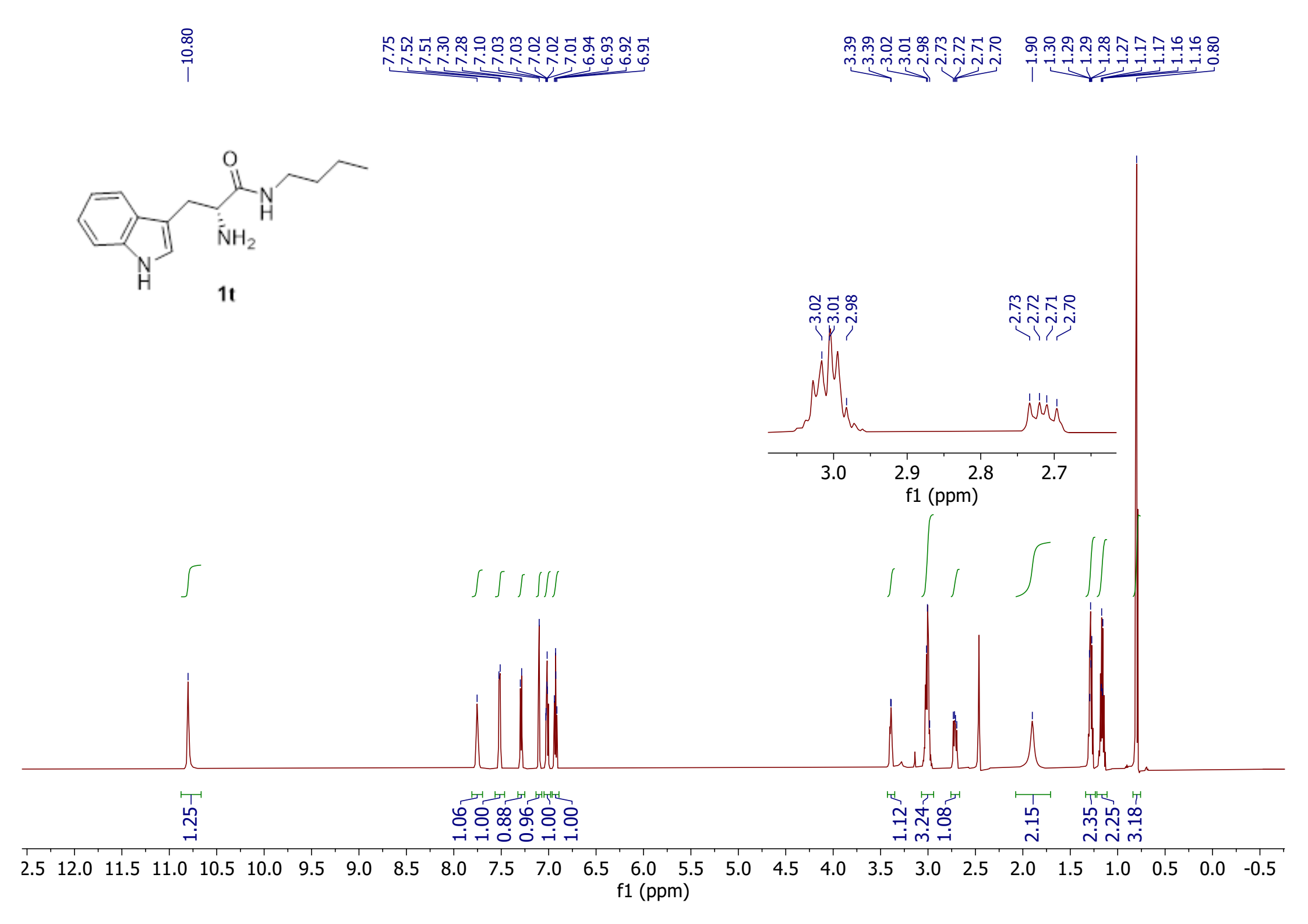

172.98
59.85
38.45
31.70
20.02
19.68
17.85
14.11
O
N
H
NH2
1q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

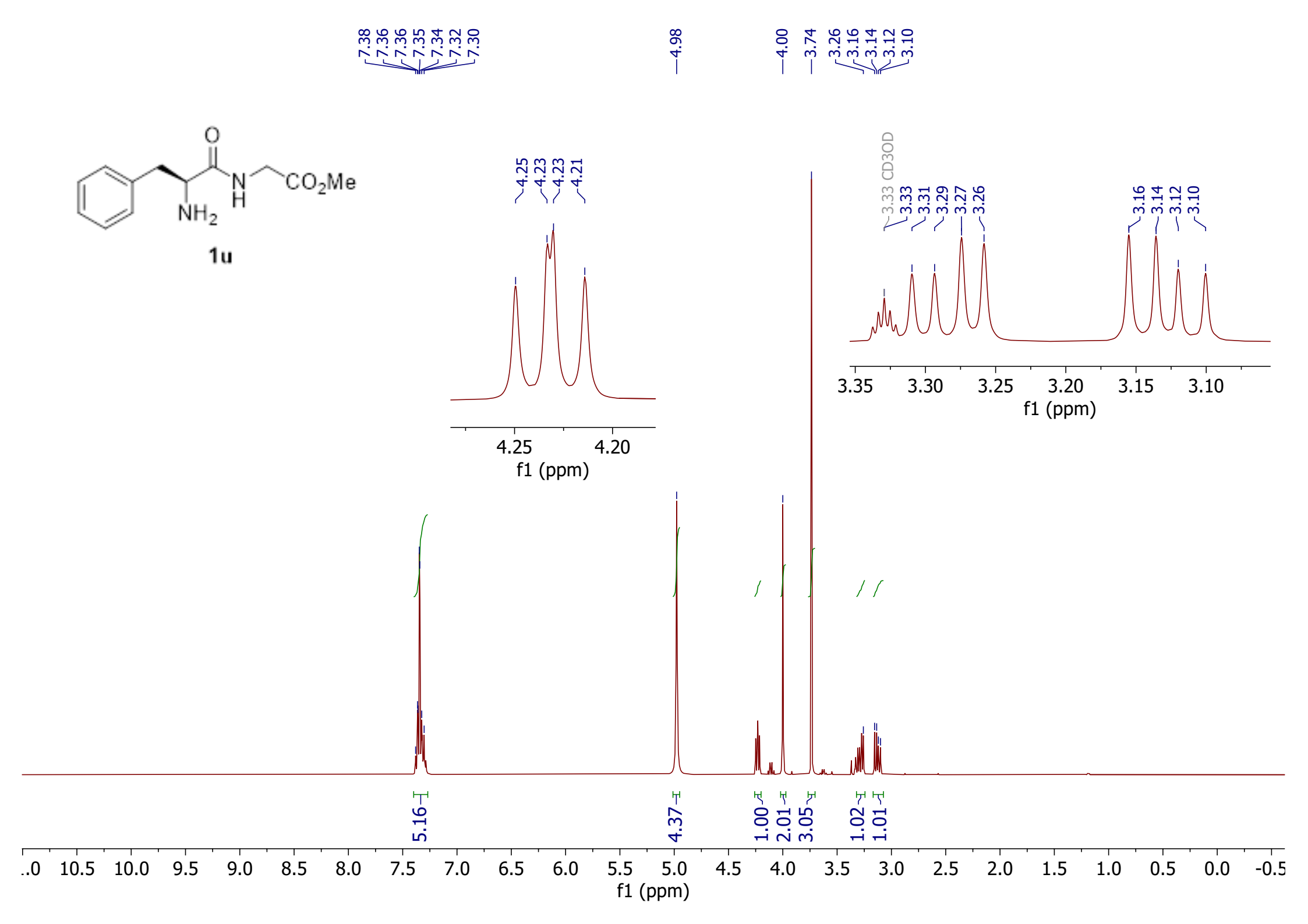

7.95
7.93
3.06
3.04
2.62
2.61
2.51
2.51
2.50
1.90
1.88
0.88
0.86
0.82
0.80
O
Me
N
H
NH2
1r
1.90
1.88
1.96 1.94 1.92 1.90 1.88 1.86 1.84 1.82
f1 (ppm)
0.99
2.39
1.00
2.98
1.02
3.01
3.04
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

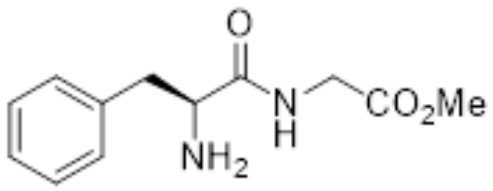

173.81
60.01
31.55
25.79
19.71
17.87
O
Me
N
H
NH2
1r
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.37
3.47
3.19
3.19
3.17
3.16
2.13
2.11
1.43
1.28
0.87
0.85
Me
O
N
H
NH2
1s
0.97
1.00
2.11
2.22
2.18
5.38
3.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


175.24
50.62
38.72
31.59
21.50
20.02
13.69
O
Me
N
H
NH2
1s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

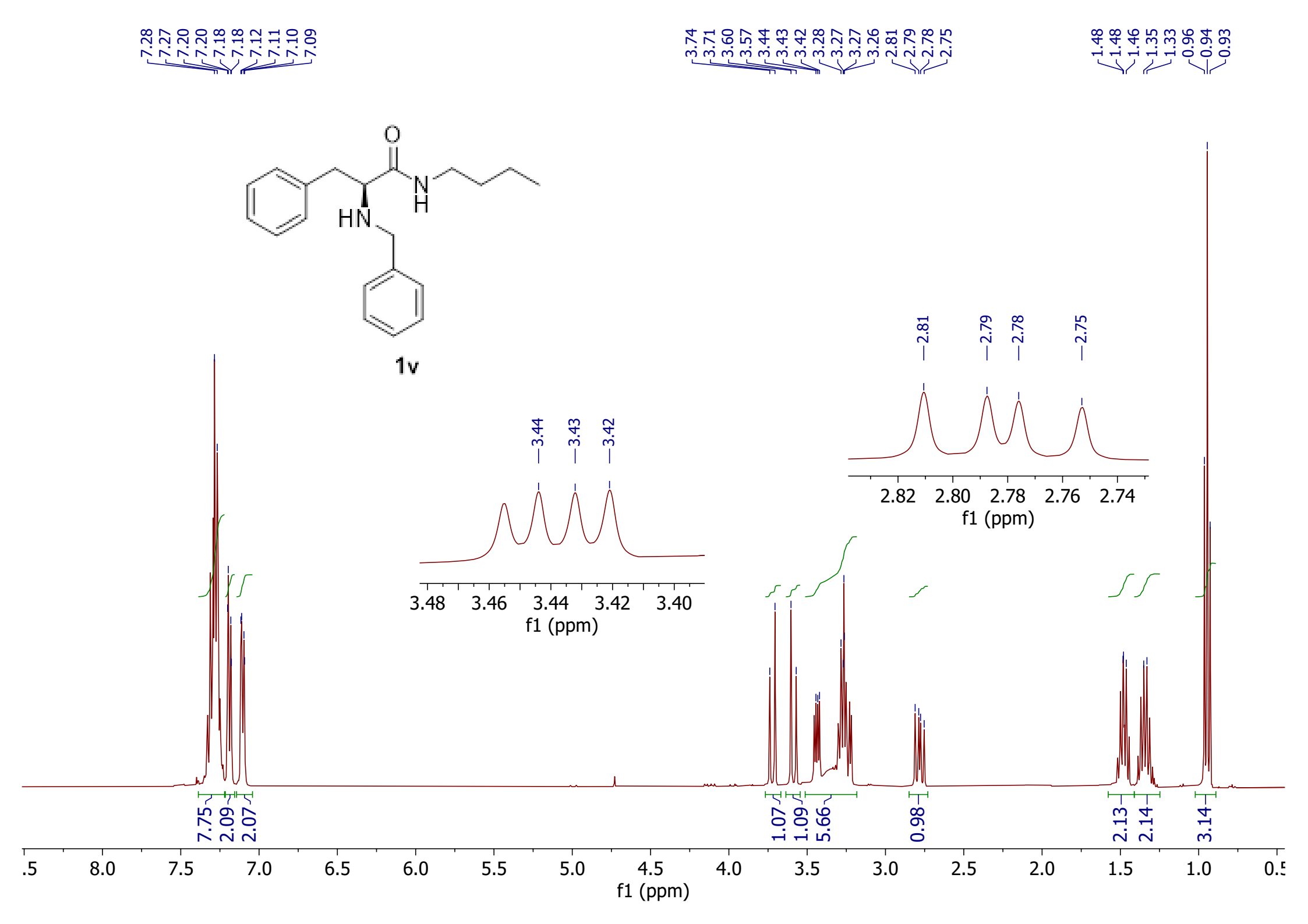

10.80
7.75
7.52
7.51
7.30
7.28
7.10
7.03
7.03
7.02
7.02
7.01
6.94
6.93
6.92
6.91
3.39
3.39
3.02
3.01
2.98
2.73
2.72
2.71
2.70
1.90
1.30
1.29
1.29
1.28
1.27
1.17
1.17
1.16
1.16
0.80
O
N
H
NH2
N
H
1t
3.02
3.01
2.98
2.73
2.72
2.71
2.70
3.0
2.9
2.8
2.7
f1 (ppm)
1.25
1.06
1.00
0.88
0.96
1.00
1.00
1.12
3.24
1.08
2.15
2.35
2.25
3.18
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

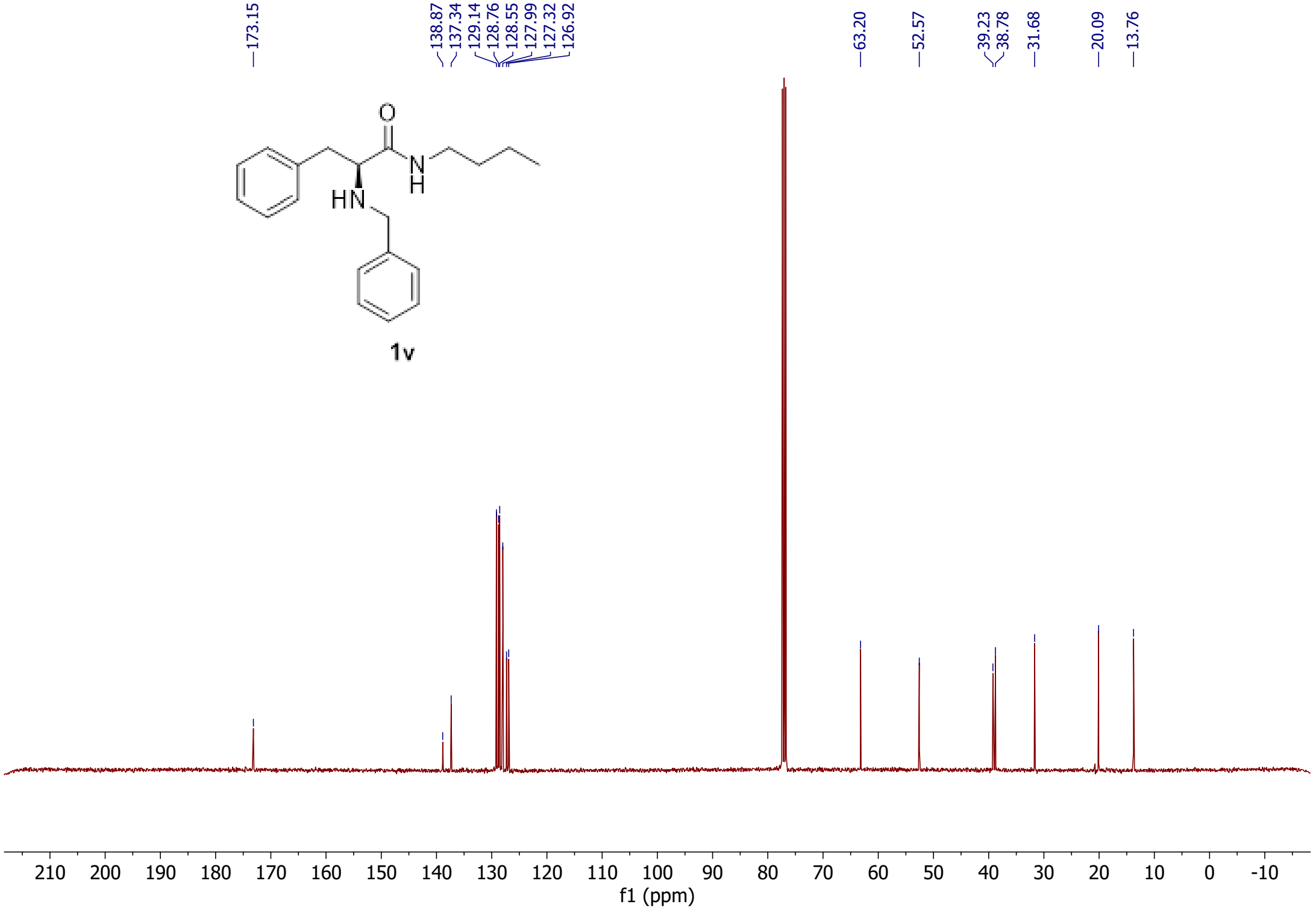

7.38
7.36
7.36
7.35
7.34
7.32
7.30
4.98
4.00
3.74
3.26
3.16
3.14
3.12
3.10
O
N
H
CO2Me
NH2
1u
4.25
4.23
4.23
4.21
4.25
4.20
f1 (ppm)
3.33 CD3OD
3.33
3.31
3.29
3.27
3.26
3.16
3.14
3.12
3.10
3.35
3.30
3.25
3.20
3.15
3.10
f1 (ppm)
5.16
4.37
1.00
2.01
3.05
1.02
1.01
f1 (ppm)

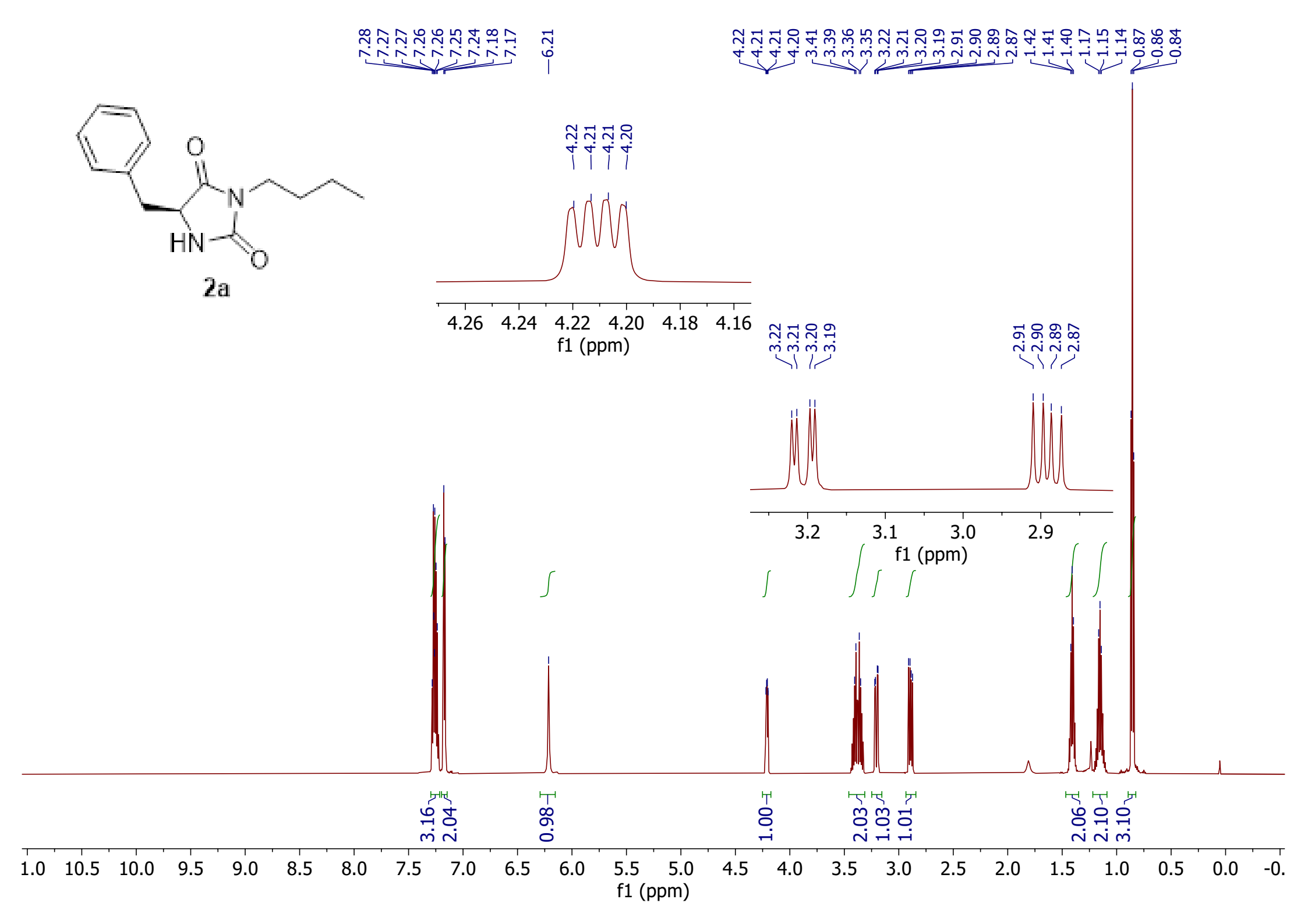

O
N
H
CO2Me
NH2

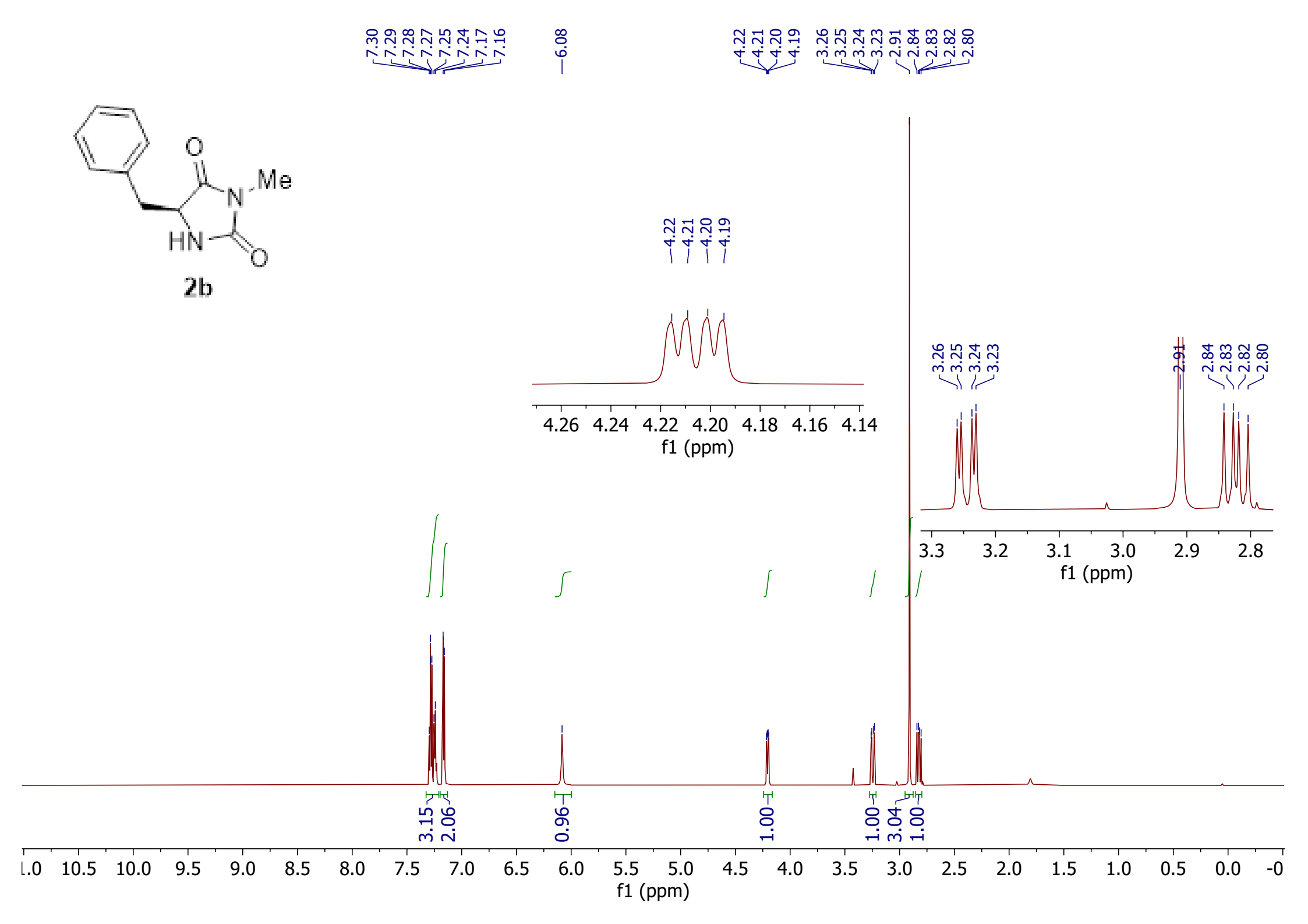
1u

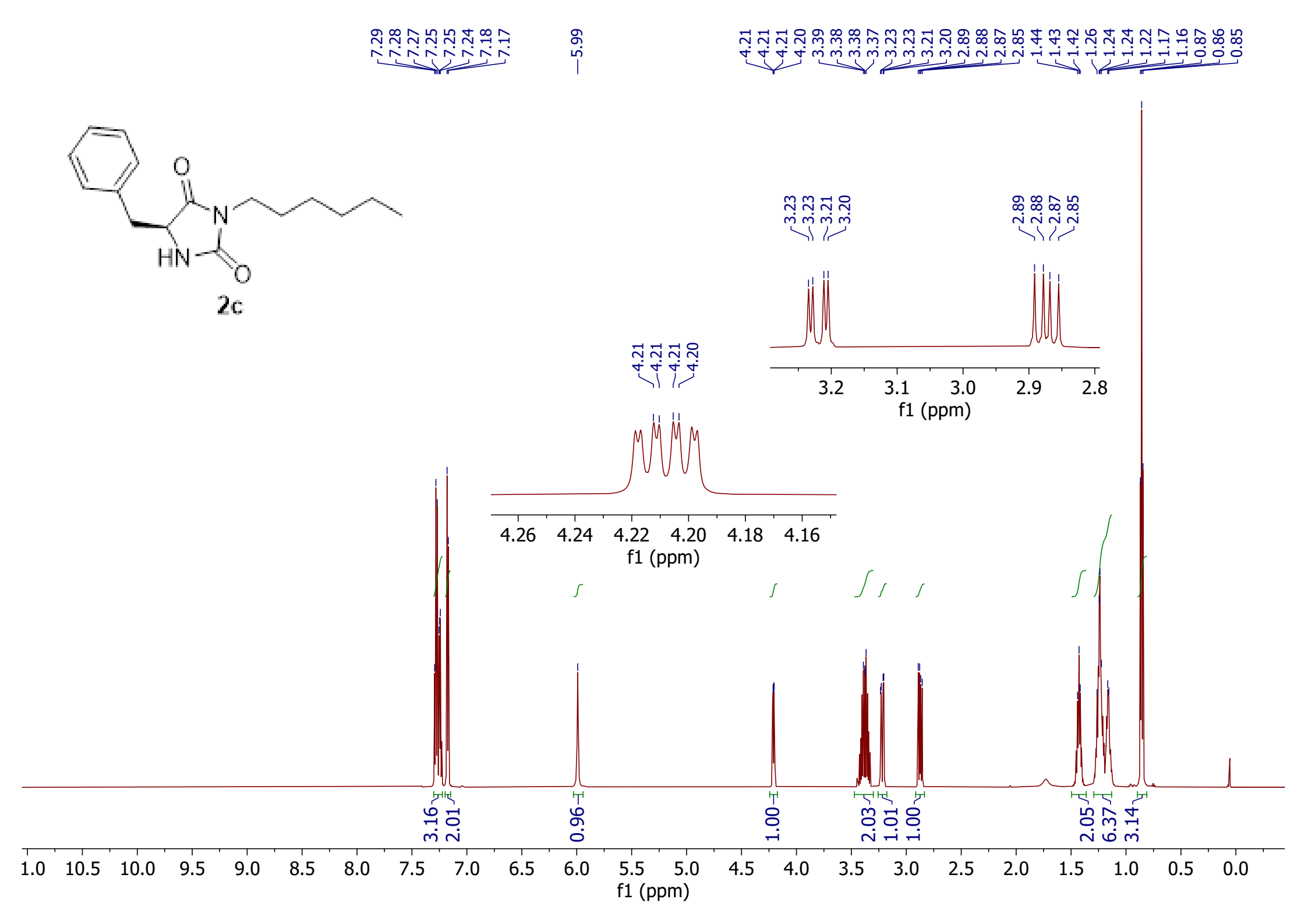
170.15
169.08
134.15
129.24
128.66
127.42
54.32
51.49
40.55
37.11
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

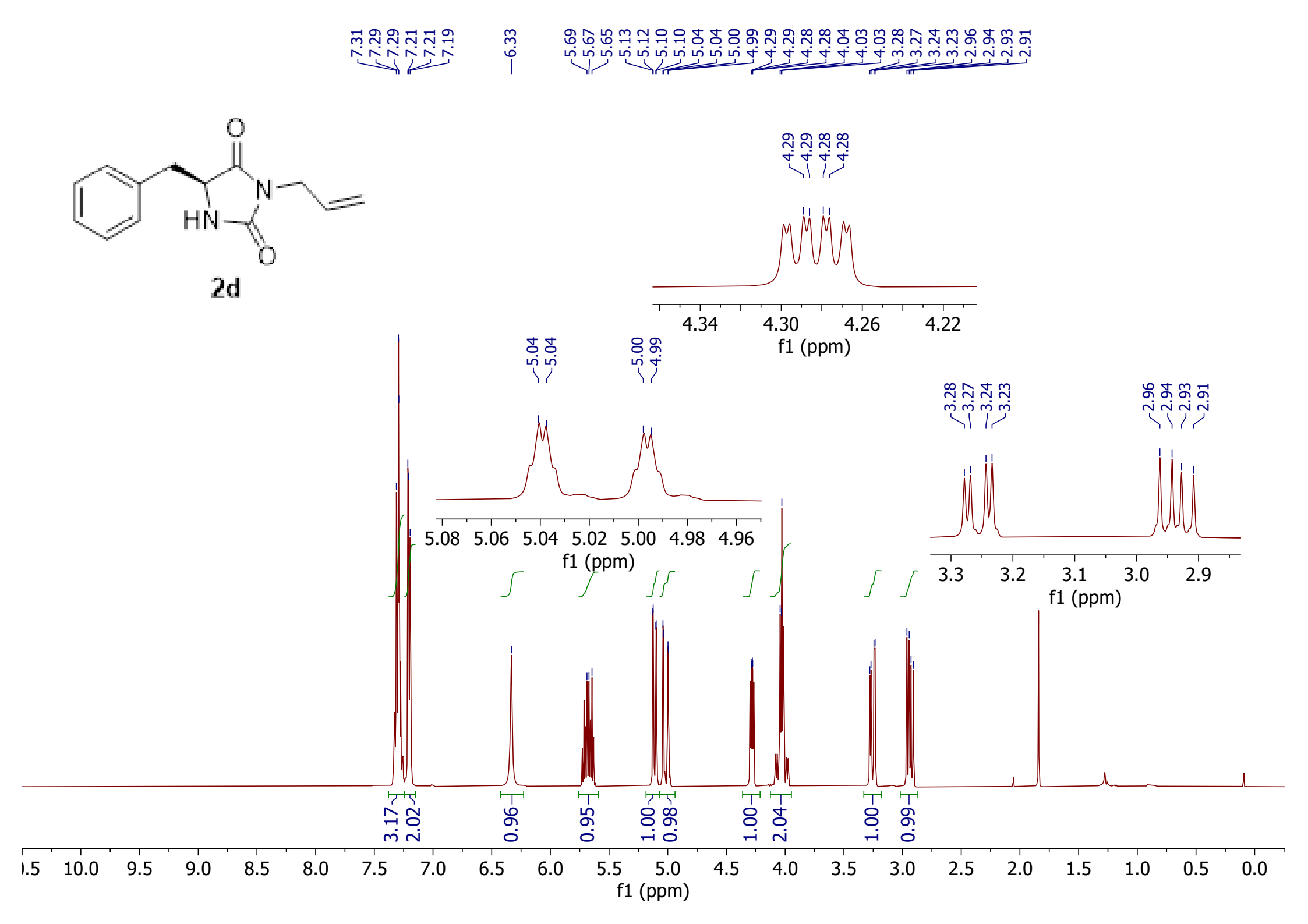

7.28
7.27
7.20
7.20
7.18
7.18
7.12
7.11
7.10
7.09
3.74
3.71
3.60
3.57
3.44
3.43
3.42
3.28
3.27
3.27
3.26
2.81
2.79
2.78
2.75
1.48
1.48
1.46
1.35
1.33
0.96
0.94
0.93
O
N
H
HN
1v
3.44
3.43
3.42
3.48
3.46
3.44
3.42
3.40
f1 (ppm)
2.81
2.79
2.78
2.75
2.82
2.80
2.78
2.76
2.74
f1 (ppm)
7.75
2.09
2.07
1.07
1.09
5.66
0.98
2.13
2.14
3.14
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

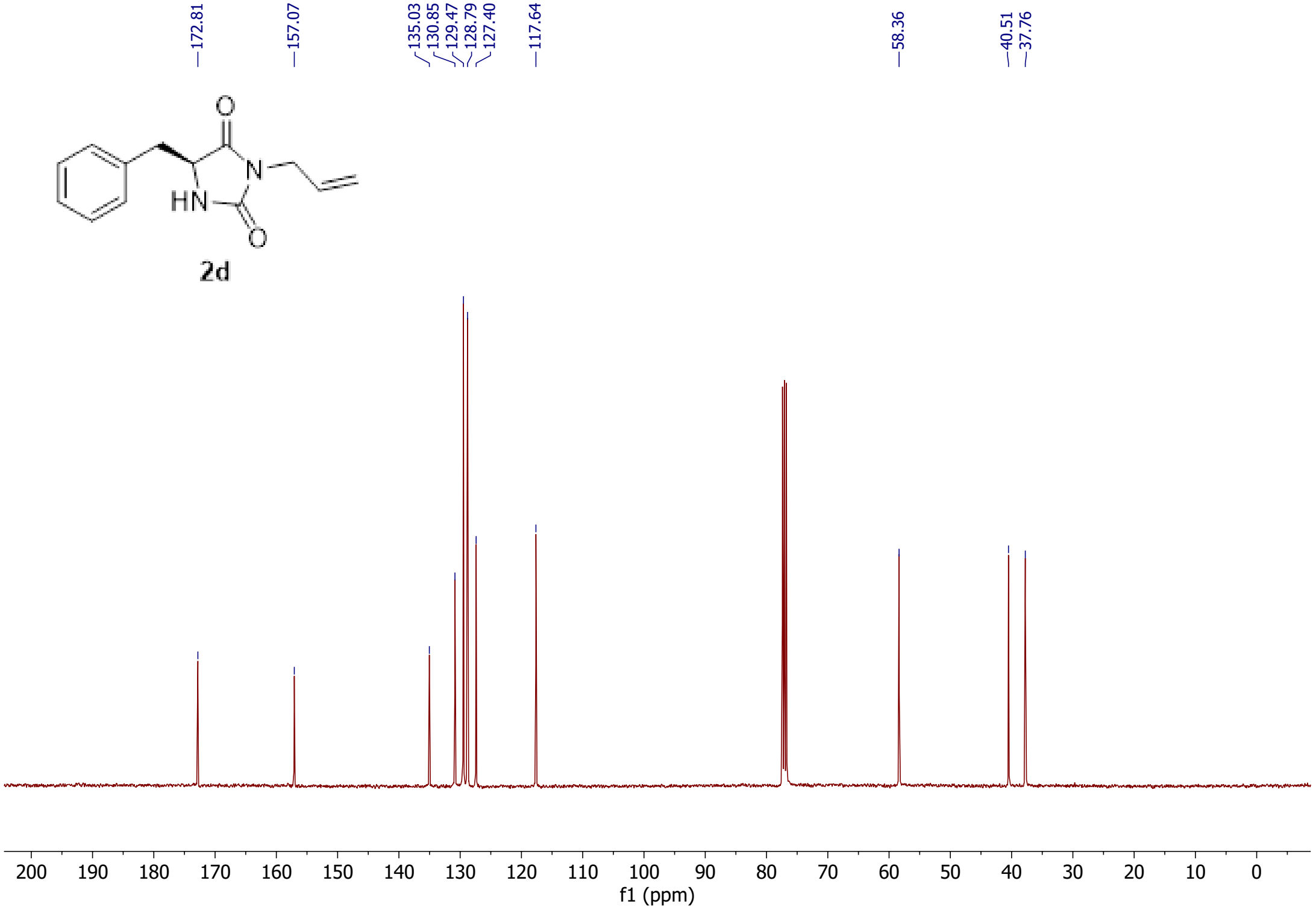

173.15
138.87
137.34
129.14
128.76
128.55
127.99
127.32
126.92
63.20
52.57
39.23
38.78
31.68
20.09
13.76
O
N
H
HN
1v
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

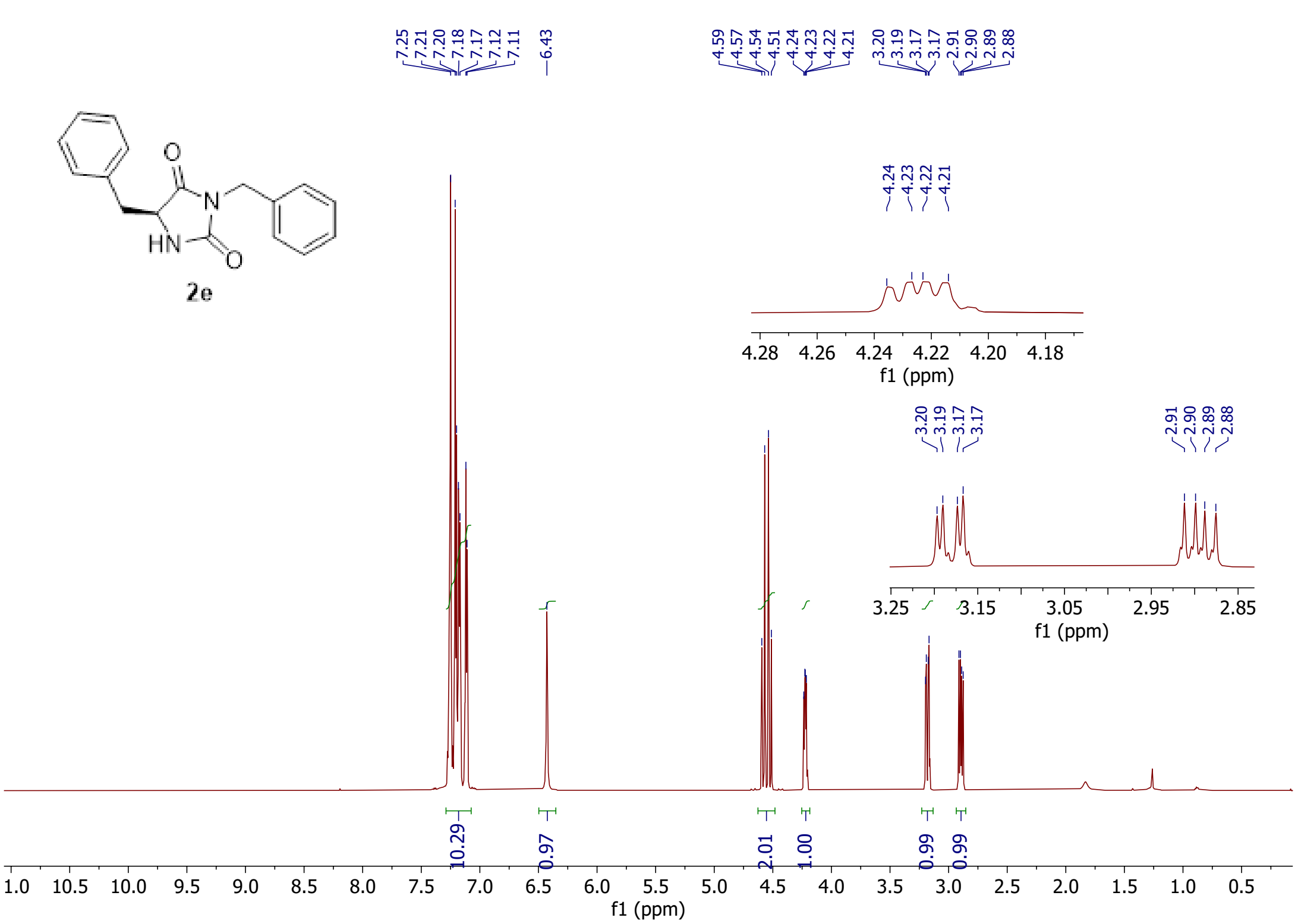

7.28
7.27
7.27
7.26
7.26
7.25
7.24
7.18
7.17
6.21
4.22
4.21
4.21
4.20
3.41
3.39
3.36
3.35
3.22
3.21
3.20
3.19
2.91
2.90
2.89
2.87
1.42
1.41
1.40
1.17
1.15
1.14
0.87
0.86
0.84
O
N
HN
O
2a
4.26 4.24 4.22 4.20 4.18 4.16
f1 (ppm)
3.2 3.1 3.0 2.9
f1 (ppm)
3.16
2.04
0.98
1.00
2.03
1.03
1.01
2.06
2.10
3.10
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

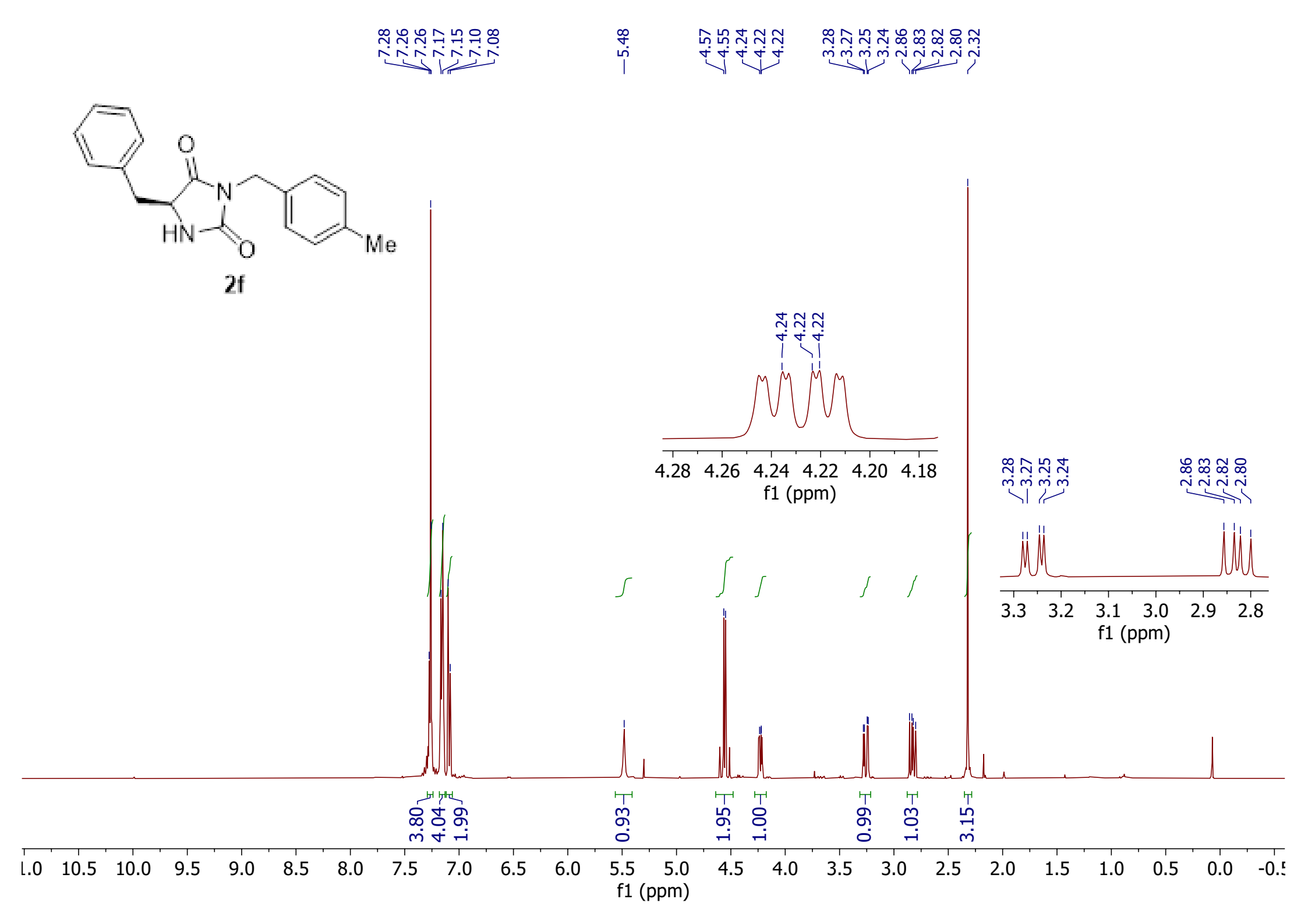

7.30
7.29
7.28
7.27
7.25
7.24
7.17
7.16
6.08
4.22
4.21
4.20
4.19
3.26
3.25
3.24
3.23
2.91
2.84
2.83
2.82
2.80
O
N
Me
HN
O
2b
4.26 4.24 4.22 4.20 4.18 4.16 4.14
f1 (ppm)
3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)
3.15
2.06
0.96
1.00
1.00
3.04
1.00
f1 (ppm)

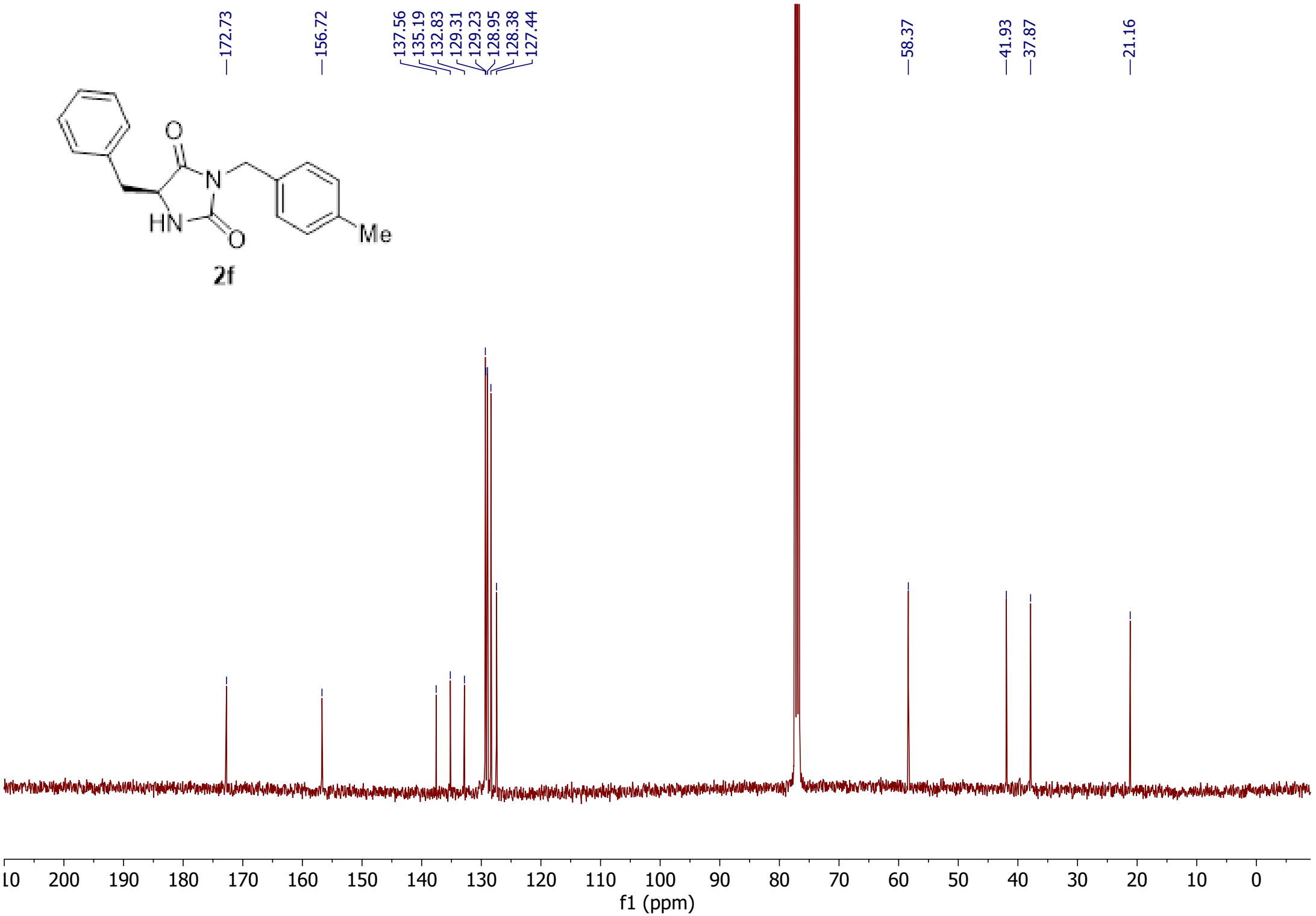

7.29
7.28
7.27
7.25
7.25
7.24
7.18
7.17
5.99
4.21
4.21
4.21
4.20
3.39
3.38
3.38
3.37
3.23
3.23
3.21
3.20
2.89
2.88
2.87
2.85
1.44
1.43
1.42
1.26
1.24
1.24
1.22
1.17
1.16
0.87
0.86
0.85
O
N
HN
O
2c
3.23
3.23
3.21
3.20
2.89
2.88
2.87
2.85
3.2
3.1
3.0
2.9
2.8
f1 (ppm)
4.21
4.21
4.21
4.20
4.26
4.24
4.22
4.20
4.18
4.16
f1 (ppm)
3.16
2.01
0.96
1.00
2.03
1.01
1.00
2.05
6.37
3.14
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


7.31
7.29
7.29
7.21
7.21
7.19
6.33
5.69
5.67
5.65
5.13
5.12
5.10
5.10
5.04
5.04
5.00
4.99
4.29
4.29
4.28
4.28
4.04
4.03
4.03
3.28
3.27
3.24
3.23
2.96
2.94
2.93
2.91
O
N
HN
O
2d
4.29
4.29
4.28
4.28
4.34
4.30
4.26
4.22
f1 (ppm)
5.04
5.04
5.00
4.99
5.08
5.06
5.04
5.02
5.00
4.98
4.96
f1 (ppm)
3.28
3.27
3.24
3.23
2.96
2.94
2.93
2.91
3.3
3.2
3.1
3.0
2.9
f1 (ppm)
3.17
2.02
0.96
0.95
1.00
0.98
1.00
2.04
1.00
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.81
157.07
135.03
130.85
129.47
128.79
127.40
117.64
58.36
40.51
37.76
O
N
HN
O
2d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.25
7.21
7.20
7.18
7.17
7.12
7.11
6.43
4.59
4.57
4.54
4.51
4.24
4.23
4.22
4.21
3.20
3.19
3.17
3.17
2.91
2.90
2.89
2.88
O
N
HN
O
2e
4.24
4.23
4.22
4.21
4.28
4.26
4.24
4.22
4.20
4.18
f1 (ppm)
3.20
3.19
3.17
3.17
2.91
2.90
2.89
2.88
3.25
3.15
3.05
2.95
2.85
f1 (ppm)
10.29
0.97
2.01
1.00
0.99
0.99
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


7.28
7.26
7.26
7.17
7.15
7.10
7.08
5.48
4.57
4.55
4.24
4.22
4.22
3.28
3.27
3.25
3.24
2.86
2.83
2.82
2.80
2.32
O
N
HN
O
Me
2f
4.24
4.22
4.22
4.28 4.26 4.24 4.22 4.20 4.18
f1 (ppm)
3.28
3.27
3.25
3.24
2.86
2.83
2.82
2.80
3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)
3.80
4.04
1.99
0.93
1.95
1.00
0.99
1.03
3.15
f1 (ppm)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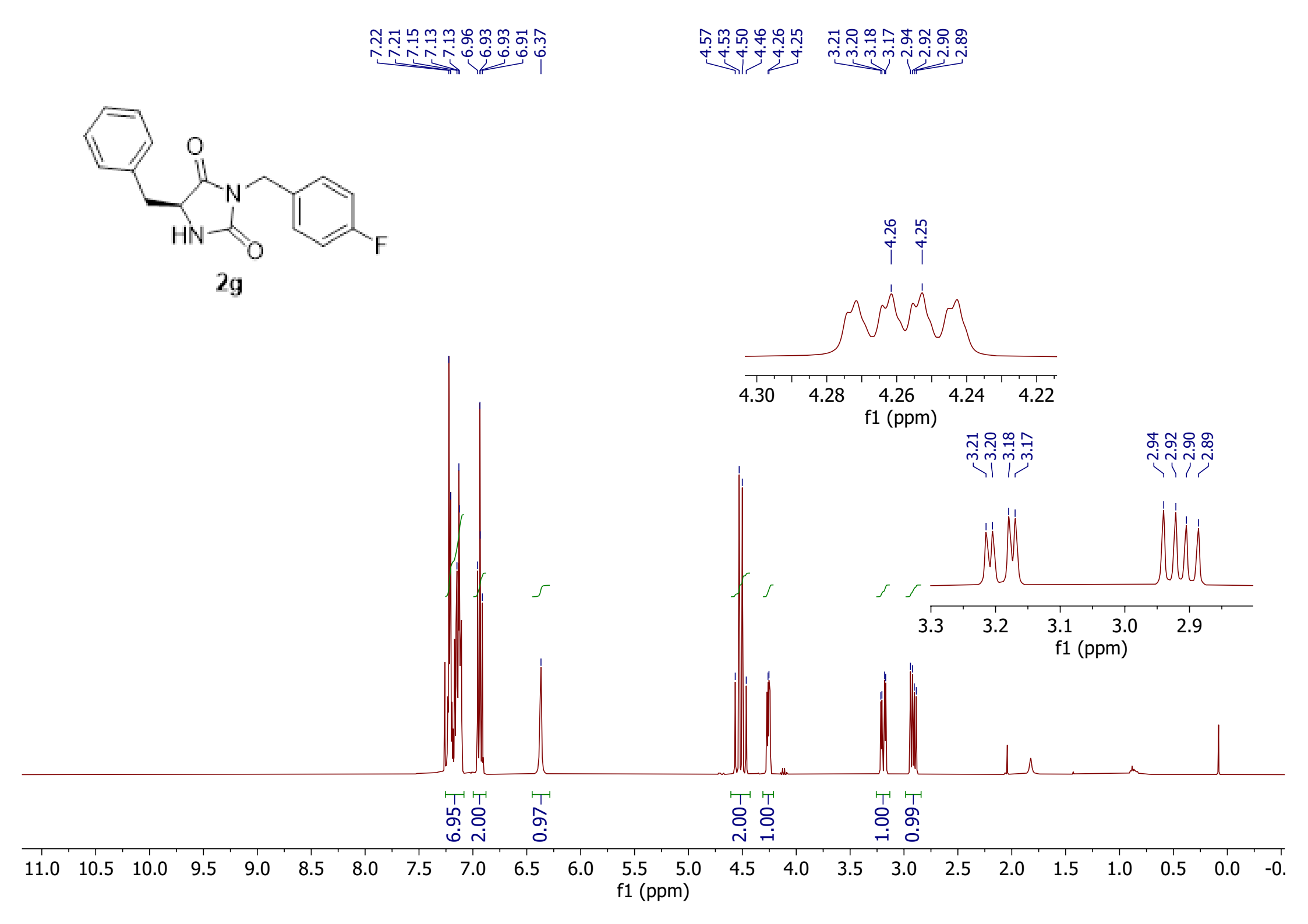
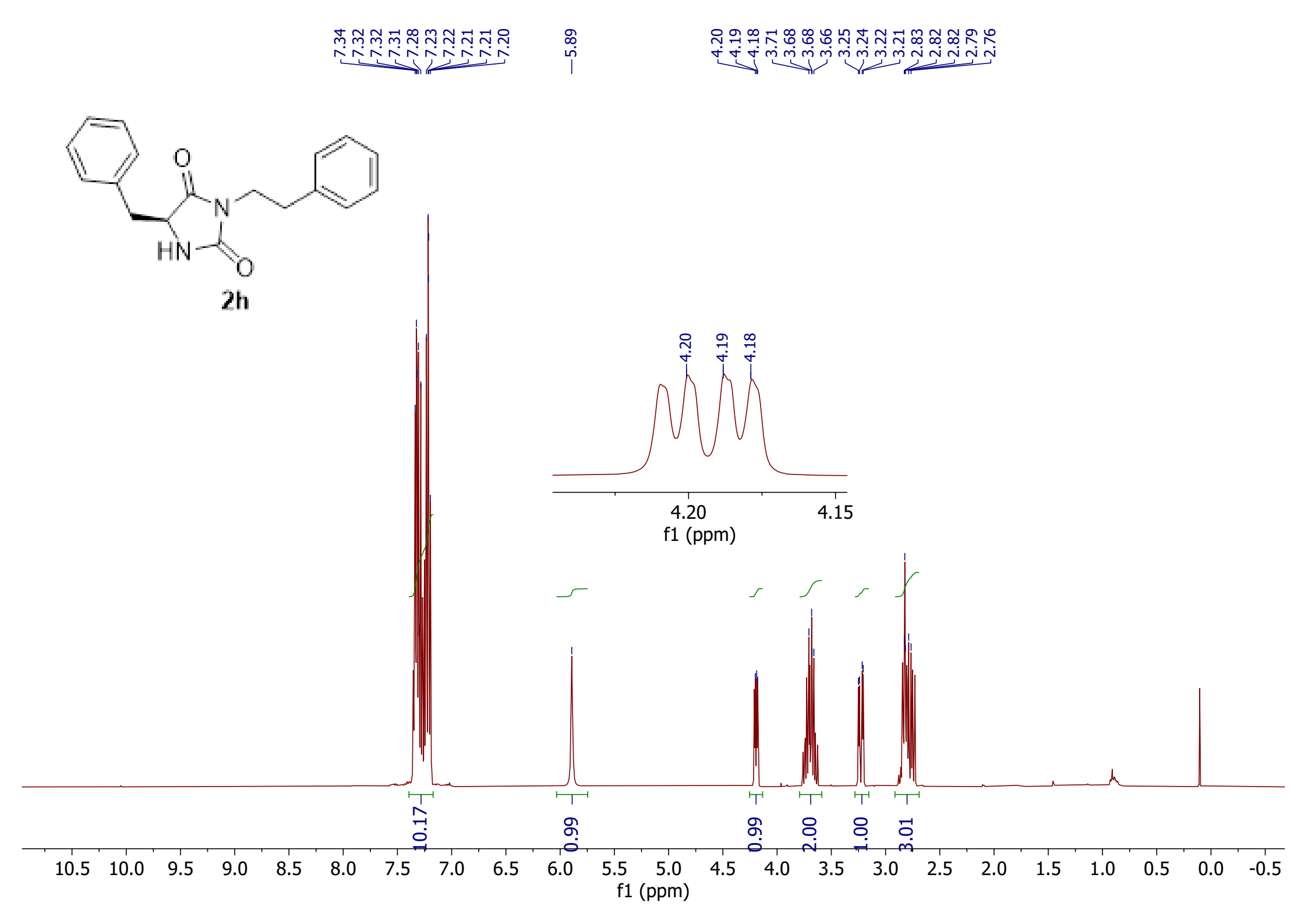
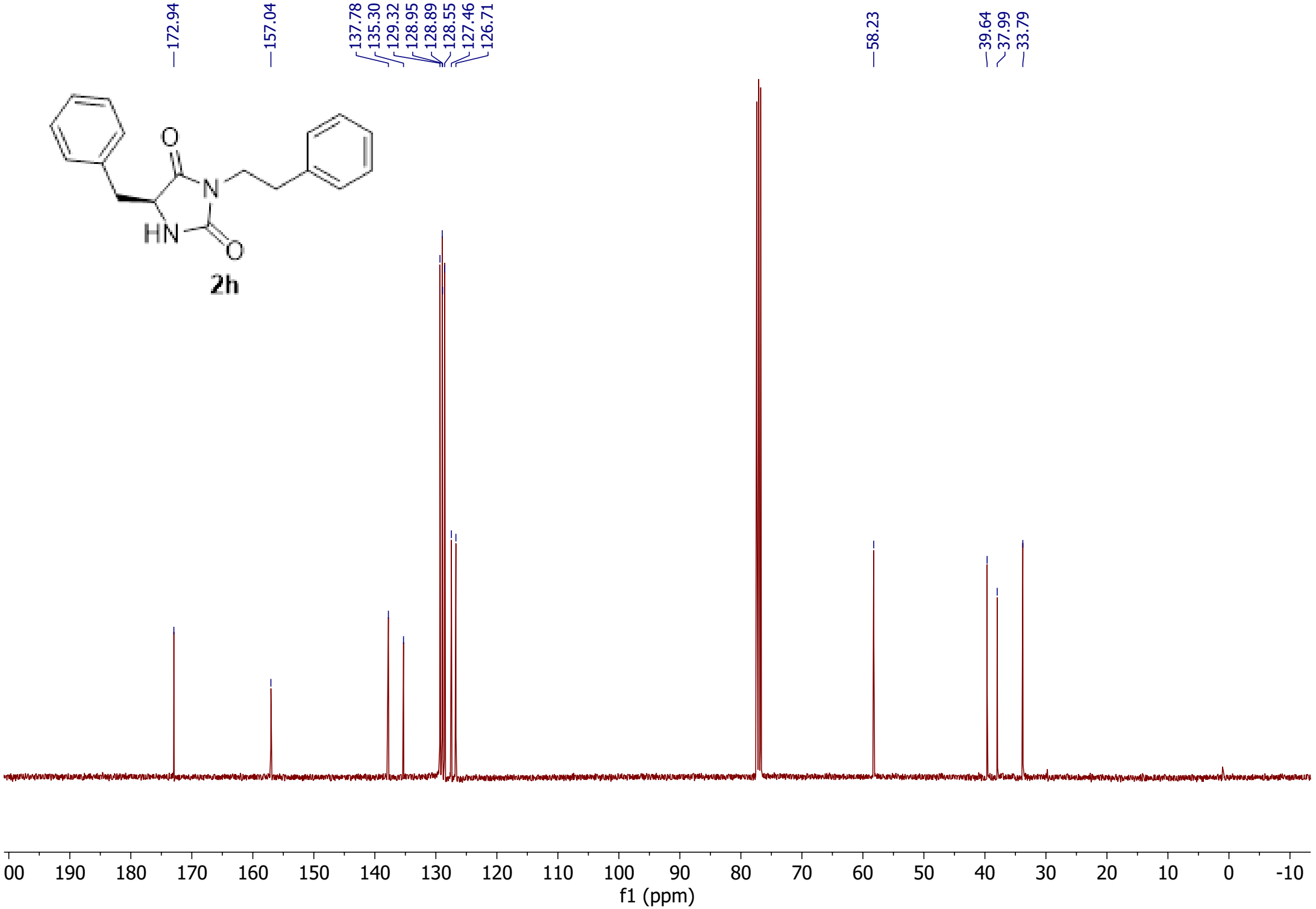
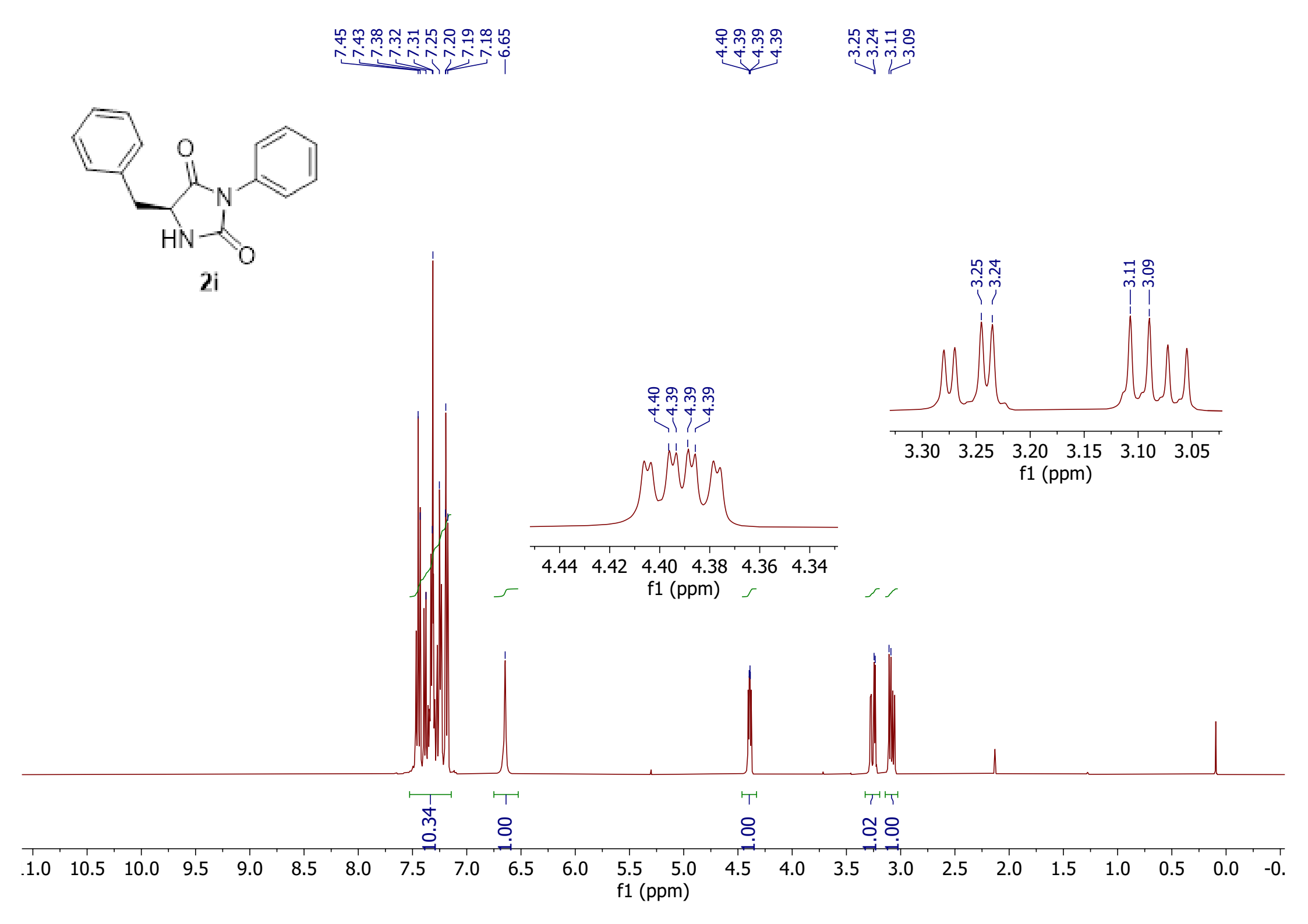
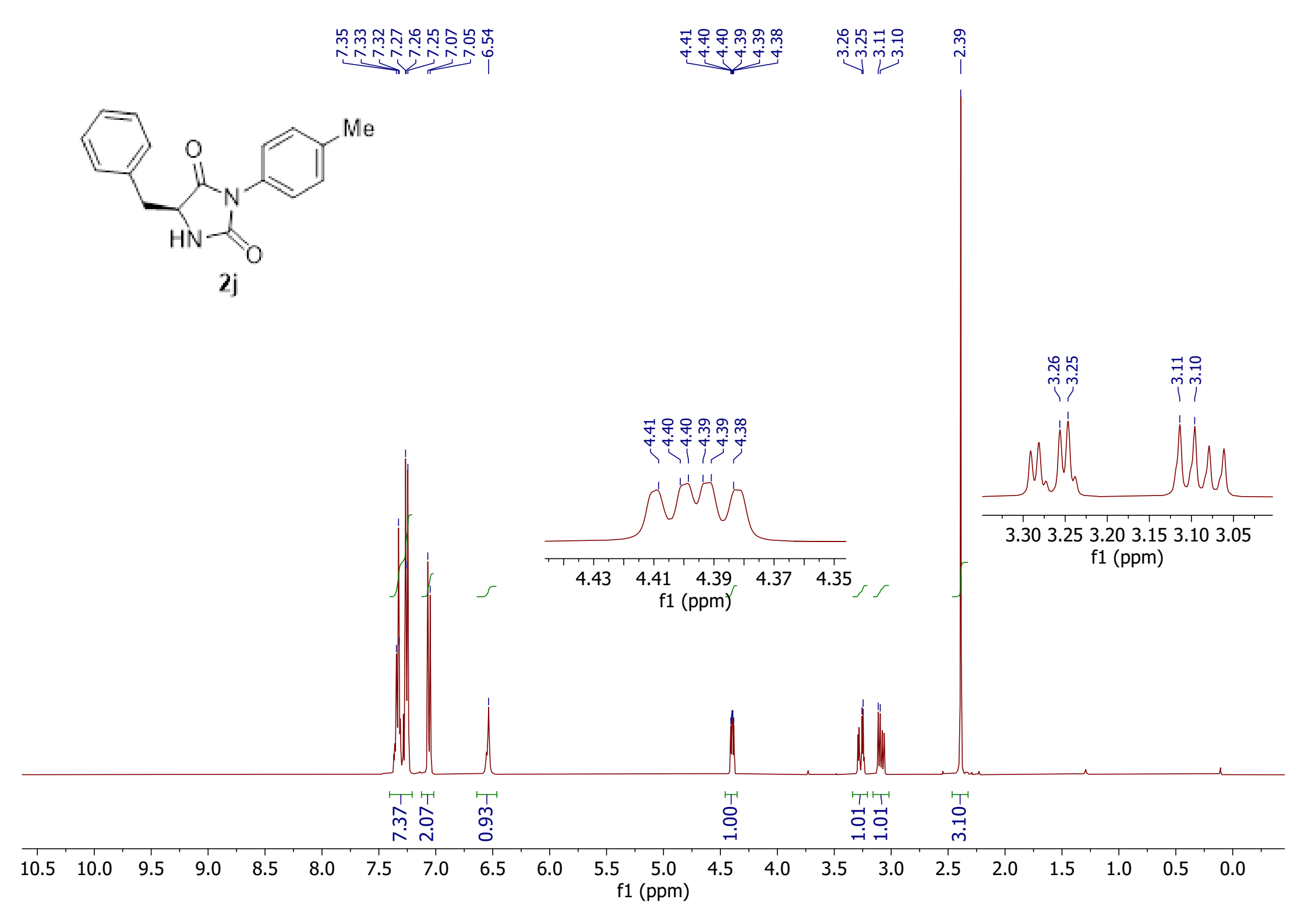
156.72
137.56
135.19
132.83
129.31
129.23
128.95
128.38
127.44
58.37
41.93
37.87
21.16
O
N
HN
O
Me
2f
f1 (ppm)

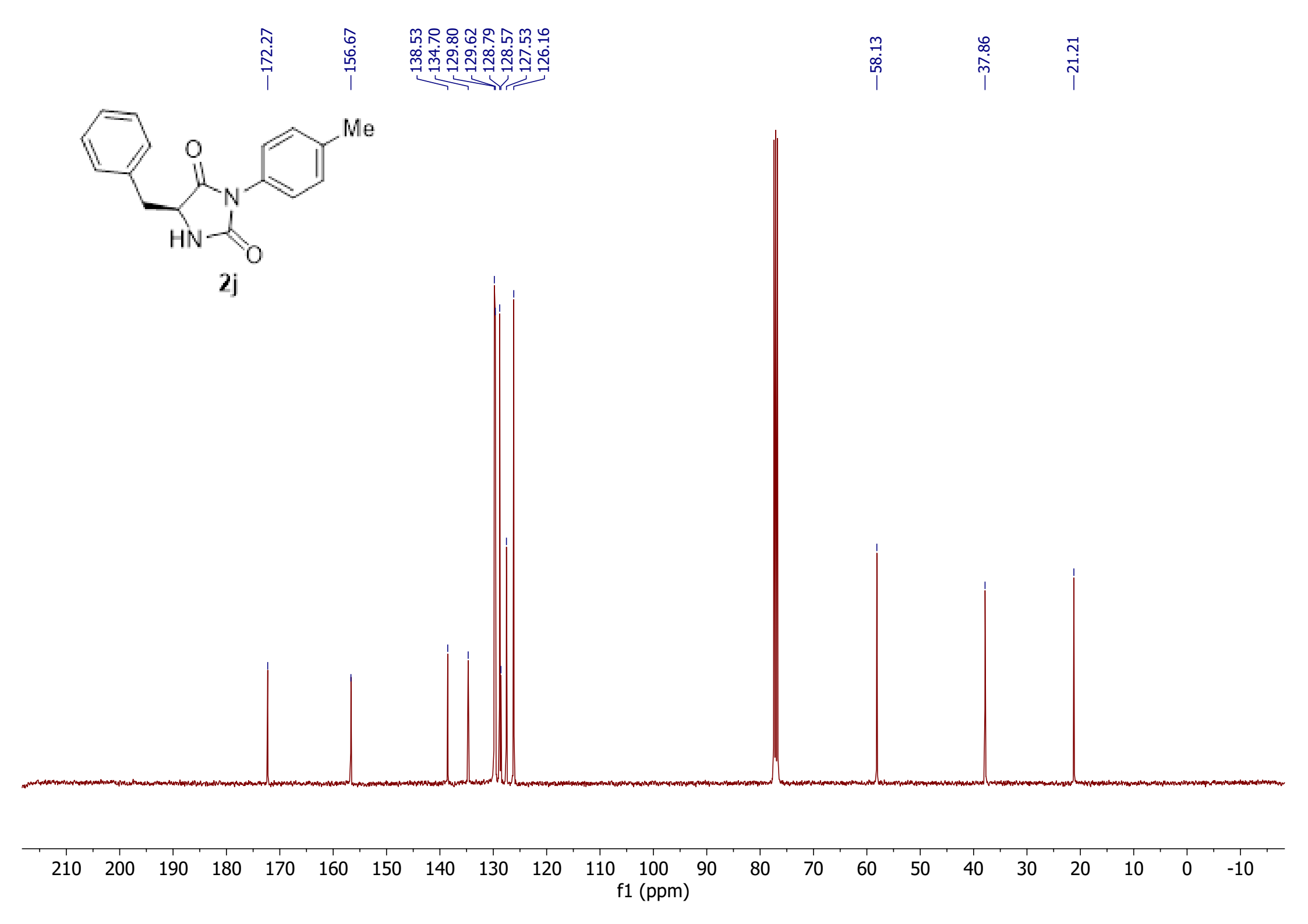

7.22
7.21
7.15
7.13
7.13
6.96
6.93
6.93
6.91
6.37
4.57
4.53
4.50
4.46
4.26
4.25
3.21
3.20
3.18
3.17
2.94
2.92
2.90
2.89
O
N
HN
O
F
2g
4.26
4.25
4.30
4.28
4.26
4.24
4.22
f1 (ppm)
3.21
3.20
3.18
3.17
2.94
2.92
2.90
2.89
3.3
3.2
3.1
3.0
2.9
f1 (ppm)
6.95
2.00
0.97
2.00
1.00
1.00
0.99
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)

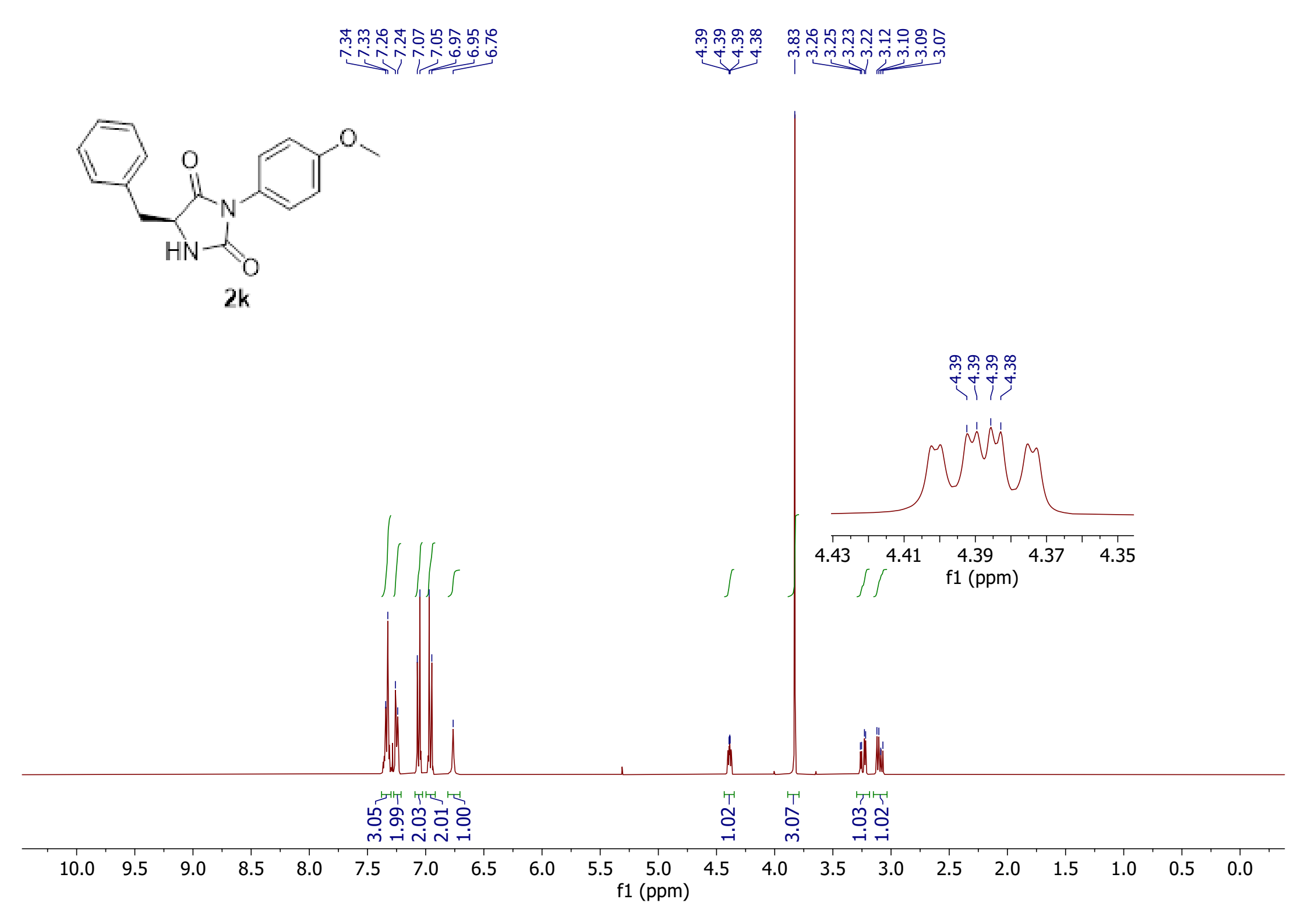

7.34
7.32
7.32
7.31
7.28
7.23
7.22
7.21
7.21
7.20
5.89
4.20
4.19
4.18
3.71
3.68
3.68
3.66
3.25
3.24
3.22
3.21
2.83
2.82
2.82
2.79
2.76
O
N
HN
O
2h
4.20
4.19
4.18
4.20
4.15
f1 (ppm)
10.17
0.99
0.99
2.00
1.00
3.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

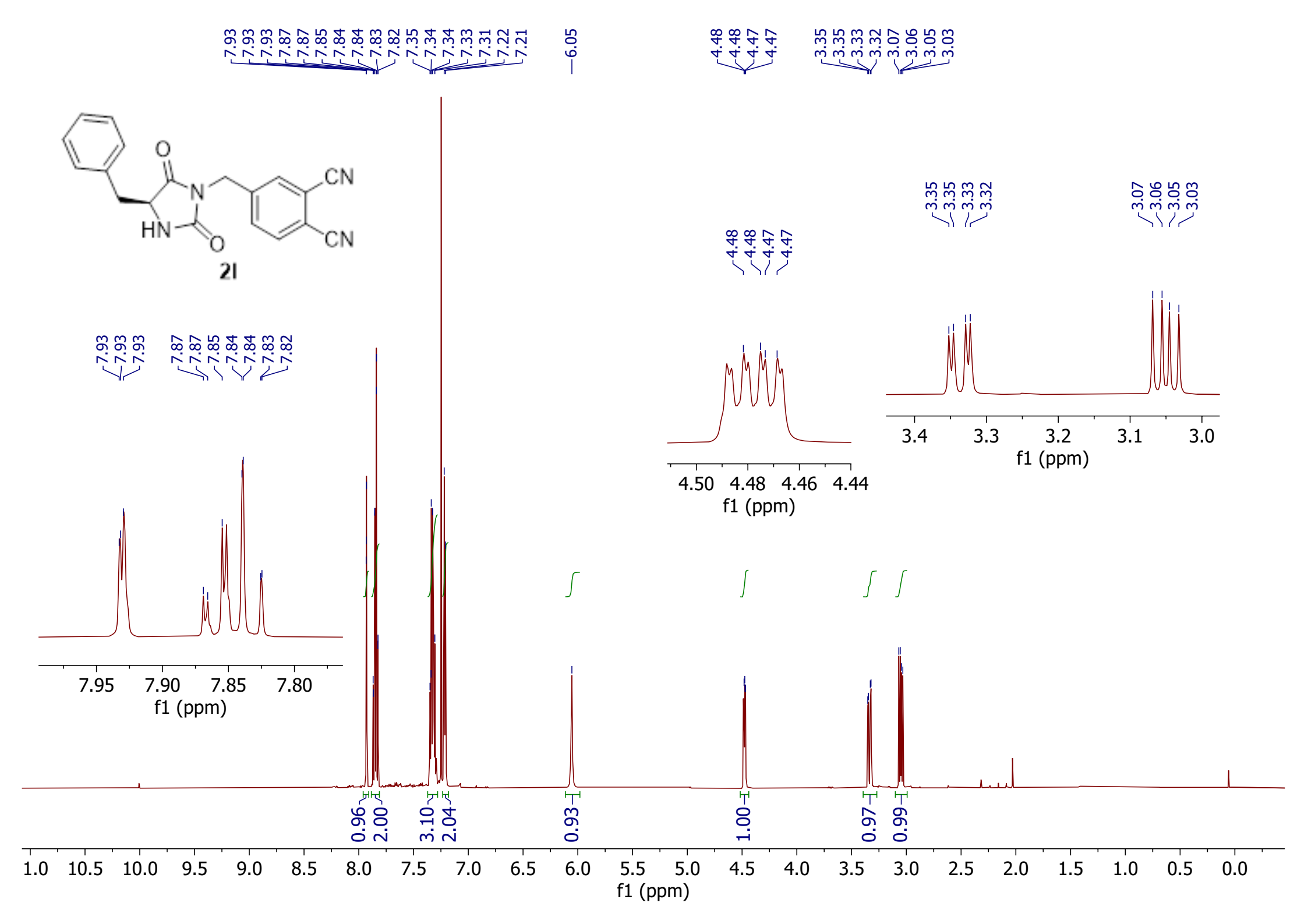

172.94
157.04
137.78
135.30
129.32
128.95
128.89
128.55
127.46
126.71
58.23
39.64
37.99
33.79
O
N
HN
O
2h
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

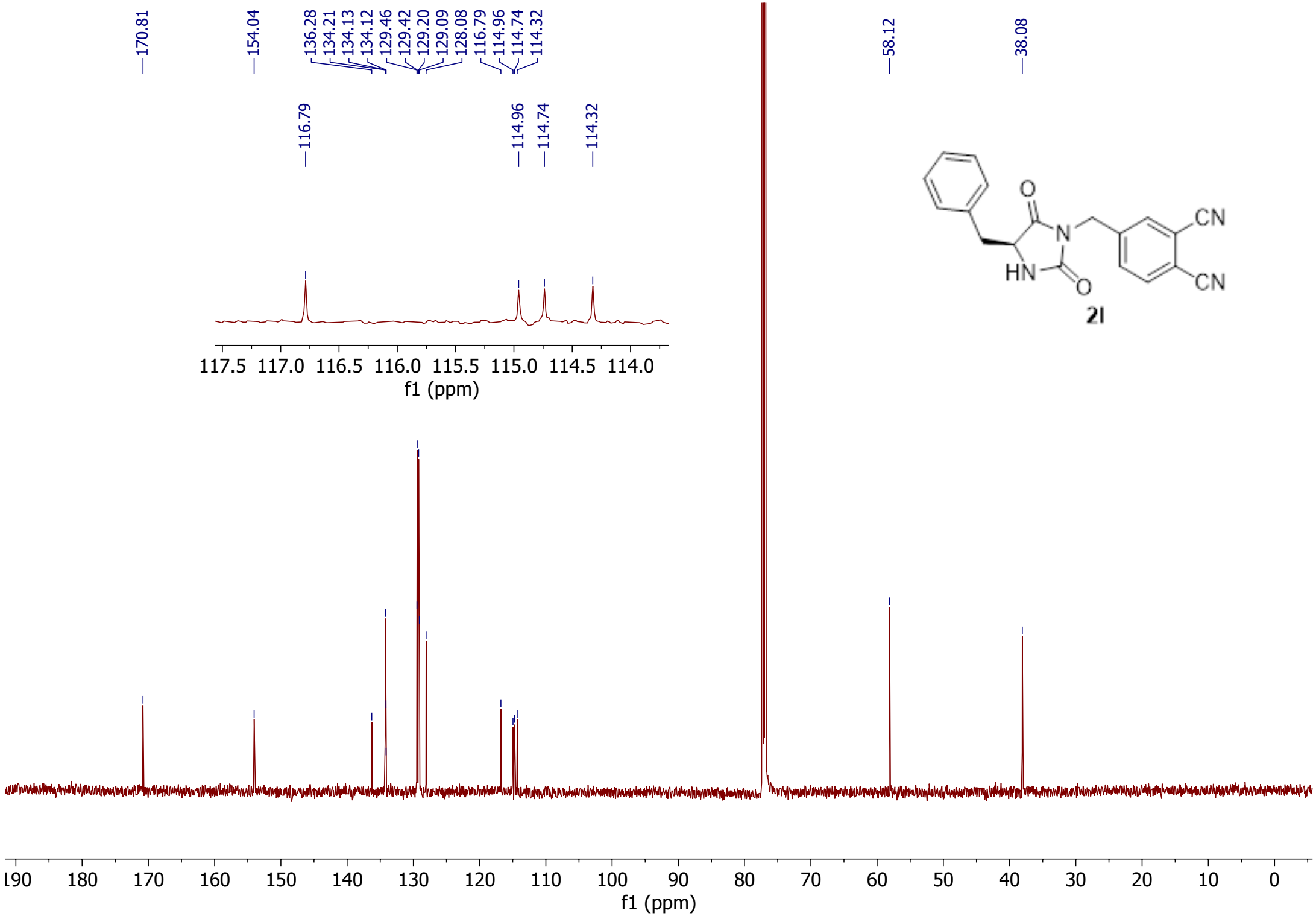

7.45
7.43
7.38
7.32
7.31
7.25
7.20
7.19
7.18
6.65
4.40
4.39
4.39
4.39
3.25
3.24
3.11
3.09
O
N
HN
O
2i
4.40
4.39
4.39
4.39
4.44 4.42 4.40 4.38 4.36 4.34
f1 (ppm)
3.25
3.24
3.11
3.09
3.30 3.25 3.20 3.15 3.10 3.05
f1 (ppm)
10.34
1.00
1.00
1.02
1.00
.1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

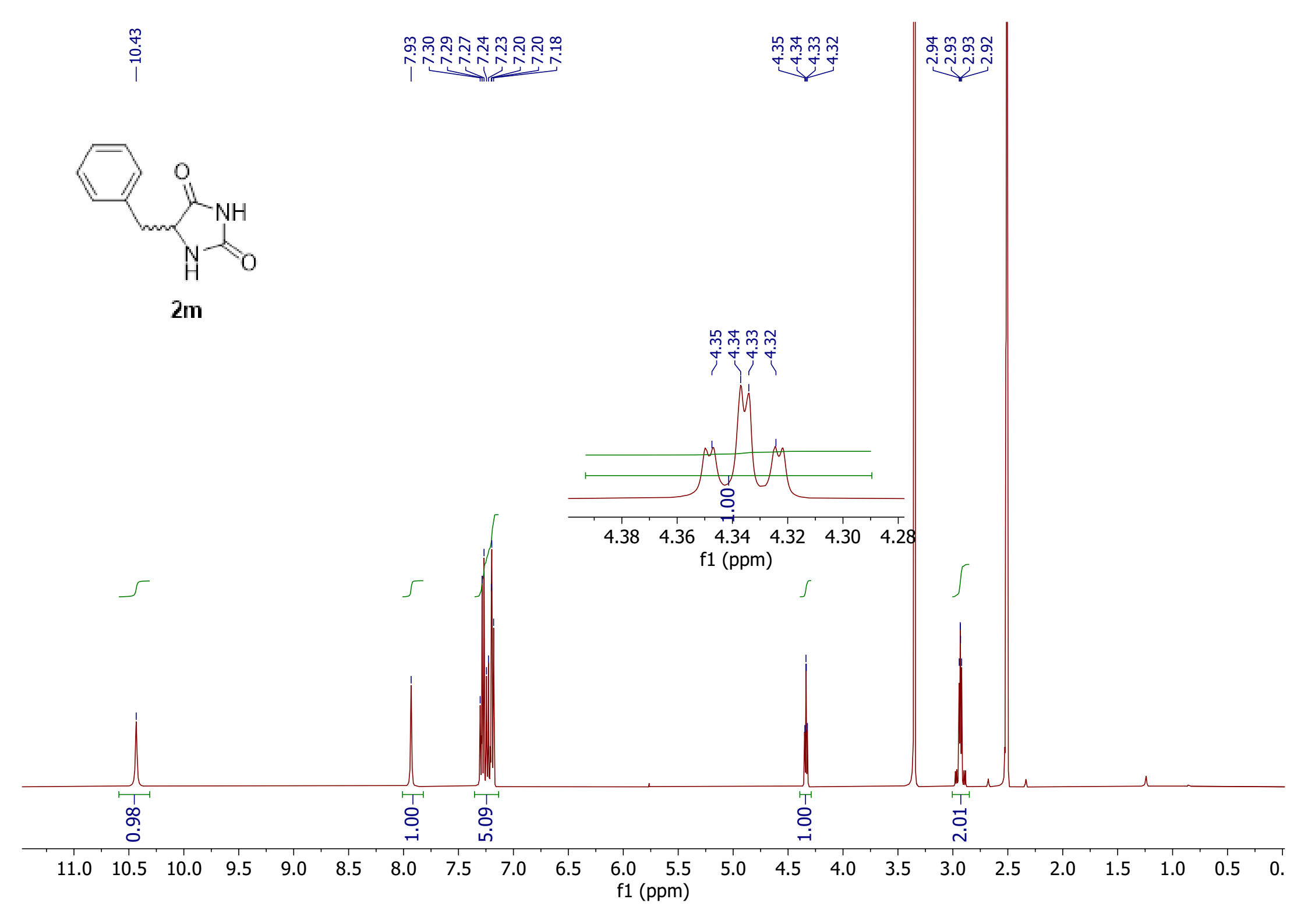

7.35
7.33
7.32
7.27
7.26
7.25
7.07
7.05
6.54
4.41
4.40
4.40
4.39
4.39
4.38
3.26
3.25
3.11
3.10
2.39
Me
O
N
HN
O
2j
4.43 4.41 4.39 4.37 4.35
f1 (ppm)
3.30 3.25 3.20 3.15 3.10 3.05
f1 (ppm)
7.37
2.07
0.93
1.00
1.01
1.01
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

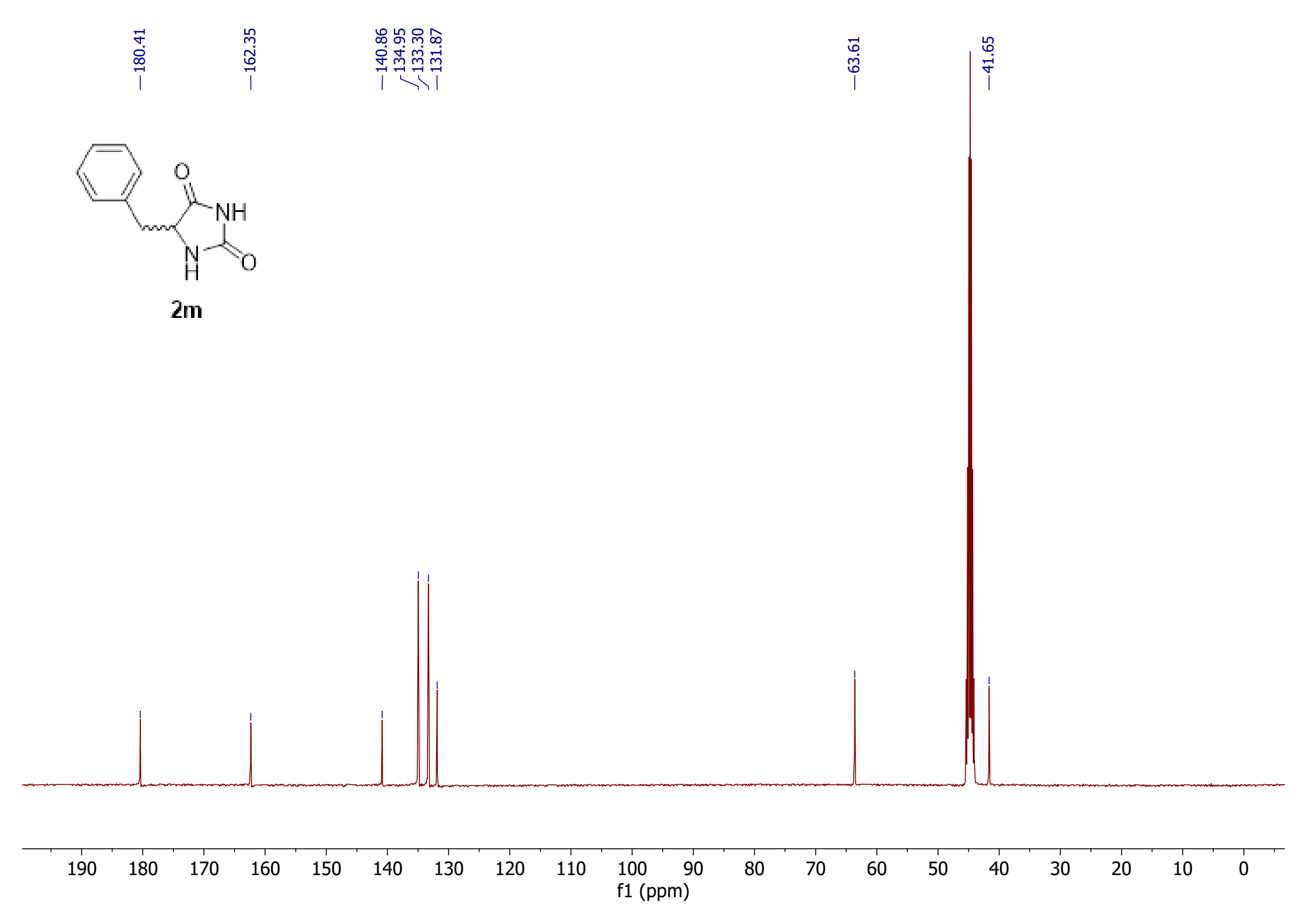

172.27
156.67
138.53
134.70
129.80
129.62
128.79
128.57
127.53
126.16
58.13
37.86
21.21
Me
O
N
HN
O
2j
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

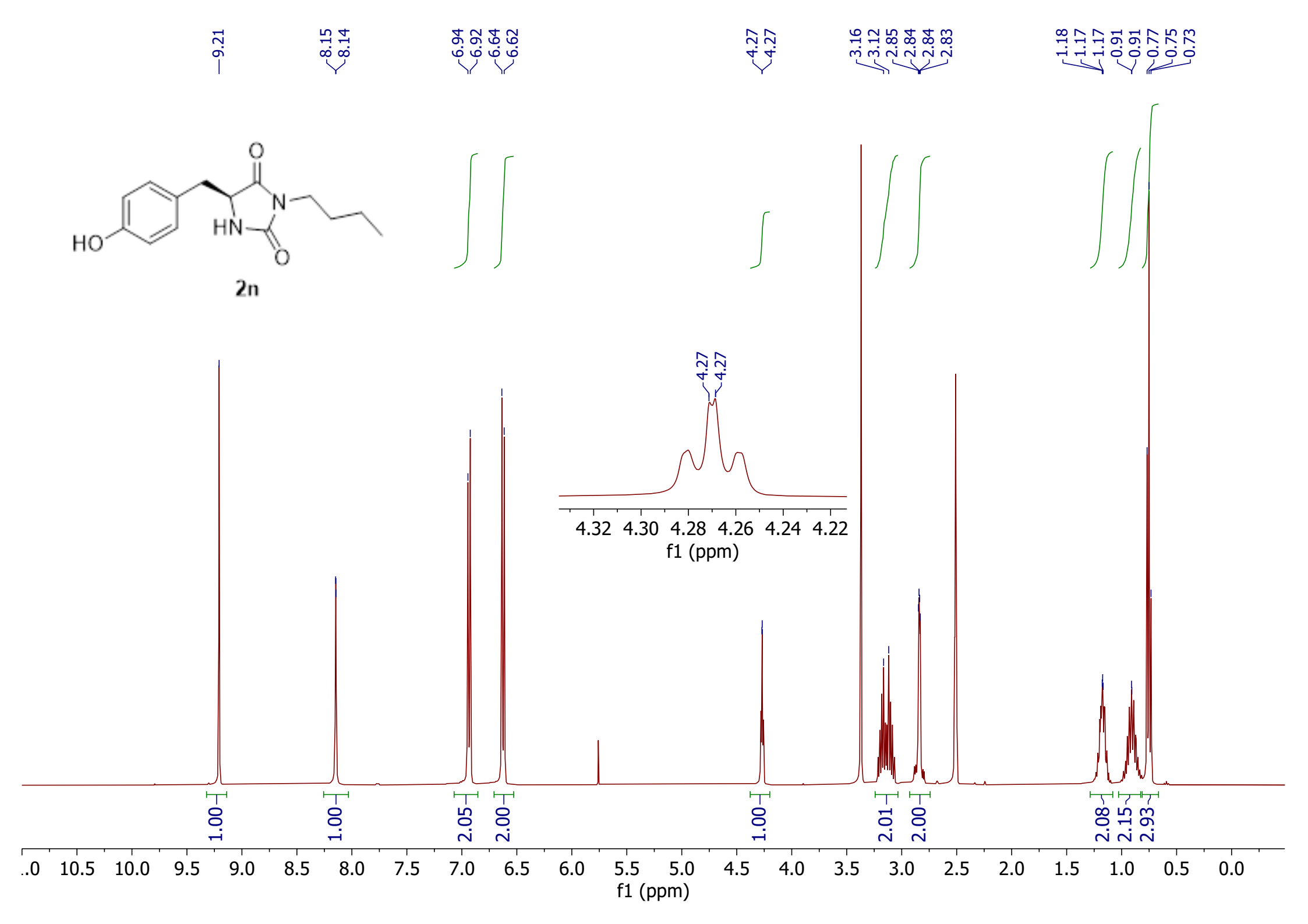

7.34
7.33
7.26
7.24
7.07
7.05
6.97
6.95
6.76
4.39
4.39
4.39
4.38
3.83
3.26
3.25
3.23
3.22
3.12
3.10
3.09
3.07
O
O
N
HN
O
O
2k
4.39
4.39
4.39
4.38
4.43
4.41
4.39
4.37
4.35
f1 (ppm)
3.05
1.99
2.03
2.01
1.00
1.02
3.07
1.03
1.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

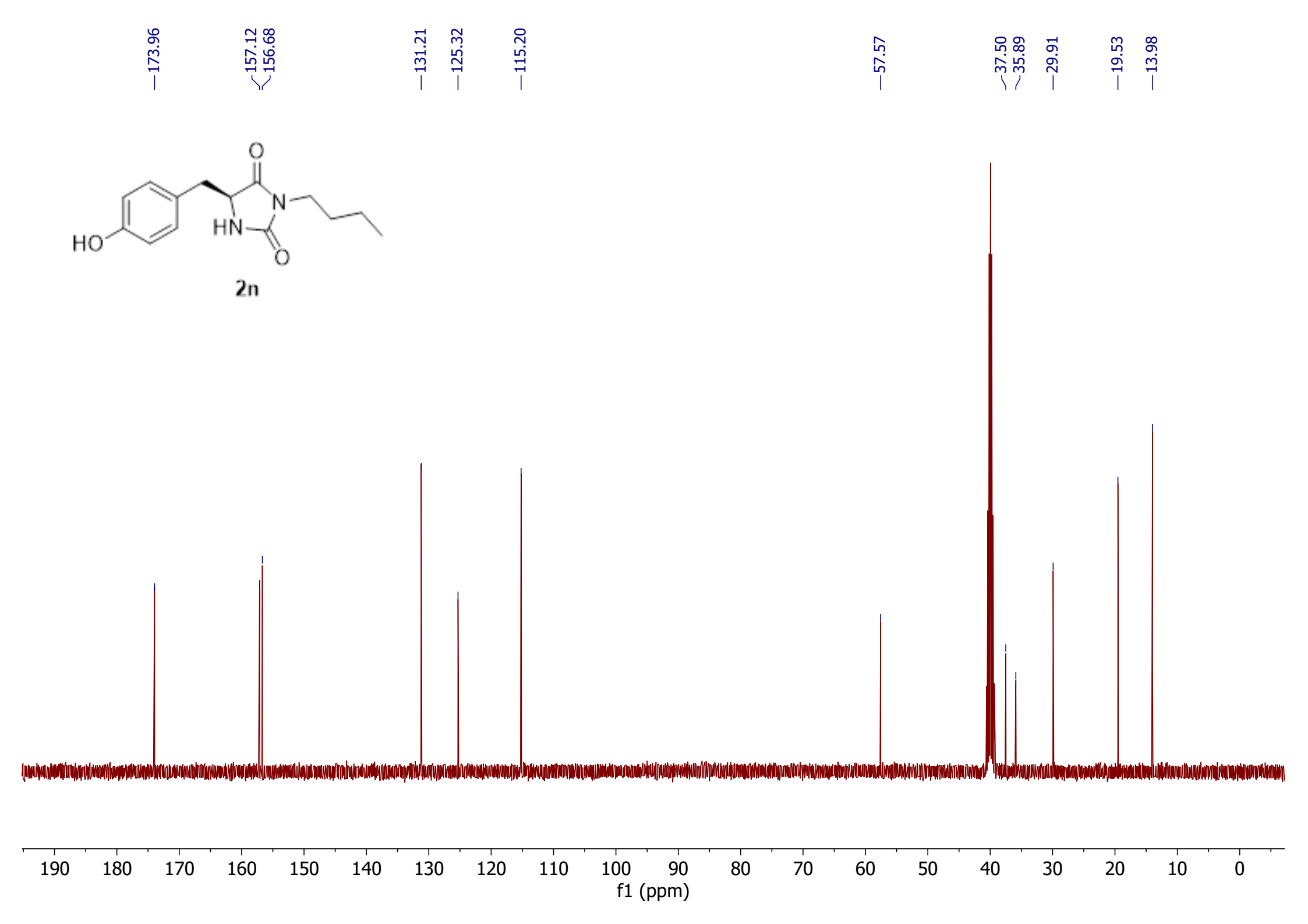

7.93
7.93
7.93
7.87
7.87
7.85
7.84
7.84
7.83
7.82
7.35
7.34
7.34
7.33
7.31
7.22
7.21
6.05
4.48
4.48
4.47
4.47
3.35
3.35
3.33
3.32
3.07
3.06
3.05
3.03
O
N
HN
O
CN
CN
2l
f1 (ppm)
0.96
2.00
3.10
2.04
0.93
1.00
0.97
0.99

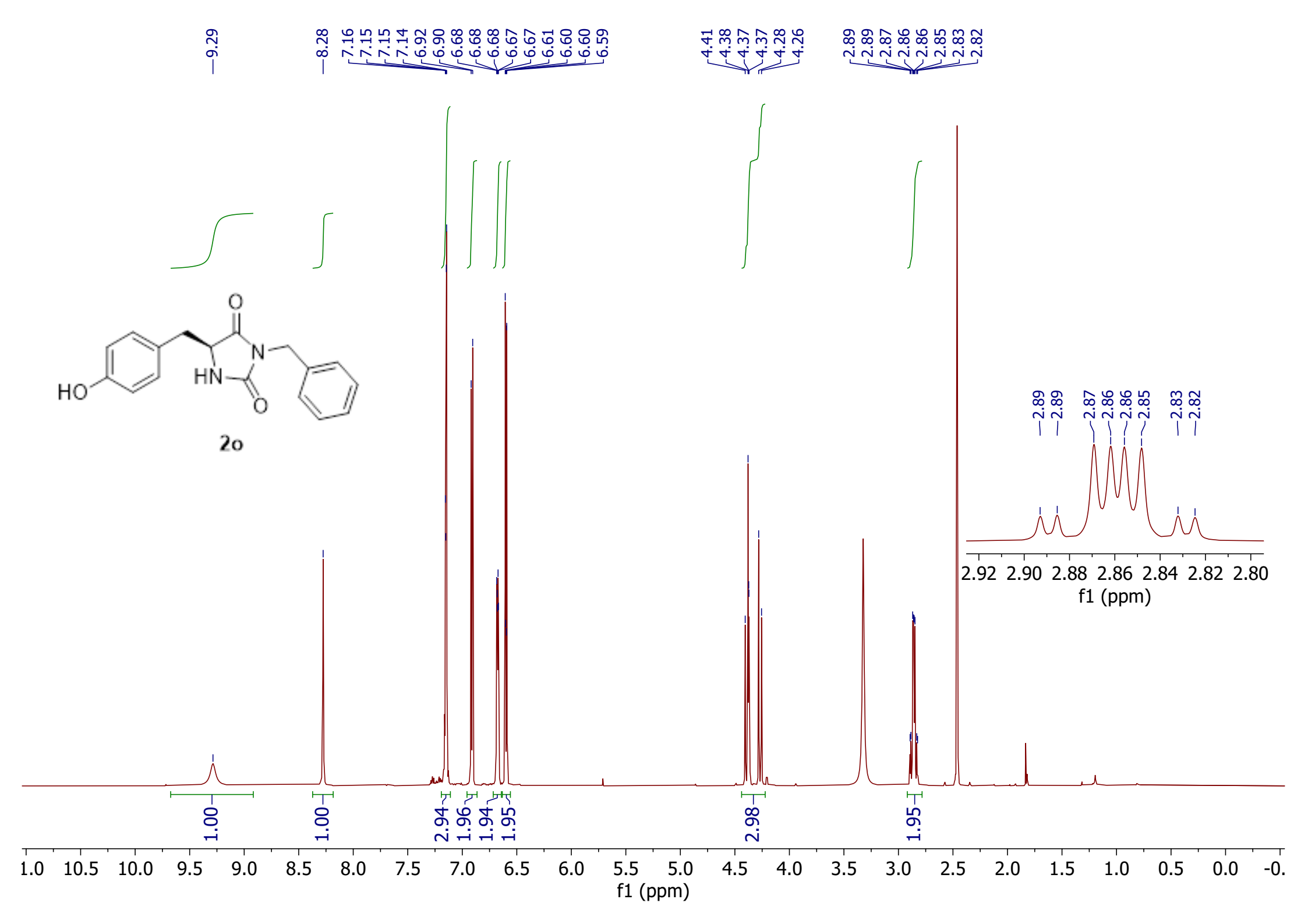

170.81
154.04
136.28
134.21
134.13
134.12
129.46
129.42
129.20
129.09
128.08
116.79
114.96
114.74
114.32
58.12
38.08
116.79
114.96
114.74
114.32
117.5 117.0 116.5 116.0 115.5 115.0 114.5 114.0
f1 (ppm)
O
N
HN
O
CN
CN
2l
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

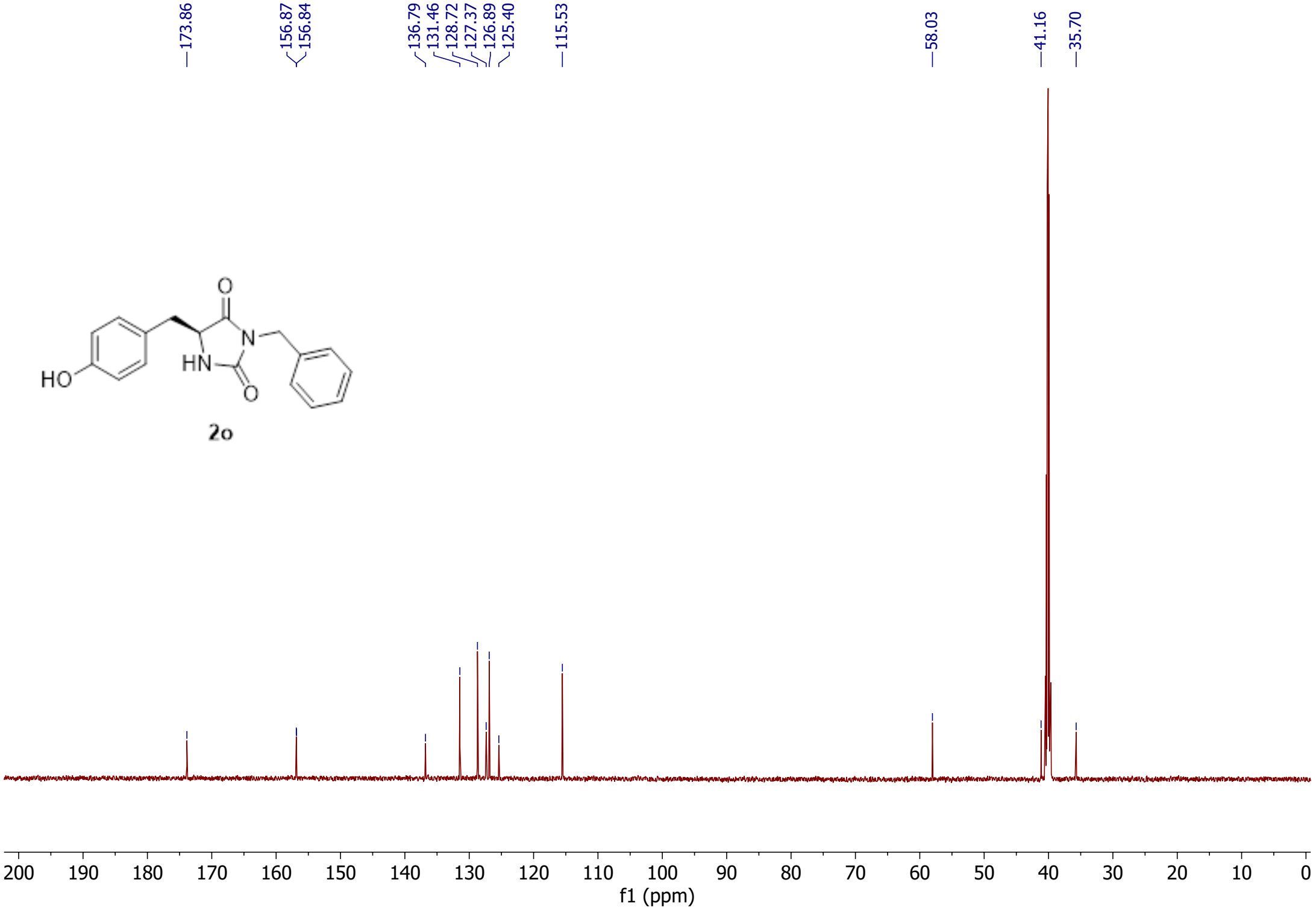

10.43
7.93
7.30
7.29
7.27
7.24
7.23
7.20
7.20
7.18
4.35
4.34
4.33
4.32
2.94
2.93
2.93
2.92
NH
N
H
O
O
2m
1.00
4.38
4.36
4.34
4.32
4.30
4.28
f1 (ppm)
0.98
1.00
5.09
1.00
2.01
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

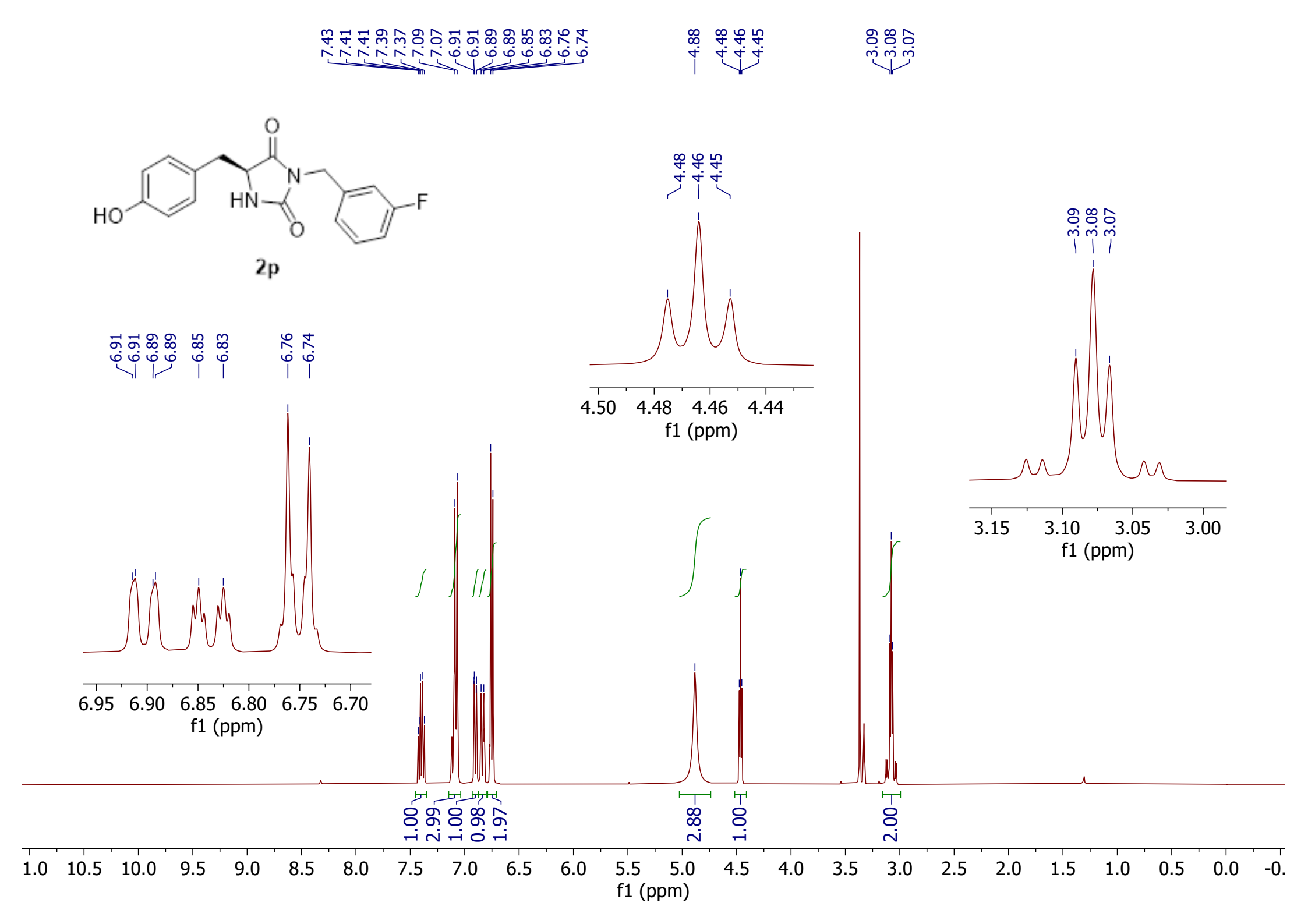

180.41
162.35
140.86
134.95
133.30
131.87
63.61
41.65
O
NH
N
H
O
2m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

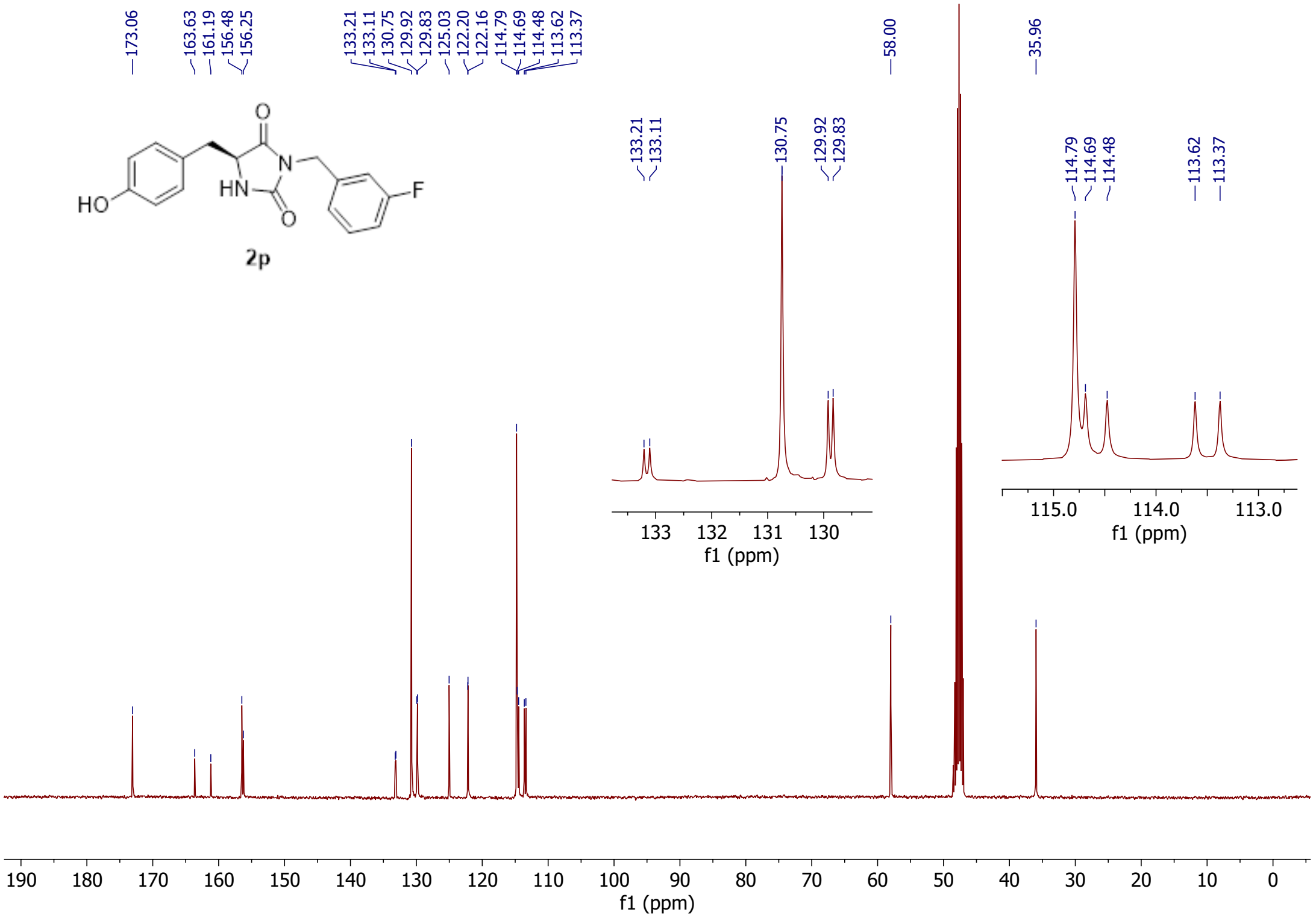

9.21
8.15
8.14
6.94
6.92
6.64
6.62
4.27
4.27
3.16
3.12
2.85
2.84
2.84
2.83
1.18
1.17
1.17
0.91
0.91
0.77
0.75
0.73
HO
HN
N
O
O
2n
4.27
4.27
4.32 4.30 4.28 4.26 4.24 4.22
f1 (ppm)
1.00
1.00
2.05
2.00
1.00
2.01
2.00
2.08
2.15
2.93
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

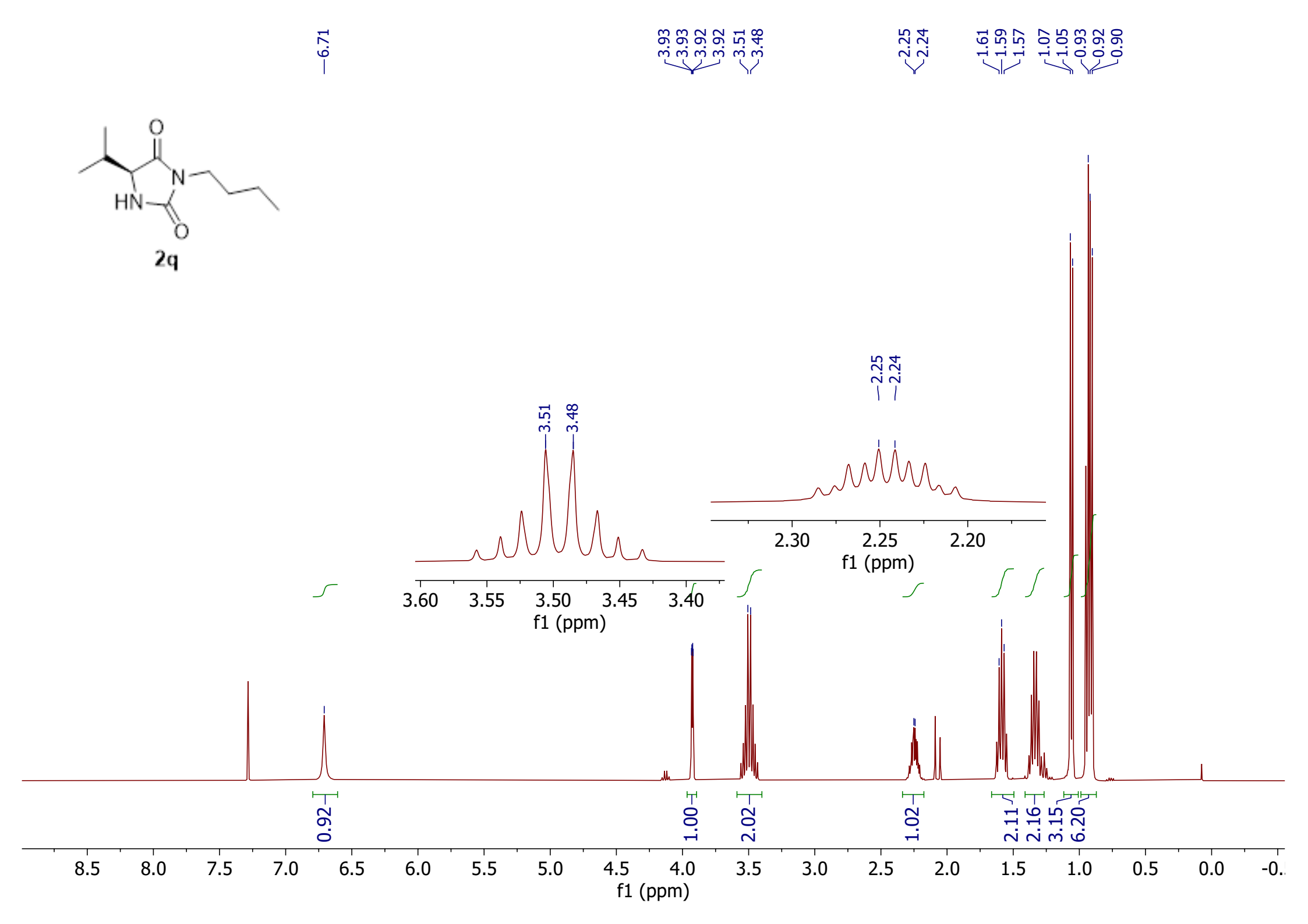

173.96
157.12
156.68
131.21
125.32
115.20
57.57
37.50
35.89
29.91
19.53
13.98
O
N
HN
O
HO
2n
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

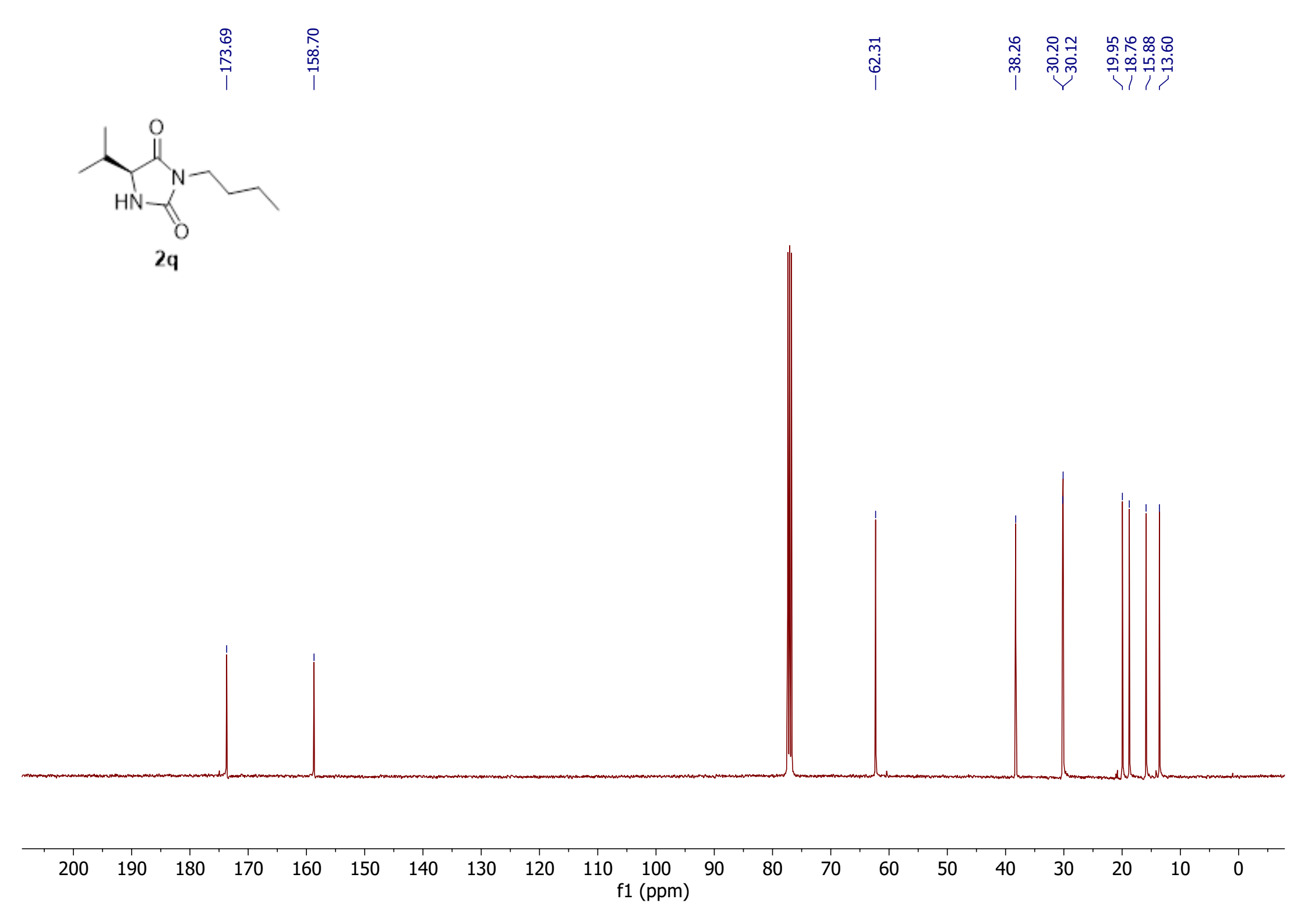

9.29
8.28
7.16
7.15
7.15
7.14
6.92
6.90
6.68
6.68
6.68
6.67
6.67
6.61
6.60
6.60
6.59
4.41
4.38
4.37
4.37
4.28
4.26
2.89
2.89
2.87
2.86
2.86
2.85
2.83
2.82
HO
HN
O
N
O
2o
1.00
1.00
2.94
1.96
1.94
1.95
2.98
1.95
f1 (ppm)
2.92 2.90 2.88 2.86 2.84 2.82 2.80
f1 (ppm)

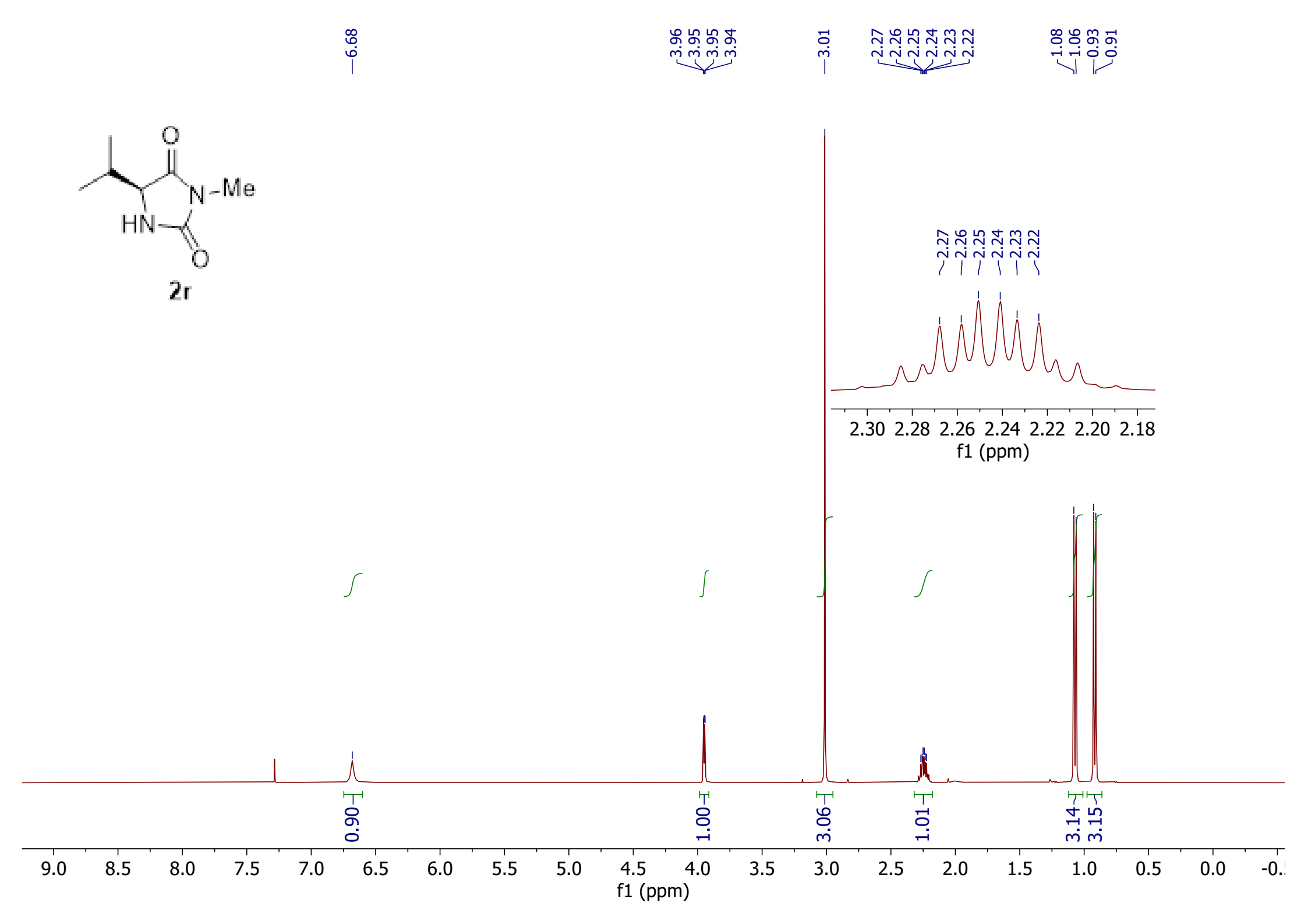

173.86
156.87
156.84
136.79
131.46
128.72
127.37
126.89
125.40
115.53
58.03
41.16
35.70
HO
HN
N
O
O
O
2o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

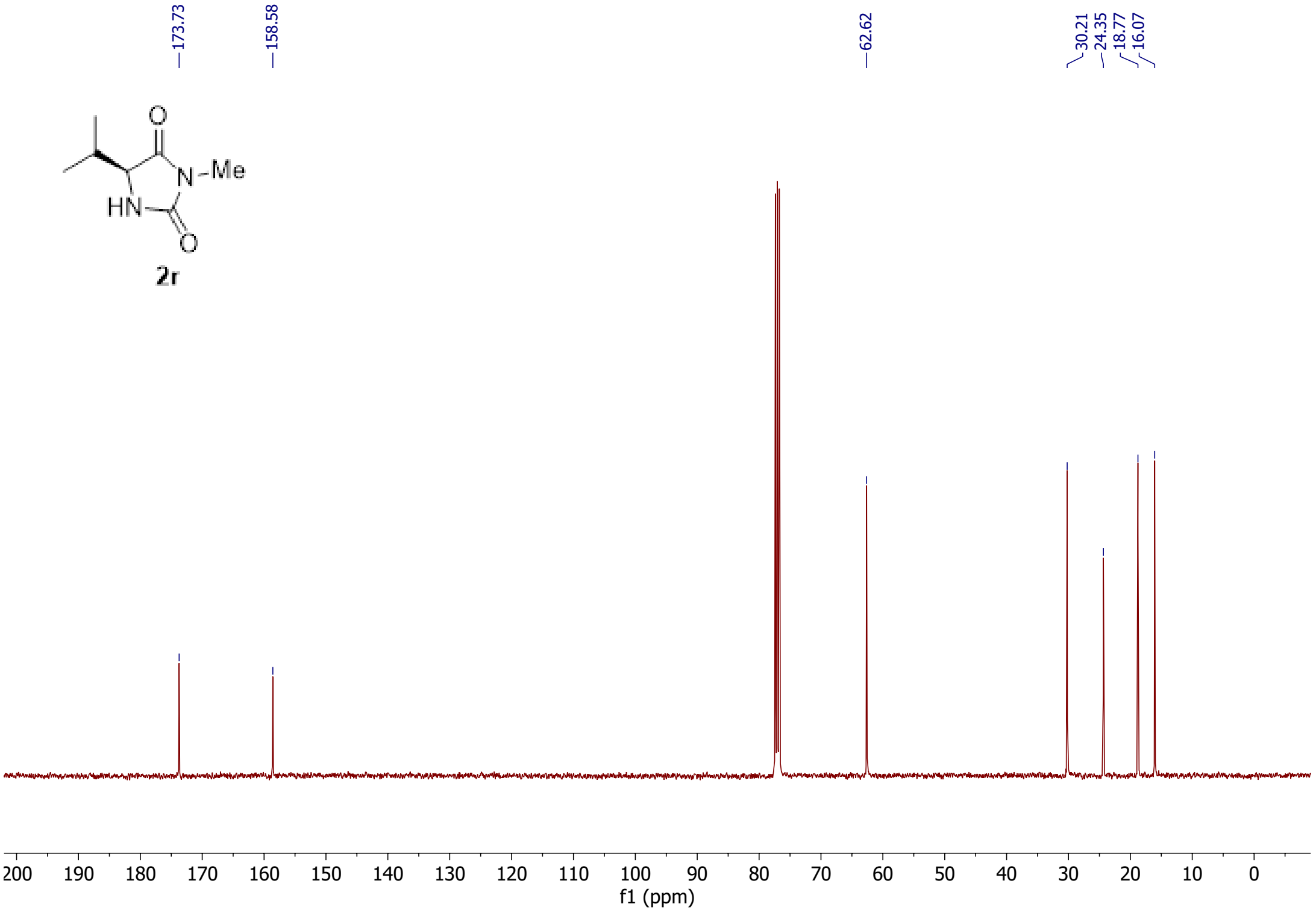

7.43
7.41
7.41
7.39
7.37
7.09
7.07
6.91
6.91
6.89
6.89
6.85
6.83
6.76
6.74
4.88
4.48
4.46
4.45
3.09
3.08
3.07
HO
HN
N
O
O
F
2p
6.91
6.91
6.89
6.89
6.85
6.83
6.76
6.74
6.95 6.90 6.85 6.80 6.75 6.70
f1 (ppm)
4.48
4.46
4.45
4.50 4.48 4.46 4.44
f1 (ppm)
3.09
3.08
3.07
3.15 3.10 3.05 3.00
f1 (ppm)
1.00
2.99
1.00
0.98
1.97
2.88
1.00
2.00
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

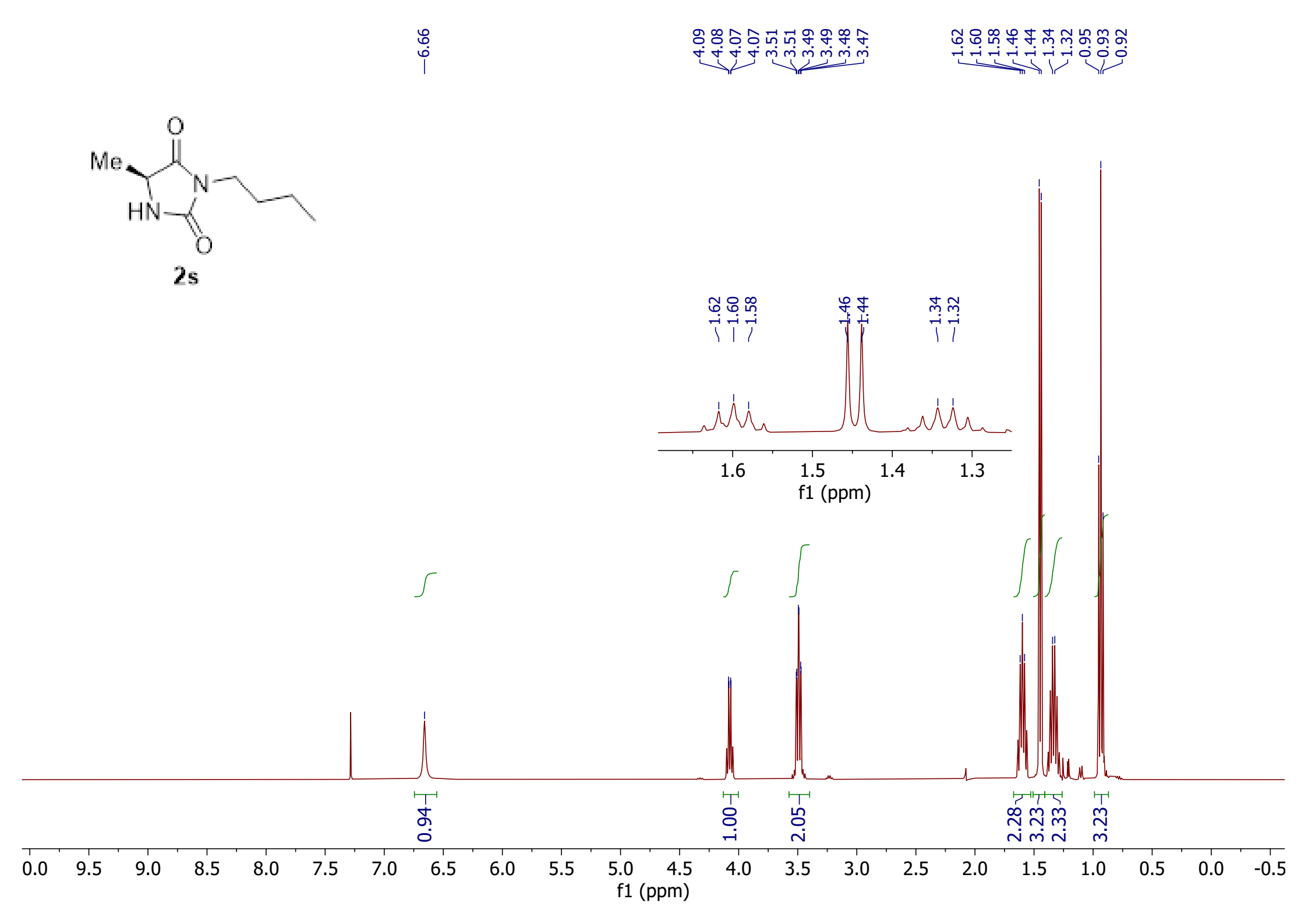

173.06
163.63
161.19
156.48
156.25
133.21
133.11
130.75
129.92
129.83
125.03
122.20
122.16
114.79
114.69
114.48
113.62
113.37
58.00
35.96
HO
HN
N
O
O
F
2p
133.21
133.11
130.75
129.92
129.83
133
132
131
130
f1 (ppm)
114.79
114.69
114.48
113.62
113.37
115.0
114.0
113.0
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

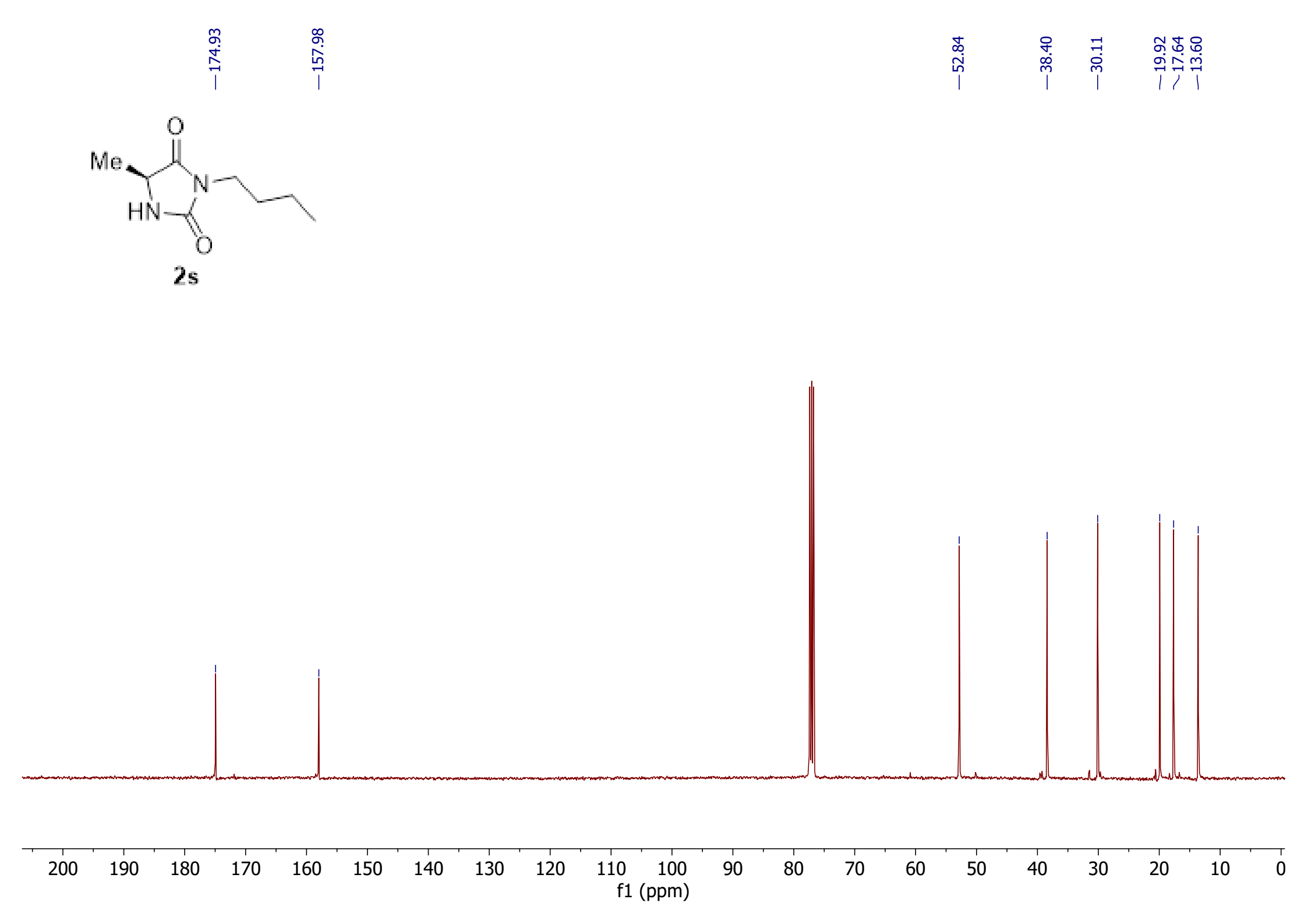

6.71
3.93
3.93
3.92
3.92
3.51
3.48
2.25
2.24
1.61
1.59
1.57
1.07
1.05
0.93
0.92
0.90
O
N
HN
O
2q
3.51
3.48
3.60
3.55
3.50
3.45
3.40
f1 (ppm)
2.25
2.24
2.30
2.25
2.20
f1 (ppm)
0.92
1.00
2.02
1.02
2.11
2.16
3.15
6.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

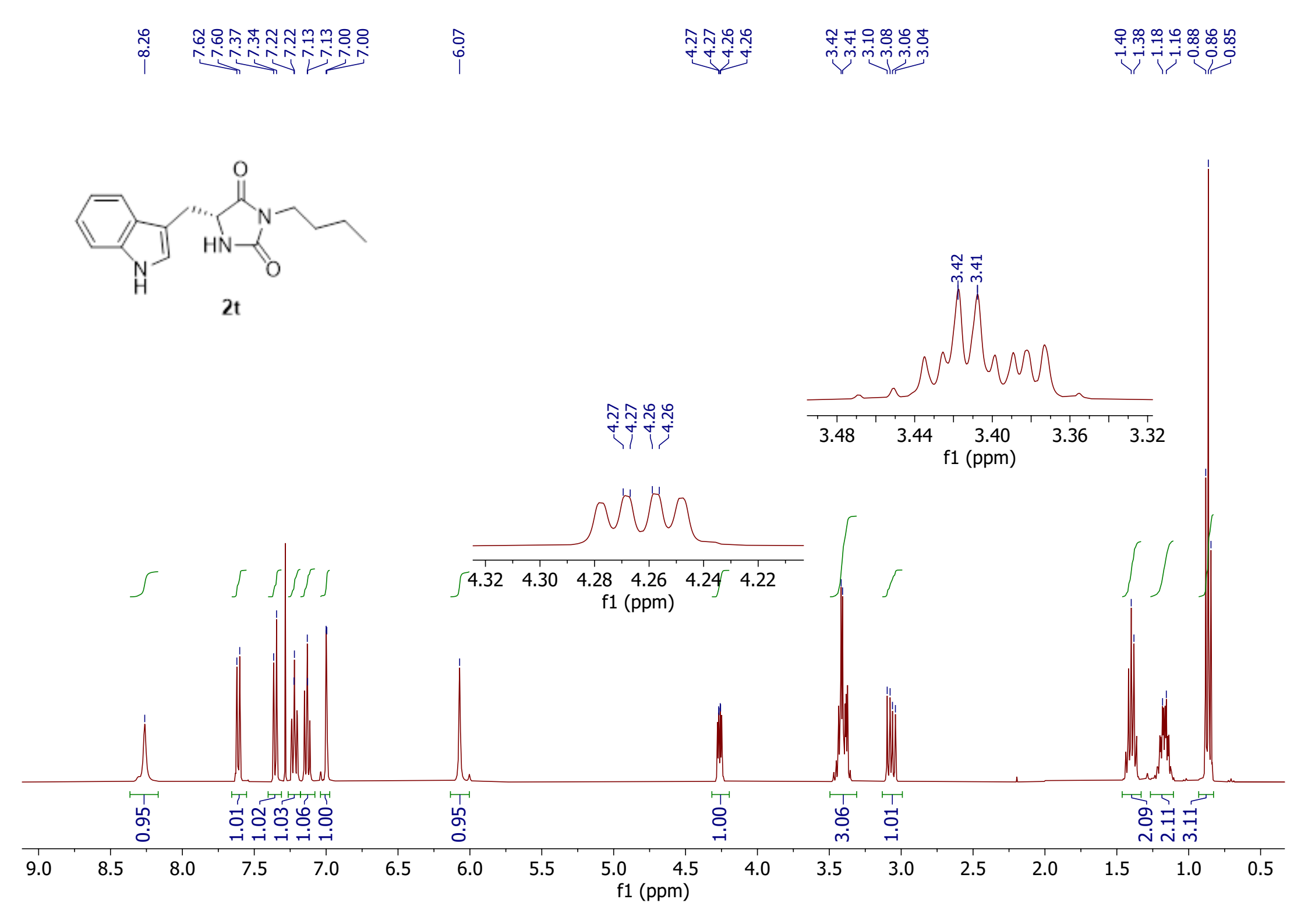

173.69
158.70
62.31
38.26
30.20
30.12
19.95
18.76
15.88
13.60
O
N
HN
O
2q
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

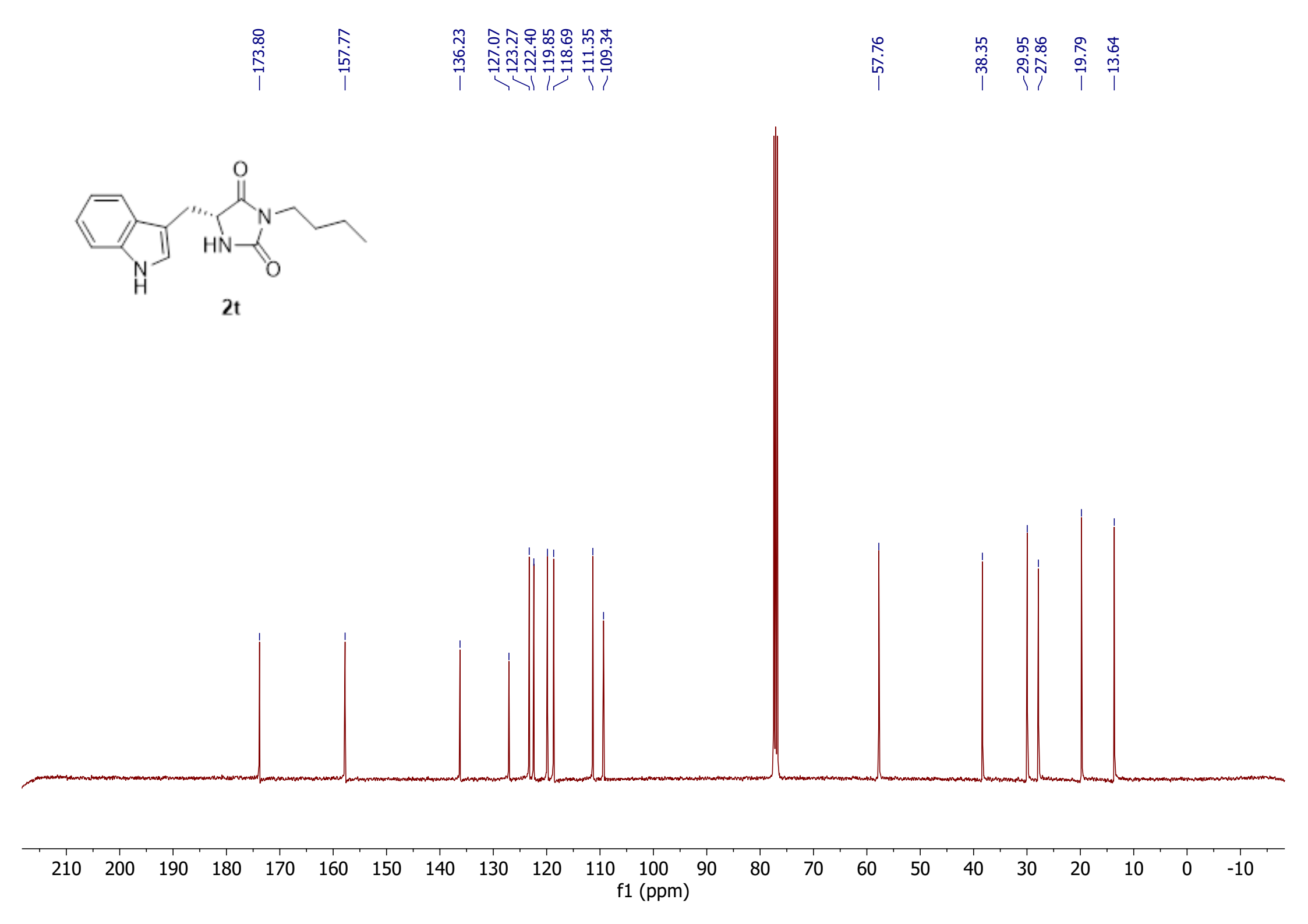

6.68
3.96
3.95
3.95
3.94
3.01
2.27
2.26
2.25
2.24
2.23
2.22
1.08
1.06
0.93
0.91
O
N-Me
HN
O
2r
2.27
2.26
2.25
2.24
2.23
2.22
2.30 2.28 2.26 2.24 2.22 2.20 2.18
f1 (ppm)
0.90
1.00
3.06
1.01
3.14
3.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

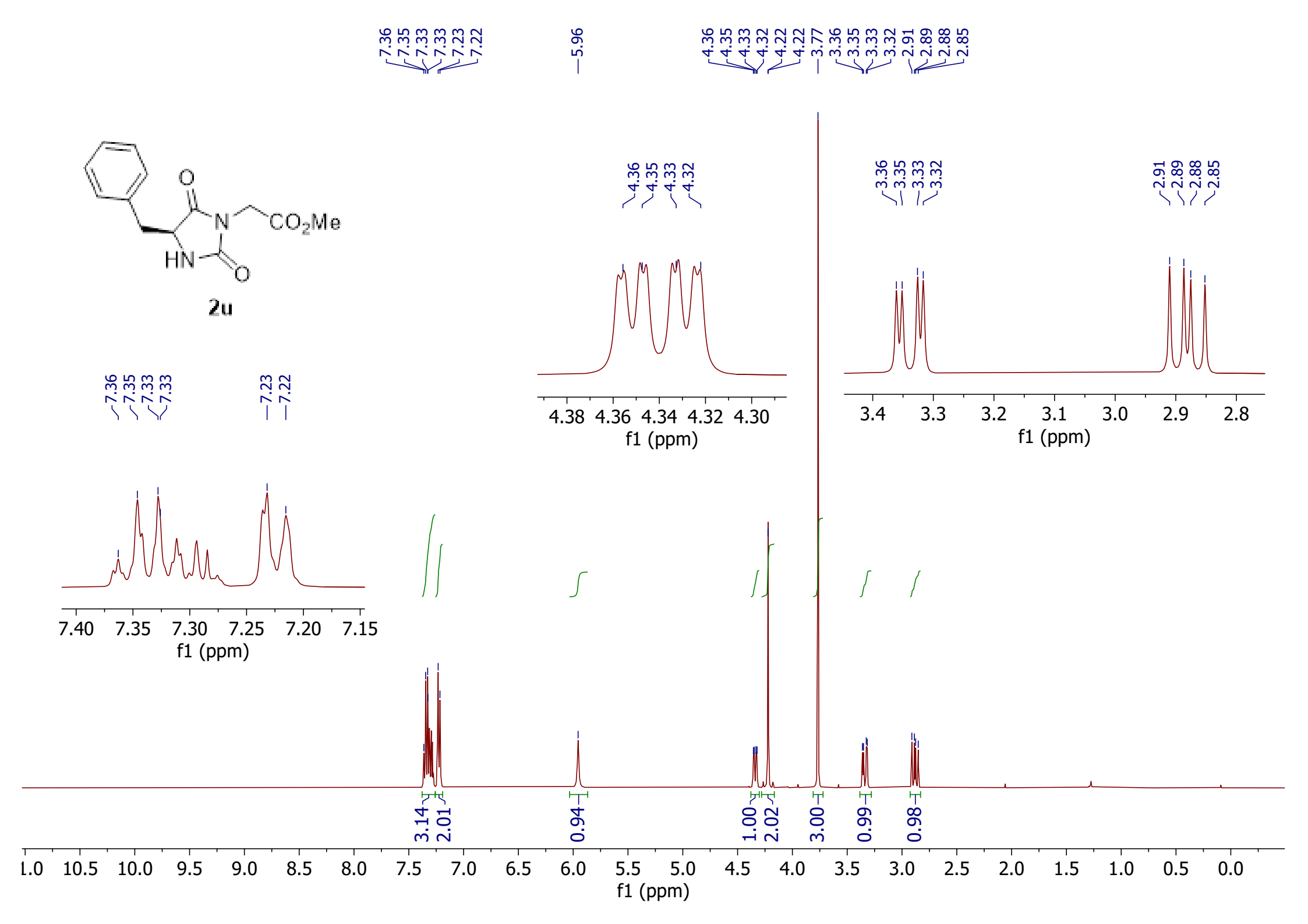

173.73
158.58
62.62
30.21
24.35
18.77
16.07
O
N
Me
HN
O
2r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

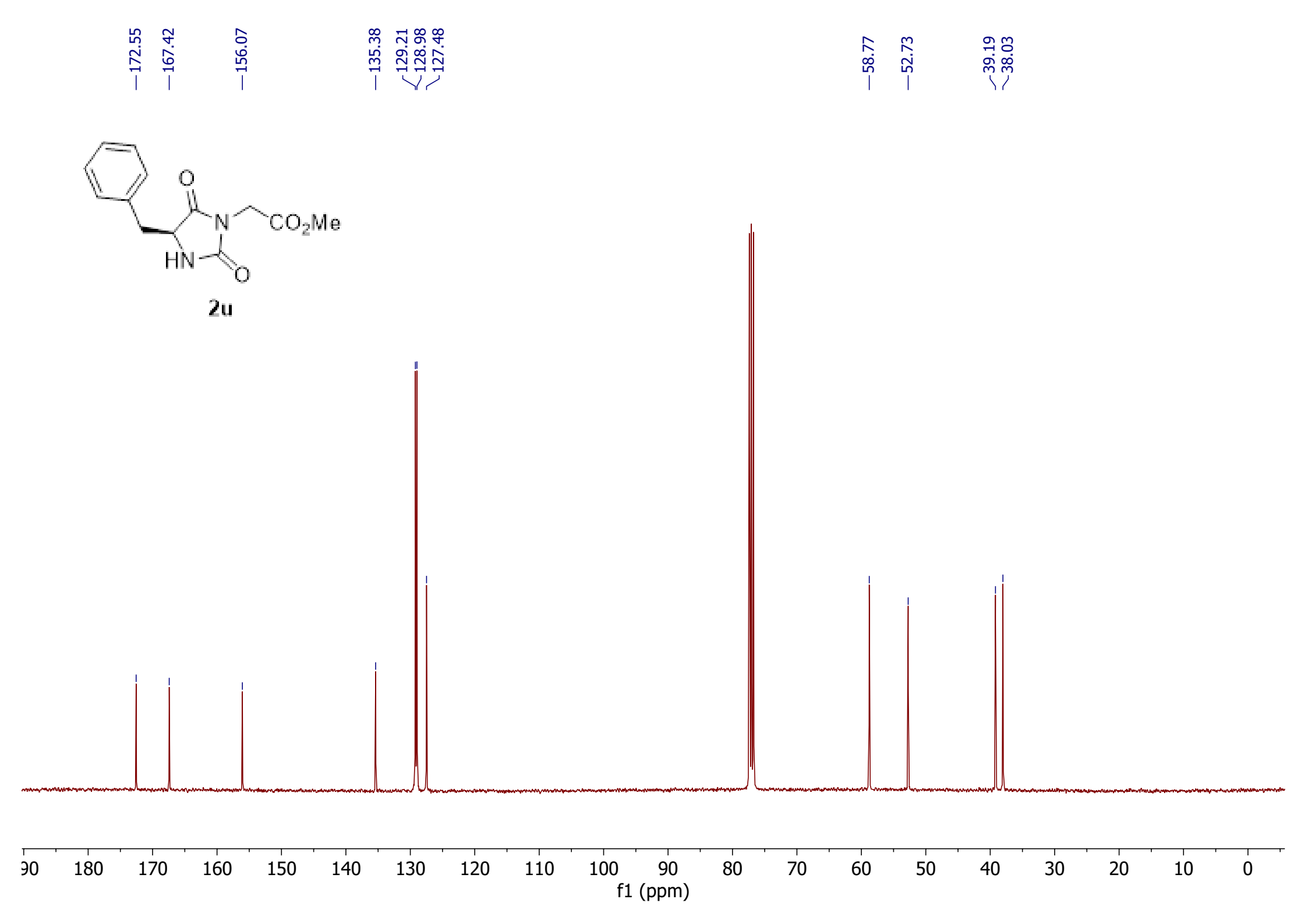

6.66
4.09
4.08
4.07
4.07
3.51
3.51
3.49
3.49
3.48
3.47
1.62
1.60
1.58
1.46
1.44
1.34
1.32
0.95
0.93
0.92
Me
HN
O
O
N
2s
1.62
1.60
1.58
1.46
1.44
1.34
1.32
1.6
1.5
1.4
1.3
f1 (ppm)
0.94
1.00
2.05
2.28
3.23
2.33
3.23
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

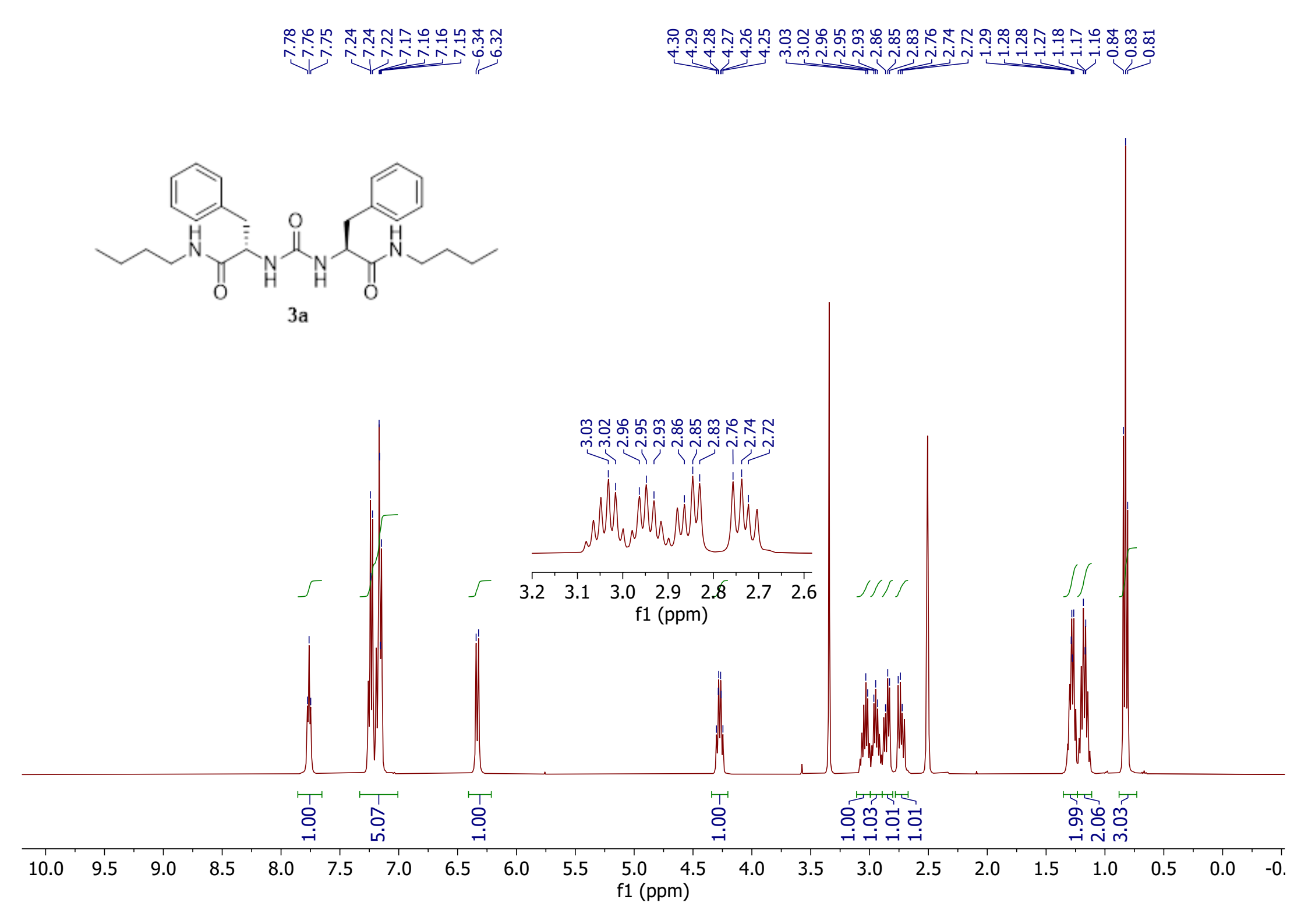

174.93
157.98
52.84
38.40
30.11
19.92
17.64
13.60
Me
HN
O
O
N
2s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

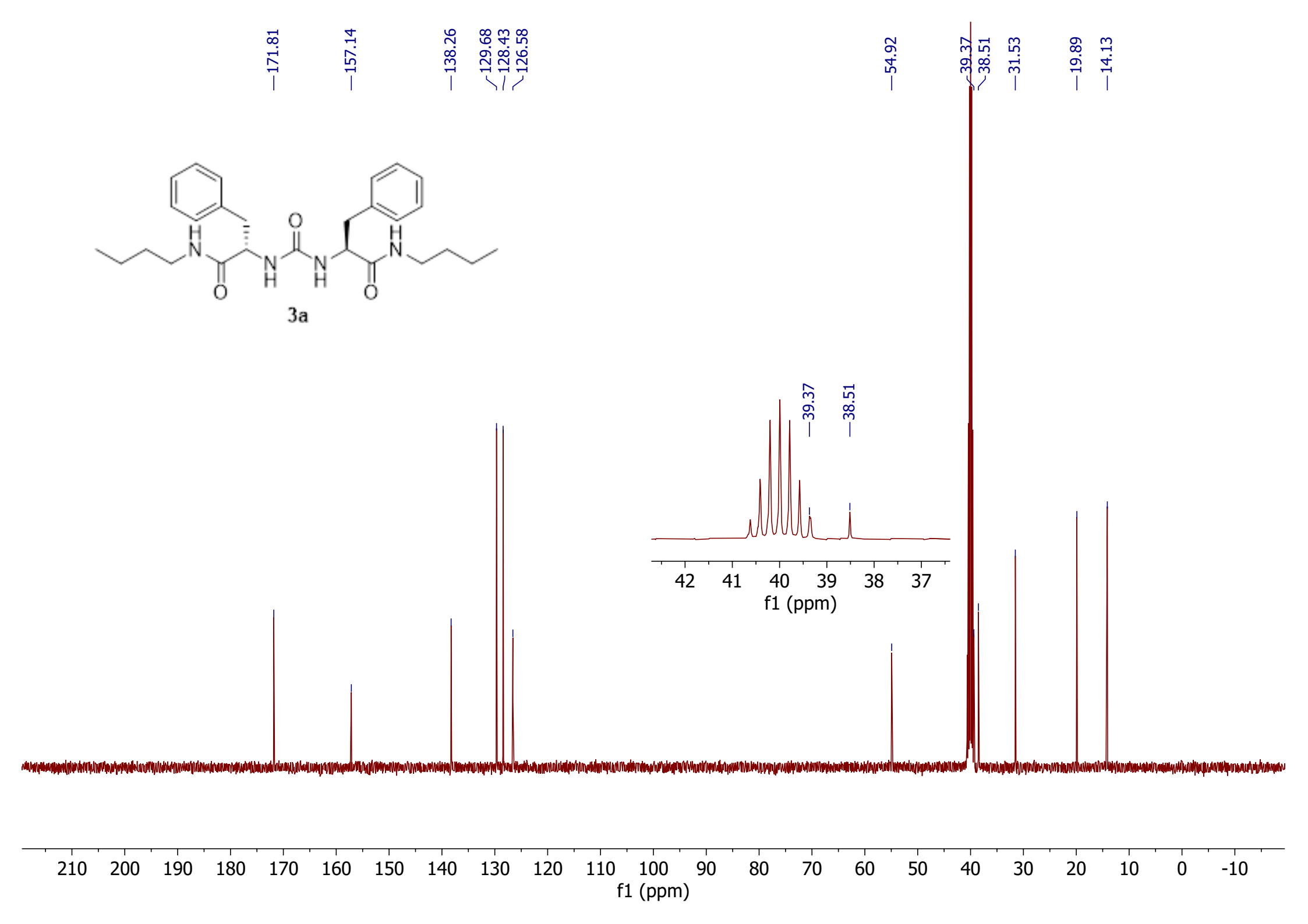

8.26
7.62
7.60
7.37
7.34
7.22
7.22
7.13
7.13
7.00
7.00
6.07
4.27
4.27
4.26
4.26
3.42
3.41
3.10
3.08
3.06
3.04
1.40
1.38
1.18
1.16
0.88
0.86
0.85
O
N
HN
O
N
H
2t
3.42
3.41
3.48
3.44
3.40
3.36
3.32
f1 (ppm)
4.27
4.27
4.26
4.26
4.32
4.30
4.28
4.26
4.24
4.22
f1 (ppm)
0.95
1.01
1.02
1.03
1.06
1.00
0.95
1.00
3.06
1.01
2.09
2.11
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

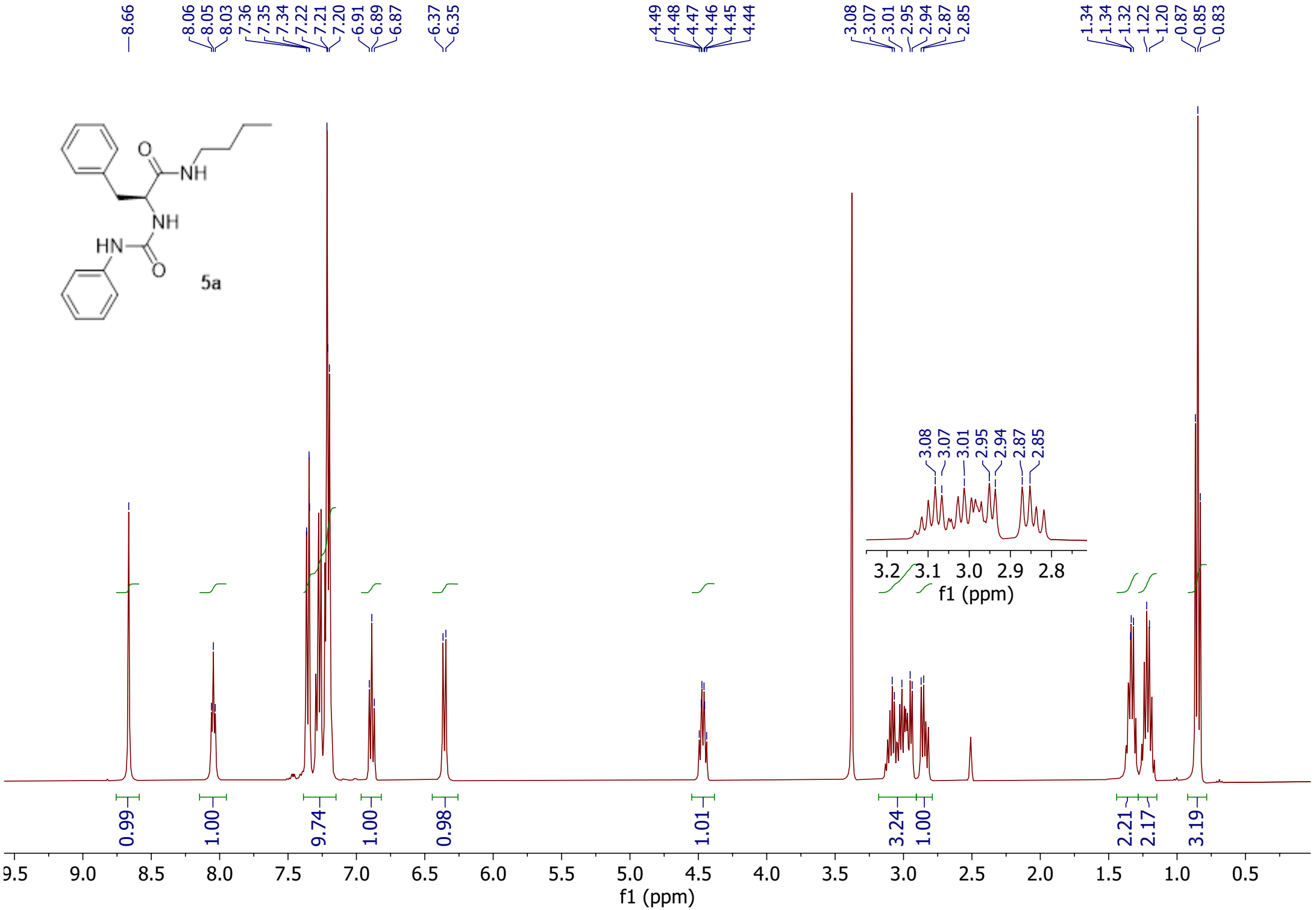

173.80
157.77
136.23
127.07
123.27
122.40
119.85
118.69
111.35
109.34
57.76
38.35
29.95
27.86
19.79
13.64
O
N
HN
O
N
H
2t
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

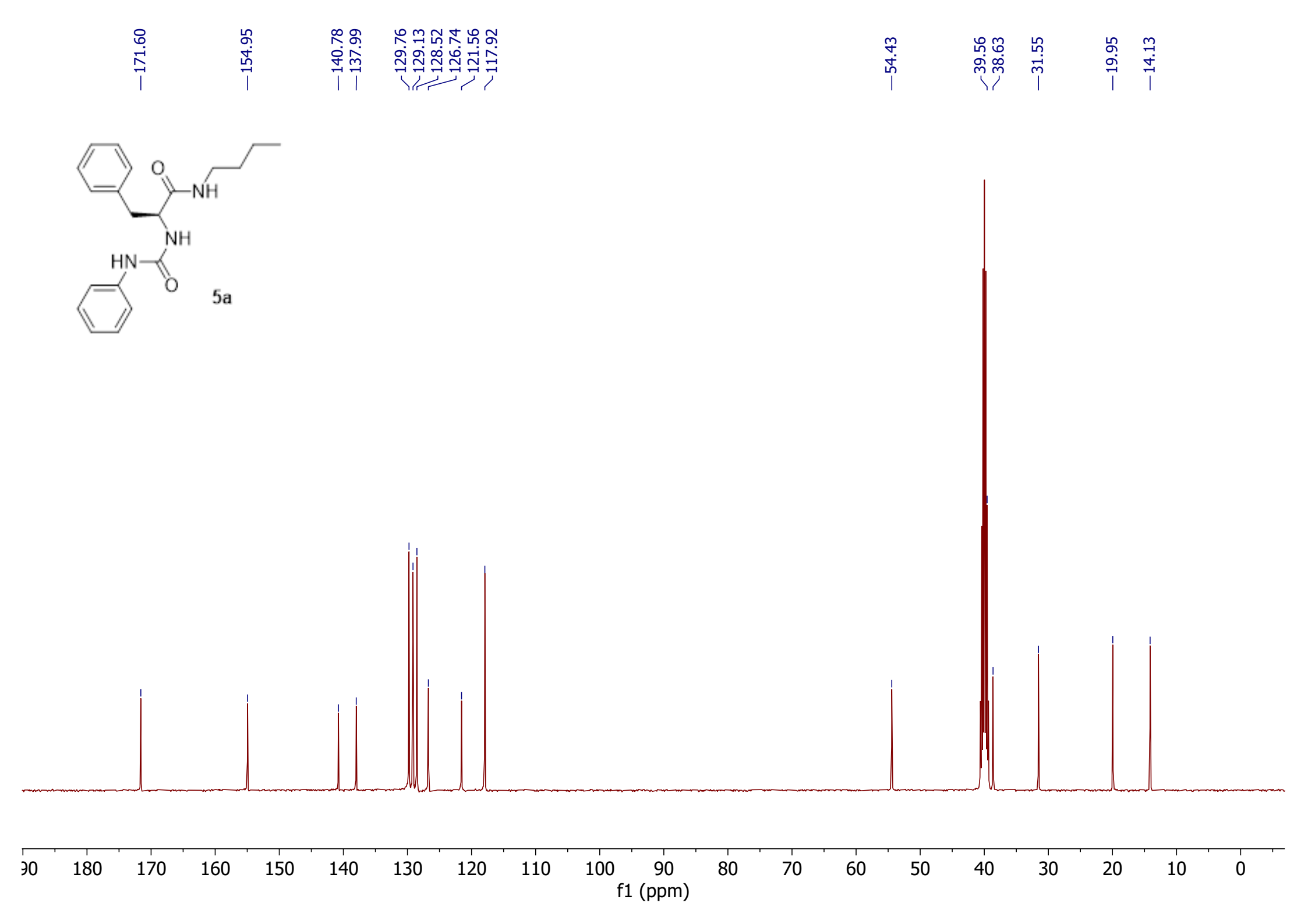

7.36
7.35
7.33
7.33
7.23
7.22
5.96
4.36
4.35
4.33
4.32
4.22
4.22
3.77
3.36
3.35
3.33
3.32
2.91
2.89
2.88
2.85
O
N
CO2Me
HN
O
2u
4.38 4.36 4.34 4.32 4.30
f1 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)
7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
3.14
2.01
0.94
1.00
2.02
3.00
0.99
0.98
f1 (ppm)


172.55
167.42
156.07
135.38
129.21
128.98
127.48
58.77
52.73
39.19
38.03
O
N
CO2Me
HN
O
2u
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.78
7.76
7.75
7.24
7.24
7.22
7.17
7.16
7.16
7.15
6.34
6.32
4.30
4.29
4.28
4.27
4.26
4.25
3.03
3.02
2.96
2.95
2.93
2.86
2.85
2.83
2.76
2.74
2.72
1.29
1.28
1.28
1.27
1.18
1.17
1.16
0.84
0.83
0.81
3a
1.00
5.07
1.00
1.00
1.00
1.03
1.01
1.01
1.99
2.06
3.03
f1 (ppm)
f1 (ppm)


171.81
157.14
138.26
129.68
128.43
126.58
54.92
39.37
38.51
31.53
19.89
14.13
3a
39.37
38.51
42
41
40
39
38
37
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.66
8.06
8.05
8.03
7.36
7.35
7.34
7.22
7.21
7.20
6.91
6.89
6.87
6.37
6.35
4.49
4.48
4.47
4.46
4.45
4.44
3.08
3.07
3.01
2.95
2.94
2.87
2.85
1.34
1.34
1.32
1.22
1.20
0.87
0.85
0.83
O
NH
NH
HN
O
5a
0.99
1.00
9.74
1.00
0.98
1.01
3.24
1.00
2.21
2.17
3.19
f1 (ppm)
f1 (ppm)


171.60
154.95
140.78
137.99
129.76
129.13
128.52
126.74
121.56
117.92
54.43
39.56
38.63
31.55
19.95
14.13
O
NH
NH
HN
O
5a
f1 (ppm)