Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Solvent free synthesis of *N*-substituted succinimides

Synthesis adapted from a literature procedure.[1] To succinic anhydride (1 eq.) was added the appropriate amine (1.0 - 1.1 eq.) and the reaction mixture was stirred for 30 minutes before heating as a melt at 175 °C on a heating block, under N_2. Evolved water was removed and collected into a separate flask via a distillation arm. When at full conversion the reaction was allowed to cool and the crude product was purified, as described, to yield the *N*-substituted succinimide.

Batch Irradiation of *N*-substituted succinimides with a 36 W low pressure Hg lamp

A solution of the appropriate *N*-substituted succinimide in degassed acetonitrile (450 mL) was irradiated using a water-cooled quartz immersion well reactor with a 36 W UVC PL-L low pressure Hg lamp (half its length surrounded by solution). Photochemical reactions were followed for their duration by NMR using 1,3,5-trimethoxybenzene as an internal standard. In all cases, a stock solution of this (0.05M, MeCN) was added to aliquots of the reaction mixture prior to NMR sample preparation. The solvent was removed *in vacuo* and the crude product was purified by flash column chromatography, where required.

Flow Irradiation of *N*-substituted succinimides

A solution of the appropriate *N*-substituted succinimide in degassed acetonitrile was irradiated with 3×36 W UVC PL-L FEP wrapped flow reactors,[2] connected in series, using an FMI valveless piston pump to control the flow rate. The solvent was removed *in vacuo* and the crude product was purified by flash column chromatography, where required.

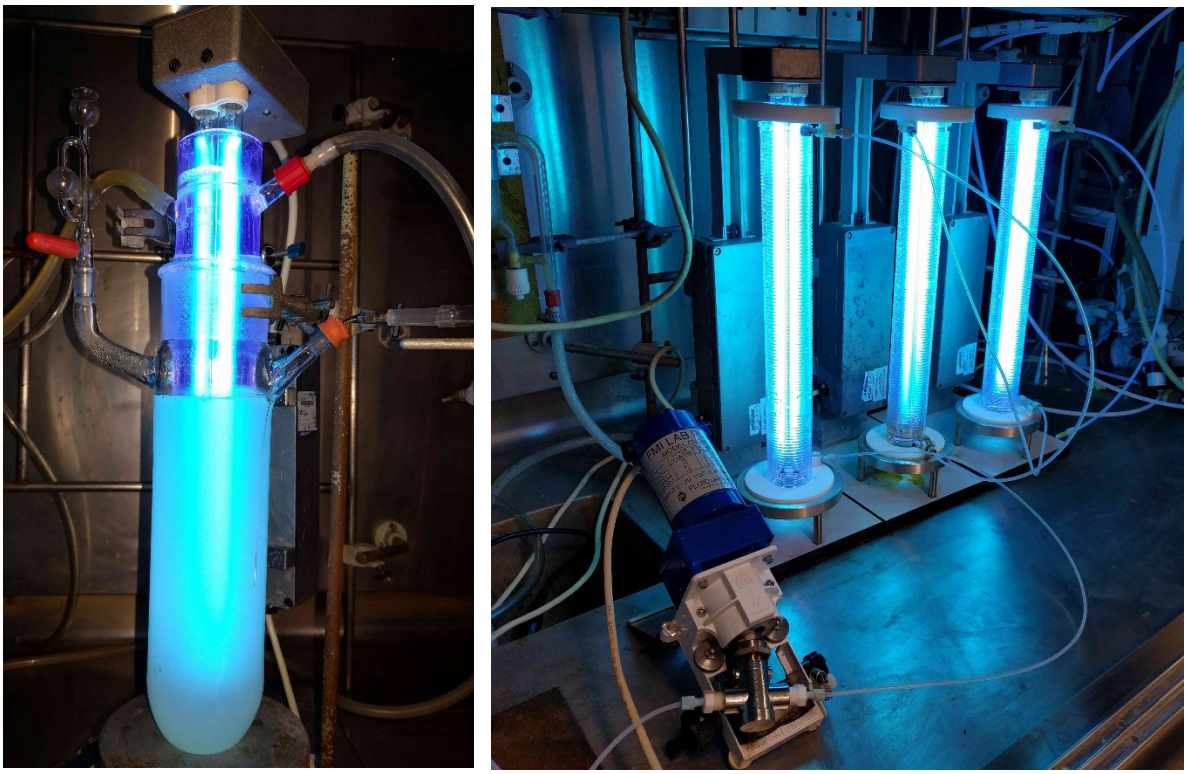
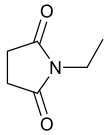


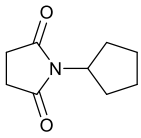
Figure 1: Left: Quartz immersion well reactor with 450 ml of solution surrounding half a 36 W UVC PL-L lamp; Right: 3 × 36 W UVC PL-L FEP wrapped flow reactors with FMI valveless piston pump

_N_-Ethylsuccinimide 5



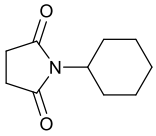
The general procedure for solvent free synthesis of *N*-substituted succinimides was followed. To succinic anhydride (160 g, 1.6 mol, 1.0 eq.) was added 2M ethylamine in THF (800 ml, 1.6 mol, 1.0 eq.) at 0 °C, and the resulting solution was stirred for 1 hour. The solvent was removed in vacuo, to give a white solid, which was heated neat at 175 °C for 16 hours. The mixture was cooled to room temperature and purified by vacuum distillation (120 °C at 2.1 mbar) to yield *N*-ethylsuccinimide **5** (194 g, 96%) as a colourless, low melting, crystalline solid; ν_{max} (neat)/cm^{-1} 1649 (CO); δ_H (400 MHz, $CDCl_3$) 3.52 (q, *J* = 7.2 Hz, 2H, -NC**H₂**CH_3), 2.66 (s, 4H, -COC**H₂**C**H₂**CO-), 1.12 (t, *J* = 7.2 Hz, 3H, -NCH_2C**H₃**); δ_C (101 MHz, $CDCl_3$) 177.1 (CO × 2), 33.7 (CH_2), 28.2 (CH_2 × 2), 13.0 (CH_3); ESI HRMS [MH^+] *m/z* 128.0709 ($C_6H_{10}NO_2$ requires 128.0706). Data in accordance with literature.[3]

***N*-(Cyclopentyl)succinimide 7a**



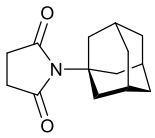
The general procedure for solvent free synthesis of *N*-substituted succinimides was followed. Succinic anhydride (100.1 g, 1.0 mol, 1.0 eq.) and cyclopentylamine (103.7 mL, 1.05 mol, 1.05 eq.) were mixed neat, to give a pale green oil, which was heated neat at 175 °C for 16 hours. The crude mixture was filtered through a silica plug (20% EtOAc in hexanes) and the solvent removed *in vacuo*, to yield *N*-(cyclopentyl)succinimide **7a** (136.9 g, 82%) as a pale yellow solid; mp 69 – 70 °C (EtOAc/hexanes); ν_{max} (neat)/cm^{-1} 2985 (CH), 1684 (CO); δ_H (400 MHz, $CDCl_3$) 4.44 (p, *J* = 8.6 Hz, 1H, -C**H**-), 2.61 (s, 4H, -COC**H$_2$**C**H$_2$**CO-), 2.02 – 1.91 (m, 2H, -CHC**H**HCH$_2$- × 2), 1.91 – 1.80 (m, 2H, -CHCH**H**CH$_2$- × 2), 1.80 – 1.71 (m, 2H, -CHCH$_2$C**H**H- × 2), 1.60 – 1.48 (m, 2H, -CHCH$_2$CH**H**- × 2); δ_C (101 MHz, $CDCl_3$) 177.3 (CO × 2), 51.6 (CH), 28.5 (CH_2 × 2), 28.0 (CH_2 × 2), 25.1 (CH_2 × 2); λ_{max} (MeCN)/nm = 215, 243; ESI HRMS [MH$^+$] *m/z* 168.1029 ($C_9H_{13}NO_2$ requires 167.0946). Data in accordance with literature.[4]

***N*-(Cyclohexyl)succinimide 7b**



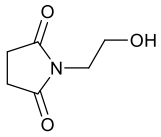
The general procedure for solvent free synthesis of *N*-substituted succinimides was followed. Succinic anhydride (100.1 g, 1.0 mol, 1.0 eq.) and cyclohexylamine (120.1 mL, 1.05 mol. 1.05 eq.) were mixed neat, to give a white solid, which was heated neat at 175 °C for 12 hours. The crude mixture was refluxed in MeCN (equal volume), cooled to room temperature and the precipitate filtered off. The solvent of the filtrate was removed *in vacuo*, to yield *N*-(cyclohexyl)succinimide **7b** (135.6 g, 74%) as a pale yellow solid; mp 47 °C (EtOAc/hexanes) (lit. 44 – 46 °C)[5]; ν_{max} (neat)/cm^{-1} 2983 (CH), 1684 (CO); δ_H (400 MHz, $CDCl_3$) 3.90 (tt, *J* = 12.3, 3.9 Hz, 1H, -NC**H**-), 2.58 (s, 4H, -COC**H$_2$**C**H$_2$**CO-), 2.07 (qd, *J* = 12.4, 3.2 Hz, 2H, -CHC**H**H- × 2), 1.81 – 1.67 (m, 2H, -CHCH$_2$C**H**H- × 2), 1.58 (m, 1H –CHCH$_2$CH$_2$C**H**H), 1.55 – 1.46 (m, 2H, -CHCH**H**- × 2), 1.30 – 1.07 (m, 3H, -CHCH$_2$CH**H**- × 2, -CHCH$_2$CH$_2$CH**H**); δ_C (101 MHz, $CDCl_3$) 177.3 (CO × 2), 51.6 (CH), 28.7 (CH_2 x 2), 28.0 (CH_2 x 2), 25.8 (CH_2 x 2), 24.9 (CH_2).; λ_{max} (MeCN)/nm = 210, 252; ESI HRMS [MH$^+$] *m/z* 196.1331 ($C_{11}H_{18}NO_2$ requires 196.1332). Data in accordance with literature.[5]

***N*-(Adamantyl)succinimide 7c**



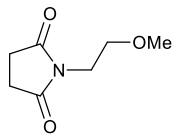
The general procedure for solvent free synthesis of *N*-substituted succinimides was followed. Succinic anhydride (16.5 g, 165 mmol, 1.0 eq.) and adamantan-1-amine (25.0 g, 165 mmol, 1.0 eq.) were mixed neat at room temperature to give a pale green oil, which was heated at 175 °C for 16 hours. The crude mixture was refluxed in MeCN (200 mL) for 30 minutes, cooled, and the precipitate filtered off. The solvent was removed *in vacuo* to yield *N*-(adamantyl)succinimide **7c** (27.2 g, 70%) as a yellow solid; mp 117 - 118 °C (hexanes) (lit. 118 °C, hexanes)[6]; ν_{max} (neat)/cm^{-1} 2915 (CH), 1689 (CO); δ_H (400 MHz, $CDCl_3$) 2.52 (s, 4H, -COC**H₂**C**H₂**CO-), 2.37 (d, *J* = 3.0 Hz, 6H, -NC(C**H₂**)**₃**), 2.15 – 2.00 (m, 3H, C**H** × 3), 1.67 (m, 6H, C**H₂** × 3); δ_C (101 MHz, $CDCl_3$) 178.56 (CO × 2), 61.06 (C), 39.29 (CH_2 × 3), 36.14 (CH × 3), 29.71 (CH_2 × 3), 28.61 (CH_2 × 2).; λ_{max} (MeCN)/nm = 216, 260; ESI HRMS [MNa^+] *m/z* 256.1307 ($C_{14}H_{19}NNaO_2$ requires 256.1308). Data in accordance with literature.[6]

***N*-(Hydroxyethyl)succinimide 7d**



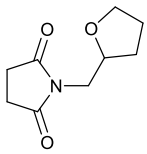
The general procedure for solvent free synthesis of *N*-substituted succinimides was followed. Ethanolamine (66 mL, 1.1 mol, 1.1 eq.) was added slowly to succinic anhydride (101 g, 1.0 mol, 1.0 eq.) at 0 °C to give a green oil, which was heated to 170 °C for 12 hours. The crude mixture was filtered through a silica plug (5% MeOH in DCM) to remove any baseline materials and the solvent removed *in vacuo*. The mixture was then dissolved in MeCN (150 mL) and the solids filtered off. The filtrate was evaporated to dryness and the solid was recrystallized from EtOAc (equal volume of EtOAc) to yield *N*-(hydroxyethyl)succinimide **7d** (95.9 g, 67%) as pale brown crystals; mp 63 - 65 °C (TBME) (lit. 61 - 62 °C)[7]; ν_{max} (neat)/cm^{-1} 3397 (OH), 2884 (CH), 1692 (CO); δ_H (400 MHz, CD_3OD) 3.67 (2H, m, -NC**H₂**-), 3.61 (2H, m, -C**H₂**OH), 2.69 (4H, s, -COC**H₂**C**H₂**CO-); δ_C (101 MHz, CD_3OD) 177.9 (CO × 2), 60.2 (CH_2), 41.5 (CH_2), 28.2 (CH_2 × 2); λ_{max} (MeCN)/nm = 221, 245; CI HRMS [MH^+] *m/z* 144.0662 ($C_6H_{10}NO_3$ requires 144.0661). Data in accordance with literature.[7]

***N*-(2-Methoxyethyl)succinimide 7e**



The general procedure for solvent free synthesis of *N*-substituted succinimides was followed by adding 2-methoxyethylamine (63.9 mL, 735 mmol, 1.05 eq.) to succinic anhydride (70.7 g, 700 mmol, 1.0 eq.) in THF (200 mL) at 0°C. The solvent was removed *in vacuo* to give a white solid which was heated to 175 °C for 12 hours. The crude mixture was purified by flash column chromatography (5% MeOH in DCM) to yield *N*-(2-methoxyethyl)succinimide **7e** (94.1 g, 85%) as an orange oil; ν_{max} (neat)/cm^{-1} 2943 (CH), 1770 (CO), 1689 (CO); δ_H (400 MHz, $CDCl_3$) 3.63 (2H, t, *J* = 5.6 Hz, -NC**H$_2$**-), 3.46 (2H, t, *J* = 5.8 Hz, -C**H$_2$**OCH$_3$), 3.24 (3H, s, -OC**H$_3$**), 2.65 (4H, s, -COC**H$_2$**C**H$_2$**CO-) ; δ_C (101 MHz, $CDCl_3$) 117.2 (CO × 2), 65.6 (CH_2), 58.4 (CH_3), 37.9 (CH_2), 28.1 (CH_2 × 2); λ_{max} (MeCN)/nm = 210, 245; CI HRMS [MH^+] *m/z* 158.0813 ($C_7H_{12}NO_3$ requires 158.0817).

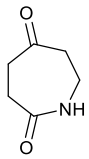
***N*-(Tetrahydrofurfuryl)succinimide 7f**



The general procedure for solvent free synthesis of *N*-substituted succinimides was followed by adding tetrahydrofurfurylamine (79.5 mL, 770 mmol, 1.1 eq.) to succinic anhydride (70.7 g, 700 mmol, 1.0 eq.) in THF (200 mL) at 0°C. The solvent was removed *in vacuo* to give a green oil which was heated at 175 °C for 6 hours. The crude mixture was purified by flash column chromatography (EtOAc) to yield *N*-(tetrahydrofurfuryl)succinimide **7f** (116.8 g, 90%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2943 (CH), 1772 (CO), 1691 (CO); δ_H (400 MHz, $CDCl_3$) 4.15 – 4.09 (1H, m , -NCH$_2$C**H**-THF), 3.81 (1H, m, -CHOC**H**HCH$_2$CH$_2$-), 3.66 (1H, m, -CHOCH**H**CH$_2$CH$_2$-), 3.58 (1H, dd, *J* = 13.4, 8.8, -NC**H**HCH-THF), 3.38 (1H, dd, *J* = 13.4, 4.3, NCH**H**CH-THF), 2.66 (4H, s, -COC**H$_2$**C**H$_2$**CO-), 1.98 – 1.76 (3H, m, -CHOCH$_2$C**H$_2$**C**H**H-), 1.58 – 1.49 (1H, m, -CHOCH$_2$CH$_2$CH**H**-); δ_C (101 MHz, $CDCl_3$) 177.2 (CO × 2), 75.3 (CH), 67.7 (CH_2), 42.5 (CH_2), 29.1 (CH_2), 28.1 (CH_2 × 2), 25.2 (CH_2); λ_{max} (MeCN)/nm = 206, 275; CI HRMS [MH^+] *m/z* 184.0981 ($C_9H_{14}NO_3$ requires 184.0974).

Batch and flow irradiation of N-substituted succinimides

Azepane-2,5-dione 6



The standard batch irradiation procedure was followed by quantitative NMR at 0.04 and 0.12 M using *N*-ethylsuccinimide **5** (2.27 g, 18 mmol) *or* (6.87 g, 54 mmol) in degassed MeCN (450 mL). The solvent was removed *in vacuo* and the crude mixture was purified by flash column chromatography (3% MeOH in DCM) to yield azepane-2,5-dione **6** (1.32 g, 58%) *or* (4.23 g, 62%) as a pale yellow solid; mp 138 °C (MeCN) (Lit. = 139 – 140 °C, MeCN)[8]; ν_{max} (neat)/cm^{-1} 3207 (NH), 1695 (CO), 1650 (CO); δ_H (400 MHz, $CDCl_3$) 3.41 – 3.32 (m, 2H, -NHC**H$_2$**-), 2.57 (m, 6H, -NHCOC**H$_2$**C**H$_2$**COC**H$_2$**-); δ_C (101 MHz, $CDCl_3$) 207.8 (CO), 176.8 (CO), 45.4 (CH_2), 39.2 (CH_2), 38.0 (CH_2), 30.4 (CH_2); ESI HRMS [MH$^+$] *m/z* 128.0709 ($C_6H_{10}NO_2$ requires 128.0706).

Time (hrs)	Yield X (0.12 M)	Yield X (0.04M)
0	0	0
1	25	45
2	39	61
3	47	64
4	51	65
6	62	
8	65	
10	64	
Isolated	4.23 g, **62%**	1.32 g, **58%**

*Table 1: quantitative NMR results of batch irradiation of **5** at 0.04 and 0.12 M*

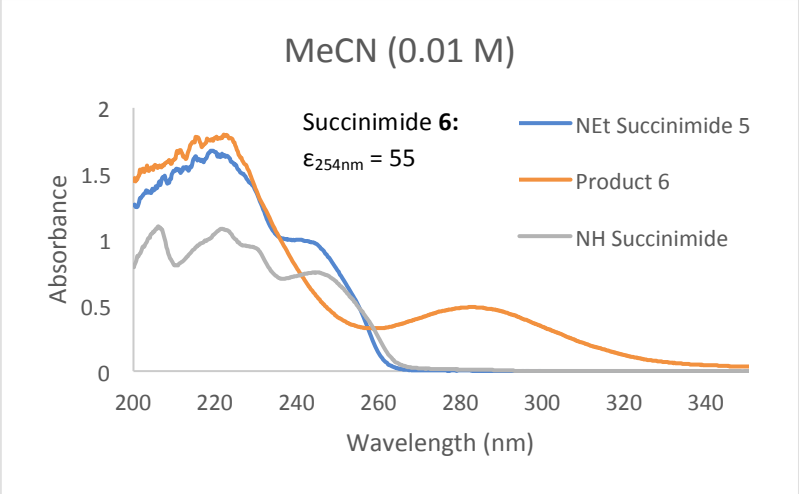


*Figure 2: UV absorption spectrum of succinimide **6** and product **7***

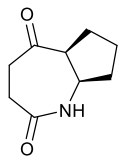
Optimised Flow Irradiation

A solution of *N*-ethylsuccinimide **5** (38.14 g, 300 mmol) in degassed MeCN (2.5 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 8 mL min^{-1}. The solvent was removed *in vacuo* and the product triturated with Et_2O/petrol to remove any residual starting material. Chromatography on silica (10% MeOH in DCM) yielded product **6** as an off-white solid (21.0 g, 55%)

Flow irradiation: further scale-up

A solution of *N*-ethylsuccinimide **5** (76.3 g, 600 mmol) in degassed MeCN (5.0 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* to $1/10^{th}$ of its original volume, and the precipitate was filtered off, to yield azepane-2,5-dione **6** (43 g, 57%) as a pale yellow solid.

(±)-Octahydrocyclopenta[*b*]azepine-2,5-dione 8a



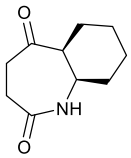
Batch irradiation

The standard batch irradiation procedure was followed over 4.5 hrs by quantitative NMR using *N*-(cyclopentyl)succinimide **7a** (3.00 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* and the crude mixture was purified by trituration using MeCN to yield (±)-octahydrocyclopenta[*b*]azepine-2,5-dione **8a** (1.35 g, 45%) as a yellow solid; mp 188 °C (Toluene); ν_{max} (neat)/cm^{-1} 3259 (NH), 1709 (CO), 1661 (CONH); δ_H (400 MHz, $CDCl_3$) 6.22 (br. s, 1H, N**H**), 4.26 (app. dtd, *J* = 9.1, 6.8, 2.4 Hz, 1H, -NHC**H**-), 3.11 (app. q, *J* = 8.4 Hz, 1H, -COC**H**-), 3.07 – 2.96 (m, 1H, -NHCOC**H**H-), 2.67 – 2.60 (m, 2H, -COC**H_2**-), 2.48 – 2.39 (m, 1H, -NHCOCH**H**-), 2.28 – 2.16 (m, 1H, -COCHC**H**H-), 2.14 – 2.03 (m, 1H, -NHCHC**H**H-), 1.84 – 1.67 (m, 2H, -COCHCH**H**- and –$COCHCH_2C$**H**H-), 1.58 – 1.44 (m, 2H, -$COCHCH_2CH$**H**- and –NHCHCH**H**-); δ_C (101 MHz, $CDCl_3$) 207.0 (CO), 175.1 (CONH), 54.6 (CH), 53.9 (CH), 39.4 (CH_2), 34.7 (CH_2), 30.5 (CH_2), 25.9 (CH_2), 23.4 (CH_2); λ_{max} (MeCN)/nm = 217, 300; CI HRMS [MH^+] *m/z* 167.0941 ($C_9H_{13}NO_2$ requires 167.0946).

Flow irradiation

A solution of *N*-(cyclopentyl)succinimide **7a** (100.12 g, 600 mmol) in degassed MeCN (5.0 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* to $1/10^{th}$ of its original volume, and the precipitate was filtered off, to yield (±)-octahydrocyclopenta[*b*]azepine-2,5-dione **8a** (39.1 g, 38%) as a yellow solid.

(±)-Octahydro-1H-benzo[*b*]azepine-2,5-dione 8b



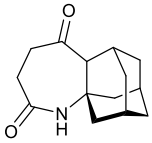
Batch irradiation

The standard batch irradiation procedure was followed over 4.5 hrs by quantitative NMR using *N*-(cyclohexyl)succinimide **7b** (3.26 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* and the crude mixture was purified by trituration using MeCN to yield (±)-octahydro-1H-benzo[*b*]azepine-2,5-dione **8b** (1.53 g, 47%) as a pale yellow solid; mp 166 °C (Toluene); ν_{max} (neat)/cm^{-1} 3227 (NH), 1695 (CO), 1643 (CONH); δ_H (400 MHz, dmso) 7.45 (br. s, 1H, N**H**), 4.17 – 4.11 (m, 1H, -NHC**H**-) 2.78 (ddd, *J* = 14.9, 8.9, 5.9 Hz, 1H, -COC**H**HCHHCO-), 2.74 – 2.66 (m, 1H, -COCHHC**H**HCO-), 2.47 (app. dt, *J* = 11.4, 3.3 Hz, 1H, -COC**H**-), 2.38 (ddd, *J* = 14.3, 8.9, 5.5 Hz, 1H, -COCHHCH**H**CO-), 2.25 – 2.17 (m, 1H, -COCH**H**CHHCO-), 1.77 – 1.17 (m, 8H, 4×C**HH**); δ_C (101 MHz, dmso) 210.7 (CO), 173.5 (CO), 54.4 (CH), 47.1 (CH), 36.2 (CH_2), 30.5 (CH_2), 29.4 (CH_2), 24.4 (CH_2), 23.0 (CH_2), 19.7 (CH_2); λ_{max} (MeCN)/nm = 217, 294; ESI HRMS [MH^+] *m/z* 182.1180 ($C_{10}H_{16}NO_2$ requires 182.1176).

Flow irradiation

A solution of *N*-(cyclohexyl)succinimide **7b** (109.9 g, 600 mmol) in degassed MeCN (5.0 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* to $1/10^{th}$ of its original volume, and the precipitate was filtered off, to yield (±)-octahydro-1H-benzo[*b*]azepine-2,5-dione **8b** (53.6 g, 49%) as a pale yellow solid.

(±)-Octahydro-6,10:8,11a-dimethanocycloocta[*b*]azepine-2,5(1H,5aH)-dione 8c



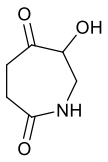
Batch irradiation

The standard batch irradiation procedure was followed over 13 hrs by quantitative NMR using *N*-(adamantyl)succinimide **7c** (4.19 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* and the crude mixture was purified by trituration with MeCN to yield the title compound **8c** (3.27 g, 78%) as a pale yellow solid; mp 211 °C (MeCN); ν_{max} (neat)/cm^{-1} 3113 (NH), 2917 (CH), 1695 (CO), 1647 (CONH); δ_H (400 MHz, $CDCl_3$) 5.81 (br. s, 1H, N**H**), 2.89 (br. s, 1H, -COC**H**-), 2.75 (ddd, *J* = 15.3, 8.5, 3.9 Hz, 1H, -NHCOC**H**HCH$_2$CO-), 2.68 – 2.60 (m, 2H, -NHCOCH$_2$C**H$_2$**CO-), 2.54 (ddd, *J* = 15.3, 8.5, 3.6 Hz, 1H, -NHCOCH**H**CH$_2$CO-), 2.48 (br. s, 1H, -COCHC**H**-), 2.13 (br. s, 1H, -NHCCH$_2$C**H**-), 2.10 – 2.01 (m, 2H, -NHCCH$_2$CHC**H$_2$**-, –NHCCH$_2$C**H**-), 1.92 (apr. t, *J* = 12.2, 2.4 Hz, 2H, -NHCC**H$_2$**-, –NHCC**H$_2$**-), 1.84 – 1.72 (m, 2H, -NHCC**H$_2$**-, –NHCCH$_2$CHC**H$_2$**-), 1.71 – 1.55 (m, 4H, -NHCC**H$_2$**-, -NHCCH$_2$CHC**H$_2$**-, –COCHCHC**H$_2$**- × 2), 1.53 – 1.46 (m, 1H, -NHCCH$_2$CHC**H$_2$**-); δ_C (101 MHz, $CDCl_3$) 208.8 (CO), 174.5 (CONH), 58.7 (CH), 53.6 (C), 47.7 (CH_2), 42.1 (CH_2), 39.8 (CH_2), 36.9 (CH_2), 35.5 (CH_2), 31.7 (CH_2), 31.4 (CH_2), 29.7 (CH), 29.2 (CH), 29.1 (CH); λ_{max} (MeCN/H_2O)/nm = 221, 306; ESI HRMS [MH^+] *m/z* 234.1484 ($C_{14}H_{20}NO_2$ requires 234.1489).

Flow irradiation

A solution of *N*-(adamantyl)succinimide **7c** (9.78 g, 45 mmol) in degassed MeCN (5.0 L, 0.01 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 1 mL min^{-1}. The solvent was removed *in vacuo* to 1/10th of its original volume, and the precipitate was filtered off, to yield the title compound **8c** (6.84 g, 69%) as a pale yellow solid.

6-Hydroxyazepane-2,5-dione 8d



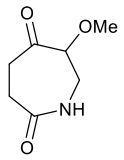
Batch irradiation

The standard batch irradiation procedure was followed over 4 hrs by quantitative NMR using *N*-(hydroxyethyl)succinimide **7d** (2.59 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* to 1/50th of the original volume. Trituration in $CHCl_3$ yielded 6-hydroxyazepane-2,5-dione **8d** (0.86 g, 33%) as a pale yellow powder; mp 156 – 159 °C (lit. 159 – 163 °C)[9] ; ν_{max} (neat)/cm^{-1} 3477 (NH,) 3123 (OH), 1707 (CO), 1652 (CONH); δ_H (400 MHz, $C_6D_5NO_2$) 6.89 (1H, br. s, N**H**), 4.59 – 4.54 (1H, m, -C**H**-), 4.25 (1H, d, *J* = 3.6, -O**H**), 3.86 – 3.79 (1H, m, -NHC**H**H-), 3.64 – 3.57 (1H, m, -NHCH**H**-), 3.09 – 2.97 (2H, m, -COC**H$_2$**-), 2.91 – 2.83 (2H, m, -NHCOC**H$_2$**-); δ_C (101 MHz, $C_6D_5NO_2$) 205.9 (CO), 176.3 (CONH), 76.7 (CH), 44.9 (CH_2), 36.9 (CH_2), 30.3 (CH_2); λ_{max} (MeCN)/nm = 216; ESI HRMS [MH$^+$] *m/z* 144.0655 ($C_6H_{10}NO_3$ requires 144.0658).

Flow irradiation

A solution of *N*-(hydroxyethyl)succinimide **7d** (85.8 g, 600 mmol) in degassed MeCN (5.0 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* to 1/50th of its original volume. Trituration in $CHCl_3$ yielded 6-hydroxyazepane-2,5-dione **8d** (29.0 g, 34%) as a yellow powder.

6-Methoxyazepane-2,5-dione 8e



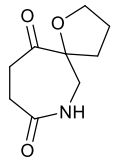
Batch irradiation

The standard batch irradiation procedure was followed over 4.5 hrs by quantitative NMR using *N*-(2-methoxyethyl)succinimide **7e** (2.82 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* and the crude product was purified *via* trituration using EtOAc to yield 6-methoxyazepane-2,5-dione **8e** (1.1 g, 41%) as an orange powder; mp 123 – 125 °C (EtOH); ν_{max} (neat)/cm^{-1} 3293 (NH), 2943 (CO), 1713 (CO), 1665 (CONH); δ_H (400 MHz, $CDCl_3$) 6.12 (1H, Br. s, N**H**), 3.74 (1H, dd, *J* = 7.3 Hz, 3.1 Hz, -C**H**-), 3.51 – 3.36 (5H, m, -OC**H$_3$**, -NHC**H$_2$**-), 2.87 – 2.81 (1H, m, -C**H**HCOCH-), 2.63 – 2.45 (3H, m, -COCH**HCH$_2$**CONH-); δ_C (101 MHz, $CDCl_3$) 207.4 (CO), 175.7 (CONH), 84.5 (CH), 58.0 (CH_3), 43.3 (CH_2), 36.5 (CH_2), 30.9 (CH_2); λ_{max} (MeCN)/nm = 206; CI HRMS [MH$^+$] *m/z* 158.0822 ($C_7H_{12}NO_3$ requires 158.0817).

Flow irradiation

A solution of *N*-(2-methoxyethyl)succinimide **7e** (94.3 g, 600 mmol) in degassed MeCN (5.0 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* and the crude mixture was purified by trituration using Et_2O, Hexane and MeCN to yield 6-methoxyazepane-2,5-dione **8e** (42.3 g, 44.8%) as an orange powder.

1-Oxa-7-azaspiro[4.6]undecane-8,11-dione 8f



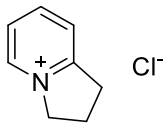
Batch irradiation

The standard batch irradiation procedure was followed over 4 hrs by quantitative NMR using *N*-(tetrahydrofurfuryl)succinimide **7f** (3.29 g, 18 mmol) in degassed MeCN (450 mL, 0.04 M). The solvent was removed *in vacuo* and the crude product was purified *via* flash column chromatography (EtOAc, then 5% MeOH in DCM) to yield 1-oxa-7-azaspiro[4.6]undecane-8,11-dione **8f** (1.3 g, 39%) as a yellow powder; mp 94 – 96 °C (TBME) (lit. 96 – 98 °C)[10] ; ν_{max} (neat)/cm^{-1} 3194 (NH), 3088 (CH), 1703 (CO), 1659 (CONH); δ_H (400 MHz, $CDCl_3$) 6.85 (1H, Br. s, N**H**), 3.96 (1H, m, -OC**H**H-), 3.88 (1H, m, -OCH**H**-), 3.38 (1H, dd, *J* = 15.3, 5.9, -CONHC**H$_2$**-), 3.23 (1H, dd, *J* = 15.3 Hz, 6.2 Hz, -CONHC**H**H-), 2.91 (1H, m, -COC**H**H-), 2.61 (2H, m, -NHC**H$_2$**-), 2.48 (1H, m, -COCH**H**-), 2.33 (1H, m, -NHCOCH**H**-), 1.93 (2H, m, -OCH_2C**H$_2$**-), 1.74 (1H, m, -NHCOCH**H**-); δ_C (101 MHz, $CDCl_3$) 207.4 (CO), 175.9 (CONH), 88.1 (C), 69.3 (CH_2), 48.1 (CH_2), 36.1 (CH_2), 31.4 (CH_2), 30.9 (CH_2), 25.3 (CH_2); λ_{max} (MeCN)/nm = 208; CI HRMS [MH^+] *m/z* 184.0972 ($C_9H_{14}NO_3$ requires 184.0974).

Flow irradiation

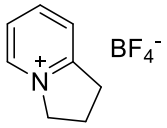
A solution of *N*-(tetrahydrofurfuryl)succinimide **7f** (115.9 g, 633 mmol) in degassed MeCN (5 L, 0.12 M) was irradiated with 3×36 W UVC PL-L / FEP flow reactors, connected in series, at 4 mL min^{-1}. The solvent was removed *in vacuo* and the crude mixture was purified by flash column chromatography (EtOAc, then 5% MeOH in DCM) to yield 1-oxa-7-azaspiro[4.6]undecane-8,11-dione **8f** (43.6 g, 38%) as a yellow powder.

2,3-dihydro-1H-indolizinium chloride 11-Cl



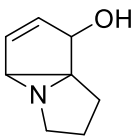
To a solution of 2-pyridinepropanol (129 ml, 1 mol) in DCM (250 ml) cooled in an ice bath was added thionyl chloride (109 ml, 1.5 mol) dropwise over 1 hour. The ice bath was removed and the solution heated to 45°C for 1 hr before quenching over ice water (400 ml) and neutralising with 15% NaOH (~800 ml) and extracting with DCM (8×400 ml). The organic extracts were dried ($MgSO_4$), the solvent was removed *in vacuo* and the resulting oil heated to 50°C on the rotary evaporator to induce cyclisation. Et_2O was added to triturate the chloride salt as a crystalline solid which was washed with toluene and Et_2O (under N_2) to give **11-Cl** as a colourless crystalline solid (120 g, 77%): δ_H (400 MHz, D_2O) 8.60 (1H, d, *J* = 6.2 Hz), 8.25 (1H, app. t, *J* = 7.9 Hz), 7.83 (1H, d, *J* = 8.1 Hz), 7.70 (1H, app. t, *J* = 7.0 Hz), 4.71 (2H, t, *J* = 7.8 Hz), 3.40 (2H, t, *J* = 7.8 Hz), 2.38 (2H, p, *J* = 7.8 Hz)

2,3-dihydro-1H-indolizinium tetrafluoroborate 11b



$NaBF_4$ (88.8 g, 809 mmol) was added to chloride salt **11-Cl** (120 g, 770 mmol) in acetone (700 ml) and the mixture stirred at room temp for 45 hrs. The mixture was filtered through celite and the solvent removed *in vacuo*. Et_2O was added to triturate the product as a crystalline solid which was washed with further Et_2O and filtered under N_2 to give tetrafluoroborate salt **11b** as a white granular solid (161 g, 100%): δ_H (400 MHz, D_2O) 8.61 (1H, d, *J* = 6.2 Hz), 8.26 (1H, app. t, *J* = 7.9 Hz), 7.85 (1H, d, *J* = 8.2 Hz), 7.72 (1H, app. t, *J* = 7.0 Hz), 4.72 (2H, t, *J* = 7.8 Hz), 3.41 (2H, t, *J* = 7.7 Hz), 2.39 (2H, p, *J* = 7.8 Hz)

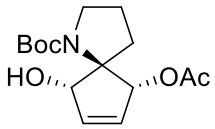
Tricyclic aziridine S1



A solution of BF_4^- pyridinium salt **11b** (1.86 g, 9.0 mmol) in degassed water (450 ml) was irradiated in a 400 ml quartz immersion well batch reactor with a 36 W PL-L UVC lamp (half its length surrounded by solution) for 22 hrs. Quantitative NMR indicated the reaction was at full conversion with aziridine product at 40% yield. The solution was basified with K_2CO_3 (10 mmol, 1.38 g) and concentrated to 50

ml *in vacuo*. The solution was further basified with K_2CO_3 (2.0 g) and KOAc (10 g) added before extraction with DCM (8×100 ml). The combined extracts were dried ($MgSO_4$), filtered and concentrated to an orange oil which was purified by chromatography on silica (10 – 20% (ethanol/ammonia) in DCM) to give aziridine **S1** as a pale orange oil which sets to a soft solid on standing (541 mg, 41%): δ_H (400 MHz, $CDCl_3$) 6.18 (1H, d, *J* = 5.6 Hz, C**H**=CH), 5.86 (1H, d, *J* = 5.6 Hz, CH=C**H**), 4.44 (1H, s, C**H**OH), 3.14 (1H, br. s, O**H**), 3.02 – 2.85 (2H, m, NC**H**HCH$_2$, NCH**H**CH$_2$), 2.56 (1H, s, NC**H**), 2.35 (1H, dd, *J* = 13.2, 7.7 Hz, C**H**H), 2.22 – 2.11 (1H, m, CH**H**), 1.82 – 1.71 (1H, m, C**H**H), 1.59 – 1.44 (1H, m, CH**H**); δ_C (101 MHz, $CDCl_3$) 137.7 (CH), 135.0 (CH), 75.7 (CH), 62.6 (C), 53.3 (CH_2), 46.3 (CH), 23.6 (CH_2), 22.6 (CH_2)

***N*Boc spirocyclic acetate 12**

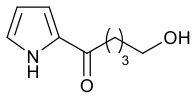


A solution of BF_4^- salt **11b** (16.56 g, 80 mmol) in degassed deionised water (4 L) was irradiated with 3×36 W UVC flow reactors (in series) at a flow rate of 3 ml/min. The photolysate was basified with K_2CO_3 (11 g) and the water concentrated *in vacuo* to around 50 ml. KOAc (15 g) was added and the product extracted with DCM (8×100 ml). The combined extracts were dried ($MgSO_4$) and the solvent removed *in vacuo*. Chromatography on silica (40% MeOH in EtOAc) yielded aziridine **S1** as a yellow oil (6.7 g) which was immediately subject to acidic ring-opening conditions:

To a solution aziridine **S1** (6.7 g) in DCM (100 ml) was added AcOH (30 ml) and the solution stirred for 16 hrs. The solvent was removed *in vacuo* and acetic acid removed by further azeotroping with heptane. The resulting residue of ring opened acetate was re-dissolved in DCM (100 ml) before the addition of Et_3N (28 ml, 200 mmol) and Boc_2O (13 g, 60 mmol). The solution was stirred at room temp for 16 hrs before quenching with water, separating and re-extracting with DCM. The dried solvent was removed *in vacuo* and chromatography on silica (60% Et_2O in petrol) yielded Boc protected spirocycle **12** as a thick oil (10.3 g, 43%): δ_H (500 MHz, DMSO) Rotamer mixture (0.55 : 0.45); 6.22 (0.55H, app. q, *J* = 1.8 Hz, OC**H**), 6.11 (0.45H, app. q, *J* = 1.8 Hz, OC**H**), 5.88 – 5.84 (1H, m, C**H**=CH), 5.69 – 5.66 (1H, m, CH=C**H**), 5.40 (0.45H, d *J* = 6.4 Hz, O**H**), 5.33 (0.55H, d *J* = 6.3 Hz, O**H**), 5.11 – 5.08 (0.55H, m, OC**H**), 4.95 – 4.91 (0.45H, m, OC**H**), 3.30 – 3.18 (2H, m, NC**H$_2$**), 2.22 – 2.10 (1H, C**H**HCH$_2$), 2.04 (1.35H, s, COC**H$_3$**), 2.03 (1.65H, s, COC**H$_3$**), 1.86 – 1.52 (3H, m, CH**H**CH$_2$, CHHC**H$_2$**), 1.40 (4.95H, s, 3×C**H$_3$**), 1.37 (4.05H, s, 3×C**H$_3$**); δ_C (126 MHz, DMSO) δ 70.0 (C), 170.0 (C), 152.9 (C), 152.4 (C), 137.4 (CH), 137.1 (CH), 129.3 (CH), 129.2 (CH), 79.0 (CH), 78.9 (C), 78.5 (C), 78.1 (C), 77.5 (CH),

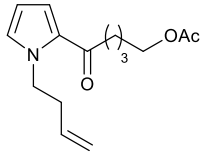
77.1 (C), 76.7 (CH), 74.6 (CH), 47.6 (CH_2), 47.5 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 27.6 (CH_2), 26.2 (CH_2), 22.6 (CH_2), 22.2 (CH_2), 20.8 (CH_3), 20.8 (CH_3)

3-hydroxy-1-(1H-pyrrol-2-yl)pentan-1-one S2



Using an adapted literature procedure.[11] To anhydrous toluene (1.00 L) at 0 °C under nitrogen was added MeMgBr (148 mL of 3.2 M in Me-THF, 470 mmol), followed by freshly distilled pyrrole (32 mL, 460 mmol) dropwise over 30 min. The reaction was stirred for 30 min, warmed to 50 °C, stirred for a further 1 h and δ-valerolactone (20.8 mL, 224 mmol) added dropwise over 20 min. The reaction was stirred for 30 min and heated to reflux. After 4.5 h the reaction was cooled to rt, stirred for 12 h and quenched by the addition of sat. aq. NH_4Cl (400 mL). The phases were separated, the aqueous phase extracted with EtOAc (3 × 300 mL), the toluene phase evaporated and partititioned between EtOAc (300 mL) and the aqueous phase, separated and extracted with EtOAc (300 mL). The combined organic phase was washed with brine, dried ($MgSO_4$) and evaporated to give a brown oil. Purification by silica gel chromatography (EtOAc/petrol, 1:3 to 1:0 as eluent) afforded the title compound (29.2 g, 78%) as a yellow oil. ν_{max} /cm^{-1} (film) 3276, 2936, 1623, 1545, 1399 and 1302; δ_H (400 MHz, $CDCl_3$) 1.60 – 1.68 (2H, m, C*H*$_2$-CH_2OH), 1.78 – 1.87 (2H, m, C*H*$_2$-CH_2-C=O), 2.83 (2H, t, J 7.2, CH_2-C=O), 3.66 (2H, t, J 6.4, C*H*$_2$OH), 6.26 – 6.29 (1H, m, pyrrole CH), 6.93 (1H, ddd, J 3.8, 2.5, 1.4, pyrrole CH), 7.02 – 7.04 (1H, m, pyrrole CH) and 9.55 (1H, brs, NH); δ_C (101 MHz, $CDCl_3$) 21.0 (*C*H_2-CH_2-C=O), 32.4 (*C*H_2-CH_2OH), 37.5 (*C*H_2-C=O), 62.4 (*C*H_2OH), 110.8 (pyrrole CH), 116.3 (pyrrole CH), 124.7 (pyrrole CH), 132.0 (Cq) and 191.0 (C=O); HRMS (Cl^+) 168.1019 ($C_9H_{14}NO_2$, $[M+H]^+$ requires 168.1025).

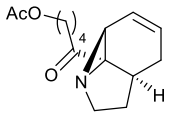
5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate 15



To a stirred solution of 3-hydroxy-1-(1H-pyrrol-2-yl)pentan-1-one **S2** (22.2 g, 133 mmol), DMAP (1.00 g, 8.20 mmol) and Hünig's base (35.5 mL, 204 mmol) in anhydrous DCM (400 mL) at 0 °C under nitrogen was added acetic anhydride (13.3 mL, 141 mmol) dropwise. The mixture was stirred for 4 h, washed with 1M HCl (300 mL), the aqueous phase extracted with DCM (100 mL) and the combined organic phase washed with sat. aq. $NaHCO_3$ (250 mL). Drying ($MgSO_4$) and evaporation gave a yellow

solid which was redissolved in butanone (350 mL) under nitrogen. K_2CO_3 (51 g, 370 mmol), tetrabutylammonium iodide (4.40 g, 11.9 mmol) and 4-bromo-1-butene (40.0 mL, 394 mmol) were added and the stirred mixture heated to reflux. After 48 h further K_2CO_3 (12.0 g, 87 mmol) and 4-bromo-1-butene (10.0 mL, 99 mmol) were added, stirred for a further 24 h and cooled to rt. The mixture was filtered and evaporated to give a brown oil which was purified by silica gel chromatography (EtOAc/petrol, 1:9 as eluent) to afford the title compound (31.2 g, 89%) as a light yellow oil. ν_{max} /cm^{-1} (film) 2952, 1734, 1643, 1468, 1409 and 1233; δ_H (400 MHz, $CDCl_3$) 1.66 – 1.74 (2H, m, C*H*$_2$CH$_2$OAc), 1.74 – 1.82 (2H, m, C*H*$_2$CH$_2$C=O), 2.04 (3H, s, Me), 2.48 (2H, q, J 7.3, NCH$_2$C*H*$_2$), 2.82 (2H, t, J 7.2, C*H*$_2$C=O), 4.09 (2H, t, J 6.4, C*H*$_2$OAc), 4.37 (2H, t, J 7.1, NCH$_2$), 4.99 – 5.06 (2H, m, CH=C*H*$_2$), 5.75 (1H, ddt, J 17.1, 10.2, 6.9, C*H*=CH$_2$), 6.11 (1H, dd, J 4.0, 2.5, pyrrole CH), 6.84 (1H, dd, J 2.4, 2.0, pyrrole CH) and 6.97 (1H, dd, J 4.1, 1.7, pyrrole CH); δ_C (101 MHz, $CDCl_3$) 21.2 (Me), 21.7 (*C*H$_2$CH$_2$C=O), 28.4 (*C*H$_2$CH$_2$OAc), 35.9 (NCH$_2$*C*H$_2$), 38.6 (*C*H$_2$C=O), 49.5 (NCH$_2$), 64.4 (*C*H$_2$OAc), 108.0 (pyrrole CH), 117.3 (CH=*C*H$_2$), 119.8 (pyrrole CH), 129.9 (Cq), 130.5 (pyrrole CH), 134.8 (*C*H=CH$_2$), 171.4 (Me*C*O$_2$) and 190.6 (C=O); HRMS (ES$^+$) 286.1411 ($C_{15}H_{21}NO_3Na$, [M+Na]$^+$, requires 286.1413).

(±)-5-oxo-5-((31*R*,3a*S*,6a*S*)-1,3a,6,6a-tetrahydroazirino[2,3,1-hi]indol-31(2*H*)-yl)pentyl acetate 13



Batch procedure: MeCN, 14.6 mM

A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (1.73 g, 6.58 mmol) in degassed MeCN (450 mL) under nitrogen was irradiated with a 50% immersed 36 W UVC lamp. After 7 h the reaction was evaporated and the resulting oil purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (1.05 g, 61%) as a yellow oil. ν_{max} /cm^{-1} (film) 2952, 1735, 1690, 1365 and 1232; δ_H (400 MHz, $CDCl_3$) 1.46 – 1.53 (1H, m, NCH$_2$CH*H*), 1.57 – 1.67 (4H, m, C*H*$_2$CH$_2$C=O and C*H*$_2$CH$_2$OAc), 1.94 (1H, ddd, J 18.1, 6.2, 1.4, allylic CH*H*), 2.02 (3H, s , Me), 2.23 – 2.33 (2H, m, CH*H*C=O and allylic C*H*H), 2.42 (1H, app. dq, J 12.5, 10.1, NCH$_2$C*H*H), 2.51 – 2.60 (2H, m, C*H*HC=O and NCH*H*), 2.80 (1H, d, J 3.8, NCH), 3.14 (1H, td, J 11.1, 2.6, NC*H*H), 3.22 – 3.27 (1H, m, CH$_2$C*H*CH$_2$), 4.02 – 4.06 (2H, m, C*H*$_2$OAc), 5.77 (1H, dt, J 10.1, 3.6, C*H*=CH-CH$_2$) and 6.22 (1H, ddd, J 10.0, 6.1, 1.7, CH$_2$-C*H*=CH); δ_C (101 MHz, $CDCl_3$) 20.2 (*C*H$_2$CH$_2$C=O), 21.1 (*Me*CO$_2$), 28.2 (*C*H$_2$CH$_2$OAc), 29.9 (allylic CH$_2$), 32.3 (CH$_2$*C*HCH$_2$), 35.6 (*C*H$_2$C=O), 41.0 (NCH$_2$*C*H$_2$), 44.0 (NCH), 49.9 (NCH$_2$), 59.1 (*C*q-C=O), 64.3 (*C*H$_2$OAc), 120.1 (*C*H=CH-CH$_2$), 135.7 (CH=*C*H-CH$_2$), 171.3 (Me*C*O$_2$) and 209.8 (C=O); HRMS (ES$^+$) 286.1417 ($C_{15}H_{21}NO_3Na$, [M+Na]$^+$, requires 286.1413).

Flow procedure: MeCN

A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (14.6 mM in degassed MeCN) was passed through 3 FEP flow reactors in series, with irradiation from 3 × 36 W UVC lamps at 6.6 mL min^{-1}. The reaction was run for 12 h, plus 2 × 30 min slugs of pure MeCN for reactor cleaning (13 h total time), flowing 4.75 L (17.94 g substrate, 68.2 mmol). Evaporation gave a brown oil which was purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (10.95 g, 61%) as a yellow oil.

Batch procedure: EtOAc/cyclohexane, 14.6 mM

A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (1.73 g, 6.58 mmol) in degassed EtOAc (68 mL) and degassed cyclohexane (382 mL) under nitrogen was irradiated with a 50% immersed 36 W UVC lamp. After 6 h the reaction was evaporated and the resulting oil purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (1.28 g, 74%) as a yellow oil.

Flow procedure: EtOAc/cyclohexane, 14.6 mM

A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (3.0 g, 11.4 mmol) in degassed EtOAc/cyclohexane (15:85, 780 mL) was passed through 3 FEP flow reactors in series, with irradiation from 3 × 36 W UVC lamps at 7.5 mL min^{-1}. Evaporation gave a brown oil which was purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (2.17 g, 72%) as a yellow oil.

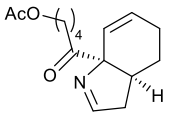
Batch procedure: EtOAc/cyclohexane, 2.5 mM

A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (300 mg, 1.14 mmol) in degassed EtOAc (68 mL) and degassed cyclohexane (382 mL) under nitrogen was irradiated with a 50% immersed 36 W UVC lamp. After 55 min the reaction was evaporated and the resulting oil purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (214 mg, 71%) as a yellow oil.

Batch procedure: EtOAc/cyclohexane, 29 mM

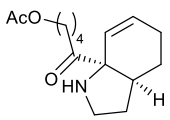
A solution of 5-(1-(but-3-en-1-yl)-1H-pyrrol-2-yl)-5-oxopentyl acetate **15** (3.46 g, 13.1 mmol) in degassed EtOAc (68 mL) and degassed cyclohexane (382 mL) under nitrogen was irradiated with a 50% immersed 36 W UVC lamp. After 12 h the reaction was evaporated and the resulting oil purified by silica gel chromatography (EtOAc/petrol, 1:9 to 7:3 as eluent) to afford the title compound (2.32 g, 67%) as a yellow oil.

(±)-5-((2*S*,3*S*)-3-methyl-2-vinyl-3,4-dihydro-2*H*-pyrrol-2-yl)-5-oxopentyl acetate 16



A stirred solution of (±)-5-oxo-5-((31*R*,3a*S*,6a*S*)-1,3a,6,6a-tetrahydroazirino[2,3,1-hi]indol-31(2*H*)-yl)pentyl acetate **13** (16.0 g, 60.8 mmol) in anhydrous toluene (500 mL) was heated to reflux under nitrogen. After 16.5 h the reaction was cooled to rt and evaporated to give a brown oil. Purification by silica gel chromatography (EtOAc/petrol, 3:7 to 7:3 as eluent) afforded the title compound (15.56 g, 97%) as a yellow oil. ν_{max} /cm^{-1} (film) 2929, 1734, 1709, 1646, 1614, 1365 and 1234; δ_H (400 MHz, $CDCl_3$) 1.32 -1.42 (1H, m, =CH-CH_2-CH*H*), 1.55 – 1.67 (4 H, m, 2 × CH_2), 1.82 – 1.91 (1H, m, =CH-CH_2-C*H*H), 1.95 – 2.08 (5H, m, =CH-C*H*$_2$ and *Me*CO_2), 2.37 (1H, dd, J 16.3, 3.9, N=CH-CH*H*), 2.64 – 2.76 (4H, m, N=CH-C*H*H, CH_2C*H*CH_2 and C*H*2C=O), 4.04 (2H, t, J 6.0, C*H*$_2$OAc), 5.93 (1H, dt, J 10.1, 1.9 Hz, C*H*=CH-CH_2), 6.03 (1H, ddd, J 10.1, 4.5, 3.5, =C*H*-CH_2) and 7.61 (1H, s, N=C*H*); δ_C (101 MHz, $CDCl_3$) 20.1 (CH_2), 21.0 (*Me*CO_2), 21.8 (allylic CH_2), 24.7 (=CH-CH_2-*C*H_2), 28.0 (CH_2), 35.2 (CH_2*C*HCH_2), 37.9 (*C*H_2C=O), 42.4 (N=CH-*C*H_2), 64.2 (*C*H_2OAc), 86.3 (*C*q-C=O), 125.7 (*C*H=CH-CH_2), 131.8 (=*C*H-CH_2), 167.5 (N=*C*H), 171.1 (Me*C*O_2) and 209.2 (C=O); HRMS (ESI$^+$) 264.1595 ($C_{15}H_{22}NO_3$, $[M+H]^+$, requires 264.1594).

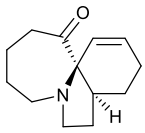
(±)-5-((3a*S*,7a*R*)-1,2,3,3a,4,5-hexahydro-7a*H*-indol-7a-yl)-5-oxopentyl acetate 17



To a stirred solution of (±)-5-((2*S*,3*S*)-3-methyl-2-vinyl-3,4-dihydro-2*H*-pyrrol-2-yl)-5-oxopentyl acetate **16** (15.2 g, 57.8 mmol) in anhydrous DCM (450 mL) at 0 °C under nitrogen was added acetic

acid (4.1 mL, 72 mmol) dropwise, followed by $NaBH(OAc)_3$ (13.5 g, 63.7 mmol). The reaction was stirred for 2 h, quenched by the addition of sat. aq. $NaHCO_3$ (200 mL), stirred for 25 min, the phases separated and the aqueous phase extracted with DCM (2 × 100 mL). The combined organic phase was dried ($MgSO_4$) and evaporated to afford the title compound (15.2 g, 100%) as a yellow oil which was used directly in the next stage. ν_{max} /cm^{-1} (film) 2931, 1735, 1703, 1645, 1566, 1451, 1365 and 1235; ν_{max} /cm^{-1} (film) 3327, 2930, 1734, 1703, 1450, 1365 and 1234; δ_H (400 MHz, $CDCl_3$) 1.46 – 1.69 (6H, m, C*H*$_2$C*H*$_2$CH$_2$C=O, NCH$_2$CH*H* and =CH-CH$_2$-CH*H*), 1.75 – 1.85 (2H, m, NCH$_2$C*H*H and =CH-CH$_2$-C*H*H), 1.98 – 2.09 (4H, m, Me and allylic CH*H*), 2.09 – 2.20 (1H, m, allylic C*H*H), 2.27 – 2.36 (1H, m, C*H*), 2.50 – 2.62 (3H, m, N*H* and C*H*$_2$C=O), 2.89 – 3.03 (2H, m, NC*H*$_2$), 4.04 (2H, t, J 6.2, C*H*$_2$O), 5.50 (1H, dt, J 10.0., 2.0, C*H*=CH-CH$_2$) and 6.04 (1H, ddd, J 10.0, 4.7, 3.6, CH=C*H*-CH$_2$); δ_C (101 MHz, $CDCl_3$) 20.7 (*C*H$_2$CH$_2$C=O), 21.1 (Me), 22.5 (allylic CH$_2$), 24.8 (=CH-CH$_2$-*C*H$_2$), 28.2 (*C*H$_2$CH$_2$OAc), 31.5 (NCH$_2$*C*H$_2$), 37.0 (*C*H$_2$C=O), 39.5 (*C*H), 44.9 (N*C*H$_2$), 64.2 (*C*H$_2$OAc), 72.8 (*C*q-C=O), 127.9 (*C*H=CH-CH$_2$), 131.3 (CH=*C*H-CH$_2$), 171.3 (Me*C*O$_2$) and 212.5 (*C*=O); HRMS (Cl^+) 266.1757 ($C_{15}H_{24}NO_3$, $[M+H]^+$, requires 266.1756).

(±)-(8a*S*,12a*R*)-2,3,4,5,8,8a,9,10-octahydro-1*H*,7*H*-azepino[2,1-i]indol-1-one 14



(±)-5-((3a*S*,7a*R*)-1,2,3,3a,4,5-hexahydro-7a*H*-indol-7a-yl)-5-oxopentyl acetate **17** (15.2 g, 57.8 mmol) was cooled to 0 °C under nitrogen and dissolved in 48% aq. HBr (95 mL, 850 mmol) with stirring. Sulphuric acid (7.6 mL, 140 mmol) was added dropwise (exotherm) and the stirred mixture heated to 80 °C. After 1 h the reaction was cooled to 0 °C and added slowly to a cold, stirred mixture of 15% aq. NaOH (320 mL), brine (200 mL) and DCM (200 mL). The phases were separated and the aqueous phase extracted with DCM (2 × 100 mL). The combined organic phase was dried ($MgSO_4$) and evaporated to give a brown oil which was immediately redissolved in anhydrous MeCN (1.2 L) under nitrogen. $^iPr_2NEt$ (29.0 mL, 166 mmol) was added and the stirred mixture heated to 80 °C. After 3 h the reaction was cooled, evaporated, and partitioned between DCM (100 mL), 15% aq. NaOH (50 mL) and brine (50 mL). The phases were separated, the aqueous phase extracted with DCM (2 × 50 mL) and the combined organic phase dried ($MgSO_4$) and evaporated to give a brown oil. Purification by silica gel chromatography (0% to 2% EtOH/aq. NH_3 (8:1) in DCM as eluent) afforded the title compound (5.65 g, 48%) as a yellow oil. ν_{max} /cm^{-1} (film) 2926, 1698, 1649, 1453 and 1333; δ_H (400 MHz, $CDCl_3$) 1.48 – 1.95 (8H, m, =CH-CH$_2$-C*H*$_2$, NCH$_2$C*H*$_2$CH and NCH$_2$C*H*$_2$C*H*$_2$), 1.95 – 2.14 (2H, m,

allylic CH_2), 2.22 – 2.33 (2H, m, CH_2CHCH_2 and CHHC=O), 2.62 – 2.71 (1H, m, NCHH), 2.75 (1H, ddd, J 13.3, 8.2, 3.3, NC'HH), 2.95 (1H, ddd, J 13.4, 7.2, 4.1, NC'HH), 3.03 – 3.18 (2H, m, NCHH and CHHC=O), 5.52 (1H, d, J 10.3, CH=CH-CH_2) and 6.05 (1H, ddd, J 10.3, 4.8, 1.9, CH=CH-CH_2); δ_C (101 MHz, $CDCl_3$) 20.5 (allylic CH_2), 22.0 (CH_2), 23.6 (CH_2), 26.0 (=CH-CH_2-CH_2), 26.5 (CH_2), 38.7 (CH_2C=O), 40.5 (CH_2CHCH_2), 48.2 (NCH_2), 50.8 (NCH_2), 71.9 (Cq-C=O), 122.9 (CH=CH-CH_2), 131.1 (CH=CH-CH_2) and 216.4 (C=O); HRMS (Cl^+) 206.1542 ($C_{13}H_{20}NO$, $[M+H]^+$, requires 206.1545).

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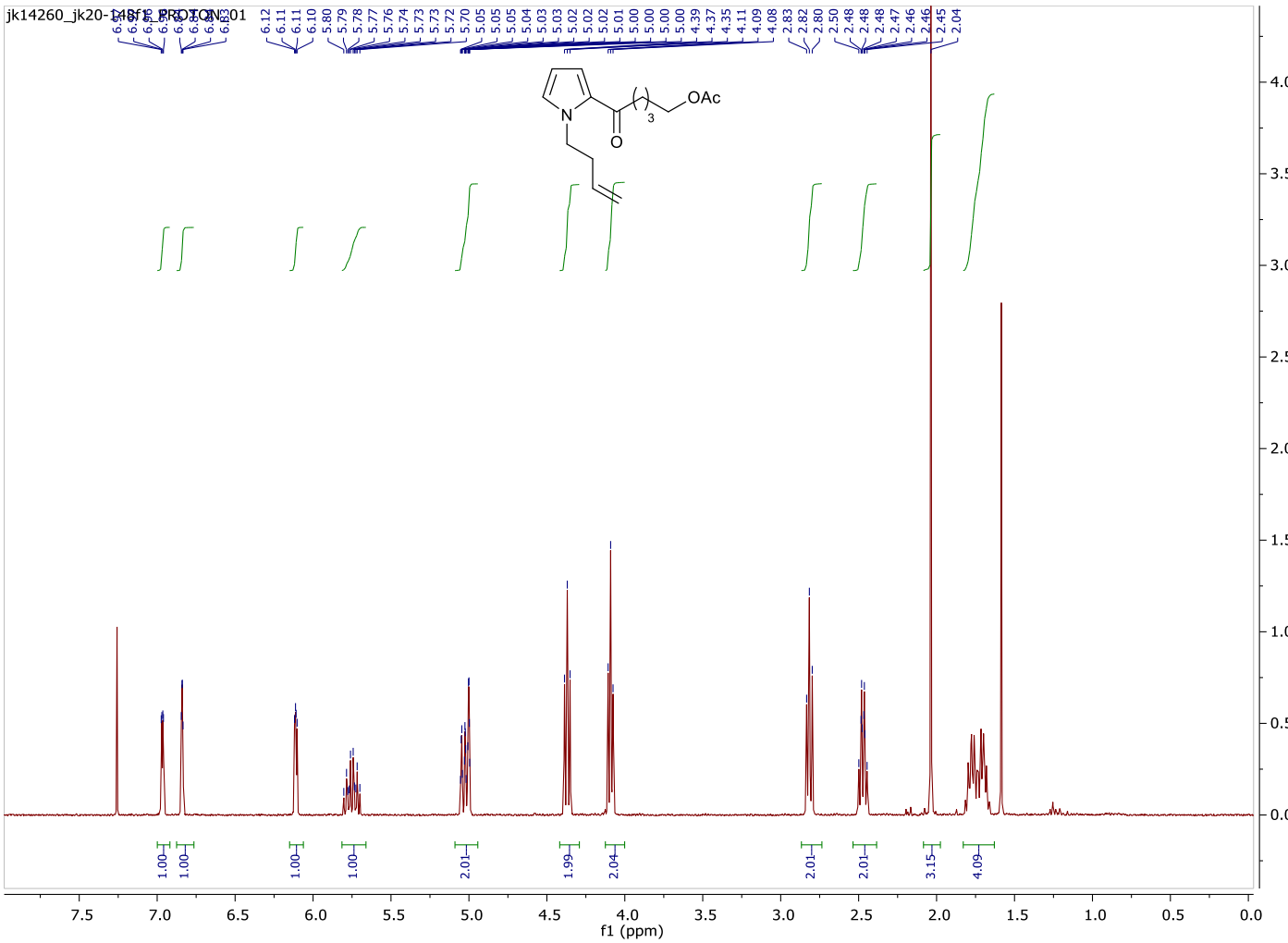
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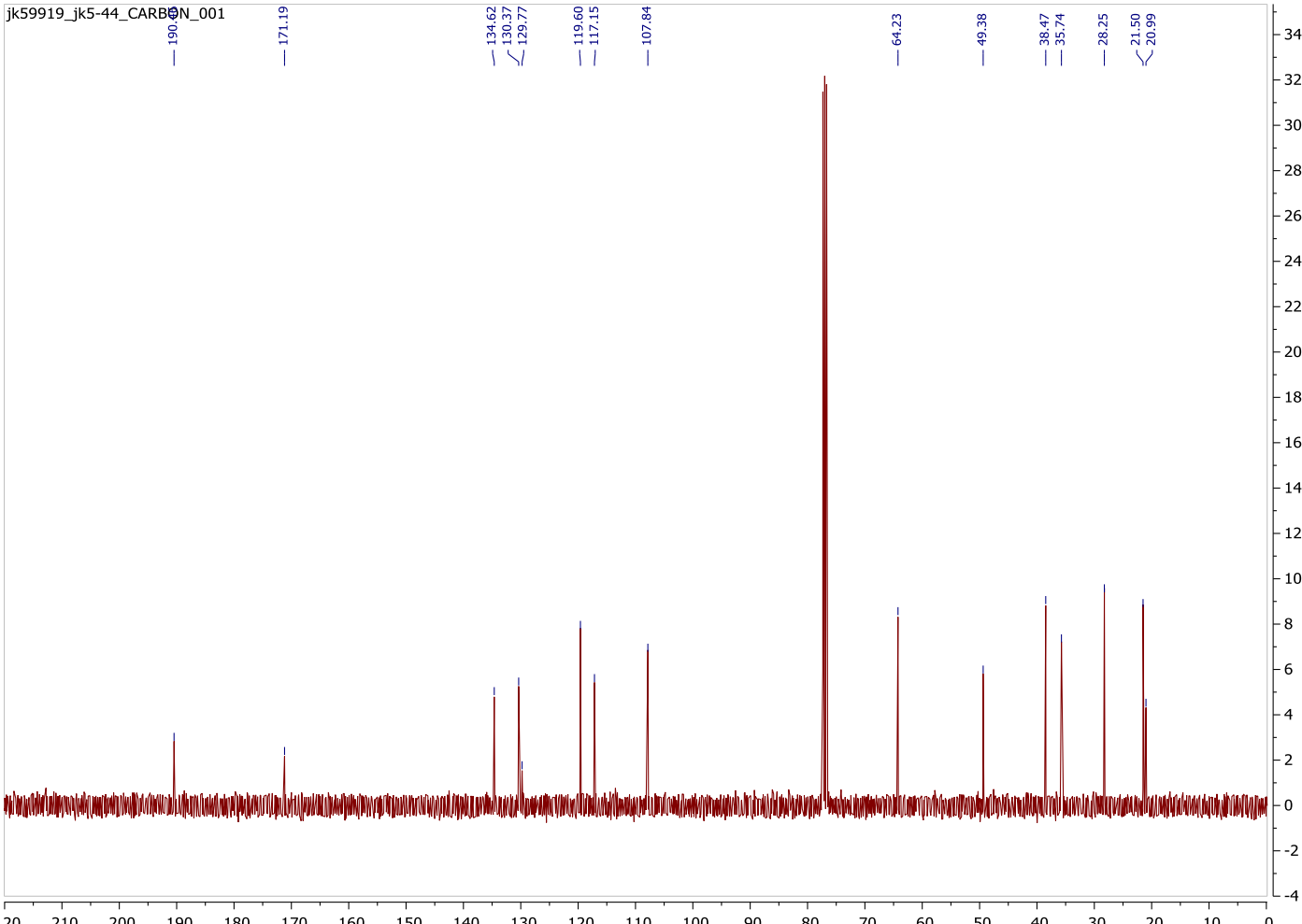
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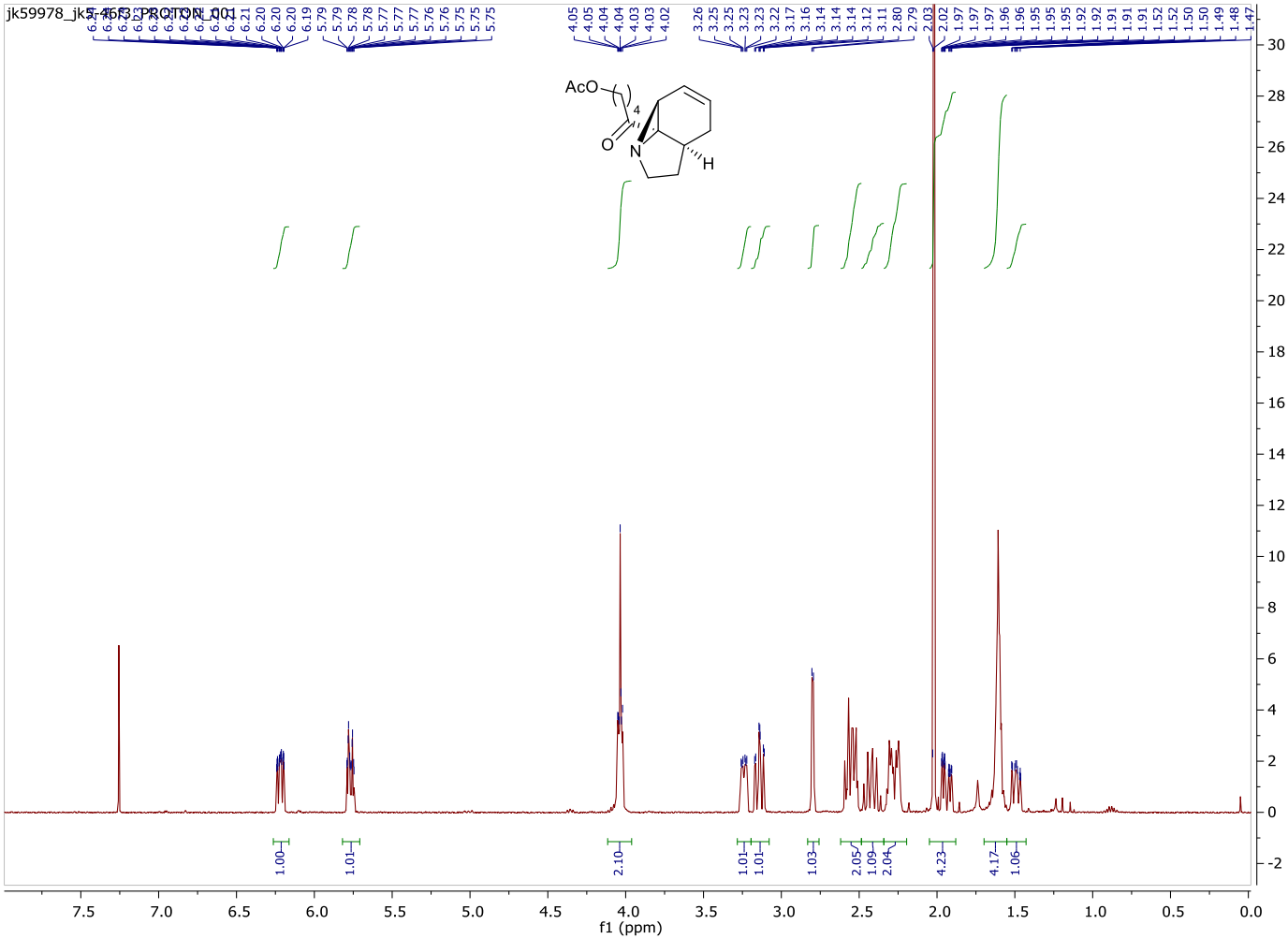
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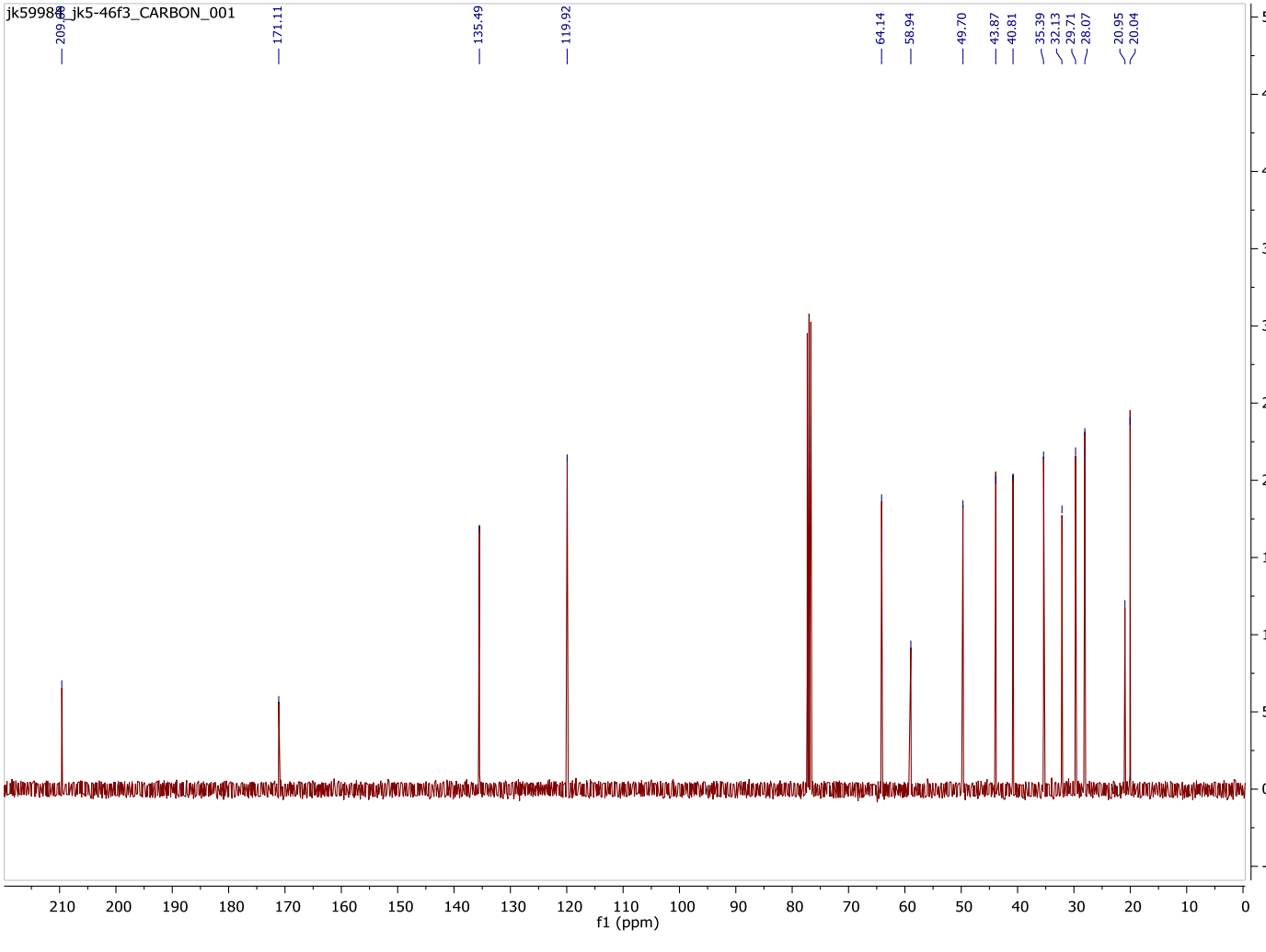
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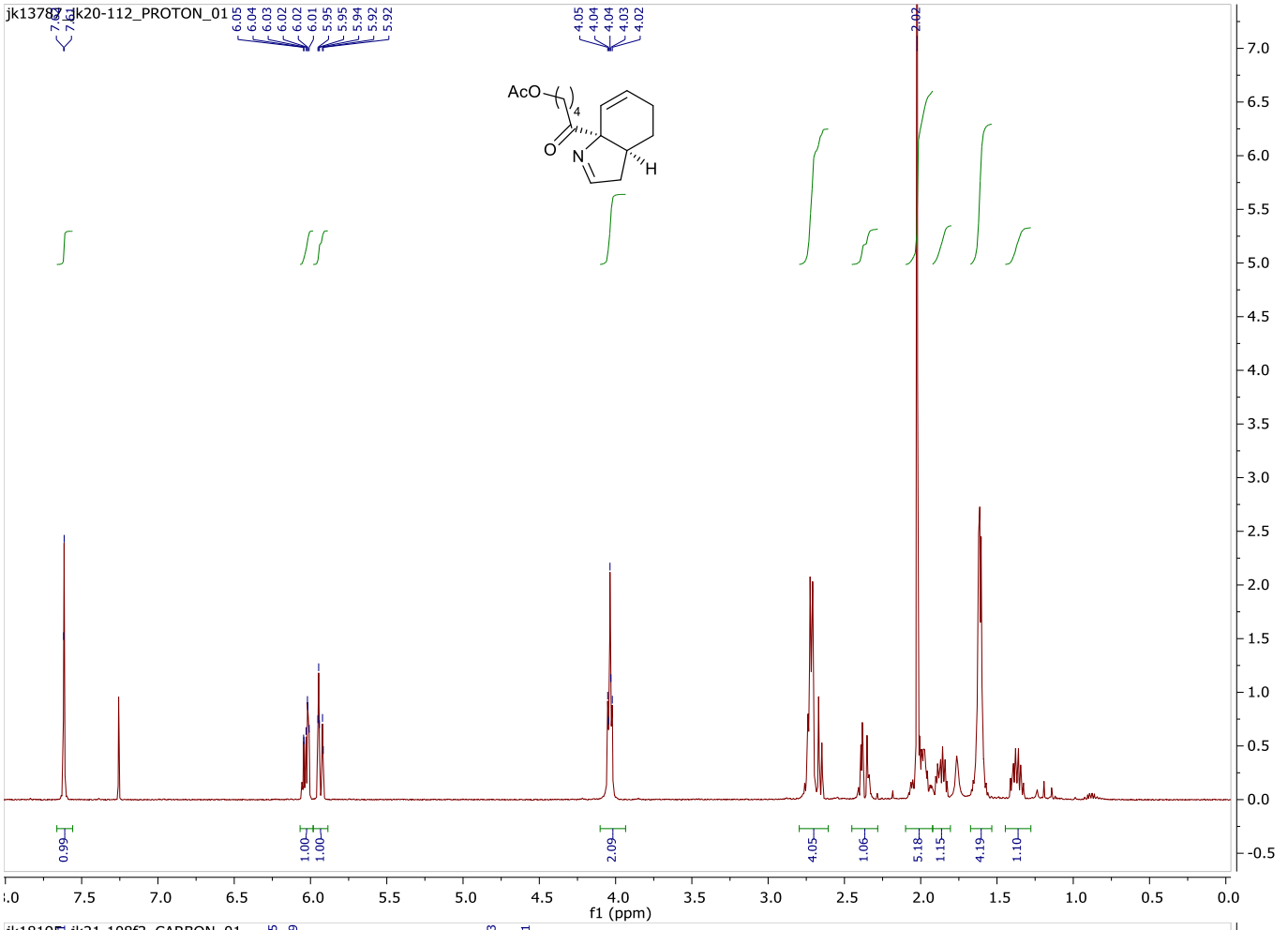
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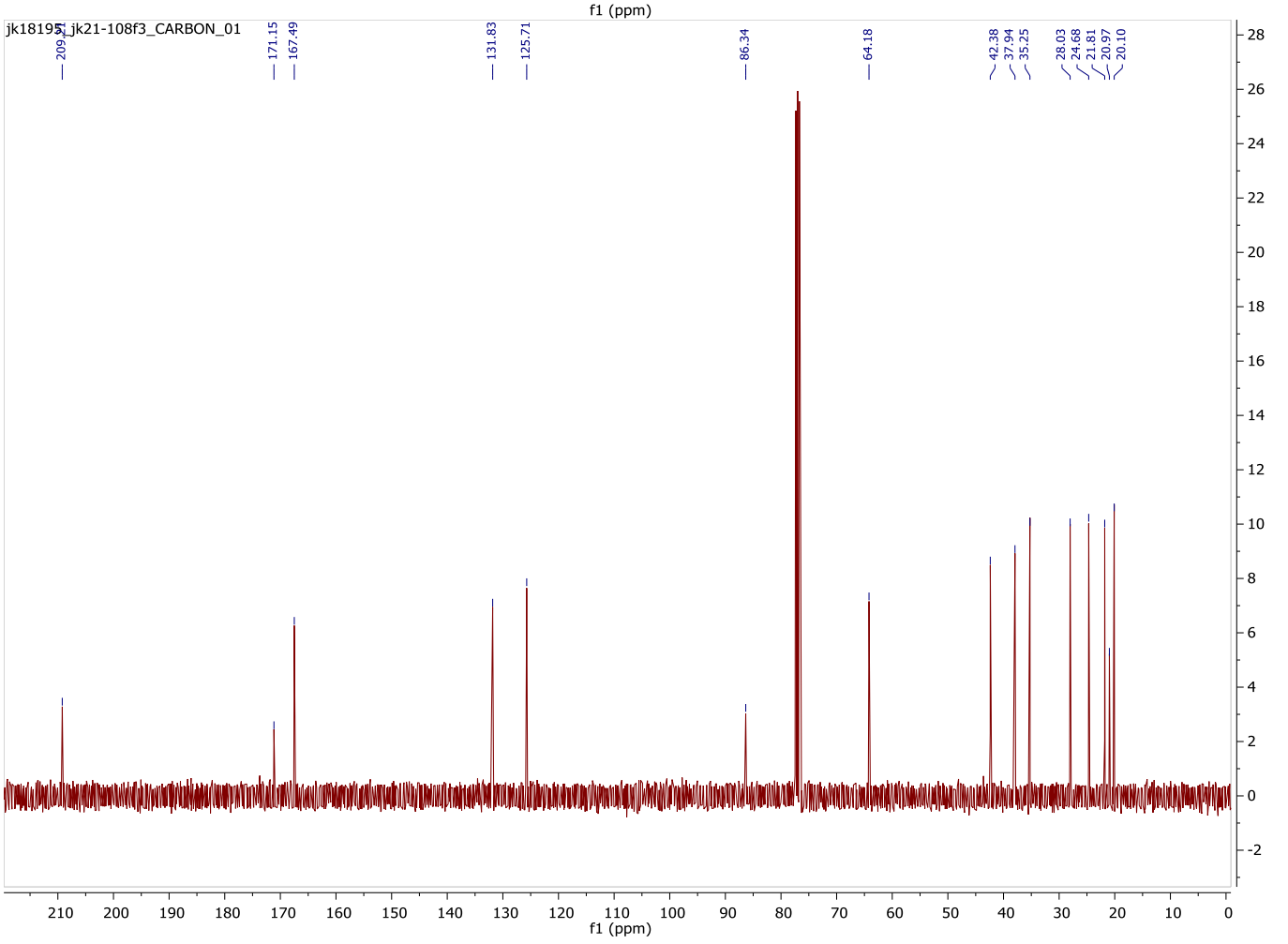
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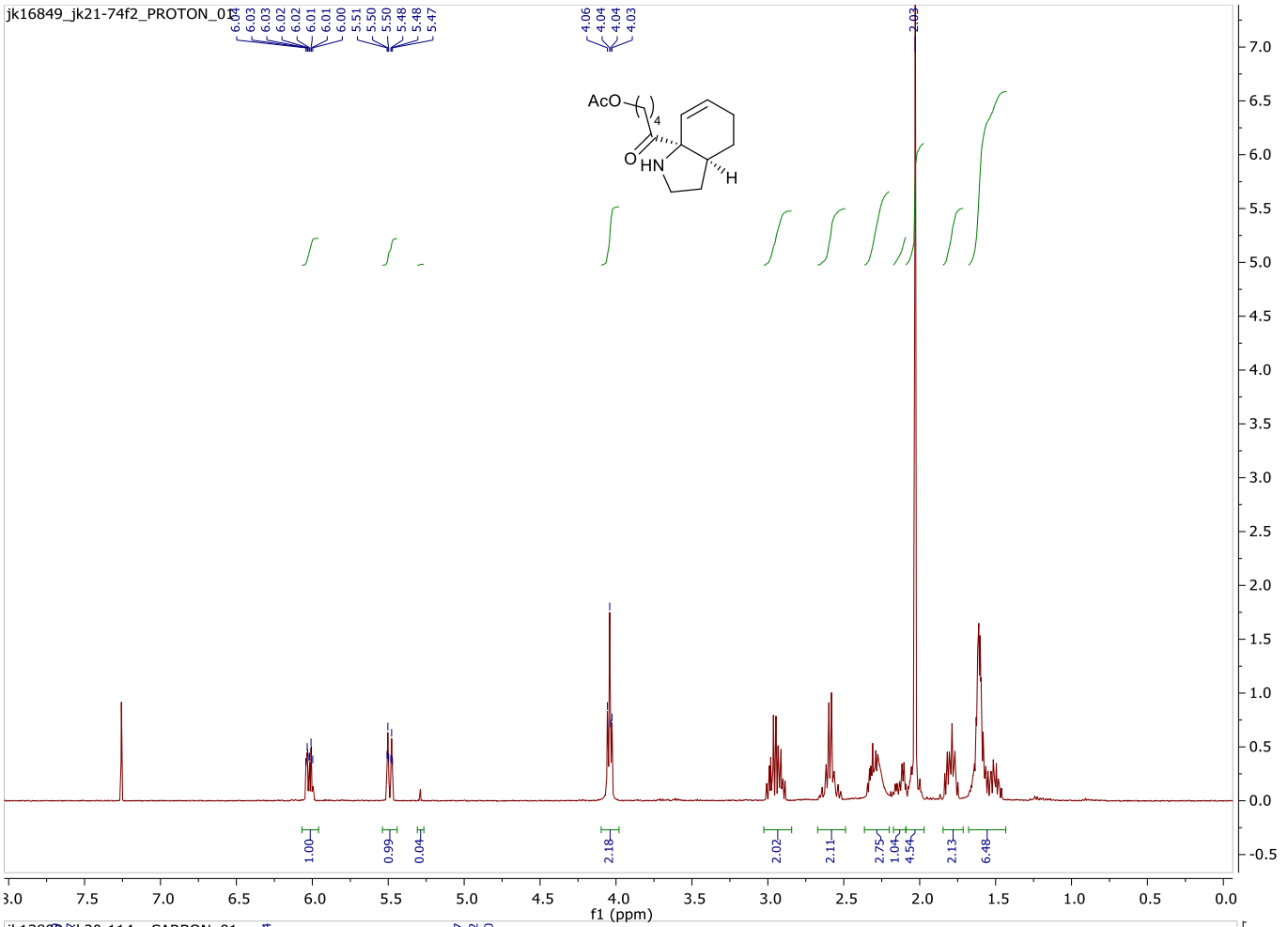
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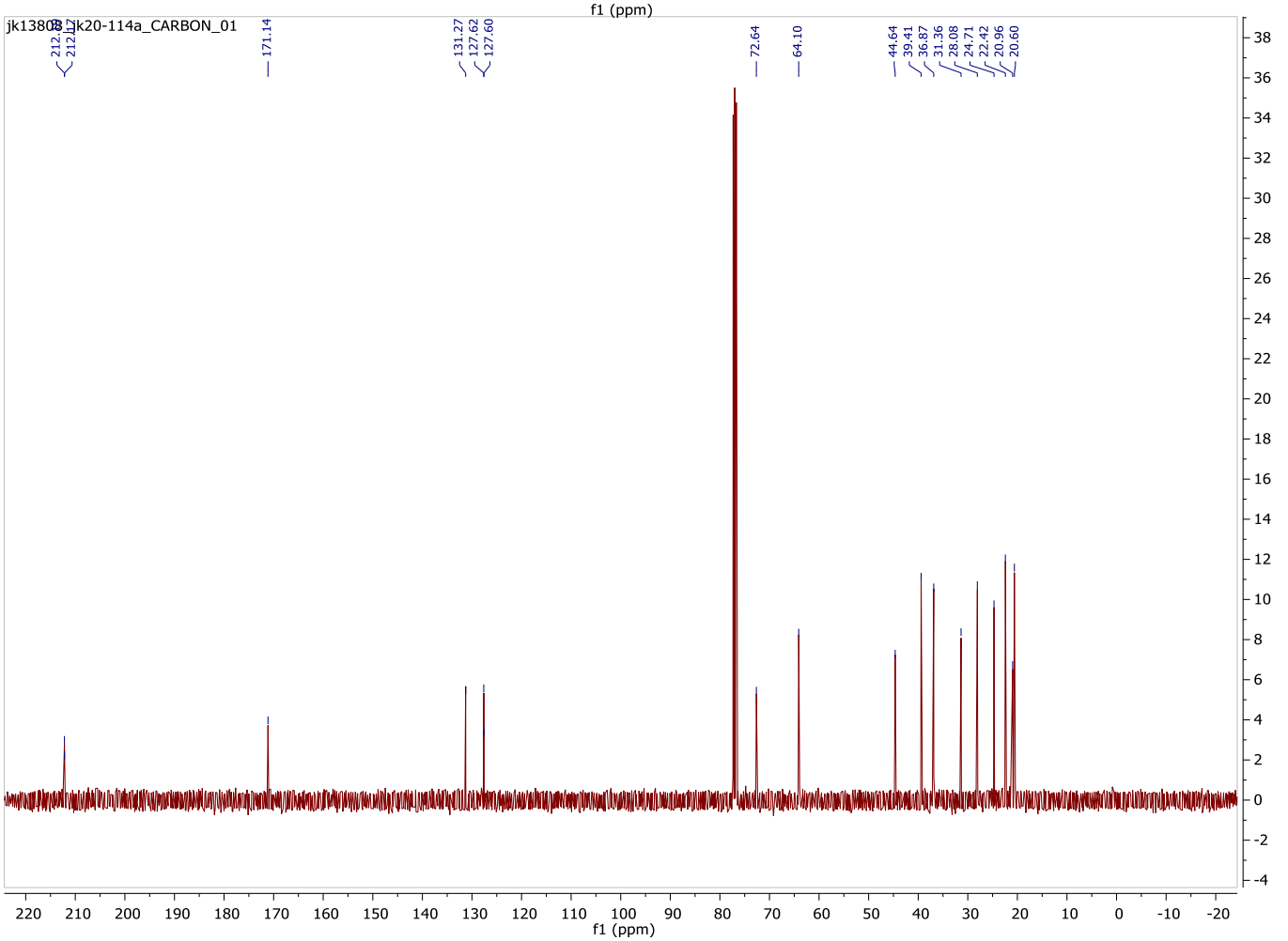
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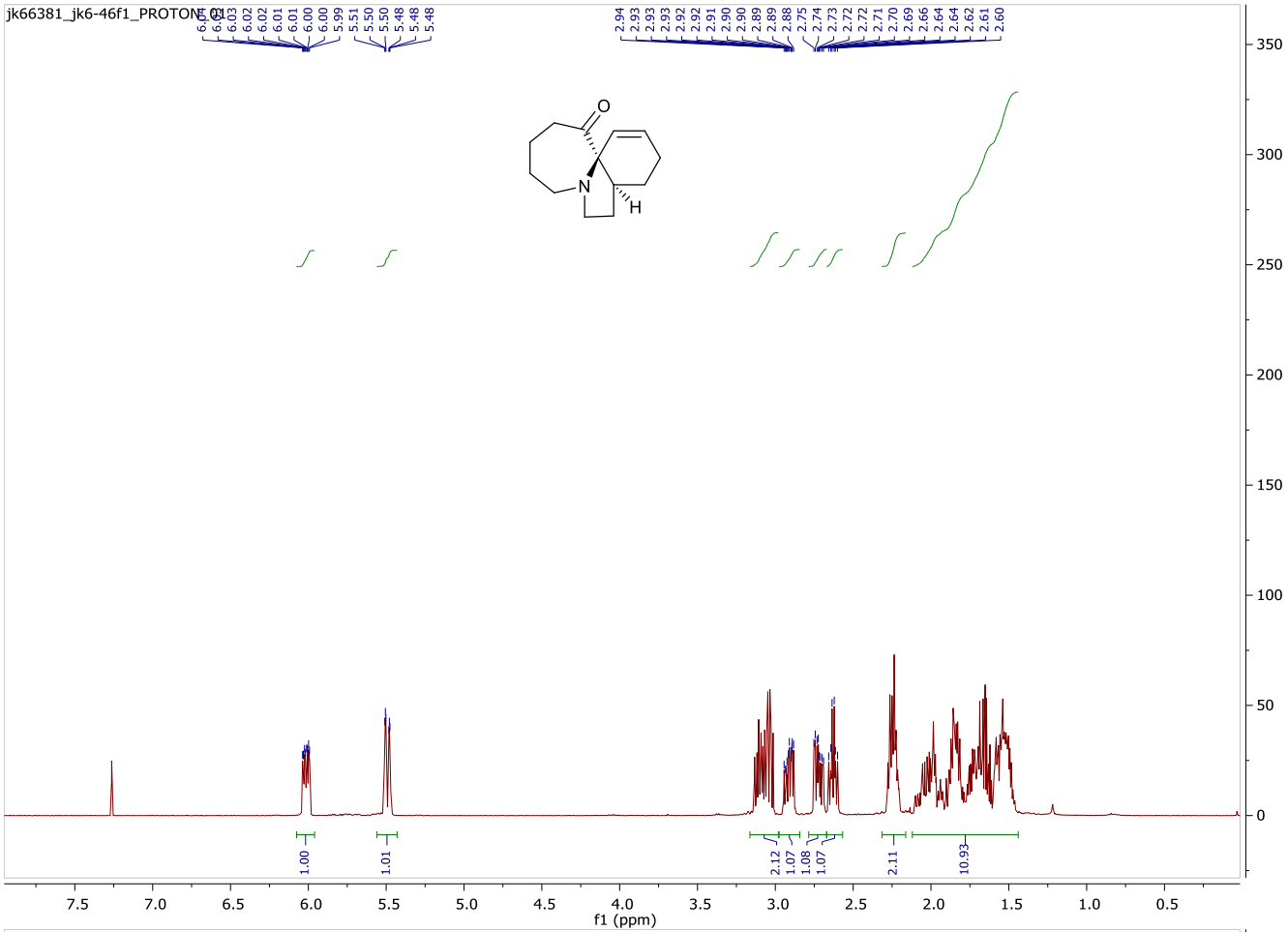
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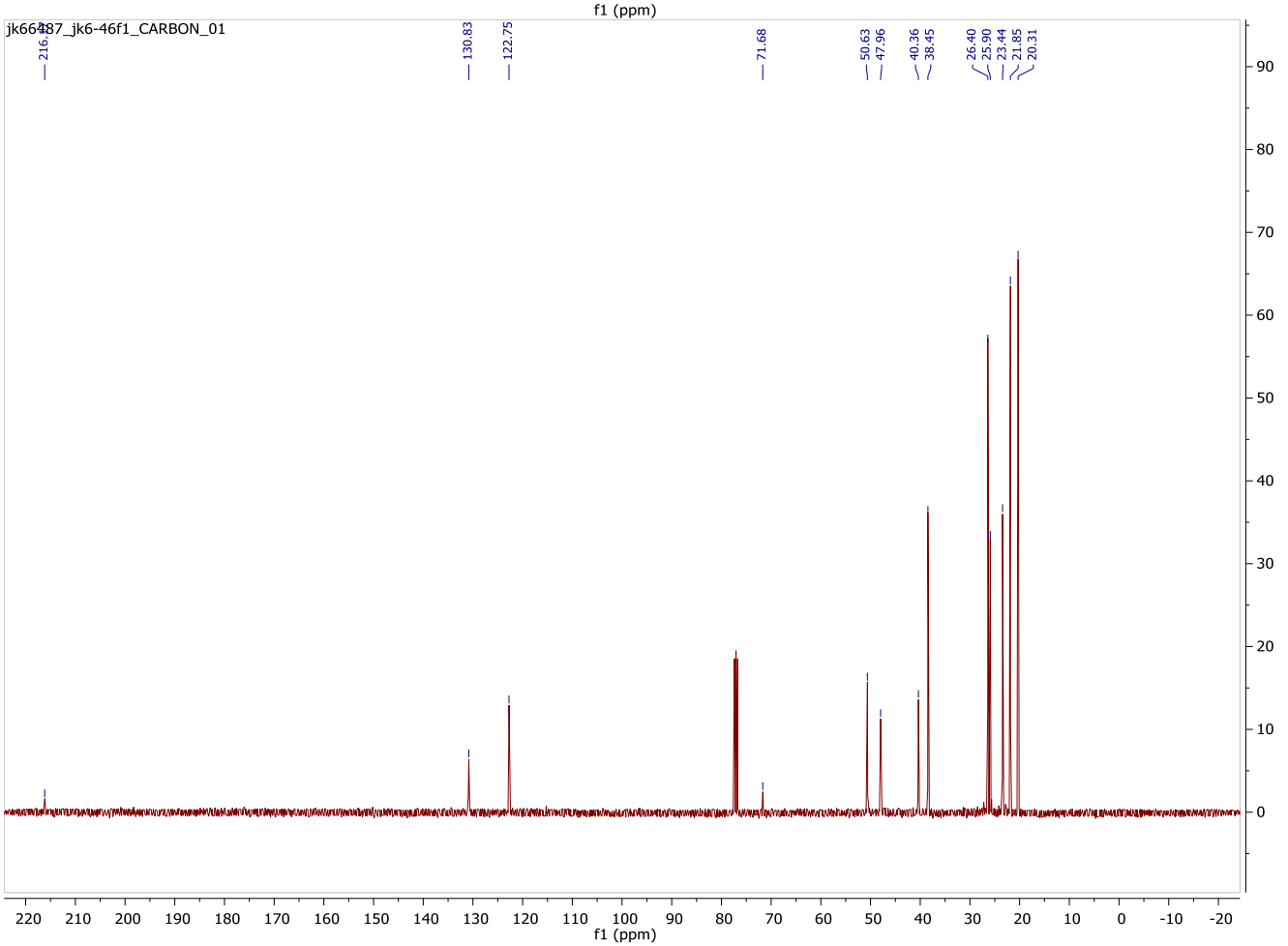
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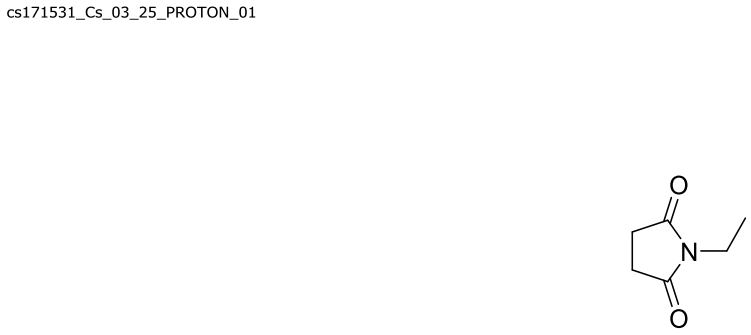

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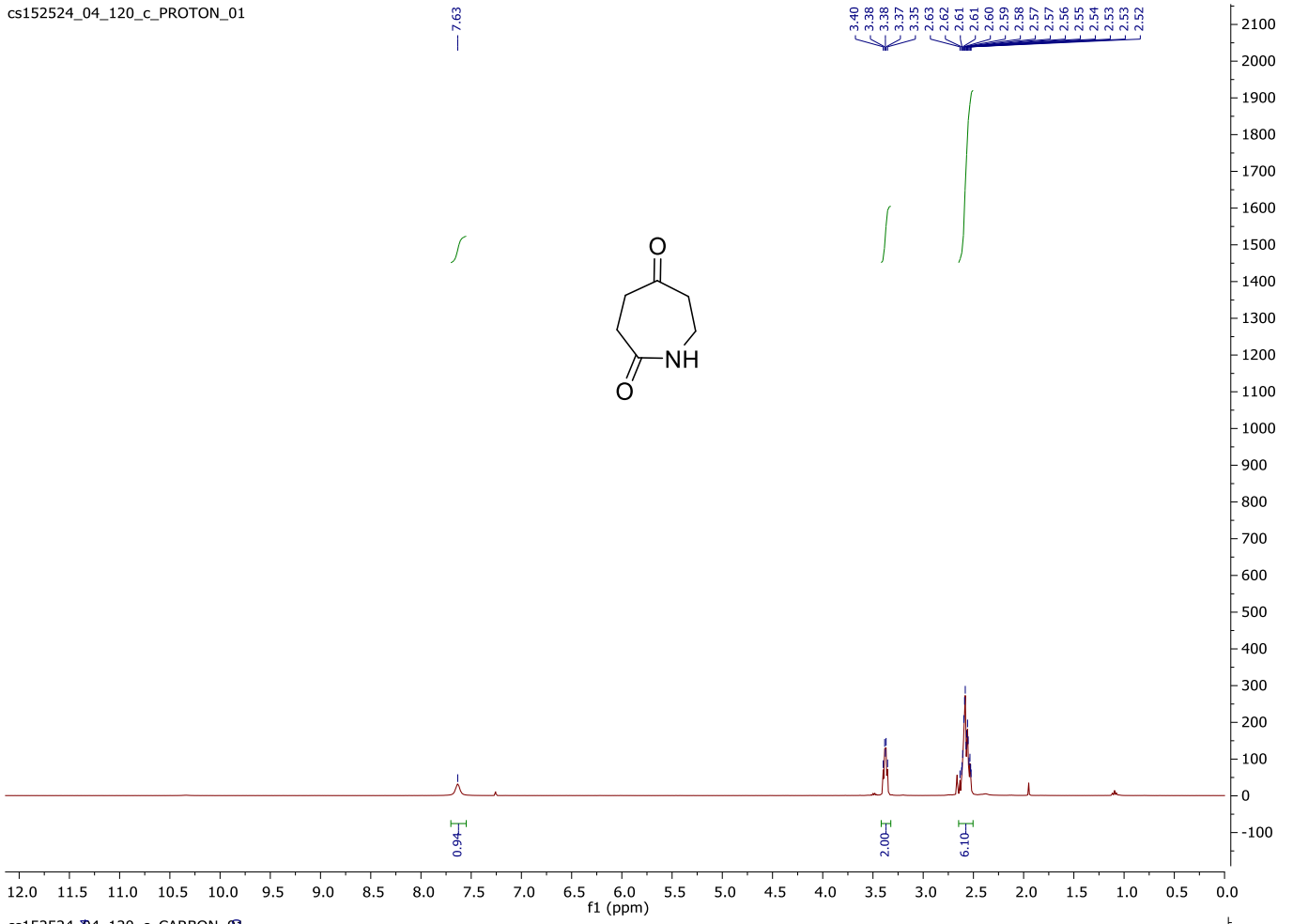

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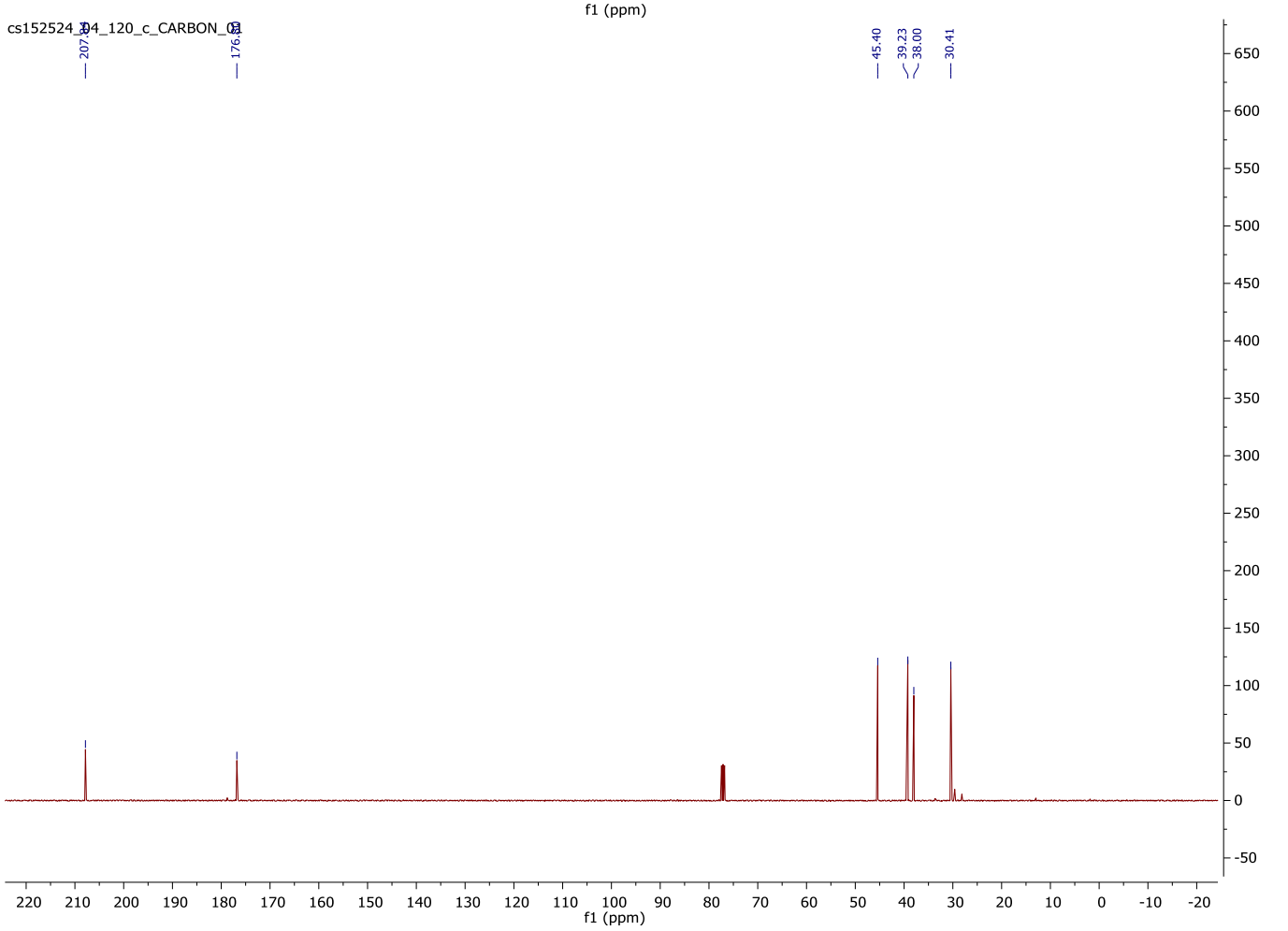
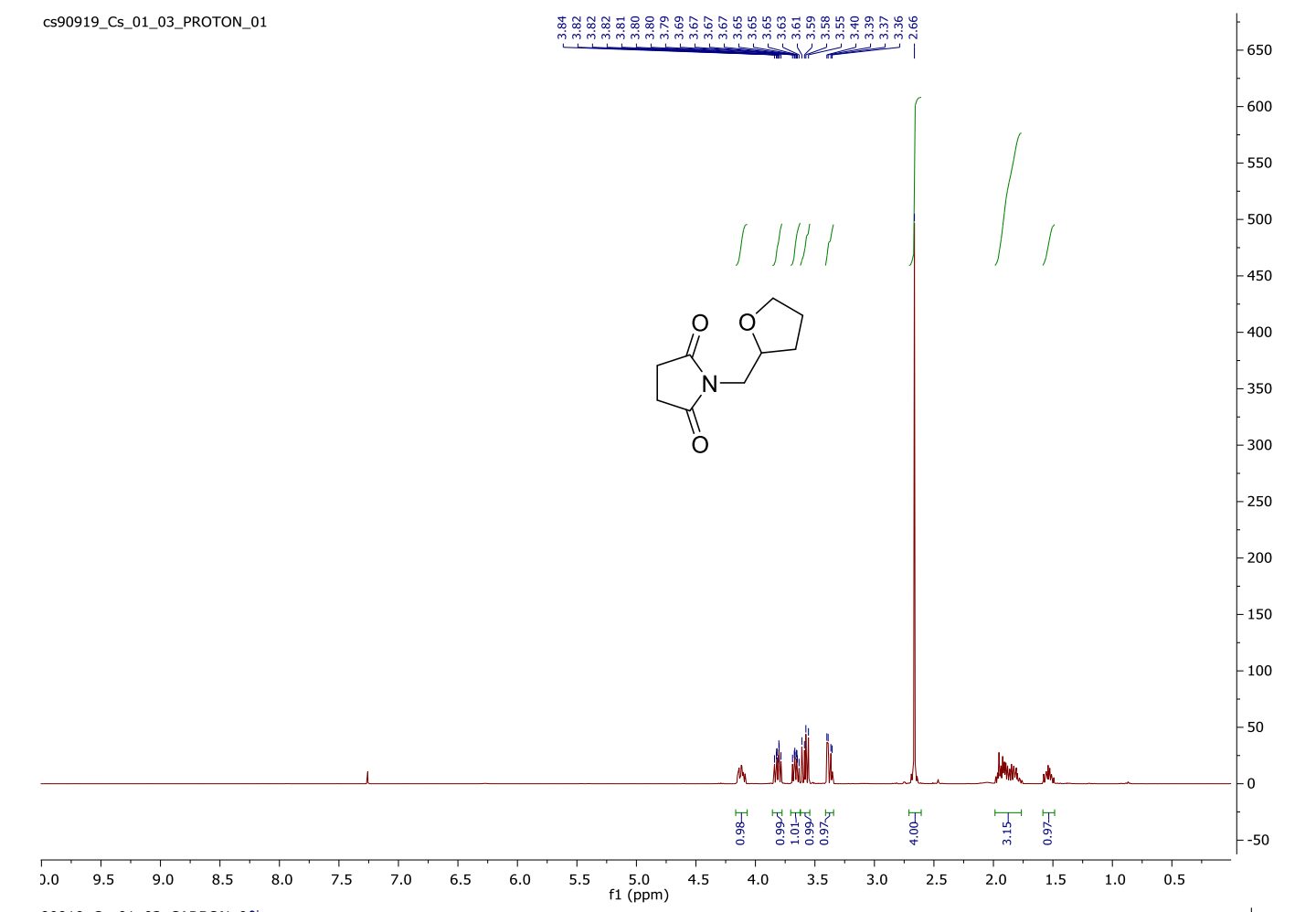
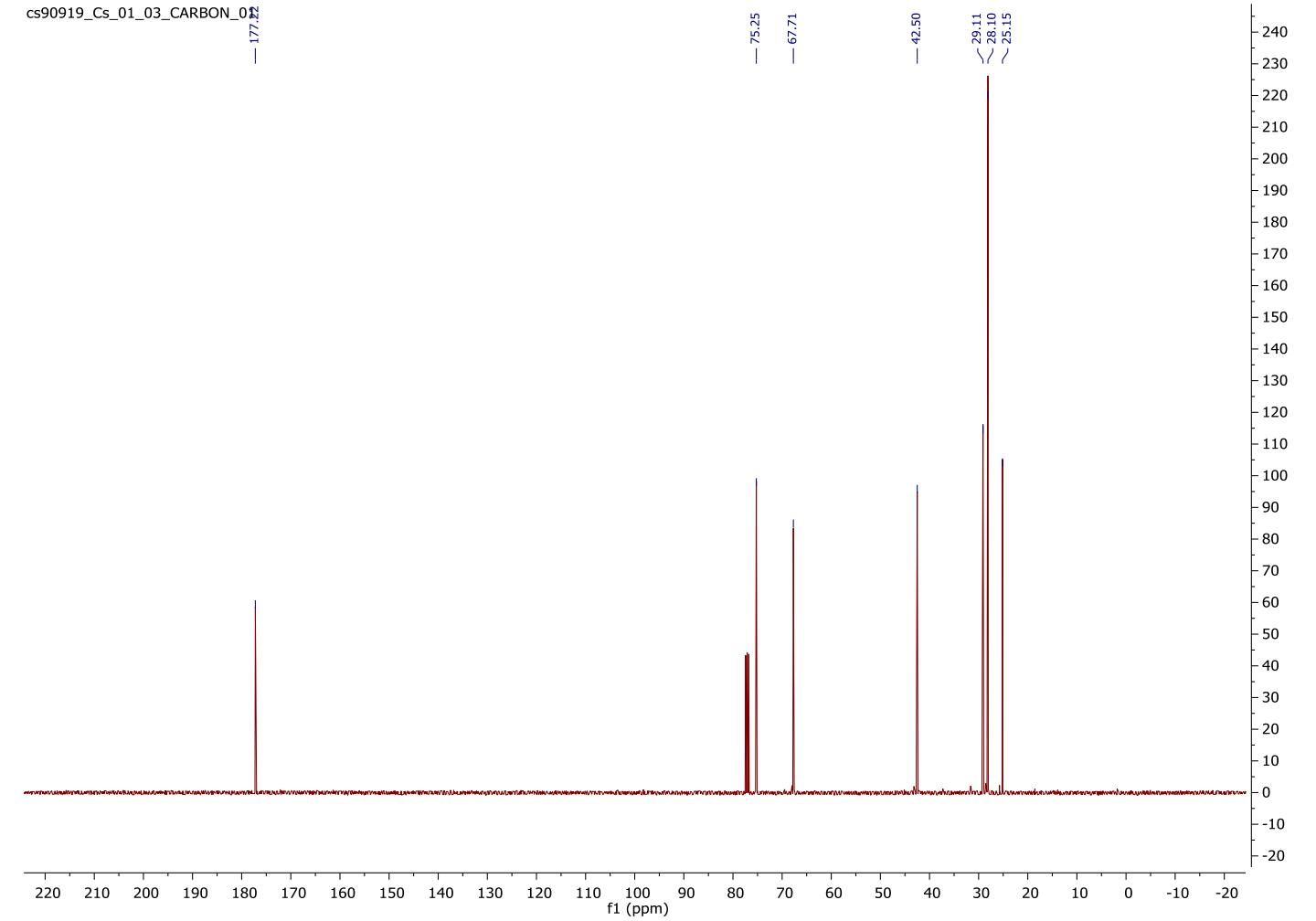
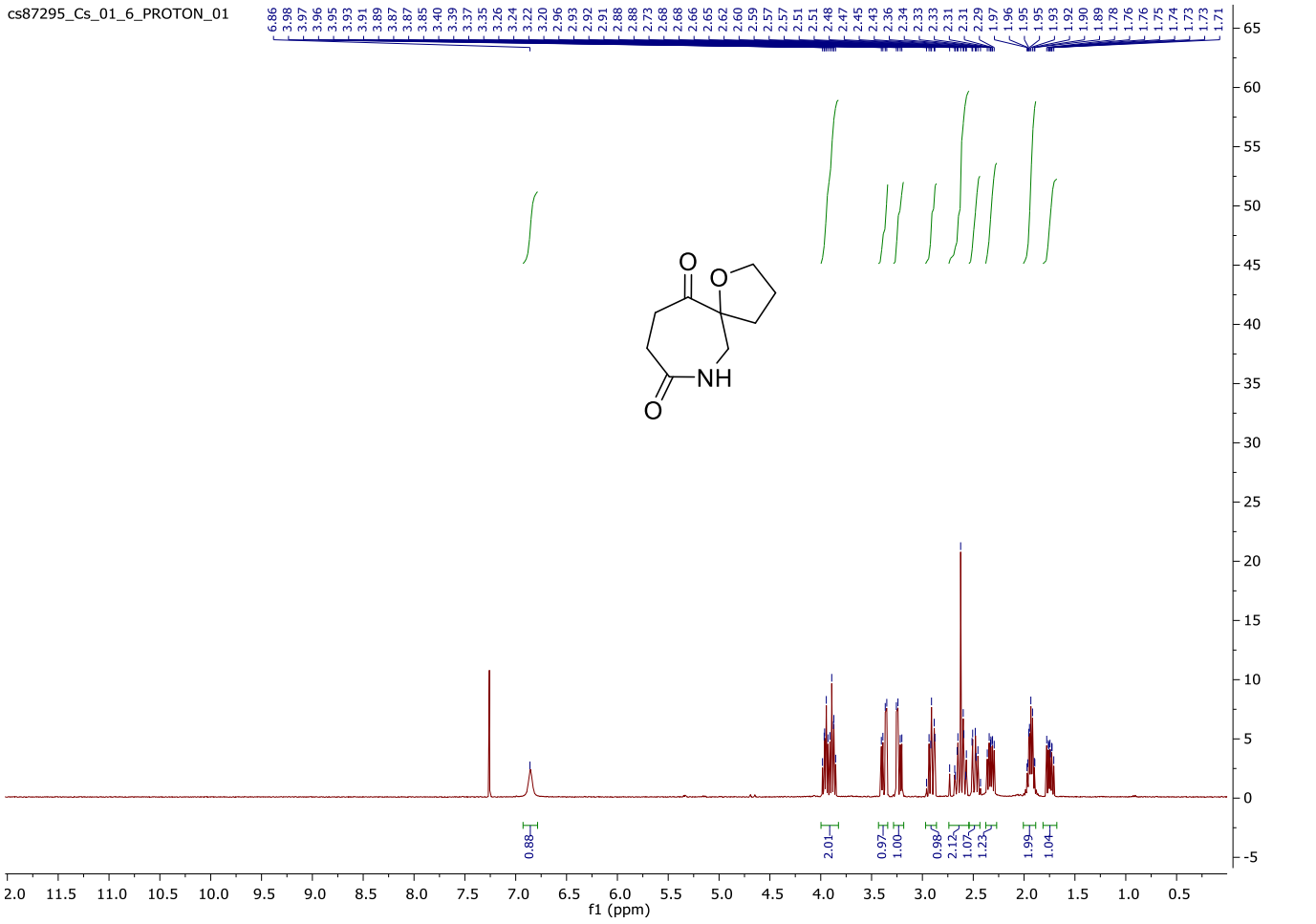
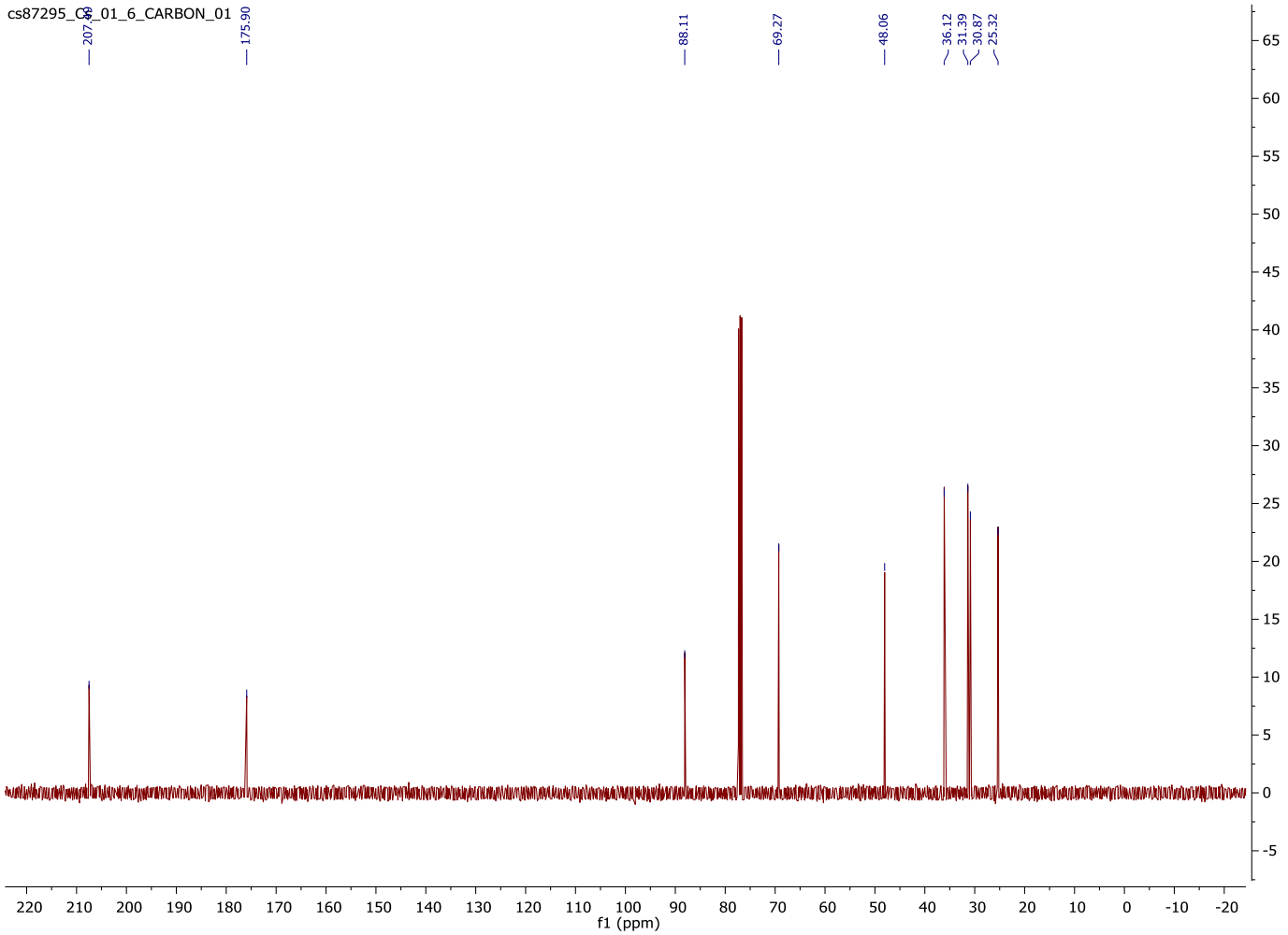


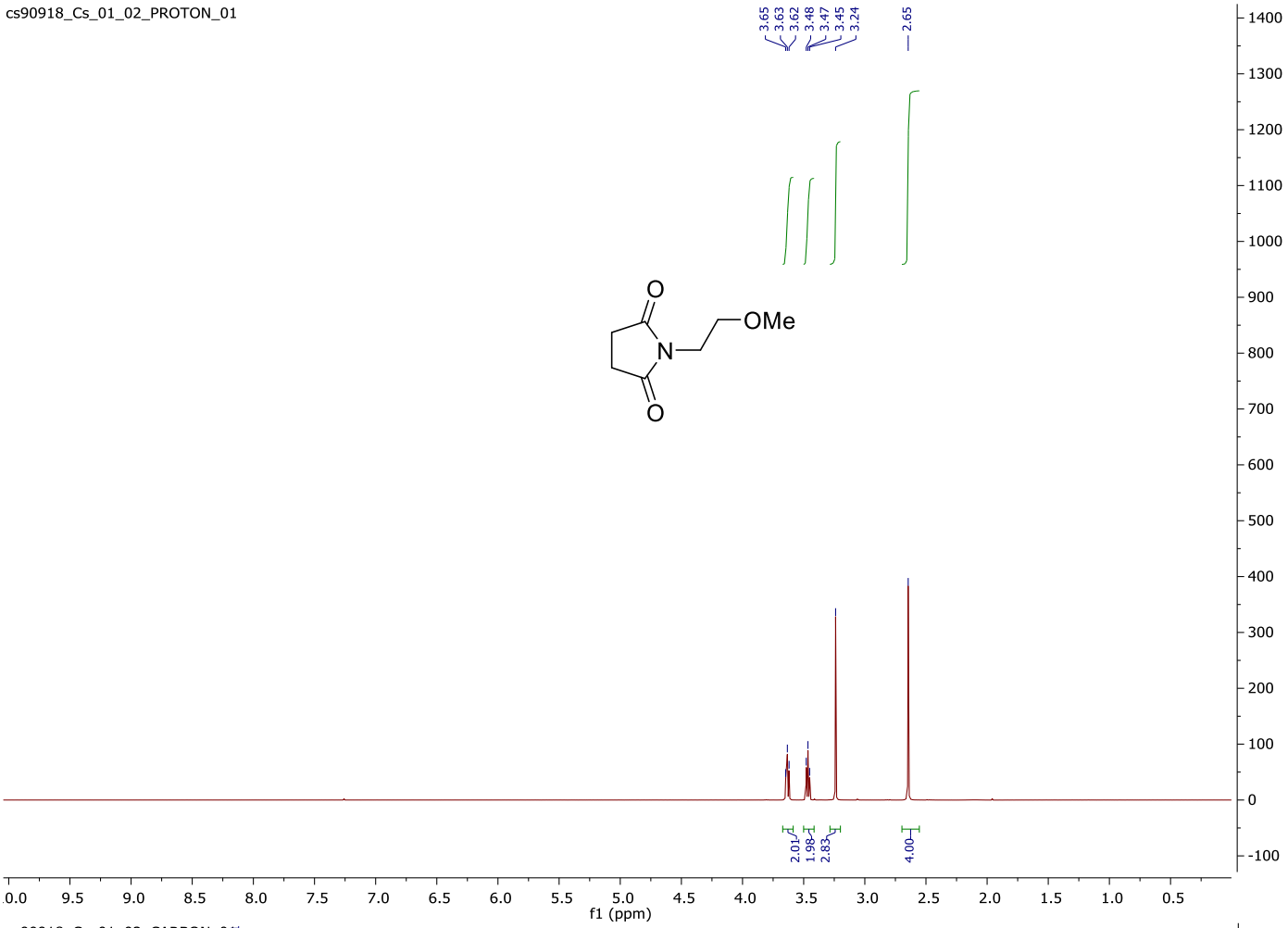

cs90919_Cs_01_03_PROTON_01
3.84
3.82
3.82
3.82
3.81
3.80
3.80
3.79
3.69
3.67
3.67
3.67
3.65
3.65
3.65
3.63
3.61
3.59
3.58
3.55
3.40
3.39
3.37
3.36
2.66
O
O
N
O
0.98
0.99
1.01
0.99
0.97
4.00
3.15
0.97
f1 (ppm)


cs90919_Cs_01_03_CARBON_01
177.22
75.25
67.71
42.50
29.11
28.10
25.15
f1 (ppm)

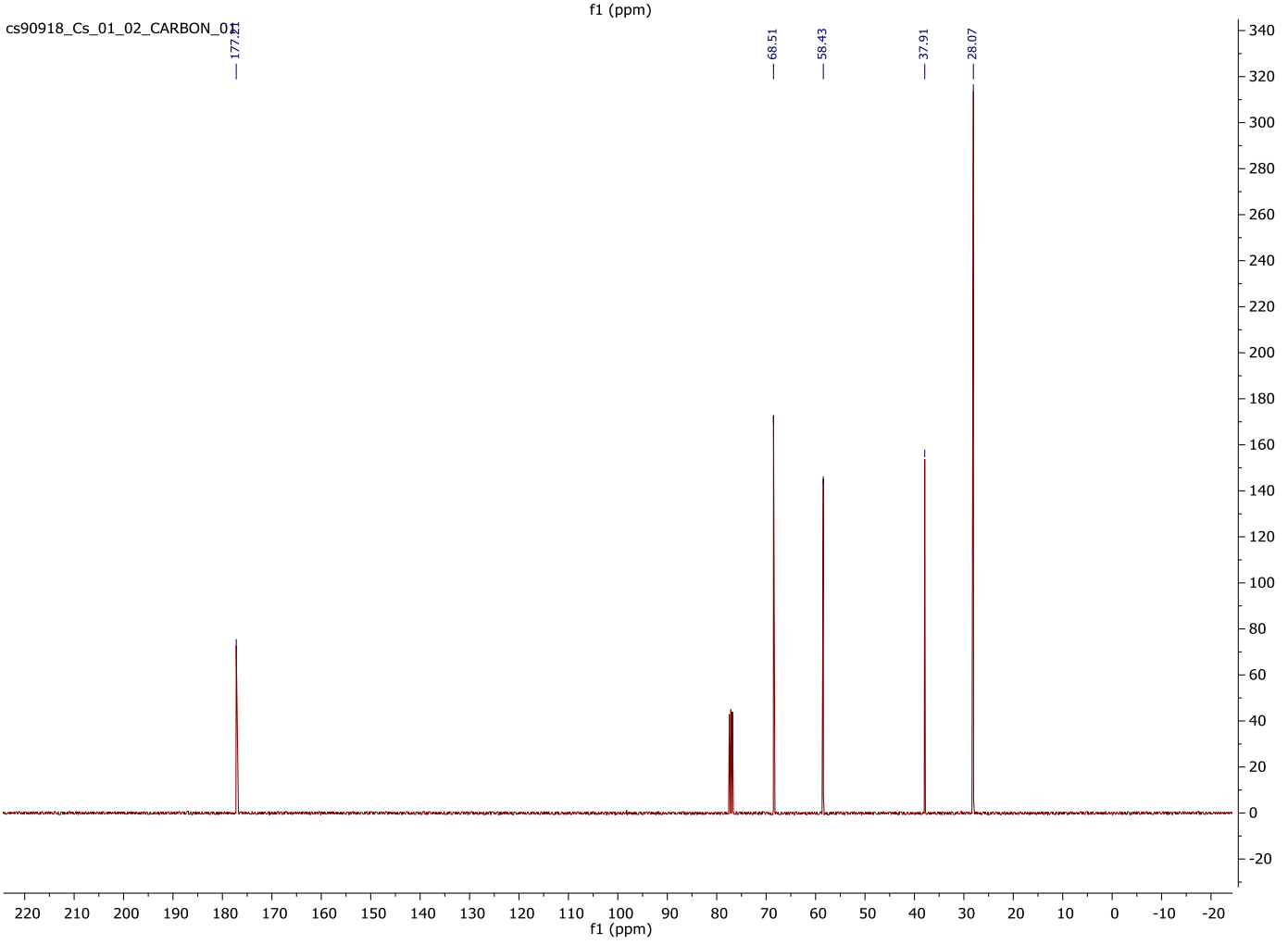

cs87295_Cs_01_6_PROTON_01
6.86 3.98 3.97 3.96 3.95 3.93 3.91 3.89 3.87 3.87 3.85 3.40 3.39 3.37 3.35 3.26 3.24 3.22 3.20 2.96 2.93 2.92 2.91 2.88 2.88 2.73 2.68 2.68 2.66 2.65 2.62 2.60 2.59 2.57 2.57 2.51 2.51 2.48 2.47 2.45 2.43 2.36 2.34 2.33 2.33 2.31 2.31 2.29 1.97 1.96 1.95 1.95 1.93 1.92 1.90 1.89 1.78 1.76 1.76 1.75 1.74 1.73 1.73 1.71
O
O
NH
O
0.88
2.01
0.97
1.00
0.98
2.12
1.07
1.23
1.99
1.04
f1 (ppm)

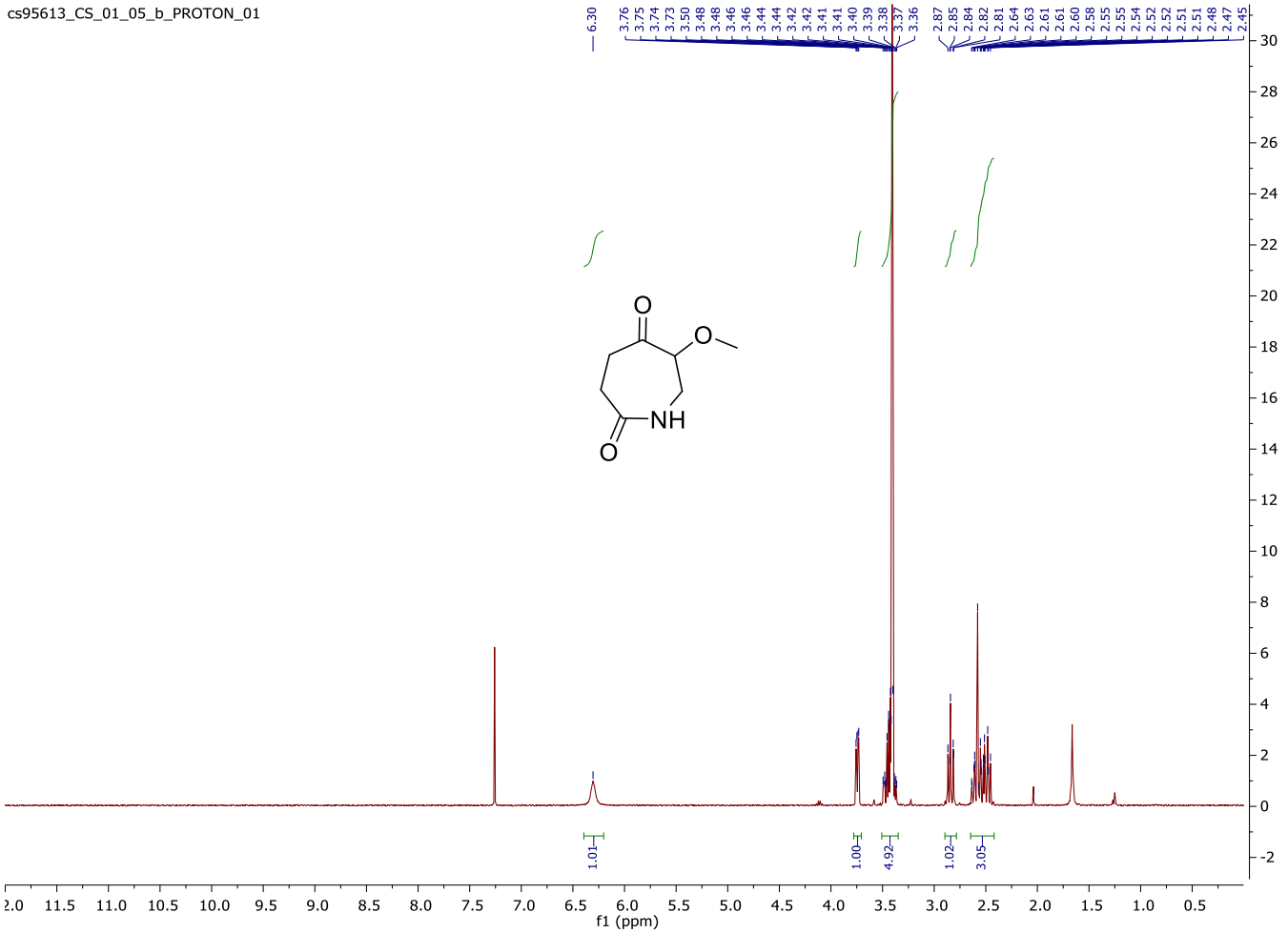

cs87295_Cs_01_6_CARBON_01
207.48
175.90
88.11
69.27
48.06
36.12
31.39
30.87
25.32
f1 (ppm)

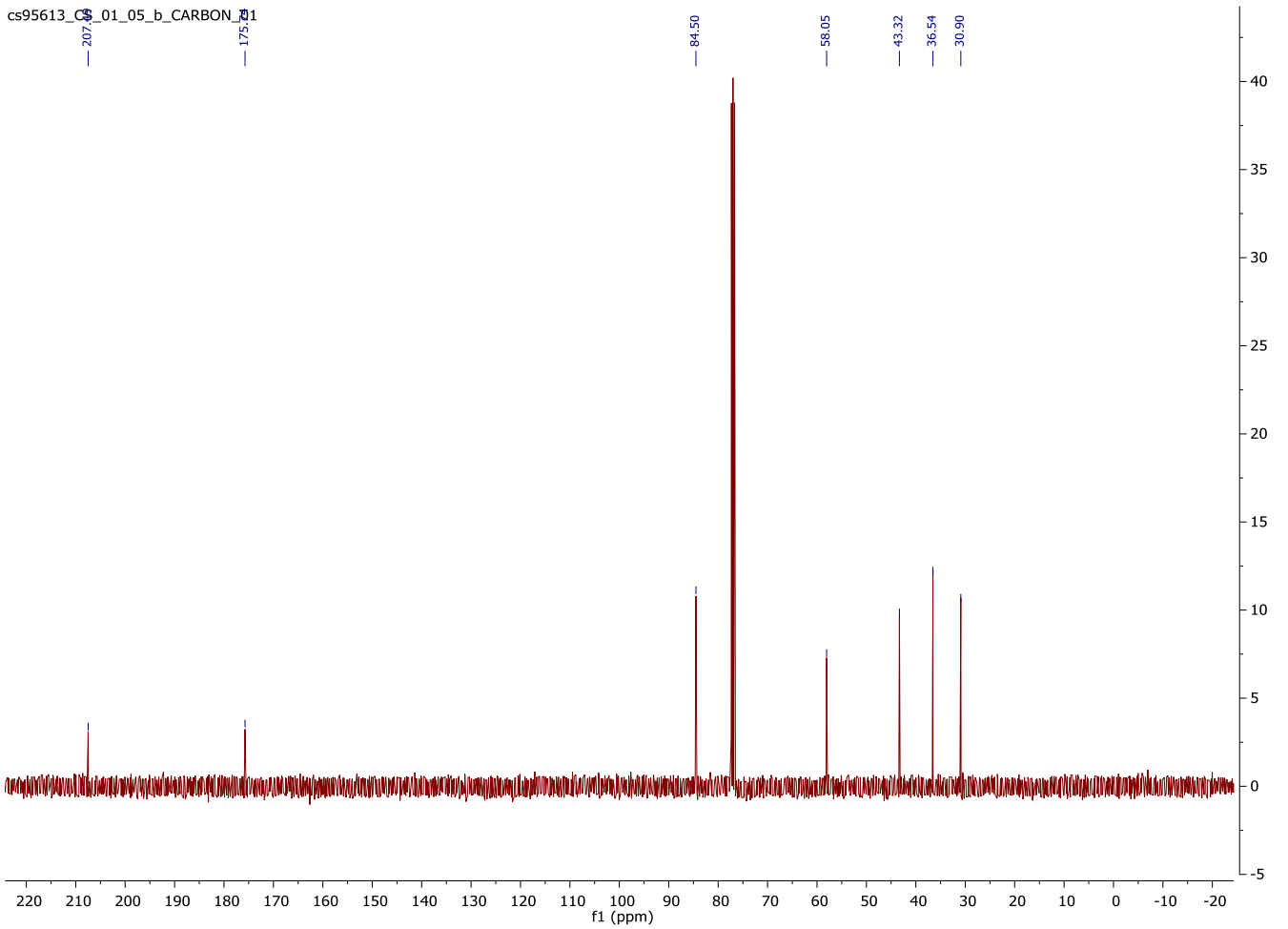
cs90918_Cs_01_02_PROTON_01

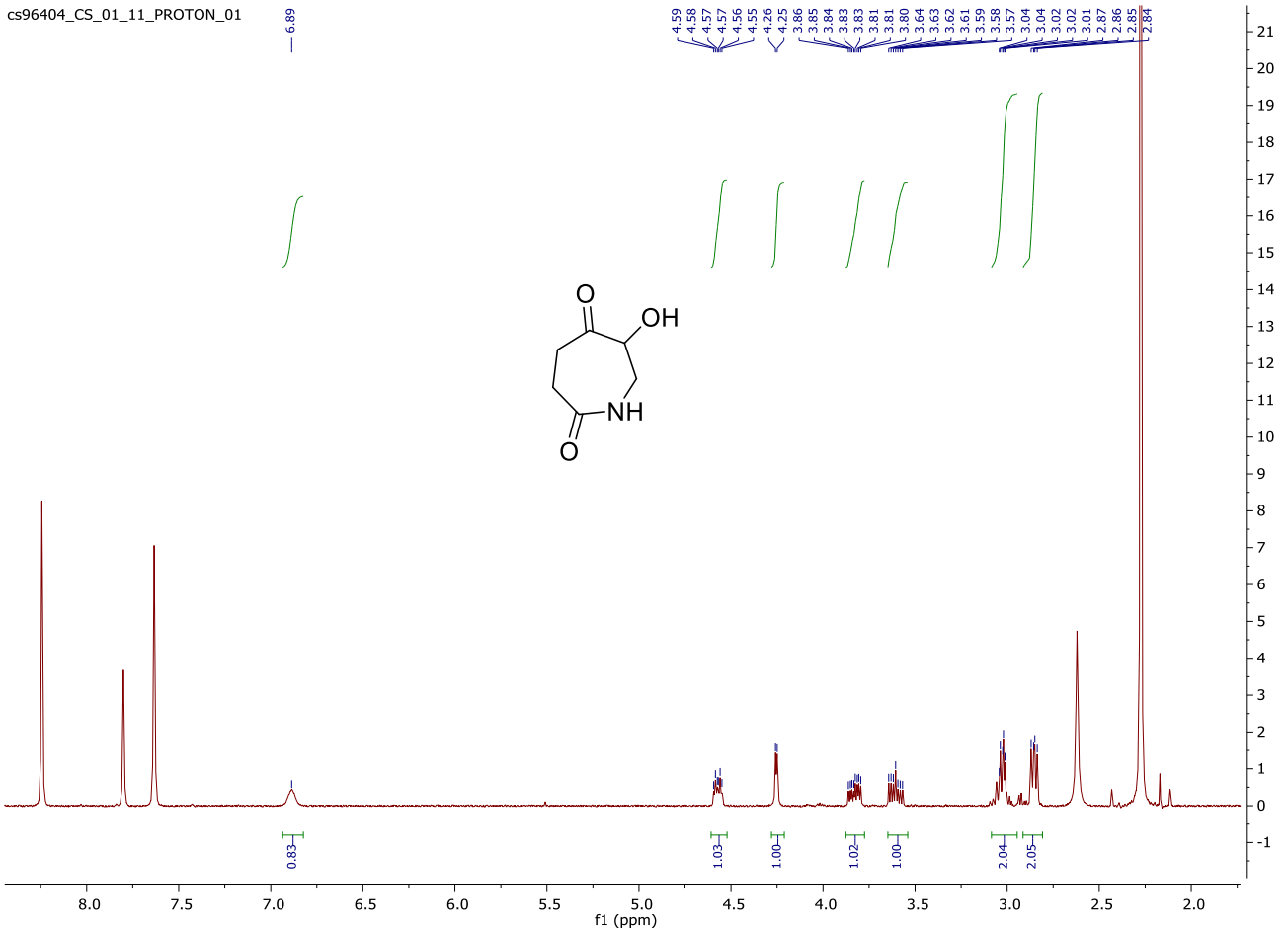


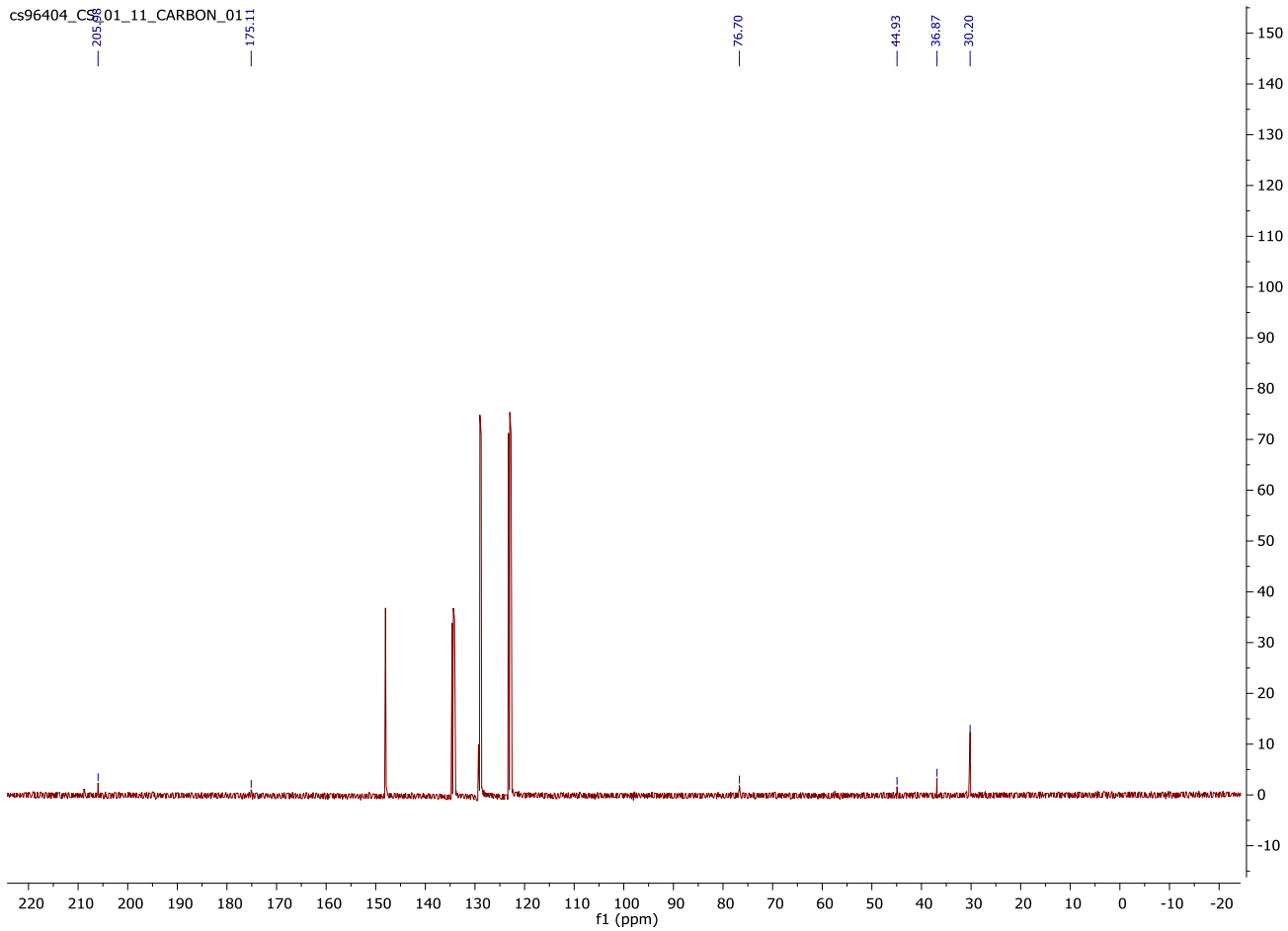
cs90918_Cs_01_02_CARBON_01

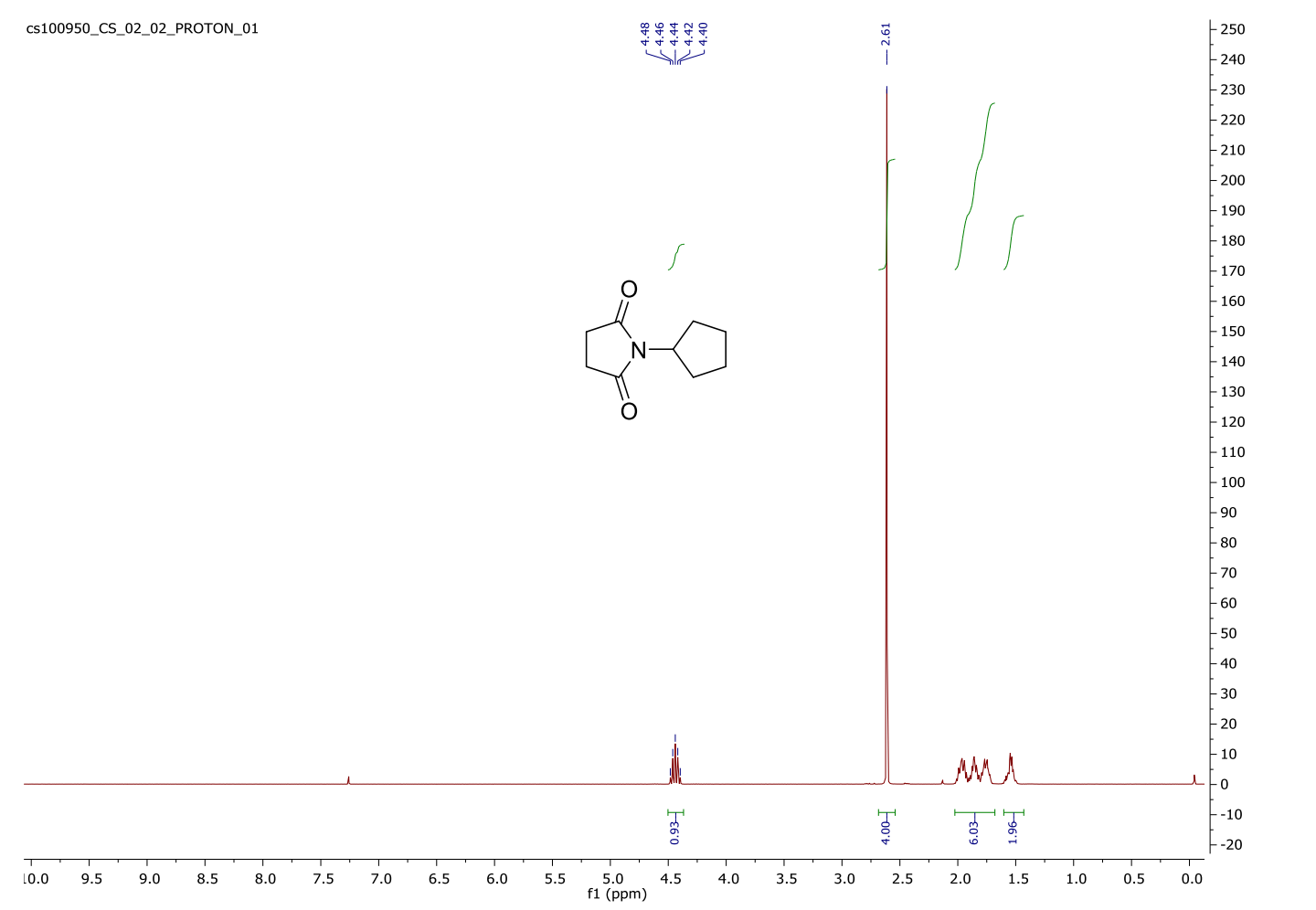


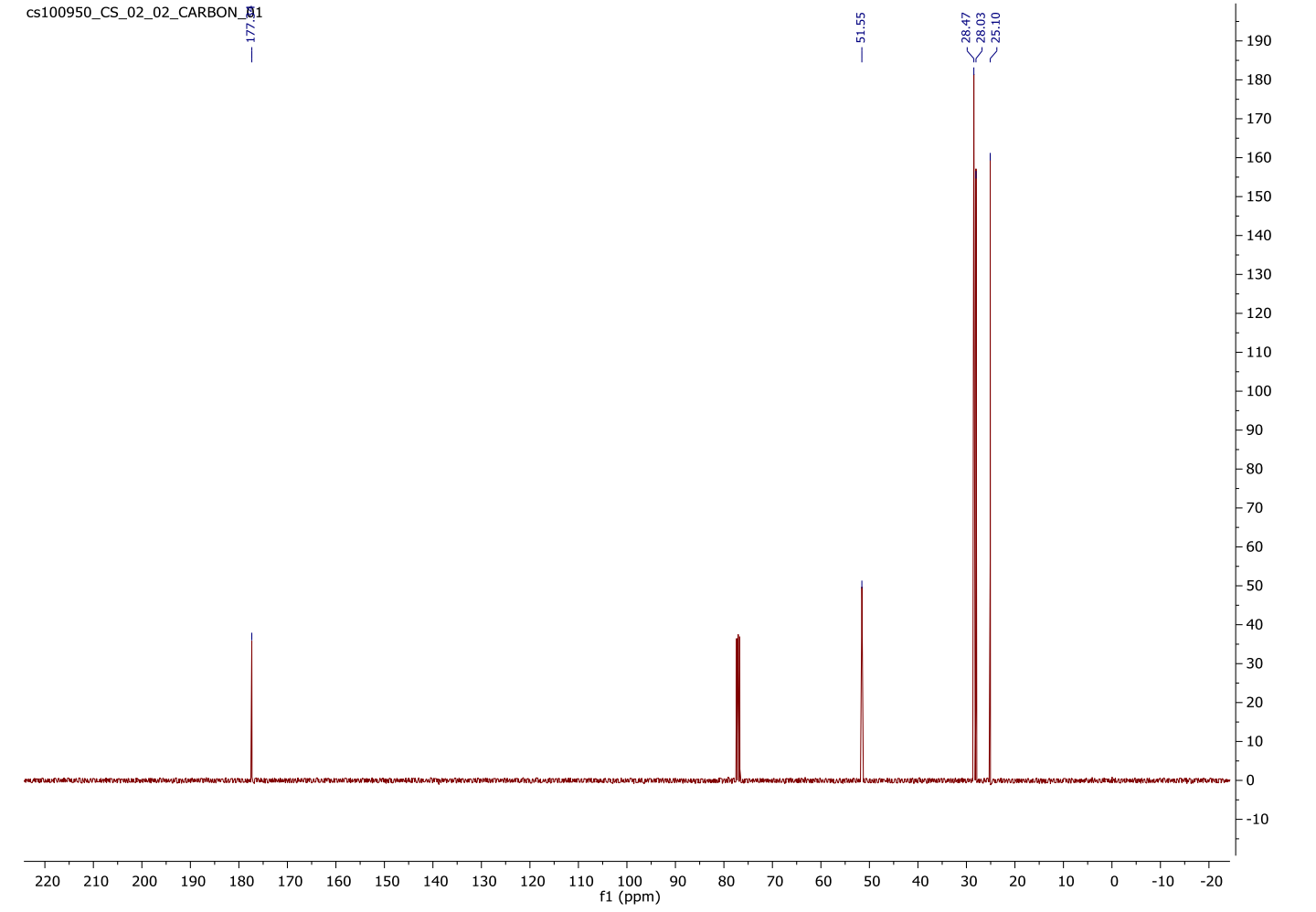

cs95613_CS_01_05_b_PROTON_01
6.30
3.76 3.75 3.74 3.73 3.50 3.48 3.48 3.46 3.46 3.44 3.44 3.42 3.42 3.41 3.41 3.40 3.39 3.38 3.37 3.36
2.87 2.85 2.84 2.82 2.81 2.64 2.63 2.61 2.61 2.60 2.58 2.55 2.55 2.54 2.52 2.52 2.51 2.51 2.48 2.47 2.45
O
O
NH
O
1.01
1.00
4.92
1.02
3.05
f1 (ppm)

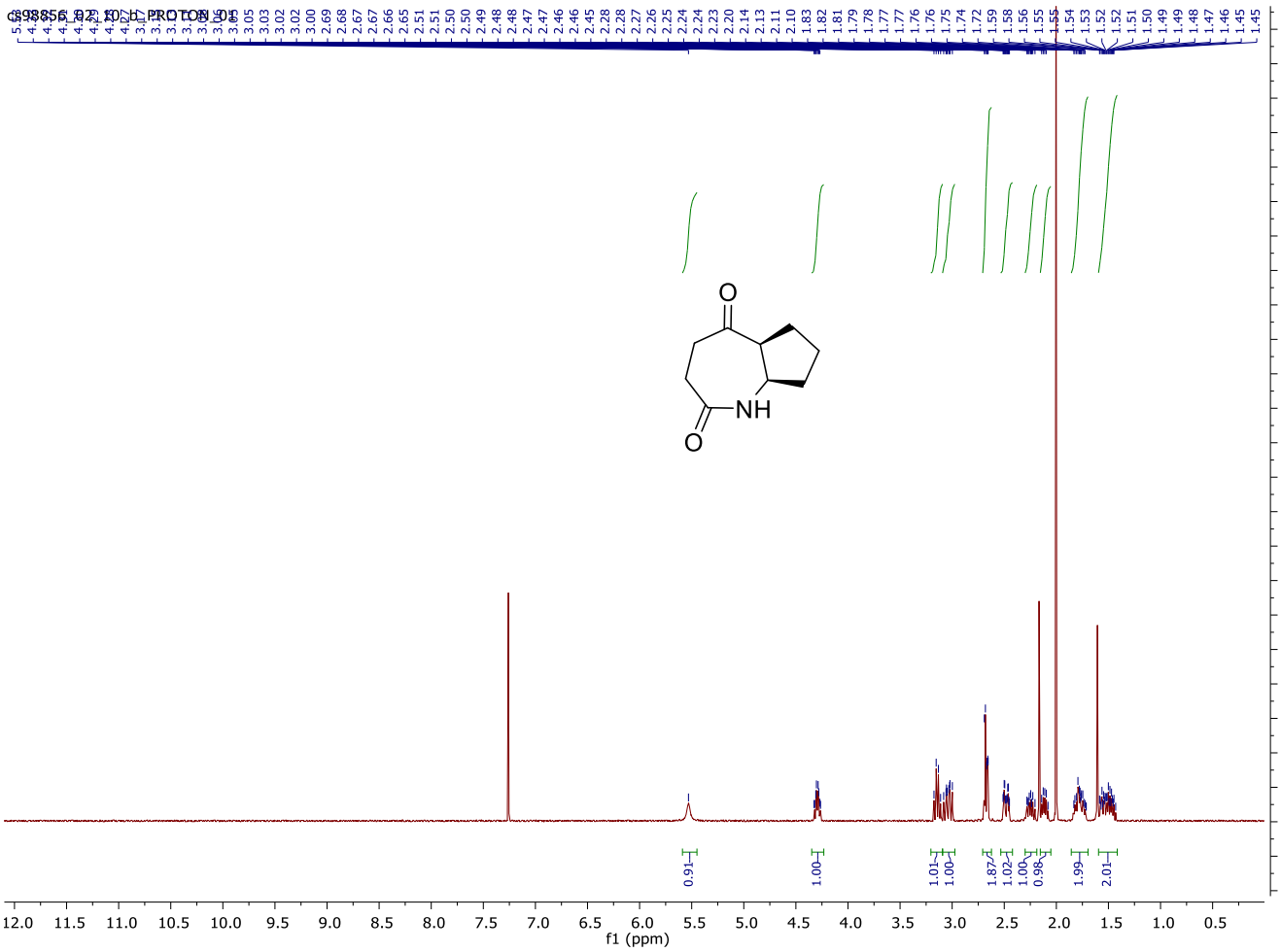

cs95613_CS_01_05_b_CARBON_01
207.43
175.21
84.50
58.05
43.32
36.54
30.90
f1 (ppm)

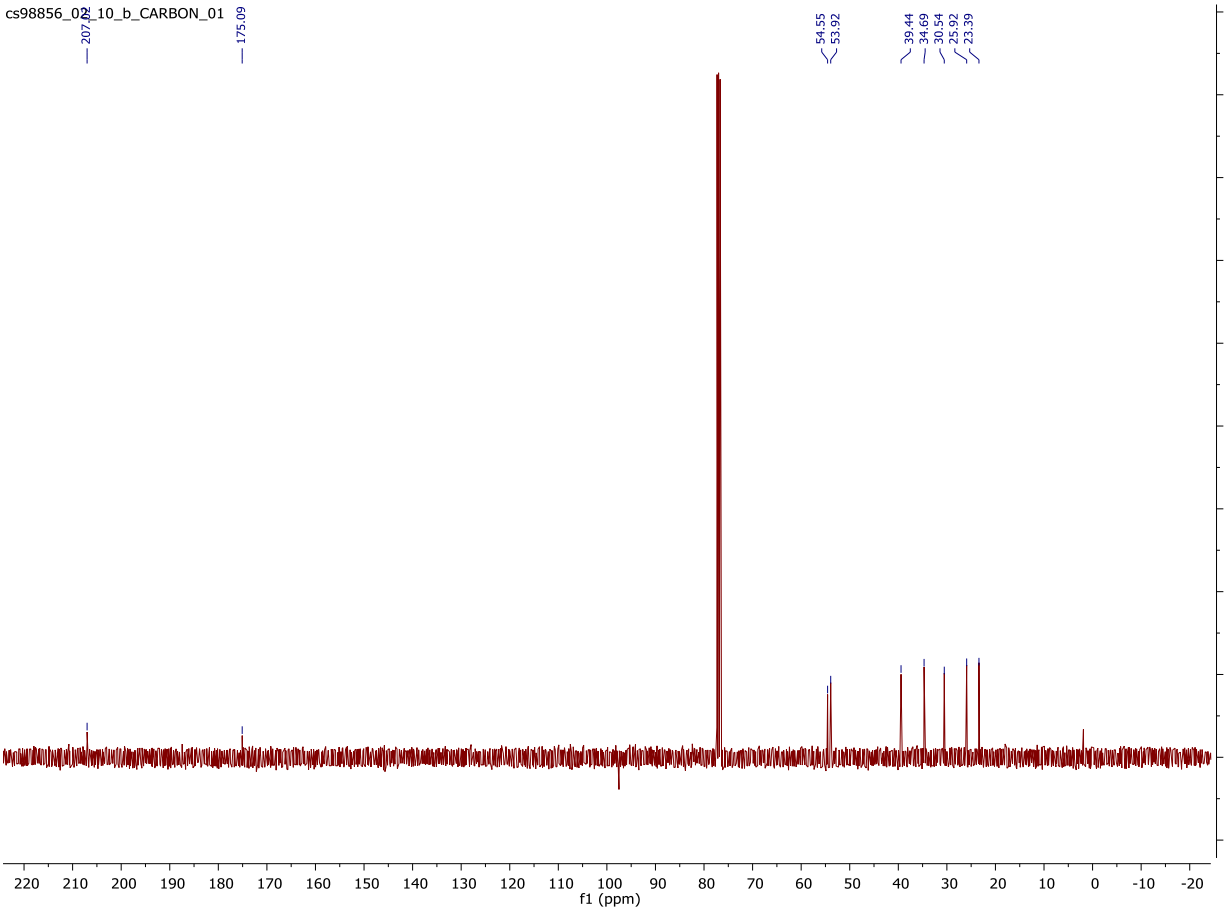

cs96404_CS_01_11_PROTON_01
6.89
4.59
4.58
4.57
4.57
4.56
4.55
4.26
4.25
3.86
3.85
3.84
3.83
3.83
3.81
3.81
3.80
3.64
3.63
3.62
3.61
3.59
3.58
3.57
3.04
3.04
3.02
3.01
2.87
2.86
2.85
2.84
O
OH
NH
O
0.83
1.03
1.00
1.02
1.00
2.04
2.05
f1 (ppm)


cs96404_CS_01_11_CARBON_01
205.98
175.11
76.70
44.93
36.87
30.20
f1 (ppm)

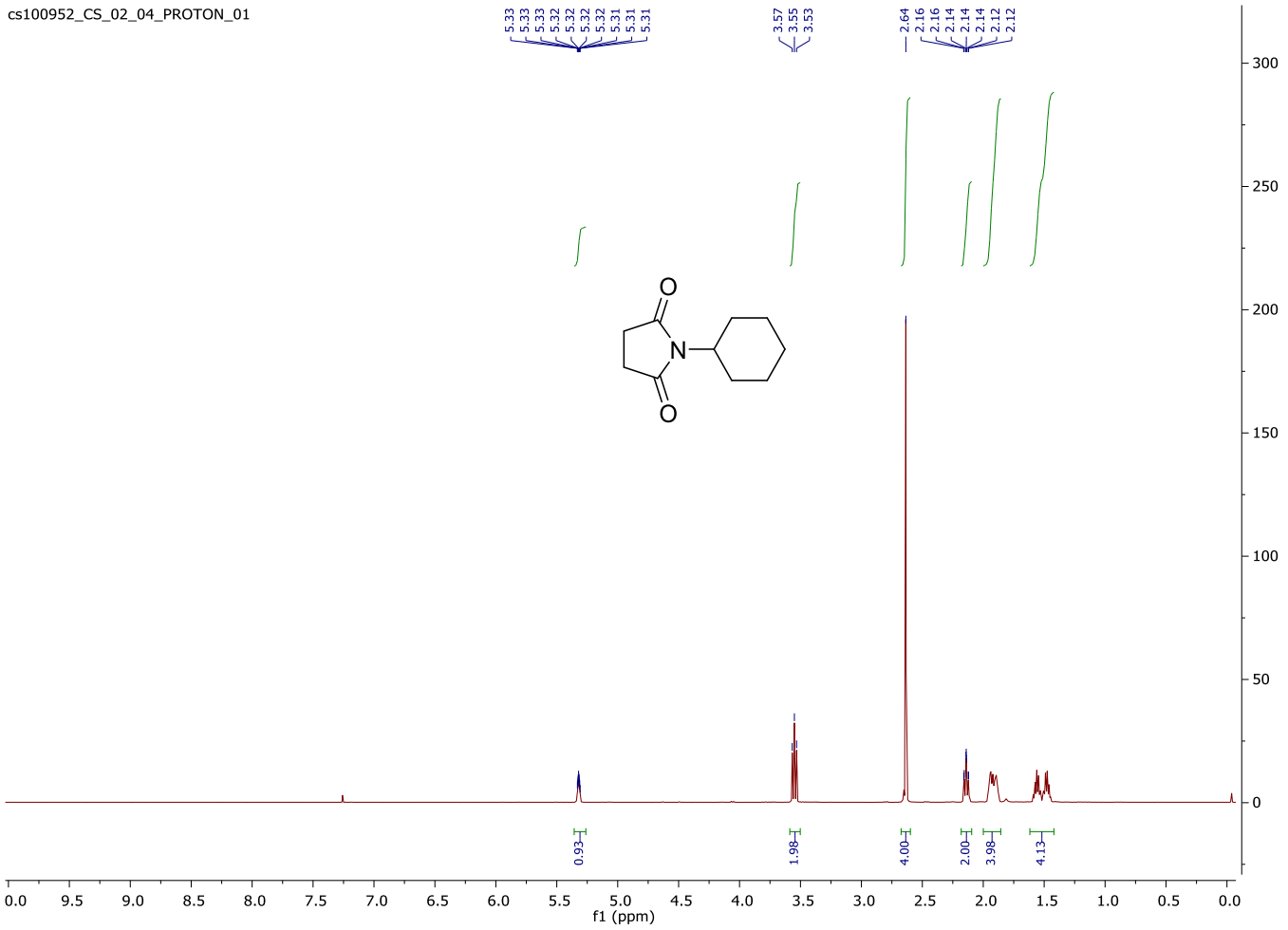

cs100950_CS_02_02_PROTON_01
4.48
4.46
4.44
4.42
4.40
2.61
O
N
O
0.93
4.00
6.03
1.96
f1 (ppm)


cs100950_CS_02_02_CARBON_01
177.81
51.55
28.47
28.03
25.10
f1 (ppm)

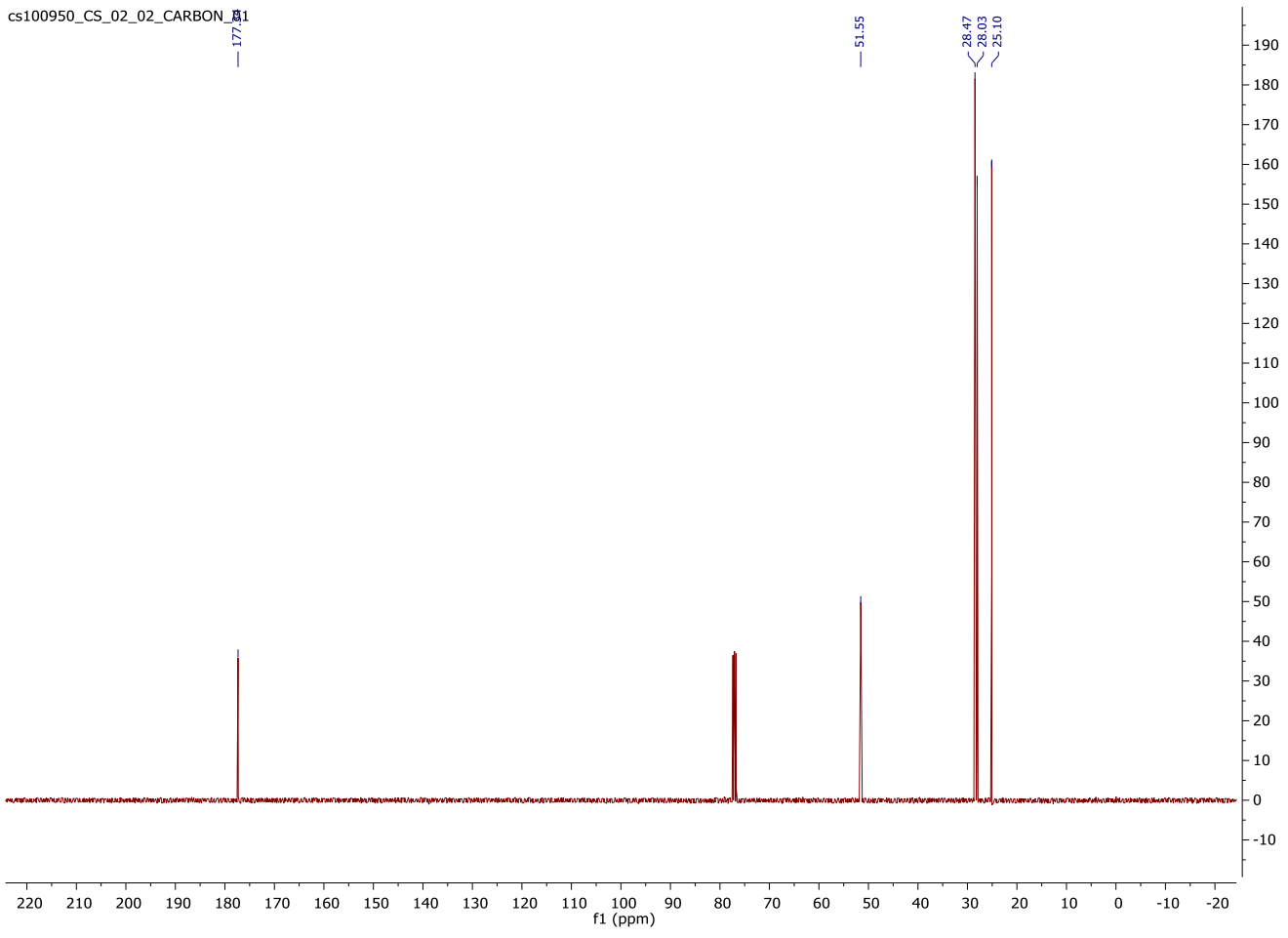

cs98856_02_10_b_PROTON_01
O
NH
O
0.91
1.00
1.01
1.00
1.87
1.02
1.00
0.98
1.99
2.01
f1 (ppm)

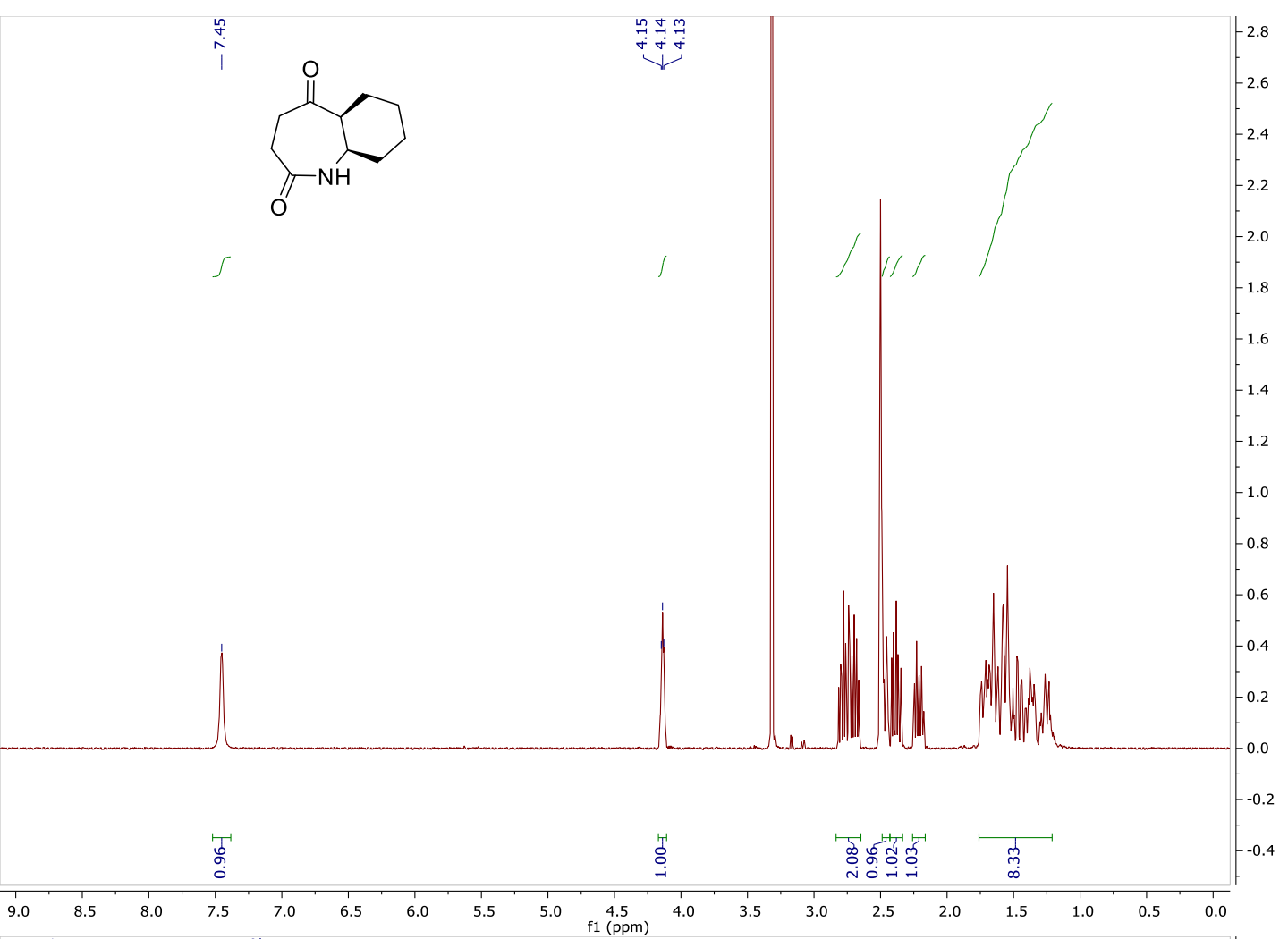

cs98856_02_10_b_CARBON_01
207.22
175.09
54.55
53.92
39.44
34.69
30.54
25.92
23.39
f1 (ppm)

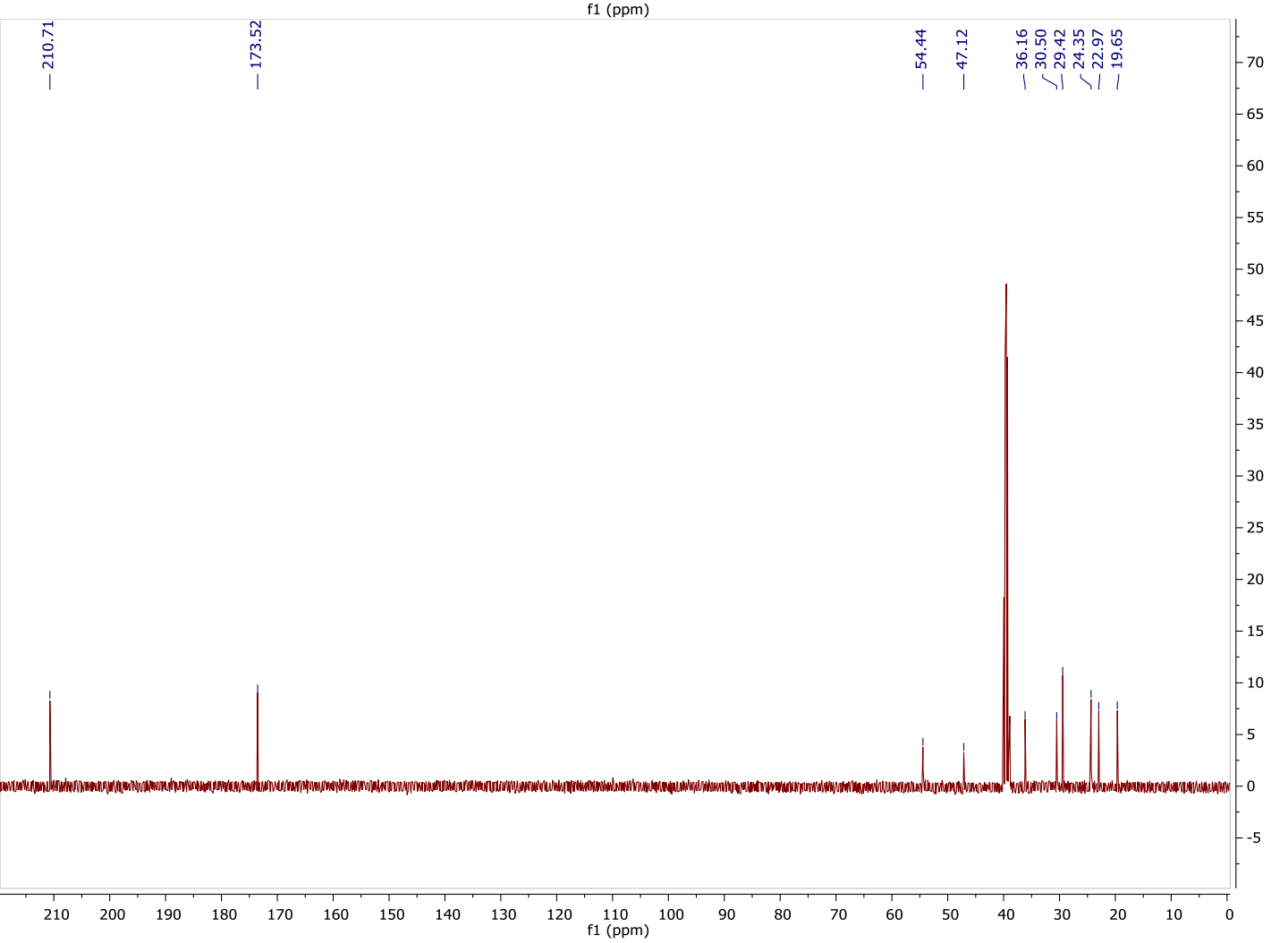
cs100952_CS_02_04_PROTON_01



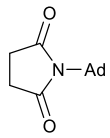
cs100950_CS_02_02_CARBON_01




7.45
4.15
4.14
4.13
O
NH
O
0.96
1.00
2.08
0.96
1.02
1.03
8.33
f1 (ppm)


210.71
173.52
54.44
47.12
36.16
30.50
29.42
24.35
22.97
19.65
f1 (ppm)

cs120701_cs_02_adm_sm_PROTON_01



2.52
2.37
2.36

4.00
5.94
2.98
6.12

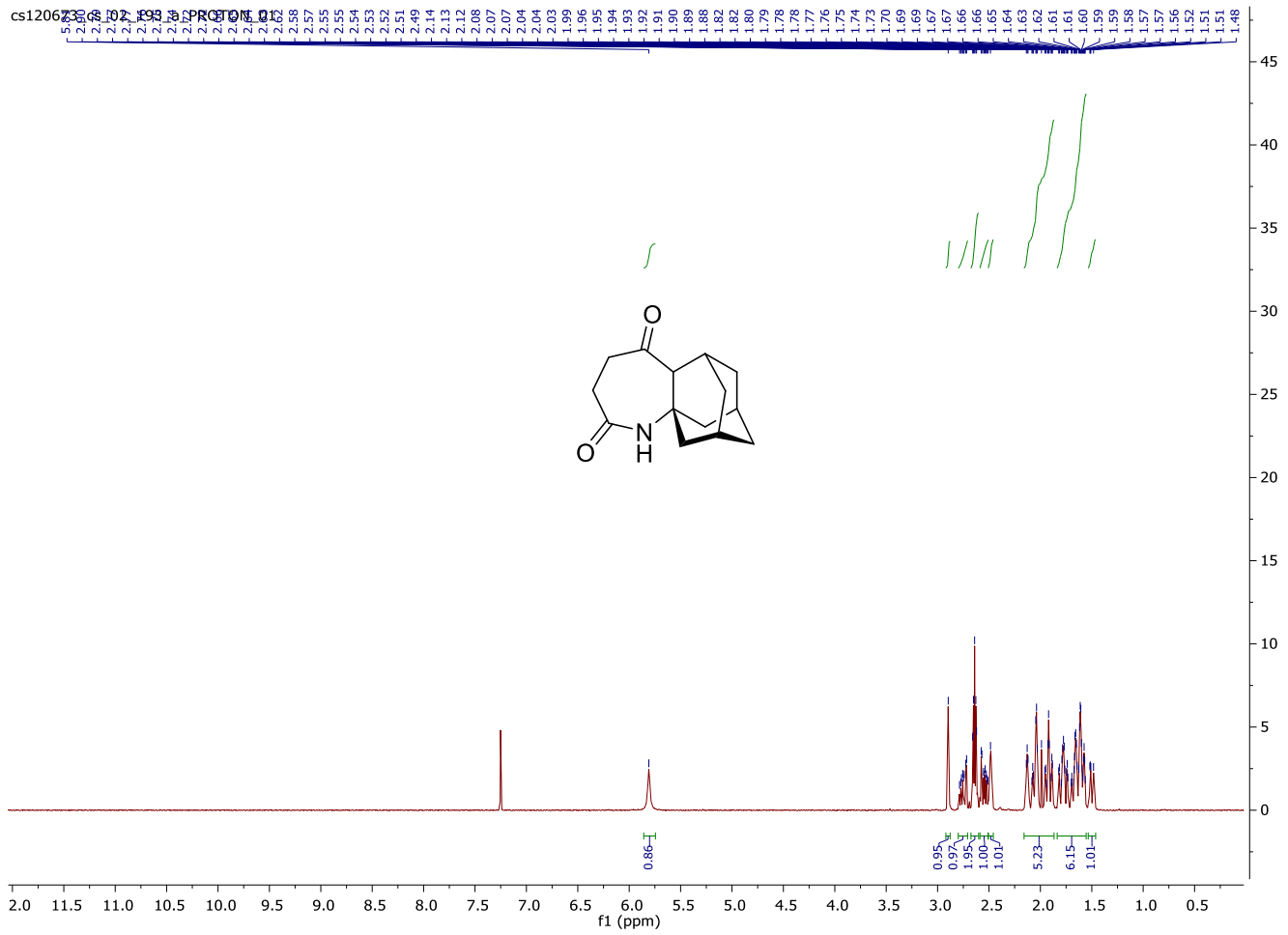
f1 (ppm)

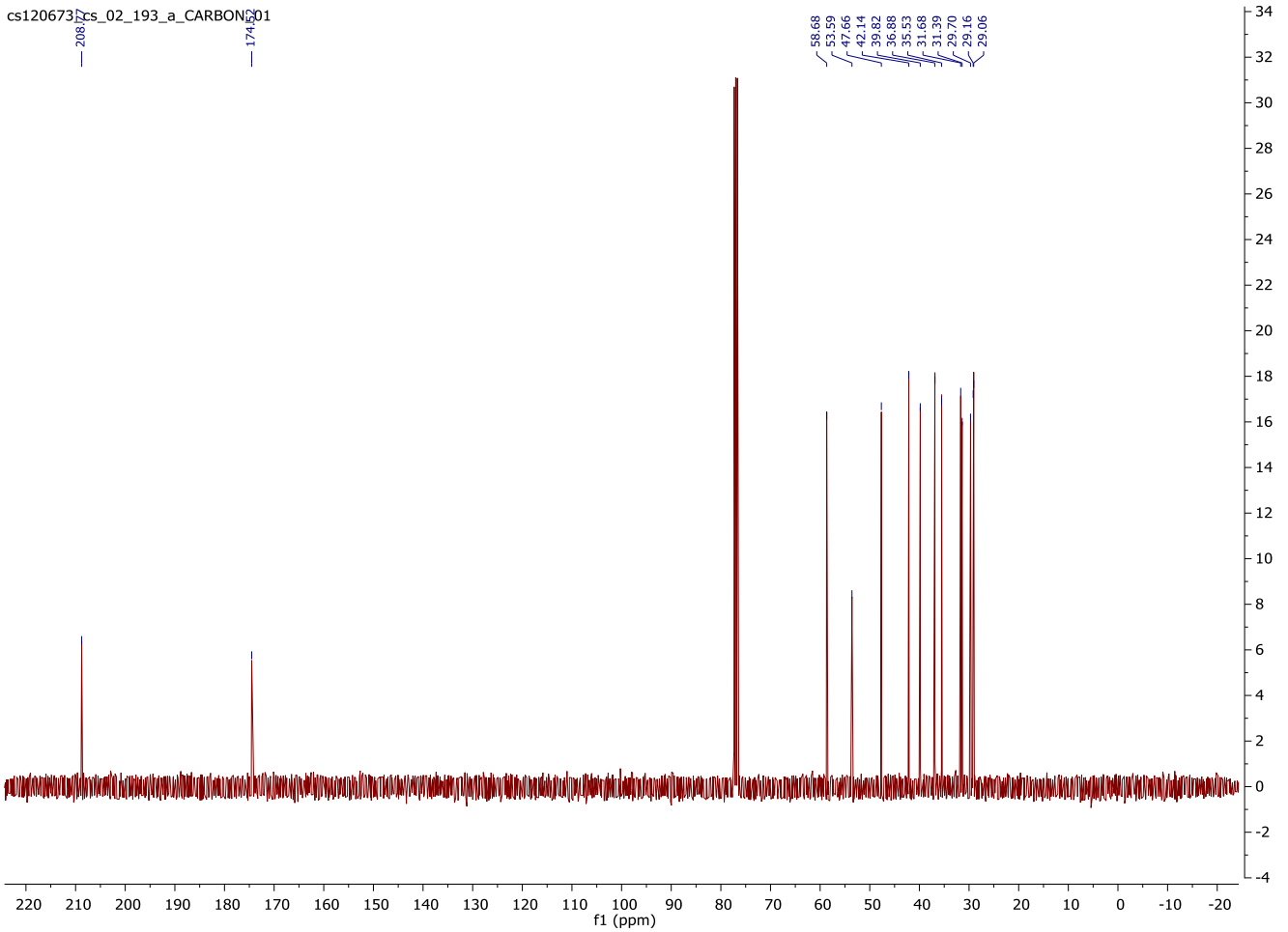
cs120701_cs_02_adm_sm_CARBON_01

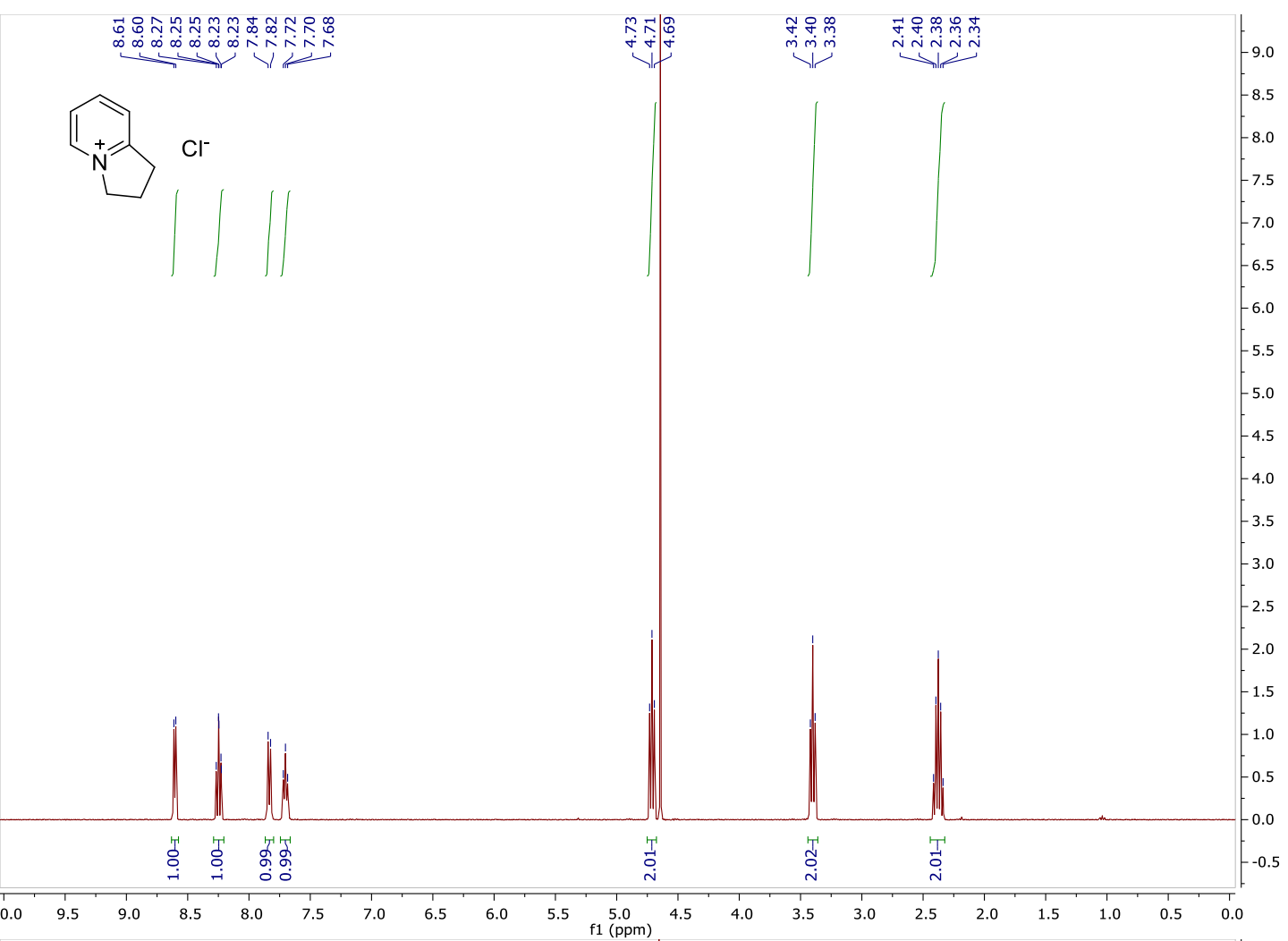
178.23

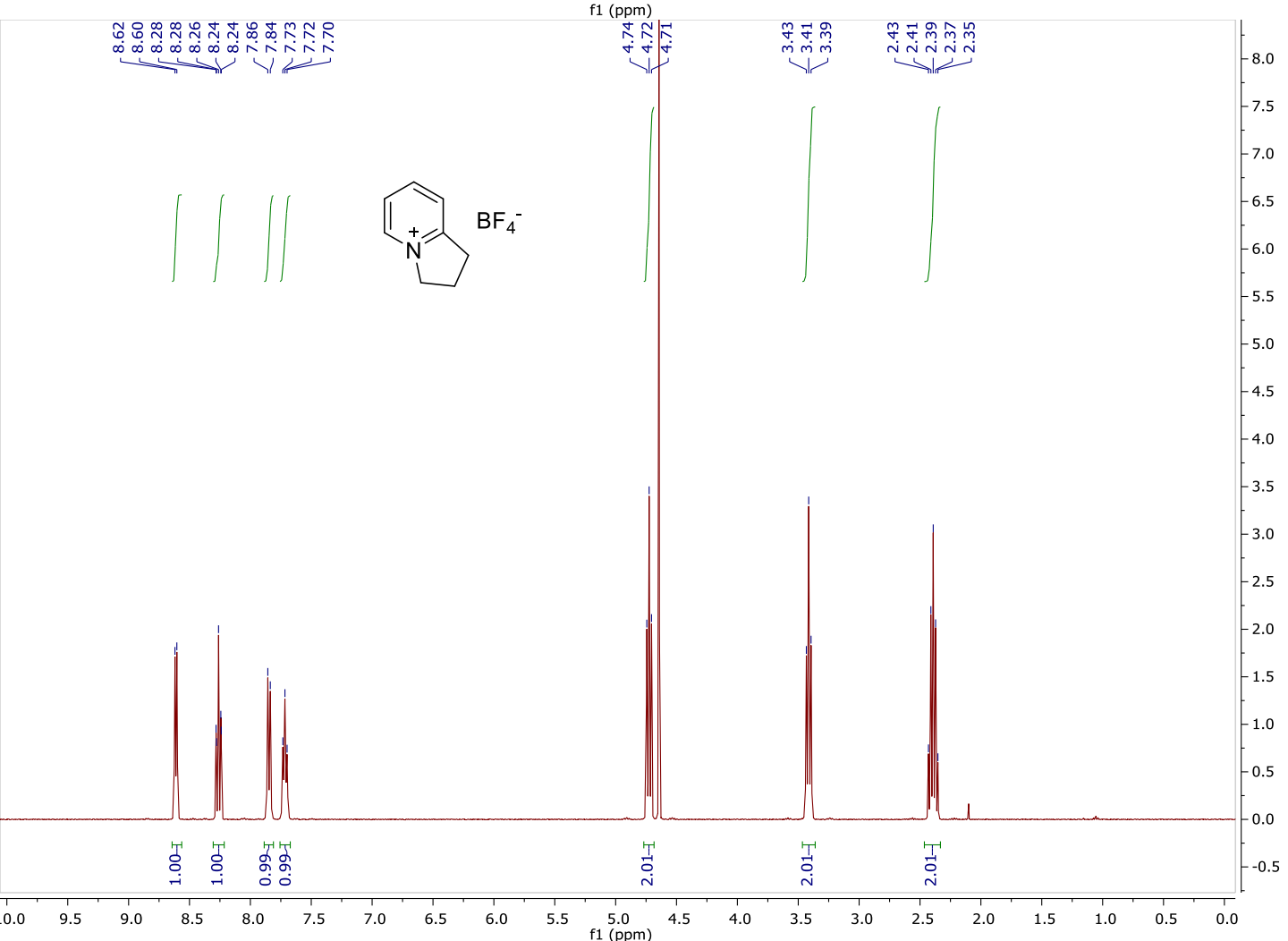
39.29
36.14
29.71
28.61

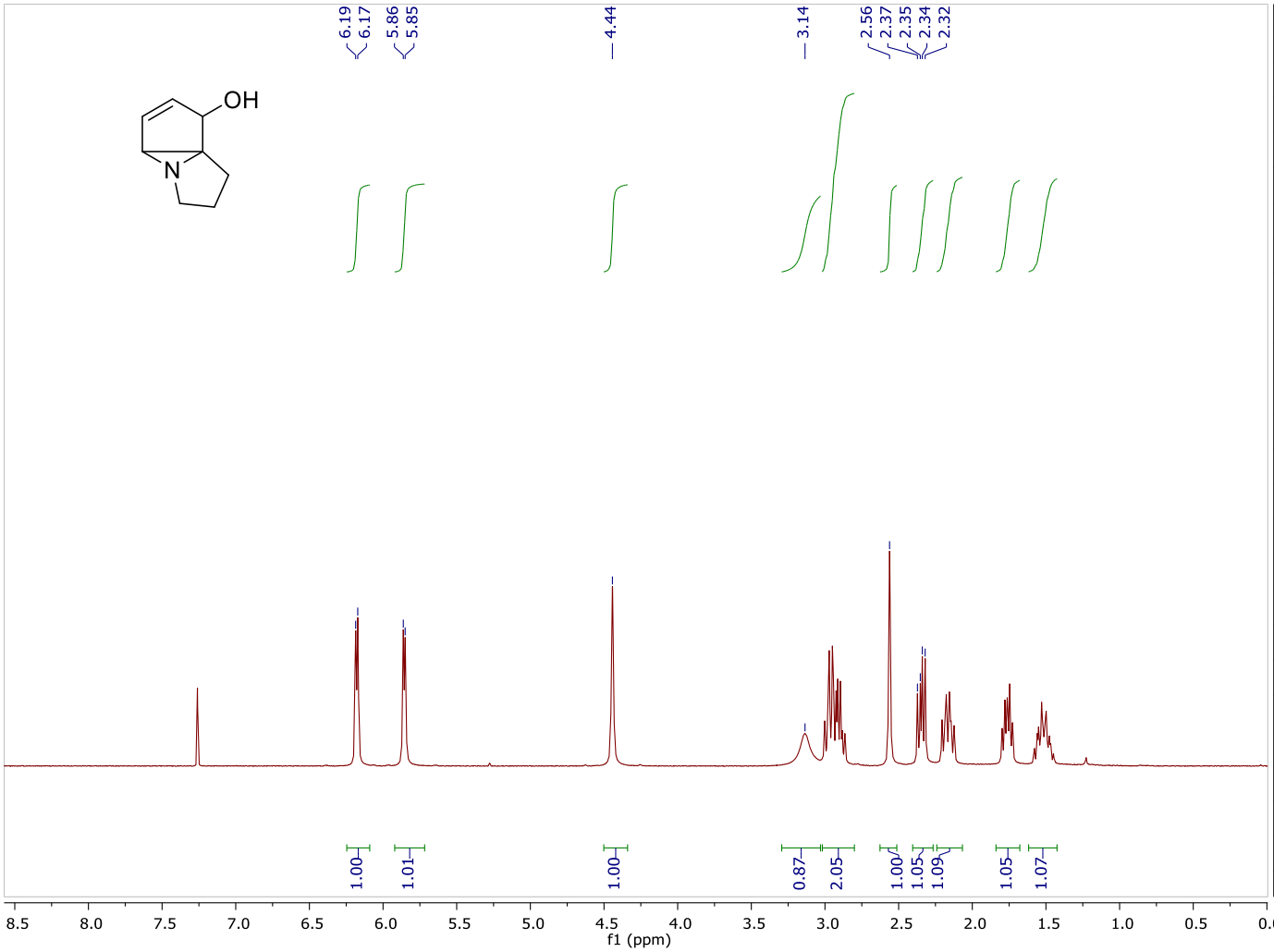
f1 (ppm)

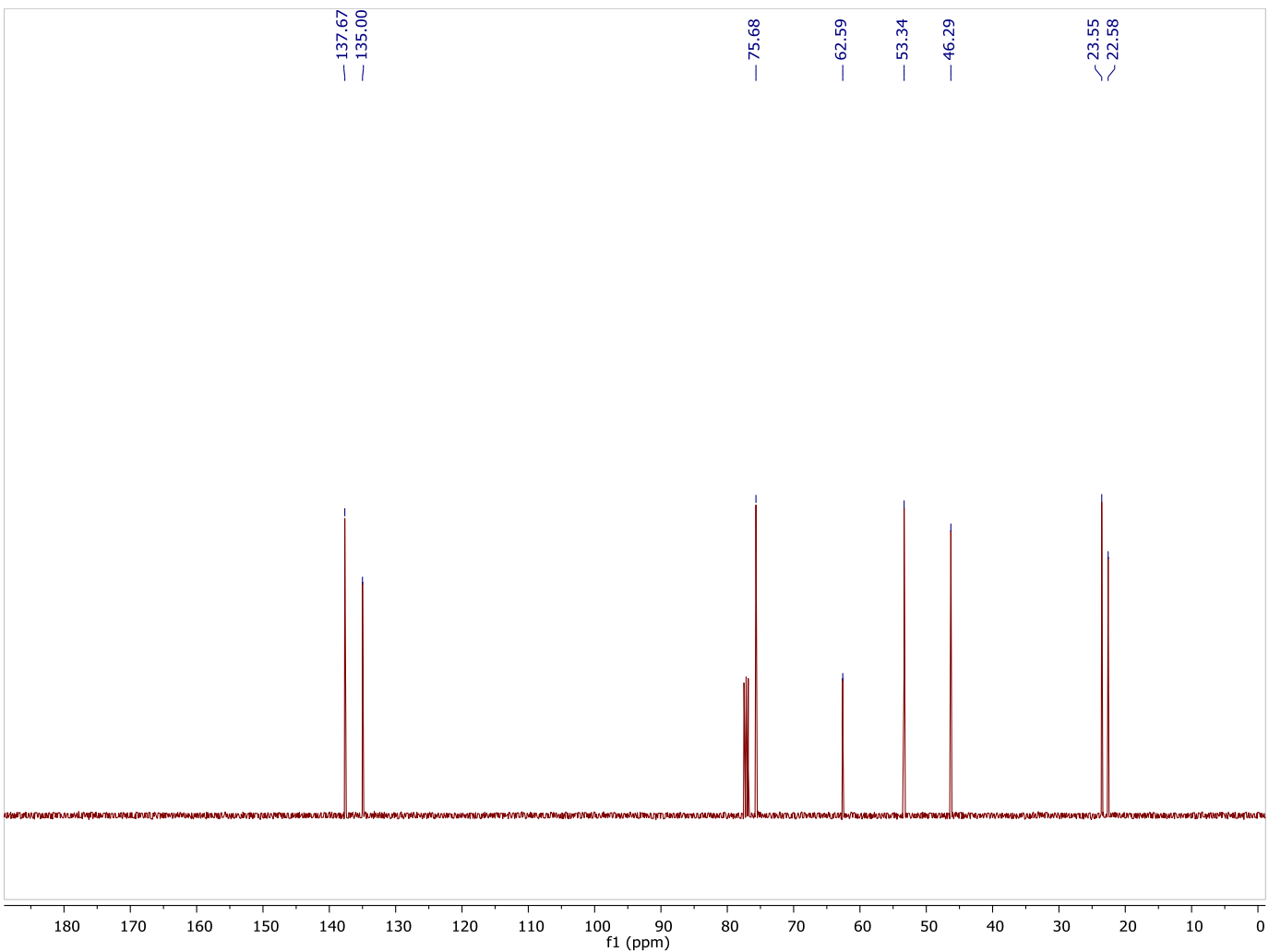

cs120623cs_02_193_a_PROTON_01
O
O
N
H
0.86
0.95
0.97
1.95
1.00
1.01
5.23
6.15
1.01
f1 (ppm)

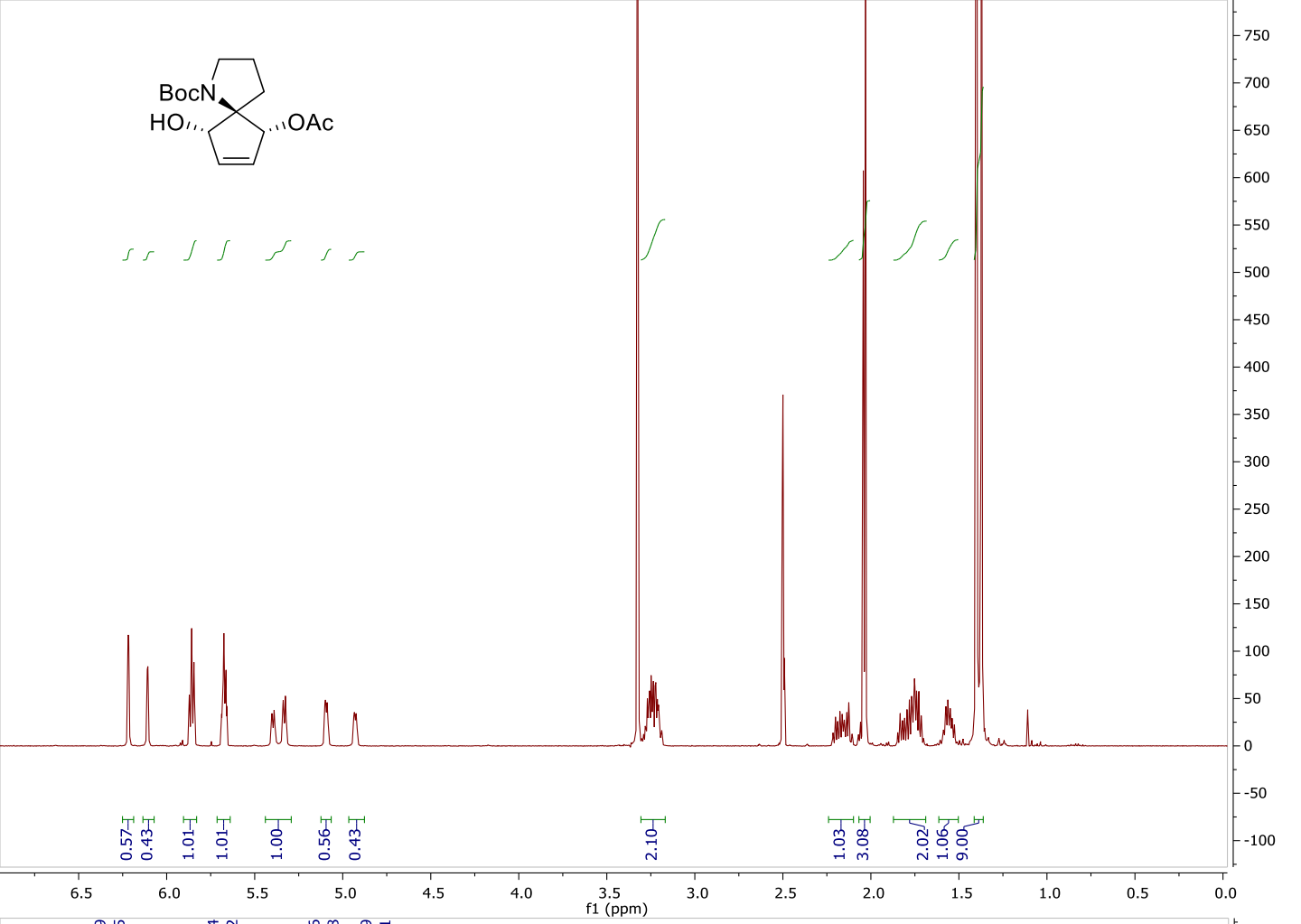

cs120673cs_02_193_a_CARBON_01
208.77
174.52
58.68
53.59
47.66
42.14
39.82
36.88
35.53
31.68
31.39
29.70
29.16
29.06
f1 (ppm)

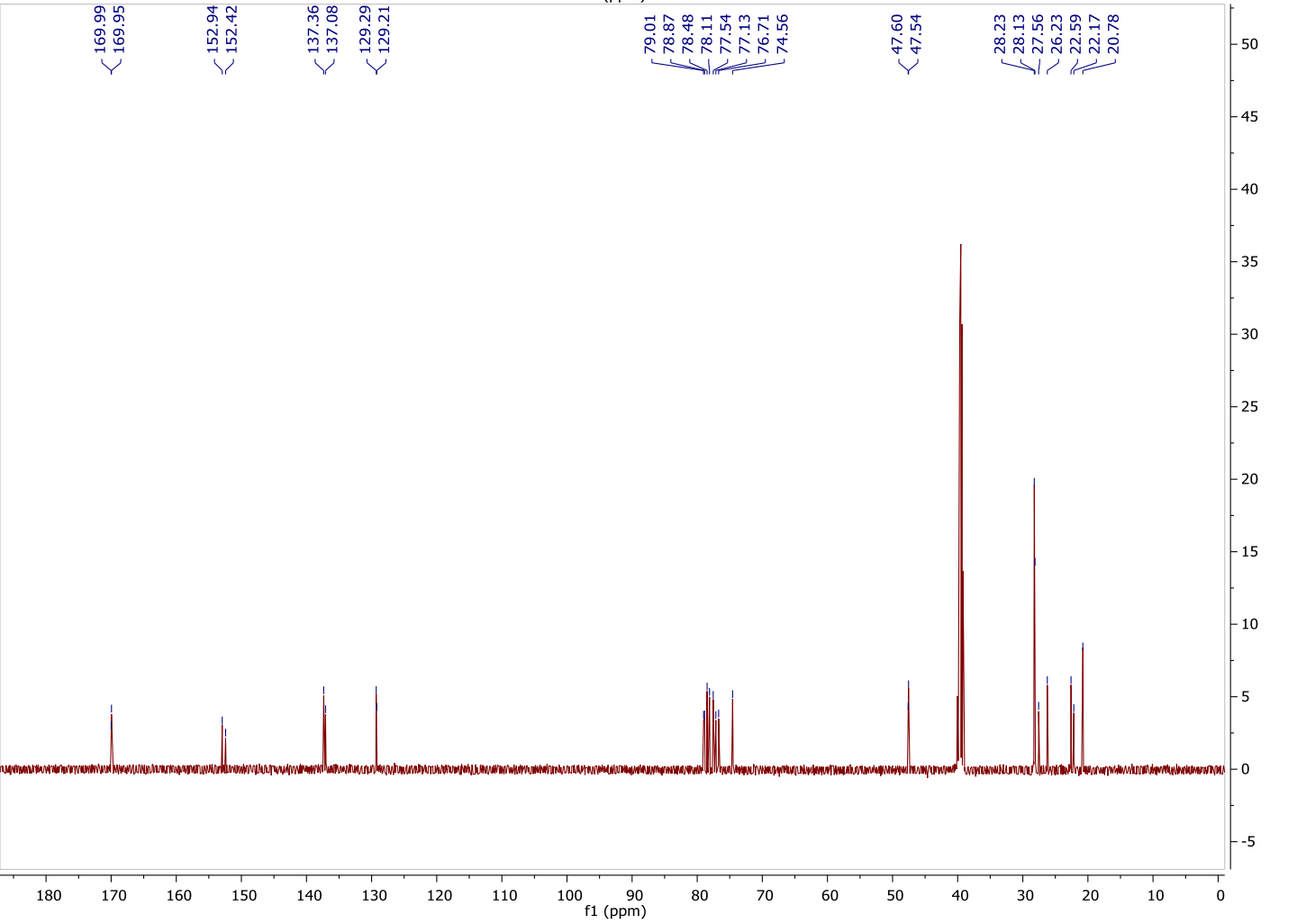

8.61
8.60
8.27
8.25
8.25
8.23
8.23
7.84
7.82
7.72
7.70
7.68
4.73
4.71
4.69
3.42
3.40
3.38
2.41
2.40
2.38
2.36
2.34
Cl-
1.00
1.00
0.99
0.99
2.01
2.02
2.01
f1 (ppm)


8.62
8.60
8.28
8.26
8.24
8.24
7.86
7.84
7.73
7.72
7.70
4.74
4.72
4.71
3.43
3.41
3.39
2.43
2.41
2.39
2.37
2.35
BF4-
1.00
1.00
0.99
0.99
2.01
2.01
2.01
f1 (ppm)


6.19
6.17
5.86
5.85
4.44
3.14
2.56
2.37
2.35
2.34
2.32
OH
N
1.00
1.01
1.00
0.87
2.05
1.00
1.05
1.09
1.05
1.07
f1 (ppm)


137.67
135.00
75.68
62.59
53.34
46.29
23.55
22.58
f1 (ppm)


BocN
HO
OAc
0.57
0.43
1.01
1.01
1.00
0.56
0.43
2.10
1.03
3.08
2.02
1.06
9.00
f1 (ppm)


169.99
169.95
152.94
152.42
137.36
137.08
129.29
129.21
79.01
78.87
78.48
78.11
77.54
77.13
76.71
74.56
47.60
47.54
28.23
28.13
27.56
26.23
22.59
22.17
20.78
f1 (ppm)