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Mild Calcium Catalysed Beckmann Rearrangements

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Contents

1 - General Experimental

Solvents and reagents

All solvents were purchased from commercial sources and used without purification (HPLC or analytical grade). Anhydrous solvents were purchased from Acros Organics stored under a nitrogen atmosphere with activated molecular sieves. Standard vacuum line techniques were used and glassware was oven dried prior to use. Deionised water was sourced using an Elga DV 25 system. Organic sovents were dried during workup using anhydrous Na_2SO_4.

Purification and chromatography

Thin Layer Chromatography (TLC) was carried out using aluminium plates coated with 60 F254 silica gel. Plates were visualised using UV light (254 or 365 nm) or staining with Ninhydrin (1 M, EtOH) or 1% aq. KMnO4. Normal-phase silica gel chromatography was carried out using Biotage Isolera One flash column chromatography system (LPLC). Reverse-phase high pressure liquid chromatography (RP-HPLC) was performed using a Waters system equipped with a Waters 2545 Binary Gradient Module, a SecurityGuard™ ULTRA cartridges for EVO-C18 UHPLC HPLC, Kinetex 5 µM EVO C18 100 Å 100 x 3.0 mm column and a Waters SQ Detector 2 using the stated eluent system.

Characterisation

Infrared spectroscopy was carried out with a Thermo Scientific Nicolet iS5 FT-IR spectrometer fitted with an iD7-ATR accessory, selected absorption maxima (νmax) recorded in wavenumbers (cm^{-1}). NMR spectra were recorded using a Bruker Avance 400 MHz spectrometer using the deuterated solvent stated. Chemical shifts (δ) quoted in parts per million (ppm) and referenced to the residual solvent peak. Multiplicities are denoted as s- singlet, d- doublet, t- triplet, q- quartet and quin- quintet and derivatives thereof (br denotes a broad resonance peak). Coupling constants recorded as Hz and round to the nearest 0.1 Hz. Low Resolution mass spectra were recorded on a Waters SQ Detector 2 (LC-MS). High Resolution Mass Spectrometry (HRMS) was recorded using an Agilent 6530 QTOF. Compound names were generated using ChemBioDraw Ultra v14 systematic naming

2 - General Procedures

General procedure **A –** Synthesis of non-commercial oximes.

To a 22 mL vial equipped with a magnetic stirrer bar was added the correspoinding ketone, hydroxylamine hydrochloride (1.5 equiv.), sodium acetate (2 equiv.) and a 4:1 mixture of water/ethanol (4 mL). The mixture was stirred at reflux for 2 hours before being cooled to room temperature where-upon the corresponding oxime precipitated and was filtered, washed with cold ethanol and dried under vacuum to afford the pure oxime, which was used without further purification.

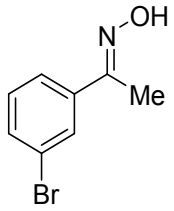
General procedure **B** - Calcium catalysed Beckmann rearrangement

To a oven dried 4 mL vial is equipped with a magnetic stirrer bar added the corresponding oxime, 10 mol% $Ca(NTf_2)_2$, 10 mol% $n Bu_4PF_6$ and 4:1 DCE:DME (approx. 2 mL) and the mixture was stirred at 80 ^oC until TLC or LCMS analysis indicated complete consumption of the starting material. Once complete, the solvent was removed in vacuo and the residue purified by flash column chromatography to afford the desired amide.

NB It was noted during the course of this study that the catalytic efficiency of the calcium salt slowly degrades over time. To ensure optimum activity, the commercial calcium salt should be thoroughly dried at 100^{o}C under vacuum for 12 hours before use and stored under an inert atmosphere.

3 - Synthesis of non-commerical oximes

1-(3-bromophenyl)ethan-1-one oxime (1c)



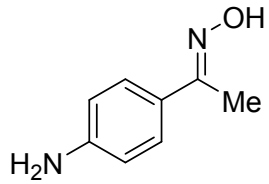
The title compound was prepared according to general procedure A, from 1-(3-bromophenyl)ethan-1-one (150 mg, 0.75 mmol) using sodium acetate (124 mg, 1.51 mmol) and hydroxylamine hydrochloride (79 mg, 1.13 mmol) in water/ethanol, which following conversion to the oxime and filtratation afforded **1c** as a white solid (117 mg, 73 %)

^{1}H NMR (400 MHz, DMSO-d6) δ 11.40 (s, 1H), 7.81 (t, J = 2.0 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 7.9 Hz, 1H), 2.15 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 152.3, 139.8, 131.8, 131.01, 128.5, 125.1, 122.3, 11.9.

All spectral data is consistent with previously published findings[1]

1-(4-aminophenyl)ethan-1-one oxime (1d)



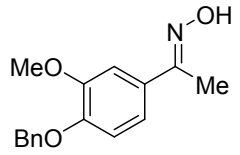
The title compound was prepared according to general procedure A, from 1-(4-aminophenyl)ethan-1-one (248 mg, 1.84 mmol) using sodium acetate (301 mg, 3.67 mmol) and hydroxylamine hydrochloride (191 mg, 2.75 mmol) in water/ethanol, which following conversion to the oxime and filtration afforded **1d** as a white solid (191 mg, 69 %)

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 7.37 – 7.25 (m, 2H), 6.57 – 6.46 (m, 2H), 5.27 (s, 2H), 2.04 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 153.2, 149.8, 126.9, 124.8, 113.79, 11.7.

All spectral data is consistent with previously published findings[2]

1-(4-(benzyloxy)-3-methoxyphenyl)ethan-1-one oxime (1e)



The title compound was prepared according to general procedure A, from 1-(4-(benzyloxy)-3-methoxyphenyl)ethan-1-one (500 mg, 1.951 mmol) using sodium acetate (320 mg, 3.90 mmol) and hydroxylamine hydrochloride (203 mg, 2.93 mmol) in water/ethanol, which following conversion to the oxime and filtration afforded **1e** as a white solid (520 mg, 98 %)

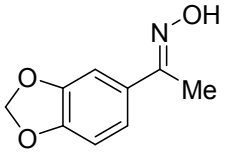
IR υ_{max} (cm^{-1}) 3241, 1599, 1416, 1218, 1017, 697

HR-ESI-MS: $C_{16}H_{18}NO_3$ $[M+H]^+$ *m/z* found 272.1290, cald 272.1287.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.00 (s, 1H), 7.47 – 7.30 (m, 5H), 7.28 (d, *J* = 2.1 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 5.11 (s, 2H), 3.78 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 152.4, 148.8, 148.4, 137.0, 130.0, 128.40, 127.9, 127.8, 118.4, 113.0, 108.71, 69.8, 55.4, 11.4.

1-(benzo[d][1,3]dioxol-5-yl)ethan-1-one oxime (1f)



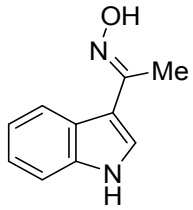
The title compound was prepared according to general procedure A, from c 1-(benzo[d][1,3]dioxol-5-yl)ethan-1-one (150 mg, 0.91 mmol) using sodium acetate (150 mg, 1.83 mmol) and hydroxylamine hydrochloride (95 mg, 1.37 mmol) in water/ethanol, which following conversion to the oxime and filtratation afforded **1f** as a white solid (106 mg, 65 %)

^{1}H NMR (400 MHz, DMSO-d6) δ 11.04 (s, 1H), 7.21 (d, J = 1.7 Hz, 1H), 7.14 (d, J = 1.8 Hz, 0H), 7.12 (d, J = 1.8 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H), 6.04 (s, 2H), 2.11 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 152.5, 147.8, 147.5, 131.2, 119.8, 108.0, 105.4, 101.1, 11.7.

All spectral data is consistent with previously published findings[3]

1-(1H-indol-3-yl)ethan-1-one oxime (1g)



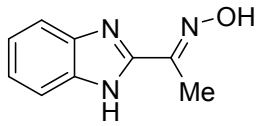
The title compound was prepared according to general procedure A, from 1-(1H-indol-3-yl)ethan-1-one (150 mg, 0.94 mmol) using sodium acetate (155 mg, 1.86 mmol) and hydroxylamine hydrochloride (98 mg, 1.41 mmol) in water/ethanol, which following conversion to the oxime and filtratation afforded **1g** as a white solid (96 mg, 59 %)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 – 8.23 (m, 1H), 7.43 (d, *J* = 2.7 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.28 – 7.18 (m, 2H), 2.35 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 151.6, 137.4, 126.7, 124.8, 122.1, 120.1, 113.7, 111.9, 12.7.

All spectral data is consistent with previously published findings[4]

1-(1*H*-benzo[*d*]imidazole-2-yl)ethan-1-one oxime (1h)



The title compound was prepared according to general procedure A, from 1-(1H-benzo[d]imidazol-2-yl)ethan-1-one (252 mg, 1.57 mmol) using sodium acetate (258 mg, 3.15 mmol) and hydroxylamine hydrochloride (164 mg, 2.36 mmol) in water/ethanol, which following conversion to the oxime and filtration afforded **1h** as a white solid (186 mg, 68 %)

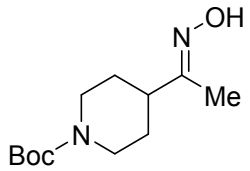
IR υ_{max} (cm^{-1}) 3727, 2999, 1651, 1574, 1100, 565

HR-ESI-MS: $C_9H_{10}N_3O$ $[M+H]^+$ *m/z* found 176.0829, cald 176.0824.

^{1}H NMR (400 MHz, Solvent) δ 12.46 (s, 1H), 11.72 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.19 (dd, *J* = 17.2, 7.8 Hz, 2H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, Solvent) δ 149.6, 148.2, 143.5, 135.1, 123.7, 121.9, 119.6, 112.0, 11.4.

tert-butyl-4-(1-(hydroxyimino)ethyl)piperidine-1-carboxylate (1j)



The title compound was prepared according to general procedure A, from tert-butyl 4-acetylpiperidine-1-carboxylate (250 mg, 1.10 mmol) using sodium acetate (180 mg, 2.20 mmol) and hydroxylamine hydrochloride (115 mg, 1.66 mmol) in water/ethanol, which following conversion to the oxime and column chromatography (0-10% MeOH in DCM) afforded **1J** as a white solid (242 mg, 91 %)

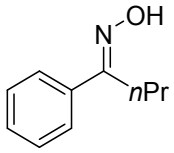
IR υ_{max} (cm^{-1}) 3347, 2932, 1691, 1670, 1427, 1240, 950

HR-ESI-MS: $C_{12}H_{23}N_2O_3$ $[M+H]^+$ *m/z* found 243.1716, cald 243.1709, $C_8H_{14}N_2O_3$ $[M\text{-}tBu]^+$ *m/z* found 186.1004, cald 186.1015.

^{1}H NMR (400 MHz, DMSO-d6) δ 10.37 (s, 1H), 3.96 (d, J = 13.5 Hz, 2H), 2.73 (s, 2H), 2.25 (tt, J = 11.7, 3.5 Hz, 1H), 1.71 (s, 3H), 1.68 (d, J = 7.5 Hz, 2H), 1.40 (s, 9H), 1.36 – 1.22 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d6) δ 157.9, 154.3, 79.0, 42.1, 29.4, 28.6, 12.2.

1-phenylbutan-1-one oxime (1n)



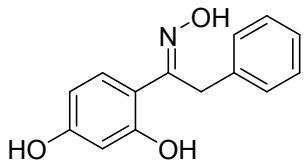
The title compound was prepared according to general procedure A, from 1-phenylbutan-1-one (100 mg, 0.67 mmol) using sodium acetate (113 mg, 1.38 mmol) and hydroxylamine hydrochloride (69 mg, 1.00 mmol) in water/ethanol, which following conversion to the oxime and filtration afforded **1n** as a white solid (97 mg, 89 %)

^{1}H NMR (400 MHz, DMSO-d6) δ 11.11 (s, 1H), 7.74 – 7.53 (m, 2H), 7.47 – 7.28 (m, 2H), 2.79 – 2.65 (m, 2H), 1.62 – 1.27 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 157.03, 136.65, 128.91 (d, J = 10.3 Hz), 126.21, 27.21, 19.86, 14.56.

All spectral data is consistent with previously published findings[5]

1-(2,4-dihydroxyphenyl)-2-phenylethan-1-one oxime (1o)



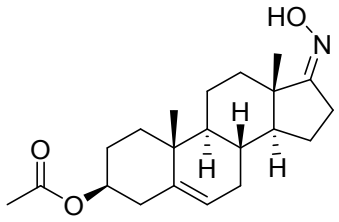
The title compound was prepared according to general procedure A, from 1-(2,4-dihydroxyphenyl)-2-phenylethan-1-one (217 µl, 1.771 mmol) using sodium acetate (291 mg, 3.54 mmol) and hydroxylamine hydrochloride (185 mg, 2.66 mmol) in water/ethanol, which following conversion to the oxime and filtration afforded as a white solid (239 mg, 41 %)

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.74 (s, 1H), 11.44 (s, 1H), 9.69 (s, 1H), 7.30 – 7.22 (m, 4H), 7.21-7.17 (M, 1H), 6.26-6.21 (M, 3H), 4.16 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d6) δ 159.8, 159.8, 159.5, 137.4, 129.8, 129.0, 128.8, 126.6, 110.4, 107.3, 103.4, 30.3.

All spectral data is consistent with previously published findings[6]

Prasterone Acetate Oxime (3)



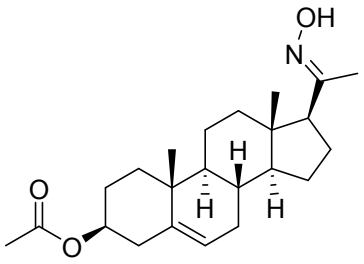
To a 22 mL vial equipped with a magnetic stirrer bar was added prasterone acetate (485 mg, 1.47 mmol) and the vial purged with nitrogen before anhydrous pyridine (4.1 mL) was added and the mixture stirred for 5 minutes to allow complete solubilisation. Hydroxylamine hydrochloride (510 mg, 7.34 mmol) was then added and the mixture stirred at room temperature overnight. Pyridine was removed *in vacuo* and the mixture was applied directly to the top of a column and purified (0 – 20% DCM in MeOH) to afforded the oxime as a white solid (399 mg, 79%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.07 (s, 1H), 5.37 (dt, J = 3.5, 1.6 Hz, 1H), 4.51 – 4.40 (m, 1H), 2.41 – 2.20 (m, 4H), 2.04 (s, 1H), 1.99 (s, 3H), 1.90 – 1.67 (m, 4H), 1.66 – 1.55 (m, 4H), 1.56 – 1.49 (m, 1H), 1.49 – 1.41 (m, 2H), 1.41 – 1.26 (m, 2H), 1.17 – 1.02 (m, 2H), 1.01 (s, 3H), 0.84 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 170.2, 168.2, 140.1, 122.3, 73.6, 54.1, 50.2, 43.3, 38.1, 36.9, 36.7, 34.5, 31.2, 27.8, 25.3, 23.3, 21.5, 20.6, 19.4, 17.5

All spectral data is consistent with previously published findings[7]

3β-Acetoxypregn-5-en-20-one Oxime (5)



To a 22 mL vial was added progenone acetate (597 mg, 1.67 mmol), anhydrous pyridine (3.5 mL), hydrozylamine hydrochloride (231 mg, 3.33 mmol) and triethylamine (3.5 mL) and the mixture stirred at reflux for 10 hours. The solution was poured directly onto ice water (25 mL) and the residue was collected via vacuum filtration. Flash column chromatography (0-10% DCM in MeOH) afforded the oxime as a white solid (427 mg, 67%).

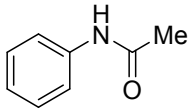
^{1}H NMR (400 MHz, Chloroform-d) δ 8.45 (s, 1H), 5.42 – 5.35 (m, 1H), 4.62 (tdd, J = 10.6, 6.4, 4.2 Hz, 1H), 2.37 – 2.29 (m, 2H), 2.25 (dd, J = 10.1, 8.2 Hz, 1H), 2.15 – 2.05 (m, 2H), 2.04 (s, 3H), 2.01 – 1.92 (m, 1H), 1.90 (s, 3H), 1.87 – 1.84 (m, 2H), 1.76 – 1.66 (m, 2H), 1.63 – 1.39 (m, 5H), 1.32 (td, J = 12.5, 4.1 Hz, 1H), 1.27 – 1.08 (m, 2H), 1.03 (s, 3H), 1.02 – 0.95 (m, 2H), 0.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 158.8, 139.7, 122.4, 73.9, 56.8, 56.1, 50.1, 43.8, 38.6, 38.1, 37.00, 36.6, 32.0, 31.8, 27.8, 24.2, 23.1, 21.4, 21.0, 19.4, 15.2, 13.1.

All spectral data is consistent with previously published findings.[8]

4 - Calcium catalyzed Beckmann Rearrangements

N-phenylacetamide (2a)



The title compound was prepared according to general procedure B, from commericially available 1-phenylethan-1-one oxime (300 mg, 2.22 mmol) using $Ca(NTf_2)_2$ (133 mg, 0.222 mmol) and $n$$Bu_4PF_6$ (54mg, 0.222 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2a** as a white solid (279 mg, 93%)

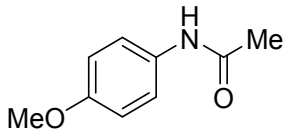
RF (50:50 EtOAc/CycHex) = 0.2

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 7.65 – 7.49 (m, 2H), 7.37 – 7.19 (m, 2H), 7.02 (tt, J = 7.3, 1.2 Hz, 1H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 168.7, 139.8, 129.1, 123.4, 119.4, 24.5.

All spectral data is consistent with previously published findings[9]

N-(4-methoxyphenyl)acetamide (2b)



The title compound was prepared according to general procedure B, from commericially available 4-methoxyacetophenone oxime (100 mg, 0.61 mmol) using $Ca(NTf_2)_2$ (36 mg, 0.061 mmol) and $n$$Bu_4PF_6$ (23 mg, 0.061 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2b** as a white solid (88 mg, 88%)

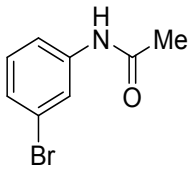
Rf (50:50 EtOAc/CycHex) = 0.19

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 7.57 – 7.37 (m, 2H), 7.01 – 6.74 (m, 2H), 3.71 (s, 3H), 2.00 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 168.1, 155.5, 133.0, 121.0, 114.2, 55.6, 24.3.

All spectral data is consistent with previously published findings[10]

N-(3-bromophenyl)acetamide (2c)



The title compound was prepared according to general procedure B, from **1c** (43 mg, 0.20 mmol) using $Ca(NTf_2)_2$ (12 mg, 0.02 mmol) and nBu_4PF_6 (8 mg, 0.03 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2c** as an off-white solid (37 mg, 86%)

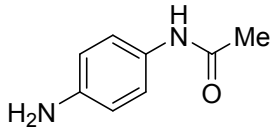
Rf (50:50 EtOAc/CycHex) = 0.36

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (s, 1H), 7.94 (t, J = 2.0 Hz, 1H), 7.52 – 7.38 (m, 1H), 7.33 – 7.16 (m, 2H), 2.05 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 169.1, 141.3, 131.2, 126.0, 122.0, 121.7, 118.1, 24.5.

All spectral data is consistent with previously published findings[11]

***N*-(4-aminophenyl)acetamide (2d)**



The title compound was prepared according to general procedure B, from **1d** (80 mg, 0.533 mmol) using $Ca(NTf_2)_2$ (32 mg, 0.053 mmol) and nBu_4PF_6 (21 mg, 0.053 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2d** as an off-white solid (57 mg, 72 %)

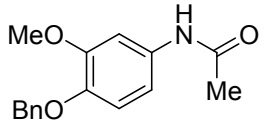
Rf (50:50 EtOAc/CycHex) = 0.12

^{1}H NMR (400 MHz, DMSO-d6) δ 9.46 (s, 1H), 7.30 – 7.01 (m, 2H), 6.65 – 6.33 (m, 2H), 4.81 (s, 2H), 1.95 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 167.6, 145.0, 129.0, 121.3, 114.2, 24.1.

All spectral data is consistent with previously published findings[12]

***N*-(4-(benzyloxy)-3-methoxyphenyl)acetamide (2e)**



The title compound was prepared according to general procedure B, from **1e** (107 mg, 0.394 mmol) using $Ca(NTf_2)_2$ (23.68 mg, 0.039 mmol) and $n$$Bu_4PF_6$ (15.28 mg, 0.039 mmol) in 4:1 DCE/DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2e** as pink solid (87mg, 81 %)

Rf (50:50 EtOAc/Hexane) = 0.31

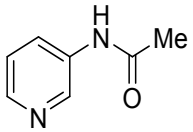
IR υ_{max} (cm^{-1}) 3241, 1599, 1416, 1218, 1017, 1017, 697

HR-ESI-MS: $C_{16}H_{18}NO_3$ $[M+H]^+$ *m/z* found 272.1292,

^{1}H NMR (400 MHz, DMSO-d6) δ 9.78 (s, 1H), 7.47 – 7.31 (m, 5H), 7.30 (d, J = 2.5 Hz, 1H), 7.04 (dd, J = 8.7, 2.3 Hz, 1H), 6.94 (d, J = 8.7 Hz, 1H), 5.02 (s, 2H), 3.74 (s, 3H), 2.01 (s, 3H)

^{13}C NMR (101 MHz, DMSO-d6) δ 168.2, 149.5, 144.0, 137.8, 133.9, 128.8, 128.2, 114.6, 111.3, 104.1, 70.8, 55.9, 24.4.

N-(pyridin-3-yl)acetamide (2f)



The title compound was prepared according to general procedure B, from commericially available 1-(pyridin-3-yl)ethan-1-one oxime (100 mg, 0.73 mmol) using $Ca(NTf_2)_2$ (44 mg, 0.073 mmol) and $n$$Bu_4PF_6$ (29 mg, 0.073 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2f** as a white solid (82 mg, 82%)

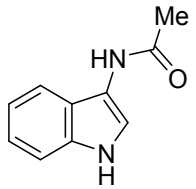
Rf (50:50 EtOAc/CycHex) = 0.1

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.50 (s, 1H), 8.85 (dd, *J* = 2.3, 0.9 Hz, 1H), 8.56 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.01 (ddd, *J* = 8.0, 2.3, 1.6 Hz, 1H), 7.42 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 2.19 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 151.6, 149.9, 147.1, 133.4, 133.0, 123.9, 40.5, 39.9, 11.8.

All spectral data is consistent with previously published findings[13]

N-(1H-indol-3-yl)acetamide (2g)



The title compound was prepared according to general procedure B, **1g** (50mg, 0.29 mmol) using $Ca(NTf_2)_2$ (17 mg, 0.03 mmol) and nBu_4PF_6 (12 mg, 0.03 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2g** as an off-white solid (45 mg, 89%)

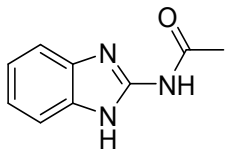
Rf (50:50 EtOAc/CycHex) = 0.15

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 (s, 1H), 8.46 – 8.38 (m, 1H), 7.89 (d, *J* = 3.0 Hz, 1H), 7.47 – 7.40 (m, 1H), 7.37 – 7.29 (m, 2H), 2.58 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.5, 136.2, 131.3, 125.4, 123.7, 122.7, 122.46, 118.7, 111.3, 27.7.

All spectral data is consistent with previously published findings[14]

***N*-(1*H*-benzo[d]imidazole-2-yl)acetamide (2h)**



The title compound was prepared according to general procedure B, **1h** (80 mg, 0.457 mmol) using $Ca(NTf_2)_2$ (27.4 mg, 0.046 mmol) and nBu_4PF_6 (17.69 mg, 0.046 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2h** as an beige solid (63 mg, 79 %)

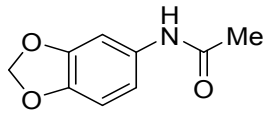
Rf (50:50 EtOAc/CycHex) = 0.15

^{1}H NMR (400 MHz, DMSO- d_6) δ 13.28 (s, 1H), 7.70 (m, 2H), 7.34 (s, 2H), 2.70 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 191.6, 148.2, 125.6, 123.0, 121.2, 112.8, 26.1.

All spectral data is consistent with previously published findings[15]

N-(benzo[d][1,3]dioxol-5-yl)acetamide (2i)



The title compound was prepared according to general procedure B, from **1i** (50mg, 0.28 mmol) using $Ca(NTf_2)_2$ (17 mg, 0.03 mmol) and nBu_4PF_6 (12 mg, 0.03 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2i** as an off-white solid (39 mg, 78%)

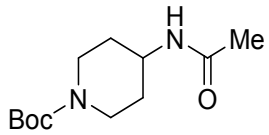
Rf (50:50 EtOAc/CycHex) = 0.21

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (s, 1H), 7.11 (d, *J* = 2.1 Hz, 1H), 6.74 – 6.61 (m, 2H), 5.86 (s, 2H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.5, 147.8, 144.3, 132.1, 113.4, 108.0, 103.1, 101.2, 24.3.

All spectral data is consistent with previously published findings[16]

tert-butyl 4-acetamidopiperidine-1-carboxylate (2j)



The title compound was prepared according to general procedure B, from **1j** (100mg, 0.41 mmol) using $Ca(NTf_2)_2$ (74 mg, 0.12 mmol) and nBu_4PF_6 (48 mg, 0.12 mmol) in 4:1 DCE:DME (3 mL), which following conversion to the amide and column chromatography (0-10% MeOH in DCM) afforded **2j** as a colourless oil (86 mg, 86%)

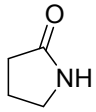
Rf (90:10 DCM/MeOH) = 0.16

^{1}H NMR (400 MHz, DMSO-d6) δ 7.79 (d, J = 7.8 Hz, 1H), 3.82 (d, J = 13.3 Hz, 2H), 3.76 – 3.63 (m, 1H), 2.83 (s, 2H), 1.79 (s, 3H), 1.69 (dt, J = 11.3, 3.4 Hz, 2H), 1.40 (s, 9H), 1.27 – 1.13 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d6) δ 168.8, 154.4, 79.1, 46.0, 31.9, 28.5, 23.2.

All spectral data is consistent with previously published findings[17]

Pyrrolidin-2-one (2k)



The title compound was prepared according to general procedure B, from commerically available cyclobutanone oxime (60mg, 0.71 mmol) using $Ca(NTf_2)_2$ (42 mg, 0.08 mmol) and nBu_4PF_6 (27 mg, 0.0 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-10% MeOH in DCM) afforded **2k** as a colourless oil (47 mg, 79%)

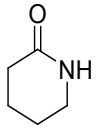
Rf (90:10 DCM/MeOH) = 0.21

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (s, 1H), 3.28 – 3.09 (m, 2H), 2.07 (ddd, J = 8.4, 7.4, 1.4 Hz, 2H), 2.02 – 1.89 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 177.7, 41.8, 30.4, 20.9.

All spectral data is consistent with previously published findings[18]

Piperidin-2-one (2l)



The title compound was prepared according to general procedure B, from commercially available cyclopentanone oxime (100 mg, 1.00 mmol) using $Ca(NTf_2)_2$ (61 mg, 0.1 mmol) and nBu_4PF_6 (39 mg, 0.1 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-10% MeOH in DCM) afforded **2l** as a white solid (81mg, 81 %)

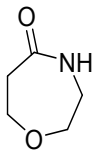
Rf (90:10 DCM/MeOH) = 0.15

^{1}H NMR (400 MHz, DMSO- d_6) δ 7.38 (s, 1H), 3.11 (td, J = 5.8, 2.2 Hz, 2H), 2.11 (t, J = 6.5 Hz, 2H), 1.75 – 1.48 (m, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 41.7, 31.9, 22.5, 21.2.

All spectral data is consistent with previously published findings[19]

1,4-oxazepan-5-one (2m)



The title compound was prepared according to general procedure B, **1m** (56 mg, 0.49 mmol) using $Ca(NTf_2)_2$ (28 mg, 0.05 mmol) and $n$$Bu_4PF_6$ (12 mg, 0.05 mmol) in 4:1 DCE:DME (2 mL),, which following conversion to the amide and column chromatography (0-10% MeOH in DCM) afforded **2m** as an off-white solid (40 mg, 69 %)

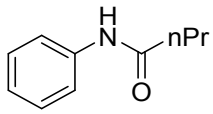
Rf (90:10 DCM/MeOH) = 0.13

^{1}H NMR (400 MHz, DMSO- d_6) 7.63 (s, 1H), 3.66 – 3.56 (m, 4H), 3.20 – 3.11 (m, 2H), 2.63 – 2.41 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 176.3, 71.7, 65.1, 44.0, 41.2.

All spectral data is consistent with previously published findings[20]

N-phenylpentanamide (2n)



The title compound was prepared according to general procedure B, from **1n** (75 mg, 0.46 mmol) using $Ca(NTf_2)_2$ (27mg, 0.05 mmol) and $n$$Bu_4PF_6$ (18 mg, 0.05 mmol) in 4:1 DCE:DME (2 mL), which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2l** as an white solid (71 mg, 95%)

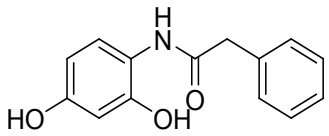
RF (50:50 EtOAc/CycHex) = 0.31

^{1}H NMR (400 MHz, DMSO-d6) δ 9.84 (s, 1H), 7.68 – 7.52 (m, 2H), 7.28 (dd, J = 8.6, 7.3 Hz, 2H), 7.12 – 6.89 (m, 1H), 2.28 (t, J = 7.3 Hz, 2H), 1.61 (h, J = 7.3 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d6) δ 171.6, 139.8, 129.1, 123.35, 119.5, 38.8, 19.0, 14.1.

All spectral data is consistent with previously published findings[21]

***N*-(2,4-dihydroxyphenyl)-2-phenylacetamide (2o)**



The title compound was prepared according to general procedure B, from (E)-1-(2,4-dihydroxyphenyl)-2-phenylethan-1-one oxime (100 mg, 0.411 mmol) using $Ca(NTf_2)_2$ (24 mg, 0.041 mmol) and nBu_4PF_6 (16 mg, 0.041 mmol) in 4:1 DCE/DME, which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2o** as an off-white solid (77 mg, 77 %)

RF (50:50 EtOAc/CycHex) = 0.33

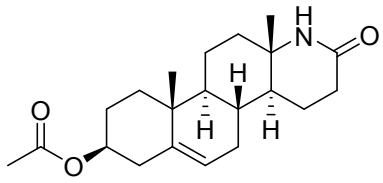
HR-ESI-MS: $C_{14}H_{14}NO_3$ $[M+H]^+$ *m/z* found 244.0969, cald 244.0974.

IR υ_{max} (cm^{-1}) 3200, 3001, 2907, 1566, 1000, 890, 544

^{1}H NMR (400 MHz, DMSO- d_6) δ 9.56 (s, 1H), 9.22 (s, 1H), 9.10 (s, 1H), 7.36 – 7.28 (m, 5H), 7.24 (d, *J* = 6.5 Hz, 1H), 6.30 (d, *J* = 2.6 Hz, 1H), 6.16 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.66 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d6) δ 169.1, 154.9, 149.5, 136.3, 129.1, 128.3, 126.5, 123.8, 117.9, 105.7, 103.1, 42.7.

17-oxo-17a-aza-D-homo-5-androsten-3β-yl acetate (4)



The title compound was prepared according to general procedure B, **3** (100 mg, 0.289 mmol) using $Ca(NTf_2)_2$ (17 mg, 0.29 mmol) and nBu_4PF_6 (11 mg, 0.029 mmol) in 4:1 DCE/DME, which following conversion to the amide and column chromatography (0-50% EtOAc in cyclohexane) afforded **2o** as an off-white solid (79 mg, 79 %).

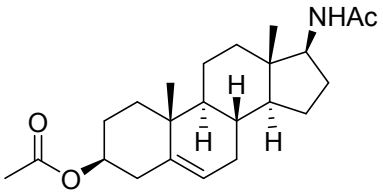
R_F (50:50 EtOAc/CycHex) = 0.16

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 (s, 1H), 5.36 (d, J = 5.1 Hz, 1H), 4.75 – 4.24 (m, 1H), 2.35 – 2.07 (m, 5H), 1.99 (s, 3H), 1.90 – 1.68 (m, 5H), 1.68 – 1.48 (m, 3H), 1.50 – 1.24 (m, 4H), 1.18 (ddd, J = 13.3, 10.6, 3.2 Hz, 1H), 1.13 – 1.07 (m, 1H), 1.06 (s, 3H), 0.96 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.0, 144.5, 127.0, 78.3, 58.4, 54.1, 52.5, 43.9, 42.7, 41.5, 41.4, 37.0, 35.9, 35.9, 32.5, 26.9, 26.3, 25.7, 25.0, 24.0.

All spectral data is consistent with previously published findings[22]

3β-acetoxy-5-androstene-17β-acetamide (6)



The title compound was prepared according to general procedure B, **5** (47 mg, 0.13 mmol) using $Ca(NTf_2)_2$ (8 mg, 0.013 mmol) and $n$$Bu_4PF_6$ (5 mg, 0.013 mmol) in 4:1 DCE/DME, which following conversion to the amide and column chromatography (0-10% MeOH in DCM) afforded **6** as an white solid (41 mg, 87 %).

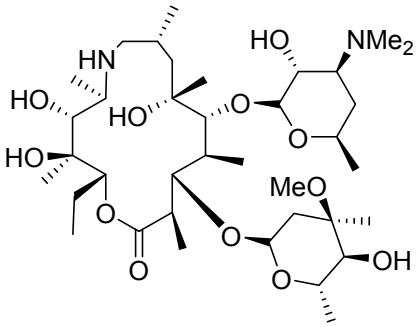
R_F (90:10 DCM/MeOH) = 0.21

^{1}H NMR (400 MHz, DMSO-d6) δ 7.48 (d, J = 8.6 Hz, 1H), 5.42 – 5.25 (m, 1H), 4.45 (qt, J = 7.8, 4.5 Hz, 1H), 3.69 (q, J = 9.2 Hz, 1H), 2.62 – 2.52 (m, 1H), 2.28 (d, J = 7.7 Hz, 2H), 1.99 (s, 3H), 1.98 – 1.89 (m, 2H), 1.85 (t, J = 4.5 Hz, 1H), 1.81 (s, 3H), 1.77 (d, J = 3.5 Hz, 1H), 1.68 – 1.48 (m, 5H), 1.5 – 1.27 (m, 3H), 1.24 – 0.99 (m, 4H), 0.98 (s, 3H), 0.96 – 0.87 (m, 1H), 0.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 158.8, 139.7, 122.4, 73.9, 56.8, 56.1, 50.1, 43.8, 38.6, 38.1, 37.0, 36.6, 32.0, 31.8, 27.8, 24.2, 23.1, 21.4, 21.0, 19.3, 15.2, 13.1.

All spectral data is consistent with previously published findings[22]

Synthesis of Azithromycin via Calcium Catalysed Beckmann Rearrangement.



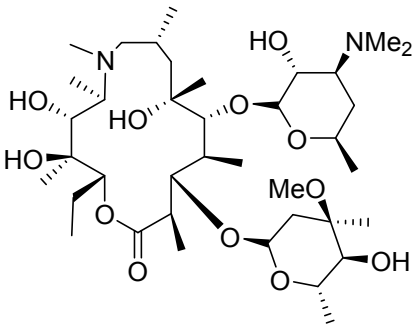
To erythromycin oxime[23] (100 mg, 0.13 mmol) in a 4 mL vial was added $Ca(NTf_2)_2$ (8 mg, 0.013 mmol) and $n$$Bu_4PF_6$ (5 mg, 0.013 mmol) in 4:1 DCE/DME and the mixture stirred at 80 °C for 5 hours. TLC/LCMS analysis indicated complete consumption of starting material. The solvent was removed under vacuum, and CH_2Cl_2 (5 mL) was added. The mixture was then acidified with 2 M HCl to pH 5 and the layers separated followed by further extraction of the aqueous layer with CH_2Cl_2. The extraction was repeated at pH 6 and 8 (achieved through addition of 1 M NaOH). The combined organic extracts obtained at pH8 were then dried (Na_2CO_3), filtered and concentrated to afford the trapped intermediate, which was used without further purification. The obtained intermediate was dissolved in MeOH (15 mL) and cooled to 0 °C, followed by the addition of $NaBH_4$ over 1 hour (4 portions of 25 mg, 2.6 mmol). The mixture was stirred at 0 °C for 3 hours before warming to room

temperature and stirring for 48 hours. Once the reduction was deemed complete by TLC, the mixture was concentrated and then redissolved in 2:1 chloroform/water, and the organic layer subsequently separated, dried and concentrated. Purification by flash column chromatograpy (10% ammonicial MeOH in DCM) afforded **8** as a white solid (74 mg, 78%).

^{1}H NMR (400 MHz, Chloroform-d) δ 5.12 (d, J = 4.7 Hz, 1H), 4.74 (dd, J = 10.3, 2.4 Hz, 1H), 4.43 (d, J = 7.3 Hz, 1H), 4.34 (d, J = 2.3 Hz, 1H), 4.09 (dq, J = 9.4, 6.2 Hz, 1H), 3.65 (d, J = 7.4 Hz, 1H), 3.51 (ddd, J = 10.9, 6.1, 2.0 Hz, 1H), 3.45 (d, J = 1.9 Hz, 1H), 3.35 (s, 3H), 3.23 (dd, J = 10.2, 7.3 Hz, 1H), 3.12 – 3.01 (m, 2H), 2.96 (s, 1H), 2.77 (dd, J = 7.5, 4.2 Hz, 1H), 2.57 (dd, J = 6.4, 1.9 Hz, 1H), 2.50 – 2.39 (m, 1H), 2.40 – 2.32 (m, 1H), 2.29 (s, 6H), 2.18 (d, J = 10.4 Hz, 1H), 2.00 – 1.72 (m, 4H), 1.67 (ddd, J = 12.7, 4.0, 2.1 Hz, 1H), 1.59 (dd, J = 15.2, 5.0 Hz, 1H), 1.49 (ddd, J = 14.3, 10.3, 7.2 Hz, 1H), 1.42 – 1.36 (m, 1H), 1.33 (d, J = 6.2 Hz, 3H), 1.30 (s, 3H), 1.25 (s, 3H), 1.22 (dd, J = 8.5, 6.8 Hz, 6H), 1.15 (d, J = 6.5 Hz, 3H), 1.09 (s, 3H), 1.06 (d, J = 7.6 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9, 103.0, 94.8, 83.4, 78.2, 78.0, 77.9, 77.2, 73.8, 73.1, 73.0, 70.9, 68.8, 65.8, 65.6, 57.4, 56.9, 49.5, 45.4, 42.2, 40.4, 34.8, 29.9, 28.7, 27.5, 21.9, 21.6, 21.4, 21.0, 18.3, 16.2, 14.9, 13.9, 11.1, 9.1.

All spectral data is consistent with previously published findings.[23]



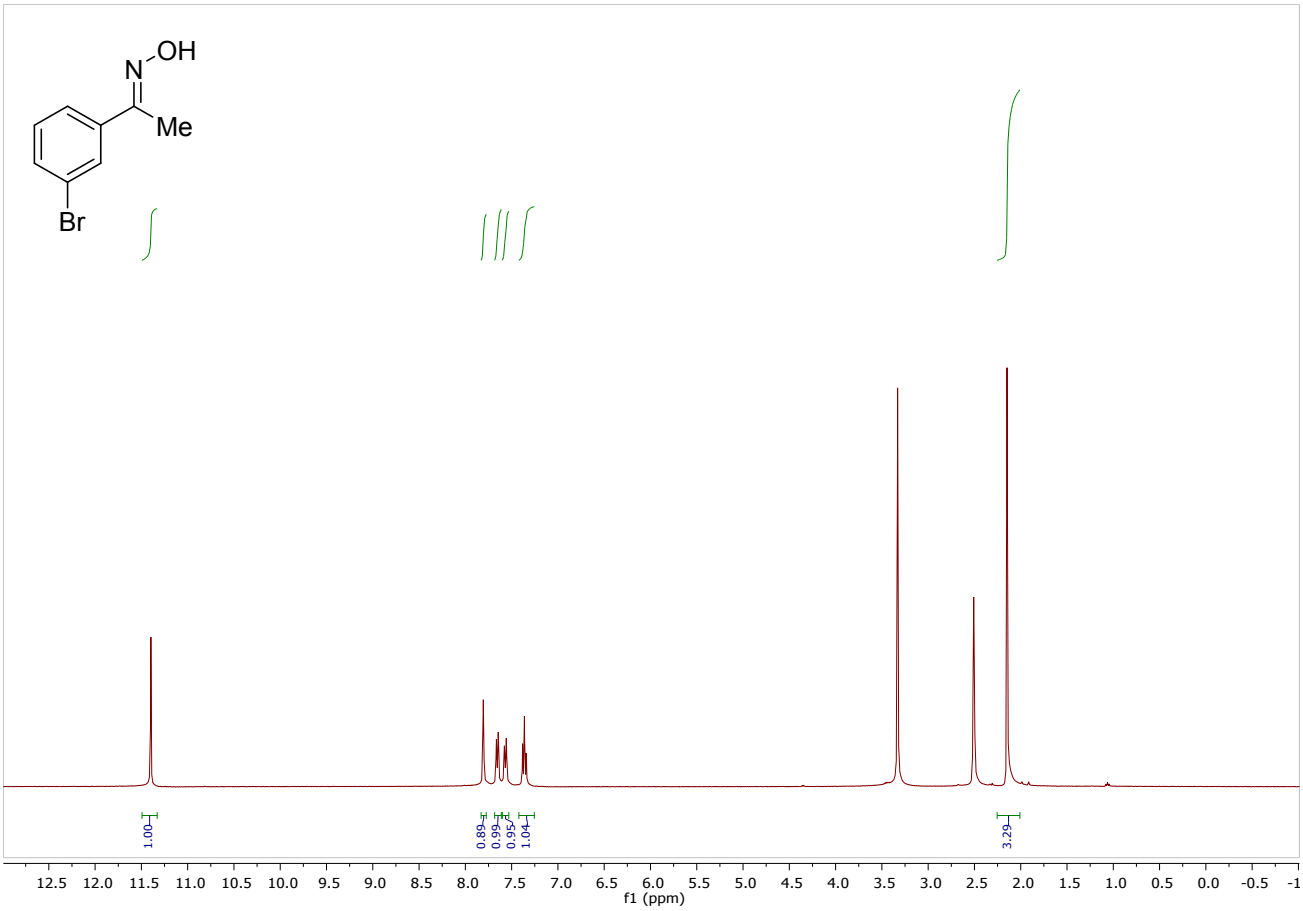
To a mixture of **8** (40 mg, 0.05 mmol), formaldehyde (37% aq. 50 uL, 0.13 mmol) and formic acid (5 uL, 0.13 mmol) in chloroform (1 mL) and the mixture stirred at 70 ^{o}C for 4 hours, until TLC analysis indicated complete consumption of the starting material., The mixture was cooled to room temperature and sat. aq. K_2CO_3 (2.5 mL) and chloroform (2.5 mL) were added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography (15% ammonical MeOH in DCM) afforded **9** as a white solid (21 mg, 57%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.69 (s, 1H), 5.38 (d, J = 6.7 Hz, 1H), 5.19 (d, J = 4.8 Hz, 1H), 4.69 (dd, J = 9.8, 2.7 Hz, 1H), 4.43 (d, J = 7.3 Hz, 1H), 4.32 – 4.24 (m, 1H), 4.09 (dq, J = 9.5, 6.2 Hz, 1H), 3.67 (dd, J = 6.6, 1.7 Hz, 1H), 3.62 (d, J = 7.5 Hz, 1H), 3.50 (ddd, J = 10.9, 6.2, 2.0 Hz, 1H), 3.37 (s, 1H), 3.22 (dd, J = 10.2, 7.3 Hz, 1H), 3.11 – 2.97 (m, 6H), 2.71 (tdd, J = 14.0, 7.2, 4.4 Hz, 2H), 2.54 (d, J = 9.6 Hz, 1H), 2.43 (ddd, J = 12.2, 10.1, 3.9 Hz, 1H), 2.36 (d, J = 15.3 Hz, 1H), 2.31 (s, 3H), 2.28 (s, 6H), 2.15 (d, J = 10.5 Hz, 1H), 2.08 – 1.84 (m, 3H), 1.78 (d, J = 14.6 Hz, 1H), 1.66 (ddd, J = 12.7, 4.0, 2.0 Hz, 1H), 1.58 (dd, J = 15.3, 5.0 Hz, 1H), 1.45 (ddd, J = 14.3, 9.8, 7.3 Hz, 1H), 1.33 (d, J = 6.2 Hz, 3H), 1.31 (s, 3H), 1.22 (d, J = 6.1 Hz, 3H), 1.18 (d, J = 7.5 Hz, 3H), 1.10 – 1.02 (m, 8H), 0.92 – 0.89 (m, 4H), 0.87 (d, J = 7.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.0, 102.9, 94.4, 83.2, 78.2, 77.6, 77.5, 74.2, 73.7, 73.4, 73.0, 70.8, 70.1, 68.8, 65.9, 65.6, 62.6, 49.5, 45.4, 42.5, 42.2, 40.4, 36.1, 34.7, 28.7, 27.6, 26.76, 21.98, 21.60, 21.4, 21.3, 18.2, 16.3, 14.5, 11.2, 9.0, 7.2.

All spectral data is consistent with previously published findings.[23]

5 – Copies of Spectra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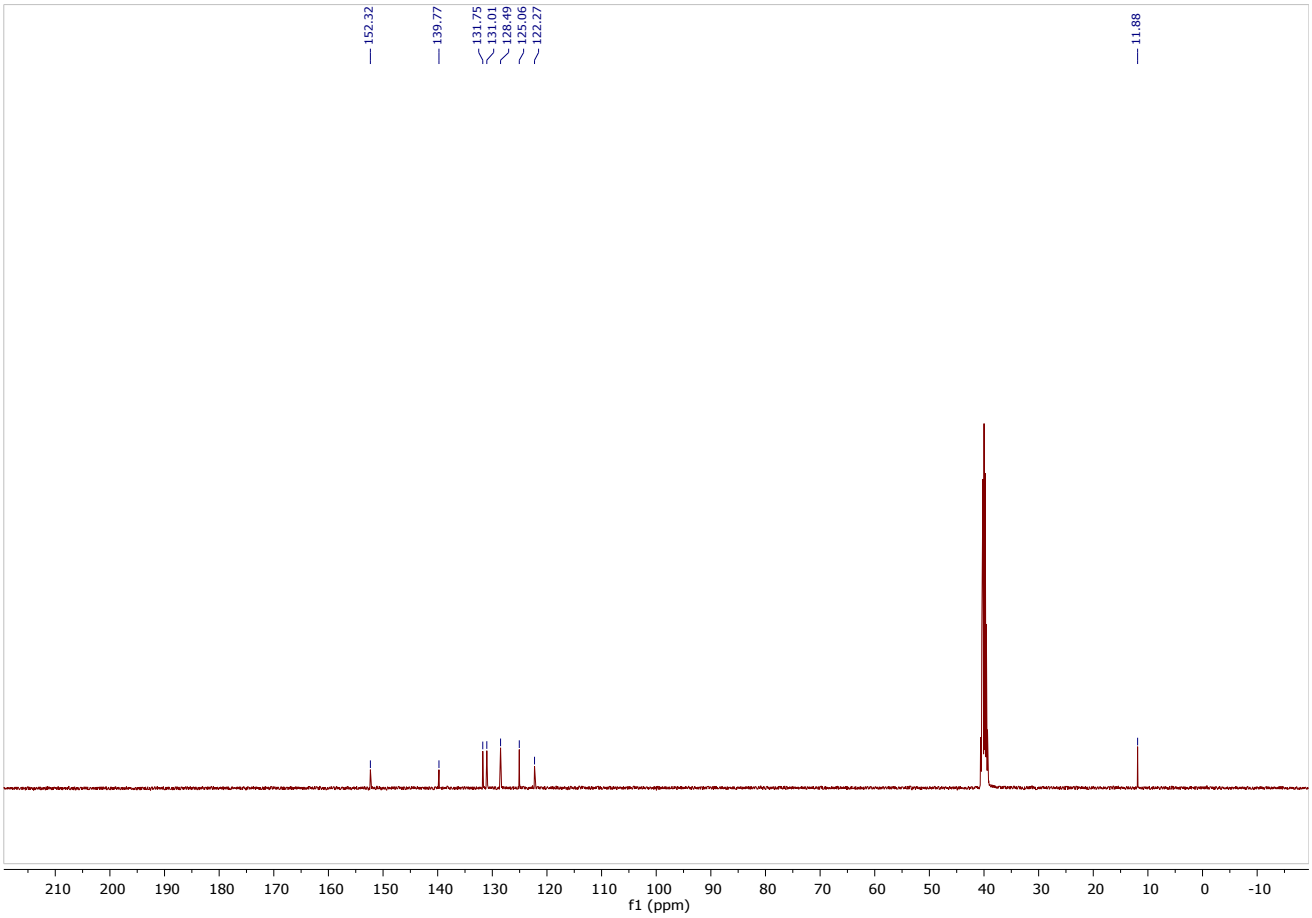
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125.06
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11.88
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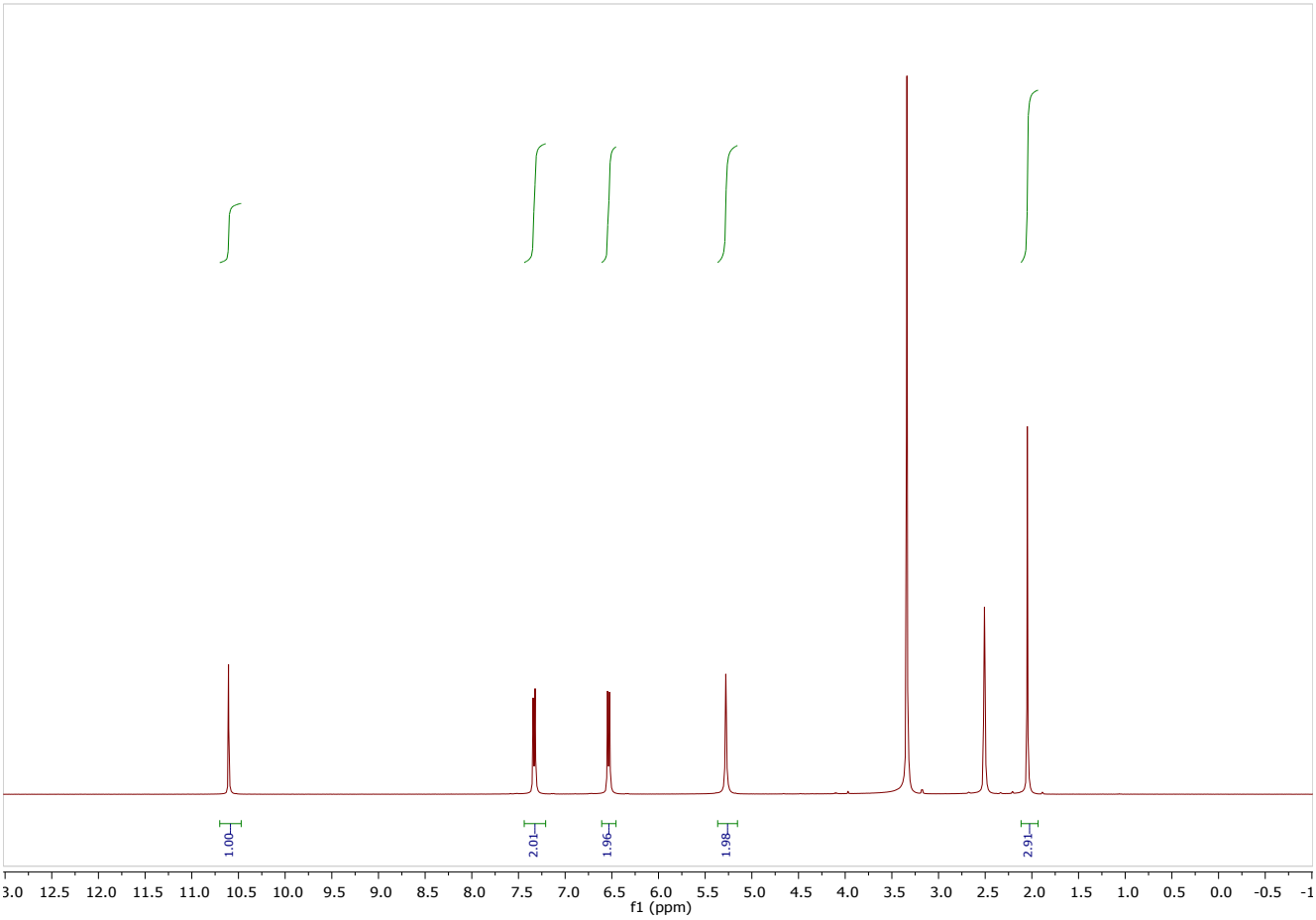
f1 (ppm)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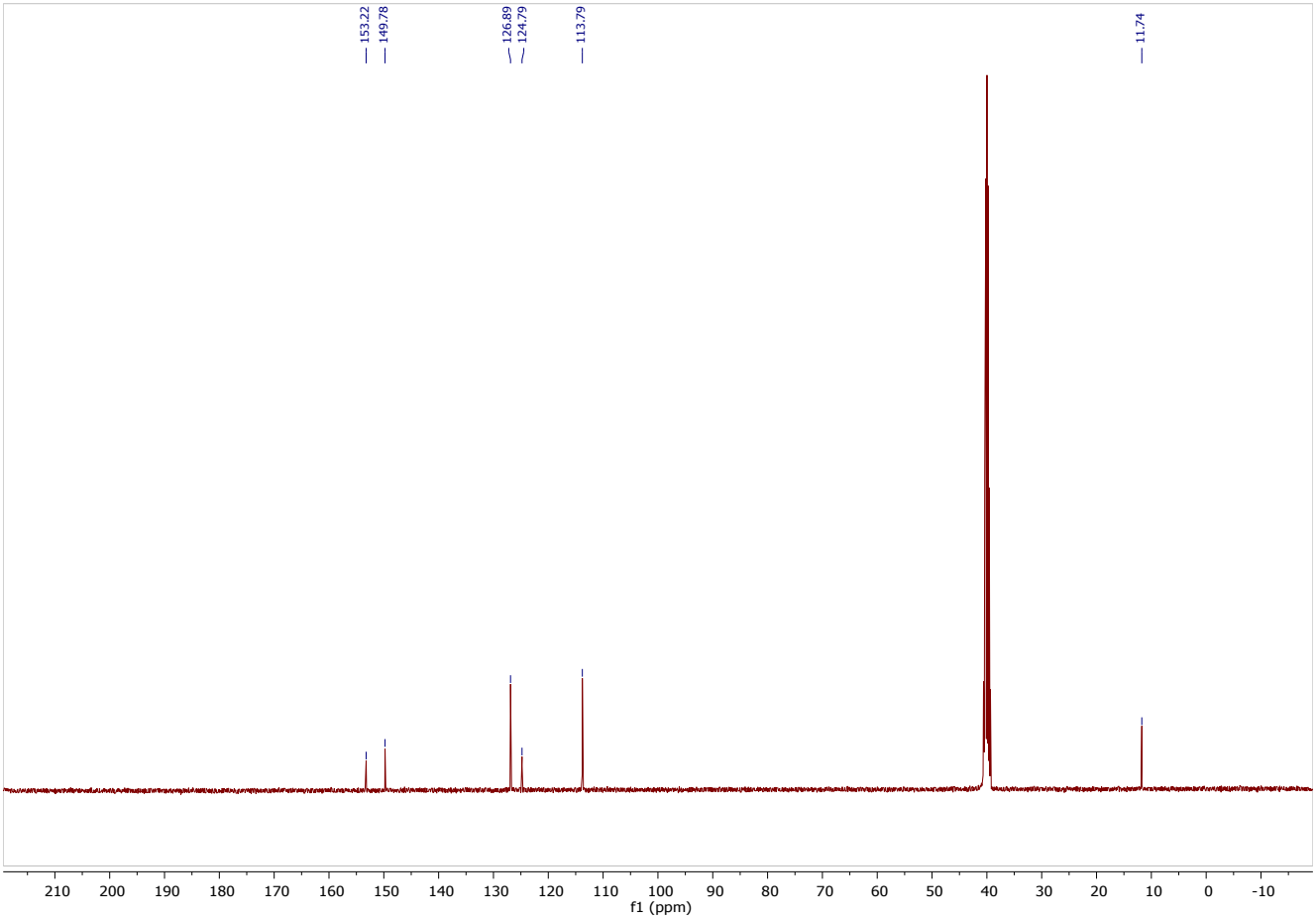
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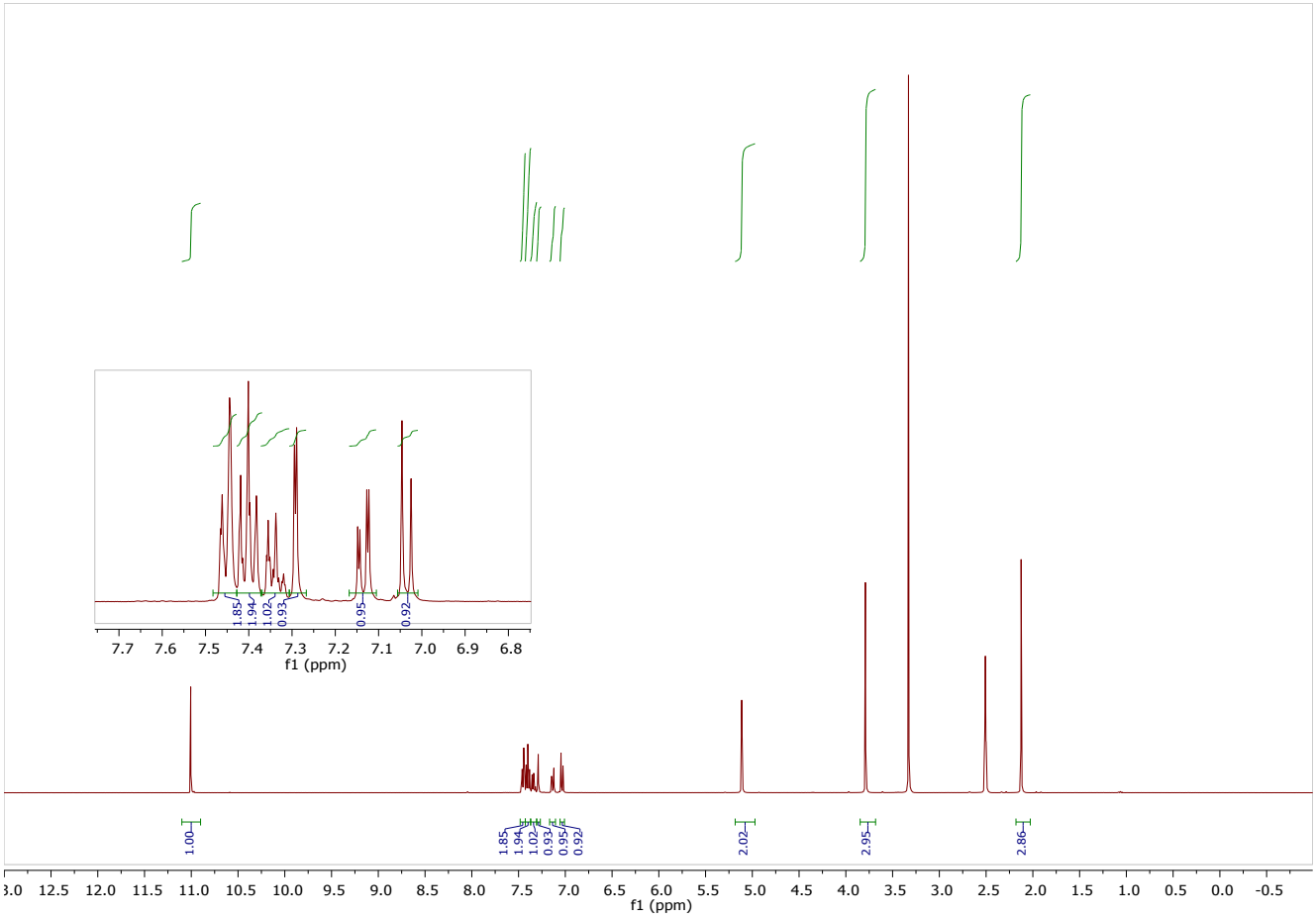
113.79
11.74
f1 (ppm)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1.02
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0.95
0.92
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
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0.93
0.95
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2.95
2.86
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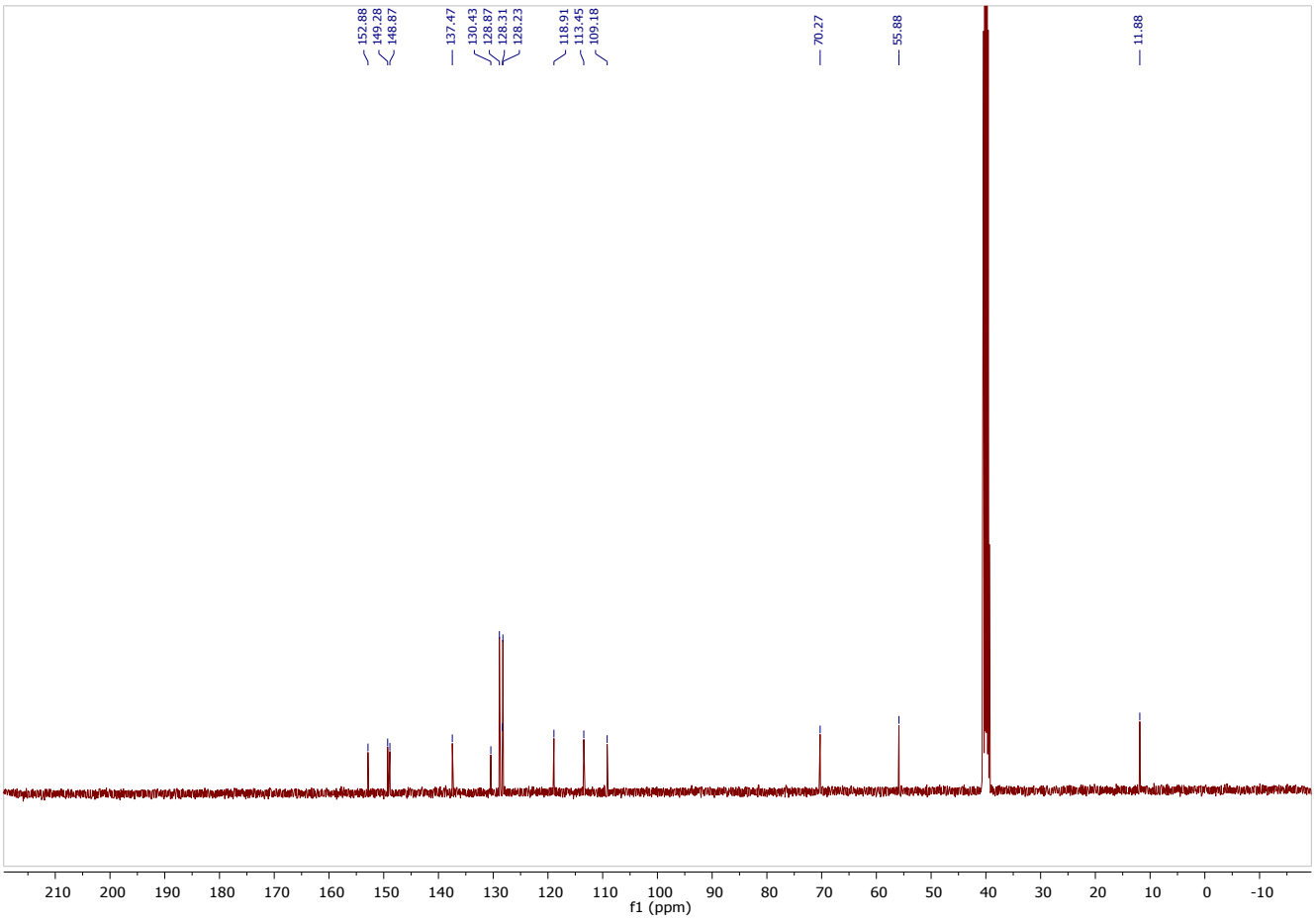
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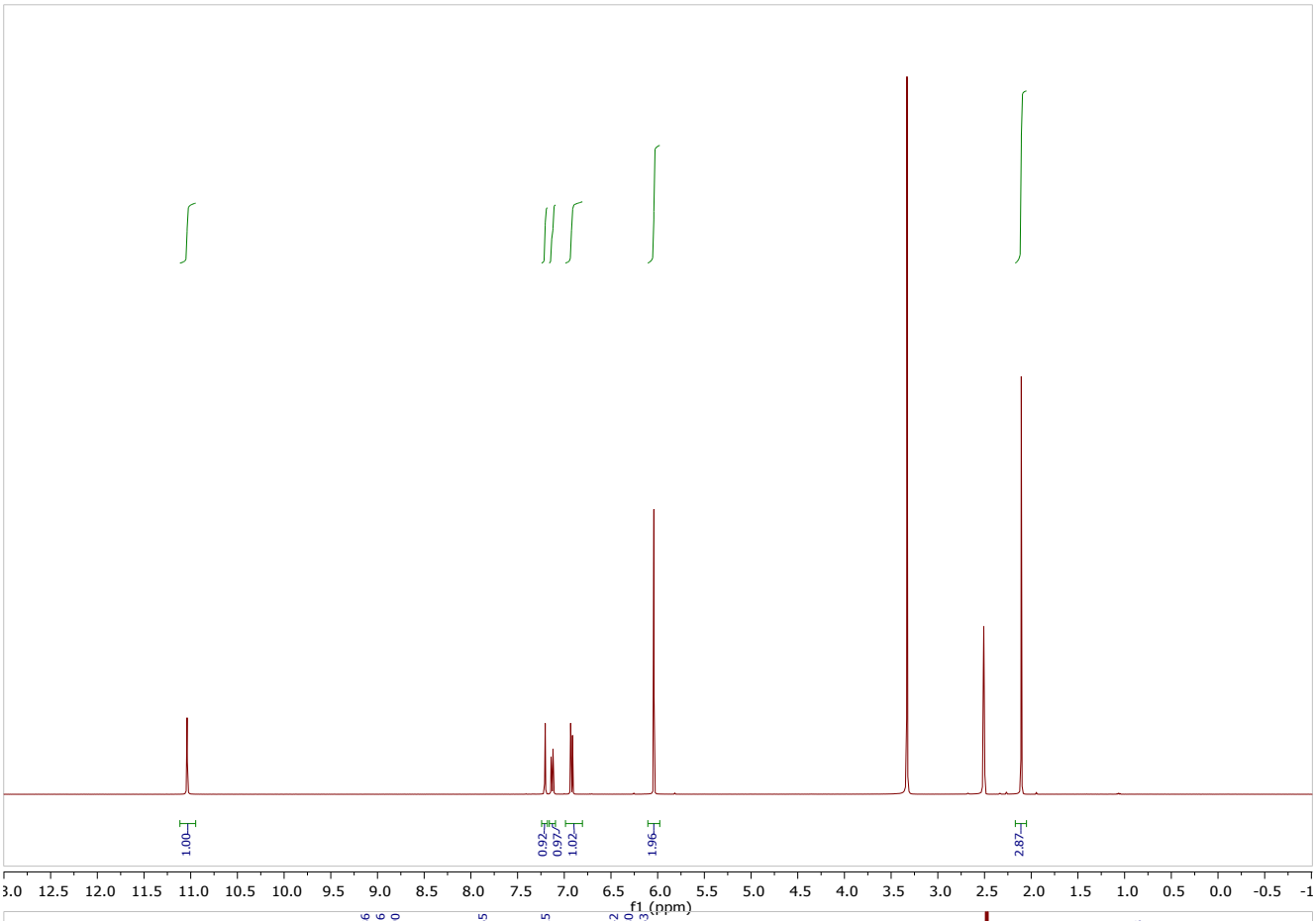
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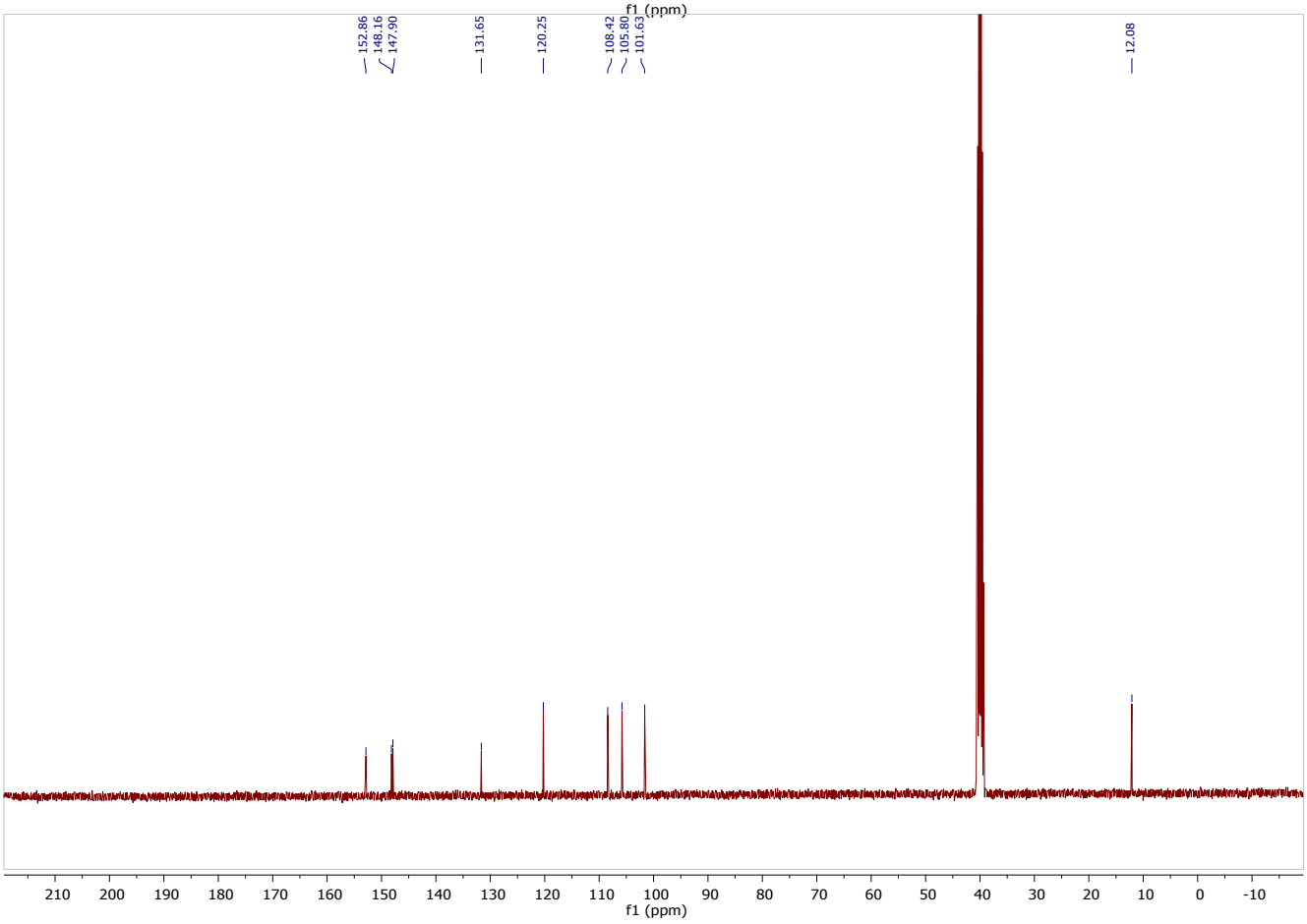
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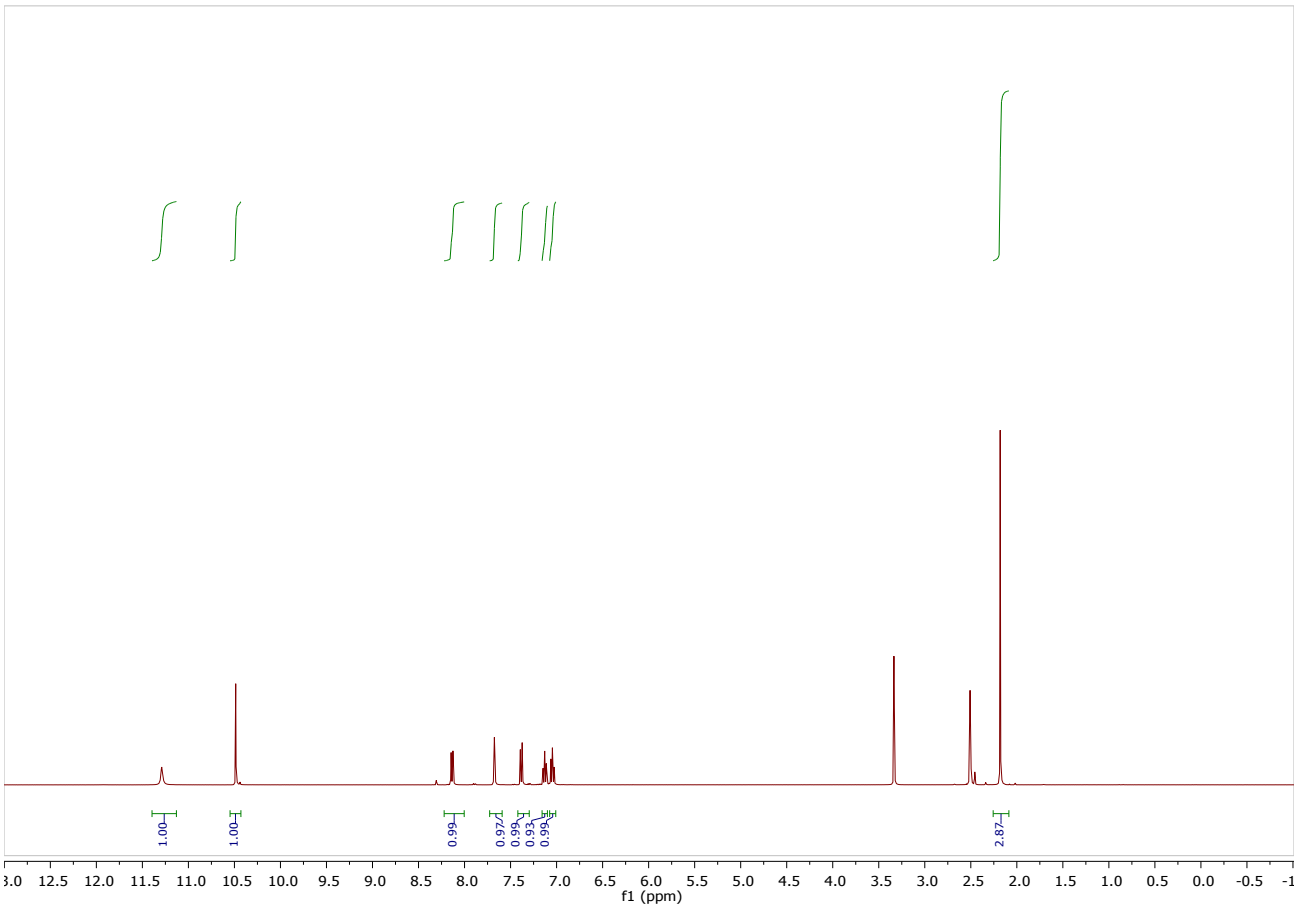
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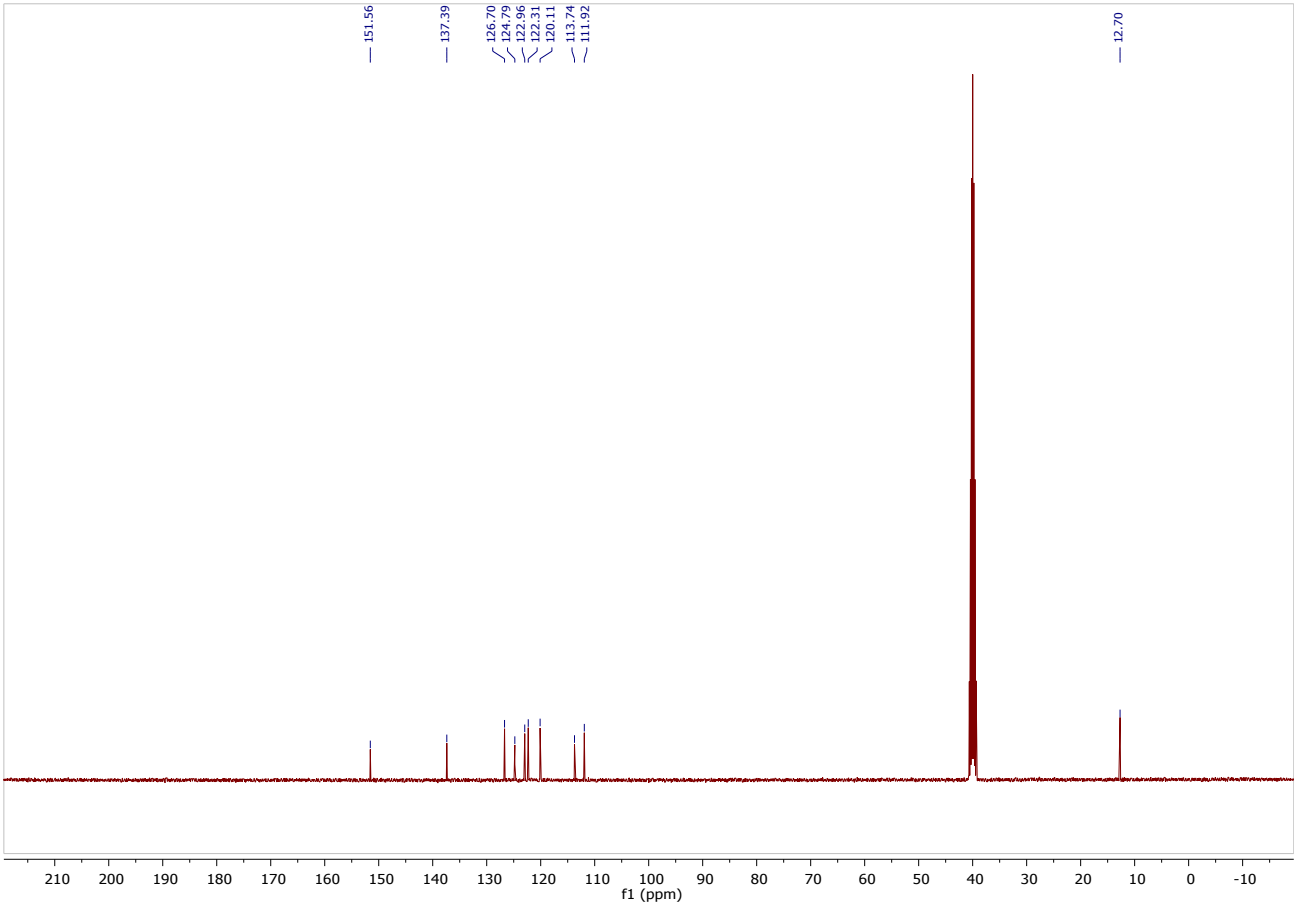
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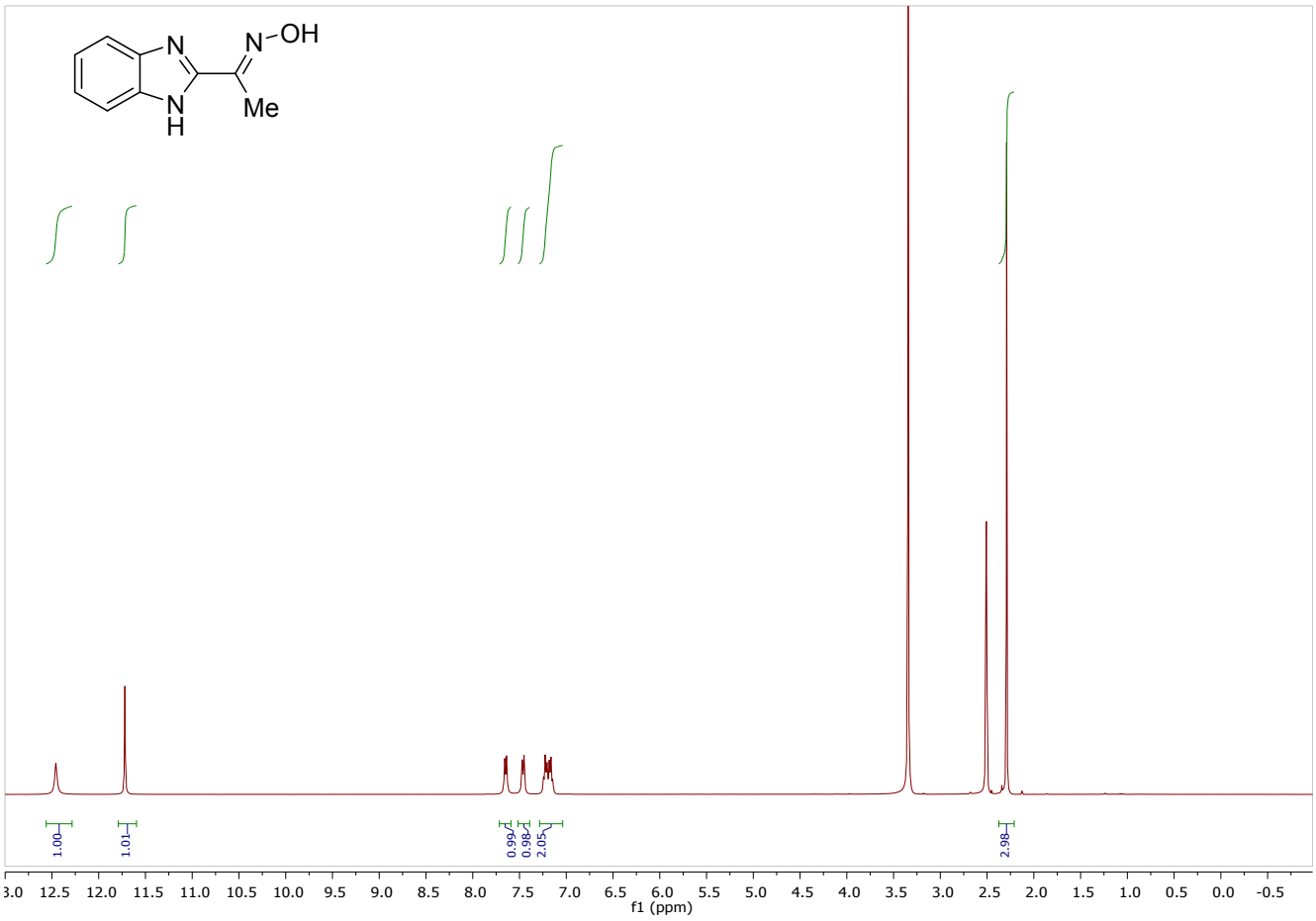
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H
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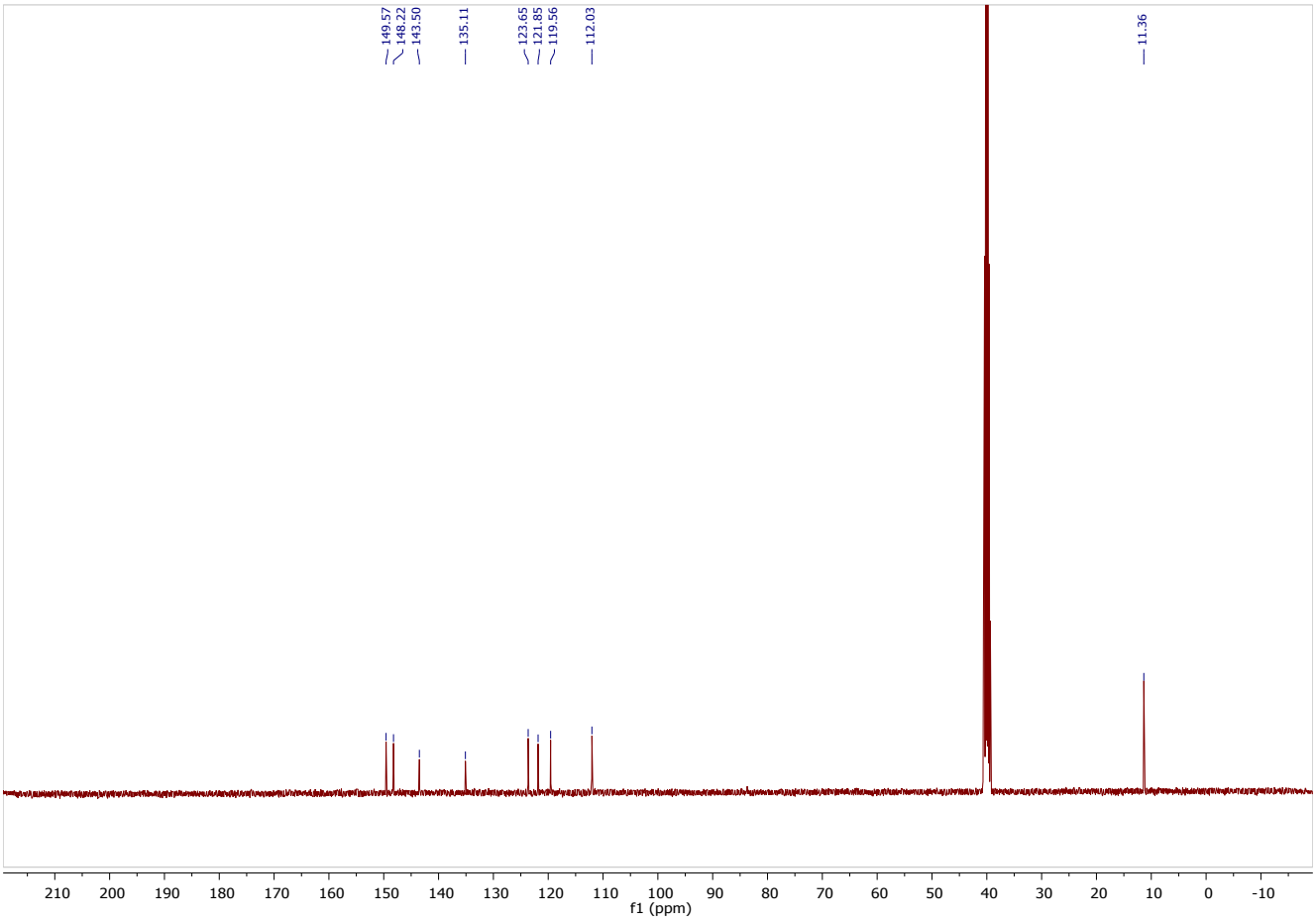
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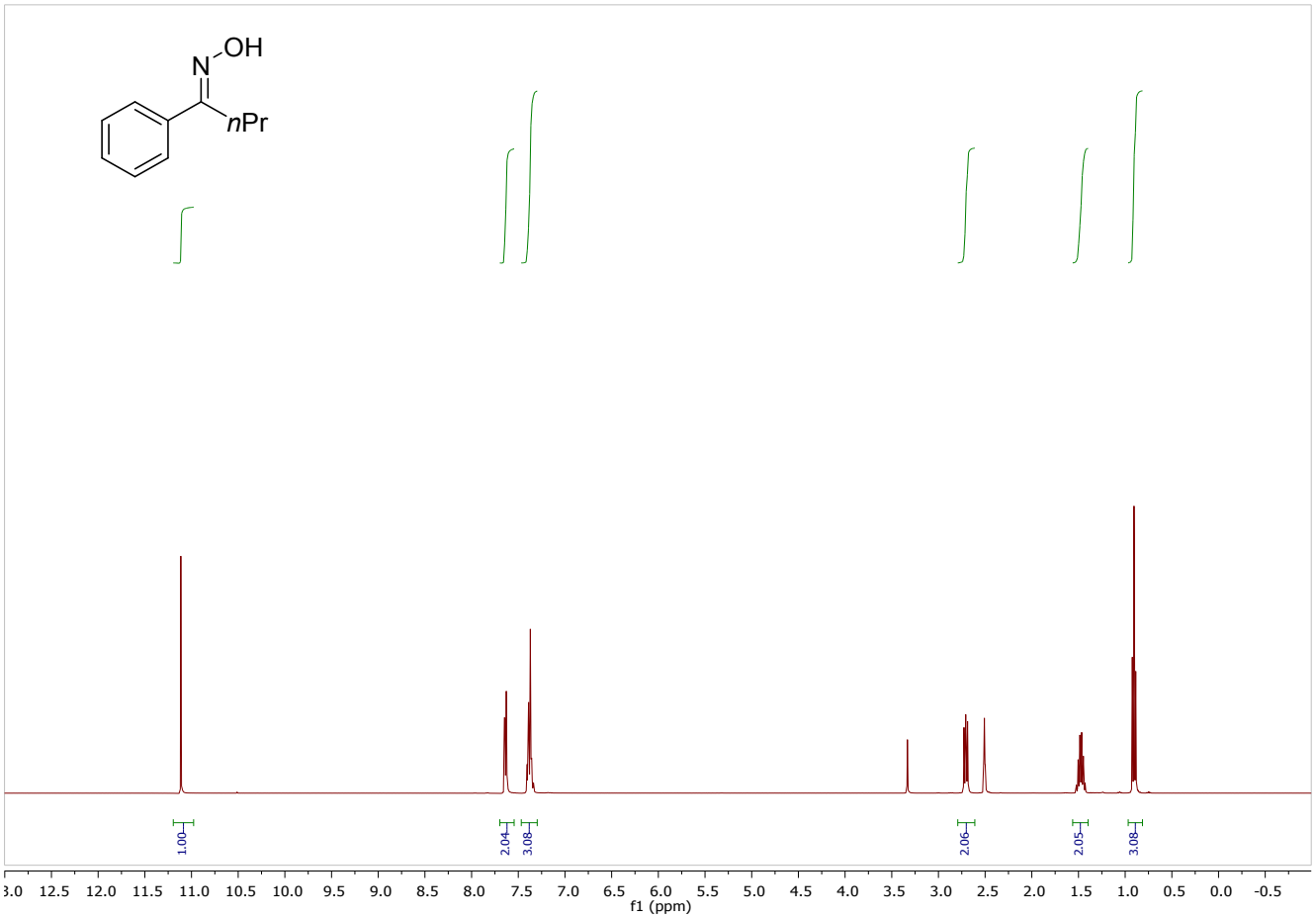
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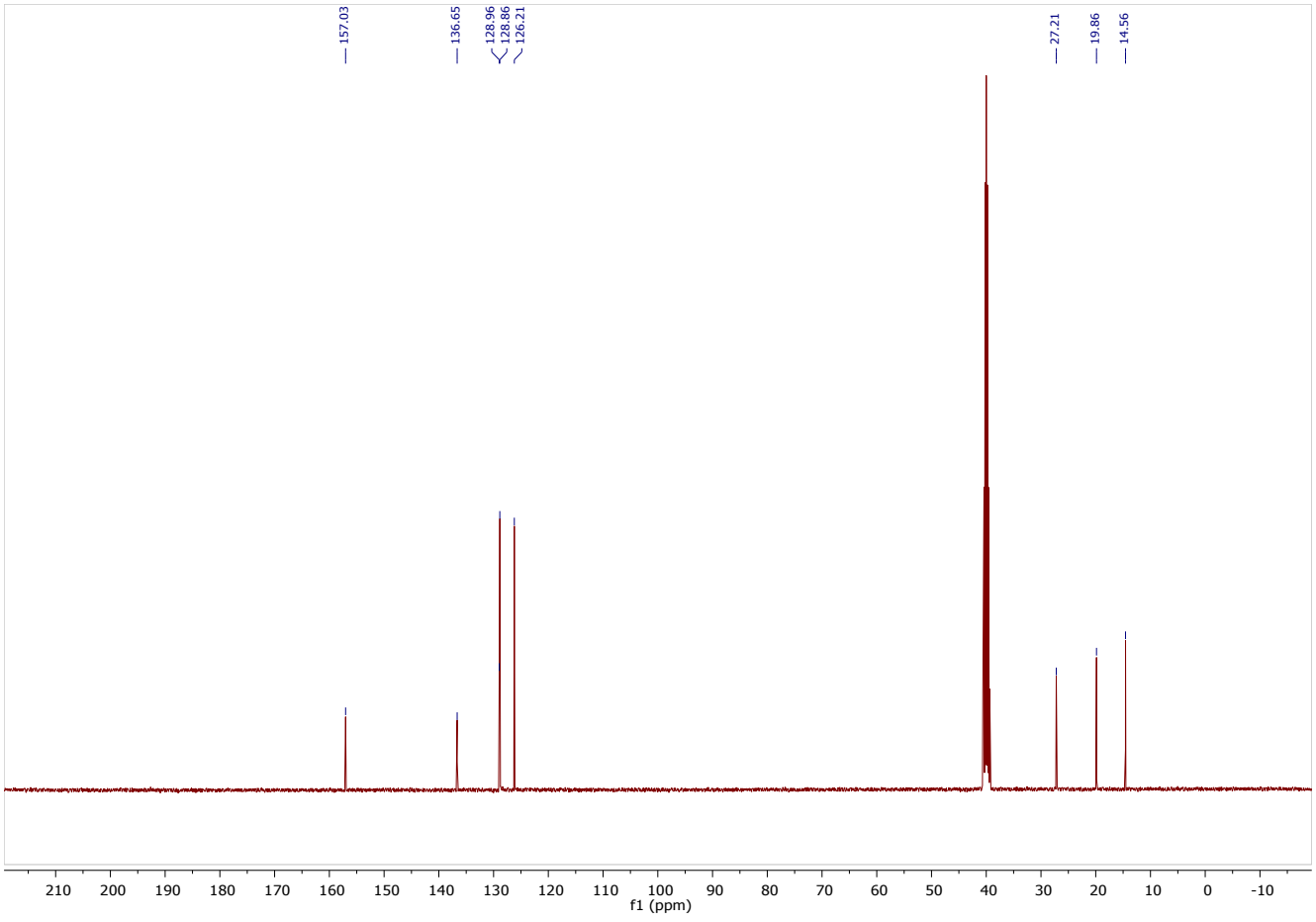
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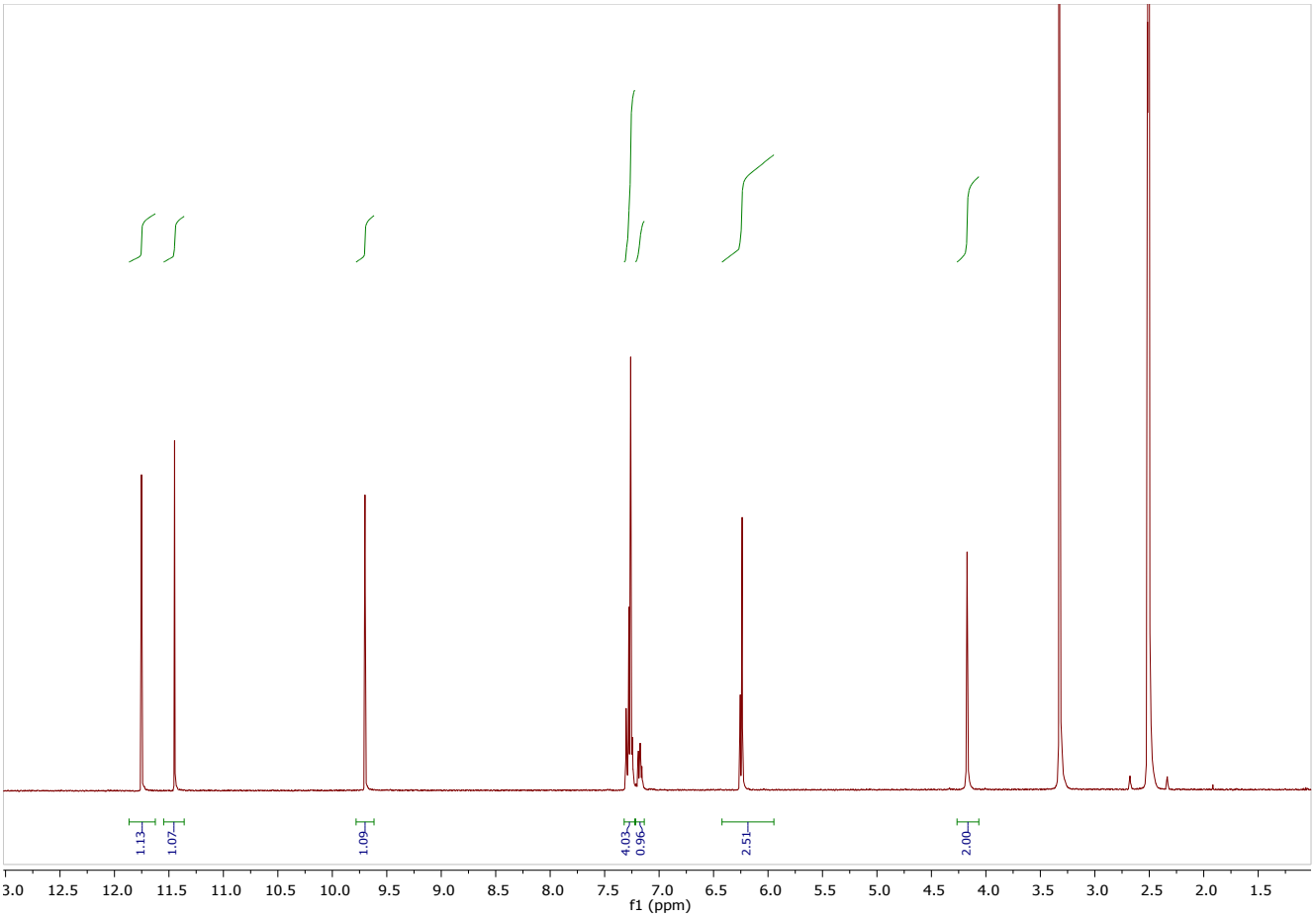
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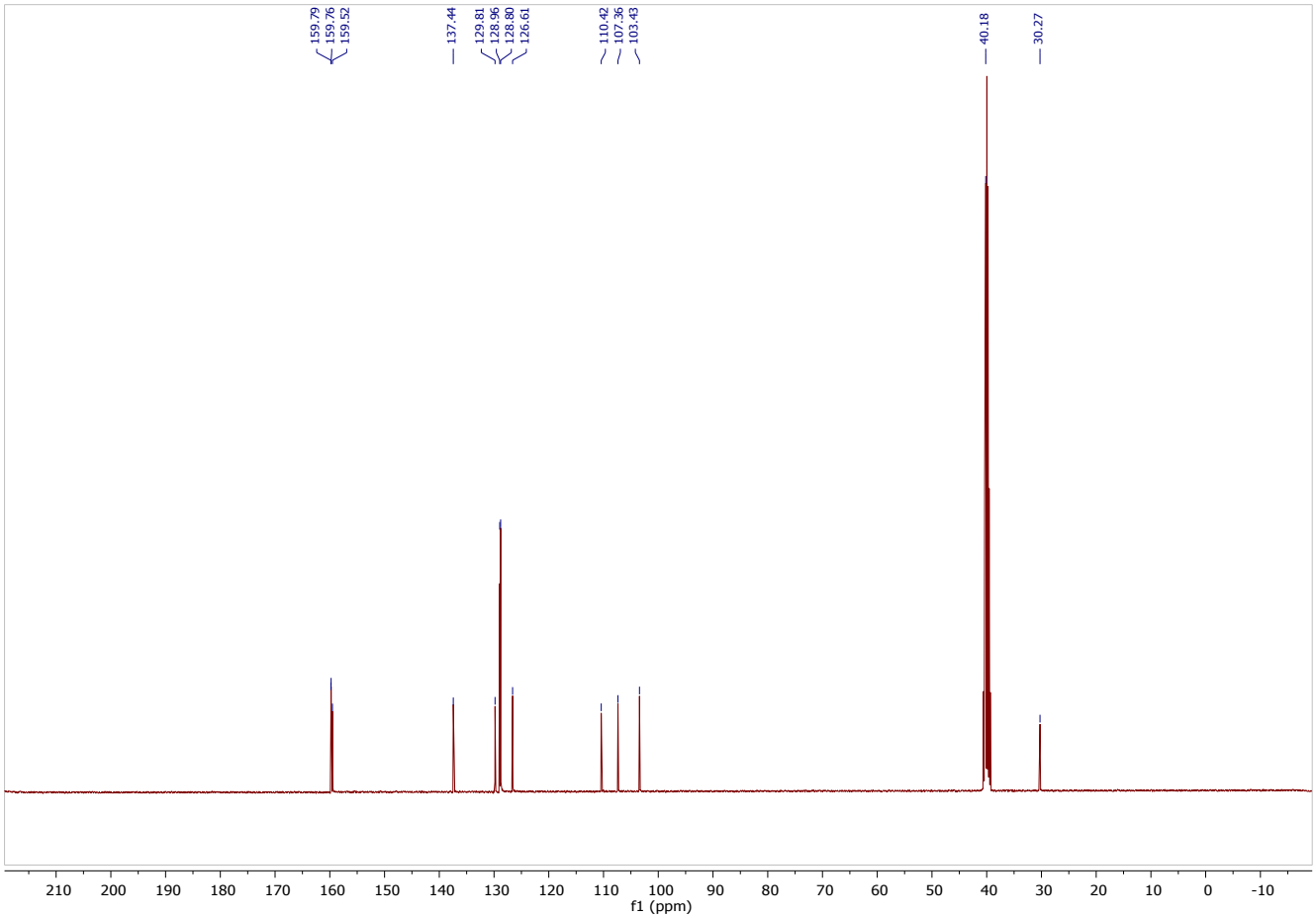
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30.27
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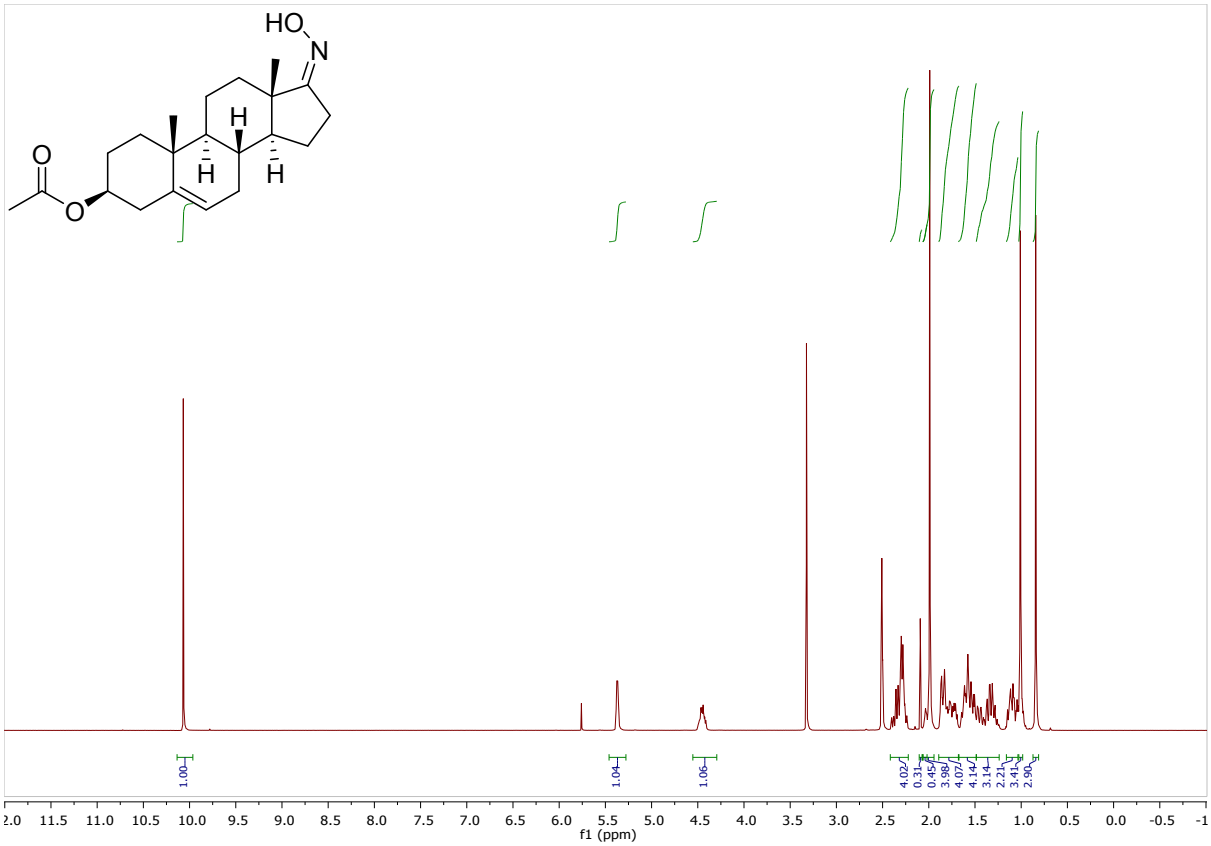
f1 (ppm)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H
O
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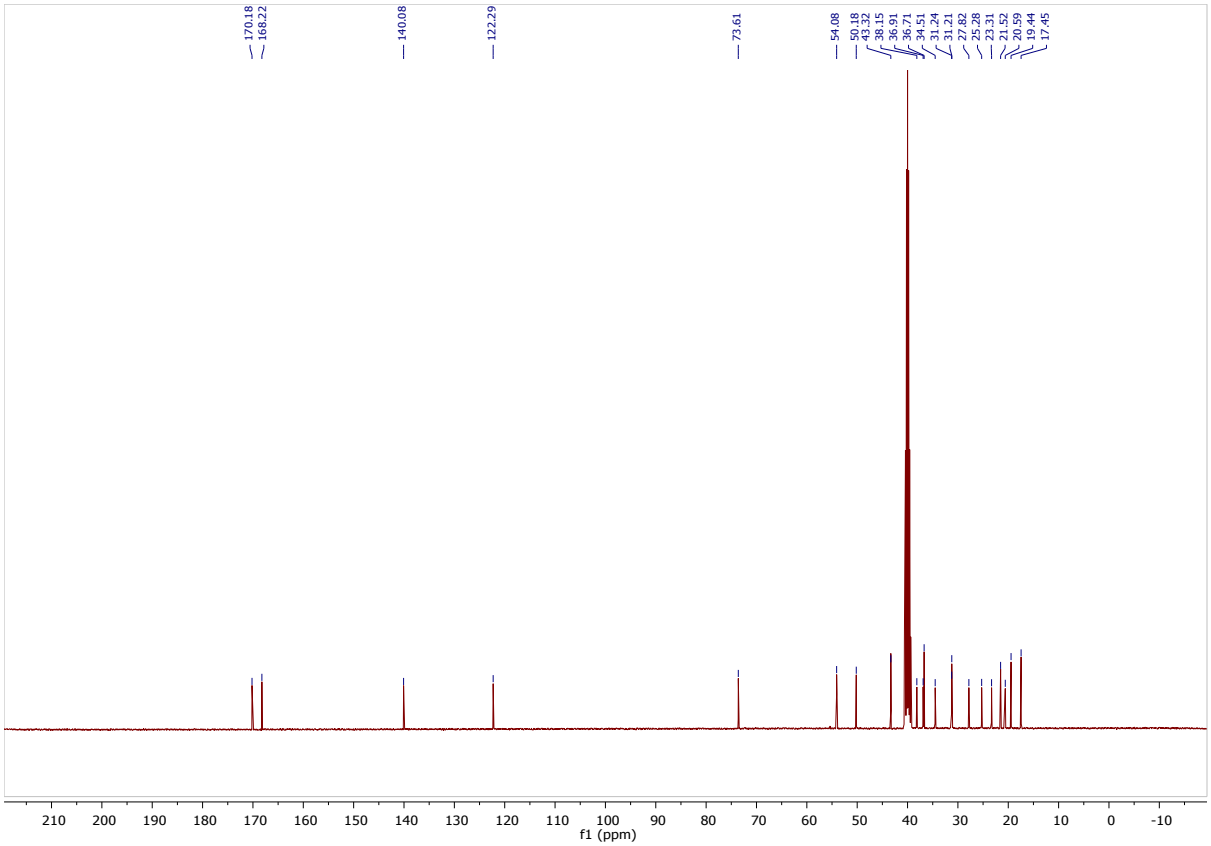
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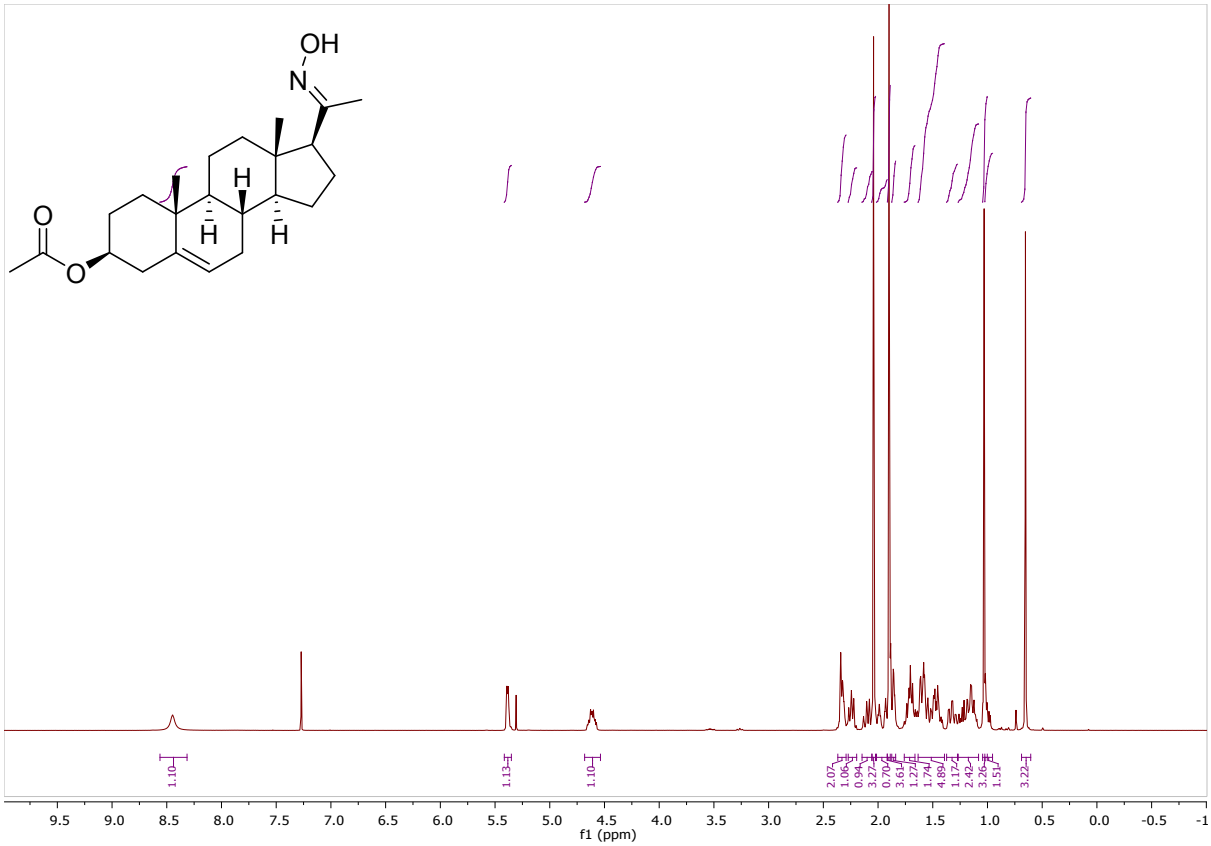
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1.27
1.74
4.89
1.17
2.42
3.26
1.51
3.22
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
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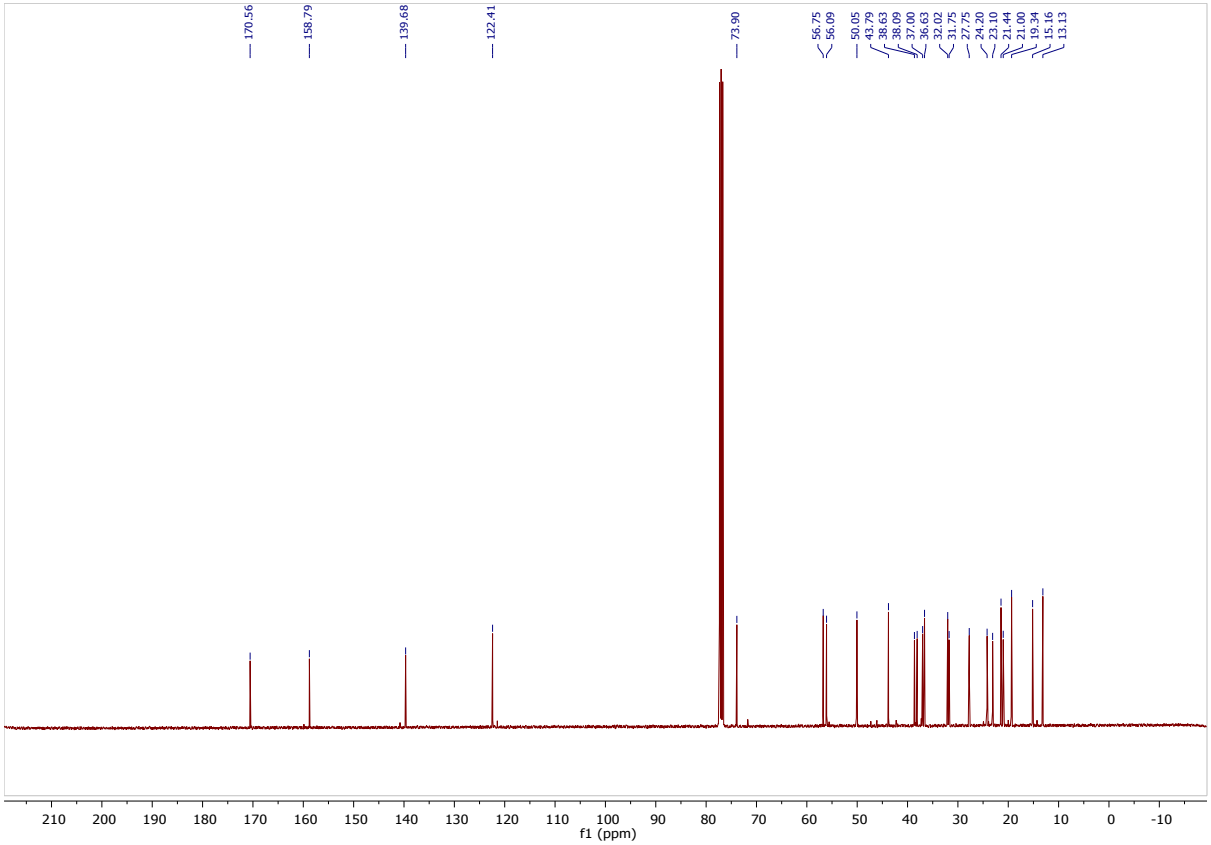
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31.75
27.75
24.20
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15.16
13.13
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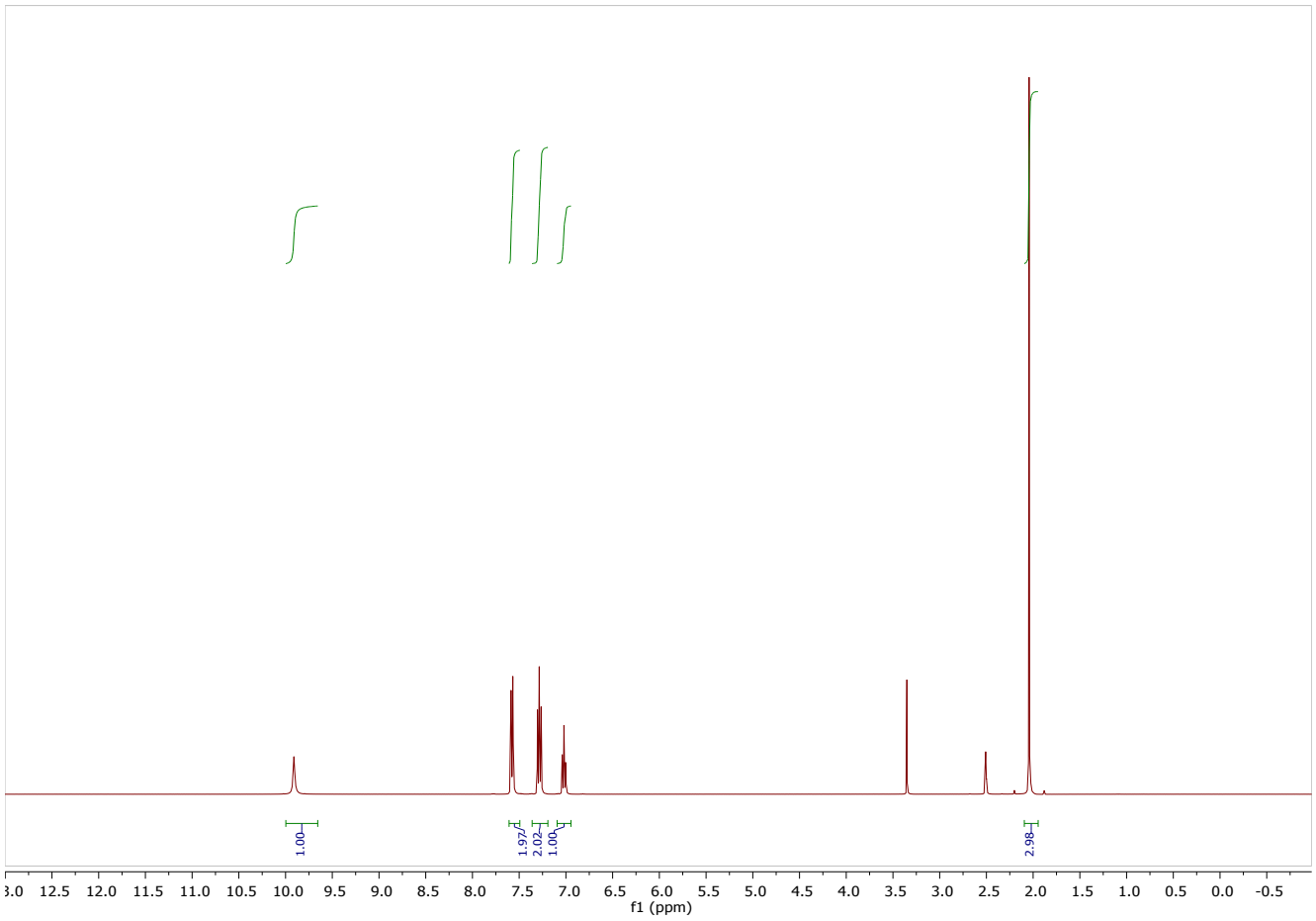
f1 (ppm)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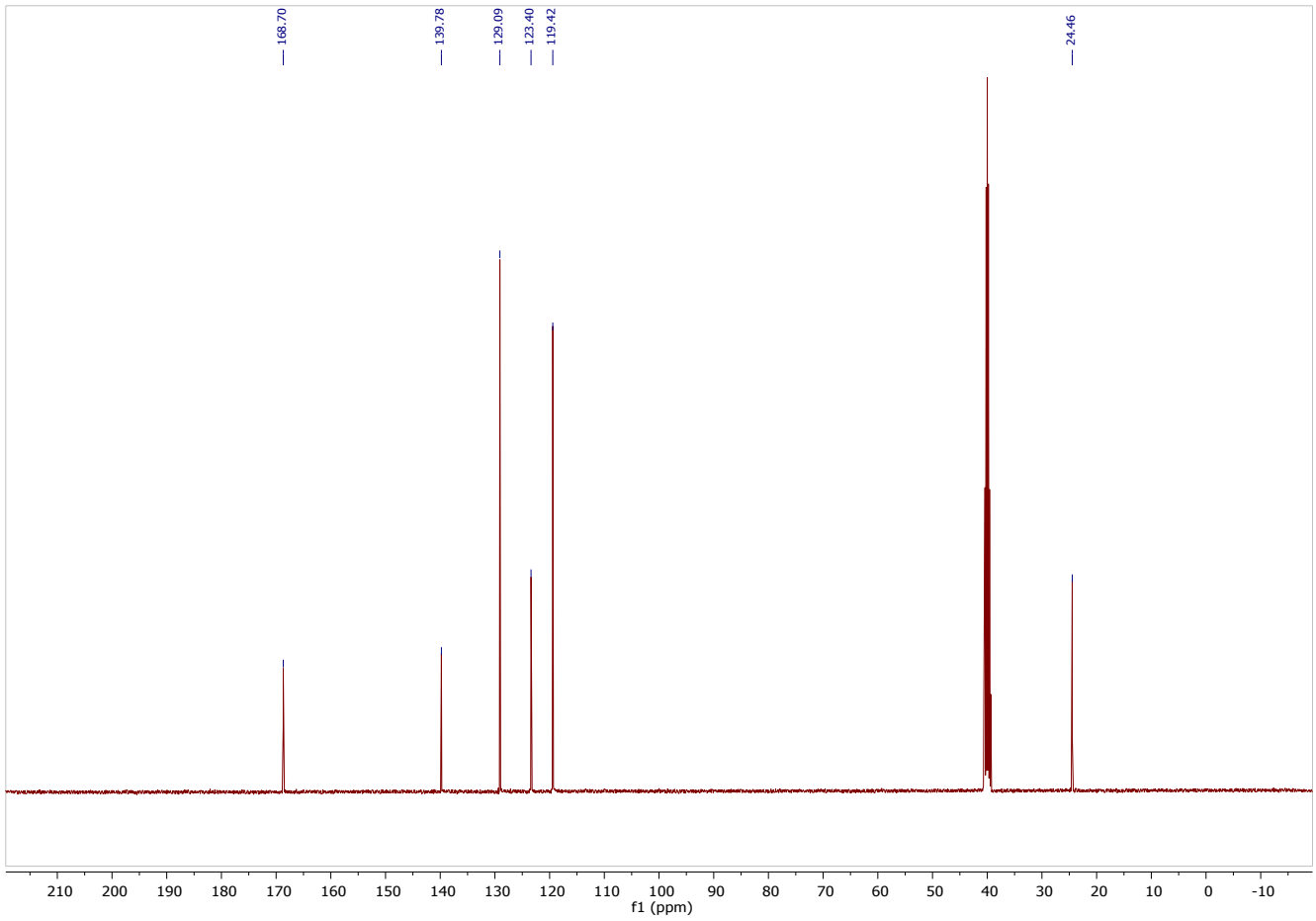
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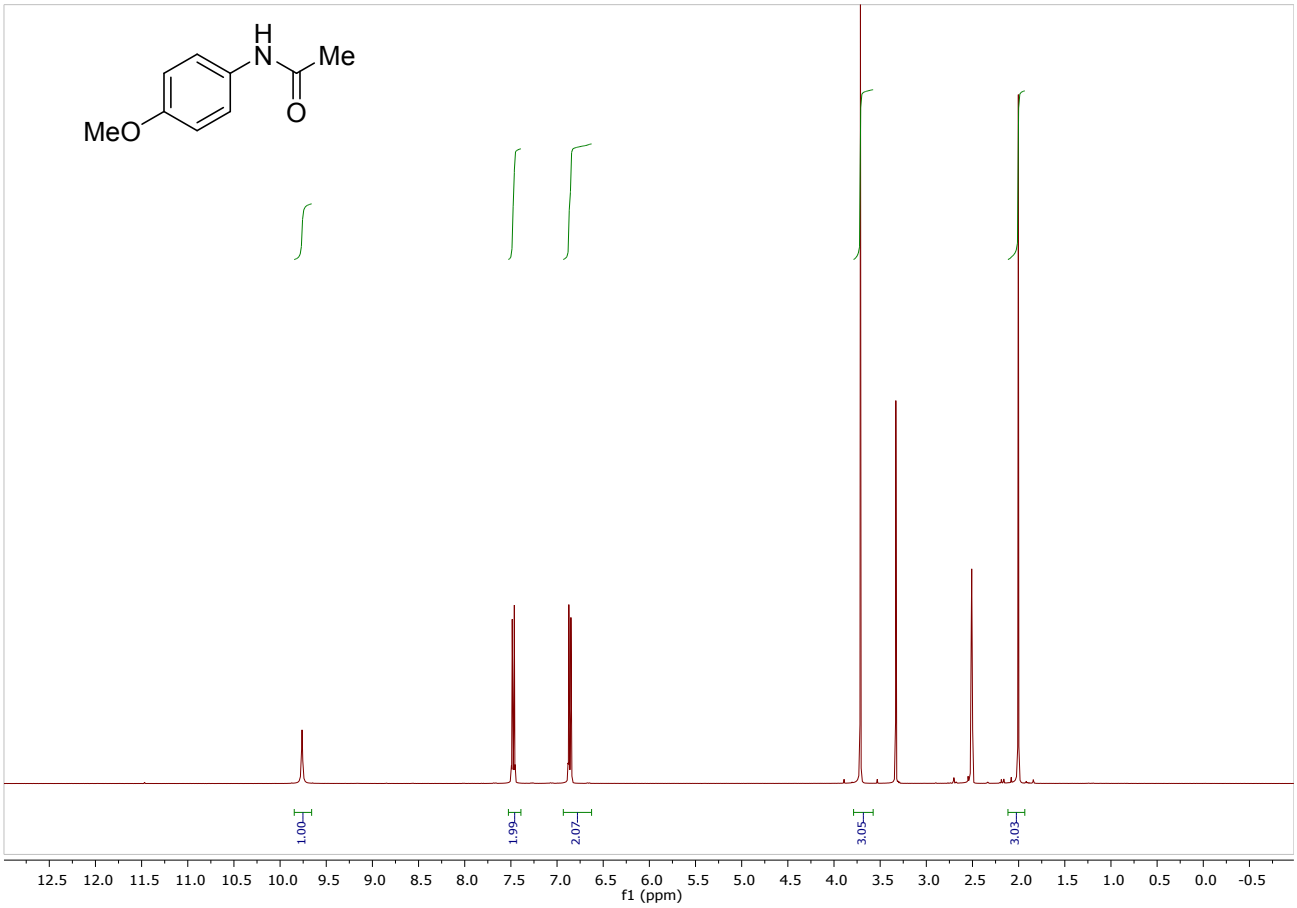
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MeO
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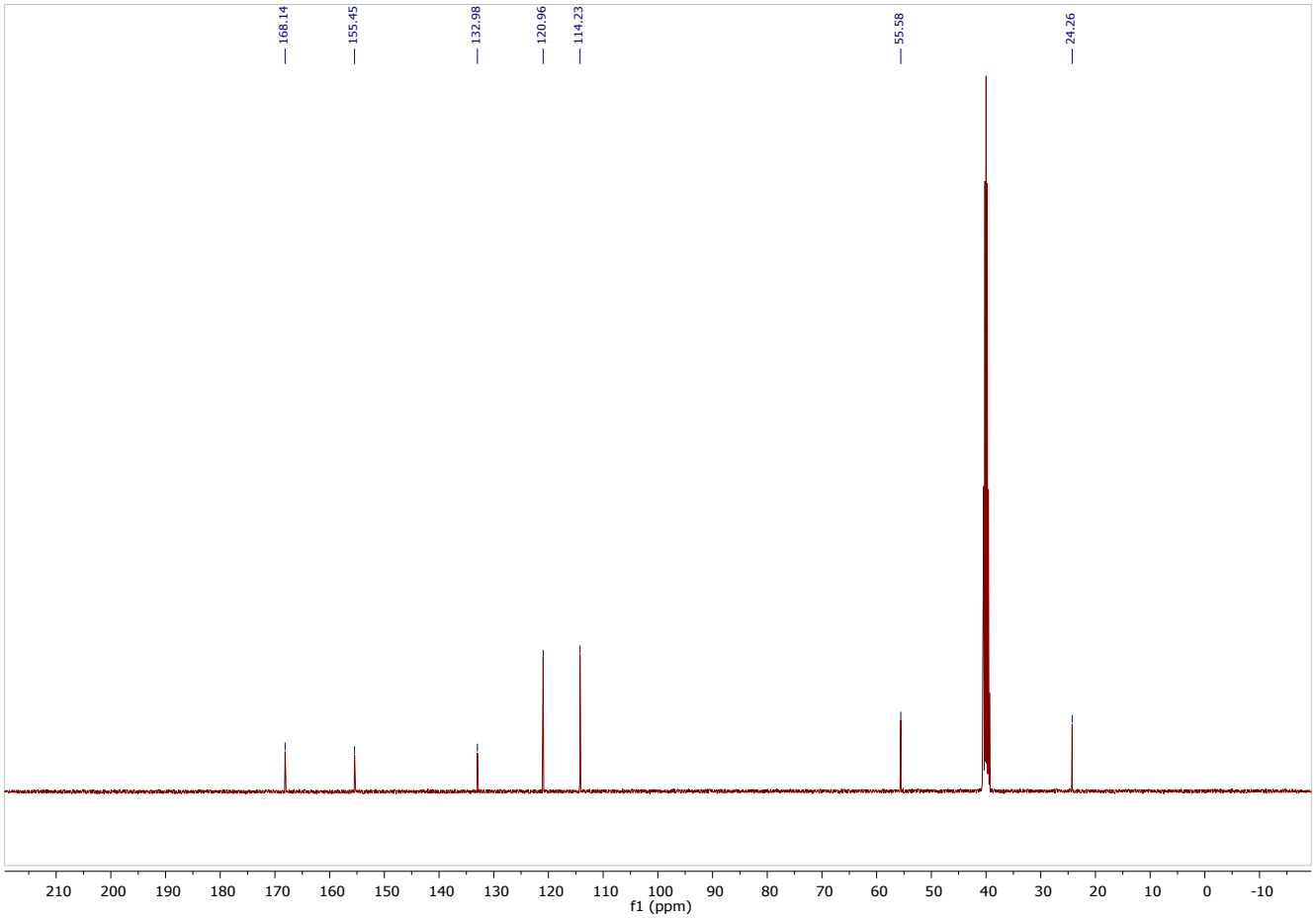
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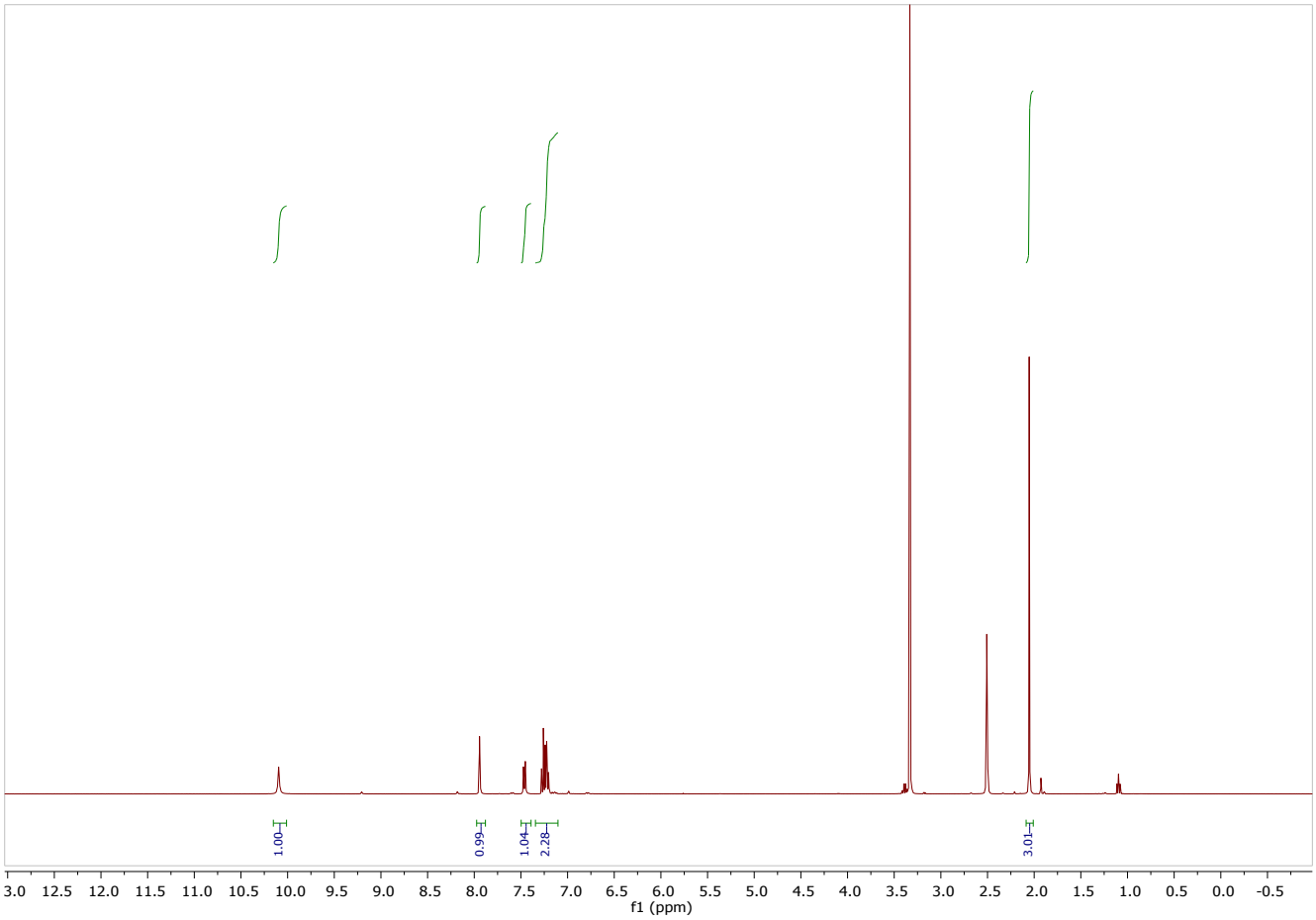
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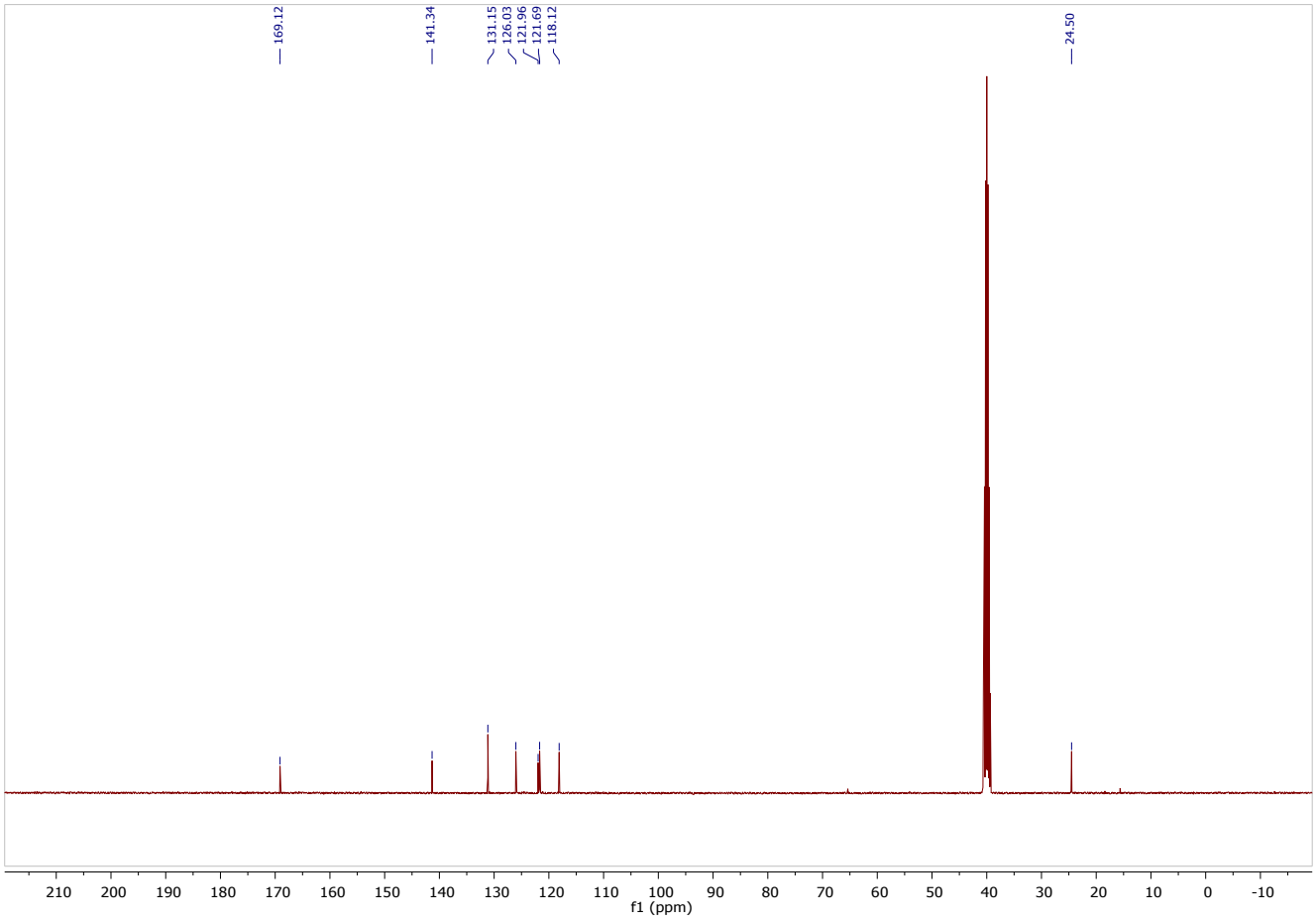
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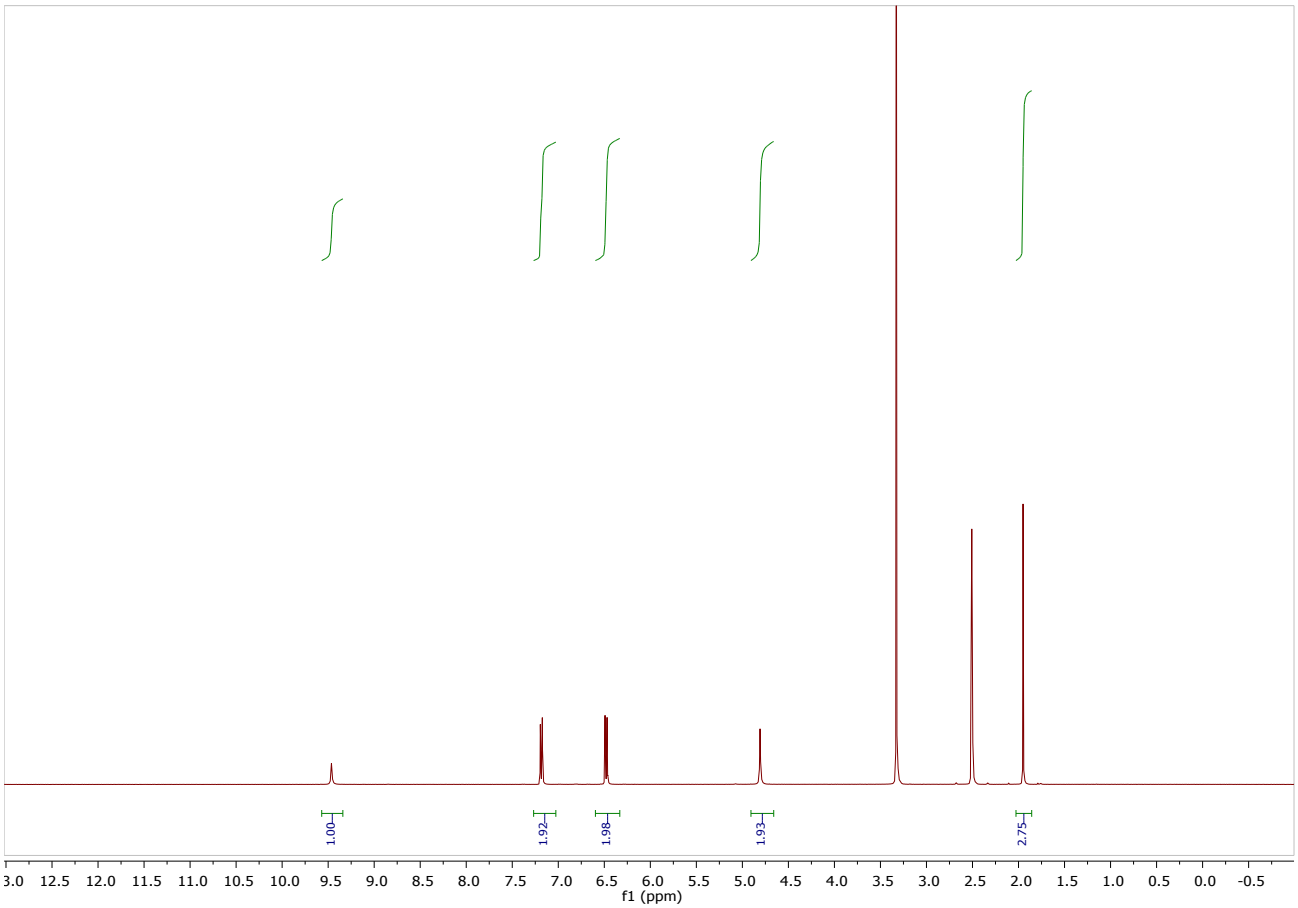
f1 (ppm)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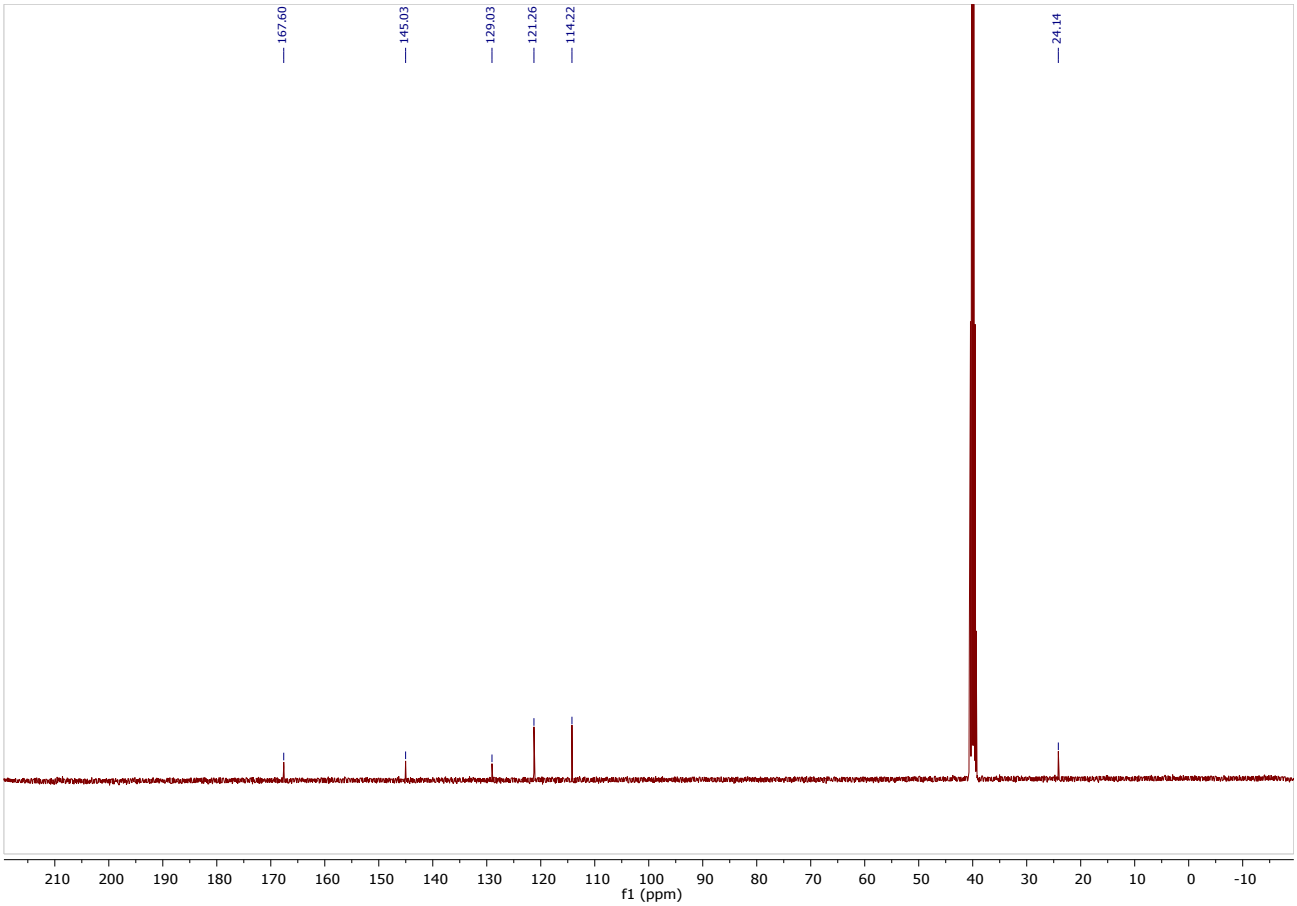
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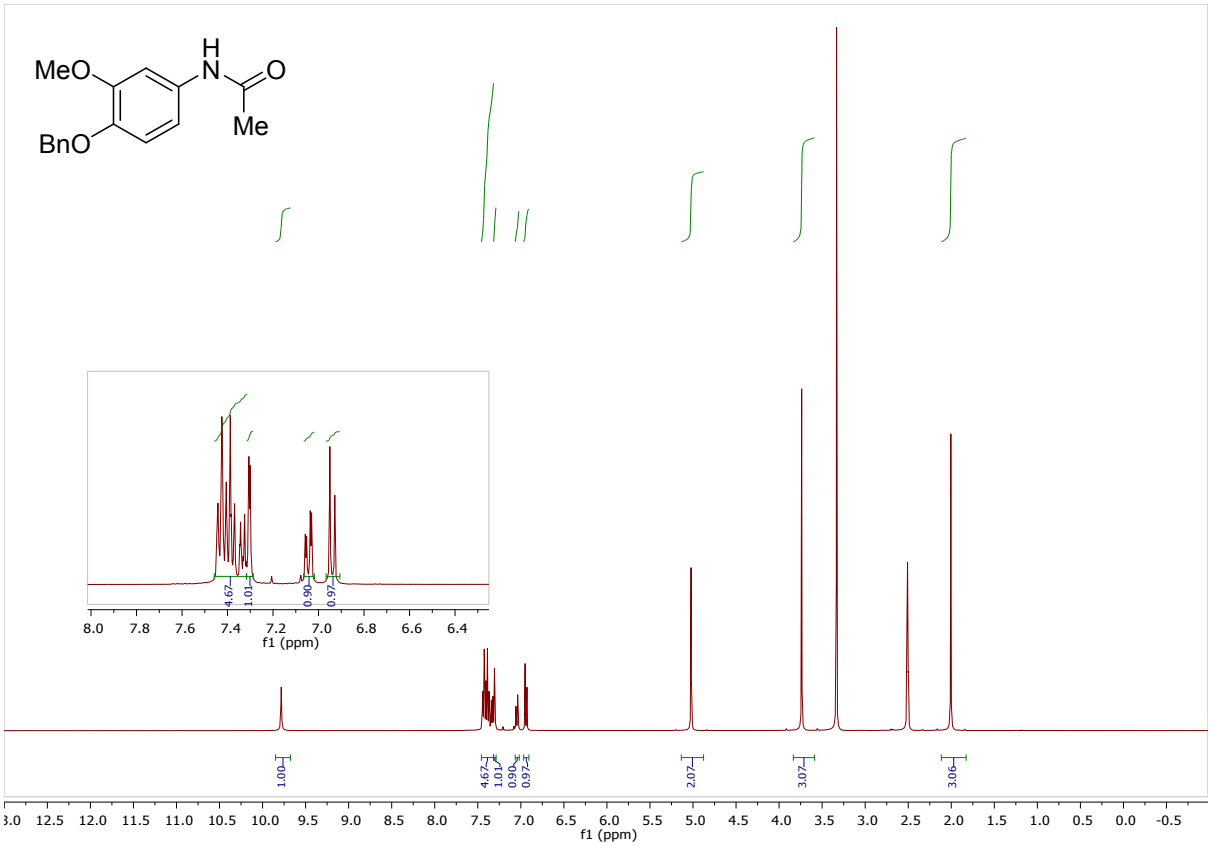
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Me
BnO
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0.97
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4
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2.07
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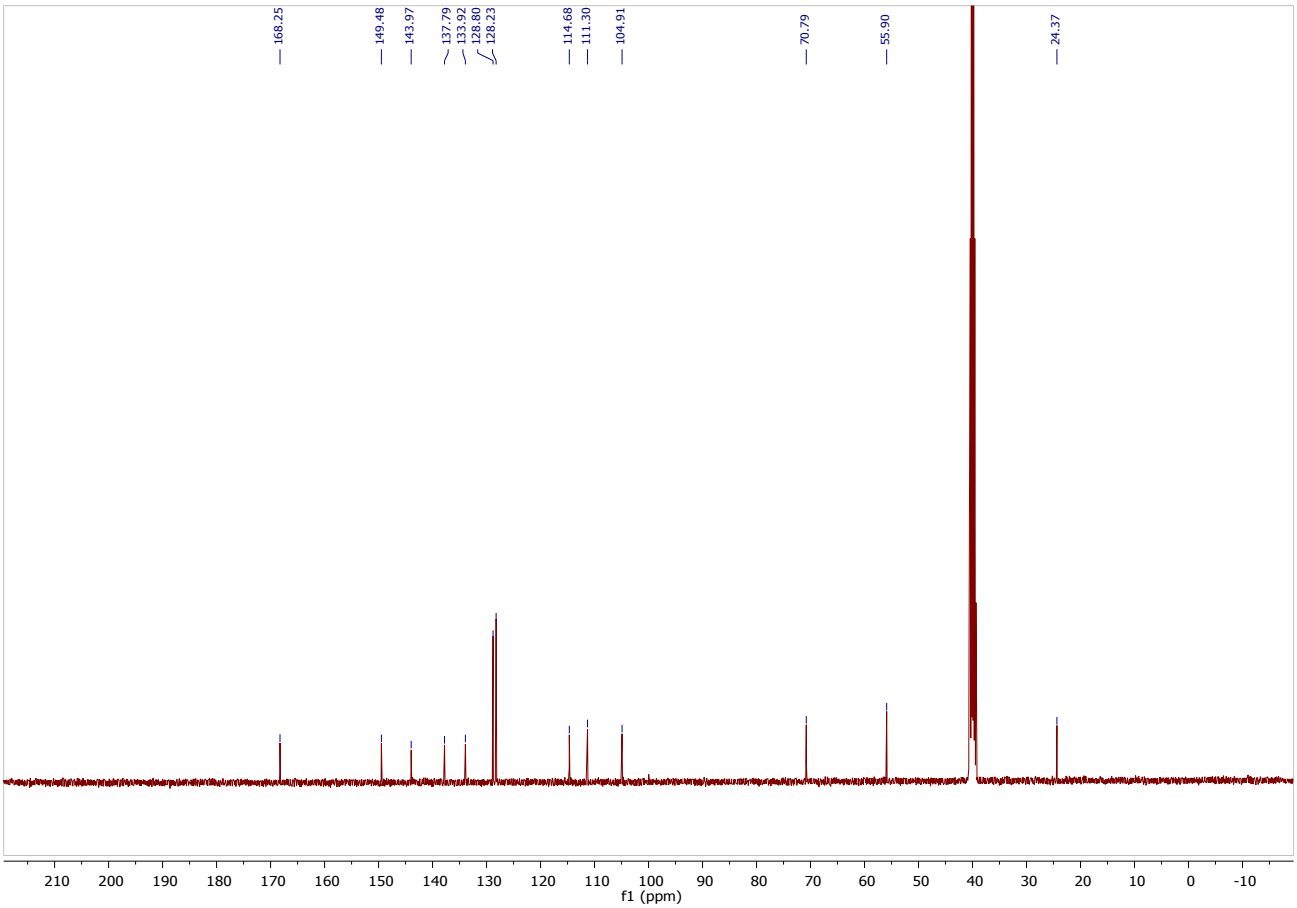
3.06
f1 (ppm)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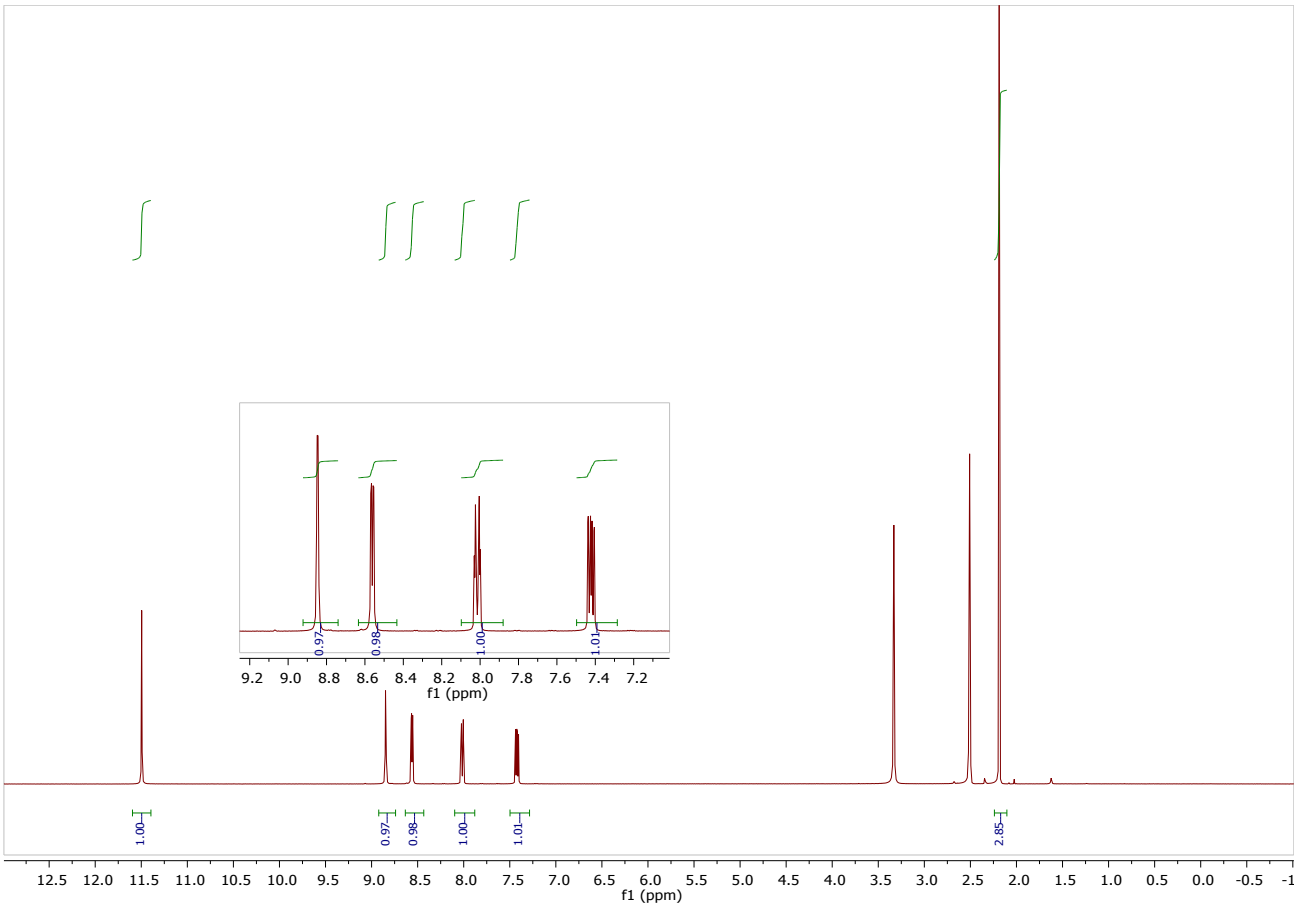
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1.00
1.01
9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2
f1 (ppm)
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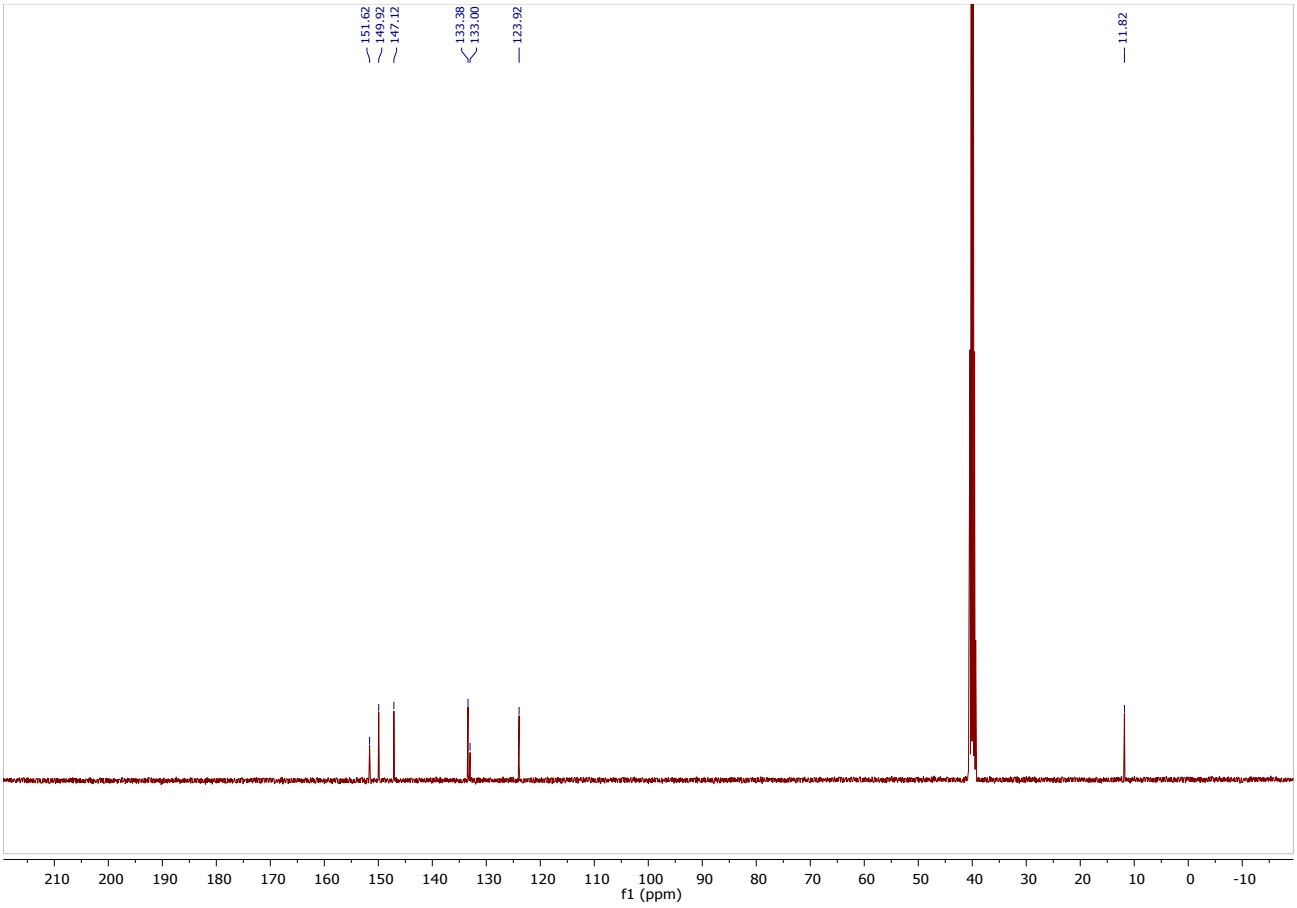
0.97
0.98
1.00
1.01
2.85
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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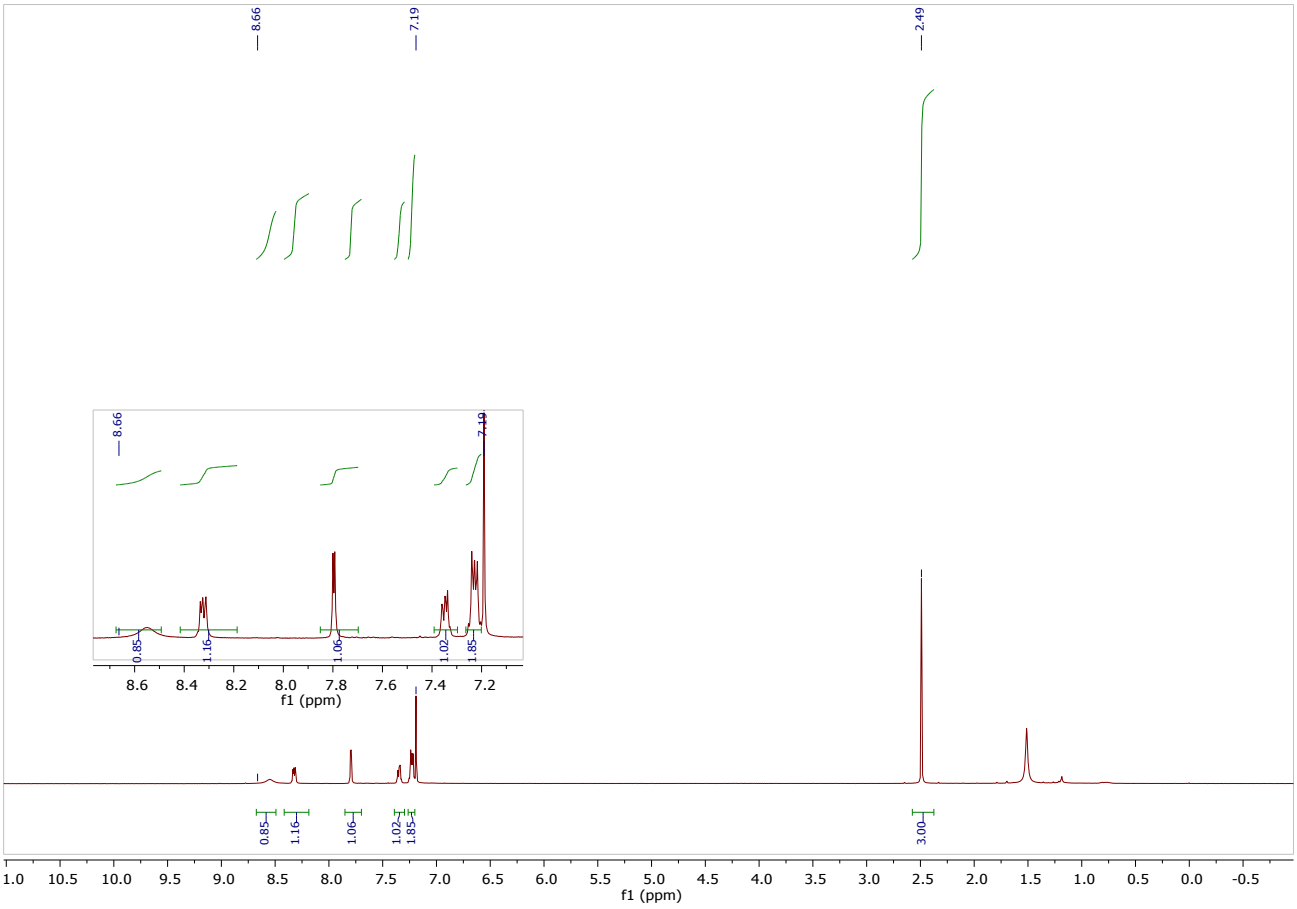
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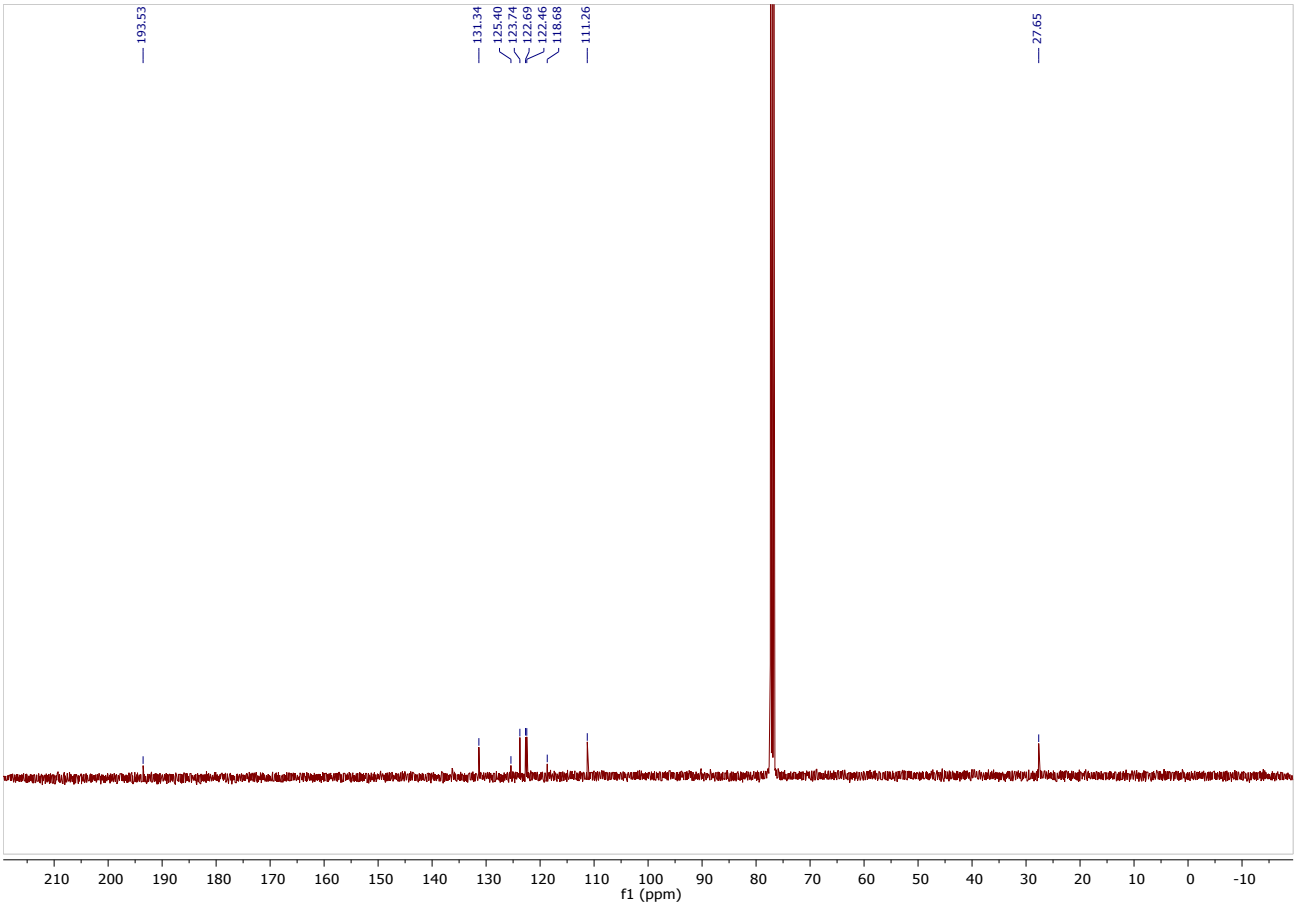
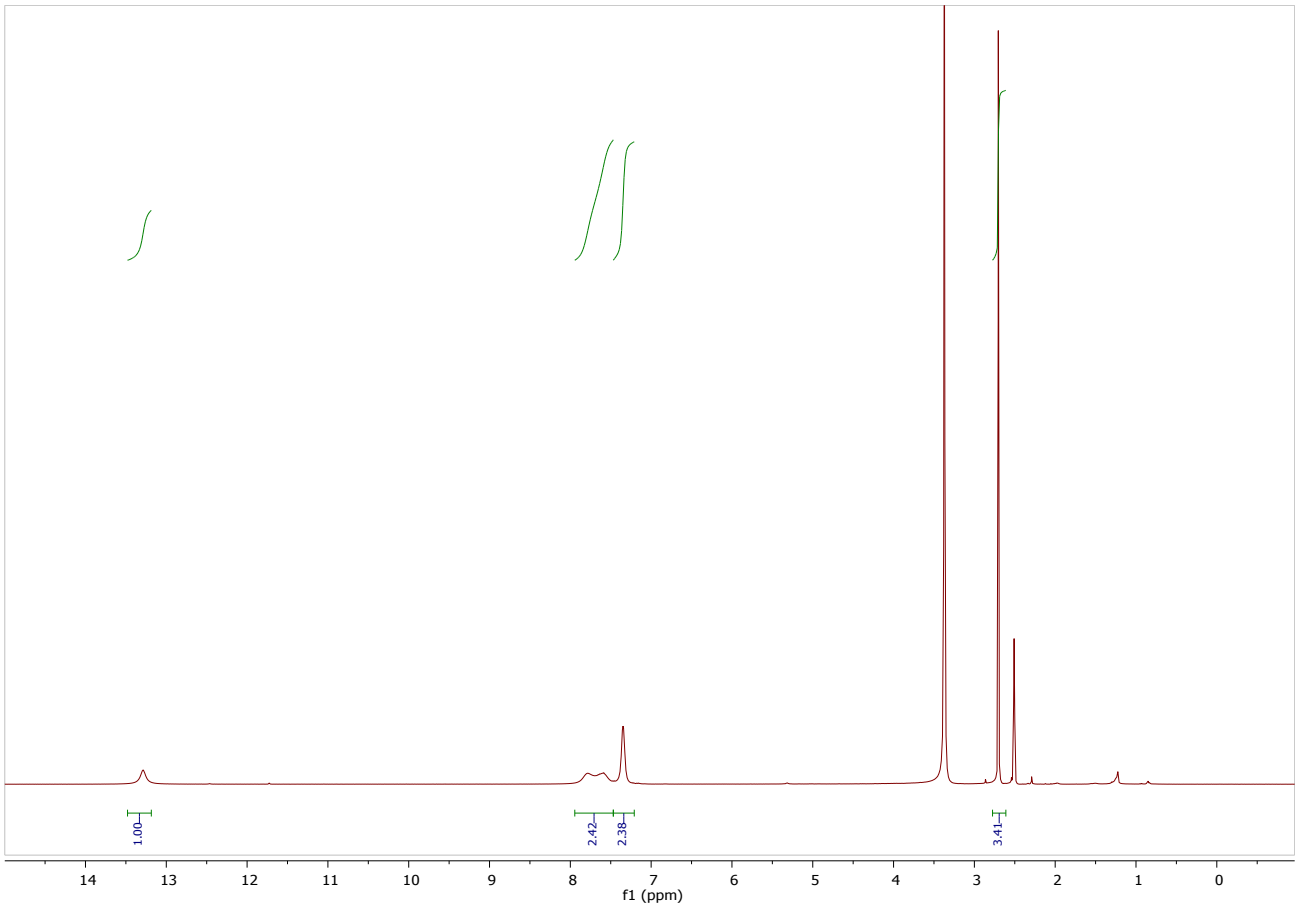
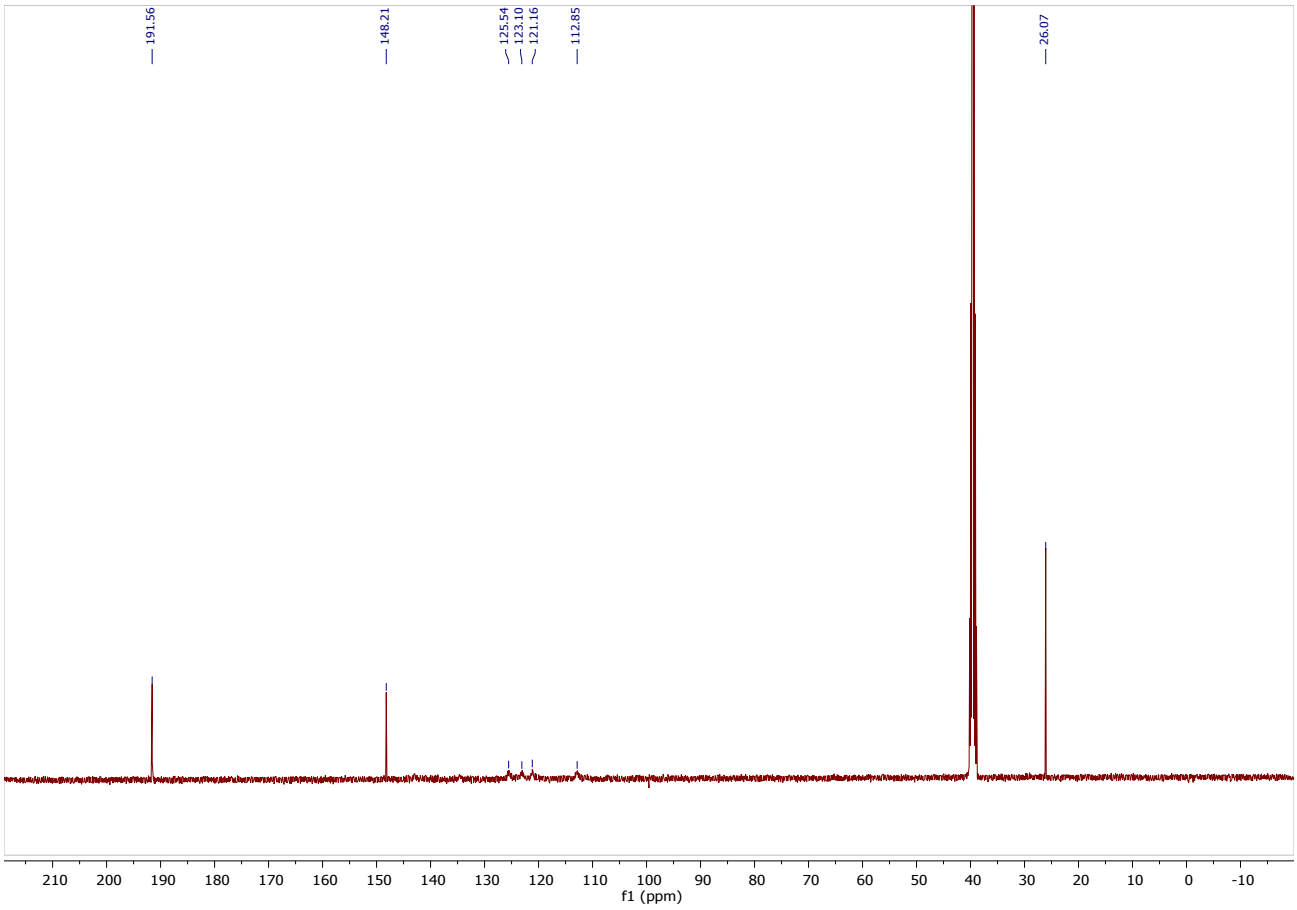
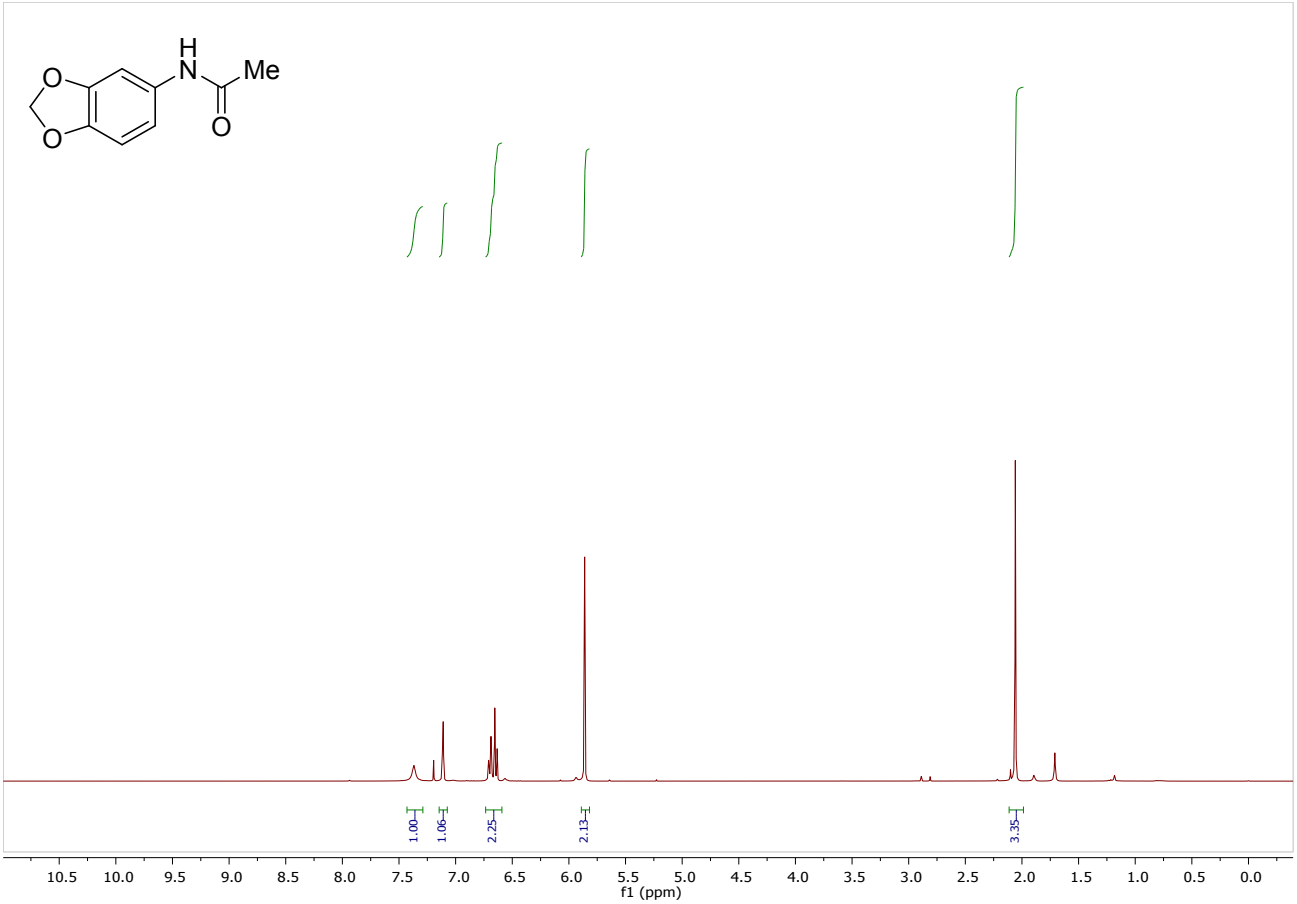
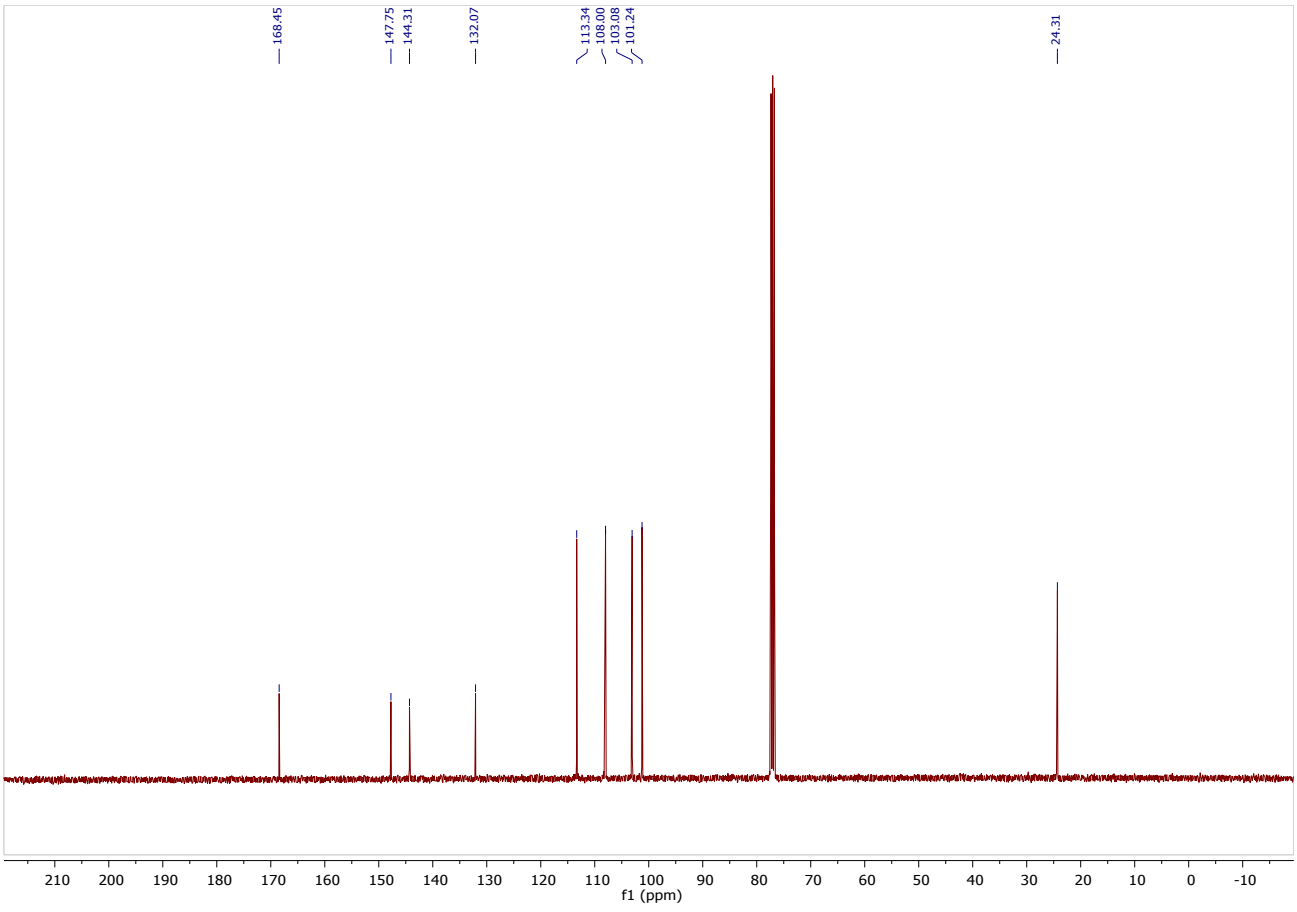
3.00
f1 (ppm)

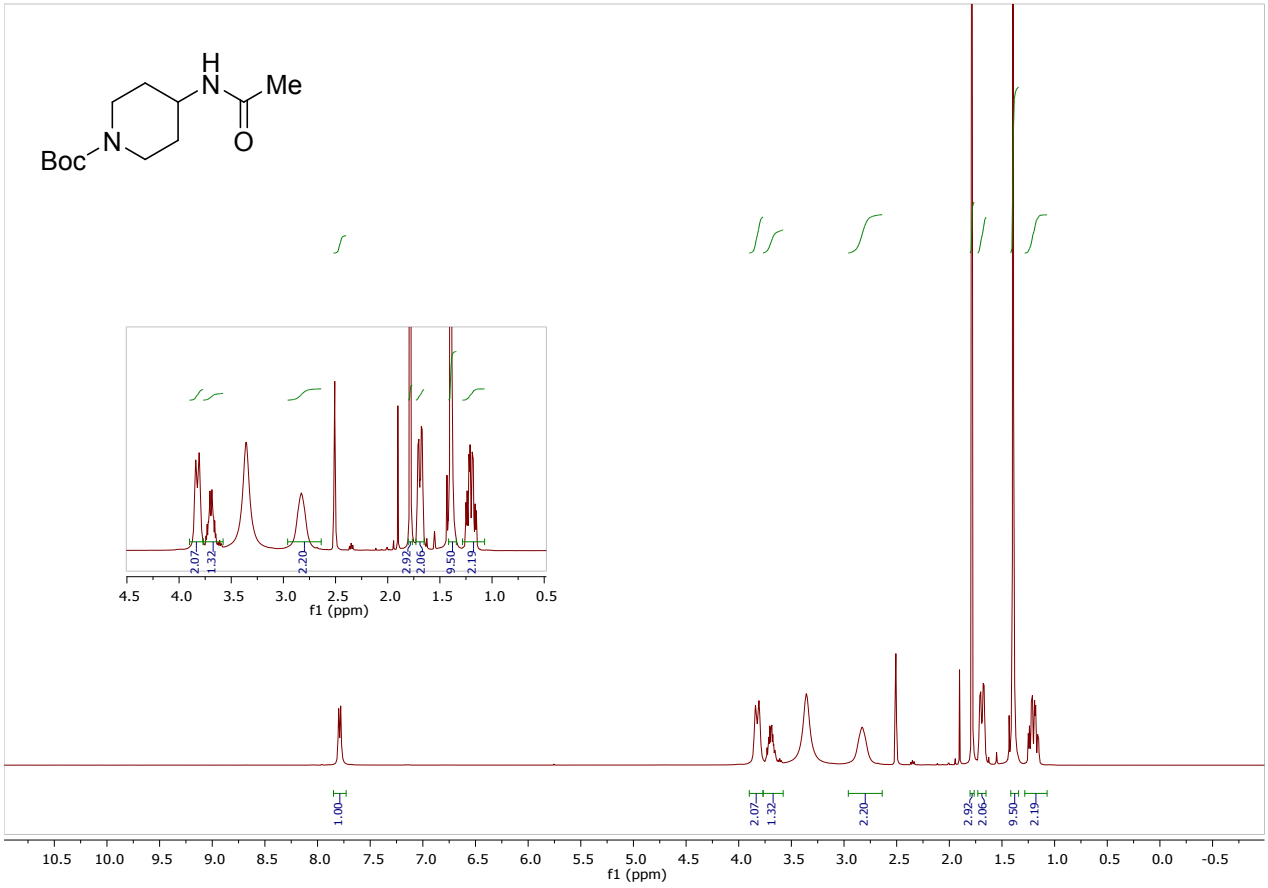

193.53
131.34
125.40
123.74
122.69
122.46
118.68
111.26
27.65
f1 (ppm)

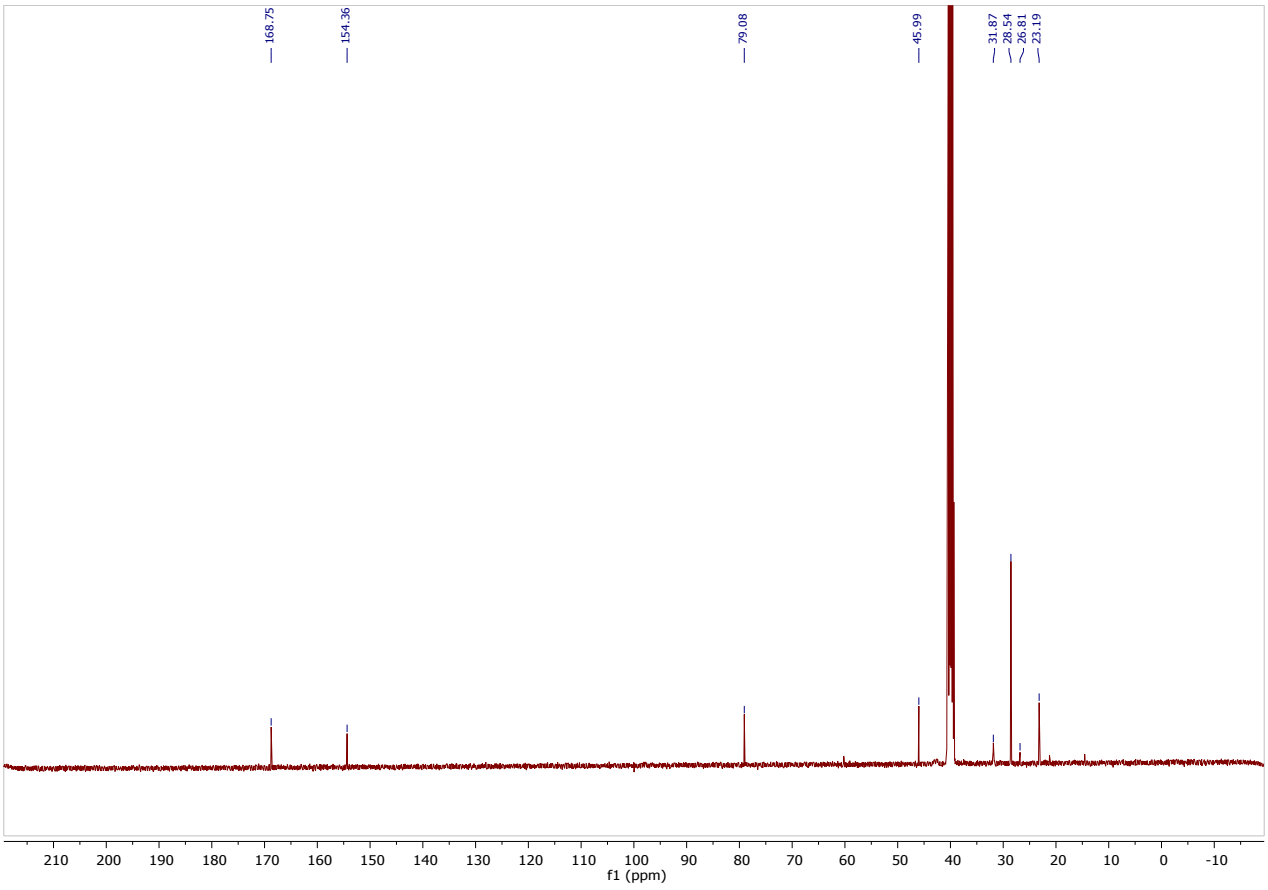

1.00
2.42
2.38
3.41
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

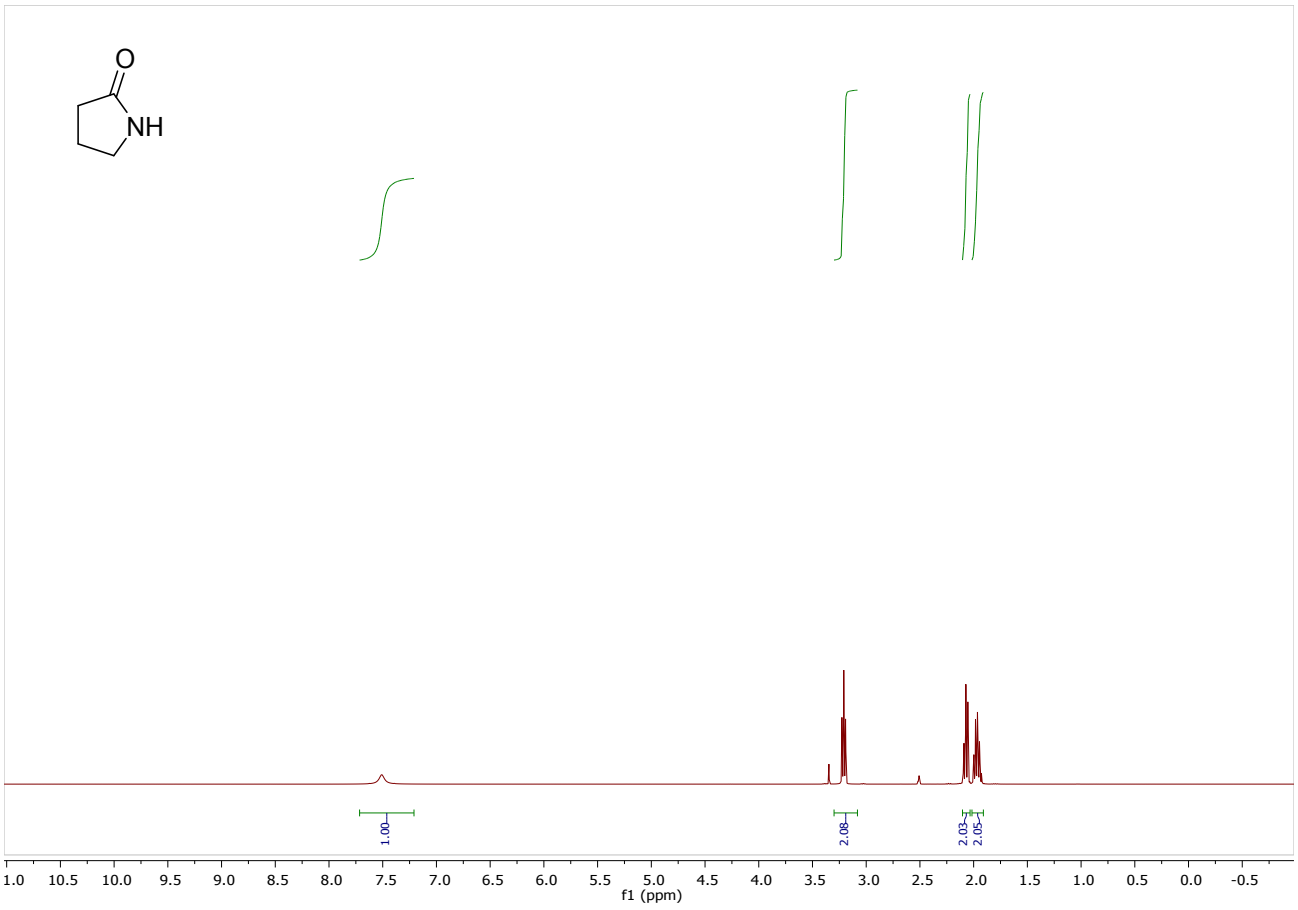

191.56
148.21
125.54
123.10
121.16
112.85
26.07
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

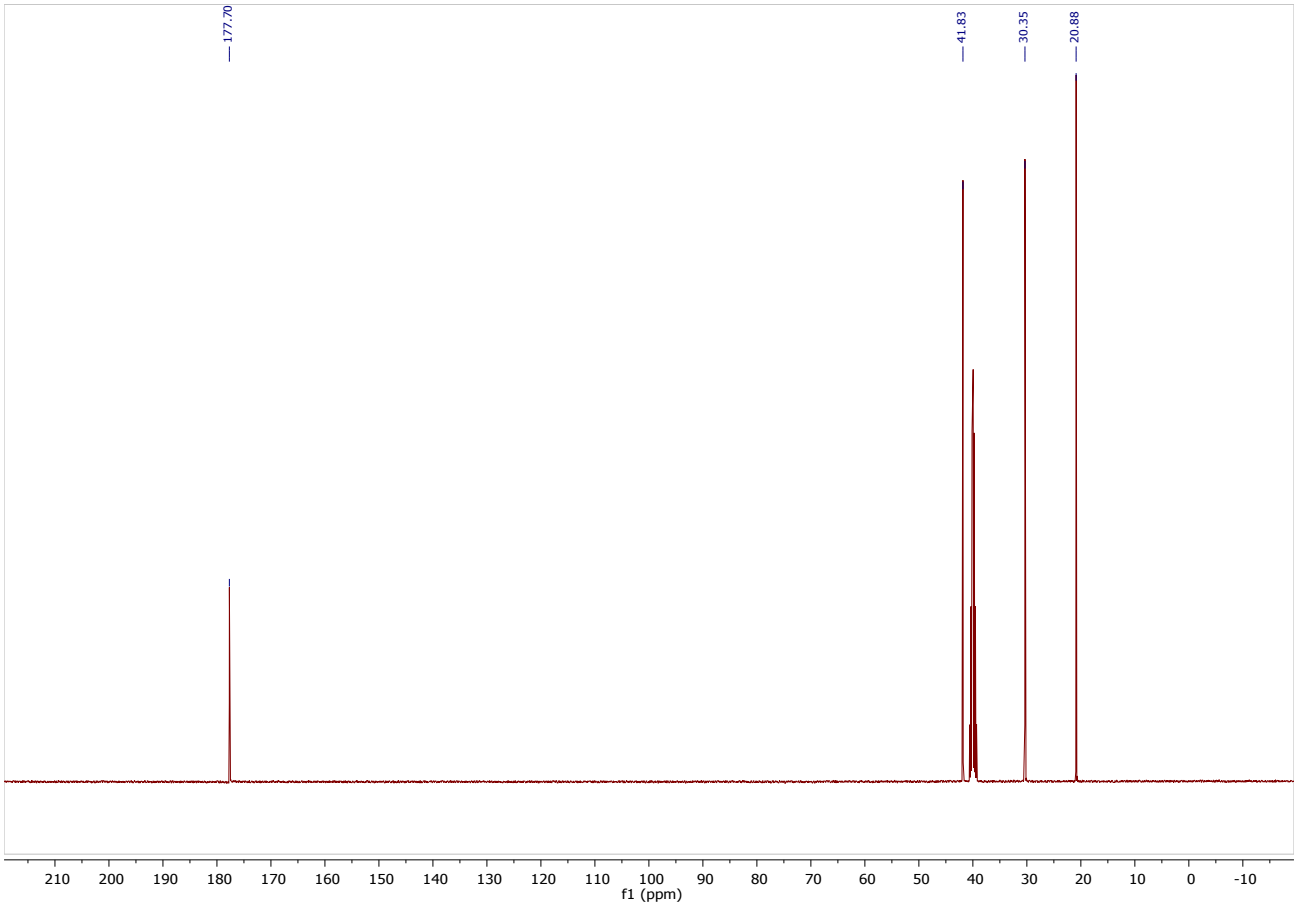

H
N
Me
O
O
O
1.00
1.06
2.25
2.13
3.35
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

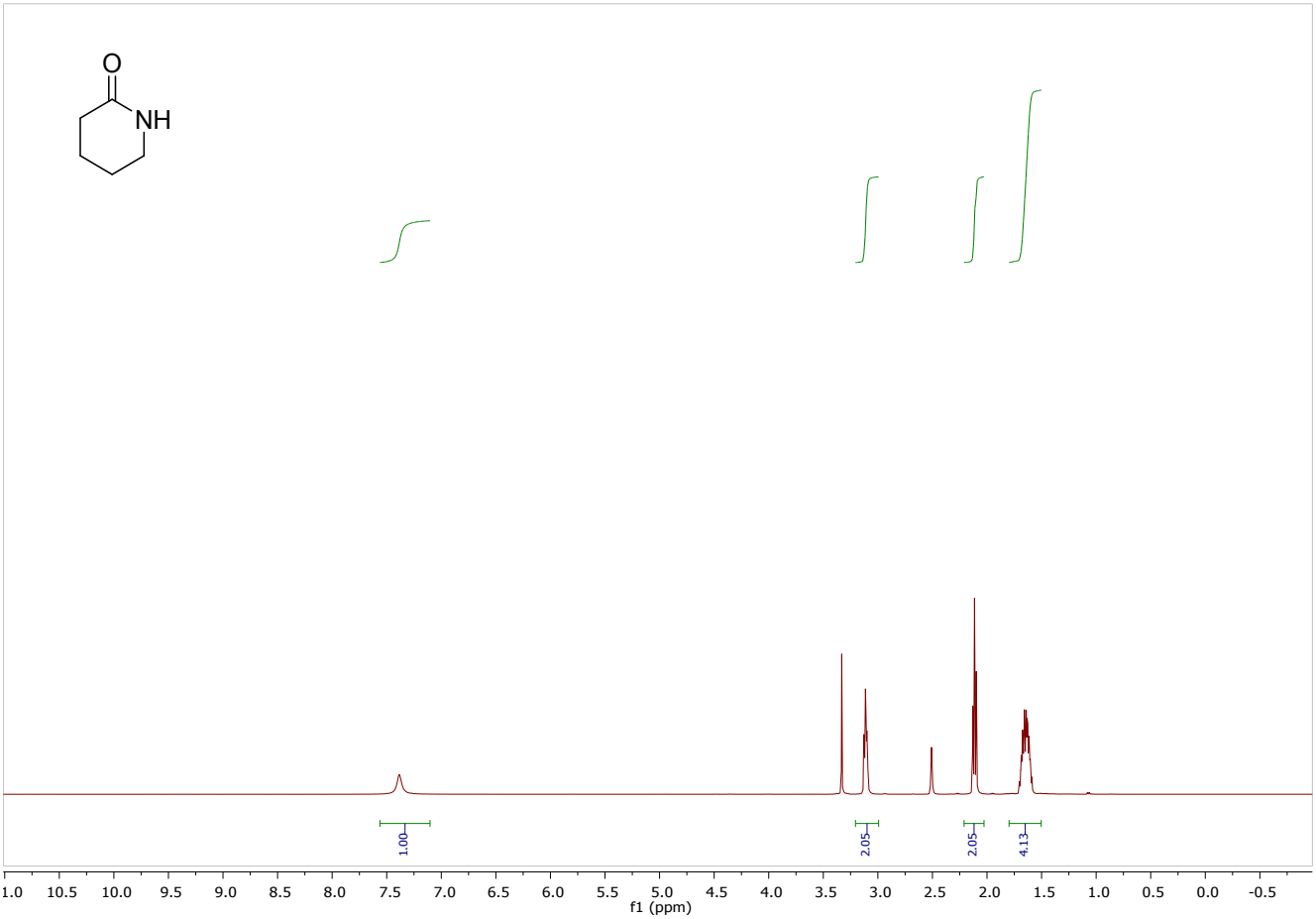

168.45
147.75
144.31
132.07
113.34
108.00
103.08
101.24
24.31
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

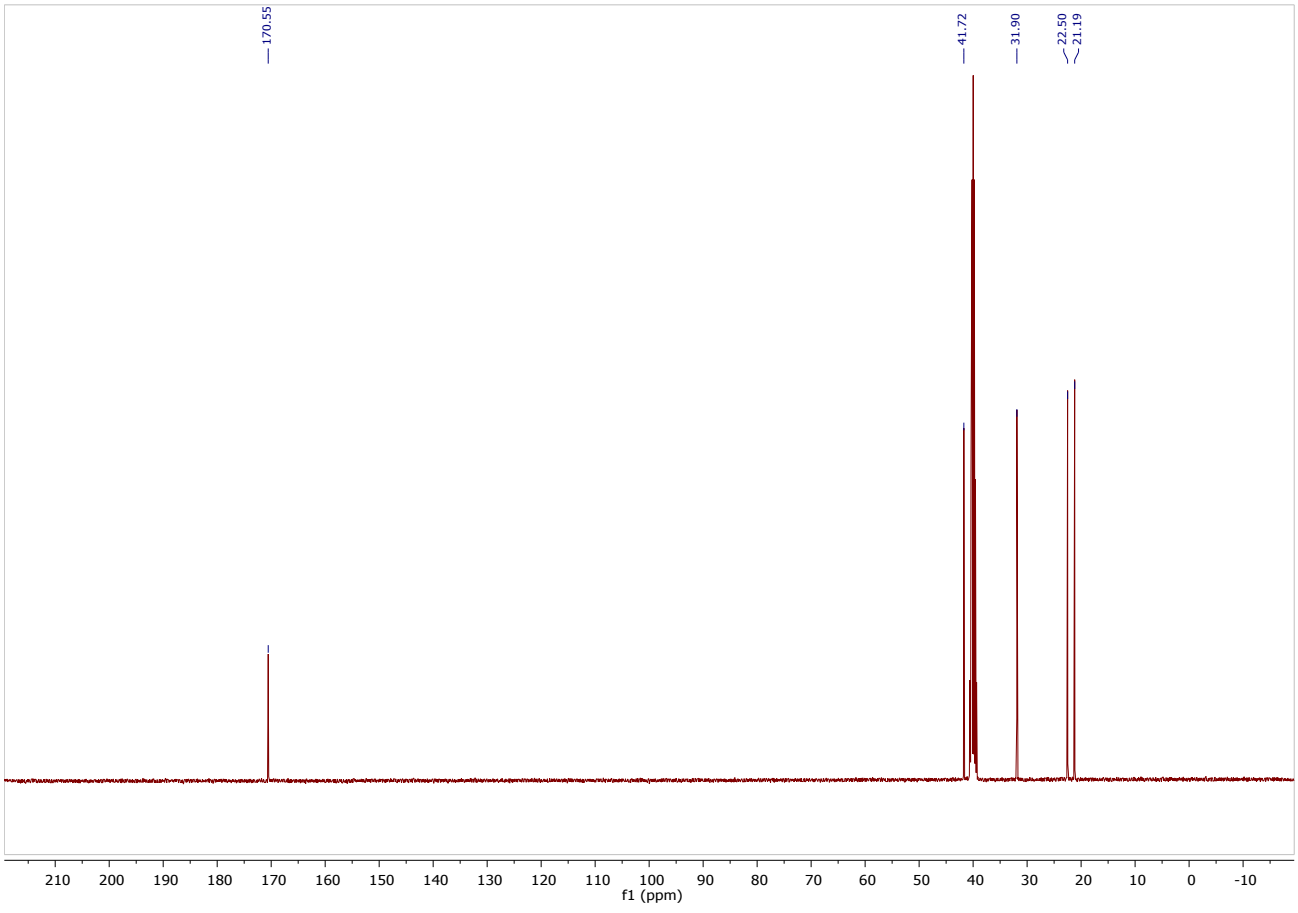

H
N
Me
O
N
Boc
2.07
1.32
2.20
2.92
2.06
9.50
2.19
4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
1.00
2.07
1.32
2.20
2.92
2.06
9.50
2.19
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

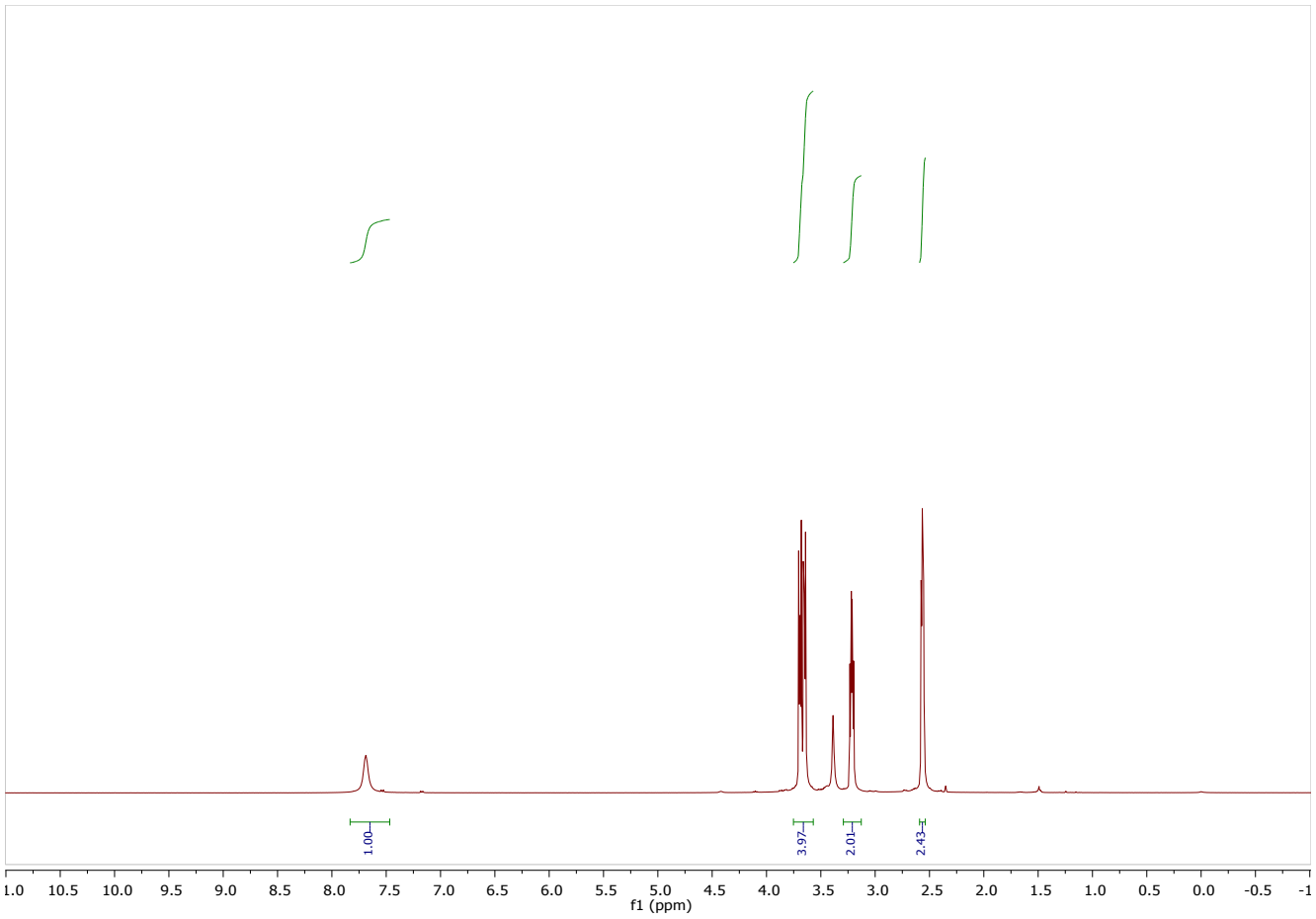

168.75
154.36
79.08
45.99
31.87
28.54
26.81
23.19
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

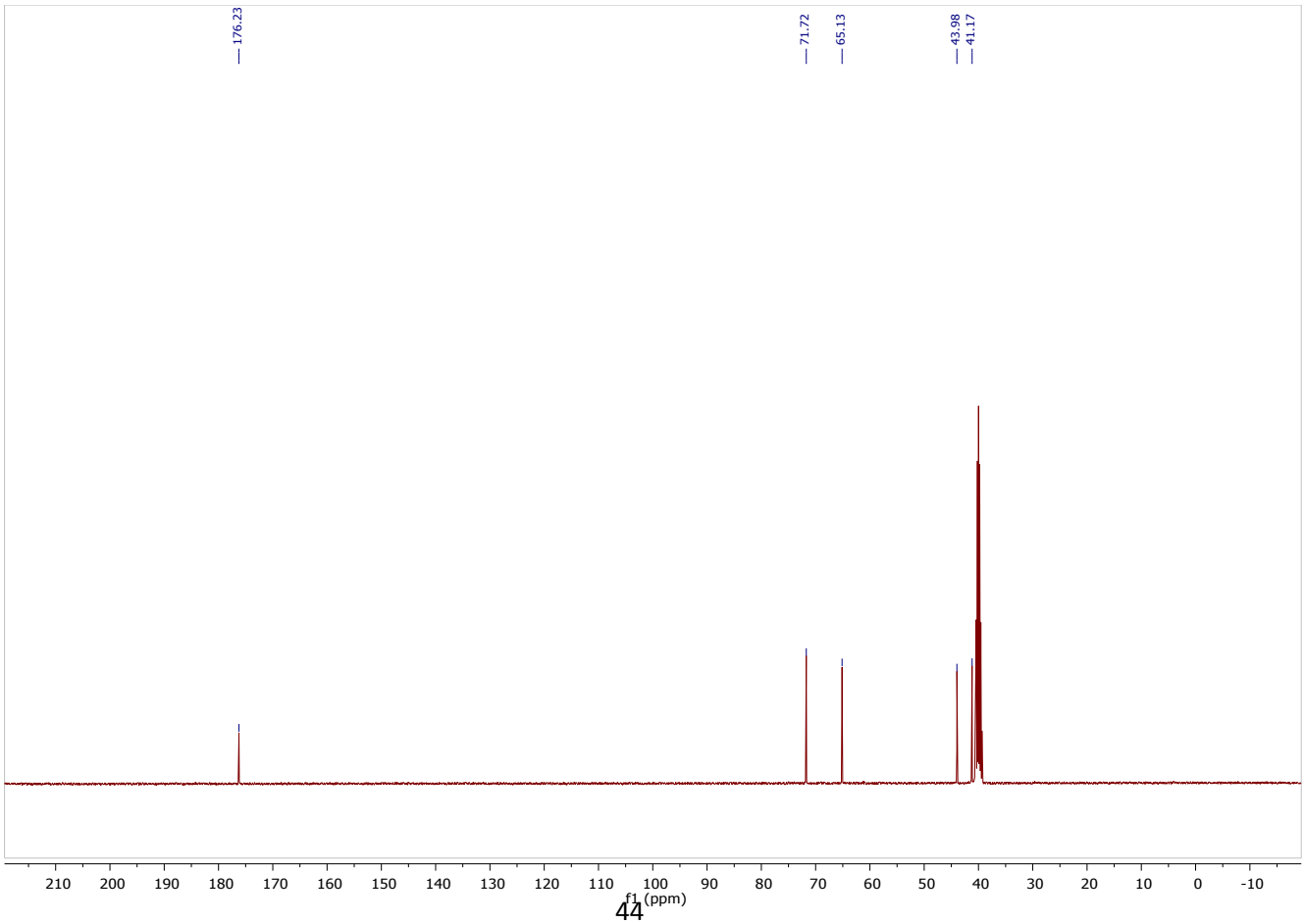

O
NH
1.00
2.08
2.03
2.05
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

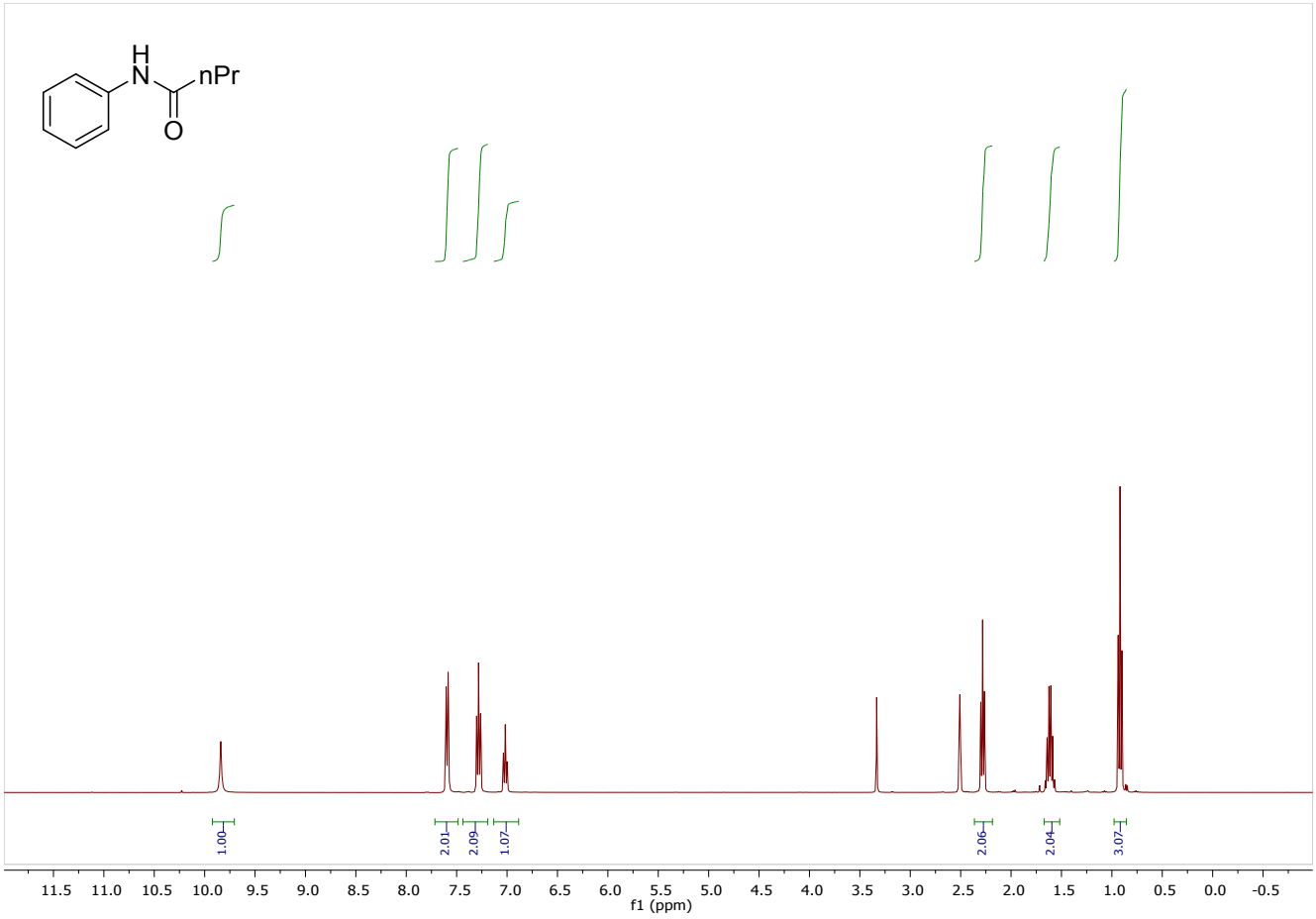

177.70
41.83
30.35
20.88
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

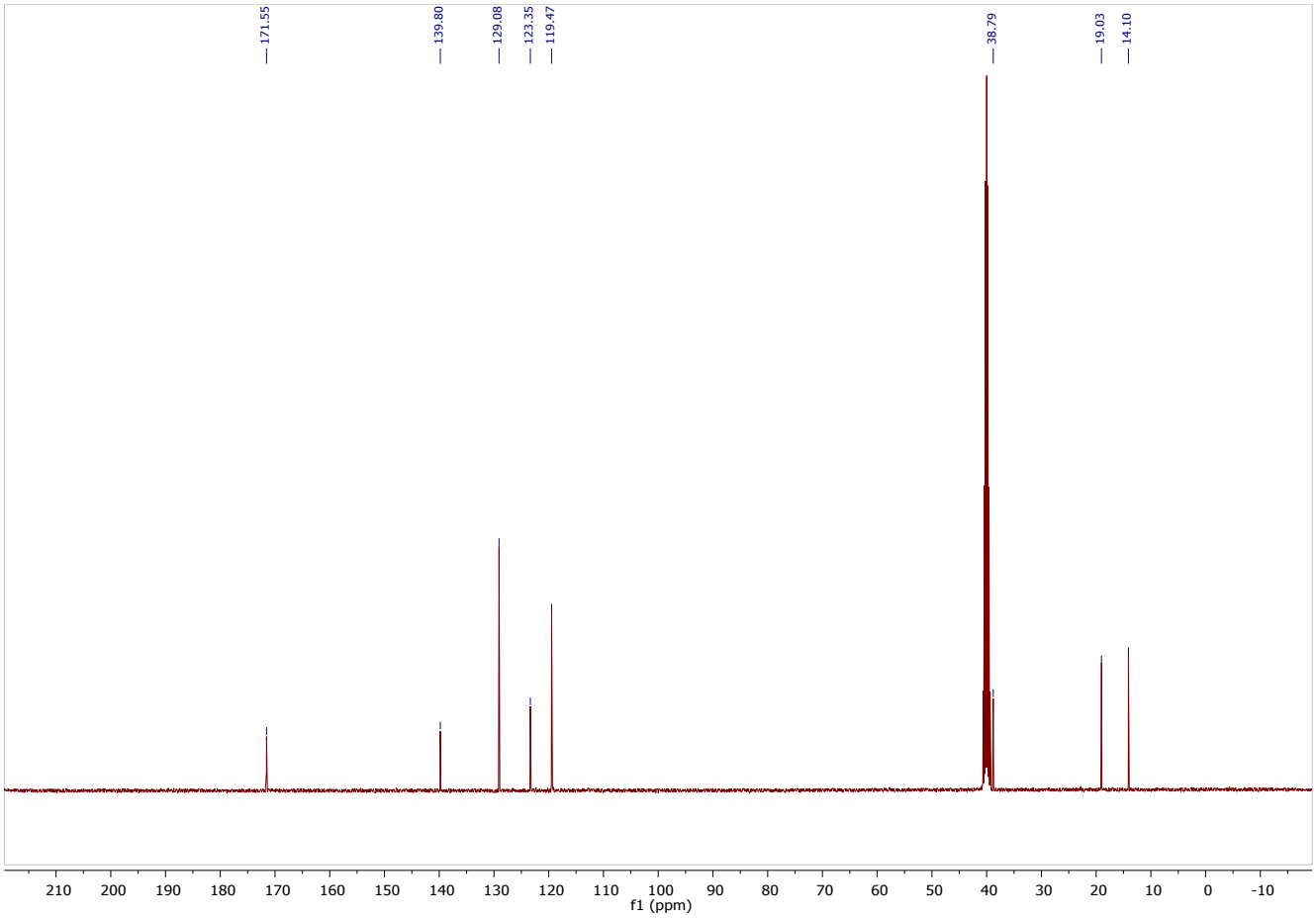

O
NH
1.00
2.05
2.05
4.13
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

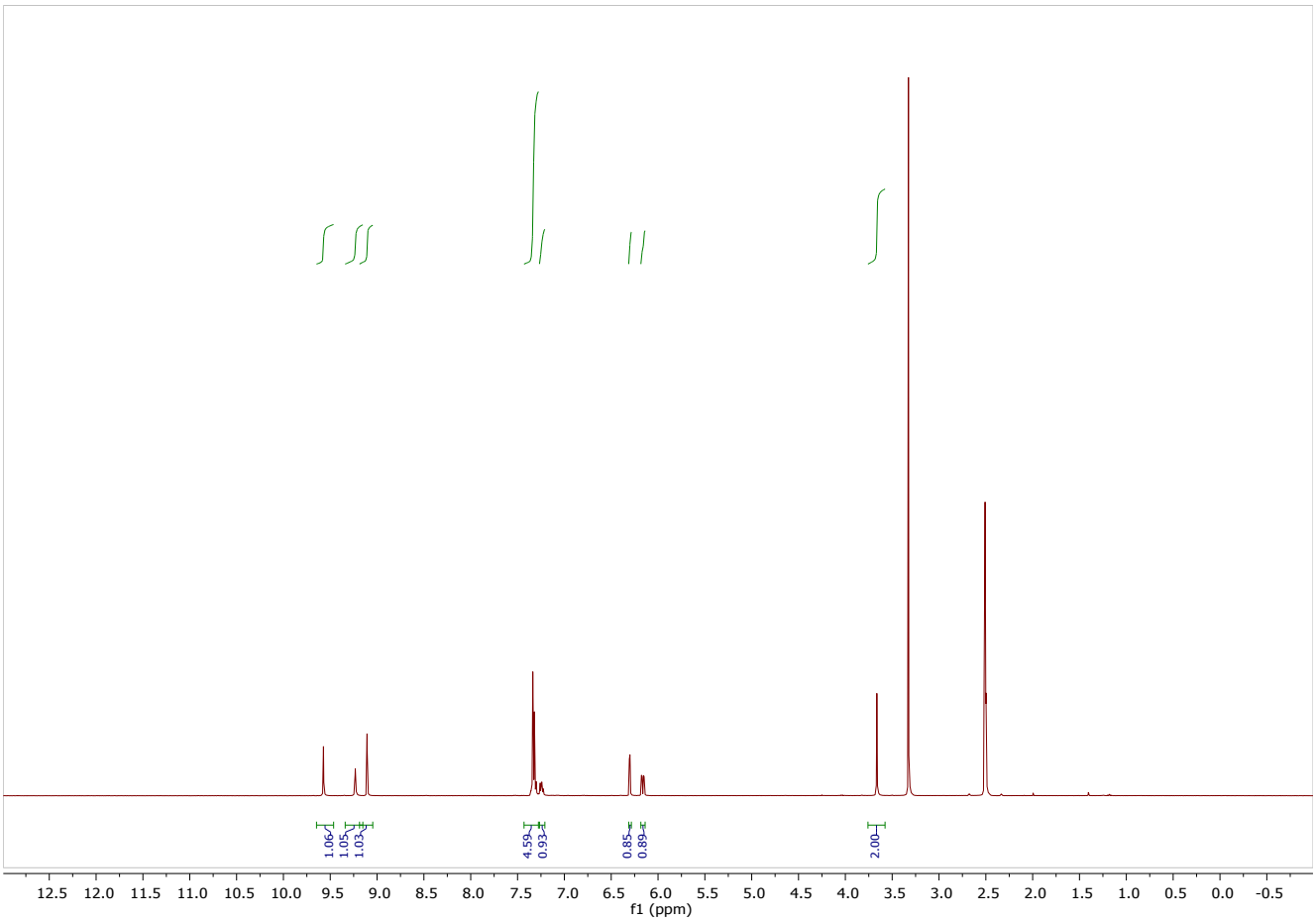

170.55
41.72
31.90
22.50
21.19
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

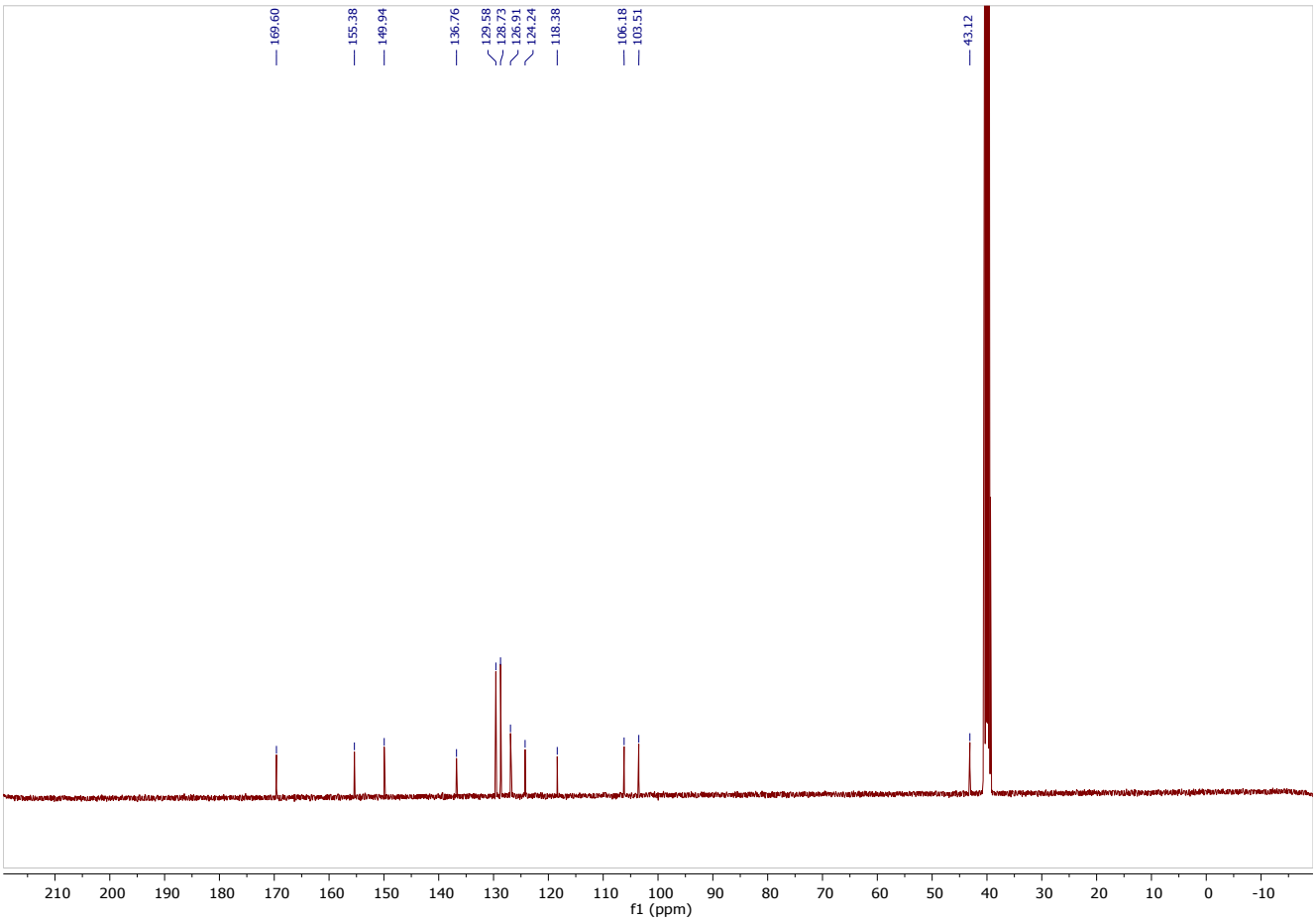

1.00
3.97
2.01
2.43
f1 (ppm)

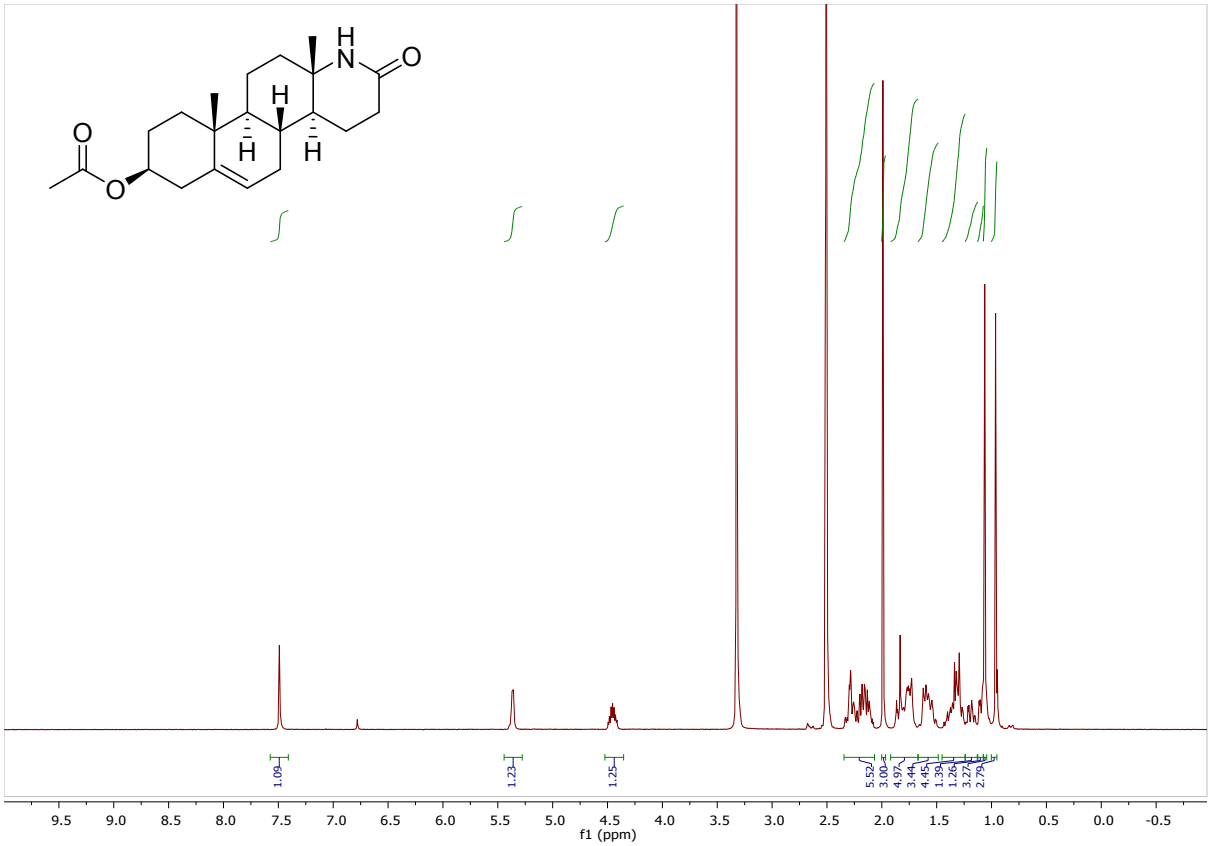

176.23
71.72
65.13
43.98
41.17
f1 (ppm)

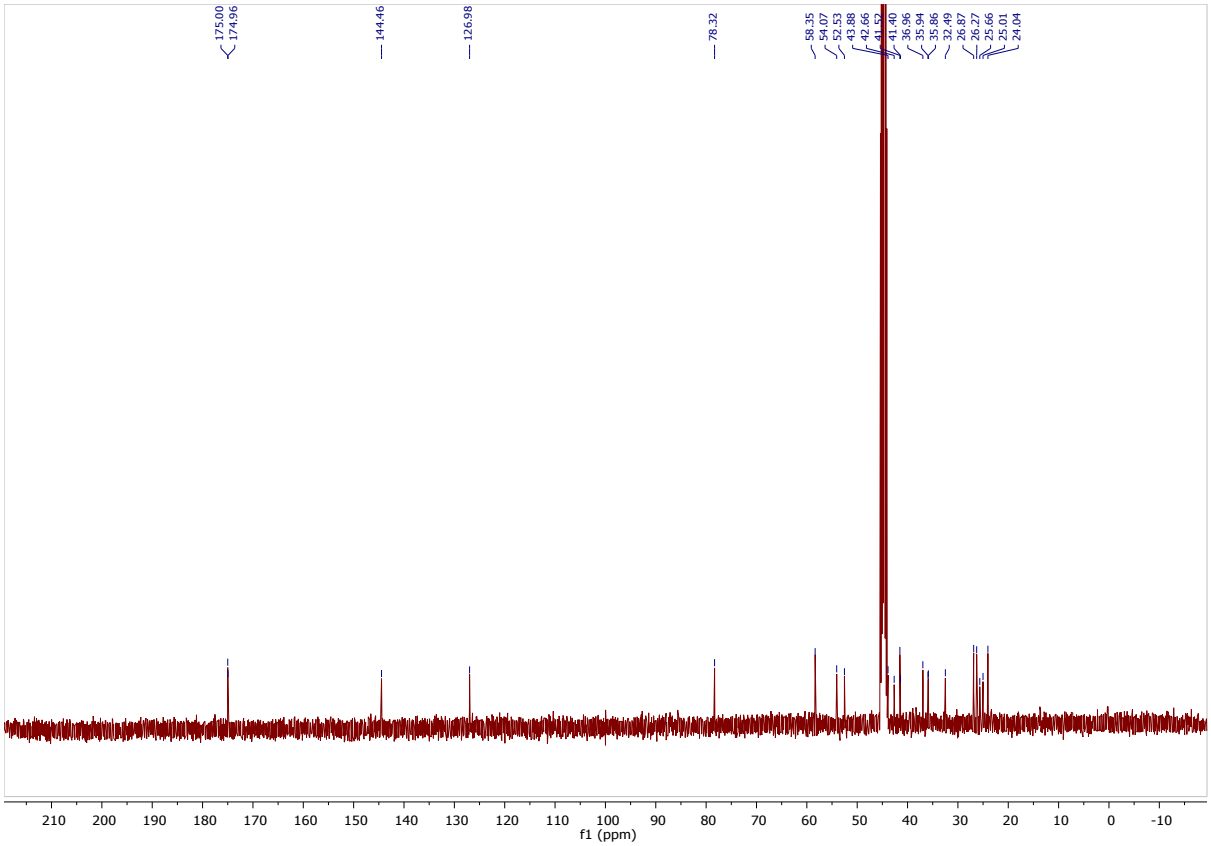

H
N
nPr
O
1.00
2.01
2.09
1.07
2.06
2.04
3.07
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

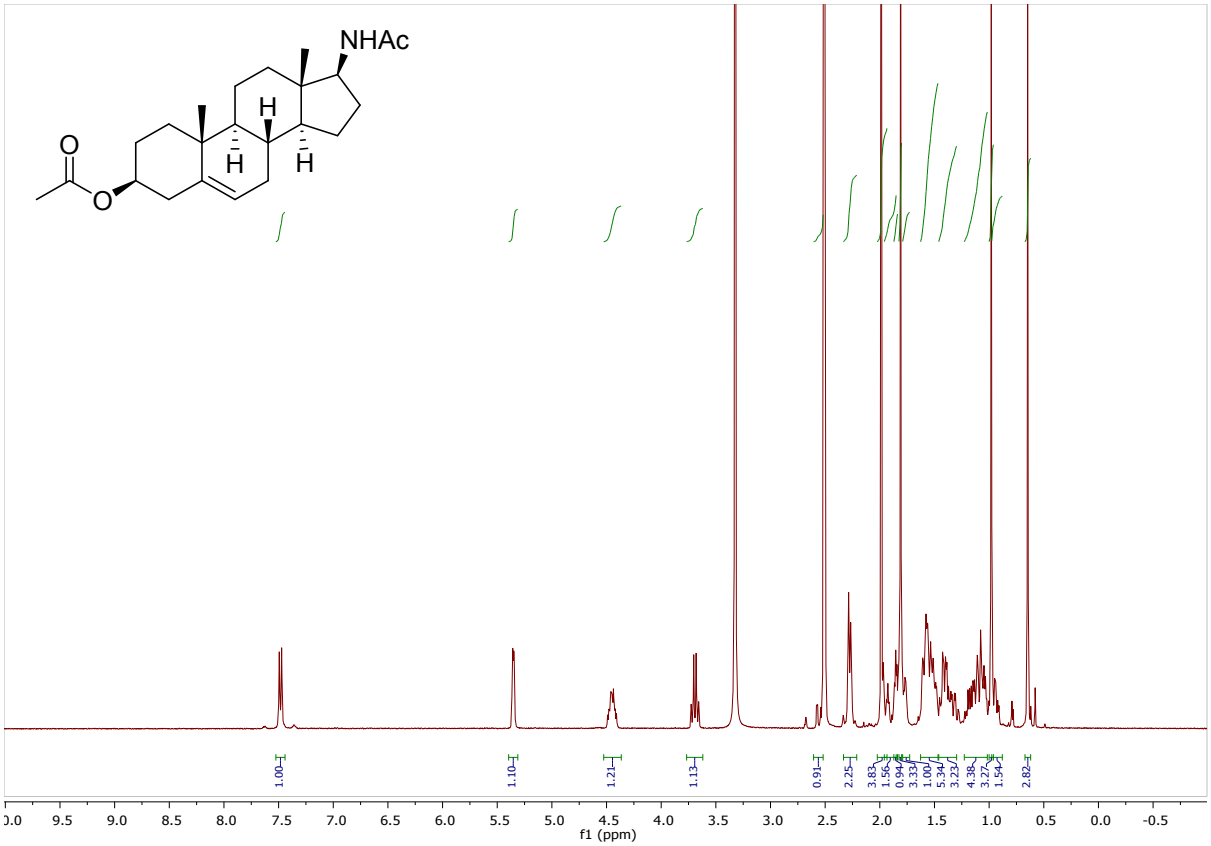

171.55
139.80
129.08
123.35
119.47
38.79
19.03
14.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

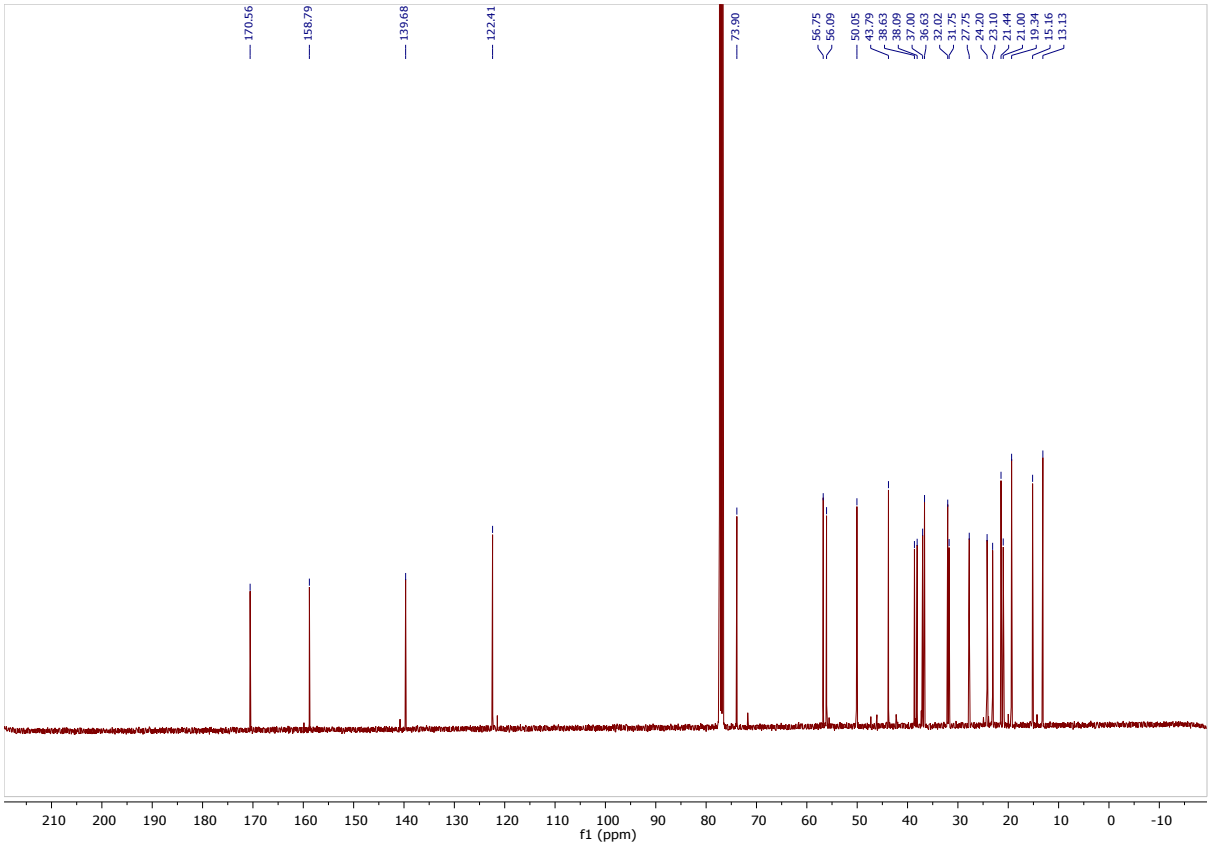

1.06
1.05
1.03
4.59
0.93
0.85
0.89
2.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

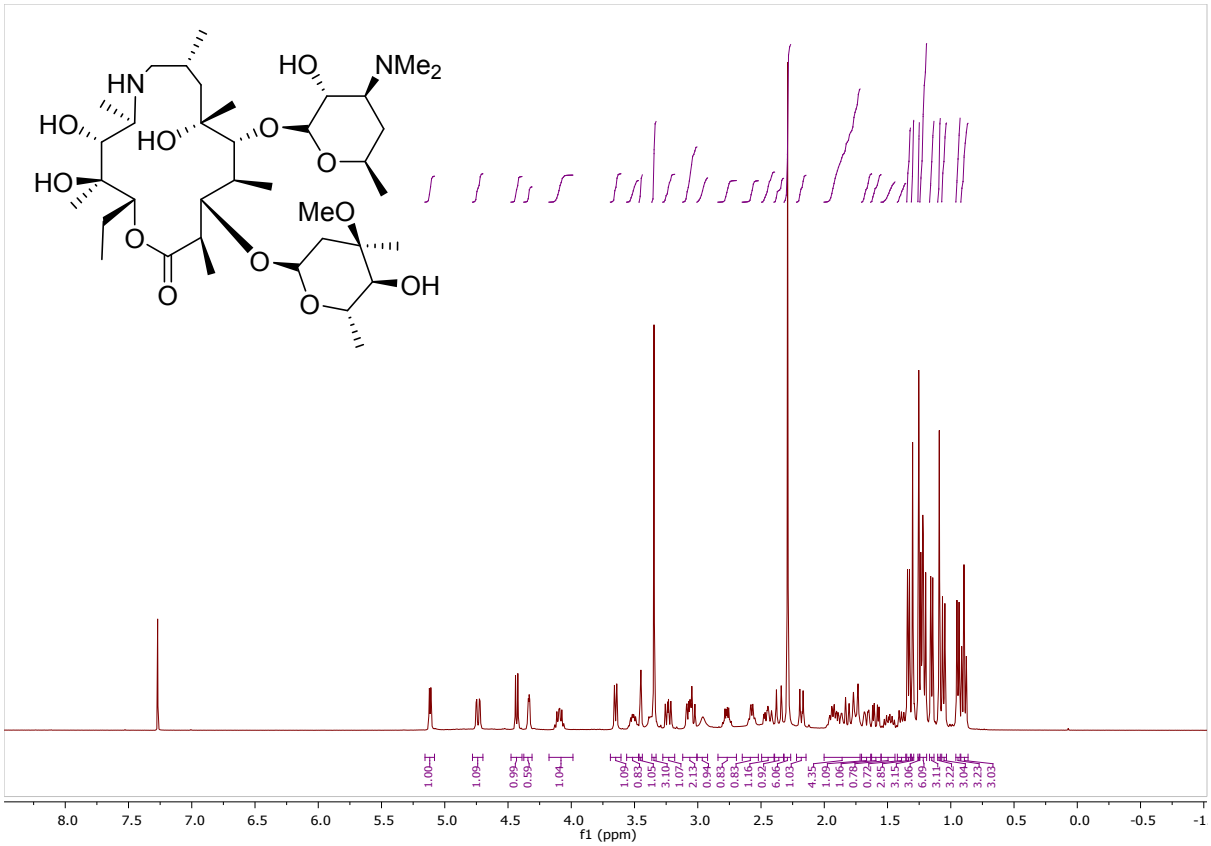

169.60
155.38
149.94
136.76
129.58
128.73
126.91
124.24
118.38
106.18
103.51
43.12
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

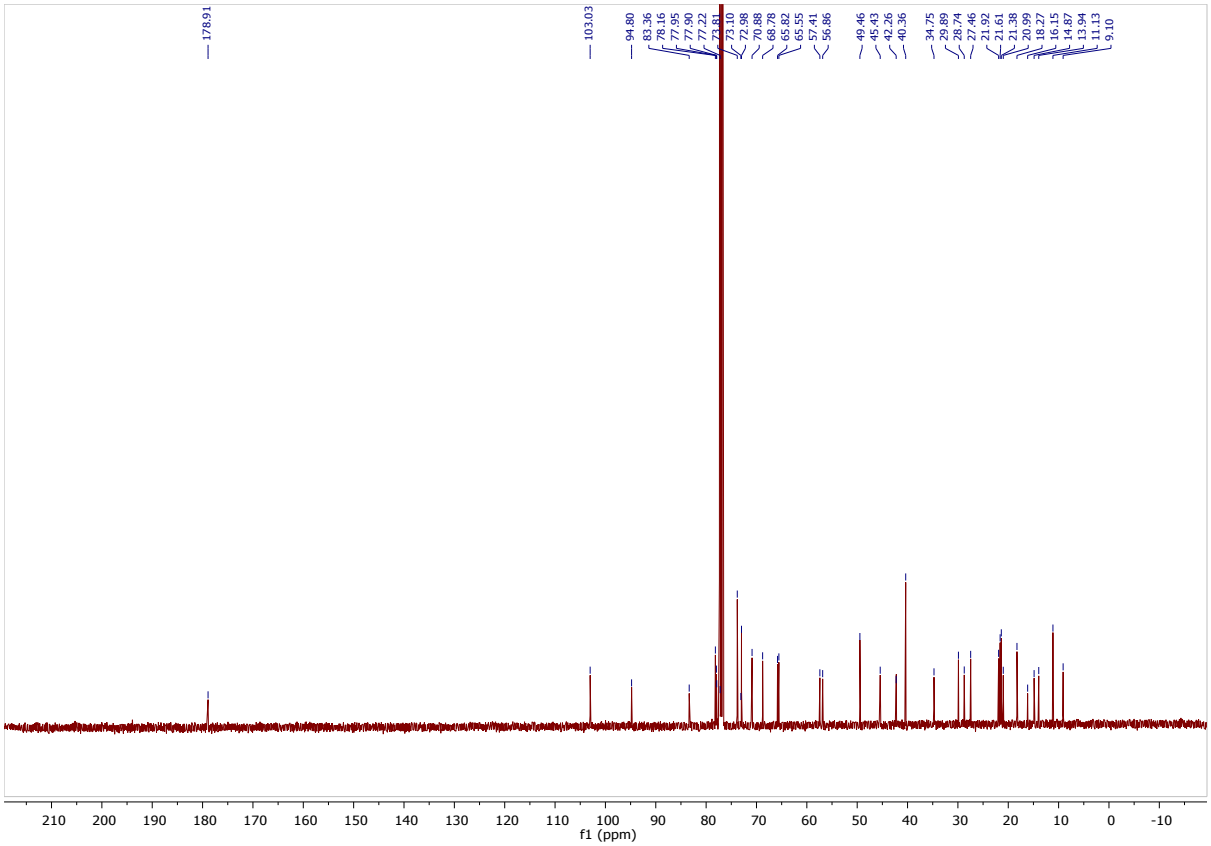

H
N
O
H
H
H
O
O
1.09
1.23
1.25
5.52
3.00
4.97
3.44
4.45
1.39
1.26
3.27
2.79
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

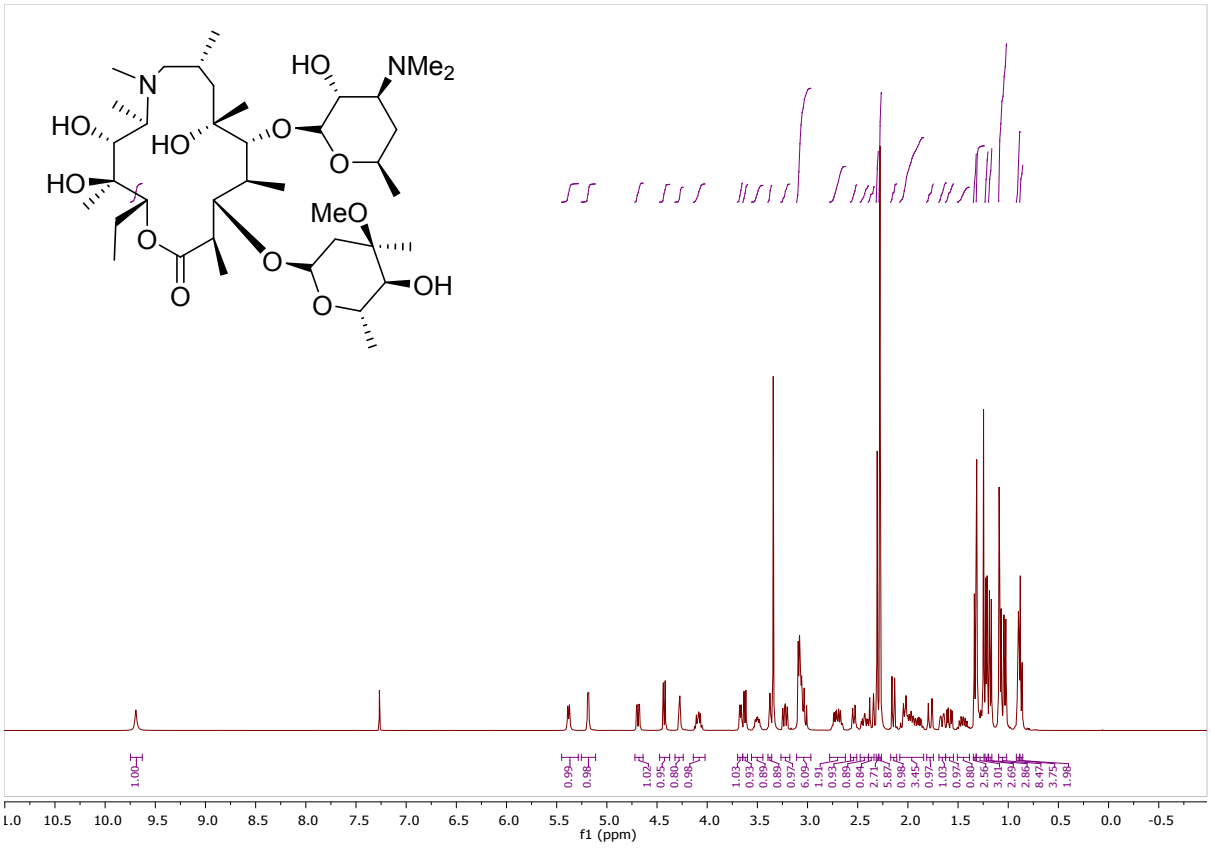

175.00
174.96
144.46
126.98
78.32
58.35
54.07
52.53
43.88
42.66
41.52
41.40
36.96
35.94
35.86
32.49
26.87
26.27
25.66
25.01
24.04
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


NHAc
O
O
H
H
H
1.00
1.10
1.21
1.13
0.91
2.25
3.83
1.56
0.94
3.33
1.00
5.34
3.23
4.38
3.27
1.54
2.82
f1 (ppm)


170.56
158.79
139.68
122.41
73.90
56.75
56.09
50.05
43.79
38.63
38.09
37.00
36.63
32.02
31.75
27.75
24.20
23.10
21.44
21.00
19.34
15.16
13.13
f1 (ppm)


HO
NMe2
HN
HO
HO
HO
O
O
MeO
O
O
O
OH
f1 (ppm)


178.91
103.03
94.80
83.36
78.16
77.95
77.90
77.22
73.81
73.10
72.98
70.88
68.78
65.82
65.55
57.41
56.86
49.46
45.43
42.26
40.36
34.75
29.89
28.74
27.46
21.92
21.61
21.38
20.99
18.27
16.15
14.87
13.94
11.13
9.10
f1 (ppm)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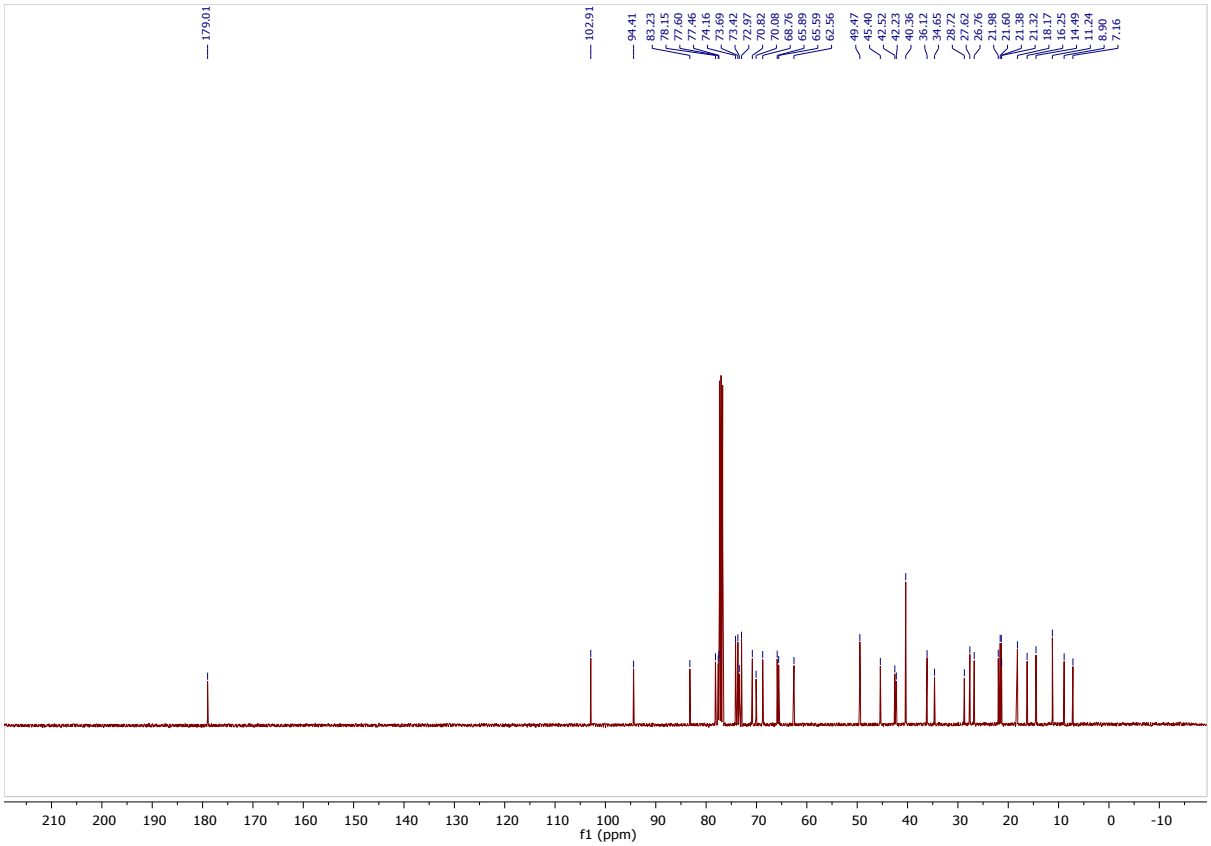
NMe2
N
HO
HO
HO
O
O
MeO
O
O
OH
O
O
1.00
0.99
0.98
1.02
0.95
0.80
0.98
1.03
1.93
0.89
0.89
0.97
6.09
1.91
0.93
0.89
0.84
2.71
5.67
0.98
3.45
0.97
1.03
0.97
0.80
2.56
3.01
2.69
2.86
8.47
3.75
1.98
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


179.01
102.91
94.41
83.23
78.15
77.60
77.46
74.16
73.69
73.42
72.97
70.82
70.08
68.76
65.89
65.59
62.56
49.47
45.40
42.52
42.23
40.36
36.12
34.65
28.72
27.62
26.76
21.98
21.60
21.38
21.32
18.17
16.25
14.49
11.24
8.90
7.16
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)

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