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A base promoted multigram synthesis of aminoisoxazoles: valuable building blocks for drug discovery and peptidomimetics.

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Supplementary Information

Table of Contents

Experimental Section.

General: All reagents were available from Enamine Ltd. Solvents were purified according to standard procedures. When organic solutions were concentrated under reduced pressure, 35–40 °C bath temperature was used. Column chromatography was performed with silica gel 60 (230–400 mesh) as the stationary phase. ^{1}H, ^{13}C NMR spectra were recorded at the NMR spectrometers operating at 400 and 500 ^{1}H frequency (101 and 126 MHz for ^{13}C experiments). NMR chemical shifts are reported in ppm, in the δ scale and are referenced using residual NMR solvent peaks at 7.26 and 77.16 ppm for ^{1}H and ^{13}C in $CDCl_3$, 2.50 and 39.52 ppm for ^{1}H and ^{13}C in DMSO-d_6, for 4.79 and ^{1}H in D_2O. For peptides NMR analysis was performed in 5 mM peptide solutions in CD_3OD at 700 MHz (^{1}H frequency) spectrometer. ^{1}H NMR spectra were recorded 25 min after the peptides were dissolved (fresh) and therefore contained few of the non-exchanged amide resonances. The ^{1}H NMR spectra were in addition recorded after overnight measurements when the NH-to-ND exchange was already completed. ^{1}H HOHAHA (dipsi2 of 60 ms) and ROESY (spin-lock 300 ms) spectra were recorded to complete the assignment of the ^{1}H resonances. ^{13}C {^{1}H} dept45 and ^{1}H {^{13}C} HSQC experiments were performed in order to assign accompanied ^{13}C resonances. The following abbreviations are used in reported NMR data: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), brs (broad singlet). Coupling constants (J) are in Hz. Spectra are reported as follows: chemical shift (δ, ppm), multiplicity, integration, coupling constants (Hz). Measured melting points are uncorrected. Boiling points were measured at 0.8 mm Hg unless otherwise specified herein. LC-MS data were acquired on Agilent 1200 HPLC system equipped with DAD/ELSD/LCMS-6120 diode-matrix and mass-selective detector, column: Poroshell 120 SB-C18, 4.6 mm × 30 mm. Eluent, A, acetonitrile − water with 0.1 % of FA (99 : 1); B, water with 0.1% of FA. Optical rotations were measured on polarimeter in methanol using 1-dm cell; optical rotation values are given in 10^{-1} deg cm^2 g^{-1}; concentrations (c) are given in mmol/L, wavelength 589 nm at 20 °C. The enantiomeric excess and retention time (t_R) was determined for major signal by HPLCs: Daicel CHIRALPACK IA, 5 μm, 4.6×250 mm, Daicel CHIRALPACK IB, 5 μm, 4.6×250 mm, Daicel CHIRALPACK OJ-H, 5 μm, 4.6×250 mm, Daicel CHIRALPACK AS-H, 5 μm, 4.6×250 mm chiral columns, injection volume 0.1 μL, eluent (hexanes : 2-propanol). Solid compounds were recrystallized from acetonitrile unless other is specified.

General methodology for the reduction of amino acids

tert-Butyl 2-(hydroxymethyl)azetidine-1-carboxylate

A 250 mL round bottomed flask was charged with a magnetic stirrer, Boc-azetidine carboxylic acid (37.3 g, 185.4 mmol) and THF (120 mL). The flask was placed in an ice cooling bath and to the vigorously stirred solution $NaBH_4$ (11.3 g, 298.7 mmol) was added portionwise over 30 min (Caution: formation of foam!). Next, BF_3•Et_2O was added dropwise, the cooling bath was removed and the resulting mixture was stirred overnight. Then, the reaction mixture was poured into 2% $NaOH_{(aq)}$ solution (240 mL). From the resulting mixture THF was evaporated and the product was extracted with EtOAc (4×100 mL). Combined organic phases were washed with 10% $K_2CO_{3(aq)}$ solution (2×50 mL) and brine (1×50 mL). Organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The resulting oily mixture was purified *via* distillation (115-117 °C) yielding title compound as a colorless oil (93%, 32.3 g). The corresponding analogues bearing Boc-group for glycinol-, (R)- and (S)-alaninol-, (R)- and (S)-prolinol- and 4-piperidinol moieties were synthesized by the same procedure and spectral data are in agreement with the previously reported in the literature.[1]

General methodology for the oxidation of alcohols

tert-Butyl 3-formylazetidine-1-carboxylate

A 2 L round bottomed flask was charged with a magnetic stirrer, *tert*-butyl 3-(hydroxymethyl)azetidine-1-carboxylate (52.0 g, 277.7 mmol) and dry CH_2Cl_2 (600 mL) under argon atmosphere. Triethylamine (122 mL, 875 mmol) and DMSO (100 mL) were added and the reaction mixture was cooled down to 0 °C. To the vigorously stirred reaction mixture Py•SO_3 (132.6 g, 833 mmol) was added portionwise while the temperature was maintained at 0 °C. Then, the reaction mixture was allowed to warm up to the ambient temperature and the stirring was continued for additional 1 h. Next, the reaction mixture was poured into a brine: ice mixture (100 mL: 100 g). DCM was evaporated and the aqueous phase was extracted with EtOAc (3×100 mL). Combined organic phases were washed with brine (1×100 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated furnishing the oily product which was further purified by distillation *in vacuo* (80-83 °C) yielding the title compound (76%, 39.1 g). The

corresponding analogues bearing Boc-group for (R)- and (S)-alaninal-, (R)- and (S)-prolinal- and piperidinal moieties were synthesized by the same procedure and spectral data are in agreement with the previously reported in the literature.[2]

General methodology for the synthesis of oximes

tert-Butyl 2-((hydroxyimino)methyl)azetidine-1-carboxylate

A 50 mL round bottomed flask was charged with a magnetic stirrer and tert-butyl 3-formylazetidine-1-carboxylate (3.7 g, 20 mmol). Hydroxylamine hydrochloride (1.5 g, 22 mmol), $NaHCO_3$ (2.2 g, 26 mmol) and THF or MeOH (20 mL) were added at 0 °C. Then, the reaction mixture was stirred at ambient temperature overnight. When the reaction was complete (^{1}H NMR control) the reaction mixture was concentrated washed with brine (2×10 mL) and the product was extracted with EtOAc (4×20 mL). Organic phase was dried over Na_2SO_4. The resulting mixture was filtered through a silica pad and the solution was concentrated furnishing the corresponding oxime (95%, 3.8 g) as an yellow
oil.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.75, 11.75 (two s, 1H, *OH mixture of syn- and anty-isomers*), 7.53-7.51, 7.00-6.99 (two m, 1H, *CH-imine mixture of syn- and anty- isomers*), 4.06 (br, 2H, *CH_2-azetidine*), 3.90 (m, 2H, *CH_2-azetidine*), 3.72-3.67 (m, 1H, *CH-azetidine*), 1.38 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 155.4, 137.0, 78.9, 51.6, 33.8, 28.0.

The corresponding analogues bearing Boc-group (R) and (S)-Ala-, (R)- and (S)-Pro- and 4-Pip moieties were synthesized by the same procedure and spectral data are in agreement with the previously reported in the literature.[3]

Due low stability of Boc-glycinal it was synthesized by the same procedure as tert-Butyl 3-formylazetidine-1-carboxylate, but after completion of the reaction (NMR control) hydroxylamine hydrochloride (1.1 eq) was added in to the reaction mixture followed by addition of saturated aqueous $NaHCO_3$ (1.2 eq).

General methodology for the synthesis of chloroximes

***tert-butyl (E)-3-(chloro(hydroxyimino)methyl)azetidine-1-carboxylate* (6)**

A three-necked 100 mL reactor was charged with a magnetic stirrer, tert-butyl [(Z, E) -3-((hydroxyimino)methyl)]azetidine-1-carboxylate (2.7 g, 13.5 mmol) and DMF (19 mL). To the vigorously stirred solution catalytic amount of 10 mol% HCl in dioxane (0.5 mL) was added at 0 °C. Next, NCS (1.93 g, 14.4 mmol) was added portionwise within 30 min, while the temperature of the reaction mixture was kept below 0 °C. Then, the reaction mixture was stirred for additional 3 h at ambient temperature. After the completion of the reaction (^{1}H NMR control) the reaction mixture was diluted with water (50 mL) and the product was extracted with EtOAc (5×10 mL). Combined organic phases were washed with a water: brine mixture [(1: 1,5) ×10 mL], brine (3×10 mL) and then dried over anhydrous Na_2SO_4. The resulting mixture was filtered and concentrated to yield **6** (2.8 g, 89%) as a white powder, mp 160 °C (dec). **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 11.92 (s, 1H, *OH*), 4.06 (br, 2H, *CH_2-azetidine*), 3.90 (br, 2H, *CH_2-azetidine*), 3.72-3.67 (m, 1H, *CH-azetidine*), 1.38 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 155.4, 137.0, 78.9, 51.6, 33.8, 28.0.

The corresponding analogues bearing Boc-group Gly, (R)- and (S)-Ala-, (R)- and (S)-Pro- and 4-Pip-moieties were synthesized by the same procedure.

***tert-butyl (E)-(2-chloro-2-(hydroxyimino)ethyl)carbamate* (1)**: white powder 49%, mp 90 °C (dec). **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 13.29 and 11.73 (s, 1H, *OH*), 7.35 and 6.97 (brs, 1H, *NH*), 3.88 (br, 2H, *CH_2*), 1.38 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 155.5, 135.4, 78.3, 44.2, 28.2.

***tert-butyl (E)-(1-chloro-1-(hydroxyimino)propan-2-yl)carbamate* (2-3)**: 85%, white powder, mp 120 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 11.66 (s, 1H, *OH*), 7.35-7.33 (d, 1H, *J* = 8.5, *NH*), 4.36 (m, 1H, *CH*), 1.37 (s, 9H, *CH_3-Boc*), 1.24 (d, 3H, *J* = 7.5, *CH_3*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 154.7, 139.3, 78.2, 50.3, 28.2, 18.4.

***tert-butyl 2-(chloro(hydroxyimino)methyl)pyrrolidine-1-carboxylate* (4-5)**: 80%, white powder, mp 135 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 11.65 (brs, 1H, *OH*), 4.43 (br, 1H, *CH-pyrrolidine*), 3.37 (br, 2H, *CH_2-pyrrolidine*), 2.54 (s, 1H, *CH-pyrrolidine*), 2.17 (br, 1H, *CH-pyrrolidine*), 1.89-1.79 (m, 2H, *CH-pyrrolidine*), 1.39-1.33 (m, 9H, *CH_3-Boc*).

^{13}C NMR (125 MHz, DMSO-d_6): δ 179.8, 153.4, 138.9, 138.7, 79.2, 60.7, 47.1, 46.9, 41.0, 31.1, 30.3, 30.0, 28.5, 28.4, 23.7, 23.1.

***tert-butyl (E)-4-(chloro(hydroxyimino)methyl)piperidine-1-carboxylate* (7)**: 85%, white powder, mp 130 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 11.62 (s, 1H, *OH*), 3.95-3.93 (m, 2H, *CH_2-piperidine*), 2.78 (br, 2H, *CH_2-piperidine*), 2.66-2.64 (m, 1H, *CH*), 1.86-1.83 (m, 2H, *CH_2-piperidine*), 1.40 (s, 11H, *CH_2-piperidine*, 2H + *CH_3-Boc, 9H*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 153.8, 139.8, 78.9, 43.0, 42.5, 29.2, 28.0.

Analytical data for 3,4-disubstituted isoxazoles

Boc-2A-CO_2Me: *S*-isomer, 97%, yellowish oil, $[\alpha]_D^{20}$= -28.14 (*c* = 36.99), 99.4% *ee*, t_R = 13.59 min;

Boc-3A-CO_2Me: *R*-isomer, 98%, yellowish oil, $[\alpha]_D^{20}$= +34.9 (*c* = 36.99), 97.6% *ee*, t_R = 11.25 min.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (s, 1H, C-H, *isoxaz*), 5.69 (br, 1H, *NH*), 5.35 (s, 1H, *CH*), 3.88 (s, 3H, *OCH_3*), 1.48 (d, 3H, *J* = 7.0, *CH_3*), 1.42 (s, 9H, CH_3-Boc). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 165.2, 164.1, 161.1, 154.7, 111.3, 78.1, 51.9, 43.0, 28.1, 19.8. **MS** (APCI) *m/z* $[M\text{-Boc}+H]^+$ calculated for $C_7H_{11}N_2O_3$: 171.2; found: 171.0. Anal. calcd for $C_{12}H_{18}N_2O_5$: C, 53.33; H, 6.71; N, 10.36. Found: C, 53.14; H, 6.44; N, 10.59.

Boc-4A-CO_2Me: *S*-isomer, 92%, yellowish oil, $[\alpha]_D^{20}$= -38.36 (*c* = 33.75), 99.6% *ee*, t_R = 11.98 min;

Boc-5A-CO_2Me: *R*-isomer, 90%, yellowish oil, $[\alpha]_D^{20}$= +39.7 (*c* = 33.75), 99.7% *ee*, t_R = 20.99 min.

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.60-9.57 (m, 1H, C-H, *isoxaz*), 5.27 (m, 1H, *pyrrolidine*), 3.80 (m, 3H, *OCH_3*), 3.46 (m, 1H, *pyrrolidine*), 3.35 (m, 1H, *pyrrolidine*), 2.35-2.17 (m, 1H, *pyrrolidine*), 1.89-1.86 (m, 3H, *pyrrolidine*), 1.37 (s, 4H, *CH_3-Boc*) + 1.17 (s, 5H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 165.0, 164.9, 163.4, 161.2, 161.1, 153.1, 152.7, 111.2, 106.8, 78.6, 78.3, 53.0, 52.7, 51.9, 46.2, 46.0, 31.9, 31.0, 28.0, 27.7, 22.9, 22.4. **MS** (APCI) sample did not dissolve. Anal. calcd for $C_{14}H_{20}N_2O_5$: C 56.75; H, 6.80; N, 9.45. Found: C, 56.94; H, 6.68; N, 9.52.

Boc-6A-CO_2Me: 91%, yellowish oil. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.89 (s, 1H, C-H, *isoxaz*), 4.34-4.29 (m, 2H, *azetidine*), 4.24-4.16 (m, 2H, *azetidine*), 4.14-4.07 (m, H, *azetidine*), 3.85 (s, 3H, *OCH_3*), 1.43 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.5, 161.6, 160.9, 155.5, 112.1, 78.7, 53.1, 51.9, 28.0, 25.2. **MS** (APCI) *m/z* [M-CO_2Me+3H]$^+$ calculated for $C_{11}H_{19}N_2O_3$: 227.1; found: 227.2. Anal. calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.25; H, 6.62; N, 9.46.

Boc-7A-CO_2Me: 91%, yellowish oil. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 9.57 (s, 1H, C-H, *isoxaz*), 4.01-3.98 (m, 2H, *piperidine*), 3.80 (s, 3H, *OCH_3*), 3.30 (br, 1H, *piperidine*), 2.86 (m, 2H, *piperidine*), 1.93-1.90 (m, 2H, *piperidine*), 1.55-1.53 (m, 2H, *piperidine*), 1.40 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.0, 164.3, 161.2, 153.8, 111.4, 78.6, 75.5, 51.7, 33.0, 29.7, 28.0. **MS** (APCI) *m/z* [M-CO_2Me+3H]$^+$ calculated for $C_{13}H_{23}N_2O_3$: 255.1; found: 255.2. Anal. calcd for $C_{15}H_{22}N_2O_5$: C, 58.05; H, 7.15; N, 9.03. Found: C, 58.24; H, 6.98; N, 8.87.

Boc-1A-CN: 89%, yellowish oil. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 9.80 (s, 1H, *isoxaz*), 7.60, (s, 1H, *NH, major rotamer*), 7.24 (br, *NH, minor rotamer*), 4.34 (d, 2H, *J* = 6.0, *CH_2*), 1.39 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 167.9, 161.4, 155.6, 110.0, 92.6, 78.6, 35.1, 28.2. **MS** (APCI) sample did not dissolve. Anal. calcd for $C_{10}H_{13}N_3O_3$: C, 53.80; H, 5.87; N, 18.82. Found: C, 53.71; H, 5.77; N, 18.74.

Boc-2A-CN: *S*-isomer, 96%, yellowish powder, mp 85-90 °C, $[\alpha]_D^{20}$= -54.20 (*c* = 42.15) 99.4% *ee*, t_R = 20.31 min;

Boc-3A-CN: *R*-isomer, 97%, yellowish powder, mp 87-90 °C, $[\alpha]_D^{20}$= +49.72 (*c* = 42.15), 98.8% *ee*, t_R = 16.23 min.

^{1}H NMR (500 MHz, DMSO-*d_6*): *δ* 9.78 (s, 1H, C-H, *isoxaz*), 7.66 (br, 1H, *NH*), 4.83 (m, 1H, *CH*), 1.42 (d, 3H, *J* = 9.0, *CH_3*), 1.39 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 167.9, 164.9, 154.9, 110.1, 92.0, 78.4, 42.9, 28.1, 19.0. **MS** (APCI) *m/z* [M-Boc+1H]$^+$ calculated for $C_6H_8N_3O$: 138.1; found: 138.1. Anal. calcd for $C_{11}H_{15}N_3O_3$: C, 55.69; H, 6.37; N, 17.71. Found: C, 55.54; H, 6.04; N, 17.44.

Boc-4A-CN: *S*-isomer, 95%, yellowish oil, $[\alpha]_D^{20}$= -175.75 (*c* = 37.98), 99.6% *ee*, t_R = 15.63 min.

Boc-5A-CN: *R*-isomer, 93%, yellowish oil, $[\alpha]_D^{20}$ = +174.12 (*c* = 37.98), 99.7% *ee*, t_R = 12.56 min.

^{1}H NMR (500 MHz, DMSO-d_6): *δ* 9.83, (s, 1H, C-H, *isoxaz major rotamer*), 9.78 (m, C-H, *isoxaz minor rotamer*), 4.96 (br, 1H, *CH*), 3.45 (m, 2H, *pyrrolidine*), 2.37 (m, 1H, *pyrrolidine*), 1.92 (br, 3H, *CH$_3$-pyrrolidine*), 1.39 (s, 5H, *CH$_3$-Boc*) 1.20 (s, 4H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 167.8, 165.9, 165.4, 153.4, 152.6, 109.9, 91.4, 91.2, 79.2, 79.1, 52.5, 46.9, 46.6, 33.1, 32.5, 27.9, 27.6, 23.9, 23.3. **MS** (APCI) *m/z* [M-Boc+1H]$^+$ calculated for $C_8H_{10}N_3O$: 164.1; found: 164.1. Anal. calcd for $C_{13}H_{17}N_3O_3$: C, 59.30; H, 6.51; N, 15.96. Found: C, 59.47; H, 6.44; N, 16.12.

Boc-6A-CN: 94%, white powder, mp 79-81 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.91 (s, 1H, C-H, *isoxaz*), 4.37-4.35 (m, 2H, *azetidine-CH$_2$*), 4.24-4.22 (m, 2H, *azetidine-CH$_2$*), 3.97-3.95 (m, 1H, *azetidine-CH*), 1.43 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 168.1, 162.7, 155.3, 110.1, 92.5, 79.0, 52.7, 28.0, 24.2. **MS** (APCI) *m/z* [M]$^+$ calculated for $C_{12}H_{15}N_3O_3$: 249.1; found: 194.0 – could not be assigned to any possible fragments (either after substraction of Boc- or –CN groups). Anal. calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.17; H, 5.79; N, 17.03.

Boc-7A-CN: 92%, white powder, mp 85-87 °C, **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.80 (s, 1H, C-H, *isoxaz*), 4.00-3.98 (m, 2H, *CH*), 3.18-3.13 (m, 1H, *CH*), 2.91 (br, 2H, *pyperidine-CH$_2$*), 1.94-1.92 (m, 2H, *pyperidine-CH$_2$*), 1.59 (s, 2H, *pyperidine-CH$_2$*), 1.40 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 167.9, 164.6, 153.8, 110.7, 92.0, 78.8, 42.8, 32.9, 29.3, 28.0. **MS** (APCI) *m/z* [M]$^+$ calculated for $C_{14}H_{19}N_3O_3$: 277.1; found: 255.2 – could not be assigned to any possible fragments (either after substraction of Boc- or –CN groups). Anal. calcd for $C_{14}H_{19}N_3O_3$: C, 60.63; H, 6.91; N, 15.15. Found: C, 60.34; H, 6.55; N, 15.34.

Boc-1A-COMe: 88%, white powder, mp 74-76 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.75 (s, 1H, *isoxaz*), 7.13 (brs, 1H, *NH, major rotamer*), 6.75 (brs, *NH, minor rotamer*), 4.40-4.38 (d, 2H, *J* = 6.0, *CH$_2$*), 2.46 (s, 3H, *CH$_3$-Ac*), 1.38 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 191.8, 165.6, 159.6, 155.5, 119.7, 78.2, 36.4, 28.9, 28.2. **MS** (APCI) *m/z* [M-Boc+1]$^+$ calculated for $C_6H_9N_2O_2$: 141.1; found: 141.2. Anal. calcd for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. Found: C, 55.35; H, 6.52; N, 11.40.

Boc-2A-COMe: *S*-isomer, 89%, beige powder, mp 45 °C, bp 133-135 °C, $[\alpha]_D^{20}$= -37.78 (*c* = 39.33); 94.76% *ee*, t_R = 16.11 min.

Boc-3A-COMe, *R*-isomer: 91%, white powder, mp 45 °C, bp 133-135 °C, $[\alpha]_D^{20}$= +34.90 (*c* = 39.33), 96.2% *ee*, t_R = 12.49 min.

^{1}H NMR (500 MHz, $CDCl_3$): *δ* 8.90 (s, 1H, C-H, *isoxaz*), 5.81 (br, 1H, *NH*), 5.32 (s, 1H, *CH*), 2.50 (s, 3H, *CH_3-Ac*), 1.41 (m, 12H, *CH_3-Boc* + *CH_3*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 191.8, 166.3, 163.7, 154.7, 119.2, 78.01, 43.1, 29.1, 28.1, 19.8. **MS** (APCI) *m/z* $[M\text{-}Boc+1]^+$ calculated for $C_7H_{11}N_2O_2$: 155.1; found: 155.1. Anal. calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.29; H, 6.95; N, 11.09.

Boc-4A-COMe: *S*-isomer, 87%, beige powder, mp 139-142°C, $[\alpha]_D^{20}$= -68.64 (*c* = 35.67) 99.5% *ee*, t_R = 20.64 min;

Boc-5A-COMe: *R*-isomer, 89%, beige powder, mp 140-142°C, $[\alpha]_D^{20}$= +63.55 (*c* = 35.67), 99.4% *ee*, t_R = 18.86 min.

^{1}H NMR (500 MHz, $CDCl_3$): *δ* 8.88-8.84 (m, 1H, C-H, *isoxaz*), 5.46-5.43 (m, 1H, *CH-pyrrolidine*), 3.64 (brs, 1H, *CH-pyrrolidine*), 3.50-3.43 (m, 1H, *CH-pyrrolidine*), 2.48 (s, 3H, *CH_3-Ac*), 2.33 (br, 1H, *CH-pyrrolidine*), 1.92-1.85 (m, 3H, *CH-pyrrolidine*), 1.43 (s, 5H, *CH_3-Boc*), 1.26 (s, 4H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 191.5, 165.9, 165.8, 163.6, 162.8, 153.1, 152.7, 119.1, 119.0, 78.5, 78.2, 53.3, 53.0, 46.3, 46.0, 31.7, 30.8, 29.0, 28.0, 27.7, 22.8, 22.2. **MS** (APCI) *m/z* $[M\text{-}Boc+1]^+$ calculated for $C_9H_{13}N_2O_2$: 181.1; found: 181.2. Anal. calcd for $C_{14}H_{20}N_2O_4$: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.28; H, 7.28; N, 9.54.

Boc-6A-COMe: 95%, yellowish oil. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 9.81 (s, 1H, C-H, *isoxaz*), 4.25-4.16 (m, 2H, *azetidine-CH_2*), 4.09-4.03 (m, 1H, *azetidine-CH*), 3.97-3.95 (m, 2H, *azetidine-CH_2*), 2.45 (s, 3H, *CH_3-Ac*), 1.37(s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 191.5, 166.2, 160.1, 155.5, 119.9, 78.6, 53.2, 28.8, 28.0, 25.5. **MS** (APCI) *m/z* $[M1]^+$ calculated for $C_{13}H_{18}N_2O_4$: 266.1; found: 211.2 - could not be assigned to any possible fragments. Anal. calcd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N, 10.52. Found: C, 58.25; H, 6.64; N, 10.33.

Boc-7A-COMe: 94%, white powder, mp 84-86 °C, **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.87 (s, 1H, C-H, *isoxaz*), 4.16 (br, 2H, *pyperidine*), 3.40-3.35 (br, 1H, *CH*), 2.87 (br, 2H,

pyperidine), 2.48 (s, 3H, *CH$_3$-Ac*), 1.97-1.95 (m, 2H, *pyperidine*), 1.73-1.64 (m, 2H, *pyperidine*), 1.40 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d$_6$*): *δ* 191.6, 166.0, 163.7, 153.8, 119.3, 78.5, 43.2, 33.1, 29.6, 29.2, 28.0. **MS** (APCI) *m/z* [M1]$^+$ calculated for $C_{10}H_{15}N_2O_2$: 195.1; found: 195.2. Anal. calcd for $C_{15}H_{22}N_2O_4$: C, 61.21; H, 7.53; N, 9.52. Found: C, 61.34; H, 7.49; N, 9.44.

Analytical data for 3,5-disubstituted isoxazoles

Boc-2B-CO$_2$Me: *S*-isomer, 87%, white powder, mp 95-97 °C, $[\alpha]_D^{20}$= -82.22 (*c* = 36.99), 99.74% *ee*, t_R = 15.55 min;

Boc-3B-CO$_2$Me: *R*-isomer, 88%, white powder, mp 95-97 °C, $[\alpha]_D^{20}$= +89.57 (*c* = 36.99), 99.1% *ee*, t_R = 13.27 min.

^{1}H NMR (500 MHz, DMSO-*d$_6$*): *δ* 7.48 (brs, 1H, *NH*), 7.13 (s, 1H, *isoxaz*), 4.81-4.77 (m, 1H, *-CH*), 3.89 (s, 3H, *OCH$_3$*), 3.33 (s, 3H, *CH$_3$ + H$_2$O*), 1.38 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d$_6$*): *δ* 167.6, 159.4, 156.7, 154.9, 108.1, 78.3, 52.9, 42.9, 28.2, 20.0. **MS** (APCI) *m/z* [M-Boc+1H]$^+$ calculated for $C_7H_{10}N_2O_3$: 170.1; found: 171.0 - could not be assigned to any possible fragments. Anal. calcd for $C_{12}H_{18}N_2O_5$: C, 53.33; H, 6.71; N, 10.36. Found: C, 53.90; H, 6.59; N, 10.41.

Boc-4B-CO$_2$Me: *S*-isomer, 91%, yellowish oil, $[\alpha]_D^{20}$= -81.43 (*c* = 33.75), 99.8% *ee*, t_R = 20.06 min;

Boc-5B-CO$_2$Me: *R*-isomer, 92%, yellowish oil, $[\alpha]_D^{20}$= +93.80 (*c* = 33.75), 99.6% *ee*, t_R = 15.21 min.

^{1}H NMR (500 MHz, DMSO-*d$_6$*): *δ* 7.24 (s, 1H, *isoxaz, major rotamer*), 7.16 (s, *isoxaz, minor rotamer*), 4.94-4.89 (m, 1H, *-CH, mixture of rotamers*), 3.89 (s, 3H, *OCH$_3$*), 3.48-3.37 (m, 2H, *CH$_2$-pyrrolidine*), 2.29-2.23 (m, 1H, *CH-pyrrolidine*), 1.89 (m, 3H, *CH-pyrrolidine*), 1.38 (s, 4H, *CH$_3$-Boc*), 1.21 (s, 5H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d$_6$*): *δ* 167.6, 167.0, 159.3, 156.7, 152.9, 108.4, 108.0, 79.1, 78.7, 53.1, 52.8, 46.4, 46.1, 32.7, 31.4, 28.0, 27.8, 23.6, 22.9. **MS** (APCI) *m/z* [M-Boc+1H]$^+$ calculated for $C_9H_{13}N_2O_3$: 197.1; found: 197.1. Anal. calcd for $C_{14}H_{20}N_2O_5$: C, 56.75; H, 6.80; N, 9.45. Found: C, 56.44; H, 6.63; N, 9.52.

Boc-6B-CO_2Me: 95%, yellowish oil. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 7.00 (s, 1H, C-H, *isoxaz*), 4.37-4.32 (t, 2H, *J* = 11.0, azetidine-*CH_2*), 4.05-4.03 (m, 2H, azetidine-*CH*), 3.97 (s, 3H, OCH_3), 3.96-3.89 (m, 1H, azetidine-*CH*), 1.45 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.4, 159.8, 156.7, 155.4, 109.0, 78.8, 53.7, 52.8, 28.0, 25.0. **MS** (APCI) *m/z* $[M\text{-}CO_2Me+3H]^+$ calculated for $C_{11}H_{19}N_2O_3$: 227.1; found: 227.2. Anal. calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.16; H, 6.65; N, 9.47.

Boc-7B-CO_2Me: 88%, white powder, mp 74-76 °C (dec). **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 6.81 (s, 1H, C-H, *isoxaz*), 4.15 (brs, 2H, piperidine-*CH_2*), 3.94 (s, 3H, O*CH_3*), 2.95-2.86 (m, 3H, piperidine-*CH_2*), 1.95-1.92 (m, 2H, piperidine-*CH_2*), 1.67-1.58 (m, 2H, piperidine-*CH_2*), 1.45 (s, 9H, *CH_3-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 167.8, 159.3, 156.8, 153.8, 108.6, 78.6, 52.8, 43.2, 42.5, 33.2, 30.0, 28.0. **MS** (APCI) *m/z* $[M\text{-}CO_2Me+3H]^+$ calculated for $C_{13}H_{23}N_2O_3$: 255.1; found: 255.2. Anal. calcd for $C_{15}H_{22}N_2O_5$: C, 58.05; H, 7.15; N, 9.03. Found: C, 57.93; H, 7.28; N, 9.16.

Boc-1B-TMS: 87%, white powder, mp = 49-51 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 7.37 (brs, 1H, *NH*), 6.57 (s, 1H, *isoxaz*), 4.19 (d, 2H, *J* = 6.0, *CH_2*), 1.39 (s, 9H, *CH_3-Boc*), 0.30 (s, 9H, *CH_3-TMS*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 177.27, 160.5, 155.7, 112.32, 78.1, 35.2, 28.1, -2.1. **MS** (APCI) *m/z* $[M]^+$ calculated for $C_{12}H_{22}N_2O_3Si$: 270.1; found: 215.2– could not be assigned to any possible fragments (either after substraction of Boc- or –TMS groups). Anal. calcd for $C_{12}H_{22}N_2O_3Si$: C, 53.30; H, 8.20; N, 10.36. Found: C, 53.25; H, 8.40; N, 10.42.

Boc-2B-TMS: *S*-isomer, 75%, white powder, mp = 74-76 °C, bp = 113-117 °C, $[\alpha]_D^{20}$ = - 26.41 (*c* = 35.16), 98.3% *ee*, t_R = 11.12 min;

Boc-3B-TMS: *R*-isomer, 77%, white powder, mp = 74-76 °C, bp = 113-115 °C, $[\alpha]_D^{20}$ = +41.58 (*c* = 35.16), mp 75-76 °C, 95.9% *ee*, t_R = 10.30 min.
^{1}H NMR (500 MHz, $CDCl_3$): *δ* 6.36 (s, 1H, *isoxaz*), 5.03-4.95 (m, 2H, *NH* + *CH*), 1.52 (t, 3H, *J* = 6.5, *CH_3*), 1.45 (s, 9H, *CH_3-Boc*), 0.33 (s, 9H, *CH_3-TMS*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 177.1, 164.5, 154.8, 111.5, 78.0, 42.5, 28.1, 20.4, -2.06. **MS** (APCI) *m/z* $[M]^+$ calculated for $C_{13}H_{24}N_2O_3Si$: 284.1; found: 229.1– could not be assigned to any

possible fragments (either after substraction of Boc- or –TMS groups). Anal. calcd for $C_{13}H_{24}N_2O_3Si$: C, 54.90; H, 8.51; N, 9.85. Found: C, 54.66; H, 8.37; N, 9.45.

Boc-4B-TMS: *S*-isomer, 85%, white powder, mp = 64-66 °C $[\alpha]_D^{20}$= -80.97 (*c* = 32.21), 99.8% *ee*, t_R = 9.66 min;

Boc-5B-TMS: *R*-isomer, 84%, white powder, mp = 64-65 °C $[\alpha]_D^{20}$= +95.32 (*c* = 32.21), 99.6% *ee*, t_R = 8.20 min.

^{1}H NMR (500 MHz, $CDCl_3$): *δ* 6.36-6.28 (m, 1H, *isoxaz*), 5.07-4.98 (m, 1H, -*CH*), 3.54-3.41 (m, 2H, *CH_2-pyrrolidine*), 2.28-1.93 (m, 4H, *CH_2-pyrrolidine*), 1.47-1.30 (m, 9H, *CH_3-Boc*), 0.31 (s, 9H, *CH_3-TMS*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *mixture of rotamers δ* 176.8, 164.6, 163.9, 153.5, 153.0, 111.7, 111.2, 78.5, 78.3, 52.8, 46.2, 46.1, 32.8, 31.4, 28.0, 27.7, 23.5, 23.0, -2.15. **MS** (APCI) *m/z* $[M+H]^+$ calculated for $C_{10}H_{19}N_2OSi$: 211.1; found: 211.2. Anal. calcd for $C_{15}H_{26}N_2O_3Si$: C, 58.03; H, 8.44; N, 9.02. Found: C, 58.21; H, 8.42; N, 9.24.

Boc-6B-TMS: 76%, yellowish oil, bp = 114-116 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 6.46 (s, 1H, C-H, *isoxaz*), 4.33-4.29 (t, 2H, *J* = 10.5, azetidine-*CH_2*), 4.04-4.02 (m, 2H, azetidine-*CH_2*), 3.93-3.88 (m, 1H, azetidine-*CH*), 1.45 (s, 9H, *CH_3-Boc*), 0.34 (s, 9H, *CH_3-TMS*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 178.1, 162.5, 155.5, 112.0, 79.2, 78.7, 54.3, 48.6, 28.0, 24.5, -2.1. **MS** (APCI) *m/z* $[M]^+$ calculated for $C_{14}H_{24}N_2O_3Si$: 296.2; found: 241.2- could not be assigned to any possible fragments (either after substraction of Boc- or –TMS groups). Anal. calcd for $C_{14}H_{24}N_2O_3Si$: C, 56.72; H, 8.16; N, 9.45. Found: C, 56.67; H, 8.28; N, 9.52.

Boc-7B-TMS: 63%, beige powder, mp 67-69 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 6.73 (s, 1H, C-H, *isoxaz*), 3.98-3.95 (m, 2H, piperidine-*CH_2*), 2.93-2.85 (m, 3H, piperidine-*CH*), 1.86-1.83 (m, 2H, piperidine-*CH*), 1.52-1.46 (m, 2H, piperidine-*CH*), 1.40 (s, 9H, *CH_3-Boc*), 0.29 (s, 9H, *CH_3-TMS*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 176.9, 164.6, 153.8, 111.7, 78.5, 43.1, 40.4, 32.8, 30.6, 28.0, -2.1. **MS** (APCI) *m/z* $[M]^+$ calculated for $C_{16}H_{28}N_2O_3Si$: 324.2; found: 269.2- could not be assigned to any possible fragments (either after substraction of Boc- or –TMS groups). Anal. calcd for $C_{16}H_{28}N_2O_3Si$: C, 59.22; H, 8.70; N, 8.63. Found: C, 59.34; H, 8.49; N, 8.87.

Analytical data for deprotected aminoisoxazoles

1A-CO_2Me•HCl: 98%, white powder, mp 169-171 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 9.76 (s, 1H, C-H, *isoxaz*), 8.79 (brs, 3H, *NH_2 • HCl*), 4.33 (s, 2H, *CH_2*), 3.83 (s, 3H, *OCH_3*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.3, 160.85, 156.4, 112.5, 52.3, 33.9.
MS (APCI) *m/z* $[M\text{-}Cl]^+$ calculated for $C_6H_8N_2O_3$: 156.1, found: not informative. Anal. calcd for $C_6H_9ClN_2O_3$: C, 37.42; H, 4.71; N, 14.54. Found: C, 37.28; H, 4.57; N, 14.37.

2A-CO_2Me•HCl: *S*-isomer, 99%, white powder, mp 149-151 °C, $[\alpha]_D^{20}$= -9.11 (*c* = 48.39);

3A-CO_2Me•HCl: *R*-isomer, 97%, white powder mp 149-151 °C, $[\alpha]_D^{20}$= +20.40 (*c* = 48.39).
^{1}H NMR (500 MHz, DMSO-*d_6*): *δ* 9.77 (s, 1H, *isoxaz*), 8.95 (brs, 3H, C-H, *NH_2 • HCl*), 4.80 (brs, 1H, *CH*), 3.84 (s, 3H, *OCH_3*), 1.58 (d, 3H, *J* = 8.5, *CH_3*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.7, 160.8, 160.4, 111.7, 52.3, 42.7, 18.0. **MS** (APCI) *m/z* $[M\text{-}Cl]^+$ calculated for $C_7H_{10}N_2O_3$: 171.1, found: 171.2. Anal. calcd for $C_7H_{11}ClN_2O_3$: C, 40.69; H, 5.37; N, 13.56. Found: C, 40.87; H, 5.59; N, 13.76.

4A-CO_2Me•HCl: *S*-isomer, 96%, white powder, mp 158-160 °C, $[\alpha]_D^{20}$= -10.17 (*c* = 42.98); **5A-CO_2Me•HCl**: *R*-isomer, 94%, white powder, mp 158-160 °C, $[\alpha]_D^{20}$= +10.03 (*c* = 42.98). **^{1}H NMR** (500 MHz, DMSO-*d_6*): *δ* 10.48 (brs, 1H, *NH • HCl*), 9.79 (s, 1H, C-H, *isoxaz*), 9.40 (brs, 1H, *NH • HCl*), 5.09 (m, 1H, *CH*), 3.86 (s, 3H, *OCH_3*), 3.32-3.27 (m, 2H, *pyrrolidine-CH_2*), 2.41-2.35 (m, 1H, *pyrrolidine-CH*), 2.26-2.19 (m, 1H, *pyrrolidine-CH*), 2.05-2.00 (m, 2H, *pyrrolidine-CH_2*).**^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.8, 160.8, 158.1, 112.8, 53.0, 52.3, 45.1, 28.8, 23.3. **MS** (APCI) *m/z* $[M\text{-}Cl]^+$ calculated for $C_9H_{12}N_2O_3$: 197.1, found: 197.2. Anal. calcd for $C_9H_{13}ClN_2O_3$: C, 46.46; H, 5.63; N, 12.04. Found: C, 46.67; H, 5.39; N, 12.37.

6A-CO_2Me•HCl: 93%, white powder, mp 190-192 °C. **^{1}H NMR** (500 MHz, DMSO-*d_6*,): *δ* 10.01 (br, 1H, C-H, *HCl*), 9.59 (br, 1H, *NH*), 9.49 (s, 1H, C-H, *isoxaz*), 4.46-4.41 (m, 1H, *azetidine-CH*), 4.35-4.28 (m, 2H, *azetidine-CH*), 4.26-4.20 (m, 2H, *azetidine-CH*), 3.80 (s, 3H, *OCH_3*). **^{13}C NMR** (125 MHz, DMSO-*d_6*): *δ* 165.2, 160.7, 159.8, 111.9, 95.6, 51.9,

48.2, 28.1. **MS** (APCI) *m/z* $[M\text{-}Cl]^+$ calculated for $C_8H_{10}N_2O_3$: 182.1, found: not informative. Anal. calcd for $C_8H_{11}ClN_2O_3$: C, 43.95; H, 5.07; N, 12.81. Found: C, 44.25; H, 4.87; N, 12.92.

7A-CO_2Me•HCl: 95%, white powder, mp 195-197 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 9.62 (s, 1H, C-H, *isoxaz*), 9.34 (brs, 1H, NH_2 • *HCl*), 9.21 (brs, 1H, NH_2 • *HCl*), 3.81 (s, 3H, OCH_3), 3.44-3.40 (m, 1H, *pyperidine-CH*), 3.31-3.29 (m, 2H, *piperidine-CH*), 3.02-3.00 (m, 2H, *piperidine-CH*), 2.11-2.09 (m, 2H, *pyperidine-CH*), 1.96-1.90 (m, 2H, *pyperidine-CH*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 165.2, 163.6, 161.2, 111.6, 52.0, 42.6, 30.9, 26.3. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_{10}H_{14}N_2O_3$: 211.1, found: 211.2. Anal. calcd for $C_{10}H_{15}ClN_2O_3$: C, 48.69; H, 6.13; N, 11.36. Found: C, 48.23; H, 6.29; N, 11.52.

1A-CN•HCl: 99%, white powder, mp 94-96 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 9.98 (s, 1H, *isoxaz*), 9.01 (brs, 3H, NH_2 • *HCl*), 4.32 (s, 2H, CH_2). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 168.1, 157.3, 109.8, 93.6, 33.2. **MS** (APCI) *m/z* $[M+Cl\text{-}1H]^+$ calculated for $C_5H_4ClN_3O$: 157.0, found: 157.2. Anal. calcd for $C_5H_6ClN_3O$: C, 37.63; H, 3.79; N, 26.33. Found: C, 37.30; H, 3.94; N, 26.08.

2A-CN•HCl: *S*-isomer, 97%, white powder, mp 189-191 °C, $[\alpha]_D^{20}$= -38.13 (*c* = 57.60);

3A-CN•HCl: *R*-isomer, 98%, white powder, mp 189-190 °C, $[\alpha]_D^{20}$= +36.83 (*c* = 57.60).

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.00 (s, 1H, *isoxaz*), 9.10 (brs, 3H, NH_2 • *HCl*), 4.77 (q, 1H, *J* = 8.5, *CH*), 1.63 (d, 3H, *J* = 9.0, CH_3). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 168.7, 160.8, 109.9, 92.5, 42.3, 17.7. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_6H_8N_3O$: 138.1, found: 138.2. Anal. calcd for $C_6H_8ClN_3O$: C, 41.51; H, 4.64; N, 24.21. Found: C, 41.26; H, 4.45; N, 24.72.

4A-CN•HCl: *S*-isomer, 96%, beige powder, mp 165 °C (dec), $[\alpha]_D^{20}$= -42.58 (*c* = 50.09);

5A-CN•HCl: *R*-isomer, 95%, beige powder, mp 165 °C (dec), $[\alpha]_D^{20}$= +42.25 (*c* = 50.09).

^{1}H NMR (500 MHz, D_2O-d_2): δ 9.49 (s, 1H, *isoxaz*), 5.16-5.12 (m, 1H, *CH*), 3.62-3.56 (m, 2H, *pyrrolidine*), 2.76-2.71 (m, 1H, *pyrrolidine*), 2.35-2.24 (m, 3H, *pyrrolidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 168.7, 158.9, 109.9, 93.4, 52.5, 45.0, 29.0, 23.2.

MS (APCI) *m/z* $[M+1H]^+$ calculated for $C_8H_{10}N_3O$: 164.1, found: 164.2. Anal. calcd for $C_8H_{10}ClN_3O$: C, 48.13; H, 5.05; N, 21.05. Found: C, 48.02; H, 5.28; N, 21.73.

6A-CN•HCl: 94%, yellowish oil. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 9.91 (s, 1H, *isoxaz*), 9.82-9.33 (br, 2H, NH_2 • *HCl*), 4.29-4.22 (m, 5H, *azetidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 168.1, 161.2, 110.1, 93.1, 48.7, 27.2. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_7H_8N_3O$: 150.1, found: 150.2. Anal. calcd for $C_7H_8ClN_3O$: C, 45.30; H, 4.34; N, 22.64. Found: C, 45.59; H, 4.22; N, 22.32.

7A-CN•HCl: 92%, white powder, mp 154-156 °C. **^{1}H NMR** (500 MHz, D_2O-d_2): δ 9.34 (s, 1H, *isoxaz*), 3.60-3.57 (m, 2H, *pyperidine*), 3.47-3.41 (m, 1H, *pyperidine*), 2.28-3.21 (m, 2H, *pyperidine*), 2.40-2.36 (m, 2H, *pyperidine*), 2.11-2.05 (m, 2H, *pyperidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 168.1, 164.0, 110.5, 92.2, 42.2, 30.7, 26.1. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_9H_{12}N_3O$: 178.1, found: 178.2. Anal. calcd for $C_9H_{12}ClN_3O$: C, 50.59; H, 5.66; N, 19.67. Found: C, 50.98; H, 5.39; N, 19.32.

2A-COMe•HCl: *S*-isomer, 96%, white powder, mp 174-176 °C, $[\alpha]_D^{20}$= -32.92 (*c* = 52.46);

3A-COMe•HCl: *R*-isomer, 94%, white powder, mp 174-176 °C, $[\alpha]_D^{20}$= +33.43 (*c* = 52.46).

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.01 (s, 1H, *isoxaz*), 8.88 (brs, 3H, NH_2•*HCl*), 4.78 (brs, 1H, *CH*), 2.52 (s, 3H, CH_3-Ac), 1.53 (d, 3H, *J* = 8.5, CH_3). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 192.1, 166.8, 159.8, 119.1, 42.9, 29.2, 17.9. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_7H_{11}N_2O_2$: 155.2, found: 155.2. Anal. calcd for $C_7H_{11}ClN_2O_2$: C, 44.10; H, 5.82; N, 14.70. Found: C, 43.96; H, 5.88; N, 14.93.

4A-COMe•HCl: *S*-isomer, 97%, white powder, mp 175 °C (dec), $[\alpha]_D^{20}$= -12.94 (*c* = 46.15);

5A-COMe•HCl: *R*-isomer, 98%, white powder, mp 175 °C (dec), $[\alpha]_D^{20}$= +12.59 (*c* = 46.15). **^{1}H NMR** (500 MHz, DMSO-d_6): δ 10.49 (brs, 1H, NH_2•*HCl*), 10.02 (s, 1H, *isoxaz*), 9.43 (brs, 1H, NH_2×*HCl*), 5.03 (t, 1H, *J* = 8.5, *CH*), 3.29 (brs, 2H, *pyrrolidine-*CH_2), 2.52 (s, 3H, CH_3-Ac), 2.41-2.32 (m, 1H, *pyrrolidine-CH*), 2.14-1.97 (m, 3H,

pyrrolidine-CH_2). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 191.8, 166.6, 157.5, 119.9, 53.4, 45.0, 29.1, 28.9, 23.1. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_9H_{13}N_2O_2$: 181.1, found: 181.2. Anal. calcd for $C_9H_{13}ClN_2O_2$: C, 49.89; H, 6.05; N, 12.93. Found: C, 50.03; H, 6.13; N, 12.88.

6A-COMe•HCl: 93%, white powder, mp 134-136 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.92 (s, 1H, *isoxaz*), 9.75 (brs, 1H, *NH•HCl*), 9.38 (brs, 1H, *NH•HCl*), 4.35-4.33 (m, 1H, azetidine-*CH*), 4.23 (brs, 2H, azetidine -*CH_2*), 4.12 (brs, 2H, azetidine-*CH_2*), 2.47 (s, 3H, CH_3-Ac). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 191.7, 166.3, 159.3, 119.8, 48.0, 28.9, 28.3. **MS** (APCI) *m/z* $[M+1H]^+$ calculated for $C_8H_{11}N_2O_2$: 167.1, found: 167.2. Anal. calcd for $C_8H_{11}ClN_2O_2$: C, 47.42; H, 5.47; N, 13.82. Found: C, 47.24; H, 5.62; N, 13.67.

7A-COMe•HCl: 90%, white powder, mp 149-151 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.84 (s, 1H, *isoxaz*), 9.28-9.18 (m, 2H, *NH•HCl*), 3.43-3.40 (m, 2H, piperidine-*CH_2*), 3.30-3.28 (m, 1H, piperidine-*CH_2*), 3.03-2.97 (m, 2H, piperidine-*CH_2*), 2.48 (s, 3H, CH_3-Ac), 2.08-2.05 (m, 2H, piperidine-*CH_2*), 1.93-1.86 (m, 2H, piperidine-*CH_2*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 191.7, 166.1, 162.9, 119.2, 42.5, 30.8, 29.2, 26.1.
MS (APCI) *m/z* $[M+1H]^+$ calculated for $C_{10}H_{15}N_2O_2$: 195.1, found: 195.2. Anal. calcd for $C_{10}H_{15}ClN_2O_2$: C, 52.06; H, 6.55; N, 12.14. Found: C, 52.17; H, 6.71; N, 12.25.

1B-CO_2Me•HCl: 98%, white powder, mp 168-170 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 8.90 (brs, 3H, *NH_2•HCl*), 7.50 (s, 1H, *isoxaz*), 4.22 (s, 2H, *CH_2*), 3.92 (s, 3H, *OCH_3*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 159.8, 159.6, 156.5, 110.0, 53.2, 34.1. **MS** (APCI) *m/z* $[M-Cl+1H]^+$ calculated for $C_6H_9N_2O_3$: 157.1, found: 157.2. Anal. calcd for $C_6H_9ClN_2O_3$: C, 37.42; H, 4.71; N, 14.54. Found: C, 37.28; H, 4.89; N, 14.36.

2B-CO_2Me•HCl: *S*-isomer, 99%, white powder, mp 149-151 °C, $[\alpha]_D^{20}$ = -13.88 (*c* = 48.39); **3B-CO_2Me•HCl**: *R*-isomer, 97%, white powder, mp 150 °C, $[\alpha]_D^{20}$ = +12.50 (*c* = 48.39).
^{1}H NMR (500 MHz, DMSO-d_6): *δ* 9.07 (brs, 3H, *NH•HCl*), 7.61 (s, 1H, *isoxaz*), 4.65 (q, 1H, *J* = 8.5, *CH*), 3.91 (s, 3H, *OCH_3*), 1.59 (d, 3H, *J* = 8.5, *CH_3*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 163.7, 160.0, 156.5, 108.9, 53.2, 43.0, 18.1. **MS**

(APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_7H_{11}N_2O_3$: 171.1, found: 171.2. Anal. calcd for $C_7H_{11}ClN_2O_3$: C, 40.69; H, 5.37; N, 13.56. Found: C, 40.63; H, 5.44; N, 13.37.

4B-CO_2Me•HCl: *S*-isomer, 96%, white powder, mp 160-162 °C. $[\alpha]_D^{20}$= -23.09 (*c* = 35.42); **5B-CO_2Me•HCl**: *R*-isomer: 95%, white powder, mp 161 °C. $[\alpha]_D^{20}$= +21.2 (*c* = 35.42). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 10.57 (brs, 1H, *NH•HCl*), *δ* 9.79 (brs, 1H, *NH•HCl*), 7.62 (s, 1H, *isoxaz*), 4.82-4.81 (m, 1H, *CH*), 3.92 (s, 3H, *OCH_3*), 3.33-3.29 (m, 2H, *CH_2-pyrrolidine*), 2.41-2.38 (m, 1H, *CH-pyrrolidine*), 2.12-1.98 (m, 3H, *CH-pyrrolidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 161.2, 160.1, 156.4, 109.5, 53.6, 53.1, 44.5, 29.2, 22.8. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_6H_{13}N_2O_3$: 197.1, found: 197.2. Anal. calcd for $C_9H_{13}ClN_2O_3$: C, 46.46; H, 5.63; N, 12.04. Found: C, 46.32; H, 5.83; N, 11.87.

6B-CO_2Me•HCl: 94%, white powder, mp 189-191 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.53 (brs, 2H, *NH•HCl*), 7.62 (s, 1H, C-H, *isoxaz*), 4.33-4.23 (m, 3H, azetidine-*CH_2*), 4.13-4.11 (m, 2H, azetidine-*CH_2*), 3.91 (s, 3H, *OCH_3*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 164.0, 159.9, 156.6, 109.2, 53.0, 49.2, 27.8. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_8H_{11}N_2O_3$: 183.1, found: 183.2. Anal. calcd for $C_8H_{11}ClN_2O_3$: C, 43.95; H, 5.07; N, 12.81. Found: C, 44.06; H, 4.88; N, 12.93.

7B-CO_2Me•HCl: 93%, beige powder, mp 192-194 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.14 (brs, 1H, *NH•HCl*), *δ* 8.97 (brs, 1H, *NH•HCl*), 7.32 (s, 1H, *isoxaz*), 3.89 (s, 3H, *OCH_3*), 3.30-3.28 (m, 2H, piperidine-*CH_2*), 3.17-3.12 (m, 1H, piperidine-*CH*), 3.04-2.97 (m, 2H, piperidine-*CH_2*), 2.14-2.12 (m, 2H, piperidine-*CH_2*), 2.91-1.84 (m, 2H, piperidine-*CH_2*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 166.8, 159.5, 156.7, 108.6, 52.9, 42.3, 31.0, 26.5. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_{10}H_{15}N_2O_3$: 211.1, found: 211.2. Anal. calcd for $C_{10}H_{15}ClN_2O_3$: C, 48.69; H, 6.13; N, 11.36. Found: C, 48.85; H, 6.02; N, 11.44.

1B-H: 86%, yellowish oil. **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 8.75 (s, 1H, *CH-isoxaz*), 6.56 (s, 1H, *CH-isoxaz*), 3.74 (brs, 2H, *CH_2*), 2.40 (br, 2H, *-NH_2*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 164.9, 159.2, 103.8, 37.1. Anal. calcd for $C_4H_6N_2O$: C, 48.97; H, 6.16; N, 28.56. Found: C, 48.56; H, 6.33; N, 28.38.

2B-H•HCl: *S*-isomer, 96%, white powder, mp 119-121 °C, $[\alpha]_D^{20}$= -6.20 (*c* = 67.30);

3B-H•HCl: *R*-isomer: 97%, white powder, mp 120 °C, $[\alpha]_D^{20}$= +7.20 (*c* = 67.30).

^{1}H NMR (500 MHz, DMSO-d_6): *δ* 8.94-8.90 (m, 4H, *NH•HCl* + 1H, *isoxaz*), 6.87 (s, 1H, *isoxaz*), 4.55 (q, 1H, *J* = 8.5, *CH*), 1.52 (d, 3H, *J* = 8.5, CH_3). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 161.7, 160.9, 103.7, 43.0, 18.4. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_5H_9N_2O$: 113.1, found: 113.2. Anal. calcd for $C_5H_9ClN_2O$: C, 40.42; H, 6.10; N, 18.85. Found: C, 40.26; H, 6.18; N, 18.67.

4B-H•HCl: *S*-isomer, 95%, white powder, mp 134-136 °C. $[\alpha]_D^{20}$= -20.92 (*c* = 57.26);

5B-H•HCl: *R*-isomer, 94%, white powder, mp 134-136 °C $[\alpha]_D^{20}$= +21.1 (*c* = 57.26).

^{1}H NMR (500 MHz, DMSO-d_6): *δ* 10.53 (br, 1H, *NH•HCl*), 9.63 (br, 1H, *NH•HCl*), 9.03 (s, 1H, *isoxaz*), 6.91 (d, 1H, *J* = 1.5, *isoxaz*), 4.76 (m, 1H, *CH-pyrrolidine*), 3.32-3.28 (m, 2H, CH_2-*pyrrolidine*), 2.39-2.36 (m, 1H, *CH-pyrrolidine*), 2.04 (brs, 3H, *CH-pyrrolidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 161.0, 159.2, 104.3, 53.8, 44.5, 29.4, 22.8. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_7H_{11}N_2O$: 139.1, found: 139.2. Anal. calcd for $C_7H_{11}ClN_2O$: C, 48.15; H, 6.35; N, 16.04. Found: C, 48.03; H, 6.24; N, 16.13.

6B-H•HCl: 98%, white powder, mp 140 °C (dec). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.67 (br, 2H, *NH•HCl*), 8.95 (s, 1H, C-H, *isoxaz*), 6.89 (s, 1H, C-H, *isoxaz*), 4.29-4.06 (m, 5H, azetidine). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 161.8, 160.7, 103.8, 49.4, 27.6. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_6H_9N_2O$: 125.1, found: 125.2. Anal. calcd for $C_6H_9ClN_2O$: C, 44.87; H, 5.65; N, 17.44. Found: C, 44.75; H, 5.81; N, 17.28.

7B-H: 84%, colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): *δ* 8.31(s, 1H, *CH-isoxaz*), 6.23 (s, 1H, *CH-isoxaz*), 3.18-3.16 (m, 2H, CH_2-*piperidine*), 2.95-2.91 (br, 1H, *CH-piperidine*), 2.75 (t, 2H, *J* = 11.0, *CH-piperidine*),1.96-1.93 (m, 2H, *CH-piperidine*), 1.88 (brs, 1H, *NH-piperidine* + H_2O), 1.70-1.63 (m, 2H, CH_2-*piperidine*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 166.2, 159.4, 103.1, 45.0, 33.5, 31.0. **MS** (APCI) *m/z* $[M\text{-}Cl+1H]^+$ calculated for $C_8H_{12}N_2O$: 153.1, found: 153.1. Anal. calcd for $C_8H_{12}N_2O$: C, 63.13; H, 7.95; N, 18.41. Found: C, 63.42; H, 7.73; N, 18.56.

Analytical data for isoxazole-based acids

Boc-2A-CO_2H: *S*-isomer, 97%, white powder, mp 144-146 °C, $[\alpha]_D^{20}$= -29.70 (*c* = 39.02);

Boc-3A-CO_2H: *R*-isomer, 98%, white powder, mp 144-146 °C, $[\alpha]_D^{20}$= +28.87 (*c* = 39.02). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 13.28 (br, 1H, C-OOH), 9.45 (s, 1H, C-H, *isoxaz*), 7.29-7.27 (br, 1H, *NH*), 5.12-5.08 (m, 1H, *CH*), 1.36 (s, 12H, CH_3 + CH_3-*Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 165.1, 164.5, 162.4, 154.8, 112.4, 78.1, 43.0, 28.2, 20.1. **MS** (APCI) *m/z* $[M-1H]^+$ calculated for $C_{11}H_{15}N_2O_5$: 255.1, found: 255.1. Anal. calcd for $C_{11}H_{16}N_2O_5$: C, 51.56; H, 6.29; N, 10.93. Found: C, 51.69; H, 6.27; N, 11.08.

Boc-4A-CO_2H: *S*-isomer, 92%, white powder, mp 139-141 °C, $[\alpha]_D^{20}$= -40.79 (*c* = 35.42);

Boc-5A-CO_2H: *R*-isomer, 90%, white powder, mp 139-141 °C, $[\alpha]_D^{20}$= +44.80 (*c* = 35.42). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.42 (s, 1H, C-H, *isoxaz, major rotamer*), 9.40 (s, C-H, *isoxaz, minor rotamer*), 5.33-5.32, (m, 1H, *pyrrolidine-CH, major-rotamer*), 5.31-5.30 (m, *pyrrolidine-CH, minor rotamer*), 3.45 (brs, 1H, *pyrrolidine-CH*), 3.33 (brs, 1H, *pyrrolidine-CH*), 2.29-2.21 (brs, 1H, *pyrrolidine-CH_2*), 1.86-1.80 (brs, 3H, *pyrrolidine-CH_2*), 1.37 (s, 4H, CH_3-*Boc*), 1.17 (s, 5H, CH_3-*Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 164.5, 164.4, 164.3, 163.7, 162.5, 153.2, 152.9, 113.2, 78.6, 78.3, 53.1, 52.8, 45.3, 45.1, 32.1, 31.2, 28.2, 27.8, 22.9, 22.4. **MS** (APCI) *m/z* $[M-1H]^+$ calculated for $C_{13}H_{17}N_2O_5$: 281.1, found: 281.1. Anal. calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.46; H, 6.31; N, 9.77.

Boc-6A-CO_2H: 91%, white powder, mp 155 °C (dec). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.52 (s, 1H, C-H, *isoxaz*), 4.19-4.02 (m, 5H), 1.37 (s, 9H, CH_3-*Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 165.3, 162.1, 161.9, 155.6, 113.2, 78.8, 53.4, 52.2, 28.1, 25.3. **MS** (APCI) *m/z* $[M-1H]^+$ calculated for $C_{12}H_{15}N_2O_5$: 267.1, found: 267.2. Anal. calcd for $C_{12}H_{16}N_2O_5$: C, 53.73; H, 6.01; N, 10.44. Found: C, 53.91; H, 5.87; N, 10.62.

Boc-7A-CO_2H: 91%, white powder, mp 150 °C (dec). **^{1}H NMR** (500 MHz, DMSO-d_6): *δ* 9.45 (s, 1H, C-H, *isoxaz*), 4.00-3.97 (m, 2H, piperidine-CH_2), 3.34-3.29 (m, 1H, piperidine-*CH* + H_2O), 2.85 (br, 2H, piperidine-CH_2), 1.93-1.90 (m, 2H, piperidine-CH_2),

1.55-1.53 (m, 2H, piperidine-*CH*$_2$), 1.40 (s, 9H, *CH*$_3$-*Boc*). **^{13}C NMR** (125 MHz, DMSO-*d*$_6$): *δ* 164.9, 164.6, 162.3, 153.9, 112.6, 78.7, 43.7, 43.0, 32.9, 29.8, 28.1.
MS (APCI) *m/z* [M-1H]$^+$ calculated for $C_{14}H_{19}N_2O_5$: 295.1, found: 295.0. Anal. calcd for $C_{14}H_{20}N_2O_5$: C, 56.75; H, 6.80; N, 9.45. Found: C, 56.66; H, 6.94; N, 9.27.

Boc-1B-CO$_2$H: 84%, white powder, mp 149-151 °C. **^{1}H NMR** (500 MHz, DMSO-*d*$_6$): *δ* 14.23 (br, 1H, C-OOH), 7.49 (br, 1H, *NH*), 6.94 (s, 1H, *isoxaz*), 4.22-4.21 (d, 2H, *J* = 7.0, -*CH*$_2$), 1.39 (s, 9H, *CH*$_3$-*Boc*). **^{13}C NMR** (125 MHz, DMSO-*d*$_6$): *δ* 163.6, 161.0, 157.7, 155.8, 108.5, 78.5, 35.7, 28.2. **MS** (APCI) *m/z* [M-1H]$^+$ calculated for $C_{10}H_{13}N_2O_5$: 241.1, found: 241.1. Anal. calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.56. Found: C, 49.66; H, 5.73; N, 11.44.

Boc-2B-CO$_2$H: *S*-isomer, 90%, white powder, mp 129-131 °C, $[\alpha]_D^{20}$= -45.62 (*c* = 39.02);

Boc-3B-CO$_2$H: *R*-isomer, 89%, white powder, mp 129-131 °C, $[\alpha]_D^{20}$= +55.68 (*c* = 39.02). **^{1}H NMR** (500 MHz, DMSO-*d*$_6$): *δ* 9.95 (br, 1H, C-OOH), 7.35-7.33 (m, 1H, *NH*), 6.96 (s, 1H, *isoxaz*), 4.79-4.75 (m, 1H, -*CH*), 1.33 (s, 12H, *CH*$_3$ + *CH*$_3$-*Boc*).
^{13}C NMR (125 MHz, DMSO-*d*$_6$): *δ* 167.7, 161.5, 158.1, 155.2, 107.7, 78.6, 43.2, 28.4, 20.2. **MS** (APCI) *m/z* [M-1H]$^+$ calculated for $C_{11}H_{17}N_2O_5$: 257.1, found: 257.1. Anal. calcd for $C_{11}H_{16}N_2O_5$: C, 51.56; H, 6.29; N, 10.93. Found: C, 51.48; H, 6.21; N, 10.77.

Boc-4B-CO$_2$H: *S*-isomer, 87%, white powder, mp 160 °C (dec), $[\alpha]_D^{20}$= -80.00 (*c* = 35.42);

Boc-5B-CO$_2$H: *R*-isomer, 83%, white powder, mp 160 °C (dec), $[\alpha]_D^{20}$= +81.84 (*c* = 35.42).
^{1}H NMR (500 MHz, DMSO-*d*$_6$): *δ* 7.10, (s, 1H, *isoxaz, major rotamer*), 7.03 (s, *isoxaz, minor rotamer*), 4.91-4.86 (m, 1H, -*CH-pyrrolidine*), 3.47-3.34 (m, 3H, *CH*$_2$ + *CH-pyrrolidine*), 1.87 (br, 3H, *CH-pyrrolidine*), 1.39 (m, 3H, *CH*$_3$-*Boc*), 1.21 (s, 6H, *CH*$_3$-*Boc*). **^{13}C NMR** (125 MHz, DMSO-*d*$_6$): *δ* 167.5, 167.0, 160.8, 157.7, 153.6, 153.0, 108.0, 107.6, 79.0, 78.6, 53.2, 46.5, 46.2, 32.7, 31.4, 28.1, 27.9, 23.6, 23.0. **MS** (APCI) *m/z* [M-1H]$^+$ calculated for $C_{13}H_{17}N_2O_5$: 281.1, found: 281.1. Anal. calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.44; H, 6.28; N, 10.06.

Boc-6B-CO_2H: 85%, white powder, mp 119-121 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 13.00 (br, 1H, C-OOH), 7.27 (s, 1H, C-H, *isoxaz*), 4.22 (br, 2H, azetidine-CH_2), 3.95 (br, 3H, azetidine-CH_2+ *CH*), 1.38 (s, 9H, CH_3-*Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 165.3, 161.6, 157.7, 155.5, 108.4, 78.9, 54.1, 53.6, 28.1, 25.1. **MS** (APCI) *m/z* $[M-1H]^+$ calculated for $C_{12}H_{15}N_2O_5$: 267.1, found: 267.2. Anal. calcd for $C_{12}H_{16}N_2O_5$: C, 53.73; H, 6.01; N, 10.44. Found: C, 53.88; H, 6.05; N, 10.57.

Boc-7B-CO_2H: 81%, beige powder, mp 129-131 °C. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 7.19 (s, 1H, C-H, *isoxaz*), 3.98-3.96 (m, 2H, piperidine-CH_2), 2.99-2.96 (m, 1H, piperidine-*CH*), 2.94 (br, 2H, piperidine-CH_2), 1.89-1.87 (m, 2H, piperidine-CH_2), 1.55-1.48 (m, 2H, piperidine-CH_2), 1.40 (s, 9H, CH_3-*Boc*). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 167.6, 161.0, 157.8, 153.9, 108.0, 78.7, 43.5, 42.8, 33.3, 30.1, 28.1. **MS** (APCI) *m/z* $[M-1H]^+$ calculated for $C_{14}H_{19}N_2O_5$: 295.1, found: 295.0. Anal. calcd for $C_{14}H_{20}N_2O_5$: C, 56.75; H, 6.80; N, 9.45. Found: C, 56.63; H, 6.87; N, 9.32.

Analytical data for 3-substituted isoxazoles

Boc-2-H: *S*-isomer, 92%, white powder, mp 54-56 °C, bp = 80-82 °C, $[\alpha]_D^{20}$= -61.59 (*c* = 47.11), 99.2% *ee*, t_R =16.8 min;

Boc-3-H: *R*-isomer, 93%, white powder, mp 54-56 °C, bp = 80-82 °C, $[\alpha]_D^{20}$= +65.58 (*c* = 47.11), 97.6% *ee*, t_R = 15.56 min.**^{1}H NMR** (500 MHz, DMSO-d_6): δ 8.79 (brs, 1H, *CH-isoxaz*), 7.42 - 7.40 (m, 1H, *NH*), 6.46 (m, 1H, *isoxaz*), 4.78 (m, 1H, -*CH*), 1.38 (m, 12H, CH_3-*Boc* + CH_3). **^{13}C NMR** (125 MHz, DMSO-d_6): δ 165.5, 159.6, 154.9, 102.9, 78.1, 42.8, 28.2, 20.2. **MS** (APCI) *m/z* $[M+Boc+1H]^+$ calculated for $C_5H_9N_2O$: 113.1, found: 113.2. Anal. calcd for $C_{10}H_{16}N_2O_3$: C, 56.59; H, 7.60; N, 13.20. Found: C, 56.72; H, 7.47; N, 13.36.

Boc-4-H: *S*-isomer, 95%, white powder, mp 59-61 °C, $[\alpha]_D^{20}$= -70.00 (*c* = 41.97), 99.7% *ee*, t_R = 10.75 min;

Boc-5-H: *R*-isomer, 93%, white powder, mp 59-61 °C, $[\alpha]_D^{20}$= +68.6 (*c* = 41.97), 99.4% *ee*, t_R = 8.55 min. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 8.80 (brs, 1H, *isoxaz*), 6.47-

6.44 (m, 1H, *isoxaz*), 4.92-4.88 (m, 1H, -*CH*), 3.43-3.38 (m, 2H, *CH$_2$-pyrrolidine*), 2.25 (m, 1H, *CH-pyrrolidine*), 1.87 (brs, 3H, *CH-pyrrolidine*), 1.39-1.22 (m, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d$_6$*): *δ* 165.4, 164.9, 159.5, 153.5, 153.1, 103.2, 102.7, 78.8, 78.5, 53.1, 46.3, 46.1, 32.8, 31.5, 28.1, 27.8, 23.6, 22.9. **MS** (APCI) *m/z* $[M+Boc+1H]^+$ calculated for $C_7H_{11}N_2O$: 139.1, found: 139.2. Anal. calcd for $C_{12}H_{18}N_2O_3$: C, 60.49; H, 7.61; N, 11.76. Found: C, 60.37; H, 7.64; N, 11.93.

Boc-6-H: 89%, colorless oil, bp 84-86 °C. **^{1}H NMR** (500 MHz, DMSO-*d$_6$*): *δ* 8.89 (s, 1H, *J* = 1.5, C-H, *isoxaz*), 6.70 (d, 1H, *J* = 2.0, C-H, *isoxaz*), 4.23 (brs, 2H, azetidine-*CH$_2$*), 3.92 (brs, 3H, azetidine-*CH$_2$*), 1.39 (s, 9H, *CH$_3$-Boc*). **^{13}C NMR** (125 MHz, DMSO-*d$_6$*): *δ* 163.2, 160.1, 155.6, 103.2, 78.7, 54.4-53.7 (m), 27.9, 25.0. **MS** (APCI) *m/z* $[M+Boc+1H]^+$ calculated for $C_6H_9N_2O$: 125.1, found: 125.2. Anal. calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 58.86; H, 7.32; N, 12.28.

Peptide synthesis

Peptide chain was grown on 100 mg of Fmoc-Rink-Amide AM resin (Opregen; load 0.9-1.3 mmol/g; 0.09-0.13 mmol, 1 eq.) each. Fmoc-group was removed by treatment with 1 ml of 22 % (w/w) piperidine in DMF for 30 min. Coupling was performed with 4 eq. Fmoc-Val, 4 eq. Fmoc-Leu, and 1.5 eq. of Fmoc-AlaIso in corresponding steps. Coupling reagents were: TBTU (1 eq: 1 eq. to Fmoc-amino acid), HOBt·H_2O (1:1) and DIPEA (2:1). Coupling was performed in DMF (2 ml); Fmoc-amino acid and coupling reagents were pre-mixed for about 2 min before addition to the resin. Coupling time was 50-80 min. At the end the Fmoc-deprotected peptide chains were capped by shaking with DIPEA (300 µl) and acetic anhydride (150 µl) in DMF (3 ml) for 20 min.

Cleavage was performed by treatment of the dry resin with the cleavage cocktail of the following content: 88 % TFA/2%TIS/10% water (v/v/v). The resins were shacked with the cleavage cocktail for 1 h twice, the liquids were collected, and the volatiles were blown off by nitrogen stream during 1 h. Residues were dissolved in acetonitrile-water (1:1, v/v) mixture and freeze-dried. Crude peptides were analyzed on RP-HPLC and NMR, where it was found that **Ac-Leu-AlaIso-Val-NH$_2$** was racemized by 15 %.

Crude peptides were purified on preparative RP-HPLC on Agilent 1260 Infinity HPLC system, equipped with an Agilent-Prep-C18 column (21.2×250 mm). Water-acetonitrile gradient was used as the mobile phase (5 mM hydrochloric acid was used

as ion-paring agent). Pure peptides were obtained in 8 mg dry weight each (yield 15-22 % depending from the actual starting load).

Peptide analysis

Fmoc-AlaIso-CO_2H (17): This compound was synthesized from Boc-2**B**-CO_2H (after Boc-cleavage) and FmocOSuc by knowing similar procedure,[4] 87%, white powder, $[\alpha]_D^{20}$ = -25.69 (c = 26.43);

^{1}H NMR (500 MHz, DMSO-d_6): *δ* 7.86 (d, 1H, *J* = 7.0, *CH-arom*), *δ* 7.81 (d, 2H, *J* = 7.0, *CH-arom*), 7.66 (brs, 2H, CH-*arom* + NH), 7.39-7.37 (m, 2H, *arom*), 7.32-7.27 (m, 2H, *arom*), 6.96 (brs, 1H, *isoxaz*), 4.87-4.83 (m, 1H, *-CH*), 4.33-4.28 (m, 2H, *-CH_2*), 4.22-4.18 (m, 1H, *-CH*), 1.46 (d, 3H, *J* = 6.5, *CH_3*). **^{13}C NMR** (125 MHz, DMSO-d_6): *δ* 167.3, 161.0, 157.7, 155.6, 143.9, 140.8, 127.7, 127.1, 125.2, 120.2, 107.8, 65.5, 46.8, 43.5, 19.9. **MS** (APCI) *m/z* $[M]^+$ calculated for $C_{21}H_{18}N_2O_5$: 125.1, found: not informative.
Anal. calcd for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N, 7.40. Found: C, 66.37; H, 4.60; N, 7.16.

Ac-Leu-AlaIso-Val-NH_2: ^{1}H NMR (700 MHz, CD_3OD):

	NH (before exchange)			AlaIso arom.	α-CH (after NH→ND exchange)			β-CH	CH_3	γ-CH	β-CH_2	β-CH_3	CH_3-groups			
	AlaIso	Val	Leu		AlaIso	Leu	Val	Val	Ac	Leu	Leu	AlaIsio	Val	Val	Leu	Leu
^{1}H NMR (MeOD, 700 MHz):																
δ, ppm	8.64	8.49	8.15	6.95	5.19	4.41	4.39	2.20	2.00	1.67	1.57	1.56	1.04	1.02	0.97	0.94
mult.	d	d	D	s	q	dd	d	oct.	s	m	m	d	d	d	d	d
J, Hz	8	8	6		7	6&9	8	7				7	7	7	6.5	6.5
int.	-	-	-	1H	1H	1H	1H	1H	3H	1H	2H	3H	3H	3H	3H	3H
^{13}C{1H} NMR (MeOD, 176 MHz):																
δ, ppm	-	-	-	105.0	42.1	51.9	58.7	30.5	21.0	24.5	40.6	18.2	18.3	17.4	22.0	20.6

ESI-MS: Calcd. $[M]^+$ 409.2, detect. 410.2 $[M+H]^+$ and 432.2 $[M+Na]^+$.

Ac-Leu-Val-AlaIso-NH_2: ^{1}H NMR (700 MHz, CD_3OD):

	NH (before exchange)			AlaIso arom.	α-CH (after NH→ND exchange)			β-CH	CH_3	γ-CH	β-CH_2	β-CH_3	CH_3-groups			
	AlaIso	Val	Leu		AlaIso	Leu	Val	Val	Ac	Leu	Leu	AlaIso	Val	Val	Leu	Leu
^{1}H NMR (MeOD, 700 MHz):																
δ, ppm	8.63	7.91	-	6.91	5.18	4.41	4.17	2.05	1.99	1.67	1.57	1.53	0.96	0.94-0.91		
mult.	d	d	-	s	q	t	d	oct.	s	m	t	d	d	m		
J, Hz	8	8	-		7	7	7	7			7	7	7			
int.	-	-	-	1H	1H	1H	1H	1H	3H	1H	2H	3H	3H	9H		
^{13}C{1H} NMR (MeOD, 176 MHz):																
δ, ppm	-	-	-	105.0	42.1	52.0	58.6	30.8	21.0	24.5	40.2	18.30	22.0	20.6; 18.33; 17.2		

ESI-MS: Calcd. $[M]^+$ 409.2, detect. 410.2 $[M+H]^+$ and 432.2 $[M+Na]^+$.

X-ray measurement details for compound Boc-6A-CO_2H:

The structure of compound Boc-**6A**-CO_2H was corroborated by X-ray crystallography (Fig. 1, Tables 1-3).

Azetidine core (Fig. 1) is flat with 0.01 Å precision. Atom (N2) has pyramidal configuration and the sum of valence angles which are centered on it is 355°. Isoxazole core is in pseudoaxial position (the torsion angle C(1)-C(4)-C(5)-N(2) 115.2(2)°) and is twisted in a way, that the angle between the planes of two heterocycles is 121°. This leads to the attractive interaction C(5)-H(5b)…N(1) 2.47 Å (the sum of Van der Waals radii is 2.67 Å),[5] which itself should not be considered as a hydrogen bond because of too acute angle C-H…N (104°). Carboxylic group is almost coplanar with the plane of isoxazole core (the torsion angle C(1)-C(2)-C(12)-O(4) 4.1(3)°). The carboxylic group is almost coplanar with the plane of isoxazole core (the torsion angle C(1)-C(2)-C(12)-O(4) 4.1(3)°). *Tert*-butyloxycarbonyl substituent is slightly twisted relative to the plane of isoxazole core (the torsion angle C(5)-N(2)-C(7)-O(2) 16.1(3)°), and its *tert*-butyloxycarbonyl substituent is in *ar*-conformation relating to N(2)-C(7) bond and is twisted in a way that C(8)-C(11) bond is almost antiperiplanar to C(7)-O(3) bond (the torsion angles C(8)-O(3)-C(7)-N(2) -167.5(2)°, C(7)-O(3)-C(8)-C(11) 168.6(2)°).

The molecules in the crystal lattice of Boc-**6A**-CO_2H are represented as endless chains (Fig. 2) toward the crystallographic direction [0 1 0] because of strong hydrogen intermolecular interaction O(5)-H…O(2)' (x, y-1, z) H…O 1.76 Å O-H…O 173°, which leads to the elongation of the bond C(7)-O(2) up to 1.227(2) Å compared to its average value being 1.210 Å.[6]

X-ray: Experimental part.

The crystals of Boc-**6A**-CO_2H are monoclinic, $C_{12}H_{16}N_2O_5$ at -173°C ***a*** = 16.0117(9), ***b*** = 9.6657(9), ***c*** = 17.4382(9) Å, β = 101.948(7)°, V = 2640.3(3) $Å^3$, M_r = 268.27, Z = 8, the spatial group C2/c, d_{ded}= 1.350 g/cm^3, $\mu(MoK_\alpha)$ = 0.106 mm^{-1}, F(000) = 1136. The parameters of elementary cell with intencities 12594 of reflections (3848 independent, R_{int}=0.054) are recorder on «Xcalibur-3» difractometer (with CCD-detector, graphite-monochromated radiation MoK_α, ω-scanning, $2\theta_{max}$= 60°).

The structures were solved by direct methods approach using the SHELXS-97 12 program and refined with the SHELXTL.[7] The positions of hydrogen atoms are refined by deductive synthesis of electron density and are corrected using a "riding model" with $U_{iso} = nU_{equiv}$ non-hydrogen atom, which is connected with that hydrogen one (n=1.5 for methyl groups and n=1.2 for the other hydrogen atoms). Carboxylic hydrogen, which is taking part in the formation of intermolecular hydrogen, is corrected by isotropic approximation. The structure is corrected by F^2 matrical least square analysis in anisotropic approximation for non-hydrogen atoms to wR_2 = 0.128 by 3826 reflections (R_1 = 0.058 by 2055 reflections c F>4σ(F), S = 1.009). The data collection namely coordinates of the corresponding atoms are depicted in Table **1**, bond lengths and valence angels are depicted in Tables **2** and **3** respectively.

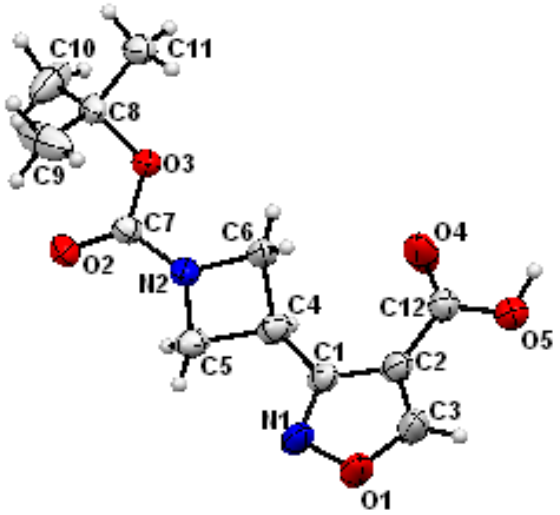

Figure 1. ORTEP representation of Boc-**6A**-CO2H. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

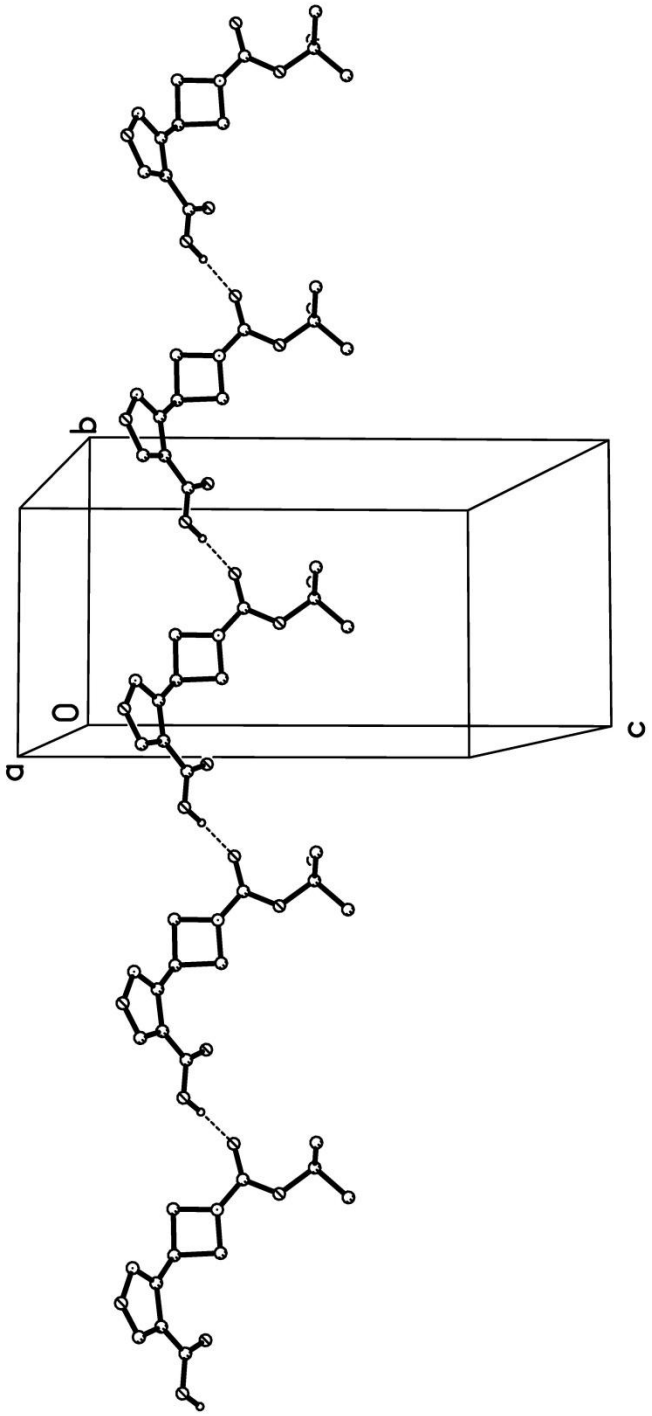

Figure 2. Packing of molecules in the crystal lattice of Boc-**6A**-CO_2H.

Table 1. Coordinates ($\times 10^4$), equivalent isotropic heat parameters ($Å^2 \times 10^3$) of atoms in structure Boc-**6A**-CO_2H.

	x	y	z	U(eq)
O(1)	-426(1)	507(1)	616(1)	65(1)
O(2)	1546(1)	5584(1)	3097(1)	43(1)
O(3)	1625(1)	3846(1)	3992(1)	33(1)
O(4)	1652(1)	-1169(1)	2582(1)	68(1)
O(5)	740(1)	-2758(1)	1974(1)	47(1)
N(1)	164(1)	1564(2)	926(1)	50(1)
N(2)	1338(1)	3348(2)	2740(1)	42(1)
C(1)	731(1)	956(2)	1470(1)	39(1)
C(2)	552(1)	-474(2)	1536(1)	43(1)
C(3)	-170(2)	-668(2)	992(1)	57(1)
C(4)	1449(1)	1776(2)	1937(1)	41(1)
C(5)	1357(1)	3370(2)	1901(1)	40(1)
C(6)	1451(1)	1846(2)	2829(1)	42(1)
C(7)	1510(1)	4356(2)	3267(1)	33(1)
C(8)	1653(1)	4741(2)	4682(1)	37(1)
C(9)	888(2)	5688(3)	4545(1)	87(1)
C(10)	2495(2)	5507(3)	4845(1)	73(1)
C(11)	1605(1)	3720(2)	5325(1)	44(1)
C(12)	1042(1)	-1485(2)	2083(1)	42(1)

Table 2. Bond lengths (Å) in structure Boc-**6A**-CO_2H**.**

O(1)-C(3)	1.334(2)	O(1)-N(1)	1.420(2)
O(2)-C(7)	1.227(2)	O(3)-C(7)	1.334(2)
O(3)-C(8)	1.475(2)	O(4)-C(12)	1.204(2)
O(5)-C(12)	1.323(2)	N(1)-C(1)	1.309(2)
N(2)-C(7)	1.329(2)	N(2)-C(6)	1.467(2)
N(2)-C(5)	1.469(2)	C(1)-C(2)	1.421(3)

C(1)-C(4)	1.491(3)	C(2)-C(3)	1.347(3)
C(2)-C(12)	1.474(2)	C(4)-C(5)	1.548(3)
C(4)-C(6)	1.556(3)	C(8)-C(9)	1.508(3)
C(8)-C(11)	1.507(2)	C(8)-C(10)	1.514(3)

Table 3. Valence angles [°] for structure Boc-**6A**-CO_2H**.**

C(3)-O(1)-N(1)	108.2(1)	C(7)-O(3)-C(8)	122.1(1)
C(1)-N(1)-O(1)	105.1(2)	C(7)-N(2)-C(6)	130.5(1)
C(7)-N(2)-C(5)	129.3(2)	C(6)-N(2)-C(5)	95.3(1)
N(1)-C(1)-C(2)	111.9(2)	N(1)-C(1)-C(4)	119.9(2)
C(2)-C(1)-C(4)	128.2(2)	C(3)-C(2)-C(1)	103.8(2)
C(3)-C(2)-C(12)	128.9(2)	C(1)-C(2)-C(12)	127.4(2)
O(1)-C(3)-C(2)	111.0(2)	C(1)-C(4)-C(5)	116.8(2)
C(1)-C(4)-C(6)	114.3(2)	C(5)-C(4)-C(6)	88.7(1)
N(2)-C(5)-C(4)	88.1(1)	N(2)-C(6)-C(4)	87.9(1)
O(2)-C(7)-N(2)	123.8(2)	O(2)-C(7)-O(3)	125.6(2)
N(2)-C(7)-O(3)	110.6(1)	O(3)-C(8)-C(9)	109.9(2)
O(3)-C(8)-C(11)	103.1(1)	C(9)-C(8)-C(11)	110.5(2)
O(3)-C(8)-C(10)	108.4(2)	C(9)-C(8)-C(10)	113.3(2)
C(11)-C(8)-C(10)	111.2(2)	O(4)-C(12)-O(5)	123.9(2)
O(4)-C(12)-C(2)	122.9(2)	O(5)-C(12)-C(2)	113.2(2)

X-ray measurement details for compound Boc-4A-COMe:

The structure of compound Boc-**4A**-COMe was corroborated by X-ray crystallography (Fig. 3, Tables 4-6).

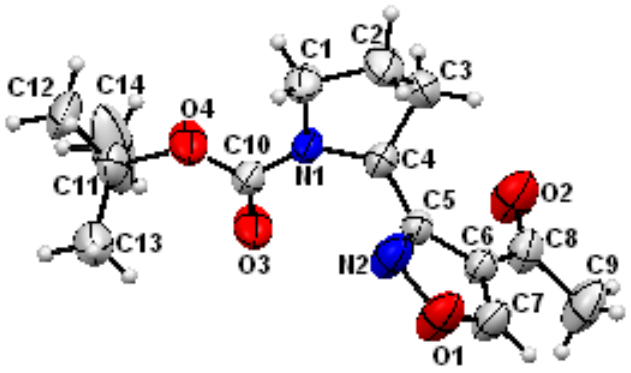

Figure 3. ORTEP representation of Boc-**4A**-COMe. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

Pyrrolidine core is in a twist conformation with a slight deviations for atoms C(2) and C(3) (0.24 Å and -0.36 Å, respectively) from the plane of other atoms resided in the cycle. Spatial orientation of isoxazole core is axial (torsion angle C(1)-N(1)-C(4)-C(5) 106.5(2)º) and slightly twisted relating to the endocyclic bond N(1)-C(4) (torsion angle N(1)-C(4)-C(5)-N(2) -17.3(2)º). Slight steric repulsion between atoms of isoxazole core and substituent at atom C(6) (shortened intermolecular interaction H(7)...C(9) 2.78 Å with regards of Van der Waals radii[5] 2.87 Å) leads to their slight noncomplanarity (torsion angle C(5)-C(6)-C(8)-O(2) 7.0(3)º). Carboxylic fragment of the substituent on atom N(1) is slightly twisted toward endocyclic bond C(4)-N(1) (torsion angle C(4)-N(1)-C(10)-O(3) 10.5(2)º), and *tert*-butyl group is situated at ar-position toward N(1)-C(10) bond and is twisted in a way that C(11)-C(12) bond is antiperiplanar to C(10)-O(4) bond (torsion angles C(11)-O(4)-C(10)-N(1) 172.5(1)º, C(10)-O(4)-C(11)-C(12) - 176.1(2)º).

In the crystal lattice between molecules of Boc-**4A**-COMe we have observed a weak intermolecular hydrogen interaction C(7)-H...O(3)' (0.5+x, 1.5-y, 1-z) H...O 2.32 Å C-H...O 174º.

The crystals of Boc-**4A**-COMe are rhomboidal, $\cdot C_{14}H_{20}N_2O_4$ at 20°C ***a*** = 8.7120(4), ***b*** = 11.1379(7), ***c*** = 15.7491(8) Å, V = 1528.2(1) $Å^3$, M_r = 280.32, Z = 4, spatial group $P2_12_12_1$, d_{ded}= 1.218 g/cm^3, $\mu(MoK_\alpha)$ = 0.090 mm^{-1}, F(000) = 600. Parameters of elementary cell and intencities 8931 reflections (4444 independed, R_{int}=0.023) were recorded on) are recorder on «Xcalibur-3» difractometer (with CCD-detector, graphite-monochromated radiation MoK_α, ω-scanning, $2\theta_{max}$= 60°).

The structures were solved by direct methods approach using the SHELXTL program.[7] The positions of hydrogen atoms are refined by deductive synthesis of electron density and are corrected using a "riding model" with $U_{iso} = nU_{equiv}$ non-hydrogen atom, which is connected with that hydrogen one (n=1.5 for methyl groups and n=1.2 for the other hydrogen atoms). Carboxylic hydrogen, which is taking part in the formation of intermolecular hydrogen, is corrected by isotropic approximation. The structure is corrected by F^2 matrical least square analysis in anisotropic approximation for non-hydrogen atoms to wR_2 = 0.114 by 4353 reflections (R_1 = 0.048 by 3089 reflections c $F>4\sigma(F)$, S = 0.990). The data collection namely coordinates of the corresponding atoms are depicted in Table **4**, bond lengths and valence angels are depicted in Tables **5** and **6** respectively.

Table 4. Coordinates ($\times 10^4$), equivalent isotropic heat parameters ($Å^2 \times 10^3$) of atoms in structure Boc-**4A**-COMe.

	x	y	z	U(eq)
O(1)	5811(2)	8217(1)	4597(1)	88(1)
O(2)	3375(2)	4654(1)	4671(1)	86(1)
O(3)	1368(1)	7797(1)	2876(1)	68(1)
O(4)	2234(1)	8136(1)	1532(1)	57(1)
N(1)	3595(1)	7012(1)	2398(1)	49(1)
N(2)	5240(2)	7907(1)	3772(1)	71(1)
C(1)	4680(2)	6764(2)	1709(1)	60(1)
C(2)	5813(2)	5919(2)	2119(1)	72(1)
C(3)	4876(2)	5272(2)	2787(1)	63(1)
C(4)	3827(2)	6252(1)	3133(1)	46(1)
C(5)	4544(2)	6891(1)	3875(1)	45(1)
C(6)	4604(2)	6497(1)	4736(1)	47(1)
C(7)	5403(2)	7369(2)	5136(1)	65(1)

C(8)	3949(2)	5411(2)	5111(1)	57(1)
C(9)	4002(3)	5289(2)	6061(1)	88(1)
C(10)	2307(2)	7663(2)	2314(1)	47(1)
C(11)	871(2)	8772(2)	1218(1)	64(1)
C(12)	1324(4)	9039(3)	311(1)	123(1)
C(13)	664(3)	9927(2)	1689(1)	82(1)
C(14)	-513(3)	7977(3)	1285(3)	159(2)

Table 5. Bond lengths (Å) in structure Boc-**4A**-COMe**.**

O(1)-C(7)	1.319(2)	O(1)-N(2)	1.433(2)
O(2)-C(8)	1.200(2)	O(3)-C(10)	1.215(2)
O(4)-C(10)	1.341(2)	O(4)-C(11)	1.469(2)
N(1)-C(10)	1.342(2)	N(1)-C(4)	1.449(2)
N(1)-C(1)	1.465(2)	N(2)-C(5)	1.294(2)
C(1)-C(2)	1.509(2)	C(2)-C(3)	1.514(3)
C(3)-C(4)	1.524(2)	C(4)-C(5)	1.504(2)
C(5)-C(6)	1.426(2)	C(6)-C(7)	1.351(2)
C(6)-C(8)	1.462(2)	C(8)-C(9)	1.504(2)
C(11)-C(13)	1.495(3)	C(11)-C(14)	1.500(3)
C(11)-C(12)	1.512(3)		

Table 6. Valence angles [°] for structure Boc-**4A**-COMe**.**

C(7)-O(1)-N(2)	108.5(1)	C(10)-O(4)-C(11)	122.6(1)
C(10)-N(1)-C(4)	120.7(1)	C(10)-N(1)-C(1)	124.6(1)
C(4)-N(1)-C(1)	113.1(1)	C(5)-N(2)-O(1)	105.1(1)
N(1)-C(1)-C(2)	102.8(1)	C(1)-C(2)-C(3)	104.0(1)
C(2)-C(3)-C(4)	103.4(1)	N(1)-C(4)-C(5)	113.7(1)
N(1)-C(4)-C(3)	102.5(1)	C(5)-C(4)-C(3)	111.6(1)
N(2)-C(5)-C(6)	111.8(1)	N(2)-C(5)-C(4)	120.8(1)
C(6)-C(5)-C(4)	127.4(1)	C(7)-C(6)-C(5)	104.0(1)
C(7)-C(6)-C(8)	127.4(1)	C(5)-C(6)-C(8)	128.6(1)
O(1)-C(7)-C(6)	110.7(1)	O(2)-C(8)-C(6)	120.8(1)

O(2)-C(8)-C(9)	121.5(2)	C(6)-C(8)-C(9)	117.7(2)
O(3)-C(10)-O(4)	126.0(1)	O(3)-C(10)-N(1)	123.9(1)
O(4)-C(10)-N(1)	110.1(1)	O(4)-C(11)-C(13)	110.2(1)
O(4)-C(11)-C(14)	109.9(2)	C(13)-C(11)-C(14)	112.1(2)
O(4)-C(11)-C(12)	101.7(2)	C(13)-C(11)-C(12)	109.4(2)
C(14)-C(11)-C(12)	113.1(3)		

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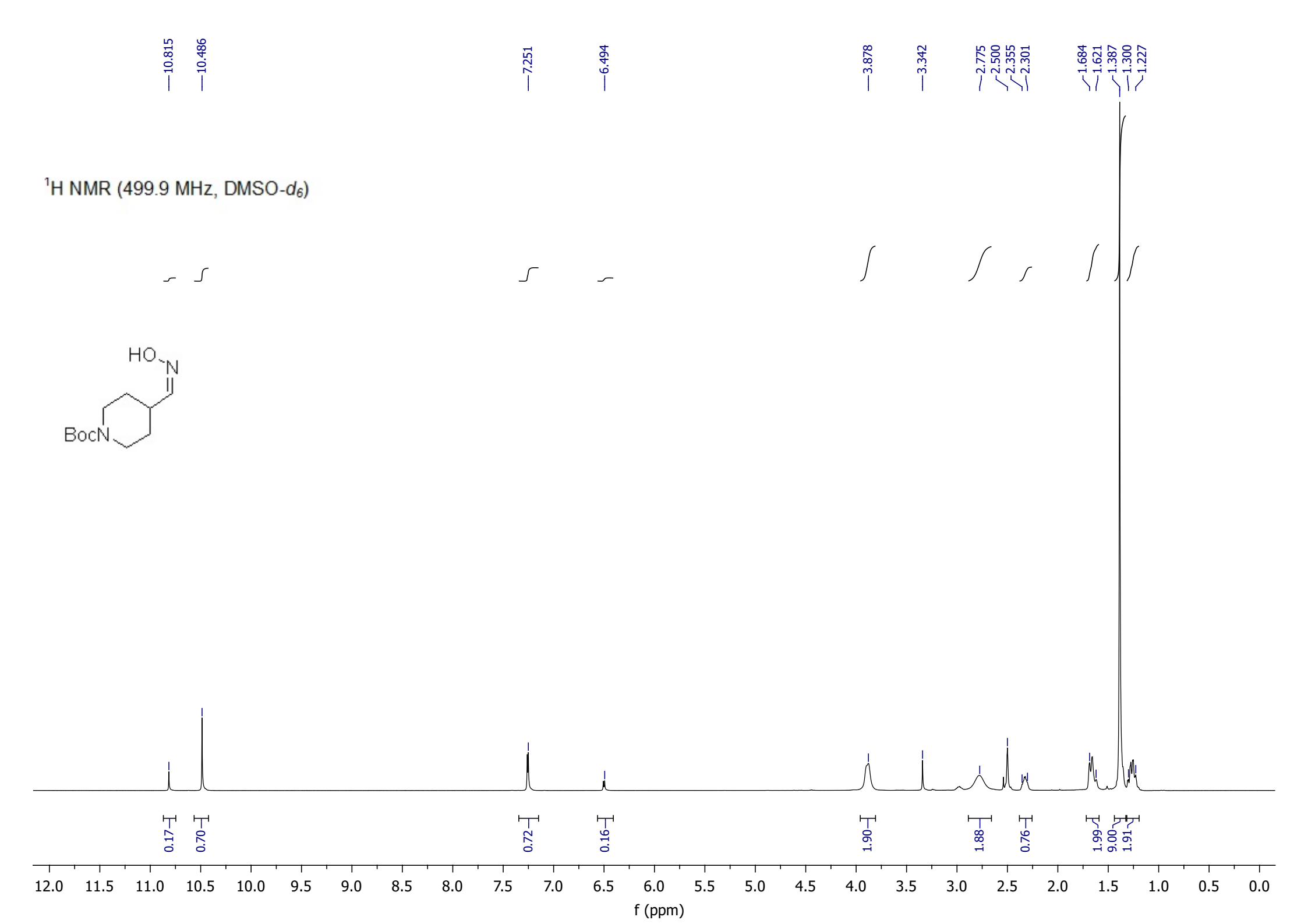
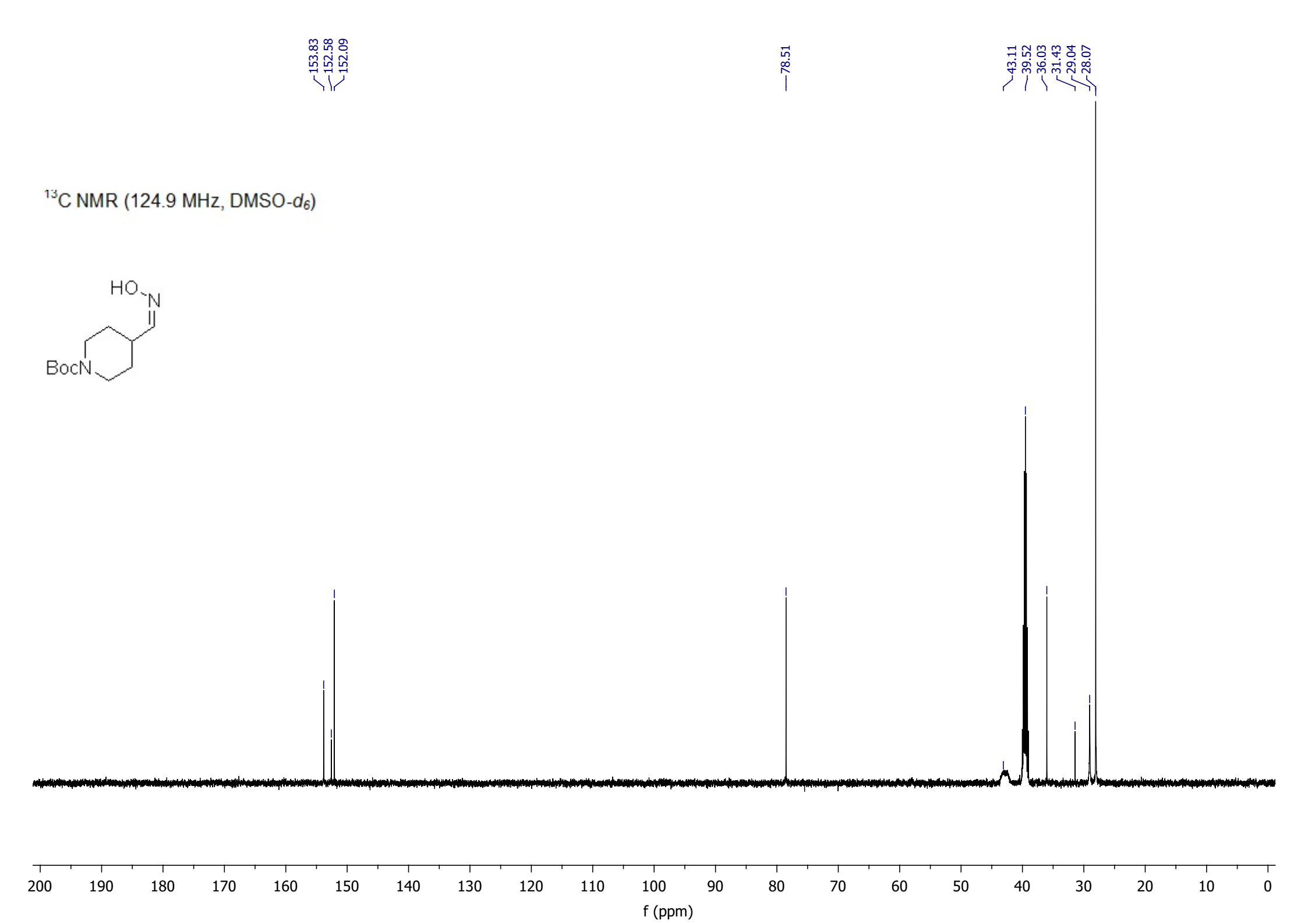
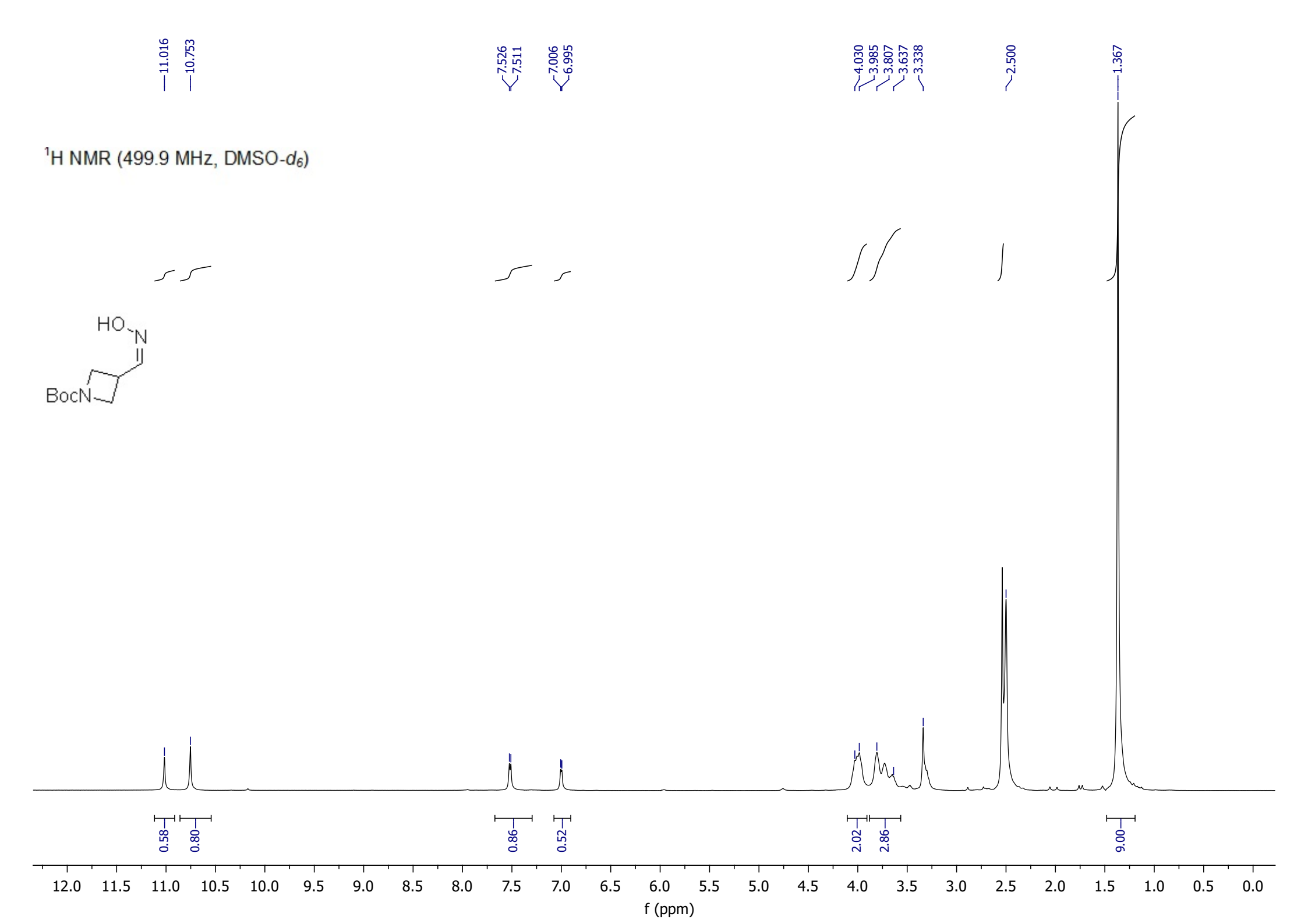
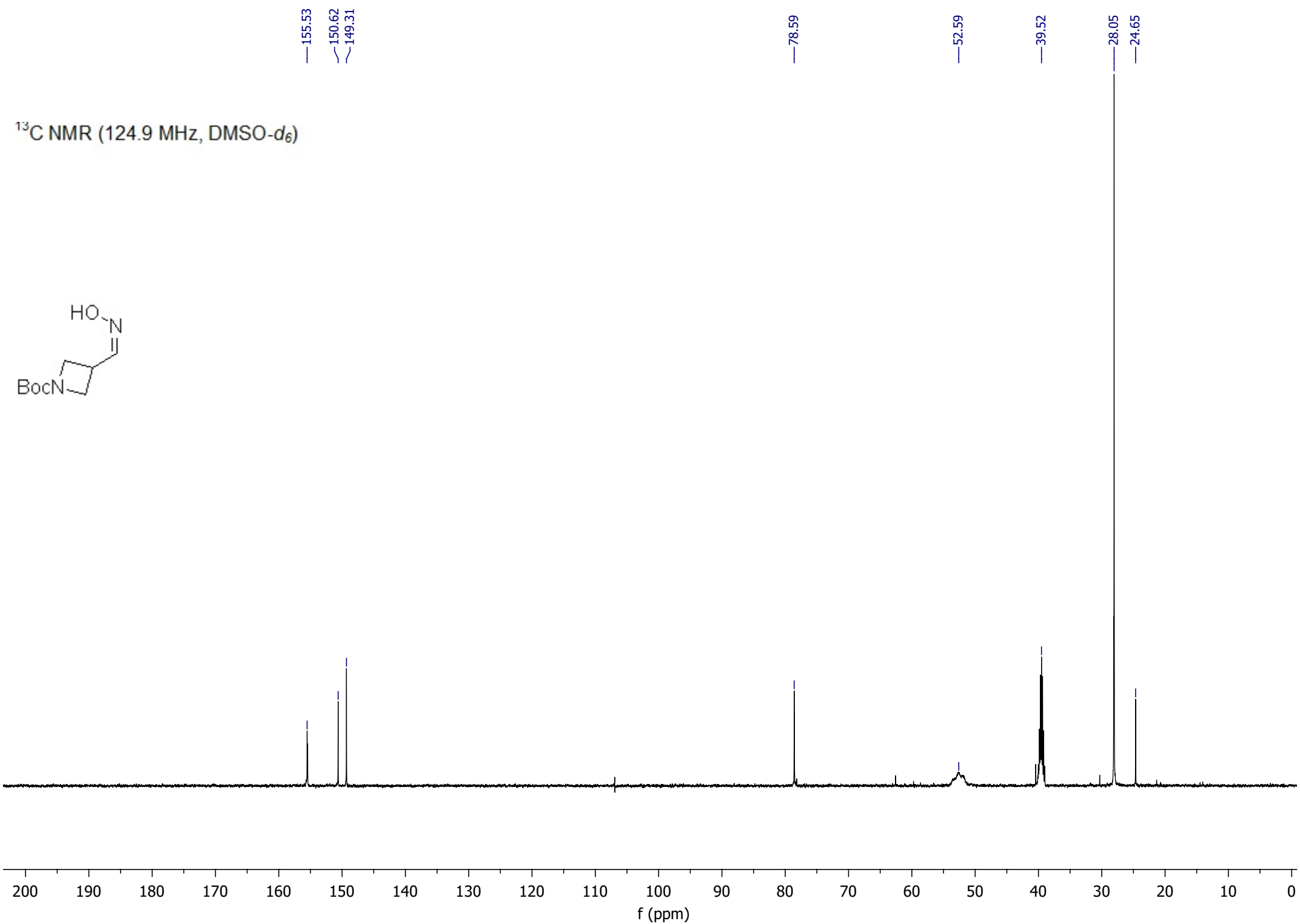
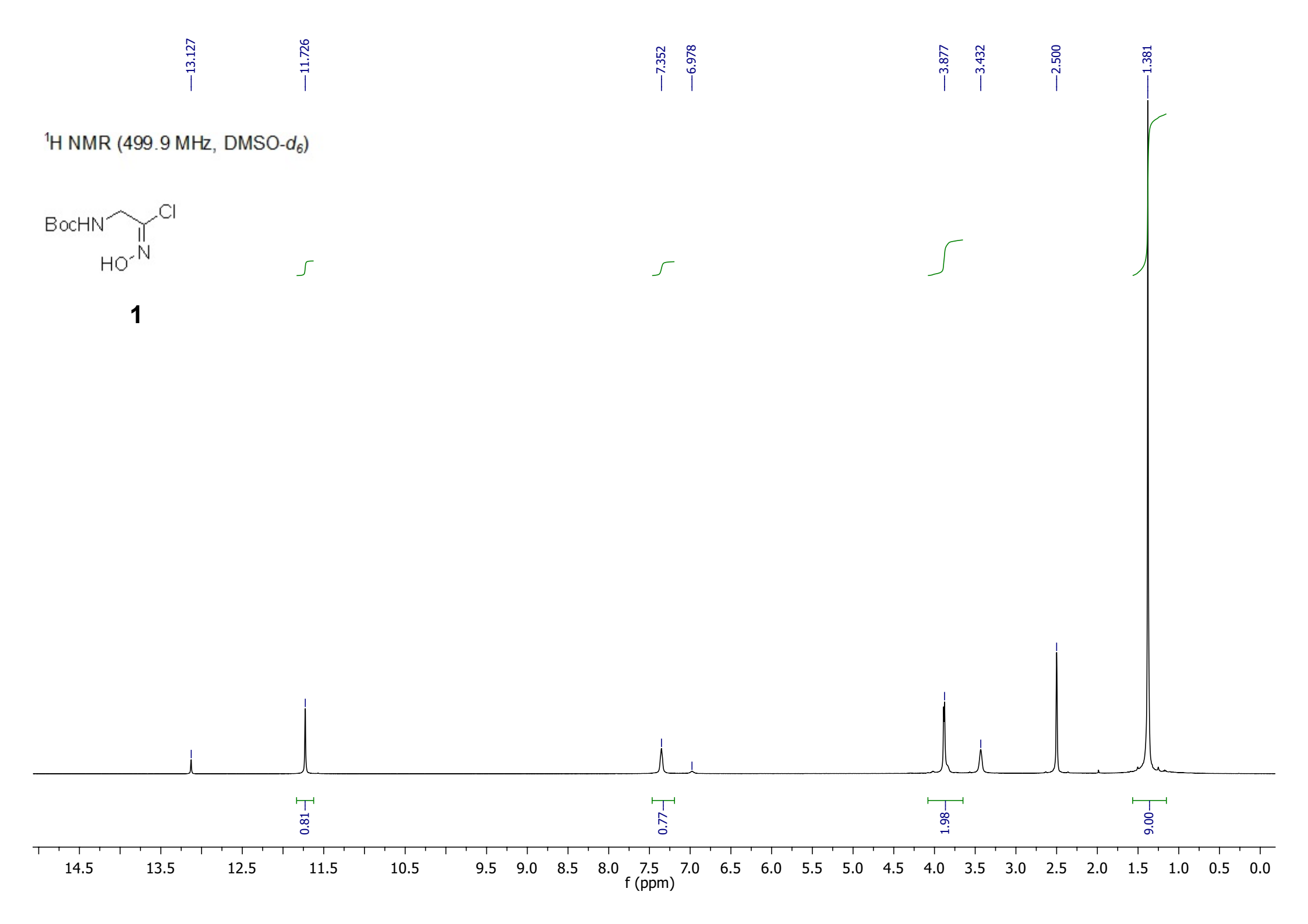
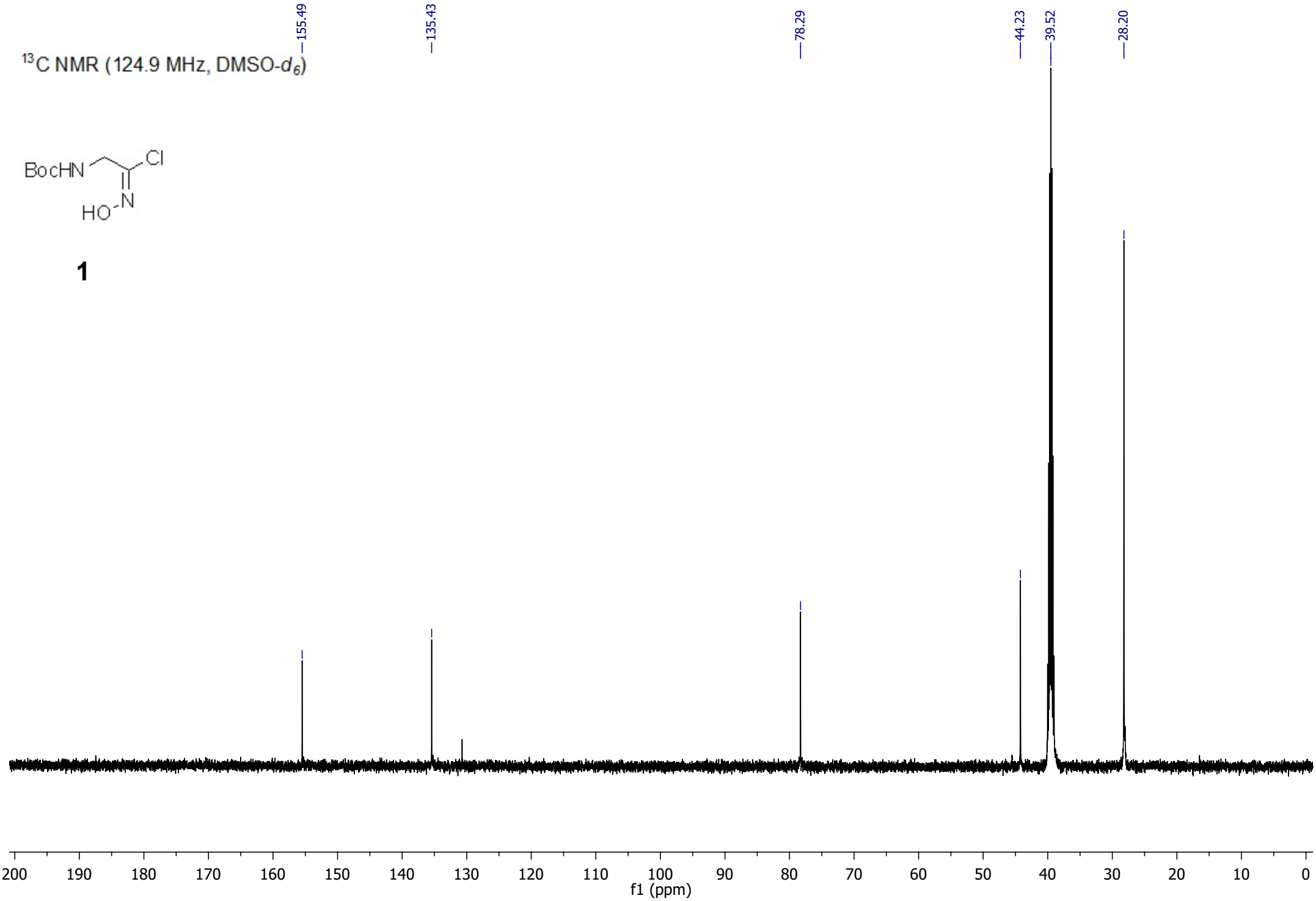

10.815
10.486
7.251
6.494
3.878
3.342
2.775
2.500
2.355
2.301
1.684
1.621
1.387
1.300
1.227
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
N
BocN
0.17
0.70
0.72
0.16
1.90
1.88
0.76
1.99
9.00
1.91
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f (ppm)

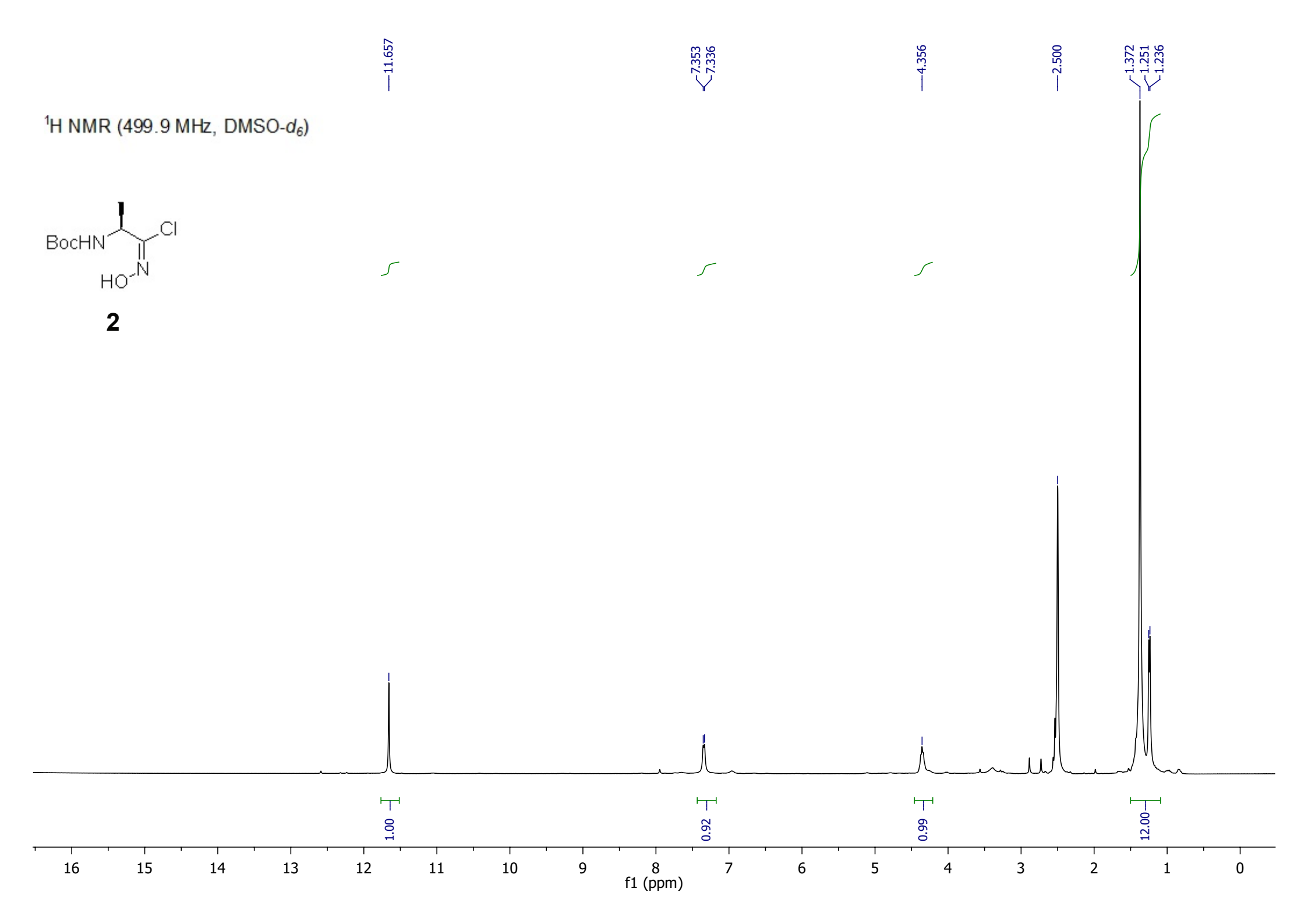

153.83
152.58
152.09
78.51
43.11
39.52
36.03
31.43
29.04
28.07
^{13}C NMR (124.9 MHz, DMSO-d_6)
HO
N
BocN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)


11.016
10.753
7.526
7.511
7.006
6.995
4.030
3.985
3.807
3.637
3.338
2.500
1.367
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
N
BocN
0.58
0.80
0.86
0.52
2.02
2.86
9.00
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
f (ppm)

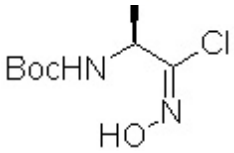

155.53
150.62
149.31
78.59
52.59
39.52
28.05
24.65
^{13}C NMR (124.9 MHz, DMSO-d_6)
HO
N
BocN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)


13.127
11.726
7.352
6.978
3.877
3.432
2.500
1.381
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
Cl
N
HO
1
0.81
0.77
1.98
9.00
14.5 13.5 12.5 11.5 10.5 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
f (ppm)


155.49
135.43
78.29
44.23
39.52
28.20
13C NMR (124.9 MHz, DMSO-d6)
BocHN
Cl
HO
N
1
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11.657
7.353
7.336
4.356
2.500
1.372
1.251
1.236
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
Cl
N
HO
2
1.00
0.92
0.99
12.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

^{13}C NMR (124.9 MHz, DMSO-d_6)



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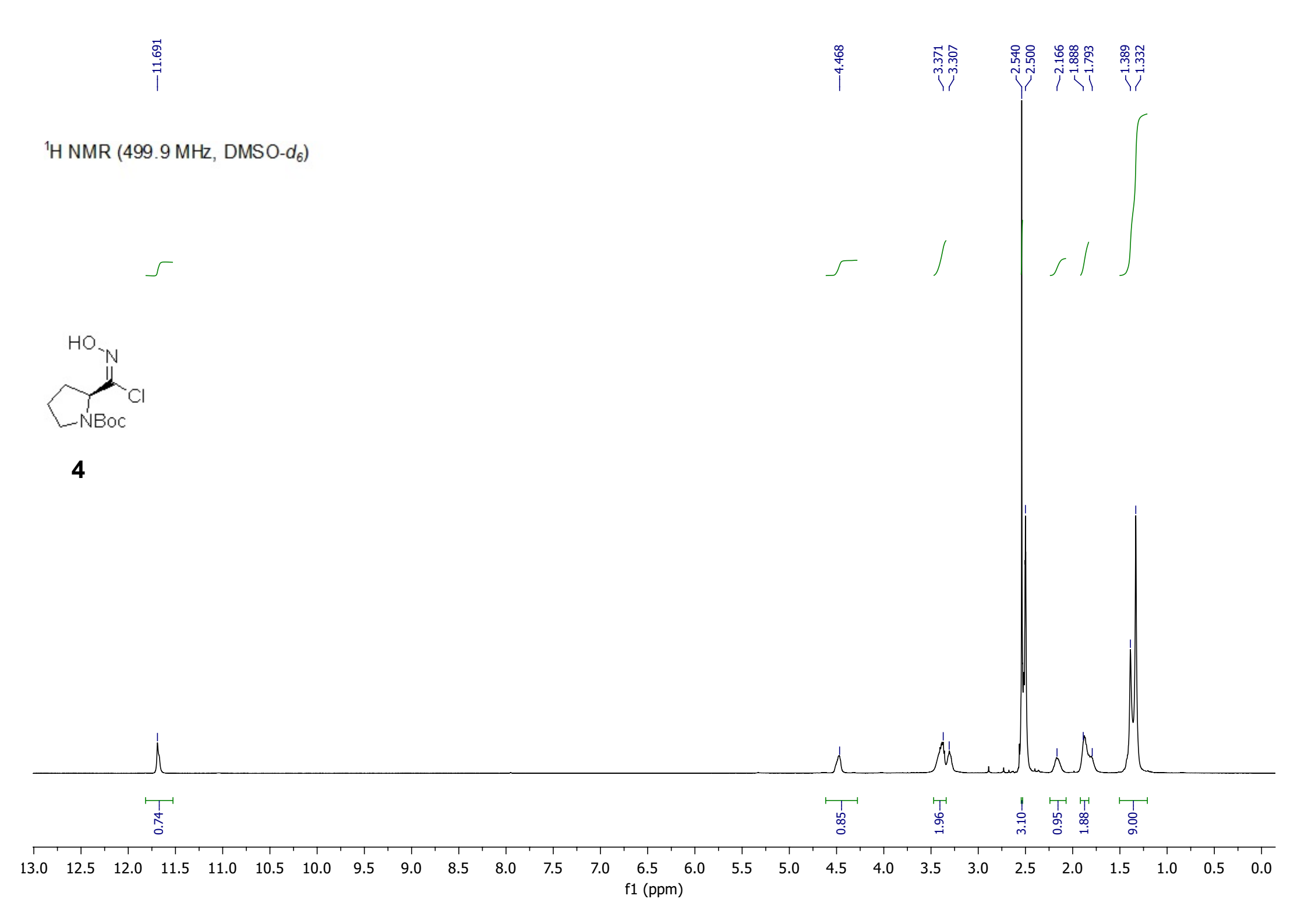
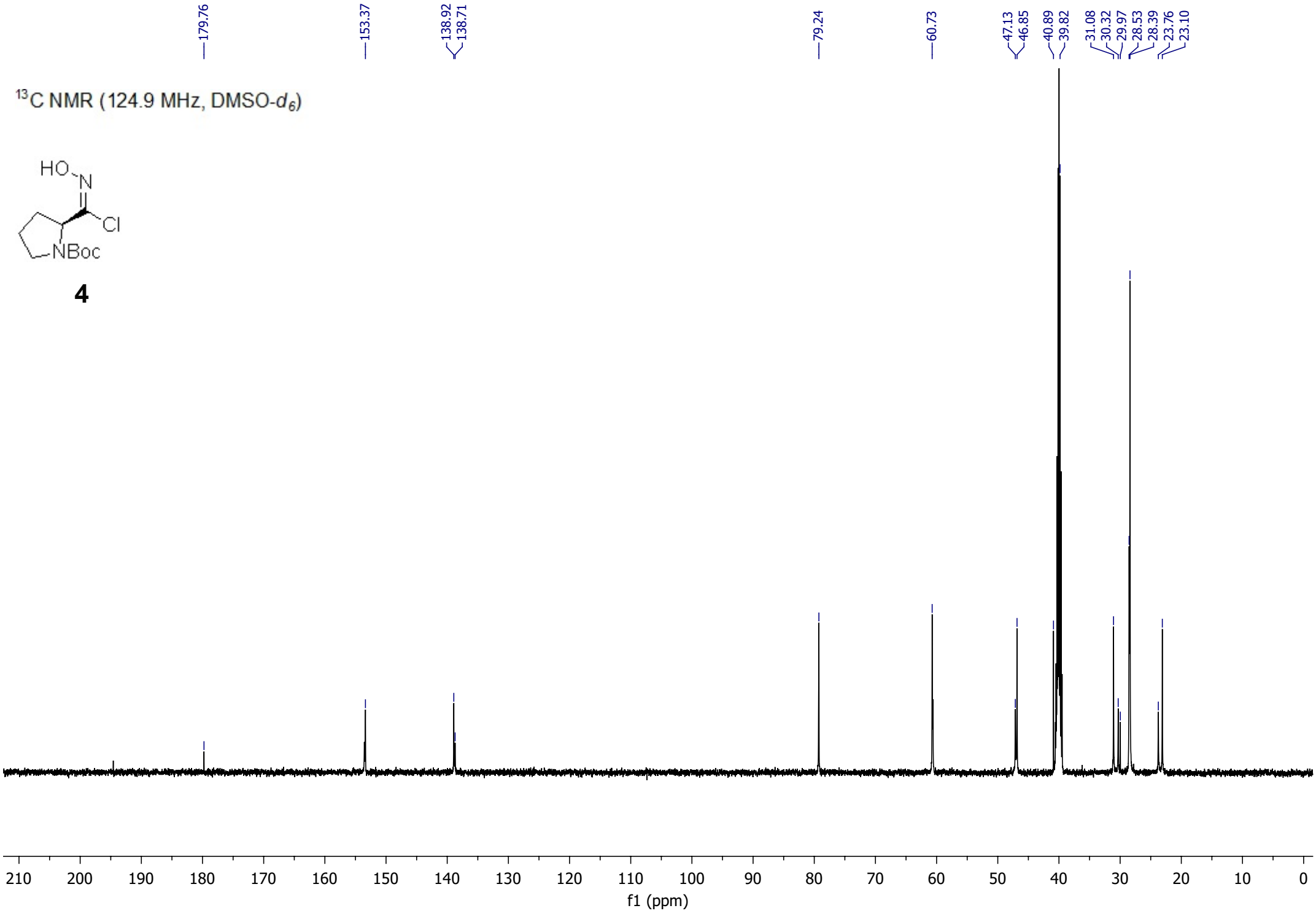
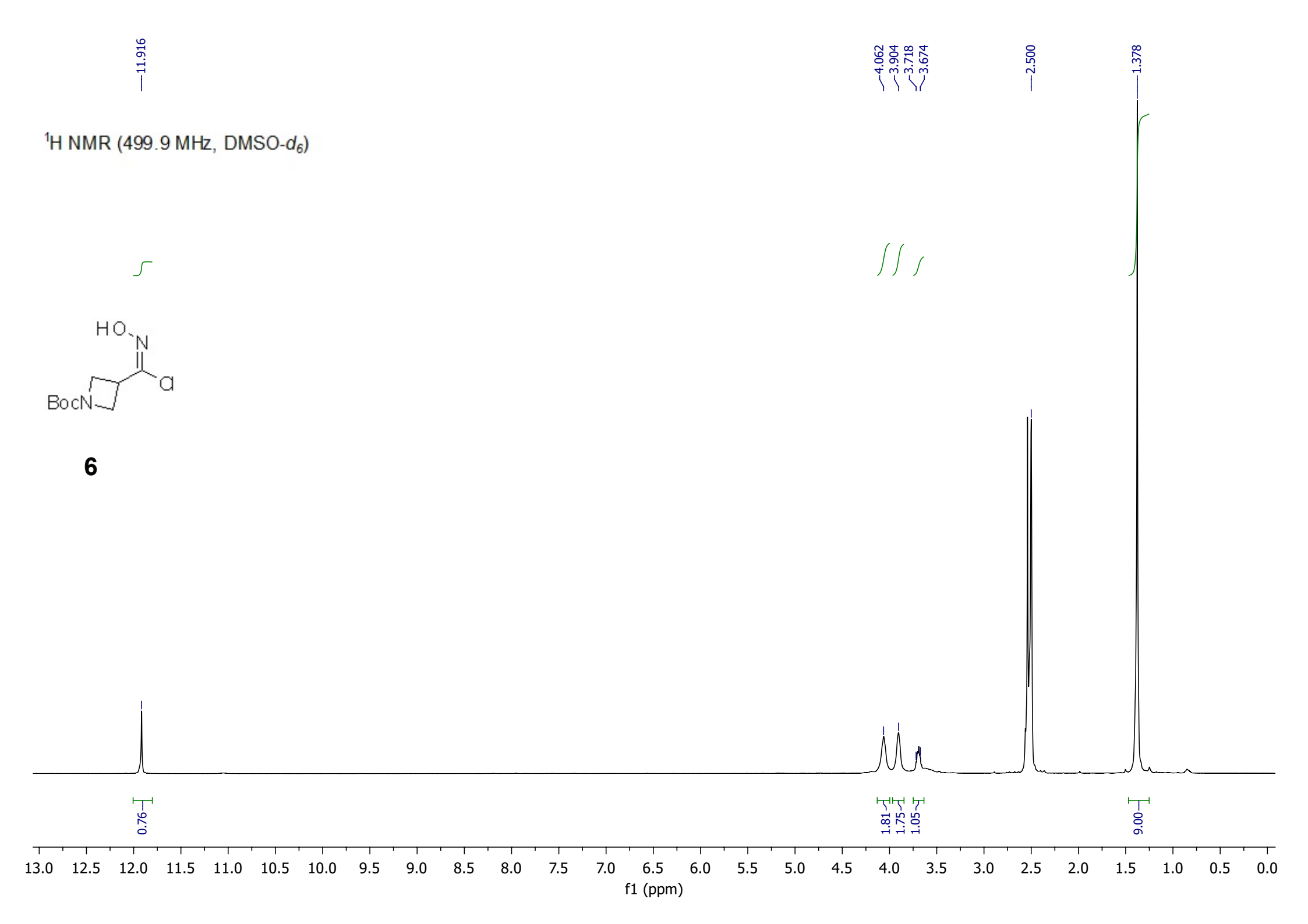
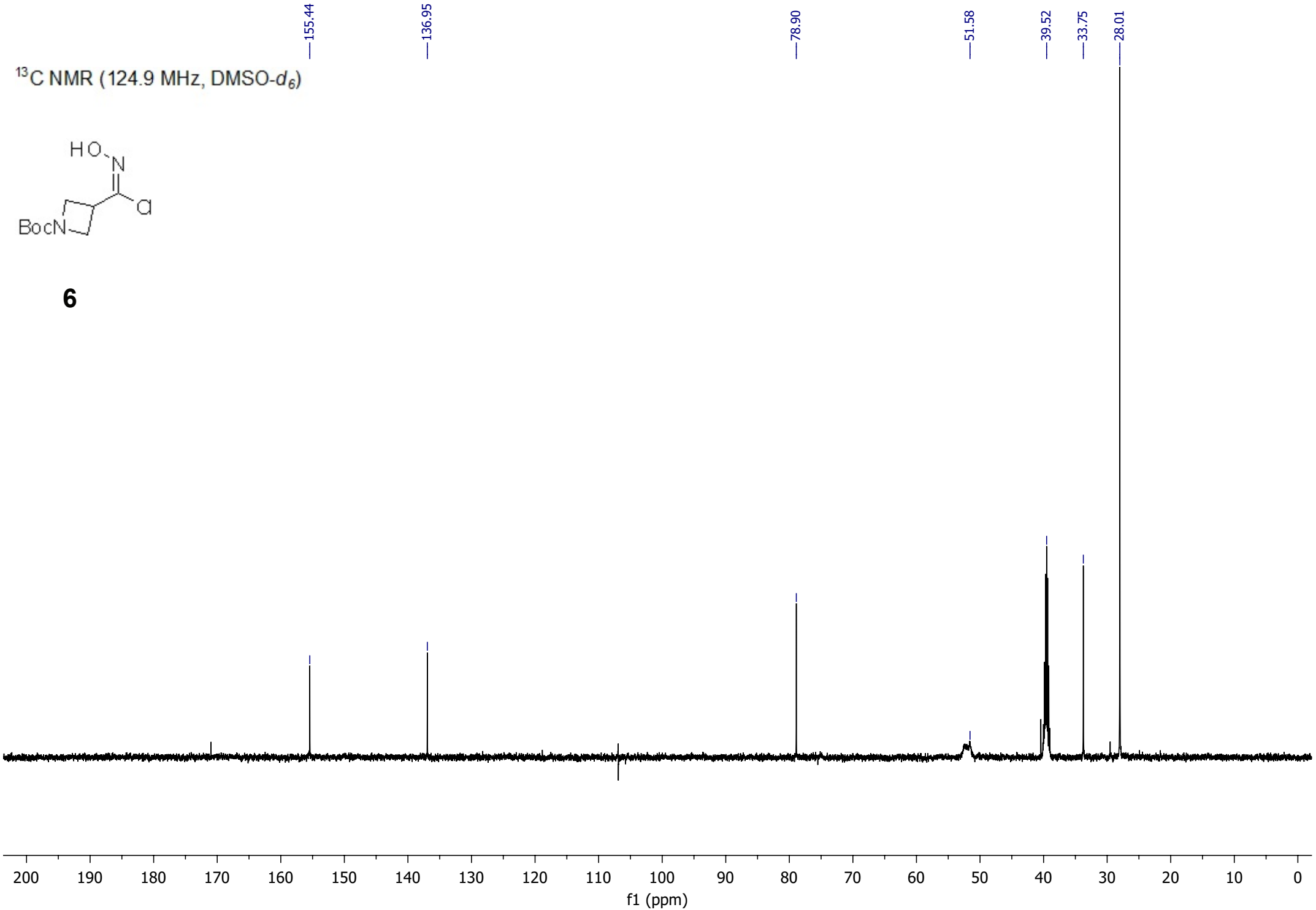
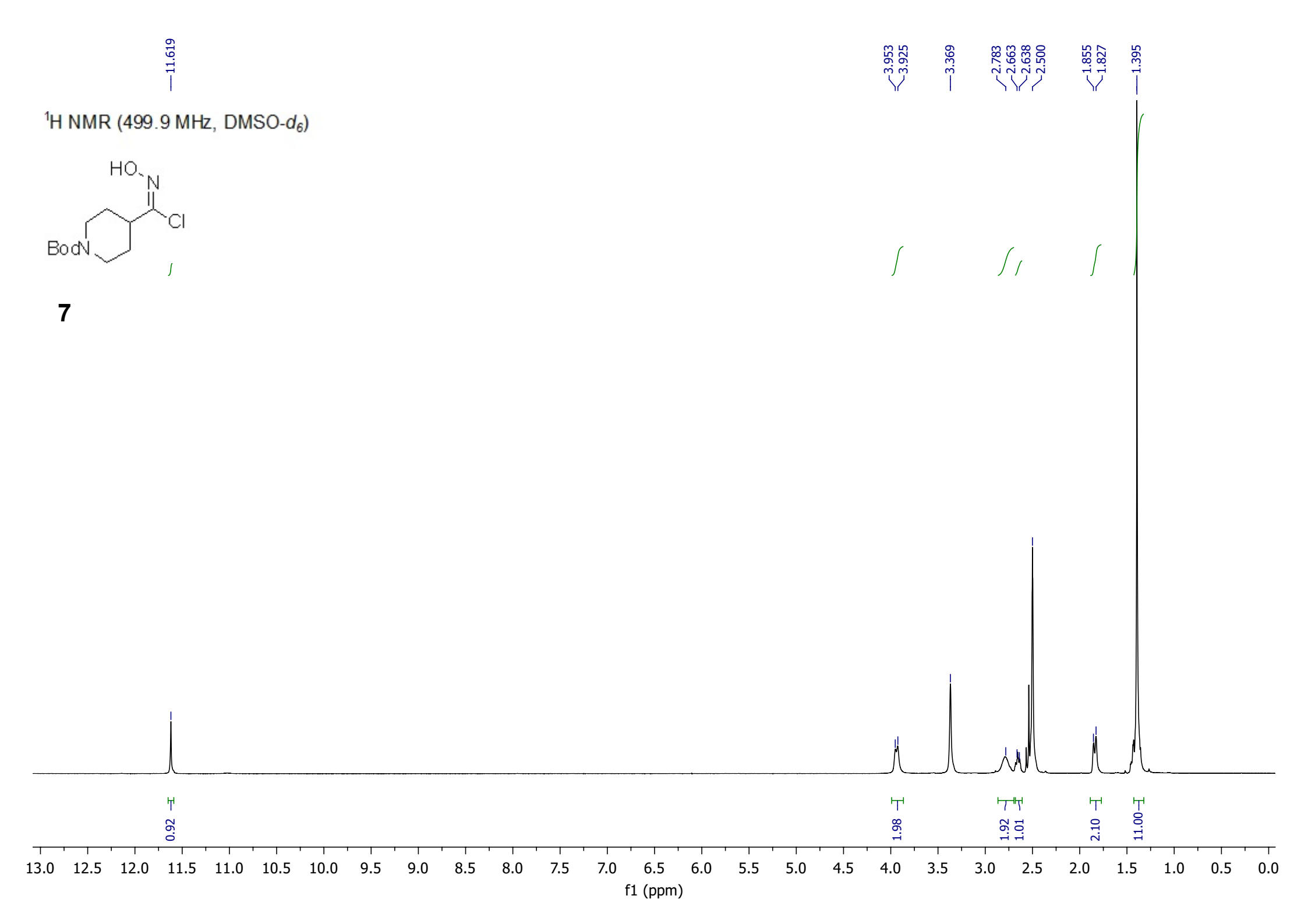
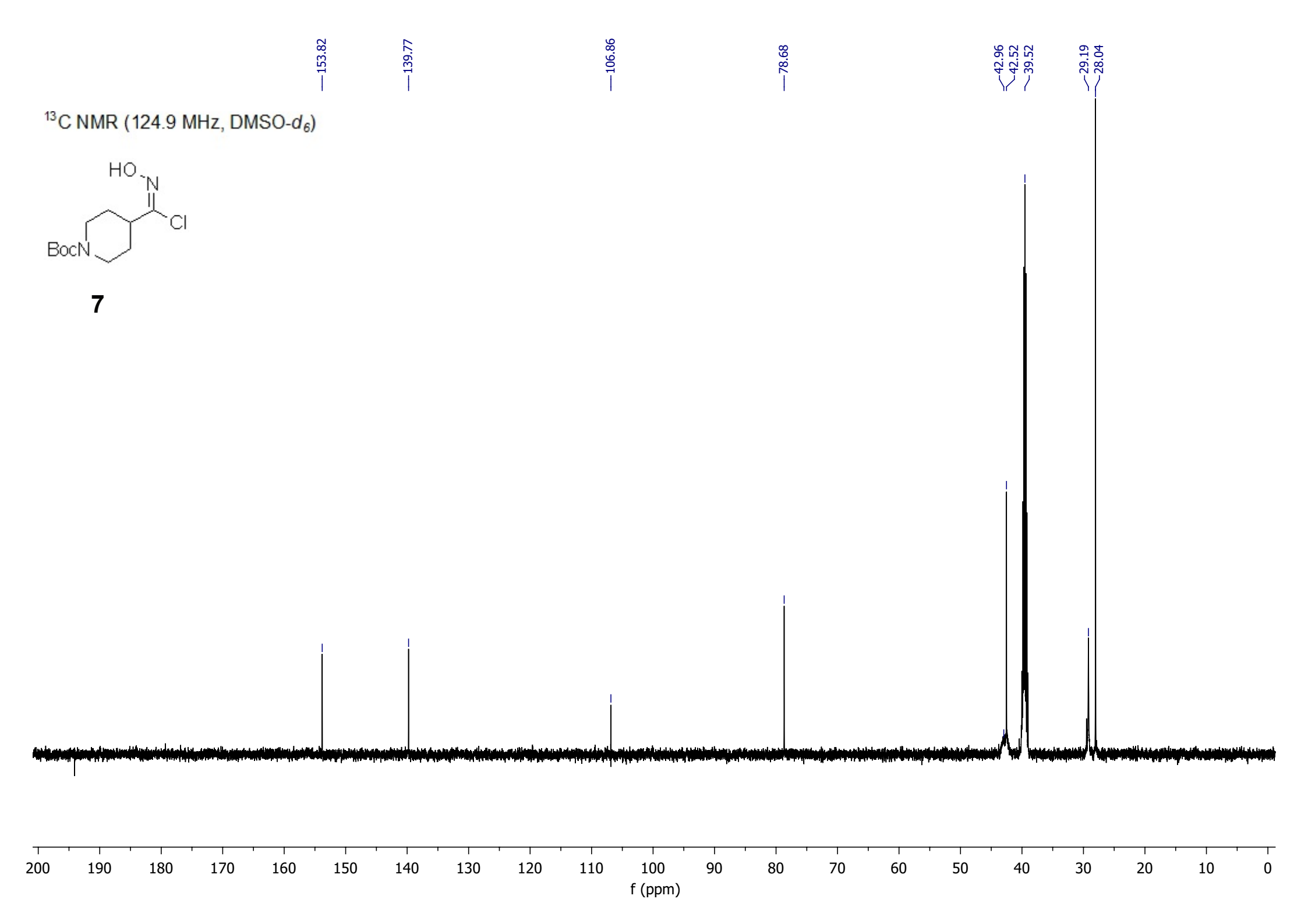

11.691
4.468
3.371
3.307
2.540
2.500
2.166
1.888
1.793
1.389
1.332
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
N
Cl
NBoc
4
0.74
0.85
1.96
3.10
0.95
1.88
9.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

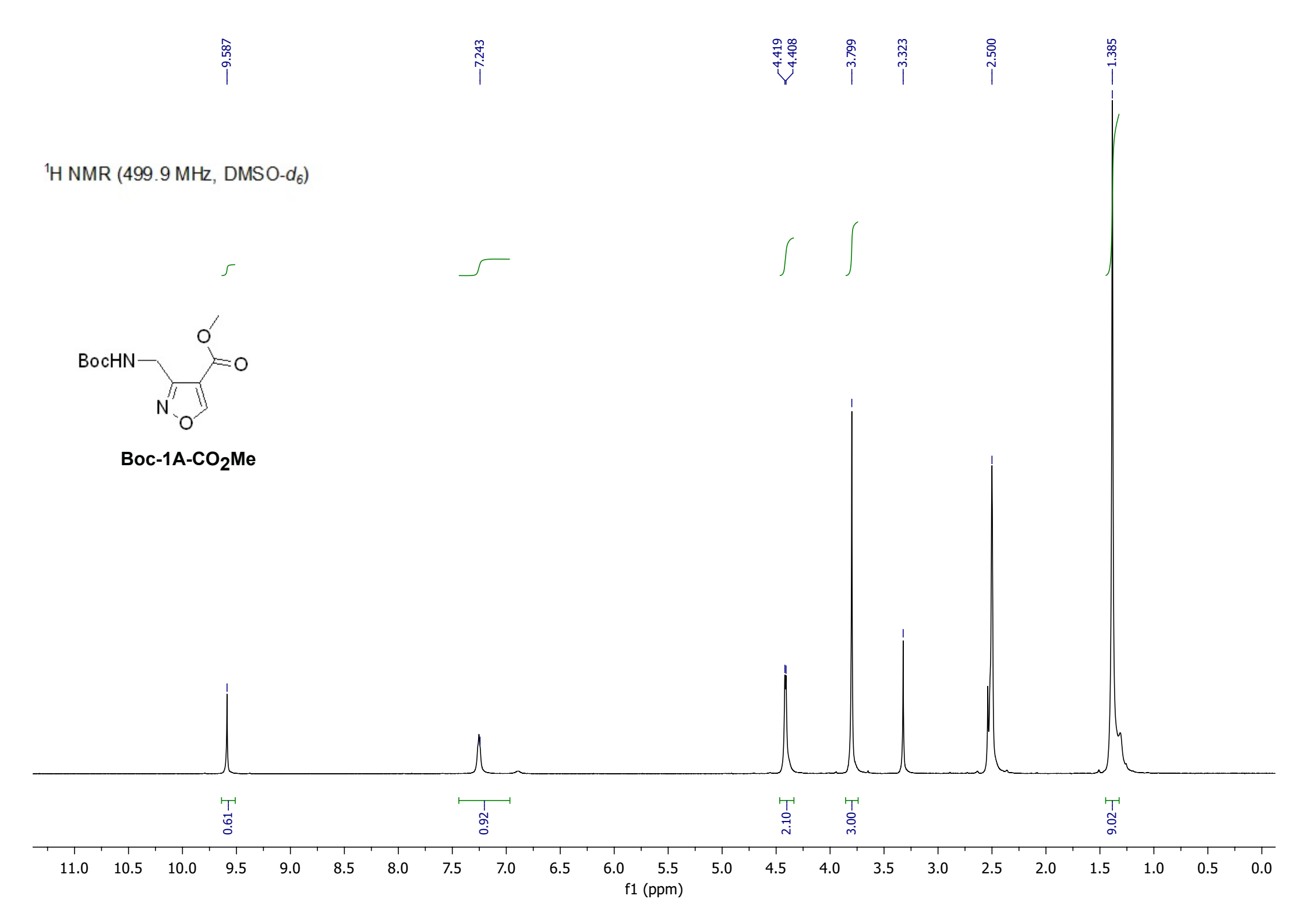

179.76
153.37
138.92
138.71
79.24
60.73
47.13
46.85
40.89
39.82
31.08
30.32
29.97
28.53
28.39
23.76
23.10
13C NMR (124.9 MHz, DMSO-d6)
HO
N
Cl
NBoc
4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

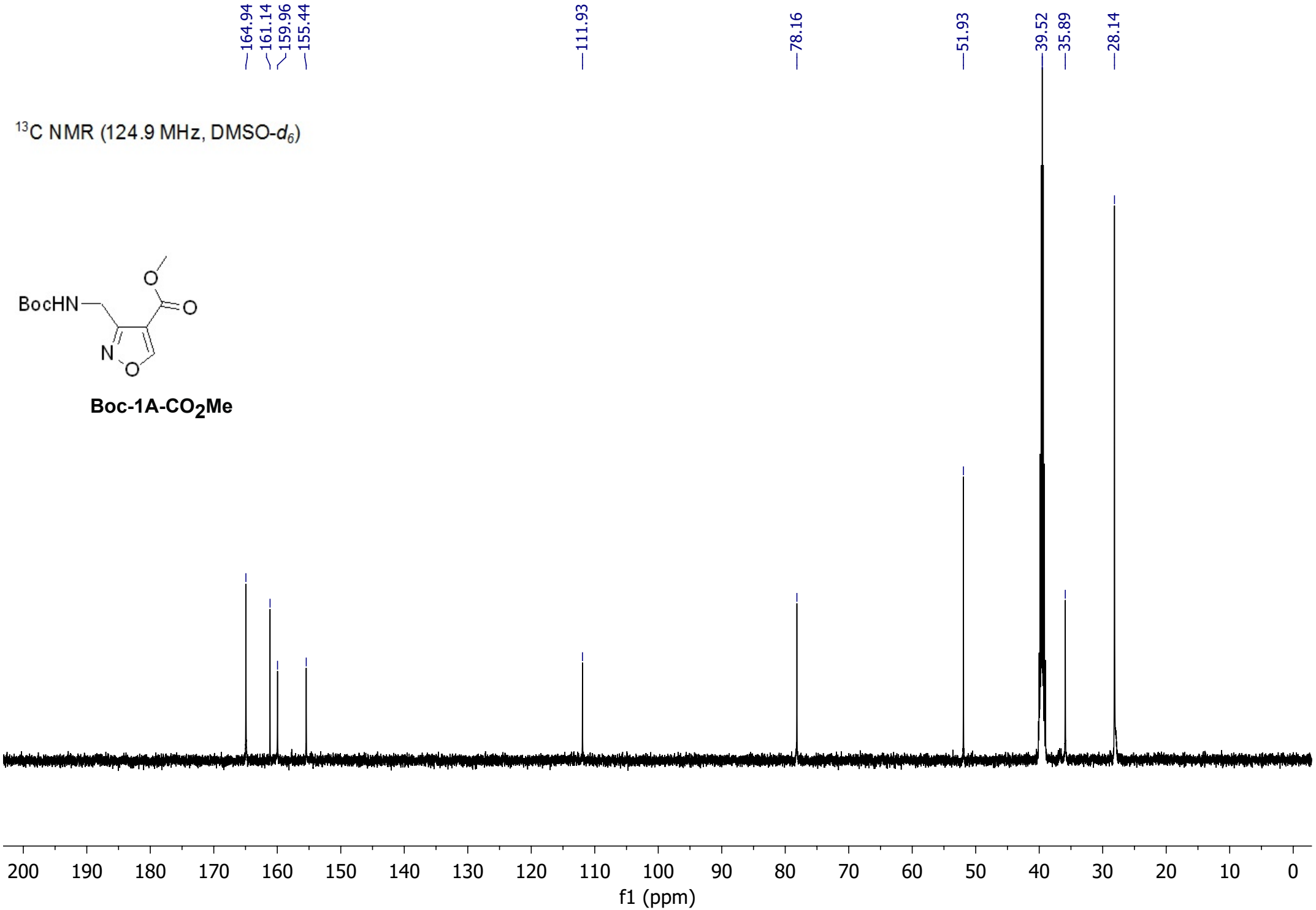

11.916
4.062
3.904
3.718
3.674
2.500
1.378
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
N
Cl
BocN
6
0.76
1.81
1.75
1.05
9.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

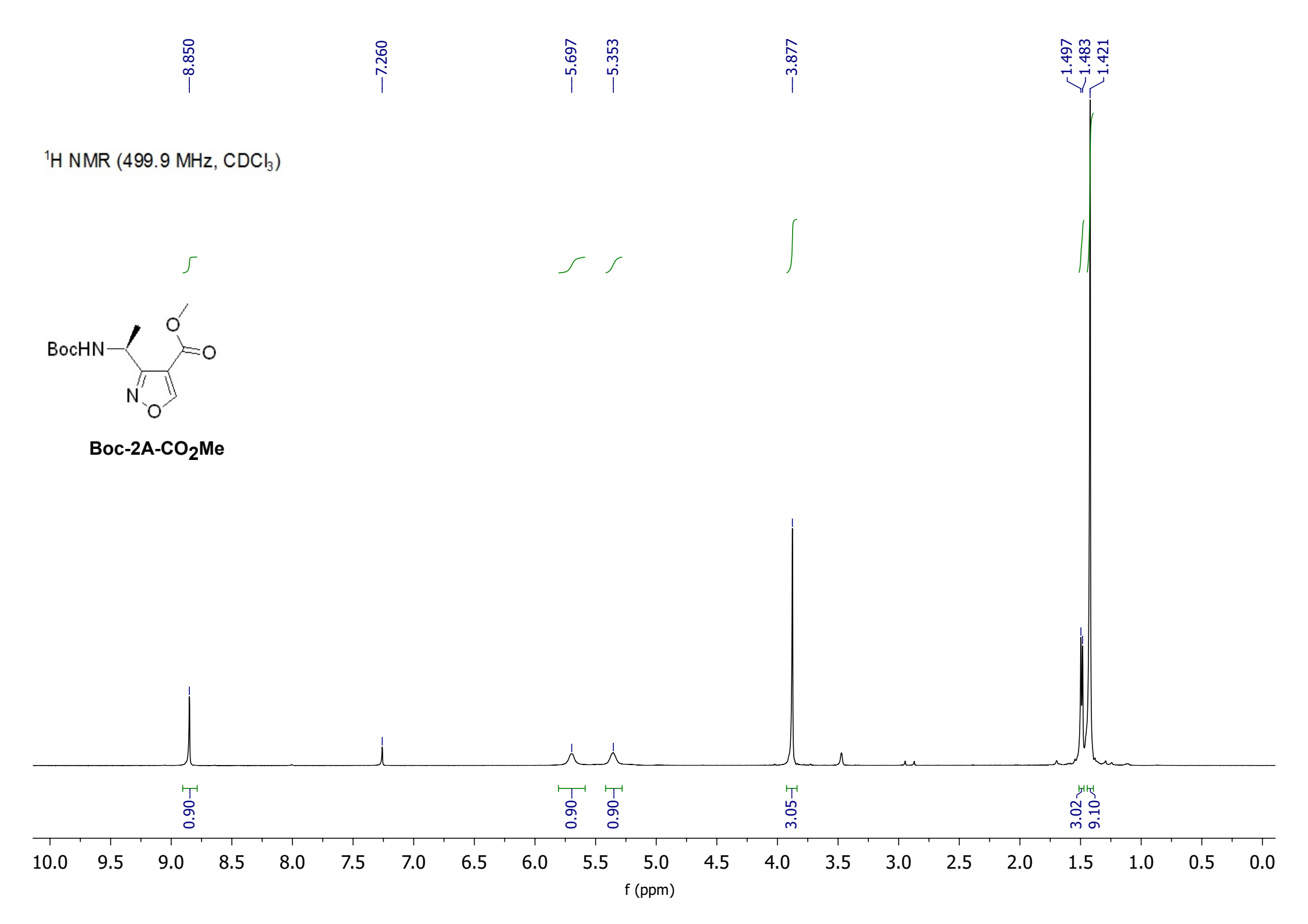

155.44
136.95
78.90
51.58
39.52
33.75
28.01
13C NMR (124.9 MHz, DMSO-d6)
HO
N
Cl
BocN
6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11.619
3.953
3.925
3.369
2.783
2.663
2.638
2.500
1.855
1.827
1.395
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
N
Cl
Boc
N
7
0.92
1.98
1.92
1.01
2.10
11.00
13.0 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
f1 (ppm)

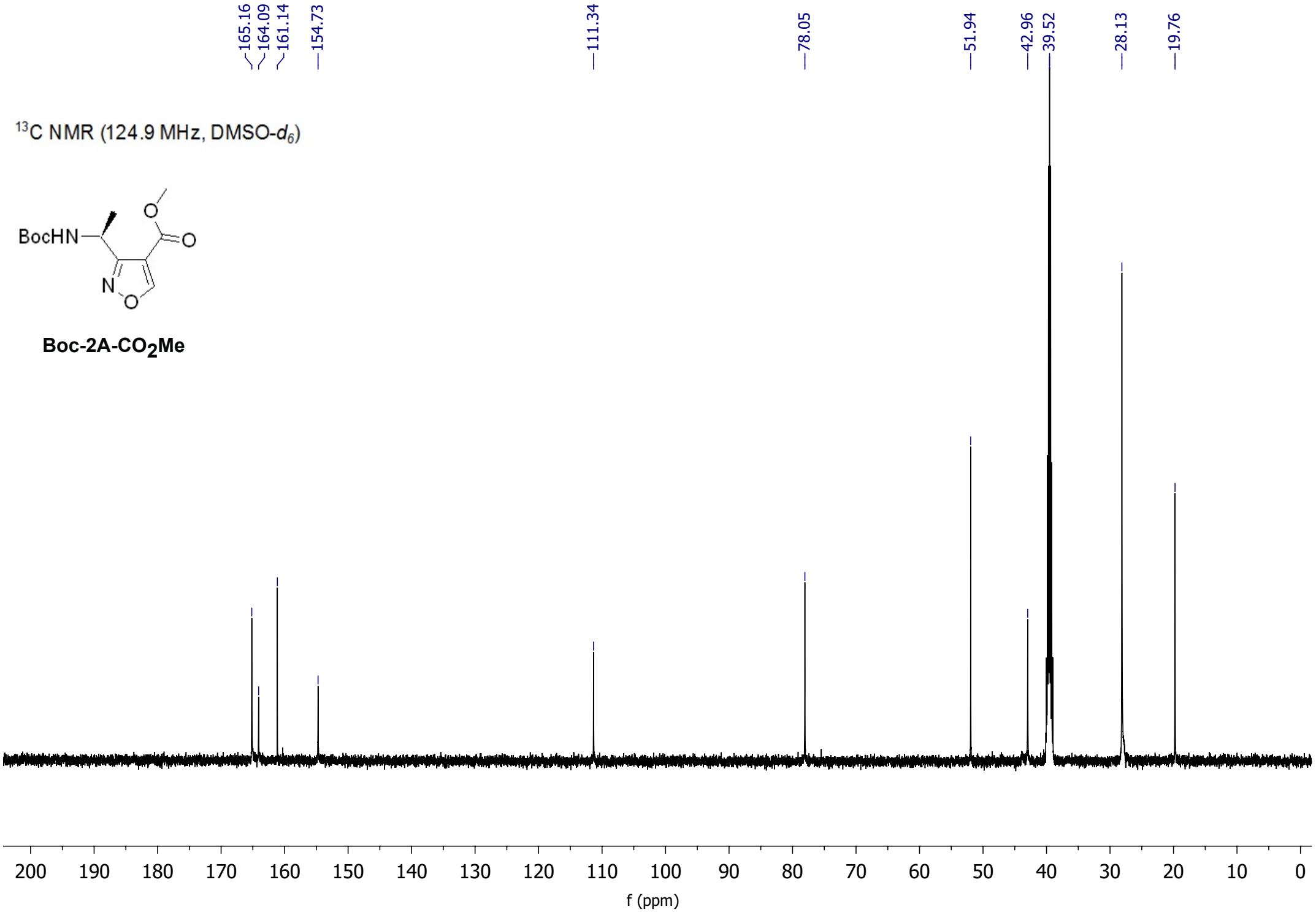

153.82
139.77
106.86
78.68
42.96
42.52
39.52
29.19
28.04
13C NMR (124.9 MHz, DMSO-d6)
HO
N
Cl
BocN
7
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)


9.587
7.243
4.419
4.408
3.799
3.323
2.500
1.385
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
O
O
N
O
Boc-1A-CO$_2$Me
0.61
0.92
2.10
3.00
9.02
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

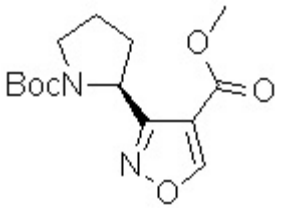

164.94
161.14
159.96
155.44
111.93
78.16
51.93
39.52
35.89
28.14
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
O
O
N
O
Boc-1A-CO$_2$Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.850
7.260
5.697
5.353
3.877
1.497
1.483
1.421
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocHN
O
O
N
O
0.90
0.90
0.90
3.05
3.02
9.10
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
f (ppm)

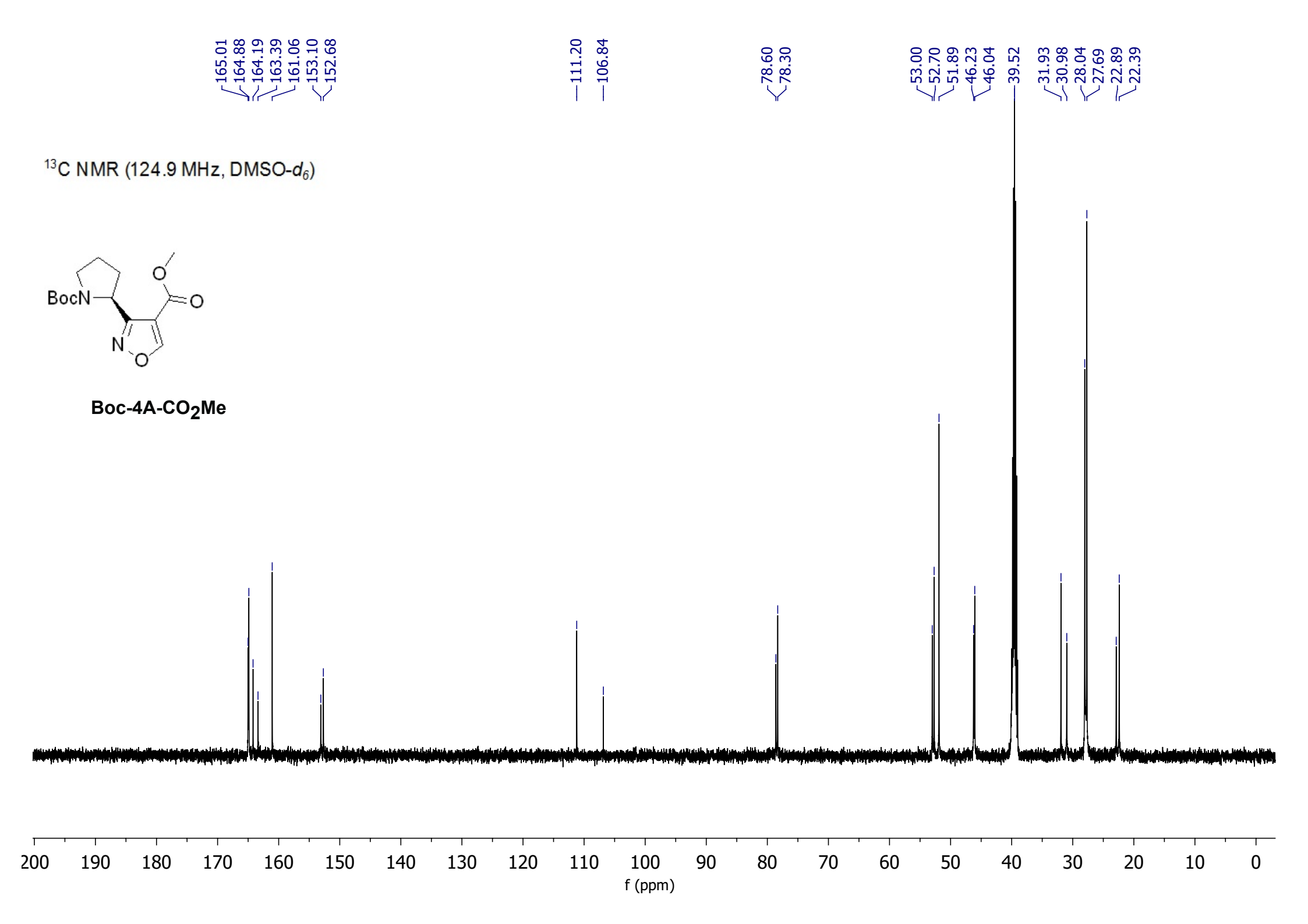
Boc-2A-CO_2Me

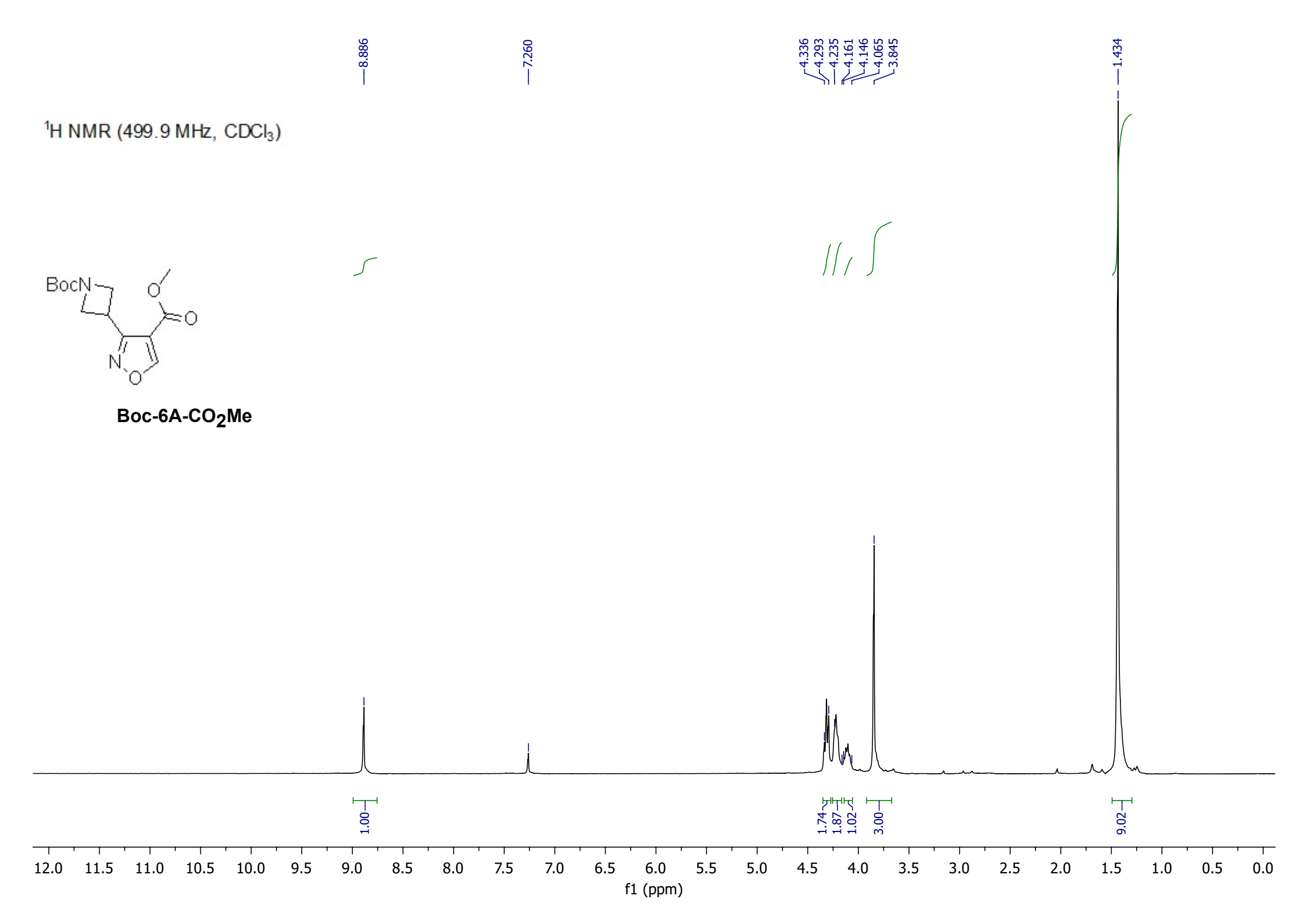

165.16
164.09
161.14
154.73
111.34
78.05
51.94
42.96
39.52
28.13
19.76
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
O
O
N
O
Boc-2A-CO$_2$Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

^{1}H NMR (499.9 MHz, DMSO-d_6)

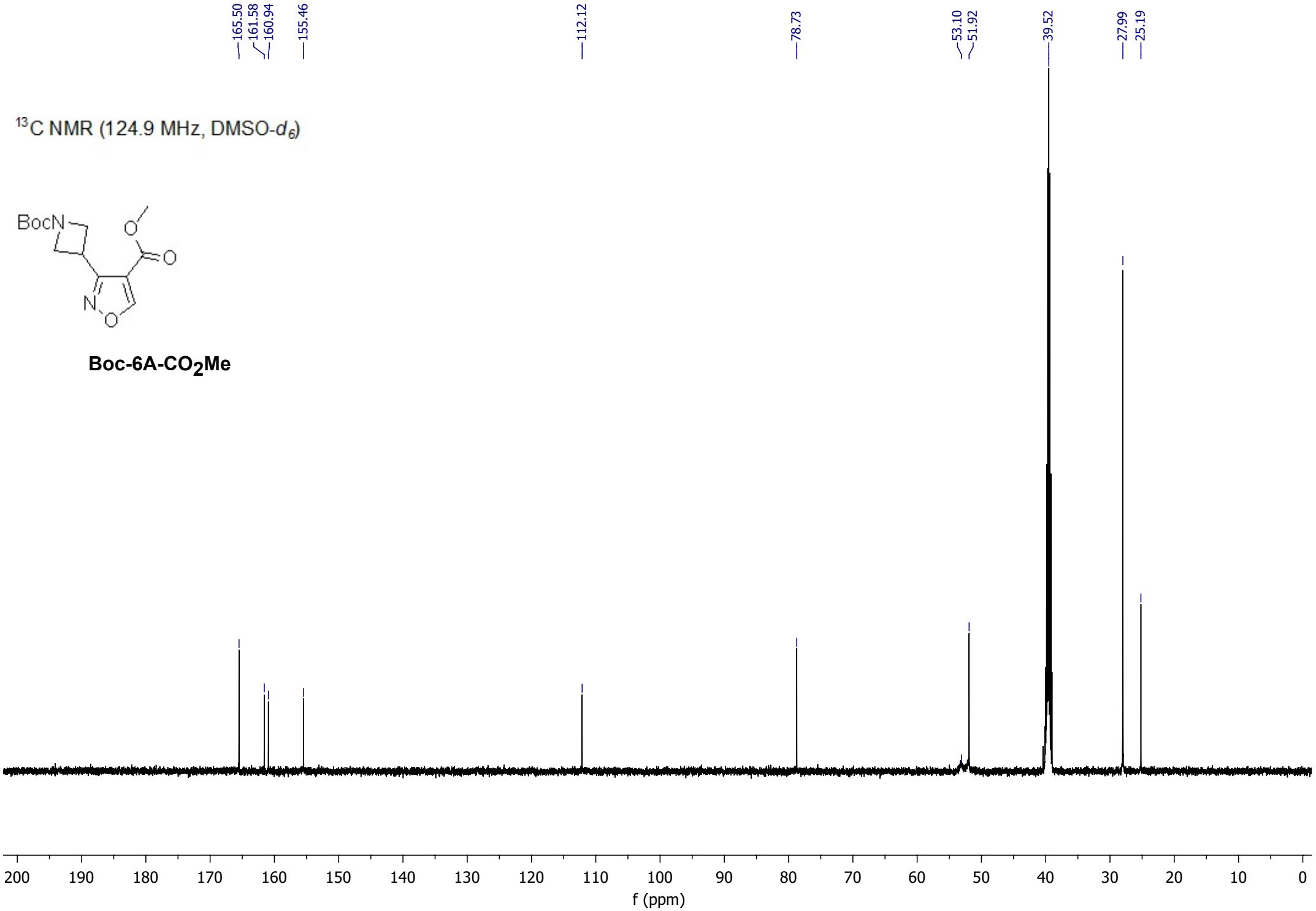


Boc-4A-CO_2Me

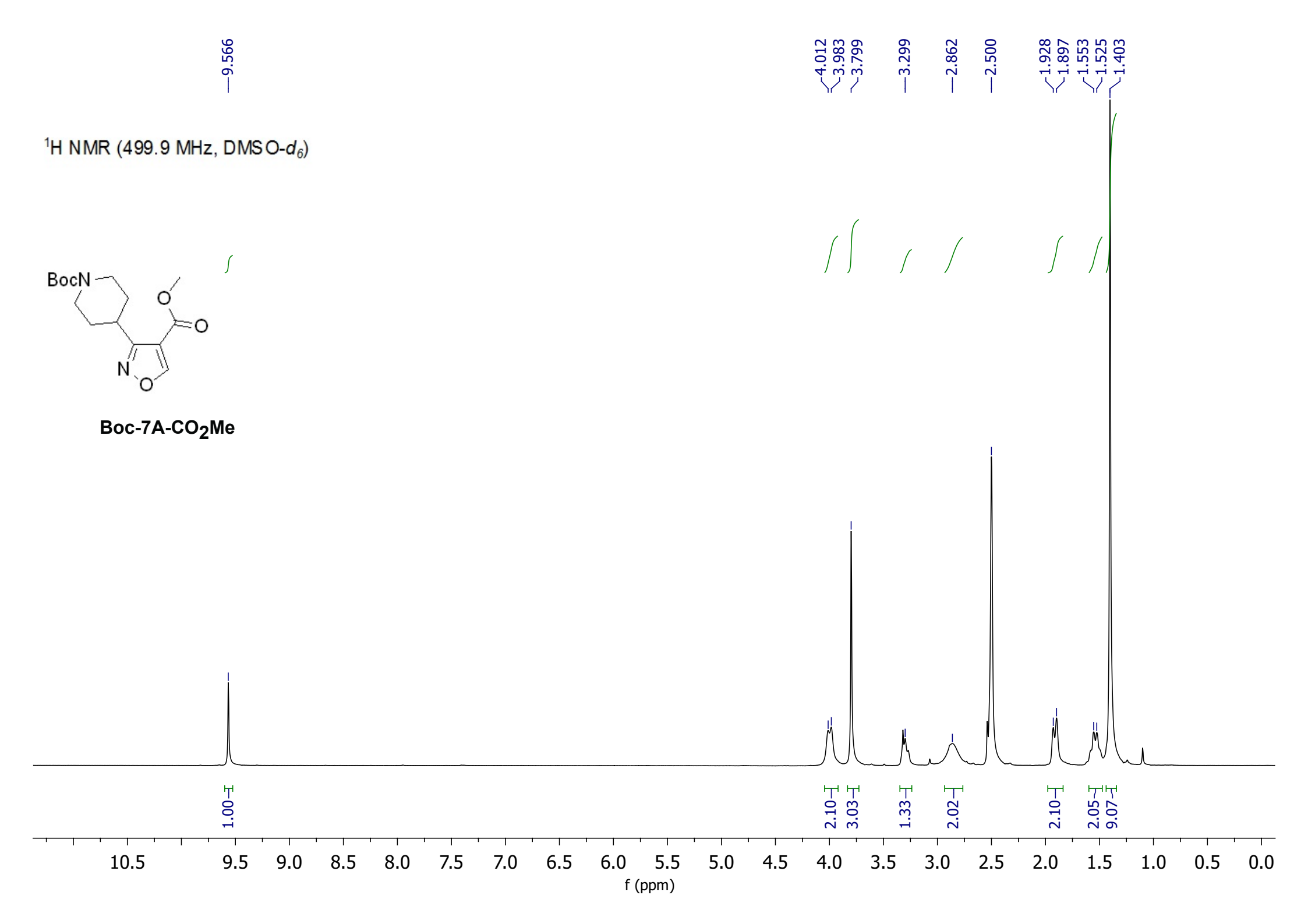

165.01
164.88
164.19
163.39
161.06
153.10
152.68
111.20
106.84
78.60
78.30
53.00
52.70
51.89
46.23
46.04
39.52
31.93
30.98
28.04
27.69
22.89
22.39
13C NMR (124.9 MHz, DMSO-d6)
BocN
O
O
N
O
Boc-4A-CO2Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

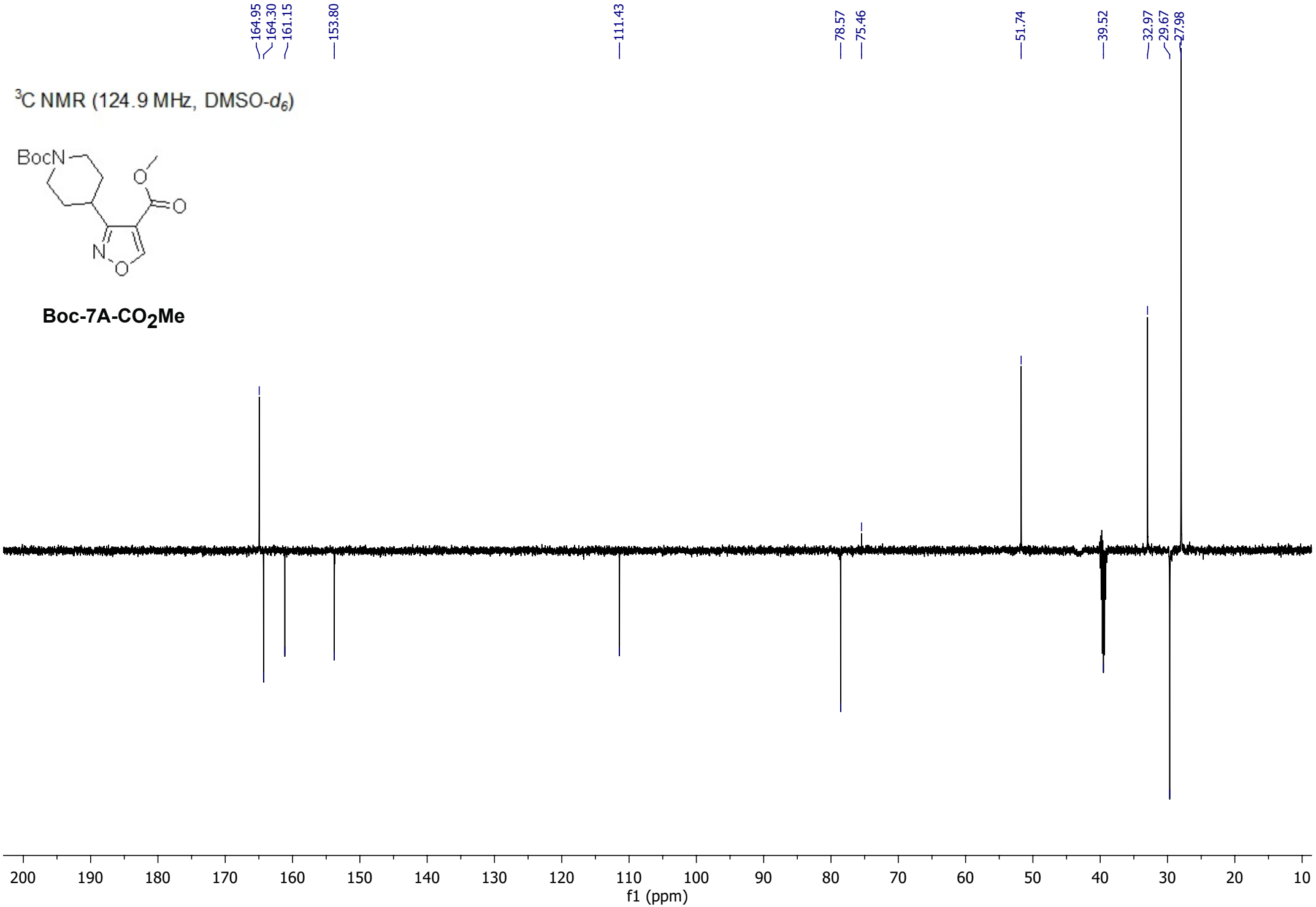

8.886
7.260
4.336
4.293
4.235
4.161
4.146
4.065
3.845
1.434
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
O
O
N
O
1.00
1.74
1.87
1.02
3.00
9.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

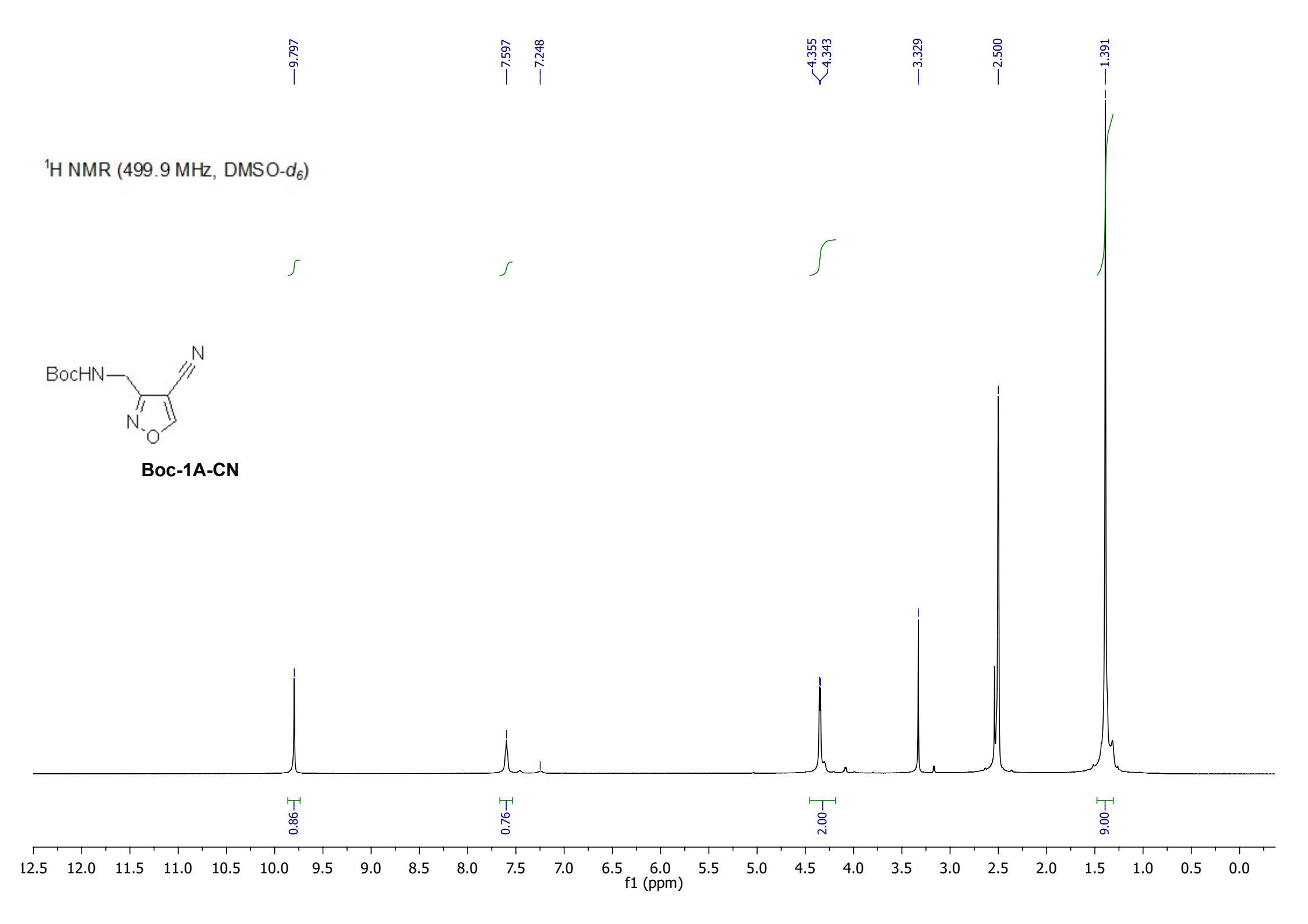
Boc-6A-CO_2Me

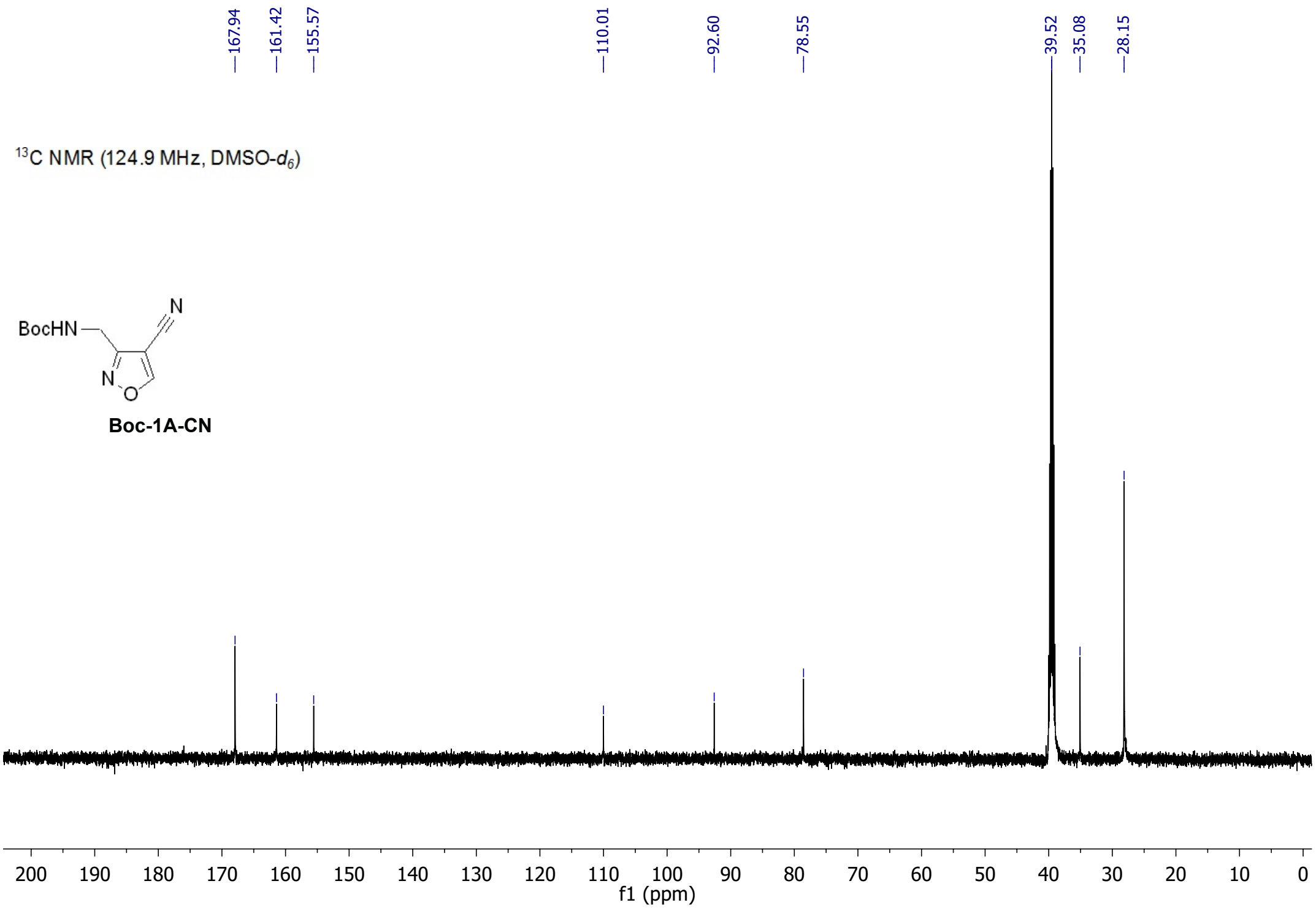

165.50
161.58
160.94
155.46
112.12
78.73
53.10
51.92
39.52
27.99
25.19
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
O
O
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

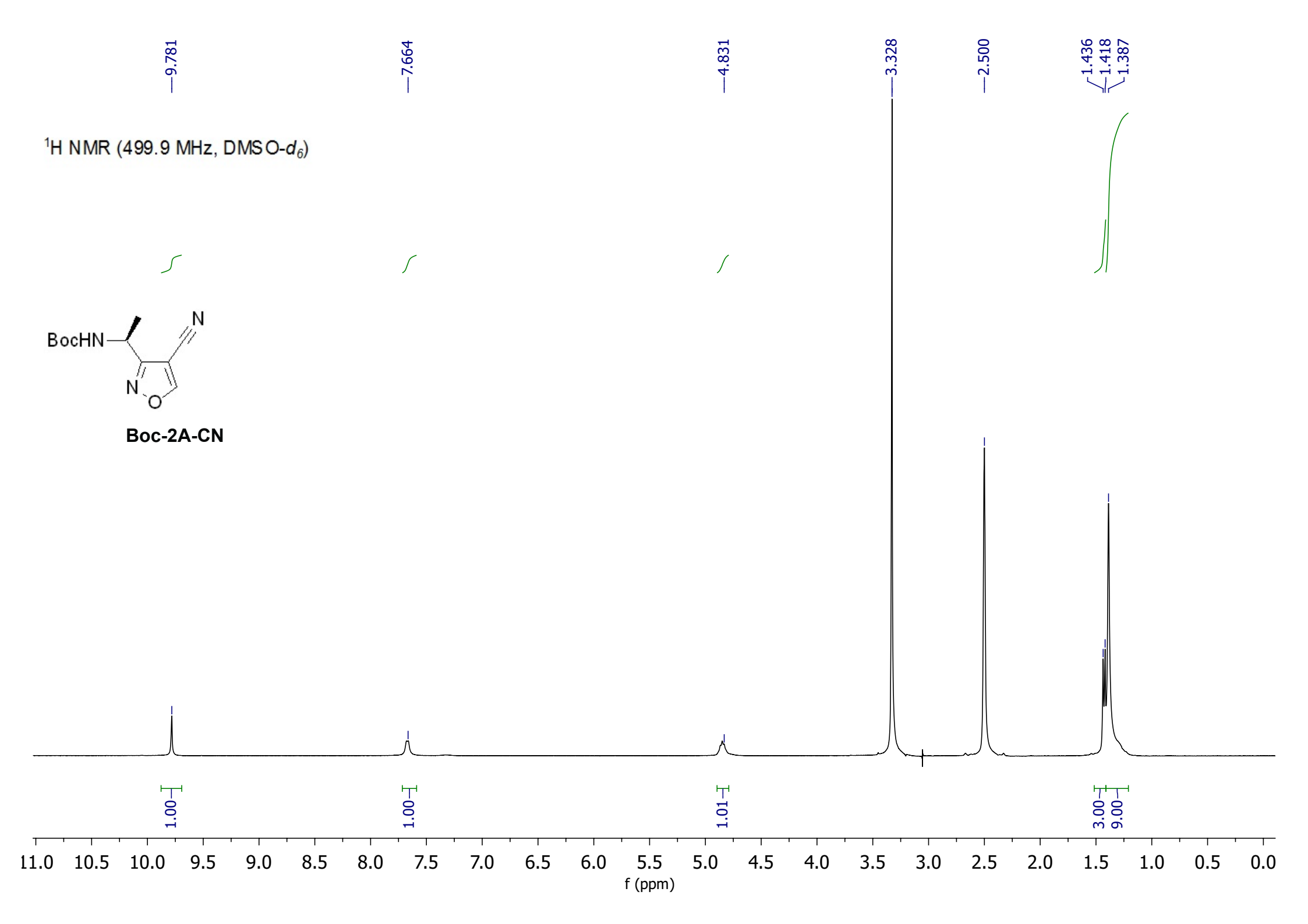
Boc-6A-CO_2Me

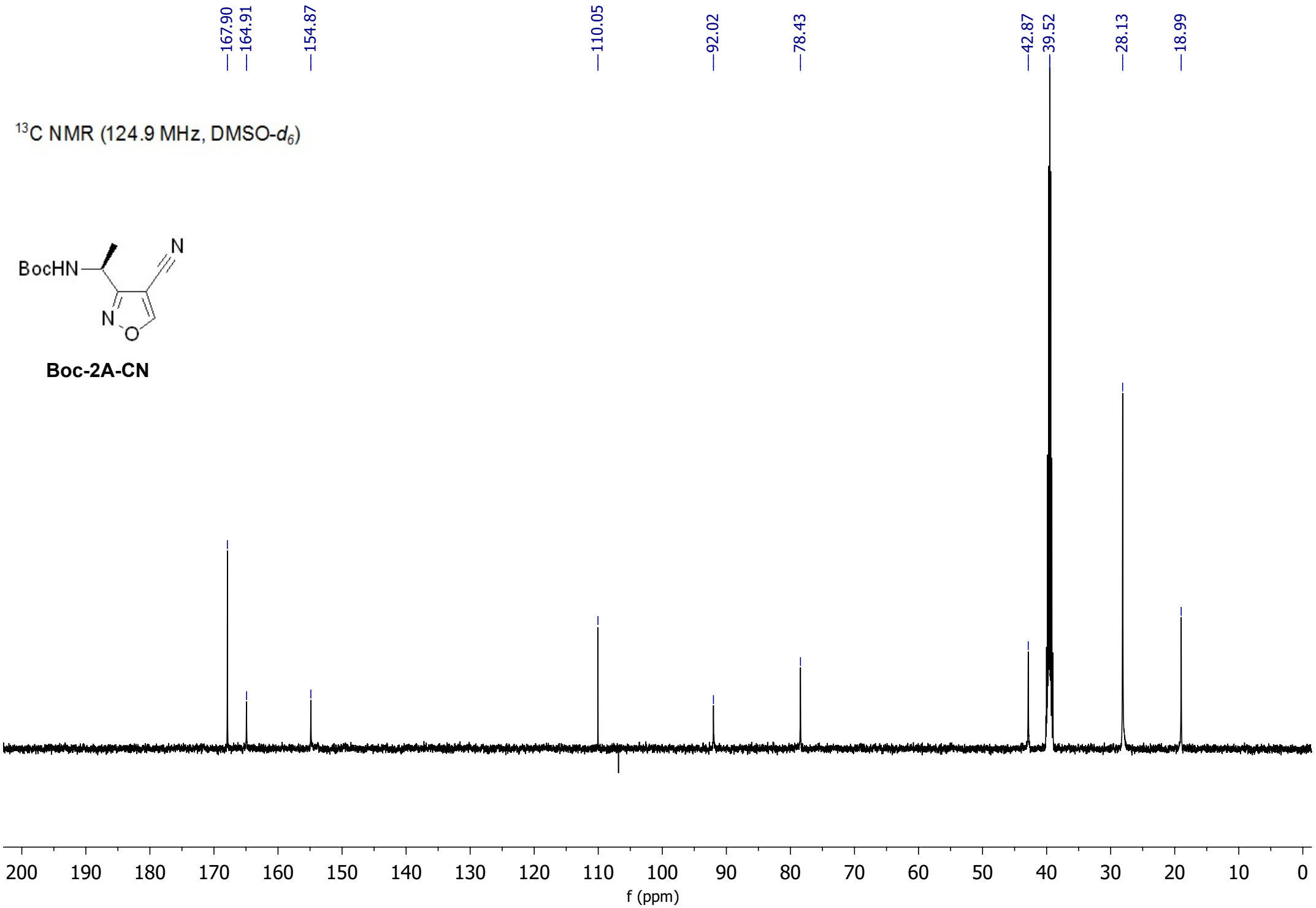

9.566
4.012
3.983
3.799
3.299
2.862
2.500
1.928
1.897
1.553
1.525
1.403
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
O
O
N
O
Boc-7A-CO$_2$Me
1.00
2.10
3.03
1.33
2.02
2.10
2.05
9.07
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f (ppm)

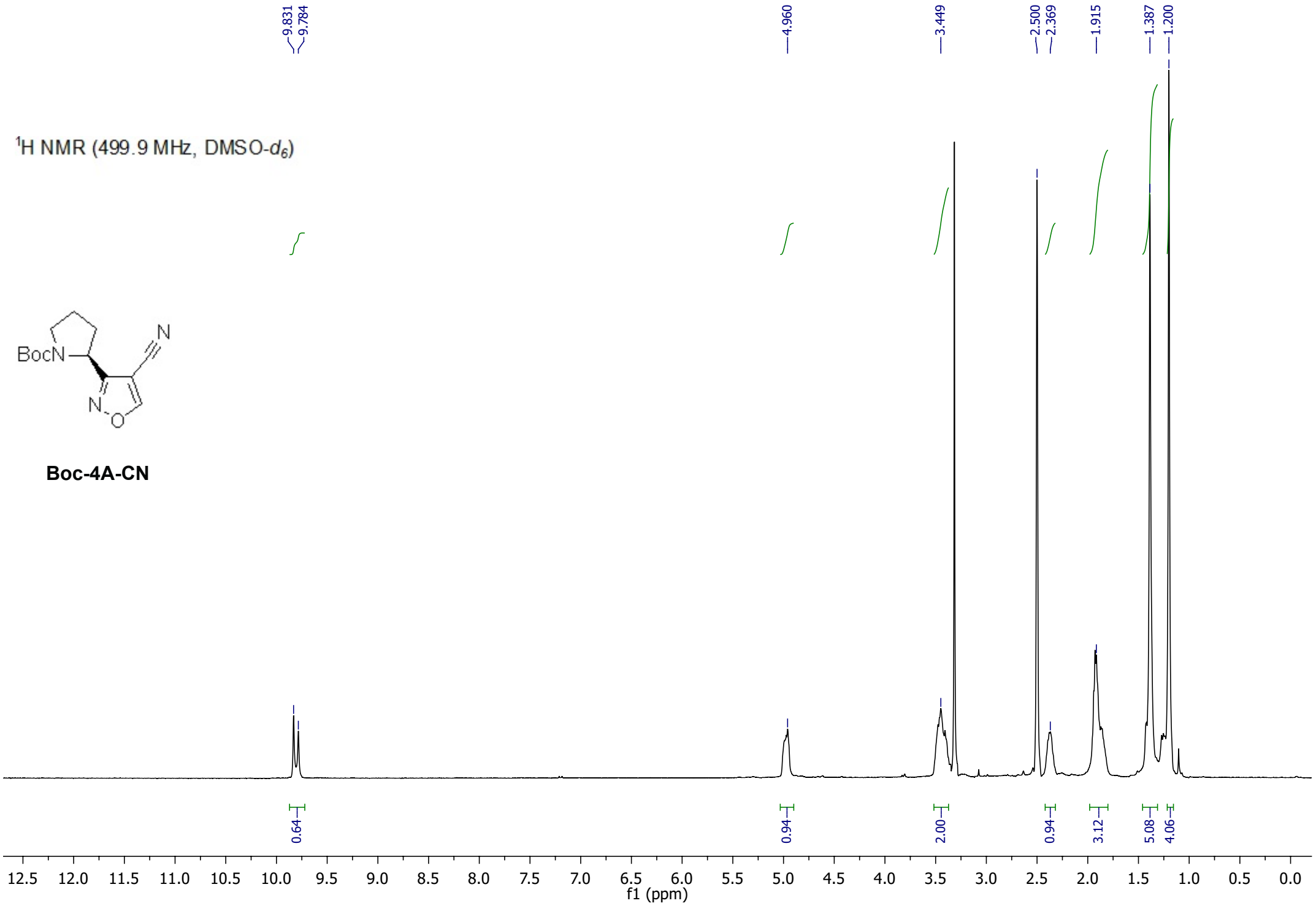

164.95
164.30
161.15
153.80
111.43
78.57
75.46
51.74
39.52
32.97
29.67
27.98
^{3}C NMR (124.9 MHz, DMSO-d_6)
BocN
O
O
N
O
Boc-7A-CO$_2$Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


9.797
7.597
7.248
4.355
4.343
3.329
2.500
1.391
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
N
O
Boc-1A-CN
0.86
0.76
2.00
9.00
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
f1 (ppm)

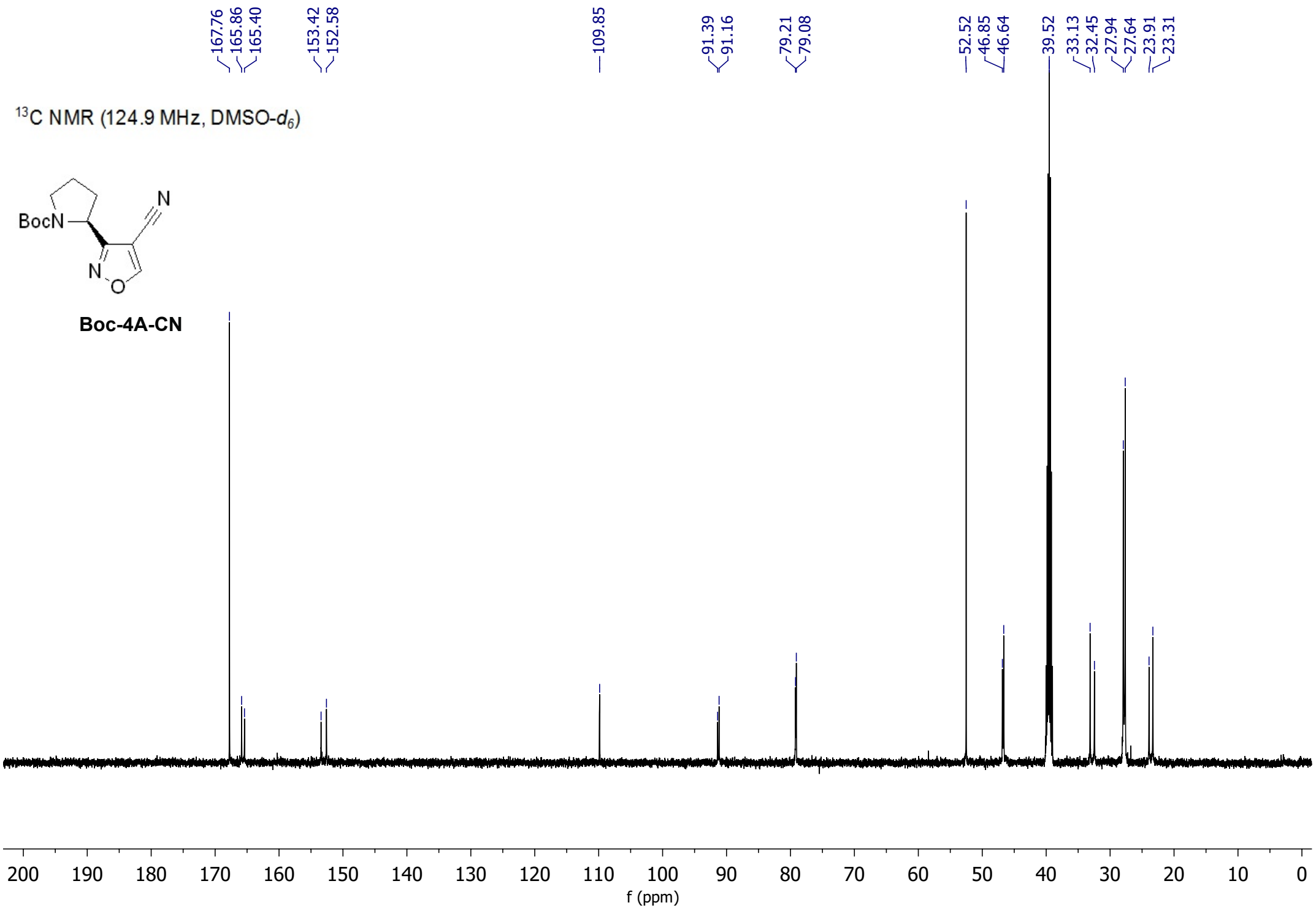

167.94
161.42
155.57
110.01
92.60
78.55
39.52
35.08
28.15
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
N
O
Boc-1A-CN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

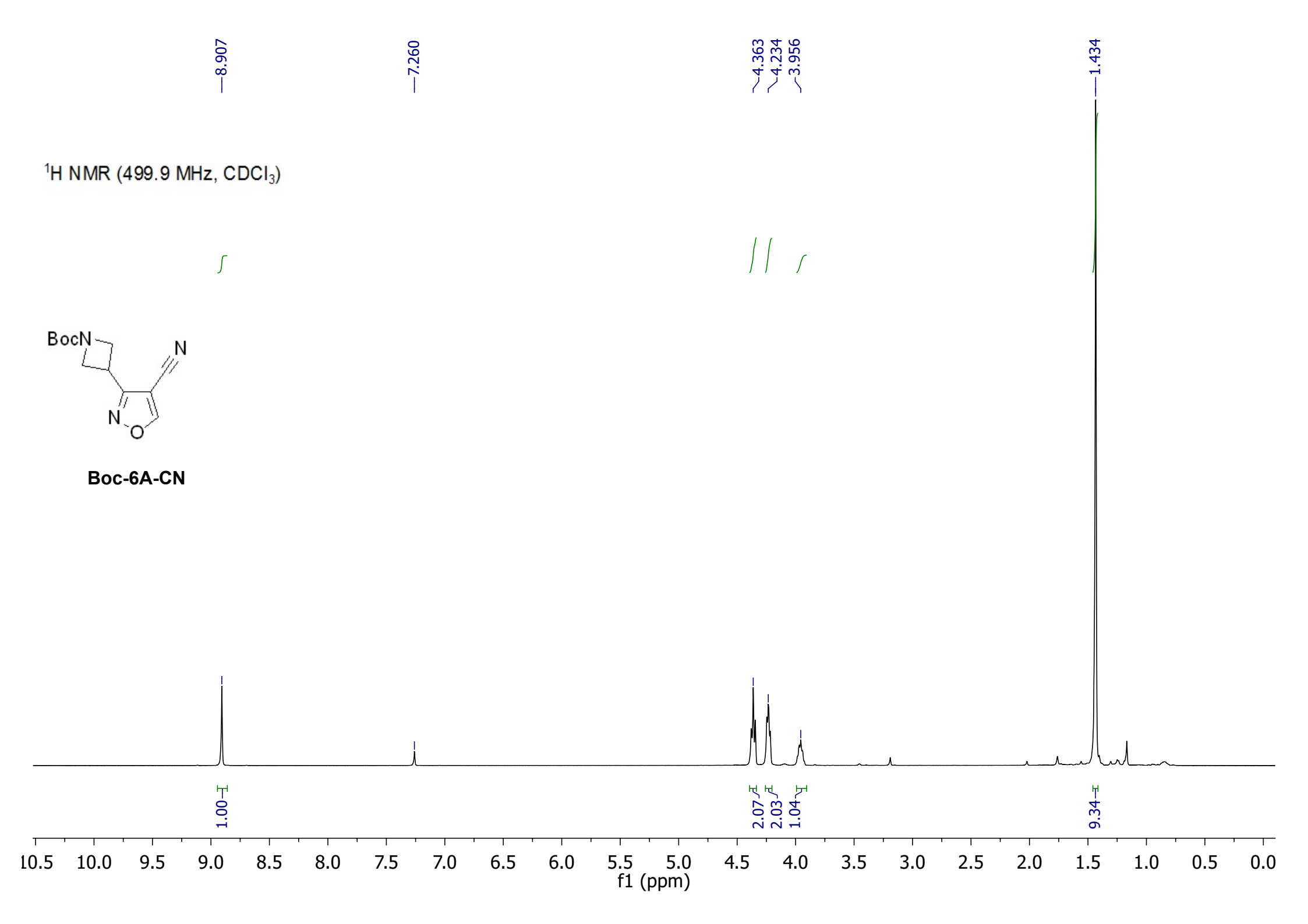

9.781
7.664
4.831
3.328
2.500
1.436
1.418
1.387
1H NMR (499.9 MHz, DMSO-d6)
BocHN
N
N
O
Boc-2A-CN
1.00
1.00
1.01
3.00
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f (ppm)

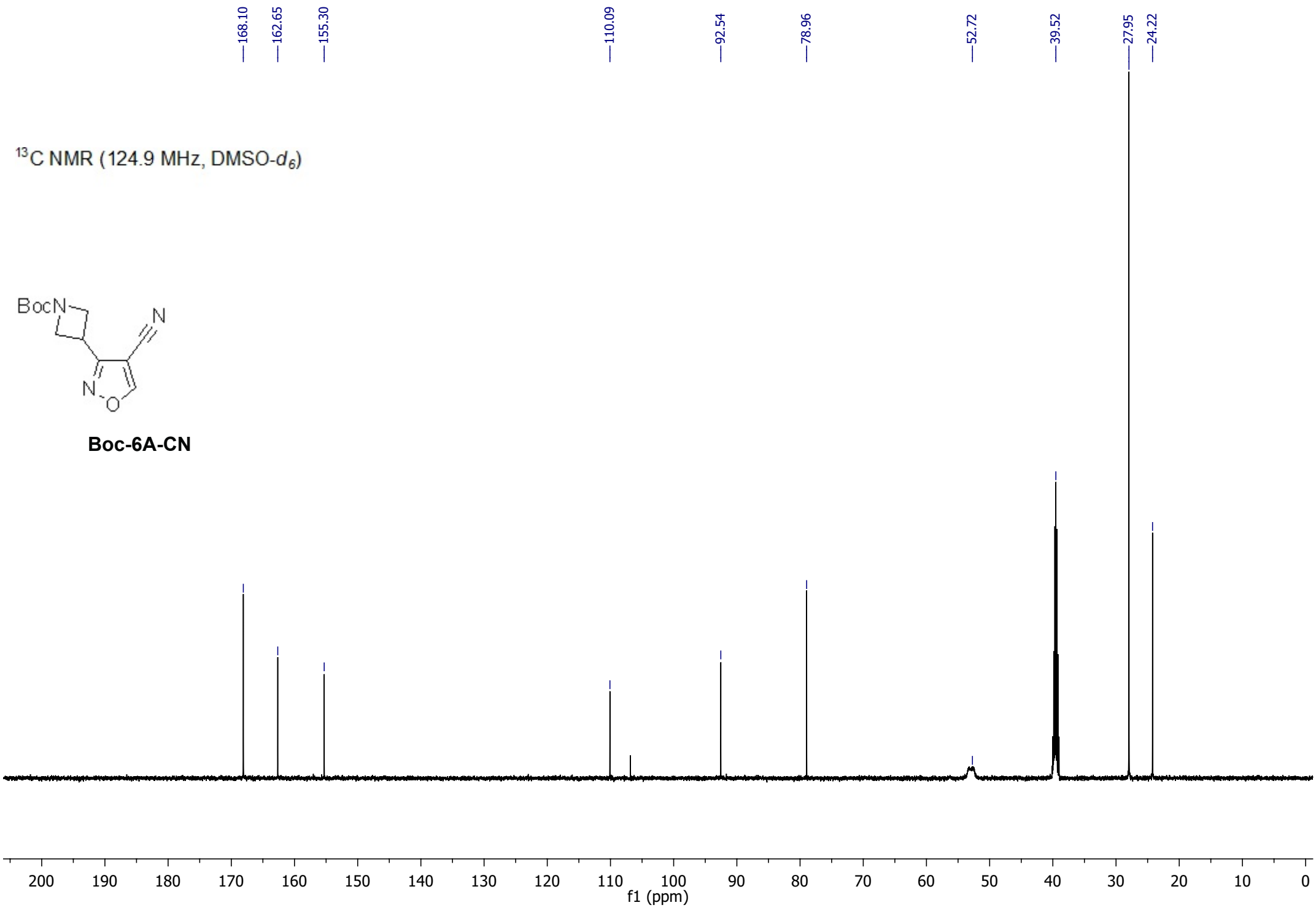

167.90
164.91
154.87
110.05
92.02
78.43
42.87
39.52
28.13
18.99
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
N
N
O
Boc-2A-CN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

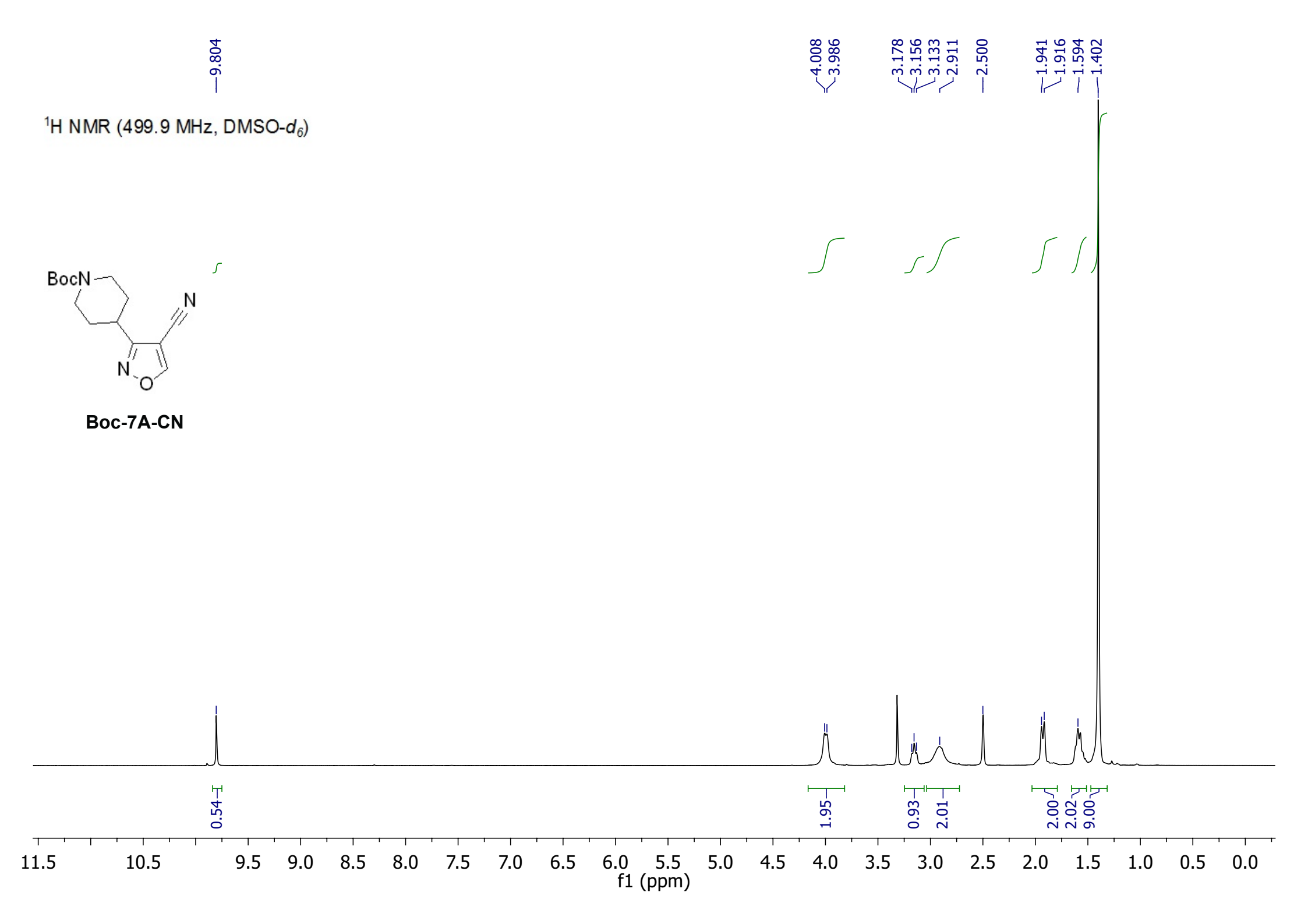

9.831
9.784
4.960
3.449
2.500
2.369
1.915
1.387
1.200
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
N
O
0.64
0.94
2.00
0.94
3.12
5.08
4.06
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

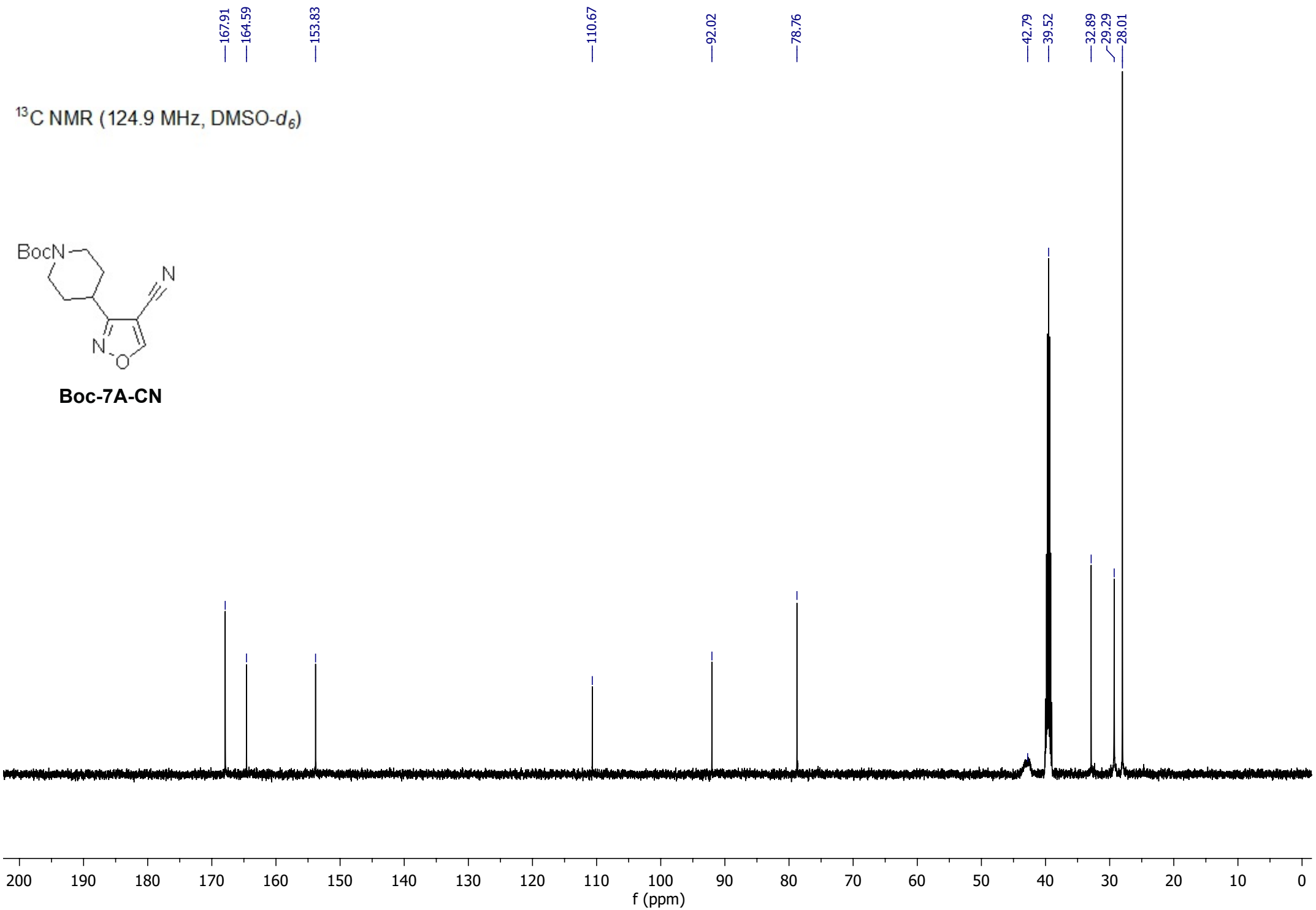
Boc-4A-CN

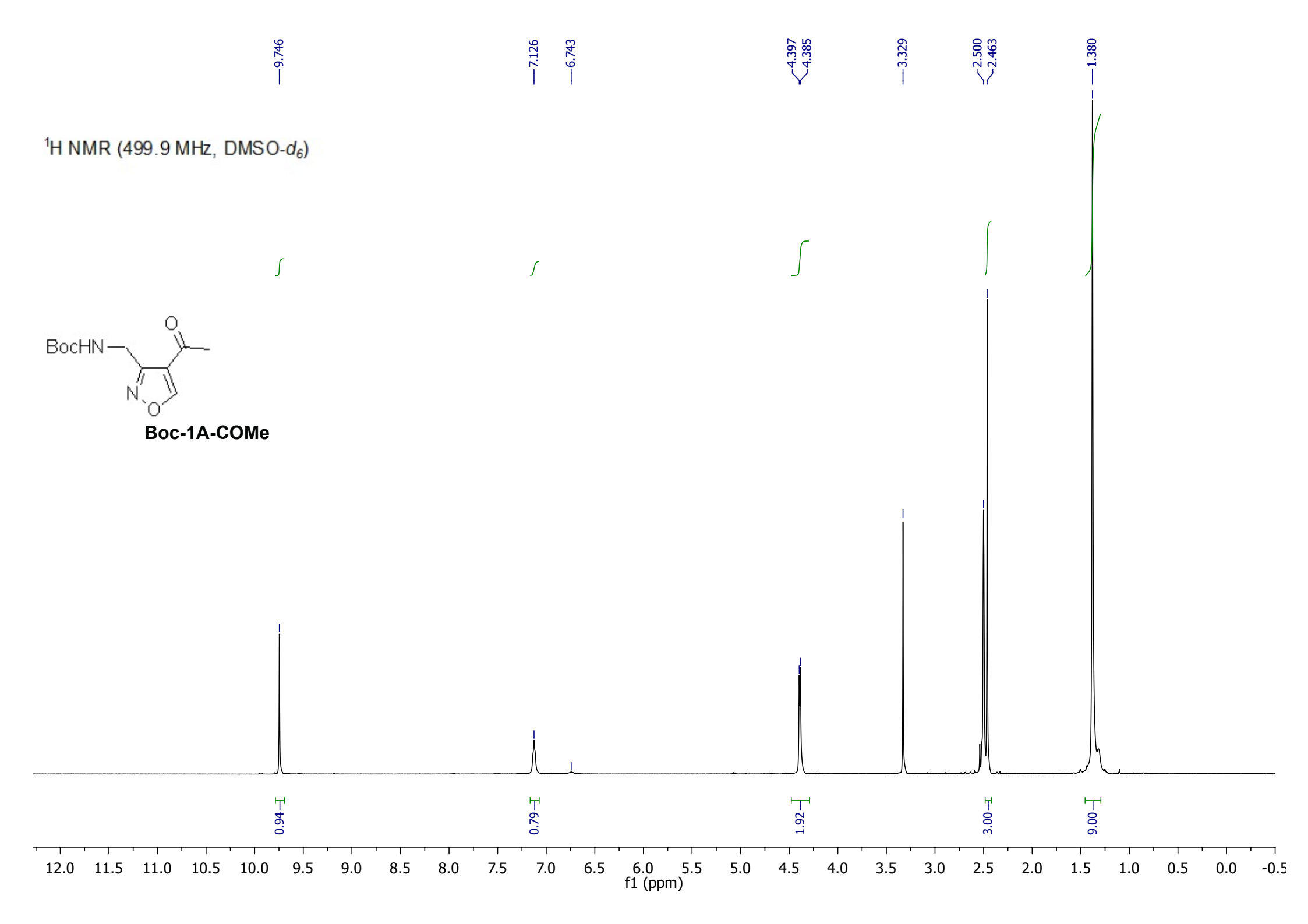

167.76
165.86
165.40
153.42
152.58
109.85
91.39
91.16
79.21
79.08
52.52
46.85
46.64
39.52
33.13
32.45
27.94
27.64
23.91
23.31
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
N
O
Boc-4A-CN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

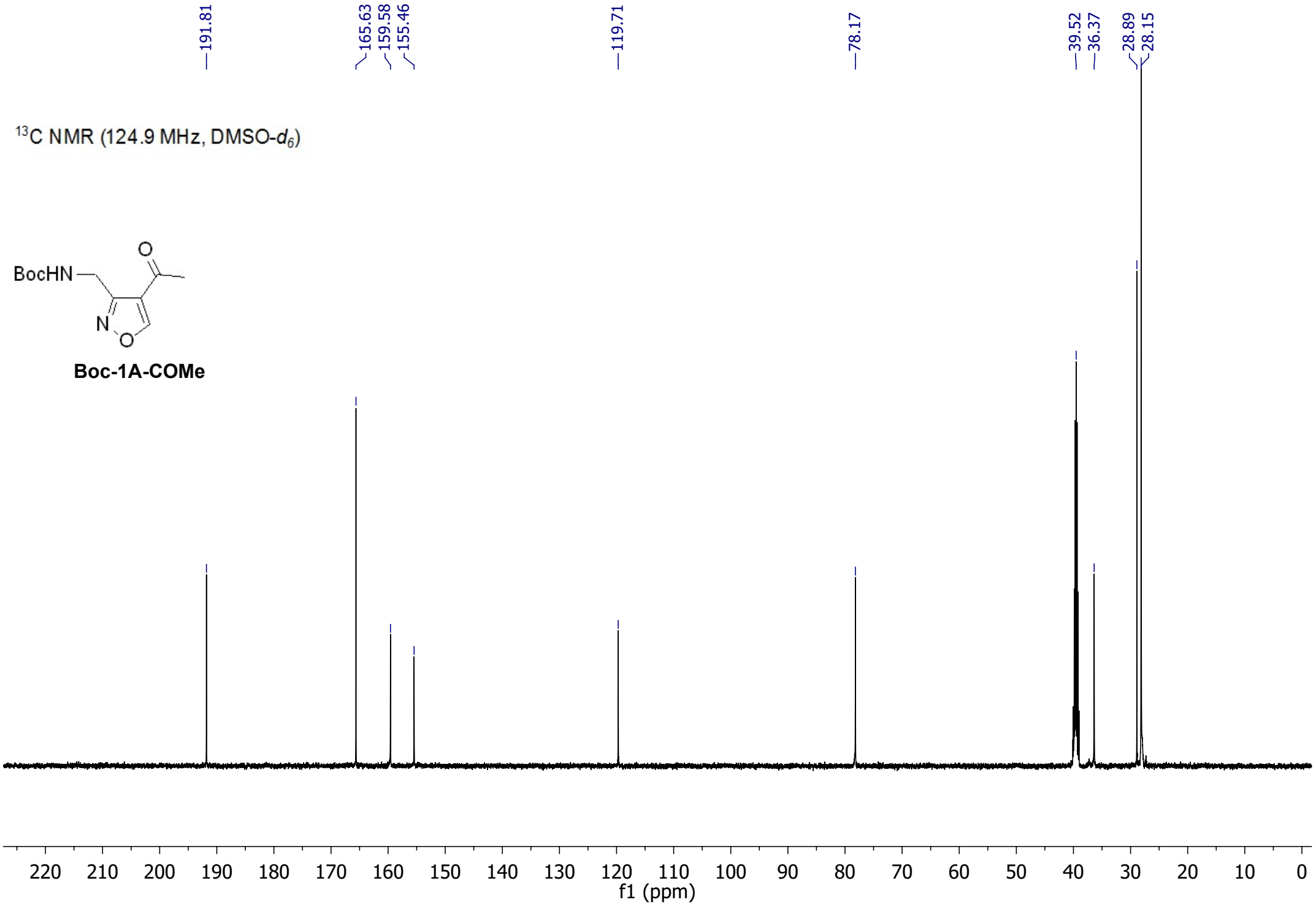

8.907
7.260
4.363
4.234
3.956
1.434
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
N
N
O
Boc-6A-CN
1.00
2.07
2.03
1.04
9.34
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

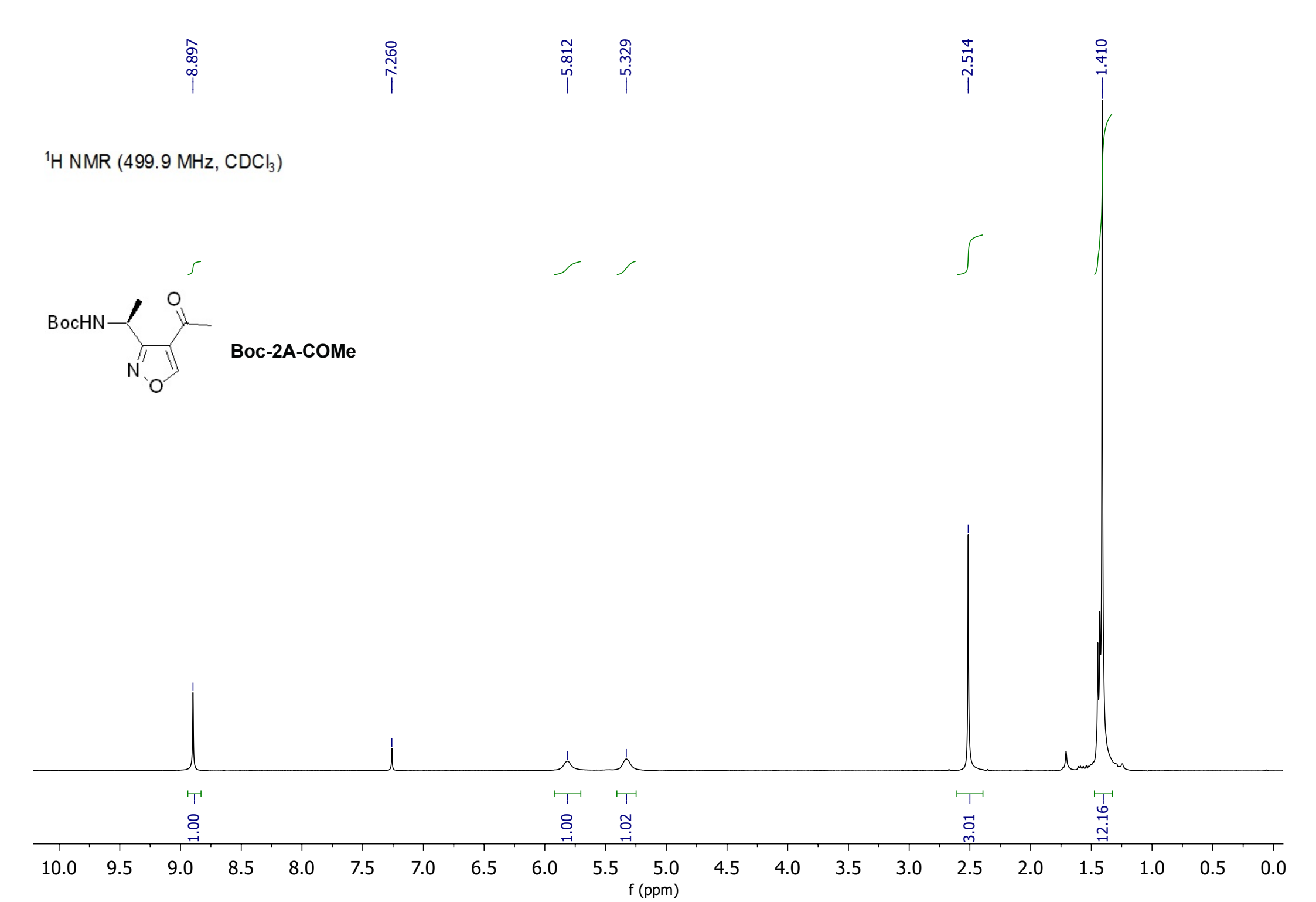

168.10
162.65
155.30
110.09
92.54
78.96
52.72
39.52
27.95
24.22
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
N
O
Boc-6A-CN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

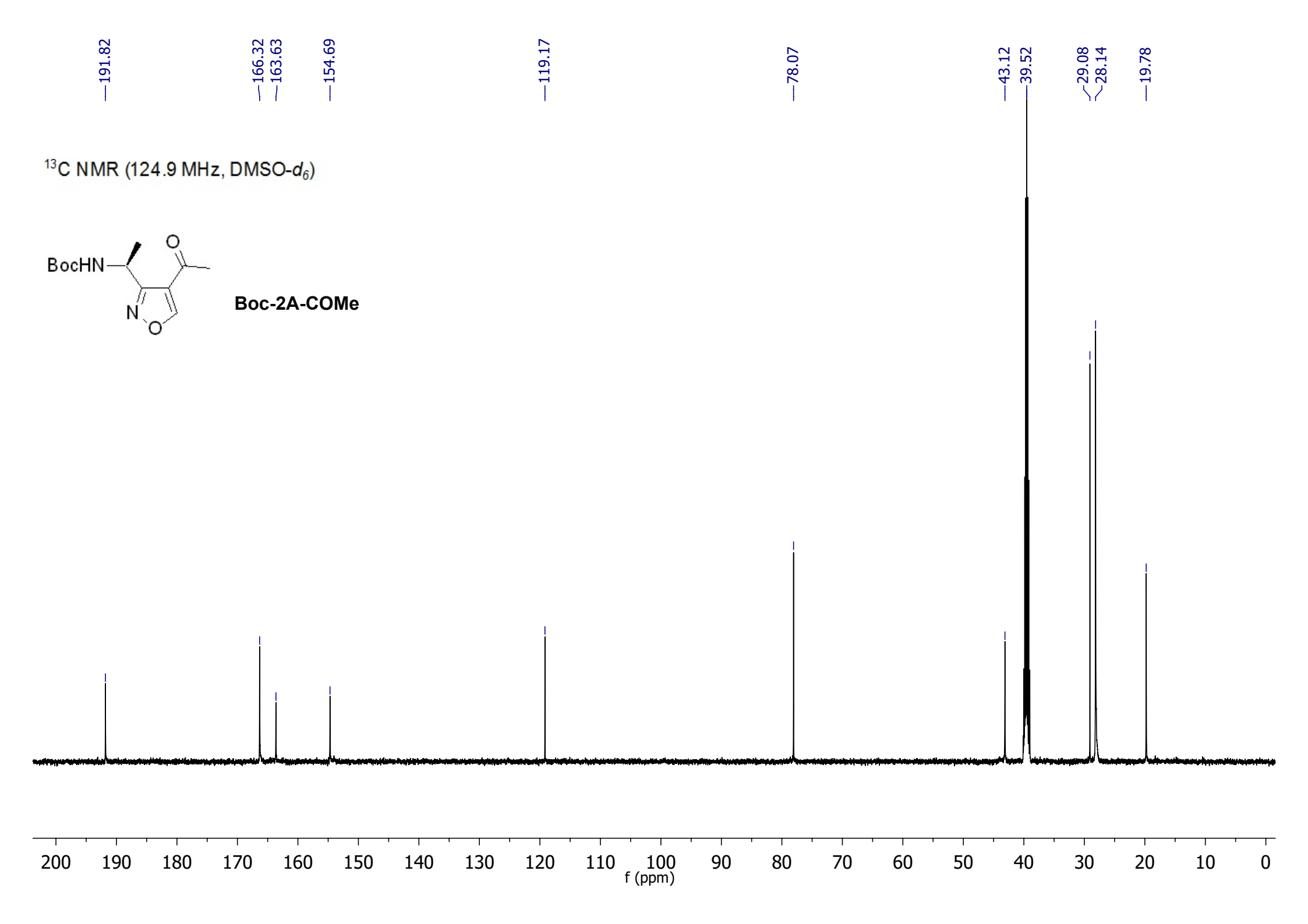

9.804
4.008
3.986
3.178
3.156
3.133
2.911
2.500
1.941
1.916
1.594
1.402
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
N
O
Boc-7A-CN
0.54
1.95
0.93
2.01
2.00
2.02
9.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

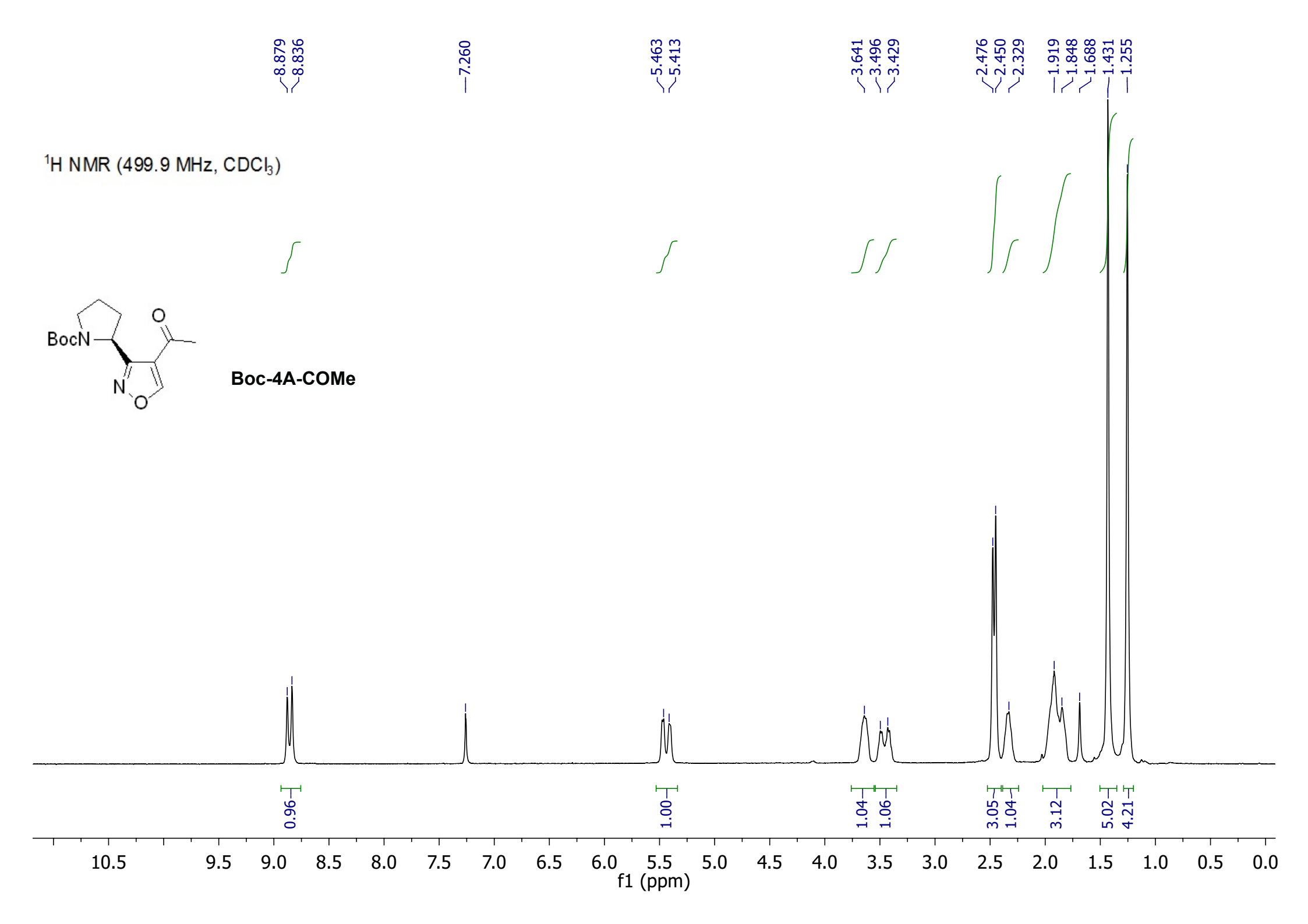

167.91
164.59
153.83
110.67
92.02
78.76
42.79
39.52
32.89
29.29
28.01
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
N
O
Boc-7A-CN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

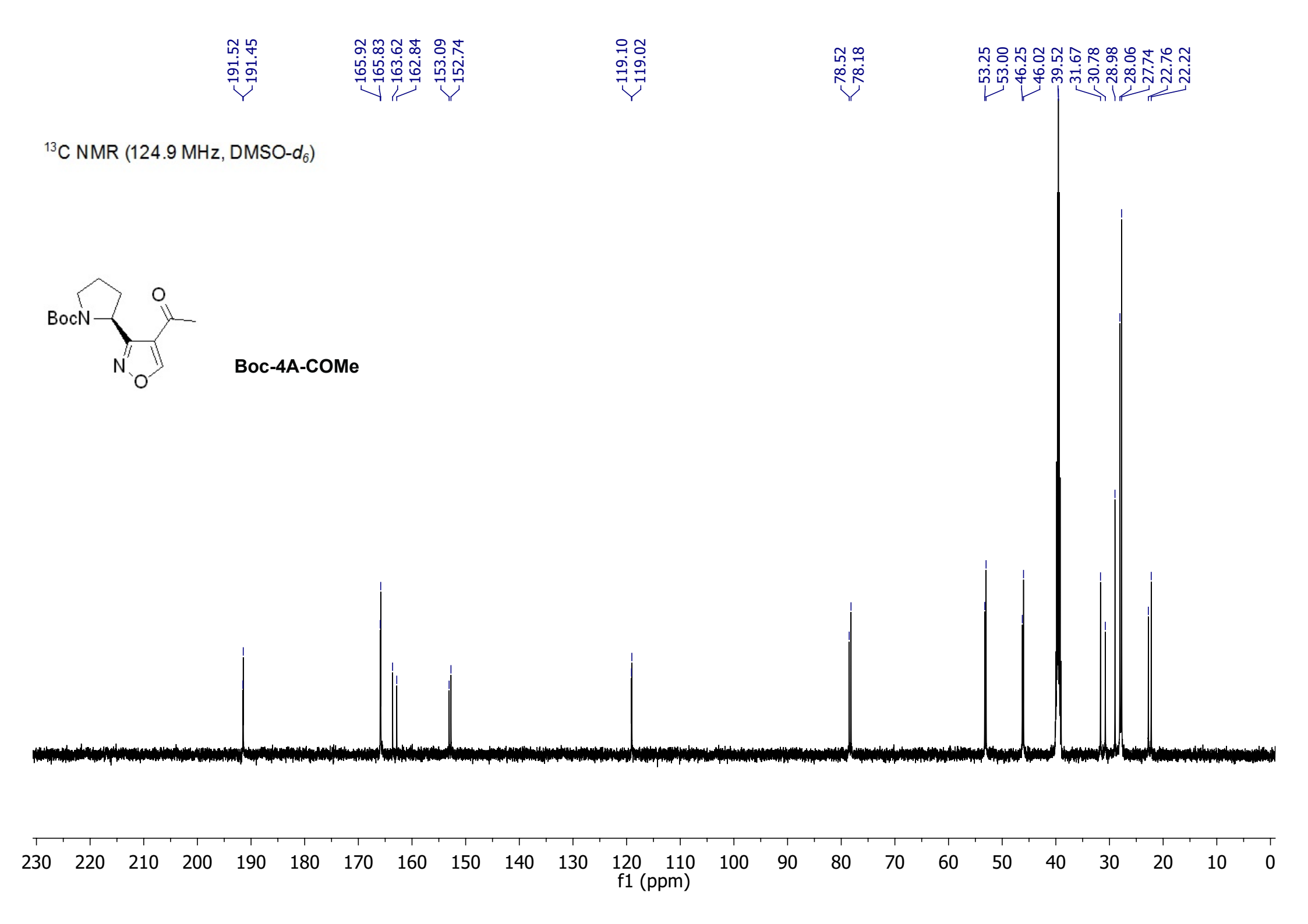

9.746
7.126
6.743
4.397
4.385
3.329
2.500
2.463
1.380
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
O
N
O
Boc-1A-COMe
0.94
0.79
1.92
3.00
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

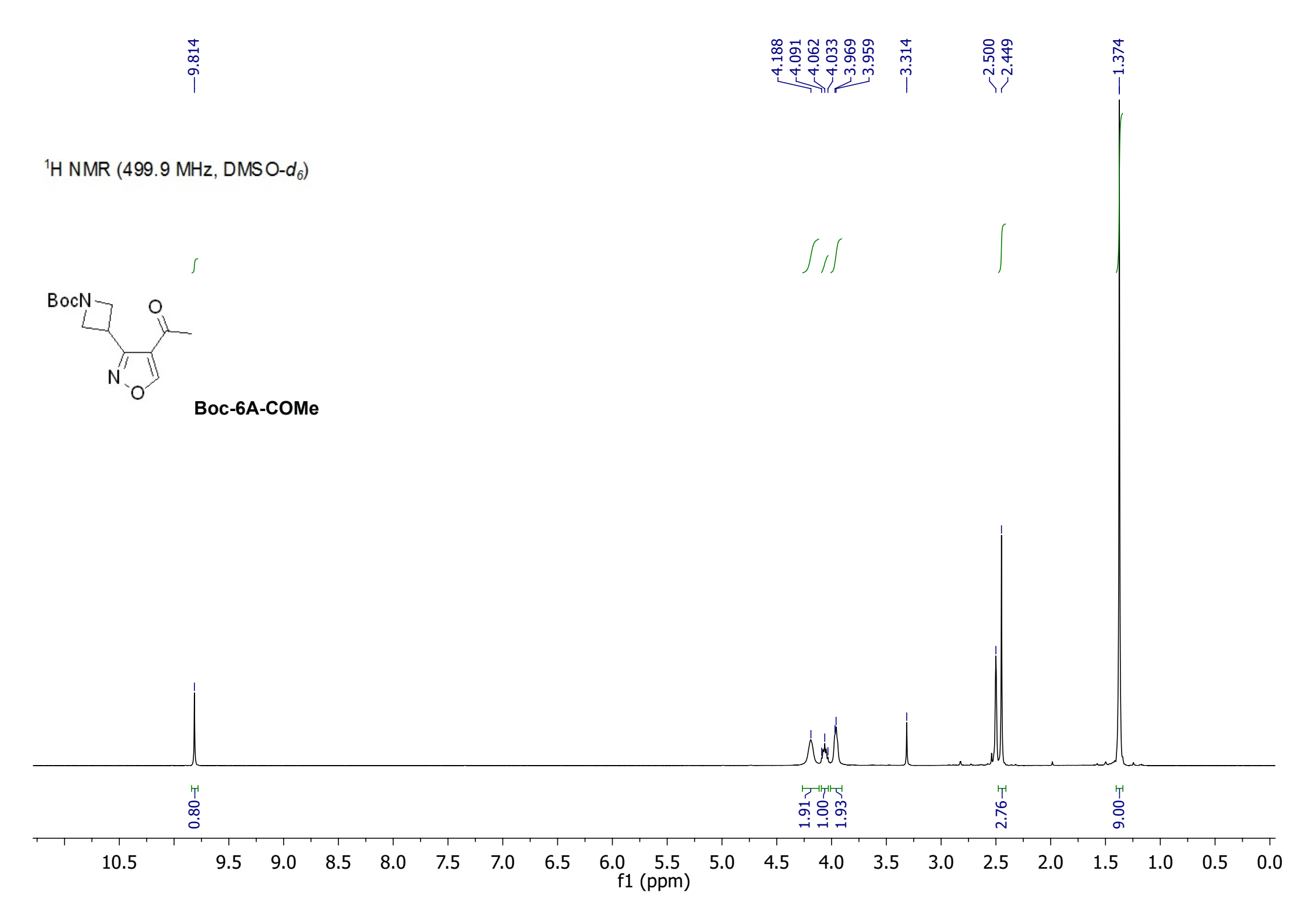

191.81
165.63
159.58
155.46
119.71
78.17
39.52
36.37
28.89
28.15
13C NMR (124.9 MHz, DMSO-d6)
BocHN
O
N
O
Boc-1A-COMe
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

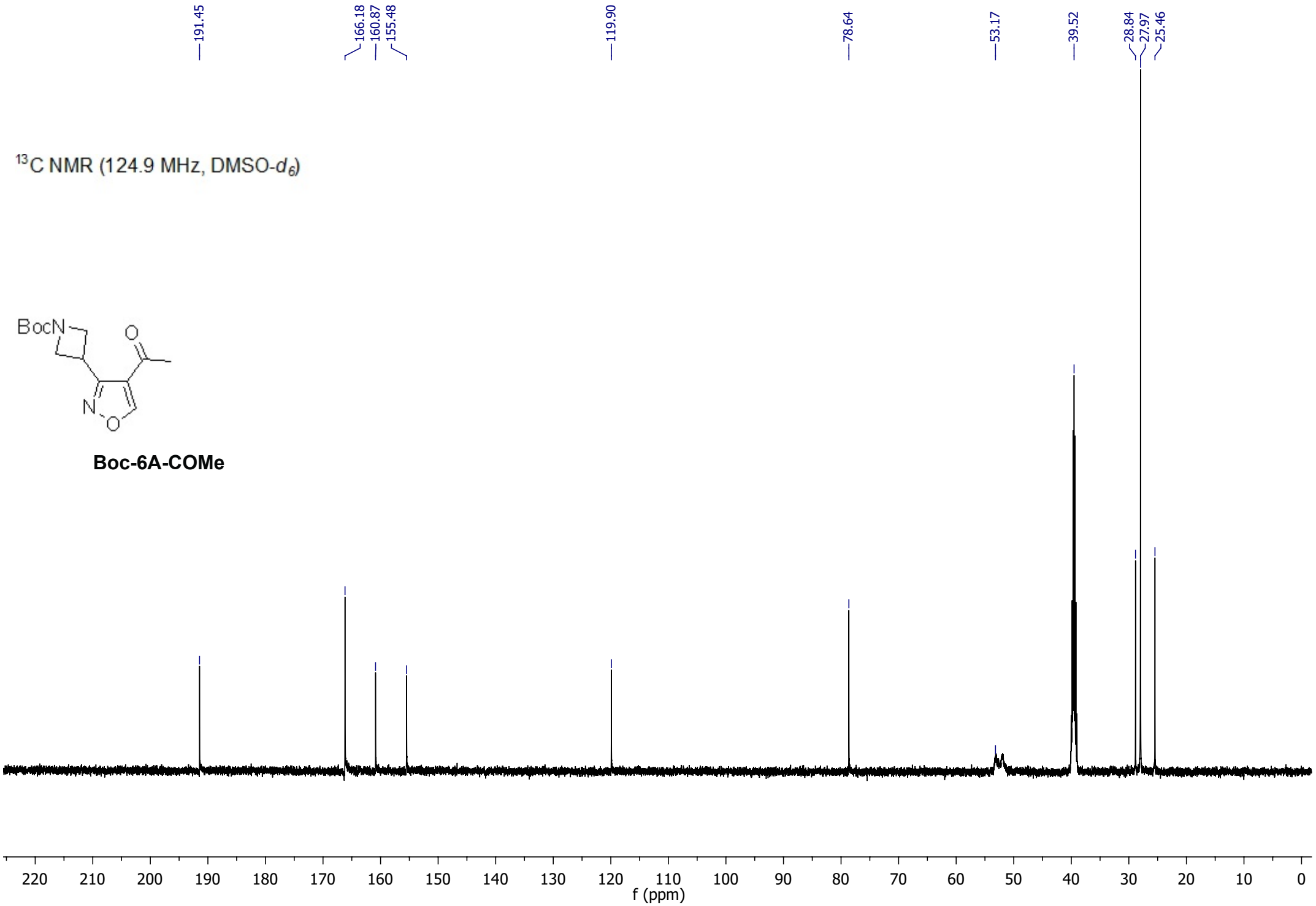

8.897
7.260
5.812
5.329
2.514
1.410
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocHN
O
N
O
Boc-2A-COMe
1.00
1.00
1.02
3.01
12.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f (ppm)

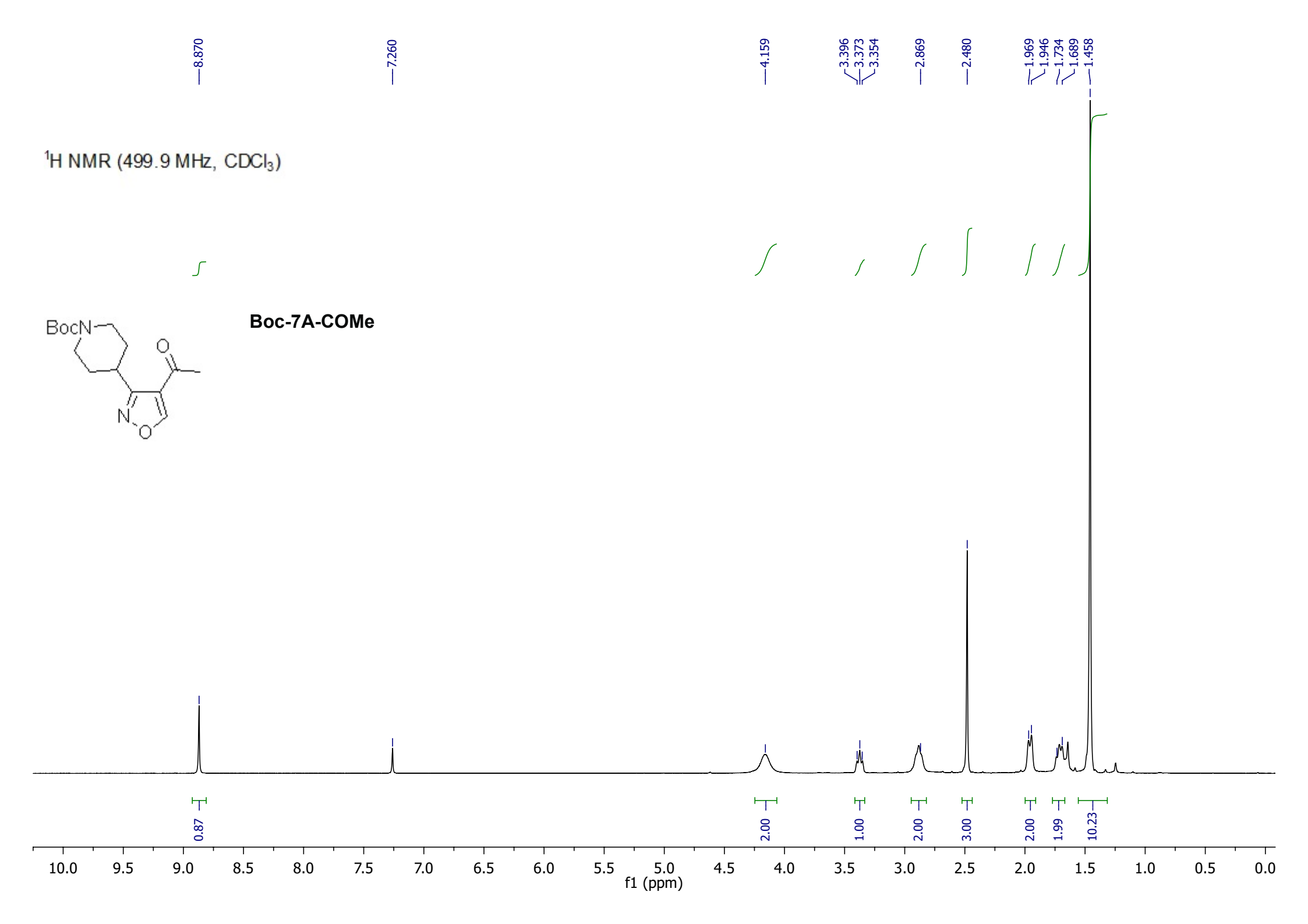

191.82
166.32
163.63
154.69
119.17
78.07
43.12
39.52
29.08
28.14
19.78
13C NMR (124.9 MHz, DMSO-d6)
BocHN
O
N
O
Boc-2A-COMe
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

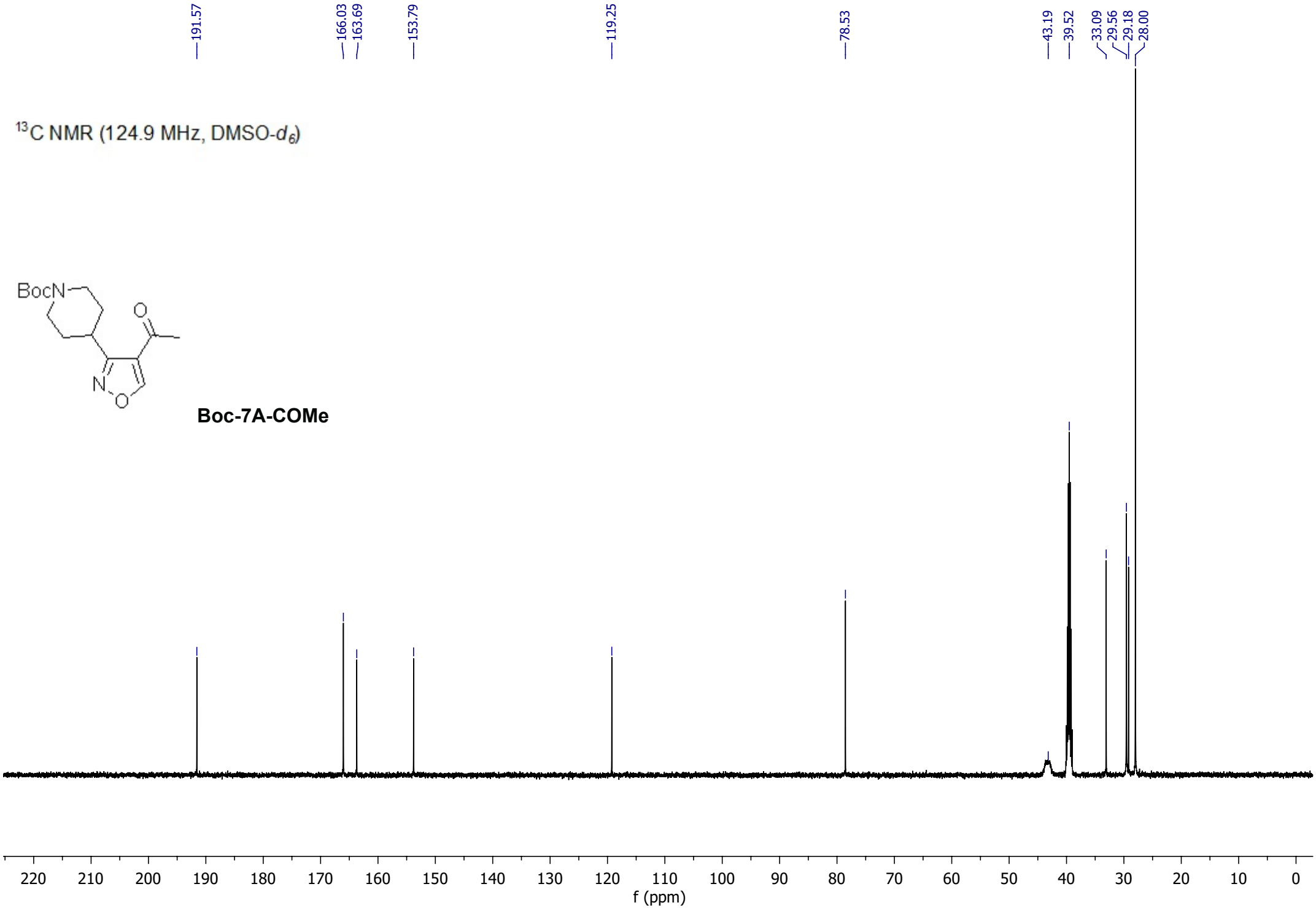

8.879
8.836
7.260
5.463
5.413
3.641
3.496
3.429
2.476
2.450
2.329
1.919
1.848
1.688
1.431
1.255
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
O
N
O
Boc-4A-COMe
0.96
1.00
1.04
1.06
3.05
1.04
3.12
5.02
4.21
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

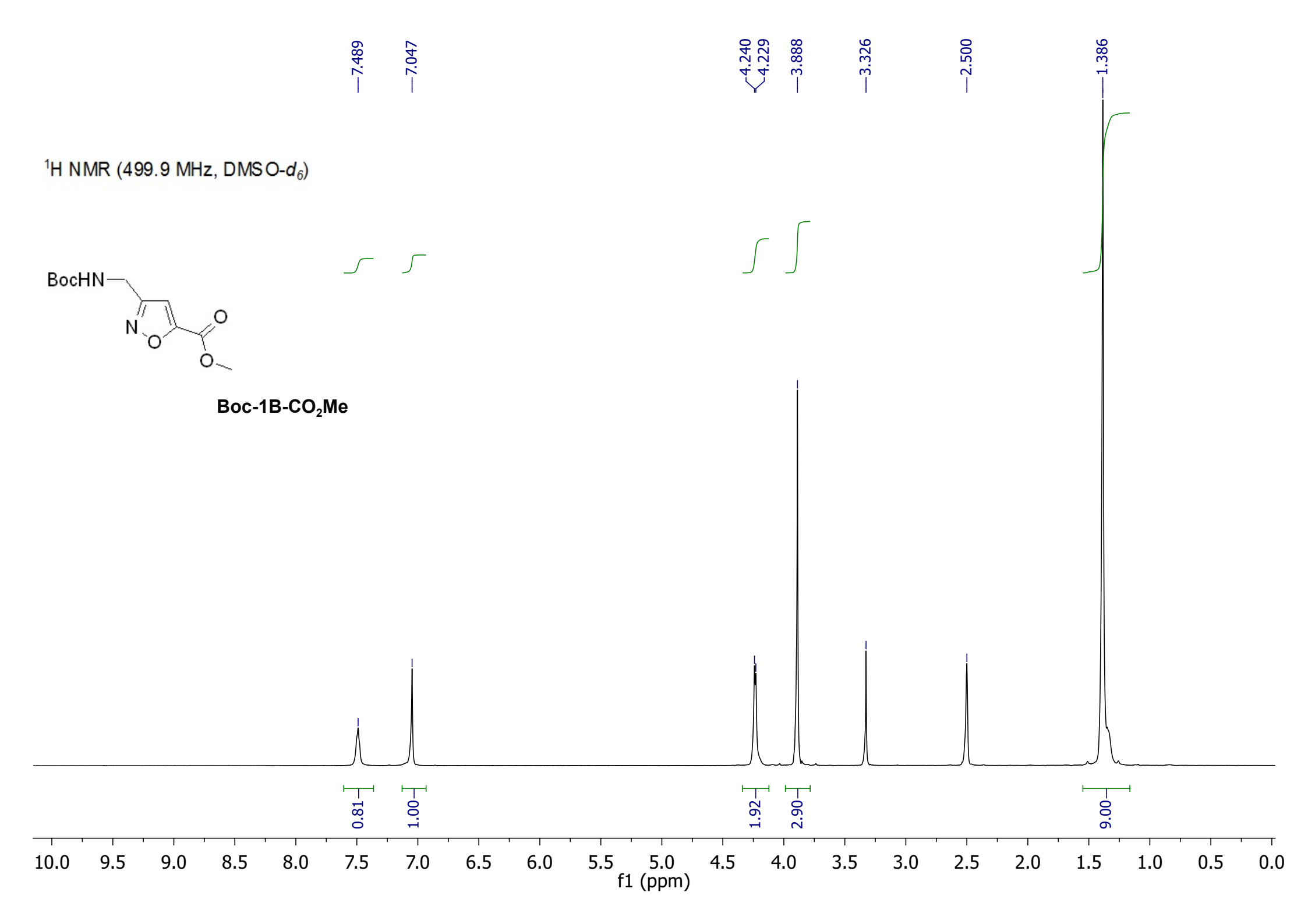

191.52
191.45
165.92
165.83
163.62
162.84
153.09
152.74
119.10
119.02
78.52
78.18
53.25
53.00
46.25
46.02
39.52
31.67
30.78
28.98
28.06
27.74
22.76
22.22
13C NMR (124.9 MHz, DMSO-d6)
BocN
O
N
O
Boc-4A-COMe
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

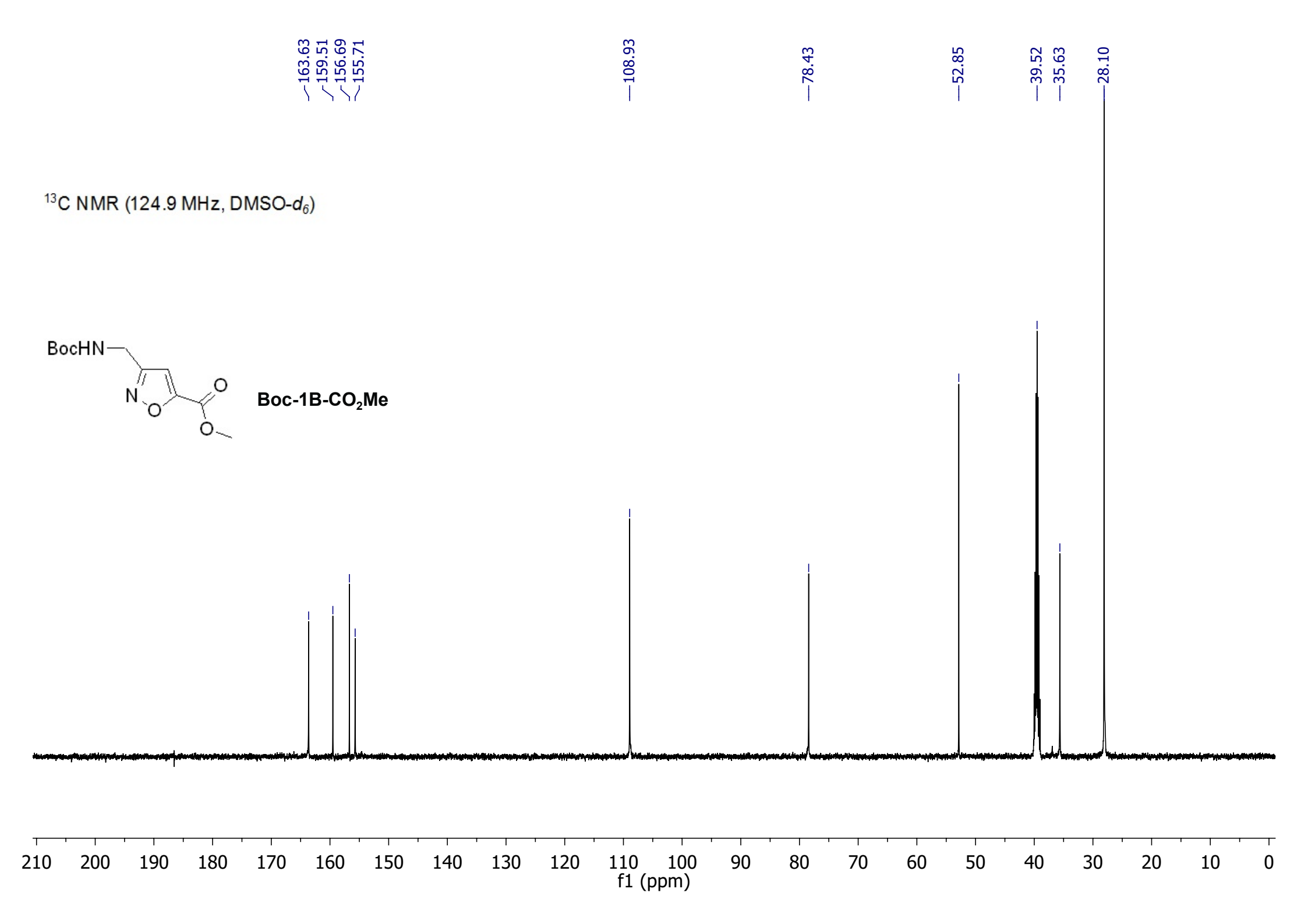

9.814
4.188
4.091
4.062
4.033
3.969
3.959
3.314
2.500
2.449
1.374
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
O
N
O
Boc-6A-COMe
0.80
1.91
1.00
1.93
2.76
9.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


191.45
166.18
160.87
155.48
119.90
78.64
53.17
39.52
28.84
27.97
25.46
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
O
N
O
Boc-6A-COMe
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

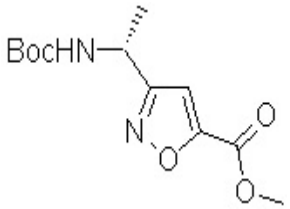

8.870
7.260
4.159
3.396
3.373
3.354
2.869
2.480
1.969
1.946
1.734
1.689
1.458
^{1}H NMR (499.9 MHz, $CDCl_3$)
Boc-7A-COMe
BocN
O
N
O
0.87
2.00
1.00
2.00
3.00
2.00
1.99
10.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


191.57
166.03
163.69
153.79
119.25
78.53
43.19
39.52
33.09
29.56
29.18
28.00
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
O
N
O
Boc-7A-COMe
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

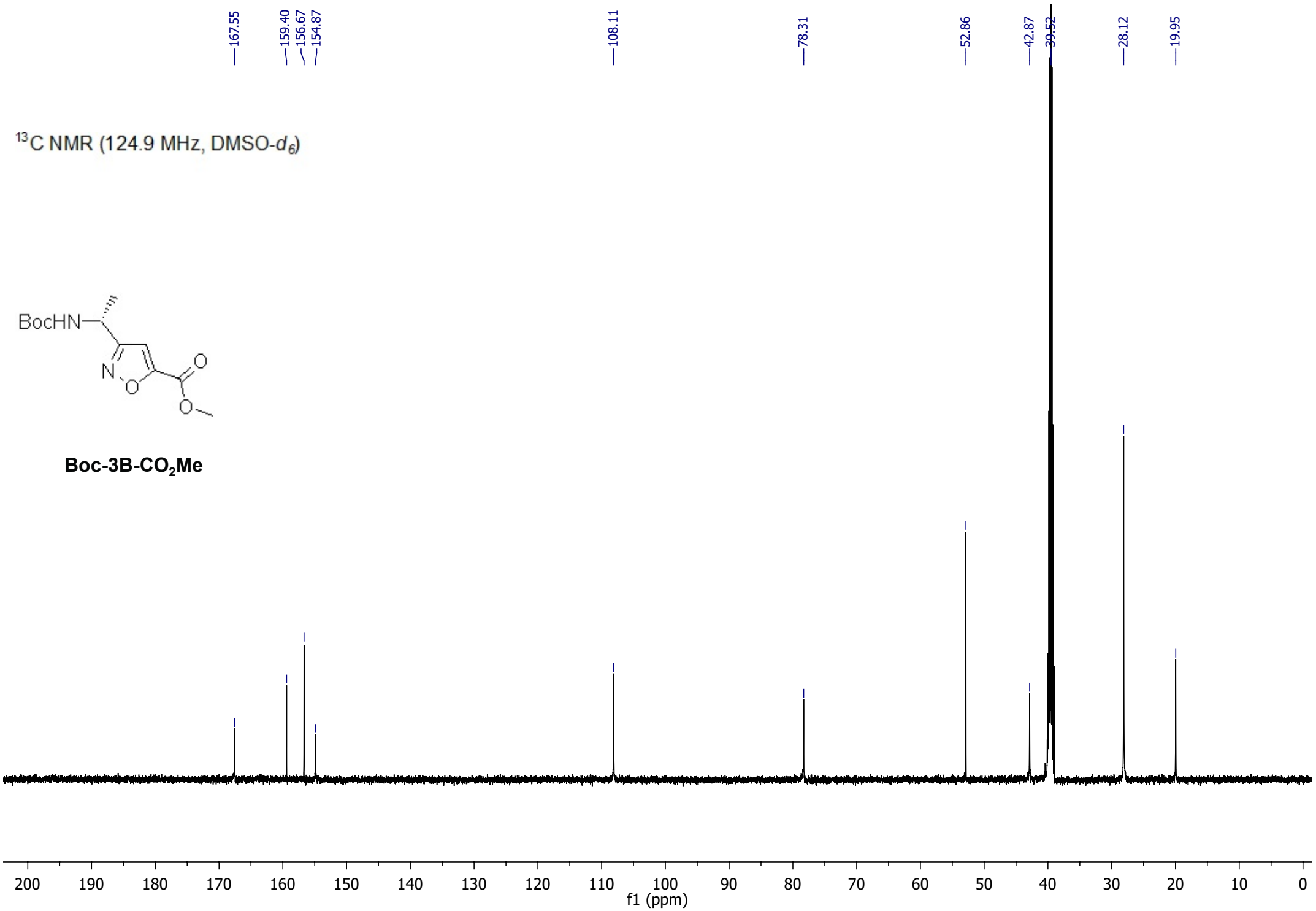

7.489
7.047
4.240
4.229
3.888
3.326
2.500
1.386
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
O
O
Boc-1B-CO$_2$Me
0.81
1.00
1.92
2.90
9.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

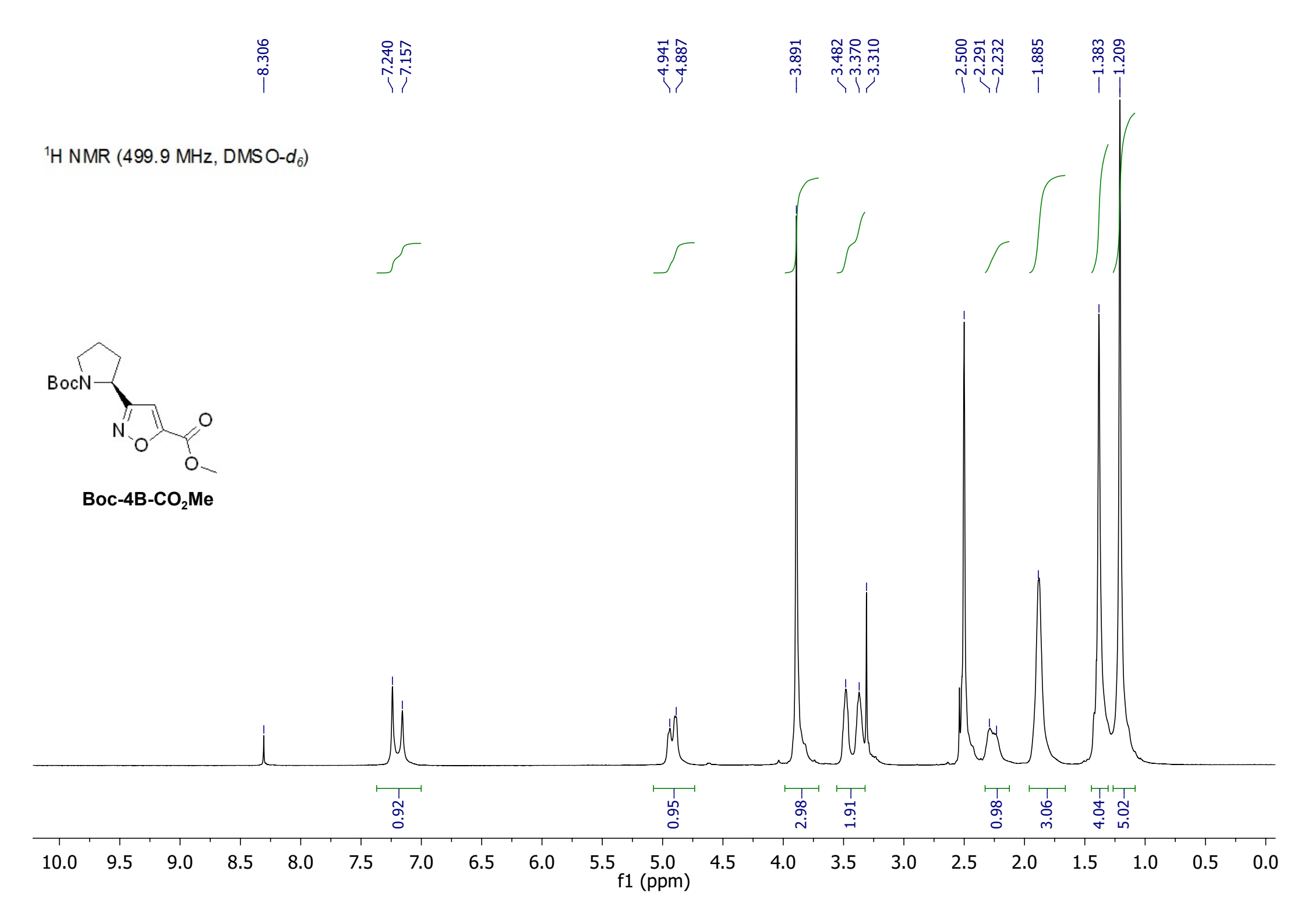

163.63
159.51
156.69
155.71
108.93
78.43
52.85
39.52
35.63
28.10
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
N
O
O
O
O
Boc-1B-CO$_2$Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

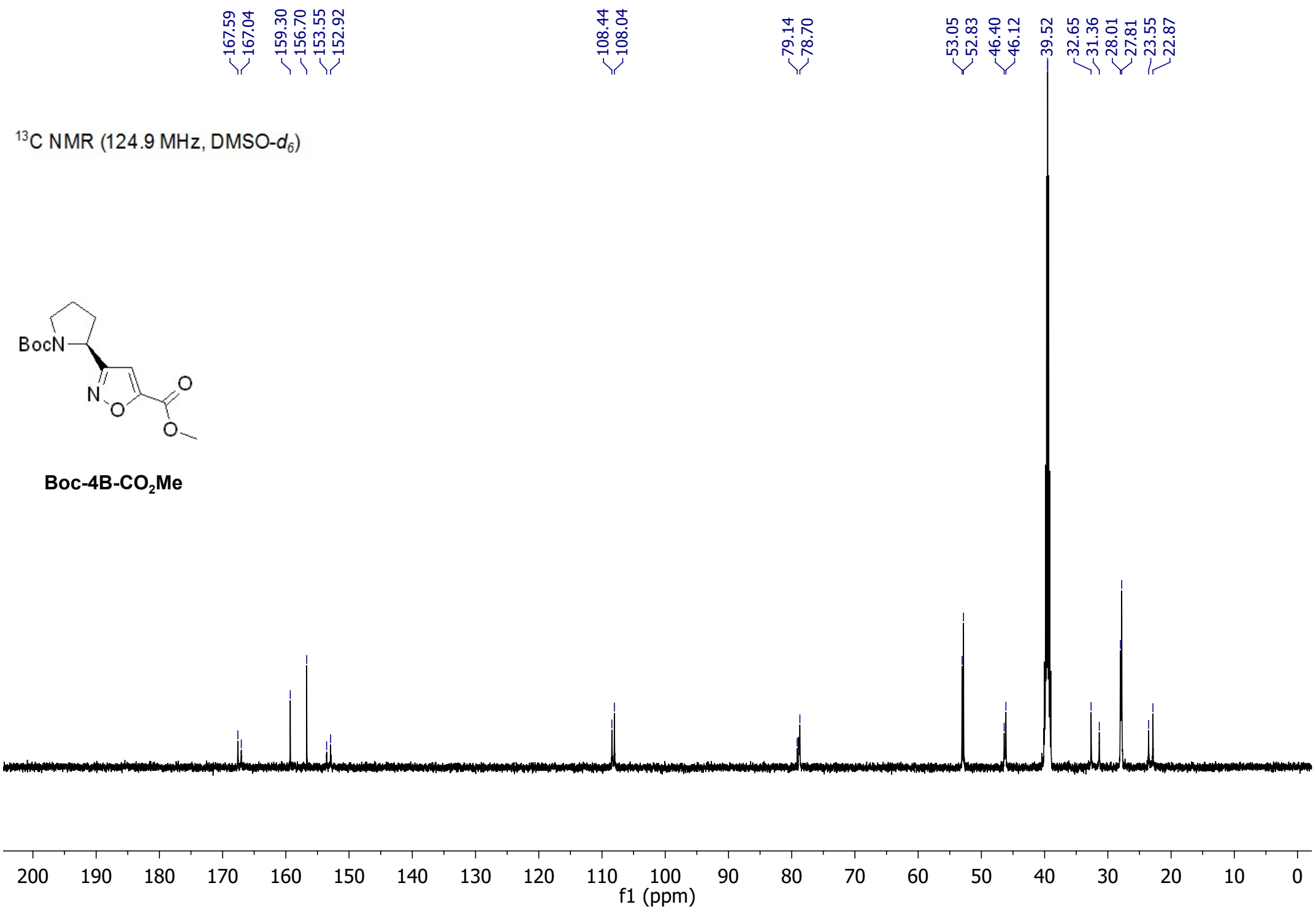
^{1}H NMR (499.9 MHz, DMSO-d_6)



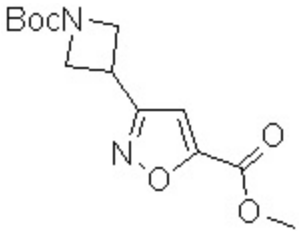
Boc-3B-CO_2Me


167.55
159.40
156.67
154.87
108.11
78.31
52.86
42.87
39.52
28.12
19.95
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
O
O
O
Boc-3B-CO2Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

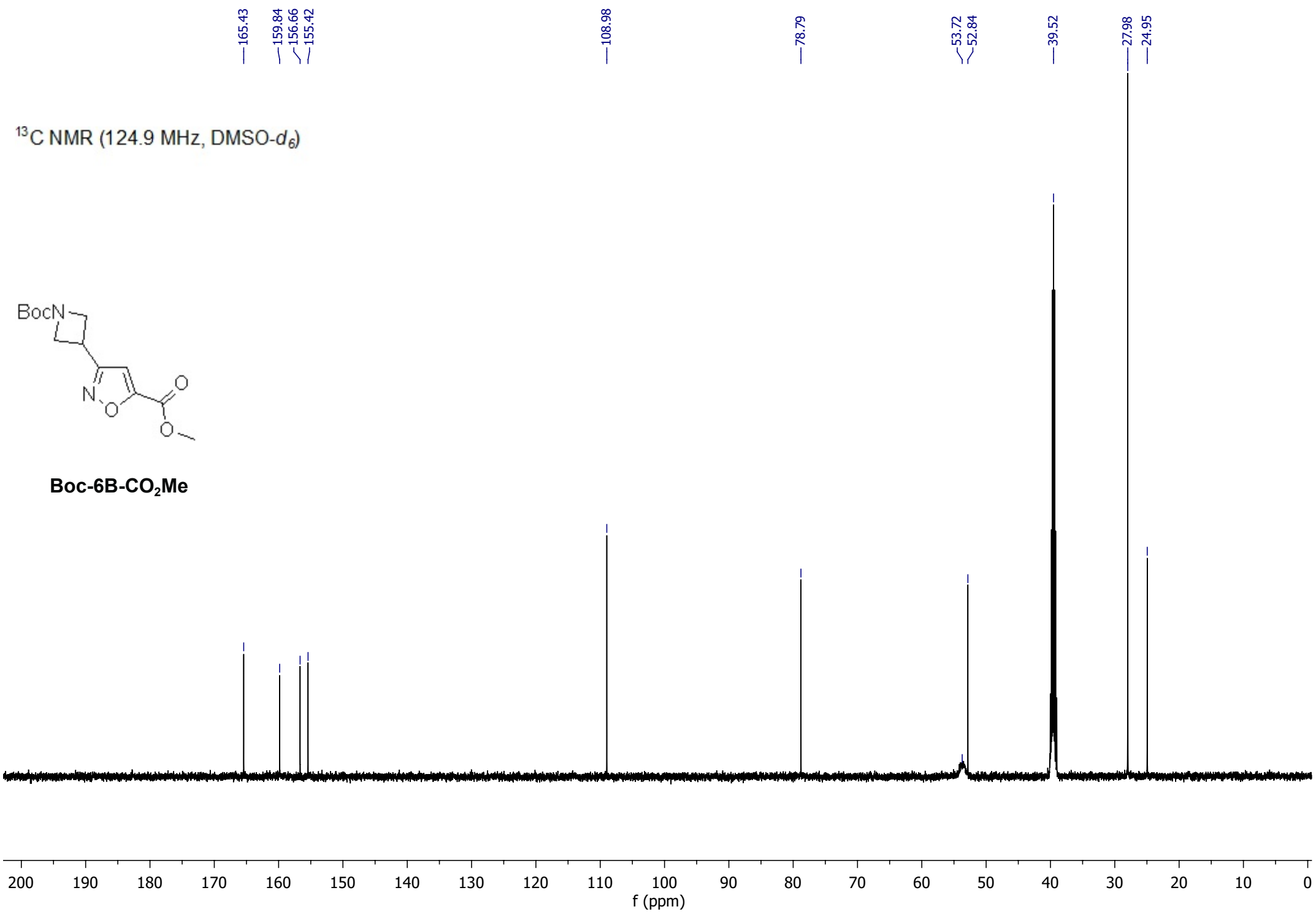

8.306
7.240
7.157
4.941
4.887
3.891
3.482
3.370
3.310
2.500
2.291
2.232
1.885
1.383
1.209
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
O
O
Boc-4B-CO$_2$Me
0.92
0.95
2.98
1.91
0.98
3.06
4.04
5.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.59
167.04
159.30
156.70
153.55
152.92
108.44
108.04
79.14
78.70
53.05
52.83
46.40
46.12
39.52
32.65
31.36
28.01
27.81
23.55
22.87
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
O
O
Boc-4B-CO$_2$Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

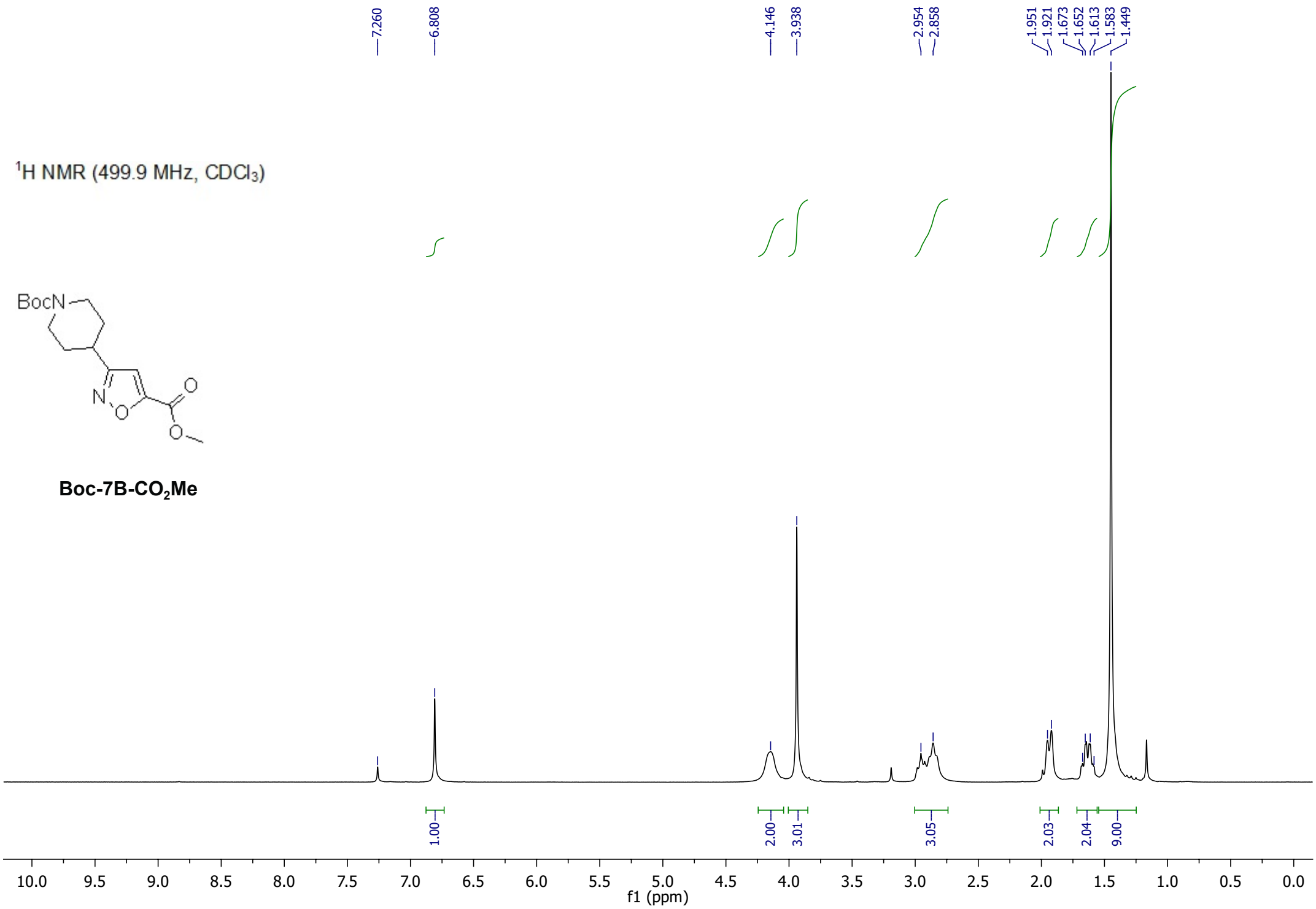
^{1}H NMR (499.9 MHz, $CDCl_3$)



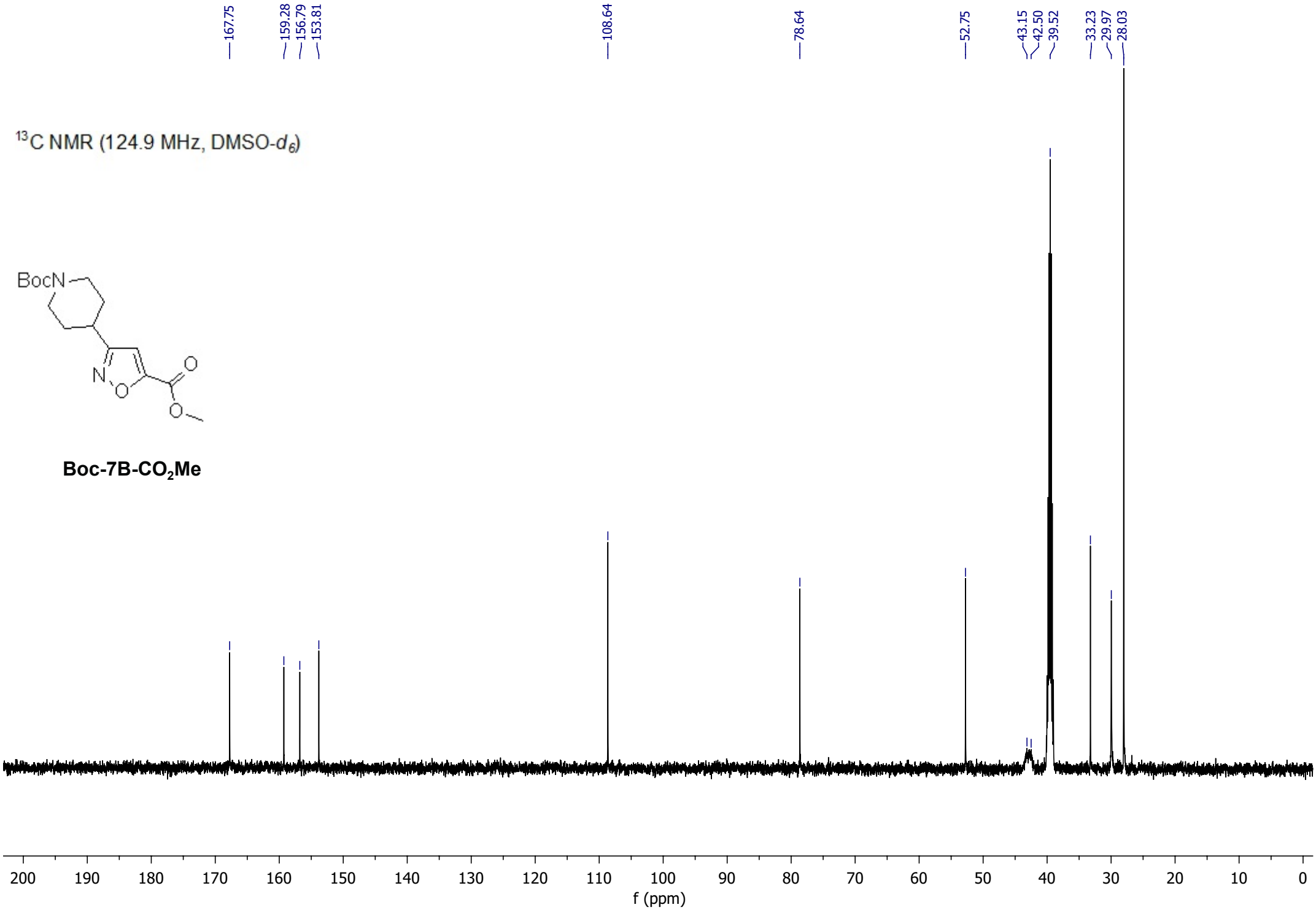
Boc-6B-CO_2Me


165.43
159.84
156.66
155.42
108.98
78.79
53.72
52.84
39.52
27.98
24.95
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
O
N
O
O
f (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

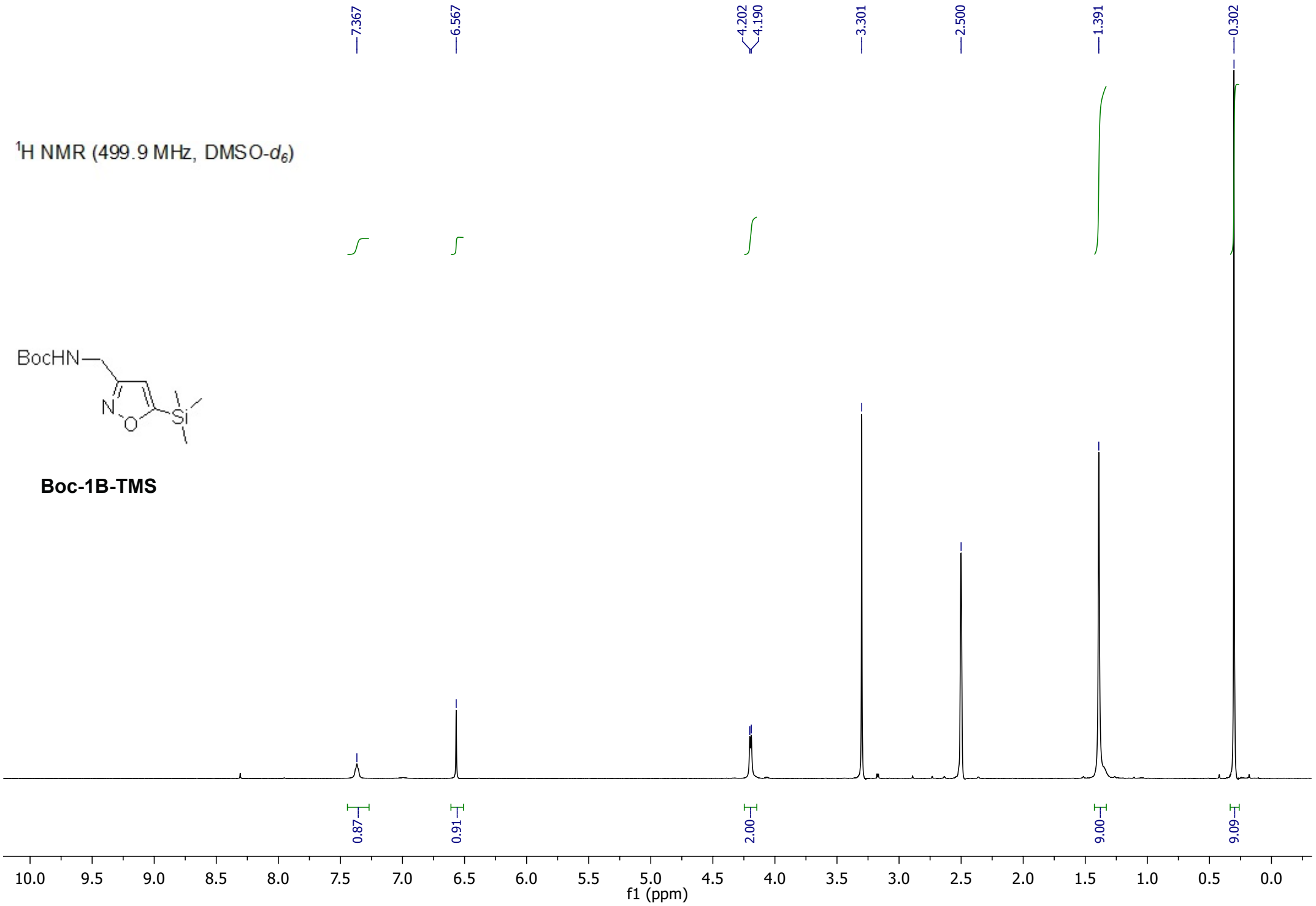
Boc-6B-CO_2Me

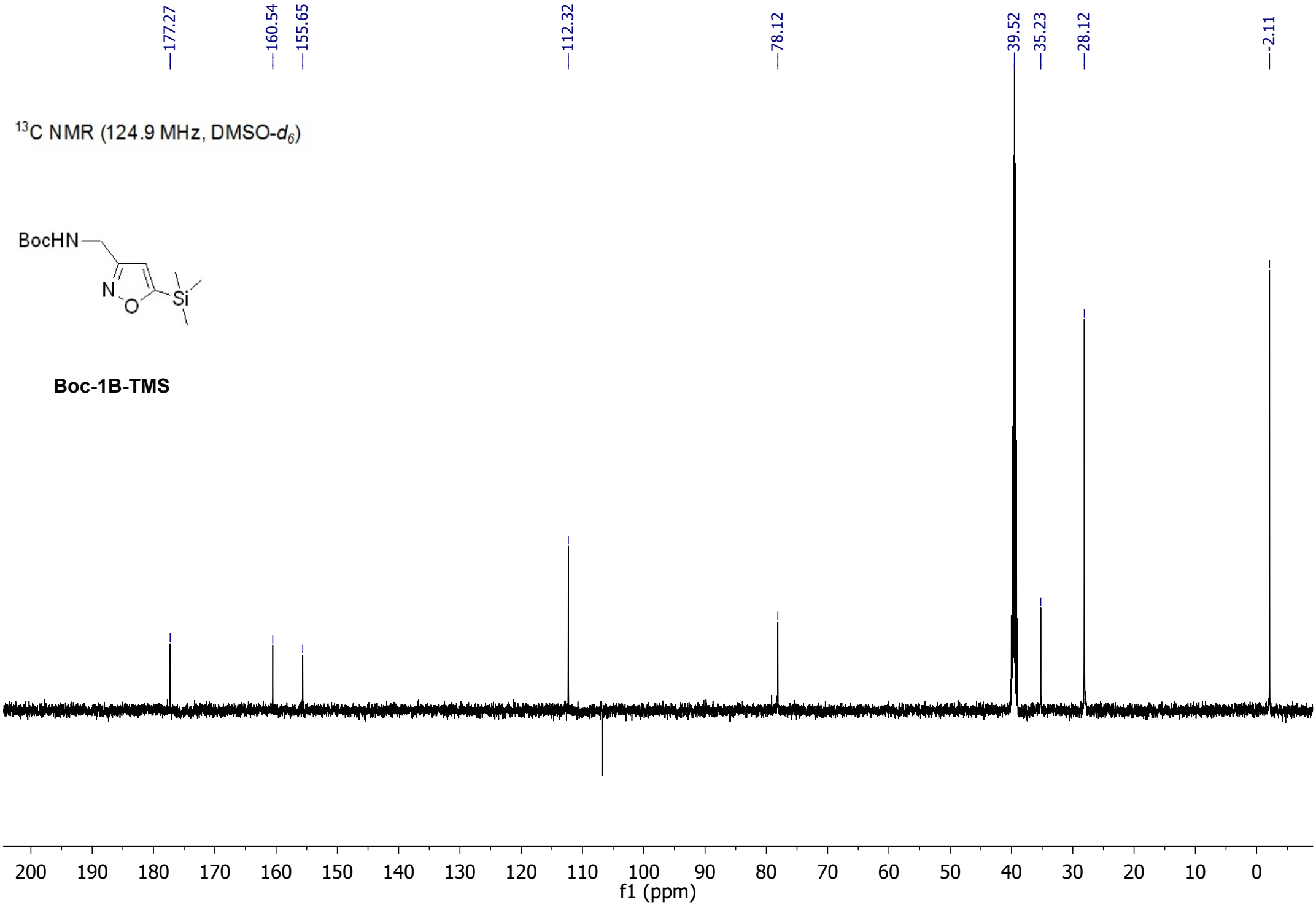

7.260
6.808
4.146
3.938
2.954
2.858
1.951
1.921
1.673
1.652
1.613
1.583
1.449
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
N
O
O
O
1.00
2.00
3.01
3.05
2.03
2.04
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

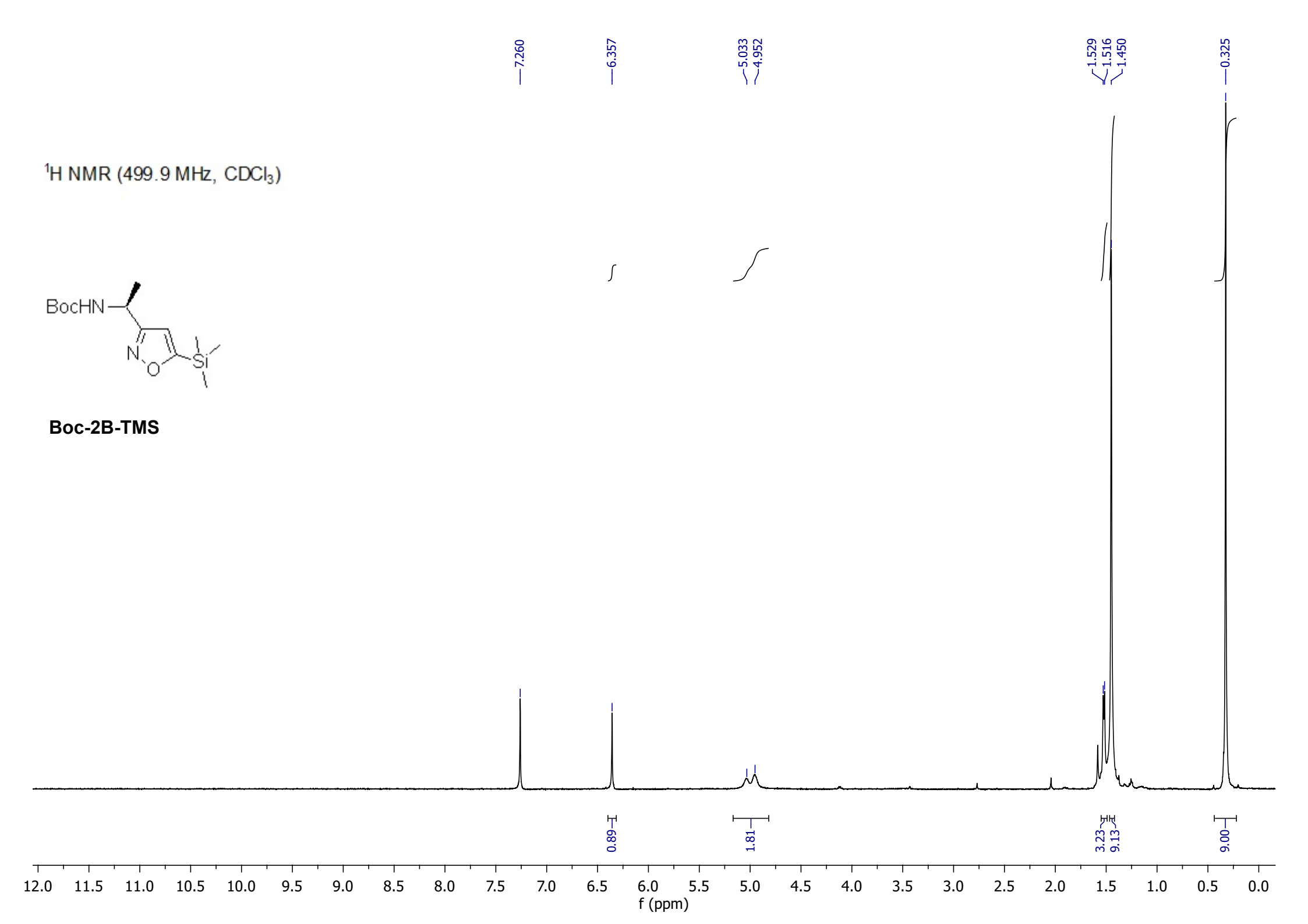
Boc-7B-CO_2Me

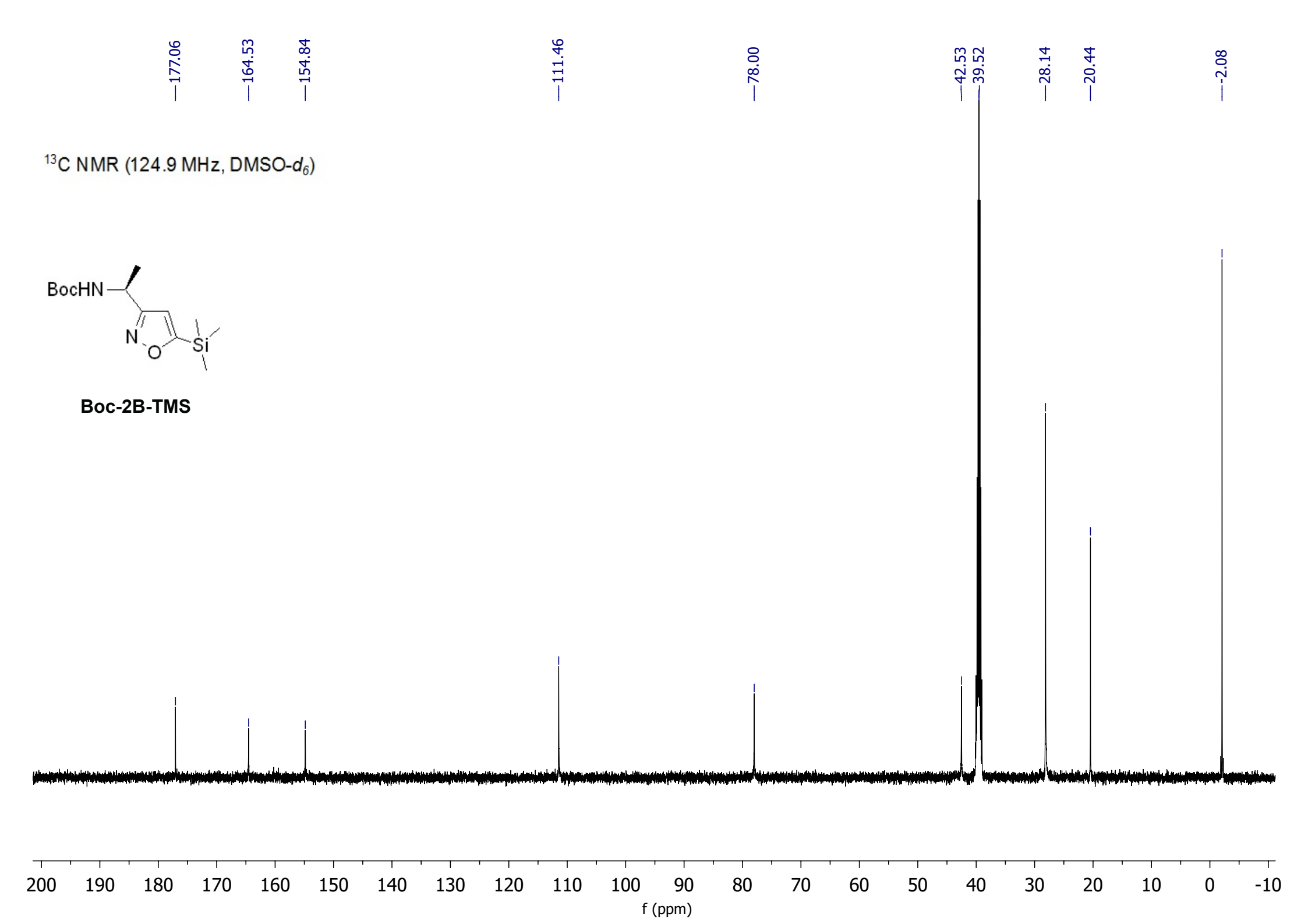

167.75
159.28
156.79
153.81
108.64
78.64
52.75
43.15
42.50
39.52
33.23
29.97
28.03
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

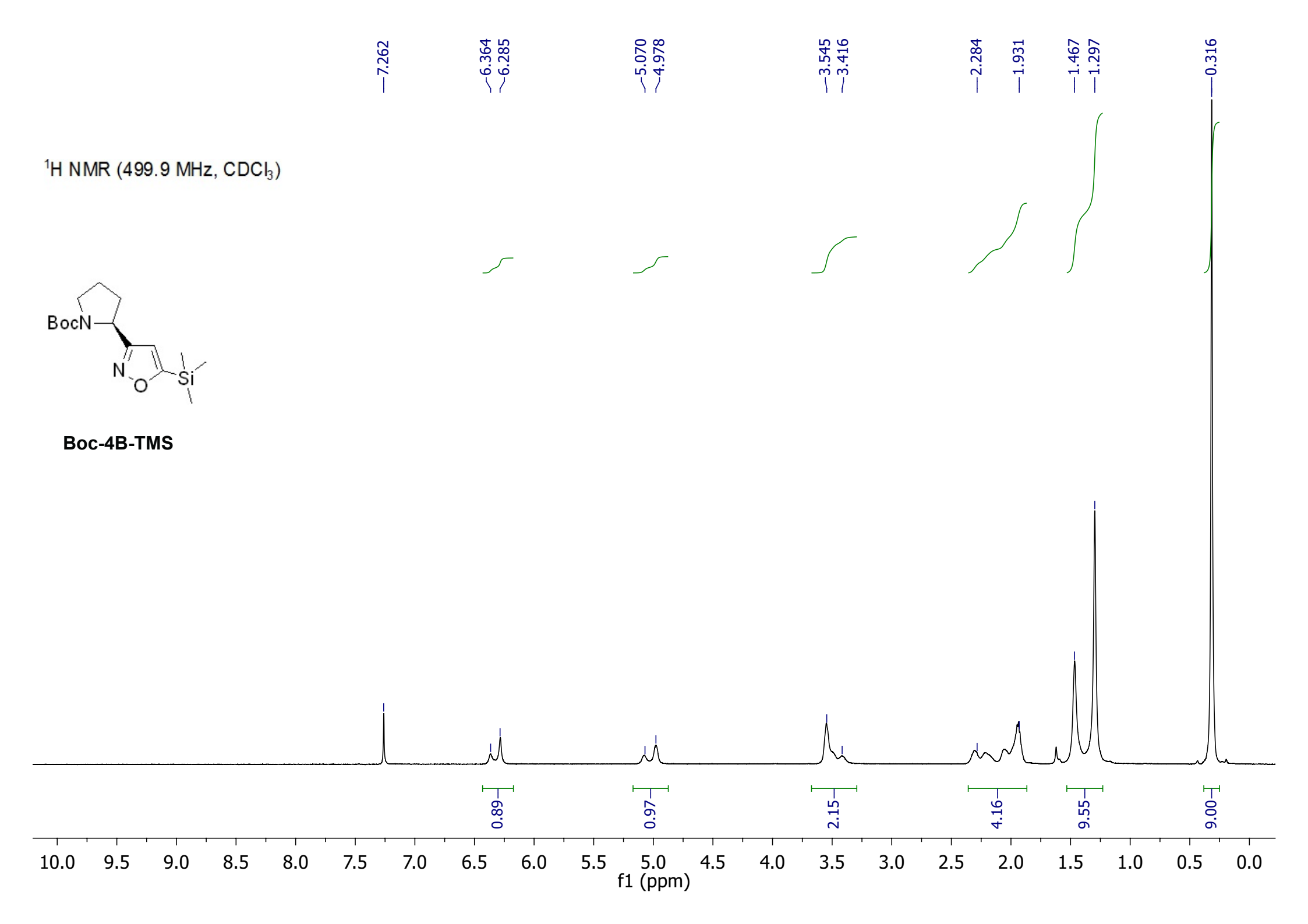
Boc-7B-CO_2Me

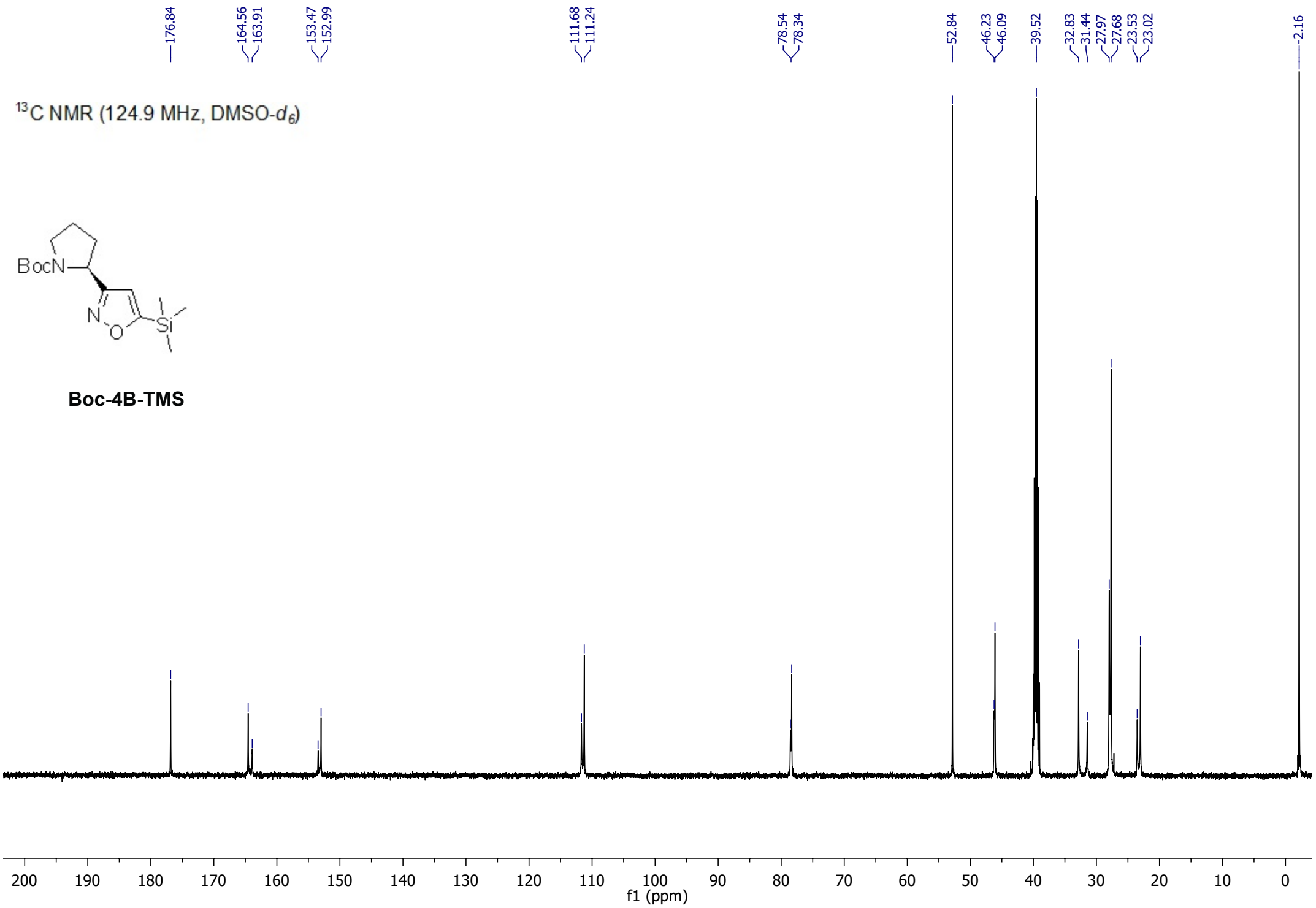

7.367
6.567
4.202
4.190
3.301
2.500
1.391
0.302
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
Si
Boc-1B-TMS
0.87
0.91
2.00
9.00
9.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


177.27
160.54
155.65
112.32
78.12
39.52
35.23
28.12
2.11
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
O
Si
Boc-1B-TMS
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

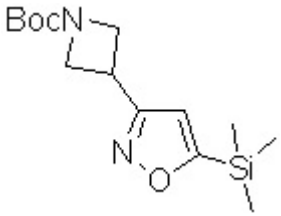

7.260
6.357
5.033
4.952
1.529
1.516
1.450
0.325
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocHN
N
O
Si
Boc-2B-TMS
0.89
1.81
3.23
9.13
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f (ppm)


177.06
164.53
154.84
111.46
78.00
42.53
39.52
28.14
20.44
-2.08
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
O
Si
Boc-2B-TMS
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f (ppm)

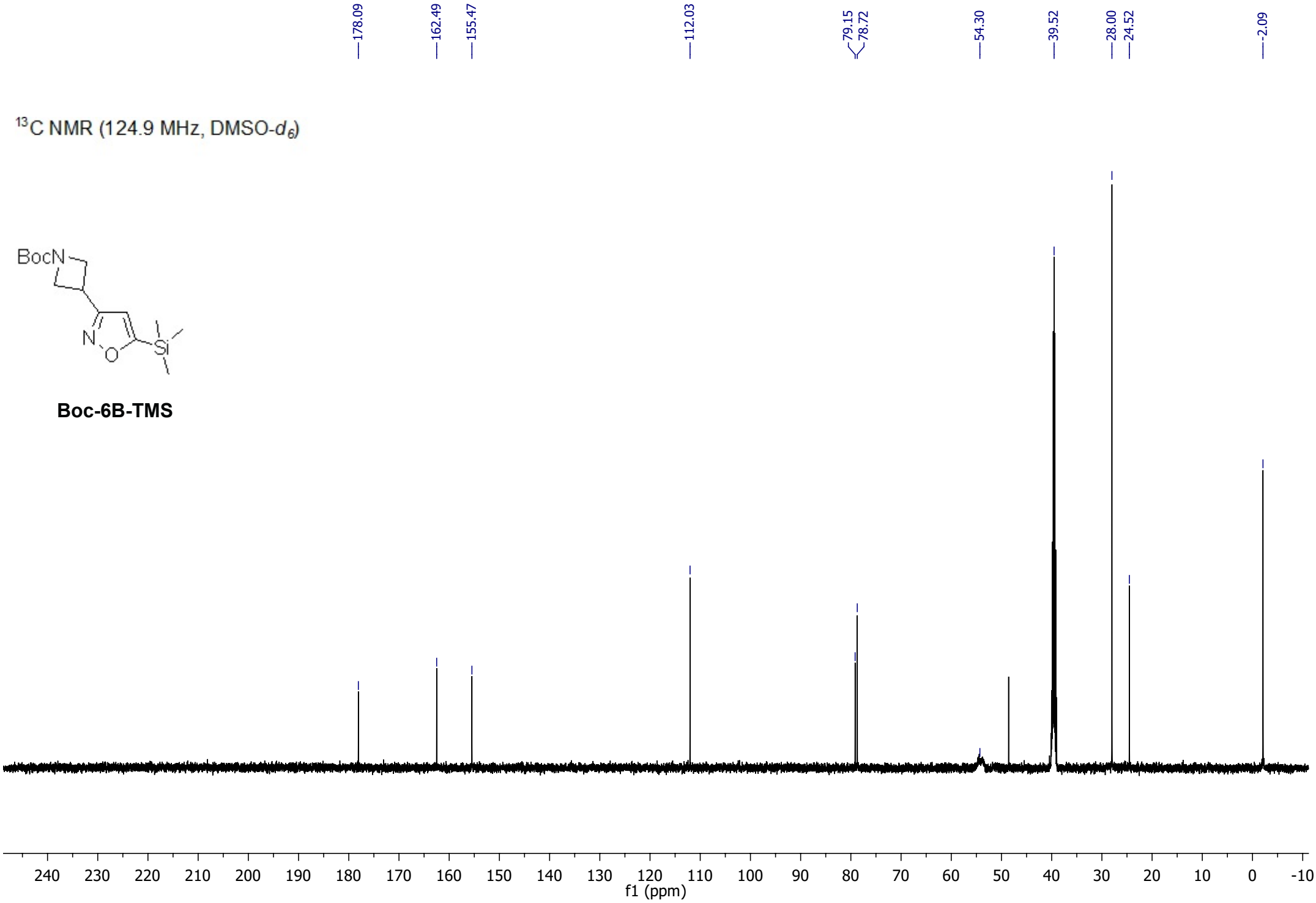

7.262
6.364
6.285
5.070
4.978
3.545
3.416
2.284
1.931
1.467
1.297
0.316
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
N
O
Si
Boc-4B-TMS
0.89
0.97
2.15
4.16
9.55
9.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

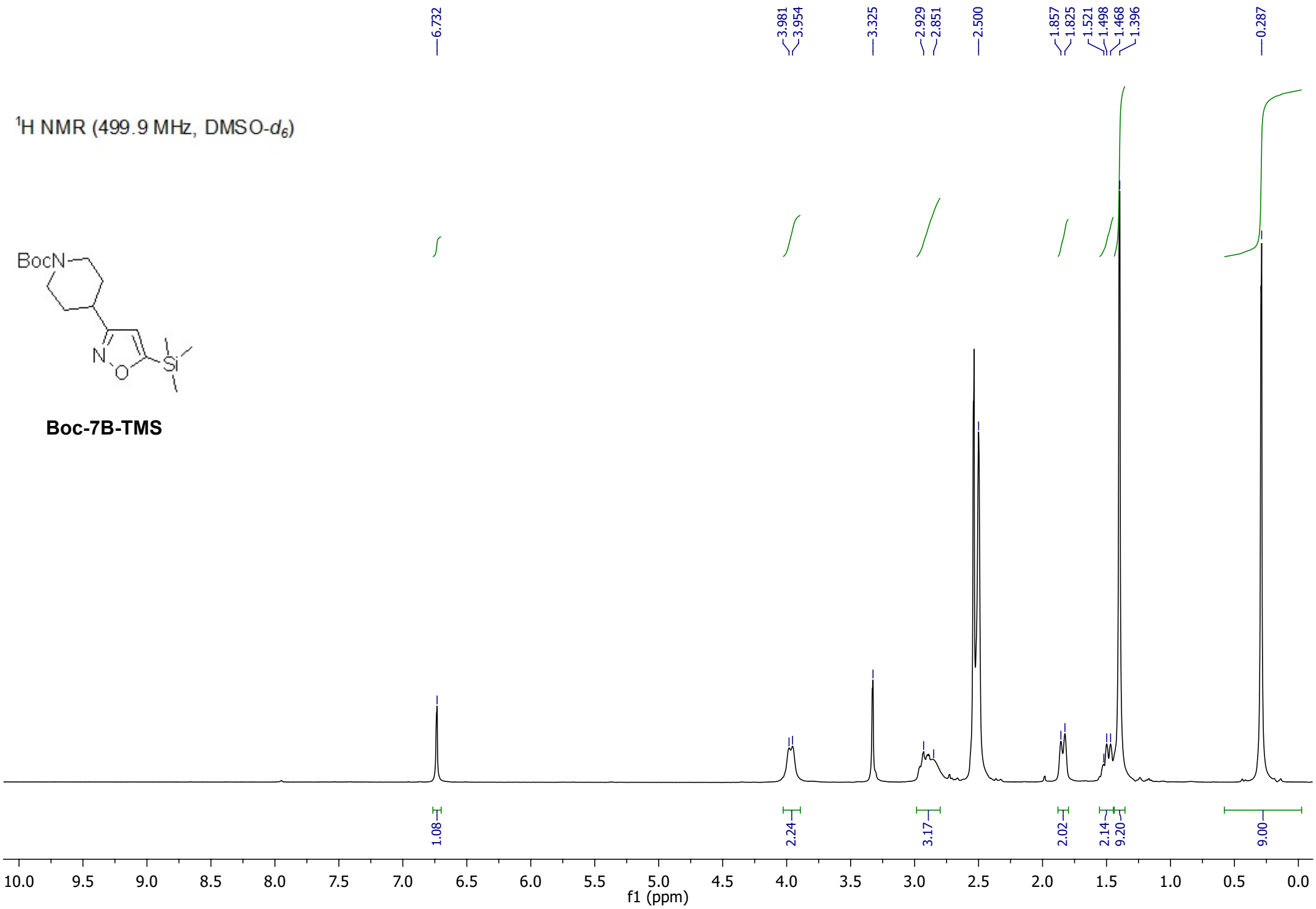

176.84
164.56
163.91
153.47
152.99
111.68
111.24
78.54
78.34
52.84
46.23
46.09
39.52
32.83
31.44
27.97
27.68
23.53
23.02
-2.16
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
O
Si
Boc-4B-TMS
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

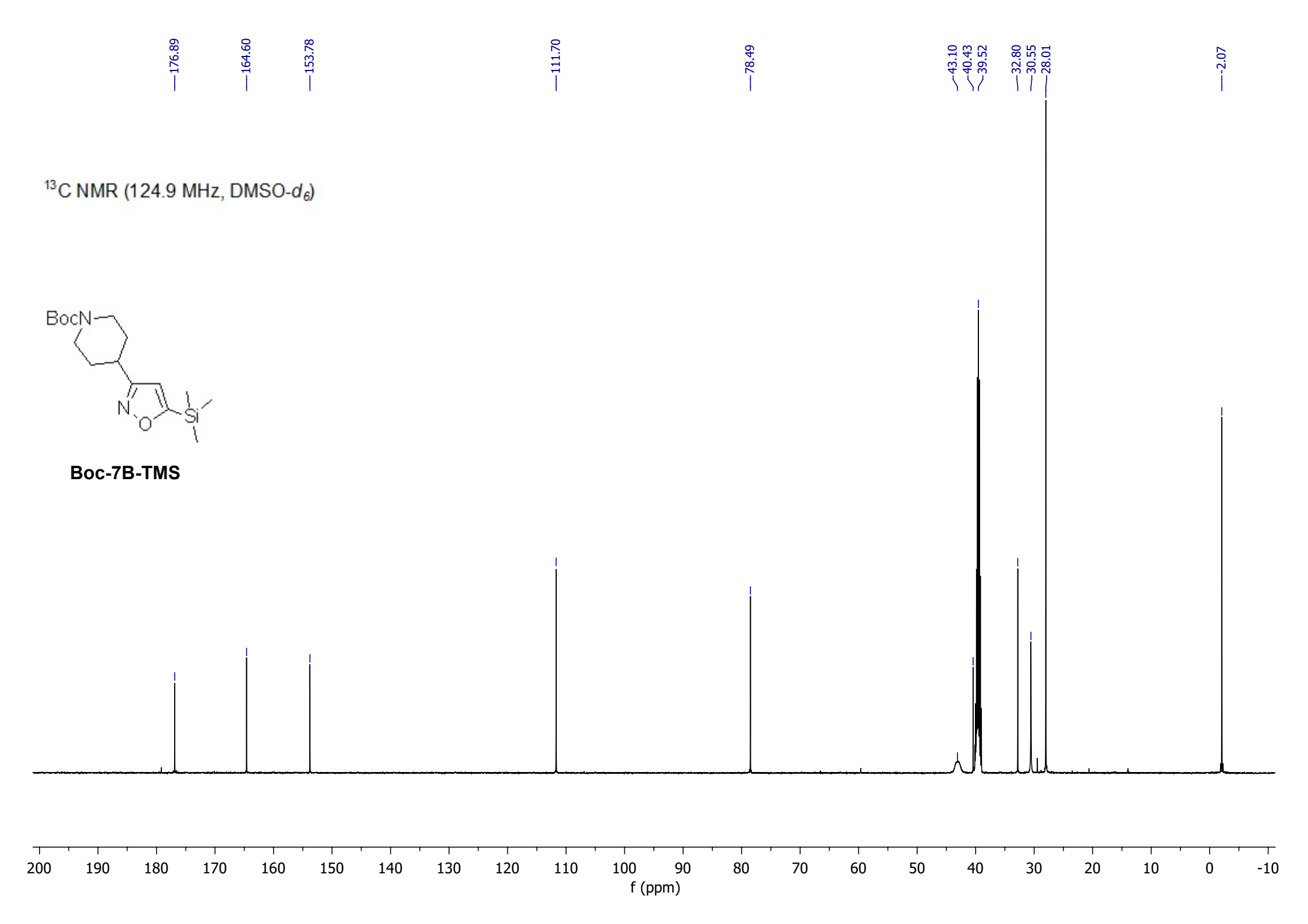
^{1}H NMR (499.9 MHz, $CDCl_3$)

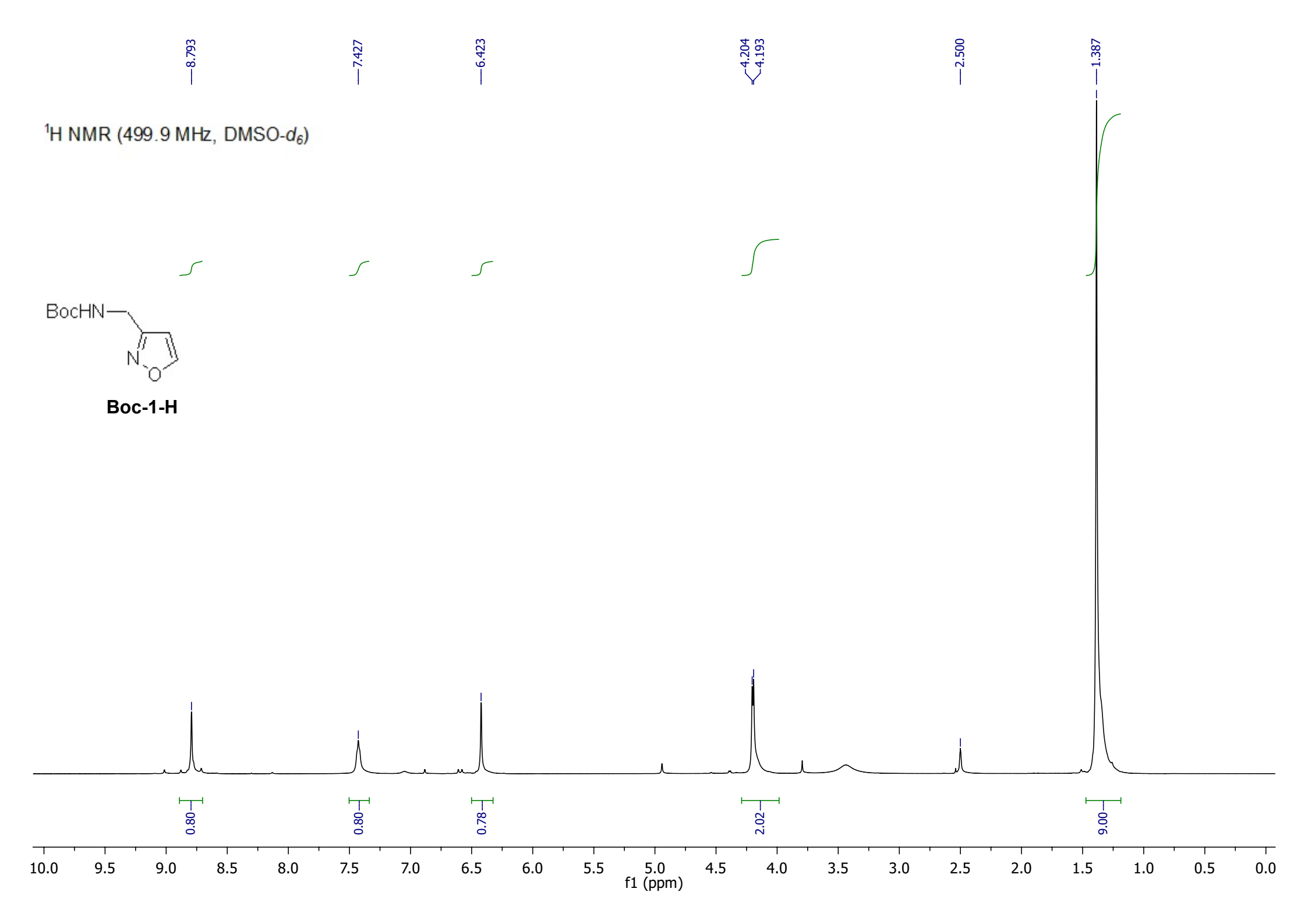


Boc-6B-TMS

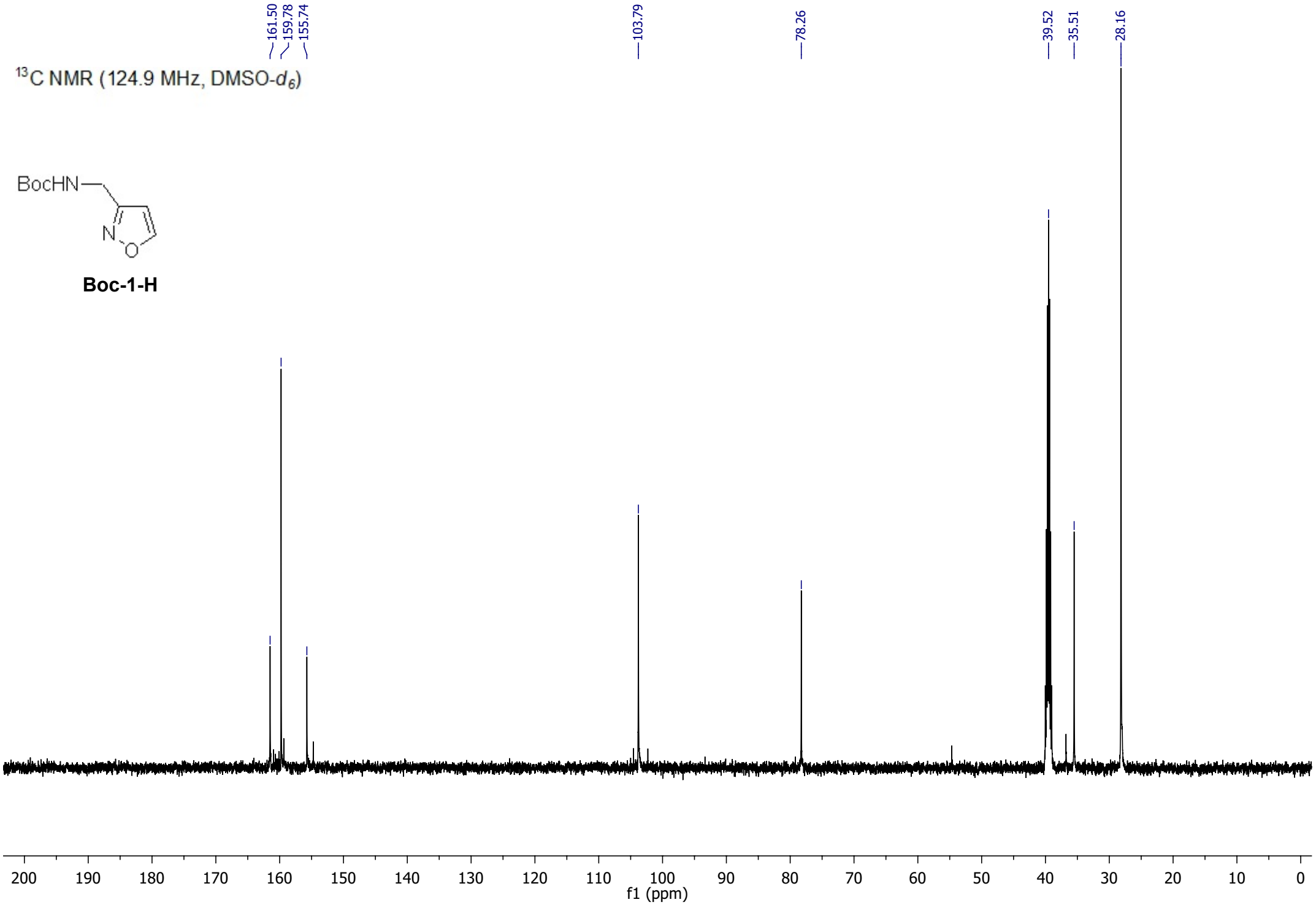

178.09
162.49
155.47
112.03
79.15
78.72
54.30
39.52
28.00
24.52
-2.09
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
Si
Boc-6B-TMS
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

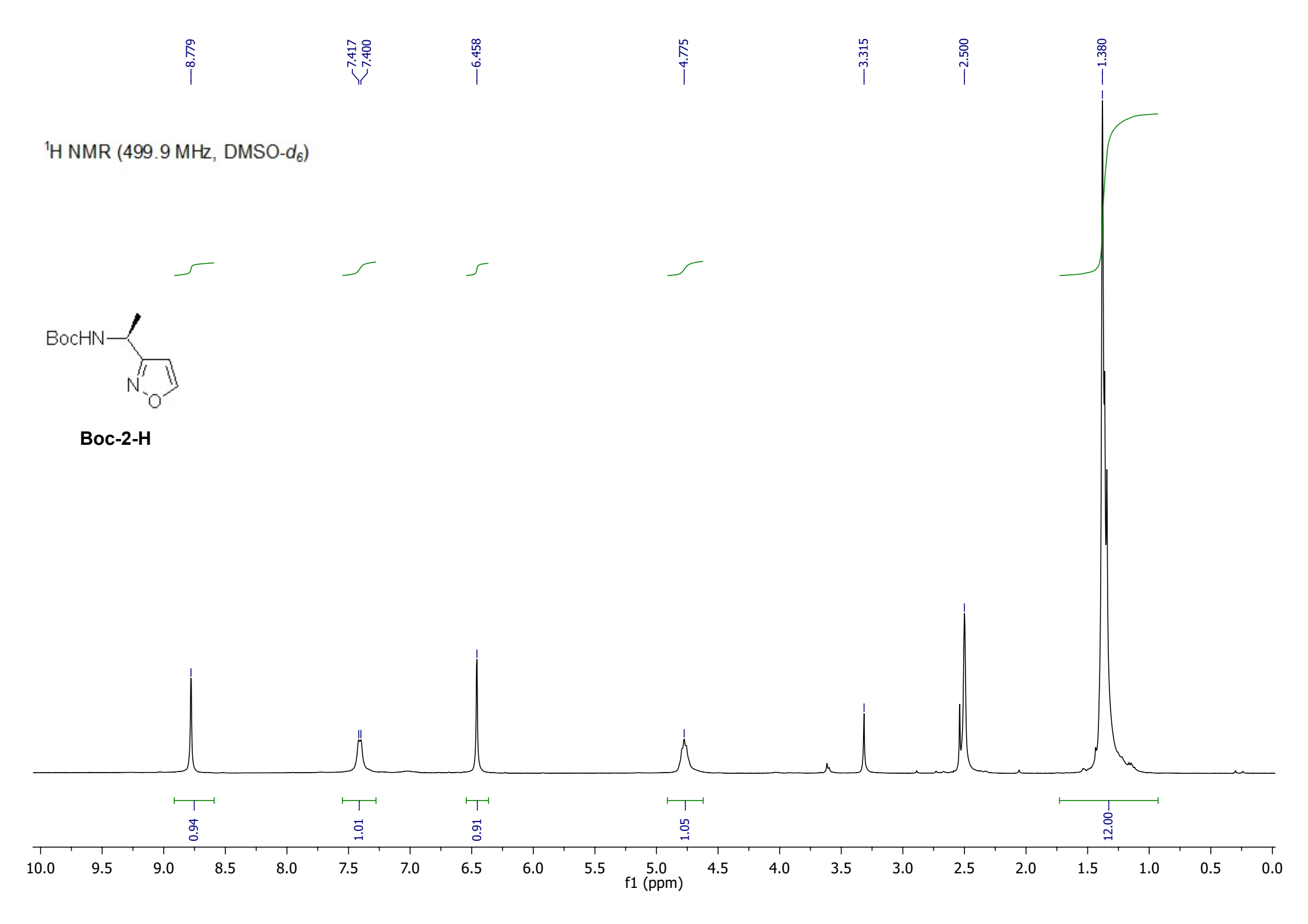

6.732
3.981
3.954
3.325
2.929
2.851
2.500
1.857
1.825
1.521
1.498
1.468
1.396
0.287
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
Si
Boc-7B-TMS
1.08
2.24
3.17
2.02
2.14
9.20
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


176.89
164.60
153.78
111.70
78.49
43.10
40.43
39.52
32.80
30.55
28.01
-2.07
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
Si
Boc-7B-TMS
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f (ppm)

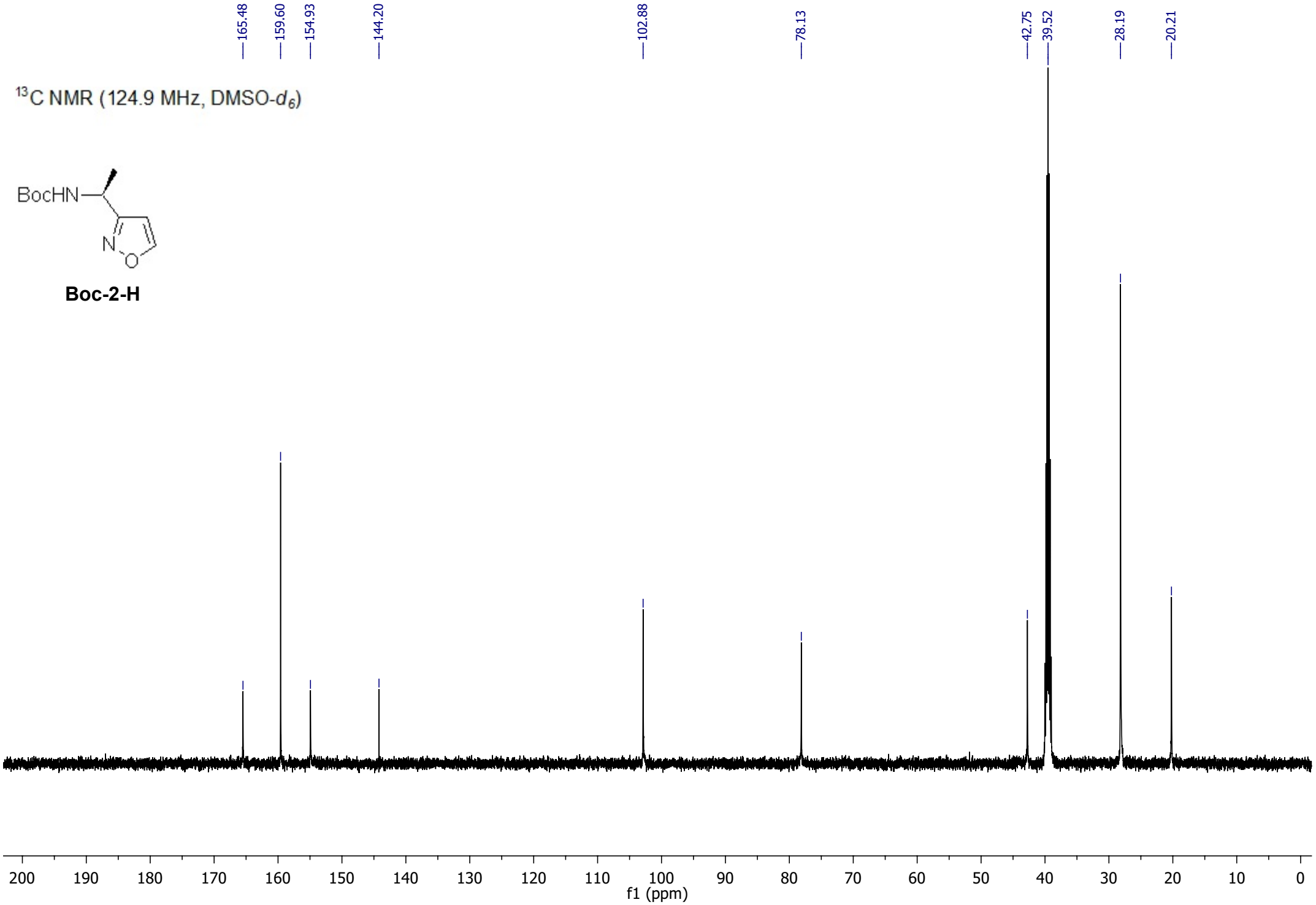

8.793
7.427
6.423
4.204
4.193
2.500
1.387
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
0.80
0.80
0.78
2.02
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

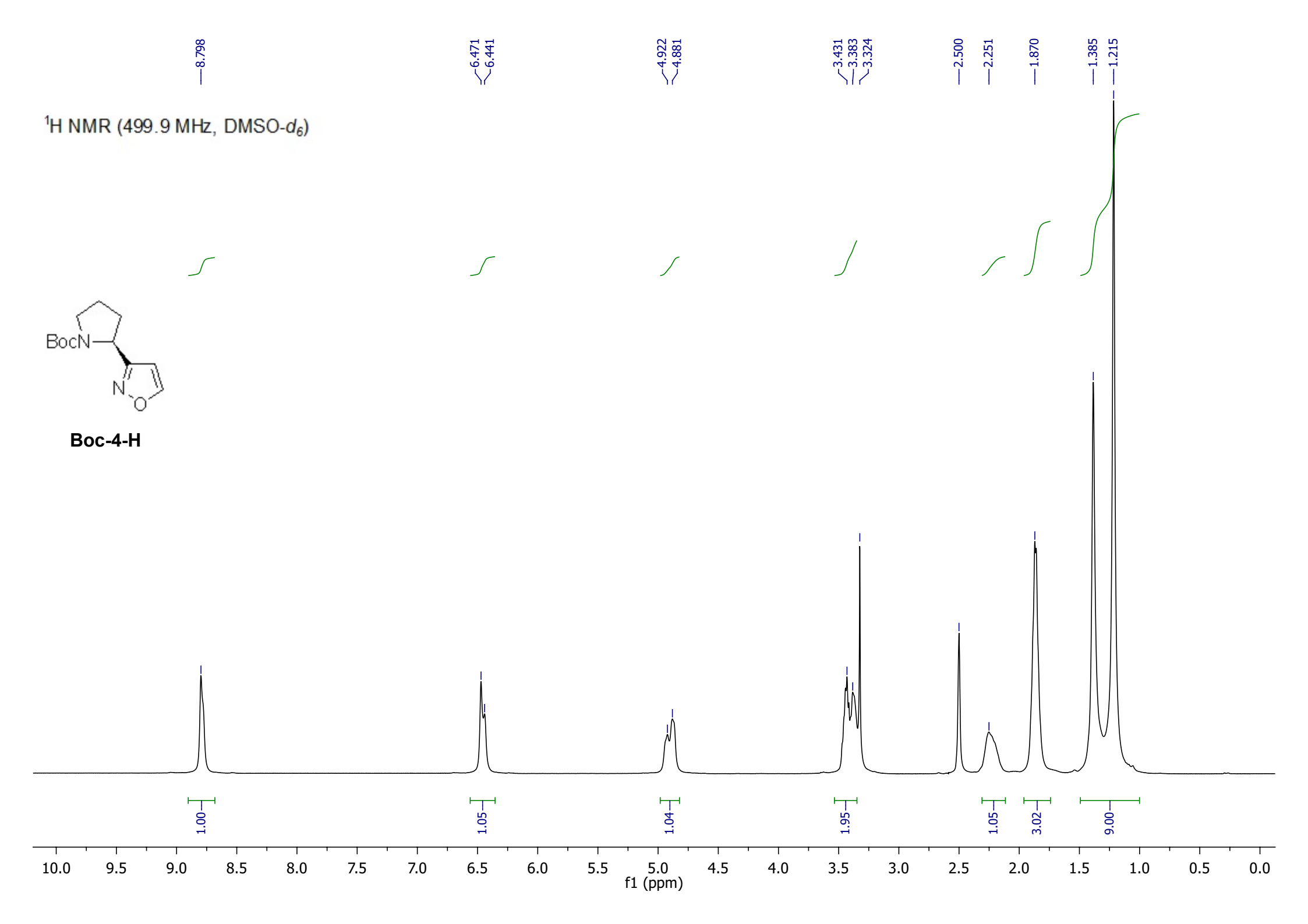
Boc-1-H

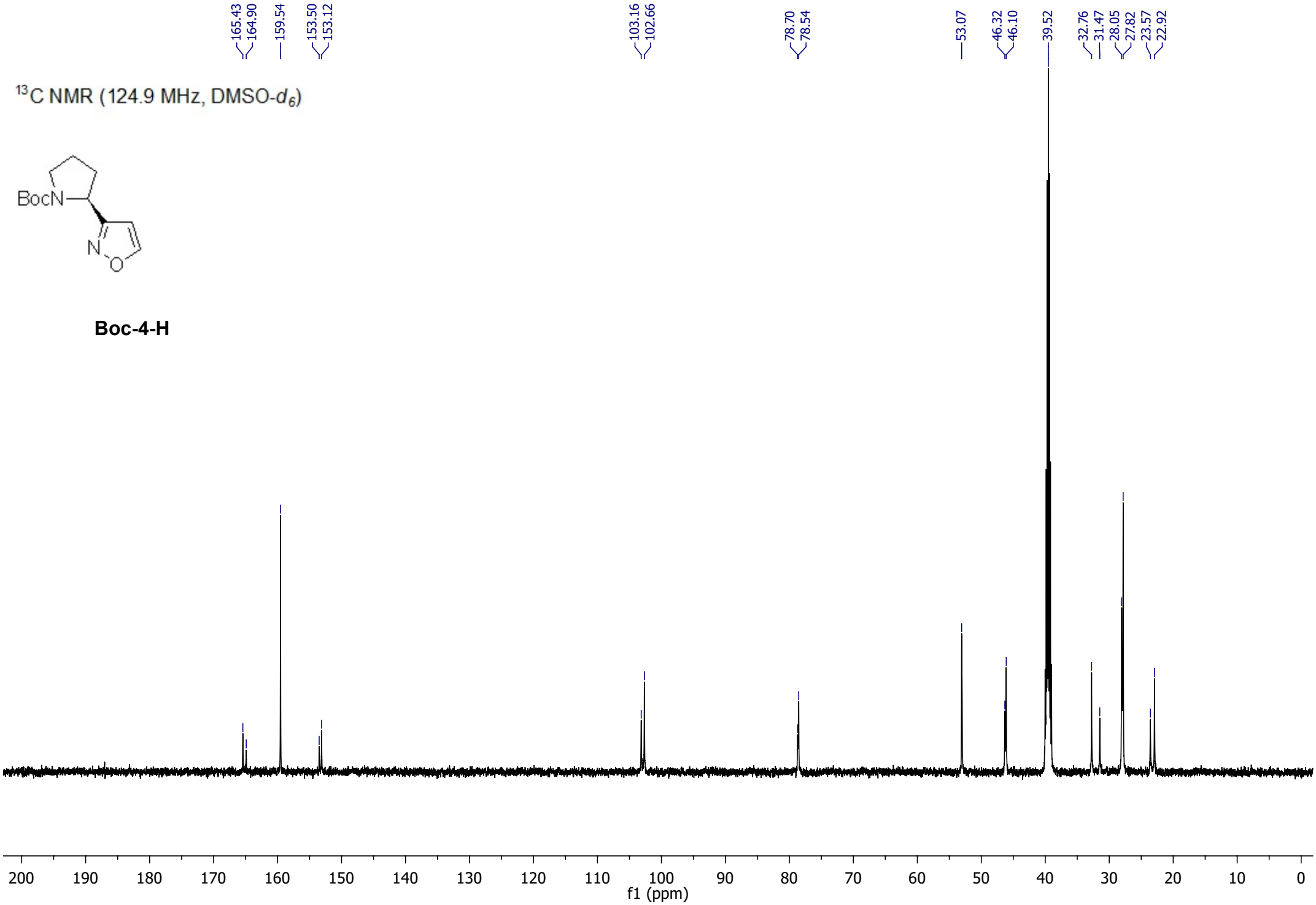

161.50
159.78
155.74
103.79
78.26
39.52
35.51
28.16
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
O
Boc-1-H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

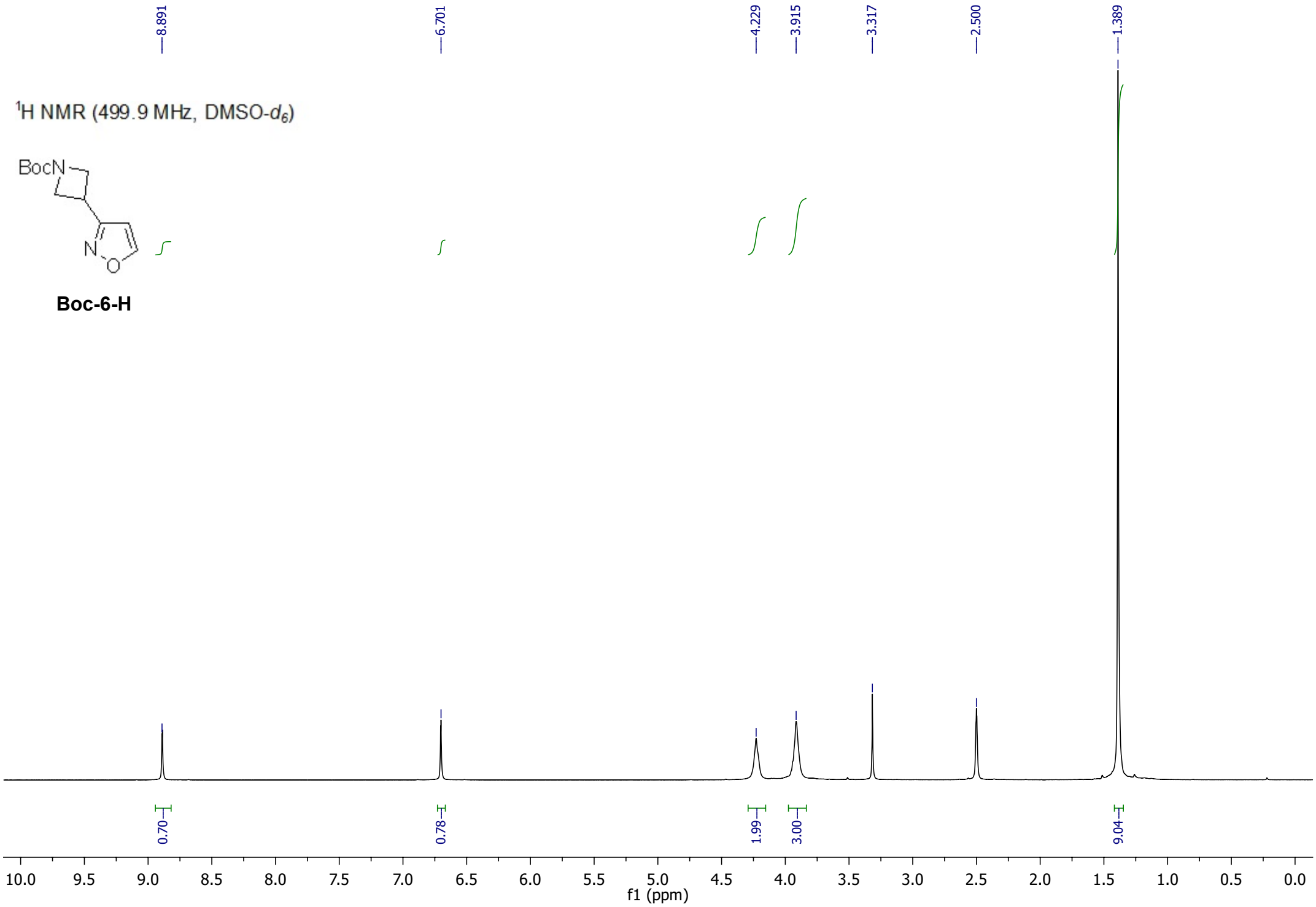

8.779
7.417
7.400
6.458
4.775
3.315
2.500
1.380
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
0.94
1.01
0.91
1.05
12.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

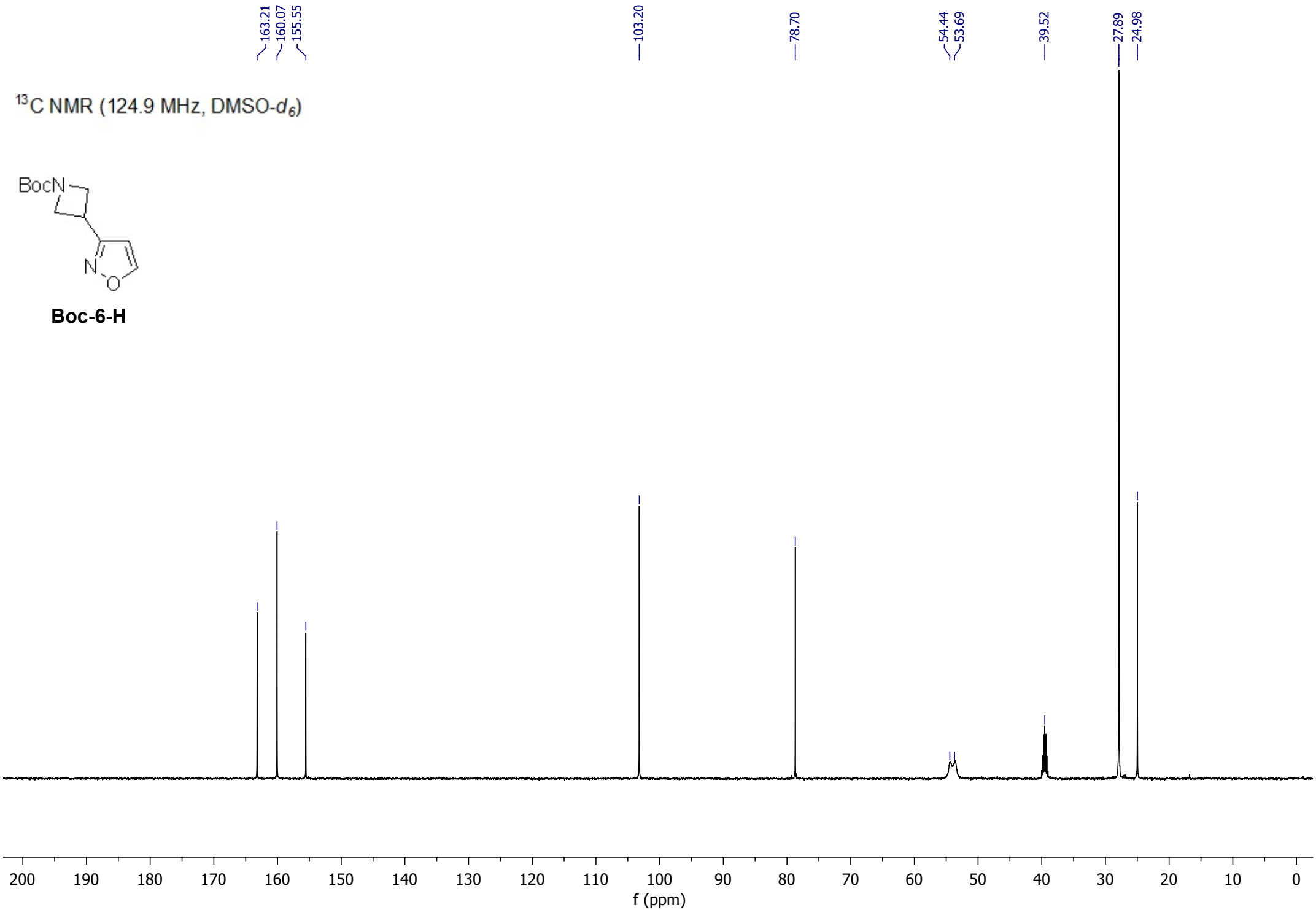
Boc-2-H


165.48
159.60
154.93
144.20
102.88
78.13
42.75
39.52
28.19
20.21
13C NMR (124.9 MHz, DMSO-d6)
BocHN
N
O
Boc-2-H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

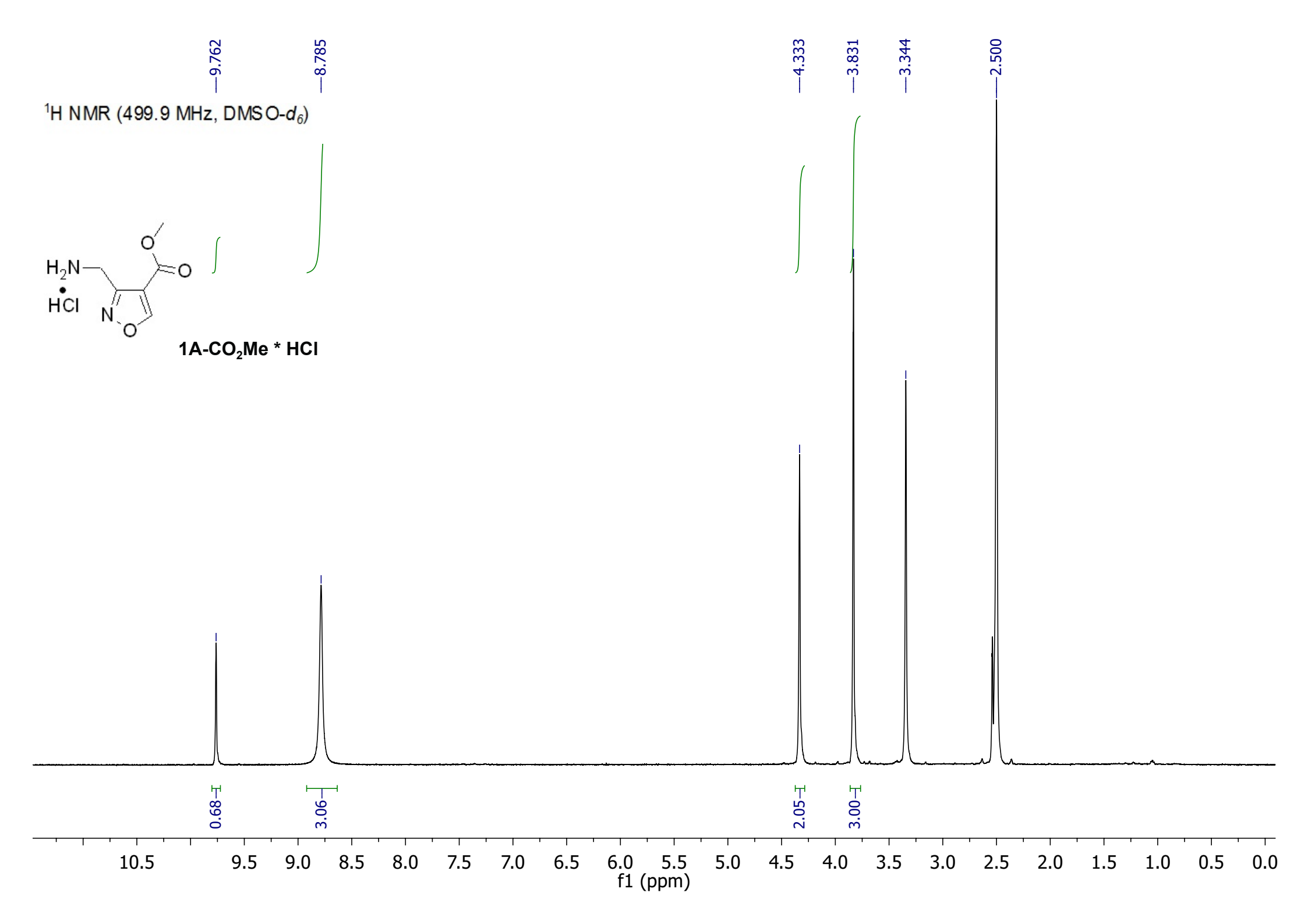

8.798
6.471
6.441
4.922
4.881
3.431
3.383
3.324
2.500
2.251
1.870
1.385
1.215
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
Boc-4-H
1.00
1.05
1.04
1.95
1.05
3.02
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

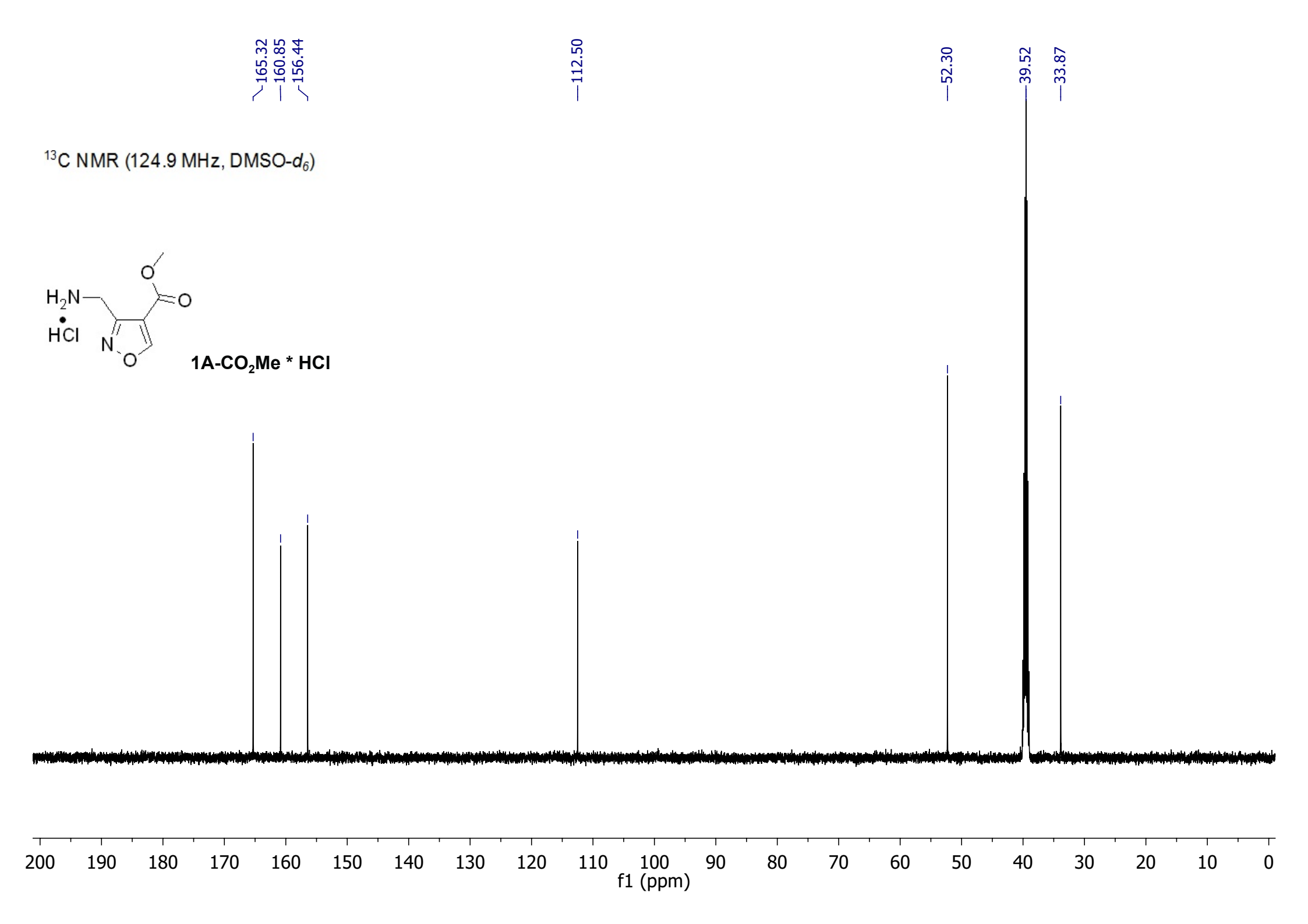

165.43
164.90
159.54
153.50
153.12
103.16
102.66
78.70
78.54
53.07
46.32
46.10
39.52
32.76
31.47
28.05
27.82
23.57
22.92
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
Boc-4-H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

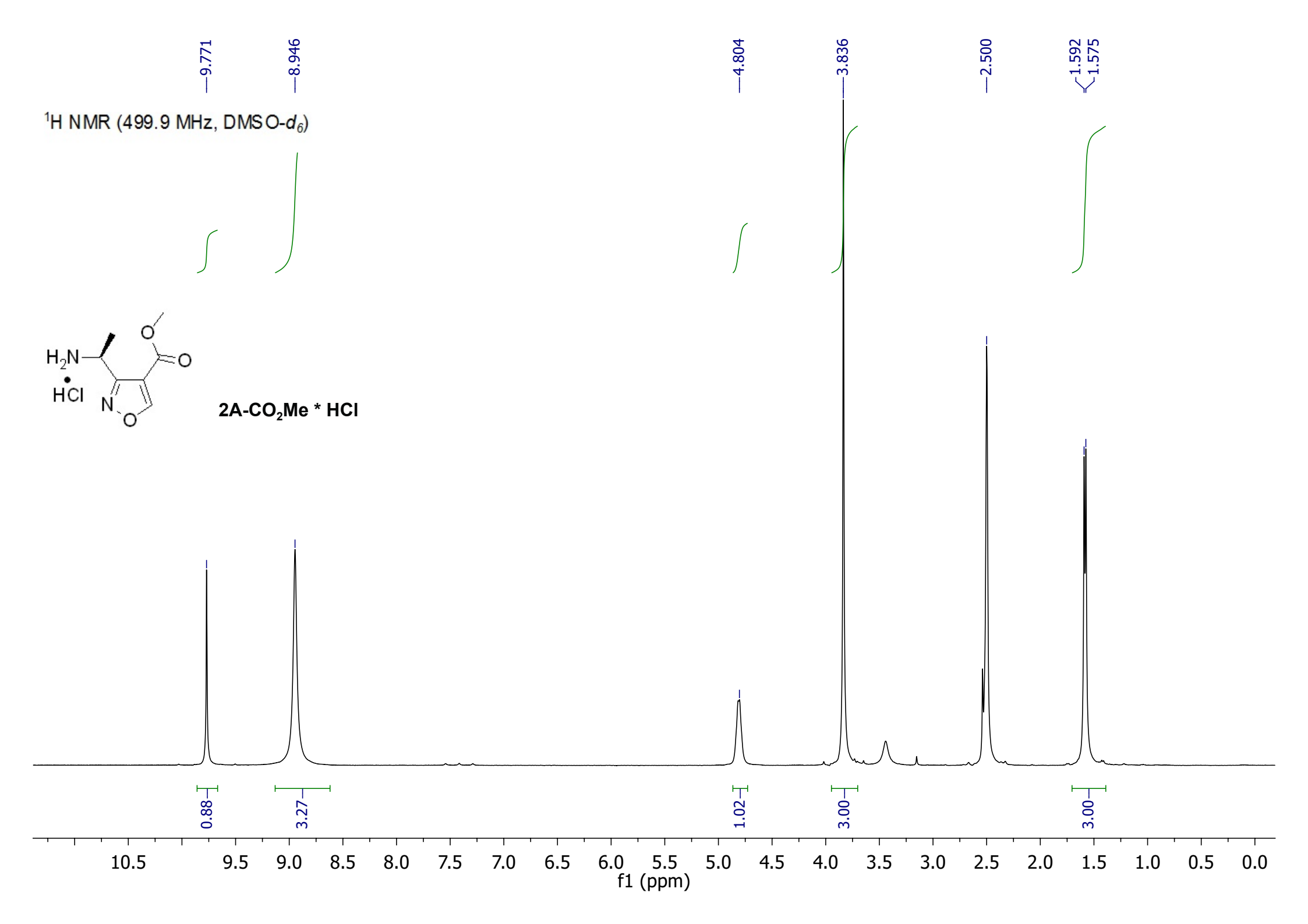

8.891
6.701
4.229
3.915
3.317
2.500
1.389
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
Boc-6-H
0.70
0.78
1.99
3.00
9.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

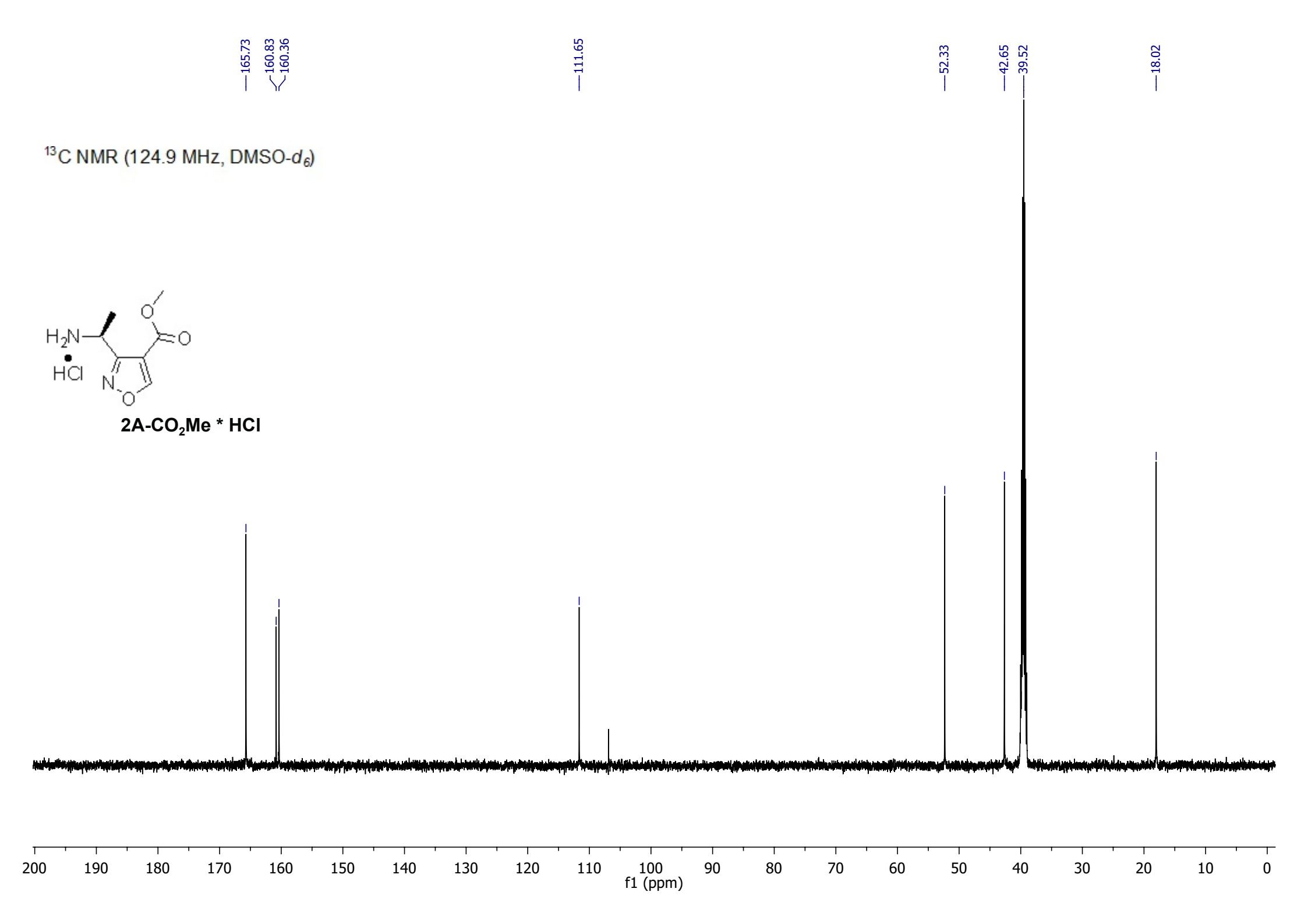

163.21
160.07
155.55
103.20
78.70
54.44
53.69
39.52
27.89
24.98
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

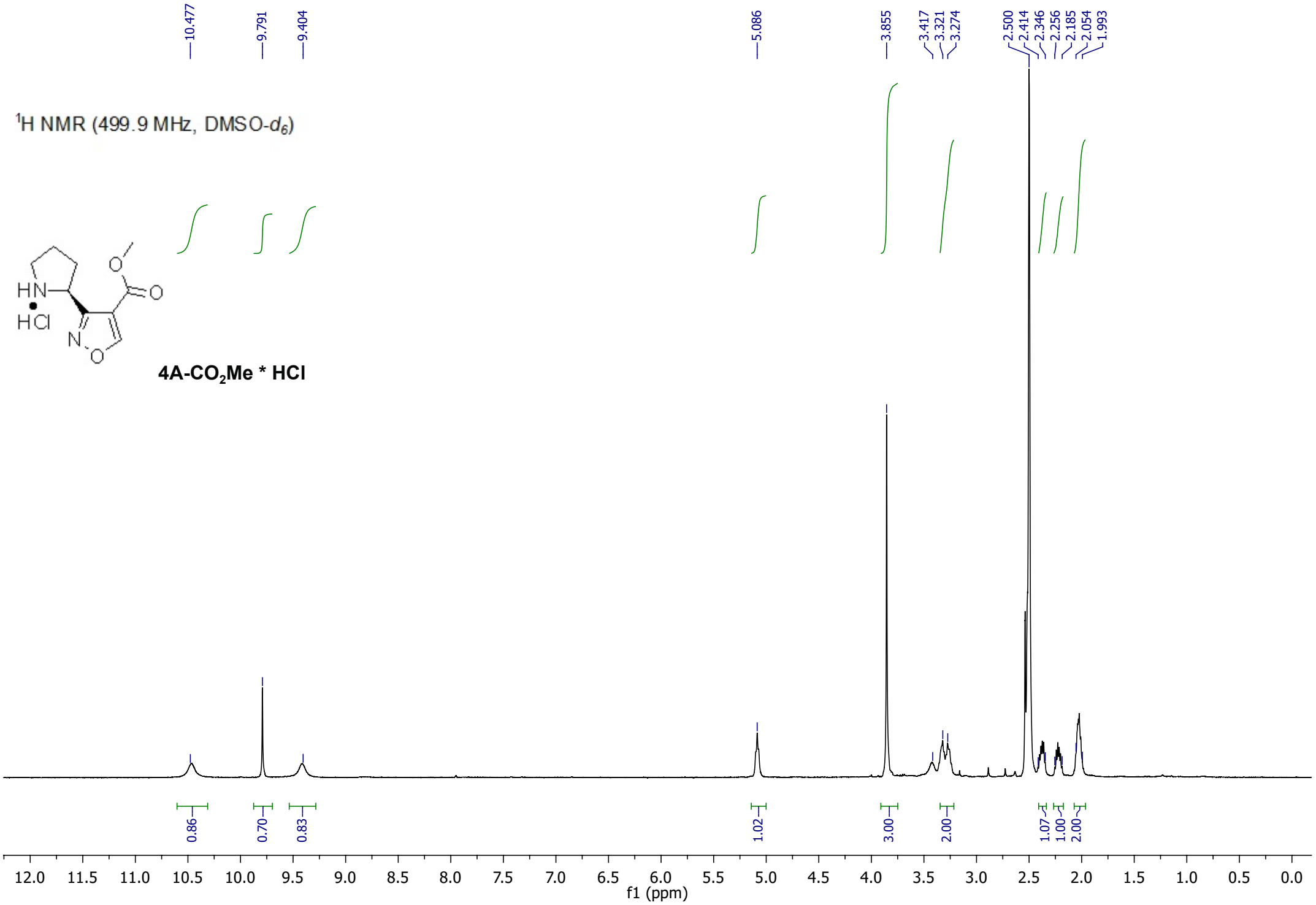
Boc-6-H

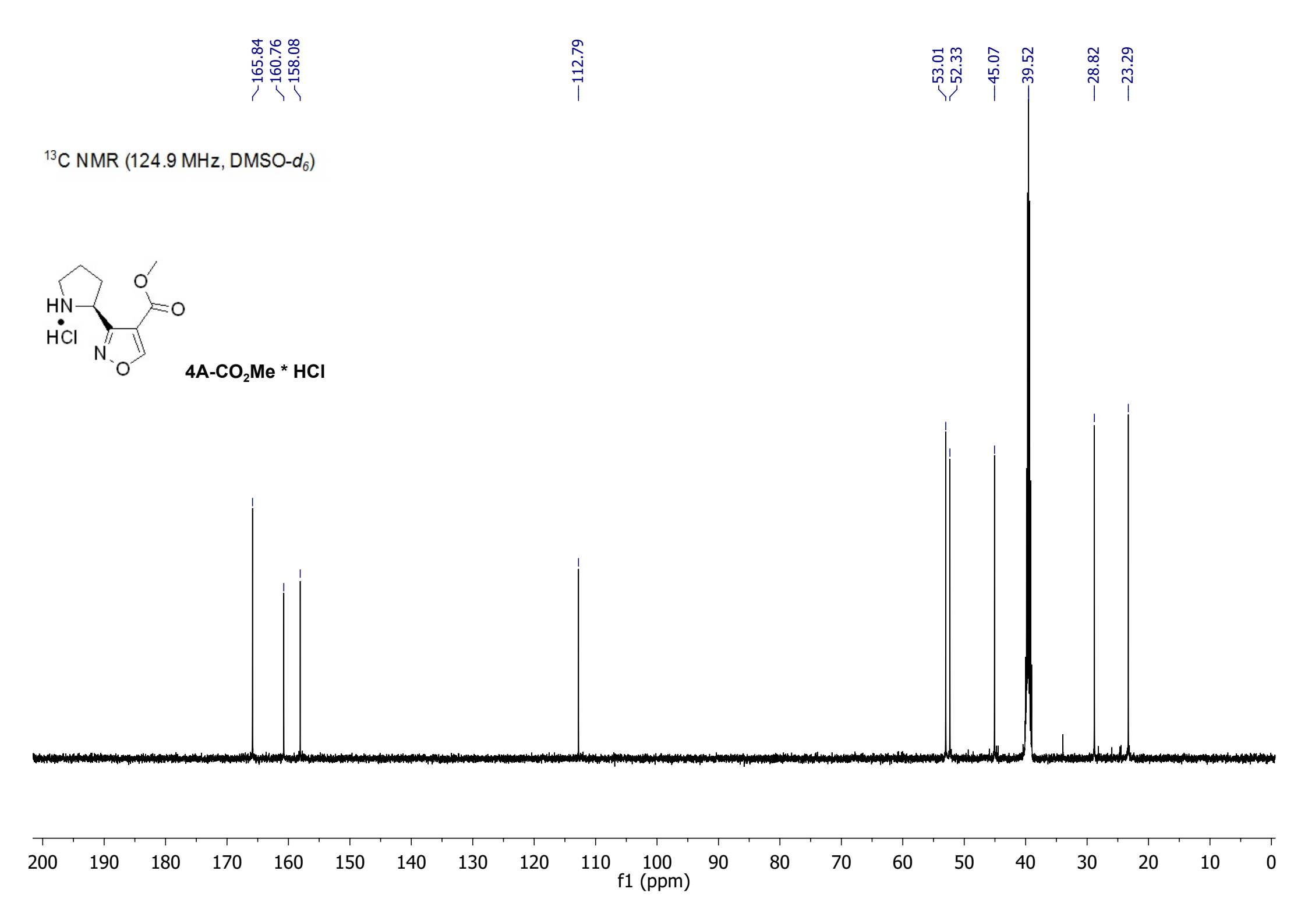

9.762
8.785
4.333
3.831
3.344
2.500
1H NMR (499.9 MHz, DMSO-d6)
H2N
HCl
O
O
N
O
1A-CO2Me * HCl
0.68
3.06
2.05
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

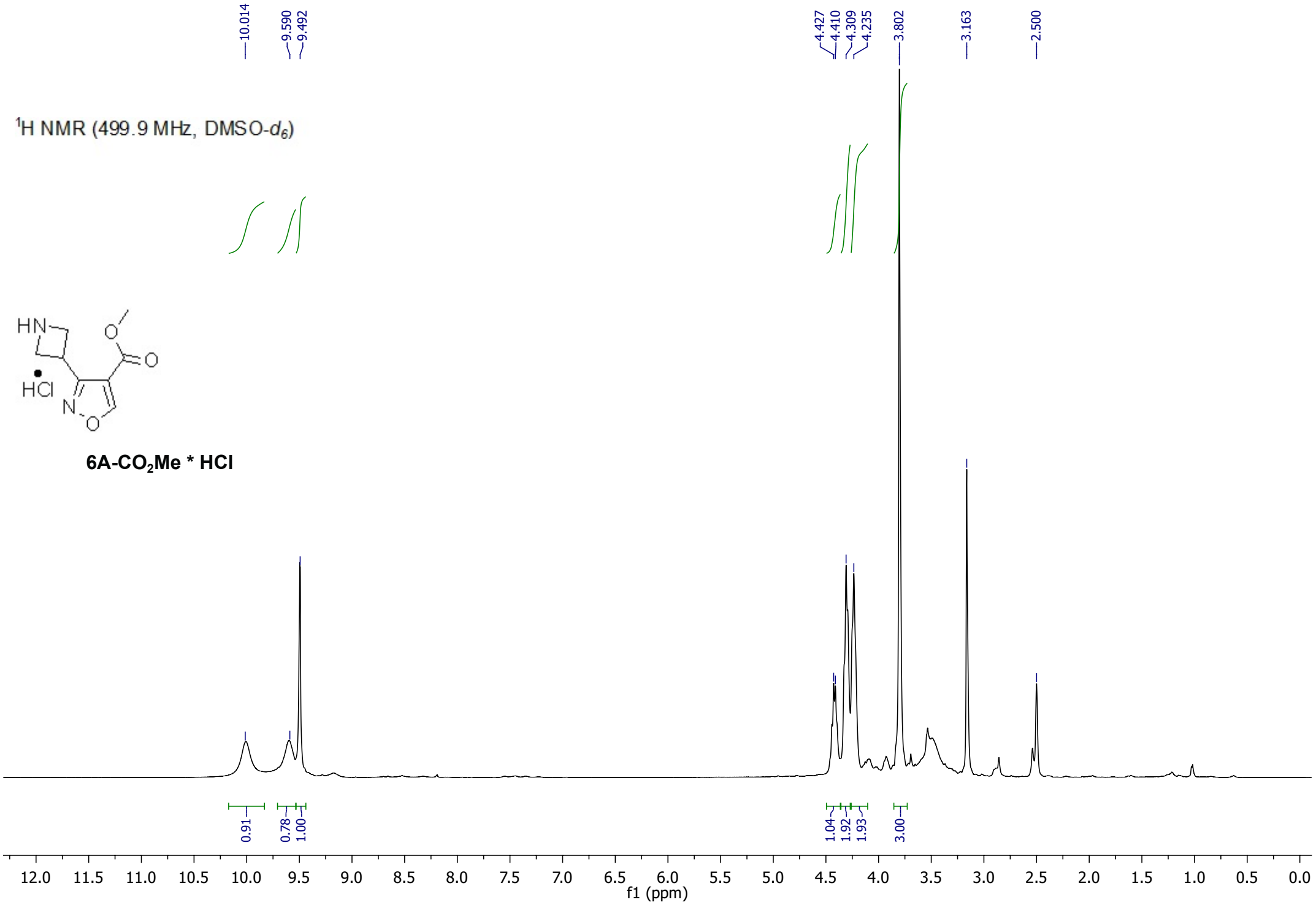

165.32
160.85
156.44
112.50
52.30
39.52
33.87
13C NMR (124.9 MHz, DMSO-d6)
H2N
HCl
O
O
N
O
1A-CO2Me * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.771
8.946
4.804
3.836
2.500
1.592
1.575
^{1}H NMR (499.9 MHz, DMSO-d_6)
H_2N
HCl
O
O
N
O
2A-CO_2Me * HCl
0.88
3.27
1.02
3.00
3.00
10.5
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)

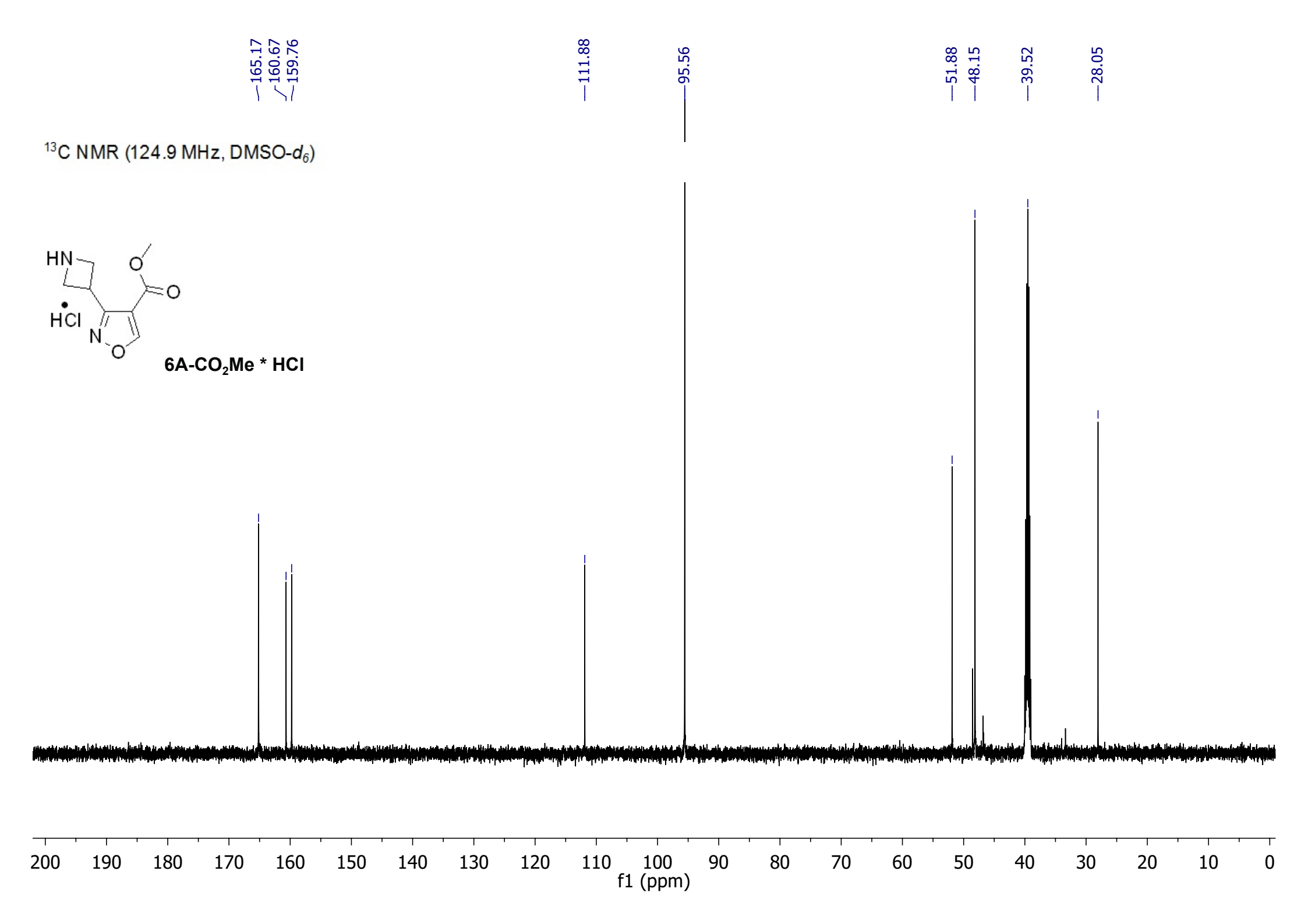

165.73
160.83
160.36
111.65
52.33
42.65
39.52
18.02
^{13}C NMR (124.9 MHz, DMSO-d_6)
H_2N
HCl
O
O
N
O
2A-CO_2Me * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

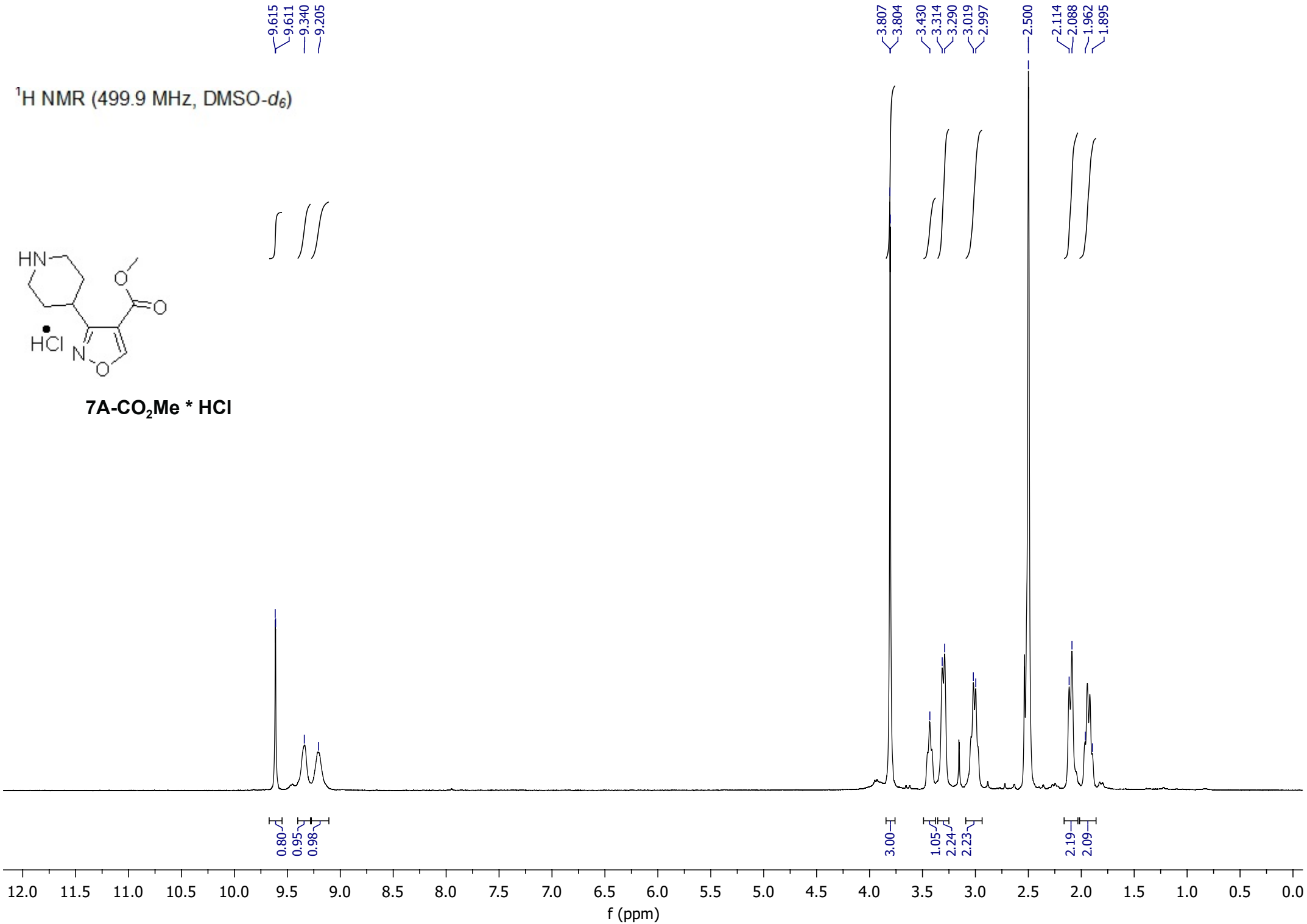

10.477
9.791
9.404
5.086
3.855
3.417
3.321
3.274
2.500
2.414
2.346
2.256
2.185
2.054
1.993
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
O
O
N
O
4A-CO$_2$Me * HCl
0.86
0.70
0.83
1.02
3.00
2.00
1.07
1.00
2.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.84
160.76
158.08
112.79
53.01
52.33
45.07
39.52
28.82
23.29
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
N
O
O
O
4A-CO2Me * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10.014
9.590
9.492
4.427
4.410
4.309
4.235
3.802
3.163
2.500
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
O
O
HCl
N
O
0.91
0.78
1.00
1.04
1.92
1.93
3.00
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
f1 (ppm)

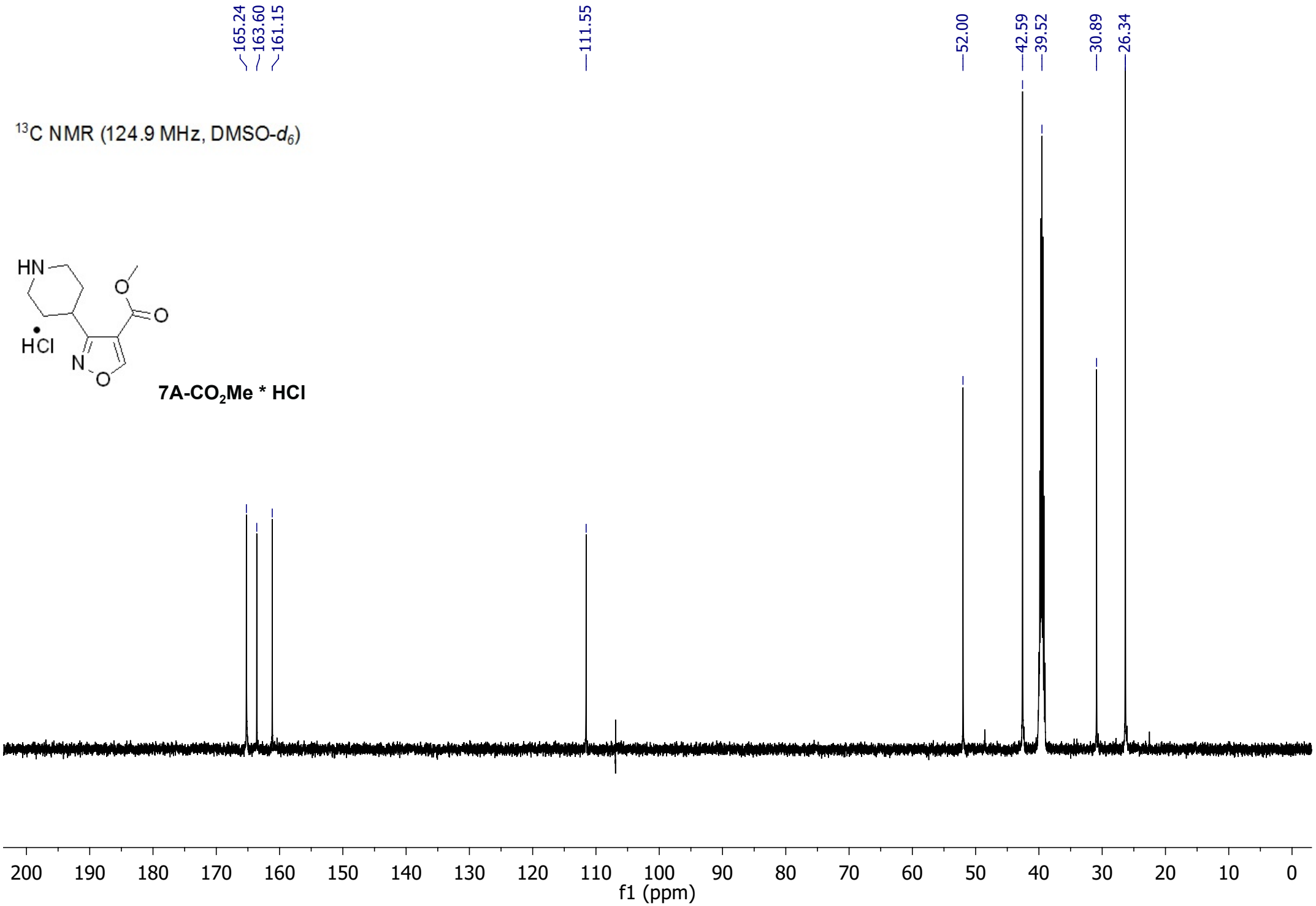
6A-CO_2Me * HCl

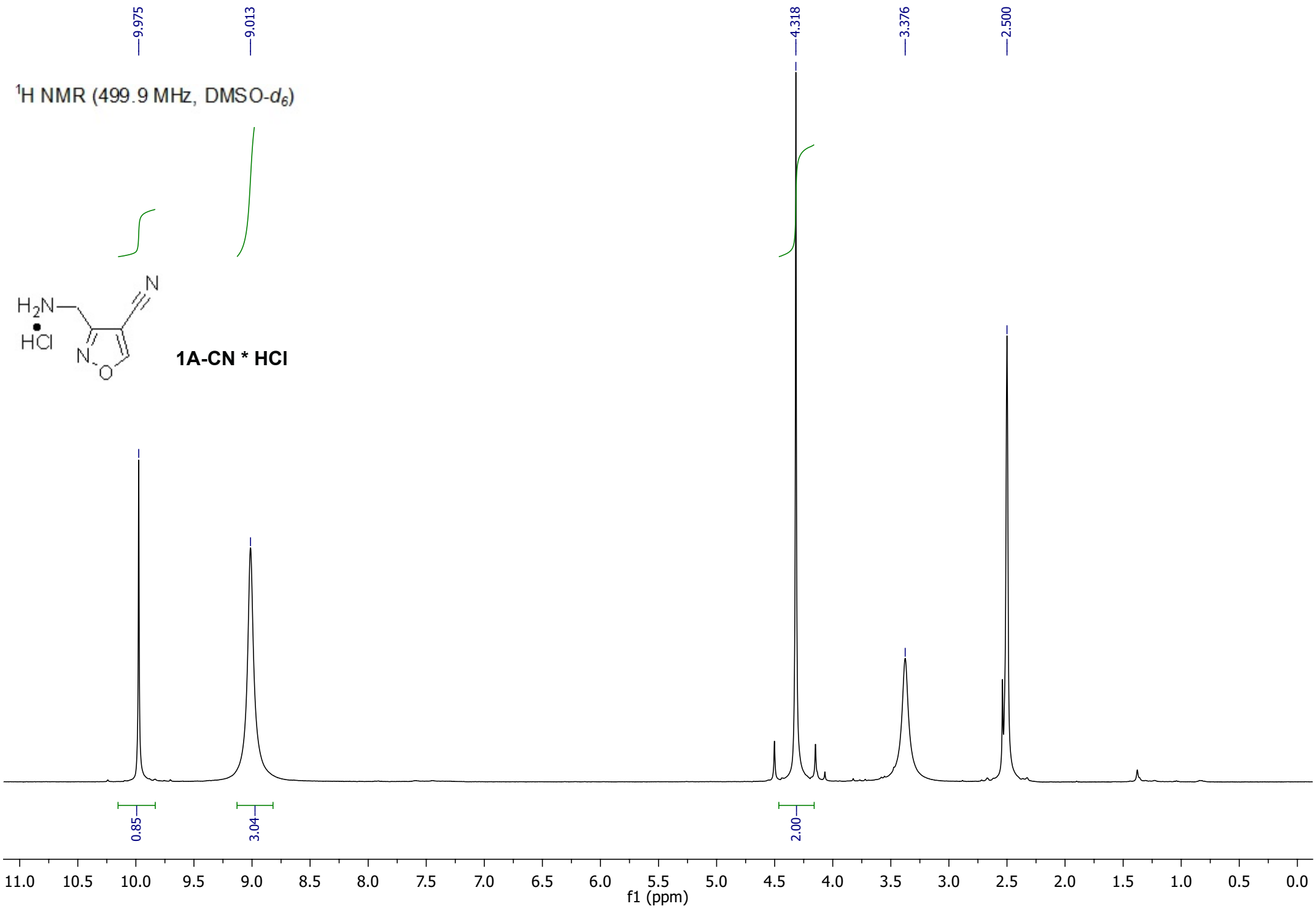

165.17
160.67
159.76
111.88
95.56
51.88
48.15
39.52
28.05
13C NMR (124.9 MHz, DMSO-d6)
HN
O
O
HCl
N
O
6A-CO2Me * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

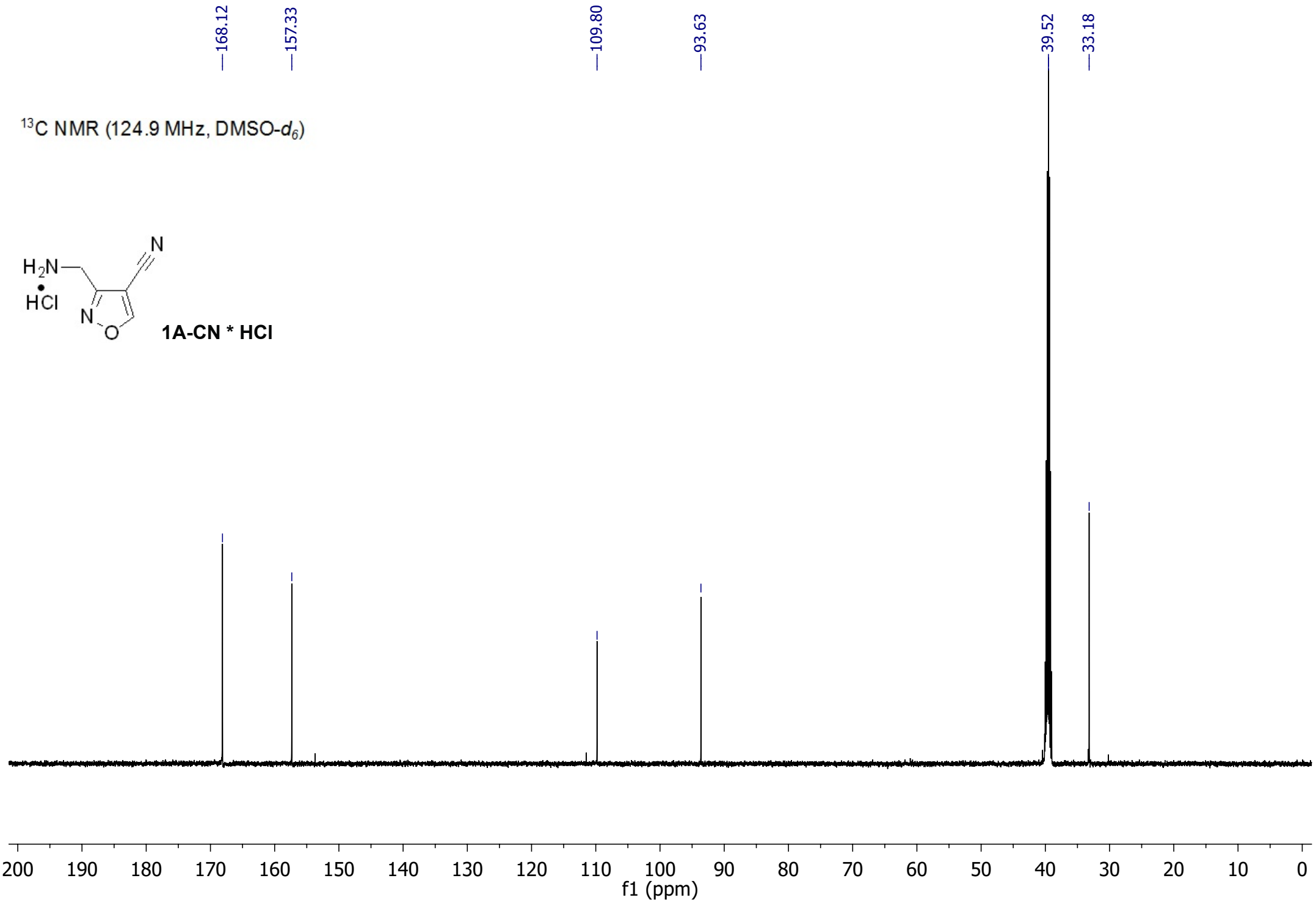


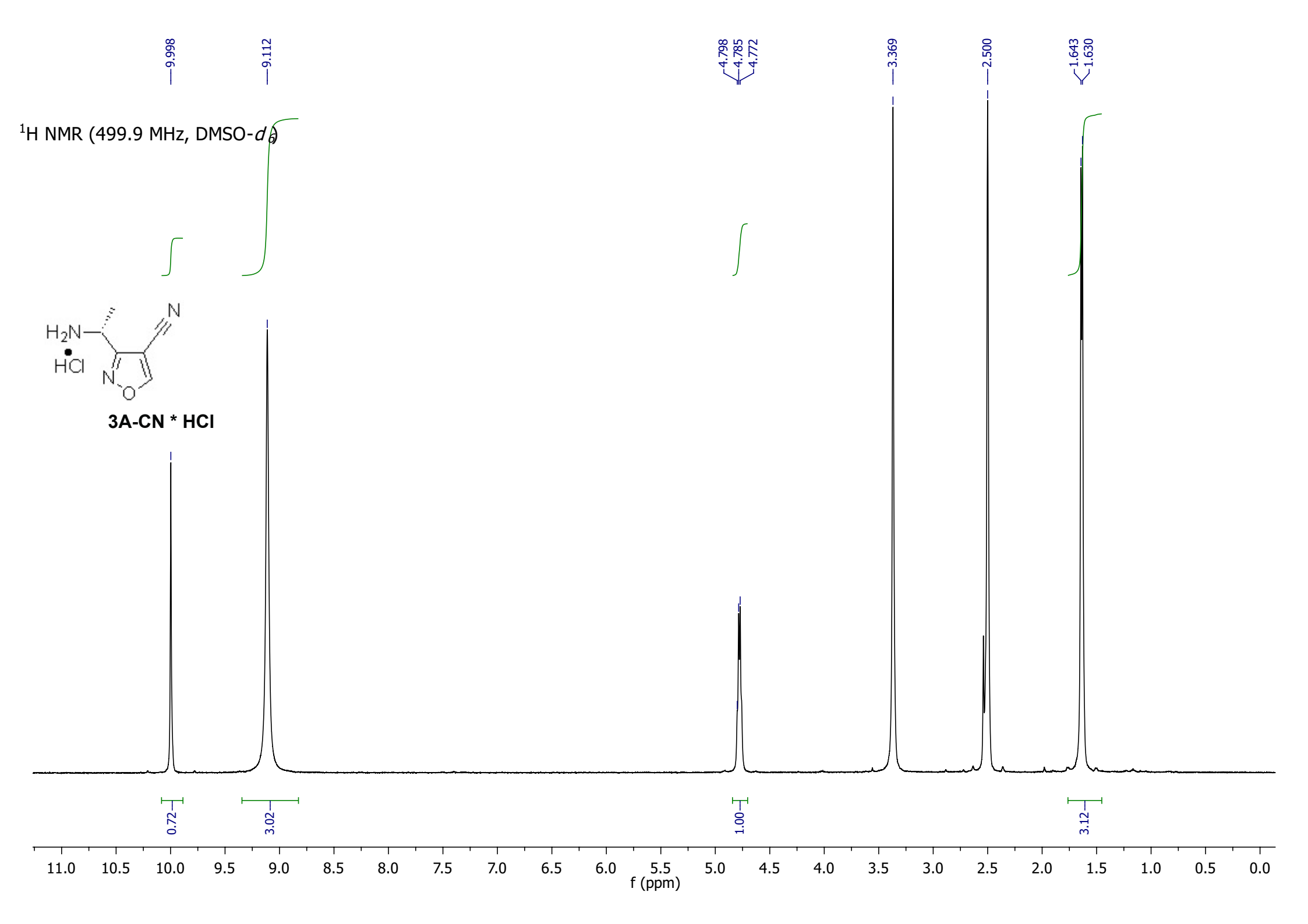
^{1}H NMR (499.9 MHz, DMSO-d_6)

7A-CO_2Me * HCl

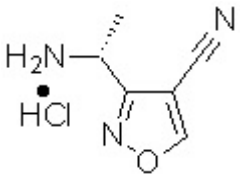

165.24
163.60
161.15
111.55
52.00
42.59
39.52
30.89
26.34
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
O
O
HCl
N
O
7A-CO$_2$Me * HCl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.975
9.013
4.318
3.376
2.500
^{1}H NMR (499.9 MHz, DMSO-d_6)
H_2N
HCl
N
N
O
1A-CN * HCl
0.85
3.04
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

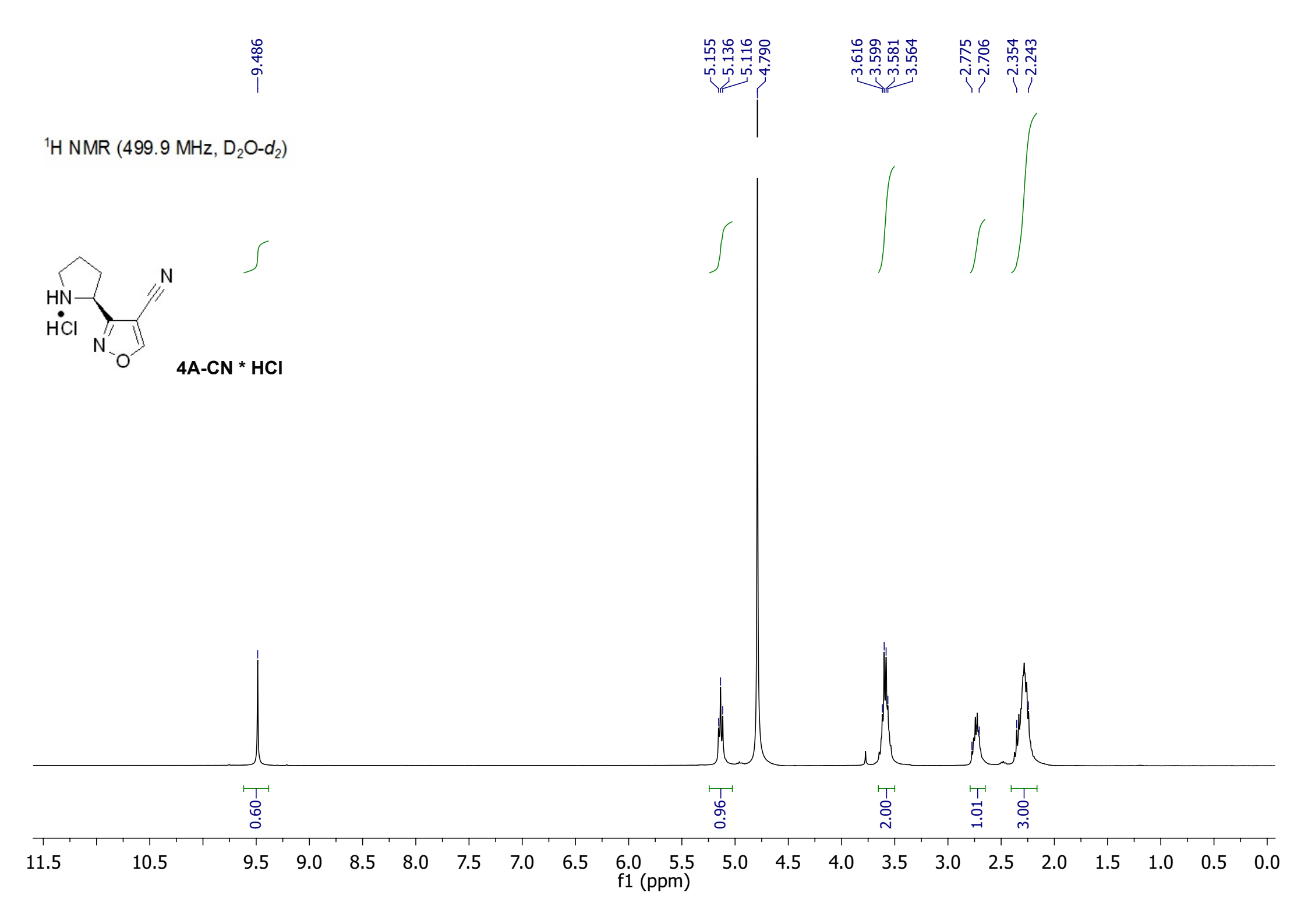

168.12
157.33
109.80
93.63
39.52
33.18
13C NMR (124.9 MHz, DMSO-d6)
H2N
HCl
N
N
O
1A-CN * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

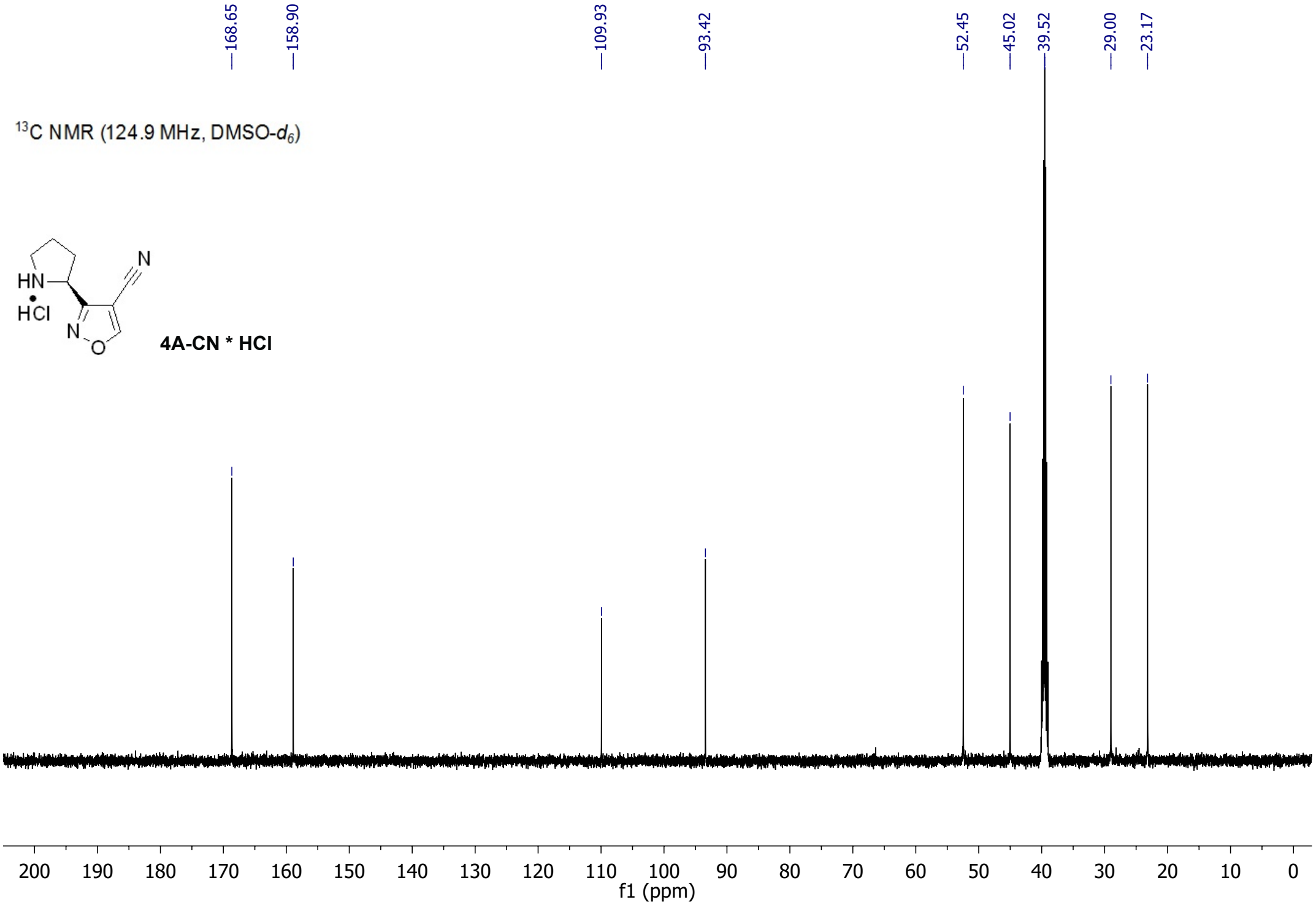

9.998
9.112
4.798
4.785
4.772
3.369
2.500
1.643
1.630
^{1}H NMR (499.9 MHz, DMSO-d_6)
H_2N
HCl
N
N
O
3A-CN * HCl
0.72
3.02
1.00
3.12
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f (ppm)

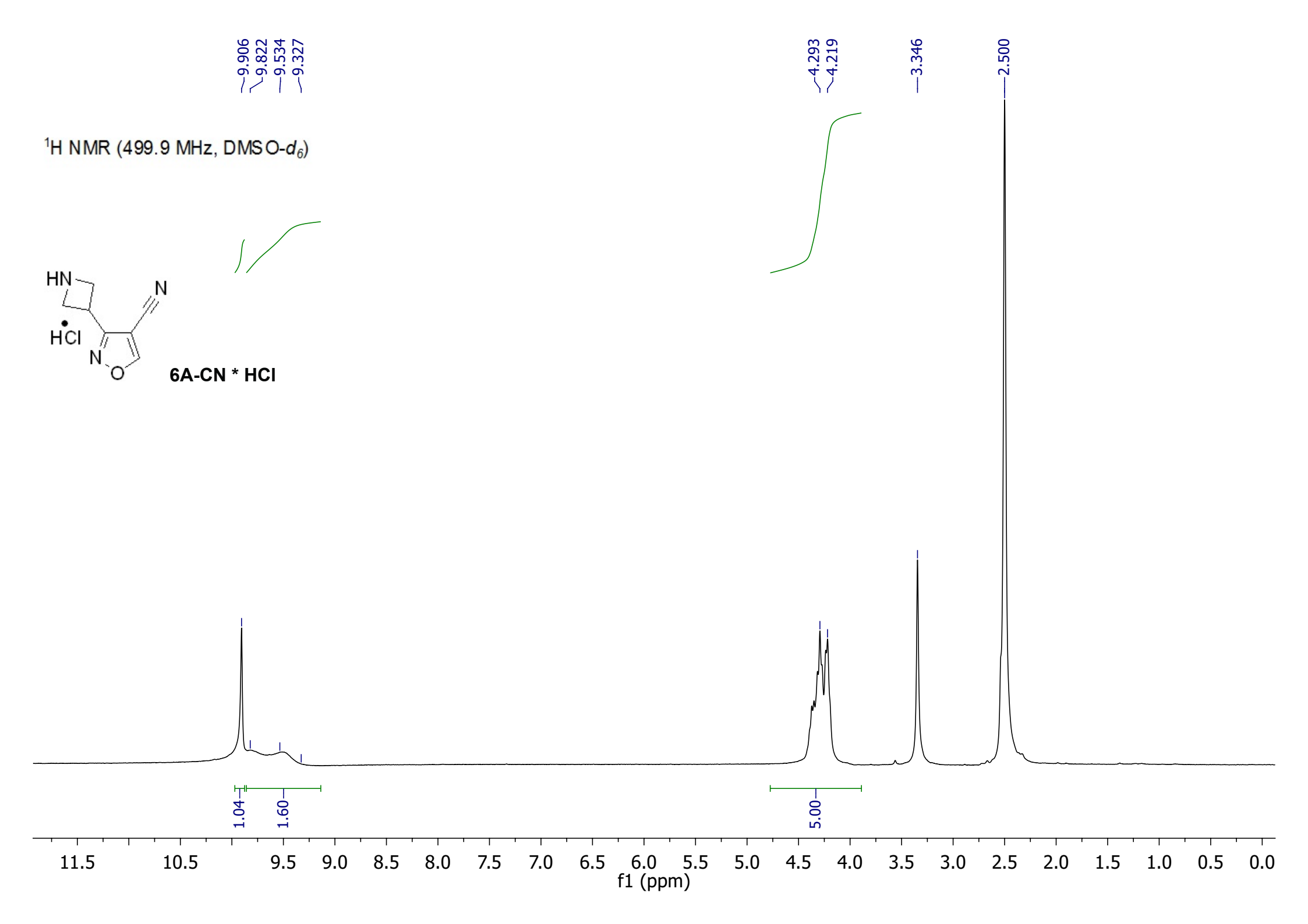
^{13}C NMR (124.9 MHz, DMSO-d_6)

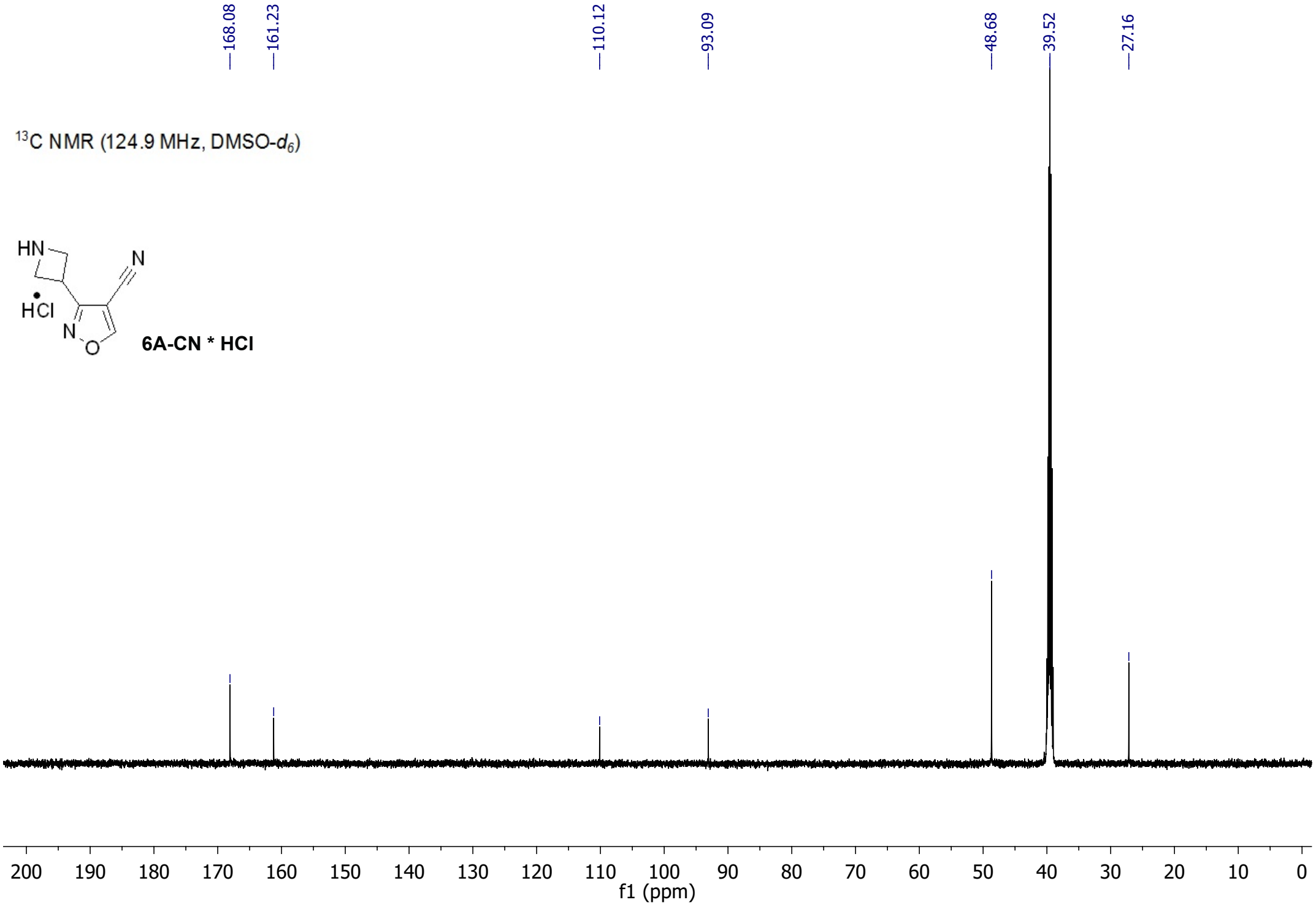


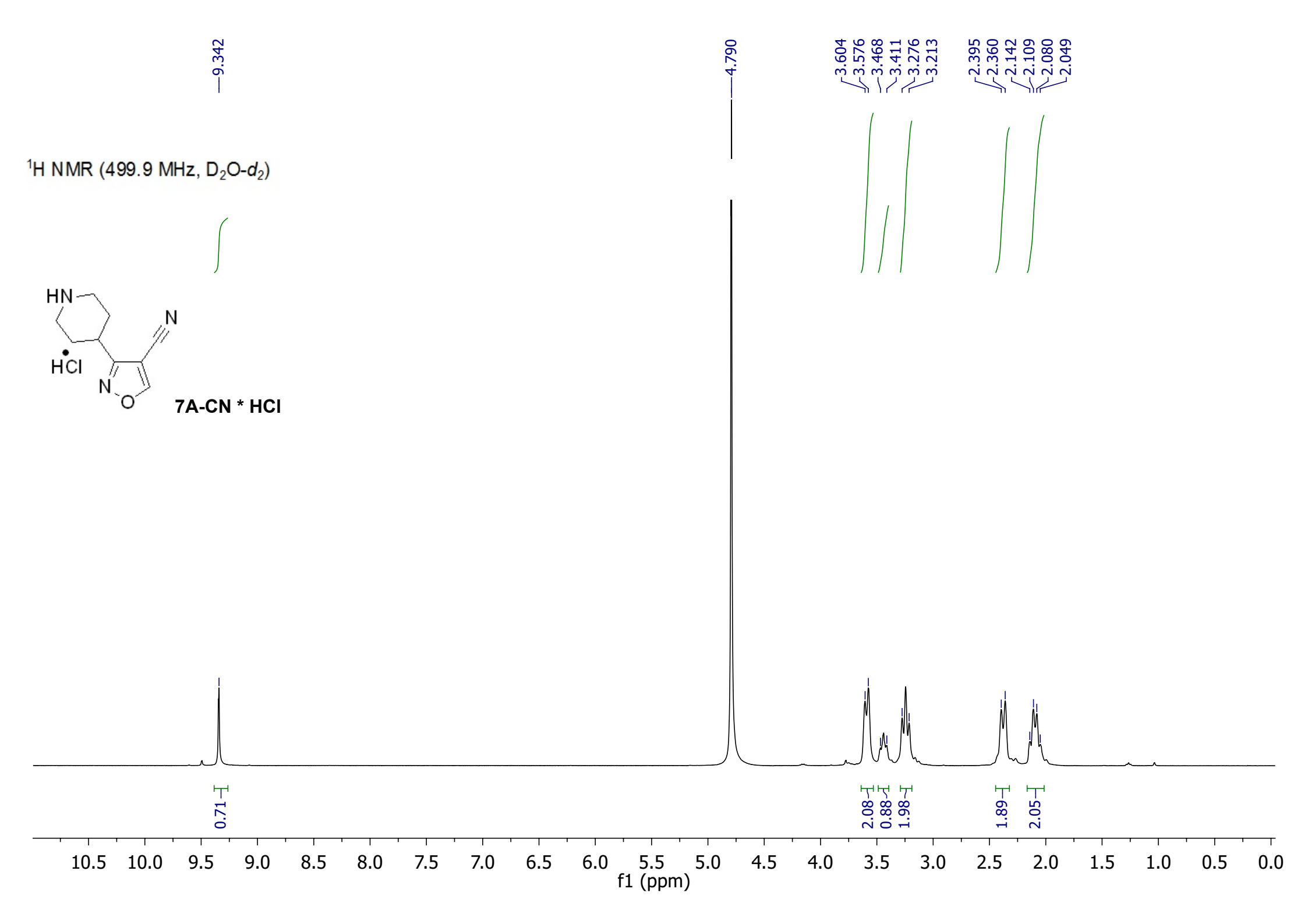
3A-CN * HCl

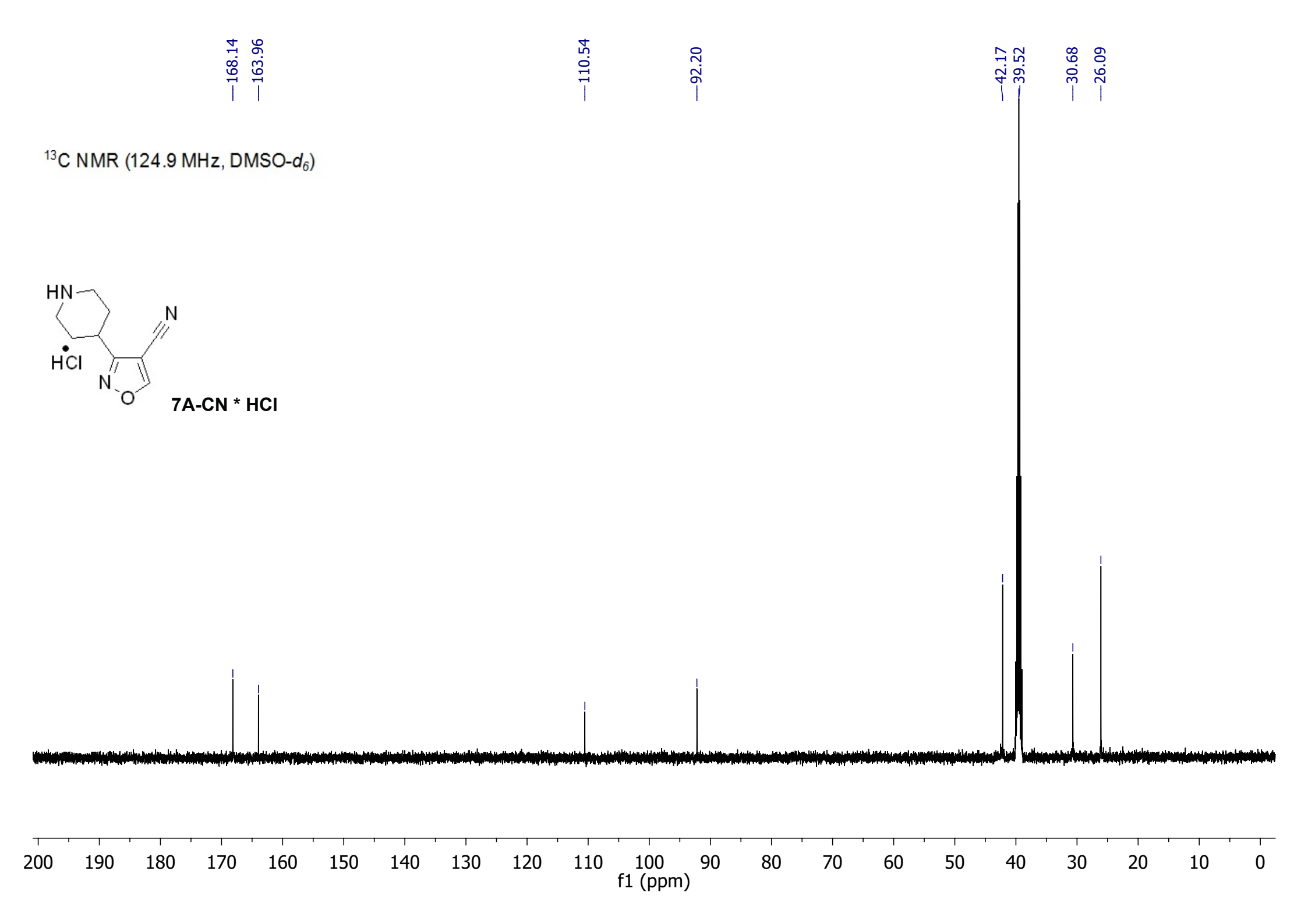

9.486
5.155
5.136
5.116
4.790
3.616
3.599
3.581
3.564
2.775
2.706
2.354
2.243
^{1}H NMR (499.9 MHz, D_2O-d_2)
HN
HCl
N
N
O
4A-CN * HCl
0.60
0.96
2.00
1.01
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

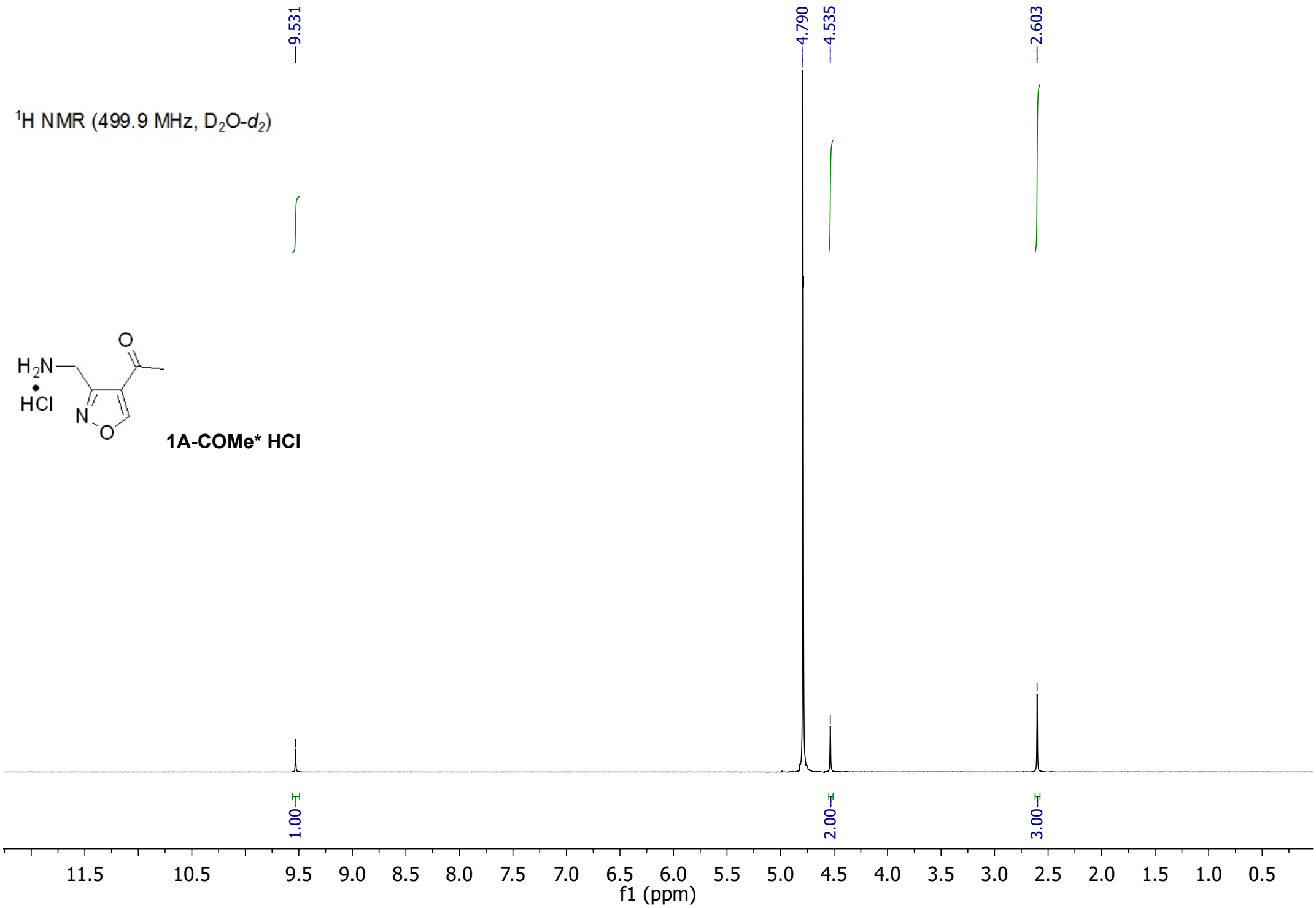

168.65
158.90
109.93
93.42
52.45
45.02
39.52
29.00
23.17
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
N
N
O
4A-CN * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

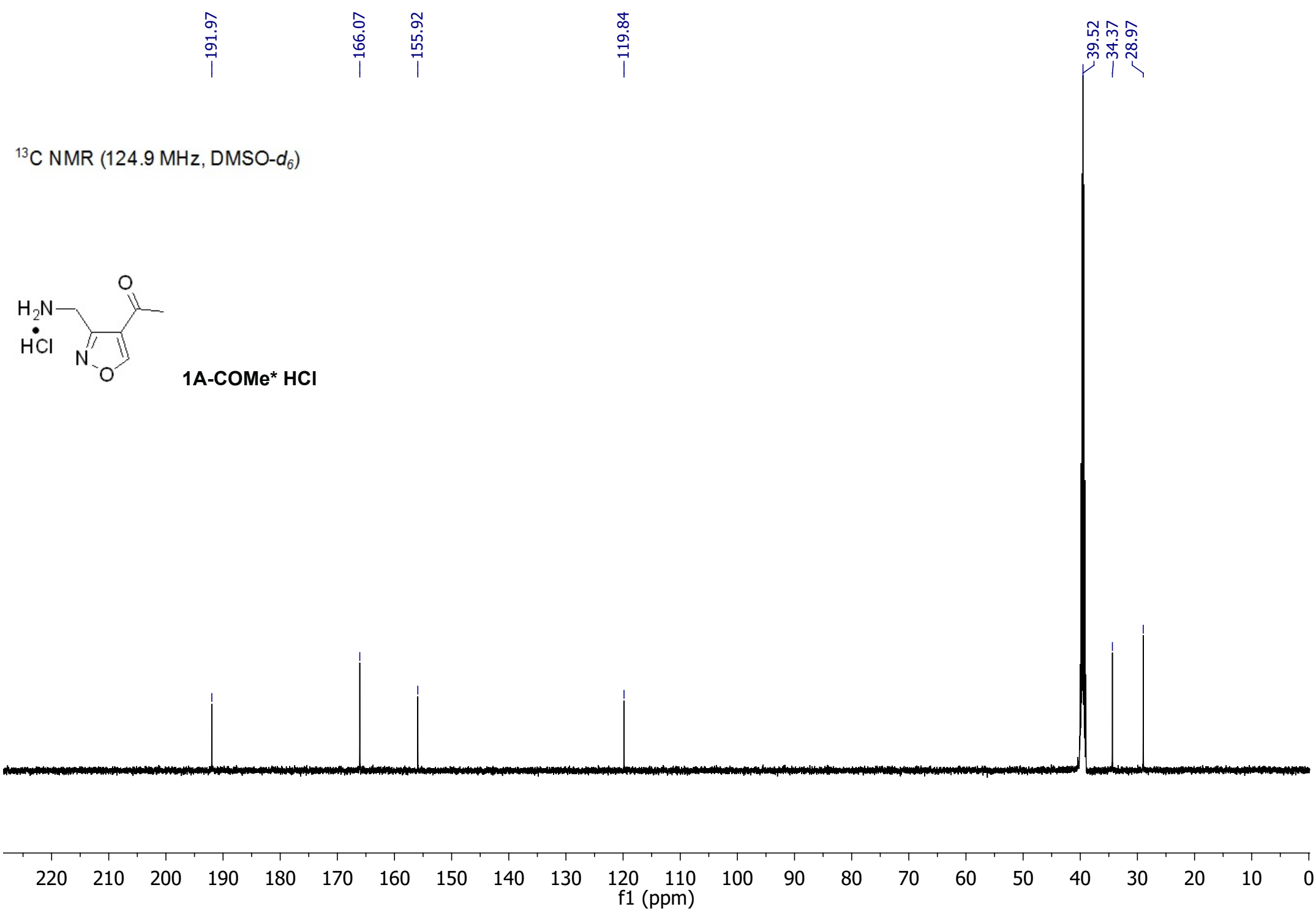

9.906
9.822
9.534
9.327
4.293
4.219
3.346
2.500
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
N
HCl
N
O
6A-CN * HCl
1.04
1.60
5.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

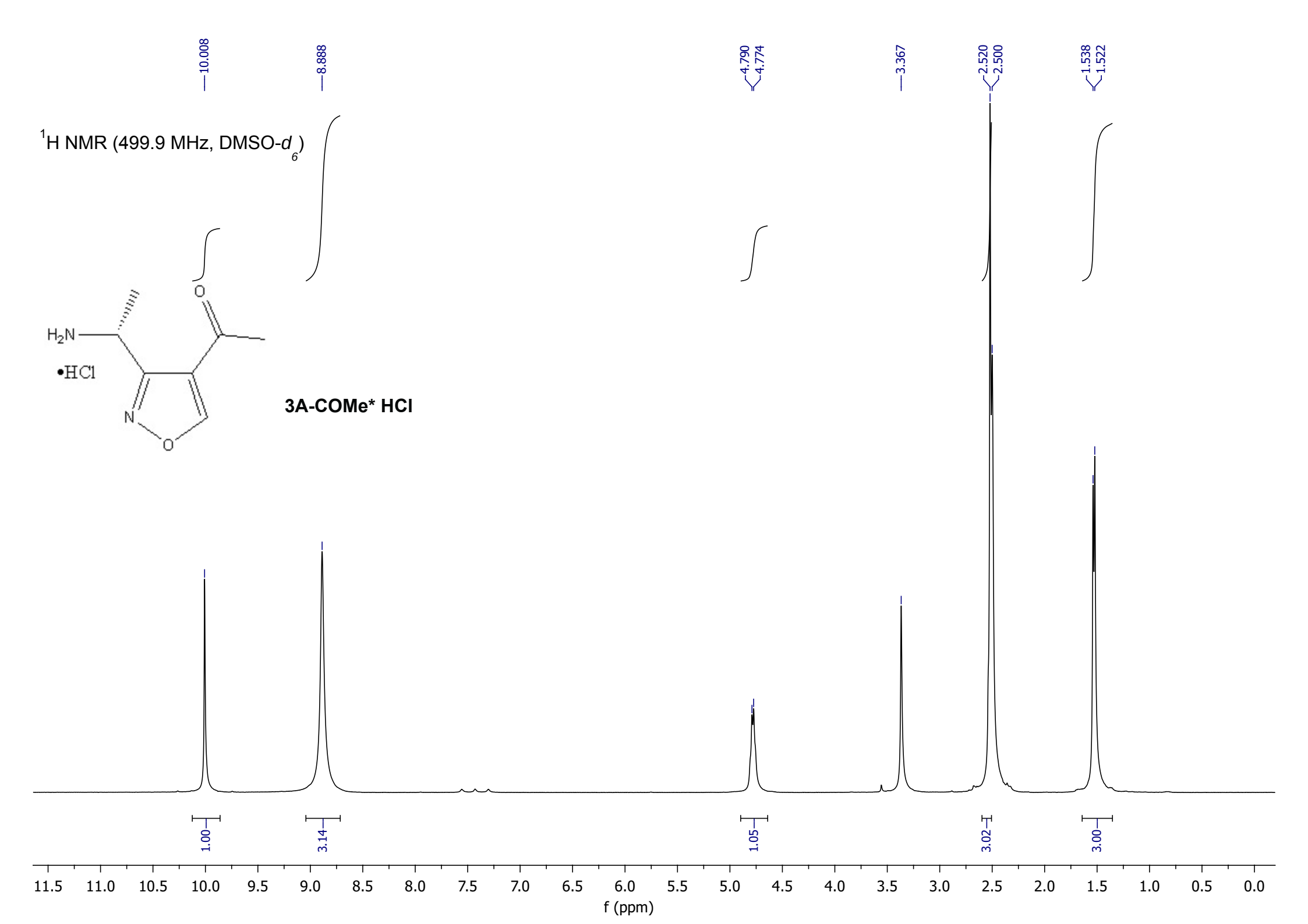

168.08
161.23
110.12
93.09
48.68
39.52
27.16
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
N
HCl
N
O
6A-CN * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

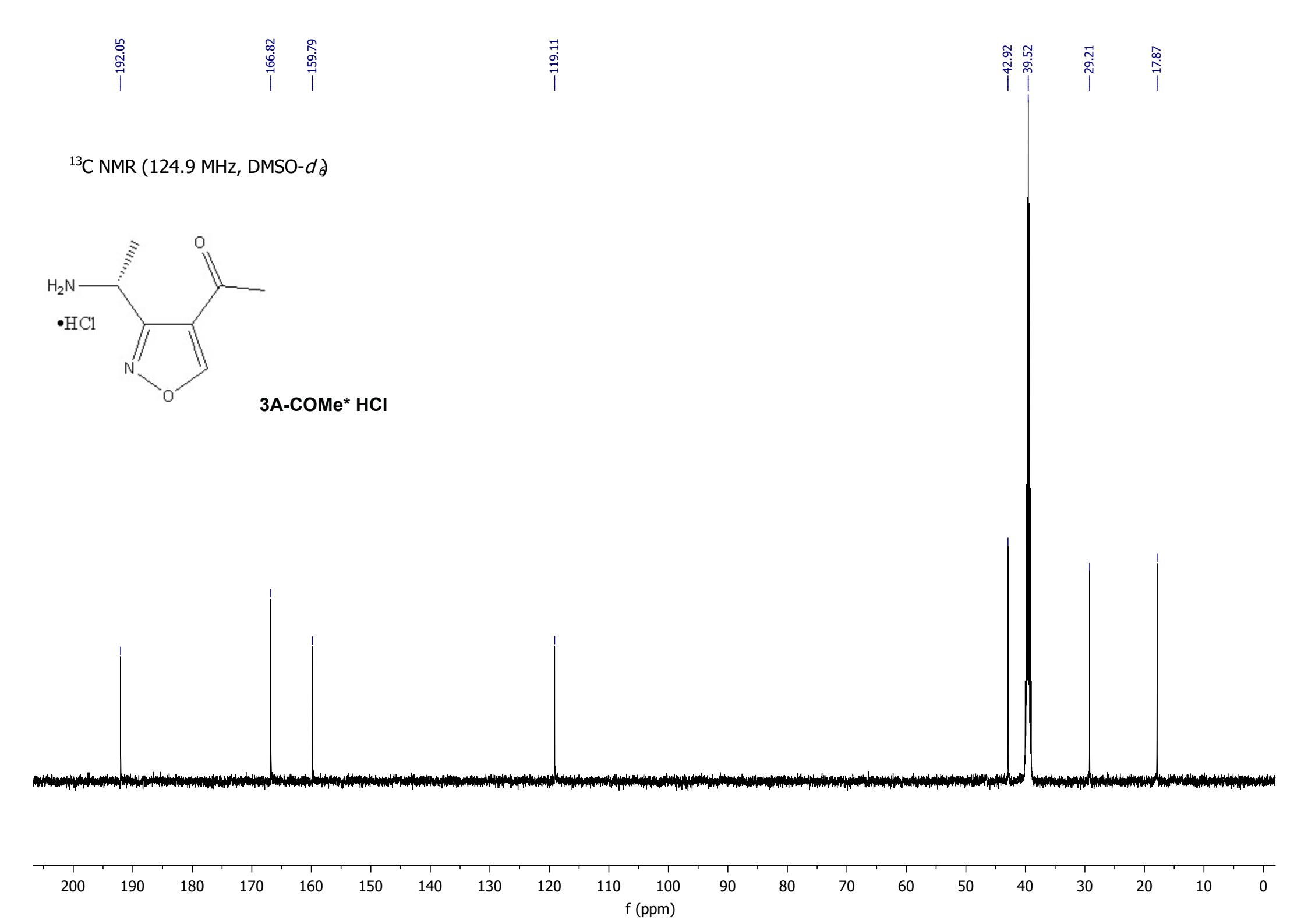

9.342
4.790
3.604
3.576
3.468
3.411
3.276
3.213
2.395
2.360
2.142
2.109
2.080
2.049
1H NMR (499.9 MHz, D2O-d2)
HN
HCl
N
N
O
7A-CN * HCl
0.71
2.08
0.88
1.98
1.89
2.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

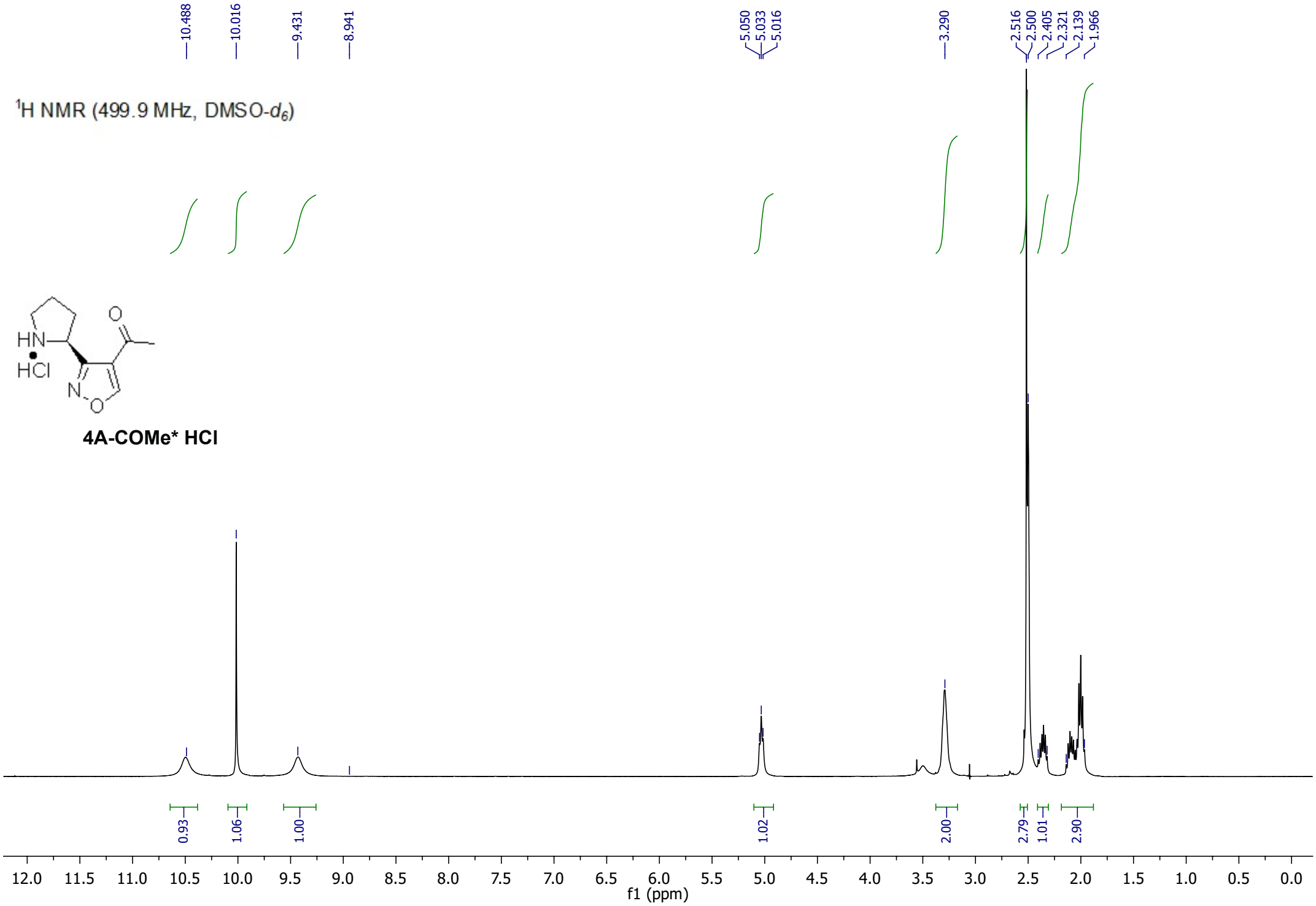

168.14
163.96
110.54
92.20
42.17
39.52
30.68
26.09
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
HCl
N
N
O
7A-CN * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.531
4.790
4.535
2.603
1H NMR (499.9 MHz, D2O-d2)
H2N
HCl
O
N
O
1A-COMe* HCl
1.00
2.00
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

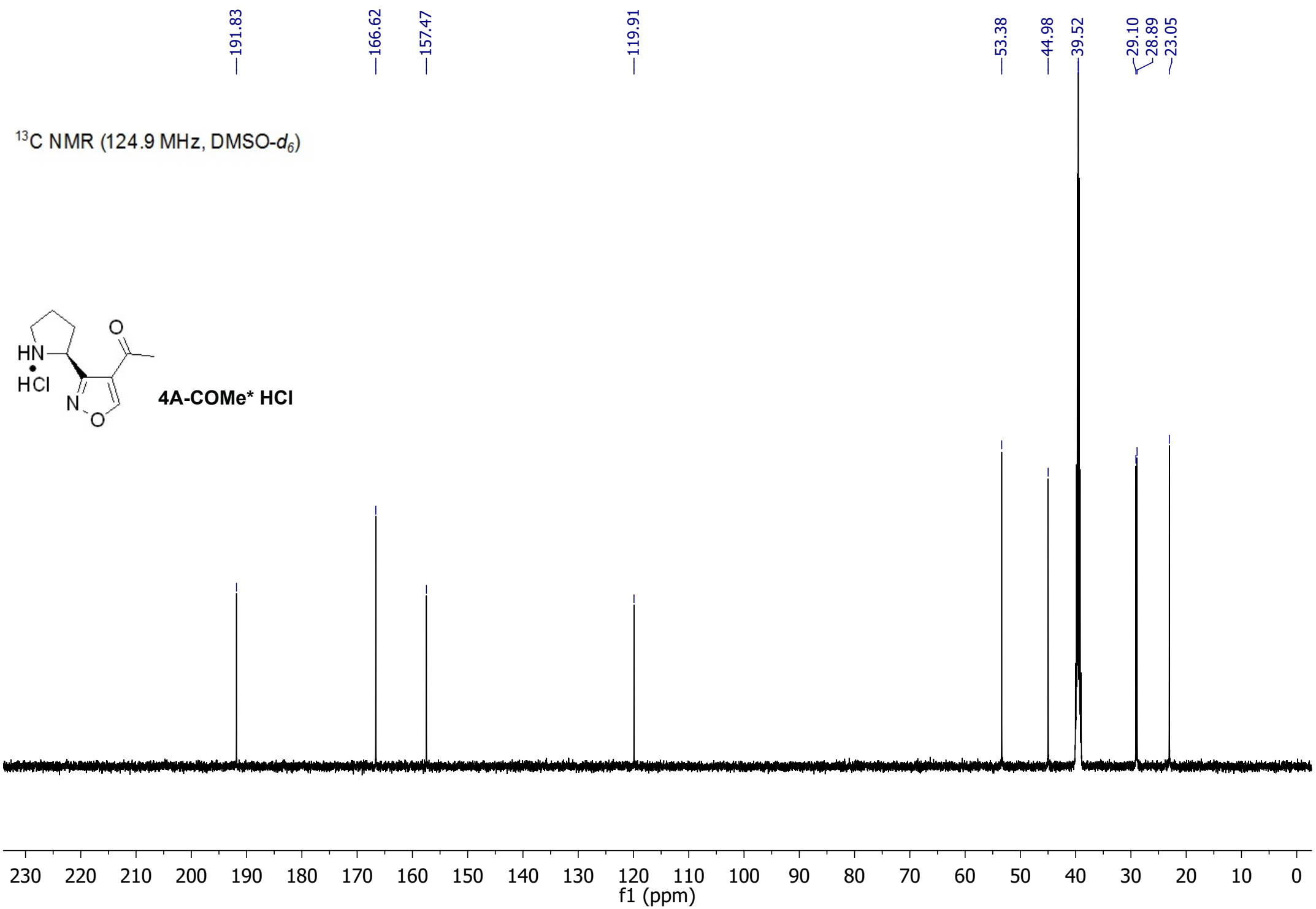

191.97
166.07
155.92
119.84
39.52
34.37
28.97
13C NMR (124.9 MHz, DMSO-d6)
H2N
HCl
O
N
O
1A-COMe* HCl
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

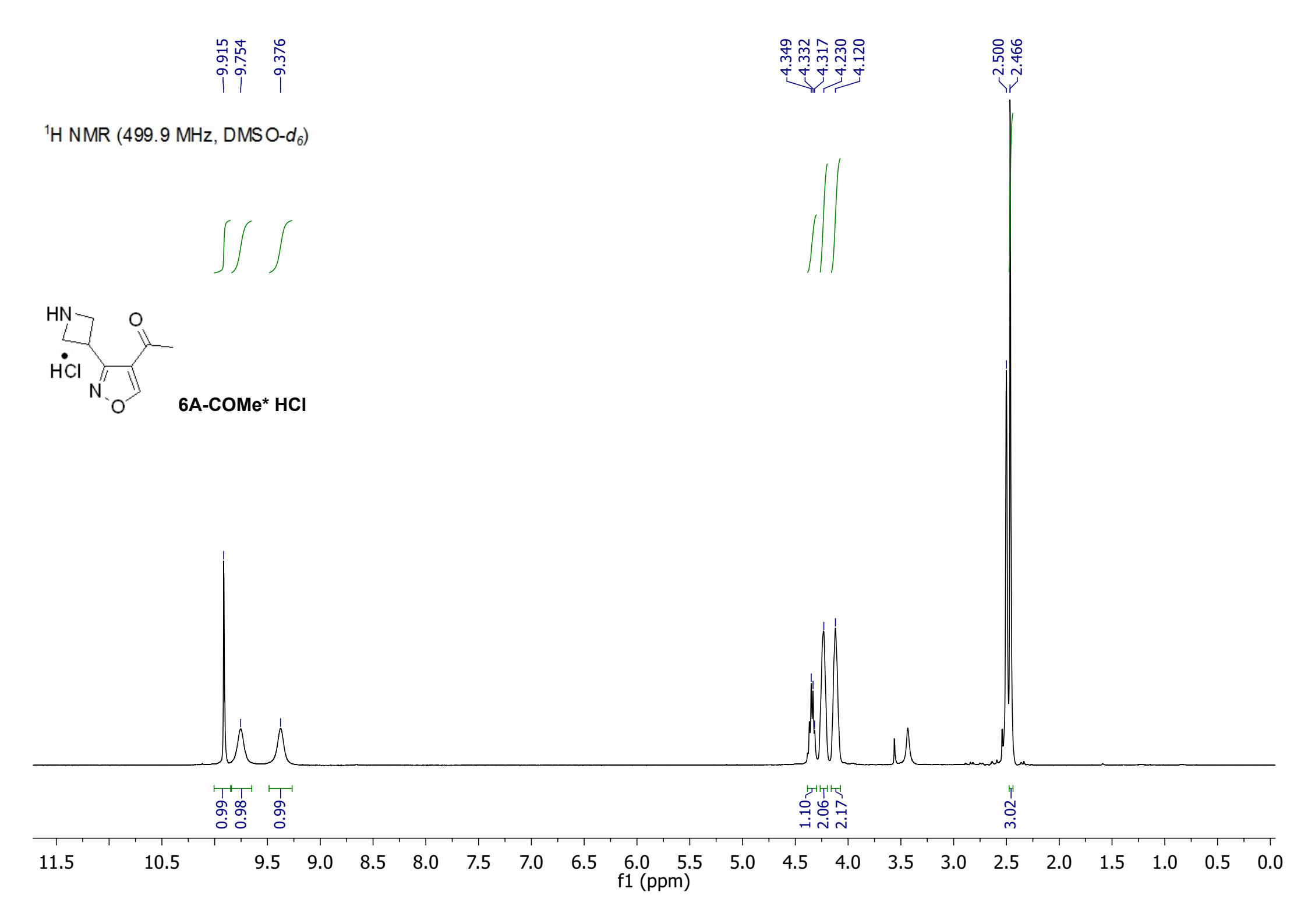

10.008
8.888
4.790
4.774
3.367
2.520
2.500
1.538
1.522
1H NMR (499.9 MHz, DMSO-d6)
H2N
•HCl
O
N
O
3A-COMe* HCl
1.00
3.14
1.05
3.02
3.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f (ppm)

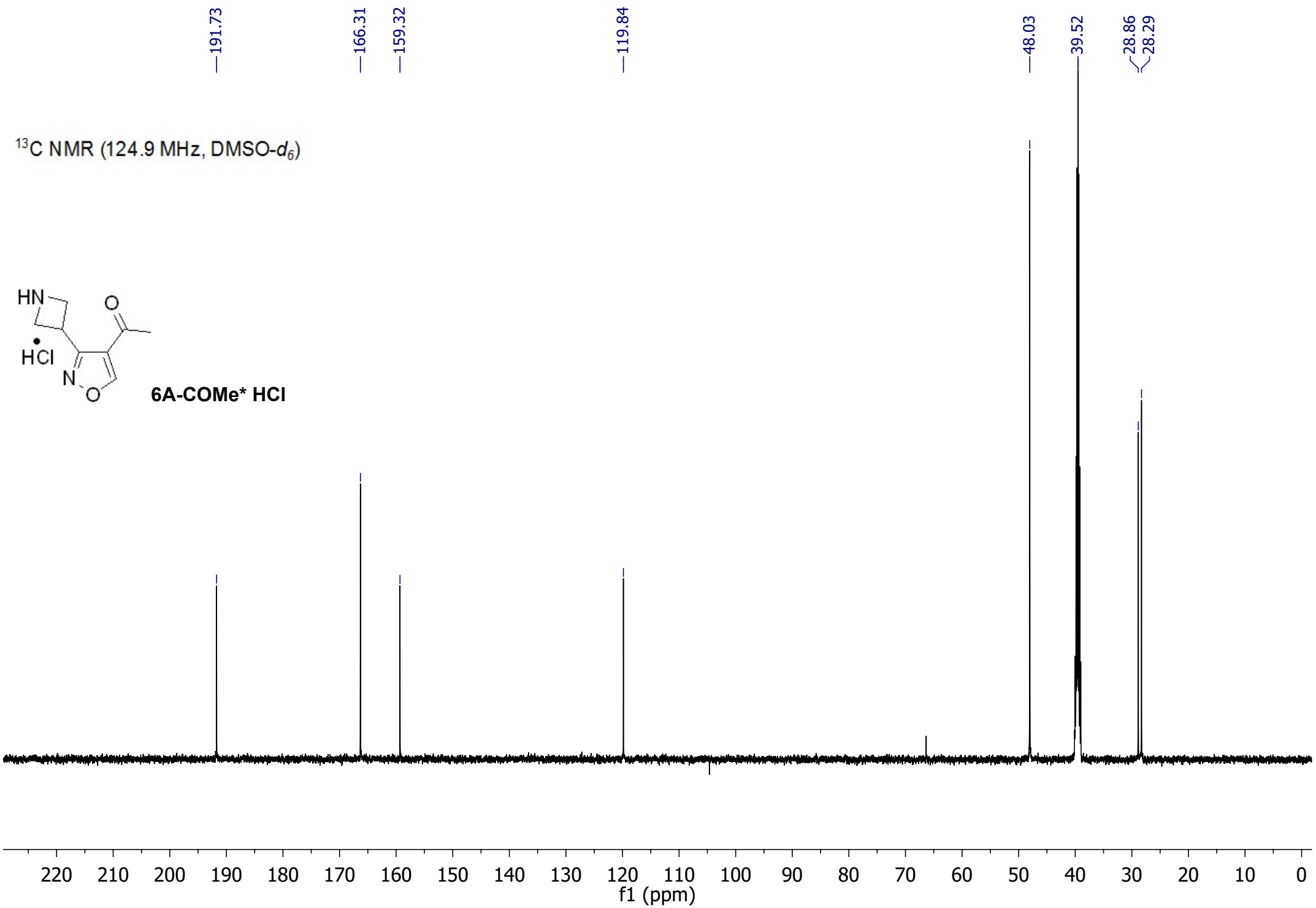

192.05
166.82
159.79
119.11
42.92
39.52
29.21
17.87
^{13}C NMR (124.9 MHz, DMSO-d_6)
H_2N
•HCl
O
N
O
3A-COMe* HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

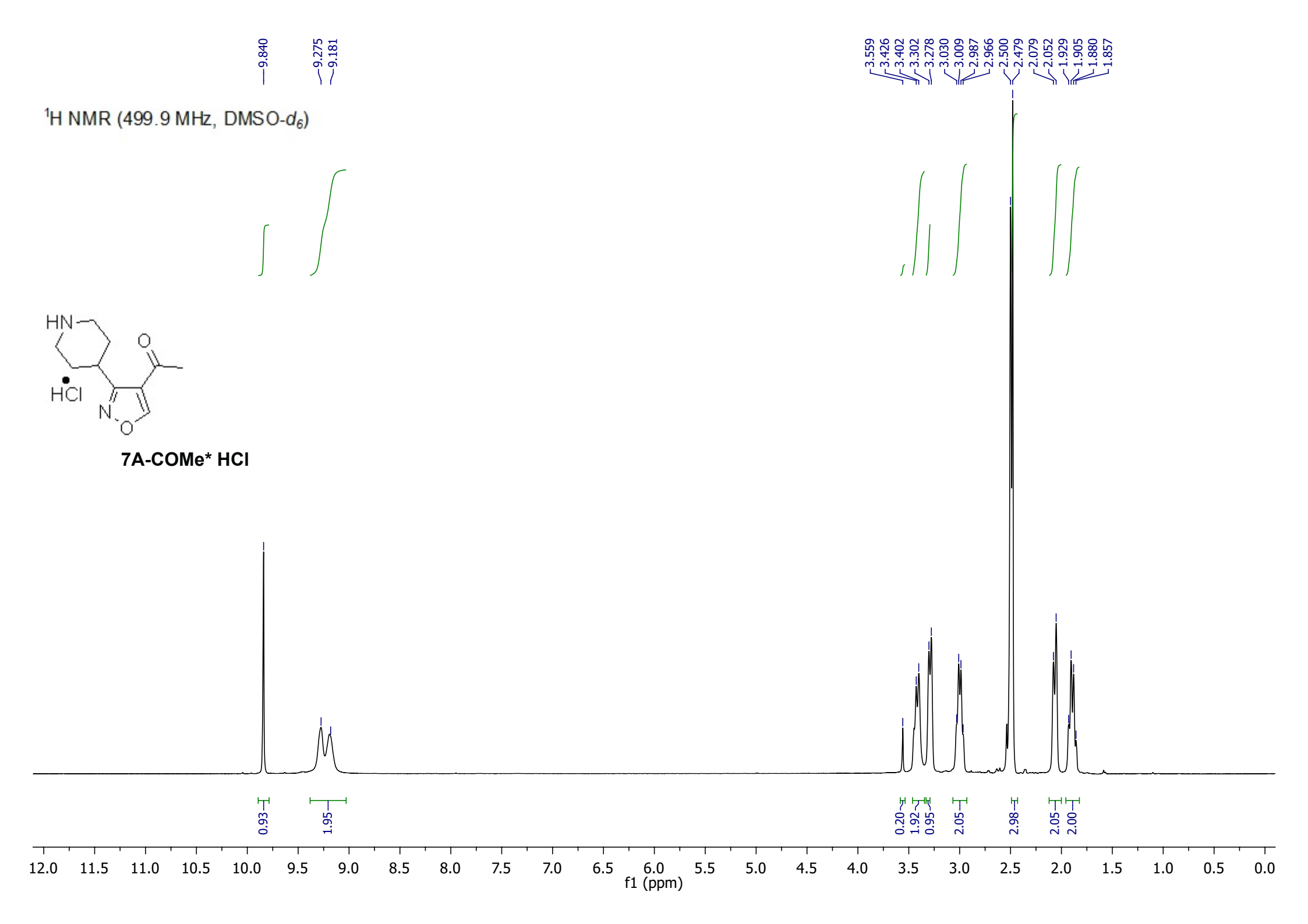

10.488
10.016
9.431
8.941
5.050
5.033
5.016
3.290
2.516
2.500
2.405
2.321
2.139
1.966
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
O
N
O
0.93
1.06
1.00
1.02
2.00
2.79
1.01
2.90
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

4A-COMe* HCl

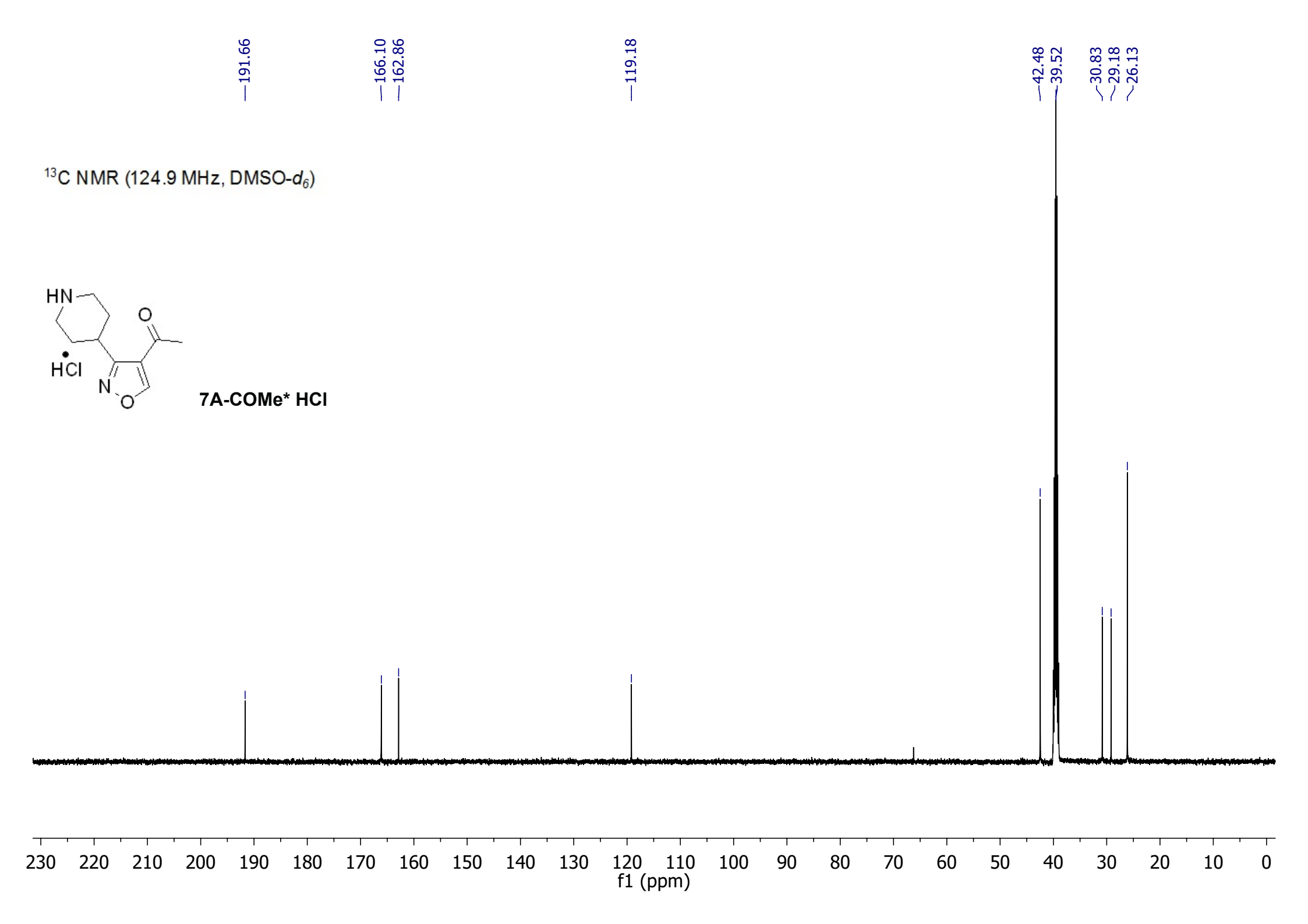

191.83
166.62
157.47
119.91
53.38
44.98
39.52
29.10
28.89
23.05
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
O
N
O
4A-COMe* HCl
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

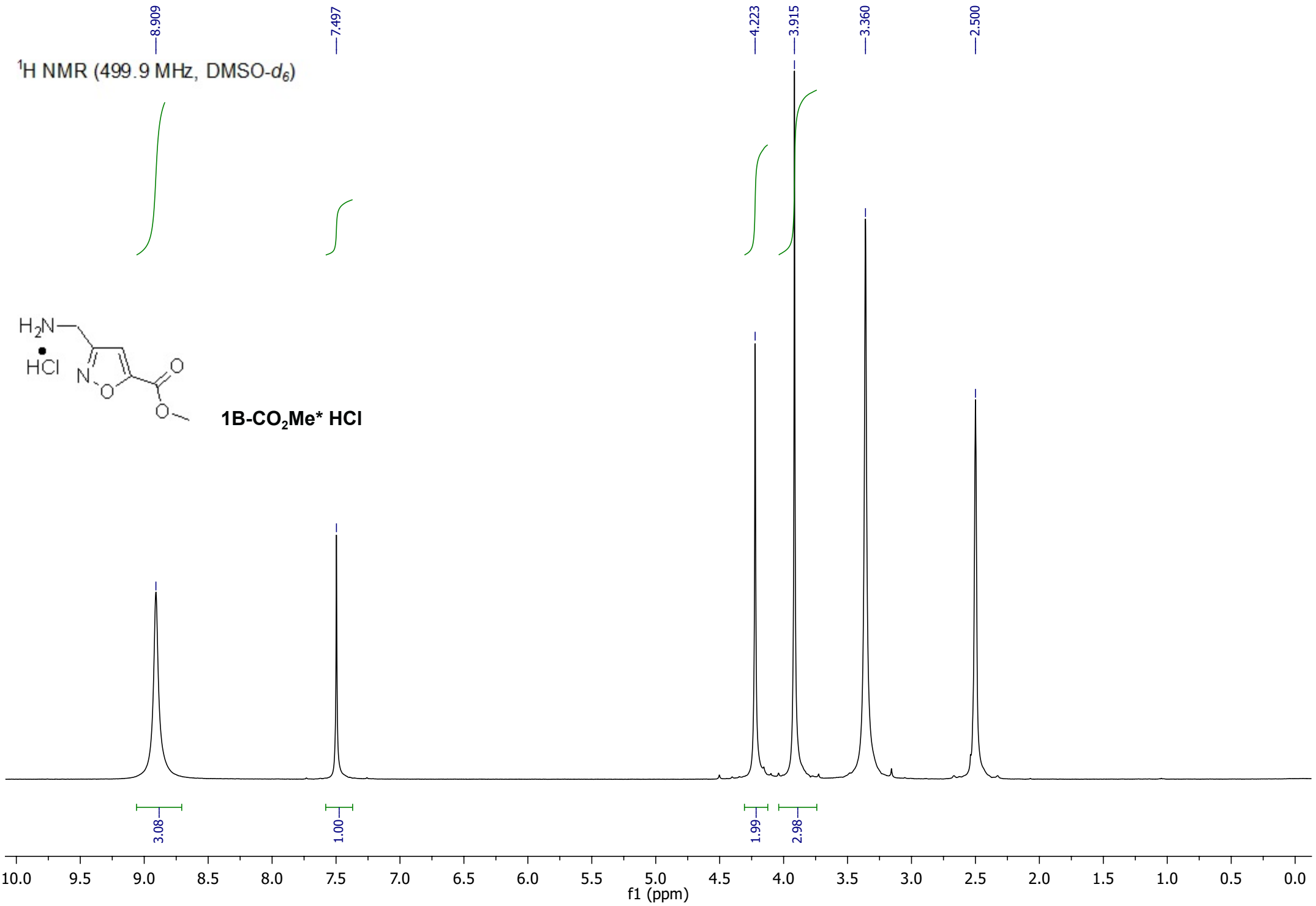

9.915
9.754
9.376
4.349
4.332
4.317
4.230
4.120
2.500
2.466
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
O
HCl
N
O
6A-COMe* HCl
0.99
0.98
0.99
1.10
2.06
2.17
3.02
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

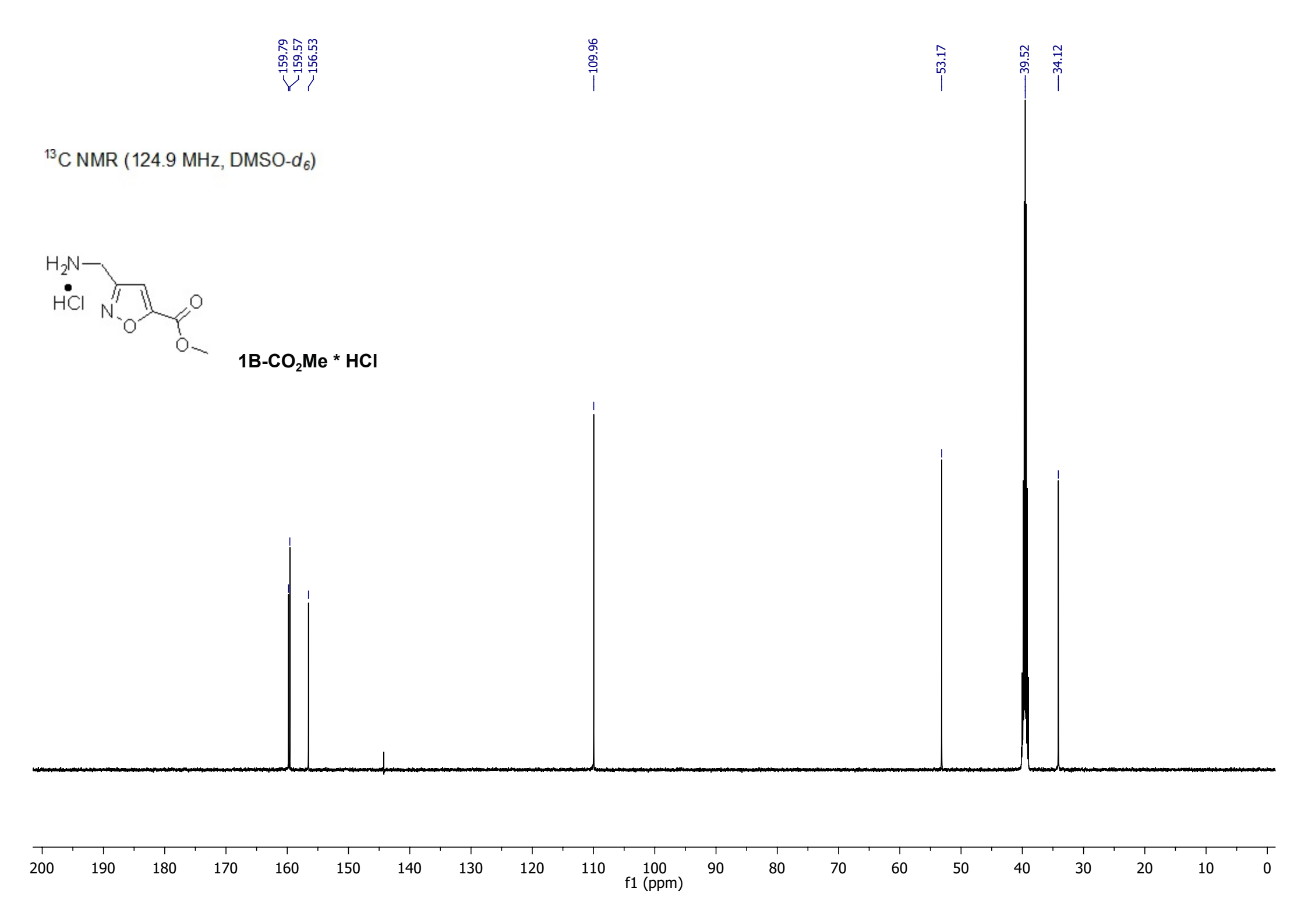

191.73
166.31
159.32
119.84
48.03
39.52
28.86
28.29
13C NMR (124.9 MHz, DMSO-d6)
HN
O
HCl
N
O
6A-COMe* HCl
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

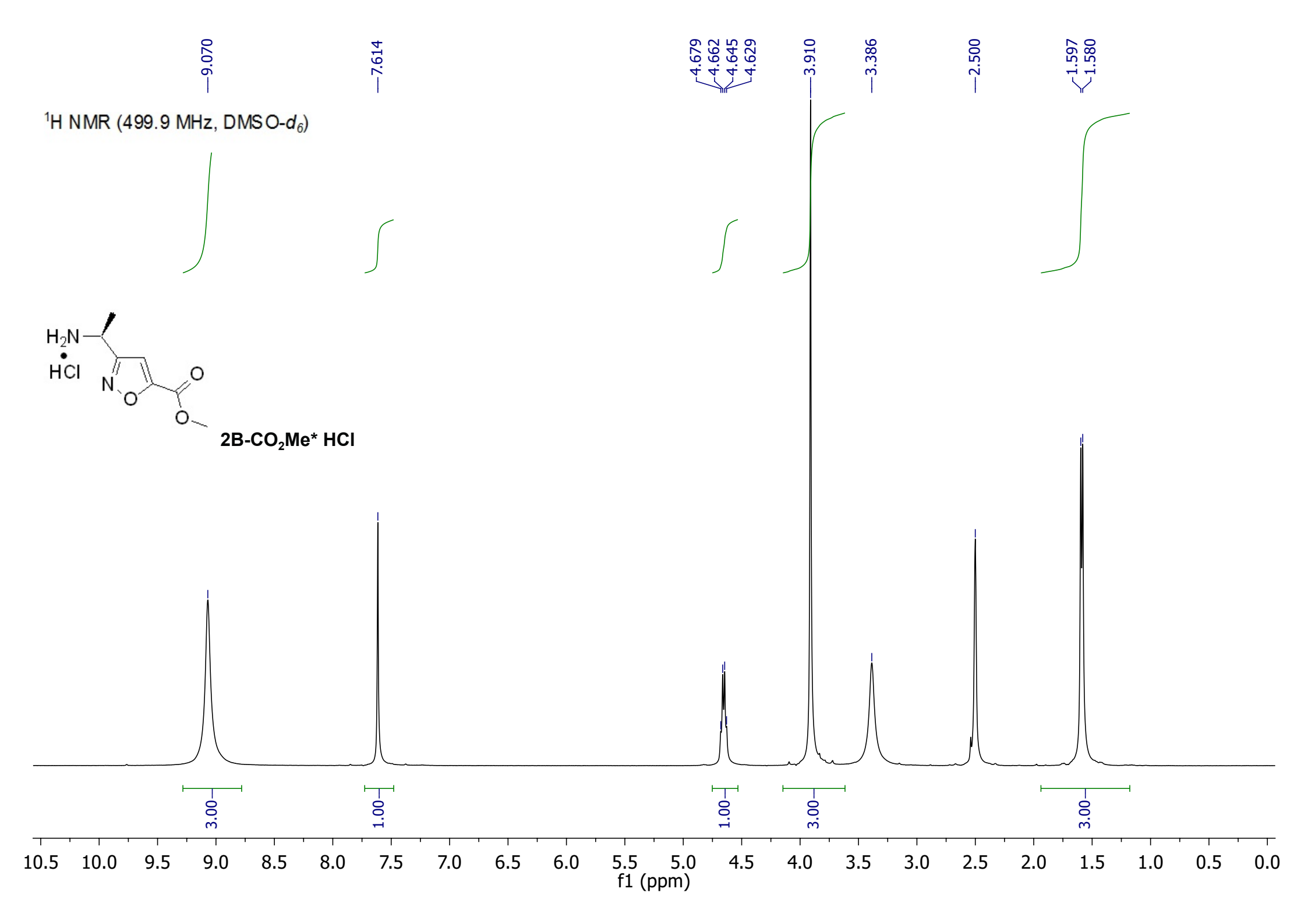

9.840
9.275
9.181
3.559
3.426
3.402
3.302
3.278
3.030
3.009
2.987
2.966
2.500
2.479
2.079
2.052
1.929
1.905
1.880
1.857
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
O
HCl
N
O
0.93
1.95
0.20
1.92
0.95
2.05
2.98
2.05
2.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

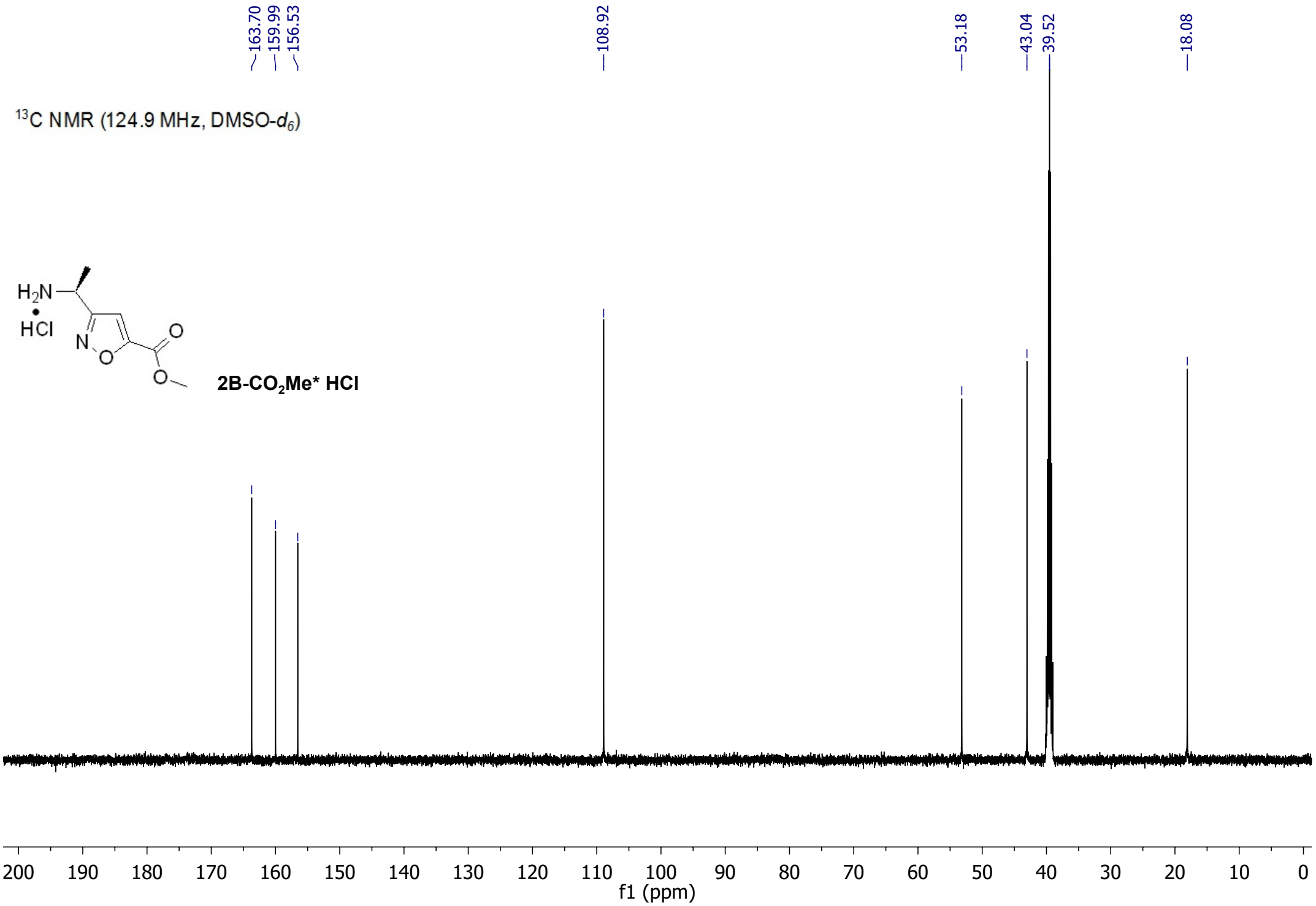
7A-COMe* HCl

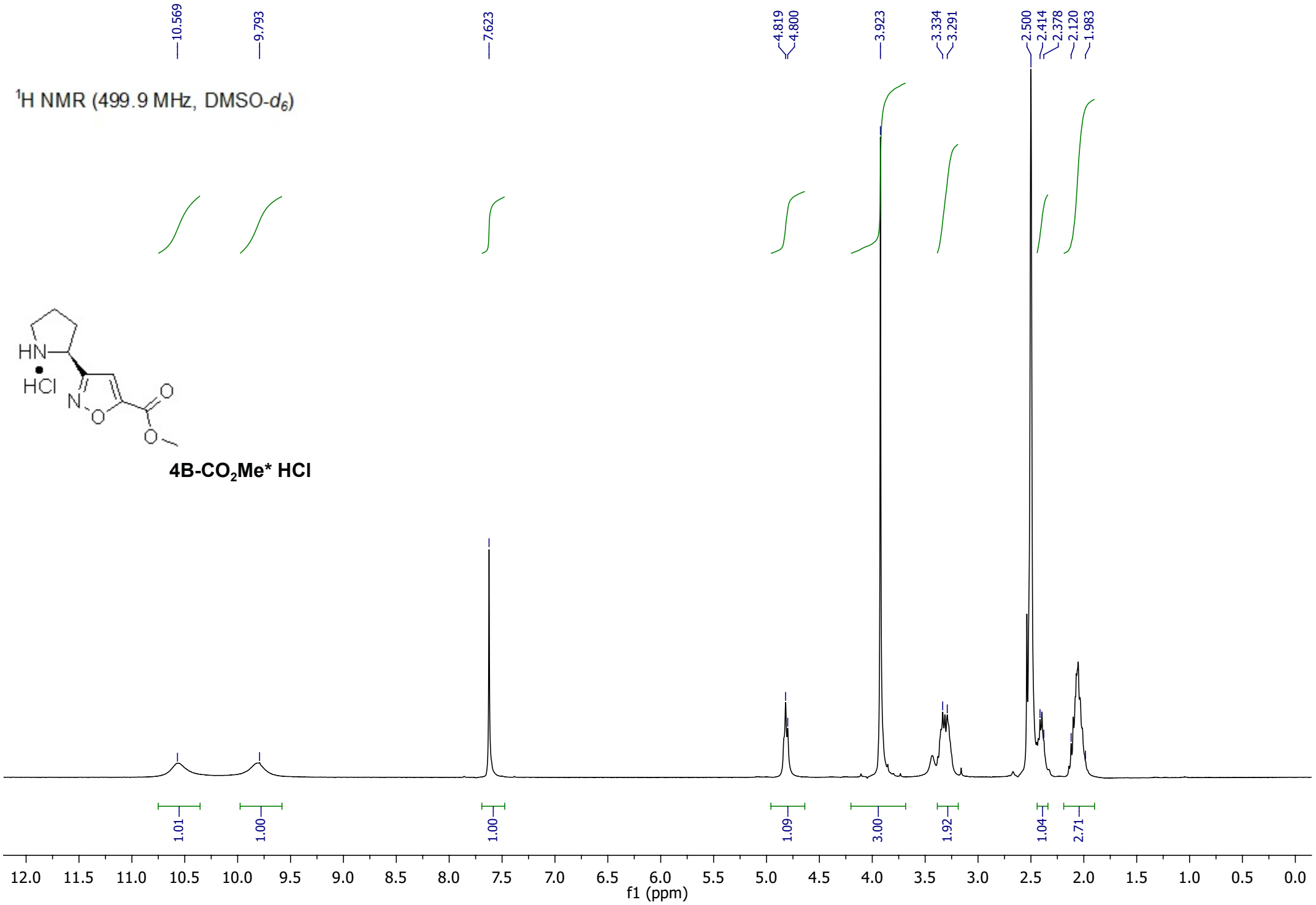

191.66
166.10
162.86
119.18
42.48
39.52
30.83
29.18
26.13
13C NMR (124.9 MHz, DMSO-d6)
HN
O
HCl
N
O
7A-COMe* HCl
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.909
7.497
4.223
3.915
3.360
2.500
1H NMR (499.9 MHz, DMSO-d6)
H2N
HCl
N
O
O
O
1B-CO2Me* HCl
3.08
1.00
1.99
2.98
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)

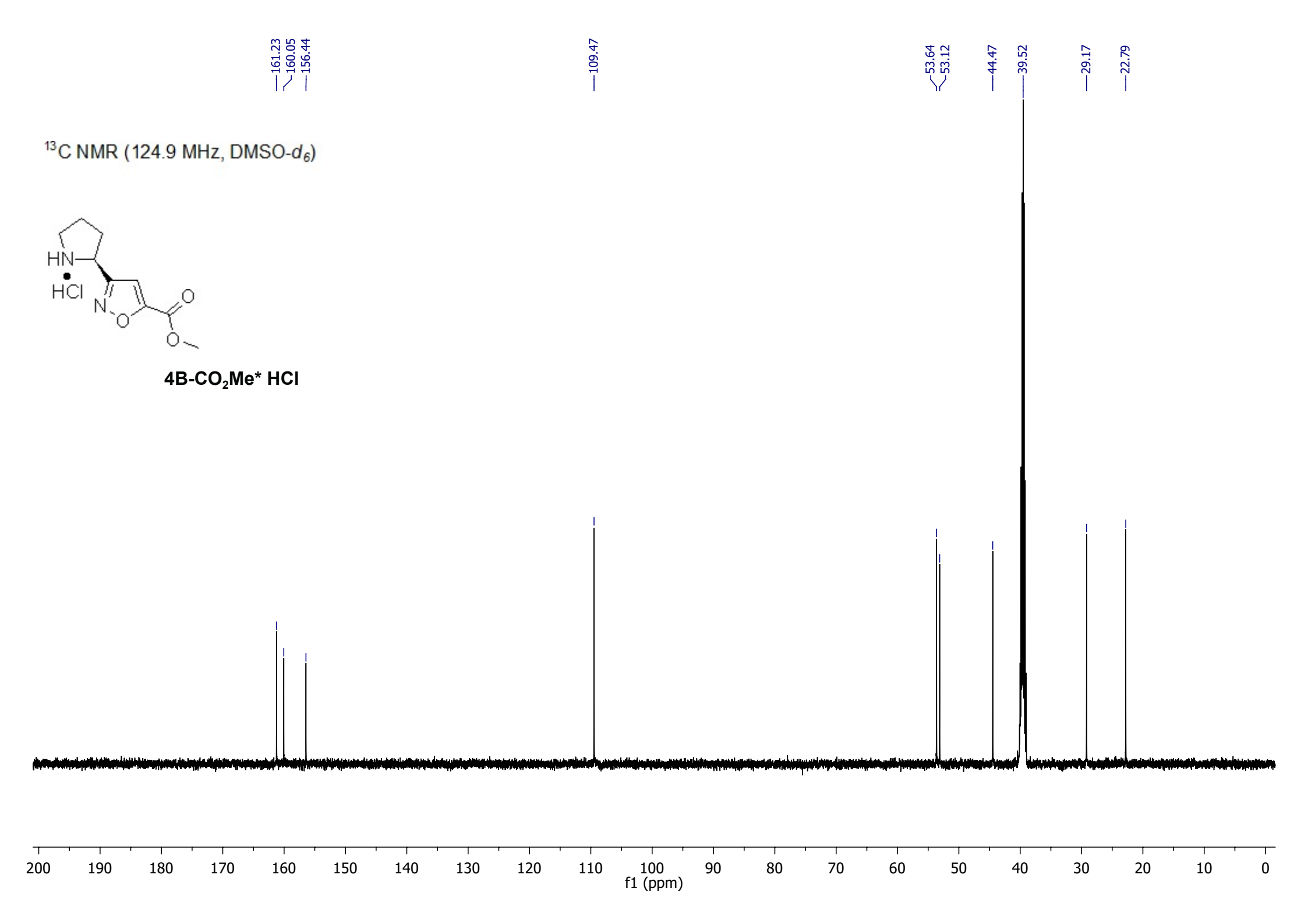

159.79
159.57
156.53
109.96
53.17
39.52
34.12
13C NMR (124.9 MHz, DMSO-d6)
H2N
HCl
N
O
O
O
1B-CO2Me * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

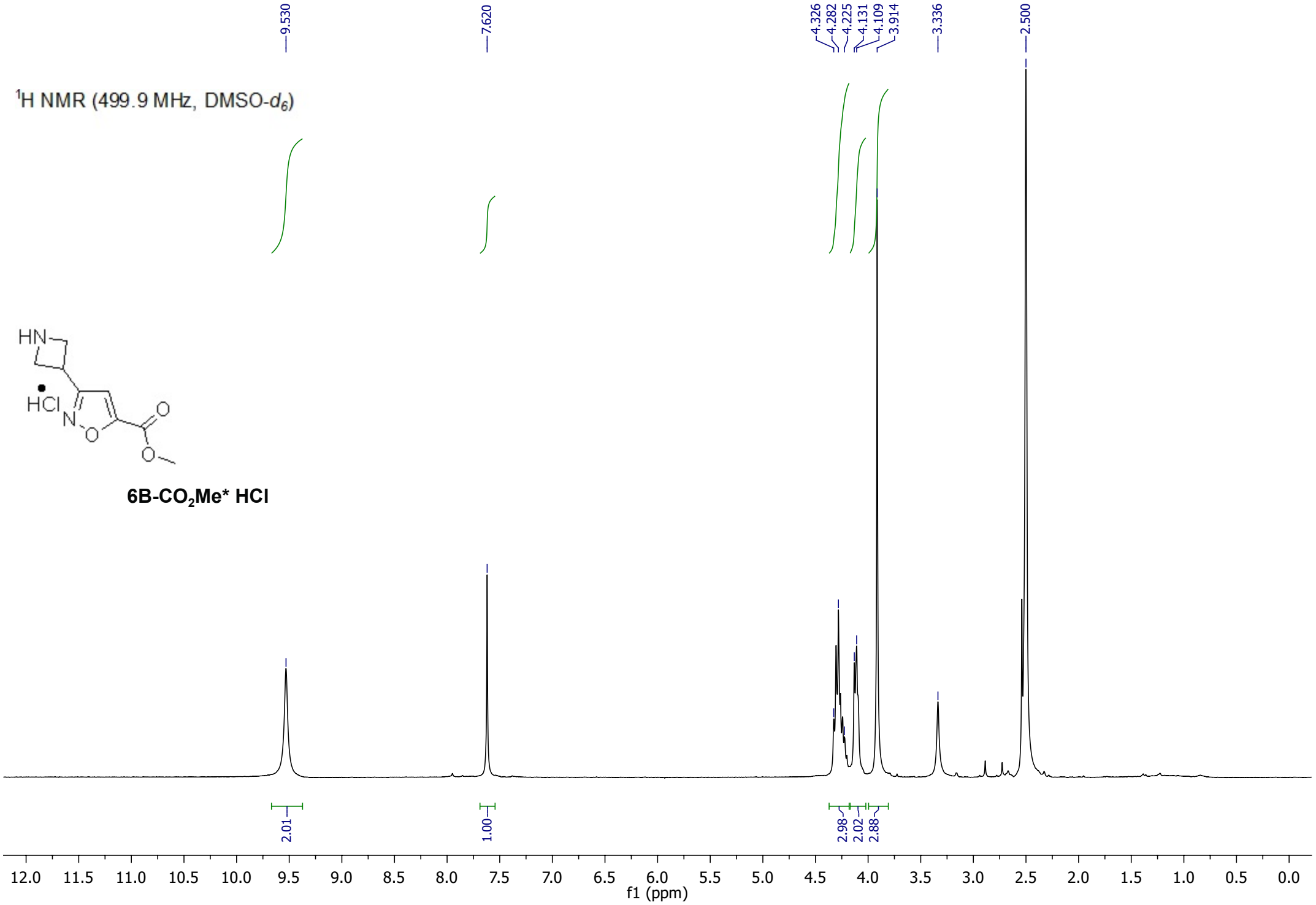

9.070
7.614
4.679
4.662
4.645
4.629
3.910
3.386
2.500
1.597
1.580
^{1}H NMR (499.9 MHz, DMSO-d_6)
H_2N
HCl
N
O
O
O
2B-CO_2Me* HCl
3.00
1.00
1.00
3.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


163.70
159.99
156.53
108.92
53.18
43.04
39.52
18.08
^{13}C NMR (124.9 MHz, DMSO-d_6)
H_2N
HCl
N
O
O
O
2B-CO_2Me* HCl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

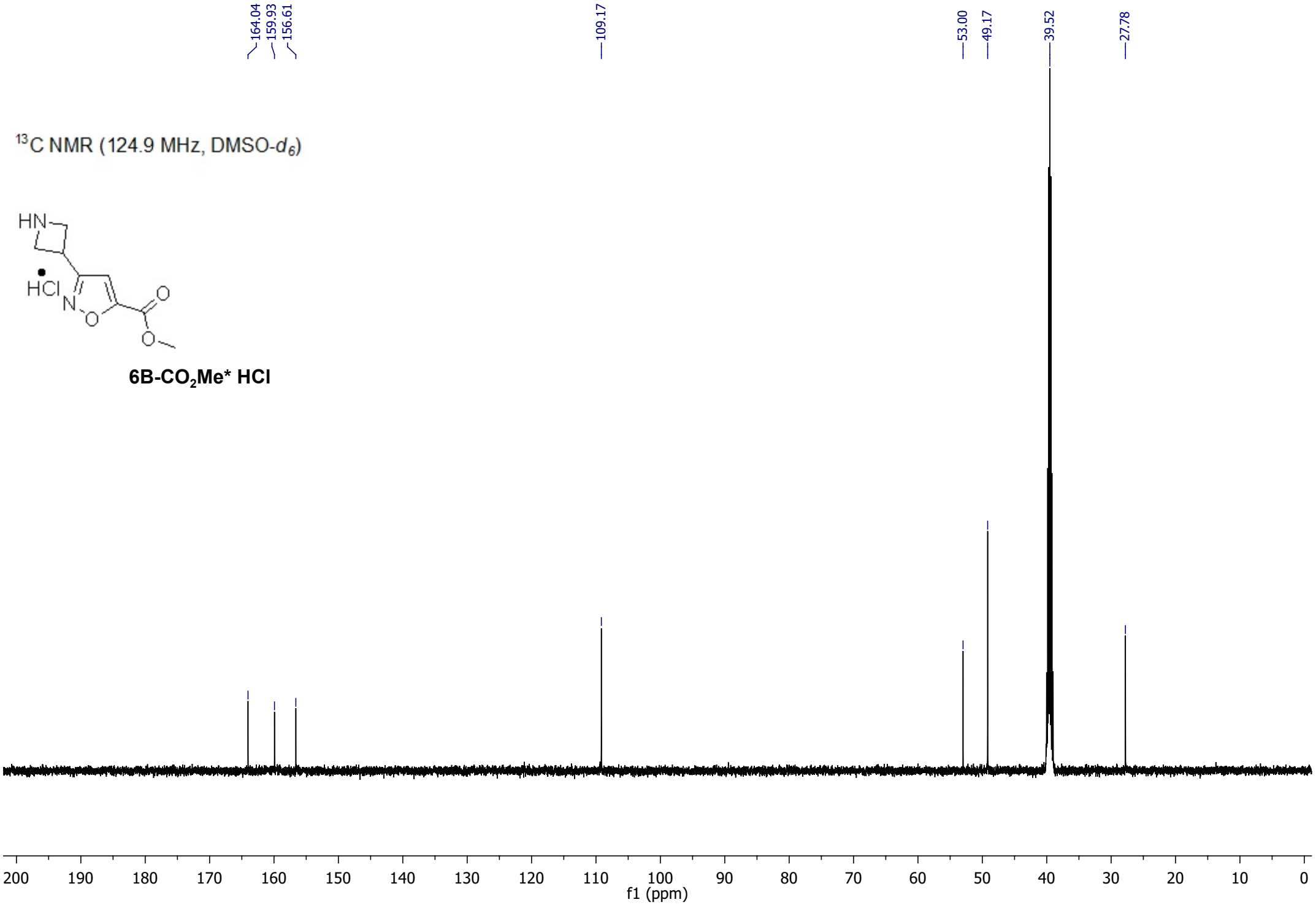

10.569
9.793
7.623
4.819
4.800
3.923
3.334
3.291
2.500
2.414
2.378
2.120
1.983
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
N
O
O
O
1.01
1.00
1.00
1.09
3.00
1.92
1.04
2.71
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

4B-CO_2Me* HCl

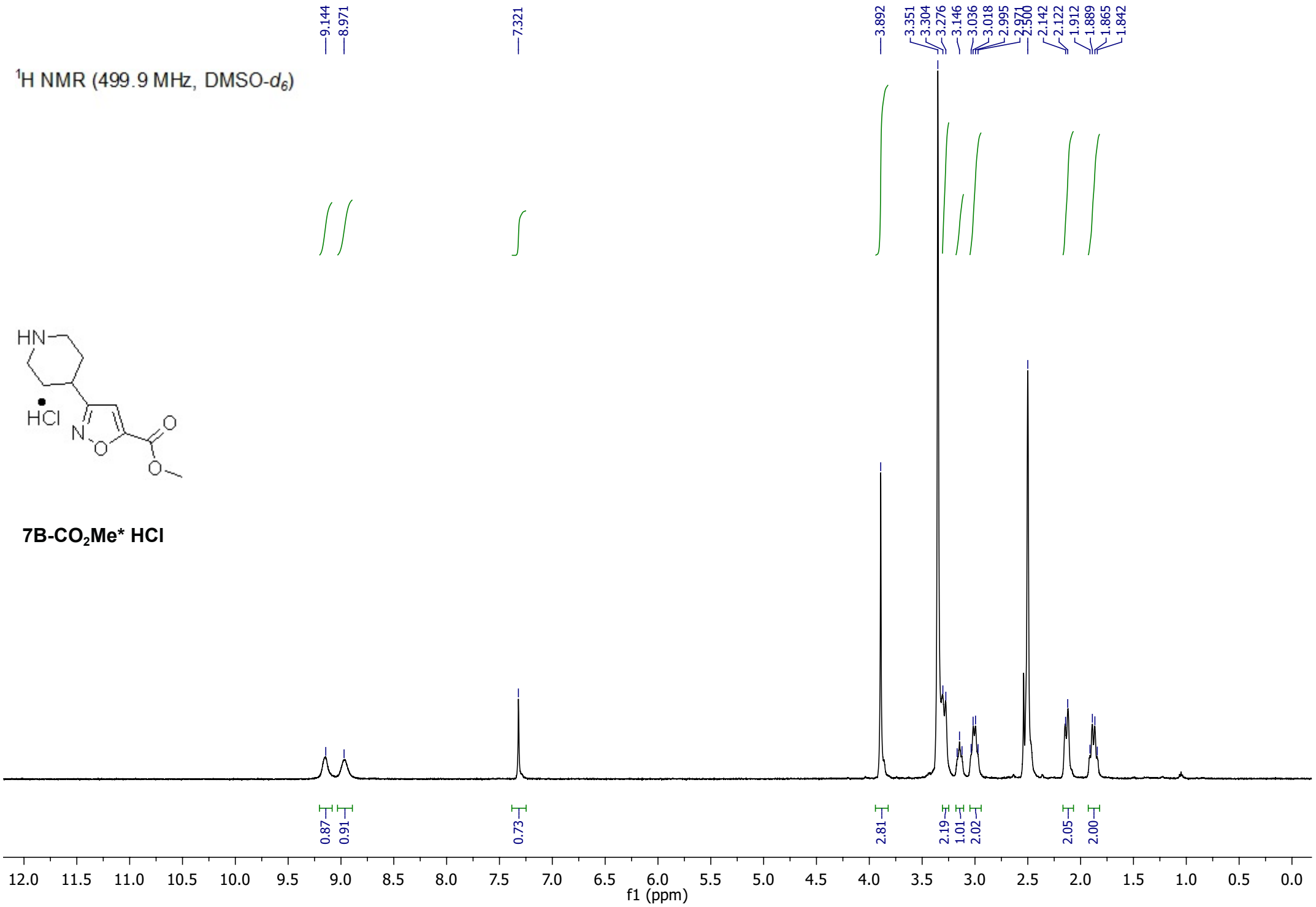

161.23
160.05
156.44
109.47
53.64
53.12
44.47
39.52
29.17
22.79
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
N
O
O
O
4B-CO2Me* HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.530
7.620
4.326
4.282
4.225
4.131
4.109
3.914
3.336
2.500
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
N
O
O
O
2.01
1.00
2.98
2.02
2.88
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
f1 (ppm)

6B-CO_2Me* HCl


164.04
159.93
156.61
109.17
53.00
49.17
39.52
27.78
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
HCl
N
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

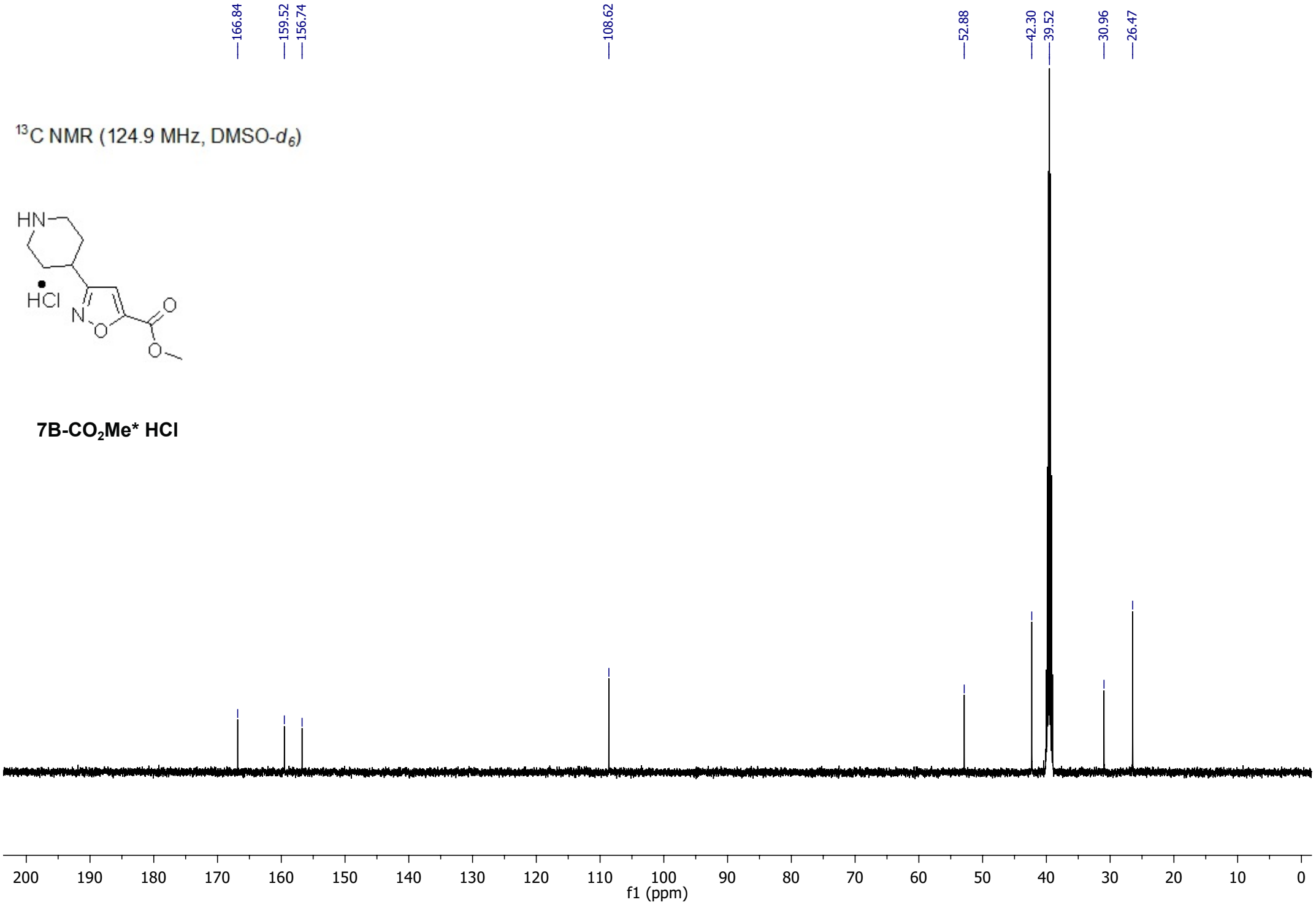
6B-CO_2Me* HCl

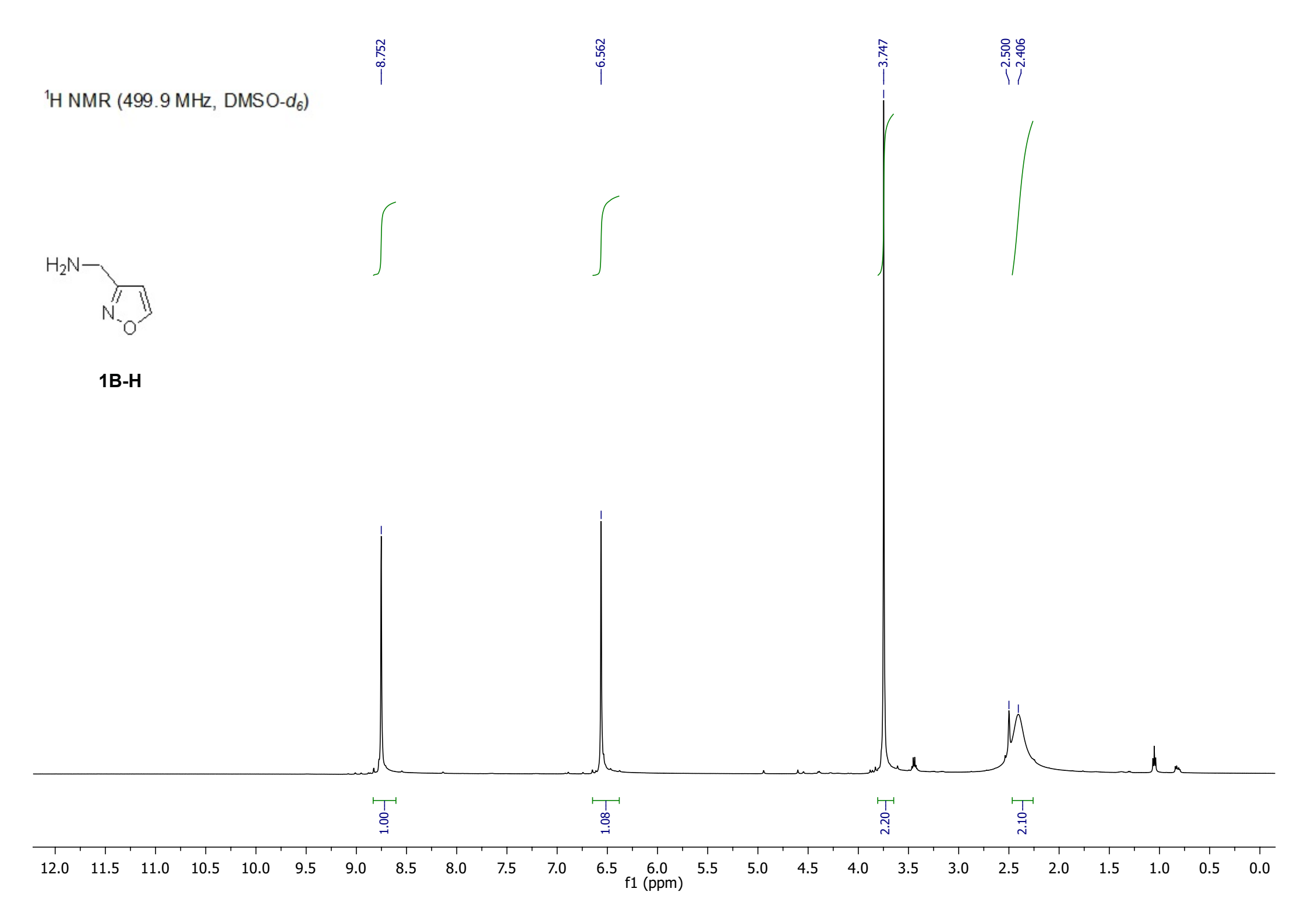


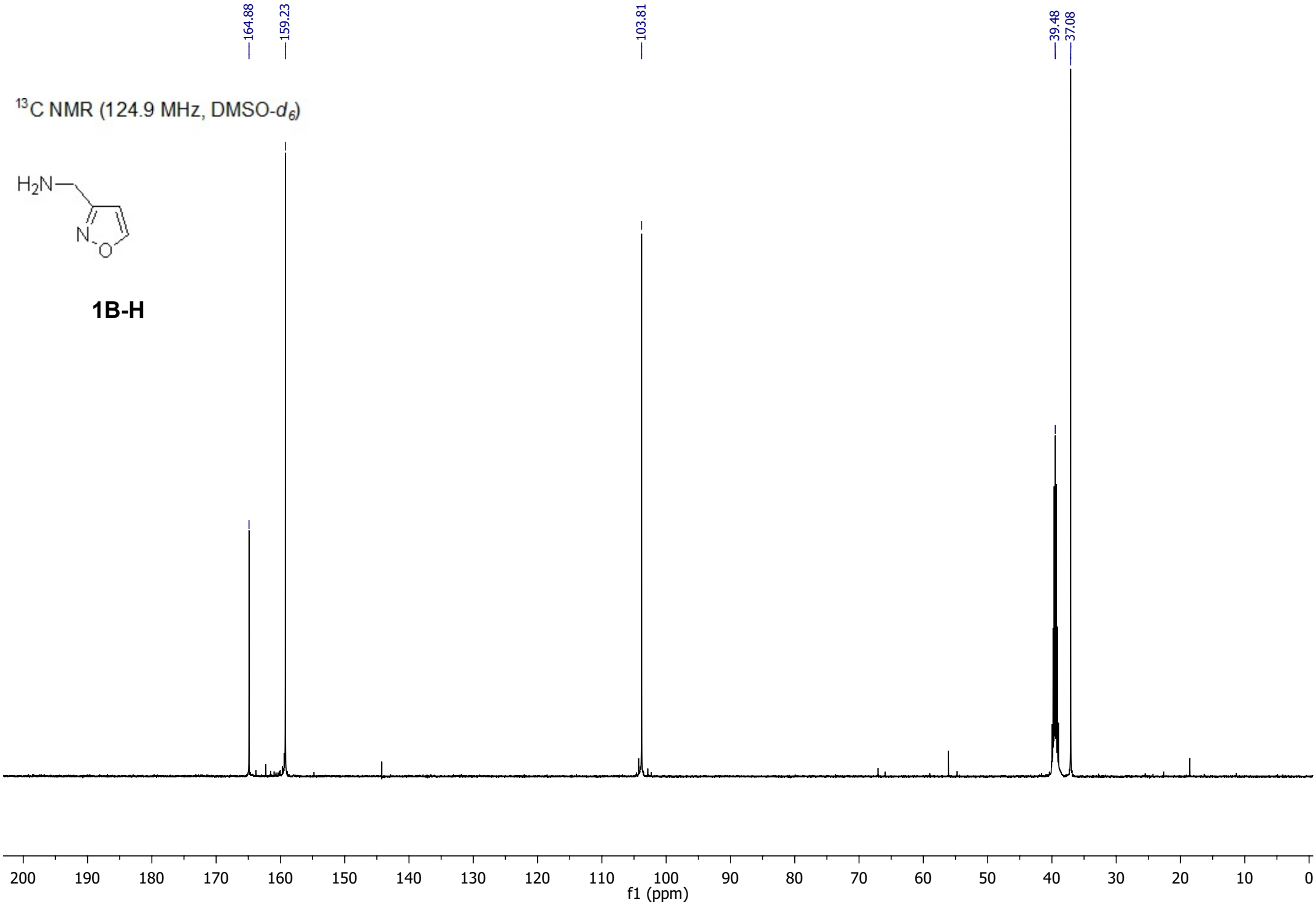
^{1}H NMR (499.9 MHz, DMSO-d_6)

HN
HCl
N
O
O
O

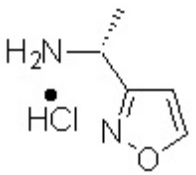
7B-CO_2Me* HCl


166.84
159.52
156.74
108.62
52.88
42.30
39.52
30.96
26.47
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
HCl
N
O
O
O
7B-CO$_2$Me* HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

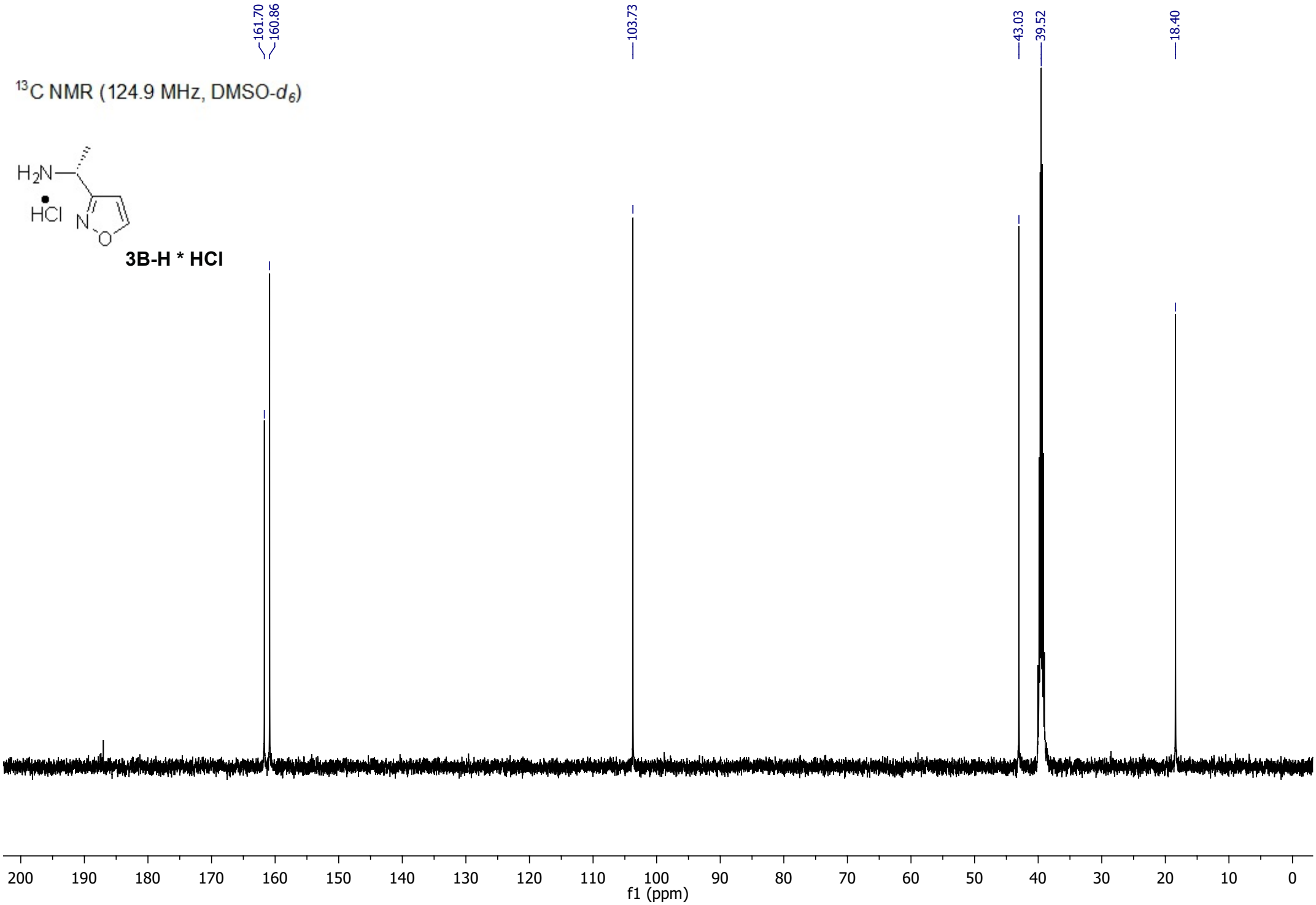

8.752
6.562
3.747
2.500
2.406
1H NMR (499.9 MHz, DMSO-d6)
H2N
N
O
1B-H
1.00
1.08
2.20
2.10
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

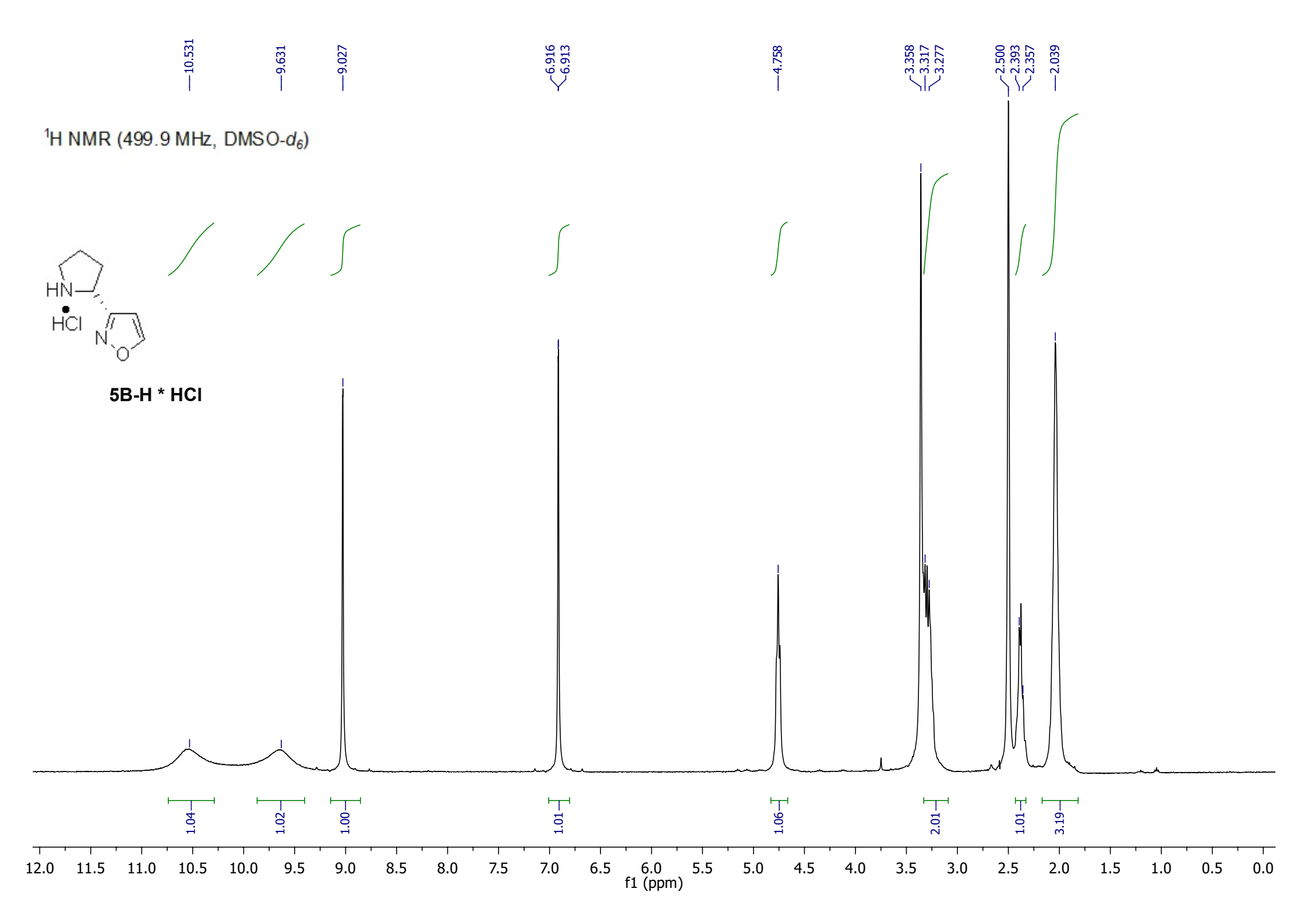

164.88
159.23
103.81
39.48
37.08
13C NMR (124.9 MHz, DMSO-d6)
H2N
N
O
1B-H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

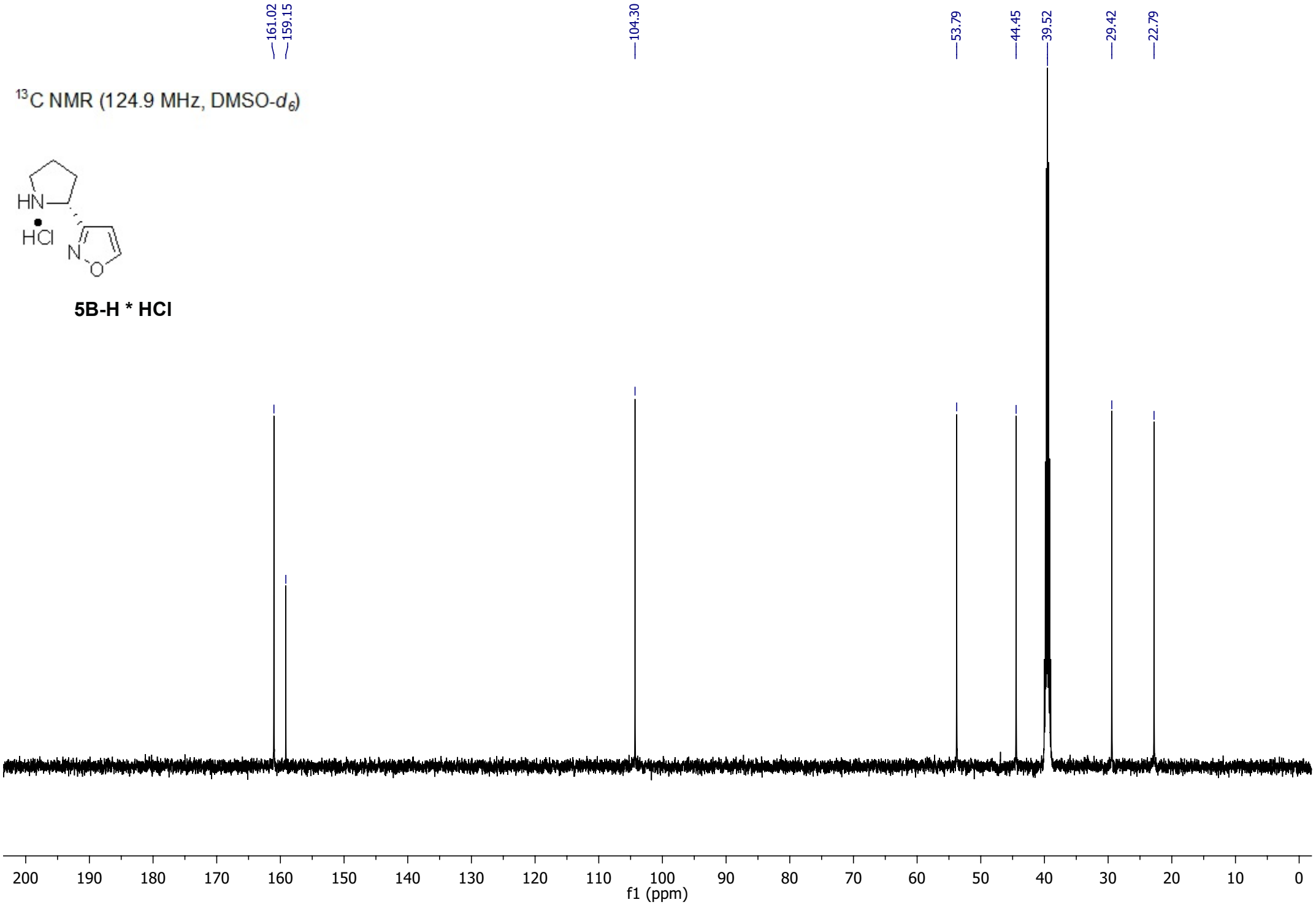
^{1}H NMR (499.9 MHz, DMSO-d_6)

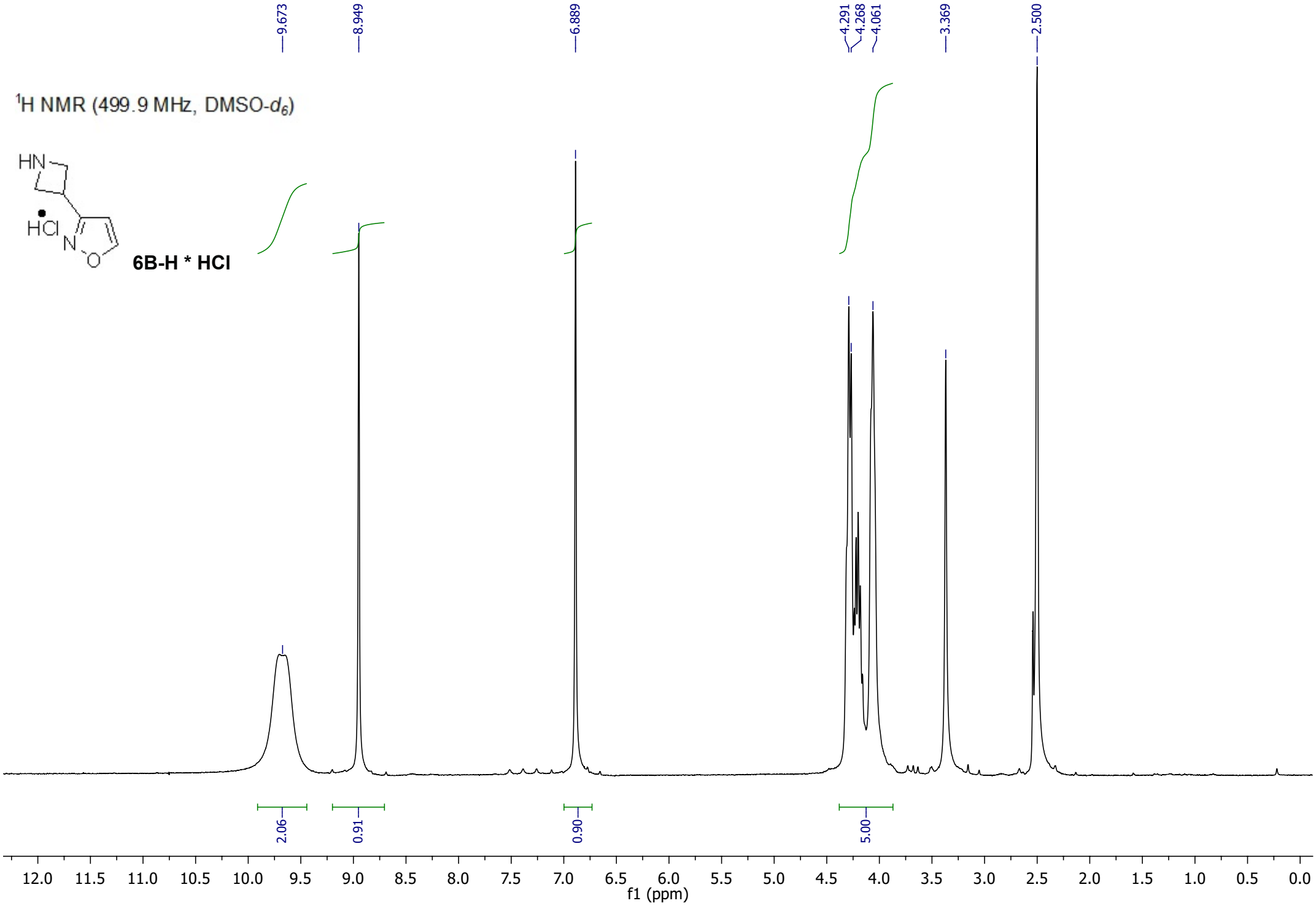


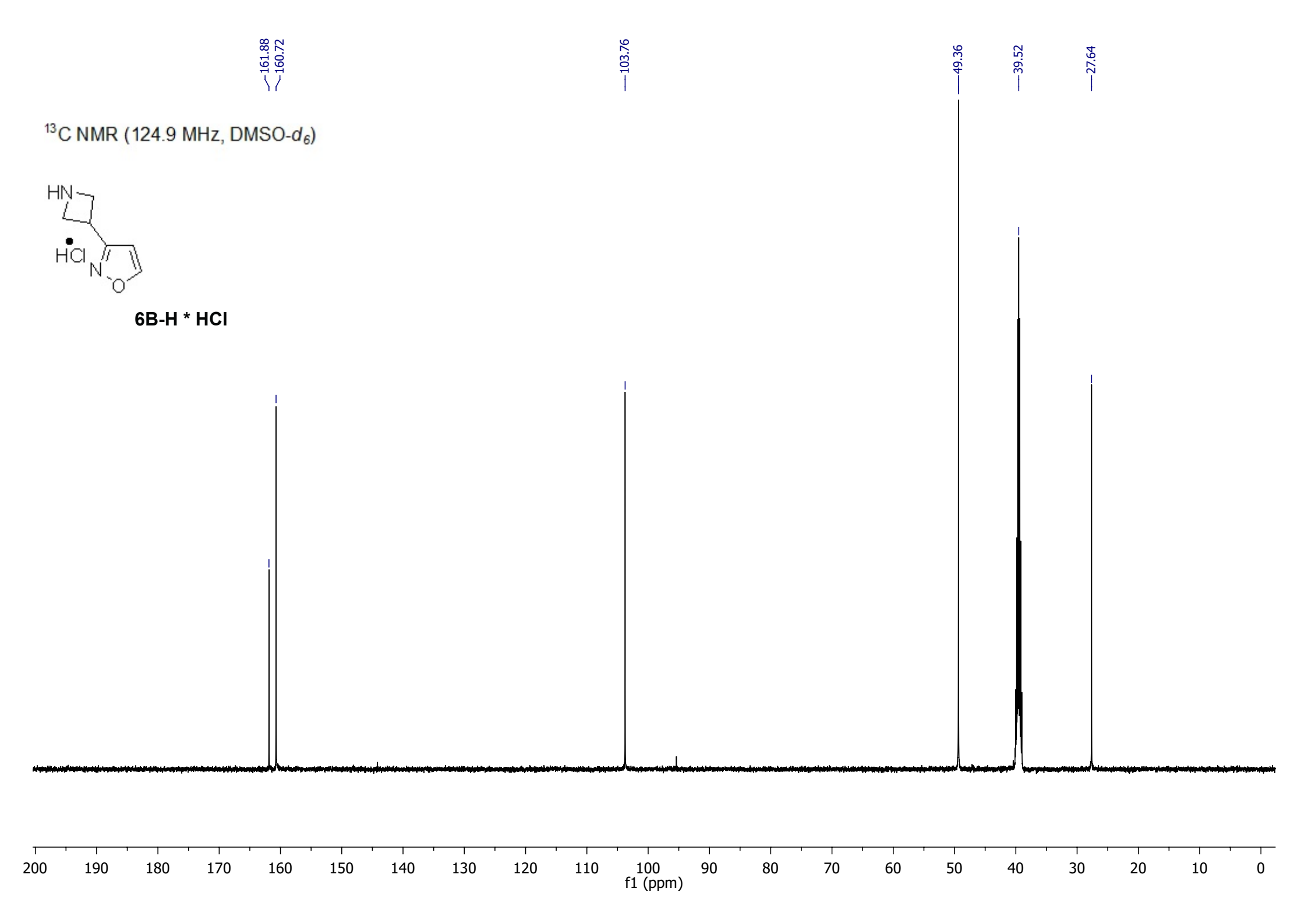
3B-H * HCl


161.70
160.86
103.73
43.03
39.52
18.40
13C NMR (124.9 MHz, DMSO-d6)
H2N
HCl
N
O
3B-H * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

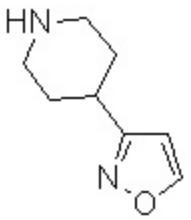

10.531
9.631
9.027
6.916
6.913
4.758
3.358
3.317
3.277
2.500
2.393
2.357
2.039
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
N
O
5B-H * HCl
1.04
1.02
1.00
1.01
1.06
2.01
1.01
3.19
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.02
159.15
104.30
53.79
44.45
39.52
29.42
22.79
^{13}C NMR (124.9 MHz, DMSO-d_6)
HN
HCl
N
O
5B-H * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

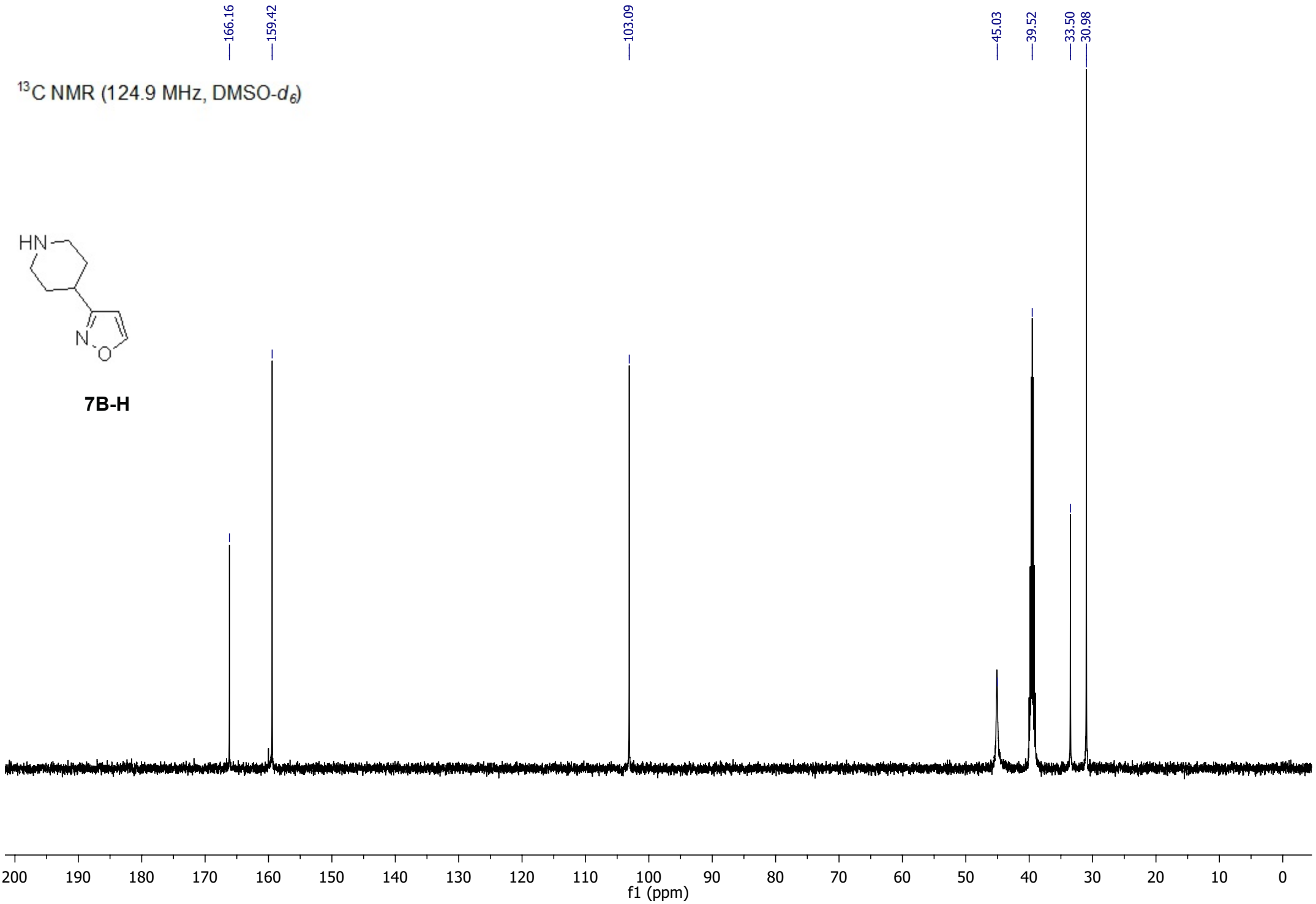

9.673
8.949
6.889
4.291
4.268
4.061
3.369
2.500
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
N
O
6B-H * HCl
2.06
0.91
0.90
5.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

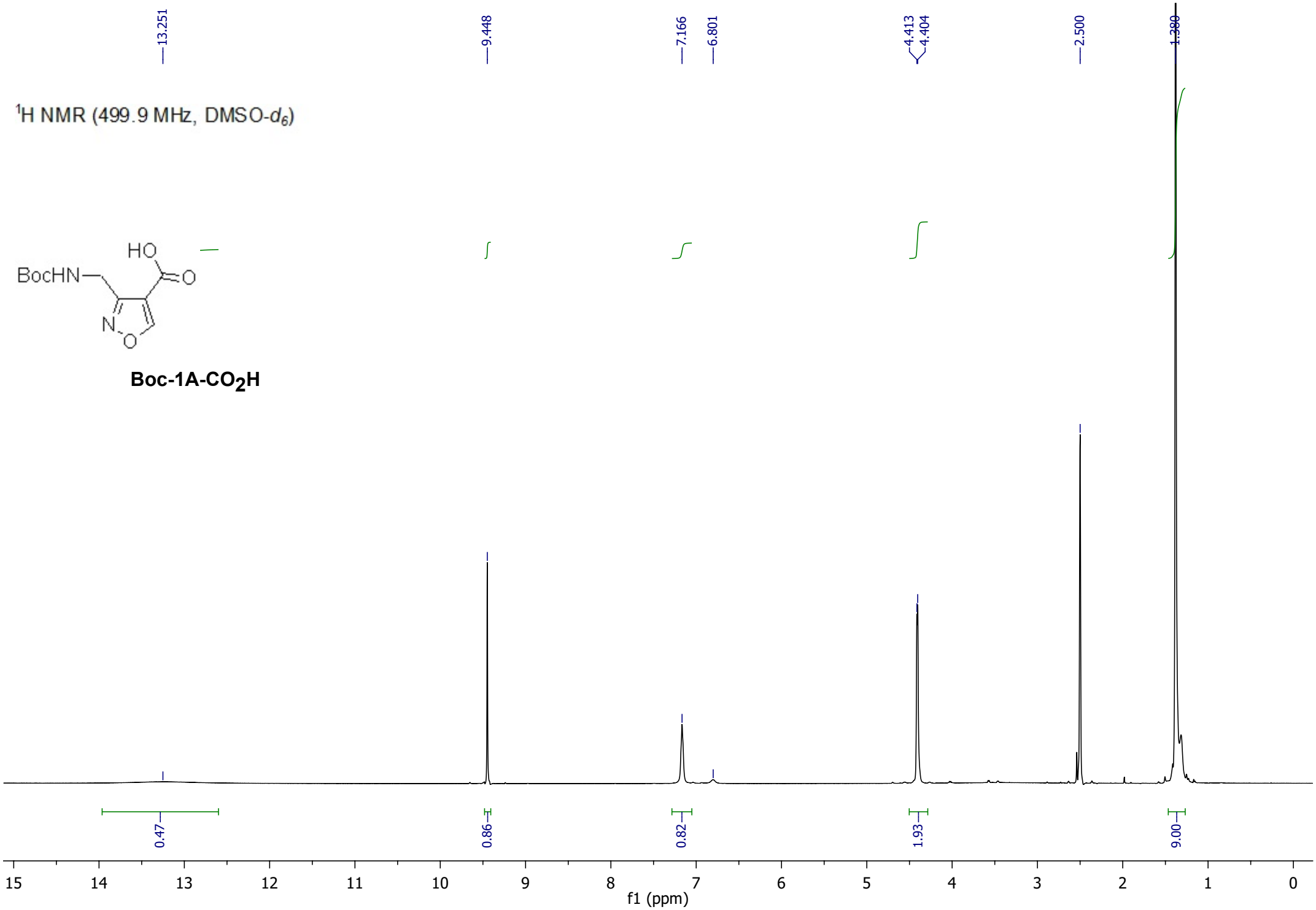

161.88
160.72
103.76
49.36
39.52
27.64
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
N
O
6B-H * HCl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

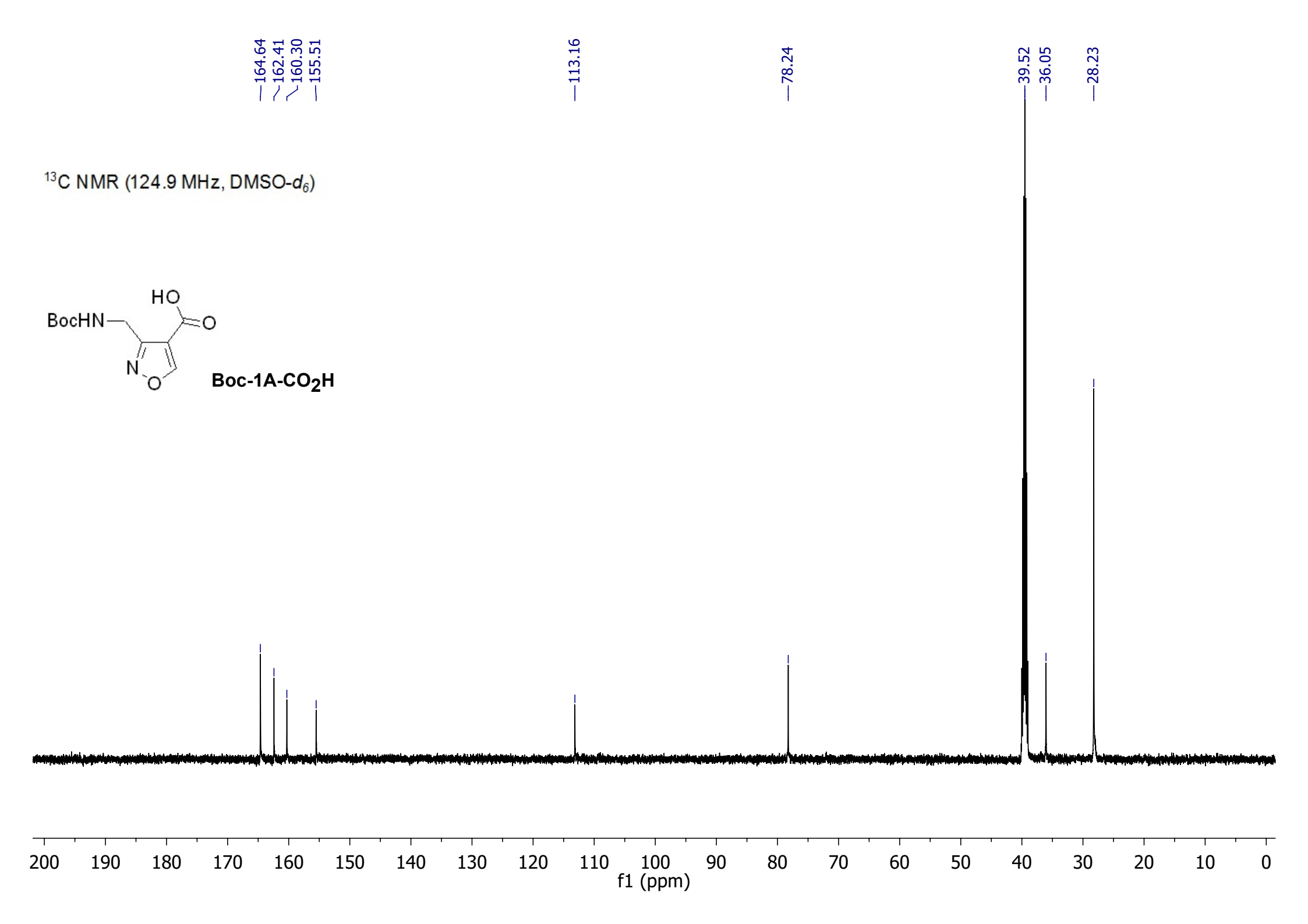
^{1}H NMR (499.9 MHz, $CDCl_3$)

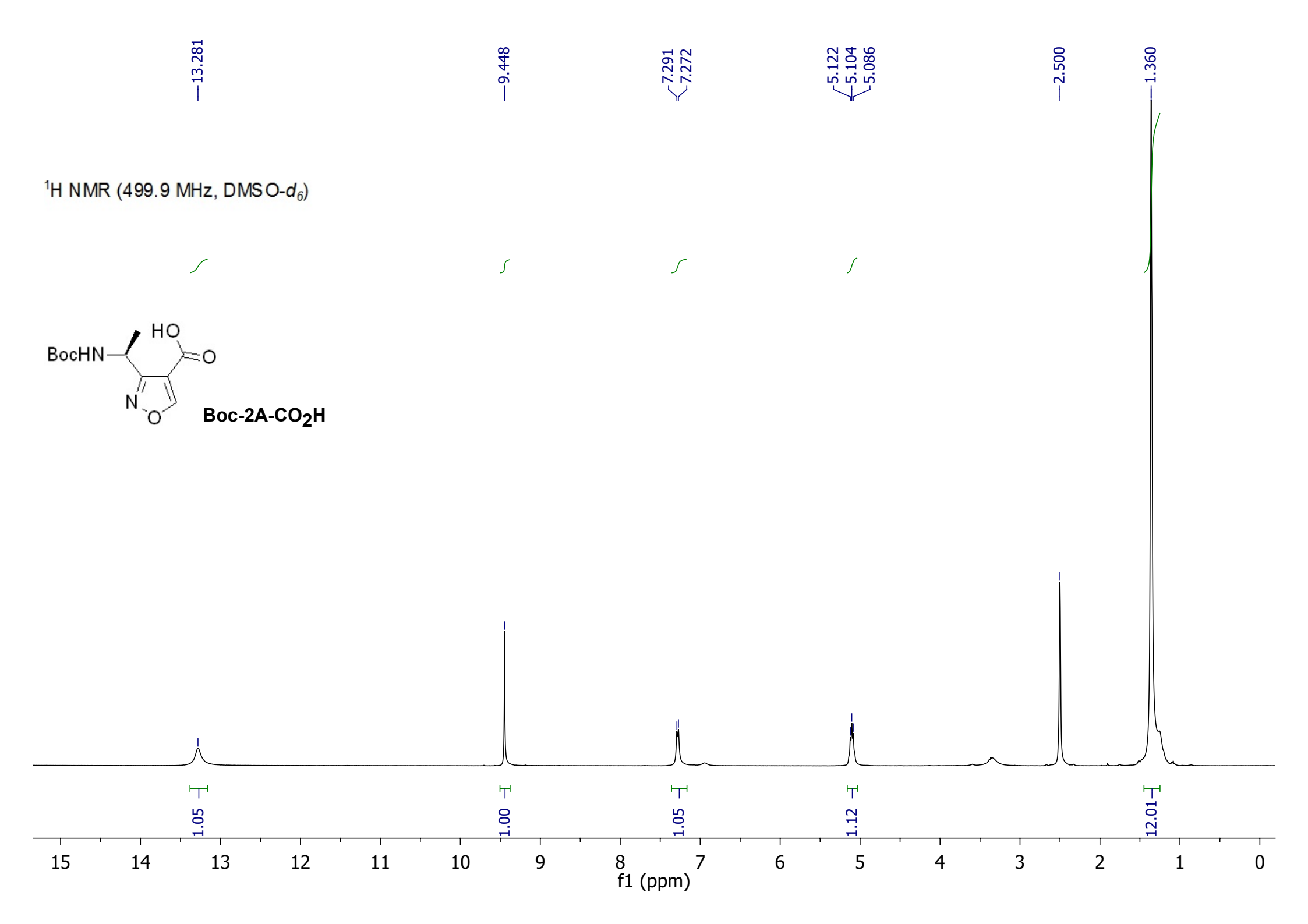


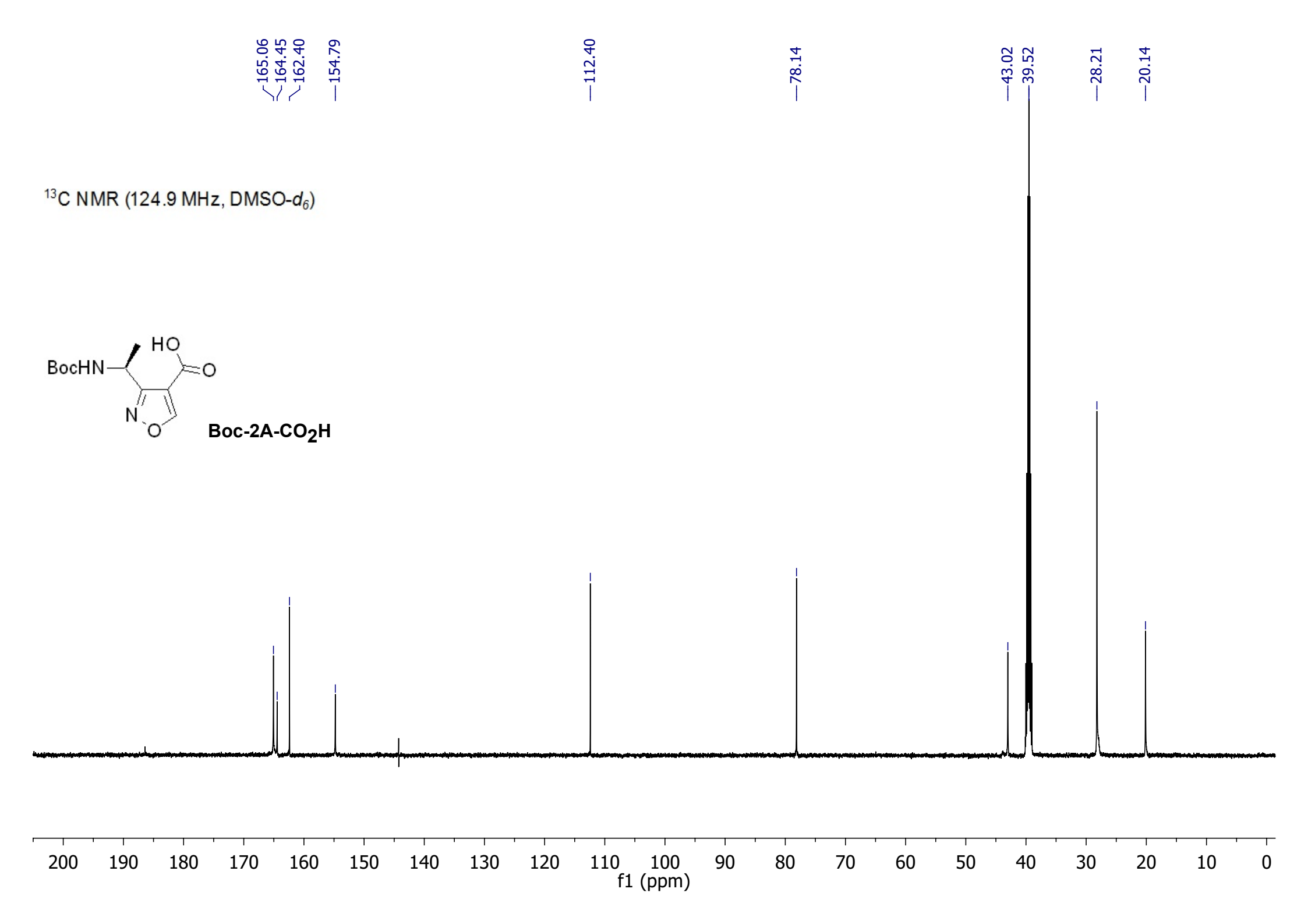
7B-H

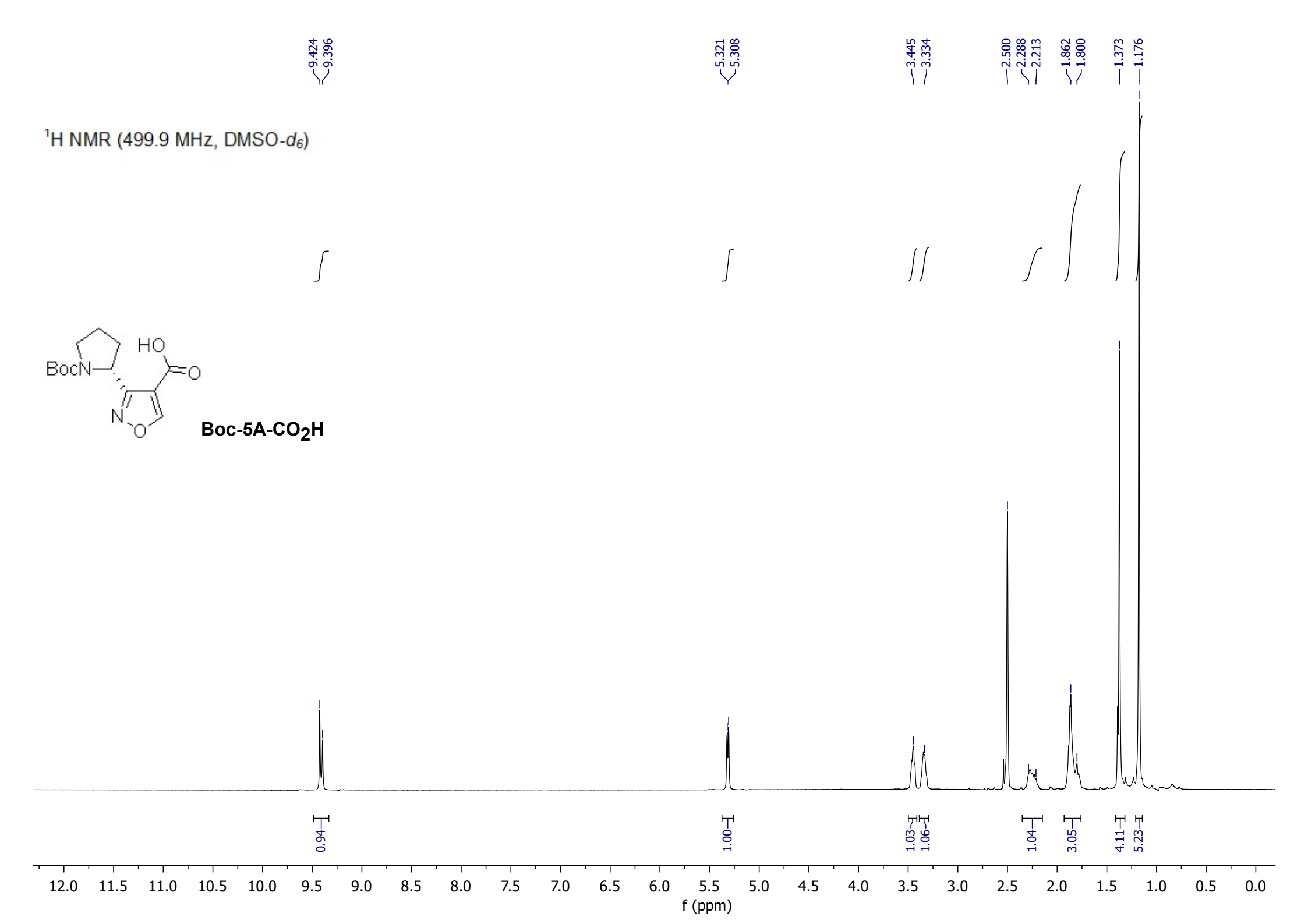

166.16
159.42
103.09
45.03
39.52
33.50
30.98
13C NMR (124.9 MHz, DMSO-d6)
HN
N
O
7B-H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

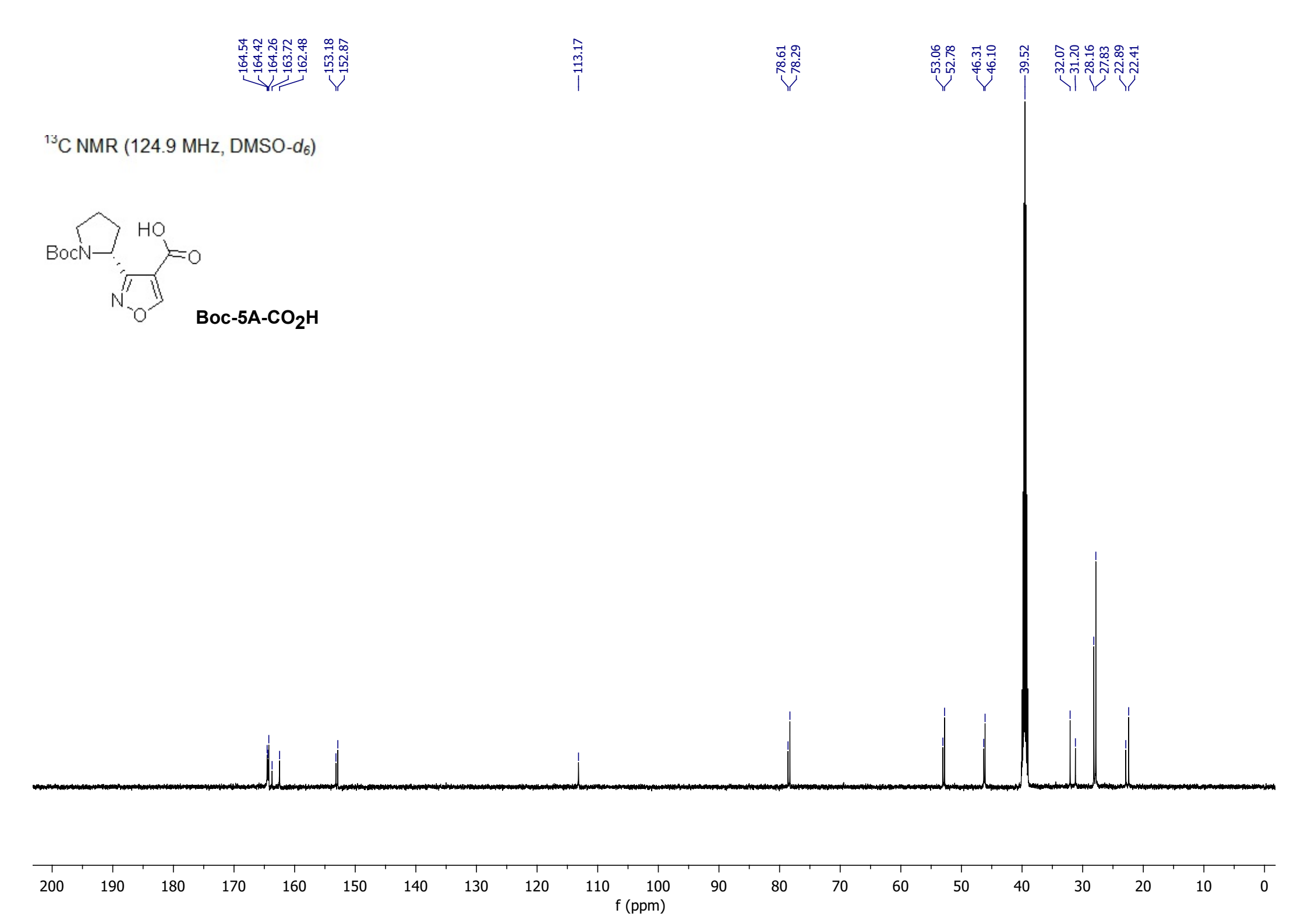

13.251
9.448
7.166
6.801
4.413
4.404
2.500
1.380
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
BocHN
O
N
O
Boc-1A-CO$_2$H
0.47
0.86
0.82
1.93
9.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

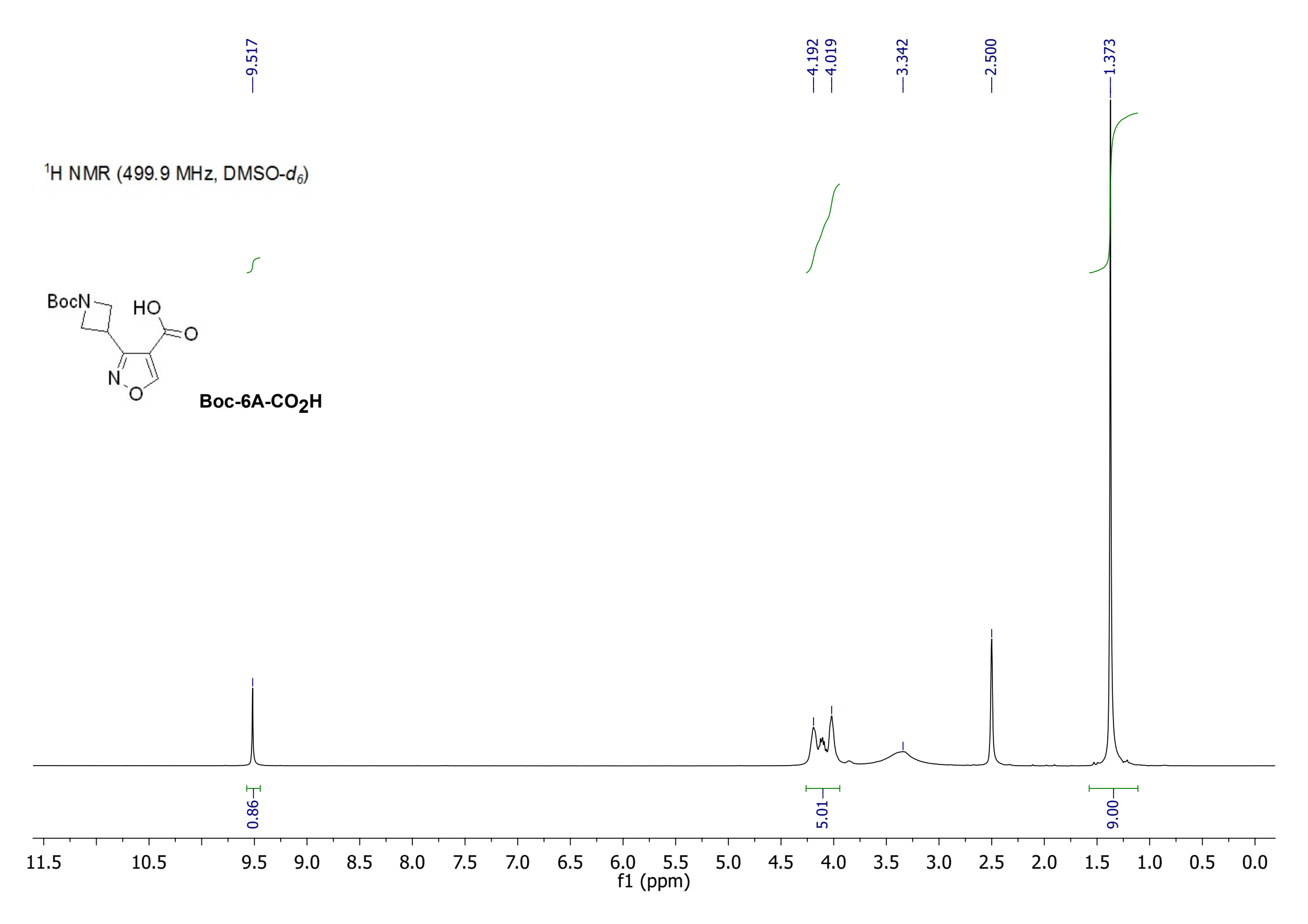

164.64
162.41
160.30
155.51
113.16
78.24
39.52
36.05
28.23
^{13}C NMR (124.9 MHz, DMSO-d_6)
HO
BocHN
O
N
O
Boc-1A-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

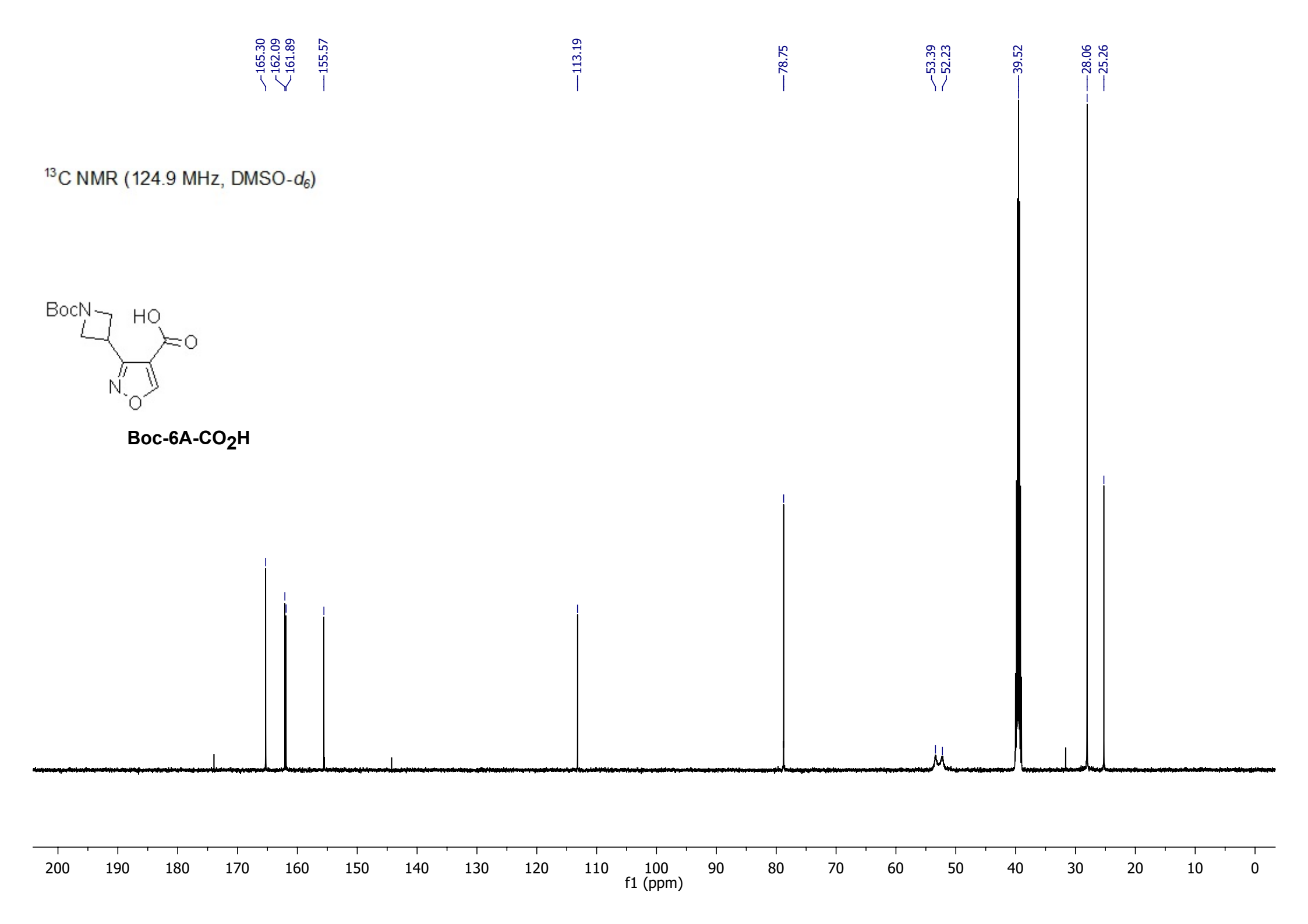

13.281
9.448
7.291
7.272
5.122
5.104
5.086
2.500
1.360
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
BocHN
O
N
O
Boc-2A-CO$_2$H
1.05
1.00
1.05
1.12
12.01
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

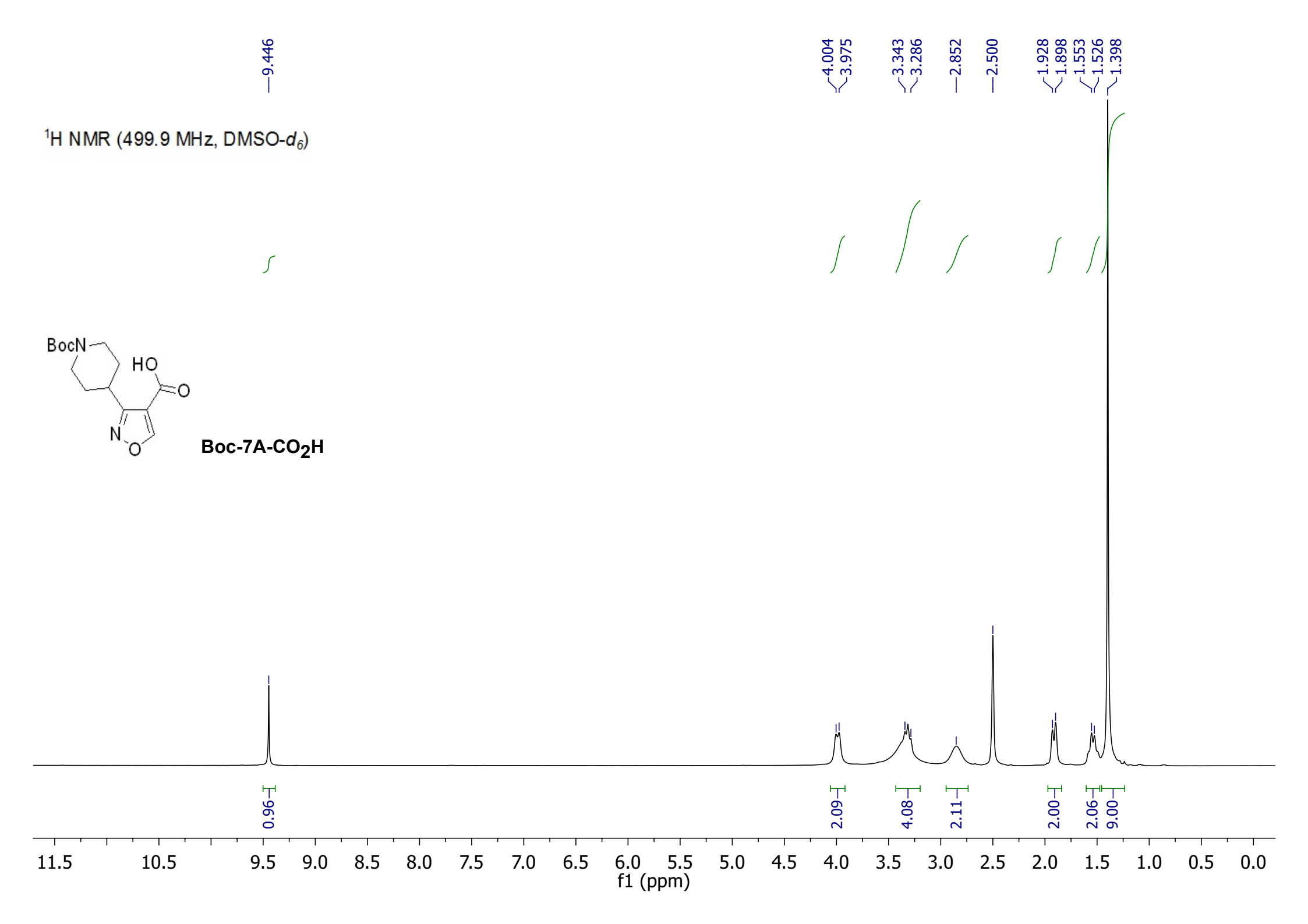

165.06
164.45
162.40
154.79
112.40
78.14
43.02
39.52
28.21
20.14
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
HO
O
N
O
Boc-2A-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

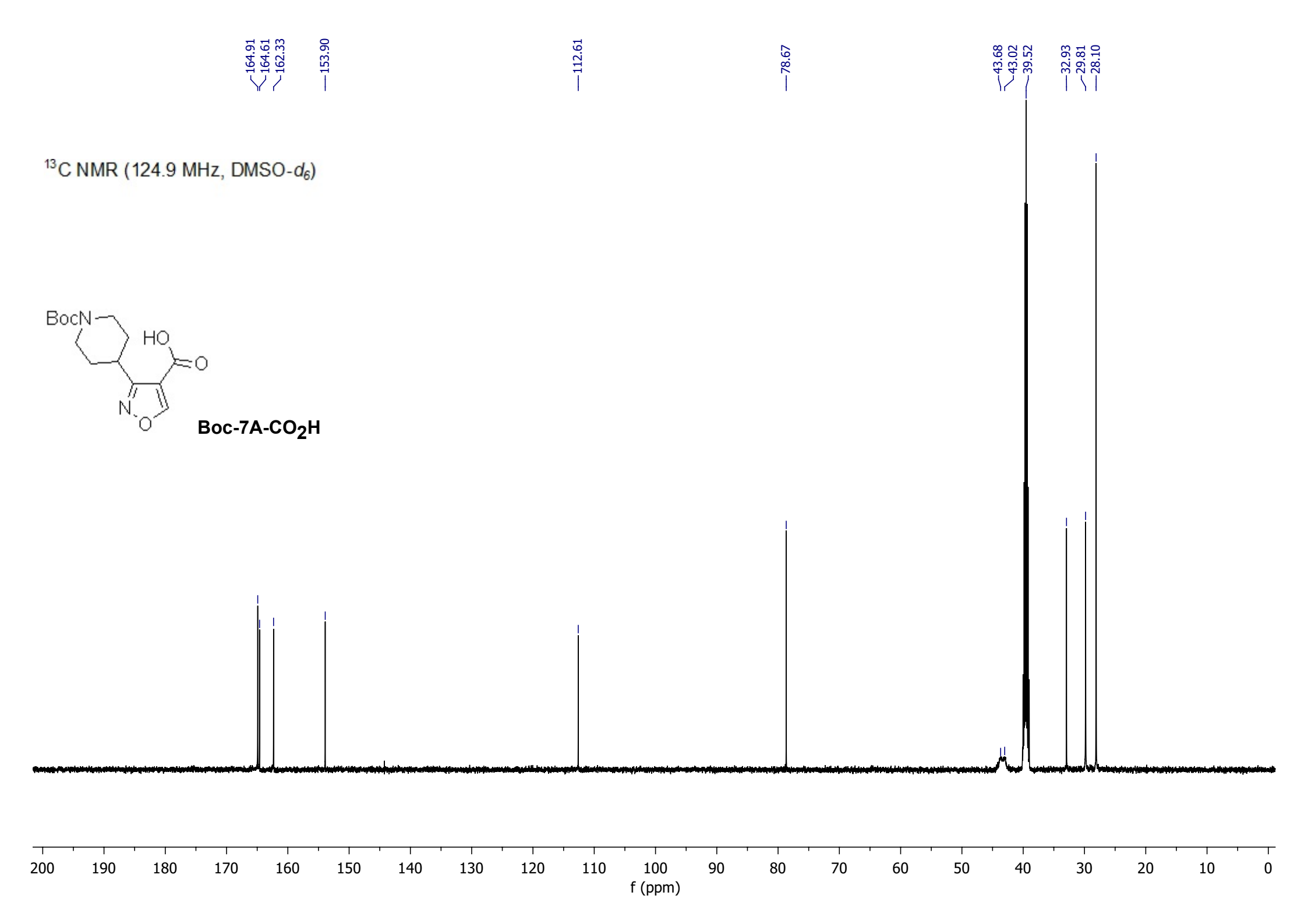

9.424
9.396
5.321
5.308
3.445
3.334
2.500
2.288
2.213
1.862
1.800
1.373
1.176
^{1}H NMR (499.9 MHz, DMSO-d_6)
HO
BocN
O
N
O
Boc-5A-CO$_2$H
0.94
1.00
1.03
1.06
1.04
3.05
4.11
5.23
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f (ppm)

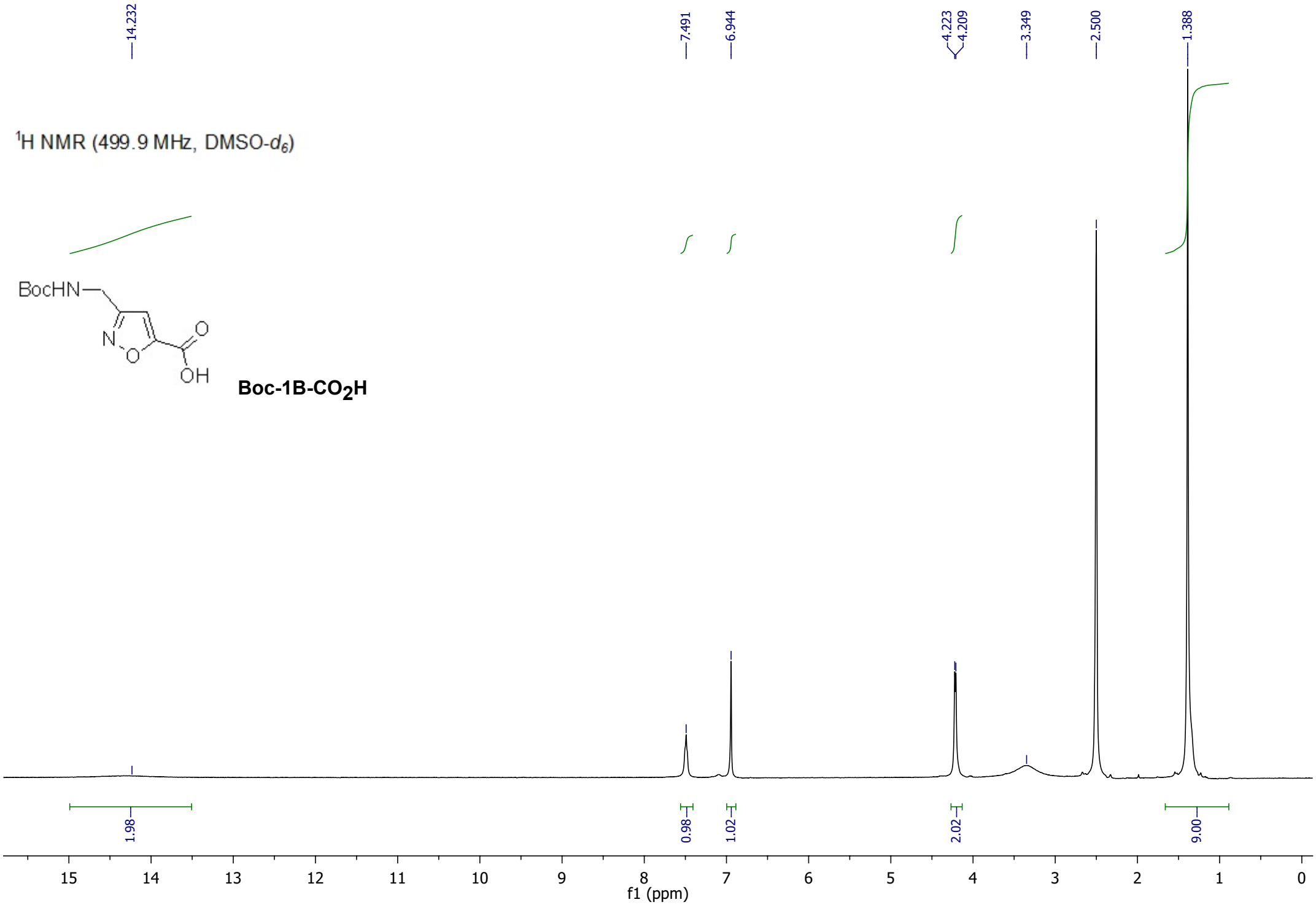

164.54
164.42
164.26
163.72
162.48
153.18
152.87
113.17
78.61
78.29
53.06
52.78
46.31
46.10
39.52
32.07
31.20
28.16
27.83
22.89
22.41
13C NMR (124.9 MHz, DMSO-d6)
HO
BocN
O
N
O
Boc-5A-CO2H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

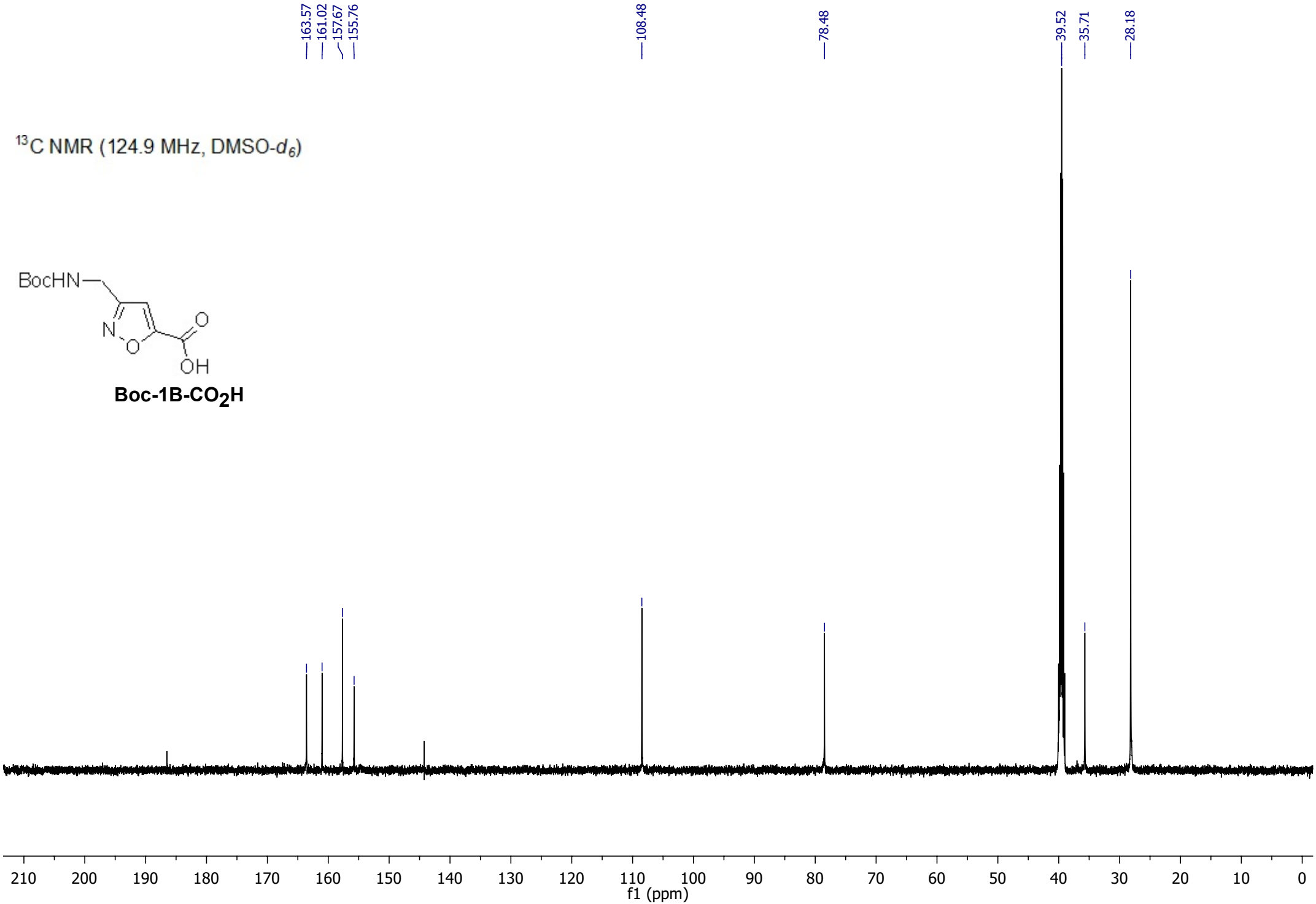

9.517
4.192
4.019
3.342
2.500
1.373
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
HO
O
N
O
Boc-6A-CO$_2$H
0.86
5.01
9.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

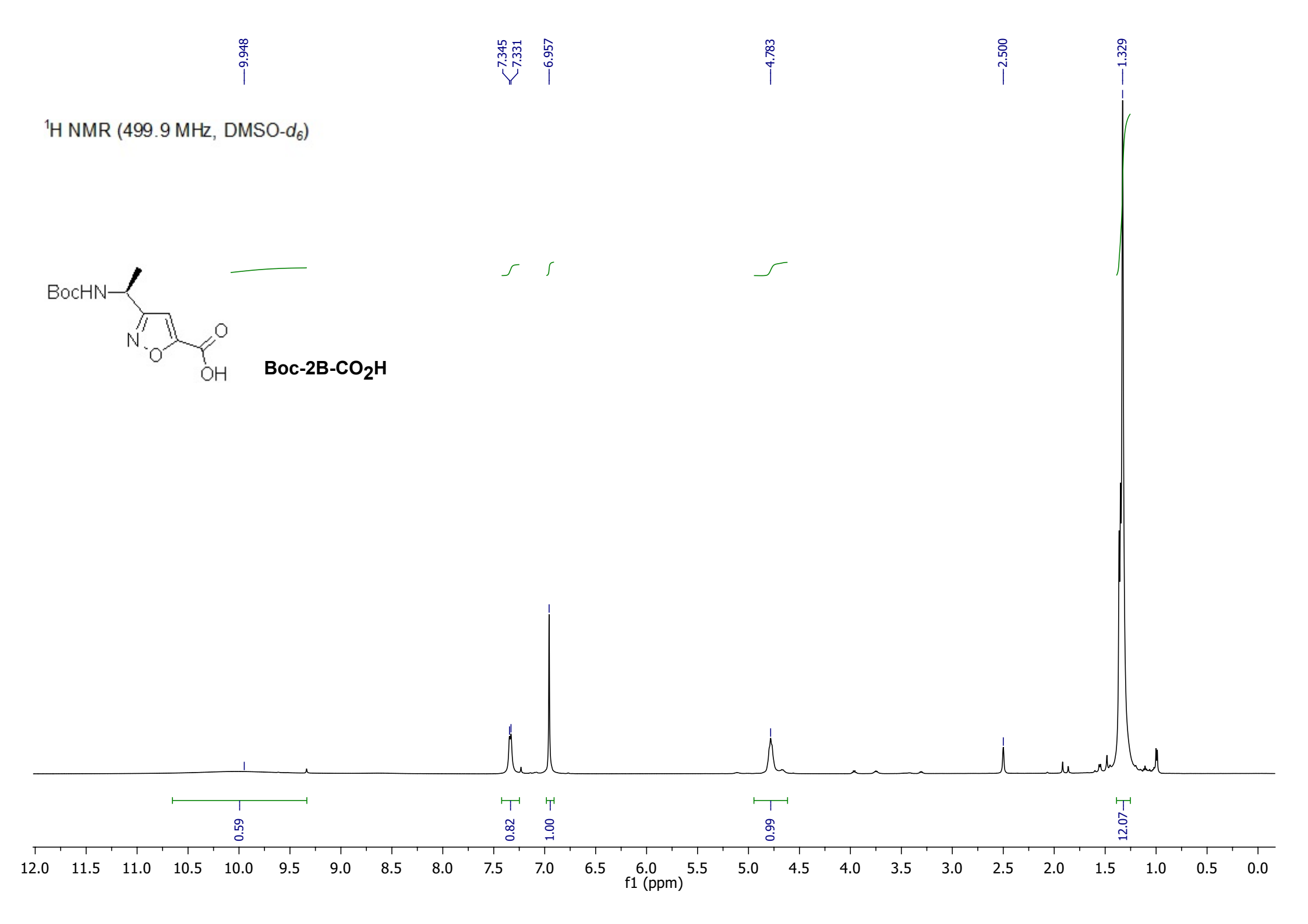

165.30
162.09
161.89
155.57
113.19
78.75
53.39
52.23
39.52
28.06
25.26
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
HO
O
N
O
Boc-6A-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

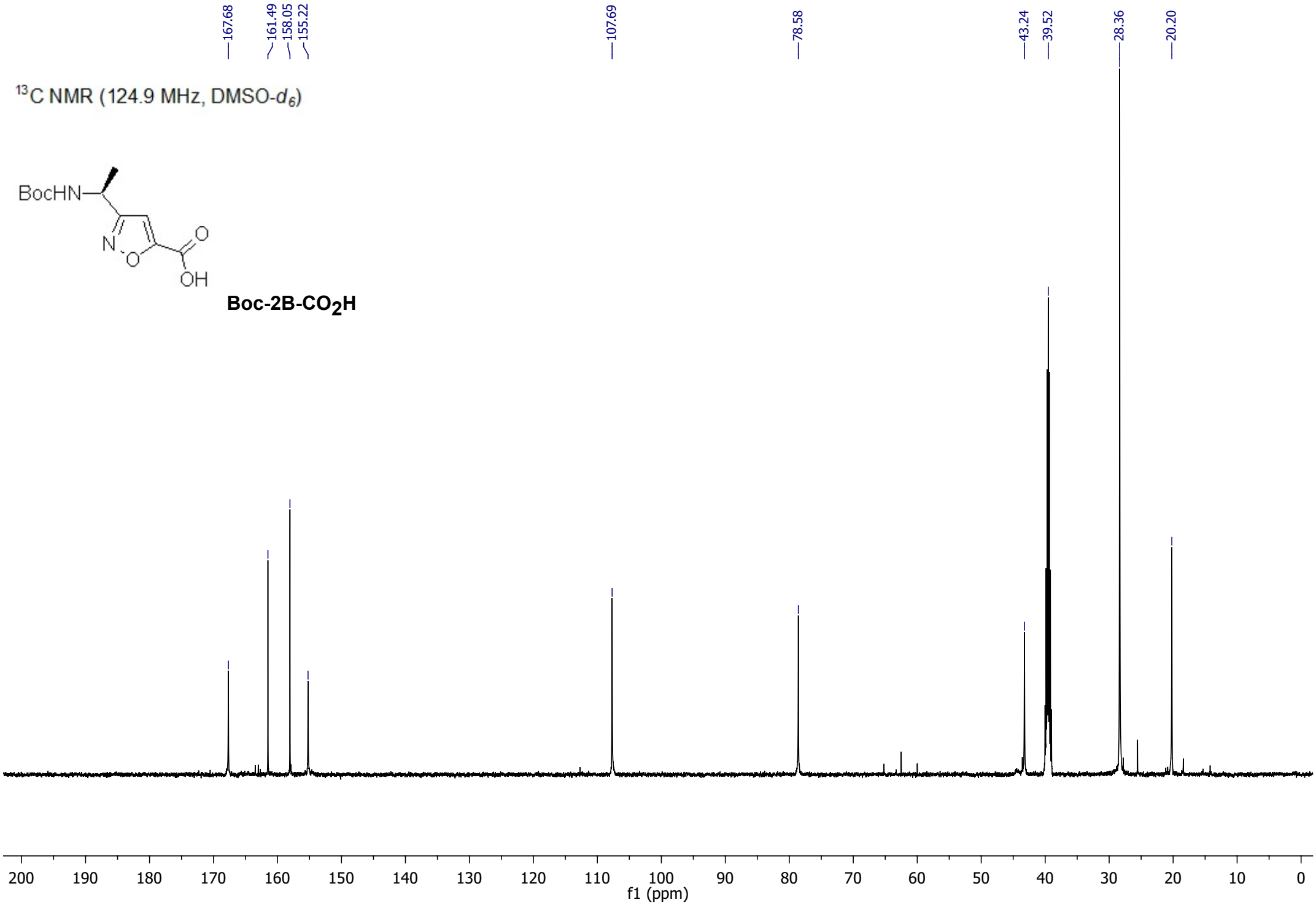

9.446
4.004
3.975
3.343
3.286
2.852
2.500
1.928
1.898
1.553
1.526
1.398
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
HO
O
N
O
Boc-7A-CO$_2$H
0.96
2.09
4.08
2.11
2.00
2.06
9.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.91
164.61
162.33
153.90
112.61
78.67
43.68
43.02
39.52
32.93
29.81
28.10
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
HO
O
N
O
Boc-7A-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

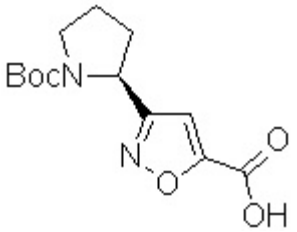

14.232
7.491
6.944
4.223
4.209
3.349
2.500
1.388
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
O
OH
Boc-1B-CO$_2$H
1.98
0.98
1.02
2.02
9.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


163.57
161.02
157.67
155.76
108.48
78.48
39.52
35.71
28.18
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
N
O
O
OH
Boc-1B-CO_2H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

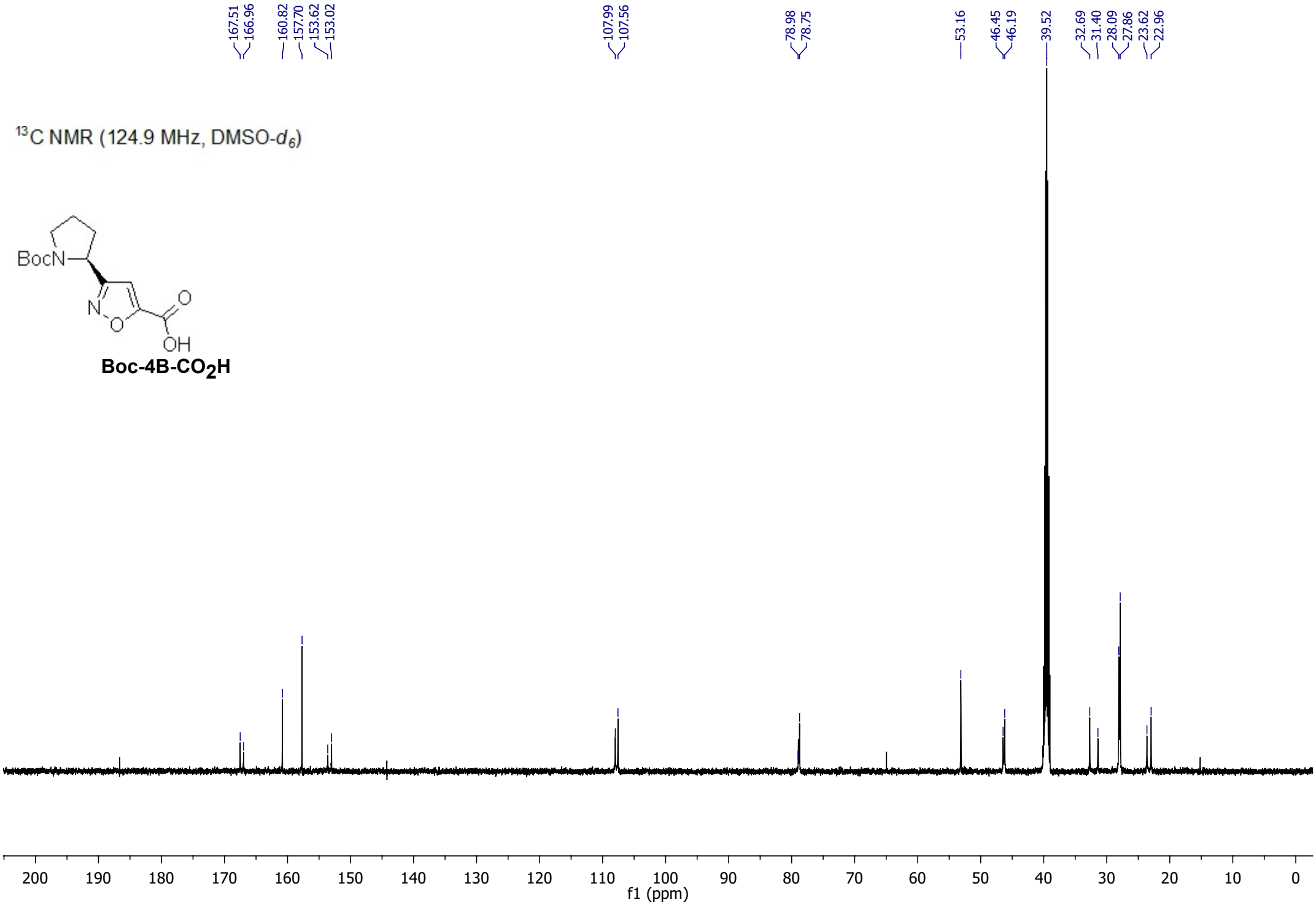

9.948
7.345
7.331
6.957
4.783
2.500
1.329
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocHN
N
O
O
OH
Boc-2B-CO$_2$H
0.59
0.82
1.00
0.99
12.07
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

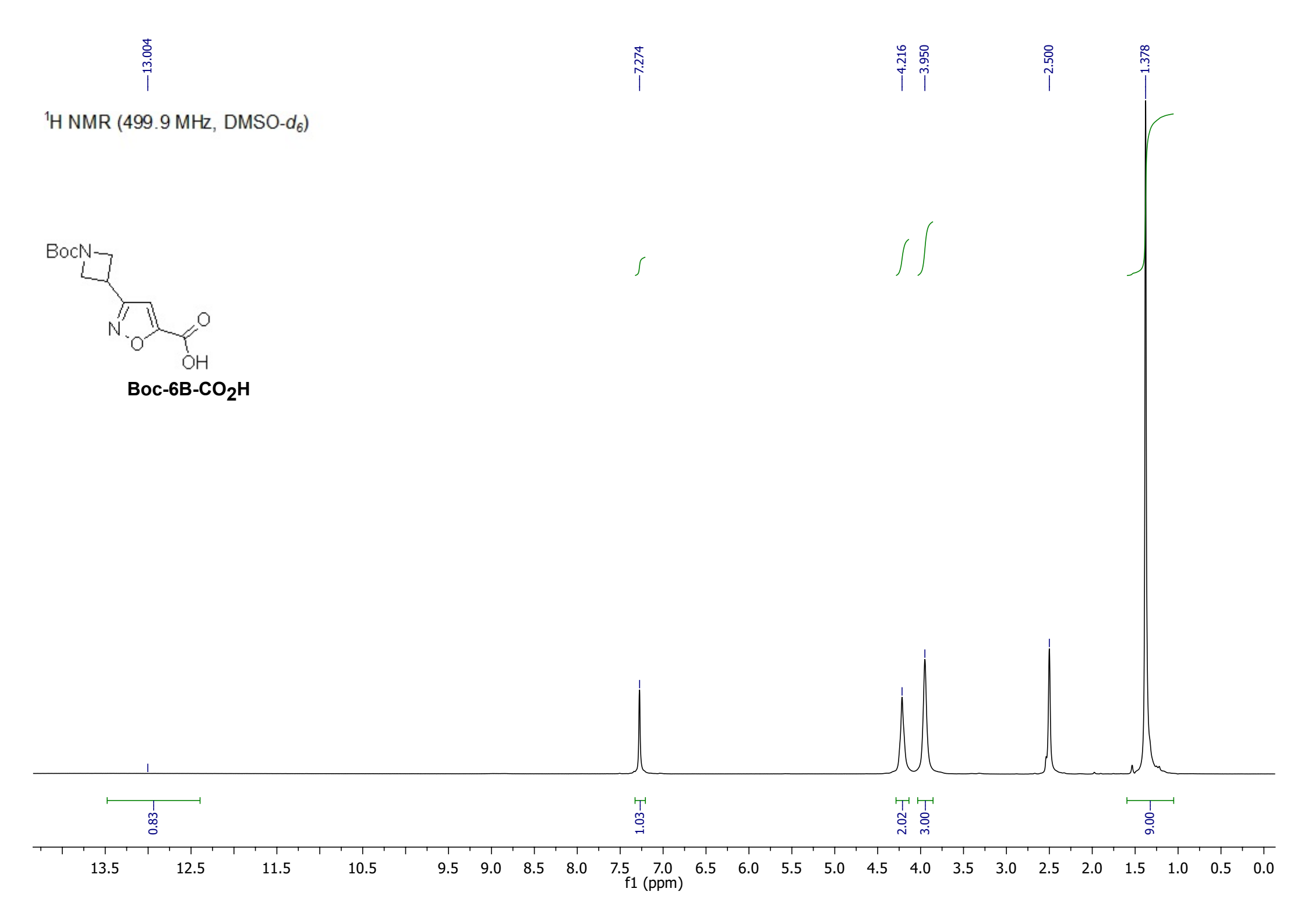

167.68
161.49
158.05
155.22
107.69
78.58
43.24
39.52
28.36
20.20
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocHN
N
O
O
OH
Boc-2B-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (499.9 MHz, DMSO-d_6)

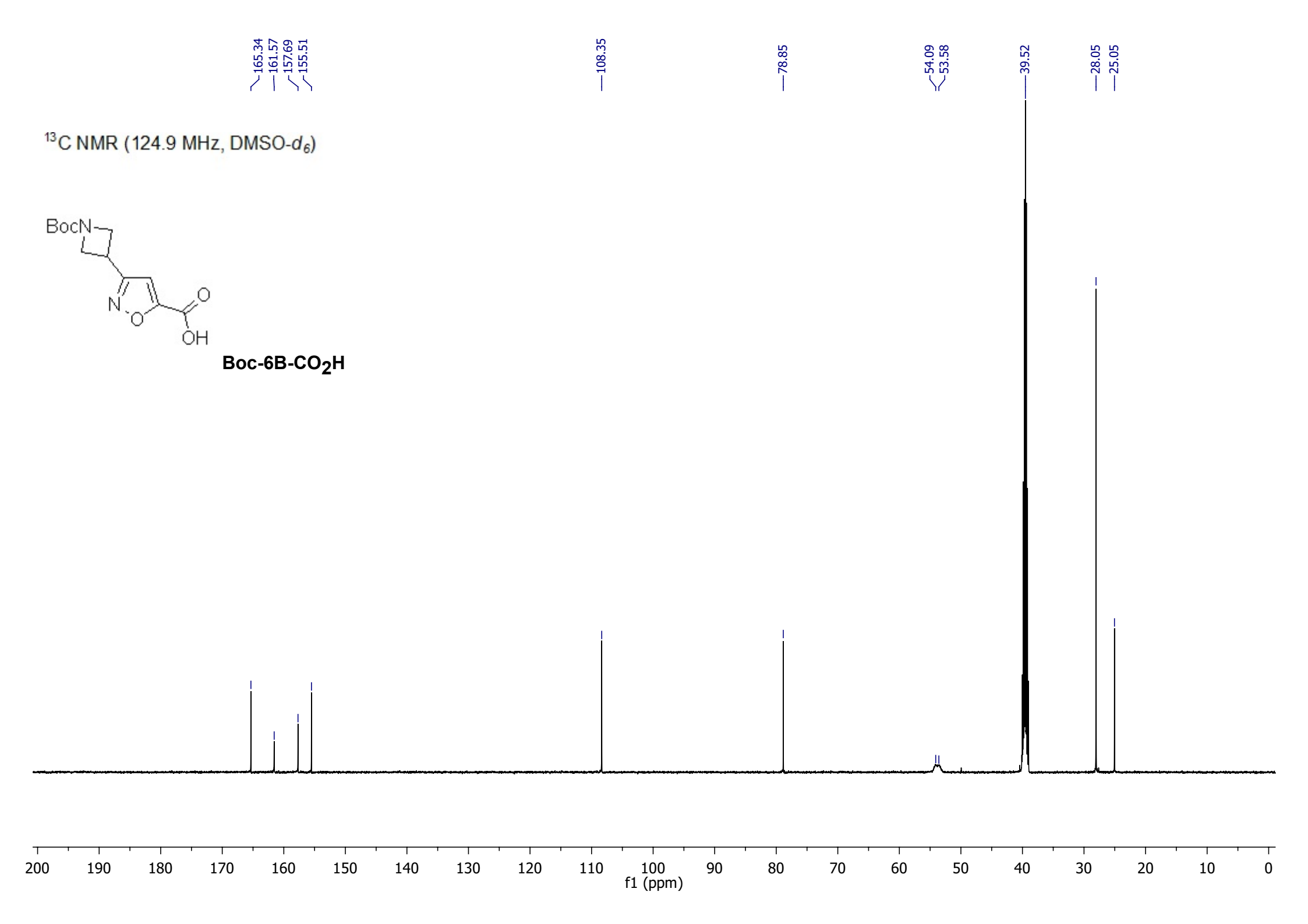


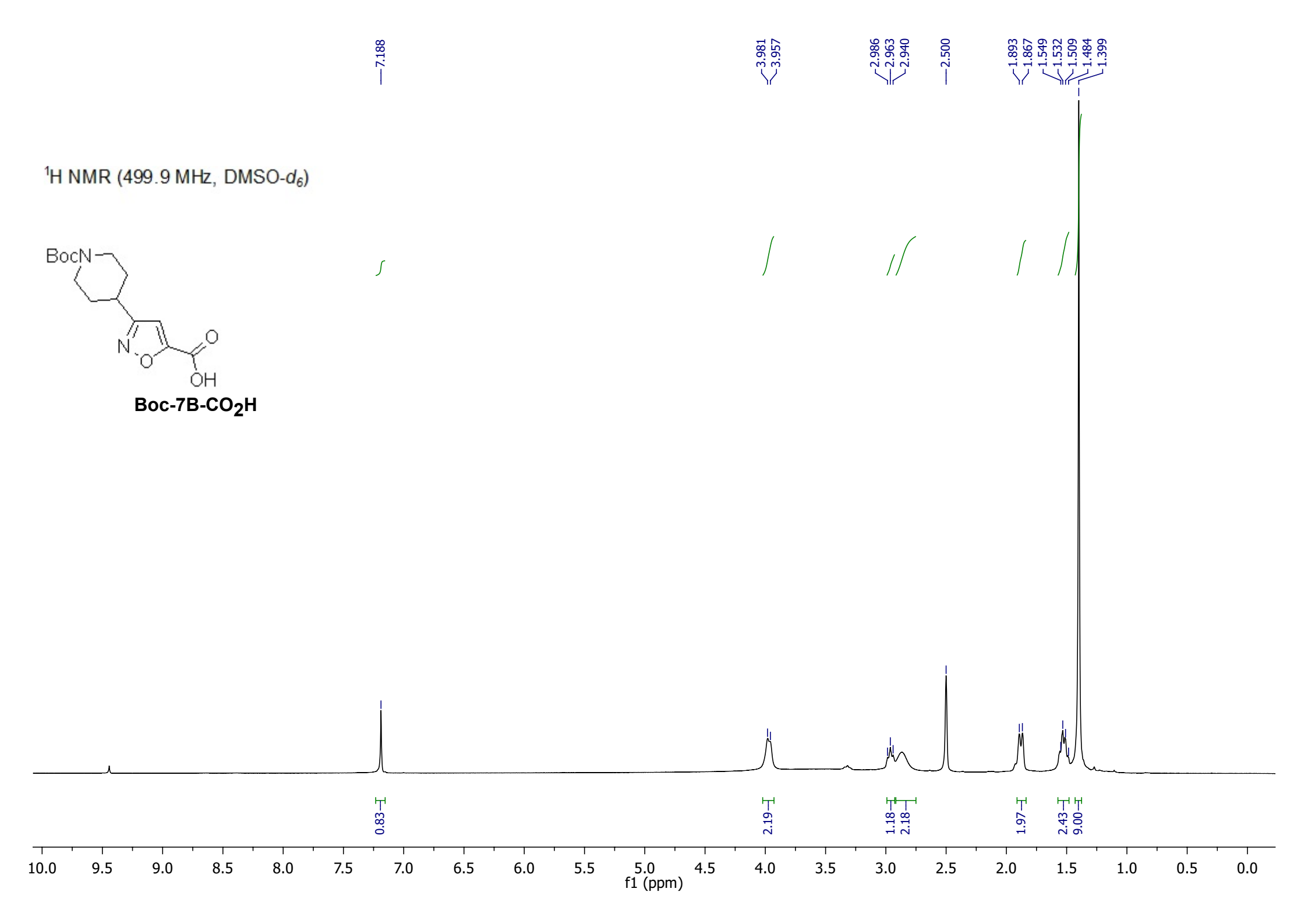
Boc-4B-CO_2H

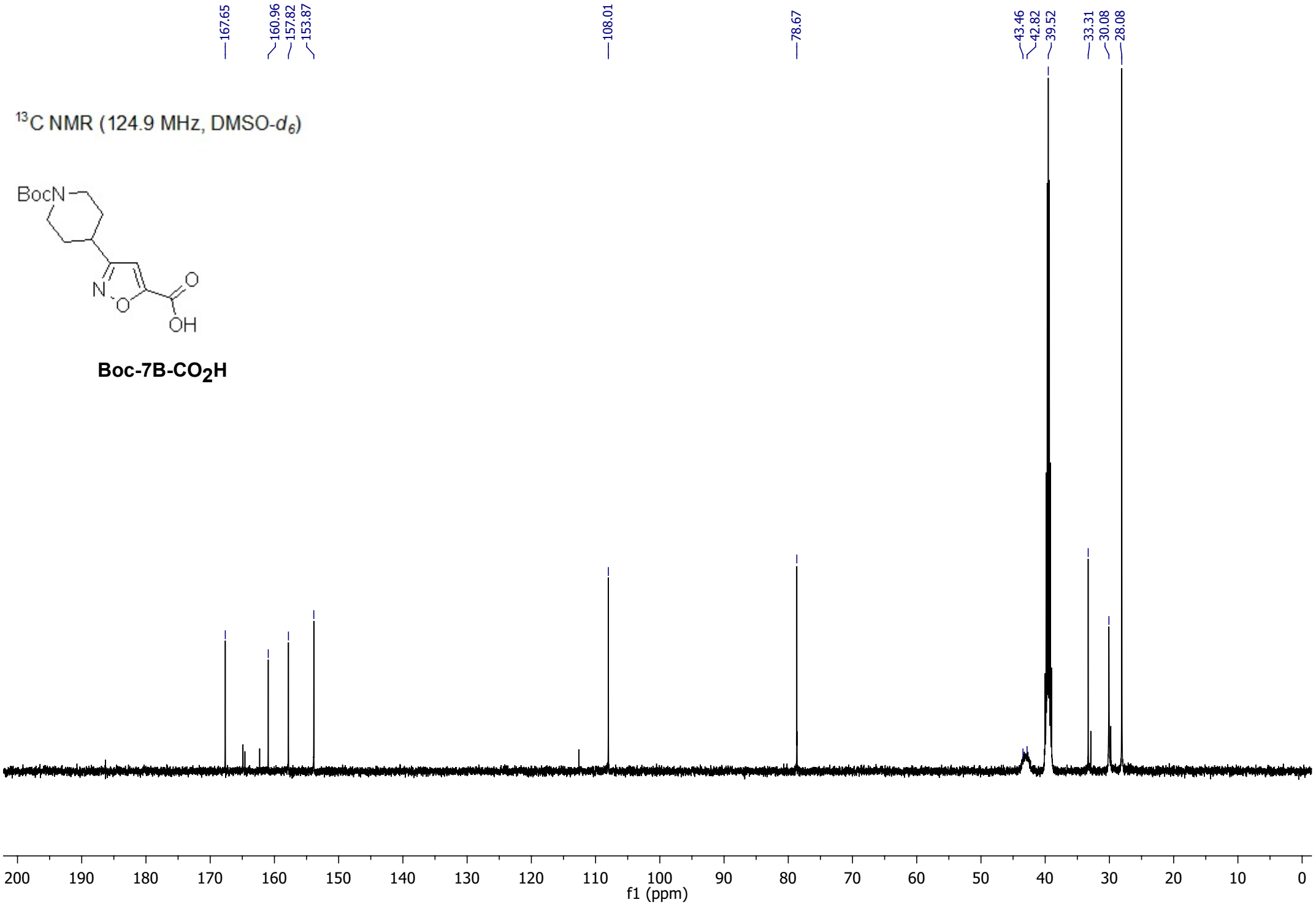

167.51
166.96
160.82
157.70
153.62
153.02
107.99
107.56
78.98
78.75
53.16
46.45
46.19
39.52
32.69
31.40
28.09
27.86
23.62
22.96
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
O
O
OH
Boc-4B-CO2H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

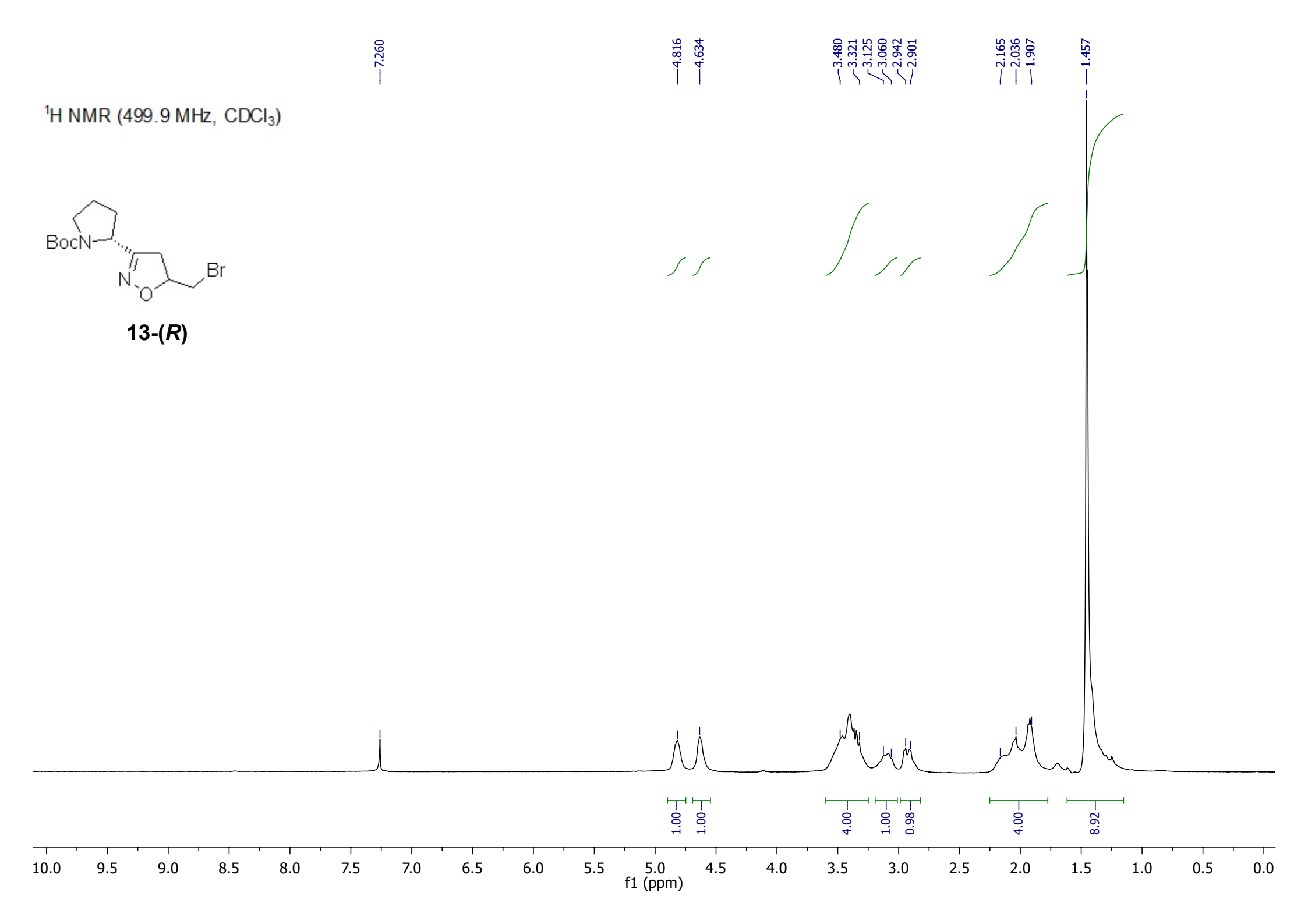

13.004
7.274
4.216
3.950
2.500
1.378
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
O
OH
0.83
1.03
2.02
3.00
9.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

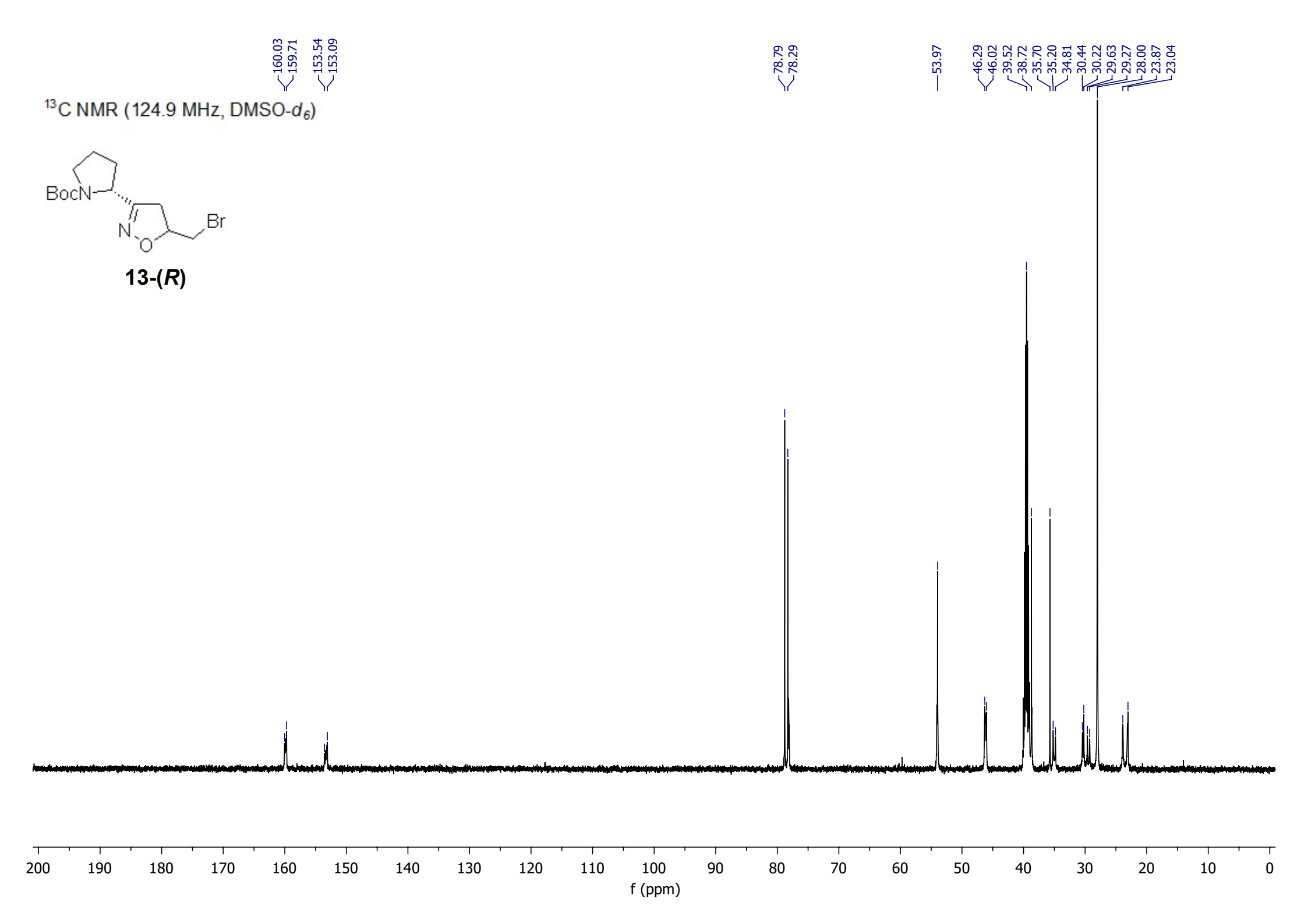
Boc-6B-CO_2H


165.34
161.57
157.69
155.51
108.35
78.85
54.09
53.58
39.52
28.05
25.05
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
O
O
OH
Boc-6B-CO2H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

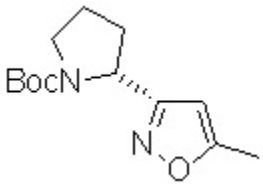

7.188
3.981
3.957
2.986
2.963
2.940
2.500
1.893
1.867
1.549
1.532
1.509
1.484
1.399
^{1}H NMR (499.9 MHz, DMSO-d_6)
BocN
N
O
O
OH
Boc-7B-CO$_2$H
0.83
2.19
1.18
2.18
1.97
2.43
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.65
160.96
157.82
153.87
108.01
78.67
43.46
42.82
39.52
33.31
30.08
28.08
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
O
OH
Boc-7B-CO$_2$H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

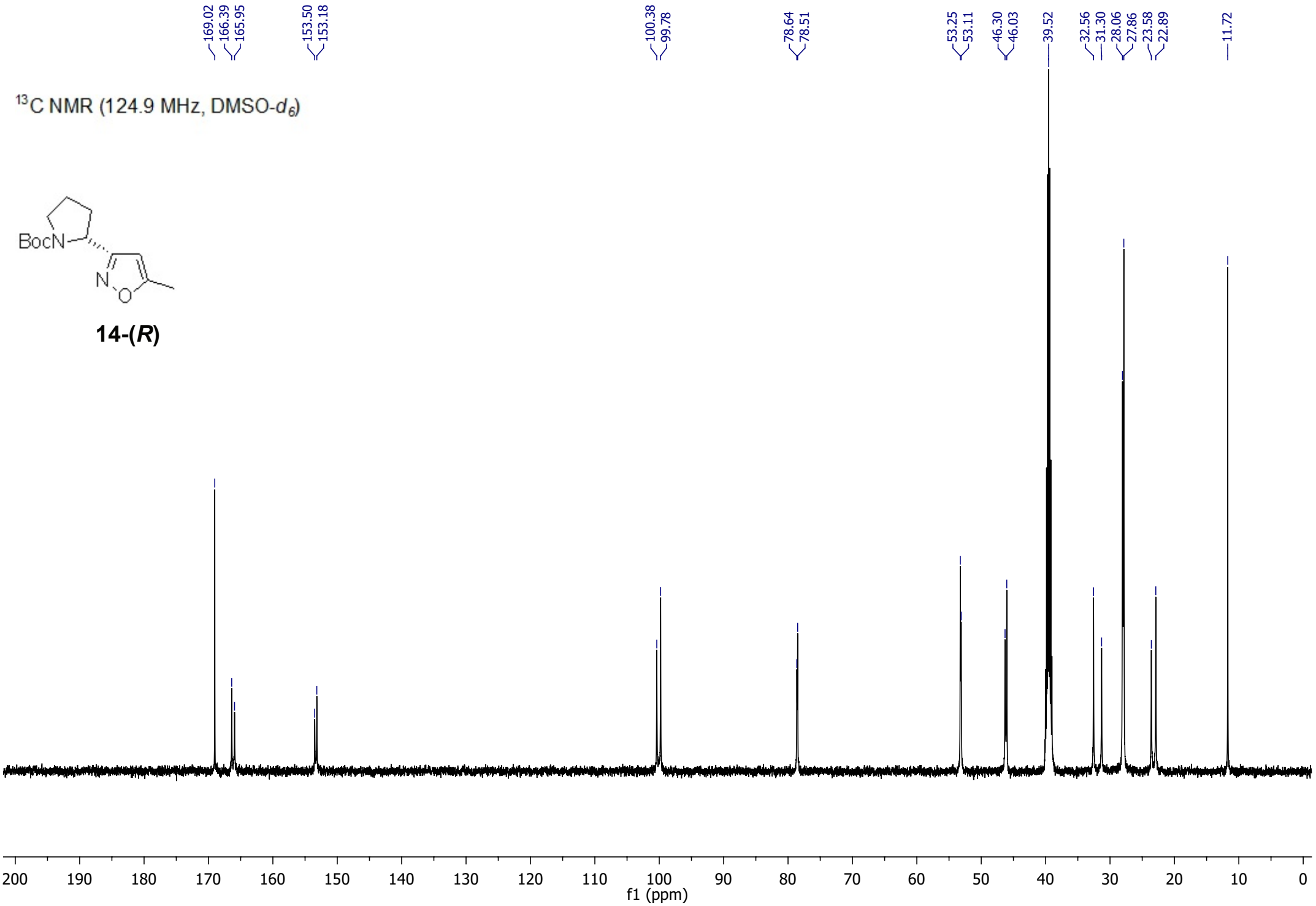

7.260
4.816
4.634
3.480
3.321
3.125
3.060
2.942
2.901
2.165
2.036
1.907
1.457
^{1}H NMR (499.9 MHz, $CDCl_3$)
BocN
N
O
Br
13-(*R*)
1.00
1.00
4.00
1.00
0.98
4.00
8.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

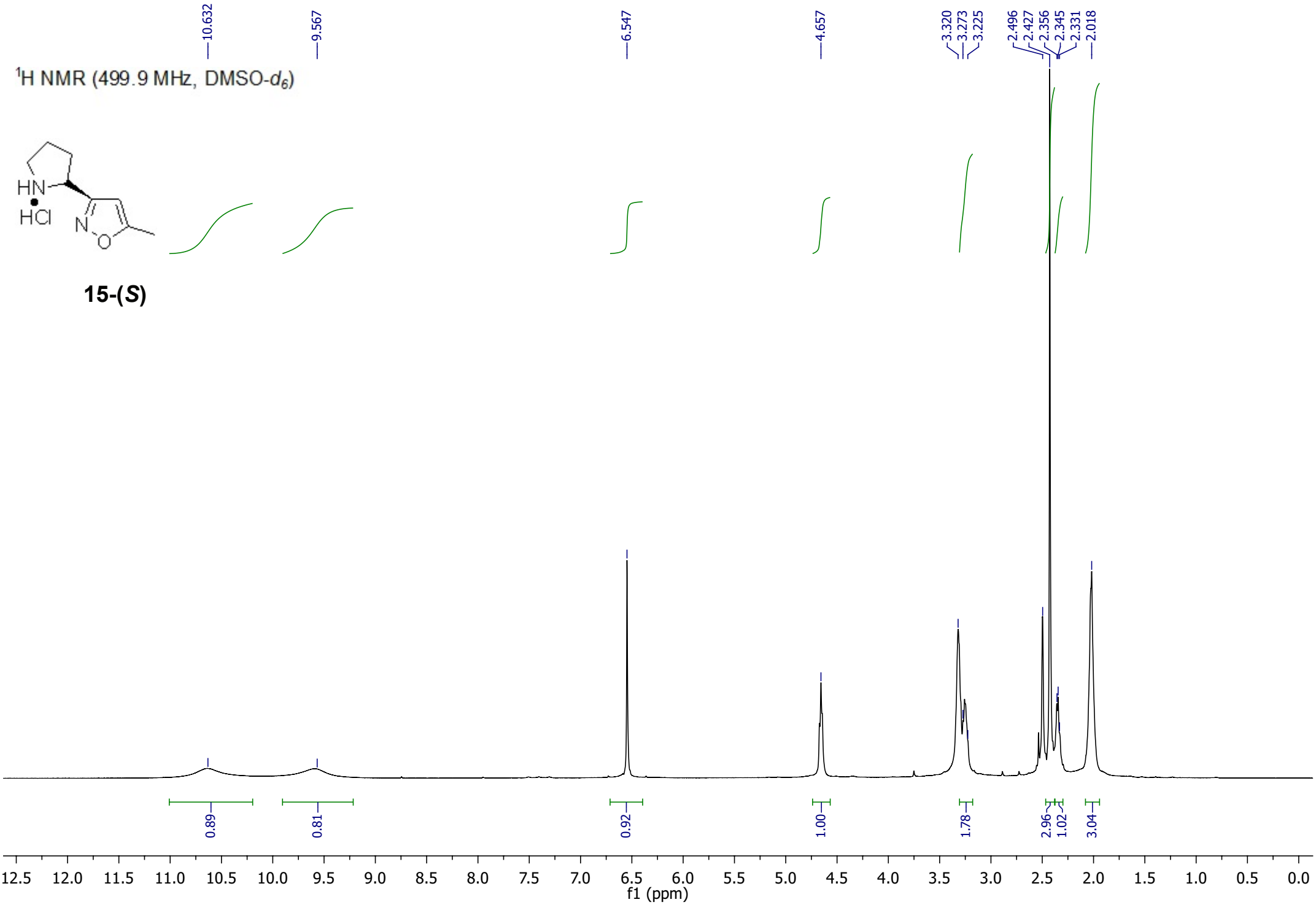

160.03
159.71
153.54
153.09
78.79
78.29
53.97
46.29
46.02
39.52
38.72
35.70
35.20
34.81
30.44
30.22
29.63
29.27
28.00
23.87
23.04
13C NMR (124.9 MHz, DMSO-d6)
BocN
N
O
Br
13-(R)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f (ppm)

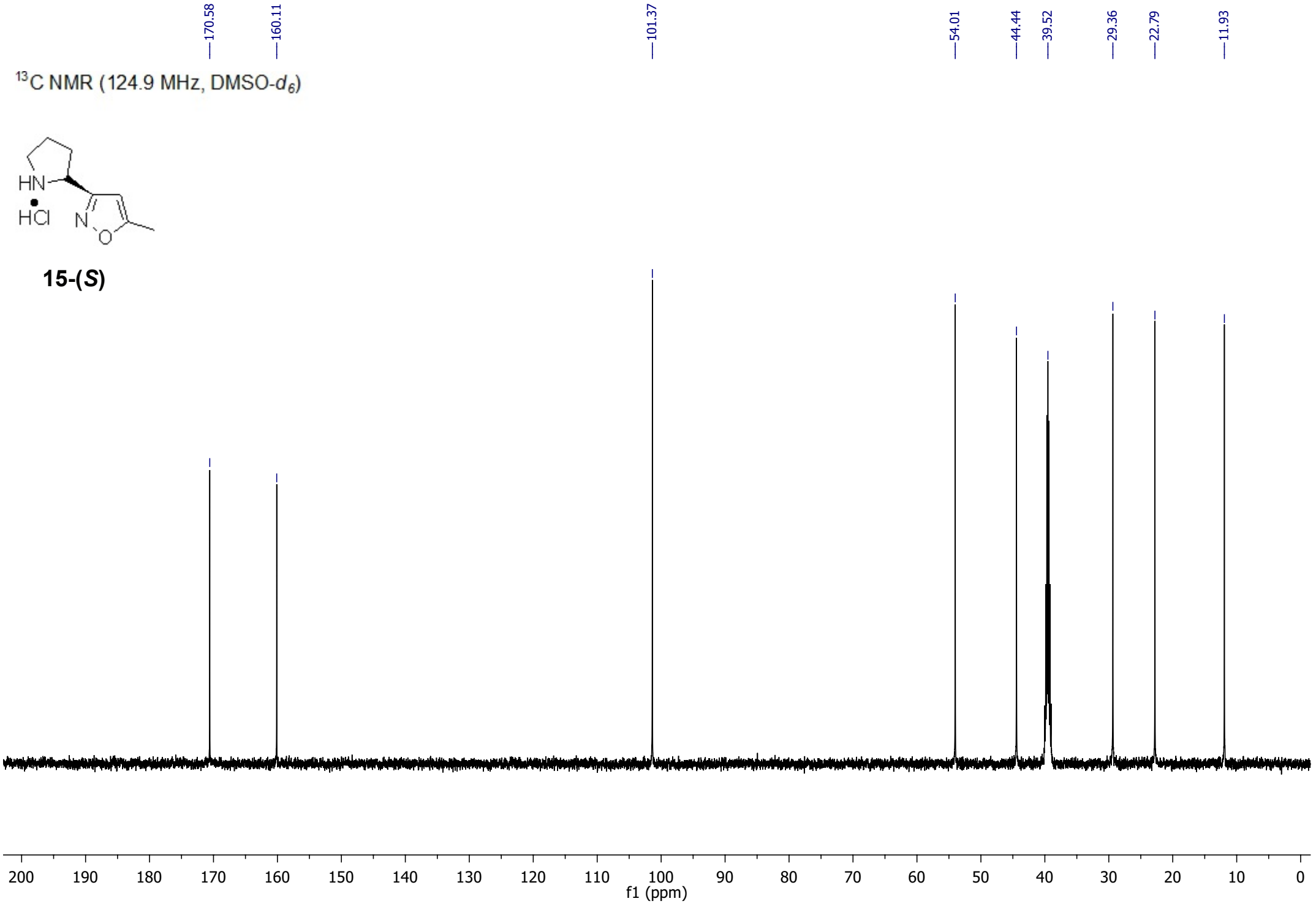
^{1}H NMR (499.9 MHz, DMSO-d_6)



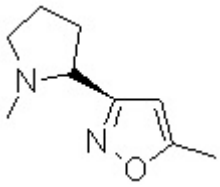
14-(*R*)


169.02
166.39
165.95
153.50
153.18
100.38
99.78
78.64
78.51
53.25
53.11
46.30
46.03
39.52
32.56
31.30
28.06
27.86
23.58
22.89
11.72
^{13}C NMR (124.9 MHz, DMSO-d_6)
BocN
N
O
14-(*R*)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

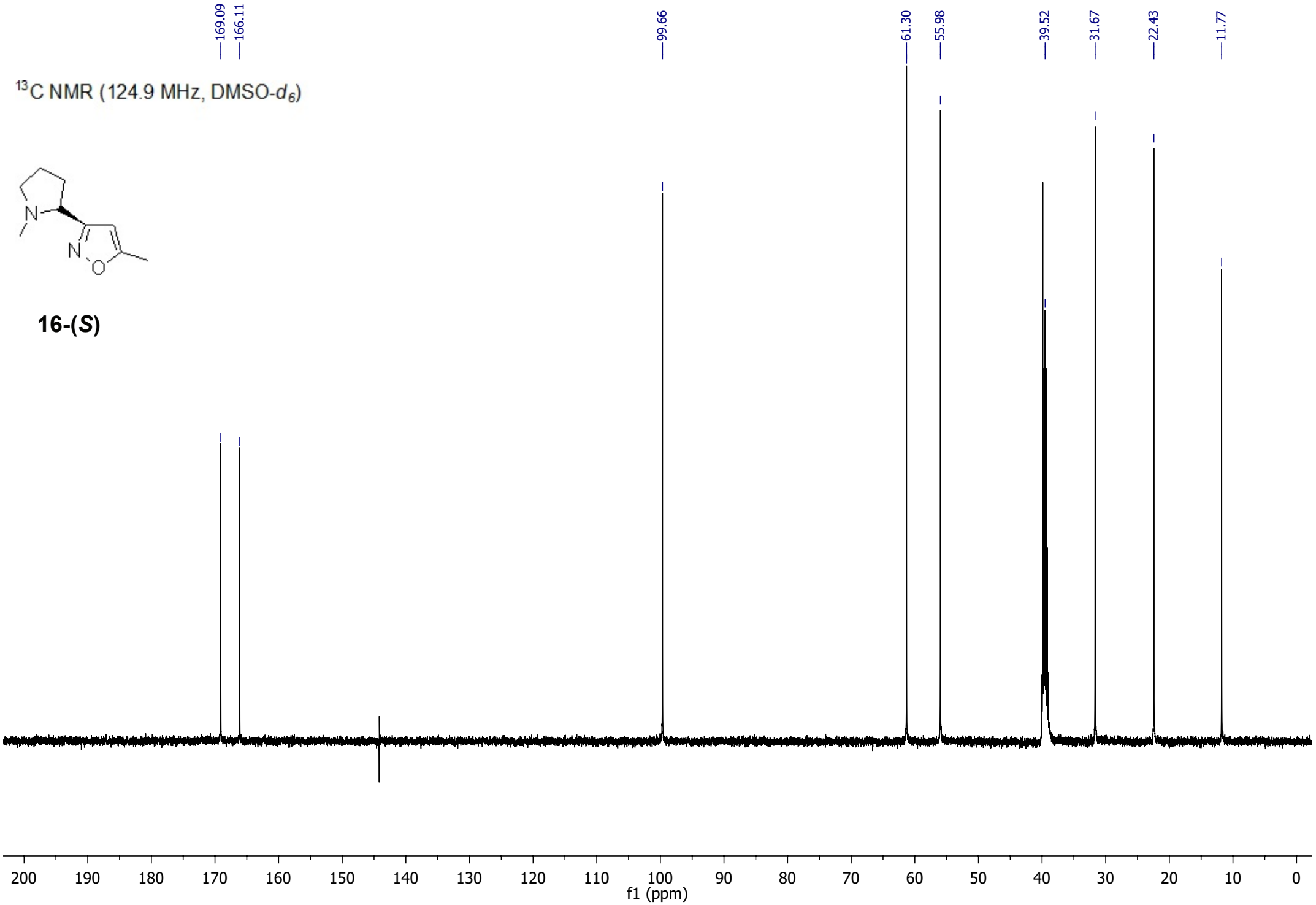

10.632
9.567
6.547
4.657
3.320
3.273
3.225
2.496
2.427
2.356
2.345
2.331
2.018
^{1}H NMR (499.9 MHz, DMSO-d_6)
HN
HCl
N
O
15-(*S*)
0.89
0.81
0.92
1.00
1.78
2.96
1.02
3.04
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.58
160.11
101.37
54.01
44.44
39.52
29.36
22.79
11.93
13C NMR (124.9 MHz, DMSO-d6)
HN
HCl
N
O
15-(S)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

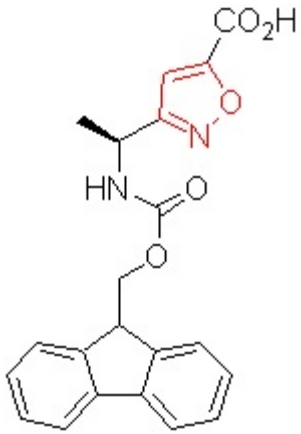
^{1}H NMR (499.9 MHz, DMSO-d_6)



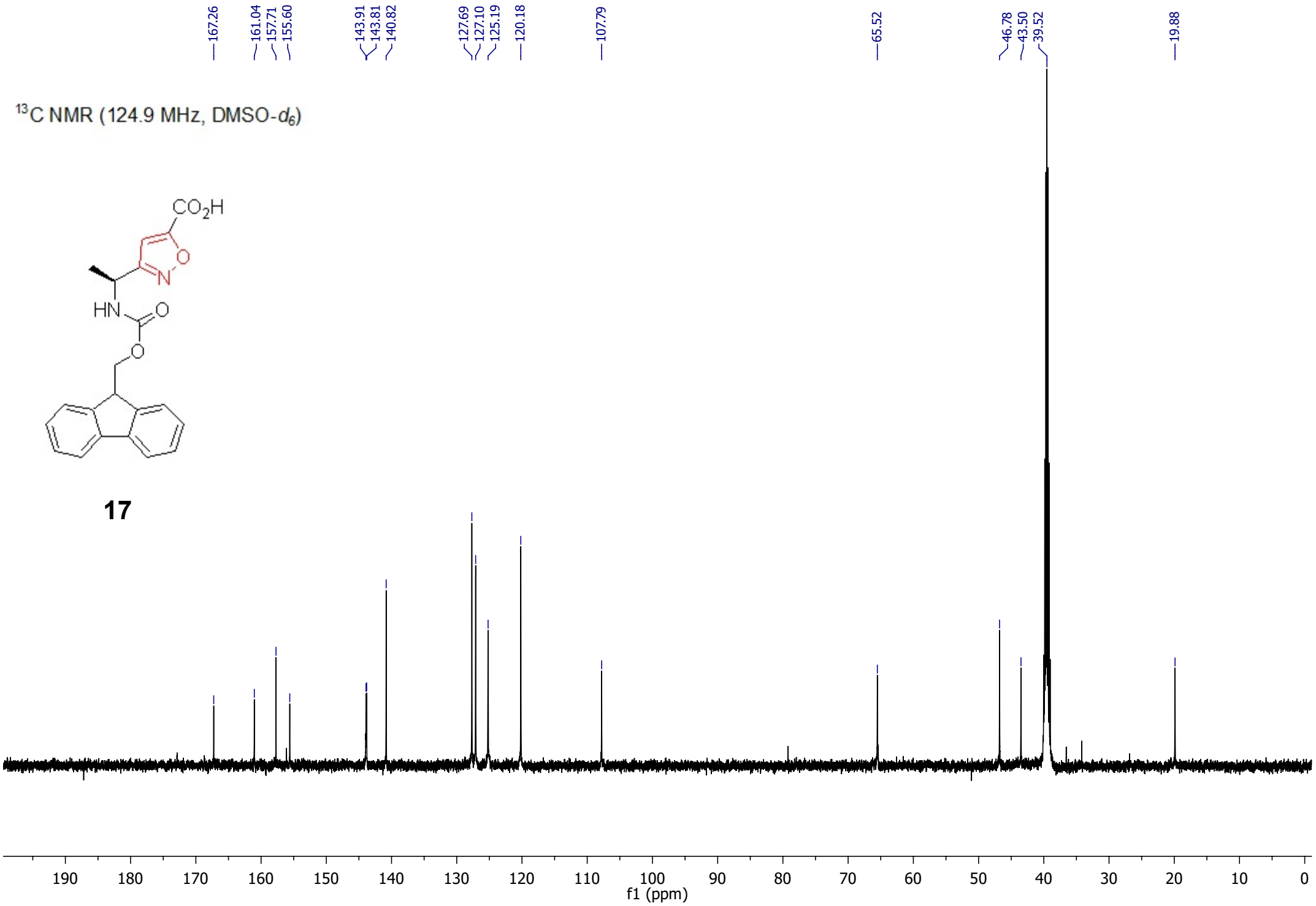
16-(*S*)


169.09
166.11
99.66
61.30
55.98
39.52
31.67
22.43
11.77
^{13}C NMR (124.9 MHz, DMSO-d_6)
N
N
O
16-(*S*)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

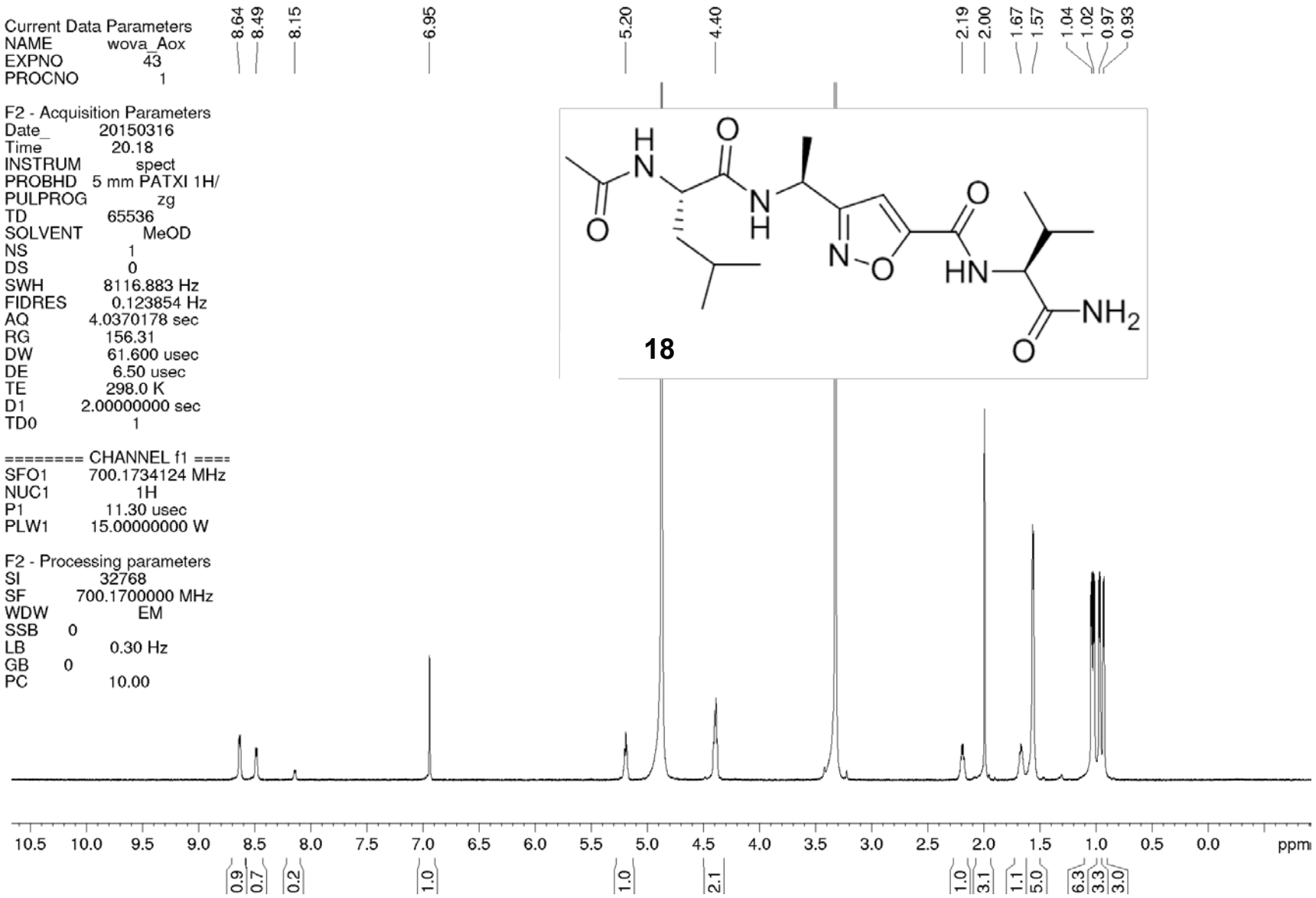
^{1}H NMR (499.9 MHz, DMSO-d_6)



17


167.26
161.04
157.71
155.60
143.91
143.81
140.82
127.69
127.10
125.19
120.18
107.79
65.52
46.78
43.50
39.52
19.88
13C NMR (124.9 MHz, DMSO-d6)
CO2H
O
N
HN
O
O
17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR of **18** (fresh):

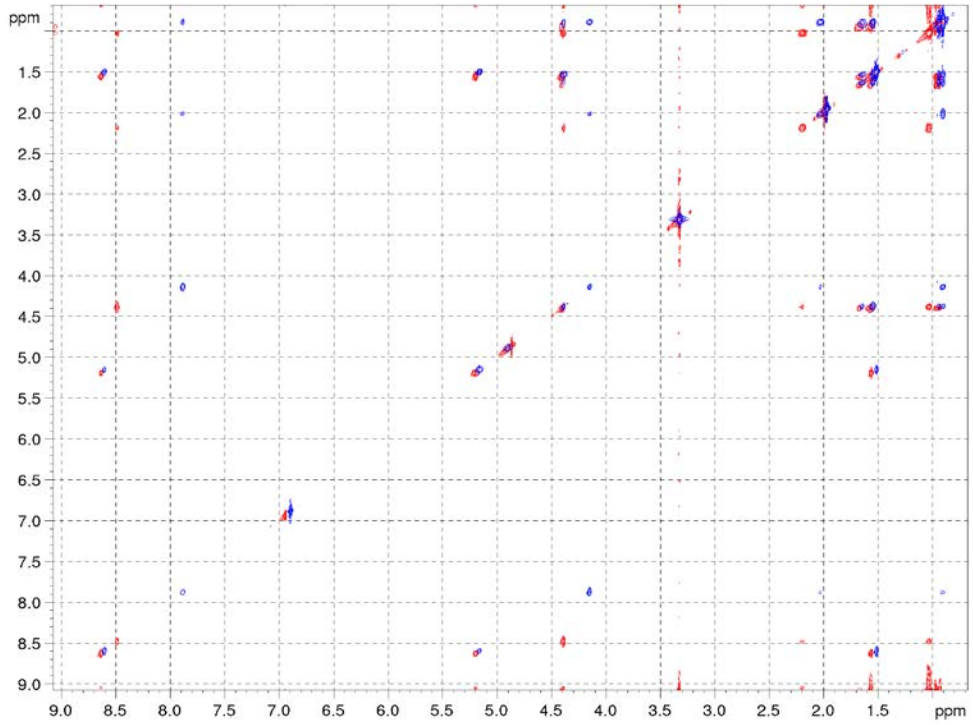


f (ppm)

^{1}H NMR of **19** (fresh):

f (ppm)

^{1}H HOHAHA (mixing 60 ms) of **18** (red) and **19** (blue):



^{1}H{^{13}C} HSQC of **18** (red) and **19** (blue):