Supplementary Information (SI) for Chemical Science.

Driving *tert*-Butyl Axial: The Surprising Cyclopropyl Effect

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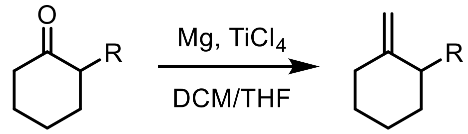
1. General information

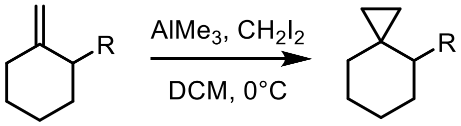
The following supporting information contains representative experimental procedures for the isolation and characterization all new compounds. All reactions were performed in standard glassware under argon unless otherwise noted. THF and DCM were distilled from sodium/benzophenone and calcium hydride respectively. All deuterated solvents were purchased from Sigma Aldrich and used as received, except for $CDCl_3$ which was stored over activated 4 Å molecular sieves. Chromatographic separations were performed on standard 230-400 mesh silica gel, unless otherwise noted. Rotary evaporation was always performed at 40 °C. DCM was used to azeotrope residual ethyl acetate following chromatography as appropriate. Unless otherwise noted, all products were colourless oils.

NMR spectra for characterization of stable products were recorded at ambient temperature using Bruker AVIIIHD 500 MHz or VNMRS 500 MHz NMR spectrometers. Low temperature (< -10°C) experiments were recorded on a Bruker AVIIIHD 400 MHz. All NMR chemical shifts are reported in ppm (δ) units with residual solvent peaks used for reference. NMR data is reported using the following abbreviations: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; m, multiplet, etc. Unless otherwise stated, spectra were acquired at 25 °C.

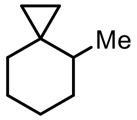
Preparation of Spirocyclic 6-membered compounds



General Procedure A[1]: To acid-washed magnesium strips (8 eq.) in dry DCM (2 ml/mmol ketone) under argon is added neat $TiCl_4$ (2 eq.). The mixture is cooled to 0 °C and a solution of ketone (1 eq.) in 3:2 DCM/THF (5 ml/mmol) is added dropwise by cannula over 30 minutes. The reaction is stirred 1 hr at room temperature (though it can be left for up to 24 hrs with no negative consequence). Dilute with DCM (5 ml/mmol), cool to 0 °C and quench with sat. Na_2CO_3 (2 ml/mmol) dropwise. Stir 10 minutes then add Na_2SO_4 until the solution becomes translucent (the black sludge should adsorb to the Na_2SO_4, greatly simplifying workup). Filter through Celite, dry further with $MgSO_4$ filter through cotton and evaporate solvent. A silica plug sufficed to purifiy all compounds made .



General Procedure B[2]: To a solution of olefin (1 eq.) and methylene iodide (1.2 eq.) in dry DCM (2 ml/mmol) at 0 °C is added trimethyl aluminum (1.3 eq., 2M in hexanes). The solution is stirred for 4 hrs, (can be left up for up to 24 hrs, even at RT, with no negative consequence), then cooled to 0 °C. Standard Fieser workup (dilute with Et_2O, slowly add 0.4 ml 3M NaOH/ mmol $AlMe_3$, then 0.4 ml H_2O / mmol $AlMe_3$, then 1 ml H_2O/ mmol $AlMe_3$. Warm to room temperature and add $MgSO_4$ until solution is clear. **Note: Much more caution must be taken quenching this reaction than with DIBAL.** The mixture is filtered, and solvent evaporated, chromatograph as necessary.



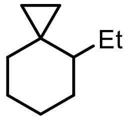
Compound **S1:** Prepared according to general procedure B from known olefin, with modification to the isolation procedure due to the volatility of this product. A Hickman distillation was performed following chromatography in pentane to remove residual hexanes and pentane. **Crude Yield:** 205 mg (38%). On distilling, much of the product was lost, leaving only about 5 mg.

^{1}H NMR (800 MHz, *d$_6$*-Acetone) δ 1.59 – 1.50 (overlapping peaks, 3H), 1.42 (m, 2H), 1.36 – 1.29 (m, 1H), 1.22 (overlapping peaks, 3H), 0.72 (d, J = 6.6 Hz, 3H), 0.26 (dt, J = 9.0, 4.5 Hz, 1H), 0.20 (dt, J = 9.2, 4.6 Hz, 1H), 0.05 (ddd, J = 9.0, 5.2, 3.8 Hz, 1H), 0.00 (ddd, J = 9.1, 5.2, 3.9 Hz, 1H).

^{13}C NMR (201 MHz, $CDCl_3$) δ 35.83, 32.74, 25.54, 23.24, 22.38, 22.08, 15.34, 11.04, 8.44.

FTIR (film, cm^{-1}): 2957, 2921, 2852, 1460,1445, 1375, 1008.

HRMS (APCI) for C_9H_{15} [M-H]$^+$: Calculated: 123.1168 Found: 123.1174



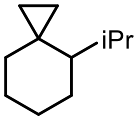
Compound **S2:** Prepared according to general procedure B from known olefin. **Yield:** 71 mg (37 %).

^{1}H NMR (500 MHz, *d$_6$*-acetone) δ 1.65-1.25 (overlapping signals, 9H, see HSQC for distinct shifts), 0.86 (t, *J* = 7.5 Hz, 3H), 0.85, (overlapping, 1 H), 0.80 (m, 1H) 0.27 (second order- apparent q, 2H), 0.15 (overlapping second order dd, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 43.8, 32.5, 28.3, 25. 5, 22.5, 22.3, 21.9, 12.0, 11.6, 10.6.

FTIR (film, cm^{-1}): 2958, 2922, 2852, 1459, 1444

HRMS (APCI) for $C_{10}H_{17}$ [M-H]$^+$: Calculated: 137.1325 Found: 137.1326



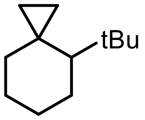
Compound **S3:** Prepared according to general procedure B from known olefin. **Yield:** 93 mg (66%).

^{1}H NMR (500 MHz, CDCl$_3$) δ ^{1}H NMR (500 MHz, acetone) δ 2.01 (m, 1H), 1.87 – 1.75 (m, 2H), 1.67 – 1.59 (m, 1H), 1.55 (tdd, *J* = 12.7, 5.4, 3.9 Hz, 1H), 1.48 – 1.43 (overlapping peaks, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 4H), 0.57 (dtd, *J* = 13.5, 2.9, 1.4 Hz, 1H), 0.49 (ddd, *J* = 9.5, 5.6, 4.3 Hz, 1H), 0.38 – 0.30 (m, 2H), 0.12 (ddd, *J* = 9.2, 5.5, 3.9 Hz, 1H), 0.04 (dddd, *J* = 9.3, 5.6, 3.9, 1.9 Hz, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 49.30, 31.30, 27.56, 26.94, 25.43, 21.22, 21.12, 20.42, 14.27, 10.49.

FTIR (film, cm^{-1}): 2926, 2855, 1447

HRMS (APCI) for C$_{11}$H$_{19}$ [M-H]$^{+}$: Calculated: 151.1481 Found: 151.1479

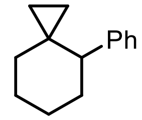


Compound **S4:** Prepared according to general procedure B from known olefin. Yield: 111 mg (73%) **^{1}H NMR** (500 MHz, CDCl$_3$) δ 1.98 (tdd, *J* = 13.4, 3.7, 2.0 Hz, 1H), 1.93 – 1.87 (m, 1H), 1.69 – 1.62 (m, 3H), 1.58 – 1.46 (m, 2H), 1.14 – 1.02 (m, 9H), 0.73 – 0.66 (m, 1H), 0.65 – 0.59 (m, 1H), 0.57 – 0.50 (m, 1H), 0.47 – 0.39 (m, 1H), 0.12 – 0.00 (m, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) 50.81, 36.09, 33.10, 31.62, 26.73, 25.39, 22.67, 21.20, 14.95, 13.46., 14.07, 13.46.~~,~~

FTIR (film, cm^{-1}): 2952, 2926, 1466

HRMS (APCI) for C$_{12}$H$_{22}$ [M]$^{+}$: Calculated: 166.1716 Found: 166.1713

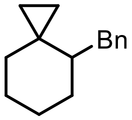


Compound **S5:** Prepared according to general procedure B from known olefin. Yield: 53 mg (72%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.21 (m, 3H), 2.82 (dd, *J* = 9.9, 4.0 Hz, 1H), 1.98 – 1.88 (m, 2H), 1.85 (ddt, *J* = 17.2, 8.9, 4.1 Hz, 1H), 1.75 (dddd, *J* = 19.1, 16.6, 8.5, 3.6 Hz, 2H), 1.63 – 1.45 (m, 2H), 1.22 (dt, *J* = 13.4, 3.9 Hz, 1H), 0.27 – 0.19 (m, 1H), 0.19 – 0.14 (m, 1H), 0.09 (ddd, *J* = 9.2, 5.4, 4.0 Hz, 1H), 0.03 (ddd, *J* = 9.4, 5.3, 4.0 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.70, 129.07, 127.62, 125.94, 47.23, 37.28, 31.44, 26.13, 25.85, 22.59, 9.79, 7.81.

FTIR (film, cm^{-1}): 3062, 3027, 2994, 2852, 1446

HRMS (APCI) for $C_{14}H_{19}$ [M+H]$^+$: Calculated: 187.1481 Found: 187.1480



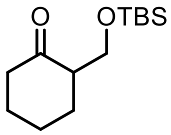
Compound **S6:** Prepared according to general procedure B from known olefin. Yield: 61 mg (88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.18 – 7.13 (m, 2H), 2.73 (dd, *J* = 13.4, 4.7 Hz, 1H), 2.63 (dd, *J* = 13.4, 10.4 Hz, 1H), 1.81 – 1.71 (m, 1H), 1.70 – 1.58 (m, 2H), 1.55 – 1.37 (m, 4H), 1.22 (dd, *J* = 10.2, 4.8 Hz, 1H), 0.92 (apparent d [small unreadable couplings present], *J* = 11.9 Hz, 1H), 0.37 – 0.21 (overlapping signals, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.07, 129.10, 128.12, 125.52, 44.54, 36.71, 33.03, 28.17, 25.66, 22.63, 21.75, 12.65, 10.95.

FTIR (film, cm^{-1}): 3064, 3026, 2993, 2923, 2852, 1454

HRMS (APCI) for $C_{15}H_{19}$ [M-H]$^+$: Calculated: 199.1481 Found: 199.1485.



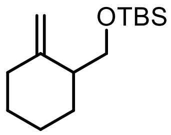
Compound **S7a:** To 2-(hydroxymethyl)cyclohexan-1-one (330 mg, 2.58 mmol) in dry DCM (6 mL) at 0 °C is added imidazole (526 mg, 3 eq.) and TBSCl (585 mg, 1.5 eq) at 0°C. The reaction is allowed to stir at room temperature for 2 hours, then quenched with aqueous sodium bicarbonate. The organic layer is washed with water and brine, dried over $MgSO_4$ and solvent removed by rotary evaporation. The crude is chromatographed (1→4% Et_2O-Hexanes) to yield compound **7a** (620 mg, 99%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.98 (dd, *J* = 10.4, 4.7 Hz, 1H), 3.57 (dd, *J* = 10.4, 8.0 Hz, 1H), 2.49 (m, 1H), 2.41 – 2.26 (m, 3H), 2.06 (m, 1H), 1.95 – 1.84 (m, 1H), 1.74 – 1.61 (m, 2H), 1.40 (m, 1H), 0.89 (s, 9H), 0.058 (s, 3H), 0.052 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 212.29, 62.38, 52.84, 42.21, 31.01, 27.69, 25.91, 24.63, 18.30, -5.40, -5.45.

FTIR (neat, cm^{-1}): 2929, 2857, 1707, 1251, 832, 774.

HRMS (APCI) for $C_{13}H_{27}O_2Si$ $[M+H]^+$: Calculated: 243.1775 Found: 243.1775



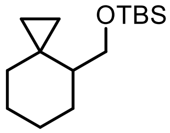
Compound **S7b:** Following general procedure A with **S7a. Yield:** (431 mg, 71%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.69 (s, 1H), 4.56 (s, 1H), 3.79 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.61 (dd, *J* = 9.8, 8.1 Hz, 1H), 2.28 – 2.15 (m, 2H), 2.11 – 2.02 (m, 1H), 1.93 – 1.82 (m, 1H), 1.76 – 1.62 (m, 3H), 1.52 – 1.42 (m, 2H), 1.38 – 1.21 (m, 3H), 0.92 (s, 9H), 0.08 (d, *J* = 1.2 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.51, 105.94, 64.96, 45.30, 35.54, 30.50, 28.59, 25.98, 24.45, 18.38, -5.30, -5.33.

FTIR (film, cm^{-1}): 2927, 2856, 1630 (w), 1254, 832, 773.

HRMS (ESI) for $C_{14}H_{29}OSi$ $[M+H]^+$: Calculated: 241.1982 Found: 241.1974



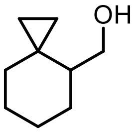
Compound **S7c**: To methylene iodide (221 µL, 1.6 eq) in DCM (10 mL) is added diethyl zinc (2.5 mL, 2.5 mmol, 1.5 eq.) at 0 °C. Stir 30 minutes, then add a solution of **S7b** (400 mg, 1.67 mmol). Stir 24 hours at RT. Quench with saturated NH_4Cl (5 mL), dilute with water (25 mL). Extract with DCM. Dry over $MgSO_4$. Chromatograph 2% Et_2O-Hexane. Yield: 311 mg (73%). The product was a thin colourless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ δ 3.65 (t, J = 9.5 Hz, 1H), 3.59 (dd, J = 10.0, 5.3 Hz, 1H), 1.70 (dd, J = 13.1, 4.3 Hz, 1H), 1.61 – 1.41 (m, 6H), 1.10 (dq, J = 9.5, 4.7 Hz, 1H), 0.90 (s, 9H), 0.86 – 0.79 (m, 1H), 0.38 (ddd, J = 6.9, 4.6, 3.2 Hz, 1H), 0.31 – 0.26 (m, 1H), 0.21 – 0.11 (m, 2H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 63.51, 44.45, 33.52, 26.53, 25.99, 25.53, 21.81, 20.06, 18.33, 12.16, 10.52, -5.31, -5.36.

FTIR (film, cm^{-1}): 2928, 2856, 1254, 834, 773.

HRMS (ESI) for $C_{15}H_{30}NaOSi$ $[M+Na]^+$: Calculated: 277.1958 Found: 277.1966



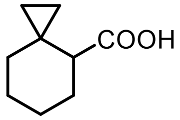
Compound **S7**: To **S7c** (100 mg, 0.39 mmol) in methanol (1 mL) is added acetyl chloride (3 µL, 0.1 eq.). Stir 1 hr, remove volatiles. No purification was necessary. The product was a thick, colourless oil Yield: 54 mg (99%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (dd, *J* = 10.7, 6.3 Hz, 1H), 3.67 (dd, *J* = 10.7, 8.3 Hz, 1H), 1.68 – 1.57 (overlapping signals, 4H), 1.56 – 1.42 (overlapping signal, 3H), 1.33 – 1.26 (m, 1H), 1.14 (mf, 1H), 0.83 (mf, 1H), 0.42 (ddd, *J* = 8.6, 5.1, 3.4 Hz, 1H), 0.34 – 0.18 (overlapping signals, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 63.63, 44.57, 33.01, 26.78, 25.46, 21.70, 19.91, 11.71, 10.58.

FTIR (neat, cm^{-1}): 3319 (br), 3067, 2993, 2922, 2852, 1445, 1036.

HRMS (ESI) for $C_{19}H_{16}NaO$ $[M+Na]^+$: Calculated: 163.1093 Found: 163.1087



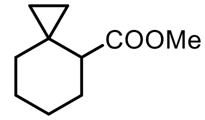
Compound **S8**: To compound **S7** (15 mg, 0.1 mmol) in acetonitrile (500μL) was added H_5IO_6(1.5 eq.) and CrO_3 (1 mol %) in acetonitrile (prepared as a stock solution[3]) at 0 °C. The mixture was allowed to warm overnight. The reaction mixture was diluted with ether (5 ml), filtered through celite, and then poured into 1M HCl (5 ml). The organic layer was washed thrice with 1M HCl until the yellow colour was completely washed away. Dry over $MgSO_4$. Chromatograph in 30% EtOAc/Hexanes and visualize with bromocresol green. The product was a thick, colourless oil. Yield: 15 mg (93%)

^{1}H NMR (500 MHz, *d$_6$*-acetone) δ10.42 (br s, 1H), 2.08 – 2.05 (m, [overlapping with solvent], 1H), 1.94 – 1.85 (overlapping signals, 1H), 1.74 – 1.65 (overlapping signals, 2H), 1.64 – 1.54 (overlapping signals, 2H), 1.48 (overlapping signals, 2H), 1.03 (m, 1H), 0.56 (m, 1H), 0.36 (m, 1H), 0.30 (m, 1H), 0.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.74, 52.70, 38.92, 32.93, 30.12, 28.16, 24.83, 16.83, 16.08

FTIR (neat, cm^{-1}): 3400-2500 (br), 3072, 2998, 2926, 2854, 1697, 1446.

HRMS (ESI) for $C_9H_{13}O_2$ $[M-H]^-$: Calculated: 153.0921 Found: 153.0921



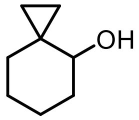
Compound **S9**: To compound **S8** (11 mg, 0.07 mmol) in dry DMF (700 µL) was added K_2CO_3 (20 mg, 0.14 mmol, 2 eq.). Methyl iodide (10 µL, 0.16 mmol, 2.3 eq.) is added, and the mixture is stirred for 16 hrs at RT. Pour into water (10 mL), and extract with ether (4 x 1 mL). Dry over $MgSO_4$. Concentrate and chromatograph (5% Et_2O-Hexanes). The product was a thin colourless liquid with a pleasant, fruity aroma. **Yield:** 10 mg (85%)

^{1}H NMR (500 MHz, *d$_6$*-acetone) δ 3.62 (s, 3H), 2.10 (t, *J* = 5.1 Hz, 1H), 1.88 (m, 1H), 1.73 – 1.63 (m, 2H), 1.58 (m, 1H), 1.50 m, 1H), 1.05 (d, *J* = 13.4 Hz, 1H), 0.57 – 0.48 (m, 1H), 0.34 – 0.22 (m, 3H).

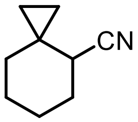
^{13}C NMR (126 MHz, *d$_6$*-acetone/ *d$_3$*-acetonitrile): 174.2, 50.5, 47.8, 33.7, 27.7, 24.8, 23.0, 19.7, 11.5, 10.7. Note that mixing deuterated solvents was unintentional, no peaks were obstructed in carbon or proton spectra.

FTIR (film, cm^{-1}): 2929, 2856, 1736, 1165

HRMS (ESI) for $C_{10}H_{16}NaO_2$ $[M+Na]^+$: Calculated 191.1043 Found: 191.1038



Compound **S10**: Prepared according to literature procedure.[2]



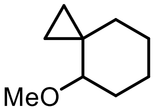
Compound **S11**: 2-spirocyclopropyl-cyclohexanone was prepared by DMP oxidation of compound **S10**, spectral data matched literature. To KOtBu (409 mg, 3.65 mmol) in dry DMSO (1.2 mL) was added TosMIC (212 mg, 1.09 mmol,). The mixture is stirred for 15 minutes. A solution of methanol (32 µL, 0.8 mmol) and 2-spirocyclopropyl-cyclohexanone (90 mg, 0.73 mmol) in DMSO (0.6 mL) was added. Stir overnight. Quench with water (4 mL), extract with pentane (3 x 2 mL). Wash with water. Dry over $MgSO_4$, pass through a small plug of alumina and concentrate, leaving some pentane. This compound is very volatile, handle with care. Chromatograph in 1-5% Et_2O/pentane, evaporate solvent with a stream of argon to yield a colourless oil. (54 mg, 55%).

^{1}H NMR (500 MHz, acetone) δ 2.51 (t, *J* = 5.2 Hz, 1H), 1.89 – 1.78 (overlapping m, 2H), 1.73 – 1.59 (overlapping m, 4H), 1.57 – 1.47 (m, 1H), 1.18 (d, *J* = 13.3 Hz, 1H), 0.59 – 0.50 (m, 2H), 0.47 – 0.37 (m, 2H)

^{13}C NMR (126 MHz, acetone) δ 121.5, 36.5, 33.5, 29.3, 25.3, 23.7, 20.7, 12.7, 11.2

FTIR (film, cm^{-1}): 2932, 2857, 2236

HRMS (APCI) for $C_9H_{14}N$ $[M+H]^+$: Calculated: 136.11208 Found: 136.11240



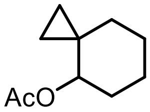
Compound **S12**: To **S10** (100 mg, 0.8 mml) in dry DMF (4 ml) is added NaH (40 mg, 1 mmol, 1.25 eq.), stir 30 minutes. Methyl iodide (62 µL) is added, and the mixture is stirred overnight at RT. The reaction is poured into water and extracted with pentane. Wash twice with an equal amount of water. Concentrate, chromatograph in pentane→ 1% ether to yield a thin, volatile, colourless liquid. Note that removing the last bit of solvent is most easily achieved by blowing argon into a small vial containing the compound. This proved to be far superior to careful rotary evaporation, which often lead to near complete loss of the desired product. (52 mg, 46%)

^{1}H NMR (500 MHz, Acetone) δ 3.28 (s, 3H), 2.70 (d, *J* = 4.3 Hz, 1H), 1.75 – 1.59 (m, 4H), 1.59 – 1.50 (m, 1H), 1.50 – 1.36 (m, 2H), 0.98 – 0.86 (m, 1H), 0.58 – 0.50 (m, 1H), 0.26 (td, *J* = 10.1, 9.1, 4.8 Hz, 2H), 0.18 – 0.09 (m, 1H).

^{13}C NMR (126 MHz, Acetone) δ 81.8, 55.5, 31.9, 29.6, 24.9, 21.3, 21.2, 10.5, 8.1.

FTIR (film, cm^{-1}): 2954, 2922, 2853, 1460, 1096

HRMS (ESI) for $C_7H_{14}NaO$ [M+Na]$^+$: Calculated: 163.1093 Found: 163.1085



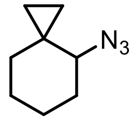
Compound **S13**: To **S10** (32mg) in dry DCM (1 mL) with triethylamine (52 μL) and DMAP (2 mg) is added AcCl (30 μL, 1.5 eq.) dropwise at 0°C. Stir overnight. Pour into water, extract with DCM. Dry over $MgSO_4$. Chromatograph 5→10% Et_2O/Hexanes to yield a thin colourless oil (28.4 mg, 68%). Some ring-opening was observed, but was separated by chromatography.

^{1}H NMR (500 MHz, Acetone) δ 4.35 (br s, 1H), 2.00 (s, 3H), 1.79 (dd, 12, 11.5 Hz 1H), 1.72-1.67 (overlapping m, 2H), 1.66-1.58 (overlapping m, 2H), 1.58 – 1.45 (m, 2H), 1.01 (d, *J* = 12.8 Hz, 1H), 0.52 (ddd, *J* = 9.4, 5.3, 3.7 Hz, 1H), 0.42 (dddd, *J* = 9.0, 5.0, 3.8, 1.3 Hz, 1H), 0.29 (ddd, *J* = 9.2, 5.3, 3.9 Hz, 1H), 0.24 (ddd, *J* = 8.9, 5.2, 3.7 Hz, 1H).

^{13}C NMR (126 MHz, Acetone) δ 169.5, 75.4, 31.9, 30.0, 24.5, 21.4, 21.4, 20.2, 10.0, 9.8

FTIR (film, cm^{-1}): 2930, 1735, 1704, 1240.

HRMS (ESI) for $C_{10}H_{16}NaO_2$ [M+Na]$^+$: Calculated: 191.1043 Found: 191.1041

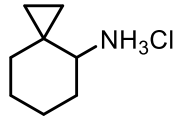


Compound **S14**: To a solution of **10** (60 mg, 0.48 mmol) in DCM (1 mL) with $TMSN_3$(150µL, 1.14 mmol, 2.4 eq.) at 0°C was added TfOH (5 µL, 0.11 eq.). Stir 1 hr at 0 °C, then pour into saturated aqueous $NaHCO_3$. Extract with DCM. Dry over $MgSO_4$. Chromatograph 5-10% Et_2O-Hexanes. **Yield**: 62 mg (87%). Note that an inseparable impurity was present, and modifying reaction temperature and time, or equivalents of acid or $TMSN_3$ did not seem to affect the ratio. As such, clean ^{13}C NMR was not obtainable.

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.24 (t, *J* = 3.9 Hz, 1H), 1.83 – 1.70 (m, 3H), 1.68 – 1.57 (m, 2H), 1.56 – 1.43 (m, 2H), 0.99 (d, *J* = 13.5 Hz, 1H), 0.61 (ddd, *J* = 9.3, 5.5, 4.0 Hz, 1H), 0.42 (dddd, *J* = 9.2, 5.3, 3.8, 1.4 Hz, 1H), 0.39 – 0.32 (m, 1H), 0.29 (ddd, *J* = 8.9, 5.5, 3.8 Hz, 1H)

FTIR (film, cm^{-1}): 2923, 2854, 2095.

HRMS (APCI) for $C_8H_{14}N$ $[M-N_2+H]^+$: Calculated: 124.1121 Found: 124.1125 (Note that even under mild ESI conditions the loss of N_2 was detected.)



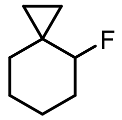
Compound **S15**: To a solution of **S11** (45 mg, 0.3 mmol) in dry THF (3 mL) at 0°C was added LAH (30 mg, 0.8 mmol). Stir 2 hrs at RT, then work up with a standard Fieser workup. Rinse solids thoroughly with ether. To the filtrate is added a saturated solution of HCl in ether. The filtrate is then evaporated and recrystallized in DCM/Et_2O to yield pure amine hydrochloride **Yield**: 37.5 mg (78%). The hydrochloride could be neutralized with aqueous hydroxide after being suspended in DCM. Note that the free amine is quite volatile, and loss of yield is likely as the DCM is evaporated.

^{1}H NMR (500 MHz, $CDCl_3$) δ δ 8.33 (s, 3H), 2.80 (t, J = 3.7 Hz, 1H), 2.15 – 2.01 (m, 2H), 1.91 – 1.79 (m, 2H), 1.75 (m, 1H), 1.65 (m, 1H), 1.52 – 1.42 (m, 1H), 0.97 (m, 1H), 0.93 – 0.85 (m, 1H), 0.57 (m, 1H), 0.44 (overlapping m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.12, 31.14, 29.00, 24.56, 20.42, 16.47, 12.53, 10.79

FTIR (film, cm^{-1}): 3335 (br), 2924, 2854, 1445.

HRMS (APCI) for $C_8H_{16}N$ $[M+H]^+$: Calculated: 126.1277 Found: 126.1278



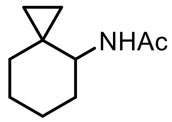
Compound **S16**: To a solution of **S10** (60 mg, 0.48 mmol) in DCM (1 mL) at 0°C was added DAST (100 µL, 0.75 mmol, 1.5 eq). Stir overnight at room temperature, then pour into saturated aqueous $NaHCO_3$. Extract with DCM. Dry over $MgSO_4$. Chromatograph in pentane. Note that to obtain a solution containing minimal solvent, very significant losses of desired compound resulted. Likewise, a sufficient amount for ^{13}C NMR could not be obtained. In lieu we provide ^{19}F NMR which showed a single peak.

^{1}H NMR (500 MHz, *d$_6$*-acetone) δ 3.03 (d, *J* = 55.9 Hz, 1H), 1.75 – 1.36 (m, 7H), 1.10 (d, *J* = 18.5 Hz, 1H), 0.59 – 0.46 (m, 1H), 0.41 (s, 1H), 0.14 (dtd, *J* = 19.8, 9.4, 8.9, 5.3 Hz, 2H).

^{19}F NMR(376.7 MHz**,** *d$_6$*-acetone, -78 °C)**:** -126.39

FTIR (film, cm^{-1}): 2919, 2856.

HRMS (APCI) for $C_8H_{12}F$ $[M-H]^+$: Calculated: 127.0918 Found: 127.0923



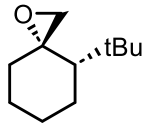
Compound **S17**: To a solution of **S10** (31 mg) in MeCN (1 mL) with H_2O (50 µL) was added TfOH (20 µL, 1 eq.). The solution was stirred and heated at 60 °C for 14 hours, then poured into saturated aqueous $NaHCO_3$. Extract with DCM. Dry over $MgSO_4$. Chromatograph 1:1 Hexanes:EtOAc. A ring opened product co-eluted with the desired product, but the desired product could be selectively crystallized out by dissolving in a minimal volume of DCM, diluting with hexanes until slightly cloudy, then boiling just until the solution clarified. The solution was capped until cooled to room temperature, then allowed to slowly evaporate until white crystals formed. The crystals were filtered and washed with 5% DCM in hexanes to yield the product as white crystals. **Yield:** 21 mg (48%).

^{1}H NMR (500 MHz, Acetone) δ 6.81 (s, 1H), 3.63 (s, 1H), 1.82 (s, 3H), 1.64 (m, 2H), 1.48 (overlapping m, 5H), 1.26 (br s, 1H), 0.46 (dt, *J* = 9.4, 4.6 Hz, 1H), 0.36 (dt, *J* = 9.2, 4.7 Hz, 1H), 0.15 (ddd, *J* = 9.2, 5.3, 4.0 Hz, 1H), 0.07 (ddd, *J* = 9.2, 5.3, 4.1 Hz, 1H).

^{13}C NMR (126 MHz, *d*$_6$-acetone) δ 169.3, 51.5, 34.4, 32.1, 25.7, 24.1, 23.0, 22.8, 11.0, 9.0.

FTIR (film, cm^{-1}): 3304 (sharp), 3075, 2997, 2922, 2850, 1636, 1543 .

HRMS (ESI) for $C_{10}H_{17}NNaO$ $[M+Na]^+$: Calculated: 190.1202 Found: 190.1204



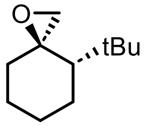
Compound **S18**: To a suspension of trimethylsulfonium iodide (1.6g, 8 mmol, 2 eq.) in THF (25 mL) at -10 °C is added nBuLi (3.1 mL, 2.5 M in hexanes, 1.9 eq.) dropwise. Stir 1 hour. A solution of 2-tertbutyl-cyclohexanone (616 mg, 4 mmol, 1 eq.) in THF (3 mL) is then added via cannula. Stir 3 hrs at RT. The reaction is quenched with NH_4Cl (1 ml/mmol base), diluted with water, and extracted with ether. The organic layer was washed with brine, then dried over $MgSO_4$. The solvent is removed, and the crude oil is chromatograph in 5% ether to yield pure **15** as a thin oil. **Yield:** 604 mg (90%) Note that this reaction yielded only one detectable diastereomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.75 (d, J = 5.1 Hz, 1H), 2.47 (d, J = 5.0 Hz, 1H), 1.89 – 1.79 (m, 2H), 1.76 (mf, 1H), 1.72 – 1.64 (m, 2H), 1.55 (m, 1H), 1.46 (m, 1H), 1.32 (m, 1H), 1.29 – 1.22 (m, 1H), 1.00 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 61.85, 55.03, 49.68, 34.32, 33.98, 30.31, 27.03, 25.44, 23.87.

FTIR (film, cm^{-1}): 2932, 2864, 1469, 1446, 1365

HRMS (APCI) for $C_{11}H_{21}O$ $[M+H]^+$: Calculated: 169.15869 Found: 169.15840



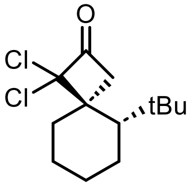
Compound **S19**: To a solution of 1-(tert-butyl)-2-methylenecyclohexane (616 mg, 4 mmol) in DCM (16 mL) was added mCPBA (<70% purity, 1.0 g, 1.4 eq.). The solution is stirred overnight. Pentane is added to triturate byproducts, the solution is filtered through silica, then concentrated to yield a 10:1 diastereomeric mixture of **S16** : **S15**. The isomers could be separated by chromatography in 2-5% Et_2O: Hexanes with ample silica. Combined yield: 499 mg (74%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87 (d, J = 4.5 Hz, 1H), 2.68 (d, J = 4.6 Hz, 1H), 1.90 – 1.79 (m, 3H), 1.75 – 1.60 (m, 3H), 1.54 (mz, 1H), 1.22 (dt, J = 13.3, 4.2 Hz, 1H), 1.11 (td, J = 4.7, 1.4 Hz, 1H), 1.02 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 60.60, 55.72, 50.02, 34.09, 32.56, 30.55, 25.69, 24.01, 22.57.

FTIR (film, cm^{-1}): 2936, 2865, 1470, 1365.

HRMS (APCI) for $C_{11}H_{21}O$ $[M+H]^+$: Calculated: 169.15869 Found: 169.15845



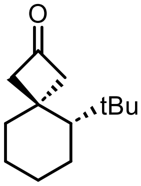
Compound **S20a**: To a solution of 1-(tert-butyl)-2-methylenecyclohexane (250 mg, 1.64 mmol) in Et_2O (4 mL) with Zinc dust (131 mg, 2 mmol, 1.2 eq) is added trichloroacetyl chloride (222 µL,2 mmol, 1.2 eq.). Stir 2 hours at room temperature. Filter through a small pad of silica, and concentrate solution. Typically, chromatography was not required, but 5% Et_2O-Hexanes is what can be used if impurities are present. Only one diastereomer was detectable in the crude. **Yield:** 361 mg (84%) of a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) 3.81 (d, J = 16.5 Hz, 1H), 2.65 (d, J = 16.5 Hz, 1H), 2.52 – 2.43 (m, 1H), 2.17 – 2.06 (m, 3H), 1.83 – 1.77 (m, 1H), 1.70 – 1.64 (m, 1H), 1.58 (m, 2H), 1.53 – 1.45 (m, 1H), 1.14 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.27, 94.24, 53.40, 49.87, 43.89, 34.63, 32.73, 32.68, 27.00, 22.18, 19.52

FTIR (film, cm^{-1}): 2960, 2926, 2870, 1806, 1463.

HRMS (APCI) for $C_{13}H_{21}OCl_2$ $[M+H]^+$: Calculated: 263.0964 Found: 263.0960. Isotope patterns were consistent with 2 chlorine atoms



Compound **S20**: To a solution of **S20a** (350 mg, 1.33 mmol) in acetic acid (5 mL) was added Zinc dust (533 mg, >5 eq.), the mixture was heated to 60°C. Stir 2 hours, or until the solution becomes translucent. The mixture is cooled and slowly added to an aqueous solution of sodium carbonate

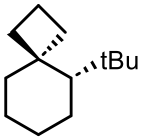
(50 mL). Extract with DCM. Wash with $NaHCO_3$ twice. Concentrate and chromatograph (5% Et_2O-Hexanes) Yield: 293 mg (92 %)

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 3.28 (dt, *J* = 17.2, 2.9 Hz, 1H), 3.24 – 3.16 (d, 17.2 Hz 1H), 2.74 (ddd, *J* = 17.3, 6.2, 2.5 Hz, 1H), 2.63 (ddd, *J* = 17.2, 6.2, 2.5 Hz, 1H), 1.88 – 1.76 (m, 1H), 1.71 – 1.62 (m, 2H), 1.59 – 1.49 (m, 5H), 1.39 (mf, 1H), 1.08 (s, 9H).[1]

^{3}**C NMR** (126 MHz, $CDCl_3$) δ 209.45, 59.65, 54.99, 51.74, 38.60, 35.62, 35.46, 31.99, 26.72, 24.21, 23.63.

FTIR (film, cm^{-1}): 2927, 2860, 1783.

HRMS (APCI) for $C_{13}H_{21}O$ $[M+H]^+$: Calculated: 195.1741 Found: 195.1743



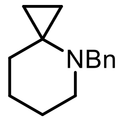
Compound **S21**: To a solution of **S20** (30 mg, 0.15 mmol) in Diethylene glycol (300 µL) was added anhydrous hydrazine (30 µL, 6 eq.), then KOH (25 mg, 3 eq.). Heat to 200 °C for 3 hours. The mixture is cooled and poured into an excess of 0.1M HCl. Extract thrice with pentane. Wash twice with 1 M HCl. Concentrate and chromatograph (pentane) **Yield:** 22 mg (81 %)

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 2.37 – 2.28 (m, 1H), 2.03 – 1.96 (m, 1H), 1.91 – 1.79 (m, 3H), 1.77 – 1.70 (m, 1H), 1.69 – 1.61 (m, 1H), 1.58 (m, 1H), 1.53 m, 3H), 1.46 (m, 2H), 1.29 – 1.24 (m, 2H), 1.04 (s, 9H).

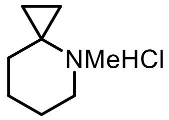
^{13}**C NMR** (126 MHz, $CDCl_3$) δ 58.51, 50.08, 40.22, 40.15, 39.81, 36.97, 36.83, 29.61, 28.68, 27.42, 20.91.

FTIR (film, cm^{-1}): 2925, 2858, 1463, 1446.

HRMS (ESI) for $C_{13}H_{23}$ $[M-H]^+$: Calculated: 179.1794 Found: 179.1796



Compound **S22**: Prepared according to literature procedure[4]. Characterization data was consistent. The product was a pale yellow oil that would discolour to a light pink over time, no notable difference was observed by NMR despite this.



Compound **S23**: To Ti(OiPr)$_4$ (1.33 mL, 4.4 mmol) in dry THF (20 mL) at -78 °C is added EtMgBr (3.33 mL, 10 mmol) dropwise. Stir 10 minutes. N-Me-valerolactam (450 mg) is added in THF (5 mL), and the solution is heated to reflux under argon for 24 hours. The solution is cooled to RT then quenched with 3M NaOH. NaOH pellets are added, and the mixture is stirred until the colour becomes light yellow or green. The mixture is distilled until about most of the THF has distilled. To the distillate is added sat. HCl in Et$_2$O, a white solid precipitates out. The volatiles are removed and the crude solid is recrystallized. The free base could be isolated by dissolving in DCM and shaking with 3M NaOH. The free base is quite volatile, evaporate cautiously.

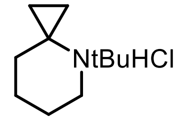
Yield: 169 mg (34 %)

^{1}H NMR (500 MHz, CDCl$_3$) δ 2.79 – 2.73 (m, 2H), 2.32 (s, 3H), 1.68 – 1.59 (m, 3H), 1.48 (m, 2H), 1.35 (dd, J = 6.3, 3.2 Hz, 4H), 0.48 (q, J = 4.0 Hz, 2H), 0.27 – 0.23 (m, 2H).

^{13}C NMR (126 MHz, *d$_6$*-acetone) δ 51.3, 44.5, 35.9, 27.0, 21.9, 18.0, 11.5, 10.6.

FTIR (film, cm^{-1}): 2926, 2854, 1457, 1446.

HRMS (ESI) for $C_8H_{16}N$ $[M+H]^+$: Calculated: 126.1277 Found: 126.1277



Compound **S24**: Following the same reaction conditions as **S20**. Following quenching, the reaction is extracted with Et_2O. Dry over $MgSO_4$ and precipitate with sat. HCl in Et_2O, remove volatiles to yield an off-white solid **Yield**: 202 mg (50 %)

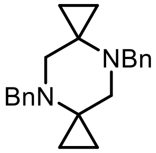
Crystallization conditions: The initially obtained solid was dissolved in toluene, and allowed to slowly evaporate until rectangular prisms grew.

^{1}H NMR (500 MHz, $CDCl_3$) δ10.46 (s, 1H), 3.63 (dd, *J* = 13.6, 3.9 Hz, 1H), 3.48 (tt, *J* = 14.1, 4.2 Hz, 1H), 246 (dddd, 15.0, 12.6, 4.0, 2.6 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.06 – 1.96 (m, 1H), 1.95 – 1.77 (overlapping H, 4H), 1.71 (s, 9H), 1.04 (dt, *J* = 10.0, 6.6 Hz, 1zH), 0.93 – 0.85 (br d, 15.4Hz, 1H), 0.46 (ddd, *J* = 9.9, 6.9, 5.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) ^{13}C NMR (126 MHz, $CDCl_3$) δ 68.1, 48.5, 43.8, 30.4, 29.5, 21.5, 20.6, 16.5, 11.4.

FTIR (solid, cm^{-1}): 3390, 2952, 2556, 1177

HRMS (ESI) for $C_{11}H_{22}N$ $[M+H]^+$: Calculated: 168.1747 Found: 168.1747



Compound **S25**: To $Ti(OiPr)_4$ (150 µL) in dry THF (5 mL) at 0°C is added EtMgBr () over 15 minutes. 1,4-dibenzylpiperazine-2,5-dione (100mg, 0.33 mmol) dissolved in THF (2 mL) is added. Stir overnight at RT. Note that attempts to promote double cyclopropanation by heating to 60°C yielded nearly identical results. Quench with 3M NaOH and saturated rochelle's salt solution and water (5 mL each), stir 30 minutes. Dilute further with water until the aqueous phase is clear.

Extract with ether. Dry over $MgSO_4$. Chromatograph 5→60% EtOAc/Hexanes. This compound elutes in 5% EtOAc, which after solvent removal yields a white powder. Yield (7mg, 7%)

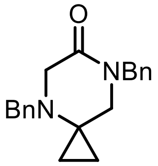
Crystallization conditions: The white powder obtained from the column was nearly dissolved in toluene, then heated until full dissolution occurred. The vial was sealed and allowed to recrystallize overnight, yielding small colourless prisms.

^{1}H NMR: δ 7.32 (s, 4H), 7.24 (s, 1H), 4.09 (s, 2H), 3.06-2.46 (br s, 2H), 0.75 (s, 2H), 0.45 (s, 2H).

^{13}C NMR (126 MHz, cdcl$_3$) δ 140.3, 128.4, 128.2, 126.7, 54.2, 49.1, 37.8, 12.4.

FTIR (film, cm^{-1}):3062, 3028, 2944, 2849

HRMS (ESI) for $C_{22}H_{27}N_2$ $[M+H]^+$: Calculated: 319.2169 Found: 319.2173



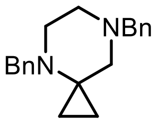
Compound **S26**: Isolated as the major product from the reaction above. Yield (49 mg, 49%).

^{1}H NMR: δ 7.40 – 7.34 (m, 2H), 7.34 – 7.29 (m, 5H), 7.29 – 7.24 (m, 3H), 4.68 (s, 2H), 3.83 (s, 2H), 3.45 (s, 2H), 3.22 (s, 2H), 0.87 – 0.79 (m, 2H), 0.56 – 0.47 (m, 2H).

^{13}C NMR (126 MHz, cdcl$_3$) δ 168.6, 138.1, 136.8, 128.8, 128.7, 128.4, 127.9, 127.6, 127.3, 56.2, 53.0, 49.5, 48.6, 39.1, 13.7

FTIR (film, cm^{-1}): 3028, 2915, 1642

HRMS (ESI) for $C_{20}H_{22}N_2NaO$ $[M+Na]^+$: Calculated: 329.1624 Found: 329.1630



Compound **S27:** To **S26** in dry THF(3 mL) is added LAH (20 mg, 0.5 mmol) at RT. Heat to 50 °C overnight. Standard Fieser workup. The filtrate was concentrated to ~1 ml, then acidified with sat. HCl in Et_2O, causing a white solid to crash out. The solid was broken up to a fine powder, and the solvent was decanted. The solid washed with ether three times, leaving pure **S24** x 2HCl. The solid is dissolved in DCM, washed with 3M NaOH, then dried and the solvent is removed, leaving high purity **S26** as a colourless oil (37 mg, 84%).

Crystallization conditions: No SCXRD quality crystals were obtained using HCl or TFA in a large variety of solvents. Addition of exactly 2 equivalents of pTsOH hydrate to the compound in acetonitrile followed by slow evaporation yielded very thin, white needles, which were washed with acetonitrile, then recrystallized, which yielded higher quality crystals.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 10H), 3.83 (s, 2H), 3.56 (s, 2H), 2.89 (s, 2H), 2.52 (t, *J* = 5.1 Hz, 2H), 2.29 (s, 2H), 0.73 (s, 2H), 0.47 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 134.9, 133.0, 123.9, 123.4, 123.0, 123.0, 121.8, 121.5, 58.3, 49.9, 48.4, 42.6, 41.7, 37.2, 8.3 (broad).

FTIR (film, cm^{-1}): 3026, 2924, 2802

HRMS (ESI) for $C_{20}H_{25}N_2$ [M+H]$^+$: Calculated: 293.2012 Found: 293.2003

2. Single-Crystal X-Ray Data

Single crystal X-ray diffraction (SCXRD) data were measured on a Bruker D8 Venture diffractometer equipped with a Photon 200 area detector, and *IμS* microfocus X-ray source (Bruker AXS, Cu*K*α source). All measurements were carried out at room temperature for all structures. All crystals were coated with a thin layer of amorphous oil to decrease crystal deterioration, structural disorder, or any related thermal motion effects and to improve the accuracy of the structural results. Structure solution was carried out using the SHELXTL package from Bruker.[6] The parameters were refined for all data by full-matrix-least- squares or F2 using SHELXL.[7]

All of the non-hydrogen atoms were refined with anisotropic thermal parameters. All hydrogen atom thermal parameters were constrained to ride on the carrier atom. Structure **S27 x 2TsOH x H_2O** was found to have two disordered units. The first in one of the tosylates, in which the oxygen atoms were split into two groups by a rotation. Another disorder is found around the water solvate which is forming hydrogen bonding between two tosylates. Both disorders were successfully modelled.

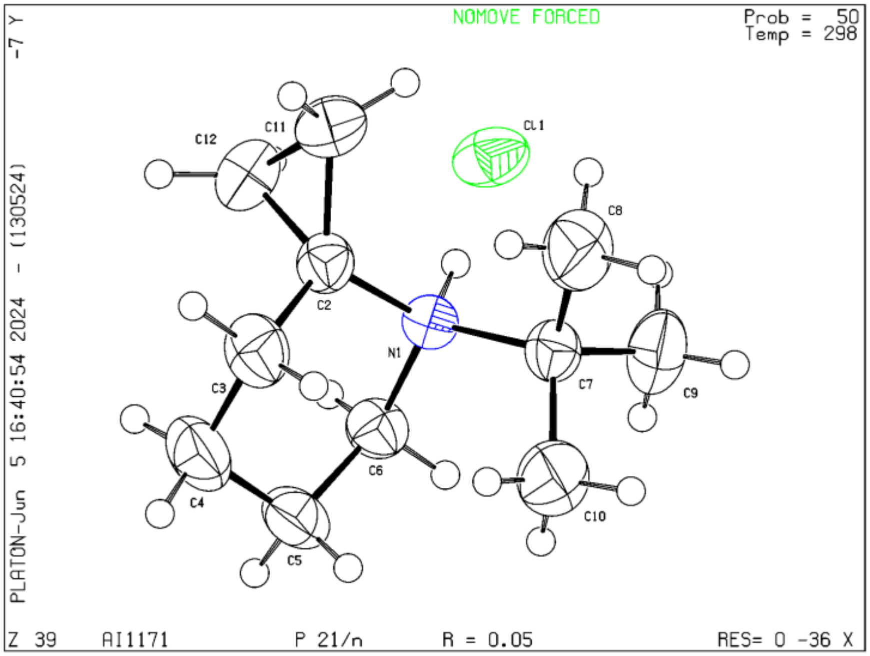


Table 1 Crystal data and structure refinement for S24

Empirical formula	$C_{11}H_{22}ClN$
Formula weight	203.74
Temperature/K	298(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	8.2410(3)
b/Å	15.6585(7)
c/Å	9.0543(4)
α/°	90

β/°	92.0640(10)
γ/°	90
Volume/Å^3	1167.62(8)
Z	4
ρ_{calc}g/cm^3	1.159
μ/mm^{-1}	2.541
F(000)	448.0
Crystal size/mm^3	0.796 × 0.264 × 0.214
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	12.142 to 145.196
Index ranges	$-7 \le h \le 10$, $-19 \le k \le 19$, $-11 \le l \le 11$
Reflections collected	18713
Independent reflections	2268 [R_{int} = 0.0414, R_{sigma} = 0.0254]
Data/restraints/parameters	2268/0/119
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0461, wR_2 = 0.1321
Final R indexes [all data]	R_1 = 0.0478, wR_2 = 0.1348
Largest diff. peak/hole / e Å^{-3}	0.31/-0.18

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for AI1171. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	2640.3(5)	6086.8(3)	3073.4(4)	56.1(2)
N1	3128.3(14)	6128.5(7)	6539.6(14)	36.0(3)
C2	1502.9(18)	6240.9(10)	7201.7(18)	42.6(4)
C5	3425(2)	4812.4(11)	8200(2)	56.8(5)
C4	1820(3)	5012.2(13)	8897(2)	66.6(5)
C3	1449(2)	5961.6(12)	8788(2)	55.9(5)
C8	3802(3)	7654.9(12)	7161(3)	77.1(7)
C7	4512.7(18)	6774.9(9)	6970.3(17)	43.4(4)
C6	3580.7(19)	5193.8(9)	6670.0(17)	44.1(4)
C9	5672(2)	6783.8(15)	5693(2)	67.5(5)
C10	5500(3)	6514.1(15)	8358(2)	68.4(6)
C11	387(2)	6909.3(12)	6571(2)	59.6(5)
C12	82(2)	5988.3(12)	6202(2)	58.2(5)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S24. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	51.6(3)	75.6(4)	40.7(3)	0.42(15)	-4.45(18)	13.11(17)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S24. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N1	38.2(6)	35.8(6)	34.1(6)	-0.9(4)	1.1(5)	1.0(4)
C2	40.4(8)	42.1(7)	45.8(8)	-0.8(6)	6.7(6)	1.2(6)
C5	65.9(11)	42.3(8)	62.3(11)	13.4(7)	3.6(8)	3.6(7)
C4	76.1(12)	62.5(11)	62.3(11)	20.1(9)	17.6(9)	-4.1(9)
C3	61.4(10)	60.5(10)	46.9(9)	0.9(7)	17.8(8)	-0.4(8)
C8	66.3(12)	40.0(9)	125(2)	-7.2(10)	2.0(12)	-7.3(8)
C7	43.1(8)	40.1(7)	46.9(8)	-1.6(6)	0.1(6)	-5.7(6)
C6	49.3(8)	34.8(7)	48.3(8)	-3.4(6)	3.5(6)	3.6(6)
C9	52.0(10)	87.9(14)	63.3(11)	-2.2(10)	10.1(8)	-20.1(9)
C10	68.7(12)	76.4(13)	58.8(11)	-0.1(9)	-17.0(9)	-18.7(10)
C11	47.7(9)	58.1(10)	73.0(12)	3.7(8)	3.2(8)	13.2(7)
C12	41.7(9)	66.8(11)	66.0(12)	-5.0(8)	1.4(8)	-3.5(7)

Table 4 Bond Lengths for S24

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C2	1.497(2)	C5	C6	1.519(2)
N1	C7	1.5640(18)	C4	C3	1.520(3)
N1	C6	1.5139(17)	C8	C7	1.509(2)

Table 4 Bond Lengths for S24

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C2	C3	1.503(2)	C7	C9	1.526(2)
C2	C11	1.493(2)	C7	C10	1.528(2)
C2	C12	1.507(2)	C11	C12	1.500(3)
C5	C4	1.518(3)			

Table 5 Bond Angles for S24

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C2	N1	C7	118.63(11)	C2	C3	C4	109.50(15)
C2	N1	C6	107.68(11)	C8	C7	N1	109.68(13)
C6	N1	C7	115.52(11)	C8	C7	C9	109.52(16)
N1	C2	C3	113.95(14)	C8	C7	C10	110.32(17)
N1	C2	C12	114.57(14)	C9	C7	N1	106.73(13)
C3	C2	C12	116.62(15)	C9	C7	C10	107.24(15)
C11	C2	N1	118.47(14)	C10	C7	N1	113.21(13)
C11	C2	C3	122.02(14)	N1	C6	C5	115.01(12)
C11	C2	C12	59.98(12)	C2	C11	C12	60.48(12)
C4	C5	C6	113.66(15)	C11	C12	C2	59.54(11)
C5	C4	C3	110.54(14)				

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for AI1171.

Atom	***x***	***y***	***z***	**U(eq)**
H1	2973.9	6202	5468.06	54
H5A	3546.61	4197.54	8135.4	68
H5AB	4303.07	5027.04	8839.68	68
H4A	1871.13	4840.87	9927.09	80
H4AB	957.33	4690.67	8397.12	80
H3A	380.92	6074.18	9160.83	67
H3AB	2240.03	6281.06	9383.19	67
H8A	4648.93	8045.72	7460.87	116
H8B	2998.56	7637.01	7901.5	116
H8C	3307.53	7841.63	6240.23	116
H6A	4694.08	5125.81	6377.46	53
H6AB	2895.4	4870.92	5978.7	53
H9A	6146.67	6228.12	5590.95	101
H9B	6513.61	7196.37	5890.11	101
H9C	5083.76	6932.58	4795.29	101
H10A	5983.6	5964.78	8206.72	103
H10B	4798.78	6485.15	9181.04	103
H10C	6337.42	6928.49	8559.7	103

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for AI1171.

Atom	*x*	*y*	*z*	U(eq)
H11A	791.41	7274.08	5800.27	71
H11B	-345.57	7186.57	7235.21	71
H12A	305.88	5797.25	5210.88	70
H12B	-831.81	5709.69	6646.72	70

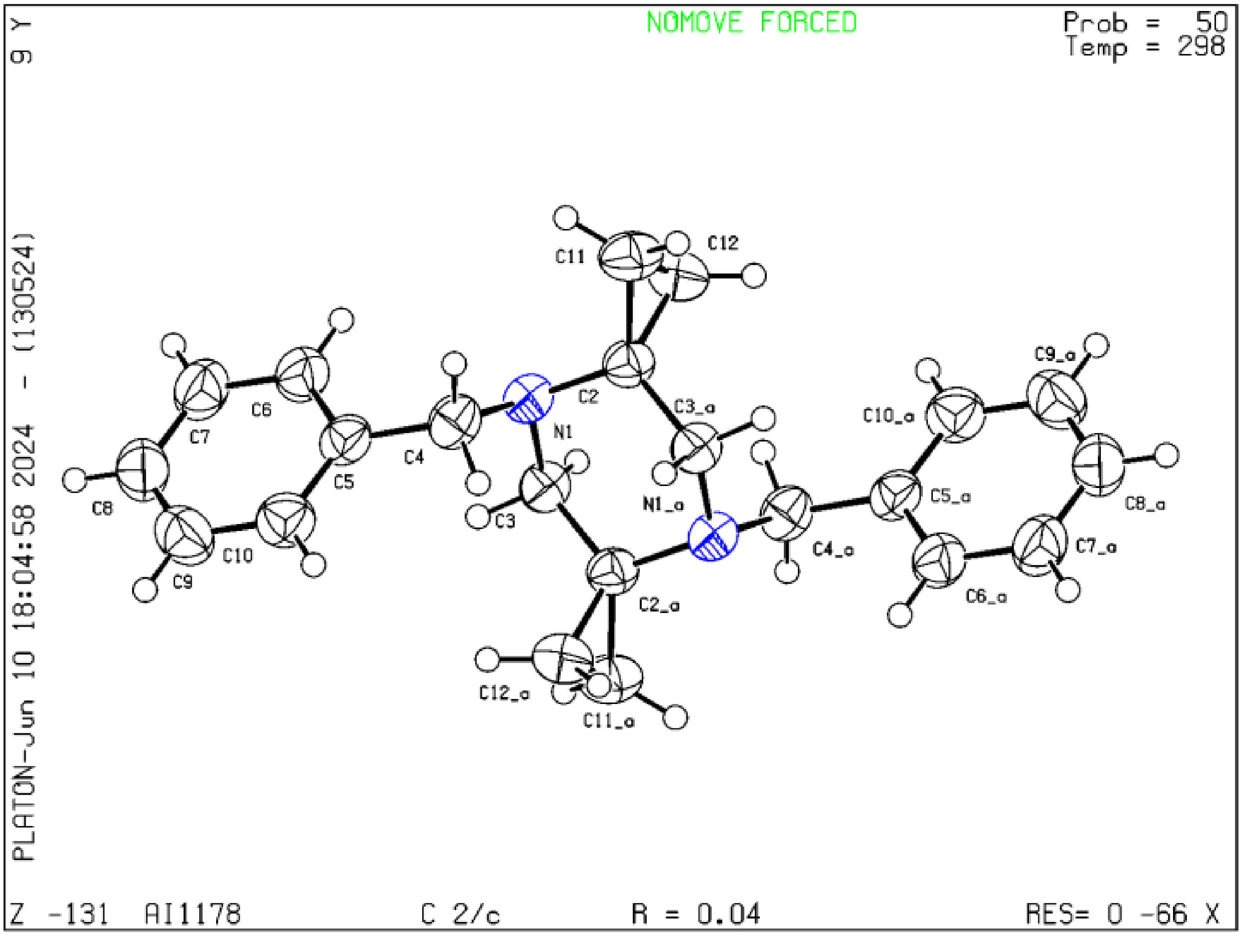


Table 1 Crystal data and structure refinement for S25

Empirical formula	$C_{22}H_{26}N_2$
Formula weight	318.45
Temperature/K	298(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	16.1970(5)
b/Å	5.7050(2)
c/Å	20.8080(6)
α/°	90
β/°	110.3740(10)
γ/°	90
Volume/Å^3	1802.45(10)
Z	4
ρ_{calc}g/cm^3	1.173
μ/mm^{-1}	0.519
F(000)	688.0
Crystal size/mm^3	0.346 × 0.264 × 0.063
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	12.024 to 145.32
Index ranges	$-20 \leq h \leq 17$, $-7 \leq k \leq 7$, $-25 \leq l \leq 25$
Reflections collected	14634
Independent reflections	1767 [R_{int} = 0.0455, R_{sigma} = 0.0259]
Data/restraints/parameters	1767/0/110
Goodness-of-fit on F^2	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.0438, wR_2 = 0.1070
Final R indexes [all data]	R_1 = 0.0523, wR_2 = 0.1165
Largest diff. peak/hole / e Å^{-3}	0.14/-0.14

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for S25. U$_{eq}$ is defined as 1/3 of the trace of the orthogonalised U$_{IJ}$ tensor.

Atom	*x*	*y*	*z*	U(eq)
N1	3280.4(6)	2232.6(18)	4788.7(5)	41.8(3)
C2	3337.8(8)	2258(2)	5501.7(6)	42.3(3)
C3	2394.6(7)	1433(2)	4360.8(6)	43.2(3)
C4	3526.2(8)	4499(2)	4570.4(7)	48.3(4)
C6	4068.0(9)	2520(3)	3710.2(8)	55.4(4)
C5	3620.8(8)	4364(2)	3874.9(7)	45.6(3)
C8	3836.1(10)	4173(3)	2605.1(8)	61.3(4)
C7	4174.1(11)	2429(3)	3080.8(8)	61.8(4)
C10	3285.2(9)	6107(2)	3392.8(7)	55.5(4)
C11	4249.3(9)	2279(3)	6022.3(7)	57.8(4)
C12	3707.0(9)	73(3)	5906.2(7)	55.5(4)
C9	3391.0(10)	6019(3)	2760.6(8)	63.7(4)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S25. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U$_{11}$	U$_{22}$	U$_{33}$	U$_{23}$	U$_{13}$	U$_{12}$
N1	38.3(5)	42.8(6)	45.3(6)	-2.9(4)	15.9(4)	0.2(4)
C2	37.9(6)	44.3(7)	42.4(6)	-2.9(5)	11.1(5)	-0.3(5)
C3	42.3(6)	44.4(7)	43.1(6)	-5.8(5)	14.9(5)	-1.9(5)
C4	47.3(7)	45.0(7)	56.1(8)	-3.2(6)	22.3(6)	-2.7(5)
C6	55.8(8)	54.2(8)	62.6(8)	9.5(6)	28.5(7)	11.3(6)
C5	38.7(6)	45.5(7)	54.8(7)	1.3(5)	18.9(5)	-1.6(5)
C8	61.9(9)	72.3(10)	53.7(8)	2.6(7)	25.2(7)	-6.6(7)
C7	63.7(9)	63.2(9)	68.6(9)	2.0(7)	35.8(7)	9.3(7)
C10	55.2(8)	47.5(8)	64.4(8)	3.8(6)	21.6(7)	5.7(6)
C11	41.2(7)	65.6(9)	57.0(8)	-4.8(7)	5.0(6)	1.1(6)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S25. The Anisotropic displacement factor exponent takes the form: -2π^2[h^{2}a*^{2}U$_{11}$+2hka*b*U$_{12}$+…].

Atom	U$_{11}$	U$_{22}$	U$_{33}$	U$_{23}$	U$_{13}$	U$_{12}$
C12	51.3(7)	54.3(8)	55.5(8)	6.2(6)	11.6(6)	7.9(6)
C9	69.1(9)	60.9(9)	58.3(9)	13.0(7)	18.7(7)	2.4(7)

Table 4 Bond Lengths for S25.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C2	1.4539(15)	C6	C5	1.3865(18)
N1	C3	1.4730(15)	C6	C7	1.380(2)
N1	C4	1.4706(16)	C5	C10	1.3821(19)
C2	C3^1	1.5109(16)	C8	C7	1.376(2)
C2	C11	1.4966(17)	C8	C9	1.377(2)
C2	C12	1.5063(18)	C10	C9	1.385(2)
C4	C5	1.5094(17)	C11	C12	1.505(2)

^{1}1/2-X,1/2-Y,1-Z

Table 5 Bond Angles for S25.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	N1	C3	108.82(9)	C7	C6	C5	120.76(13)
C2	N1	C4	112.24(9)	C6	C5	C4	120.78(12)
C4	N1	C3	113.39(10)	C10	C5	C4	120.92(12)
N1	C2	C3^1	115.00(10)	C10	C5	C6	118.28(12)
N1	C2	C11	115.79(11)	C7	C8	C9	119.59(14)
N1	C2	C12	115.71(11)	C8	C7	C6	120.39(14)
C11	C2	C3^1	120.05(11)	C5	C10	C9	121.04(13)
C11	C2	C12	60.17(9)	C2	C11	C12	60.23(8)
C12	C2	C3^1	119.23(11)	C11	C12	C2	59.60(9)

Table 5 Bond Angles for S25.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	C3	C2[1]	113.34(10)	C8	C9	C10	119.92(14)
N1	C4	C5	112.35(10)				

[1] 1/2-X,1/2-Y,1-Z

Table 6 Hydrogen Atom Coordinates (Å×10⁴) and Isotropic Displacement Parameters (Å²×10³) for S25.

Atom	*x*	*y*	*z*	U(eq)
H3A	2340.7	-224.11	4442.57	52
H3AB	2327.1	1623.78	3881.91	52
H4A	4079.26	5017.5	4905.34	58
H4AB	3080.31	5653.24	4555.94	58
H6	4299.13	1330.07	4027.63	67
H8	3907.71	4105.38	2181	74
H7	4475.88	1180.89	2977.63	74
H10	2983.59	7358.31	3494.41	67
H11A	4344.46	3134.4	6444.95	69
H11B	4739.31	2317.22	5856.1	69
H12A	3474.83	-394.18	6258.21	67
H12B	3869.85	-1211.71	5669.11	67
H9	3161.75	7205.39	2441.67	76

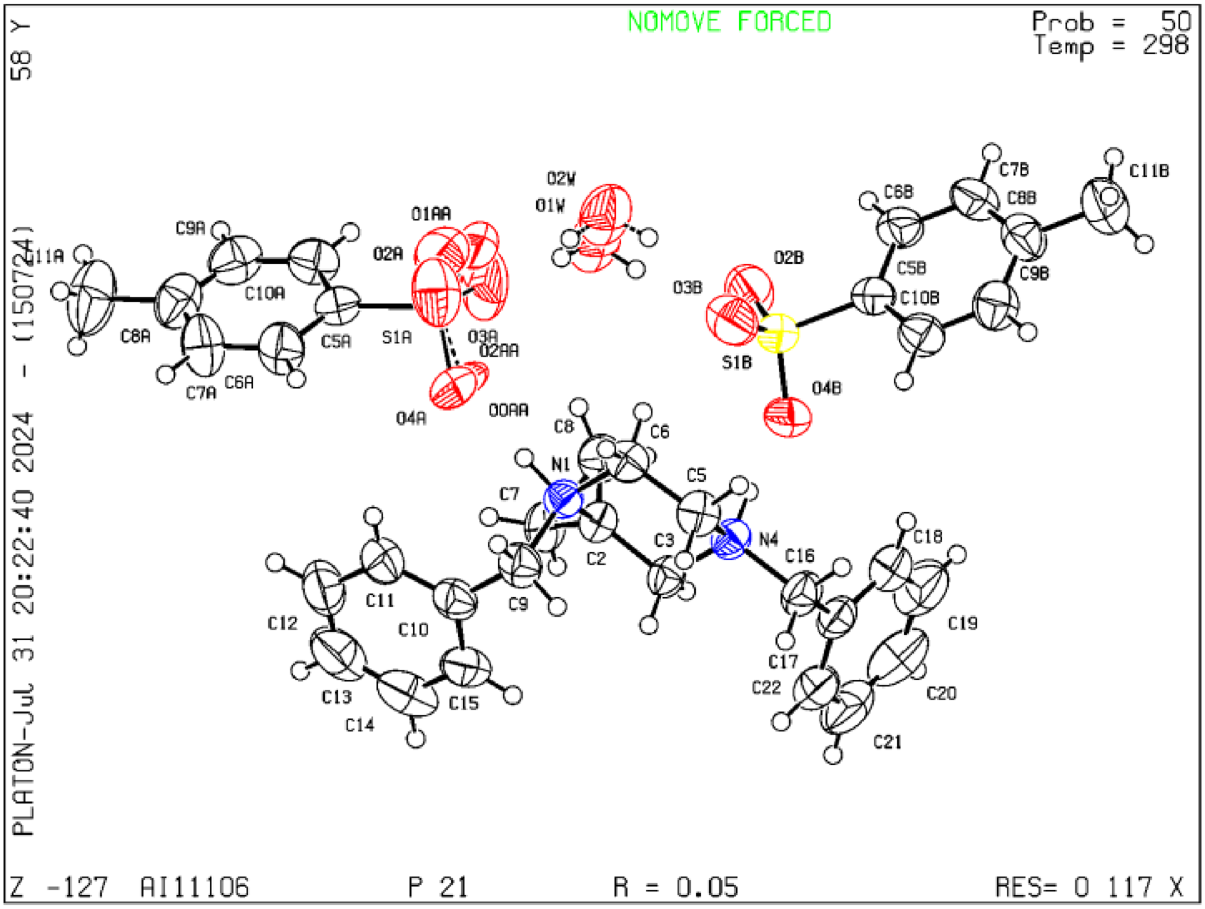

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Table 1 Crystal data and structure refinement for S27 X 2TSOH X H_2O.

Empirical formula	$C_{34}H_{42}N_2O_7S_2$
Formula weight	654.81
Temperature/K	298(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	14.120(3)
b/Å	9.381(2)
c/Å	14.431(3)
α/°	90
β/°	118.580(14)
γ/°	90
Volume/$Å^3$	1678.5(7)
Z	2
ρ_{calc}g/cm^3	1.296
μ/mm^{-1}	1.847
F(000)	696.0
Crystal size/mm^3	0.65 × 0.074 × 0.053
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.976 to 144.822
Index ranges	$-17 \leq h \leq 17, -11 \leq k \leq 11, -17 \leq l \leq 17$
Reflections collected	29994
Independent reflections	6534 [R_{int} = 0.1585, R_{sigma} = 0.0952]
Data/restraints/parameters	6534/394/445
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0502, wR_2 = 0.1277
Final R indexes [all data]	R_1 = 0.0758, wR_2 = 0.1453
Largest diff. peak/hole / e Å^{-3}	0.26/-0.31
Flack parameter	0.038(12)

Table 2 Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times10^3$) for S27 X 2TSOH X H_2O. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
N1	4935(3)	3270(4)	6951(3)	44.5(8)
C2	3837(3)	3514(4)	6829(3)	43.4(9)
C3	3037(4)	2457(5)	6108(3)	46.1(9)
N4	2937(3)	2546(4)	5029(3)	46.5(8)
C6	4855(4)	3351(5)	5879(3)	51.2(10)
C5	4034(4)	2334(5)	5110(4)	52.8(10)
C9	5506(4)	1930(5)	7559(4)	55.6(11)
C8	3509(5)	5027(5)	6798(4)	61.6(13)
C7	3744(4)	4112(5)	7738(3)	57.6(12)
C10	5607(4)	1910(5)	8636(4)	55.8(11)
C11	6427(5)	2676(6)	9448(4)	68.4(14)
C12	6480(6)	2766(7)	10430(4)	87.8(19)
C13	5697(7)	2097(7)	10591(5)	97(2)
C14	4918(7)	1309(7)	9824(5)	88.2(18)
C17	1025(4)	1702(5)	4141(3)	55.1(11)
C16	2127(4)	1480(5)	4268(4)	58.0(11)
C15	4875(5)	1200(6)	8847(5)	70.3(14)
C18	345(5)	2709(6)	3436(4)	69.5(14)
C19	-673(6)	2977(8)	3347(6)	92.0(19)
C20	-992(6)	2217(8)	3962(7)	97(2)
O1W	3767(12)	9028(10)	6438(12)	101(4)
O2W	4060(30)	9140(30)	6110(30)	101(4)
S1B	2557.9(10)	6362.0(12)	4061.4(9)	55.4(3)
S1A	6614.9(11)	6776.1(14)	8059.5(9)	63.8(4)
C21	-346(6)	1194(8)	4634(5)	90.2(19)
C22	663(5)	940(7)	4730(4)	74.9(16)

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for S27 X 2TSOH X H_2O. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O2A	7314(15)	7070(20)	7637(10)	101(5)
O3A	5658(14)	7630(20)	7604(11)	122(6)
O2B	2401(4)	7649(4)	4509(3)	92.1(15)
O4A	6368(16)	5269(13)	8026(8)	91(4)
O3B	3668(3)	6048(5)	4374(3)	85.4(13)
C5A	7339(4)	7214(5)	9408(4)	53.5(11)
O4B	2023(3)	5156(4)	4237(3)	63.5(9)
C6A	8108(4)	6282(6)	10115(4)	68.9(14)
C5B	1904(4)	6629(5)	2678(4)	51.0(10)
C7A	8700(5)	6650(8)	11169(4)	80.7(17)
C6B	1576(4)	7967(5)	2249(4)	60.2(12)
C8A	8554(5)	7933(7)	11551(5)	74.7(15)
C7B	1093(5)	8144(6)	1173(4)	67.6(14)
C9A	7782(5)	8828(6)	10836(5)	73.7(15)
C8B	917(4)	7022(6)	501(4)	65.5(13)
C10A	7187(5)	8496(6)	9783(4)	65.8(13)
C9B	1263(5)	5683(6)	944(4)	65.1(13)
C11A	9232(6)	8315(12)	12700(5)	113(3)
C11B	380(6)	7227(8)	-681(5)	91(2)
C10B	1751(4)	5481(5)	2020(4)	58.5(12)
O0AA	5890(20)	5750(30)	8021(15)	72(6)
O1AA	6090(20)	8020(20)	7502(18)	95(7)
O2AA	7404(19)	6290(40)	7762(16)	90(7)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S27X2TSOHXH2O. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N1	42.3(19)	41.2(18)	47.9(18)	0.6(14)	19.9(15)	1.1(15)
C2	40(2)	44(2)	46(2)	-5.8(16)	20.9(17)	2.3(17)
C3	45(2)	52(2)	42(2)	-7.8(17)	21.3(17)	-5.3(18)
N4	49(2)	44.7(19)	46.4(18)	-7.5(14)	23.7(16)	-3.4(15)
C6	49(3)	55(3)	55(2)	2.5(19)	29(2)	3(2)
C5	54(3)	57(3)	54(2)	-6.0(19)	31(2)	4(2)
C9	54(3)	50(2)	58(2)	4(2)	22(2)	12(2)
C8	69(3)	46(3)	62(3)	-7(2)	25(2)	12(2)
C7	60(3)	65(3)	47(2)	-9(2)	25(2)	6(2)
C10	59(3)	46(2)	58(2)	10(2)	24(2)	11(2)
C11	67(3)	63(3)	58(3)	10(2)	17(2)	5(3)
C12	108(5)	78(4)	50(3)	2(3)	16(3)	6(4)
C13	144(7)	83(5)	69(4)	18(3)	55(4)	18(4)
C14	120(5)	72(4)	91(4)	28(3)	66(4)	15(4)
C17	54(3)	56(3)	50(2)	-13(2)	21.0(19)	-16(2)
C16	63(3)	54(3)	52(2)	-15(2)	24(2)	-11(2)
C15	78(4)	56(3)	76(3)	15(3)	36(3)	-2(3)
C18	58(3)	74(3)	63(3)	-2(2)	18(2)	-15(3)
C19	62(4)	85(5)	111(5)	-13(4)	27(3)	-9(3)
C20	71(4)	92(5)	131(6)	-39(4)	52(4)	-27(3)
O1W	103(7)	62(3)	99(7)	-22(4)	17(4)	11(4)
O2W	103(7)	62(3)	99(7)	-22(4)	17(4)	11(4)
S1B	56.5(7)	48.3(6)	55.2(6)	4.8(4)	21.6(5)	-4.5(5)
S1A	69.6(8)	60.4(8)	51.9(6)	0.1(5)	21.5(6)	-11.7(6)
C21	84(4)	112(5)	88(4)	-34(4)	52(3)	-50(4)
C22	77(4)	77(4)	65(3)	-9(3)	29(3)	-30(3)
O2A	126(8)	125(10)	71(5)	-19(6)	62(5)	-56(7)
O3A	82(8)	116(10)	98(6)	0(7)	-14(6)	36(7)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for S27X2TSOHXH2O. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O2B	133(4)	58(2)	63(2)	-6.9(18)	29(2)	5(2)
O4A	103(9)	56(5)	76(4)	-4(4)	13(5)	-32(5)
O3B	46(2)	109(3)	91(3)	38(2)	24.4(18)	2(2)
C5A	54(3)	48(3)	63(3)	-0.3(19)	32(2)	-5(2)
O4B	64(2)	63(2)	64(2)	9.9(16)	32.0(17)	-9.5(17)
C6A	67(3)	60(3)	67(3)	-3(2)	22(2)	16(3)
C5B	49(2)	45(2)	61(2)	6.2(19)	27.7(19)	0.5(19)
C7A	64(3)	105(5)	58(3)	0(3)	17(2)	19(3)
C6B	72(3)	45(3)	63(3)	0(2)	32(3)	-2(2)
C8A	70(4)	98(4)	65(3)	-23(3)	40(3)	-18(3)
C7B	78(4)	56(3)	67(3)	18(2)	33(3)	7(3)
C9A	90(4)	68(3)	80(3)	-20(3)	55(3)	-12(3)
C8B	63(3)	79(3)	56(3)	12(2)	30(2)	3(3)
C10A	74(4)	58(3)	73(3)	0(2)	42(3)	5(3)
C9B	68(4)	70(3)	60(3)	-6(2)	33(2)	0(3)
C11A	92(5)	171(7)	73(4)	-43(4)	37(4)	-20(5)
C11B	97(5)	108(5)	60(3)	10(3)	30(3)	-2(4)
C10B	62(3)	48(3)	64(3)	4(2)	30(2)	8(2)
O0AA	73(11)	59(10)	79(8)	-13(7)	34(8)	-37(8)
O1AA	83(12)	69(9)	77(8)	10(6)	-6(9)	-20(7)
O2AA	86(10)	135(18)	59(8)	-14(11)	43(7)	13(11)

Table 4 Bond Lengths for S27X2TSOHXH2O.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C2	1.493(5)	S1B	O3B	1.439(4)
N1	C6	1.497(5)	S1B	O4B	1.448(3)
N1	C9	1.524(6)	S1B	C5B	1.771(5)

Table 4 Bond Lengths for S27X2TSOHXH2O.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C2	C3	1.489(6)	S1A	O2A	1.413(12)
C2	C8	1.487(6)	S1A	O3A	1.429(10)
C2	C7	1.488(6)	S1A	O4A	1.451(9)
C3	N4	1.497(5)	S1A	C5A	1.760(5)
N4	C5	1.510(6)	S1A	O0AA	1.392(15)
N4	C16	1.520(5)	S1A	O1AA	1.41(2)
C6	C5	1.502(6)	S1A	O2AA	1.446(19)
C9	C10	1.491(7)	C21	C22	1.385(9)
C8	C7	1.502(7)	C5A	C6A	1.388(7)
C10	C11	1.389(7)	C5A	C10A	1.377(7)
C10	C15	1.381(7)	C6A	C7A	1.384(7)
C11	C12	1.386(8)	C5B	C6B	1.378(7)
C12	C13	1.383(10)	C5B	C10B	1.384(7)
C13	C14	1.348(10)	C7A	C8A	1.380(9)
C14	C15	1.386(8)	C6B	C7B	1.374(7)
C17	C16	1.493(7)	C8A	C9A	1.372(9)
C17	C18	1.384(8)	C8A	C11A	1.508(8)
C17	C22	1.381(7)	C7B	C8B	1.371(8)
C18	C19	1.403(9)	C9A	C10A	1.375(8)
C19	C20	1.371(11)	C8B	C9B	1.388(8)
C20	C21	1.359(10)	C8B	C11B	1.512(7)
S1B	O2B	1.436(4)	C9B	C10B	1.377(7)

Table 5 Bond Angles for S27X2TSOHXH2O.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C2	N1	C6	108.0(3)	O3B	S1B	C5B	106.6(2)
C2	N1	C9	115.3(3)	O4B	S1B	C5B	105.8(2)
C6	N1	C9	113.3(3)	O2A	S1A	O3A	113.3(8)

Table 5 Bond Angles for S27X2TSOHXH2O.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C3	C2	N1	112.2(3)	O2A	S1A	O4A	112.4(7)
C8	C2	N1	116.1(4)	O2A	S1A	C5A	106.0(5)
C8	C2	C3	119.5(4)	O3A	S1A	O4A	111.6(7)
C8	C2	C7	60.7(3)	O3A	S1A	C5A	107.4(6)
C7	C2	N1	118.6(4)	O4A	S1A	C5A	105.5(4)
C7	C2	C3	120.7(4)	O0AA	S1A	C5A	103.5(8)
C2	C3	N4	110.7(3)	O0AA	S1A	O1AA	111.9(11)
C3	N4	C5	109.2(3)	O0AA	S1A	O2AA	115.4(12)
C3	N4	C16	112.3(3)	O1AA	S1A	C5A	107.9(10)
C5	N4	C16	111.0(3)	O1AA	S1A	O2AA	111.1(14)
N1	C6	C5	112.4(4)	O2AA	S1A	C5A	106.2(9)
C6	C5	N4	112.0(4)	C20	C21	C22	120.0(7)
C10	C9	N1	111.8(4)	C17	C22	C21	121.0(6)
C2	C8	C7	59.7(3)	C6A	C5A	S1A	120.1(4)
C2	C7	C8	59.6(3)	C10A	C5A	S1A	121.4(4)
C11	C10	C9	119.9(5)	C10A	C5A	C6A	118.4(5)
C15	C10	C9	121.8(5)	C7A	C6A	C5A	120.0(5)
C15	C10	C11	118.2(5)	C6B	C5B	S1B	121.2(4)
C12	C11	C10	120.7(6)	C6B	C5B	C10B	119.4(4)
C13	C12	C11	119.2(6)	C10B	C5B	S1B	119.3(3)
C14	C13	C12	121.0(6)	C8A	C7A	C6A	122.0(6)
C13	C14	C15	119.8(7)	C7B	C6B	C5B	119.8(5)
C18	C17	C16	120.1(5)	C7A	C8A	C11A	120.6(7)
C22	C17	C16	121.5(5)	C9A	C8A	C7A	116.8(5)
C22	C17	C18	118.4(5)	C9A	C8A	C11A	122.6(6)
C17	C16	N4	112.1(4)	C8B	C7B	C6B	122.0(5)
C10	C15	C14	121.1(6)	C8A	C9A	C10A	122.5(5)
C17	C18	C19	120.6(6)	C7B	C8B	C9B	117.7(4)
C20	C19	C18	119.1(7)	C7B	C8B	C11B	121.6(5)

Table 5 Bond Angles for S27X2TSOHXH2O.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C21	C20	C19	120.9(7)	C9B	C8B	C11B	120.7(6)
O2B	S1B	O3B	114.2(3)	C9A	C10A	C5A	120.3(5)
O2B	S1B	O4B	111.9(3)	C10B	C9B	C8B	121.3(5)
O2B	S1B	C5B	106.2(2)	C9B	C10B	C5B	119.8(5)
O3B	S1B	O4B	111.5(2)				

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for S27X2TSOHXH2O.

Atom	*x*	*y*	*z*	U(eq)
H1	5379.83	4079.96	7354.63	53
H3A	2340.75	2640.23	6064.16	55
H3B	3262.74	1504.62	6388.52	55
H4	2686.3	3505.95	4752.65	56
H6A	5554.17	3139.16	5938.59	61
H6B	4661.88	4315.49	5611.19	61
H5A	4272.09	1363.55	5332.66	63
H5B	3980.33	2469.31	4420.2	63
H9A	5104.56	1097.84	7171.33	67
H9B	6218.81	1881.73	7618.22	67
H8A	2762.24	5272.72	6325.48	74
H8B	4028.12	5759.57	6880.28	74
H7A	4404.74	4292.66	8386.64	69
H7B	3138.78	3805.78	7831.8	69
H11	6944.8	3132.28	9331	82
H12	7034.27	3270.19	10974.41	105
H13	5709.38	2192.76	11238.03	116
H14	4410.02	840.65	9950.63	106
H16A	2098.26	1569.91	3584.96	70

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for S27X2TSOHXH2O.

Atom	*x*	*y*	*z*	U(eq)
H16B	2367.18	521.59	4525.35	70
H15	4344.76	638.89	8325.31	84
H18	564.56	3213.08	3016.9	83
H19	-1125.5	3660.32	2876.86	110
H20	-1658.45	2404.81	3918.33	116
H1WA	4336.22	8542.28	6794.52	152
H1WB	3334.58	8451.64	5974.37	152
H2WA	4554.64	8595.48	6540.99	152
H2WB	3665.7	8596.32	5591.74	152
H21	-581.25	665.55	5030.49	108
H22	1103.94	244.87	5196.64	90
H6AA	8224.97	5409.23	9880.64	83
H7AA	9212.51	6013.26	11633.36	97
H6BA	1680.41	8747.52	2684.83	72
H7BA	880.32	9053.07	893	81
H9AA	7656.03	9692.98	11073.26	88
H10A	6679.7	9140.08	9322.05	79
H9BA	1162.46	4906.38	505.89	78
H11A	9173.63	9318.76	12791.27	169
H11B	9971.93	8076.17	12925.77	169
H11C	8982.31	7792.83	13113.07	169
H11D	-280.16	6692	-1007.89	137
H11E	852.65	6899	-940.93	137
H11F	225.12	8219.79	-844.46	137
H10B	1977.23	4575.41	2302.23	70

Table 7 Atomic Occupancy for S27 X 2TSOH X H_2O.

Atom	*Occupancy*	Atom	*Occupancy*	Atom	*Occupancy*
O1W	0.74(3)	H1WA	0.74(3)	H1WB	0.74(3)
O2W	0.26(3)	H2WA	0.26(3)	H2WB	0.26(3)
O2A	0.66(3)	O3A	0.66(3)	O4A	0.66(3)
O0AA	0.34(3)	O1AA	0.34(3)	O2AA	0.34(3)

3. Supplemental Information References

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2. *Angew. Chem. Int. Ed*. **2020**, 59, 11339 – 11344
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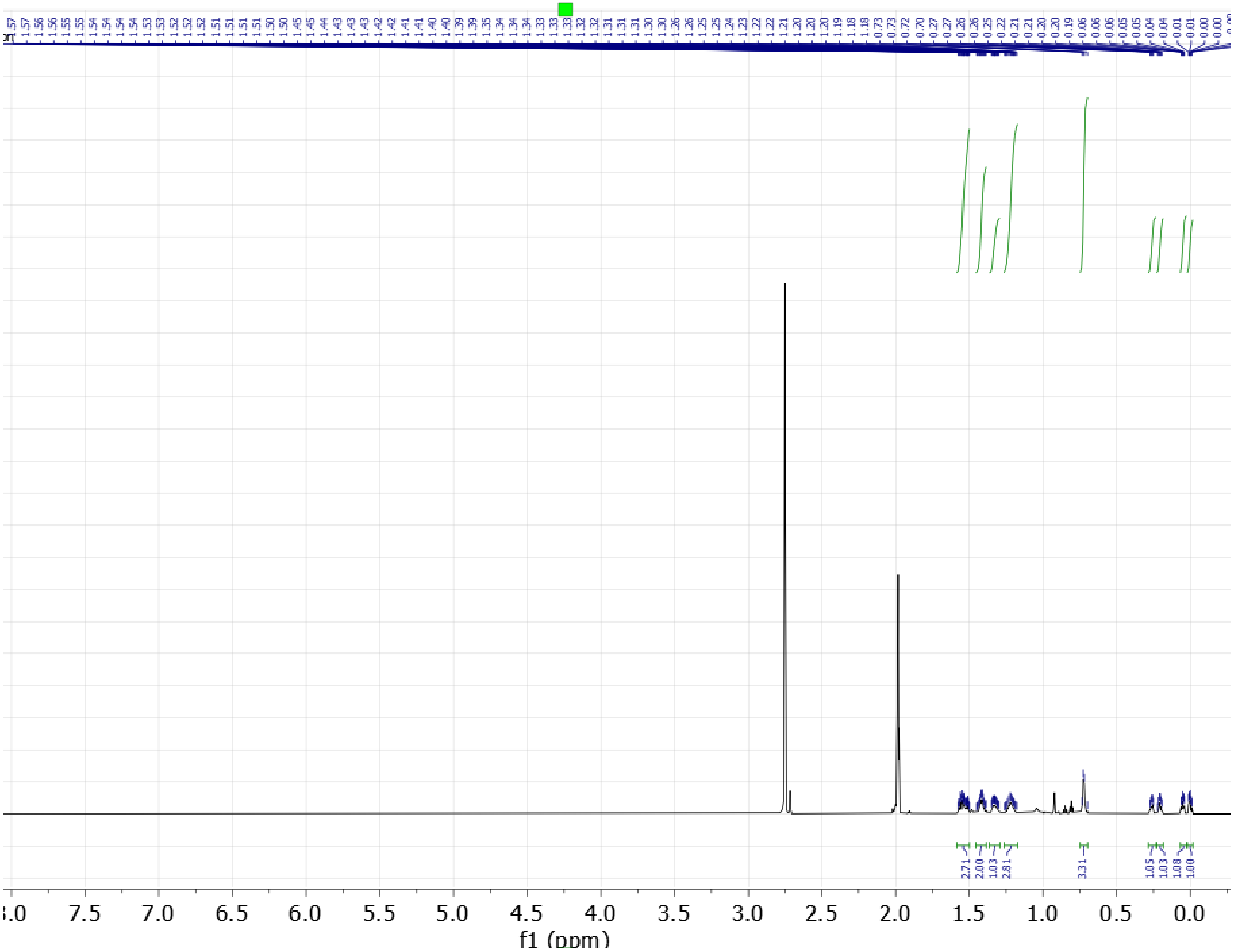
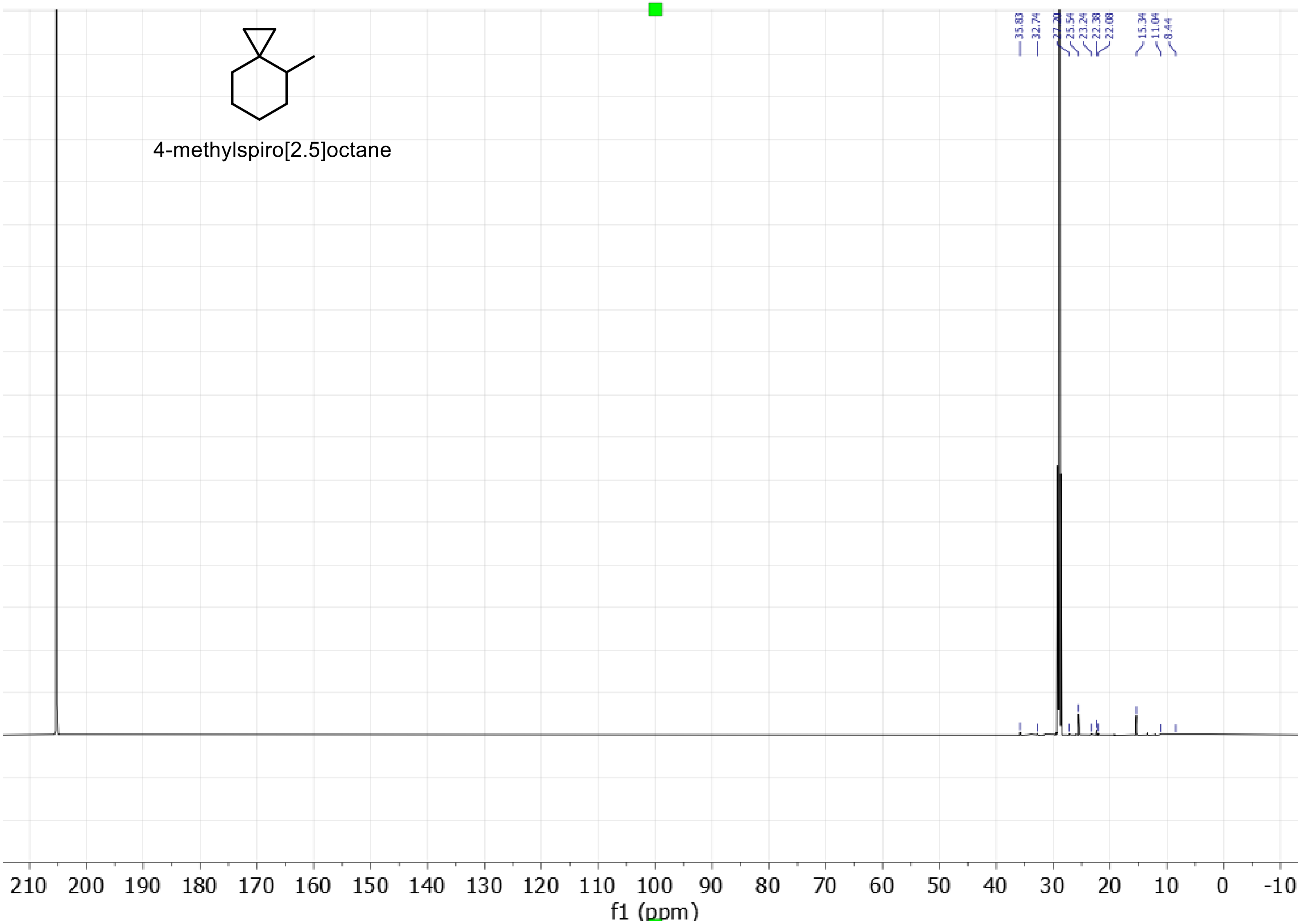
6. Sheldrick, G. M., SHELXT - Integrated space-group and crystal-structure determination. *Acta Cryst. Sect. A* **2015**, A71, 3-8. 6.
7. Sheldrick, G. M. "Crystal structure refinement with SHELXL." *Acta Cryst Sect. C*: *Structural Chemistry* 71, 1, **2015**, 3-8

4. Characterization Data: NMR Spectra

Compound **S1** **^{1}H NMR** (800 MHz, d_6-Acetone)

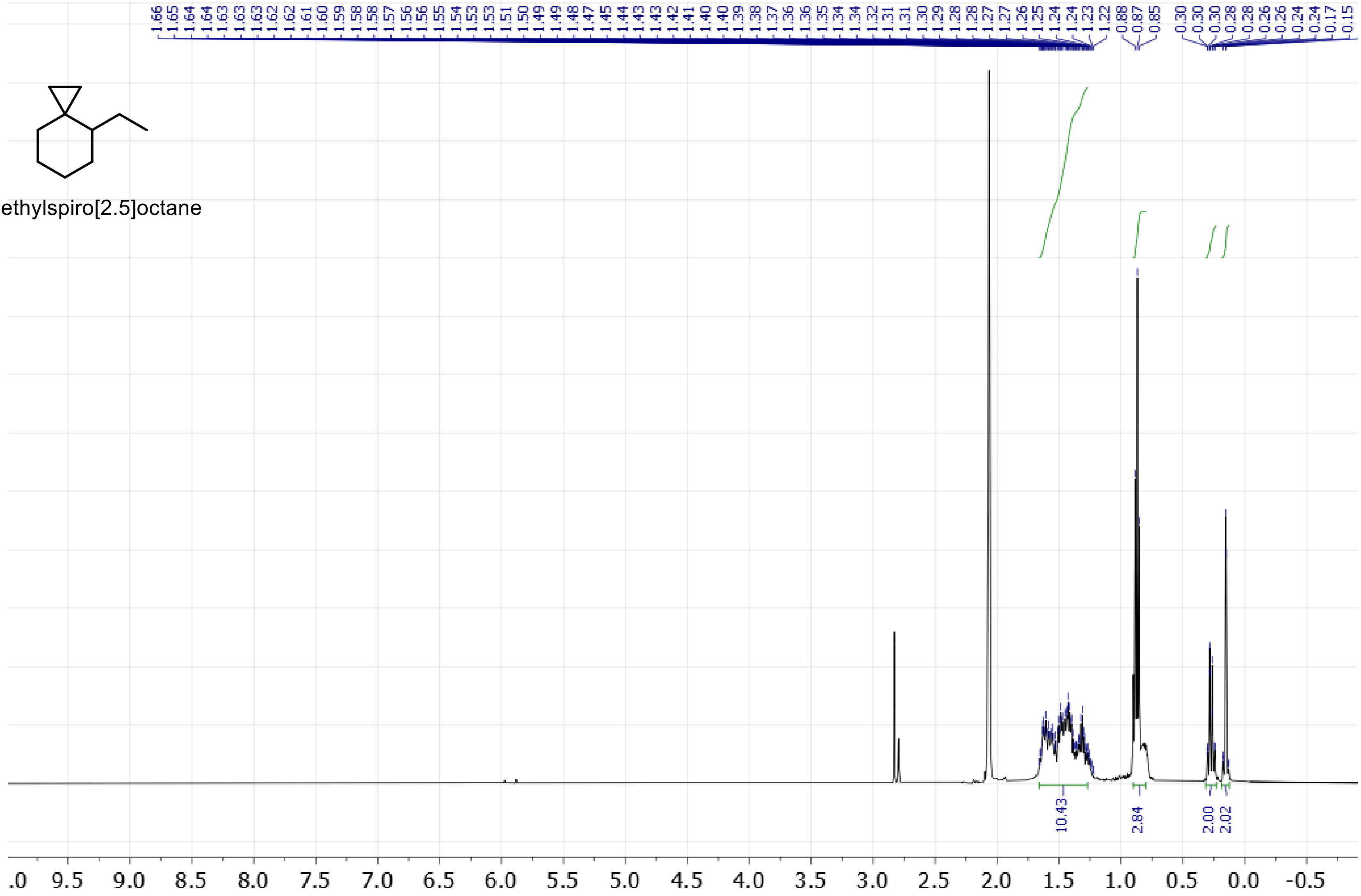


Compound **S1** ^{13}**C NMR** (201 MHz, *d*$_6$-Acetone)



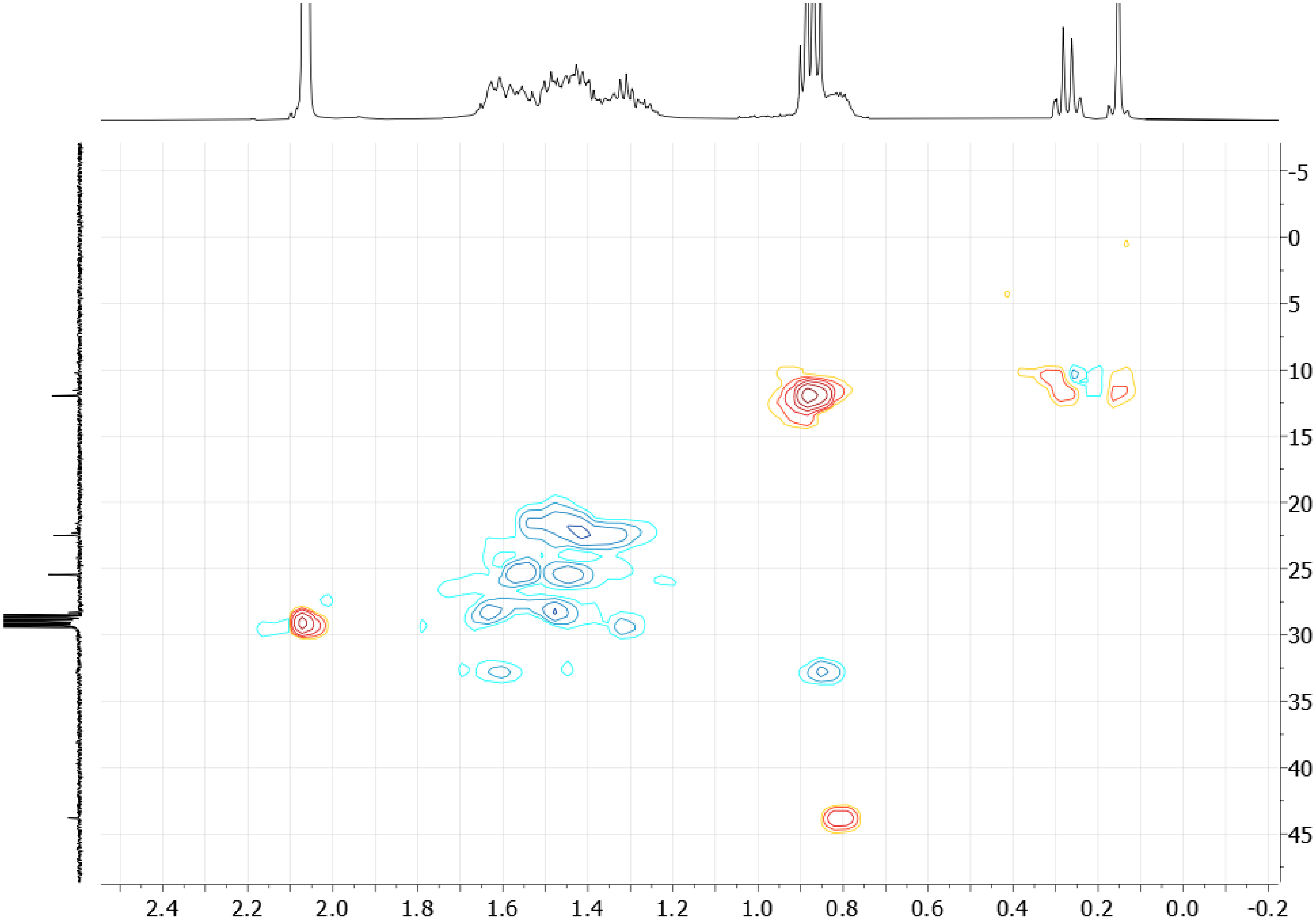
Compound **S2** **^{1}H NMR** (500 MHz, *d_6*-Acetone)

4-ethylspiro[2.5]octane

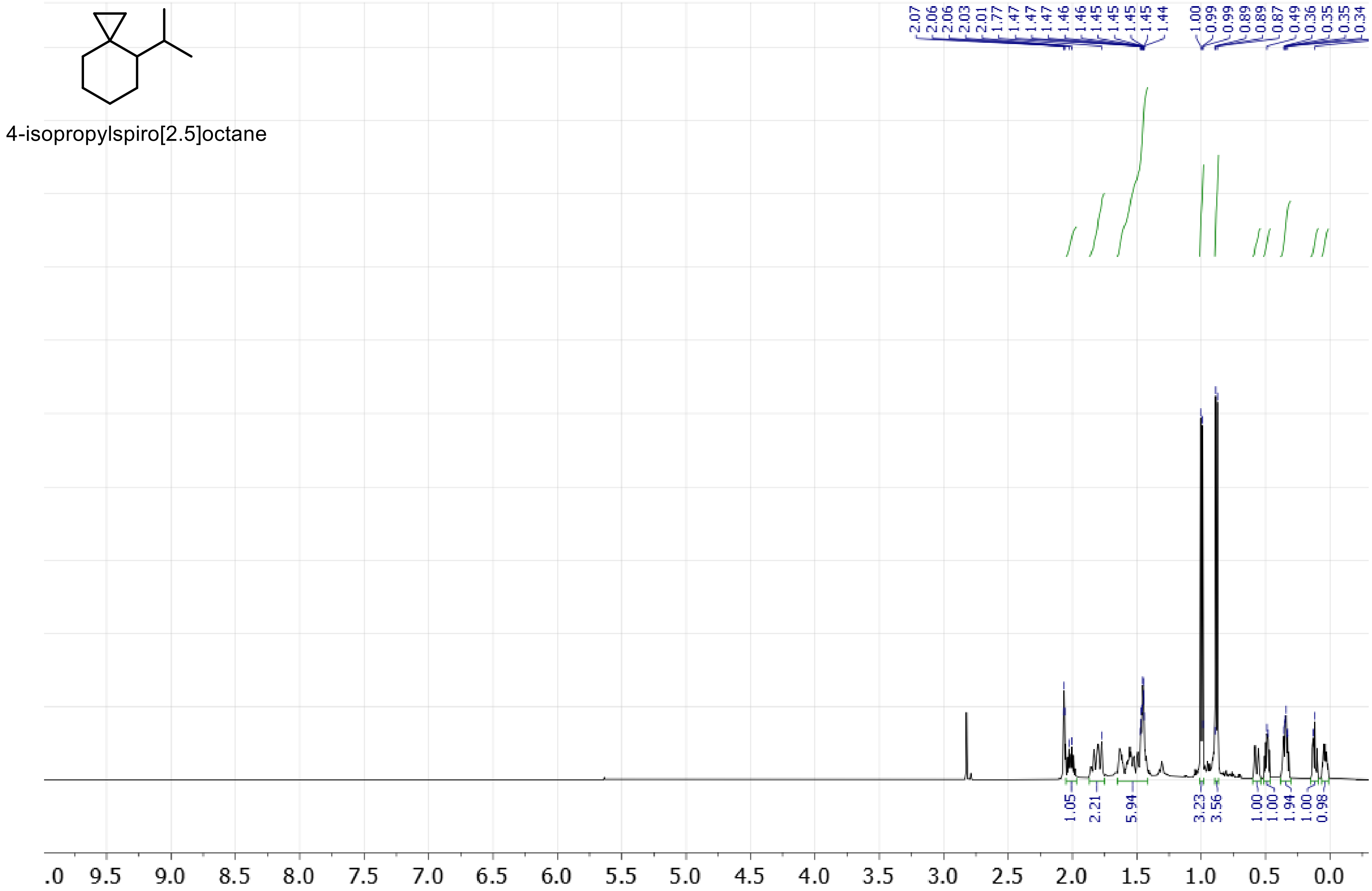


Compound **S2** **^{13}C NMR** (126 MHz, d_6-Acetone)

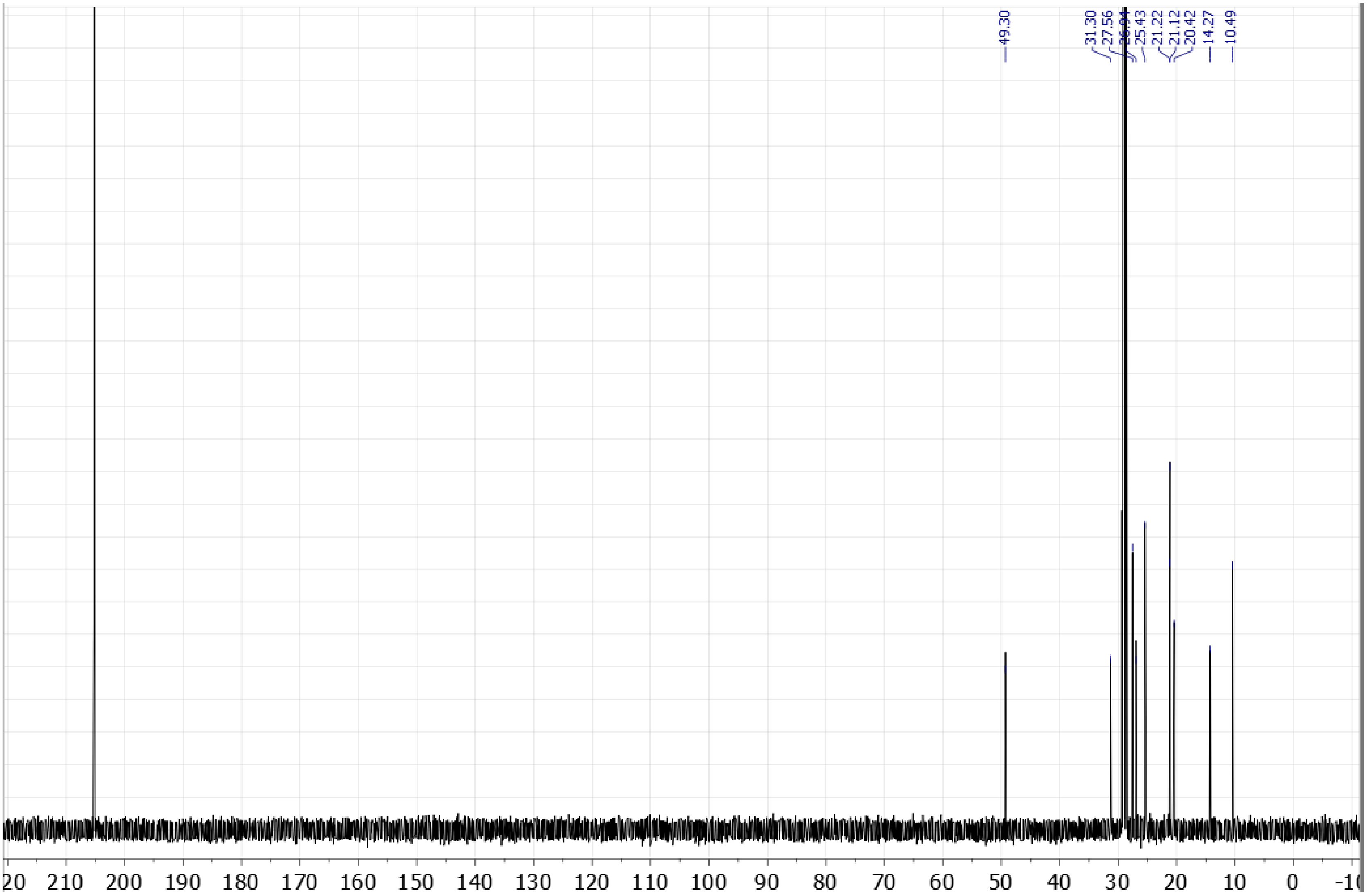
Compound **S2** **HSQC** (500 MHz, *d*$_6$-Acetone)



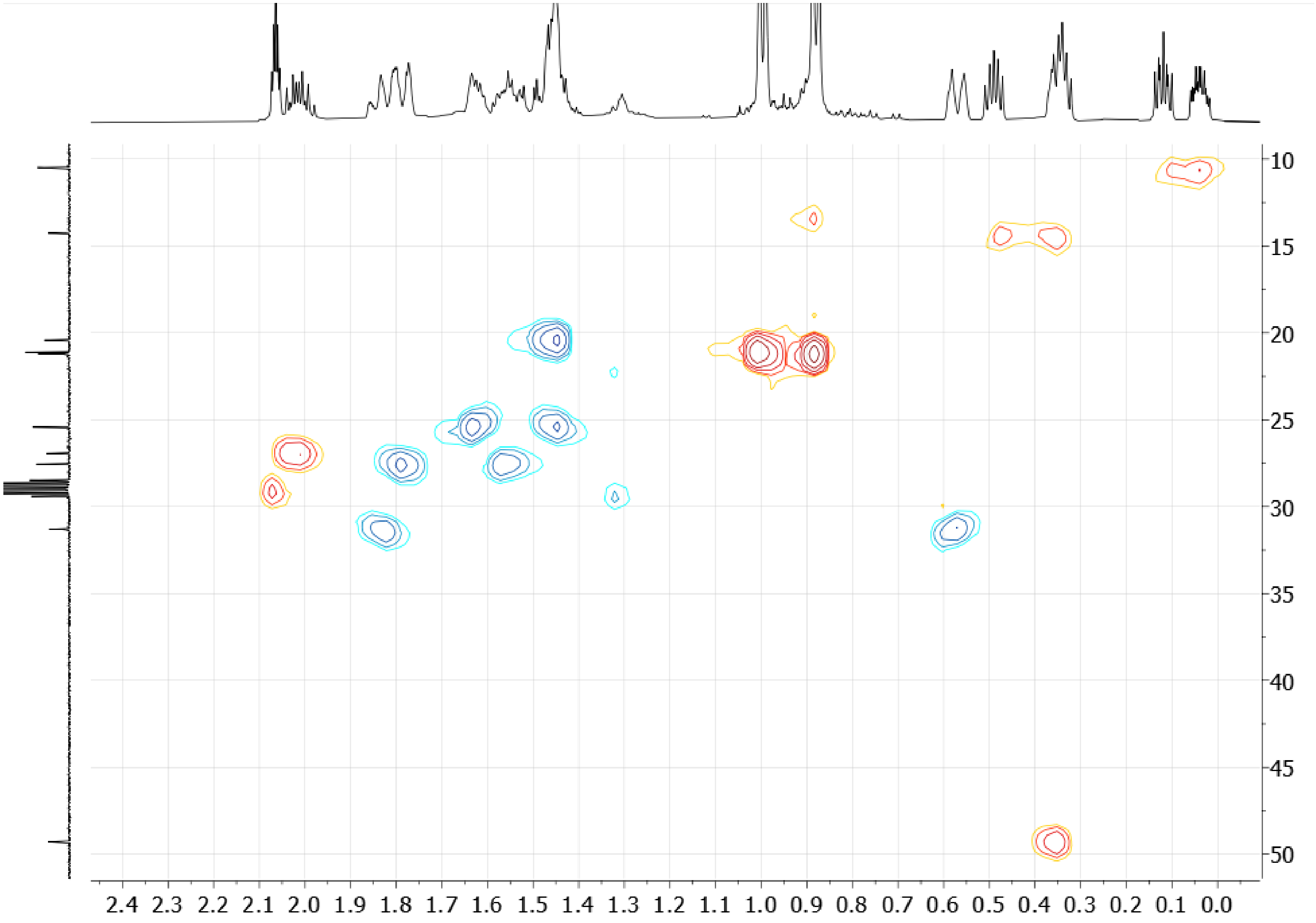
Compound **S3** **^{1}H NMR** (500 MHz, *d_6*-Acetone)


4-isopropylspiro[2.5]octane

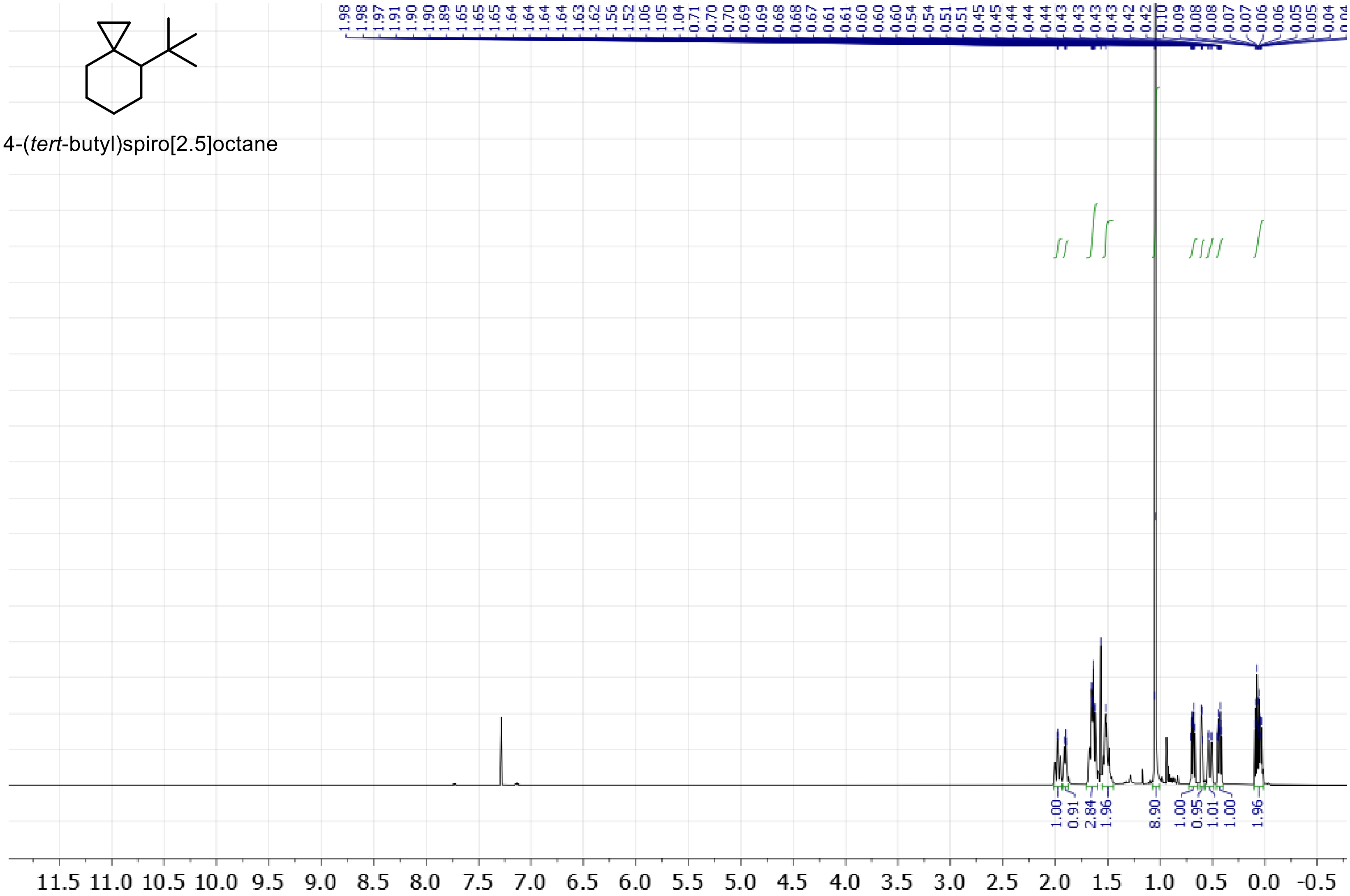
Compound **S3** **^{13}C NMR** (126 MHz, *d_6*-Acetone)



Compound **S3** **HSQC** (500 MHz, *d*$_6$-Acetone)

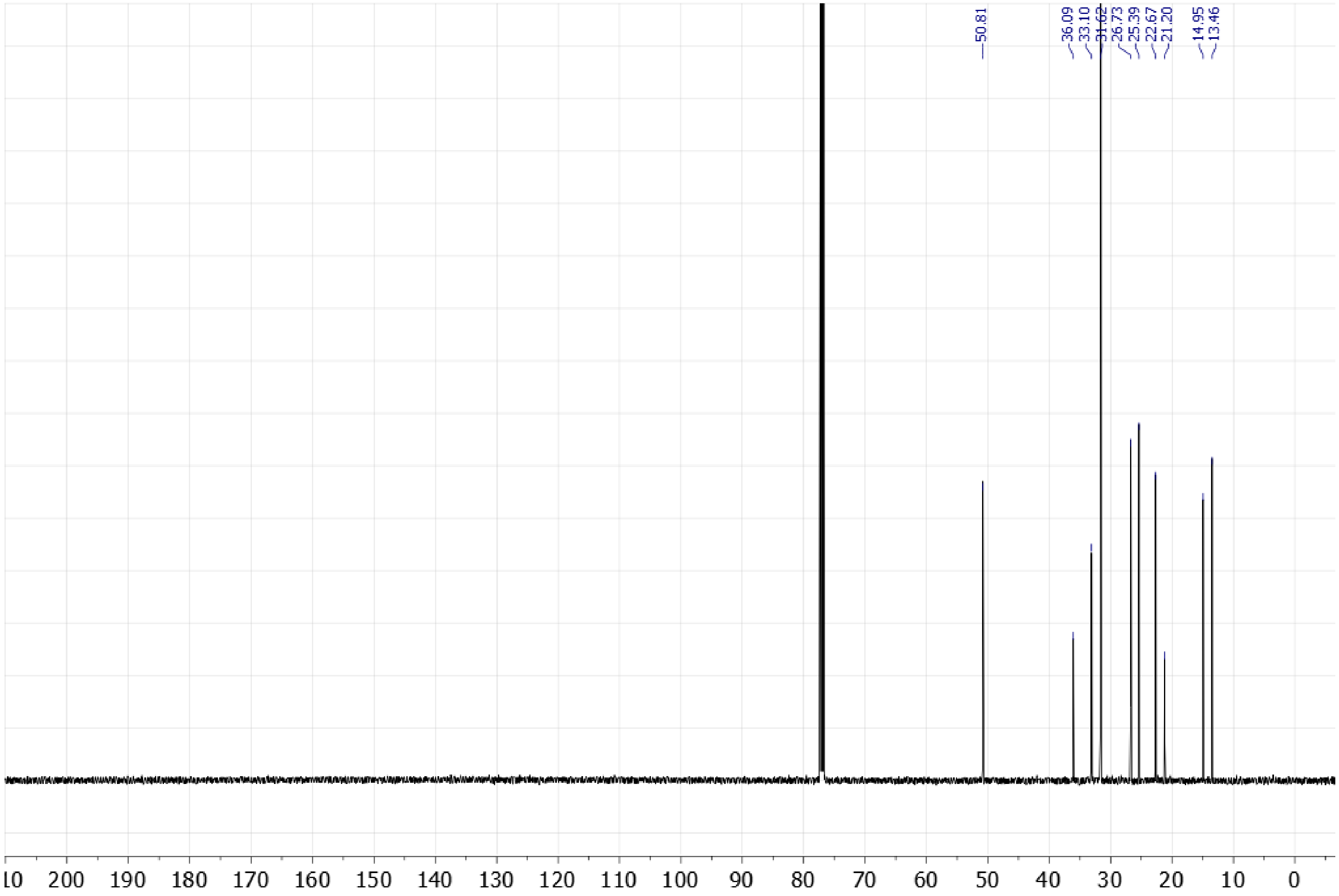


Compound **S4** **^{1}H NMR** (500 MHz, $CDCl_3$)

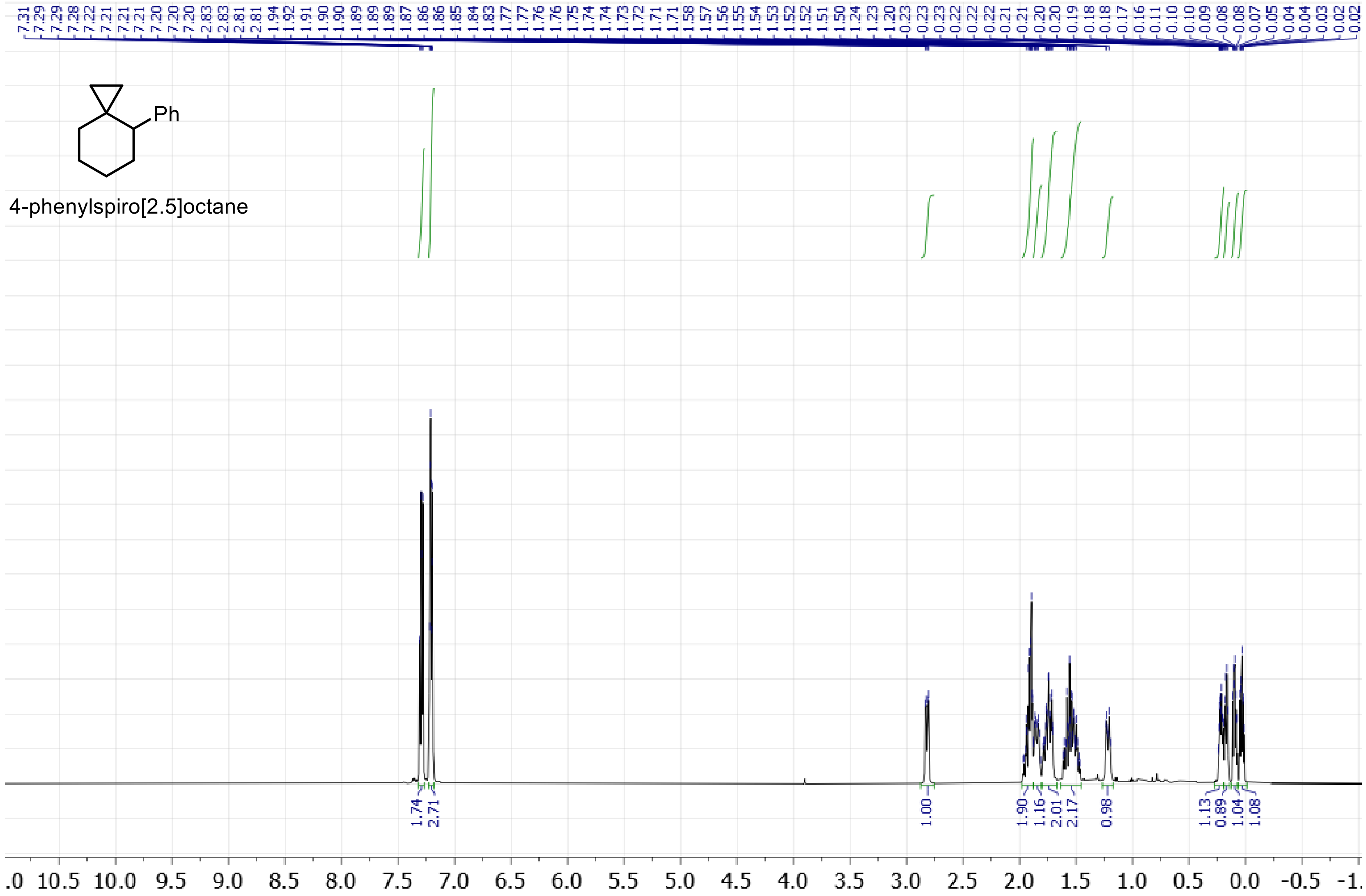


4-(*tert*-butyl)spiro[2.5]octane

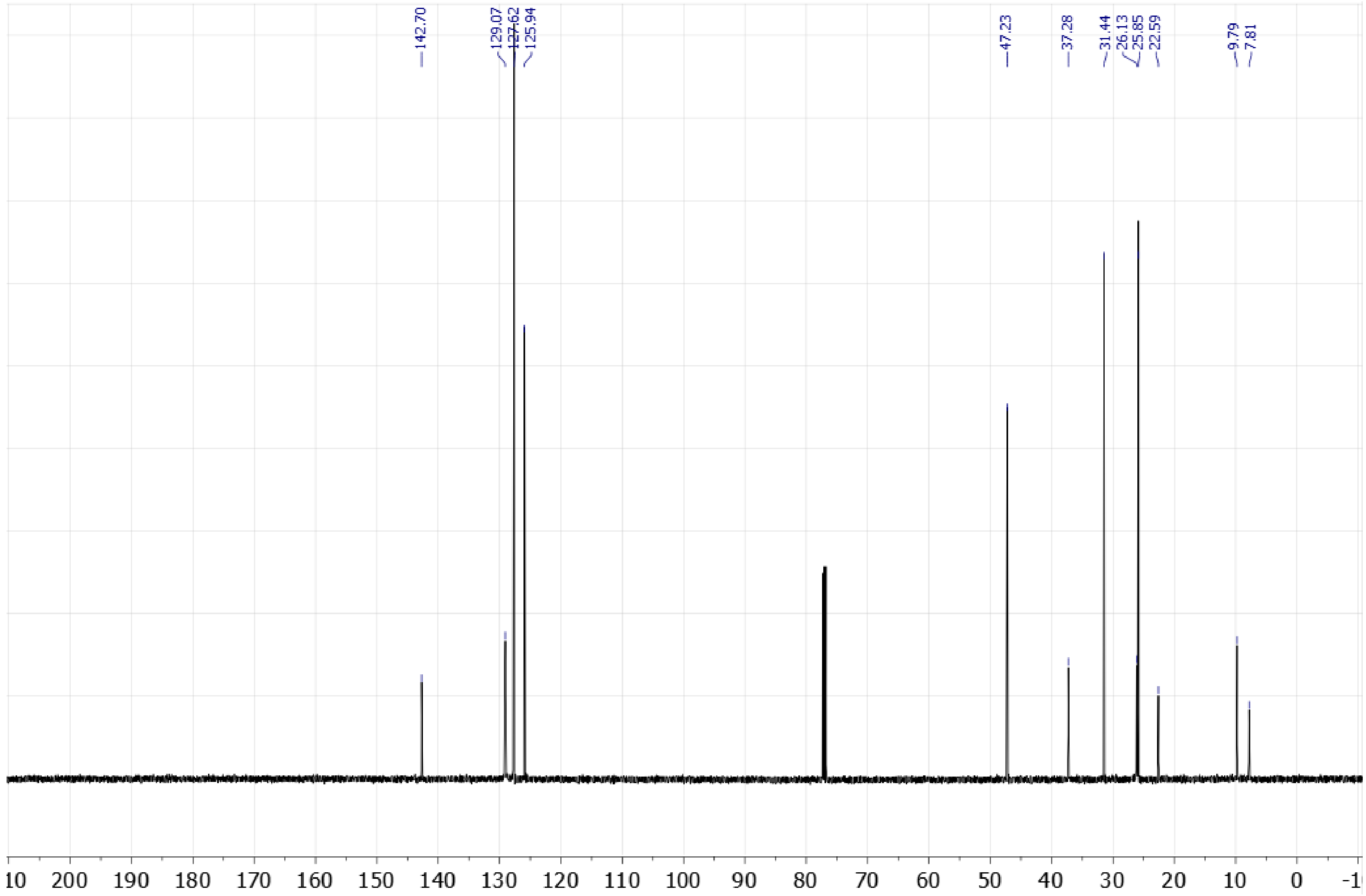
Compound **S4** ^{13}**C NMR** (126 MHz, CDCl$_3$))



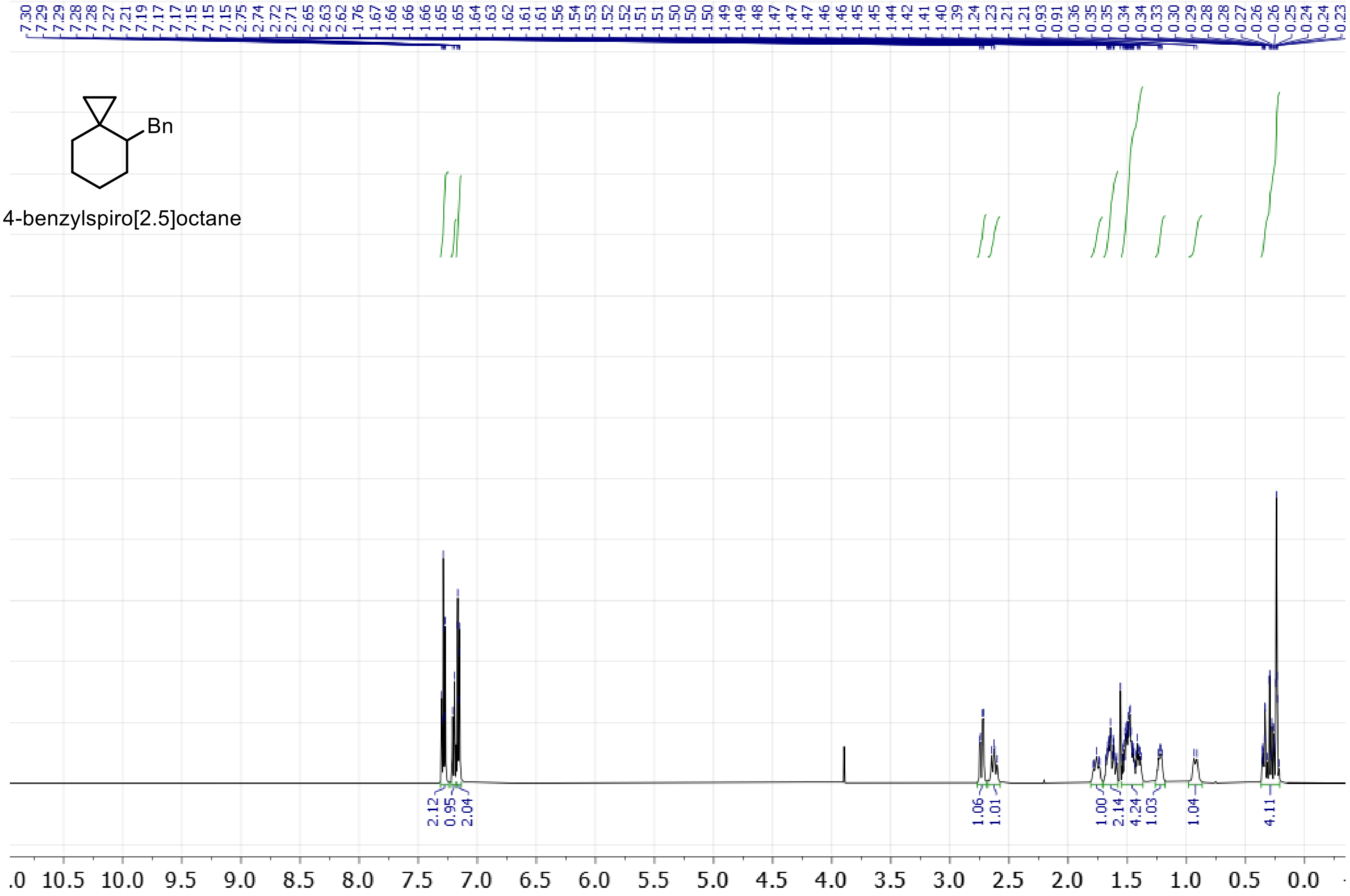
Compound **S5** ^{1}**H NMR** (500 MHz, $CDCl_3$)



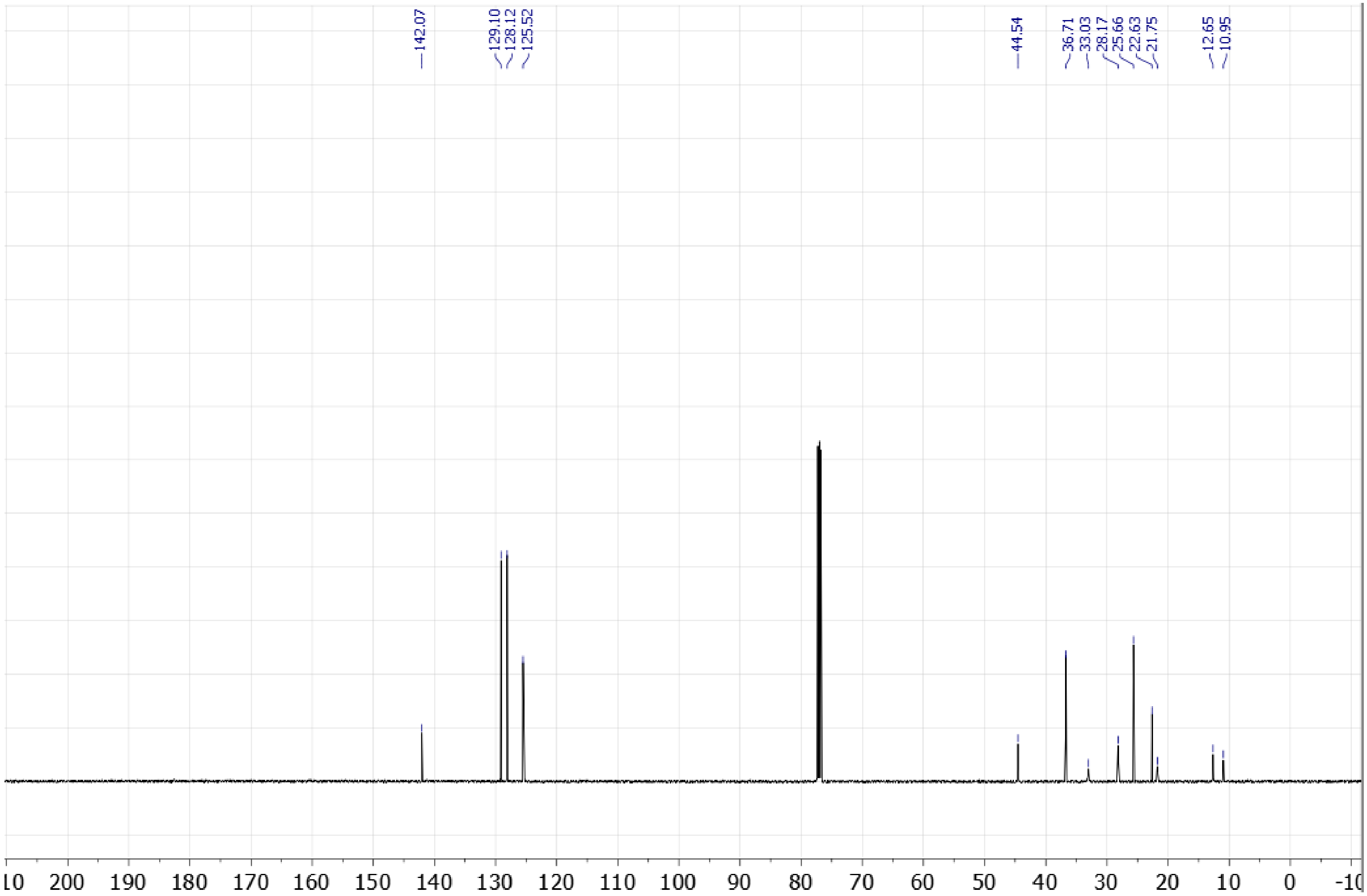
Compound **S5** **^{13}C NMR** (126 MHz, $CDCl_3$)



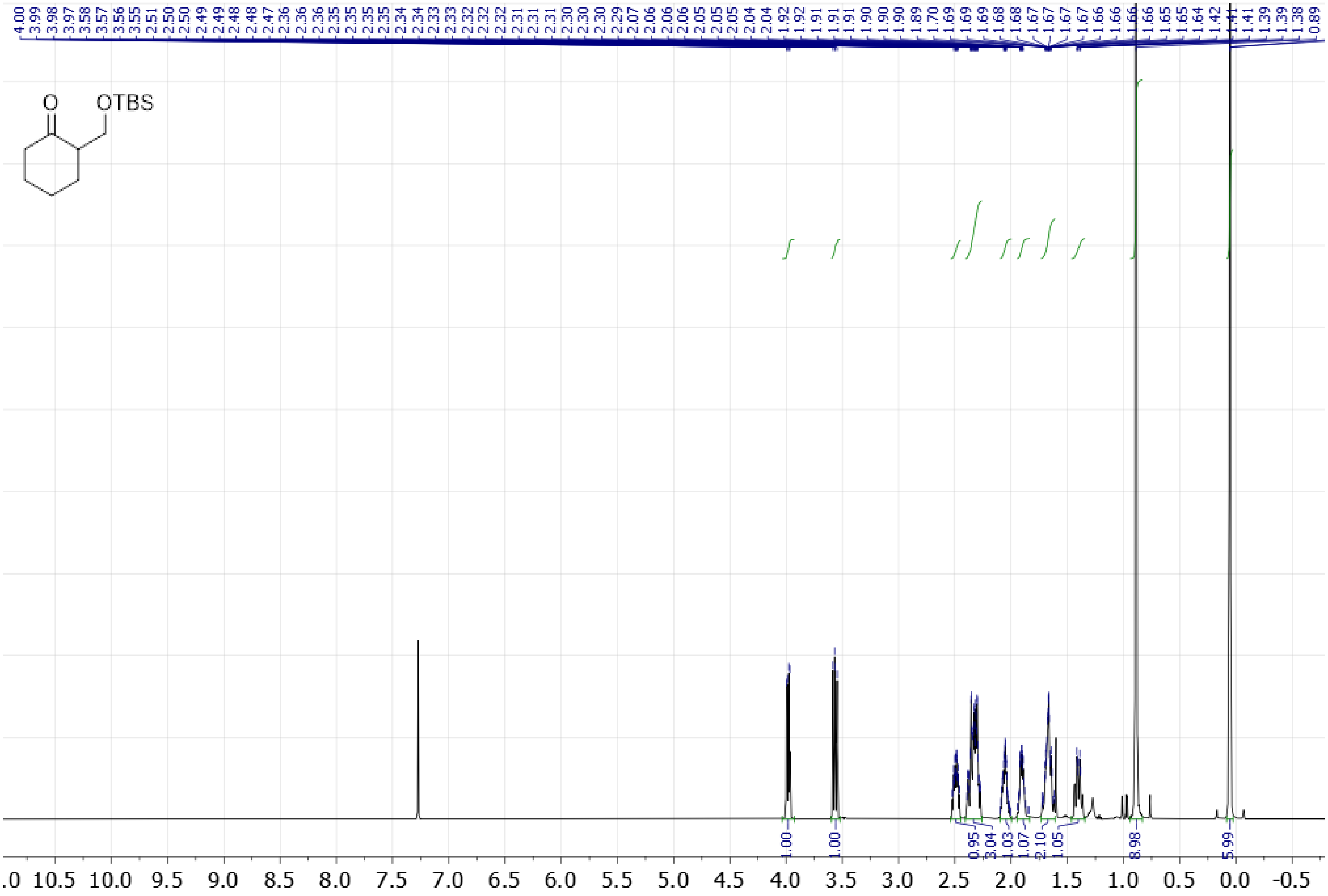
Compound **S6** ^{1}**H NMR** (500 MHz, CDCl$_3$)



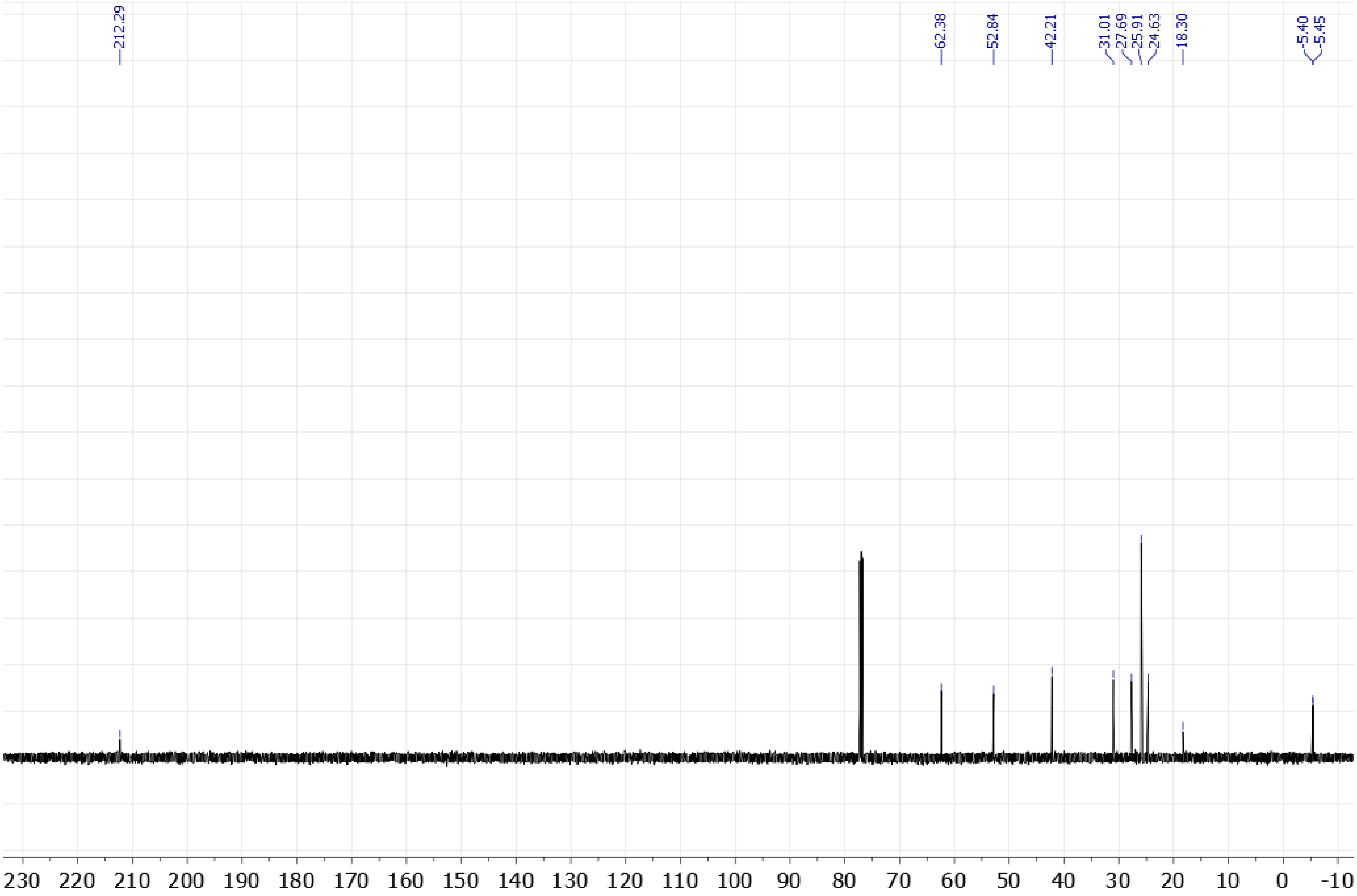
Compound **S6** **^{13}C NMR** (126 MHz, $CDCl_3$)



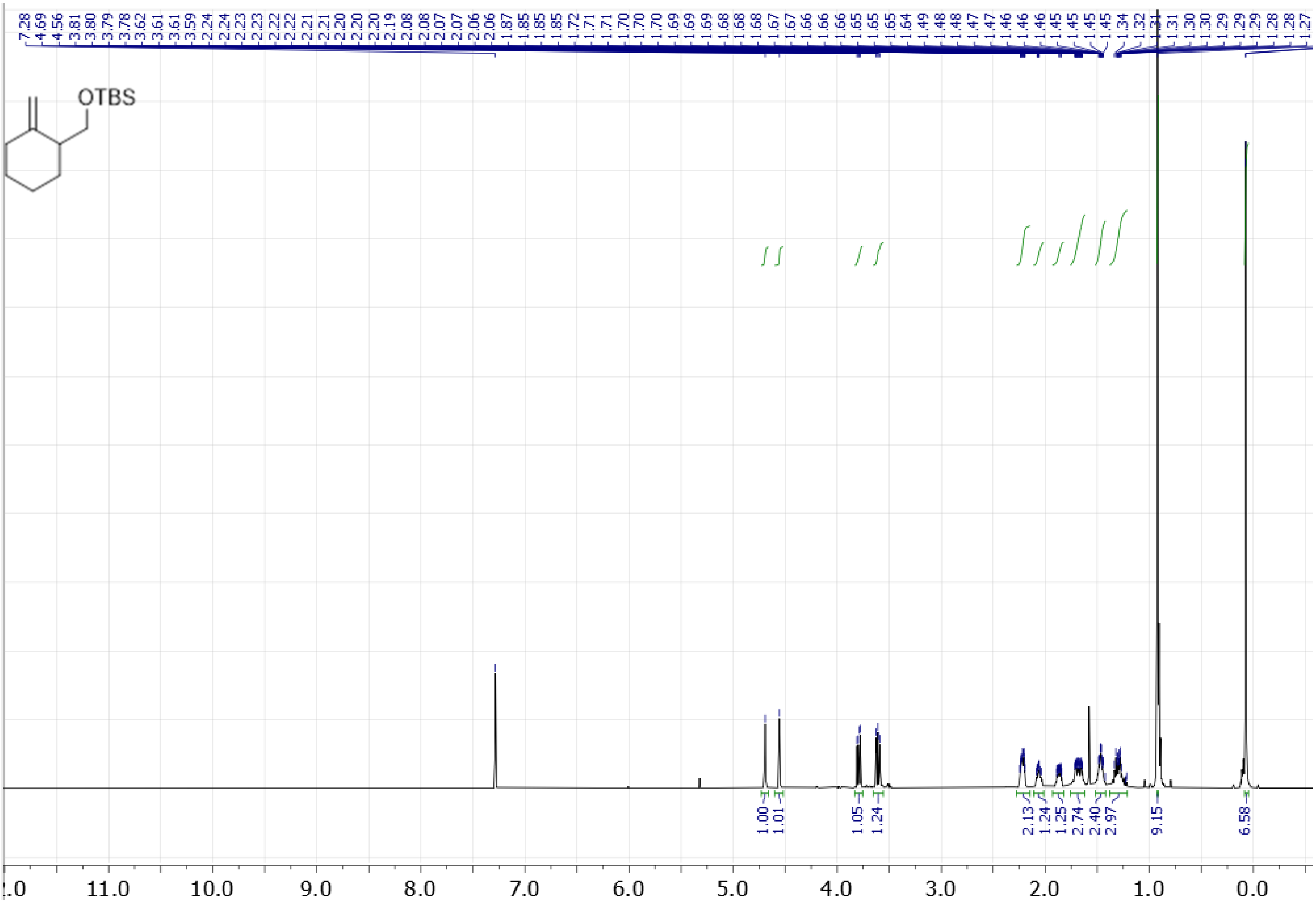
Compound **S7a** ^{1}**H NMR** (500 MHz, $CDCl_3$)



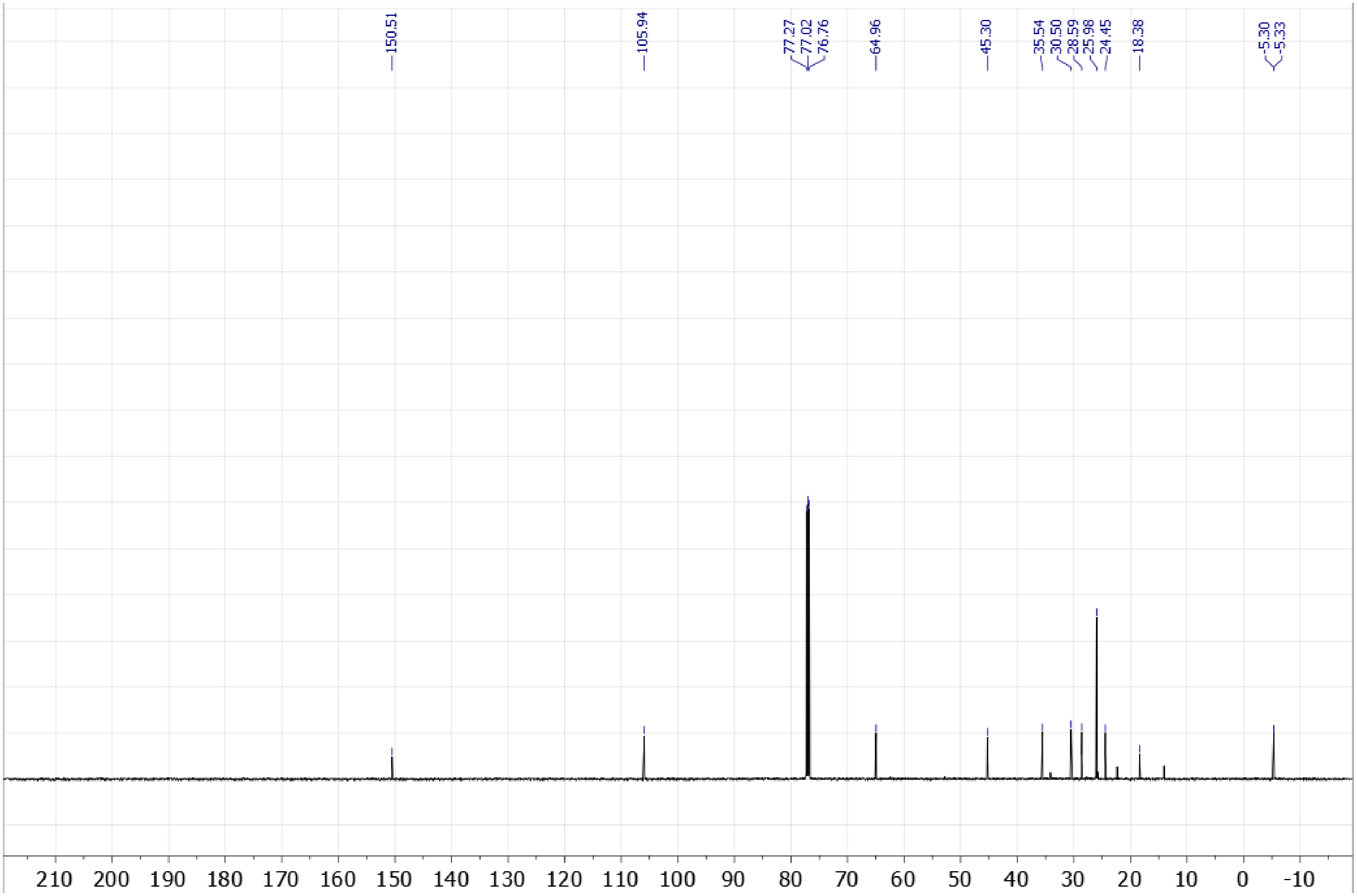
Compound **S7a** **^{13}C NMR** (126 MHz, CDCl$_3$)



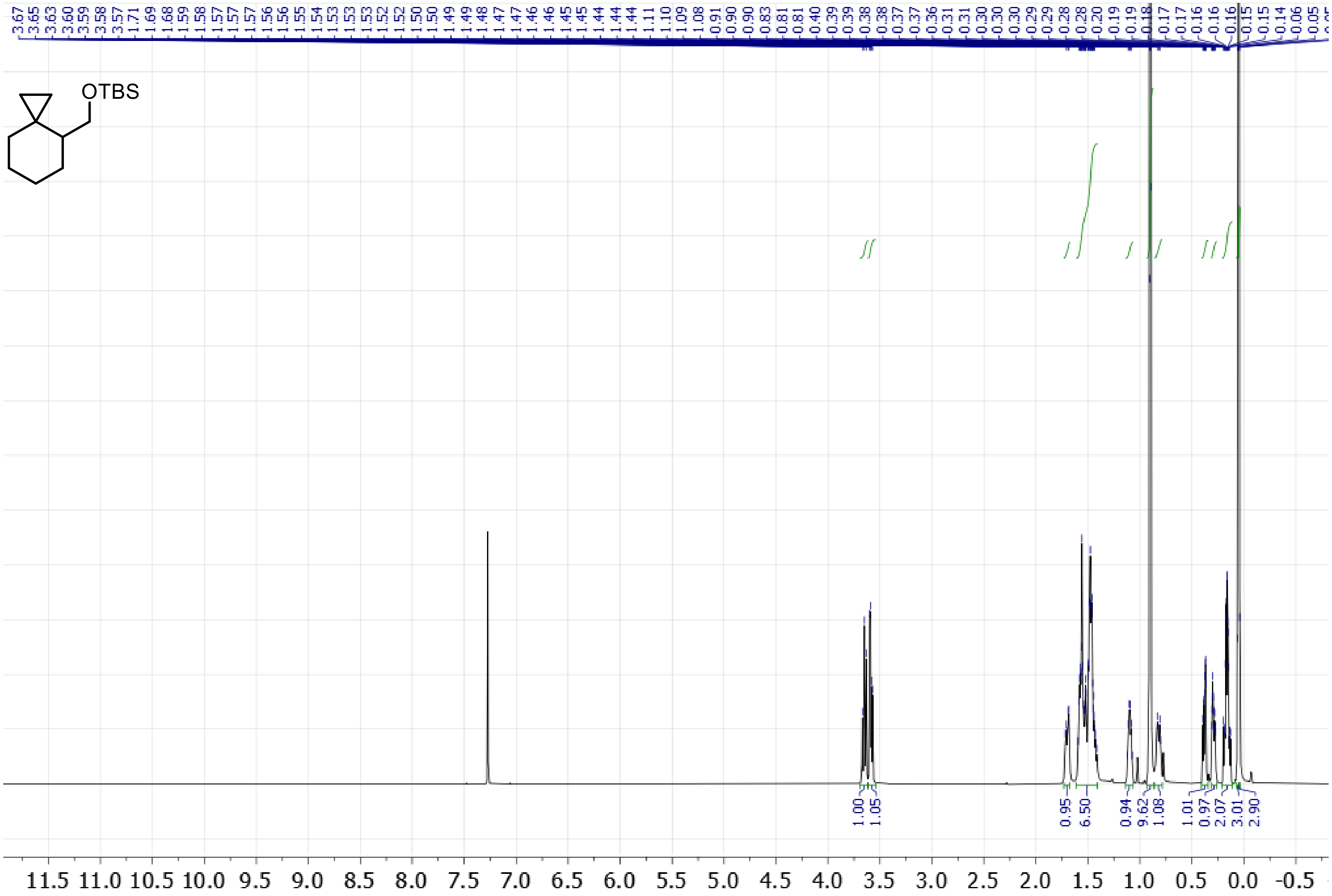
Compound **S7b** **^{1}H NMR** (500 MHz, $CDCl_3$)



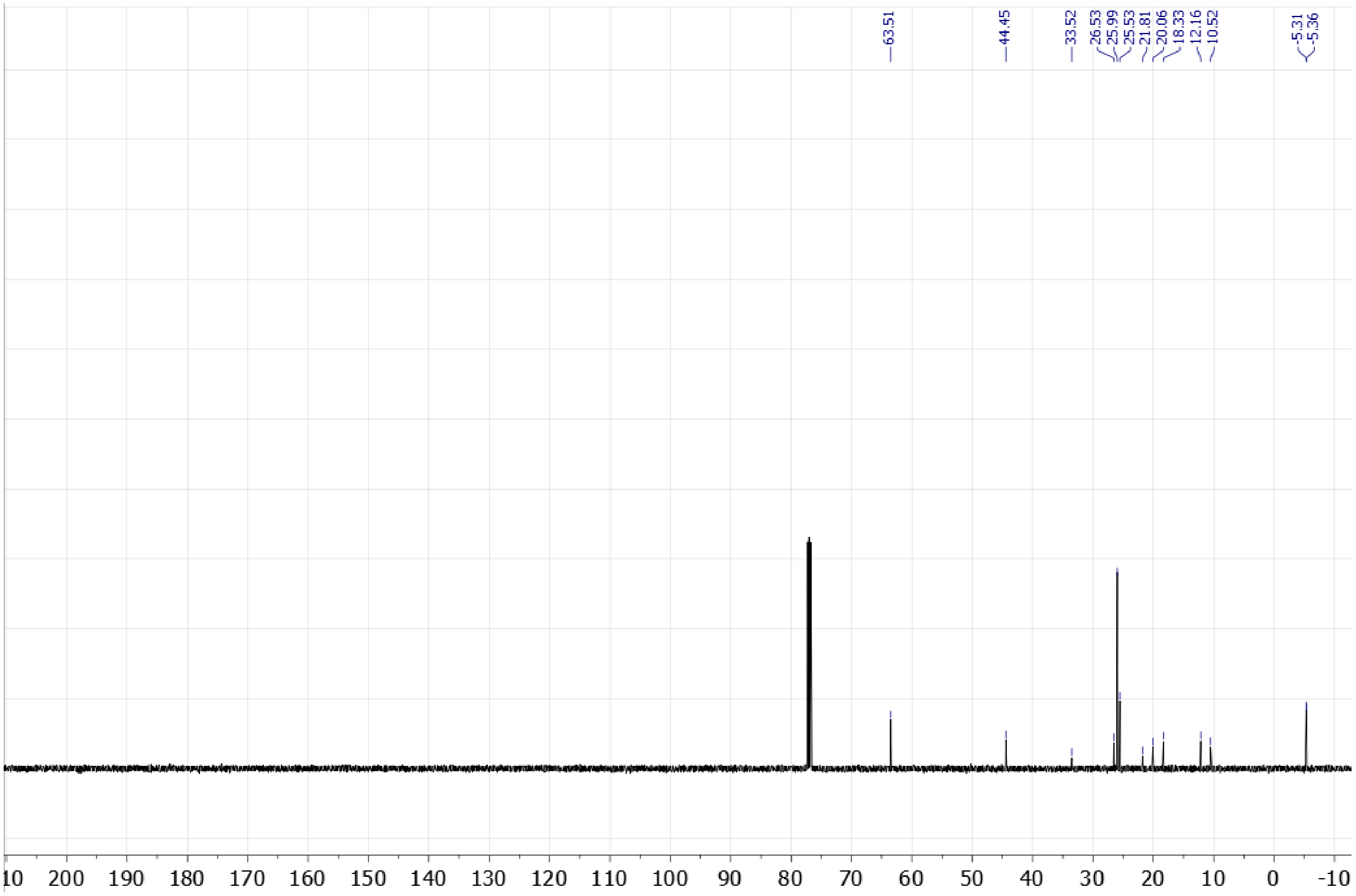
Compound **S7b** **^{13}C NMR** (126 MHz, $CDCl_3$)



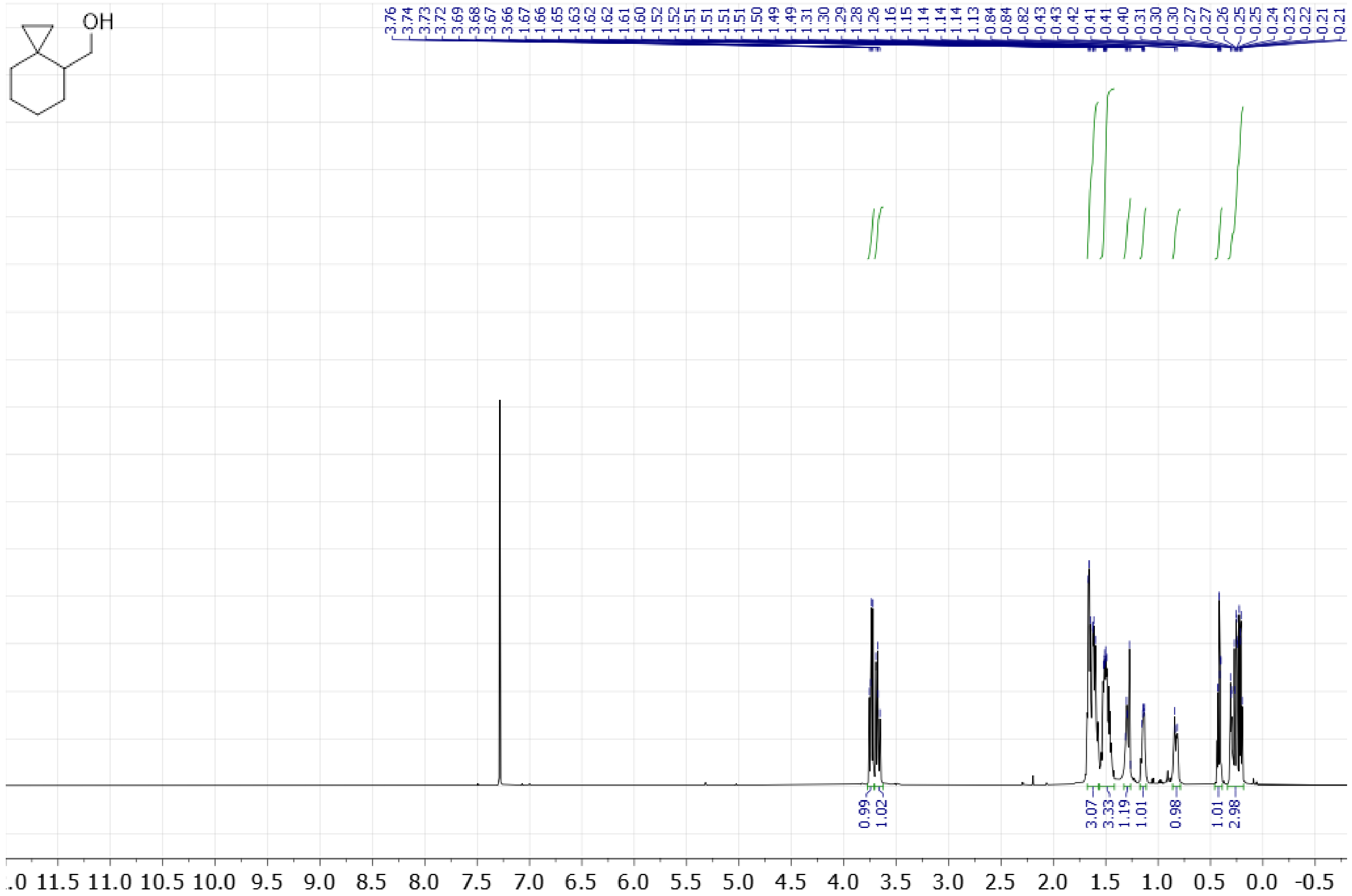
Compound 7c ^{1}**H NMR** (500 MHz, $CDCl_3$)



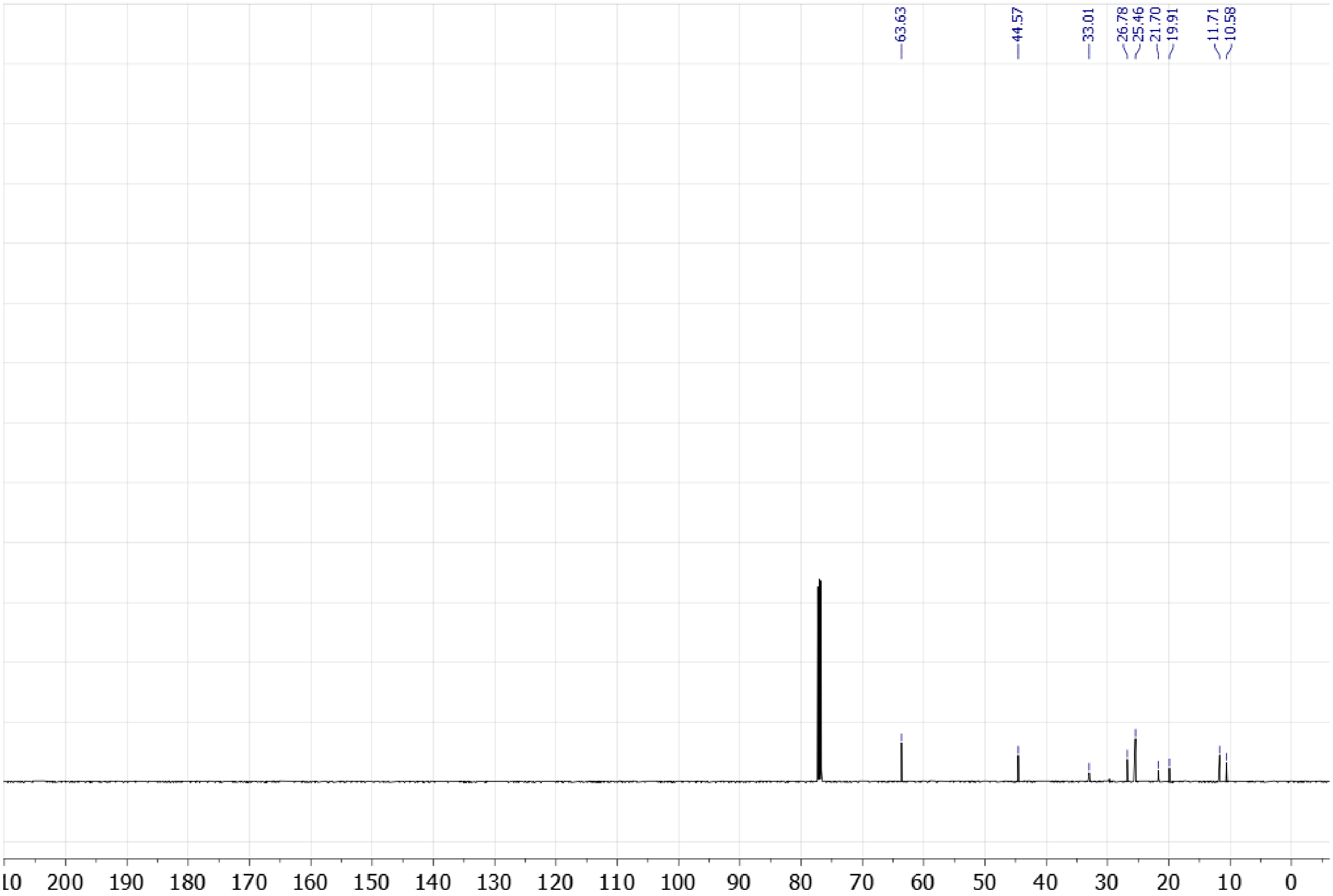
Compound 7c **^{13}C NMR** (126 MHz, CDCl$_3$)



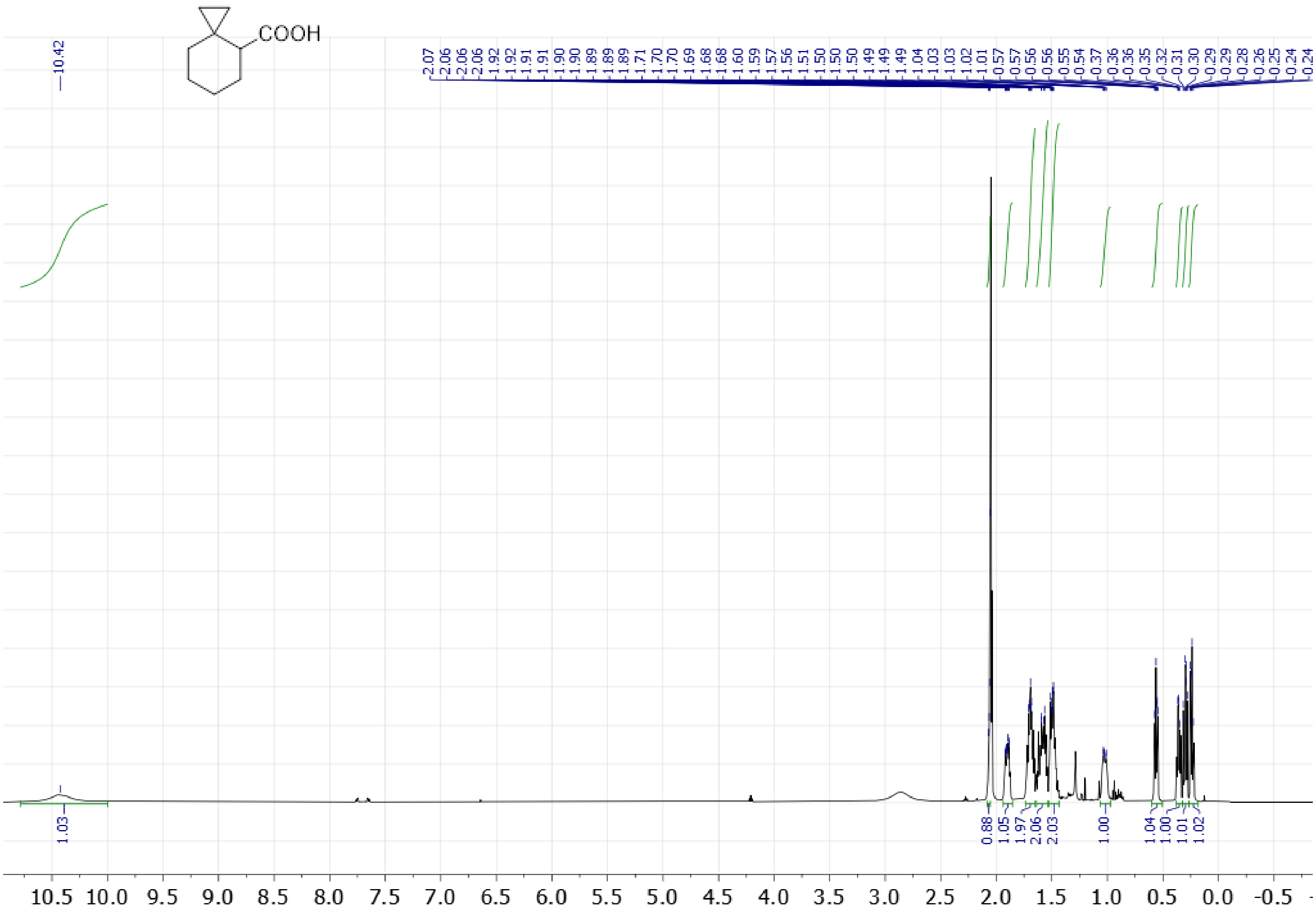
Compound 7 **^{1}H NMR** (500 MHz, $CDCl_3$)



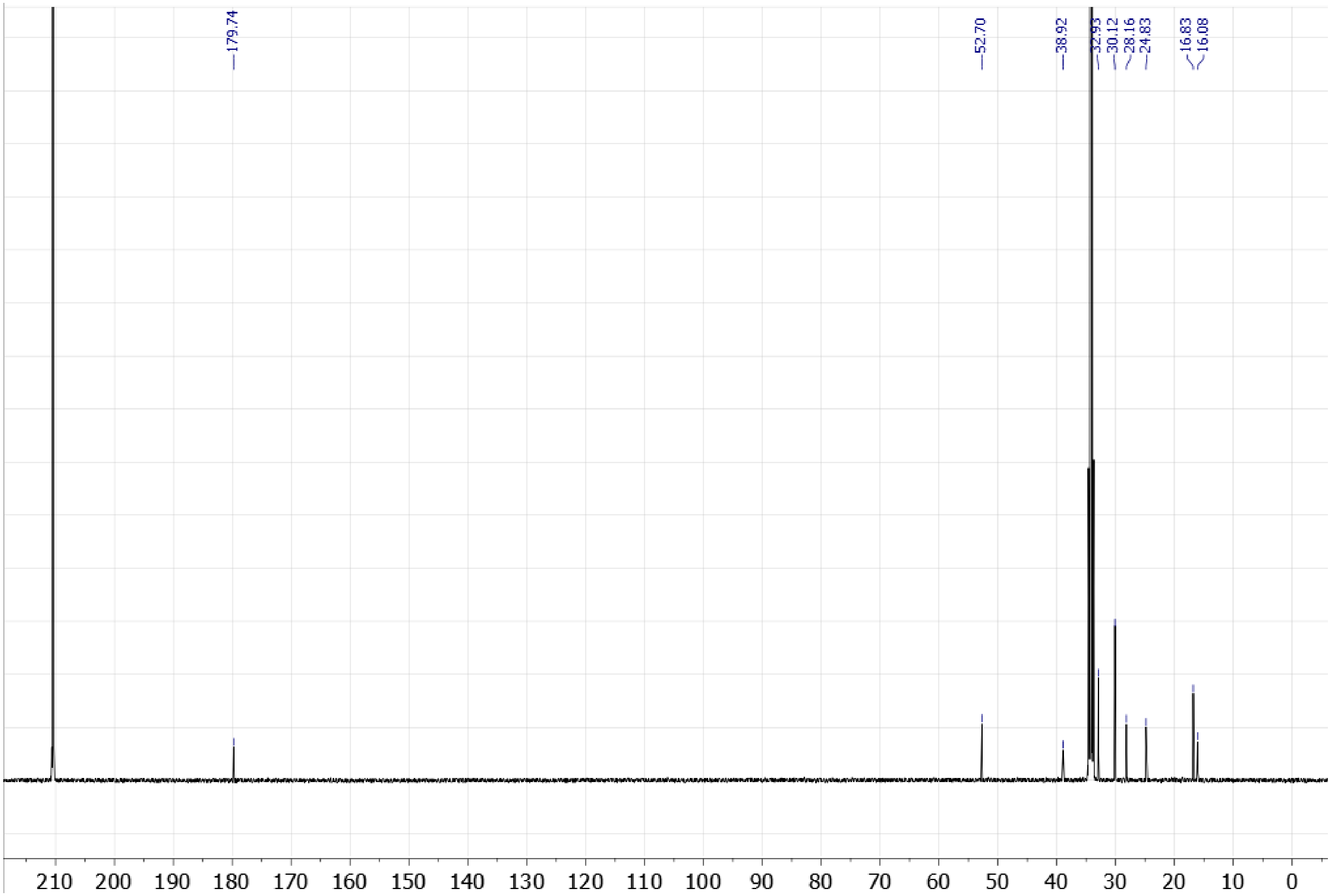
Compound 7 ^{13}**C NMR** (126 MHz, CDCl$_3$)



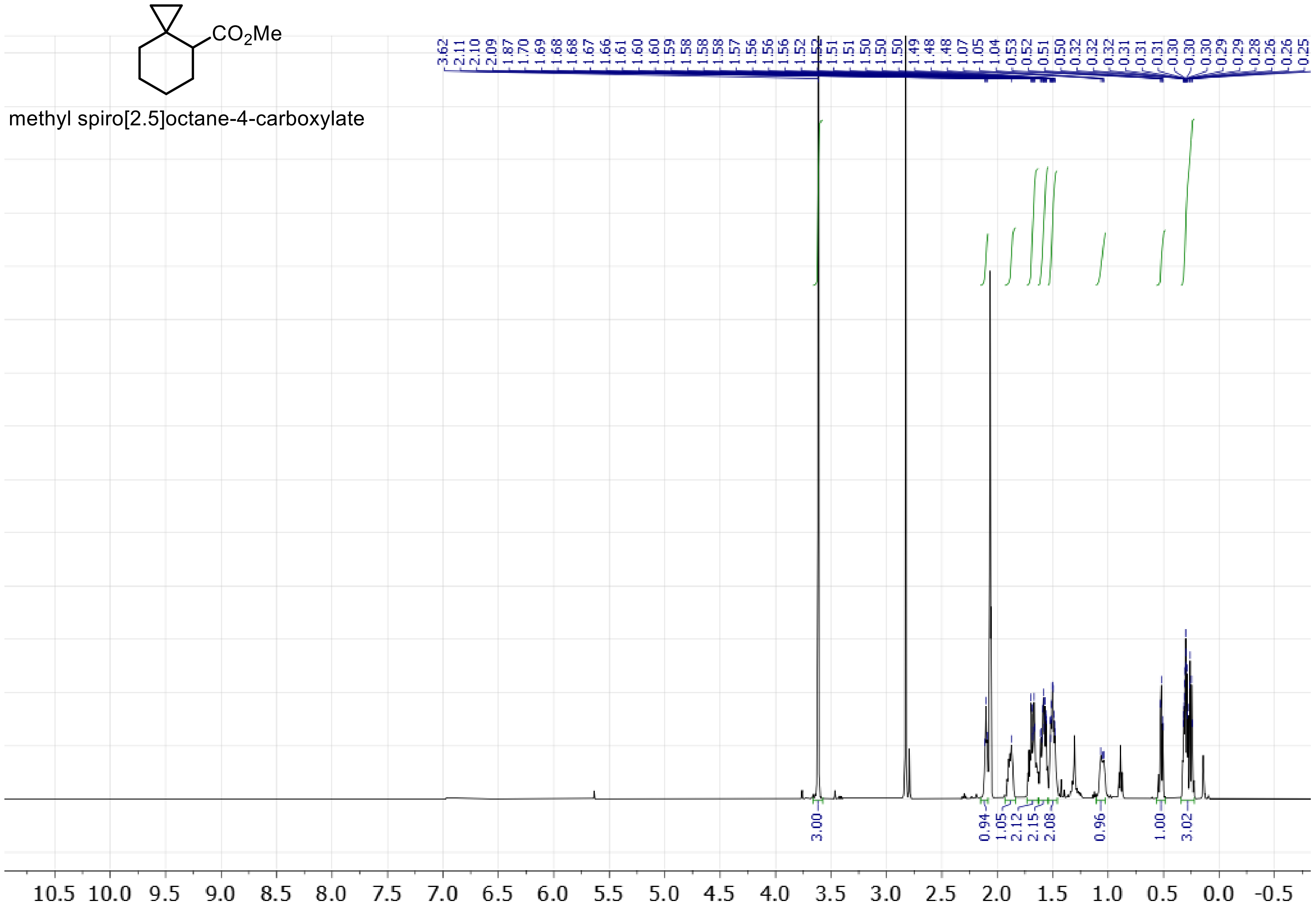
Compound 8 **^{1}H NMR** (500 MHz, *d_6*-Acetone)



Compound 8 ^{13}**C NMR** (500 MHz, d_6-Acetone)

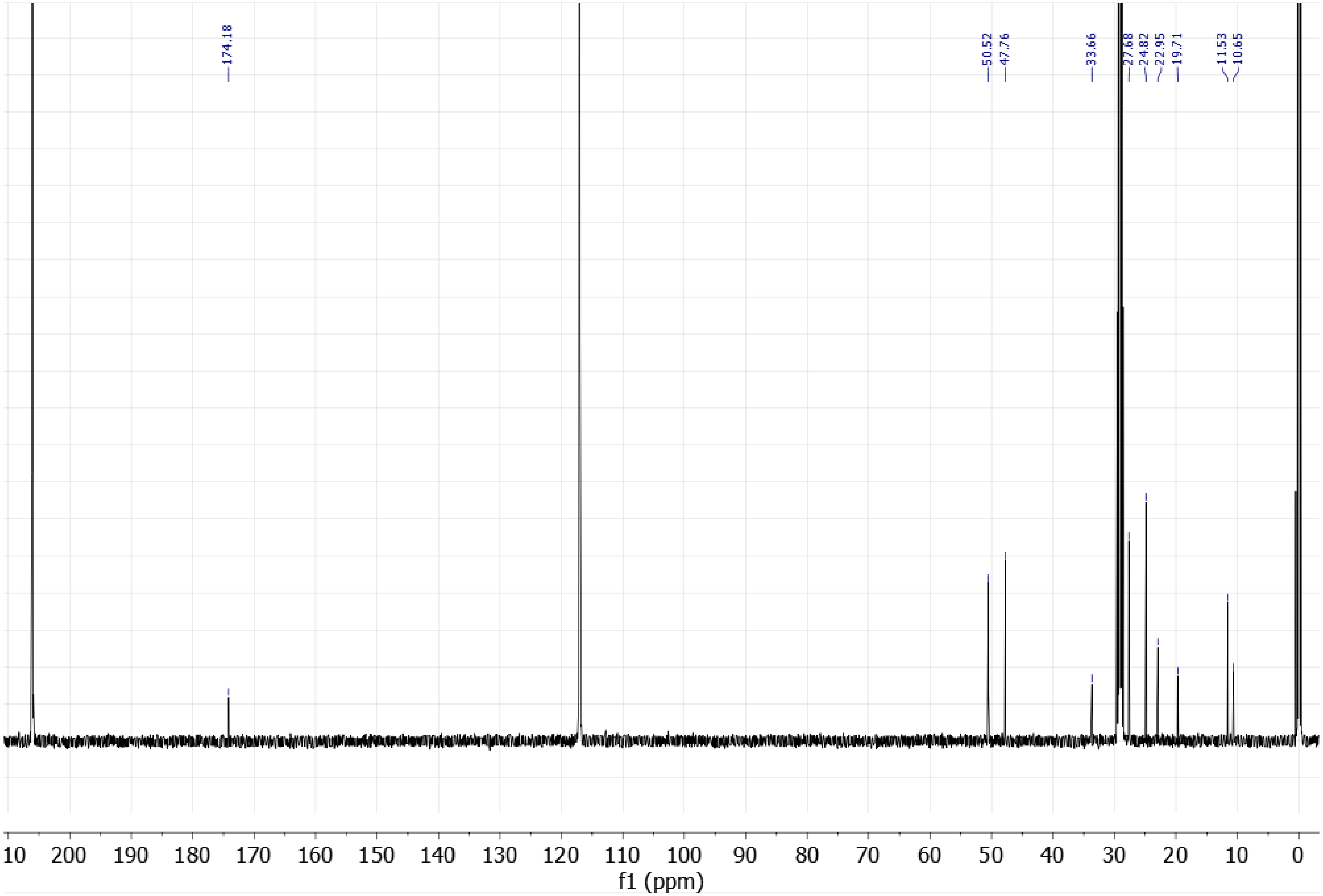


Compound 9 ^{1}**H NMR** (126 MHz, d_6-Acetone)

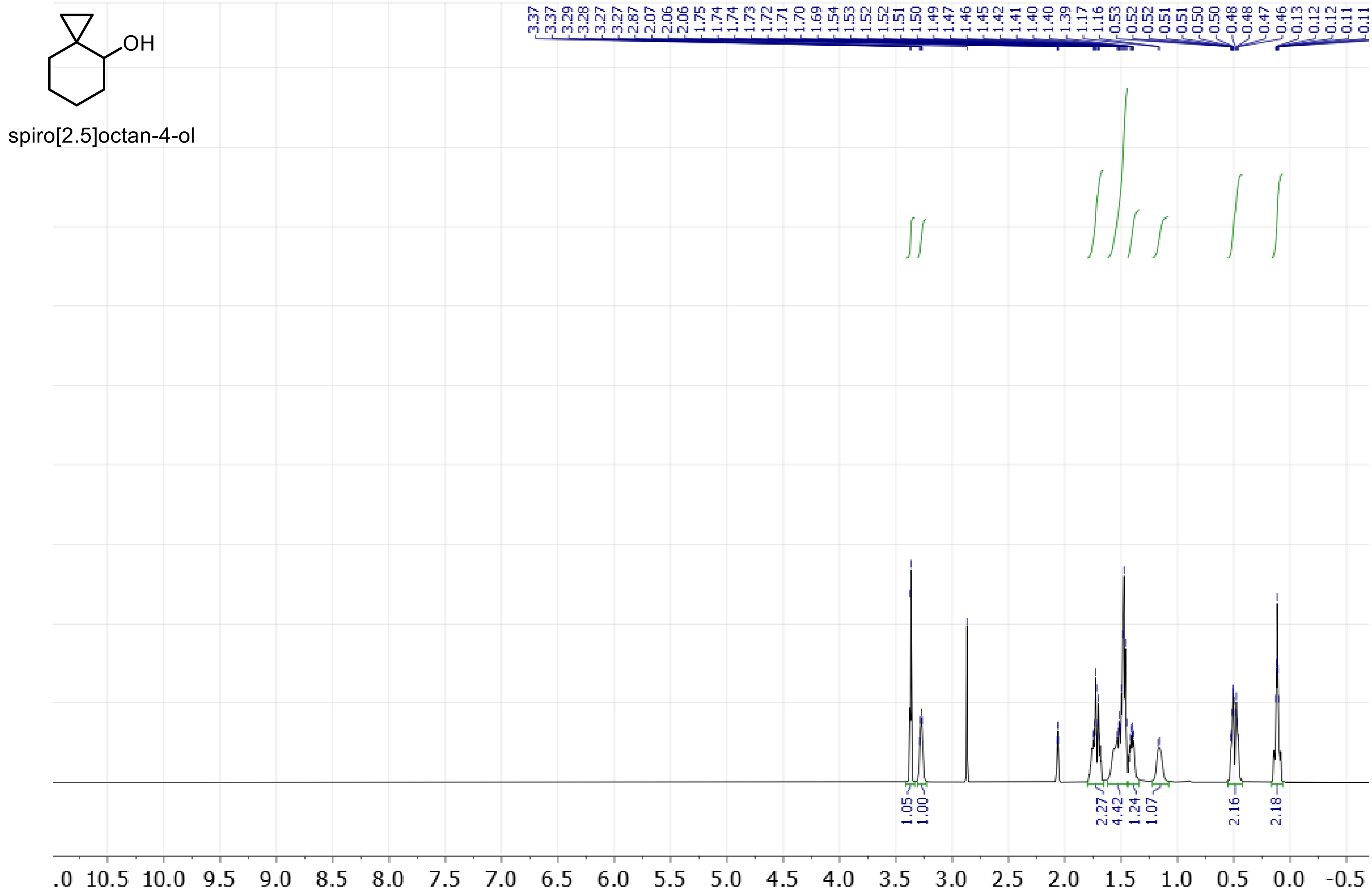


methyl spiro[2.5]octane-4-carboxylate

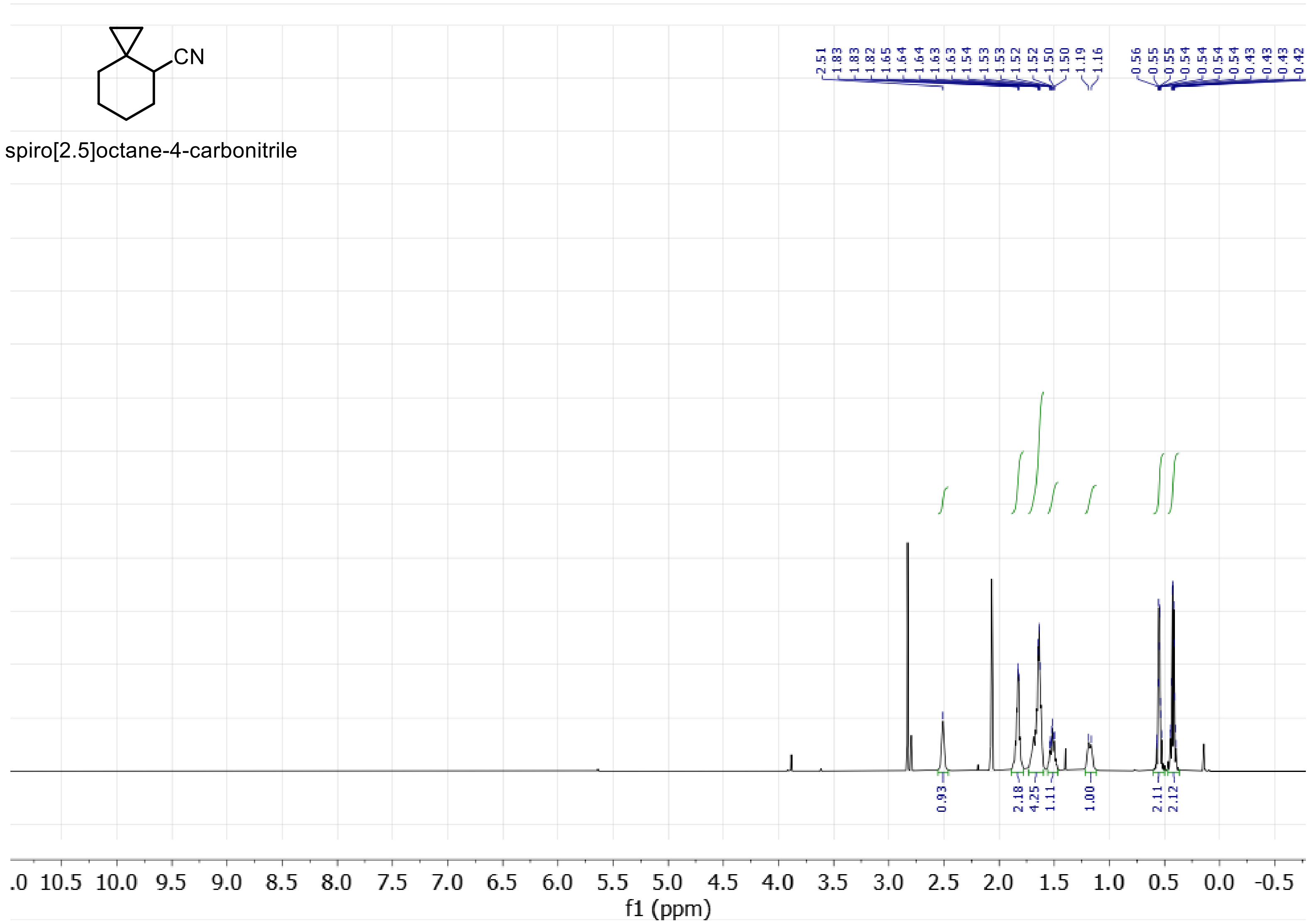
Compound **S9** ^{13}**C NMR** (500 MHz, *d*$_6$-Acetone/ *d*$_3$-acetonitrile))



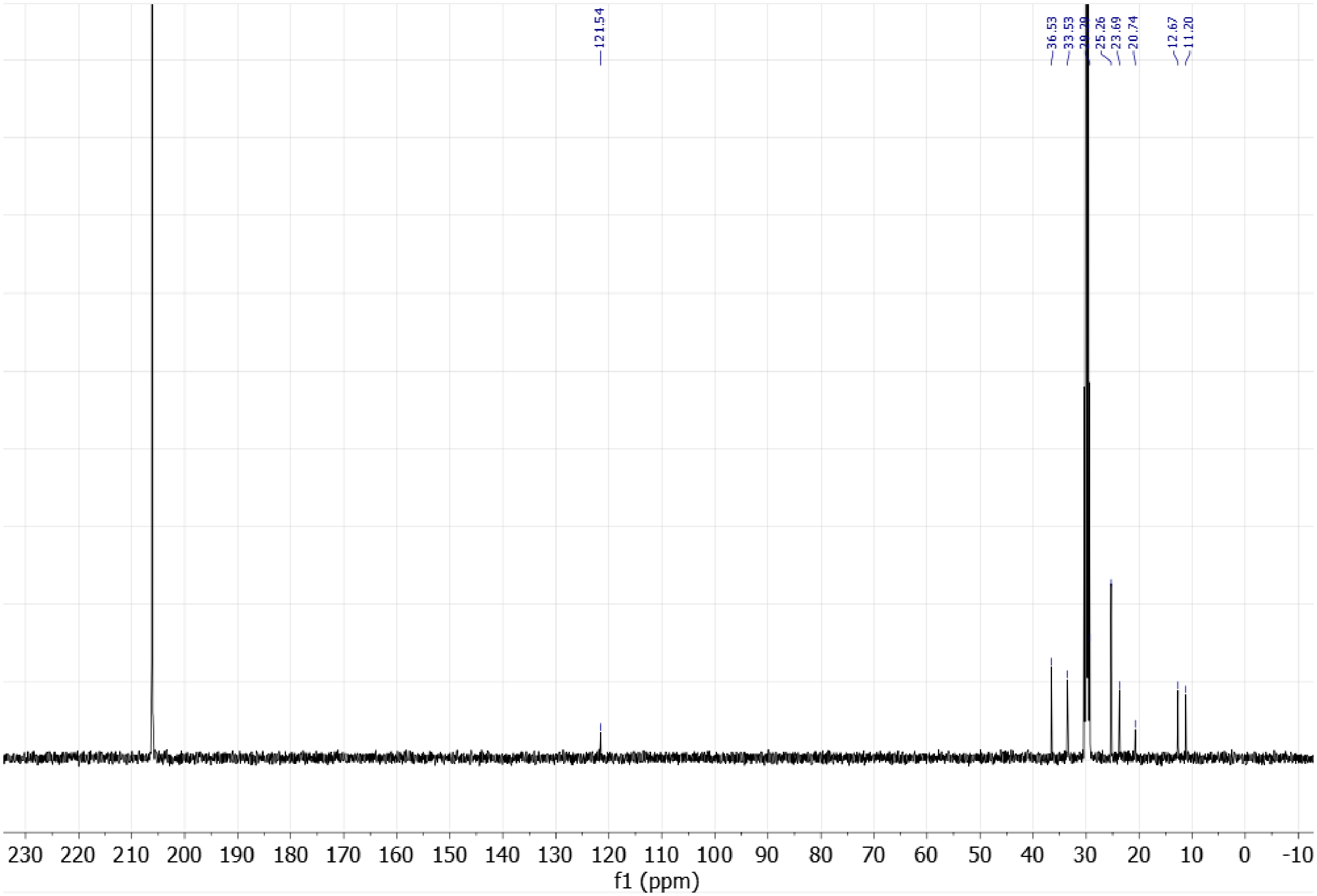
Compound **S10** ^{1}**H NMR** (500 MHz, *d*$_6$-Acetone [previously reported in chloroform])



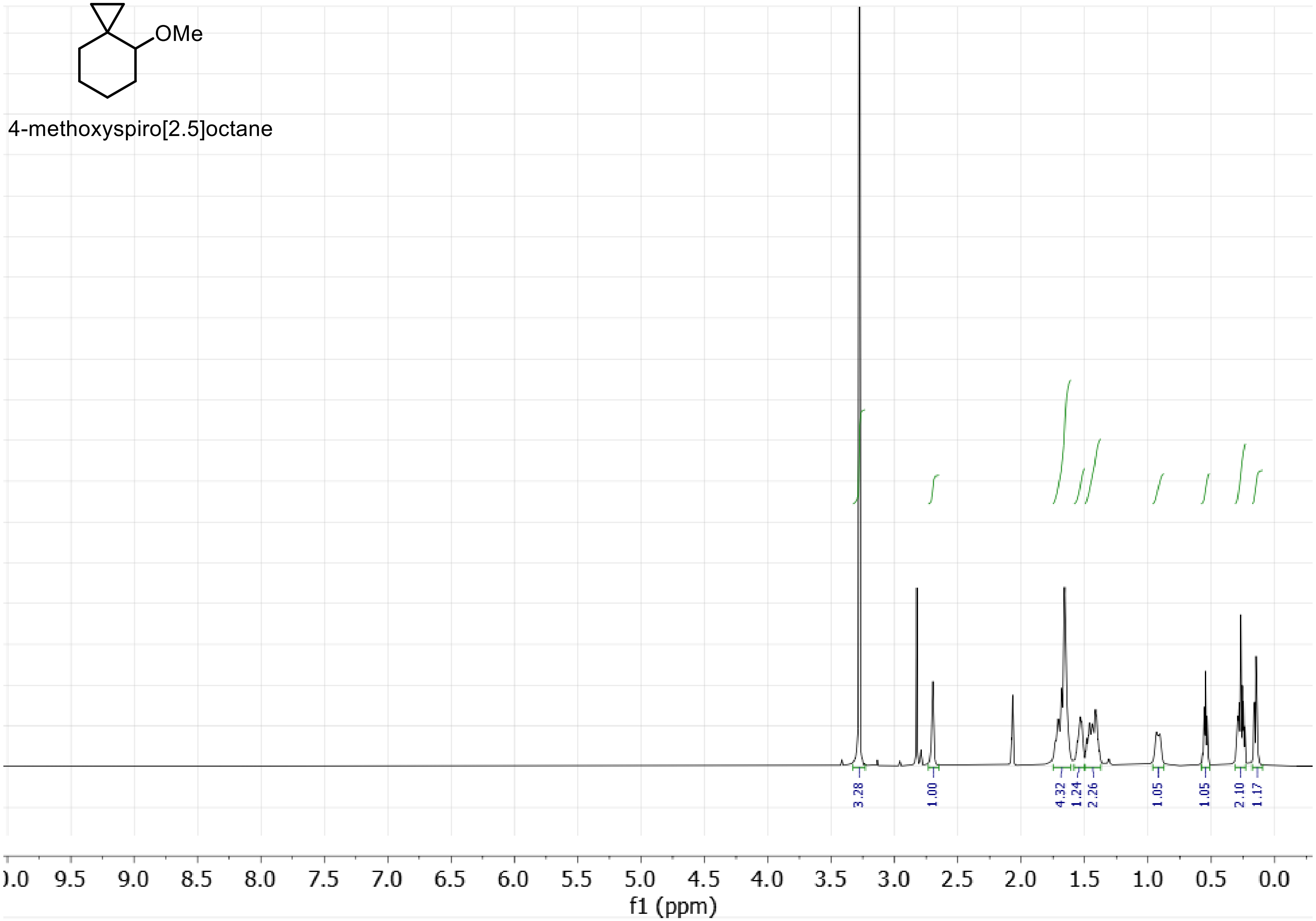
Compound **S11** **^{1}H NMR** (500 MHz, d_6-acetone)



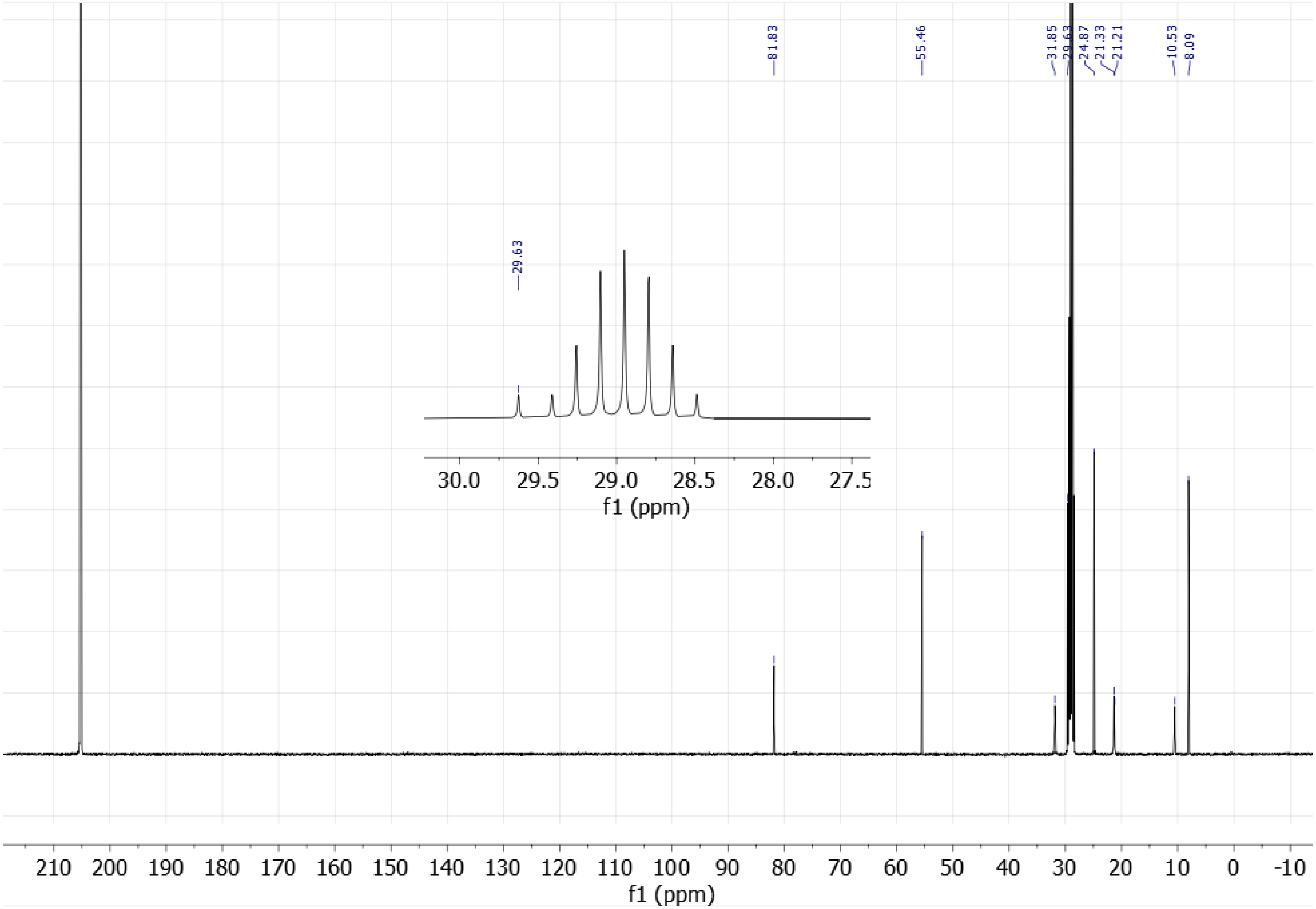
Compound **S11** **^{13}C NMR** (126 MHz, *d*$_6$-acetone)



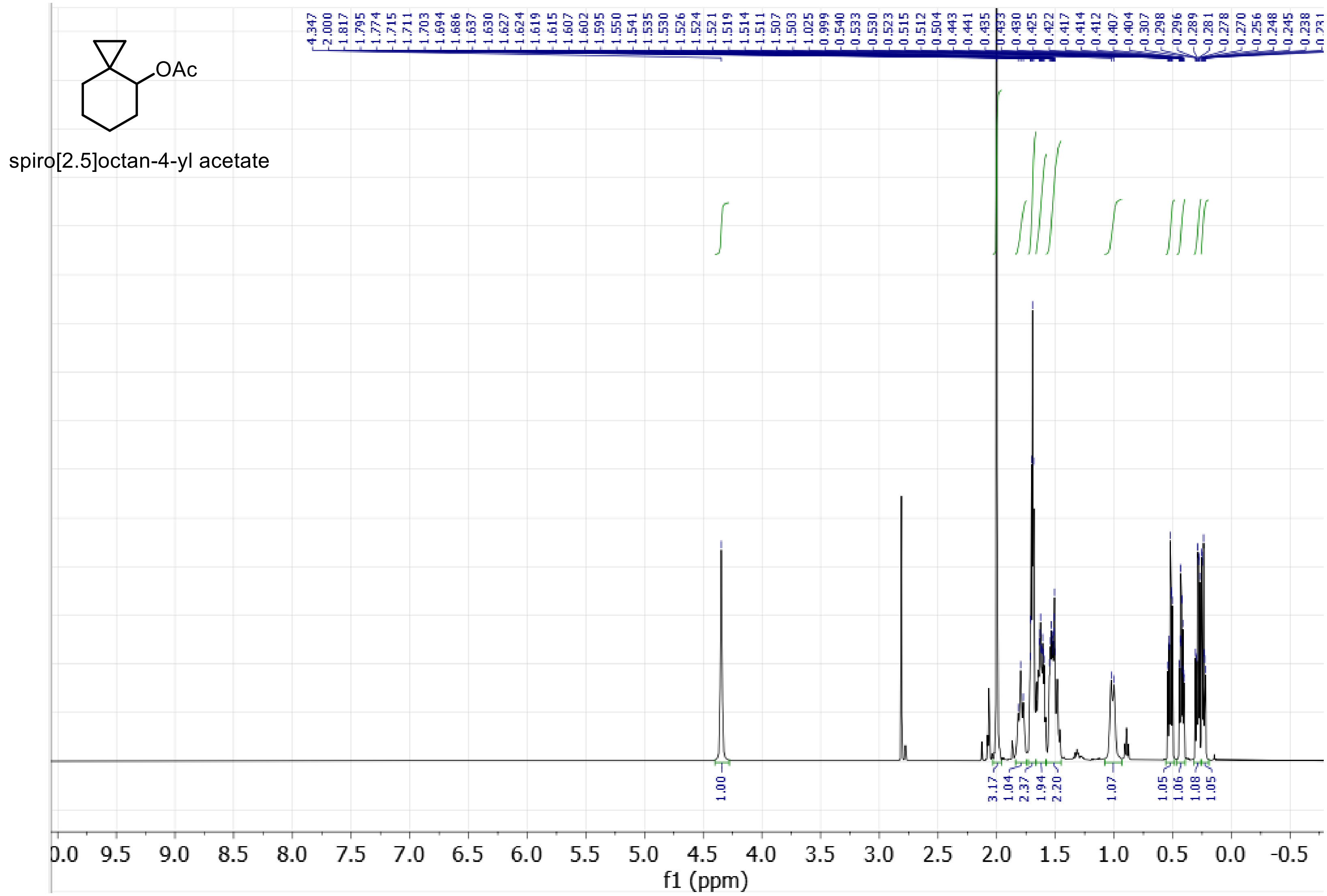
Compound **S12** ^{1}**H NMR** (500 MHz, *d*$_6$-acetone)



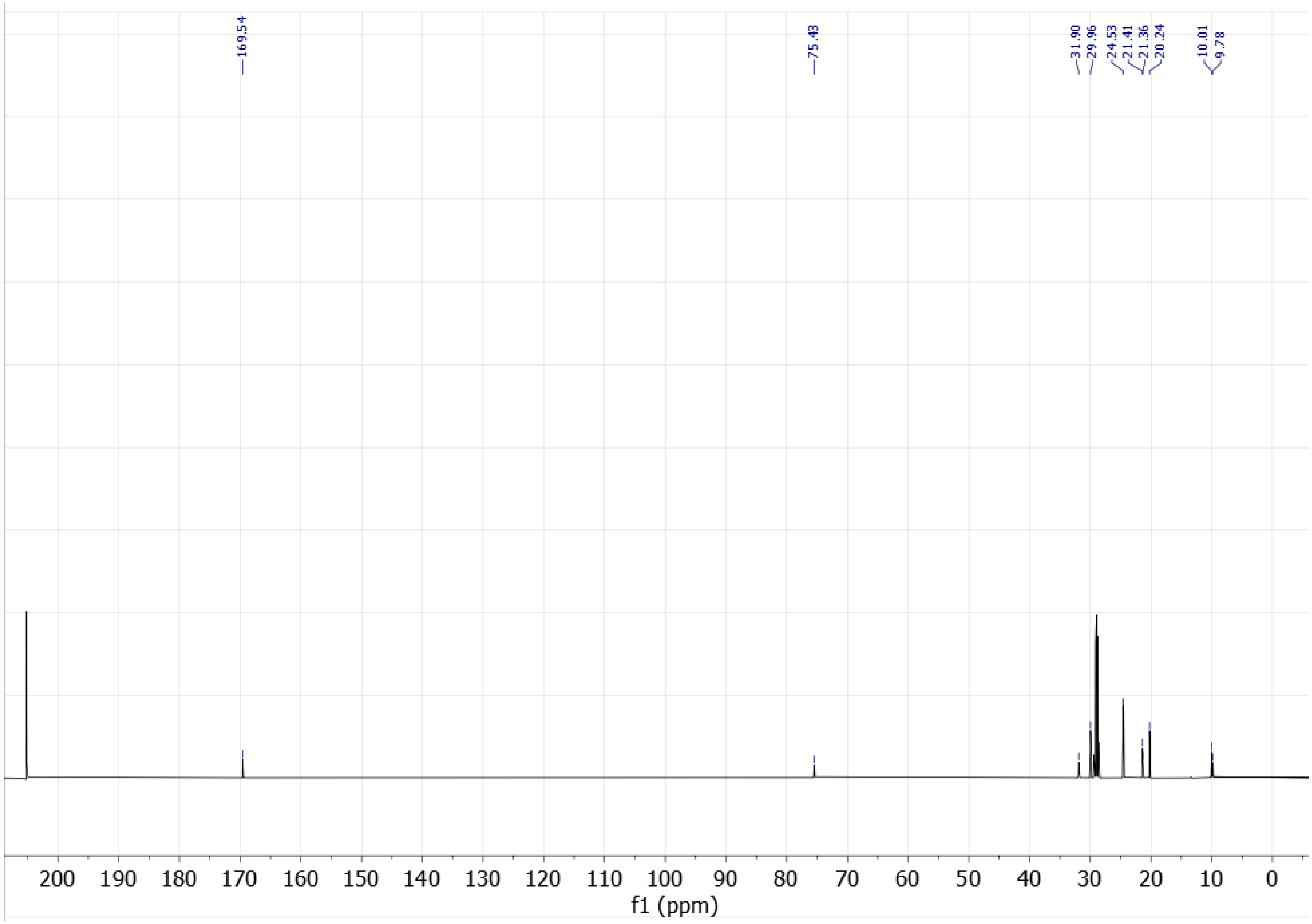
Compound **S12** **^{13}C NMR** (126 MHz, d_6-acetone)



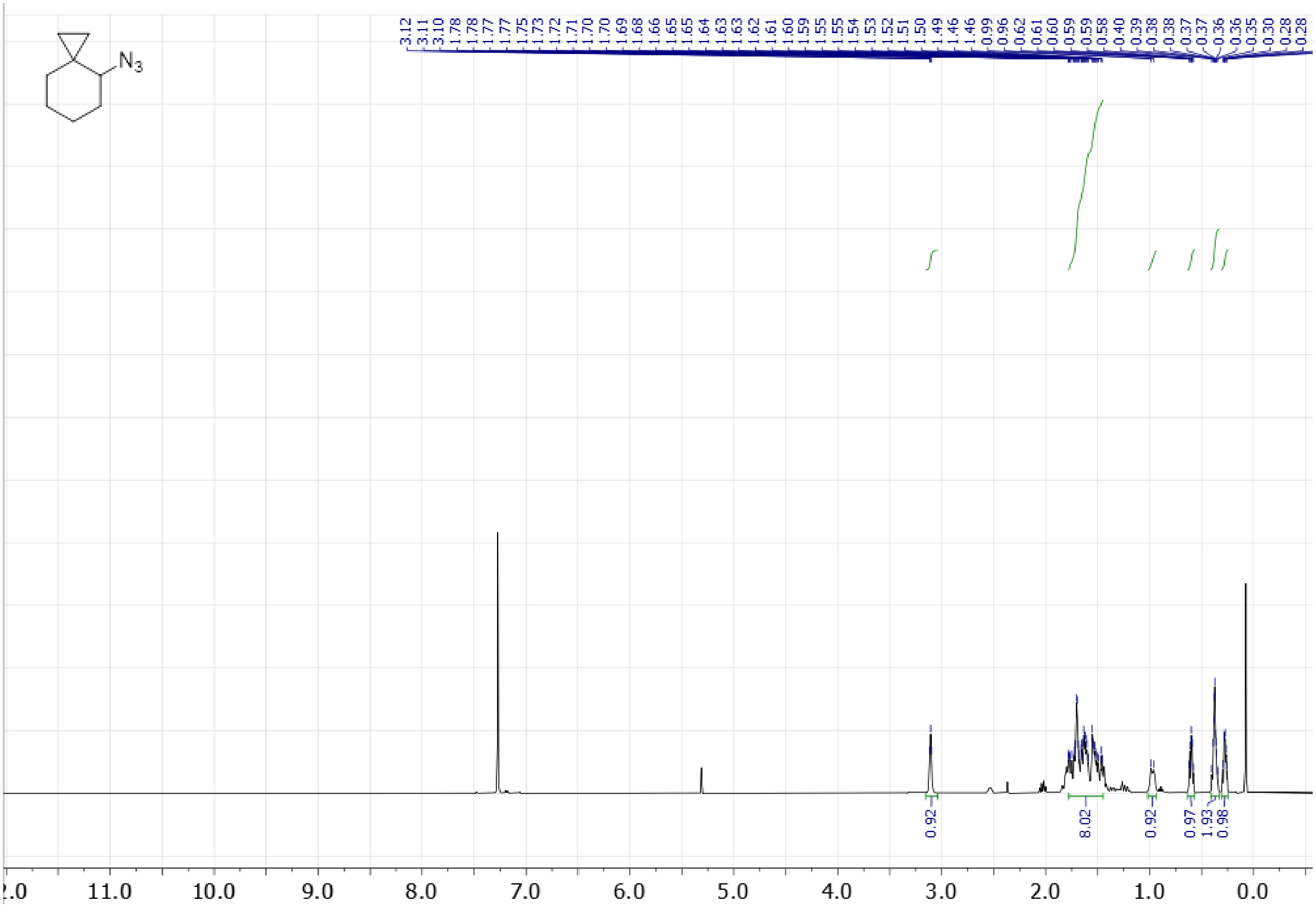
Compound **S13** ^{1}**H NMR** (500 MHz, d_6-acetone)



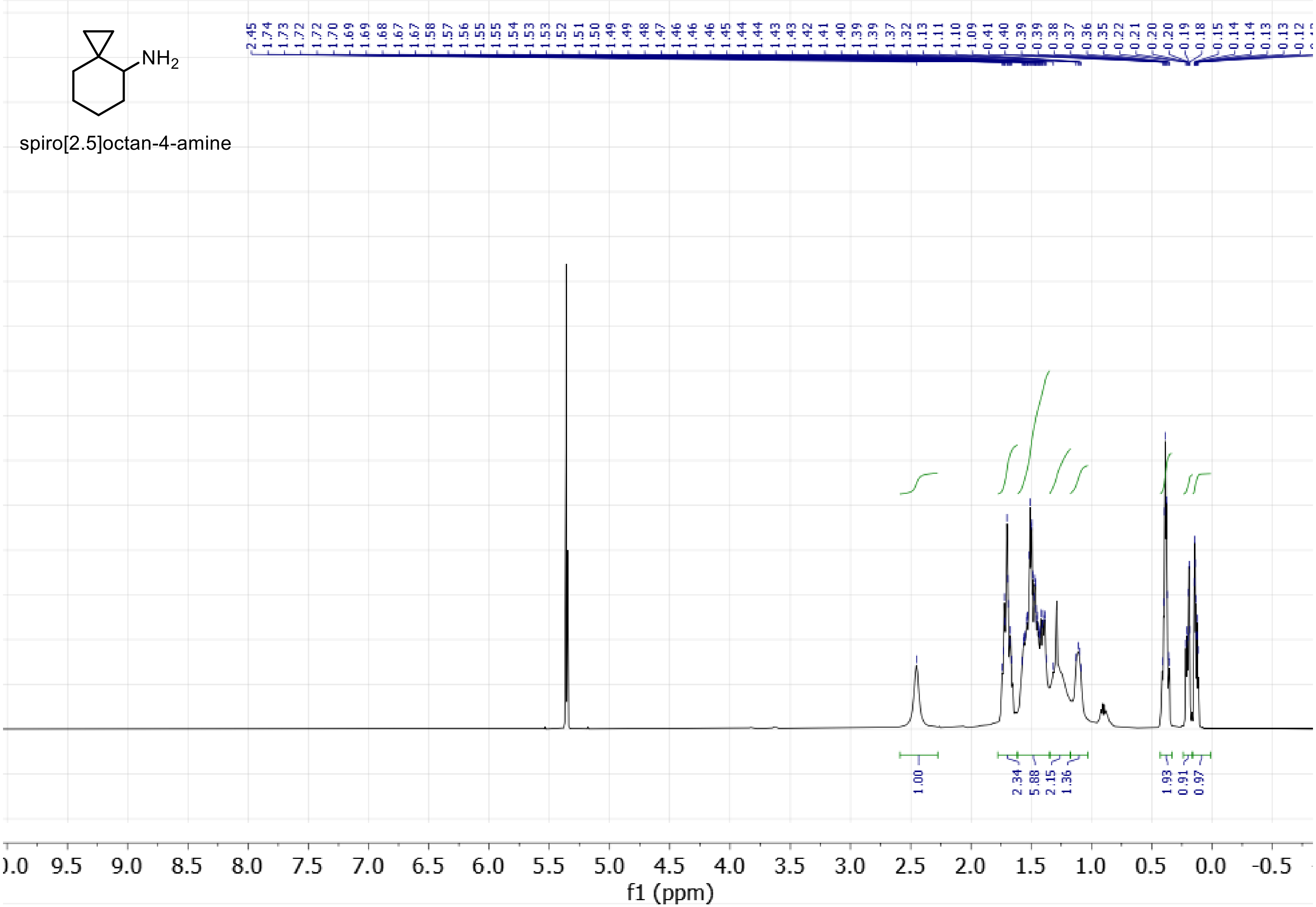
Compound **S13** **^{13}C NMR** (126 MHz, *d_6*-acetone)



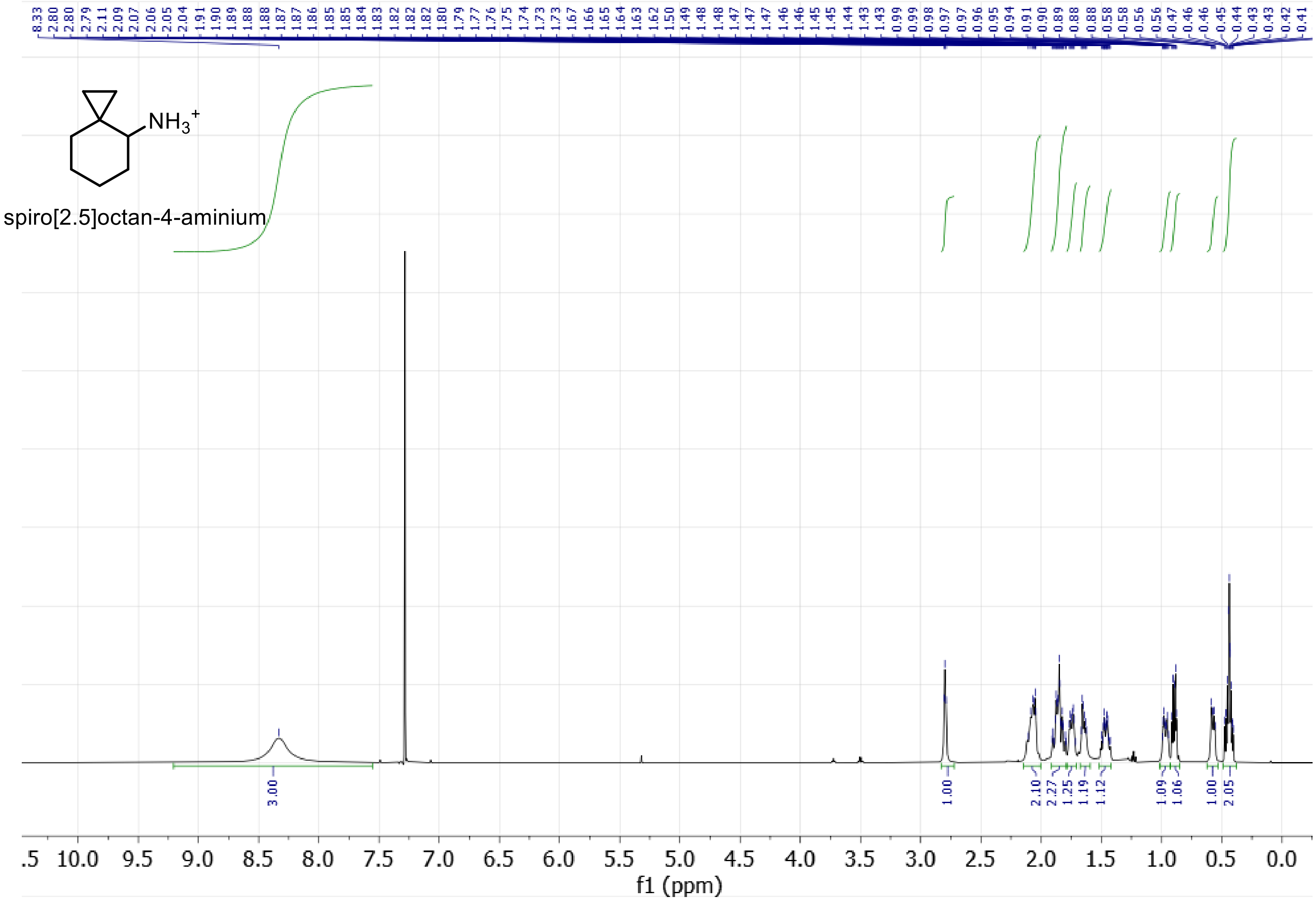
Compound **S14** ^{1}**H NMR** (126 MHz, $CDCl_3$)



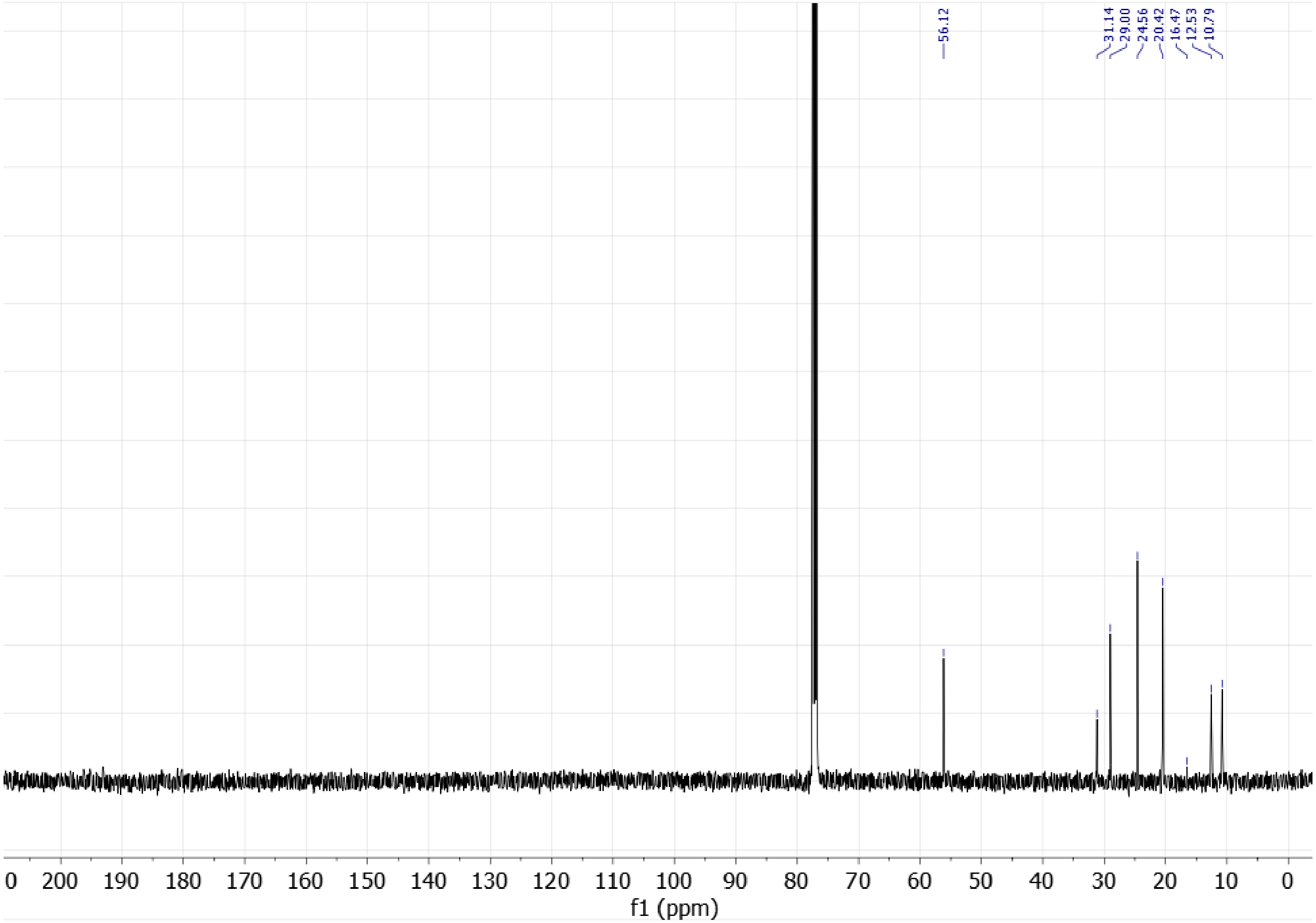
Compound **S15-neutral** **^{1}H NMR** (500 MHz, d_2-DCM



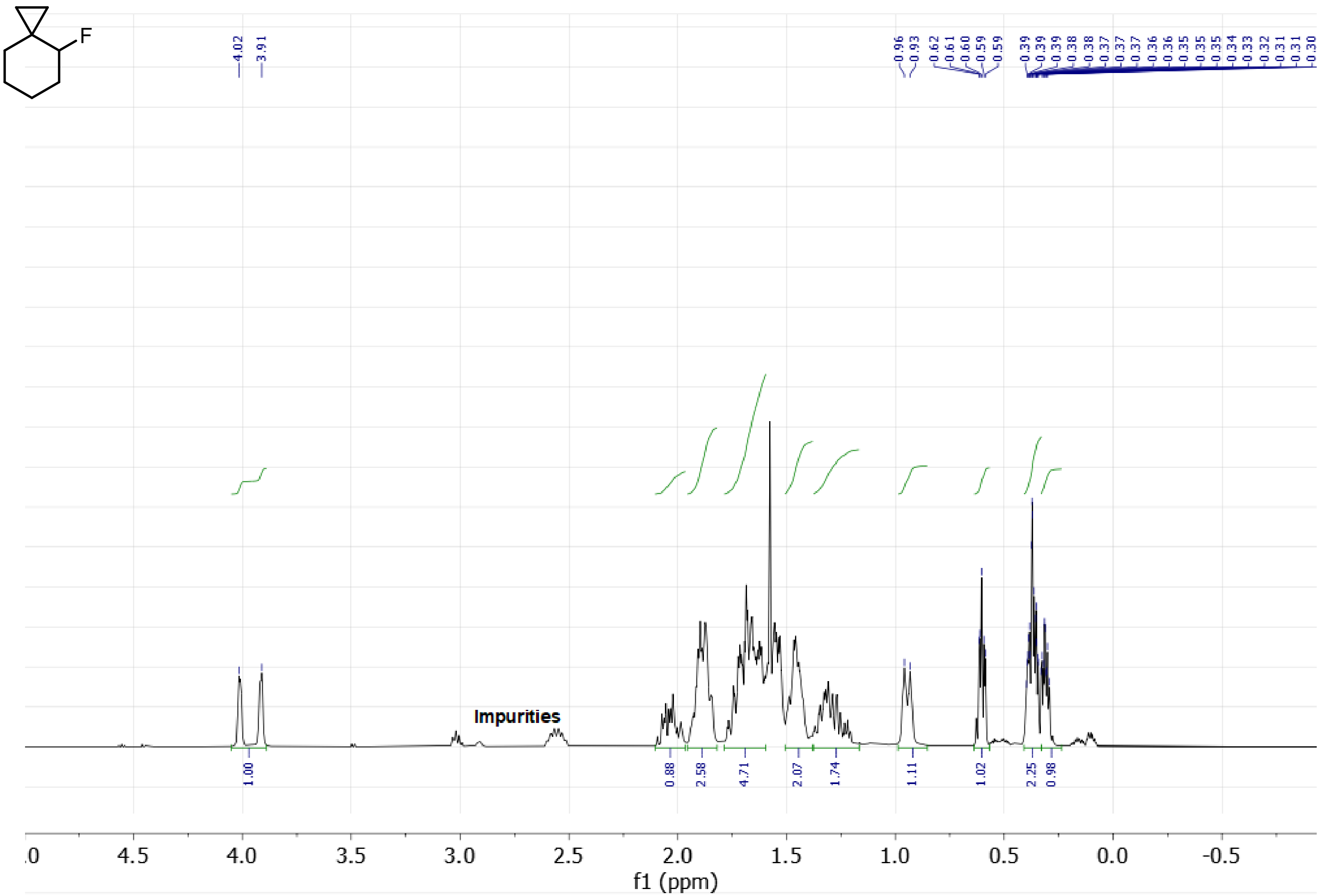
Compound **S15-HCl** **^{1}H NMR** (500 MHz, $CDCl_3$)



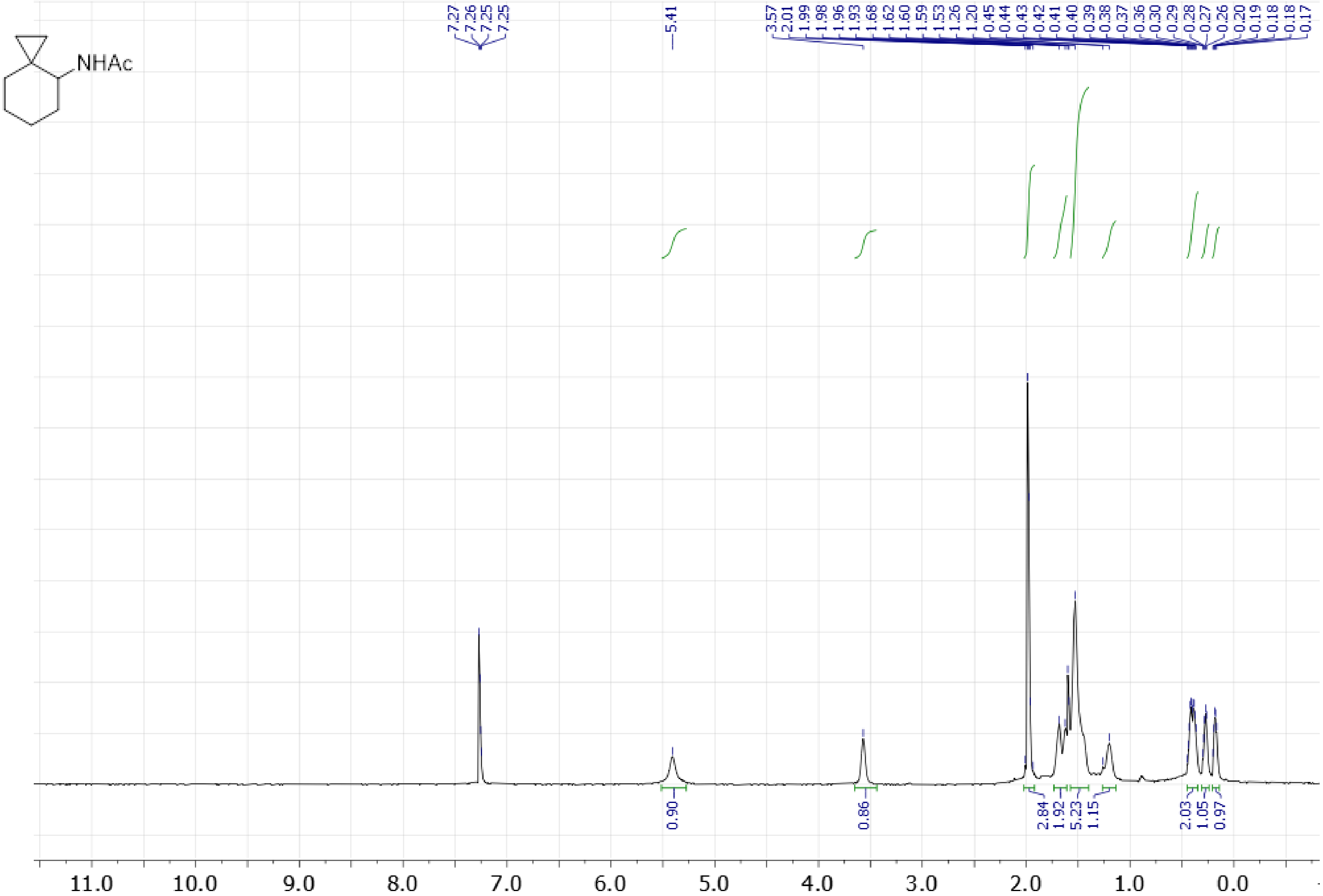
Compound **S15-HCl ^{1}H NMR** (126 MHz, $CDCl_3$)



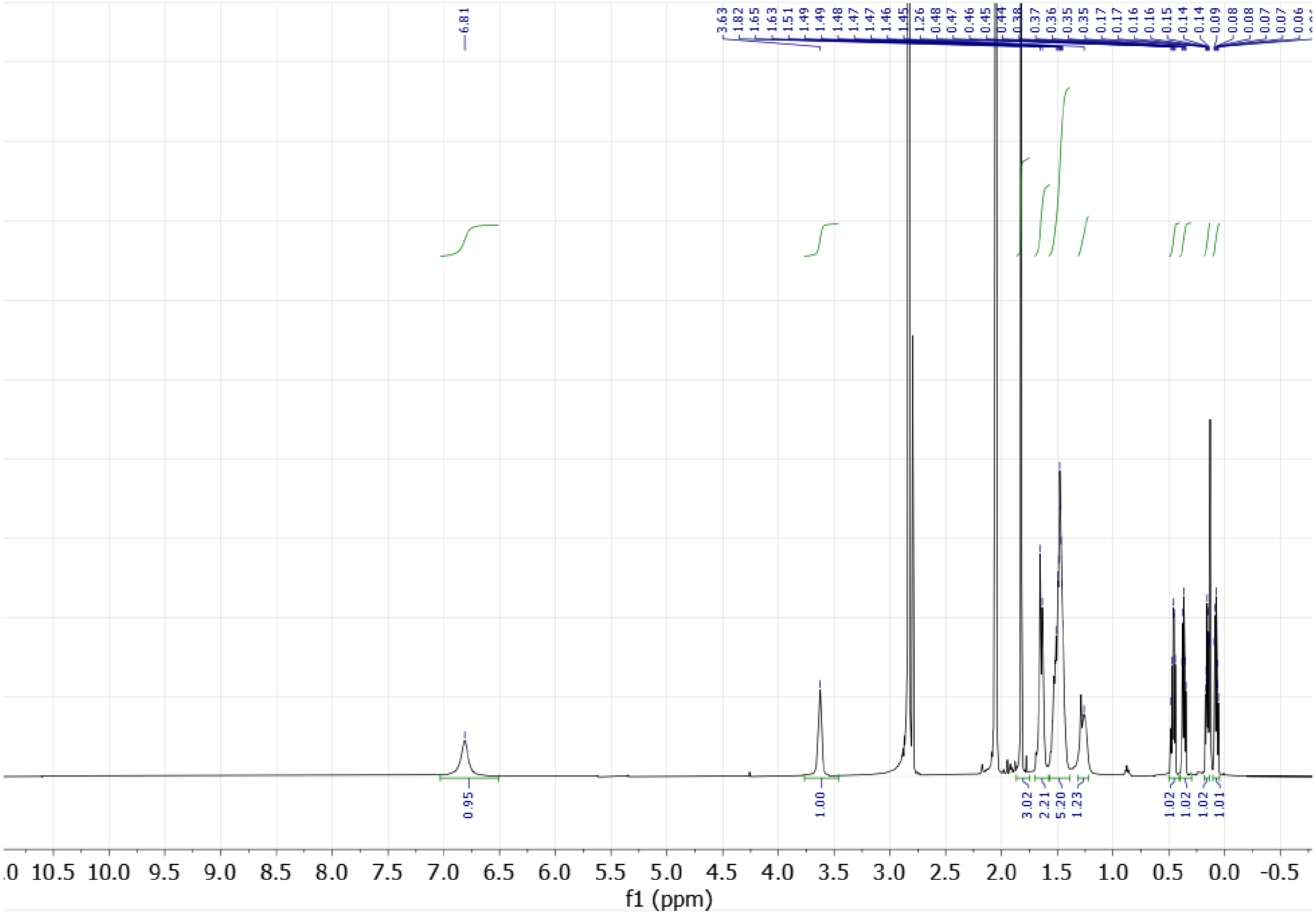
Compound 16 **crude ^{1}H NMR** (500 MHz, d_6-Acetone)



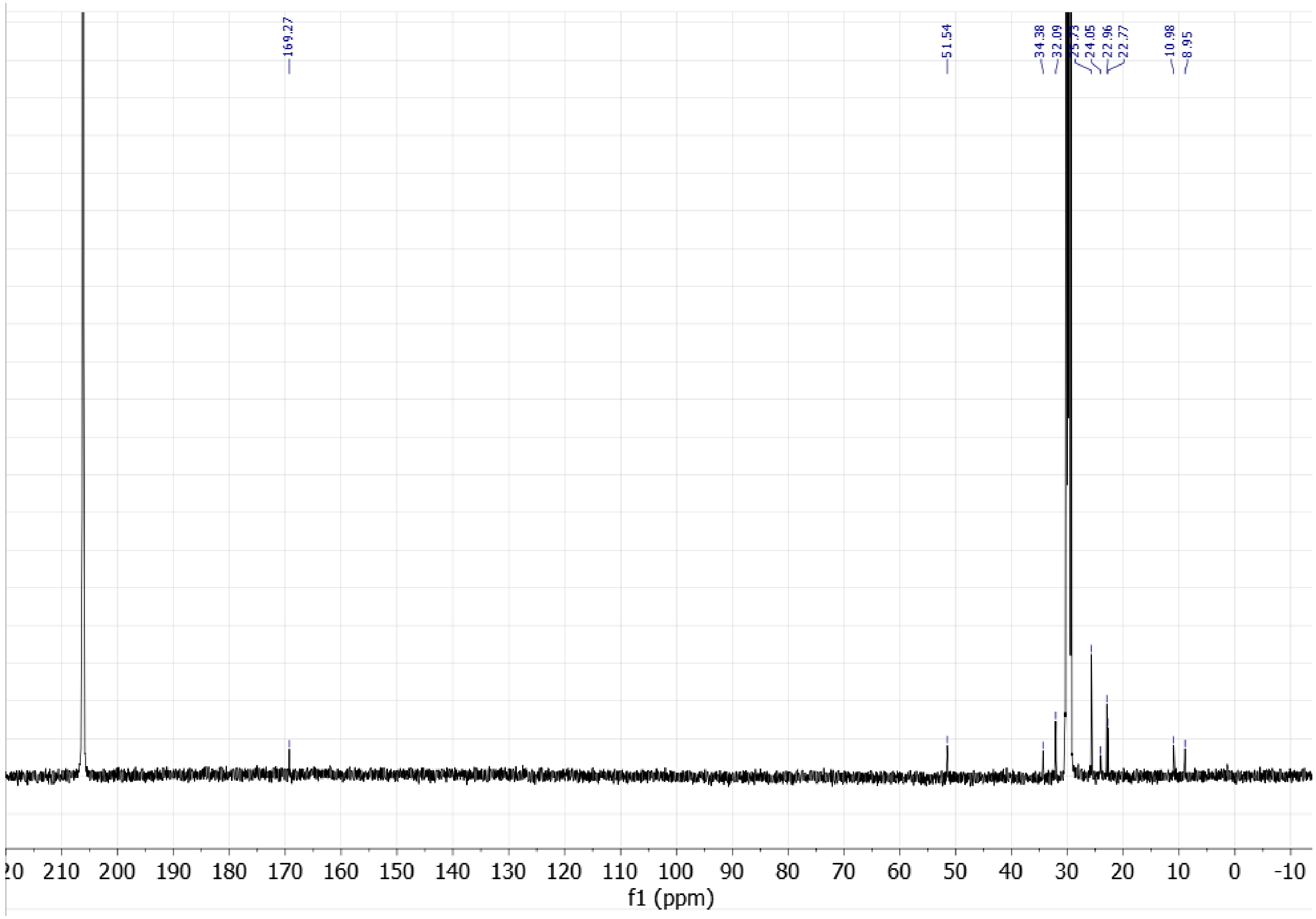
Compound **S17** **^{1}H NMR** (500 MHz,CDCl$_3$)



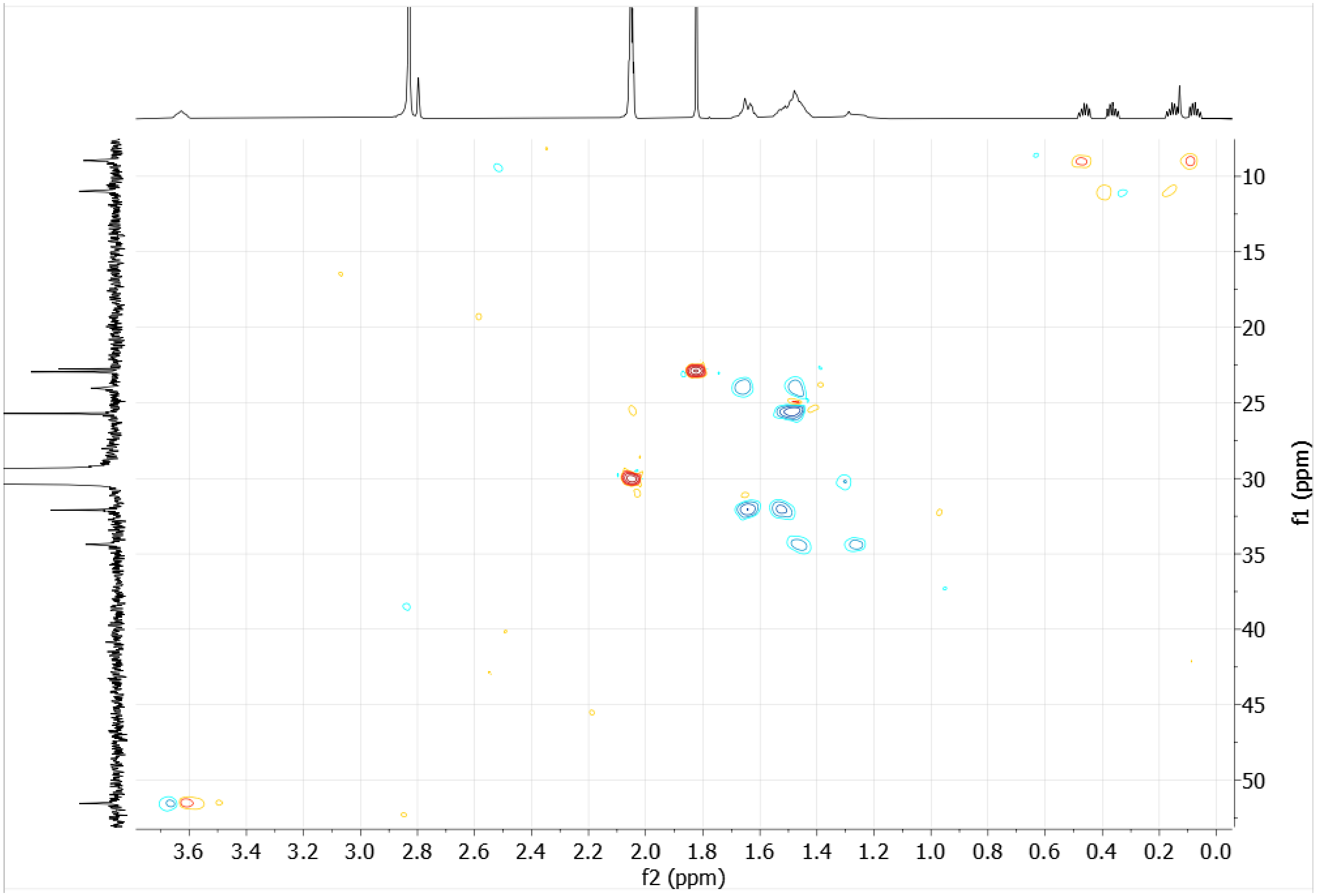
Compound **S17** **^{1}H NMR** (500 MHz, d_6-Acetone)



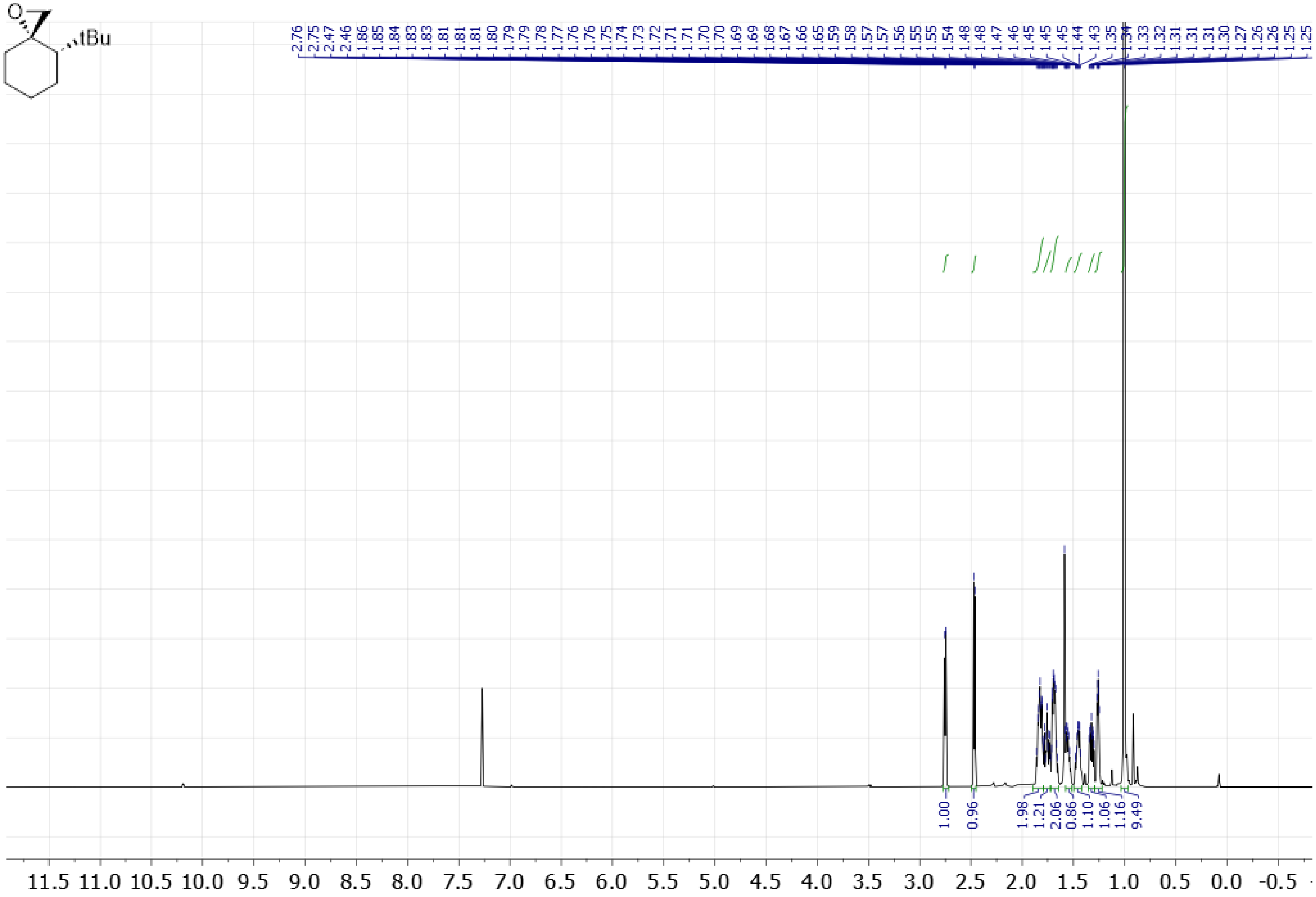
Compound **S17** **^{13}C NMR** (126 MHz, *d_6*-Acetone)



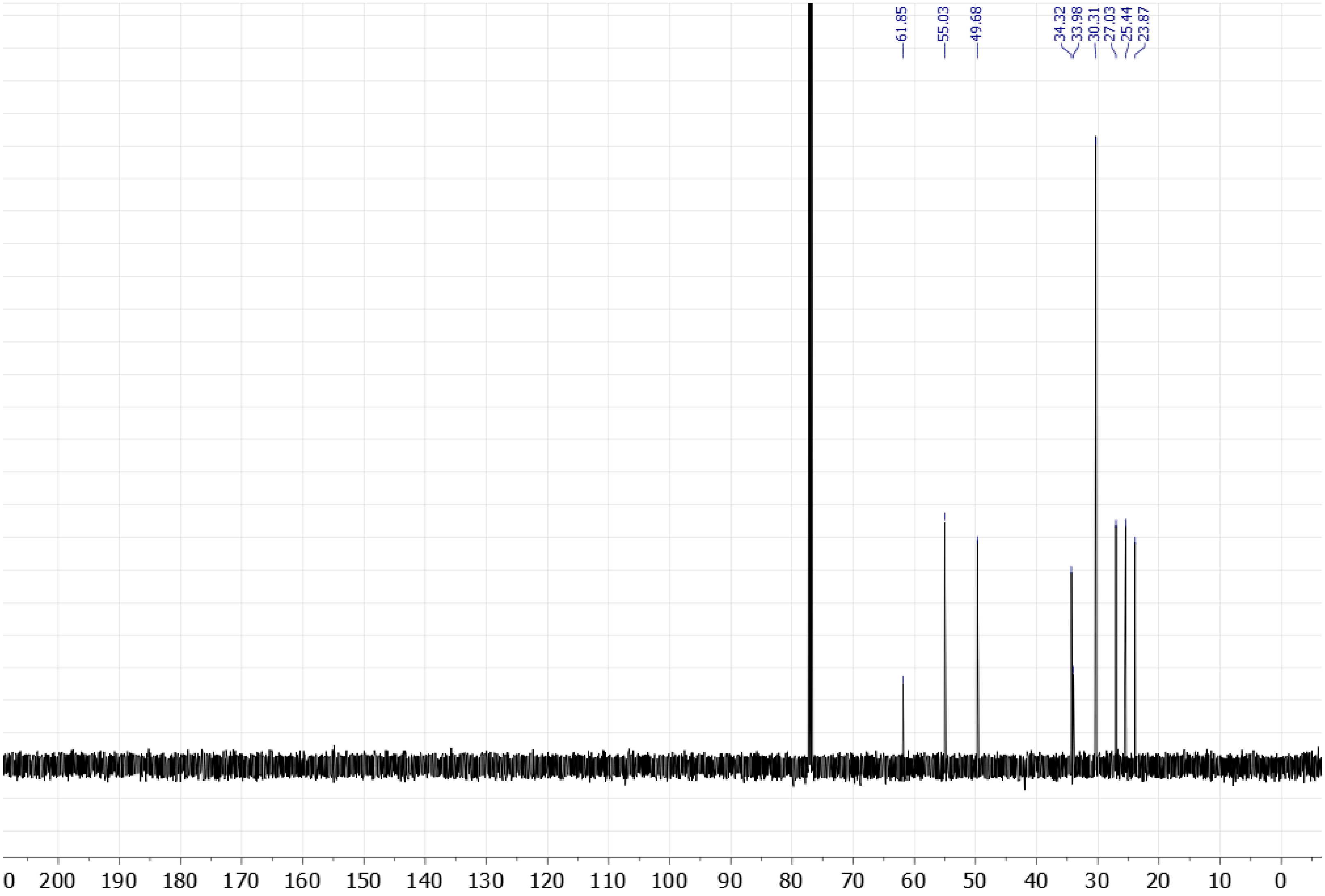
Compound **S17** **HSQC** (126 MHz, d_6-Acetone)



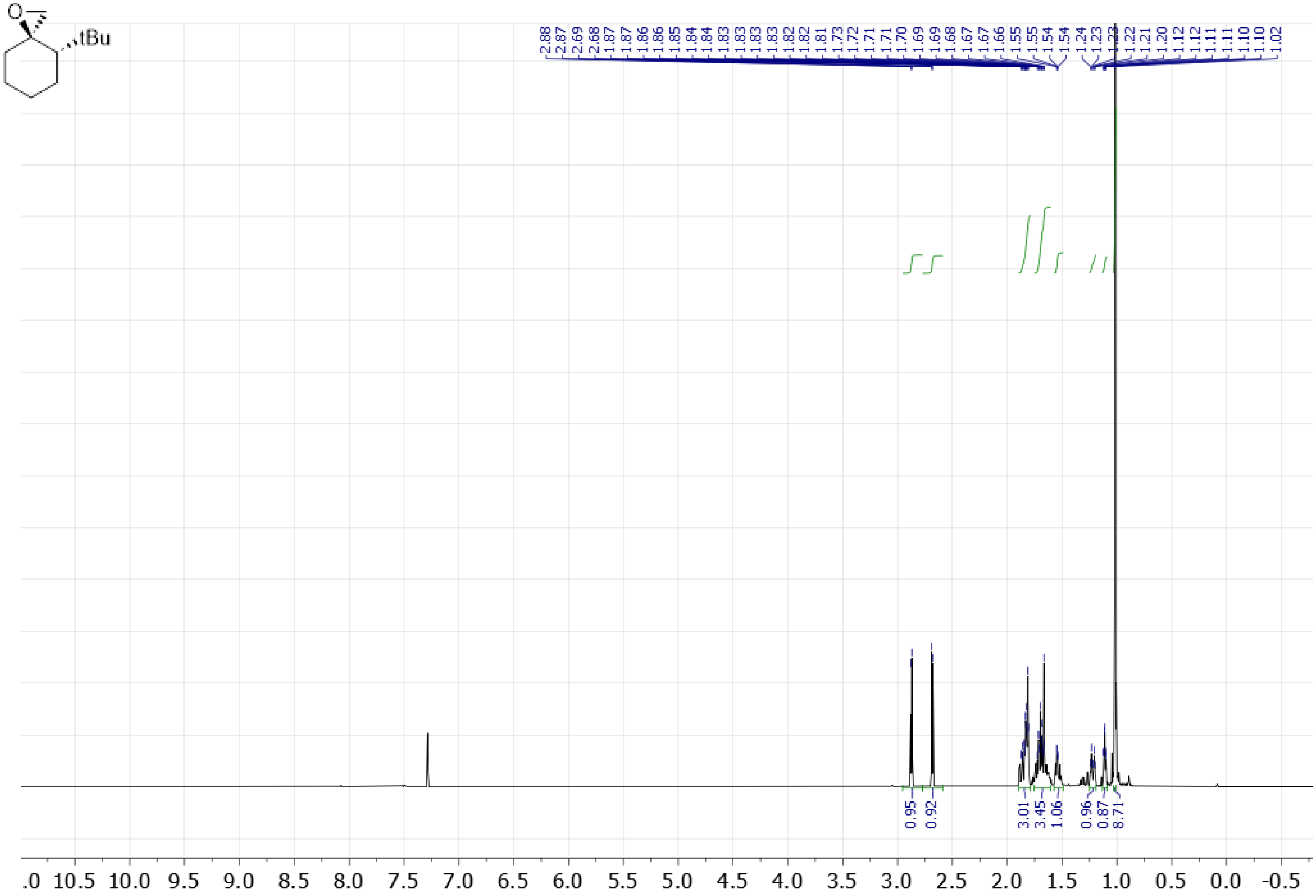
Compound **S18** **^{1}H NMR** (500 MHz, $CDCl_3$)



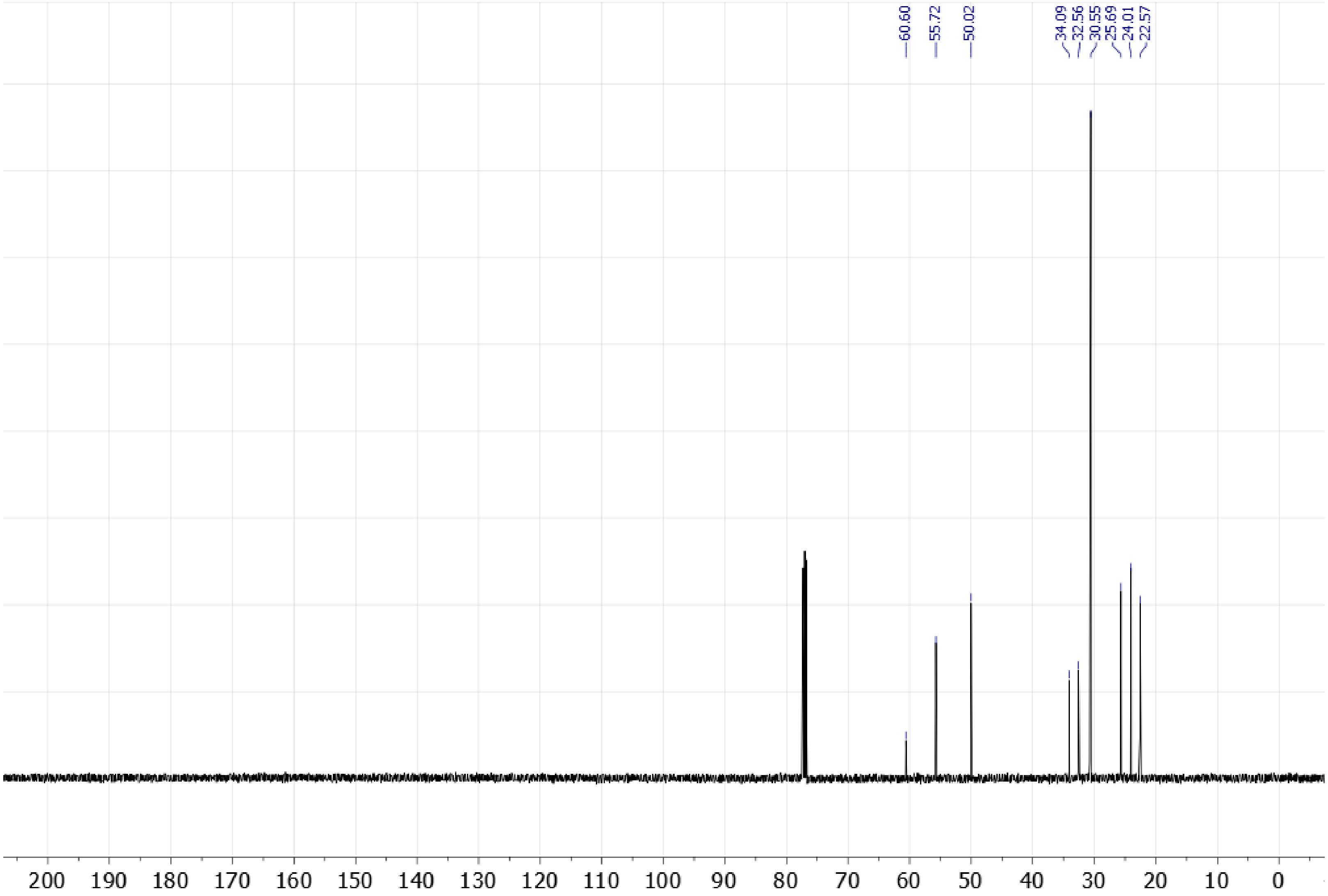
Compound **S18** **^{13}C NMR** (126 MHz, CDCl$_3$)



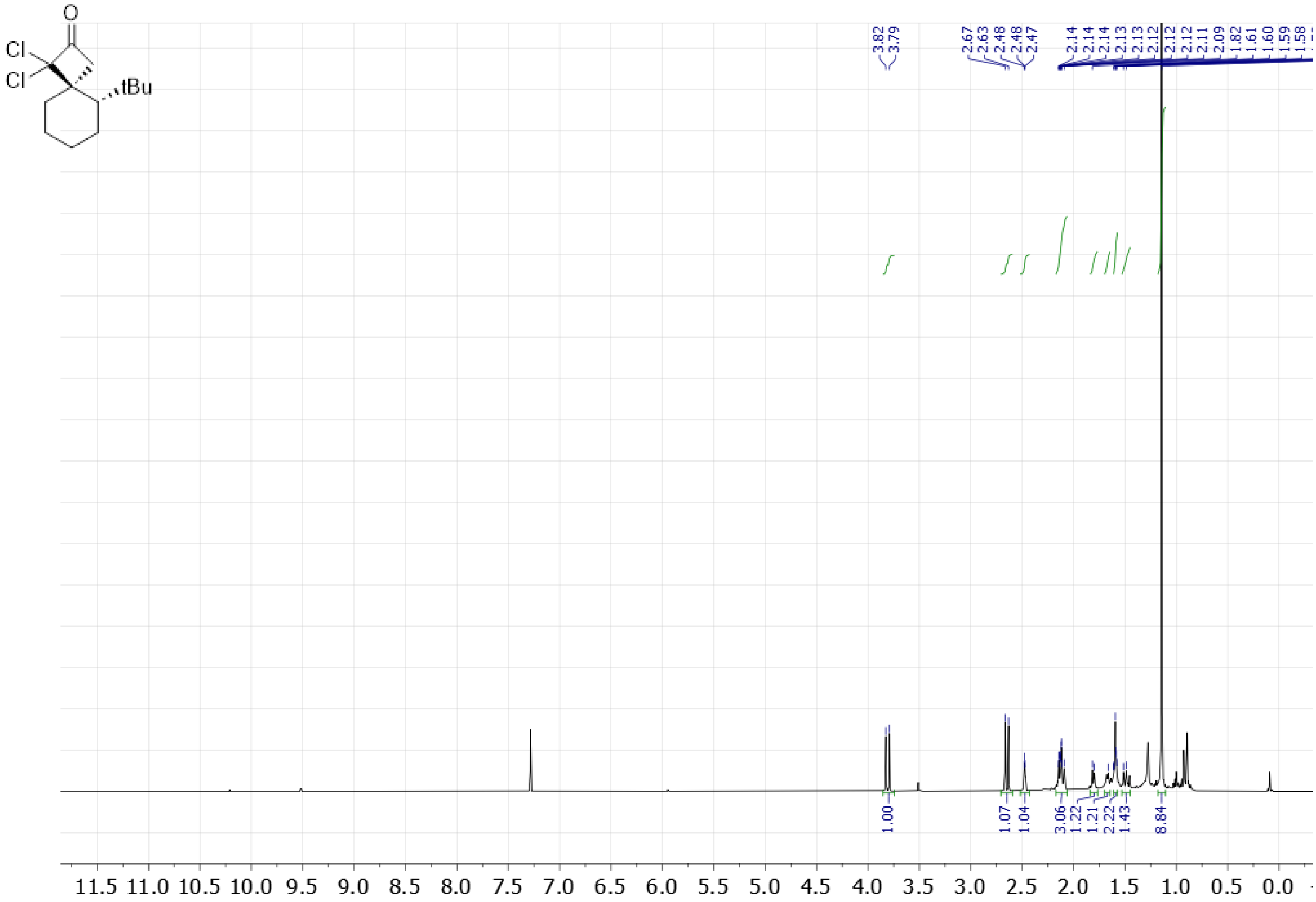
Compound **S19** **^{1}H NMR** (500 MHz, $CDCl_3$)



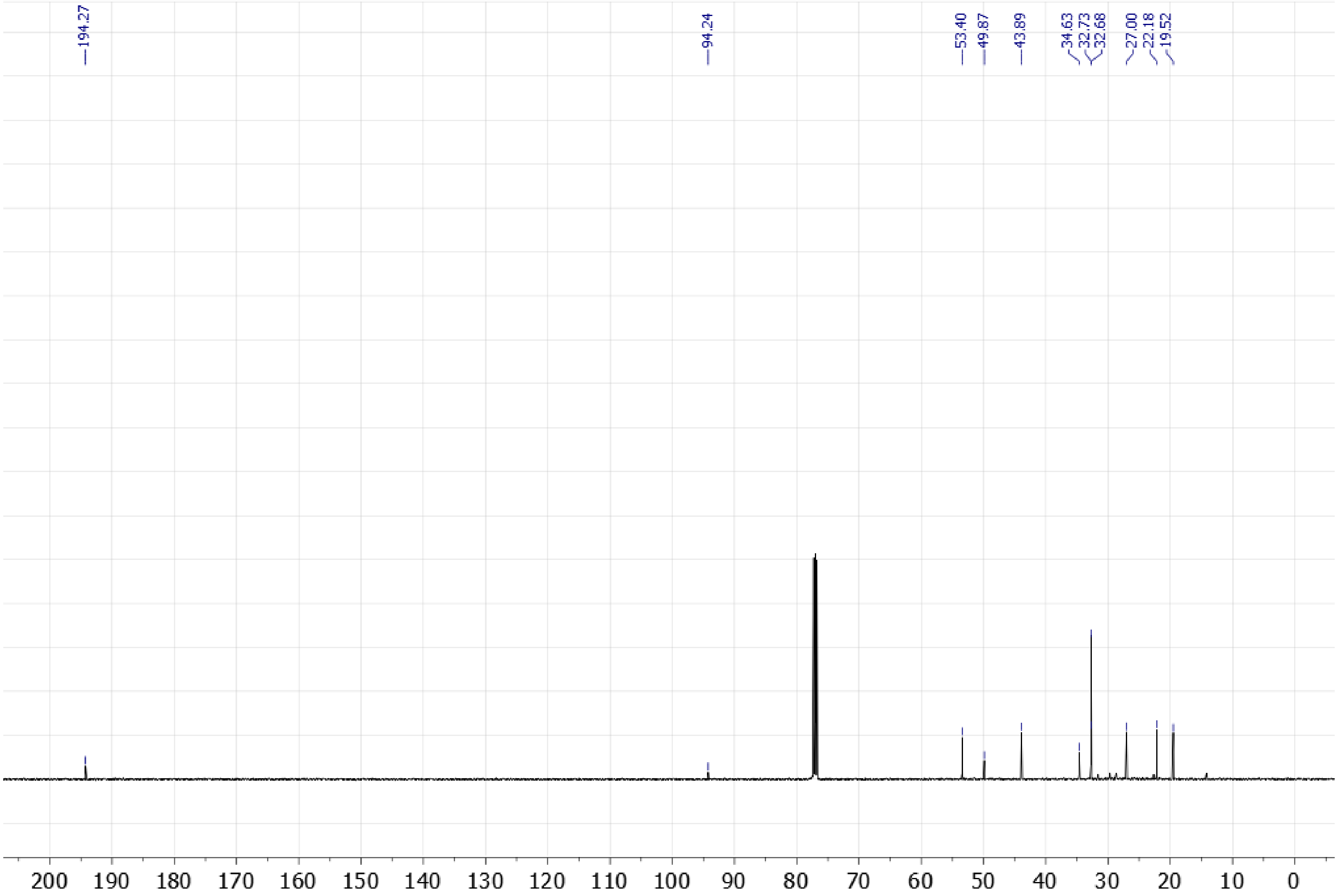
Compound **S19** ^{13}**C NMR** (126 MHz, $CDCl_3$)



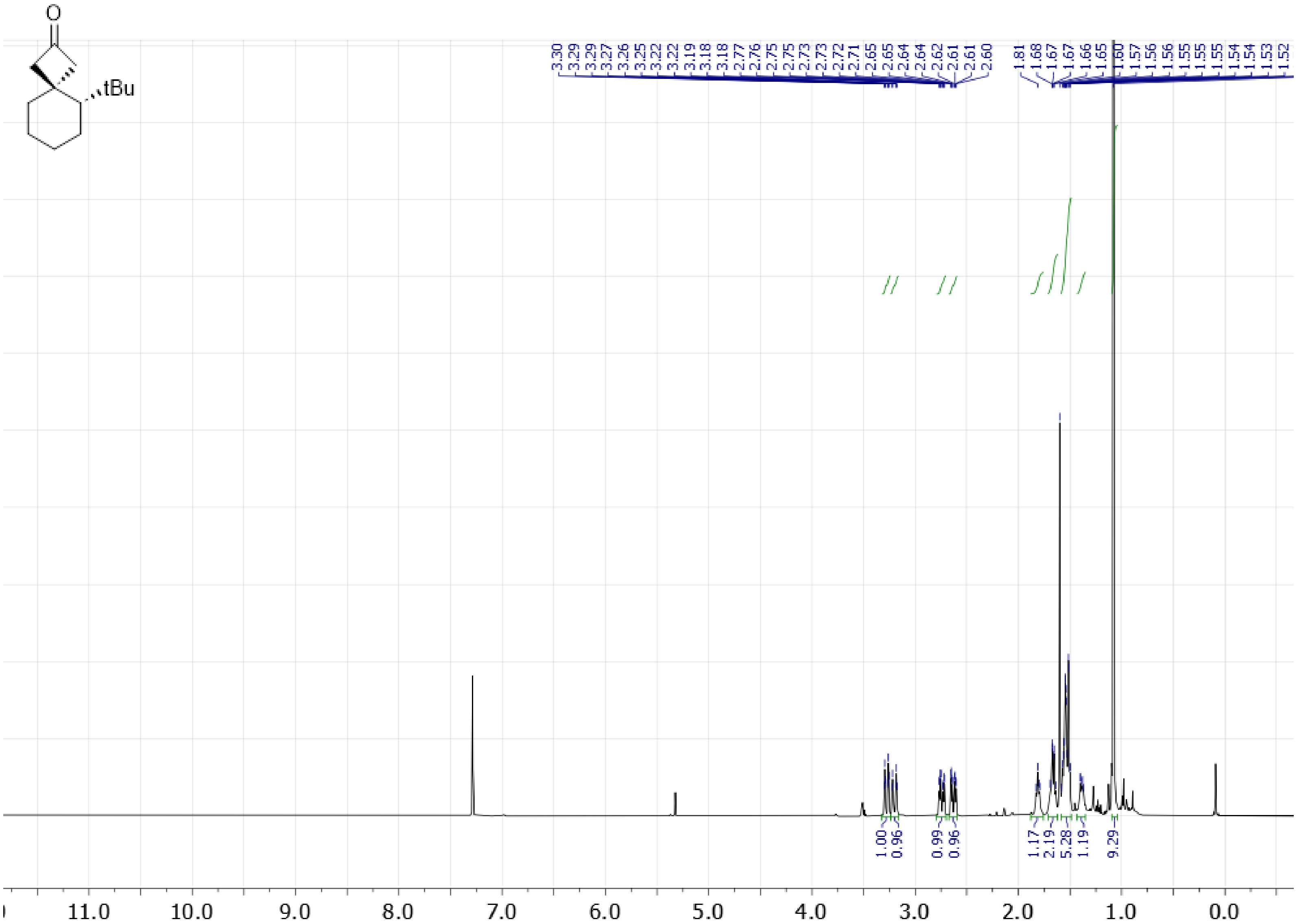
Compound **S20a** **^{1}H NMR** (500 MHz, CDCl$_3$)



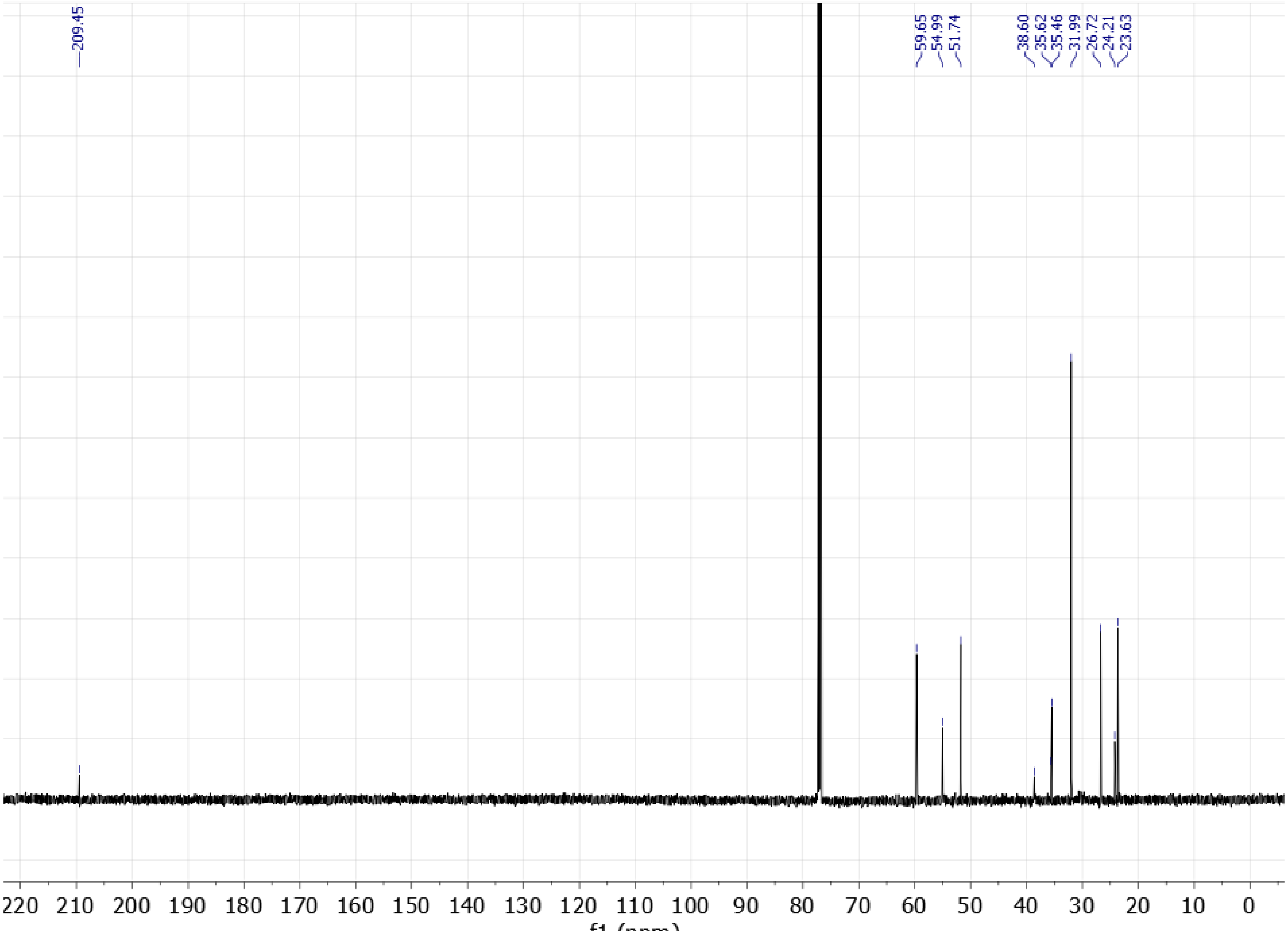
Compound **S20a** **^{13}C NMR** (126 MHz, $CDCl_3$)



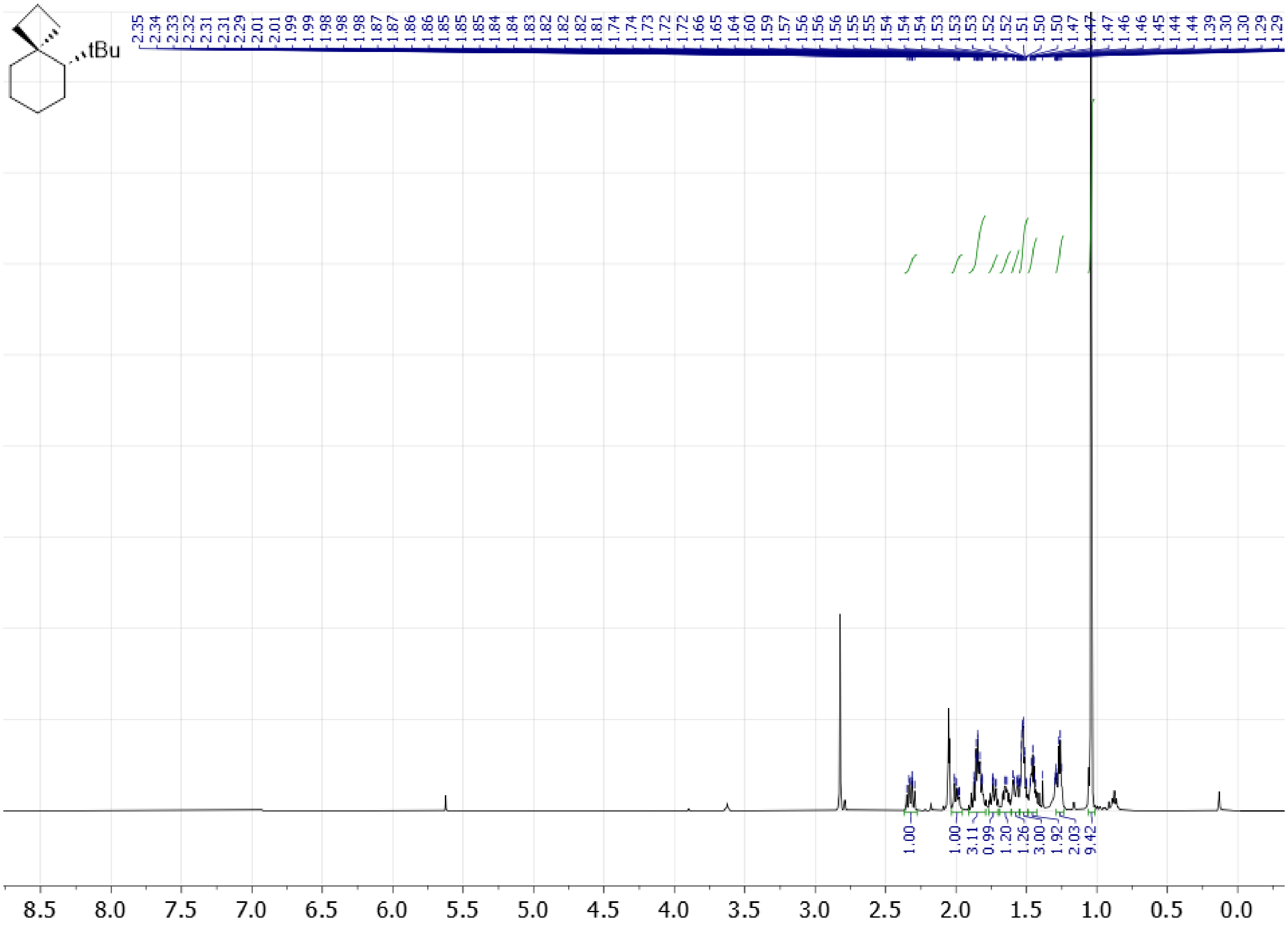
Compound **S20** **^{1}H NMR** (500 MHz, CDCl$_3$)



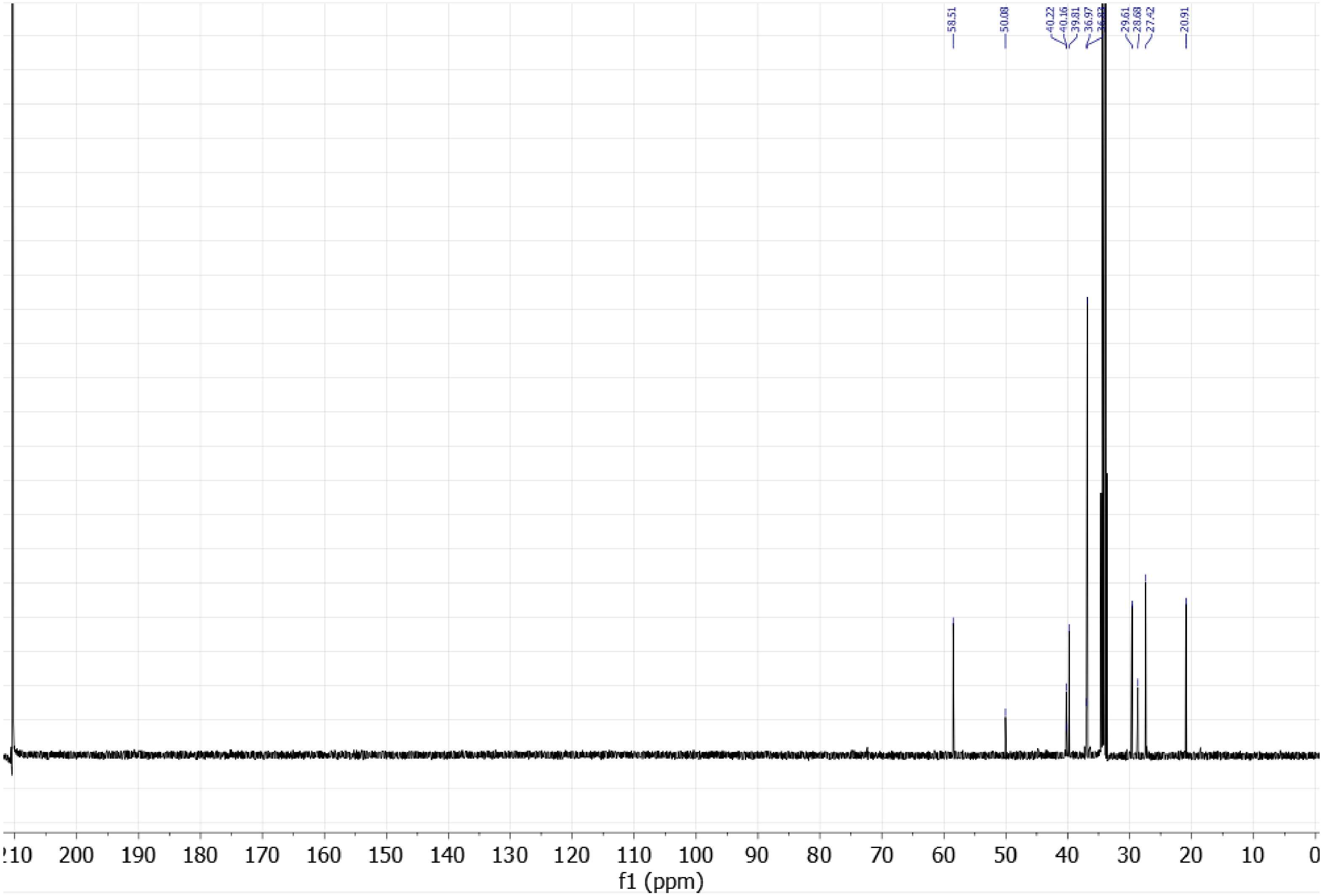
Compound **S20** **^{13}C NMR** (126 MHz, $CDCl_3$)



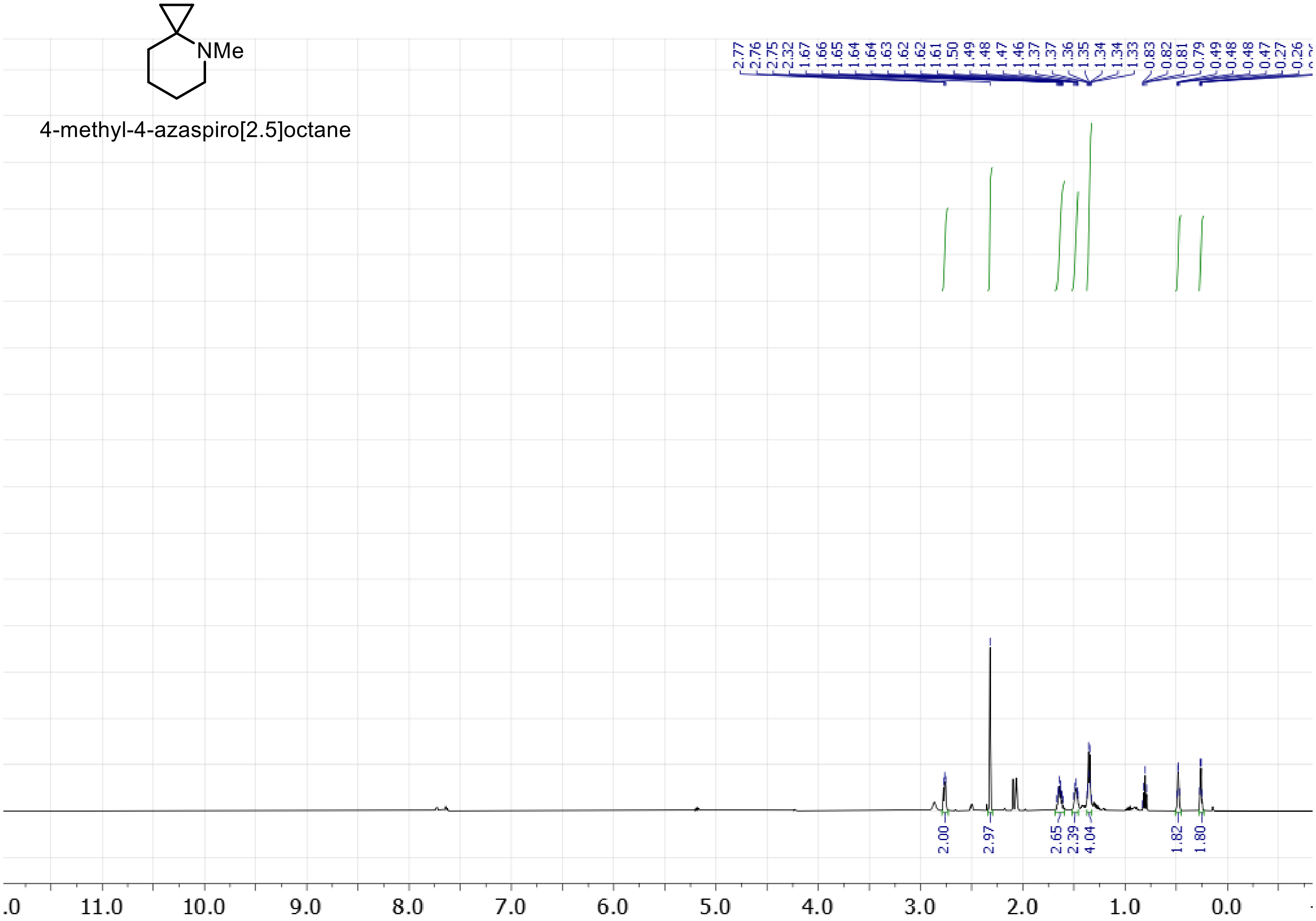
Compound **S21** **^{1}H NMR** (500 MHz, d_6-Acetone)



Compound **S21** **^{13}C NMR** (126 MHz, d_6-Acetone)

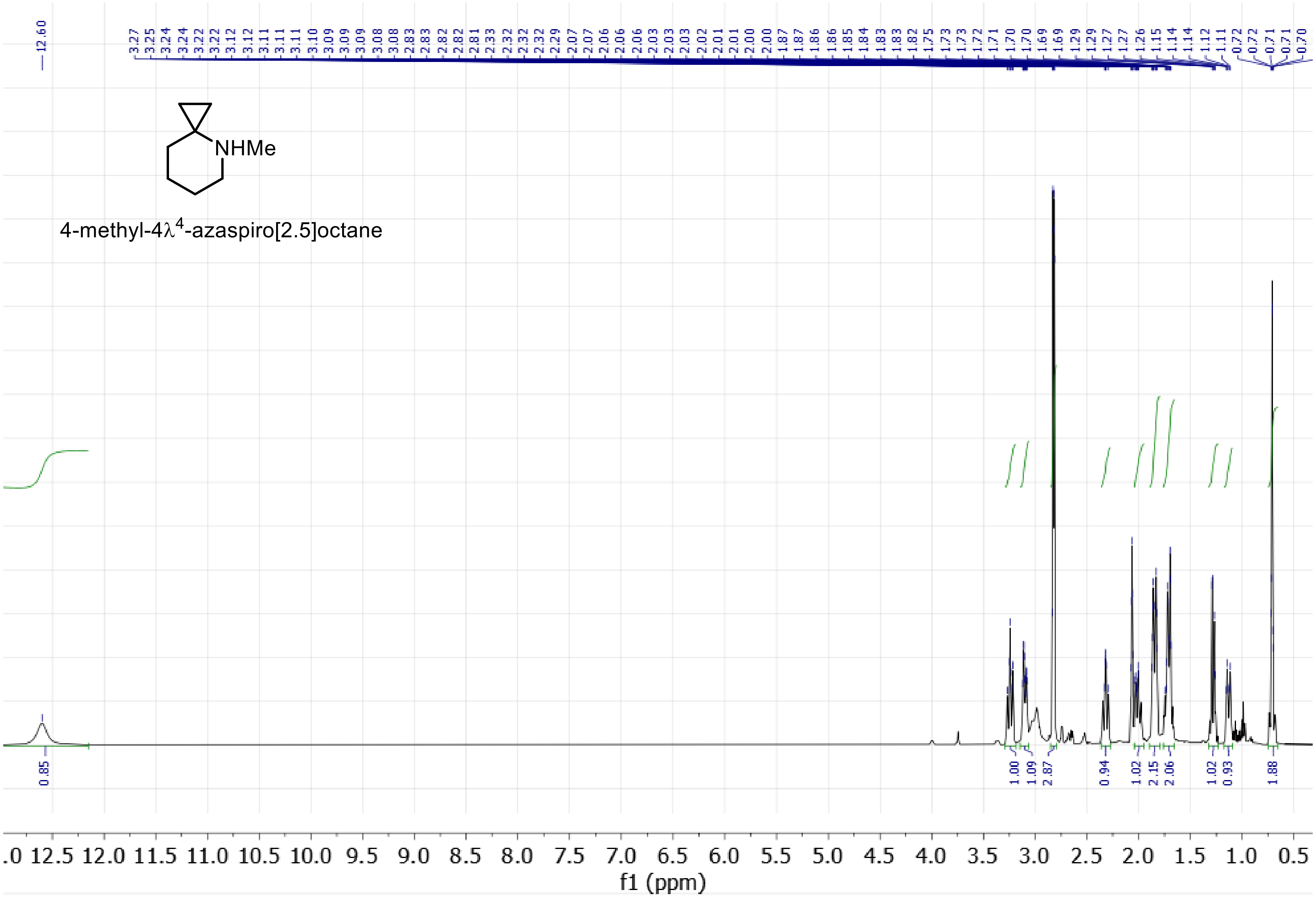


Compound **S23-**neutral ^{1}**H NMR** (500 MHz, *d*$_6$-Acetone)

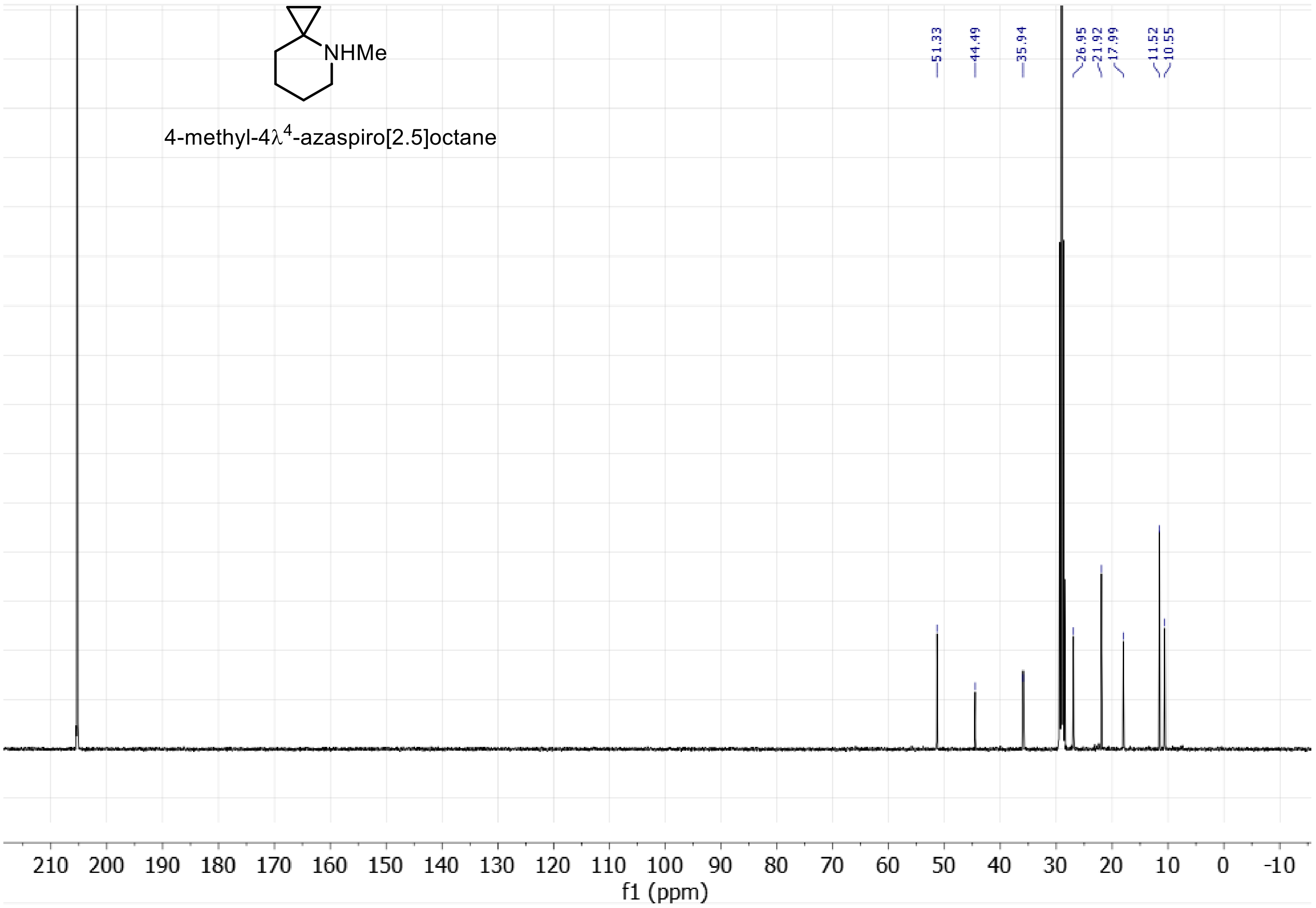


4-methyl-4-azaspiro[2.5]octane

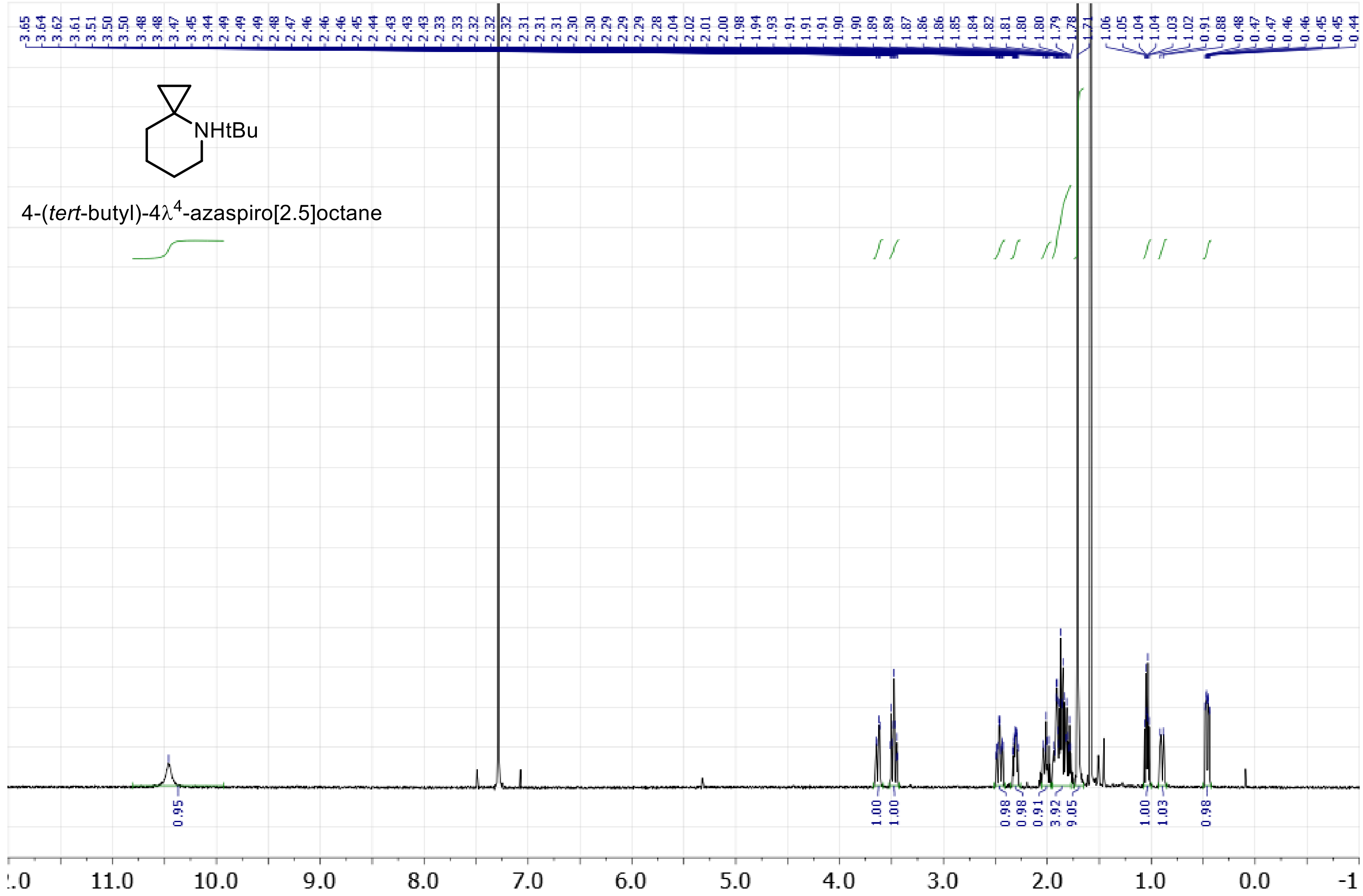
Compound **S23-**HCl ^{1}**H NMR** (500 MHz, *d*$_6$-Acetone)



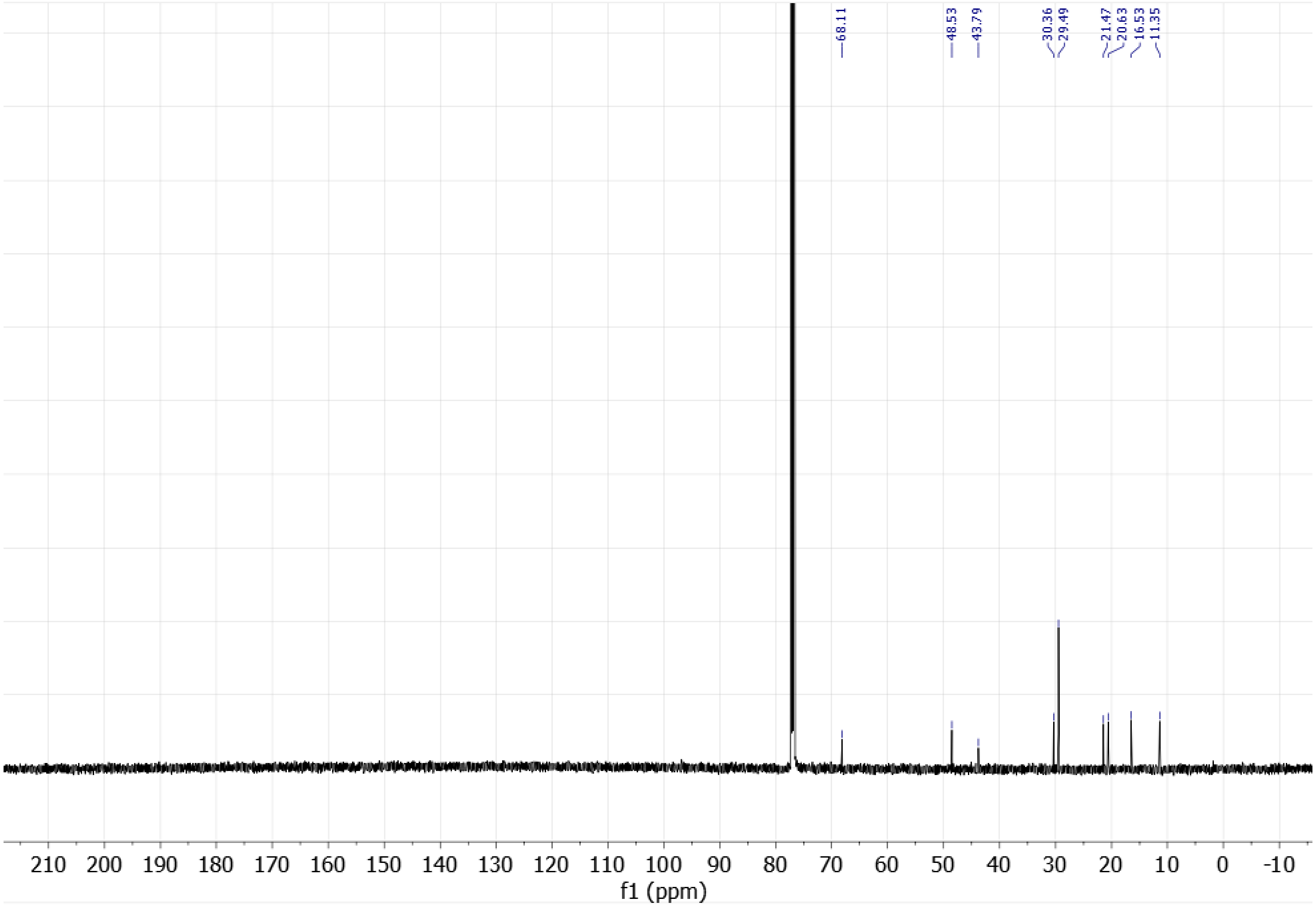
Compound **S23-HCl ^{13}C NMR** (126 MHz, d_6-Acetone)



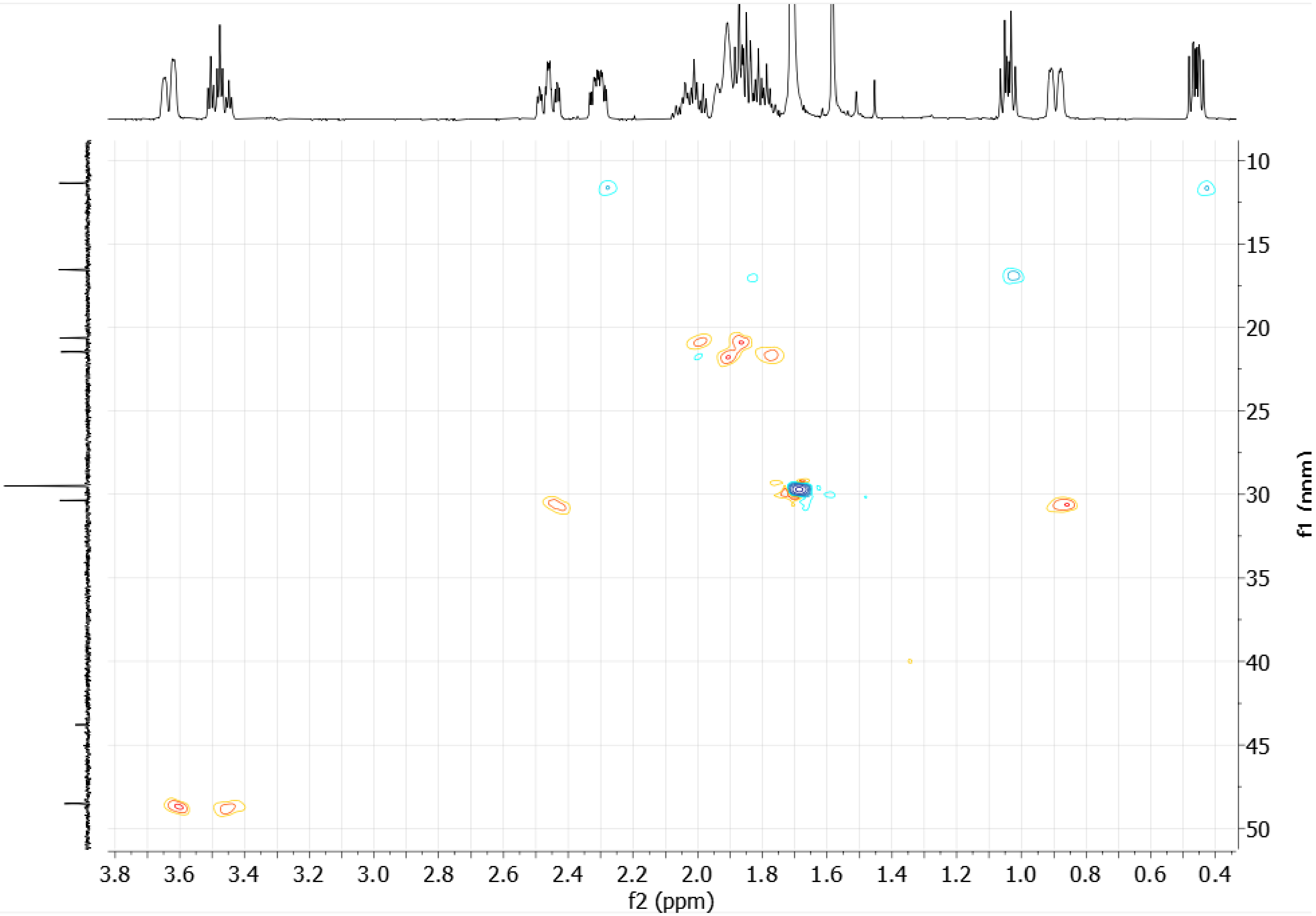
Compound **S24** **^{1}H NMR** (500 MHz, $CDCl_3$)



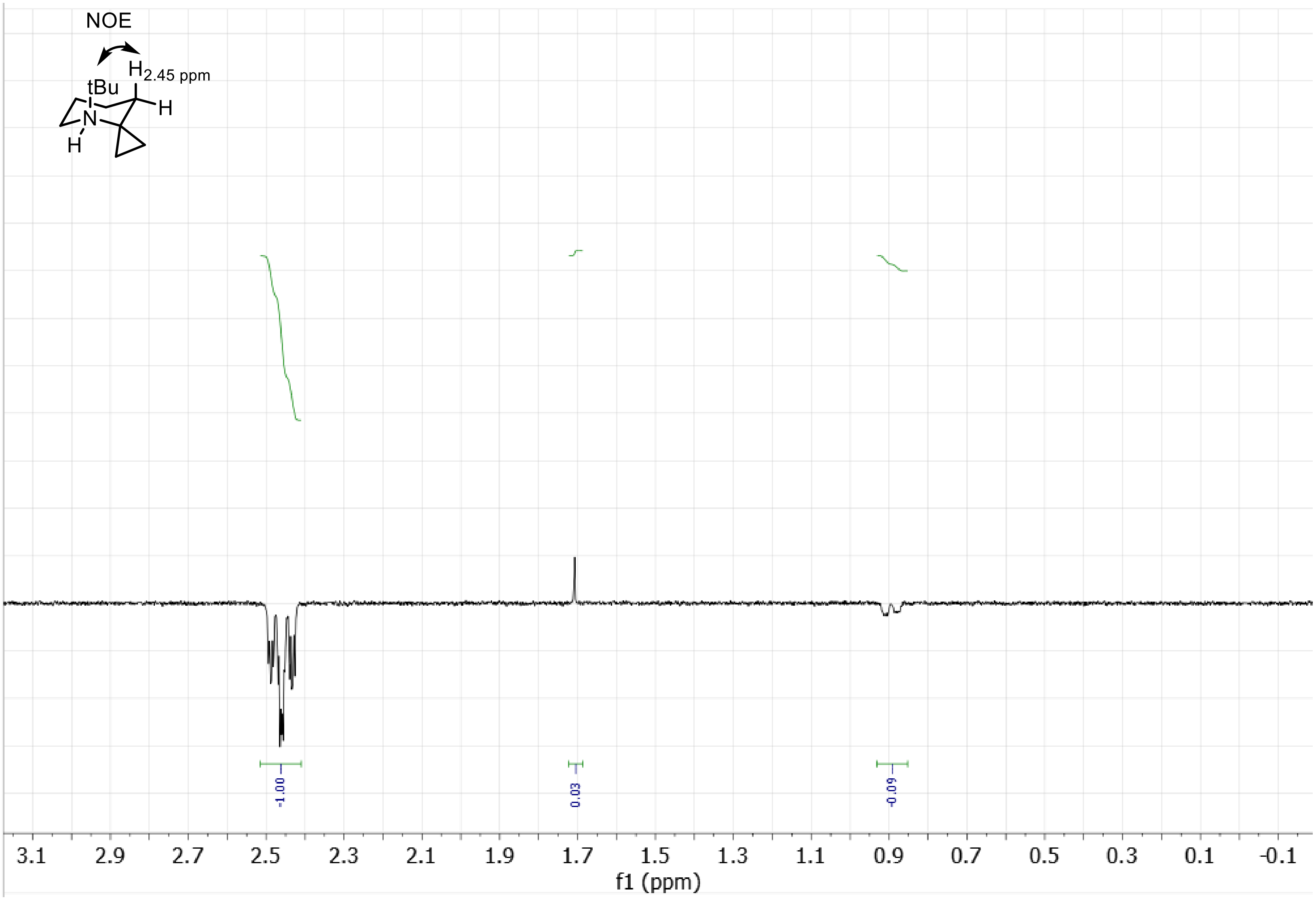
Compound **S24** **^{13}C NMR** (126 MHz, $CDCl_3$)



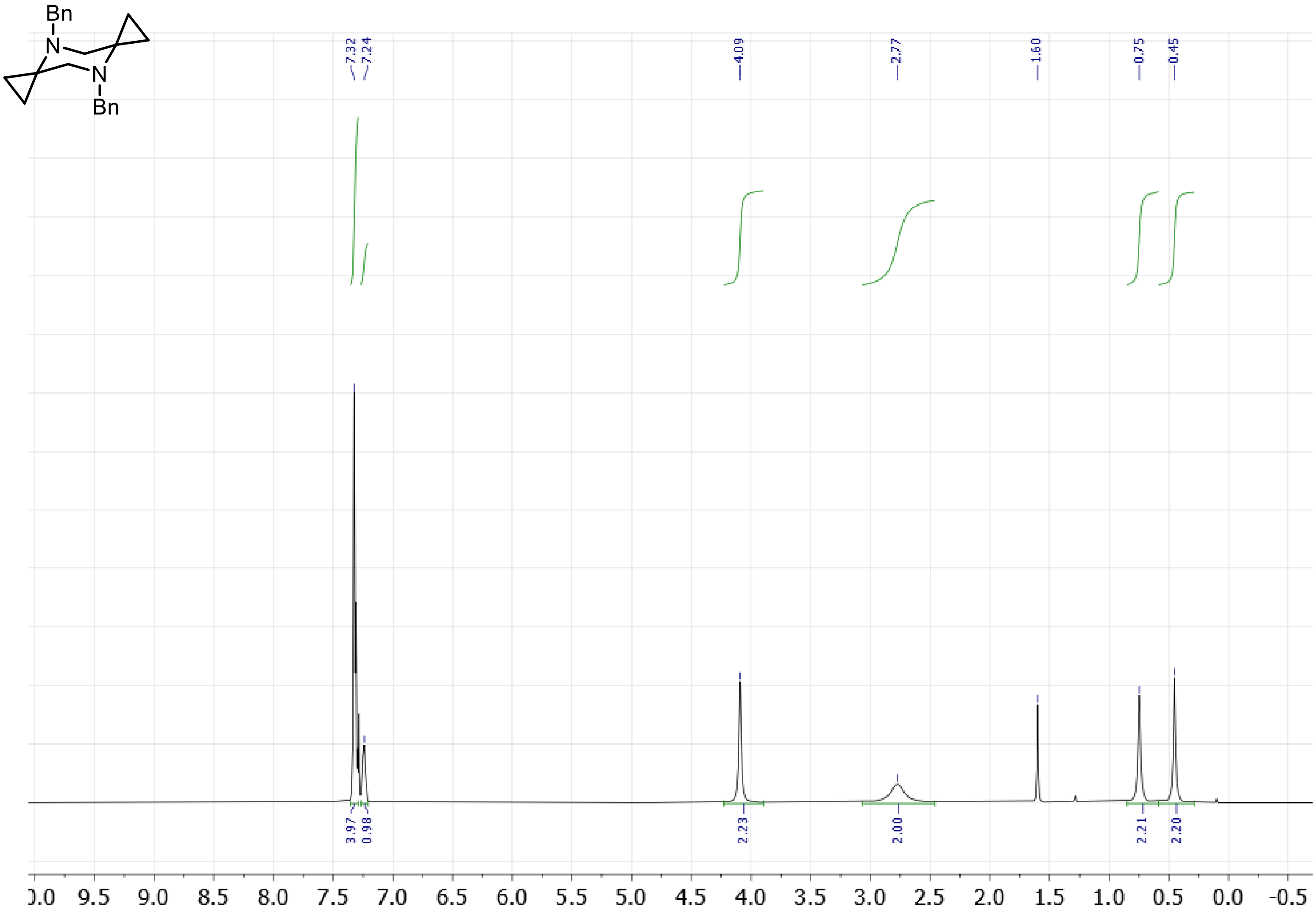
Compound **S24 HSQC** (CDCl$_3$)



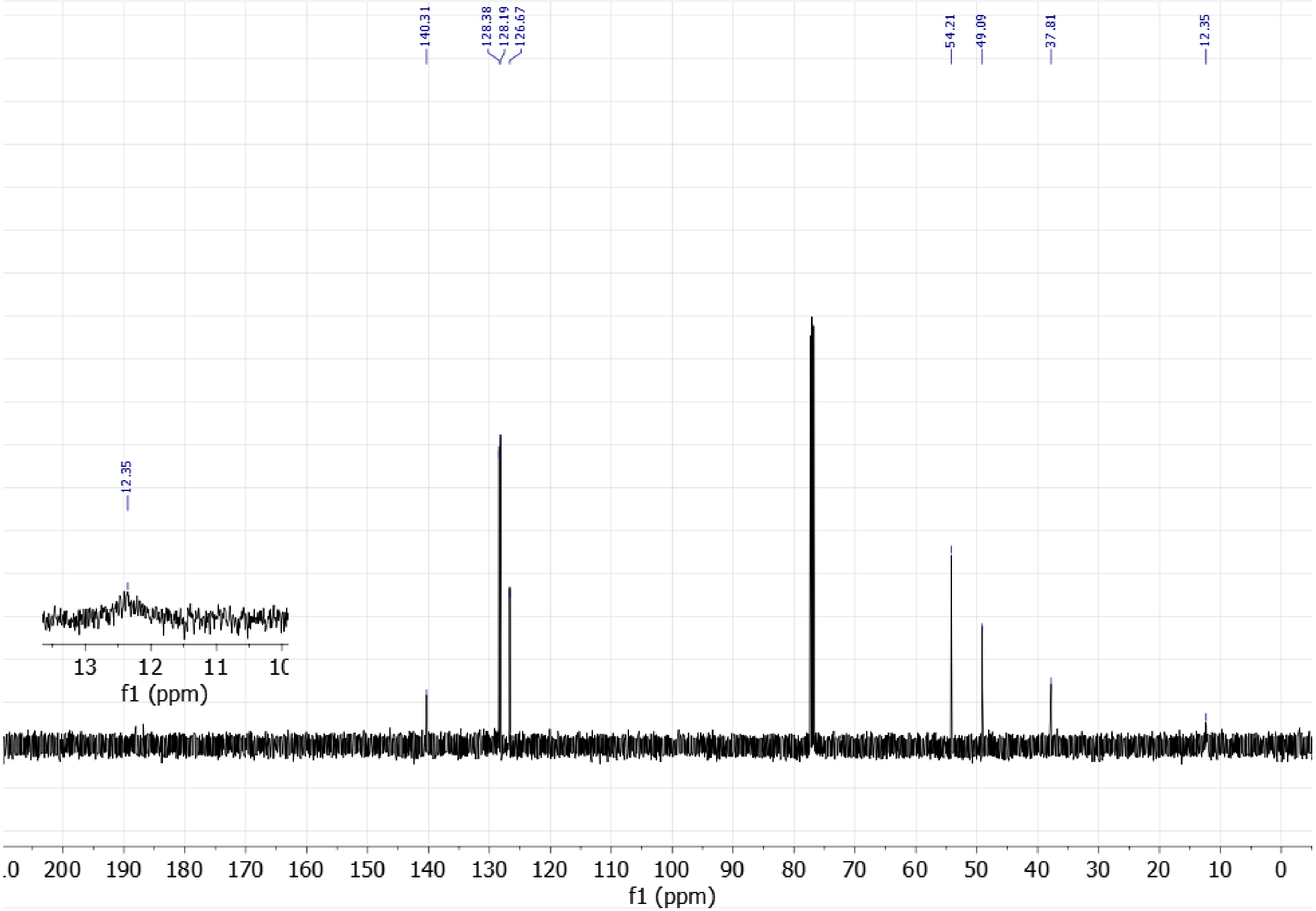
Compound **S24 1D NOE (**irradiation at 2.45 ppm, axial proton adjacent to cyclopropane)



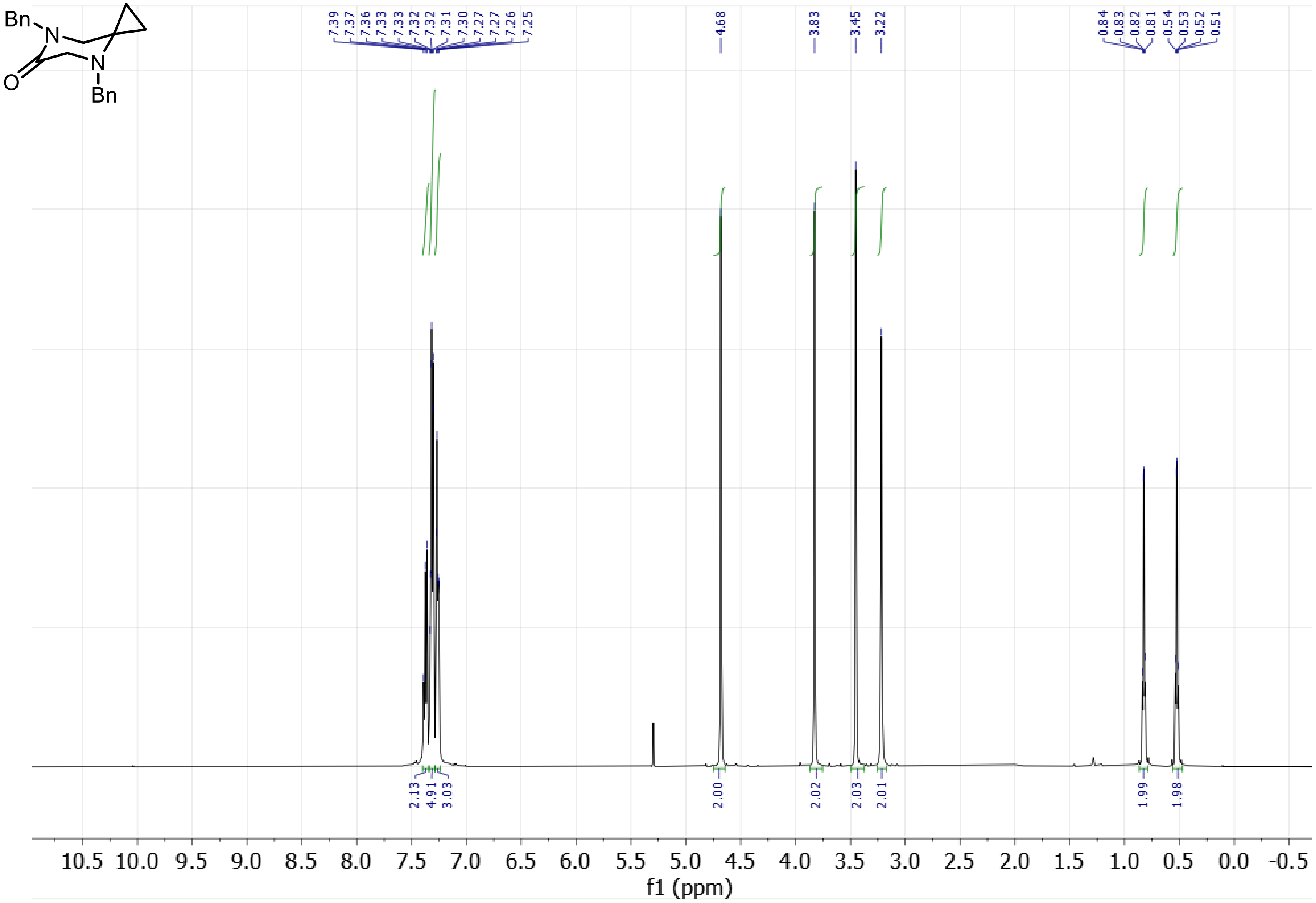
Compound **S25** **^{1}H NMR** (500 MHz, $CDCl_3$)



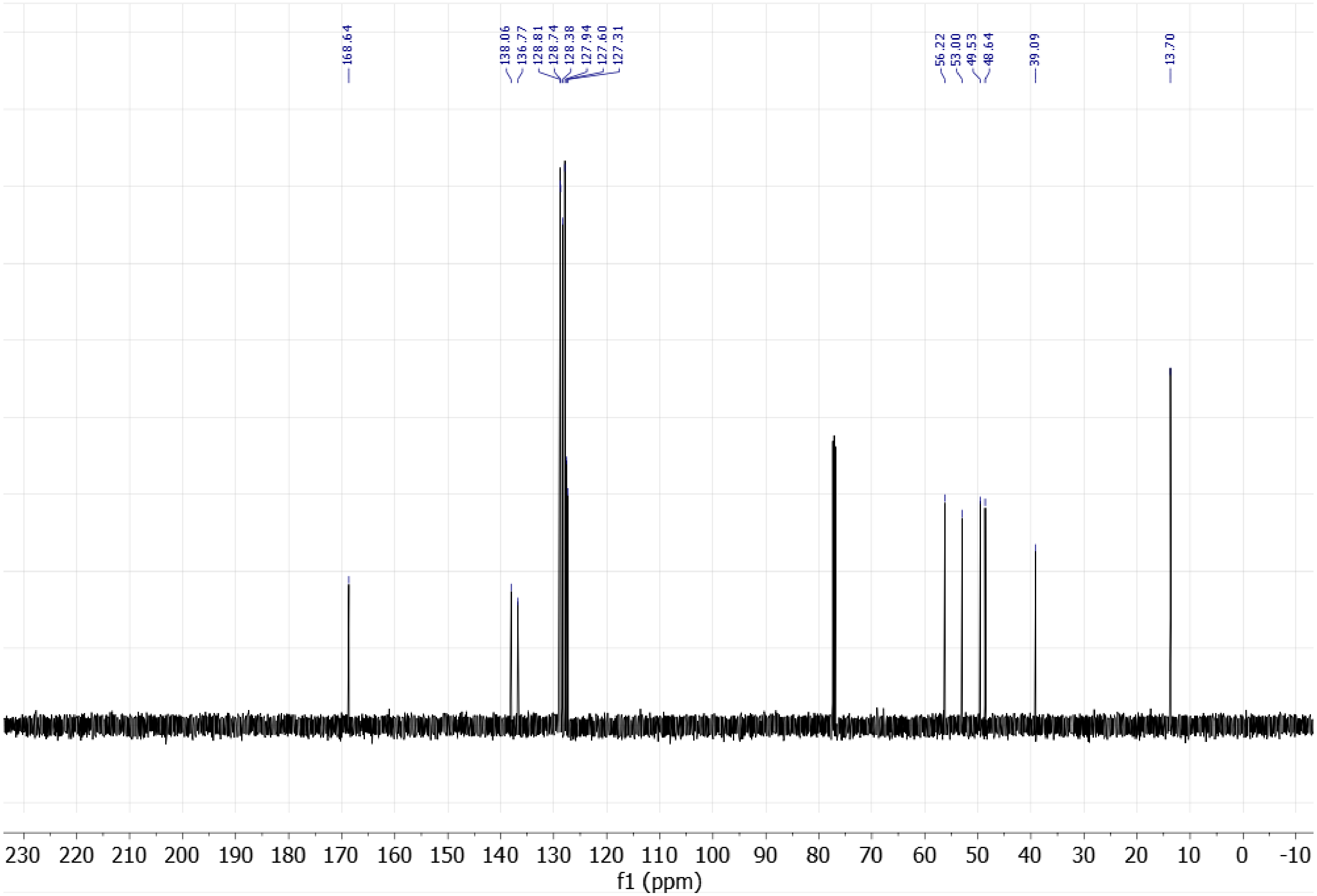
Compound **S25** ^{13}**C NMR** (126 MHz, $CDCl_3$) with zoom of broad peak at 12.35 ppm



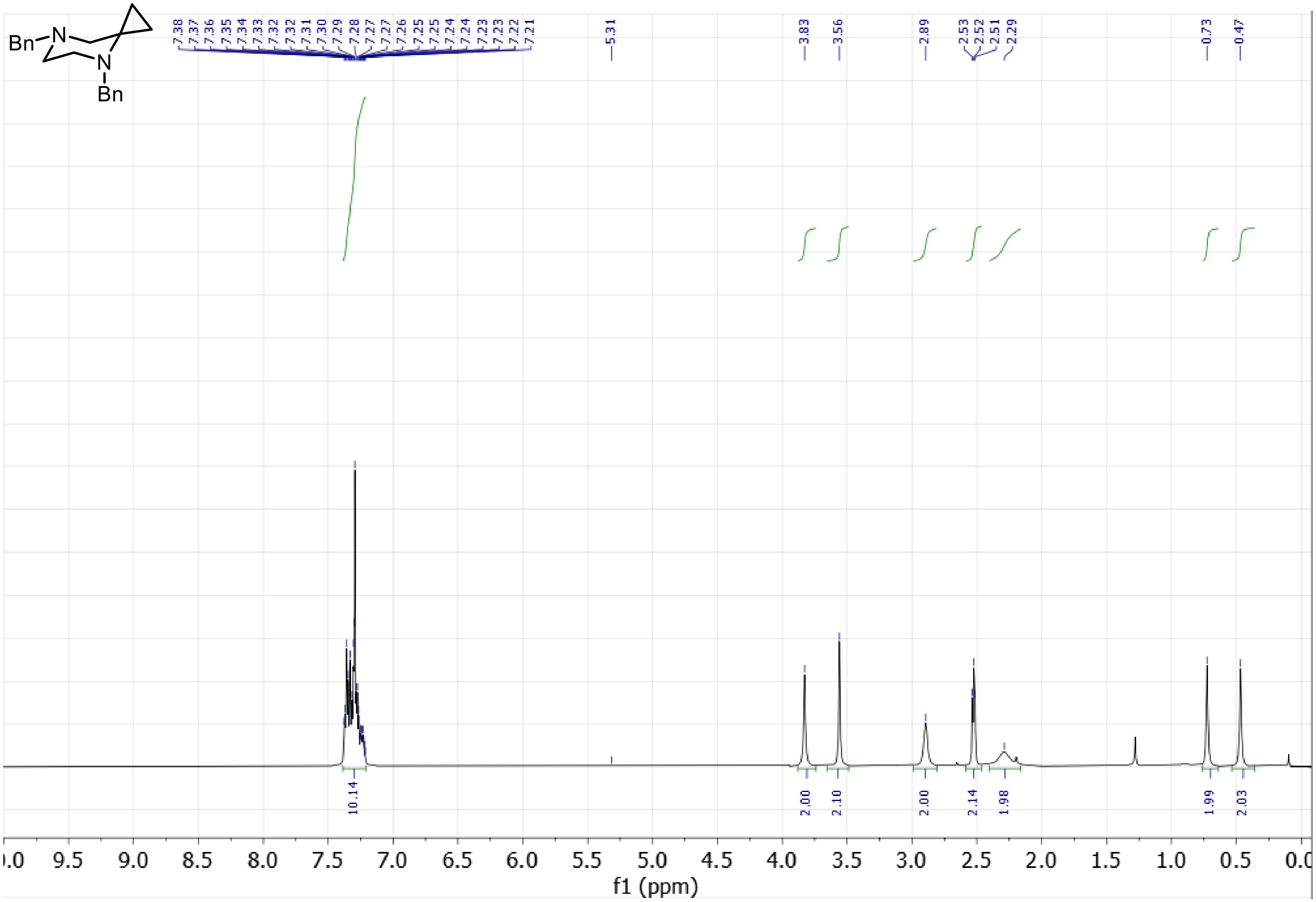
Compound **S26** **^{1}H NMR** (500 MHz, $CDCl_3$)



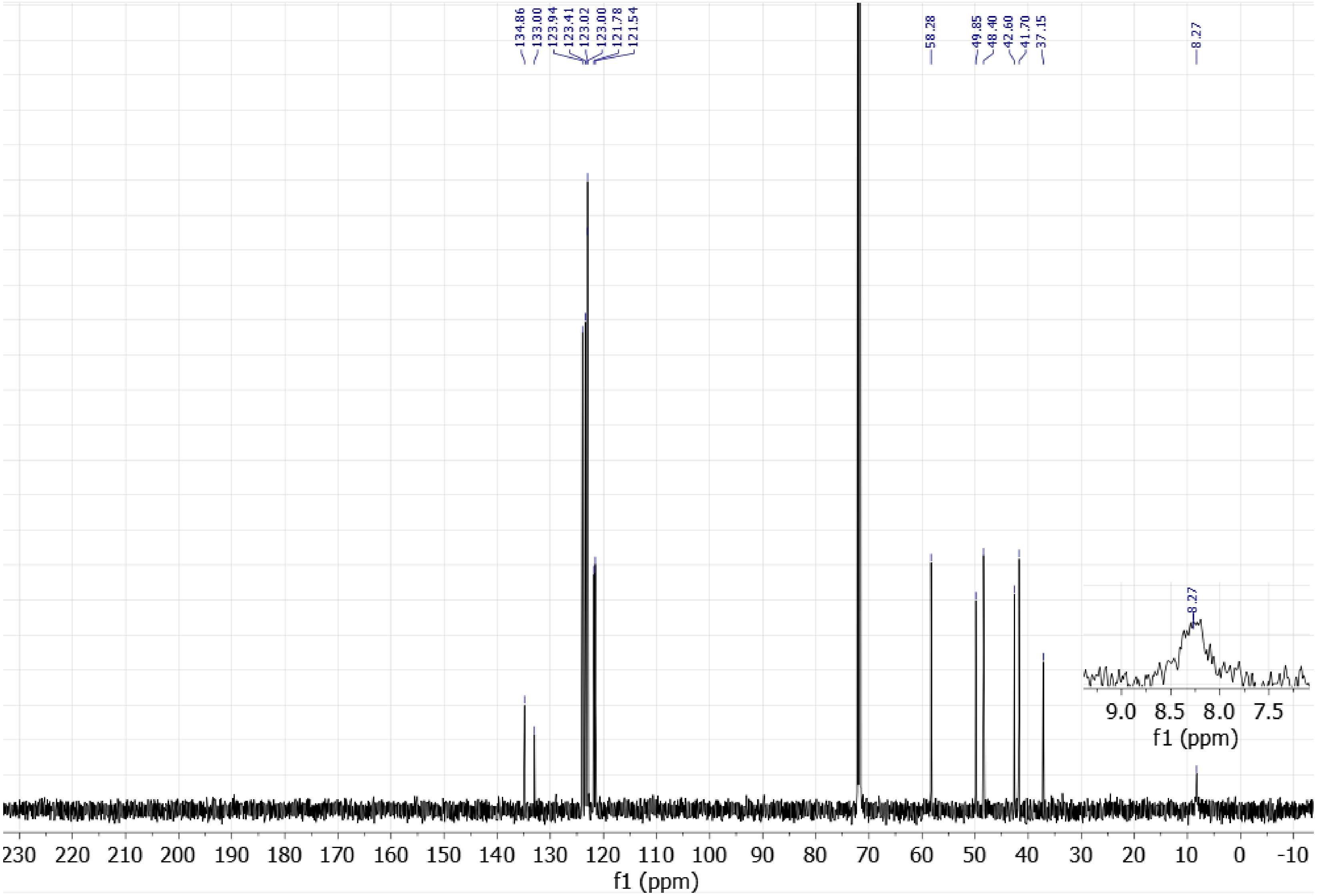
Compound **S26** ^{13}**C NMR** (126 MHz, CDCl$_3$)



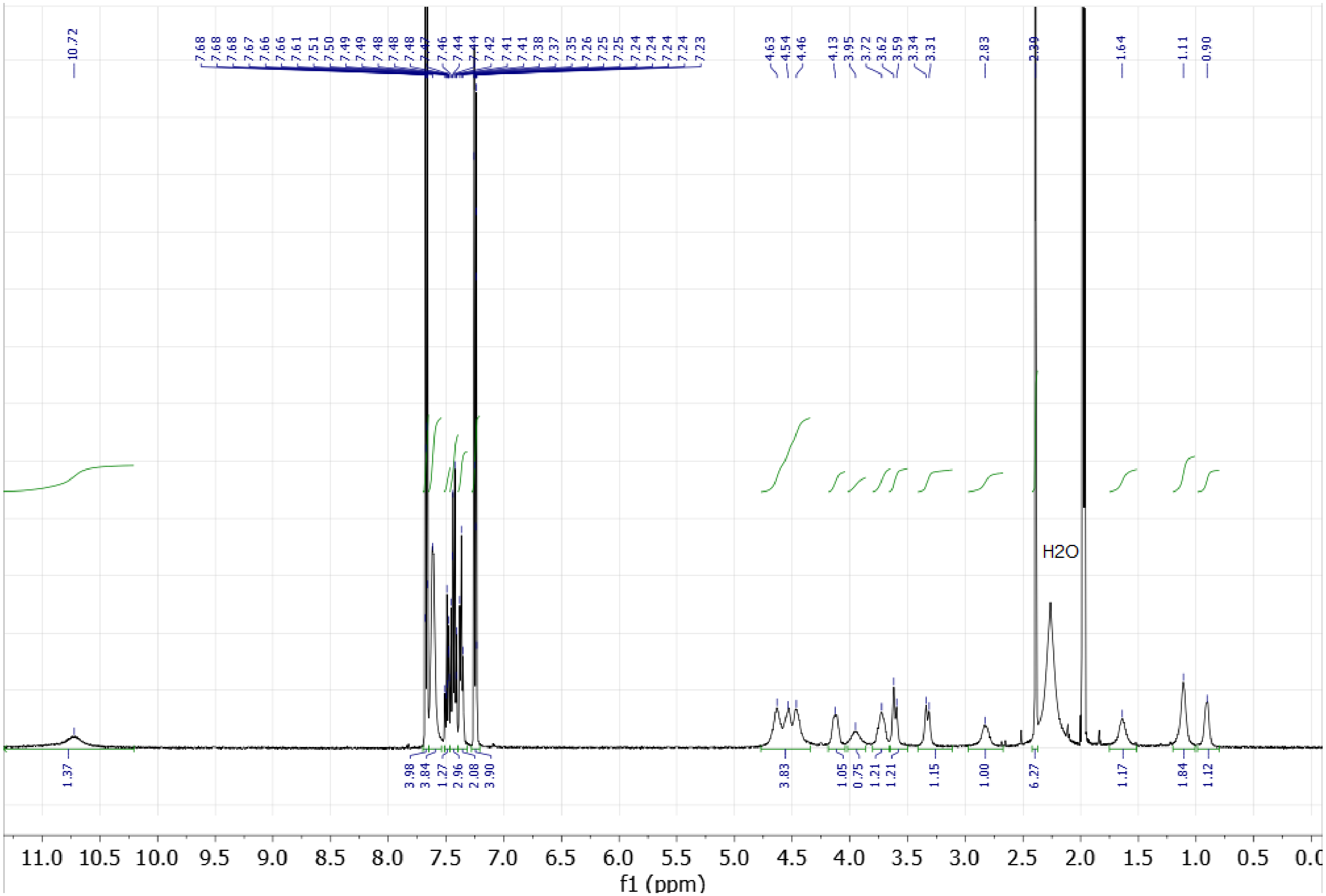
Compound **S27** **^{1}H NMR** (500 MHz, CDCl$_3$)



Compound **S27** ^{13}**C NMR** (126 MHz, CDCl$_3$) with zoom of slightly broad peak at 8.27 ppm

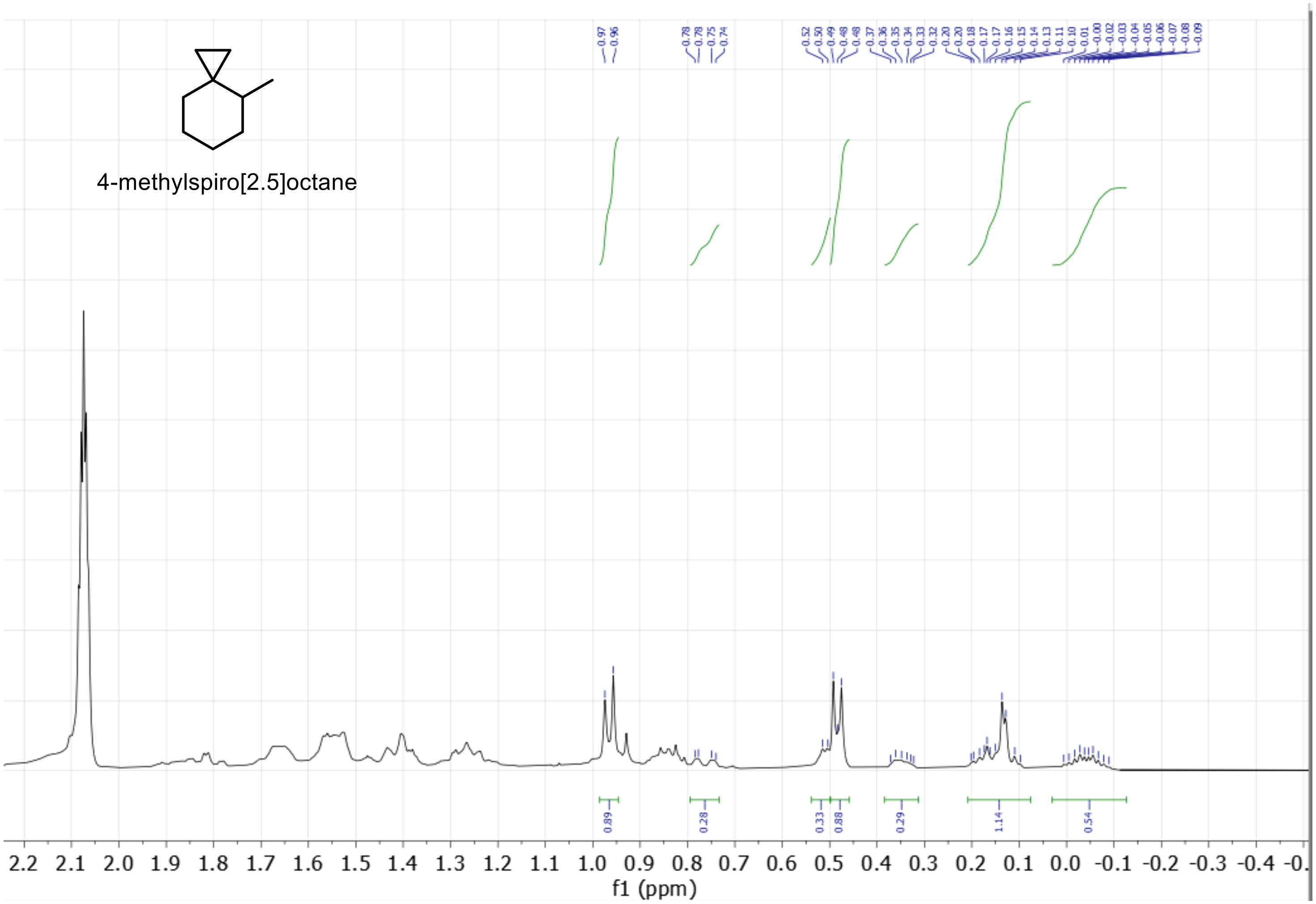


Compound **S27** x 2TsOH **^{1}H NMR** (500 MHz, CD_3CN)

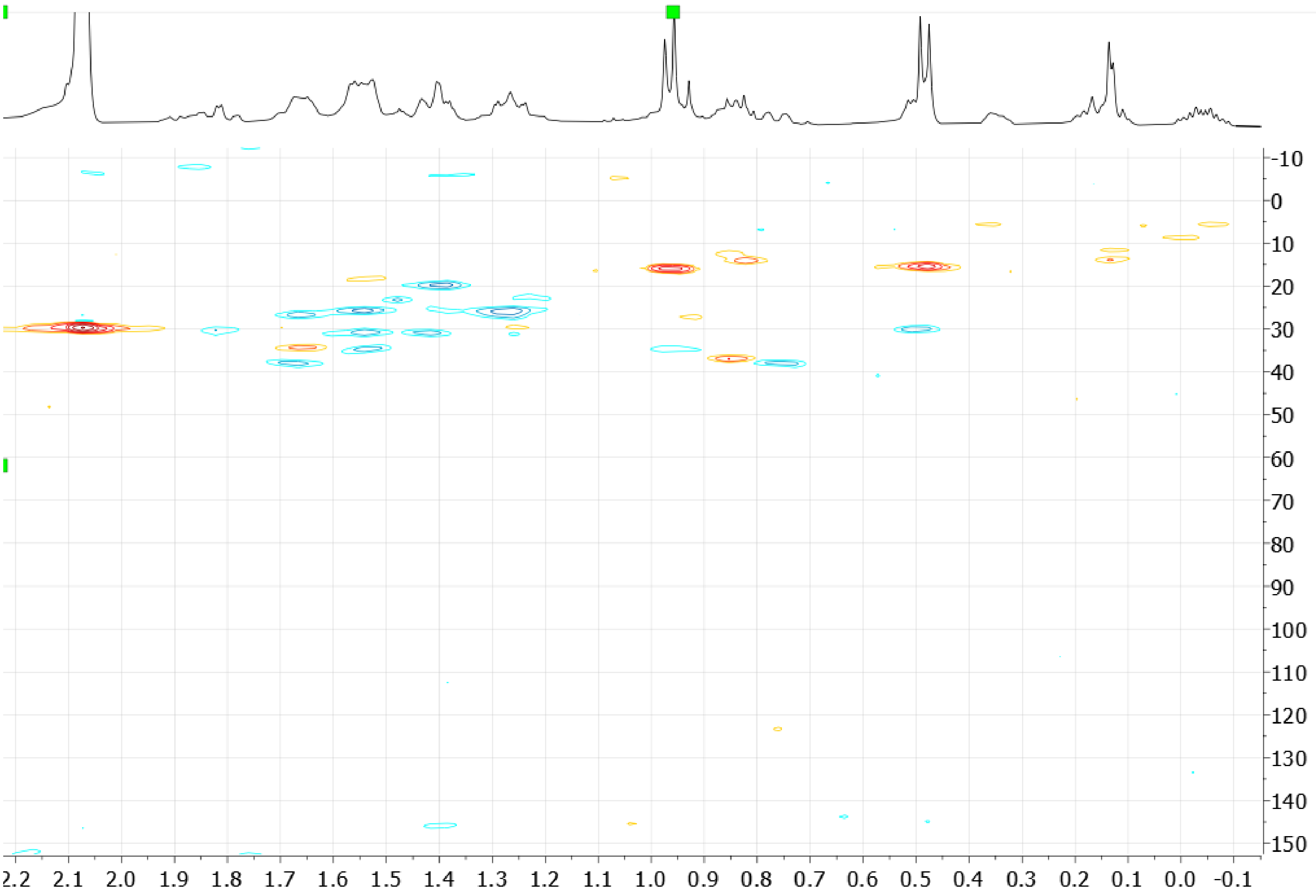


5. Low-temperature NMR

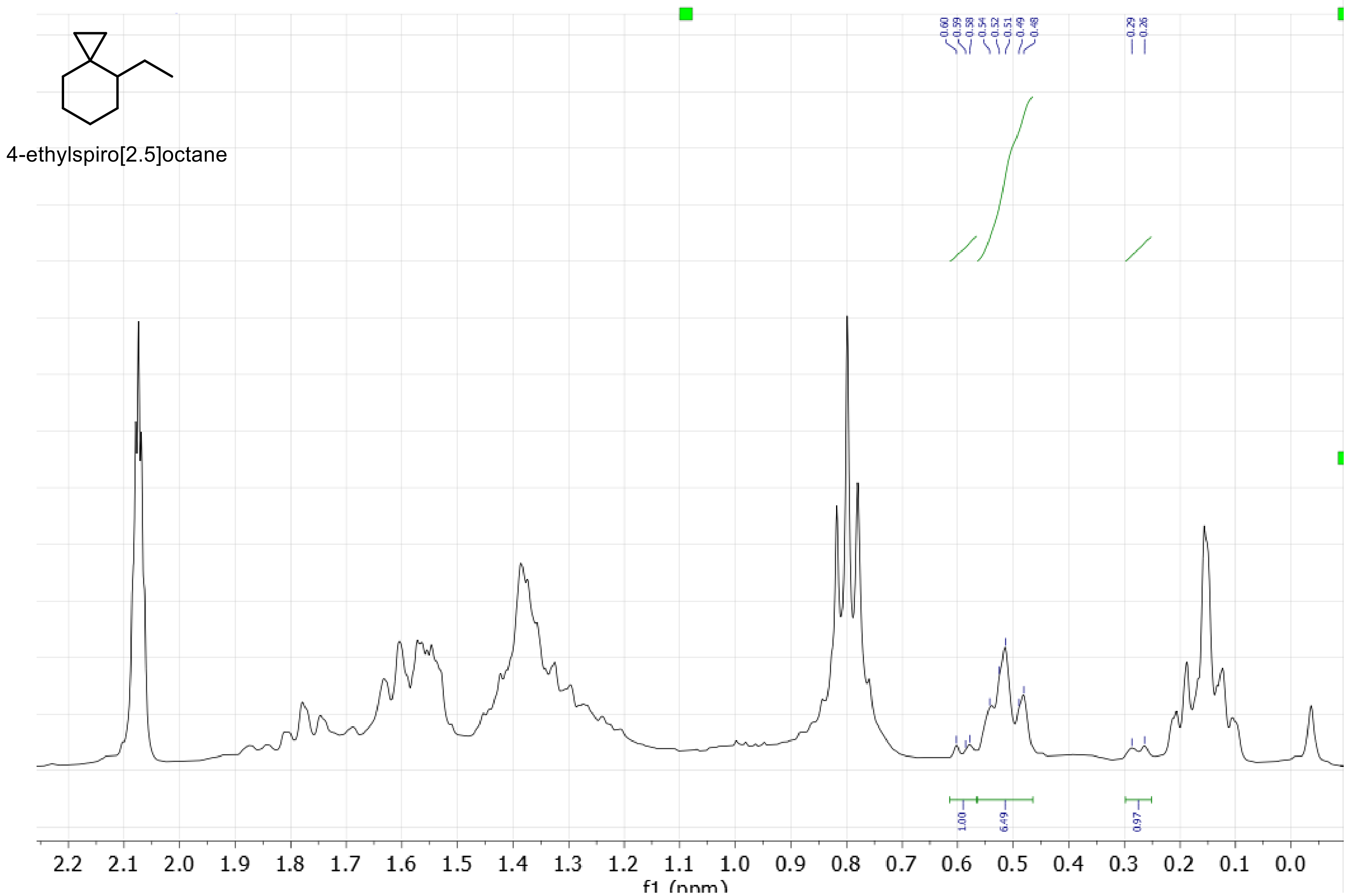
Compound **S1** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



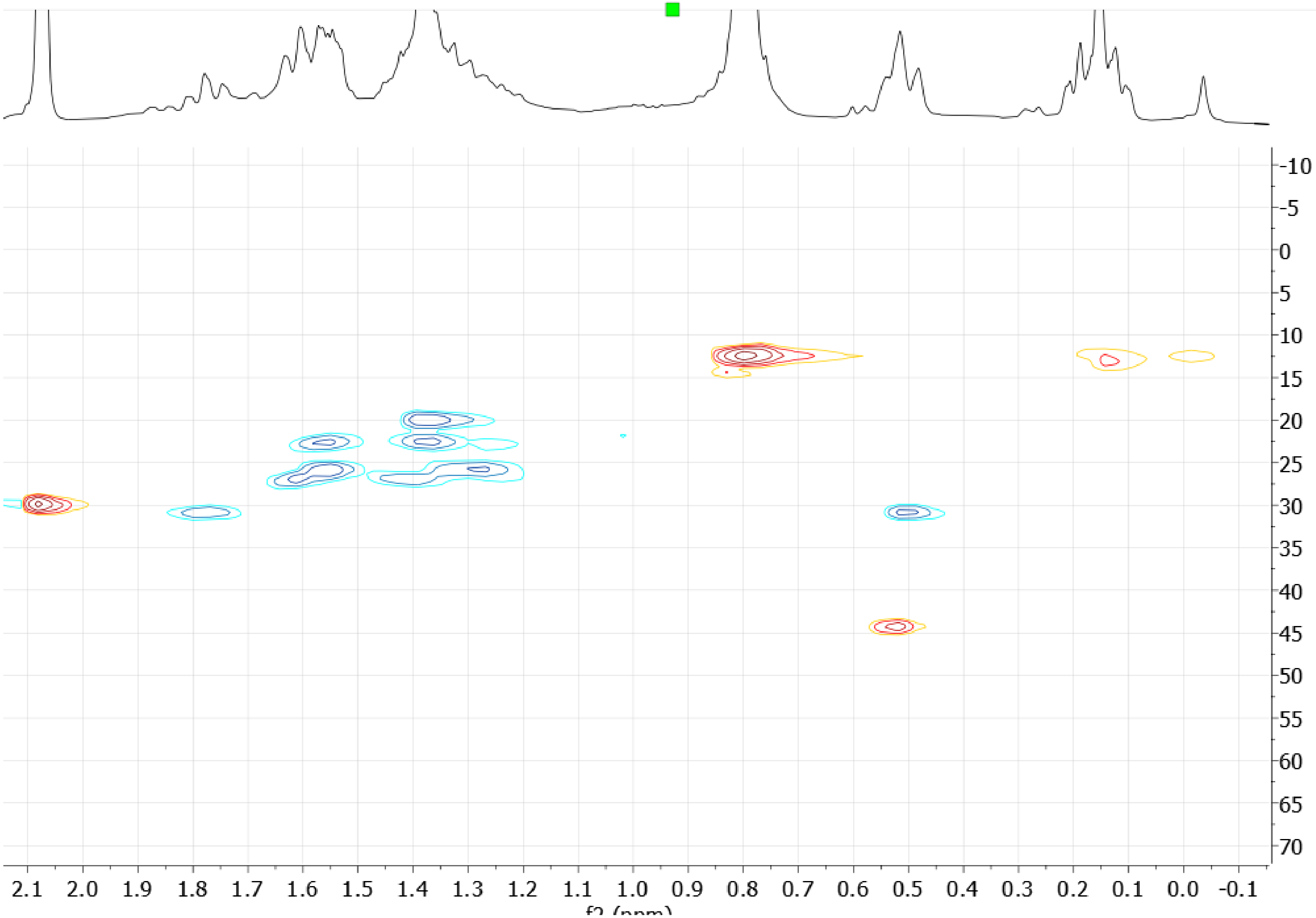
Compound **S1** **HSQC** (400 MHz, *d_6*-Acetone, -78 °C)



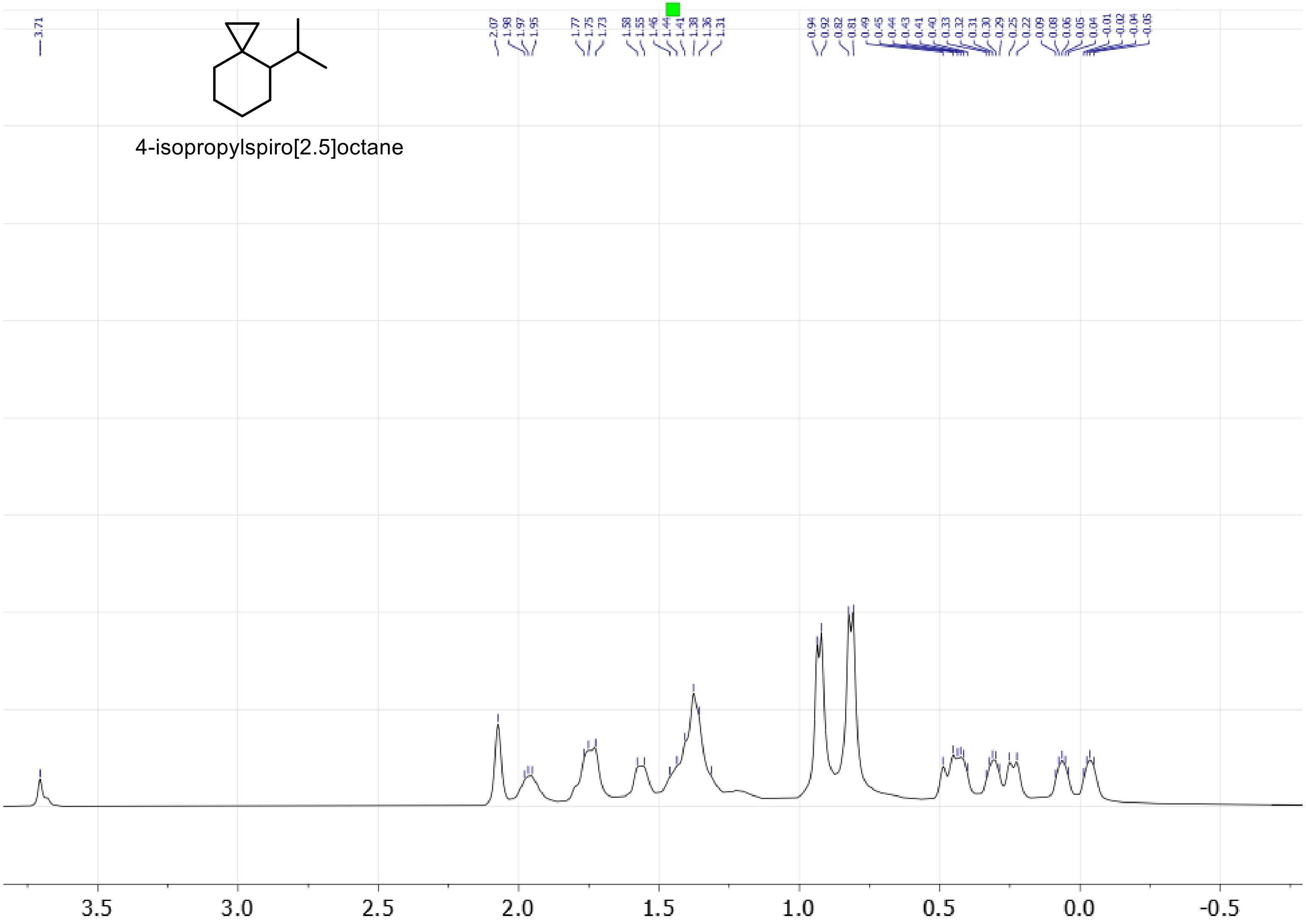
Compound **S2** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



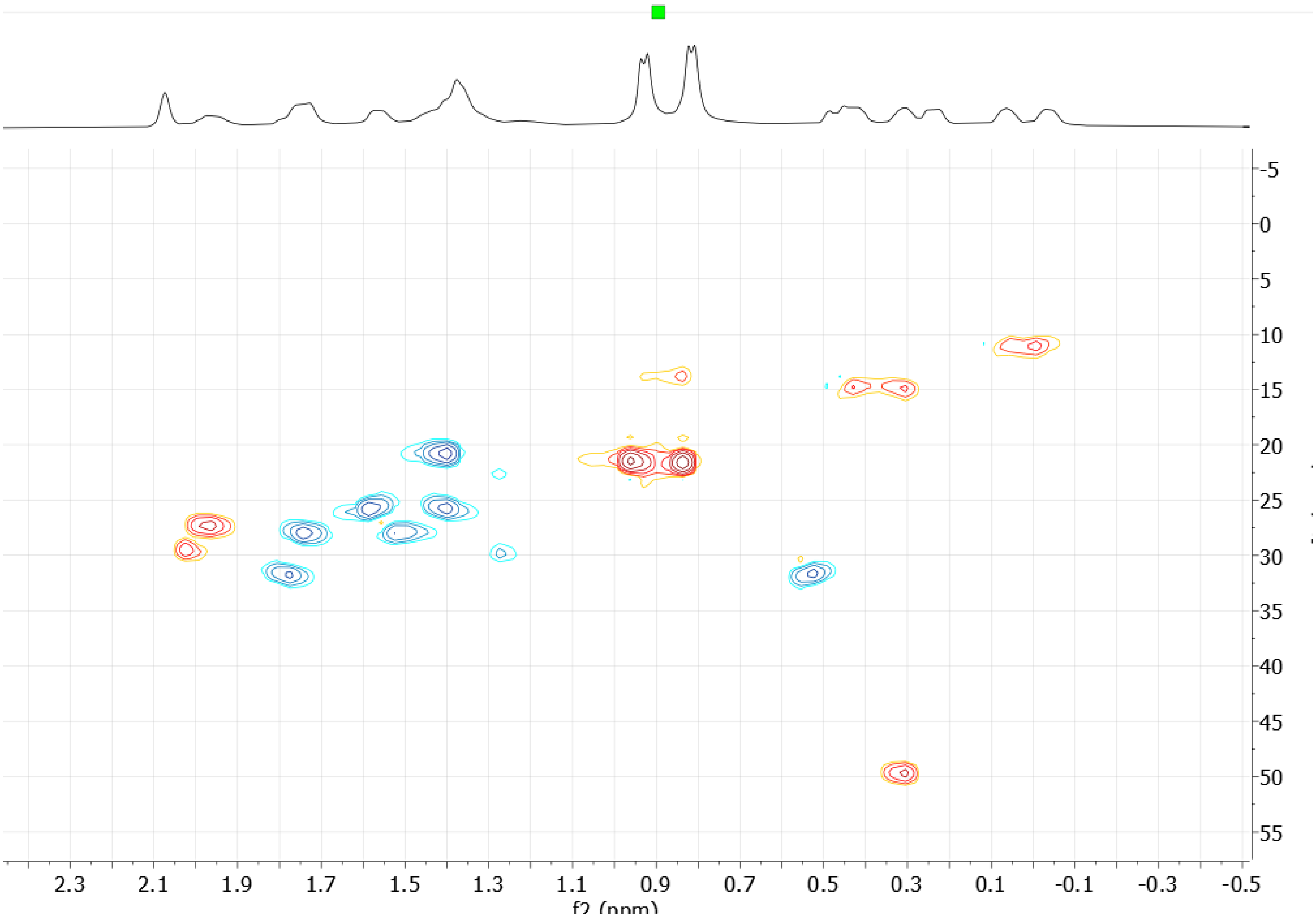
Compound **S2** **HSQC** (400 MHz, d_6-Acetone, -78 °C)



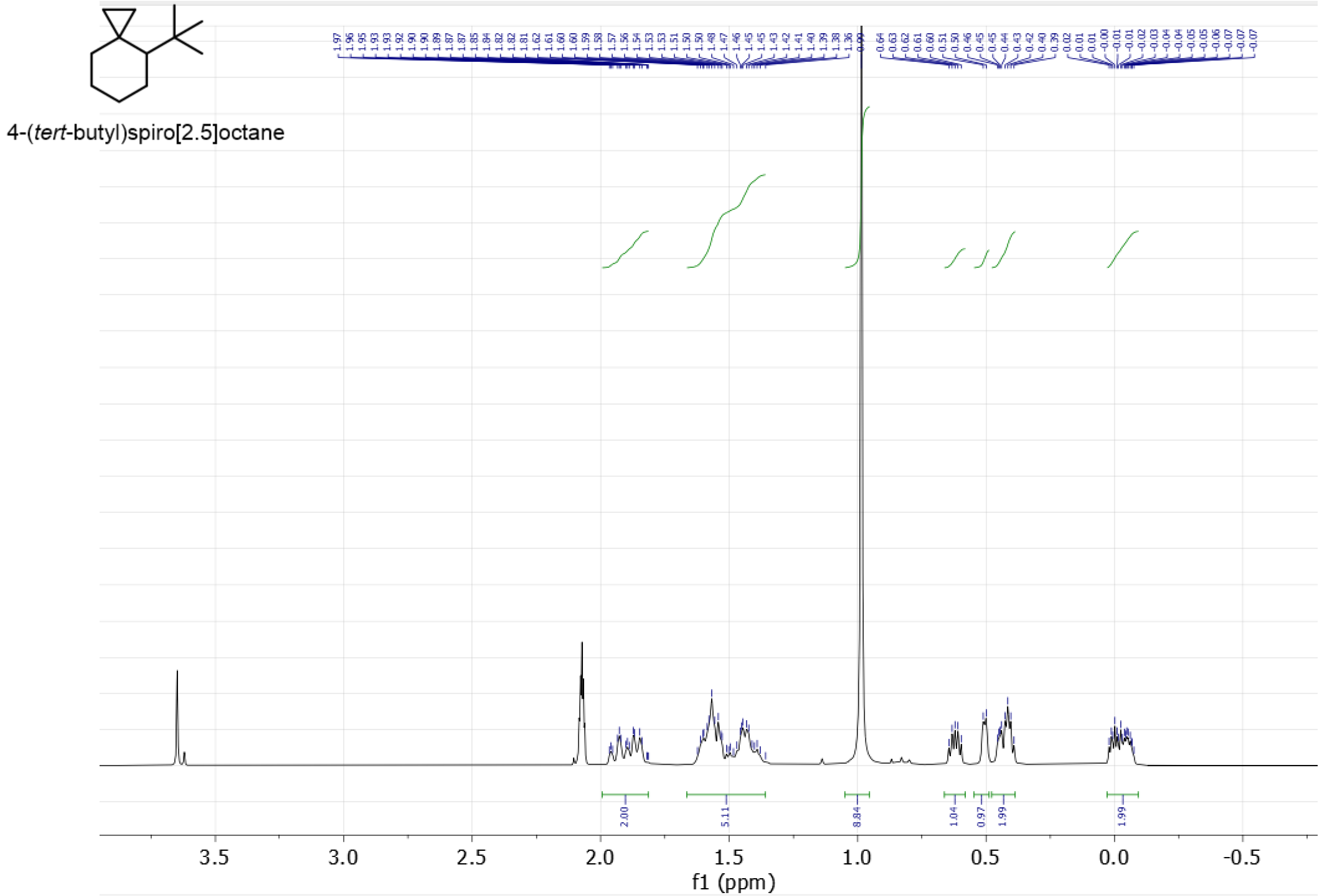
Compound **S3** **^{1}H NMR** (400 MHz, *d_6*-Acetone, -78 °C)



Compound **S3** **HSQC** (400 MHz, *d_6*-Acetone, -78 °C)

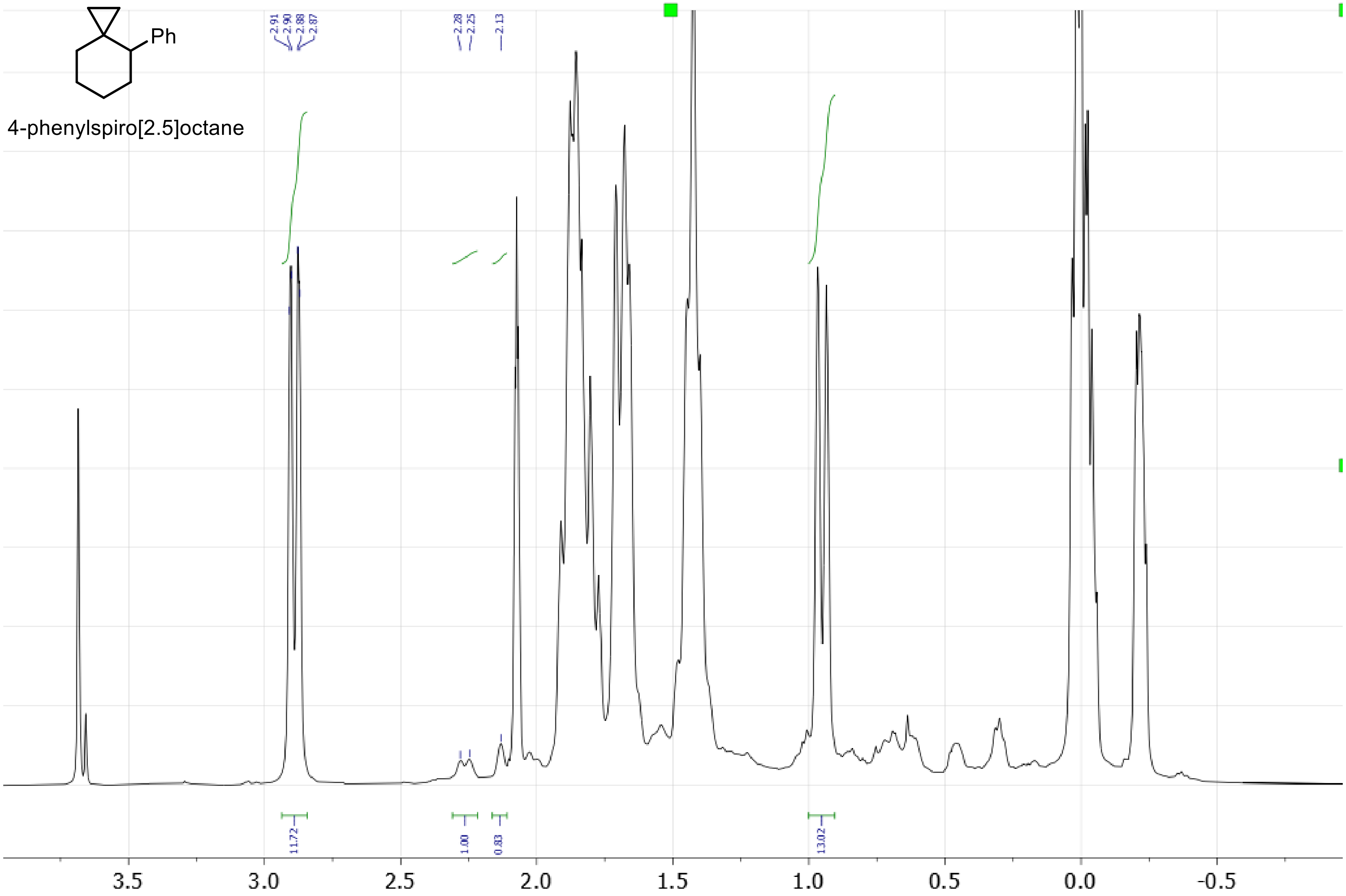


Compound **S4** **^{1}H NMR** (400 MHz, *d$_6$*-Acetone, -78 °C)

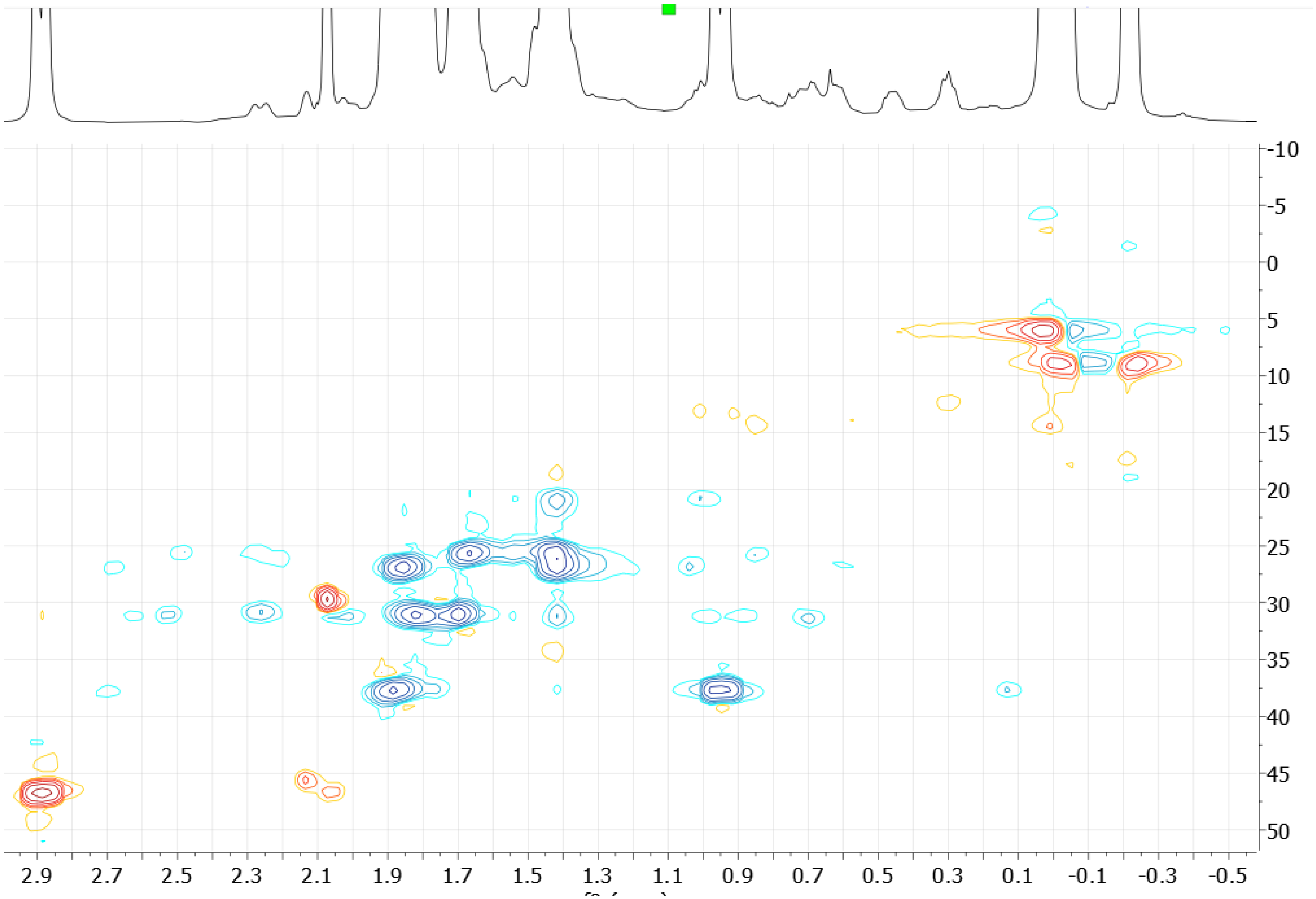


4-(*tert*-butyl)spiro[2.5]octane

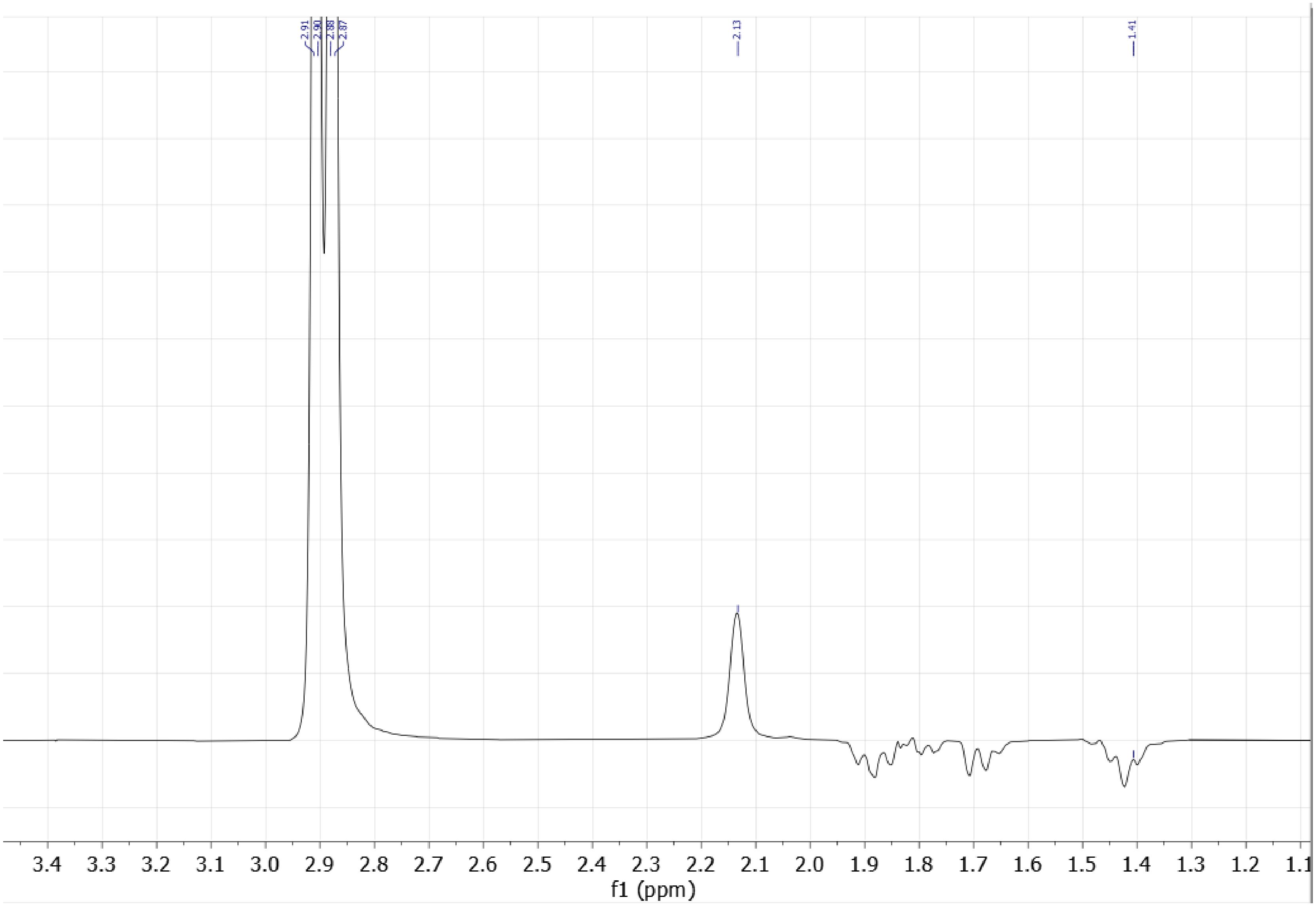
Compound **S5** ^{1}**H NMR** (400 MHz, *d*$_6$-Acetone, -78 °C)



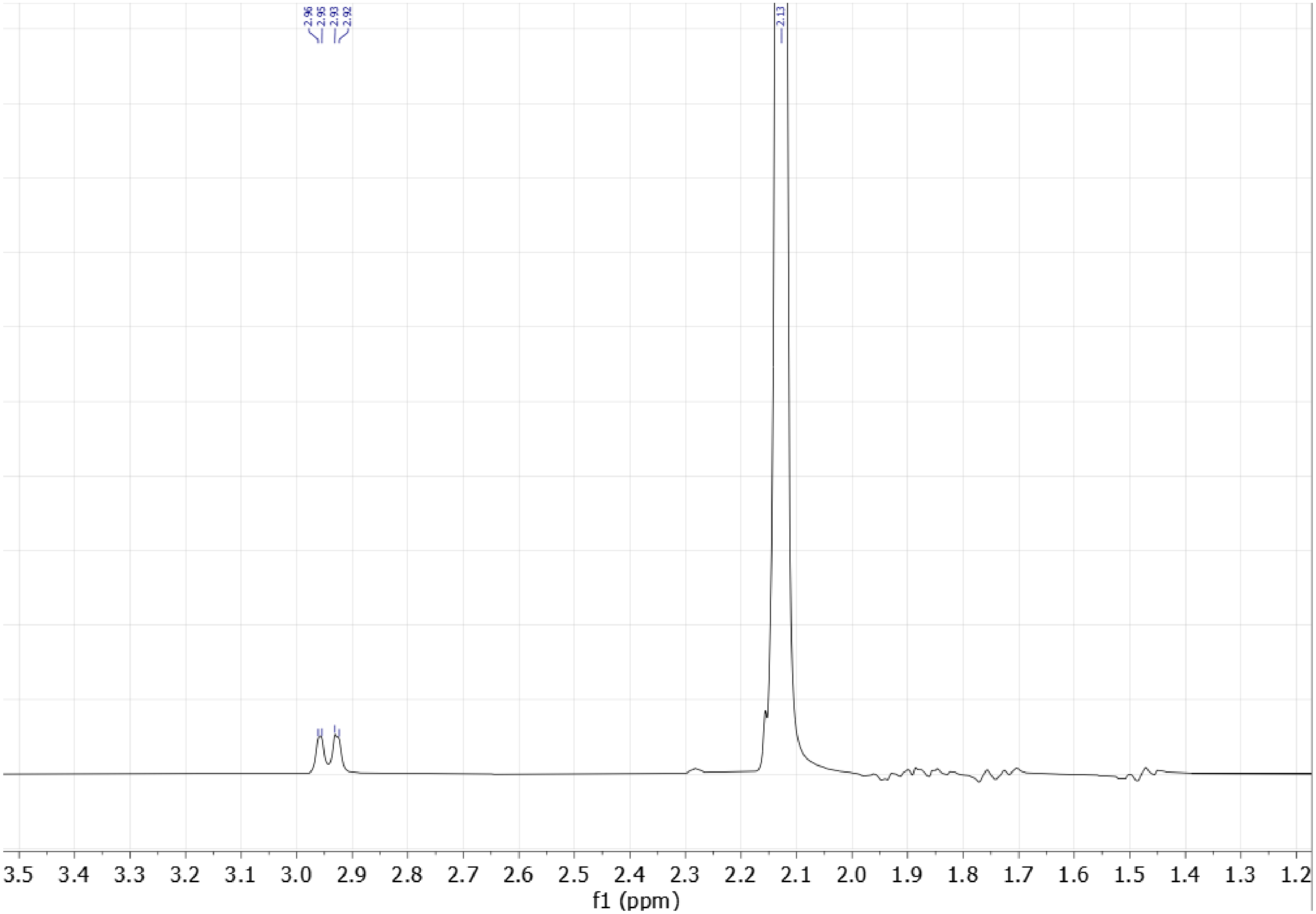
Compound **S5 HSQC** (400 MHz, d_6-Acetone, -78 °C)



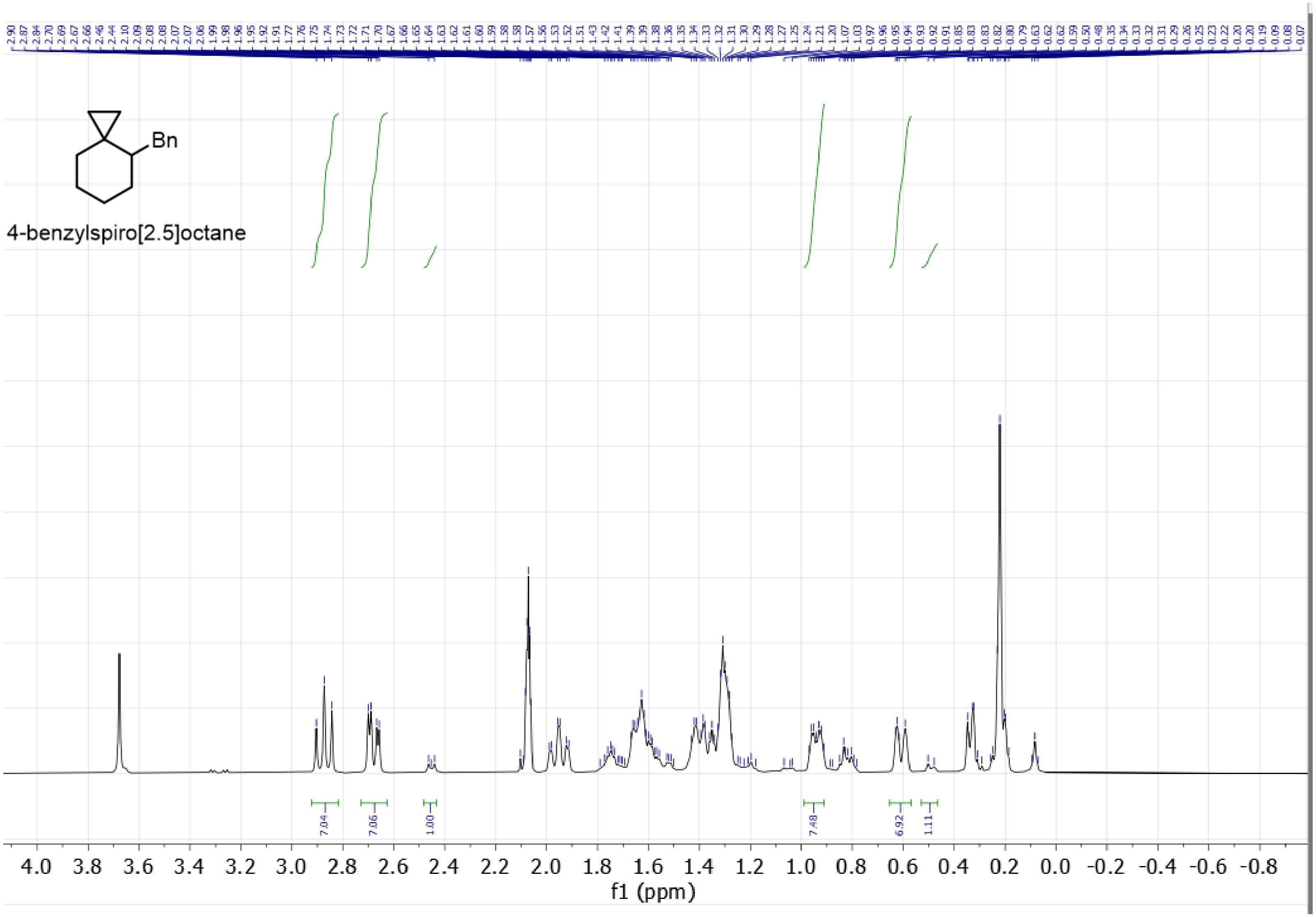
Compound **S5 1D NOE** (irradiation at 2.89 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C)



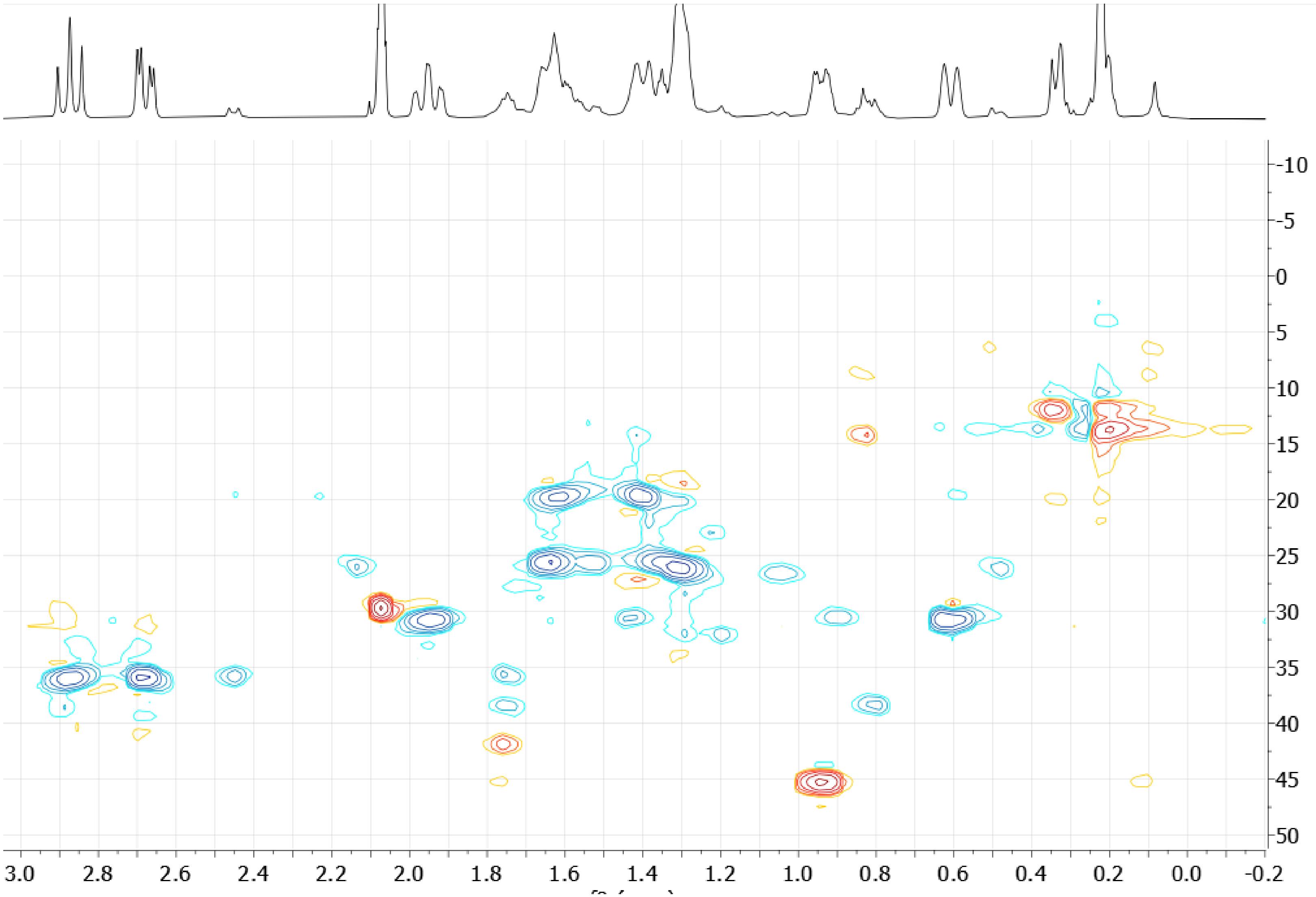
Compound **S5 1D NOE** (irradiation at 2.13 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C



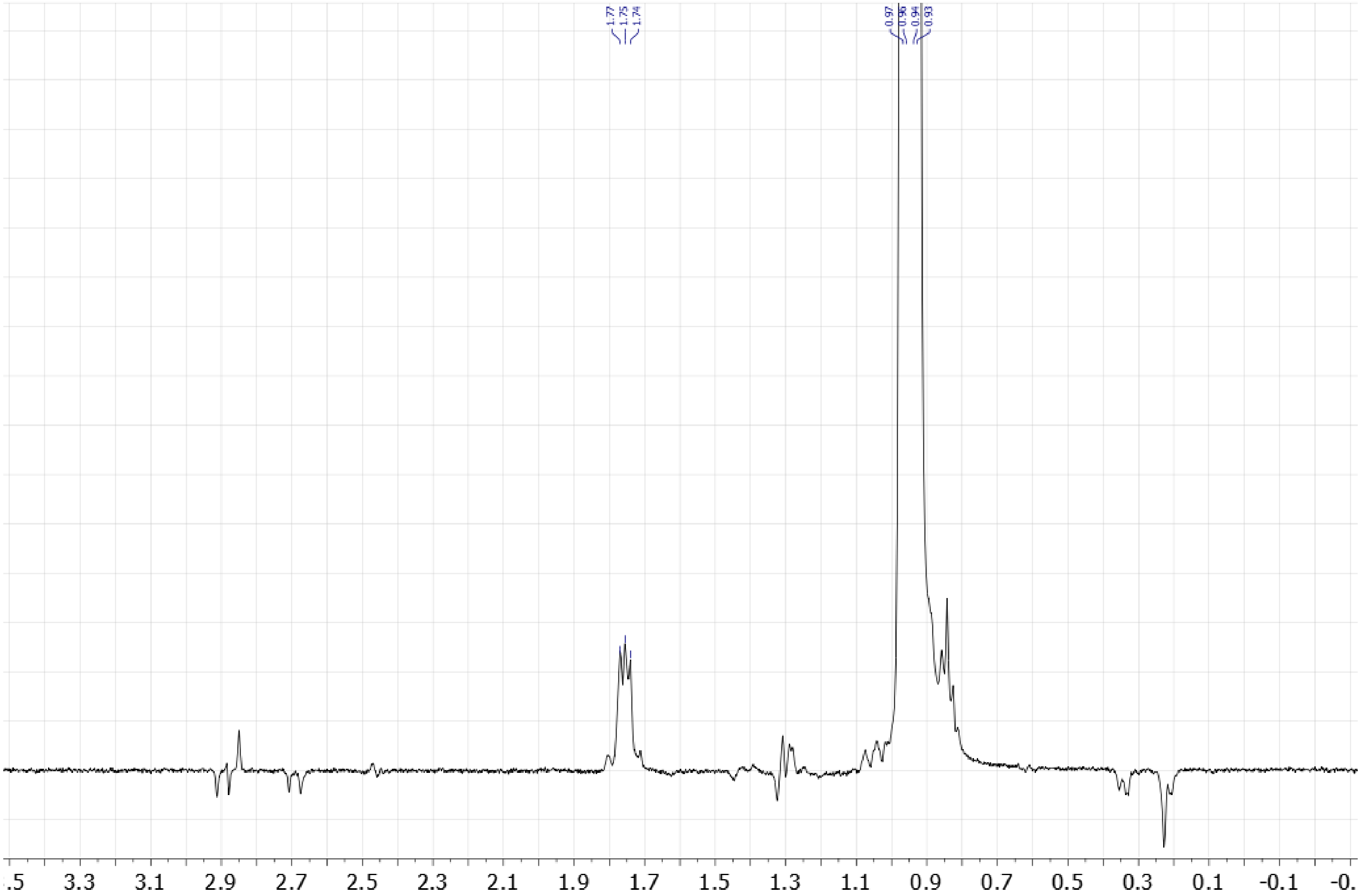
Compound **S6** ^{1}**H NMR** (400 MHz, *d$_6$*-Acetone, -78 °C)



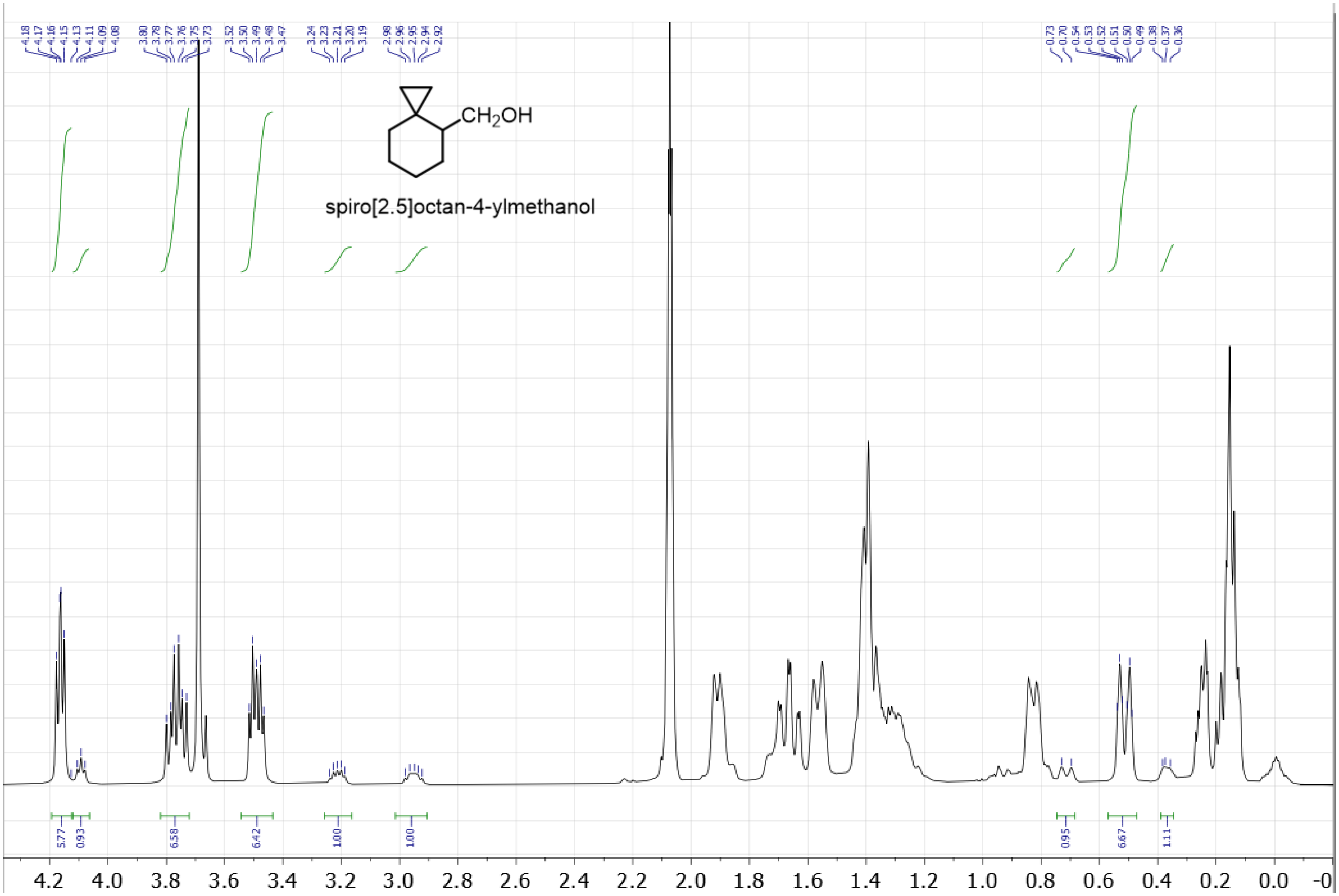
Compound **S6** **HSQC** (400 MHz, d_6-Acetone, -78 °C)



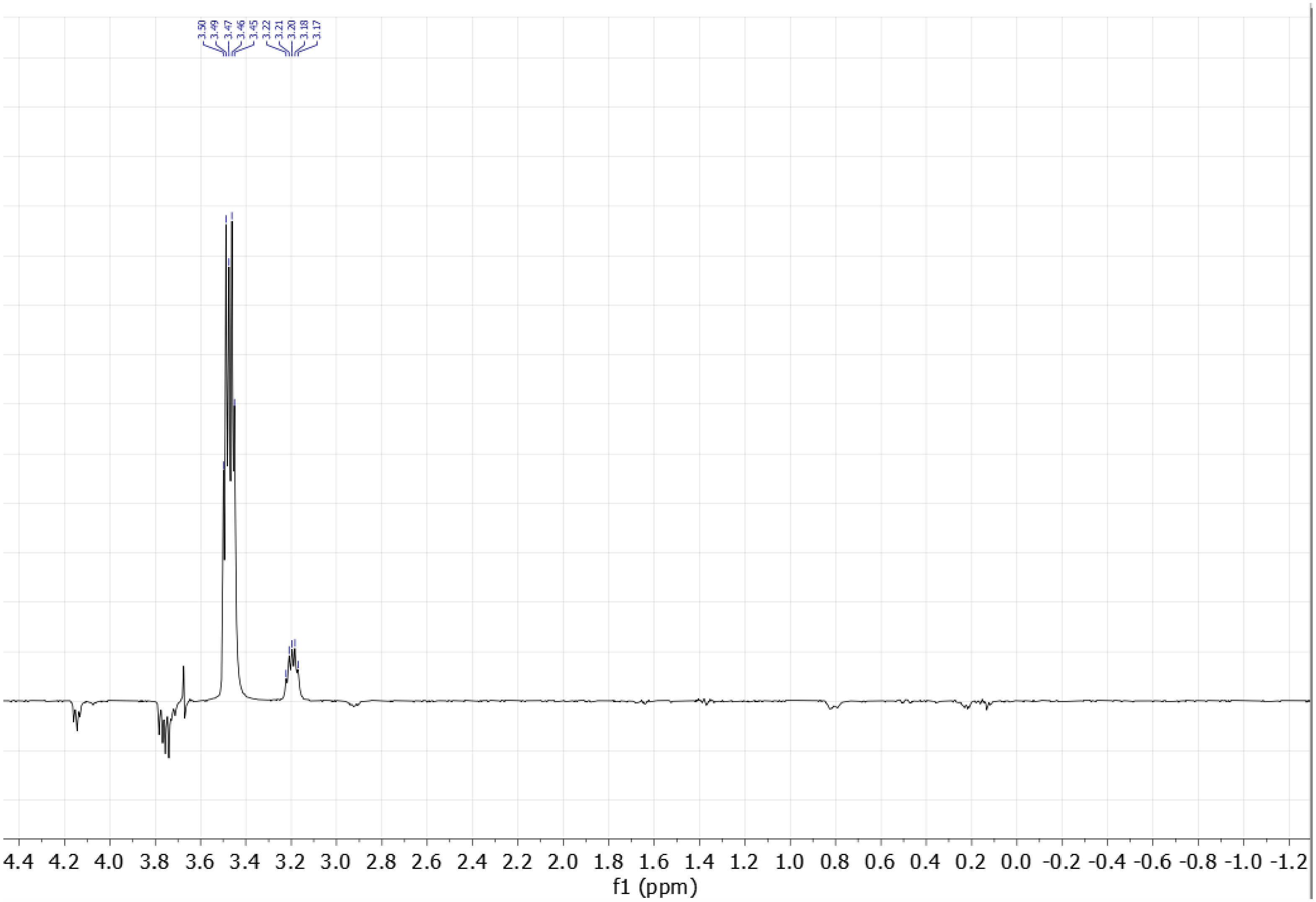
Compound **S6 1D NOE** (irradiation at 0.94 ppm, 400 MHz, d_6-Acetone, -78 °C)



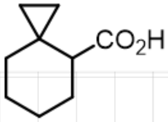
Compound **S7** **^{1}H NMR** (400 MHz, d_6-Acetone, -78 °C)



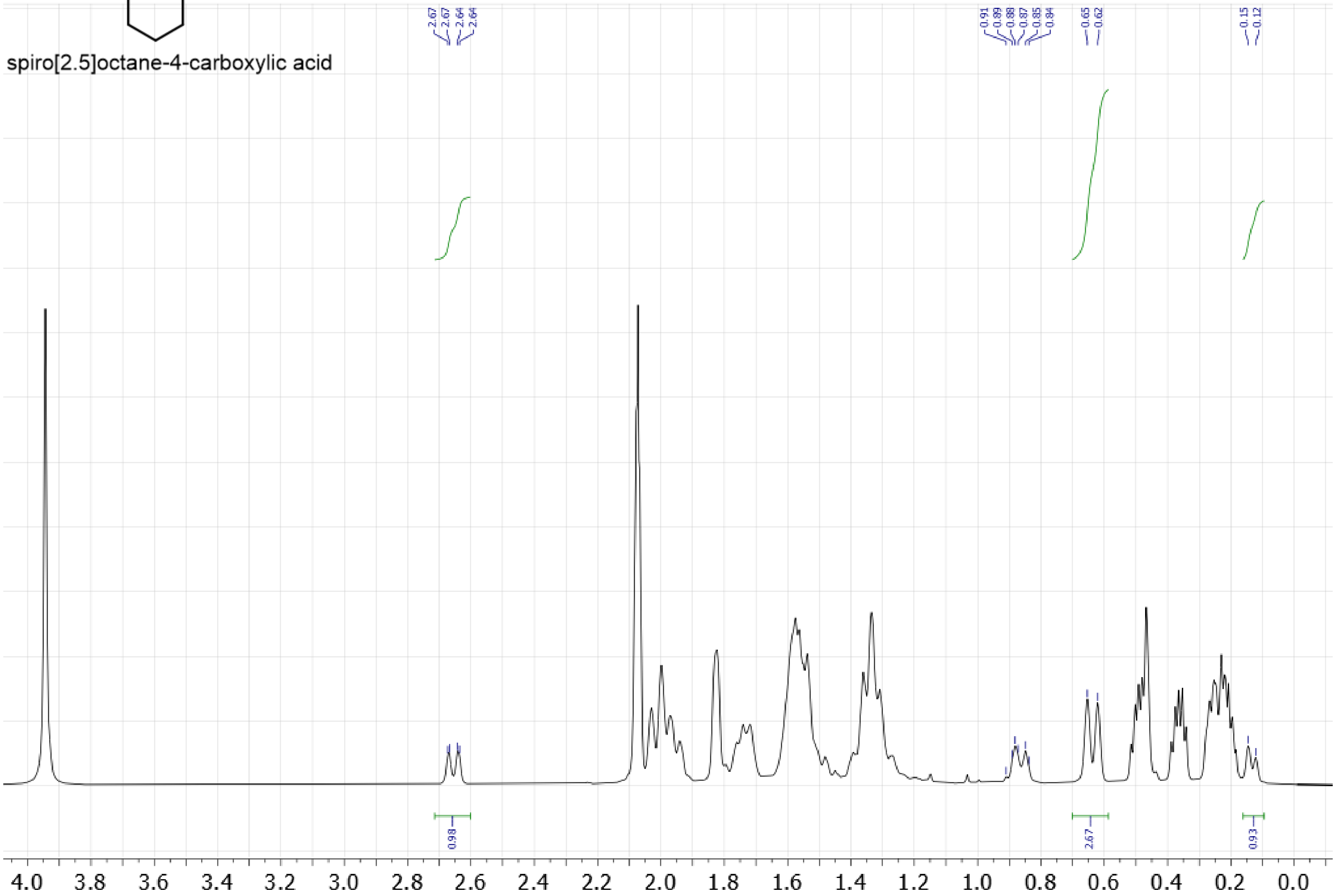
Compound **S7 1D NOE** (irradiation at 3.48 ppm, 400 MHz, d_6-Acetone, -78 °C)



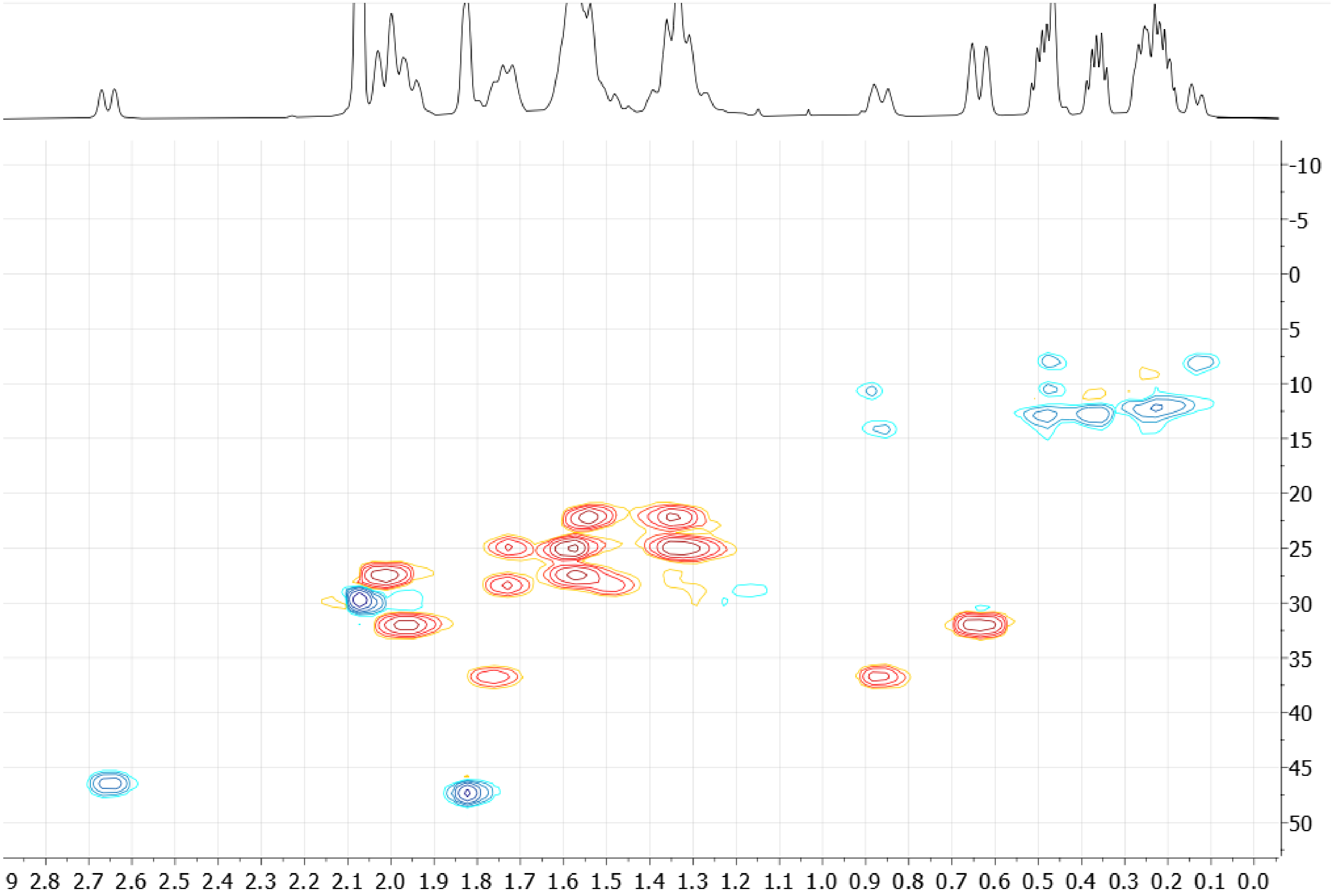
Compound **S8** **^{1}H NMR** (400 MHz, d_6-Acetone, -78 °C)



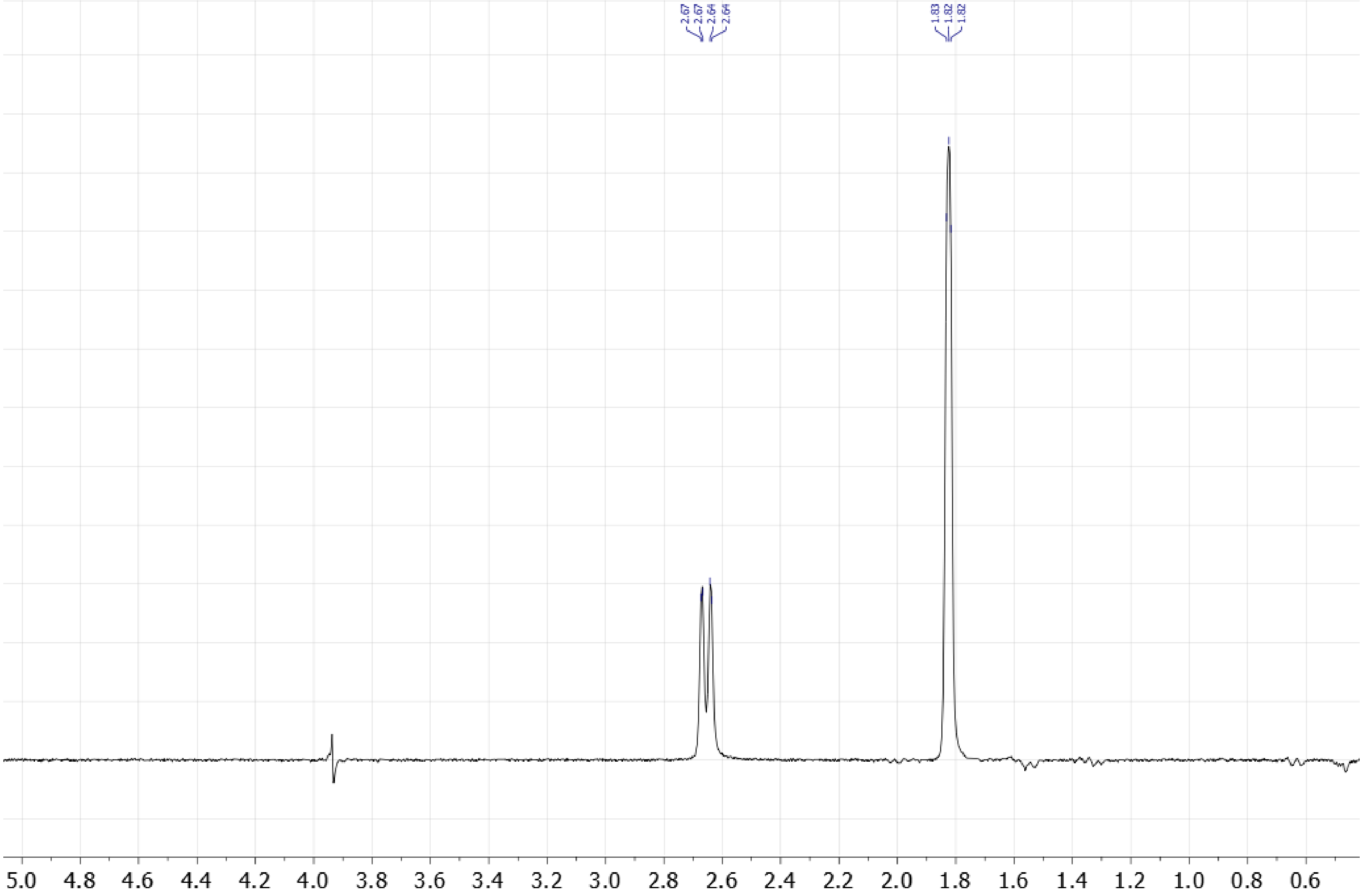
spiro[2.5]octane-4-carboxylic acid



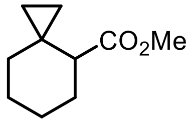
Compound **S8 HSQC** (400 MHz, *d*$_6$-Acetone, -78 °C)



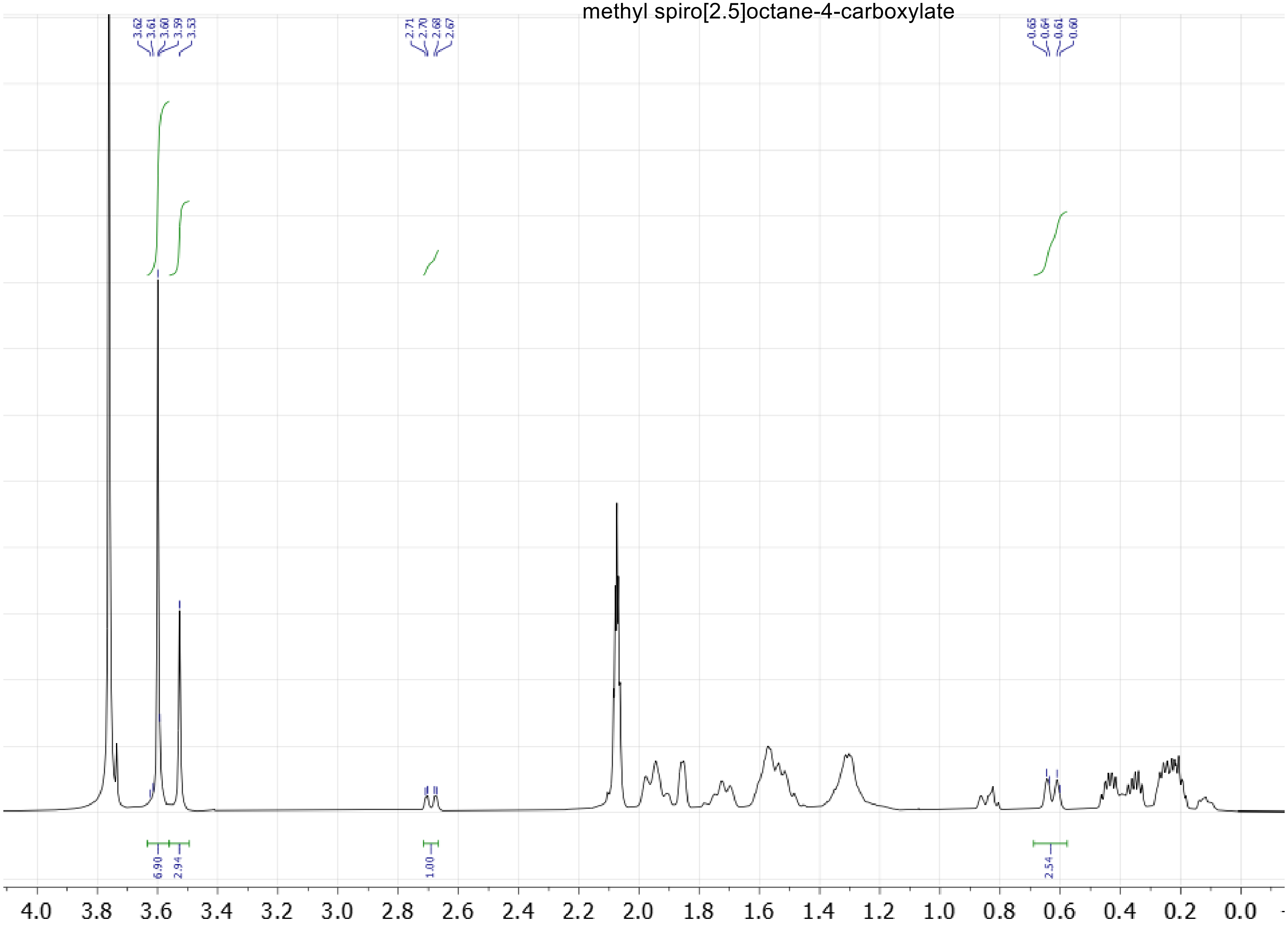
Compound **S8 1D NOE** (irradiation at 2.655 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C)



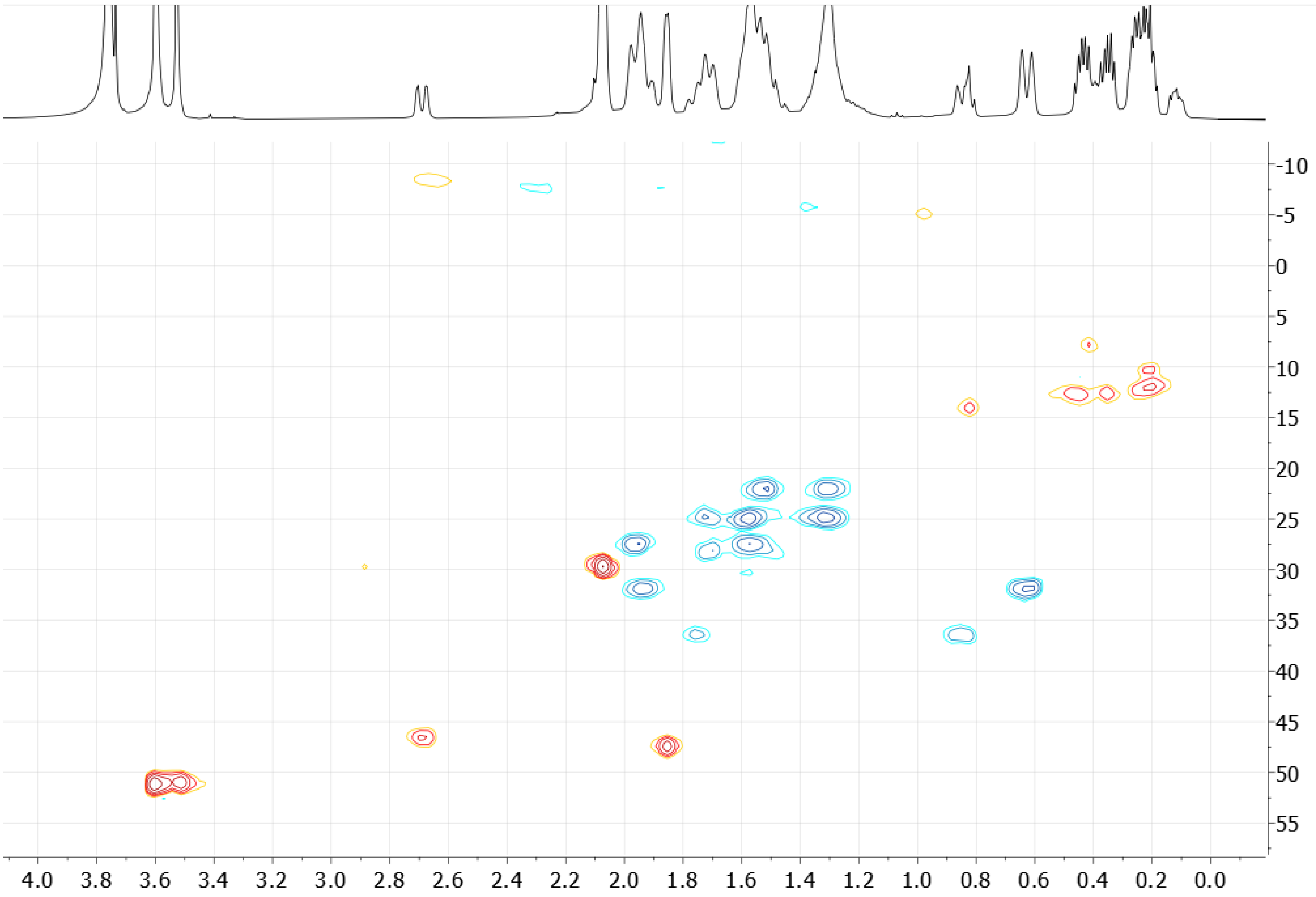
Compound **S9** ^{1}**H NMR** (400 MHz, *d₆*-Acetone, -78 °C)



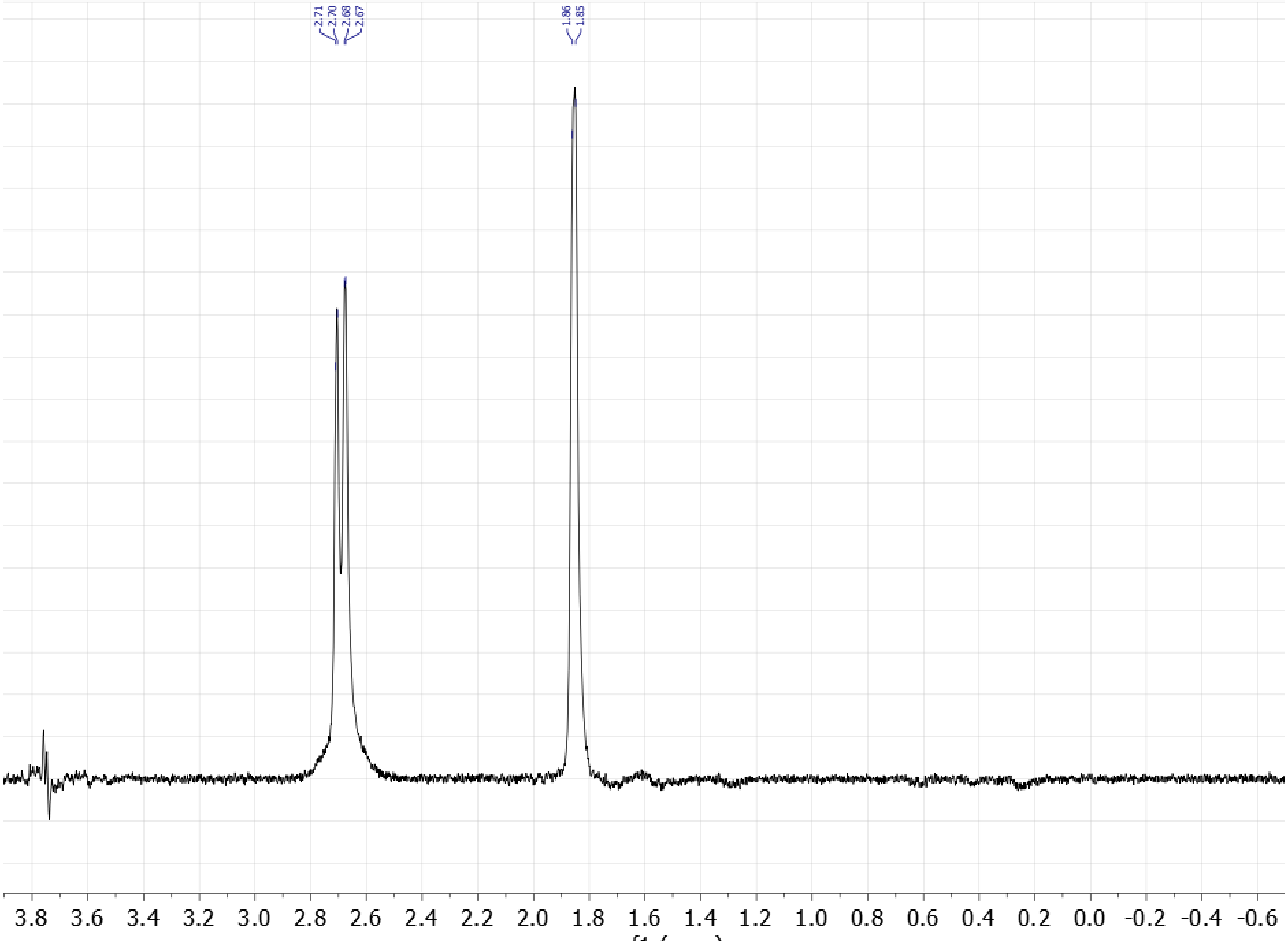
methyl spiro[2.5]octane-4-carboxylate



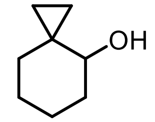
Compound **S9 HSQC** (400 MHz, d_6-Acetone, -78 °C)



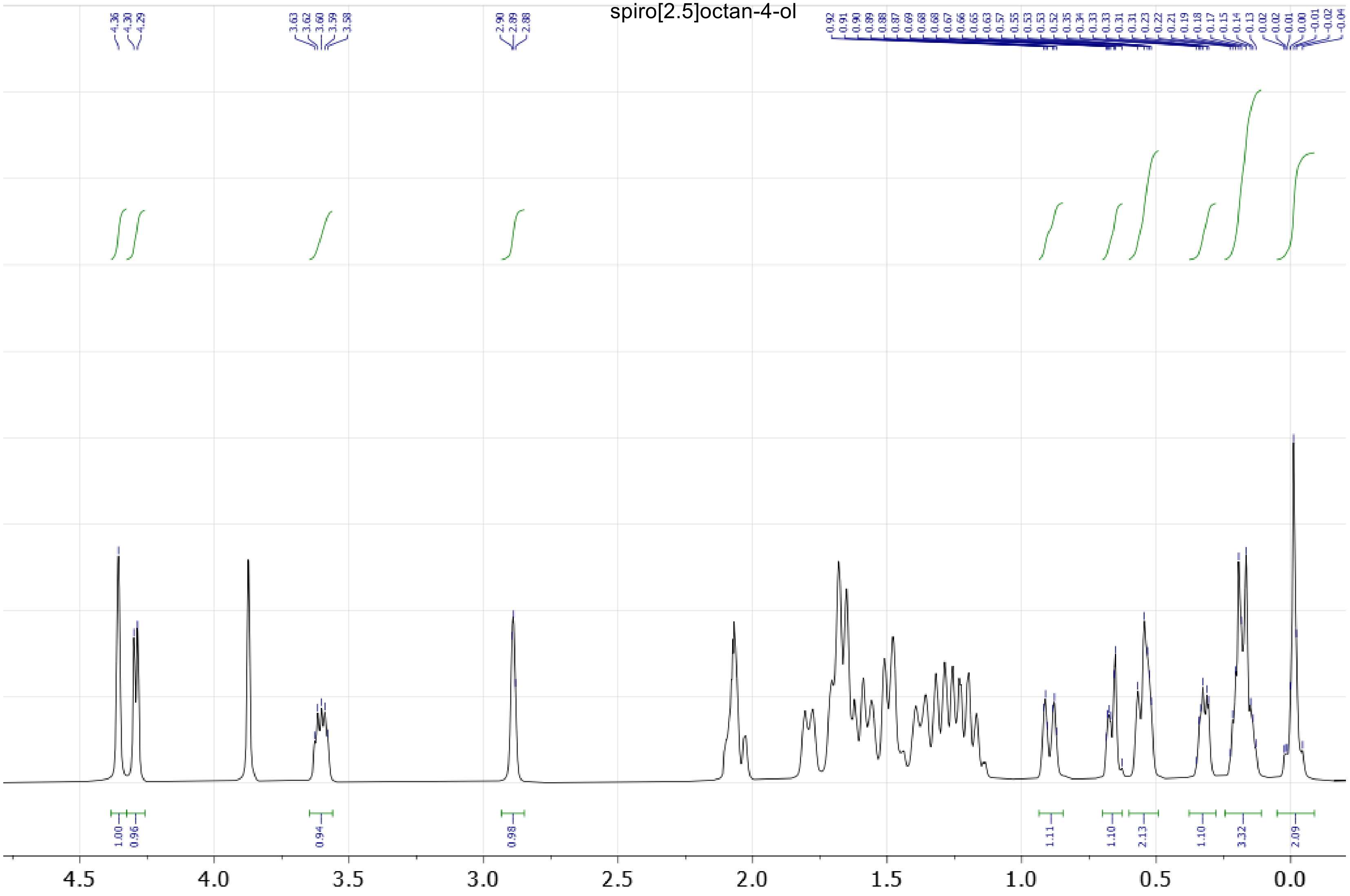
Compound **S9 1D NOE** (irradiation at 2.69 ppm, 400 MHz, d_6-Acetone, -78 °C)



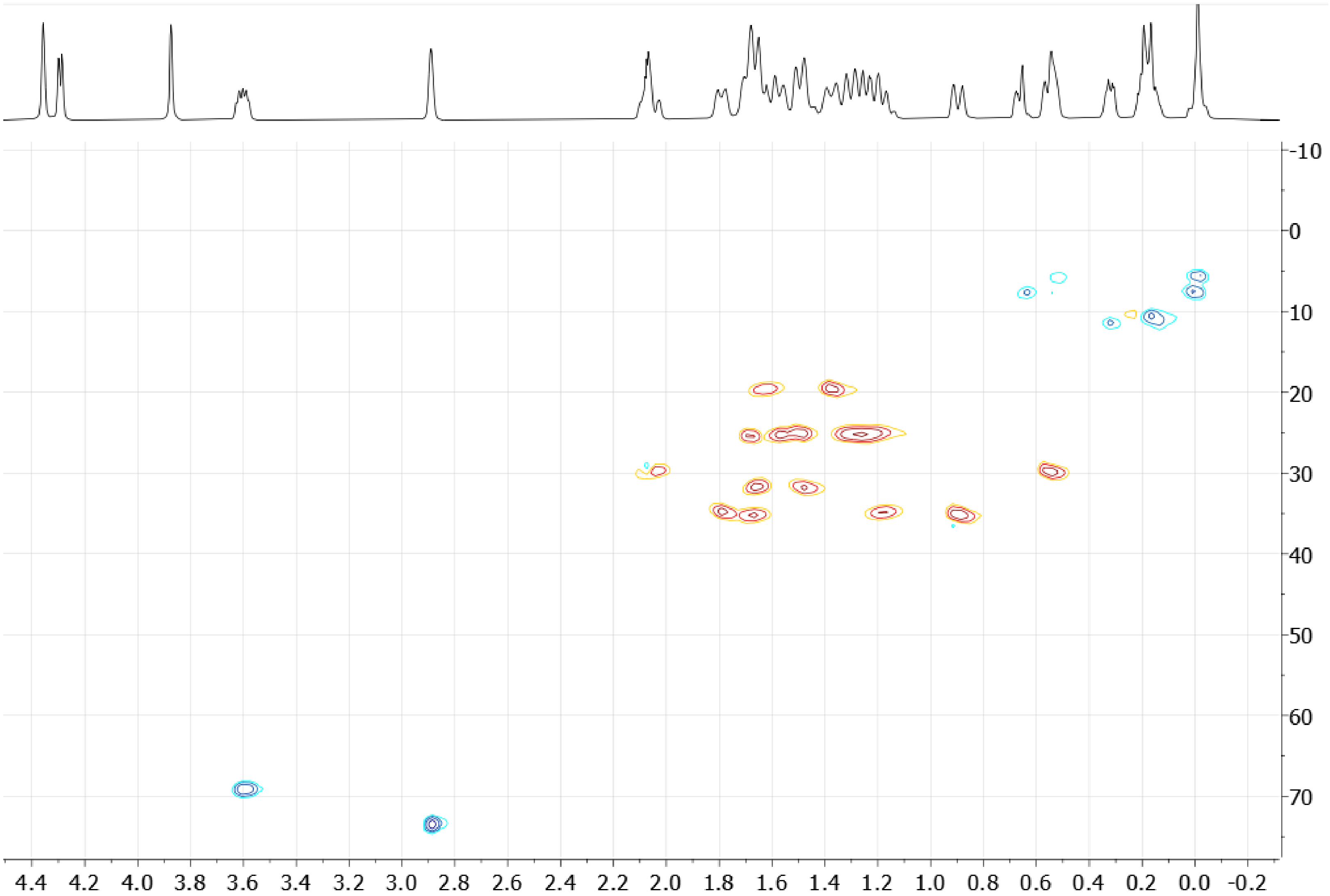
Compound **S10** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



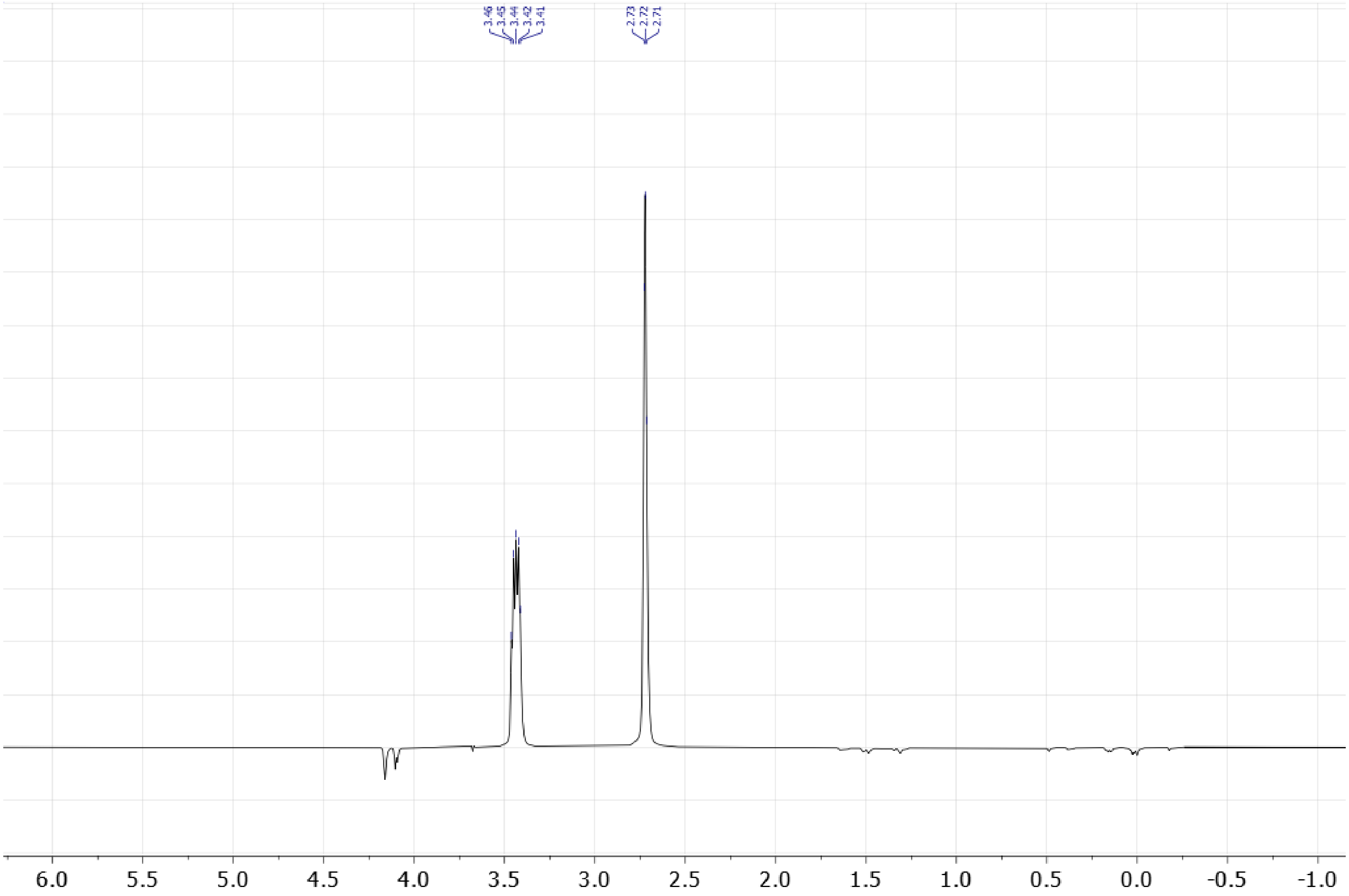
spiro[2.5]octan-4-ol



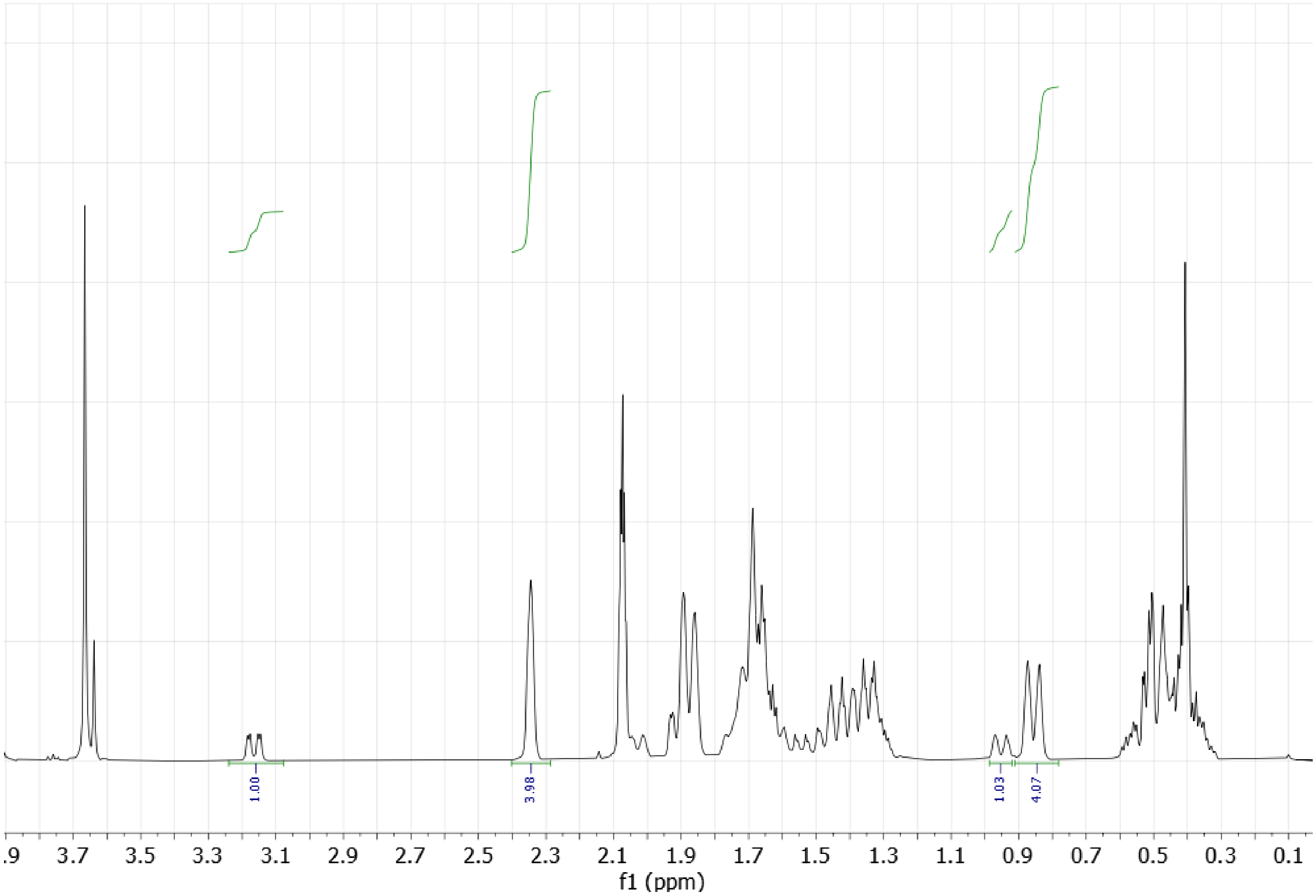
Compound **S10 HSQC** (400 MHz, d_6-Acetone, -78 °C)



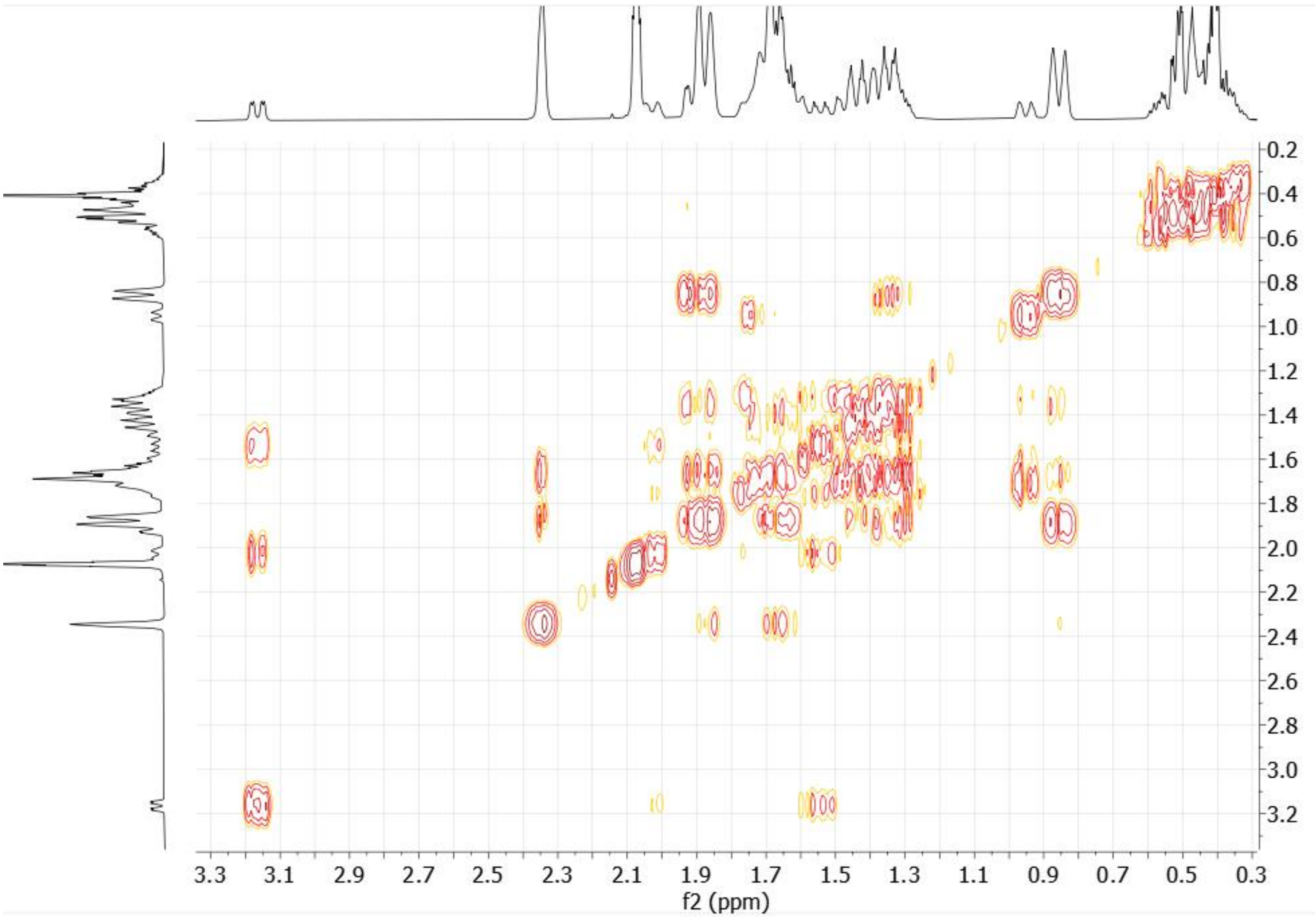
Compound **S10 1D NOE** (irradiation at 2.89 ppm, 400 MHz, d_6-Acetone, -78 °C)



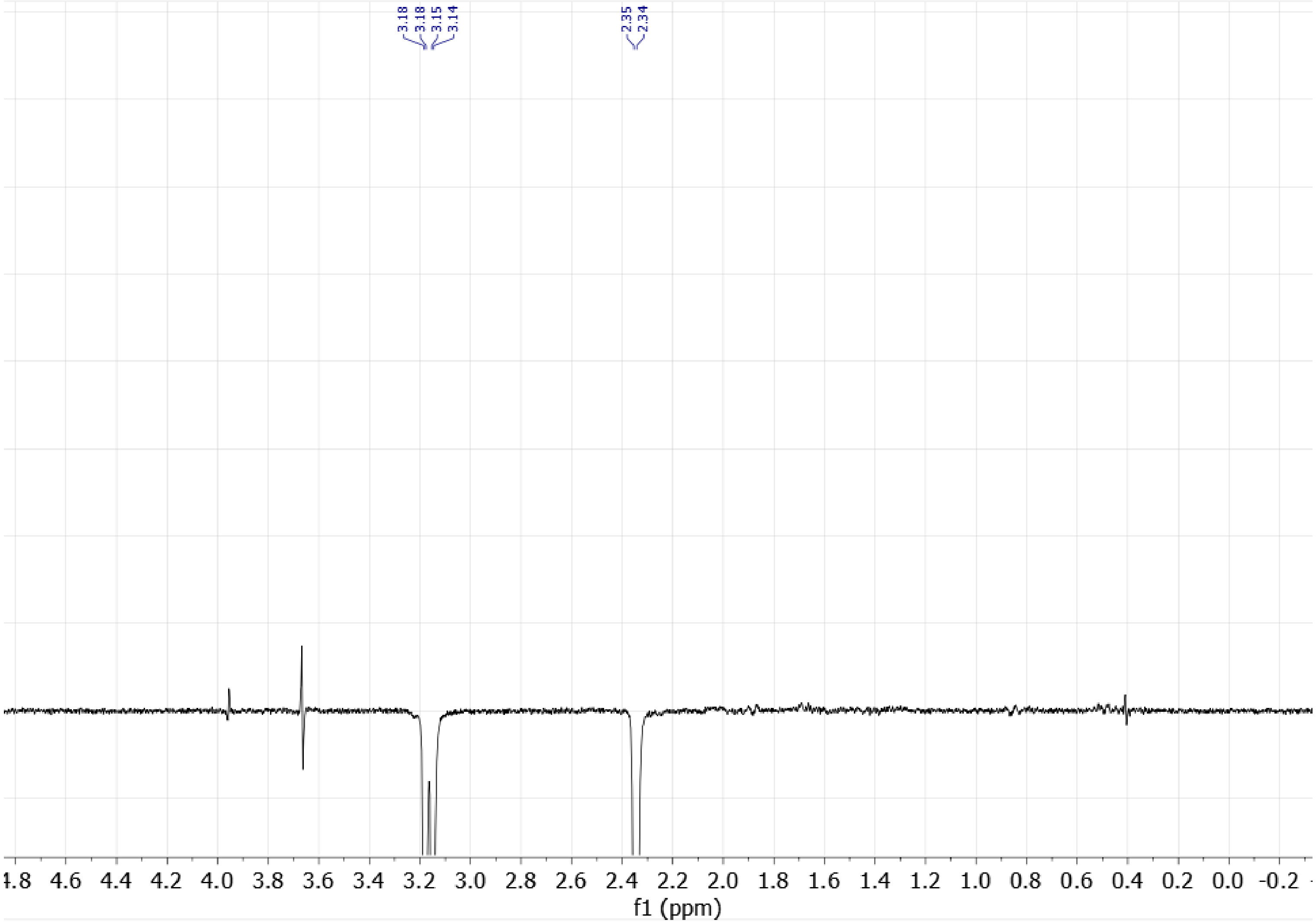
Compound **S11** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



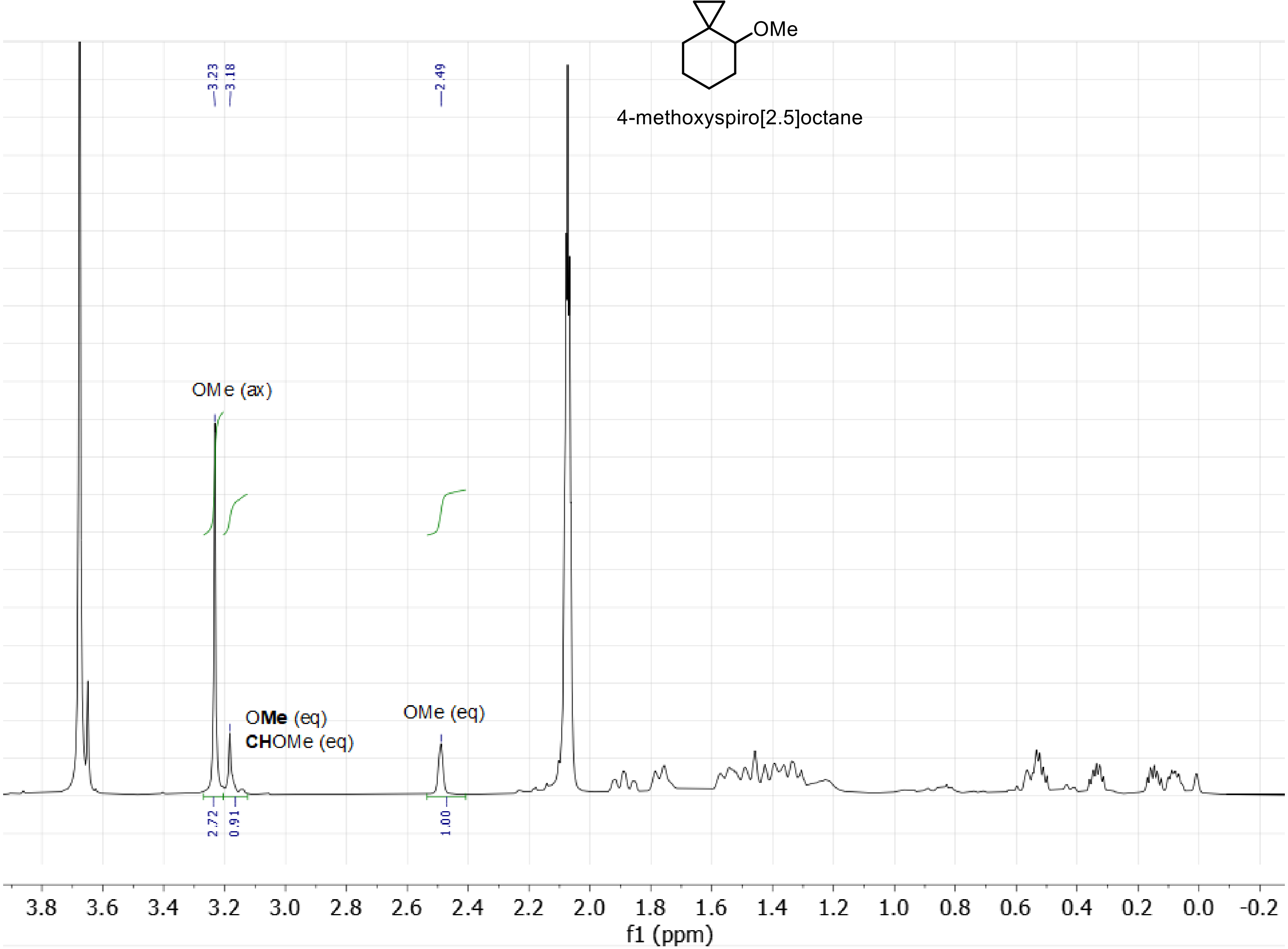
Compound **S11 COSY** (d_6-Acetone, -78 °C)



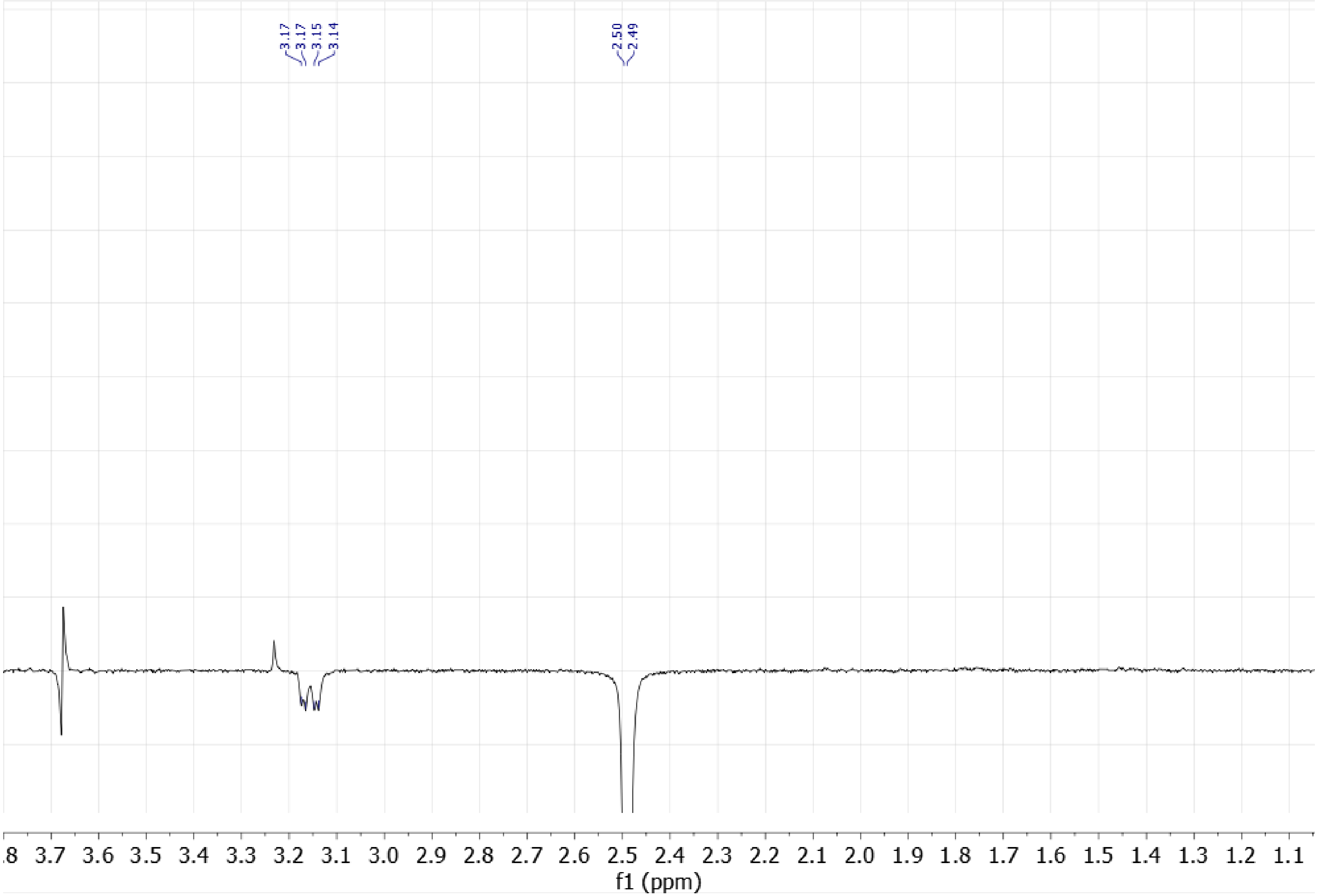
Compound **S11 1D-NOE** (d_6-Acetone, -78 °C, irradiation at 3.167 ppm)



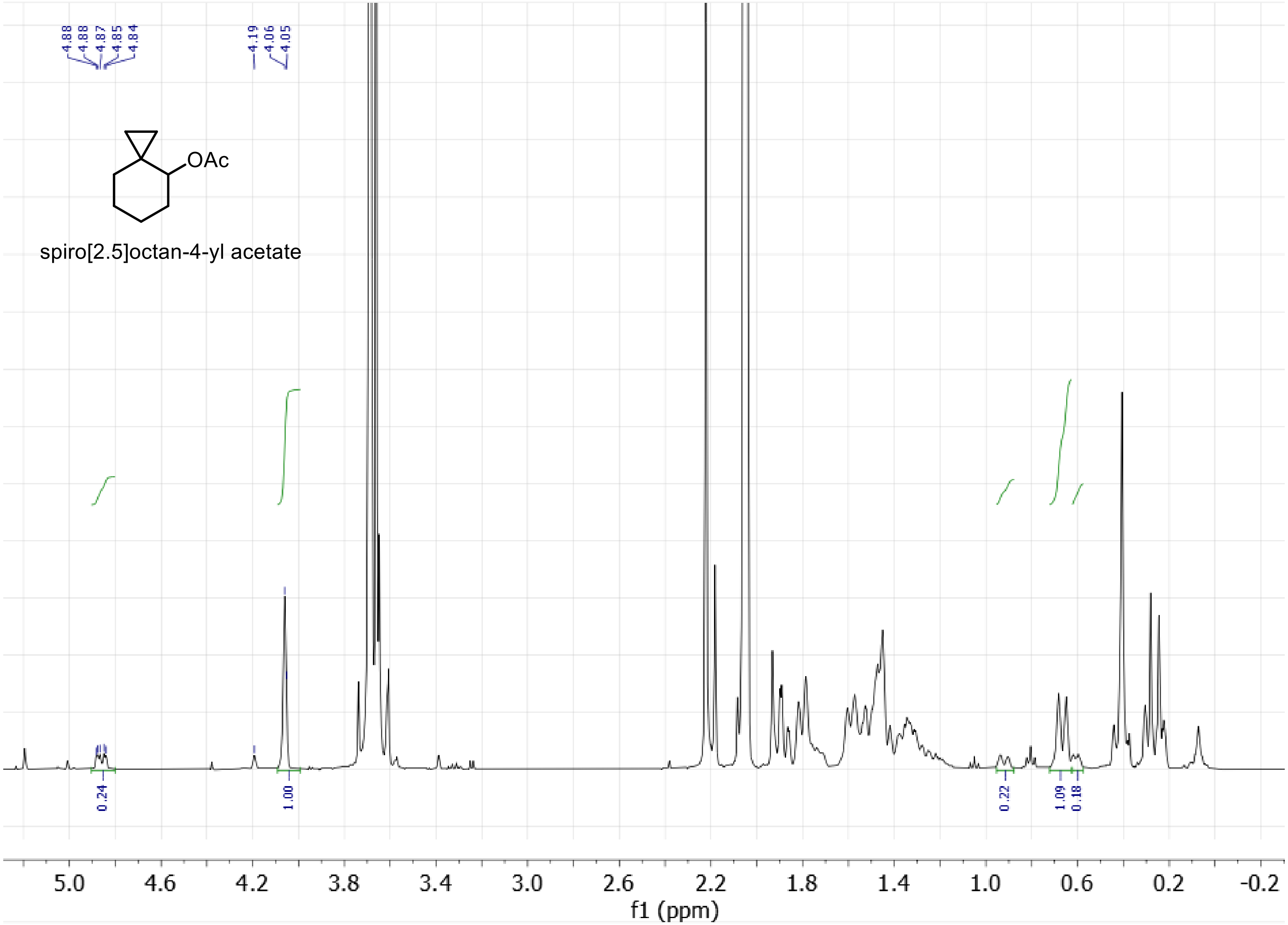
Compound **S12** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



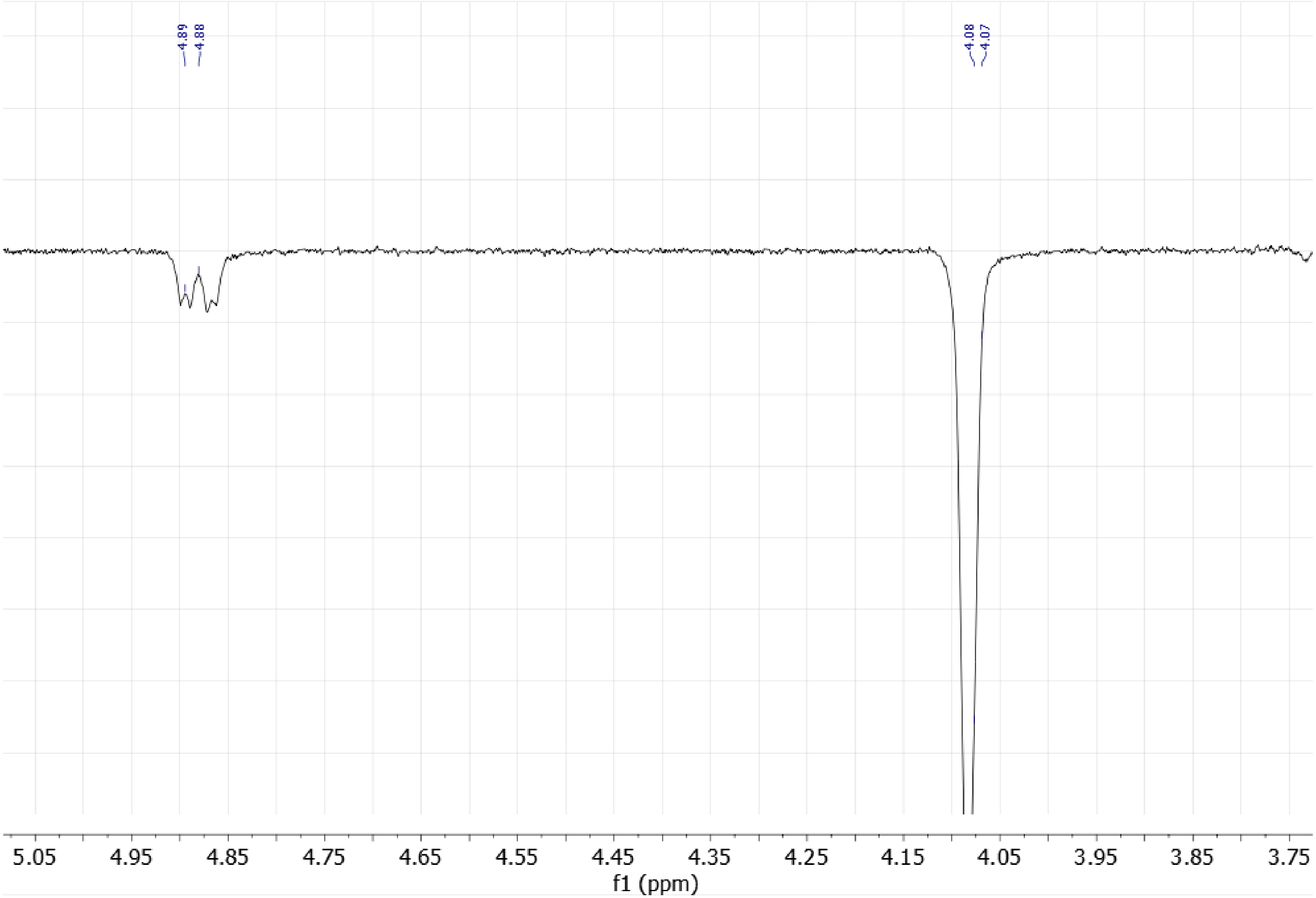
Compound **S12** **1D-NOE** (400 MHz, d_6-Acetone, -78 °C, irradiation at 2.5 ppm)



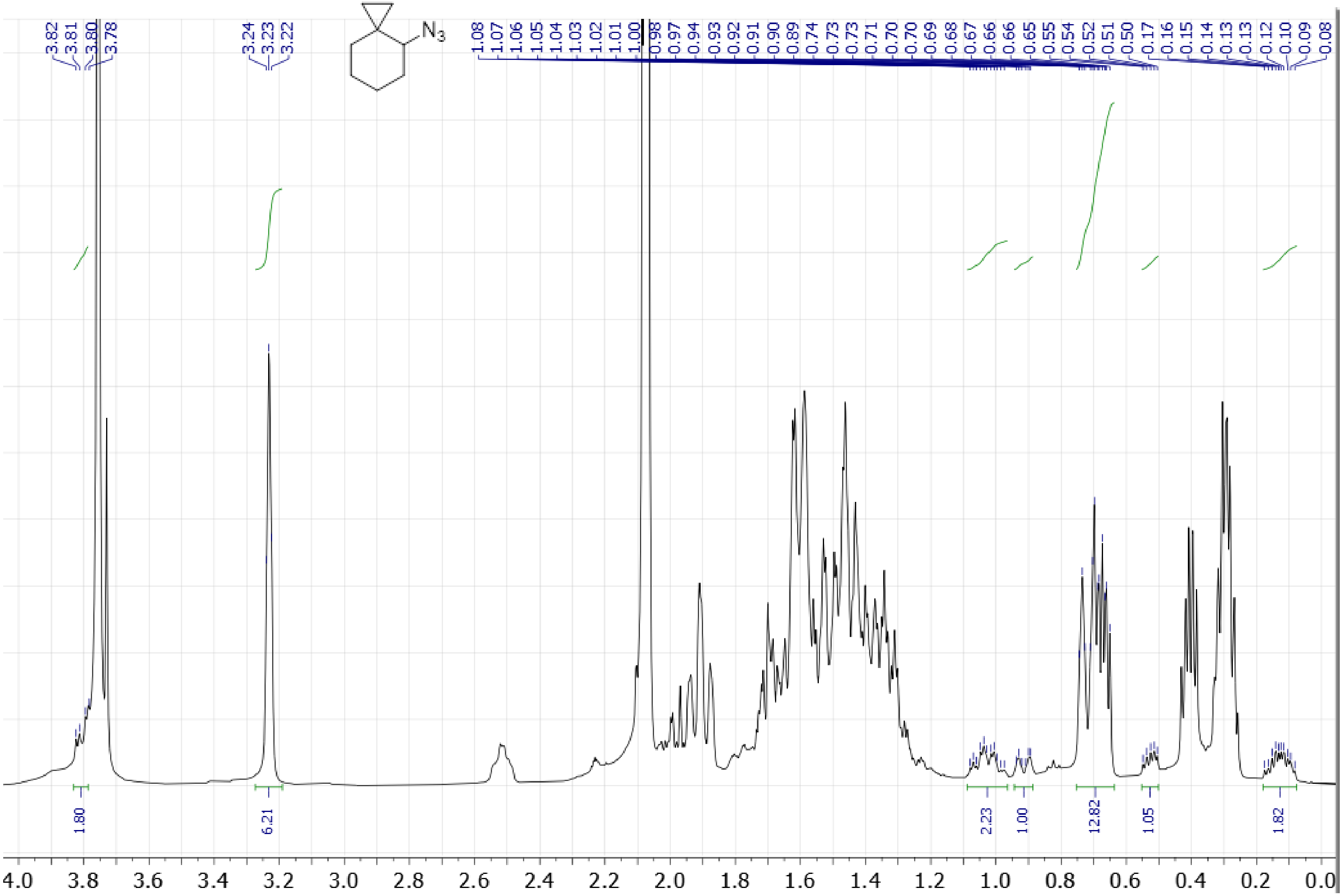
Compound **S13** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C



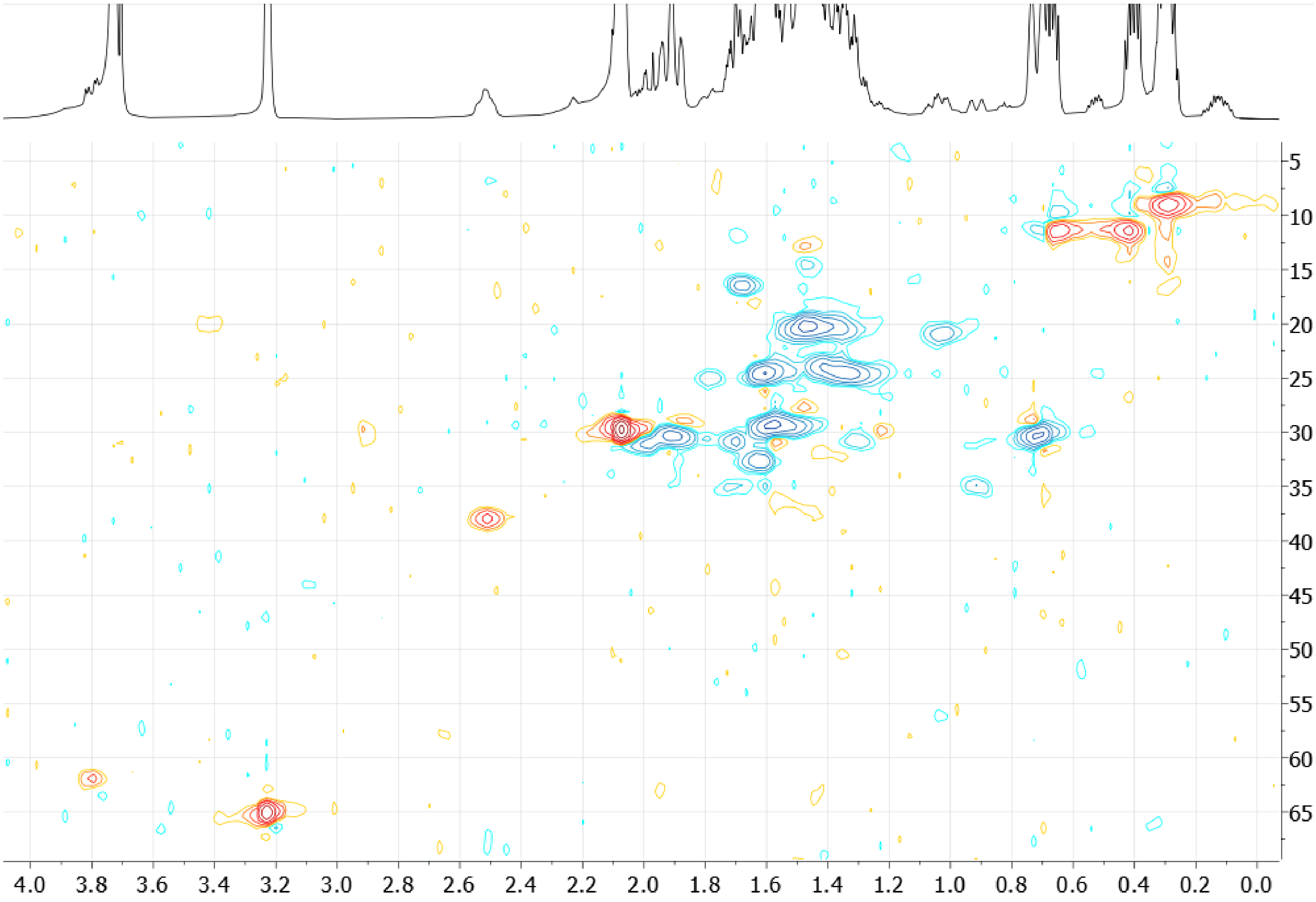
Compound **S13 1D-NOE** (400 MHz, *d*$_6$-Acetone, -78 °C, irradiation at 4.07 ppm)



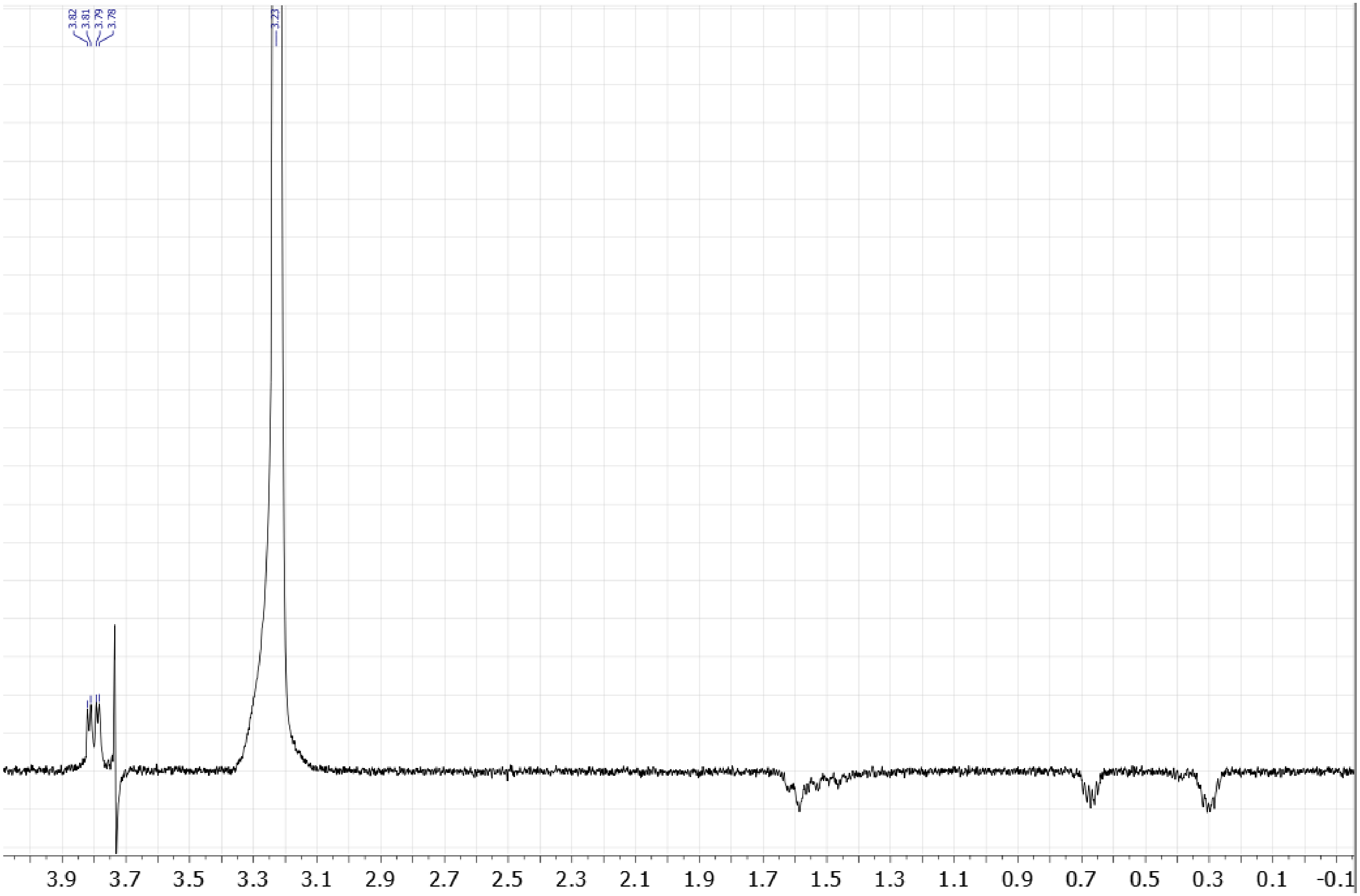
Compound **S14** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



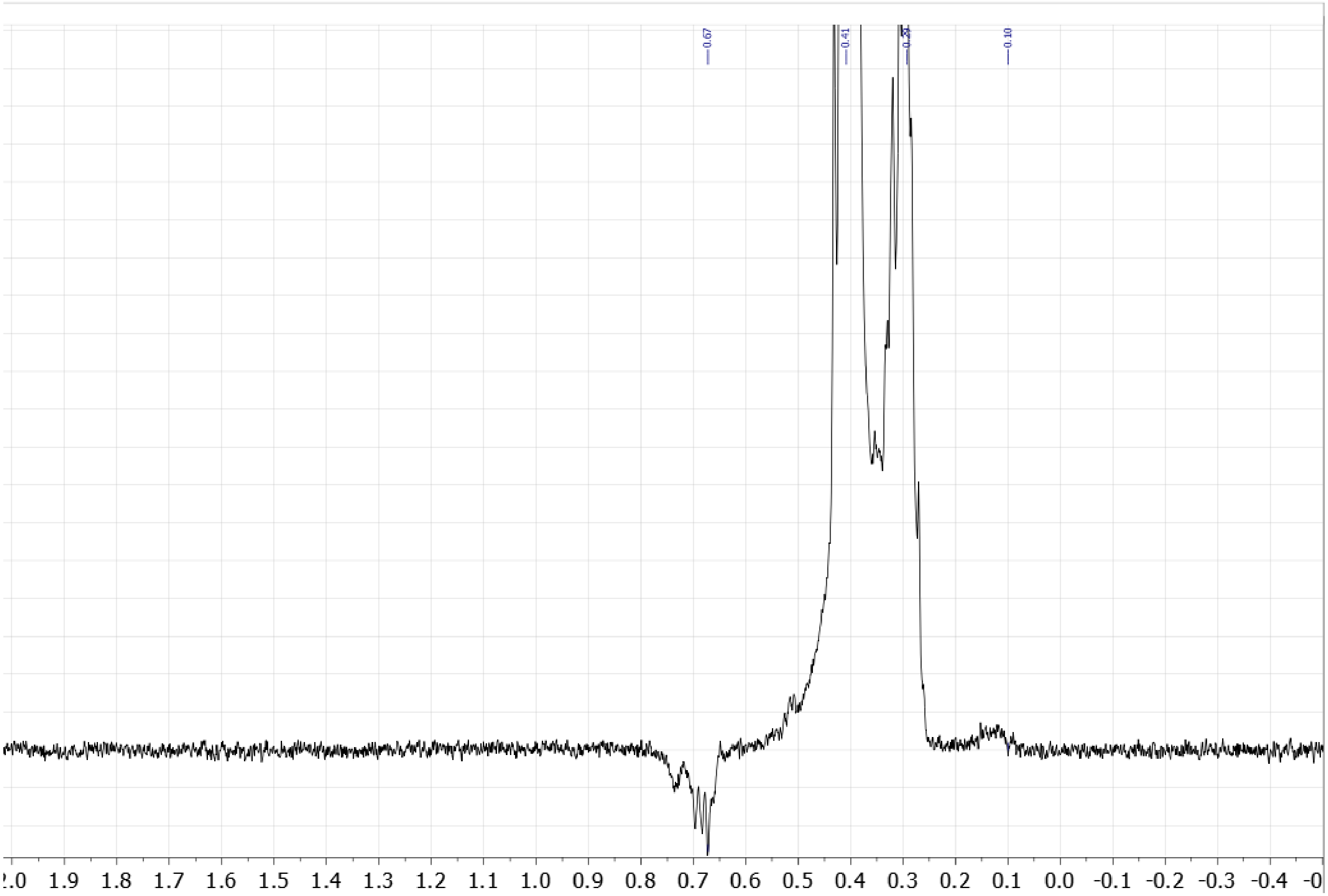
Compound **S14 HSQC** (400 MHz, *d*$_6$-Acetone, -78 °C)



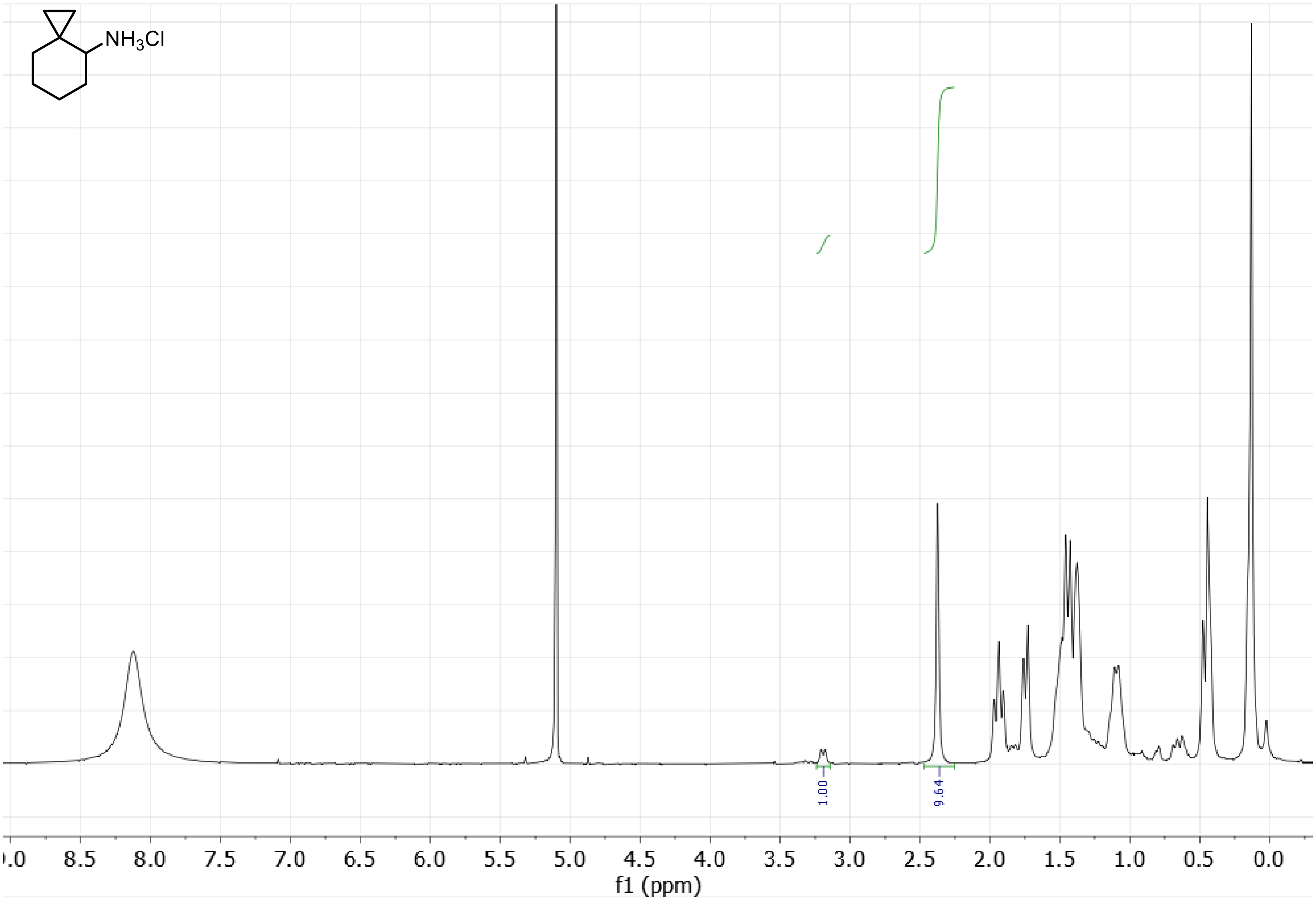
Compound **S14 1D NOE** (irradiation at 3.24 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C)



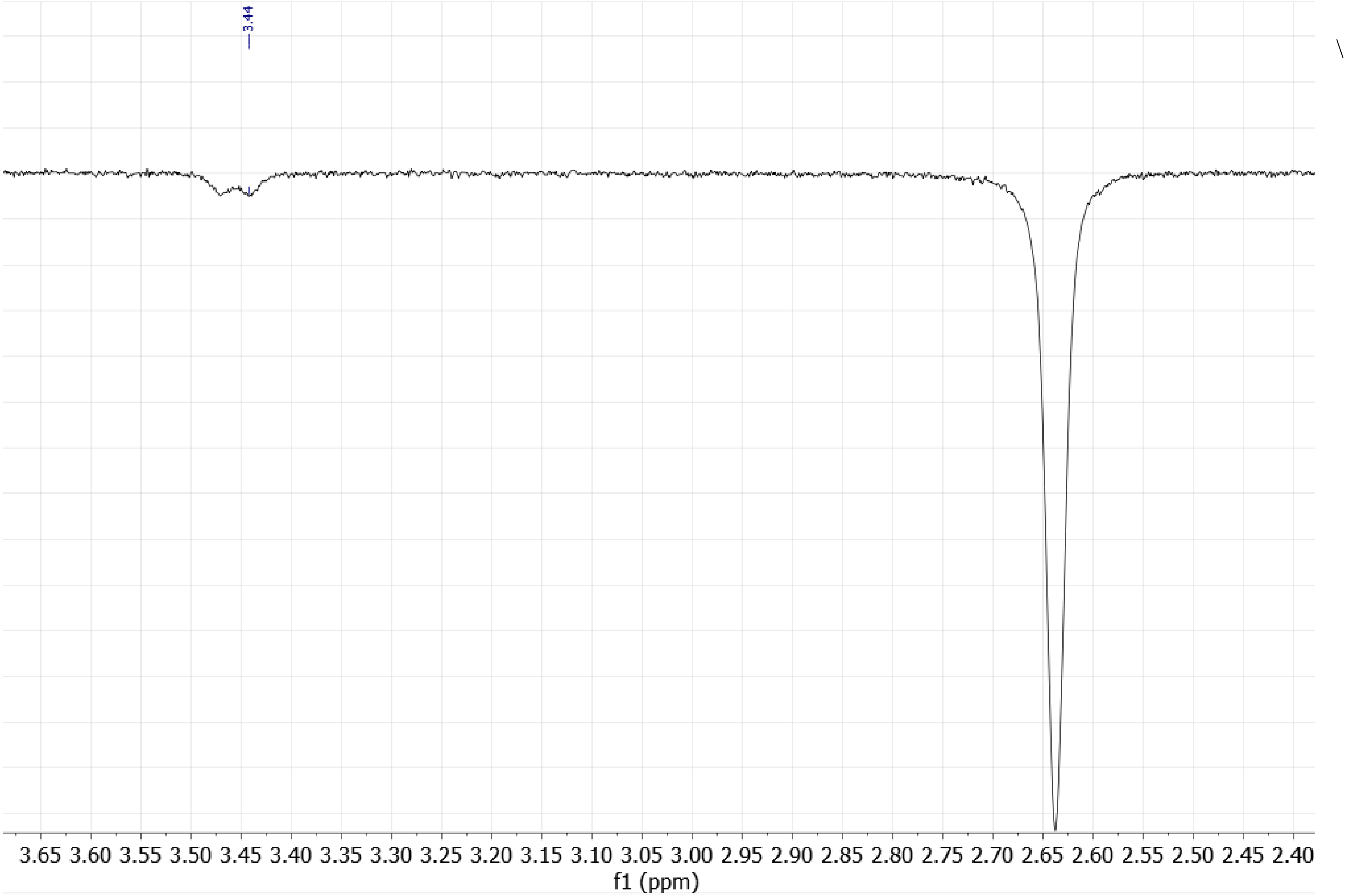
Compound **S14 1D NOE** (irradiation at 0.40 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C)



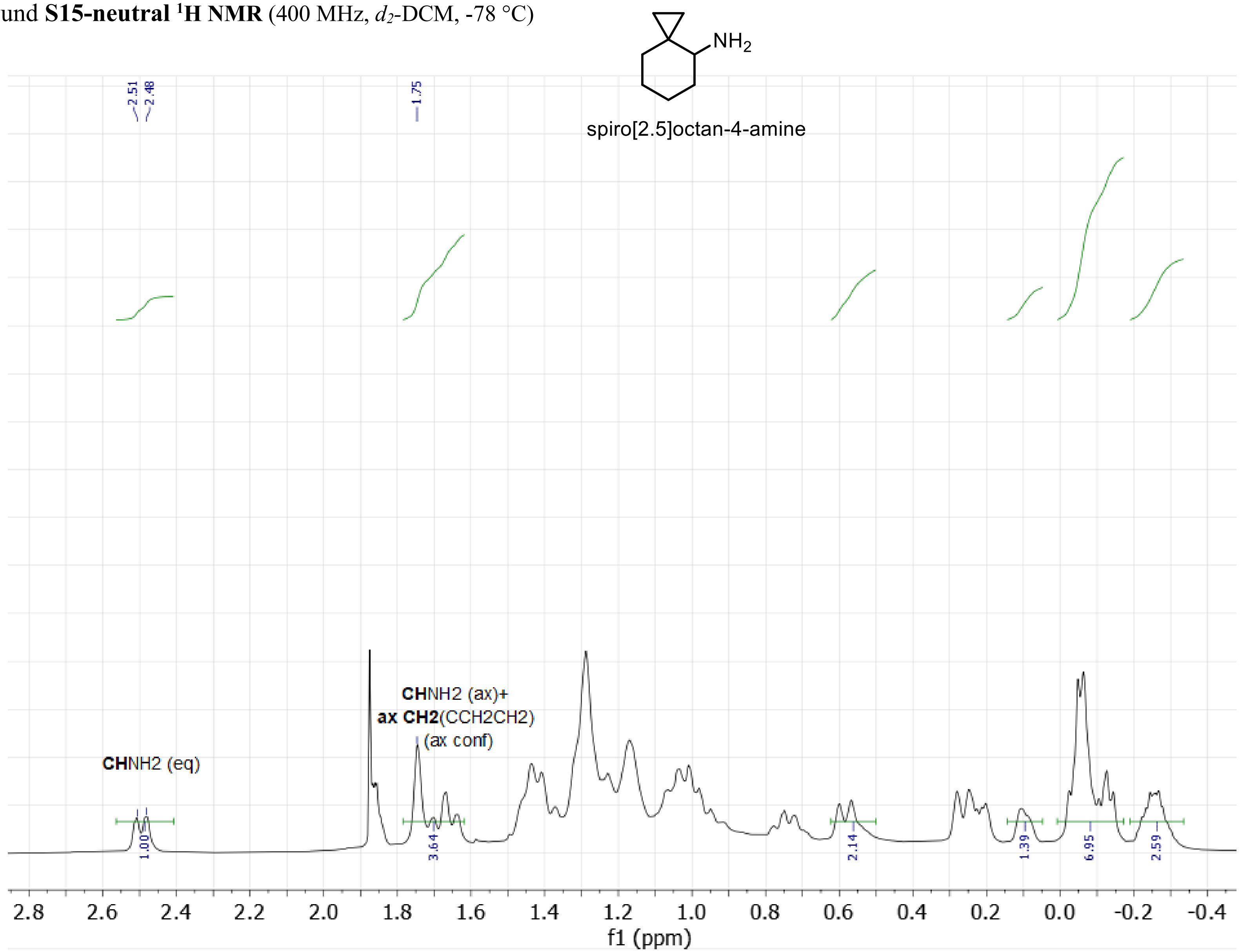
Compound **S15-HCl** ^{1}**H NMR** (400 MHz, *d*$_2$-DCM, -78 °C)



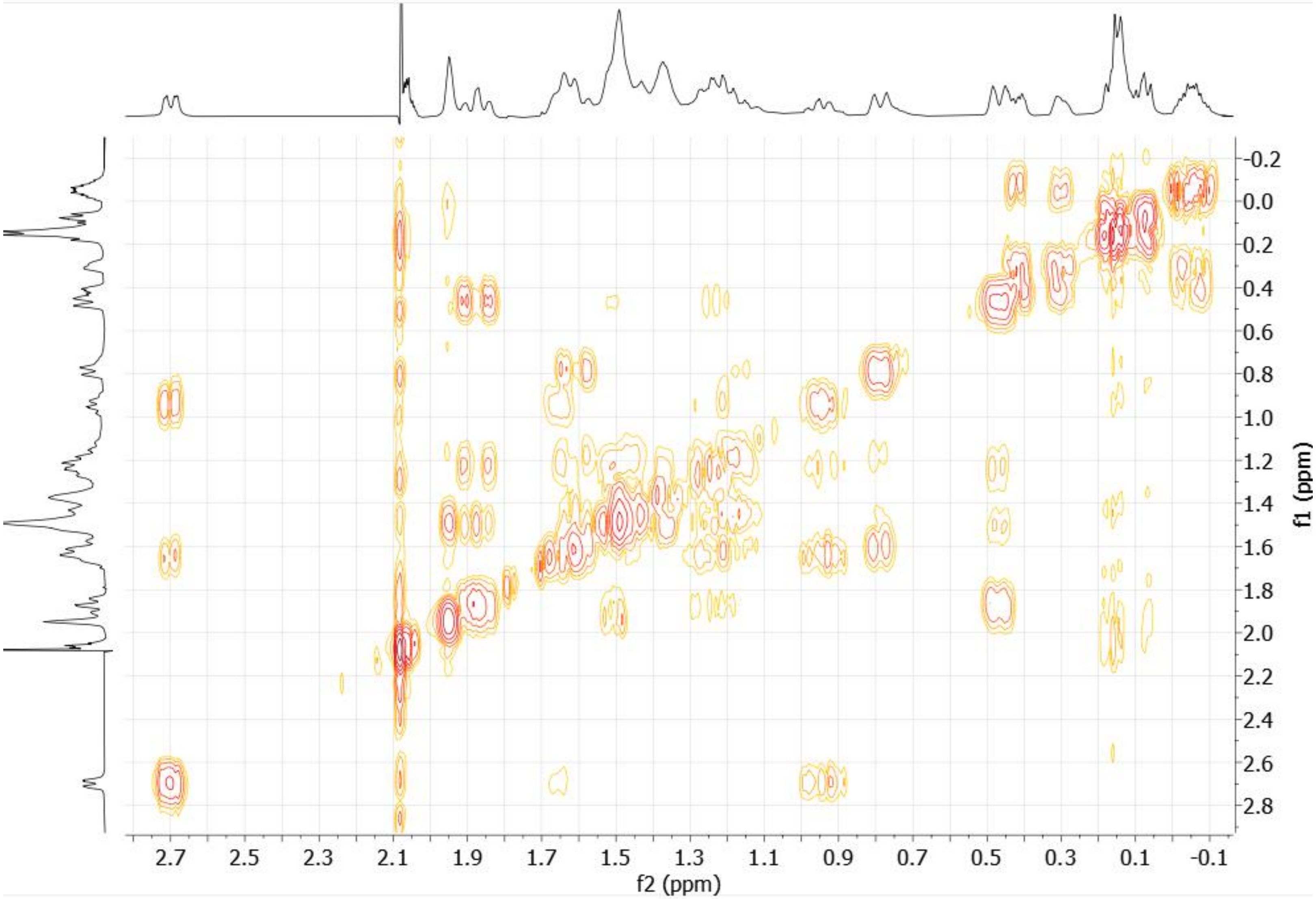
Compound **S15-HCl 1D-NOE** (400 MHz, *d*$_2$-DCM, -78 °C, irradiation at 2.64 ppm)



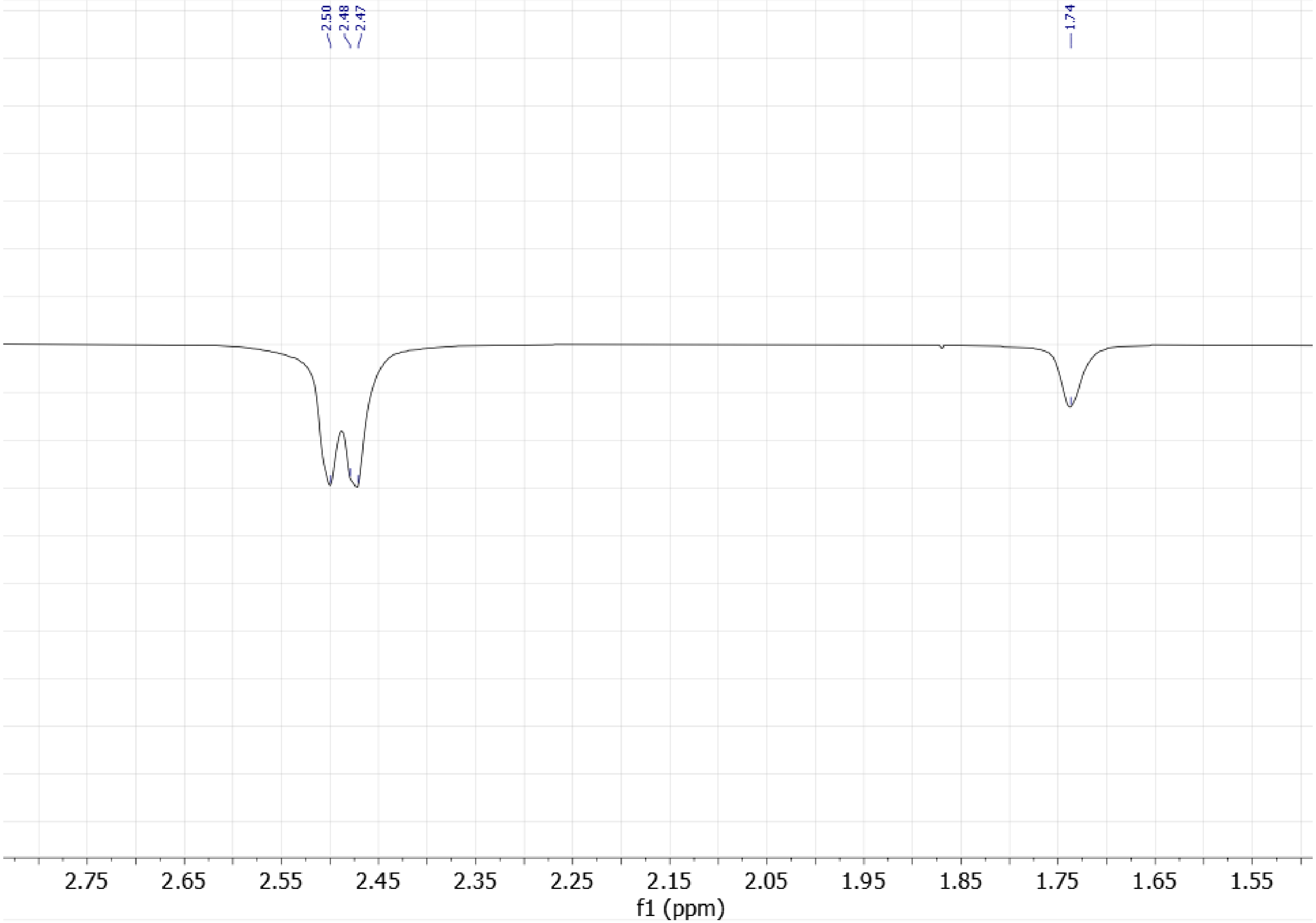
Compound **S15-neutral ^{1}H NMR** (400 MHz, d_2-DCM, -78 °C)



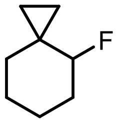
Compound **S15-neutral COSY** (400 MHz, *d*$_2$-DCM, -78 °C)


2.7
2.5
2.3
2.1
1.9
1.7
1.5
1.3
1.1
0.9
0.7
0.5
0.3
0.1
-0.1
f2 (ppm)
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
f1 (ppm)

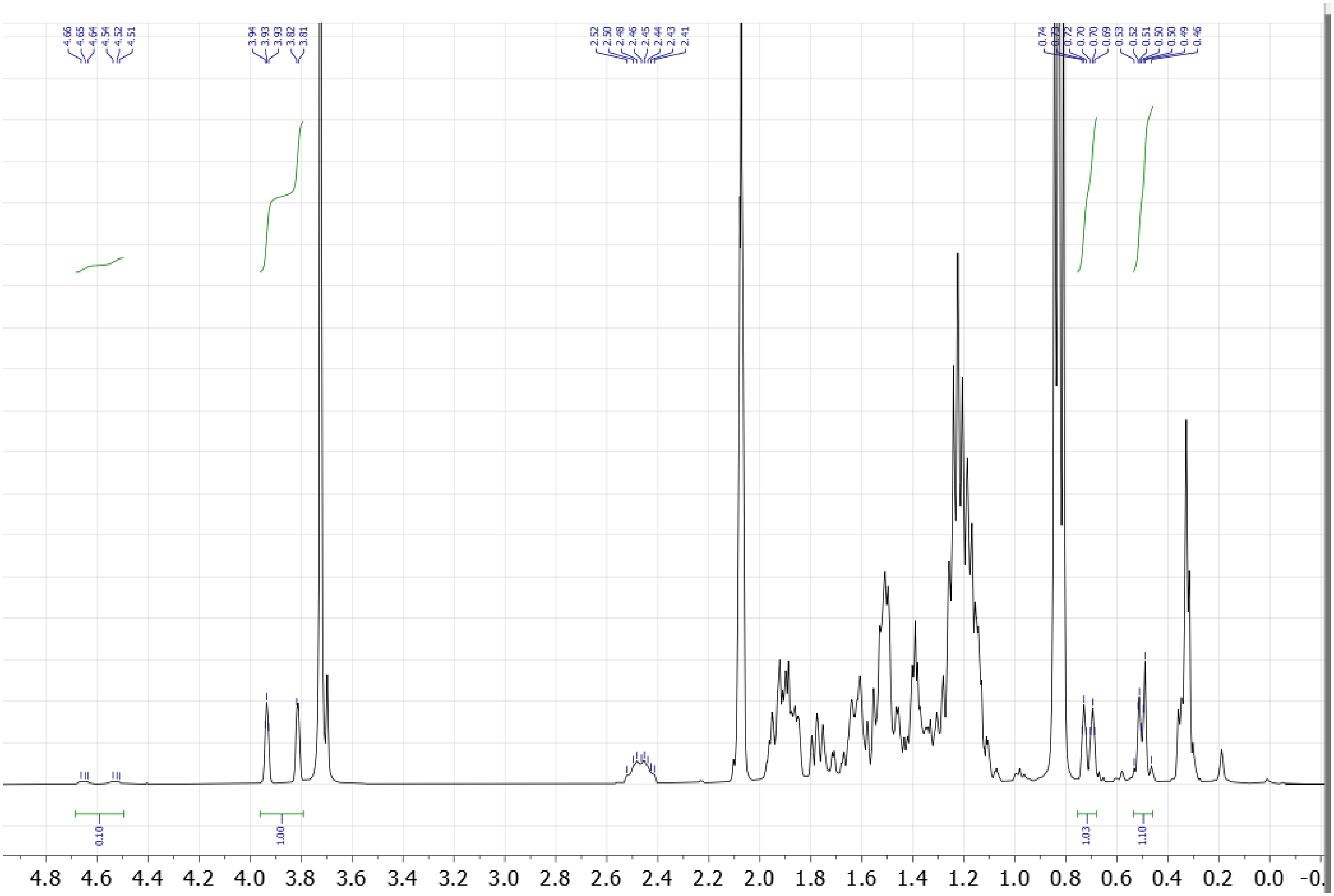
Compound **S15-neutral 1D-NOE** (400 MHz, d_2-DCM, -78 °C, irradiation at 2.46 ppm)



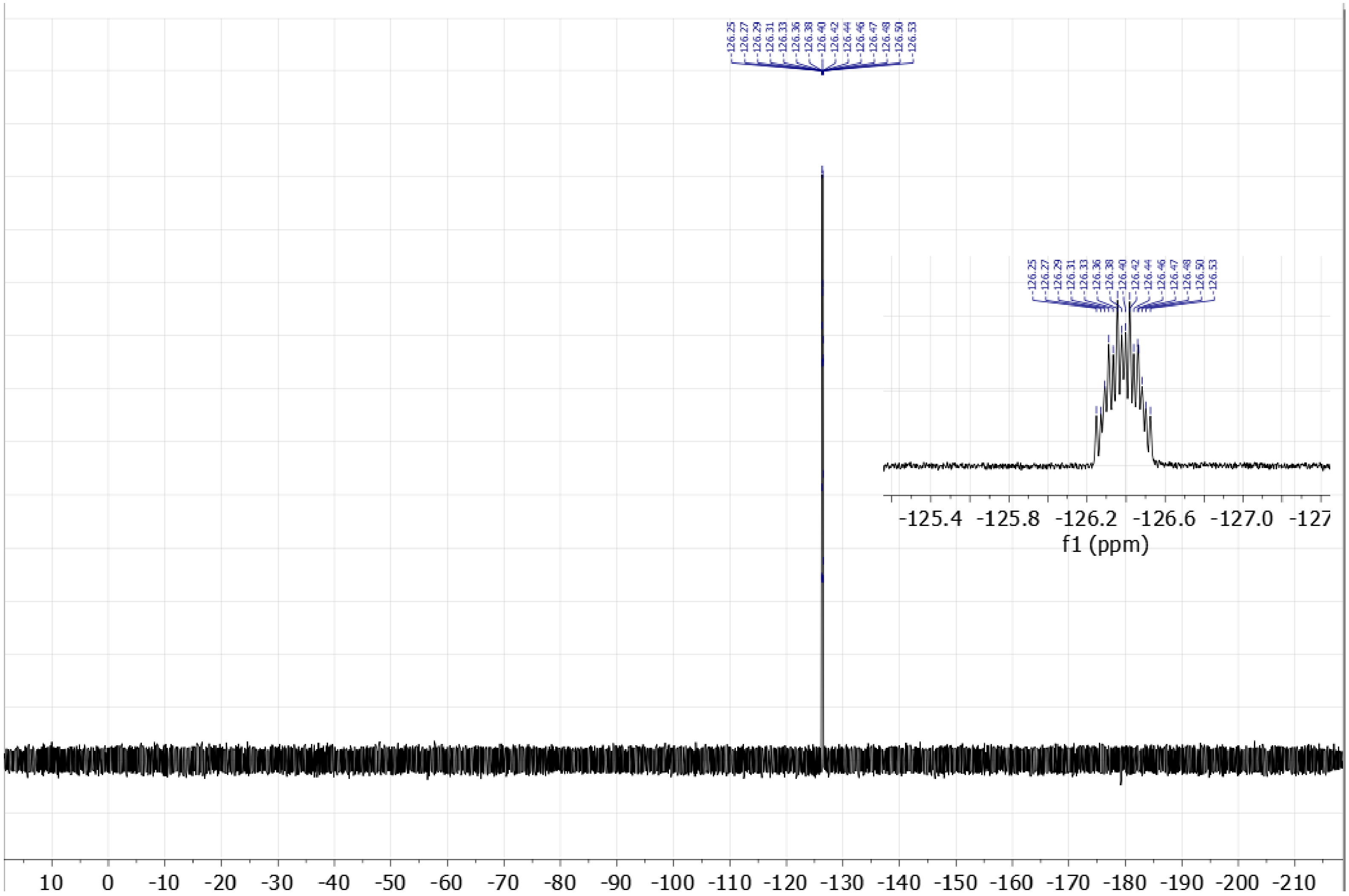
Compound **S16** ^{1}**H NMR** (400 MHz, *d$_6$*-Acetone, -78 °C)



4-fluorospiro[2.5]octane

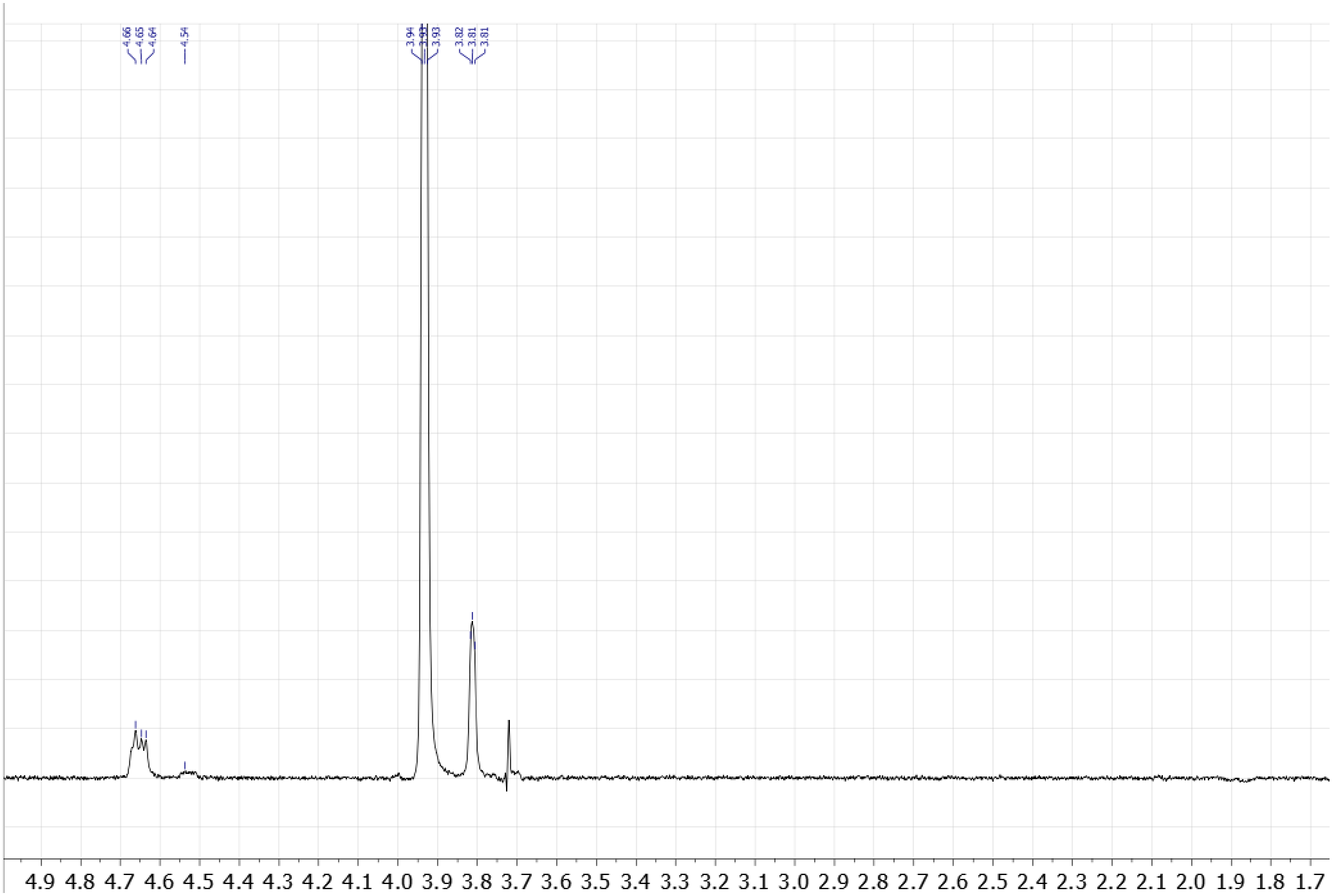

4.66
4.65
4.64
4.54
4.52
4.51
3.94
3.93
3.93
3.82
3.81
2.52
2.50
2.48
2.46
2.45
2.44
2.43
2.41
0.74
0.73
0.72
0.70
0.70
0.69
0.53
0.52
0.51
0.50
0.50
0.49
0.46
0.10
1.00
1.03
1.10
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.

Compound **S16** ^{19}**F NMR** (376.7 MHz, d_6-Acetone, -78 °C), with zoom of peak multiplicity

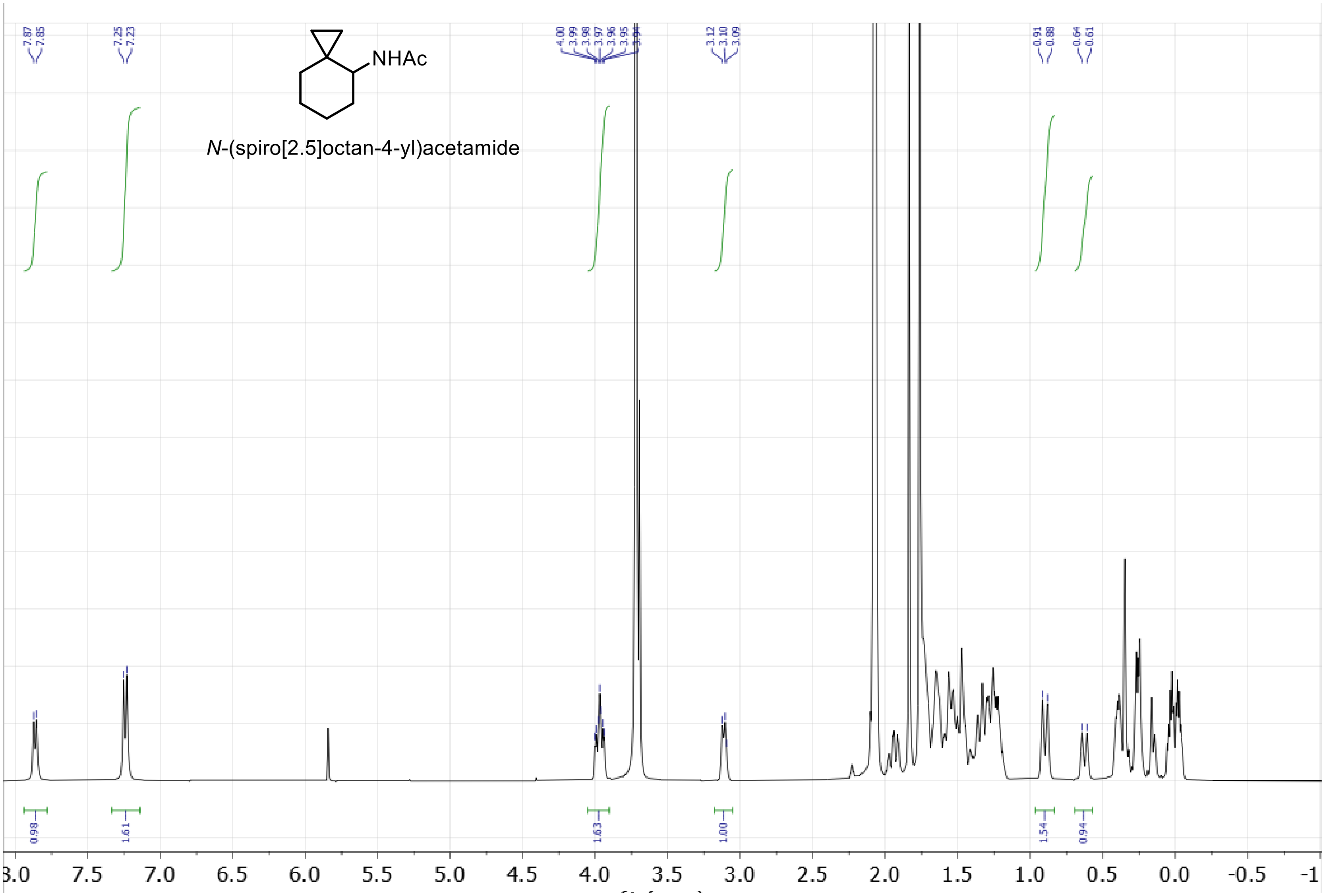


Compound **S16 1D NOE** (irradiation at 3.48 ppm, 400 MHz, d_6-Acetone, -78 °C)

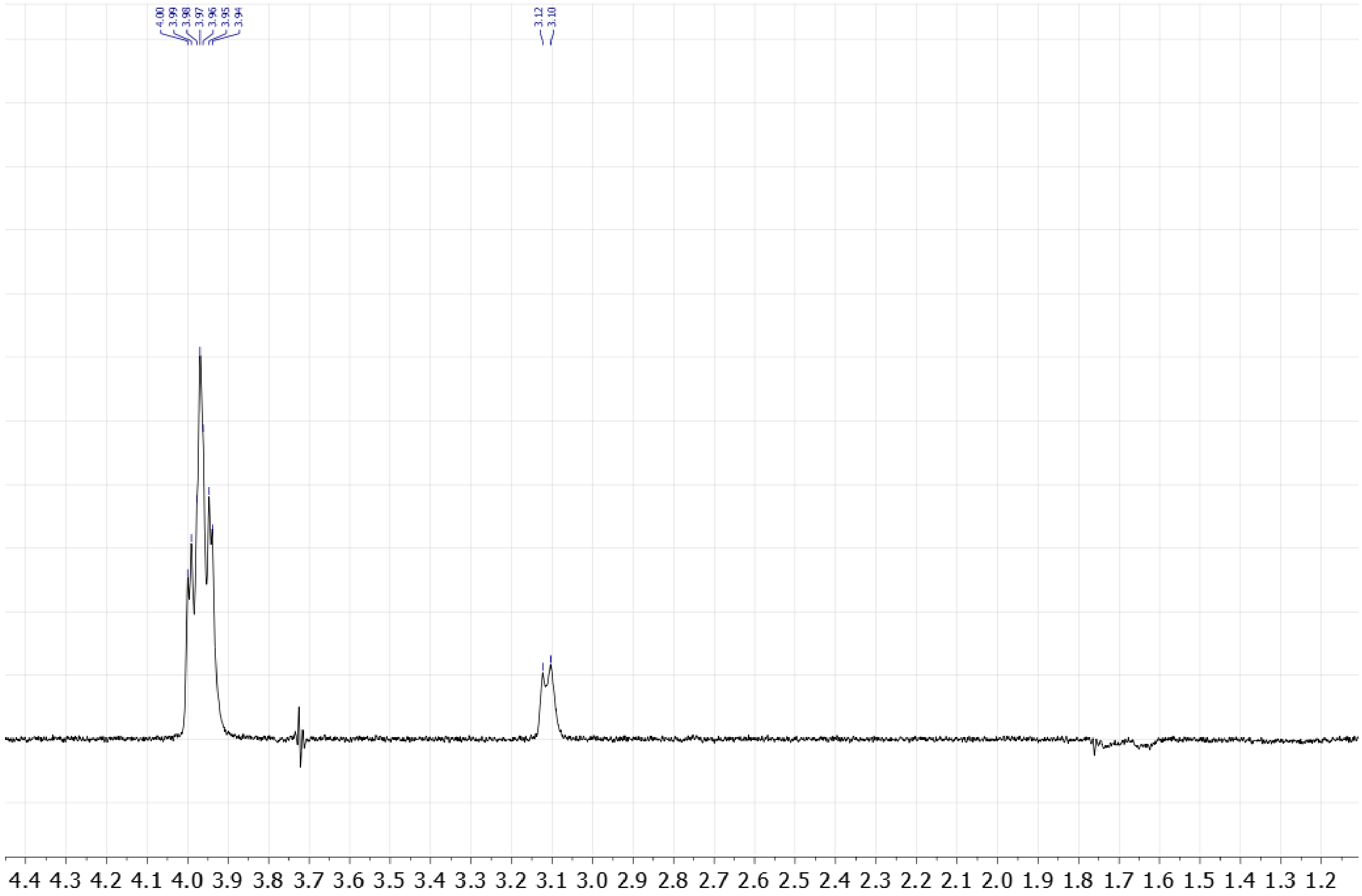
*Note that irradiating the left peak of such a doublet yields the corresponding left peak of the conformer's doublet



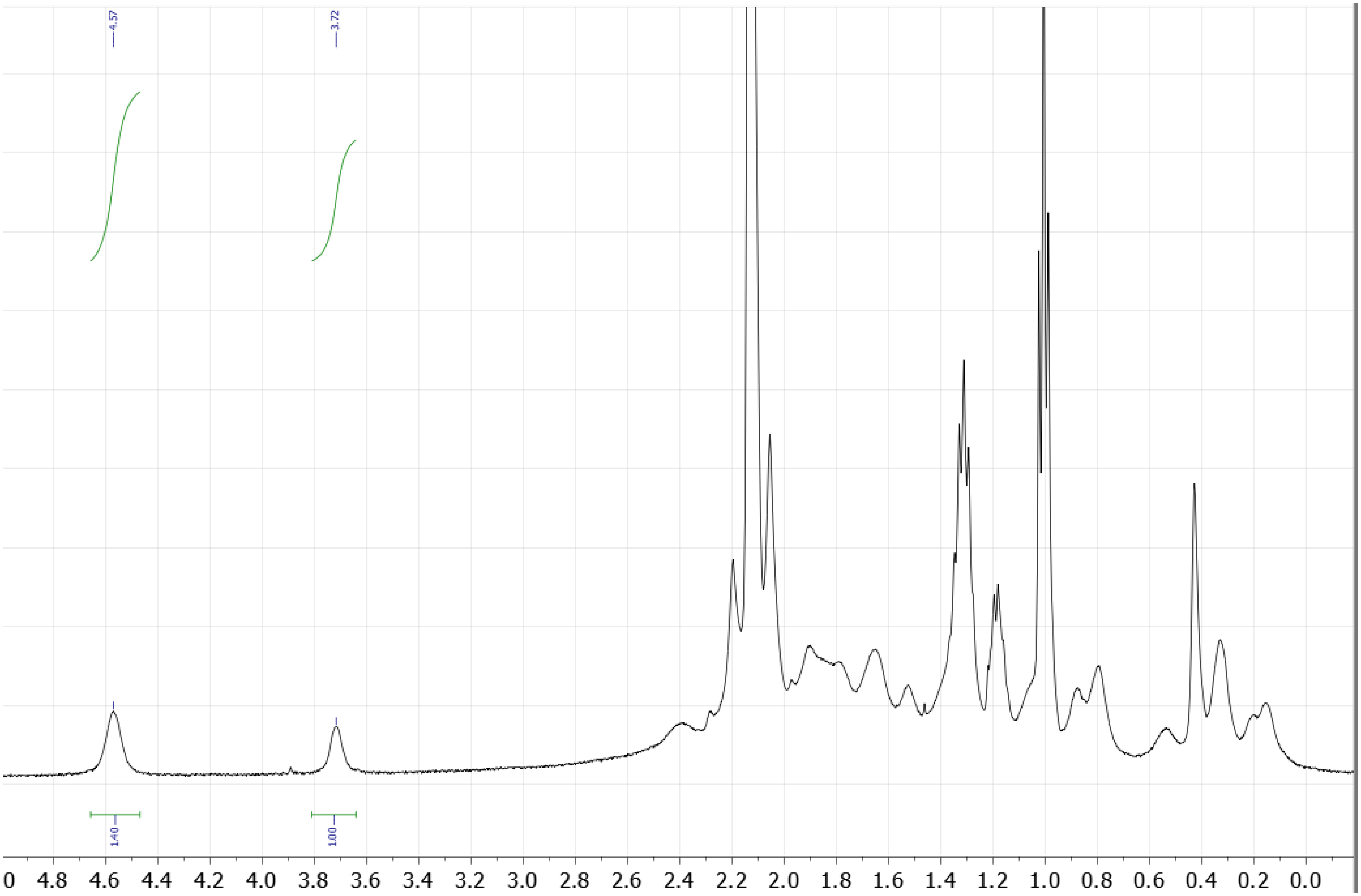
Compound **S17** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)



Compound **S17 1D NOE** (irradiation at 3.96 ppm, 400 MHz, d_6-Acetone, -78 °C)

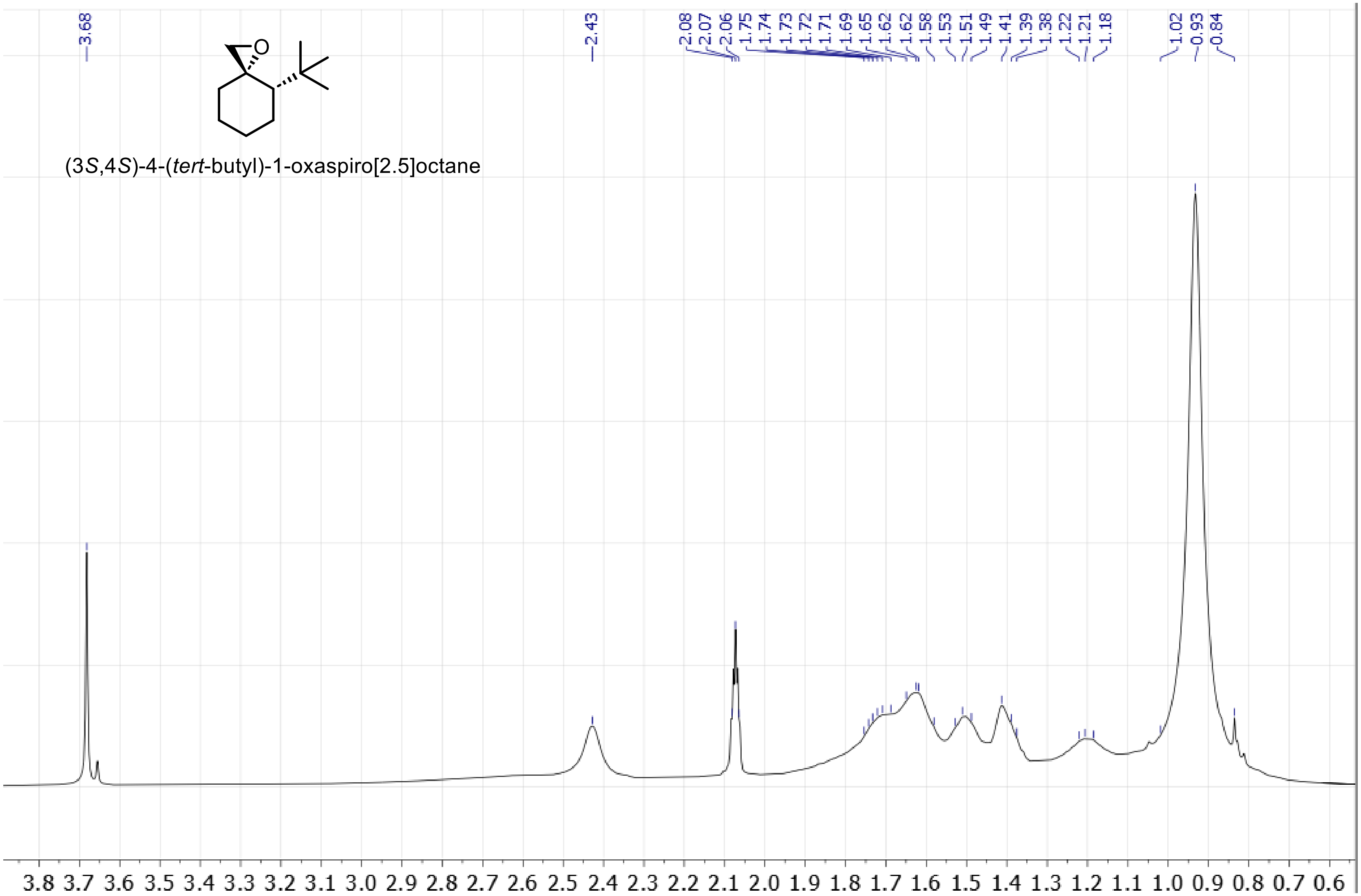


Compound **S17** **^{1}H NMR** (400 MHz, d_8-Toluene, -78 °C)



Compound **S18** ^{1}**H NMR** (400 MHz, *d*$_6$-Acetone, -78 °C)

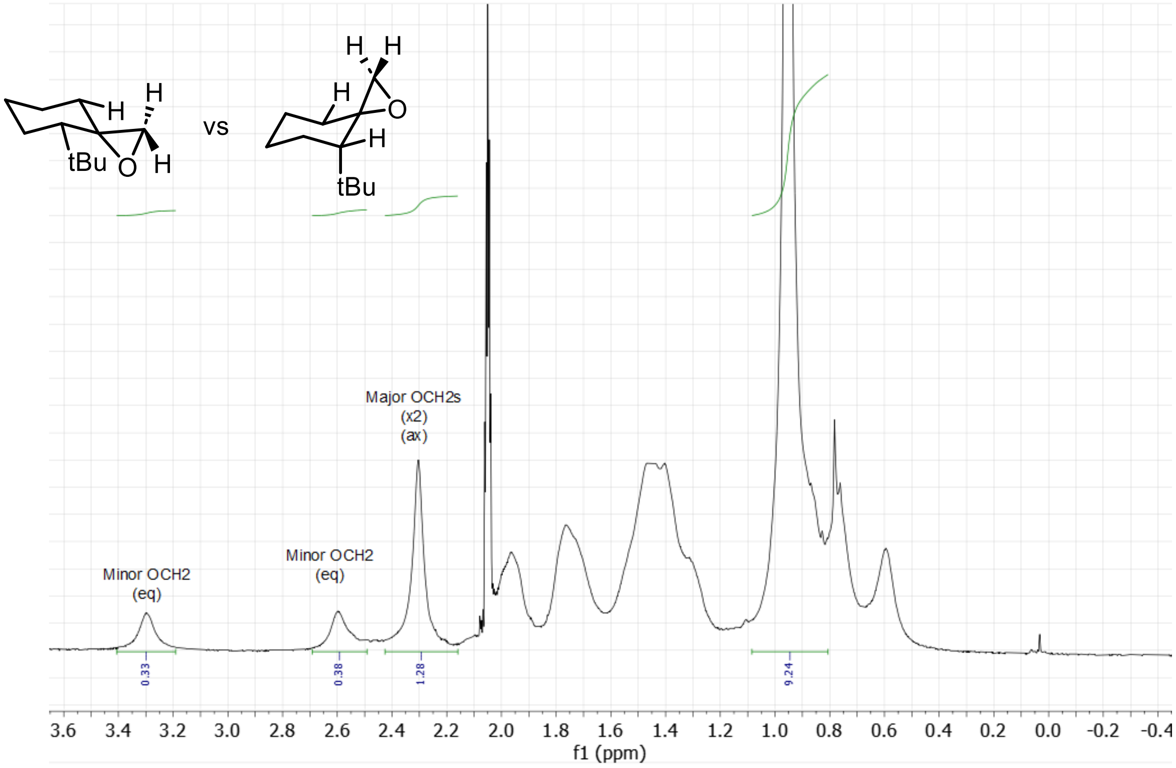
***Note: Peaks not resolved at -78**



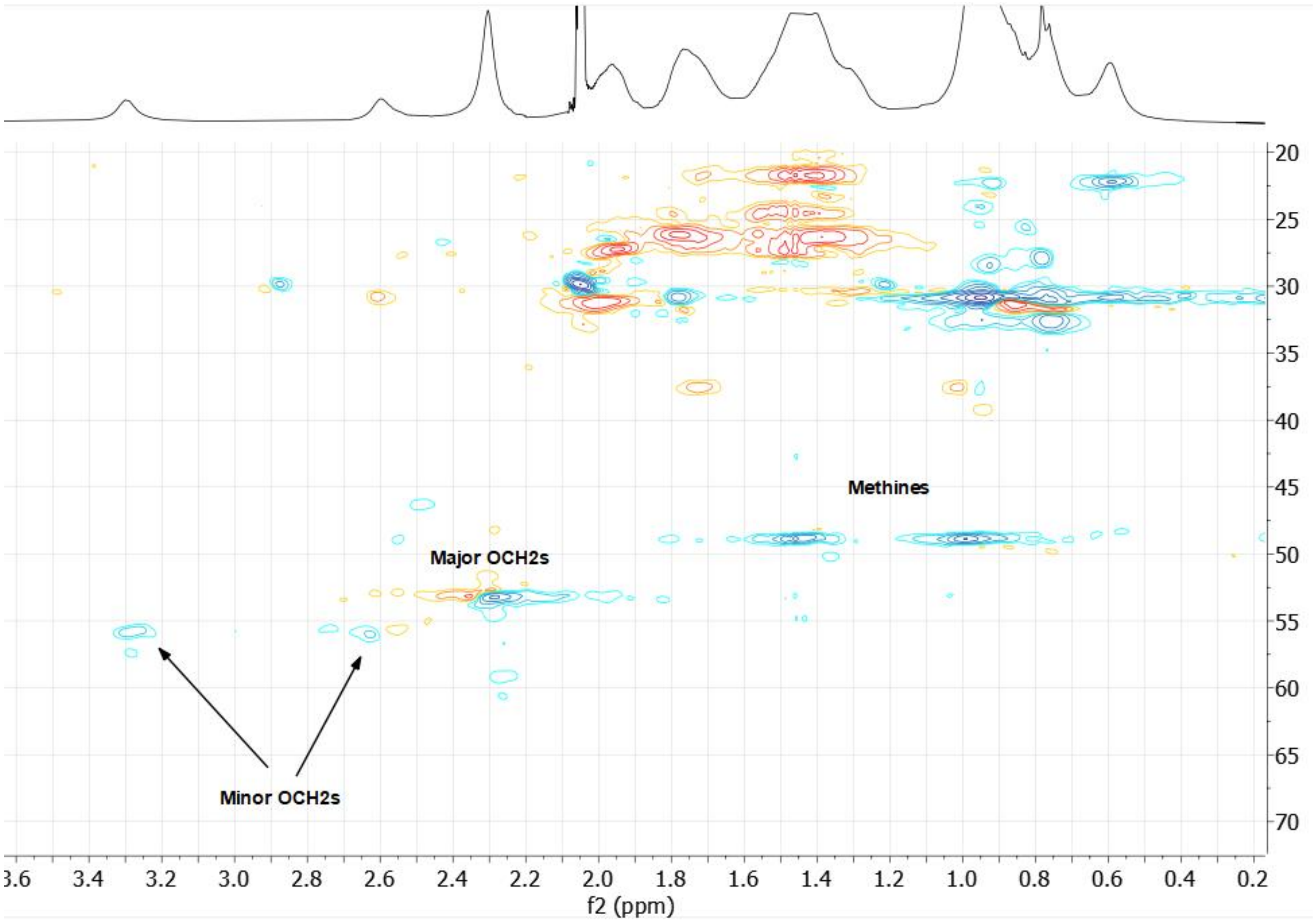
Compound **S18** **^{1}H NMR** (400 MHz, d_6-Acetone, -**98 °C**)

Note: Peaks now resolved at -98 °C

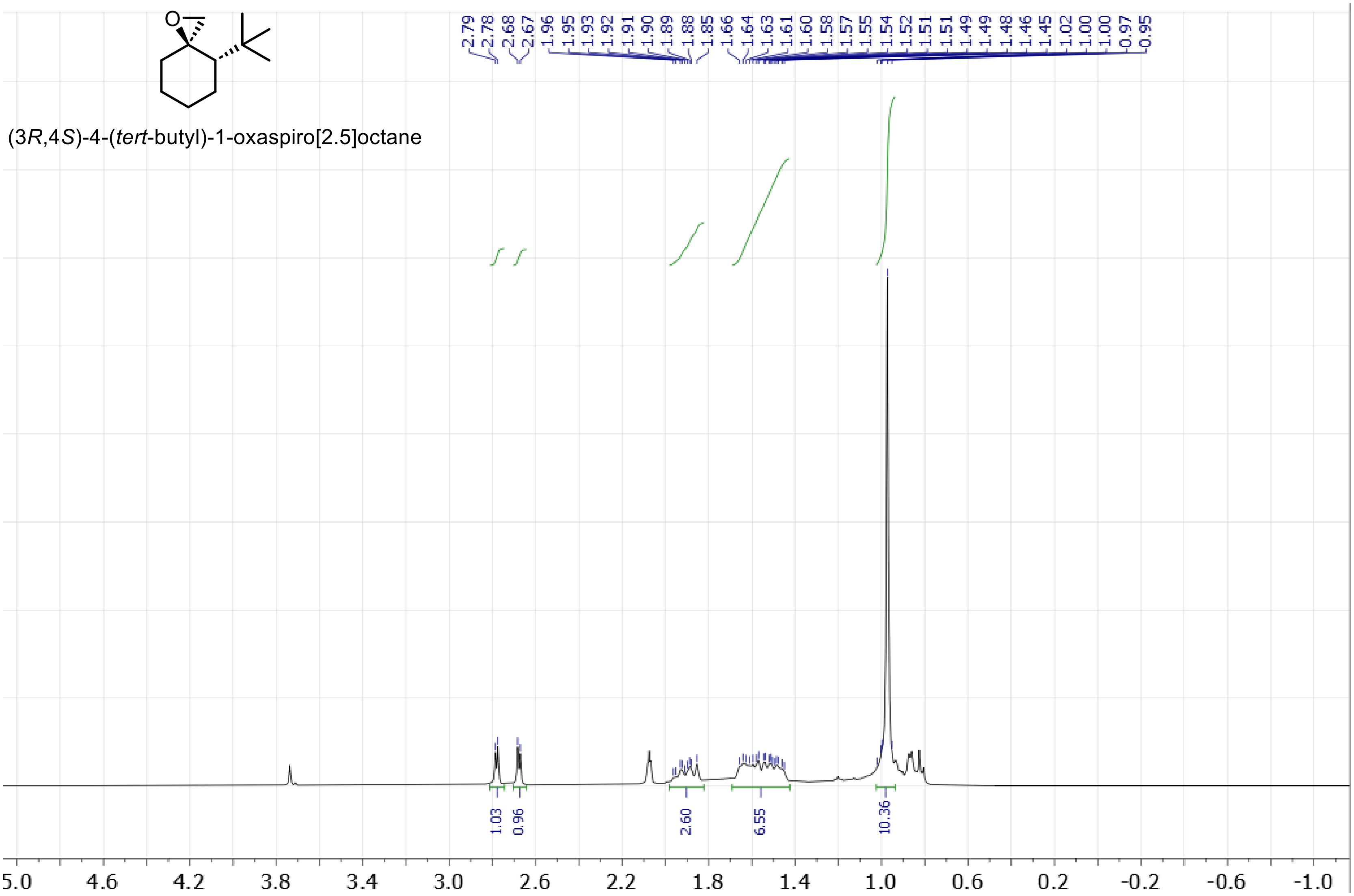
Rationale for assignment: The notable difference between major and minor conformations that we can see clearly from the spectrum is the difference in chemical shift for the epoxide methylene. The major conformer has overlapping methylenes with effectively identical shift, while the minor has a large difference. We would expect a large difference in shift for the equatorial tert-butyl methylenes, as the syn-proton will be close to the tert-butyl, and the anti-proton will be close to the equatorial proton on the other side of the ring. Conversely, the methylenes in the axial tert-butyl conformation are both closest to equatorial protons. NOES were unsuccessful at this temperature.



Compound **S18 HSQC** (400 MHz, *d*$_6$-Acetone, -**98 °C**)

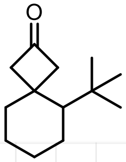


Compound **S19** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)

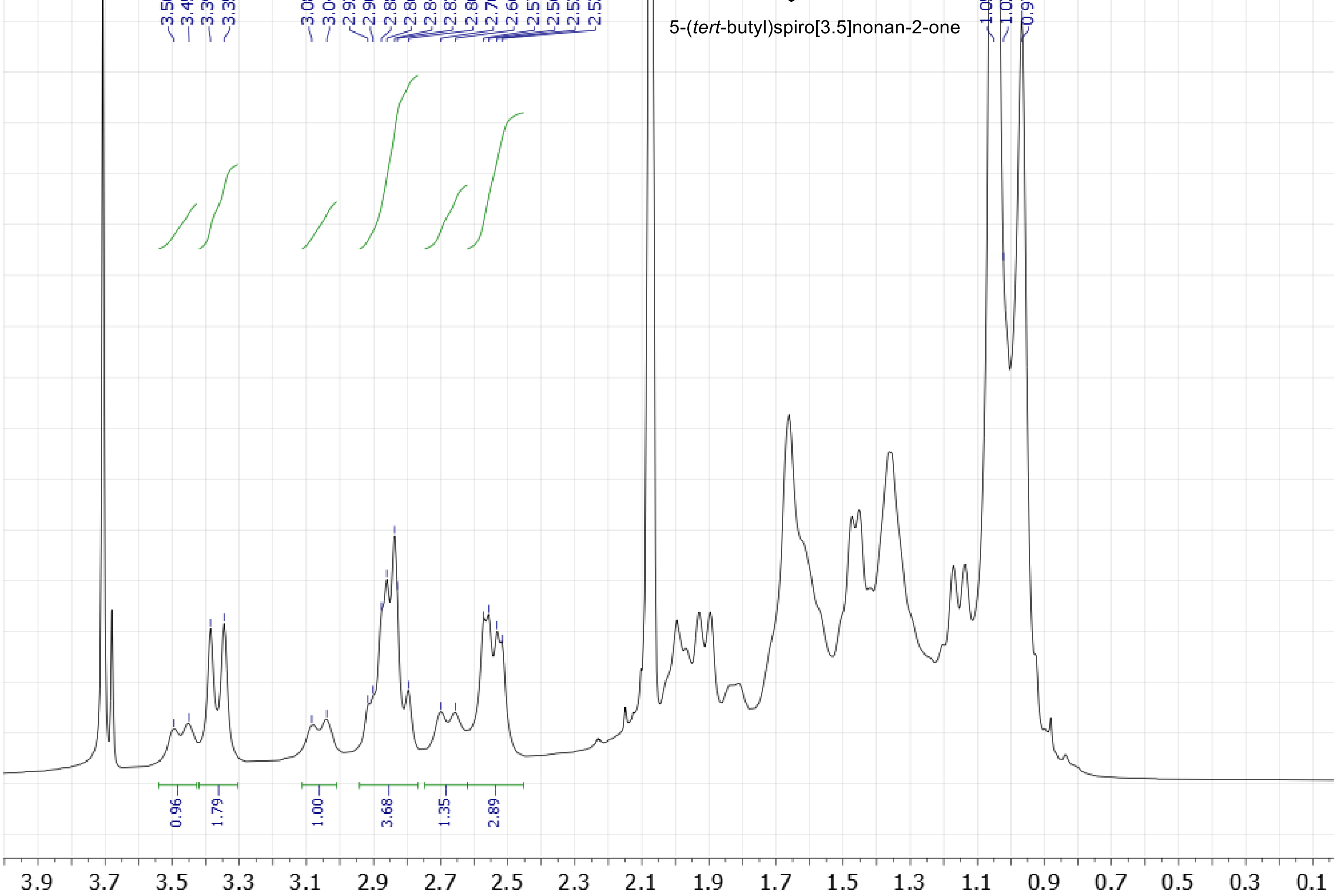


(3*R*,4*S*)-4-(*tert*-butyl)-1-oxaspiro[2.5]octane

Compound **20** **^{1}H NMR** (400 MHz, d_6-Acetone, -78 °C)



5-(*tert*-butyl)spiro[3.5]nonan-2-one

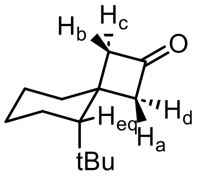


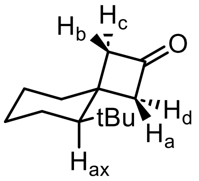
In this case we could reliably measure the ratio of conformers, but were unable to obtain conclusive NOE data. Predictions using NMR were successful at assigning the conformers as the predictions for both conformers were accurate

Chemical shift analysis method:

Shifts calculated using GIAO method at the B3LYP/6-311+G(2d,p) level with SCRF=acetone, referenced to TMS. Shifts were estimated using a Boltzmann distribution of all chair conformers.

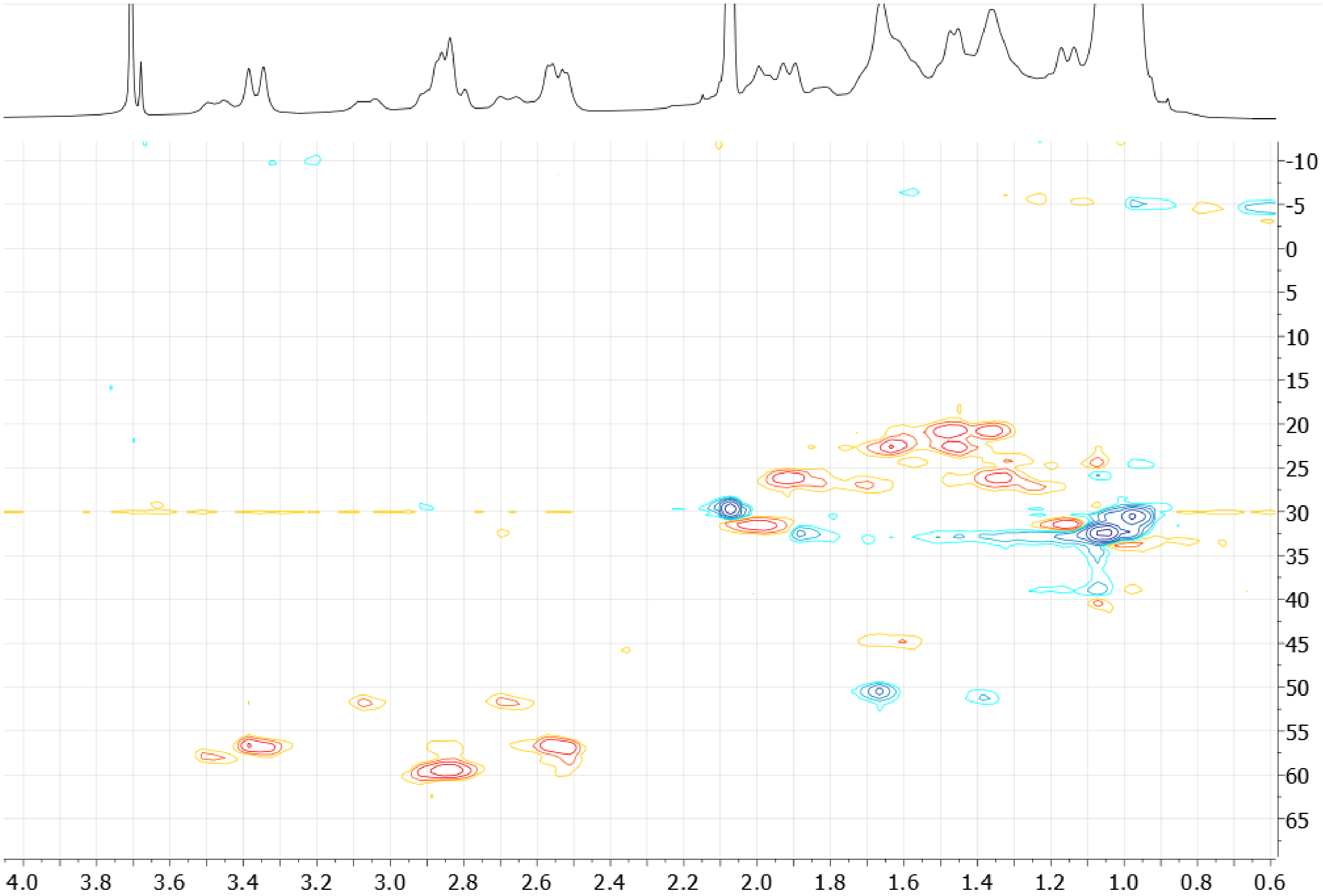
Table 1: Predicted (NMR GIAO) vs. observed NMR peaks for compound ***S20***



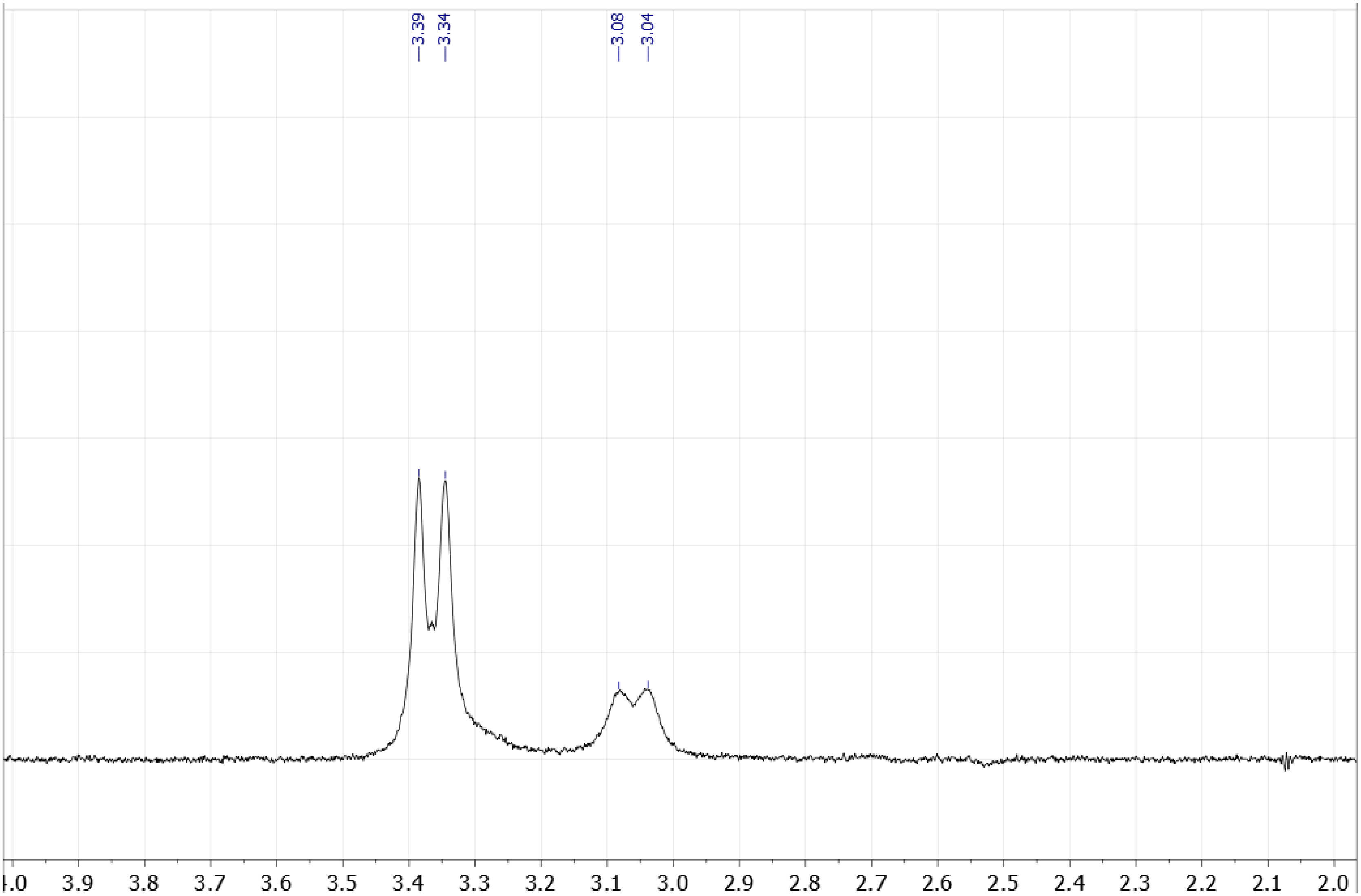


	Predicted	Observed		Predicted	Observed
H_{ax}	1.52 ppm	1.64 ppm	H_{eq}	1.34 ppm	1.36 ppm
H_a	3.39 ppm	3.38 ppm	H_a	3.63 ppm	3.46 ppm
H_b	2.72 ppm	2.75 ppm	H_b	3.19 ppm	3.04 ppm
H_c	2.92 ppm	2.85 ppm	H_c	2.63 ppm	2.65 ppm
H_d	2.46 ppm	2.52 ppm	H_d	2.43 ppm	2.51 ppm

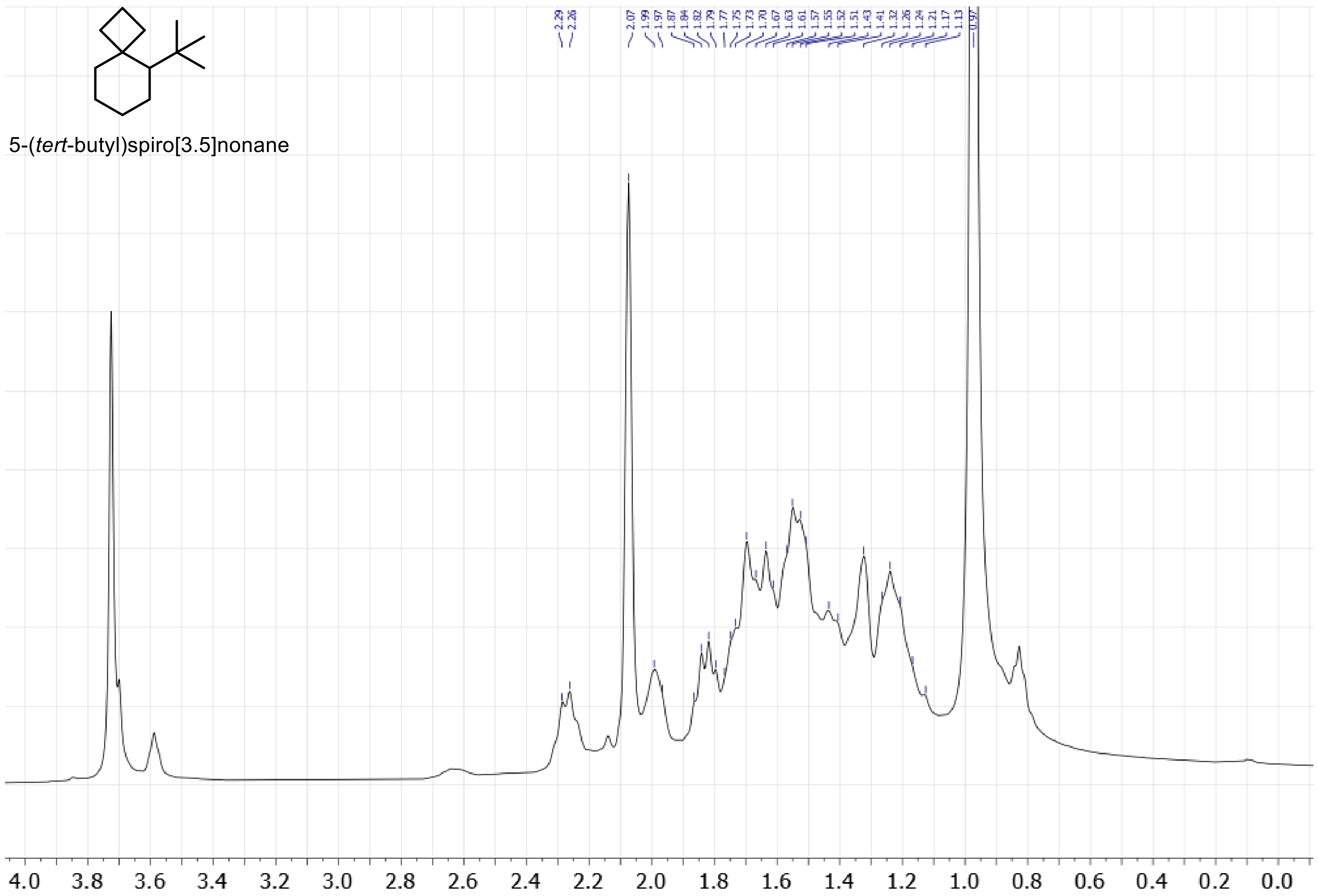
Compound **S20 HSQC** (400 MHz, d_6-Acetone, -78 °C)



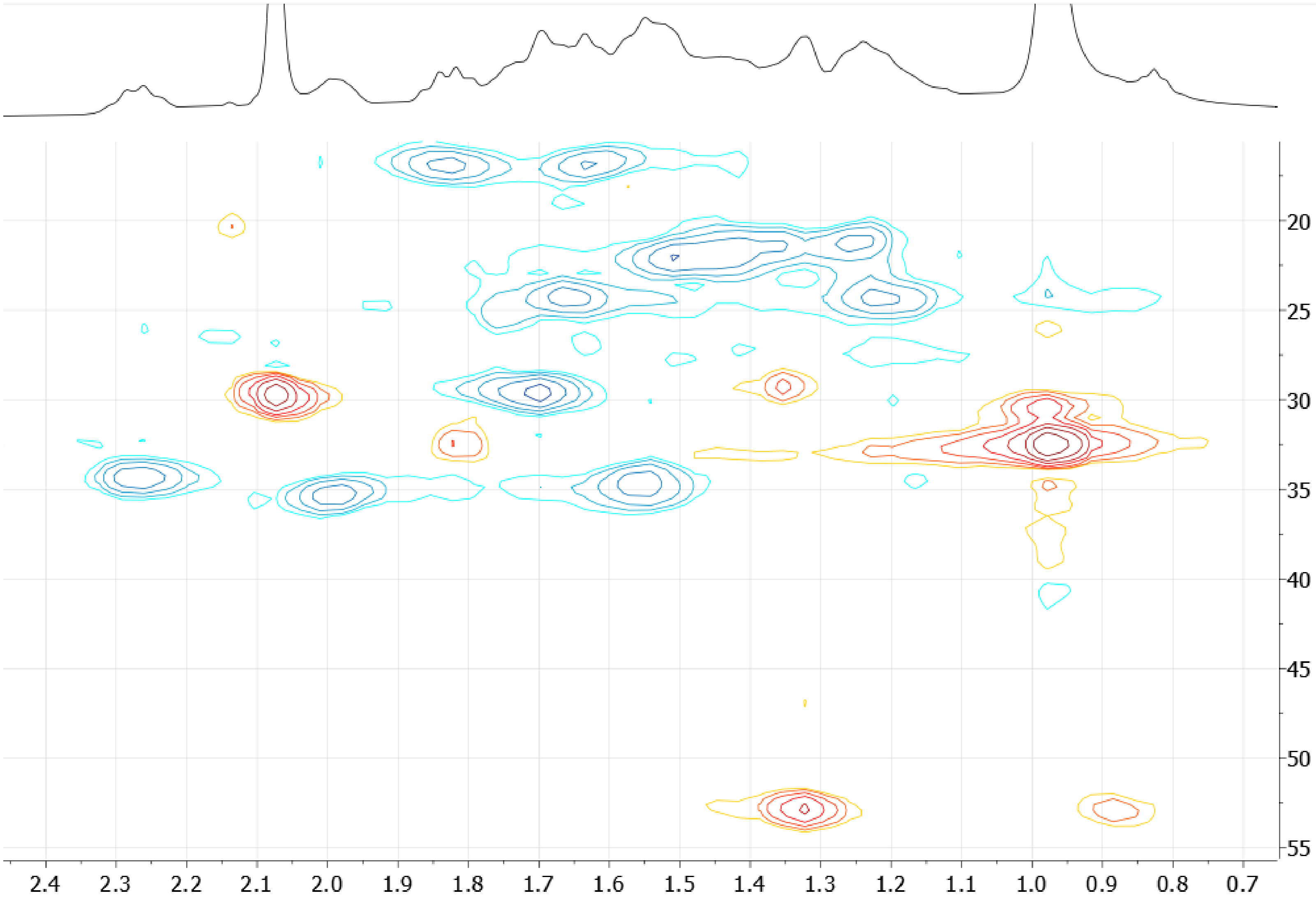
Compound **S20 1D NOE** (irradiation at 3.36 ppm, 400 MHz, d_6-Acetone, -78 °C)



Compound **S21** **^{1}H NMR** (400 MHz, d_6-Acetone, -78 °C)

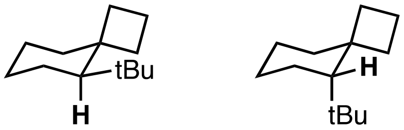


Compound **S21 HSQC** (400 MHz, *d*$_6$-Acetone, -78 °C)



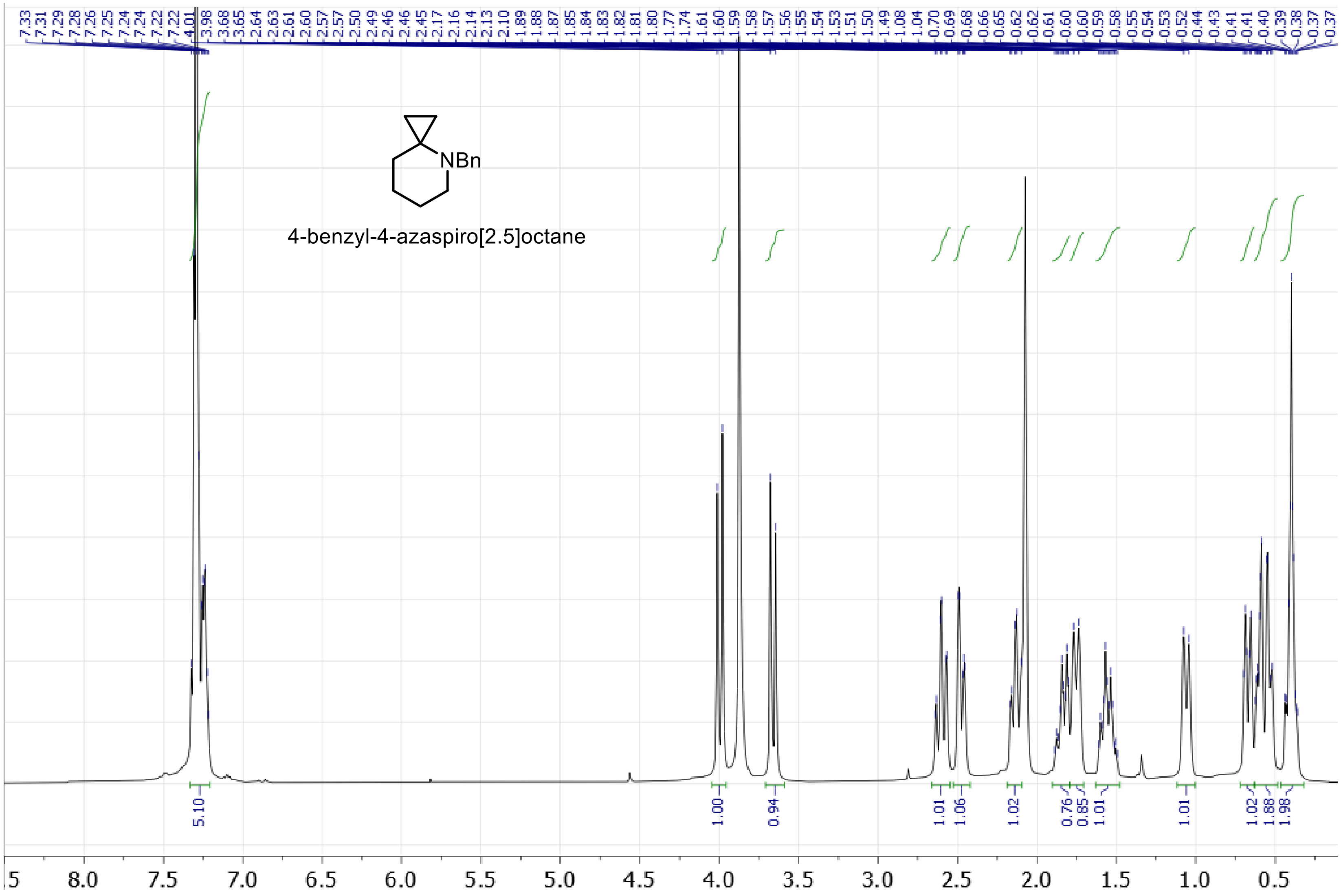
Although we could not quantify the ratio, we were able to assign overlapped methine signals using NMR prediction (see computational SI for details. The predicted vs observed are shown below in table 2.

Table 2: Predicted vs observed chemical shifts of compound S21 at -78 °C

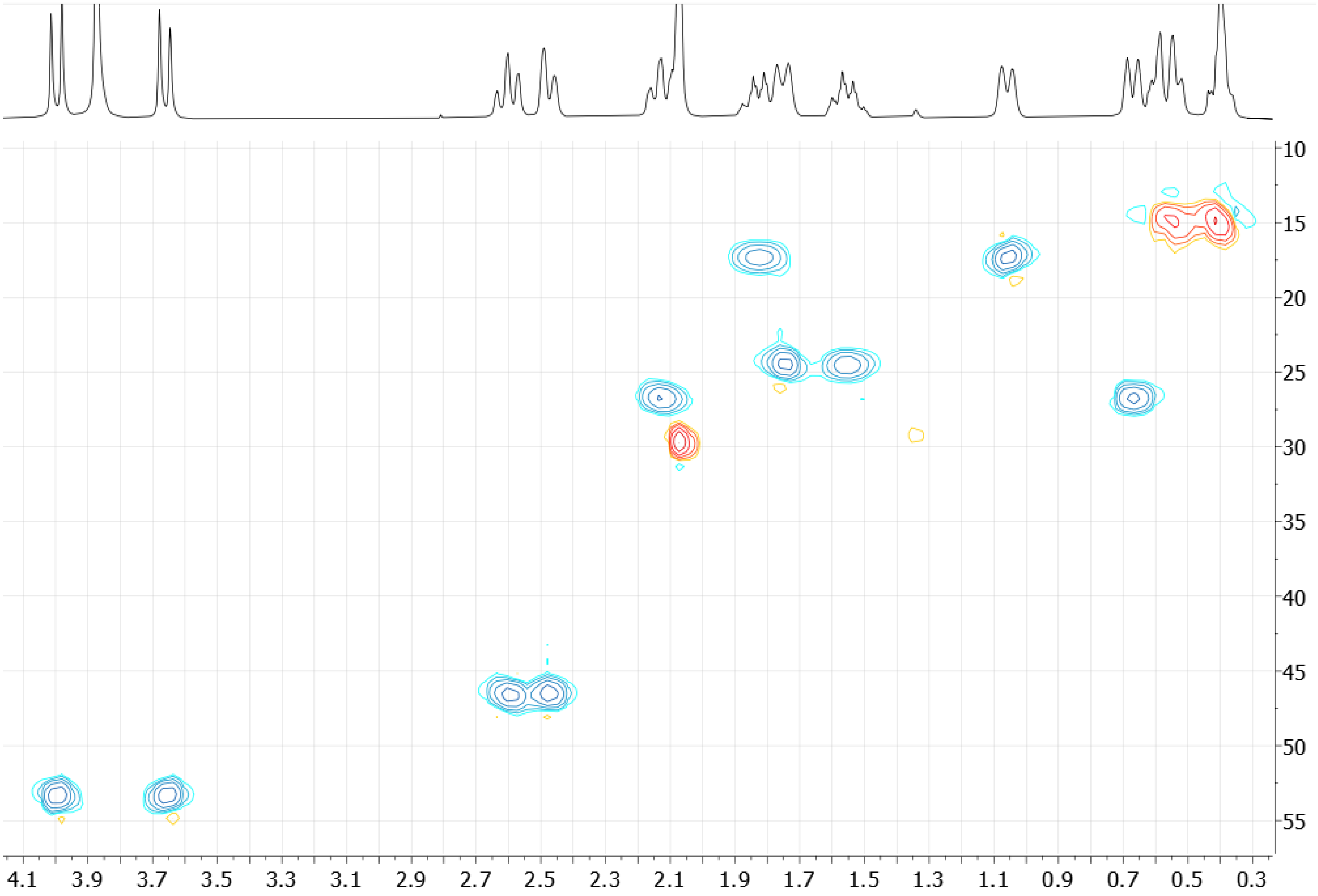


Predicted:	1.25 ppm	0.83 ppm
Observed:	1.32 ppm	0.88 ppm

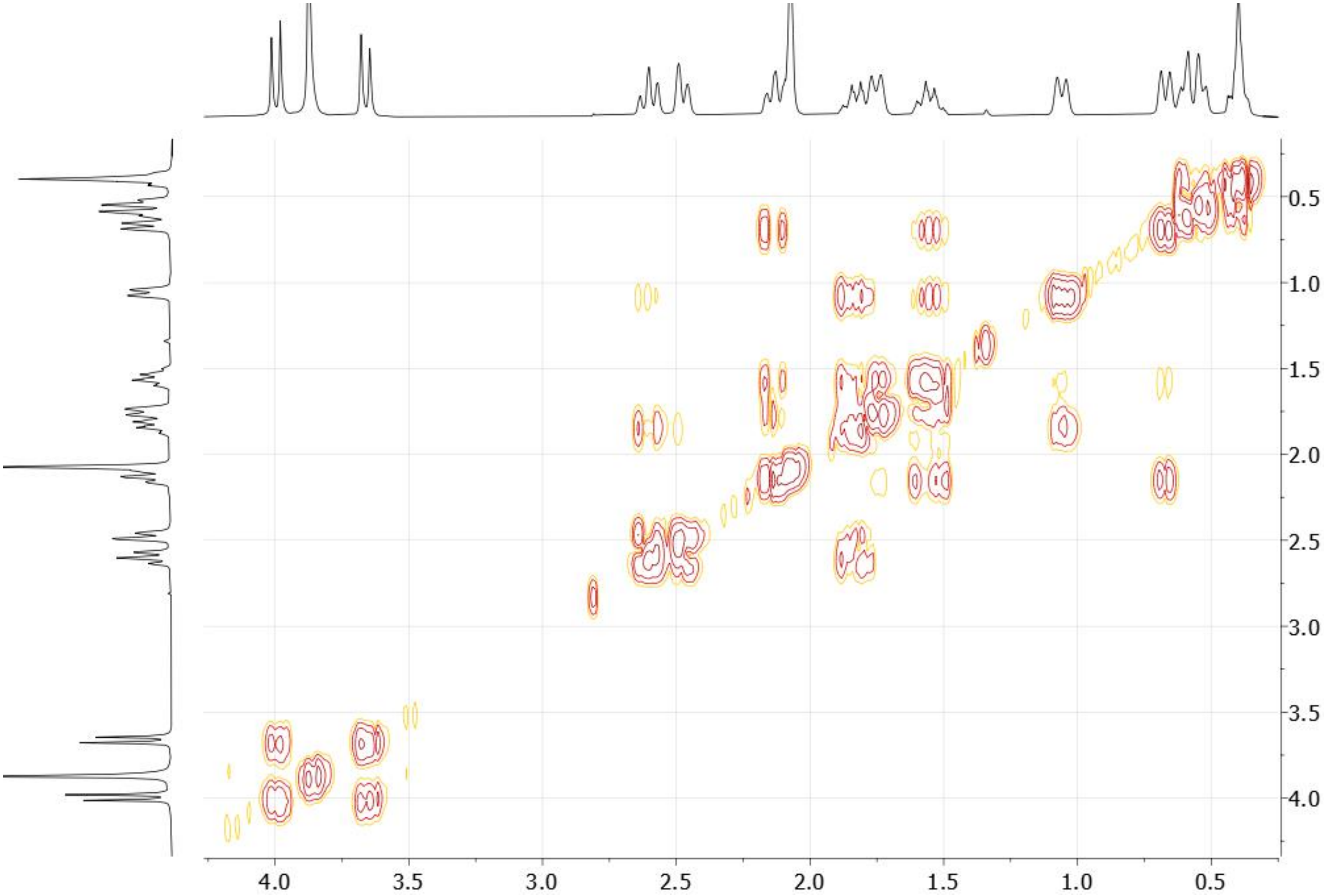
Compound **S22** ^{1}**H NMR** (400 MHz, *d_6*-Acetone, -78 °C)



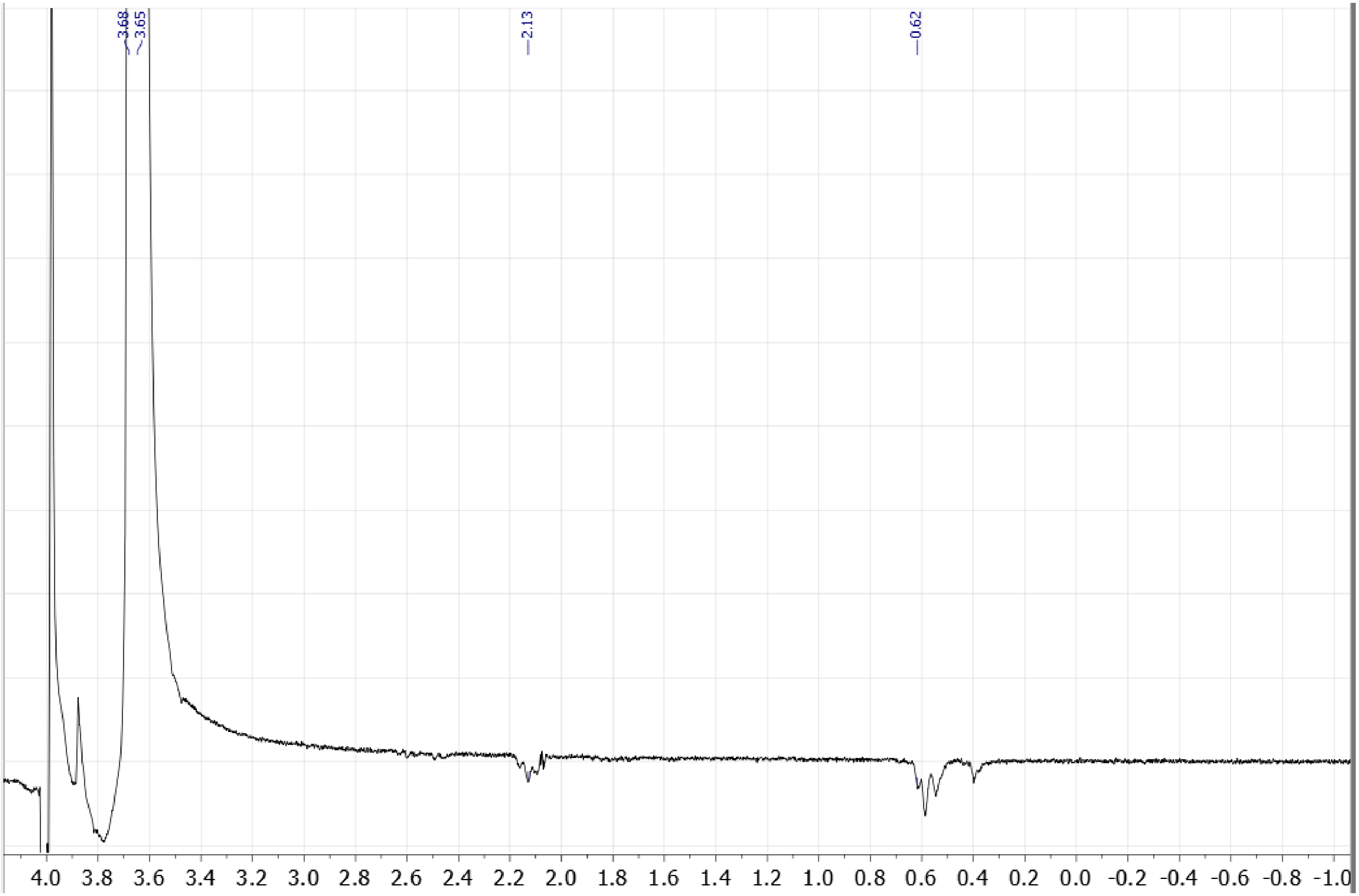
Compound **S22 HSQC** (400 MHz, d_6-Acetone, -78 °C)



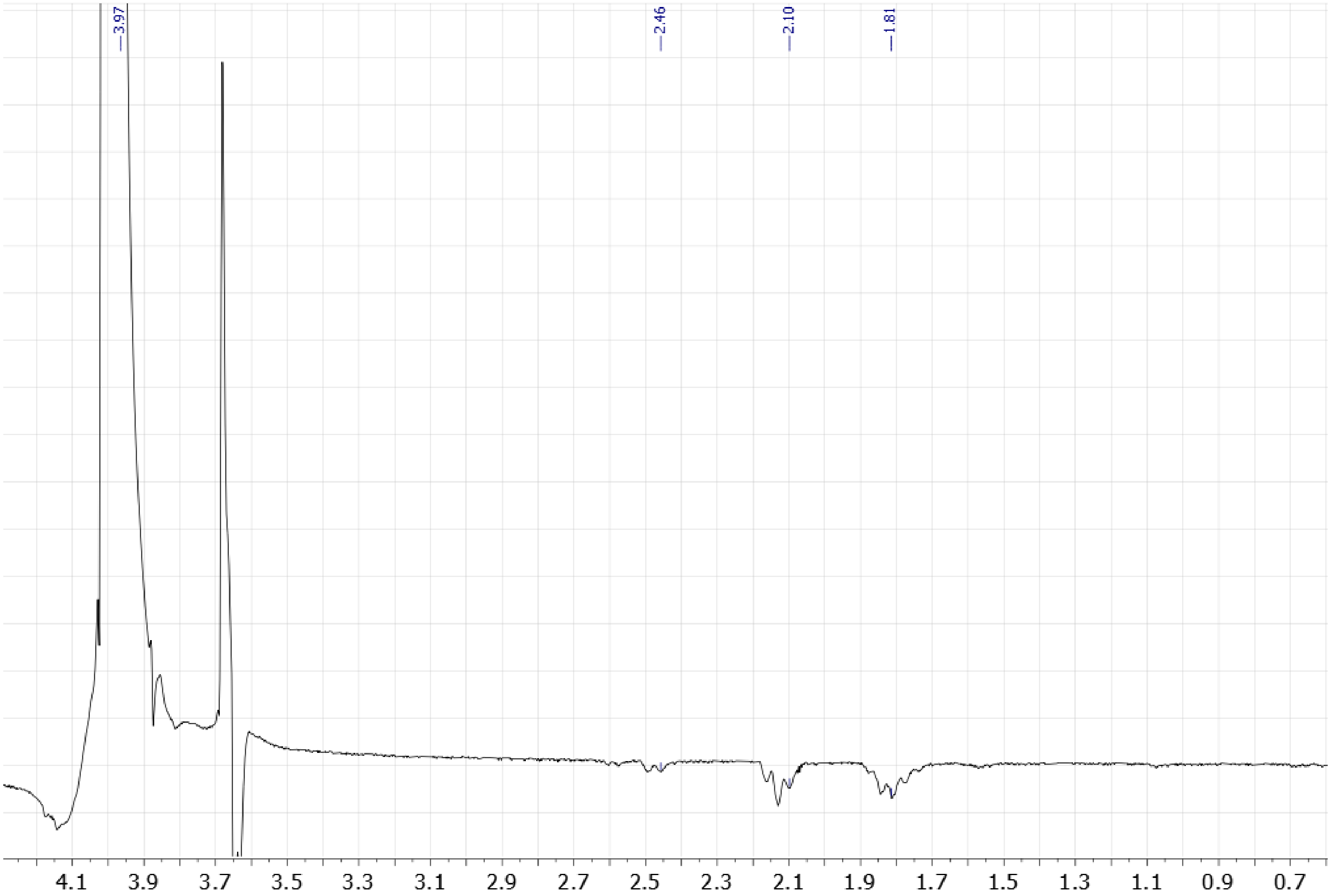
Compound **S22** **COSY** (400 MHz, d_6-Acetone, -78 °C)



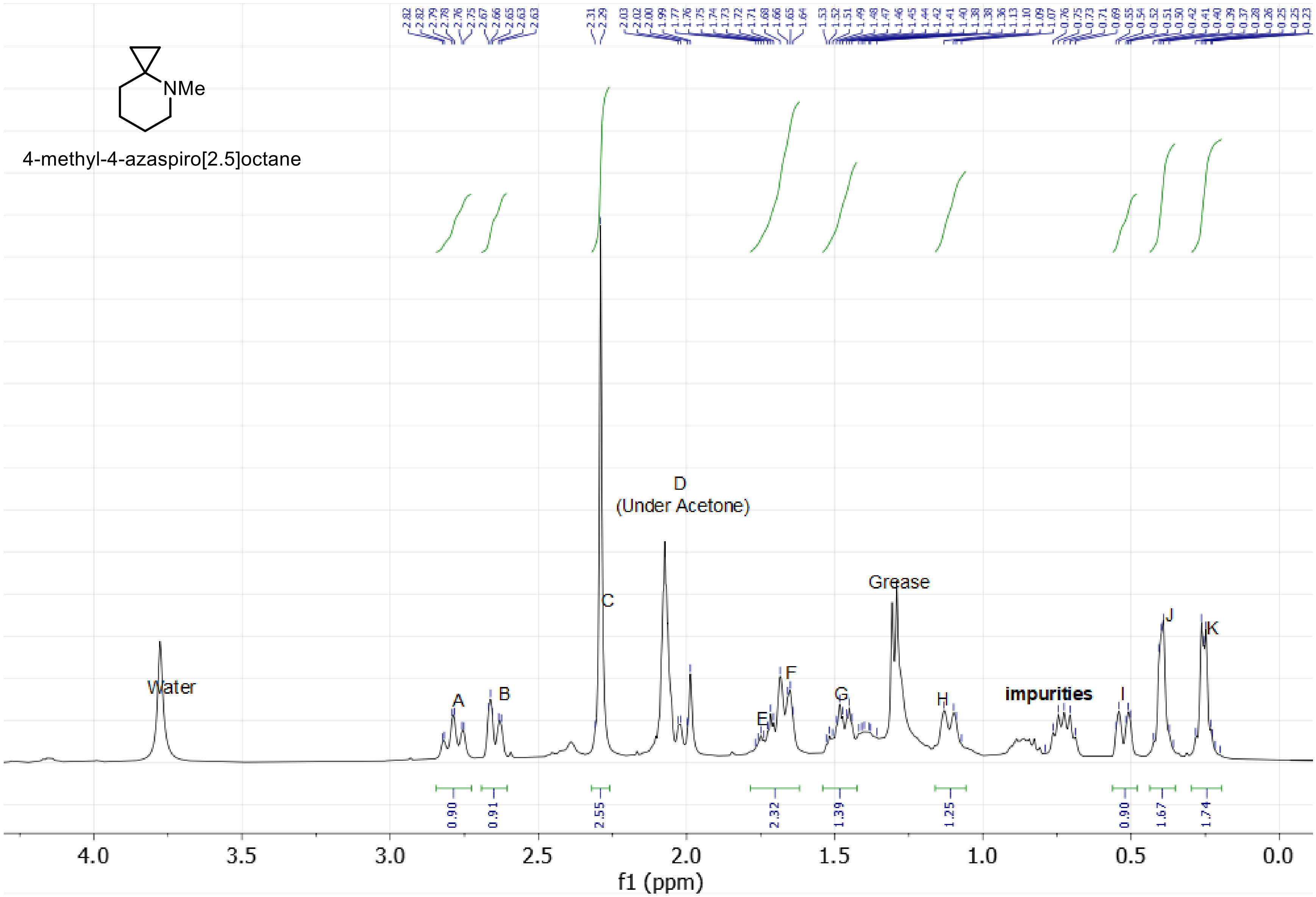
Compound **S22 1D NOE** (irradiation at 3.67 ppm, 400 MHz, d_6-Acetone, -78 °C)



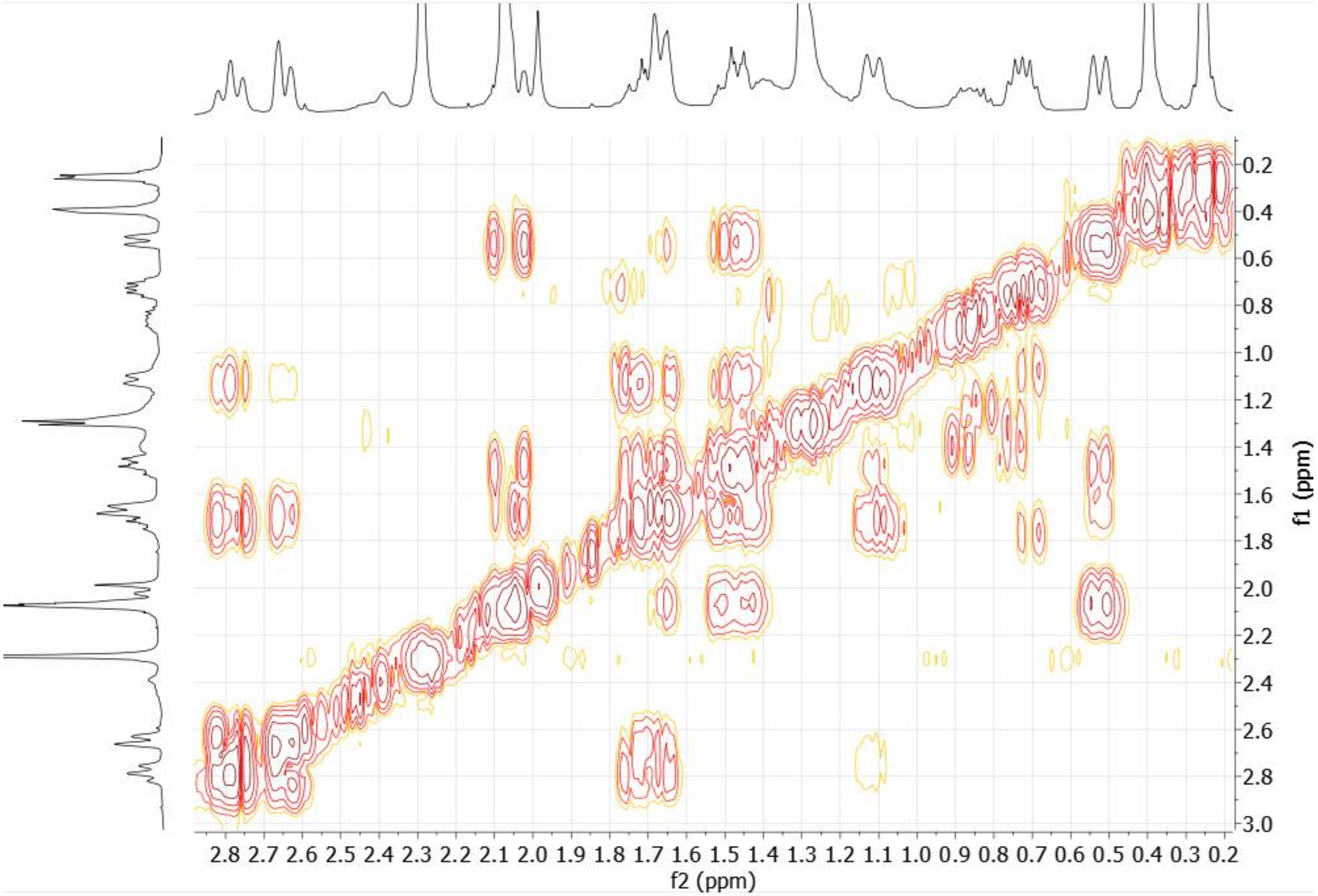
Compound **S22 1D NOE** (irradiation at 3.97 ppm, 400 MHz, *d*$_6$-Acetone, -78 °C)



Compound **S23** ^{1}**H NMR** (400 MHz, *d$_6$*-Acetone, -78 °C)



Compound **S23 COSY** (400 MHz, d_6-Acetone, -78 °C)



Compound **S23** **1D NOE** (400 MHz, d_6-Acetone, -78 °C)

NOE data was very weak though two of the expected correlations were observed similar to in the case of **S22**. However, a lack of complementary evidence led us to support the axial assignment by DFT NMR prediction (see table 3 on the following page)

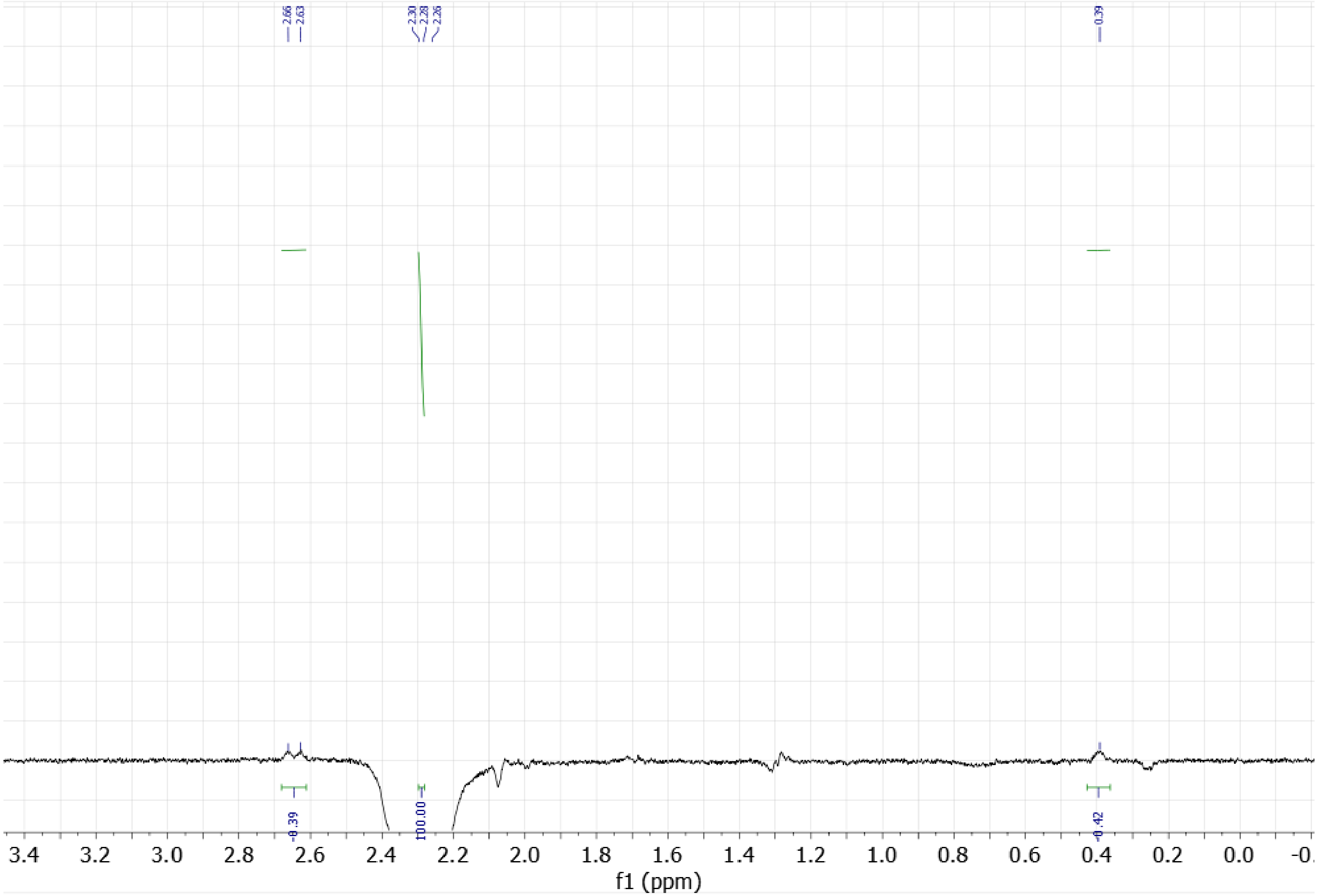
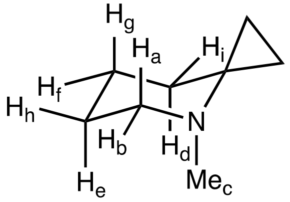


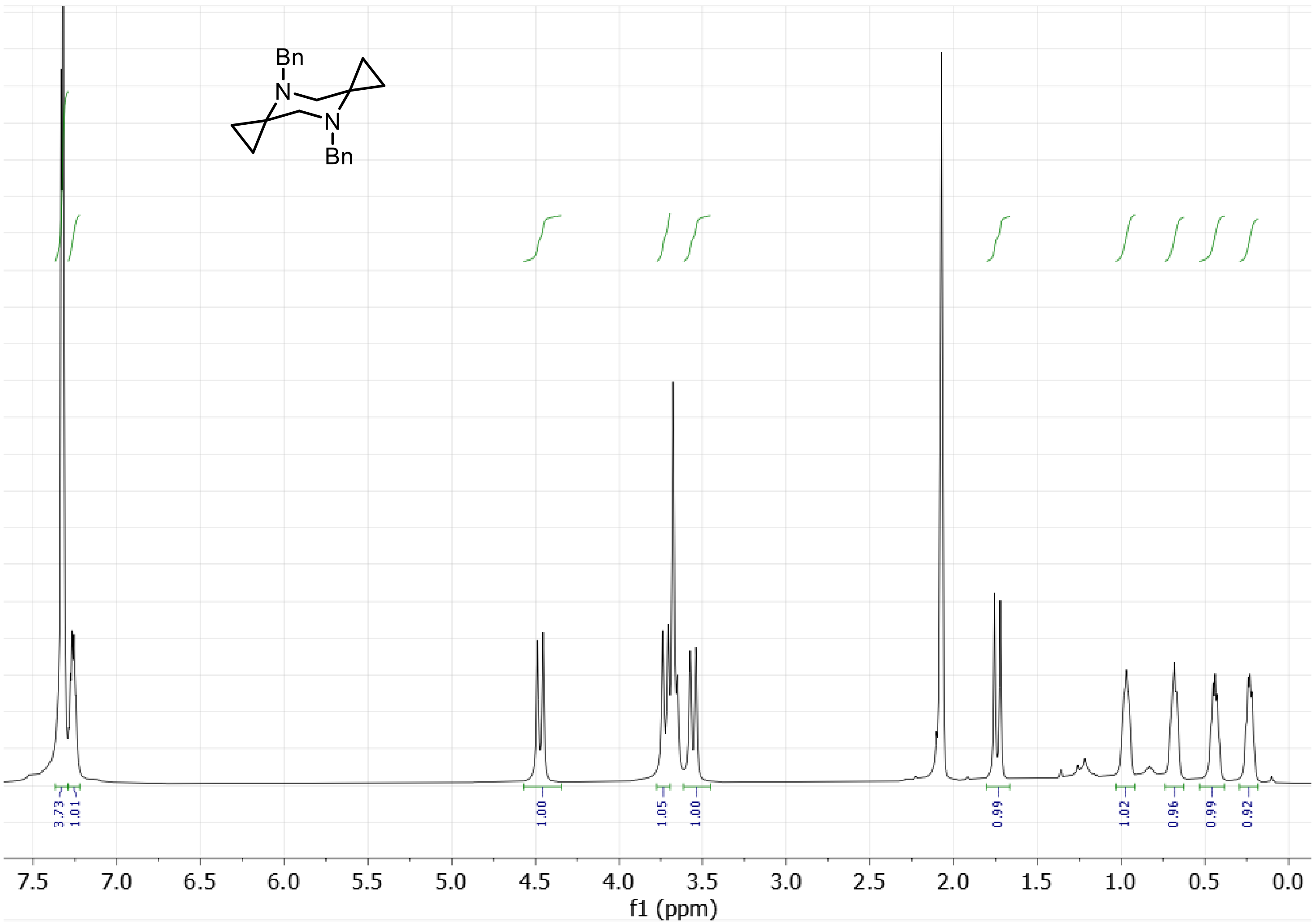
Table 3: Comparison of experimental vs. predicted chemical shifts for axial and equatorial conformations for ***S23***



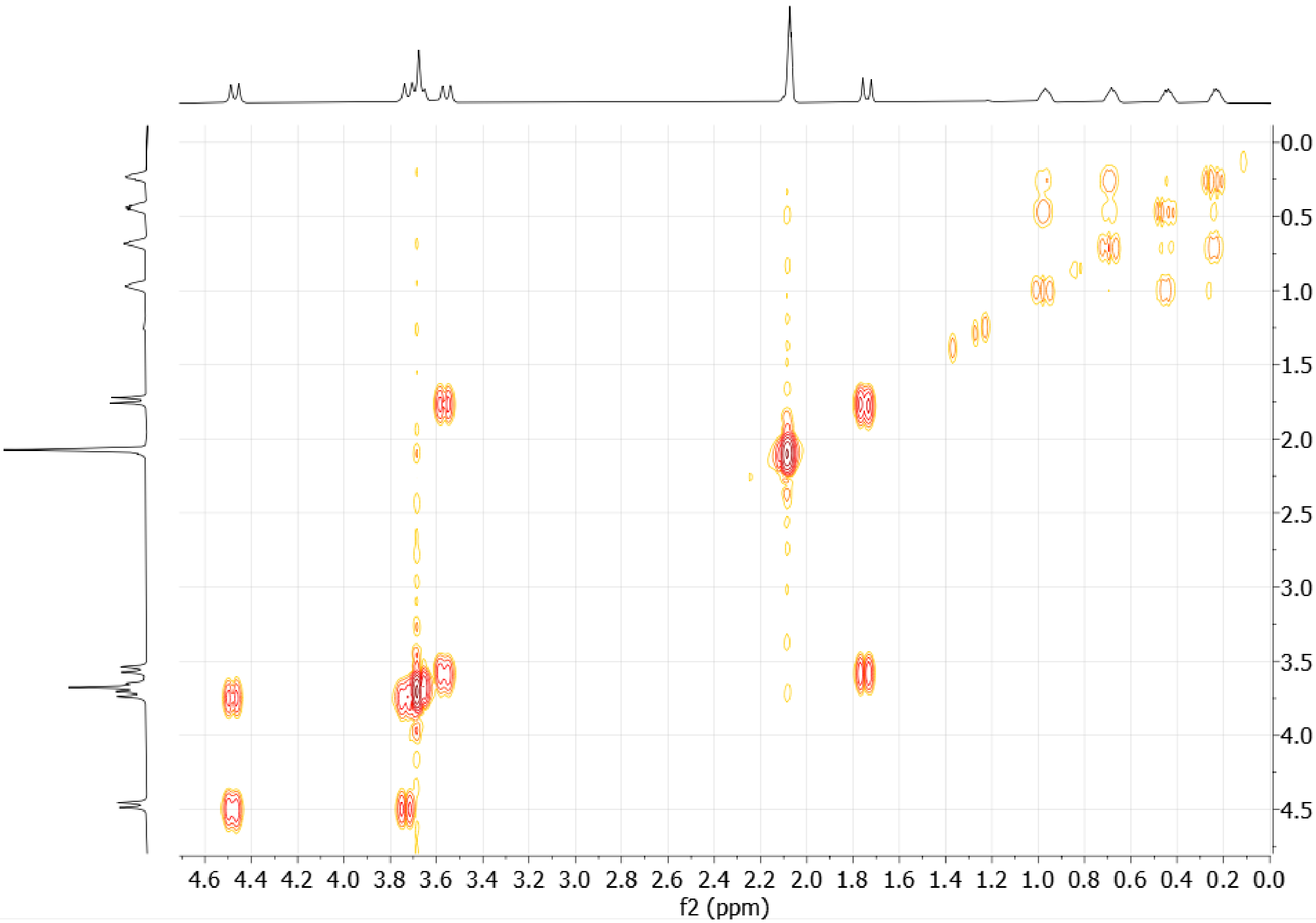
	Observed	Predicted Axial	Predicted Equatorial
a	2.79	3.04	2.22
b	2.65	2.77	2.60
c	2.29	2.45	1.95
d	2.07	2.20	1.90
e	1.73	1.85	1.60
f	1.67	1.70	1.60
g	1.48	1.60	1.41
h	1.11	1.02	1.60
i	0.53	0.48	0.81

Compound **S25** ^{1}**H NMR** (400 MHz, d_6-Acetone, -78 °C)

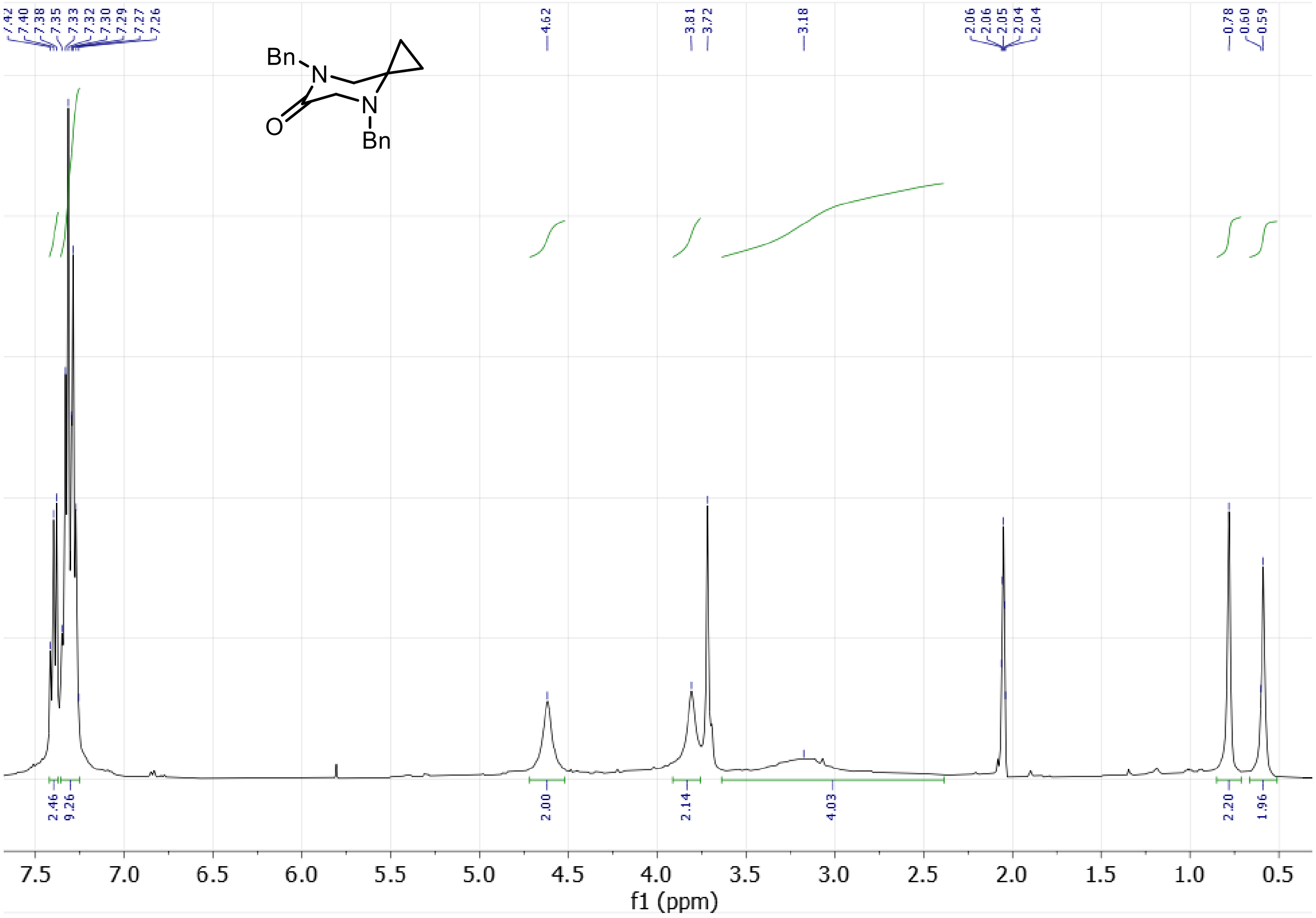
NOE experiments were conducted but inconclusive.



Compound **S25 COSY** (400 MHz, *d*$_6$-Acetone, -78 °C)



Compound **S26** **^{1}H NMR** (400 MHz, *d*$_6$-Acetone, -78 °C)



Compound **S27** ^{1}**H NMR** (400 MHz, *d*$_6$-Acetone, -78 °C)

NOE experiments were inconclusive, though they did not reveal any hidden conformers by exchange.