

## Synthesis of Quaternary $\alpha$ -Perfluoroalkyl Lactams via Electrophilic Perfluoroalkylation

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## General techniques and chemicals

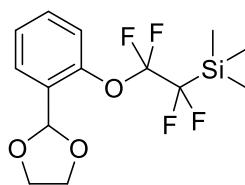
**General techniques.** All reactions were performed in a flame-dried glassware under argon atmosphere containing a Teflon-coated stir bar and dry septum. Solvents were purified and dried by standard procedures prior to use. IR spectra were measured on Thermo Scientific Nicolet 6700 IR spectrometer equipped with ATR cell.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on Bruker DPX-300 (operating at 300.1 MHz and 75.5 MHz, respectively), Bruker DPX-400 (operating at 400.1 MHz and 100.6 MHz, respectively) and Bruker DPX-500 (operating at 500.1 MHz and 126 MHz, respectively) and  $^{19}\text{F}$  NMR spectra on Bruker DPX-300 (at 282 MHz), Bruker DPX-400 (at 376 MHz) and Bruker DPX-500 (at 471 MHz). Shifts are relative to TMS as an external standard for  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra and calibrated against the solvent residual peak.<sup>[1]</sup> Mass spectra were measured by the MS service of the Labor für organische Chemie der ETH Zürich, Switzerland, and elemental analyses by the Mikroelementaranalytisches Laboratorium der ETH Zürich. TLC plates were obtained from Merck (silica gel 60 F<sub>254</sub>). Melting points were measured on a Büchi Melting Point B-540. TLC visualisation was performed either by fluorescence quenching at 254 nm or by staining with aqueous  $\text{KMnO}_4$  solution followed by heating. Chromatographic purification was (if not otherwise specified carried out) either by dry column vacuum chromatography (DCVC) according to procedure by Pedersen et al.<sup>[2]</sup> applying gradient elution from hexane to hexane: EtOAc (3:1) mixtures using TLC grade silica gel (Silica gel 60, particle size 20–45  $\mu\text{m}$ , Carl-Roth) or by flash chromatography using standard silica gel (Silica gel 60, particle size 43–63  $\mu\text{m}$ , Fluka).

**Chemicals.** 1-Trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole,<sup>[3]</sup> N-trimethylsilyl-bis(trifluoromethanesulfonyl)imide,<sup>[4]</sup> catalysts **5**,<sup>[5]</sup> **6**<sup>[5]</sup> and **7**<sup>[6]</sup> were prepared according to previously reported procedures. Chlorotrimethylsilane (99%),  $\text{BH}_3\cdot\text{Me}_2\text{S}$  in THF (10 M), n-BuLi in hexanes (1.6 M) and diisopropylamine (99%) were obtained from Aldrich. Precursors of reagents **2b–f** and **2h** ( $\text{R}-\text{CF}_2\text{CF}_2\text{Br}$ ) were obtained from CF Plus Chemicals (Brno, Czech Republic). Reagents **1**, **2a** ( $\text{R}_f = \text{CF}_3$ ),<sup>[7]</sup> **2b–d**, **2f** and **2h**<sup>[8]</sup> were prepared according to previously reported procedures. Unless otherwise noted, commercially available chemicals were used as received.

### Synthesis of new hypervalent iodine(III)- $\text{R}_f$ reagents (**2e**, **2g**, **2i–k**).

#### Synthesis of **2e**.

##### Step 1: Synthesis of (2-(2-(1,3-Dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)trimethylsilane.

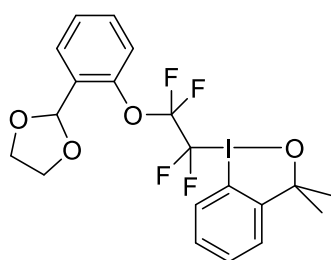


A flame-dried 100-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere subsequently with 2-(2-(2-bromo-1,1,2,2-tetrafluoroethoxy)phenyl)-1,3-dioxolane (880 mg, 2.50 mmol, 1 equiv), trimethylchlorosilane (1.3 mL, 10 mmol, 4 equiv) and anhydrous THF (20 mL). The solution was cooled to  $-65\text{ }^\circ\text{C}$  (acetone/dry ice bath). A solution of *i*-PrMgCl·LiCl (1.3 M in THF, 2.6 mL, 3.0 mmol, 1.2 equiv) was added dropwise *via* syringe, and the reaction mixture was stirred for 5 h at  $-60\text{ }^\circ\text{C}$  to rt. THF was removed on a rotary evaporator, water (30 mL) was added, and the product was extracted to a diethyl ether/hexane 1:1 mixture ( $3 \times 25\text{ mL}$ ). The combined organic fractions were washed with water ( $2 \times 20\text{ mL}$ ) and brine ( $2 \times 20\text{ mL}$ ). After drying with anhydrous sodium sulfate, filtering and concentrating to dryness, the product was obtained as a colorless oil. The ratio of product and the protodesilylated compound was 94:6 and the product was used further without purification.

Yield: 806 mg (90%).  $\text{R}_f = 0.33$  (EtOAc:hexane 1:10).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.25 (s, 3H), 3.88 – 4.11 (m, 4H), 5.97 (s, 1H), 7.17 – 7.32 (m, 3H), 7.56 (m, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  -4.4 (m),

65.3, 98.6, 119.3 (tt,  $J = 275.7, 28.1$  Hz), 120.6 (tt,  $J = 271.8, 39.7$  Hz), 121.6 (t,  $J = 1.6$  Hz), 126.2, 127.6, 130.2, 130.7; 147.7 (t,  $J = 1.7$  Hz).  $^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -129.74 (t,  $^3J_{\text{FF}} = 4.1$  Hz, 2F), -83.72 (t,  $^3J_{\text{FF}} = 4.1$  Hz, 2F). IR (ATR, neat): 2963, 2890, 1610, 1593, 1491, 1456, 1398, 1348, 1310, 1280, 1257, 1222, 1174, 1134, 1114, 1096, 1071, 1039, 963, 943, 912, 845, 820, 807, 753, 733, 632  $\text{cm}^{-1}$ . HRMS (ESI<sup>+</sup>) calcd (m/z) for  $\text{C}_{14}\text{H}_{19}\text{F}_4\text{O}_3\text{Si}$ :  $[\text{M}+\text{H}^+]$  339.1034, found: 339.1034.

**Step 2: Synthesis of 1-(2-(2-(1,3-dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxole (2e).**



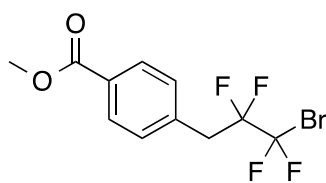
A flame-dried 100-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere with 1-fluoro-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxole (1.16 g, 3.70 mmol, 2 equiv) and anhydrous  $\text{CH}_3\text{CN}$  (20 mL). The solution was cooled to  $-30$  °C (acetone/dry ice bath). tetrabutylammonium difluorotriphenylsilicate (20.0 mg, 0.04 mmol, 0.02 equiv) was added as solid, followed by the addition of a solution of (2-(2-(1,3-dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)-

trimethylsilane (700 mg, 1.86 mmol, 90% purity, 1 equiv) in anhydrous  $\text{CH}_3\text{CN}$  (6 mL) over a period of 30 min at  $-25$  °C. The mixture was stirred at  $-25$  °C to rt for 5 h. The solvent was removed on a rotary evaporator and the mixture was anchored on Celite® (2 g). The product was isolated by flash column chromatography (gradient elution from hexane to EtOAc) as an oily yellow liquid.

Yield: 642 mg (66%).  $R_f = 0.31$  (EtOAc:hexane 1:2).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.50 (s, 6H), 3.99 – 4.13 (m, 4H), 6.06 (s, 1H), 7.30 – 7.41 (m, 5H), 7.49 (m, 1H), 7.65 (m, 1H), 7.77 (m, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  30.8, 65.3, 76.3, 98.8, 111.0, 111.5 (tt,  $J = 337.6, 38.1$  Hz), 117.4 (tt,  $J = 278.5, 26.1$  Hz), 121.4 (t,  $J = 1.5$  Hz), 126.6, 127.3, 127.6, 129.2 (t,  $J = 5.2$  Hz), 129.4, 130.3, 130.3, 130.7, 147.2, 150.0.  $^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -97.2 (br s, 2F), -84.1 (td,  $^3J_{\text{FF}} = 4.6$  Hz,  $J_{\text{HF}} = 1.5$  Hz, 2F). IR (ATR, neat): 3062, 2971, 2924, 2897, 1725, 1607, 1588, 1564, 1488, 1461, 1452, 1438, 1376, 1358, 1302, 1269, 1246, 1177, 1161, 1106, 1071, 994, 958, 896, 870, 802, 749, 718, 664, 647  $\text{cm}^{-1}$ . HRMS (MALDI) calcd (m/z) for  $\text{C}_{20}\text{H}_{20}\text{F}_4\text{IO}_4$ :  $[\text{M}+\text{H}^+]$  527.0337, found: 527.0336.

**Synthesis of 2g.**

**Step 1: Synthesis of methyl 4-(3-bromo-2,2,3,3-tetrafluoropropyl)benzoate.**

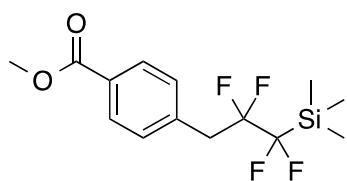


A solution of methyl 4-formylbenzoate (1.86 g, 11.4 mmol, 1 equiv) in EtOH (15 mL) was added with stirring dropwise to a solution of hydrazine hydrate (0.643 mL, 11.4 mmol, 1 equiv) in EtOH (15 mL) and the mixture was stirring at 25 °C for 12 h. Then freshly purified  $\text{CuCl}$  (112 mg, 1.14 mmol, 0.1 equiv) and 1,2-ethylenediamine (3.79 mL, 56.8 mmol, 5 equiv) were added. After 10 min,  $\text{BrCF}_2\text{CF}_2\text{Br}$  (6.78 mL, 56.8 mmol, 5 equiv) was added dropwise and the reaction mixture was stirred at 50 °C for 5 h. After cooling, reaction mixture was quenched with hydrochloric acid (1 M, 20 mL). Reaction products were extracted with DCM (5  $\times$  30 mL) and combined organic layers were washed with a saturated solution of NaCl (20 mL) and dried over  $\text{MgSO}_4$ , filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 0.5:9.5) to afford a white solid (1.39 g, 4.22 mmol, 37 %).

$R_f = 0.63$  ( $\text{SiO}_2$ ; EtOAc/Hexane 1:4; UV).  $\text{M.p.} = 45$  °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  3.43 (t,  $J = 18.0$  Hz, 2H), 3.92 (s, 3H), 7.38 (d,  $J = 8.1$  Hz, 2H), 7.38 (d,  $J = 8.1$  Hz, 2H), 8.03 (d,  $J = 8.3$  Hz, 2H).

**<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 36.83 (t, *J*<sub>C,F</sub> = 22.7 Hz), 52.33, 115.92 (tt, *J*<sub>C,F</sub> = 255 Hz, *J*<sub>C,F</sub> = 31.5 Hz), 117.65 (tt, *J*<sub>C,F</sub> = 312 Hz, *J*<sub>C,F</sub> = 39.5 Hz), 129.93, 130.21, 130.93, 134.76, 166.79. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>) δ -110.20 (t, *J* = 3.6 Hz), -65.10 (t, *J* = 3.6 Hz). **IR** (ATR, neat): 2954, 1716, 1615, 1435, 1281, 1244, 1110, 1078, 904, 889, 865, 619 cm<sup>-1</sup>. **HRMS** (ESI+) calcd (m/z) for C<sub>11</sub>H<sub>13</sub>N<sub>1</sub>O<sub>2</sub>F<sub>4</sub>Br: [M+NH<sub>4</sub>]<sup>+</sup> 346.0060 [M<sub>Br79</sub>] and 348.0041 [M<sub>Br81</sub>], found: 346.0054 [M<sub>Br79</sub>] and 348.0042 [M<sub>Br81</sub>]. **Anal.** Calcd. for C<sub>11</sub>H<sub>9</sub>O<sub>2</sub>F<sub>4</sub>Br: C 40.15, H 2.76, F 23.09, Br 24.28, found: C, 40.30, H, 2.76, F, 23.11, Br, 24.07.

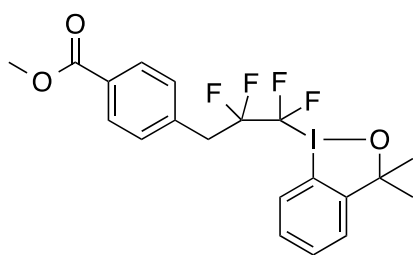
### Step 2: Synthesis of methyl 4-(2,2,3,3-tetrafluoro-3-(trimethylsilyl)propyl)benzoate.<sup>[9]</sup>



To a solution of methyl 4-(3-bromo-2,2,3,3-tetrafluoropropyl)benzoate (1.13 g, 3.43 mmol, 1 equiv) in dry THF (25 mL) under Ar. were added successively at -78 °C trimethylsilyl chloride (1.31 mL, 10.3 mmol, 3 equiv) and dropwise *i*-PrMgCl•LiCl (1.3 M in THF, 3.17 mL, 4.12 mmol, 1.2 equiv). The reaction mixture was allowed to warm up overnight until 25 °C, then quenched by addition of water (30 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with a saturated solution of NaCl (30 mL), dried over MgSO<sub>4</sub>, filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 0.5:9.5) to afford a white solid (941 mg, 2.92 mmol, 85 %).

**R<sub>f</sub>** = 0.54 (SiO<sub>2</sub>; EtOAc/Hexane 1:9; UV). **M.p.** 39 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 0.26 (s, 9H), 3.11 (t, *J* = 18.0 Hz, 2H), 3.91 (s, 3H), 7.37 (d, *J* = 8.0 Hz, 2H), 8.01 (d, *J* = 8.3 Hz, 2H). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ -4.03 (p, *J*<sub>C,F</sub> = 2.0 Hz), 35.54 (tt, *J*<sub>C,F</sub> = 23.4 Hz, *J*<sub>C,F</sub> = 2.2 Hz), 52.18, 120.42 (tt, *J*<sub>C,F</sub> = 245 Hz, *J*<sub>C,F</sub> = 31.4 Hz), 122.97 (tt, *J*<sub>C,F</sub> = 270 Hz, *J*<sub>C,F</sub> = 50.0 Hz), 129.52, 129.65, 131.05, 136.76, 166.97. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>) δ -125.90 (t, *J* = 4.4 Hz), -108.50 (tt, *J* = 18.8 Hz, *J* = 4.4 Hz). **IR** (ATR, neat): 2959, 1720, 1616, 1435, 1279, 1256, 1099, 1021, 843, 735, 607 cm<sup>-1</sup>. **HRMS** (ESI+) calcd (m/z) for C<sub>14</sub>H<sub>19</sub>O<sub>2</sub>F<sub>4</sub>Si: [M+H]<sup>+</sup> 323.1085, found: 323.1086.

### Step 3: Synthesis of methyl 4-(3-(3,3-dimethyl-1λ<sup>3</sup>-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)-2,2,3,3-tetrafluoropropyl)benzoate (2g).



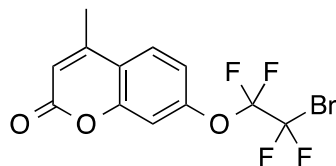
To a solution of 1-fluoro-3,3-dimethyl-1,3-dihydro-1λ<sup>3</sup>-benzo[*d*][1,2]iodaoxole (1.21 g, 4.11 mmol, 2 equiv) and TBAT (11.4 mg, 0.02 mmol, 0.01 equiv) in dry MeCN (20 mL) under Ar. was added dropwise at -35 °C a solution of methyl 4-(2,2,3,3-tetrafluoro-3-(trimethylsilyl)propyl)benzoate (662 mg, 2.05 mmol, 1 equiv) in dry MeCN (10 mL). The reaction mixture was stirred for 30 min at -35 °C and 2 h at 25 °C. The reaction mixture was evaporated to dryness with Celite® and subjected to flash chromatography (EtOAc/Hexane 1:1) to afford yellowish oil (545 mg, 1.1 mmol, 52 %).

**R<sub>f</sub>** = 0.37 (SiO<sub>2</sub>; EtOAc/Hexane 1:1; UV). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 1.43 (s, 6H), 3.35 (t, *J* = 18.5 Hz, 2H), 3.86 (s, 3H), 7.32 (q, *J* = 7.7, 6.8 Hz, 4H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 30.87, 35.77 (t, *J*<sub>C,F</sub> = 23.4 Hz), 52.10, 76.06, 110.79, 114.76 (tt, *J*<sub>C,F</sub> = 336 Hz, *J*<sub>C,F</sub> = 51.5 Hz), 118.64 (tt, *J*<sub>C,F</sub> = 247 Hz, *J*<sub>C,F</sub> = 28.5 Hz), 127.32, 128.86 (t, *J*<sub>C,F</sub> = 5.4 Hz), 129.28, 129.72, 129.82, 130.25, 130.84, 135.27, 150.00, 166.61. **<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>) δ -106.45 (t, *J* = 18.5 Hz), -92.47 (bs). **IR** (ATR, neat): 2969, 1719, 1615, 1436,

1278, 1180, 1106, 1060, 961, 869, 754, 729, 621  $\text{cm}^{-1}$ . **HRMS** (ESI+) calcd (m/z) for  $\text{C}_{20}\text{H}_{20}\text{O}_3\text{F}_4\text{I}$ :  $[\text{M}+\text{H}]^+$  511.0388, found 511.0384.

## Synthesis of 2i.

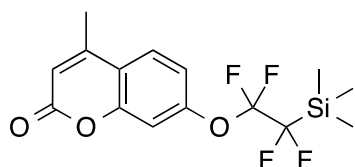
### Step 1: Synthesis of 7-(2-bromo-1,1,2,2-tetrafluoroethoxy)-4-methyl-2H-chromen-2-one.



To a suspension of sodium hydride (60%, washed with pentane, 2.49 g, 14 mmol, 1.5 equiv) in dry DMF (60 mL) under Ar. was added at 0 °C a solution of 7-hydroxy-4-methyl-2H-chromen-2-one (7.3 g, 41.5 mmol, 1 equiv) in dry DMF (20 mL). The reaction mixture was cooled to -50 °C and TBAI (2.3 g, 6.22 mmol, 0.15 eq) and  $\text{BrCF}_2\text{CF}_2\text{Br}$  (1.4 mL, 11.7 mmol, 1.25 equiv) were added dropwise. The reaction mixture was allowed to warm up to 25 °C overnight. The reaction was quenched with hydrochloric acid (1 M, 20 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed several times with water (30 mL) and a saturated solution of NaCl (30 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 2:8) to afford white solid (3.41 g, 9.60 mmol, 23%).

$R_f$  = 0.49 ( $\text{SiO}_2$ ; EtOAc/Hexane 2:3; UV). **M.p.** = 58 °C.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.37 (d,  $J$  = 1.4 Hz, 3H), 6.20 (d,  $J$  = 1.4 Hz, 1H), 7.03 – 7.16 (m, 2H), 7.56 (d,  $J$  = 8.6 Hz, 1H).  $^{13}\text{C NMR}$  (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  18.70, 110.01, 113.27 (tt,  $J_{\text{C,F}}$  = 312 Hz,  $J_{\text{C,F}}$  = 44.2 Hz), 115.11, 115.86 (tt,  $J_{\text{C,F}}$  = 277 Hz,  $J_{\text{C,F}}$  = 32.4 Hz), 117.32, 118.69, 126.05, 150.92 (t,  $J_{\text{C,F}}$  = 1.4 Hz), 151.71, 154.20, 160.01.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -86.11 (t,  $J$  = 4.5 Hz), -68.25 (t,  $J$  = 4.9 Hz). **IR** (ATR, neat): 3065, 1704, 1615, 1391, 1326, 1263, 1125, 1095, 984, 927, 878, 786, 711, 620  $\text{cm}^{-1}$ . **HRMS** (ESI+) calcd (m/z) for  $\text{C}_{12}\text{H}_8\text{O}_3\text{F}_4\text{Br}$ :  $[\text{M}+\text{H}]^+$  354.9587 [ $\text{M}_{\text{Br}79}$ ] and 356.9568 [ $\text{M}_{\text{Br}81}$ ], found 354.9586 [ $\text{M}_{\text{Br}79}$ ] and 356.9566 [ $\text{M}_{\text{Br}81}$ ].

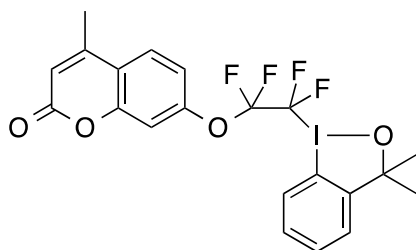
### Step 2: Synthesis of 4-methyl-7-(1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethoxy)-2H-chromen-2-one.



To a solution of 7-(2-bromo-1,1,2,2-tetrafluoroethoxy)-4-methyl-2H-chromen-2-one (3.41 g, 9.6 mmol, 1 equiv) in dry THF (50 mL) under Ar. were added successively at -78 °C trimethylsilyl chloride (3.66 mL, 28.8 mmol, 3 equiv) and dropwise *i*-PrMgCl·LiCl (1.3 M in THF, 8.85 mL, 11.5 mmol, 1.2 equiv). The reaction mixture was allowed to warm up overnight until 25 °C, then quenched by addition of water (30 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with a saturated solution of NaCl (30 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 2:8) to afford white solid (1.1 g, 3.05 mmol, 70%).

$R_f$  = 0.59 ( $\text{SiO}_2$ ; EtOAc/Hexane 2:3; UV). **M.p.** = 87 °C.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.31 (s, 9H), 2.42 (d,  $J$  = 1.4 Hz, 3H), 6.24 (d,  $J$  = 1.4 Hz, 1H), 7.05 – 7.21 (m, 2H), 7.59 (d,  $J$  = 8.6 Hz, 1H).  $^{13}\text{C NMR}$  (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  -4.27, 18.72, 109.75, 114.74, 117.25, 118.03, 119.39 (tt,  $J_{\text{C,F}}$  = 277 Hz,  $J_{\text{C,F}}$  = 27.7 Hz), 120.49 (tt,  $J_{\text{C,F}}$  = 272 Hz,  $J_{\text{C,F}}$  = 39.7 Hz), 125.83, 151.75, 151.85, 154.27, 160.27.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -129.99 (t,  $J$  = 4.3 Hz), -85.05 (t,  $J$  = 4.4 Hz). **IR** (ATR, neat): 2973, 1736, 1620, 1302, 1174, 1132, 1082, 1039, 848, 765, 628  $\text{cm}^{-1}$ . **HRMS** (ESI+) calcd (m/z) for  $\text{C}_{15}\text{H}_{17}\text{O}_3\text{F}_4\text{Si}$ :  $[\text{M}+\text{H}]^+$  349.0878, found 349.0878.

### Step 3: Synthesis of 7-(2-(3,3-Dimethyl-1 $\lambda^3$ -benzo[d][1,2]iodaoxol-1(3*H*)-yl)-1,1,2,2-tetrafluoroethoxy)-4-methyl-2*H*-chromen-2-one (2i).

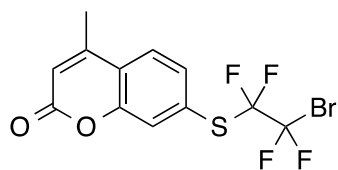


To a solution of 1-fluoro-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[d][1,2]iodaoxole (1.34 g, 4.81 mmol, 2 equiv) and TBAT (12.9 mg, 0.024 mmol, 0.01 equiv) in dry MeCN (20 mL) under Ar. was added dropwise at  $-35\text{ }^{\circ}\text{C}$  a solution of 4-methyl-7-(1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethoxy)-2*H*-chromen-2-one (837 mg, 2.40 mmol, 1 equiv) in dry MeCN (10 mL). The reaction mixture was stirring 30 min at  $-35\text{ }^{\circ}\text{C}$  and 2 h at  $25\text{ }^{\circ}\text{C}$ . The reaction mixture was evaporated to dryness with Celite® and subjected to flash chromatography (EtOAc/Hexane 4:1) to afford yellowish oil (1.0 g, 1.86 mmol, 78%).

$R_f$  = 0.39 (SiO<sub>2</sub>; EtOAc/Hexane 4:1; UV). **M.p.** =  $132\text{ }^{\circ}\text{C}$ . **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 1.47 (s, 6H), 2.40 (d,  $J$  = 1.3 Hz, 3H), 6.24 (d,  $J$  = 1.4 Hz, 1H), 7.08 – 7.20 (m, 2H), 7.30 – 7.47 (m, 2H), 7.48 (td,  $J$  = 7.4, 0.9 Hz, 1H), 7.59 (d,  $J$  = 8.6 Hz, 1H), 7.69 (d,  $J$  = 4.2 Hz, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 18.72, 30.87, 76.66, 109.82, 111.06 (tt,  $J_{C,F}$  = 337 Hz,  $J_{C,F}$  = 37.9 Hz), 111.08, 114.99, 117.18, 117.46 (tt,  $J_{C,F}$  = 279 Hz,  $J_{C,F}$  = 26.7 Hz), 118.44, 125.96, 127.51, 128.83 (t,  $J_{C,F}$  = 5.3 Hz), 129.55, 130.52, 149.89, 151.06, 151.65, 154.19, 160.04. **<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>)  $\delta$  =  $-97.50$  (t,  $J$  = 3.8 Hz),  $-84.35$  (t,  $J$  = 4.1 Hz). **IR** (ATR, neat): 2970, 1727, 1615, 1389, 1303, 1179, 1108, 1092, 869, 756, 748, 602 cm<sup>-1</sup>. **HRMS** (ESI+) calcd (m/z) for C<sub>21</sub>H<sub>18</sub>O<sub>4</sub>F<sub>4</sub>I: [M+H]<sup>+</sup> 537.0180, found 537.0176.

### Synthesis of 2j.

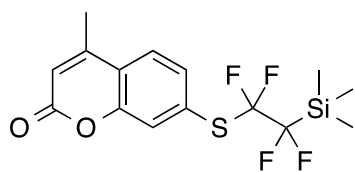
#### Step 1: Synthesis of 7-((2-bromo-1,1,2,2-tetrafluoroethyl)thio)-4-methyl-2*H*-chromen-2-one.



To a suspension of sodium hydride (60%, washed with pentane, 562 mg, 14 mmol, 1.5 equiv) in dry DMF (20 mL) under Ar. was added at  $0\text{ }^{\circ}\text{C}$  a solution of 7-mercapto-4-methyl-2*H*-chromen-2-one (1.8 g, 9.36 mmol, 1 equiv) in dry DMF (10 mL). The reaction mixture was cooled to  $-50\text{ }^{\circ}\text{C}$  and BrCF<sub>2</sub>CF<sub>2</sub>Br (1.4 mL, 11.7 mmol, 1.25 equiv) was added dropwise. The reaction mixture was allowed to warm up to  $25\text{ }^{\circ}\text{C}$  overnight. The reaction was quenched with hydrochloric acid (1 M, 20 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with Ether (3  $\times$  50 mL). The combined organic layers were washed several times with water (30 mL) and a saturated solution of NaCl (30 mL), dried over MgSO<sub>4</sub>, filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 2:8) to afford a white solid (2.17 g, 5.85 mmol, 63%).

$R_f$  = 0.54 (SiO<sub>2</sub>; EtOAc/Hexane 3:7; UV). **M.p.** =  $99\text{ }^{\circ}\text{C}$ . **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>)  $\delta$  2.46 (t,  $J$  = 1.4 Hz, 3H), 6.37 (s,  $J$  = 1.5 Hz, 1H), 7.51 – 7.64 (m, 3H). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  18.75, 116.47 (t,  $J_{C,F}$  = 313 Hz,  $J_{C,F}$  = 39.9 Hz), 116.98, 122.03, 122.18 (tt,  $J_{C,F}$  = 292 Hz,  $J_{C,F}$  = 34.2 Hz), 125.18, 125.34, 127.48 (tt,  $J_{C,F}$  = 2.7 Hz), 132.16, 151.45, 153.29, 159.74. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>)  $\delta$   $-84.51$  (t,  $J$  = 8.1 Hz),  $-62.41$  (t,  $J$  = 8.0 Hz). **IR** (ATR, neat): 3059, 1721, 1601, 1395, 1383, 1168, 1107, 1092, 950, 777, 614 cm<sup>-1</sup>. **HRMS** (ESI+) calcd (m/z) for C<sub>12</sub>H<sub>8</sub>O<sub>2</sub>F<sub>4</sub>BrS: [M+H]<sup>+</sup> 370.9359 [M<sub>Br79</sub>] and 372.9339 [M<sub>Br81</sub>], found 370.9360 [M<sub>Br79</sub>] and 372.9339 [M<sub>Br81</sub>].

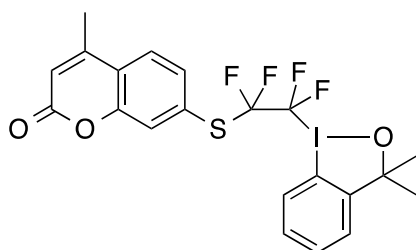
## Step 2: Synthesis of 4-methyl-7-((1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethyl)thio)-2H-chromen-2-one.



To a solution of 7-((2-bromo-1,1,2,2-tetrafluoroethyl)thio)-4-methyl-2H-chromen-2-one (1.63 g, 4.39 mmol, 1 equiv) in dry THF (35 mL) under Ar. were added successively at  $-78\text{ }^{\circ}\text{C}$  trimethylsilyl chloride (1.67 mL, 13.2 mmol, 3 equiv) and dropwise *i*-PrMgCl•LiCl (1.3 M in THF, 4.05 mL, 5.27 mmol, 1.2 equiv). The reaction mixture was allowed to warm up overnight until  $25\text{ }^{\circ}\text{C}$ , then quenched by addition of water (30 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with EtOAc ( $3 \times 40\text{ mL}$ ). The combined organic layers were washed with a saturated solution of NaCl (30 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated under vacuum. The crude residue was purified by flash chromatography on silica gel (EtOAc/Hexane 1:9) to afford white solid (2.35 g, 6.75 mmol, 70 %).

$R_f = 0.56$  ( $\text{SiO}_2$ ; EtOAc/Hexane 3:7; UV). **M.p.** =  $81\text{ }^{\circ}\text{C}$ .  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.27 (s, 9H), 2.44 (d,  $J = 1.3\text{ Hz}$ , 3H), 6.33 (d,  $J = 1.4\text{ Hz}$ , 1H), 7.50 – 7.66 (m, 3H).  $^{13}\text{C NMR}$  (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  -4.02, 18.73, 116.46, 121.28, 122.60 (tt,  $J_{\text{C,F}} = 273\text{ Hz}$ ,  $J_{\text{C,F}} = 45.5\text{ Hz}$ ), 124.79, 124.94, 127.22 (tt,  $J_{\text{C,F}} = 283\text{ Hz}$ ,  $J_{\text{C,F}} = 32.8\text{ Hz}$ ), 129.26, 131.94, 151.55, 153.21, 160.03.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -121.68 (t,  $J = 4.9\text{ Hz}$ ), -81.70 (t,  $J = 4.9\text{ Hz}$ ). **IR** (ATR, neat): 3062, 1720, 1601, 1394, 1387, 1258, 1171, 1063, 1042, 951, 848, 823, 787, 747, 709, 631, 613  $\text{cm}^{-1}$ . **HRMS** (ESI+) calcd (m/z) for  $\text{C}_{15}\text{H}_{17}\text{O}_2\text{F}_4\text{SSi}$ :  $[\text{M}+\text{H}]^+$  365.0649, found 365.0644. **Anal.** Calcd. for  $\text{C}_{15}\text{H}_{16}\text{O}_2\text{F}_4\text{SSi}$ : C 49.44, H 4.43, F 20.85, S 8.80, found C, 49.96, H, 4.59, F, 20.78, S, 8.69.

## Step 3: Synthesis of 7-((2-(3,3-Dimethyl-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)-1,1,2,2-tetrafluoroethyl)thio)-4-methyl-2H-chromen-2-one (2j).

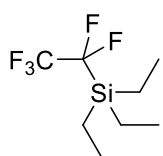


To a solution of 1-fluoro-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxole (1.40 g, 4.75 mmol, 2 equiv) and TBAT (13.2 mg, 0.024 mmol, 0.01 equiv) in dry MeCN (20 mL) under Ar. was added dropwise at  $-35\text{ }^{\circ}\text{C}$  a solution of 4-methyl-7-((1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethyl)thio)-2H-chromen-2-one (865 mg, 2.37 mmol, 1 equiv) in dry MeCN (10 mL). The reaction mixture was stirring 30 min at  $-35\text{ }^{\circ}\text{C}$  and 2 h at  $25\text{ }^{\circ}\text{C}$ . The reaction mixture was evaporated to dryness with Celite® and subjected to flash chromatography (EtOAc/Hexane 1:1) to afford yellowish oil (516 mg, 0.93 mmol, 39%).

$R_f = 0.33$  ( $\text{SiO}_2$ ; EtOAc/Hexane 1:1; UV). **M.p.:**  $111\text{ }^{\circ}\text{C}$ .  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.46 (s, 6H), 2.44 (d,  $J = 1.3\text{ Hz}$ , 3H), 6.35 (d,  $J = 1.4\text{ Hz}$ , 1H), 7.32 – 7.40 (m, 2H), 7.48 (td,  $J = 7.3\text{ Hz}$ ,  $J = 0.9\text{ Hz}$ , 1H), 7.56 (td,  $J = 6.7\text{ Hz}$ ,  $J = 3.4\text{ Hz}$ , 2H), 7.60–7.66 (m, 2H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  18.74, 30.88, 76.69, 111.27, 114.19 (tt,  $J_{\text{C,F}} = 338\text{ Hz}$ ,  $J_{\text{C,F}} = 47.6\text{ Hz}$ ), 116.76, 121.74, 124.81 (tt,  $J_{\text{C,F}} = 285\text{ Hz}$ ,  $J_{\text{C,F}} = 28.9\text{ Hz}$ ), 124.98, 125.22, 127.50, 127.96, 128.94 (t,  $J_{\text{C,F}} = 5.3\text{ Hz}$ ), 129.61, 130.50, 132.04, 150.04, 151.52, 153.25, 159.82.  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -89.89 (bs), -81.31 (t,  $J = 5.8\text{ Hz}$ ). **IR** (ATR, neat): 2970, 1725, 1598, 1396, 1174, 1093, 1072, 964, 950, 879, 769, 718, 629, 608  $\text{cm}^{-1}$ . **HRMS** (ESI+) calcd (m/z) for  $\text{C}_{21}\text{H}_{18}\text{O}_3\text{SF}_4\text{I}$ :  $[\text{M}+\text{H}]^+$  552.9952, found 552.9948.

## Synthesis of 2k.

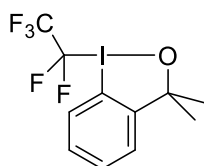
### Step 1: Synthesis of triethyl(perfluoroethyl)silane.



Anhydrous diethyl ether (150 mL) was cooled down to  $-78\text{ }^{\circ}\text{C}$  (acetone/dry ice bath). Pentafluoroethane (15.6 g, 130 mmol, 2 equiv) was condensed to the solution. A solution of *n*-BuLi (2.5 M in hexanes, 26 mL, 65 mmol, 1 equiv) was added carefully so that the internal temperature did not exceed  $-60\text{ }^{\circ}\text{C}$ . After stirring for 1 h, a solution of triethylchlorosilane (10.9 mL, 65 mmol, 1 equiv) in diethyl ether (5 mL) was added within 5 min. The mixture was allowed to warm up to rt 1 h and then concentrated near dryness. A little amount of pentane was added to finish precipitation of LiCl. The suspension was filtered and concentrated to dryness, affording the crude product. The product was distilled *in vacuo* to give a colourless oil.

Yield: 11.4 g (75%).  $R_f = 0.56$  (EtOAc:hexane 1:10).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (q,  $J = 7.9$  Hz, 6H), 1.04 (t,  $J = 7.9$  Hz, 9H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  0.9 (m), 6.5, 120.6(1) (tq,  $J = 272.5$ , 42.2 Hz), 120.6(4) (qt,  $J = 284.5$ , 30.4 Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -127.4 (br s, 2F), -82.9 (br s, 2F). **IR** (ATR, neat): 2964, 2948, 2921, 2886, 1461, 1417, 1385, 1317, 1243, 1190, 1121, 1051, 1023, 1009, 966, 945, 741, 730, 698  $\text{cm}^{-1}$ . **Anal.** calcd. for  $\text{C}_8\text{H}_{15}\text{SiF}_5$ : C 41.01, H 6.45, F 40.55, found: C 41.13, H 6.67, F 40.27.

### Step 2: Synthesis of 3,3-dimethyl-1-(perfluoroethyl)-1,3-dihydro-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxole (2k).



A flame-dried 100-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere with 1-fluoro-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxole (4.69 g, 16.7 mmol, 2 equiv) and anhydrous  $\text{CH}_3\text{CN}$  (43 mL). The solution was cooled to  $-35\text{ }^{\circ}\text{C}$  (acetone/dry ice bath). A solution of tetrabutylammonium difluorotriphenylsilicate (93.0 mg, 0.17 mmol, 0.02 equiv) in anhydrous  $\text{CH}_3\text{CN}$  (2 mL) was added at once, followed by the addition of a solution of triethyl(perfluoroethyl)silane (2.00 g, 8.37 mmol, 1 equiv) in anhydrous  $\text{CH}_3\text{CN}$  (5 mL) over a period of 30 min at  $-35\text{ }^{\circ}\text{C}$ . The mixture was stirred at  $-35\text{ }^{\circ}\text{C}$  to rt for 1 h. The solvent was removed on a rotary evaporator, yielding a yellow oil, which was treated with pentane (10 mL). The resulting suspension was filtered through a glass frit containing layers of Celite®, neutral activated alumina and Celite®, and washed with pentane ( $5 \times 10$  mL). The filtrate was concentrated on a rotary evaporator and dried *in vacuo* affording a white solid.

Yield: 2.30 g (72%).  $R_f = 0.25$  (EtOAc:hexane 1:10). **M.p.** = 68.8–71.2  $^{\circ}\text{C}$ .  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.49 (s, 6H), 7.37 – 7.42 (m, 2H), 7.52 (m, 1H), 7.56 (m, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  30.7, 77.0, 109.2 (tq,  $J = 334.8$ , 43.1 Hz), 111.1 (m), 118.9 (qt,  $J = 285.2$ , 28.6 Hz), 127.5, 128.5 (m), 129.7, 130.6, 149.7 (m).  $^{19}\text{F NMR}$  (471 MHz,  $\text{CDCl}_3$ )  $\delta$  -99.78 (br s, 2F), -81.80 (br s, 2F). **IR** (ATR, neat): 3137, 3068, 2975, 2962, 2931, 2920, 2860, 1565, 1462, 1452, 1438, 1375, 1357, 1303, 1268, 1249, 1178, 1160, 1119, 1063, 1040, 999, 959, 897, 869, 750, 729, 717, 647. **HRMS** (ESI $^+$ ) calcd (m/z) for  $\text{C}_{11}\text{H}_{11}\text{F}_5\text{IO}$ :  $[\text{M}+\text{H}^+]$  380.9769, found: 380.9776.

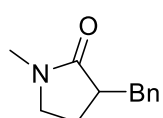
### General procedure for the synthesis of $\alpha$ -substituted $\gamma$ -, $\delta$ - and $\epsilon$ -lactams.

A flame-dried 100-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere subsequently with diisopropylamine (0.96 mL, 6.82 mmol, 1.1 equiv) and anhydrous THF (10 mL). To this well-stirred solution held at  $-18\text{ }^{\circ}\text{C}$  (ice/salt bath) was added within 5 minutes via a syringe a solution of *n*-BuLi (1.6 M in hexanes, 6.51 mmol, 1.05 equiv). The resulting



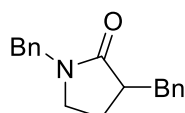
solution was stirred at this temperature for 15 minutes, then the solution was cooled to  $-78^{\circ}\text{C}$  (acetone/dry ice bath). A solution of the selected lactam (6.2 mmol, 1 equiv) in anhydrous THF (5 mL) was introduced dropwise via a syringe within 5 minutes. Lithiation was conducted for 90 minutes, then the solution of the corresponding alkylbromide (6.82 mmol, 1.1 equiv) in THF (5 mL) was slowly introduced. The resultant reaction mixture was stirred overnight allowing to gradually reach rt and then was quenched with sat.  $\text{NaHCO}_3$  solution. The aqueous phase was extracted with EtOAc ( $3 \times 30$  mL), washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , concentrated to dryness and subjected to dry column vacuum chromatography, applying gradient elution from hexane to hexane/EtOAc (3:1) to give the corresponding pure product.

### 3-Benzyl-1-methylpyrrolidin-2-one (3a). [CAS: 53101-33-0]



Yield 84%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35 – 7.30 (m, 2H), 7.27 – 7.20 (m, 3H), 3.30 – 3.21 (m, 2H), 3.12 (td,  $J = 9.2, 3.8$  Hz, 1H), 2.87 (s, 3H), 2.79 – 2.67 (m, 2H), 2.13 – 2.02 (m, 1H), 1.83 – 1.71 (m, 1H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.1, 29.7, 37.2, 43.4, 47.6, 126.3, 128.4, 129.0, 139.5, 175.9.

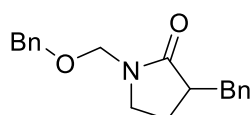
### 1,3-Dibenzylpyrrolidin-2-one (3b). [CAS: 178371-86-3]



Yield 87%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.72 – 1.90 (m, 1H), 2.03 – 2.14 (m, 1H), 2.69 – 2.98 (m, 2H), 3.01 – 3.26 (m, 2H), 3.26 – 3.43 (m, 1H), 4.49 (d, 15.0 Hz, 1H), 4.54 (d, 15.0 Hz, 1H), 7.19 – 7.50 (m, 10H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  24.2, 37.2, 43.8, 44.9, 46.9, 126.4, 127.6, 128.2, 128.6, 128.8, 129.2, 136.6, 139.5,

175.9.

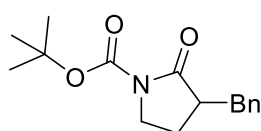
### 3-Benzyl-1-((benzyloxy)methyl)pyrrolidin-2-one (3c).



Yield 70%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.50 – 1.70 (m, 1H), 1.86 – 1.98 (m, 1H), 2.49 – 2.72 (m, 2H), 3.15 (dd,  $J = 13.0, 3.2$  Hz, 1H), 3.18 – 3.33 (m, 2H), 4.39 (d,  $J = 12.0$  Hz, 1H), 4.44 (d,  $J = 12.0$  Hz, 1H), 4.74 (d,  $J = 10.5$  Hz, 1H), 4.80 (d,  $J = 10.6$  Hz, 1H), 7.04 – 7.40 (m, 10H).  $^{13}\text{C NMR}$  (75

MHz,  $\text{CDCl}_3$ )  $\delta$  176.9, 139.3, 138.0, 129.1, 128.5, 128.4, 127.8, 126.4, 72.9, 70.8, 44.1, 43.9, 36.8, 24.3. **IR** (ATR, neat): 2933, 1690, 1453, 1264, 1062, 737, 696  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{Na}$ :  $[\text{M}+\text{Na}^+]$  318.1464, found: 318.1467.

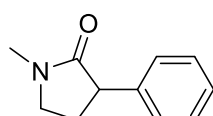
### *t*-Butyl 3-benzyl-2-oxopyrrolidine-1-carboxylate (3d). [CAS: 178371-86-3]



Yield 91%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.60 (s, 9H), 1.71 – 1.85 (m, 1H), 2.00 – 2.16 (m, 1H), 2.73 (dd,  $J = 13.5, 9.8$  Hz, 1H), 2.79 – 2.94 (m, 1H), 3.35 (dd,  $J = 13.6, 3.7$  Hz, 1H), 3.53 – 3.62 (m, 1H), 3.69 – 3.76 (m, 1H), 7.24 – 7.40 (m, 5H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  23.8, 28.1, 36.5, 44.4,

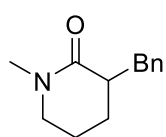
45.6, 82.9, 126.5, 128.6, 129.0, 138.9, 150.4, 175.2.

### 1-Methyl-3-phenylpyrrolidin-2-one (3e). [CAS: 54520-82-0]



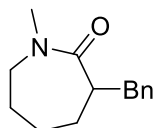
Yield 37%, white solid. **M.p.** = 62.8-64.0  $^{\circ}\text{C}$ .  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ )  $\delta$  1.97 – 2.31 (m, 1H), 2.38 – 2.68 (m, 1H), 2.96 (s, 3H), 3.30 – 3.58 (m, 2H), 3.67 (t,  $J = 8.8$  Hz, 1H), 7.07 – 7.49 (m, 5H).  $^{13}\text{C NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  28.0, 30.1, 47.7, 48.0, 126.9, 127.9, 128.7, 140.0, 174.9.

### 3-Benzyl-1-methylpiperidin-2-one (3f). [CAS: 37129-04-7]



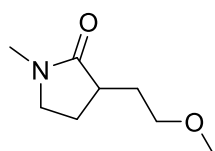
Yield 67%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.40 – 1.62 (m, 1H), 1.64 – 2.01 (m, 3H), 2.52 – 2.78 (m, 2H), 3.03 (s, 3H), 3.24 – 3.42 (m, 2H), 3.52 (dd,  $J = 12.9$ , 3.1 Hz, 1H), 7.20 – 7.31 (m, 3H), 7.33 – 7.39 (m, 2H).  $^{13}\text{C NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  21.5, 25.8, 35.0, 37.9, 43.4, 50.2, 126.0, 128.3, 129.2, 140.3, 172.0.

### 3-Benzyl-1-methylazepan-2-one (3g). [CAS: 57724-11-5]



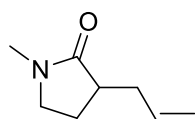
Yield 76%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.30 – 1.63 (m, 3H), 1.70 – 1.85 (m, 2H), 1.87 – 2.02 (m, 1H), 2.64 (dd,  $J = 14.1$ , 8.7 Hz, 1H), 2.80 – 2.97 (m, 1H), 3.06 (s, 3H), 3.20 (dd,  $J = 15.4$ , 5.8 Hz, 1H), 3.32 (dd,  $J = 14.0$ , 5.6 Hz, 1H), 3.70 (dd,  $J = 15.2$ , 9.9 Hz, 1H), 7.22 – 7.33 (m, 5H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  27.0, 29.2, 29.4, 36.0, 38.3, 45.5, 50.5, 126.0, 128.4, 129.4, 141.1, 176.7.

### 3-(2-Methoxyethyl)-1-methylpyrrolidin-2-one (3h).



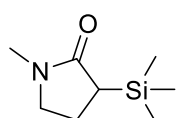
Yield 19%, colorless oil.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.90 (dd,  $J = 13.7$ , 9.4 Hz, 1H), 3.18 (s, 3H), 3.53 (dd,  $J = 13.7$ , 4.5 Hz, 1H), 3.74 (dd,  $J = 9.5$ , 4.5 Hz, 1H), 6.77 (t,  $J = 6.7$  Hz, 2H), 6.94 (t,  $J = 7.5$  Hz, 1H), 7.12 – 7.38 (m, 6H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  26.1, 36.9, 47.1, 107.9, 122.0, 124.5, 126.6, 127.9, 128.3, 128.4, 129.4, 138.0, 144.2, 177.0. **IR** (ATR, neat): 2869, 1698, 1432, 1400, 1264, 1113, 933, 714  $\text{cm}^{-1}$ . **HRMS** (EI) calcd ( $m/z$ ) for  $\text{C}_8\text{H}_{16}\text{NO}_2$ :  $[M+H]^+$  158.1176, found: 158.1177.

### 3-Allyl-1-methylpyrrolidin-2-one (3i). [CAS: 40296-20-6]



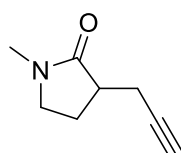
Yield 67%, yellowish oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.55 – 1.86 (m, 1H), 2.02 – 2.29 (m, 2H), 2.35 – 2.69 (m, 2H), 2.82 (s, 3H), 3.10 – 3.44 (m, 2H), 4.89 – 5.23 (m, 2H), 5.66 – 5.82 (m, 1H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  23.9, 29.7, 35.6, 41.2, 47.7, 116.8, 135.7, 176.0.

### 1-Methyl-3-(trimethylsilyl)pyrrolidin-2-one (3j). [CAS: 72578-86-0]



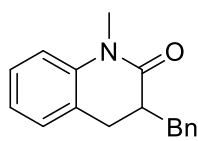
Yield 71%, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.09 (s, 9H), 1.77 – 2.07 (m, 2H), 2.09 – 2.39 (m, 1H), 2.79 (s, 3H), 3.21 – 3.33 (m, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  2.6, 20.3, 29.6, 32.7, 49.3, 177.25.

### 1-Methyl-3-(prop-2-yn-1-yl)pyrrolidin-2-one (3k). [CAS: 1616976-81-8]



Yield 56%, yellowish oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.80 – 2.04 (m, 2H), 2.17 – 2.31 (m, 1H), 2.32 – 2.46 (m, 1H), 2.49 – 2.67 (m, 2H), 2.81 (s, 3H), 3.23 – 3.40 (m, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  20.54, 23.86, 29.80, 40.73, 47.57, 69.67, 81.51, 174.56.

### 3-Benzyl-1-methyl-3,4-dihydroquinolin-2(1H)-one (3l).

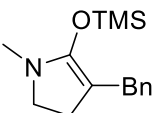


Yield 86, colorless oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.56 – 2.75 (m, 2H), 2.80 – 3.00 (m, 2H), 3.39 (dd,  $J = 13.6$ , 3.9 Hz, 1H), 3.47 (s, 3H), 7.02 – 7.19 (m, 3H), 7.21 – 7.42 (m, 6H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  29.4, 29.9, 35.6, 42.5, 114.5, 122.9, 125.1, 126.4, 127.5, 128.2, 128.5, 129.2, 139.2, 140.3, 172.1. **IR** (ATR, neat): 3025, 2945, 1663, 1601, 1470, 1366, 1269, 1162, 1078, 751, 734, 698  $\text{cm}^{-1}$ . **HRMS** (EI) calcd ( $m/z$ ) for  $\text{C}_{17}\text{H}_{18}\text{NO}$ :  $[M+H]^+$  252.1383, found: 252.1386.

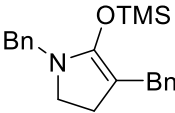
## General procedure for synthesis of lactam ketene silyl amides. (KSAs).

A flame-dried 50-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere subsequently with diisopropylamine (0.686 g, 0.95 mL, 6.78 mmol, 1.1 equiv) and anhydrous THF (10 mL). To this well-stirred solution held at  $-18\text{ }^{\circ}\text{C}$  (ice-salt bath) was added a solution of *n*-BuLi (1.6M in hexanes, 4.45 mL, 1.15 equiv) via a syringe within 2 minutes. The resulting solution was stirred at this temperature for 30 minutes, then the solution was cooled to  $-78\text{ }^{\circ}\text{C}$ . A solution of the selected lactam (6.165 mmol, 1 equiv) in anhydrous THF (5 mL) was introduced dropwise via a syringe within 2 minutes. Lithiation was conducted for 60 minutes, then neat trimethylchlorosilane (1.138 g, 1.35 mL, 10.48 mmol, 1.7 equiv) was introduced at once. The resultant reaction mixture was stirred overnight allowing to gradually reach rt. The turbid solution was concentrated in vacuo in Schlenk flask (external cold trap). To the remaining white slurry an anhydrous pentane (10 mL) was introduced and the mixture was stirred for 10 minutes. The resulting suspension was filtered into second, oven-dried Schlenk flask using a syringe filter (PTFE membrane, 3 cm diameter) under argon atmosphere and washed with dry pentane (3 mL). The clear filtrate was concentrated in vacuo (external cold trap) to give the desired ketene silyl amide (KSA). KSAs were stored in parafilm-sealed Schlenk flask in a freezer at  $-20\text{ }^{\circ}\text{C}$ .

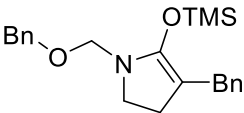
### 4-Benzyl-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole (4a). [CAS: 223714-06-5]

 Using the general procedure, compound **4a** was synthesized from **3a** (1167 mg, 6.17 mmol) and TMSCl (1.33 mL, 10.5 mmol). **4a** was obtained as colorless oil (1605 mg, 6.14 mmol, 99.6%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.29 (s, 9H), 2.19 (t,  $J = 8.4$  Hz, 2H), 2.46 (s, 3H), 2.96 (t,  $J = 8.4$  Hz, 2H), 3.36 (s, 2H), 7.21 (dd,  $J = 16.5, 7.5$  Hz, 3H), 7.30 (t,  $J = 7.3$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  0.0, 27.4, 32.2, 37.8, 52.2, 88.8, 124.98, 127.6, 127.9, 140.6, 151.4.

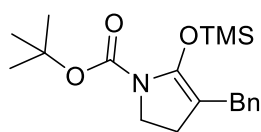
### 1,4-Dibenzyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole (4b).

 Using the general procedure, compound **4b** was synthesized from **3b** (500 mg, 1.69 mmol) and TMSCl (0.36 mL, 2.88 mmol). **4b** was obtained as colorless oil (610 mg, 1.66 mmol, 99%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.32 (s, 9H), 2.18 (t,  $J = 8.5$  Hz, 2H), 2.89 (t,  $J = 8.5$  Hz, 2H), 3.40 (s, 2H), 3.94 (s, 2H), 7.20 – 7.37 (m, 10H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  0.6, 27.9, 32.7, 49.9, 55.1, 89.6, 125.6, 126.8, 128.1, 128.2, 128.3, 128.5, 139.1, 141.2, 150.9. **IR** (ATR, neat): 2956, 2825, 1684, 1493, 1371, 1267, 1085, 865, 840, 750, 696  $\text{cm}^{-1}$ . **Anal.** calcd. for  $\text{C}_{21}\text{H}_{27}\text{NOSi}$ : C 74.32, H 8.17, N 4.18 found: C 74.37, H 8.11, N 4.16.

### 4-Benzyl-1-((benzyloxy)methyl)-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole (4c).

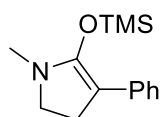
 Using the general procedure, compound **4c** was synthesized from **3c** (300 mg, 1.02 mmol) and TMSCl (0.22 mL, 1.73 mmol). **4c** was obtained as colorless oil (360 mg, 0.98 mmol, 96%).  $^1\text{H NMR}$  (500 MHz,  $\text{CD}_3\text{CN}$ )  $\delta$  0.21 (s, 9H), 2.16 – 2.27 (m, 2H), 3.26 – 3.32 (m, 4H), 4.40 (s, 2H), 4.50 (s, 2H), 7.16 – 7.19 (m, 2H), 7.25 – 7.37 (m, 8H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  0.5, 27.9, 32.7, 45.53, 70.2, 78.1, 89.7, 125.6, 127.4, 127.6, 128.2, 128.3, 128.5, 138.8, 140.99, 148.45. **IR** (ATR, neat): 2953, 1693, 1494, 1452, 1378, 1251, 1051, 866, 841, 696  $\text{cm}^{-1}$ . **Anal.** calcd. for  $\text{C}_{22}\text{H}_{29}\text{NO}_2\text{Si}$ : C 71.89, H 7.95, N 3.81 found: C 71.68, H 8.25, N 3.59.

#### *t*-Butyl 4-benzyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole-1-carboxylate (**4d**).



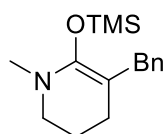
Using the general procedure, compound **4d** was synthesized from **3d** (1006 mg, 3.65 mmol) and TMSCl (0.79 mL, 6.21 mmol). **4d** was obtained as colorless oil (1200 mg, 3.45 mmol, 95%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.29 (s, 9H), 1.50 (s, 9H), 2.12 – 2.30 (m, 2H), 3.37 (s, 2H), 3.57 – 3.83 (m, 2H), 7.15 – 7.22 (m, 3H), 7.26 – 7.32 (m, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.3, 26.2, 28.5, 32.3, 44.9, 79.5, 96.4, 125.9, 128.3, 128.5, 140.0, 142.7, 151.5. IR (ATR, neat): 2975, 1744, 1716, 1494, 1390, 1293, 1248, 1153, 1103, 839, 697 cm<sup>-1</sup>. Anal. calcd. for C<sub>19</sub>H<sub>29</sub>NO<sub>3</sub>Si: C 65.67, H 8.41, N 4.03 found: C 65.44, H 8.58, N 4.21.

#### 1-Methyl-4-phenyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole (**4e**).



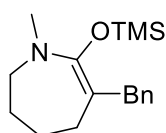
Using the general procedure, compound **4e** was synthesized from **3e** (1000 mg, 5.21 mmol) and TMSCl (1.23 mL, 9.7 mmol). **4e** was obtained as colorless oil (1379 mg, 5.57 mmol, 98%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.23 (s, 9H), 2.58 (s, 3H), 2.70 (t, *J* = 8.5 Hz, 2H), 3.13 (t, *J* = 8.5 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.3 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.4, 27.5, 37.6, 51.9, 91.1, 122.7, 124.2, 127.9, 137.5, 154.1. IR (ATR, neat): 2947, 1683, 1628, 1494, 1445, 1300, 1248, 839, 755, 715 cm<sup>-1</sup>. Anal. calcd. for C<sub>14</sub>H<sub>21</sub>NOSi: C 67.96, H 8.56, N 5.66 found: C 67.85, H 8.51, N 5.51.

#### 5-Benzyl-1-methyl-6-((trimethylsilyl)oxy)-1,2,3,4-tetrahydropyridine (**4f**). [CAS: 223714-12-3]



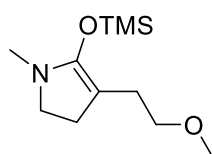
Using the general procedure, compound **4f** was synthesized from **3f** (1000 mg, 4.92 mmol) and TMSCl (1.06 mL, 8.36 mmol). **4f** was obtained as colorless oil (1350 mg, 4.9 mmol, 99%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.24 (s, 9H), 1.52 – 1.69 (m, 2H), 1.85 (t, *J* = 6.5 Hz, 2H), 2.56 (s, 3H), 2.88 – 2.99 (m, 2H), 3.38 (s, 2H), 7.05 – 7.43 (m, 5H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.2, 18.9, 26.2, 36.6, 39.0, 51.5, 95.6, 125.4, 128.0, 128.7, 142.2, 147.8.

#### 6-Benzyl-1-methyl-7-((trimethylsilyl)oxy)-2,3,4,5-tetrahydro-1*H*-azepine (**4g**).



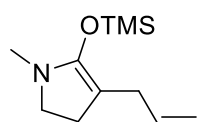
Using the general procedure, compound **4g** was synthesized from **3g** (700 mg, 3.22 mmol) and TMSCl (0.7 mL, 5.48 mmol). **4g** was obtained as colorless oil (875 mg, 3.02 mmol, 94%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.26 (s, 9H), 1.55 – 1.71 (m, 3H), 1.77 (p, *J* = 6.4 Hz, 2H), 1.89 – 2.07 (m, 2H), 2.71 (s, 3H), 3.22 (t, *J* = 6.1 Hz, 2H), 3.37 (s, 2H), 7.10 – 7.54 (m, 5H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 0.0, 25.0, 28.2, 36.2, 38.4, 50.6, 101.1, 125.1, 127.8, 128.5, 142.1, 149.7. IR (ATR, neat): 2924, 1659, 1451, 1353, 1247, 1116, 1047, 875, 836, 749, 698 cm<sup>-1</sup>. Anal. calcd. for C<sub>17</sub>H<sub>27</sub>NOSi: C 70.53, H 9.40, N 4.84 found: C 70.48, H 9.38, N 4.76.

#### 4-(2-Methoxyethyl)-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1*H*-pyrrole (**4h**).



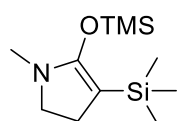
Using the general procedure, compound **4h** was synthesized from **3h** (800 mg, 5.09 mmol) and TMSCl (1.1 mL, 8.65 mmol). **4h** was obtained as colorless oil (1100 mg, 4.8 mmol, 94%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.24 (s, 9H), 2.28 (t, *J* = 7.9 Hz, 4H), 2.38 (s, 3H), 2.92 (t, *J* = 8.3 Hz, 2H), 3.34 (s, 3H), 3.38 (t, *J* = 7.4 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.4, 26.9, 28.2, 38.3, 52.8, 58.4, 72.0, 87.0, 152.0. IR (ATR, neat): 2873, 1687, 1452, 1401, 1249, 1113, 1041, 839, 754 cm<sup>-1</sup>. Anal. calcd. for C<sub>11</sub>H<sub>23</sub>NO<sub>2</sub>Si: C 56.02, H 9.78, N 5.71 found: C 56.11, H 9.84, N 5.63.

#### 4-Allyl-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (4i).



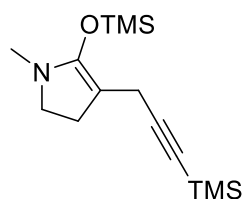
Using the general procedure, compound **4i** was synthesized from **3i** (1000 mg, 7.18 mmol) and TMSCl (1.55 mL, 12.2 mmol). **4i** was obtained as colorless oil (1442 mg, 6.82 mmol, 95%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.25 (s, 9H), 2.25 (t, *J* = 8.4 Hz, 2H), 2.40 (s, 3H), 2.75 (d, *J* = 6.4 Hz, 2H), 2.94 (t, *J* = 8.4 Hz, 2H), 4.94 – 5.00 (m, 1H), 5.04 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.76 (ddt, *J* = 16.5, 10.0, 6.4 Hz, 1H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.4, 28.0, 31.0, 38.3, 52.8, 88.4, 114.4, 137.2, 151.4. IR (ATR, neat): 2952, 1694, 1500, 1434, 1401, 1248, 977, 907, 838, 752, 665 cm<sup>-1</sup>. Anal. calcd. for C<sub>11</sub>H<sub>21</sub>NOSi: C 62.50, H 10.01, N 6.63 found: C 62.73, H 10.21, N 6.43.

#### 1-Methyl-4-(trimethylsilyl)-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (4j).



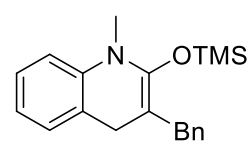
Using the general procedure, compound **4j** was synthesized from **3j** (1000 mg, 5.84 mmol) and TMSCl (1.26 mL, 9.92 mmol). **4j** was obtained as colorless oil (1380 mg, 5.67 mmol, 97%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.06 (s, 9H), 0.24 (s, 9H), 2.30 (t, *J* = 8.5 Hz, 2H), 2.43 (s, 3H), 3.00 (t, *J* = 8.5 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.4, 0.6, 28.5, 38.0, 54.9, 82.4, 162.3. IR (ATR, neat): 2954, 1675, 1605, 1499, 1398, 1297, 1246, 1109, 1052, 832, 750, 708 cm<sup>-1</sup>. HRMS (EI) calcd (m/z) for C<sub>11</sub>H<sub>26</sub>NOSi<sub>2</sub>: [M+H<sup>+</sup>] 244.1547, found: 244.1545.

#### 1-Methyl-5-((trimethylsilyl)oxy)-4-(3-(trimethylsilyl)prop-2-yn-1-yl)-2,3-dihydro-1H-pyrrole (4k).



Using the general procedure, compound **4k** was synthesized from **3k** (1000 mg, 7.29 mmol) and TMSCl (3.24 mL, 25.5 mmol). **4k** was obtained as colorless oil (1922 mg, 6.83 mmol, 94%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 0.11 (s, 9H), 0.23 (s, 9H), 2.34 (d, *J* = 8.3 Hz, 1H), 2.37 (s, 3H), 2.93 (s, 2H), 2.95 (d, *J* = 8.3 Hz, 1H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 0.1, 0.4, 17.8, 27.7, 38.0, 52.5, 83.6, 85.0, 105.5, 151.7. IR (ATR, neat): 2956, 2175, 1920, 1689, 1500, 1403, 1247, 163, 1033, 835, 757, 696 cm<sup>-1</sup>. Anal. calcd. for C<sub>14</sub>H<sub>27</sub>NOSi<sub>2</sub>: C 59.73, H 9.67, N 4.97 found: C 59.43, H 9.53, N 4.77.

#### 3-Benzyl-2-((trimethylsilyl)oxy)-1,4-dihydroquinoline (4l).



Using the general procedure, compound **4l** was synthesized from **3l** (500 mg, 1.99 mmol) and TMSCl (0.43 mL, 3.38 mmol). **4l** was obtained as colorless oil (650 mg, 1.98 mmol, 99%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.27 (s, 9H), 3.18 (s, 3H), 3.34 (s, 2H), 3.47 (s, 2H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.84 (td, *J* = 7.4, 1.0 Hz, 1H), 6.93 (d, *J* = 6.5 Hz, 1H), 7.01 – 7.36 (m, 7H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 0.4, 31.1, 33.0, 36.6, 88.1, 113.3, 120.5, 123.6, 125.9, 126.5, 128.2, 128.4, 128.7, 140.8, 142.3, 143.5. IR (ATR, neat): 2954, 1682, 1600, 1493, 1361, 1329, 1263, 1122, 1087, 839, 747, 698 cm<sup>-1</sup>. Anal. calcd. for C<sub>20</sub>H<sub>25</sub>NOSi: C 74.25, H 7.79, N 4.33 found: C 74.13, H 7.98, N 4.44.

### General procedures for $\alpha$ -trifluoromethylation of KSAs.

**General procedure 1, TMSNTf<sub>2</sub>-catalyzed:** In a flame-dried 10 mL Schlenk flask equipped with rubber septum and magnetic stirring bar, selected trimethylsilyl ketene amide (1.3 mmol) was weighed out under argon. The trimethyl silyl ketene amide was dissolved by addition of 1 mL anhydrous DCM and cooled to -78 °C (dry ice/acetone bath). Solution of TMSNTf<sub>2</sub> in DCM (0.32, 32  $\mu$ L, 0.01 mmol,

0.01 equiv) was added via a microsyringe at once. To the resulting well-stirred solution was added solid 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole **2a** (331 mg, 1 mmol, 1 equiv). The mixture was allowed to reach rt overnight (19 h) with stirring. The reaction mixture was directly subjected to chromatographic purification.

**General procedure 2, one-pot procedure:** A flame-dried 25 mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged subsequently with diisopropylamine (0.2 mL, 1.4 mmol, 1.4 equiv) and 2 ml of dry THF under argon flow. The solution was cooled to -18 °C with an ice/salt bath and a solution of n-BuLi (1.6 M in THF, 0.93 mL, 1.5 mmol, 1.5 equiv) was added dropwise. The formed LDA was stirred for 15 minutes, then cooled to -78 °C and the selected lactam (**3a-I**) (1.30 mmol, 1.30 equiv) in 1 mL of THF was added dropwise via syringe. Lithiation was proceeded for 2 hours at -78 °C, then TMSCl (0.28 mL, 2.2 mmol, 2.2 equiv) was added. The mixture was allowed to reach rt overnight (17 h) with stirring. The mixture was again cooled to -78 °C and reagent **2a** (333 mg, 1.0 mmol, 1.0 equiv) and TMSNTf<sub>2</sub> (0.15 M in DCM, 0.067 mL, 0.01 mmol, 0.01 equiv) were added and the mixture was stirred for another 19 hours while warming to rt. To the reaction mixture were then added water (10 mL) and EtOAc (10 mL), the aqueous phase was separated and extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was purified by column chromatography (Hexane/EtOAc, 3:1).

**General procedure 3, non-catalyzed:** In a flame-dried 10 mL Schlenk flask equipped with rubber septum and magnetic stirring bar, selected trimethylsilyl ketene amide (**4a-I**) (1.3 mmol, 1.3 equiv) was weighed out under argon. The trimethyl silyl ketene amide was dissolved by addition of 1 mL anhydrous DCM and cooled to -78 °C (dry ice/acetone bath). To the resulting well-stirred solution was added solid 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole **2a** (331 mg, 1 mmol, 1 equiv). The mixture was allowed to reach rt overnight (19 h) with stirring. The reaction mixture was directly subjected to chromatographic purification.

### 3-Benzyl-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (**8a**).

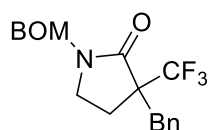


Using **general procedure 1**, compound **8a** was synthesized from **4a** (340 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8a** was obtained as yellow oil (242 mg, 0.94 mmol, 94%). **General procedure 2:** 82% yield. **General procedure 3:** 67% yield. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.83 – 2.02 (m, 2H), 2.03 – 2.20 (m, 1H), 2.51 (s, 3H), 2.62 (d, *J* = 13.2 Hz, 1H), 2.80 – 2.90 (m, 1H), 3.31 (d, *J* = 13.2 Hz, 1H), 6.99 – 7.05 (m, 2H), 7.07 – 7.16 (m, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 21.2 (d, *J* = 1.6 Hz), 28.0, 34.7 (q, *J* = 2.4 Hz), 43.8, 52.4 (q, *J* = 24.9 Hz), 124.49 (q, *J* = 282.0 Hz), 125.6, 126.6, 128.3, 132.6, 167.5. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -73.88. IR (ATR, neat): 2892, 1691, 1496, 1455, 1404, 1315, 1261, 1162, 1132, 1090, 1064, 1027, 926, 768, 702, 685 cm<sup>-1</sup>. HRMS (EI) calcd (m/z) for C<sub>13</sub>H<sub>14</sub>NOF<sub>3</sub>: [M<sup>+</sup>] 257.1022, found: 257.1024.

### 1,3-Dibenzyl-3-(trifluoromethyl)pyrrolidin-2-one (**8b**).

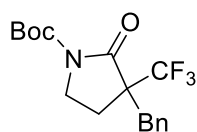
Using **general procedure 1**, compound **8b** was synthesized from **4b** (439 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8b** was obtained as colorless oil (293 mg, 0.88 mmol, 88%). **General procedure 2:** 69% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 2.04 – 2.19 (m, 1H), 2.19 – 2.38 (m, 3H), 2.85 (d, *J* = 13.2 Hz, 1H), 2.93 – 3.10 (m, 1H), 3.59 (d, *J* = 13.2 Hz, 1H), 4.26 (d, *J* = 14.8 Hz, 1H), 4.47 (d, *J* = 14.7 Hz, 1H), 6.91 – 7.10 (m, 2H), 7.19 – 7.33 (m, 12H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 22.8 (d, *J* = 1.9 Hz), 36.2 (q, *J* = 2.4 Hz), 43.1, 47.0, 54.6 (q, *J* = 24.6 Hz), 126.5 (q, *J* = 282.4 Hz), 127.4, 127.7, 128.0, 128.5, 128.6, 130.5, 134.4, 135.4, 169.2 (d, *J* = 1.8 Hz). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -73.8. IR (ATR, neat): 3031, 2933, 1695, 1495, 1454, 1268, 1190, 1071, 771, 698, 618 cm<sup>-1</sup>. HRMS (ESI) calcd (m/z) for C<sub>19</sub>H<sub>19</sub>NOF<sub>3</sub>: [M+H<sup>+</sup>] 334.1413, found: 334.1414.

### 3-Benzyl-1-((benzyloxy)methyl)-3-(trifluoromethyl)pyrrolidin-2-one (8c).



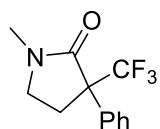
Using **general procedure 1**, compound **8c** was synthesized from **4c** (478 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8c** was obtained as colorless oil (334 mg, 0.92 mmol, 92%). **General procedure 2**: 84% yield.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.12 – 2.26 (m, 1H), 2.28 – 2.41 (m, 1H), 2.64 (td,  $J = 9.3, 5.2$  Hz, 1H), 2.88 (d,  $J = 13.4$  Hz, 1H), 3.31 (td,  $J = 9.3, 5.4$  Hz, 1H), 3.55 (d,  $J = 13.4$  Hz, 1H), 4.27 (d,  $J = 11.6$  Hz, 1H), 4.38 (d,  $J = 11.6$  Hz, 1H), 4.62 (d,  $J = 10.7$  Hz, 1H), 4.84 (d,  $J = 10.7$  Hz, 1H), 7.25 – 7.39 (m, 10H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  22.2 – 23.6 (m), 36.1 (q,  $J = 2.2$  Hz), 42.5, 55.1 (q,  $J = 24.6$  Hz), 70.4, 72.6, 126.5 (q,  $J = 283.8$  Hz), 127.6, 127.9, 128.0, 128.4, 128.6, 130.5, 134.3, 137.3, 170.3 (d,  $J = 1.6$  Hz).  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -73.65. **IR** (ATR, neat): 3031, 2936, 1705, 1455, 1275, 1161, 1070, 777, 731, 698  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{20}\text{H}_{21}\text{NO}_2\text{F}_3$ :  $[\text{M}+\text{H}^+]$  364.1519, found: 364.1522.

### *t*-Butyl 3-benzyl-2-oxo-3-(trifluoromethyl)pyrrolidine-1-carboxylate (8d).



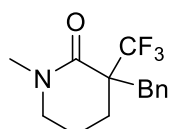
Using **general procedure 1**, compound **8d** was synthesized from **4d** (452 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8d** was obtained as a white solid (295 mg, 0.86 mmol, 86%). **General procedure 2**: 71% yield. M.p. 68.7-70.1 °C.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.49 (s, 9H), 1.97 – 2.14 (m, 1H), 2.18 – 2.34 (m, 1H), 2.56 – 2.72 (m, 1H), 2.88 (d,  $J = 13.4$  Hz, 1H), 3.33 – 3.59 (m, 2H), 7.21 – 7.34 (m, 5H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  22.0 (q,  $J = 1.7$  Hz), 27.9, 37.0 (q,  $J = 2.4$  Hz), 42.8, 56.0 (q,  $J = 25.0$  Hz), 83.5, 125.8 (q,  $J = 282.5$  Hz), 127.8, 128.7, 130.2, 133.8, 149.4, 169.0 (q,  $J = 2.25$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -73.47. **IR** (ATR, neat): 2979, 1782, 1742, 1723, 1369, 1279, 1190, 1117, 934, 777, 702  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{17}\text{H}_{21}\text{NO}_3\text{F}_3$ :  $[\text{M}+\text{H}^+]$  344.1468, found: 344.1468.

### 1-Methyl-3-phenyl-3-(trifluoromethyl)pyrrolidin-2-one (8e).



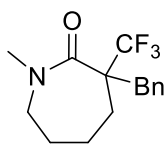
Using **general procedure 1**, compound **8e** was synthesized from **4e** (322 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8e** was obtained as a yellow solid (221 mg, 0.91 mmol, 91%). **General procedure 2**: 61% yield. **General procedure 3**: 35% yield.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.41 – 2.59 (m, 1H), 2.57 – 2.74 (m, 1H), 2.84 (s, 3H), 3.07 – 3.21 (m, 1H), 3.27 (td,  $J = 9.2, 3.4$  Hz, 1H), 7.15 – 7.39 (m, 3H), 7.49 – 7.67 (m, 2H).  $^{13}\text{C NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  28.5 (q,  $J = 1.5$  Hz), 30.1, 45.5, 56.7 (q,  $J = 26.0$  Hz), 125.4 (q,  $J = 280.0$  Hz), 128.1 (d,  $J = 1.0$  Hz), 128.7, 128.74, 133.34 (q,  $J = 1.5$  Hz), 168.86 (q,  $J = 2.0$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -71.20. **IR** (ATR, neat): 2886, 1695, 1499, 1449, 1434, 1405, 1307, 1260, 1219, 1145, 1070, 1035, 1014, 976, 937, 905, 764, 700, 665  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{12}\text{H}_{13}\text{NOF}_3$ :  $[\text{M}+\text{H}^+]$  244.0944, found: 244.0944.

### 3-Benzyl-1-methyl-3-(trifluoromethyl)piperidin-2-one (8f).



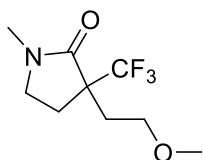
Using **general procedure 1**, compound **8f** was synthesized from **4f** (358 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8f** was obtained as colorless oil (264 mg, 0.97 mmol, 97%). **General procedure 2**: 72% yield. **General procedure 3**: 81% yield.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.06 – 1.25 (m, 1H), 1.55 – 1.74 (m, 1H), 1.75 – 1.90 (m, 2H), 1.90 – 2.07 (m, 1H), 2.68 (d,  $J = 13.2$  Hz, 1H), 2.84 – 2.92 (m, 1H), 2.88 (s, 3H), 3.06 – 3.25 (m, 1H), 3.62 (d,  $J = 13.2$  Hz, 1H), 7.05 – 7.18 (m, 2H), 7.15 – 7.27 (m, 3H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  19.3, 26.4 (q,  $J = 2.0$  Hz), 35.8, 38.9 (q,  $J = 2.5$  Hz), 49.9, 52.0 (q,  $J = 22.3$  Hz), 126.8 (q,  $J = 283.5$  Hz), 127.2, 128.4, 130.5, 135.6, 165.8 (1,  $J = 1.5$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -71.14. **IR** (ATR, neat): 2941, 1644, 1497, 1455, 1402, 1364, 1335, 1258, 1194, 1153, 1132, 1081, 1029, 974, 766, 741, 702, 668  $\text{cm}^{-1}$ . **HRMS** (EI) calcd (m/z) for  $\text{C}_{14}\text{H}_{16}\text{NOF}_3$ :  $[\text{M}^+]$  271.1179, found: 271.1181.

### 3-Benzyl-1-methyl-3-(trifluoromethyl)azepan-2-one (8g).



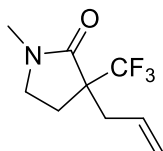
Using **general procedure 1**, compound **8g** was synthesized from **4g** (376 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8g** was obtained as colorless oil (279 mg, 0.978 mmol, 98%). **General procedure 2**: 65% yield. **General procedure 3**: 72% yield.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.69 – 0.86 (m, 1H), 1.30 – 1.50 (m, 3H), 1.80 (dd,  $J = 7.5, 2.9$  Hz, 2H), 2.63 (d,  $J = 13.1$  Hz, 1H), 2.83 (dt,  $J = 15.3, 4.8$  Hz, 1H), 2.89 (s, 3H), 3.34 – 3.58 (m, 1H), 3.74 (d,  $J = 13.1$  Hz, 1H), 7.14 (d,  $J = 3.1$  Hz, 5H).  $^{13}\text{C NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  19.2, 24.1, 25.9 (q,  $J = 1.5$  Hz), 29.8, 38.3, 40.4 (q,  $J = 2.5$  Hz), 46.5, 57.5 (q,  $J = 24.5$  Hz), 127.2 (q,  $J = 283.5$  Hz), 127.0, 128.2, 130.9, 135.9, 167.8.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -71.23. **IR** (ATR, neat): 2939, 1639, 1495, 1471, 1395, 1370, 1321, 1252, 1210, 1194, 1149, 1108, 1088, 1058, 1030, 1005, 760, 742, 703, 656  $\text{cm}^{-1}$ . **HRMS** (EI) calcd (m/z) for  $\text{C}_{15}\text{H}_{19}\text{NOF}_3$ :  $[\text{M}+\text{H}^+]$  286.1413, found: 286.1418.

### 3-(2-Methoxyethyl)-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (8h).



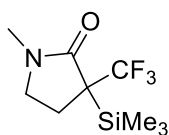
Using **general procedure 1**, compound **8h** was synthesized from **4h** (298 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8h** was obtained as colorless oil (202 mg, 0.897 mmol, 90%). **General procedure 2**: 82% yield.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.94 – 2.05 (m, 1H), 2.15 – 2.27 (m, 1H), 2.31 (t,  $J = 7.1$  Hz, 2H), 2.88 (s, 3H), 3.25 – 3.31 (m, 4H), 3.35 (t,  $J = 7.6$  Hz, 1H), 3.31 – 3.55 (m, 4H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  24.4 (q,  $J = 1.01$  Hz), 30.3, 30.6, 46.3, 52.1 (q,  $J = 25.3$  Hz), 58.8, 68.6, 126.8 (q,  $J = 282.3$  Hz), 169.63 (q,  $J = 2.02$  Hz).  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -73.82. **IR** (ATR, neat): 2891, 1737, 1698, 1437, 1373, 1240, 1183, 1111, 1044, 684  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_9\text{H}_{15}\text{NO}_2\text{F}_3$ :  $[\text{M}+\text{H}^+]$  226.1049, found: 226.1053.

### 3-Allyl-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (8i).



Using **general procedure 1**, compound **8i** was synthesized from **4i** (275 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8i** was obtained as colorless oil (177.6 mg, 0.857 mmol, 86%). **General procedure 2**: 77% yield.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.02 – 2.19 (m, 1H), 2.19 – 2.47 (m, 2H), 2.72 (dd,  $J = 13.7, 6.1$  Hz, 1H), 2.85 (s, 3H), 3.21 (td,  $J = 9.4, 4.7$  Hz, 1H), 3.26 – 3.42 (m, 1H), 5.05 – 5.27 (m, 2H), 5.50 – 5.72 (m, 1H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  23.3 (q,  $J = 1.8$  Hz), 30.0, 35.4 (q,  $J = 2.3$  Hz), 46.1, 52.8 (q,  $J = 25.0$  Hz), 120.6, 126.5 (q,  $J = 282.3$  Hz), 131.2, 169.2 (q,  $J = 1.9$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -73.54. **IR** (ATR, neat): 2924, 1695, 1643, 1504, 1441, 1406, 1341, 1262, 1169, 1129, 1097, 1070, 1029, 998, 925, 706, 666  $\text{cm}^{-1}$ . **HRMS** (EI) calcd (m/z) for  $\text{C}_9\text{H}_{12}\text{NO}_2\text{F}_3$ :  $[\text{M}^+]$  207.0866, found: 207.0870.

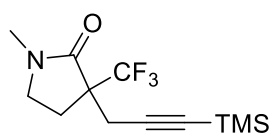
### 1-Methyl-3-(trifluoromethyl)-3-(trimethylsilyl)pyrrolidin-2-one (8j).



Using **general procedure 1**, compound **8j** was synthesized from **4j** (317 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8j** was obtained as colorless oil (223 mg, 0.932 mmol, 93%). **General procedure 2**: 83% yield.  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.19 (s, 9H), 2.11 – 2.22 (m, 1H), 2.30 – 2.42 (m, 1H), 2.86 (s, 3H), 3.20 – 3.31 (m, 1H), 3.39 – 3.50 (m, 1H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  -3.1, 22.2 (q,  $J = 3.1$  Hz), 29.9, 46.2 (q,  $J = 26.3$  Hz), 47.1, 127.8 (q,  $J = 279.3$  Hz), 170.2 (q,  $J = 4.0$  Hz).  $^{19}\text{F NMR}$  (471 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.96. **IR** (ATR, neat): 2958, 1678, 1506, 1402, 1304, 1250, 1161, 1123, 1080, 843, 700  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_9\text{H}_{17}\text{NOSiF}_3$ :  $[\text{M}+\text{H}^+]$  240.1026, found: 240.1028.

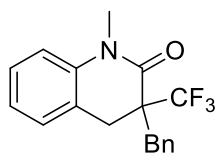


### 1-Methyl-3-(trifluoromethyl)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)pyrrolidin-2-one (8k).



Using **general procedure 1**, compound **8k** was synthesized from **4k** (366 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8k** was obtained as colorless oil (202.5 mg, 0.73 mmol, 73%). **General procedure 2**: 54% yield.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.11 (s, 9H), 2.38 (dd,  $J = 7.9, 6.5$  Hz, 2H), 2.59 (d,  $J = 16.7$  Hz, 1H), 2.89 (s, 2H), 2.93 (d,  $J = 16.9$  Hz, 1H), 3.38 (t,  $J = 7.2$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  0.0, 23.5 (q,  $J = 3.1$  Hz), 24.1 (q,  $J = 1.6$  Hz), 30.2, 46.5, 52.7 (q,  $J = 25.5$  Hz), 88.3, 100.0, 125.9 (q,  $J = 282.3$  Hz), 168.5 (q,  $J = 1.8$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -74.01. **IR** (ATR, neat): 2960, 2182, 1703, 1504, 1455, 1434, 1406, 1346, 1317, 1249, 1184, 1162, 1137, 1103, 1037, 839, 759, 688, 640  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{12}\text{H}_{18}\text{NOSiF}_3$ :  $[\text{M}^+]$  277.1105, found: 277.1109.

### 3-Benzyl-1-methyl-3-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (8l).

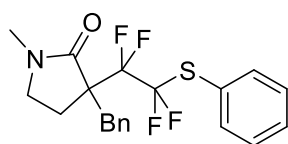


Using **general procedure 1**, compound **8l** was synthesized from **4l** (421 mg, 1.30 mmol) and **2a** (330 mg, 1.00 mmol). **8l** was obtained as a white solid (277 mg, 0.867 mmol, 87%). **General procedure 2**: 74% yield. **M.p.** 71.5–72.5 °C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.92 – 3.11 (m, 2H), 3.23 (d,  $J = 16.2$  Hz, 1H), 3.31 (s, 1H), 3.37 (d,  $J = 13.4$  Hz, 3H), 6.91 (d,  $J = 8.1$  Hz, 1H), 7.10 (d,  $J = 7.4$  Hz, 3H), 7.12 – 7.35 (m, 5H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  30.1, 30.2 (q,  $J = 3.0$  Hz), 51.9 (q,  $J = 23.2$  Hz), 114.3, 121.8, 126.3 (q,  $J = 284.4$  Hz), 123.5, 127.4, 127.9, 128.1, 128.4, 130.5, 134.3, 138.9, 165.8.  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -70.55. **IR** (ATR, neat): 2963, 1736, 1669, 1602, 1466, 1421, 1373, 1238, 1152, 1077, 1041, 965, 901, 751, 735, 698  $\text{cm}^{-1}$ . **HRMS** (ESI) calcd (m/z) for  $\text{C}_{18}\text{H}_{17}\text{NOF}_3$ :  $[\text{M}+\text{H}^+]$  320.1257, found: 320.1258.

### General procedure for $\alpha$ -perfluoroalkylation of KSA **4a**.

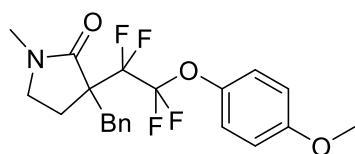
In a flame-dried 10 mL Schlenk flask equipped with rubber septum and magnetic stirring bar, ketene silyl amide (KSA) **4a** (282 mg, 0.78 mmol, 1.3 equiv) was weighed out under Ar. KSA **4a** was dissolved by addition of 1 mL anhydrous DCM and the resulting mixture was cooled to -78 °C (dry ice/acetone bath). Solution of  $\text{TMSNTf}_2$  in DCM (0.2 M, 6.0  $\mu\text{mol}$ , 0.01 equiv) was added via a microsyringe at once followed by addition of the selected reagent **2b–k** (0.6 mmol, 1 equiv). The mixture was allowed to reach rt overnight (19 h) with stirring. After evaporation of the solvent at reduced pressure the crude product was purified by column chromatography (Hexane/EtOAc, 3:1).

### 3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(phenylthio)ethyl)pyrrolidin-2-one (9ab).



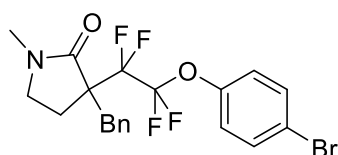
Using the general procedure, compound **9ab** was synthesized from **4a** (204 mg, 0.78 mmol) and **2b** (282 mg, 0.6 mmol). **9ab** was obtained as a white solid (217 mg, 0.55 mmol, 91%). **M.p.** = 70.7–72.5 °C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.95 – 2.14 (m, 2H), 2.37 – 2.52 (m, 1H), 2.64 (s, 3H), 2.88 – 3.03 (m, 2H), 3.56 (d,  $J = 13.1$  Hz, 1H), 7.18 – 7.27 (m, 2H), 7.24 – 7.34 (m, 4H), 7.39 – 7.46 (m, 2H), 7.46 – 7.53 (m, 1H), 7.70 (d,  $J = 7.2$  Hz, 2H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  23.0 (p,  $J = 3.4$  Hz), 29.9, 37.0 (p,  $J = 3.3$  Hz), 45.7, 54.3 (t,  $J = 20.6$  Hz), 118.05 (tt,  $J = 260.6, 32.3$  Hz), 124.1, 126.6 (tt,  $J = 290.9, 40.4$  Hz), 127.4, 128.3, 129.2, 130.6, 134.8, 137.4, 170.1.  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -111.19 (ddd,  $J_{\text{C,F}} = 275.9, 6.2, 2.3$  Hz, 1F), -109.04 (ddd,  $J_{\text{C,F}} = 276.1, 6.1, 2.2$  Hz, 1F), -81.45 (d,  $J_{\text{C,F}} = 220.5$  Hz, 1F), -80.63 (dd,  $J_{\text{C,F}} = 220.6, 5.6$  Hz, 1F). **IR** (ATR, neat): 2899, 1690, 1507, 1455, 1407, 1307, 1246, 1100, 1087, 946, 749, 729, 691  $\text{cm}^{-1}$ . **HRMS** (MALDI) calcd (m/z) for  $\text{C}_{20}\text{H}_{19}\text{NOSF}_4\text{Na}$ :  $[\text{M}+\text{Na}^+]$  420.1016, found: 420.1018.

### 3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(4-methoxyphenoxy)ethyl)pyrrolidin-2-one (9ac).



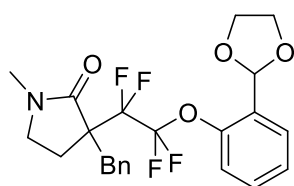
Using the general procedure, compound **9ac** was synthesized from **4a** (204 mg, 0.78 mmol) and **2c** (291 mg, 0.6 mmol). **9ac** was obtained as colorless oil (218 mg, 0.53 mmol, 88%). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 1.94 – 2.11 (m, 2H), 2.38 – 2.53 (m, 1H), 2.57 (s, 3H), 2.81 – 3.08 (m, 2H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.72 (s, 3H), 6.74 – 6.84 (m, 2H), 7.02 – 7.10 (m, 2H), 7.11 – 7.24 (m, 5H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 23.1, 29.9, 37.0, 45.9, 53.9 (t, *J* = 20.2 Hz), 55.6, 114.6, 116.4 (tt, *J* = 260.6, 34.2 Hz), 118.1 (tt, *J* = 276.9, 34.2 Hz), 123.0, 127.3, 128.3, 130.6, 135.1, 142.2 (t, *J* = 1.9 Hz), 158.0, 170.2. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>) δ -118.52 (dd, *J*<sub>C,F</sub> = 271.6, 4.9 Hz, 1F), -116.44 (dd, *J*<sub>C,F</sub> = 271.6, 5.8 Hz, 1F), -80.85 (dd, *J*<sub>C,F</sub> = 143.9, 5.7 Hz, 1F), -79.97 (dd, *J*<sub>C,F</sub> = 143.9, 5.2 Hz, 1F). **IR** (ATR, neat): 2937, 1694, 1505, 1455, 1278, 1173, 1055, 1029, 1018, 876, 728, 702, 645 cm<sup>-1</sup>. **HRMS** (MALDI) calcd (m/z) for C<sub>21</sub>H<sub>21</sub>NO<sub>3</sub>F<sub>4</sub>Na: [M+Na<sup>+</sup>] 434.1350, found: 434.1353.

### 3-Benzyl-3-(2-(4-bromophenoxy)-1,1,2,2-tetrafluoroethyl)-1-methylpyrrolidin-2-one (9ad).



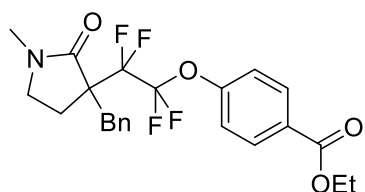
Using the general procedure, compound **9ad** was synthesized from **4a** (204 mg, 0.78 mmol) and **2d** (320 mg, 0.6 mmol). **9ad** was obtained as colorless oil (223 mg, 0.485 mmol, 81%). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 2.07 – 2.18 (m, 2H), 2.48 – 2.62 (m, 1H), 2.68 (s, 3H), 2.98 (s, 1H), 3.04 (dd, *J* = 9.0, 6.1 Hz, 1H), 3.63 (d, *J* = 13.1 Hz, 1H), 7.11 – 7.18 (m, 2H), 7.22 – 7.34 (m, 5H), 7.49 – 7.57 (m, 2H). **<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 23.03 (d, *J* = 3.03 Hz), 29.9, 36.9 (p, *J* = 2.02 Hz), 45.8, 53.8 (t, *J* = 20.2 Hz), 116.2 (tt, *J* = 260.9, 34.1 Hz), 117.9 (tt, *J* = 280.8, 29.3 Hz), 119.8, 123.5, 127.4, 128.3, 130.6, 132.8, 134.9, 147.9 (t, *J* = 2.02 Hz), 169.9. **<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>) δ -118.28 (dd, *J*<sub>C,F</sub> = 272.5, 4.7 Hz, 1F), -116.36 (dd, *J*<sub>C,F</sub> = 272.6, 5.0 Hz, 1F), -80.87 (dd, *J*<sub>C,F</sub> = 143.0, 5.0 Hz, 1F), -79.92 (dd, *J*<sub>C,F</sub> = 143.3, 4.3 Hz, 1F). **IR** (ATR, neat): 2887, 1694, 1483, 1455, 1403, 1327, 1183, 1067, 1056, 1011, 877, 782, 729, 702 cm<sup>-1</sup>. **HRMS** (MALDI) calcd (m/z) for C<sub>20</sub>H<sub>18</sub>NO<sub>2</sub>F<sub>4</sub>NaBr: [M+Na<sup>+</sup>] 482.0349, found: 482.0349.

### 3-(2-(2-(1,3-Dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)-3-benzyl-1-methylpyrrolidin-2-one (9ae).



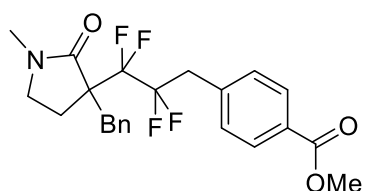
Using the general procedure, compound **9ae** was synthesized from **4a** (204 mg, 0.78 mmol) and **2e** (316 mg, 0.6 mmol). **9ae** was obtained as colorless oil (240 mg, 0.53 mmol, 88%). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 1.86 – 2.16 (m, 2H), 2.49 (dd, *J* = 9.0, 5.9 Hz, 1H), 2.54 (s, 3H), 2.91 (td, *J* = 9.2, 3.2 Hz, 1H), 2.99 (d, *J* = 13.1 Hz, 1H), 3.51 (d, *J* = 13.1 Hz, 1H), 3.84 – 4.14 (m, 4H), 6.01 (s, 1H), 7.08 – 7.45 (m, 8H), 7.57 (dd, *J* = 7.9, 1.7 Hz, 1H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>) δ 23.1 (t, *J* = 3.0 Hz), 29.9, 36.81 – 36.93 (m), 45.9, 53.9 (d, *J* = 20.2 Hz), 65.4, 98.7, 116.4 (tt, *J* = 260.3, 34.5 Hz), 118.3 (tt, *J* = 277.5, 33.7 Hz), 121.6, 126.6, 127.3, 127.7, 128.3, 130.3, 130.6, 130.8, 135.1, 147.4, 170.1. **<sup>19</sup>F NMR** (282 MHz, CDCl<sub>3</sub>) δ -118.52 (dt, *J*<sub>C,F</sub> = 271.7, 3.2 Hz, 1F), -116.26 (dt, *J*<sub>C,F</sub> = 271.8, 3.2 Hz, 1F), -79.49 (bs, 2F). **IR** (ATR, neat): 2887, 1695, 1455, 1403, 1326, 1110, 1068, 1019, 964, 942, 755, 729, 702 cm<sup>-1</sup>. **HRMS** (MALDI) calcd (m/z) for C<sub>23</sub>H<sub>23</sub>NO<sub>4</sub>F<sub>4</sub>Na: [M+Na<sup>+</sup>] 476.1455, found: 476.1454.

### Ethyl 4-(2-(3-benzyl-1-methyl-2-oxopyrrolidin-3-yl)-1,1,2,2-tetrafluoroethoxy)benzoate (**9af**).



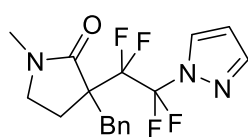
Using the general procedure, compound **9af** was synthesized from **4a** (204 mg, 0.78 mmol) and **2f** (316 mg, 0.6 mmol). **9af** was obtained as colorless oil (210 mg, 0.46 mmol, 77%).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.47 (t,  $J = 7.1$  Hz, 3H), 2.08 – 2.29 (m, 2H), 2.52 – 2.70 (m, 1H), 2.73 (s, 3H), 2.96 – 3.28 (m, 2H), 3.69 (d,  $J = 13.1$  Hz, 1H), 4.46 (q,  $J = 7.1$  Hz, 2H), 7.28 – 7.38 (m, 7H), 8.11 – 8.21 (m, 2H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  14.3, 23.0, 29.9, 36.9, 45.8, 53.8 (t,  $J = 20.2$  Hz), 61.2, 116.2 (tt,  $J = 261.1$ , 33.9 Hz), 118.1 (tt,  $J = 279.6$ , 34.5 Hz), 127.4, 128.3, 128.6, 130.6, 131.4, 134.9, 165.5, 170.0.  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -118.33 (ddd,  $J_{\text{C,F}} = 272.7$ , 4.3, 2.2 Hz, 1F), -116.27 (dd,  $J_{\text{C,F}} = 272.7$ , 4.8 Hz, 1F), -80.85 (dd,  $J_{\text{C,F}} = 143.1$ , 3.4 Hz, 1F), -79.77 (dd,  $J_{\text{C,F}} = 142.9$ , 4.1 Hz, 1F). **IR** (ATR, neat): 2979, 1696, 1605, 1503, 1404, 1274, 1162, 1098, 1056, 908, 753, 729, 702  $\text{cm}^{-1}$ . **HRMS** (MALDI) calcd (m/z) for  $\text{C}_{23}\text{H}_{23}\text{NO}_4\text{F}_4\text{Na}$ :  $[\text{M}+\text{Na}^+]$  476.1455, found: 476.1456.

### Methyl 4-(3-(3-benzyl-1-methyl-2-oxopyrrolidin-3-yl)-2,2,3,3-tetrafluoropropyl)benzoate (**9ag**).



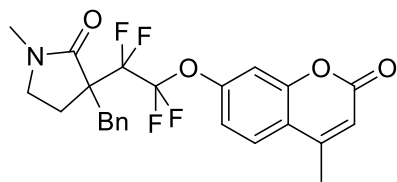
Using the general procedure, compound **9ag** was synthesized from **4a** (204 mg, 0.78 mmol) and **2g** (316 mg, 0.6 mmol). **9ag** was obtained as colorless oil (210 mg, 0.46 mmol, 91%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.07 (q,  $J = 9.5$  Hz, 2H), 2.47 (p,  $J = 9.8$  Hz, 1H), 2.64 (s, 3H), 2.89 – 3.03 (m, 2H), 3.36 – 3.63 (m, 3H), 3.94 (s, 3H), 7.16 – 7.34 (m, 5H), 7.41 (d,  $J = 8.0$  Hz, 2H), 8.03 (d,  $J = 8.2$  Hz, 2H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  22.8, 29.8, 36.9, 37.5 (t,  $J = 23.2$  Hz), 45.8, 52.1, 53.9 (t,  $J = 20.2$  Hz), 118.0 (tt,  $J = 260.6$ , 34.3 Hz), 119.6 (tt,  $J = 253.5$ , 38.4 Hz), 127.3, 128.3, 129.5, 129.6, 130.6, 131.1, 135.0, 135.9, 166.8, 170.42 (d,  $J = 4.04$  Hz).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.61 (dd,  $J_{\text{C,F}} = 279.4$ , 13.3 Hz), -112.86 (dd,  $J_{\text{C,F}} = 279.3$ , 14.3 Hz), -109.11 (dd,  $J_{\text{C,F}} = 261.5$ , 13.5 Hz), -107.76 (dd,  $J_{\text{C,F}} = 261.4$ , 14.4 Hz). **IR** (ATR, neat): 2952, 1720, 1692, 1455, 1278, 1182, 1084, 1066, 1039, 907, 772, 759, 702, 646  $\text{cm}^{-1}$ . **HRMS** (MALDI) calcd (m/z) for  $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_3\text{F}_4$ :  $[\text{M}+\text{NH}_4^+]$  455.1952, found: 455.1950.

### 3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(1H-pyrazol-1-yl)ethyl)pyrrolidin-2-one (**9ah**).



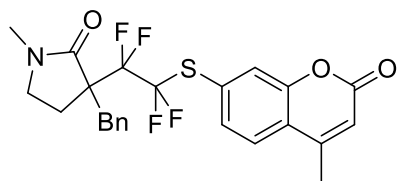
Using the general procedure, compound **9ah** was synthesized from **4a** (204 mg, 0.78 mmol) and **2h** (257 mg, 0.6 mmol). **9ah** was obtained as colorless oil (175 mg, 0.49 mmol, 82%).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.81 – 2.10 (m, 2H), 2.17 – 2.35 (m, 1H), 2.52 (s, 3H), 2.63 (d,  $J = 13.0$  Hz, 1H), 2.88 (td,  $J = 9.3$ , 3.1 Hz, 1H), 3.32 (d,  $J = 13.0$  Hz, 1H), 6.34 – 6.49 (m, 1H), 7.03 – 7.30 (m, 5H), 7.72 (d,  $J = 22.8$  Hz, 2H).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  22.6 (p,  $J = 3.2$  Hz), 29.8, 35.2 – 38.0 (m), 45.7, 54.0 (t,  $J = 20.2$  Hz), 108.4, 114.5 (tt,  $J = 268.5$ , 35.3 Hz), 117.9 (tt,  $J = 261.0$ , 38.2 Hz), 127.4, 128.3, 129.5, 130.5, 134.6, 142.6, 169.0 – 170.3 (m).  $^{19}\text{F NMR}$  (282 MHz,  $\text{CDCl}_3$ )  $\delta$  -116.69 (dt,  $J_{\text{C,F}} = 276.2$ , 5.5 Hz, 1F), -114.15 (dt,  $J_{\text{C,F}} = 275.9$ , 4.0 Hz, 1F), -93.74 (dt,  $J_{\text{C,F}} = 219.3$ , 4.0 Hz, 1F), -91.57 (dt,  $J_{\text{C,F}} = 219.2$ , 5.0 Hz, 1F). **IR** (ATR, neat): 2887, 1693, 1421, 1392, 1340, 1160, 1122, 1088, 918, 758, 730, 702, 633  $\text{cm}^{-1}$ . **HRMS** (MALDI) calcd (m/z) for  $\text{C}_{17}\text{H}_{21}\text{N}_4\text{OF}_4$ :  $[\text{M}+\text{NH}_4^+]$  373.1646, found: 373.1646.

### 3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)-pyrrolidin-2-one (9ai).



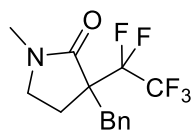
Using the general procedure, compound **9ai** was synthesized from **4a** (204 mg, 0.78 mmol) and **2i** (322 mg, 0.6 mmol). **9ai** was obtained as colorless oil (220 mg, 0.47 mmol, 79%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.88 – 2.19 (m, 2H), 2.37 (s, 3H), 2.40 – 2.54 (m, 1H), 2.59 (s, 3H), 2.90 (d, *J* = 13.1 Hz, 1H), 2.94 – 3.05 (m, 1H), 3.54 (d, *J* = 13.1 Hz, 1H), 6.16 – 6.27 (m, 1H), 7.08 – 7.27 (m, 7H), 7.50 – 7.62 (m, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 18.7, 23.0, 29.9, 36.9, 45.8, 53.9 (t, *J* = 20.2 Hz), 110.0, 114.9, 116.2 (tt, *J* = 260.2, 33.7 Hz), 117.5, 118.1 (tt, *J* = 279.0, 34.5 Hz), 118.3, 125.8, 127.5, 128.4, 130.6, 134.8, 151.2, 151.7, 154.1, 160.1, 169.9. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -118.1 (dt, *J*<sub>C,F</sub> = 273.2, 3.2 Hz, 1F), -116.1 (ddd, *J*<sub>C,F</sub> = 273.5, 2.8, 0.9 Hz, 1F), -80.98 (ddd, *J*<sub>C,F</sub> = 142.6, 4.7, 2.4 Hz), -79.90 (ddd, *J*<sub>C,F</sub> = 143.1, 5.1, 2.8 Hz, 1F). IR (ATR, neat): 2933, 1730, 1694, 1627, 1613, 1496, 1404, 1223, 1177, 1110, 1068, 1055, 1016, 979, 869, 748, 702 cm<sup>-1</sup>. HRMS (MALDI) calcd (m/z) for C<sub>24</sub>H<sub>21</sub>NO<sub>4</sub>F<sub>4</sub>Na: [M+Na<sup>+</sup>] 486.1299, found: 486.1298.

### 3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-((4-methyl-2-oxo-2H-chromen-7-yl)thio)ethyl)-pyrrolidin-2-one (9aj).



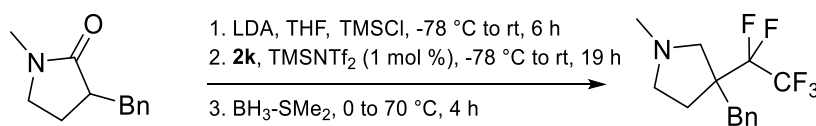
Using the general procedure, compound **9aj** was synthesized from **4a** (204 mg, 0.78 mmol) and **2j** (331 mg, 0.6 mmol). **9aj** was obtained as colorless oil (220 mg, 0.46 mmol, 76%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.99 – 2.25 (m, 2H), 2.35 – 2.51 (m, 1H), 2.53 (s, 3H), 2.69 (s, 3H), 2.97 (d, *J* = 13.1 Hz, 1H), 2.98 – 3.11 (m, 1H), 3.60 (d, *J* = 13.1 Hz, 1H), 6.40 – 6.49 (m, 1H), 7.25 – 7.37 (m, 6H), 7.63 – 7.73 (m, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 18.6, 22.9, 29.8, 37.0, 45.7, 54.2 (t, *J* = 20.2 Hz), 116.5, 117.9 (tt, *J* = 262.1, 32.7 Hz), 121.5, 124.99, 125.01, 125.6 (tt, *J* = 292.3, 41.6 Hz), 127.4, 128.3, 128.5, 130.5, 132.2, 134.6, 151.5, 153.1, 159.9, 169.88 (d, *J* = 2.5 Hz). <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -110.80 (ddd, *J*<sub>C,F</sub> = 276.5, 5.9, 2.7 Hz), -108.6 (ddd, *J*<sub>C,F</sub> = 276.5, 5.9, 2.7 Hz), -80.9 (ddd, *J*<sub>C,F</sub> = 220.1, 5.6, 2.3 Hz, 1F), -79.87 (ddd, *J*<sub>C,F</sub> = 220.3, 5.7, 2.4 Hz). IR (ATR, neat): 2886, 2247, 1722, 1690, 1624, 1602, 1495, 1397, 1385, 1173, 1075, 990, 909, 726, 702, 672 cm<sup>-1</sup>. HRMS (MALDI) calcd (m/z) for C<sub>24</sub>H<sub>21</sub>NSO<sub>3</sub>F<sub>4</sub>Na: [M+Na<sup>+</sup>] 502.1070, found: 502.1069.

### 3-Benzyl-1-methyl-3-(perfluoroethyl)pyrrolidin-2-one (9ak).



Using the general procedure, compound **9ak** was synthesized from **4a** (204 mg, 0.78 mmol) and **2k** (228 mg, 0.6 mmol). **9ak** was obtained as white solid (175 mg, 0.57 mmol, 95%). M.p. = 65.5–66.3 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.77 – 2.00 (m, 2H), 2.08 – 2.29 (m, 1H), 2.47 (s, 3H), 2.67 (d, *J* = 13.1 Hz, 1H), 2.73 – 2.88 (m, 1H), 3.35 (d, *J* = 13.1 Hz, 1H), 6.98 – 7.09 (m, 2H), 7.06 – 7.16 (m, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 22.8 (p, *J* = 2.7 Hz), 29.9, 35.2 – 38.7 (m), 45.6, 53.4 (t, *J* = 19.8 Hz), 115.4 (tq, *J* = 260.3, 36.1 Hz), 119.4 (qt, *J* = 288.7, 37.3 Hz), 127.6, 128.4, 130.4, 134.3, 169.2. <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ -119.42 (d, *J*<sub>C,F</sub> = 278.6 Hz, 1F), -117.27 (d, *J*<sub>C,F</sub> = 278.6 Hz, 1F), -78.39 (s, 3F). IR (ATR, neat): 2893, 1693, 1496, 1455, 1360, 1333, 1177, 1114, 1074, 1059, 964, 878, 747, 731, 701, 686 cm<sup>-1</sup>. HRMS (MALDI) calcd (m/z) for C<sub>14</sub>H<sub>14</sub>NONaF<sub>5</sub>: [M+Na<sup>+</sup>] 330.0888, found: 330.0885.

### Synthesis of 3-benzyl-1-methyl-3-(perfluoroethyl)pyrrolidine (**10**).



A flame-dried 25-mL Schlenk flask equipped with rubber septum and magnetic stirring bar was charged under Ar atmosphere subsequently with diisopropylamine (57.1 mg, 0.564 mmol, 1.43 equiv) and anhydrous THF (2 mL). To this well-stirred solution held at -18°C (ice/salt bath) was added a solution of n-BuLi (1.6 M in hexanes, 0.539 mmol, 1.36 equiv) via a syringe. The resulting solution was stirred at this temperature for 15 minutes, then the solution was cooled to -78°C. A solution of lactam **3a** (0.513 mmol, 1.3 equiv) in anhydrous THF (1 mL) was introduced dropwise via a syringe within 1 minute. Lithiation was conducted for 60 minutes, then neat trimethylchlorosilane (0.1 mL, 0.789 mmol, 2 equiv) was introduced at once. The resultant reaction mixture was stirred for 6 h allowing to gradually reach rt. After the reaction mixture was cooled to -78°C and the solution of TMSNTf<sub>2</sub> in DCM (0.2 M, 3.95 mmol, 0.01 equiv) was added via a microsyringe at once followed by addition of solid 3,3-dimethyl-1-(perfluoroethyl)-1,3-dihydro-1λ<sup>3</sup>-benzo[d][1,2]iodaoxole (**2k**) (150 mg, 0.395 mmol, 1 equiv). The mixture was allowed to reach rt overnight 19 h with stirring. The final solution was cooled to 0°C and BH<sub>3</sub>·Me<sub>2</sub>S (10 M in THF, 1.28 mmol, 3.25 equiv) was added dropwise over 5 minutes and after removal of the cooling bath the mixture was refluxed for 3 h. The reaction mixture was then cooled to rt and the excess of BH<sub>3</sub> was eliminated by dropwise addition of MeOH (1 mL). After removal of the solvent at reduced pressure the crude was purified by column chromatography (Hexane/EtOAc, 5:1) giving 82 mg (71%) of pure product **10** as colorless oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 1.96 – 2.10 (m, 3H), 2.18 – 2.25 (m, 4H), 2.40 – 2.51 (m, 1H), 2.65 – 2.73 (m, 1H), 2.89 – 2.98 (m, 2H), 3.03 (d, *J* = 13.9 Hz, 1H), 7.22 – 7.41 (m, 5H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 30.9, 39.3, 41.6, 51.3 (t, *J* = 18.9 Hz), 55.5, 60.1 (m), 117.5 (tq, *J* = 257.2, 35.2 Hz), 120.0 (qt, *J* = 288.1, 37.9 Hz), 126.9, 128.1, 131.3, 136.1. <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -116.9 (d, *J*<sub>C,F</sub> = 273.2 Hz, 1F), -116.2 (d, *J*<sub>C,F</sub> = 277.9 Hz, 1F), -77.6 (s, 3F). IR (ATR, neat): 2942, 2792, 1484, 1454, 1333, 1196, 1141, 1089, 1033, 989, 758, 700 cm<sup>-1</sup>. HRMS (ESI) calcd (m/z) for C<sub>14</sub>H<sub>17</sub>NF<sub>5</sub>: [M+H<sup>+</sup>] 294.1276, found: 294.1280.

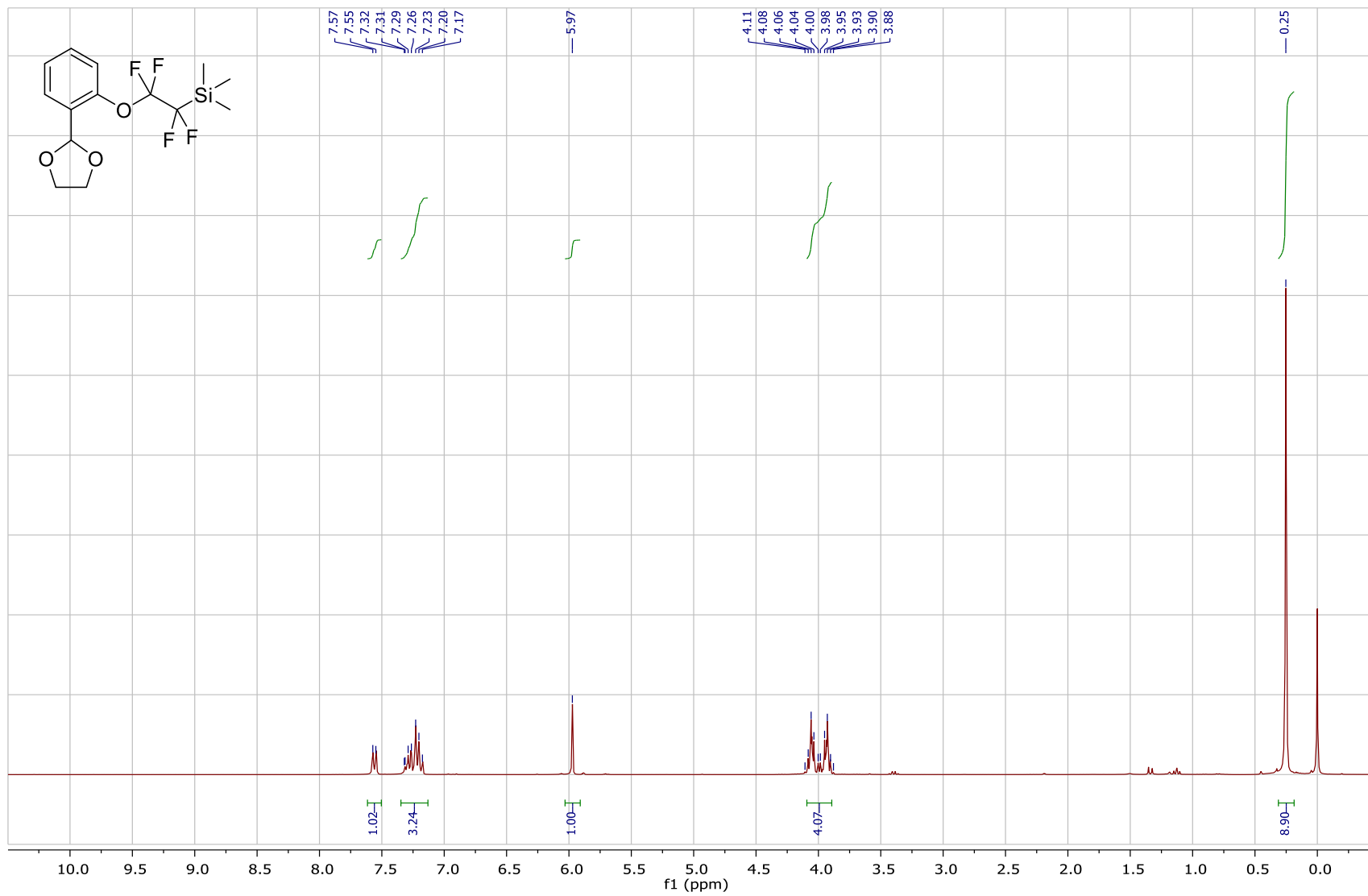
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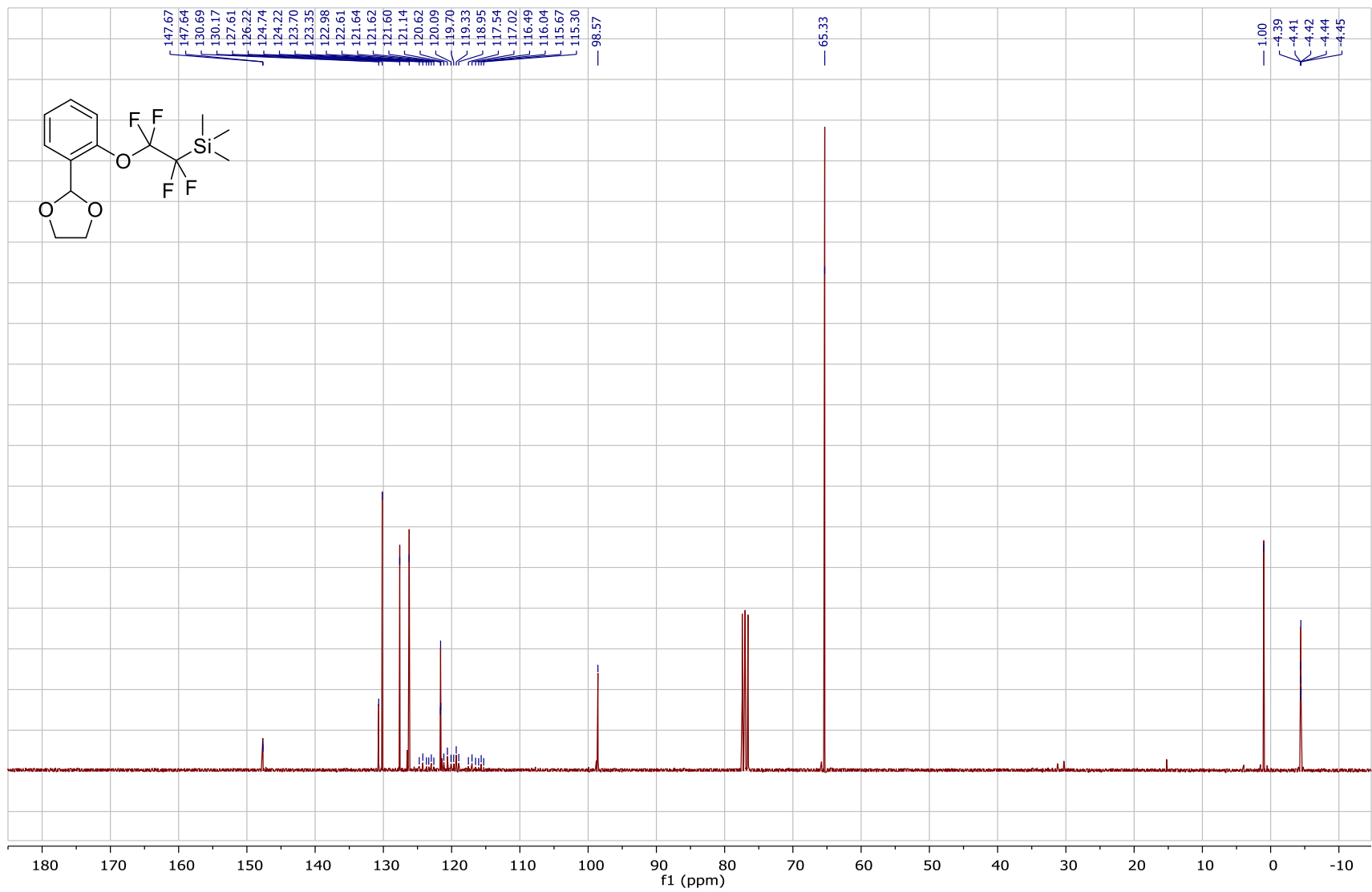


2-(2-(1,3-Dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)trimethylsilane

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

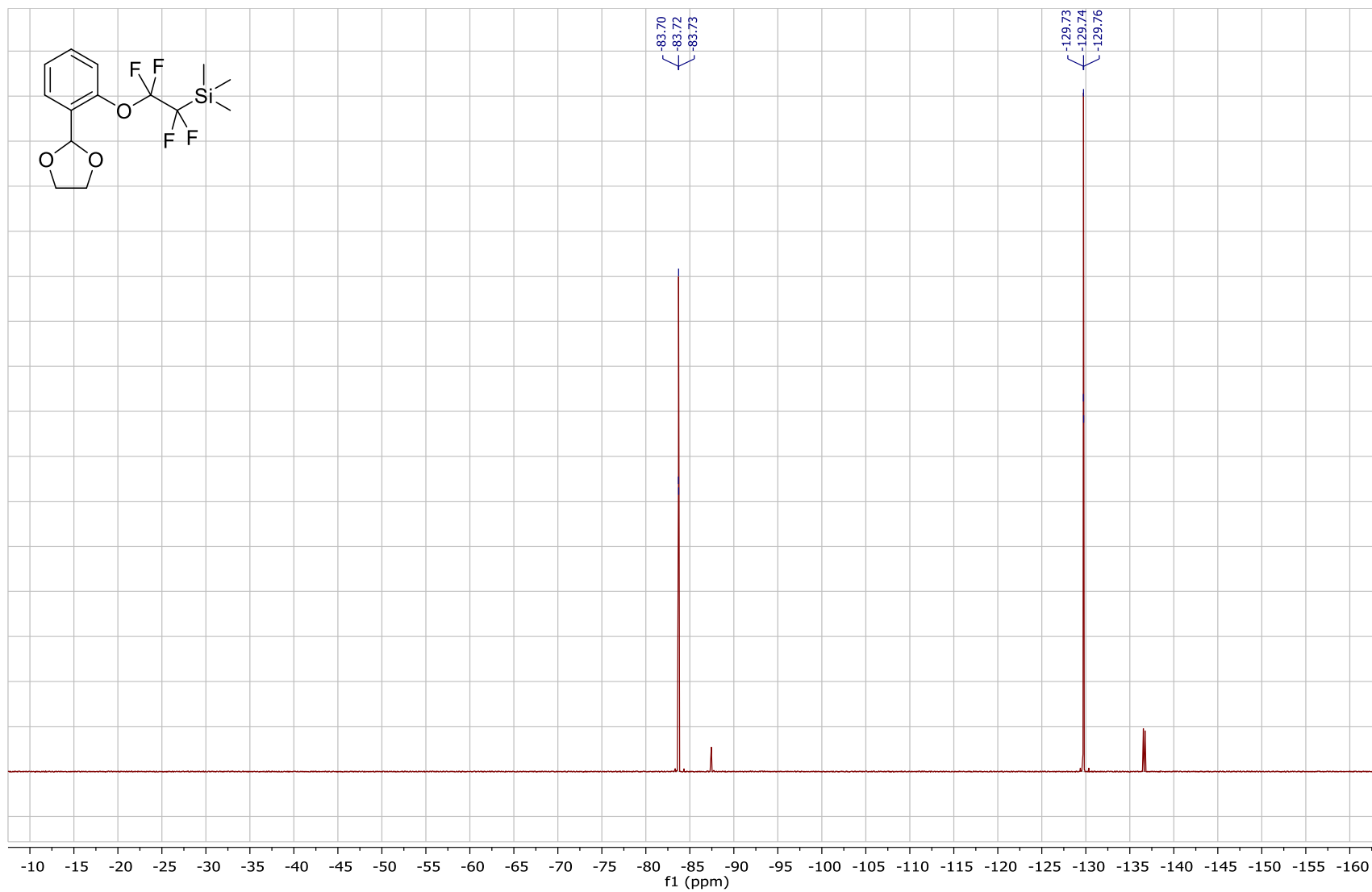


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



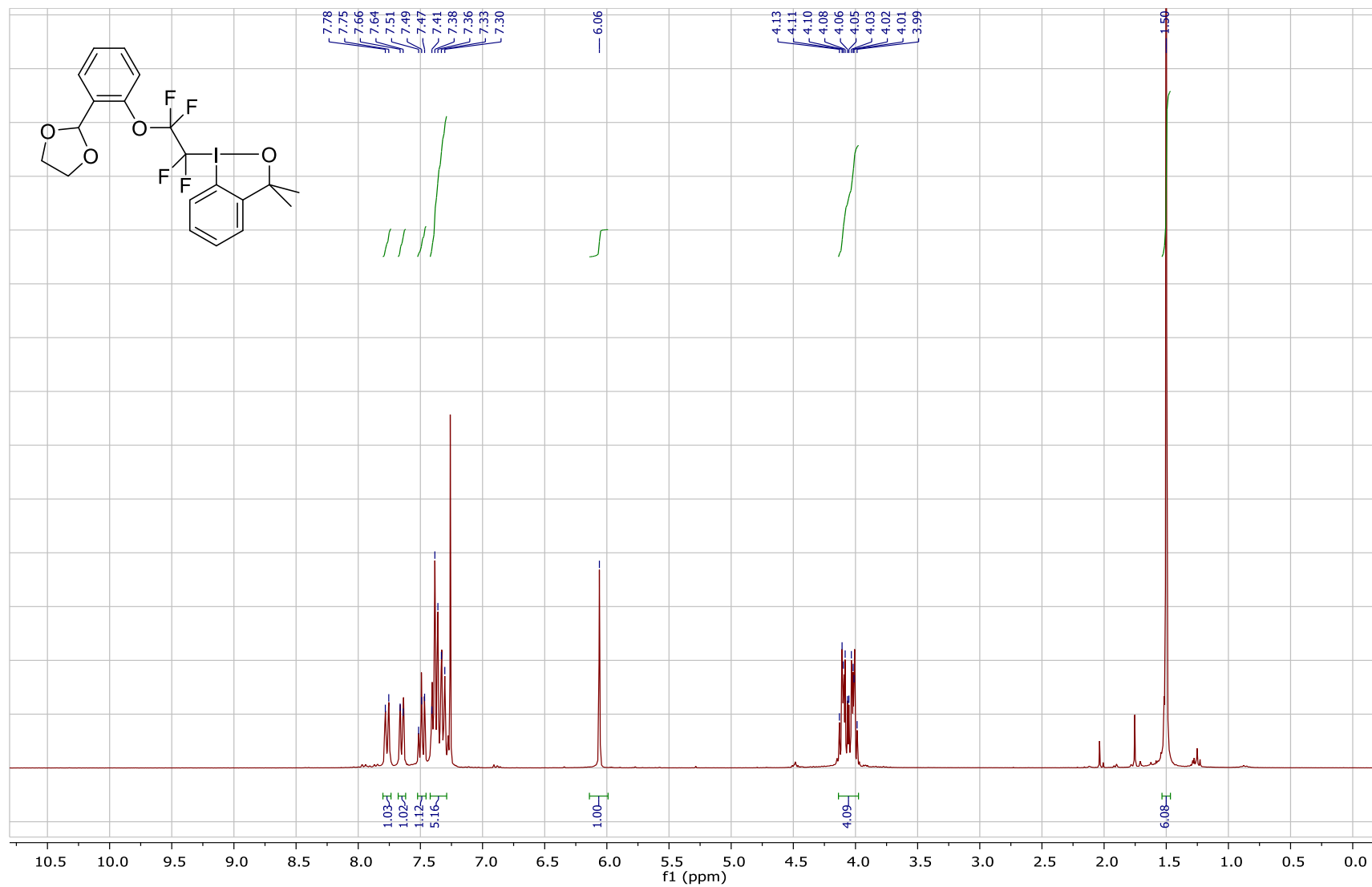


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

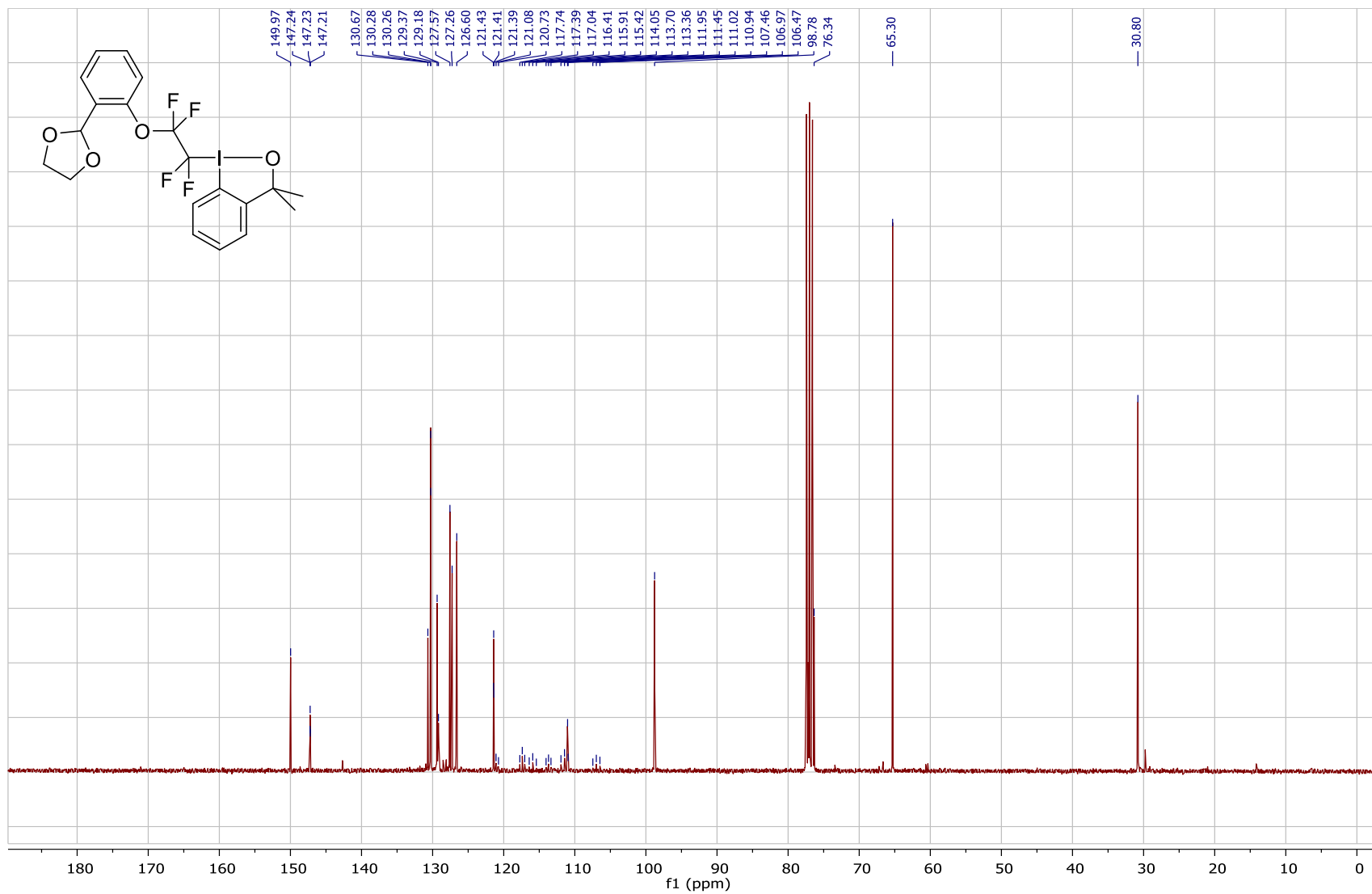


1-(2-(2-(1,3-dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)-3,3-dimethyl-1,3-dihydro-1 $\lambda^3$ -benzo[d][1,2]iodaoxole (**2e**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



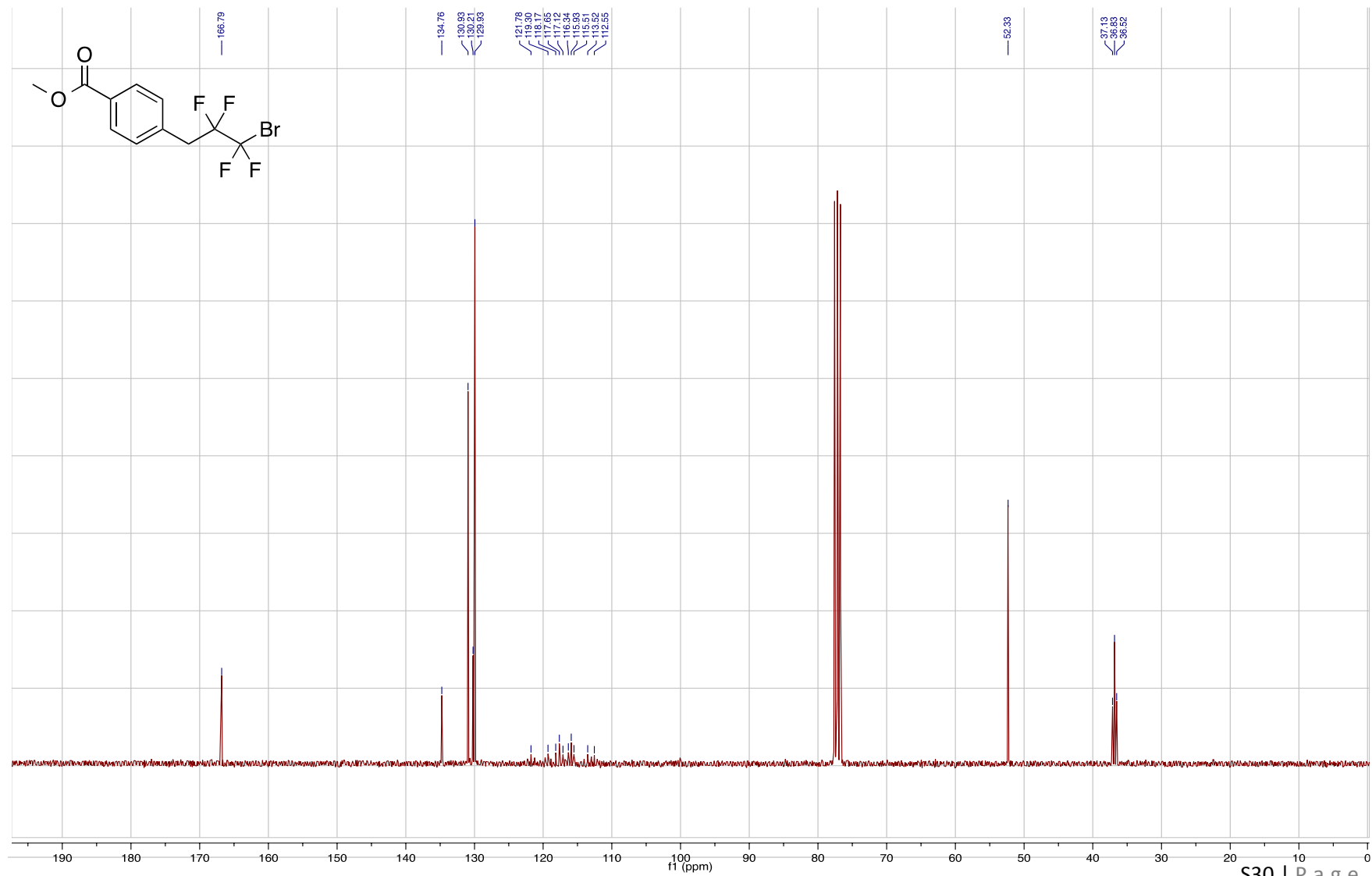


Methyl 4-(3-bromo-2,2,3,3-tetrafluoropropyl)benzoate

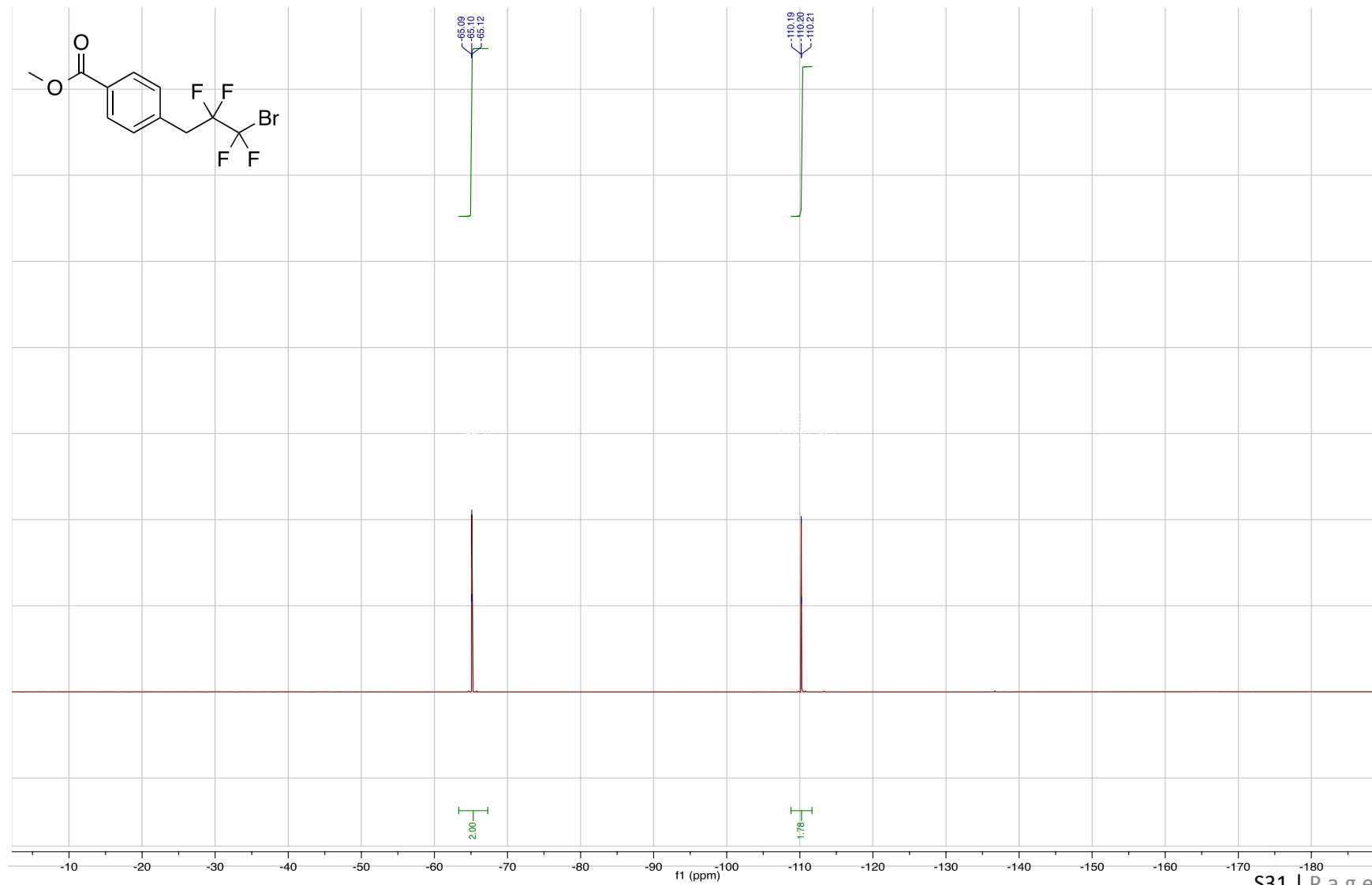
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )

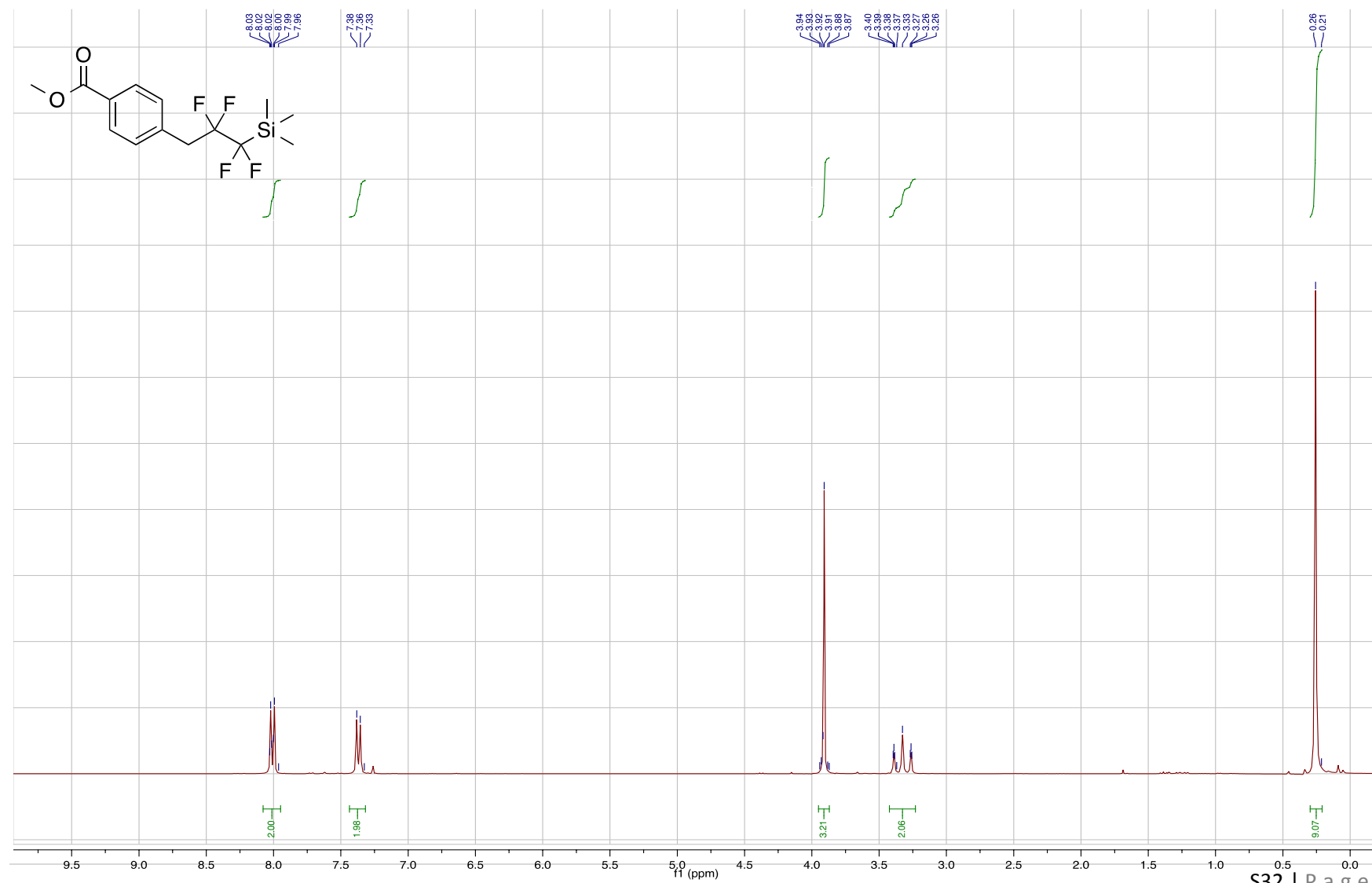


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



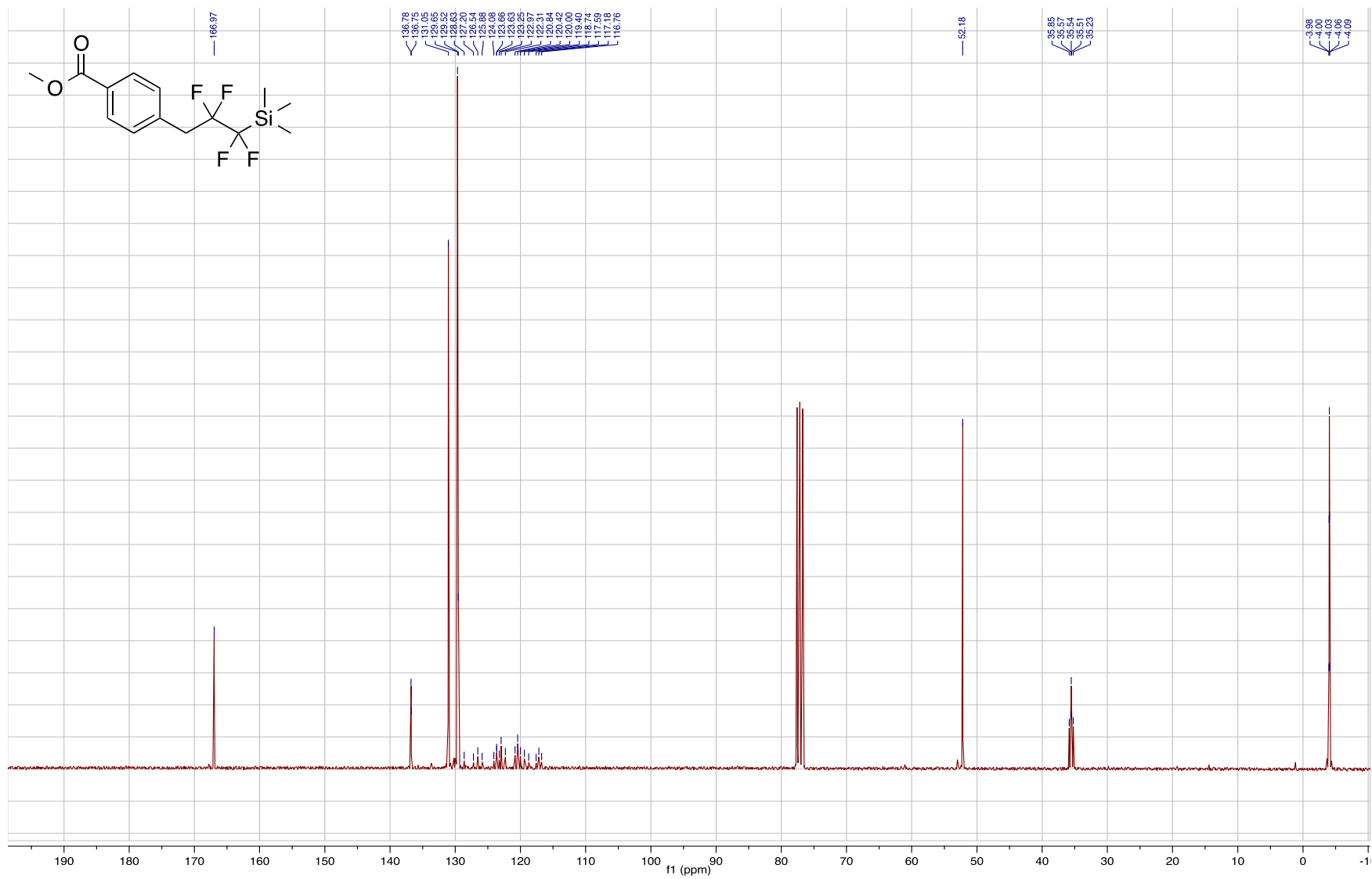
Methyl 4-(2,2,3,3-tetrafluoro-3-(trimethylsilyl)propyl)benzoate

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

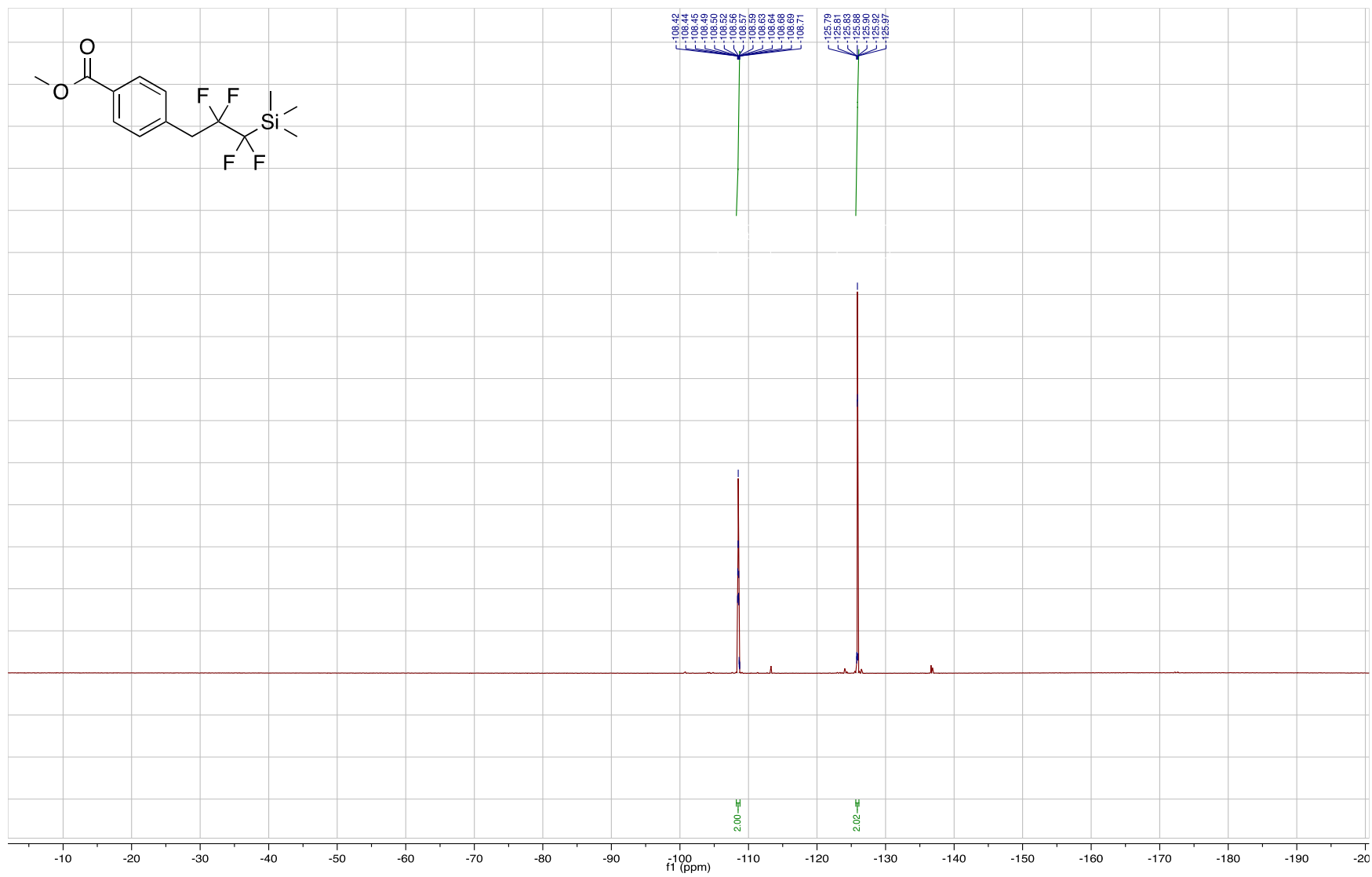




$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )

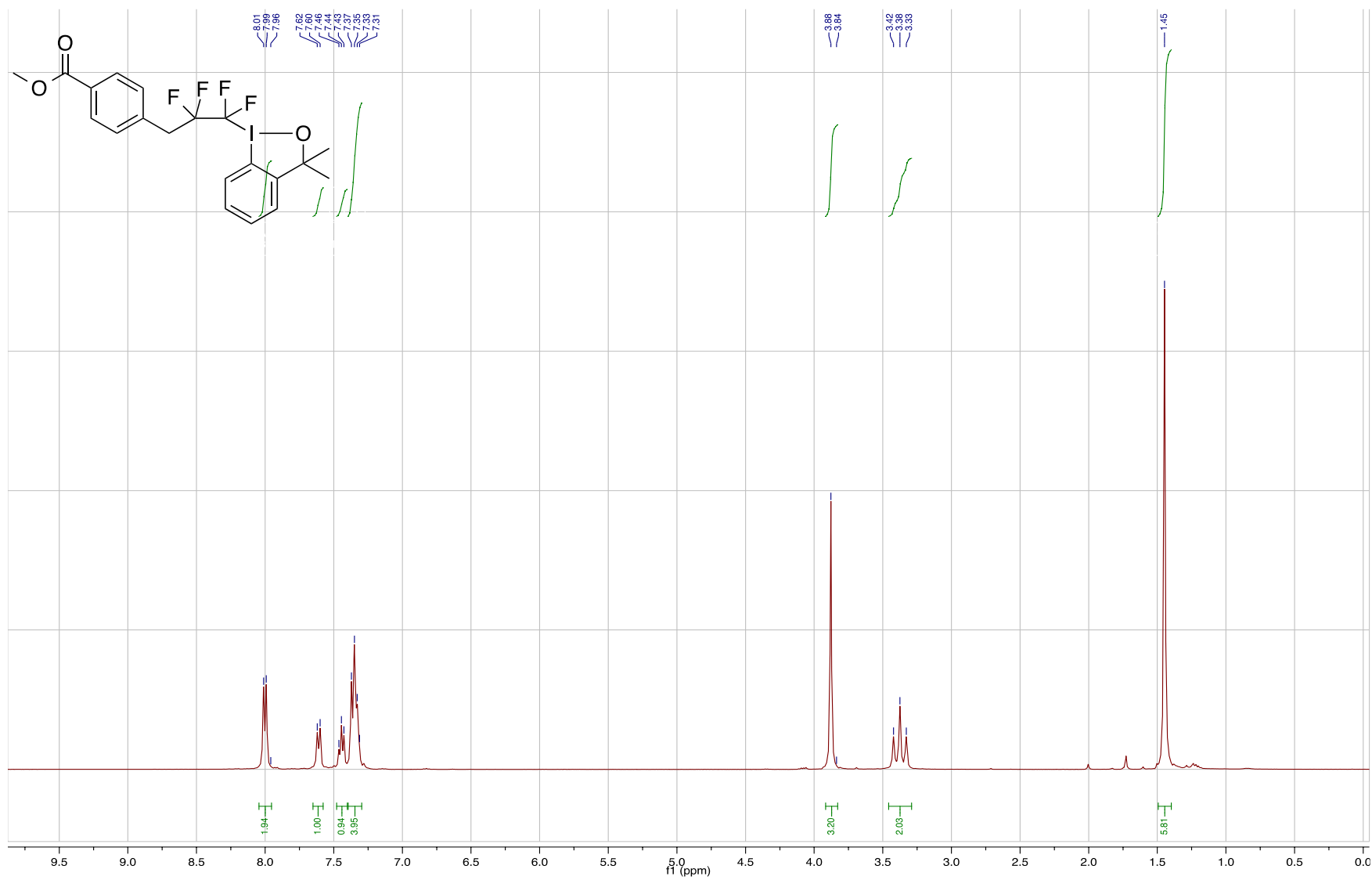


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

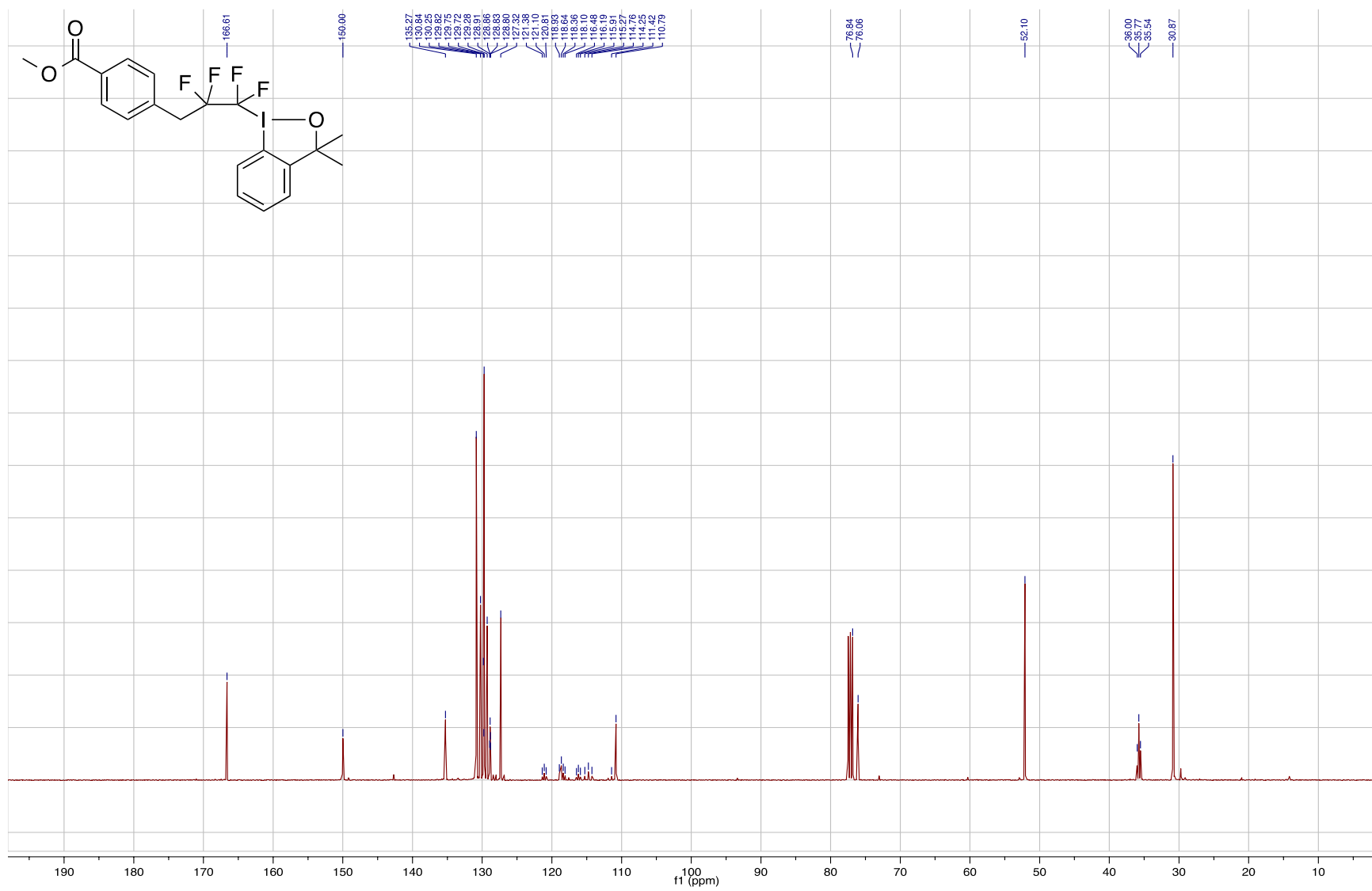


Methyl 4-(3-(3,3-dimethyl-1 $\lambda^3$ -benzo[d][1,2]iodaoxol-1(3*H*)-yl)-2,2,3,3-tetrafluoropropyl)benzoate (**2g**)

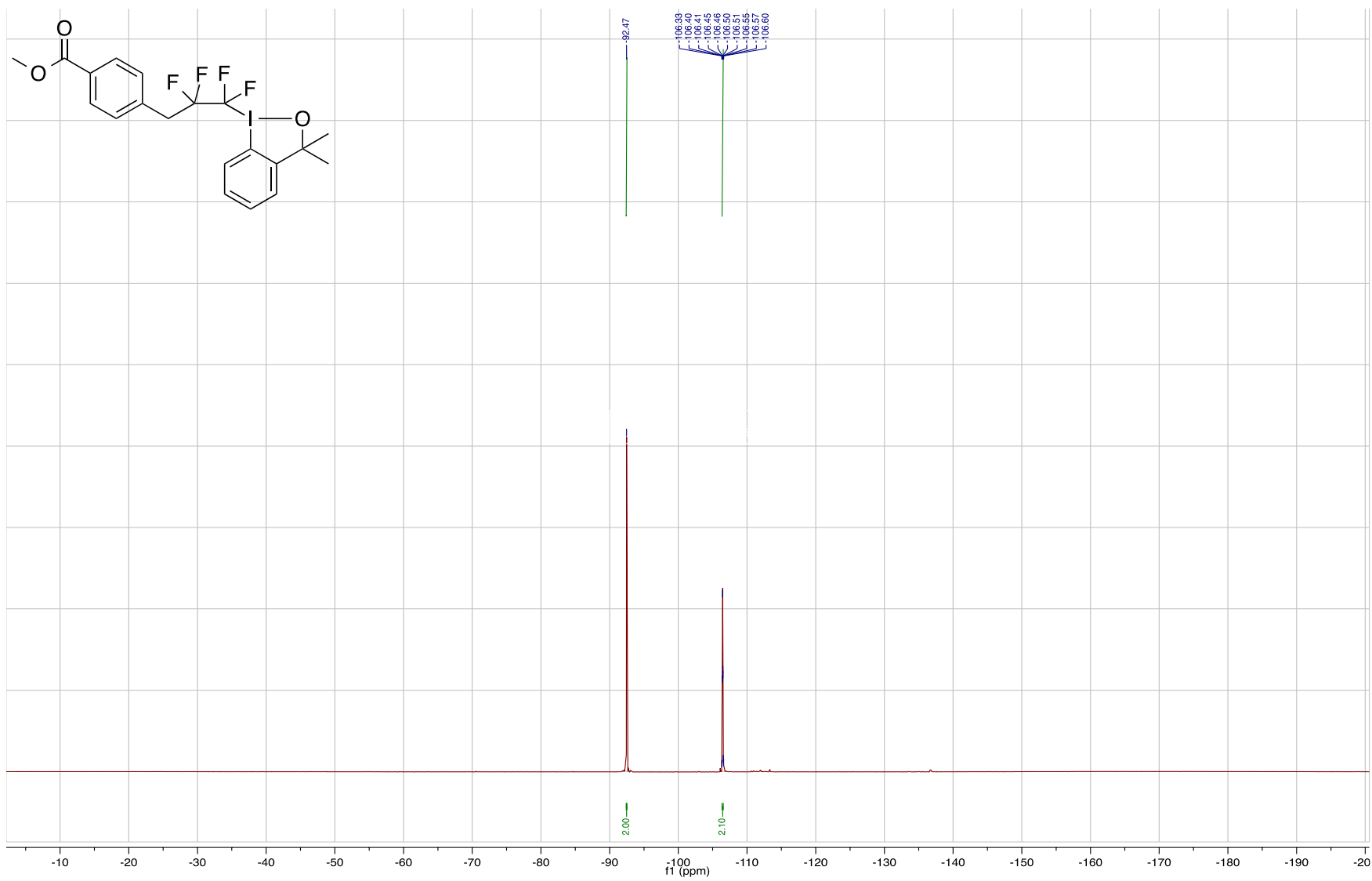
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )

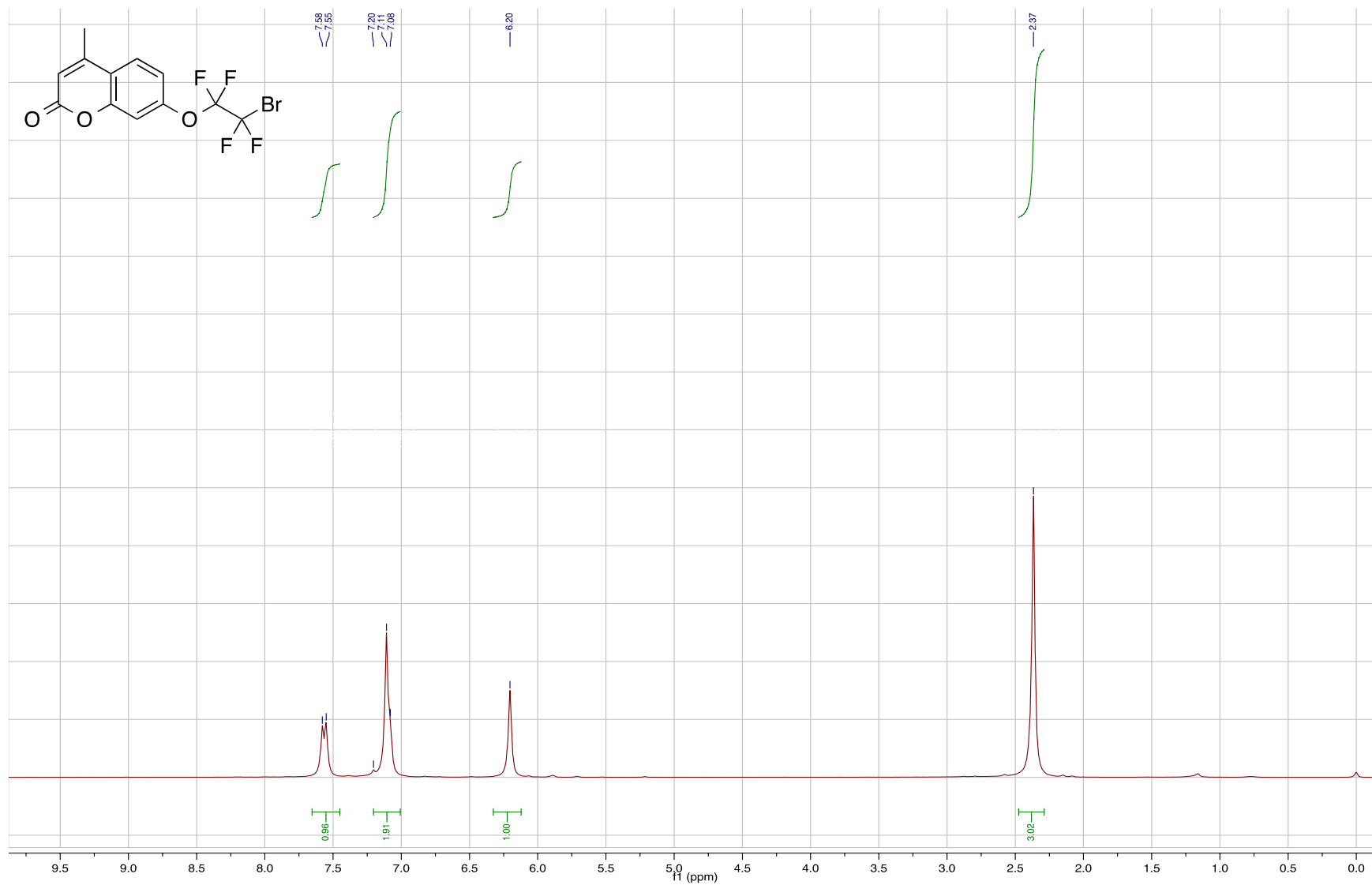


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

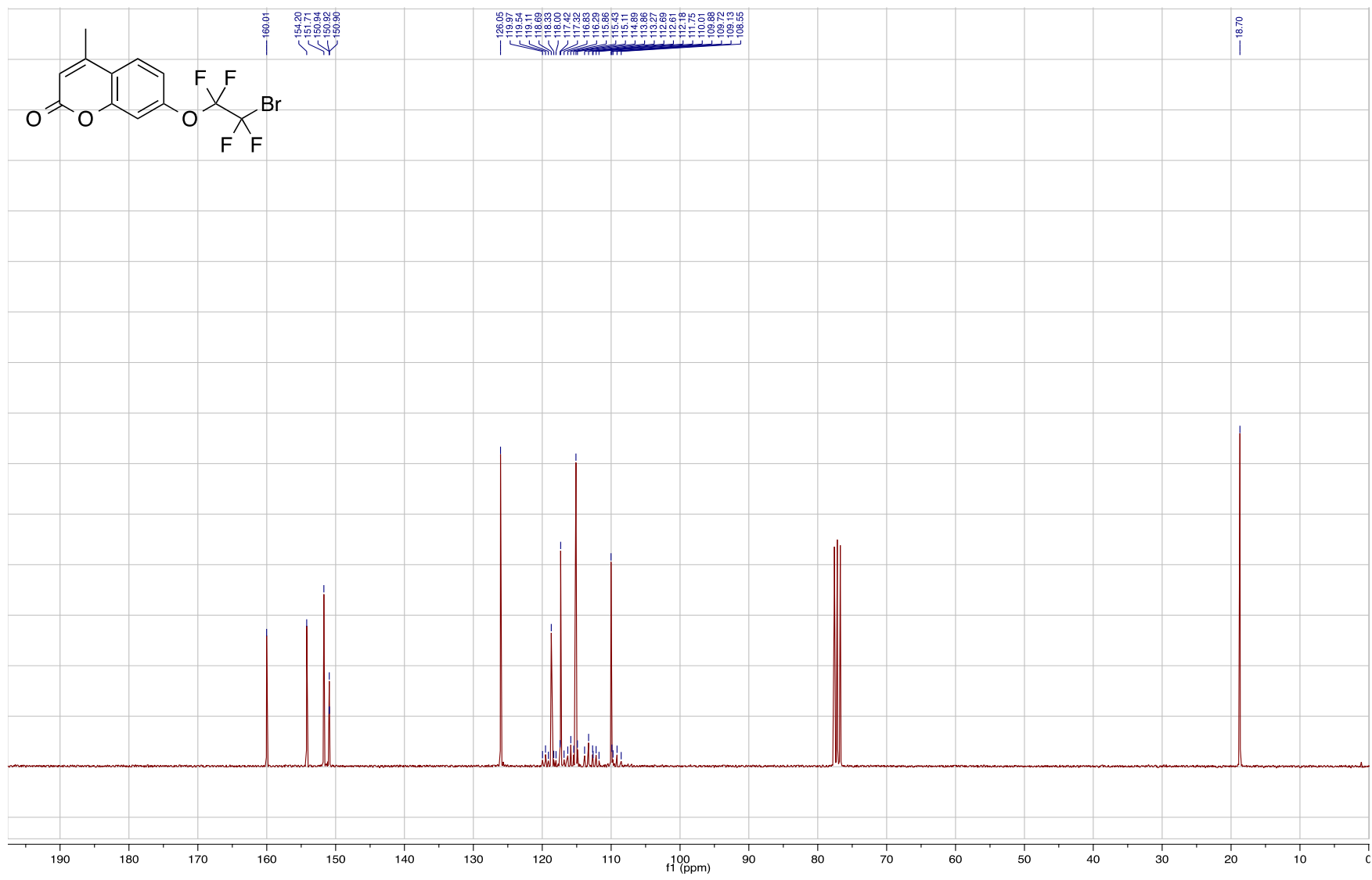


7-(2-Bromo-1,1,2,2-tetrafluoroethoxy)-4-methyl-2H-chromen-2-one

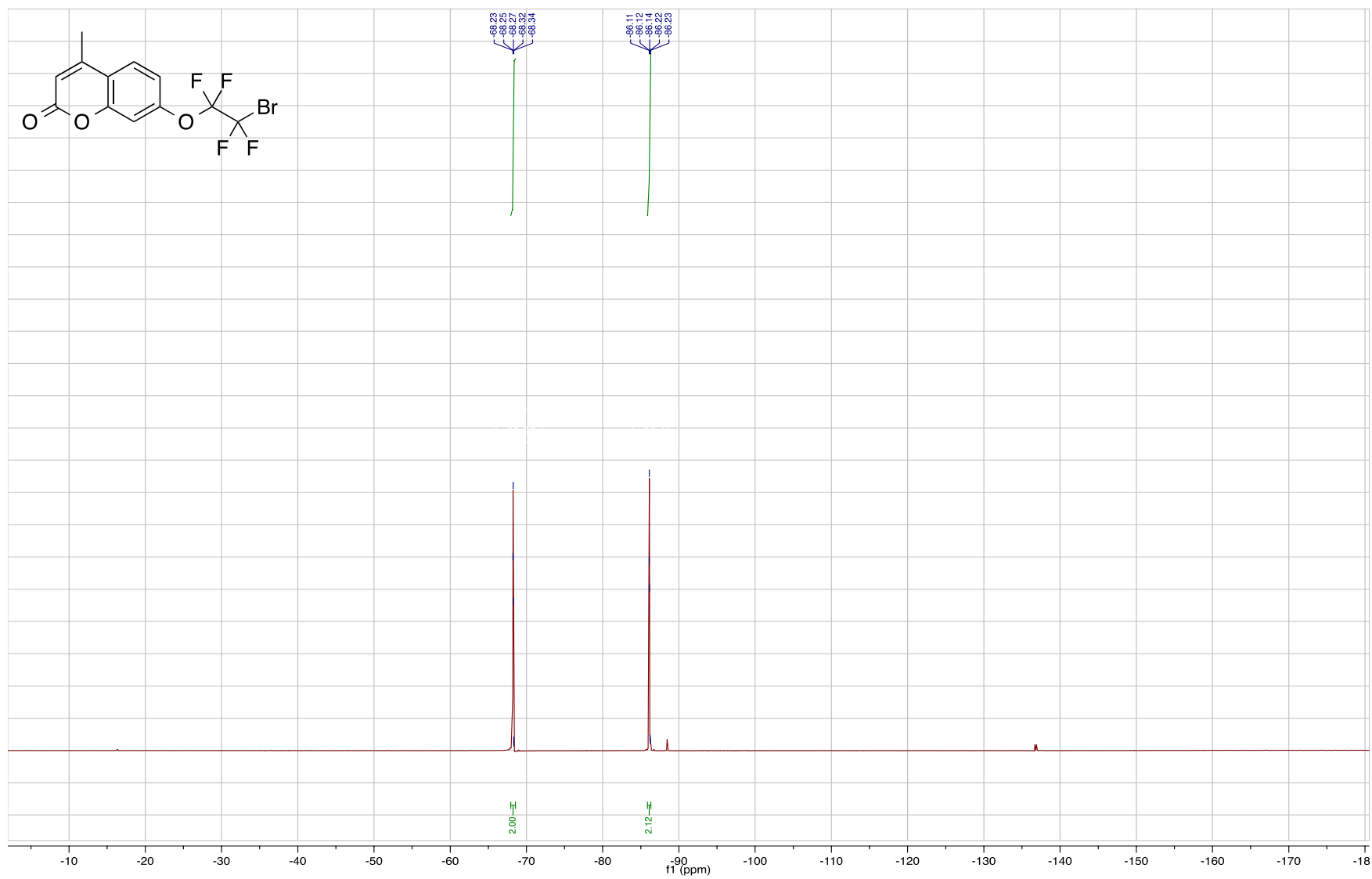
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )



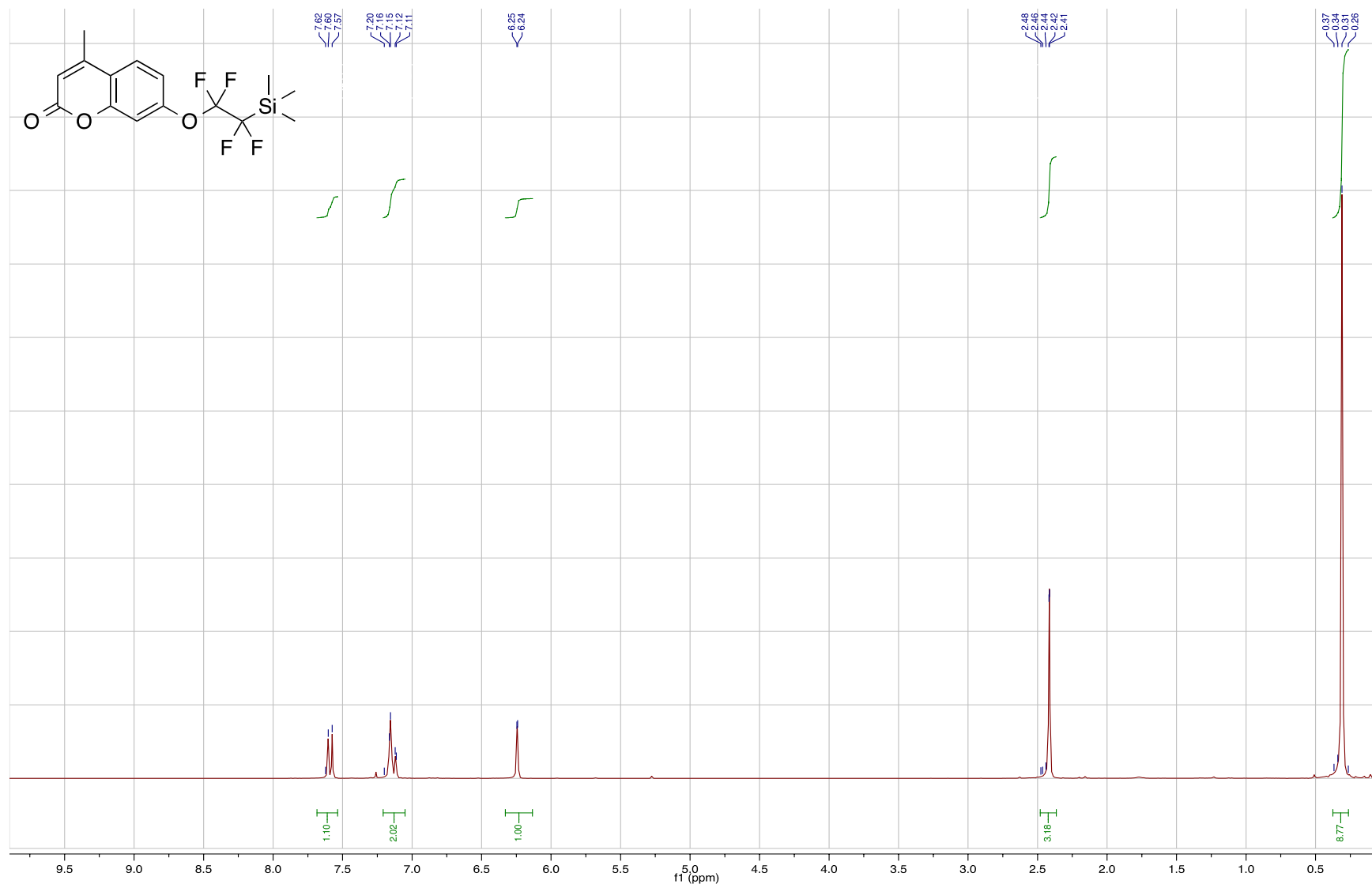
$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



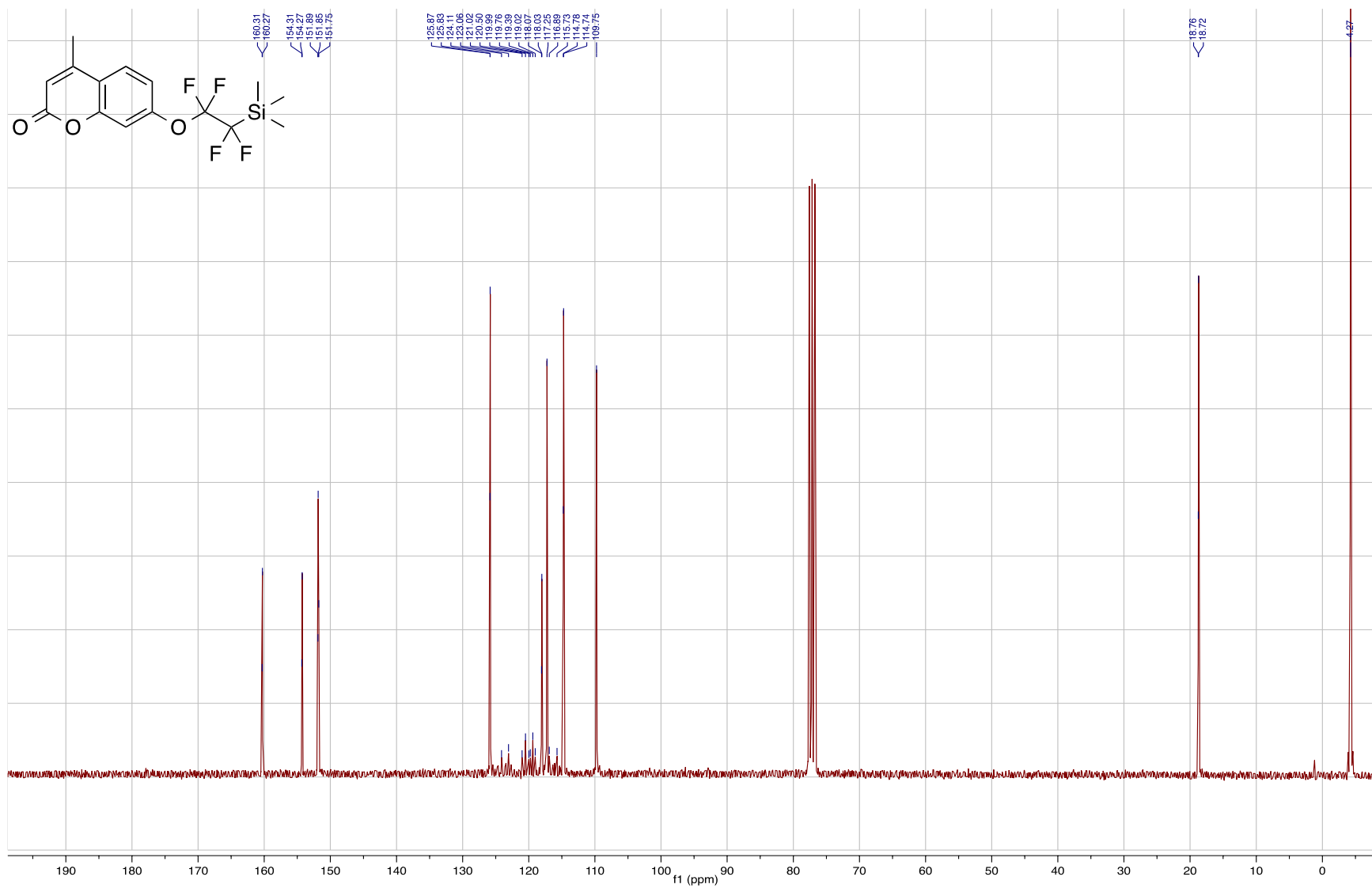


4-Methyl-7-(1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethoxy)-2H-chromen-2-one

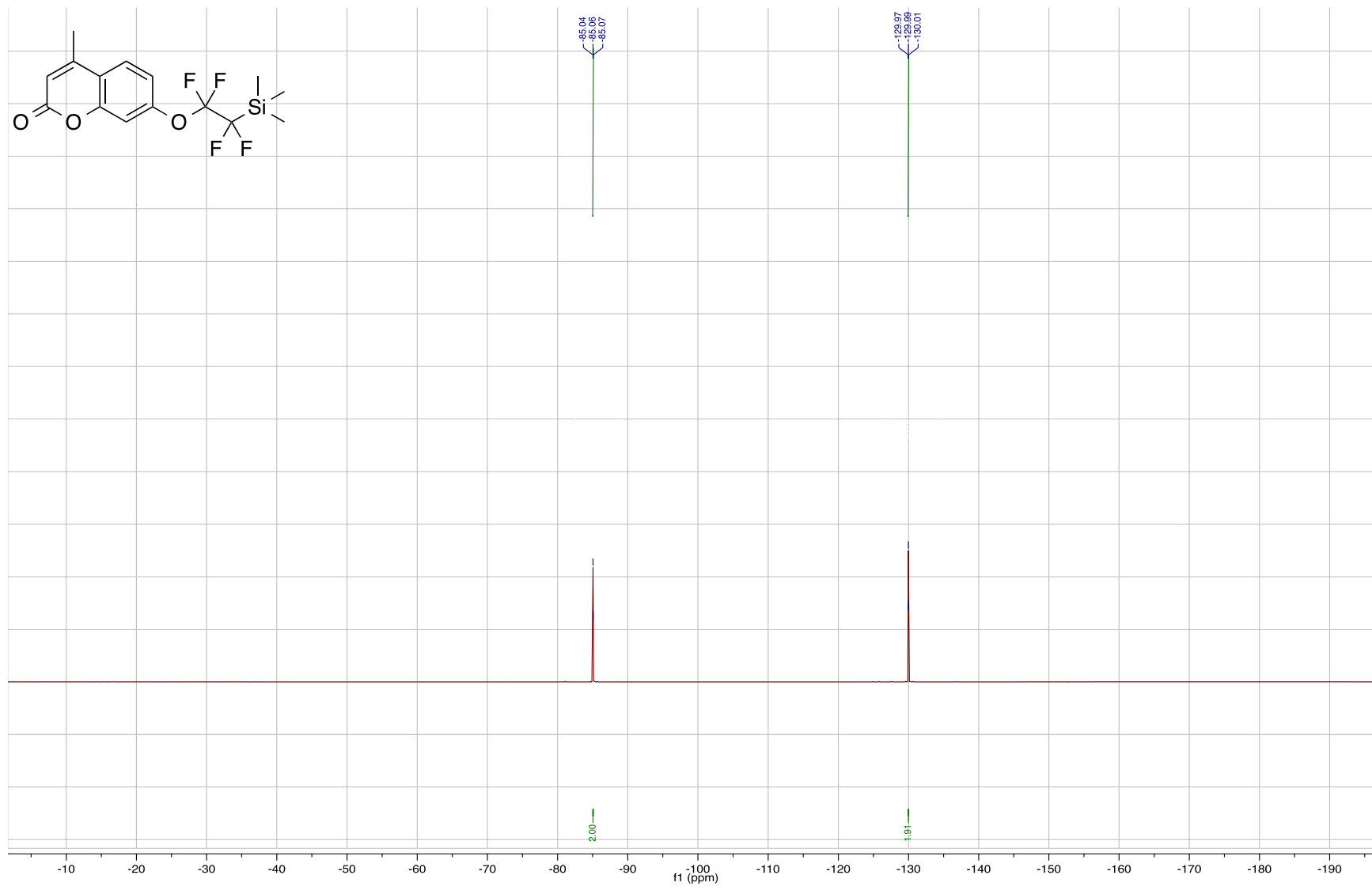
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )

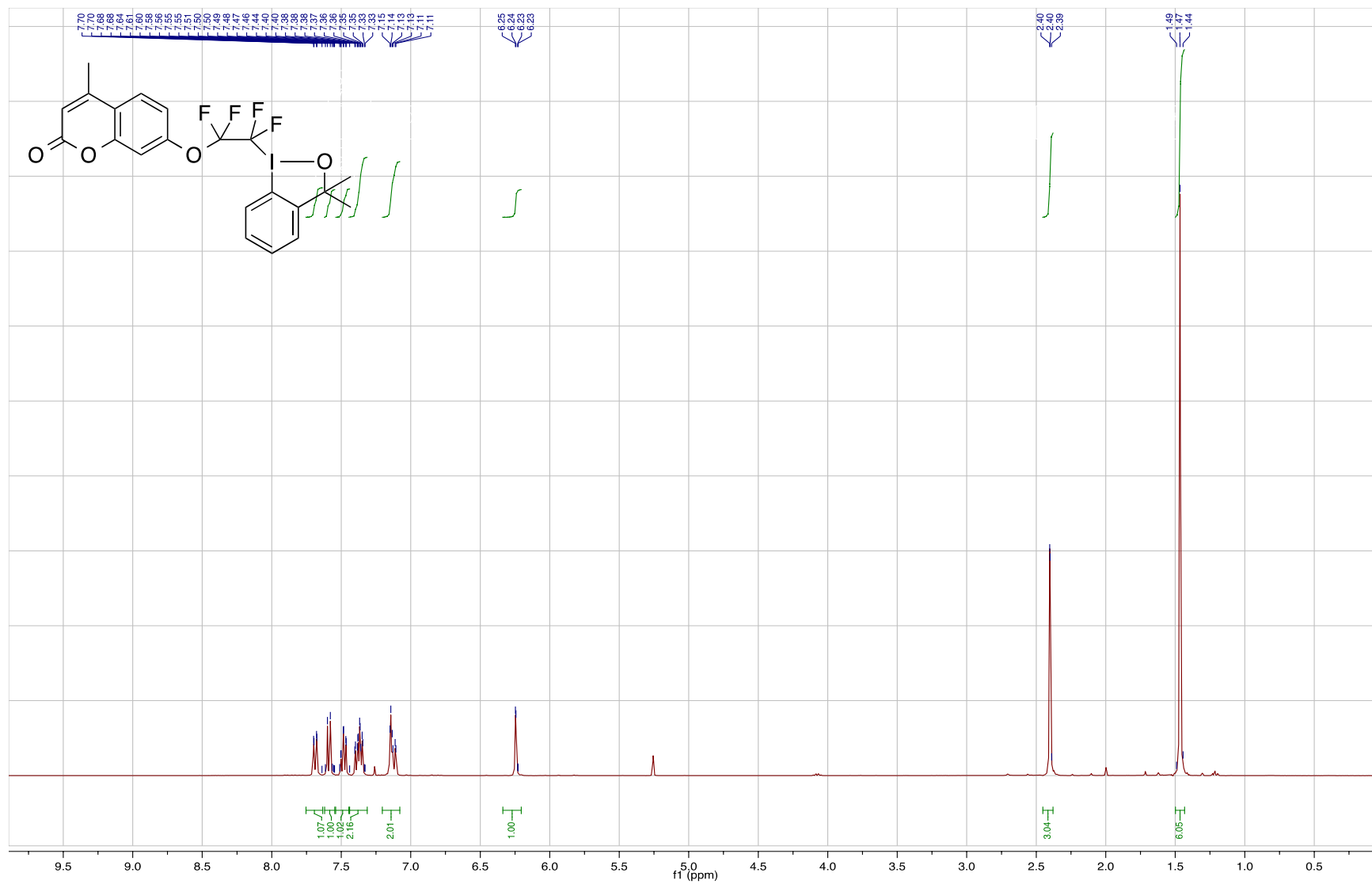


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

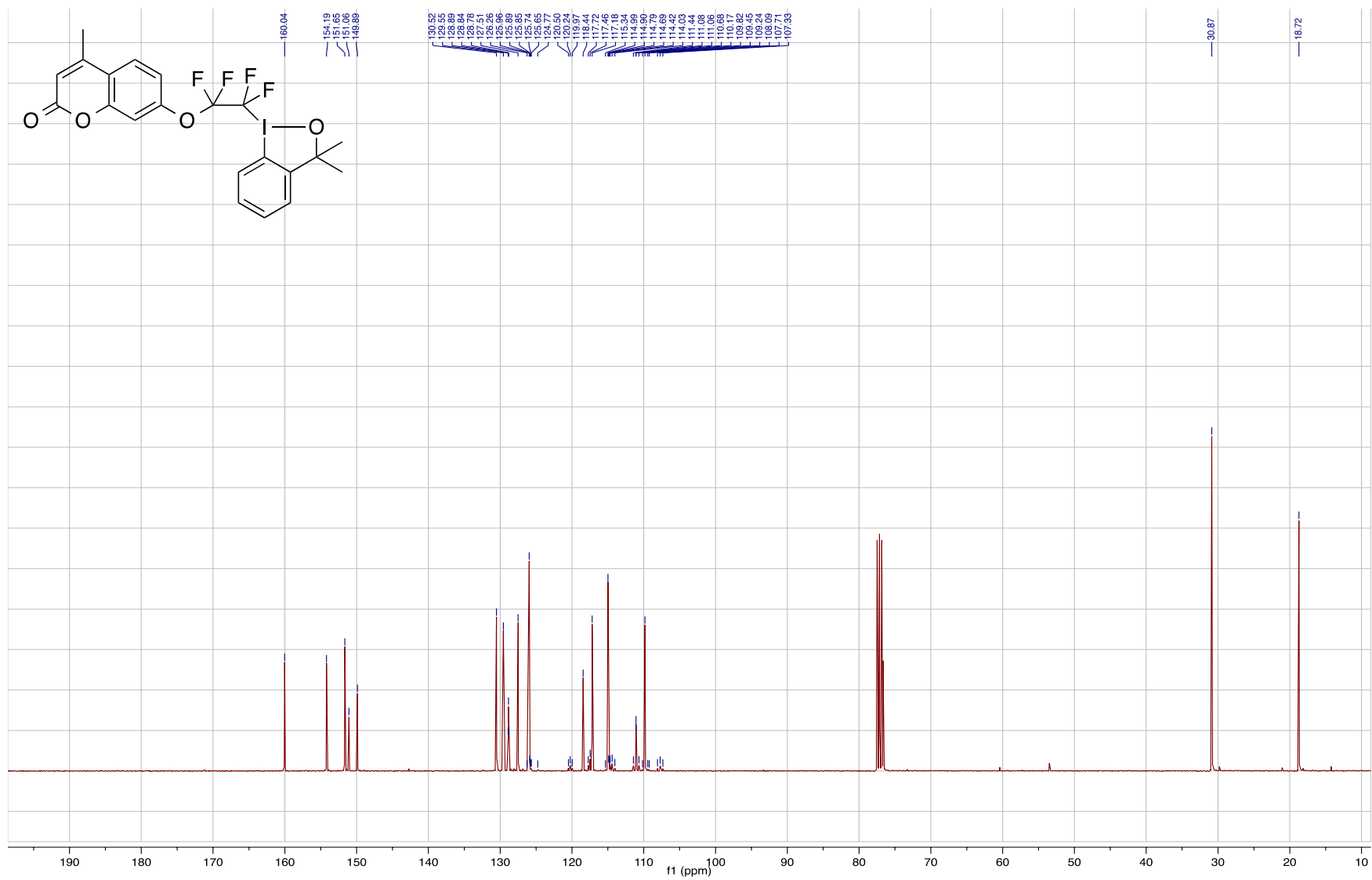


7-(2-(3,3-Dimethyl-1  $\lambda^3$ -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)-1,1,2,2-tetrafluoroethoxy)-4-methyl-2*H*-chromen-2-one (**2i**)

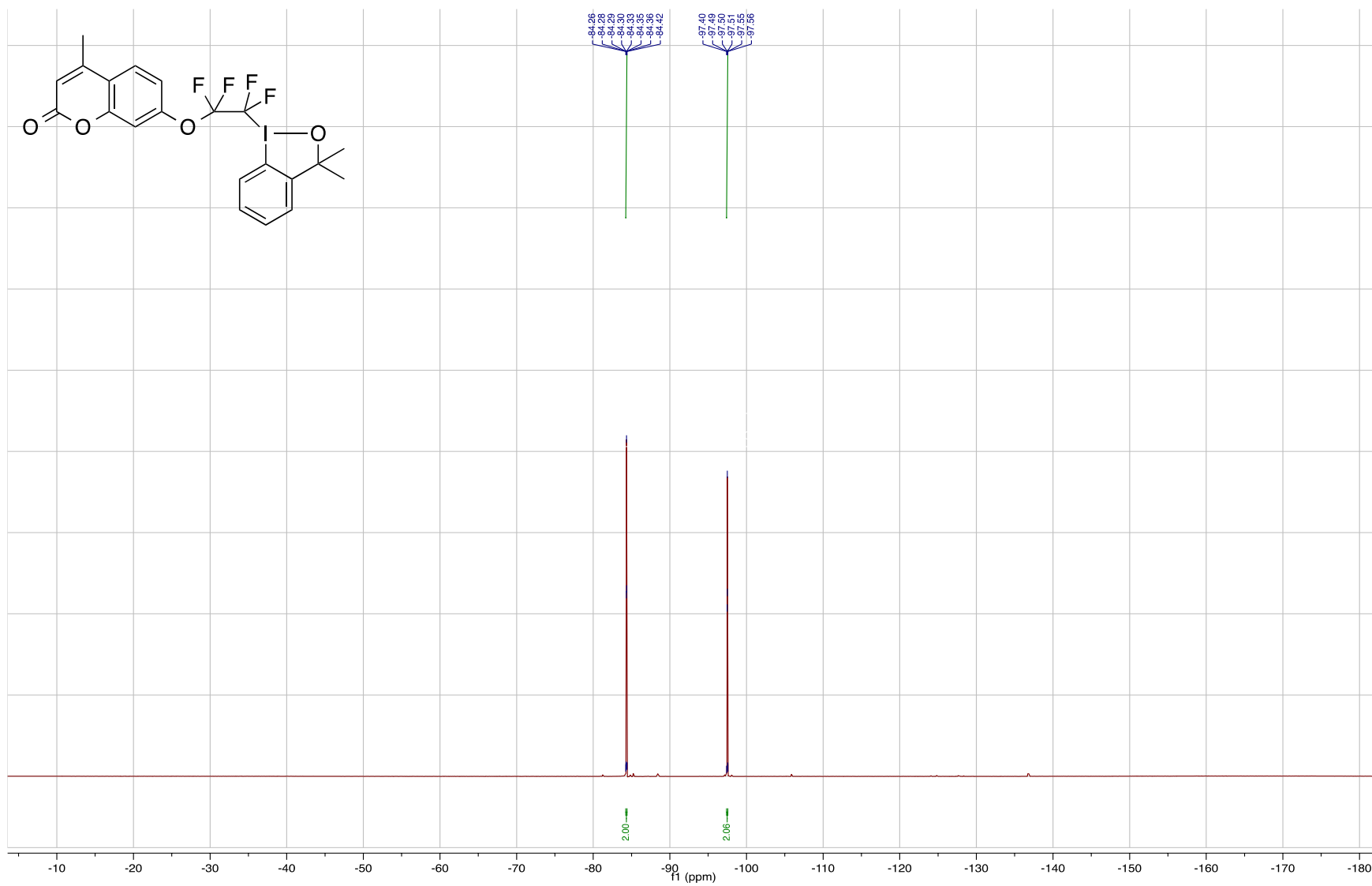
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

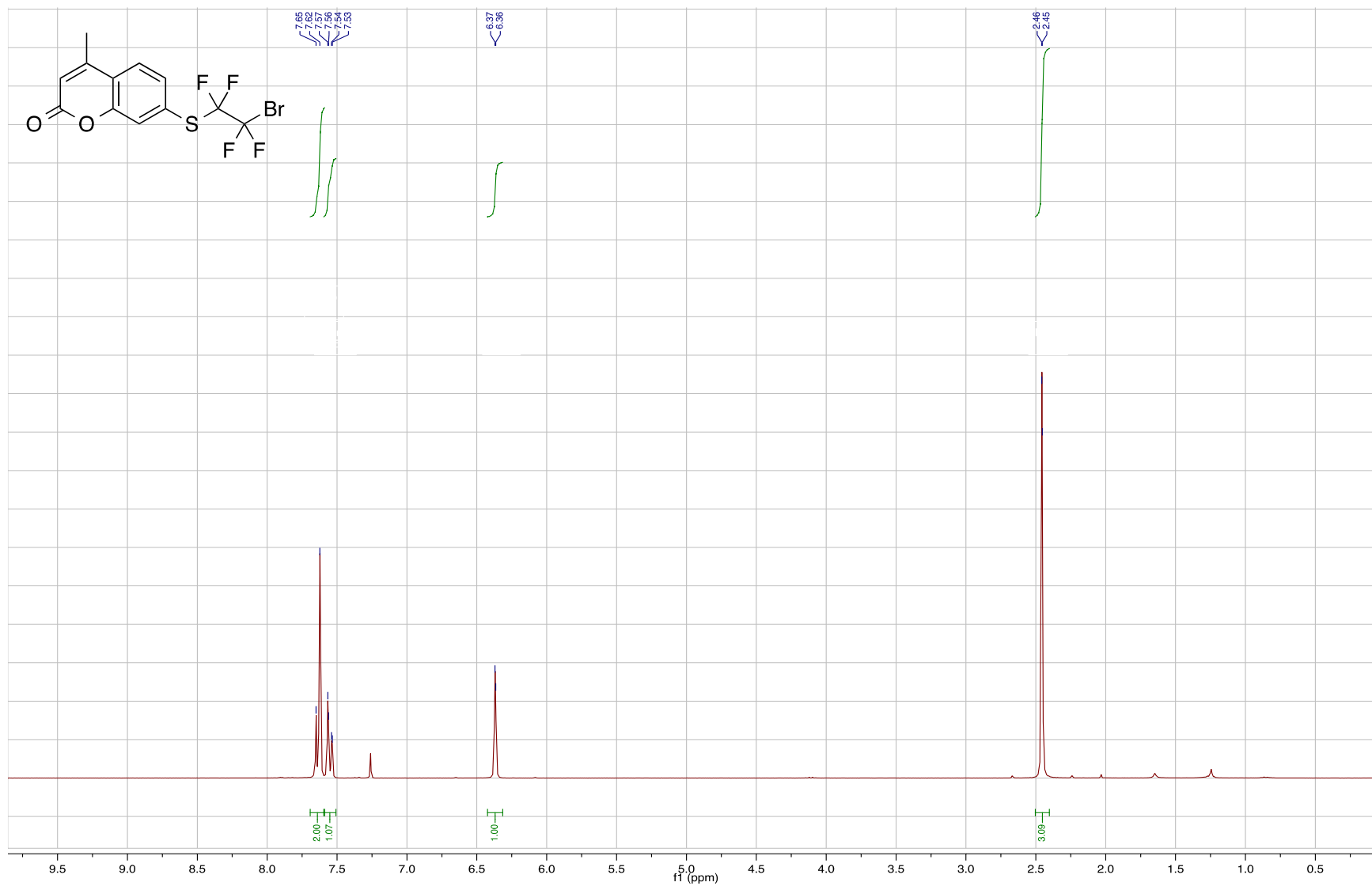


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

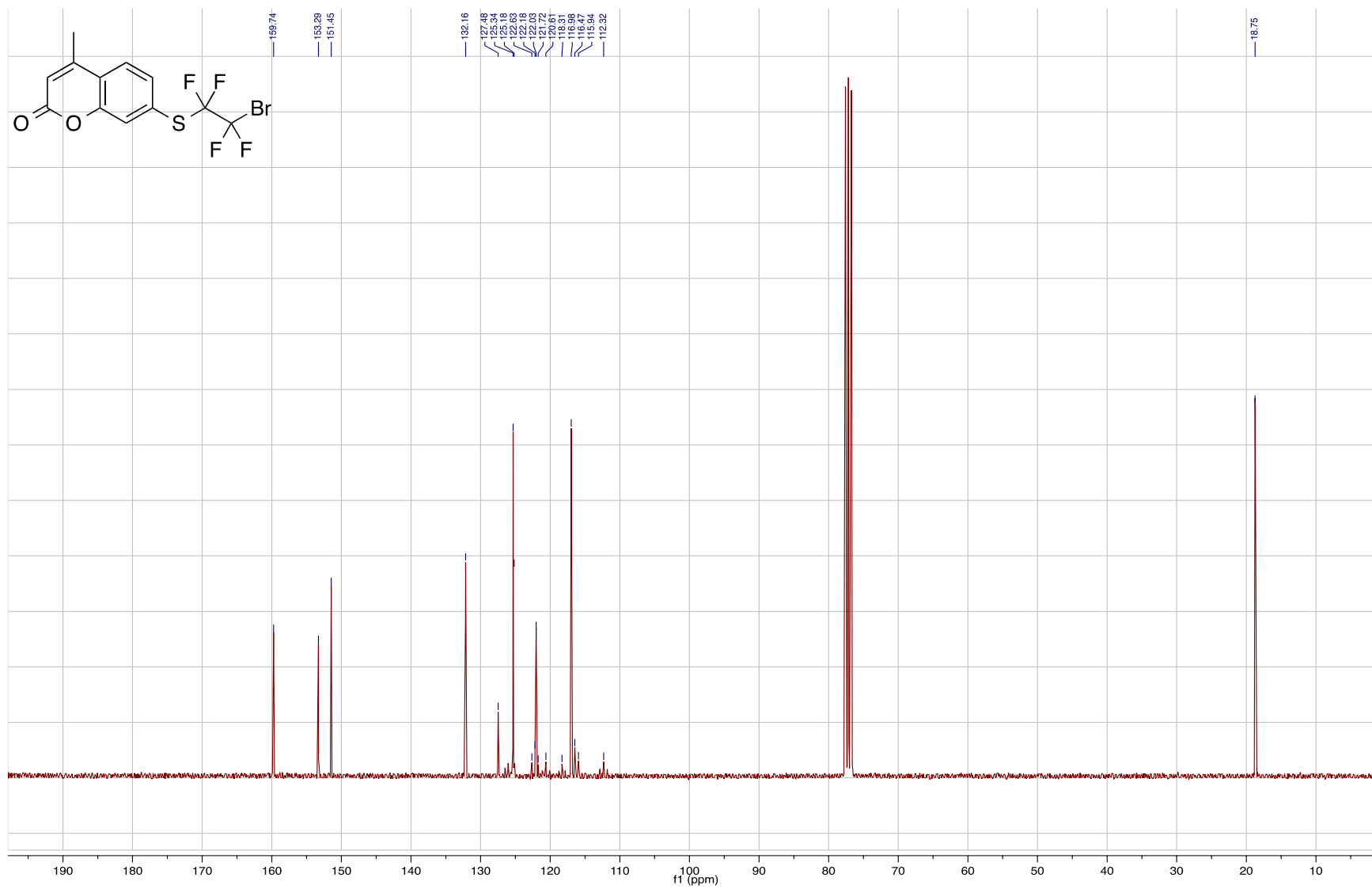


7-((2-Bromo-1,1,2,2-tetrafluoroethyl)thio)-4-methyl-2H-chromen-2-one

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

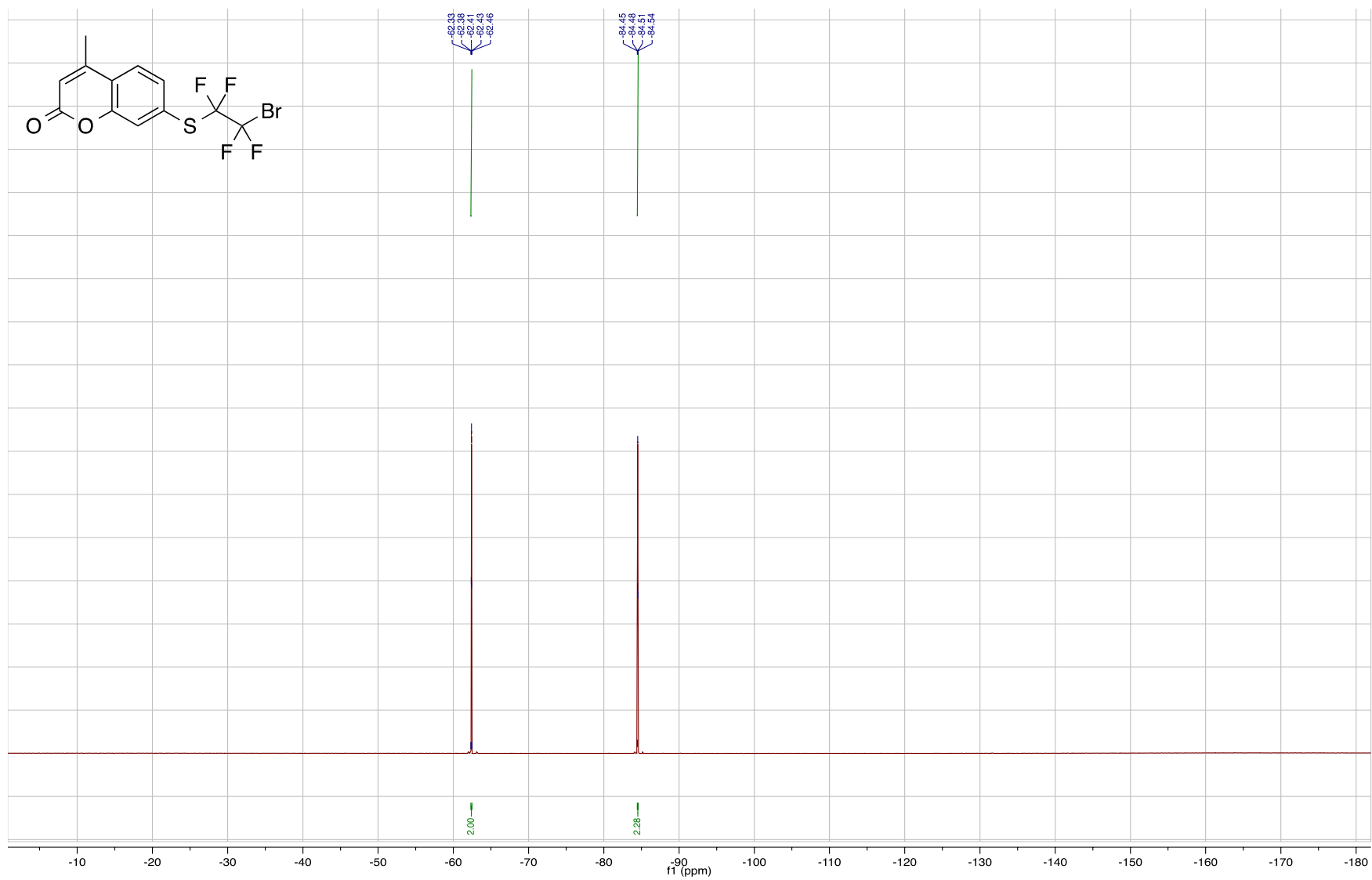


$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )



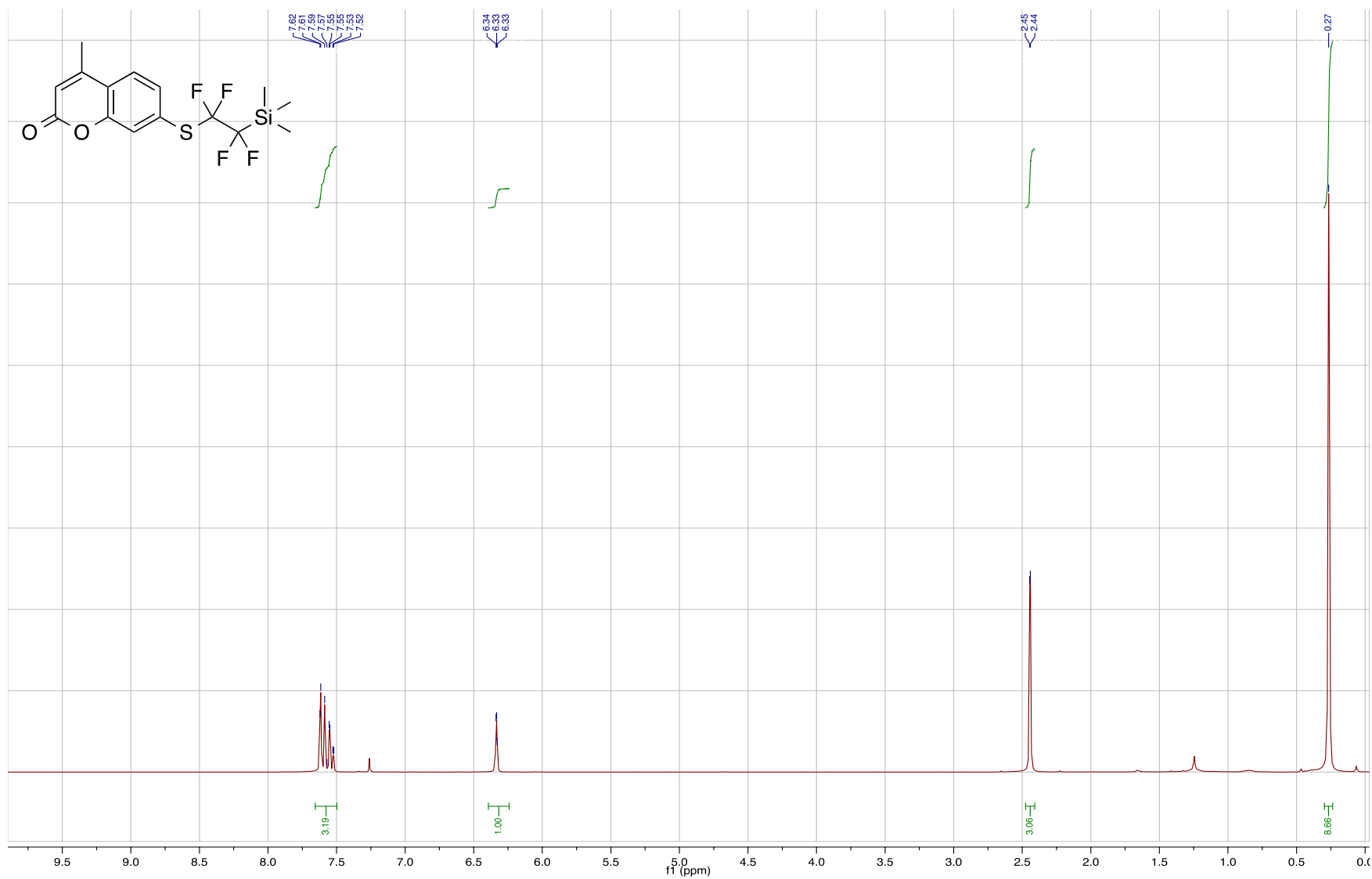


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

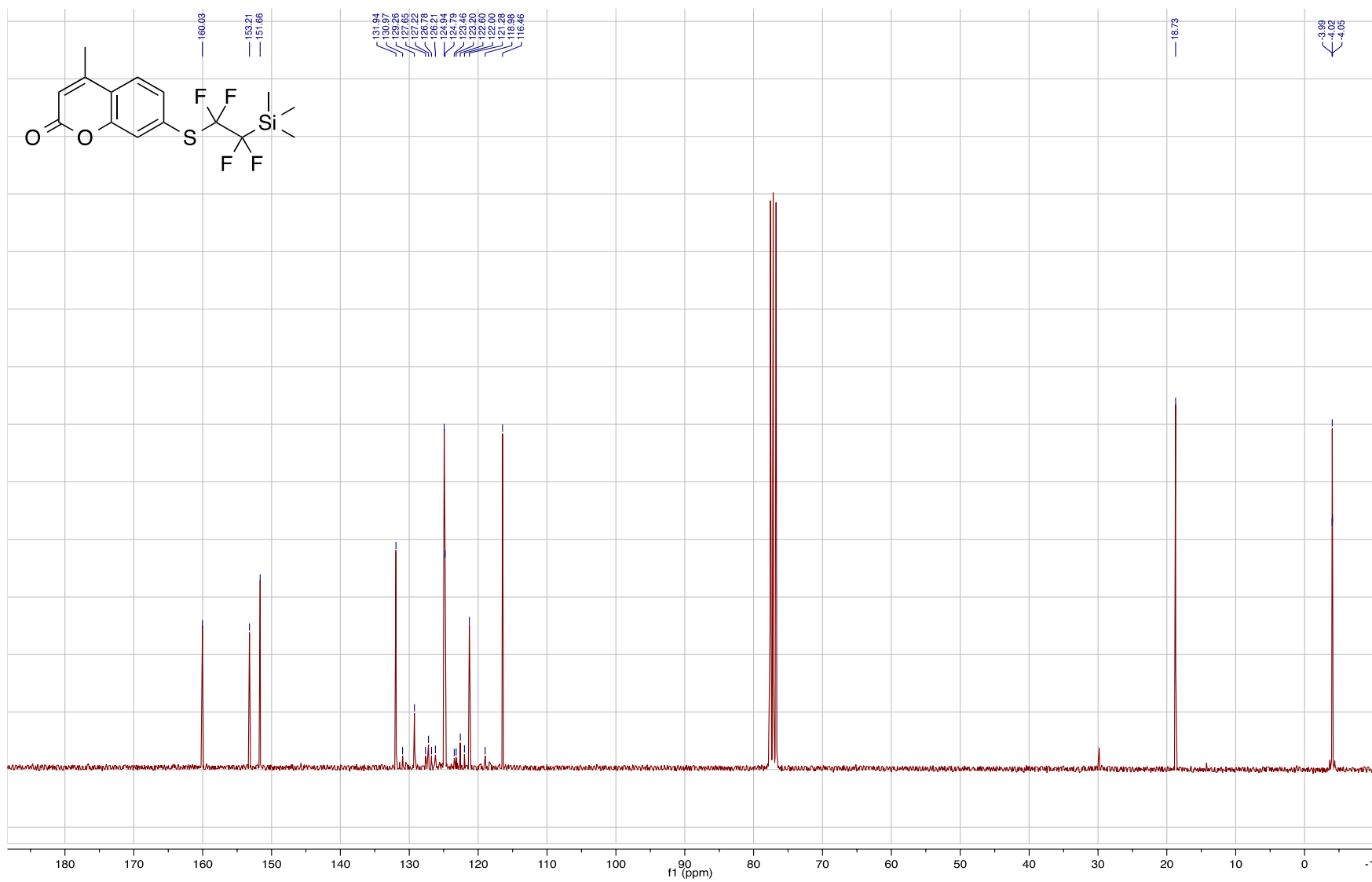


4-Methyl-7-((1,1,2,2-tetrafluoro-2-(trimethylsilyl)ethyl)thio)-2H-chromen-2-one

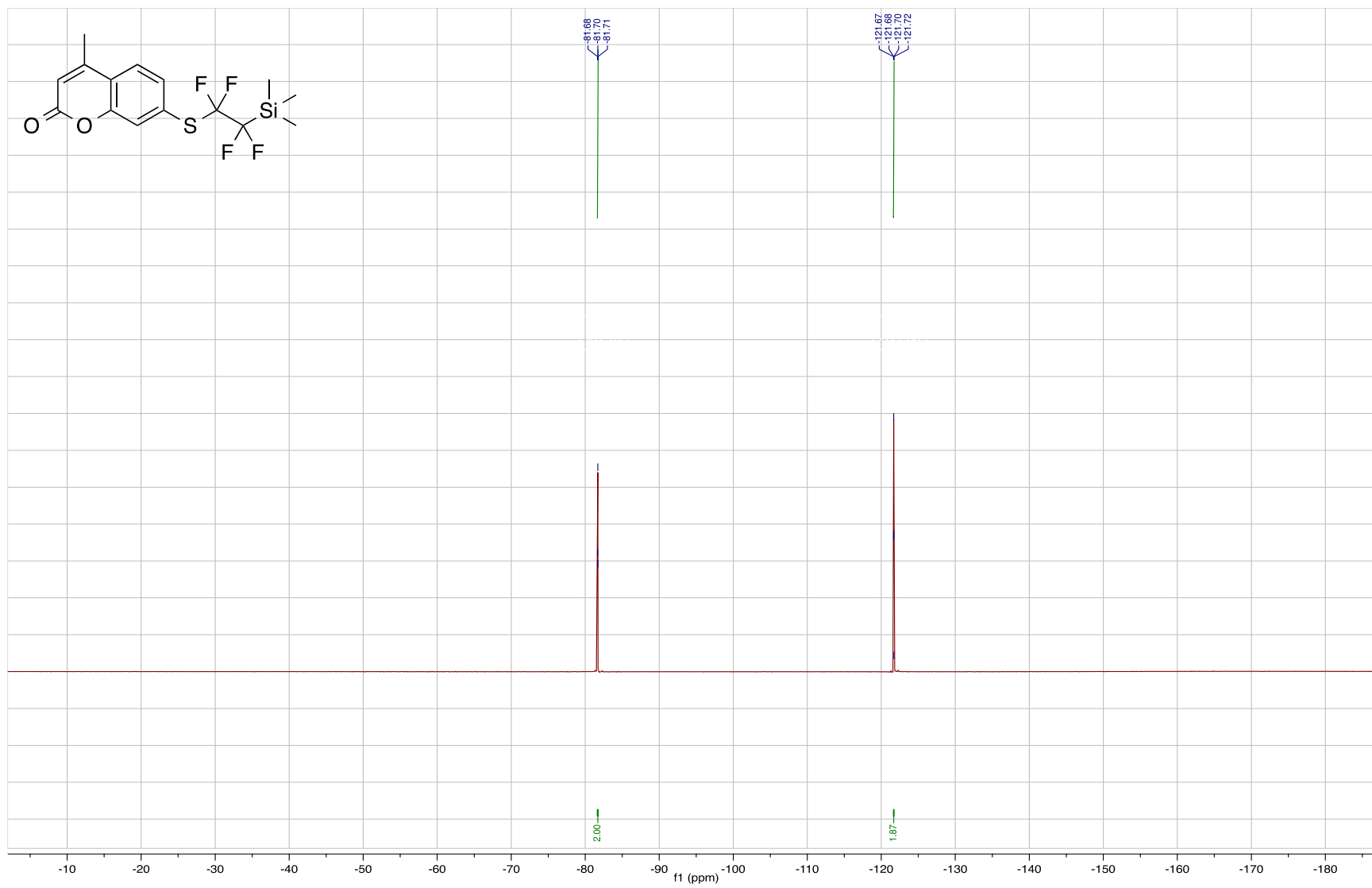
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )

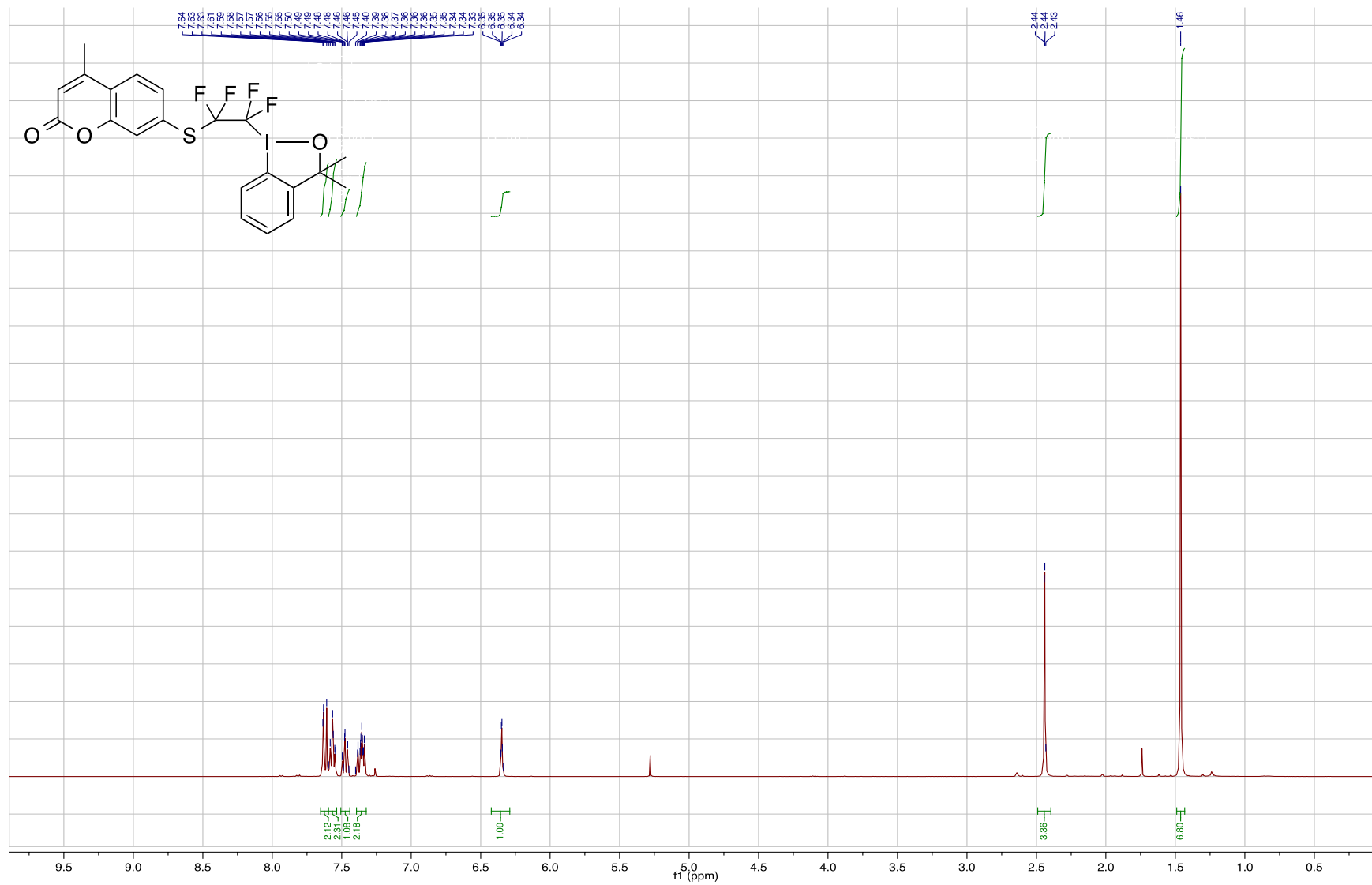


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

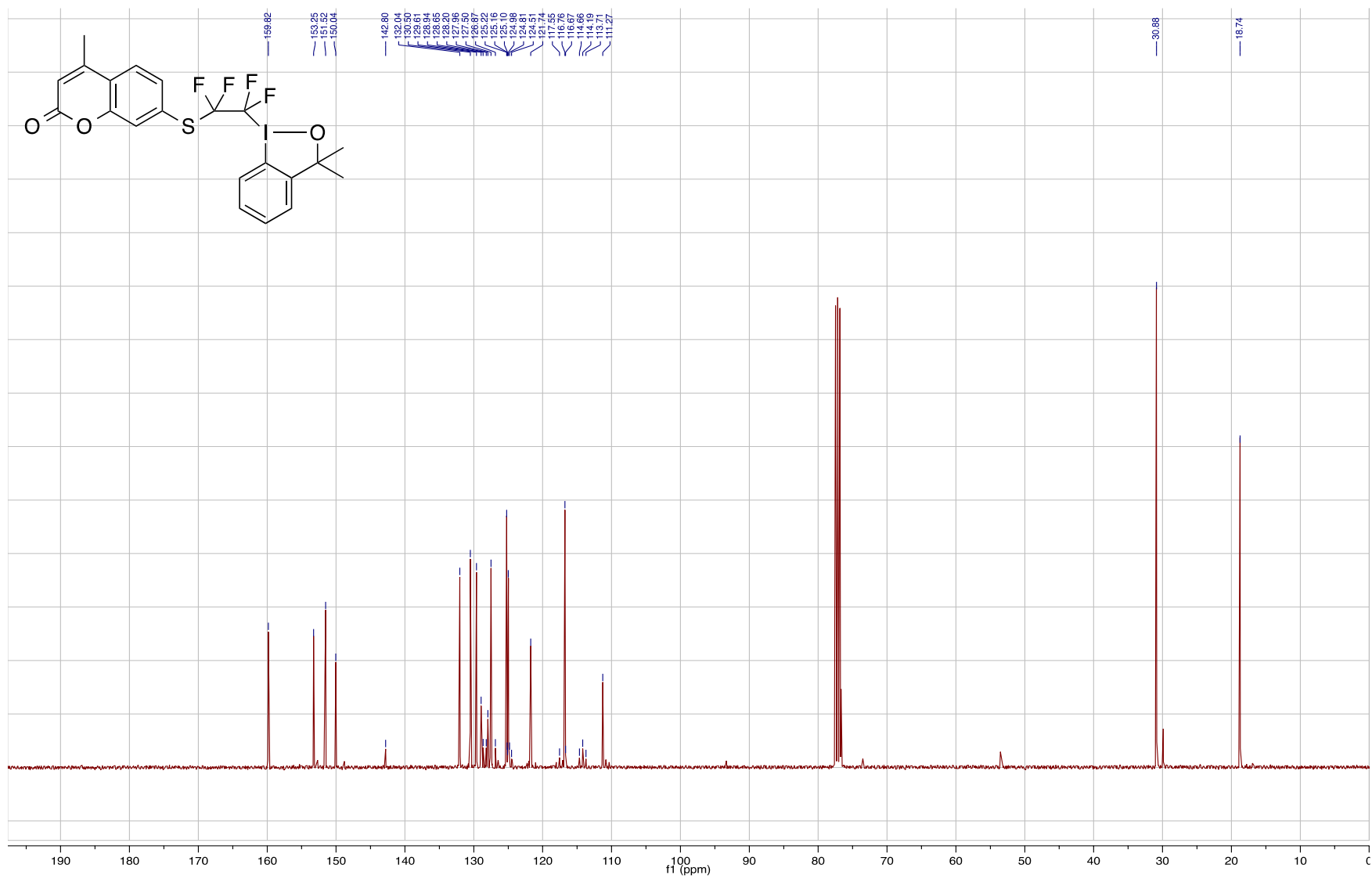


7-((2-(3,3-Dimethyl-1 $\lambda^3$ -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)-1,1,2,2-tetrafluoroethyl)thio)-4-methyl-2*H*-chromen-2-one (2j)

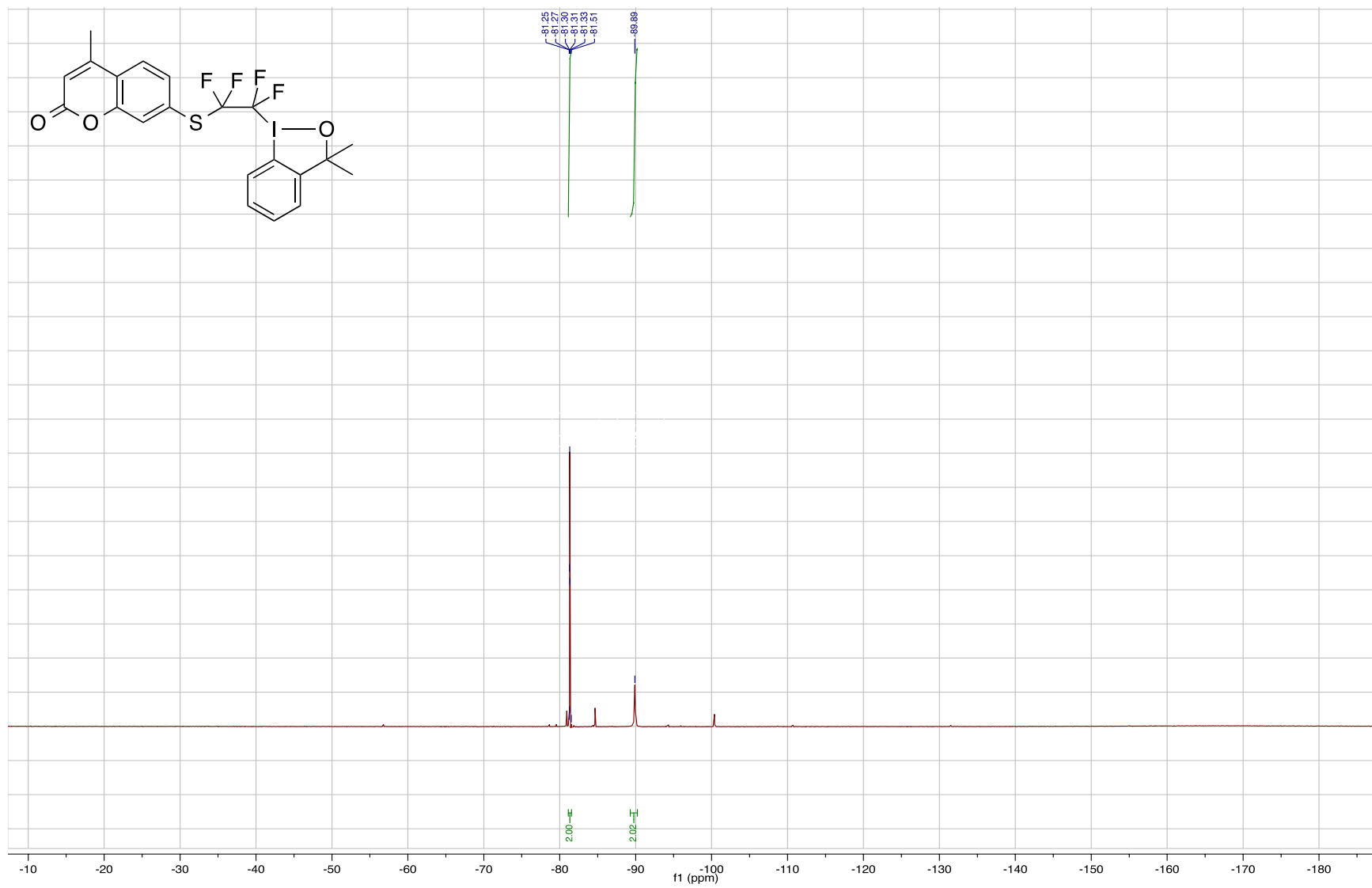
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )

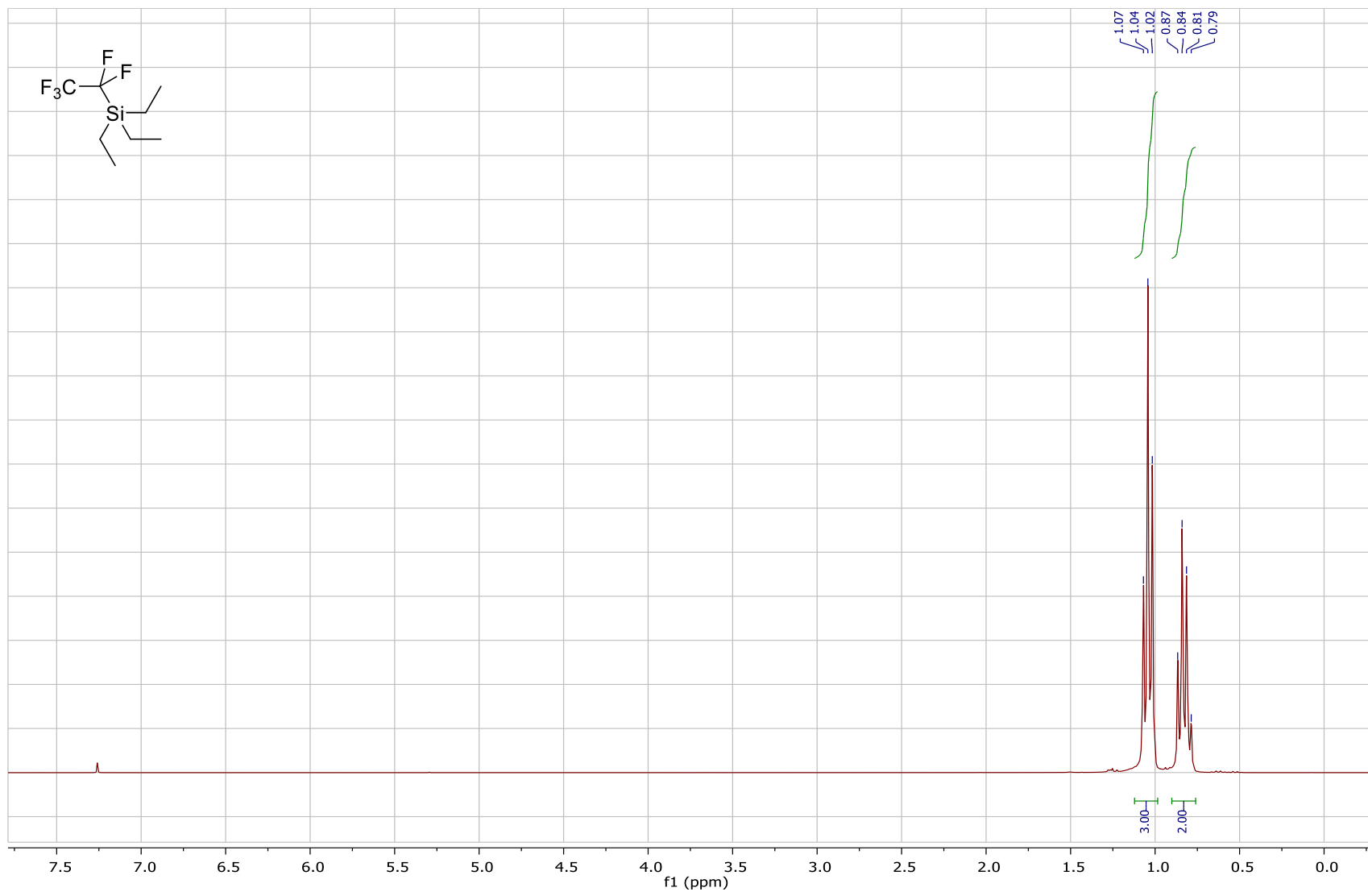


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



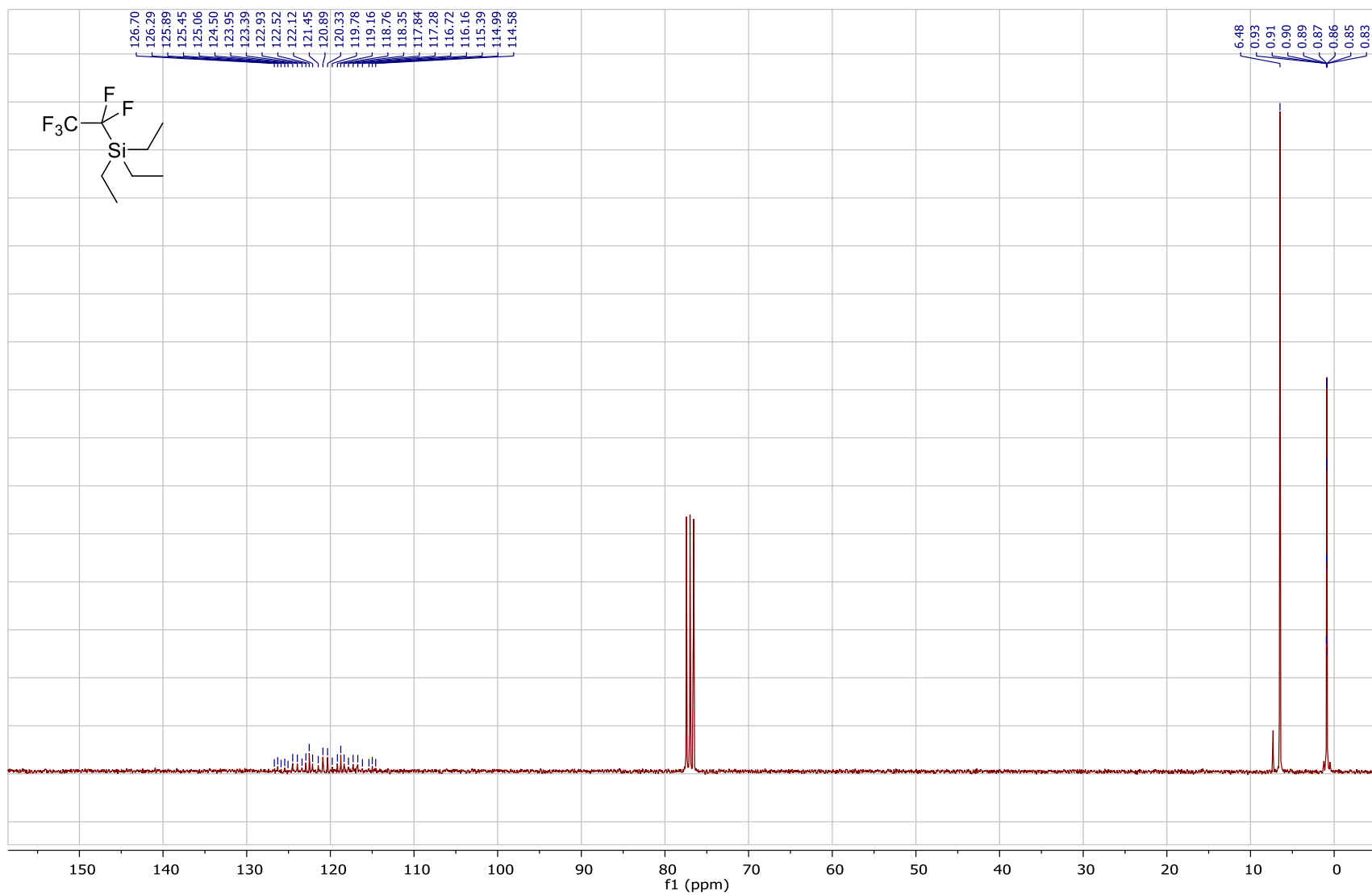
# Triethyl(perfluoroethyl)silane

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

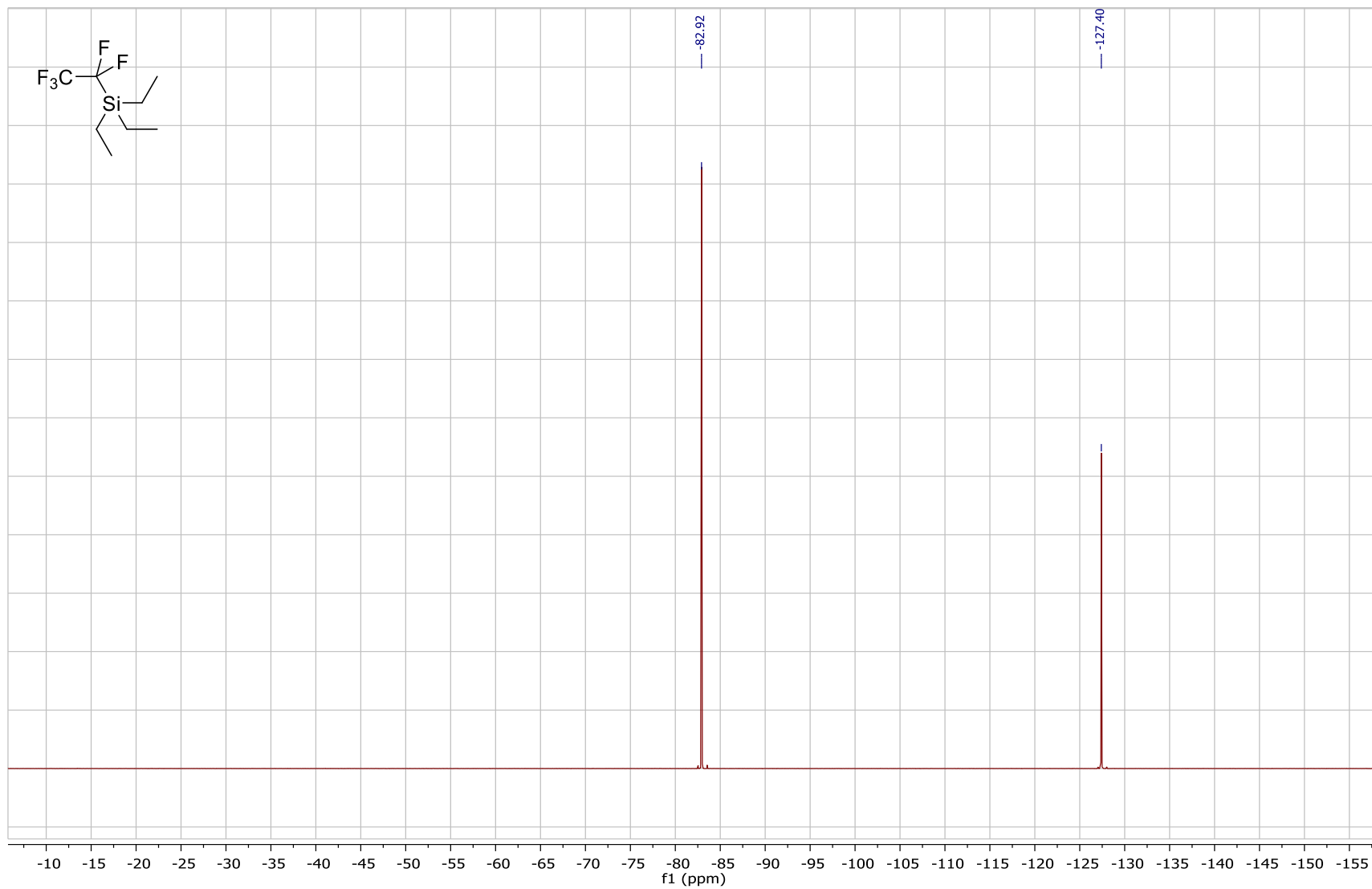




$^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ )

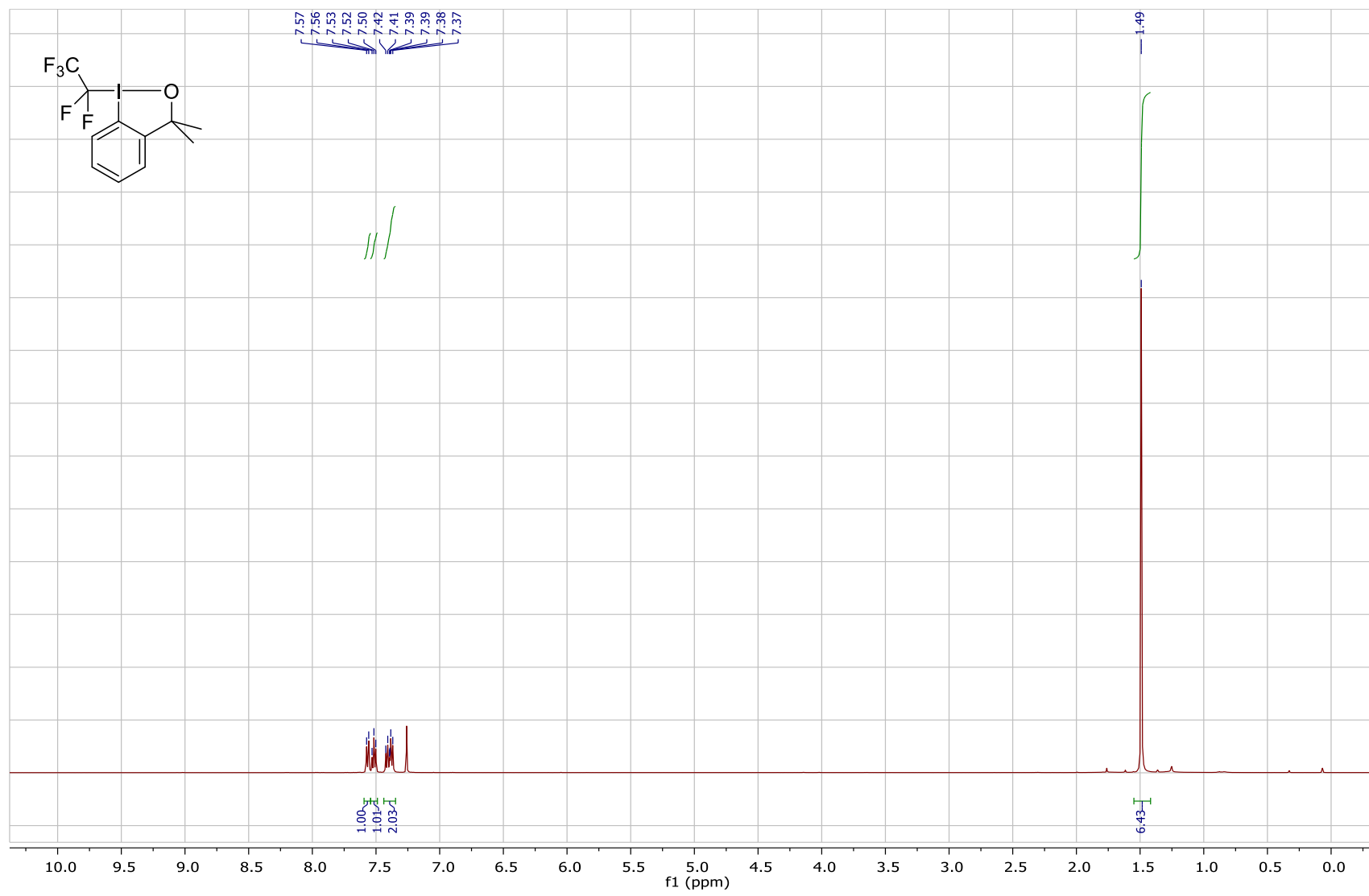


$^{19}\text{F}$  NMR (300 MHz,  $\text{CDCl}_3$ )

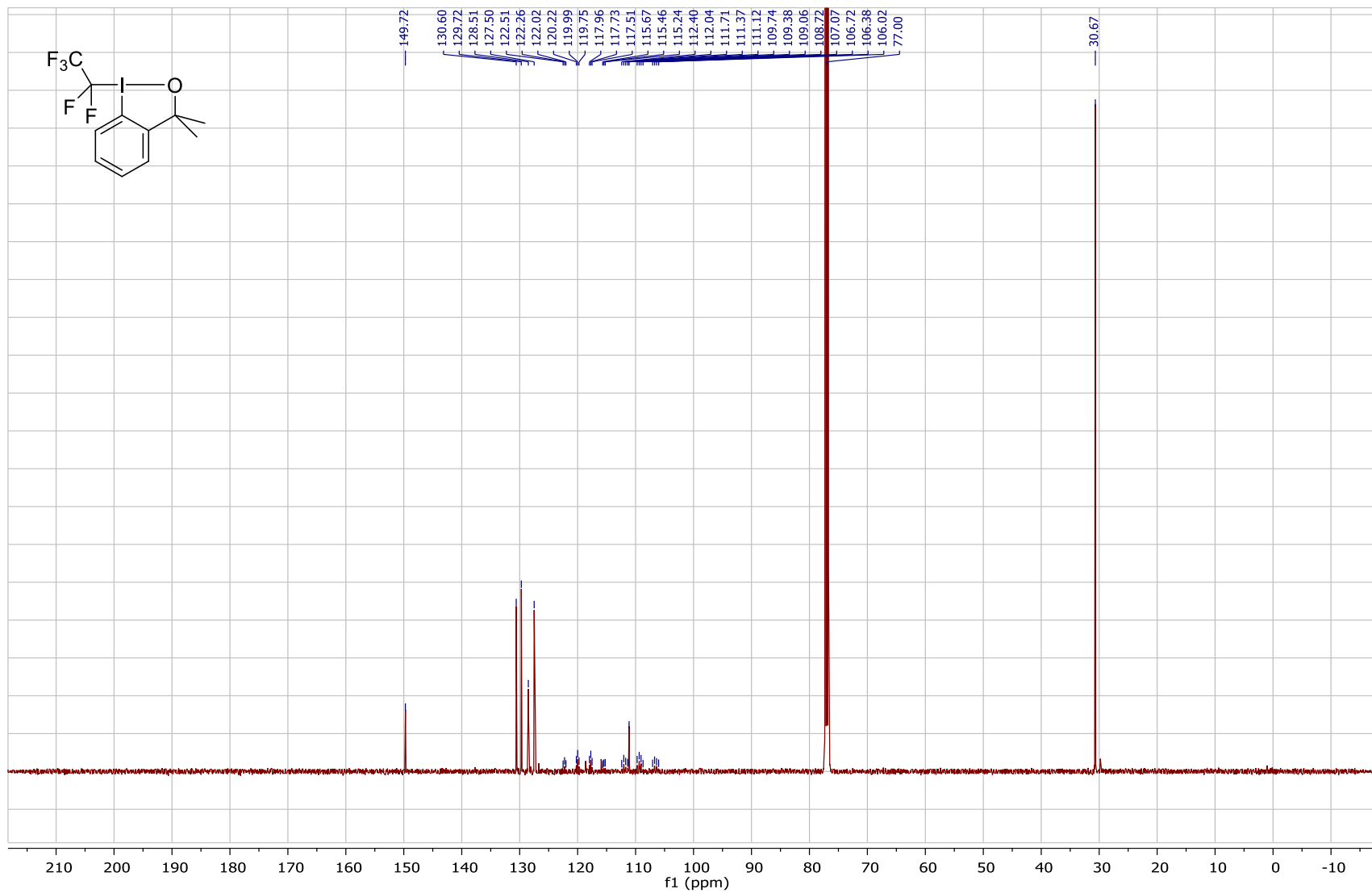


3,3-Dimethyl-1-(perfluoroethyl)-1,3-dihydro-1λ<sup>3</sup>-benzo[d][1,2]iodaoxole (**2k**)

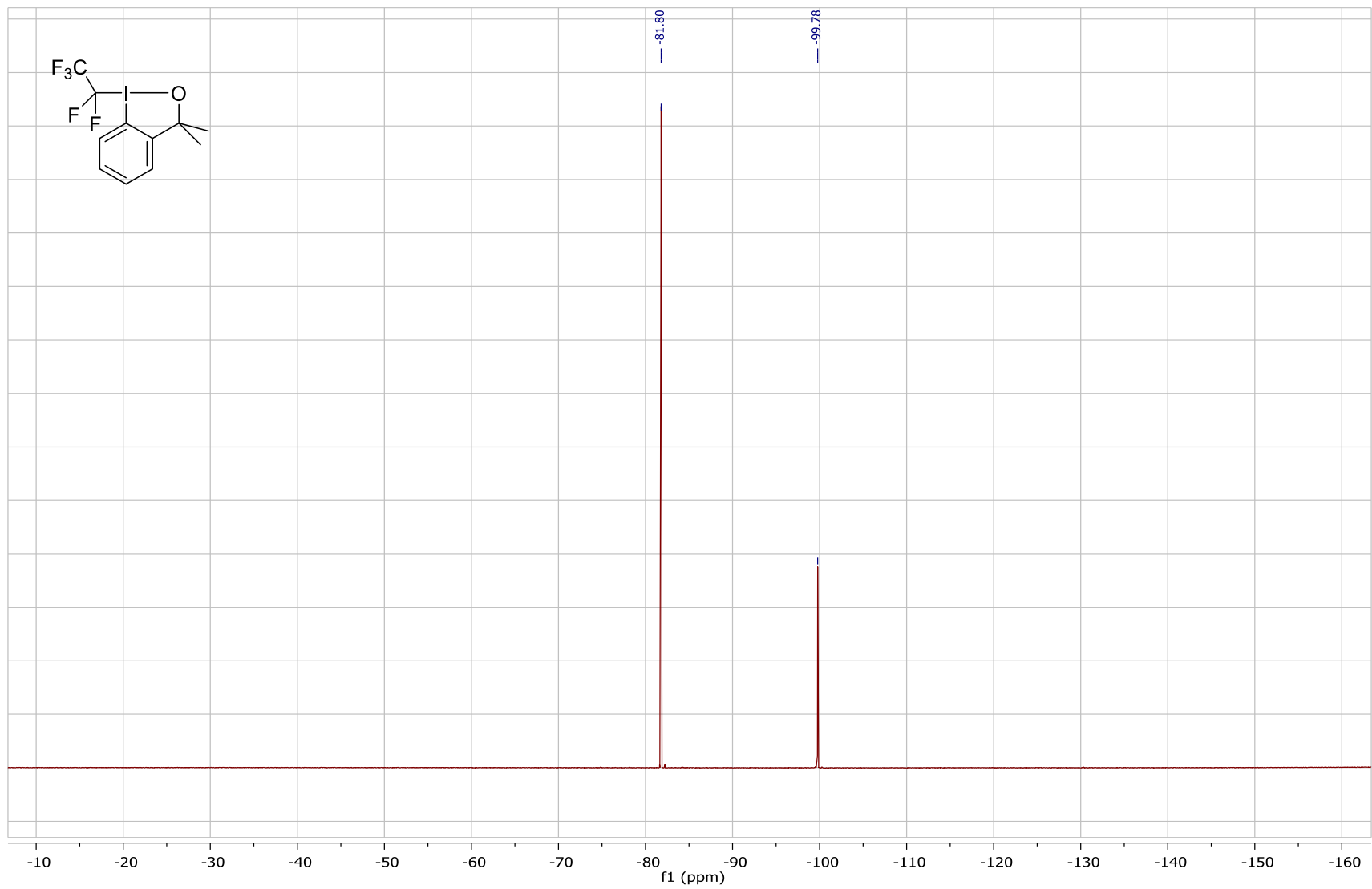
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

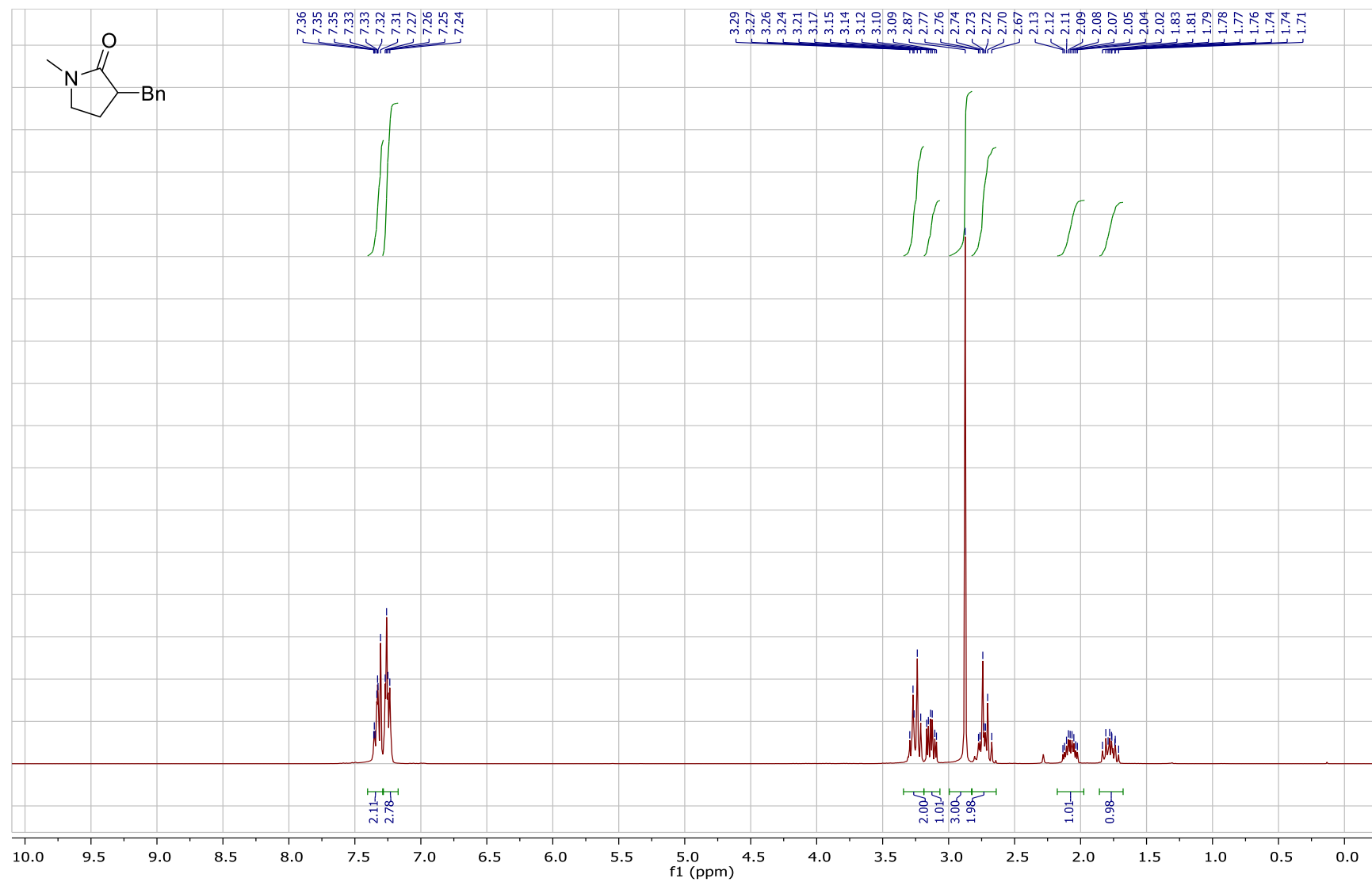


$^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )

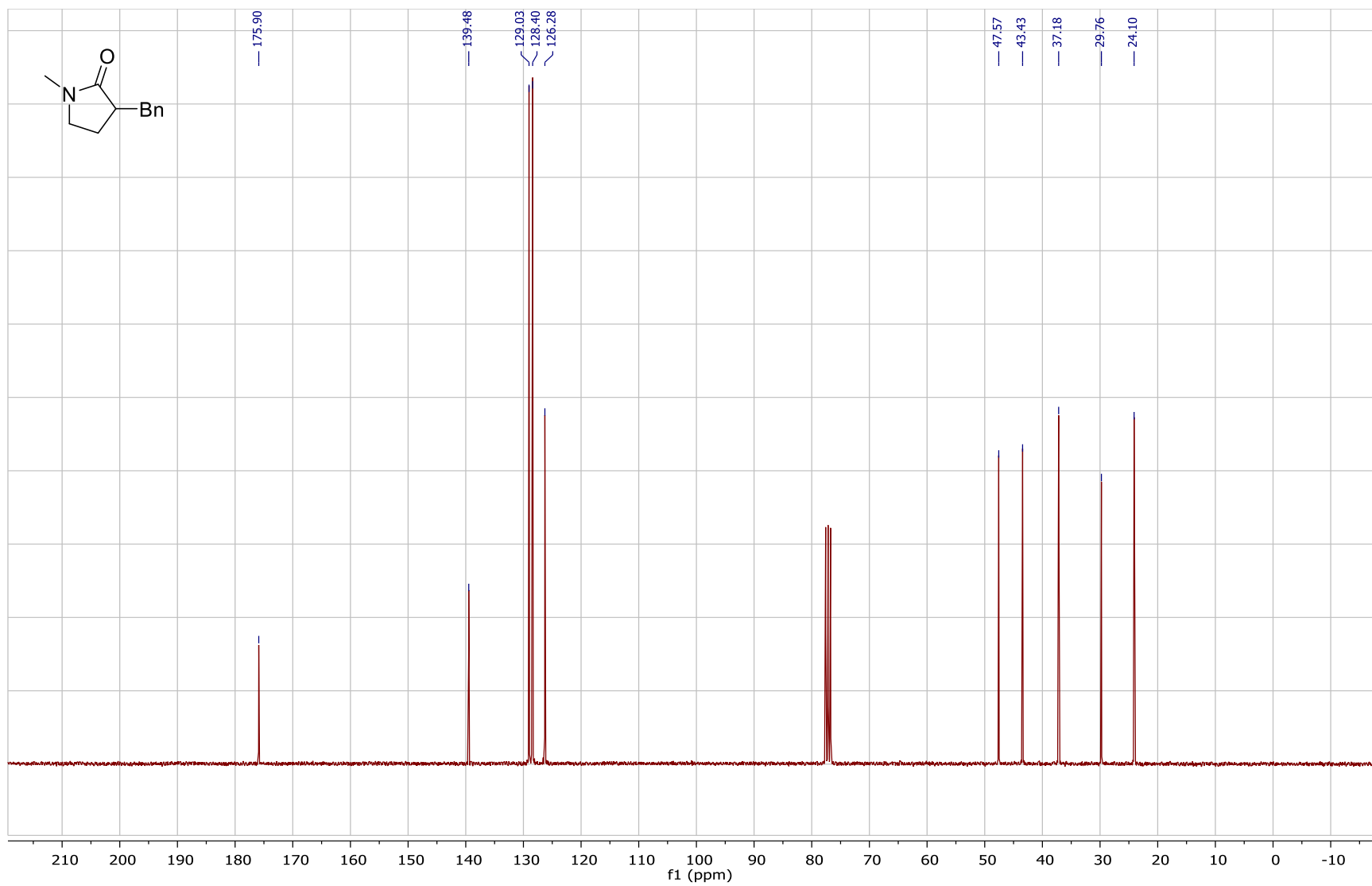


### 3-Benzyl-1-methylpyrrolidin-2-one (3a)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

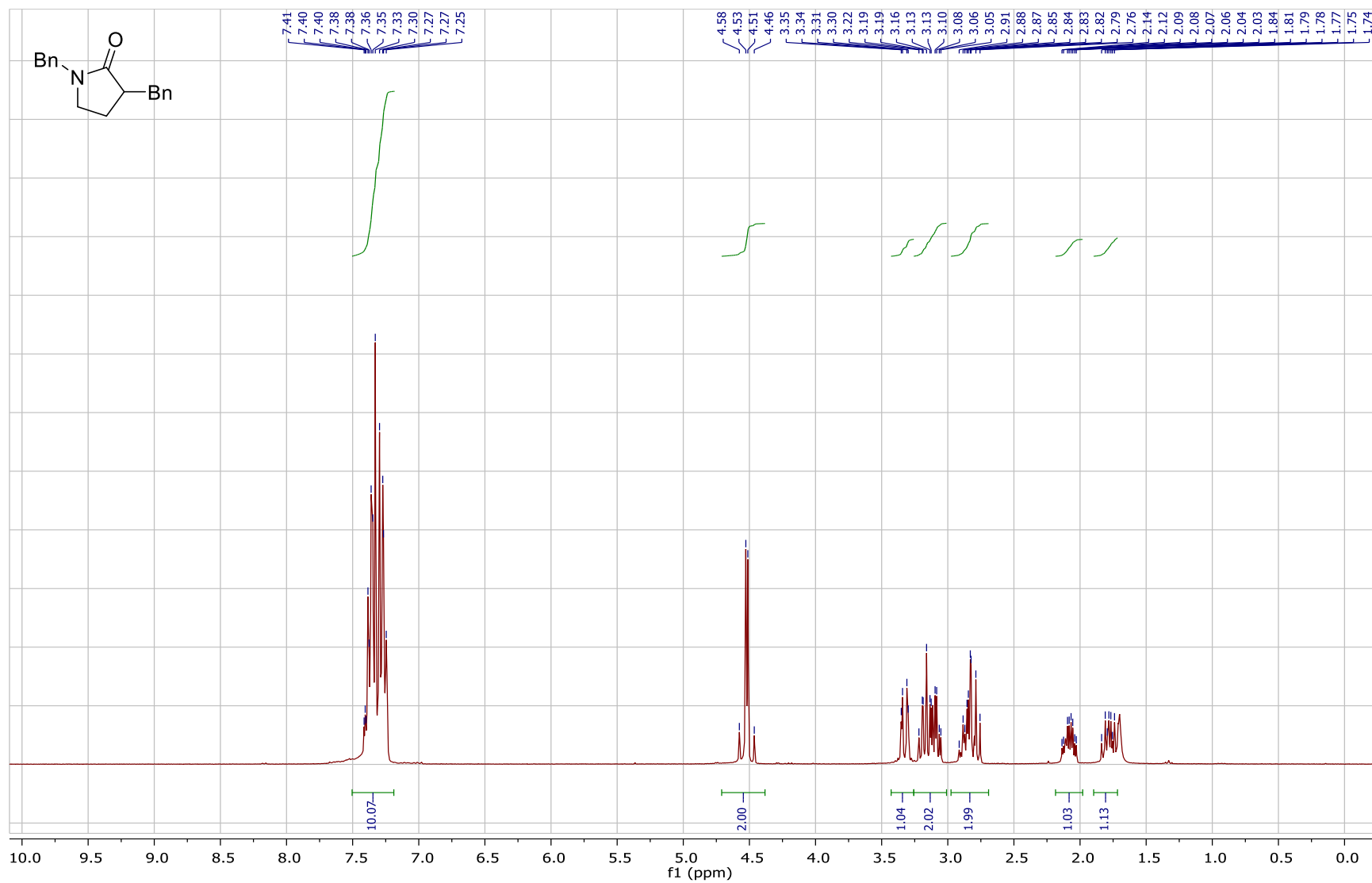


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



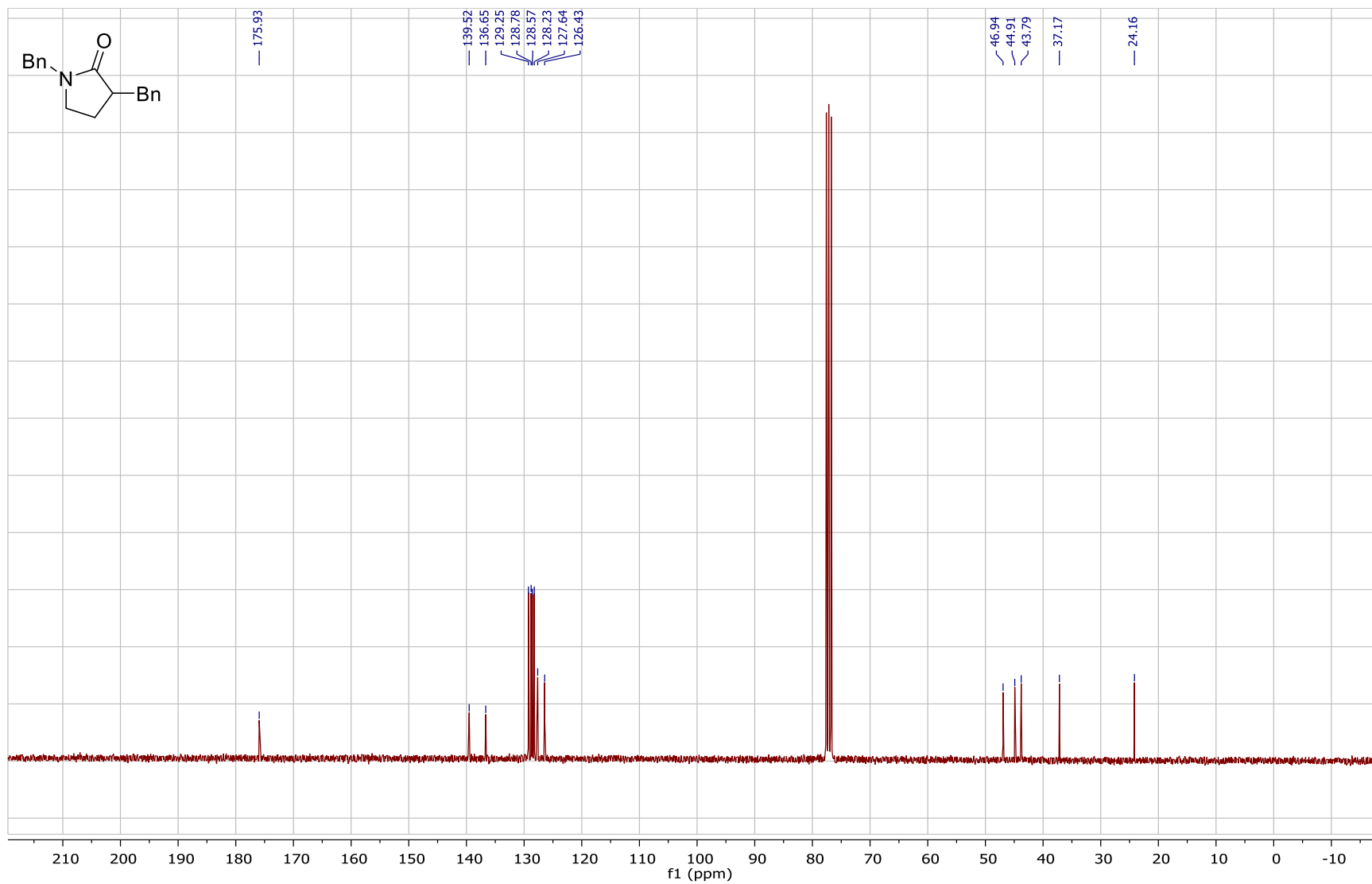
# 1,3-Dibenzylpyrrolidin-2-one (**3b**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



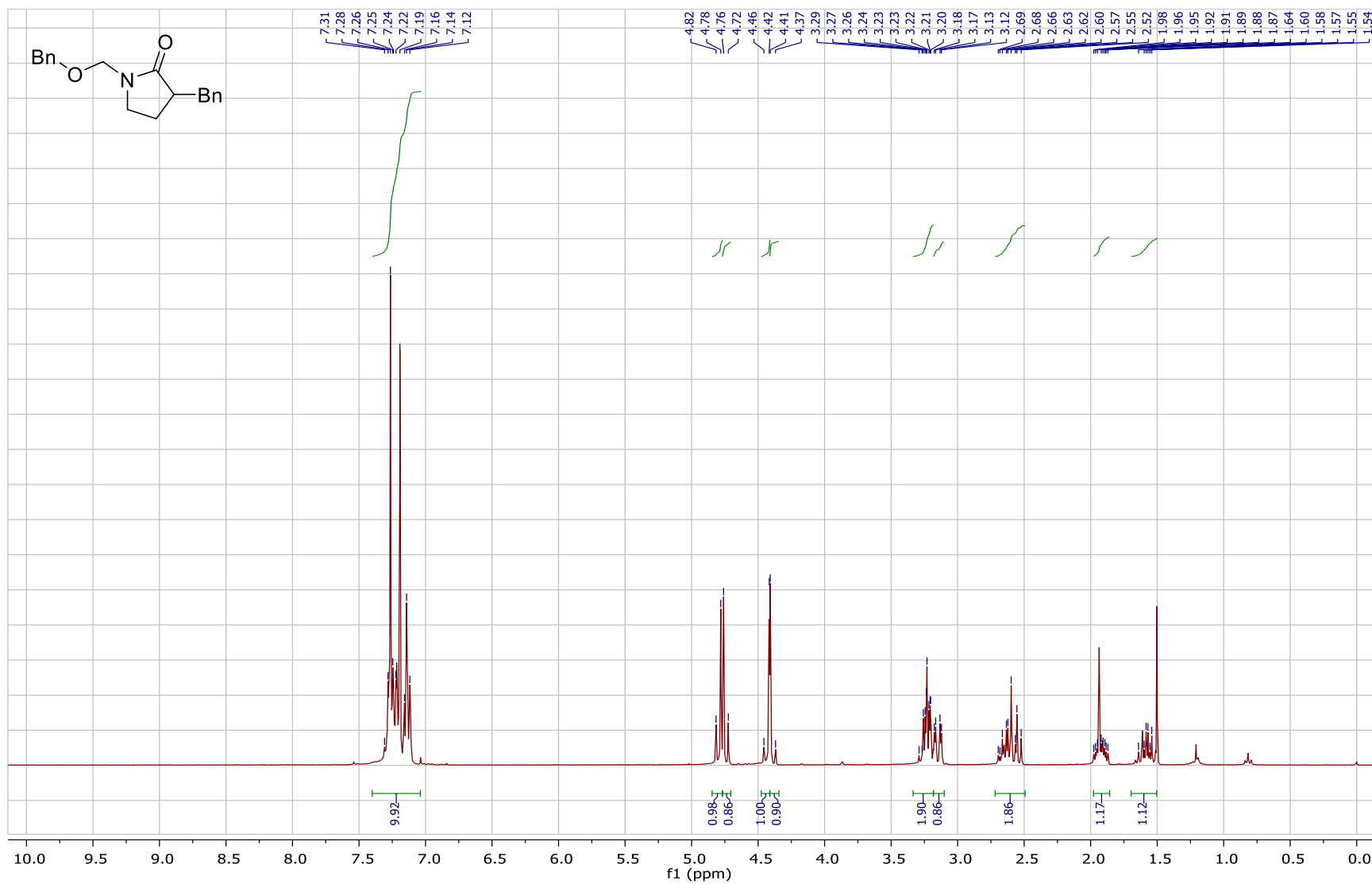


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

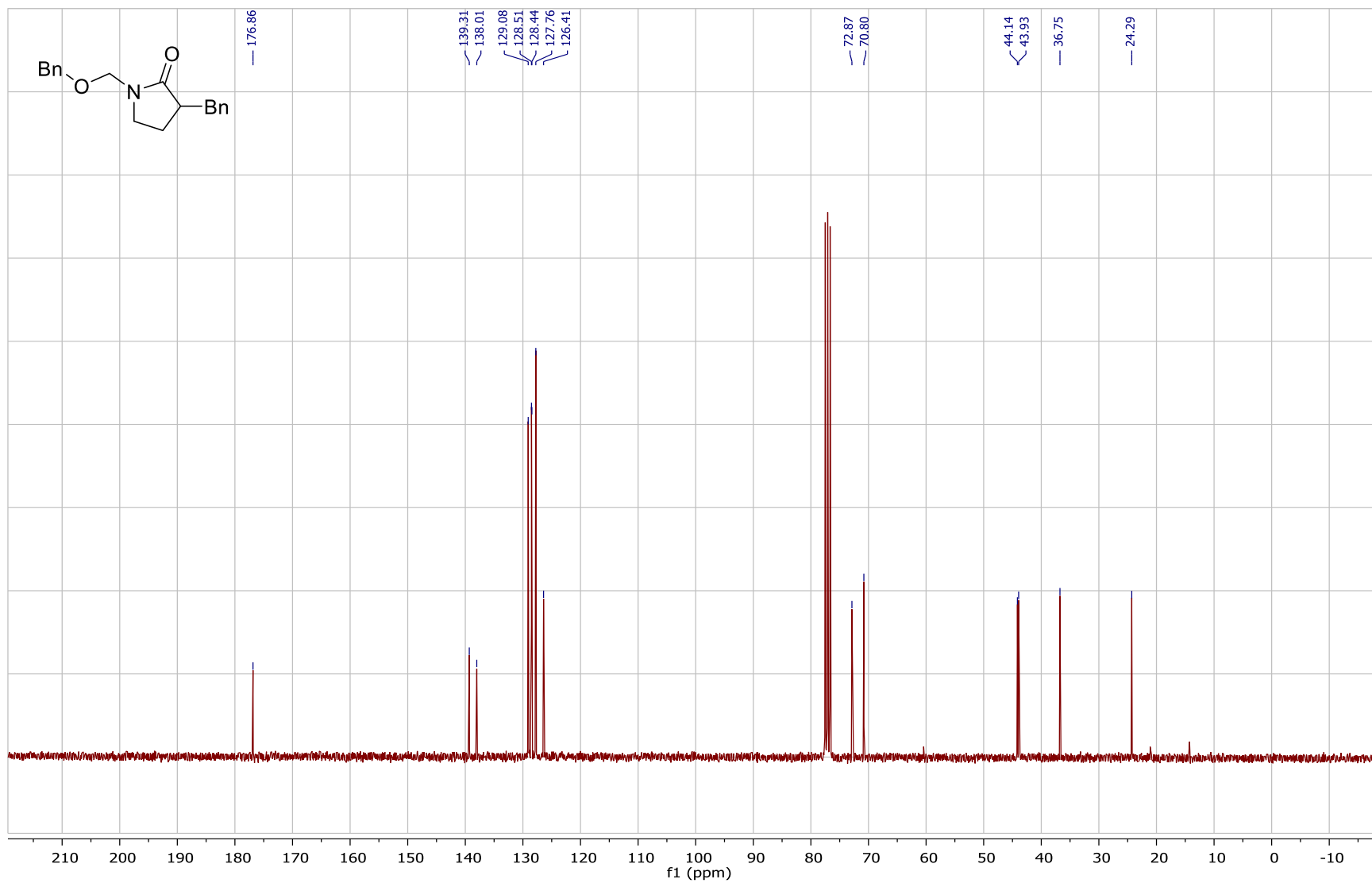


3-Benzyl-1-((benzyloxy)methyl)pyrrolidin-2-one (**3c**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

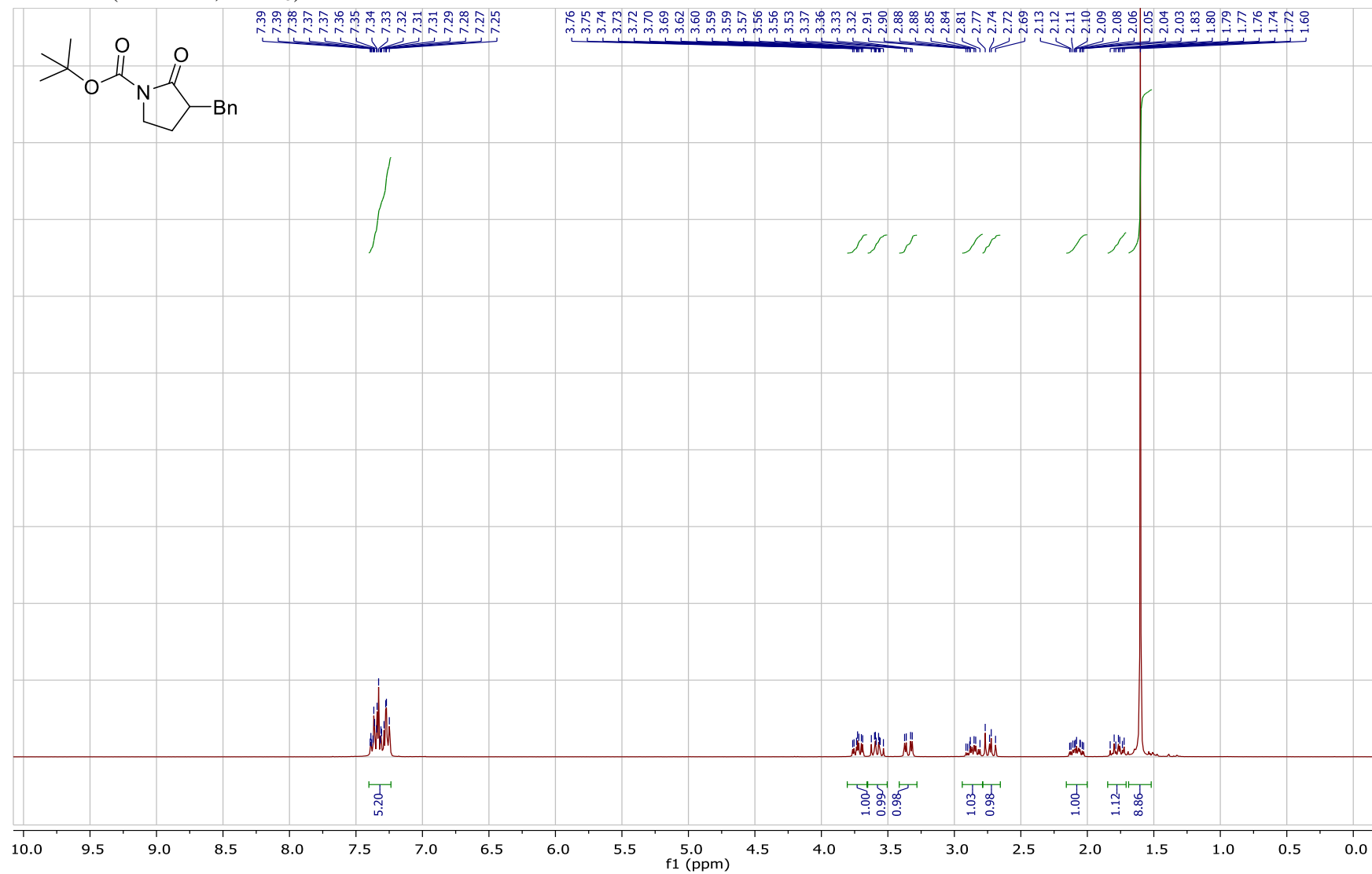


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

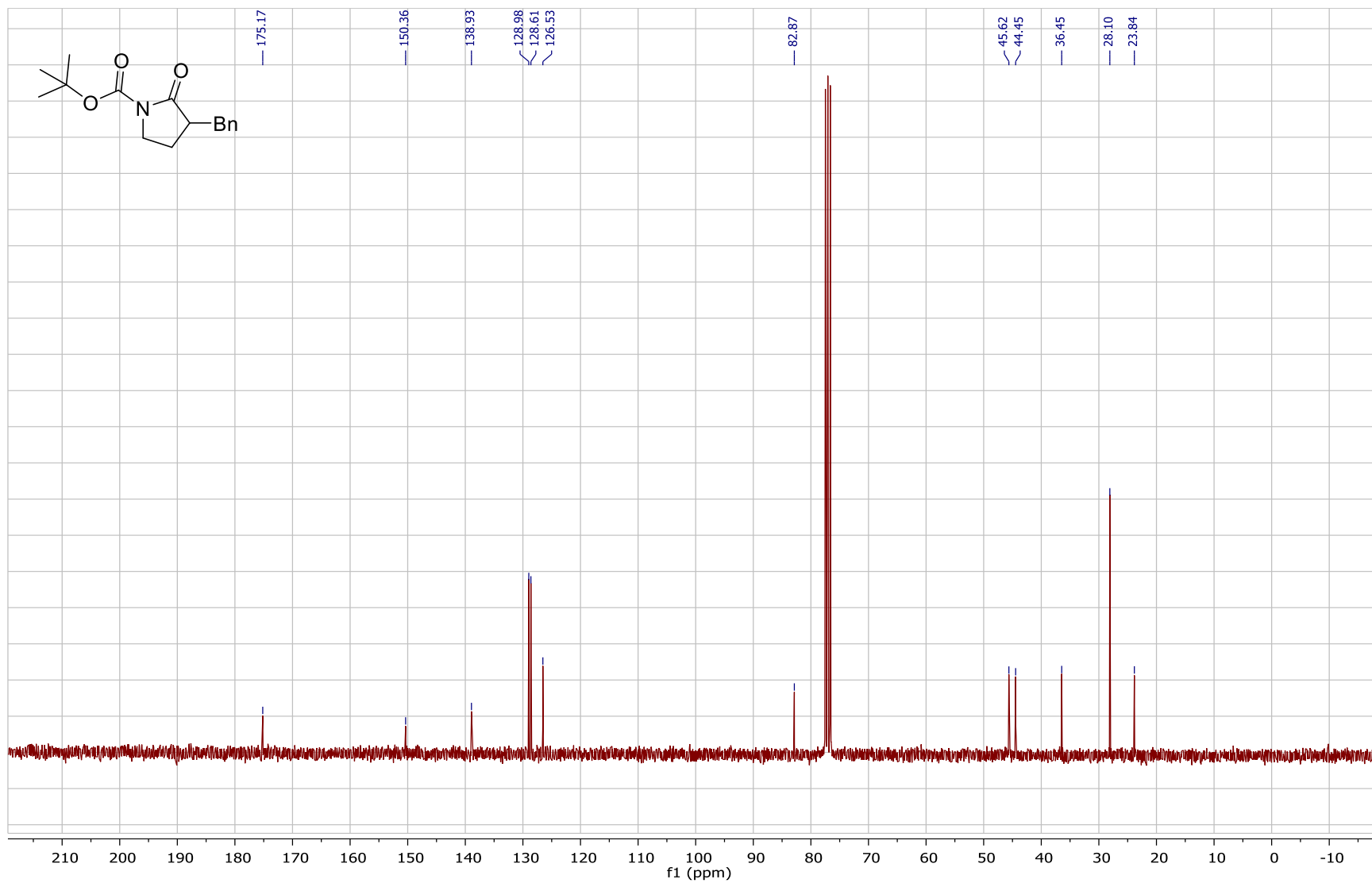


t-Butyl 3-benzyl-2-oxopyrrolidine-1-carboxylate (**3d**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

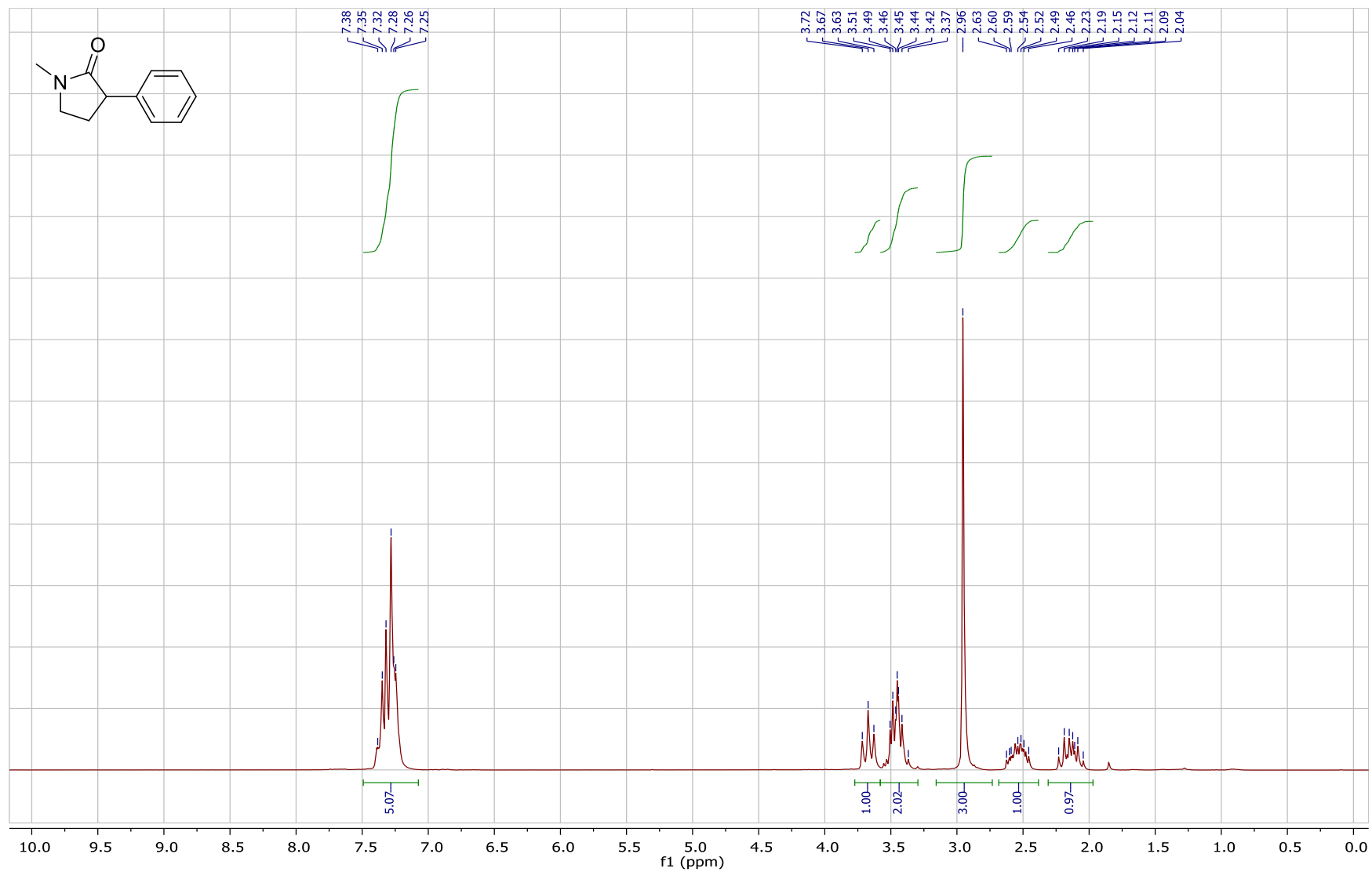


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

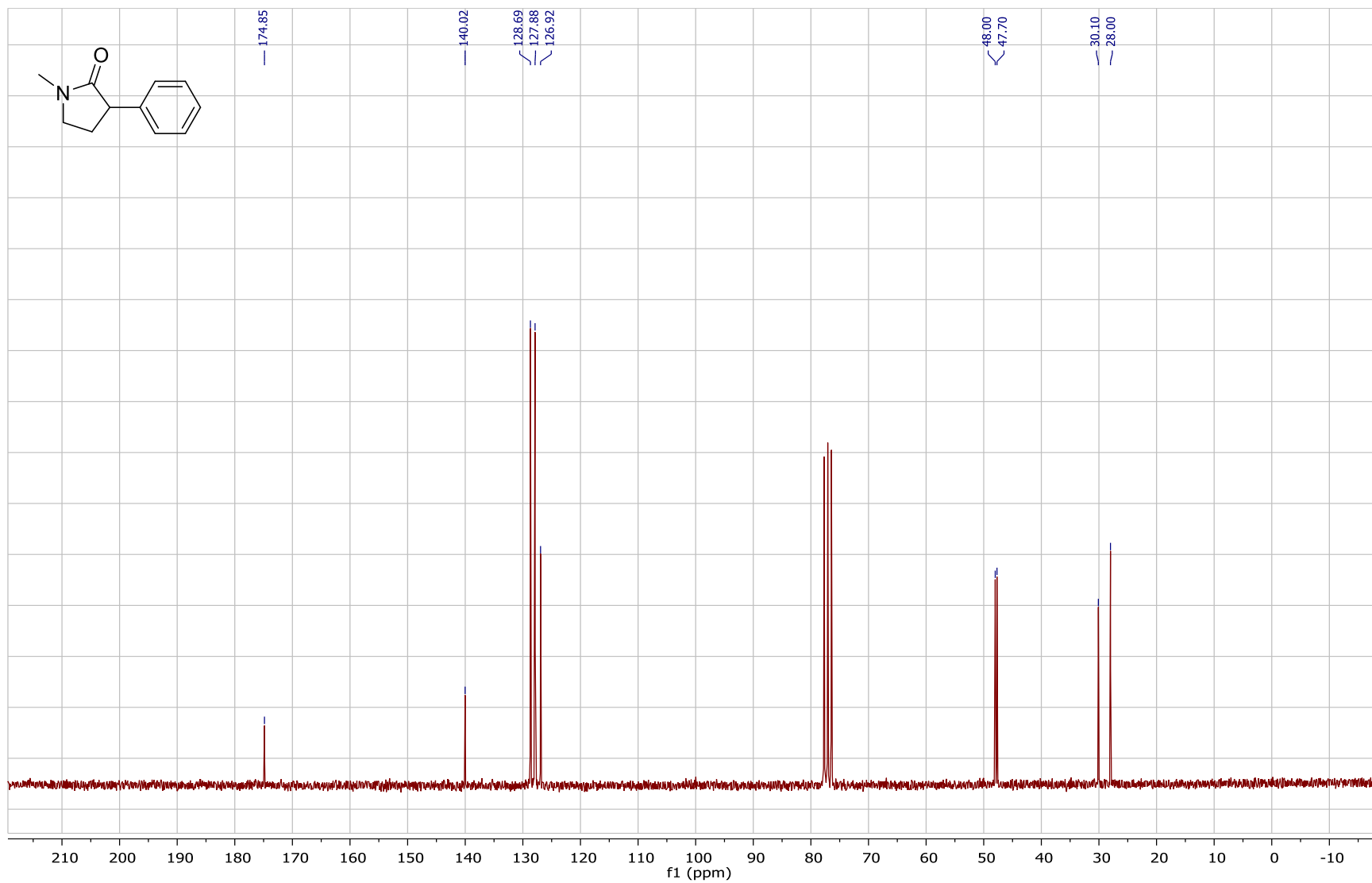


1-Methyl-3-phenylpyrrolidin-2-one (**3e**)

$^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )

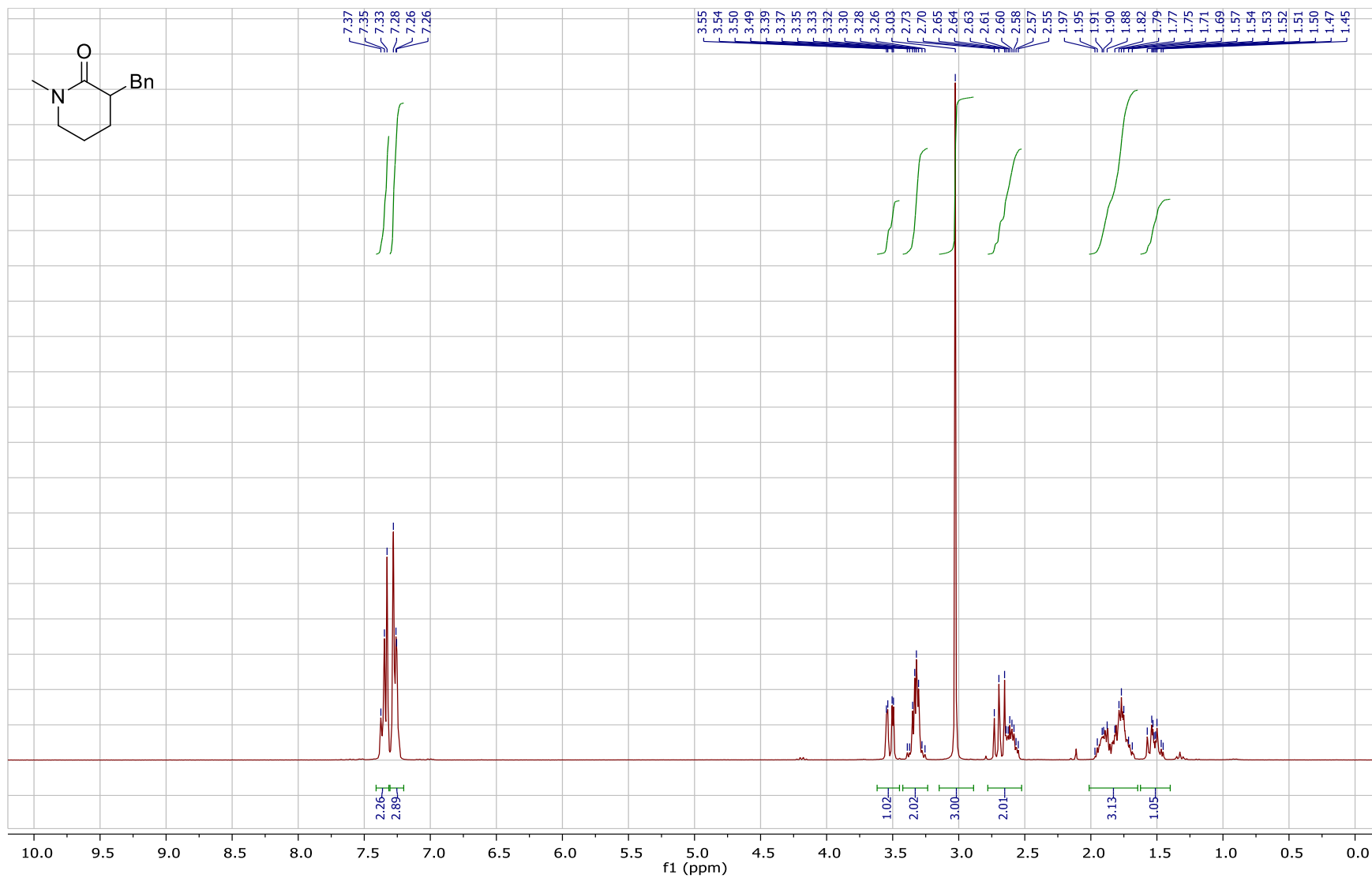


$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )



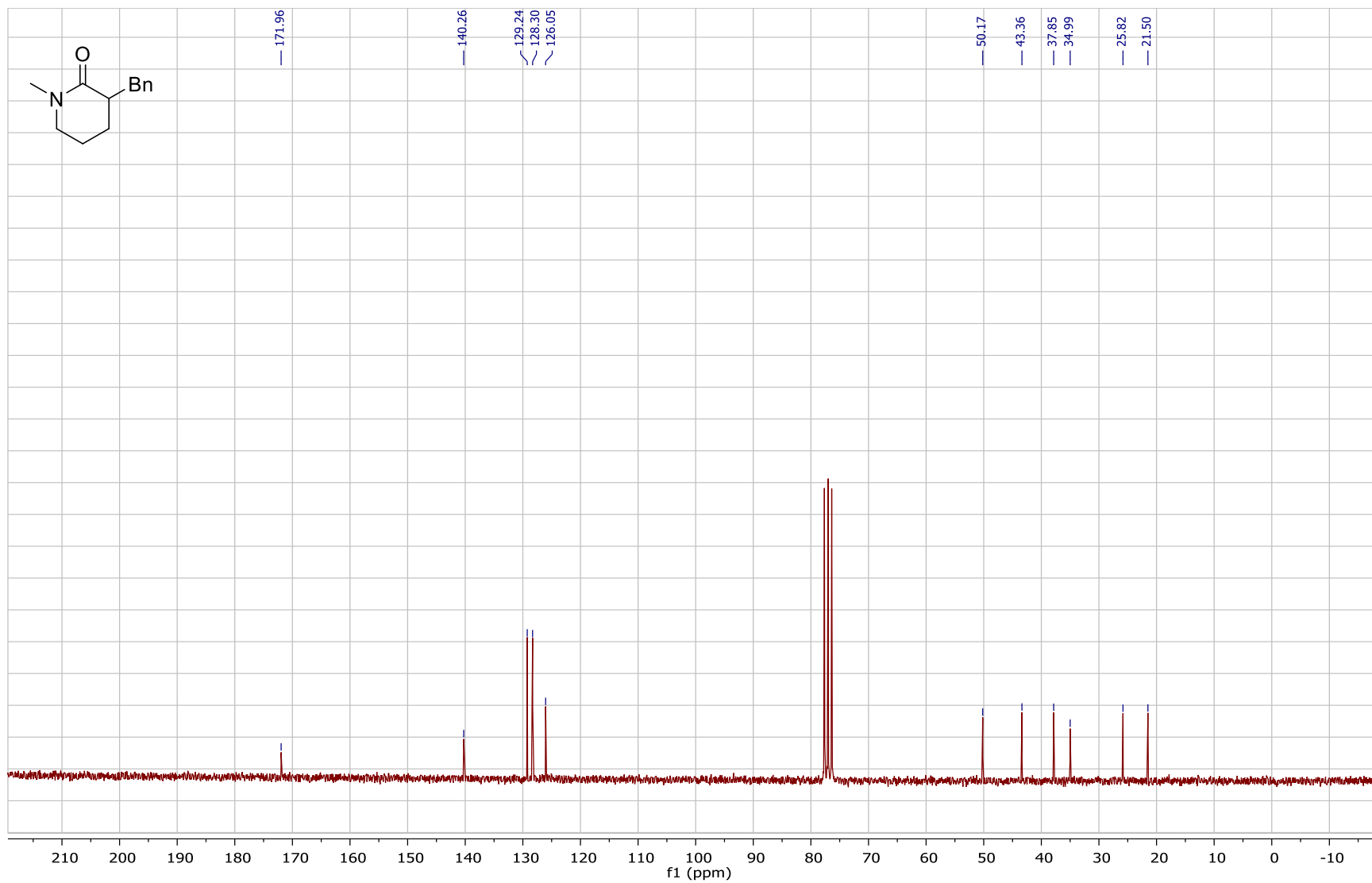
3-Benzyl-1-methylpiperidin-2-one (**3f**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



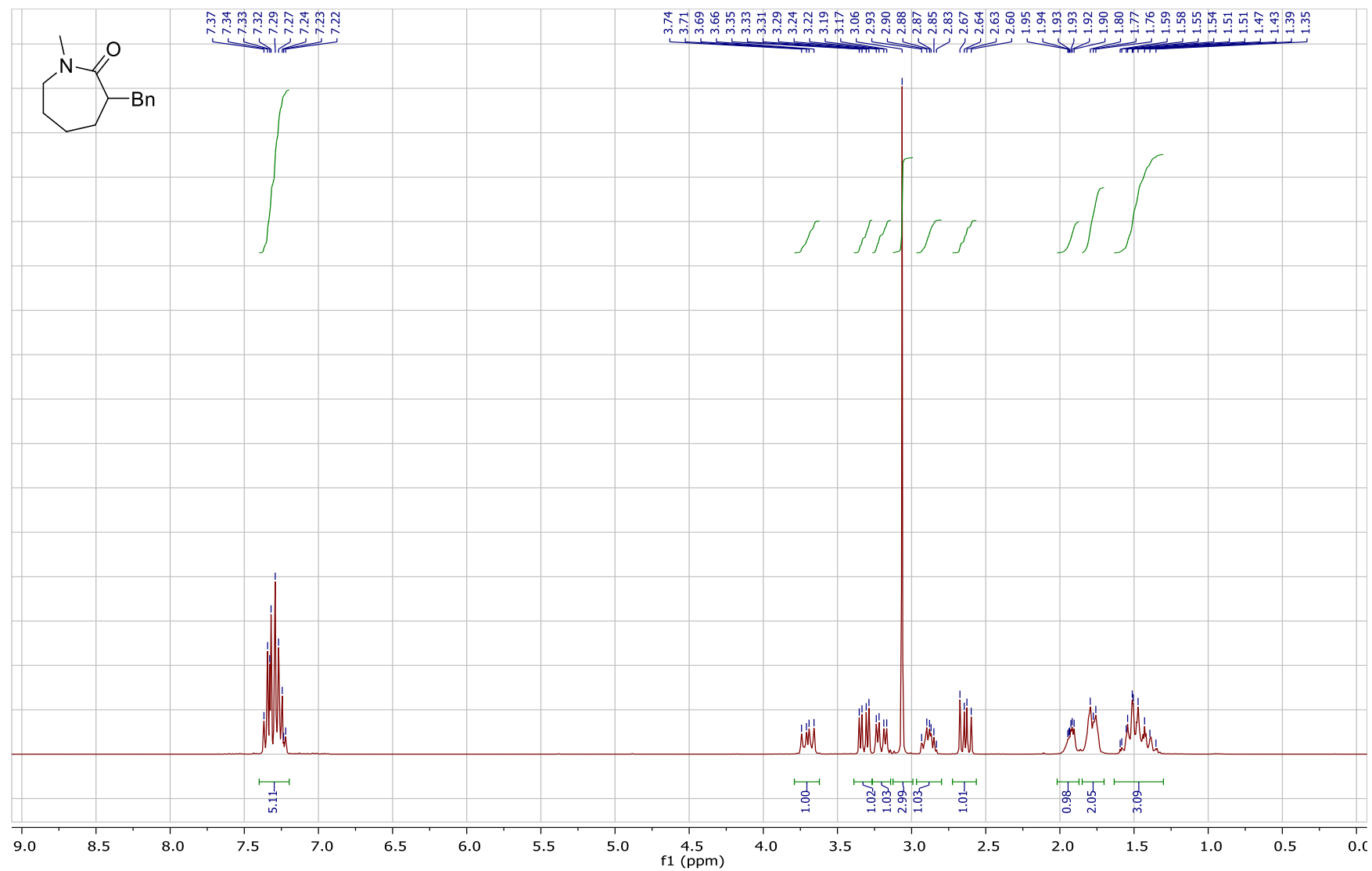


$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )

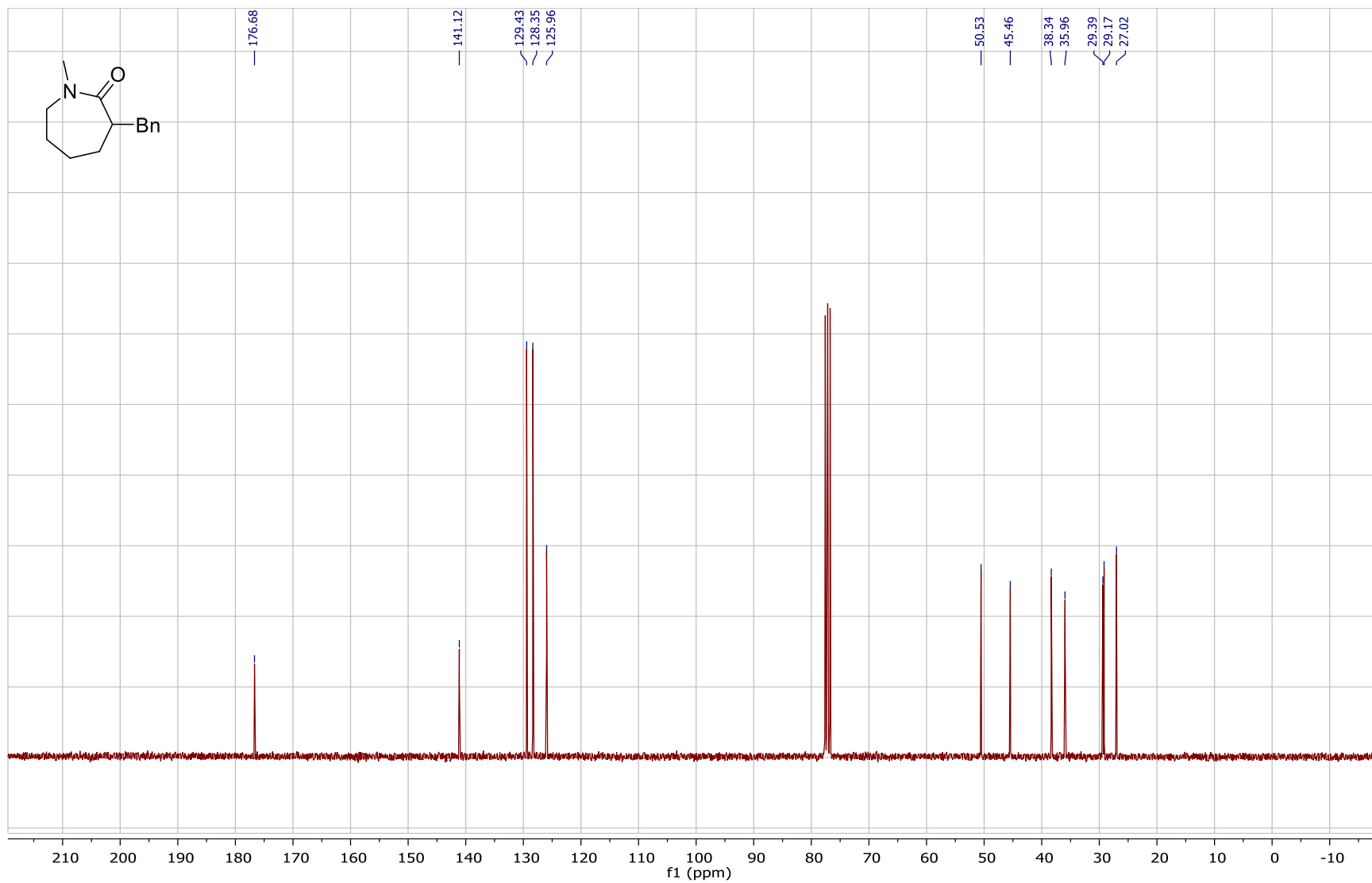


### 3-Benzyl-1-methylazepan-2-one (3g)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

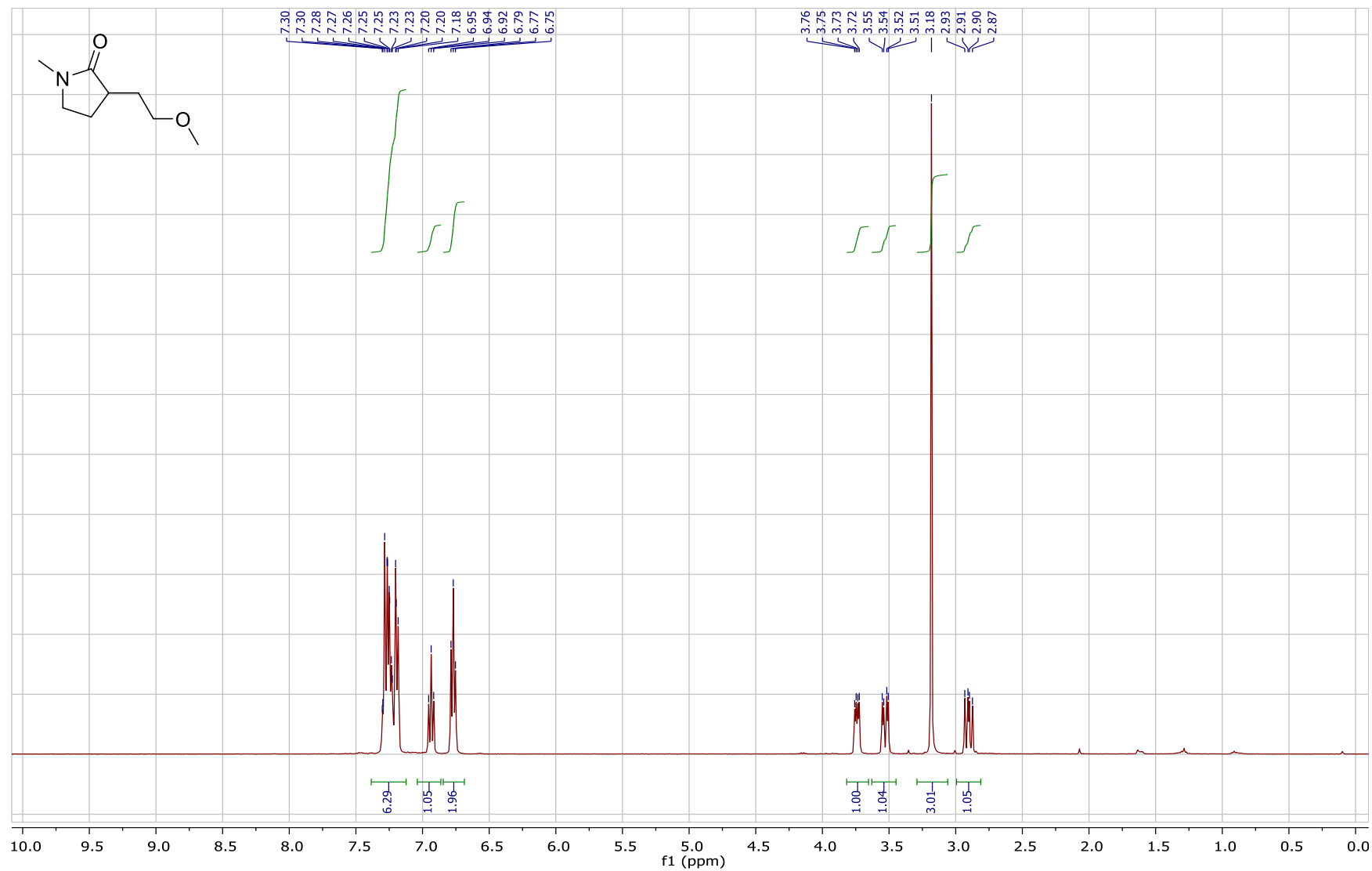


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

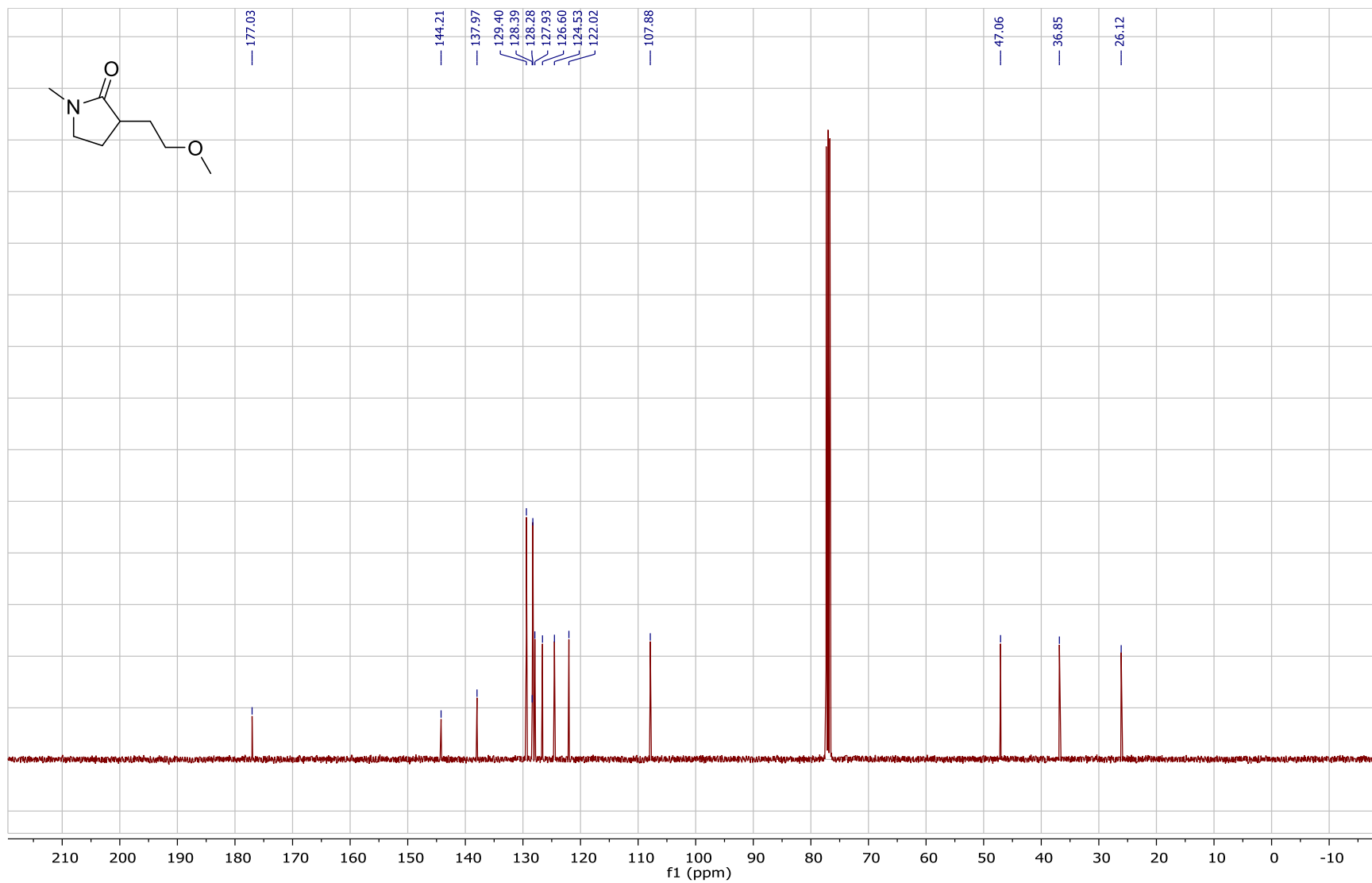


3-(2-Methoxyethyl)-1-methylpyrrolidin-2-one (**3h**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

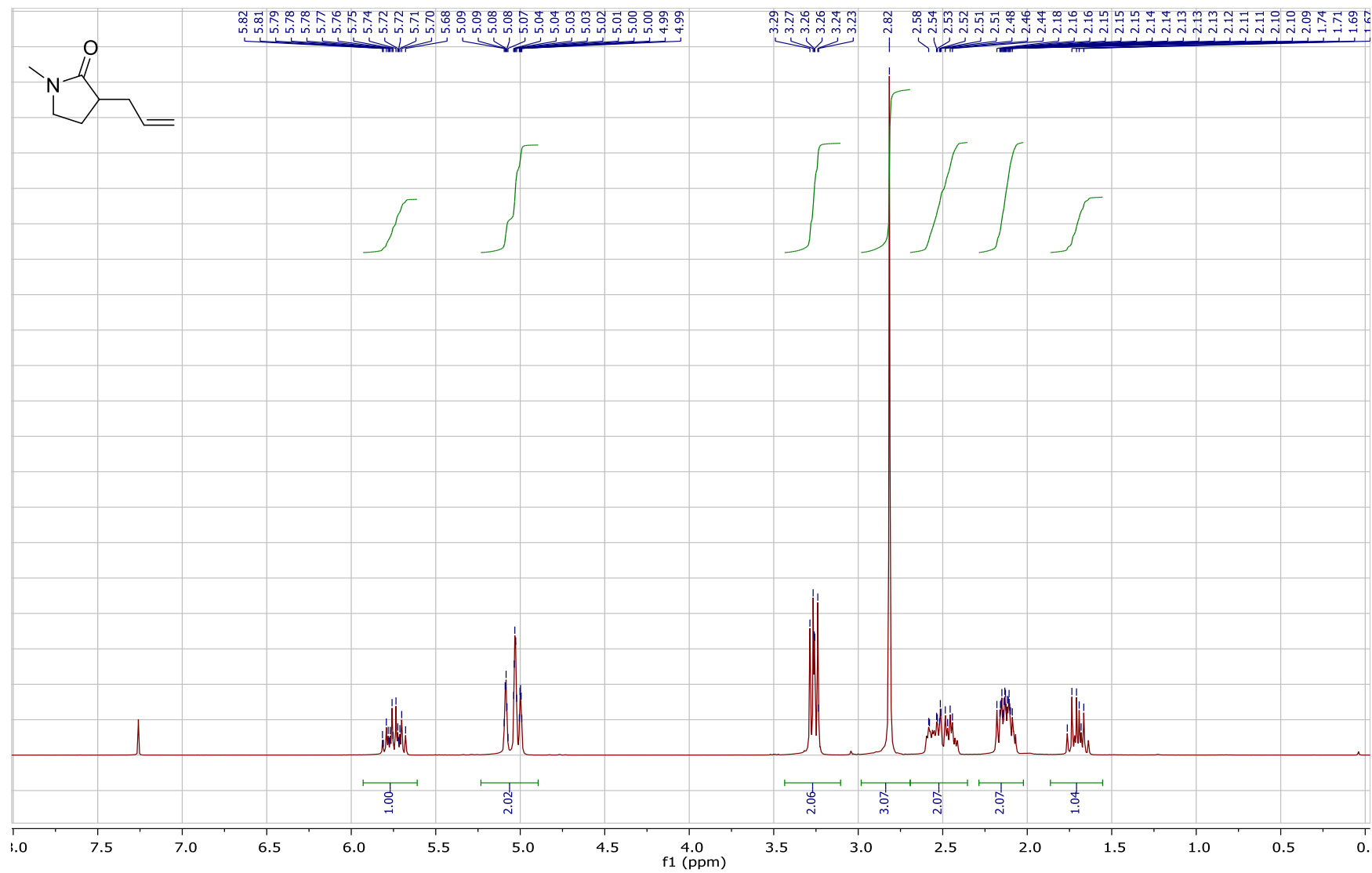


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

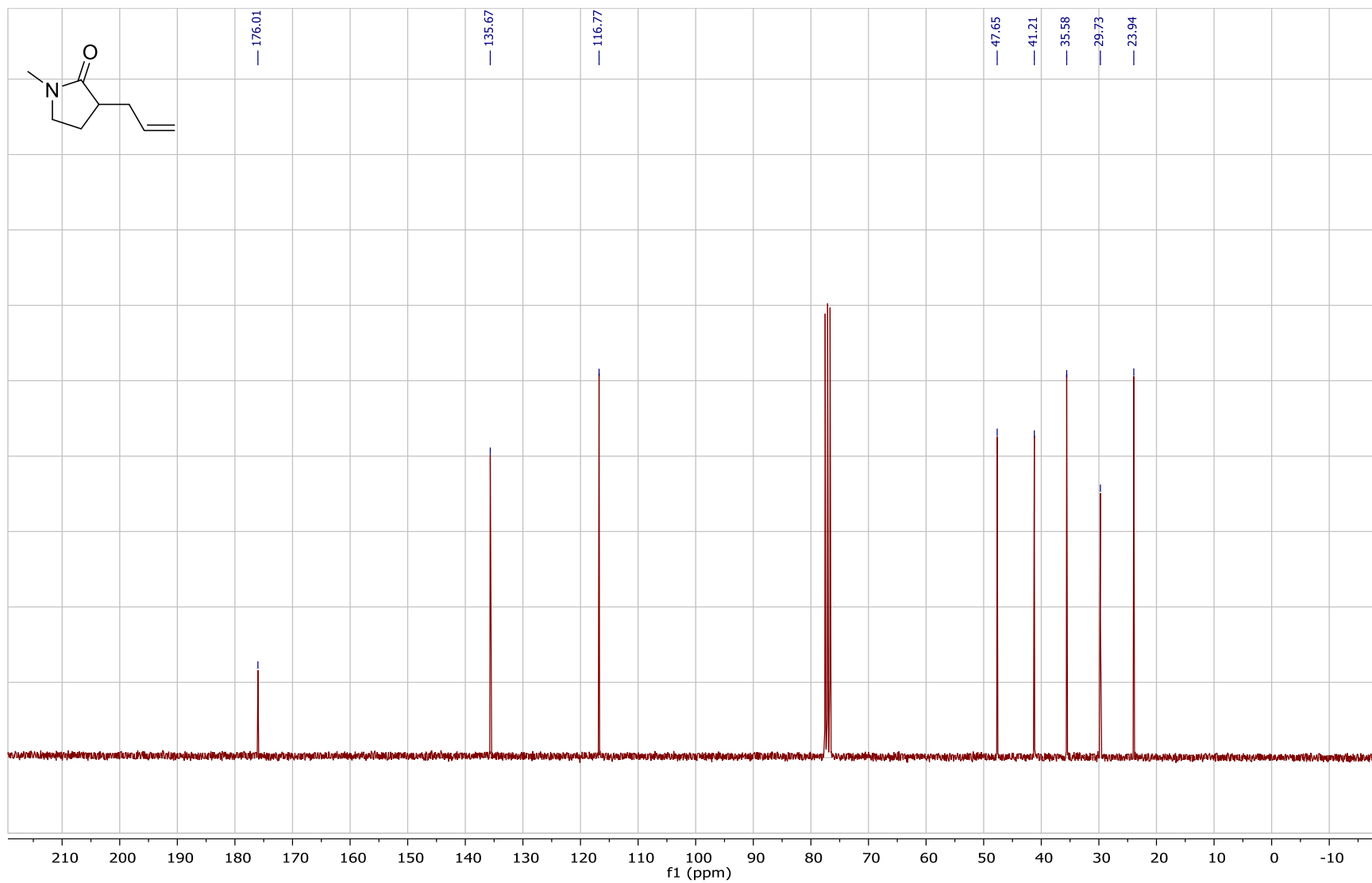


### 3-Allyl-1-methylpyrrolidin-2-one (**3i**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

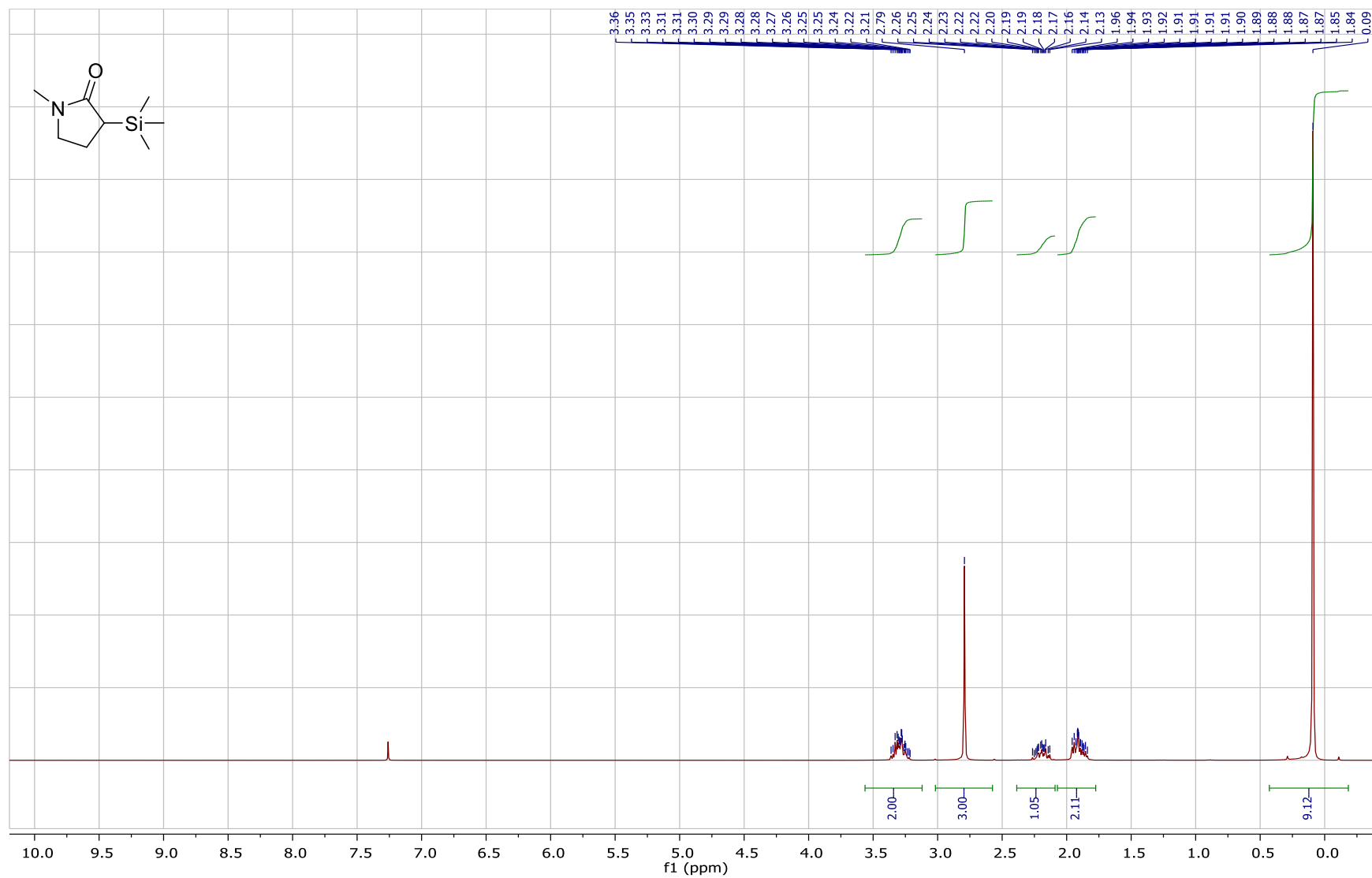


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



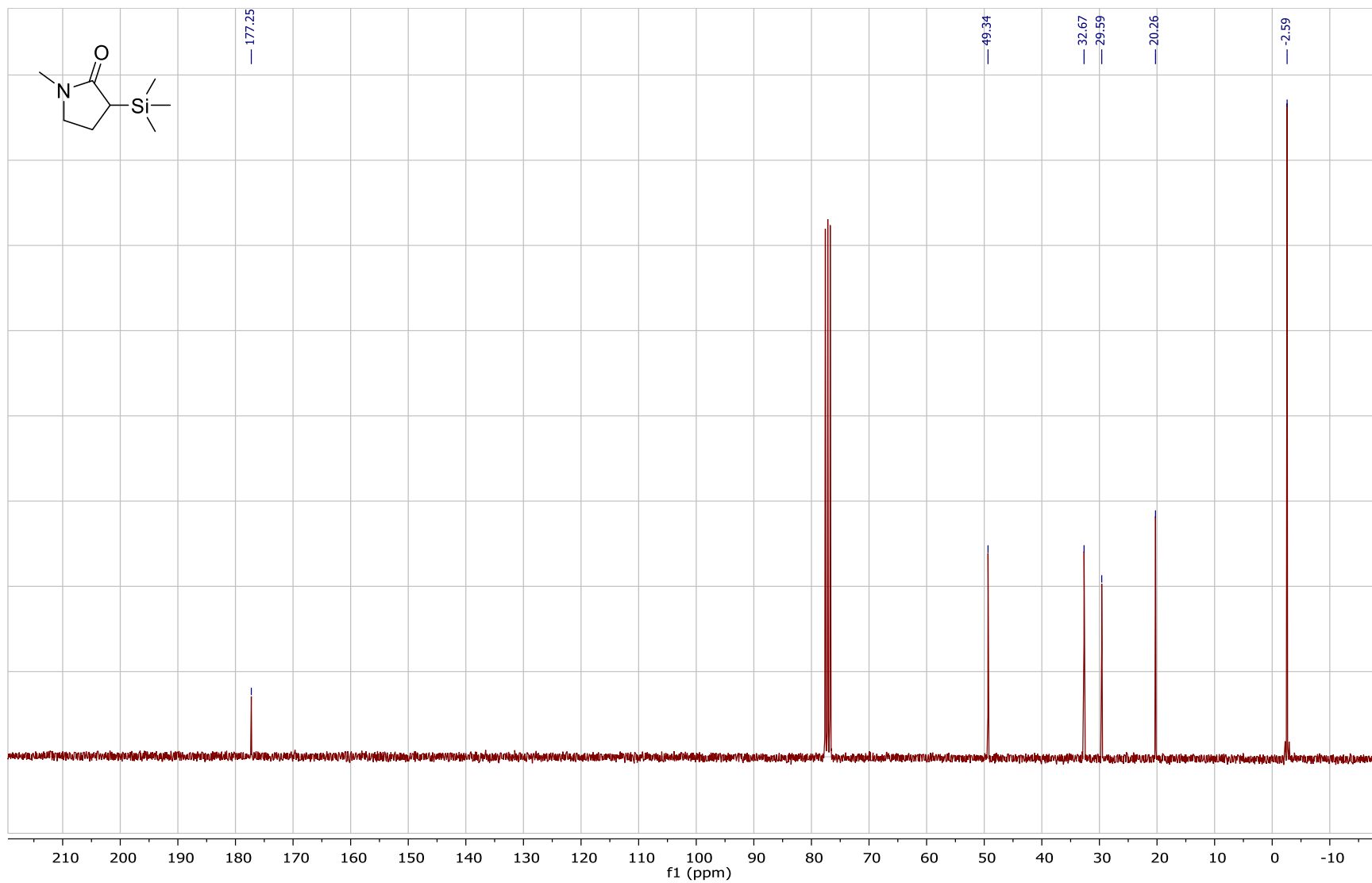
1-Methyl-3-(trimethylsilyl)pyrrolidin-2-one (**3j**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



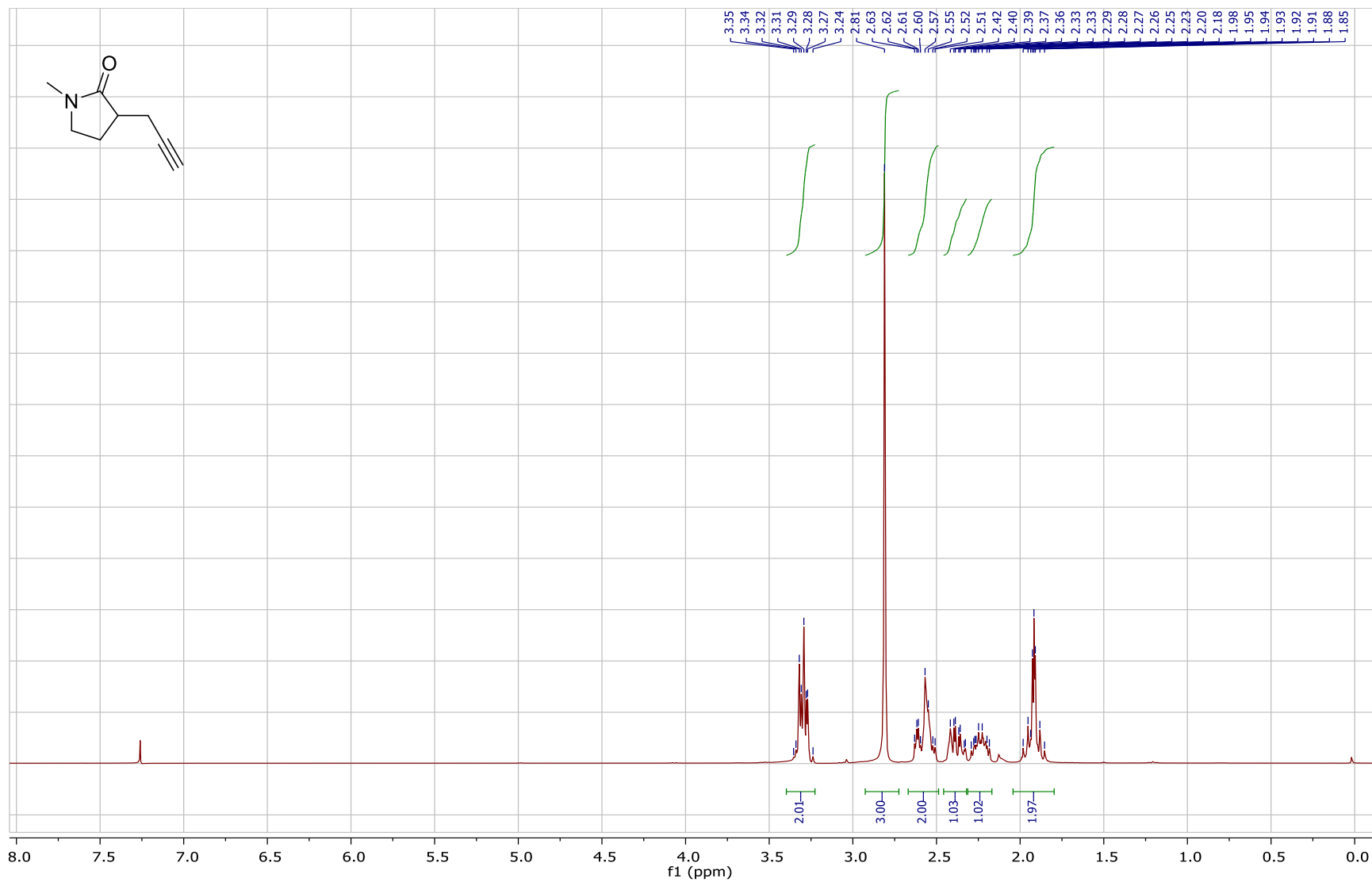


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

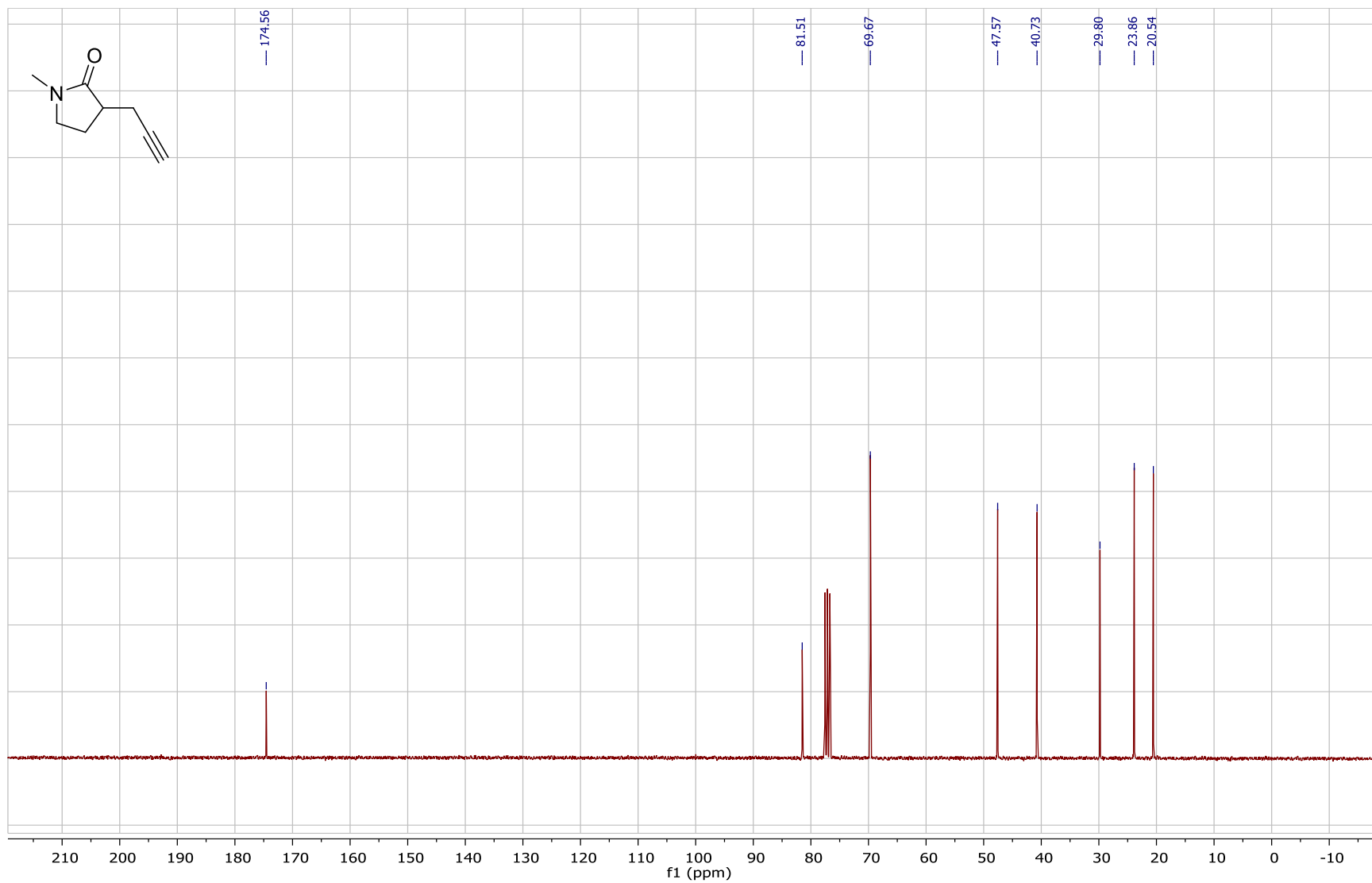


1-Methyl-3-(prop-2-yn-1-yl)pyrrolidin-2-one (**3k**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

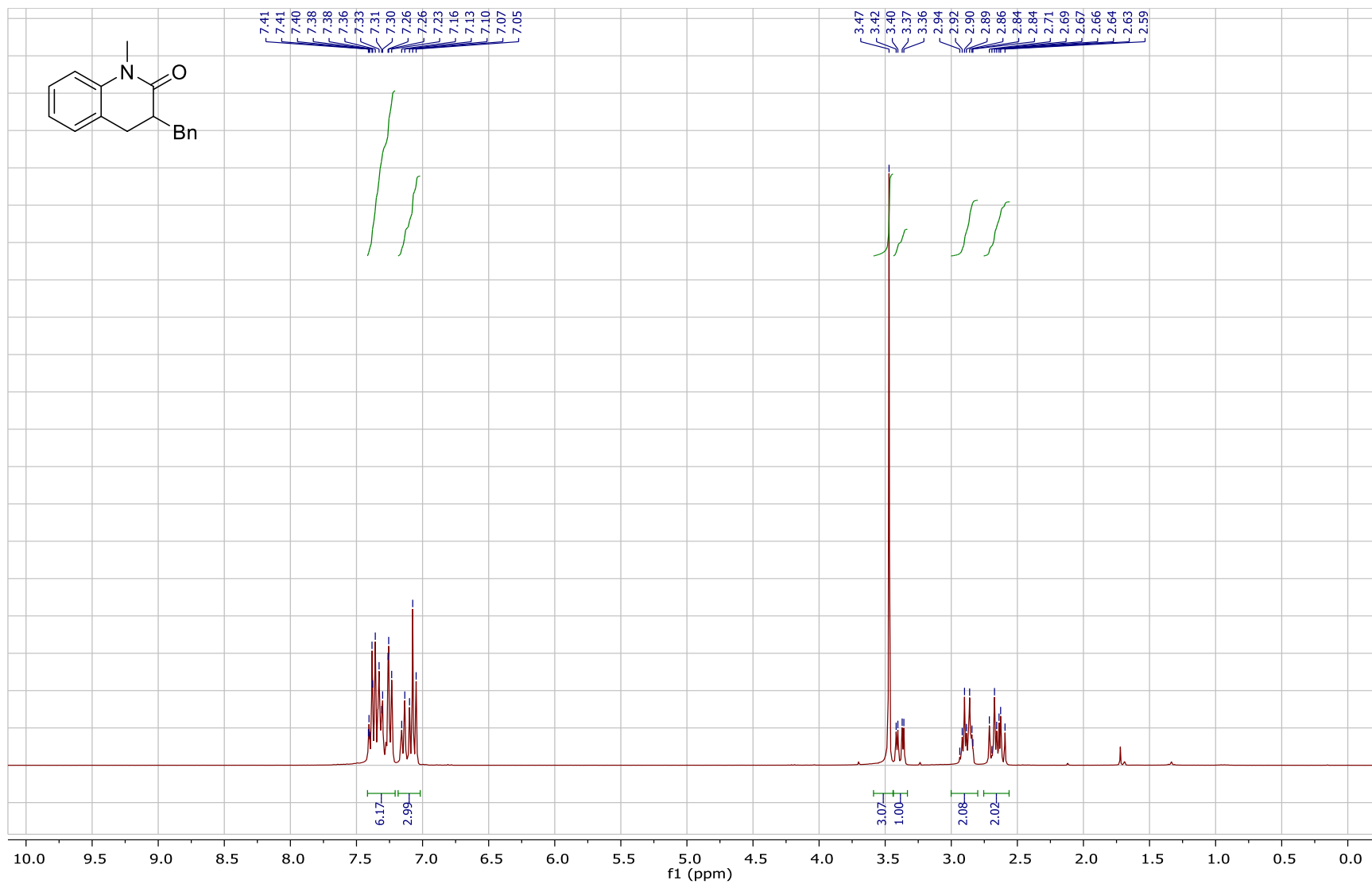


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

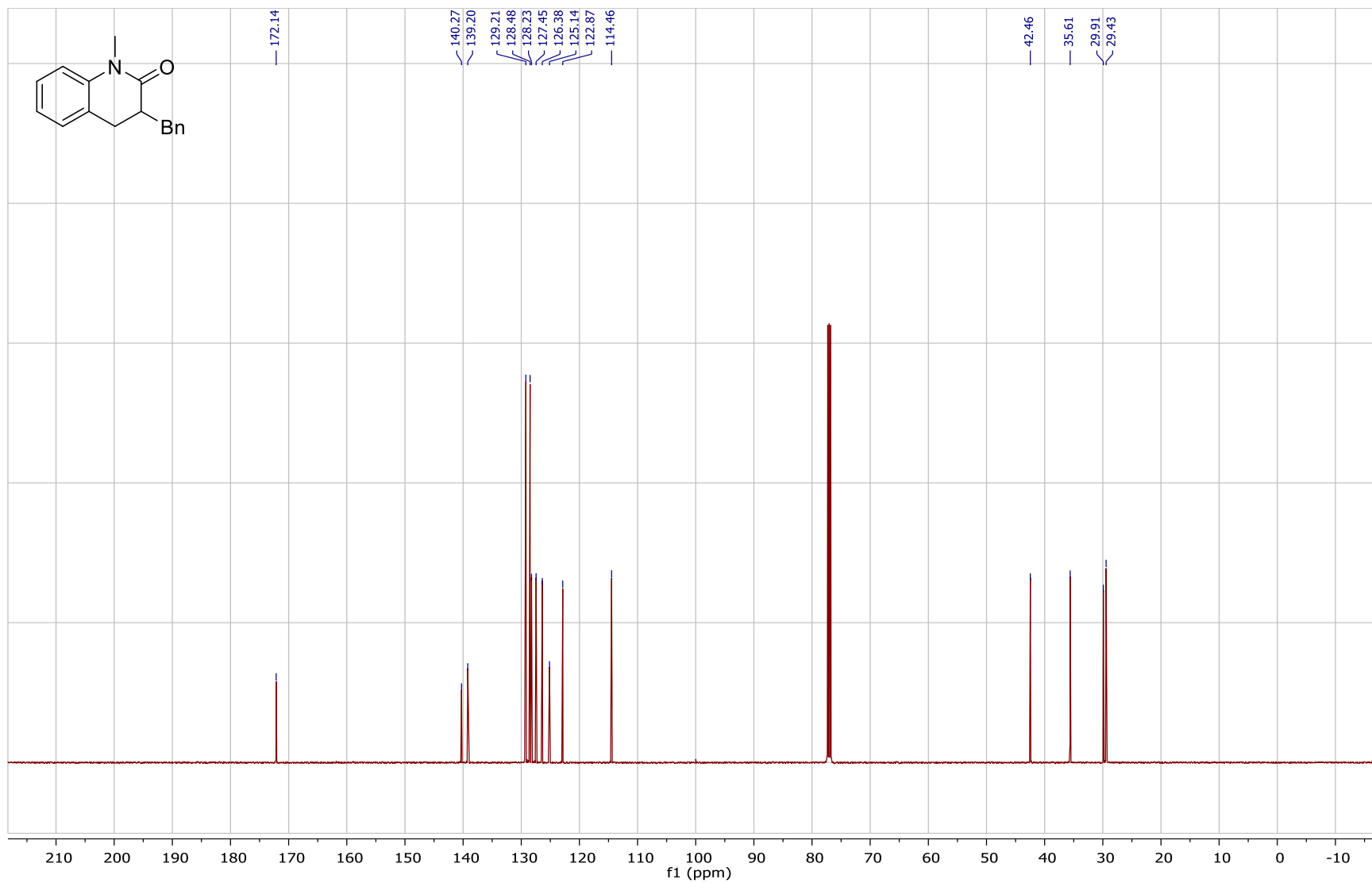


### 3-Benzyl-1-methyl-3,4-dihydroquinolin-2(1H)-one (**31**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

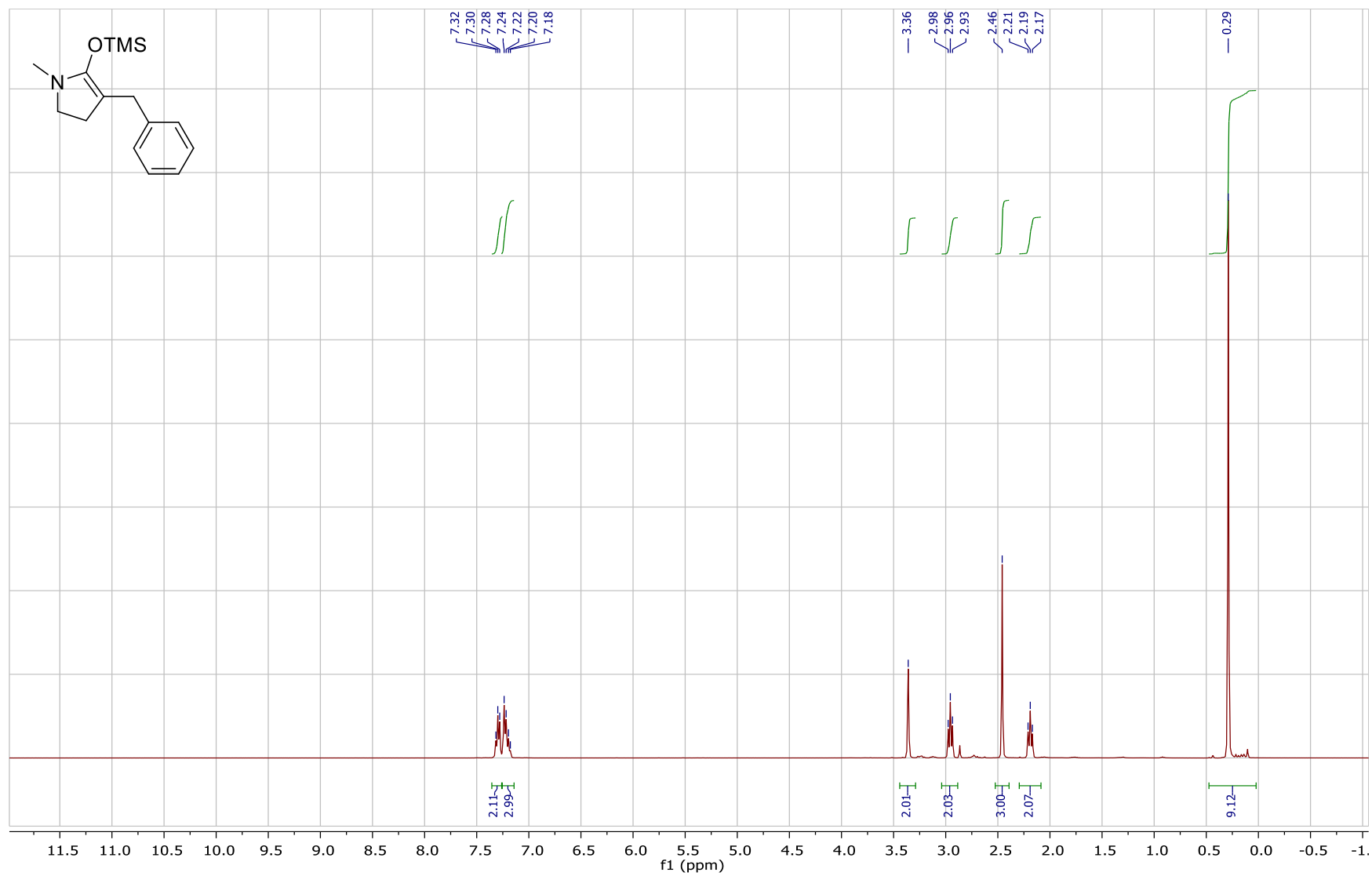


$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

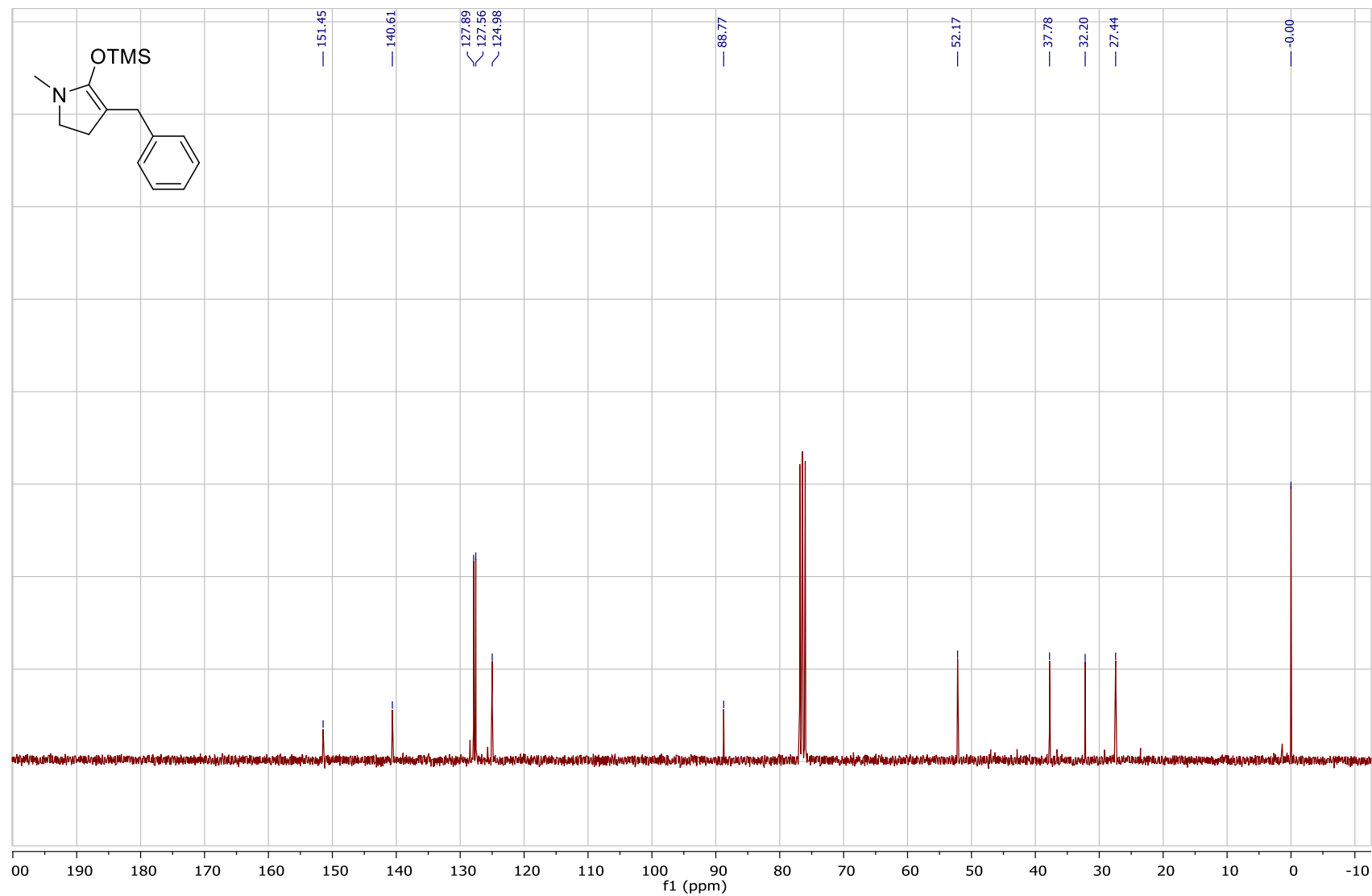


4-Benzyl-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4a**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

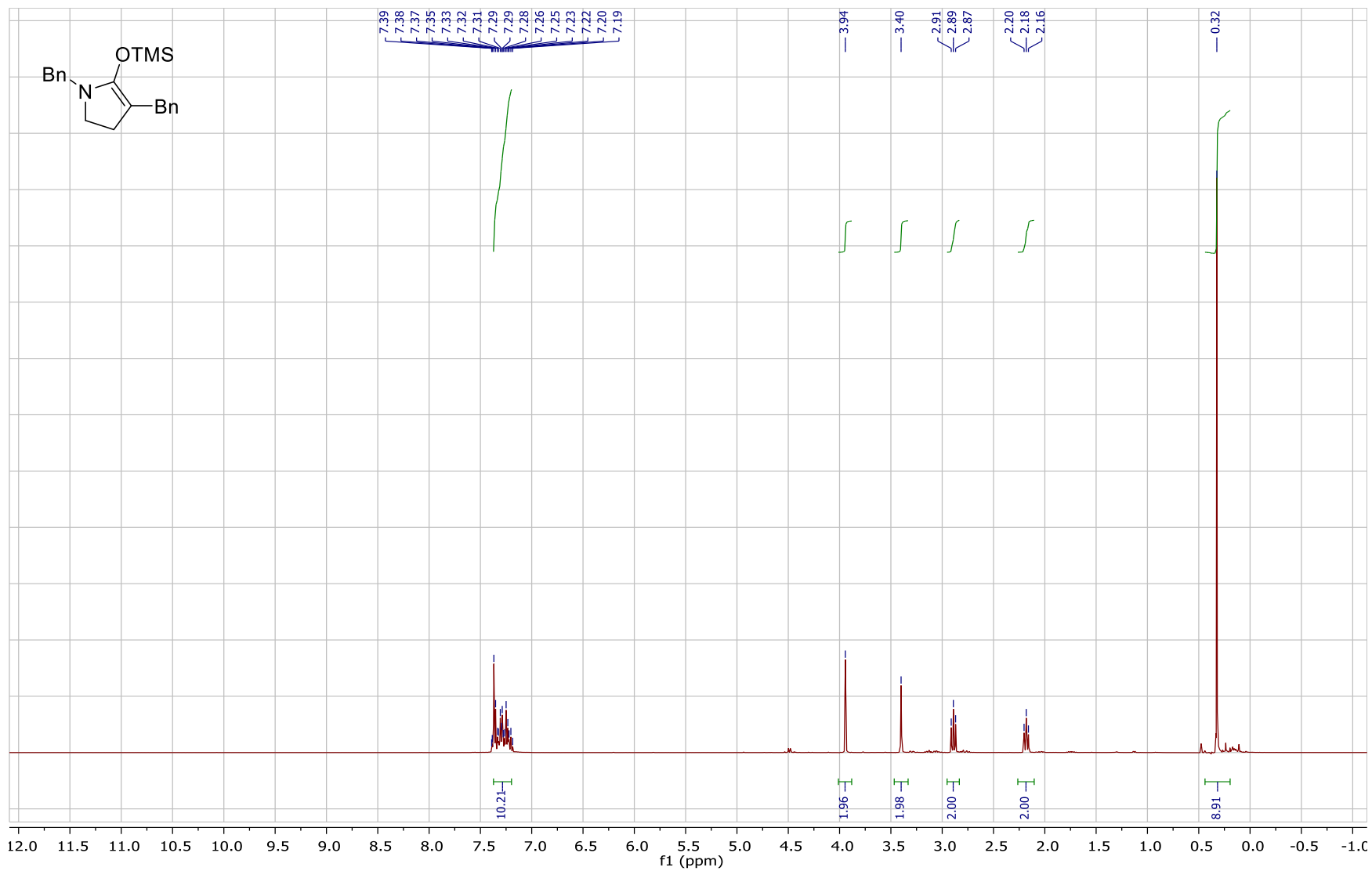


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



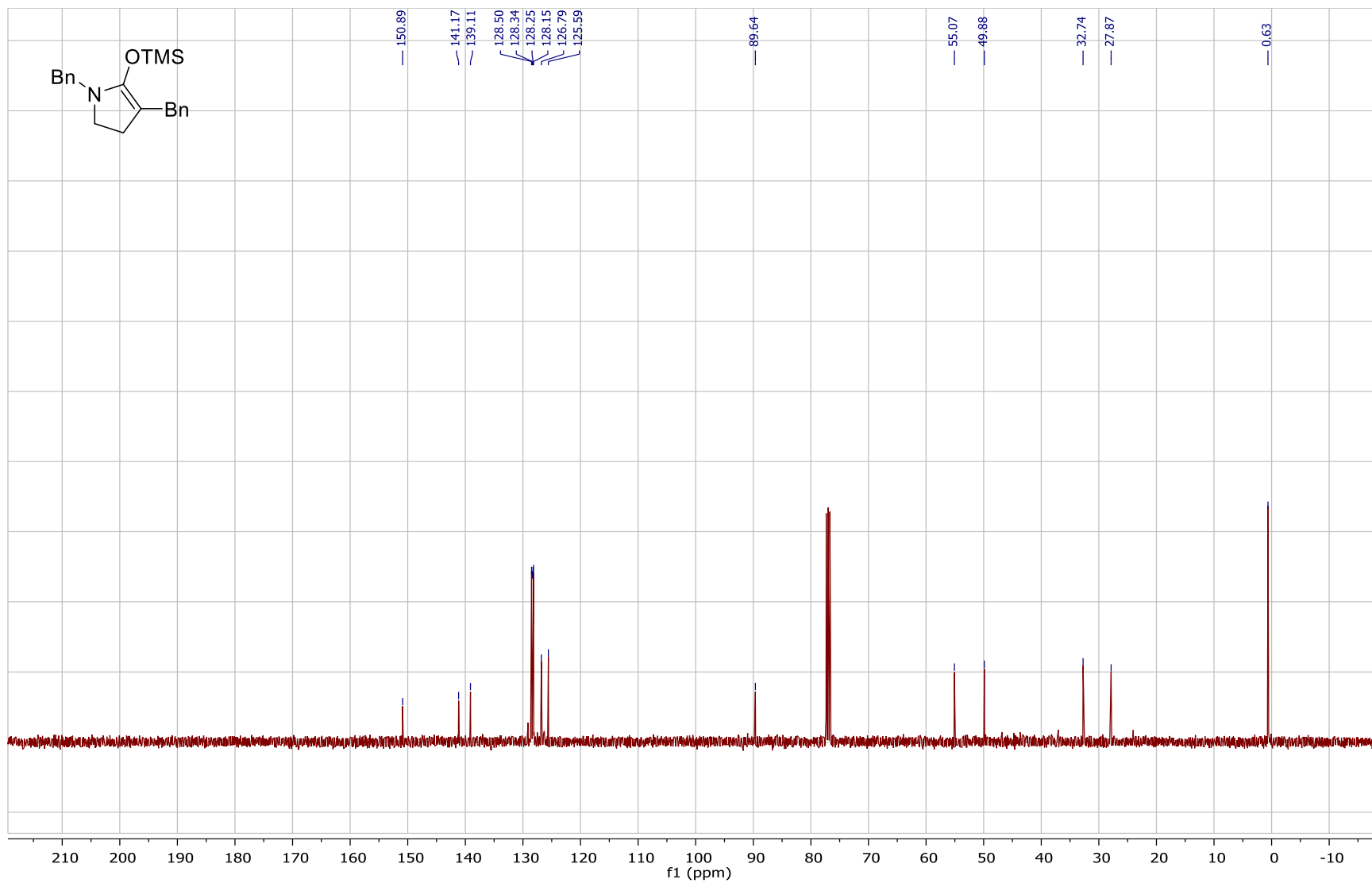
1,4-Dibenzyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4b**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



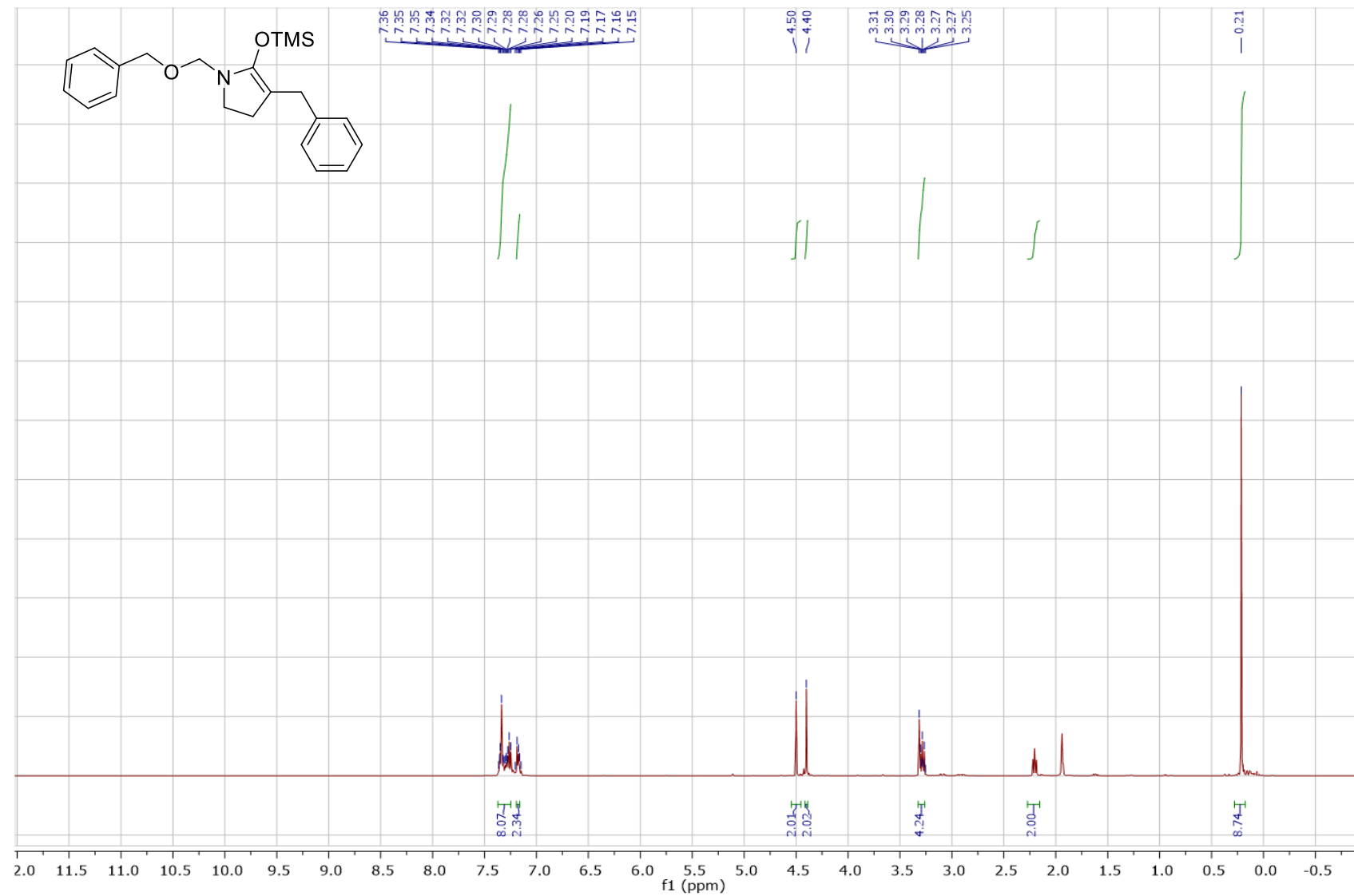


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

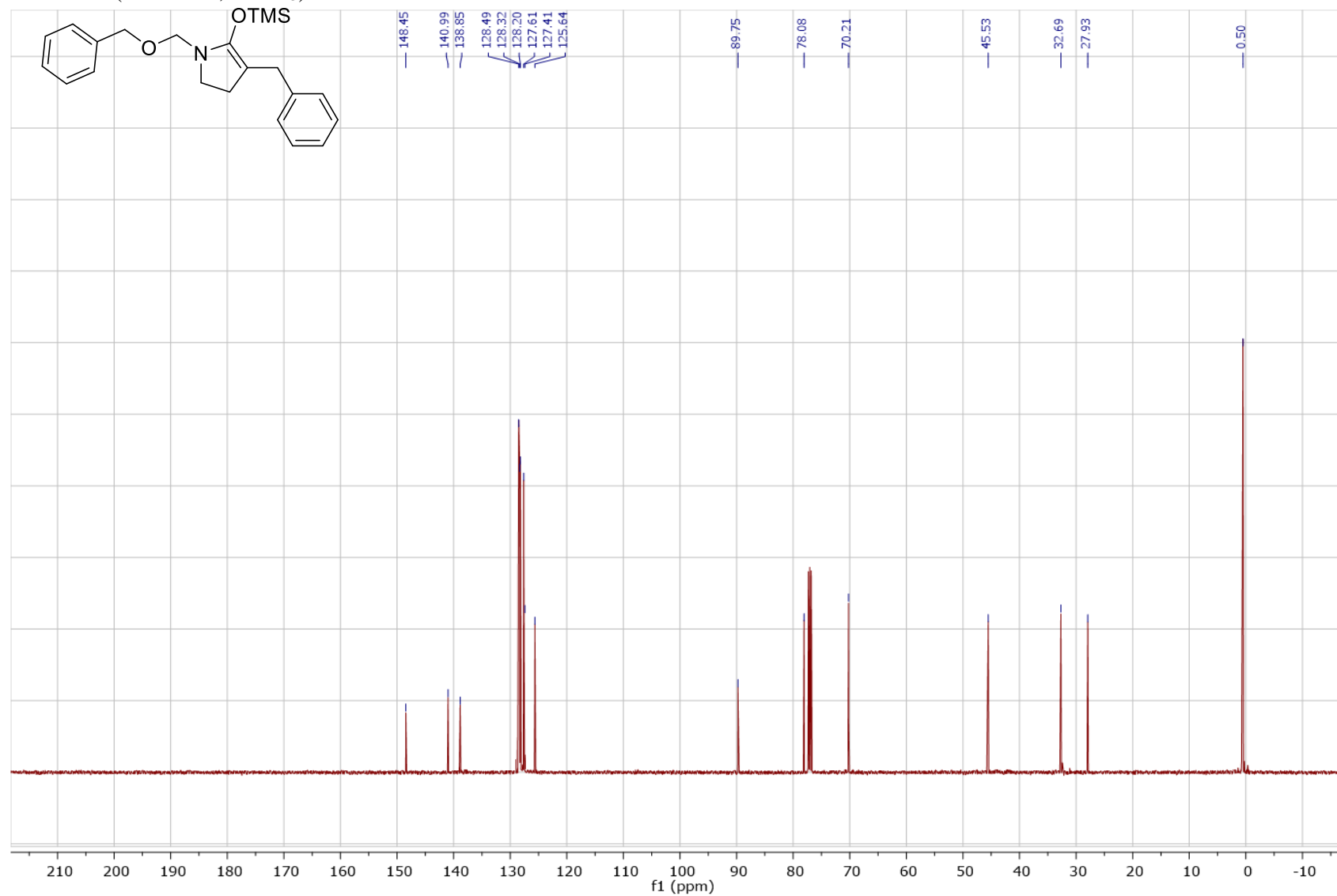


4-Benzyl-1-((benzyloxy)methyl)-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4c**)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )

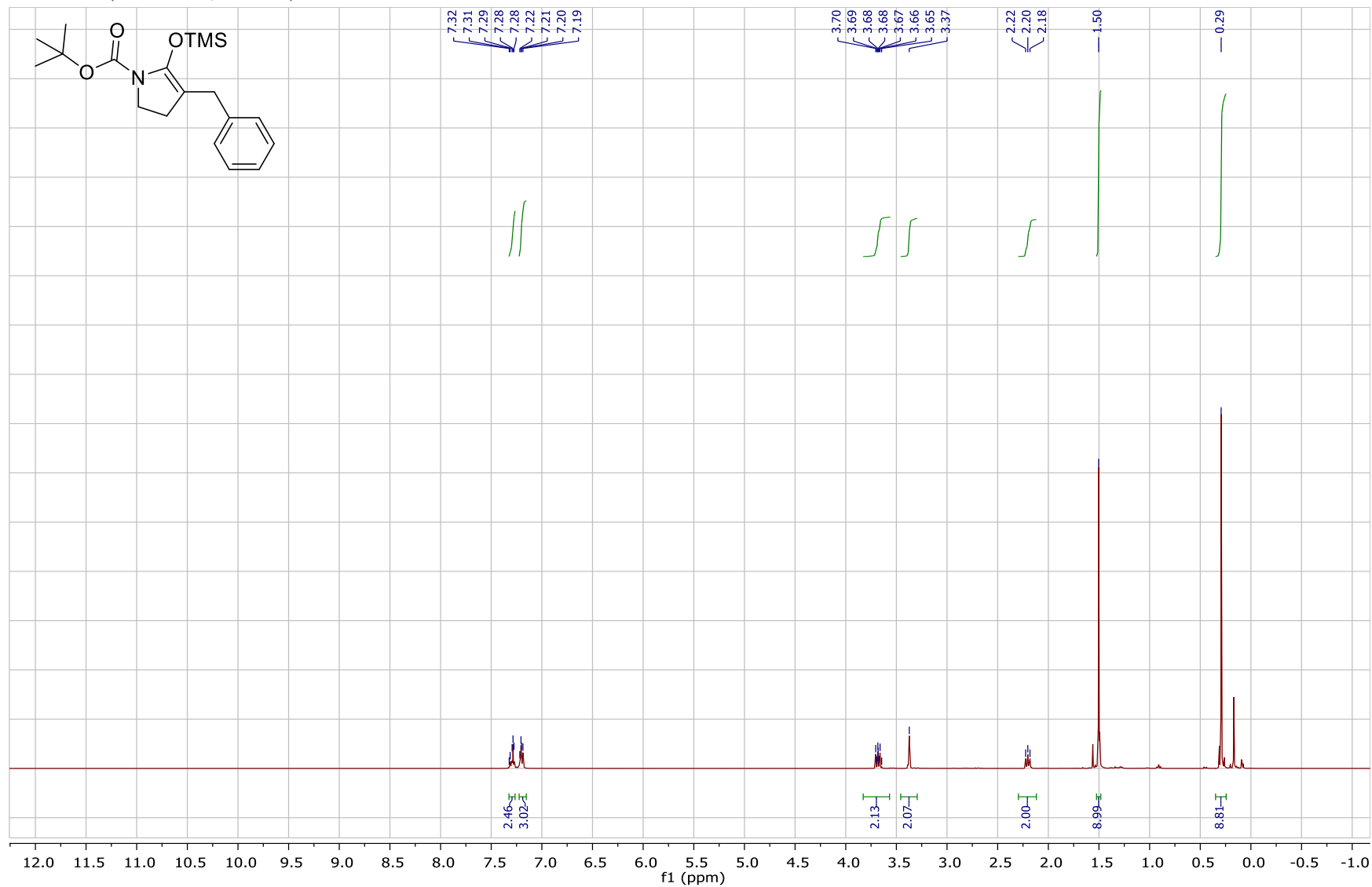


$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )

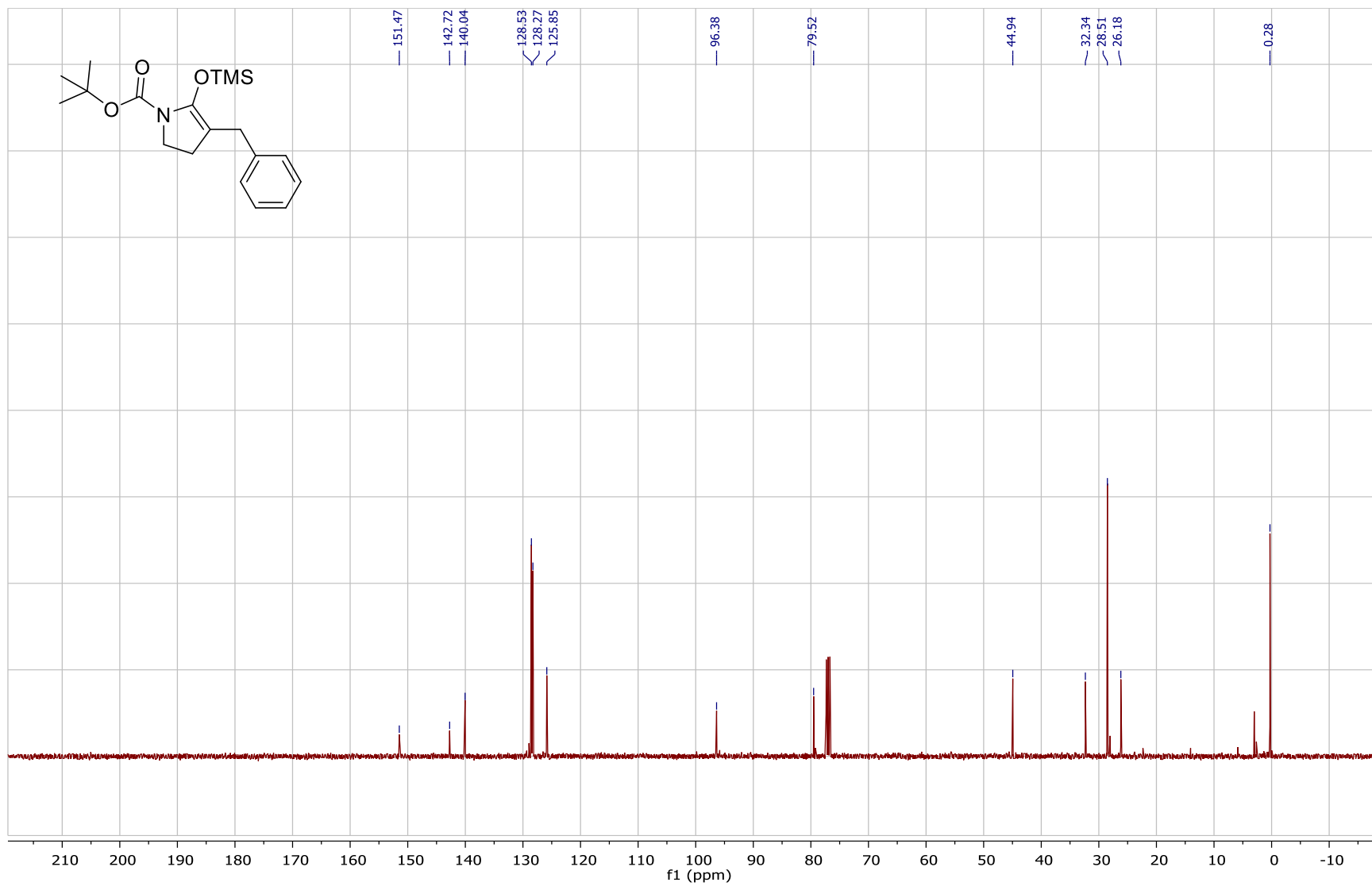


t-Butyl 4-benzyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole-1-carboxylate (**4d**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

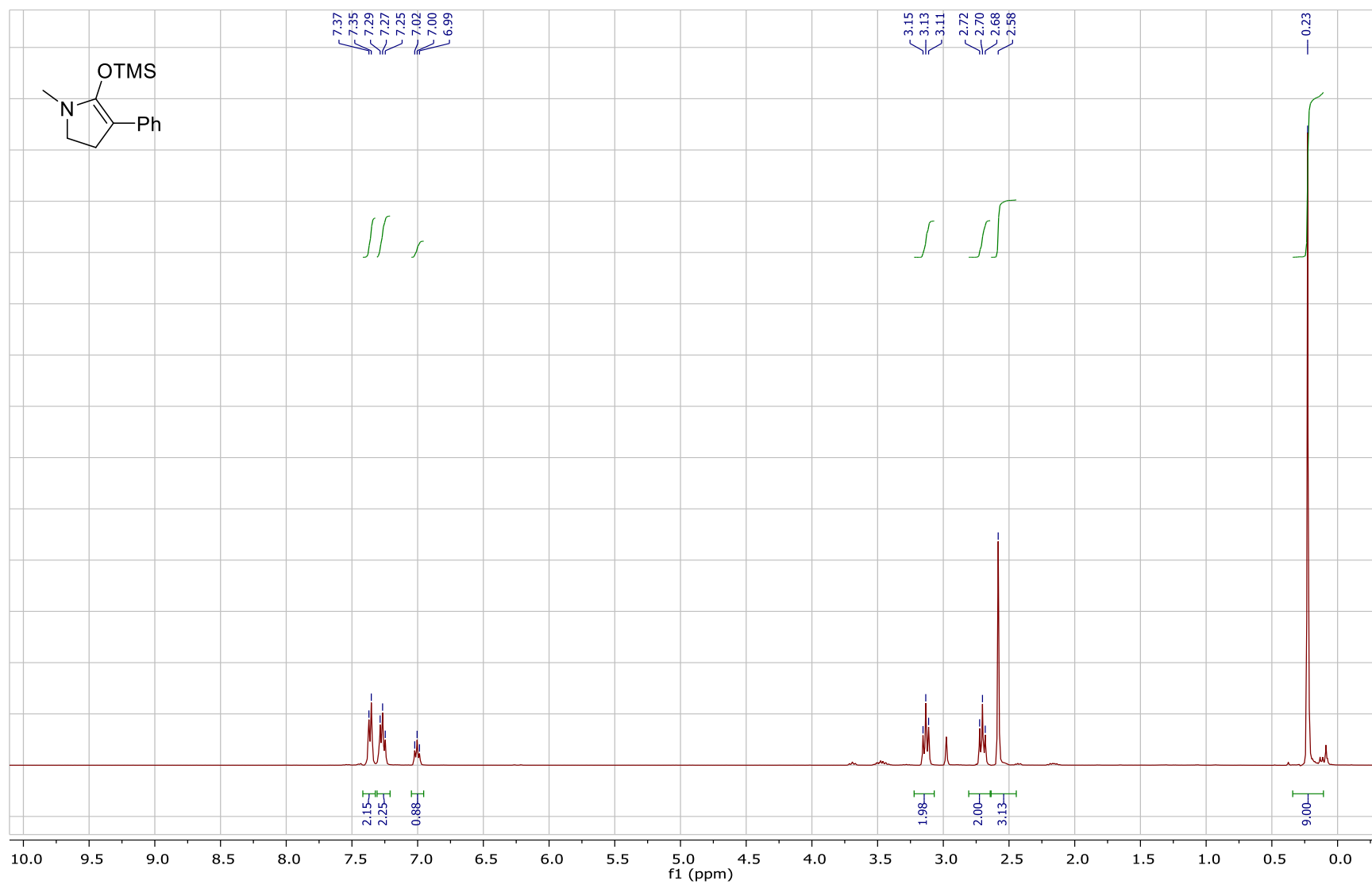


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

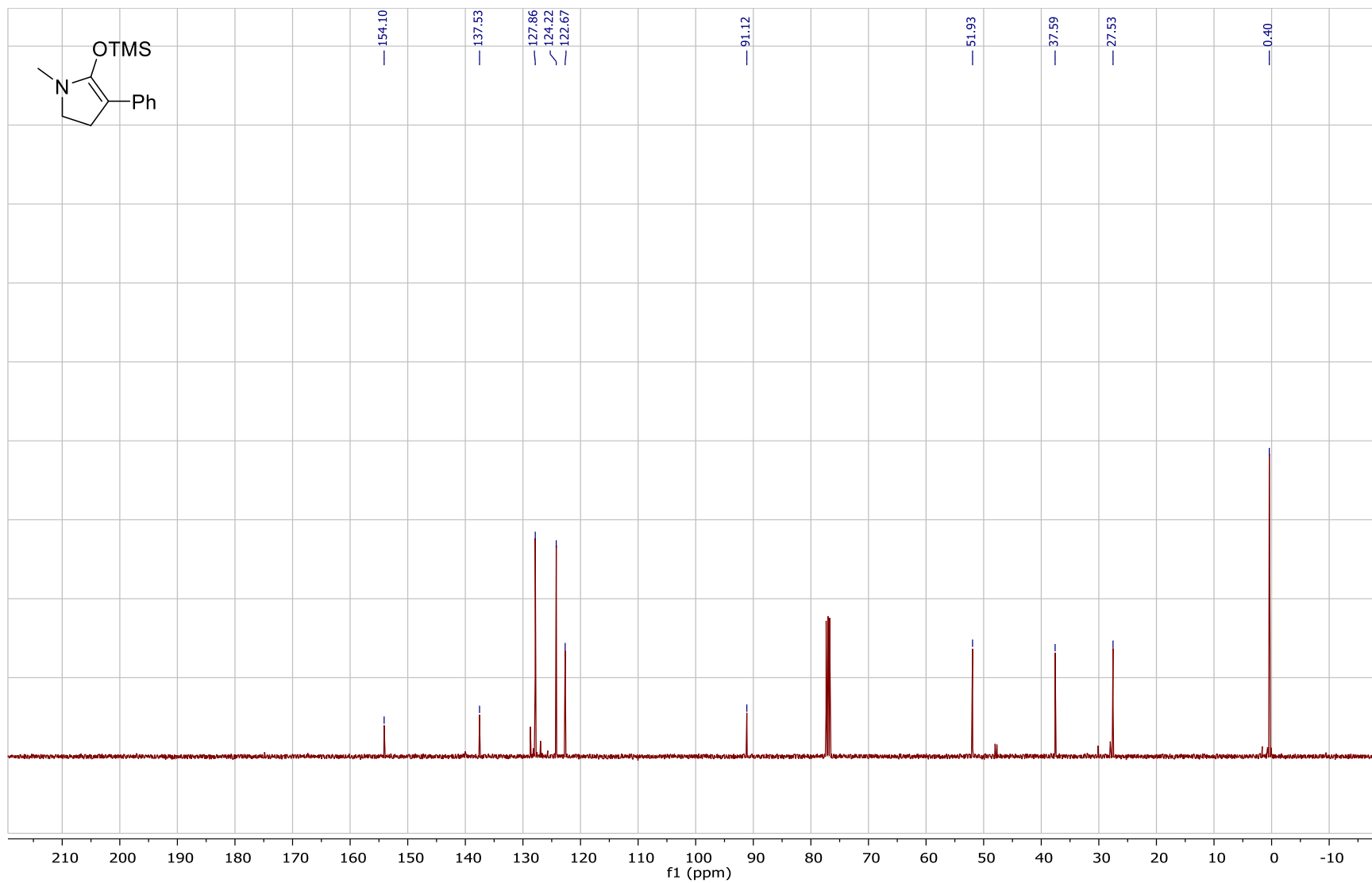


1-Methyl-4-phenyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4e**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

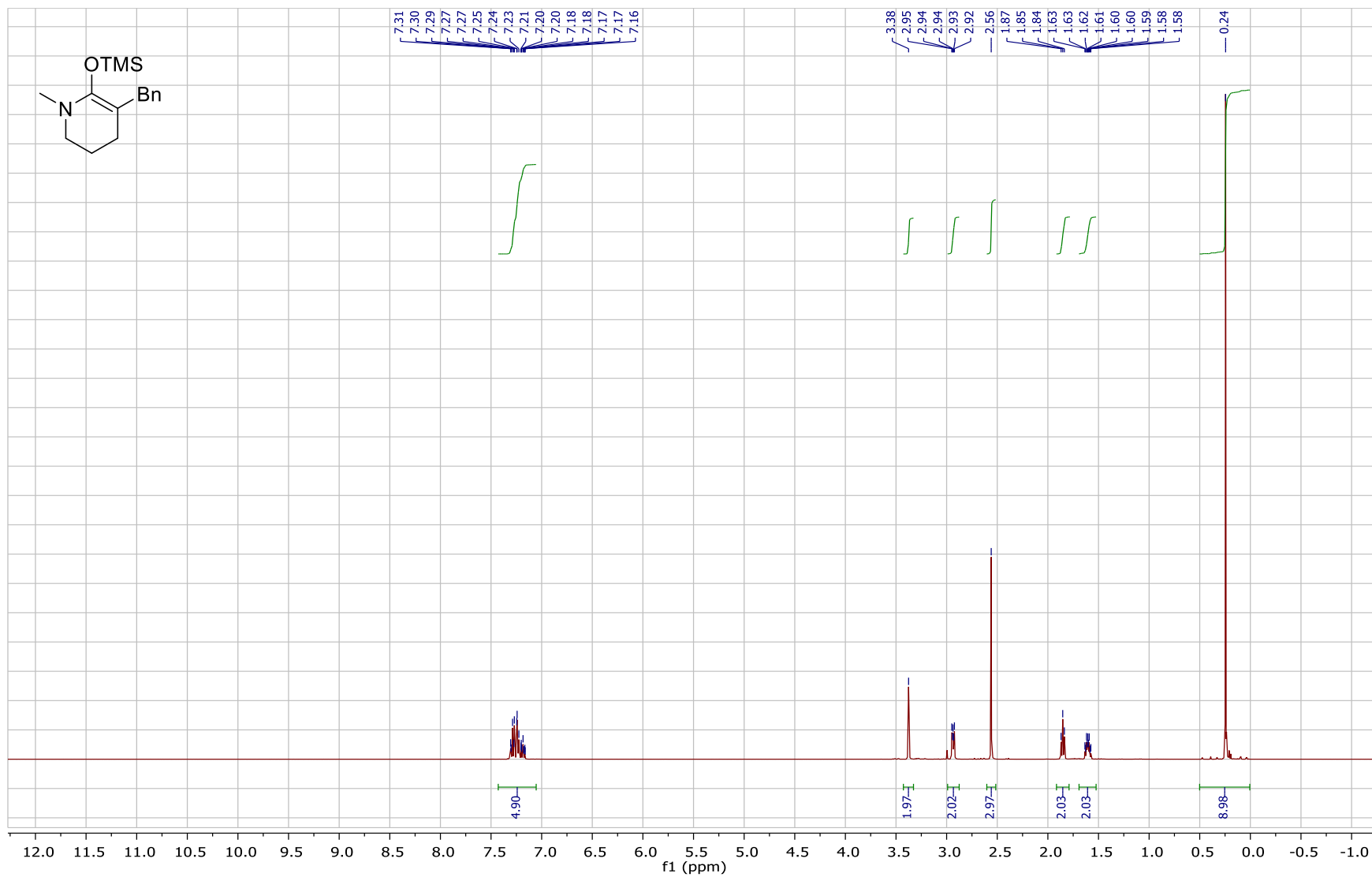


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )



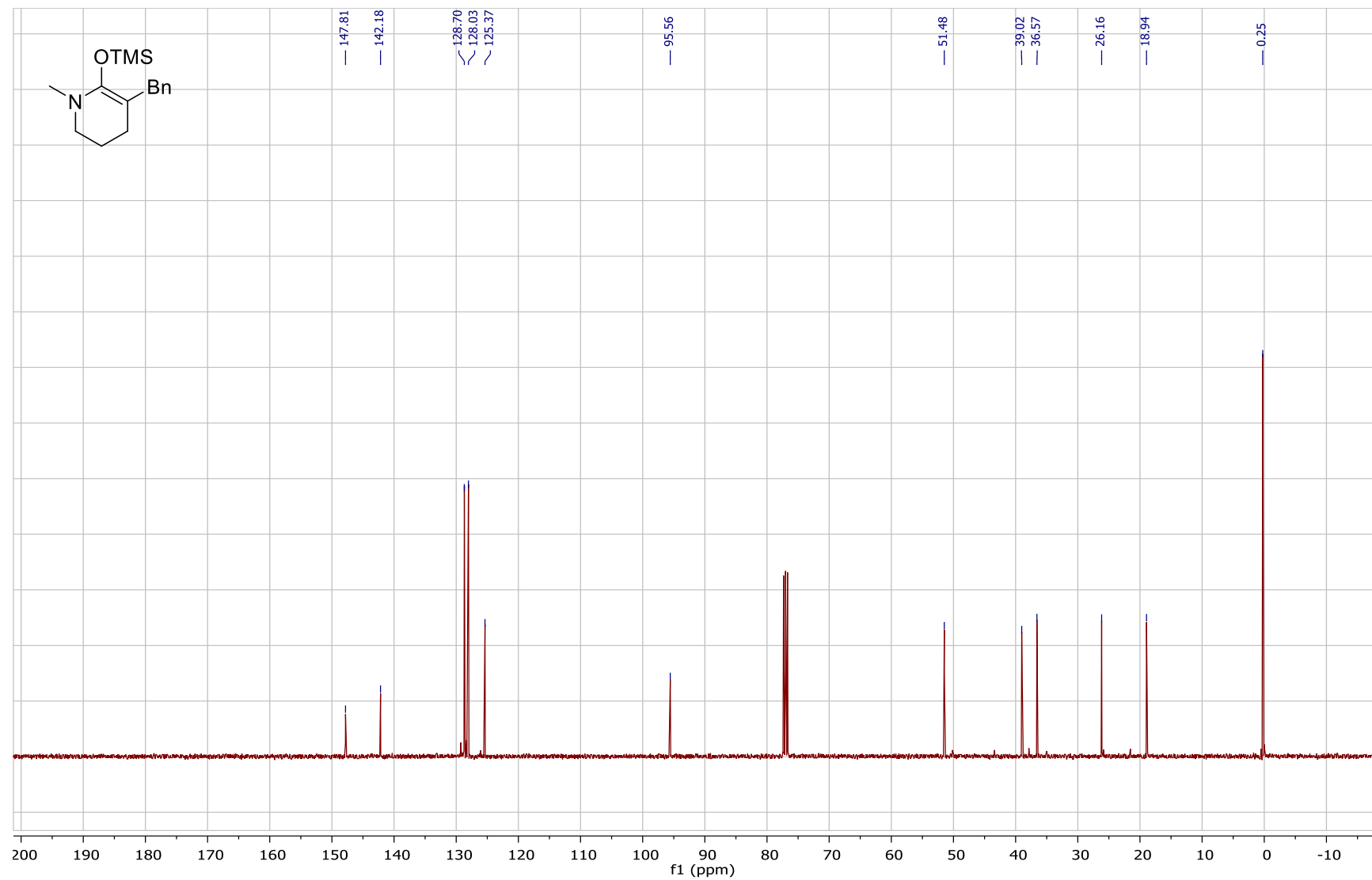
5-Benzyl-1-methyl-6-((trimethylsilyl)oxy)-1,2,3,4-tetrahydropyridine (**4f**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



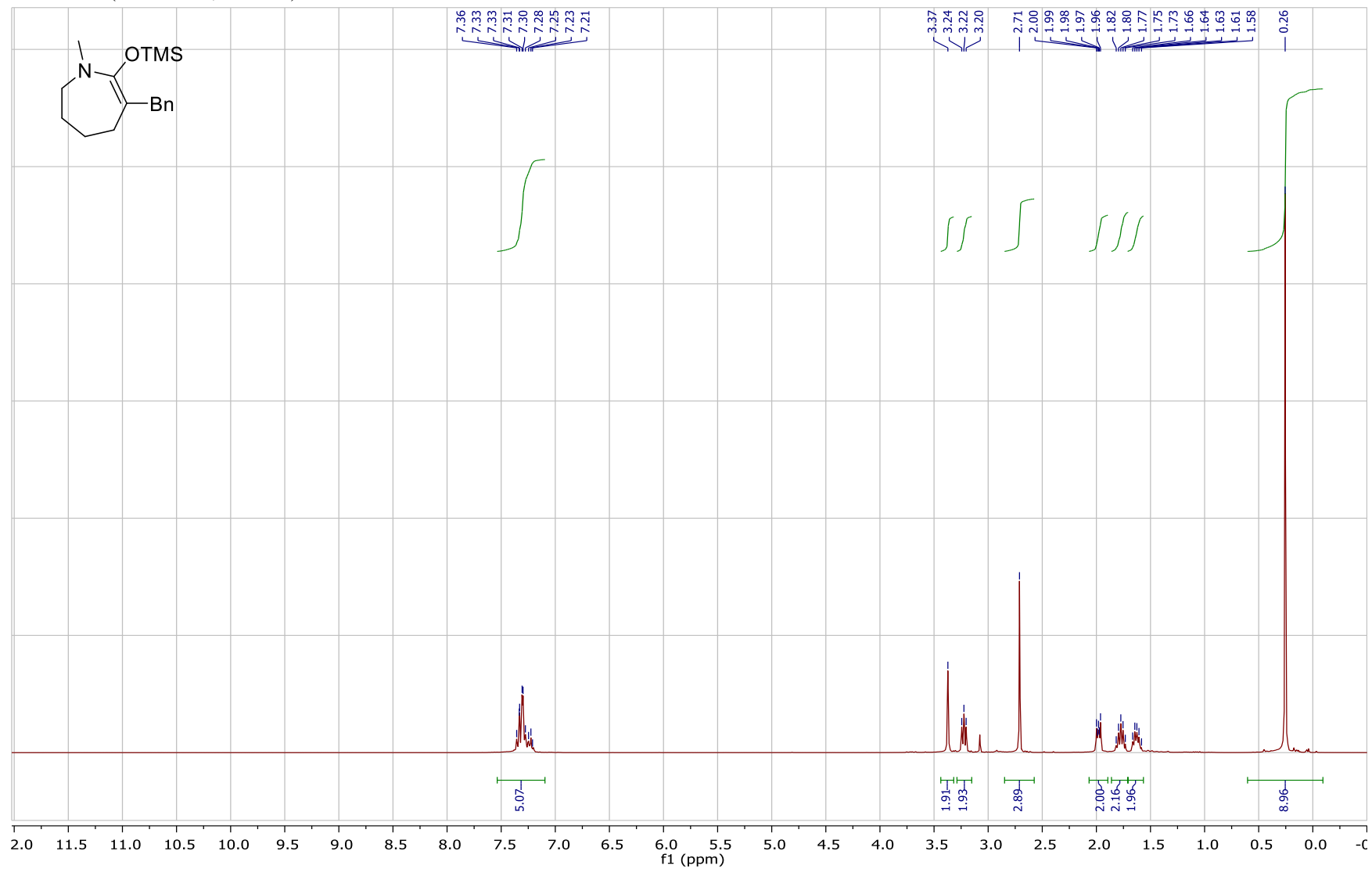


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

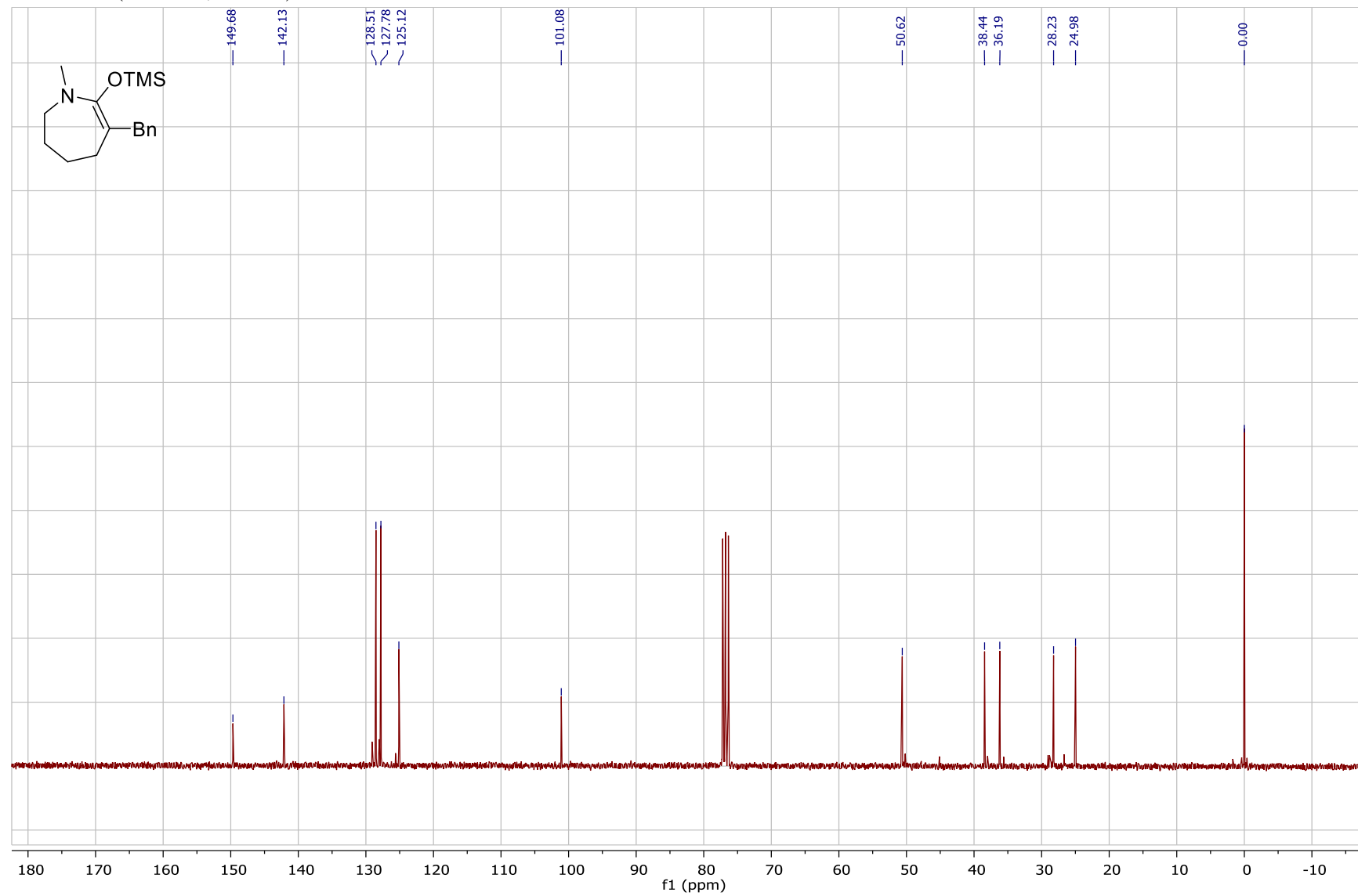


6-Benzyl-1-methyl-7-((trimethylsilyl)oxy)-2,3,4,5-tetrahydro-1H-azepine (**4g**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

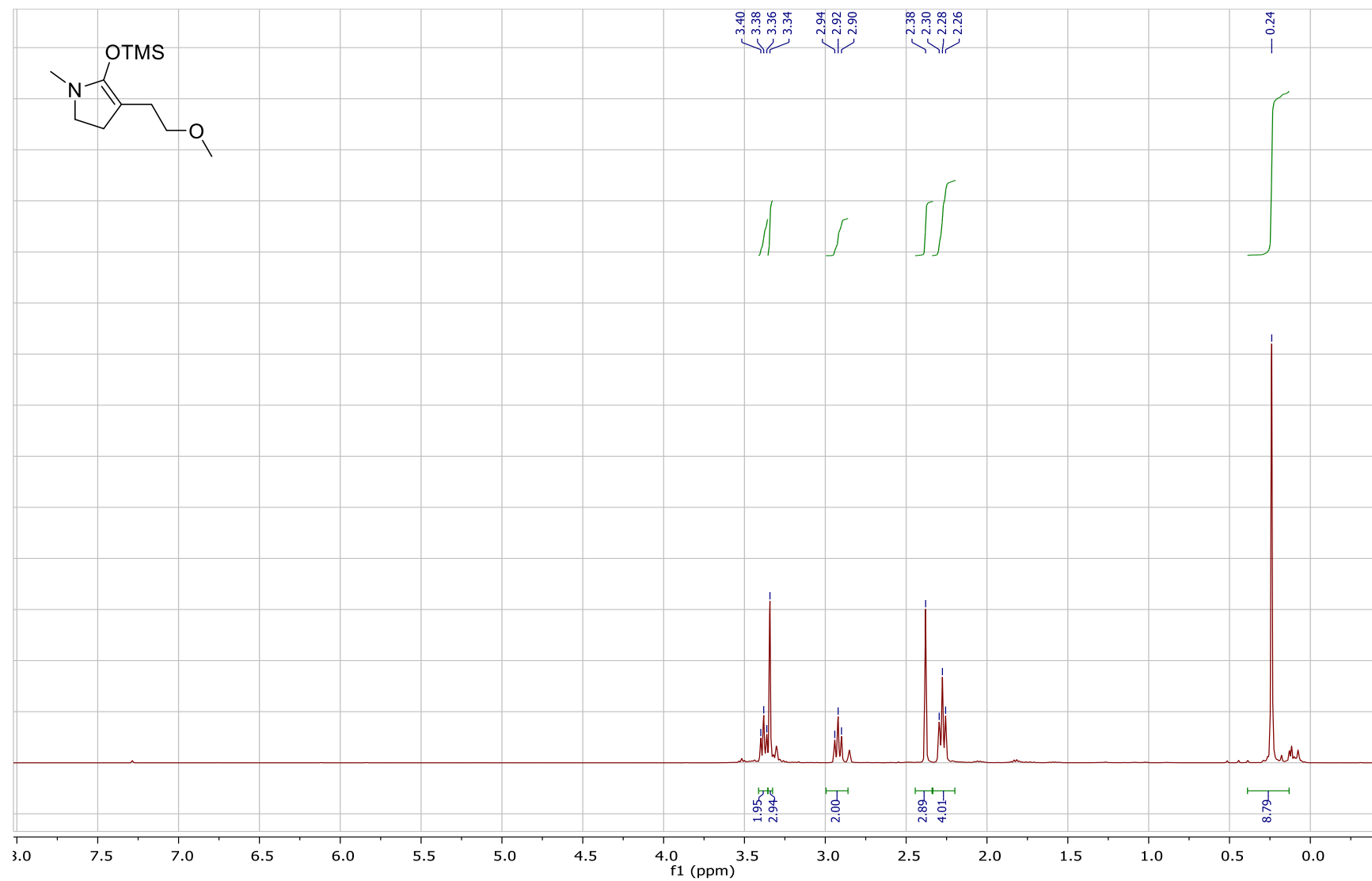


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

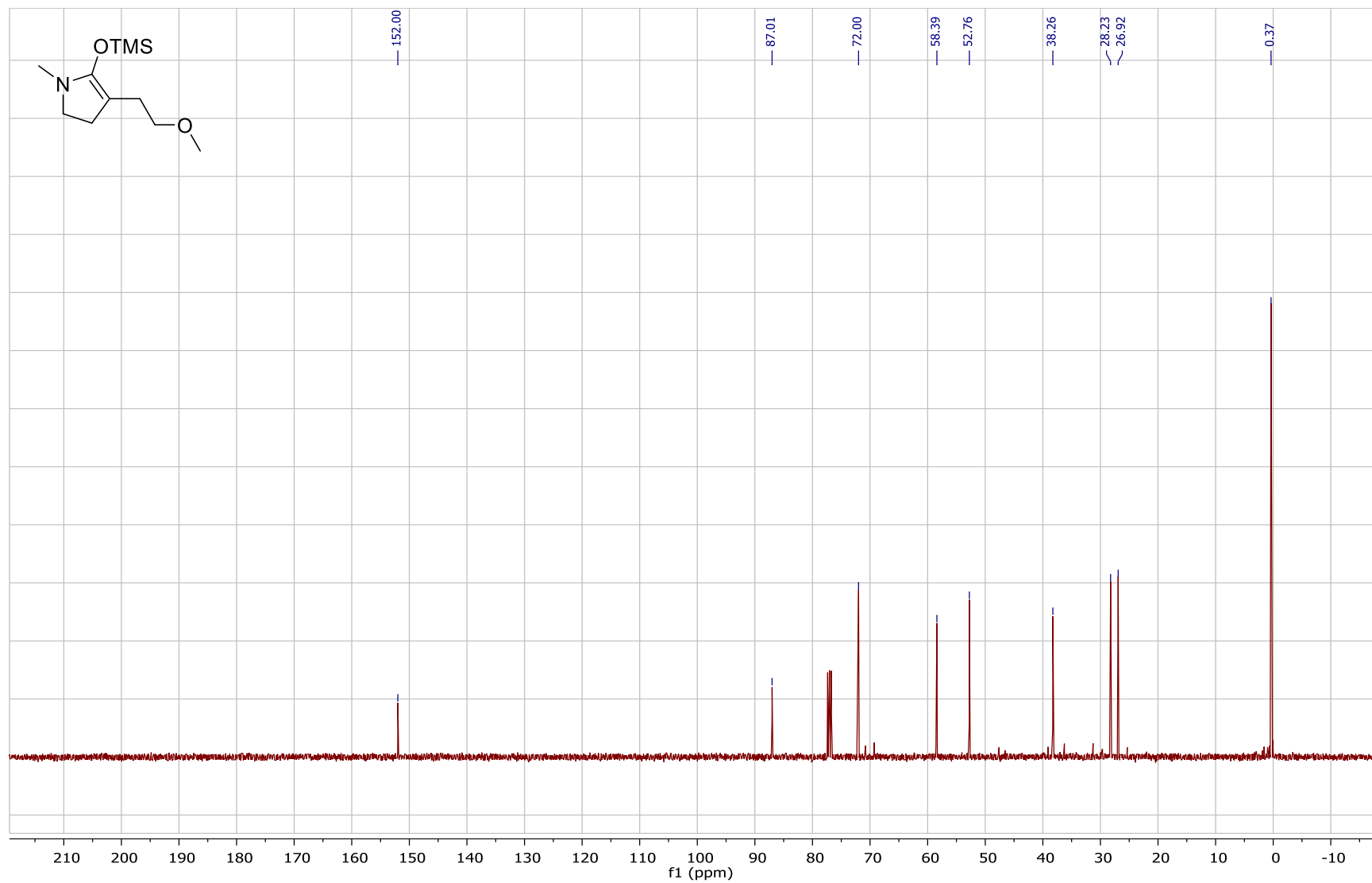


4-(2-Methoxyethyl)-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4h**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

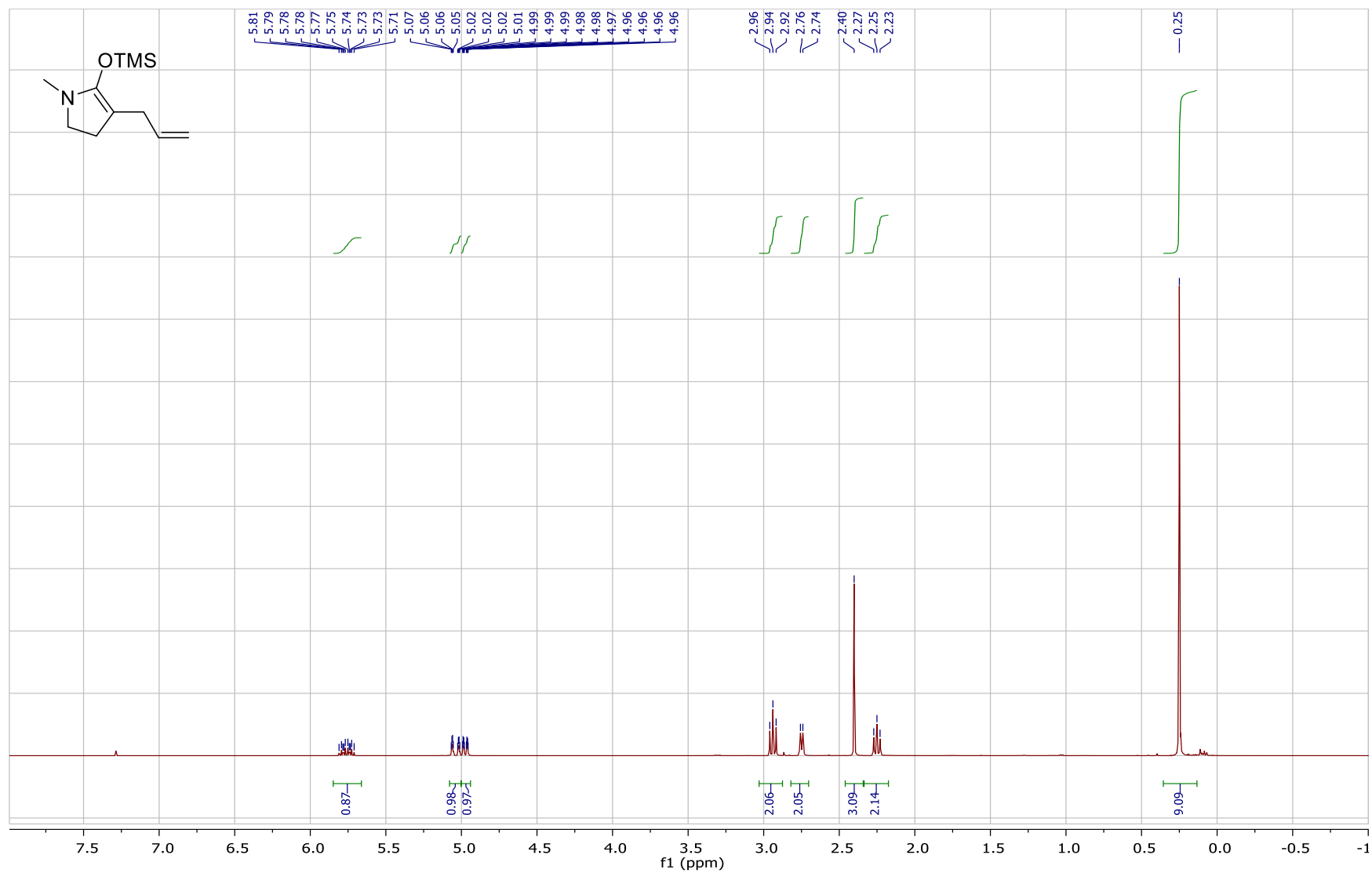


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

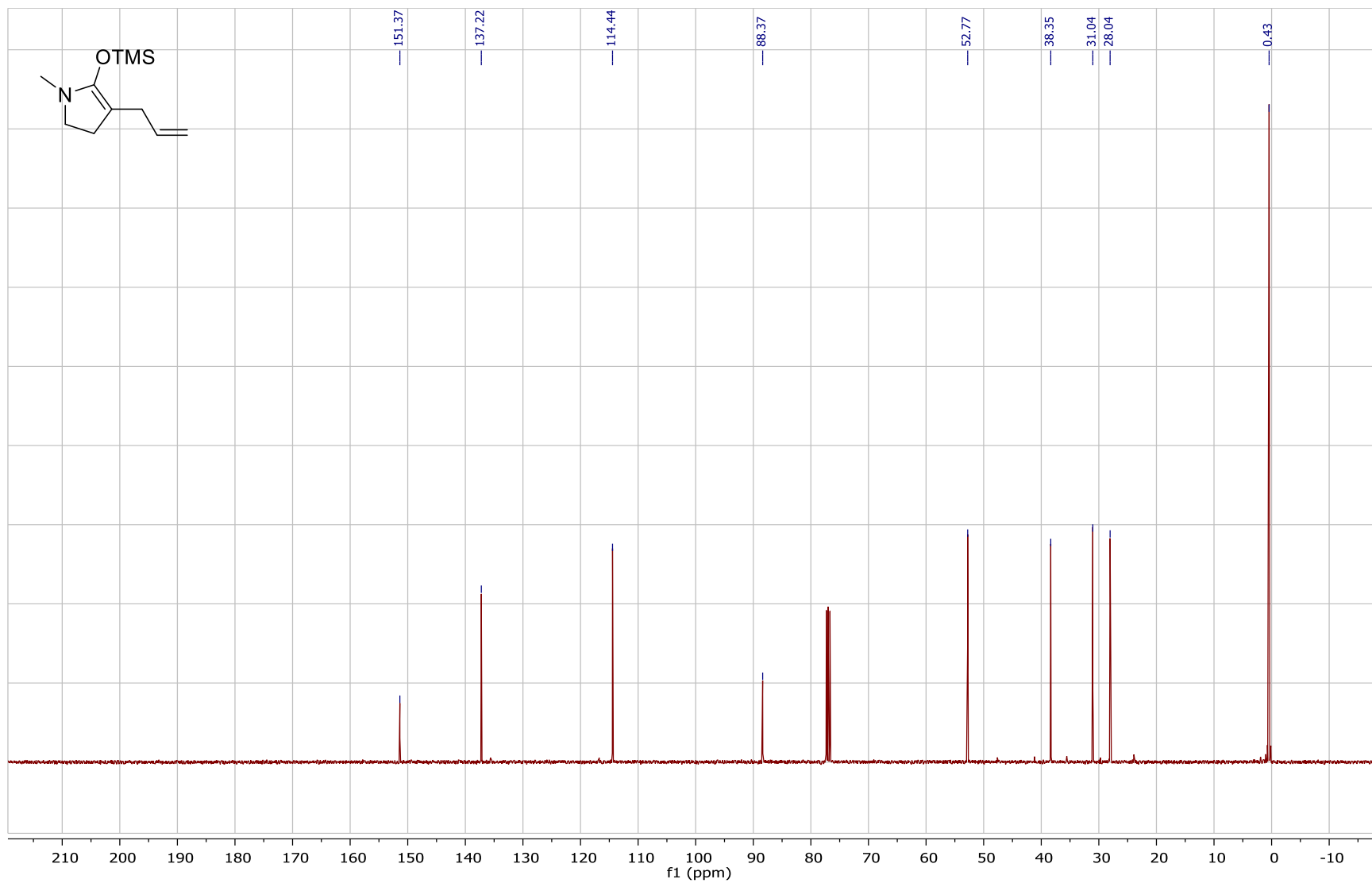


4-Allyl-1-methyl-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4i**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

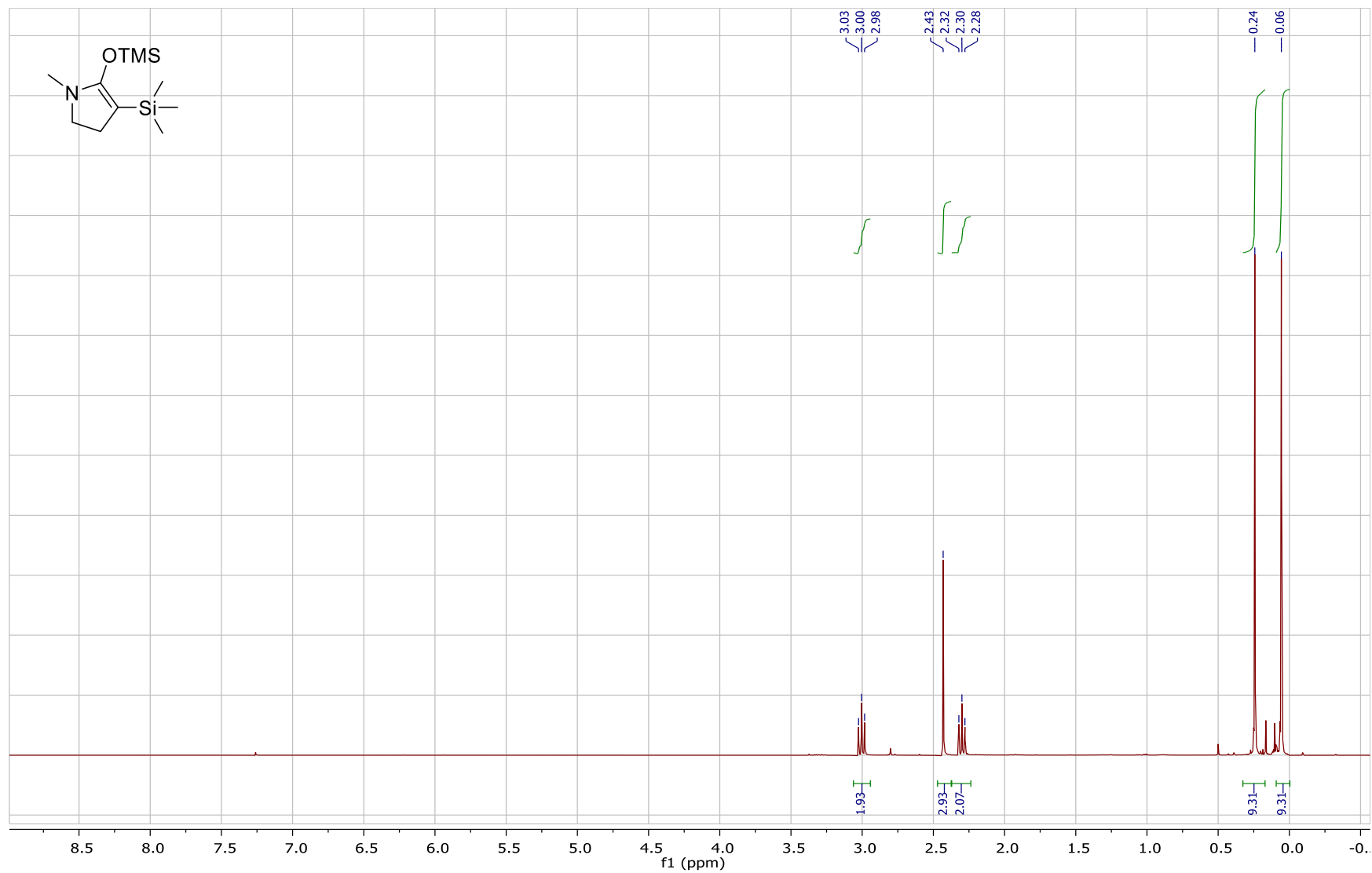


$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )



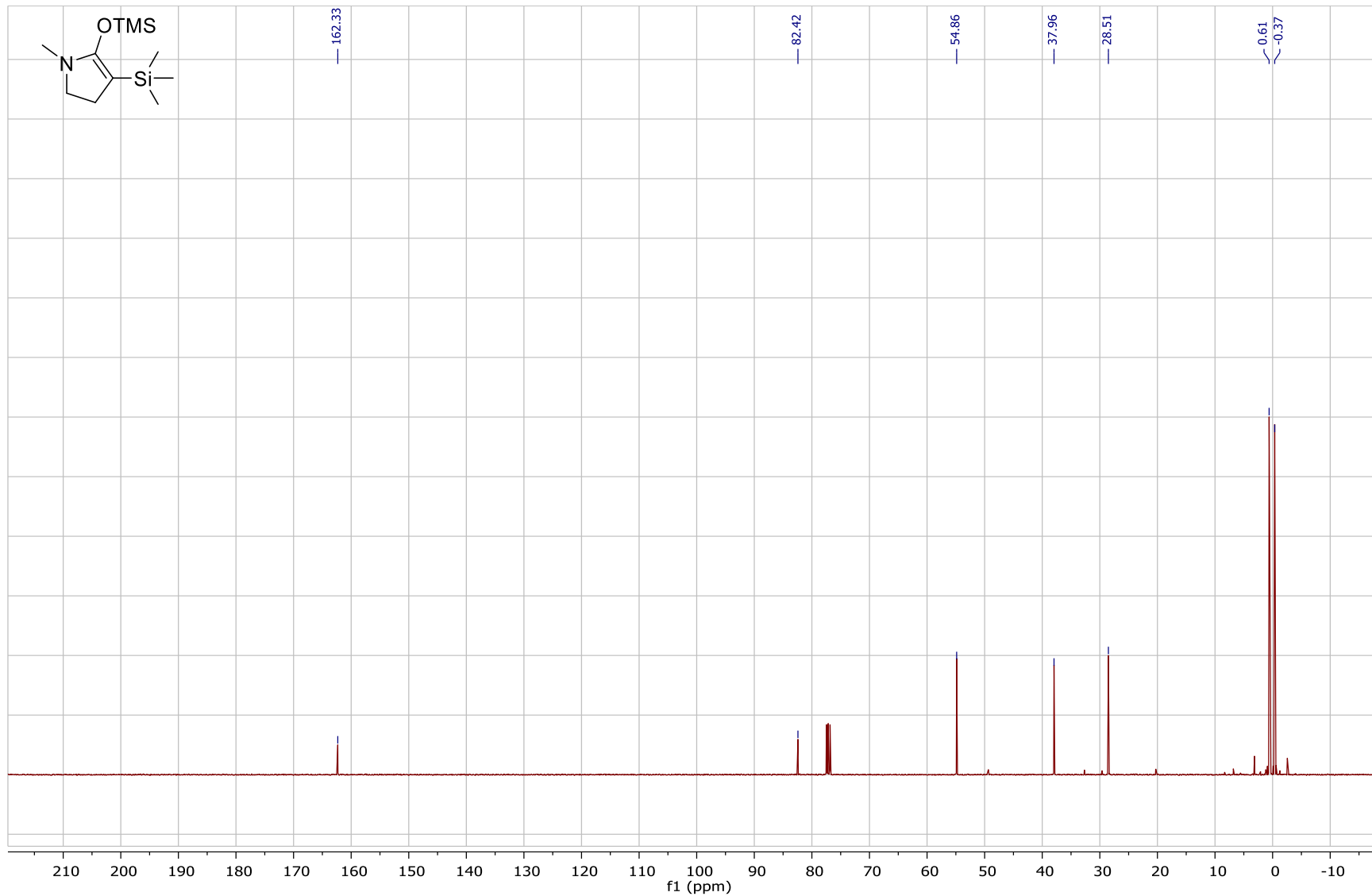
1-Methyl-4-(trimethylsilyl)-5-((trimethylsilyl)oxy)-2,3-dihydro-1H-pyrrole (**4j**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



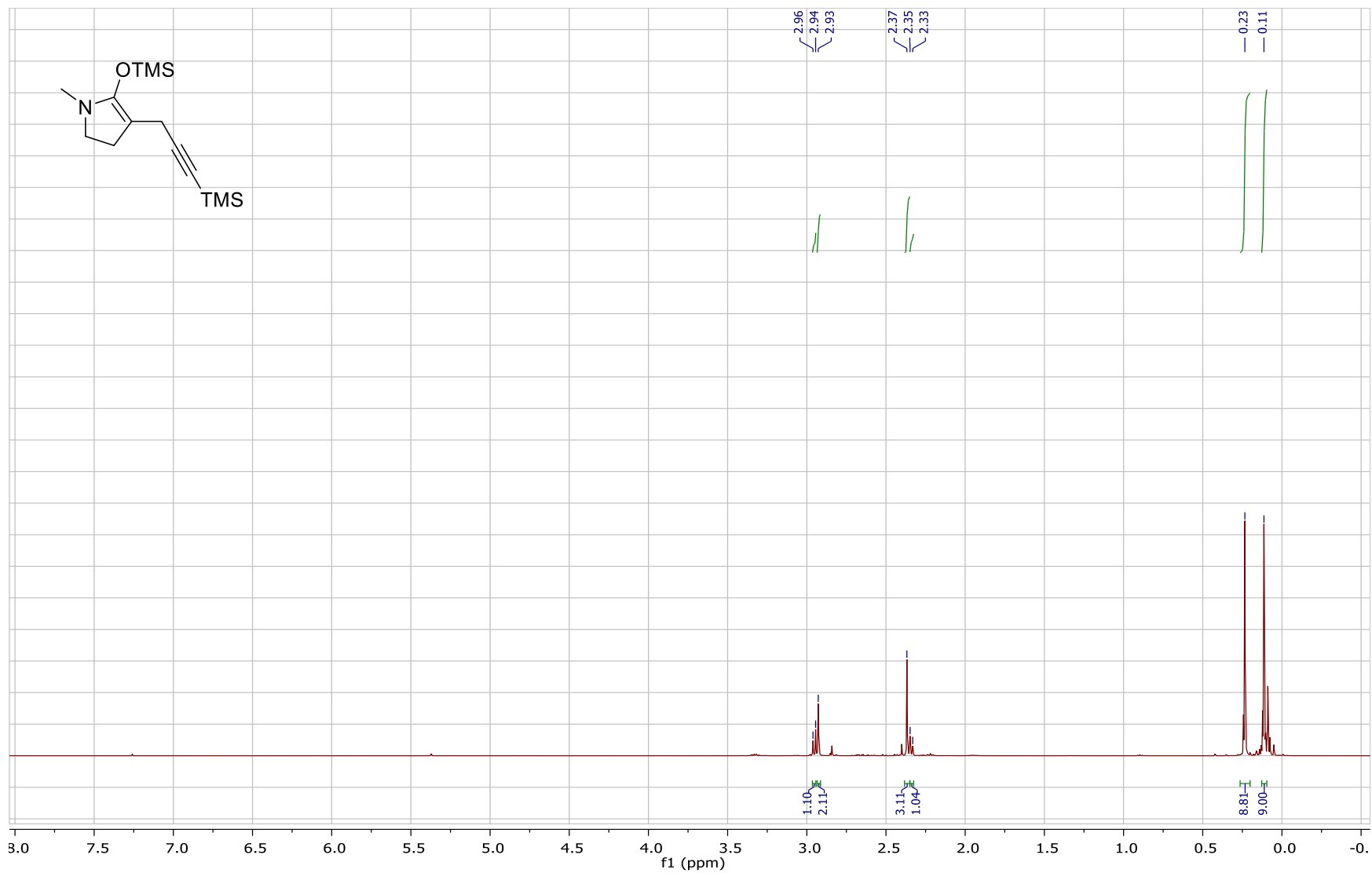


<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

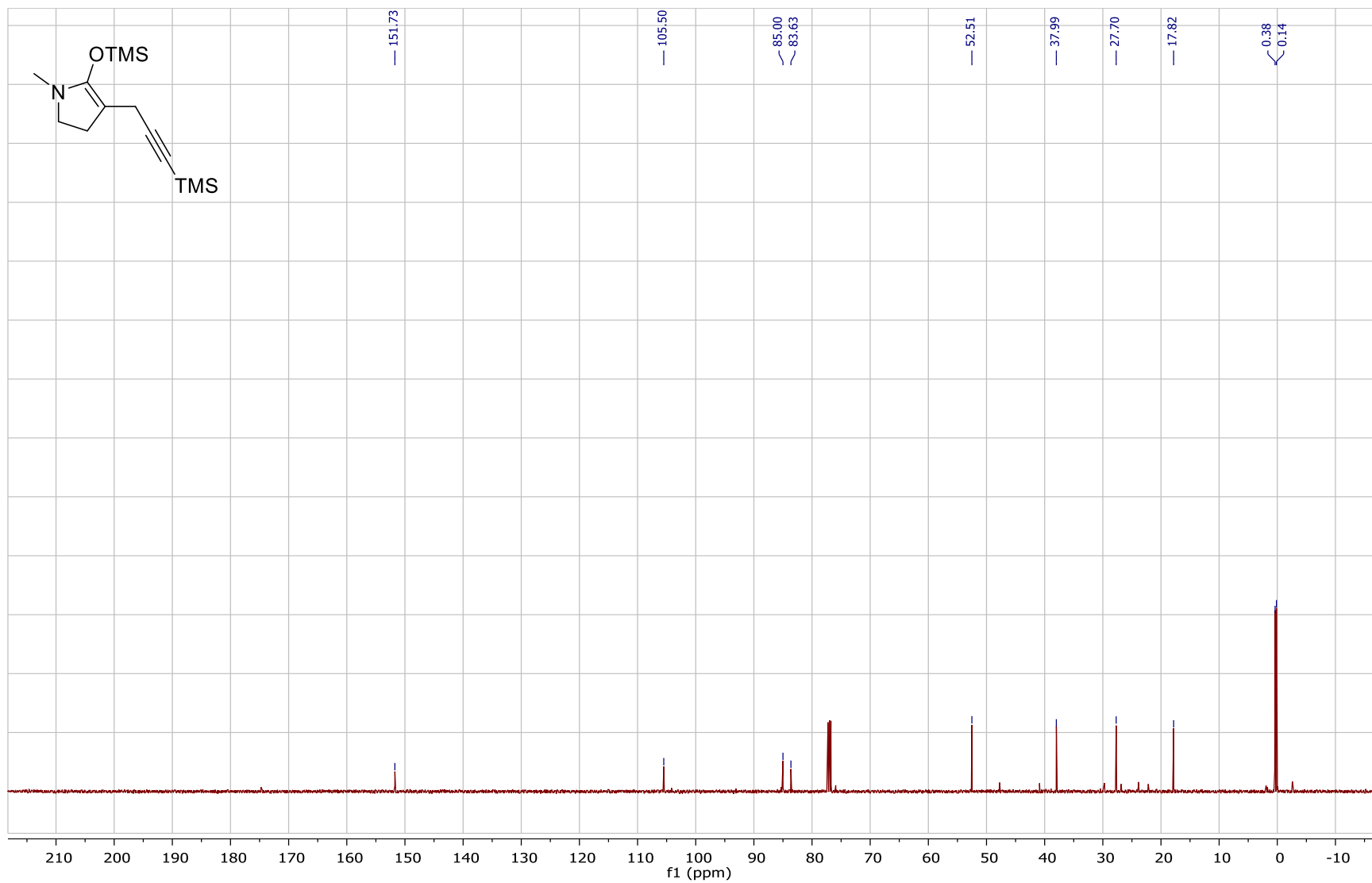


1-Methyl-5-((trimethylsilyl)oxy)-4-(3-(trimethylsilyl)prop-2-yn-1-yl)-2,3-dihydro-1H-pyrrole (**4k**)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )

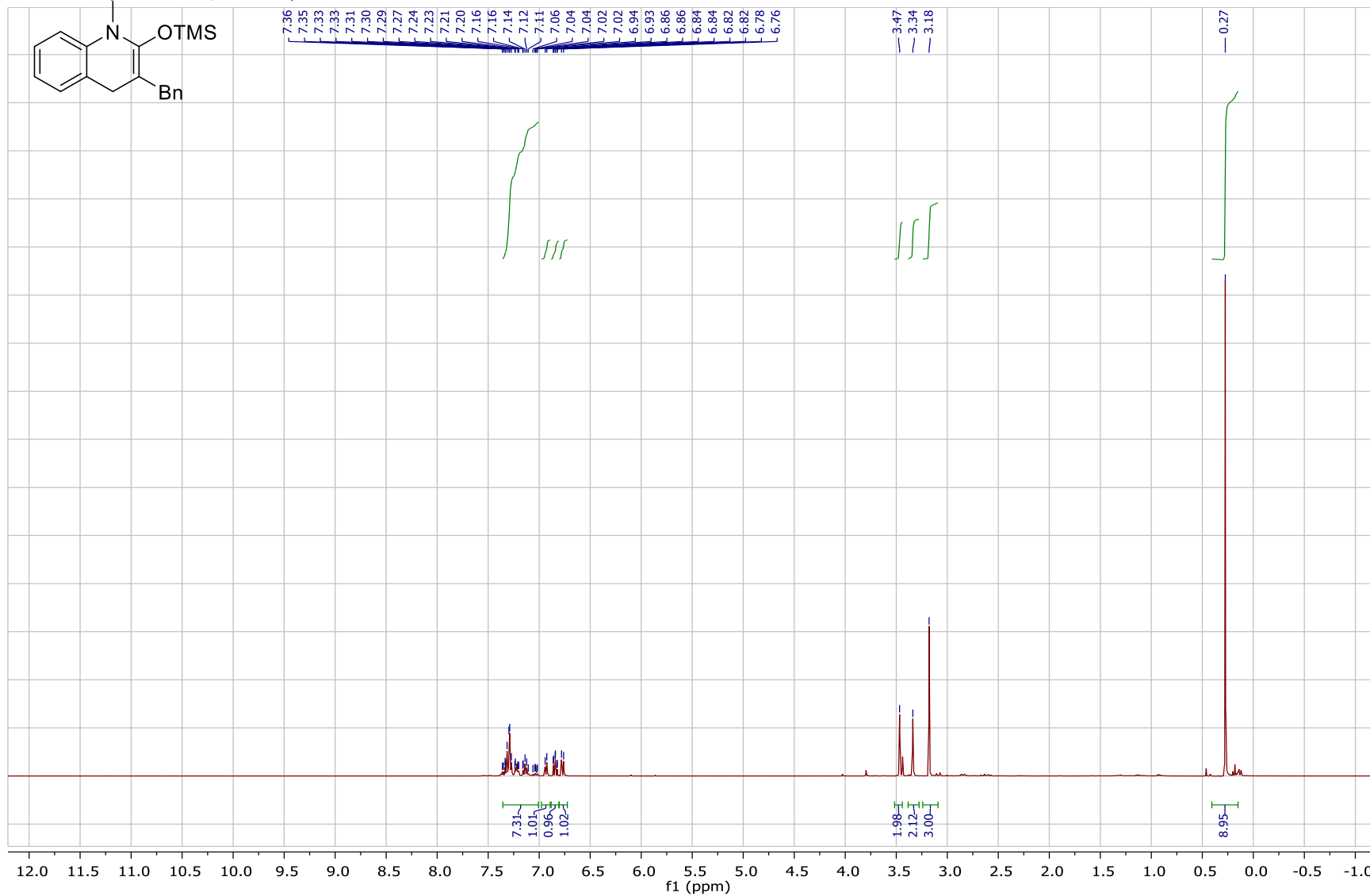


$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



3-Benzyl-2-((trimethylsilyl)oxy)-1,4-dihydroquinoline (**41**)

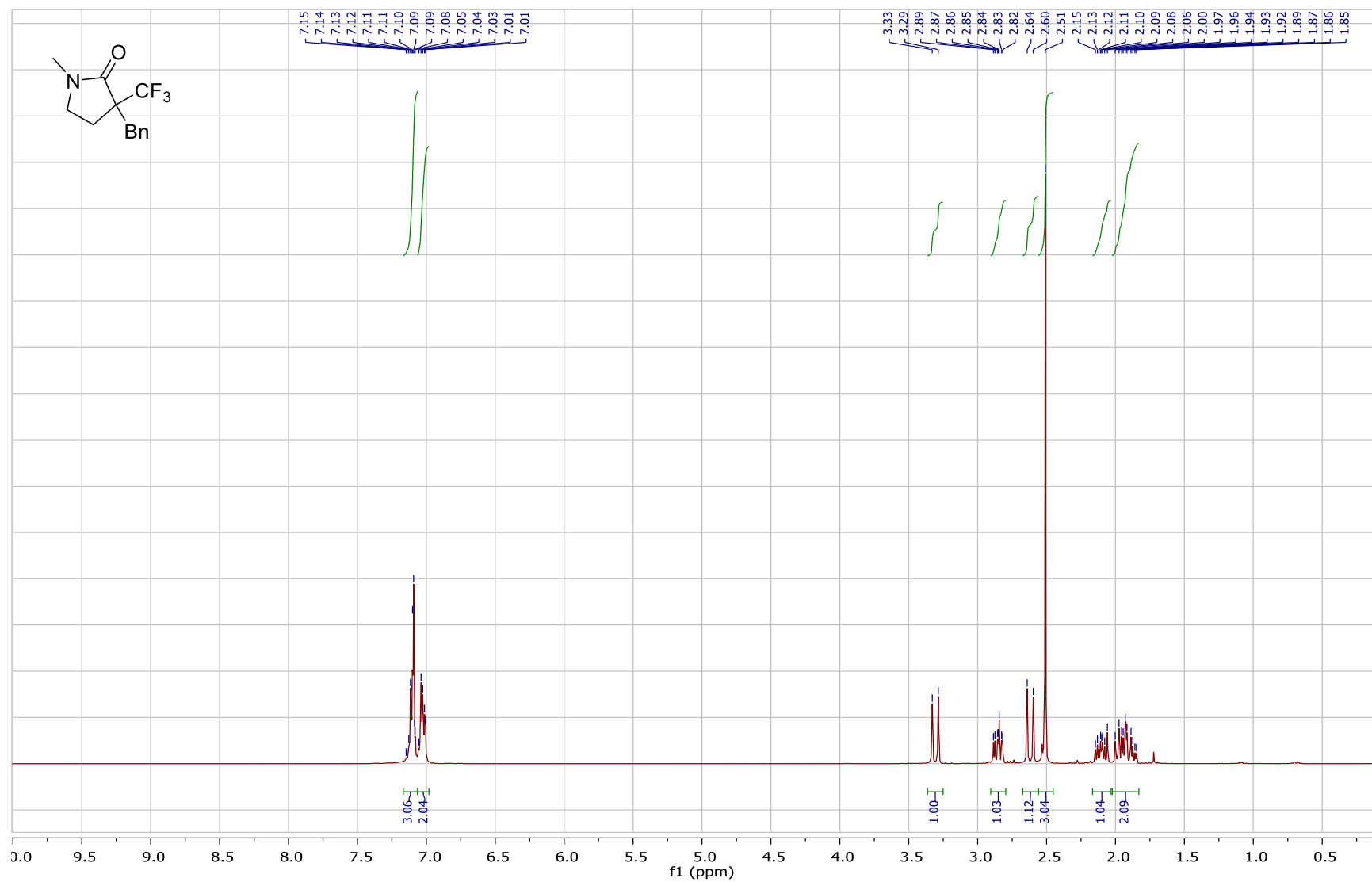
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



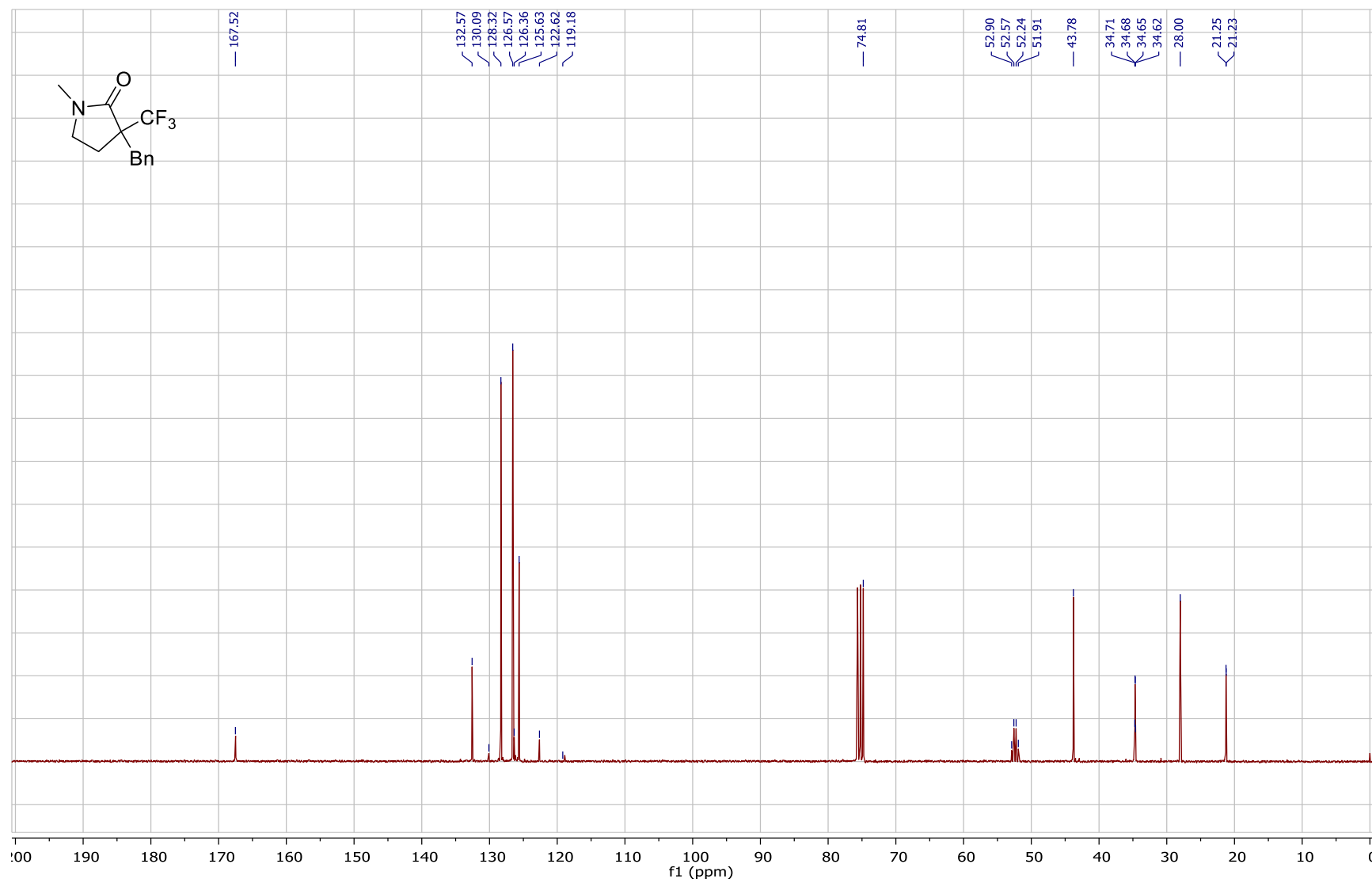


3-Benzyl-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (**8a**)

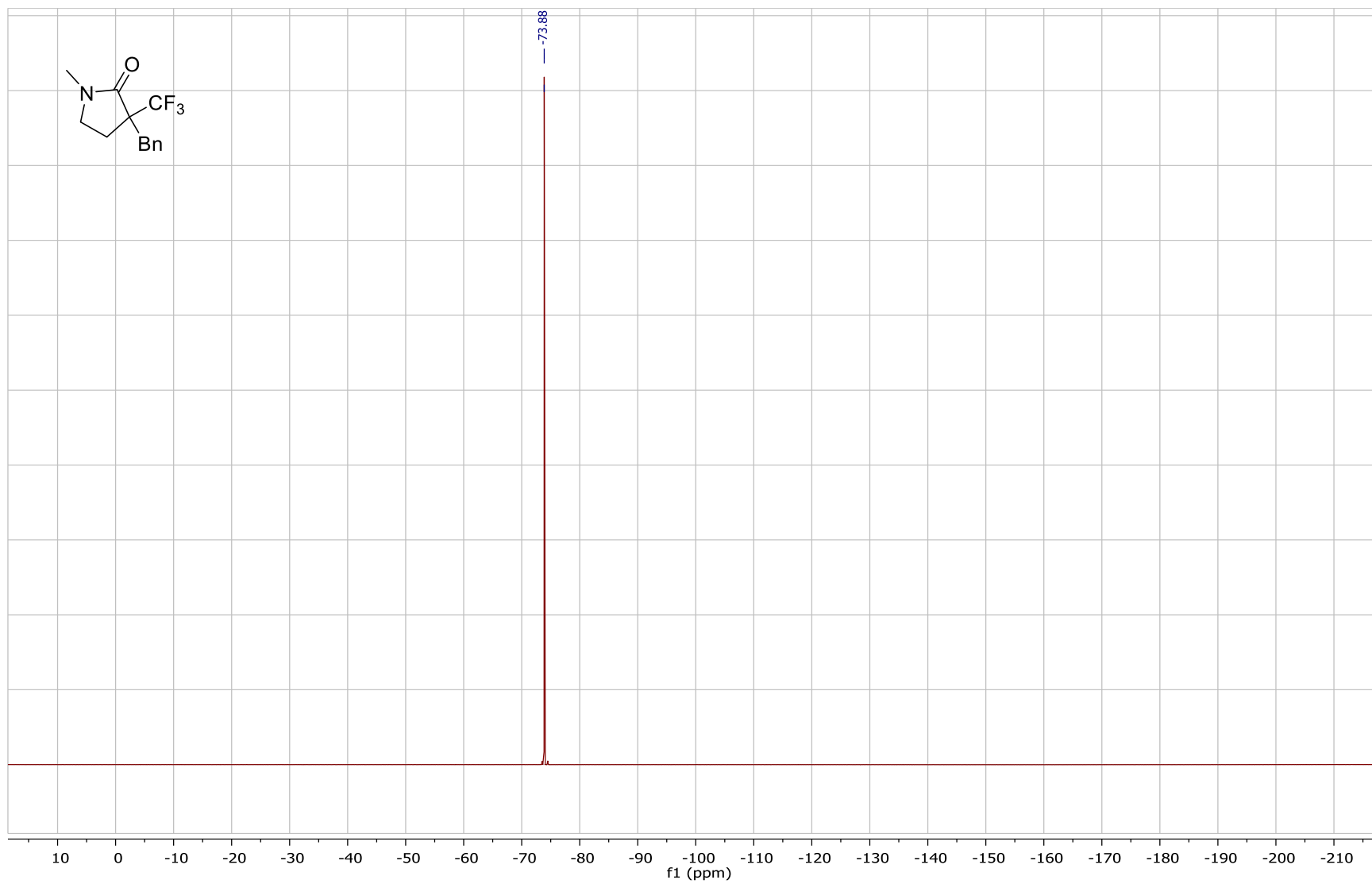
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



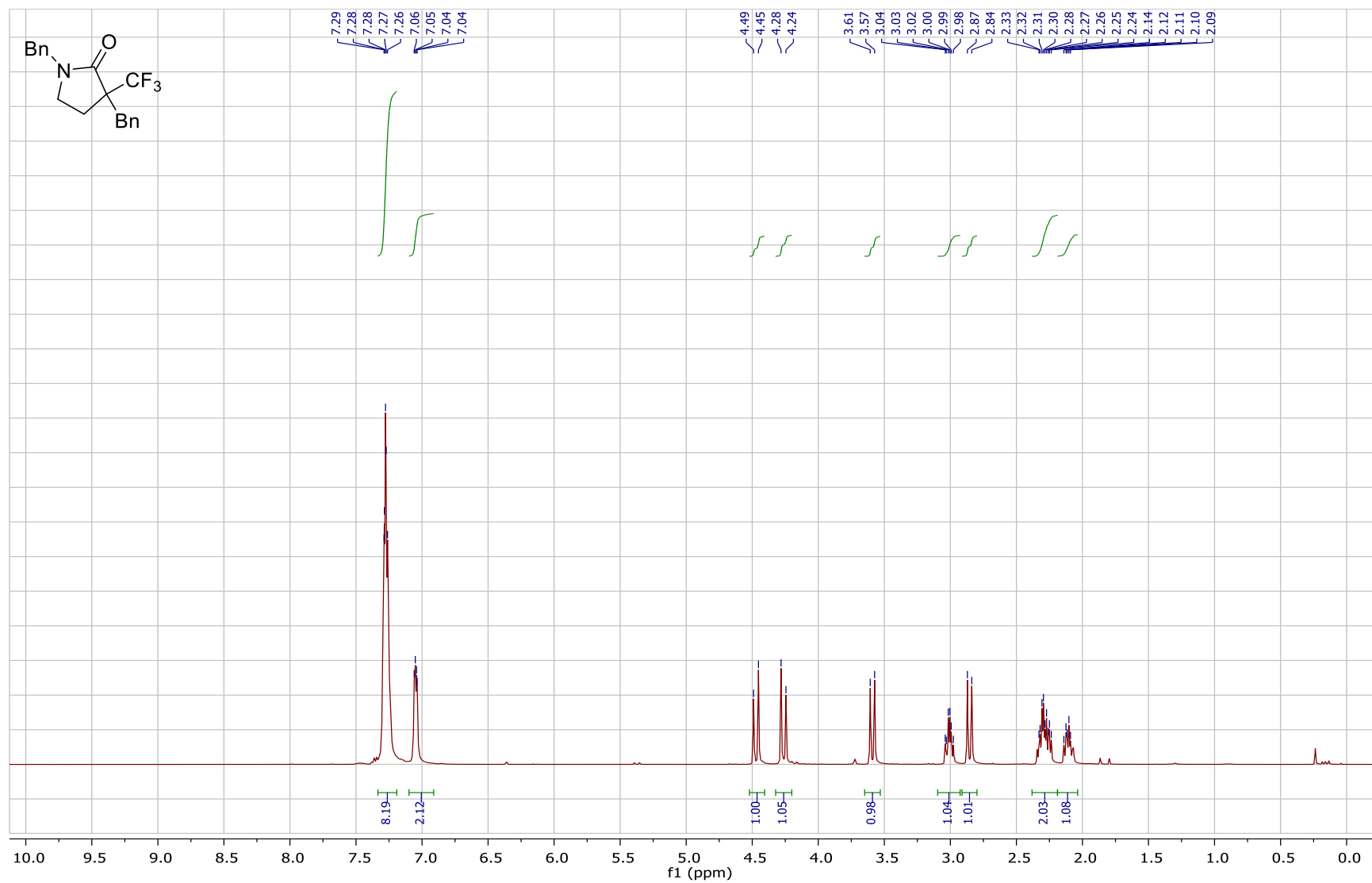
$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



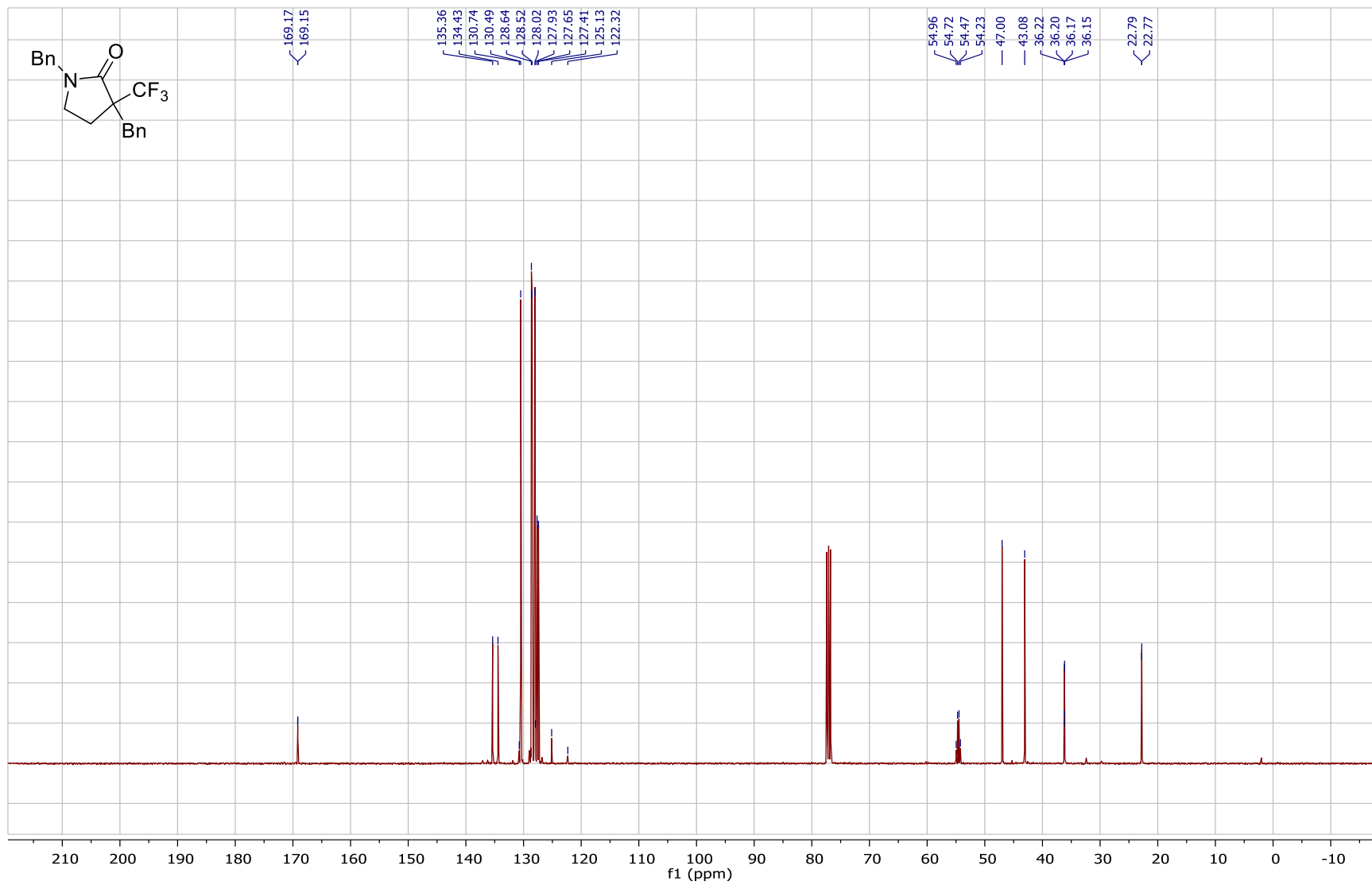


1,3-Dibenzyl-3-(trifluoromethyl)pyrrolidin-2-one (**8b**)

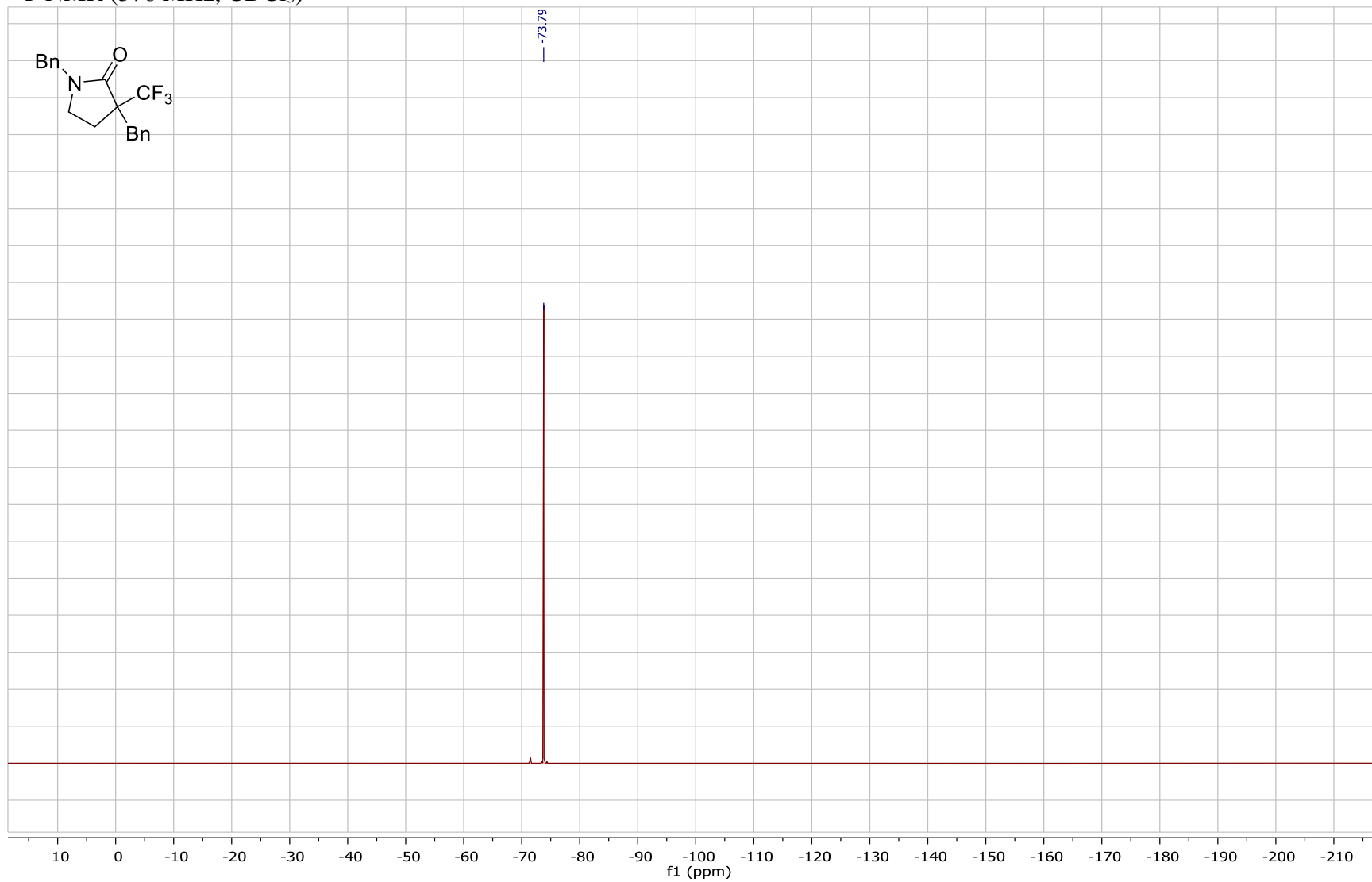
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

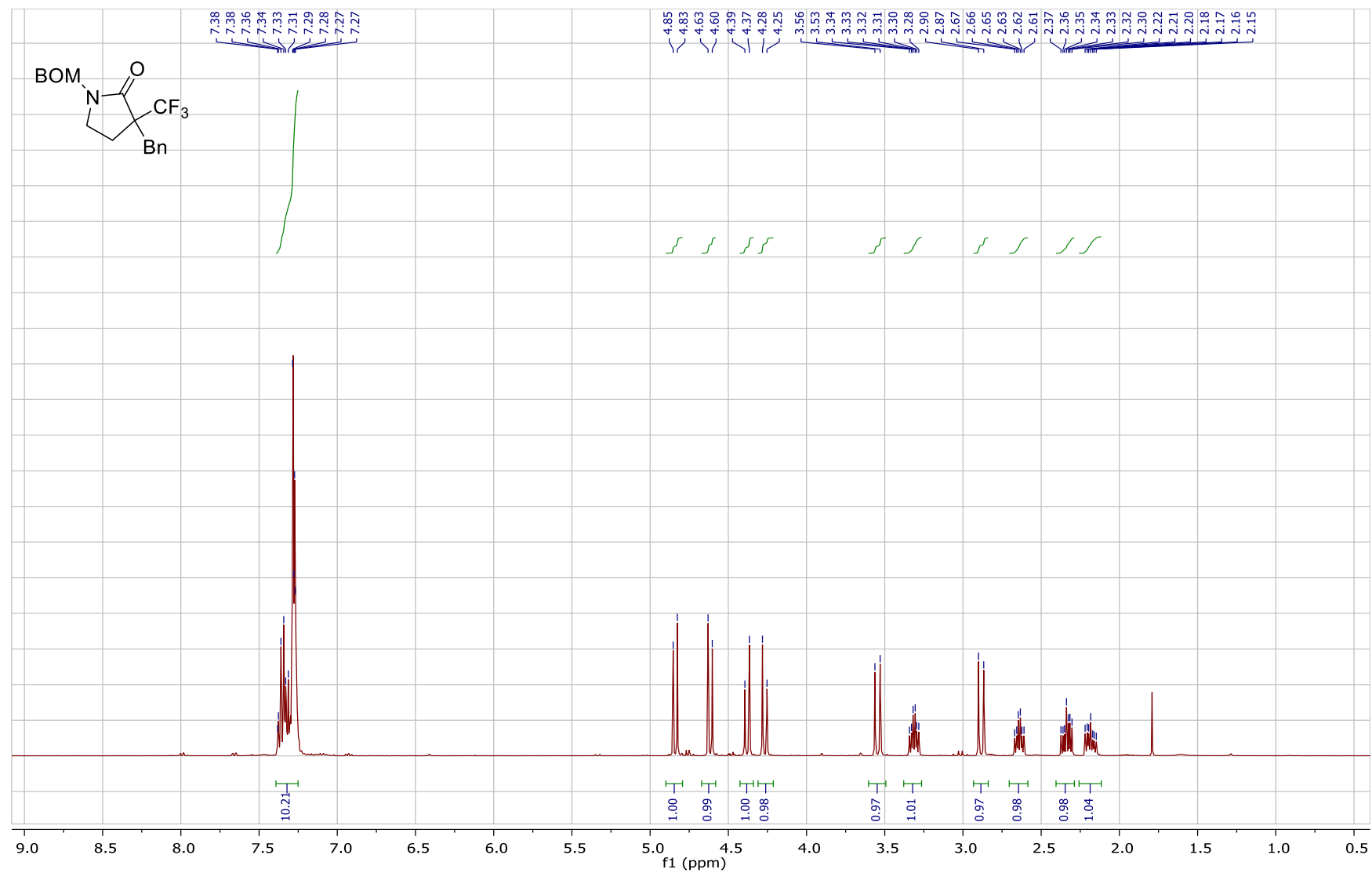


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

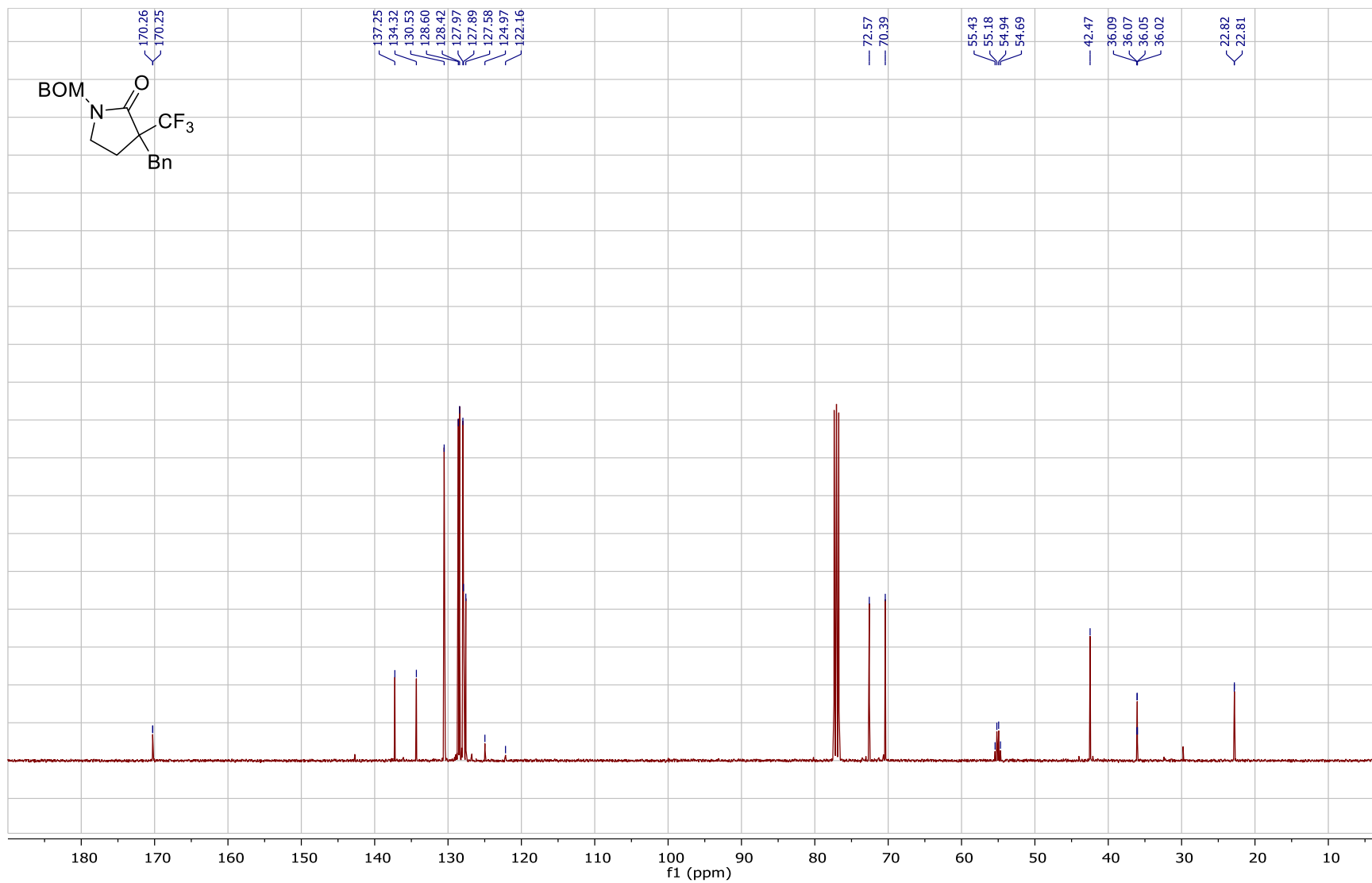


3-Benzyl-1-((benzyloxy)methyl)-3-(trifluoromethyl)pyrrolidin-2-one (**8c**)

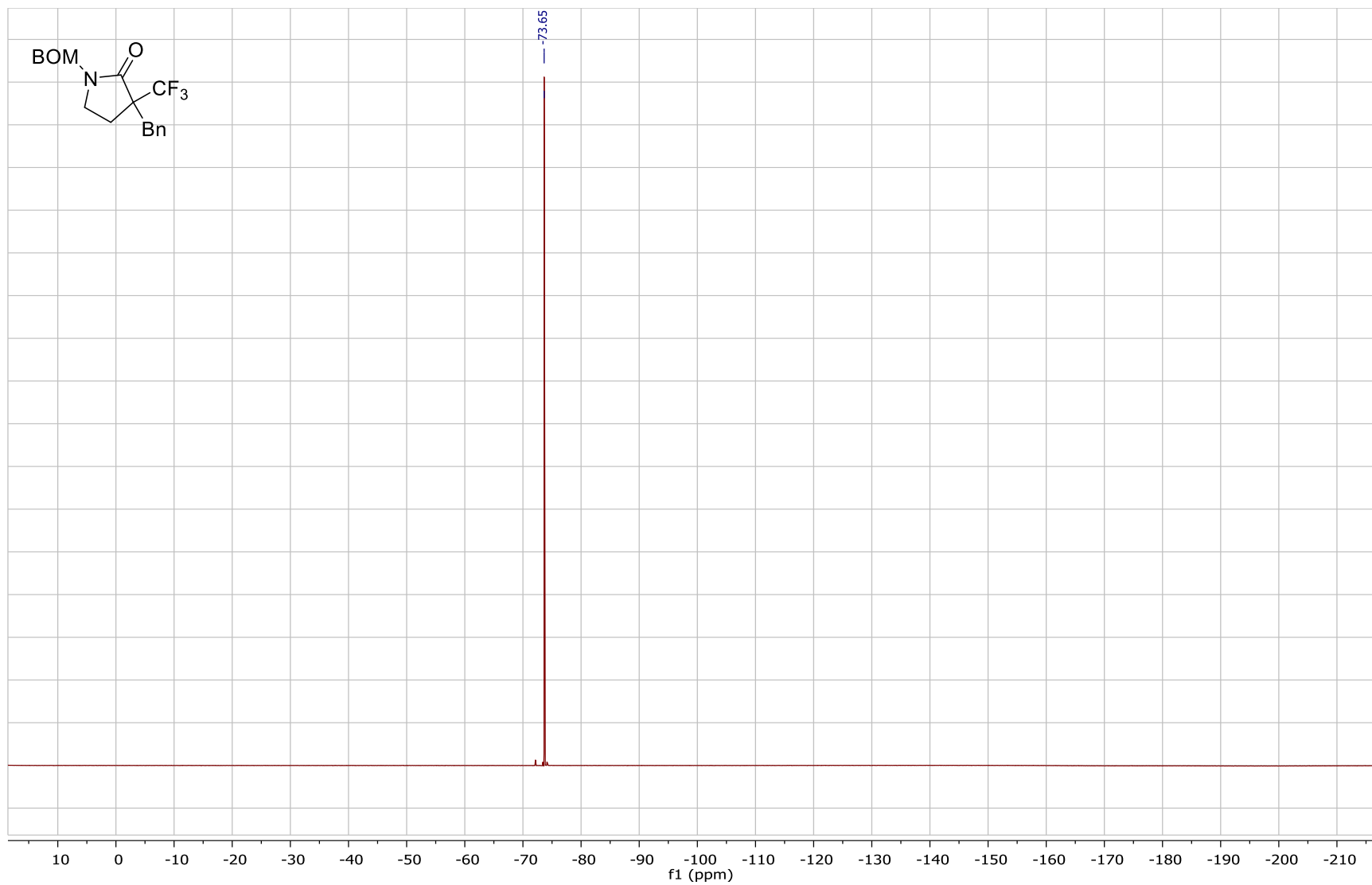
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

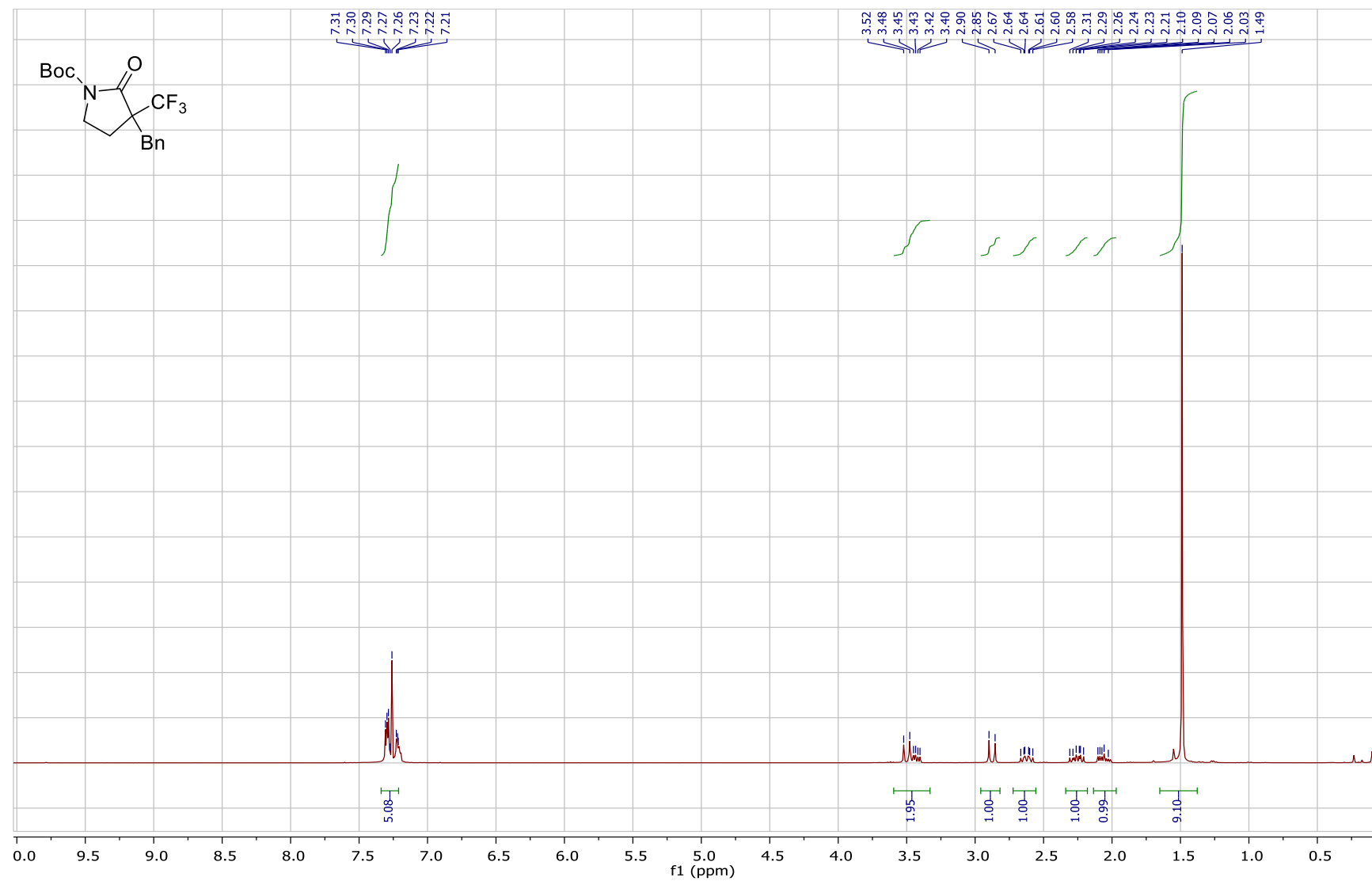


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

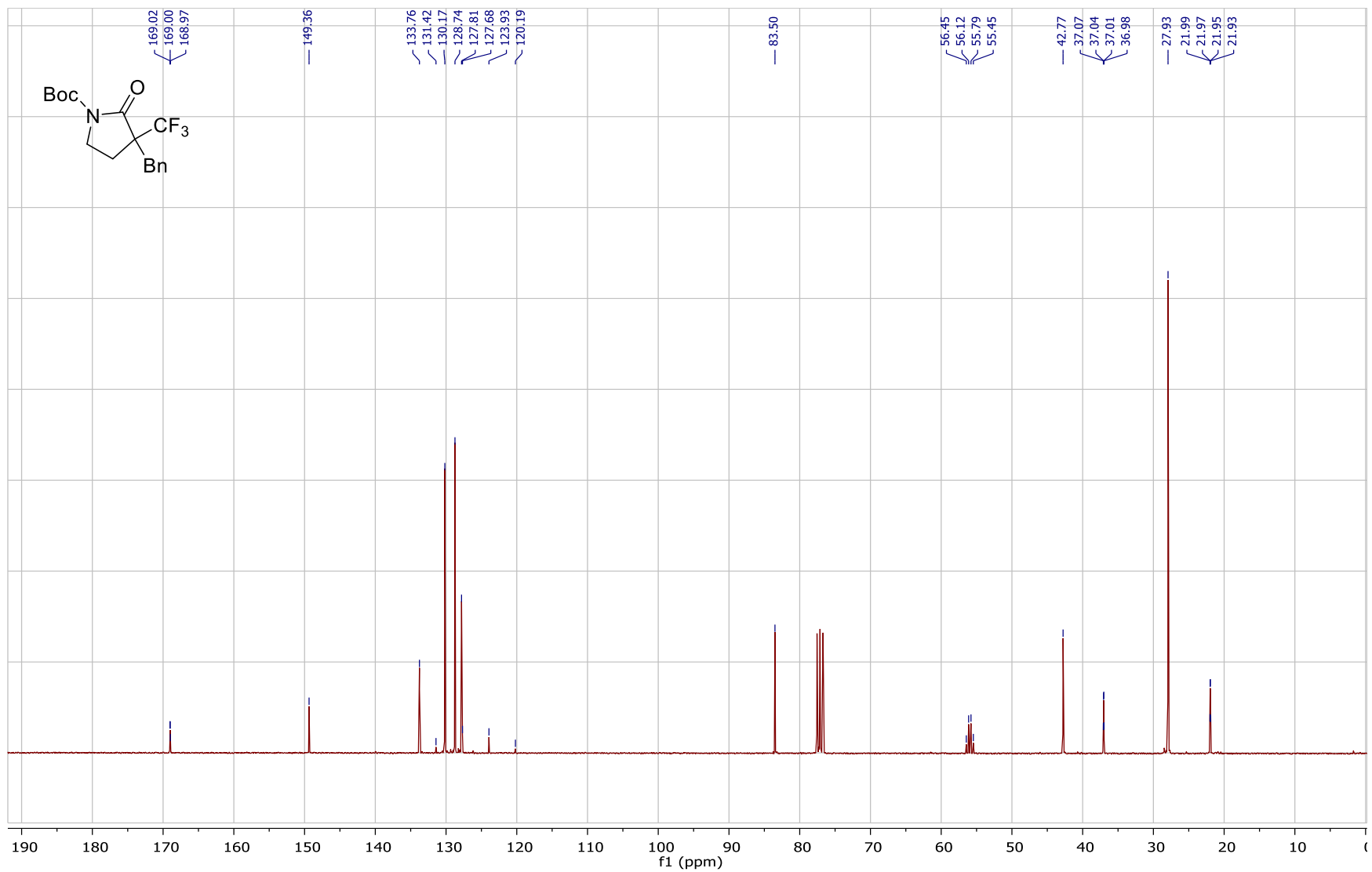


t-Butyl 3-benzyl-2-oxo-3-(trifluoromethyl)pyrrolidine-1-carboxylate (**8d**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

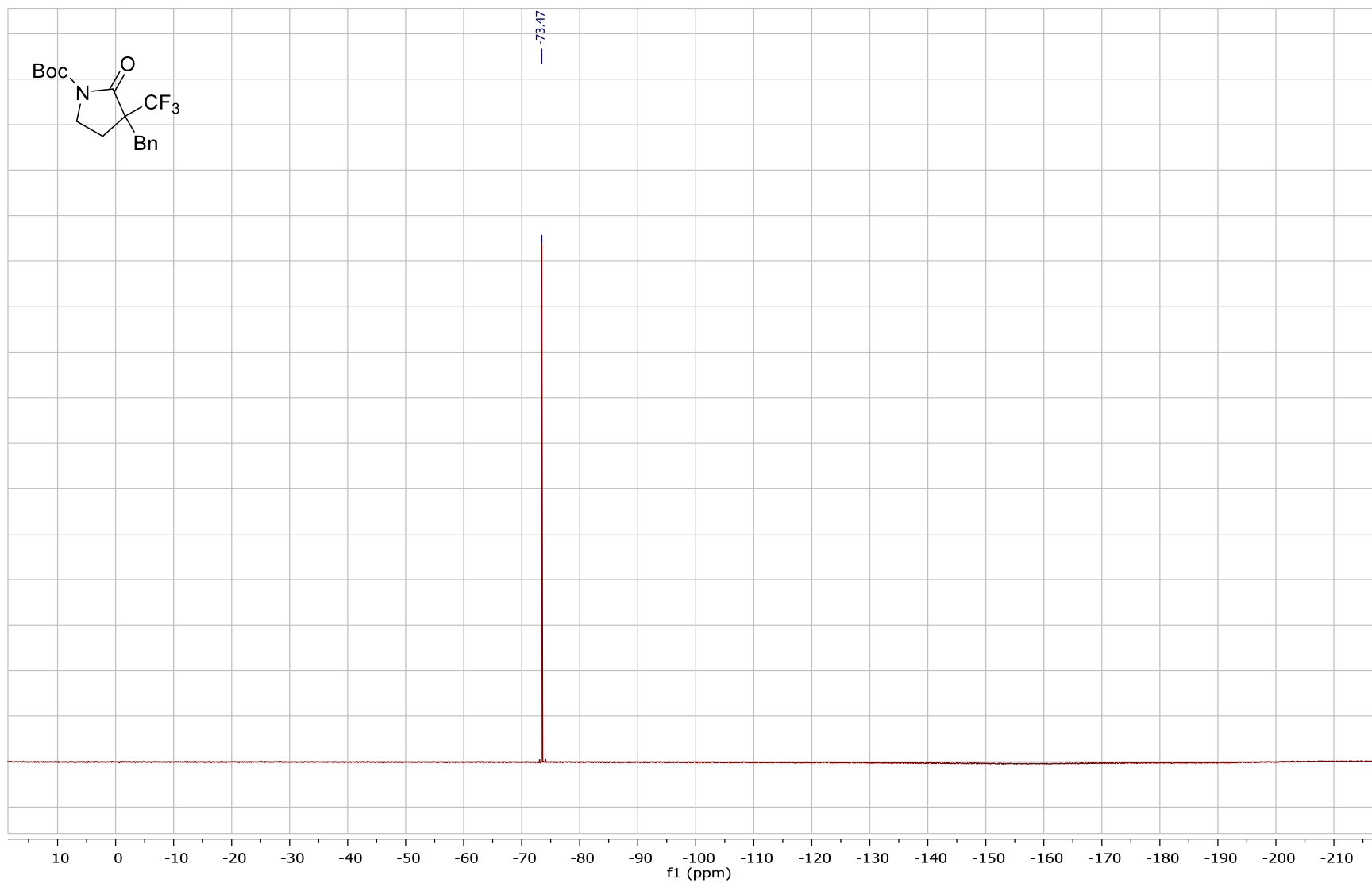


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



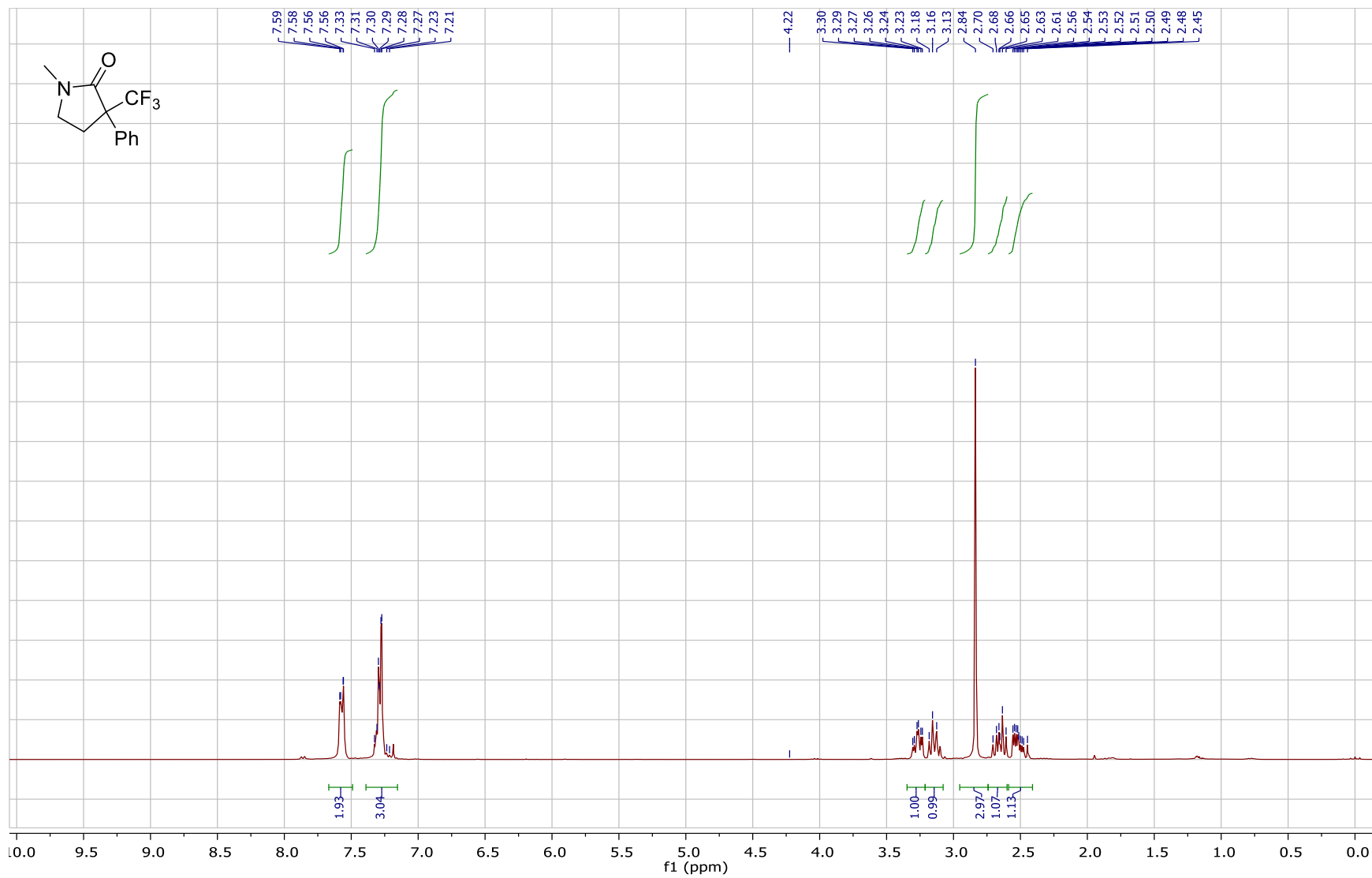


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

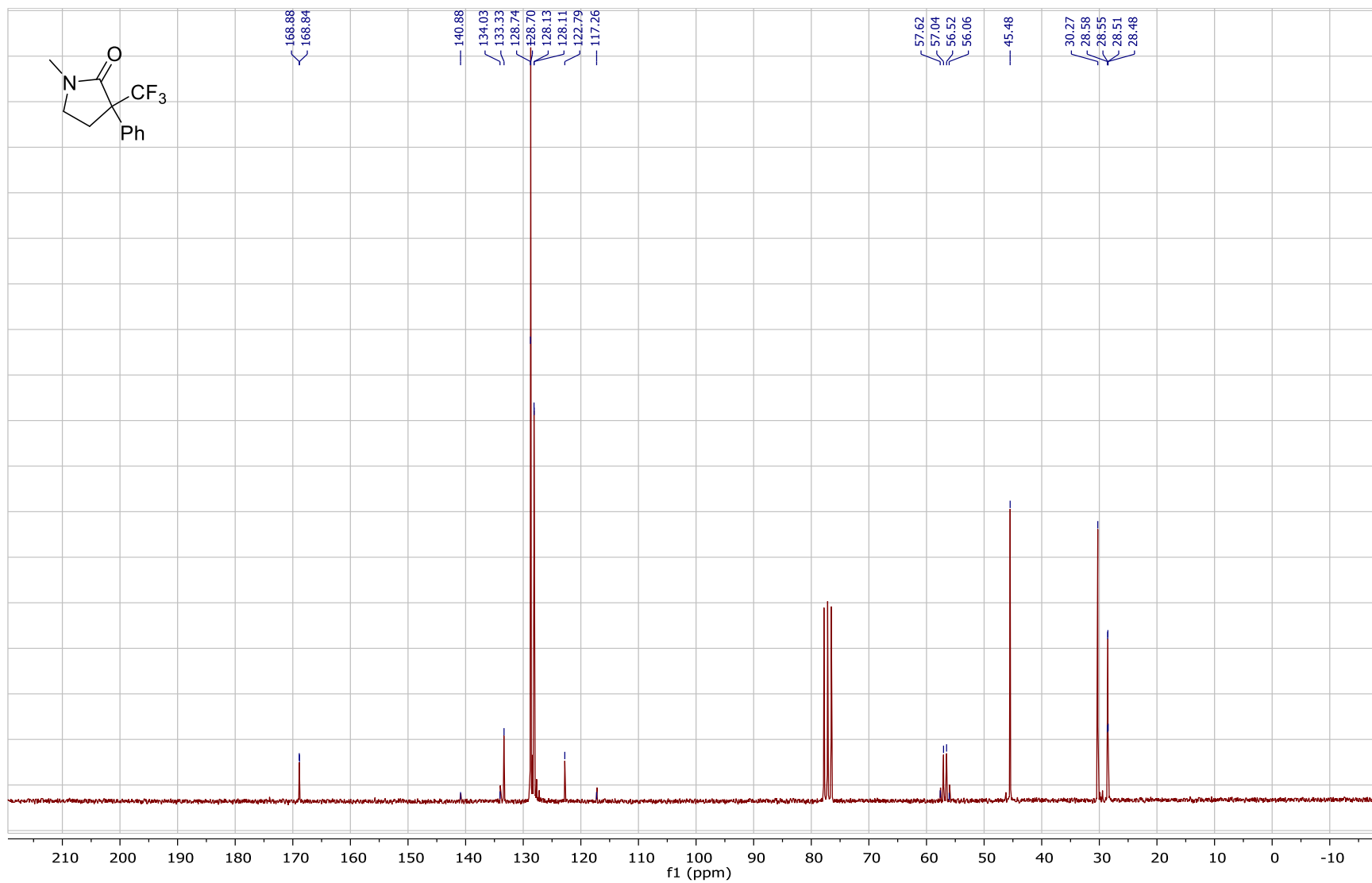


1-Methyl-3-phenyl-3-(trifluoromethyl)pyrrolidin-2-one (**8e**)

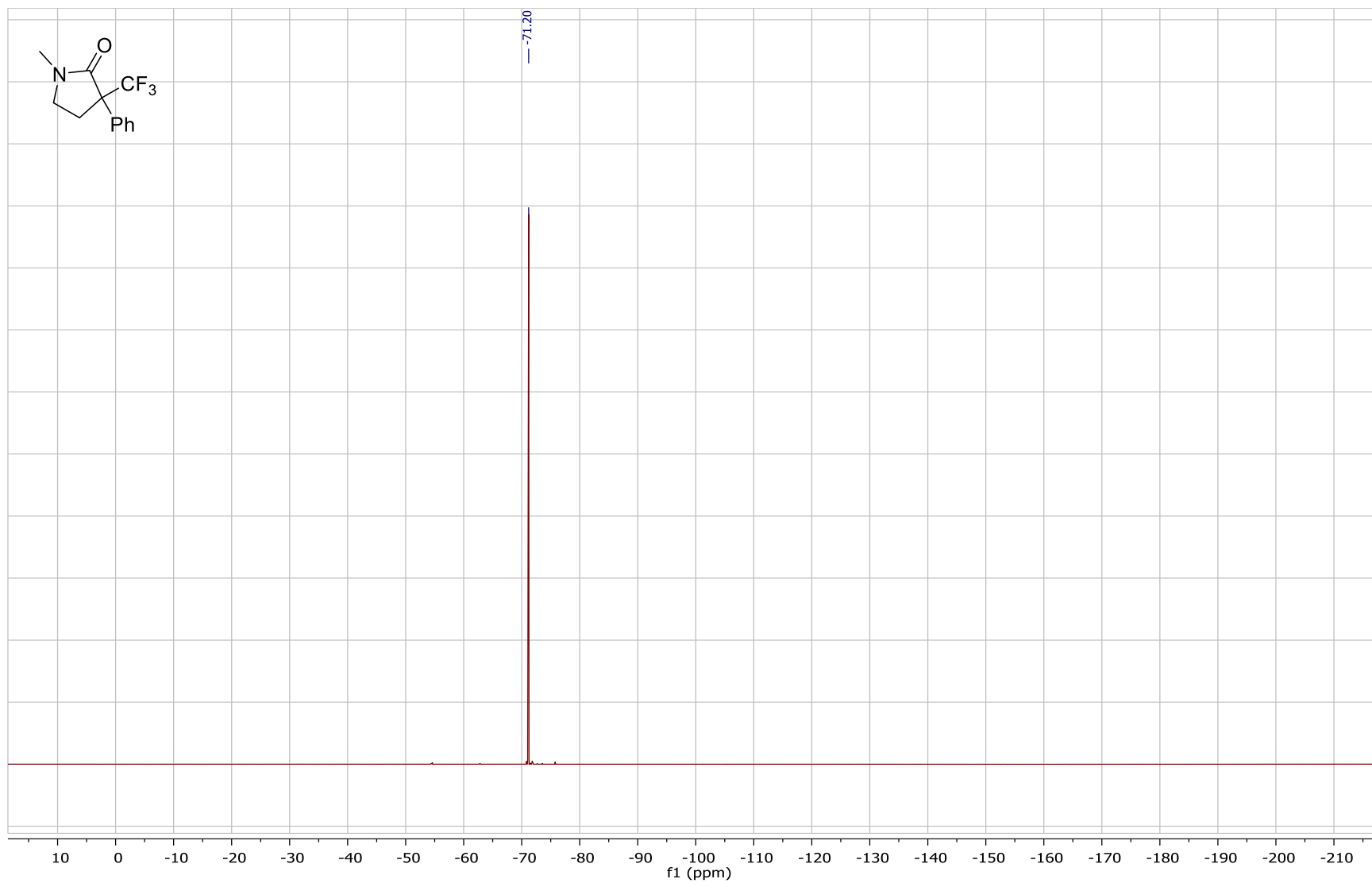
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )

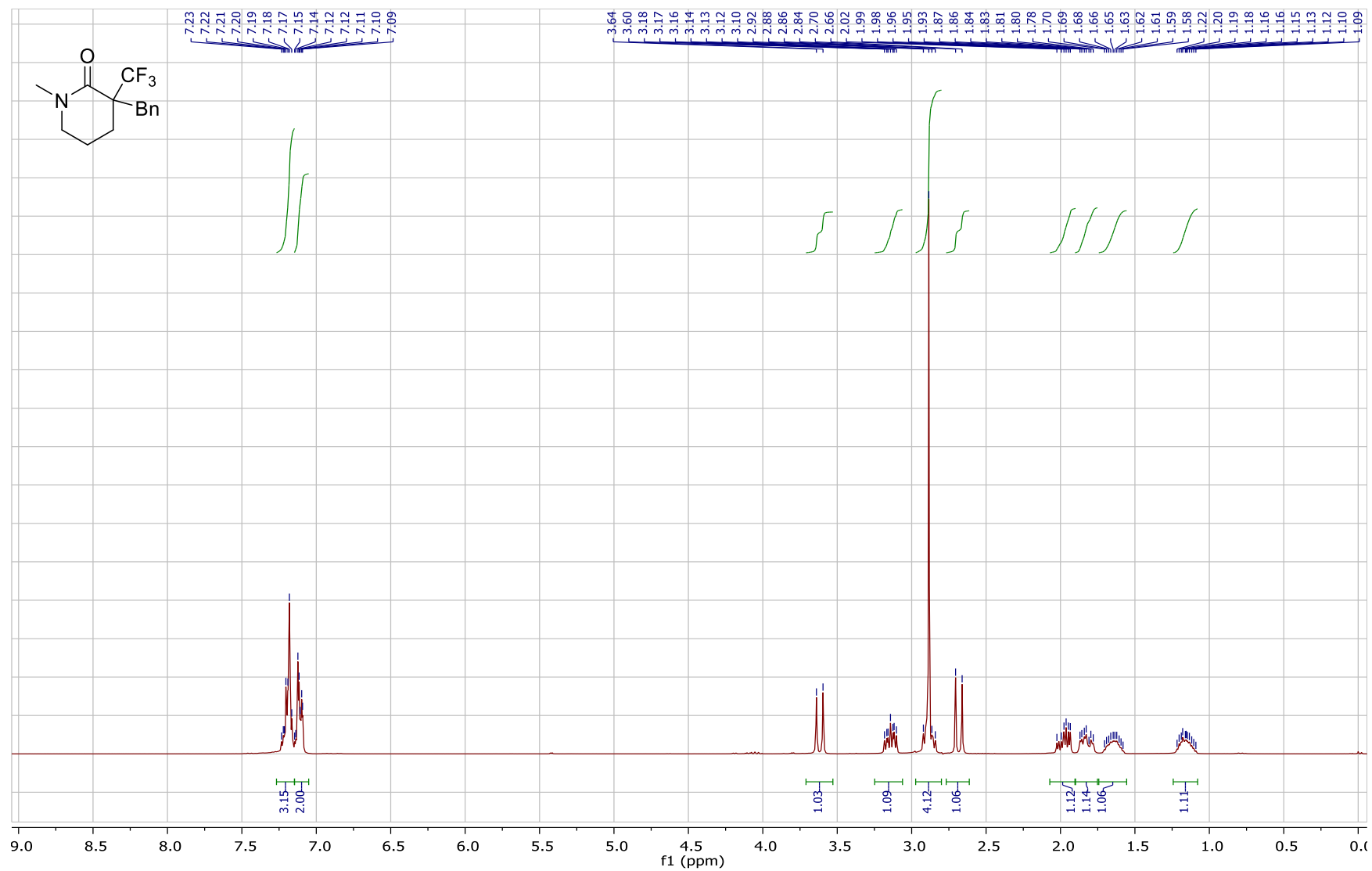


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

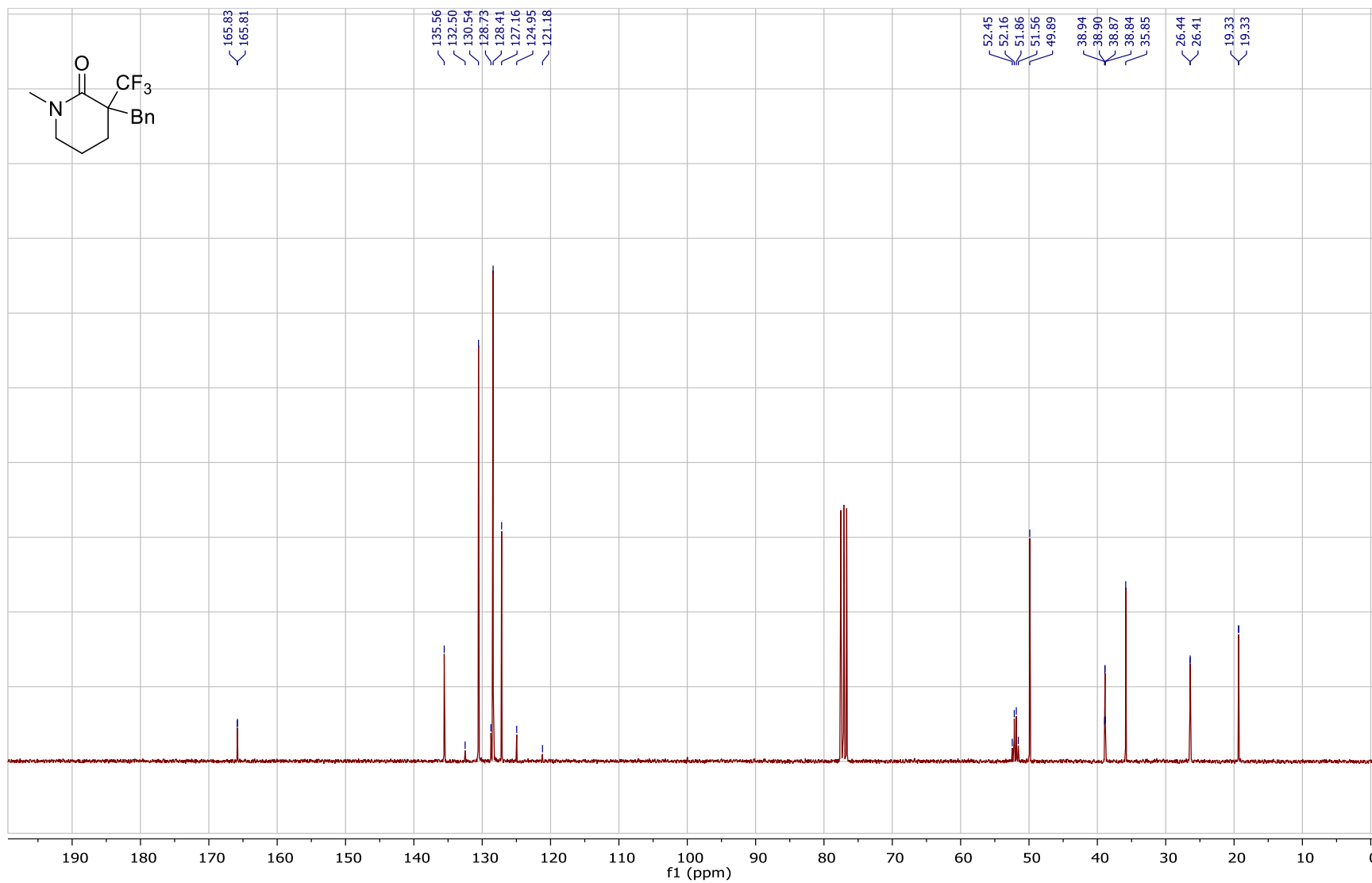


3-Benzyl-1-methyl-3-(trifluoromethyl)piperidin-2-one (**8f**)

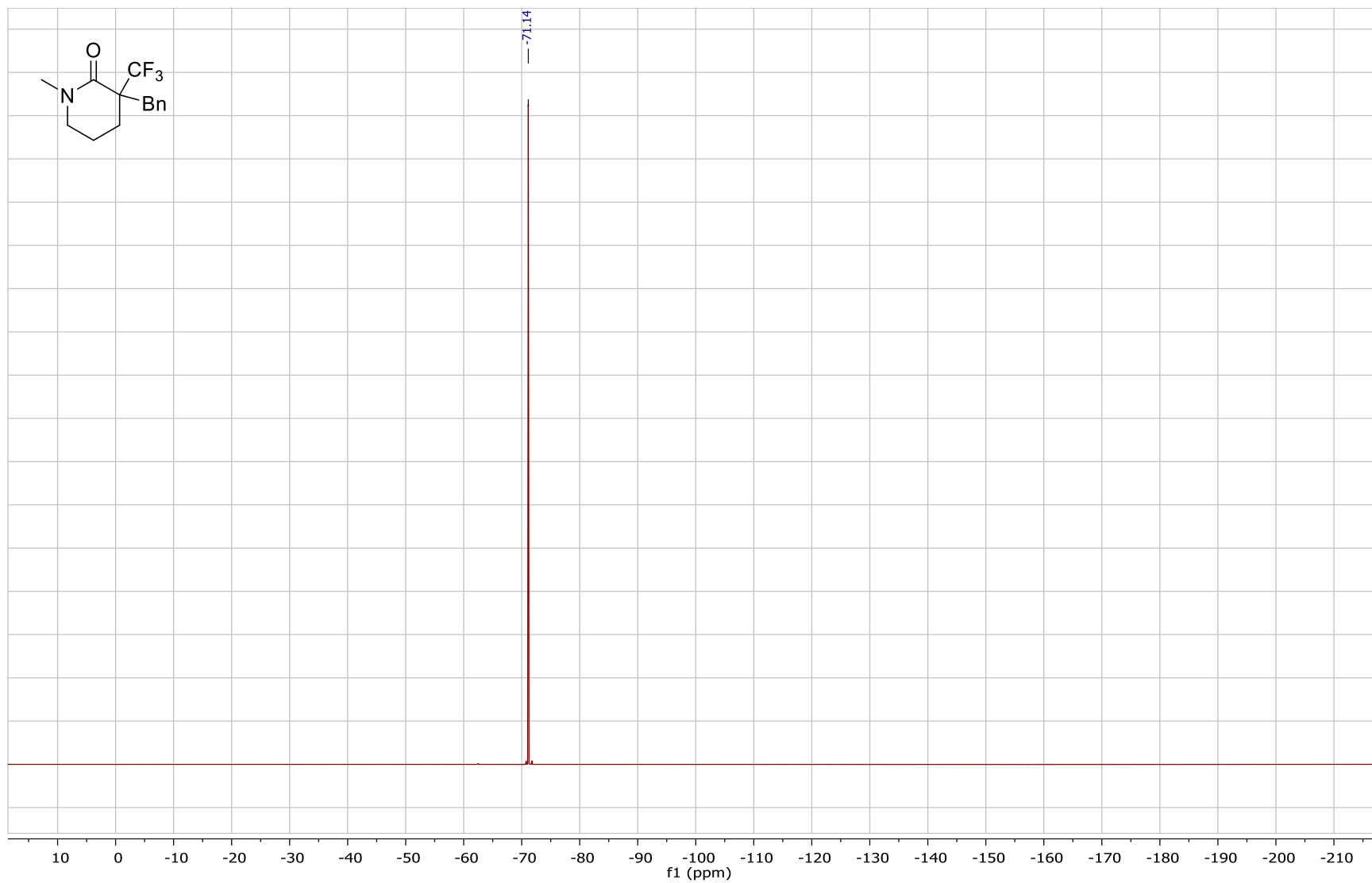
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

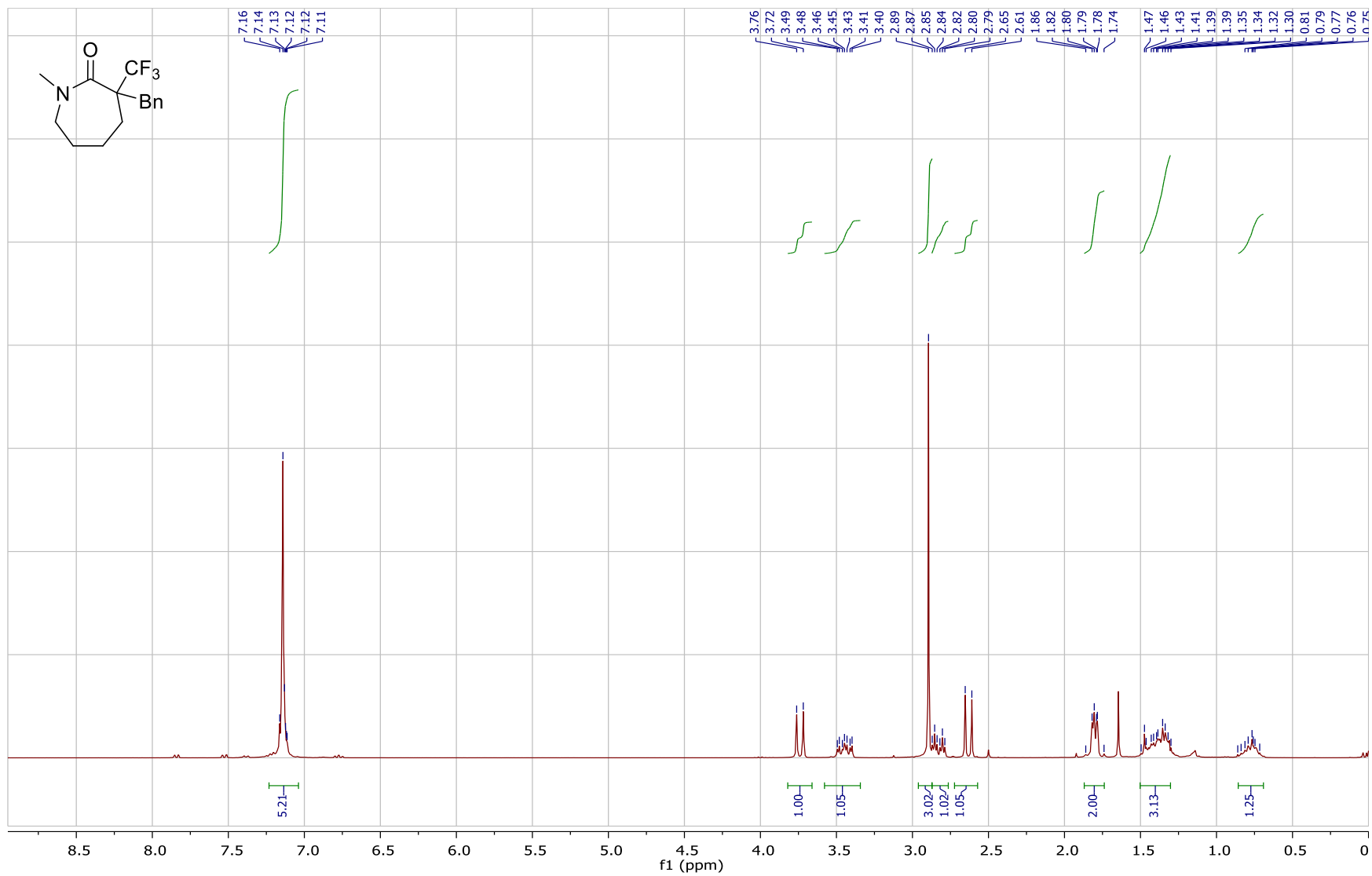


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



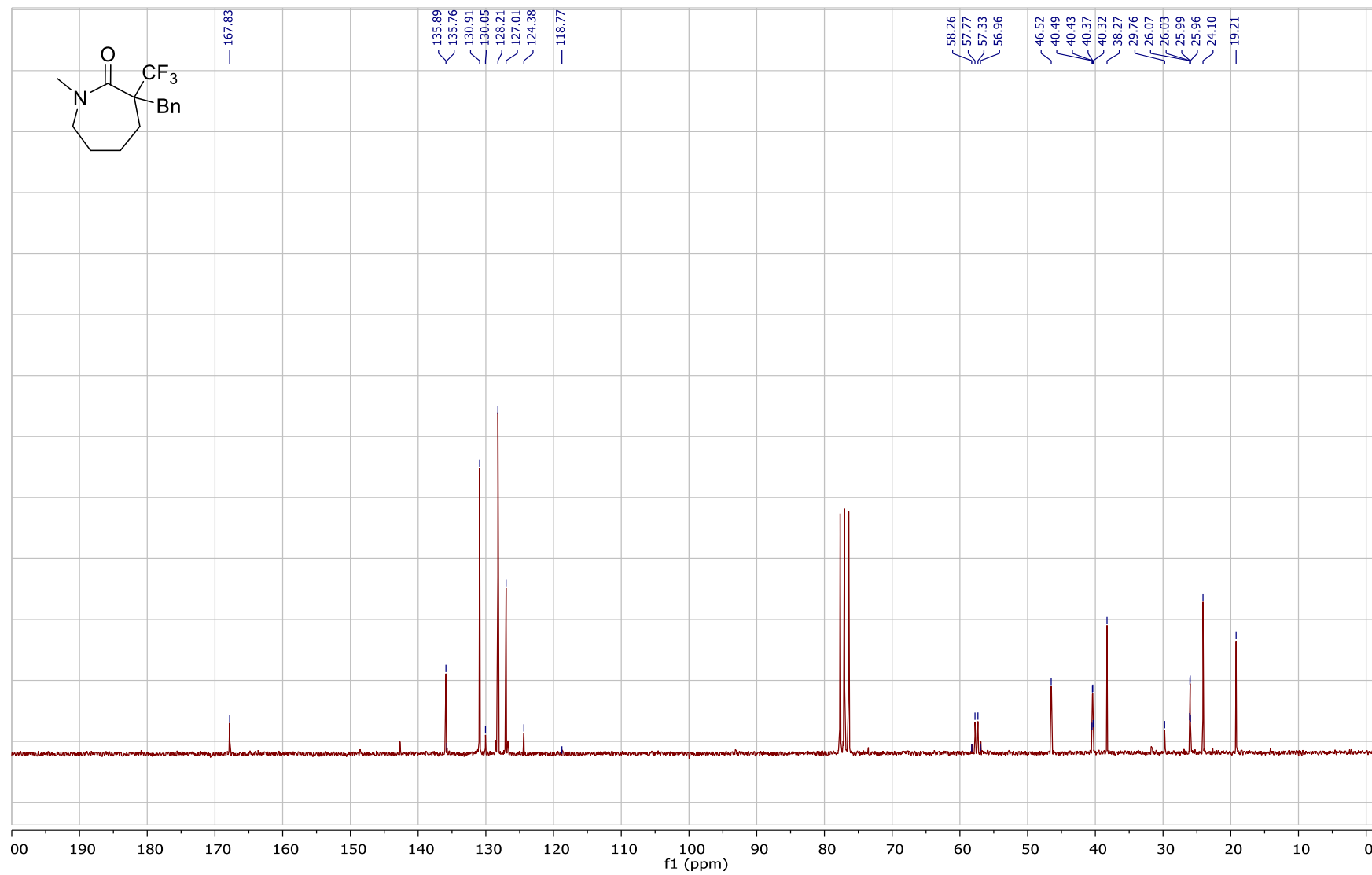
3-Benzyl-1-methyl-3-(trifluoromethyl)azepan-2-one (**8g**)

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

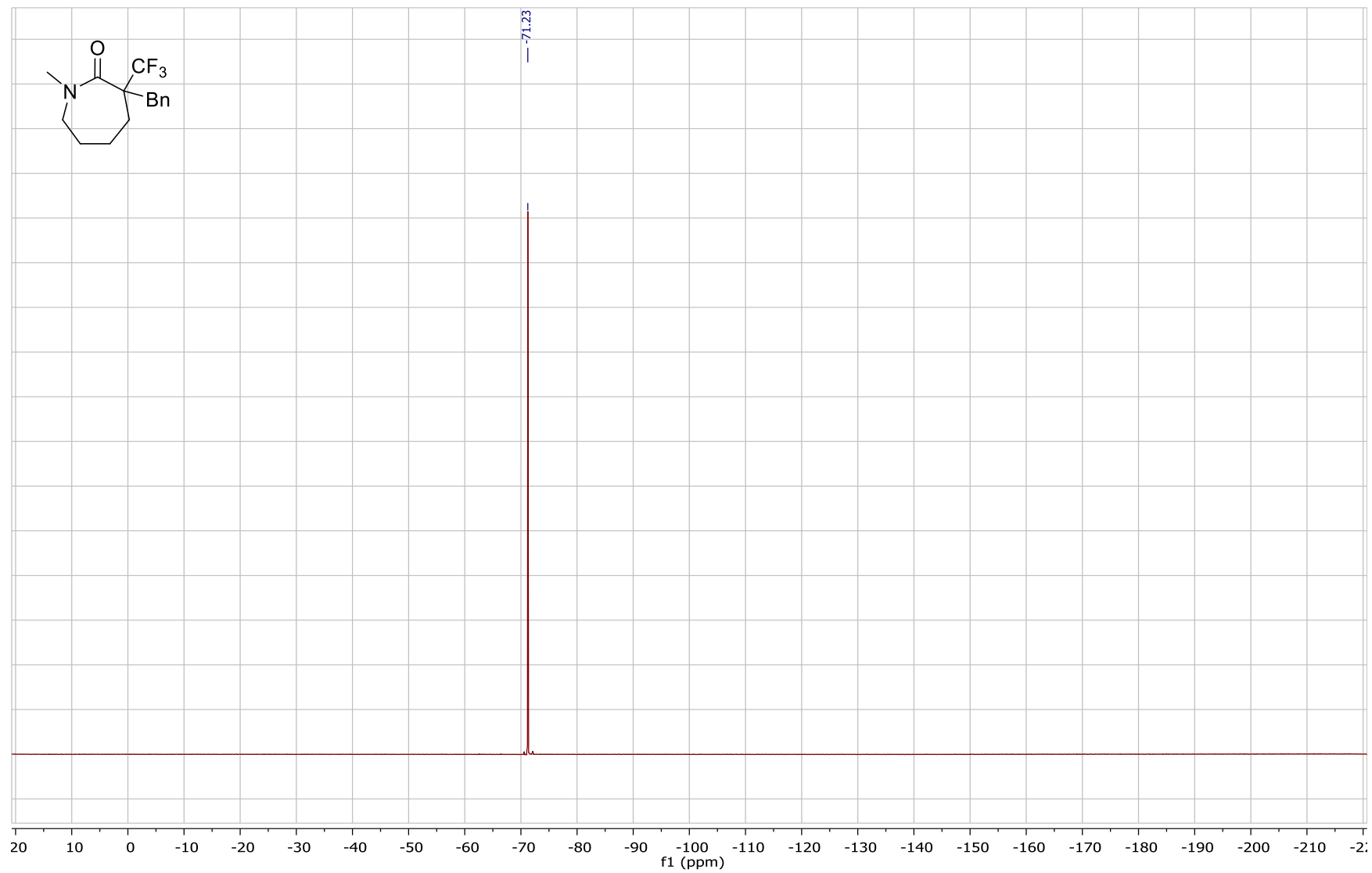




$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )

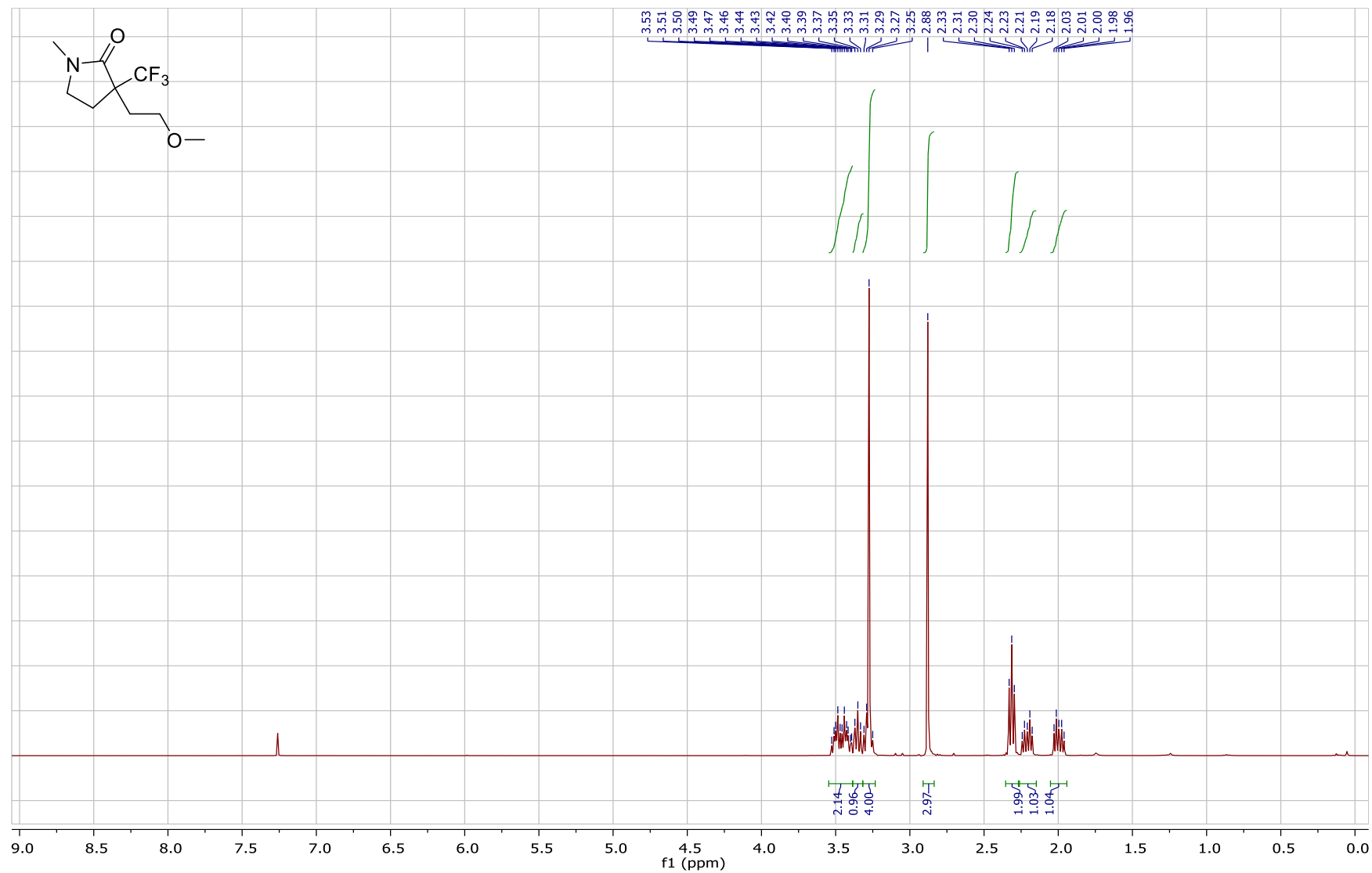


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

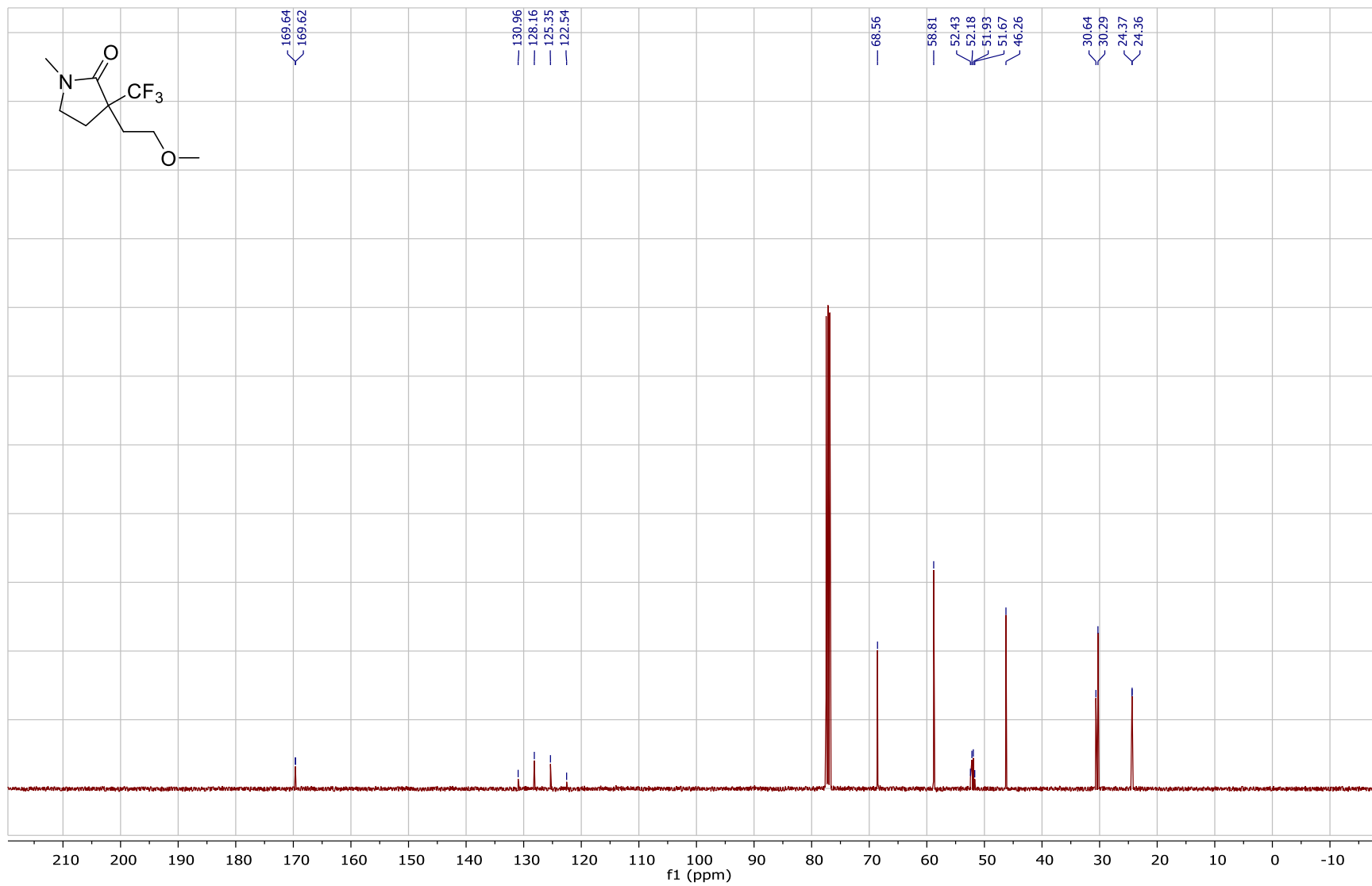


3-(2-Methoxyethyl)-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (**8h**)

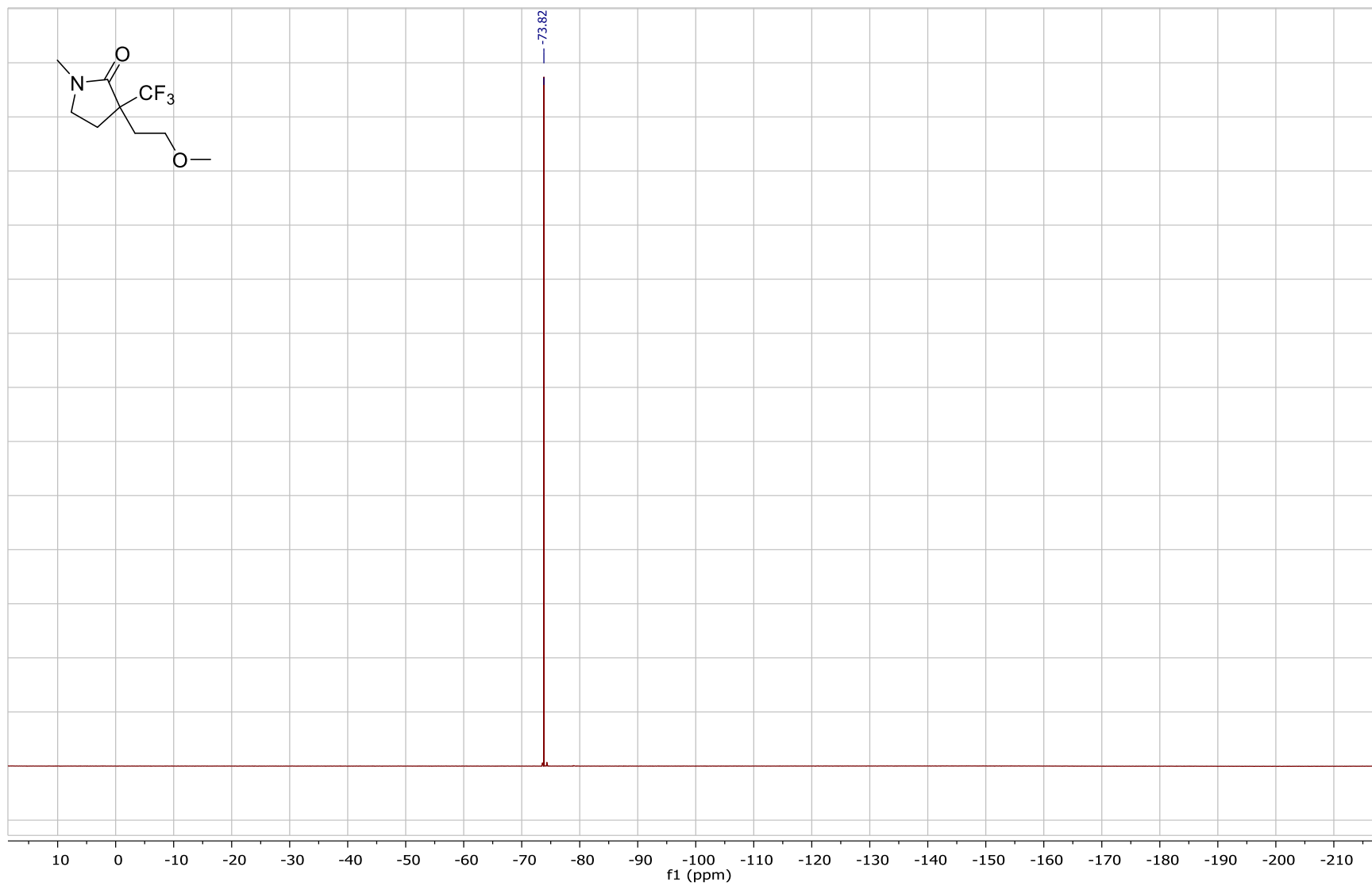
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

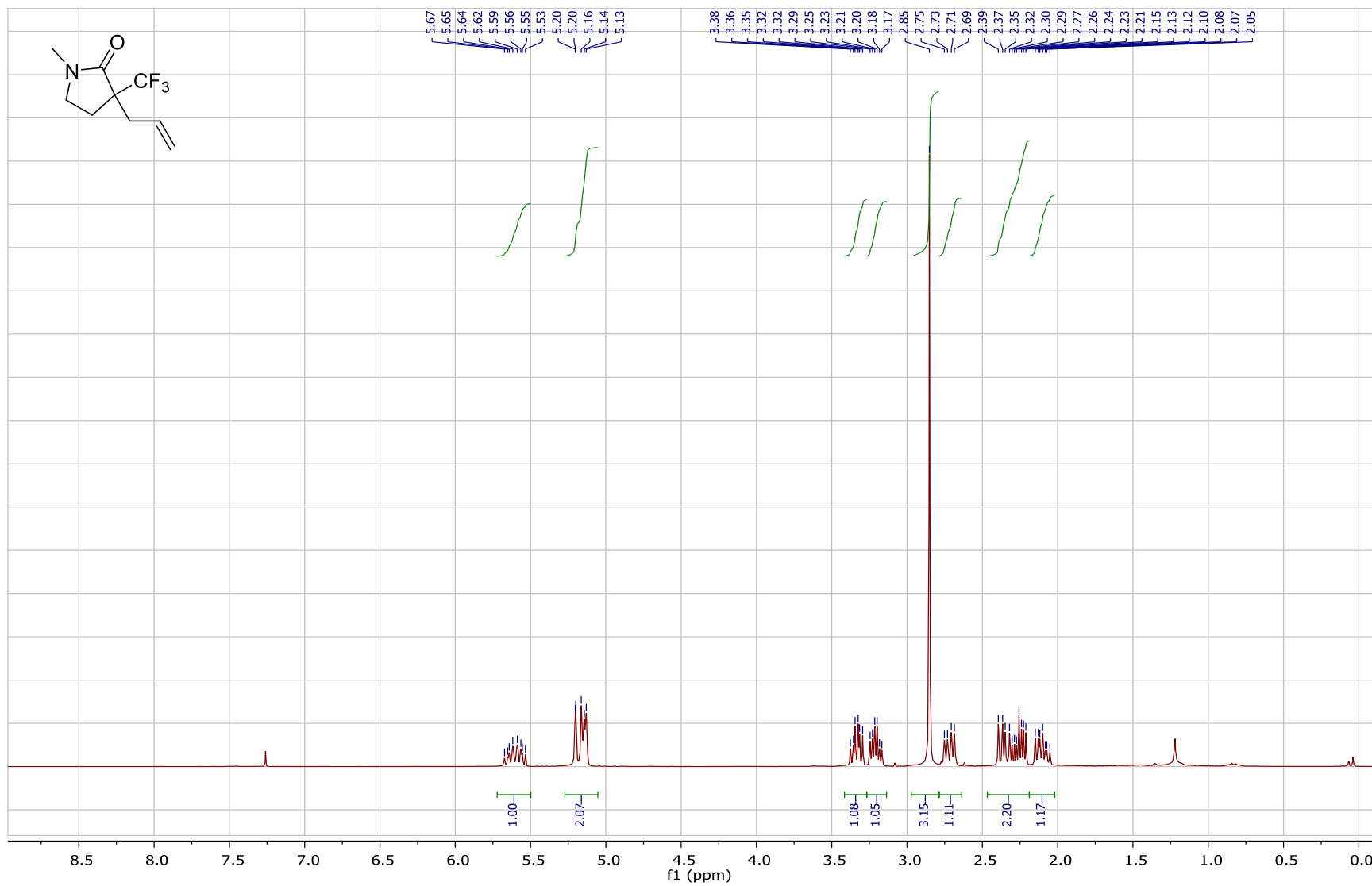


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

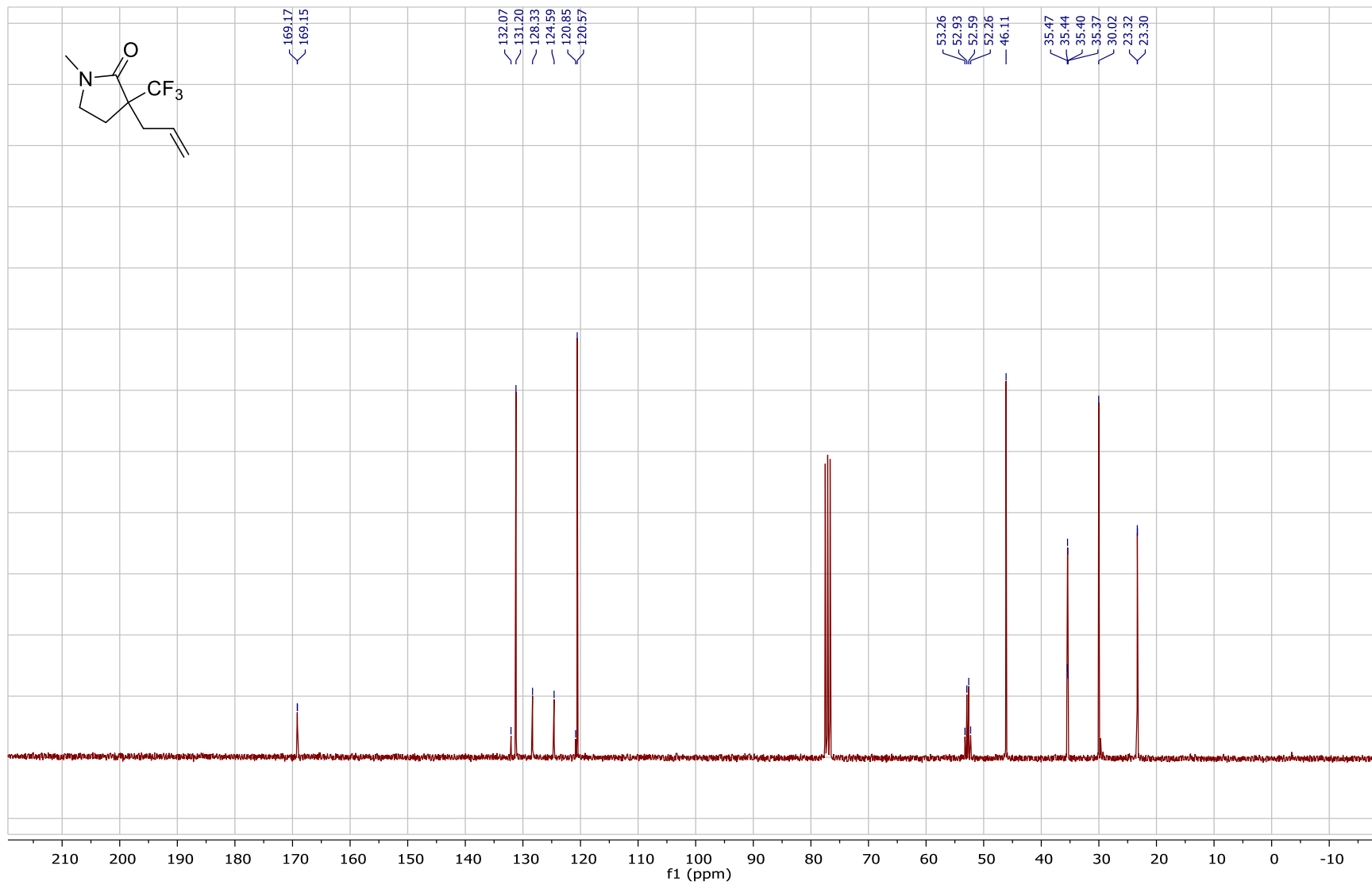


3-Allyl-1-methyl-3-(trifluoromethyl)pyrrolidin-2-one (**8i**)

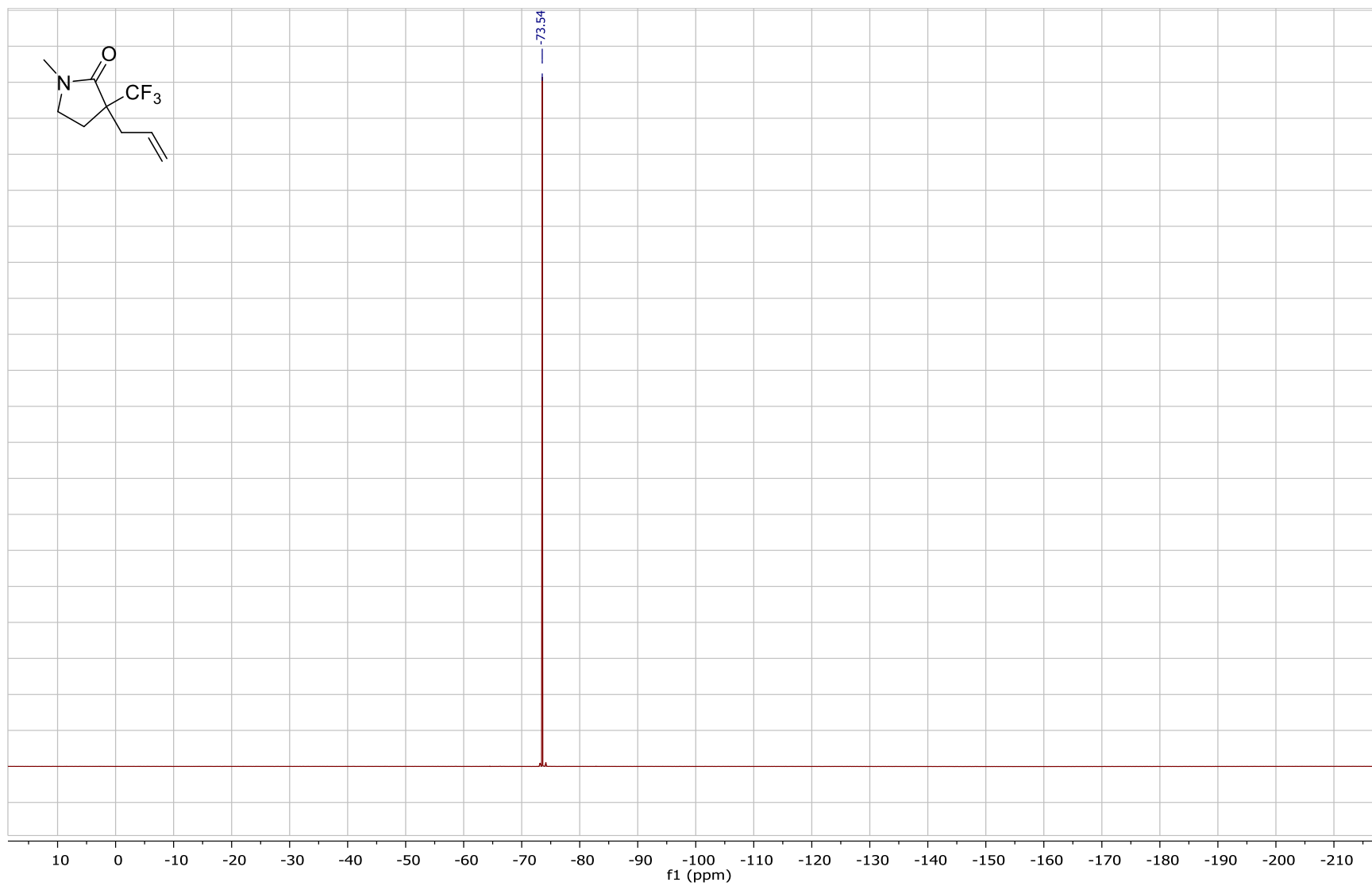
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



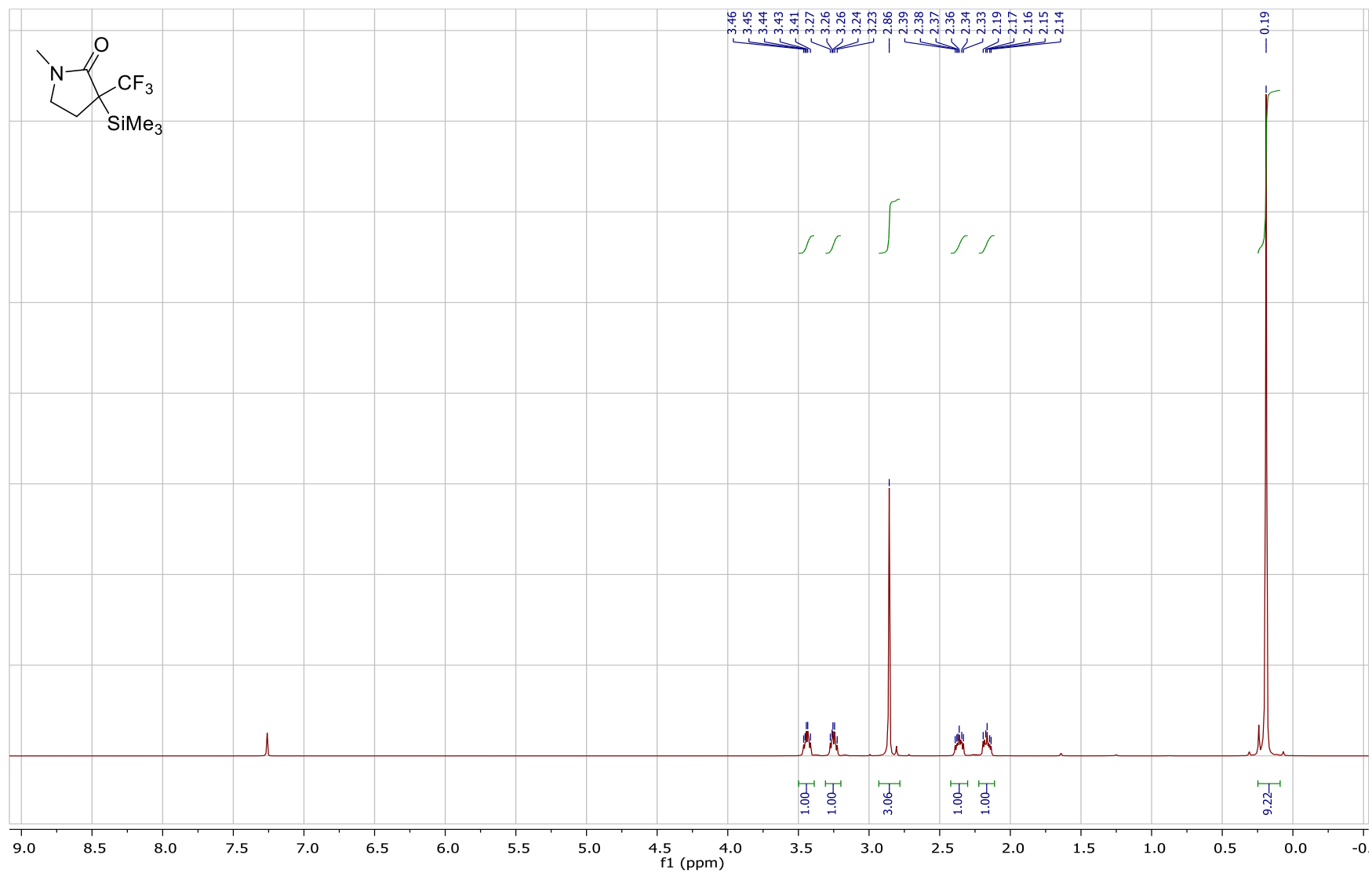
$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



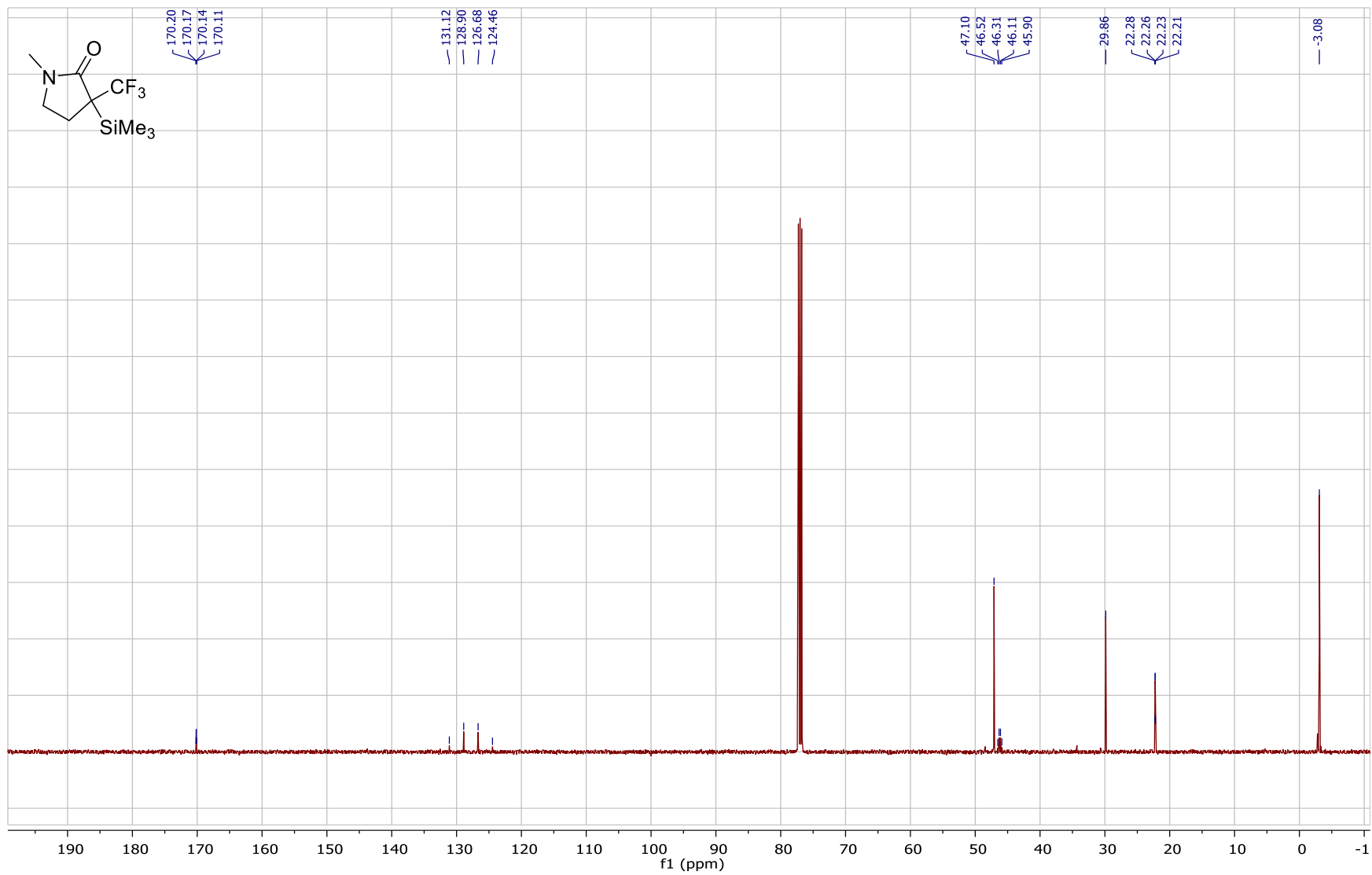


1-Methyl-3-(trifluoromethyl)-3-(trimethylsilyl)pyrrolidin-2-one (**8j**)

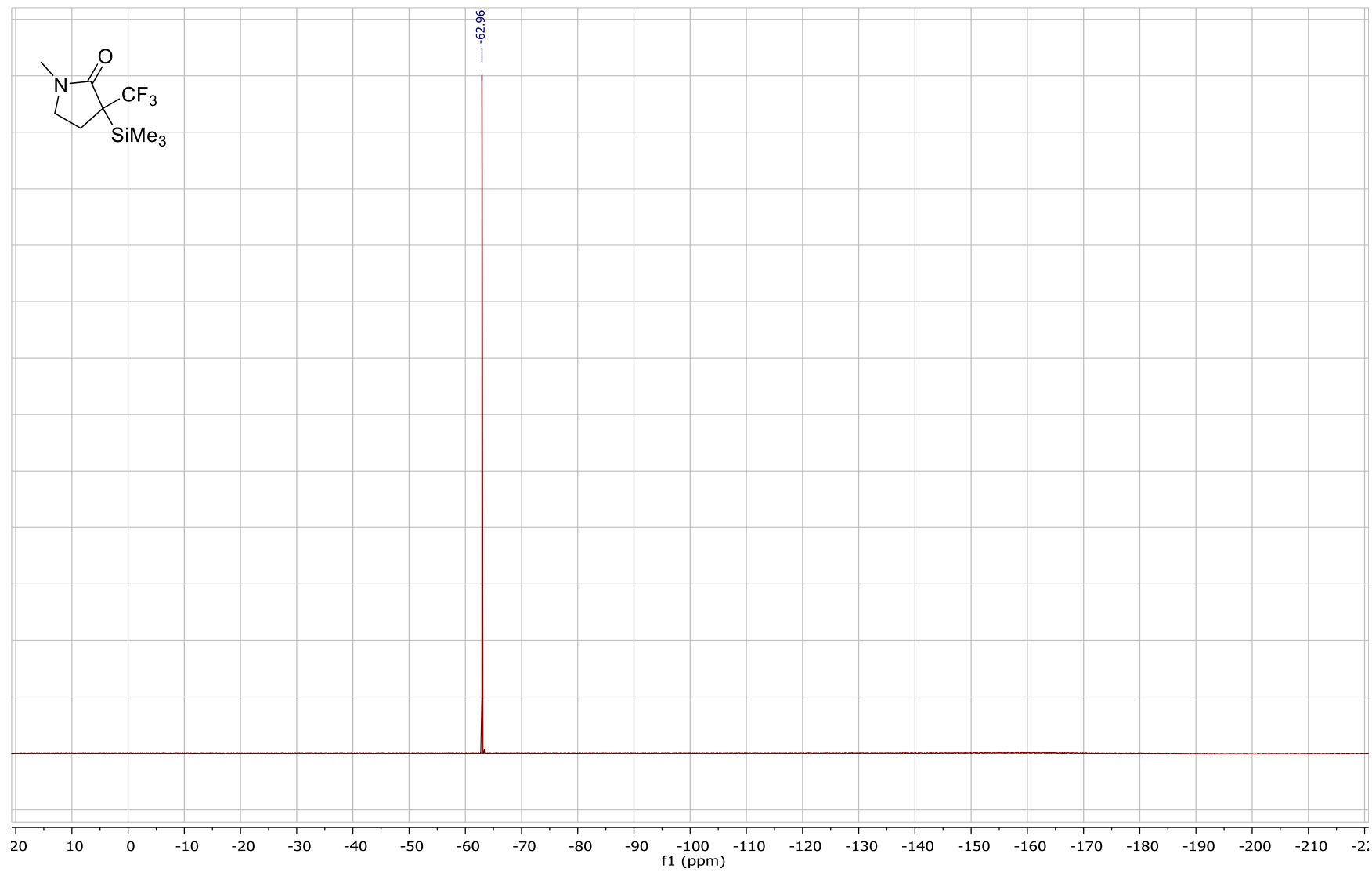
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

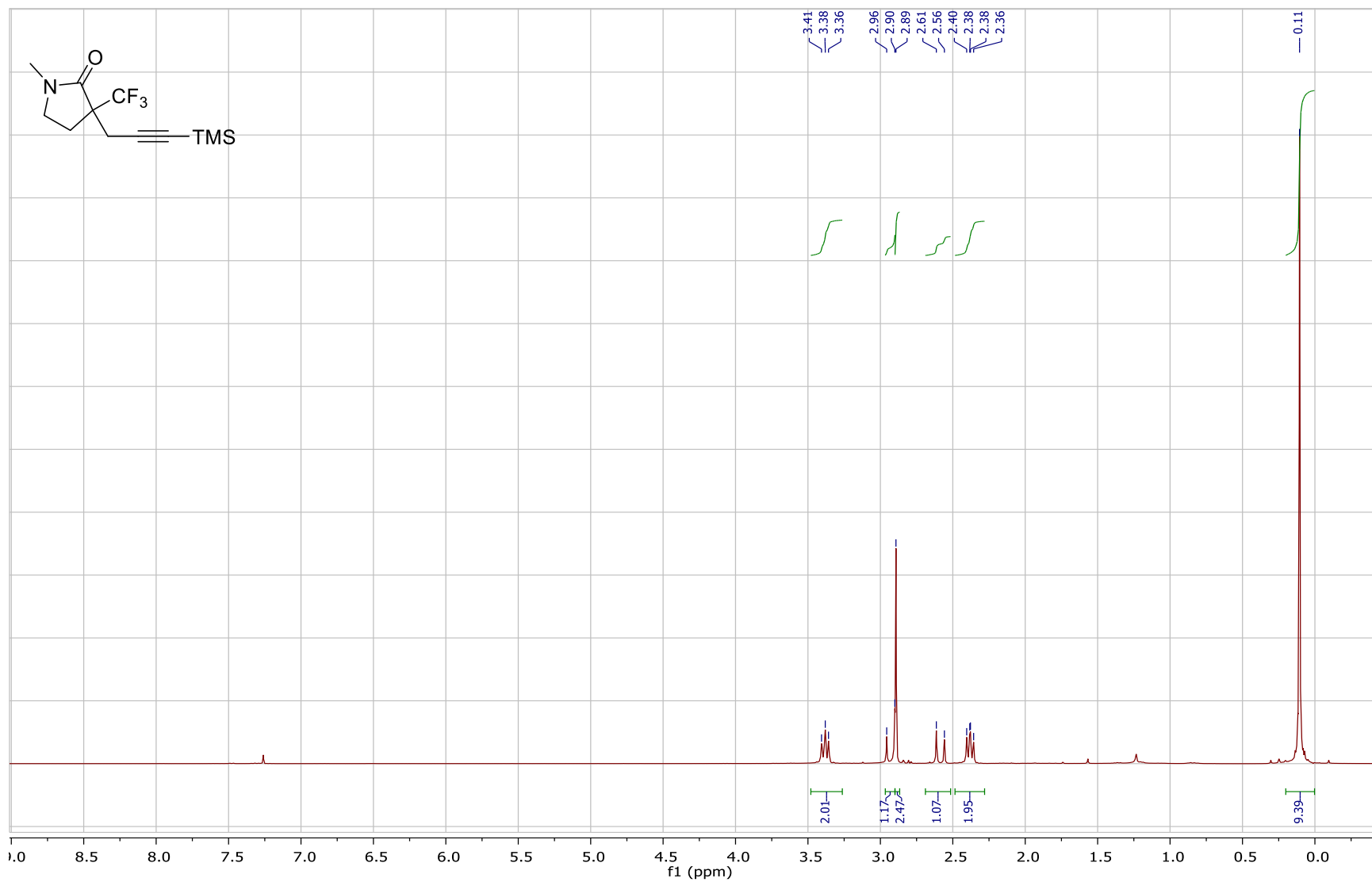


$^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )

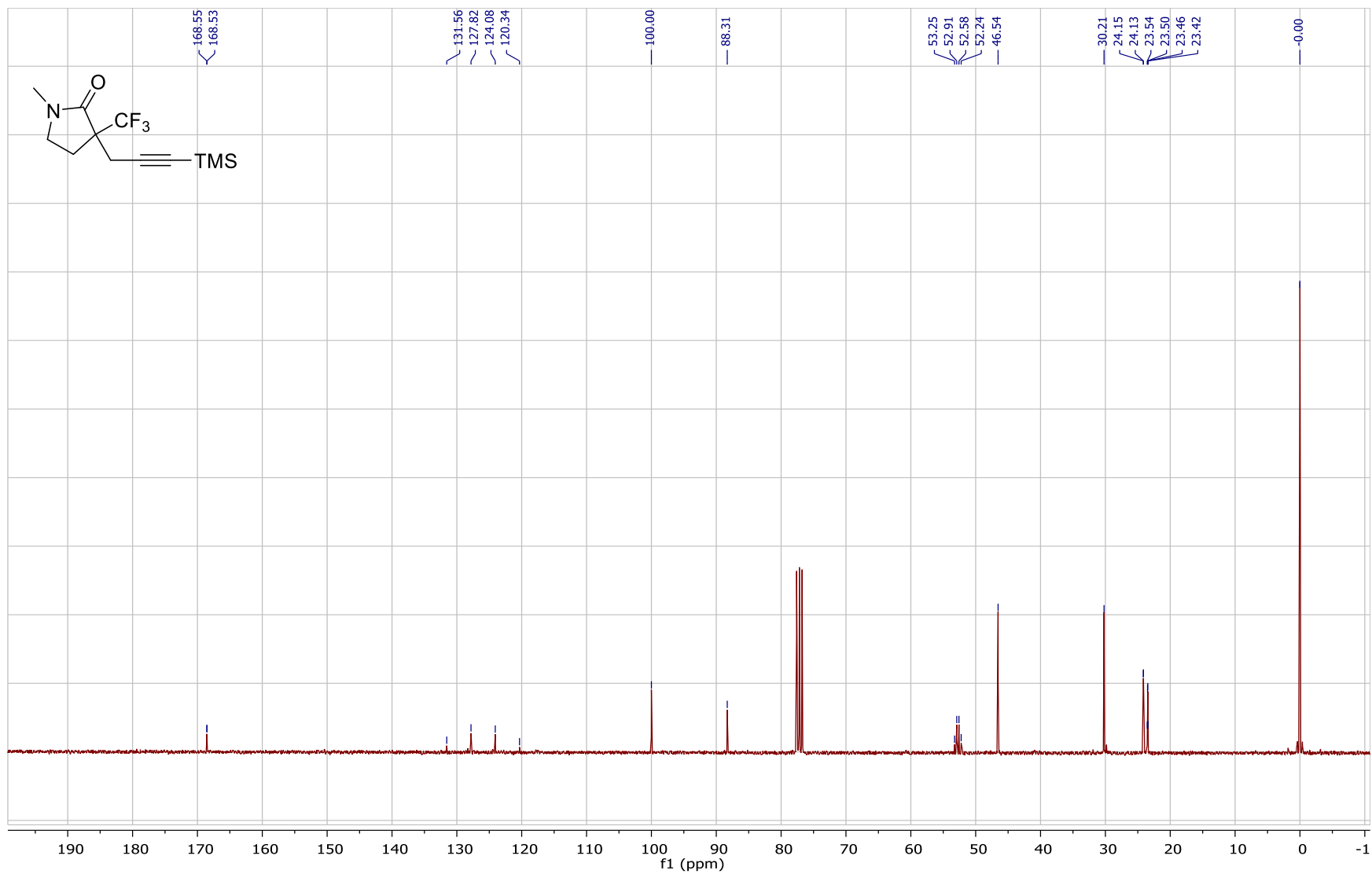


1-Methyl-3-(trifluoromethyl)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)pyrrolidin-2-one (**8k**)

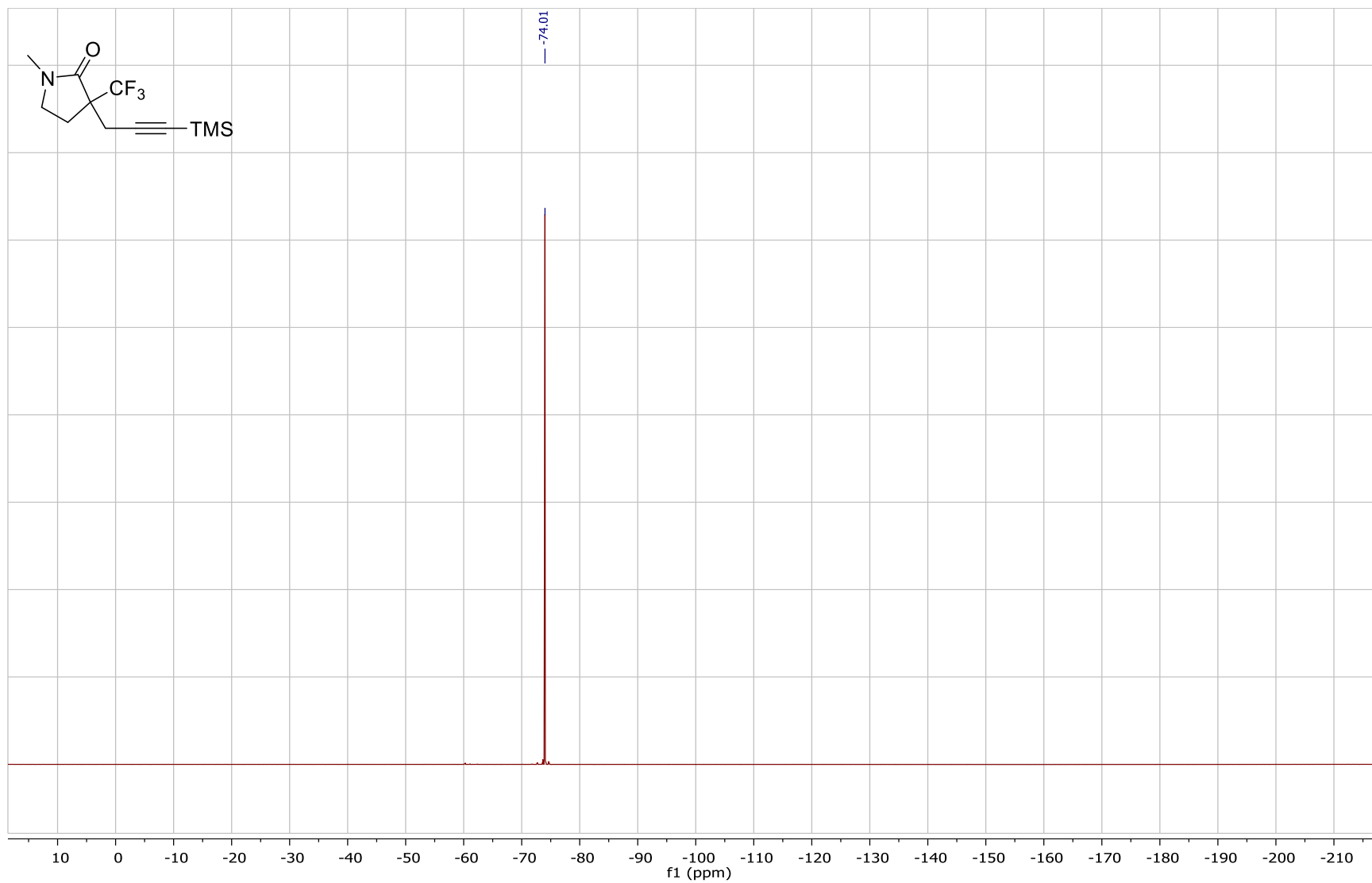
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

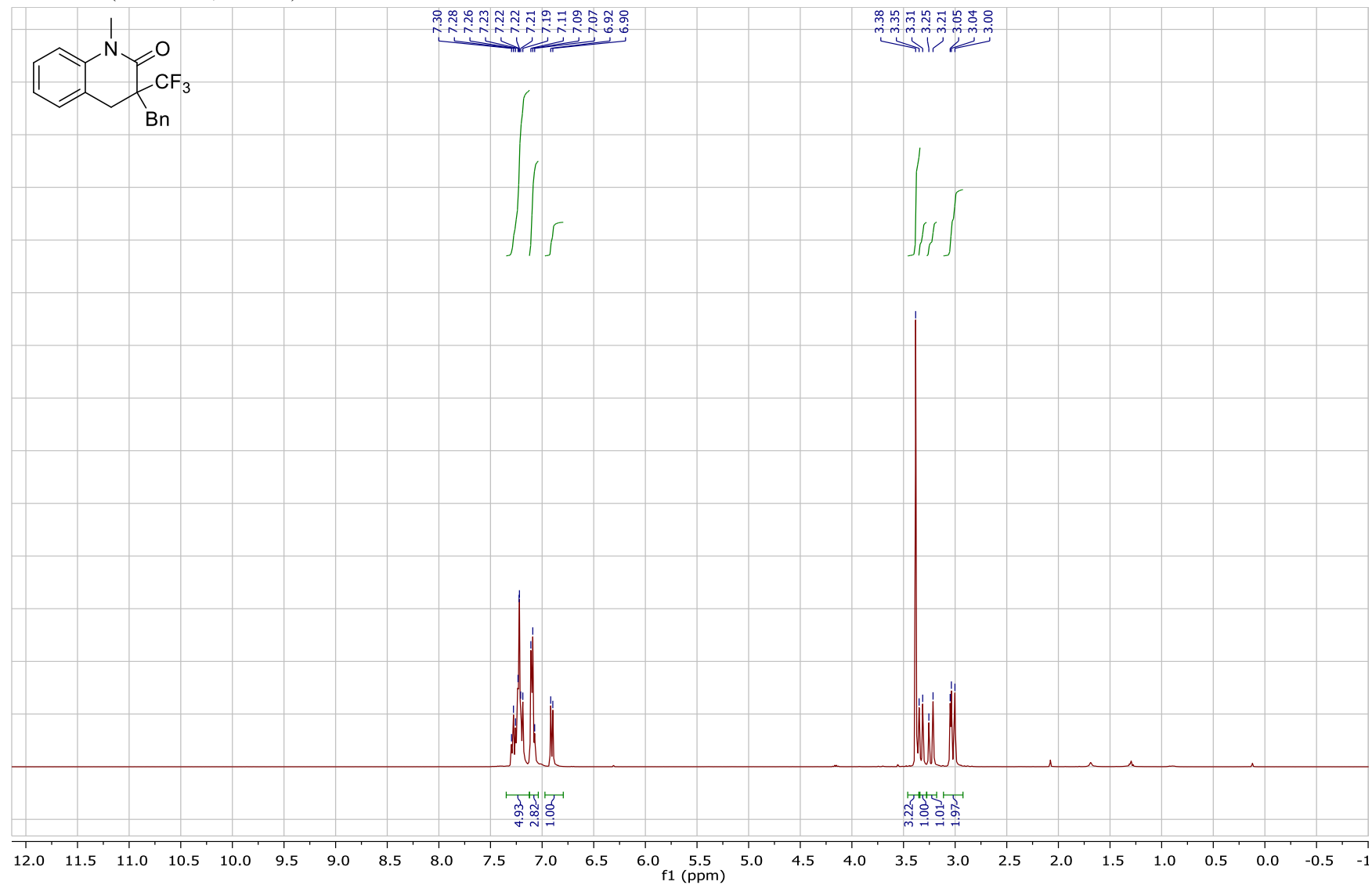


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

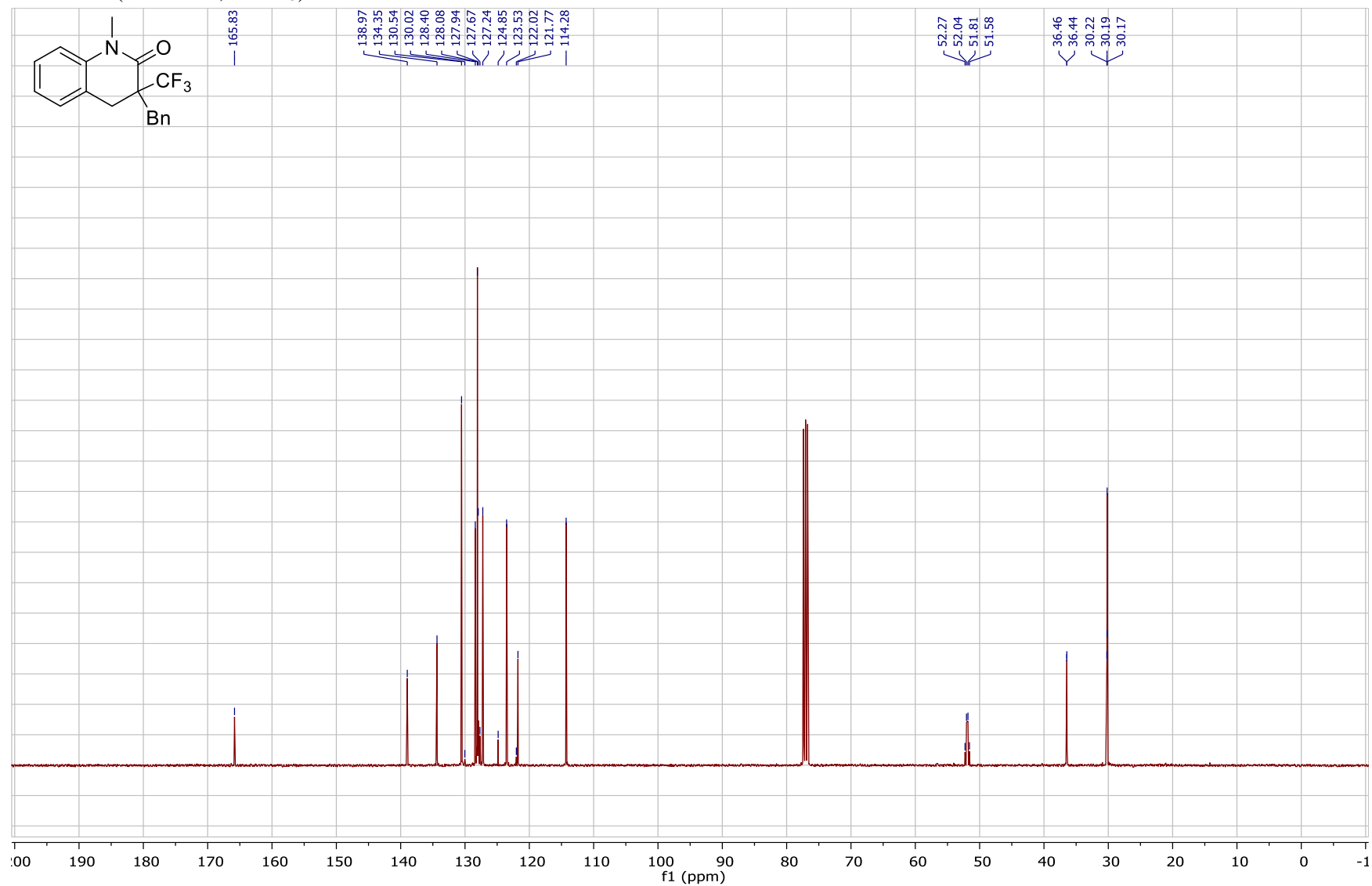


3-Benzyl-1-methyl-3-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (**81**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

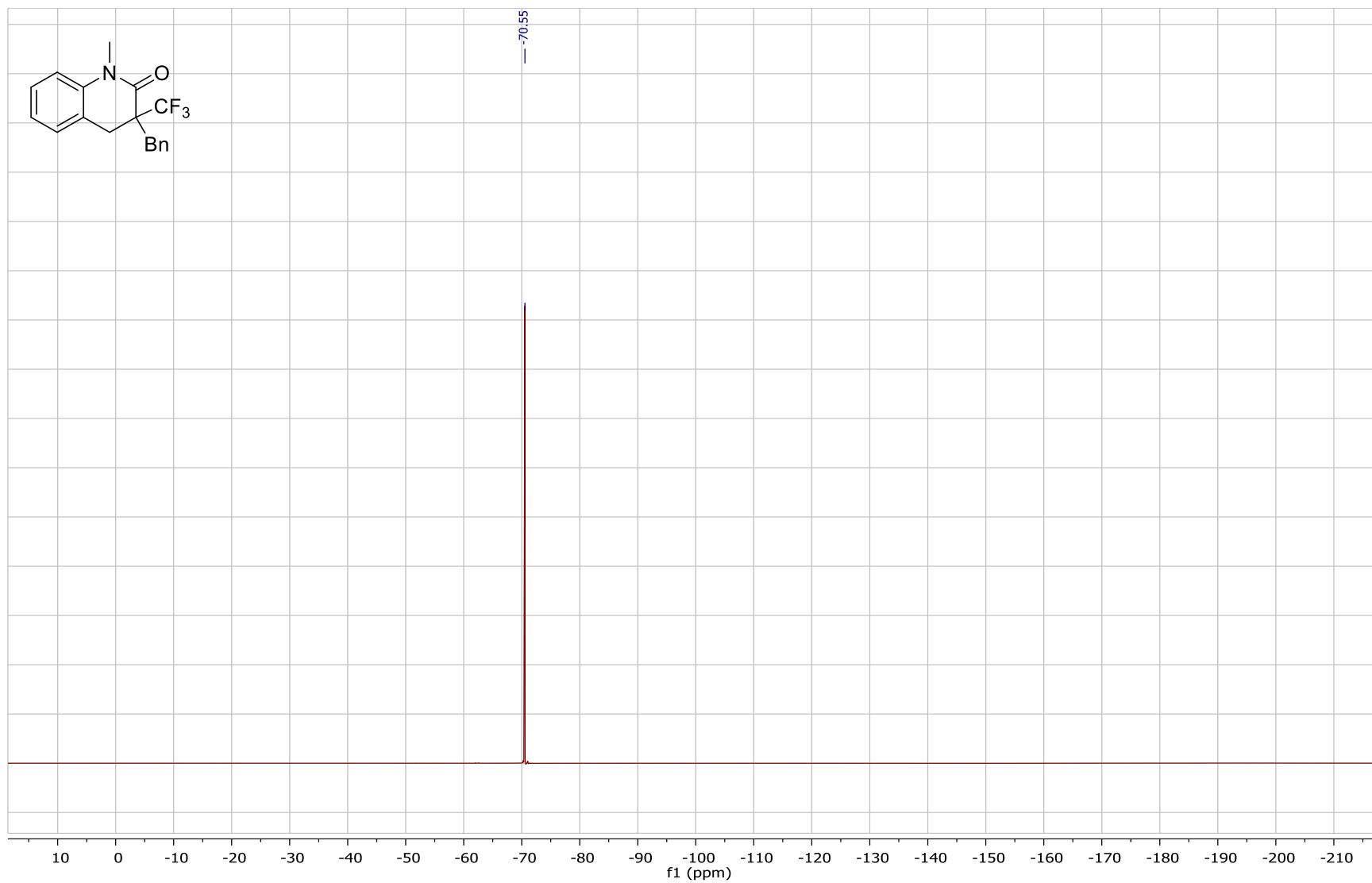


<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



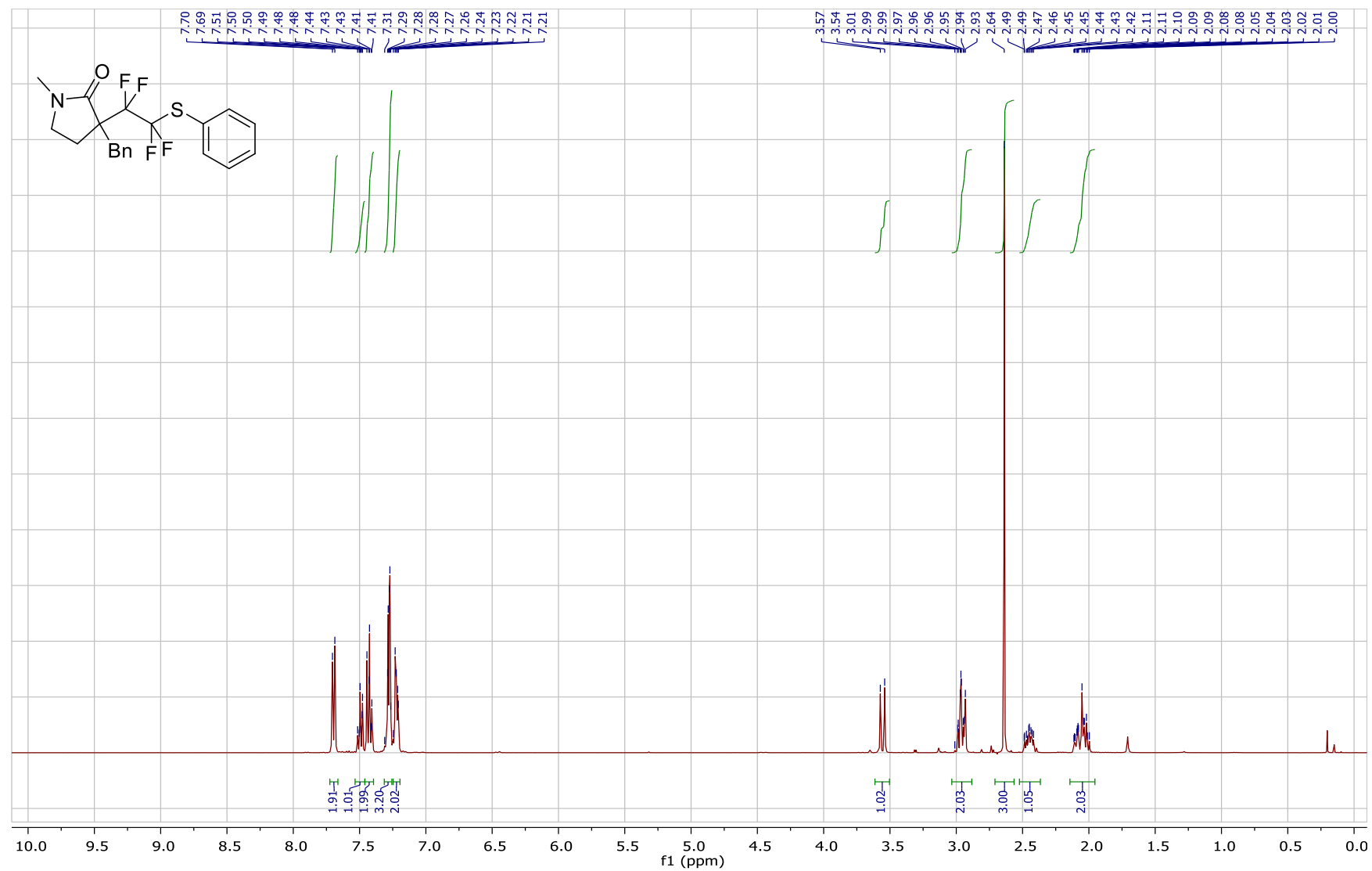


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



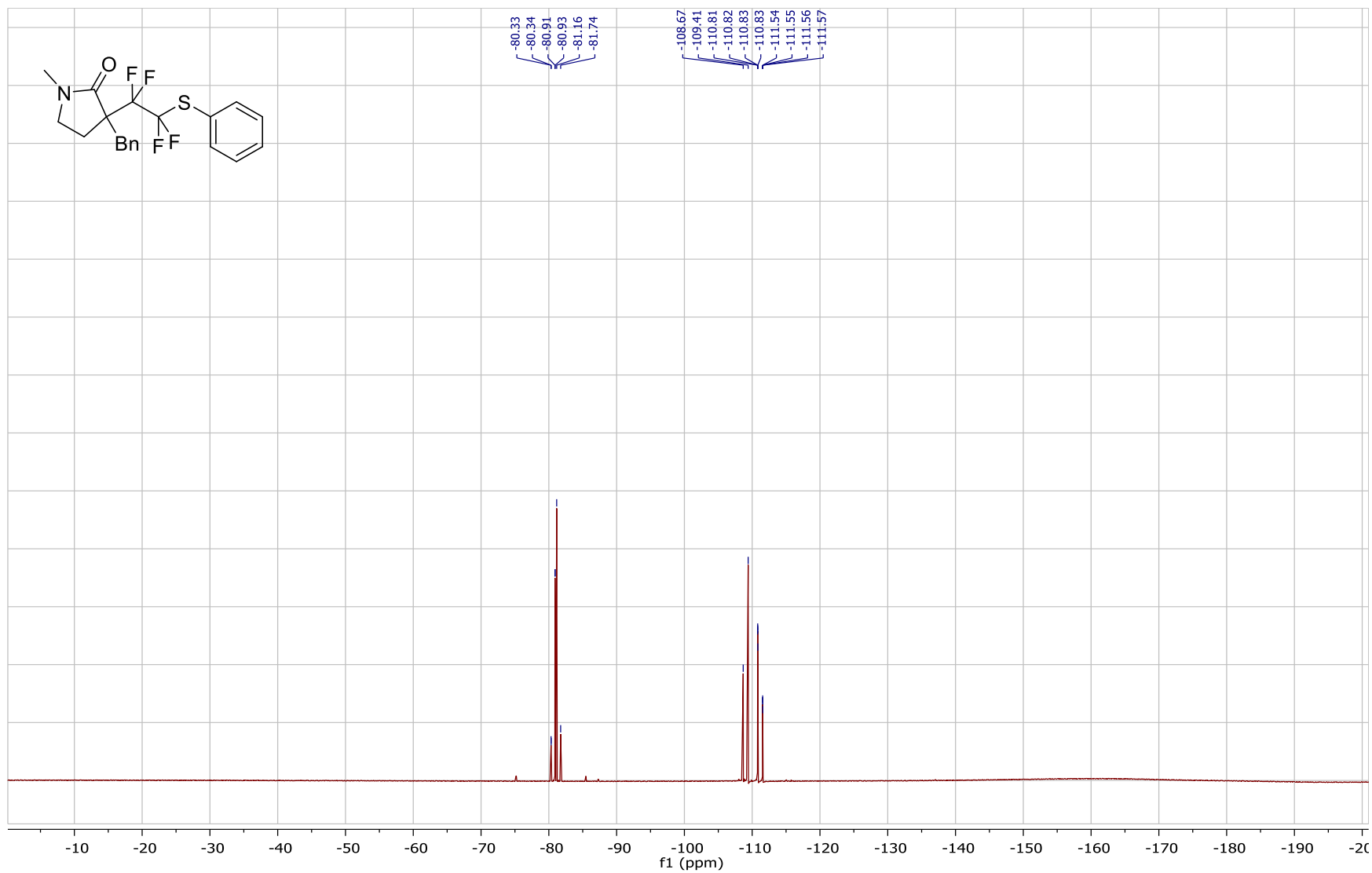
3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(phenylthio)ethyl)pyrrolidin-2-one (**9ab**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



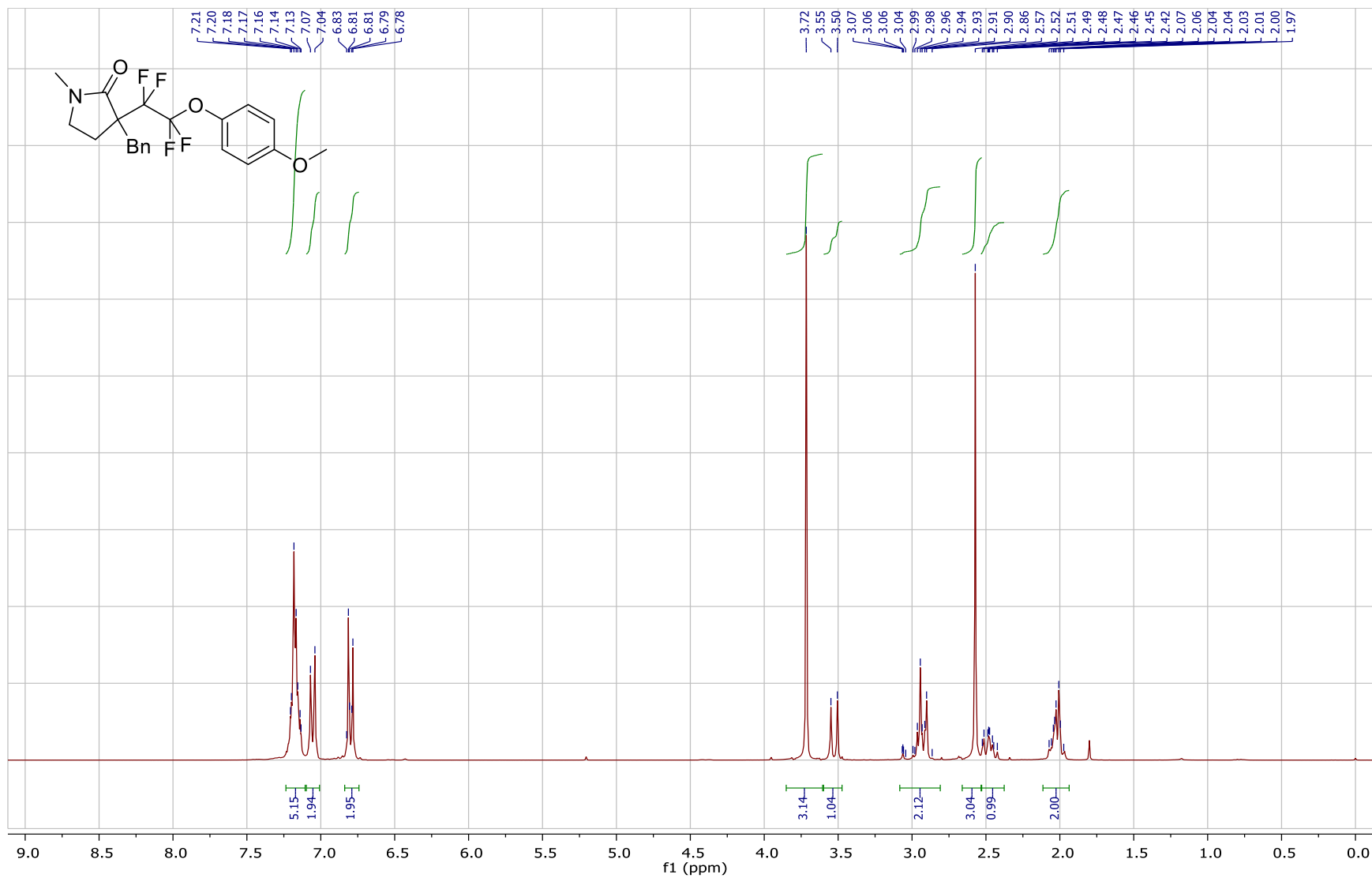


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

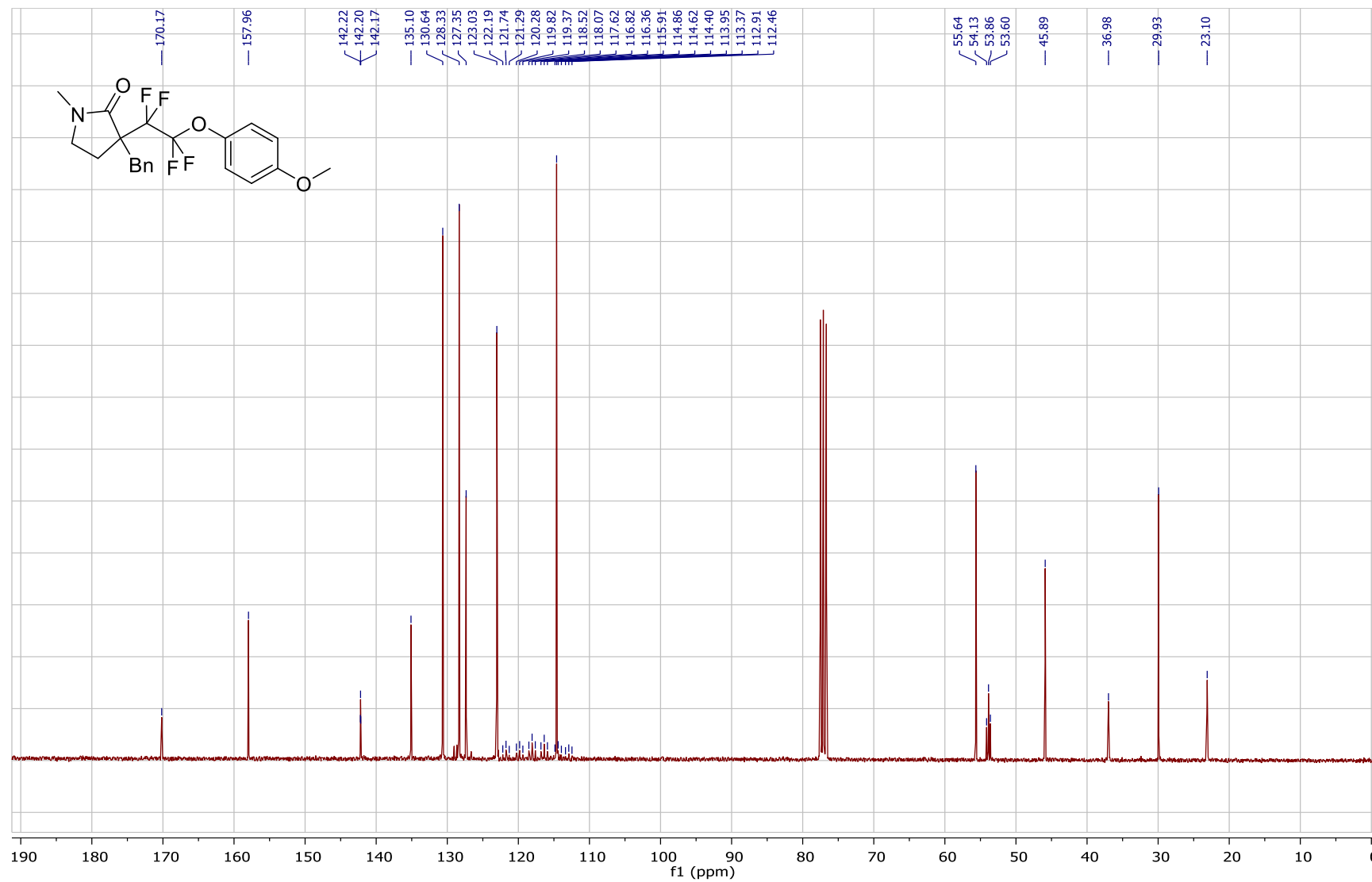


3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(4-methoxyphenoxy)ethyl)pyrrolidin-2-one (**9ac**)

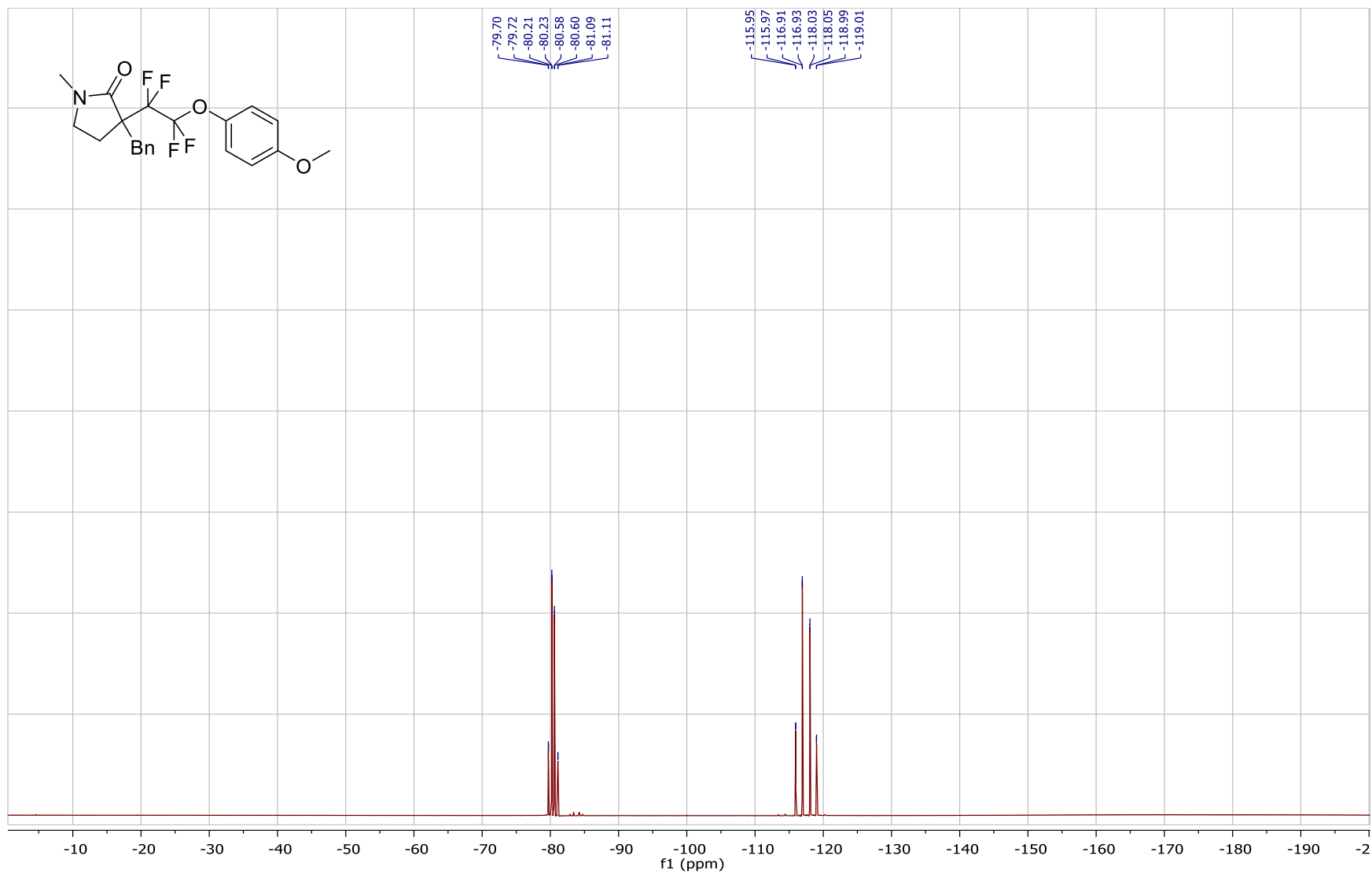
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

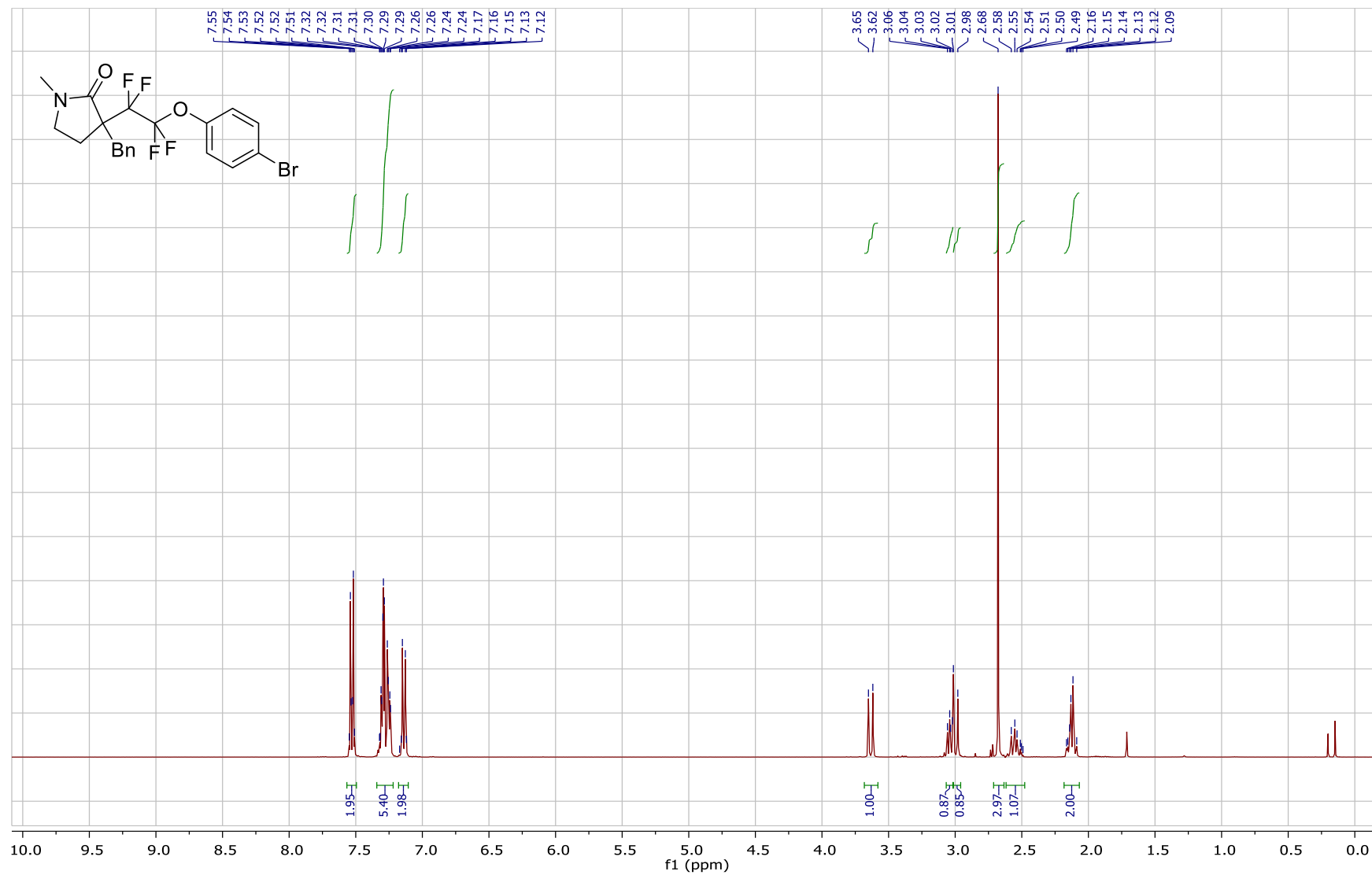


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



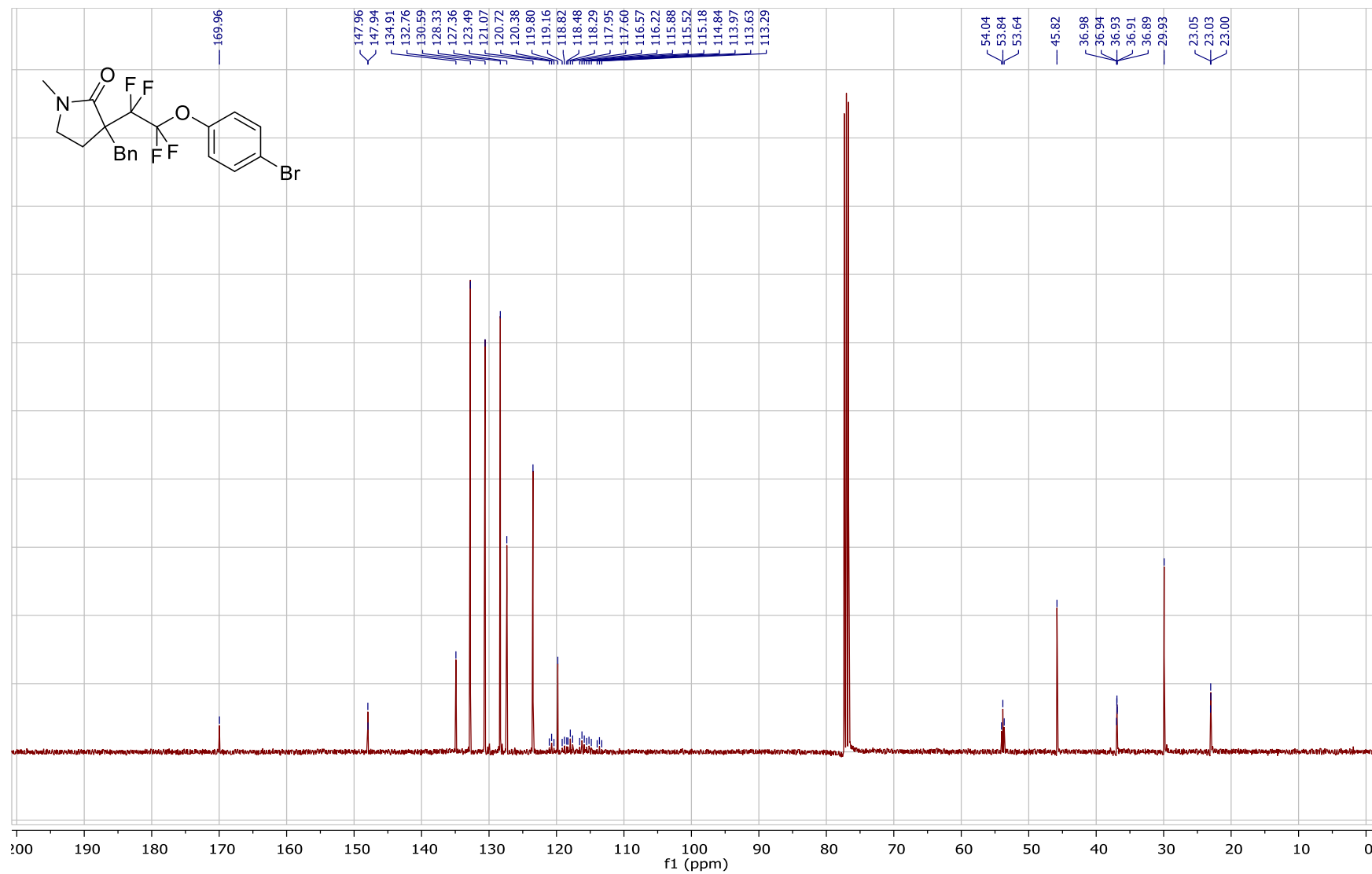
3-Benzyl-3-(2-(4-bromophenoxy)-1,1,2,2-tetrafluoroethyl)-1-methylpyrrolidin-2-one (**9ad**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

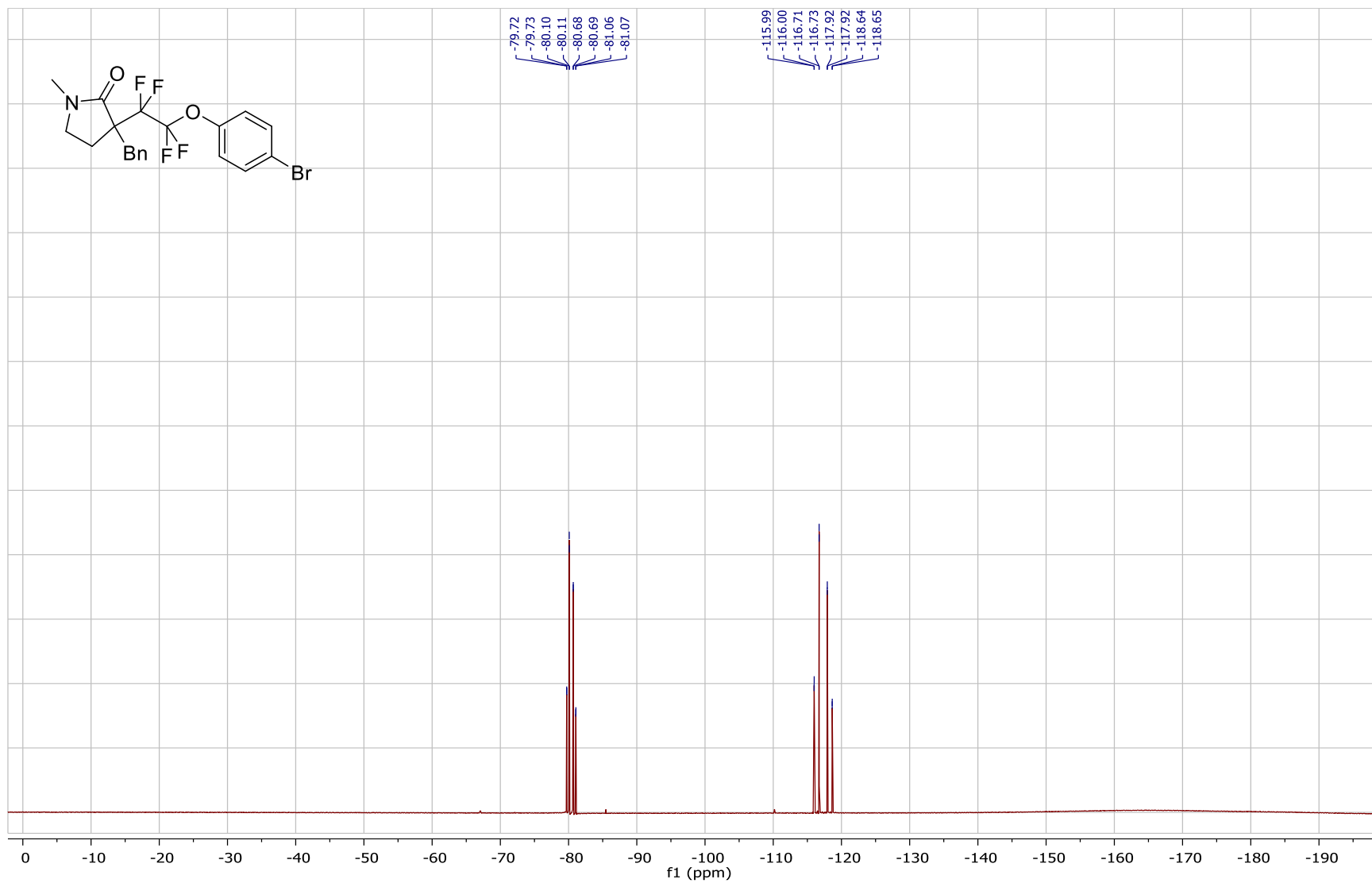




$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

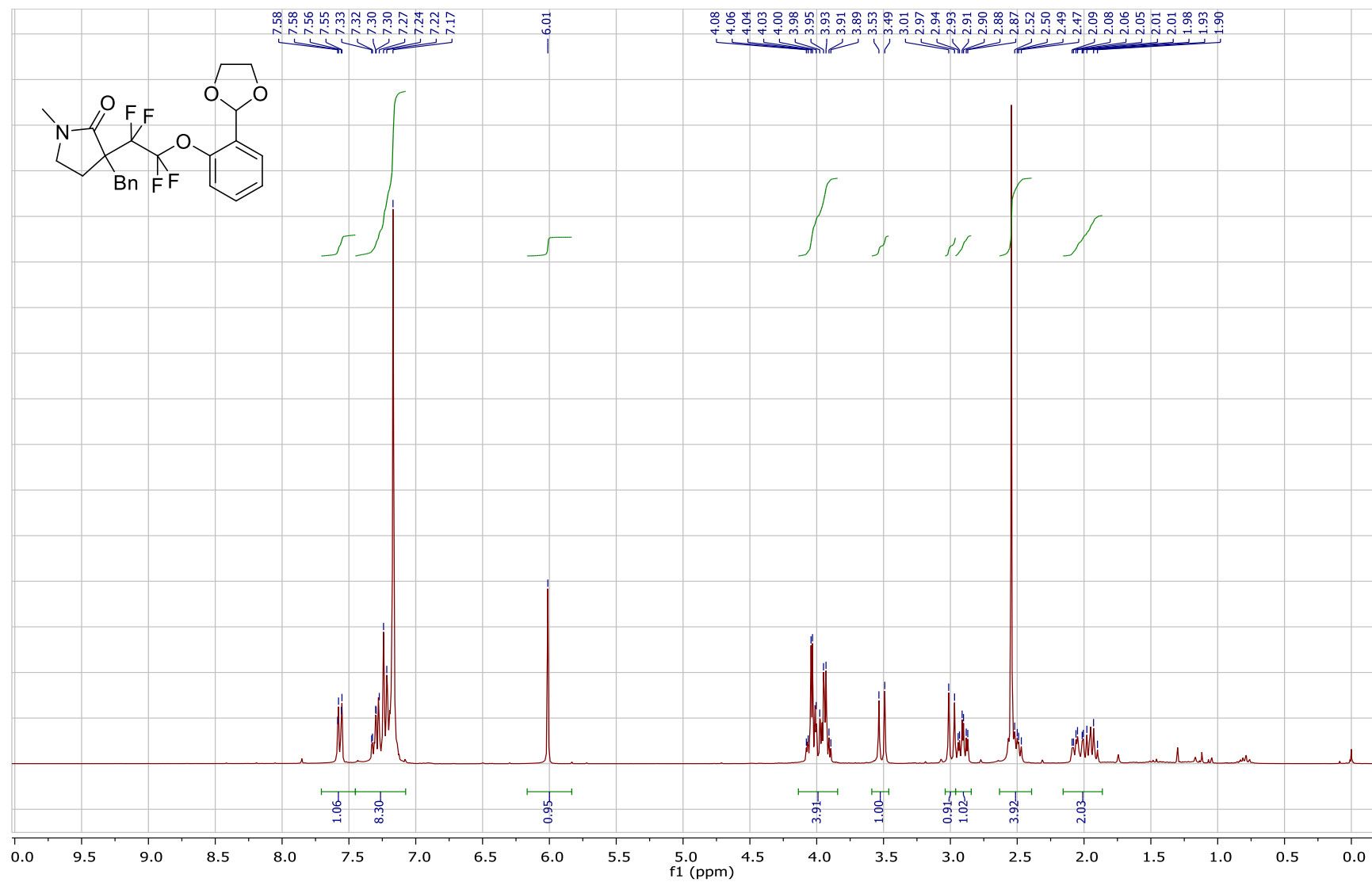


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

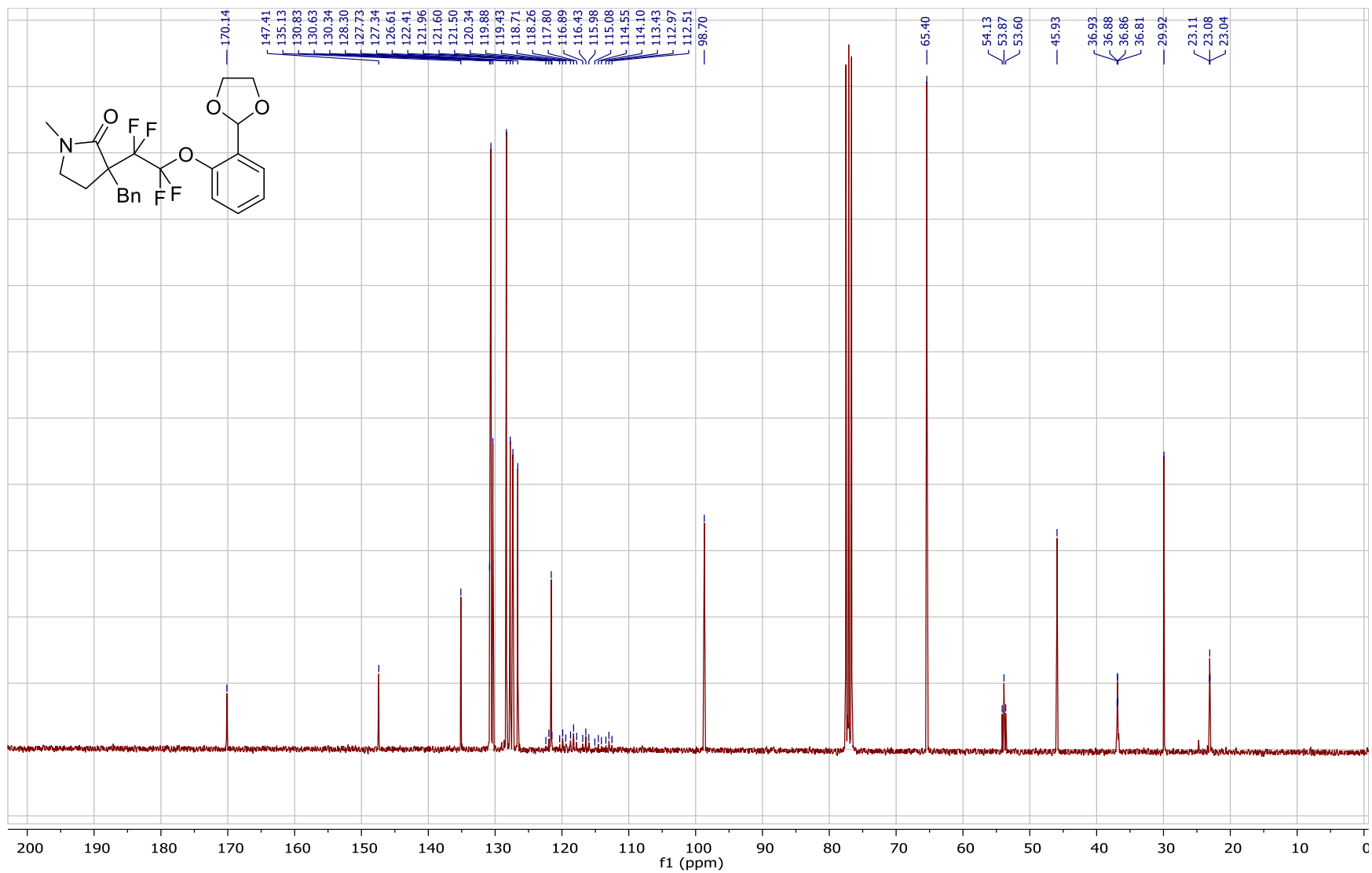


3-(2-(2-(1,3-Dioxolan-2-yl)phenoxy)-1,1,2,2-tetrafluoroethyl)-3-benzyl-1-methylpyrrolidin-2-one (**9ae**)

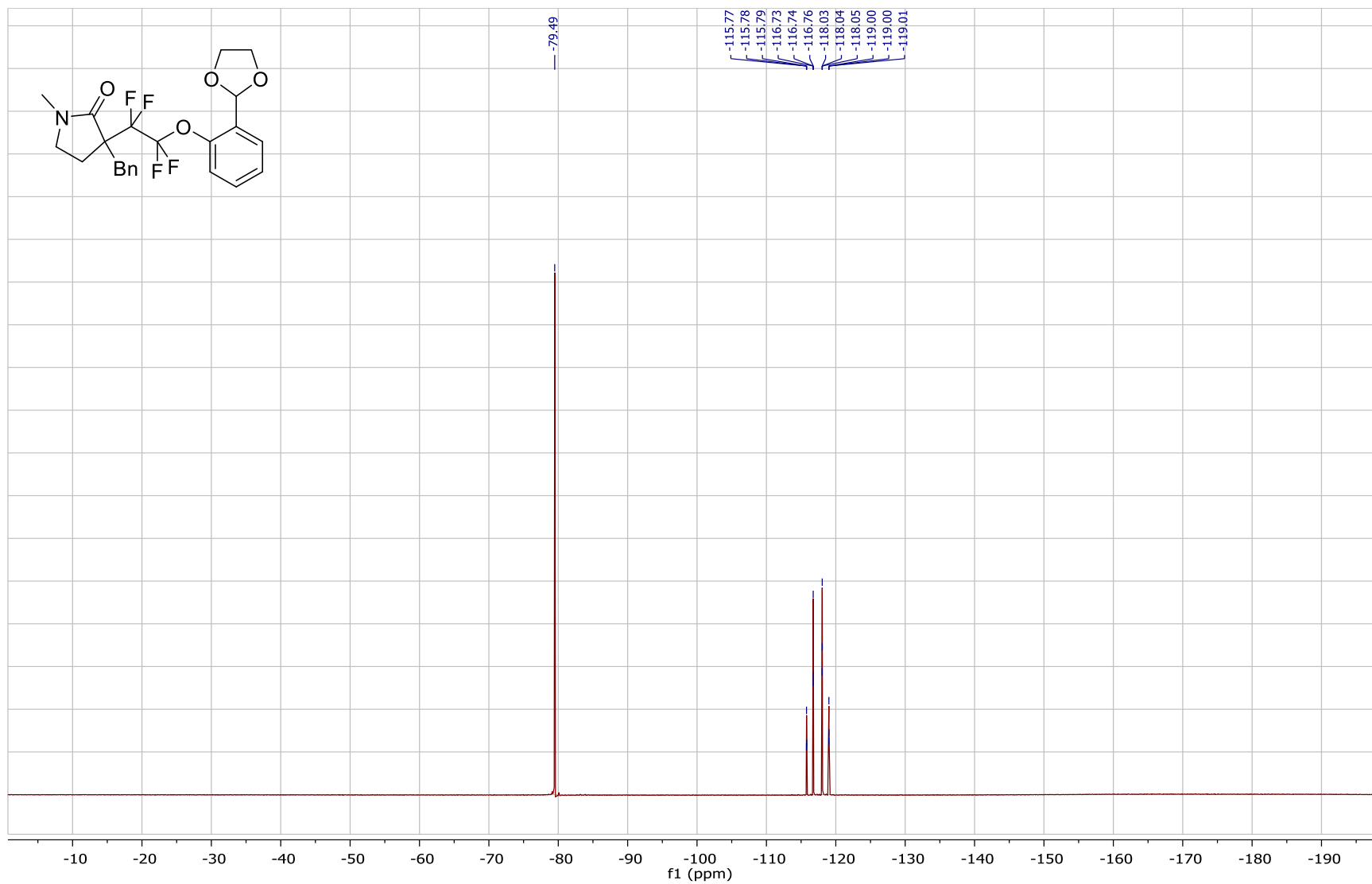
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

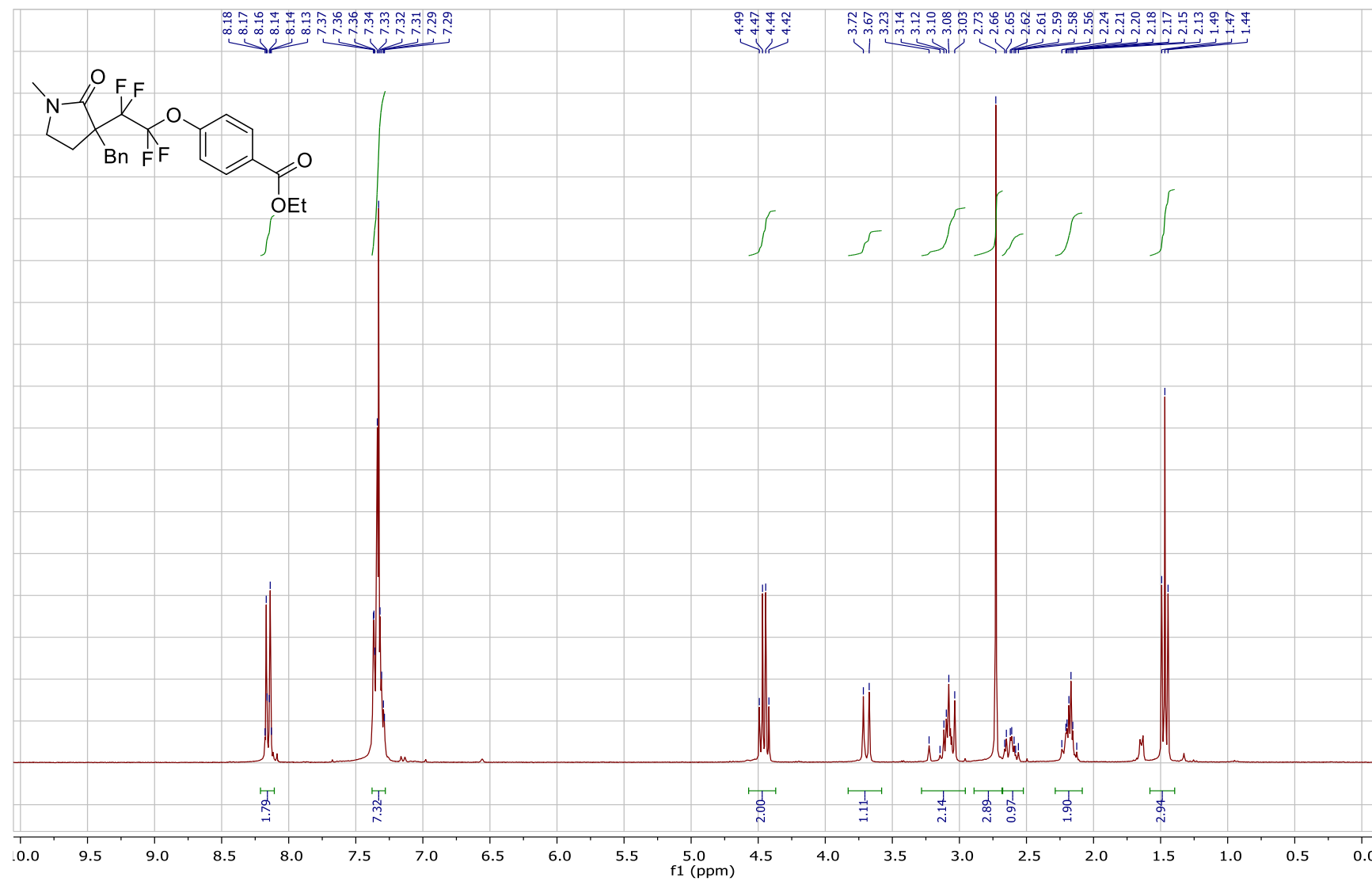


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

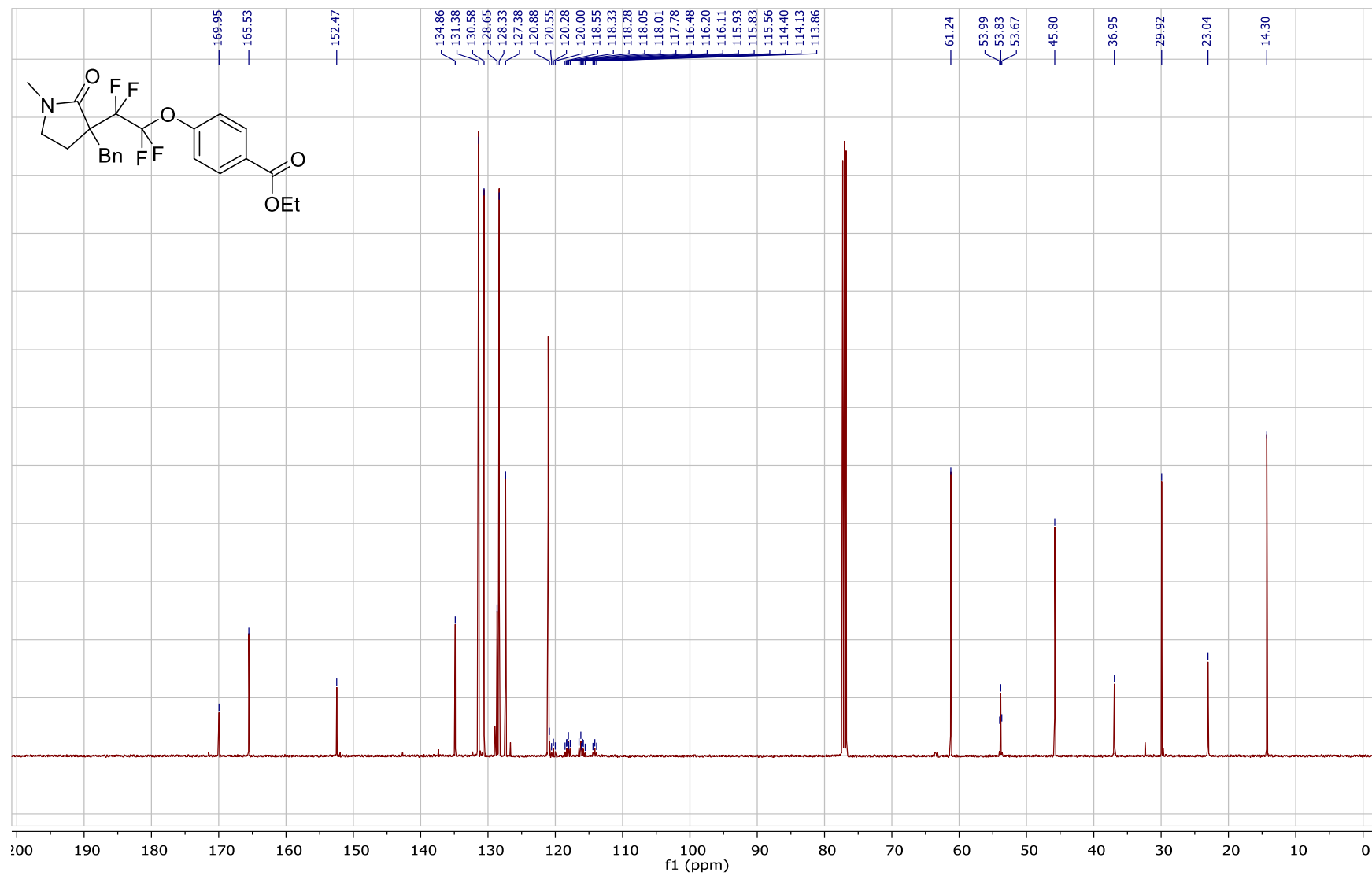


Ethyl 4-(2-(3-benzyl-1-methyl-2-oxopyrrolidin-3-yl)-1,1,2,2-tetrafluoroethoxy)benzoate (**9af**).

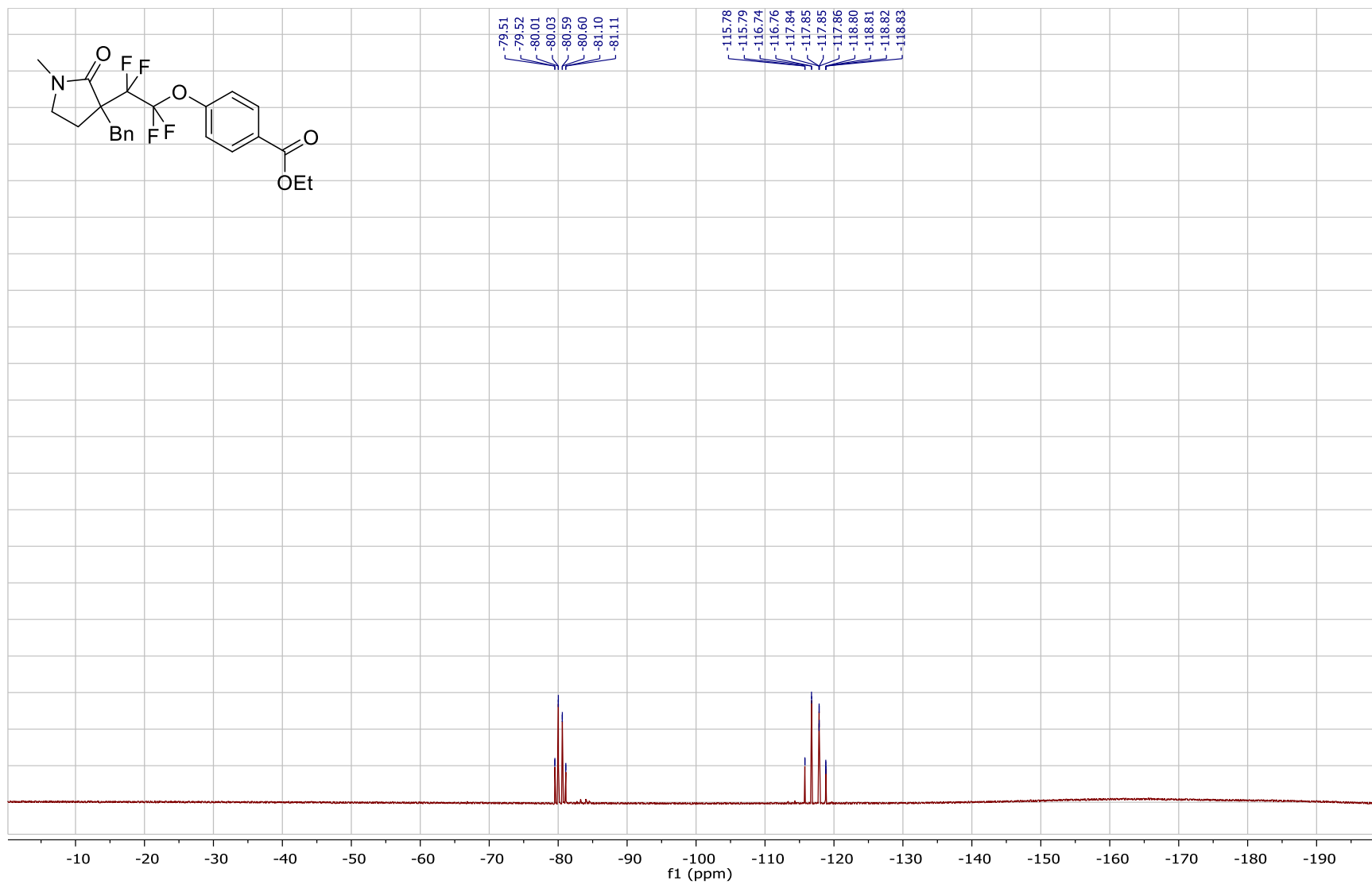
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



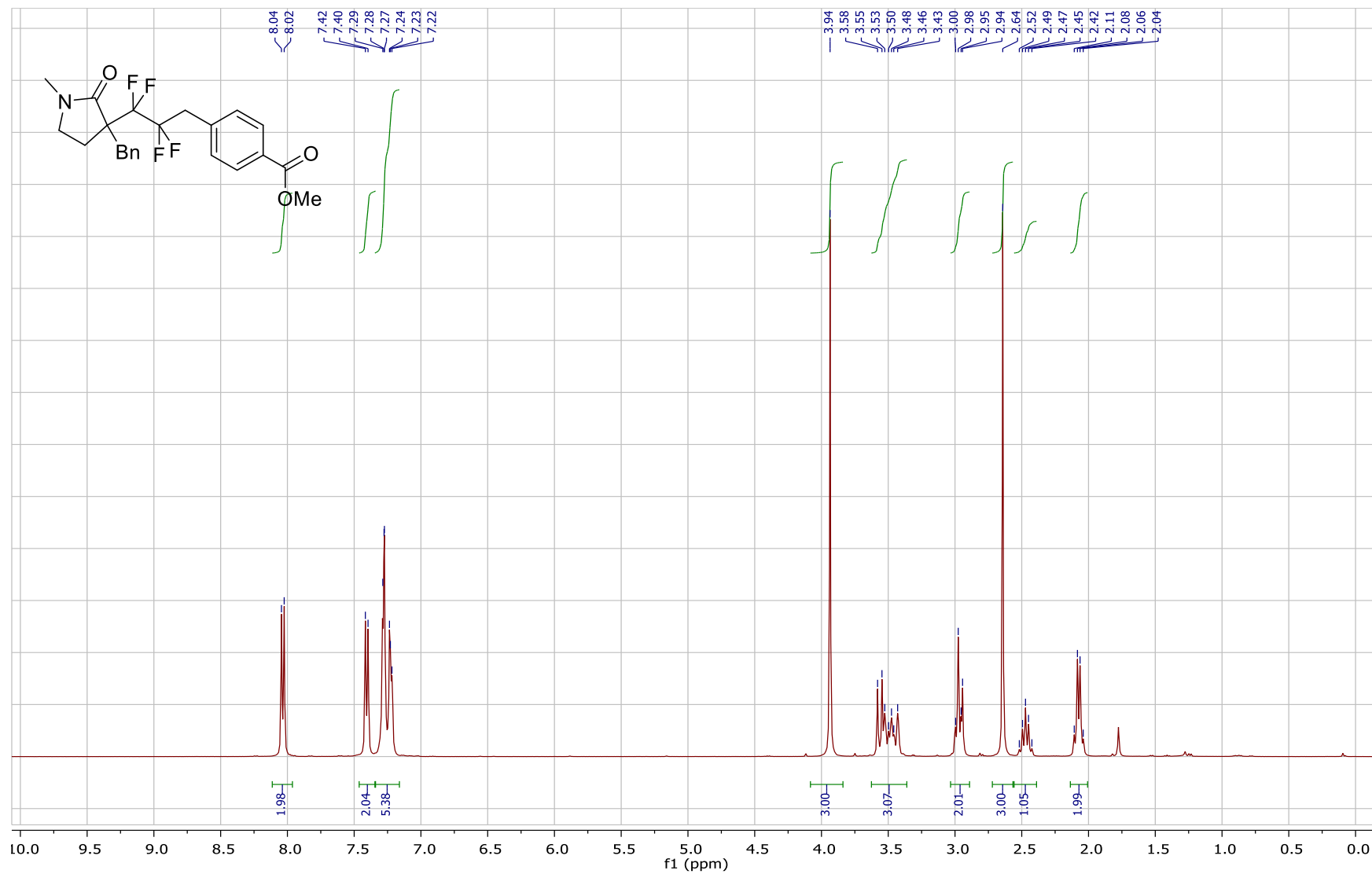
$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



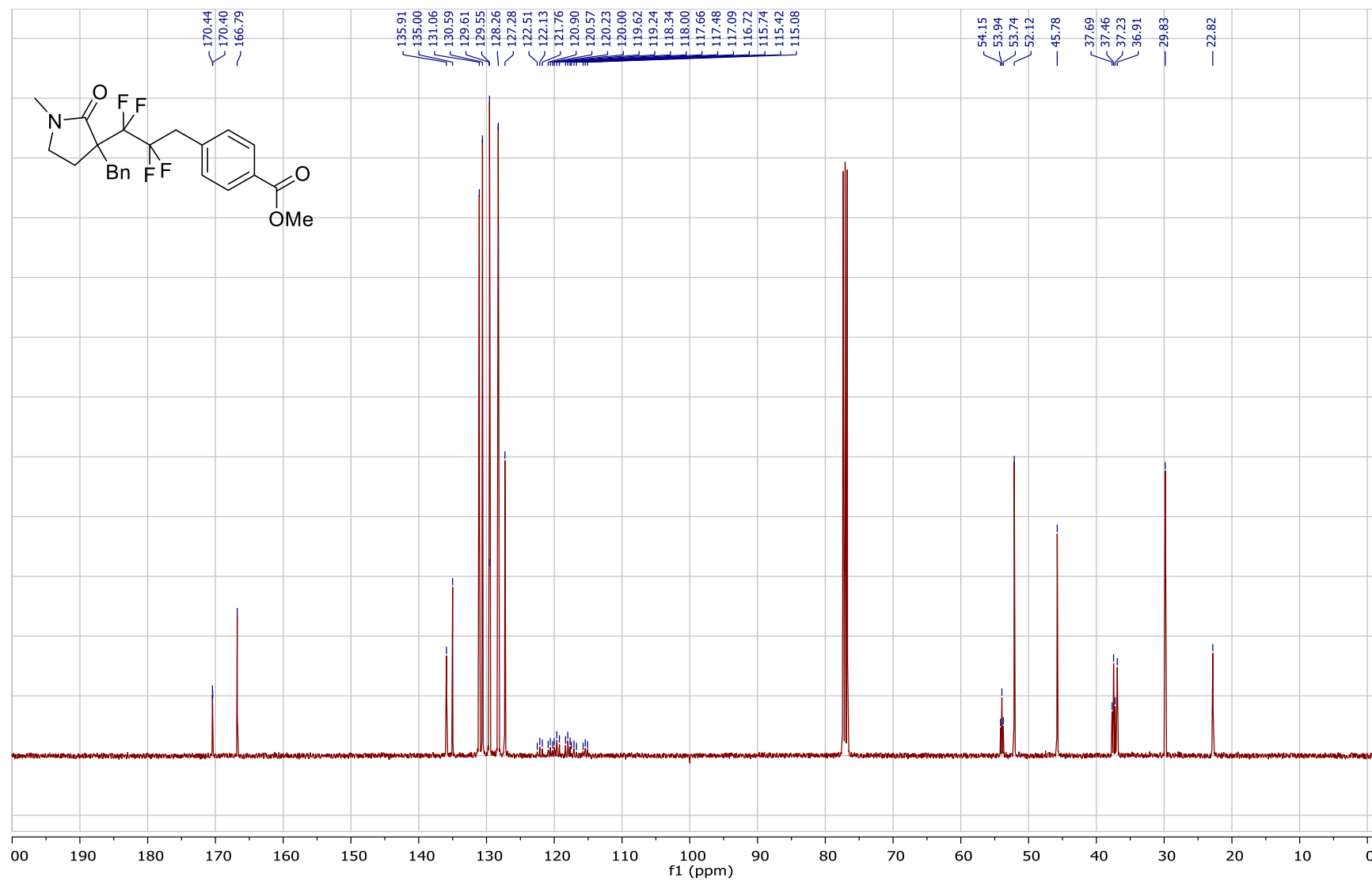


Methyl 4-(3-(3-benzyl-1-methyl-2-oxopyrrolidin-3-yl)-2,2,3,3-tetrafluoropropyl)benzoate (**9ag**)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



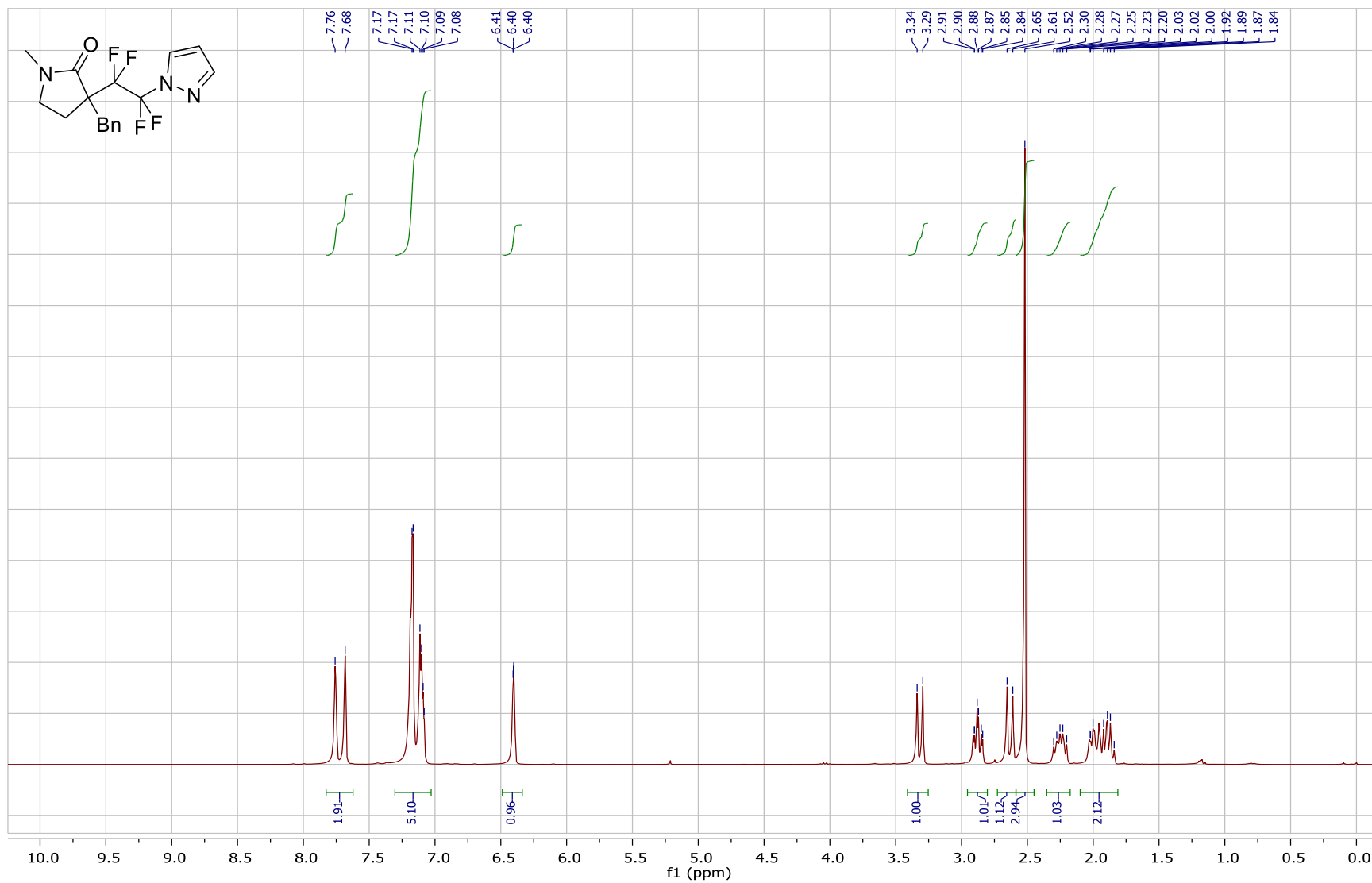
$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )



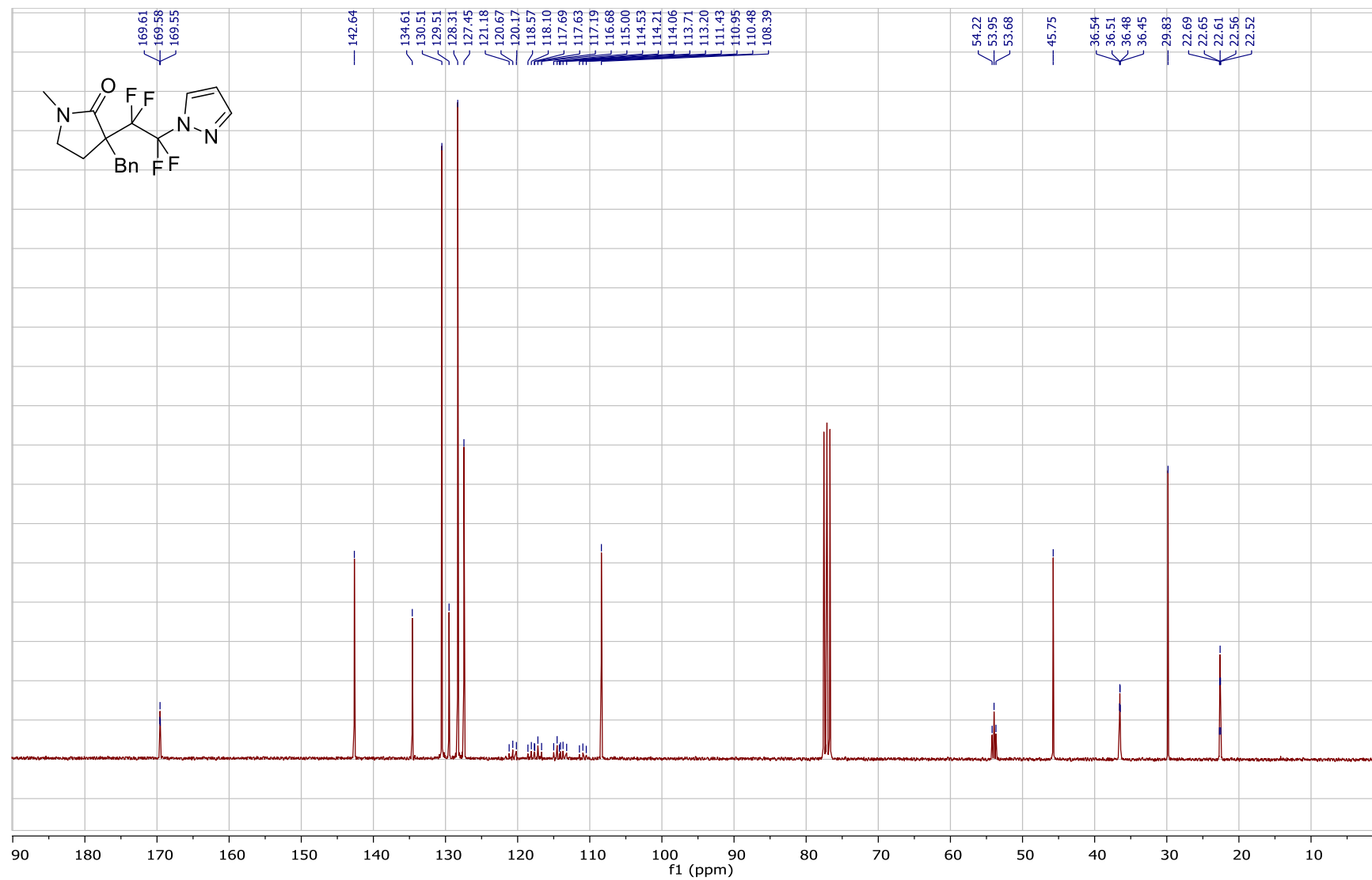


3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-(1H-pyrazol-1-yl)ethyl)pyrrolidin-2-one (**9ah**)

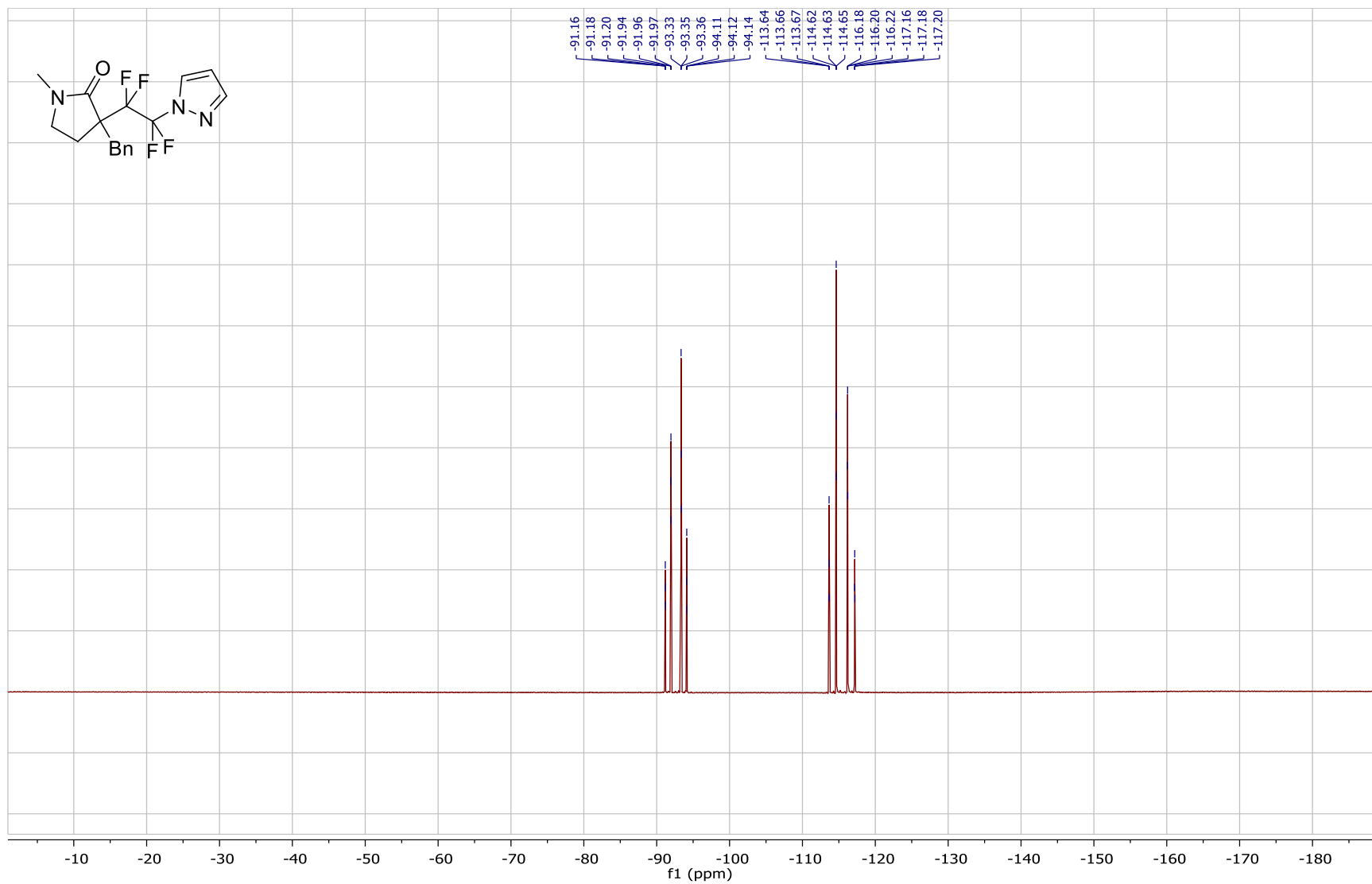
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )

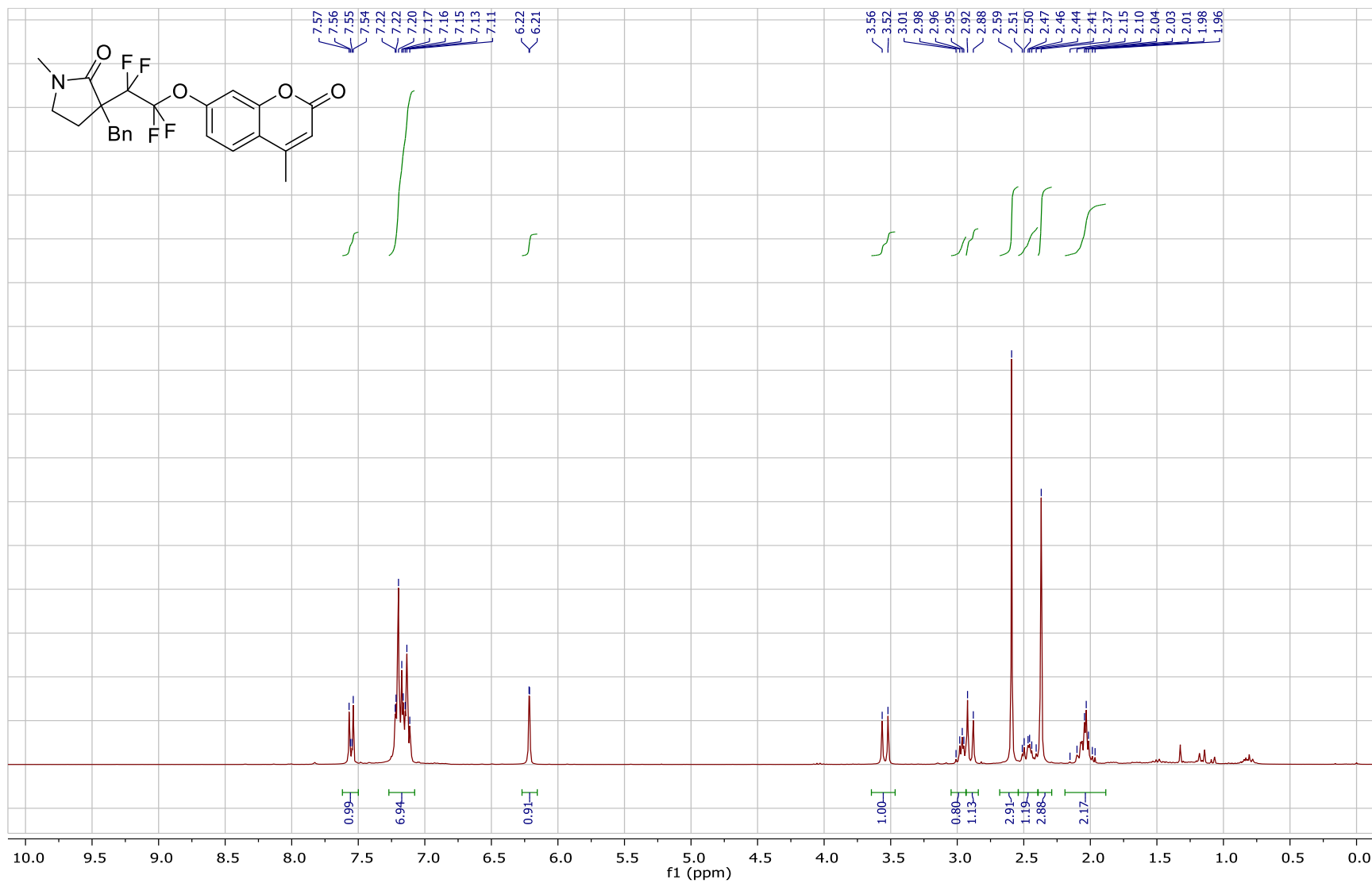


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

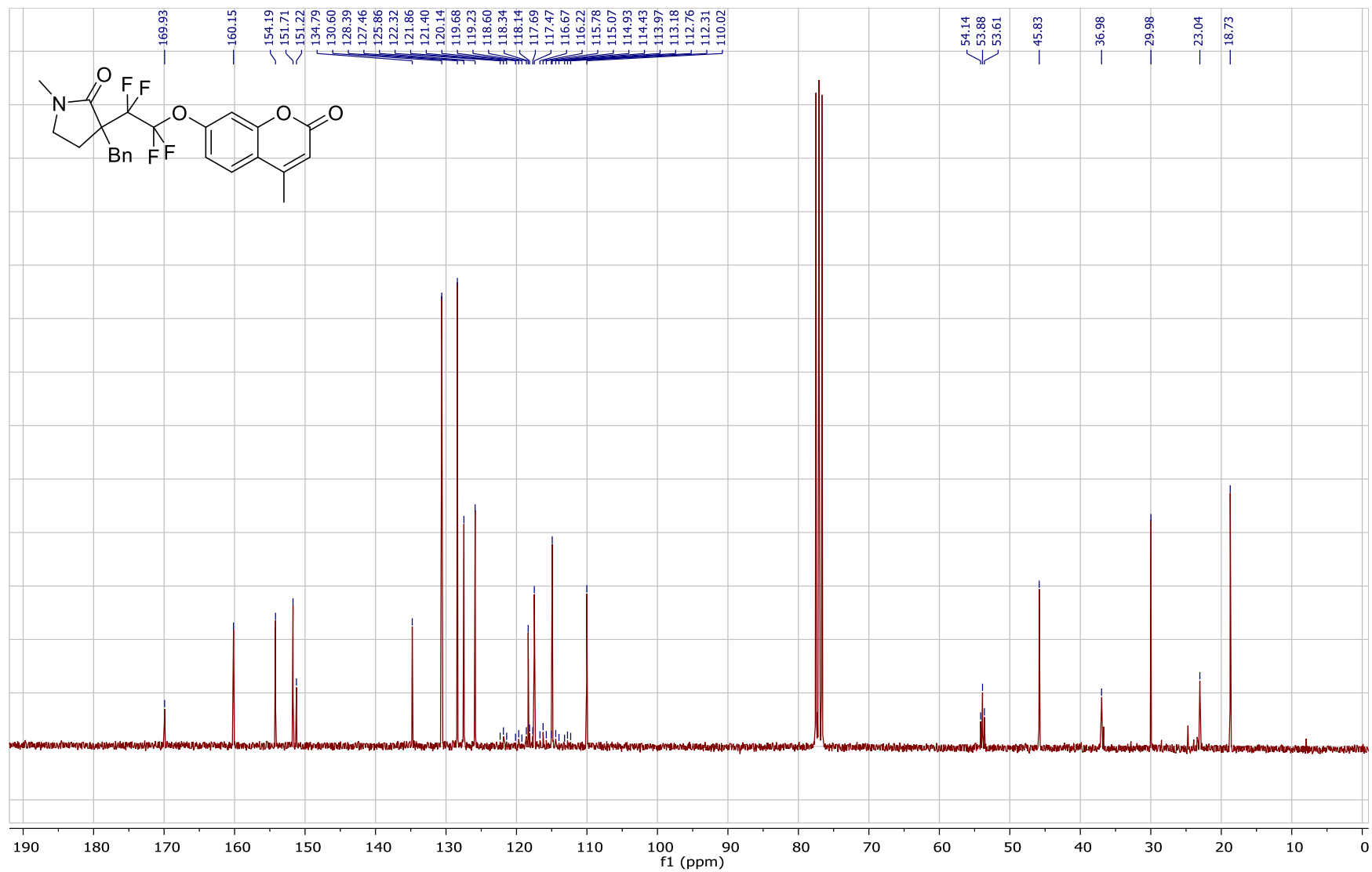


3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)pyrrolidin-2-one (**9ai**).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )

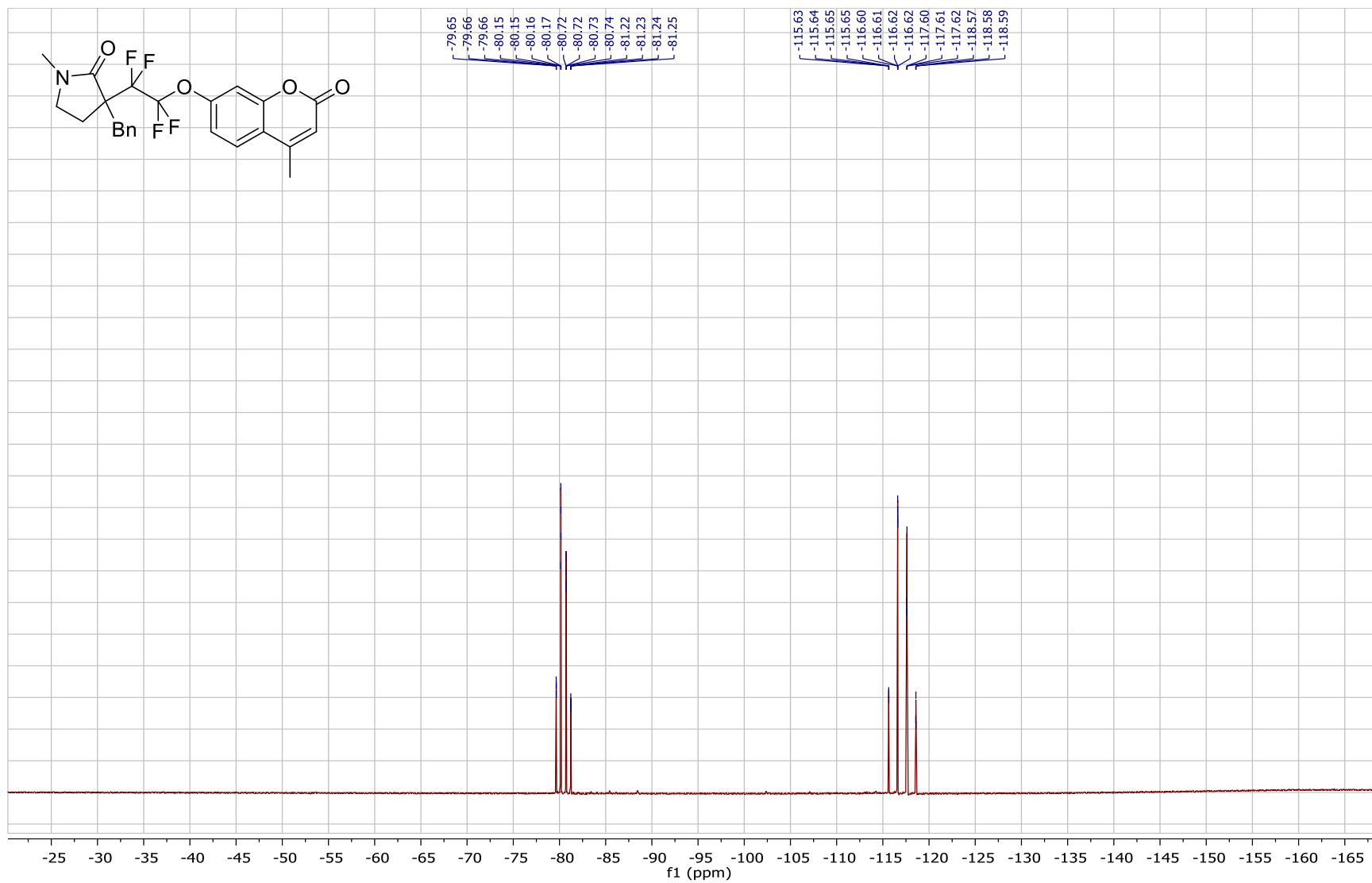


$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )



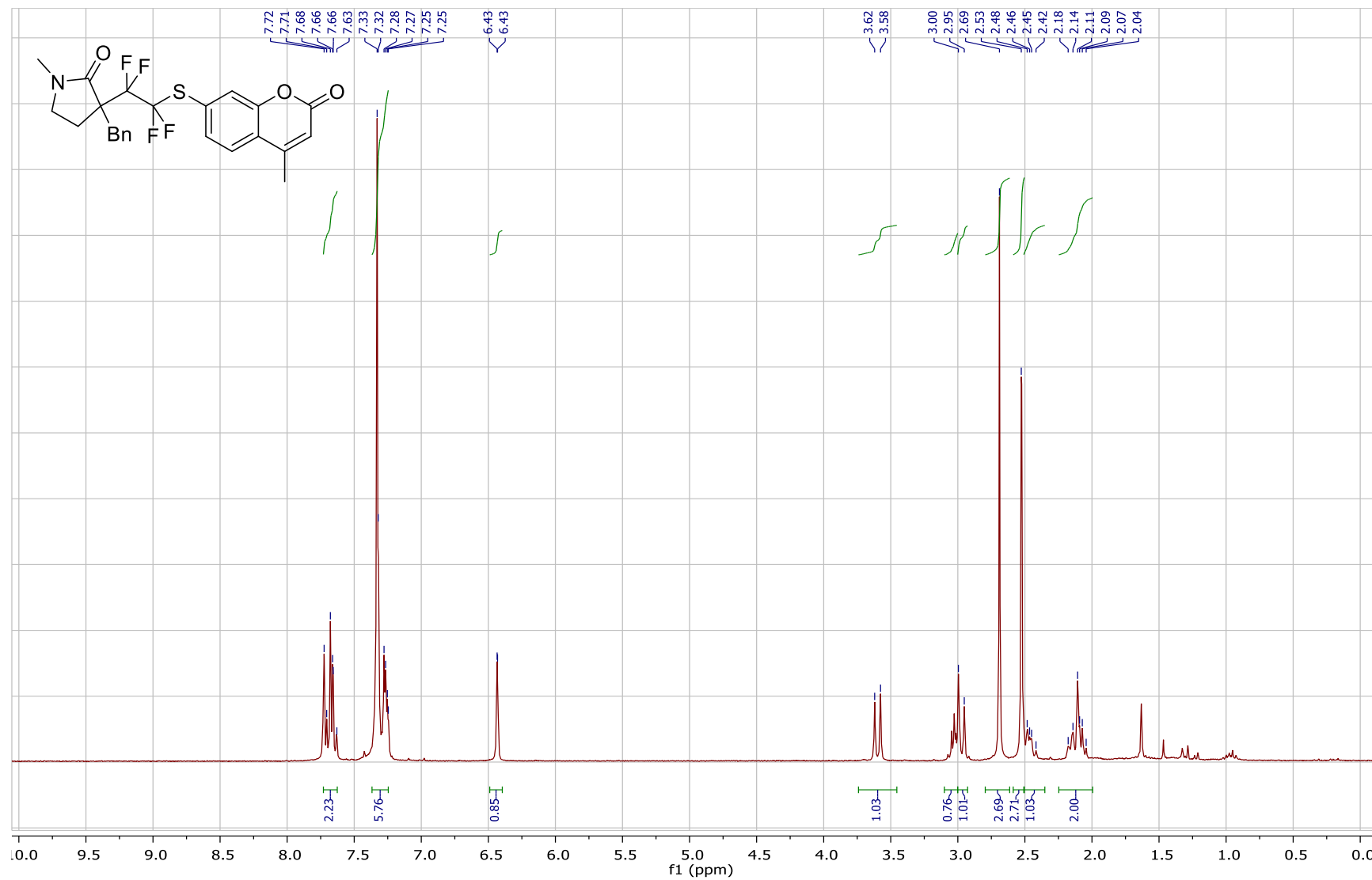


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

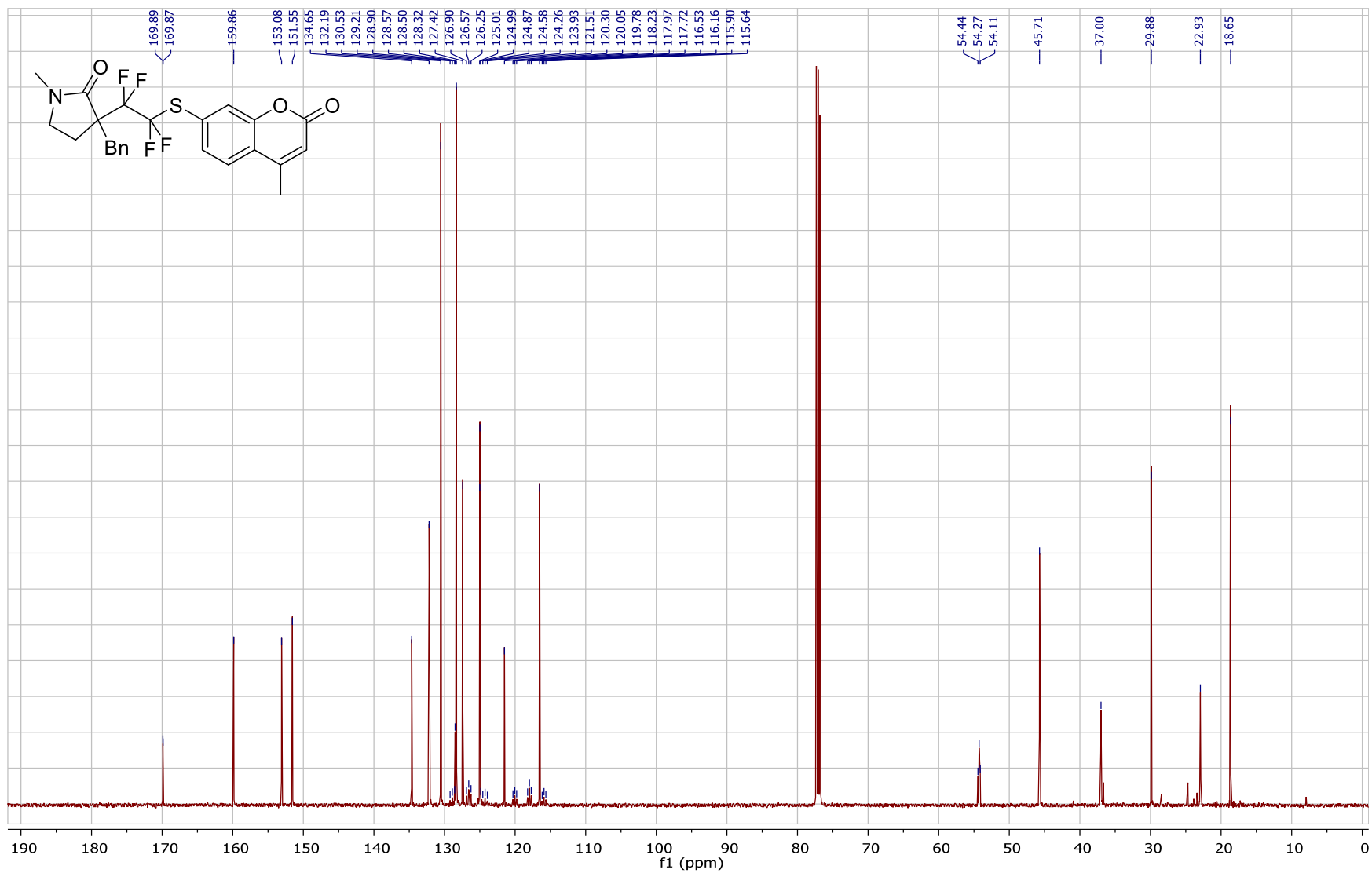


3-Benzyl-1-methyl-3-(1,1,2,2-tetrafluoro-2-((4-methyl-2-oxo-2H-chromen-7-yl)thio)ethyl)pyrrolidin-2-one (**9aj**)

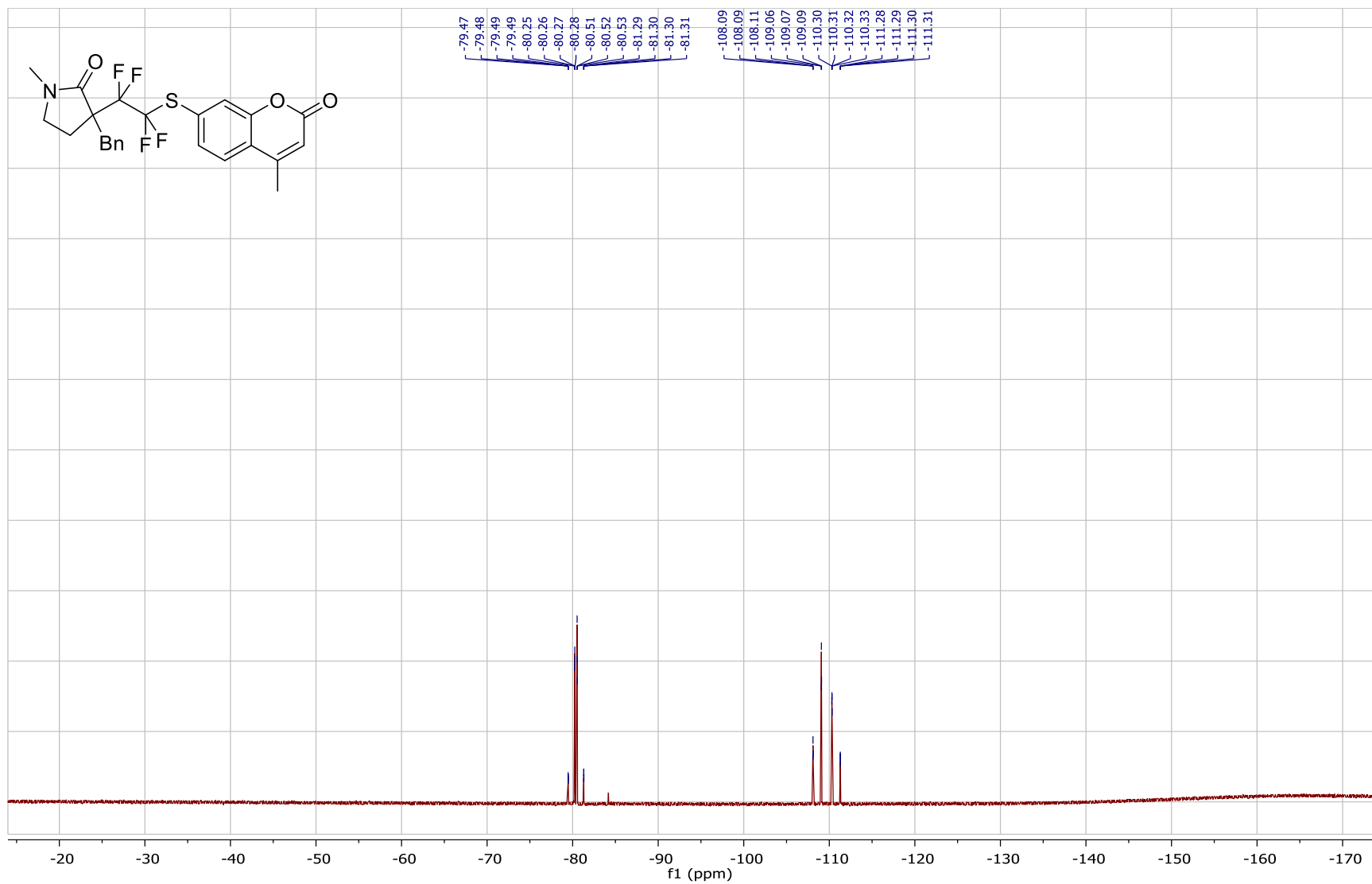
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )

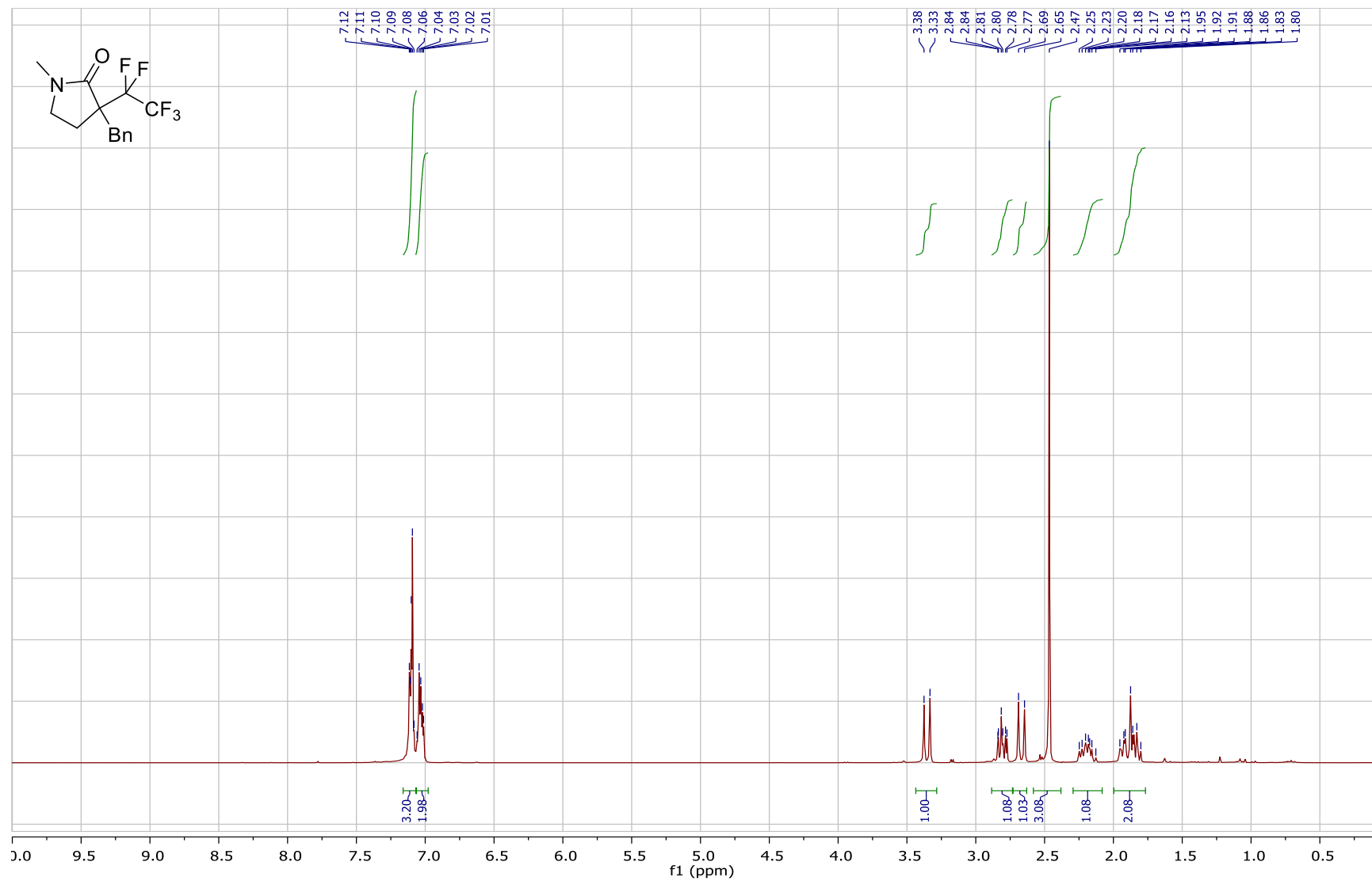


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )

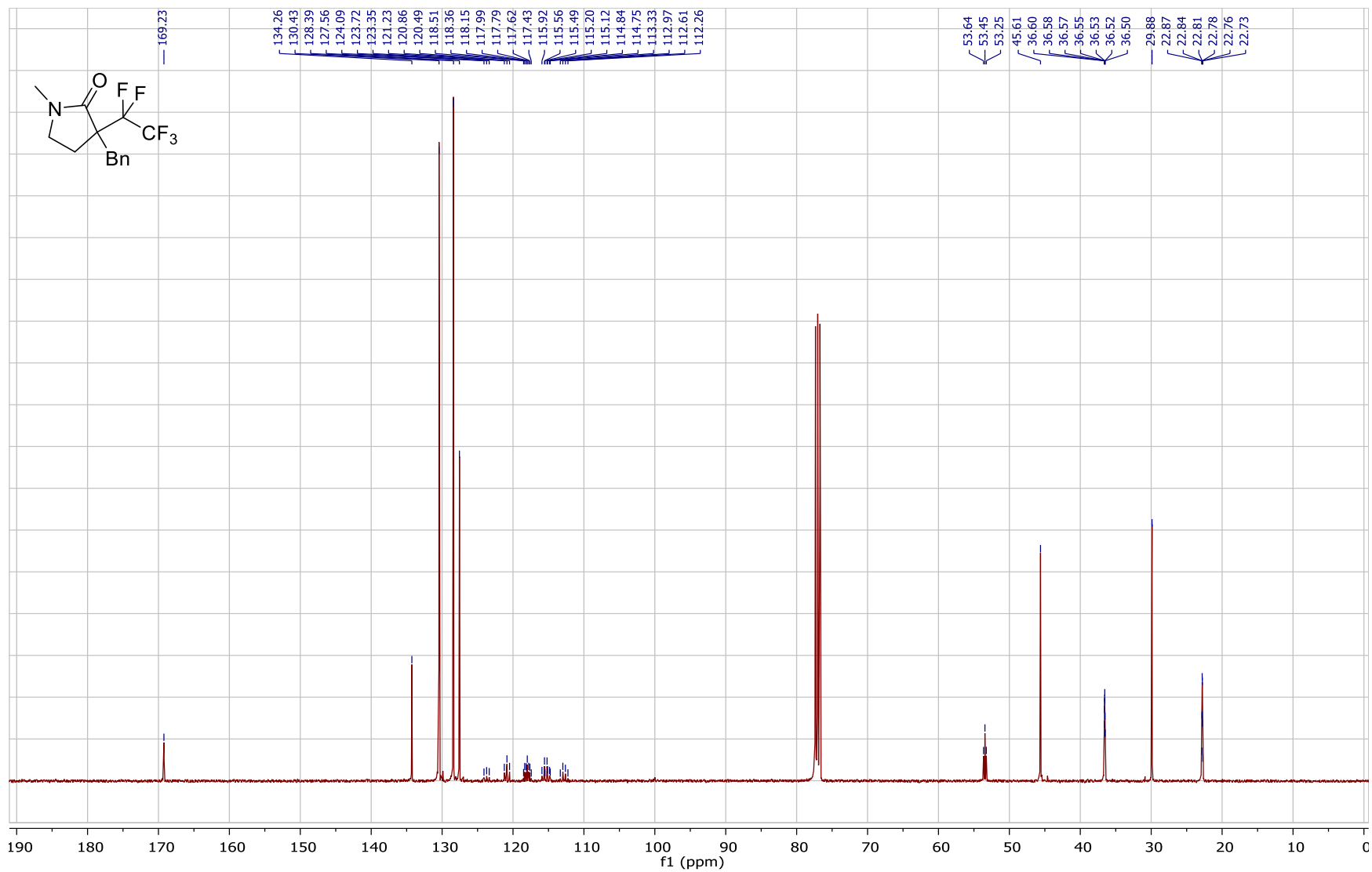


3-Benzyl-1-methyl-3-(perfluoroethyl)pyrrolidin-2-one (**9ak**)

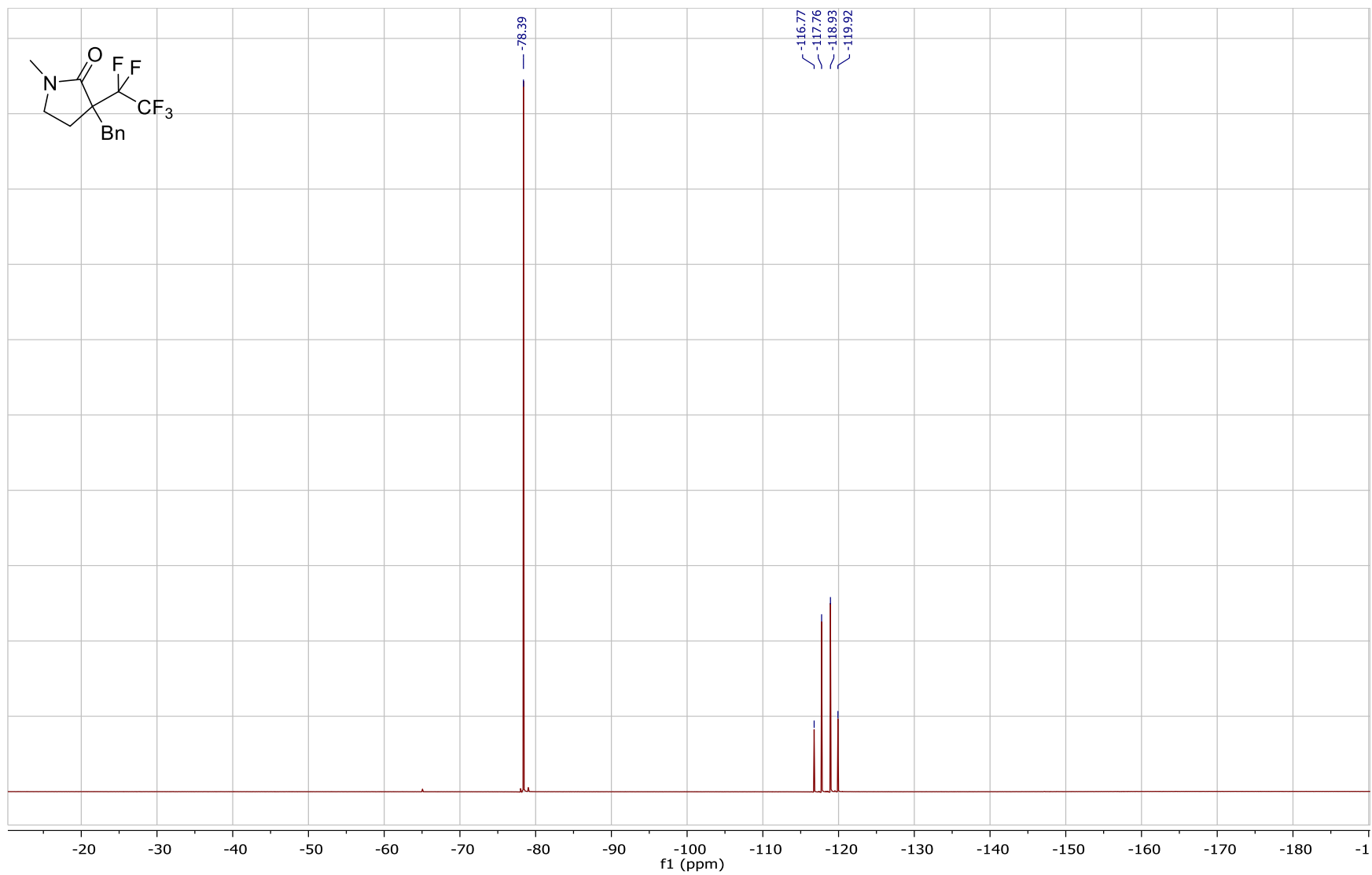
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

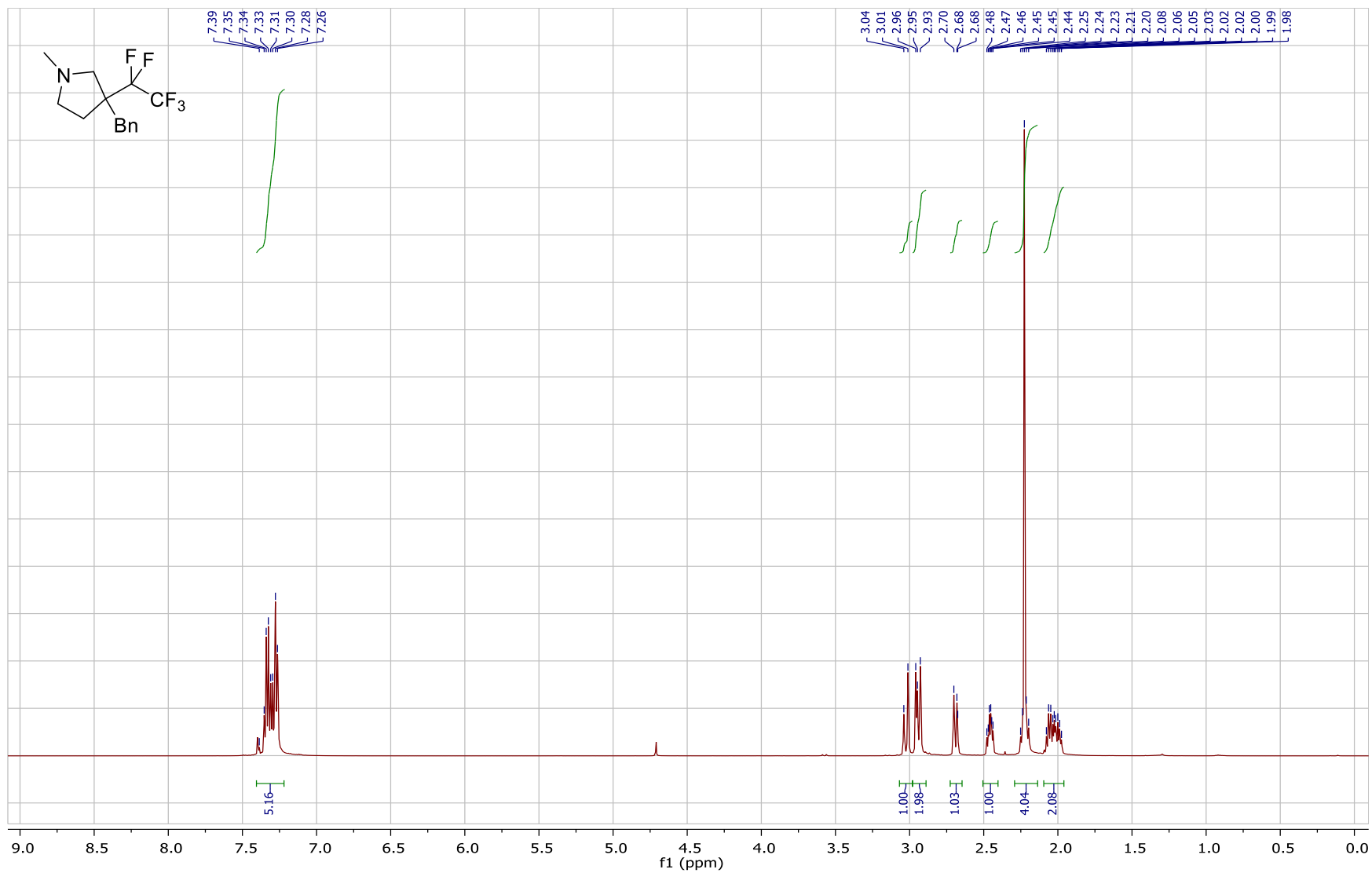


$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )



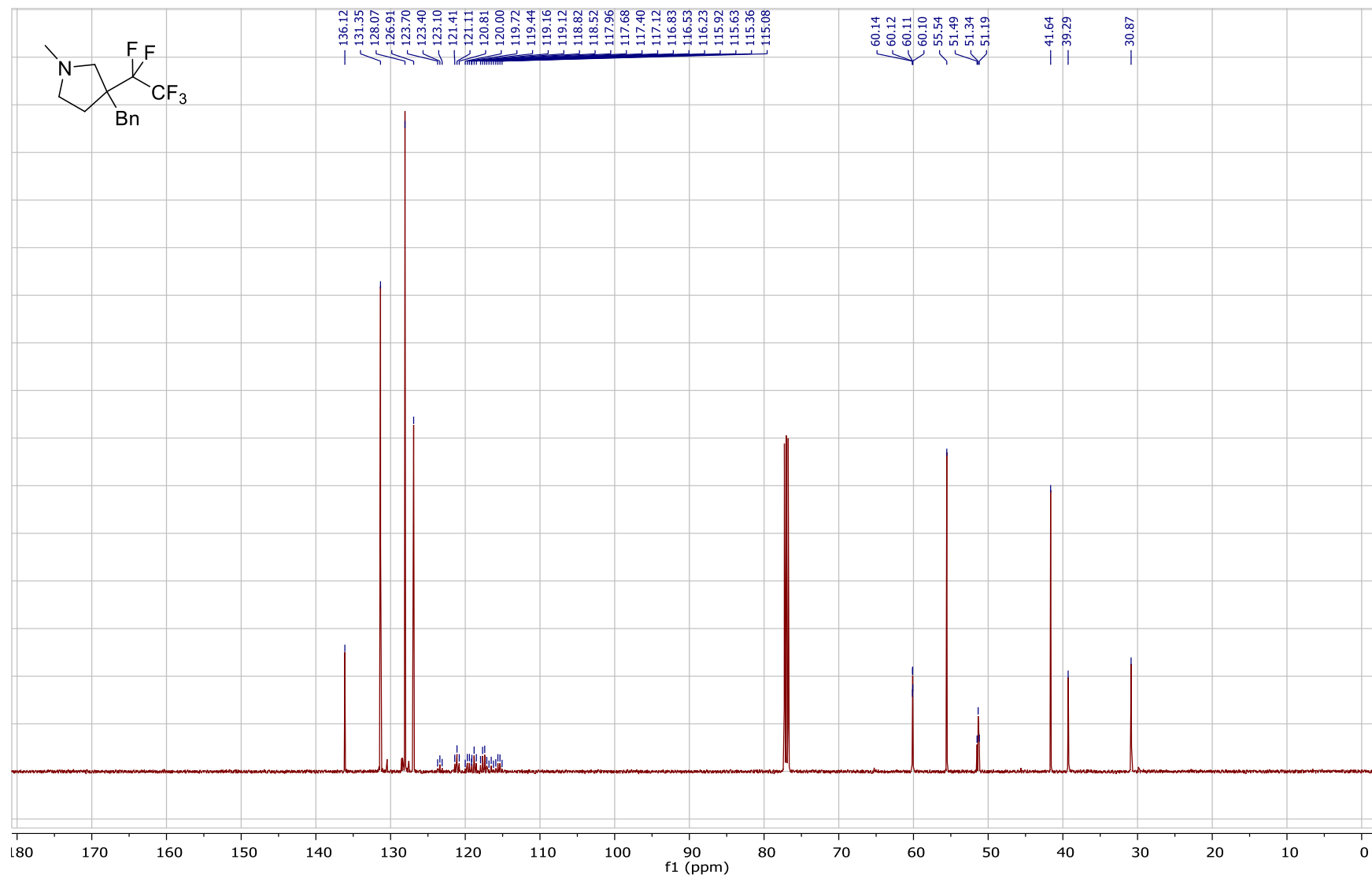
3-Benzyl-1-methyl-3-(perfluoroethyl)pyrrolidine (**10**)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )





$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )



$^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )

