Rhodium catalyzed Synthesis of Difluoromethyl Cyclopropanes

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Supporting information

General: Unless otherwise noted, all commercially available compounds were used as provided without further purification. Chemicals used in this manuscript were purchased from Sigma Aldrich, Fluorochem, ABCR, Apollo Scientific, Alfa Aesar.

Solvents used in reactions were p.A. grade, and were dried and degassed prior to use. Solvents for chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on Macherey-Nagel silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.063 – 0.2 mm). Solvent mixtures are understood as volume/volume.

^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR were recorded on a Varian AV400 or AV600 spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated br (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet)); coupling constants (J) are in Hertz (Hz).

HRMS data were recorded on a Finnigan MAT 95 using EI ionization at 70 eV.

IR spectra were recorded on a Perkin Elmer-100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}).

The following equipment was utilized for the continuous-flow generation of difluoromethyl diazomethane:

Syringe pump: Harvard Apparatus 22 syringe pump, Chemyx Inc. Model Fusion 710.

Micromixer: Little Things Factory, MR Lab, Type: MST

PTFE tubing: CS Chromatographie PTFE tubing, Art Nr. 590515, 1/16” AD, 0.8mm ID, max pressure 37 bar.

Back pressure regulator: IDEX back pressure assembly, 40 psi, article nr. P-785

Diazomethane glass equipment used: obtained from Sigma Aldrich, catalogue nr. Z411736

Safety Note:

Safety hazards of difluoromethyl diazomethane, described within this manuscript, has not been investigated. However, it should be noted that handling of diazomethane and its derivatives should only be done in a well-ventilated fume cupboard using an additional blast shield. No incidents occurred handling difluoromethyl diazomethane during the preparation of this manuscript, yet the reader should be aware of carcinogenicity and potential explosiveness of the herein described diazomethane derivatives. General safety precautions when working with diazomethane and its derivatives should be followed. Any reactions described in this manuscript should not be performed without strict risk assessment and proper safety precautions.

General procedure for the continuous-flow preparation of difluoromethyl diazomethane and subsequent cyclopropanation reaction

Two stock solutions are prepared:

- 2,2-Difluoroethylamine (c = 0.2 M) is dissolved in anhydrous, degassed $CHCl_3$
- tBuONO (c = 0.24 M) and AcOH (0.08 M) are dissolved in anhydrous, degassed $CHCl_3$

The stock solutions are transferred into two syringes and placed in a syringe pump and the syringes are connected via PTFE tubing to the micromixer with an internal volume of 0.2 mL. At a constant flow rate of 50 µL/min the reactants are transferred into the microreactor. The outlet is added to a solution of styrene (0.4 mmol) and catalyst dissolved in 4 mL $CHCl_3$ under Ar.

After complete addition the resulting solution is stirred for 10 h at room temperature. The crude reaction mixture is filtered over silica with a pentane / Et_2O (10:1) mixture. The filtrate is concentrated in vacuo and purified by column chromatography using pentane (100%) to pentane/Et_2O (20:1) as eluent.

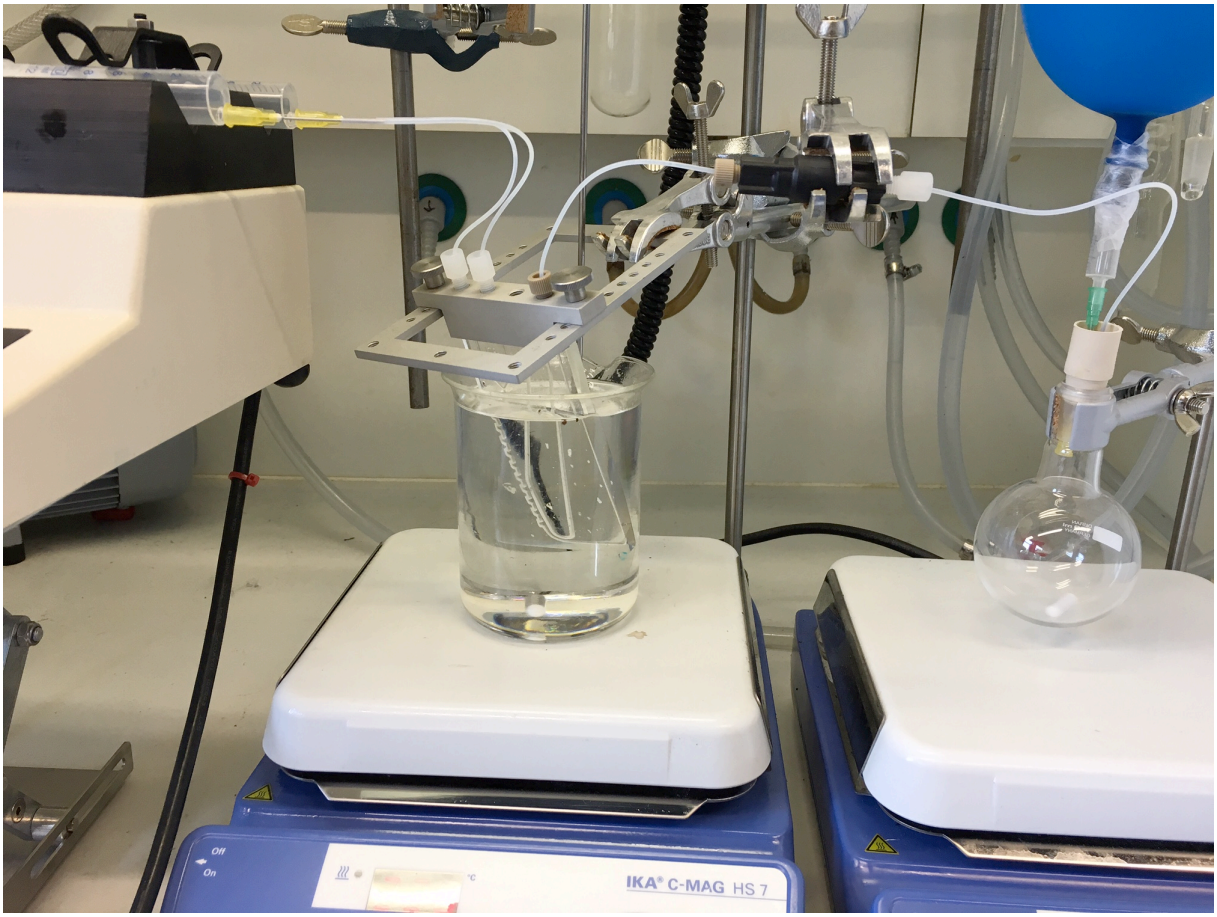
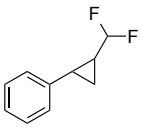


Figure 1: setup of the continuous-flow system (on the left: syringe pump with 2x 10 mL syringes; in the middle: micromixer (Little things factory, MR-Lab type MST) and back pressure vent (in black); on the right: reaction flask for the cyclopropanation reaction)

Physical data

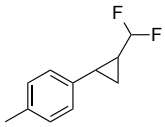
(2-(difluoromethyl)cyclopropyl)benzene



observerd isomer ratio: 1:1.5

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.34 – 7.09 (m, 5H), 5.76 (td, *J* = 57.5, 4.1 Hz, 0.6H) AND 4.93 (ddd, *J* = 56.0, 54.7, 7.7 Hz, 0.4H), 2.51 – 2.40 AND 2.24 – 2.14 (m, 1H), 1.76 – 1.56 (m, 1H), 1.29 – 1.03 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -108.14 (ddd, J = 283.0, 54.6, 8.8 Hz, 1F), -113.48 (dddd, J = 283.0, 56.1, 5.8, 3.8 Hz, 1F), -115.18 (ddd, J = 280.8, 57.5, 10.6 Hz, 1F), -116.01 (ddd, J = 280.8, 57.5, 10.9 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 140.17, 136.19, 128.99 (d, J = 79.4 Hz), 128.47, 128.45, 126.91, 126.34, 126.28, 118.08 (t, J = 235.4 Hz), 116.45 (t, J = 238.4 Hz), 23.92 (t, J = 26.7 Hz), 20.36 (dd, J = 30.9, 28.5 Hz), 18.76 (t, J = 4.6 Hz), 10.48 (t, J = 4.6 Hz), 6.12 (d, J = 7.8 Hz); IR (KBr): 2921, 2855, 2322, 2109, 1739, 1456, 1372, 1084, 1036, 803, 696; HRMS (EI): mass found: 168.07424, calculated mass for $C_{10}H_{10}F_2$: 168.07506.

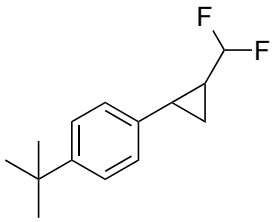
1-(2-(difluoromethyl)cyclopropyl)-4-methylbenzene



observerd isomer ratio: 1:1.2

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.17 (m, 1H), 7.10 (m, 2H), 7.01 (m, 1H), 5.74 (td, *J* = 57.5, 4.2 Hz, 0.5H) AND 4.92 (ddd, *J* = 56.2, 54.7, 7.7 Hz, 0.5H), 2.46 – 2.37 AND 2.19 – 2.13 (m, 1H), 2.32 (d, *J* = 4.3 Hz, 3H) 1.70 – 1.55 (m, 1H), 1.24 – 1.02 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -108.14 (ddt, J = 116.5, 70.7, 35.3 Hz, 1F), -113.58 (dddd, J = 83.2, 36.6, 19.2, 15.4 Hz, 1F), -114.90 (ddd, J = 280.5, 57.6, 10.5 Hz, 1F), -115.98 (ddd, J = 280.6, 57.5, 10.9 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 137.09, 136.52, 135.95, 133.08, 129.14, 129.10, 126.22, 118.21 (t, J = 235.1 Hz), 116.58 (t, J = 238.3 Hz), 23.77 (t, J = 26.7 Hz), 21.02, 20.96, 20.26 (dd, J = 30.9, 28.4 Hz), 19.50 (d, J = 8.7 Hz), 18.62 – 18.07 (m), 10.29 (t, J = 4.5 Hz), 6.12 (d, J = 7.8 Hz); IR (KBr): 3443 ,2925, 2859, 2316, 2107, 1739, 1431, 1368, 1218, 1031, 808; HRMS (EI): mass found: 182.09070, calculated mass for $C_{11}H_{12}F_2$: 182.09071.

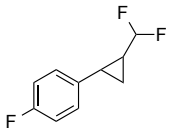
1-(2-(difluoromethyl)cyclopropyl)-4-*tert*-butylbenzene



observerd isomer ratio: 1:1.2

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.31 (dd, *J* = 8.3, 1.9 Hz, 2H), 7.22 – 7.02 (m, 2H), 5.73 (td, *J* = 57.5, 4.1 Hz, 0.6H), 4.94 (ddd, *J* = 56.0, 54.5, 7.7 Hz, 0.4H), 2.50 – 2.09 (m, 1H), 1.70 – 1.57 (m, 1H), 1.41 – 1.04 (m, 11H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 149.81, 149.31, 137.14, 133.08, 128.92, 125.94, 125.37 (d, *J* = 5.0 Hz), 118.20 (d, *J* = 14.7 Hz), 116.57, 114.99, 31.33, 23.81 (t, *J* = 26.7 Hz), 20.27 (dd, *J* = 30.9, 28.3 Hz), 19.44 (d, *J* = 8.9 Hz), 18.35 (t, *J* = 4.6 Hz), 10.41 (t, *J* = 4.6 Hz), 6.18 (d, *J* = 7.9 Hz); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -107.85 (ddd, *J* = 282.4, 54.5, 9.0 Hz), -113.43 (ddt, *J* = 282.8, 55.9, 5.1 Hz), -114.93 (ddd, *J* = 280.3, 57.4, 10.4 Hz), -115.92 (ddd, *J* = 280.5, 57.6, 11.0 Hz).

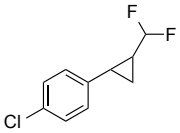
1-(2-(difluoromethyl)cyclopropyl)-4-fluorobenzene



observerd isomer ratio: 1:1.2

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.34 – 6.86 (m, 4H), 5.74 (td, *J* = 57.5, 4.1 Hz, 0.5H) AND 4.90 (ddd, *J* = 56.0, 54.8, 7.6 Hz, 0.5H), 2.45 – 2.32 AND 2.25 – 2.07 (m, 1H), 1.76 – 1.44 (m, 1H), 1.31 – 0.93 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -108.34 (ddd, J = 283.6, 54.7, 8.7 Hz, 1F), -113.66 (dddd, J = 283.7, 55.9, 6.2, 3.4 Hz, 1F), -115.70 (m, 3F), -116.25 (m, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 162.70, 135.73, 130.88, 130.80, 127.92 (d, J = 8.1 Hz), 116.43 – 113.73 (m), 23.76 (t, J = 26.6 Hz), 20.24 (t, J = 29.6 Hz), 19.11 (d, J = 8.2 Hz), 18.06, 10.26 (t, J = 4.4 Hz), 6.41 (d, J = 7.9 Hz); IR (KBr): 2923, 2856, 2287, 2232, 2114, 2018, 1733, 1641, 1602, 1513, 1460, 1344, 1232, 1083, 1037, 832; HRMS (EI): mass found: 186.06576, calculated mass for $C_{10}H_9F_3$: 186.06563.

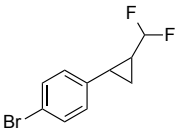
1-(2-(difluoromethyl)cyclopropyl)-4-chlorobenzene



observerd isomer ratio: 1:1.5

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.32 – 7.18 (m, 4H), 7.07 – 6.99 (m, 1H), 5.76 (td, J = 57.4, 4.0 Hz, 0.6H) AND 4.93 (ddd, J = 55.9, 54.7, 7.5 Hz, 0.4H), 2.43 – 2.34 AND 2.22 – 2.12 (m, 1H), 1.76 – 1.55 (m, 1H), 1.31 – 1.00 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -108.37 (ddd, J = 284.0, 54.7, 8.6 Hz, 1F), -113.56 (dddd, J = 283.9, 55.9, 6.2, 3.1 Hz, 1F), -115.91 (dd, J = 57.4, 10.8 Hz, 2F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 138.68, 134.76, 132.78, 132.06, 130.64, 128.59 (d, J = 6.5 Hz), 127.71, 117.82 (t, J = 235.8 Hz), 116.15 (t, J = 238.6 Hz), 23.98 (t, J = 26.8 Hz), 20.41 (dd, J = 30.6, 28.6 Hz), 19.27 (d, J = 8.3 Hz), 18.19 (t, J = 4.7 Hz), 10.50 (t, J = 4.6 Hz), 6.35 (d, J = 7.6 Hz); IR (KBr): 2922, 2856, 2310, 2103, 1897, 1740, 1367, 1218, 1087, 1038, 824; HRMS (EI): mass found: 202.03608, calculated mass for $C_{10}H_9F_2Cl$: 202.03582.

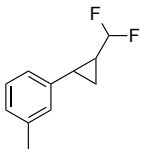
1-(2-(difluoromethyl)cyclopropyl)-4-bromobenzene



observerd isomer ratio: 1:1.3

^{1}H NMR (400MHz, $CDCl_3$): δ = 7.47 – 7.35 (m, 2H), 7.16 (d, J = 8.3 Hz, 1H), 7.02 – 6.94 (m, 1H), 5.76 (td, J = 57.4, 4.0 Hz, 0.6H) AND 5.04 – 4.82 (m, 0.4H), 2.41 – 2.33 AND 2.19 – 2.11 (m, 1H), 1.74 – 1.52 (m, 1H), 1.30 – 1.00 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -108.37 (ddd, J = 284.0, 54.7, 8.6 Hz, 1F), -113.55 (dddd, J = 284.0, 55.9, 6.2, 3.1 Hz, 1F), -115.95 (dd, J = 57.5, 10.5 Hz, 2F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 139.24, 135.30, 131.56, 131.51, 131.01, 128.08, 120.86, 120.01, 117.79 (t, *J* = 235.8 Hz), 116.11 (t, J = 238.6 Hz), 23.99 (t, J = 26.8 Hz), 20.39 (dd, J = 30.5, 28.8 Hz), 19.35 (d, J = 8.4 Hz), 18.26 (t, J = 4.6 Hz), 10.50 (t, J = 4.6 Hz), 6.31 (d, J = 7.5 Hz); IR (KBr): 2923, 2860, 1460, 1372, 1044, 906, 822, 730; HRMS (EI): mass found: 245.98493, calculated mass for $C_{10}H_9BrF_2$: 245.98557.

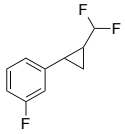
1-(2-(difluoromethyl)cyclopropyl)-3-methylbenzene



observerd isomer ratio: 1:1.4

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.22 – 7.14 (m, 1H), 7.12 – 7.00 (m, 2H), 6.95 – 6.87 (m, 1H), 5.74 (td, J = 57.5, 4.1 Hz, 0.6H) AND 4.93 (ddd, J = 56.1, 54.6, 7.7 Hz, 0.4H), 2.45 – 2.37 AND 2.19 – 2.11 (m, 1H), 1.74 – 1.56 (m, 1H), 1.25 – 1.03 (m, 2H); ^{19}F NMR (367 MHz, $CDCl_3$): δ = -108.05 (ddd, J = 282.9, 54.5, 8.4 Hz, 1F), -113.47 (dd, J = 282.7, 56.3 Hz, 1F), -114.99 (ddd, J = 280.6, 57.5, 10.6 Hz, 1F), -116.04 (ddd, J = 280.6, 57.5, 10.8 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 139.12 (d, J = 300.8 Hz), 137.08 (d, J = 300.7 Hz), 130.01, 128.38, 128.31, 127.66, 127.09, 126.18, 123.24, 118.11 (d, *J* = 240.4 Hz), 116.53 (t, J = 238.4 Hz), 29.70, 23.86 (t, J = 26.7 Hz), 21.37, 20.33 (dd, J = 31.0, 28.4 Hz), 19.83 (d, J = 8.7 Hz), 18.69 (t, J = 4.6 Hz), 10.41 (t, J = 4.5 Hz), 6.07 (d, J = 7.7 Hz); IR (KBr): 2930, 2259, 1738, 1431, 1366, 1035, 904, 425; HRMS (EI): mass found: 182.09026, calculated mass for $C_{11}H_{12}F_2$: 182.09071.

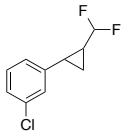
1-(2-(difluoromethyl)cyclopropyl)-3-fluorobenzene



observed isomer ratio: 1:1.2

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.26 – 7.20 (m, 1H), 7.09 – 6.87 (m, 3H), 5.77 (td, *J* = 57.5, 3.9 Hz, 0.6H) AND 4.95 (ddd, *J* = 55.8, 54.7, 7.6 Hz, 0.4H), 2.54 – 2.13 (m, 1H), 1.83 – 1.58 (m, 1H), 1.34 – 0.93 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$) δ = -108.31 (ddd, *J* = 284.5, 55.6, 8.7 Hz), -113.05 – -113.87 (m), -116.11 (dd, *J* = 57.6, 10.8 Hz); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 163.78, 162.15, 142.90 (d, *J* = 7.7 Hz), 129.93 (d, *J* = 8.5 Hz), 122.04 (d, *J* = 2.8 Hz), 117.62, 117.11 – 115.68 (m), 113.96 (d, *J* = 21.3 Hz), 113.61 – 112.98 (m), 24.16 (t, *J* = 26.7 Hz), 20.58 (dd, *J* = 30.6, 28.9 Hz), 19.67, 18.50, 10.69, 6.36 (d, *J* = 7.5 Hz).

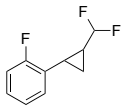
1-(2-(difluoromethyl)cyclopropyl)-3-chlorobenzene



observed isomer ratio 1:1.2

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.31 – 7.14 (m, 2H), 7.11 – 6.92 (m, 2H), 5.77 (td, *J* = 57.4, 4.0 Hz, 0.6H) AND 4.96 (ddd, *J* = 55.8, 54.7, 7.5 Hz, 0.4H), 2.29 (ddt, *J* = 141.3, 10.1, 4.2 Hz, 1H), 1.83 – 1.59 (m, 1H), 1.28 – 1.05 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$) δ = -108.35 (ddd, *J* = 284.2, 54.8, 8.9 Hz), -113.52 (dddd, *J* = 284.1, 56.0, 6.6, 3.3 Hz), -116.12 (ddd, *J* = 57.6, 10.9, 7.3 Hz); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 142.31, 138.37, 134.33, 129.70, 129.36, 127.53, 127.21, 126.51, 124.61, 117.64, 116.01, 114.43, 24.05 (t, *J* = 26.8 Hz), 20.54 (t, *J* = 29.8 Hz), 19.57 (d, *J* = 8.4 Hz), 18.42 (d, *J* = 4.7 Hz), 10.58 (t, *J* = 4.7 Hz), 6.29 (d, *J* = 7.6 Hz).

1-(2-(difluoromethyl)cyclopropyl)-2-fluorobenzene

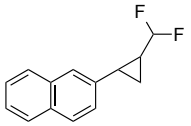


observed isomer ratio 1:1.2

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.25 – 6.94 (m, 4H), 5.79 (td, *J* = 57.5, 4.0 Hz, 0.6H), 5.01 (td, *J* = 55.7, 6.9 Hz, 0.4H), 2.46 – 2.28 (m, 1H), 1.82 – 1.61 (m, 1H), 1.29 – 1.09 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$) δ = -107.90 – -108.98 (m), -114.01 (dddd, *J* = 284.0, 56.1, 8.0, 2.9 Hz), -115.19 (ddd, *J* = 281.3, 57.6, 10.2 Hz), -115.63, -116.86 (ddd, *J* = 281.3, 57.3, 11.4 Hz), -119.03 (dt, *J* = 11.5, 5.7 Hz); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 162.58 (d, *J* = 247.4 Hz), 161.70 (d, *J* = 246.0 Hz), 129.65 (d, *J* = 3.7 Hz), 128.71 (d, *J* = 8.4 Hz), 127.81 (d, *J* = 7.8 Hz), 127.05 (d, *J* = 3.8 Hz), 123.95 (dd, *J* = 26.6, 3.7 Hz), 123.65 (d, *J* = 14.9 Hz), 118.52 (d, *J* = 183.4 Hz), 116.94 (d, *J* = 185.8 Hz), 115.37 (d, *J* = 21.4 Hz), 115.29 (d, *J* = 22.1 Hz), 23.39 – 21.83 (m), 20.08 (dd, *J* = 30.6, 28.2 Hz), 14.74 – 13.47

(m), 12.71 (d, *J* = 5.0 Hz), 9.25 (d, *J* = 4.4 Hz), 5.51 (d, *J* = 6.9 Hz); IR (KBr): 2924, 2858, 1459, 1215, 907, 745; HRMS (EI): mass found: 186.06524, calculated mass for $C_{10}H_9F_3$: 186.06563.

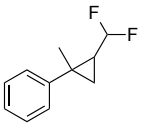
2-(2-(difluoromethyl)cyclopropyl)naphthalene



observerd isomer ratio: 1:1.2

^{1}H NMR (400MHz, $CDCl_3$): δ = 7.88 – 7.37 (m, 6H), 7.23 (dd, *J* = 8.5, 1.8 Hz, 1H), 5.81 (td, *J* = 57.5, 4.1 Hz, 0.6H) AND 4.94 (ddd, *J* = 56.1, 54.7, 7.7 Hz, 0.4H), 2.73 – 2.52 AND 2.43 – 2.29 (m, 1H), 1.86 – 1.65 (m, 1H), 1.41 – 1.13 (m, 2H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -107.72 (ddd, J = 283.1, 54.6, 8.6 Hz, 1F), -113.50 (dddd, J = 283.2, 56.1, 5.5, 3.7 Hz, 1F), -115.21 (ddd, J = 280.9, 57.5, 10.7 Hz, 1F), -115.88 (ddd, J = 280.9, 57.5, 10.8 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 137.58, 133.86, 133.36, 133.28, 132.44, 132.19, 128.18, 128.14, 127.89, 127.63 , 127.61, 127.56, 127.35, 127.27, 126.25, 126.22, 125.81, 125.45, 124.81, 124.75, 118.09 (t, J = 235.9 Hz), 116.46 (t, J = 238.4 Hz), 23.93 (t, J = 26.8 Hz), 20.56 (dd, J = 30.9, 28.7 Hz), 20.15 (d, J = 8.6 Hz), 19.01 (t, J = 4.6 Hz), 10.44 (t, J = 4.6 Hz), 6.28 (d, J = 7.7 Hz); IR (KBr): 3050, 2925, 2858, 1634, 1430, 1371, 1152, 1032, 905, 815, 736; HRMS (EI): mass found: 218.09012, calculated mass for $C_{14}H_{12}F_2$: 218.09071.

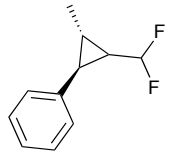
(2-(difluoromethyl)-1-methylcyclopropyl)benzene



observerd isomer ratio: 1:1.7

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.36 – 7.16 (m, 5H), 5.69 (td, J = 56.2, 6.9 Hz, 0.6H) AND 4.77 (ddd, J = 56.1, 54.6, 7.8 Hz, 0.4H), 1.67 – 1.50 (m, 1H), 1.49 – 1.39 (m, 3H), 1.33 – 1.17 (m, 1H), 1.06 – 0.93 (m, 1H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -106.23 (ddd, J = 285.1, 56.4, 8.3 Hz, 1F), -107.76 (ddd, J = 281.8, 54.5, 8.4 Hz, 1F), -112.04 (ddd, J = 285.2, 56.0, 9.5 Hz, 1F), -112.93 (ddd, J = 281.8, 56.1, 5.6 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 145.67, 141.19, 129.17, 128.60, 128.49, 127.55, 126.97, 126.51, 118.57 (t, J = 235.5 Hz), 118.11 (t, J = 236.6 Hz), 27.95, 27.08 (dd, J = 31.4, 27.0 Hz), 26.54 (dd, J = 29.8, 27.6 Hz), 26.27, 25.16 (d, J = 7.5 Hz), 21.6, 16.80 (d, J = 7.5 Hz), 14.30 (d, J = 7.7 Hz); IR (KBr): 2922, 2857, 1725, 1458, 1374, 1261, 1088, 1031,802, 759; HRMS (EI): mass found: 182.09046, calculated mass for $C_{11}H_{12}F_2$: 182.09071.

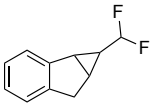
(2-(difluoromethyl)-3-methylcyclopropyl)benzene



observerd isomer ratio: 1:1.2

^{1}H NMR (600MHz, $CDCl_3$): δ =7.37 – 7.16 (m, 4H), 7.10 – 7.03 (m, 1H), 5.73 (td, *J* = 56.2, 6.4 Hz, 0.6 H) AND 4.98 (ddd, *J* = 56.4, 54.7, 7.6 Hz, 0.4 H), 2.21 – 2.12 AND 1.97 – 1.92 (m, 1H), 1.71 – 1.61 AND 1.48 – 1.40 (m, 2H) 1.33 – 1.28 (m, 3H);^{19}F NMR (564 MHz, $CDCl_3$): δ = -107.56 (ddd, *J* = 285.3, 56.3, 10.0 Hz, 1F), -108.06 (ddd, *J* = 283.3, 54.8, 9.2 Hz, 1F), -112.27 (ddd, *J* = 285.3, 56.3, 9.5 Hz), -112.27 (ddd, *J* = 285.3, 56.3, 9.5 Hz, 1F), -112.94 (m, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 140.42, 136.53, 133.28, 129.01, 128.45 (d, *J* = 2.8 Hz), 127.52, 126.76, 126.18 (d, *J* = 14.4 Hz), 117.76 (t, *J* = 236.5 Hz)117.25 (t, *J* = 237.2 Hz) 29.70, 28.57 (dd, *J* = 28.5, 13.3 Hz), 28.36 – 28.08 (m), 27.83 (d, *J* = 6.6 Hz), 20.07 (d, *J* = 6.9 Hz), 17.64, 14.48 (d, *J* = 7.5 Hz), 13.43; MS-EI: m/z(%): 181.9 [M] 21%, 166.9 [M-CH_3] 18%, 146,9 [M-CH_4F] 41%, 131.0 [M-CF_2H] 100%, 115.0 [M-$C2H_4F_2$] 53%;IR (KBr): υ = 3026, 2964, 2929, 2326, 2108, 1927, 1602, 1499, 1444, 1393, 1130, 1070, 1030, 744, 696

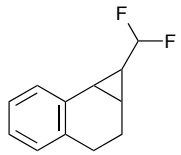
1-(difluoromethyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene



observerd isomer ratio: 1:1.4

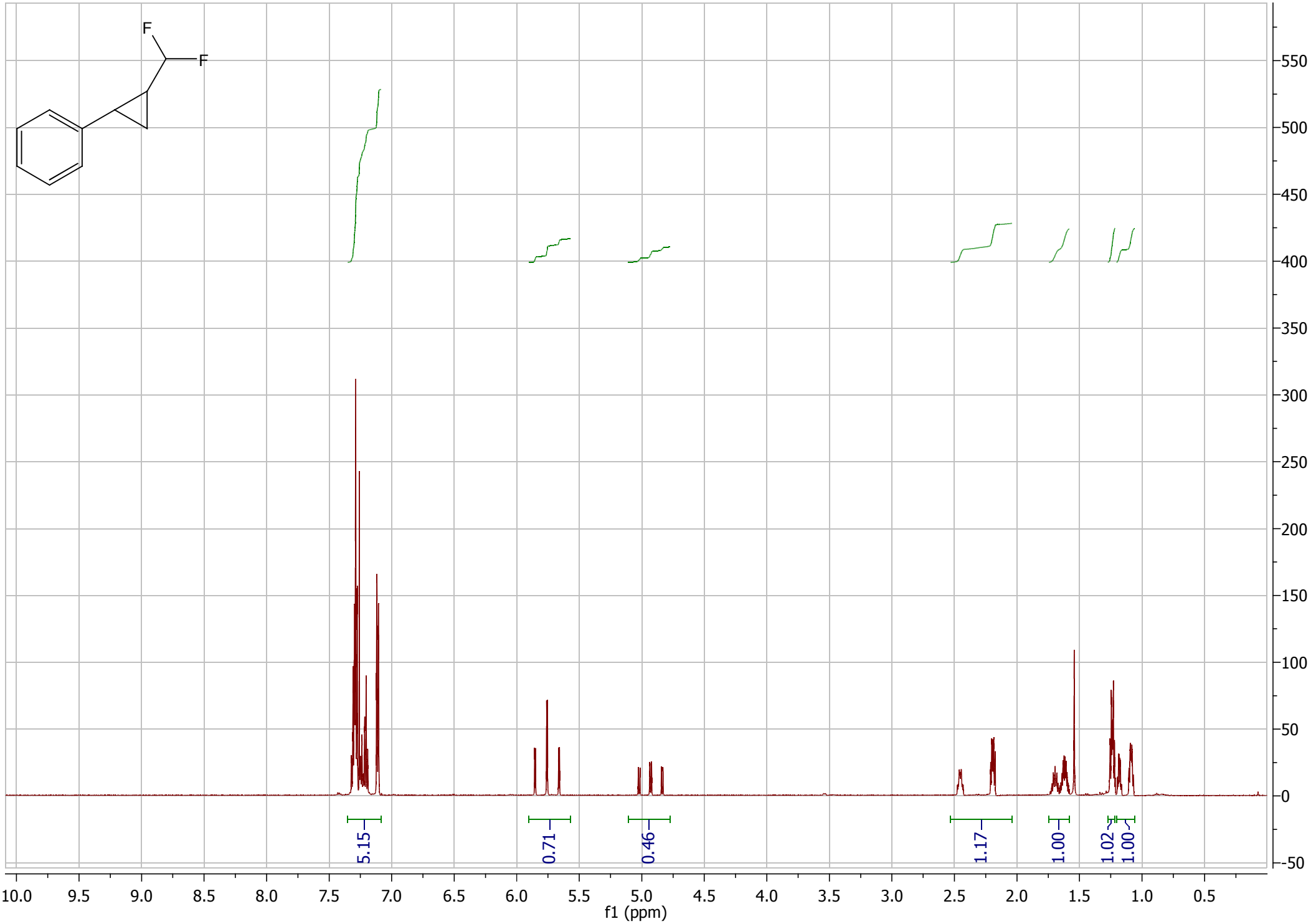
^{1}H NMR (600MHz, $CDCl_3$): δ = 7.40 – 7.08 (m, 4H), 5.73 (ddd, J = 61.6, 50.3, 4.2 Hz, 0.6H) AND 4.75 (ddd, J = 56.2, 54.9, 8.0 Hz, 0.4H), 3.31 – 3.21 (m, 1H), 3.05 – 2.98 (m, 1H), 2.85 – 2.79 (m, 1H), 2.68 – 2.63 (m, 1H), 2.21 – 2.05 (m, 1H), 1.70 – 1.59 AND 1.36 – 1.28 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): δ = -110.55 (dd, J = 54.6, 9.9 Hz, 1F), -111.32 (dd, J = 54.7, 10.0 Hz, 1F), -114.53 (dt, J = 35.5, 17.7 Hz, 1F), -115.23 (ddd, J = 38.4, 31.4, 7.5 Hz, 1F); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 142.72 (d, J = 305.4 Hz), 141.34 (d, J = 328.4 Hz), 126.99, 126.73, 126.29, 126.24, 125.36, 124.94, 124.44, 123.78, 115.97 (t, J = 234.7 Hz), 115.88 (t, J = 238.3 Hz), 34.84, 32.01, 30.49 (t, J = 26.1 Hz), 29.70, 28.28 (d, J = 9.2 Hz), 26.97 (t, J = 4.8 Hz), 24.21 (t, J = 30.9 Hz), 20.06 (d, J = 9.1 Hz), 18.88 (t, J = 4.8 Hz); IR (KBr): 2920, 2860, 1721, 1640, 1547, 1476, 1340, 1266, 1209, 1135, 1052, 859, 723; HRMS (EI): mass found: 182.07452, calculated mass for $C_{11}H_{10}F_2$: 180.07506.

1-(difluoromethyl)-1a,2,3,7b-tetrahydro-1H-cyclopropa[a]naphthalene



observerd isomer ratio: 1:3,3

^{1}H NMR (600MHz, $CDCl_3$): δ = 7.34 – 7.27 (m, 1H), 7.20 – 7.01 (m, 3H), 5.74 (td, *J* = 57.6, 4.2 Hz, 0.8H) AND 5.12 (ddd, *J* = 56.9, 54.1, 8.0 Hz, 0.2H), 2.95 – 2.75 AND 2.72 – 2.59 (m, 1H), 2.50 – 2.37 (m, 1H), 2.33 – 2.08 (m, 2H), 1.98 – 1.58 (m, 2H), 1.35 – 1.25 (m, 1H); ^{19}F NMR (564 MHz, $CDCl_3$): δ = -109.07 (ddd, *J* = 288.7, 54.3, 14.3 Hz), -113.79 – -116.06 (m); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 135.33, 133.74, 130.40, 128.67, 128.58, 128.47, 126.68, 126.47, 126.23, 125.72, 116.65 (t, *J* = 238.3 Hz), 27.93, 25.51, 22.92 (t, *J* = 26.2 Hz), 22.33, 18.53, 18.21, 16.83, 14.06; MS-EI: m/z(%): 193.9 [M] 21%, 143.0 [M-CF_2H]38%, 128.0 [M-$C_2H_4F_2$] 100%; IR (KBr): υ = 3022, 2928, 2859, 2326, 2108, 1910, 1491, 1442, 1380, 1192, 1141, 1079, 1031, 747, 682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F
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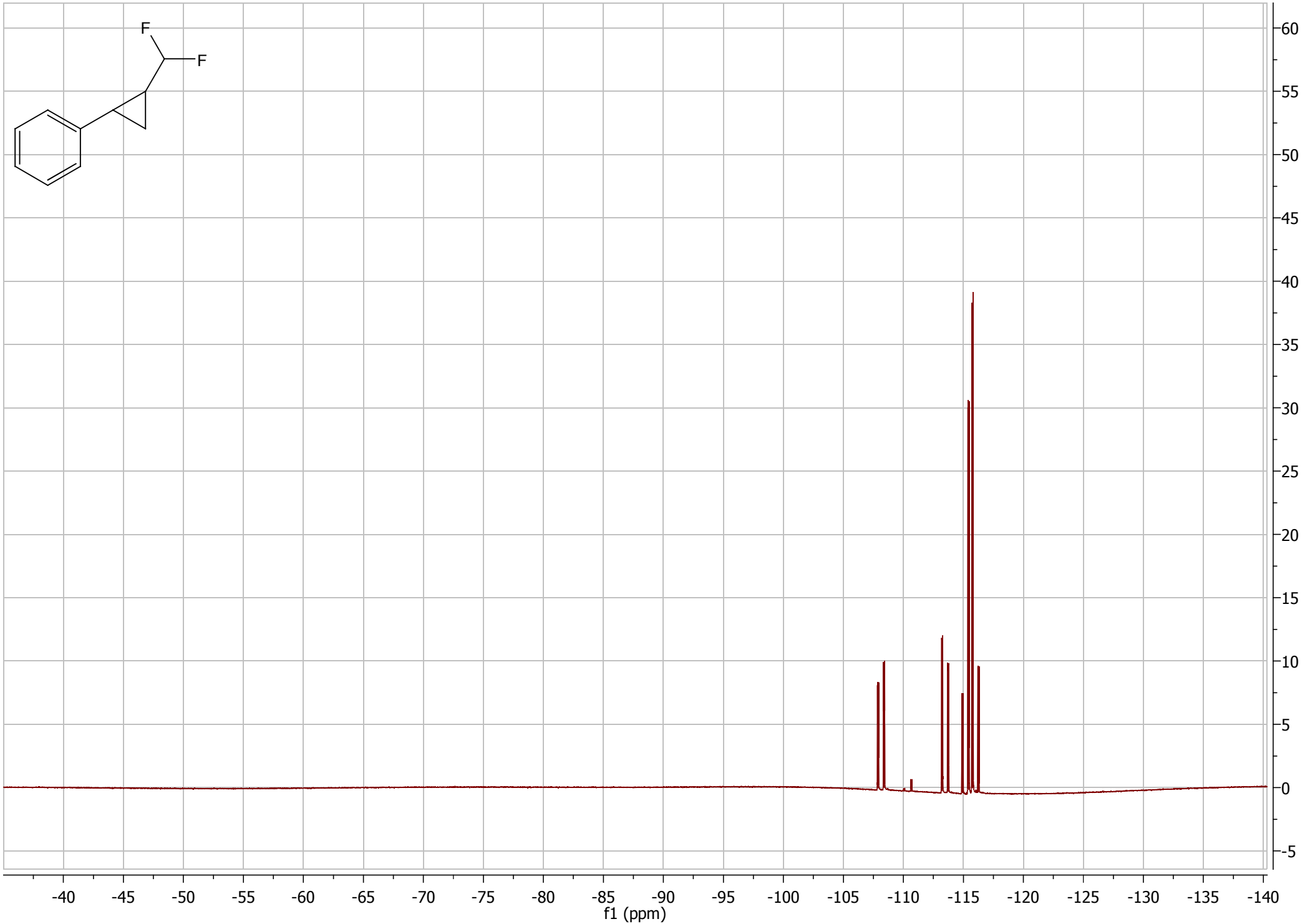
0.71
0.46
1.17
1.00
1.02
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
550
500
450
400
350
300
250
200
150
100
50
0
-50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F
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
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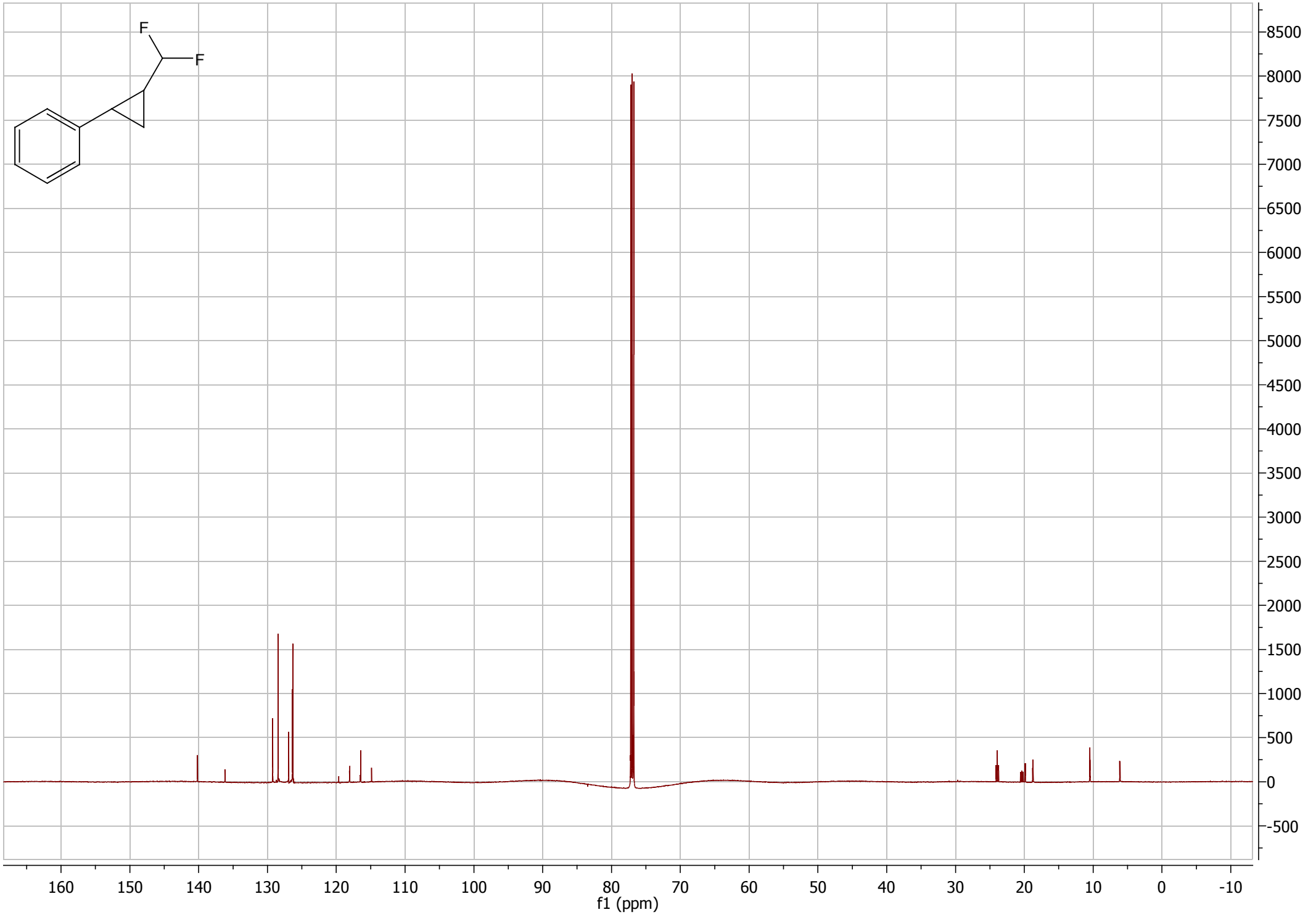
-120
-125
-130
-135
-140
f1 (ppm)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F
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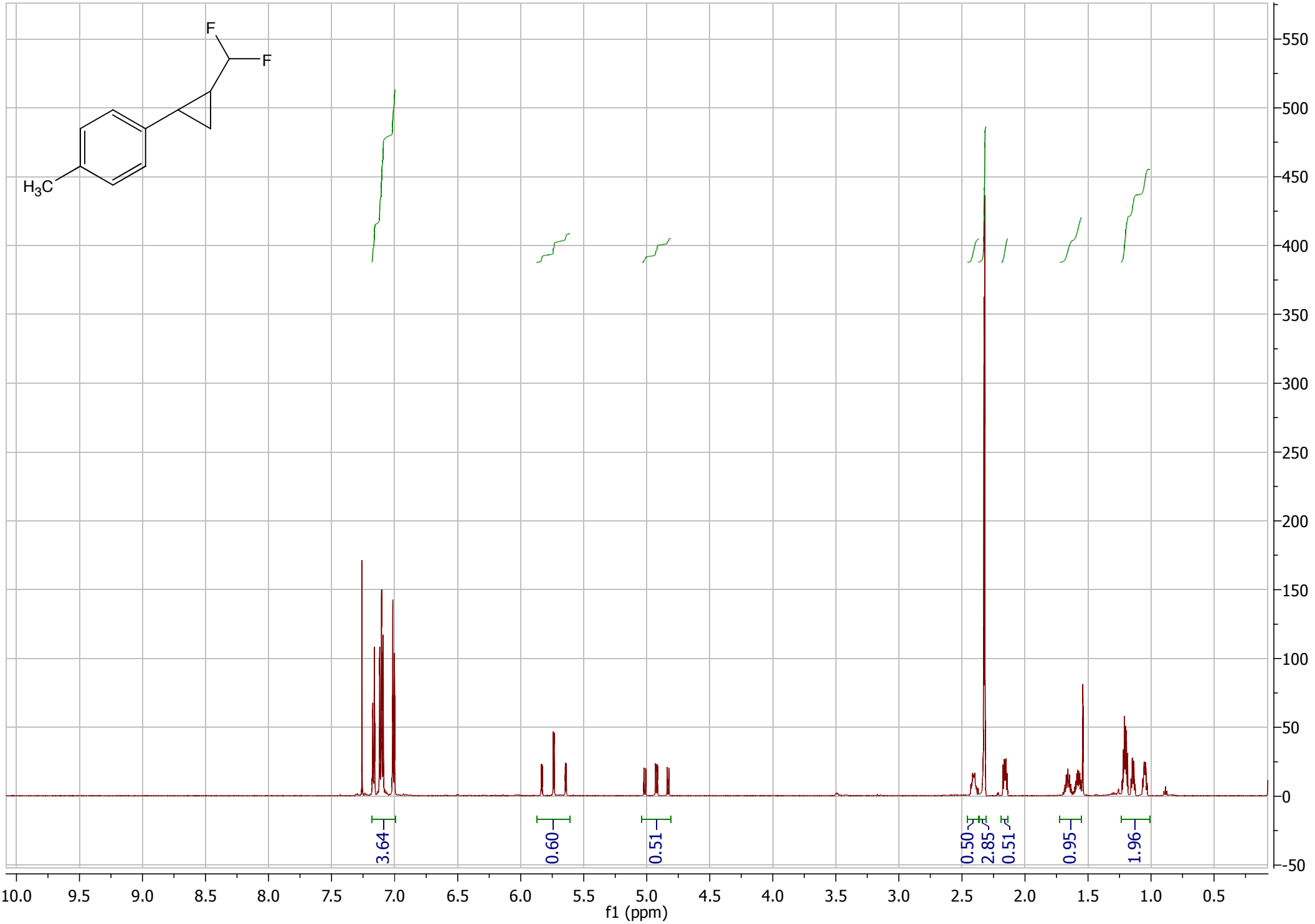
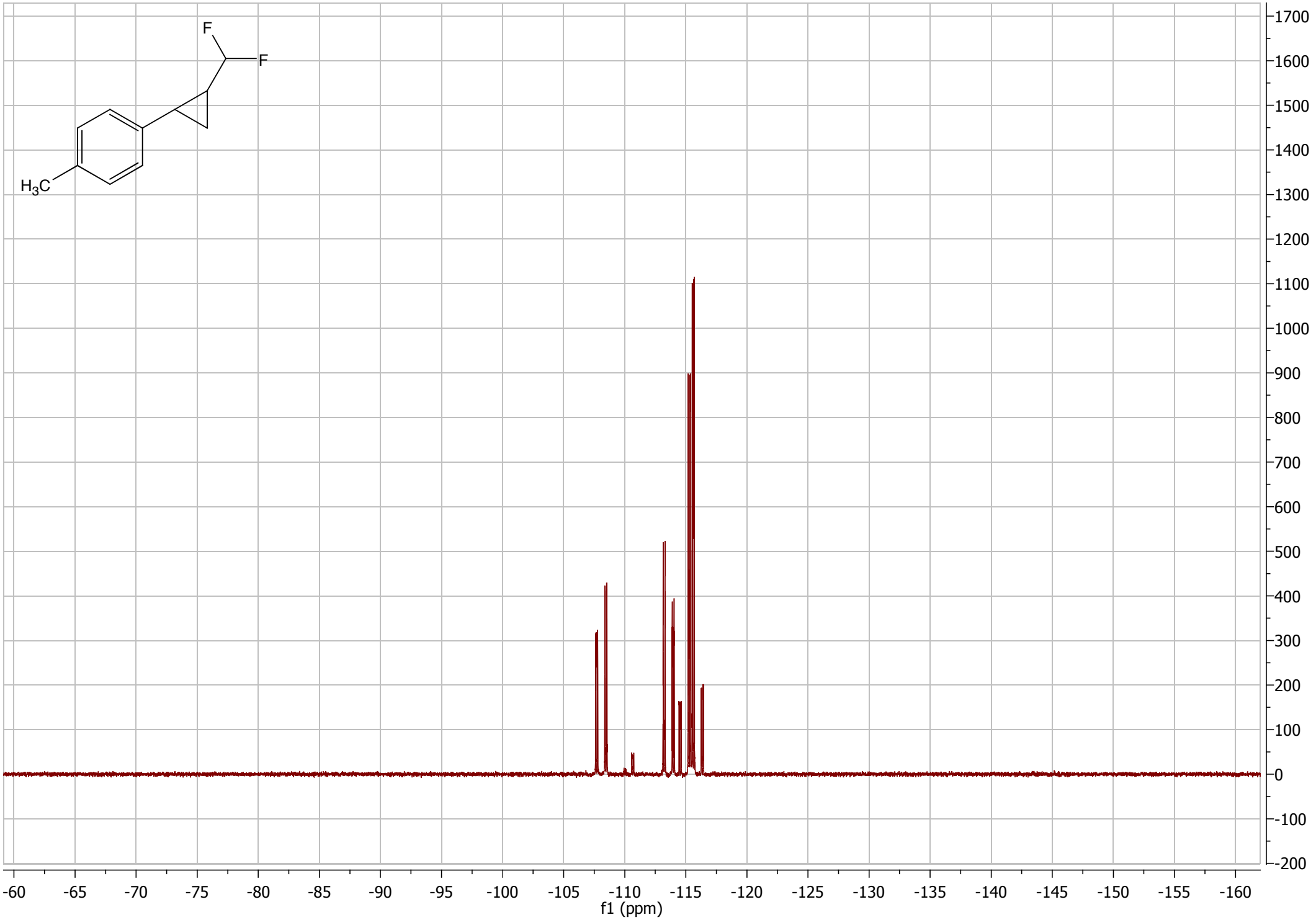
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


F
F
H3C
3.64
0.60
0.51
0.50
2.85
0.51
0.95
1.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
550
500
450
400
350
300
250
200
150
100
50
0
-50


F
F
H3C
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
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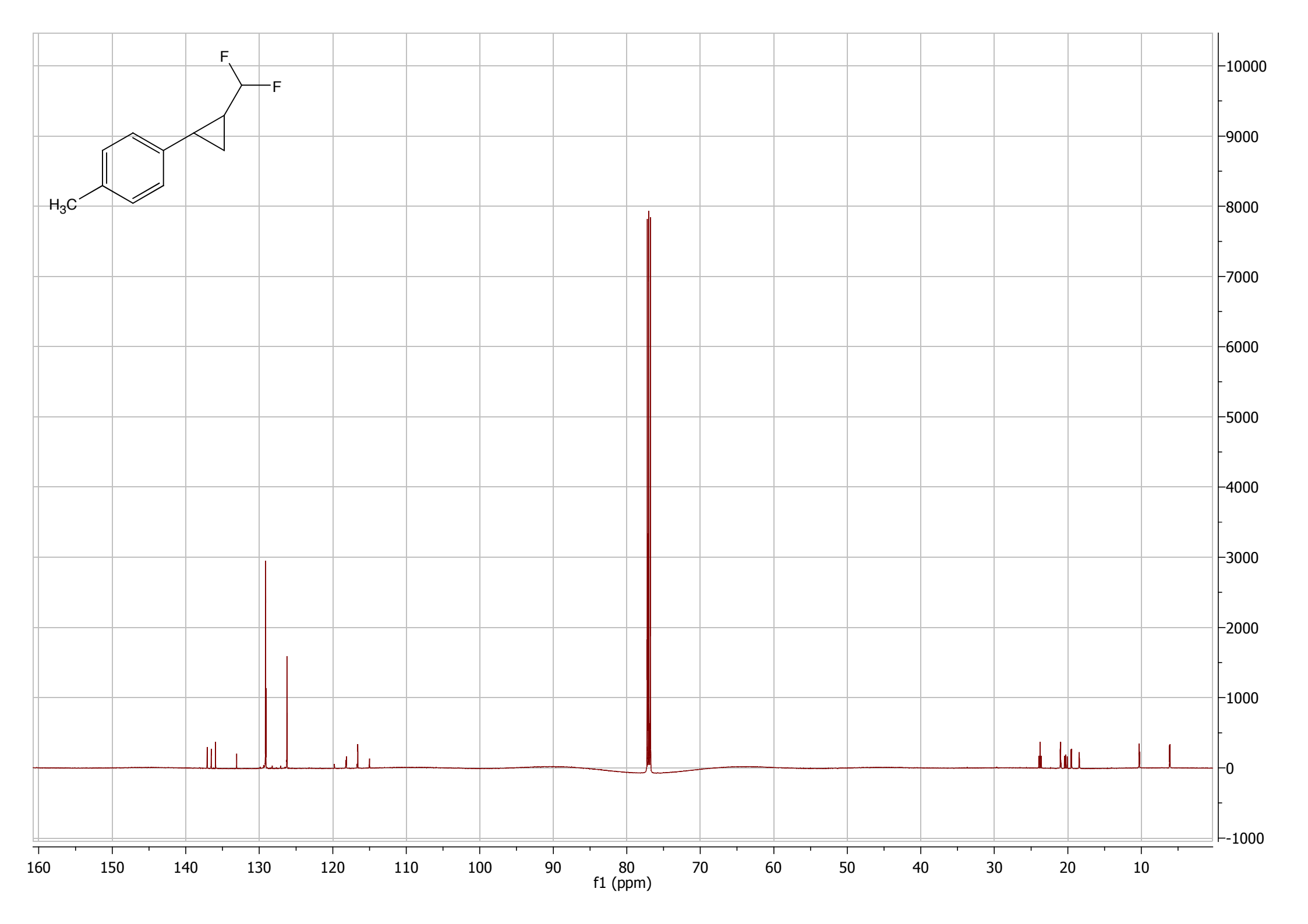
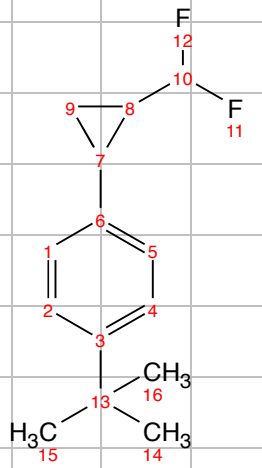
-140
-145
-150
-155
-160
f1 (ppm)


F
F
H3C
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


F
12
10
F
11
9
8
7
6
1
5
2
4
3
CH3
16
13
H3C
15
CH3
14

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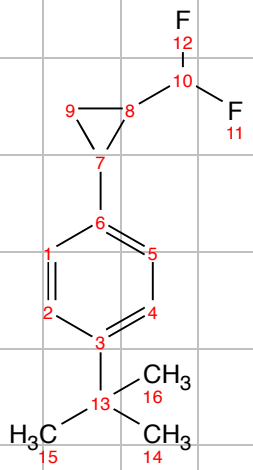
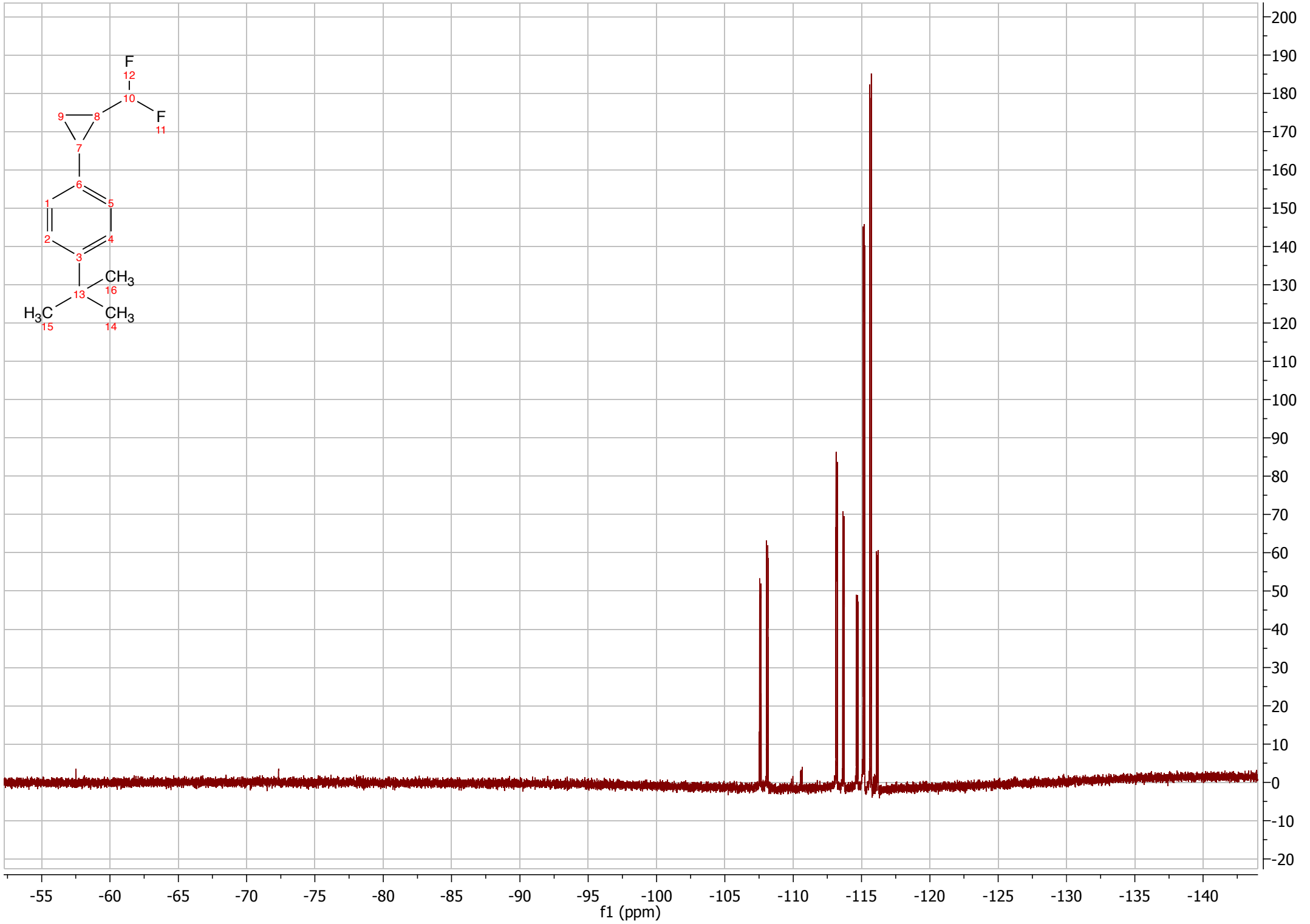
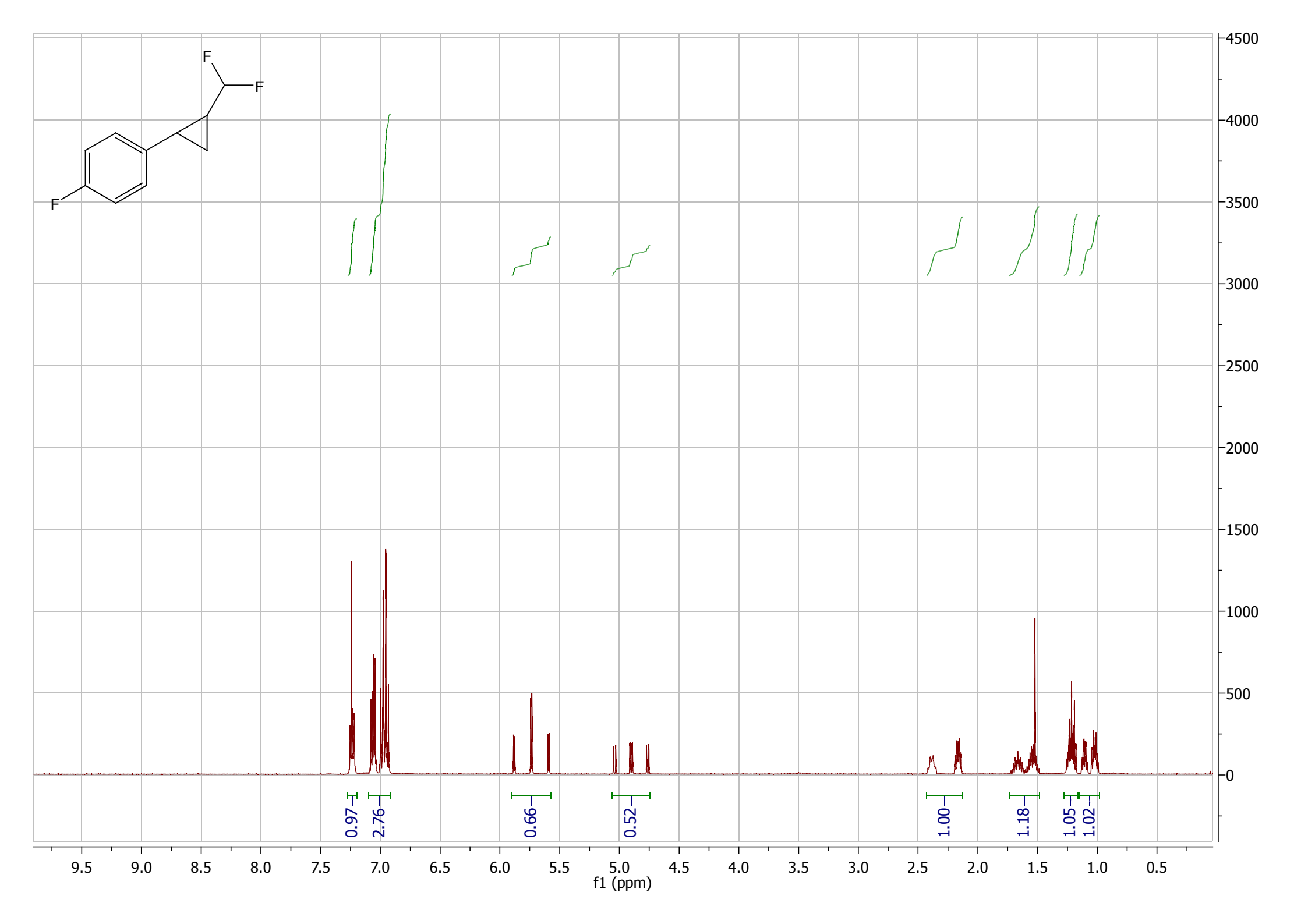
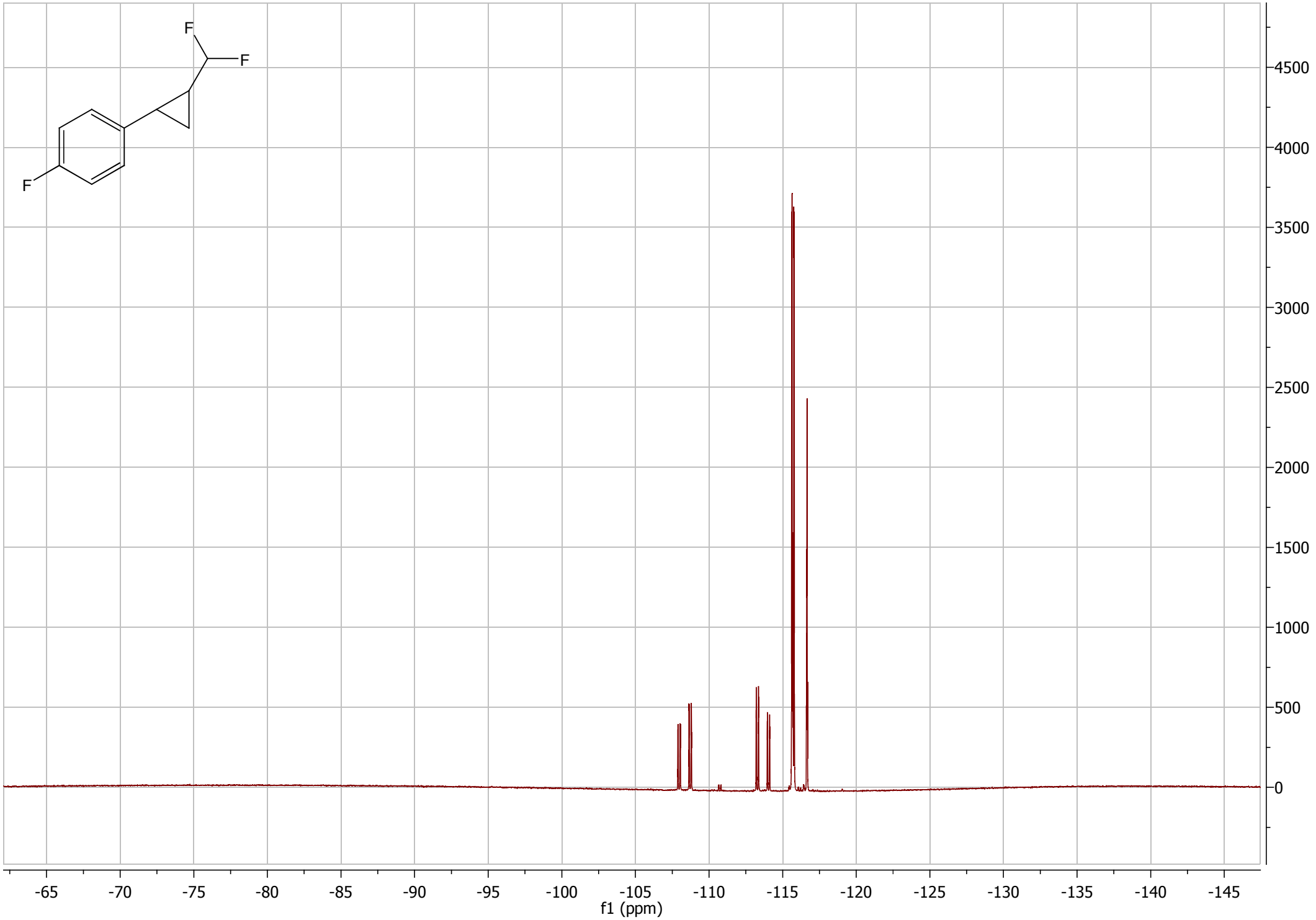
1.48
0.53
0.45
0.33
0.41
0.91
6.61
2.16
f1 (ppm)

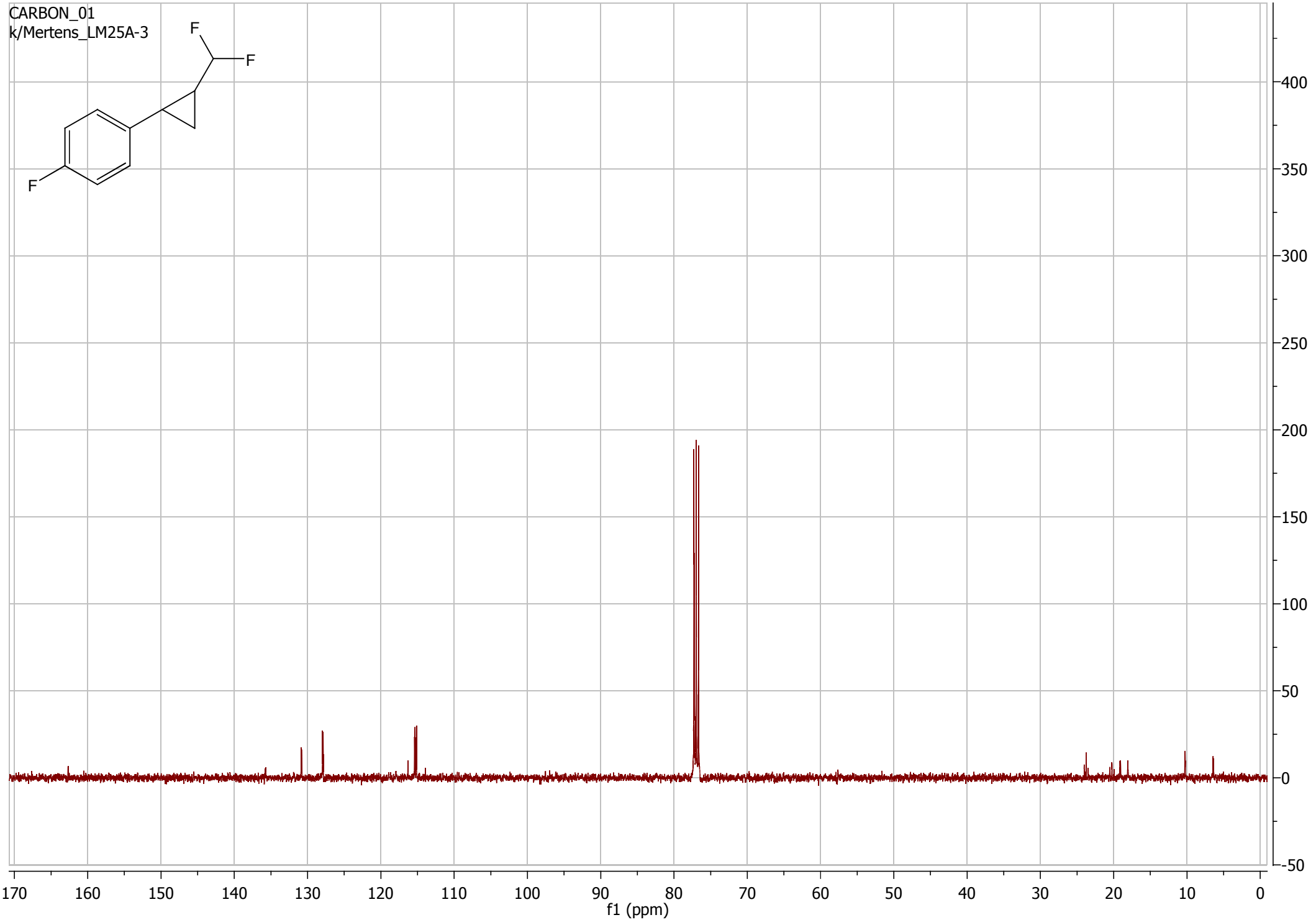

F
12
10
F
11
9
8
7
6
1
5
2
4
3
CH3
16
13
H3C
15
CH3
14

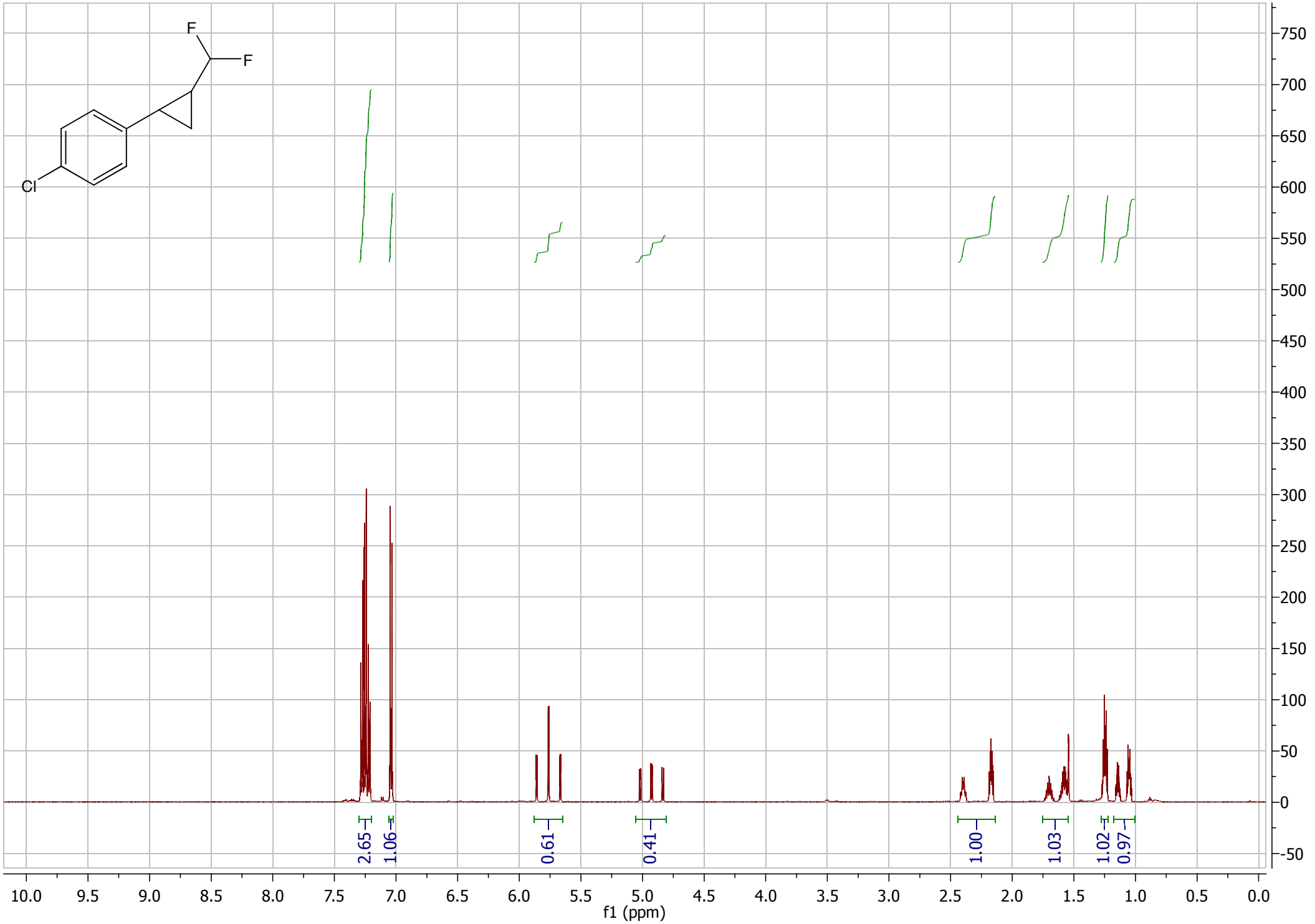
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

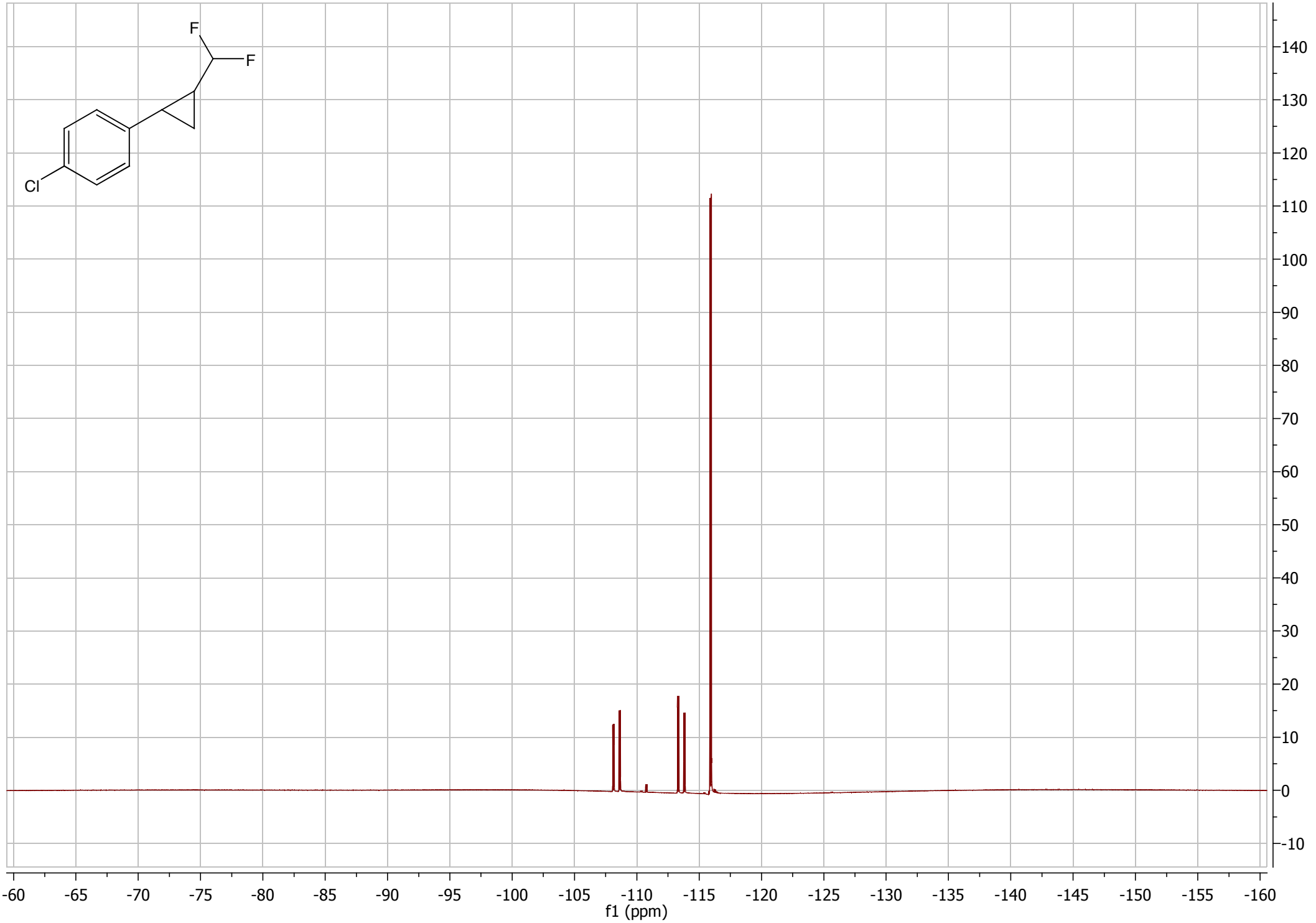

F
12
10
F
11
9
8
7
6
1
5
2
4
3
CH3
16
13
H3C
15
CH3
14
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)


F
F
F
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0.97
2.76
0.66
0.52
1.00
1.18
1.05
1.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


F
F
F
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
f1 (ppm)


CARBON_01
k/Mertens_LM25A-3
F
F
F
400
350
300
250
200
150
100
50
0
-50
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
F
Cl
2.65
1.06
0.61
0.41
1.00
1.03
1.02
0.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50


F
F
Cl
140
130
120
110
100
90
80
70
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50
40
30
20
10
0
-10
-60
-65
-70
-75
-80
-85
-90
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-120
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-130
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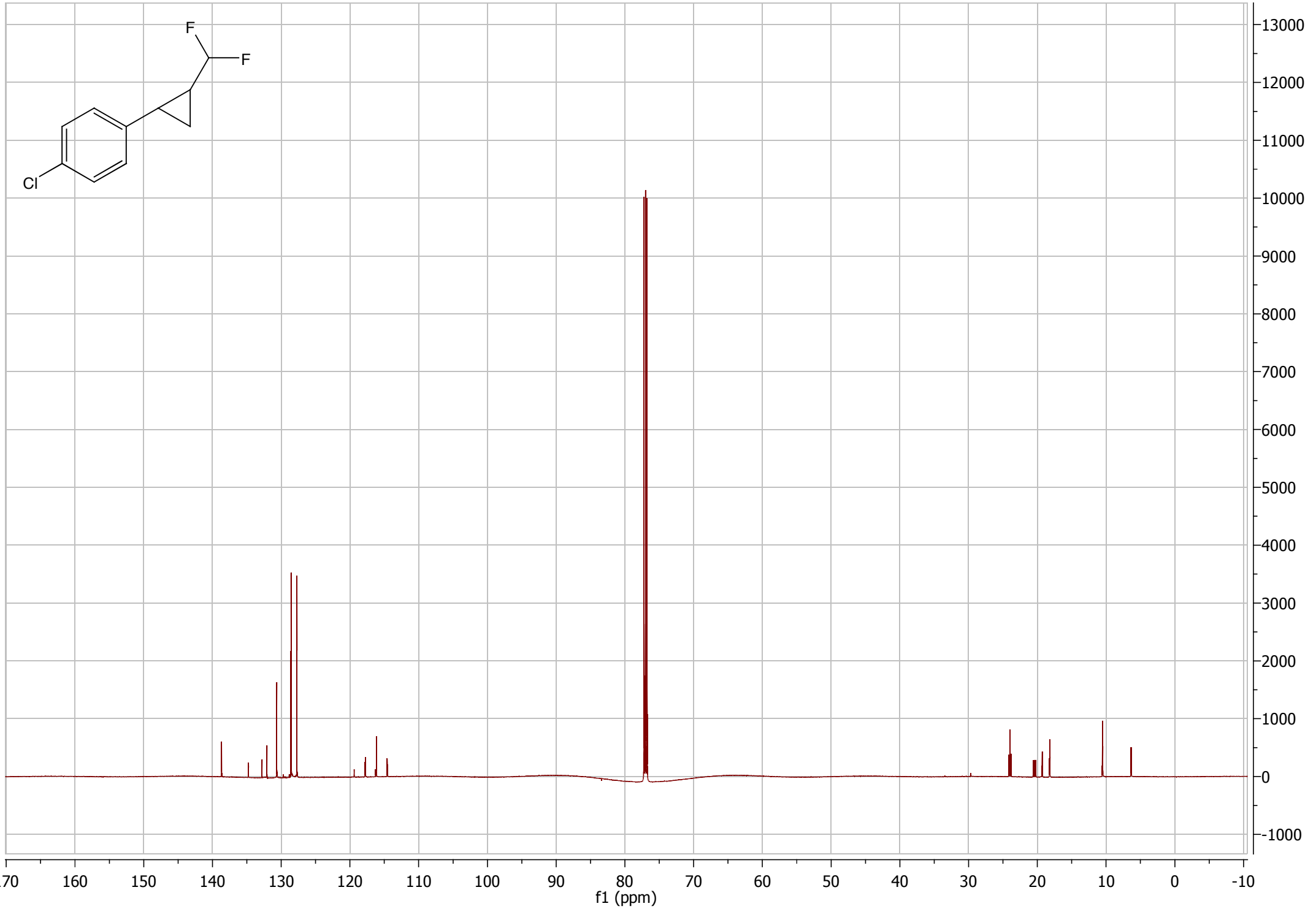
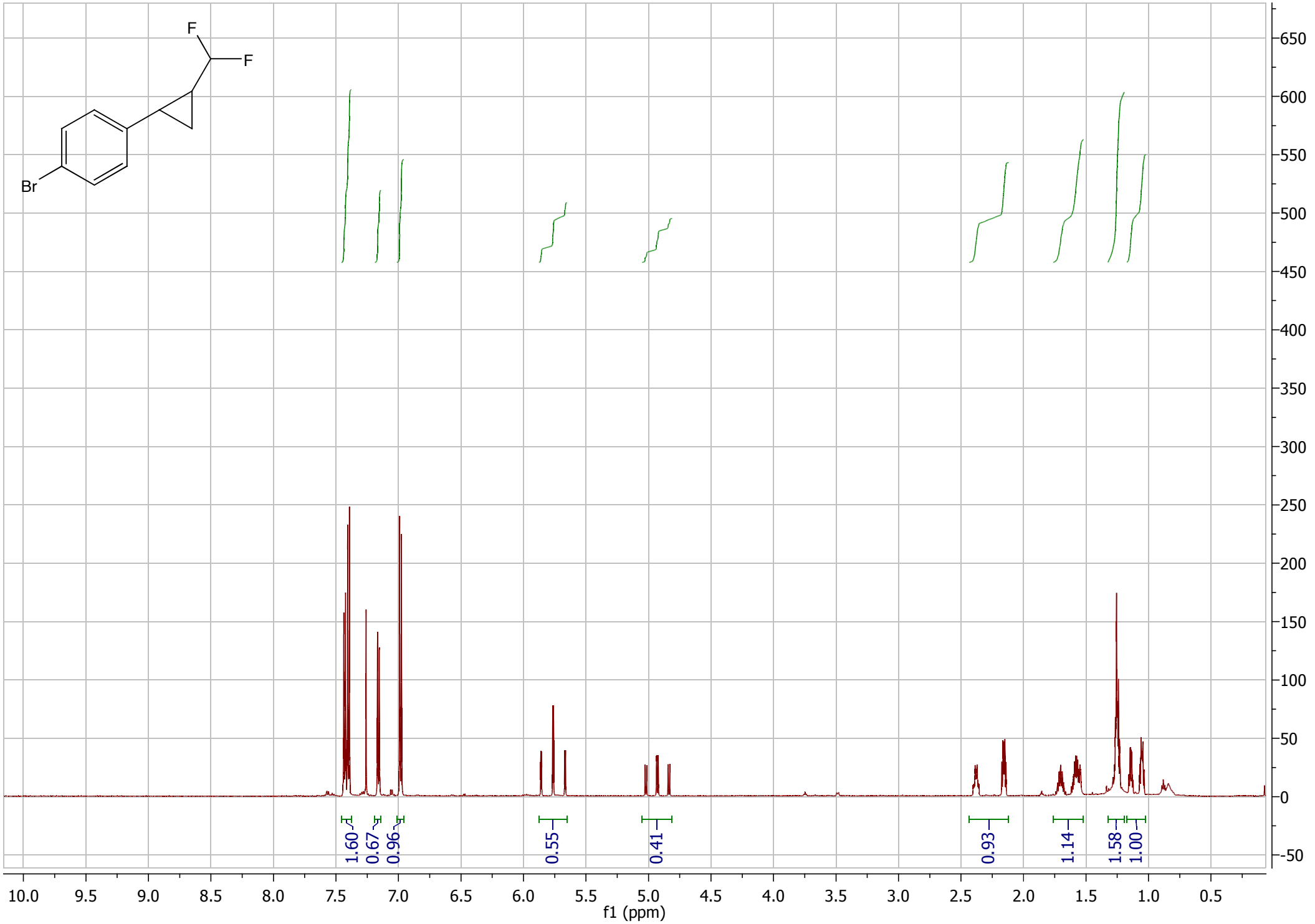
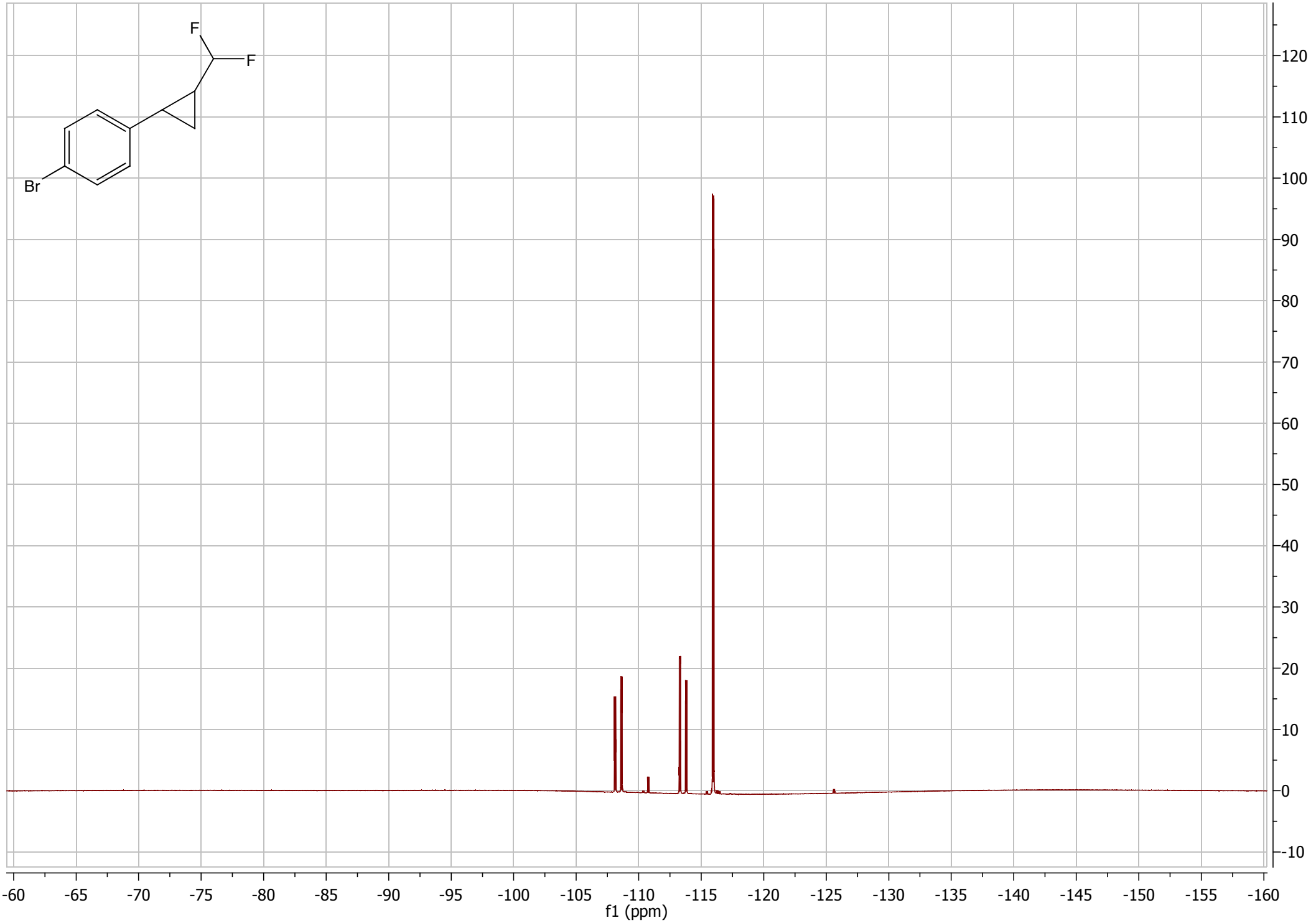
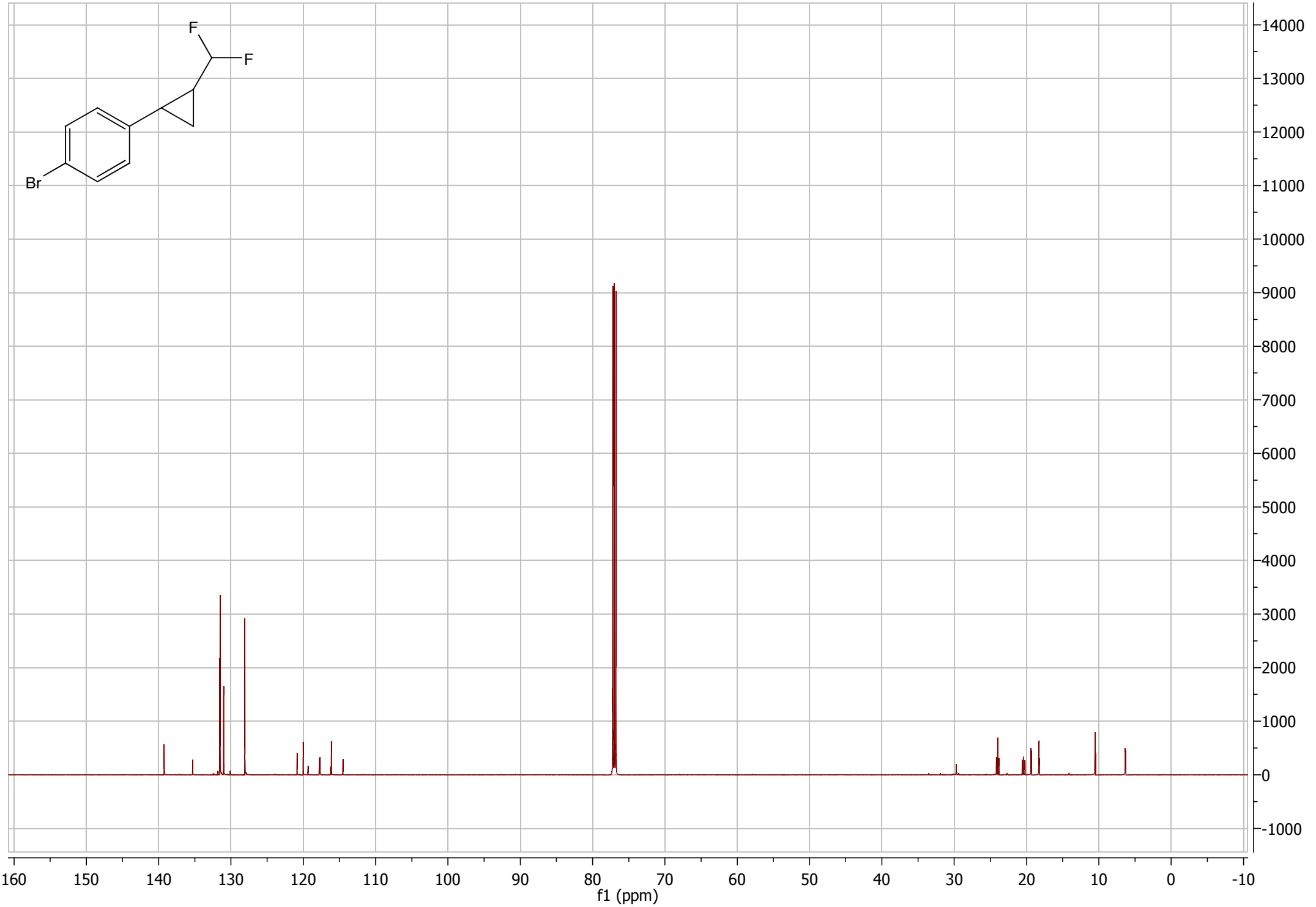
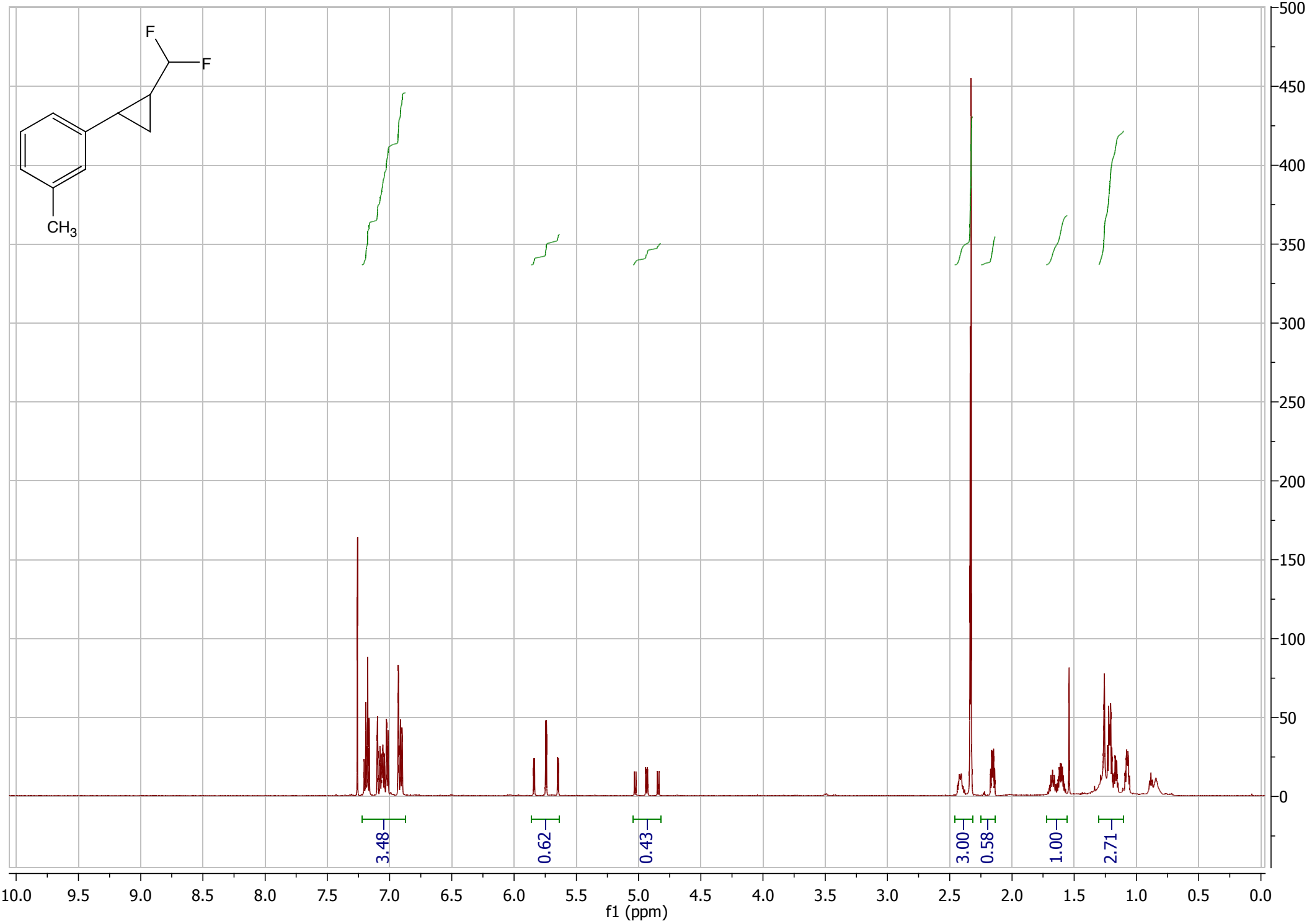
-140
-145
-150
-155
-160
f1 (ppm)

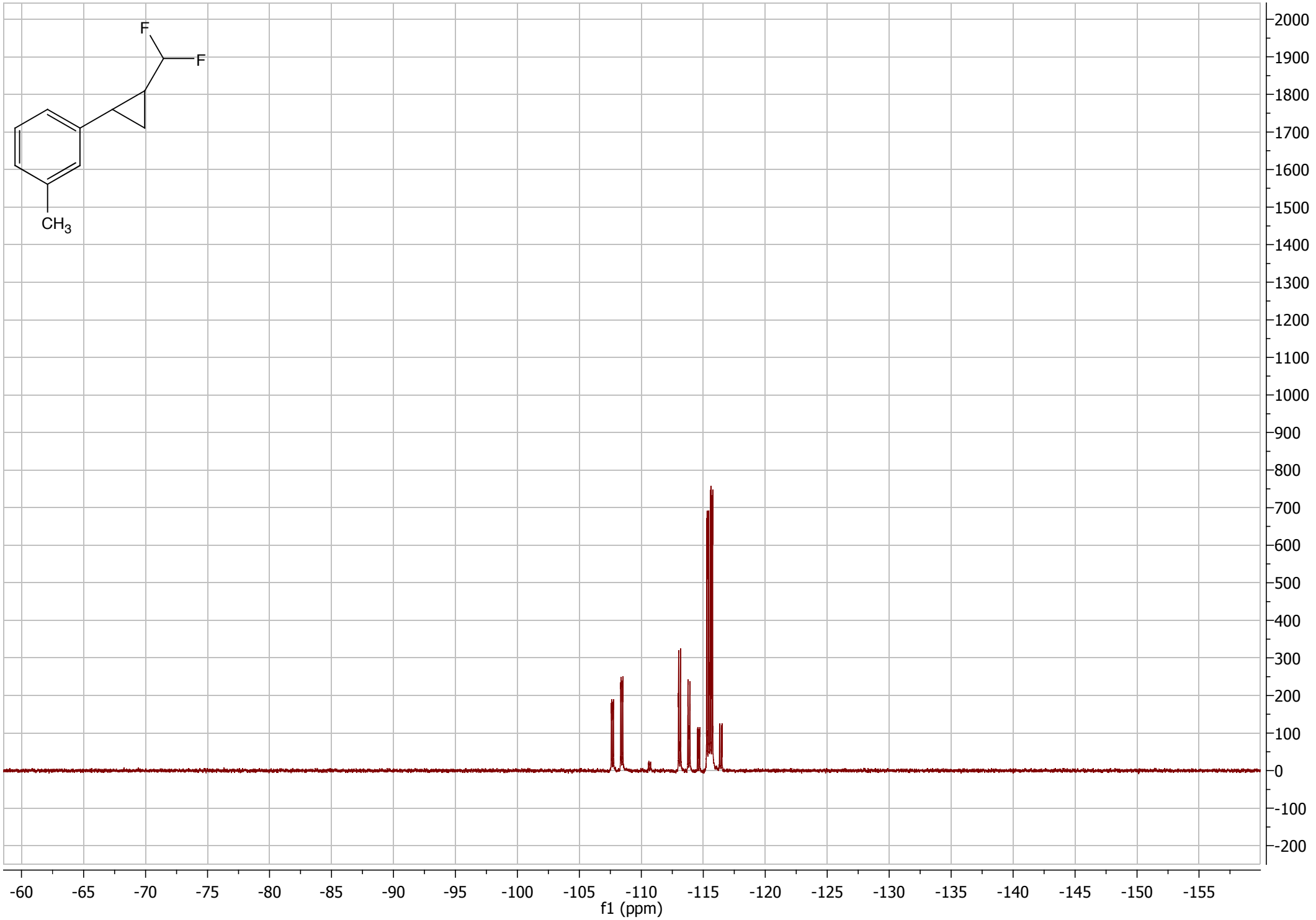

F
F
Cl
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

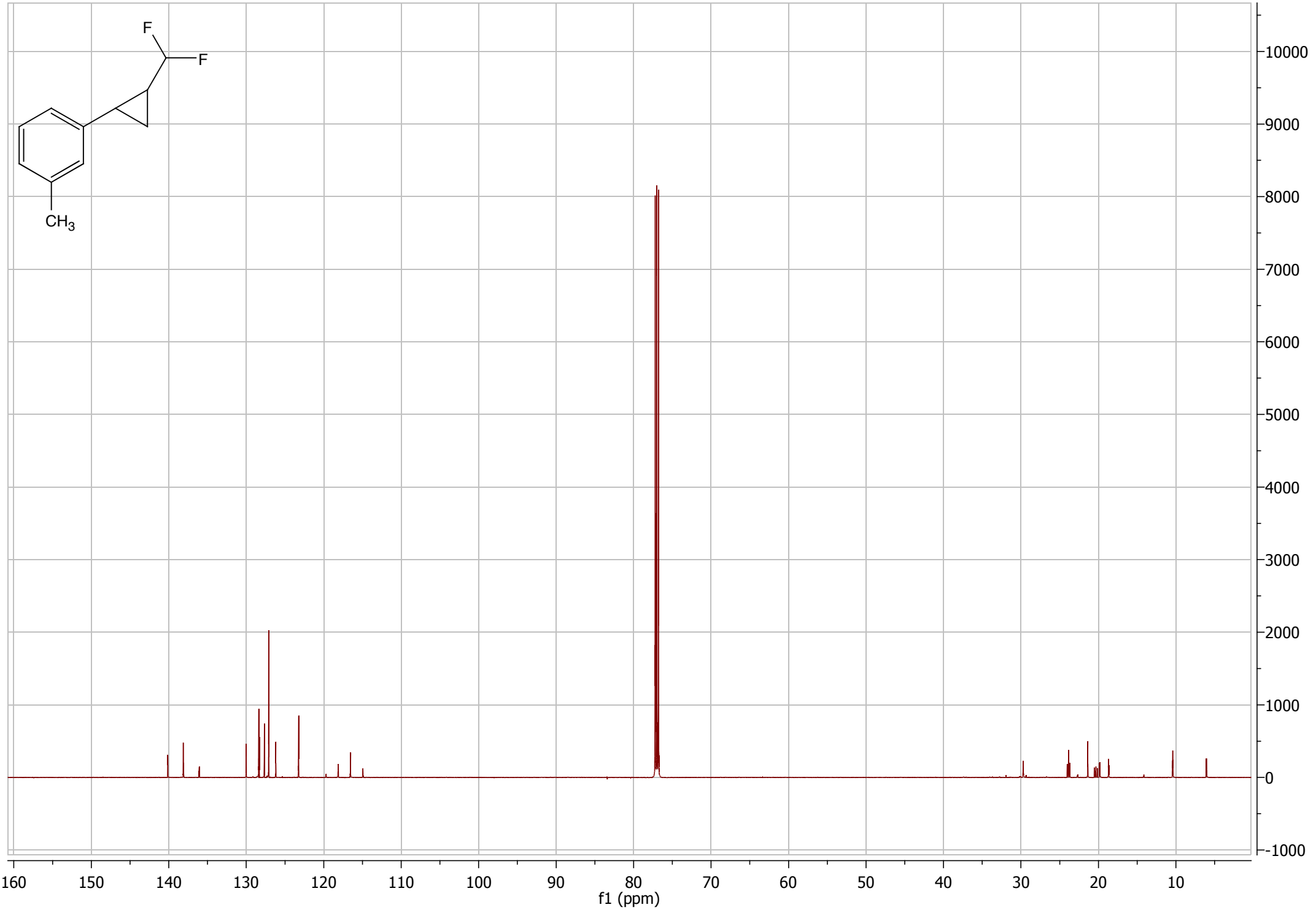

F
F
Br
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
1.60
0.67
0.96
0.55
0.41
0.93
1.14
1.58
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

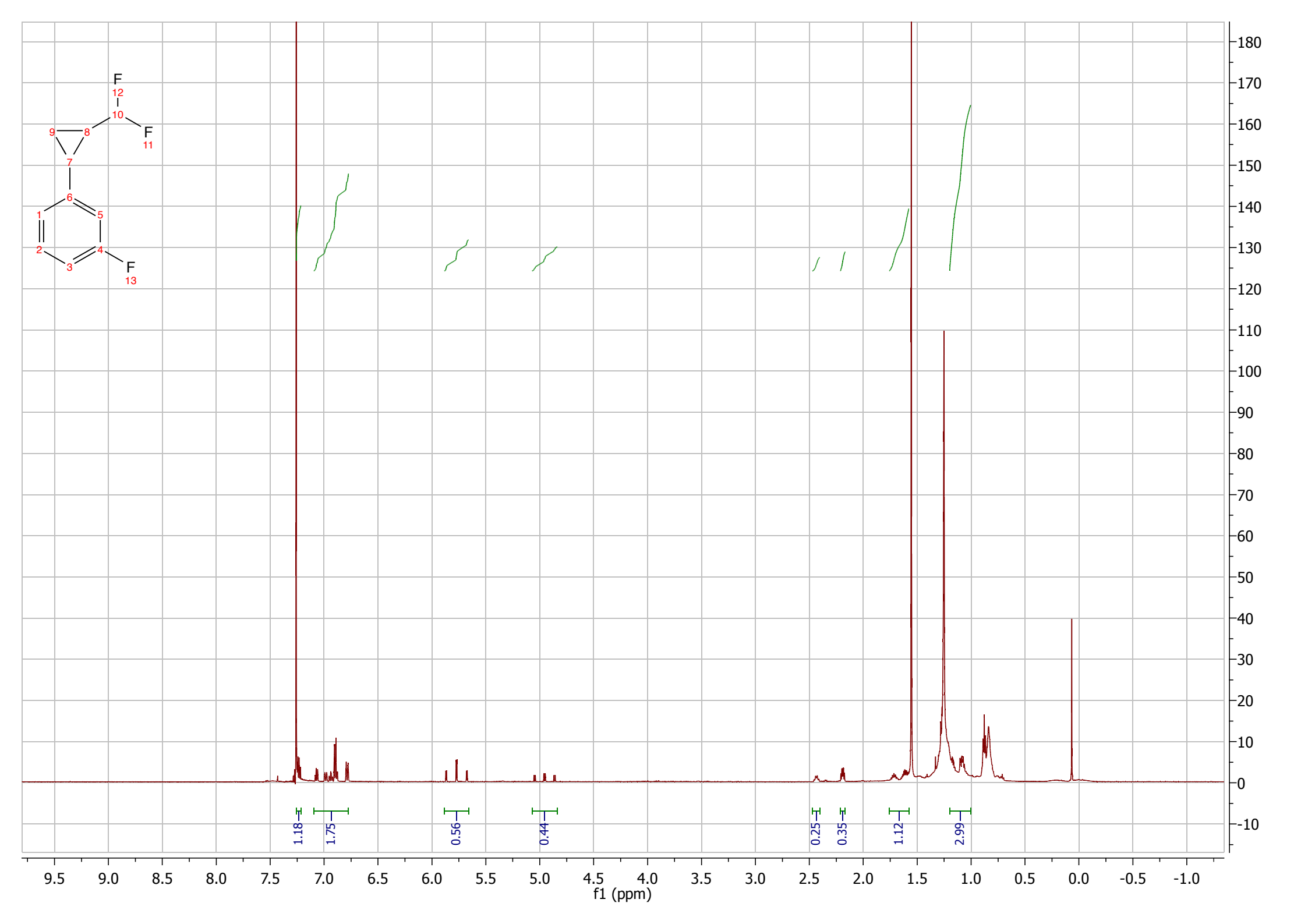

F
F
Br
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
f1 (ppm)

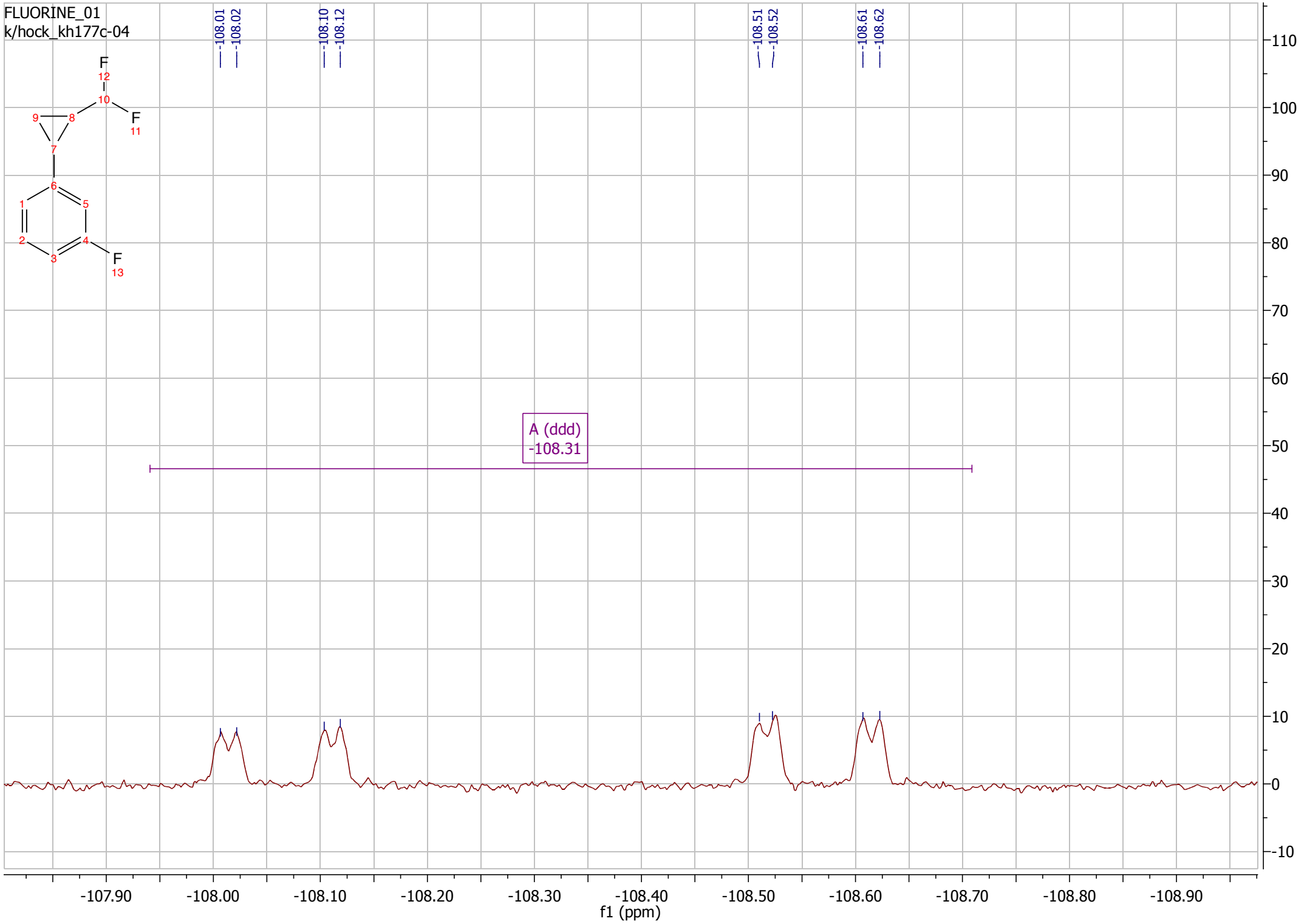

F
F
Br
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

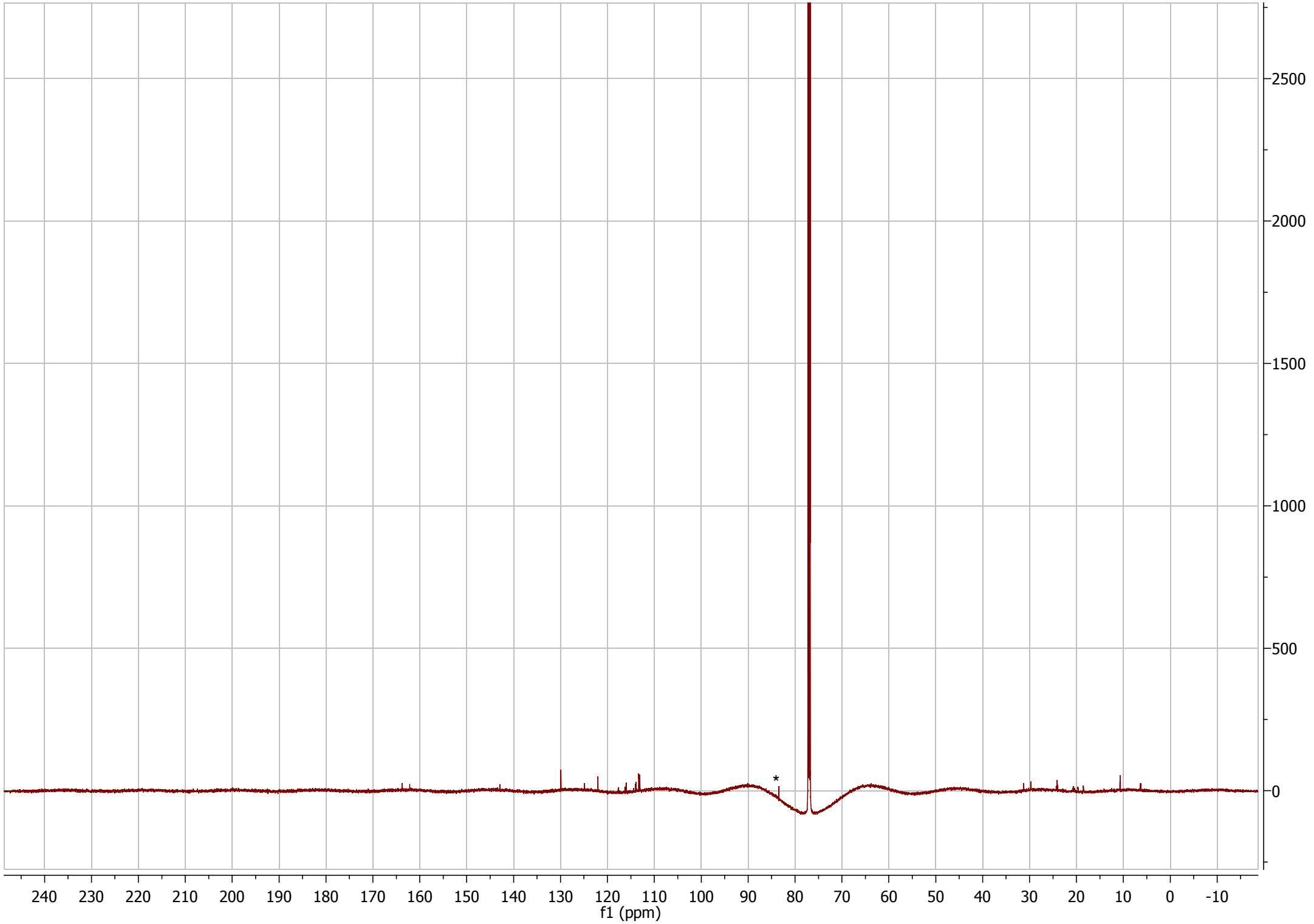

F
F
CH3
3.48
0.62
0.43
3.00
0.58
1.00
2.71
f1 (ppm)

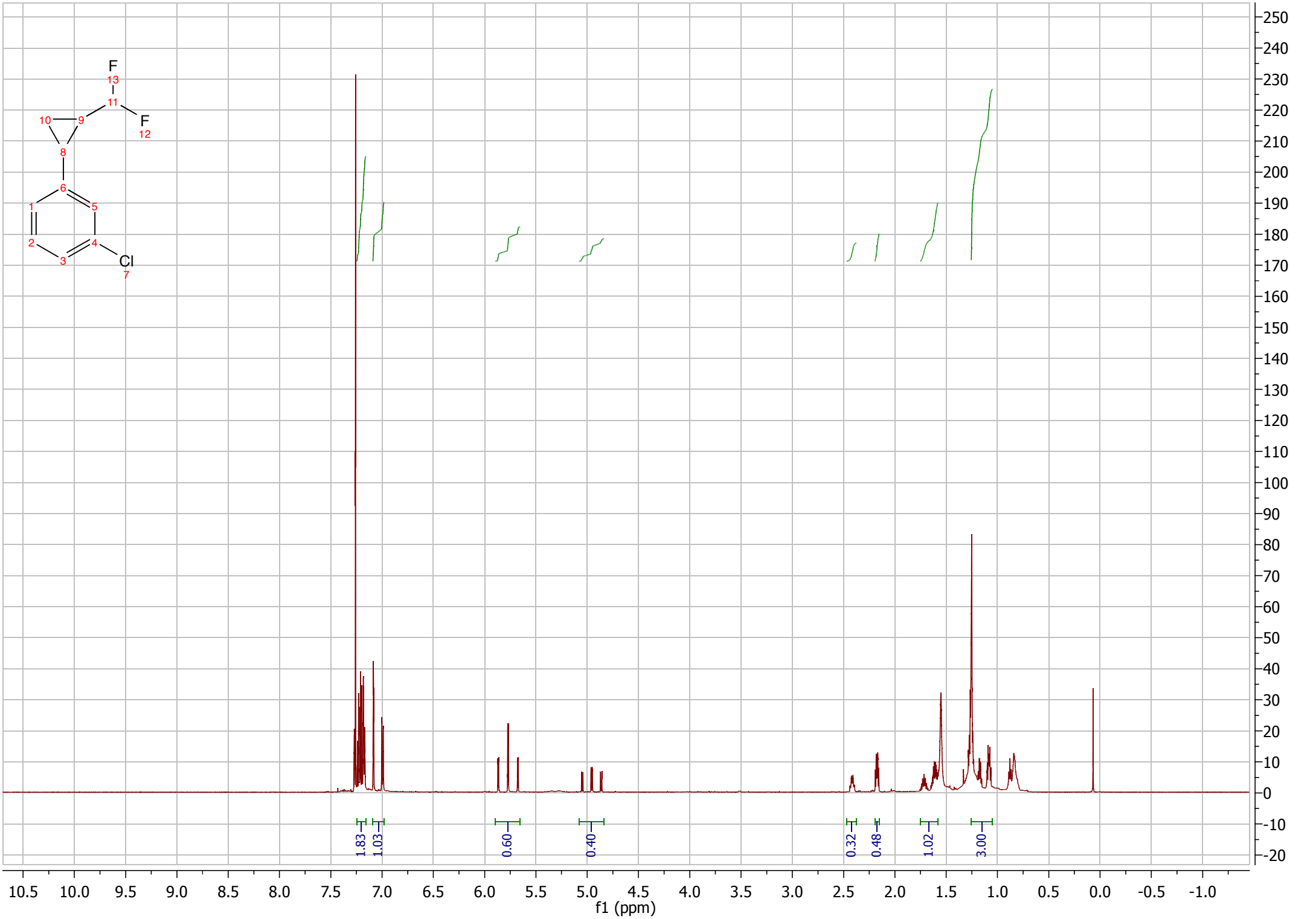

F
F
CH3
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
f1 (ppm)

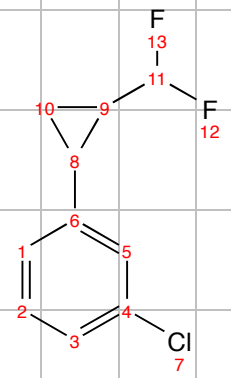

F
F
CH3
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


F
12
10
F
11
9
8
7
6
1
5
2
4
3
F
13
1.18
1.75
0.56
0.44
0.25
0.35
1.12
2.99
f1 (ppm)

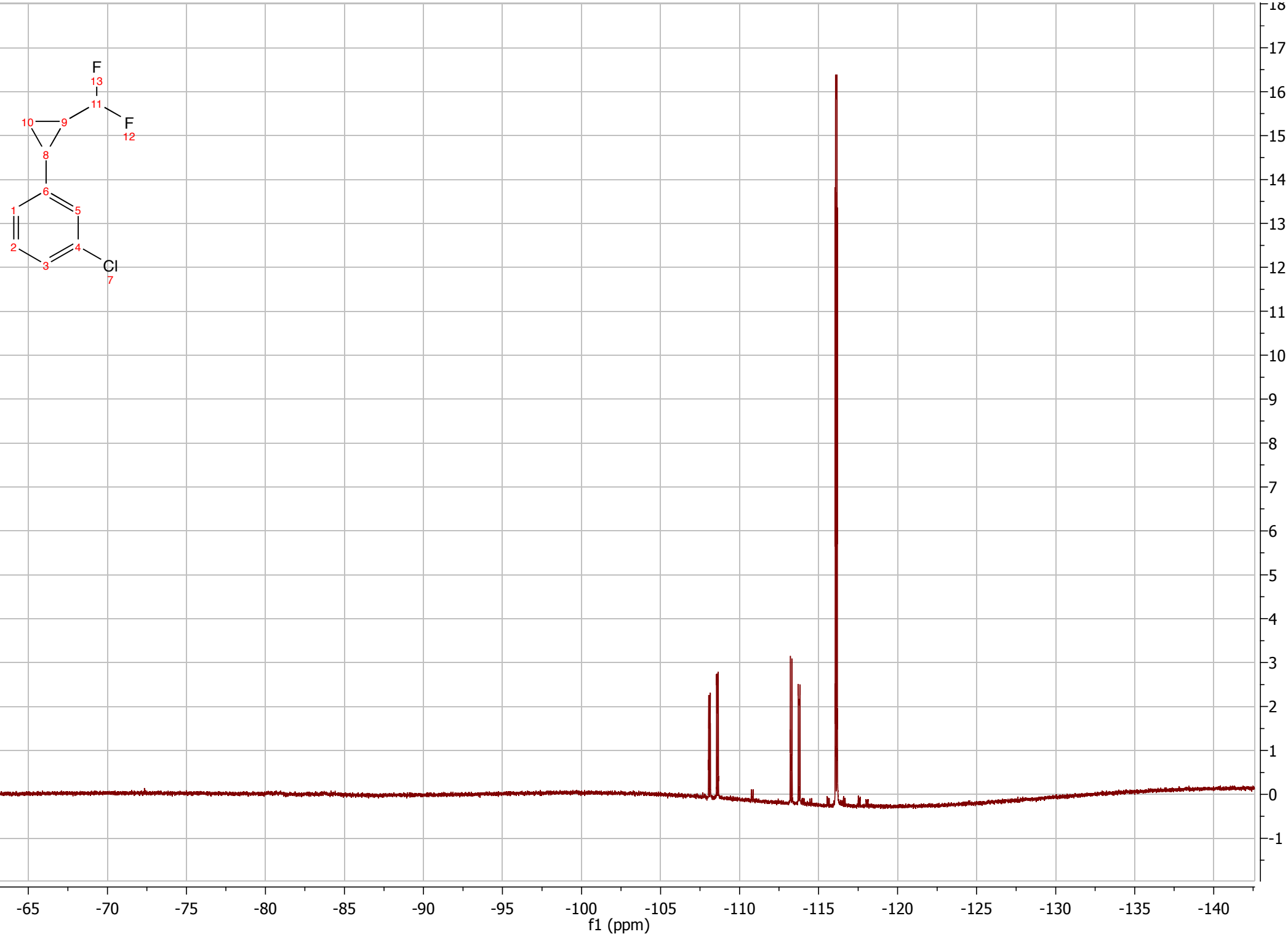

FLUORINE_01
k/hock_kh177c-04
-108.01
-108.02
-108.10
-108.12
-108.51
-108.52
-108.61
-108.62
A (ddd)
-108.31
F
12
10
F
11
9
8
7
6
1
5
2
4
3
F
13
110
100
90
80
70
60
50
40
30
20
10
0
-10
-107.90
-108.00
-108.10
-108.20
-108.30
-108.40
-108.50
-108.60
-108.70
-108.80
-108.90
f1 (ppm)

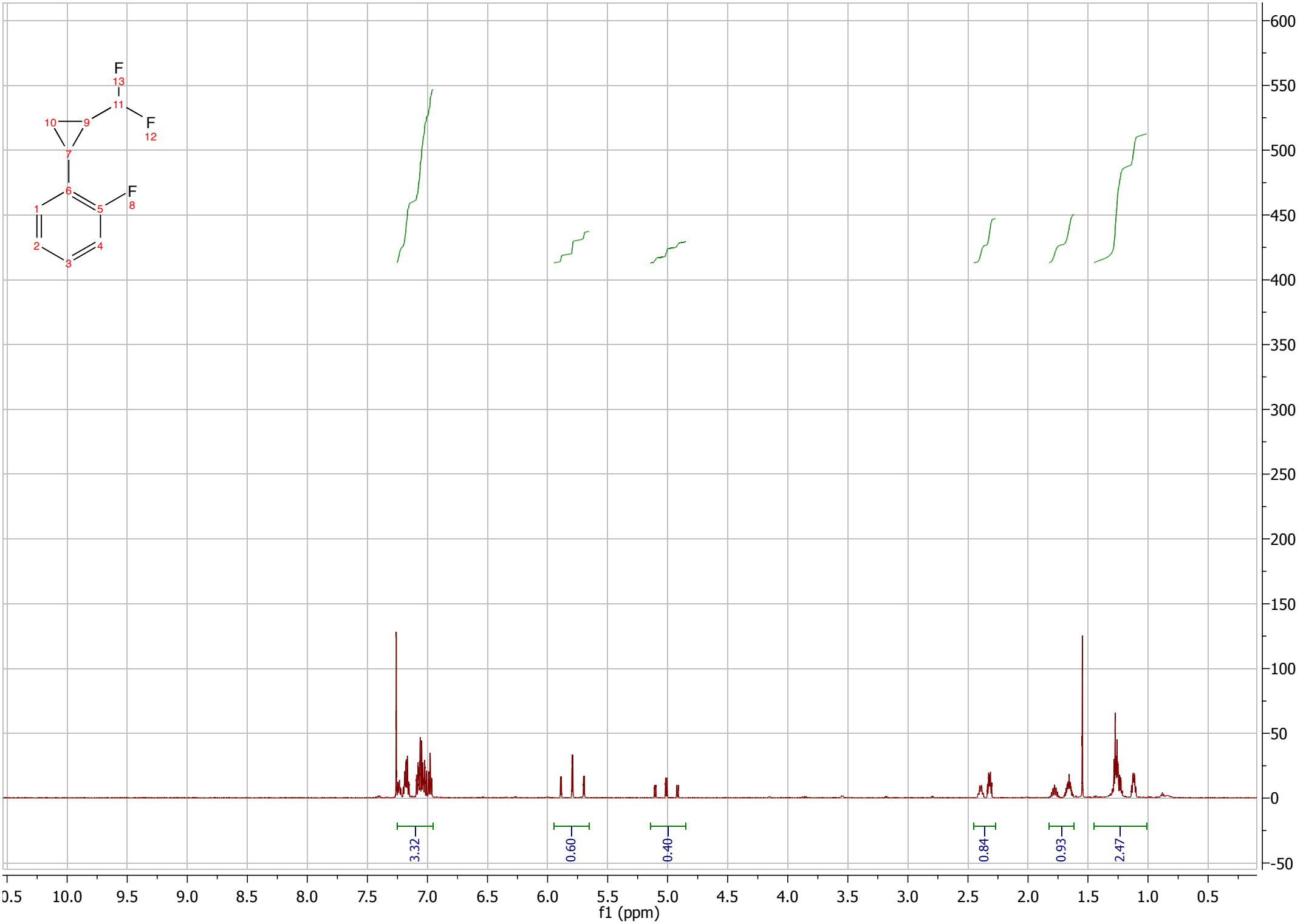

2500
2000
1500
1000
500
0
*
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

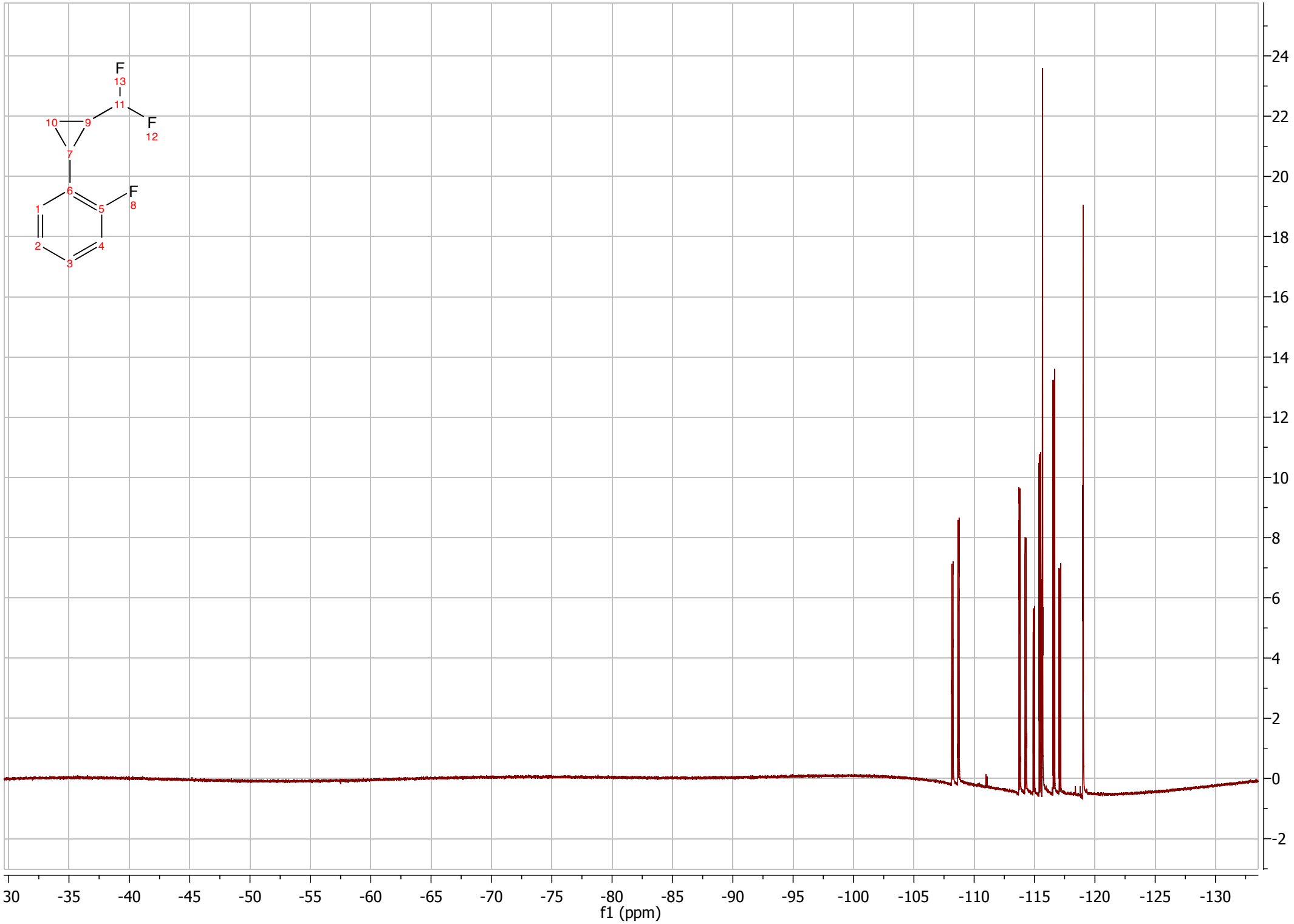

F
13
11
F
12
10
9
8
6
1
5
2
4
3
Cl
7
1.83
1.03
0.60
0.40
0.32
0.48
1.02
3.00
f1 (ppm)

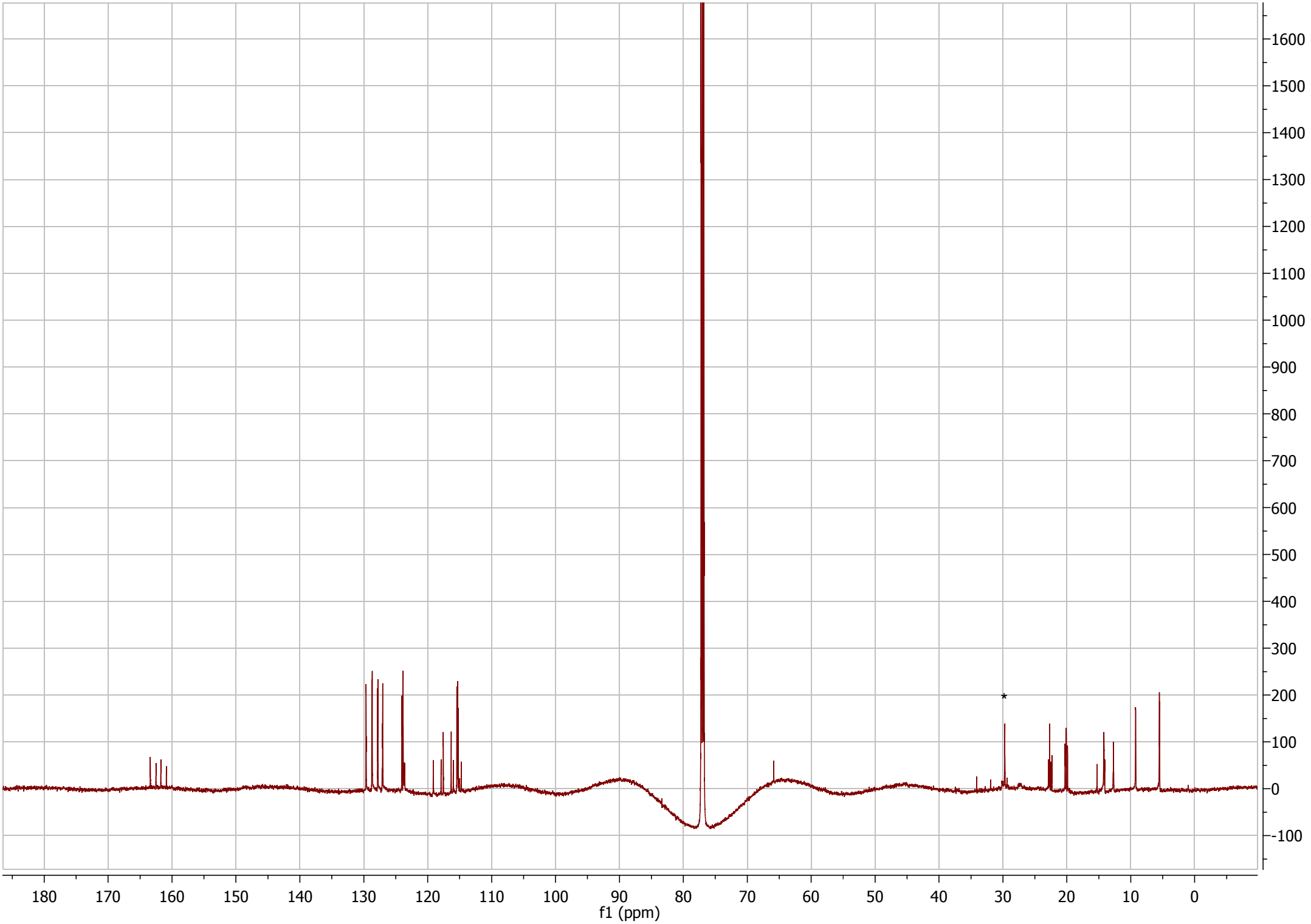

F
13
11
10
9
F
12
8
6
1
5
2
4
3
Cl
7

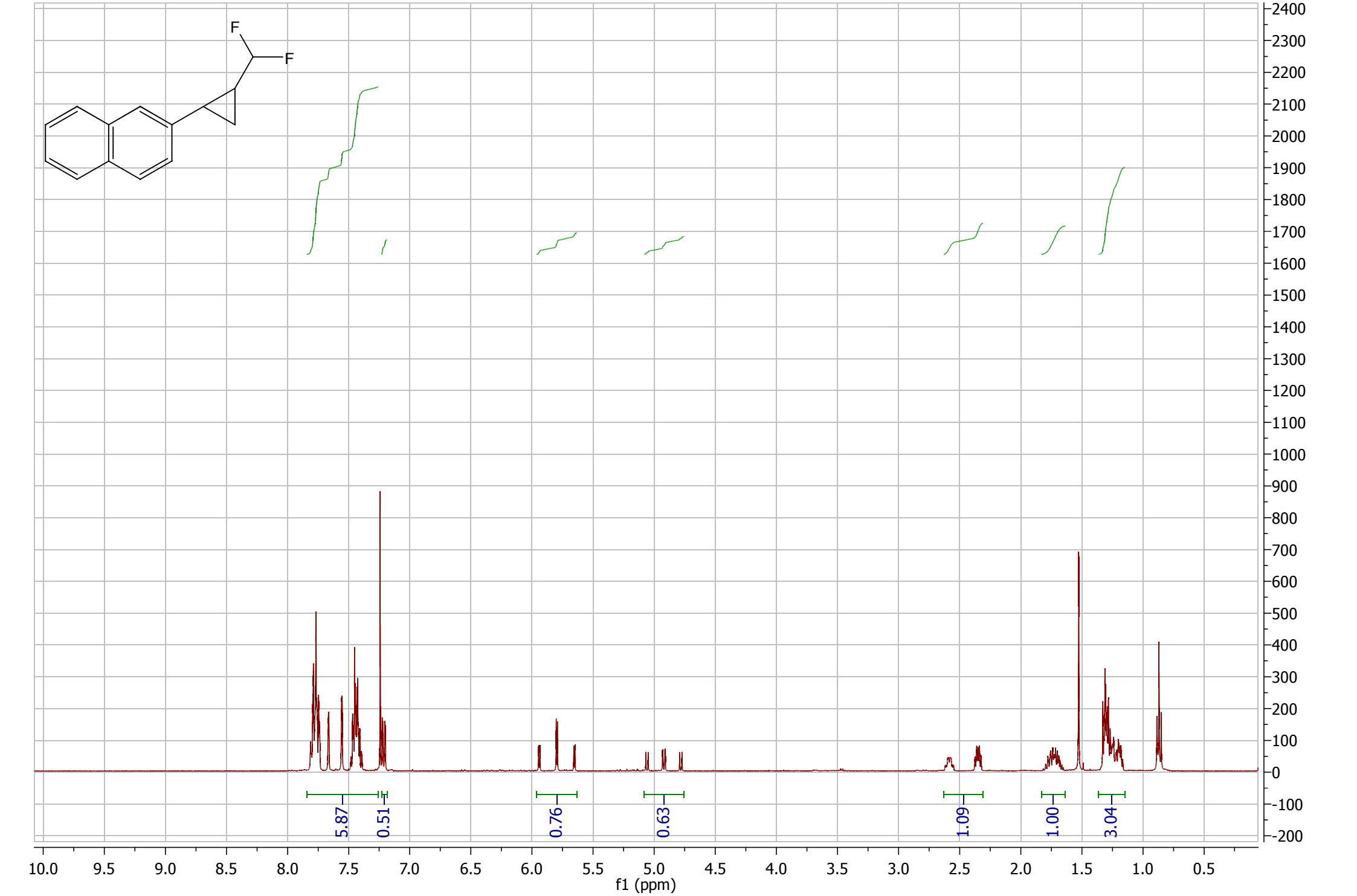
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

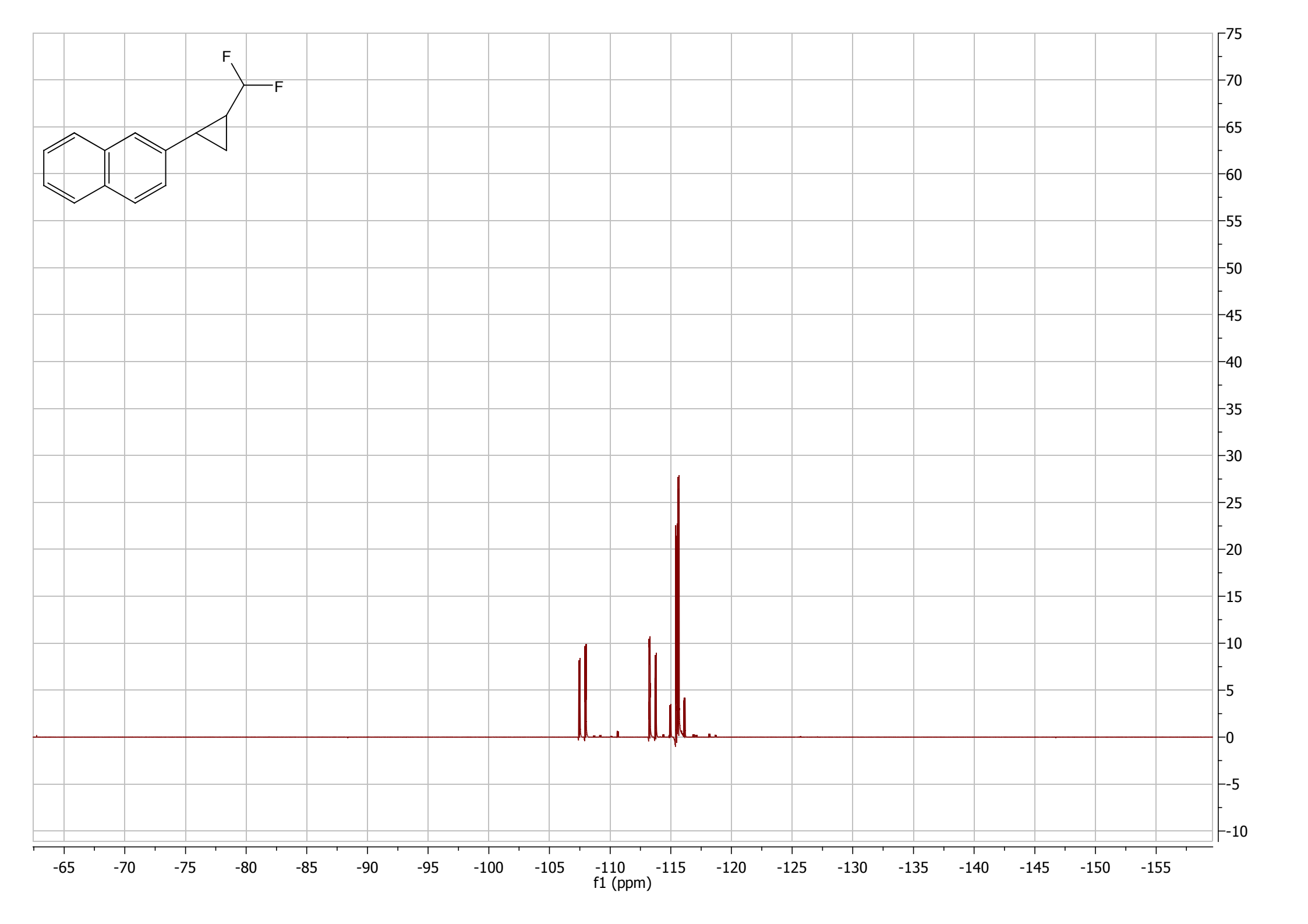

F
13
11
10
9
F
12
8
6
1
5
2
4
3
Cl
7
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
f1 (ppm)
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

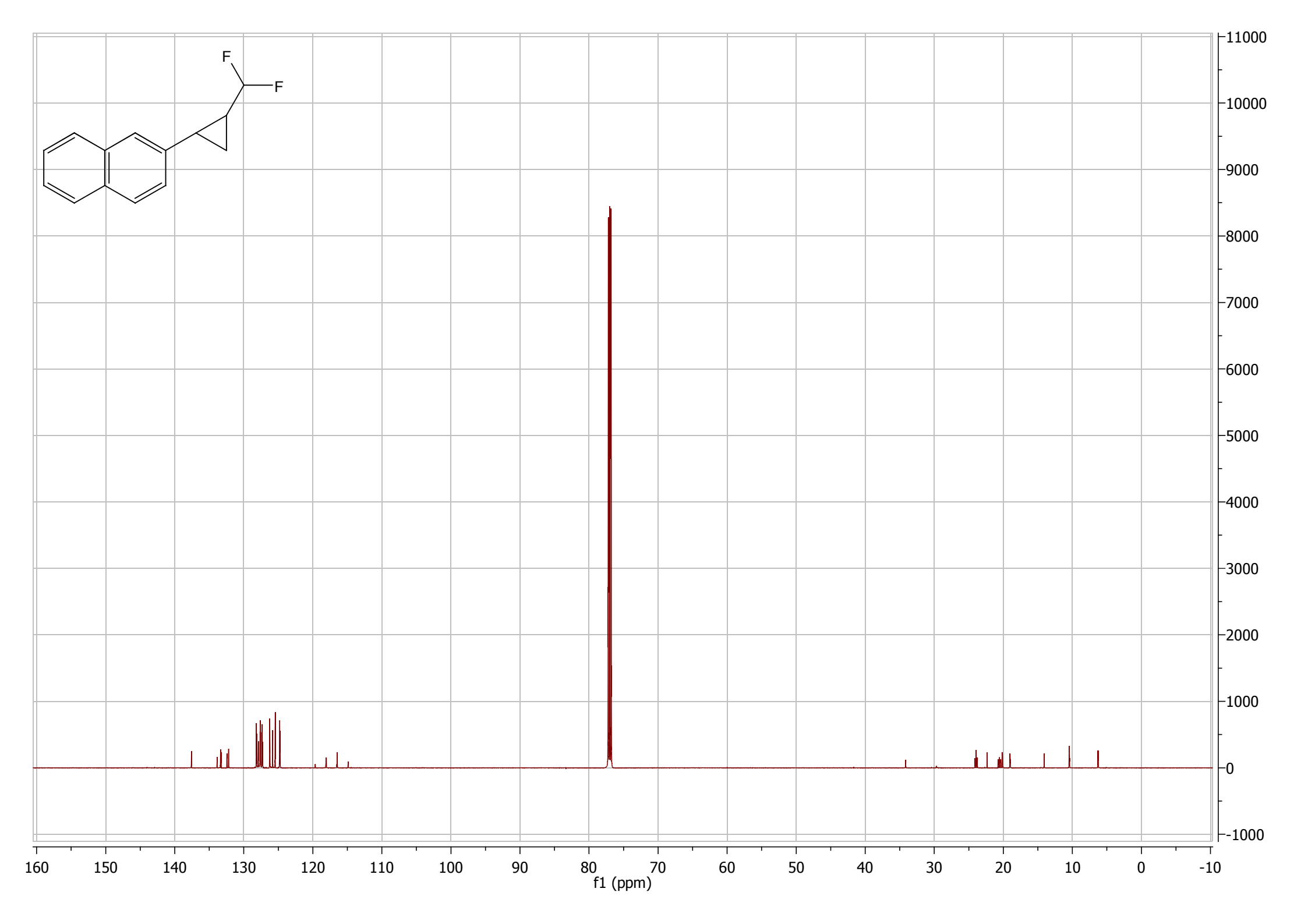

F
13
11
10
9
F
12
7
6
F
8
1
5
2
4
3
3.32
0.60
0.40
0.84
0.93
2.47
f1 (ppm)

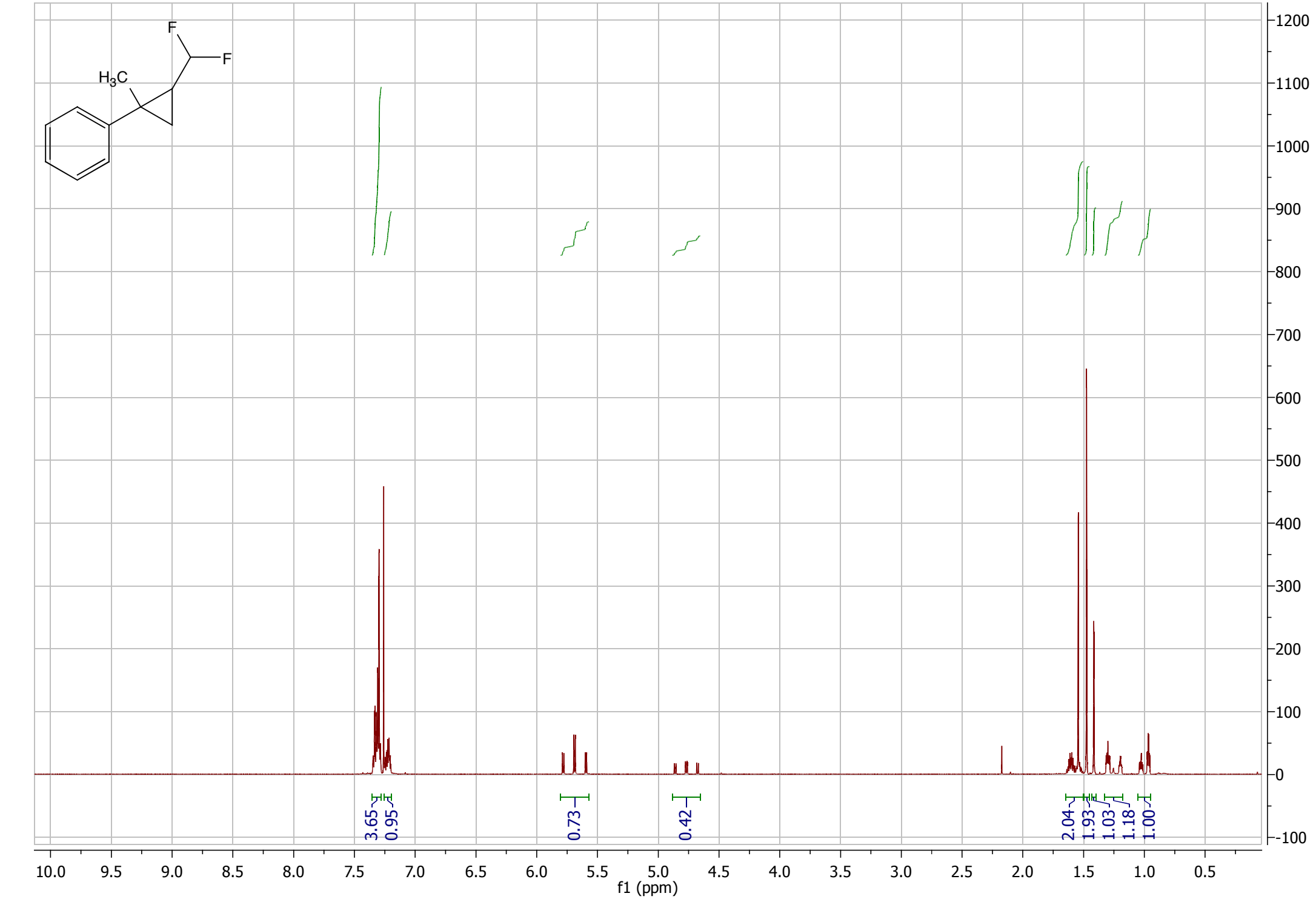

F
13
11
10
9
F
12
7
6
F
8
1
5
2
4
3
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
f1 (ppm)

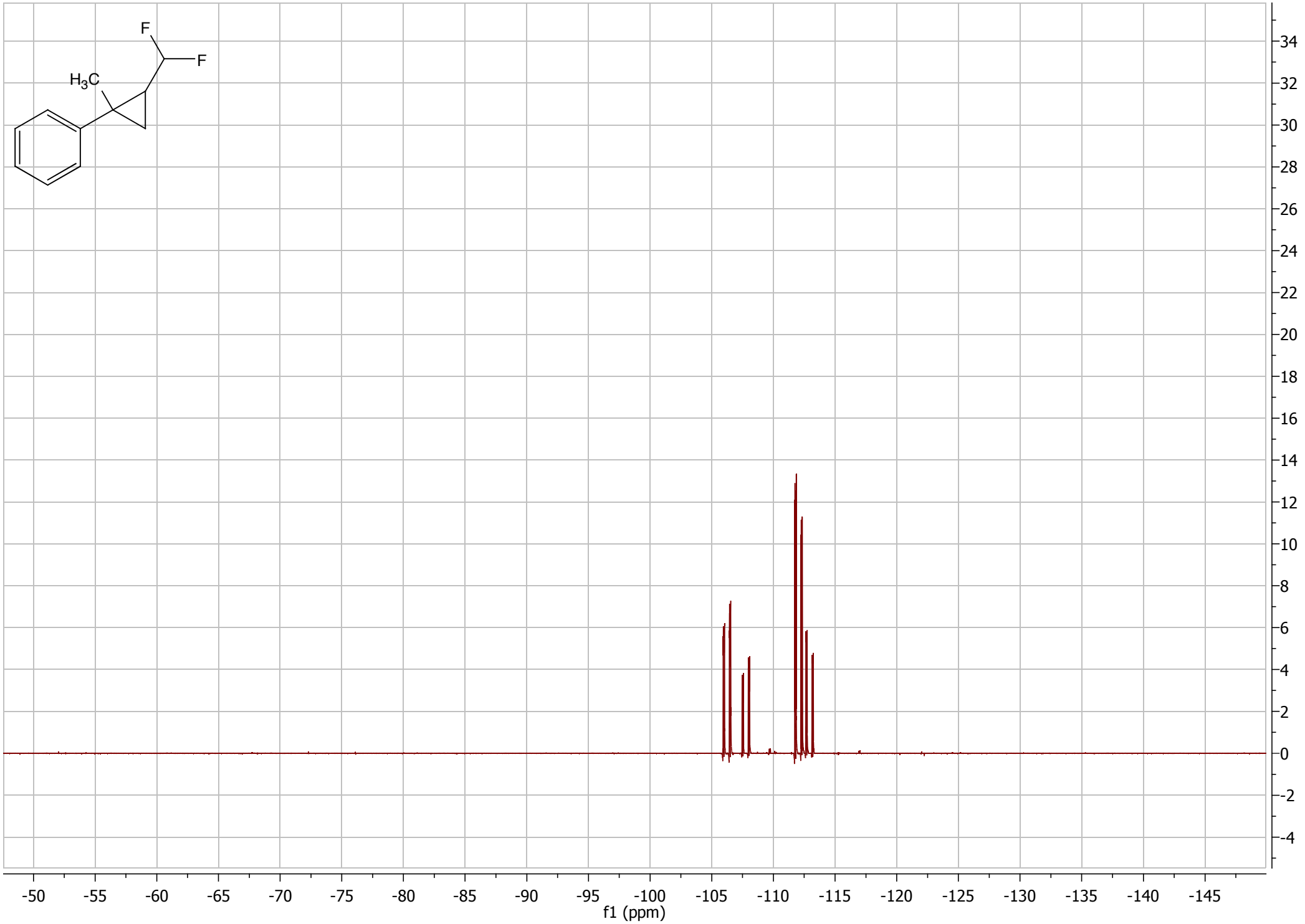

1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
*
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

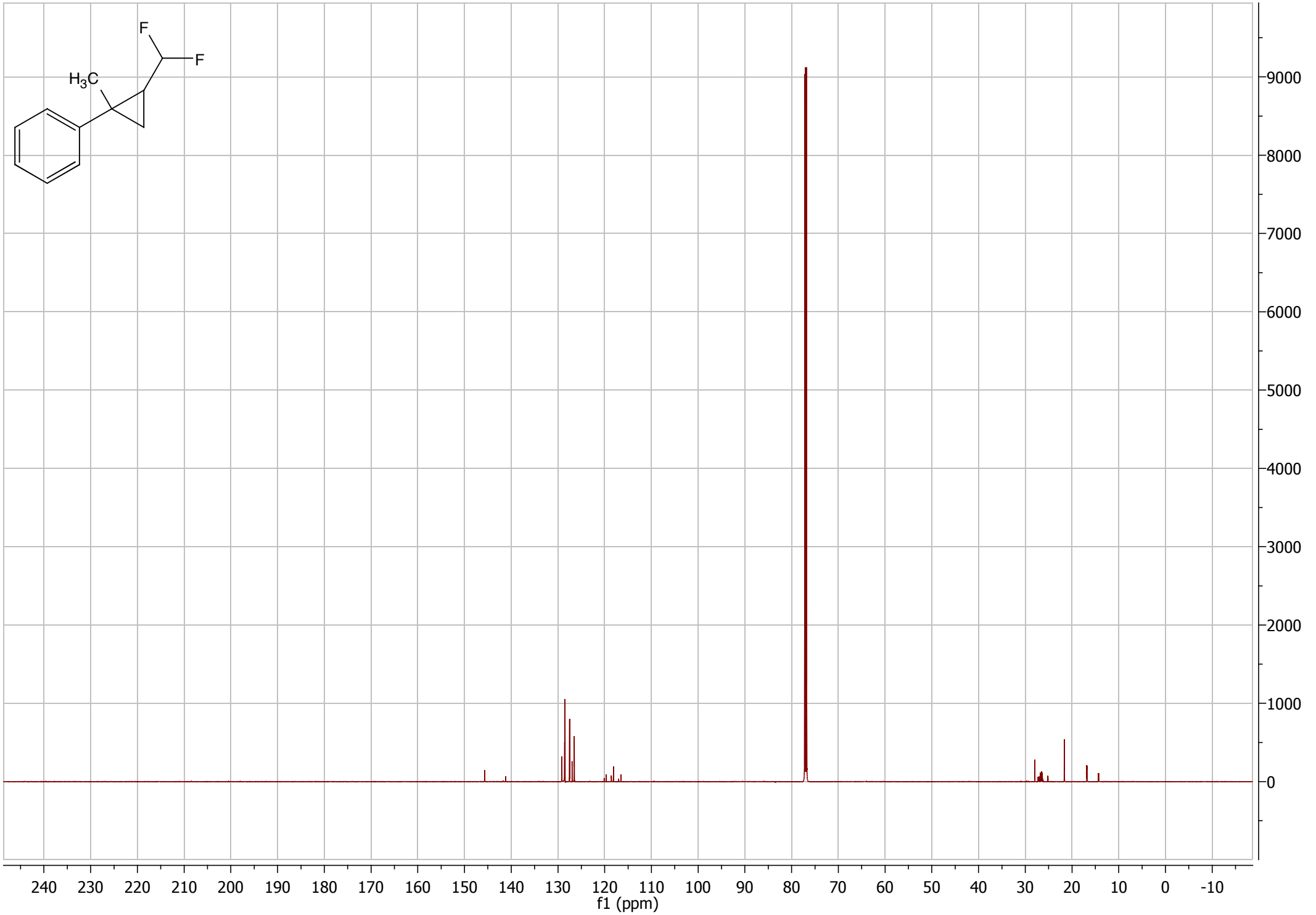

F
F
5.87
0.51
0.76
0.63
1.09
1.00
3.04
f1 (ppm)

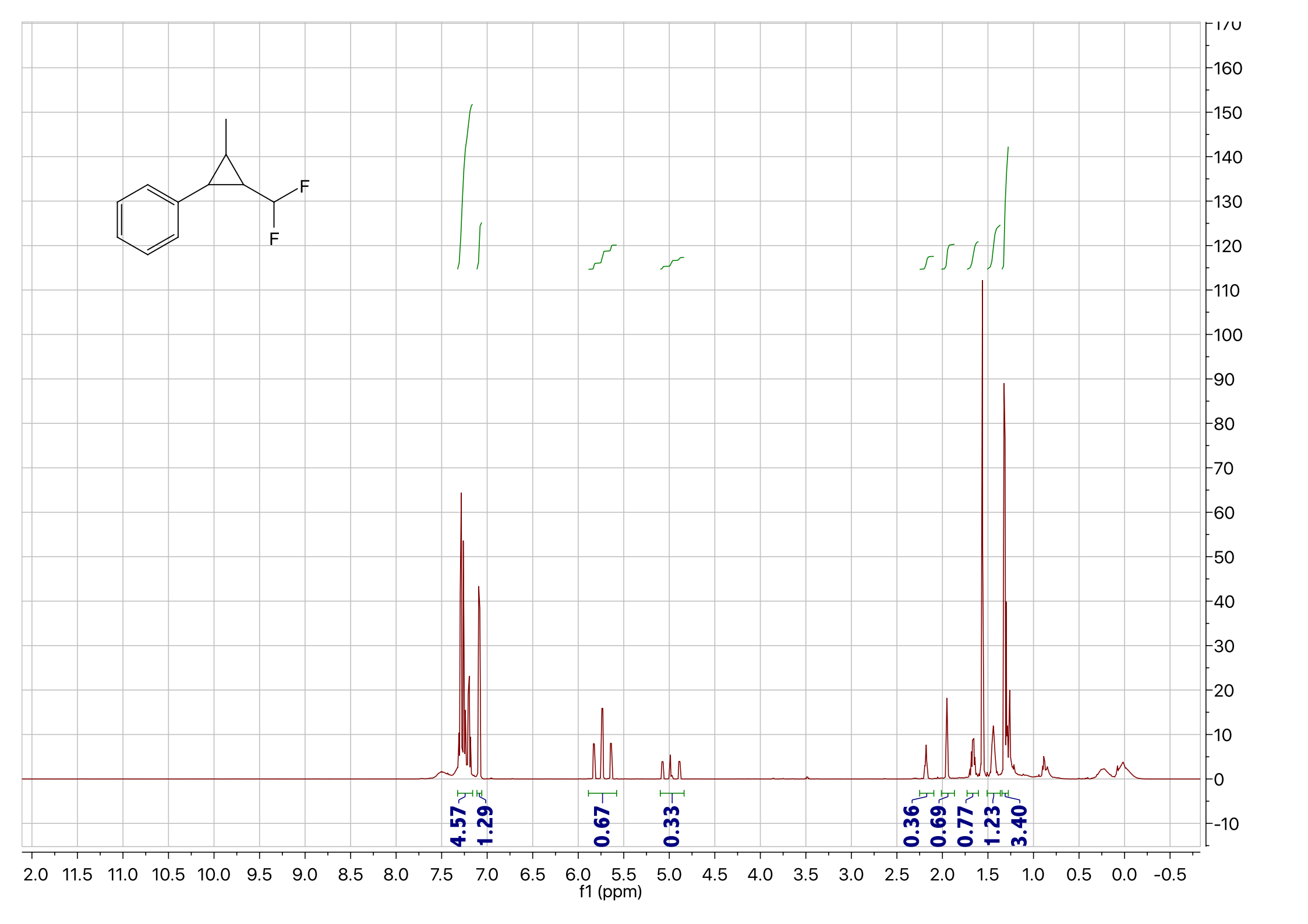

F
F
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
f1 (ppm)

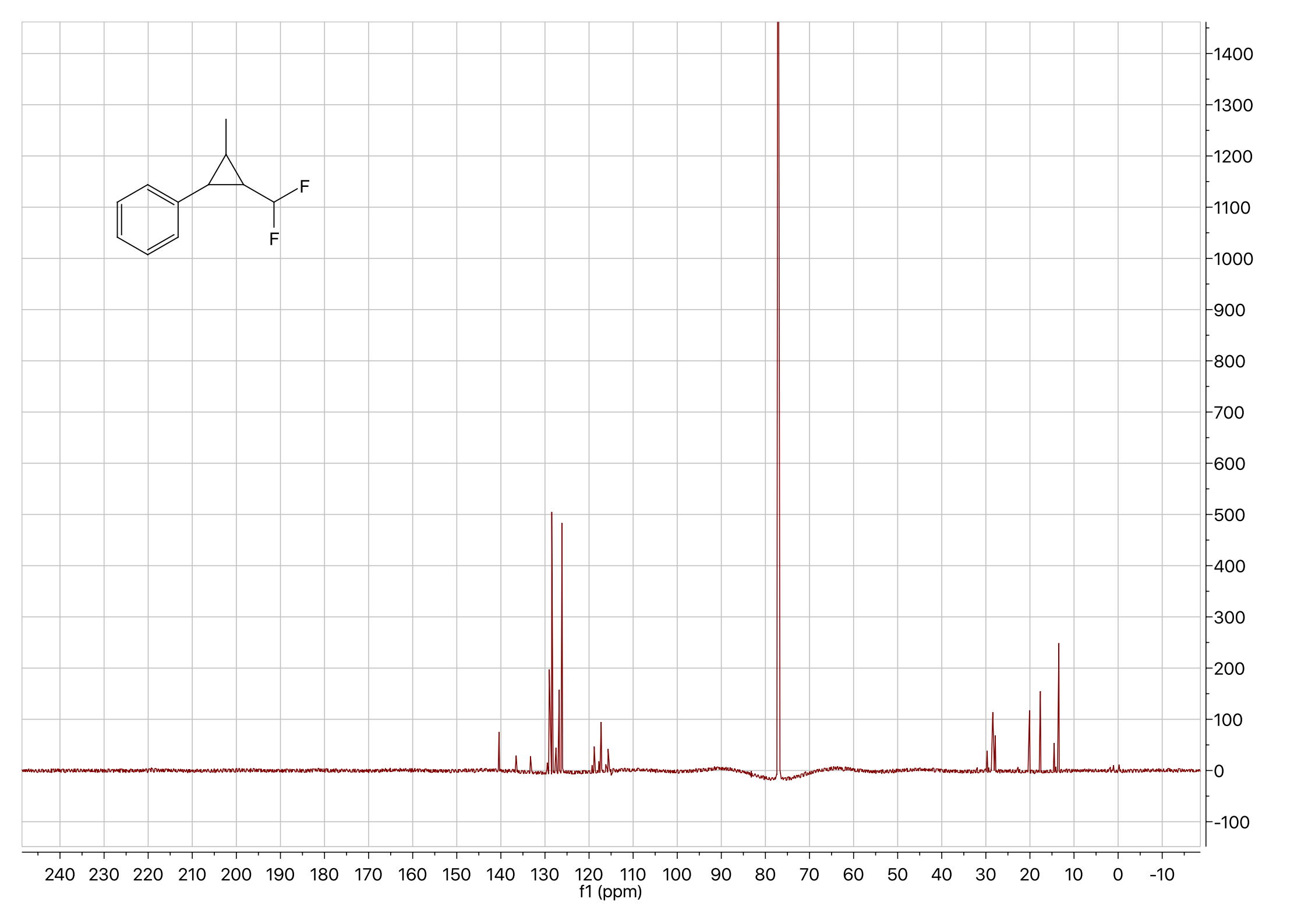

F
F
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

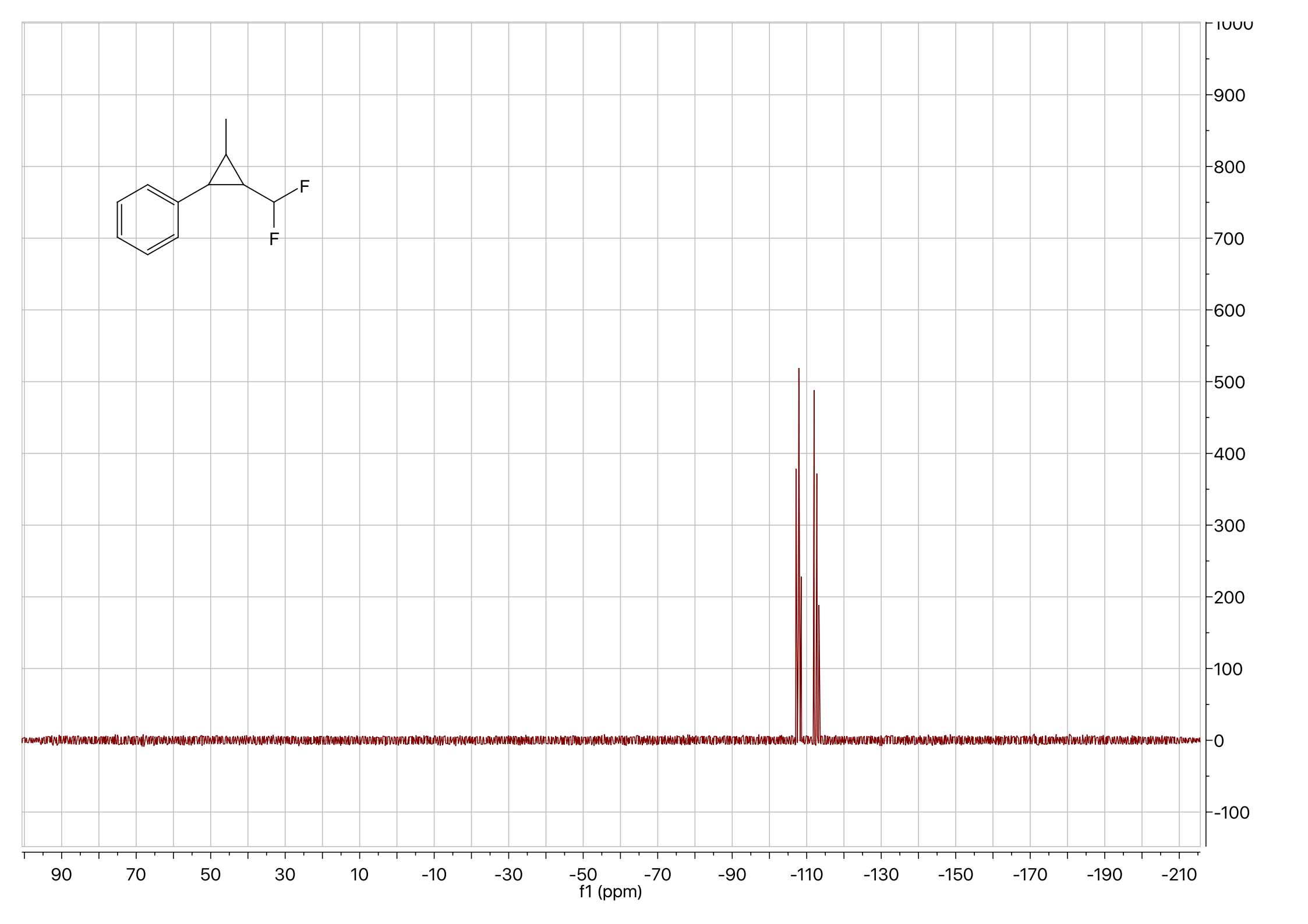

F
F
H3C
3.65
0.95
0.73
0.42
2.04
1.93
1.03
1.18
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

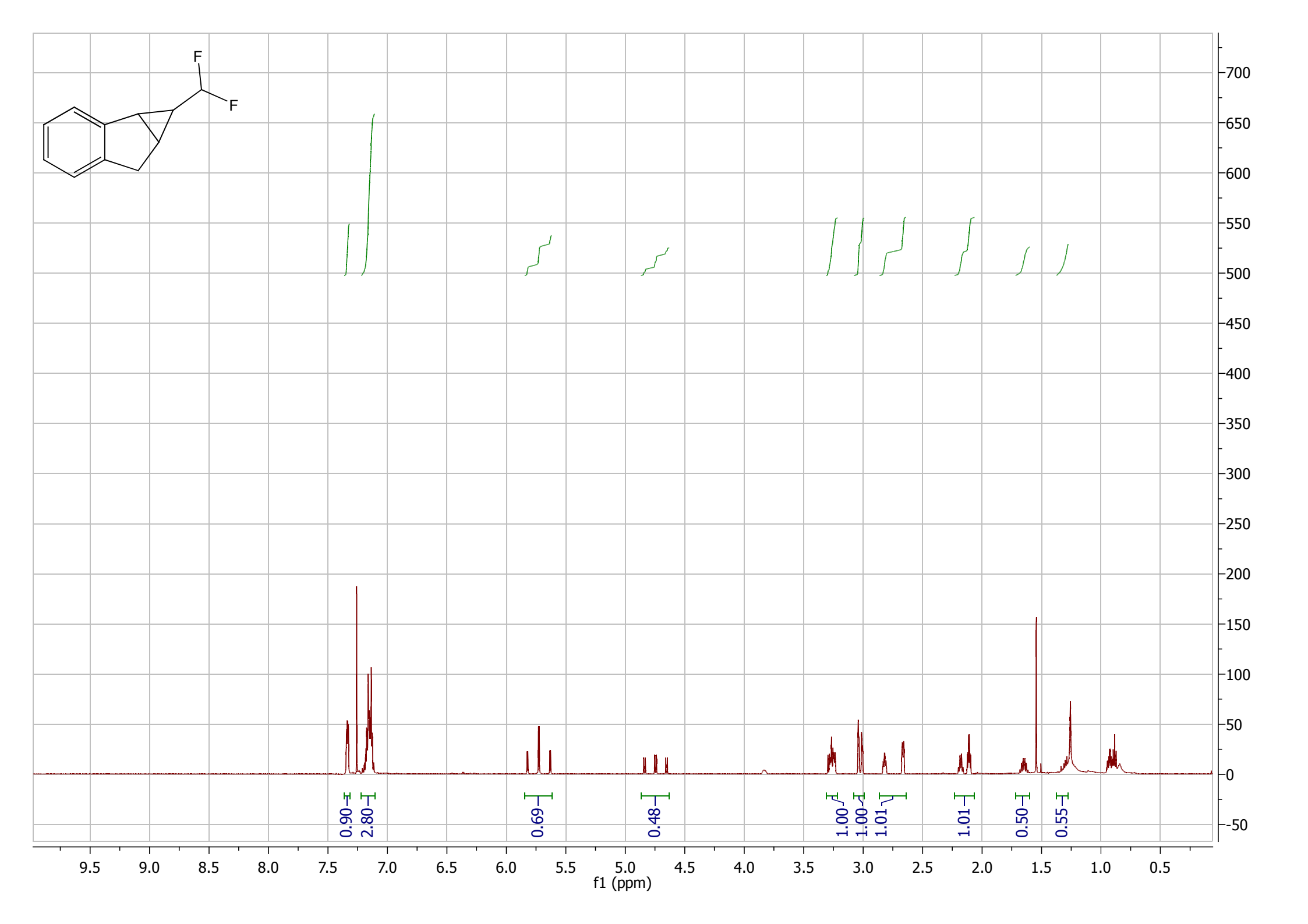

F
F
H3C
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
-4
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
f1 (ppm)

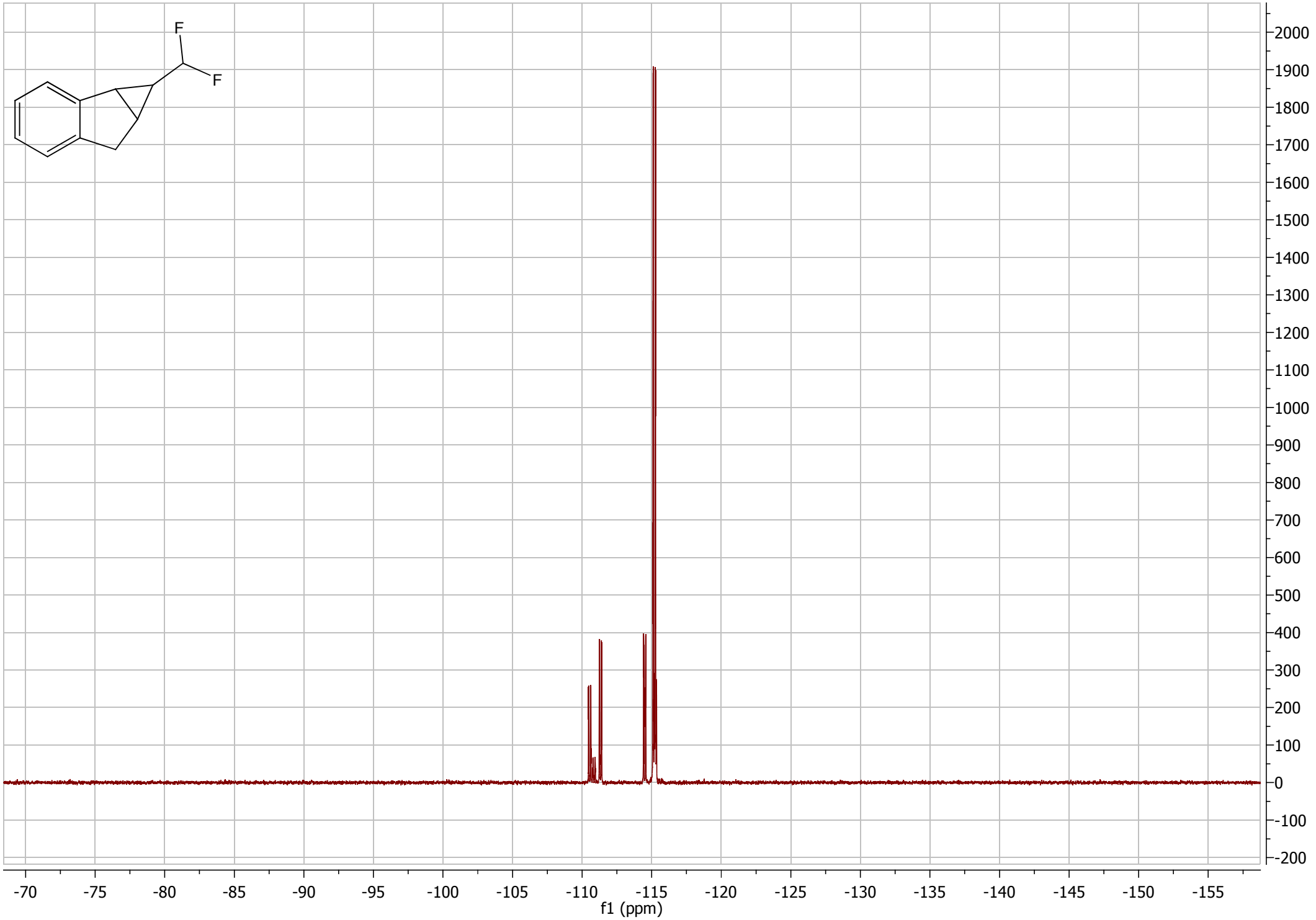

F
F
H3C
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

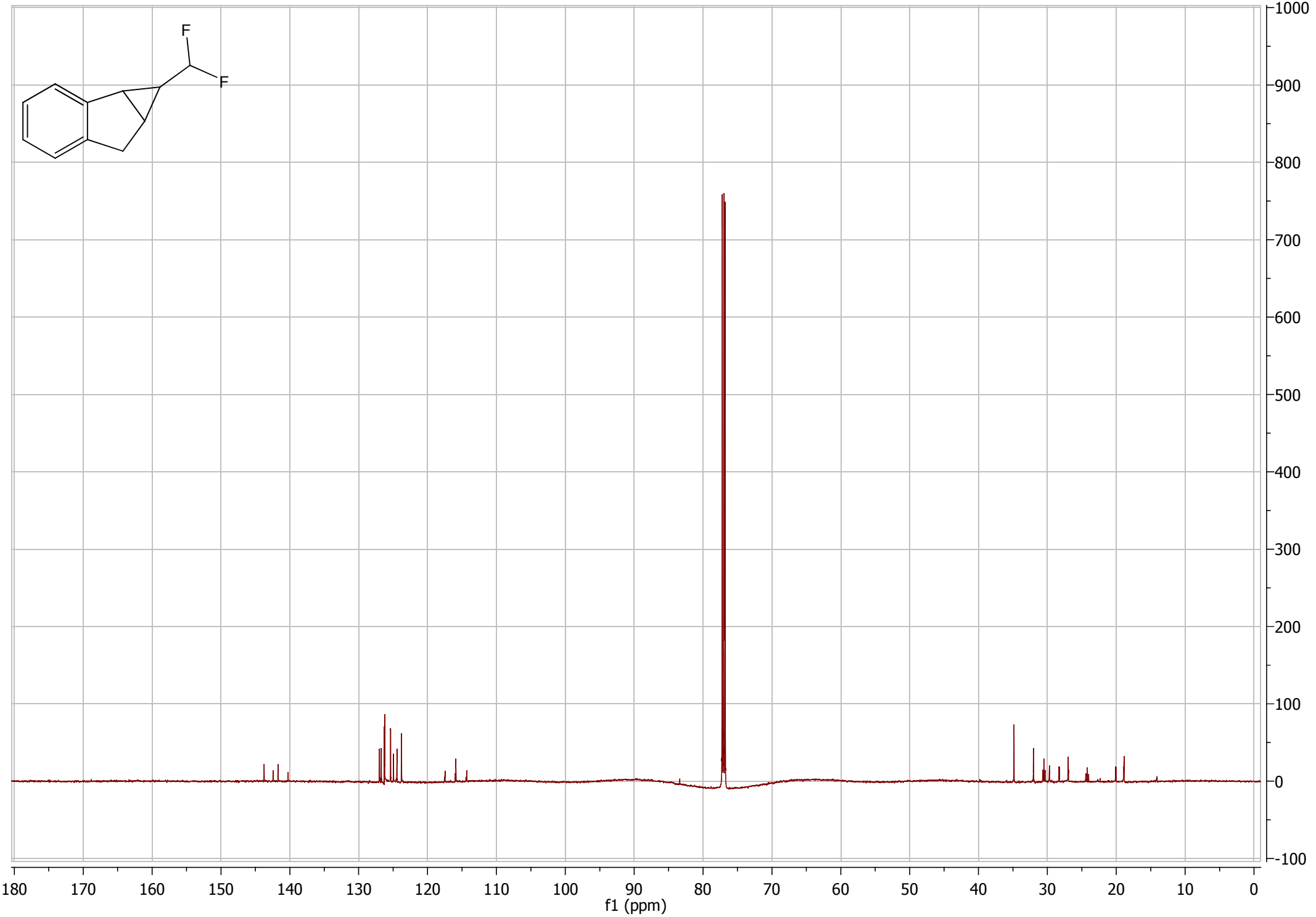

F
F
4.57
1.29
0.67
0.33
0.36
0.69
0.77
1.23
3.40
f1 (ppm)

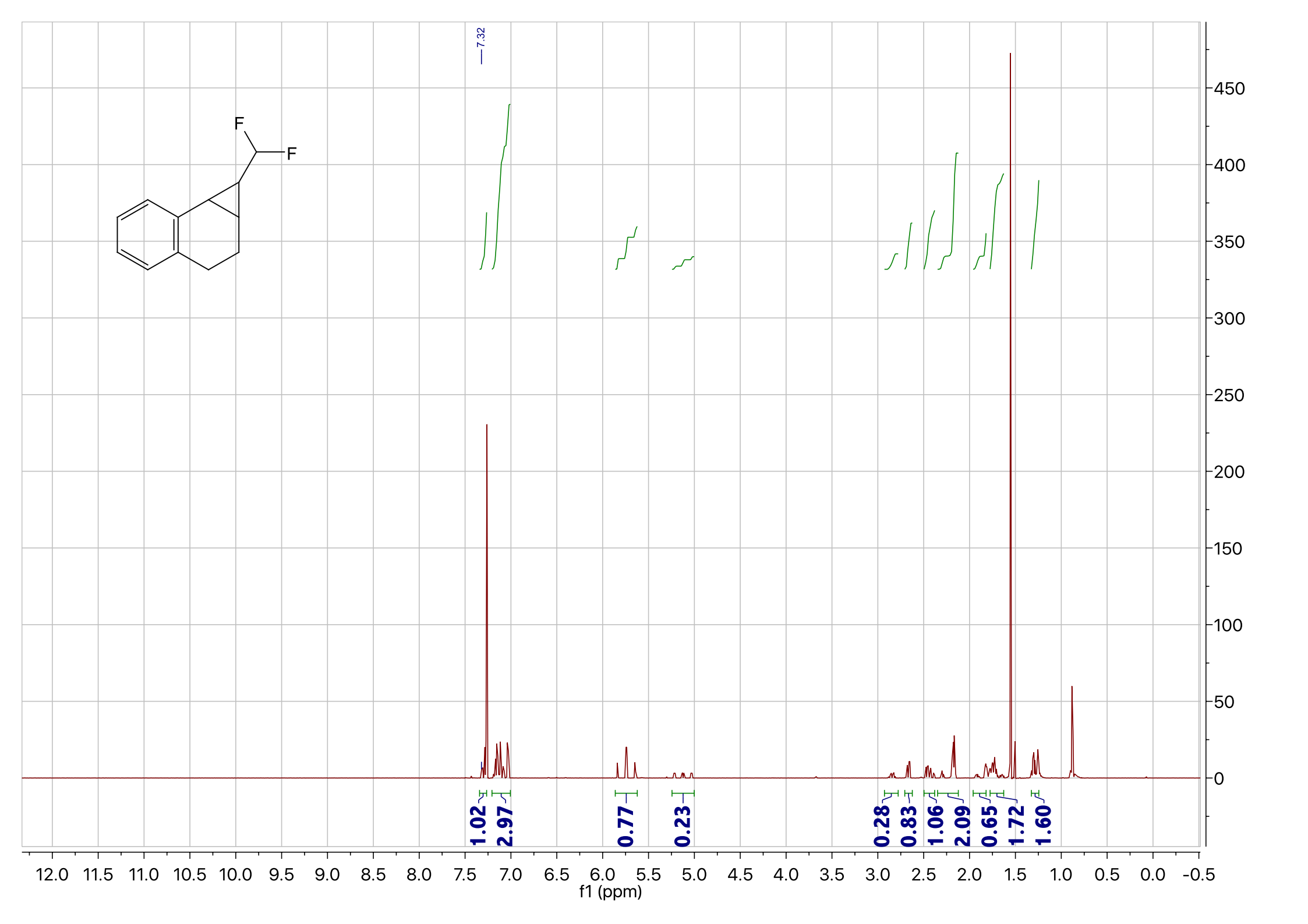

F
F
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

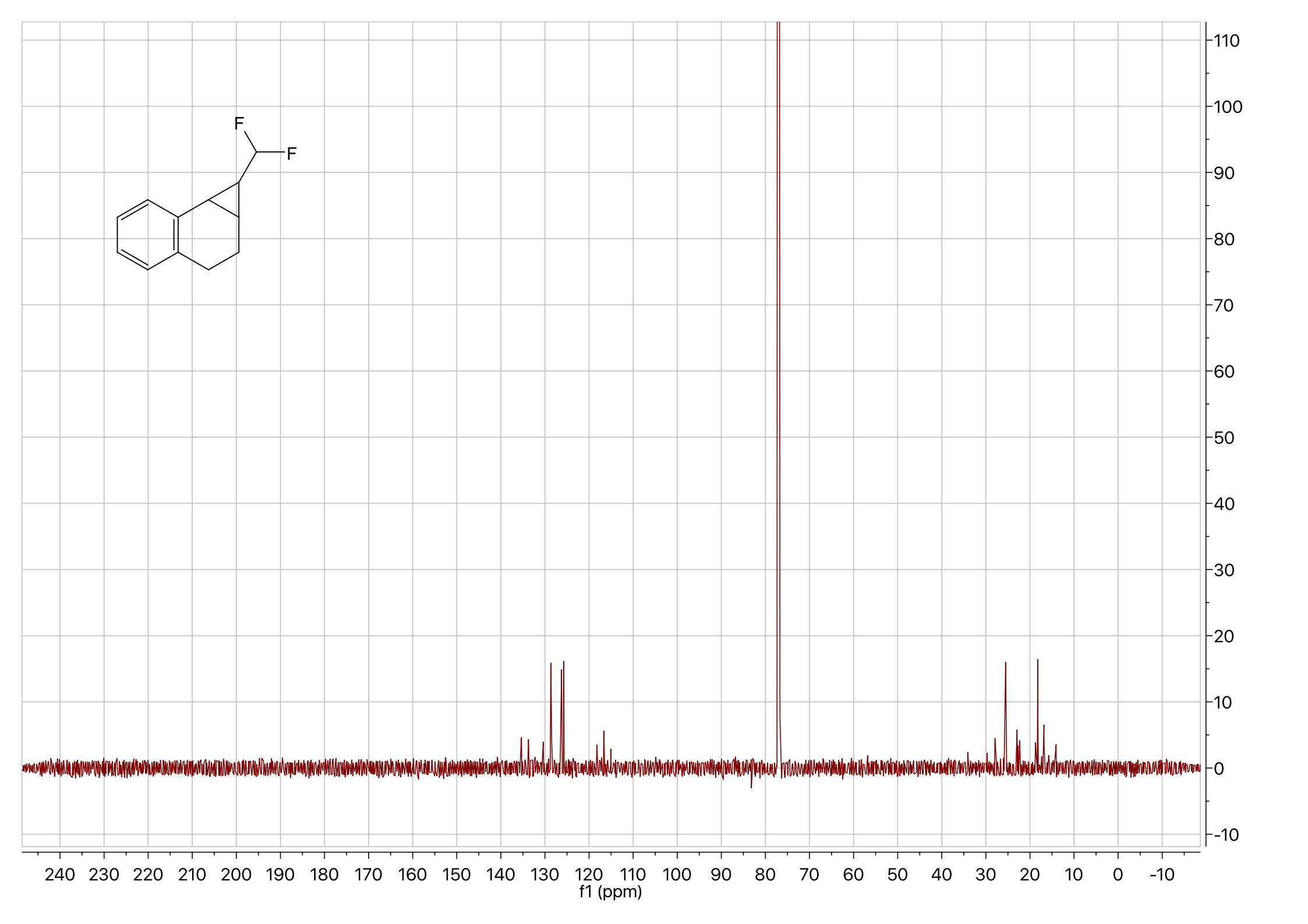

F
F
1000
900
800
700
600
500
400
300
200
100
0
-100
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

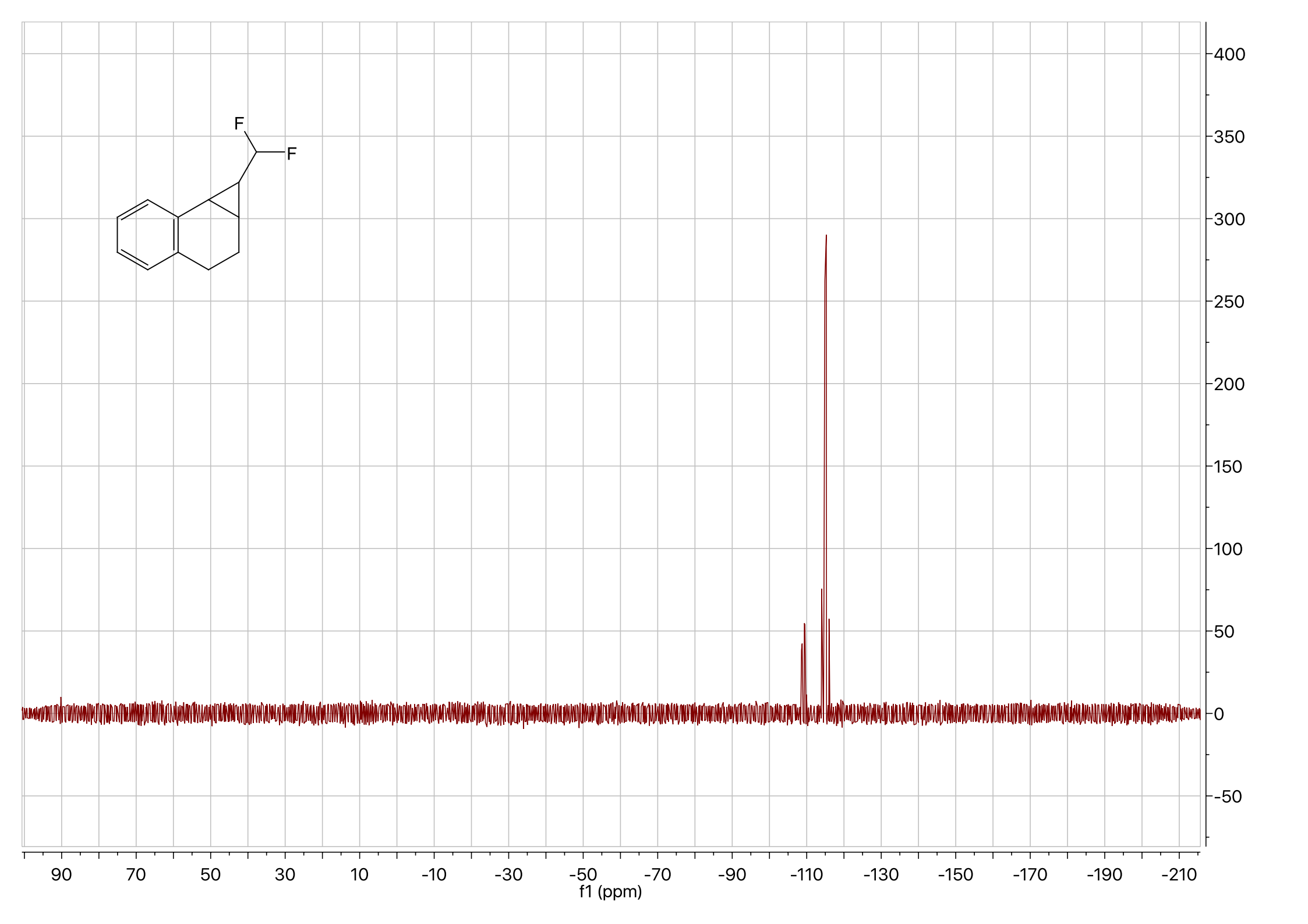

F
F
0.90
2.80
0.69
0.48
1.00
1.00
1.01
1.01
0.50
0.55
f1 (ppm)


F
F
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
f1 (ppm)


F
F
1000
900
800
700
600
500
400
300
200
100
0
-100
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
F
7.32
1.02
2.97
0.77
0.23
0.28
0.83
1.06
2.09
0.65
1.72
1.60
f1 (ppm)


F
F
110
100
90
80
70
60
50
40
30
20
10
0
-10
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F
F
400
350
300
250
200
150
100
50
0
-50
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)