

Copper-catalyzed aminotrifluoromethylation of alkenes: a facile synthesis of CF₃-containing lactams

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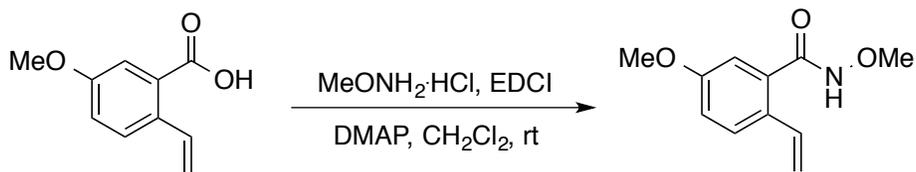
I. General Procedures.

Glassware and stir bars were dried in an oven at 140 °C for at least 12 h and then cooled in a desiccator cabinet over Drierite prior to use. Optimization and substrate screens were performed in 8-mL microwave vials. Vials were fitted with crimp top septa under a positive pressure of nitrogen that had been passed through a column (5 x 20 cm) of Drierite, unless otherwise noted. All other reactions were performed in round-bottom flasks sealed with rubber septa. Plastic syringes or glass pipets were used to transfer liquid reagents. Reactions were stirred magnetically using Teflon-coated, magnetic stir bars. Analytical thin-layer chromatography (TLC) was performed using aluminum plates pre-coated with 0.25 mm of 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light and/or exposure to KMnO₄ stain. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Flash-column chromatography was performed on silica gel (60 Å, standard grade) or with pre-packed FLASH silica gel columns.

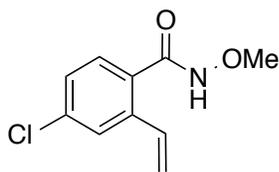
II. Materials and Instrumentation.

Nuclear magnetic resonance spectra were recorded at ambient temperature (unless otherwise stated) on 400 MHz or 500 MHz spectrometers. All values for proton chemical shifts are reported in parts per million (δ) and are referenced to the residual protium in CDCl_3 (δ 7.26). All values for carbon chemical shifts are reported in parts per million (δ) and are referenced to the carbon resonances in CDCl_3 (δ 77.0). NMR data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broad), coupling constant (Hz), and integration. Infrared spectroscopic data are reported in wavenumbers (cm^{-1}). High-resolution mass spectra were obtained using a liquid chromatography-electrospray ionization and Time-of-flight mass spectrometer.

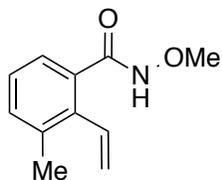
III. Synthesis of Substrates.



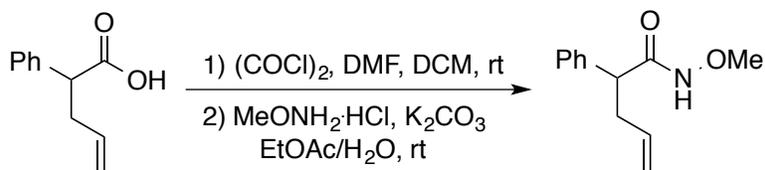
N,5-Dimethoxy-2-vinylbenzamide (1f). Follow literature procedure.¹ To a solution of 5-methoxy-2-vinylbenzoic acid (712 mg, 4 mmol) in CH_2Cl_2 (20 mL) was added $\text{MeONH}_2\cdot\text{HCl}$ (501 mg, 6 mmol), EDCI (1.54 g, 8 mmol) and DMAP (979 mg, 8 mmol) successively. The resulting mixture was stirred at room temperature overnight. The reaction was quenched by adding HCl (2M, 10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 . The combined extracts were washed with brine, dried over Na_2SO_4 , and filtrated. The filtrate was concentrated. Purification by column chromatography (50% EtOAc in hexanes) gave **1f** as a white solid (752.8 mg, 91% yield); $R_f = 0.42$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 10.32 (s, 1H), 7.24 (d, $J = 8.8$ Hz, 1H), 6.68 (d, $J = 8.8$ Hz, 1H), 6.66–6.58 (m, 2H), 5.35 (d, $J = 17.2$ Hz, 1H), 4.96 (d, $J = 10.8$ Hz, 1H), 3.54 (s, 3H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 166.3, 158.0, 132.6, 132.1, 128.3, 126.5, 116.1, 113.8, 111.9, 63.3, 54.8; IR (neat): 3175, 2938, 1640, 1601, 1480, 1292, 1234, 1030, 917, 836, 822, 623, 545 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{14}\text{NO}_3$) ($[\text{M}+\text{H}]^+$): 208.0968; found: 208.0971.



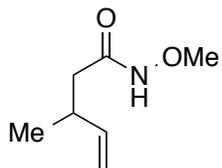
4-Chloro-N-methoxy-2-vinylbenzamide (1g). Follow the same procedure with **1f**. Purification by column chromatography (40% EtOAc in hexanes) gave **1g** as a white solid in quantitative yield; $R_f = 0.50$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, CD_3OD): δ 7.69 (s, 1H), 7.40–7.30 (m, 2H), 6.95 (dd, $J = 17.6, 10.8$ Hz, 1H), 5.85 (d, $J = 17.6$ Hz, 1H), 5.42 (d, $J = 10.8$ Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD): δ 167.9, 139.5, 137.7, 133.6, 131.8, 130.4, 128.6, 126.8, 118.6, 64.4; IR (neat): 3126, 2959, 2812, 1739, 1634, 1237, 1037, 893, 836 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{10}\text{H}_{11}\text{ClNO}_2$) ($[\text{M}+\text{H}]^+$): 212.0473; found: 212.0479.



***N*-Methoxy-3-methyl-2-vinylbenzamide (1h).** Follow the same procedure with **1f**. Purification by column chromatography (40% EtOAc in hexanes) gave **1h** as a yellow oil (46% yield); $R_f = 0.42$ (50% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 9.89 (s, 1H), 7.15–7.02 (m, 1H), 7.02–6.88 (m, 2H), 6.56 (dd, $J = 17.6, 11.2$ Hz, 1H), 5.23 (d, $J = 11.6$ Hz, 1H), 5.13 (d, $J = 17.6$ Hz, 1H), 3.53 (s, 3H), 2.14 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 167.6, 136.0, 135.8, 133.2, 132.2, 131.4, 126.4, 125.3, 119.5, 63.1, 19.9; IR (neat): 3163, 2935, 1629, 1497, 1457, 1438, 1303, 1057, 1038, 924, 726 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{14}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 192.1019; found: 192.1026.

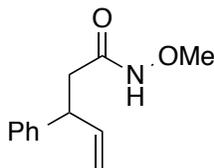


***N*-methoxy-2-phenylpent-4-enamide (1j).** Follow literature procedure.¹ To a solution of 2-phenylpent-4-enoic acid (1.76 g, 10 mmol) in CH_2Cl_2 (20 mL) was added dropwise oxalyl chloride (1.1 mL, 13 mmol) followed by a catalytic amount of DMF. The mixture was stirred at room temperature for 1 h, and then was concentrated under reduced pressure to remove the solvent. The resulting residue was added dropwise to a biphasic mixture of $\text{MeONH}_2\cdot\text{HCl}$ (1.25 g, 15 mmol) and K_2CO_3 (2.76 g, 20 mmol) in EtOAc (24 mL) and H_2O (12 mL). The reaction was stirred at room temperature for 2 h. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 , and filtrated. The filtrate was concentrated. Purification by column chromatography (25% EtOAc in hexanes) gave **1j** as a yellow oil (1.526 g, 75% yield); $R_f = 0.62$ (50% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.24 (s, 1H), 7.37–7.24 (m, 5H), 5.80–5.60 (m, 1H), 5.07 (ddd, $J = 17.0, 3.2, 1.6$ Hz, 1H), 5.03–4.97 (m, 1H), 3.69 (s, 3H), 3.40–3.20 (m, 1H), 2.98–2.78 (m, 1H), 2.60–2.40 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 170.7, 138.8, 135.1, 128.4, 127.8, 127.1, 116.8, 63.8, 48.9, 37.1; IR (neat): 3132, 3066, 2973, 2937, 1647, 1636, 1525, 1493, 1448, 1359, 1254, 1058, 912, 695, 644, 602 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{12}\text{H}_{16}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 206.1176; found: 206.1178.

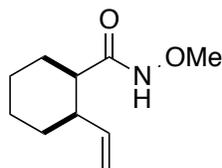


***N*-Methoxy-3-methylpent-4-enamide (1l).** Follow the same procedure with **1f**. Purification by column chromatography (50% EtOAc in hexanes) gave **1l** as a colorless oil (44% yield); $R_f = 0.40$ (50% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 10.91 (s, 1H), 5.52 (ddd, $J = 17.2, 10.4, 7.2$ Hz, 1H), 4.80 (d, $J = 17.2$ Hz, 1H), 4.71 (d, $J = 10.4$ Hz, 1H), 3.50 (s, 3H), 2.55–2.40 (m, 1H), 1.98 (dd, $J = 14.0, 7.2$ Hz, 1H), 2.51 (dd, $J = 14.0, 7.2$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 169.3, 141.8, 112.9, 63.2, 39.1, 34.1, 18.9; IR (neat): 3174, 2965, 1651, 1516, 1438,

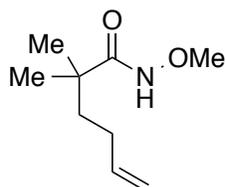
1050, 913, 672, 588 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_7\text{H}_{14}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 144.1019; found: 144.1020.



***N*-Methoxy-3-phenylpent-4-enamide (1m).** Follow the same procedure with **1f**. Purification by column chromatography (33% EtOAc in hexanes) gave **1m** as a colorless oil (68% yield); $R_f = 0.40$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 10.66 (s, 1H), 7.32–7.12 (m, 5H), 6.00 (ddd, $J = 17.2, 9.8, 7.6$ Hz, 1H), 5.15–5.00 (m, 2H), 3.92 (q, $J = 7.6$ Hz, 1H), 3.54 (s, 3H), 2.60 (dd, $J = 14.0, 7.6$ Hz, 1H), 2.51 (dd, $J = 14.0, 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 168.8, 142.1, 139.9, 128.2, 127.3, 126.4, 114.7, 63.5, 45.5, 38.4; IR (neat): 3167, 2979, 1650, 1239, 1063, 977, 915, 698 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{12}\text{H}_{16}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 206.1176; found: 206.1176.

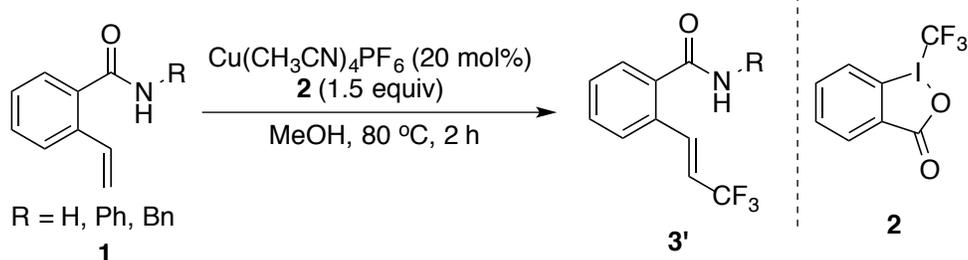


***cis*-N-Methoxy-2-vinylcyclohexane-1-carboxamide (1n).** Follow the same procedure with **1f**. *cis*-2-Vinylcyclohexane-1-carboxylic acid was synthesized according to literature procedure.² Purification by column chromatography (25% EtOAc in hexanes) gave **1k** as a colorless oil (92% yield); $R_f = 0.28$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 9.86 (s, 1H), 6.01–5.89 (m, 1H), 5.04–4.90 (m, 2H), 3.63 (s, 3H), 2.49 (s, br, 1H), 2.35 (s, br, 1H), 1.86–1.64 (m, 3H), 1.61–1.43 (m, 3H), 1.41–1.19 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.4, 138.7, 115.2, 63.8, 43.5, 41.9, 30.0, 25.0, 23.9, 22.2; IR (neat): 3173, 2927, 2854, 1651, 1509, 1446, 1071, 1047, 910, 633 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{10}\text{H}_{18}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 184.1332; found: 184.1328.

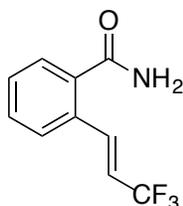


***N*-Methoxy-2,2-dimethylhex-5-enamide (1o).** Follow the same procedure with **1j**. Purification by column chromatography (33% EtOAc in hexanes) gave **1o** as a yellow oil (87% yield); $R_f = 0.51$ (50% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 8.33 (s, 1H), 5.84–5.71 (m, 1H), 5.07–4.97 (m, 1H), 4.97–4.89 (m, 1H), 3.75 (s, 3H), 2.07–1.96 (m, 2H), 1.66–1.56 (m, 2H), 1.18 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.8, 138.0, 114.0, 63.1, 40.5, 39.6, 28.7, 24.5; IR (neat): 3210, 2972, 2936, 1641, 1499, 1052, 909 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_9\text{H}_{18}\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 172.1332; found: 172.1333.

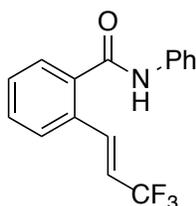
IV. Procedure for Alkene Trifluoromethylation Reaction (Table 1)



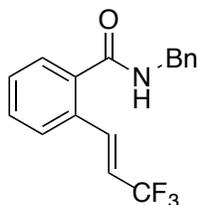
To a reaction tube charged with *N*-methoxylamide **1** (0.2 mmol, 1.0 equiv) and Togni's reagent **2** (0.4 mmol, 1.5 equiv), was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{PF}_6$ (0.04 mmol, 20 mol%) and MeOH (2.0 mL). The reaction tube was capped and the resulting mixture was stirred at 80 °C for 2 h. After cooling down to room temperature, the reaction mixture was filtered through a pale of basic Al_2O_3 . The filtrate was concentrated *in vacuo*. The resulting crude mixture was subject to flash column chromatography to provide the trifluoromethylated product **3'**.



(*E*)-2-(3',3',3'-trifluoroprop-1'-en-1'-yl)benzamide (3a'). Purification by column chromatography (50% EtOAc in hexanes) gave **3a'** as a white solid (23.3 mg, 54% yield); $R_f = 0.16$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CD_3OD): δ 7.75 (d, $J = 7.6$ Hz, 1H), 7.64 (d, $J = 16.0$ Hz, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.52 (t, $J = 7.6$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 1H), 6.44 (dq, $J = 16.0, 6.8, 1.2$ Hz, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_3OD): δ 173.9, 137.7, 136.8 (q, $J = 7.0$ Hz, 1C), 132.9, 131.6, 130.7, 128.8, 127.9, 125.0 (q, $J = 266.0$ Hz, 1C), 118.5 (q, $J = 34.0$ Hz, 1C); $^{19}\text{F NMR}$ (376 MHz, CD_3OD): δ -65.2 (dd, $J = 6.5, 2.0$ Hz, 3F); IR (neat): 2529, 2340, 1619, 1419, 1268, 1110, 750, 585 cm^{-1} ; HRMS (m/z) Calcd for $(\text{C}_{10}\text{H}_9\text{F}_3\text{NO}_2)$ ($[\text{M}+\text{H}]^+$): 216.0631; found: 216.0633.

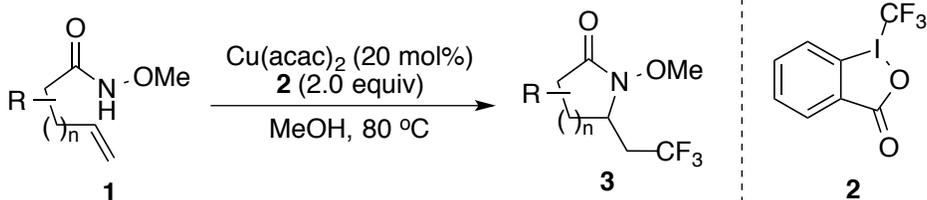


(*E*)-*N*-phenyl-2-(3',3',3'-trifluoroprop-1'-en-1'-yl)benzamide (3b'). Purification by column chromatography (20% EtOAc in hexanes) gave **3b'** as a pale yellow solid (44.6 mg, 74% yield); $R_f = 0.53$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CD_3OD): δ 7.78 (d, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 7.2$ Hz, 2H), 7.65–7.45 (m, 4H), 7.36 (t, $J = 7.2$ Hz, 2H), 7.16 (t, $J = 7.2$ Hz, 1H), 6.57–6.37 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CD_3OD): δ 169.6, 139.6, 138.3, 136.5 (q, $J = 7.0$ Hz, 1C), 133.0, 131.7, 130.9, 129.9, 128.9, 128.0, 125.8, 125.0 (q, $J = 266.0$ Hz, 1C), 121.7, 118.9 (q, $J = 33.0$ Hz, 1C); $^{19}\text{F NMR}$ (376 MHz, CD_3OD): δ -65.2 (d, $J = 6.4$ Hz, 3F); IR (neat): 3310, 1646, 1521, 1315, 1272, 1254, 1105, 750, 689 cm^{-1} ; HRMS (m/z) Calcd for $(\text{C}_{16}\text{H}_{13}\text{F}_3\text{NO}_2)$ ($[\text{M}+\text{H}]^+$): 292.0944; found: 292.0948.

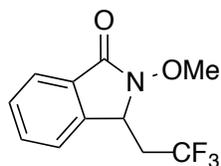


(E)-N-benzyl-2-(3',3',3'-trifluoroprop-1'-en-1'-yl)benzamide (3c'). Purification by column chromatography (20% EtOAc in hexanes) gave **3c'** as a white solid (37.2 mg, 61% yield); $R_f = 0.43$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.75–7.27 (m, 10H), 6.28–6.08 (m, 2H), 4.63 (d, $J = 5.6$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 168.3, 137.6, 136.3, 135.4 (q, $J = 6.7$ Hz, 1C), 132.0, 130.5, 129.6, 128.8, 127.8, 127.7, 127.4, 127.0, 123.2 (q, $J = 268.0$ Hz, 1C), 118.2 (q, $J = 33.7$ Hz, 1C), 44.2; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.5 (d, $J = 6.2$ Hz, 3F); IR (neat): 3298, 1632, 1530, 1311, 1270, 1129, 1103, 737, 698, 683, 603 cm^{-1} ; HRMS (m/z) Calcd for $(\text{C}_{17}\text{H}_{15}\text{F}_3\text{NO}_2)$ ($[\text{M}+\text{H}]^+$): 306.1100; found: 306.1097.

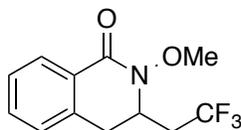
V. General Procedure for Aminotrifluoromethylation Reaction.



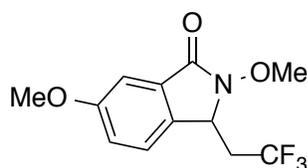
To a reaction tube charged with *N*-methoxylamide **1** (0.3 mmol, 1.0 equiv) and Togni's reagent **2** (0.6 mmol, 2.0 equiv), was added $\text{Cu}(\text{acac})_2$ (0.06 mmol, 20 mol%) and MeOH (3.0 mL). The reaction tube was capped and the resulting mixture was stirred at 80 °C for 2–5 h. After cooling down to room temperature, the reaction mixture was filtered through a pale of basic Al_2O_3 . The filtrate was concentrated *in vacuo*. The resulting crude mixture was subject to flash column chromatography to provide the aminotrifluoromethylated product **3**.



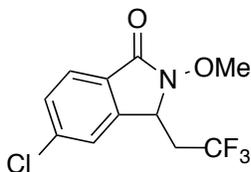
2-Methoxy-3-(2',2',2'-trifluoroethyl)isoindolin-1-one (3d). Purification by column chromatography (20% EtOAc in hexanes) gave **3d** as a white solid (60.0 mg, 82% yield); $R_f = 0.33$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.72 (d, $J = 7.6$ Hz, 1H), 7.52 (d, $J = 7.6$ Hz, 1H), 7.45–7.38 (m, 2H), 4.84 (dd, $J = 6.8, 4.0$ Hz, 1H), 3.88 (s, 3H), 2.95–2.75 (m, 1H), 2.56–2.40 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 164.6, 140.4, 132.5, 129.1, 129.0, 125.3 (q, $J = 276.0$ Hz, 1C), 124.0, 122.9 (q, $J = 2.0$ Hz, 1C), 63.6, 53.8 (q, $J = 3.2$ Hz, 1C), 35.5 (q, $J = 28.6$ Hz, 1C); $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -62.6 (t, $J = 10.9$ Hz, 3F); IR (neat): 2944, 1708, 1250, 1130, 1088, 684, 573 cm^{-1} ; HRMS (m/z) Calcd for $(\text{C}_{11}\text{H}_{11}\text{F}_3\text{NO}_2)$ ($[\text{M}+\text{H}]^+$): 246.0736; found: 246.0744.



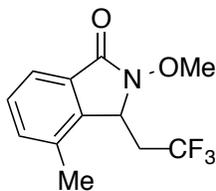
2-Methoxy-3-(2',2',2'-trifluoroethyl)-3,4-dihydroisoquinolin-1(2H)-one (3e). Purification by column chromatography (15% EtOAc in hexanes) gave **3e** as a yellow oil (69.3 mg, 89% yield); $R_f = 0.43$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.27 (t, $J = 7.6$ Hz, 1H), 7.15 (t, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 7.6$ Hz, 1H), 4.15–4.03 (m, 1H), 3.71 (s, 3H), 3.31 (dd, $J = 16.4, 5.6$ Hz, 1H), 2.92 (dd, $J = 16.4, 2.4$ Hz, 1H), 2.60–2.35 (m, 1H), 2.15–1.95 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 162.8, 134.1, 132.4, 127.7, 127.6, 127.4, 126.9, 125.2 (q, $J = 275.2$ Hz, 1C), 62.9, 53.3 (q, $J = 2.7$ Hz, 1C), 33.3 (q, $J = 28.0$ Hz, 1C), 32.5; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.6 (t, $J = 11.0$ Hz, 3F); IR (neat): 2939, 1677, 1238, 1136, 1099, 984, 726 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{12}\text{H}_{13}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 260.0893; found: 260.0896.



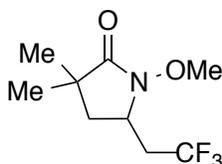
2,6-Dimethoxy-3-(2',2',2'-trifluoroethyl)isoindolin-1-one (3f). Purification by column chromatography (20% EtOAc in hexanes) gave **3f** as a colorless oil (26.3 mg, 32% yield); $R_f = 0.33$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.38 (d, $J = 8.4$ Hz, 1H), 7.33 (d, $J = 2.4$ Hz, 1H), 7.15 (dd, $J = 8.4, 2.4$ Hz, 1H), 4.87 (dd, $J = 7.6, 4.0$ Hz, 1H), 3.98 (s, 3H), 3.85 (s, 3H), 3.05–2.85 (m, 1H), 2.55–2.40 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 164.8, 160.5, 132.6, 130.7, 125.5 (q, $J = 275.5$ Hz, 1C), 124.2 (q, $J = 2.2$ Hz, 1C), 120.6, 106.8, 63.8, 55.7, 53.7 (q, $J = 3.3$ Hz, 1C), 36.0 (q, $J = 28.5$ Hz, 1C); $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -62.6 (t, $J = 10.9$ Hz, 3F); IR (neat): 2943, 1708, 1493, 1435, 1282, 1248, 1131, 1096, 1021, 1002, 832, 580 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{12}\text{H}_{13}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 276.0842; found: 276.0841.



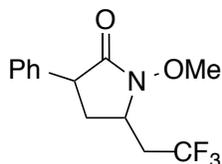
5-Chloro-2-methoxy-3-(2',2',2'-trifluoroethyl)isoindolin-1-one (3g). Purification by column chromatography (20% EtOAc in hexanes) gave **3g** as a pale yellow solid (40.8 mg, 49% yield); $R_f = 0.44$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.79 (d, $J = 8.6$ Hz, 1H), 7.54–7.47 (m, 2H), 4.90 (dd, $J = 7.2, 4.0$ Hz, 1H), 3.99 (s, 3H), 3.09–2.86 (m, 1H), 2.62–2.44 (m, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 163.7, 142.0, 139.0, 129.8, 127.7, 125.8 (q, $J = 275.5$ Hz, 1C), 125.2, 123.6 (q, $J = 2.3$ Hz, 1C), 63.8, 53.7 (q, $J = 3.3$ Hz, 1C), 35.6 (q, $J = 28.8$ Hz, 1C); $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -62.6 (t, $J = 10.9$ Hz, 3F); IR (neat): 2947, 1705, 1296, 1248, 1142, 1093, 1066, 845, 571 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{10}\text{ClF}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 280.0347; found: 280.0347.



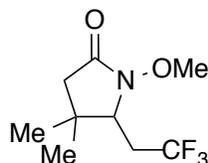
2-Methoxy-4-methyl-3-(2',2',2'-trifluoroethyl)isoindolin-1-one (3h). Purification by column chromatography (20% EtOAc in hexanes) gave **3h** as a white solid (57.0 mg, 74% yield); $R_f = 0.25$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.68–7.60 (m, 1H), 7.41–7.33 (m, 2H), 4.96 (dd, $J = 5.2, 2.7$ Hz, 1H), 3.93 (s, 3H), 3.02–2.84 (m, 1H), 2.80–2.64 (m, 1H), 2.37 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 164.8, 138.1, 134.2, 132.7, 129.5, 129.2, 125.2 (q, $J = 276.3$ Hz, 1C), 121.5, 63.6, 53.3 (q, $J = 2.8$ Hz, 1C), 33.8 (q, $J = 28.4$ Hz, 1C), 17.7; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.2 (t, $J = 10.6$ Hz, 3F); IR (neat): 2947, 1713, 1292, 1250, 1126, 1094, 740, 572 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{12}\text{H}_{13}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 260.0893; found: 260.0896.



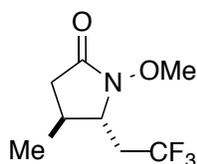
1-Methoxy-3,3-dimethyl-5-(2',2',2'-trifluoroethyl)pyrrolidin-2-one (3i). Purification by column chromatography (20% EtOAc in hexanes) gave **3i** as a yellow oil (55.4 mg, 82% yield); $R_f = 0.44$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 3.84–3.73 (m, 1H), 3.69 (s, 3H), 2.85–2.65 (m, 1H), 2.15–1.95 (m, 2H), 1.56 (dd, $J = 12.8, 8.4$ Hz, 1H), 1.10 (s, 3H), 1.02 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 175.7, 125.4 (q, $J = 275.2$ Hz, 1C), 62.1, 49.3 (q, $J = 3.3$ Hz, 1C), 38.4, 37.2 (q, $J = 27.6$ Hz, 1C), 37.0, 25.0, 23.9; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.5 (t, $J = 10.7$ Hz, 3F); IR (neat): 2970, 1714, 1247, 1135, 1074, 658 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_9\text{H}_{15}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 226.1049; found: 226.1053.



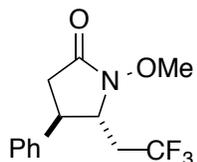
1-Methoxy-3-phenyl-5-(2',2',2'-trifluoroethyl)pyrrolidin-2-one (3j). The crude reaction mixture contains two diastereoisomers with d.r. = 1:1 detected by GC-MS. Purification by column chromatography (20% EtOAc in hexanes) gave **3j** as a yellow oil (59.9 mg, 73% yield, as an inseparable mixture of two diastereomers); $R_f = 0.40$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.40–7.15 (m, 5H), 4.20–4.10 (m, 0.5H), 3.97–3.87 (m, 0.5H), 3.85 (s, 1.5H), 3.83 (s, 1.5H), 3.63 (dd, $J = 9.2, 7.2$ Hz, 0.5H), 3.56 (t, $J = 9.8$ Hz, 0.5H), 2.96–2.72 (m, 1.5H), 2.50–2.16 (m, 2H), 1.90–1.78 (m, 0.5H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 172.2, 170.4, 138.1, 137.7, 128.8, 128.7, 127.6, 127.4, 127.3, 125.58 (q, $J = 275.2$ Hz, 1C), 125.1 (q, $J = 275.2$ Hz, 1C), 63.2, 62.6, 51.2 (q, $J = 2.8$ Hz, 1C), 50.0 (q, $J = 2.8$ Hz, 1C), 44.6, 42.8, 37.7 (q, $J = 27.8$ Hz, 1C), 33.3 (q, $J = 27.8$ Hz, 1C), 32.8, 31.1; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.2 (t, $J = 10.7$ Hz, 3F), -63.3 (t, $J = 10.7$ Hz, 3F); IR (neat): 2942, 1715, 1247, 1135, 1114, 1043, 697 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 274.1049; found: 274.1047.



1-Methoxy-4,4-dimethyl-5-(2',2',2'-trifluoroethyl)pyrrolidin-2-one (3k). Purification by column chromatography (20% EtOAc in hexanes) gave **3k** as a colorless oil (32.5 mg, 48% yield); $R_f = 0.32$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 3.78 (s, 3H), 3.67 (dd, $J = 6.6, 4.4$ Hz, 1H), 2.60–2.30 (m, 2H), 2.17 (s, 2H), 1.20 (s, 3H), 1.09 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 169.9, 125.7 (q, $J = 274.6$ Hz, 1C), 62.1, 60.6, 43.2, 33.7, 32.2 (q, $J = 28.8$ Hz, 1C), 27.1, 23.1; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.1 (t, $J = 11.0$ Hz, 3F); IR (neat): 2967, 1715, 1252, 1131, 1092, 638 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_9\text{H}_{15}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 226.1049; found: 226.1052.

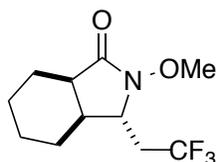


1-Methoxy-4-methyl-5-(2',2',2'-trifluoroethyl)pyrrolidin-2-one (3j). The crude reaction mixture contains two diastereoisomers with d.r. = 4.5:1 detected by $^{19}\text{F NMR}$. Purification by column chromatography (33% EtOAc in hexanes) gave **3j** as a colorless oil (39.9 mg, 63% yield, an inseparable mixture of two diastereoisomers, major isomer shown, relative stereochemistry was assigned on the basis of NOESY. The signals of methyne protons at C-5 in the *trans* isomers were reported to appear at a higher field than those of the *cis* isomers.³); $R_f = 0.35$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3 , signals for the minor diastereoisomer are reported in *italics*): δ 3.96–3.89 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.56–3.48 (m, 1H), 2.90–2.78 (m, 1H), 2.72–2.58 (m, 1H), 2.60–2.46 (m, 1H), 2.60–2.30 (m, 3H), 2.27–2.10 (m, 2H), 2.00–1.85 (m, 1H, both), 1.15 (d, $J = 6.8$ Hz, 3H), 1.05 (d, $J = 6.4$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , signals for the minor diastereoisomer are reported in *italics*, some signals corresponding to the minor diastereoisomer were not detected): δ 171.5, 169.4, 125.5 (q, $J = 275.2$ Hz, 1C), 62.7, 62.2, 58.4 (q, $J = 3.0$ Hz, 1C), 55.1 (q, $J = 3.0$ Hz, 1C), 35.9 (q, $J = 27.7$ Hz, 1C), 35.8, 34.7, 31.2 (q, $J = 28.2$ Hz, 1C), 29.7, 26.9, 19.6, 15.2; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.2 (t, $J = 10.9$ Hz, 3F), -63.6 (t, $J = 10.9$ Hz, 3F); IR (neat): 2940, 1714, 1351, 1289, 1249, 1132, 1061, 947, 623 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_8\text{H}_{13}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 212.0893; found: 212.0896.

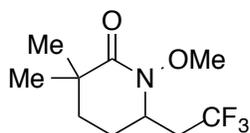


1-Methoxy-4-phenyl-5-(2',2',2'-trifluoroethyl)pyrrolidin-2-one (3k). The crude reaction mixture contains two diastereoisomers with d.r. = 6.3:1 detected by $^{19}\text{F NMR}$. Purification by column chromatography (33% EtOAc in hexanes) gave **3k** as a colorless oil (40.4 mg, 50% yield, an inseparable mixture of two diastereoisomers, major isomer shown, relative stereochemistry was assigned on the basis of NOESY. The signals of methyne protons at C-5 in the *trans* isomers were reported to appear at a higher field than those of the *cis* isomers.³); $R_f =$

0.35 (33% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3 , signals for the minor diastereoisomer are reported in *italics*): δ 7.44–7.12 (m, 5H, both), 4.27–4.18 (m, 1H), 3.99–3.92 (m, 1H), 3.82 (s, 3H, both), 3.67–3.59 (m, 1H), 3.36–3.26 (m, 1H), 2.84 (dd, $J = 17.6, 9.6$ Hz, 1H), 2.78–2.62 (m, 1H, both), 2.59–2.51 (m, 1H), 2.44 (dd, $J = 17.6, 5.2$ Hz, 1H), 2.41–2.29 (m, 1H), 2.41–2.24 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , , signals for the minor diastereoisomer are reported in *italics*, some signals corresponding to the minor diastereoisomer were not detected): δ 172.1, 169.6, 141.2, 138.3, 129.1, 129.0, 128.2, 127.9, 127.6, 126.6, 125.4 (q, $J = 276.0$ Hz, 1C), 62.9, 62.6, 58.9 (q, $J = 2.8$ Hz, 1C), 40.3, 38.6, 35.8 (q, $J = 28.0$ Hz, 1C), 35.05, 35.03; ^{19}F NMR (376 MHz, CDCl_3): δ -62.7 (t, $J = 10.9$ Hz, 3F), -63.5 (t, $J = 10.9$ Hz, 3F); IR (neat): 2983, 2939, 1720, 1243, 1135, 1112, 1094, 1044, 731, 700 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 274.1049; found: 274.1053.

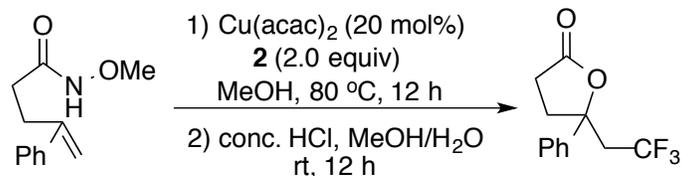


2-Methoxy-3-(2,2,2-trifluoroethyl)octahydro-1H-isoindol-1-one (31). The crude reaction mixture contains two diastereoisomers with d.r. = 5.3:1 detected by GC-MS. Purification by column chromatography (20% EtOAc in hexanes) gave the major isomer **31** as a colorless oil (31.5 mg, 42% yield, relative *trans* stereochemistry was assigned on the basis of NOESY). $R_f = 0.50$ (33% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 3.77 (s, 3H), 3.54 (ddd, $J = 9.6, 2.8, 1.6$ Hz, 1H), 2.67–2.45 (m, 2H), 2.35–2.15 (m, 2H), 2.13–2.02 (m, 1H), 1.97–1.80 (m, 1H), 1.70–1.40 (m, 3H), 1.36–1.10 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.2, 125.6 (q, $J = 275.5$ Hz, 1C), 61.9, 56.0 (q, $J = 3.0$ Hz, 1C), 36.4, 34.9, 33.5 (q, $J = 27.6$ Hz, 1C), 28.1, 23.2, 22.8, 22.4; ^{19}F NMR (376 MHz, CDCl_3): δ -63.7 (t, $J = 10.5$ Hz, 3F); IR (neat): 2932, 2857, 1715, 1250, 1133, 1111, 1044, 1030, 974 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{17}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 252.1206; found: 252.1209.

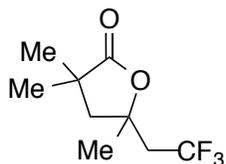


1-Methoxy-3,3-dimethyl-6-(2,2,2-trifluoroethyl)piperidin-2-one (30). Purification by column chromatography (20% EtOAc in hexanes) gave **30** as a colorless oil (31.8 mg, 44% yield); $R_f = 0.46$ (33% EtOAc in hexanes); ^1H NMR (400 MHz, CDCl_3): δ 4.02–3.94 (m, 1H), 3.69 (s, 3H), 2.90–2.70 (m, 1H), 2.35–2.20 (m, 1H), 2.20–2.10 (m, 1H), 1.96–1.84 (m, 1H), 1.73–1.63 (m, 1H), 1.62–1.52 (m, 1H), 1.20 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 173.8, 125.7 (q, $J = 275.5$ Hz, 1C), 61.2, 54.6, 39.5, 35.9 (q, $J = 27.3$ Hz, 1C), 32.1, 26.8, 26.7, 24.3; ^{19}F NMR (376 MHz, CDCl_3): δ -63.2 (t, $J = 11.0$ Hz, 3F); IR (neat): 2933, 1663, 1385, 1334, 1246, 1149, 1128, 1093, 1027, 648, 568 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{10}\text{H}_{17}\text{F}_3\text{NO}_2$) ($[\text{M}+\text{H}]^+$): 240.1206; found: 240.1210.

VI. Procedure for Oxytrifluoromethylation (Scheme 2)

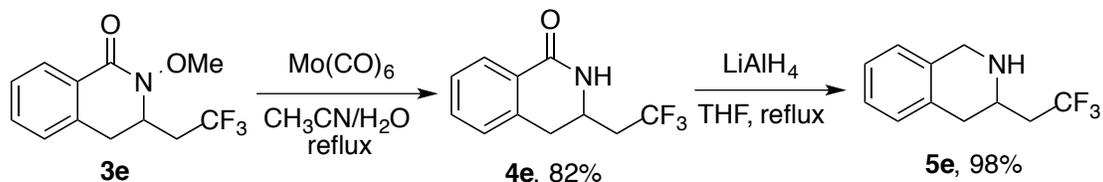


5-phenyl-5-(2',2',2'-trifluoroethyl)dihydrofuran-2(3H)-one (3p). To a reaction tube charged with *N*-methoxy-4-phenylpent-4-enamide **1p** (61.5 mg, 0.3 mmol, 1.0 equiv) and Togni's reagent **2** (189.6 mg, 0.6 mmol, 2.0 equiv), was added Cu(acac)₂ (15.7 mg, 0.06 mmol, 20 mol%) and MeOH (3.0 mL). The reaction tube was capped and the resulting mixture was stirred at 80 °C overnight. After cooling down to room temperature, the reaction mixture was filtered through a pale of basic Al₂O₃. The filtrate was concentrated *in vacuo*. The residue was dissolved in concentrated aqueous solution of HCl (12 M, 2 mL) and MeOH (4 mL). The resulting mixture was stirred at room temperature overnight. The reaction mixture was concentrated. Purification by flash column chromatography (20% EtOAc in hexanes) provided the oxytrifluoromethylated product 5-phenyl-5-(2',2',2'-trifluoroethyl)dihydrofuran-2(3H)-one (**3p**) as a pale yellow solid (35.6 mg, 49% yield); *R*_f = 0.55 (33% EtOAc in hexanes); ¹H NMR (400 MHz, CDCl₃): δ 7.45–7.26 (m, 5H), 2.93–2.70 (m, 2H), 2.68–2.52 (m, 3H), 2.48–2.34 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 175.2, 140.9, 128.6, 128.3, 124.5 (q, *J* = 276.8 Hz, 1C), 124.4, 84.1 (q, *J* = 2.2 Hz, 1C), 44.9 (q, *J* = 27.4 Hz, 1C), 34.1, 27.7; ¹⁹F NMR (376 MHz, CDCl₃): δ -60.5 (t, *J* = 10.1 Hz, 3F); IR (neat): 1777, 1379, 1261, 1247, 1231, 1195, 1118, 926, 702, 651 cm⁻¹; HRMS (*m/z*) Calcd for (C₁₂H₁₂F₃O₂) ([M+H]⁺): 245.0784; found: 245.0782.



3,3,5-trimethyl-5-(2',2',2'-trifluoroethyl)dihydrofuran-2(3H)-one (3q). Follow the procedure described for **3p**. Purification by column chromatography (20% EtOAc in hexanes) gave 3,3,5-trimethyl-5-(2',2',2'-trifluoroethyl)dihydrofuran-2(3H)-one (**3q**) as a colorless oil (32.8 mg, 52% yield); *R*_f = 0.42 (20% EtOAc in hexanes); ¹H NMR (400 MHz, CDCl₃): δ 2.65–2.45 (m, 2H), 2.30 (d, *J* = 13.6 Hz, 1H), 2.10 (d, *J* = 13.6 Hz, 1H), 1.56 (s, 3H), 1.36 (s, 3H), 1.32 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 180.8, 124.9 (q, *J* = 276.0 Hz, 1C), 78.5 (q, *J* = 2.2 Hz, 1C), 47.4 (q, *J* = 1.4 Hz, 1C), 45.3 (q, *J* = 27.2 Hz, 1C), 40.4, 28.1 (q, *J* = 1.8 Hz, 1C), 27.6, 27.3; ¹⁹F NMR (376 MHz, CDCl₃): δ -60.7 (t, *J* = 10.5 Hz, 3F); IR (neat): 2975, 1762, 1375, 1239, 1097, 1070, 951, 919, 644 cm⁻¹; HRMS (*m/z*) Calcd for (C₉H₁₄F₃O₂) ([M+H]⁺): 211.0940; found: 211.0939.

VII. Deprotection Conditions for 3e.



To a solution of **3e** (77.7 mg, 0.3 mmol) in CH₃CN-H₂O (4.8 mL, 15:1) at room temperature was added Mo(CO)₆ (95.1 mg, 0.36 mmol).⁴ The resulting mixture was refluxed for 2 h, then cooled down and concentrated under reduced pressure. Purification by column chromatography (30%

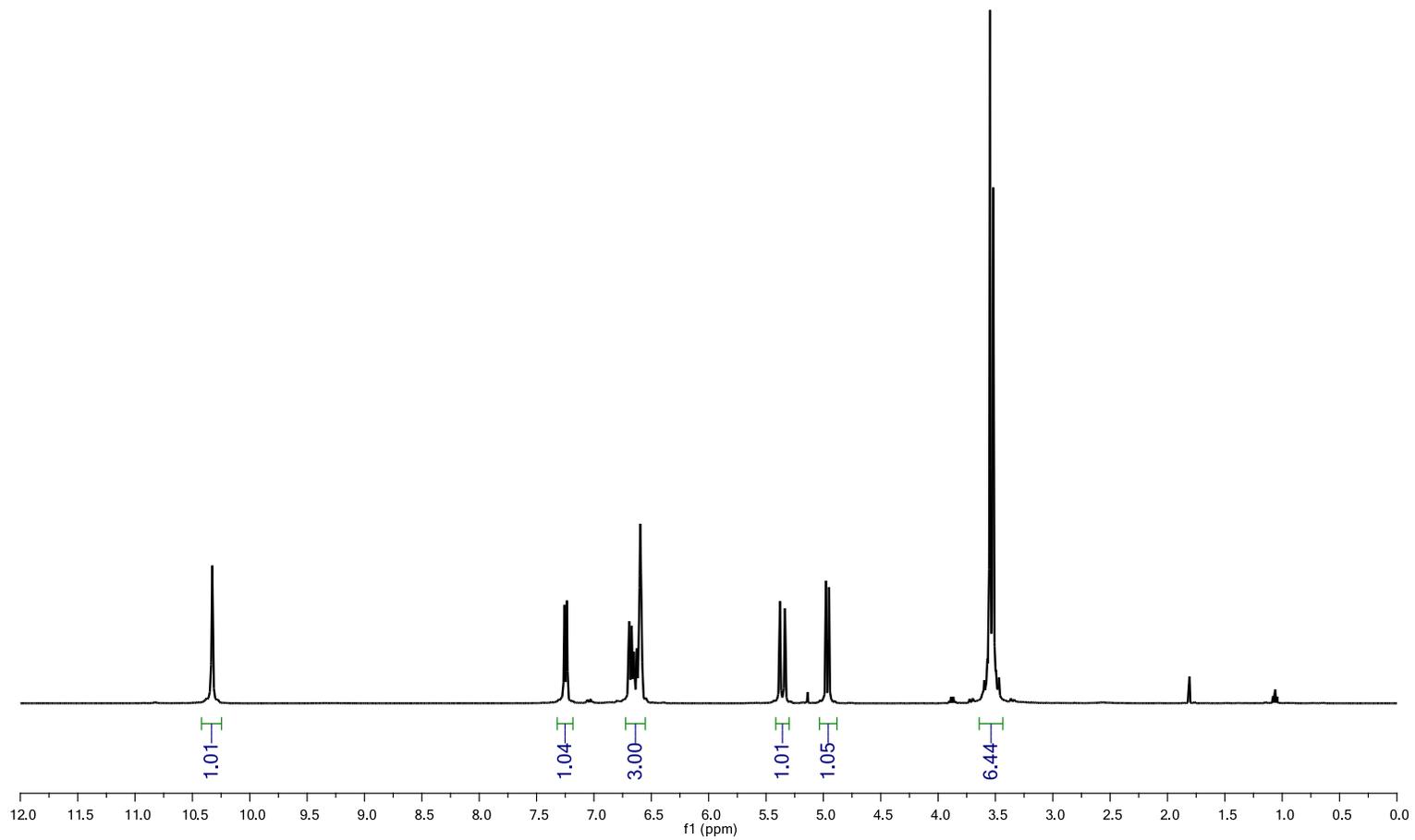
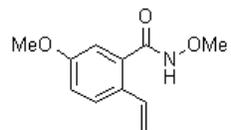
EtOAc in hexanes) gave **4e** as a white solid (56.2 mg, 82% yield); $R_f = 0.37$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.06 (d, $J = 7.6$ Hz, 1H), 7.48 (td, $J = 7.6, 1.2$ Hz, 1H), 7.38 (t, $J = 7.6$ Hz, 1H), 7.22 (d, $J = 7.6$ Hz, 1H), 6.91 (s, br, 1H), 4.17–4.05 (m, 1H), 3.19 (dd, $J = 15.6, 4.8$ Hz, 1H), 2.92 (dd, $J = 15.6, 8.4$ Hz, 1H), 2.58–2.44 (m, 1H), 2.44–2.30 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , one carbon missing): δ 165.7, 136.3, 132.6, 128.0, 127.6, 127.5, 125.7 (q, $J = 275.7$ Hz, 1C), 45.9 (q, $J = 2.8$ Hz, 1C), 39.0 (q, $J = 27.4$ Hz, 1C), 33.7; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.4 (t, $J = 10.7$ Hz, 3F); IR (neat): 3179, 3052, 2943, 1661, 1383, 1356, 1246, 1155, 1122, 1103, 1009, 737, 651 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{11}\text{F}_3\text{NO}$) ($[\text{M}+\text{H}]^+$): 230.0787; found: 230.0791.

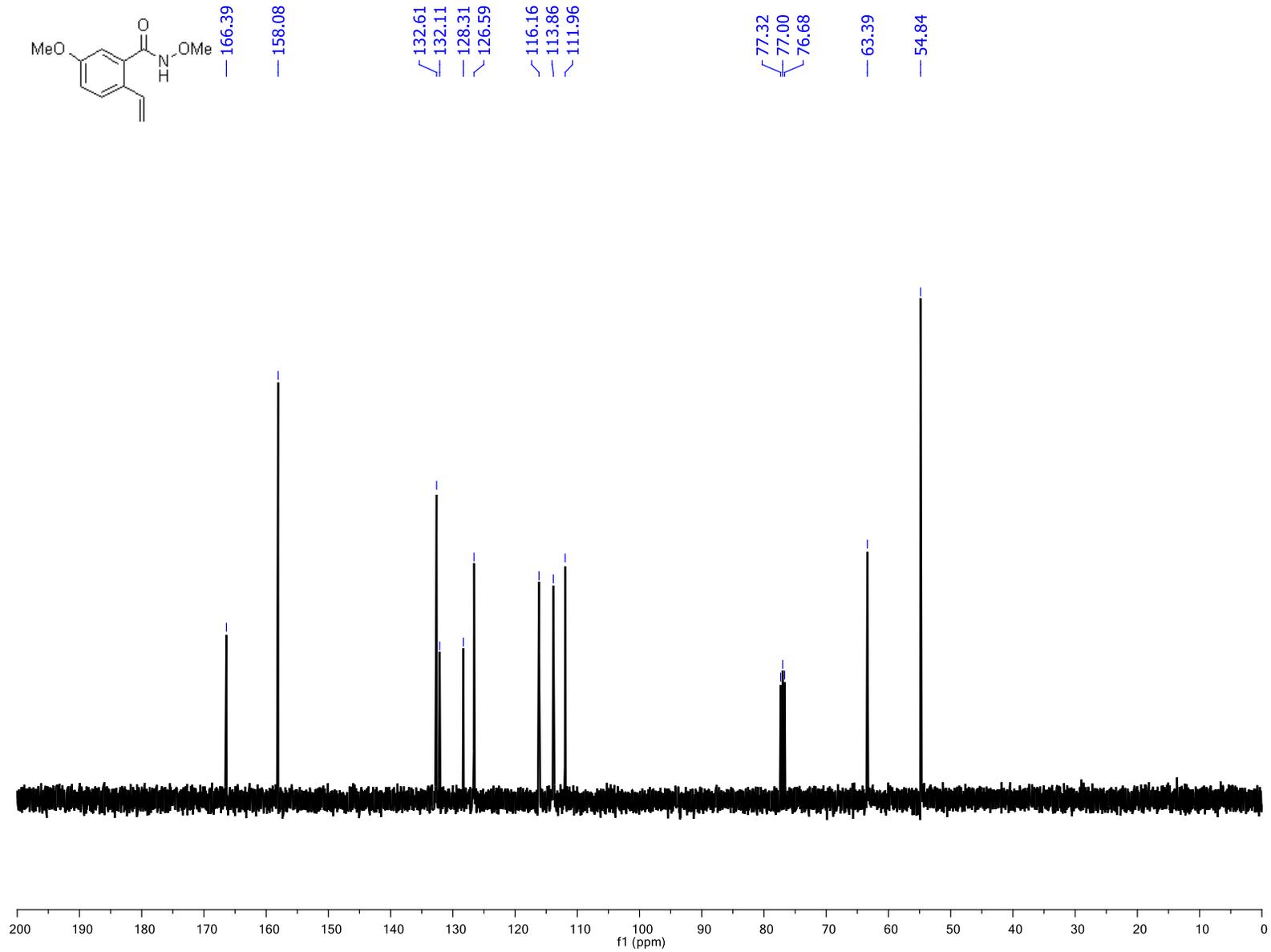
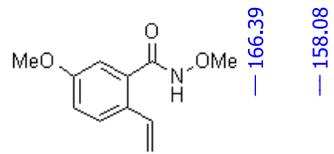
To a 25 mL round-bottomed flask charged with LiAlH_4 (38 mg, 1 mmol), was added THF (5 mL) and a solution of **4e** (45.8 mg, 0.2 mmol) in THF (5 mL) at room temperature. The resulting mixture was refluxed overnight. The reaction was quenched with the addition of an aqueous solution of NaOH (2 M, 2 mL). The mixture was filtered through a pale of Celite. The solvent was removed under reduced pressure. Purification by column chromatography (33% EtOAc in hexanes containing 2% TEA) gave **5e** as a colorless oil (42.0 mg, 98% yield); $R_f = 0.18$ (33% EtOAc in hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.22–7.00 (m, 4H), 4.14 (d, $J = 16.0$ Hz, 1H), 4.05 (d, $J = 16.0$ Hz, 1H), 3.38–3.24 (m, 1H), 2.89 (dd, $J = 16.0, 4.0$ Hz, 1H), 2.67 (dd, $J = 16.0, 10.4$ Hz, 1H), 2.48–2.22 (m, 2H), 1.86 (s, br, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 134.6, 133.2, 129.0, 126.4 (q, $J = 275.3$ Hz, 1C), 126.2, 126.08, 126.06, 48.4 (q, $J = 2.8$ Hz, 1C), 47.9, 40.2 (q, $J = 27.2$ Hz, 1C), 35.2; $^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ -63.2 (t, $J = 11.2$ Hz, 3F); IR (neat): 2933, 2835, 1251, 1234, 1148, 1124, 1098, 743, 660 cm^{-1} ; HRMS (m/z) Calcd for ($\text{C}_{11}\text{H}_{13}\text{F}_3\text{N}$) ($[\text{M}+\text{H}]^+$): 216.0995; found: 216.0999.

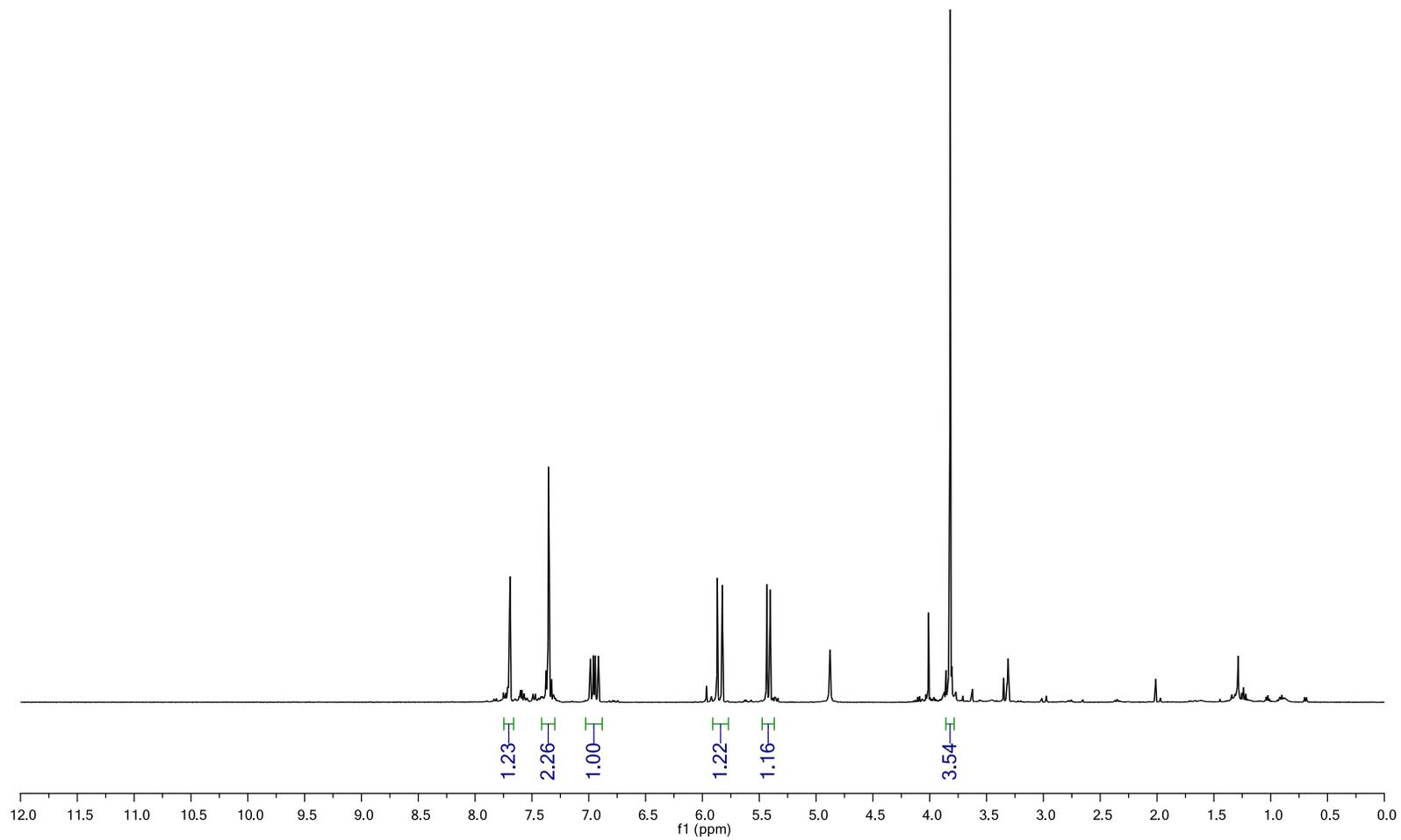
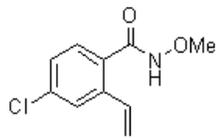
VIII. References.

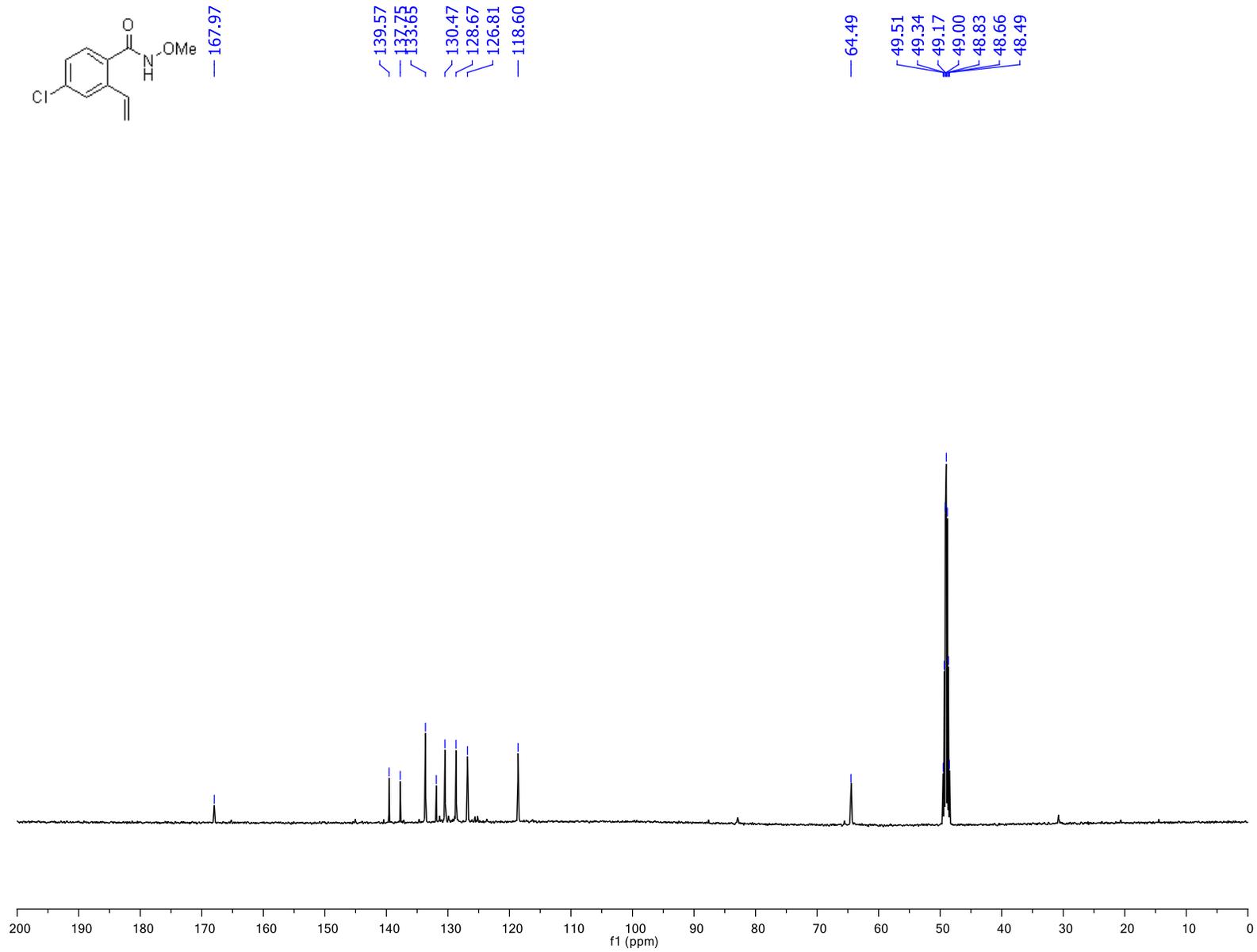
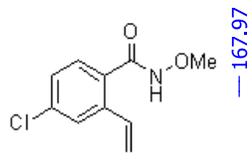
1. K. Shen and Q. Wang, *Chem. Sci.* 2015, **6**, 4279.
2. S. Nicolai, C. Piemontesi and J. Waser, *Angew. Chem. Int. Ed.* 2011, **50**, 4680.
3. H. Takahata, T. Takamatsu and T. Yamazaki, *J. Org. Chem.* 1989, **54**, 4812.
4. D. J. Wardrop, E. G. Bowen, R. E. Forslund, A. D. Sussman and S. L. Weerasekera, *J. Am. Chem. Soc.* 2010, **132**, 1188.

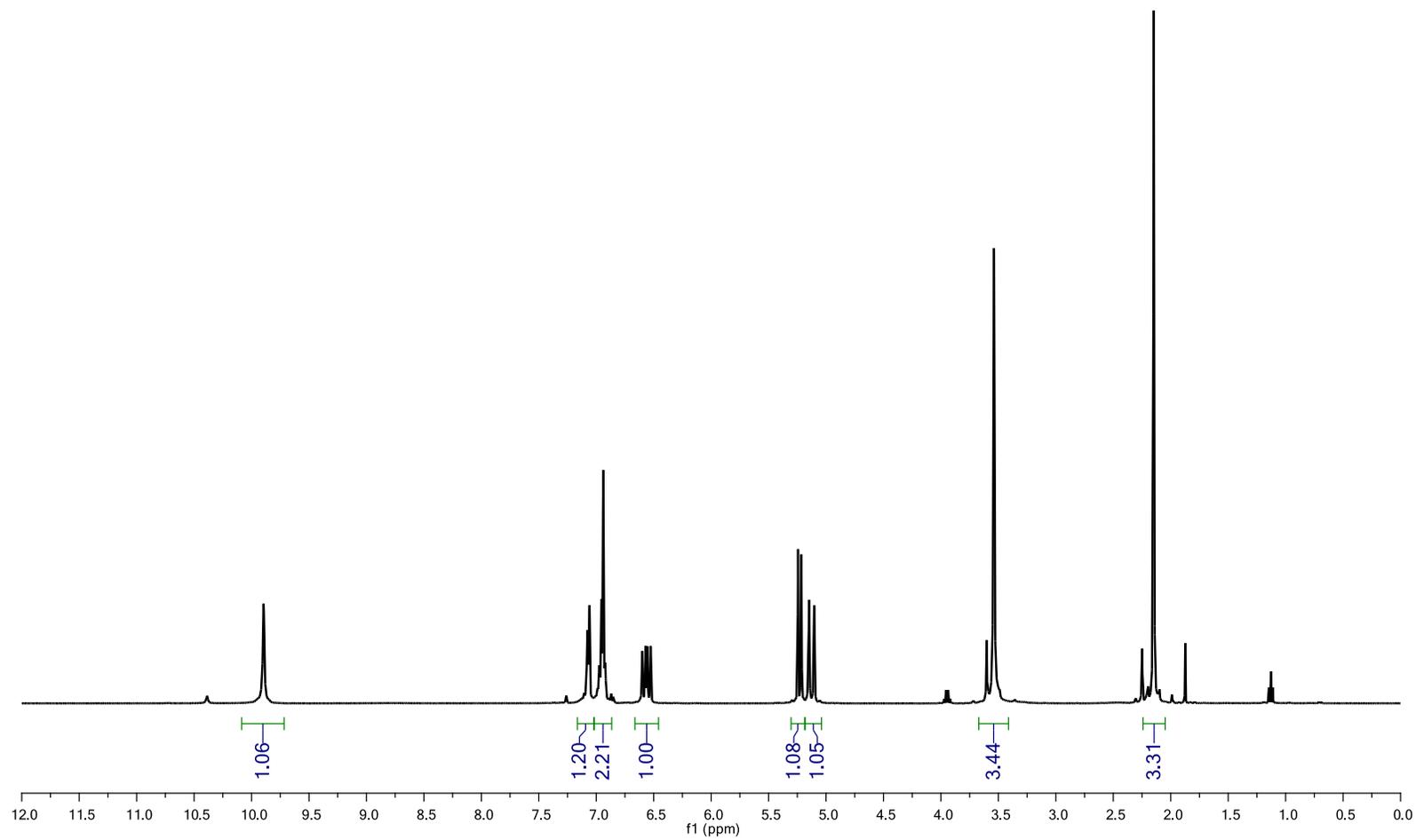
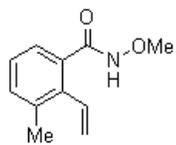
IX. NMR Spectra

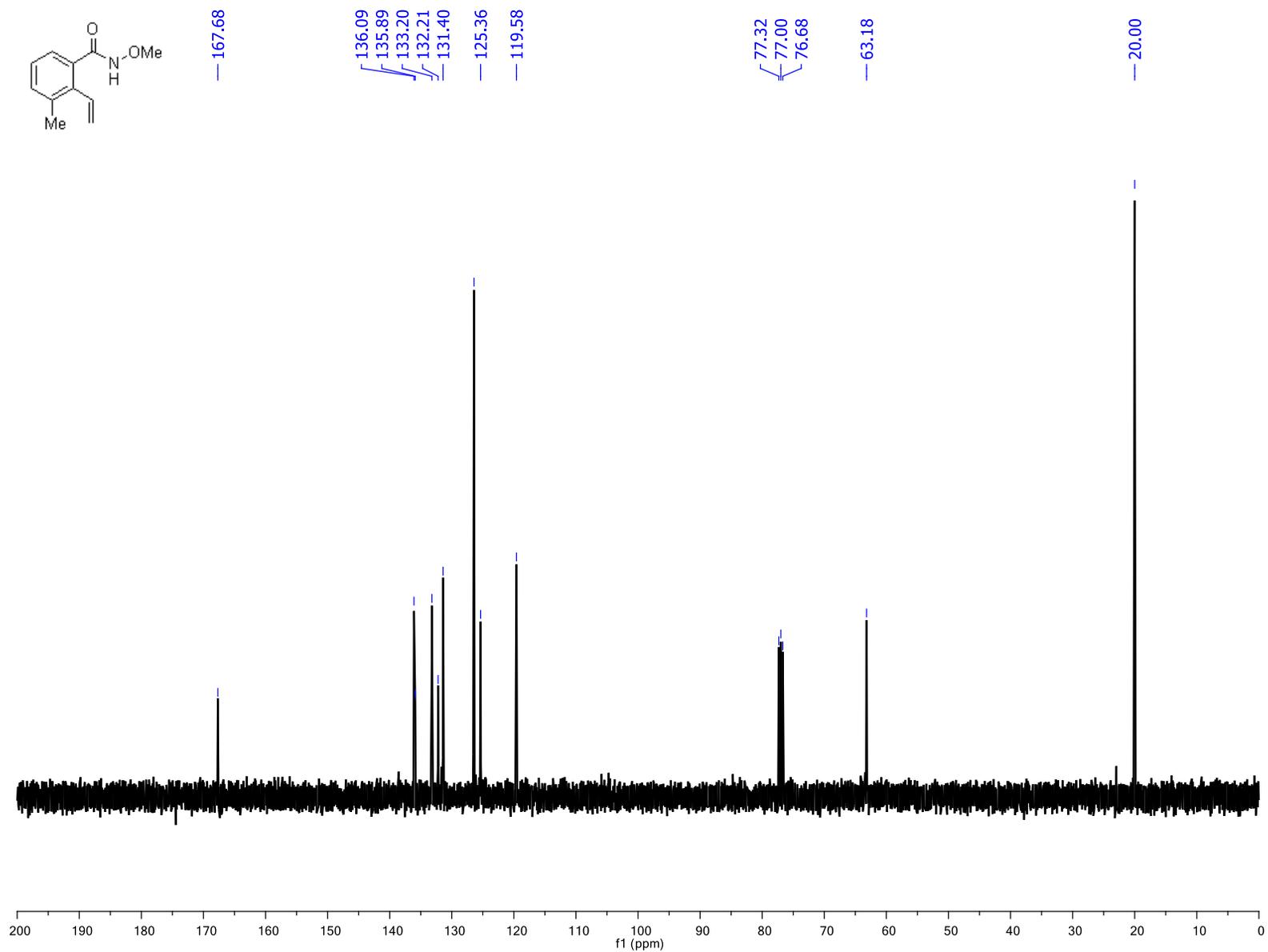
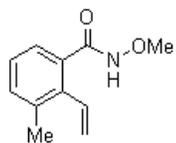


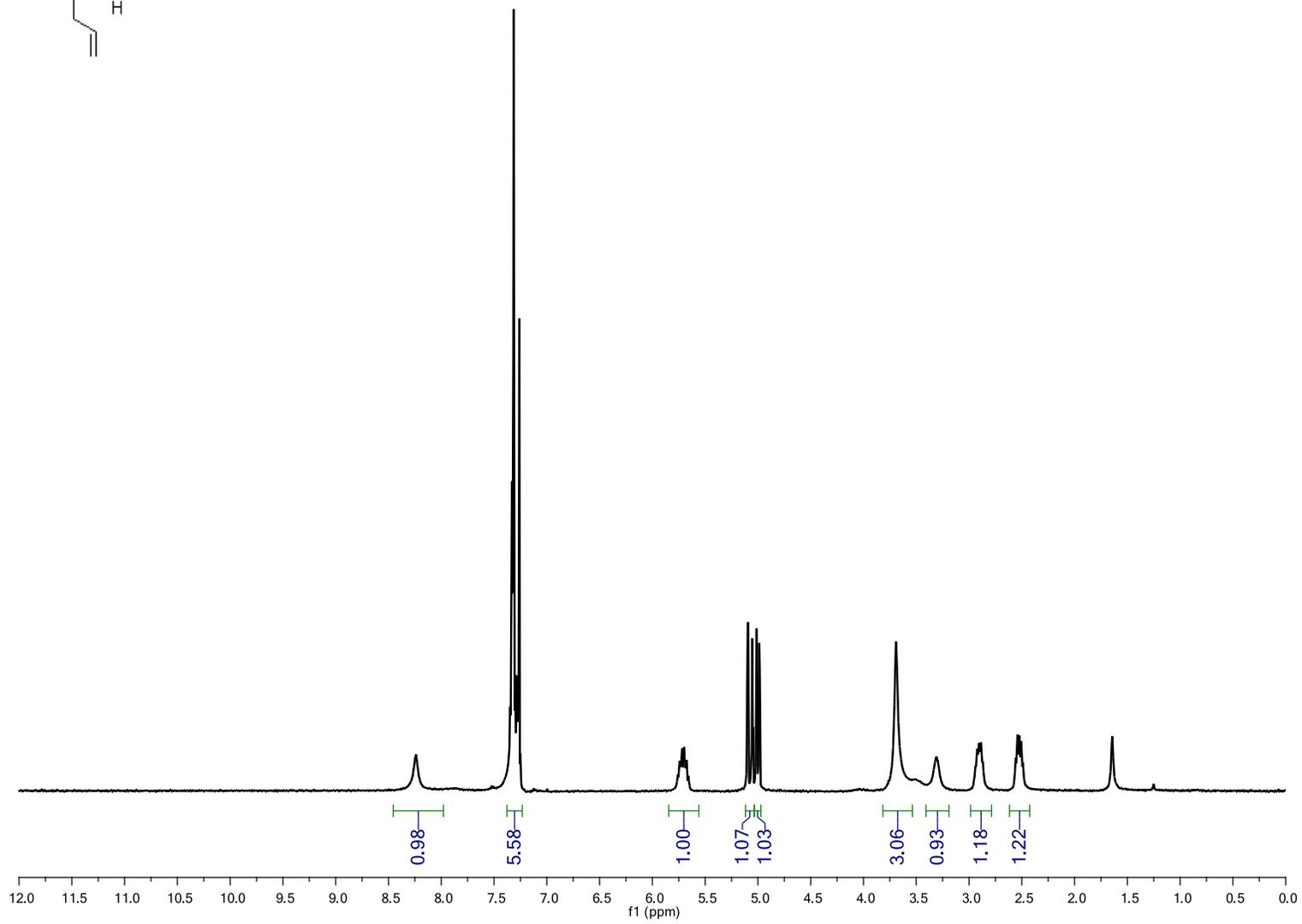
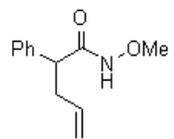


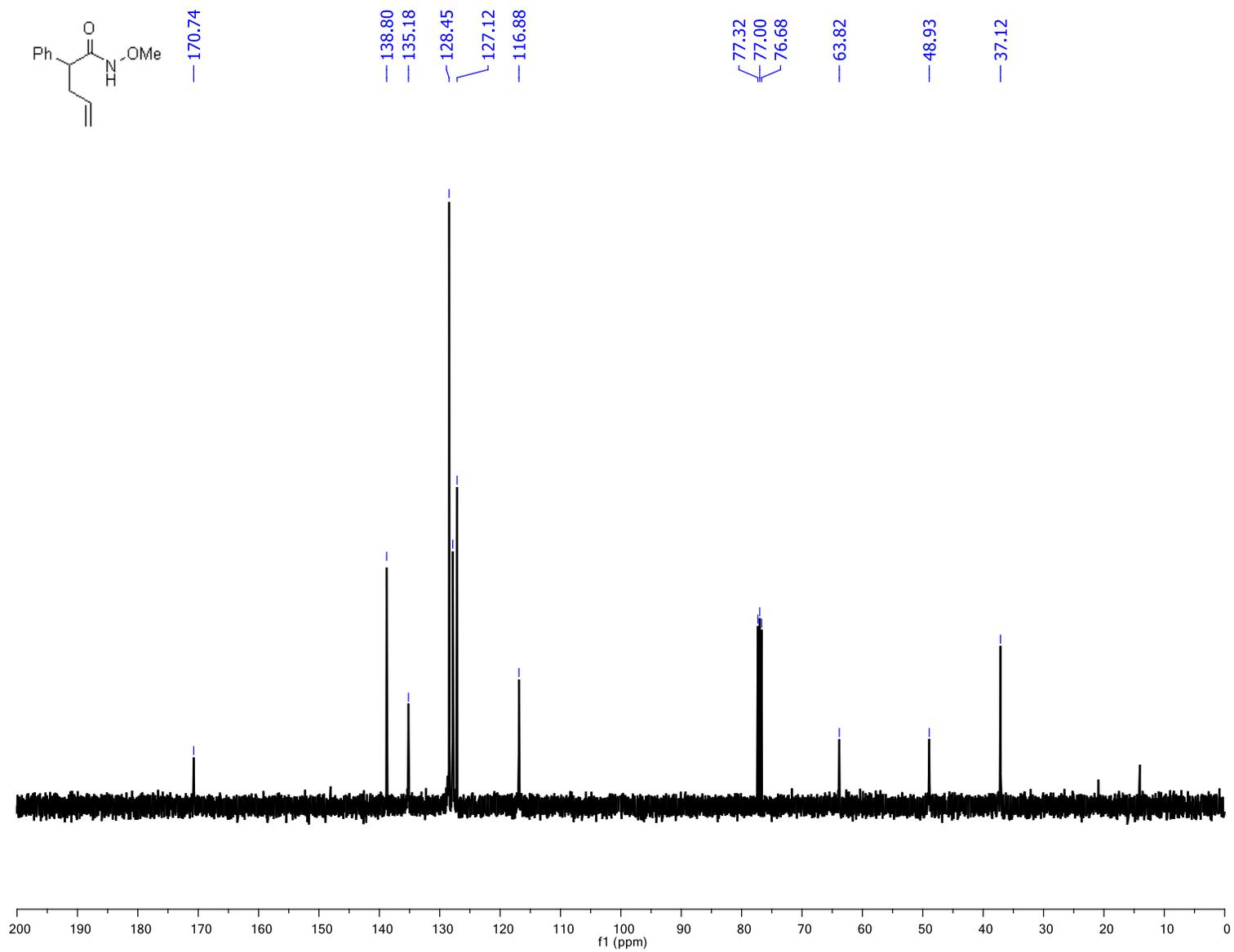
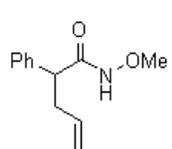


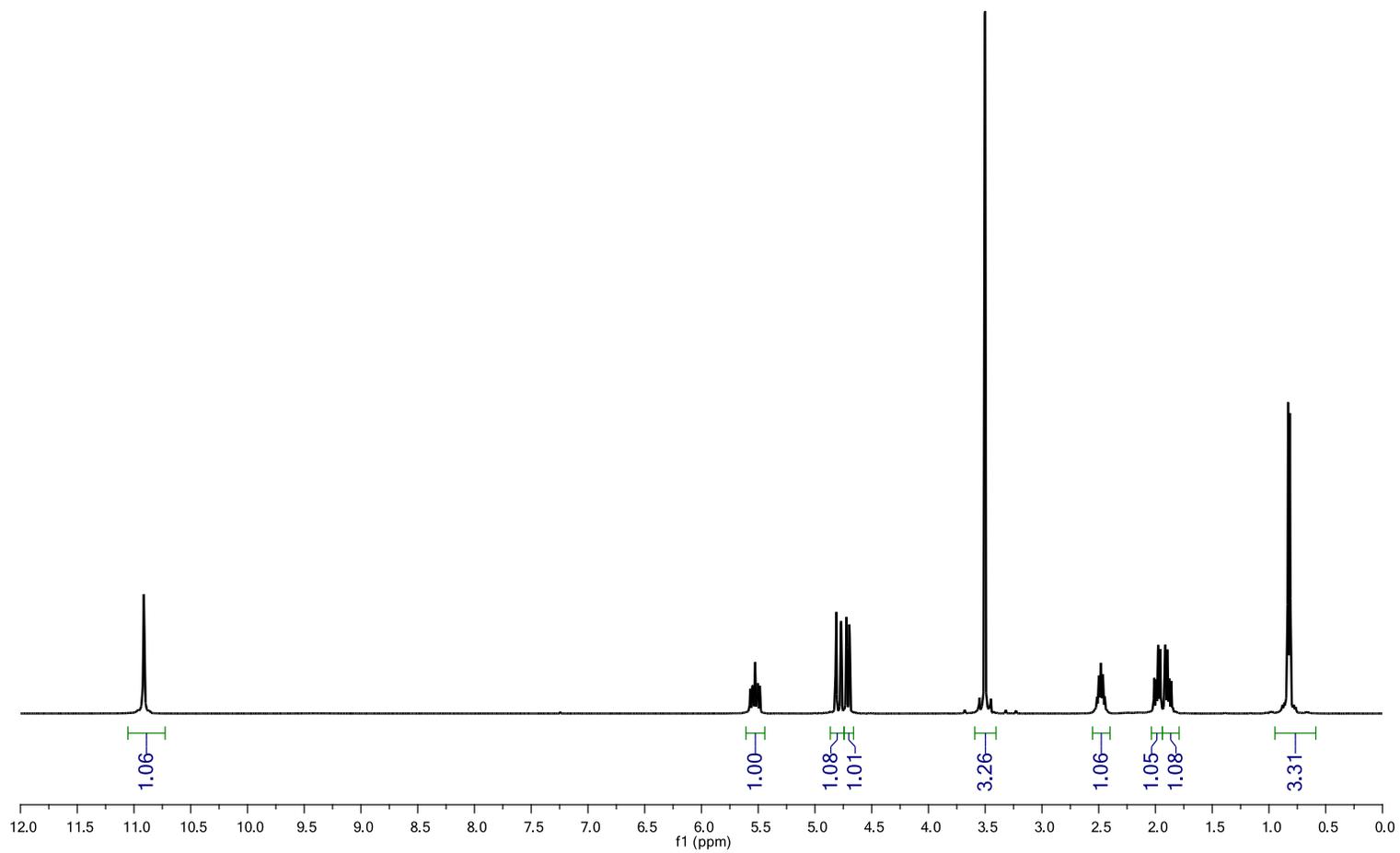
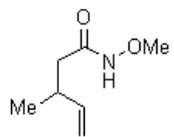


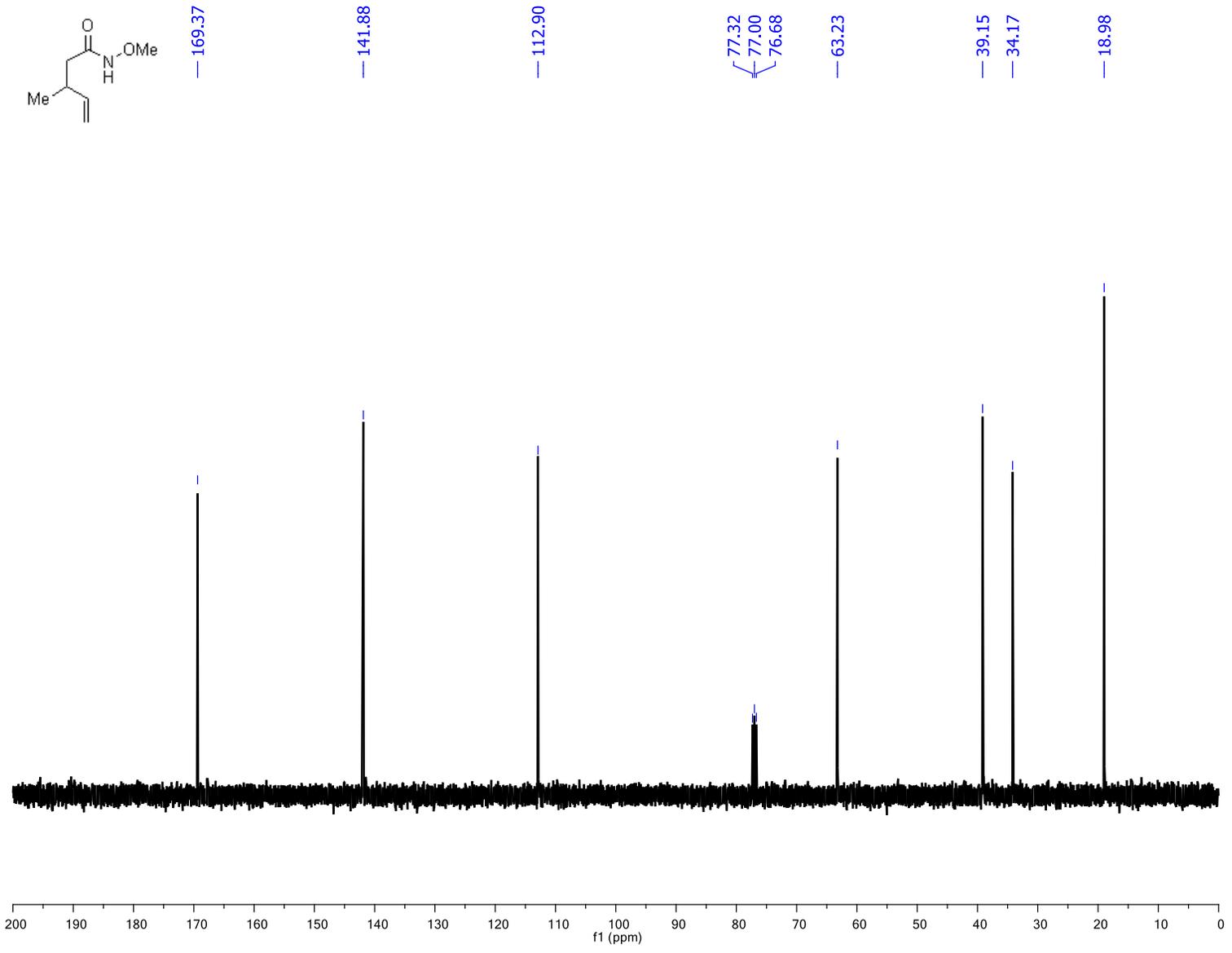


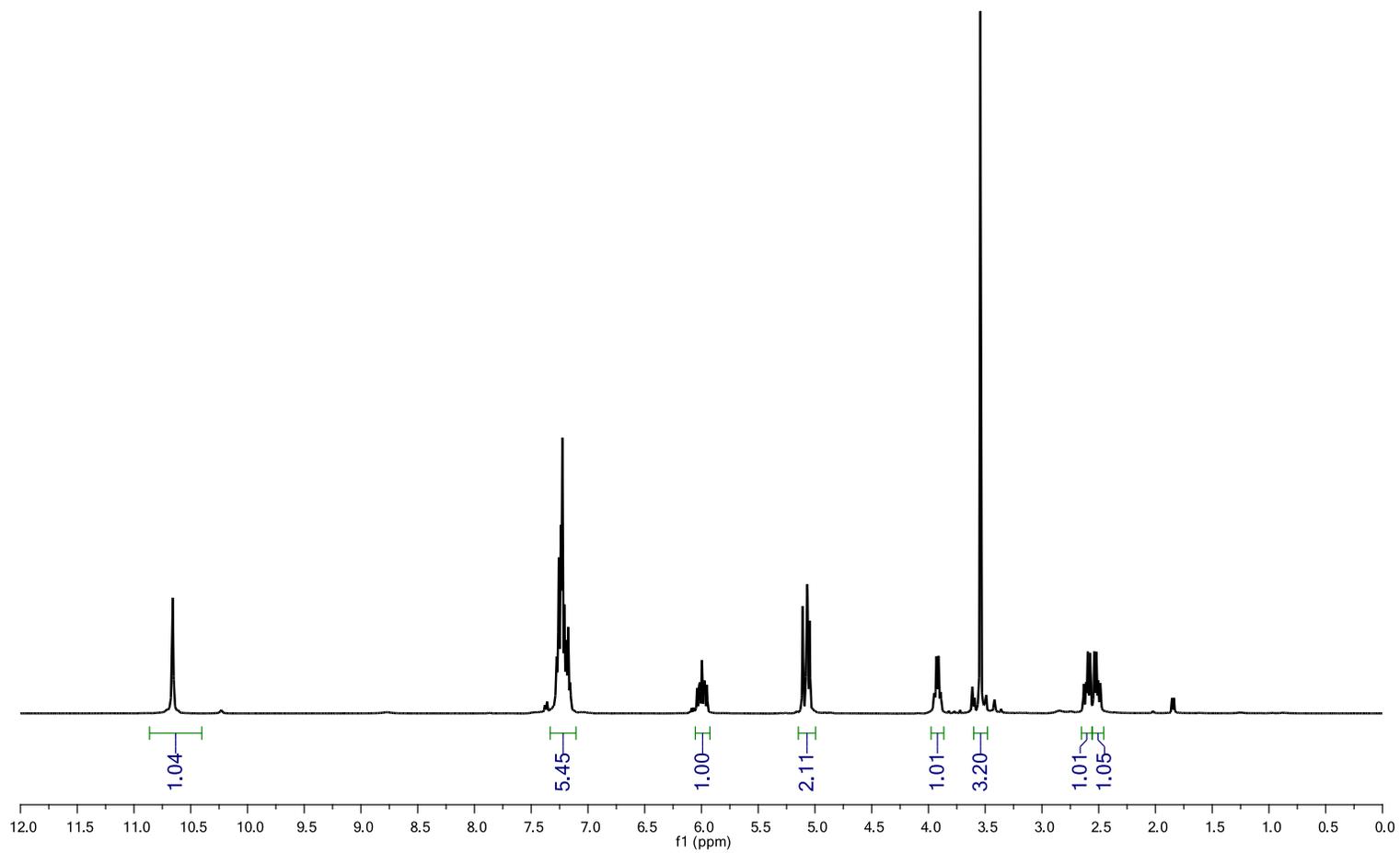
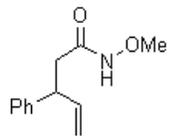


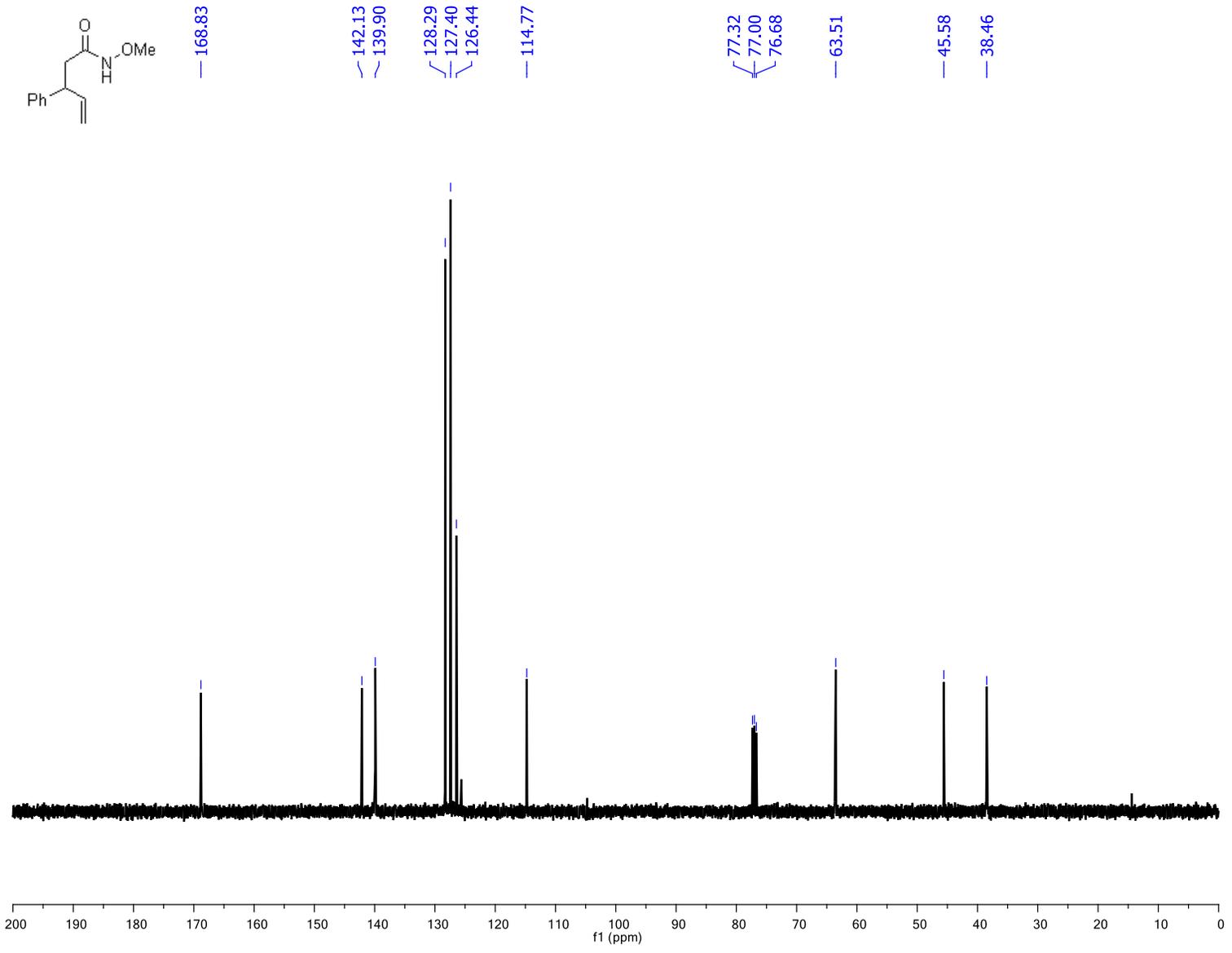


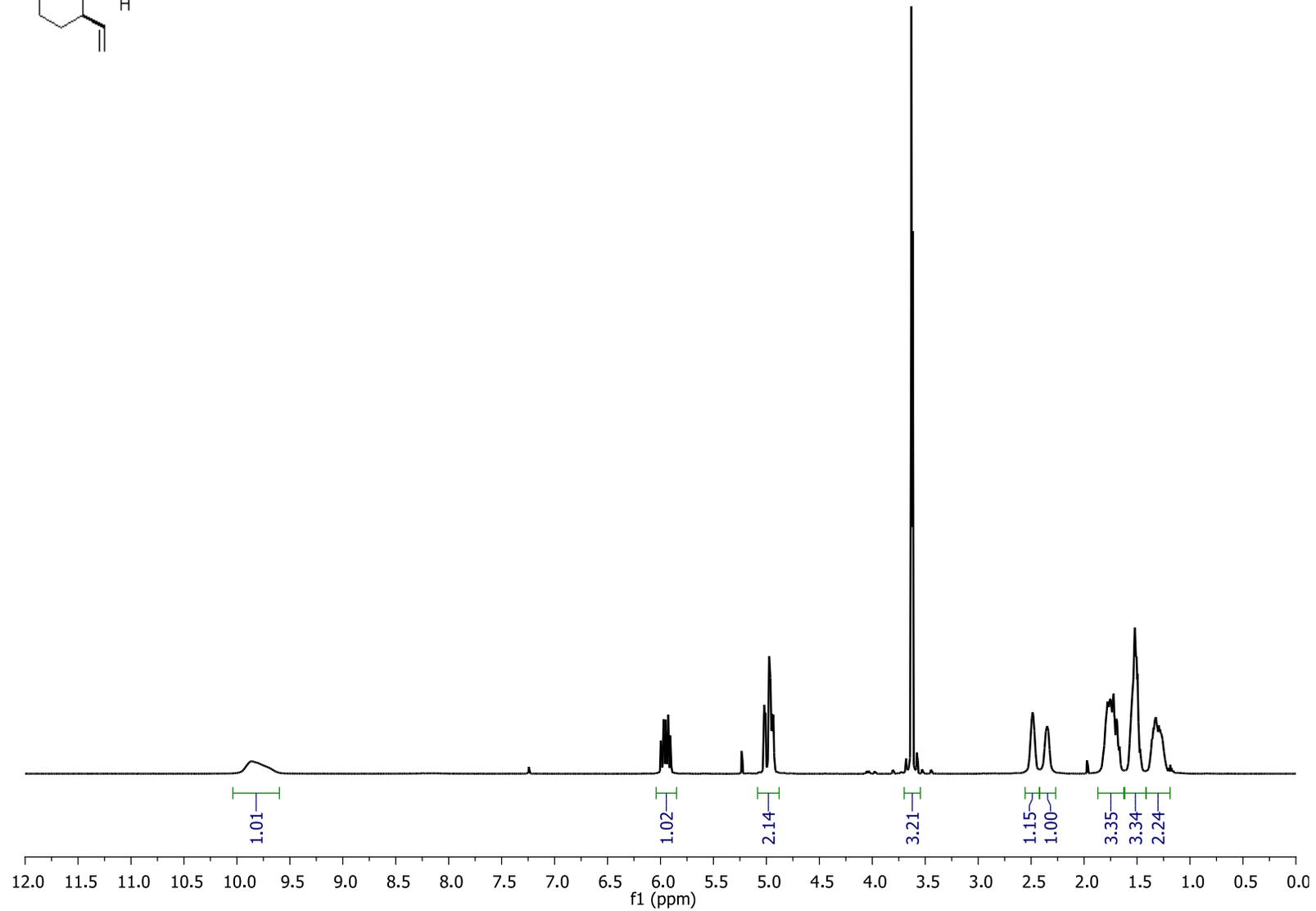
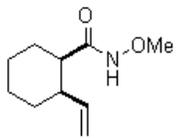


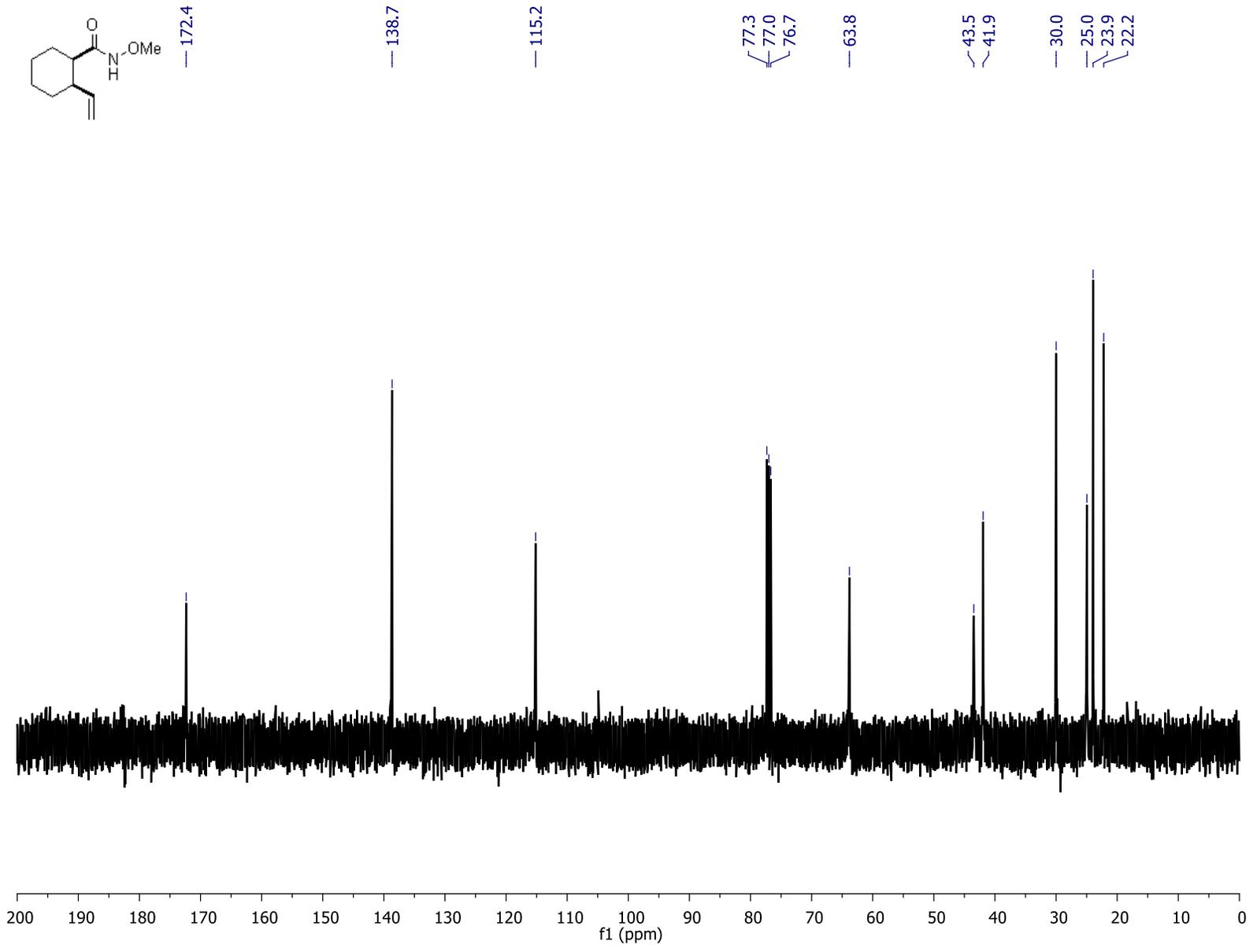
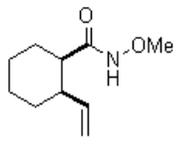


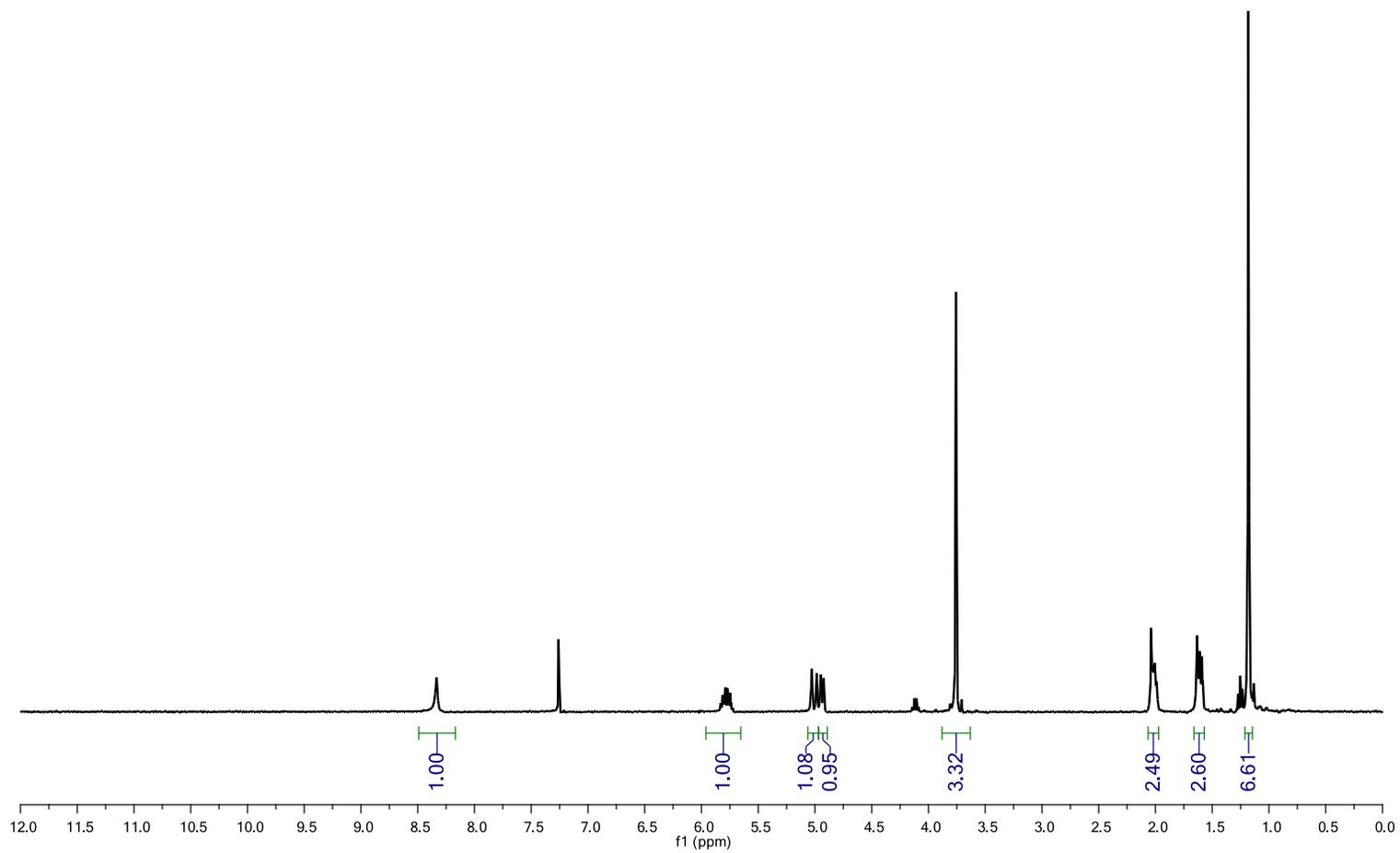
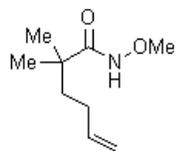


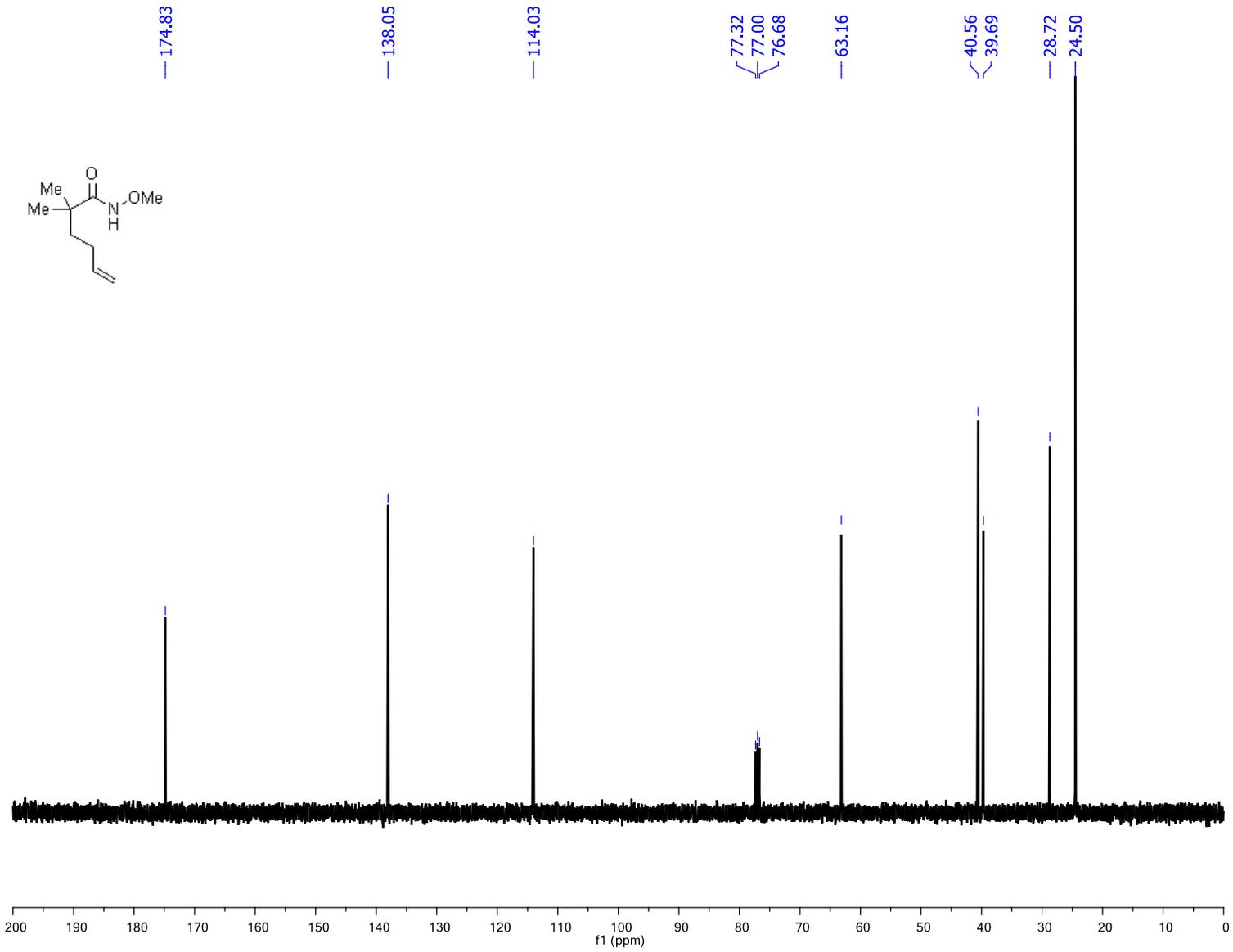


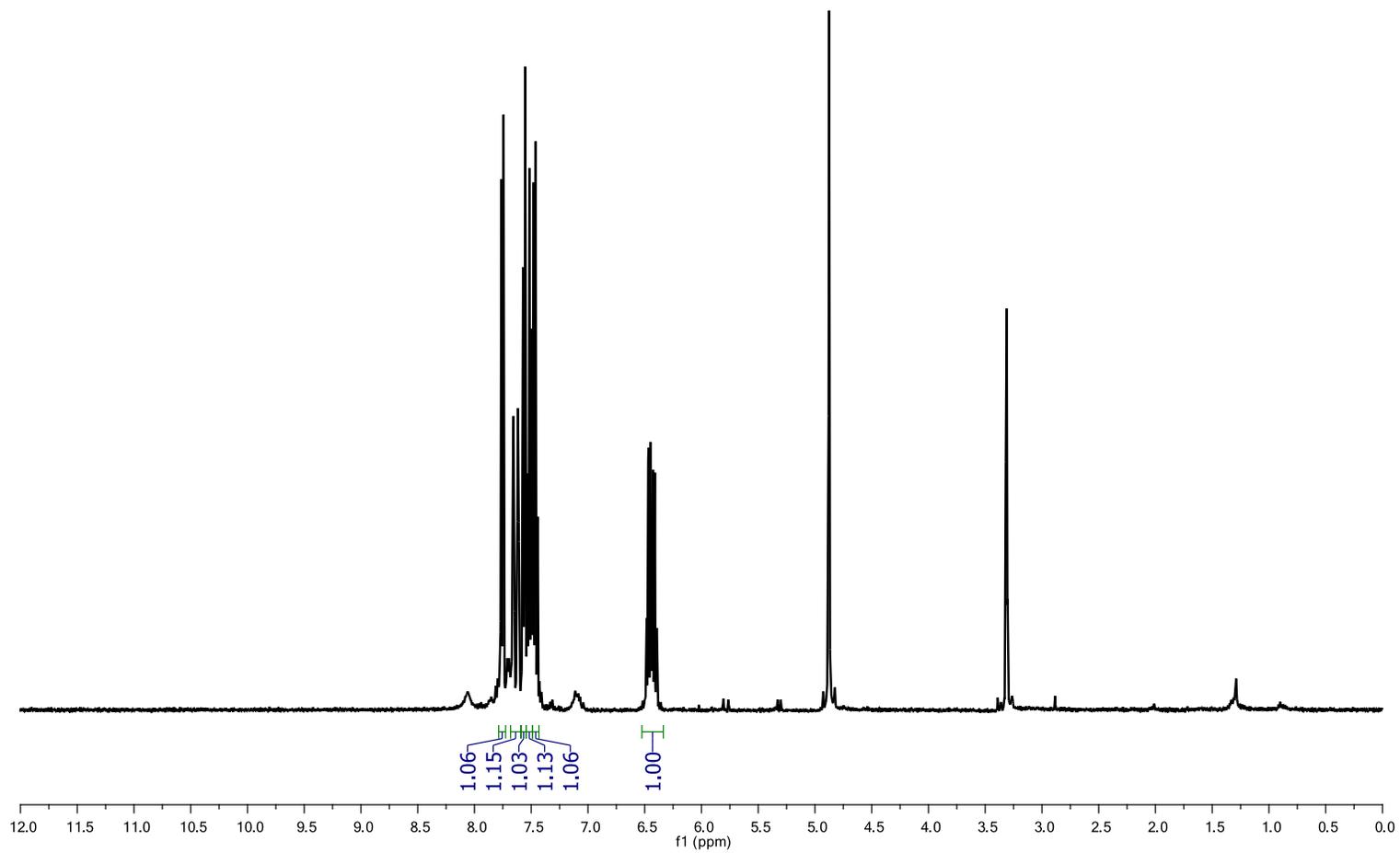
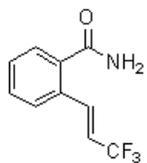


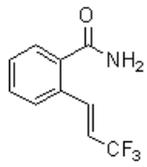




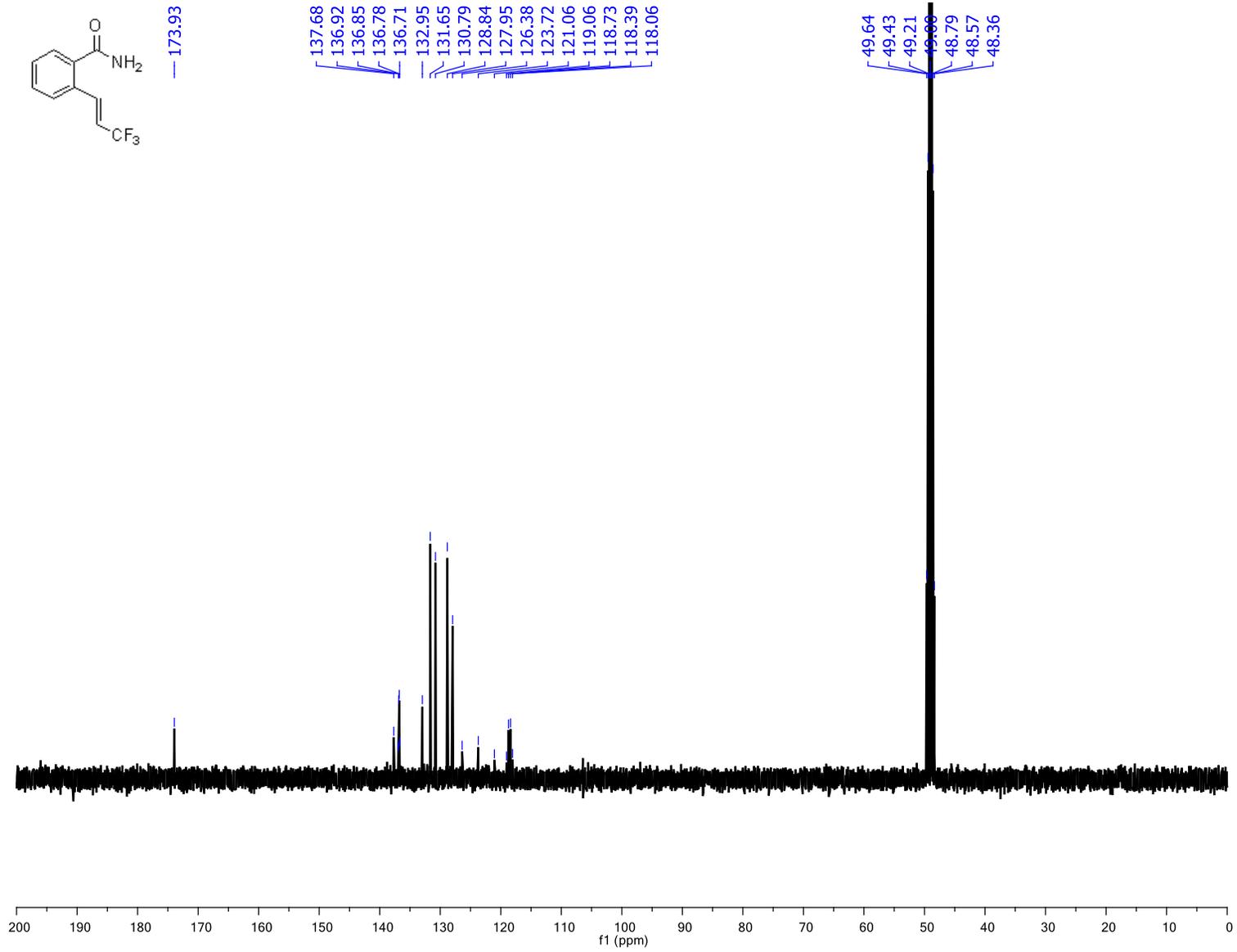


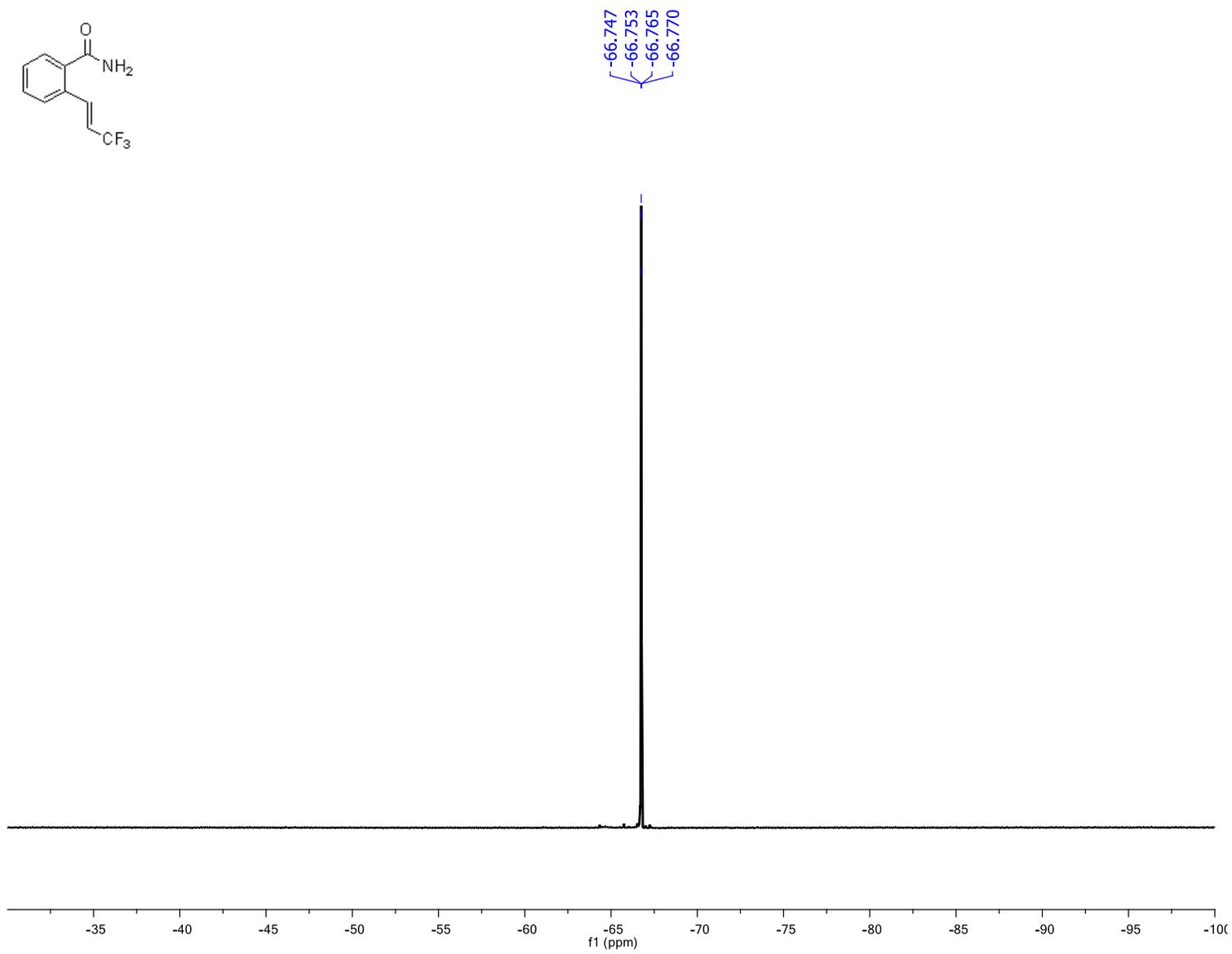
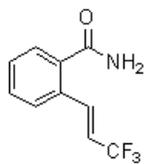


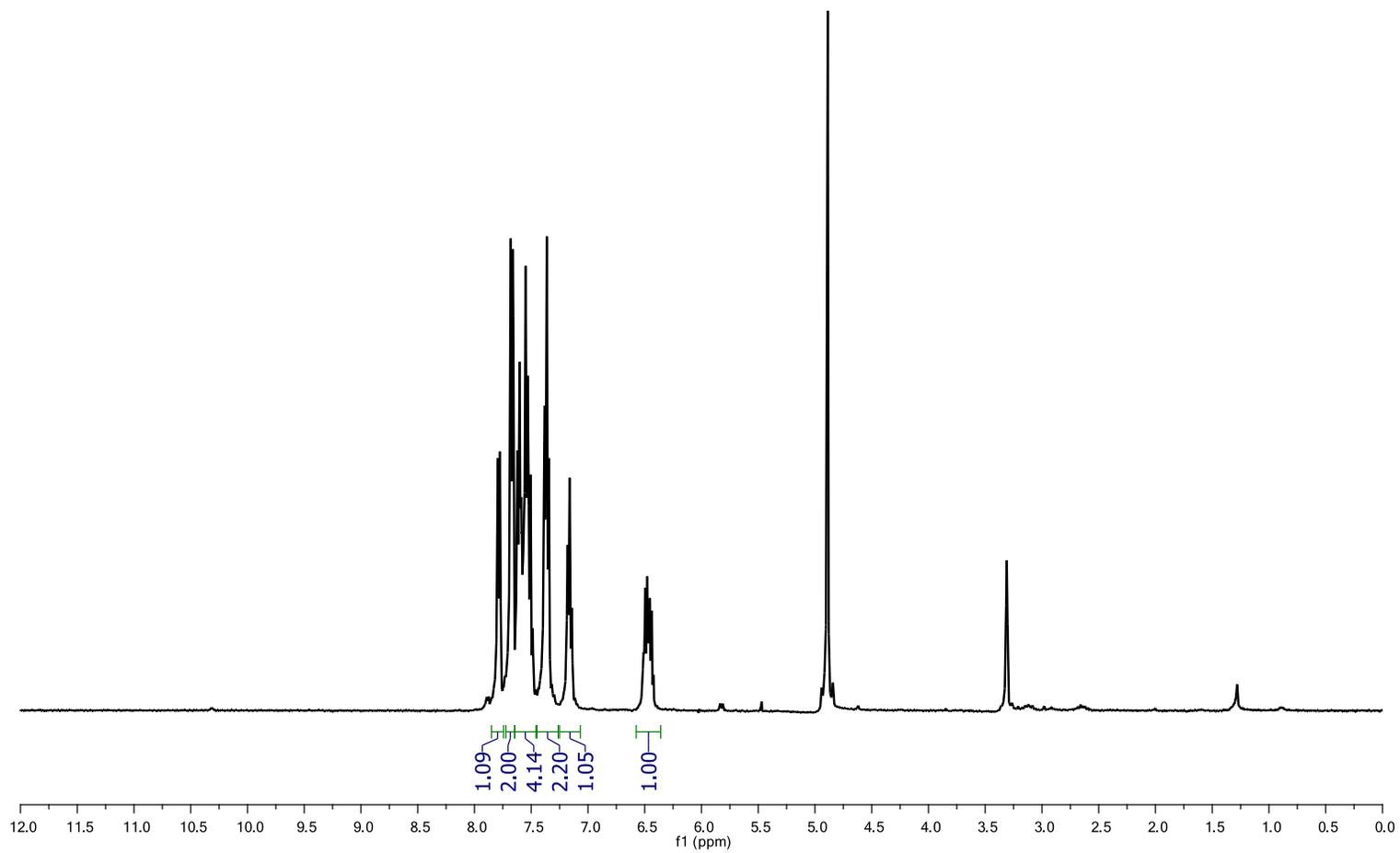
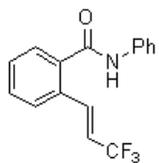


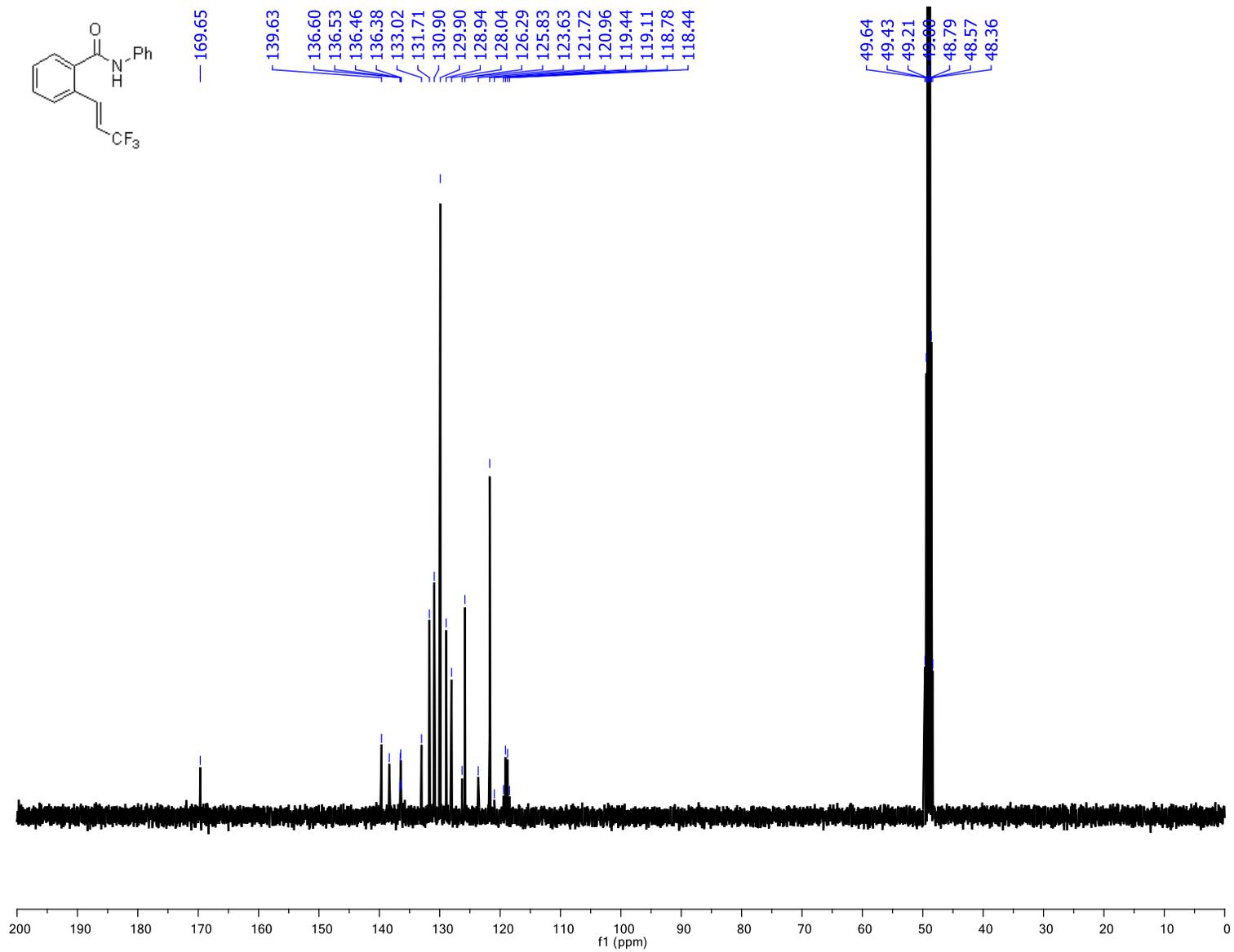
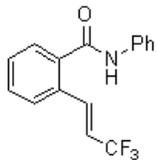


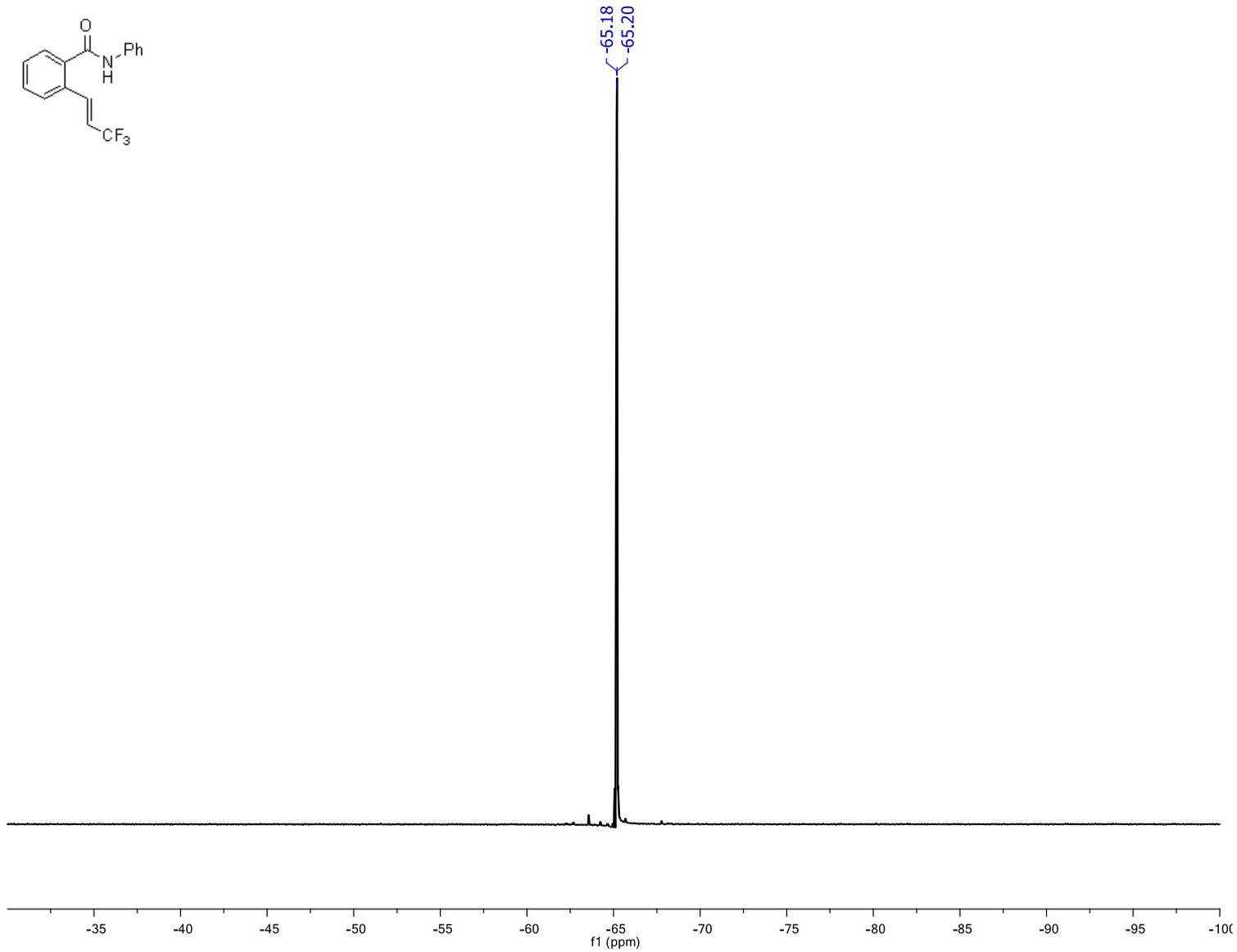
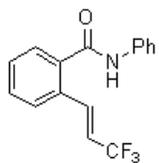
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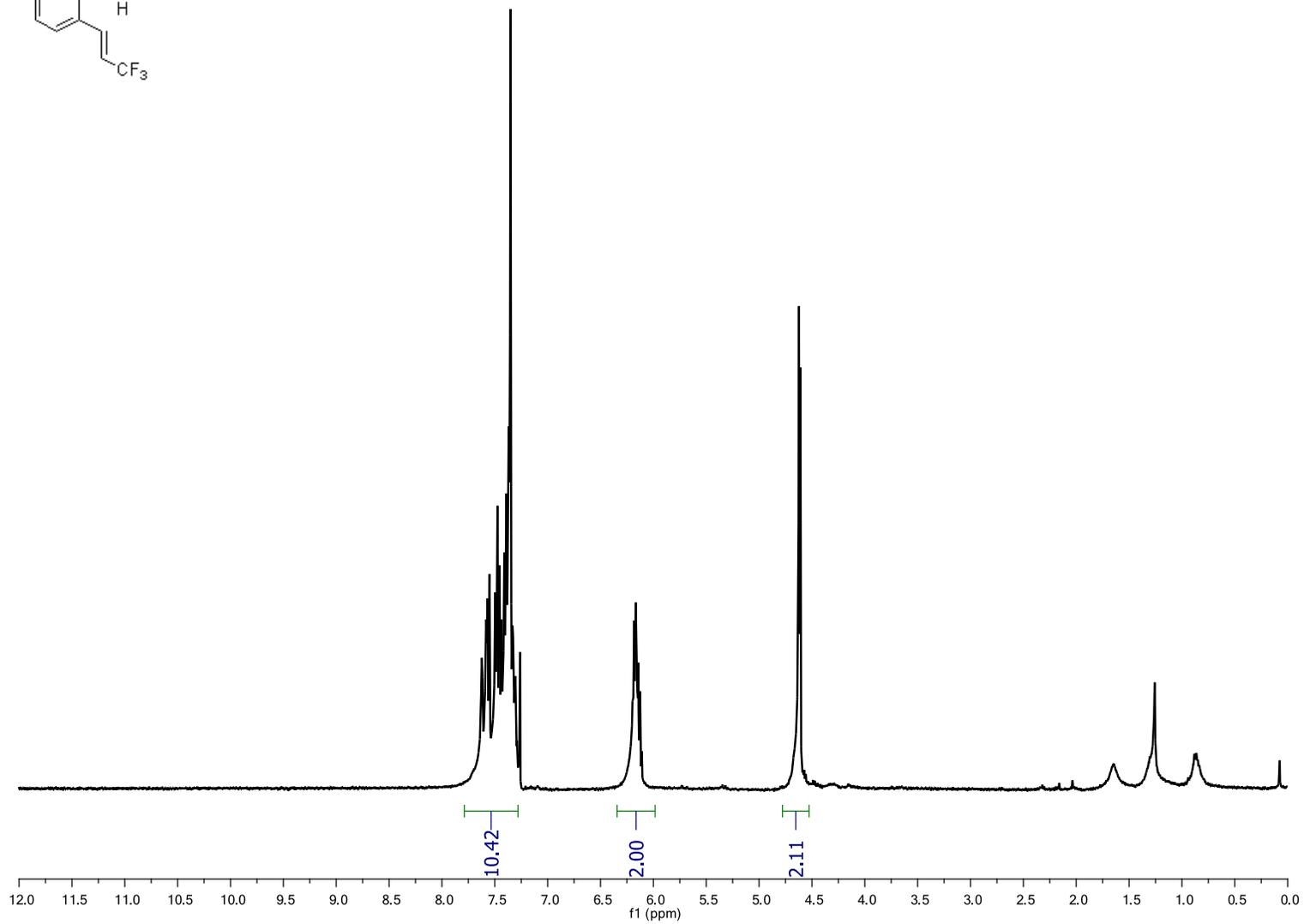
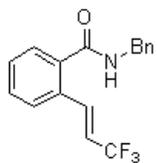


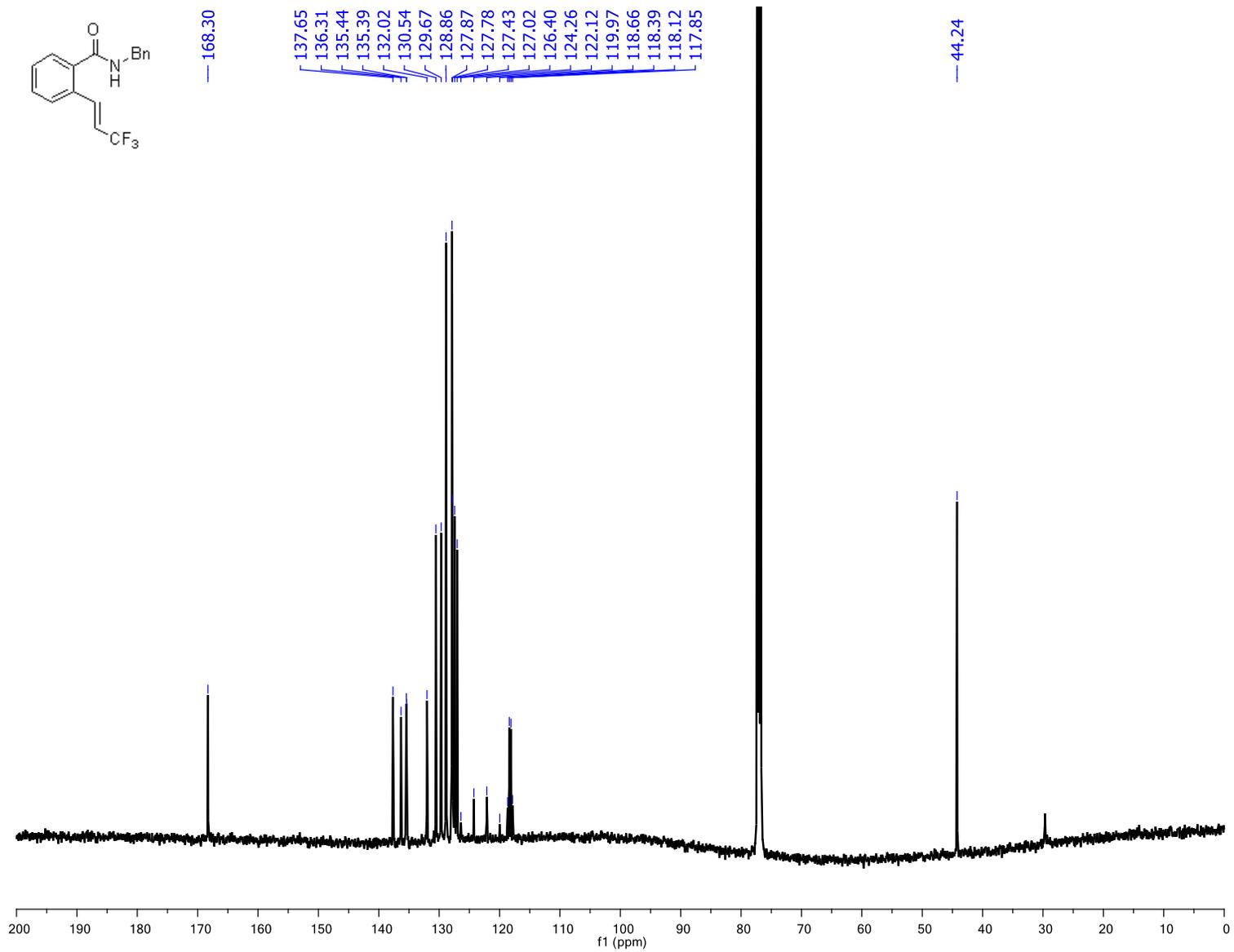
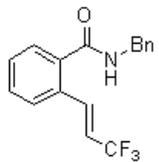


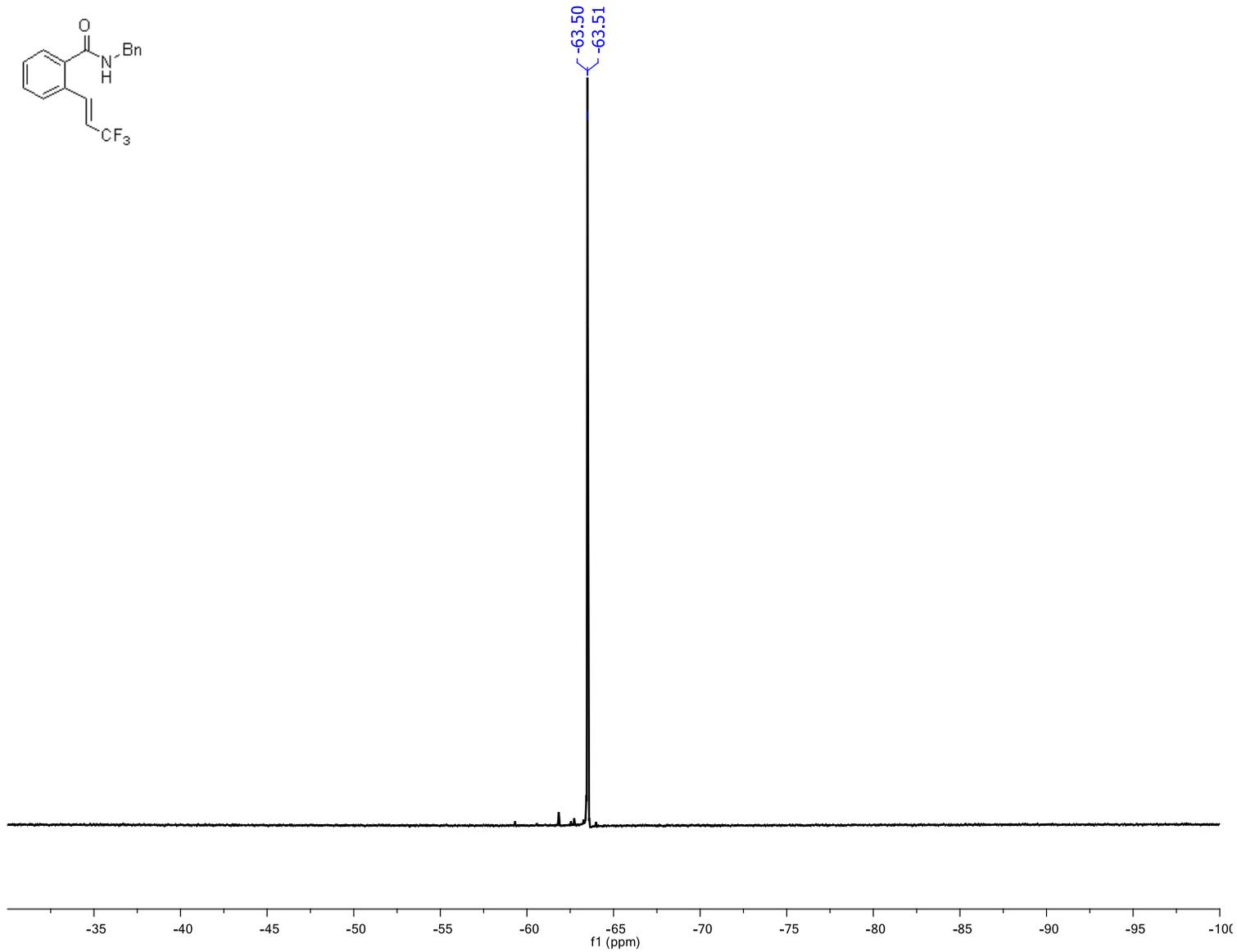
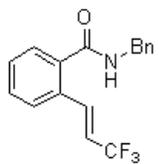


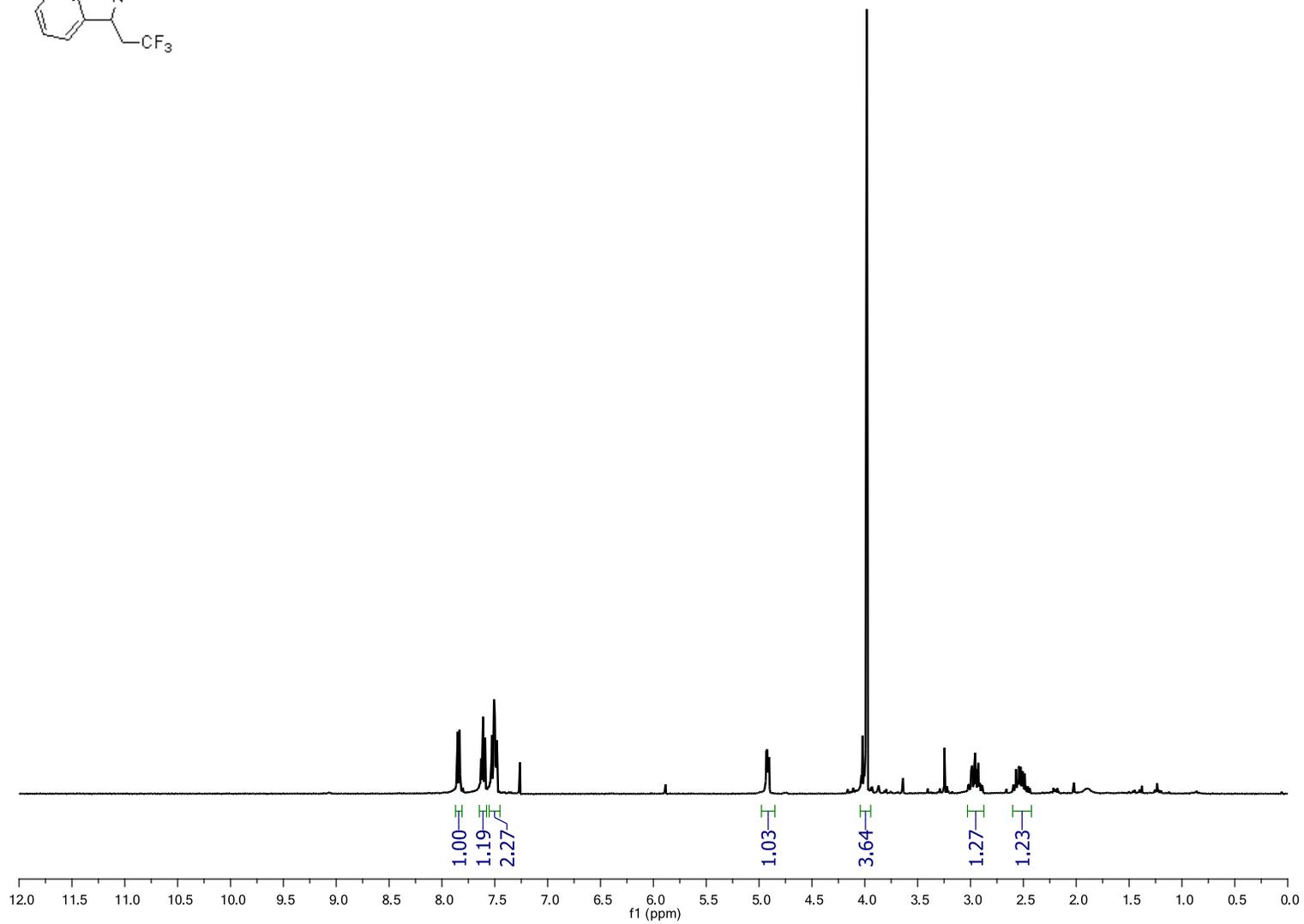
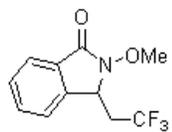


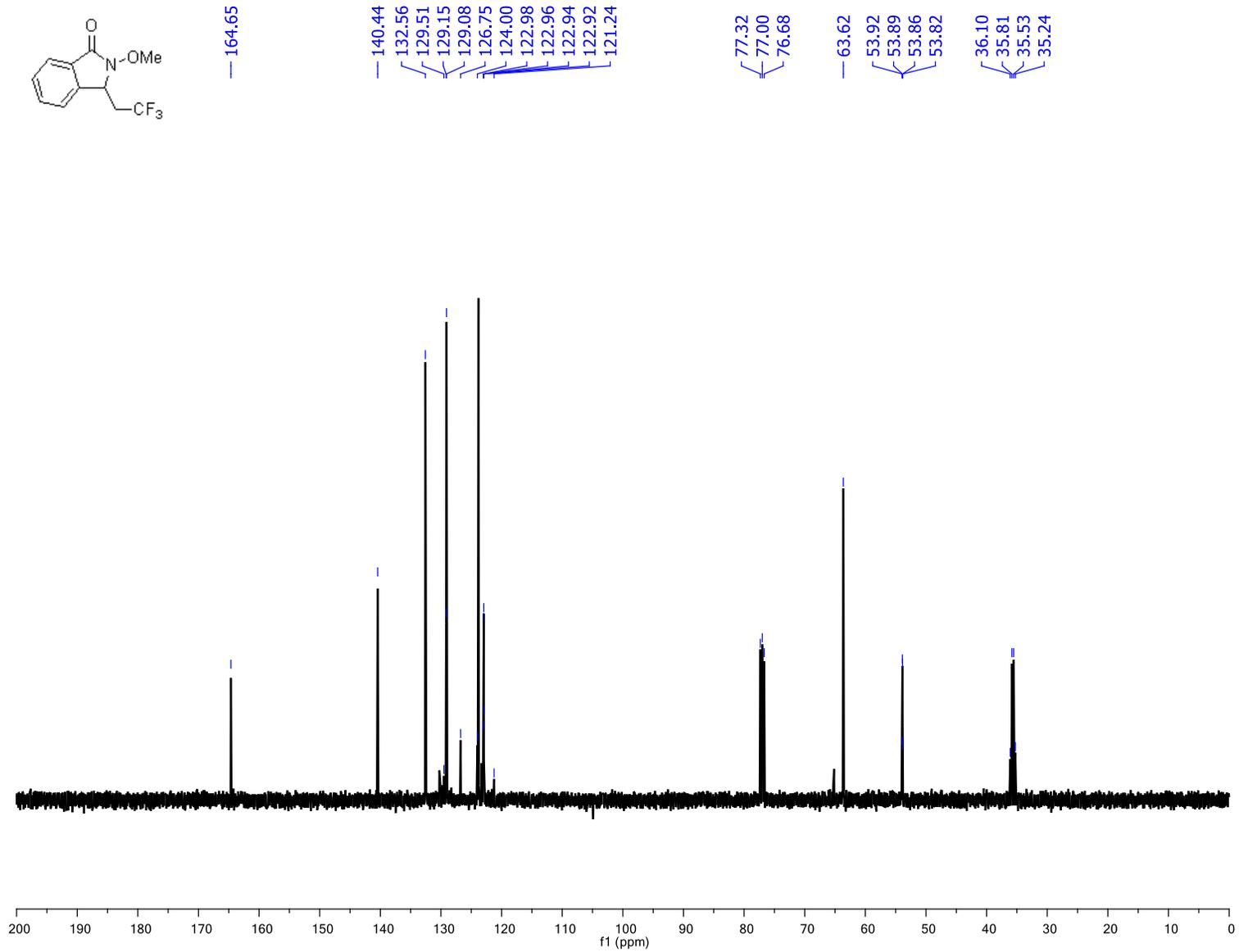
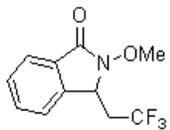


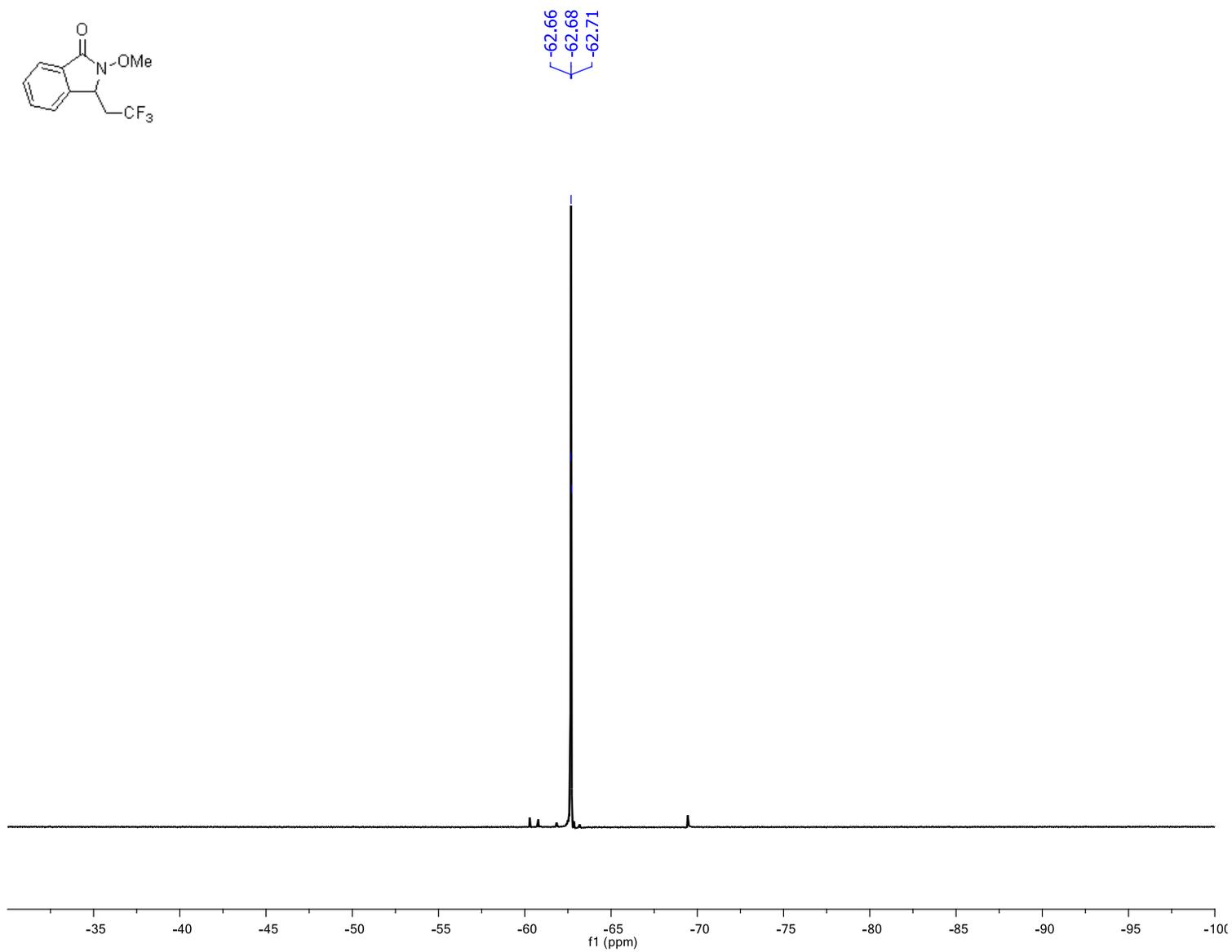
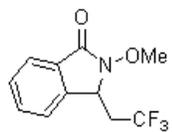


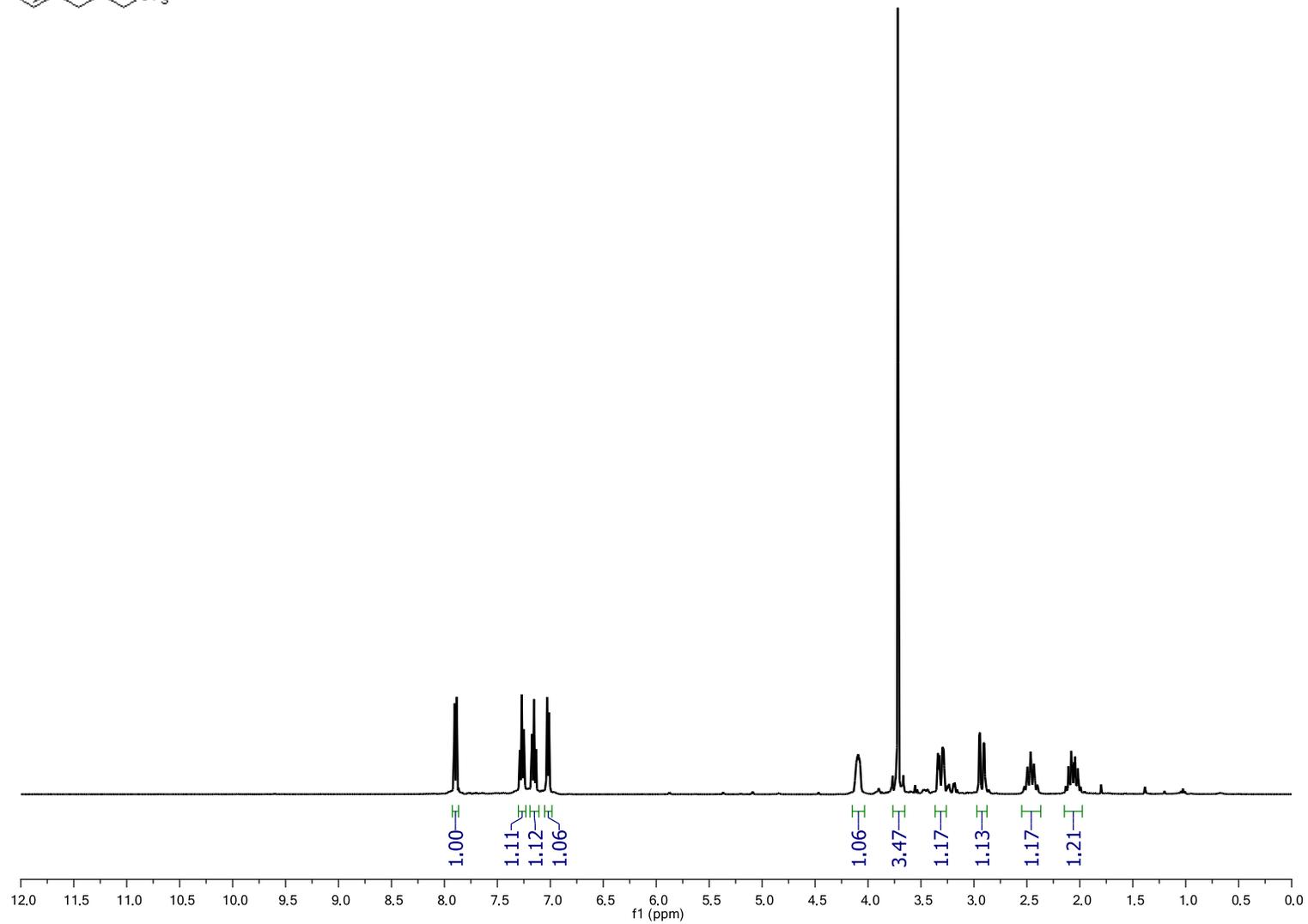
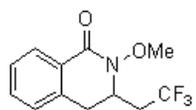


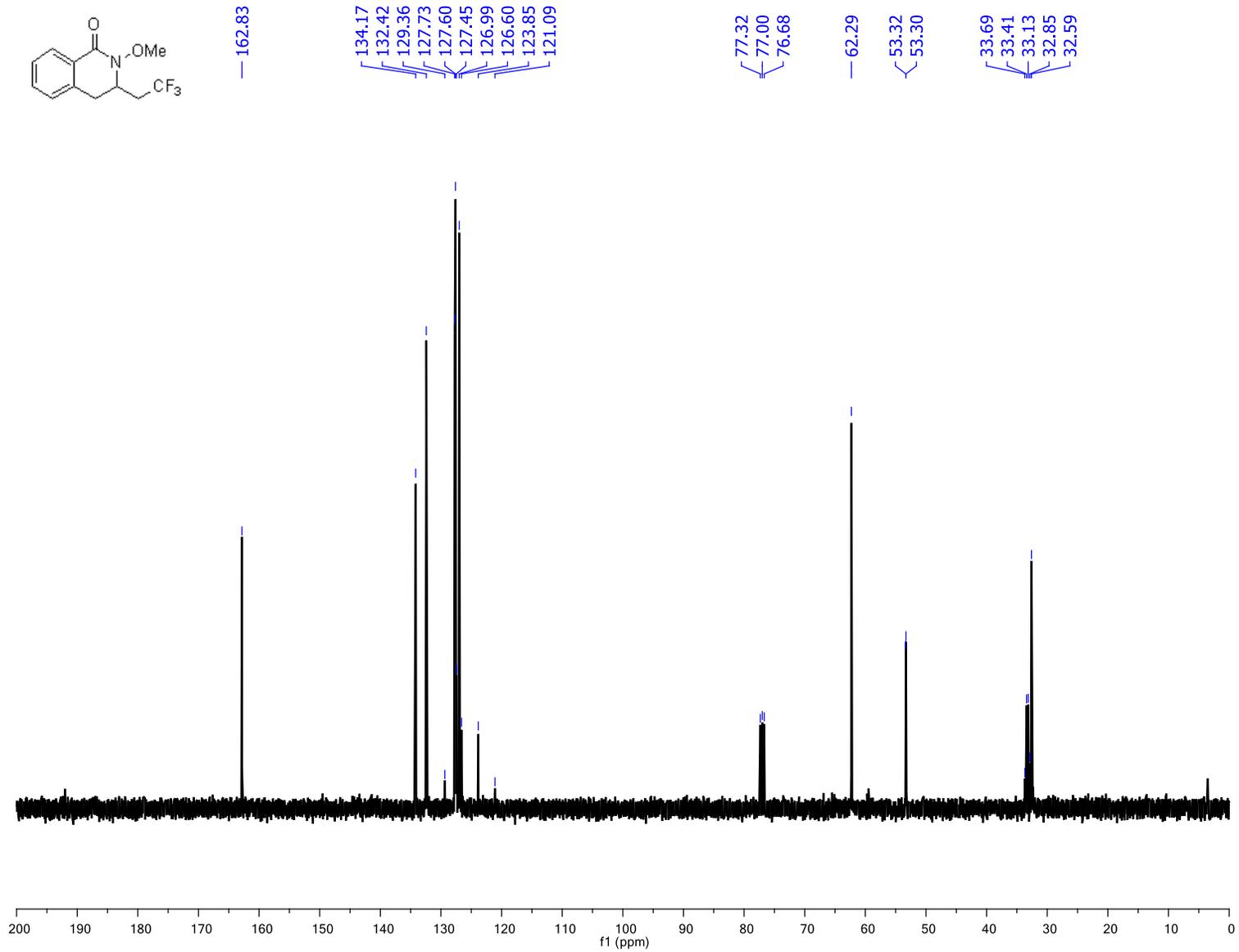
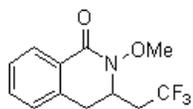


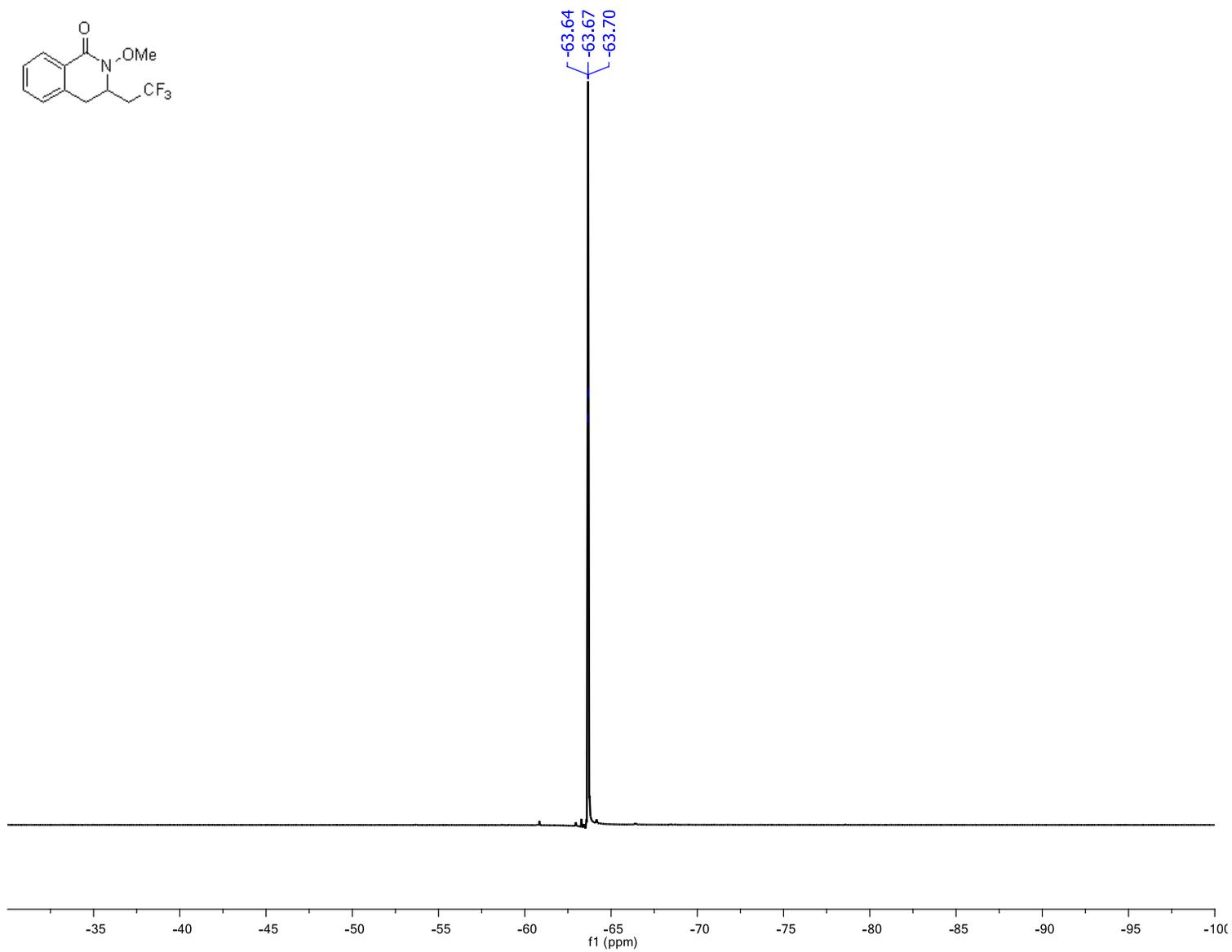
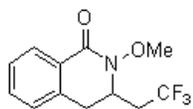


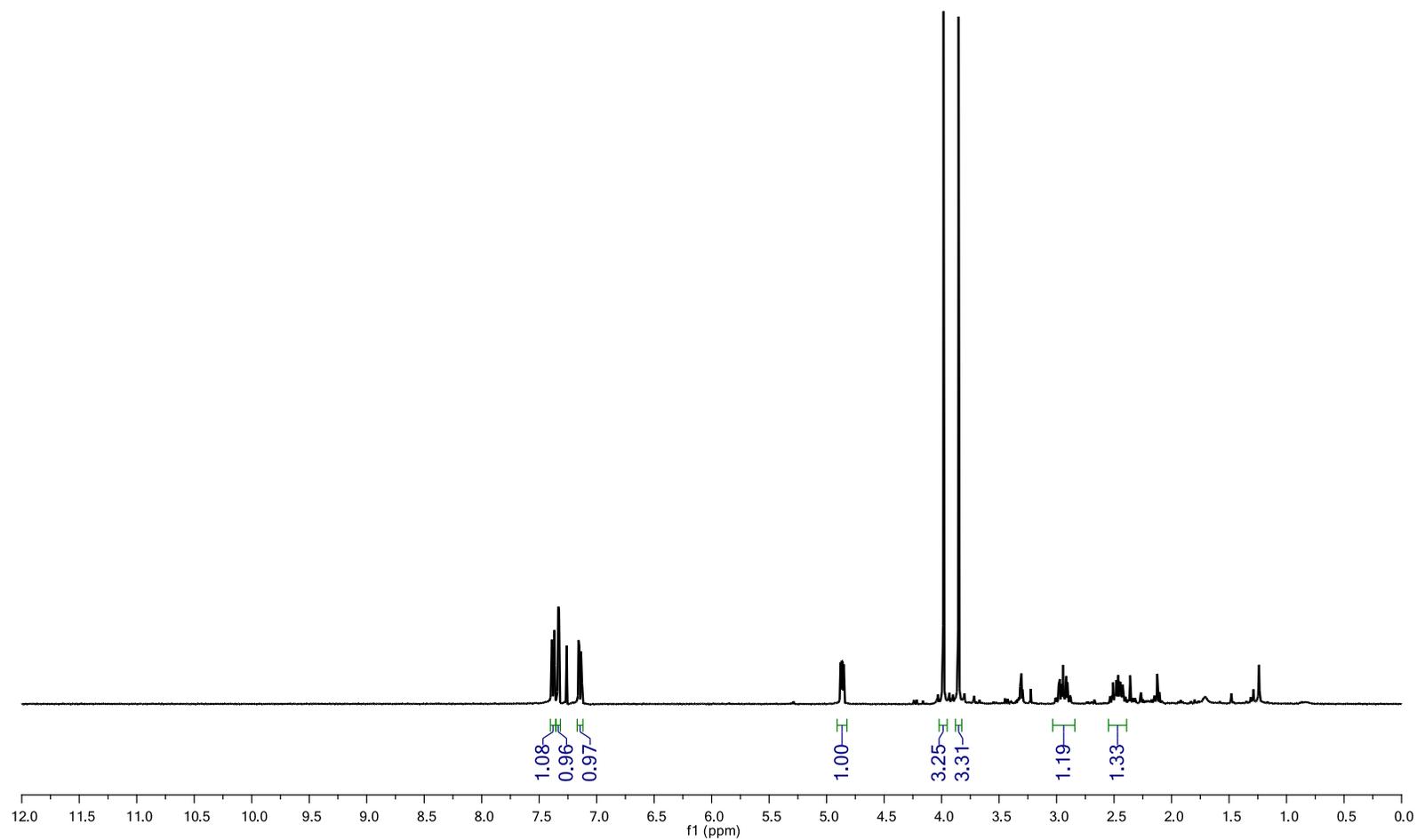
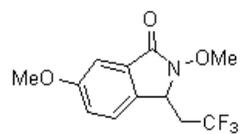


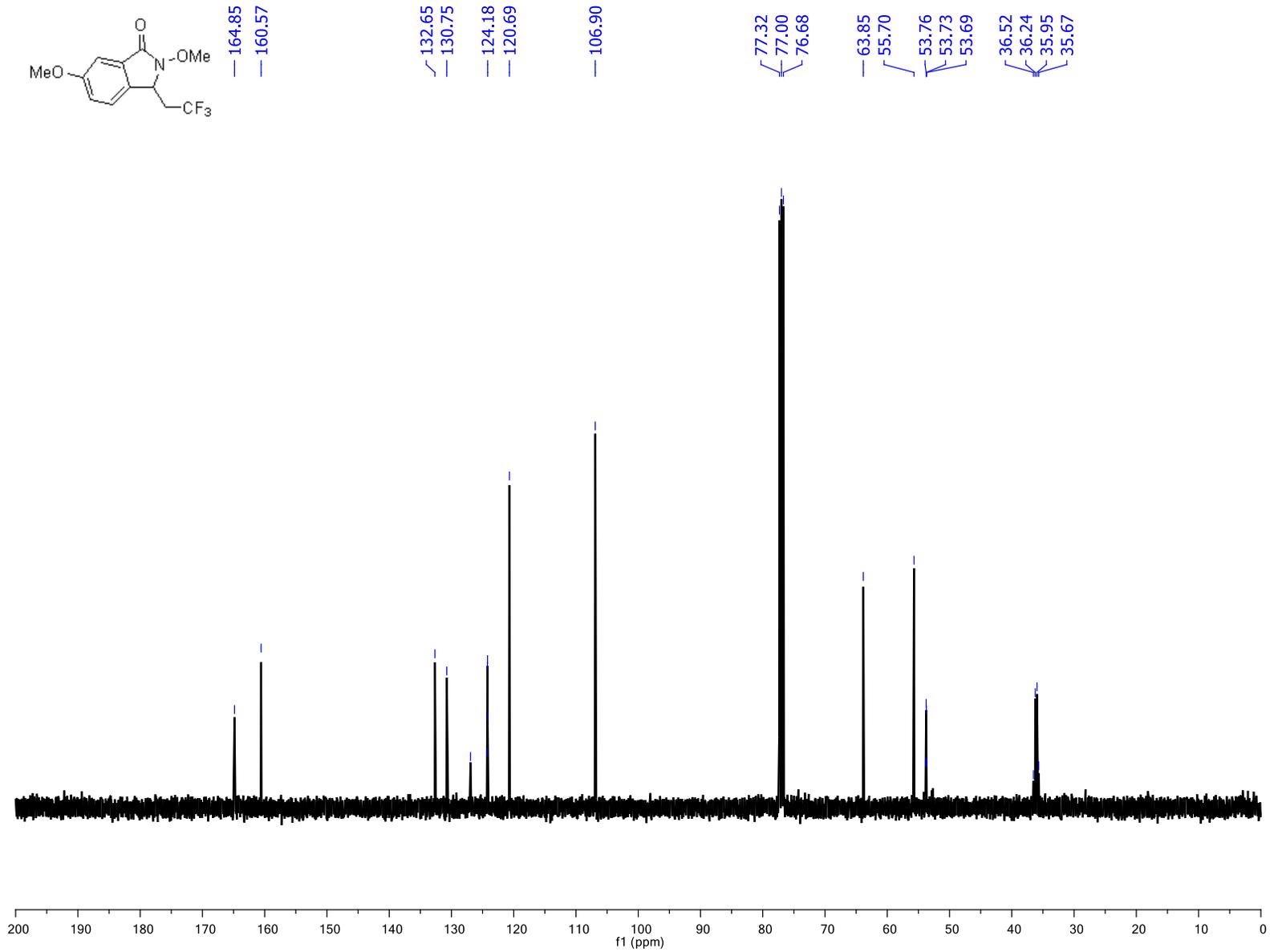


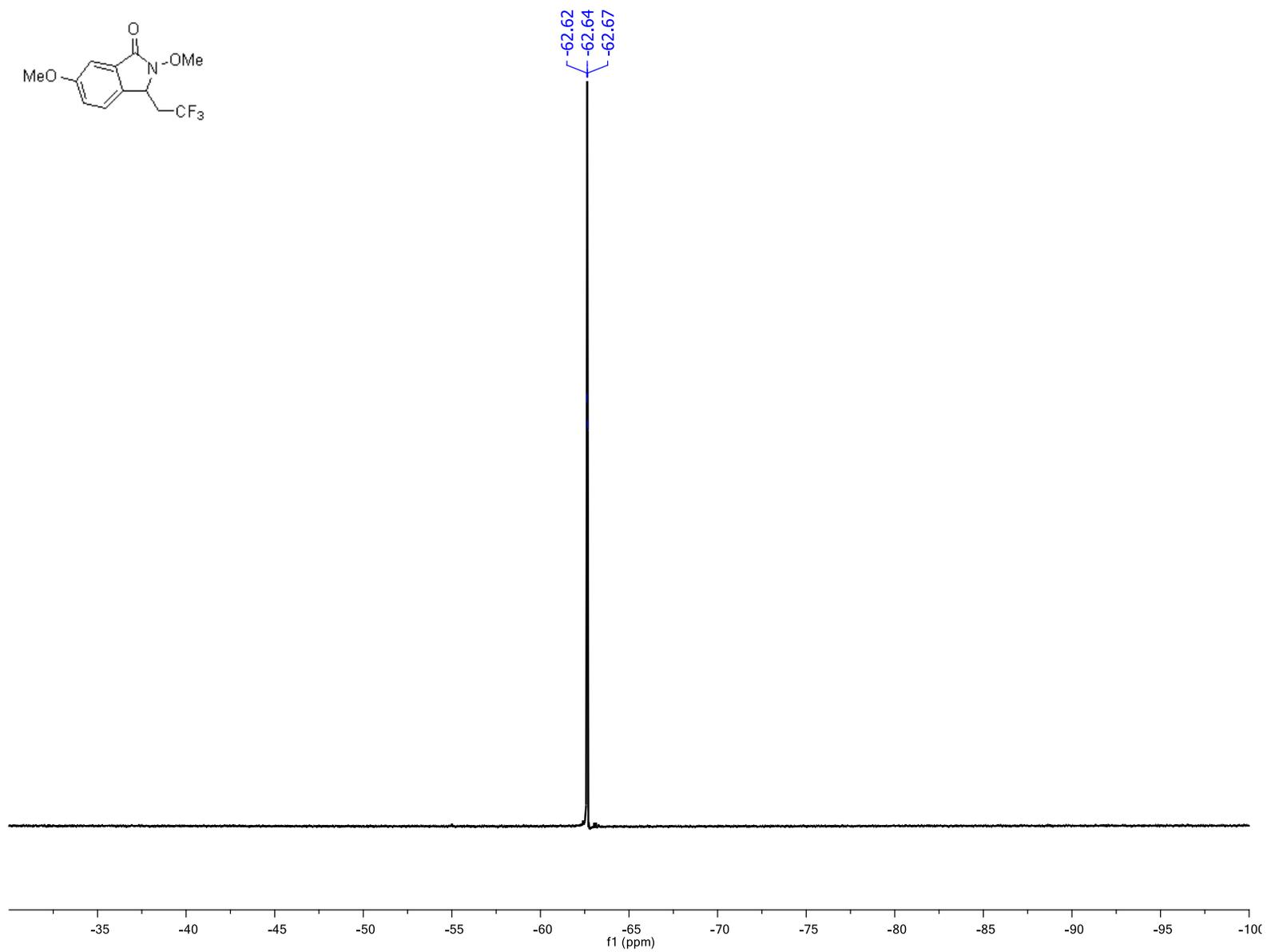
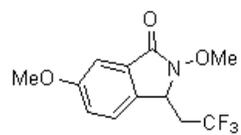


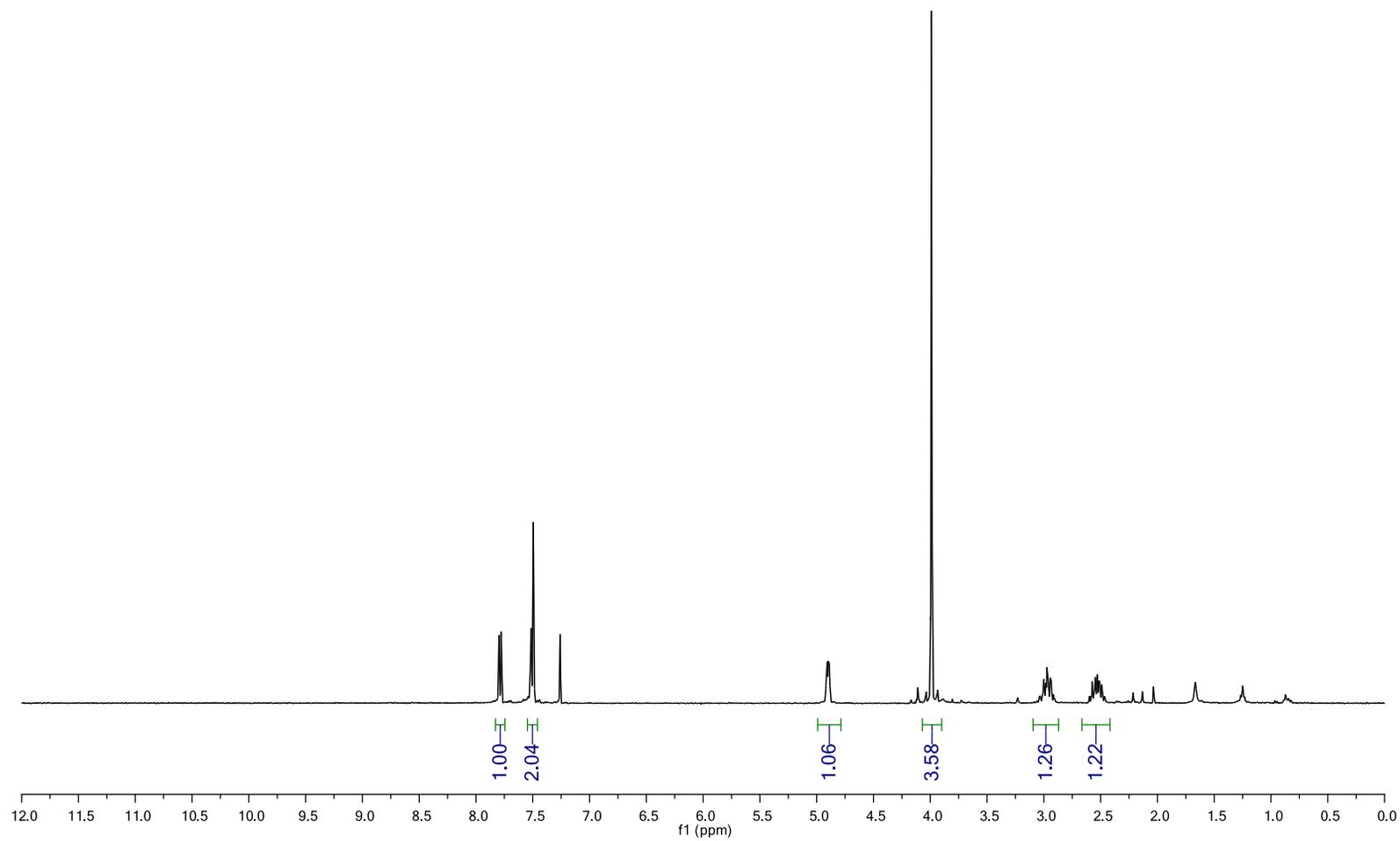
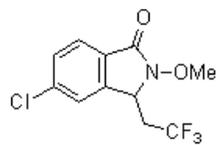


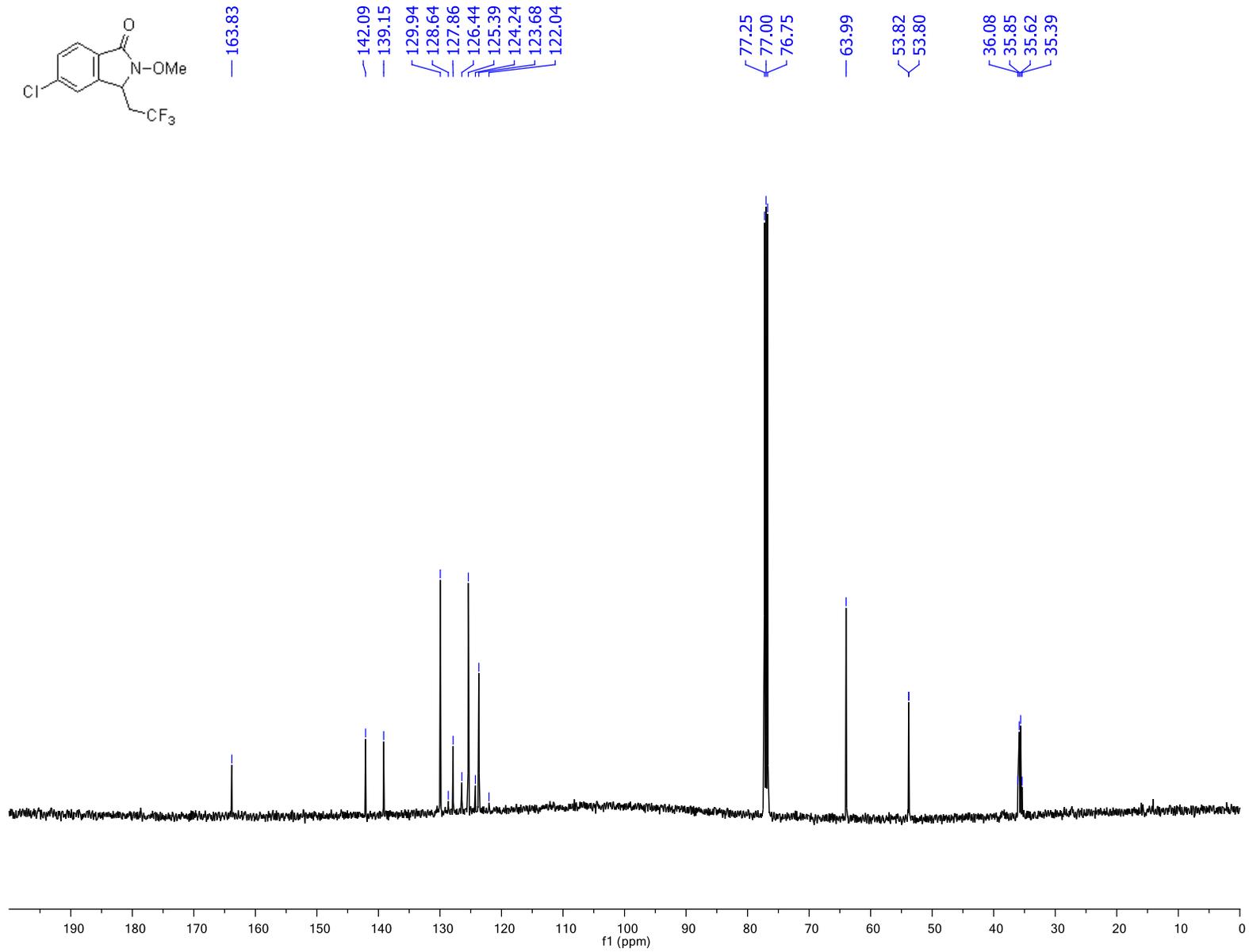
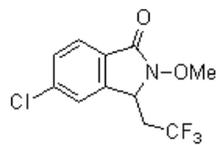


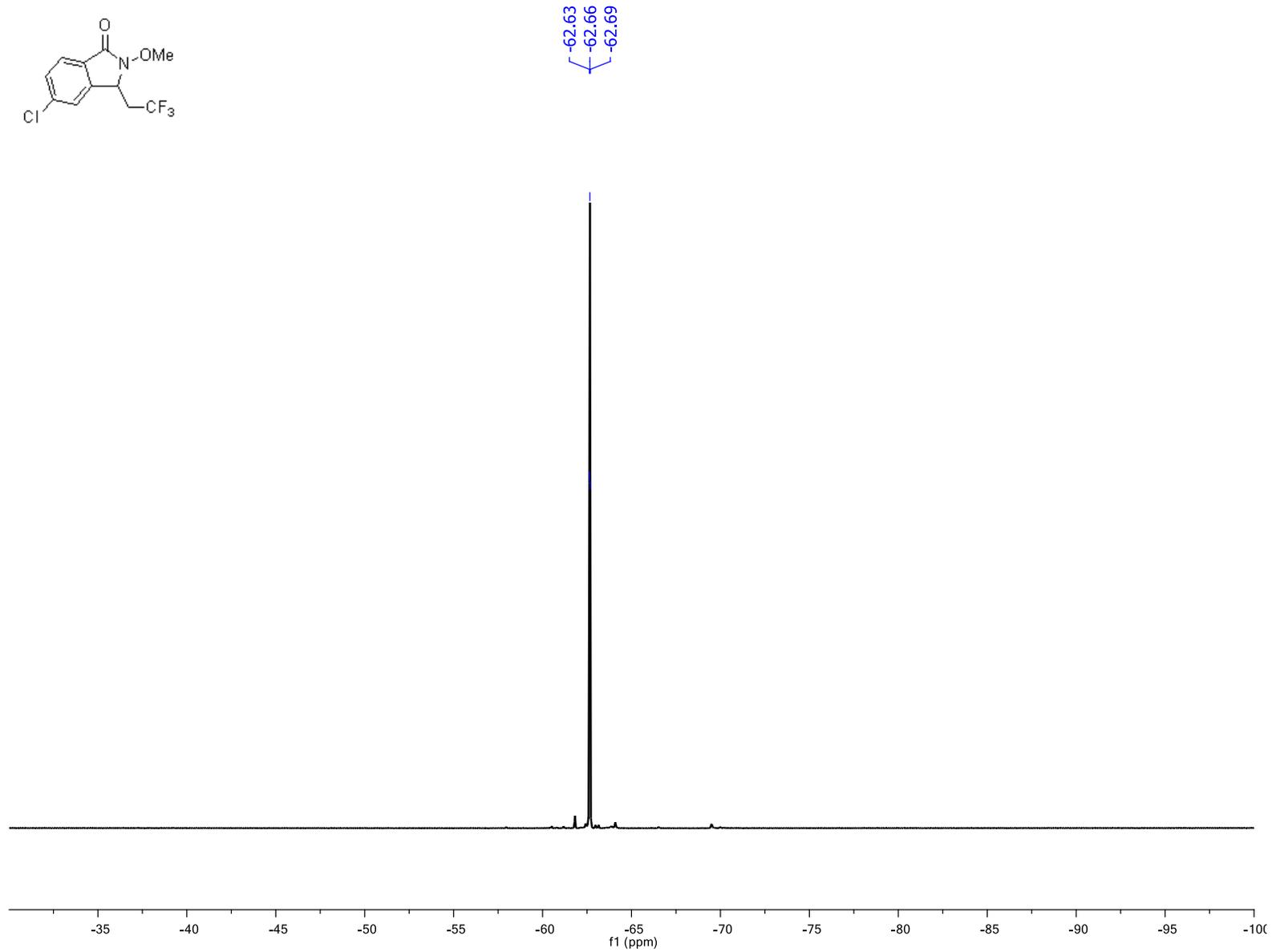
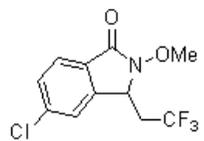


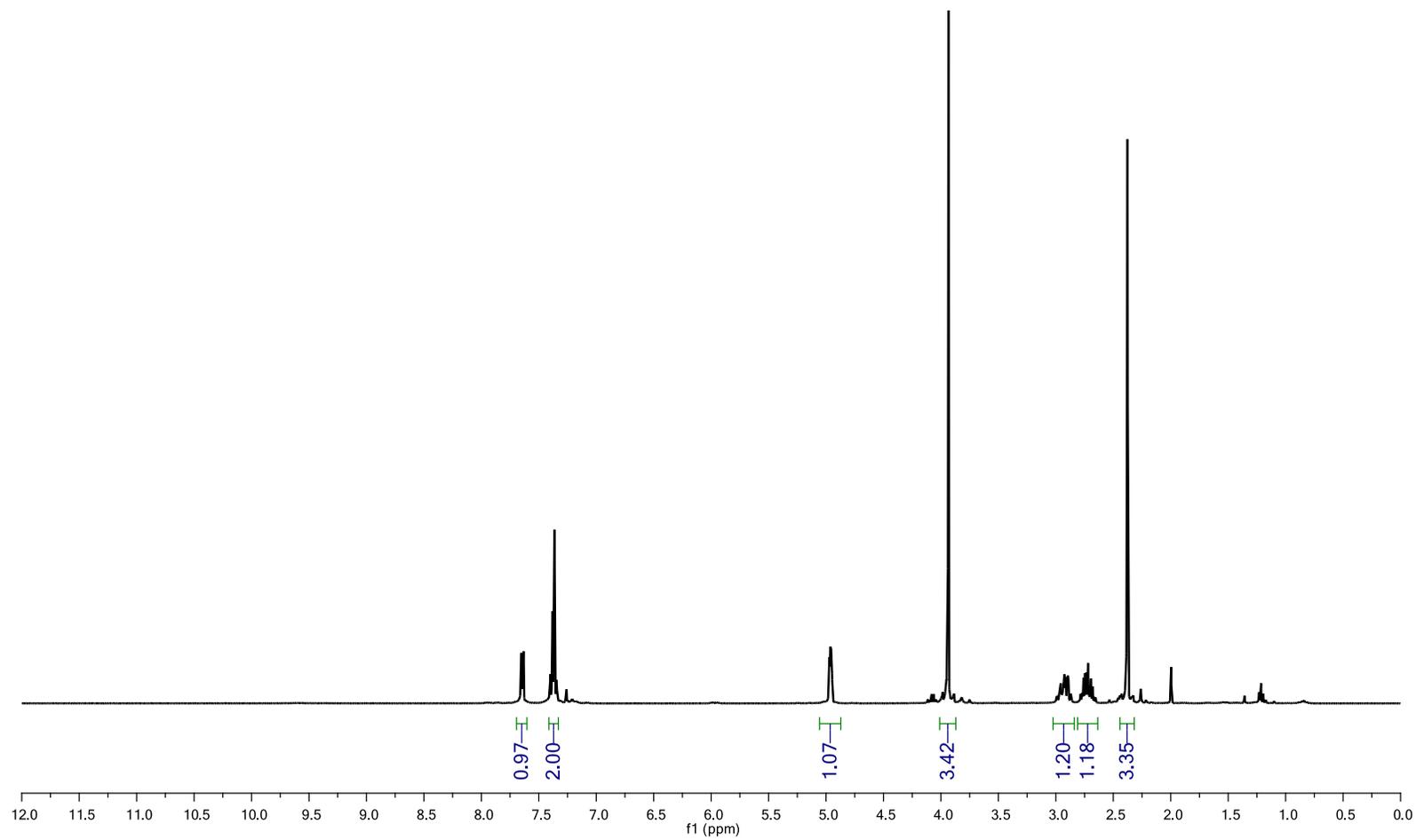
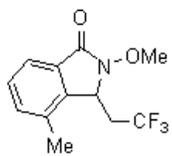


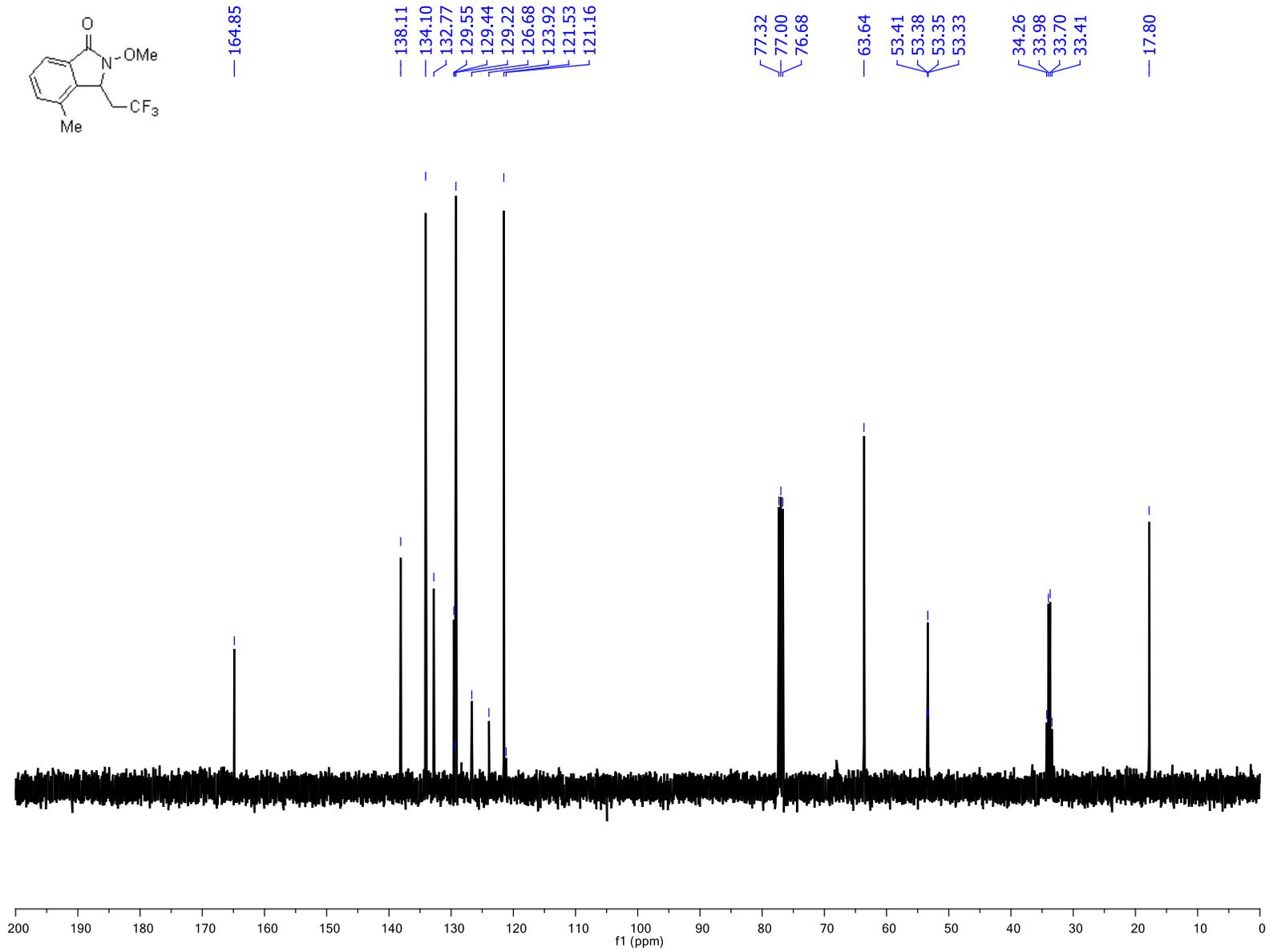
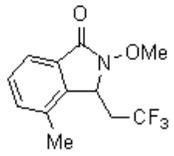


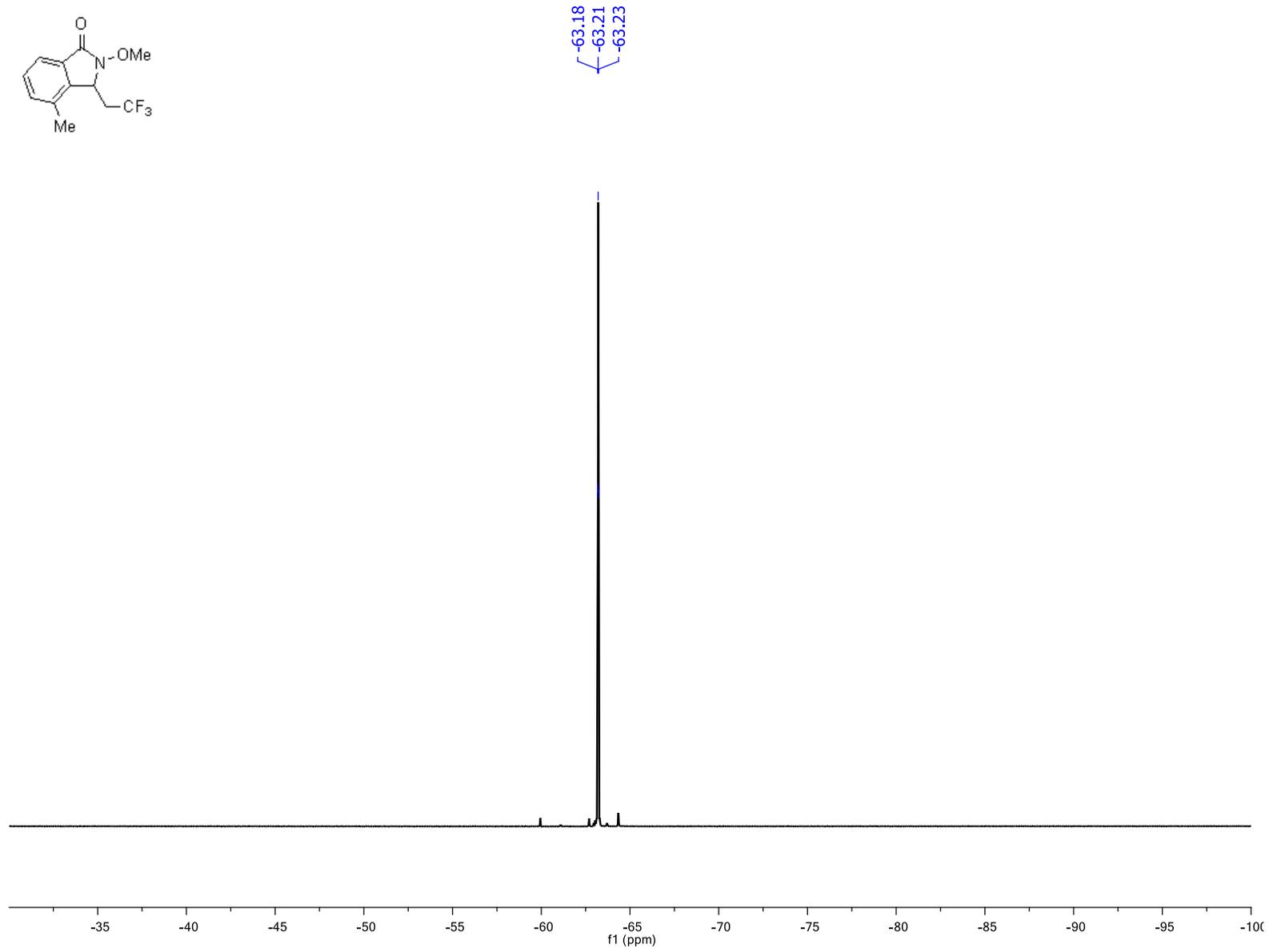
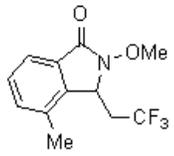


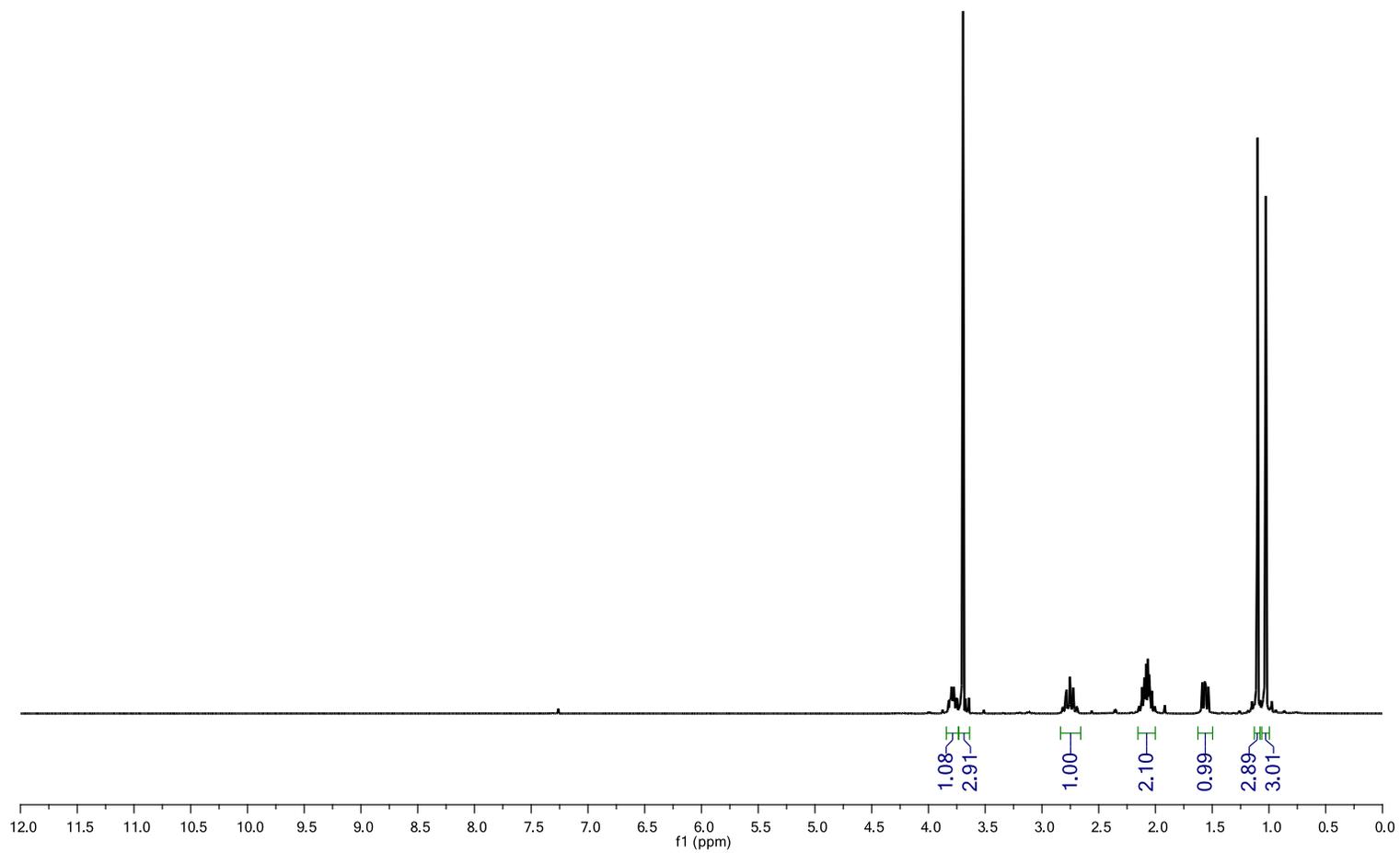
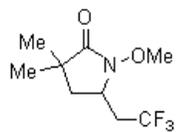


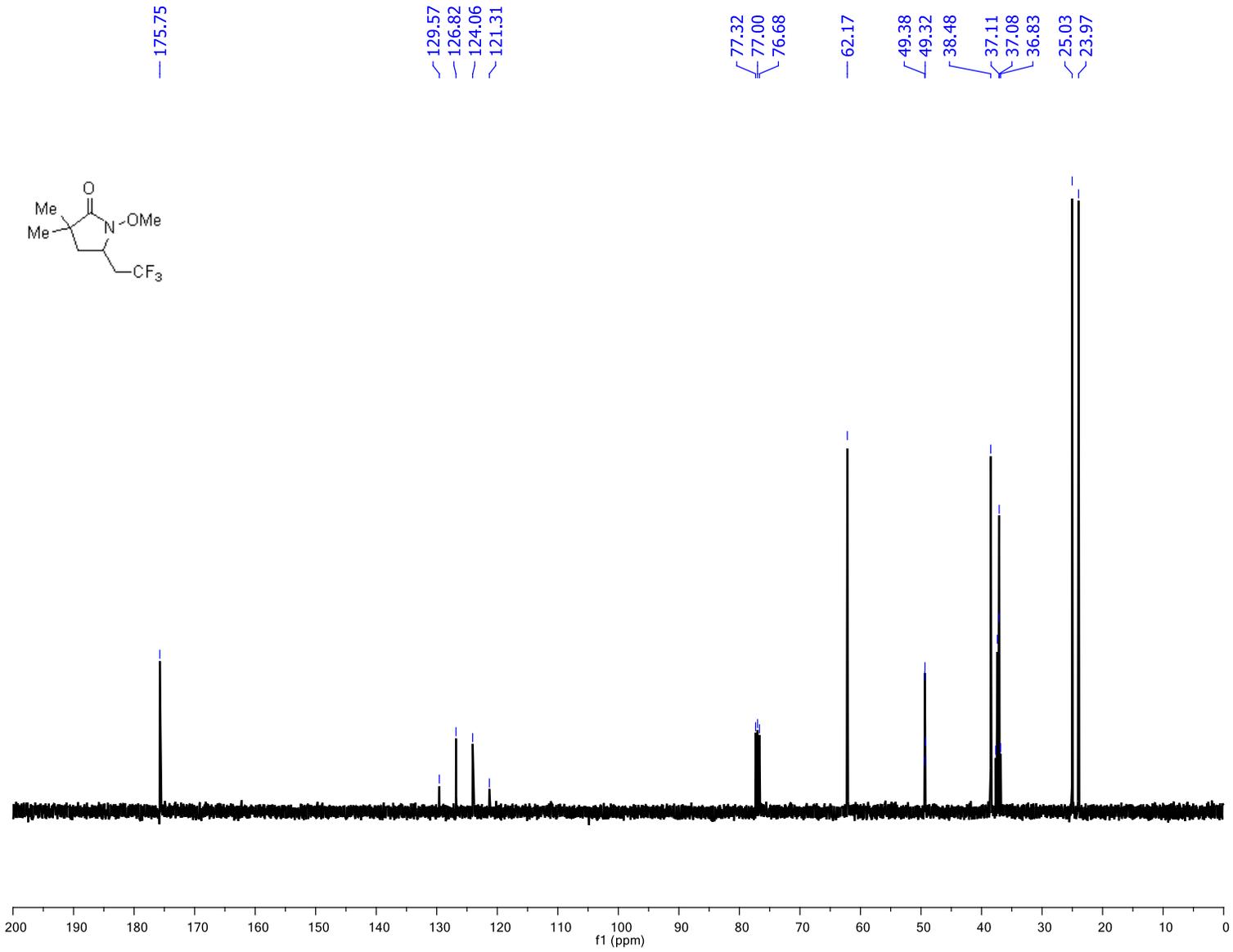


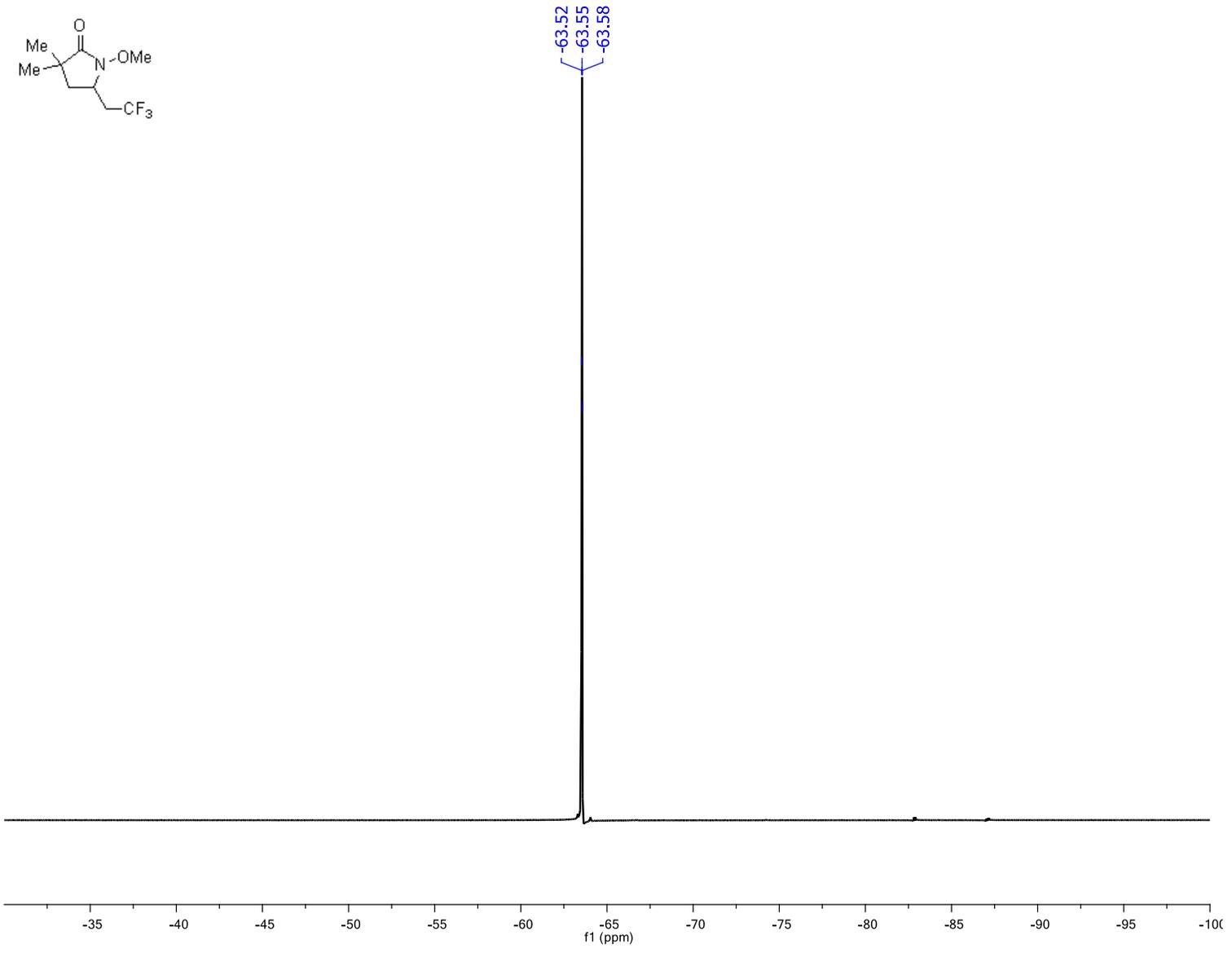
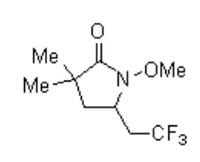


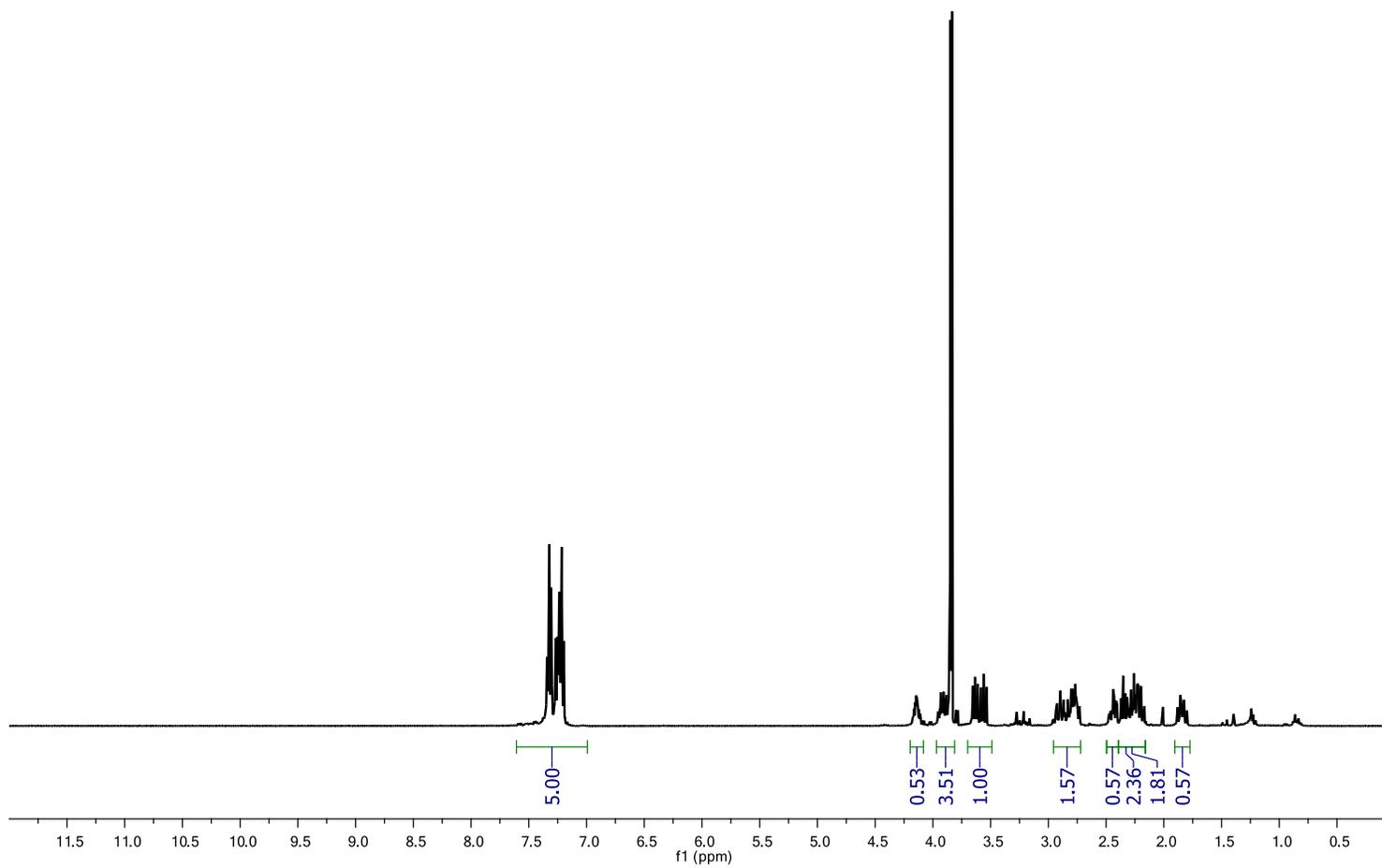
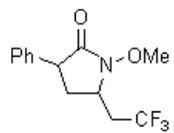


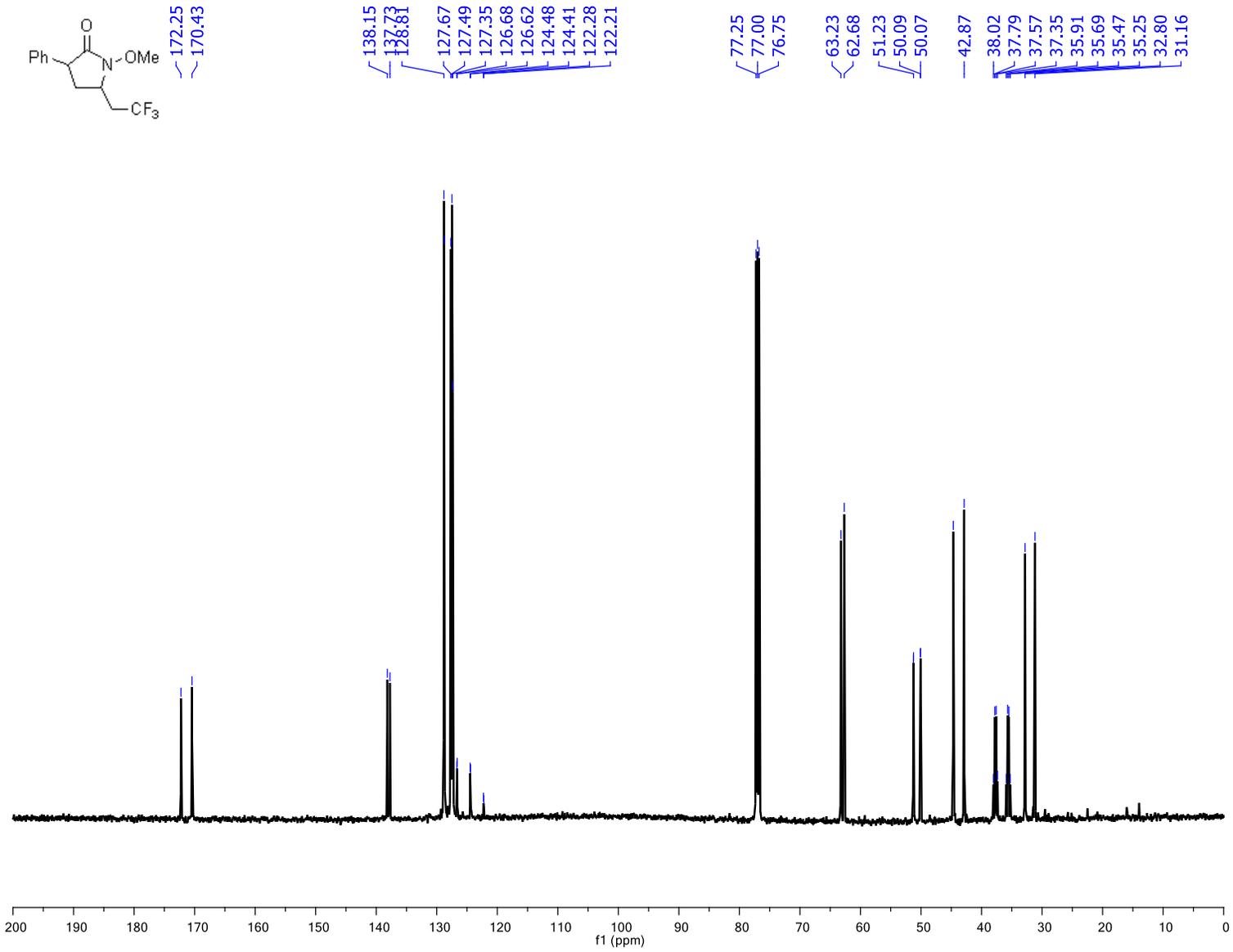


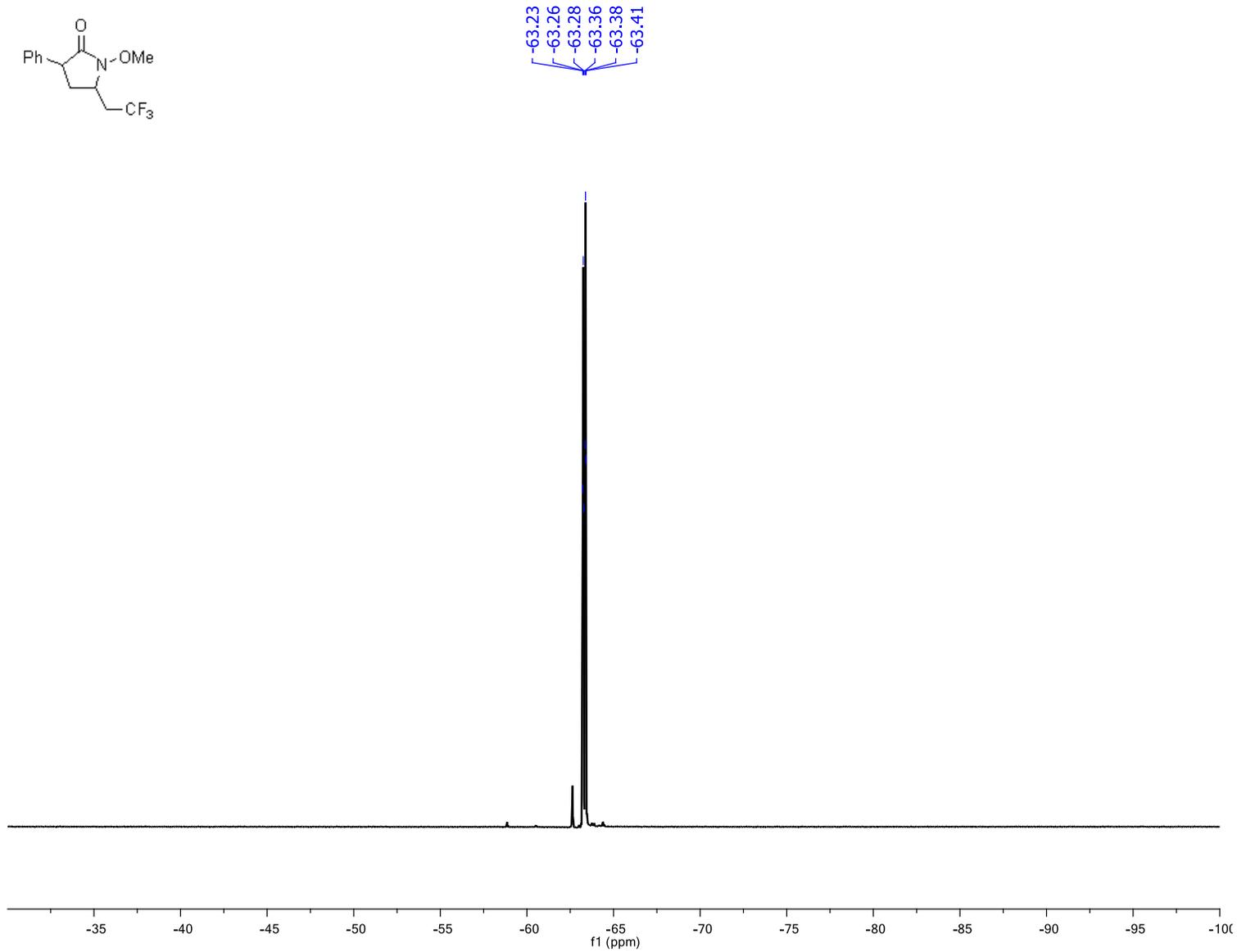
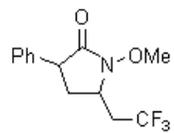


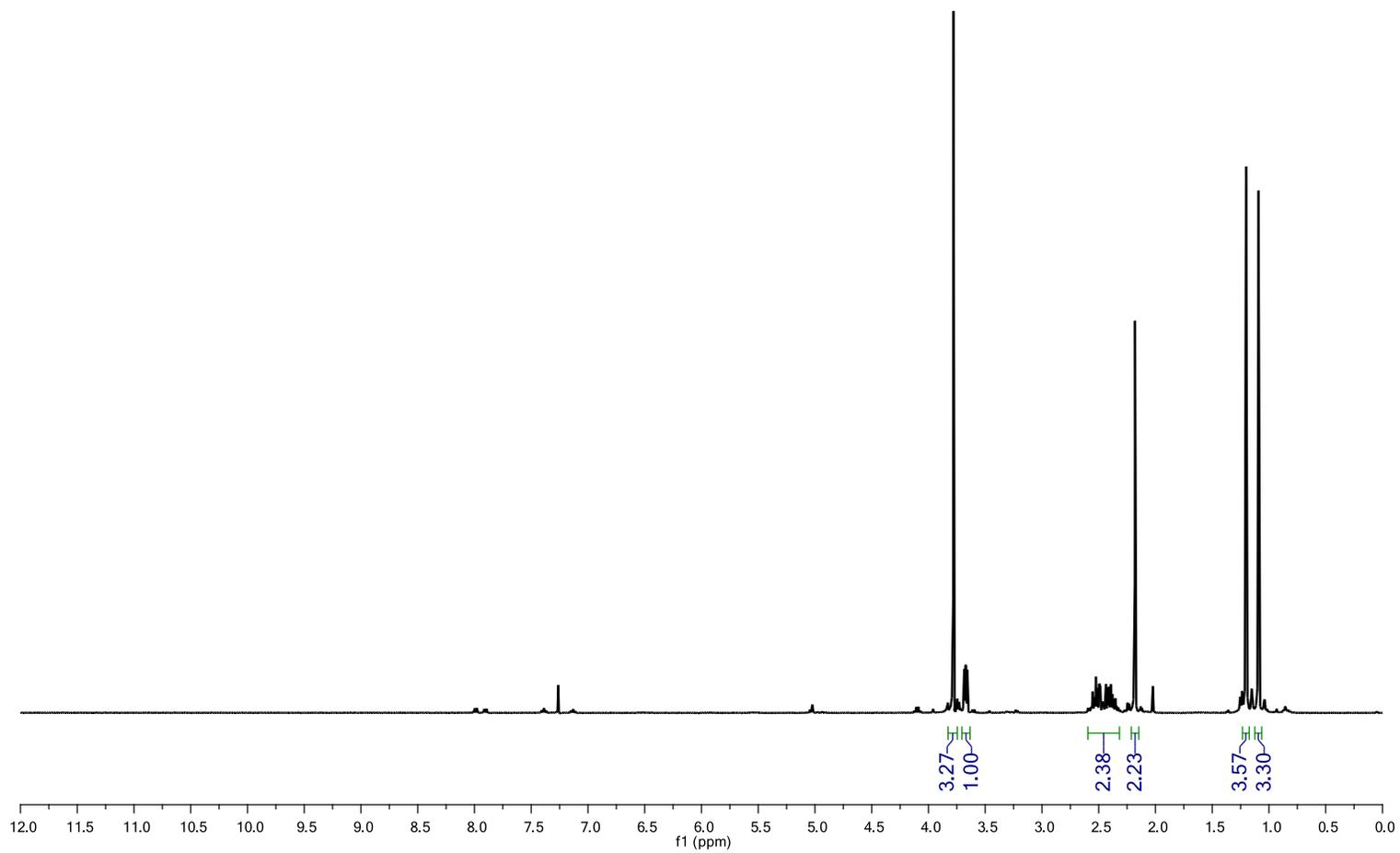
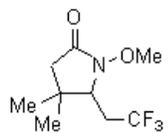


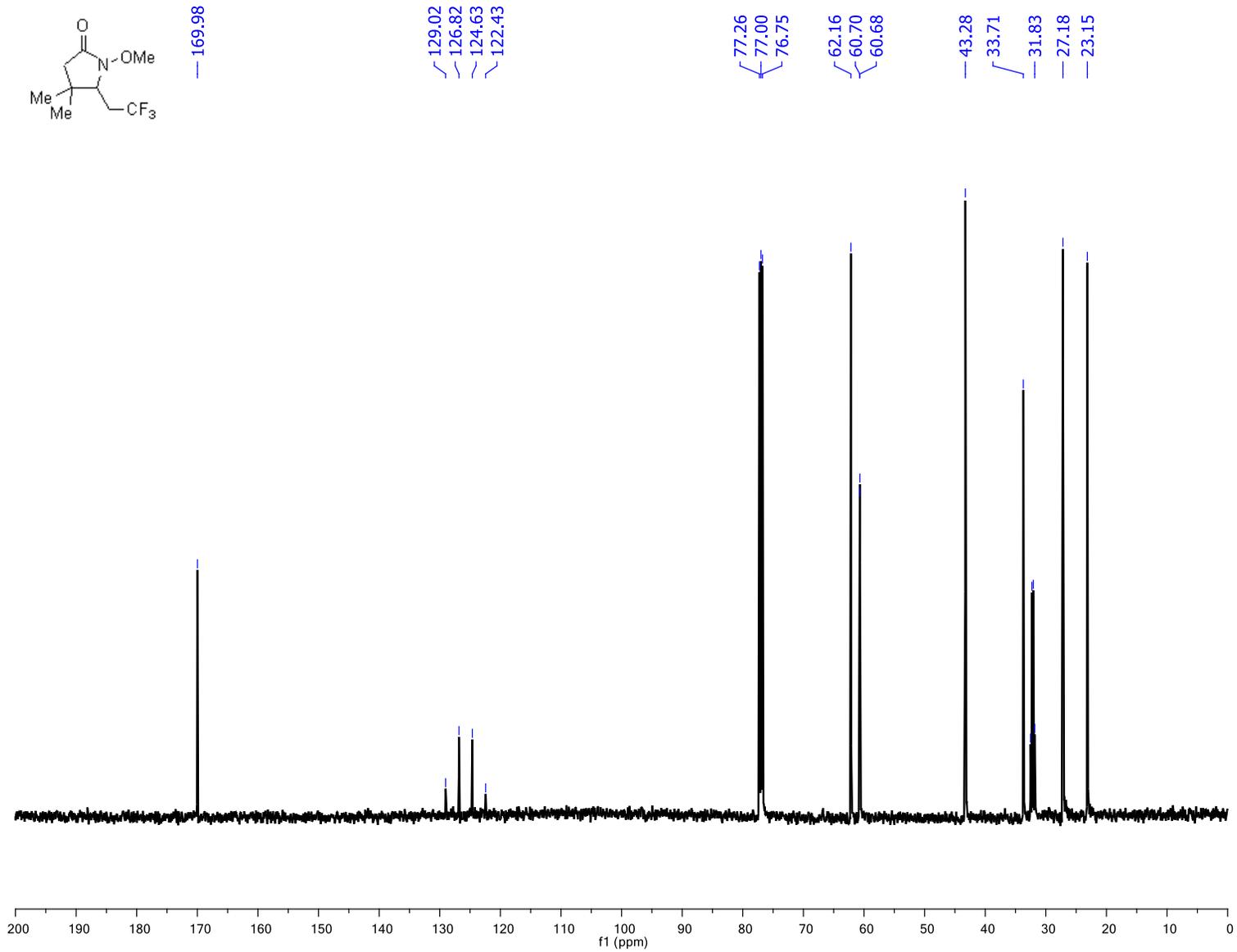
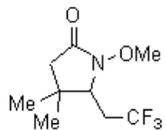


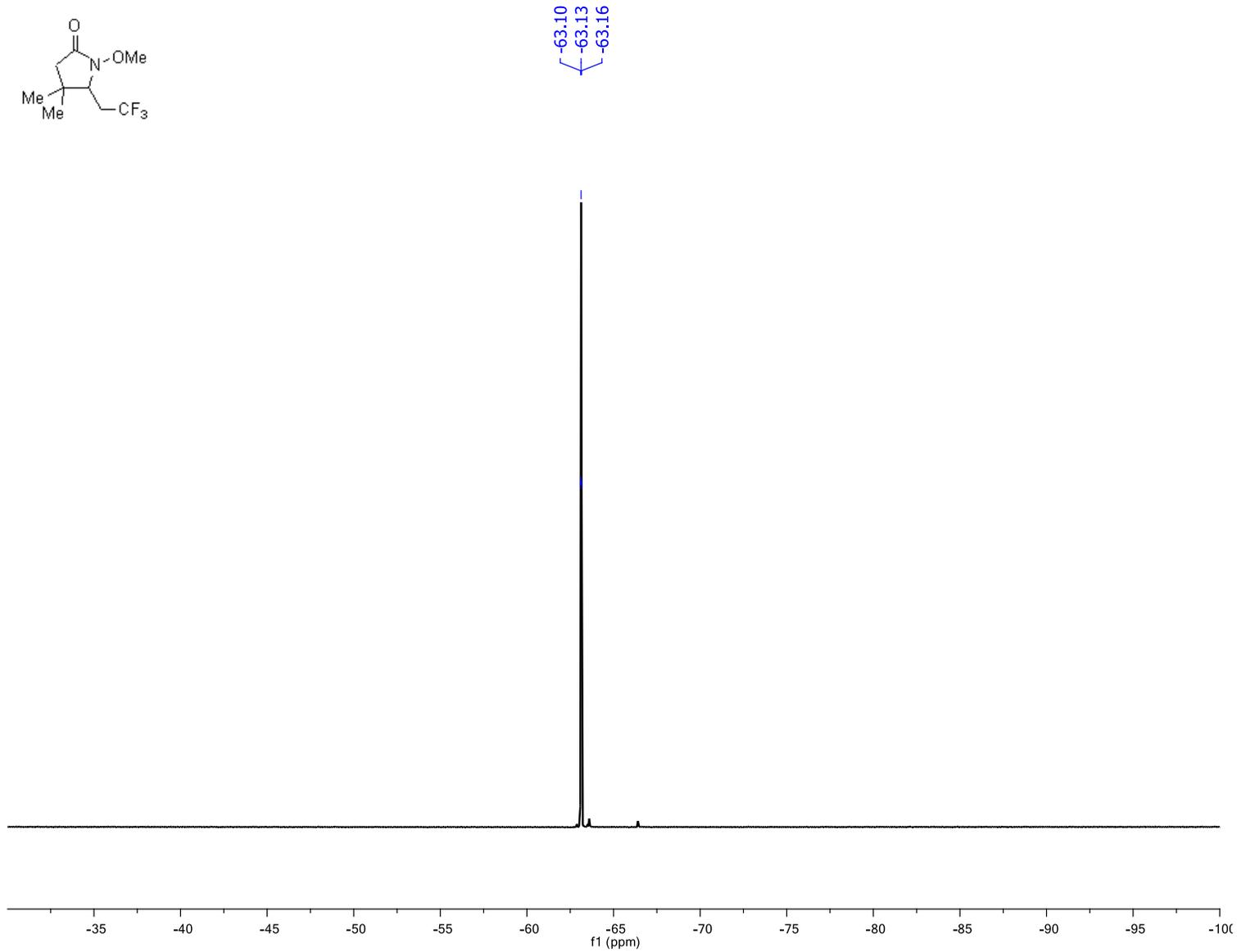
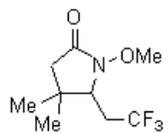


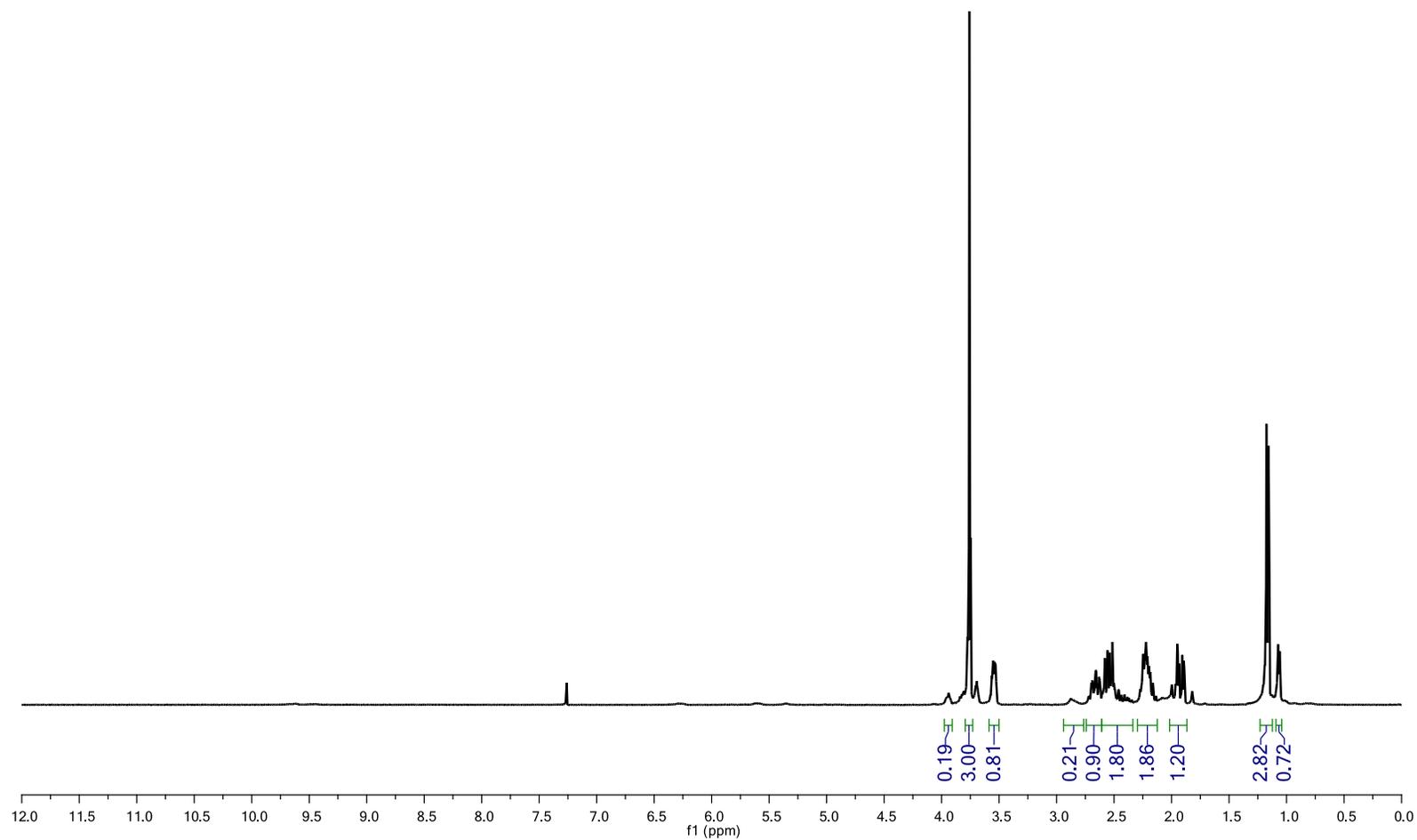
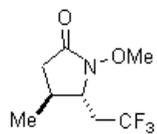


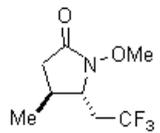












~ 171.57
~ 169.48

~ 129.68
~ 126.93
~ 124.18
~ 121.42

~ 77.32
~ 77.00
~ 76.68

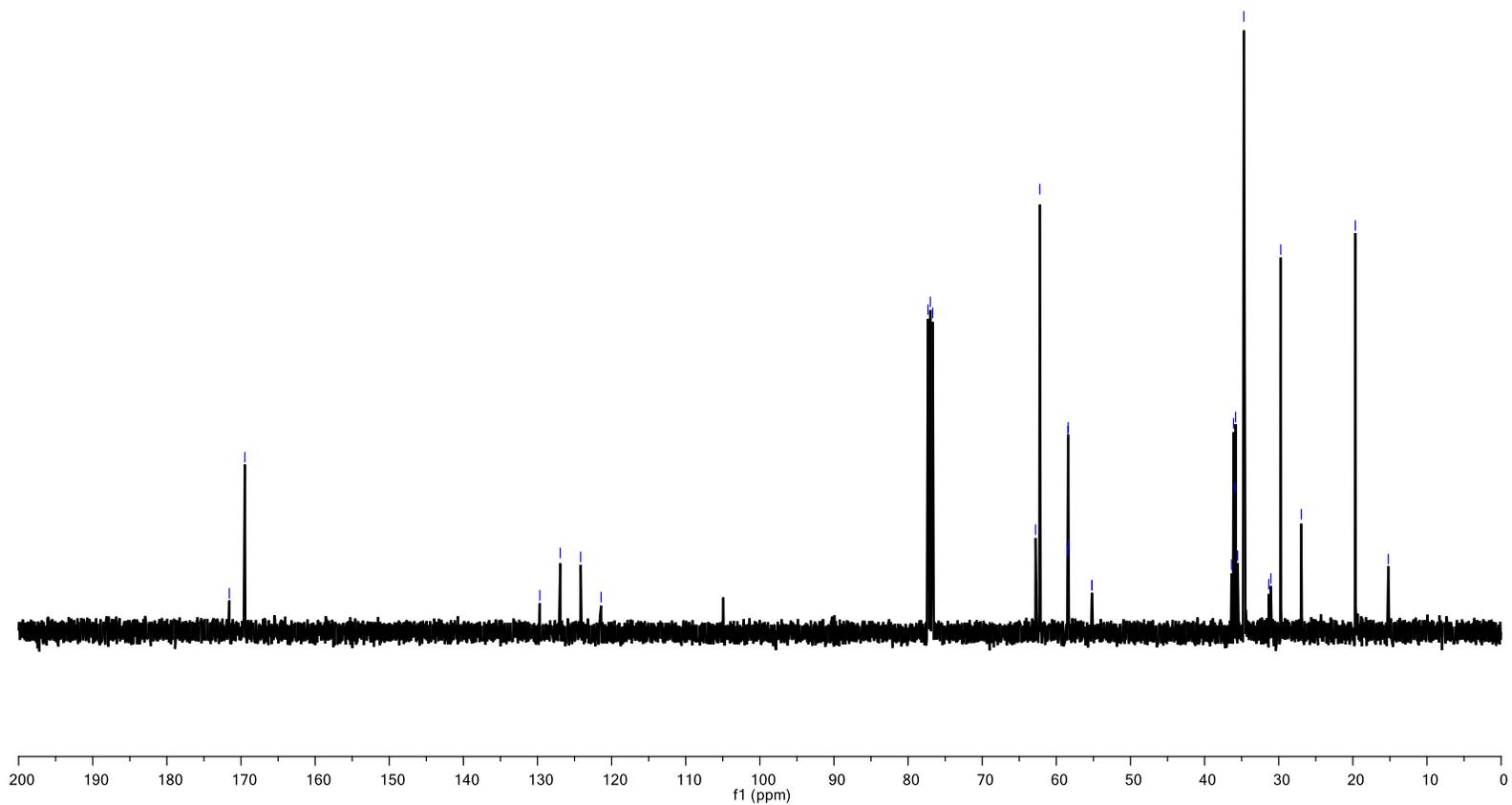
~ 62.79
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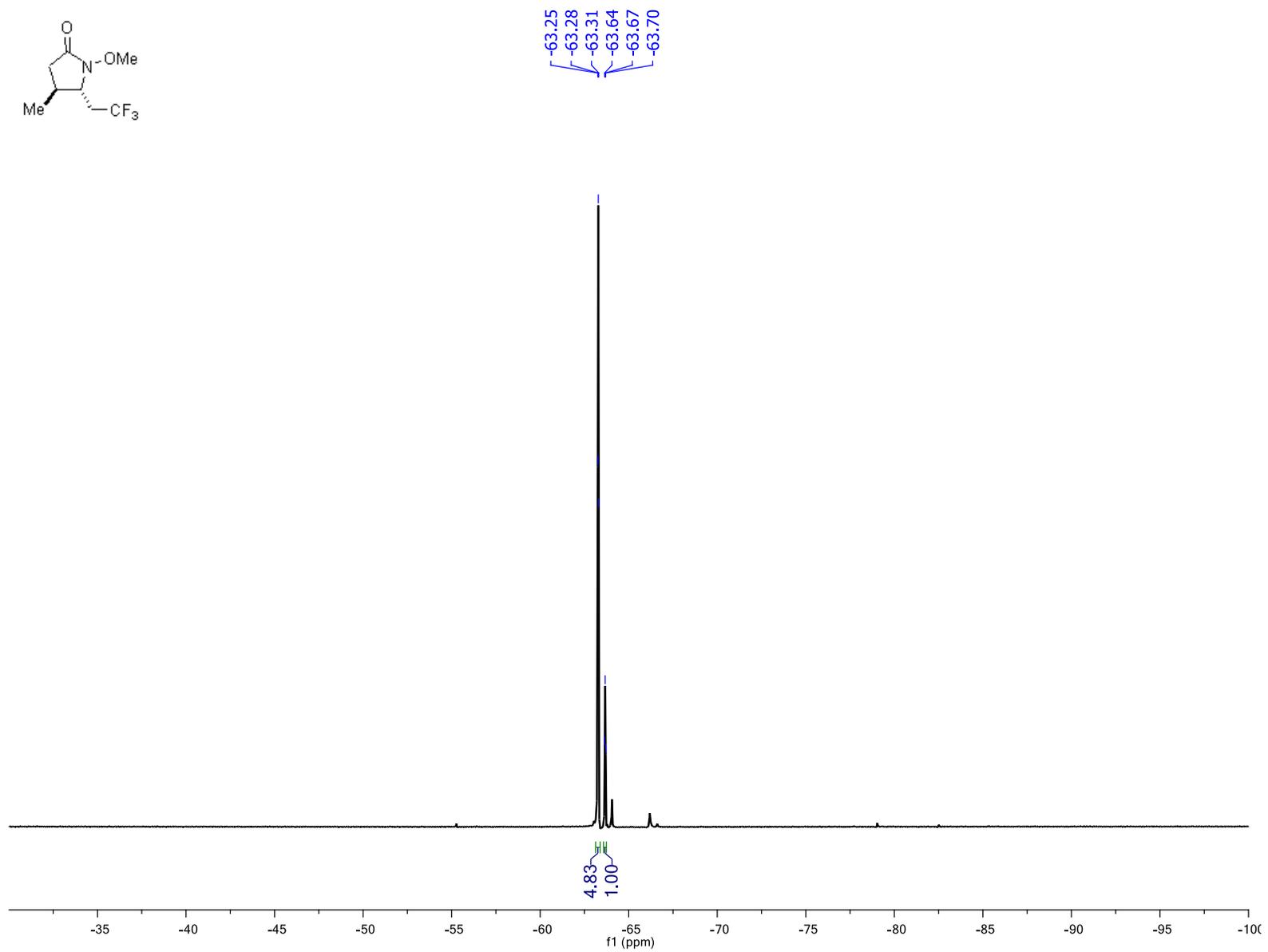
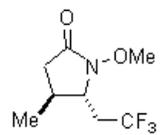
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~ 58.38
~ 56.09
~ 55.18

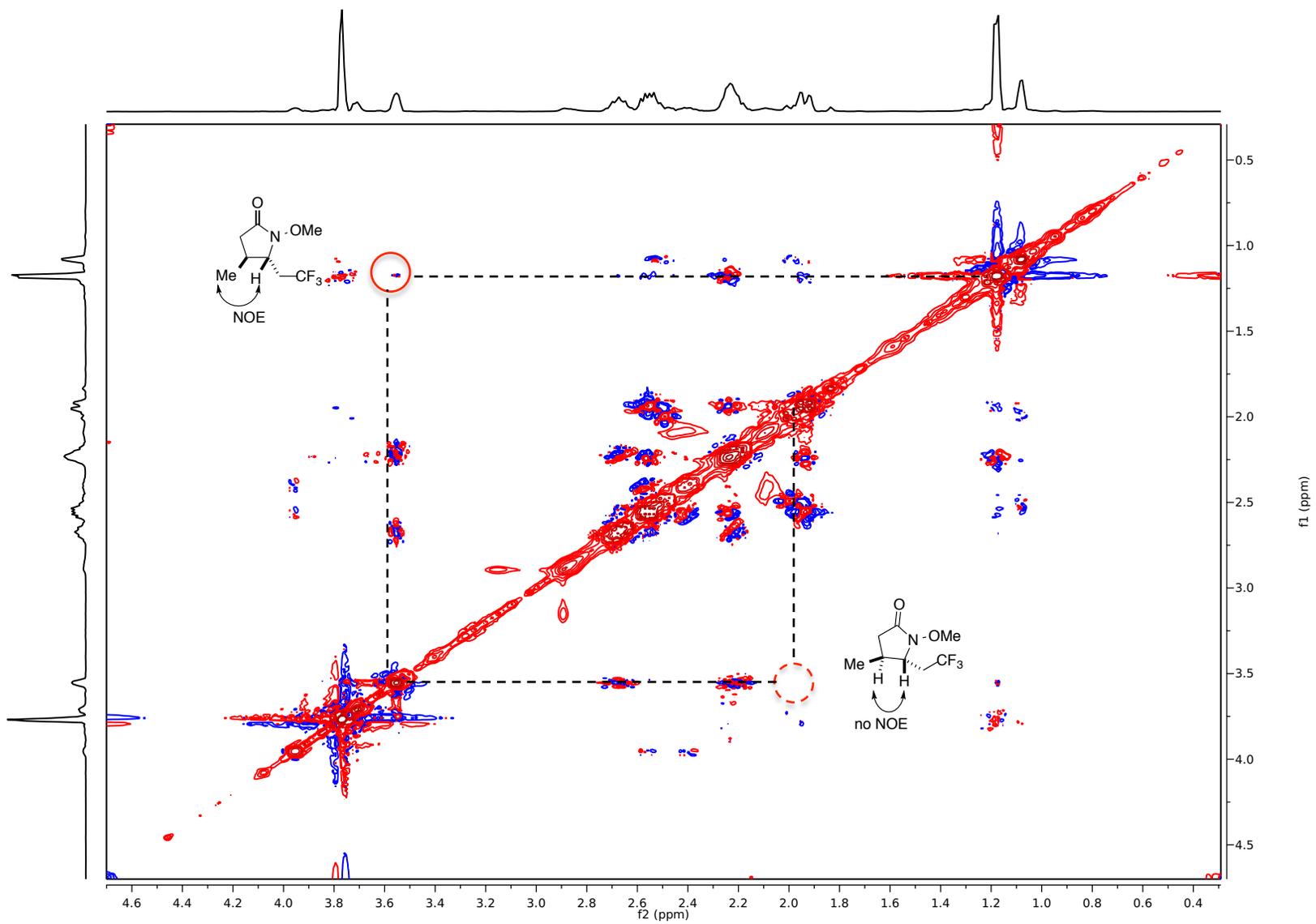
~ 35.81
~ 35.54
~ 34.71

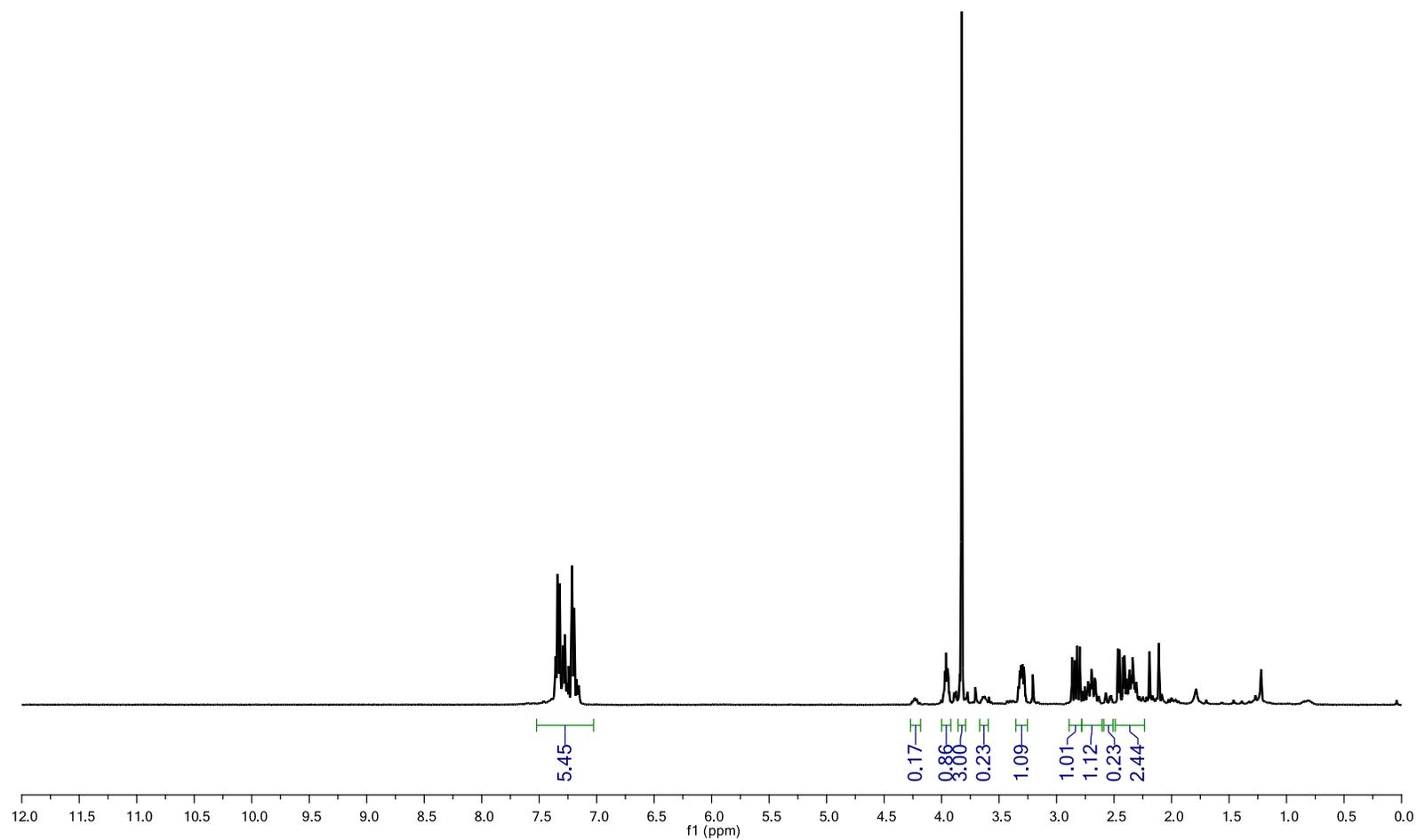
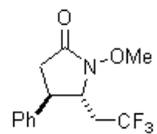
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~ 29.73
~ 26.96

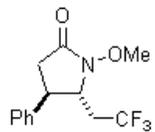
~ 19.66
~ 15.22











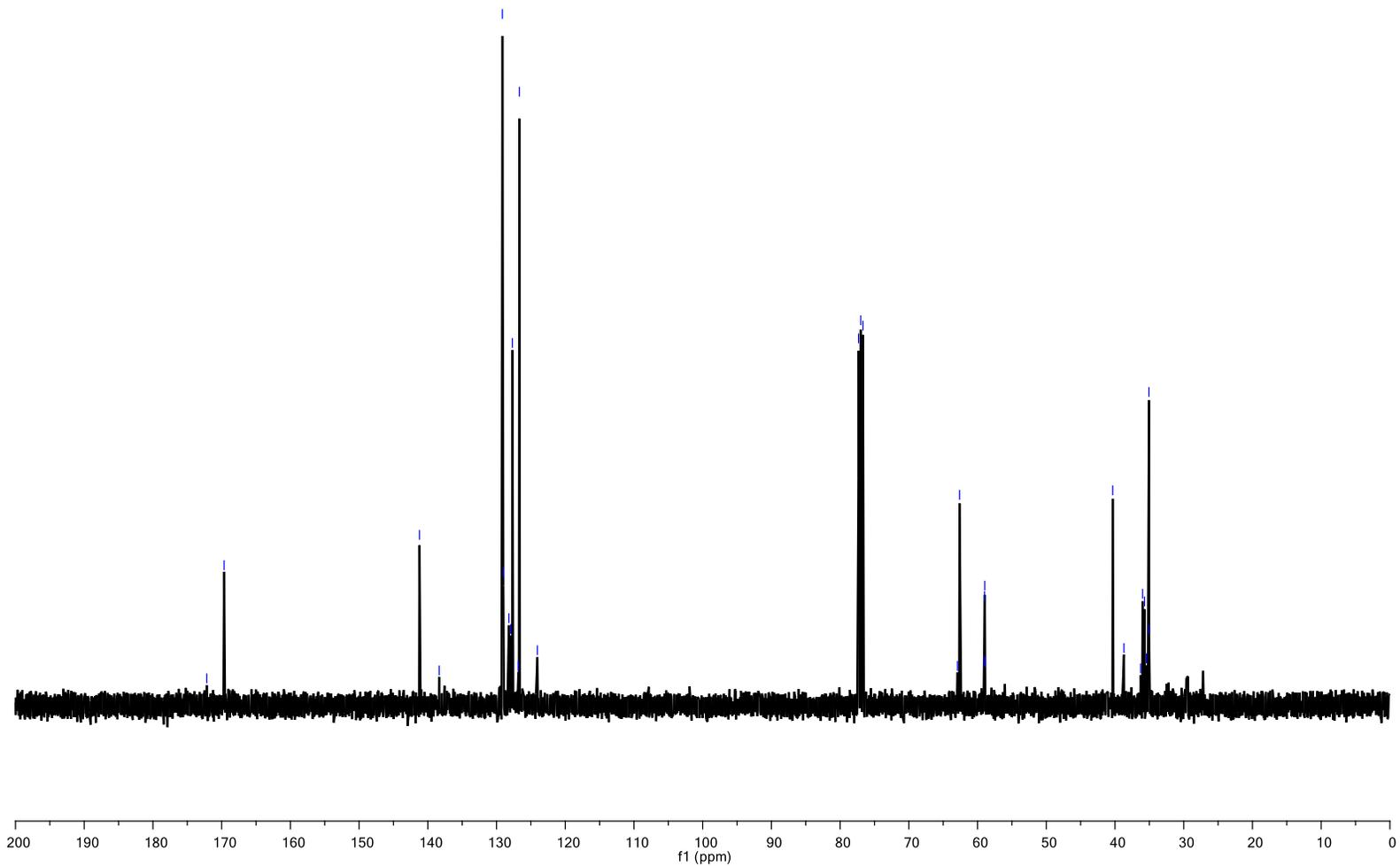
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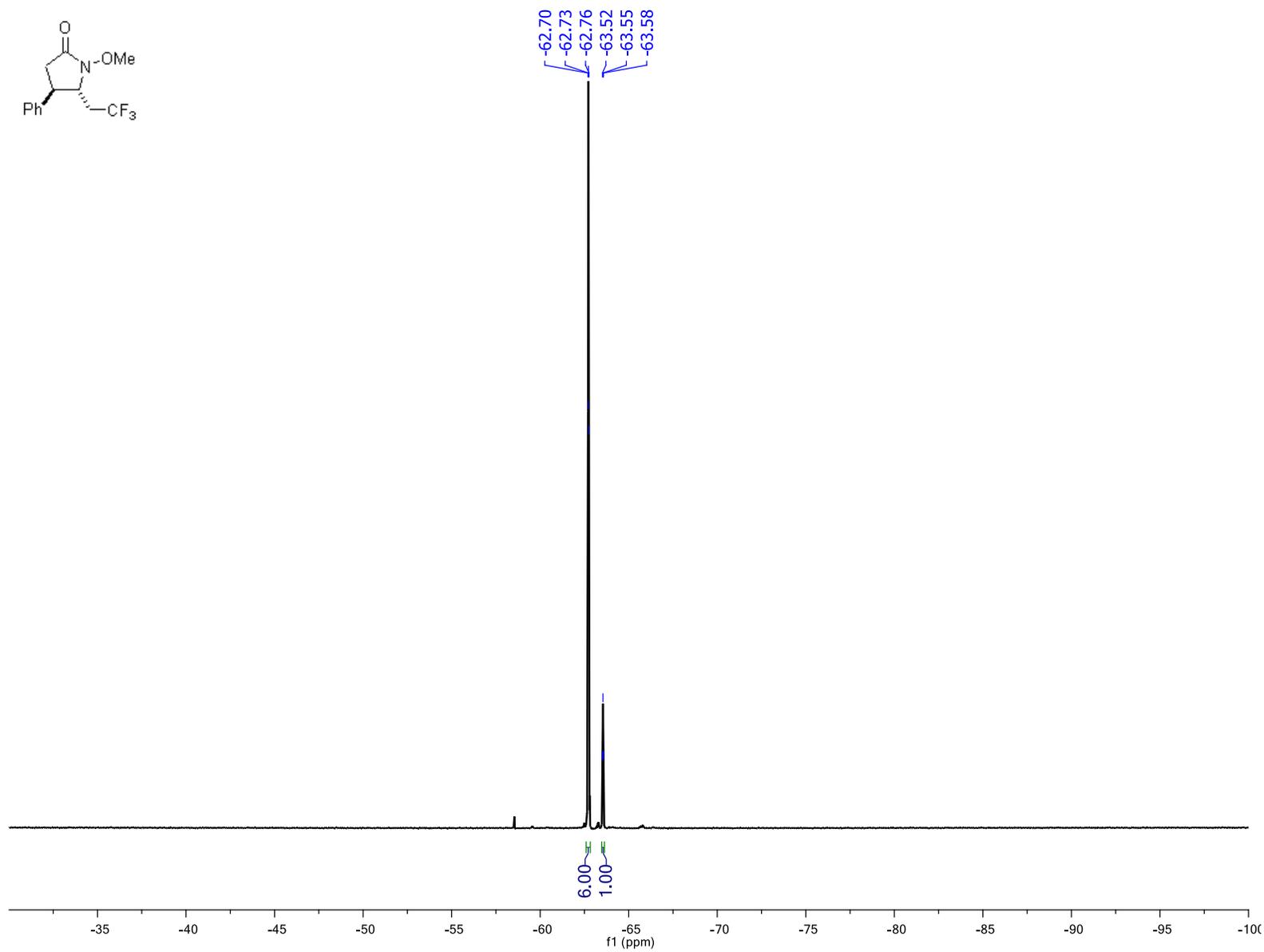
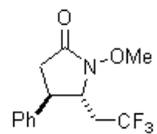
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126.81
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124.05

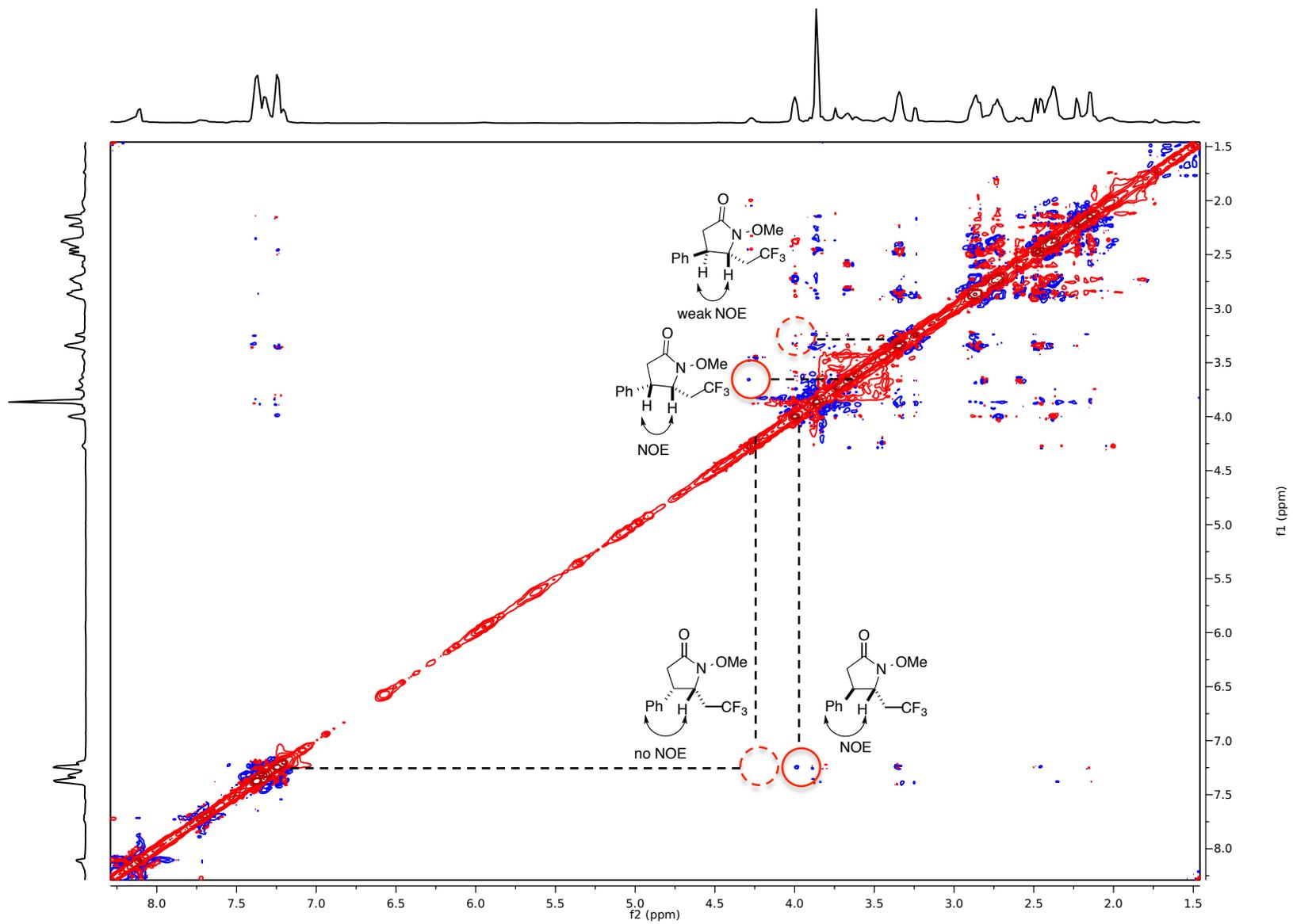
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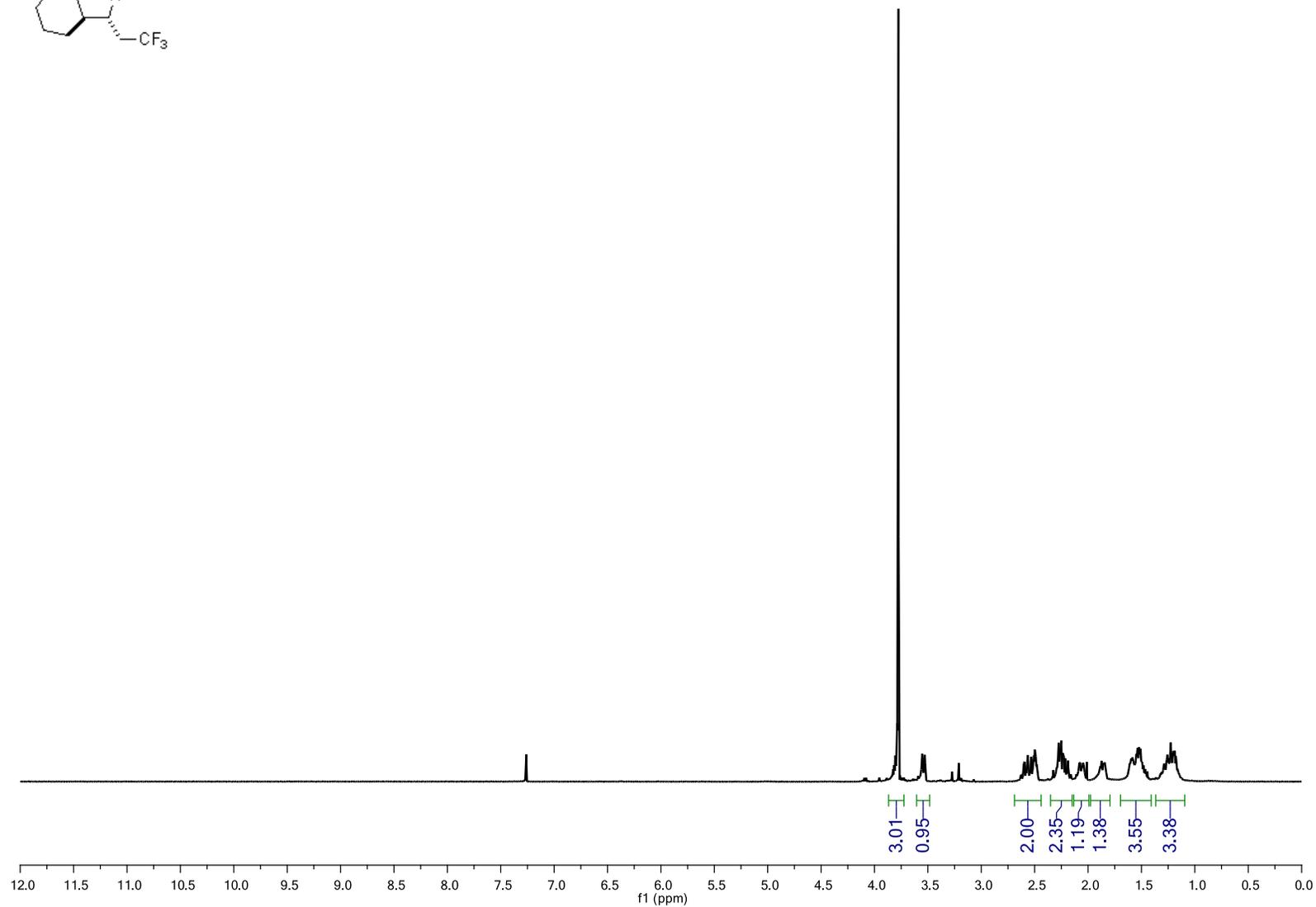
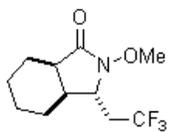
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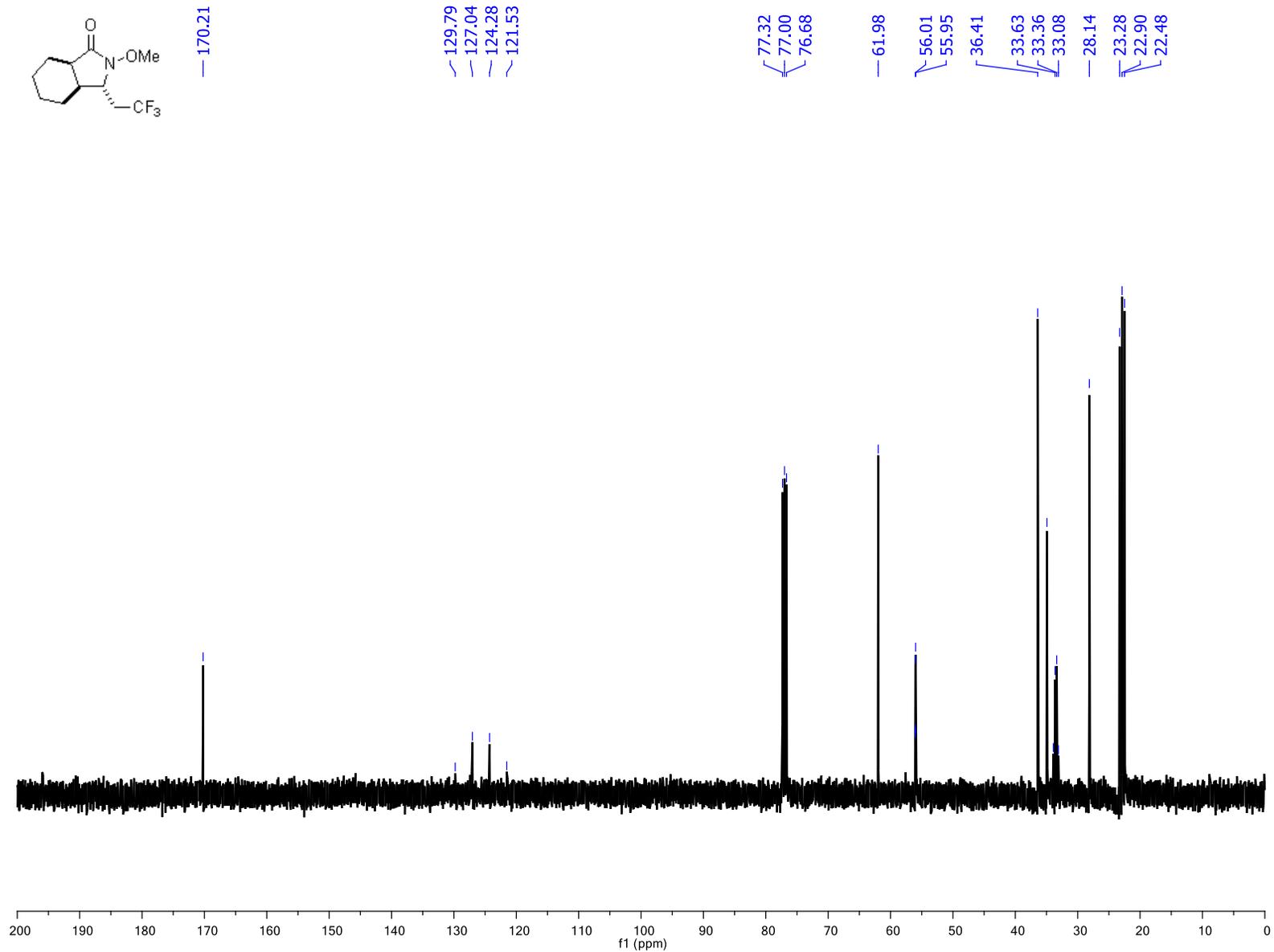
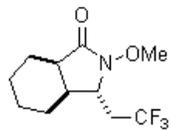
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35.06

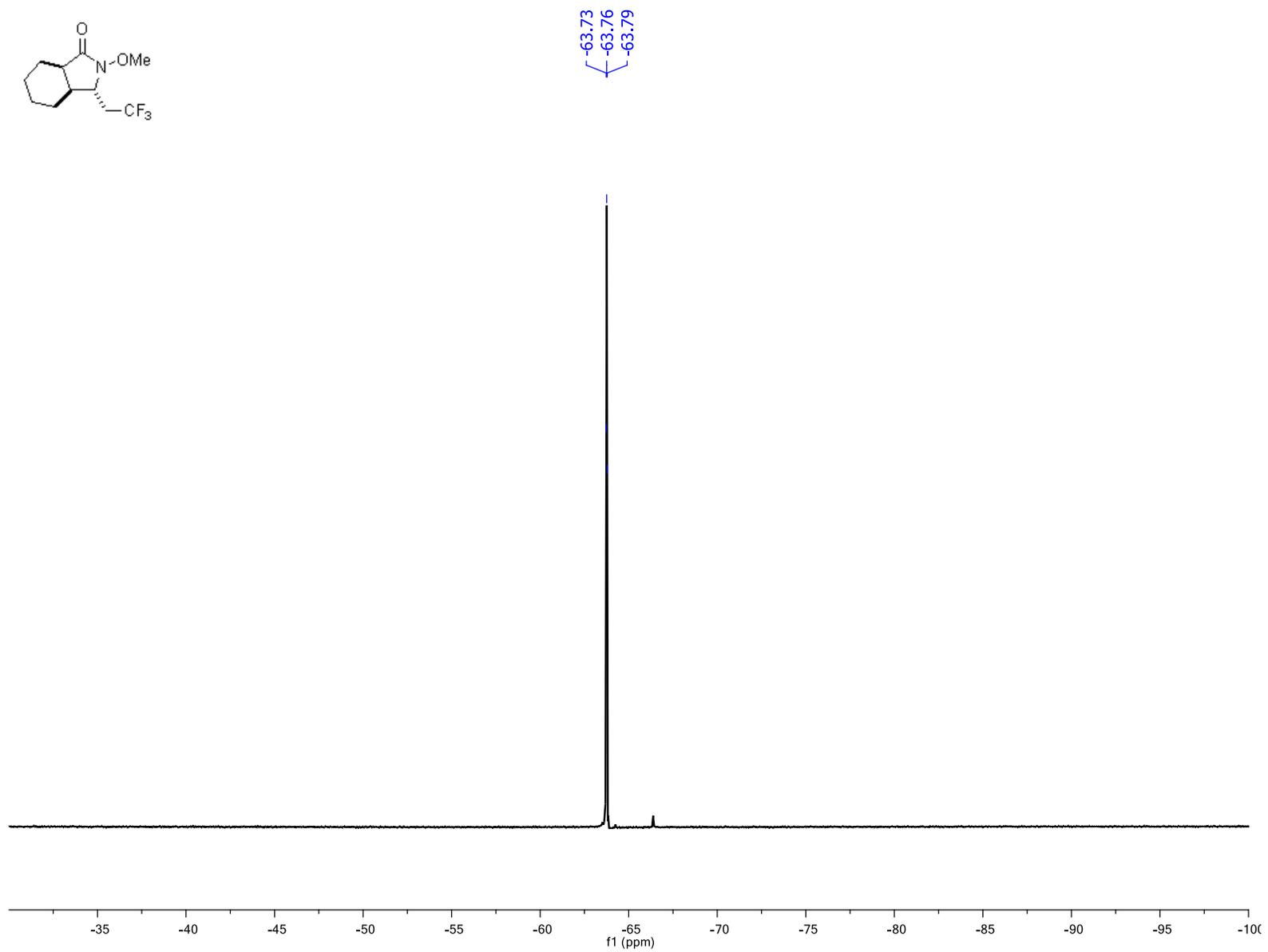
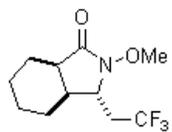


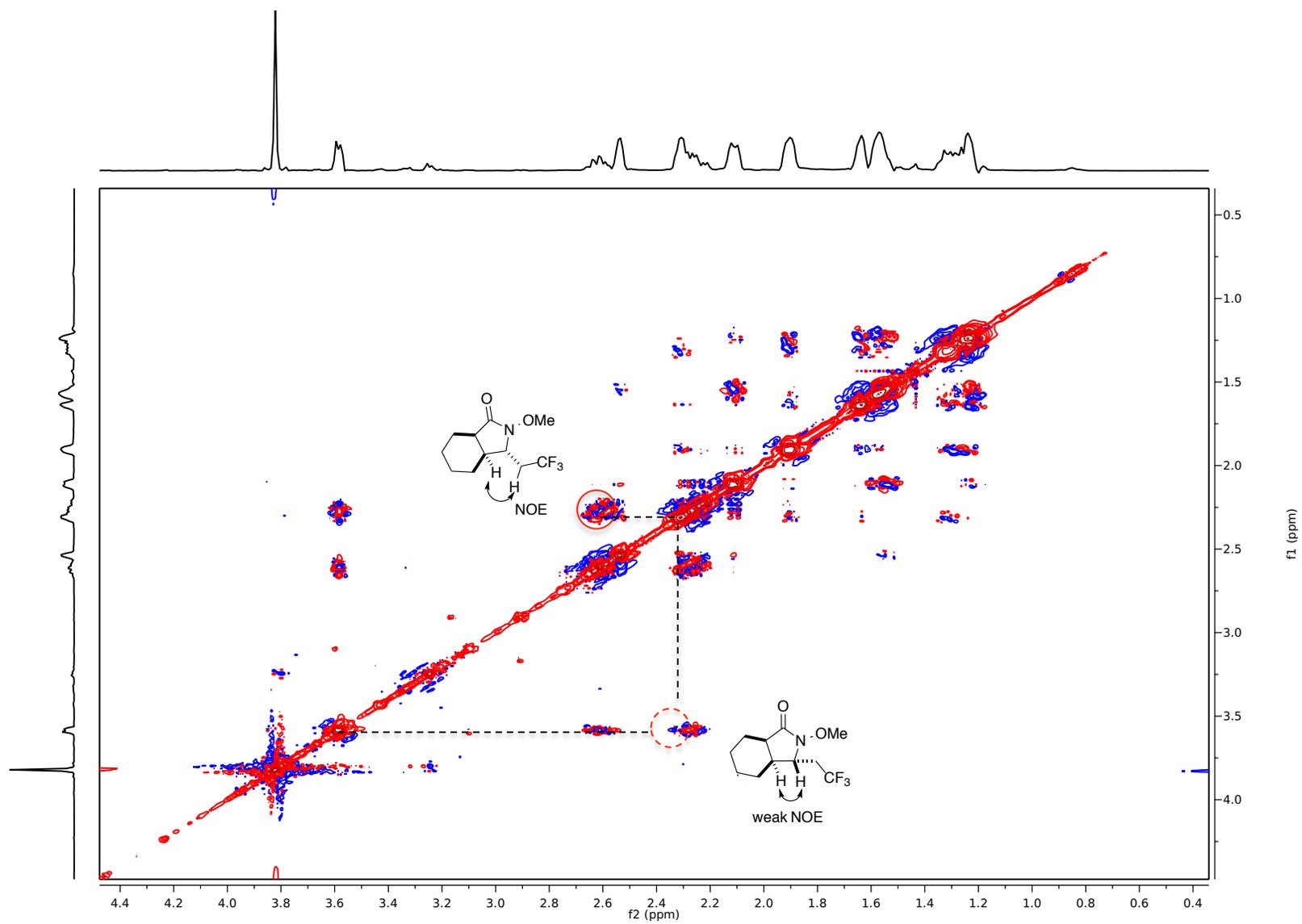


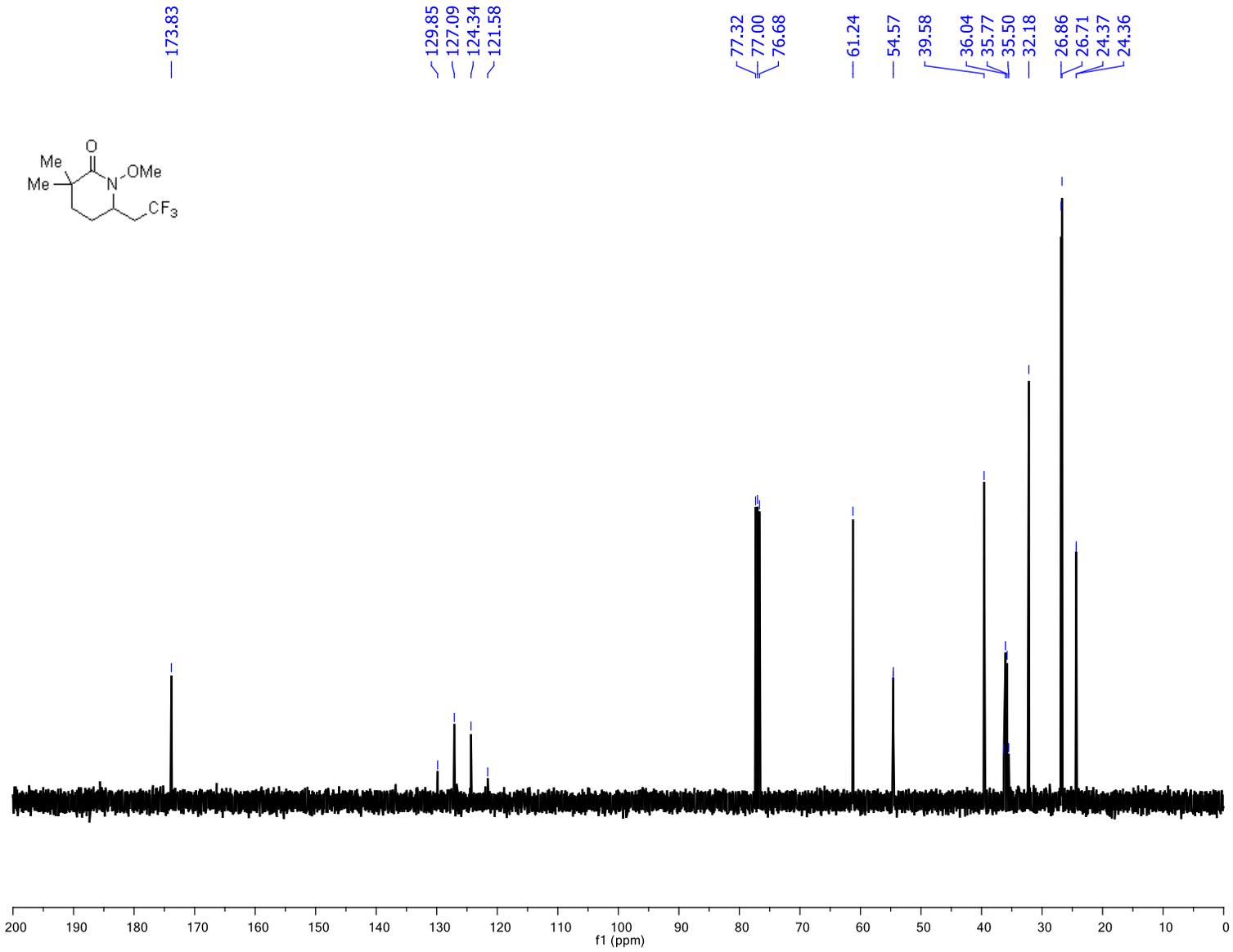


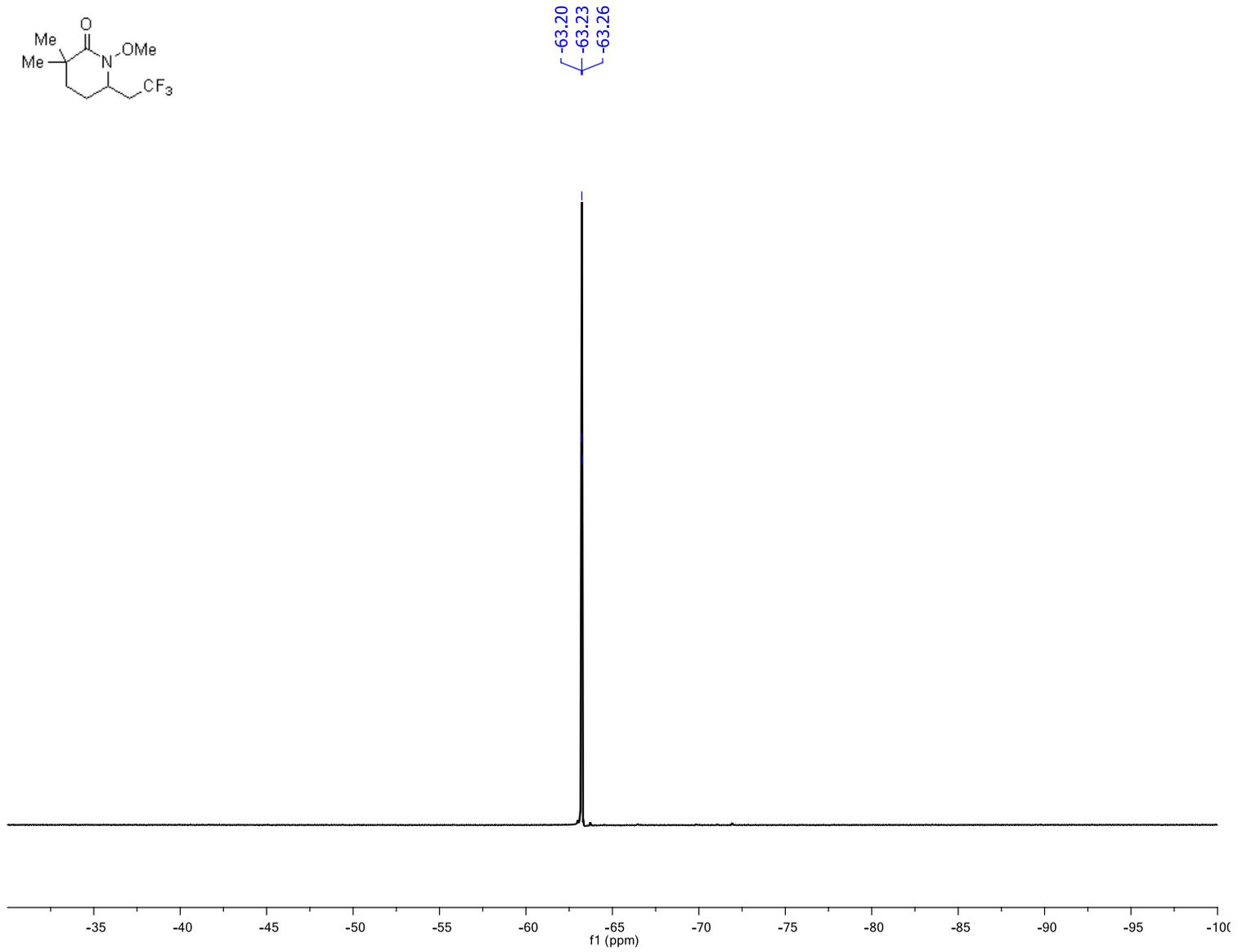
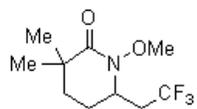


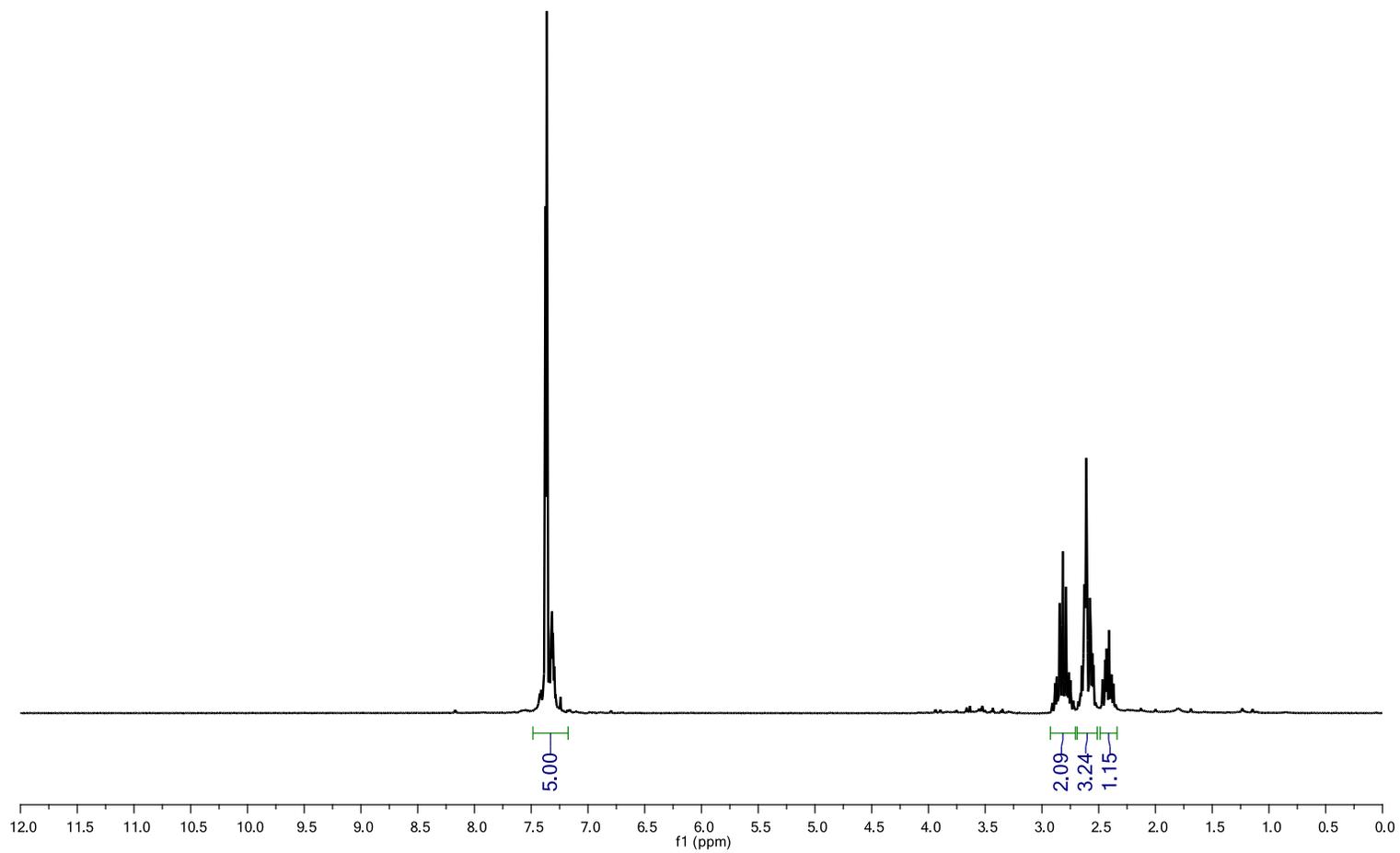
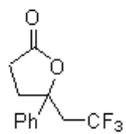


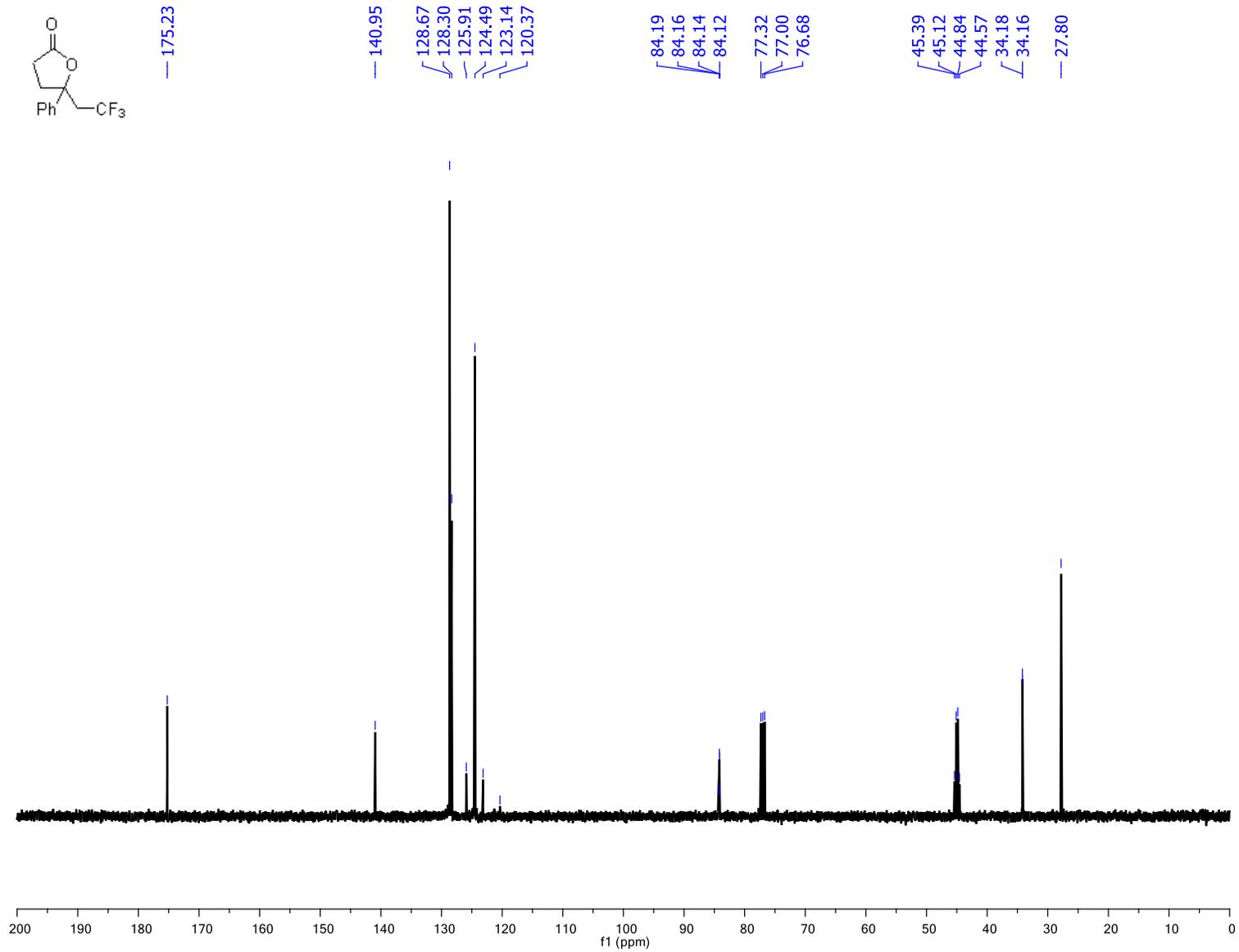
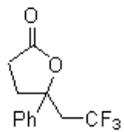


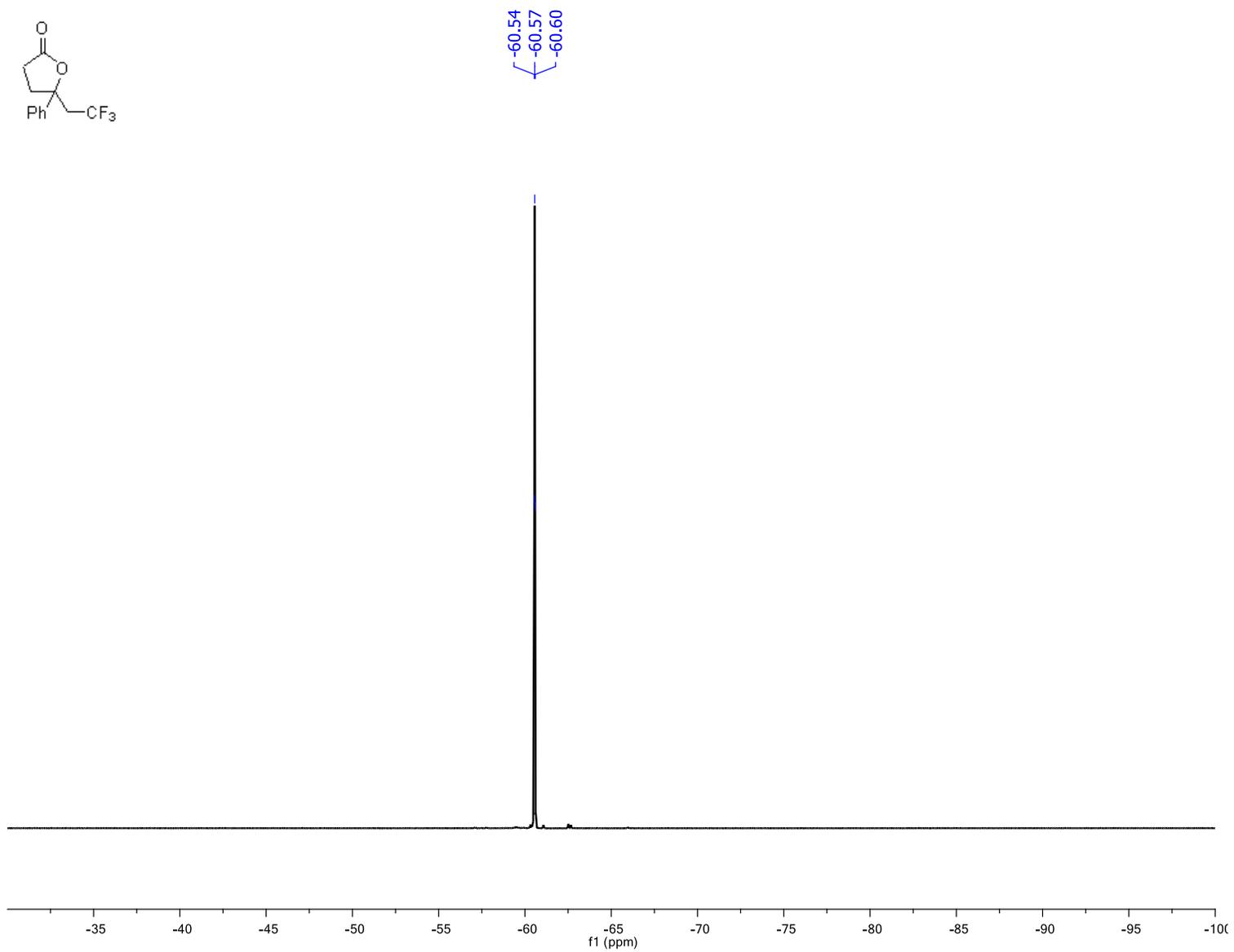
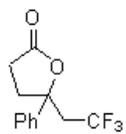


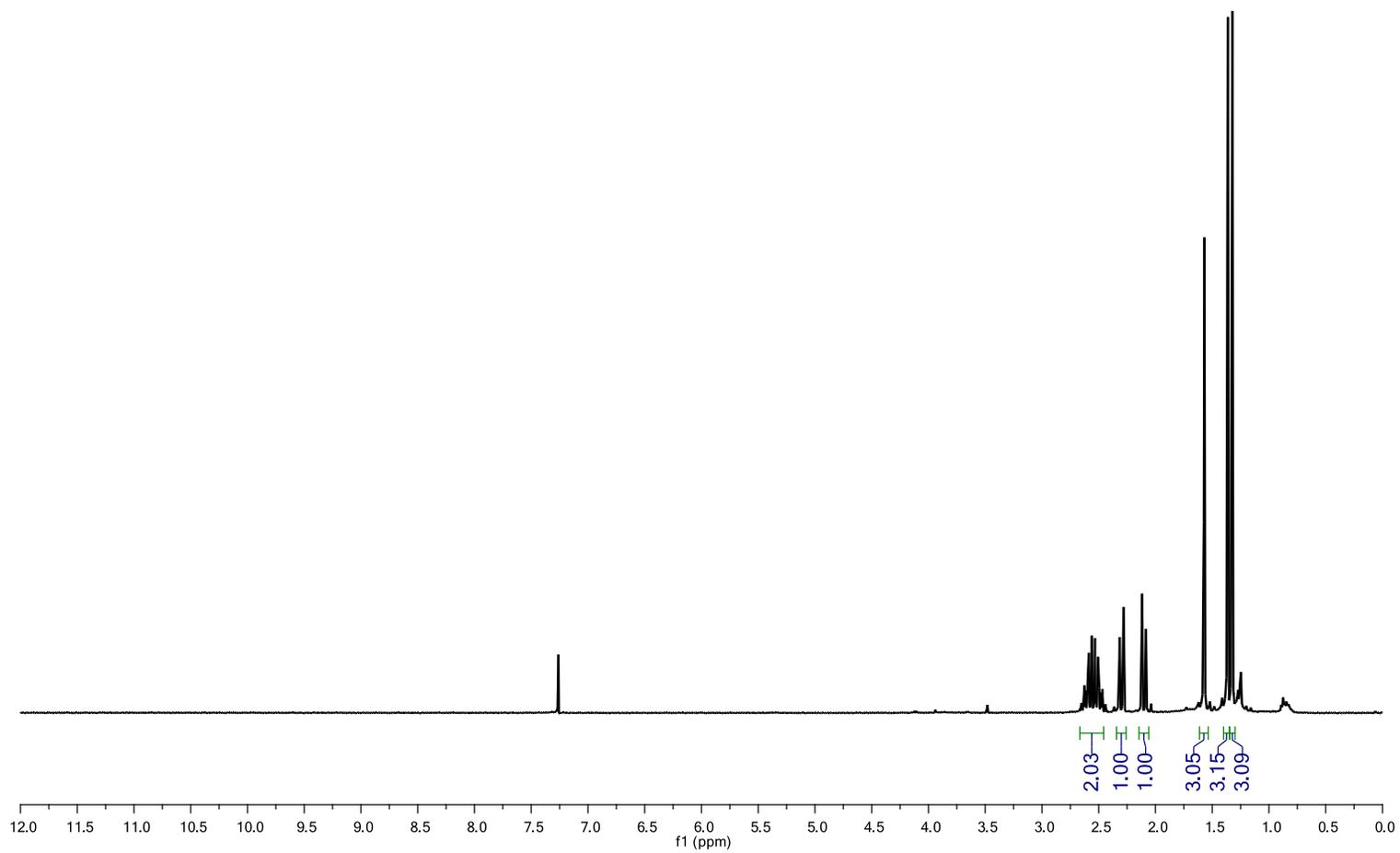
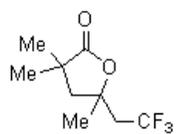


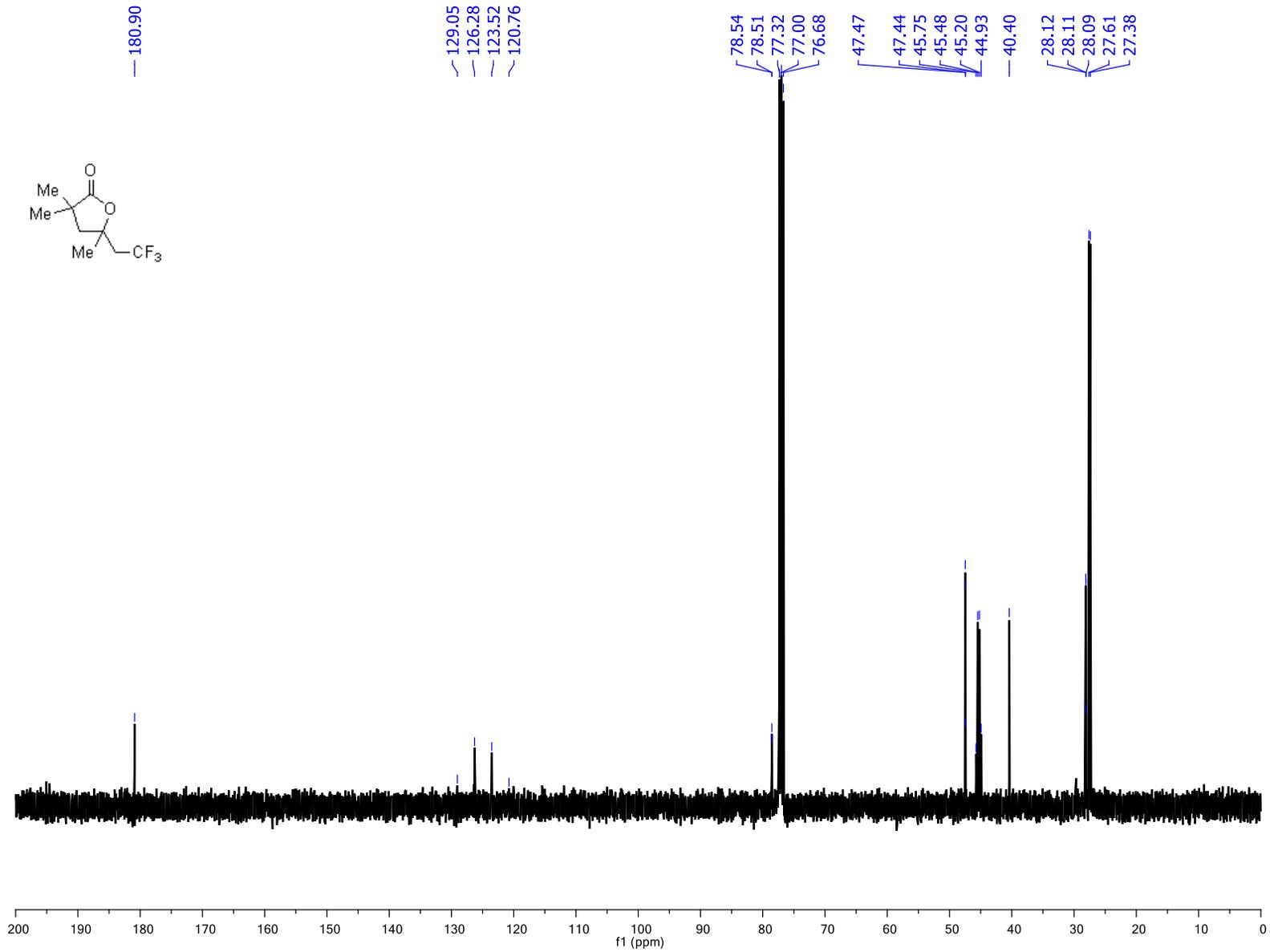


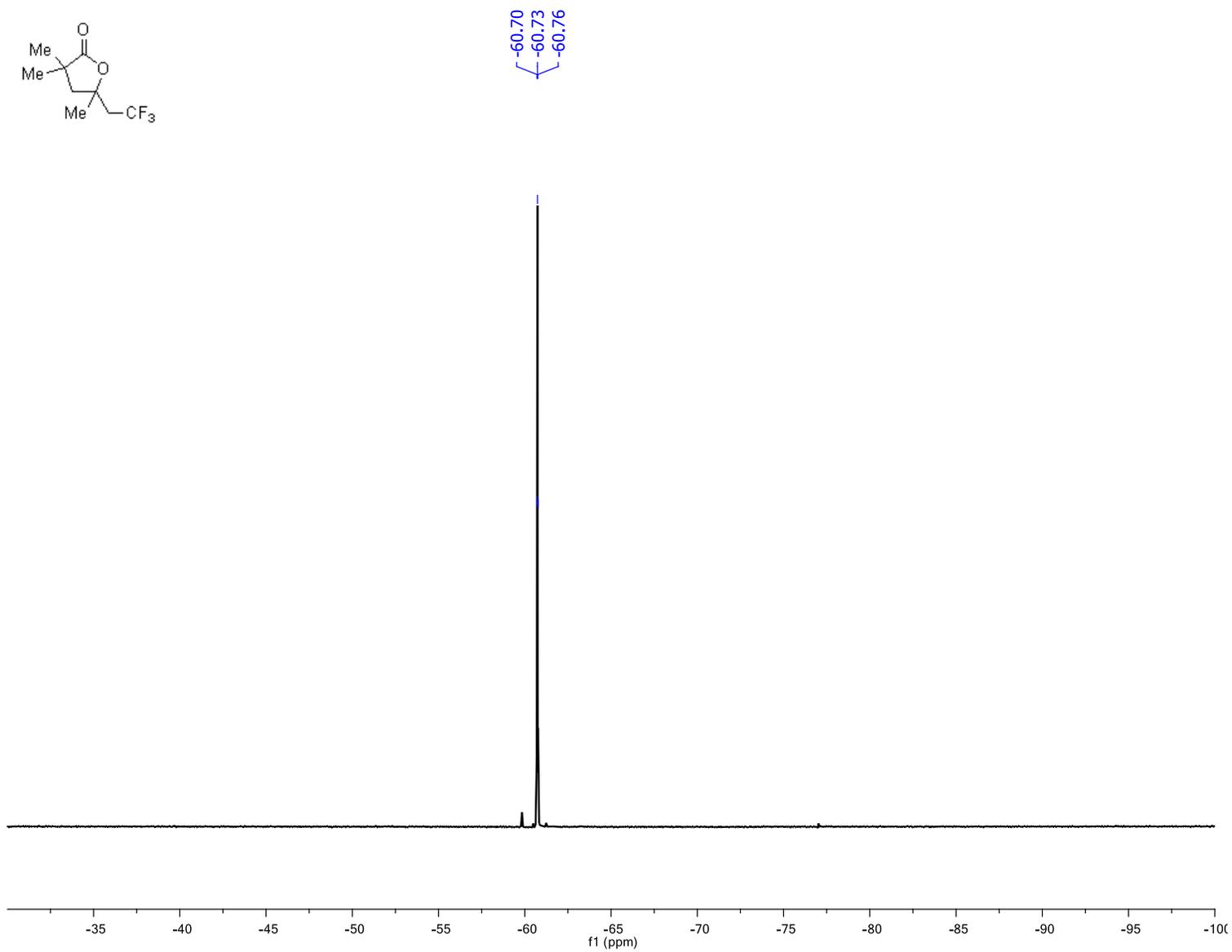
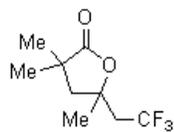


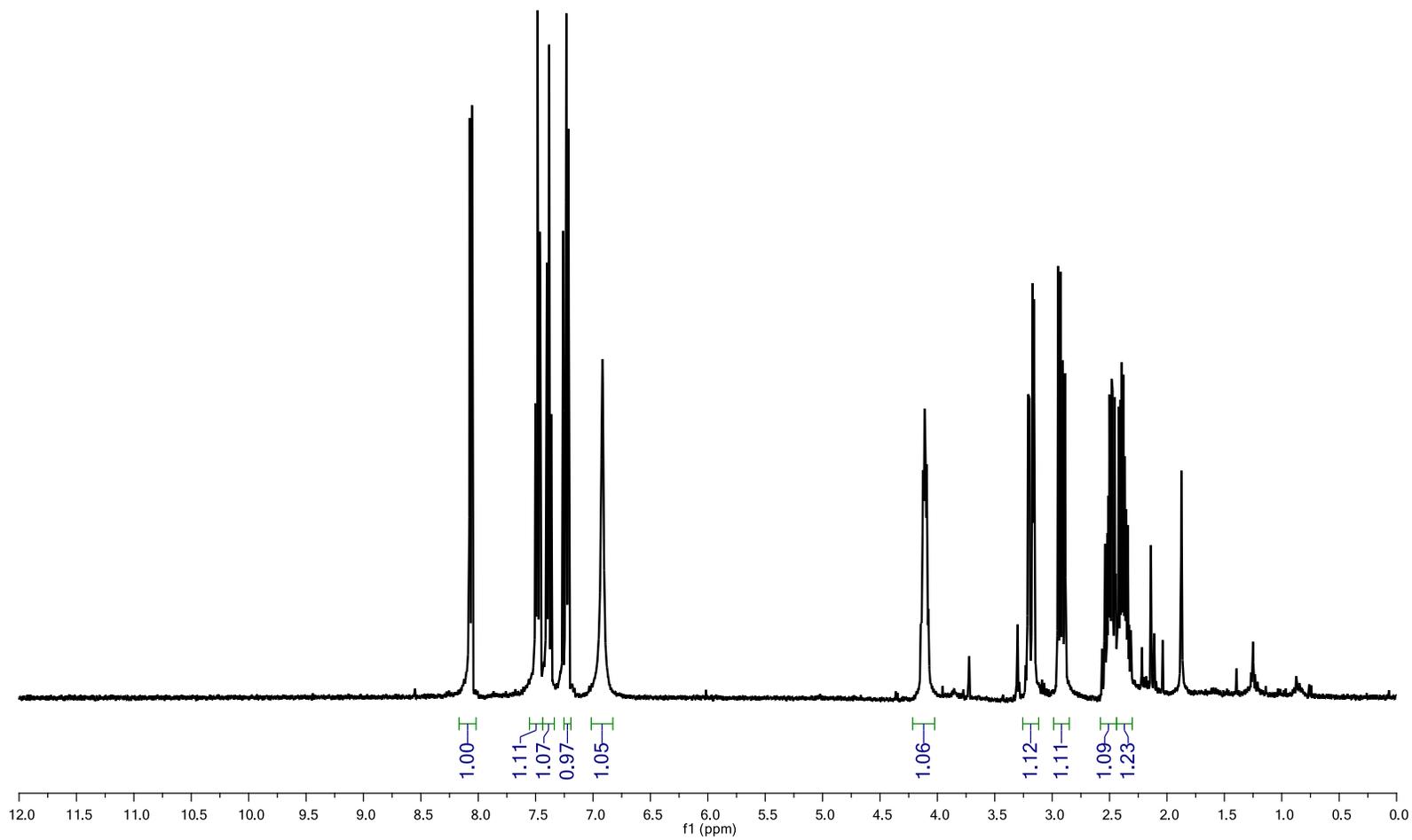
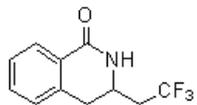


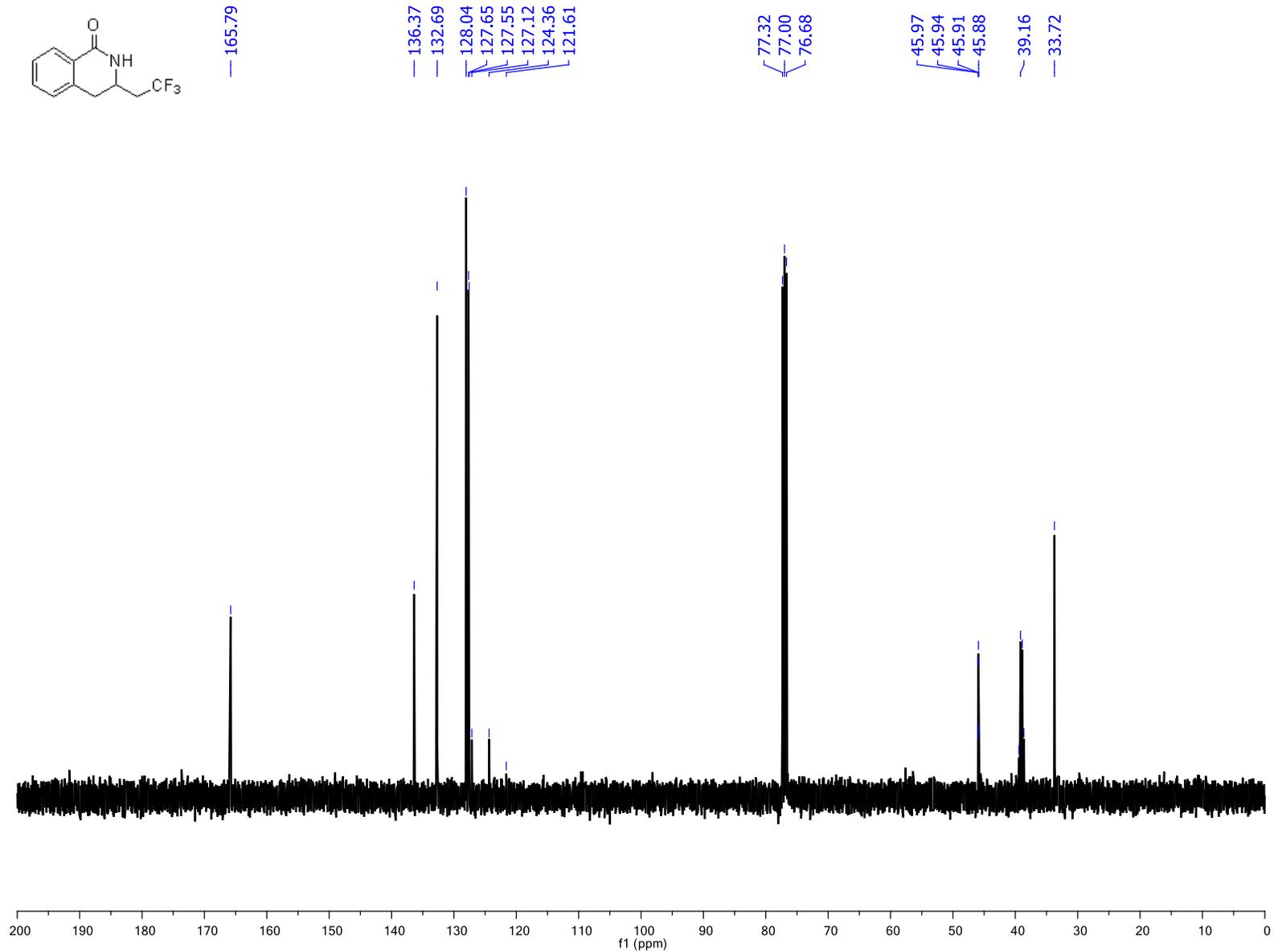
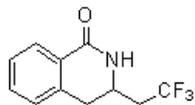


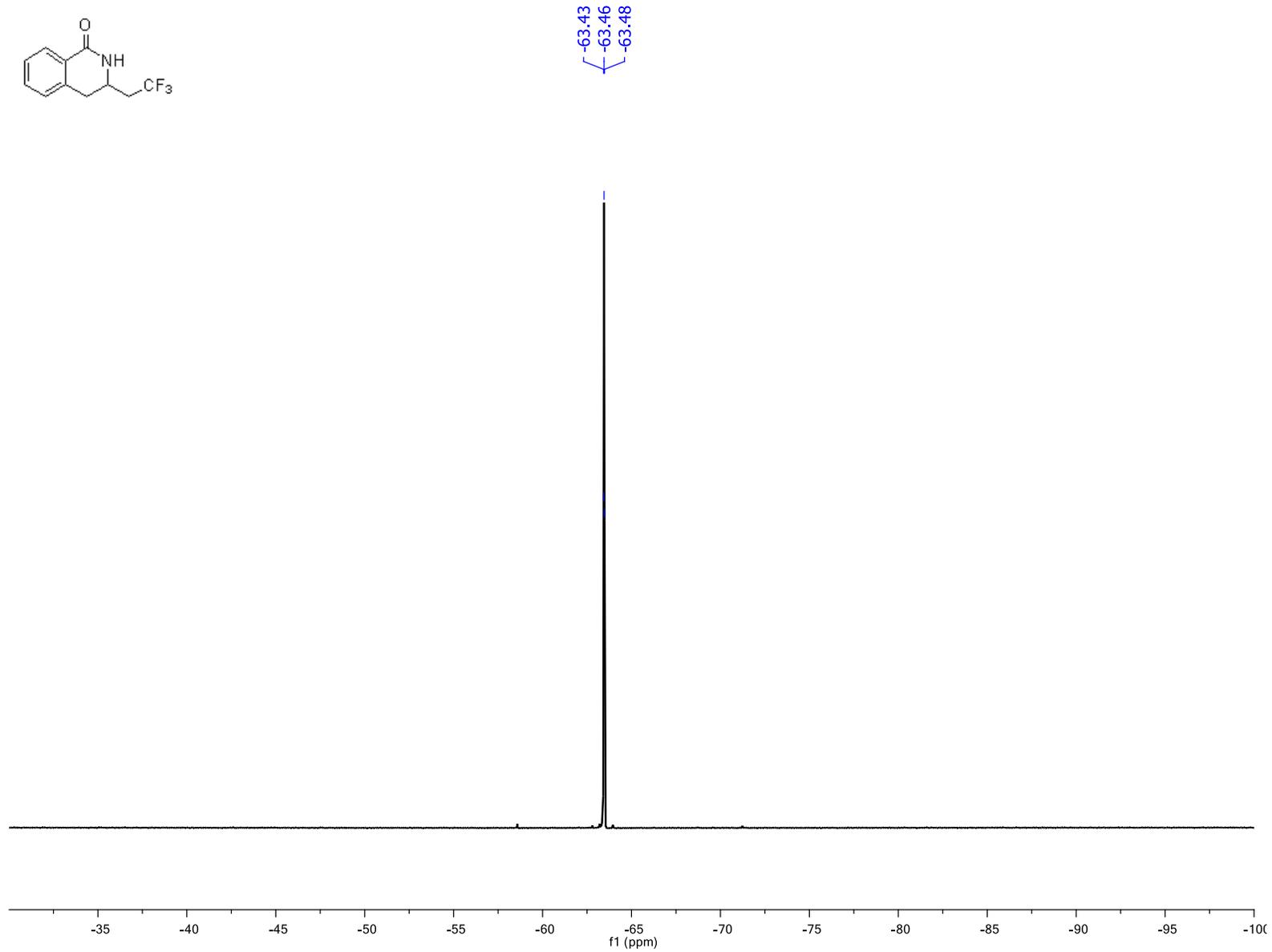
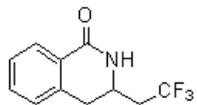


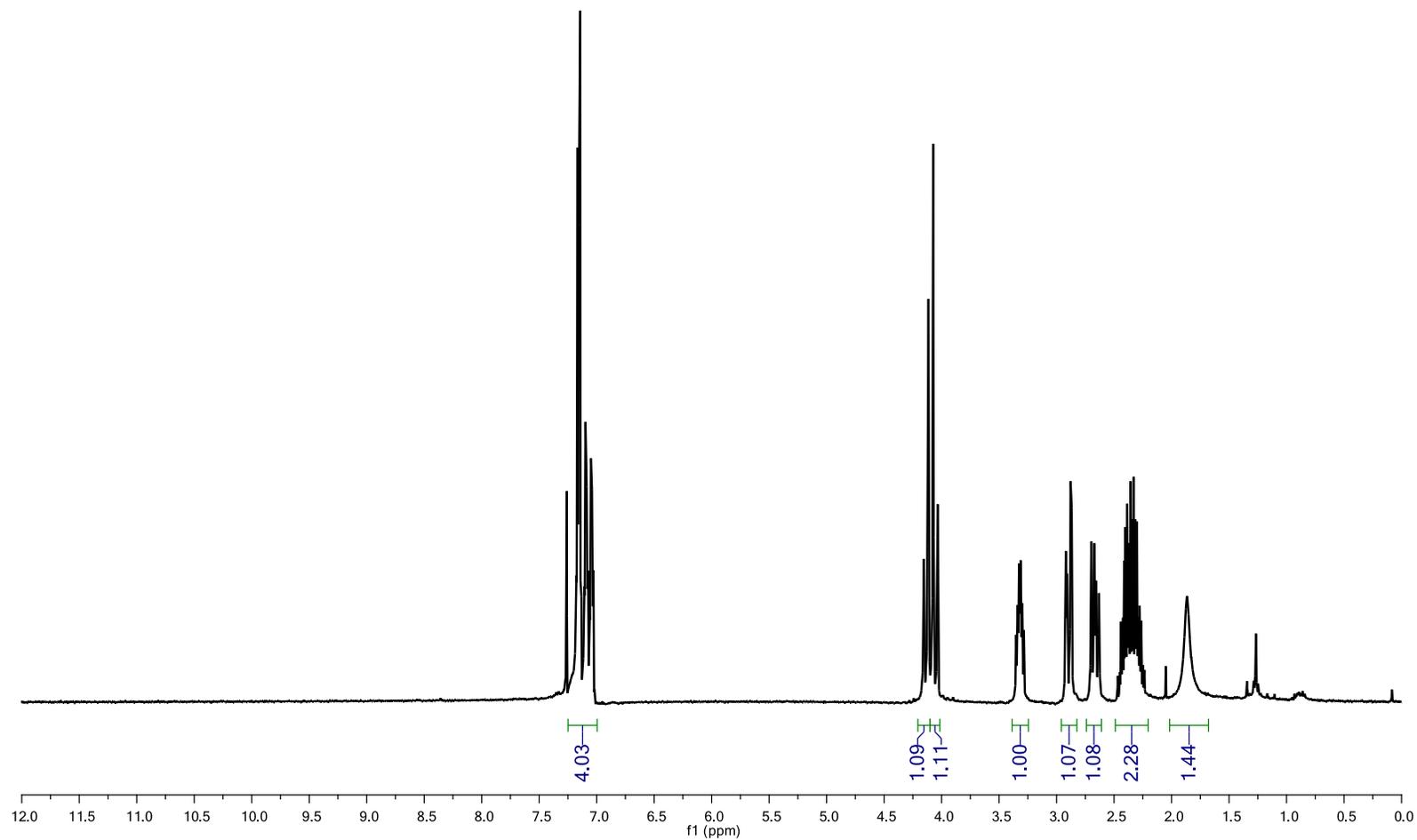
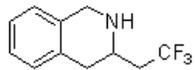


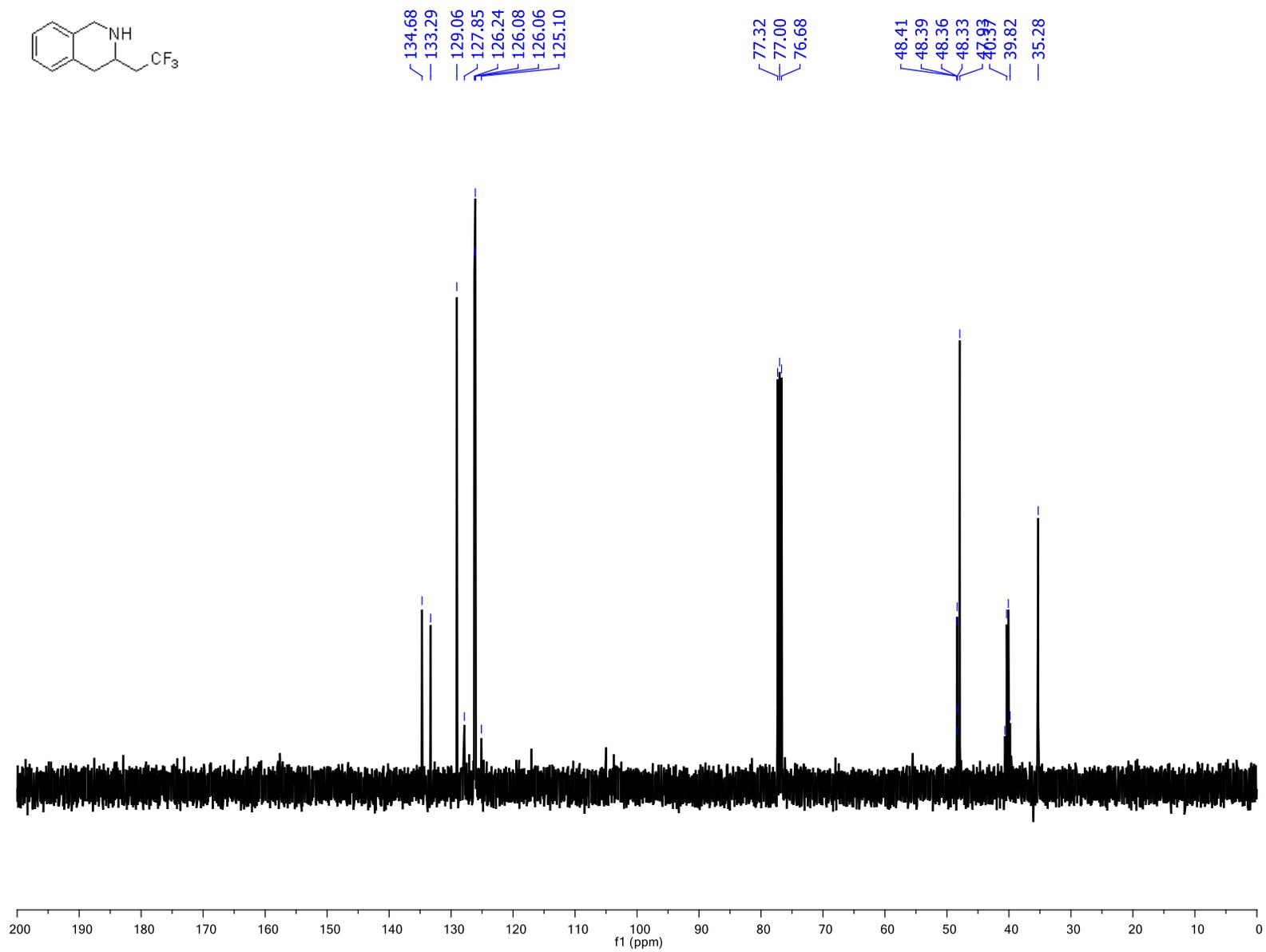
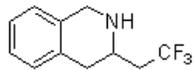


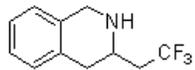












-63.16
-63.19
-63.22

