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Supporting Information

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Copper-Catalyzed Electrophilic Amination of Heteroarenes and Arenes by C−H Zincation**

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Supporting Information

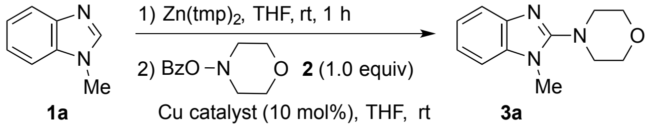
Content

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 Biotage 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. Reaction vials were sealed with Teflon tape. 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 $KMnO_4$ stain. Organic solutions were concentrated under reduced pressure using a Büchi rotary evaporator. Flash-column chromatography was performed on silica gel (60 Å, standard grade) or on a CombiFlash companion system with pre-packed FLASH silica gel columns (Teledyne ISCO, Inc.).

Materials. Commercial reagents and solvents were purchased from Sigma-Aldrich, Alfa Aesar, Matrix, or Acros and used as received. Dry THF and CH_2Cl_2 were obtained using an Innovative Technologies solvent purification system. Zn(tmp)$_2$ (0.5 M solution in toluene) was purchased from Sigma-Aldrich. tmpZnCl•LiCl was prepared according to literature procedure.[1a] *O*-acylhydroxylamine derivatives were prepared according to literature procedure.[1b-c]

Instrumentation. Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded on a Varian INOVA 400 or Bruker 500 spectrometer at ambient temperature unless otherwise indicated. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm, δ) and referenced to residual protium in the NMR solvent (CDCl3: δ 7.26, CD_2Cl_2: δ 5.32). Chemical shifts for ^{13}C NMR are reported in ppm and referenced to the carbon resonances of the solvent (CDCl3: δ 77.0 CD_2Cl_2: δ 54.0). 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), integration. Infrared spectroscopic data were obtained using a Thermo Scientific Nicolet 380 and are reported in wavennumbers (cm^{-1}). High-resolution mass spectra were obtained through the Duke University Mass Spectrometry Facility using an Agilent 1100 Series liquid chromatography-electrospray ionization mass spectrometer.

Condition Screenings for the Reaction of 1a and 2a.



entry	**1a** (equiv)	$Zn(tmp)_2$ (equiv)	copper catalyst	time[a] (h)	**3a** (%)[b]
1	2.1	1.0	–	24[c]	0
2	2.1	1.0	CuI	4	82
3	2.1	1.0	CuBr	19	80
4	2.1	1.0	CuCl	4	88
5	2.1	1.0	CuCN	19	81
6	2.1	1.0	CuOT•ftol	4	71
7	2.1	1.0	$CuCl_2$	3.5	89
8	2.1	1.0	$Cu(acac)_2$	3.5	82
9	2.1	1.0	$Cu(OTf)_2$	5	76
10	**2.1**	**1.0**	**$Cu(OAc)_2$**	**5**	**99**
11	1.4	0.6	$Cu(OAc)_2$	72[c]	56
12	1.05	0.5	$Cu(OAc)_2$	72[c]	40

[a] Time required for complete consumption of **2** in step 2. [b] Yields determined by ^{1}H NMR spectroscopy with CH_2Br_2 as a quantitative internal standard. [c] **2** not fully consumed after 72 h.

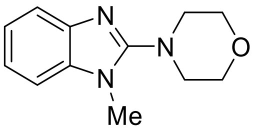
Typical Procedure 1 (TP1): General Experimental Procedure for C–H Amination via $Zn(tmp)_2$ Mediated Metalation.

To an 8 mL microwave tube charged with heteroaryl compound (0.420 mmol, 2.1 equiv) was added THF (1 mL) followed by dropwise addition of $Zn(tmp)_2$ (0.5 M solution in tol, 0.40 mL, 0.200 mmol, 1.0 equiv) under N_2. The reaction was stirred at room temperature for 1−2 h and then a mixture of *O*-acylhydroxylamine (0.200 mmol, 1.0 equiv) and $Cu(OAc)_2$ (0.020 mmol, 0.10 equiv) in THF (1 mL) was added to the reaction. The reaction mixture was allowed to stir at room temperature. Upon complete consumption of *O*-acylhydroxylamine (monitored by TLC–50% ethyl acetate–hexanes), the reaction mixture was flushed through a plug of aluminum oxide and washed with Et_2O. The filtrate was concentrated under reduced pressure. The crude reaction mixture was purified by either column chromatography or Kugelrohr distillation.

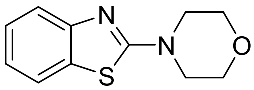
Typical Procedure 2 (TP2): General Experimental Procedure for C–H Amination via tmpZnCl•LiCl Mediated Metalation.

To an 8 mL microwave tube charged with heteroaryl compound (0.200 mmol, 1.0 equiv) was added THF (1 mL) followed by dropwise addition of tmpZnCl·LiCl solution (0.200 mmol, 1.0 equiv) under N_2. The resulting mixture was stirred vigorously at room temperature for 1 h. Then a mixture of $Cu(OAc)_2$ (0.020 mmol, 0.10 equiv) and *O*-acylhydroxylamine (0.240 mmol, 1.2 equiv) in THF (1 mL) was added dropwise to the heteroarylzinc mixture under N_2. Upon complete consumption of the heteroarene (determined by TLC analysis with a small aliquot reaction sample that was quenched with a saturated aqueous solution of $NaHCO_3$ and extracted into EtOAc), the reaction was quenched by dropwise addition of a saturated aqueous solution of NH_4Cl (1 mL). The reaction mixture was subsequently basified with saturated aqueous solution of Na_2CO_3 (5 mL) and extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure. The crude reaction mixture was purified by flash-column chromatography.

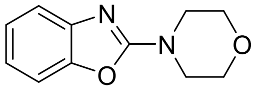
Characterization Data of New Compounds.



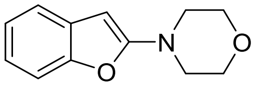
4-(1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)morpholine (3a). Compound prepared according to TP1. Purification by flash-column chromatography (100% ethyl acetate) gave **3a** as a white solid (41.6 mg, 96%); $R_f = 0.32$ (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.63–7.60 (m, 1H), 7.22–7.17 (m, 3H), 3.90 (t, *J* = 4.6 Hz, 4H), 3.62 (s, 3H), 3.32 (t, *J* = 4.6 Hz, 4H); Spectroscopic data was identical to that reported previously.[2]



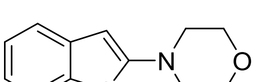
4-(Benzo[*d*]thiazol-2-yl)morpholine (3b). Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3b** as a pale yellow solid (40.6 mg, 93%); $R_f =$ 0.57 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.10 (td, *J* = 7.6, 1.2 Hz, 1H), 3.83 (t, *J* = 4.8 Hz, 4H), 3.62 (t, *J* = 4.8 Hz, 4H); Spectroscopic data was identical to that reported previously.[2]



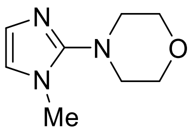
2-Morpholinobenzo[*d*]oxazole (3c). Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **3c** as a yellow solid (38.9 mg, 95%); $R_f = 0.64$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.27 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.18 (td, *J* = 7.6, 1.2 Hz, 1H), 7.04 (td, *J* = 7.6, 1.2 Hz, 1H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.69 (t, *J* = 4.8 Hz, 4H); Spectroscopic data was identical to that reported previously.[2]



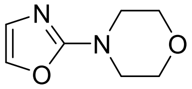
4-(Benzofuran-2-yl)morpholine (3d). Compound prepared according to TP1. Deprotonation of **1d** achieved with $Zn(tmp)_2$•LiCl•$MgCl_2$ at room temperature for 24 h. Purification by flash-column chromatography (10% ethyl acetate–hexanes) gave **3d** as a white solid (28.9 mg, 71%); $R_f = 0.64$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.04 (t, *J* = 8.0 Hz, 1H), 5.47 (s, 1H), 3.86 (t, *J* = 4.8 Hz, 4H), 3.29 (t, *J* = 4.8 Hz, 4H); Spectroscopic data was identical to that previously reported.[3]



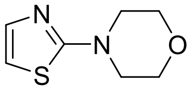
4-(Benzo[*b*]thiophen-2-yl)morpholine (3e). Compound prepared according to TP1. Deprotonation of **1e** achieved with $Zn(tmp)_2$•LiCl•$MgCl_2$ at room temperature for 24 h. Purification by flash-column chromatography (10% ethyl acetate–hexanes) gave **3e** as a white solid (30.7 mg, 70%); $R_f = 0.66$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.23 (s, 1H), 3.87 (t, *J* = 4.8 Hz, 4H), 3.25 (t, *J* = 4.8 Hz, 4H); Spectroscopic data was identical to that reported previously.[4]



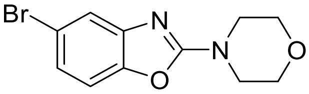
4-(1-Methyl-1*H*-imidazol-2-yl)morpholine (3f). Compound prepared according to TP1. Purification by flash-column chromatography (100% ethyl acetate) gave **3f** as a colorless oil (27.4 mg, 82%); R_f = 0.07 (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.80 (d, *J* = 1.4 Hz, 1H), 6.67 (d, *J* = 1.4 Hz, 1H), 3.83 (t, *J* = 4.8 Hz, 4H), 3.50 (s, 3H), 3.08 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.8, 125.0, 118.3, 66.8, 51.1, 31.9; FTIR (thin film): cm^{-1} 2854, 1527, 1285, 1115; HRMS-ESI (m/z) Calcd for ($C_8H_{14}N_3O$) ([M+H]$^+$): 168.1131; found: 168.1133.



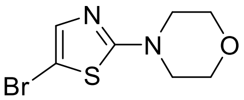
4-(Oxazol-2-yl)morpholine (3g). Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3g** as a white solid (28.3 mg, 92%); R_f = 0.27 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23 (s, 1H), 6.83 (s, 1H), 3.78 (t, *J* = 4.9 Hz, 4H), 3.48 (t, *J* = 4.9 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 161.8, 132.8, 126.8, 66.2, 46.0; FTIR (thin film): cm^{-1} 2922, 1655, 1483, 1116; HRMS-ESI (m/z) Calcd for ($C_7H_{11}N_2O_2$) ([M+H]$^+$): 155.0815; found: 155.0811.



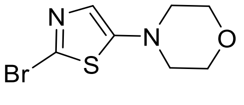
4-(Thiazol-2-yl)morpholine (3h). Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **3h** as a colorless oil (32.3 mg, 95%); R_f = 0.49 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (d, *J* = 3.6 Hz, 1H), 6.60 (d, *J* = 3.6 Hz, 1H), 3.81 (t, *J* = 5.0 Hz, 4H), 3.46 (t, *J* = 5.0 Hz, 4H); Spectroscopic data was identical to that reported previously.[2]



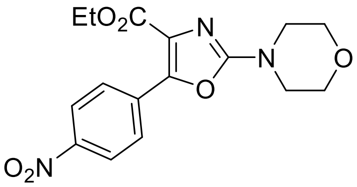
5-Bromo-2-morpholinobenzo[*d*]oxazole (3i). Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3i** as a white solid (54.3 mg, 96%); R_f = 0.52 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46 (dd, *J* = 2.0, 0.8 Hz, 1H), 7.15–7.09 (m, 2H), 3.81 (t, *J* = 4.6 Hz, 4H), 3.68 (t, *J* = 4.6 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.6, 147.7, 144.7, 123.5, 119.4, 116.8, 109.9, 66.1, 45.6; FTIR (thin film): cm^{-1} 2869, 1567, 1452, 1113, 791; HRMS-ESI (m/z) Calcd for ($C_{11}H_{12}BrN_2O_2$) ([M+H]$^+$): 283.0077; found: 283.0080.



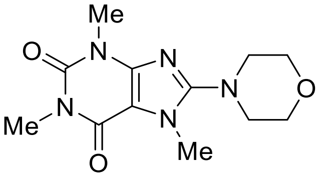
4-(5-Bromothiazol-2-yl)morpholine (3j). Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3j** as a pale yellow solid (42.3 mg, 85%); R_f = 0.71 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.09 (s, 1H), 3.80 (t, *J* = 5.0 Hz, 4H), 3.40 (t, *J* = 5.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.8, 140.4, 95.3, 66.0, 48.2; FTIR (thin film): cm^{-1} 2869, 1537, 1448, 1114, 634; HRMS-ESI (m/z) Calcd for ($C_7H_{10}BrN_2OS$) ([M+H]$^+$): 248.9692; found: 248.9691.



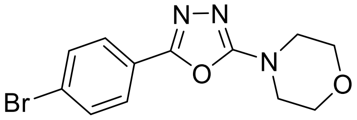
4-(2-Bromothiazol-5-yl)morpholine (3k). Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3k** as a white solid (44.7 mg, 90%); R_f = 0.65 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.75 (s, 1H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.05 (t, *J* = 4.8 Hz, 4H); Spectroscopic data was identical to that reported previously.[5]



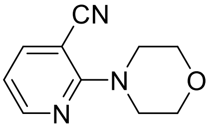
Ethyl-2-morpholino-5-(4-nitrophenyl)oxazole-4-carboxylate (3l). Compound prepared according to TP1. Purification by flash-column chromatography (60% ethyl acetate–hexanes) gave **3l** as a neon yellow solid (61.8 mg, 89%); R_f = 0.18 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26 (dt, *J* = 8.8, 2.0 Hz, 2H), 8.19 (dt, *J* = 8.8, 2.0 Hz, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 3.83 (t, *J* = 4.8 Hz, 4H), 3.66 (t, *J* = 4.8 Hz, 4H), 1.42 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.3, 159.6, 147.2, 146.2, 133.3, 130.2, 127.7, 123.6, 66.0, 61.8, 45.6, 14.2; FTIR (thin film): cm^{-1} 2859, 1713, 1619, 1323, 1116; HRMS-ESI (m/z) Calcd for ($C_{17}H_{18}N_3O_6$) ([M+H]$^+$): 348.1190; found: 348.1193.



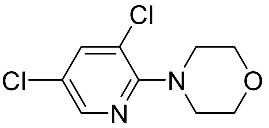
1,3,7-Trimethyl-8-morpholino-3,7-dihydro-1*H*-purine-2,6-dione (3m). Compound prepared according to TP1. Deprotonation of **1m** was done in CH_2Cl_2 due to low solubility in THF. Purification by flash-column chromatography (80% ethyl acetate–hexanes) gave **3m** as a white solid (45.8 mg, 82%); R_f = 0.24 (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.84 (t, *J* = 4.8 Hz, 4H), 3.76 (s, 3H), 3.52 (s, 3H), 3.38 (s, 3H), 3.26 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 155.9, 155.0, 151.7, 147.3, 105.5, 66.3, 49.9, 32.4, 29.7, 27.7; FTIR (thin film): cm^{-1} 2852, 1693, 1647, 1611, 1432, 1114; HRMS-ESI (m/z) Calcd for ($C_{12}H_{18}N_5O_3$) ([M+H]$^+$): 280.1404; found: 280.1405.



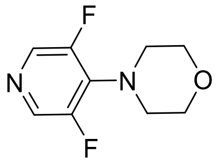
4-(5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl)morpholine (3n). Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **3n** as a white solid (56.4 mg, 91%); R_f = 0.08 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 3.82 (t, *J* = 4.6 Hz, 4H), 3.57 (t, *J* = 4.6 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.0, 158.8, 132.1, 127.1, 125.0, 123.3, 65.9, 46.1; FTIR (thin film): cm^{-1} 2857, 1547, 1481, 1273, 1116; HRMS-ESI (m/z) Calcd for ($C_{12}H_{13}BrN_3O_2$) ([M+H]$^+$): 310.0186; found: 310.0188.



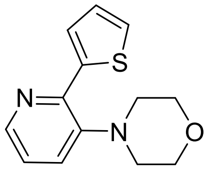
2-Morpholinonicotinonitrile (3o). Compound prepared according to TP1. Amination step run at 50 °C. Purification by flash-column chromatography (20% ethyl acetate–hexanes) gave **3o** as a pale yellow solid (30.6 mg, 81%); R_f = 0.50 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.36 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.79 (dd, *J* = 7.6, 2.0 Hz, 1H), 6.79 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.84 (t, *J* = 4.8 Hz, 4H), 3.71 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.7, 151.9, 143.9, 117.9, 114.5, 95.2, 66.7, 48.4; FTIR (thin film): cm^{-1} 3026, 2845, 2210, 1580, 1552, 1231, 1116; HRMS-ESI (m/z) Calcd for ($C_{10}H_{12}N_3O$) ([M+H]$^+$): 190.0975; found: 190.0975.



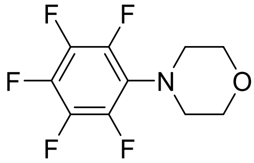
4-(3,5-Dichloropyridin-2-yl)morpholine (3p). Compound prepared according to TP1. Amination step run at 50 °C. Purification by flash-column chromatography (20% ethyl acetate–hexanes) gave **3p** as a pale yellow solid (36.8 mg, 91%); $R_f = 0.82$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13 (d, $J = 2.4$ Hz, 1H), 7.61 (d, $J = 2.4$ Hz, 1H), 3.85 (t, $J = 4.8$ Hz, 4H), 3.34 (t, $J = 4.8$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 156.6, 144.3, 138.3, 124.5, 122.6, 66.8, 49.5; FTIR (thin film): cm^{-1} 2961, 2852, 2360, 1573, 1436, 1271, 1117; HRMS-ESI (m/z) Calcd for ($C_9H_{11}Cl_2N_2O$) ($[M+H]^+$): 233.0243; found: 233.0243.



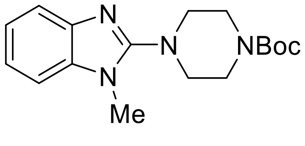
4-(3,5-Difluoropyridin-4-yl)morpholine (3q). Compound prepared according to TP1. Amination step run at 50 °C. Purification by flash-column chromatography (30% ethyl acetate–hexanes) gave **3q** as a pale yellow solid (36.2 mg, 91%); $R_f = 0.48$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16 (br s, 2H), 3.81 (t, $J = 4.4$ Hz, 4H), 3.41 (t, $J = 4.4$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.6 (d, $J = 251.7$ Hz), 134.9 (d, $J = 23.9$ Hz), 134.0 (t, $J = 8.6$ Hz), 67.1, 50.5; FTIR (thin film): cm^{-1} 2970, 2920, 2872, 1603, 1506, 1447, 1254, 1114, 1016; HRMS-ESI (m/z) Calcd for ($C_9H_{11}F_2N_2O$) ($[M+H]^+$): 201.0834; found: 201.0837.



4-(2-(Thiophen-2-yl)pyridin-3-yl)morpholine (3r). Compound prepared according to TP1. Amination step run at 50 °C. Compound prepared according to TP1. Purification by flash-column chromatography (20% ethyl acetate–hexanes) gave **3r** as a pale yellow solid (36.4 mg, 74%); $R_f = 0.53$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.55−8.53 (m, 1H), 8.34−8.31 (m, 1H), 7.71−7.66 (m, 1H), 7.32 (d, $J = 5.6$ Hz, 1H), 7.10−7.07 (m, 1H), 7.02 (d, $J = 5.6$ Hz, 1H), 3.86 (t, $J = 4.4$ Hz, 4H), 3.00 (t, $J = 4.4$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 133.9, 130.5, 129.2, 128.4 (2C), 128.3 (2C), 127.7, 107.6, 65.0, 40.0; FTIR (thin film): cm^{-1} 3051, 2956, 2848, 1578, 1535, 1214, 1028; HRMS-ESI (m/z) Calcd for ($C_{13}H_{15}N_2OS$) ($[M+H]^+$): 247.0900; found: 247.0909.

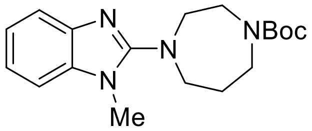


4-(Perfluorophenyl)morpholine (3s). Compound prepared according to TP1. Purification by kugelrohr distillation gave **3p** as a yellow oil (37.9 mg, 75%); $R_f = 0.88$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.81 (t, $J = 4.6$ H, 4H), 3.20 (t, $J = 4.6$ Hz, 4H); Spectroscopic data was identical to that reported previously.[6]

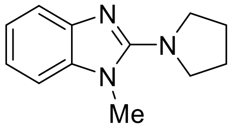


***tert*-Butyl-4-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)piperazine-1-carboxylate (4).** Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **4** as a white solid (54.1 mg, 86%); $R_f = 0.36$ (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61–7.58 (m, 1H), 7.22–7.17 (m, 3H), 3.62 (s, 3H), 3.62 (t, $J = 5.2$ Hz, 4H), 3.26 (t, $J = 5.2$ Hz, 4H), 1.49 (s, 9H);

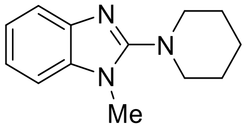
^{13}C NMR ($CDCl_3$, 125 MHz, 60 °C): δ 157.5, 154.7, 141.4, 135.7, 121.6, 121.2, 118.1, 108.3, 79.9, 50.2, 43.4, 30.2, 28.3; FTIR (thin film): cm^{-1} 2935, 1634, 1575, 1459, 739; HRMS-ESI (m/z) Calcd for ($C_{17}H_{25}N_4O_2$) ([M+H]$^+$): 317.1972; found: 317.1974.



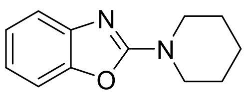
tert**-Butyl-4-(1-methyl-1*****H*****-benzo[*****d*****]imidazol-2-yl)-1,4-diazepane-1-carboxylate (5).** Compound prepared according to TP1. Purification by flash-column chromatography (90% ethyl acetate–hexanes) gave **5** as a colorless oil (44.1 mg, 67%); $R_f = 0.34$ (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 500 MHz, 60 °C): δ 7.53 (d, *J* = 6.5 Hz, 1H), 7.18–7.07 (m, 3H), 3.69–3.45 (m, 8H), 3.59 (s, 3H), 1.99 (br s, 2H), 1.47 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz, 60 °C) as a mixture of conformers: δ 158.5, 155.3 141.7, 136.0, 121.6, 120.8, 117.6, 108.1, 79.6, 53.5, 52.0, 48.1, 47.5, 46.1, 45.5, 30.9, 28.5; FTIR (thin film): cm^{-1} 2971, 1682, 1526, 1159, 738; HRMS-ESI (m/z) Calcd for ($C_{18}H_{27}N_4O_2$) ([M+H]$^+$): 331.2129; found: 331.2129.



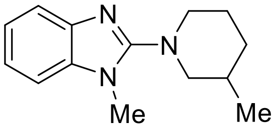
1-Methyl-2-(pyrrolidin-1-yl)-1***H*****-benzo[*****d*****]imidazole (6).** Compound prepared according to TP1. Purification by flash-column chromatography (100% ethyl acetate) gave **6** as a white solid (27.1 mg, 67%); $R_f = 0.31$ (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.13–7.05 (m, 3H), 3.63 (s, 3H), 3.64–3.60 (m, 4H), 2.00–1.92 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.3, 142.1, 136.2, 121.3, 119.6, 116.5, 107.4, 50.3, 31.1, 25.6; FTIR (thin film): cm^{-1} 2968, 1541, 1469, 1285, 740; HRMS-ESI (m/z) Calcd for ($C_{12}H_{16}N_3$) ([M+H]$^+$): 202.1339; found: 202.1341.



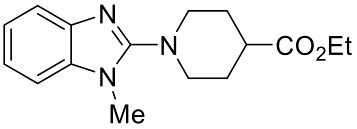
1-Methyl-2-(piperidin-1-yl)-1***H*****-benzo[*****d*****]imidazole (7).** Compound prepared according to TP1. Purification by flash-column chromatography (30% ethyl acetate−hexanes) gave **7** as white solid (36.9 mg, 86%); $R_f = 0.45$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60−7.58 (m, 1H), 7.19−7.14 (m, 3H), 3.59 (s, 3H), 3.25 (t, *J* = 5.2 Hz, 4H), 1.79−1.73 (m, 4H), 1.68−1.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.9, 141.5, 135.6, 121.4, 120.8, 117.8, 108.2, 51.5, 30.4, 25.7, 24.2; FTIR (thin film): cm^{-1} 2932, 2849, 1522, 1469, 1283; HRMS-ESI (m/z) Calcd for ($C_{12}H_{18}N_3$) ([M+H]$^+$): 214.1495; found: 214.1497.



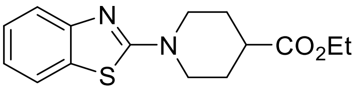
2-(Piperidin-1-yl)benzo[***d*****]oxazole (8).** Compound prepared according to TP1. Purification by kugelröhr distillation followed by flash-column chromatography (15% ethyl acetate–hexanes) gave **8** as a white solid (35.0 mg, 87%); $R_f = 0.28$ (15% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (d, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 3.65 (br s, 4H), 1.67 (br s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.4, 148.7, 143.4, 123.8, 120.2, 116.0, 108.5, 46.6, 25.2, 24.1; FTIR (thin film): cm^{-1} 2935, 1634, 1575, 1459, 739; HRMS-ESI (m/z) Calcd for ($C_{12}H_{15}N_2O$) ([M+H]$^+$): 203.1179; found: 203.1181.



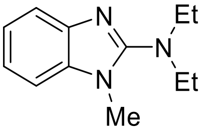
1-Methyl-2-(3-methylpiperidin-1-yl)-1*H*-benzo[*d*]imidazole (9). Compound prepared according to TP1. Purification by flash-column chromatography (10% ethyl acetate–hexanes) gave **9** as a white solid (37.0 mg, 81%); R_f = 0.26 (30% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59–7.57 (m, 1H), 7.16–7.14 (m, 3H), 3.57 (s, 3H), 3.49–3.44 (m, 2H), 2.90 (td, *J* = 11.2, 3.6 Hz, 1H), 2.65 (dd, *J* = 12.4, 10.4 Hz, 1H), 1.87–1.76 (m, 4H), 1.14–1.09 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.7, 141.5, 135.6, 121.4, 120.8, 117.8, 108.2, 58.0, 51.1, 32.7, 30.9, 30.4, 25.2, 19.2; FTIR (thin film): cm^{-1} 2925, 1521, 1280, 1122, 742; HRMS-ESI (m/z) Calcd for ($C_{14}H_{20}N_3$) ($[M+H]^+$): 230.1652; found: 230.1555.



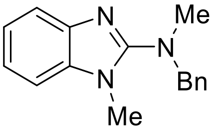
Ethyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)piperidine-4-carboxylate (10). Compound prepared according to TP1. Purification by flash-column chromatography (40% ethyl acetate–hexanes) gave **10** as a yellow oil (43.9 mg, 76%); R_f = 0.36 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60–7.58 (m, 1H), 7.19–7.16 (m, 3H), 4.17, (q, *J* = 7.2 Hz, 2H), 3.60 (s, 3H), 3.56 (dt, *J* = 12.8, 3.2, 2H), 3.05 (td, 12.4, 2.4 Hz, 2H), 2.52 (tt, 11.2, 4.0 Hz, 1H), 2.10–2.06 (m, 2H), 1.99–1.89 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.5, 158.1, 141.3, 135.3, 121.5, 121.0, 117.9, 108.3, 60.4, 50.0, 40.8, 30.3, 27.9, 14.1; FTIR (thin film): cm^{-1} 2926, 1723, 1520, 1041, 743; HRMS-ESI (m/z) Calcd for ($C_{16}H_{22}N_3O_2$) ($[M+H]^+$): 288.1707; found: 288.1707.



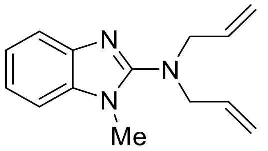
Ethyl-1-(benzo[*d*]thiazol-2-yl)piperidine-4-carboxylate (11). Compound prepared according to TP1. Purification by flash-column chromatography (gradient from 5% ethyl acetate–hexanes to 15% ethyl acetate–hexanes) gave **11** as a yellow powder (46.1 mg, 79%); R_f = 0.20 (15% ethyl acetate–hexanes); ^{1}H NMR (CD_2Cl_2, 500 MHz): δ 7.65 (d, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.33–7.29 (m, 1H), 7.11–7.08 (m, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 4.07 (tt, *J* = 13.5, 3.5 Hz, 2H), 3.23 (ddd, *J* = 13.5, 11.5, 3.0 Hz, 2H), 2.57 (tt, *J* = 11.0, 3.8 Hz, 1H), 2.04–2.01 (m, 2H), 1.86–1.72 (m, 2H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_2Cl_2, 125 MHz): δ 174.5, 169.1, 153.6, 131.6, 126.4, 121,7, 121.2, 119.3, 61.1, 48.5, 41.3, 28.1, 16.6; FTIR (thin film): cm^{-1} 2925, 1726, 1529, 1174, 1038, 752; HRMS-ESI (m/z) Calcd for ($C_{15}H_{19}N_2O_2S$) ($[M+H]^+$): 291.1162; found: 291.1164.



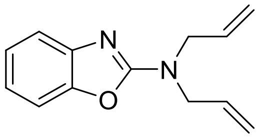
***N*,*N*-Diethyl-1-methyl-1*H*-benzo[*d*]imidazol-2-amine (12).** Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **12** as a clear oil (37.3 mg, 92%); R_f = 0.35 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60–7.58 (m, 1H), 7.19–7.12 (m, 3H), 3.59 (s, 3H), 3.32 (q, *J* = 7.2 Hz, 4H), 1.16 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.8, 141.6, 135.5, 121.4, 120.7, 117.7, 108.2, 46.0, 30.4, 12.9; FTIR (thin film): cm^{-1} 2969, 1521, 1439, 1323, 741; HRMS-ESI (m/z) Calcd for ($C_{12}H_{18}N_3$) ($[M+H]^+$): 204.1495; found: 204.1499.



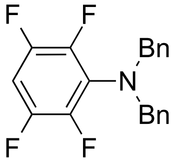
***N*-Benzyl-*N*,1-dimethyl-1*H*-benzo[*d*]imidazol-2-amine (13).** Compound prepared according to TP1. Purification by flash-column chromatography (50% ethyl acetate–hexanes) gave **13** as a white solid (45.2 mg, 90%); R_f = 0.46 (50% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62–7.60 (m, 1H), 7.41–7.35 (m, 4H), 7.32–7.30 (m, 1H), 7.22–7.16 (m, 3H), 4.47 (s, 2H), 3.65 (s, 3H), 2.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.9, 141.3, 137.3, 135.8, 128.6, 127.8, 127.5, 121.6, 120.9, 117.7, 108.3, 58.2, 39.3, 30.7; FTIR (thin film): cm^{-1} 3029, 1532, 1445, 1392, 740; HRMS-ESI (m/z) Calcd for ($C_{16}H_{18}N_3$) ($[M+H]^+$): 252.1495; found: 252.1504.



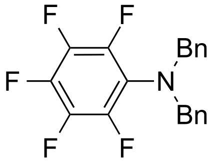
***N,N*-Diallyl-1-methyl-1*H*-benzo[*d*]imidazol-2-amine (14).** Compound prepared according to TP1. Purification by flash-column chromatography (5% ethyl acetate–dichloromethane) gave **14** as a clear oil (36.5 mg, 80%); R$_f$ = 0.17 (15% ethyl acetate–hexanes); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.59–7.57 (m, 1H), 7.20–7.14 (m, 3H), 5.94 (ddt, *J* = 17.2, 10.0, 6.0 Hz, 2H), 5.28 (dd, *J* = 17.2, 1.6 Hz, 2H), 5.20 (dd, *J* = 10.0, 1.6 Hz, 2H), 3.92 (d, *J* = 6.0 Hz, 4H), 3.62 (s, 3H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ157.8, 141.5, 135.7, 133.9, 121.5, 120.8, 118.0, 117.8, 108.2, 53.7, 30.6; FTIR (thin film): cm^{-1} 2920, 1533, 1393, 1284, 923, 741; HRMS-ESI (m/z) Calcd for ($C_{14}H_{18}N_3$) ($[M+H]^+$): 228.1495; found: 228.1494.



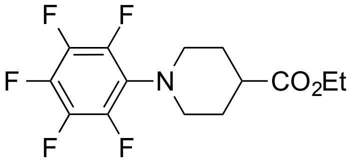
***N,N*-Diallylbenzo[*d*]oxazol-2-amine (15).** Compound prepared according to TP1. Purification by kugelröhr distillation followed by flash-column chromatography (15% ethyl acetate–hexanes) gave **15** as a clear oil (28.1 mg, 66%); R$_f$ = 0.51 (15% ethyl acetate–hexanes); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.38–7.35 (m, 1H), 7.26–7.24 (m, 1H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 7.00 (td, *J* = 7.6, 1.2 Hz, 1H), 5.87 (ddt, *J* = 22.4, 10.4, 5.8 Hz, 2H), 5.27–5.26 (m, 2H), 5.22 (t, *J* = 1.2 Hz, 2H), 4.16 (d, *J* = 5.8 Hz, 4H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 162.3, 148.9, 143.3, 132.5, 123.9, 120.3, 117.8, 116.1, 108.7, 49.9; FTIR (thin film): cm^{-1} 2923, 1631, 1577, 1459, 1243, 740; HRMS-ESI (m/z) Calcd for ($C_{13}H_{15}N_2O$) ($[M+H]^+$): 215.1178; found: 215.1178.



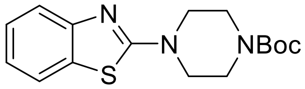
***N,N*-Dibenzyl-2,3,5,6-tetrafluoroaniline (16).** Compound prepared according to TP1. Purification by flash-column chromatography (100% hexanes) gave **16** as a clear oil (58.7 mg, 85%); R$_f$ = 0.33 (100% hexanes); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.31–7.26 (m, 10H), 6.71 (tt, *J* = 10.0, 7.2 Hz, 1H), 4.30 (s, 4H); Spectroscopic data was identical to that reported previously.[7b]



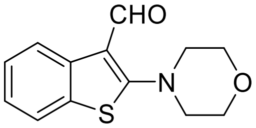
***N,N*-Dibenzyl-2,3,4,5,6-pentafluoroaniline (17).** Compound prepared according to TP1. Purification by flash-column chromatography (5% dichloromethane–hexanes) gave **17** as a clear oil (58.1 mg, 80%); R$_f$ = 0.39 (5% dichloromethane–hexanes); ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.30–7.22 (m, 10H), 4.23 (s, 4H); Spectroscopic data was identical to that reported previously.[7b]



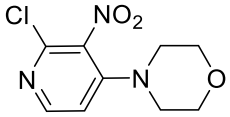
Ethyl-1-(perfluorophenyl)piperidine-4-carboxylate (18). Compound prepared according to TP1. Purification by flash-column chromatography (gradient of 100% hexanes to 20% ethyl acetate–hexanes) gave **18** as a yellow oil (50.6 mg, 78%); $R_f = 0.35$ (5% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.16 (q, $J = 7.2$ Hz, 2H), 3.28–3.24 (m, 2H), 3.14–3.07 (m, 2H), 2.43 (tt, $J = 11.2$, 4.0 Hz, 1H), 2.00–1.96 (m, 2H), 1.89–1.81 (m, 2H), 1.27 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.3 (dd, $J_{C\text{-}F} = 246.3$, 5.5 Hz), 139.0–135.9 (m, 2C), 126.5 (t, $J_{C\text{-}F} = 11.3$ Hz); FTIR (thin film): cm^{-1} 2959, 1730, 1516, 1498, 985; HRMS-ESI (m/z) Calcd for ($C_{14}H_{15}F_5NO_2$) ([M+H]$^+$): 324.1017; found: 324.1014.



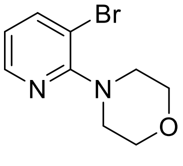
tert**-Butyl-4-(benzo[*****d*****]thiazol-2-yl)piperazine-1-carboxylate (19).** Compound prepared according to TP2. Purification by flash-column chromatography (gradient from 5% ethyl acetate–hexanes to 20% ethyl acetate–hexanes) gave **19** as a white solid (55.0 mg, 86%); $R_f = 0.28$ (20% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62–7.59 (m, 1H), 7.57–7.55 (m, 1H), 7.33–7.28 (m, 1H), 7.11–7.07 (m, 1H), 3.63–3.54 (m, 8H), 1.48 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.5, 154.6, 152.7, 130.9, 126.0, 121.6, 120.7, 119.4, 80.3, 48.3, 43.2, 28.4; FTIR (thin film): cm^{-1} 2974, 1696, 1536, 1444, 1167; HRMS-ESI (m/z) Calcd for ($C_{16}H_{22}N_3O_2S$) ([M+H]$^+$): 320.1427; found: 320.1429.



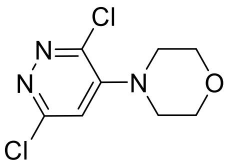
2-Morpholinobenzo[***b*****]thiophene-3-carbaldehyde (20).** Compound prepared according to TP2. Purification by flash-column chromatography (30% ethyl acetate−hexanes) gave **20** as a white solid (35.6 mg, 72%); $R_f = 0.25$ (30% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.18 (s, 1H), 8.31 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.45−7.38 (m, 1H), 7.30−7.26 (m, 1H), 3.93 (t, $J = 4.8$ Hz, 4H), 3.45 (t, $J = 4.8$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 182.4, 151.5, 137.3, 131.4, 124.0, 121.6, 116.6, 66.2, 55.0; FTIR (thin film): cm^{-1} 2854, 1650, 1514, 1462, 1437, 1115, 1011, 754; HRMS-ESI (m/z) Calcd for ($C_{13}H_{14}NO_2S$) ([M+H]$^+$): 248.0740; found: 248.0734.



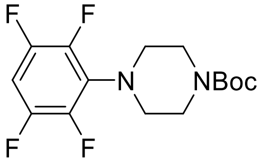
4-(2-Chloro-3-nitropyridin-4-yl)morpholine (21). Compound prepared according to TP2. Reaction run on a 0.400 mmol scale. Purification by flash-column chromatography (40% ethyl acetate−hexanes) gave **21** as a bright yellow solid (78.9 mg, 81%); $R_f = 0.30$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, $J = 6.0$ Hz, 1H), 6.81 (d, $J = 6.0$ Hz, 1H), 3.76 (t, $J = 4.8$ Hz, 4H), 3.20 (t, $J = 4.8$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 150.4, 149.8, 144.0, 137.3, 112.7, 66.1, 49.4; FTIR (thin film): cm^{-1} 3053, 2862, 1585, 1530, 1263, 968; HRMS-ESI (m/z) Calcd for ($C_9H_{11}ClN_3O_3$) ([M+H]$^+$): 244.0483; found: 244.0485.



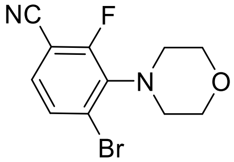
4-(3-Bromopyridin-2-yl)morpholine (22). Compound prepared according to TP2. Reaction run on a 0.400 mmol scale. Purification by flash-column chromatography (20% ethyl acetate−hexanes) gave **22** as a yellow oil (50.6 mg, 90%); $R_f = 0.74$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24 (dd, $J = 4.8$, 1.6 Hz, 1H), 7.79 (dd, $J = 7.6$, 1.6 Hz, 1H), 6.80 (dd, $J = 7.6$, 4.8 Hz, 1H), 3.87 (t, $J = 4.8$ Hz, 4H), 3.34 (t, $J = 4.8$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.2, 146.5, 142.3, 118.7, 112.8, 66.9, 50.0; FTIR (thin film): cm^{-1} 2956, 2847, 1717, 1575, 1427, 1110, 1011, 941; HRMS-ESI (m/z) Calcd for ($C_9H_{12}BrN_2O$) ([M+H]$^+$): 243.0128; found: 243.0127.



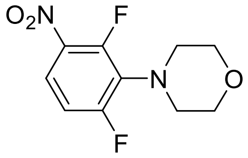
4-(3,6-Dichloropyridazin-4-yl)morpholine (23). Compound prepared according to TP2. Reaction run on a 0.400 mmol scale. Purification by flash-column chromatography (40% ethyl acetate−hexanes) gave **23** as a yellow solid (84.1 mg, 90%); $R_f = 0.40$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.86 (s, 1H), 3.87 (t, *J* = 4.8 Hz, 4H), 3.30 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 155.7, 149.3, 149.2, 115.8, 66.0, 49.5; FTIR (thin film): cm^{-1} 2962, 2853, 1714, 1548, 1110, 966; HRMS-ESI (m/z) Calcd for ($C_8H_{10}Cl_2N_3O$) ([M+H]$^+$): 234.0195; found: 234.0195.



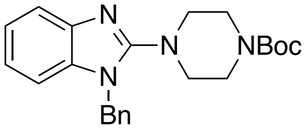
***tert*-Butyl-4-(2,3,5,6-tetrafluorophenyl)piperazine-1-carboxylate (24).** Compound prepared according to TP2. Purification by flash-column chromatography (5% ethyl acetate–dichloromethane) gave **24** as a clear oil (59.6 mg, 89%); $R_f = 0.51$ (15% ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.71 (tt, *J* = 9.6, 7.1 Hz, 1H), 3.54 (t, *J* = 5.0 Hz, 4H), 3.19 (br s, 4H), 1.48 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz, 60 °C): δ 154.7, 147.7–145.5 (m), 143.5–141.4 (m), 130.8 (t, *J* = 9.9 Hz), 99.2 (t, *J* = 23.0 Hz), 50.8, 44.4, 28.4; FTIR (thin film): cm^{-1} 2976, 2859, 1696, 1503, 1005, 924; HRMS-ESI (m/z) Calcd for ($C_{15}H_{19}F_4N_2O_2$) ([M+H]$^+$): 335.1377; found: 335.1378.



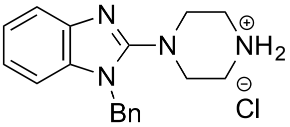
4-Bromo-2-fluoro-3-morpholinobenzonitrile (25). Compound prepared according to TP2. Reaction run on a 0.400 mmol scale. Purification by flash-column chromatography (10% ethyl acetate−hexanes) gave **25** as a yellow solid (102.6 mg, 90%); $R_f = 0.74$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48 (d, *J* = 8.4 Hz, 1H), 7.21 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.84 (t, *J* = 4.4 Hz, 4H), 3.18 (br s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.7 (d, *J* = 262.4 Hz), 138.4 (d, *J* = 11.3 Hz), 130.8 (d, *J* = 5.9 Hz), 129.8, 128.7, 113.2, 102.3 (d, *J* = 15.6 Hz), 67.4, 50.9 (d, *J* = 3.7 Hz); FTIR (thin film): cm^{-1} 2958, 2853, 2234, 1589, 1438, 1112, 1024; HRMS-ESI (m/z) Calcd for ($C_{11}H_{11}BrFN_2O$) ([M+H]$^+$): 285.0033; found: 285.0029.



4-(2,6-Difluoro-3-nitrophenyl)morpholine (26). Compound prepared according to TP2. Reaction run on a 0.400 mmol scale. Purification by flash-column chromatography (10% ethyl acetate−hexanes) gave **26** as a yellow solid (95.5 mg, 98%); $R_f = 0.83$ (50% ethyl acetate−hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.74–7.69 (m, 1H), 6.99–6.93 (m, 1H), 3.81 (t, *J* = 4.8 Hz, 4H), 3.26–3.23 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.7 (d, *J* = 262.4 Hz), 138.4 (d, *J* = 11.3 Hz), 130.8 (d, *J* = 5.9 Hz), 129.8, 128.7, 113.2, 102.3 (d, *J* = 15.6 Hz), 67.4, 50.9 (d, *J* = 3.7 Hz); FTIR (thin film): cm^{-1} 3062, 2971, 2861, 1578, 1528, 1380, 1068, 1019; HRMS-ESI (m/z) Calcd for ($C_{10}H_{11}F_2N_2O_2$) ([M+H]$^+$): 285.0033; found: 285.0029.

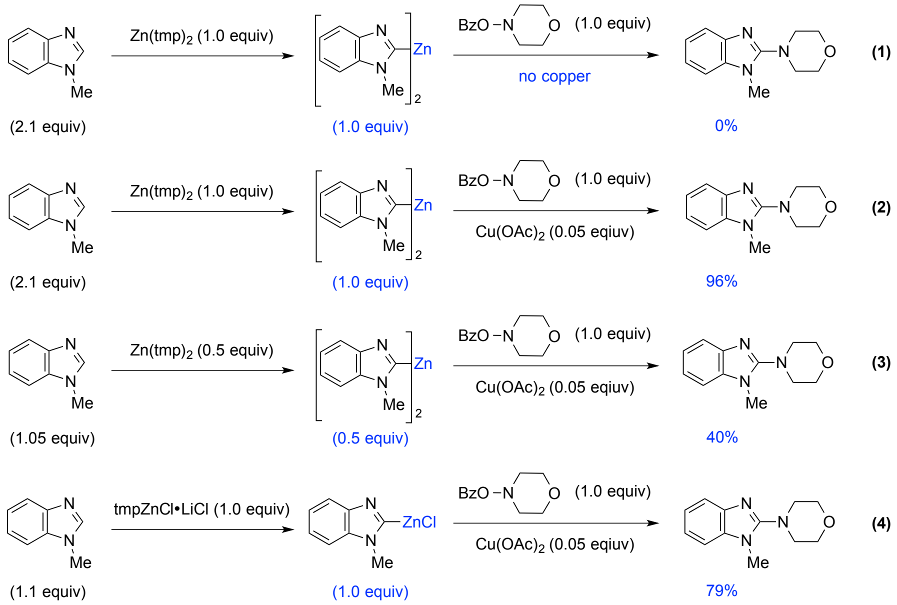


tert-Butyl-4-(1-benzyl-1H-benzo[d]imidazol-2-yl)piperazine-1-carboxylate (28). Compound prepared according to TP2. Reaction run on 0.960 mmol scale. Purification by flash-column chromatography (70% ethyl acetate–hexanes) gave **28** as a pale yellow solid (331 mg, 88%); R_f = 0.57 (100% ethyl acetate); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65 (d, J = 7.6 Hz, 1H), 7.36–7.29 (m, 3H), 7.20 (td, J = 7.6 Hz, 1.2 Hz, 1H), 7.17–7.15 (m, 2H), 7.11 (td, J = 7.6 Hz, 1.2 Hz, 1H), 7.05–7.03 (m, 1H), 5.24 (s, 2H), 3.53 (t, J = 4.8 Hz, 4H), 3.19 (t, J = 4.8 Hz, 4H), 1.46 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.7, 154.7, 141.4, 136.1, 135.4, 129.0, 127.7, 126.0, 122.1, 121.7, 118.3, 109.4, 80.1, 50.5, 47.6, 43.2, 28.4; FTIR (thin film): cm^{-1} 3070, 2845, 1691, 1520, 1114, 998; HRMS-ESI (m/z) Calcd for ($C_{23}H_{29}N_4O_2$) ($[M+H]^+$): 394.2285; found: 394.2284.

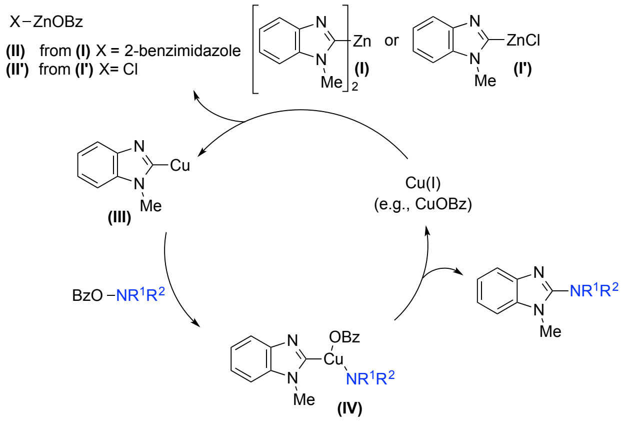


4-(1-Benzyl-1H-benzo[d]imidazol-2-yl)piperazin-1-ium chloride (29). To an 8 mL vial charged with boc-protected amine **28** (89.3 mg, 0.23 mmol, 1.0 equiv) was added Et_2O (2 mL) followed by HCl (2.0 M solution in Et_2O, 1.1 mL, 2.3 mmol, 10 equiv). The reaction was stirred at room temperature. Upon consumption of **28** (monitored by TLC–100% ethyl acetate), the reaction was filtered. The salt was washed with copious amounts of Et_2O. The salt then washed into separate filter flask with MeOH. Filtrate collected and concentrated under reduced pressure giving **29** as a pale yellow solid (73.3 mg, 98%). ^{1}H NMR (D_2O, 400 MHz): δ 7.64–7.62 (m, 1H), 7.51–7.38 (m, 6H), 7.29–7.27 (m, 2H), 5.53 (s, 2H), 3.81 (t, J = 5.2 Hz, 4H), 3.42 (t, J = 5.2 Hz, 4H); ^{13}C NMR (D_2O, 125 MHz): δ 151.8, 133.9, 132.1, 129.9, 129.1, 129.0, 129.8, 126.2, 125.8, 113.5, 112.4, 46.7, 43.1; HRMS-ESI (m/z) Calcd for ($C_{18}H_{21}N_4$) ($[M-HCl]^+$): 293.1761; found: 293.1763.

Supplementary Studies



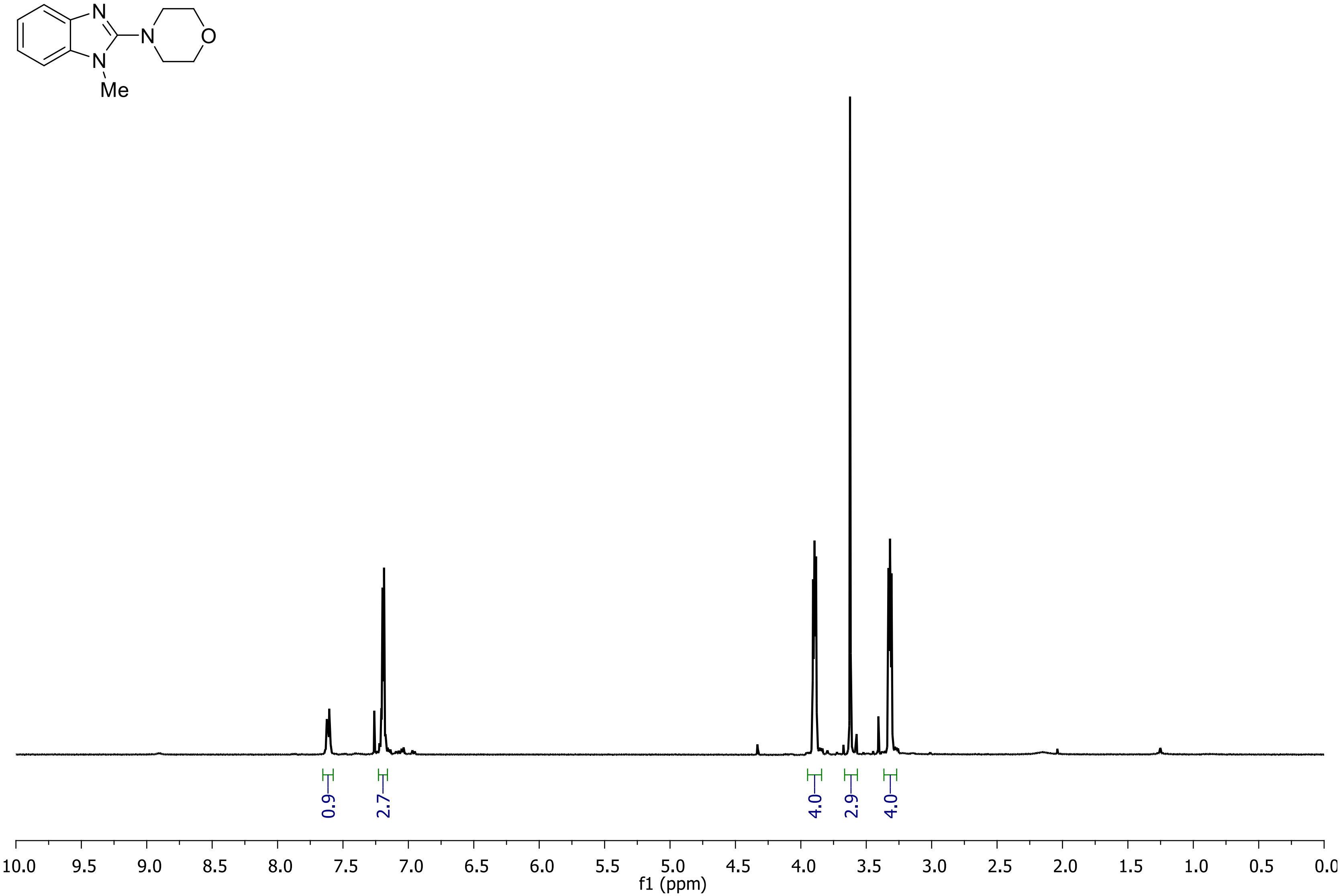
Proposed Reaction Pathway.



Based on current experimental observations and related mechanistic studies,[7] a possible mechanism is proposed for this copper-catalyzed amination reaction as above. It involves (1) the transmetalation of the pre-formed organozinc intermediate either diarylzinc **(I)** or monoarylzinc chloride **(I')** with a Cu(I) catalyst [upon initial reduction when Cu(II) catalyst was used] to form the aryl copper complex **(III)**, (2) an oxidative addition with *O*-benzoylhydroxylamine to form a high-valent copper species **(IV)**, and (3) reductive elimination to form the C−N bond and regenerate the copper catalyst. In addition, the results from eq. 2 and eq. 3 suggest that benzoyloxyarylzinc intermediate **(II)** is unable to undergo effective transmetalation under the current conditions. It should be noted that the detailed mechanism for C−N bond formation still remains obscure. For example, we cannot exclude an alternative that involves (1) oxidative addition of the hydroxylamine to the copper (I) species, (2) transmetalation with an organozinc intermediate, and (3) reductive elimination to form a C−N bond. Further studies toward understanding this process will be performed.

Reference:

1. (a) A. Unsinn, M. J. Ford, P. Knochel *Org. Lett.* **2013**, *15*, 1128; (b) A.M. Berman, J. S. Johnson *J. Am. Chem. Soc.* **2004**, *126*, 5680. (c) A. M. Berman, J. S. Johnson *J. Org. Chem.* **2006**, *71*, 219.
2. M. W. Hooper, M. Utsunomiya, J. F. Hartwig *J. Org. Chem* **2003**, *68*, 2861.
3. M. Kienle, C. Dunst, P. Knochel *Org. Lett.* **2009**, *11*, 5158.
4. M. Kienle, A. J. Wagner, C. Dunst, P. Knochel *Chem. Asian J.* **2011**, *6*, 517.
5. M. Kienle, C. Dunst, P. Knochel *Org. Lett.* **2009**, *11*, 5158.
6. W. Ge, B. Wu, W. Huang, *Huaxue Xuebao* **1985**, *43*, 859.
7. (a) M. J. Campbell, J. S. Johnson *Org. Lett.* **2007**, *9*, 1521. (b) N. Matsuda, K. Hirano, T. Satoh, M. Miura *Org. Lett.* **2011**, *13*, 2860.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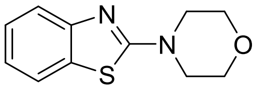
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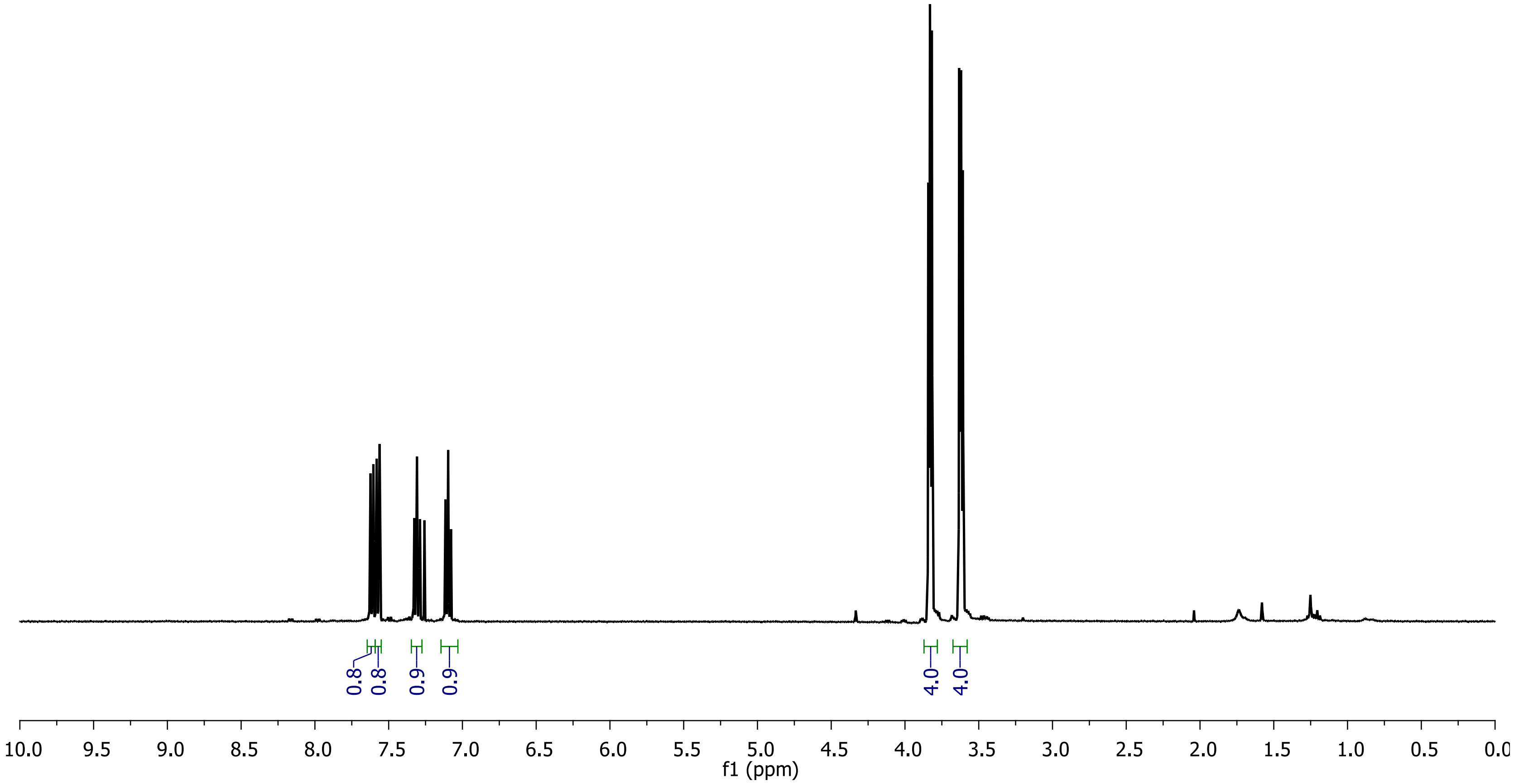
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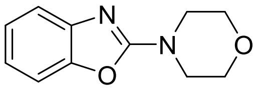
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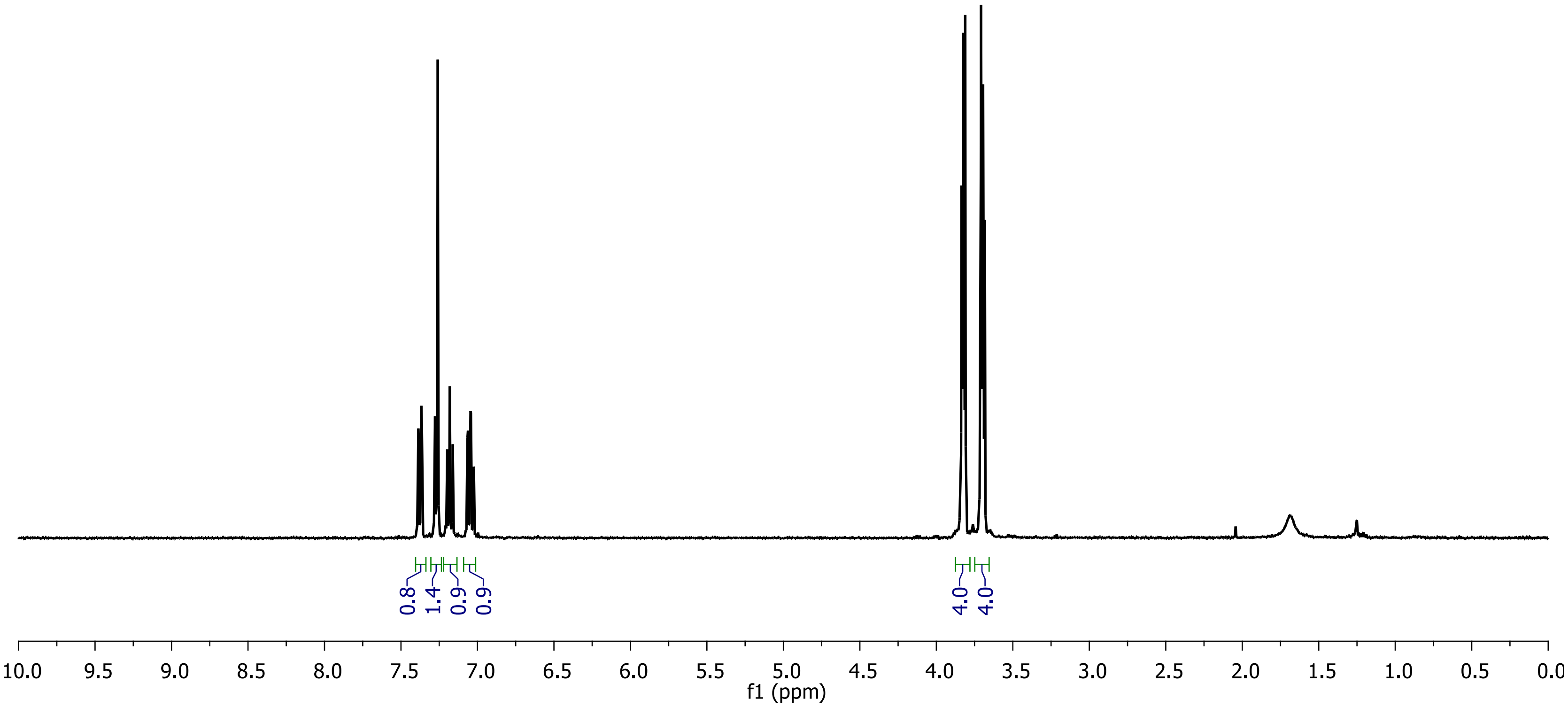
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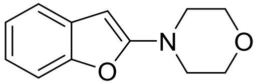
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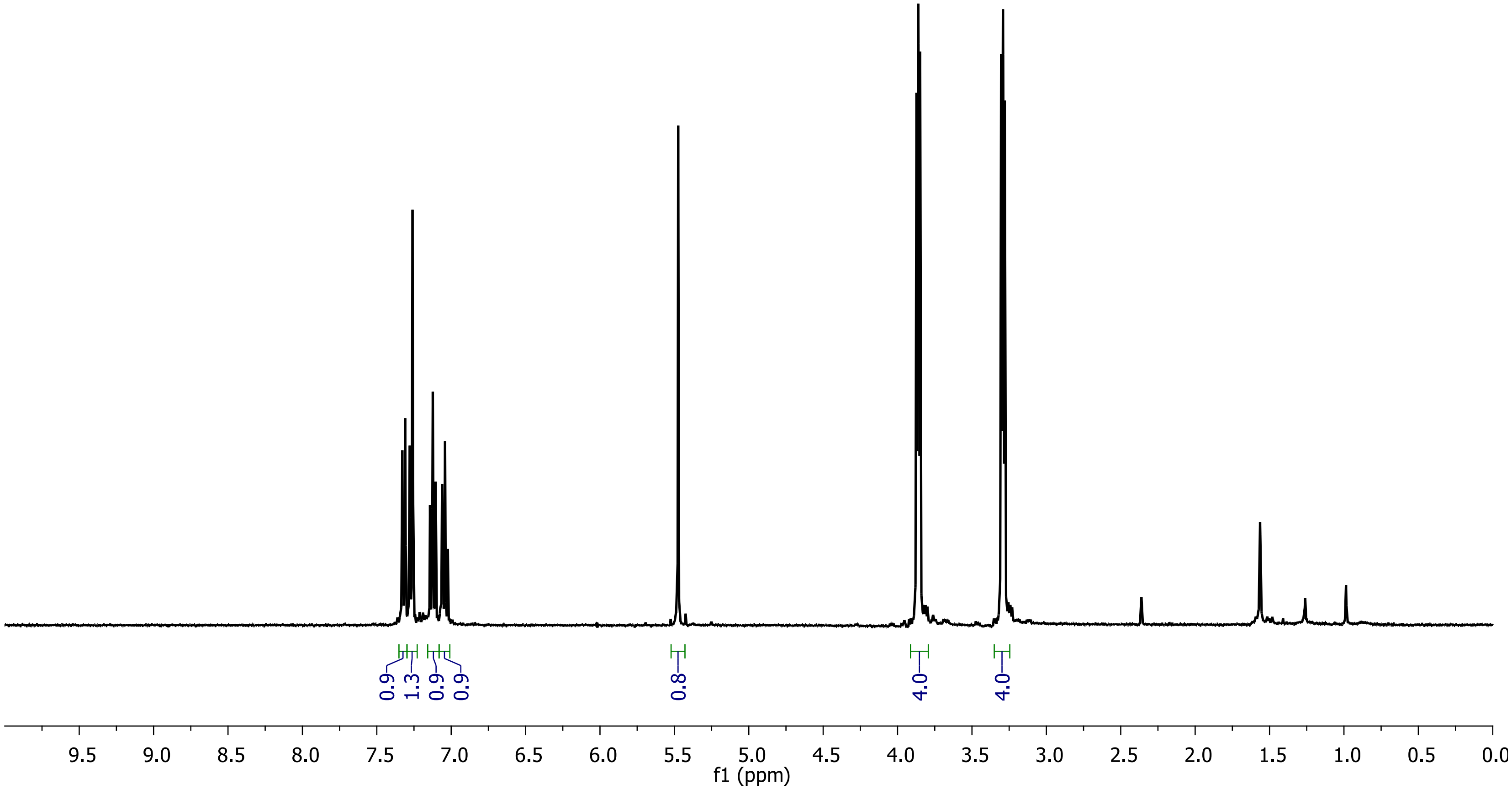
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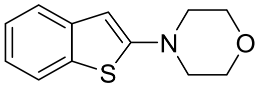
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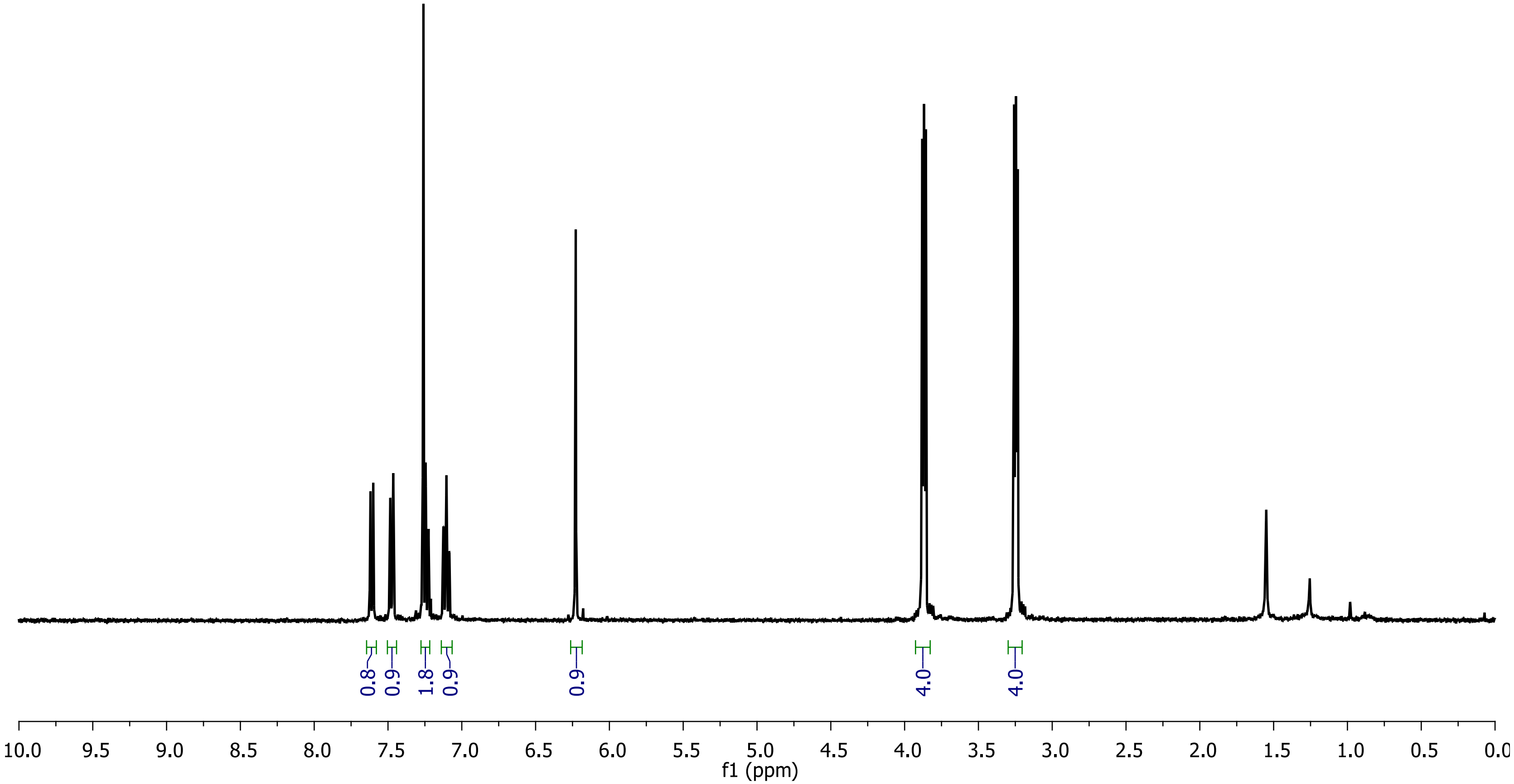
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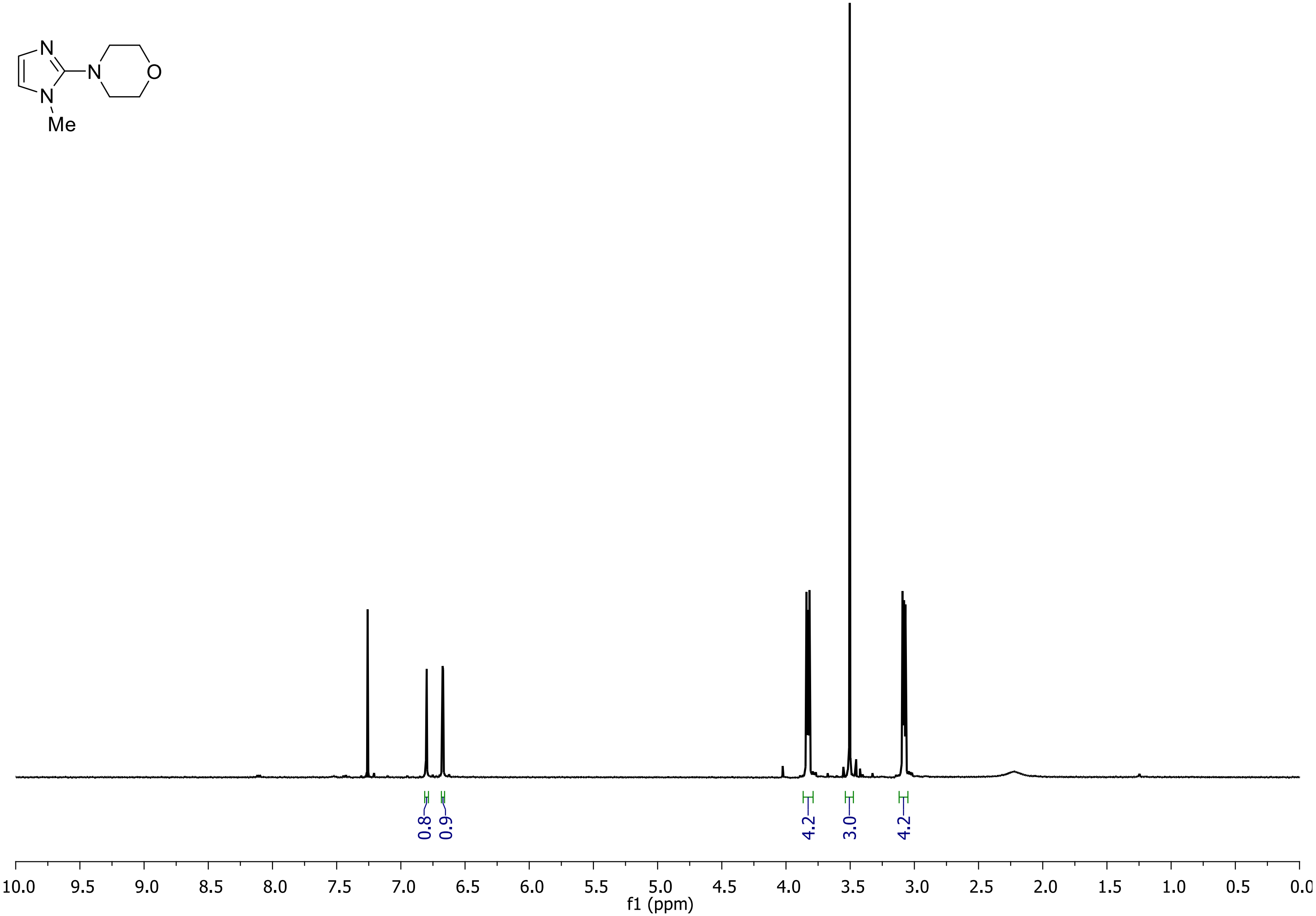
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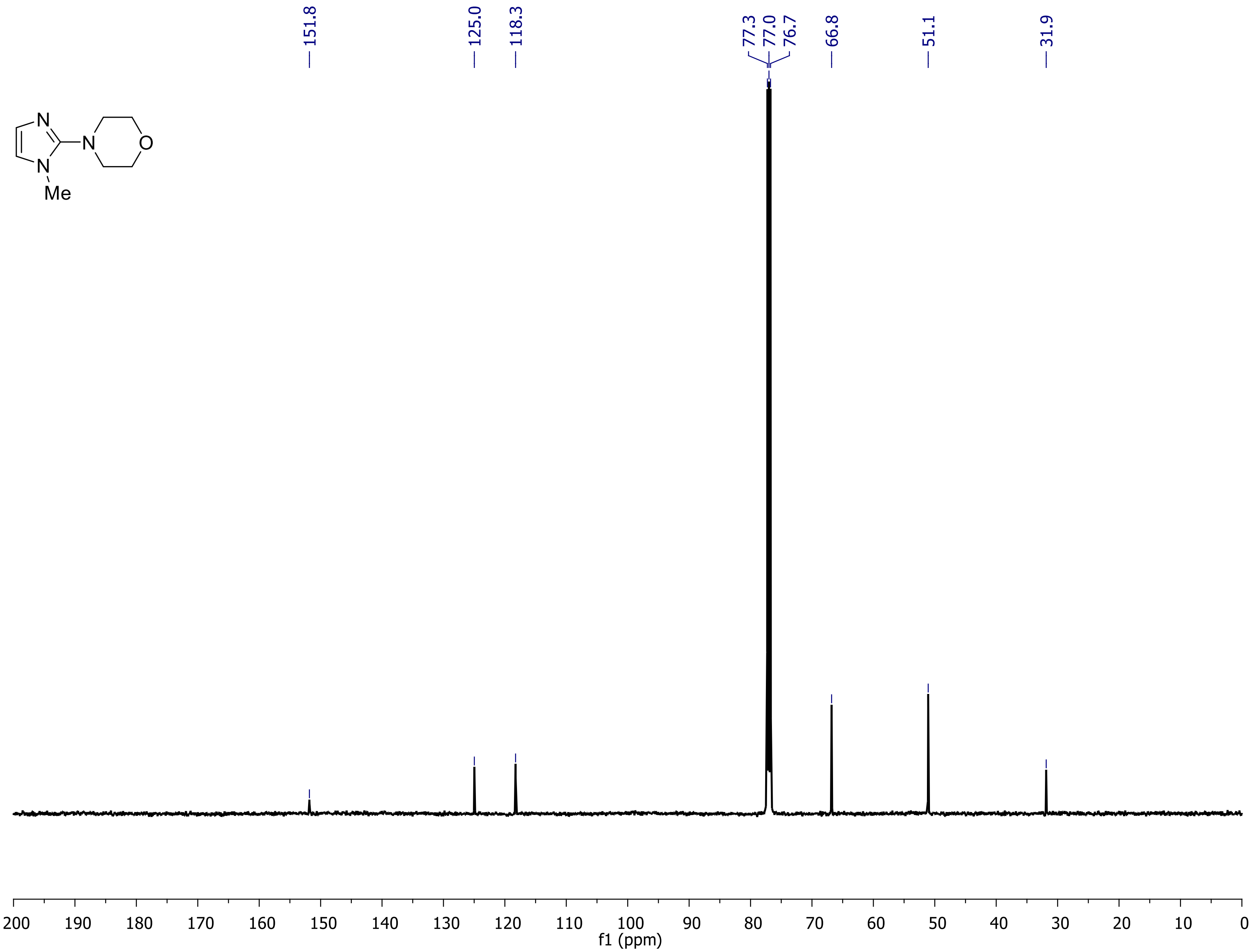151.8
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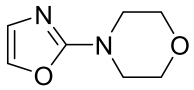

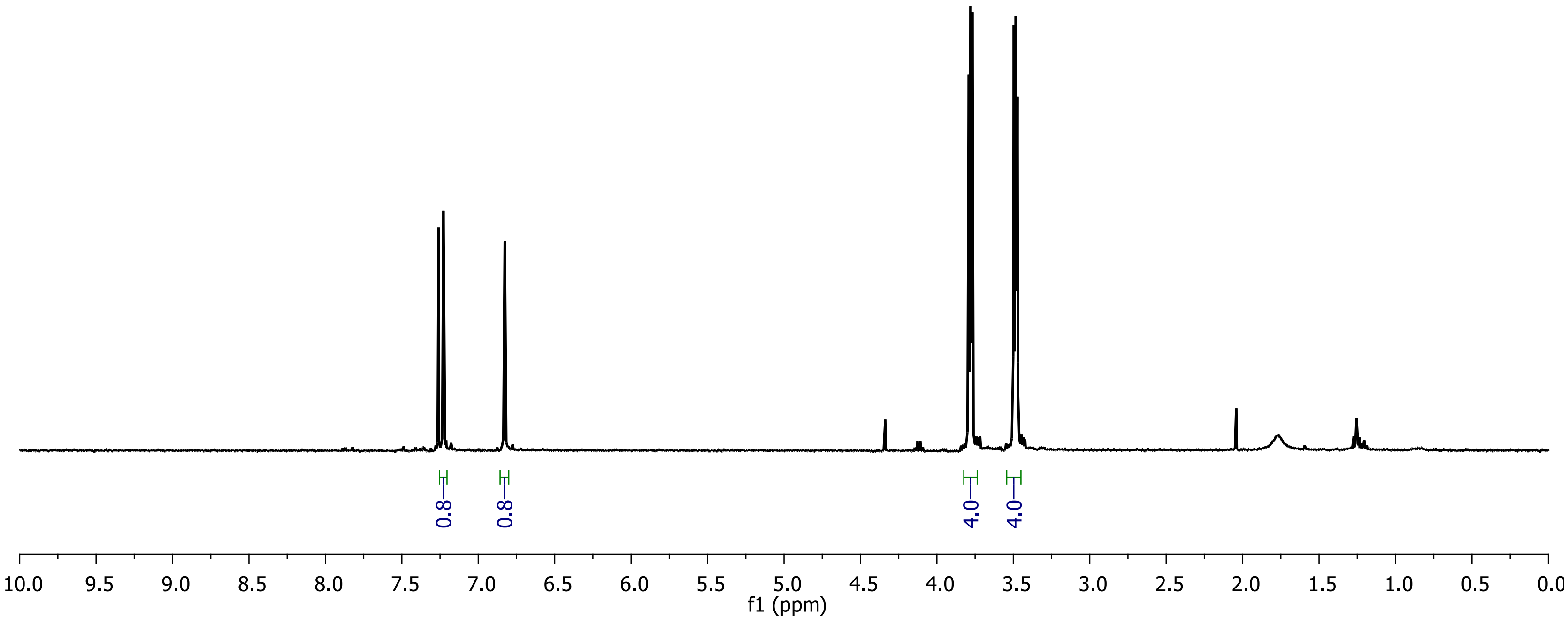
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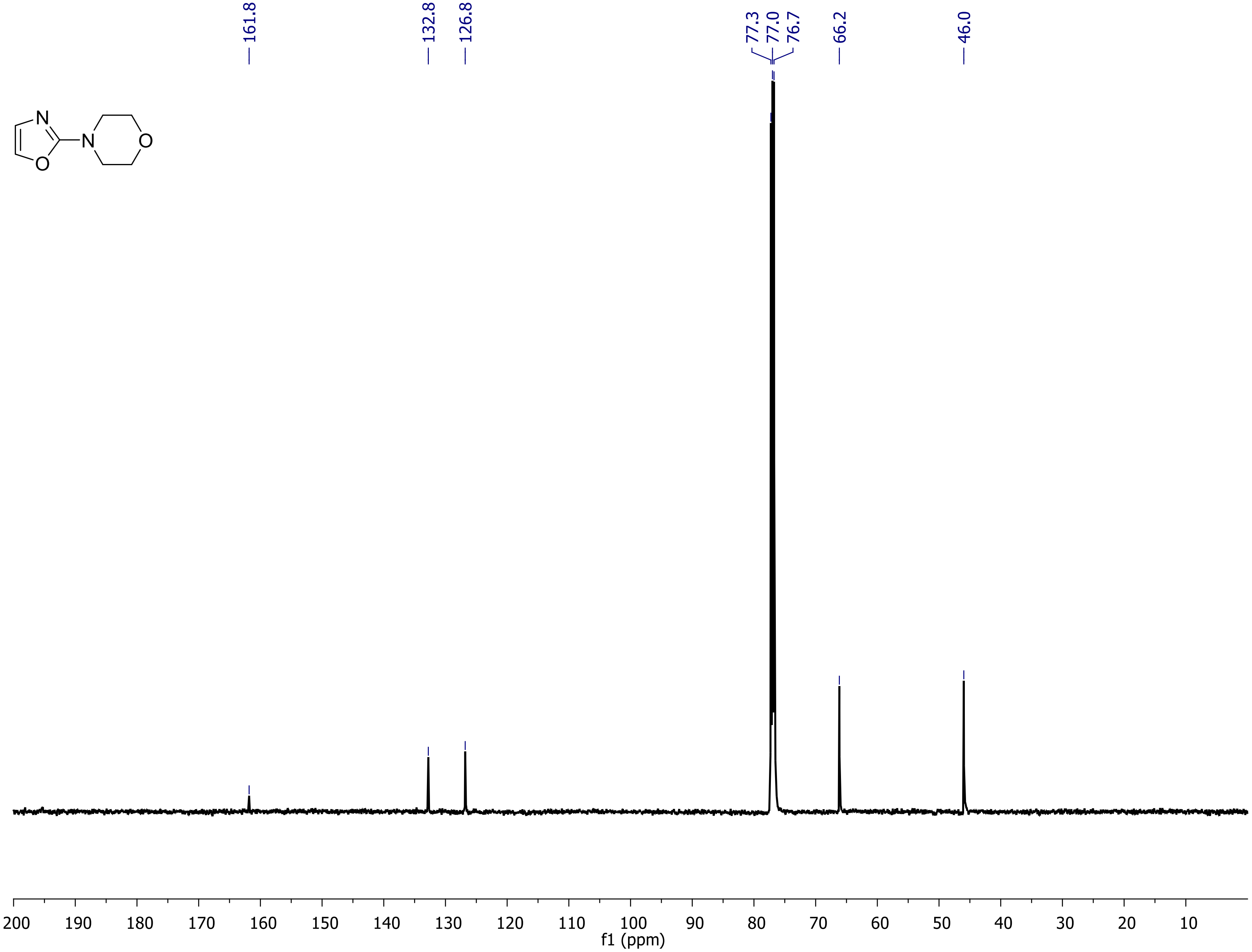
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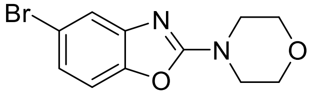
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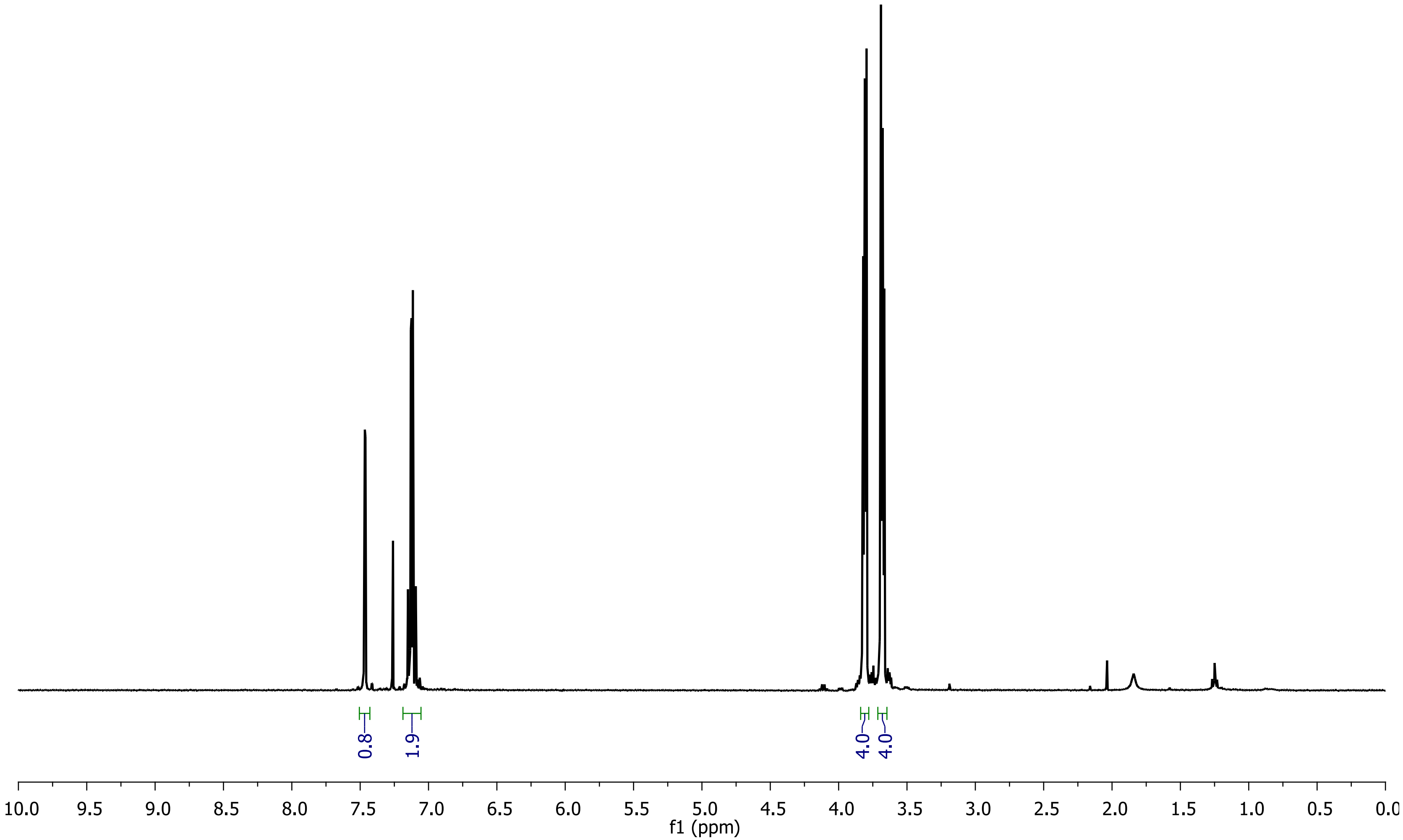
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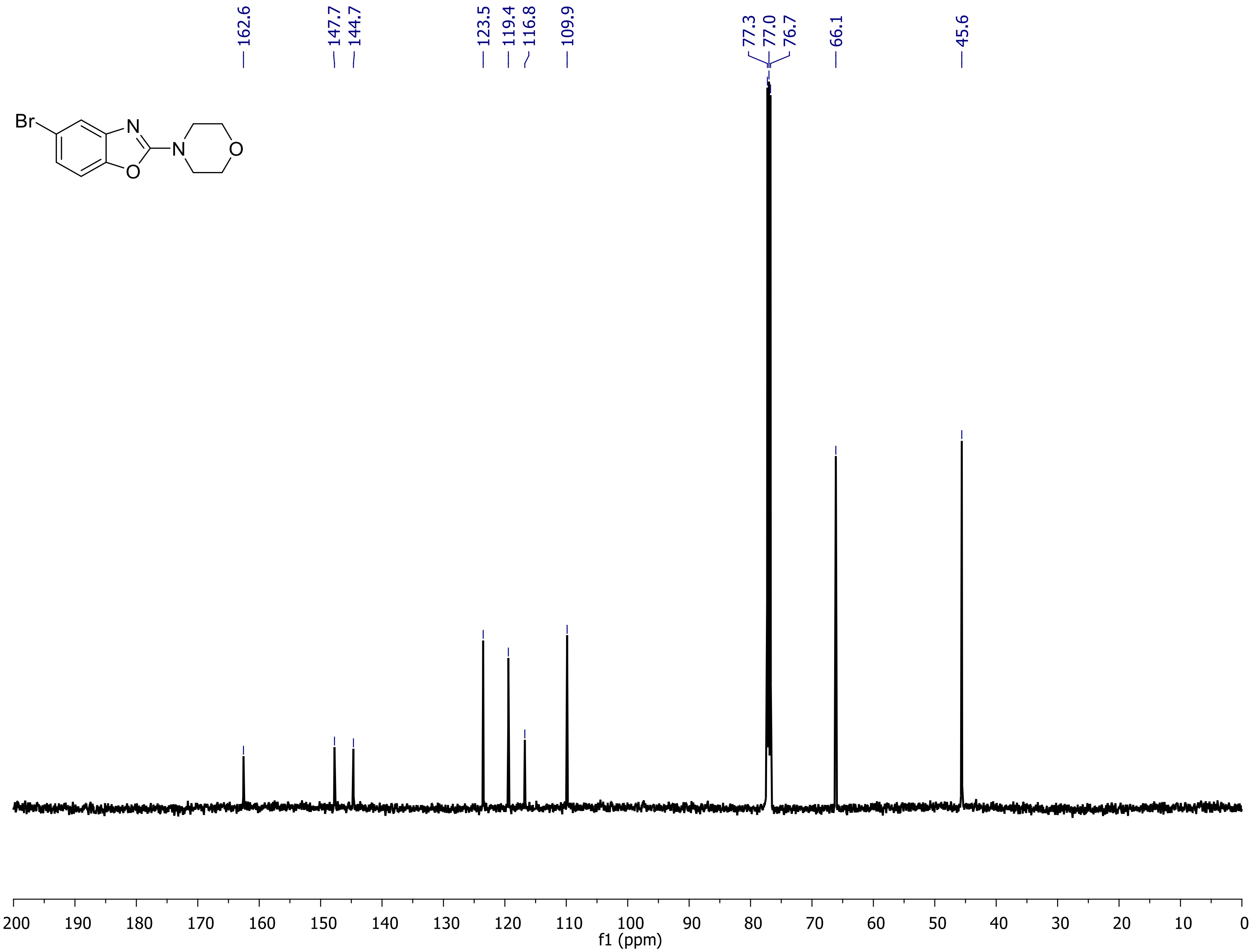
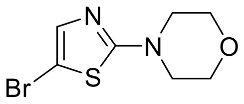
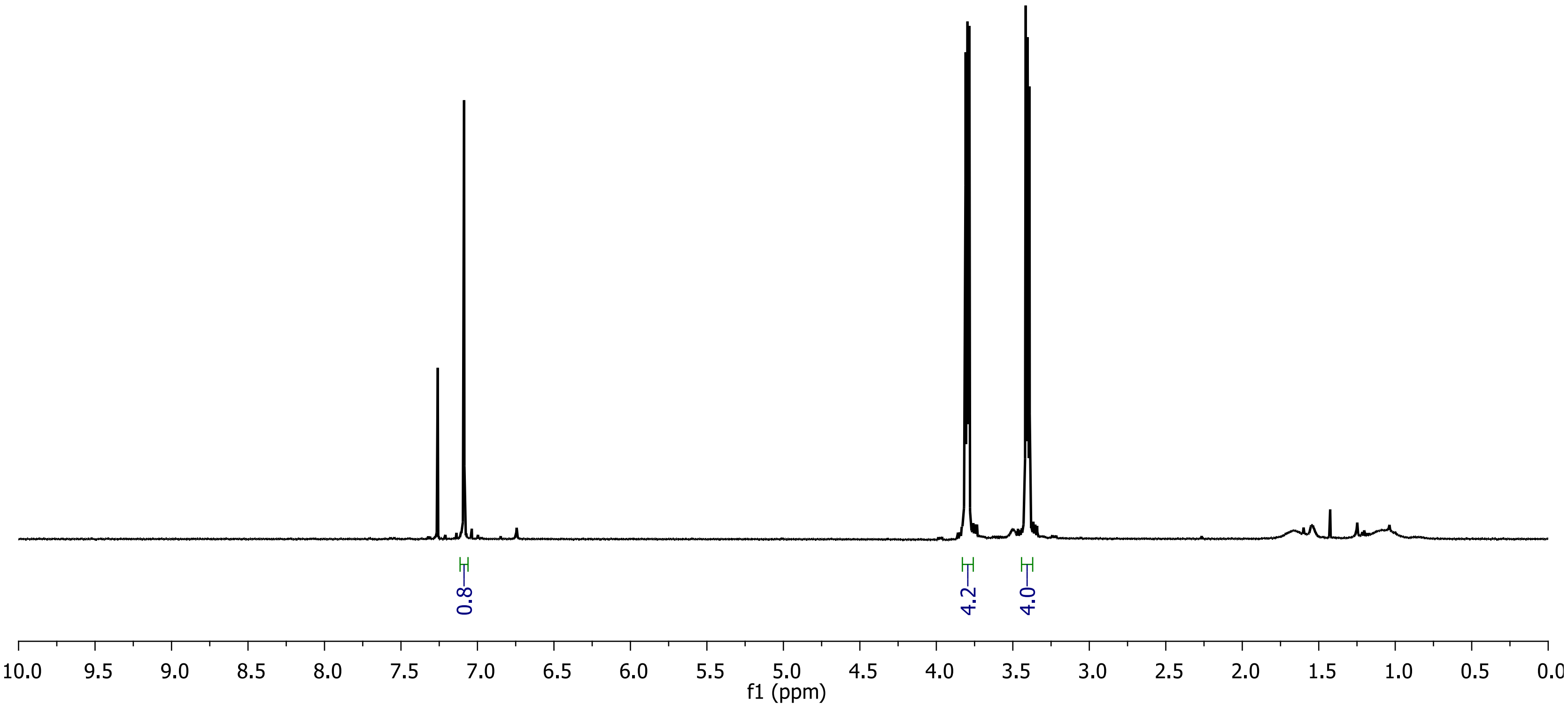
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.6
147.7
144.7
123.5
119.4
116.8
109.9
77.3
77.0
76.7
66.1
45.6
Br
N
O
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
O
N
Br
S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4.2
4.0
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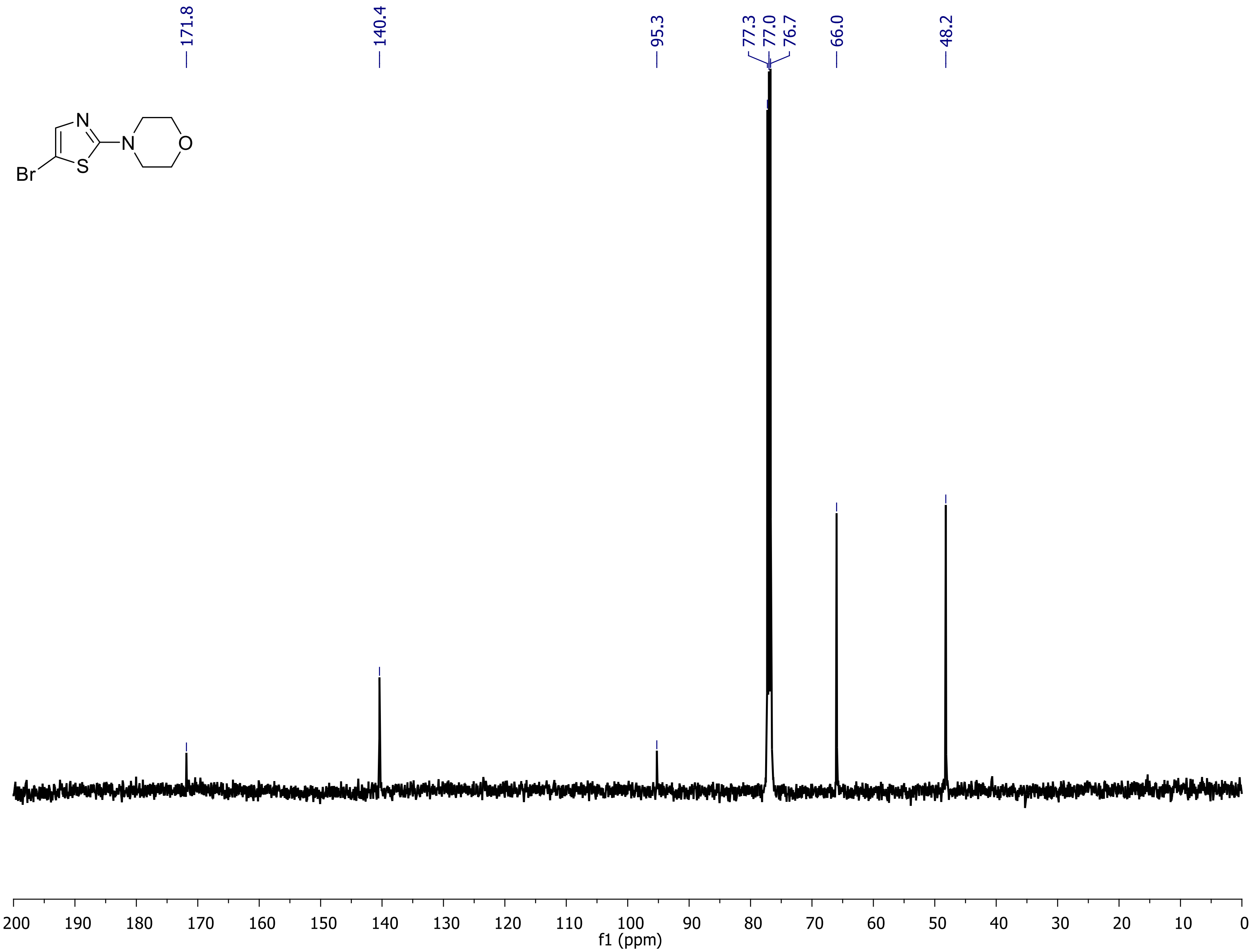
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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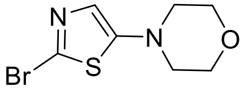
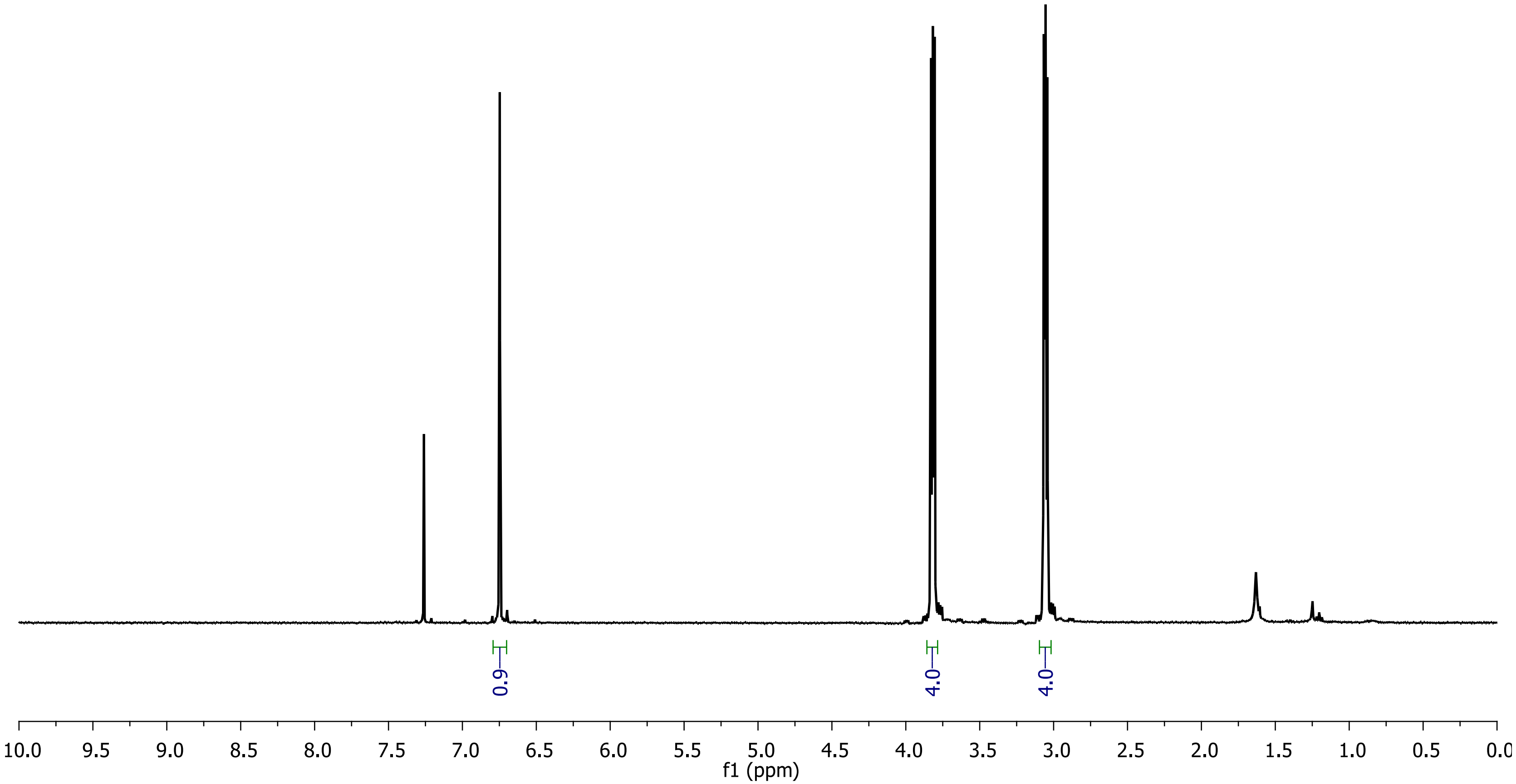
95.3
77.3
77.0
76.7
66.0
48.2
N
N
O
S
Br
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
O
Br
S


0.9
4.0
4.0
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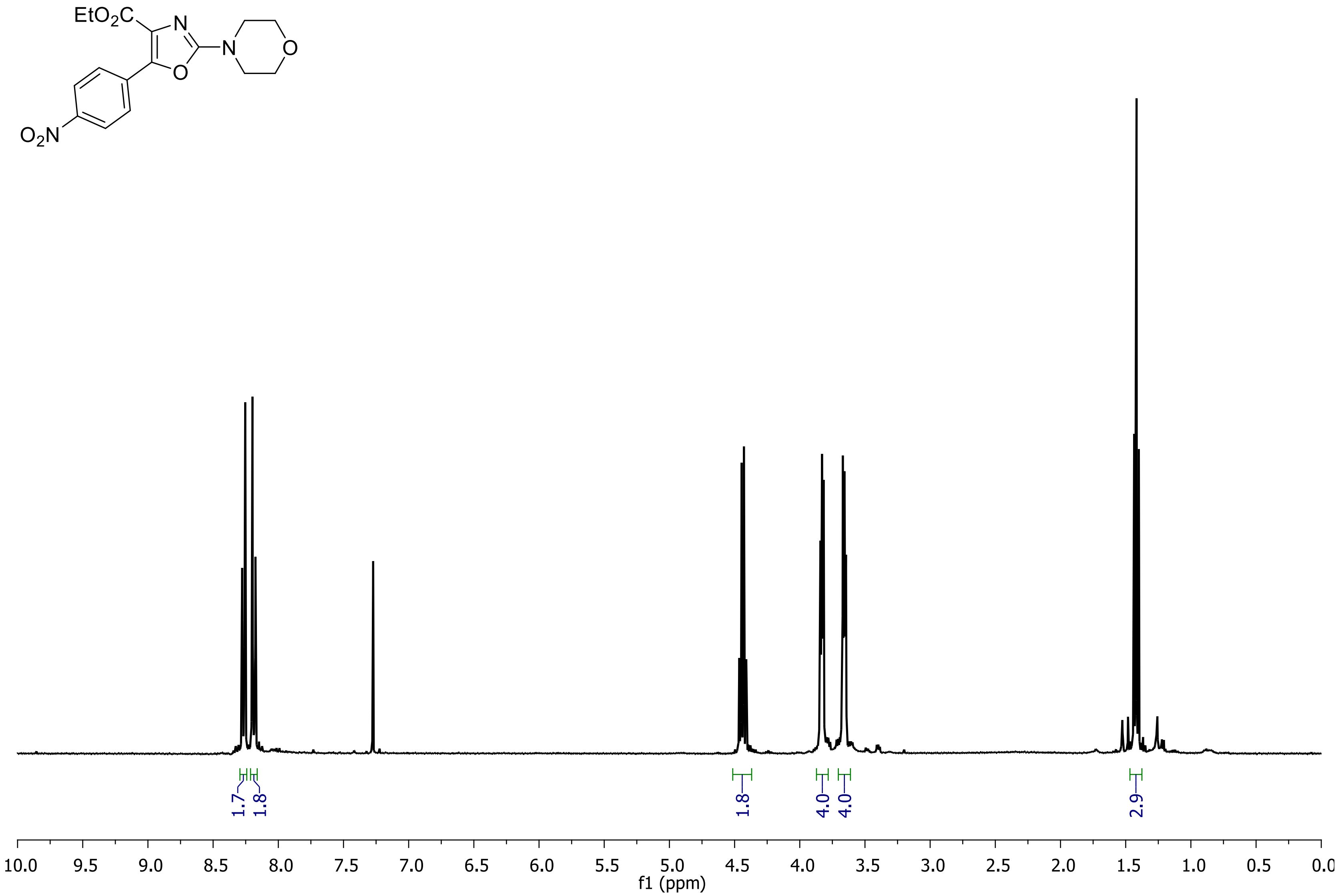
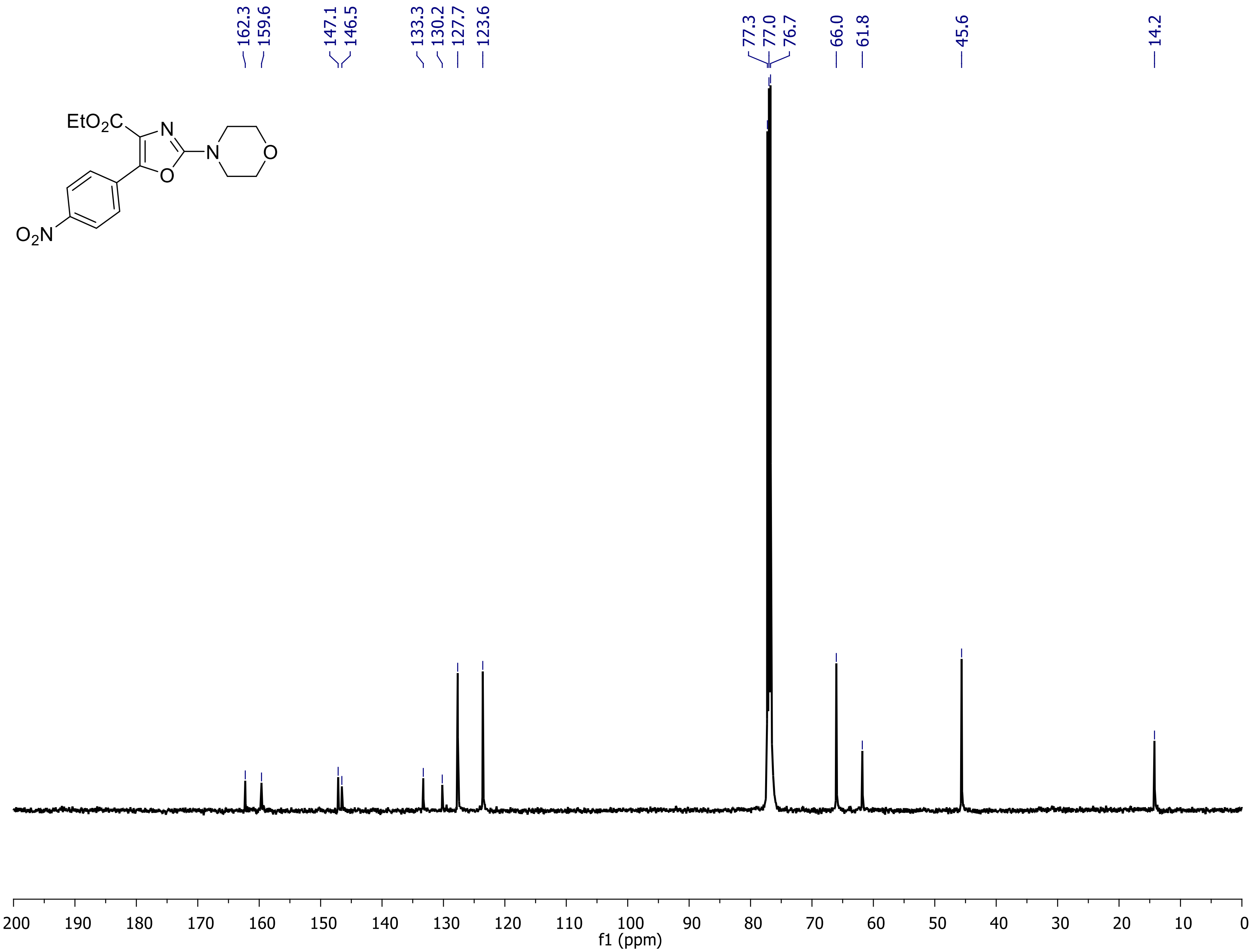
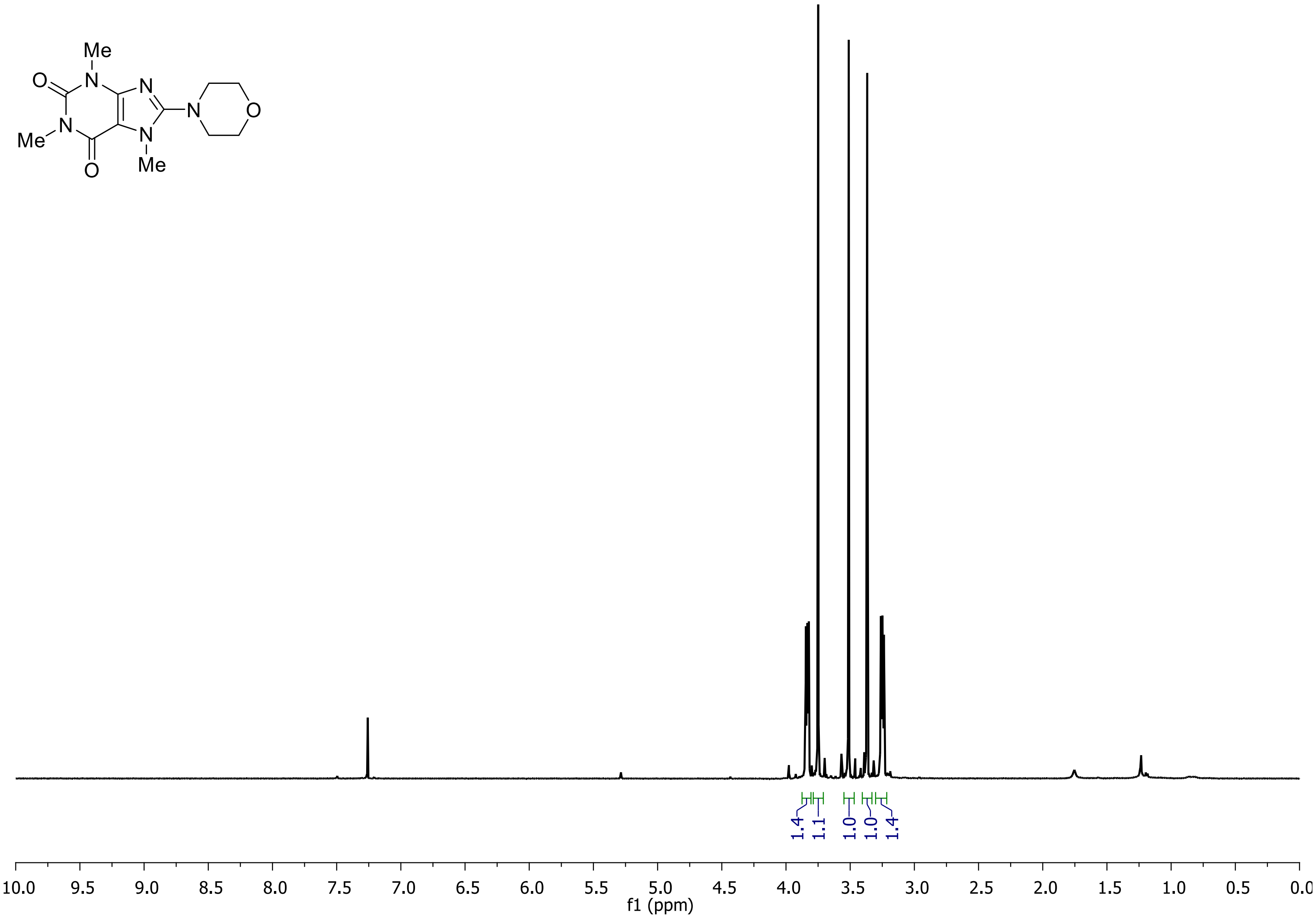
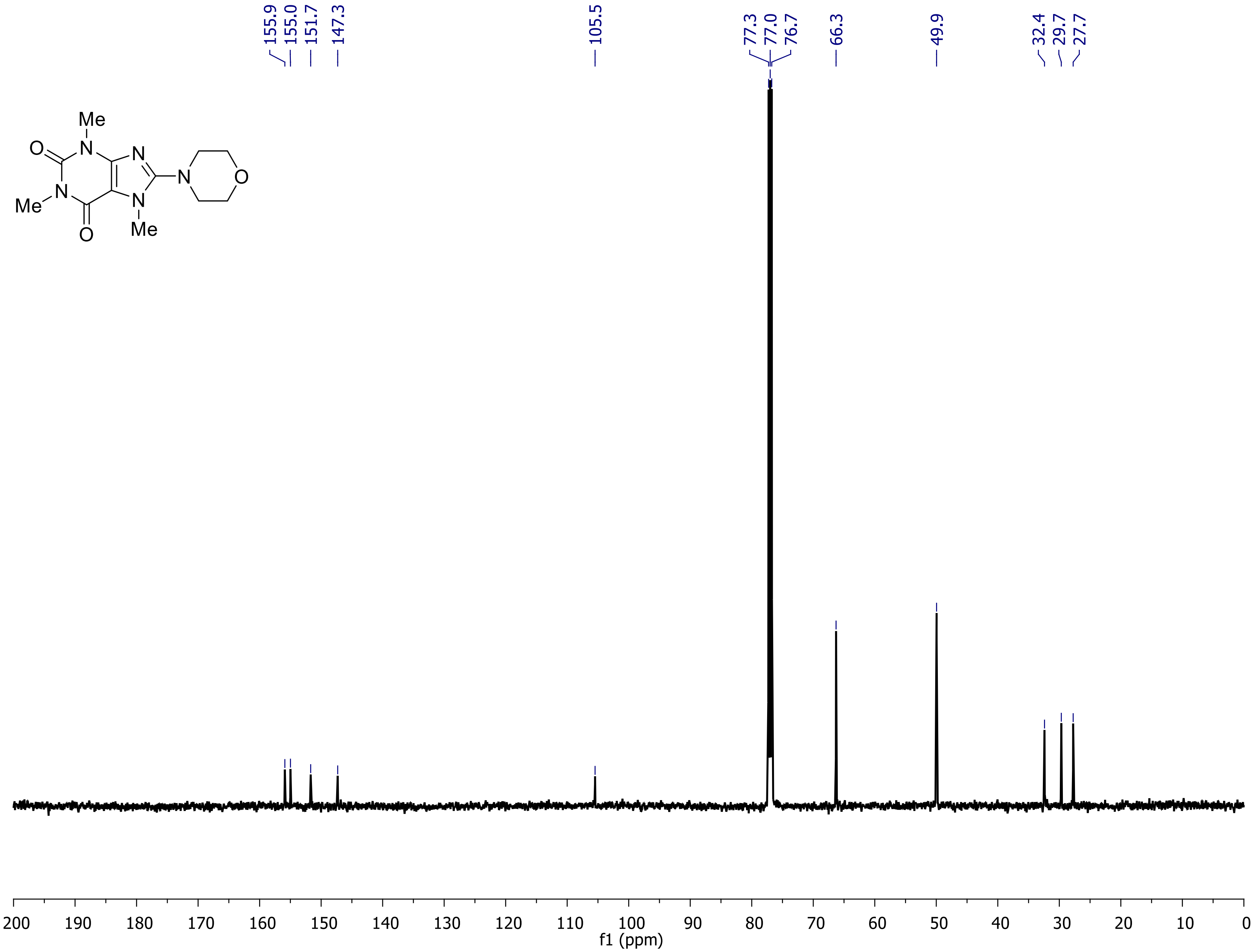
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

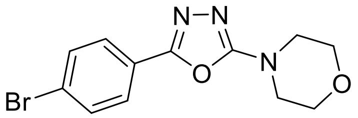

EtO$_2$C
N
O
N
O
O$_2$N
1.7
1.8
1.8
4.0
4.0
2.9
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

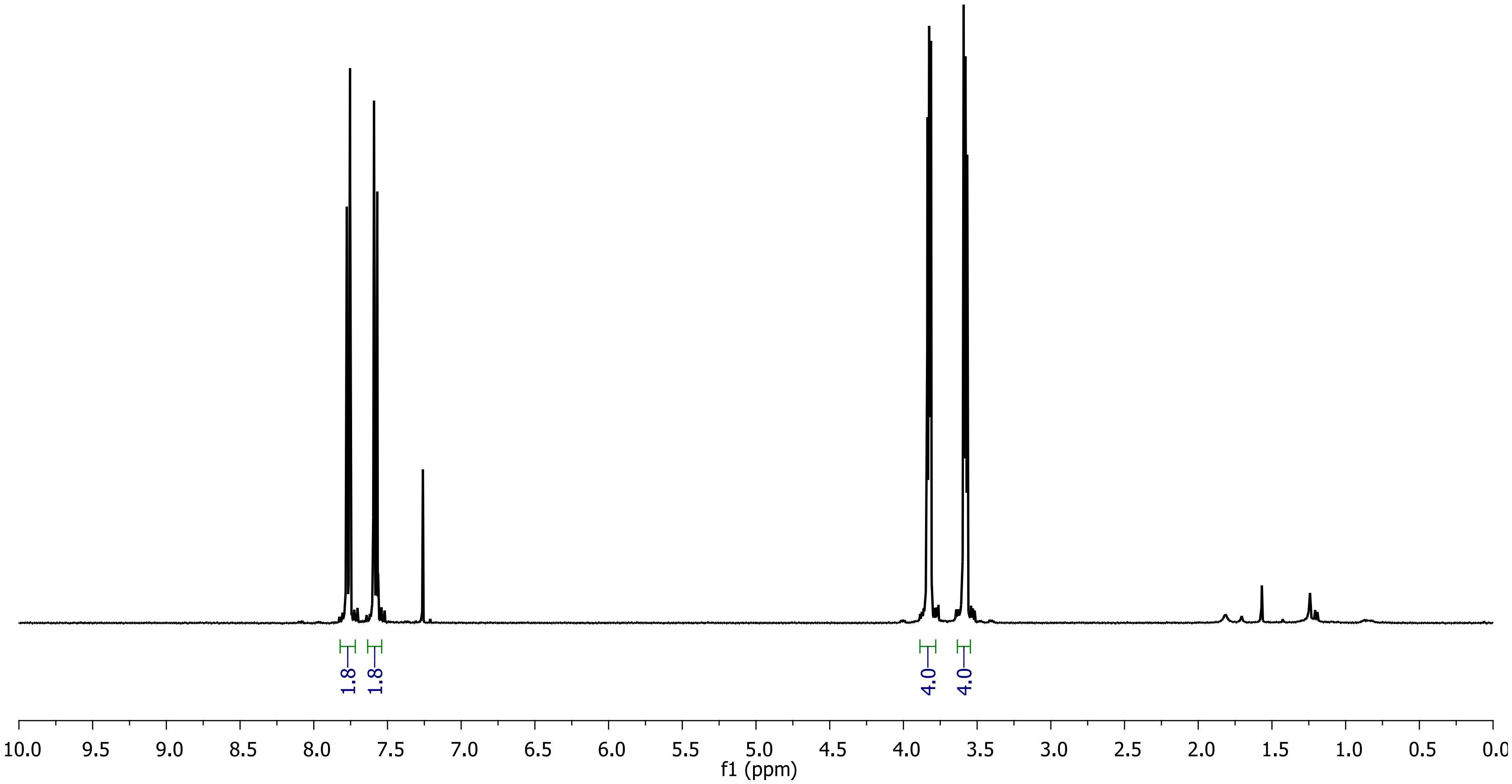

162.3
159.6
147.1
146.5
133.3
130.2
127.7
123.6
77.3
77.0
76.7
66.0
61.8
45.6
14.2
EtO2C
N
O
N
O
O2N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

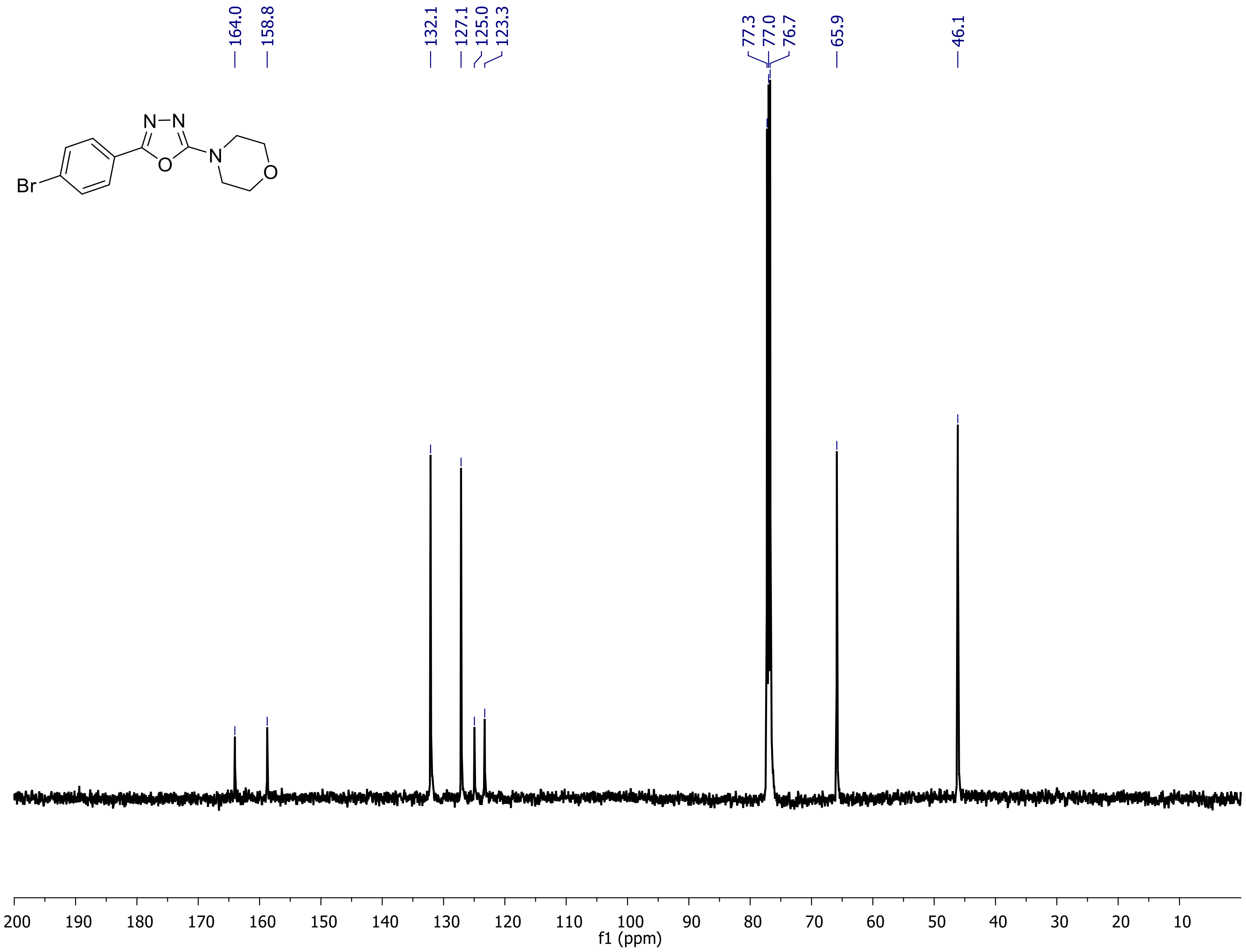


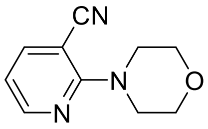
Me
O
N
N
N
O
Me
N
O
N
Me
1.4
1.1
1.0
1.0
1.4
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

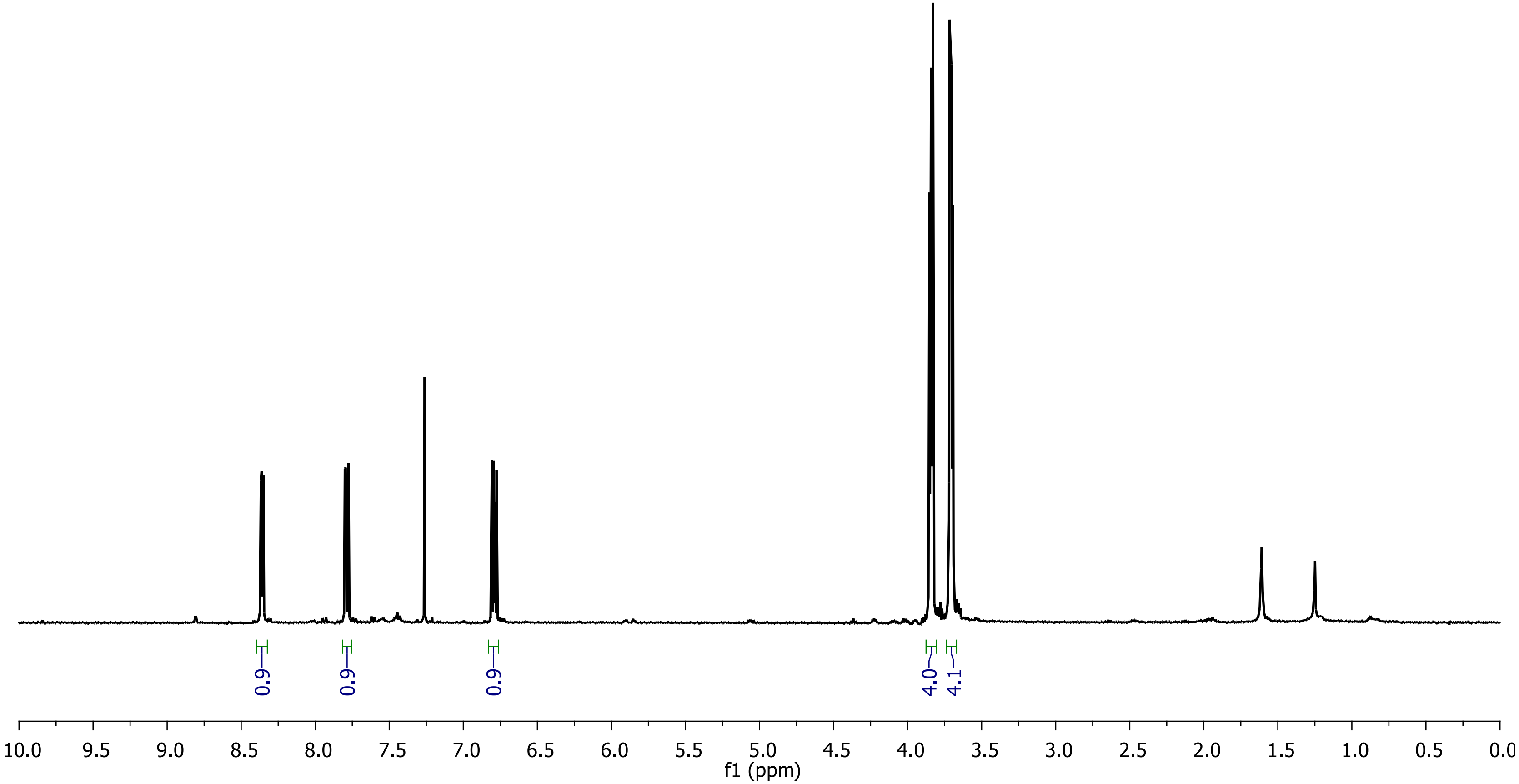

155.9
155.0
151.7
147.3
105.5
77.3
77.0
76.7
66.3
49.9
32.4
29.7
27.7
Me
O
N
N
N
N
O
Me
O
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

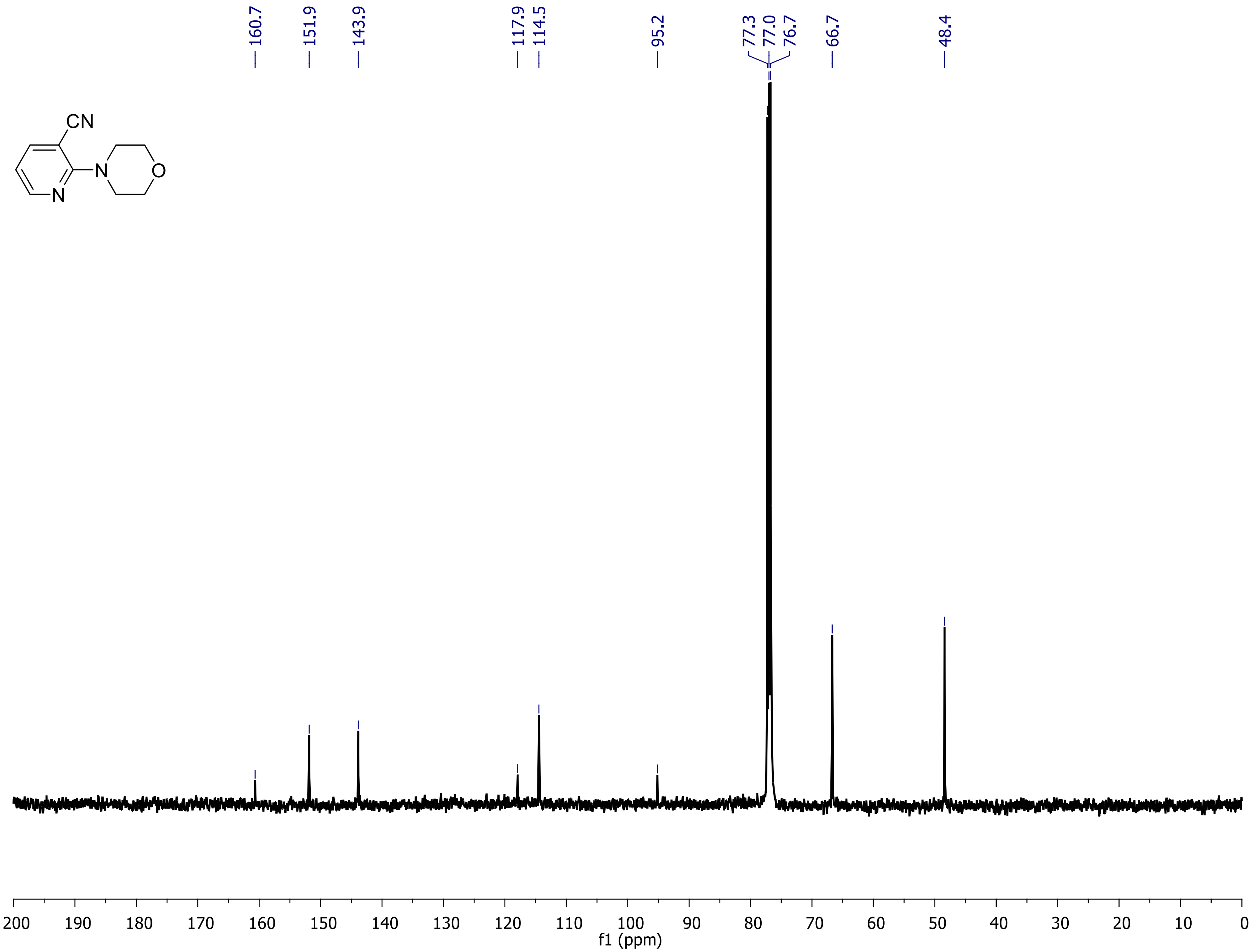

N–N
O
N
O
Br

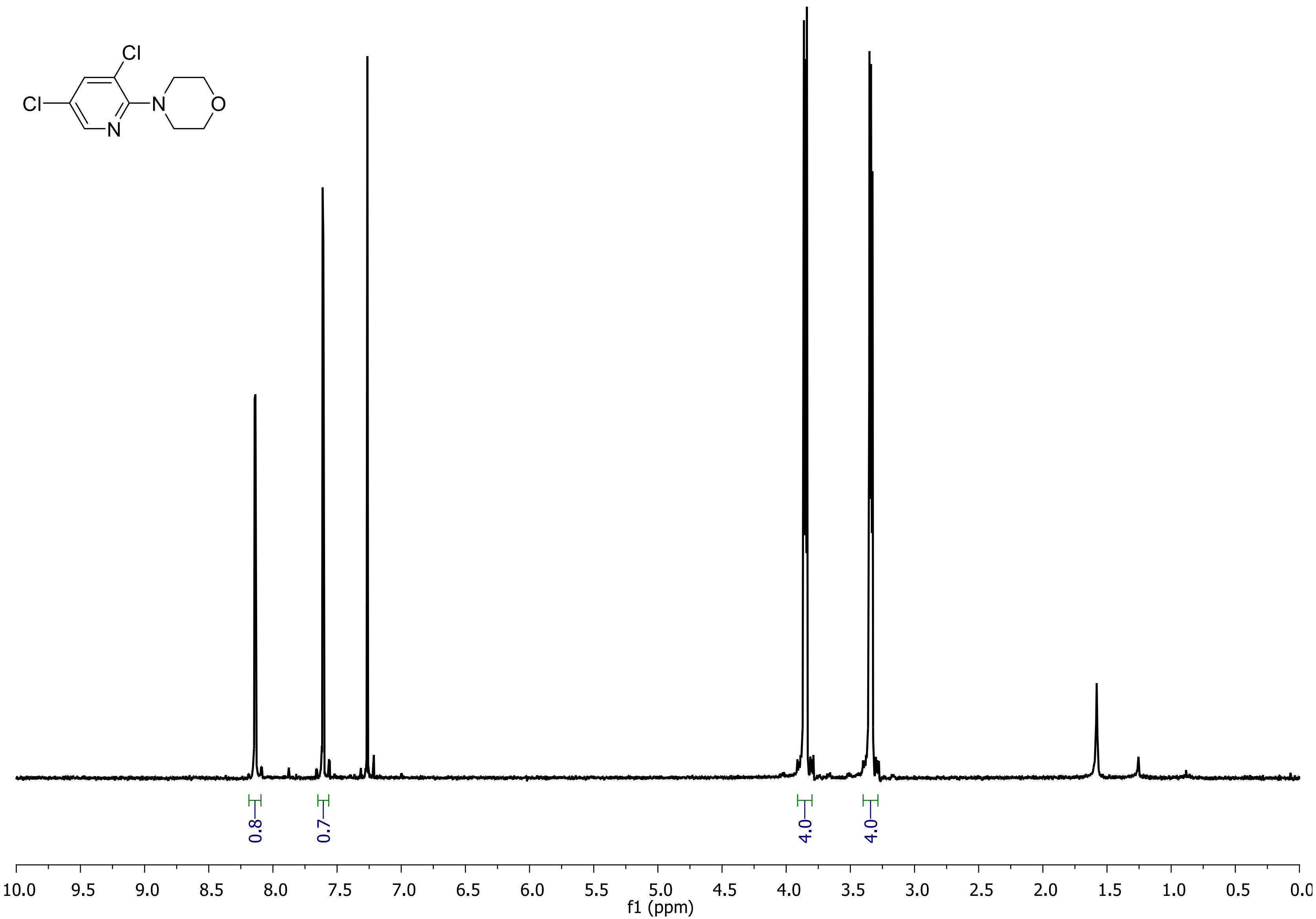

1.8
1.8
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

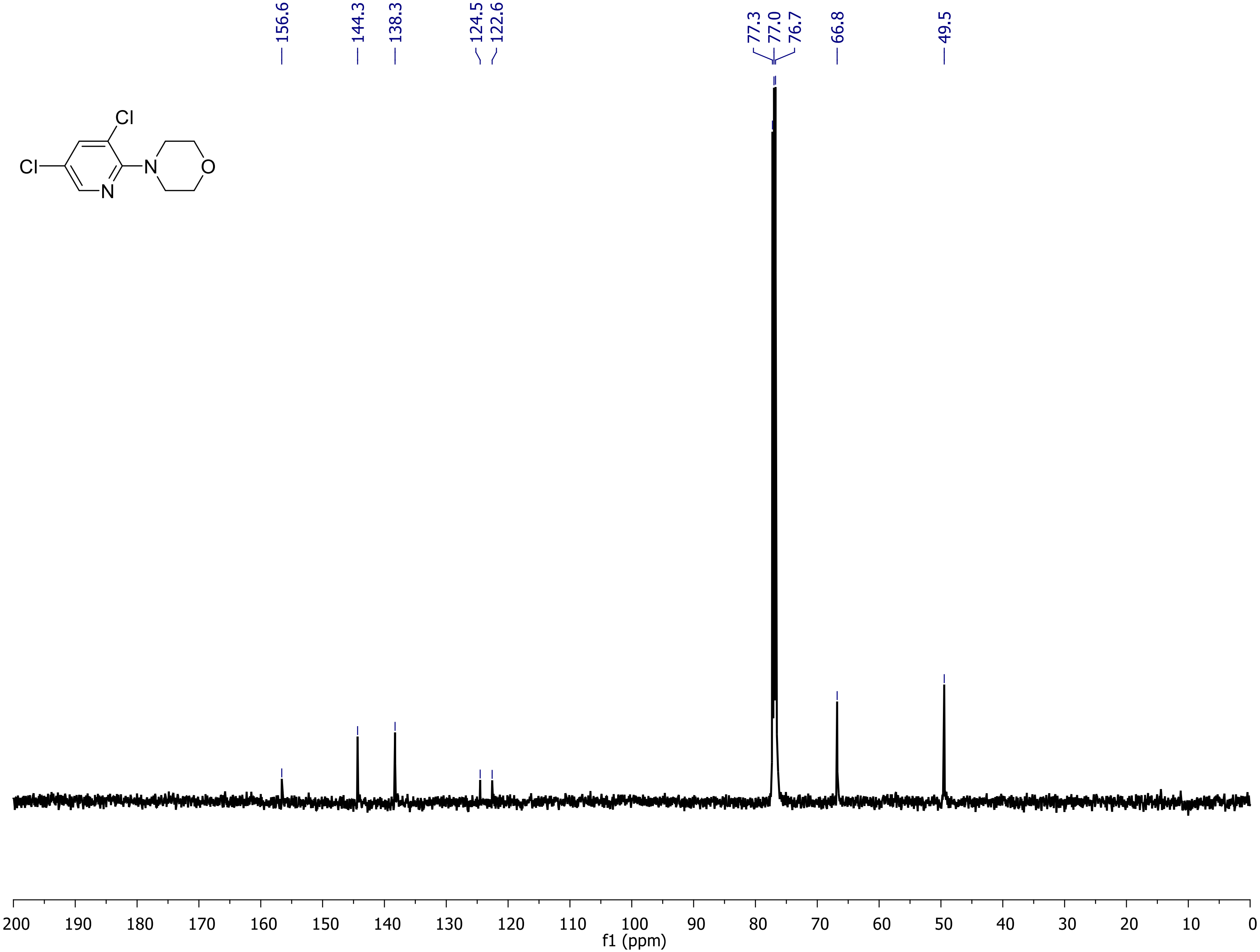

164.0
158.8
132.1
127.1
125.0
123.3
77.3
77.0
76.7
65.9
46.1
Br
N–N
O
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

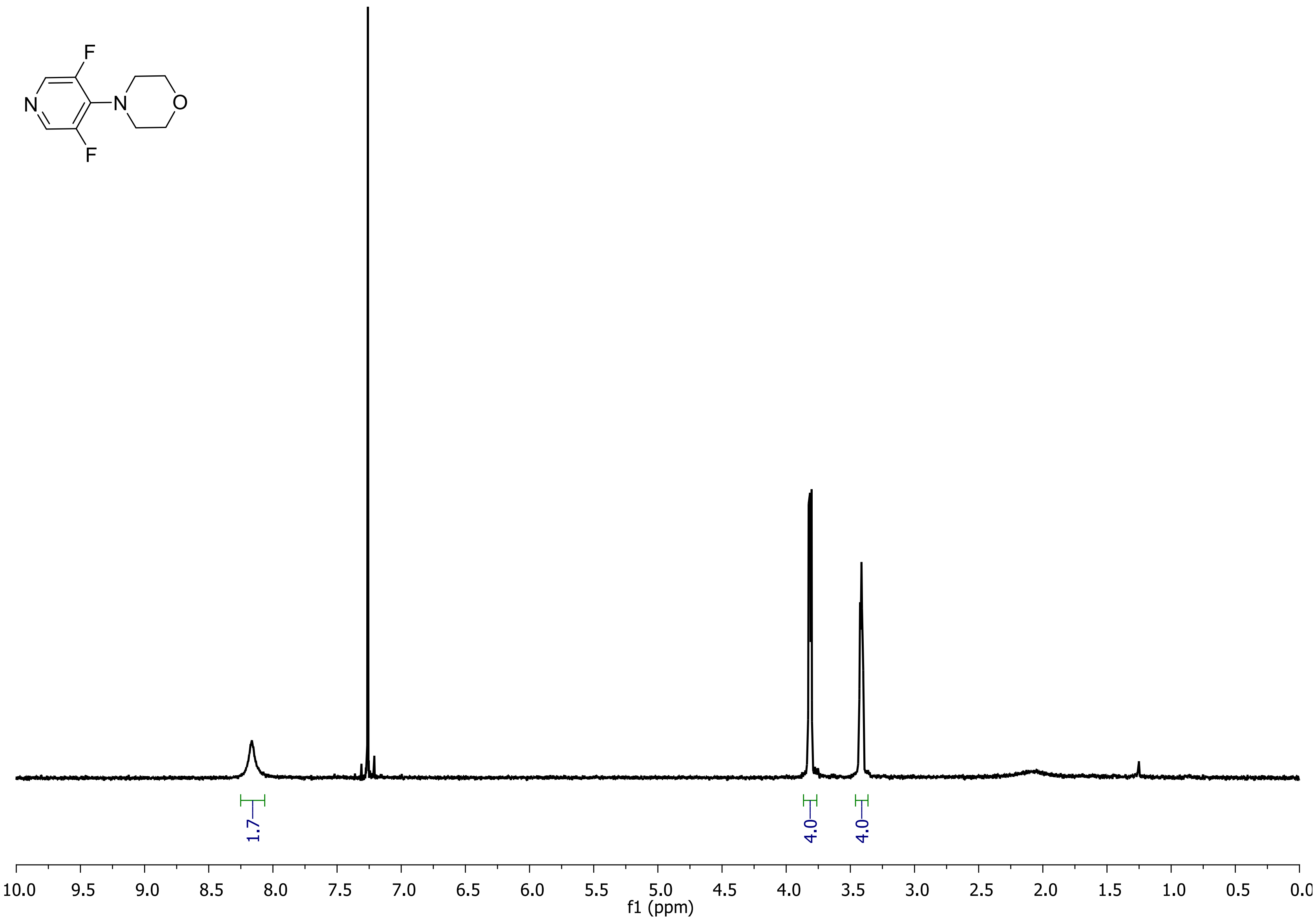

CN
N
O
N

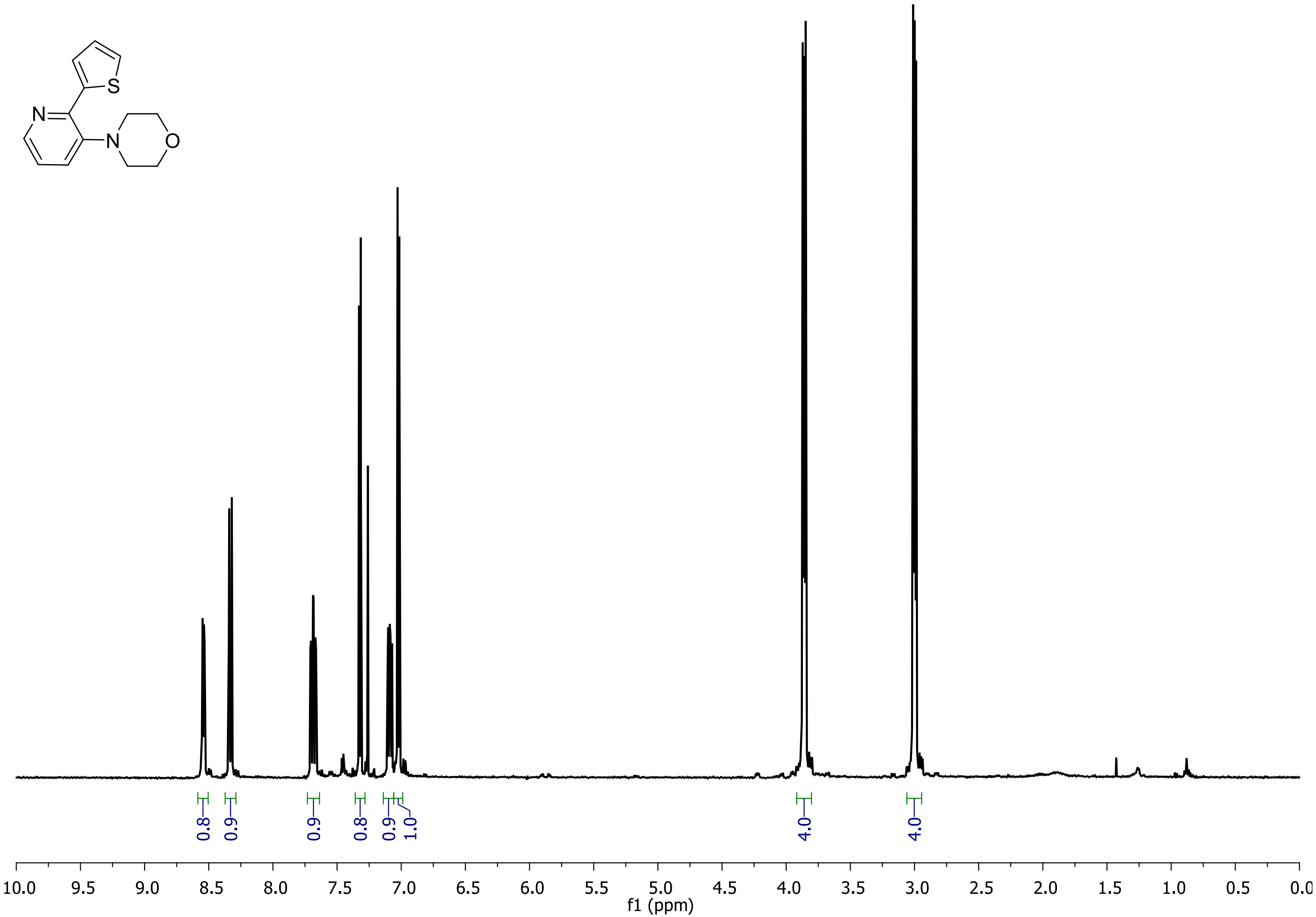

0.9
0.9
0.9
4.0
4.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

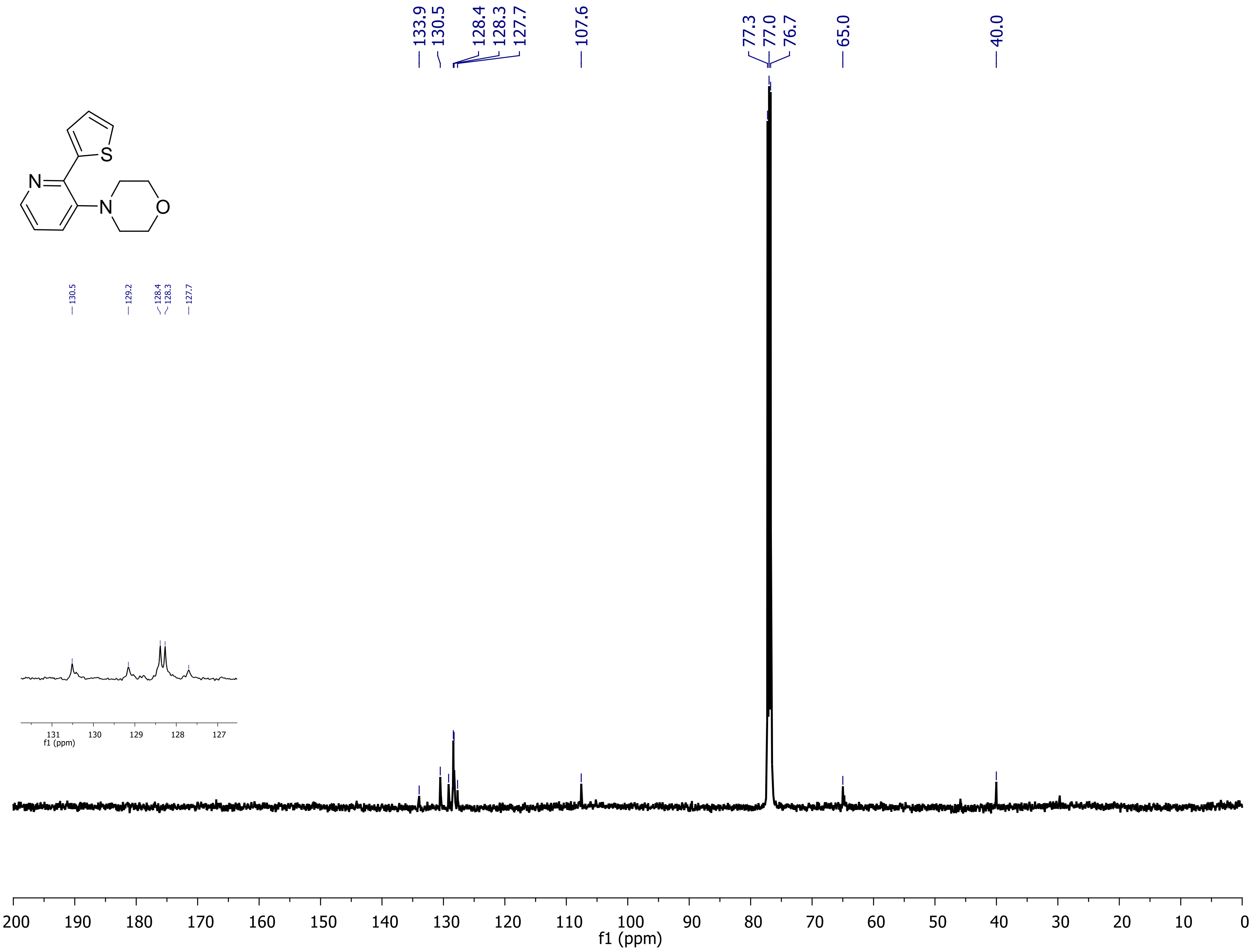

160.7
151.9
143.9
117.9
114.5
95.2
77.3
77.0
76.7
66.7
48.4
CN
N
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

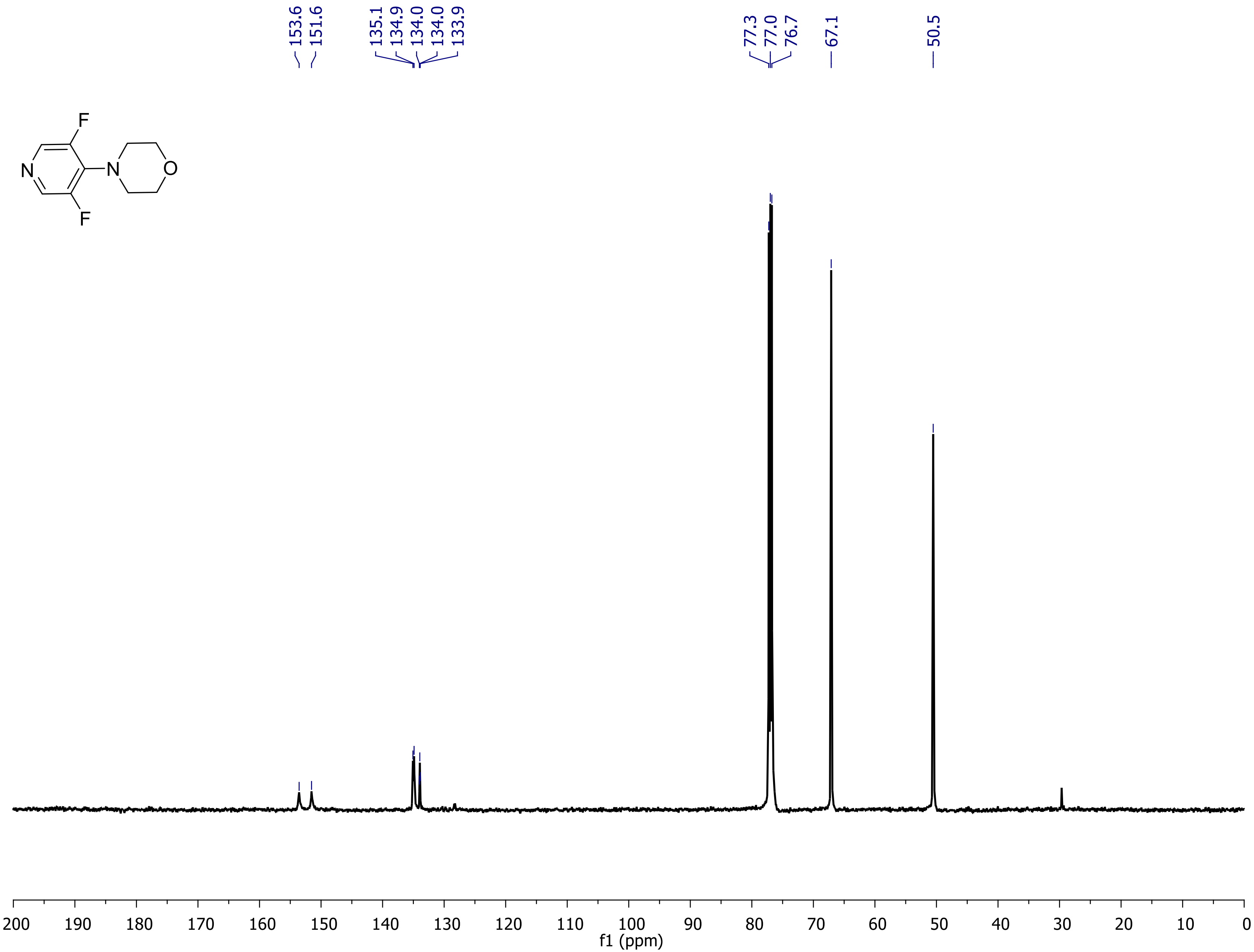

Cl
Cl
N
N
O
0.8
0.7
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

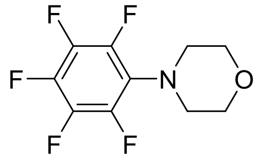

156.6
144.3
138.3
124.5
122.6
77.3
77.0
76.7
66.8
49.5
Cl
Cl
N
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

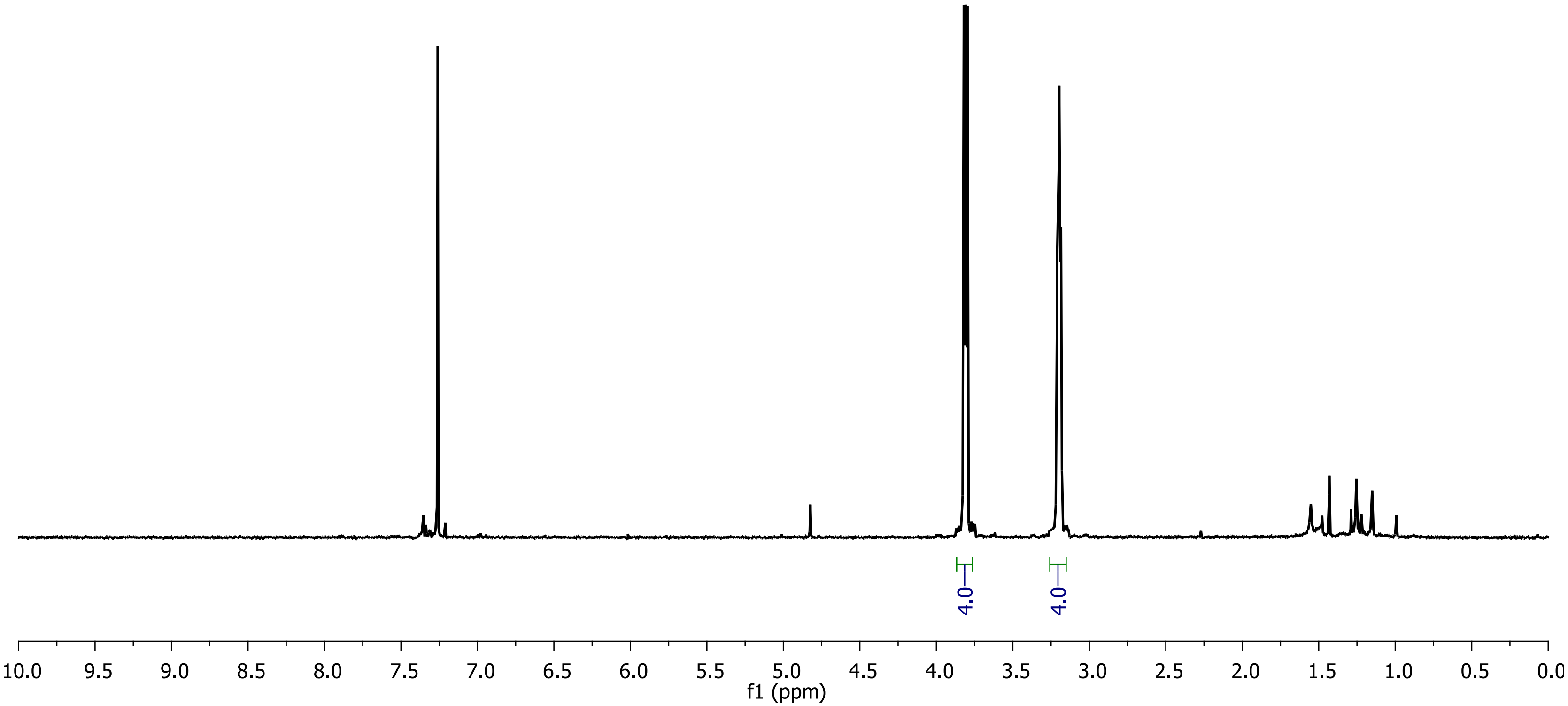

F
N
N
O
F
1.7
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

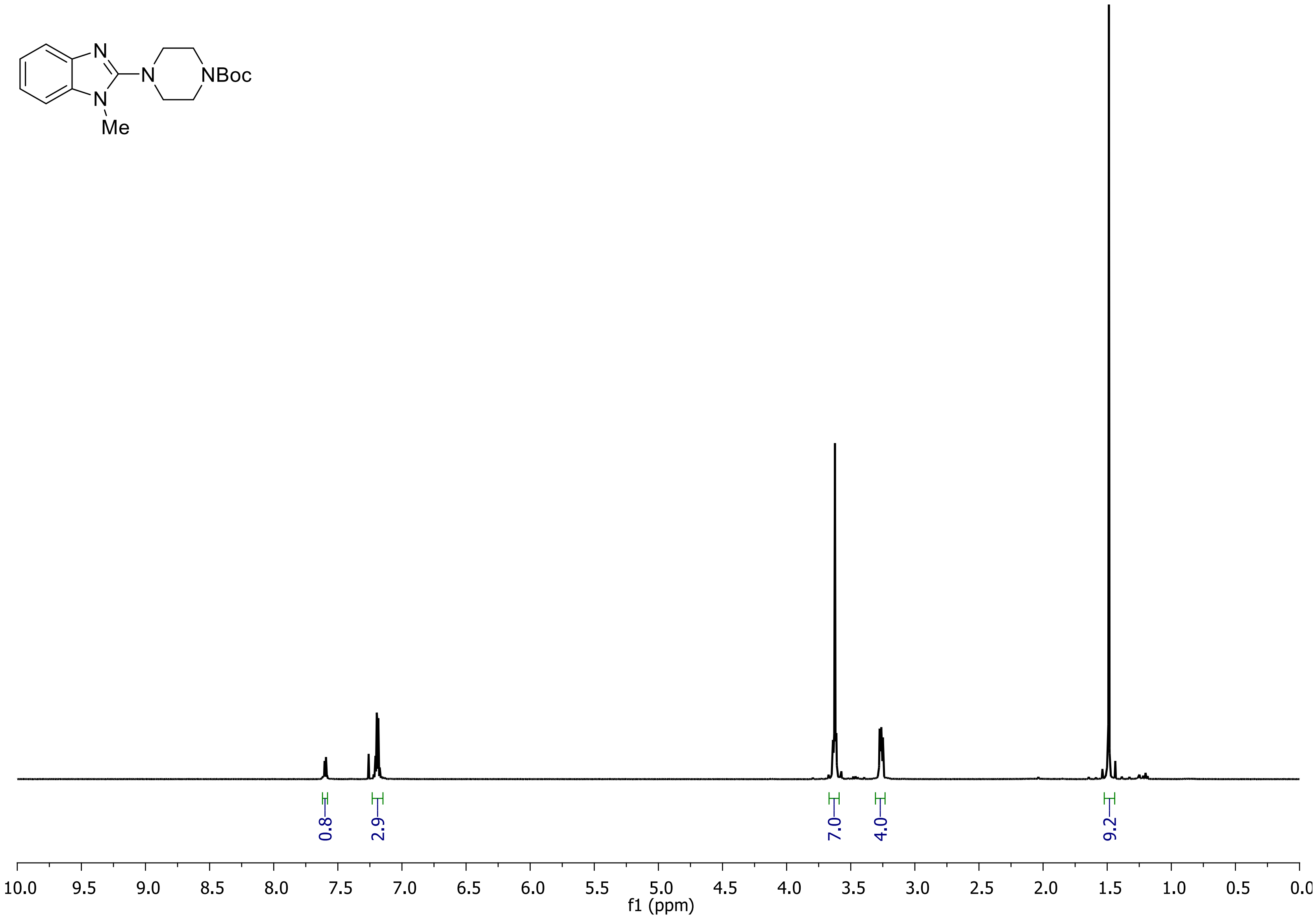

S
N
N
O
0.8
0.9
0.9
0.8
0.9
1.0
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

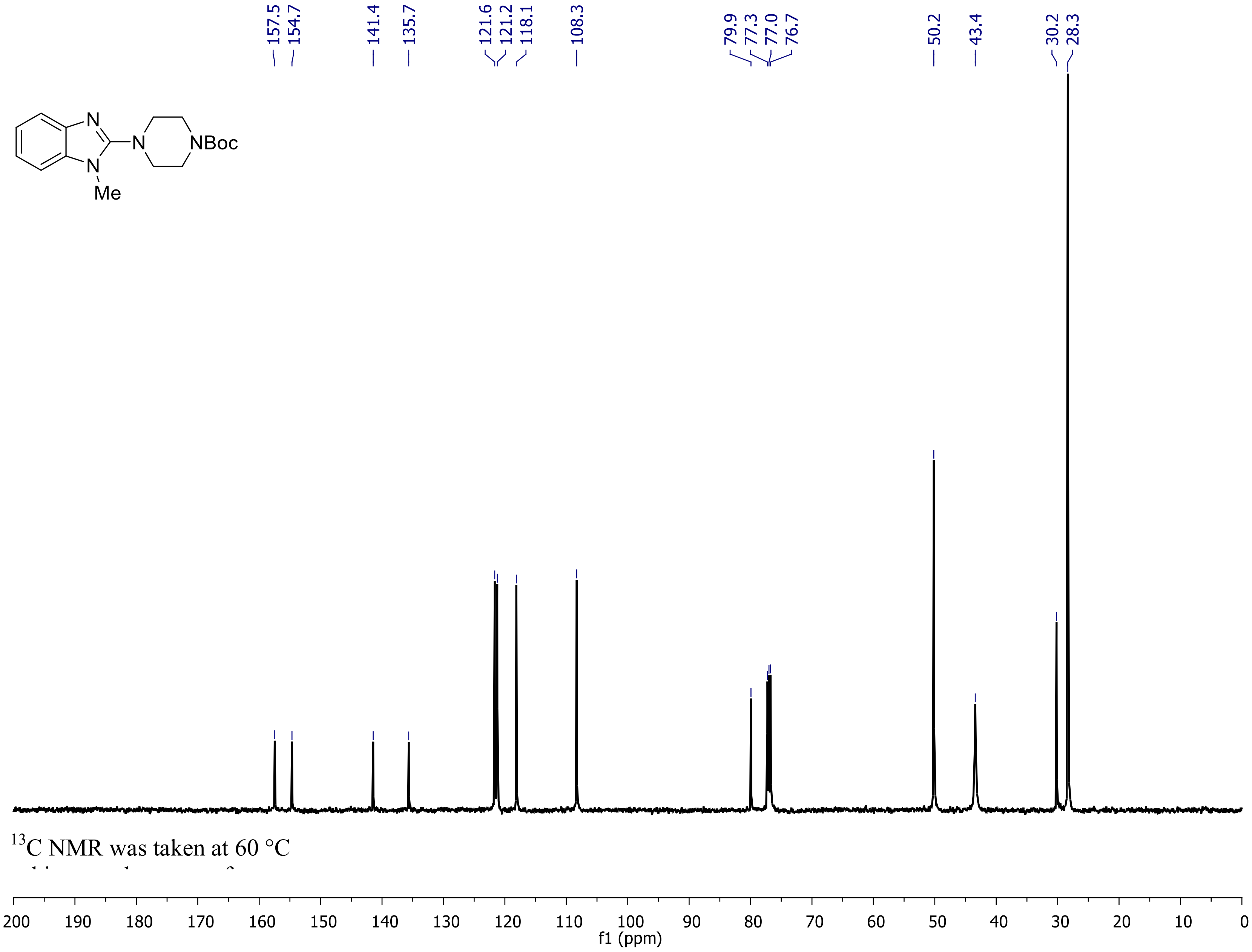

133.9
130.5
128.4
128.3
127.7
107.6
77.3
77.0
76.7
65.0
40.0
N
S
N
O
130.5
129.2
128.4
128.3
127.7
131
130
129
128
127
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


153.6
151.6
135.1
134.9
134.0
134.0
133.9
77.3
77.0
76.7
67.1
50.5
F
N
N
O
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

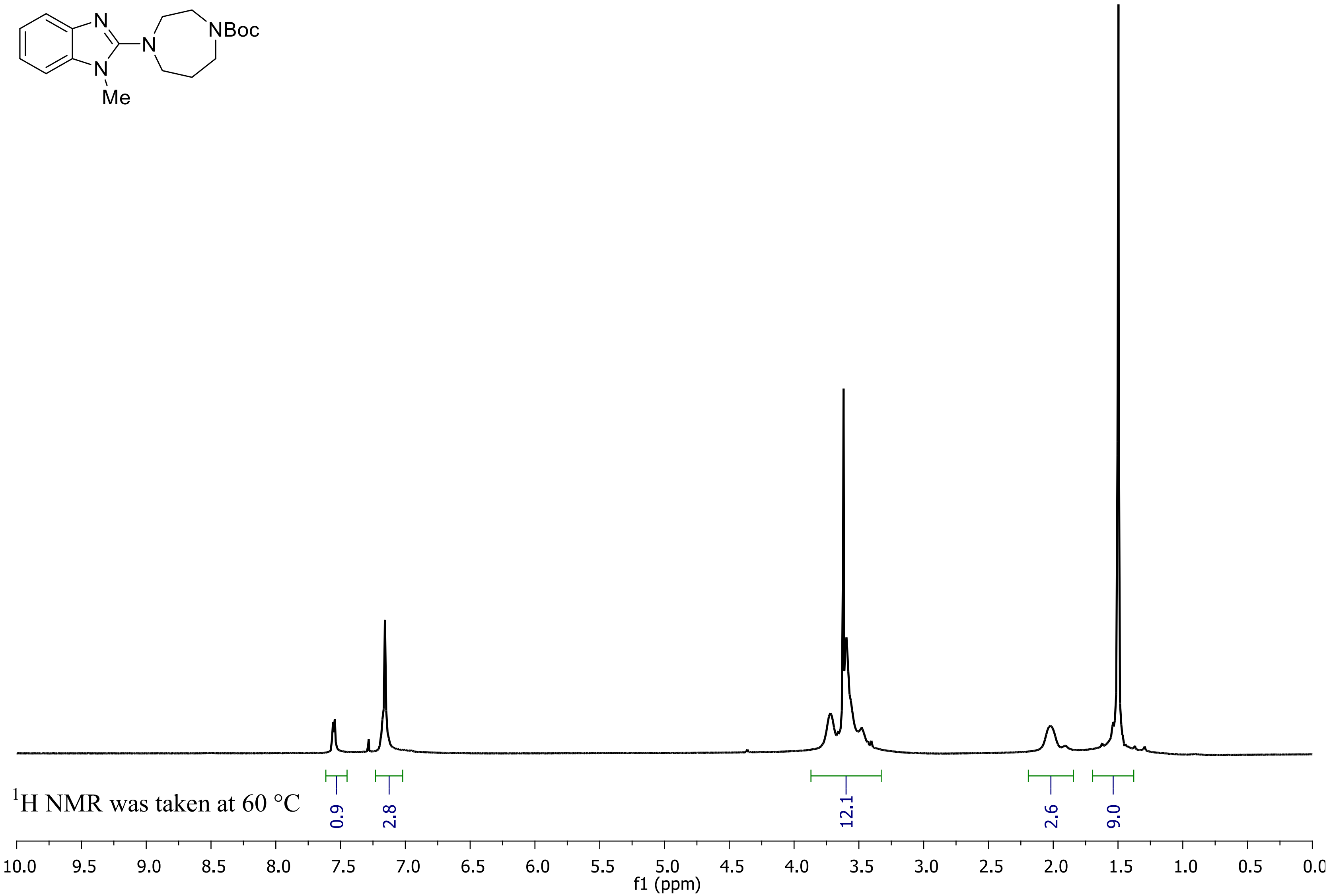

F
F
F
N
O
F
F


4.0
4.0
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)

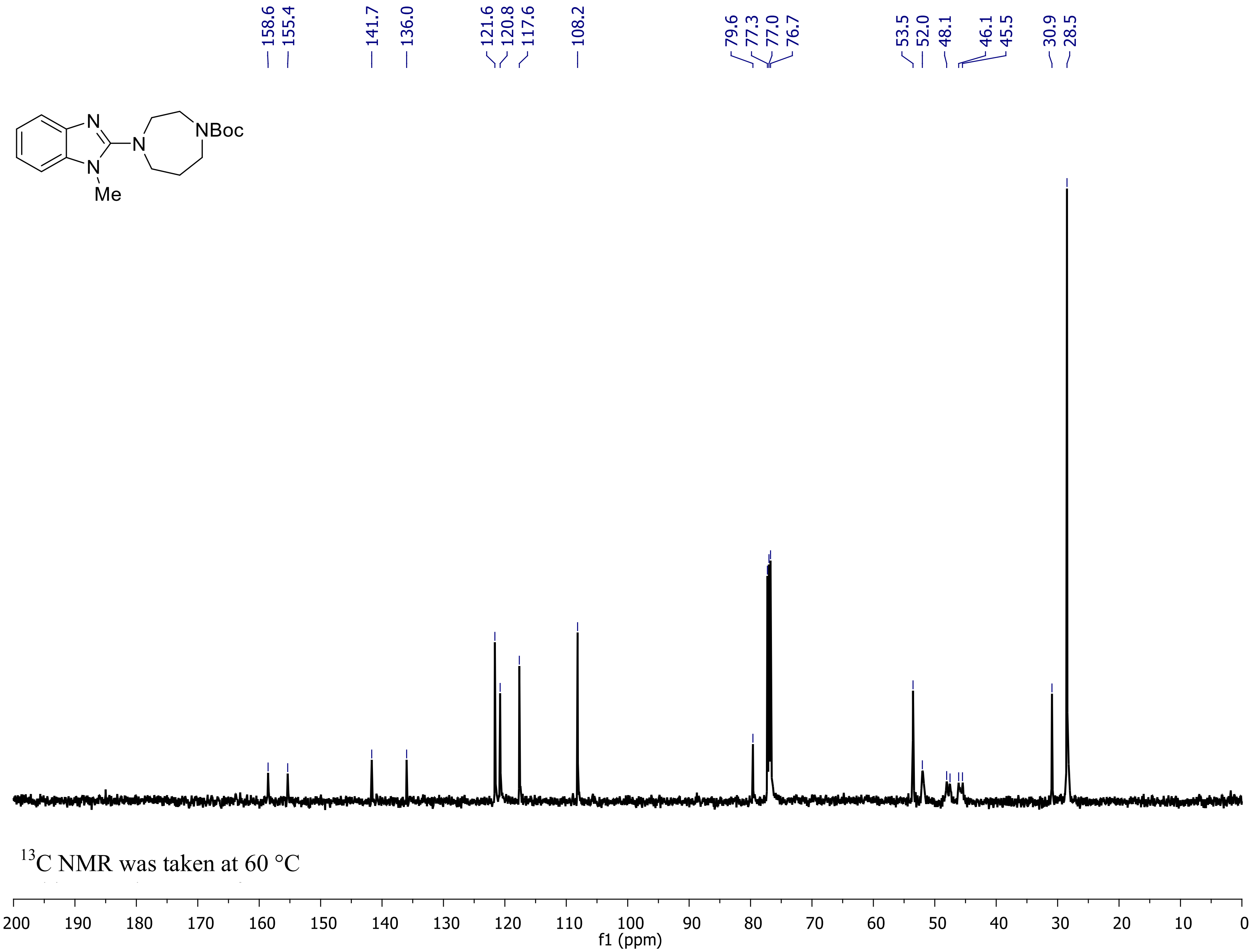

N
N
Me
N
NBoc
0.8
2.9
7.0
4.0
9.2
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



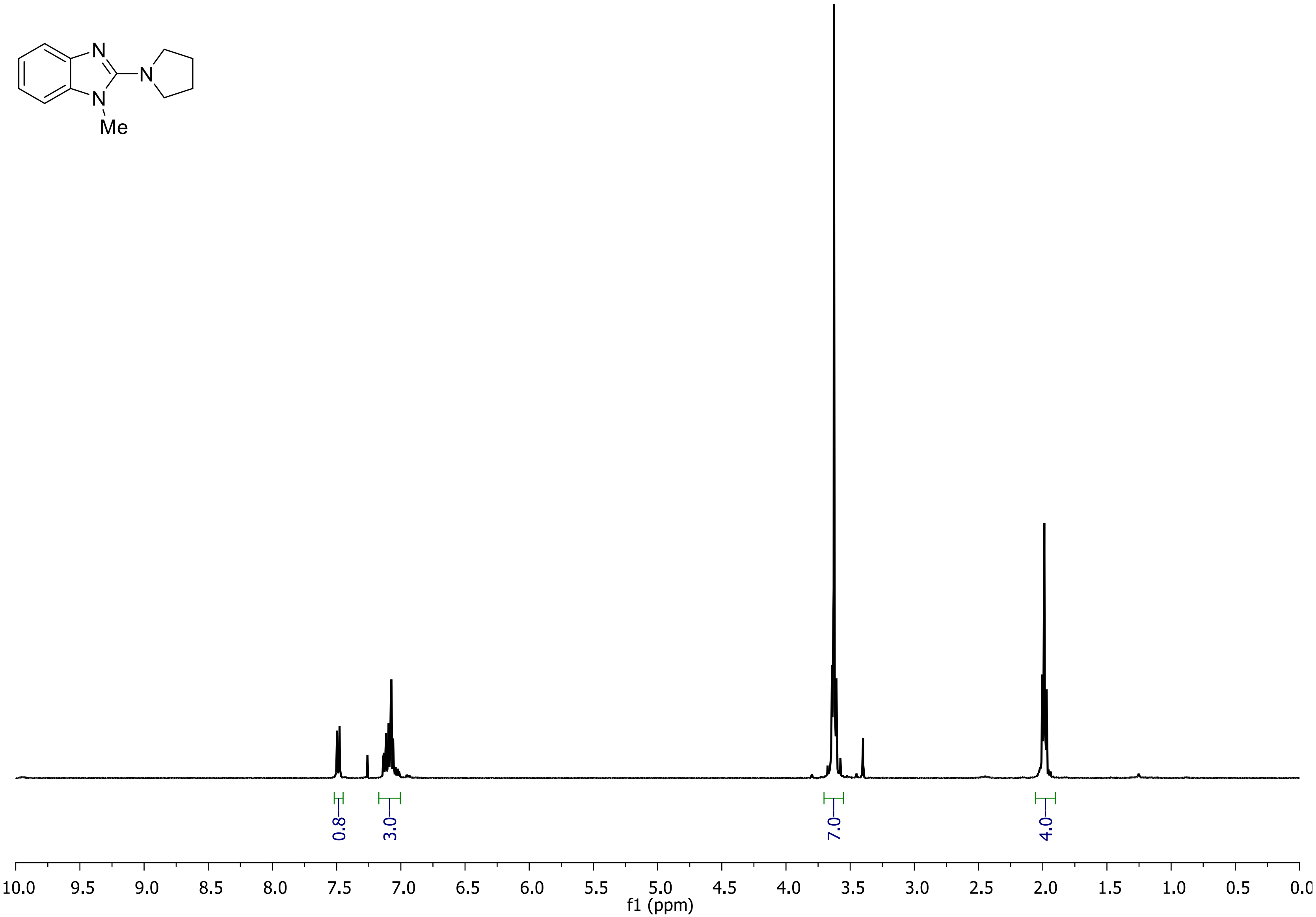
^{13}C NMR was taken at 60 °C



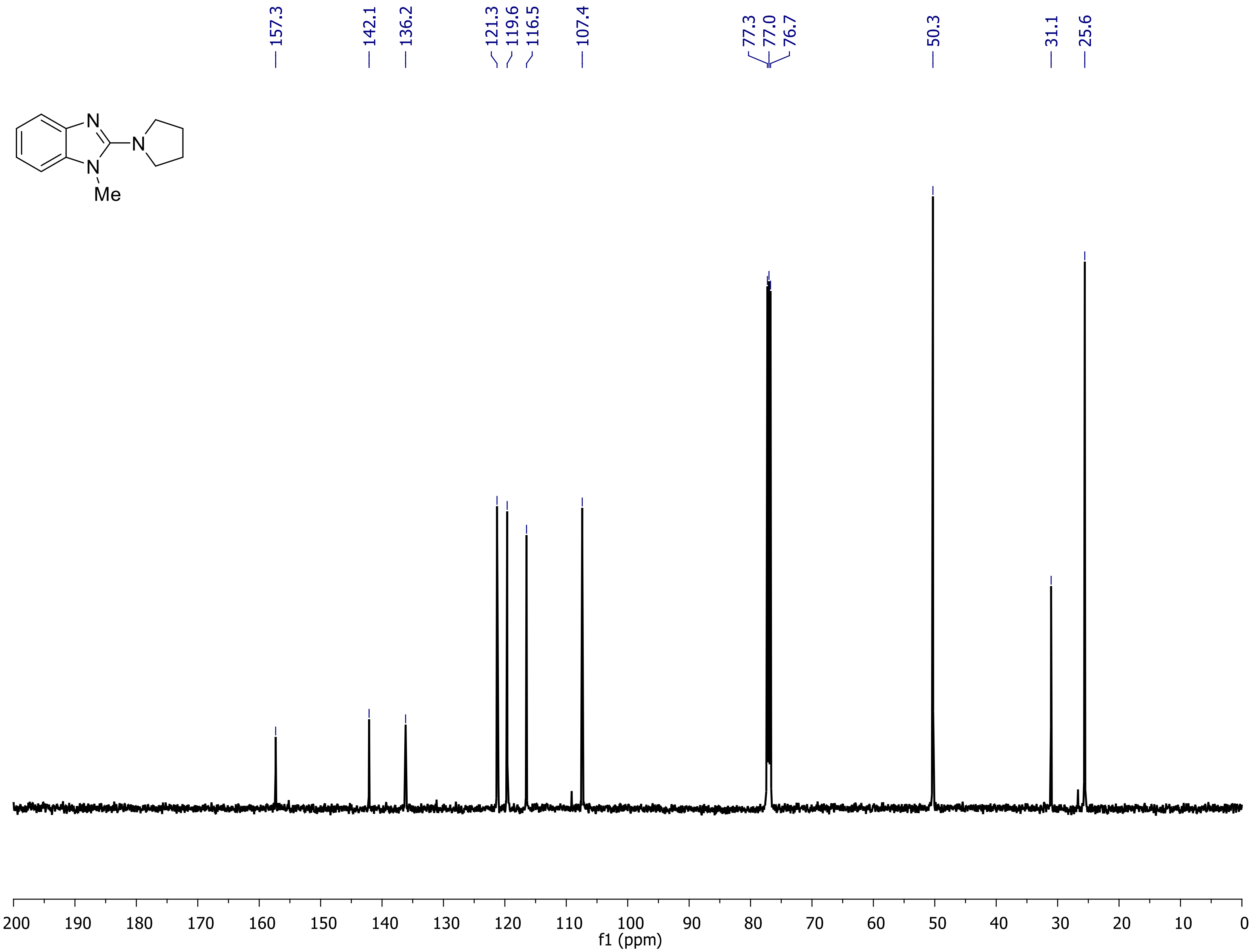
^{1}H NMR was taken at 60 °C

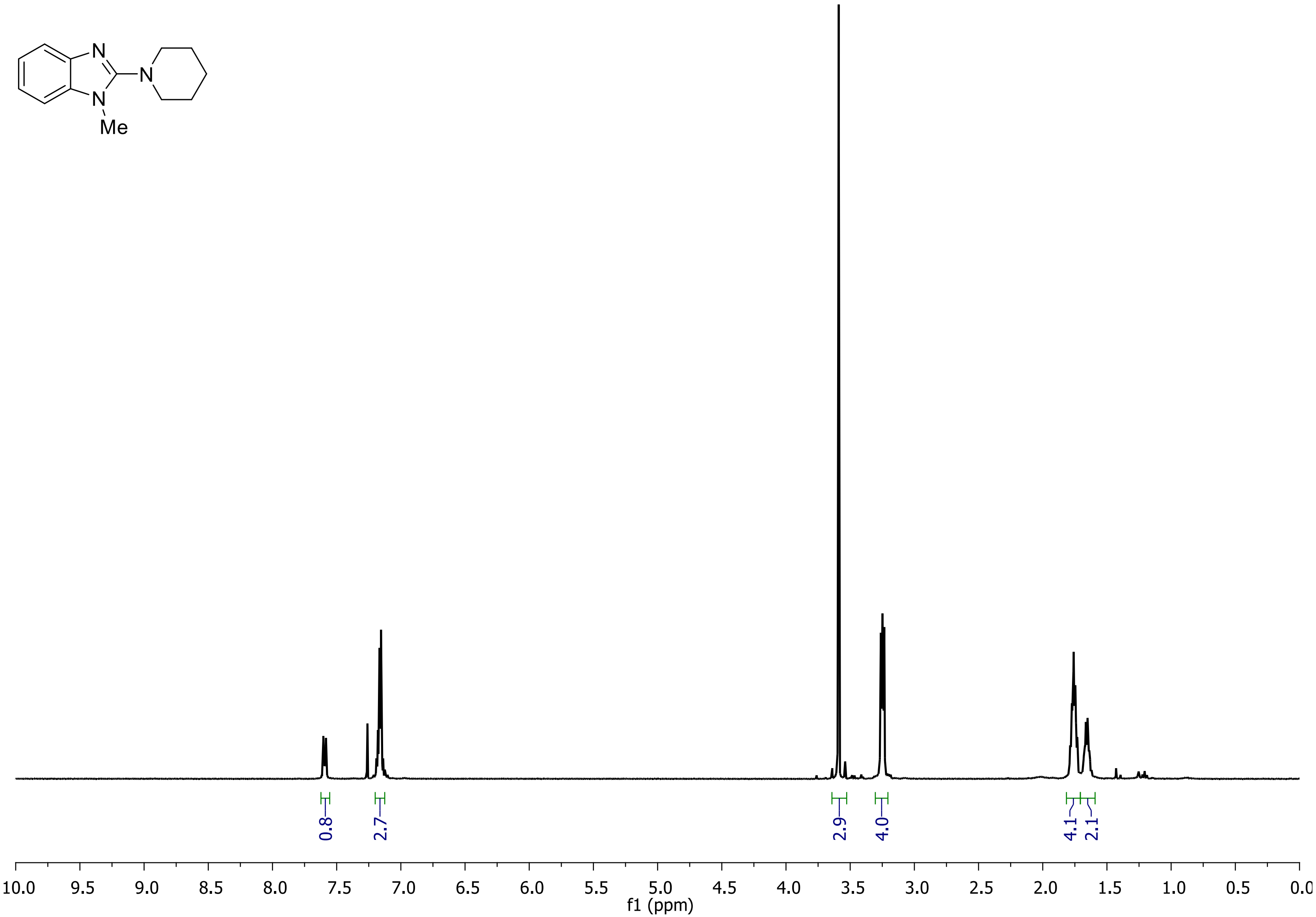


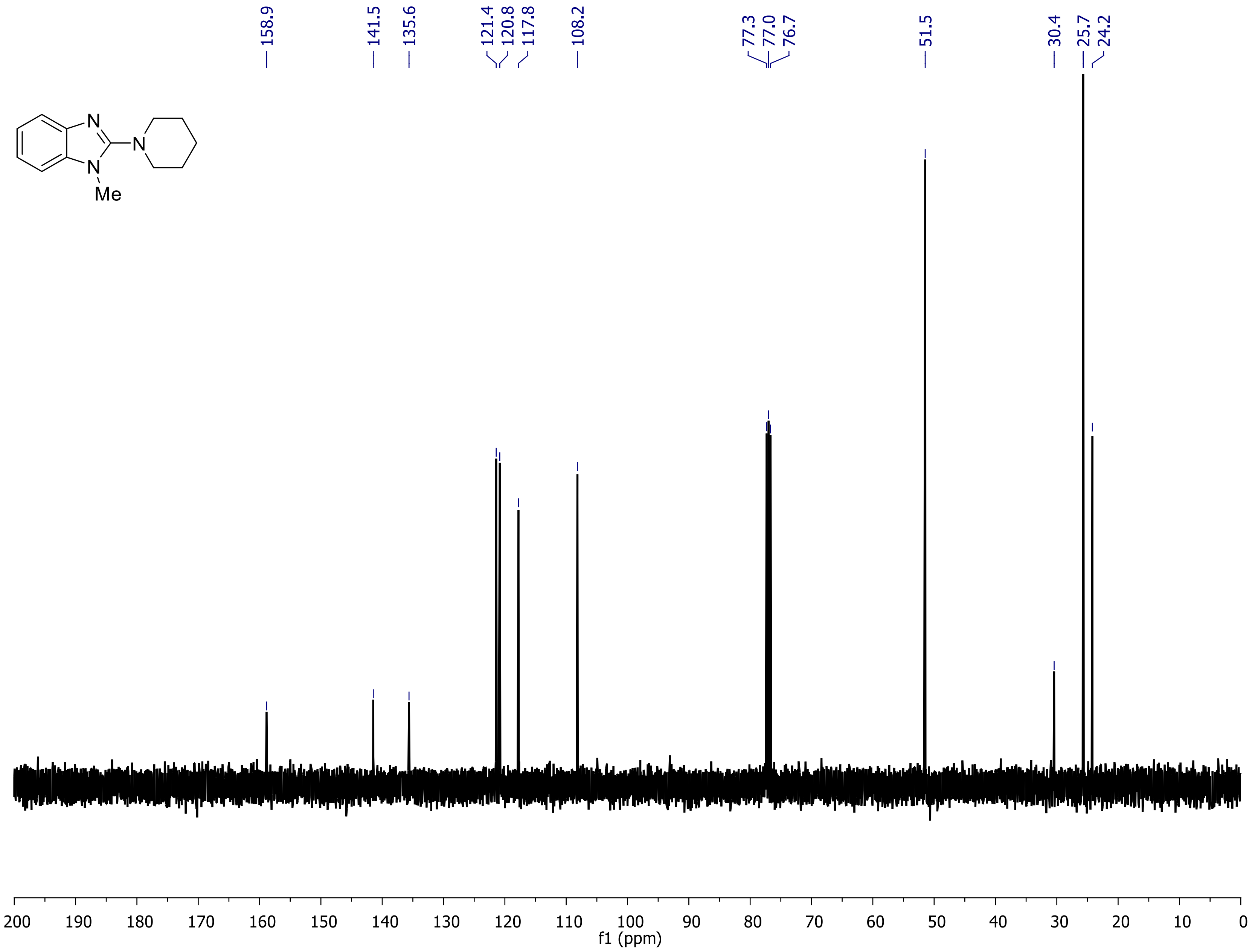
^{13}C NMR was taken at 60 °C

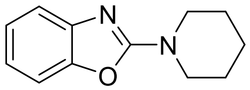


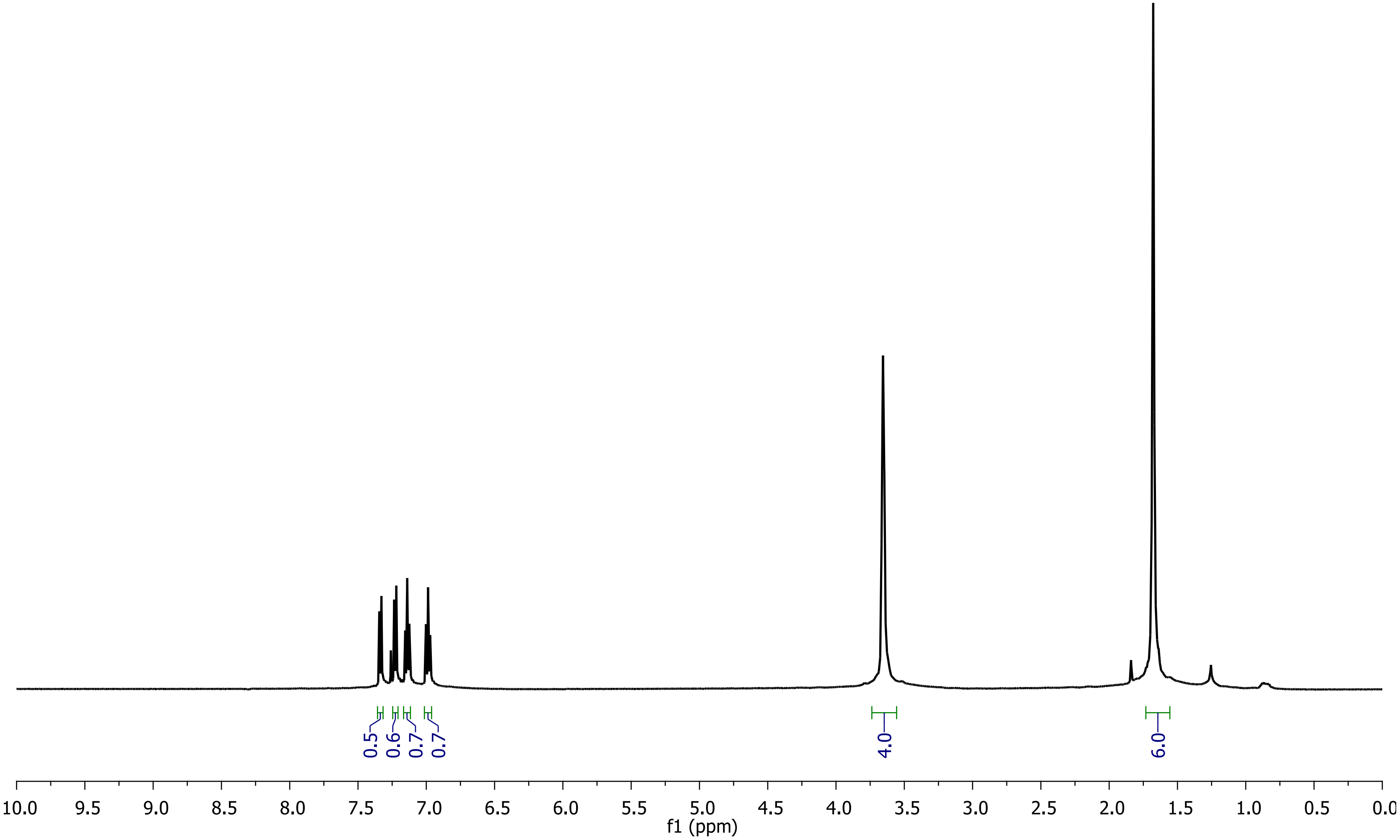
N
N
N
Me
0.8
3.0
7.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

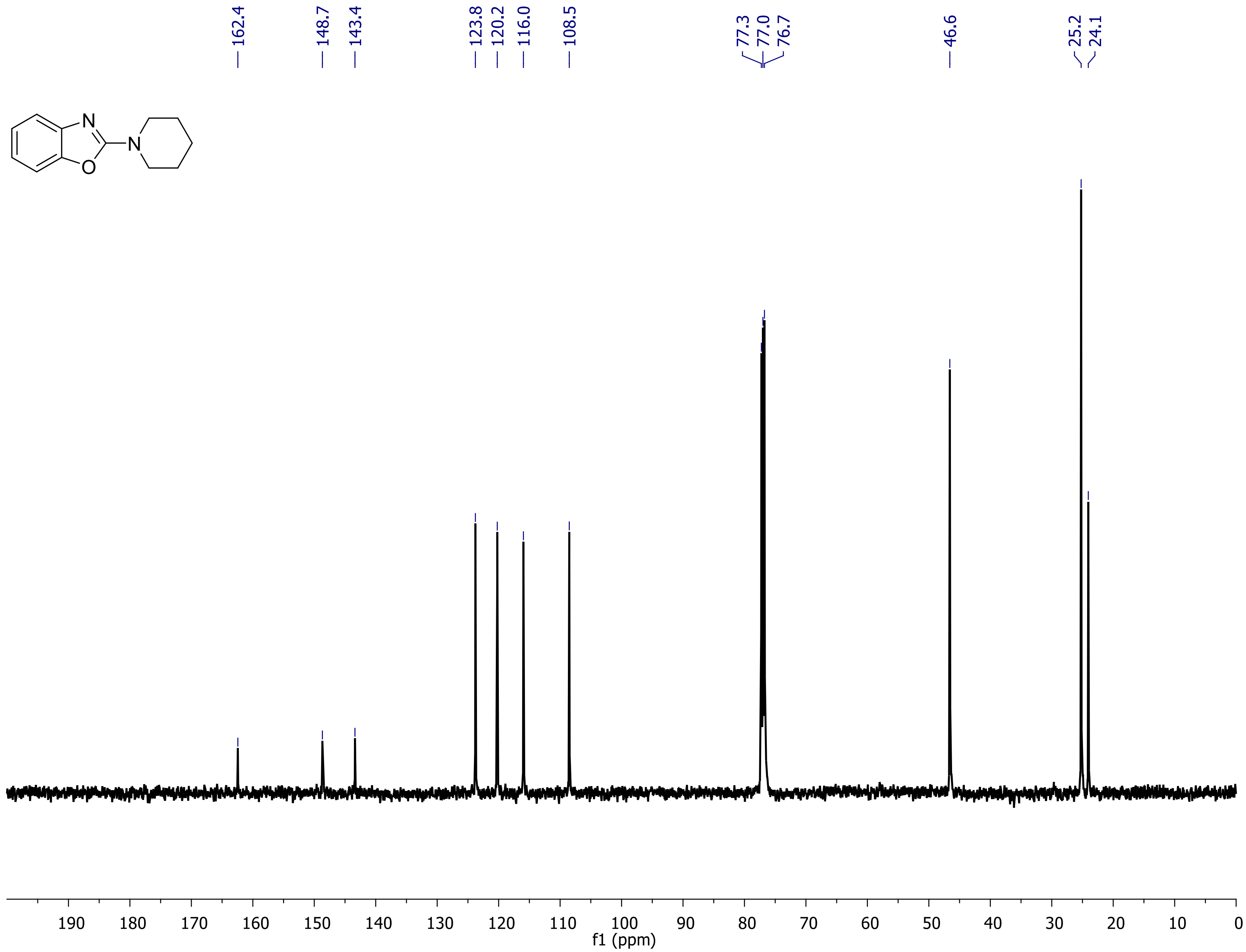

157.3
142.1
136.2
121.3
119.6
116.5
107.4
77.3
77.0
76.7
50.3
31.1
25.6
N
N
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

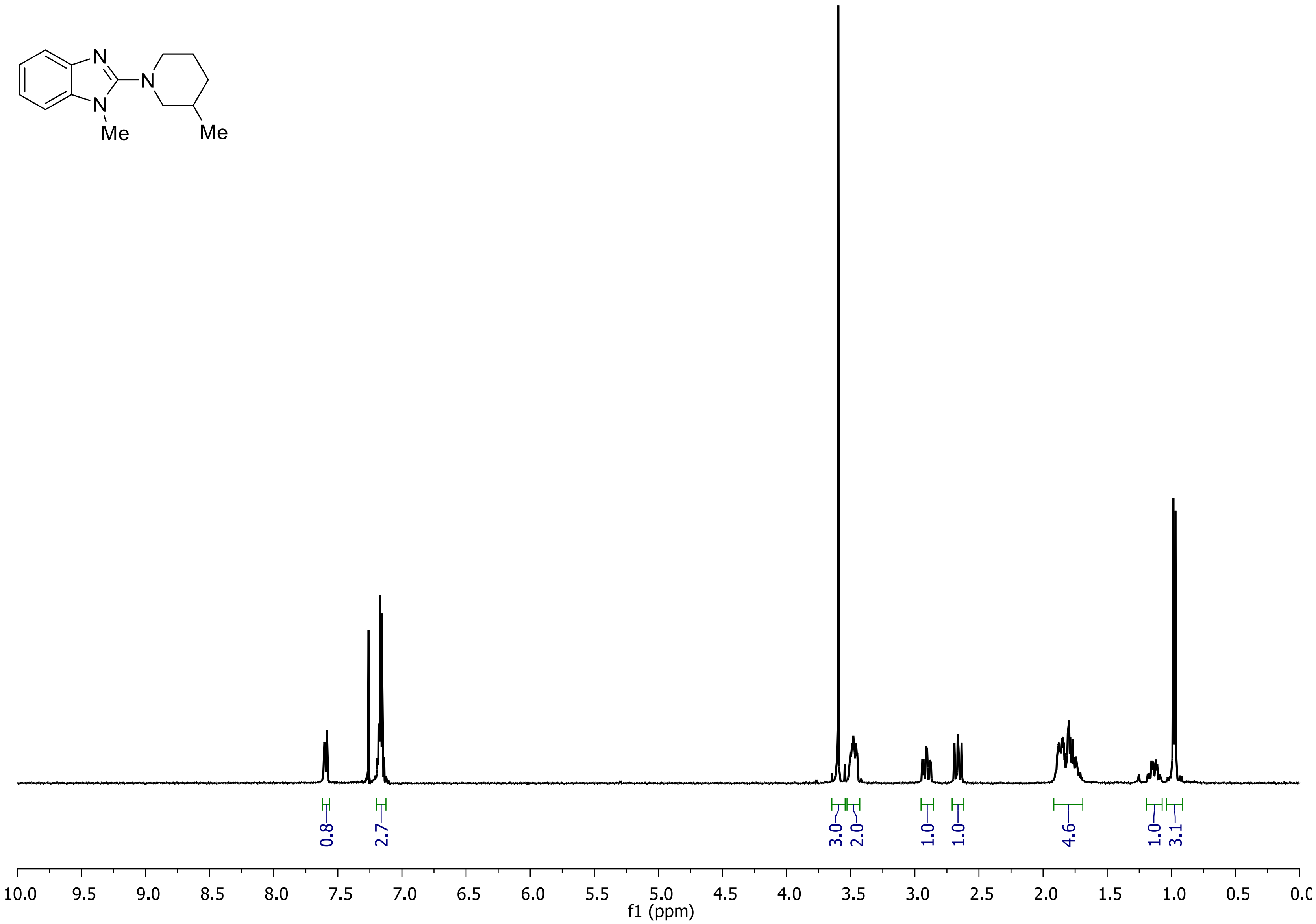

N
N
N
Me
0.8
2.7
2.9
4.0
4.1
2.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

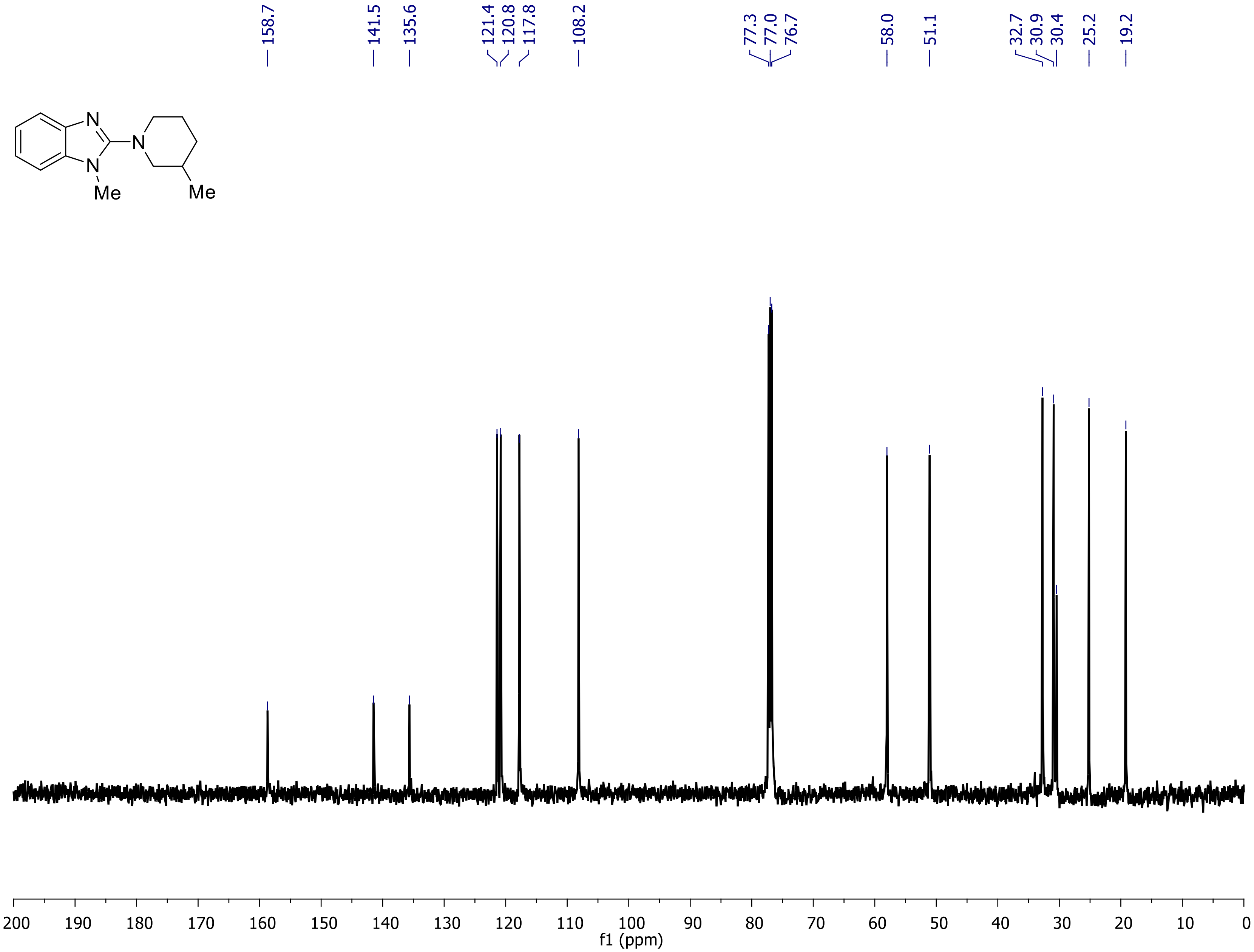

158.9
141.5
135.6
121.4
120.8
117.8
108.2
77.3
77.0
76.7
51.5
30.4
25.7
24.2
N
N
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
O


0.5
0.6
0.7
0.7
4.0
6.0
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)


162.4
148.7
143.4
123.8
120.2
116.0
108.5
77.3
77.0
76.7
46.6
25.2
24.1
N
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
Me
N
Me
0.8
2.7
3.0
2.0
1.0
1.0
4.6
1.0
3.1
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)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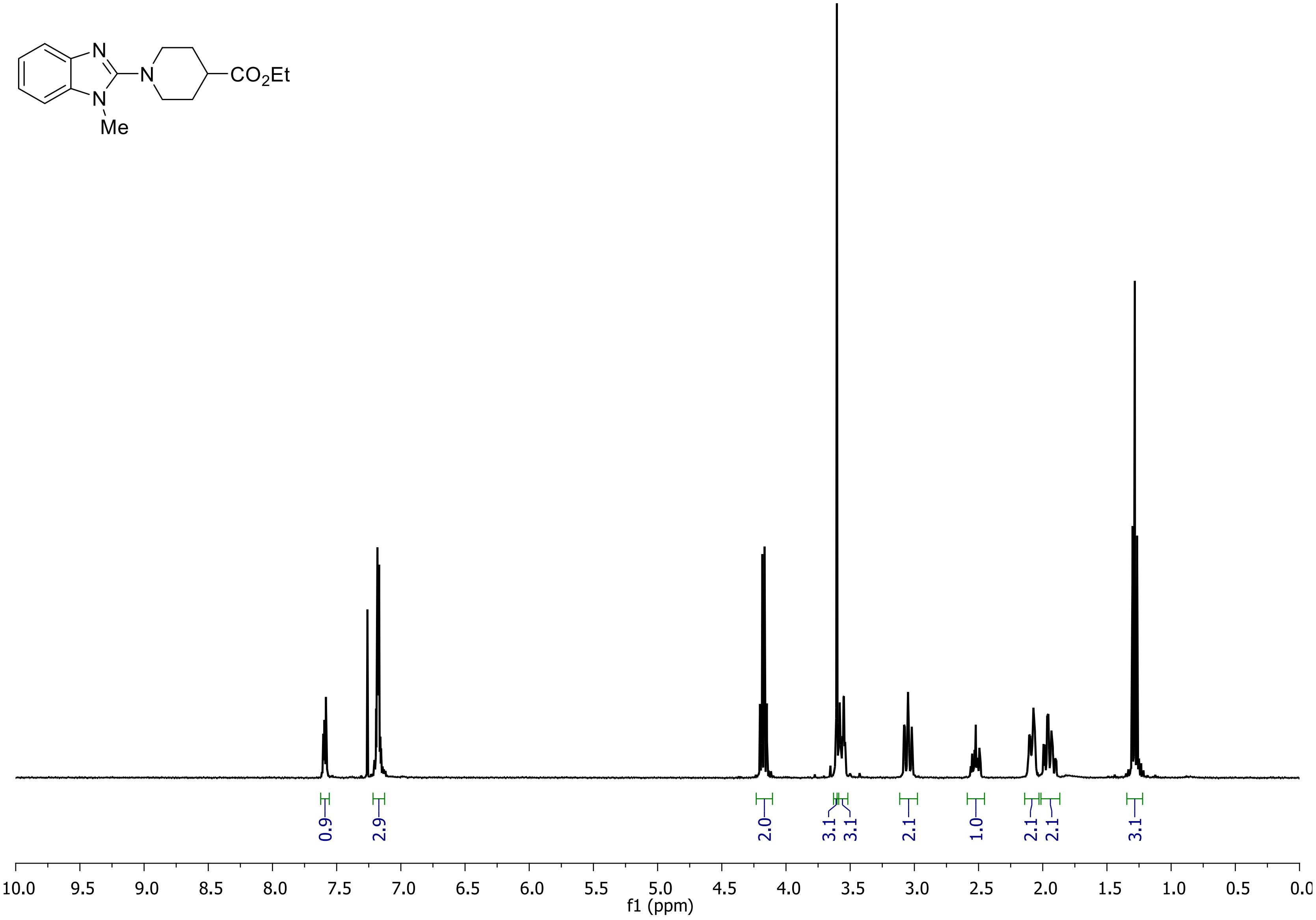
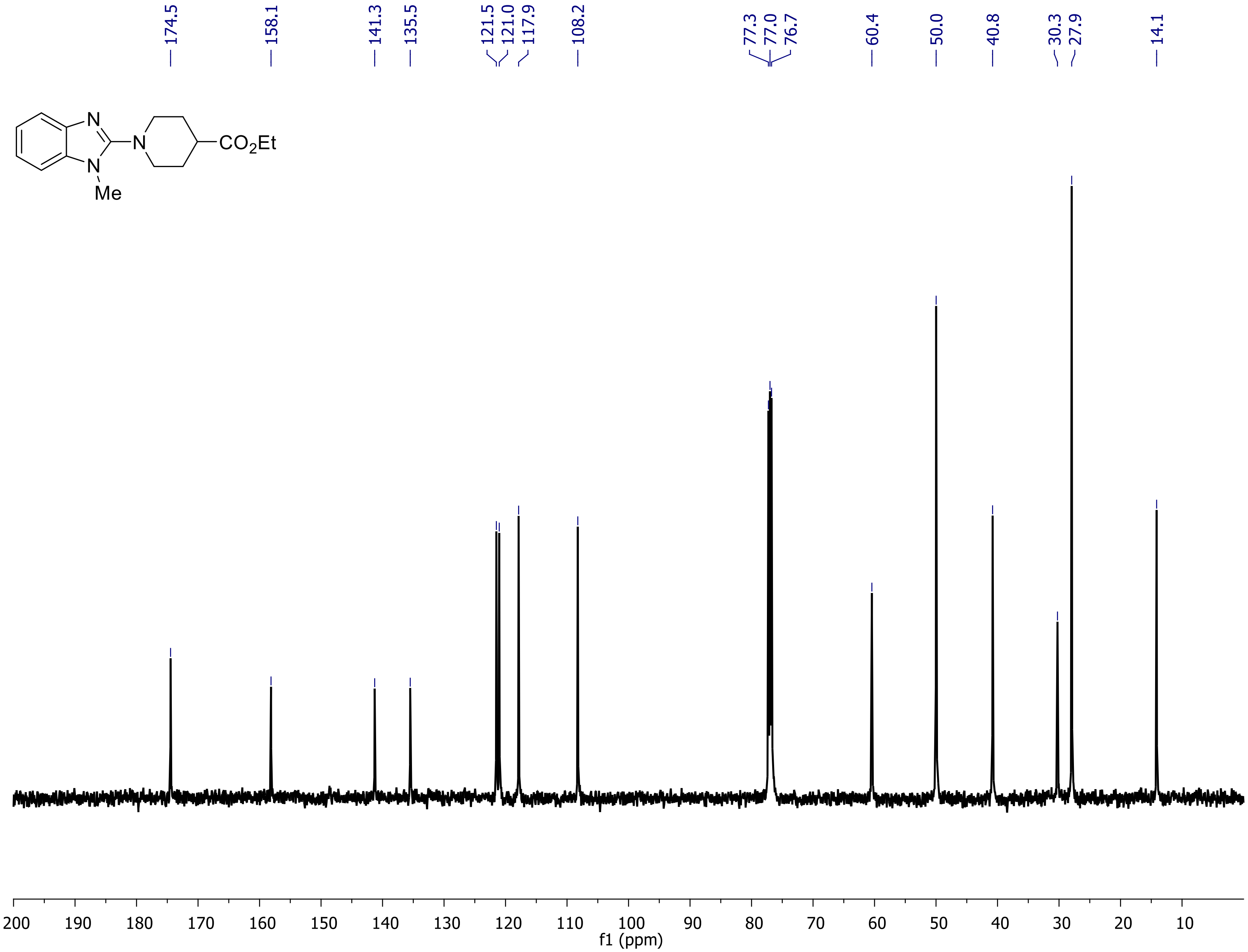
141.5
135.6
121.4
120.8
117.8
108.2
77.3
77.0
76.7
58.0
51.1
32.7
30.9
30.4
25.2
19.2
N
N
N
Me
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
Me
N
CO2Et
0.9
2.9
2.0
3.1
3.1
2.1
1.0
2.1
2.1
3.1
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)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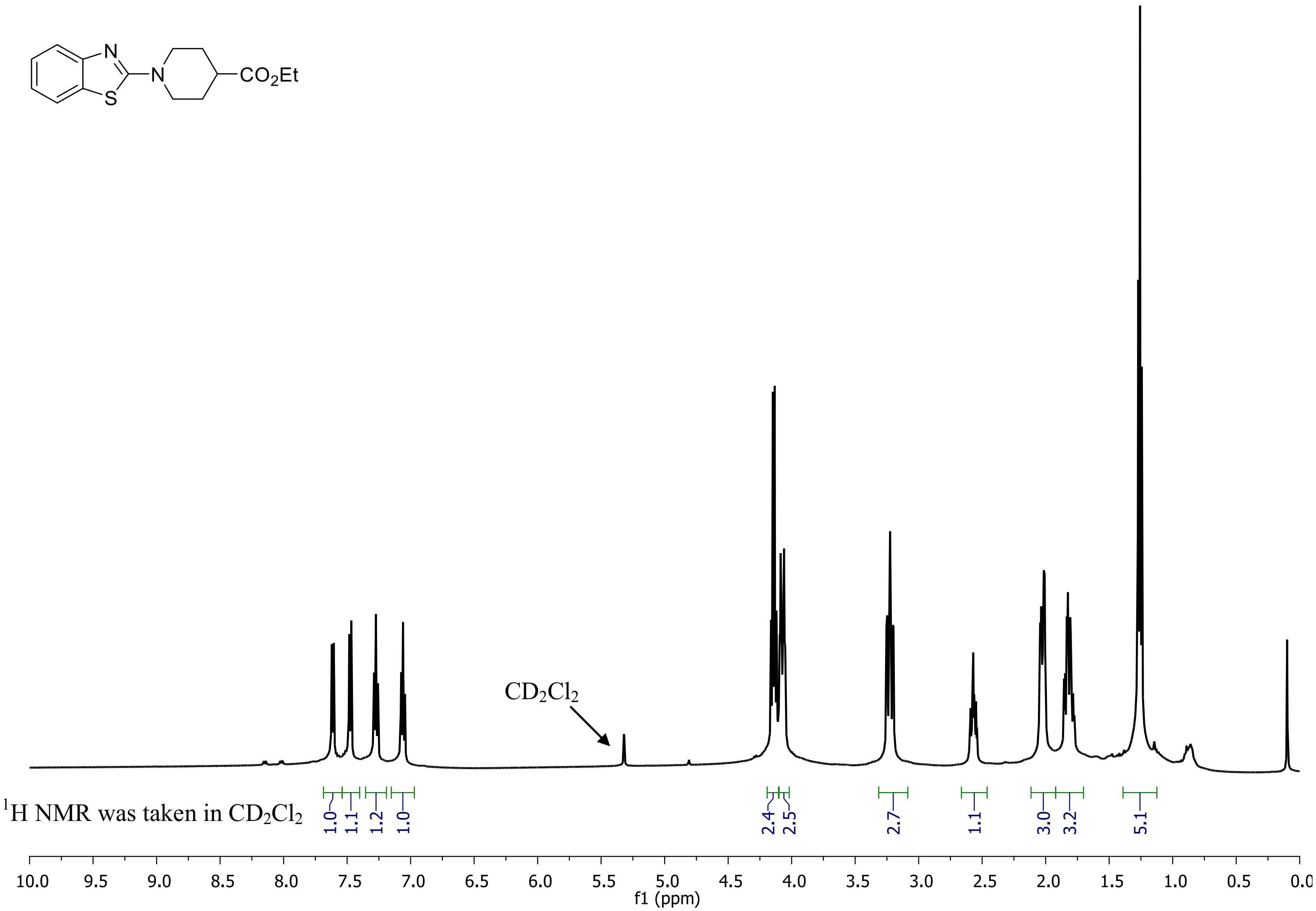
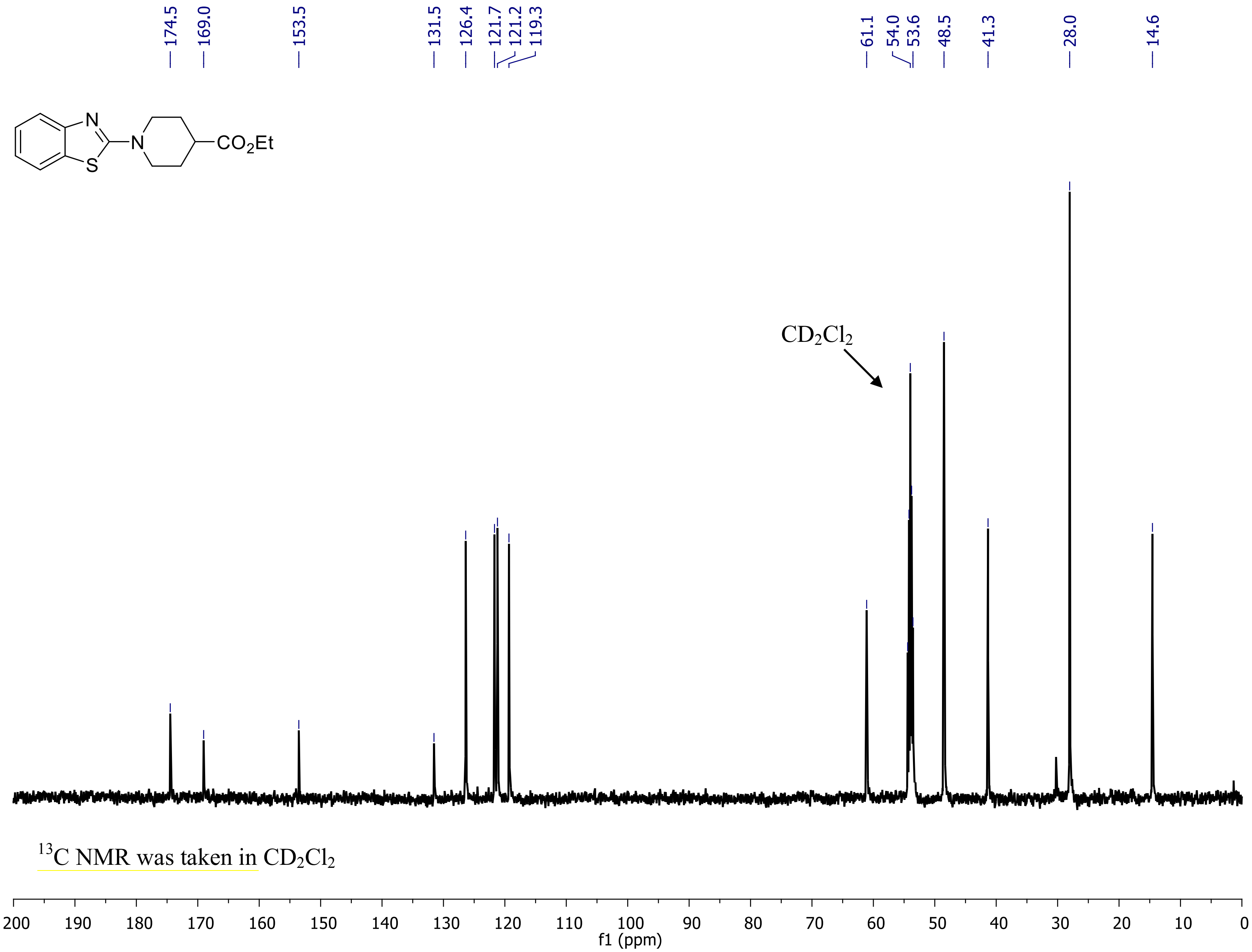
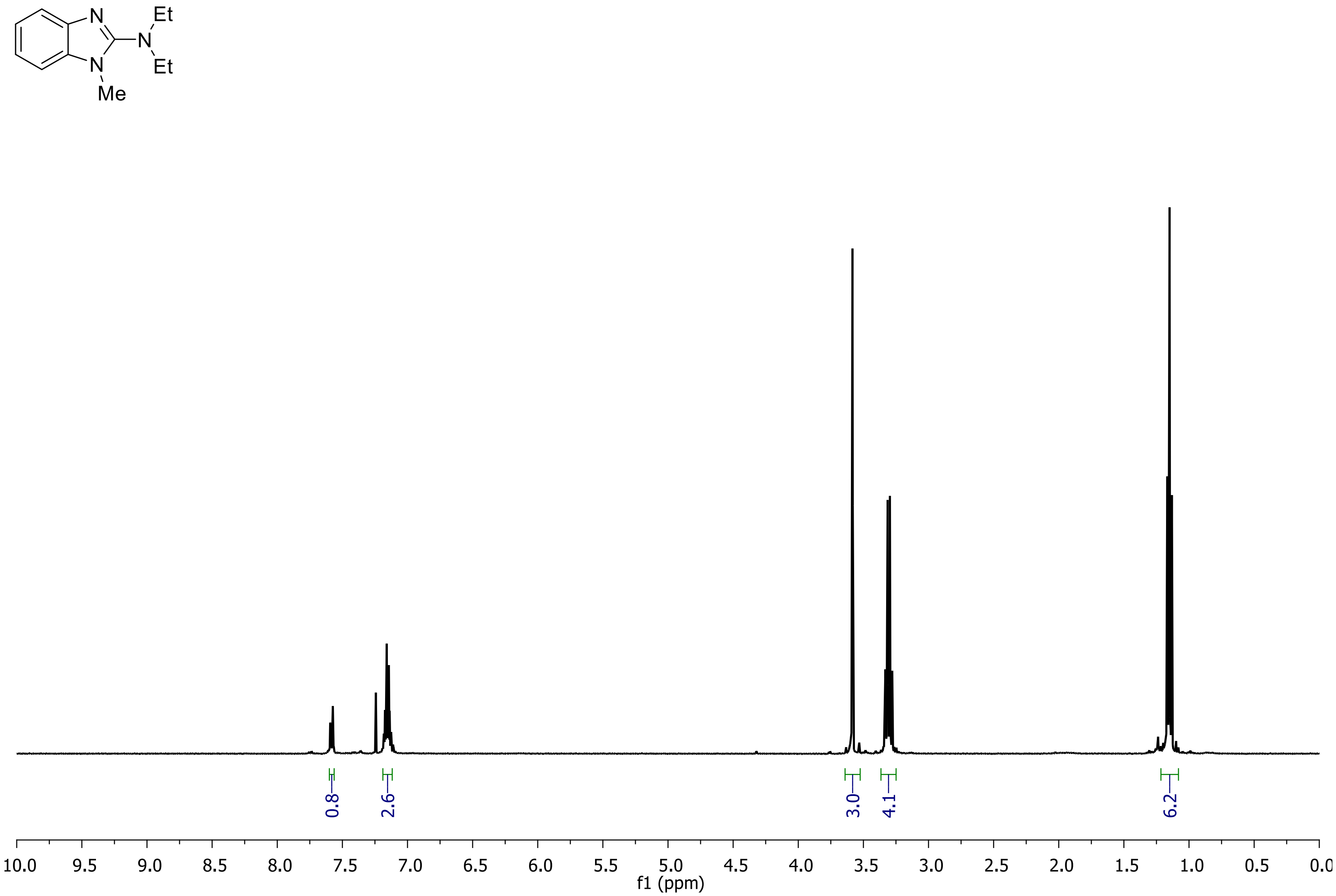
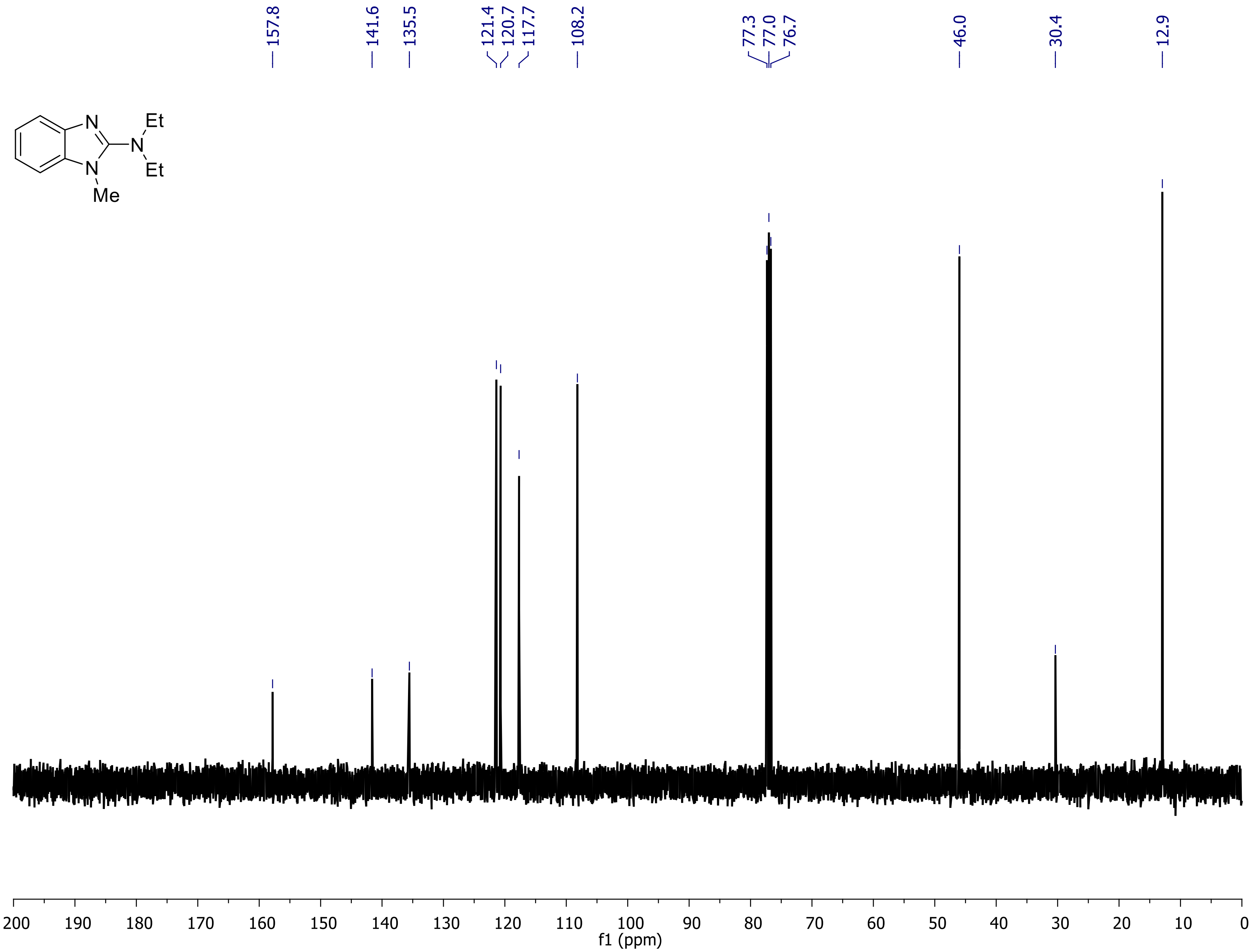
158.1
141.3
135.5
121.5
121.0
117.9
108.2
77.3
77.0
76.7
60.4
50.0
40.8
30.3
27.9
14.1
N
N
N
Me
CO2Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

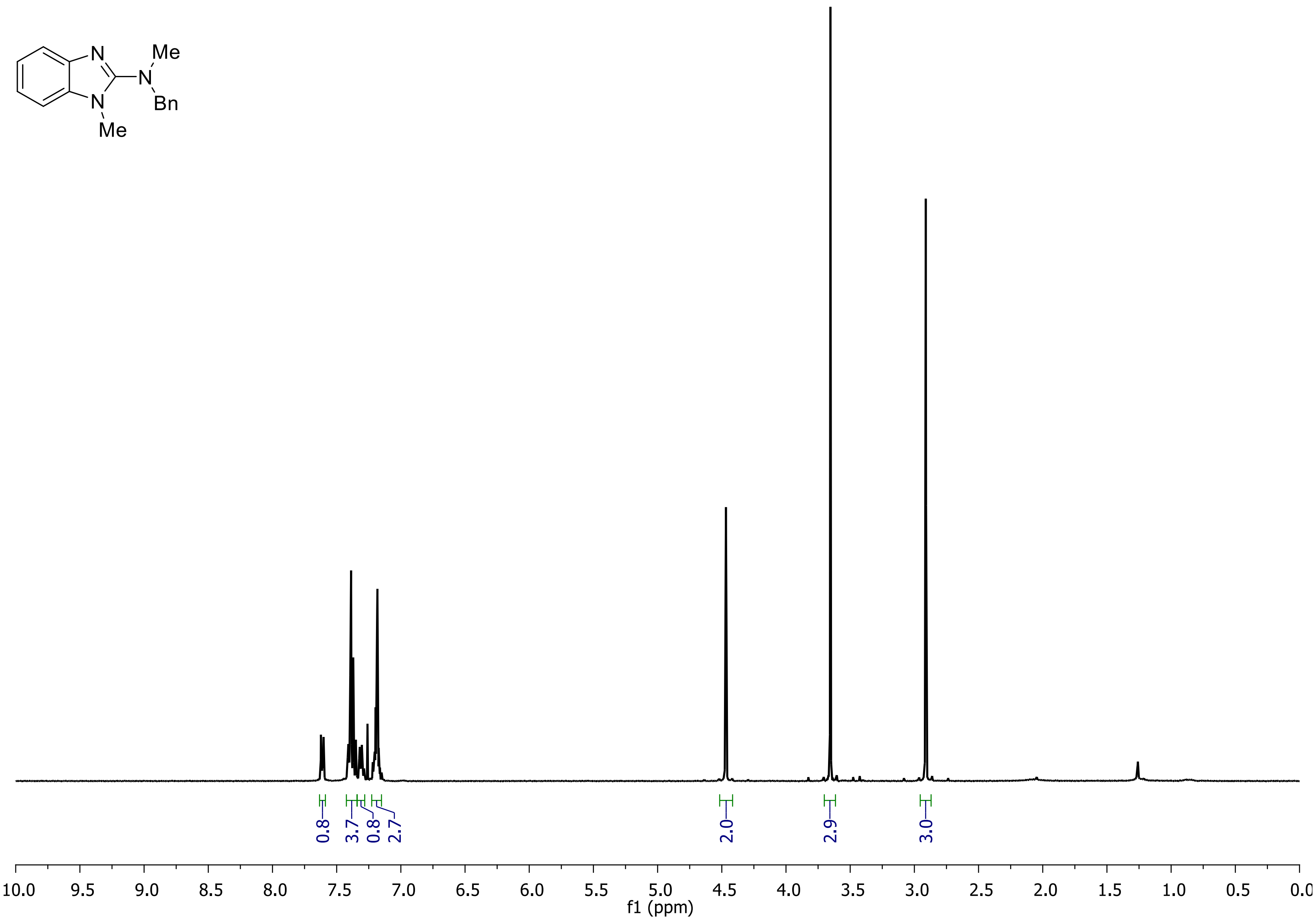

N
S
N
CO$_2$Et
CD$_2$Cl$_2$
^{1}H NMR was taken in CD$_2$Cl$_2$
1.0
1.1
1.2
1.0
2.4
2.5
2.7
1.1
3.0
3.2
5.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

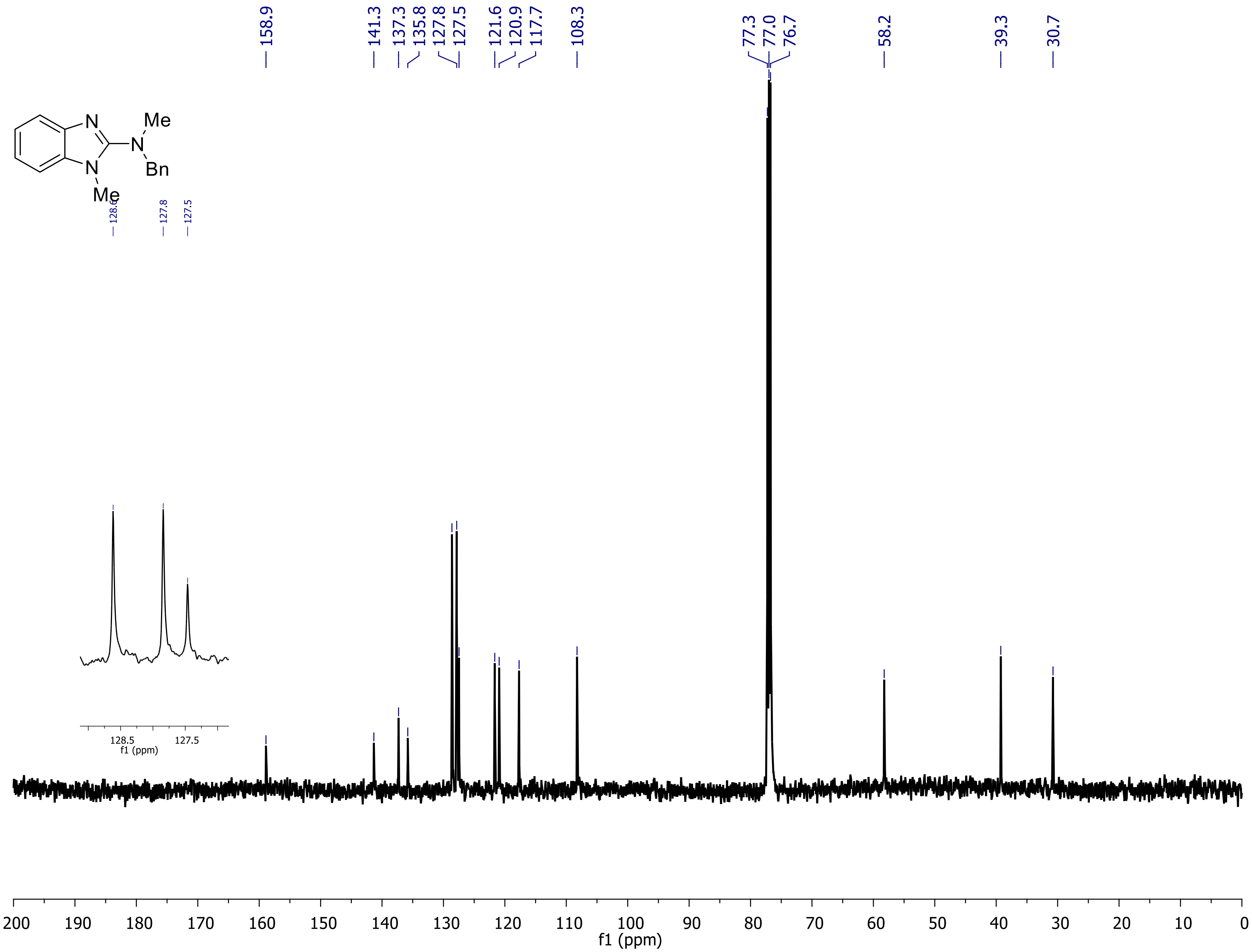


^{13}C NMR was taken in CD_2Cl_2


N
N
Me
N
Et
Et
0.8
2.6
3.0
4.1
6.2
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)


157.8
141.6
135.5
121.4
120.7
117.7
108.2
77.3
77.0
76.7
46.0
30.4
12.9
N
N
Me
N
Et
Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
Me
N
Bn
N
Me
0.8
3.7
0.8
2.7
2.0
2.9
3.0
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)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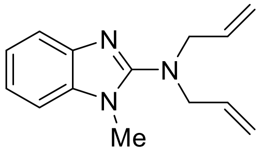
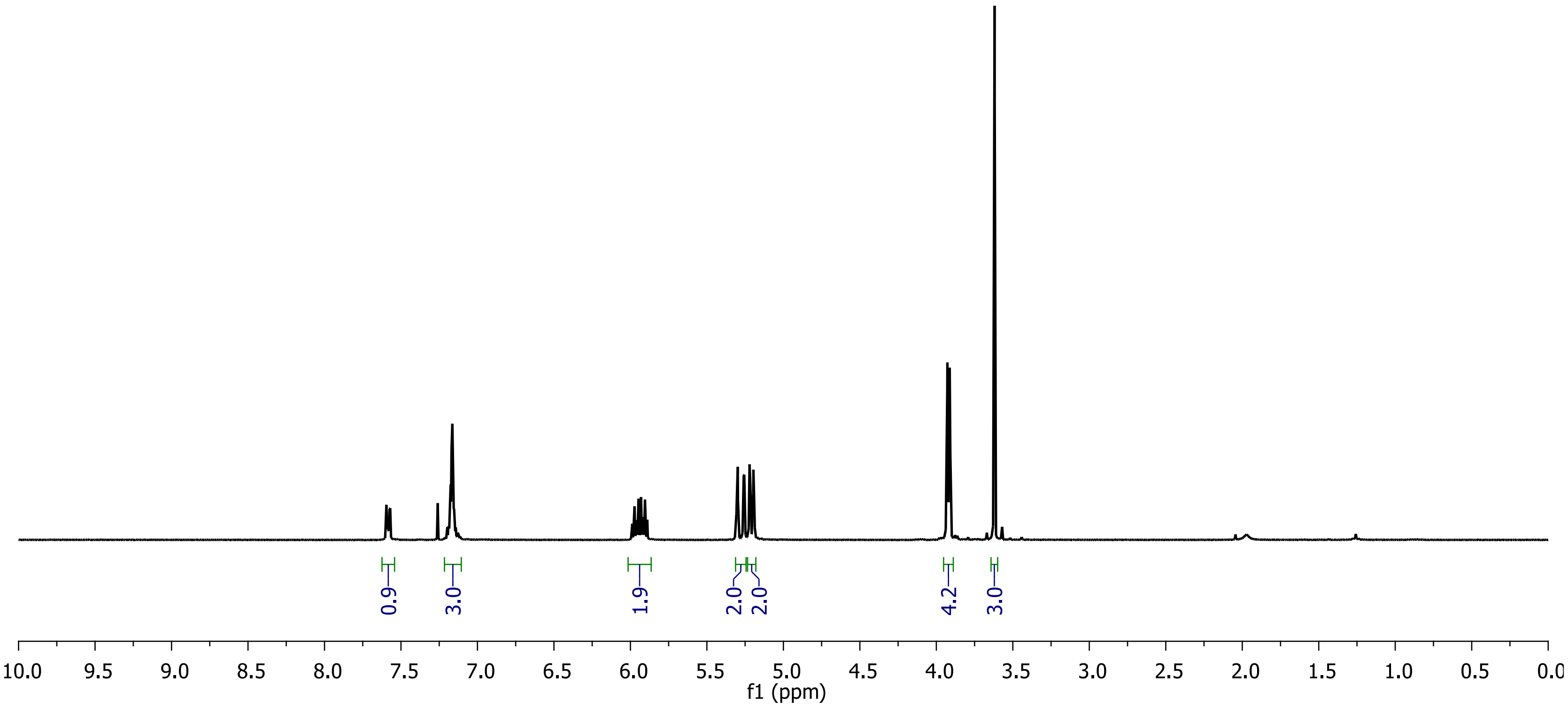
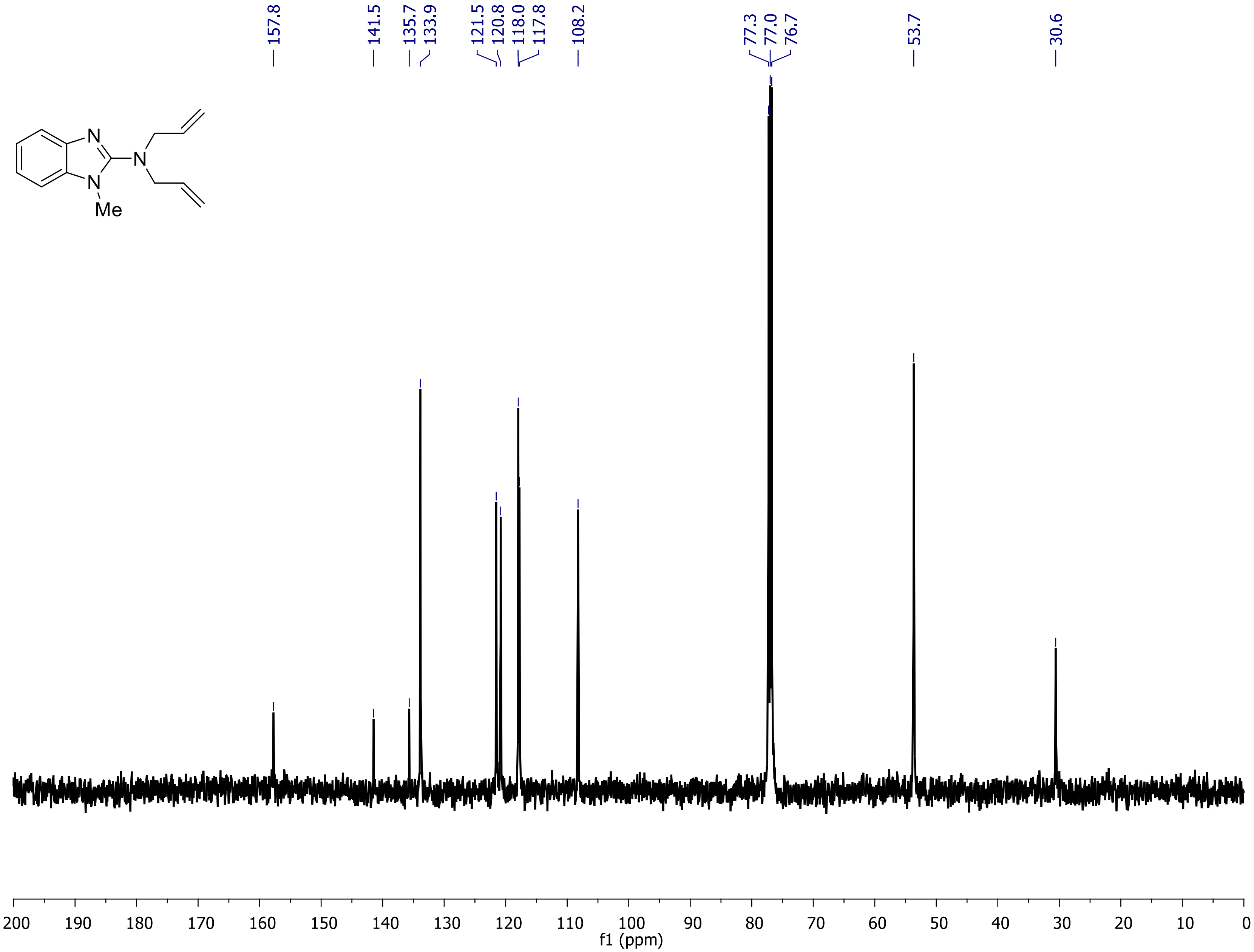
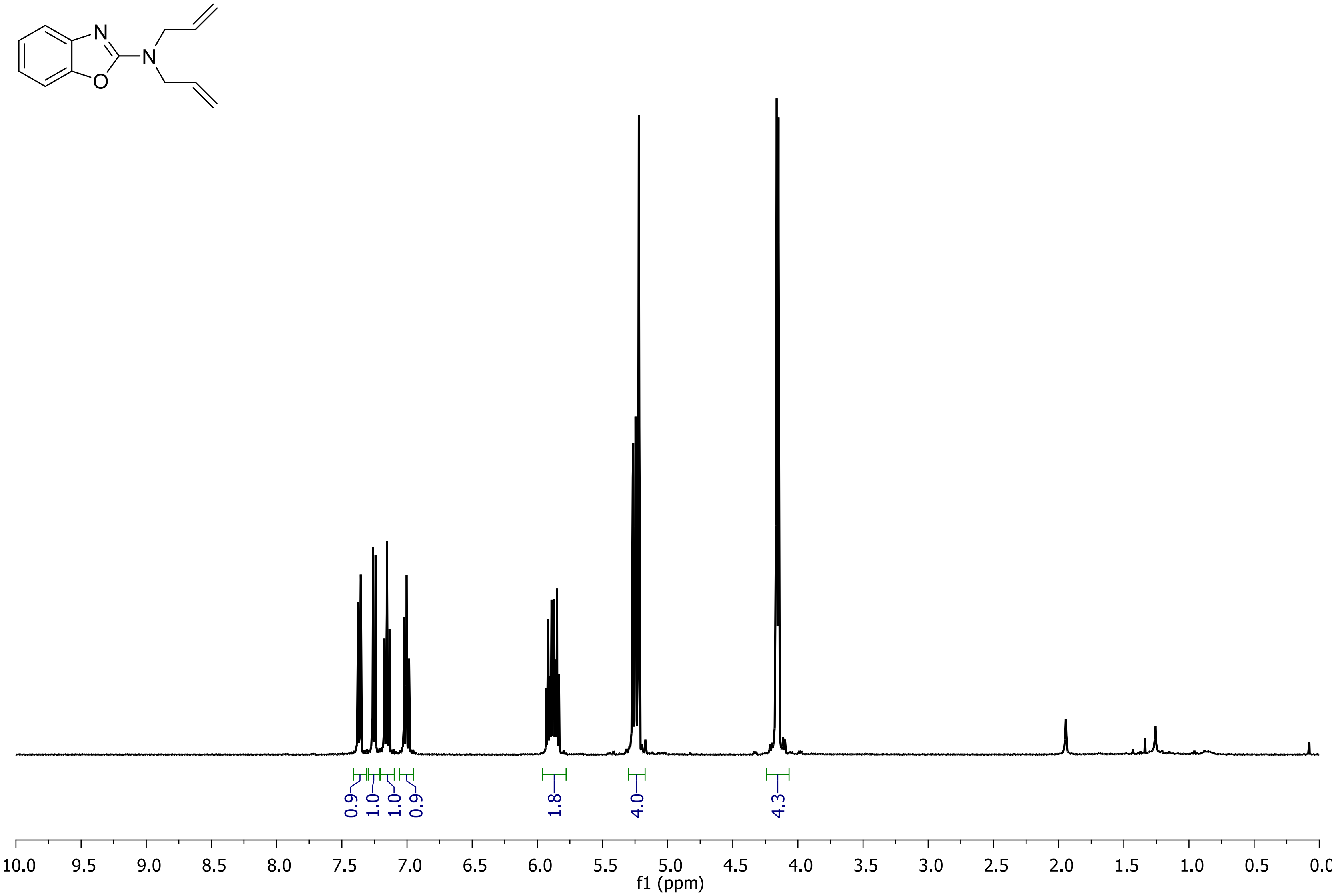
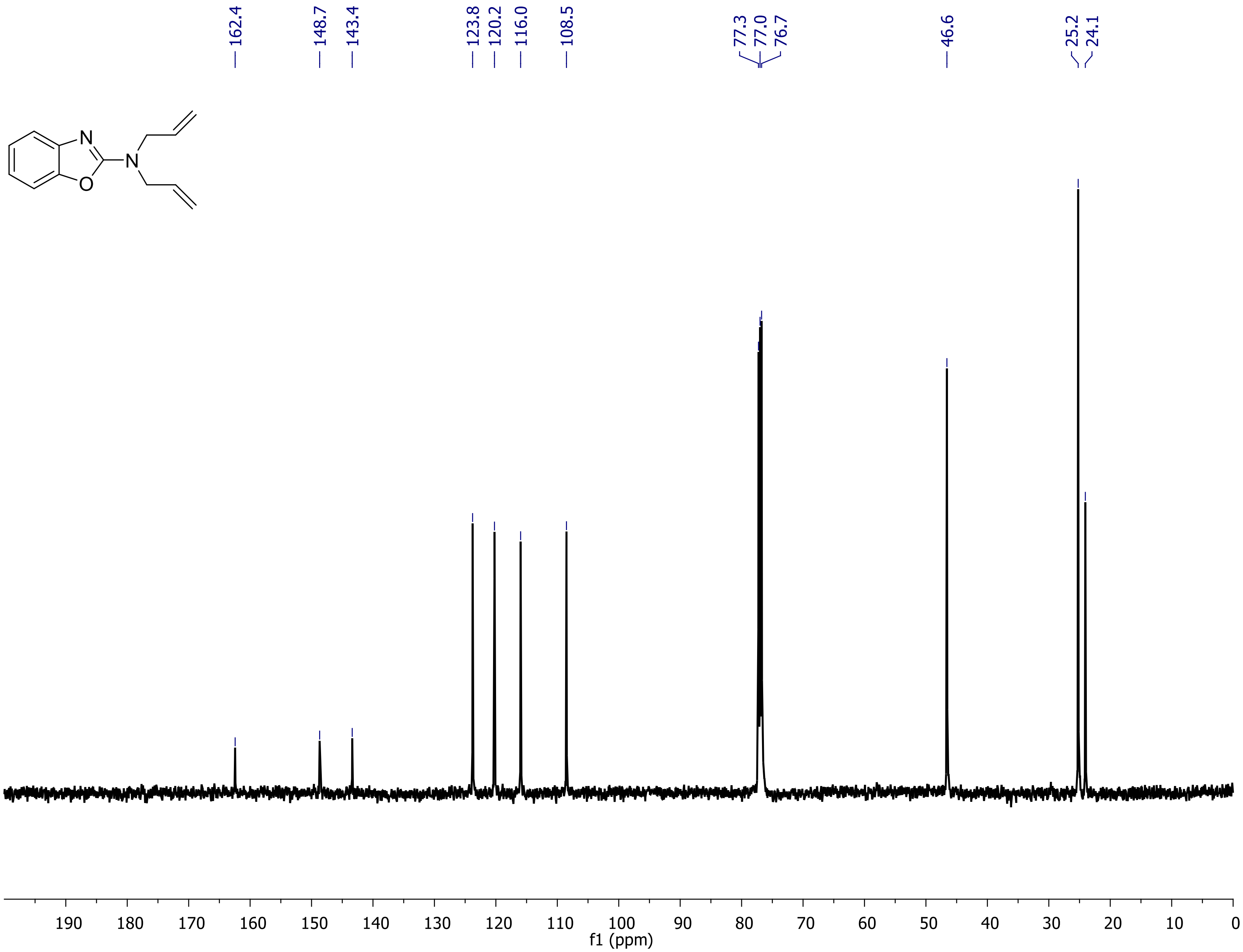
141.3
137.3
135.8
127.8
127.5
121.6
120.9
117.7
108.3
77.3
77.0
76.7
58.2
39.3
30.7
N
N
Me
N
Bn
Me
128.6
127.8
127.5
128.5
127.5
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

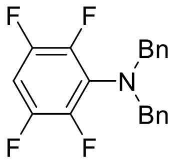

N
N
N
Me

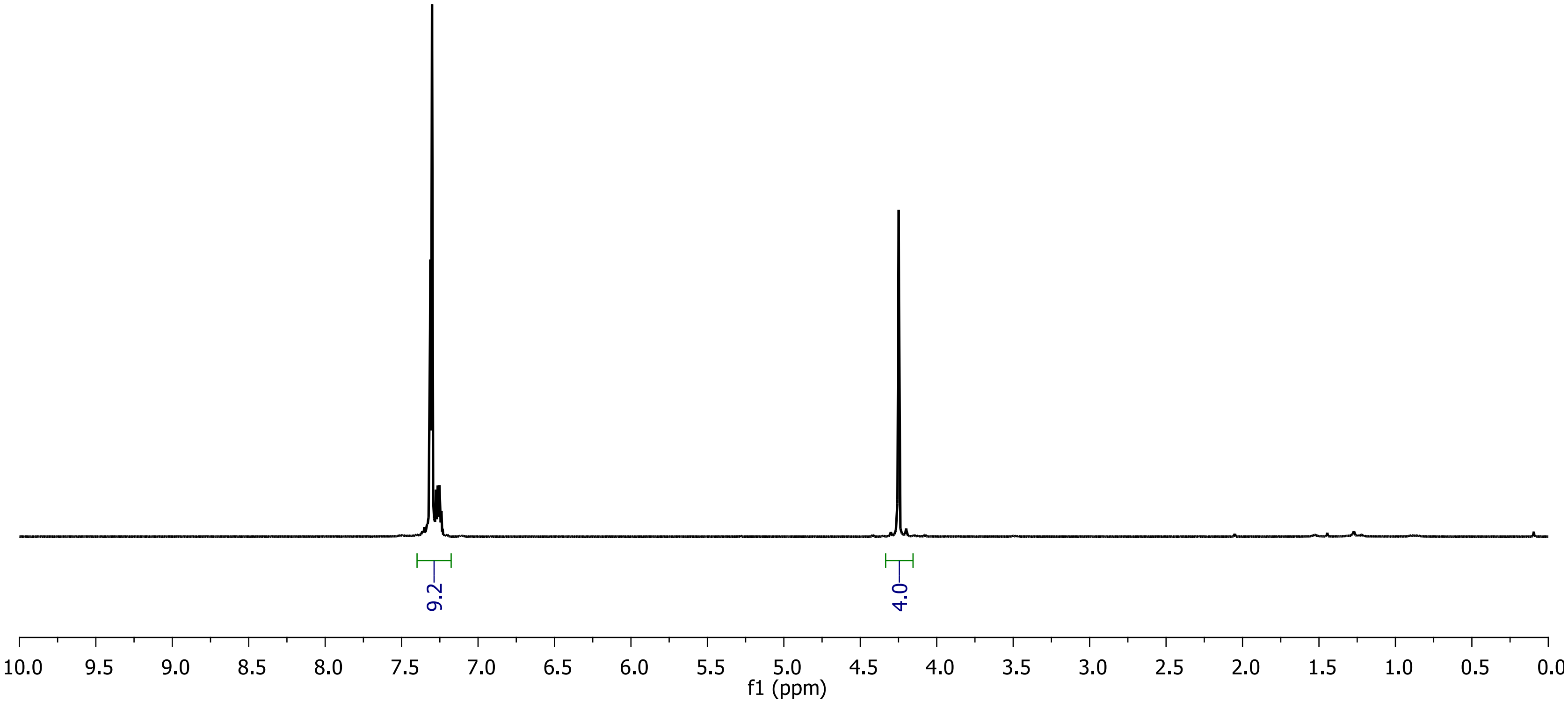

0.9
3.0
1.9
2.0
2.0
4.2
3.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

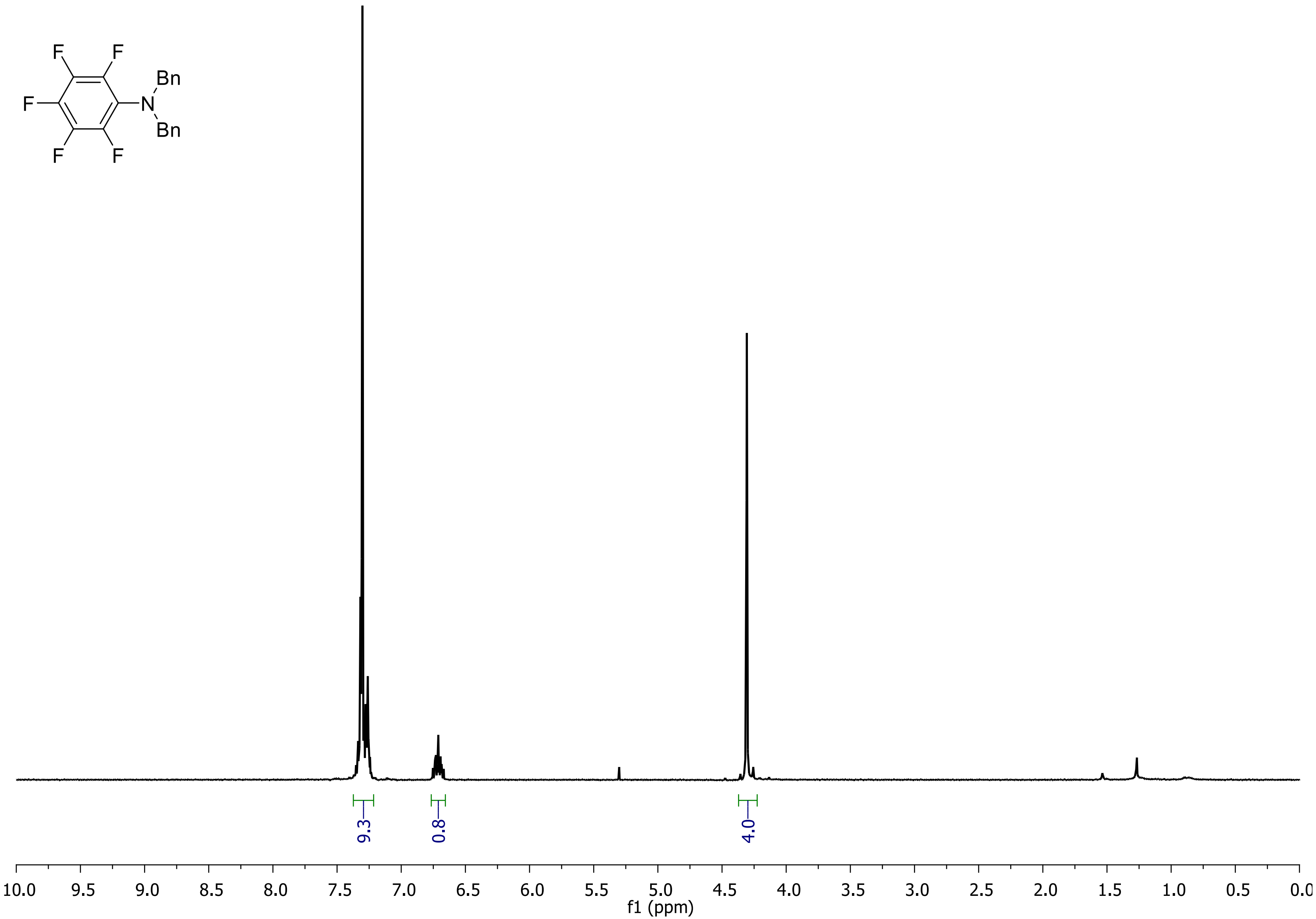

157.8
141.5
135.7
133.9
121.5
120.8
118.0
117.8
108.2
77.3
77.0
76.7
53.7
30.6
N
N
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

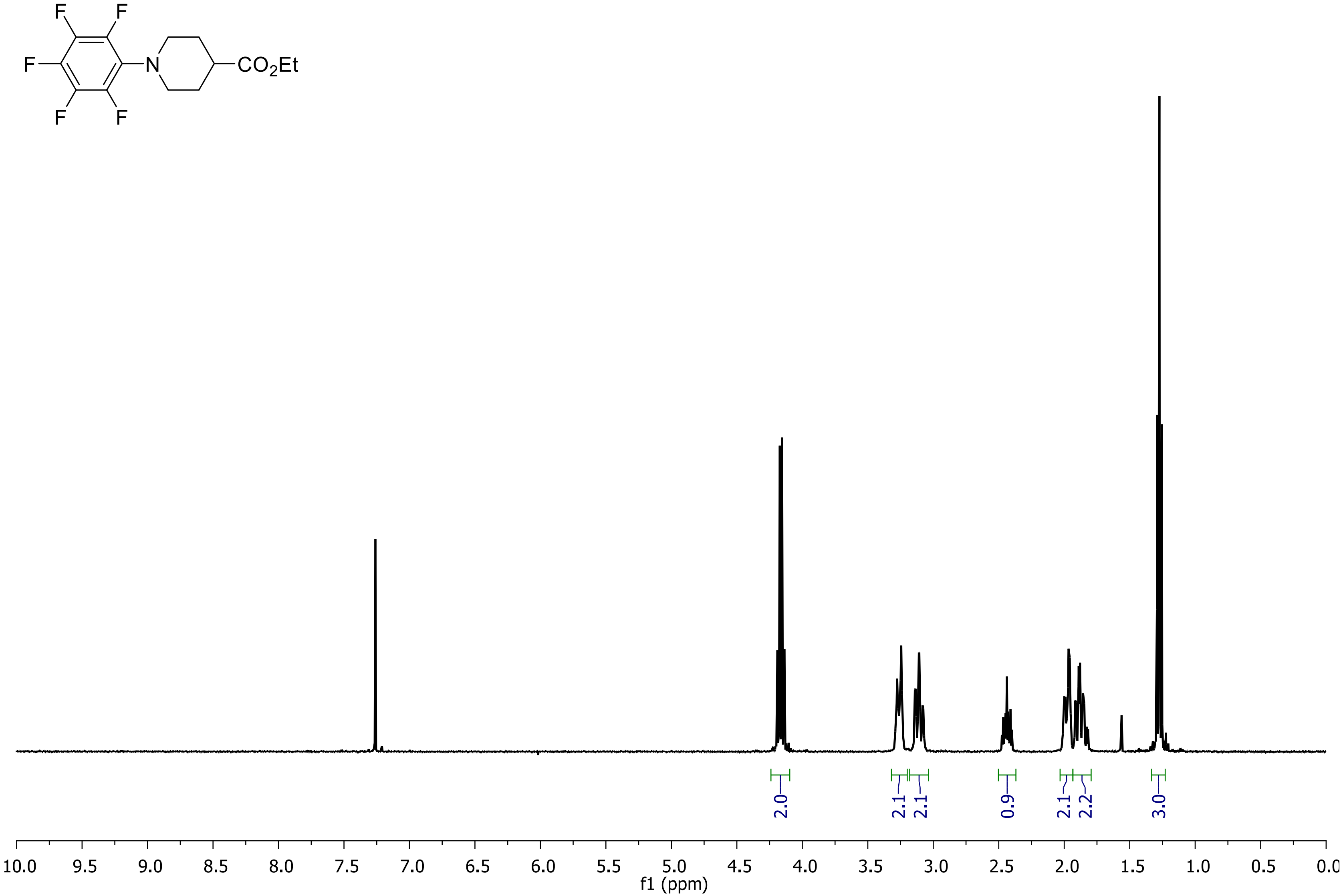

N
O
N
0.9
1.0
1.0
0.9
1.8
4.0
4.3
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

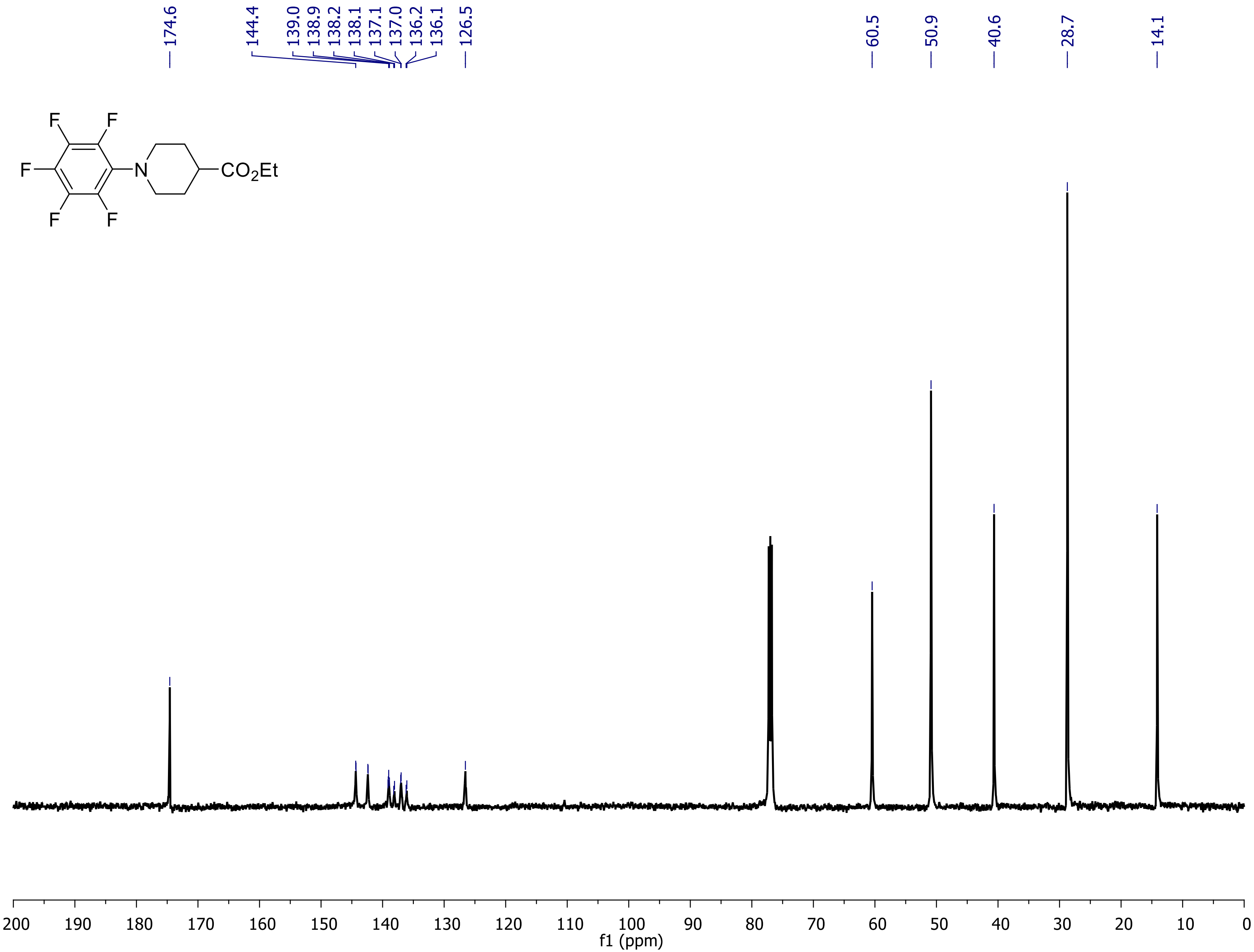

162.4
148.7
143.4
123.8
120.2
116.0
108.5
77.3
77.0
76.7
46.6
25.2
24.1
N
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

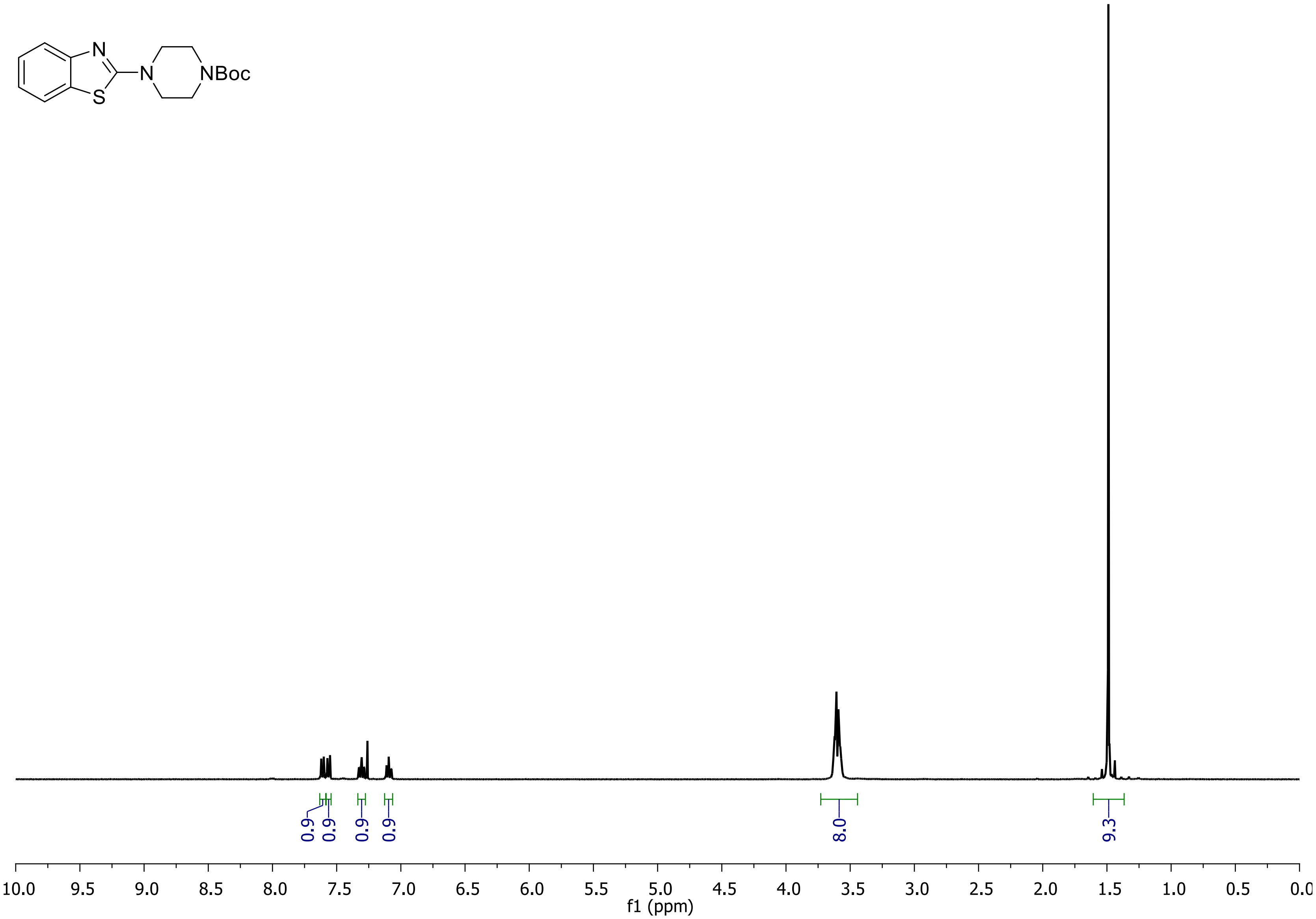

F
F
F
F
N
Bn
Bn

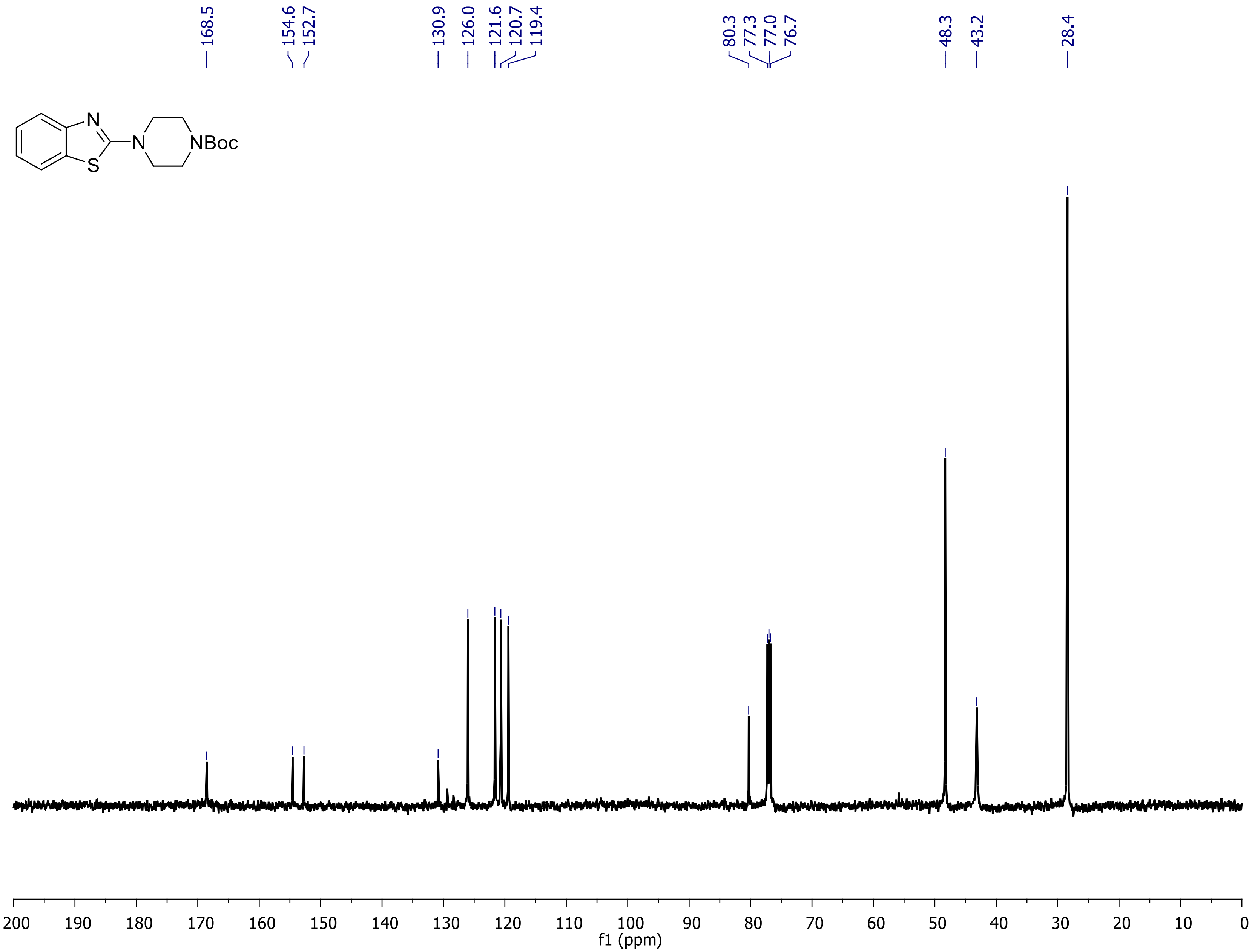

9.2
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

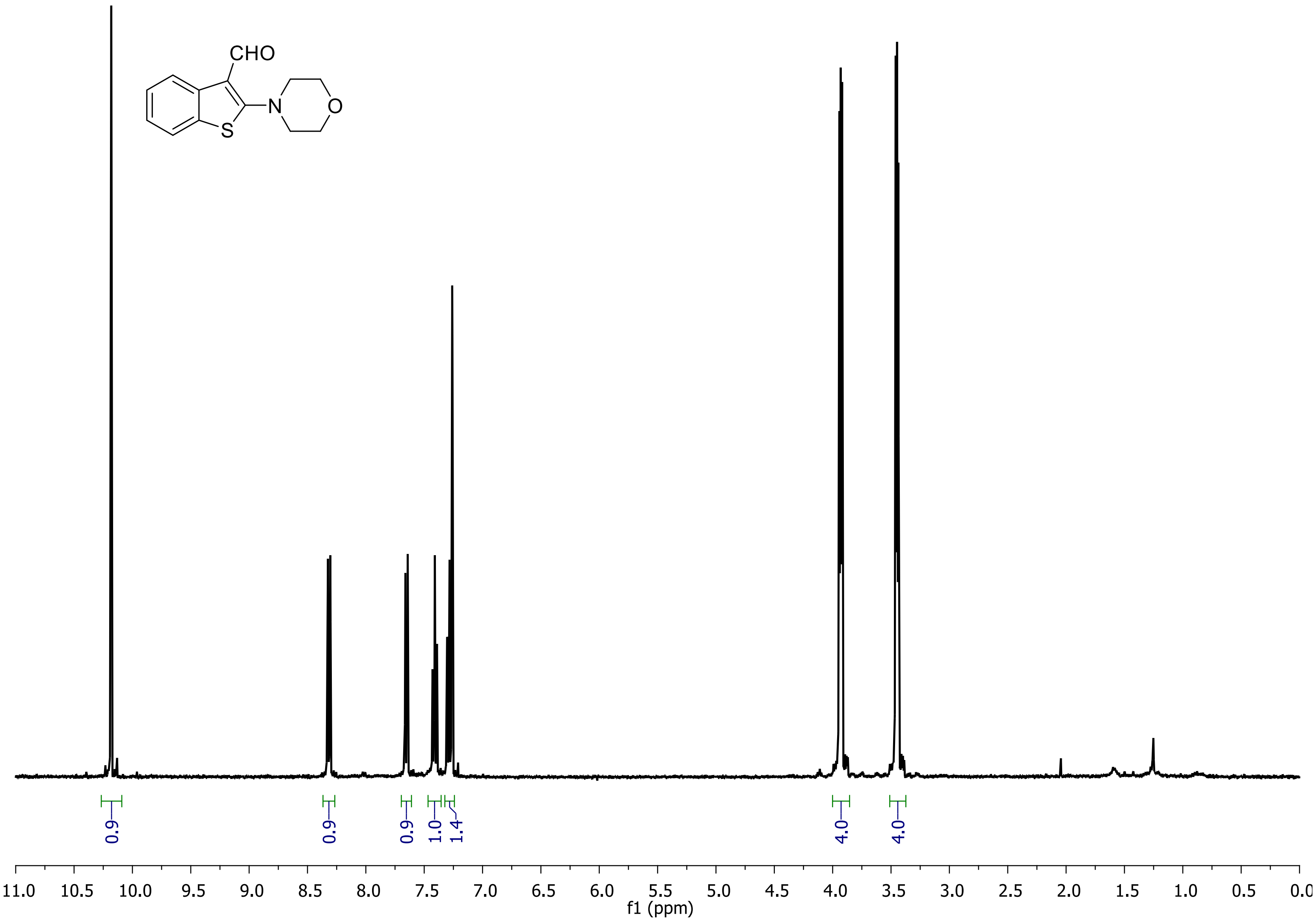

F
F
F
F
F
N
Bn
Bn
9.3
0.8
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

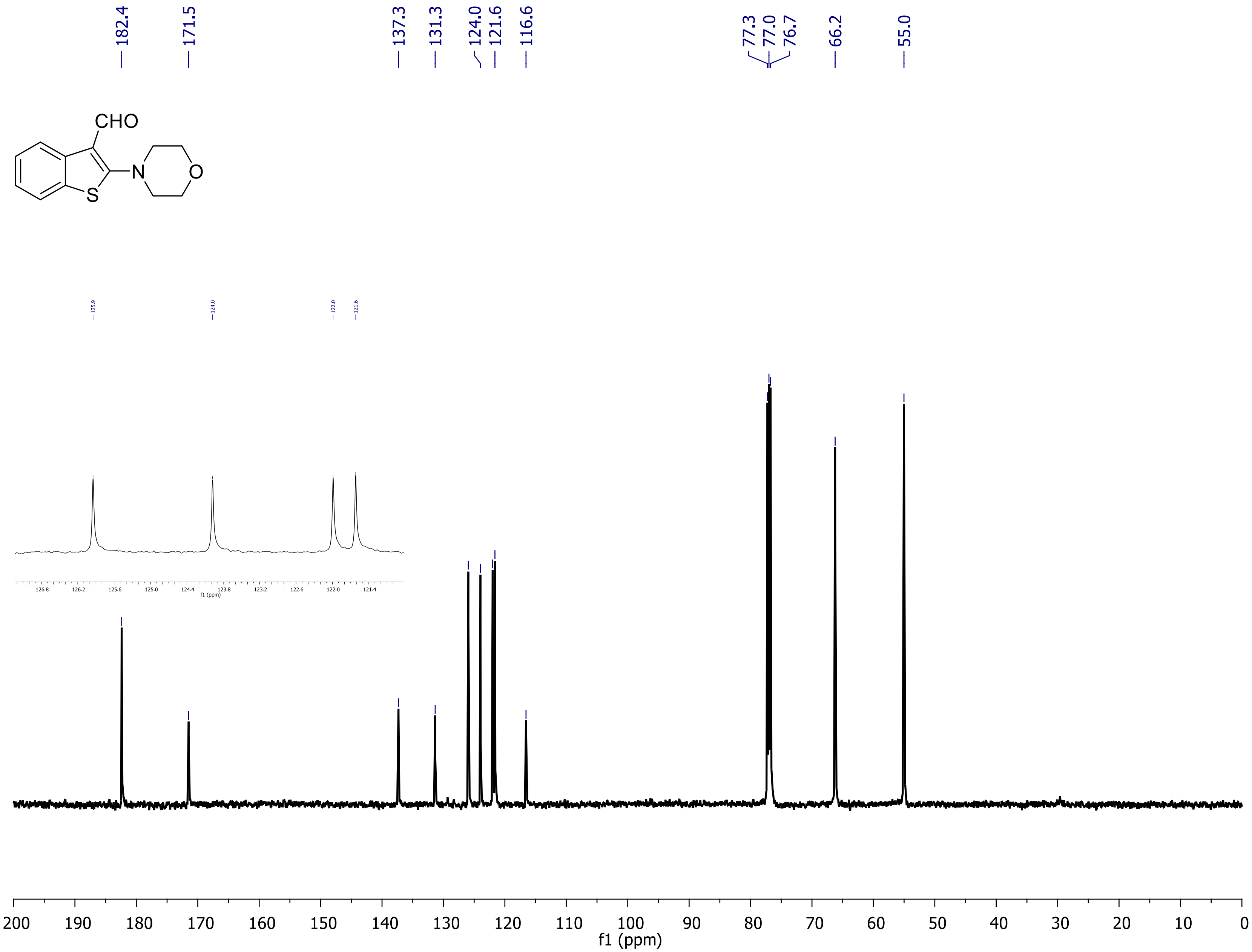

F
F
F
F
F
N
CO$_2$Et
2.0
2.1
2.1
0.9
2.1
2.2
3.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

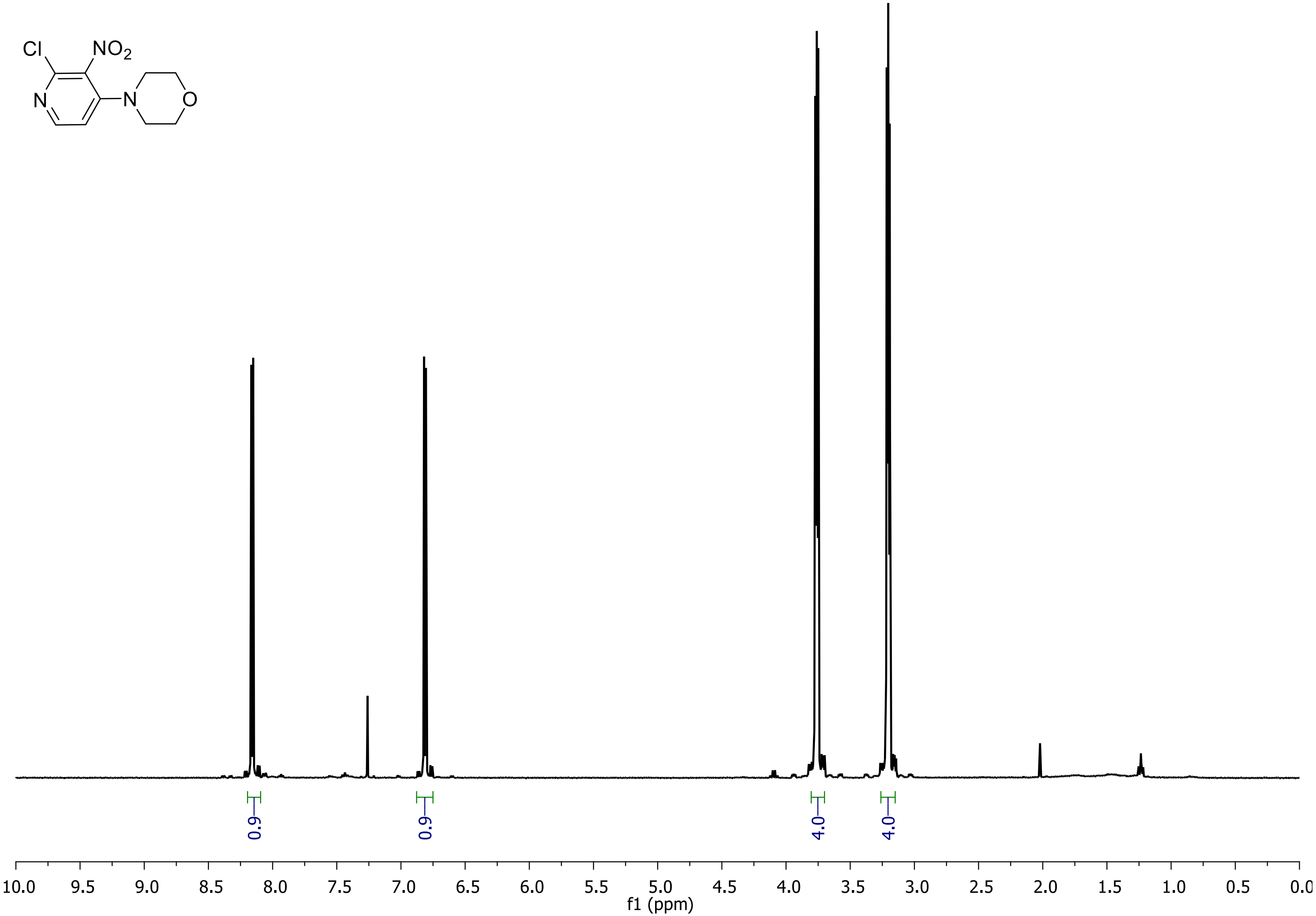

174.6
144.4
139.0
138.9
138.2
138.1
137.1
137.0
136.2
136.1
126.5
60.5
50.9
40.6
28.7
14.1
F
F
F
F
F
N
CO2Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

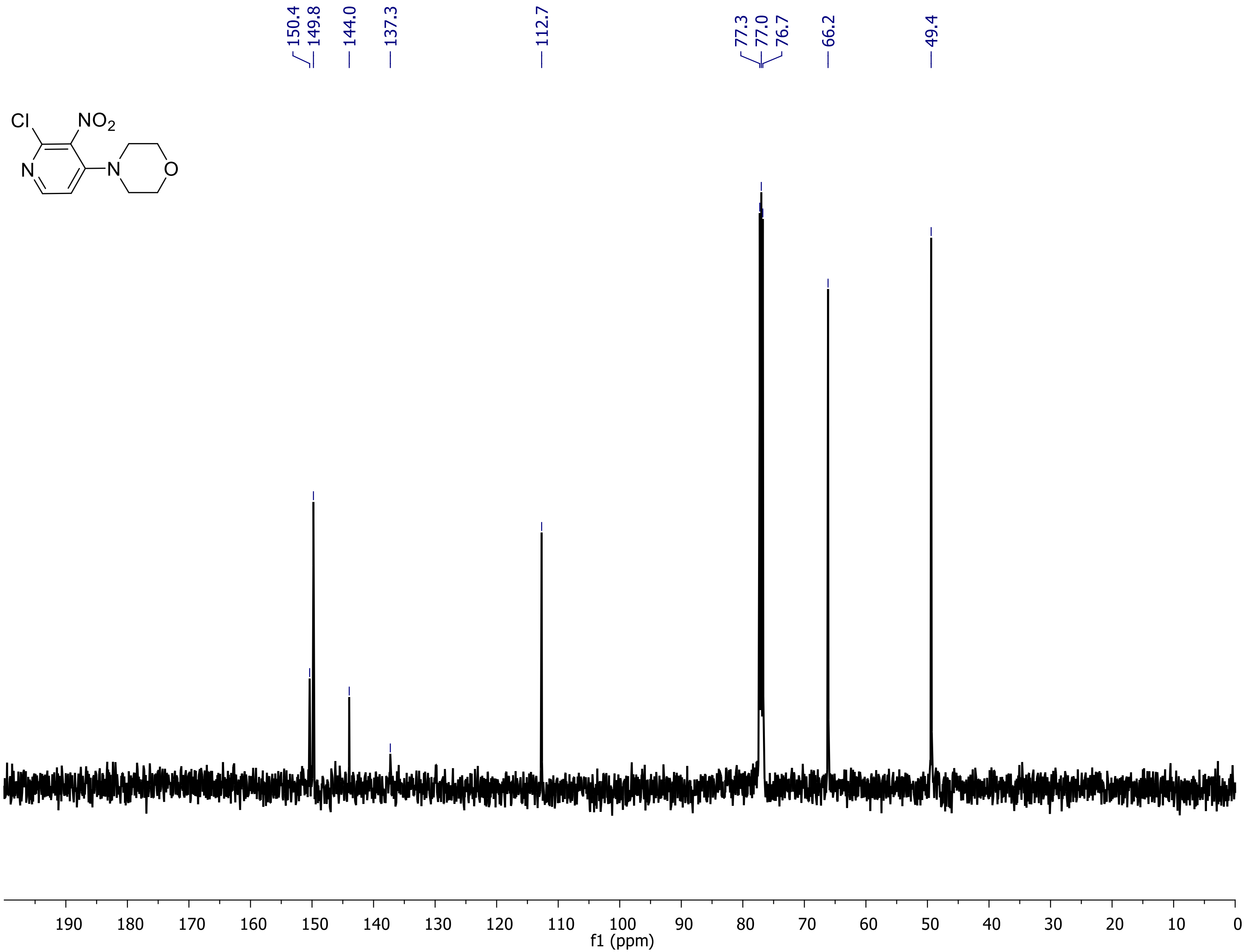

N
S
N
NBoc
0.9
0.9
0.9
0.9
8.0
9.3
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

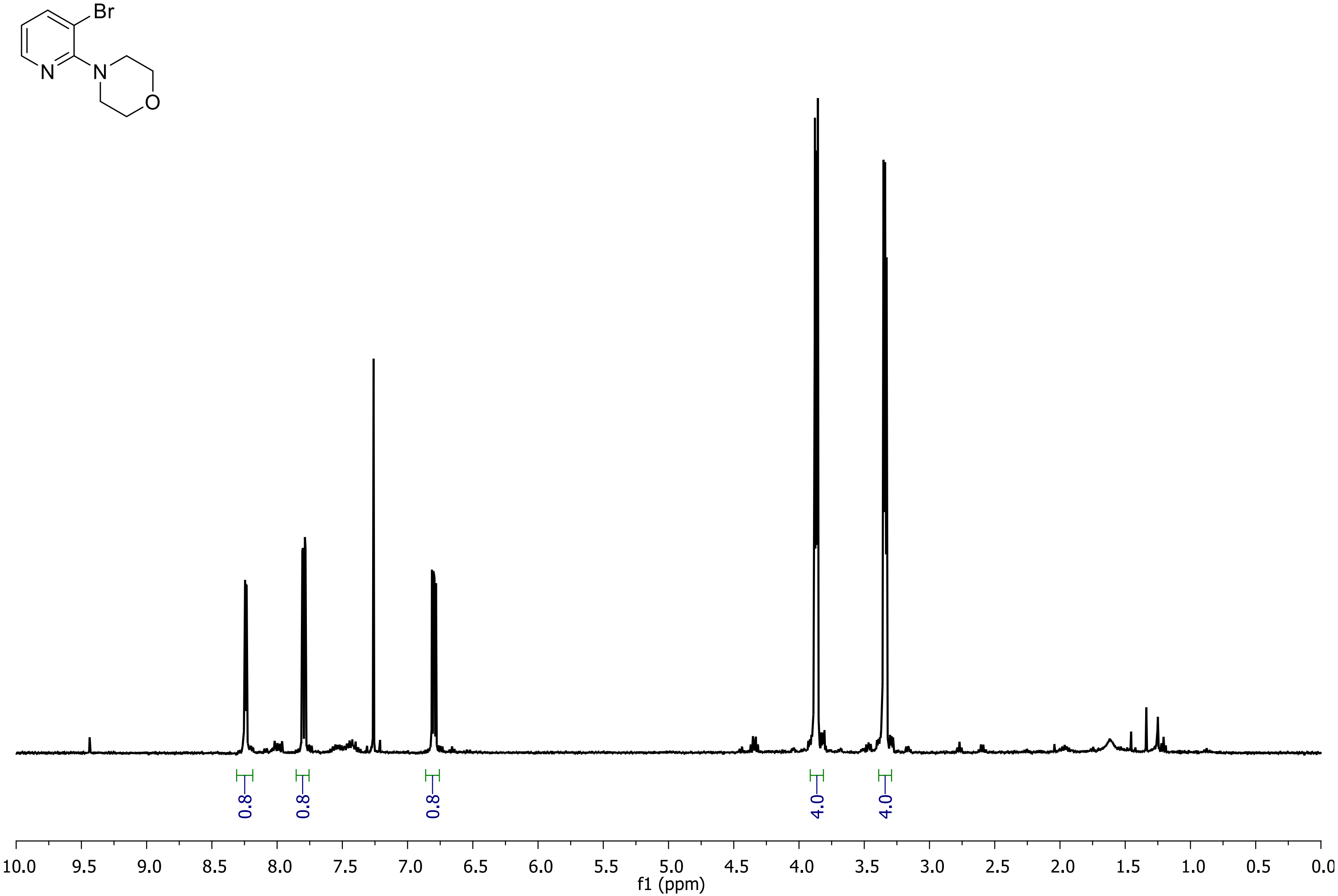

168.5
154.6
152.7
130.9
126.0
121.6
120.7
119.4
80.3
77.3
77.0
76.7
48.3
43.2
28.4
N
S
N
NBoc
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

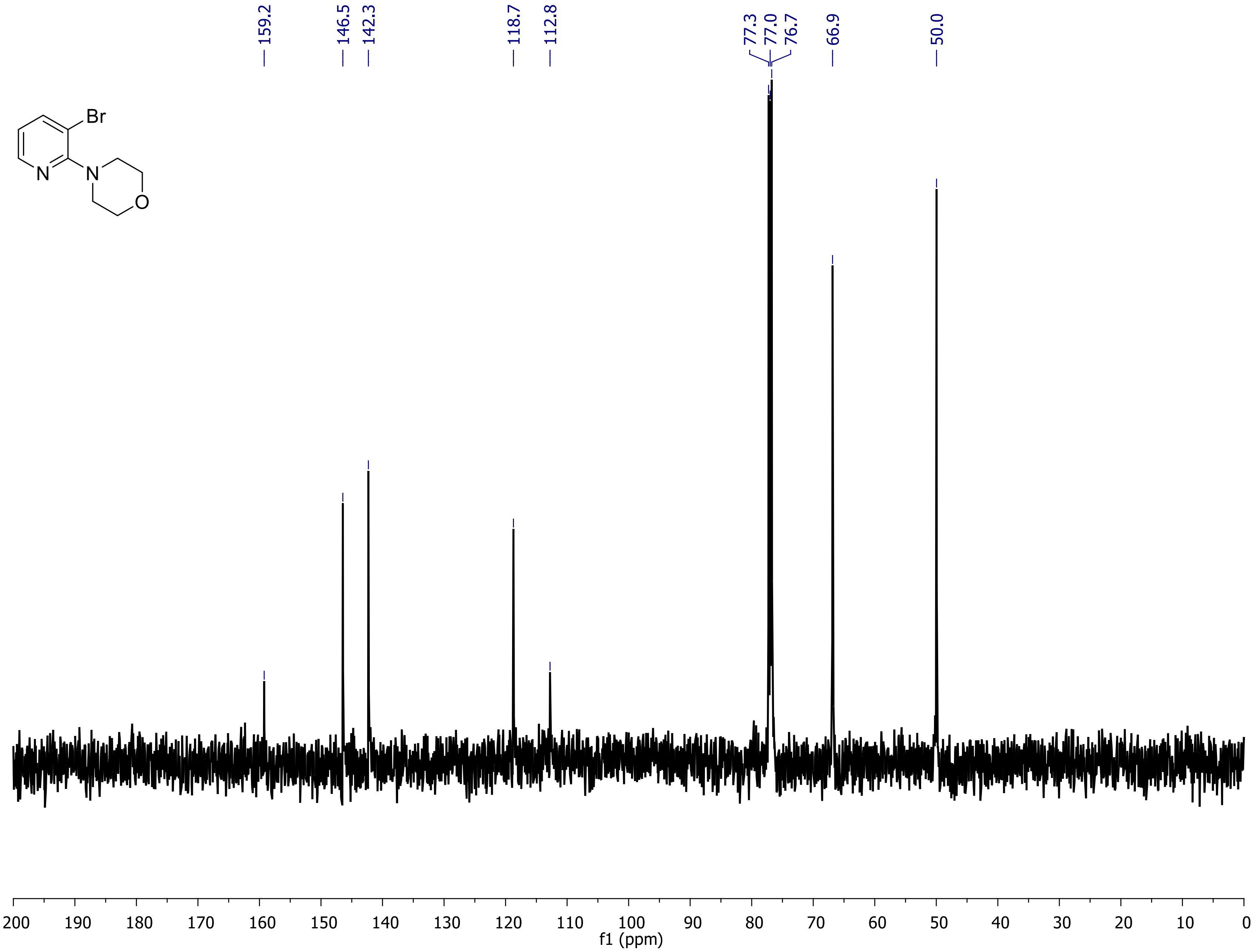

CHO
N
O
S
0.9
0.9
0.9
1.0
1.4
4.0
4.0
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

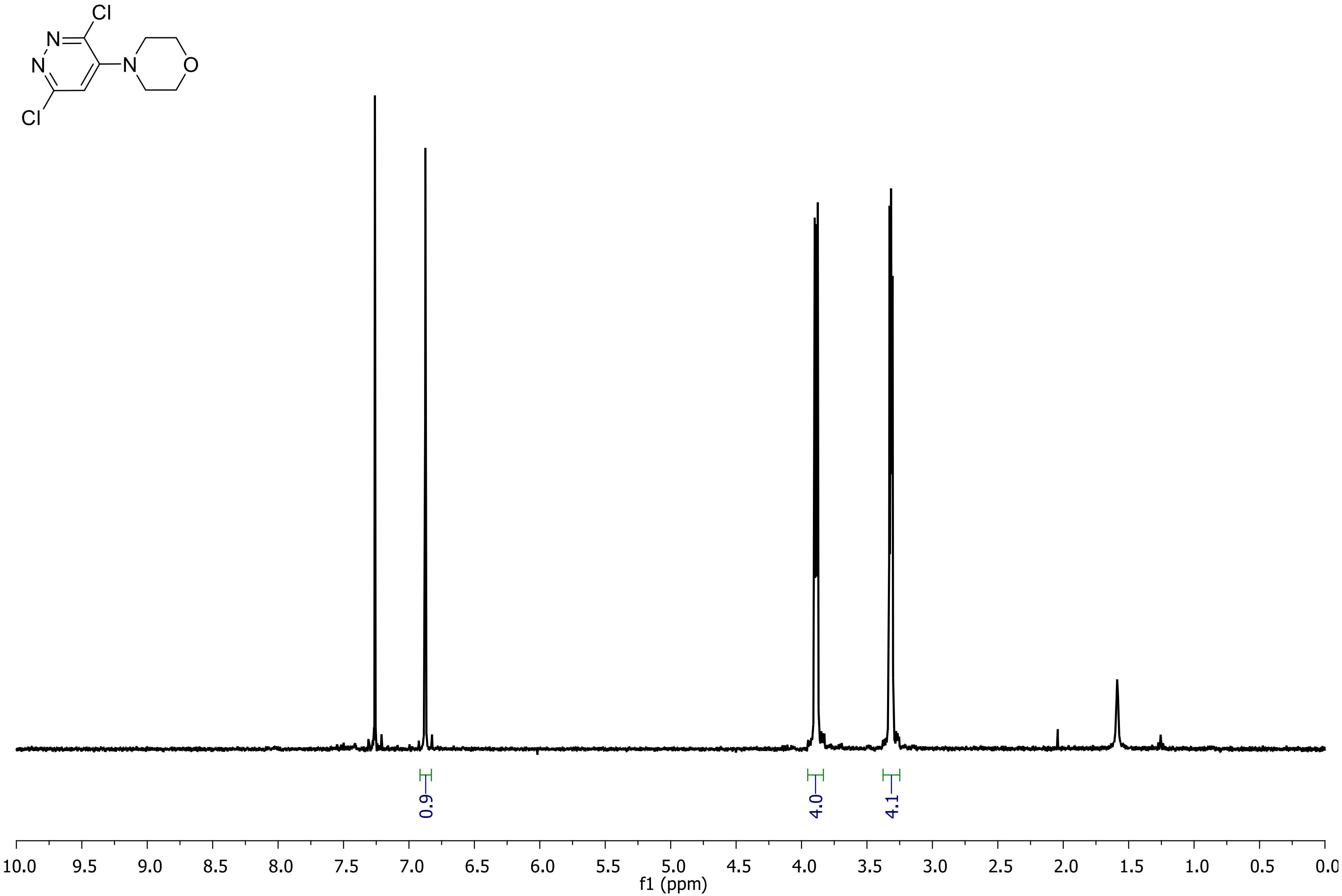

182.4
171.5
137.3
131.3
124.0
121.6
116.6
77.3
77.0
76.7
66.2
55.0
CHO
N
O
S
125.9
124.0
122.0
121.6
126.8
126.2
125.6
125.0
124.4
123.8
123.2
122.6
122.0
121.4
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

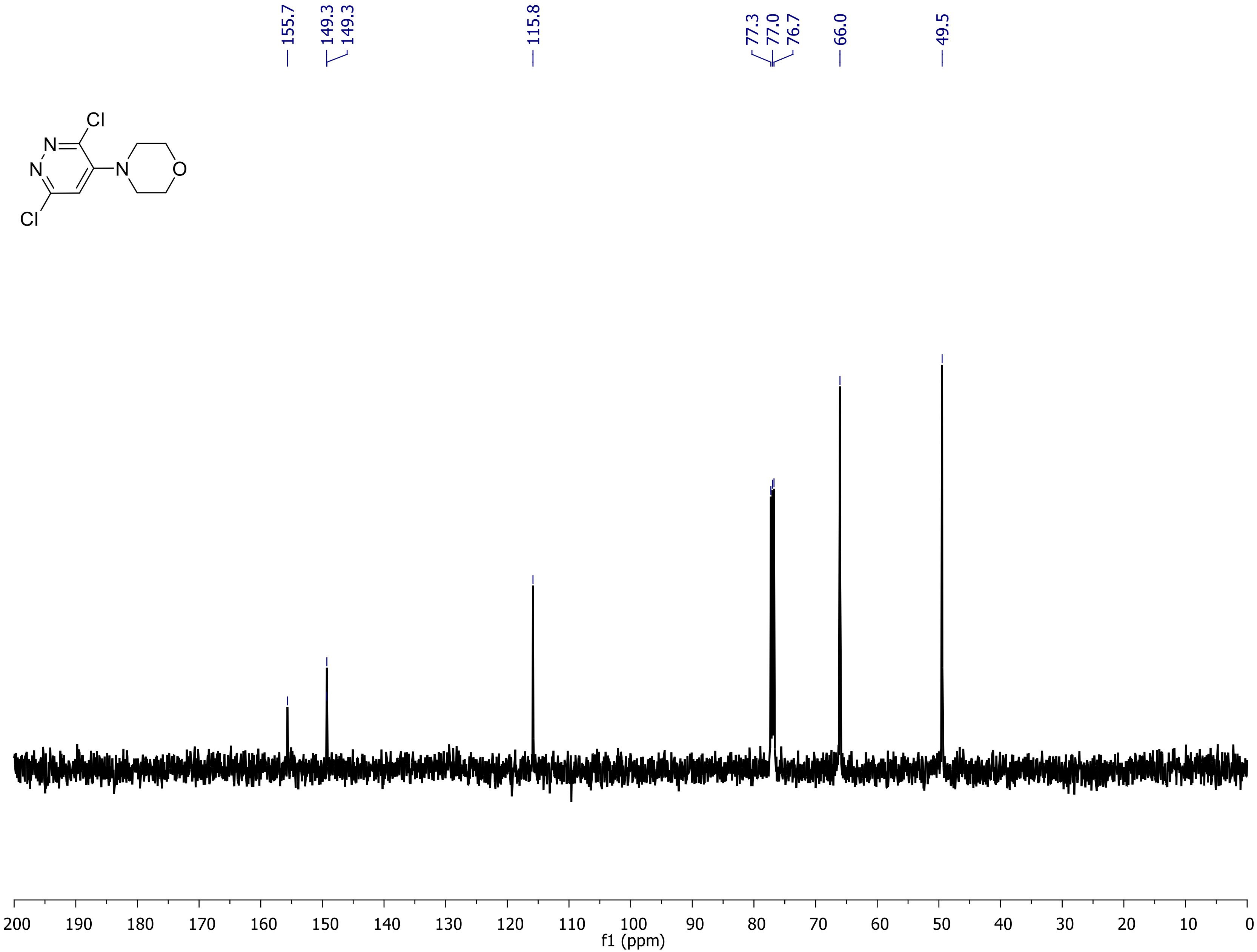

0.9
0.9
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

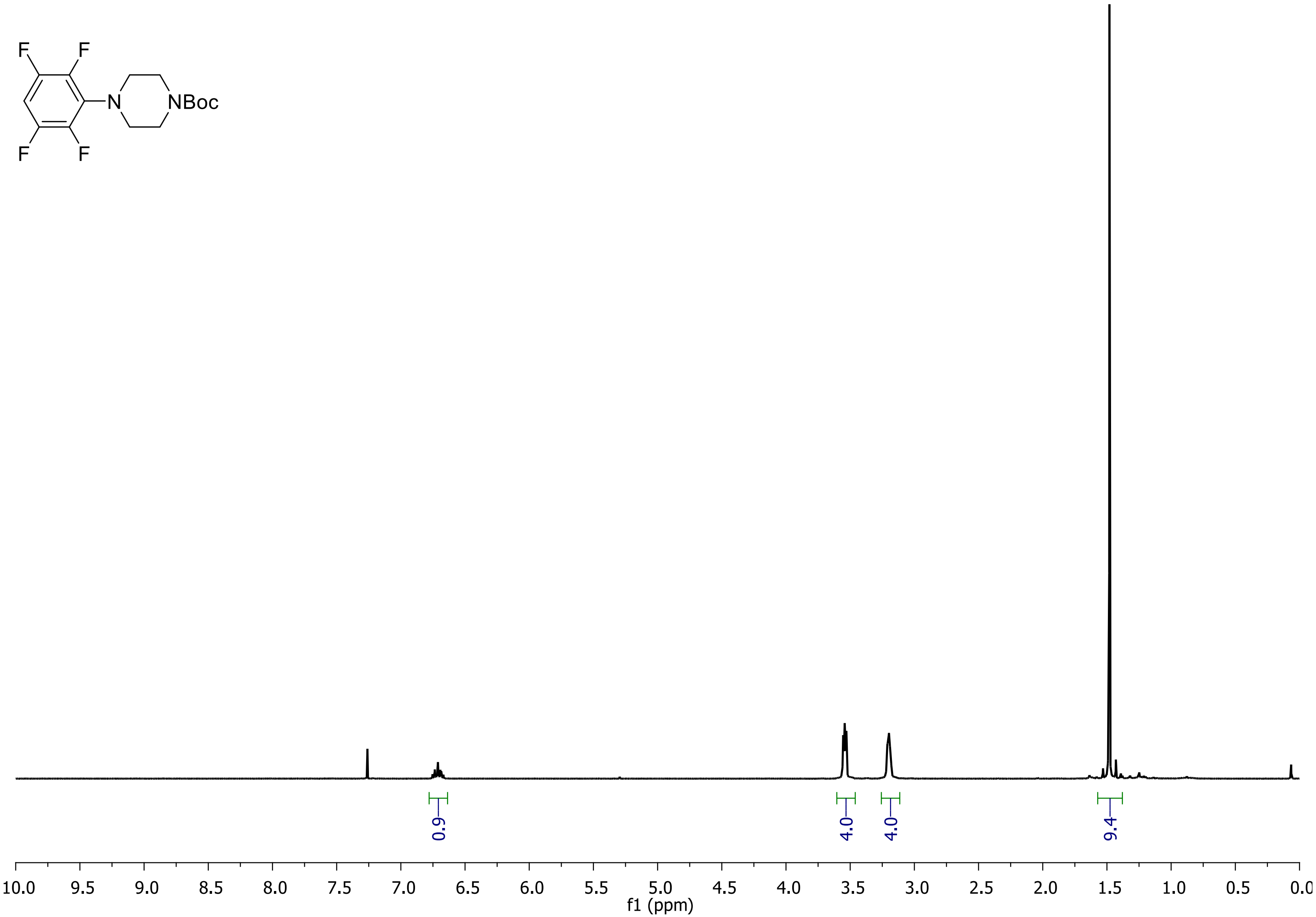

150.4
149.8
144.0
137.3
112.7
77.3
77.0
76.7
66.2
49.4
Cl
NO2
N
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

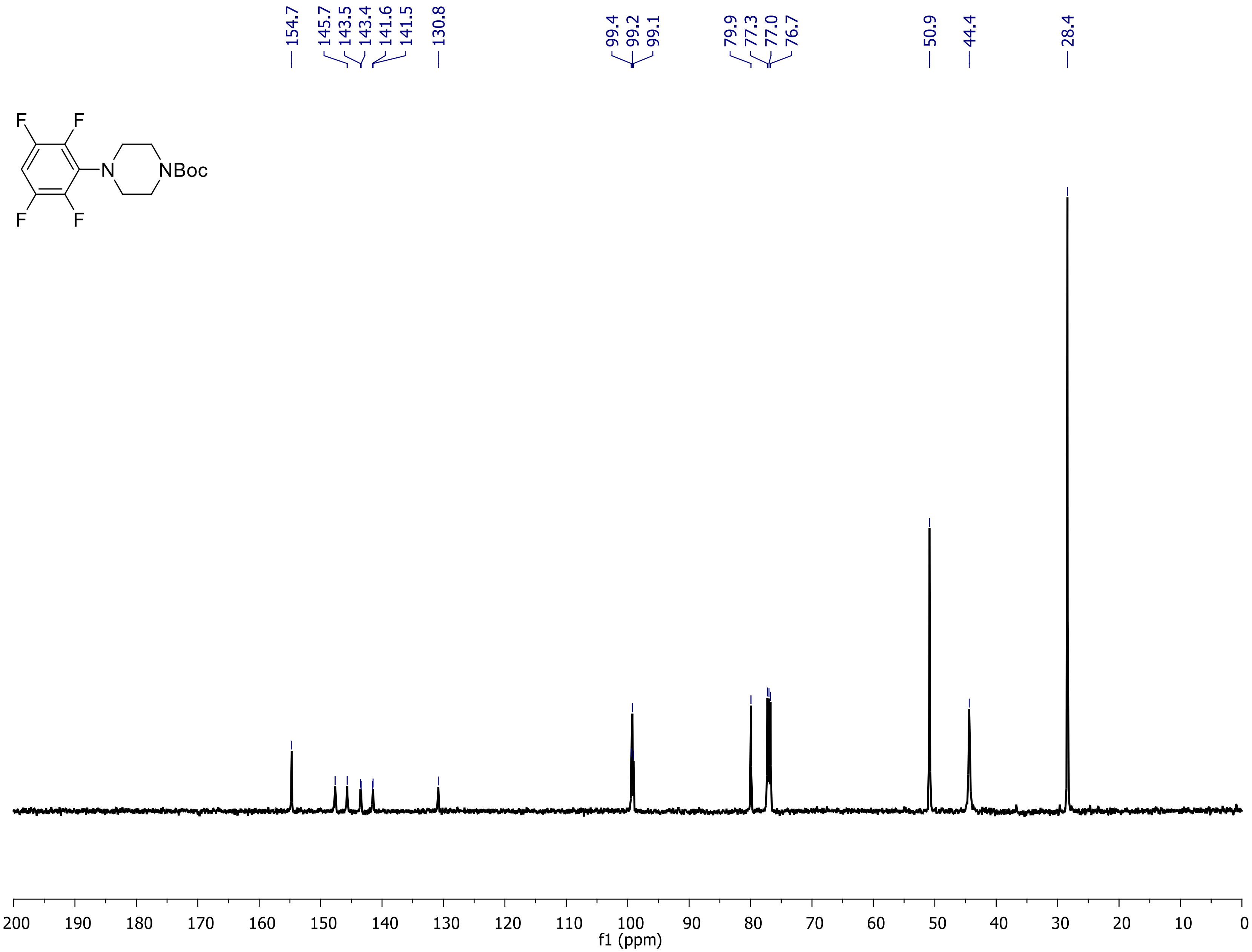

Br
N
N
O
0.8
0.8
0.8
4.0
4.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

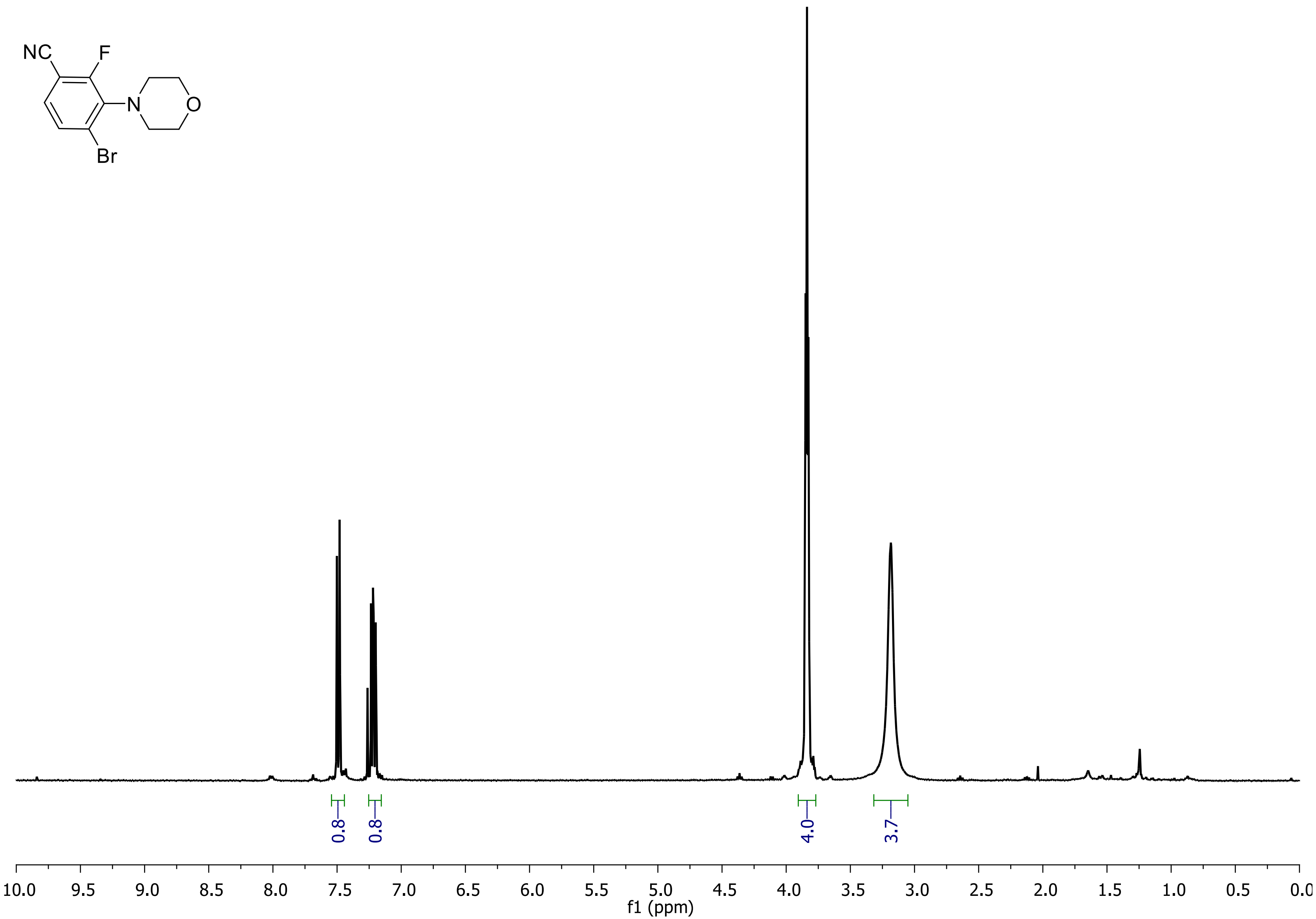

159.2
146.5
142.3
118.7
112.8
77.3
77.0
76.7
66.9
50.0
Br
N
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

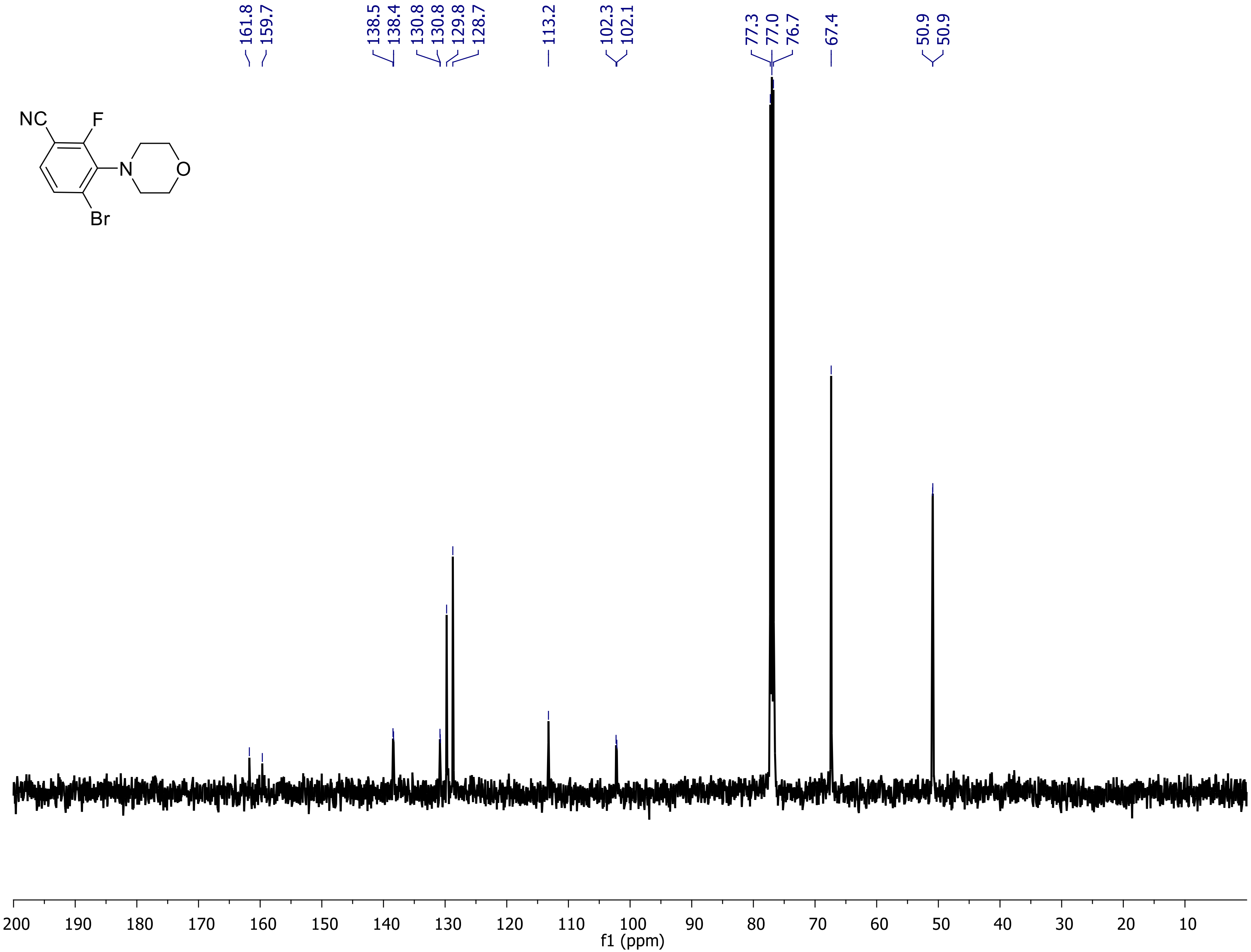

Cl
N
N
N
O
Cl
0.9
4.0
4.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

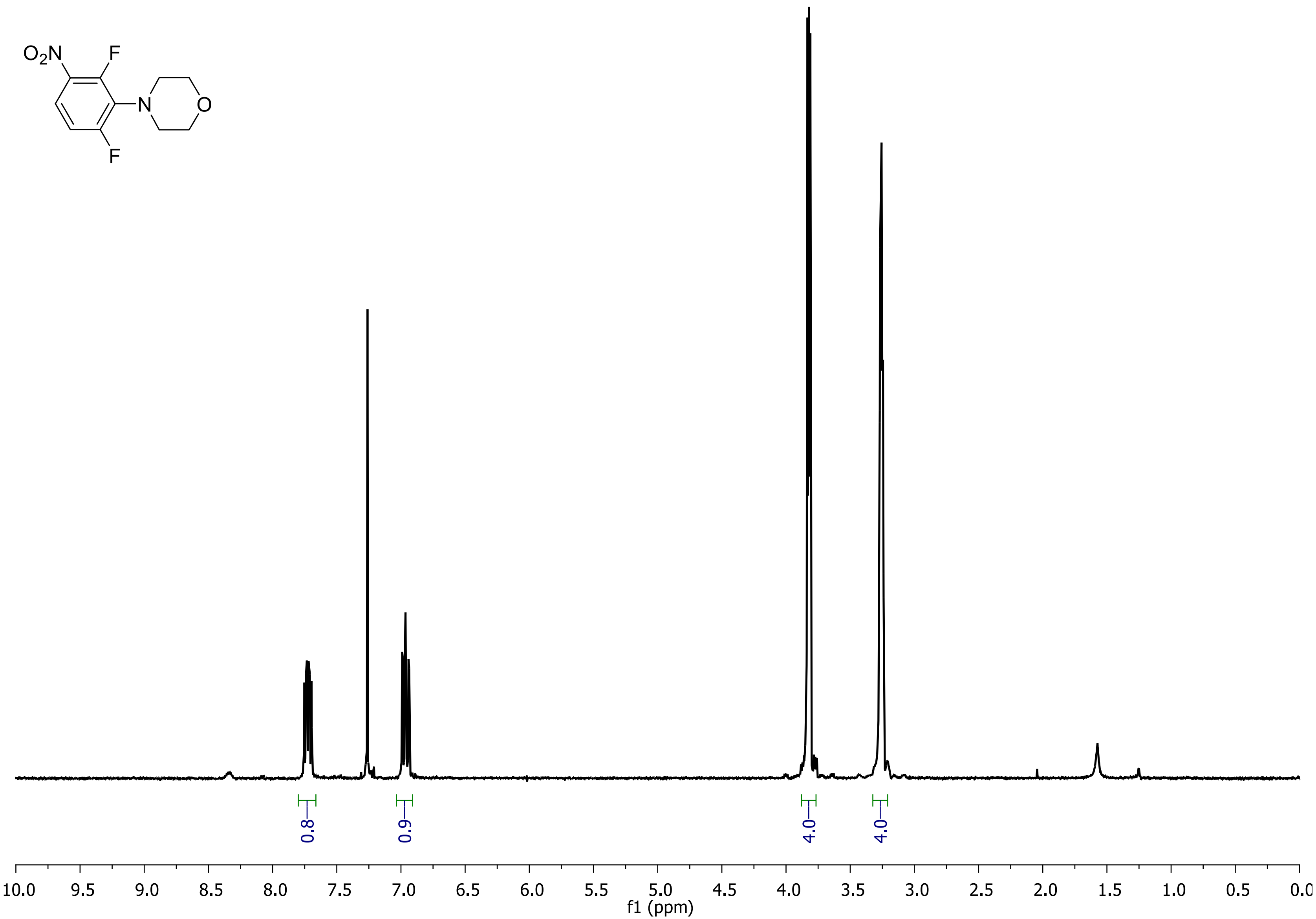

155.7
149.3
149.3
115.8
77.3
77.0
76.7
66.0
49.5
Cl
N
N
N
O
Cl
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

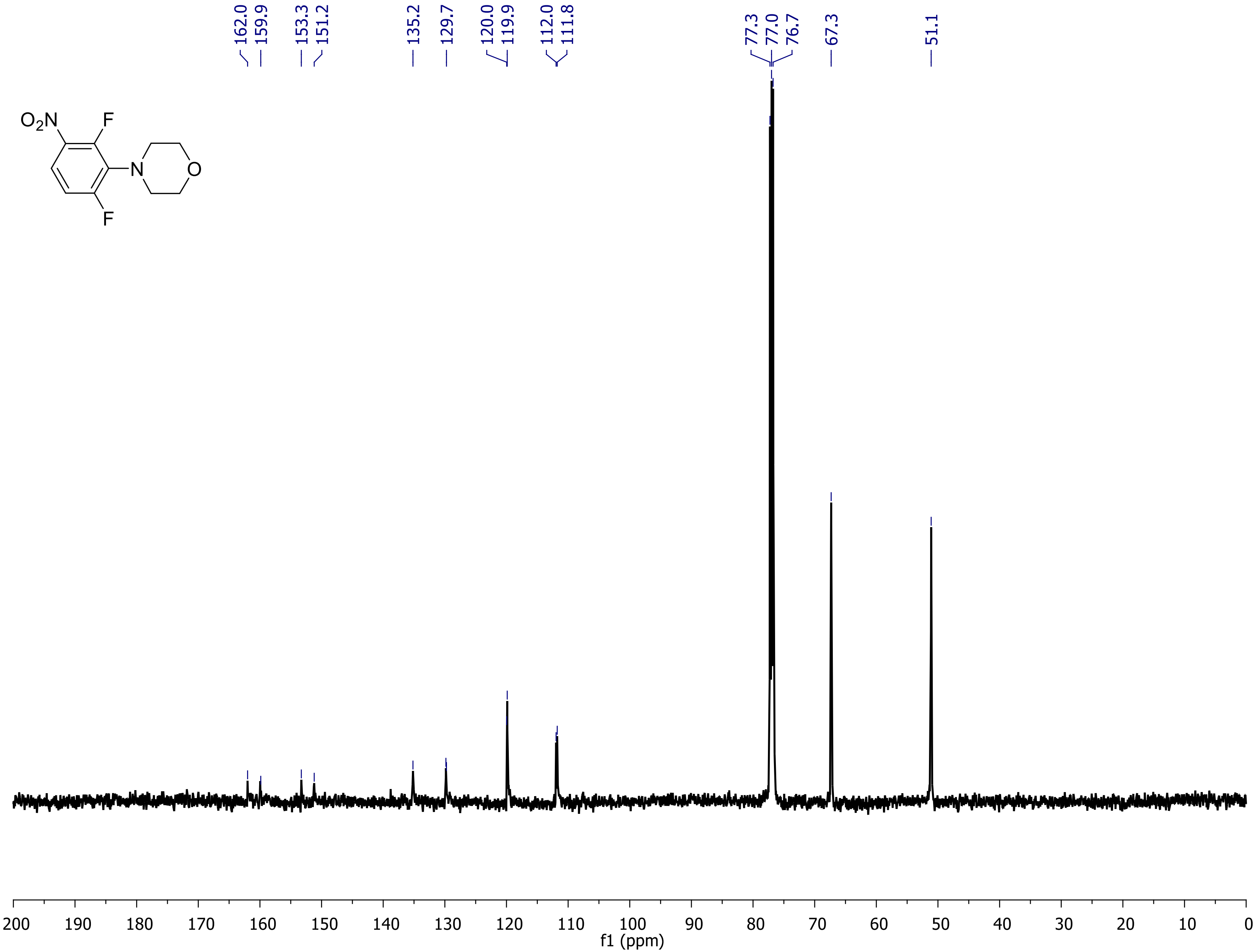

F
F
F
F
N
NBoc
0.9
4.0
4.0
9.4
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

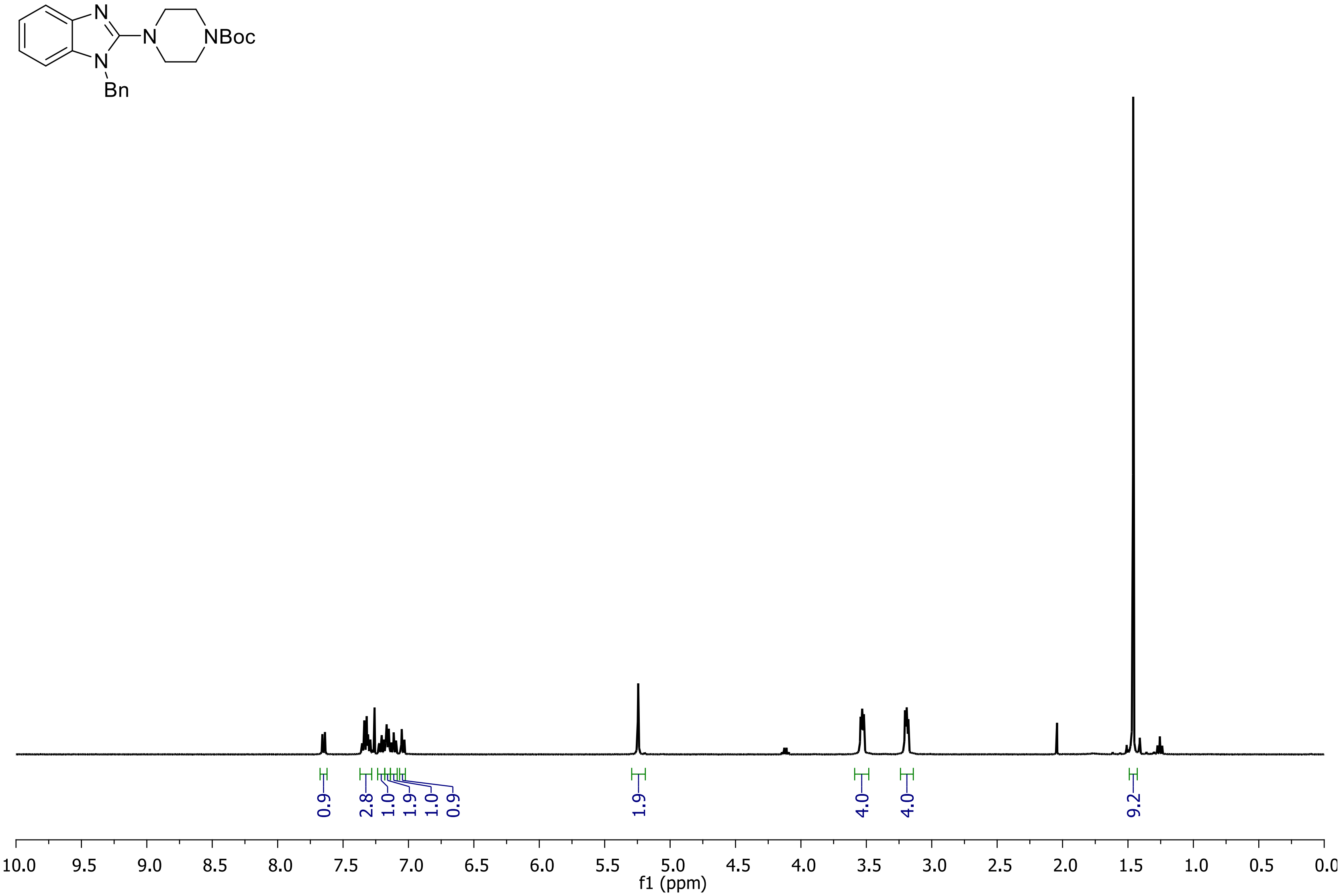

154.7
145.7
143.5
143.4
141.6
141.5
130.8
99.4
99.2
99.1
79.9
77.3
77.0
76.7
50.9
44.4
28.4
F
F
F
F
N
NBoc
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

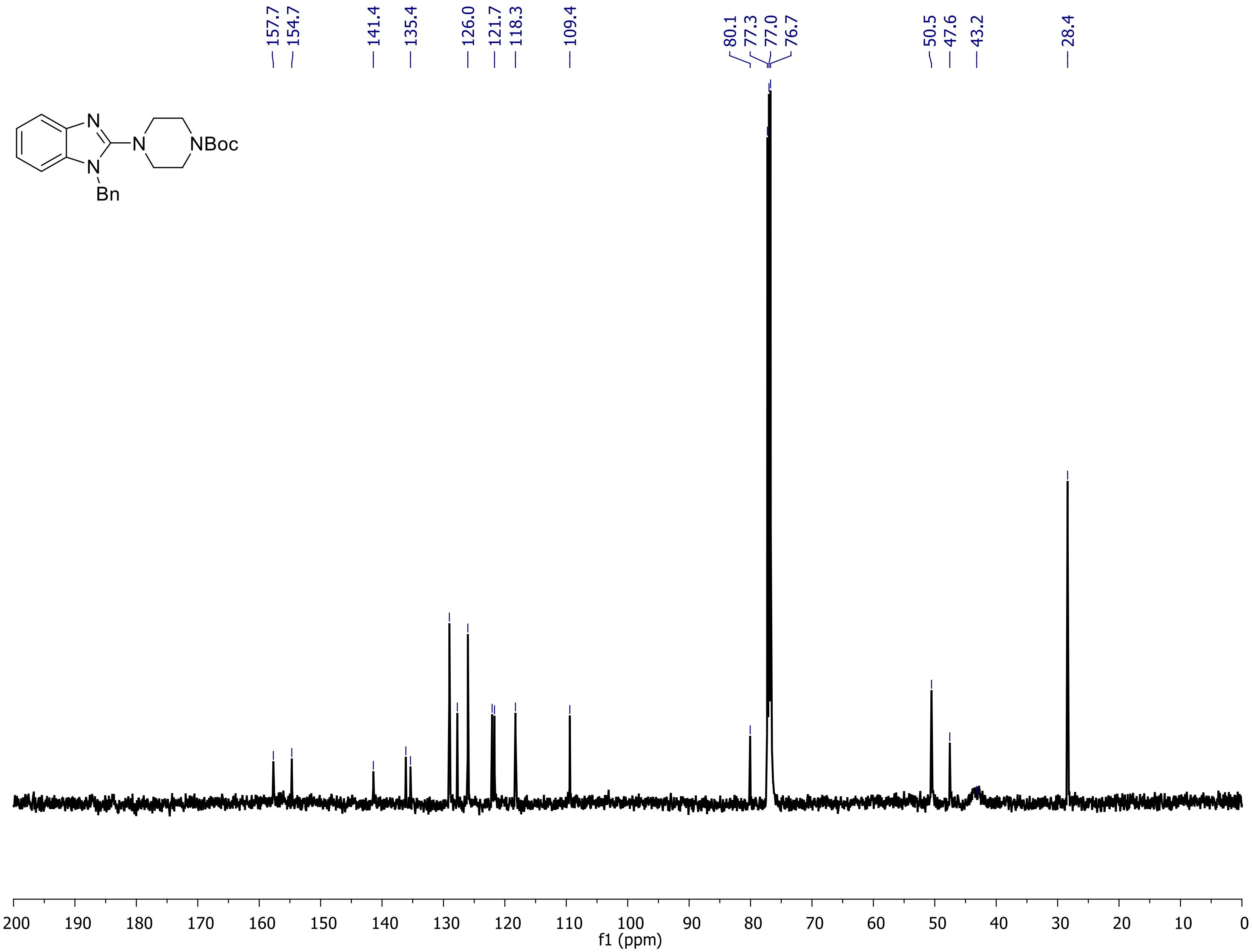

NC
F
N
O
Br
0.8
0.8
4.0
3.7
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

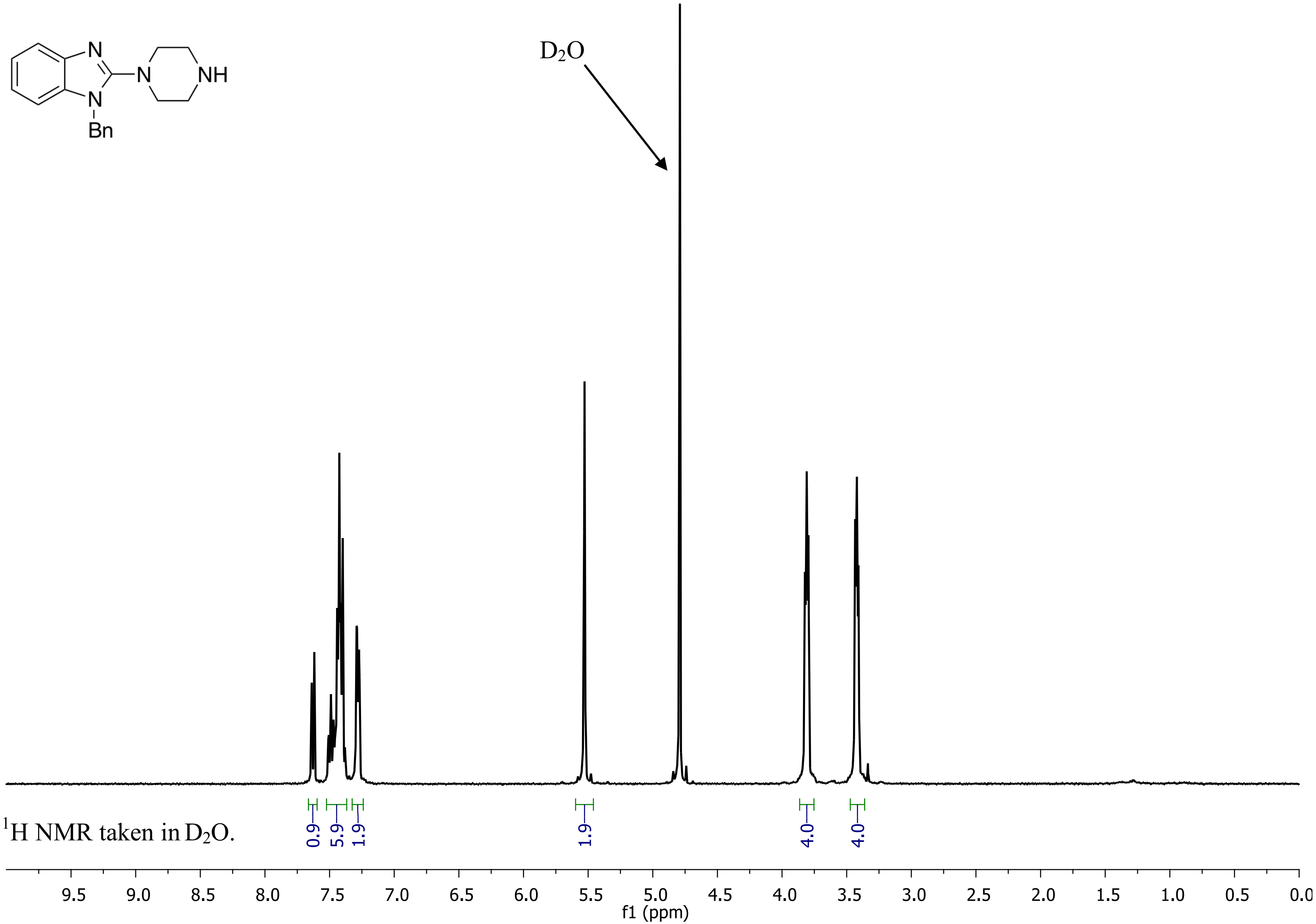

161.8
159.7
138.5
138.4
130.8
130.8
129.8
128.7
113.2
102.3
102.1
77.3
77.0
76.7
67.4
50.9
50.9
NC
F
N
O
Br
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
F
N
O
F
0.8
0.9
4.0
4.0
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)

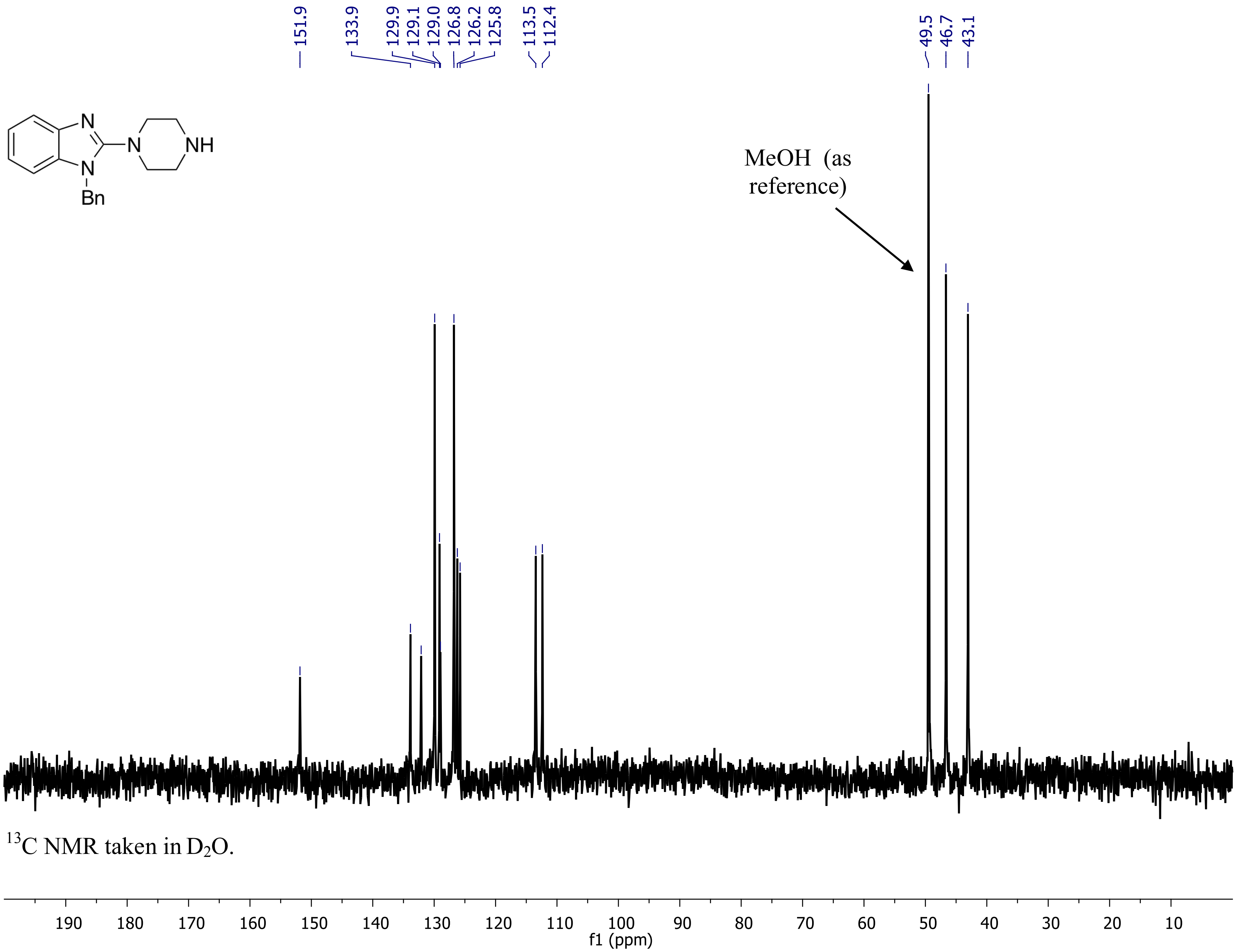

162.0
159.9
153.3
151.2
135.2
129.7
120.0
119.9
112.0
111.8
77.3
77.0
76.7
67.3
51.1
O_2N
F
N
O
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
N
N
NBoc
Bn
0.9
2.8
1.0
1.9
1.0
0.9
1.9
4.0
4.0
9.2
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)


157.7
154.7
141.4
135.4
126.0
121.7
118.3
109.4
80.1
77.3
77.0
76.7
50.5
47.6
43.2
28.4
N
N
N
NBoc
Bn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



^{1}H NMR taken in D_2O.



^{13}C NMR taken in D_2O.