Supporting information for

3-Amino-Chromanes and Tetrahydroquinolines as Selective 5-HT_{2B}, 5-HT_7, or σ_1 Receptor Ligands

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General Chemical Synthesis Information:

Azide Precautions: Organic and inorganic azides are known to be high-energy materials and explosions have been reported with their use.[1] All of the azides reported herein were synthesized without incident; however, several precautions were taken. First, all azides synthesized herein have a C/N ratio of ≥ 3:1. Second, reactions with more than 1 mmol of azide were placed behind safety shields both in the fume hood and during rotary evaporation. Third, all waste solutions (both organic and aqueous) that could be contaminated by azide were kept segregated in specially labeled containers and were kept STRICTLY free of acid to prevent incidental formation of HN_3.

General Chemical Synthesis: All reactions sensitive to air or moisture were carried out in oven-dried glassware using standard Schlenk line techniques or were conducted using a glovebox (details are provided below). All reactions were mixed by magnetic stirring (100-600 rpm). All reactions conducted at elevated temperatures used aluminum block heating with an external thermocouple. Dry DCM and THF were obtained from a commercial solvent purification system using activated alumina columns and stored under a positive pressure of argon. Other reagents and solvents were purchased from commercial suppliers and were used as received. Reactions were monitored by gas chromatography or thin layer chromatography (TLC) using pre-coated plastic plates impregnated with a fluorescent indicator (254 nm). Visualization was carried out with UV light (254 nm), $KMnO_4$, ninhydrin, or PMA stains. Column chromatography was performed using a Teledyne Isco CombiFlash R_f purification system utilizing normal phase pre-column load cartridges and gold high performance columns.

Instrumentation for Chemical Synthesis: All proton (^1H) NMR spectra were recorded at 400 or 500 MHz on a Bruker spectrometer. All carbon (^{13}C) NMR spectra were recorded at either 101 or 126 MHz on a Bruker spectrometer. Chemical shifts are expressed in ppm and are referenced to residual solvent as an internal standard (^1H: $CHCl_3$, 7.27 ppm, ^{13}C $CDCl_3$, 77.2 ppm). Infrared (IR) spectra were performed as a film on NaCl plates on a Nexus 670 FT-IR and are reported in cm^{-1}.

Note: Compounds are identified via a "number-letter" format (eg compound **4d**). For organizational convenience, compounds derived from the same starting material have the same letter designation (e.g. all compounds derived from 4-phenylphenol are denoted "**#f**"). Precursor compounds **1**, **2**, and **5-9** of substrate families **a-c**, **e**, **j-l**, **n**, and **o** were synthesized in a previous publication. Synthetic methods and characterization data for those compounds can be found in that paper.[2]

General Cellular Assay Information:

Biological Activity Assay: Compounds were assayed for biological activity at the Psychoactive Drug Screen Program via a two tiered system: an initial screen against receptors at 10 μM concentration, followed by a secondary assay to determine K_i values for compounds that exhibited over 50% activity in the primary assay.[3] Compounds were shipped to the PDSP as neat oils or solids.

Compound Preparation for Cellular Assays: 4j was prepared in 20% DMSO in 0.01 M phosphate buffered saline (PBS) and 18% 1M HCl; (+)-pentazocine (PTZ) (sourced from Sigma-Aldrich) was prepared in 10% DMSO in 0.01 M PBS and 6% 1M HCl; tert-butyl hydroperoxide (tBHP) [5.5 M in decane] (sourced from Sigma-Aldrich) was dissolved in 0.01 M PBS.

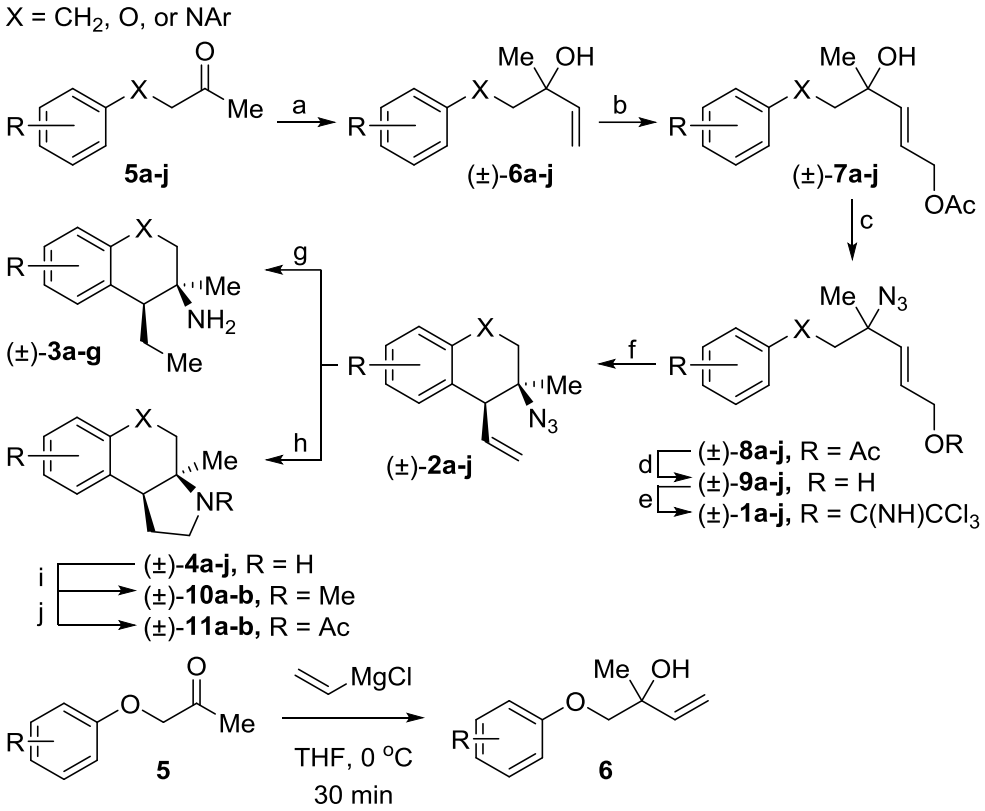
Cell Culture and Cell Viability: 661W cells, obtained from Dr. M. Al-Ubaidi (Univ. of Houston), express blue and green cone pigments, transducin and cone arrestin characteristic of

cone photoreceptor cells.[4] They were cultured in Dulbecco's modified Eagle's medium (DMEM, Thermo Fisher Scientific, Waltham, MA) supplemented with 5% FBS for regular culture or 1% FBS for treatment, and 100U/mL penicillin, 100µg/mL streptomycin. The cells were treated with tBHP [55 µM] to induce oxidative stress[5,6] in the presence/absence of compound **4j** or (+)-PTZ for 24 h. Cell viability under these various conditions was measured using the Vybrant® MTT Cell Proliferation Assay Kit as described previously.[7] Cells were solubilized in isopropanol and released, solubilized formazan reagent was measured spectrophotometrically using a Synergy H1 Hybrid Multi-Mode plate reader (Winooski, VT) at 540 nm. The assay was performed in triplicate. Cells cultured under identical conditions, but with no treatment served as control.

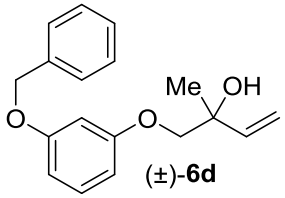
Assessment of oxidative stress: To assess effects of **4j** on oxidative stress *in vitro*, 661W cells were seeded on coverslips and were exposed to media containing tBHP (55 µM) for 2 h. In companion studies, cells were treated with **4j** (10, 30 µM) or (+)-PTZ (20, 50 µM) and tBHP (55µM) for 2 h or were treated with **4j** or (+)-PTZ alone. Control experiments were conducted in parallel in which tBHP and (+)-PTZ were omitted from the media. Following treatments, cells were rinsed with PBS and intracellular reactive oxygen species (ROS) were detected in cells using 5 µM CellROX Green Reagent (Thermo-Fisher Scientific; 30 min incubation, followed by fixation). The assay detects reactive oxygen species (ROS) including hydroxyl, peroxyl, peroxynitrite and hydroxyl radicals. DAPI was used to stain nuclei. Green fluorescent signals representing ROS were visualized using an Axioplan-2 fluorescent microscope Carl Zeiss, Göttingen, Germany) equipped with an HRM camera. Fluorescence intensity was quantified using NIH Image J 1.48v software.

Statistical Analysis: The data were analyzed using GraphPad Prism statistical analysis program (LaJolla, Calif., USA). Significance was established as $p<0.05$. Data were analyzed by one-way ANOVA followed by Tukey's post-hoc test.

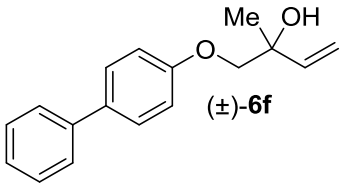
General Sequence for Substrate Synthesis



General Procedure 1: Addition of vinyl magnesium Grignard: Example given for R = *m*-OBn. **Compound (±)-6d.** An oven-dried round bottom flask was sequentially charged with THF (20 mL) and a solution of vinyl magnesium chloride (4.0 mL, 1.6 M in THF, 6.6 mmol), then cooled in an ice bath. To this solution neat **5d** (R = *m*-OBn, 1.3 g, 5.1 mmol) was added dropwise over 5 min. After 30 min, the reaction was quenched into a saturated solution of NH_4Cl (20 mL). The resulting solution was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford alcohol **5d** (1.2 g, 4.2 mmol, 83%) as a slightly yellow oil. **Note:** Substrates **6a-c**, **6e**, **6j-l**, and **6n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]

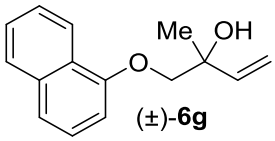


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.0 Hz, 2H), 7.44 – 7.39 (m, 2H), 7.37 – 7.33 (m, 1H), 7.20 (t, *J* = 8.2 Hz, 1H), 6.63 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.60 (t, *J* = 2.3 Hz, 1H), 6.56 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.04 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.42 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.22 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.06 (s, 2H), 3.89 (d, *J* = 8.9 Hz, 1H), 3.84 (d, *J* = 8.9 Hz, 1H), 2.43 (br s, 1H), 1.42 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.2, 160.1, 141.9, 137.1, 130.1, 128.8, 128.1, 127.7, 114.2, 107.8, 107.4, 102.3, 75.1, 72.6, 70.2, 24.6; **IR** (NaCl, thin film, cm^{-1}) 3440, 2979, 2930, 2870, 1593, 1491, 1454, 1288, 1262, 1178, 1151, 1045, 1027, 758, 737, 696; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{20}O_3Na^+$ $(M+Na)^+$ 307.1305, found 307.1304.



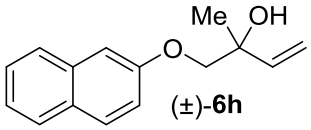
(±)-**6f**

(±)-6f: General procedure 1 was used and the product was isolated in 83% yield (1.9 g) as a white solid: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 – 7.54 (m, 4H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.08 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.46 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.25 (dd, *J* = 10.8, 1.2 Hz, 1H), 3.96 (d, *J* = 8.9 Hz, 1H), 3.92 (d, *J* = 8.9 Hz, 1H), 2.47 (br s, 1H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.4, 141.9, 140.8, 134.5, 128.9, 128.3, 126.9 (2C), 115.2, 114.2, 75.2, 72.6, 24.7; **IR** (NaCl, thin film, cm^{-1}) 3349, 3032, 2977, 2920, 2868, 1606, 1519, 1487, 1269, 1246, 1050, 924, 904, 831, 760, 736, 690; **HRMS** (ESI-TOF) *m/z* calcd for $C_{17}H_{18}O_2Na^+$ $(M+Na)^+$ 277.1199, found 277.1194.



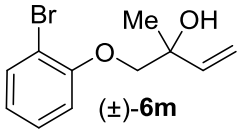
(±)-**6g**

(±)-6g: General procedure 1 was used and the product was isolated in 89% yield (2.0 g) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.28 – 8.23 (m, 1H), 7.85 – 7.81 (m, 1H), 7.54 – 7.48 (m, 2H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.15 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.52 (dd, *J* = 17.3, 1.2 Hz, 1H), 5.28 (dd, *J* = 10.8, 1.2 Hz, 1H), 4.08 (d, *J* = 8.8 Hz, 1H), 4.06 (d, *J* = 8.9 Hz, 1H), 2.50 (br s, 1H), 1.54 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.4, 142.1, 134.7, 127.8, 126.7, 126.0, 125.7, 125.5, 121.9, 121.0, 114.3, 105.2, 75.2, 72.9, 24.9; **IR** (NaCl, thin film, cm^{-1}) 3428, 3053, 2980, 2929, 2870, 1595, 1579, 1508, 1459, 1402, 1270, 1241, 1102, 1069, 1020, 790, 770; **HRMS** (ESI-TOF) *m/z* calcd for $C_{15}H_{16}O_2Na^+$ $(M+Na)^+$ 251.1043, found 251.1037.



(±)-**6h**

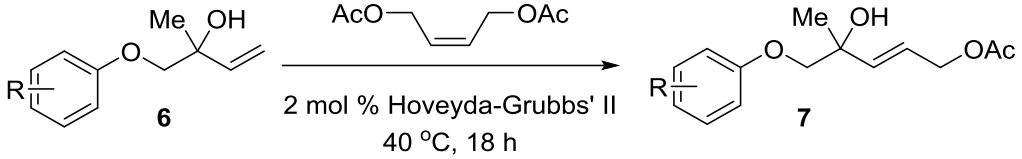
(±)-6h: General procedure 1 was used and the product was isolated in 91% yield (2.1 g) as a tan solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.75 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.47 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.20 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.17 (d, *J* = 2.6 Hz, 1H), 6.10 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.47 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.26 (dd, *J* = 10.8, 1.2 Hz, 1H), 4.03 (d, *J* = 8.9 Hz, 1H), 3.99 (d, *J* = 8.9 Hz, 1H), 2.54 (br s, 1H), 1.48 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.7, 141.9, 134.6, 129.6, 129.3, 127.8, 126.9, 126.6, 124.0, 118.9, 114.3, 107.2, 75.0, 72.6, 24.7; **IR** (NaCl, thin film, cm^{-1}), 3431, 3057, 2979, 2930, 1629, 1600, 1511, 1459, 1389, 1257, 1218, 1177, 1120, 1040, 960, 837, 746; **HRMS** (ESI-TOF) *m/z* calcd for $C_{15}H_{16}O_2Na^+$ $(M+Na)^+$ 251.1043, found 251.1053.



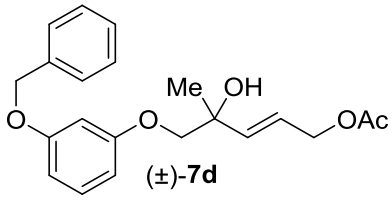
(±)-**6m**

(±)-6m: General procedure 1 was used and the product was isolated in 90% yield (2.0 g) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.26 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 6.88 (dd, *J* = 8.3, 1.4 Hz, 1H), 6.86 (td, *J* = 7.6, 1.4 Hz, 1H), 6.06 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.44 (dd, *J* = 17.4, 1.2 Hz, 1H), 5.23 (dd, *J* = 10.8, 1.2 Hz, 1H), 3.94 (d, *J* = 8.6 Hz, 1H),

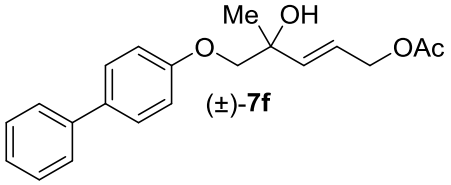
3.88 (d, *J* = 8.7 Hz, 1H), 2.68 (br s, 1H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.0, 141.5, 133.4, 128.7, 122.6, 114.4, 113.9, 112.7, 76.3, 72.6, 24.6; **IR** (NaCl, thin film, cm^{-1}) 3428, 3064, 2977, 2931, 2872, 1585, 1481, 1442, 1292, 1279, 1248, 1054, 1031, 924, 746; **HRMS** (ESI-TOF) *m/z* calcd for $C_{11}H_{13}BrO_2Na^+$ $(M+Na)^+$ 278.9991, found 278.9989.



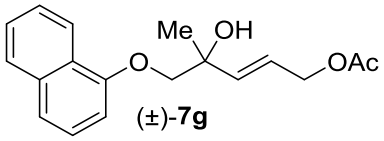
General Procedure 2: Formation of cross metathesis product: Example for R = *m*-OBn.
Compound (±)-7d: In a glovebox, a 20 mL vial was charged with Hoveyda-Grubbs' 2nd generation catalyst (48 mg, 78 μmol, 2 mol %). The vial was sealed and removed from the glovebox. The vial was uncapped and compound **6d** (1.2 g, 3.9 mmol) and *cis*-1,4-diacetoxy-2-butene (2.0 mL, 12 mmol) were added as a neat mixture. The vial was attached to a vacuum adapter, placed under reduced pressure (< 1.0 torr), and heated to 40 °C. After 18 h, the vacuum was released and the resulting mixture was loaded directly onto a column load cartridge. Final purification by column chromatography (0 to 80% gradient, EtOAc in hexanes) afforded compound **7d** (1.1 g, 2.9 mmol, 76%) as a yellow oil. **Note:** Substrates **7a-c**, **7e**, **7j-l**, and **7n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 7.34 (tt, *J* = 7.0, 2.3 Hz, 1H), 7.20 (t, *J* = 8.2 Hz, 1H), 6.62 (ddd, *J* = 8.1, 2.4, 0.8 Hz, 1H), 6.59 (t, *J* = 2.4 Hz, 1H), 6.54 (ddd, *J* = 8.3, 2.4, 0.8 Hz, 1H), 6.00 – 5.89 (m, 2H), 5.06 (s, 2H), 4.62 (d, *J* = 4.9 Hz, 2H), 3.87 (d, *J* = 8.9 Hz, 1H), 3.83 (d, *J* = 9.0 Hz, 1H), 2.56 (br s, 1H), 2.09 (s, 3H), 1.42 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 160.2, 159.9, 137.7, 137.0, 130.1, 128.7, 128.1, 127.6, 124.0, 107.7, 107.4, 102.3, 75.0, 72.0, 70.2, 64.5, 24.8, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3467, 3031, 2975, 2932, 2872, 1736, 1593, 1491, 1454, 1380, 1260, 1179, 1150, 1027, 970, 763, 741, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{21}H_{24}O_5Na^+$ $(M+Na)^+$ 379.1516, found 379.1520.

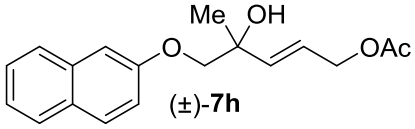


(±)-7f: General procedure 2 was used and the product was isolated in 81% (1.1 g) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 4H), 7.43 (dd, *J* = 8.5, 7.0 Hz, 2H), 7.33 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.02 – 6.98 (m, 2H), 6.02 – 5.92 (m, 2H), 4.64 (d, *J* = 4.6 Hz, 2H), 3.94 (d, *J* = 8.9 Hz, 1H), 3.90 (d, *J* = 8.9 Hz, 1H), 2.60 (br s, 1H), 2.10 (s, 3H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 158.2, 140.8, 137.7, 134.5, 128.9, 128.3, 126.93, 126.88, 124.1, 115.1, 75.1, 72.1, 64.5, 24.8, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3471, 3032, 2976, 2930, 2871, 1738, 1607, 1488, 1379, 1353, 1245, 1050, 1031, 973, 831, 761, 695; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{22}O_4Na^+$ $(M+Na)^+$ 349.1410, found 349.1418.



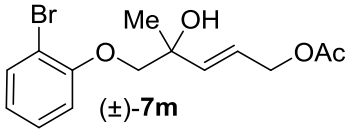
(±)-**7g**

(±)-7g: General procedure 2 was used and the product was isolated in 86% yield (1.3 g) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 – 8.21 (m, 1H), 7.84 – 7.81 (m, 1H), 7.54 – 7.48 (m, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.08 – 6.03 (m, 2H), 4.69 – 4.59 (m, 2H), 4.06 (s, 2H), 2.58 (br s, 1H), 2.09 (s, 3H), 1.54 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 154.2, 138.0, 134.7, 127.8, 126.7, 126.0, 125.7, 125.5, 124.1, 121.8, 121.0, 105.3, 75.1, 72.3, 64.5, 25.0, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3457, 3053, 2976, 2931, 1736, 1580, 1401, 1268, 1241, 1102, 1069, 1021, 970, 792, 772; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{20}O_4Na^+$ $(M+Na)^+$ 323.1254, found 323.1257.



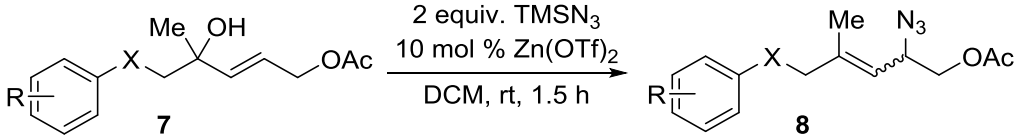
(±)-**7h**

(±)-7h: General procedure 2 was used and the product was isolated in 72% yield (1.1 g) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 9.1 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.46 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.18 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.15 (d, *J* = 2.6 Hz, 1H), 6.02 – 5.96 (m, 2H), 4.64 (d, *J* = 4.2 Hz, 2H), 4.01 (d, *J* = 8.9 Hz, 1H), 3.98 (d, *J* = 8.9 Hz, 1H), 2.59 (br s, 1H), 2.10 (s, 3H), 1.48 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 156.6, 137.7, 134.6, 129.7, 129.3, 127.8, 126.9, 126.7, 124.1, 124.0, 118.8, 107.2, 74.9, 72.1, 64.5, 24.9, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3456, 3057, 2976, 2933, 2872, 1736, 1629, 1600, 1511, 1460, 1389, 1360, 1257, 1218, 1178, 1120, 1032, 963, 838, 748; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{20}O_4Na^+$ $(M+Na)^+$ 323.1254, found 323.1257.



(±)-**7m**

(±)-7m: General procedure 2 was used and the product was isolated in 68% yield (890 mg) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.27 – 7.23 (m, 1H), 6.89 – 6.84 (m, 2H), 6.01 – 5.91 (m, 2H), 4.62 – 4.59 (m, 2H), 3.93 (d, *J* = 8.7 Hz, 1H), 3.89 (d, *J* = 8.7 Hz, 1H), 2.69 (br s, 1H), 2.08 (s, 3H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 154.9, 137.3, 133.4, 128.7, 124.2, 122.7, 113.9, 112.7, 76.2, 72.1, 64.5, 24.8, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3462, 3064, 2976, 2935, 2875, 1737, 1585, 1482, 1443, 1278, 1247, 1054, 1030, 972, 749; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{17}BrO_4Na^+$ $(M+Na)^+$ 351.0202, found 351.0202.

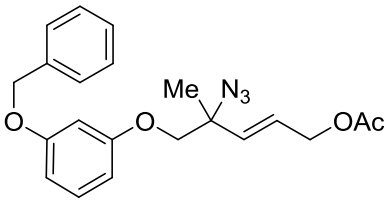


General Procedure 3: Azide Installation with $TMSN_3$: Example given for R = *m*-OBn.

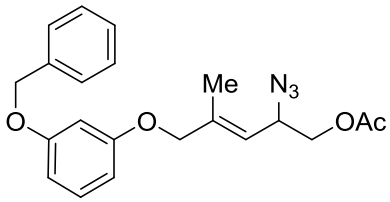
Compound (±)-8d: To a solution of alcohol **7d** (980 mg, 2.8 mmol) in DCM (0.8 mL) at room temperature, trimethylsilyl azide (0.70 mL, 5.5 mmol), and $Zn(OTf)_2$ (110 mg, 0.28 mmol, 10 mol %) were sequentially added. The vial was sealed. After 1.5 h, the solution was quenched by addition of trimethylamine (0.1 mL, 0.7 mmol) and methanol (1 mL), and stirred for 5 min. The resulting solution was filtered through a plug of basic alumina and the filtrate was concentrated *in vacuo*. Final purification by column chromatography (0 to 80% gradient, EtOAc in hexanes)

afforded azide **8d** (590 mg, 1.5 mmol, 56%) as a yellow oil. **Note:** Substrates **8a-c**, **8e**, **8j-l**, and **8n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]

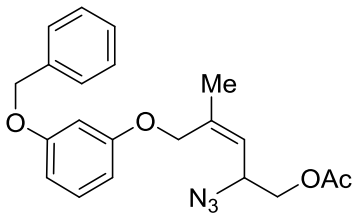
Compound **8d** was isolated as a mixture of three isomers (1.0:1.6:0.2 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture:



(±)-**8d *trans***

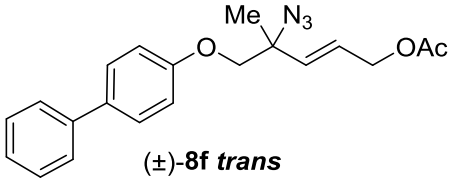


(±)-**8d *E***

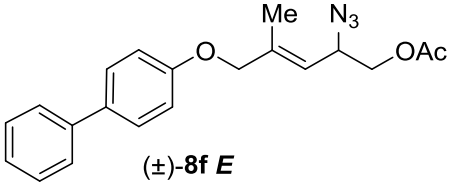


(±)-**8d *Z***

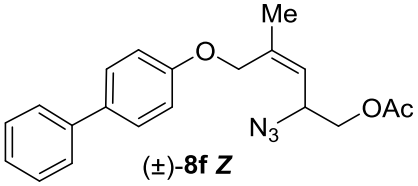
^{1}H NMR (500 MHz, $CDCl_3$) **8d *trans*** δ 7.48 – 7.38 (m, 4H), 7.37 – 7.32 (m, 1H), 7.23 – 7.17 (m, 1H), 6.65 – 6.53 (m, 3H), 5.97 (dt, *J* = 15.7, 5.6 Hz, 1H), 5.87 (dt, *J* = 15.8, 1.3 Hz, 1H), 5.06 (s, 2H), 4.64 (dd, *J* = 5.7, 1.4 Hz, 2H), 3.92 (d, *J* = 9.3 Hz, 1H), 3.90 (d, *J* = 9.3 Hz, 1H), 2.11 (s, 3H), 1.54 (s, 3H); **8d *E*** δ 7.48 – 7.38 (m, 4H), 7.37 – 7.32 (m, 1H), 7.23 – 7.17 (m, 1H), 6.65 – 6.53 (m, 3H), 5.54 (dq, *J* = 9.1, 1.5 Hz, 1H), 5.06 (s, 2H), 4.56 – 4.50 (m, 1H), 4.46 (s, 2H), 4.15 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.04 (dd, *J* = 11.4, 7.8 Hz, 1H), 2.11 (s, 3H), 1.87 (d, *J* = 1.5 Hz, 3H); **8d *Z*** δ 7.48 – 7.38 (m, 4H), 7.37 – 7.32 (m, 1H), 7.23 – 7.17 (m, 1H), 6.65 – 6.53 (m, 3H), 5.39 (dq, *J* = 9.5, 1.4 Hz, 1H), 5.07 (s, 2H), 4.60 (ddd, *J* = 9.5, 7.5, 4.5 Hz, 1H), 4.56 – 4.50 (m, 2H), 4.13 (dd, *J* = 11.4, 4.5 Hz, 1H), 4.04 (dd, *J* = 11.4, 7.6 Hz, 1H), 2.10 (s, 3H), 1.96 (d, *J* = 1.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.75, 170.72, 160.2, 159.77, 159.73, 139.4, 139.13, 137.07, 137.01, 133.2, 130.16, 130.13, 130.08, 128.7, 128.12, 128.10, 127.6, 126.60, 122.56, 120.2, 107.9, 107.8, 107.7, 107.5, 107.3, 102.39, 102.35, 102.30, 74.2, 72.2, 70.20, 70.17, 67.1, 66.0, 65.7, 64.1, 63.2, 57.7, 57.6, 22.0, 21.3, 21.0, 20.9, 14.6; **IR** (NaCl, thin film, cm^{-1}) 3064, 3032, 2934, 2872, 2108, 1743, 1592, 1491, 1454, 1381, 1228, 1177, 1150, 1028, 764, 739, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{21}H_{23}N_3O_4Na^+$ $(M+Na)^+$ 404.1581, found 404.1579.



(±)-**8f *trans***



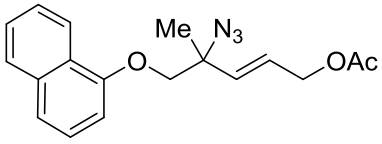
(±)-**8f *E***



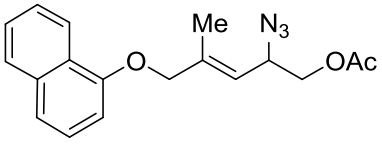
(±)-**8f *Z***

(±)-8f: General procedure 3 was used and the product was isolated in 87% yield (920 mg) as a yellow oil. Compound **8f** was isolated as a mixture of three isomers (1.0:1.6:0.25 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **8f *trans*** δ 7.60 – 7.52 (m, 4H), 7.47 – 7.41 (m, 2H), 7.35 – 7.30 (m, 1H), 7.04 – 6.98 (m, 2H), 6.00 (dt, *J* = 15.7, 5.6 Hz, 1H), 5.90 (dt, *J* = 15.6, 1.3 Hz, 1H), 4.66 (dd, *J* = 5.7, 1.3 Hz, 2H), 3.99 (d, *J* = 9.2 Hz, 1H), 3.96 (d, *J* = 9.2 Hz, 1H), 2.11 (s, 3H), 1.57 (s, 3H); **8f *E*** δ 7.60 – 7.52 (m, 4H), 7.47 – 7.41 (m, 2H), 7.35 – 7.30 (m, 1H), 7.04 – 6.98 (m, 2H), 5.58 (dq, *J* = 9.0, 1.5 Hz, 1H), 4.58 – 4.53 (m, 1H), 4.53 (s, 2H), 4.17 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.06 (dd, *J* = 11.4, 7.8 Hz, 1H), 2.11 (s, 3H), 1.90 (d, *J* = 1.5 Hz, 3H); **8f *Z*** δ 7.60 – 7.52 (m, 4H), 7.47 – 7.41 (m, 2H), 7.35 – 7.30 (m, 1H), 7.04 – 6.98 (m, 2H), 5.42 (dq, *J* = 9.5, 1.4 Hz, 1H), 4.62 – 4.60 (m, 2H), 4.58 – 4.53 (m, 1H), 4.19 – 4.14 (m, 1H), 4.08 – 4.04 (m, 1H), 2.12 (s, 3H), 1.99 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.80, 170.78, 158.12, 158.09, 158.06, 140.83, 140.80,

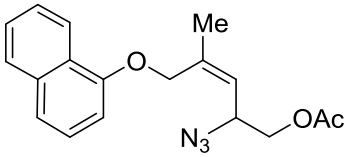
140.78, 139.5, 139.2, 134.7, 134.6, 134.4, 133.2, 128.90, 128.89, 128.49, 128.41, 128.37, 128.33, 126.97, 126.92, 126.89, 126.7, 122.7, 120.3, 119.4, 115.22, 115.12, 115.10, 74.27, 72.25, 67.1, 66.0, 65.8, 64.1, 63.3, 57.7, 57.6, 22.0, 21.3, 21.18, 20.91, 20.89, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3020, 2934, 2108, 1743, 1608, 1518, 1487, 1242, 1047, 833, 763, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{21}N_3O_3Na^+$ $(M+Na)^+$ 374.1475, found 374.1480.



(±)-**8g *trans***

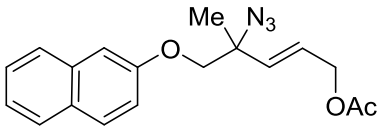


(±)-**8g *E***

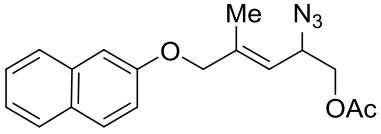


(±)-**8g *Z***

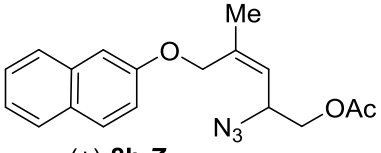
(±)-8g: General procedure 3 was used and the product was isolated in 29% yield (530 mg) as a yellow oil. Compound **8g** was isolated as a mixture of two isomers (1.0:1.0 *trans*:*E*). Trace amounts of **8g *Z*** were observed. NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **8g *trans*** δ 8.34 – 8.26 (m, 1H), 7.85 – 7.81 (m, 1H), 7.56 – 7.51 (m, 2H), 7.48 (t, *J* = 8.6 Hz, 1H), 7.40 – 7.36 (m, 1H), 6.80 (t, *J* = 7.3 Hz, 1H), 6.06 (dt, *J* = 15.7, 5.6 Hz, 1H), 5.97 (dt, *J* = 15.7, 1.4 Hz, 1H), 4.69 – 4.67 (m, 2H), 4.14 – 4.06 (m, 2H), 2.12 (s, 3H), 1.66 (s, 3H); **8g *E*** δ 8.34 – 8.26 (m, 1H), 7.85 – 7.81 (m, 1H), 7.56 – 7.51 (m, 2H), 7.48 (t, *J* = 8.6 Hz, 1H), 7.40 – 7.36 (m, 1H), 6.80 (t, *J* = 7.3 Hz, 1H), 5.68 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.67 (s, 2H), 4.59 (ddd, *J* = 9.1, 7.7, 4.3 Hz, 1H), 4.19 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.14 – 4.06 (m, 1H), 2.11 (s, 3H), 1.97 (d, *J* = 1.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.80, 170.75, 154.16, 154.15, 139.3, 134.70, 134.69, 133.3, 127.67, 127.65, 126.77, 126.73, 126.6, 125.89, 125.80, 125.78, 125.65, 125.63, 125.48, 122.11, 122.05, 121.2, 120.8, 120.3, 105.3, 104.9, 74.1, 72.3, 65.8, 64.1, 63.5, 57.7, 21.7, 21.1, 20.9, 14.8; **IR** (NaCl, thin film, cm^{-1}) 3053, 2933, 2108, 1743, 1580, 1389, 1267, 1239, 1103, 792, 772; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{19}N_3O_3Na^+$ $(M+Na)^+$ 348.1319, found 348.1330.



(±)-**8h *trans***

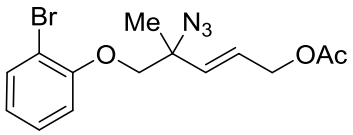


(±)-**8h *E***

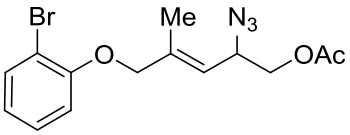


(±)-**8h *Z***

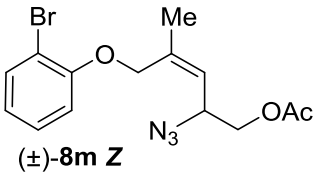
(±)-8h: General procedure 3 was used and the product was isolated in 64% yield (740 mg) as a yellow oil. Compound **8h** was isolated as a mixture of two isomers (1.0:1.2 *trans*:*E*). Trace amounts of **8h *Z*** were observed. NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$): **8h *trans*** δ 7.82 – 7.71 (m, 3H), 7.52 – 7.43 (m, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.16 (m, 1H), 7.17 – 7.13 (m, 1H), 6.01 (dt, *J* = 15.7, 5.6 Hz, 1H), 5.93 (dt, *J* = 15.7, 1.3 Hz, 1H), 4.67 (dd, *J* = 5.6, 1.3 Hz, 2H), 4.09 – 4.03 (m, 2H), 2.12 (s, 3H), 1.60 (s, 3H); **8h *E*** δ 7.82 – 7.71 (m, 3H), 7.52 – 7.43 (m, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.16 (m, 1H), 7.17 – 7.13 (m, 1H), 5.63 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.60 (s, 2H), 4.56 (ddd, *J* = 9.2, 7.7, 4.3 Hz, 1H), 4.17 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.09 – 4.03 (m, 1H), 2.09 (s, 3H), 1.92 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.79, 170.77, 156.51, 156.45, 156.43, 139.5, 139.2, 134.58, 134.57, 134.52, 133.2, 129.76, 129.72, 129.67, 129.38, 129.34, 129.27, 127.83, 127.80, 126.94, 126.92, 126.67, 126.66, 126.58, 124.09, 124.05, 123.96, 122.6, 120.3, 119.0, 118.9, 118.8, 107.4, 107.1, 107.0, 74.1, 72.1, 67.0, 66.0, 65.8, 64.1, 63.3, 57.7, 57.6, 22.0, 21.4, 21.1, 20.90, 20.86, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3057, 2942, 2108, 1743, 1629, 1600, 1510, 1468, 1389, 1365, 1255, 1219, 1177, 1120, 1046, 838, 749; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{19}N_3O_3Na^+$ $(M+Na)^+$ 348.1319, found 348.1320.



(±)-**8m *trans***

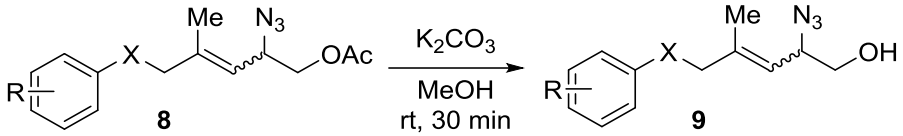


(±)-**8m *E***



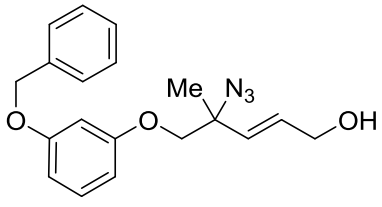
(±)-**8m *Z***

(±)-8m: General procedure 3 was used and the product was isolated in 74% yield (670 mg) as a yellow oil. Compound **8m** was isolated as a mixture of two isomers (1.0:1.0 *trans*:*E*). Trace amounts of **8m *Z*** were observed. NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **8m *trans*** δ 7.59 – 7.53 (m, 1H), 7.30 – 7.23 (m, 1H), 6.95 – 6.84 (m, 2H), 6.01 (dt, *J* = 15.7, 5.5 Hz, 1H), 5.93 (dt, *J* = 15.6, 1.2 Hz, 1H), 4.65 (dd, *J* = 5.5, 1.3 Hz, 2H), 3.95 (d, *J* = 9.0 Hz, 1H), 3.92 (d, *J* = 9.1 Hz, 1H), 2.11 (s, 3H), 1.61 (s, 3H); **8m *E*** δ 7.59 – 7.53 (m, 1H), 7.30 – 7.23 (m, 1H), 6.95 – 6.84 (m, 2H), 5.64 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.54 (s, 2H), 4.57 – 4.50 (m, 1H), 4.15 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.06 (dd, *J* = 11.4, 7.6 Hz, 1H), 2.11 (s, 3H), 1.90 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.74, 170.72, 154.9, 154.8, 138.5,133.7, 133.63, 133.60, 133.0, 128.7, 128.59, 128.56, 126.8, 122.7, 122.6, 122.5, 120.5, 113.8, 113.5, 112.6, 112.5, 74.9, 72.9, 68.1, 66.0, 65.7, 64.1, 63.3, 57.6, 57.5, 21.9, 21.3, 21.1, 20.9, 14.6; **IR** (NaCl, thin film, cm^{-1}) 2937, 2109, 1743, 1585, 1481, 1442, 1278, 1244, 1056, 1031, 750; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{16}BrN_3O_3Na^+$ $(M+Na)^+$ 376.0267, found 376.0266.

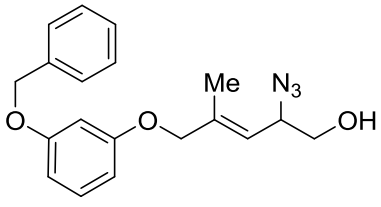


General Procedure 4: Acetate deprotection of allylic azides: Example given for R = *m*-OBn. **Compound (±)-9d:** To a solution of acetate **8d** (530 mg, 1.4 mmol) in methanol (9.0 mL) at room temperature, solid potassium carbonate (580 mg, 4.2 mmol) was added. After 30 min, the reaction was quenched by the addition of water (20 mL) and the resulting solution was extracted with DCM (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford alcohol **9d** (480 mg, 1.4 mmol, quantitative yield) as a clear oil of sufficient purity to advance without further purification. **Note:** Substrates **9a-c**, **9e**, **9j-l**, and **9n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]

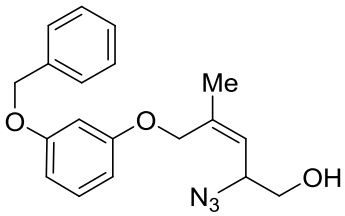
Compound **9d** was isolated as a mixture of three isomers (1.0:7.7:0.8 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture:



(±)-**9d *trans***



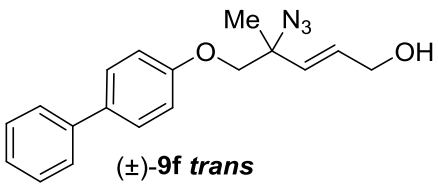
(±)-**9d *E***



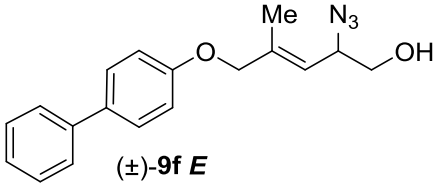
(±)-**9d *Z***

^{1}H NMR (500 MHz, $CDCl_3$) **9d *trans*** δ 7.46 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.31 (m, 1H), 7.22 – 7.17 (m, 1H), 6.64 – 6.59 (m, 1H), 6.59 – 6.56 (m, 1H), 6.56 – 6.51 (m, 1H), 6.03 (dt, *J* = 15.7, 5.0 Hz, 1H), 5.85 (dt, *J* = 15.7, 1.7 Hz, 1H), 5.06 (s, 2H), 4.25 (dd, *J* = 5.0, 1.7 Hz, 2H), 3.91 (d, *J* = 9.3 Hz, 1H), 3.89 (d, *J* = 9.3 Hz, 1H), 1.63 (br s, 1H), 1.52 (s, 3H); **9d *E*** δ 7.46 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.31 (m, 1H), 7.22 – 7.17 (m, 1H), 6.64 – 6.59 (m, 1H), 6.59

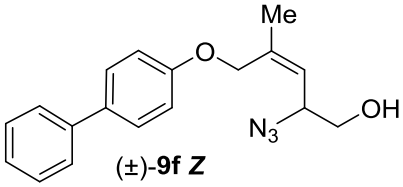
– 6.56 (m, 1H), 6.56 – 6.51 (m, 1H), 5.57 (dq, *J* = 9.3, 1.5 Hz, 1H), 5.06 (s, 2H), 4.46 (s, 2H), 4.45 – 4.40 (m, 1H), 3.63 – 3.53 (m, 2H), 1.87 (d, *J* = 1.4 Hz, 3H), 1.63 (br s, 1H); **9d *Z*** δ 7.46 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.31 (m, 1H), 7.22 – 7.17 (m, 1H), 6.64 – 6.59 (m, 1H), 6.59 – 6.56 (m, 1H), 6.56 – 6.51 (m, 1H), 5.44 (dq, *J* = 9.8, 1.0 Hz, 1H), 5.06 (s, 2H), 4.55 (d, *J* = 11.5, Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.51 – 4.47 (m, 1H), 3.63 – 3.53 (m, 2H), 1.96 (d, *J* = 1.5 Hz, 3H), 1.63 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.2, 159.8, 139.3, 139.1, 137.1, 131.7, 130.17, 130.13, 130.10, 128.7, 128.1, 127.66, 127.64, 123.3, 120.8, 107.9, 107.8, 107.7, 107.5, 107.4, 107.3, 102.4, 102.3, 74.3, 72.4, 70.22, 70.20, 67.2, 65.2, 65.0, 63.4, 62.9, 61.2, 61.1, 22.1, 21.4, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3424, 3031, 2924, 2872, 2105, 1592, 1491, 1453, 1288, 1261, 1176, 1149, 1027, 737, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{19}H_{21}N_3O_3Na^+$ $(M+Na)^+$ 362.1475, found 362.1471.



(±)-**9f *trans***

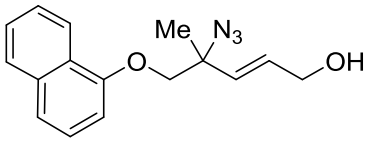


(±)-**9f *E***

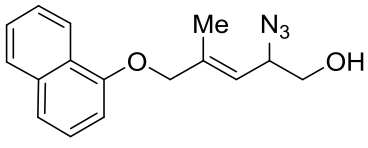


(±)-**9f *Z***

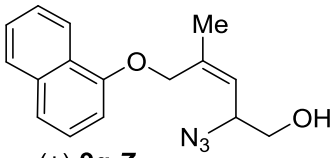
(±)-9f: General procedure 4 was used and the product was isolated in 97% (730 mg) yield as a yellow oil. Compound **9f** was isolated as a mixture of three isomers (1.0:4.2:0.75 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **9f *trans*** δ 7.59 – 7.51 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.98 (m, 2H), 6.06 (dt, *J* = 15.8, 5.0 Hz, 1H), 5.89 (dt, *J* = 15.7, 1.7 Hz, 1H), 4.28 – 4.24 (m, 2H), 3.99 (d, *J* = 9.3 Hz, 1H), 3.96 (d, *J* = 9.2 Hz, 1H), 1.87 (br s, 1H); 1.56 (s, 3H); **9f *E*** δ 7.59 – 7.51 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.98 (m, 2H), 5.62 (dq, *J* = 9.4, 1.5 Hz, 1H), 4.53 (s, 2H), 4.46 (ddd, *J* = 9.4, 7.1, 4.7 Hz, 1H), 3.66 – 3.55 (m, 2H), 1.90 (d, *J* = 1.5 Hz, 3H), 1.87 (br s, 1H); **9f *Z*** δ 7.59 – 7.51 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.98 (m, 2H), 5.47 (dq, *J* = 9.6, 1.2 Hz, 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.59 (d, *J* = 11.7 Hz, 1H), 4.55 – 4.52 (m, 1H), 3.66 – 3.55 (m, 2H), 2.00 (d, *J* = 1.5 Hz, 3H), 1.87 (br s, 1H), **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.1, 140.9, 140.8, 139.4, 139.2, 134.7, 134.4, 131.8, 130.2, 128.92, 128.91, 128.44, 128.39, 128.36, 126.97, 126.95, 126.92, 123.4, 120.8, 115.3, 115.16, 115.11, 74.4, 72.5, 67.2, 65.2, 65.0, 63.4, 63.0, 61.3, 61.2, 22.2, 21.5, 14.8; **IR** (NaCl, thin film, cm^{-1}) 3369, 2920, 2868, 2107, 1606, 1488, 1246, 1043, 831, 763, 692; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{19}N_3O_2Na^+$ $(M+Na)^+$ 332.1369, found 332.1374.



(±)-**9g *trans***



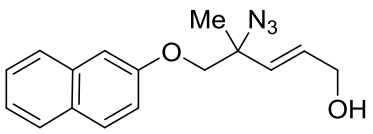
(±)-**9g *E***



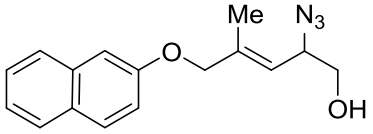
(±)-**9g *Z***

(±)-9g: General procedure 4 was used and the product was isolated in 99% yield (410 mg) as a yellow oil. Compound **9g** was isolated as a mixture of three isomers (1.0:3.8:0.6 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **9g *trans*** δ 8.34 – 8.24 (m, 1H), 7.85 – 7.80 (m, 1H), 7.56 – 7.47 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.87 – 6.77 (m, 1H), 6.11 (dt, *J* = 15.7, 5.0 Hz, 1H), 5.94 (dt, *J* = 15.7, 1.7 Hz, 1H), 4.27 (dd, *J* = 5.0, 1.7 Hz, 2H), 4.12 (d, *J* = 9.1 Hz, 1H), 4.09 (d, *J* = 9.2 Hz, 1H), 1.96 (br s, 1H), 1.65 (s, 3H); **9g *E*** δ 8.34 – 8.24 (m, 1H), 7.85 – 7.80 (m, 1H), 7.56 – 7.47 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.87 – 6.77 (m, 1H), 5.70 (dq, *J* = 9.3,

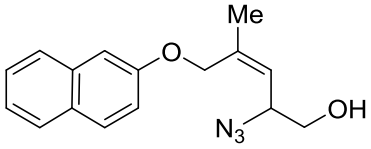
1.5 Hz, 1H), 4.68 (s, 2H), 4.50 (ddd, *J* = 9.4, 7.3, 4.7 Hz, 1H), 3.67 – 3.55 (m, 2H), 1.97 (d, *J* = 1.4 Hz, 3H), 1.96 (br s, 1H); **9g *Z*** δ 8.34 – 8.24 (m, 1H), 7.85 – 7.80 (m, 1H), 7.56 – 7.47 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.87 – 6.77 (m, 1H), 5.52 (dq, *J* = 9.3, 1.5 Hz, 1H), 4.78 (d, *J* = 11.4 Hz,1H), 4.74 (d, *J* = 11.4 Hz, 1H), 4.57 – 4.53 (m, 1H), 3.67 – 3.55 (m, 2H), 2.08 (d, *J* = 1.5 Hz, 3H), 1.96 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.4, 154.23, 154.21, 139.6, 139.2, 134.71, 134.69, 131.8, 130.3, 127.69, 127.66, 126.73, 126.70, 126.63, 125.91, 125.88, 125.83, 125.80, 125.76, 125.66, 125.57, 125.49, 123.2, 122.15, 122.08, 122.05, 121.14, 121.03, 120.84, 120.80, 105.4, 105.0, 104.9, 74.3, 72.5, 67.1, 65.2, 65.0, 63.7, 62.9, 61.3, 61.1, 53.6, 22.2, 21.8, 14.9; **IR** (NaCl, thin film, cm^{-1}) 3363, 3053, 2924, 2872, 2105, 1595, 1580, 1508, 1461, 1402, 1268, 1241, 1097, 1067, 791, 771; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{17}N_3O_2Na^+$ $(M+Na)^+$ 306.1213, found 306.1216.



(±)-**9h *trans***

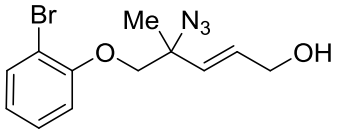


(±)-**9h *E***

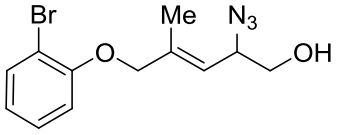


(±)-**9h *Z***

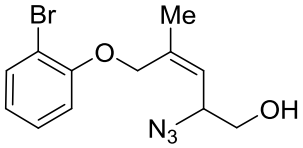
(±)-9h: General procedure 4 was used and the product was isolated in 98% yield (580 mg) as a yellow oil. Compound **9h** was isolated as a mixture of three isomers (1.0:4.0:0.7 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **9h *trans*** δ 7.81 – 7.71 (m, 3H), 7.50 – 7.42 (m, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.17 (m, 1H), 7.19 – 7.12 (m, 1H), 6.07 (dt, *J* = 15.8, 5.0 Hz, 1H), 5.91 (dt, *J* = 15.7, 1.8 Hz, 1H), 4.27 (dd, *J* = 5.0, 1.7 Hz, 2H), 4.07 (d, *J* = 9.3 Hz, 1H), 4.04 (d, *J* = 9.2 Hz, 1H), 1.95 (br s, 1H), 1.59 (s, 3H); **9h *E*** δ 7.81 – 7.71 (m, 3H), 7.50 – 7.42 (m, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.17 (m, 1H), 7.19 – 7.12 (m, 1H), 5.66 (dq, *J* = 9.4, 1.6 Hz, 1H), 4.61 (s, 2H), 4.48 (ddd, *J* = 9.3, 7.2, 4.6 Hz, 1H), 3.67 – 3.55 (m, 2H), 1.95 (br s, 1H), 1.93 (d, *J* = 1.4 Hz, 3H); **9h *Z*** δ 7.81 – 7.71 (m, 3H), 7.50 – 7.42 (m, 1H), 7.41 – 7.33 (m, 1H), 7.24 – 7.17 (m, 1H), 7.19 – 7.12 (m, 1H), 5.49 (dq, *J* = 9.7, 1.6 Hz, 1H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.67 (d, *J* = 11.4 Hz, 1H), 4.59 – 4.52 (m, 1H), 3.67 – 3.55 (m, 2H), 2.02 (d, *J* = 1.5 Hz, 3H), 1.95 (br s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.54, 156.49, 139.4, 139.1, 134.60, 134.58, 134.54, 131.8, 130.2, 129.78, 129.72, 129.68, 129.37, 129.35, 129.28, 127.84, 127.81, 127.0, 126.9, 126.69, 126.66, 126.60, 124.1, 124.0, 123.4, 120.8, 119.0, 118.9, 107.4, 107.1, 107.0, 74.3, 72.3, 67.1, 65.2, 65.0, 63.4, 62.9, 61.3, 61.2, 22.2, 21.5, 14.8; **IR** (NaCl, thin film, cm^{-1}) 3385, 3057, 2922, 2872, 2104, 1629, 1600, 1510, 1469, 1389, 1257, 1216, 1177, 1120, 1043, 1010, 837, 748; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{17}N_3O_2Na^+$ $(M+Na)^+$ 306.1213, found 306.1212.



(±)-**9m *trans***



(±)-**9m *E***



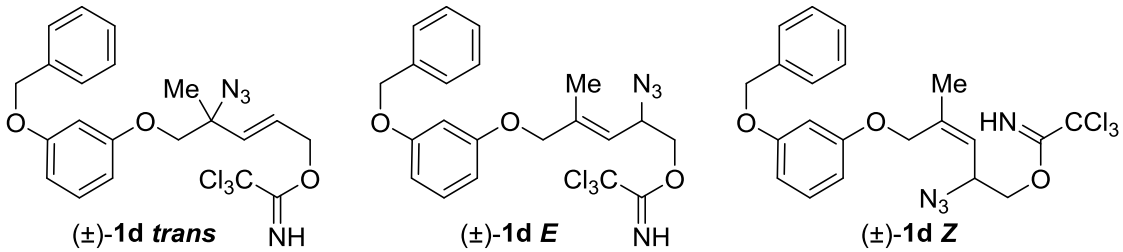
(±)-**9m *Z***

(±)-9m: General procedure 4 was used and the product was isolated in quantitative yield (540 mg) as a yellow oil. Compound **9m** was isolated as a mixture of three isomers (1.0:4.0:0.6 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **9m *trans*** δ 7.58 – 7.52 (m, 1H), 7.30 – 7.22 (m, 1H), 6.94 – 6.81 (m, 2H), 6.06 (dt, *J* = 15.7, 5.1 Hz, 1H), 5.89 (dt, *J* = 15.7, 1.7 Hz, 1H), 4.24 (m, 2H), 3.94 (d, *J* = 9.1 Hz, 1H), 3.91 (d, *J* = 9.1 Hz, 1H), 2.07 (br s, 1H), 1.60 (s, 3H); **9m *E*** δ 7.58 – 7.52 (m, 1H), 7.30 – 7.22 (m, 1H), 6.94 – 6.81 (m, 2H), 5.65 (dq, *J* = 9.4, 1.5 Hz, 1H), 4.54 (s, 2H), 4.44 (ddd, *J* = 9.3, 7.1, 4.7

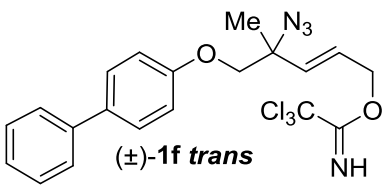
Hz, 1H), 3.64 – 3.55 (m, 2H), 2.07 (br s, 1H), 1.90 (d, *J* = 1.6 Hz, 3H); **9m *Z*** δ 7.58 – 7.52 (m, 1H), 7.30 – 7.22 (m, 1H), 6.94 – 6.81 (m, 2H), 5.46 (dq, *J* = 9.6, 1.4 Hz, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 1H), 4.58 – 4.54 (m, 1H), 3.64 – 3.55 (m, 2H), 2.07 (br s, 1H), 2.01 (d, *J* = 1.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.9, 154.8, 138.7, 138.5, 133.7, 133.61, 133.59, 131.9, 130.0, 128.66, 128.61, 128.57, 123.4, 122.72, 122.67, 122.5, 121.0, 113.9, 113.8, 113.5, 112.6, 112.5, 75.0, 73.2, 68.2, 65.2, 64.9, 63.4, 62.9, 61.2, 61.0, 22.1, 21.4, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3359, 2926, 2873, 2106, 1585, 1480, 1442, 1279, 1247, 1056, 1031, 748; **HRMS** (ESI-TOF) *m/z* calcd for $C_{12}H_{14}BrN_3O_2Na^+$ $(M+Na)^+$ 334.0162, found 334.0154.

General Procedure 5: Installation of Trichloroacetimidate: Example given for R = *m*-OBn. **Compound (±)-1d:** To solution of alcohol **1d** (437 mg, 1.3 mmol) in DCM (13 mL) at room temperature, trichloroacetonitrile (0.26 mL, 2.6 mmol), and DBU (48 μL, 0.32 mmol, 25 mol %) were sequentially added. After 90 min, the solution was concentrated *in vacuo* and loaded onto a column cartridge. Final purification by column chromatography (0 to 80% gradient, EtOAc in hexanes) afforded trichloroacetimidate **1d** (531 mg, 1.1 mmol, 85%) as a yellow oil. **Note:** Substrates **1a-c**, **1e**, **1j-l**, and **1n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]

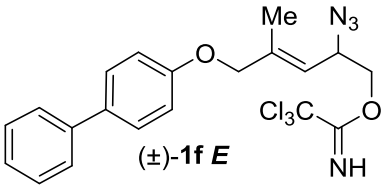
Compound **1d** was isolated as a mixture of three isomers (1:1.4:0.25 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture:



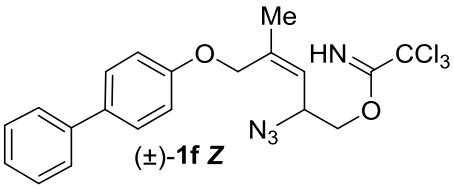
^{1}H NMR (400 MHz, $CDCl_3$) **1d *trans*** δ 8.39 (s, 1H), 7.48 – 7.38 (m, 4H), 7.38 – 7.31 (m, 1H), 7.24 – 7.16 (m, 1H), 6.66 – 6.51 (m, 3H), 6.08 (dt, *J* = 15.8, 5.1 Hz, 1H), 6.00 (dt, *J* = 15.8, 1.2 Hz, 1H), 5.05 – 4.98 (m, 2H), 4.90 (dd, *J* = 5.1, 1.1 Hz, 2H), 3.94 (d, *J* = 9.4 Hz, 1H), 3.91 (d, *J* = 9.4 Hz, 1H), 1.55 (s, 3H); **1d *E*** δ 8.43 (s, 1H), 7.48 – 7.38 (m, 4H), 7.38 – 7.31 (m, 1H), 7.24 – 7.16 (m, 1H), 6.66 – 6.51 (m, 3H), 5.63 (dq, *J* = 9.1, 1.5 Hz, 1H), 5.07 (s, 2H), 4.68 (ddd, *J* = 9.2, 7.0, 4.7 Hz, 1H), 4.46 (s, 2H), 4.37 – 4.27 (m, 2H), 1.90 (d, *J* = 1.4 Hz, 3H); **1d *Z*** δ 8.43 (s, 1H), 7.48 – 7.38 (m, 4H), 7.38 – 7.31 (m, 1H), 7.24 – 7.16 (m, 1H), 6.66 – 6.51 (m, 3H), 5.46 (dq, *J* = 9.4, 1.4 Hz, 1H), 5.07 (s, 2H), 4.78 (ddd, *J* = 9.4, 7.2, 4.6 Hz, 1H), 4.58 (s, 2H), 4.37 – 4.27 (m, 2H), 1.97 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.7, 162.5, 160.2, 159.81, 159.75, 139.3, 137.1, 137.0, 133.5, 130.20, 130.16, 130.13, 128.77, 128.74, 128.18, 128.16, 127.7, 125.8, 122.4, 120.1, 107.9, 107.8, 107.6, 107.5, 107.3, 102.4, 102.3, 91.1, 74.2, 72.2, 70.34, 70.24, 70.22, 68.6, 63.3, 57.4, 22.0, 21.4, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3339, 3032, 2918, 2871, 2107, 1664, 1592, 1490, 1453, 1290, 1150, 1083, 831, 796, 647; **HRMS** (ESI-TOF) *m/z* calcd for $C_{21}H_{21}Cl_3N_4O_3Na^+$ $(M+Na)^+$ 505.0571, found 505.0571.



(±)-**1f *trans***

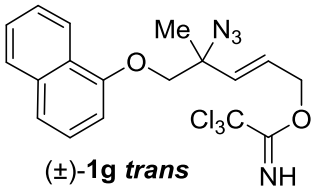


(±)-**1f *E***

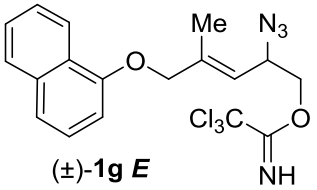


(±)-**1f *Z***

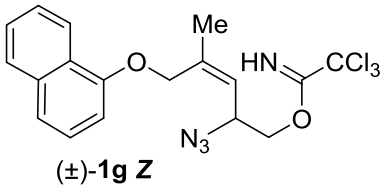
(±)-1f: General procedure 5 was used and the product was isolated in 97% yield (890 mg) as a yellow oil. Compound **1f** was isolated as a mixture of three isomers (1.0:2.6:0.4 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **1f *trans*** δ 8.38 (s, 1H), 7.58 – 7.51 (m, 4H), 7.46 – 7.40 (m, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.96 (m, 2H), 6.09 (dt, *J* = 15.8, 5.2 Hz, 1H), 6.02 (dt, *J* = 15.7, 1.2 Hz, 1H), 4.90 (dd, *J* = 5.2, 1.2 Hz, 2H), 4.00 (d, *J* = 9.2 Hz, 1H), 3.97 (d, *J* = 9.3 Hz, 1H), 1.57 (s, 3H); **1f *E*** δ 8.42 (s, 1H), 7.58 – 7.51 (m, 4H), 7.46 – 7.40 (m, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.96 (m, 2H), 5.66 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.69 (ddd, *J* = 9.1, 7.0, 4.7 Hz, 1H), 4.53 (s, 2H), 4.34 (dd, *J* = 11.1, 4.6 Hz, 1H), 4.30 (dd, *J* = 11.2, 7.1 Hz, 1H), 1.92 (d, *J* = 1.4 Hz, 3H); **1f *Z*** δ 8.42 (s, 1H), 7.58 – 7.51 (m, 4H), 7.46 – 7.40 (m, 2H), 7.35 – 7.29 (m, 1H), 7.03 – 6.96 (m, 2H), 5.48 (dq, *J* = 9.3, 1.3 Hz, 1H), 4.80 (ddd, *J* = 9.4, 7.2, 4.6 Hz, 1H), 4.65 – 4.63 (m, 2H), 4.36 – 4.32 (m, 1H), 4.32 – 4.28 (m, 1H), 1.99 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.7, 162.5, 158.17, 158.14, 158.11, 140.9, 140.8, 139.6, 139.3, 134.7, 134.6, 134.4, 133.6, 128.91, 128.89, 128.42, 128.39, 128.36, 126.98, 126.94, 126.92, 126.90, 125.8, 122.5, 120.2, 115.23, 115.17, 115.15, 91.2, 74.3, 72.3, 70.6, 70.3, 68.6, 67.3, 63.4, 57.4, 22.0, 21.4, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3339, 3032, 2922, 2107, 1666, 1608, 1518, 1487, 1292, 1243, 1075, 1005, 832, 796, 763, 647; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{19}Cl_3N_4O_2Na^+$ $(M+Na)^+$ 475.0466, found 475.0465.



(±)-**1g *trans***

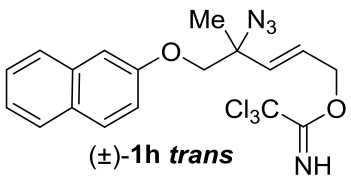


(±)-**1g *E***

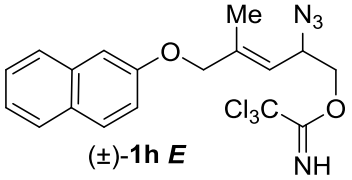


(±)-**1g *Z***

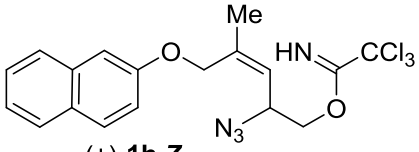
(±)-1g: General procedure 5 was used and the product was isolated in 74% yield (410 mg) as a yellow oil. Compound **1g** was isolated as a mixture of two isomers (1.0:1.4 *trans*:*E*). Trace amounts of **1g *Z*** were observed. NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **1g *trans*** δ 8.38 (s, 1H), 8.32 – 8.25 (m, 1H), 7.84 – 7.79 (m, 1H), 7.54 – 7.44 (m, 3H), 7.41 – 7.35 (m, 1H), 6.84 – 6.77 (m, 1H), 6.17 (dt, *J* = 15.8, 4.8 Hz, 1H), 6.11 (dt, *J* = 15.7, 1.2 Hz, 1H), 4.92 (dd, *J* = 4.6, 1.0 Hz, 2H), 4.14 (d, *J* = 9.2 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, 1H), 1.66 (s, 3H); **1g *E*** δ 8.43 (s, 1H), 8.32 – 8.25 (m, 1H), 7.84 – 7.79 (m, 1H), 7.54 – 7.44 (m, 3H), 7.41 – 7.35 (m, 1H), 6.84 – 6.77 (m, 1H), 5.79 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.73 (ddd, *J* = 9.2, 6.9, 4.6 Hz, 1H), 4.68 (s, 2H), 4.38 (dd, *J* = 11.1, 4.6 Hz, 1H), 4.34 (dd, *J* = 11.2, 6.9 Hz, 1H), 1.99 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.7, 162.5, 154.19, 154.17, 139.4, 134.72, 134.70, 133.60, 127.68, 127.65, 126.75, 126.65, 125.92 (2C), 125.80, 125.78, 125.70, 125.64, 125.5, 122.2, 122.1, 121.2, 120.8, 120.0, 105.2, 104.9, 91.4, 91.2, 74.2, 72.2, 70.4, 68.5, 63.6, 57.3, 21.8, 14.9; **IR** (NaCl, thin film, cm^{-1}) 3340, 3054, 2933, 2108, 1666, 1580, 1403, 1390, 1304, 1269, 1241, 1099, 1072, 1019, 827, 794, 771, 647; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{17}Cl_3N_4O_2Na^+$ $(M+Na)^+$ 449.0309, found 449.0306.



(±)-**1h *trans***

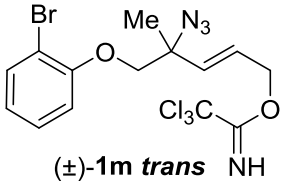


(±)-**1h *E***

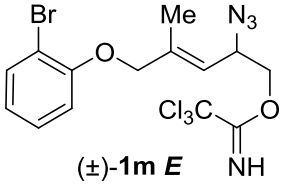


(±)-**1h *Z***

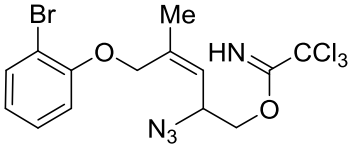
(±)-1h: General procedure 5 was used and the product was isolated in 85% yield (690 mg) as a yellow oil. Compound **1h** was isolated as a mixture of two isomers (1.0:1.8 *trans*:*E*). Trace amounts of **1h *Z*** were observed. NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **1h *trans*** δ 8.41 (s, 1H), 7.83 – 7.72 (m, 3H), 7.52 – 7.44 (m, 1H), 7.41 – 7.35 (m, 1H), 7.23 – 7.18 (m, 1H), 7.17 – 7.15 (m, 1H), 6.13 (dt, *J* = 15.8, 5.1 Hz, 1H), 6.06 (dt, *J* = 15.7, 1.2 Hz, 1H), 4.92 (dd, *J* = 5.2, 1.1 Hz, 2H), 4.09 (d, *J* = 9.3 Hz, 1H), 4.06 (d, *J* = 9.3 Hz, 1H), 1.61 (s, 3H); **1h *E*** δ 8.44 (s, 1H), 7.83 – 7.72 (m, 3H), 7.52 – 7.44 (m, 1H), 7.41 – 7.35 (m, 1H), 7.23 – 7.18 (m, 1H), 7.17 – 7.15 (m, 1H), 5.72 (dq, *J* = 9.2, 1.5 Hz, 1H), 4.75 – 4.68 (m, 1H), 4.61 (s, 2H), 4.37 (dd, *J* = 11.2, 4.7 Hz, 1H), 4.33 (dd, *J* = 11.2, 7.0 Hz, 1H), 1.96 (d, *J* = 1.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.62, 162.59, 162.4, 156.52, 156.46, 156.42, 139.5, 139.2, 134.58, 134.56, 134.51, 133.5, 129.75, 129.71, 129.66, 129.37, 129.32, 129.26, 127.82, 127.79, 126.94, 126.91, 126.66, 126.65, 126.57, 125.8, 124.1, 124.0, 123.9, 122.5, 120.2, 119.0, 118.9, 118.8, 107.3, 107.1, 107.0, 91.4, 91.1, 74.1, 72.1, 70.6, 70.3, 68.5, 67.1, 63.3, 60.5, 57.32, 57.30, 22.0, 21.4, 21.2, 14.8, 14.4; **IR** (NaCl, thin film, cm^{-1}) 3339, 3059, 2922, 2108, 1666, 1629, 1600, 1511, 1468, 1389, 1304, 1256, 1217, 1177, 1079, 1008, 835, 797, 647; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{17}Cl_3N_4O_2Na^+$ $(M+Na)^+$ 449.0309, found 449.0319.



(±)-**1m *trans***

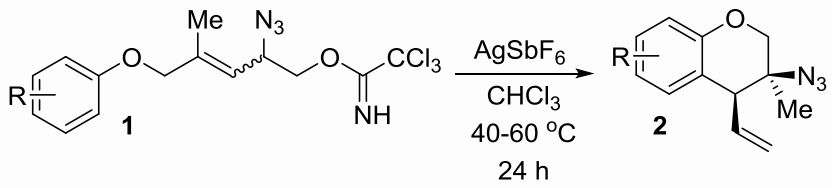


(±)-**1m *E***

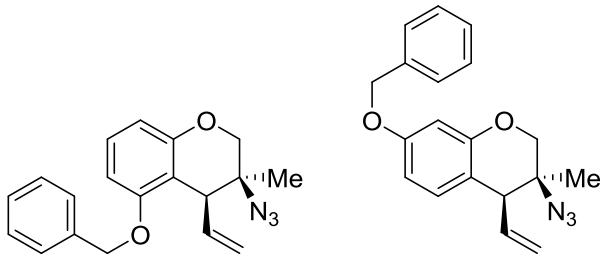


(±)-**1m *Z***

(±)-1m: General procedure 5 was used and the product was isolated in 73% yield (500 mg) as a yellow oil. Compound **1m** was isolated as a mixture of three isomers (1.0:1.6:0.3 *trans*:*E*:*Z*). NMR data given below is based off of idealized integrations of the resulting mixture: **^{1}H NMR** (500 MHz, $CDCl_3$) **1m *trans*** δ 8.38 (s, 1H), 7.59 – 7.50 (m, 1H), 7.33 – 7.20 (m, 1H), 6.96 – 6.79 (m, 2H), 6.11 (dt, *J* = 15.7, 5.1 Hz, 1H), 6.04 (dt, *J* = 15.8, 1.2 Hz, 1H), 4.89 (dd, *J* = 5.1, 1.2 Hz, 2H), 3.96 (d, *J* = 9.0 Hz, 1H), 3.93 (d, *J* = 9.1 Hz, 1H), 1.62 (s, 3H); **1m *E*** δ 8.42 (s, 1H), 7.59 – 7.50 (m, 1H), 7.33 – 7.20 (m, 1H), 6.96 – 6.79 (m, 2H), 5.71 (dq, *J* = 9.1, 1.5 Hz, 1H), 4.67 (ddd, *J* = 9.1, 7.0, 4.7 Hz, 1H), 4.55 (s, 2H), 4.34 (dd, *J* = 11.1, 4.7 Hz, 1H), 4.30 (dd, *J* = 11.1, 6.9 Hz, 1H), 1.93 (d, *J* = 1.4 Hz, 3H); **1m *Z*** δ 8.42 (s, 1H), 7.59 – 7.50 (m, 1H), 7.33 – 7.20 (m, 1H), 6.96 – 6.79 (m, 2H), 5.47 (dq, *J* = 9.4, 1.4 Hz, 1H), 4.91 – 4.85 (m, 1H), 4.68 – 4.65 (m, 2H), 4.35 (dd, *J* = 11.0, 4.6 Hz, 1H), 4.28 (dd, *J* = 11.2, 7.3 Hz, 1H), 2.00 (d, *J* = 1.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.7, 162.6, 162.5, 154.9, 154.8, 138.9, 138.7, 133.8, 133.7, 133.6, 133.3, 128.65, 128.60, 128.58, 126.0, 122.8, 122.7, 122.5, 122.4, 120.4, 113.7, 113.5, 112.7, 112.5, 91.4, 91.1, 74.9, 72.9, 70.6, 70.3, 68.6, 68.3, 63.4, 57.3, 57.2, 21.9, 21.4, 14.7; **IR** (NaCl, thin film, cm^{-1}) 3340, 2924, 2108, 1666, 1585, 1480, 1442, 1293, 1246, 1064, 1031, 1011, 830, 797, 748, 647; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{14}BrCl_3N_4O_2Na^+$ $(M+Na)^+$ 476.9258, found 476.9245.



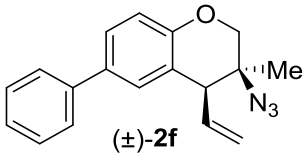
General Procedure 6: Silver Catalyzed Resolution of Allylic Azides via Friedel-Crafts Alkylation: Example given for R = *m*-OBn. **Compound (±)-2d:** In a glovebox, a 50 mL round bottom flask was sequentially charged with imidate **1a** (360 mg, 0.75 mmol) and silver hexafluoroantimonate (12.3 mg, 37 μmol, 5 mol %). To the mixture, $CHCl_3$ (7.5 mL, see note below) was added. The vial was sealed, removed from the glovebox, and placed on a hot plate set to 50 °C (external thermocouple) with a stir rate of 400 rpm. After 24 h, the resulting mixture was concentrated *in vacuo* and filtered through a short plug of silica (1:1 DCM:hexanes). Final purification by column chromatography (0 to 20% gradient, EtOAc in hexanes) afforded the product as two separable regioisomers (**2d-A** and **2d-B**) in a 1:3.5 ratio in 64% overall yield. **2d-A** (34 mg, 0.10 mmol, 14%) was isolated as a clear oil in a 15:1 dr. **2d-B** (116 mg, 0.37 mmol, 49%) was isolated as a white solid in >25:1 dr. Note: Substrates **2a-c**, **2e**, **2j-l**, and **2n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]



(±)-2d-B: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.0 Hz, 2H), 7.42 – 7.37 (m, 2H), 7.36 – 7.31 (m, 1H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.60 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 5.82 (ddd, *J* = 17.0, 10.0, 9.0 Hz, 1H), 5.42 (dd, *J* = 10.1, 1.8 Hz, 1H), 5.26 (ddd, *J* = 16.9, 1.7, 0.7 Hz, 1H), 5.03 (s, 2H), 4.18 (d, *J* = 11.3 Hz, 1H), 3.90 (dd, *J* = 11.3, 0.8 Hz, 1H), 3.34 (br d, *J* = 8.9 Hz, 1H), 1.40 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.2, 153.8, 137.1, 136.2, 130.4, 128.8, 128.1, 127.7, 120.5, 114.2, 109.1, 102.4, 70.9, 70.3, 59.0, 50.5, 20.8; **IR** (NaCl, thin film, cm^{-1}) 3065, 3033, 2970, 2930, 2873, 2107, 1618, 1502, 1285, 1264, 1179, 1164, 1116, 736, 696; **HRMS** (ESI-TOF) *m/z* calcd $C_{19}H_{19}N_3O_2Na^+$ $(M+Na)^+$ 344.1369, found 344.1367.

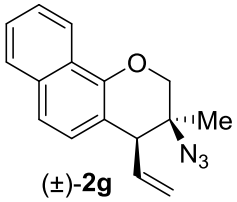
Note on solvent: This procedure used anhydrous chloroform stabilized with amylene (50-150 ppm). Chloroform stabilized with ethanol gave inferior results as did chloroform which was stored under ambient conditions. For best results, the salts, substrates, and solvent were transferred in a glovebox, after which the vials were sealed and removed from the glovebox.

Note: Several minor modifications were made based on the substrate. The most common of these are to 1) heat the reaction to different temperature (40 °C – 60 °C), 2) alter the catalyst loading catalyst loading (5% - 10% $AgSbF_6$), or 3) simplify final purification via a short pass of silica instead of a flash column. These variations are noted for each substrate below.



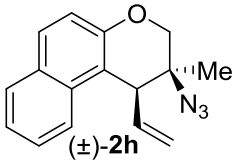
(±)-**2f**

(±)-2f: A variation of general procedure 6 was used. The reaction was conducted at 0.10 M substrate and used 10% catalyst at 40 °C for 8 h. Purification was conducted by column chromatography (0 to 20% gradient, EtOAc in hexanes). This afforded compound **2f** as a white solid in 39% yield (200 mg, 59% brsm) with >25:1 dr, along with 34 % unreacted **1f**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 – 7.50 (m, 2H), 7.43 – 7.39 (m, 3H), 7.33 – 7.29 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.88 (ddd, *J* = 17.1, 10.1, 8.9 Hz, 1H), 5.47 (dd, *J* = 10.1, 1.7 Hz, 1H), 5.33 (ddd, *J* = 17.1, 1.8, 0.8 Hz, 1H), 4.24 (d, *J* = 11.4 Hz, 1H), 3.96 (dd, *J* = 11.4, 0.9 Hz, 1H), 3.45 (br d, *J* = 8.9 Hz, 1H), 1.45 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.6, 141.0, 135.8, 134.6, 128.9, 128.5, 127.3, 127.0, 126.9, 122.0, 121.1, 117.0, 70.9, 59.0, 51.1, 20.9; **IR** (NaCl, thin film, cm^{-1}) 3030, 2975, 2928, 2109, 1482, 1263, 1234, 1055, 762, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{17}N_3ONa^+$ $(M+Na)^+$ 314.1264, found 314.1267.



(±)-**2g**

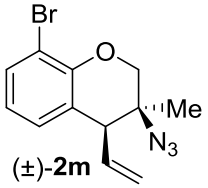
(±)-2g: A variation of general procedure 6 was used. The reaction was conducted at 0.10 M substrate and used 5% catalyst at 60 °C for 24 h. Purification was conducted by filtering through a short plug of silica (1:1 DCM:hexanes). This afforded compound **2g** (15 mg) as a white solid in 56% yield with >25:1 dr: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 – 8.21 (m, 1H), 7.79 – 7.76 (m, 1H), 7.51 – 7.47 (m, 2H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 1H), 5.93 (ddd, *J* = 17.0, 10.0, 8.8 Hz, 1H), 5.44 (dd, *J* = 10.1, 1.8 Hz, 1H), 5.30 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.35 (d, *J* = 11.2 Hz, 1H), 4.06 (dd, *J* = 11.1, 1.1 Hz, 1H), 3.53 (br d, *J* = 8.8 Hz, 1H), 1.48 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.1, 136.7, 133.7, 127.6, 127.2, 126.5, 125.7, 124.8, 122.0, 120.8, 120.4, 115.3, 70.5, 59.0, 50.9, 21.1; **IR** (NaCl, thin film, cm^{-1}) 3055, 2975, 2930, 2877, 2108, 1575, 1506, 1403, 1380, 1355, 1279, 1106, 1087, 926, 812, 766, 662; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{15}N_3ONa^+$ $(M+Na)^+$ 288.1107, found 288.1099.



(±)-**2h**

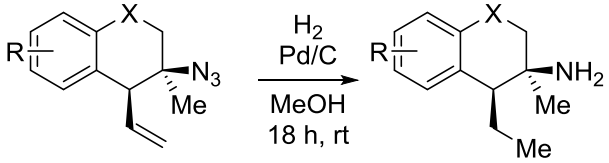
(±)-2h: A variation of general procedure 6 was used. The reaction was conducted at 0.10 M substrate and used 5% catalyst at 50 °C for 24 h. Purification was conducted by filtering through a short plug of silica (1:1 DCM:hexanes). This afforded compound **2h** as a white solid in 58% yield (15 mg) with a >25:1 dr. Compound **2h** was isolated as a single regioisomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.9 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.48 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.08 (d, *J* = 8.9 Hz, 1H), 6.18 (ddd, *J* = 17.1, 10.3, 6.8 Hz, 1H), 5.33 (dt, *J* = 10.3, 1.1 Hz, 1H), 4.97 (dt, *J* = 17.1, 1.4 Hz, 1H), 4.15 (d, *J* = 10.4 Hz, 1H), 4.01 (br d, *J* = 6.8 Hz, 1H), 3.87 (dd, *J* = 10.4, 2.0 Hz, 1H), 1.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.4, 137.3, 132.9, 129.7, 129.6, 128.8, 126.8, 123.7, 122.8, 120.2, 118.5, 112.8, 67.4, 59.7, 46.1, 22.1; **IR** (NaCl, thin film, cm^{-1}) 3063, 2974, 2885, 2099, 1623, 1600, 1514, 1472,

1434, 1403, 1258, 1230, 1075, 927, 812, 745; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{15}N_3ONa^+$ $(M+Na)^+$ 288.1107, found 288.1112.

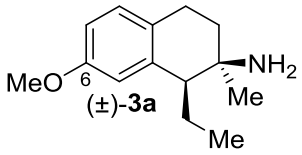


(±)-**2m**

(±)-2m: A variation of general procedure 6 was used. The reaction was conducted at 0.10 M substrate and used 10% catalyst at 60 °C for 24 h. Purification was conducted by filtering through a short plug of silica (3:2 DCM:hexanes). This afforded compound **2m** as a white solid in 69% yield (20 mg) with a >25:1 dr: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.04 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.80 (t, *J* = 7.8 Hz, 1H), 5.82 (ddd, *J* = 17.1, 10.1, 8.9 Hz, 1H), 5.45 (dd, *J* = 10.1, 1.7 Hz, 1H), 5.27 (ddd, *J* = 17.1, 1.7, 0.8 Hz, 1H), 4.31 (d, *J* = 11.4 Hz, 1H), 4.00 (dd, *J* = 11.4, 0.9 Hz, 1H), 3.40 (dt, *J* = 8.9, 1.0 Hz, 1H), 1.43 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 149.7, 135.6, 132.2, 129.1, 123.5, 122.0, 121.2, 110.7, 71.3, 58.7, 51.0, 20.7; **IR** (NaCl, thin film, cm^{-1}) 2977, 2930, 2875, 2109, 1467, 1443, 1280, 1240, 1070, 1044, 927, 770, 737; **HRMS** (ESI-TOF) *m/z* calcd for $C_{12}H_{12}BrN_3ONa^+$ $(M+Na)^+$ 316.0056, found 316.0056.

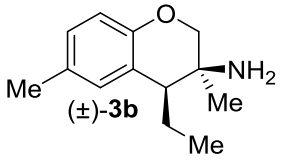


General Procedure 7: Palladium Catalyzed Hydrogenation: Example given for R = 6-OMe, X = CH_2. **Compound (±)-3a**: An oven dried 4 mL vial was charged with palladium on carbon (10 mg, 10 w % Pd) and sealed with a septa cap. The vial was then flushed with nitrogen gas (approx. 0.5 L) and charged with a solution of azide **2a**[2] (24 mg, 0.10 mmol) in MeOH (1 mL). The head space of the vial was then flushed with hydrogen gas (approx. 1 L). The vial was fitted with 2 balloons of hydrogen gas and stirred vigorously. After 18h, the reaction was diluted with MeOH and filtered through a short plug of silica gel. The filtrate was concentrated under reduced pressure to afford **3a** (14 mg, 0.7 mmol, 65%) as a clear oil. **Note:** Substrates **2a-c** and **2e**, were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]

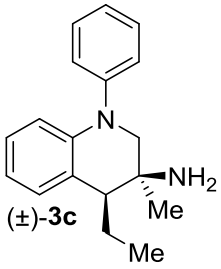


(±)-**3a**

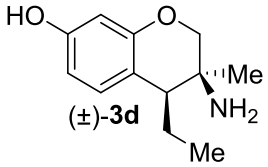
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.4 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.7 Hz, 1H), 6.61 (d, *J* = 2.7 Hz, 1H), 3.79 (s, 3H), 2.87 (ddd, *J* = 17.4, 7.8, 2.6 Hz, 1H), 2.76 (ddd, *J* = 17.6, 10.4, 7.7 Hz, 1H), 2.23 (dd, *J* = 9.4, 3.7 Hz, 1H), 1.96 (dtd, *J* = 21.7, 7.8, 3.8 Hz, 1H), 1.88 (ddd, *J* = 13.4, 10.7, 8.1 Hz, 1H), 1.56 (ddt, *J* = 12.7, 7.9, 2.3 Hz, 1H), 1.36 – 1.22 (m, 3H), 1.07 (s, 3H), 0.99 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.0, 142.0, 129.8, 126.6, 115.4, 111.8, 55.4, 53.3, 51.2, 33.8, 28.6, 26.4, 25.1, 13.9; **IR** (NaCl, thin film , cm^{-1}) 3359, 2954, 2929, 2871, 1609, 1502, 1257, 1156, 1043, 810; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{22}NO^+$ $(M+H)^+$ 220.1696, found 220.1693.



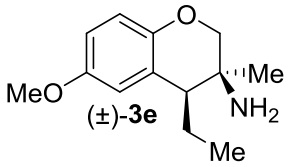
(±)-3b: Compound **2b**[2] was used as the starting material for this reaction. General procedure 7 was used and the product was isolated in 53% yield (11 mg) as a clear oil in 20:1 dr: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.93 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.89 (d, *J* = 2.2 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 3.89 (d, *J* = 10.4 Hz, 1H), 3.69 (d, *J* = 10.4 Hz, 1H), 2.36 (dd, *J* = 8.7, 4.0 Hz, 1H), 2.28 (s, 3H), 1.92 (dqd, *J* = 15.0, 7.6, 4.0 Hz, 1H), 1.43 (dp, *J* = 14.9, 7.7 Hz, 1H), 1.20 (br s, 2H), 1.16 (s, 3H), 1.08 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.4, 130.8, 129.2, 128.4, 125.2, 116.1, 73.3, 48.9, 48.1, 26.7, 25.0, 20.8, 14.0; **IR** (NaCl, thin film, cm^{-1}) 3370, 2960, 2926, 2873, 1615, 1586, 1498, 1243, 1214, 1128, 1032, 813; **HRMS** (ESI-TOF) *m/z* calcd for $C_{13}H_{20}NO^+$ $(M+H)^+$ 206.1539, found 206.1538.



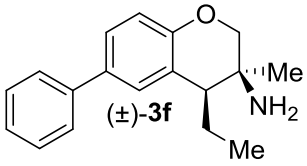
(±)-3c: Compound **2c**[2] was used as the starting material. General procedure 7 was used and the product was isolated in 95% yield (28 mg) as a white solid in 17:1 dr: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.8 Hz, 2H), 7.31 – 7.23 (m, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.10 – 7.03 (m, 1H), 6.99 (td, *J* = 7.8, 1.7 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 2H), 3.51 (d, *J* = 11.1 Hz, 1H), 3.39 (dd, *J* = 11.1, 1.6 Hz, 1H), 2.39 (dd, *J* = 3.3, 1.5 Hz, 1H), 2.25 (br s, 2H), 1.95 (dqd, *J* = 14.9, 7.6, 3.5 Hz, 1H), 1.45 – 1.31 (m, 1H), 1.23 (s, 3H), 1.05 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.7, 141.9, 130.5, 129.7, 126.9, 126.8, 125.2, 124.3, 117.7, 115.2, 60.1, 51.4, 51.0, 28.3, 24.3, 13.2; **IR** (NaCl, thin film, cm^{-1}) 3363, 3061, 3032, 2959, 2923, 2871, 1591, 1495, 1303, 1250, 747, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{23}N_2^+$ $(M+H)^+$ 267.1856, found 267.1850.



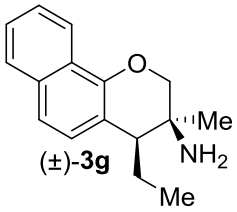
(±)-3d: General procedure 7 was used and the product was isolated in quantitative yield (11 mg) as a clear oil: **^{1}H NMR** (500 MHz, CD_3OD) δ 6.88 (d, *J* = 8.4 Hz, 1H), 6.33 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.22 (d, *J* = 2.5 Hz, 1H), 3.92 (d, *J* = 10.5 Hz, 1H), 3.66 (dd, *J* = 10.5, 1.7 Hz, 1H), 2.30 (ddd, *J* = 9.3, 3.6, 1.4 Hz, 1H), 1.90 (dqd, *J* = 15.0, 7.5, 3.9 Hz, 1H), 1.35 – 1.24 (m, 1H), 1.12 (s, 3H), 1.02 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, CD_3OD) δ 156.7, 153.1, 130.8, 116.0, 107.2, 102.2, 71.4, 48.5, 47.1, 24.7, 24.6, 12.1; **IR** (NaCl, thin film cm^{-1}) 3421, 2963, 2932, 1620, 1504, 1467, 1159, 1120, 633; **HRMS** (ESI-TOF) *m/z* calcd for $C_{12}H_{18}NO_2^+$ $(M+H)^+$ 208.1332, found 208.1331; calcd for $C_{12}H_{15}O_2^+$ $(M-NH_2)^+$ 191.1067, found 191.1064.



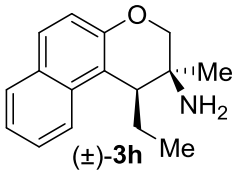
(±)-3e: Compound **2e**[2] was used as the starting material. General procedure 7 was used and the product was isolated in quantitative yield (25 mg) as a clear oil: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.79 – 6.59 (m, 3H), 3.88 (d, *J* = 10.5 Hz, 1H), 3.76 (s, 3H), 3.68 (d, *J* = 10.4 Hz, 1H), 2.38 (dd, *J* = 8.5, 3.9 Hz, 1H), 1.93 (dqd, *J* = 14.9, 7.6, 4.1 Hz, 1H), 1.53 – 1.39 (m, 3H), 1.17 (s, 3H), 1.09 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.2, 146.7, 126.2, 116.8, 115.4, 113.3, 73.3, 55.9, 49.0, 48.2, 26.5, 24.8, 14.1; **IR** (NaCl, thin film, cm^{-1}) 3369, 2960, 2874, 2832, 1496, 1209, 1050, 814; **HRMS** (ESI-TOF) *m/z* calcd for $C_{13}H_{20}NO_2^+$ $(M+H)^+$ 222.1489, found 222.1487; calcd for $C_{13}H_{17}O_2^+$ $(M-NH_2)^+$ 205.1223, found 205.1227.



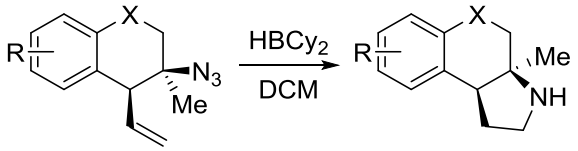
(±)-3f: General procedure 7 was used and the product was isolated in quantitative yield (28 mg) as a clear oil: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 – 7.53 (m, 2H), 7.46 – 7.40 (m, 2H), 7.38 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.35 – 7.28 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.01 (d, *J* = 10.5 Hz, 1H), 3.79 (dd, *J* = 10.5, 1.5 Hz, 1H), 2.50 (dd, *J* = 8.8, 3.9 Hz, 1H), 2.18 (br s, 2H), 2.01 (dqd, *J* = 18.9, 7.5, 3.5 Hz, 1H), 1.54 – 1.45 (m, 1H), 1.24 (s, 3H), 1.14 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.3, 141.2, 133.3, 129.2, 128.9, 126.9, 126.7, 126.6, 125.4, 116.9, 72.8, 49.3, 48.1, 26.4, 24.9, 13.8; **IR** (NaCl, thin film, cm^{-1}) 3367, 3030, 2962, 2930, 2874, 1613, 1483, 1232, 1130, 1019, 825, 763, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{22}NO^+$ $(M+H)^+$ 268.1696, found 268.1686; calcd for $C_{18}H_{19}O^+$ $(M-NH_2)^+$ 251.1430, found 251.1431.



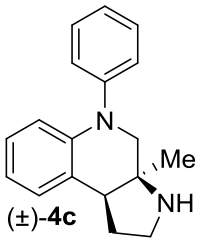
(±)-3g: General procedure 7 was used and the product was isolated in quantitative yield (17 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 – 8.16 (m, 1H), 7.79 – 7.73 (m, 1H), 7.49 – 7.43 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 4.10 (d, *J* = 10.4 Hz, 1H), 3.93 (dd, *J* = 10.4, 1.7 Hz, 1H), 2.57 (ddd, *J* = 8.1, 4.4, 1.6 Hz, 1H), 2.01 (dqd, *J* = 15.1, 7.5, 4.4 Hz, 1H), 1.74 (br s, 2H), 1.60 – 1.49 (m, 1H), 1.23 (s, 3H), 1.12 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.5, 133.5, 128.6, 127.4, 126.0, 125.3, 125.0, 122.0, 119.5, 119.0, 73.2, 49.1, 48.0, 26.7, 25.7, 14.0; **IR** (NaCl, thin film, cm^{-1}) 3369, 3053, 2961, 2930, 2874, 1575, 1401, 1378, 1107, 1092, 1011, 805, 746; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{20}NO^+$ $(M+H)^+$ 242.1539, found 242.1543; calcd for $C_{16}H_{17}O^+$ $(M-NH_2)^+$ 225.1274, found 225.1281.



(±)-3h: General procedure 7 was used and the product was isolated in 91% yield (15 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.50 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.35 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 1H), 4.07 (d, *J* = 10.4 Hz, 1H), 3.77 (dd, *J* = 10.4, 1.9 Hz, 1H), 3.03 (ddd, *J* = 6.5, 4.1, 1.9 Hz, 1H), 1.84 (dp, *J* = 14.5, 7.3 Hz, 1H), 1.69 (dqd, *J* = 15.1, 7.7, 4.0 Hz, 1H), 1.40 (br s, 2H), 1.19 (s, 3H), 1.17 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 149.5, 133.3, 129.6, 128.9, 128.3, 126.4, 123.2, 122.5, 118.7, 118.5, 71.7, 49.3, 44.2, 27.9, 27.5, 15.6; **IR** (NaCl, thin film, cm^{-1}) 3370, 3055, 2959, 2928, 2874, 1622, 1599, 1514, 1472, 1401, 1229, 1082, 1026, 812, 748; **HRMS** (ESI-TOF) *m/z* calcd for $C_{16}H_{20}NO^+$ $(M+H)^+$ 242.1539, found 242.1544; calcd for $C_{16}H_{17}O^+$ $(M-NH_2)^+$ 225.1274, found 225.1273.

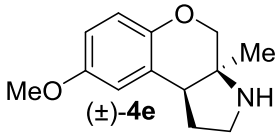


General Procedure 8: Pyrrolidine Synthesis: Example given for R = H, X = N-Ph. **Compound 4c**: In a glovebox, a 4 mL vial was charged with $HBCy_2$ (121 mg, 0.68 mmol). The vial was sealed with a septa cap and removed from the glovebox. The vial was then placed in an ice bath and charged with DCM (0.5 mL). A solution of azide **2c**[2] in DCM (104 mg, 0.34 mmol, 0.2 M) was added at 0 °C and a rinsed with additional DCM (0.2 mL). After 5 min, the ice bath was removed, and the solution was allowed to gradually warm to room temperature. After 18 h, the reaction was quenched by the addition of solid sodium fluoride (270 mg, 6.8 mmol) and DI water (61 µL, 3.4 mmol). After 1 h, the solution was filtered through a short plug of silica gel rinsed (2% NEt_3 in DCM) and the filtrate was concentrated under reduced pressure. Final purification by column chromatography (0 to 70% gradient, *i*-PrOH in 99:1 hexanes:NEt_3) afford pyrrolidine **4c** (72 mg, 0.26 mmol, 76%) as a clear oil. **Note:** Substrates **2c**, **2e**, **2j-l**, and **2n-o** were synthesized according to a previous publication. Characterization data for those compounds can be found in that paper.[2]



(±)-**4c**

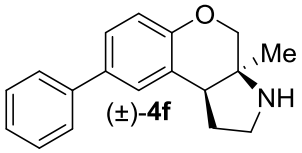
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 7.7 Hz, 2H), 7.18 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.08 (td, *J* = 7.4, 1.1 Hz, 1H), 6.97 (td, *J* = 7.7, 1.6 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 3.45 (d, *J* = 11.8 Hz, 1H), 3.30 (d, *J* = 11.8 Hz, 1H), 3.06 (dd, *J* = 8.2, 5.6 Hz, 2H), 2.96 (t, *J* = 8.2 Hz, 1H), 2.52 (ddt, *J* = 13.5, 8.1, 5.6 Hz, 1H), 1.96 (br s, 1H), 1.88 (dq, *J* = 12.6, 8.2 Hz, 1H), 1.26 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.6, 143.5, 130.5, 129.6, 128.6, 126.4, 123.8, 123.5, 119.5, 115.7, 60.2, 57.7, 48.0, 44.6, 37.6, 25.9; **IR** (NaCl, thin film, cm^{-1}) 3330, 3030, 2958, 2923, 1592, 1572, 1495, 1460, 1447, 1366, 1250, 748, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{21}N_2^+$ $(M+H)^+$ 265.1699, found 265.1700.



(±)-**4e**

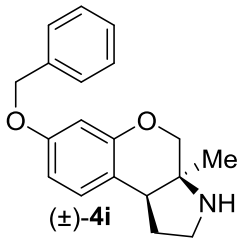
(±)-4e: Compound **2e**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 81% yield (73 mg) as a yellow oil: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.78 (d,

J = 8.5 Hz, 1H), 6.70 – 6.63 (m, 2H), 3.74 (d, *J* = 11.2 Hz, 1H), 3.74 (s, 3H), 3.66 (d, *J* = 10.9 Hz, 1H), 3.12 – 3.03 (m, 1H), 3.01 – 2.95 (m, 1H), 2.94 (br s, 1H), 2.87 (t, *J* = 7.7 Hz, 1H), 2.52 – 2.40 (m, 1H), 1.85 (dq, *J* = 11.9, 7.6 Hz, 1H), 1.22 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.2, 147.8, 126.9, 117.6, 114.5, 113.2, 71.6, 58.4, 55.7, 45.8, 44.6, 35.9, 24.2; **IR** (NaCl, thin film, cm^{-1}) 3342, 2960, 2872, 2833, 1497, 1211, 1046, 817, 722; **HRMS** (ESI-TOF) *m/z* calcd for $C_{13}H_{18}NO_2^+$ $(M+H)^+$ 220.1332, found 220.1332.



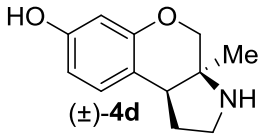
(±)-**4f**

(±)-4f: General procedure 8 was used and the product was isolated in 76% yield (69 mg) as white solid: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 2H), 7.46 – 7.41 (m, 2H), 7.40 – 7.36 (m, 2H), 7.33 (tt, *J* = 7.2, 1.4, 1.2 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 3.85 (d, *J* = 10.9 Hz, 1H), 3.80 (dd, *J* = 10.7, 1.0 Hz, 1H), 3.15 (dt, *J* = 10.7, 7.7 Hz, 1H), 3.05 (ddd, *J* = 10.6, 8.0, 4.5 Hz, 1H), 2.98 (br t, *J* = 7.9 Hz, 1H), 2.76 (br s, 1H), 2.55 (dtd, *J* = 12.5, 7.8, 4.5 Hz, 1H), 1.95 (dq, *J* = 13.0, 7.9 Hz, 1H), 1.31 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.4, 141.0, 134.6, 128.84, 128.81, 126.84, 126.83, 126.3, 126.2, 117.4, 71.5, 58.2, 45.7, 44.6, 36.0, 24.2; **IR** (NaCl, thin film, cm^{-1}) 3322, 3057, 3029, 2963, 2873, 1482, 1265, 1229, 1129, 1049, 1019, 826, 764, 732, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{20}NO^+$ $(M+H)^+$ 266.1539, found 266.1533.



(±)-**4i**

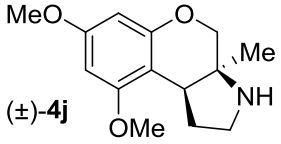
(±)-4i: General procedure 8 was used and the product was isolated in 74% yield (44 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.36 – 7.31 (m, 1H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.63 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.53 (d, *J* = 2.6 Hz, 1H), 5.02 (s, 2H), 3.78 (d, *J* = 10.9 Hz, 1H), 3.73 (d, *J* = 10.9 Hz, 1H), 3.10 (dt, *J* = 10.6, 7.6 Hz, 1H), 2.99 (ddd, *J* = 10.6, 7.9, 4.6 Hz, 1H), 2.85 (t, *J* = 7.7 Hz, 1H), 2.45 (ddd, *J* = 15.8, 8.0, 3.8 Hz, 1H), 2.40 (br s, 1H), 1.84 (dq, *J* = 12.8, 7.7 Hz, 1H), 1.25 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.2, 154.5, 137.1, 130.7, 128.7, 128.0, 127.6, 118.4, 109.3, 102.7, 71.5, 70.2, 58.1, 45.0, 44.6, 35.9, 24.2; **IR** (NaCl, thin film, cm^{-1}) 3374, 3063, 3031, 2963, 2872, 1618, 1582, 1503, 1454, 1379, 1266, 1161, 1127, 1105, 1037, 833, 735, 697; **HRMS** (ESI-TOF) *m/z* calcd for $C_{19}H_{22}NO_2^+$ $(M+H)^+$ 296.1645, found 296.1644.



(±)-**4d**

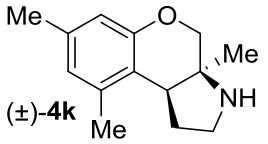
(±)-4d: Compound **4i** was used as the starting material. General procedure 7 was used and the product was isolated in quantitative yield (22 mg) as a clear oil: **^{1}H NMR** (500 MHz, CD_3OD) δ 7.01 (d, *J* = 8.3 Hz, 1H), 6.46 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.31 (d, *J* = 2.4 Hz, 1H), 3.92 (d, *J* = 11.4 Hz, 1H), 3.78 (d, *J* = 11.3 Hz, 1H), 3.19 (dt, *J* = 11.2, 7.2 Hz, 1H), 3.04 (t, *J* = 6.8 Hz, 1H), 3.02 – 2.97 (m, 1H), 2.56 (dq, *J* = 14.1, 7.3 Hz, 1H), 1.94 – 1.86 (m, 1H), 1.34 (s, 3H); **^{13}C NMR** (126 MHz, CD_3OD) δ 156.7, 154.3, 130.0, 115.4, 109.6, 102.8, 69.3, 60.6, 44.2, 43.6, 34.3, 21.3; **IR**

(NaCl, thin film, cm^{-1}) 3300, 2964, 1621, 1593, 1505, 1471, 1384, 1252, 1158, 1107, 1037, 843, 735; **HRMS** (ESI-TOF) *m/z* calcd for $C_{12}H_{16}NO_2^+$ $(M+H)^+$ 206.1176, found 206.1171.



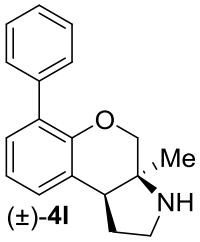
(±)-**4j**

(±)-4j: Compound **2j**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 50% yield (12 mg) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.10 (d, *J* = 2.4 Hz, 1H), 6.08 (d, *J* = 2.4 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.71 (d, *J* = 10.6 Hz, 1H), 3.67 (dd, *J* = 10.8, 1.2 Hz, 1H), 3.11 (dt, *J* = 10.3, 7.7 Hz, 1H), 2.98 (ddd, *J* = 10.5, 8.2, 3.7 Hz, 1H), 2.80 (br t, *J* = 8.3 Hz, 1H), 2.58 (dtd, *J* = 13.0, 7.6, 3.7 Hz, 1H), 2.50 (br s, 1H), 1.66 (dq, *J* = 13.0, 8.5 Hz, 1H), 1.23 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.7, 159.6, 154.9, 107.4, 93.4, 92.2, 71.5, 57.2, 55.6, 55.5, 44.7, 41.6, 34.6, 24.1; **IR** (NaCl, thin film, cm^{-1}) 3324, 2960, 1617, 1590, 1494, 1454, 1422, 1202, 1145, 1097, 1057, 813; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{20}NO_3^+$ $(M+H)^+$ 250.1438, found 250.1436.



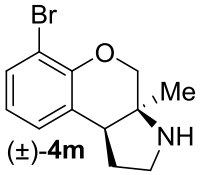
(±)-**4k**

(±)-4k: Compound **2k**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 35% yield (22 mg) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.64 (s, 1H), 6.58 (s, 1H), 3.76 (d, *J* = 10.7 Hz, 1H), 3.65 (dd, *J* = 10.7, 1.2 Hz, 1H), 3.12 (dt, *J* = 10.8, 8.0 Hz, 1H), 3.04 (ddd, *J* = 10.7, 8.5, 3.9 Hz, 1H), 2.79 (br t, *J* = 8.6 Hz, 1H), 2.59 (dtd, *J* = 12.3, 8.1, 3.9 Hz, 1H), 2.27 (s, 3H), 2.26 (s, 3H), 2.11 (br s, 1H), 1.68 (dq, *J* = 12.8, 8.5 Hz, 1H), 1.24 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.5, 138.1, 136.9, 124.2, 121.9, 115.2, 70.8, 58.2, 44.5, 44.4, 34.8, 24.0, 21.1, 19.5; **IR** (NaCl, thin film, cm^{-1}) 3334, 2961, 2920, 2873, 1618, 1575, 1455, 1296, 1137, 1075, 840; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{20}NO^+$ $(M+H)^+$ 218.1539, found 218.1535.



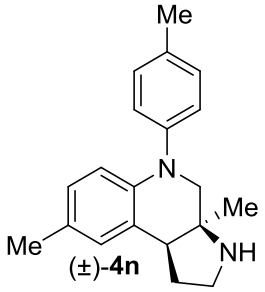
(±)-**4l**

(±)-4l: Compound **2l**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 57% yield (15 mg) as a yellow oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 – 7.52 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.33 (dt, *J* = 7.4, 1.4 Hz, 1H), 7.19 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.16 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 3.77 (d, 11.1 Hz, 1H), 3.75 (d, 10.9 Hz, 1H), 3.12 (dt, *J* = 10.5, 7.7 Hz, 1H), 3.04 (ddd, *J* = 10.6, 7.9, 4.3 Hz, 1H), 2.98 (t, *J* = 8.0 Hz, 1H), 2.55 (dtd, *J* = 12.3, 7.7, 4.3 Hz, 1H), 1.93 (dq, *J* = 12.7, 8.0 Hz, 1H), 1.90 (br s, 1H), 1.28 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 151.0, 138.6, 130.5, 129.71, 129.70, 128.7, 128.2, 127.1, 127.1, 121.3, 71.9, 58.1, 46.2, 44.9, 36.7, 24.6; **IR** (NaCl, thin film, cm^{-1}) 3319, 3056, 2961, 2923, 2871, 1586, 1465, 1429, 1213, 1072, 1024, 759, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{20}NO^+$ $(M+H)^+$ 266.1539, found 266.1547.



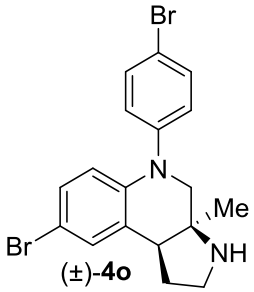
(±)-**4m**

(±)-4m: General procedure 8 was used and the product was isolated in 55% yield (22 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.09 (dd, *J* = 7.7, 2.2 Hz, 1H), 6.80 (t, *J* = 7.8 Hz, 1H), 3.87 (d, *J* = 11.2 Hz, 1H), 3.84 (d, *J* = 10.9 Hz, 1H), 3.13 (dt, *J* = 10.6, 7.8 Hz, 1H), 3.02 (ddd, *J* = 10.6, 8.0, 4.4 Hz, 1H), 2.92 (t, *J* = 8.1 Hz, 1H), 2.51 (dtd, *J* = 12.4, 7.8, 4.3 Hz, 1H), 2.37 (br s, 1H), 1.86 (dq, *J* = 12.8, 8.0 Hz, 1H), 1.28 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.5, 131.1, 129.5, 127.8, 122.3, 111.2, 72.0, 58.2, 46.0, 44.6, 36.1, 24.2; **IR** (NaCl, thin film, cm^{-1}) 3334, 2963, 2926, 2875, 1563, 1465, 1441, 1229, 1071, 1019, 771, 732; **HRMS** (ESI-TOF) *m/z* calcd for $C_{12}H_{15}BrNO^+$ $(M+H)^+$ 268.0332, found 268.0338.



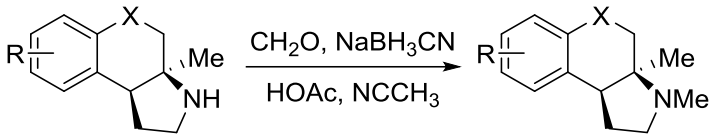
(±)-**4n**

(±)-4n: Compound **2n**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 74% yield (22 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.97 (d, *J* = 2.1 Hz, 1H), 6.78 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 3.96 (br s, 1H), 3.45 (d, *J* = 11.8 Hz, 1H), 3.30 (d, *J* = 11.7 Hz, 1H), 3.13 – 3.09 (m, 2H), 2.98 (br t, *J* = 8.1 Hz, 1H), 2.54 (dddd, *J* = 13.0, 8.2, 6.4, 5.2 Hz, 1H), 2.35 (s, 3H), 2.26 (s, 3H), 1.90 (dq, *J* = 12.8, 8.2 Hz, 1H), 1.31 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.0, 141.5, 133.3, 130.7, 130.2, 128.6, 127.4, 127.3, 123.0, 115.5, 60.9, 57.1, 47.7, 44.1, 37.0, 25.1, 21.0, 20.6; **IR** (NaCl, thin film, cm^{-1}) 3351, 2921, 1609, 1502, 1259, 810; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{25}N_2^+$ $(M+H)^+$ 293.2012, found 293.2011.

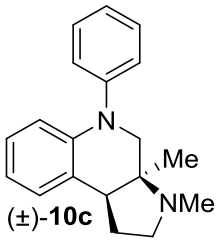


(±)-**4o**

(±)-4o: Compound **2o**[2] was used as the starting material. General procedure 8 was used and the product was isolated in 81% yield (81 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 – 7.39 (m, 2H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.09 – 7.03 (m, 3H), 6.70 (d, *J* = 8.8 Hz, 1H), 3.42 (d, *J* = 11.9 Hz, 1H), 3.27 (d, *J* = 11.9 Hz, 1H), 3.16 – 3.03 (m, 2H), 2.93 (br t, *J* = 8.4 Hz, 1H), 2.61 (br s, 1H), 2.57 – 2.45 (m, 1H), 1.86 (dq, *J* = 13.0, 8.4 Hz, 1H), 1.27 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 146.2, 141.9, 133.0, 132.8, 130.6, 129.6, 125.2, 117.6, 116.5, 112.0, 60.3, 57.2, 47.7, 44.3, 37.1, 25.4; **IR** (NaCl, thin film, cm^{-1}) 3320, 2961, 2922, 1583, 1438, 1258, 1167, 1068, 812; **HRMS** (ESI-TOF) *m/z* calcd for $C_{18}H_{19}Br_2N_2^+$ $(M+H)^+$ 420.9910, found 420.9899.

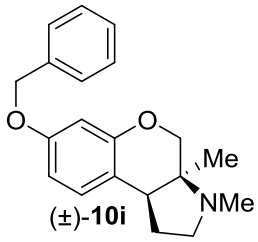


General Procedure 9: Pyrrolidine *N*-Methylation: Example given for R = H, X = N-Ph. **Compound 10c:** $NaBH_3CN$ (9.1 mg, 0.15 mmol) was add to a solution of amine **4c** (29 mg, 0.11 mmol) and CH_2O (40 µL, 37% aq. solution) in acetonitrile (0.3 mL) in an ice bath. After 15 min, glacial acetic acid (4 µL, 70 µmol) was added. After an additional 15 min, the reaction was removed from the ice bath and allowed to warm to rt. After 18 h, the reaction mixture was directly purified by column chromatography (0 to 60 % gradient, *i*-PrOH in 99:1 hexanes:NEt_3) afforded **10c** (27 mg, 0.10 mmol, 89%) as a clear oil.



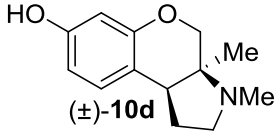
(±)-**10c**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.25 – 7.21 (m, 2H), 7.16 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.09 (tt, *J* = 7.3, 1.2 Hz, 1H), 6.96 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H), 6.83 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.79 (td, *J* = 7.4, 1.2 Hz, 1H), 3.40 (d, *J* = 11.6 Hz, 1H), 3.26 (dd, *J* = 11.6, 1.2 Hz, 1H), 3.02 – 2.96 (m, 2H), 2.87 (td, *J* = 9.1, 4.8 Hz, 1H), 2.49 (dddd, *J* = 12.6, 9.4, 7.9, 4.7 Hz, 1H), 2.40 (s, 3H), 1.83 (dtd, *J* = 12.7, 8.8, 6.5 Hz, 1H), 1.19 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.9, 143.1, 130.3, 129.5, 128.6, 126.4, 124.1, 123.5, 119.2, 115.5, 60.6, 52.8, 52.5, 48.0, 34.6, 32.9, 21.4; **IR** (NaCl, thin film, cm^{-1}) 3029, 2961, 2933, 2893, 2778, 1592, 1495, 1367, 1266, 1212, 747, 699; **HRMS** (ESI-TOF) *m/z* calcd for $C_{19}H_{23}N_2^+$ $(M+H)^+$ 279.1856, found 279.1867.



(±)-**10i**

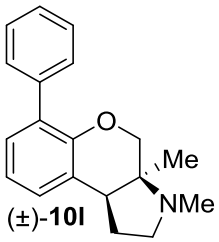
(±)-10i: General procedure 9 was used and the product was isolated in 72% yield (12 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.35 – 7.30 (m, 1H), 7.02 (d, *J* = 8.5 Hz, 1H), 6.61 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 5.02 (s, 2H), 3.79 (d, *J* = 11.0 Hz, 1H), 3.73 (d, *J* = 10.9 Hz, 1H), 2.95 – 2.82 (m, 3H), 2.43 (s, 3H), 2.43 – 2.37 (m, 1H), 1.74 (dq, *J* = 12.8, 7.6 Hz, 1H), 1.12 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.2, 154.5, 137.3, 130.4, 128.7, 128.1, 127.6, 119.7, 109.3, 102.9, 70.3, 69.0, 59.3, 53.1, 45.3, 34.7, 32.3, 18.7; **IR** (NaCl, thin film, cm^{-1}) 2962, 2931, 2783, 1618, 1583, 1503, 1454, 1266, 1163, 1036, 734, 696; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{24}NO_2^+$ $(M+H)^+$ 310.1802, found 310.1804.



(±)-**10d**

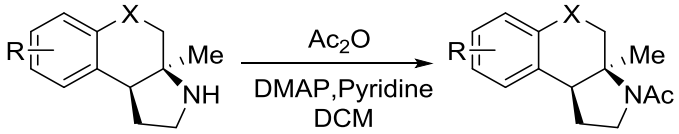
(±)-10d: 10i was used as the starting material. General procedure 7 was used and the product was isolated in 77% yield (6.5 mg) as a clear oil: **^{1}H NMR** (500 MHz, CD_3OD) δ 6.94 (d, *J* = 8.2 Hz,

1H), 6.40 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.27 (d, *J* = 2.5 Hz, 1H), 3.82 (d, *J* = 11.0 Hz, 1H), 3.73 (dd, *J* = 11.0, 1.0 Hz, 1H), 2.91 – 2.84 (m, 3H), 2.44 (ddt, *J* = 12.8, 9.4, 6.4 Hz, 1H), 2.39 (s, 3H), 1.69 (dq, *J* = 12.7, 7.7 Hz, 1H), 1.12 (s, 3H); **^{13}C NMR** (126 MHz, CD_3OD) δ 156.2, 154.1, 129.9, 117.8, 109.0, 102.7, 67.5, 59.4, 52.2, 44.7, 33.3, 31.6, 17.3; **IR** (NaCl, thin film, cm^{-1}) 3402, 2963, 1620, 1594, 1507, 1469, 1244, 1156, 1122, 1038, 842; **HRMS** (ESI-TOF) *m/z* calcd for $C_{13}H_{18}NO_2^+$ $(M+H)^+$ 220.1332, found 220.1328.

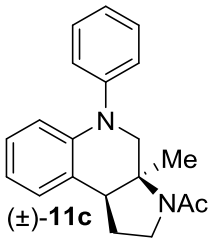


(±)-10l

(±)-10l: General procedure 9 was used and the product was isolated in 70% yield (11 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 – 7.53 (m, 2H), 7.44 – 7.38 (m, 2H), 7.33 (tt, *J* = 7.5, 1.4 Hz, 1H), 7.18 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.14 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 3.78 (s, 2H), 3.01 (t, *J* = 8.7 Hz, 1H), 2.97 – 2.90 (m, 2H), 2.49 (ddt, *J* = 12.5, 9.3, 5.9 Hz, 1H), 2.45 (s, 3H), 1.84 (dq, *J* = 12.6, 7.9 Hz, 1H), 1.18 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 151.0, 138.6, 130.5, 129.7, 129.3, 128.6, 128.1, 128.0, 127.1, 121.3, 69.3, 59.3, 53.1, 46.3, 34.8, 32.6, 19.4; **IR** (NaCl, thin film, cm^{-1}) 3056, 2963, 2932, 2871, 1466, 1430, 1209, 1179, 1072, 1022, 759, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{19}H_{22}NO^+$ $(M+H)^+$ 280.1696, found 280.1694.

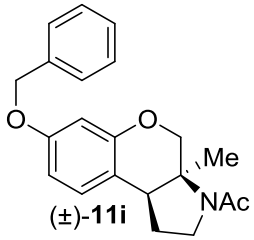


General Procedure 10: Pyrrolidine *N*-Acetylation: Example given for R = H, X = N-Ph. **Compound 11c:** To a solution of amine **4c** (29 mg, 0.11 mmol) in DCM (0.8 mL) was sequentially added DMAP (1.0 mg, 8 μmol) and pyridine (10 μL, 0.12 mmol). The solution was cooled in an ice bath and Ac_2O (12 μL, 0.12 mmol) was added. The ice bath was then removed, and the solution was allowed to warm to rt. After 18 h, the solution was purified directly by column chromatography (0 to 70% gradient, *i*-PrOH in hexanes) afforded amide **11c** (25 mg, 0.08 mmol, 73%) as a clear oil.



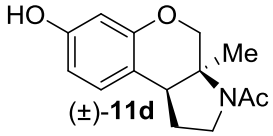
(±)-11c

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.18 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.17 – 7.14 (m, 2H), 7.05 – 7.02 (m, 1H), 7.02 – 6.99 (m, 1H), 6.92 (dd, *J* = 8.4, 1.3 Hz, 1H), 6.84 (td, *J* = 7.3, 1.3 Hz, 1H), 3.92 (d, *J* = 12.2 Hz, 1H), 3.87 (d, *J* = 12.2 Hz, 1H), 3.50 – 3.44 (m, 2H), 3.12 (t, *J* = 7.4 Hz, 1H), 2.44 (dtd, *J* = 12.2, 6.6, 5.3 Hz, 1H), 1.96 – 1.87 (m, 1H), 1.90 (s, 3H), 1.54 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.5, 147.4, 143.8, 130.0, 129.4, 126.9, 126.5, 123.1, 123.0, 119.8, 117.1, 62.6, 52.7, 48.6, 47.5, 33.1, 24.2, 22.8; **IR** (NaCl, thin film, cm^{-1}) 2967, 2929, 2869, 1644, 1496, 1408, 751; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{22}N_2ONa^+$ $(M+Na)^+$ 329.1624, found 329.1628.



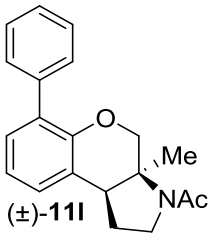
(±)-**11i**

(±)-11i: General procedure 10 was used and the product was isolated in 75% yield (14 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.0 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.31 (m, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.63 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.53 (d, *J* = 2.6 Hz, 1H), 5.02 (s, 2H), 4.34 (d, *J* = 10.8 Hz, 1H), 4.19 (d, *J* = 10.8 Hz, 1H), 3.50 (dt, *J* = 10.0, 6.8 Hz, 1H), 3.37 (dt, *J* = 10.1, 6.6 Hz, 1H), 3.02 (t, *J* = 6.7 Hz, 1H), 2.39 (dq, *J* = 12.9, 6.5 Hz, 1H), 2.06 (s, 3H), 1.84 (dq, *J* = 13.6, 6.9 Hz, 1H), 1.53 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.8, 158.6, 155.6, 137.1, 130.1, 128.8, 128.1, 127.7, 116.0, 109.7, 102.6, 70.2, 67.8, 61.1, 47.7, 45.8, 31.9, 24.5, 21.2; **IR** (NaCl, thin film, cm^{-1}) 2968, 2927, 2874, 1646, 1620, 1503, 1409, 1163, 738; **HRMS** (ESI-TOF) *m/z* calcd for $C_{21}H_{23}NO_3Na^+$ $(M+Na)^+$ 360.1570, found 360.1576.



(±)-**11d**

(±)-11d: 11i was used as the starting material. General procedure 7 was used and the product was isolated in 89% yield (8.9 mg) as a clear oil: **^{1}H NMR** (500 MHz, CD_3OD) δ 7.02 (d, *J* = 8.4 Hz, 1H), 6.44 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.26 (d, *J* = 2.5 Hz, 1H), 4.28 (d, *J* = 10.8 Hz, 1H), 4.09 (d, *J* = 10.7 Hz, 1H), 3.58 (dt, *J* = 10.1, 6.8 Hz, 1H), 3.39 (dt, *J* = 10.2, 6.7 Hz, 1H), 3.05 (t, *J* = 6.6 Hz, 1H), 2.43 (dq, *J* = 13.0, 6.6 Hz, 1H), 2.06 (s, 3H), 1.85 (dq, *J* = 12.4, 6.9 Hz, 1H), 1.49 (s, 3H); **^{13}C NMR** (126 MHz, CD_3OD) δ 171.0, 156.7, 155.2, 129.8, 114.4, 109.3, 102.5, 66.8, 61.2, 47.3, 45.5, 31.3, 22.6, 19.7; **IR** (NaCl, thin film, cm^{-1}) 3417, 2917, 1616, 1505, 1455, 1417, 1160, 1113, 1043, 848, 630; **HRMS** (ESI-TOF) *m/z* calcd for $C_{14}H_{17}NO_3Na^+$ $(M+Na)^+$ 270.1101, found 270.1099.



(±)-**11l**

(±)-11l: General procedure 10 was used and the product was isolated in 96% yield (5.9 mg) as a clear oil: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 – 7.51 (m, 2H), 7.41 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.33 (tt, *J* = 7.6, 1.4 Hz, 1H), 7.23 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.15 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 4.28 (d, *J* = 10.8 Hz, 1H), 4.21 (d, *J* = 10.7 Hz, 1H), 3.55 (dt, *J* = 10.0, 7.1 Hz, 1H), 3.46 (ddd, *J* = 10.0, 7.1, 5.3 Hz, 1H), 3.14 (t, *J* = 7.2 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.07 (s, 3H), 1.94 (dq, *J* = 12.5, 7.5 Hz, 1H), 1.58 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.8, 151.9, 138.2, 130.6, 129.7 (2C), 129.2, 128.9, 128.2 (2C), 127.2, 124.5, 121.4, 67.9, 61.0, 47.8, 46.8, 32.5, 24.5, 21.4; **IR** (NaCl, thin film, cm^{-1}) 2968, 2929, 2873, 1645, 1429, 1409, 1216, 1029, 761, 698; **HRMS** (ESI-TOF) *m/z* calcd for $C_{20}H_{21}NO_2Na^+$ $(M+Na)^+$ 330.1465, found 330.1463.

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pK_i Determination:

Compound pK_i were determined by the Psychoactive Drug Screening Program (PDSP) using the following method: The IC_{50} was first determined using the equation

$$Y = Bottom + \frac{(Top - Bottom)}{1 + 10^{X - \log(IC_{50})}}$$

where *Y* is the total binding in the presence of the test compound *X*. *Top* and *Bottom* are the total and nonspecific binding in the absence and presence of 10 μM reference antagonist. IC_{50} is the concentration at which 50% observed binding of the displaced radioligand was observed. The IC_{50} was converted to K_i according to the Cheng-Prusoff equation:

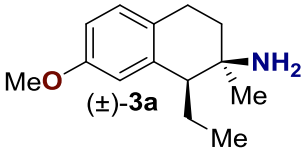
$$K_i = \frac{IC_{50}}{1 + \frac{L}{K_d}}$$

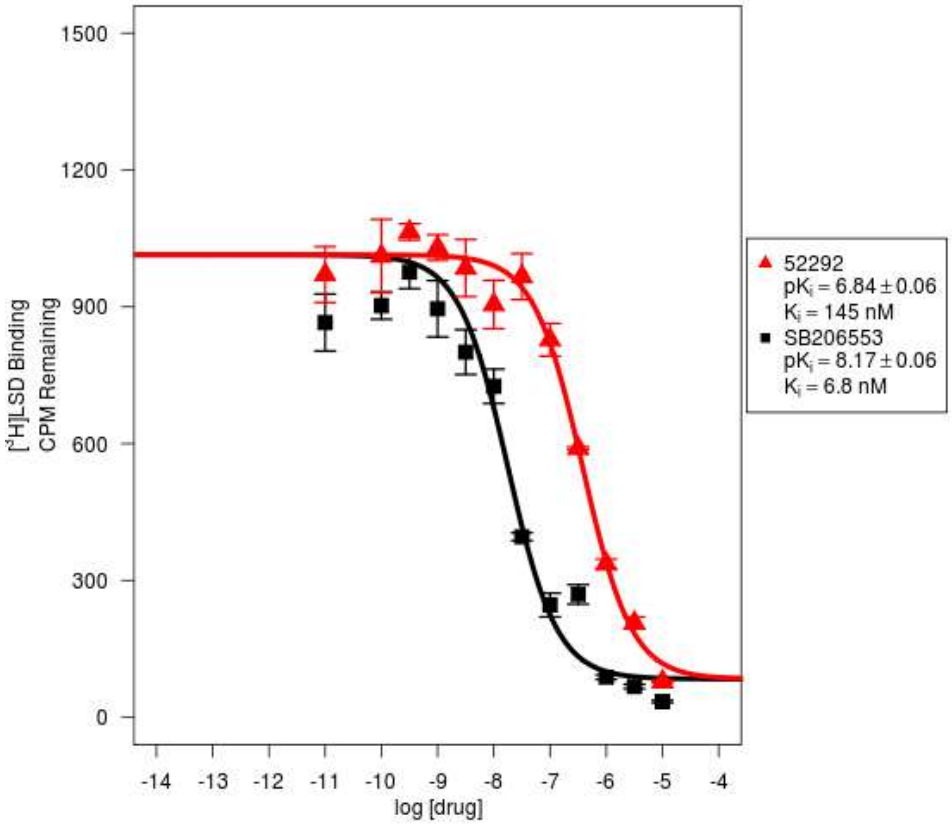
where *L* is the radioligand concentration used in the competition binding assay and K_d is the radioligand equilibrium binding affinity determined during saturation binding assays. *Top* and *Bottom* values are shared among all binding curves from the same plate if necessary.

pK_i errors were determined as follows: For pK_i values determined from triplicate measurements of a single experiment, the error reflects the error in the sigmoidal curve fit. For pK_i values determined from the average of duplicate experiments run in triplicate, the error reflects one half the difference between the two calculated pK_i values. For pK_i values determined from the average of triplicate experiments run in triplicate, the error reflects the standard deviation of the three calculated pK_i values.

For more details on the fitting process please reference the PDSP assay protocol book at: https://pdspdb.unc.edu/pdspWeb/content/UNC-CH%20Protocol%20Book.pdf

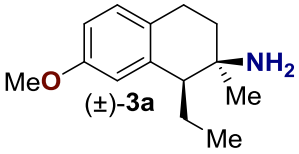
Compound **(±)-3a**, PDSP ID 52292, 5-HT_{2B} receptor:

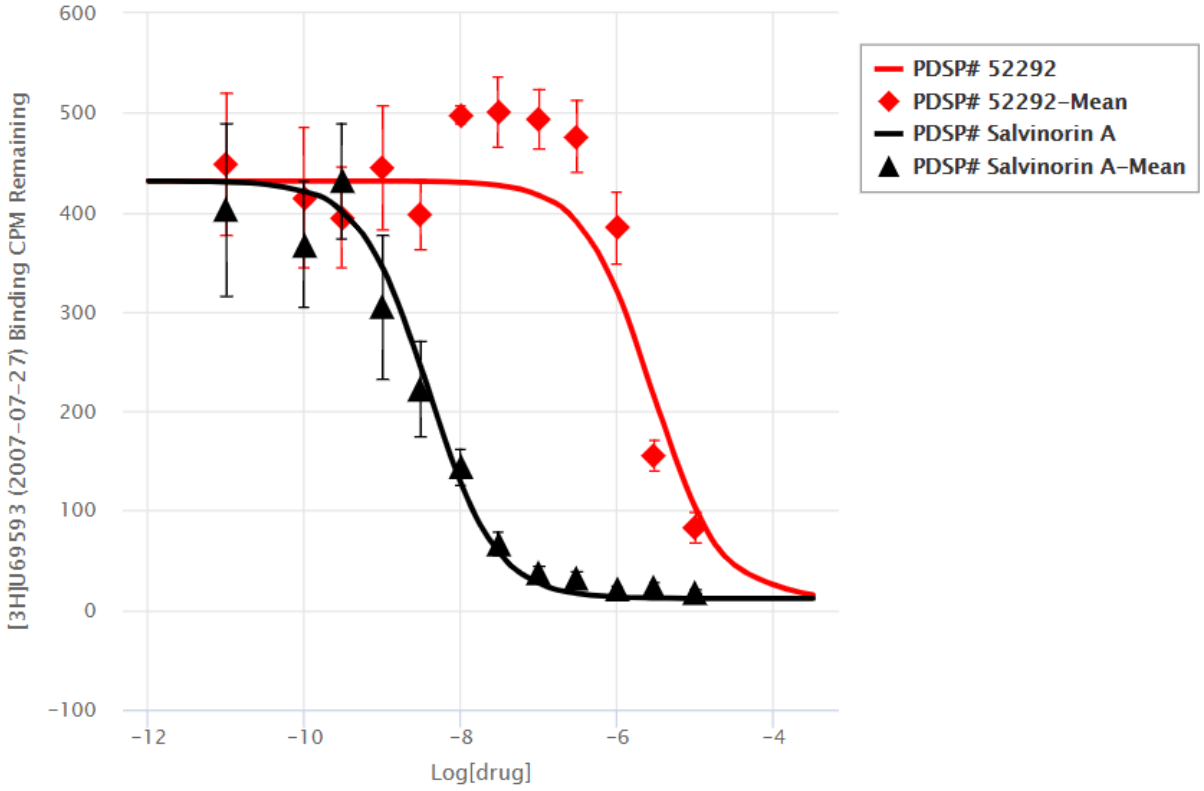




Compound: **3a**					pK*i*	± pK*i*	K*i* (nM)
PDSP ID:	52292			**3a**	6.84	±0.06	145
Receptor	5-HT_{2B}			SB206553	8.17		
log[**3a**]	1	2	3	log[SB 206553]	1	2	3
-11	1122	1082	1022	-11	928	803	757
-10	944	981	855	-10	961	862	885
-9.5	1174	1140	1049	-9.5	1024	905	999
-9	955	792	793	-9	961	772	954
-8.5	982	1099	1002	-8.5	811	711	880
-8	962	1056	1140	-8	801	688	688
-7.5	1118	904	1069	-7.5	413	388	386
-7	836	782	855	-7	620	272	220
-6.5	600	619	603	-6.5	299	228	281
-6	358	387	376	-6	81	97	85
-5.5	209	202	238	-5.5	70	58	74
-5	428	259	338	-5	38	36	29

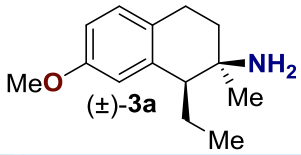
Compound **(±)-3a**, PDSP ID 52292, κ-opioid receptor:

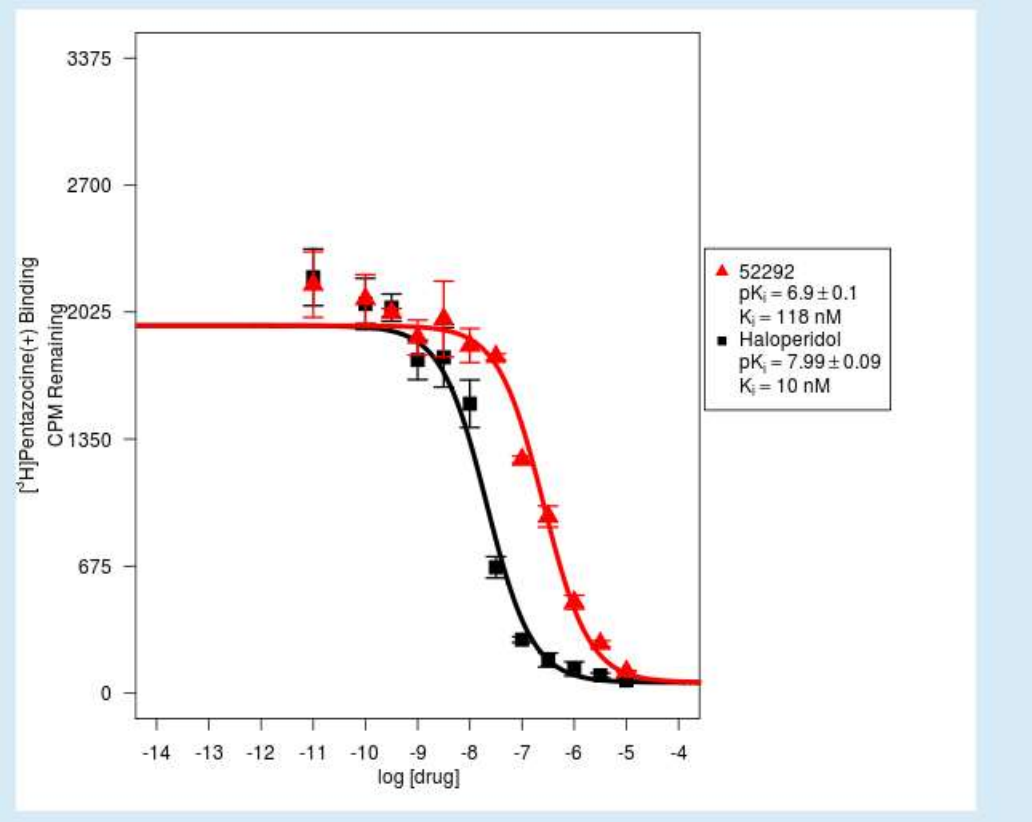




Compound: **3a**					pK*i*	± pK*i*	K*i* (nM)
PDSP ID:	52292			**3a**	6.5	±0.1	350
Receptor	κ-OR			Salvinorin A	9.3		
log[**3a**]	1	2	3	log[Salvinorin A]	1	2	3
-11	294	451	599	-11	567	437	203
-10	256	435	552	-10	502	367	232
-9.52	273	466	445	-9.52	499	504	290
-9	331	410	591	-9	444	330	139
-8.52	472	400	321	-8.52	338	169	157
-8	480	493	520	-8	187	111	133
-7.52	537	551	413	-7.52	95	45	61
-7	449	465	567	-7	37	26	50
-6.52	416	450	562	-6.52	47	26	22
-6	429	296	428	-6	27	21	17
-5.52	134	138	194	-5.52	26	11	31
-5	77	53	117	-5	20	13	21

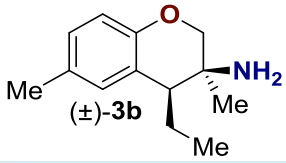
Compound **(±)-3a**, PDSP ID 52292, σ_1 receptor:

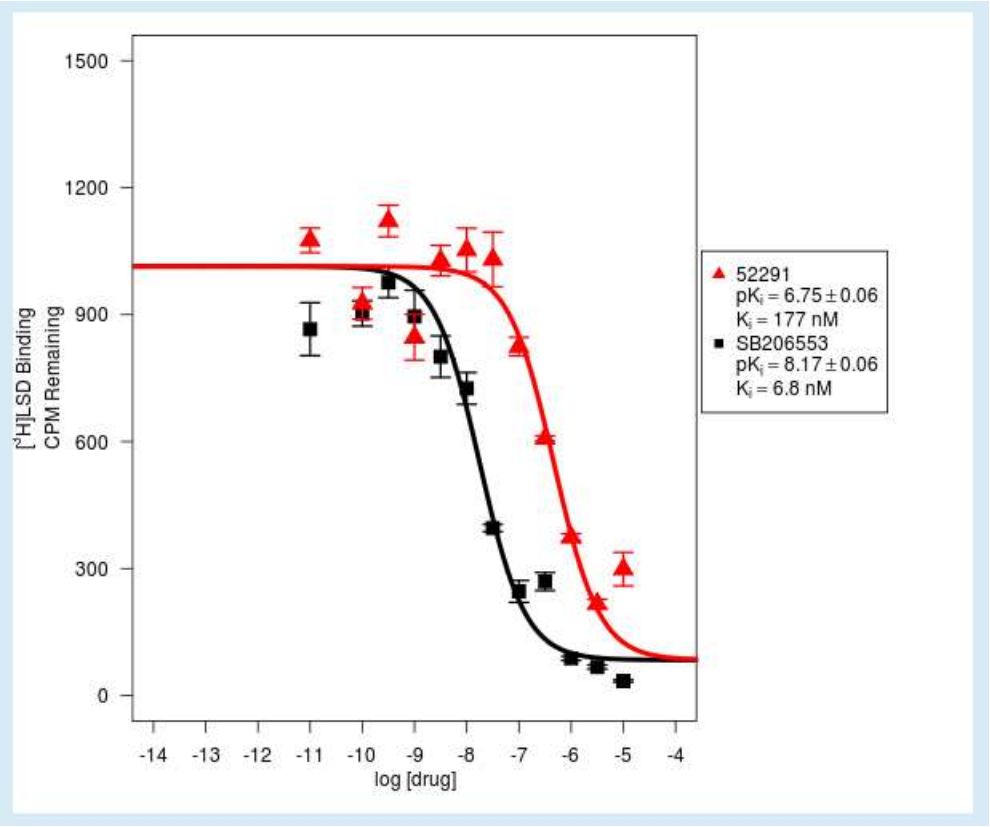




Compound: **3a**					pK_i	± pK_i	K_i (nM)
PDSP ID:	52292			**3a**	6.9	±0.1	120
Receptor	σ_1			Haloperidol	7.99		
log[**3a**]	1	2	3	log[Haloperidol]	1	2	3
-11	2512	2068	1934	-11	2313	1913	2404
-10	2352	1975	1957	-10	2063	1835	2307
-9.5	2023	2059	1981	-9.5	2054	1921	2171
-9	2049	1893	1726	-9	1824	1569	1919
-8.5	2204	2174	1585	-8.5	1835	1489	2030
-8	1787	2025	1729	-8	1593	1297	1724
-7.5	1772	1818	1773	-7.5	773	579	653
-7	1272	1243	1208	-7	274	264	314
-6.5	1045	855	914	-6.5	132	146	249
-6	527	409	512	-6	80	103	203
-5.5	285	232	270	-5.5	80	82	119
-5	125	107	111	-5	62	58	81

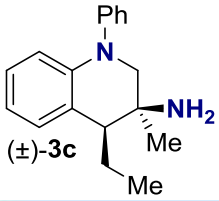
Compound **(±)-3b**, PDSP ID 52291, 5-HT_{2B} receptor:

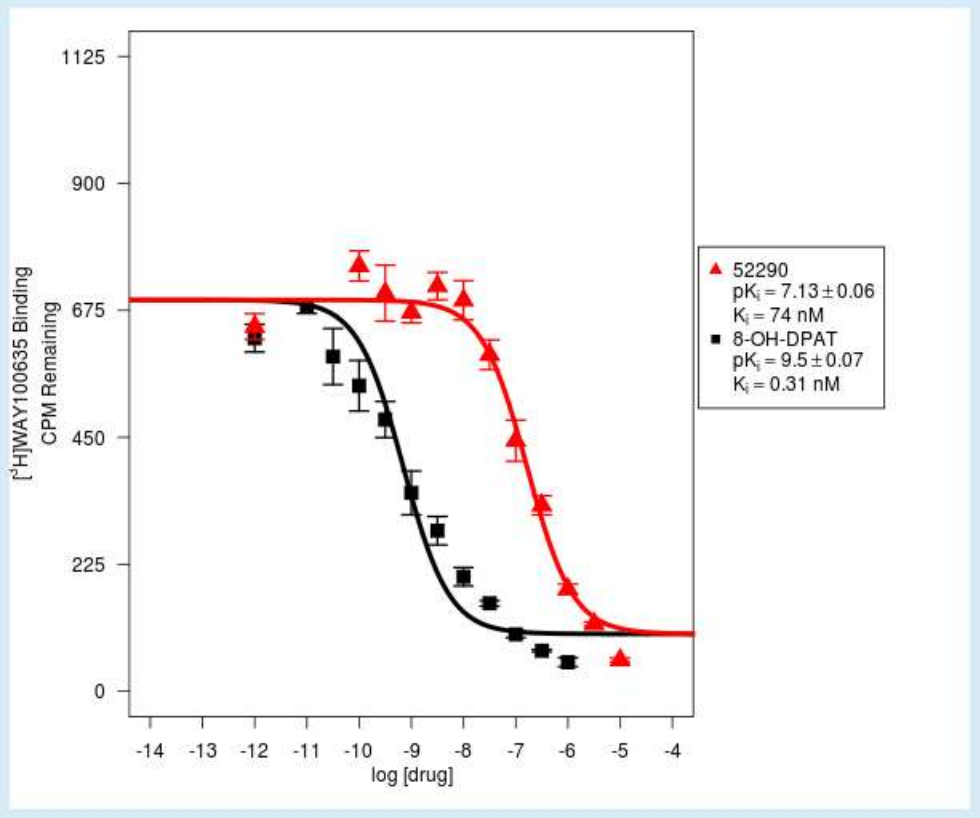




Compound: **3b**					pK*i*	± pK*i*	K*i* (nM)
PDSP ID:	52291			**3b**	6.75	±0.06	177
Receptor	5-HT_{2B}			SB 206553	8.17		
log[**3b**]	1	2	3	log[SB 206553]	1	2	3
-11	1122	1082	1022	-11	928	803	757
-10	944	981	855	-10	961	862	885
-9.5	1174	1140	1049	-9.5	1024	905	999
-9	955	792	793	-9	961	772	954
-8.5	982	1099	1002	-8.5	811	711	880
-8	962	1056	1140	-8	801	688	688
-7.5	1118	904	1069	-7.5	413	388	386
-7	836	782	855	-7	620	272	220
-6.5	600	619	603	-6.5	299	228	281
-6	358	387	376	-6	81	97	85
-5.5	209	202	238	-5.5	70	58	74
-5	428	259	338	-5	38	36	29

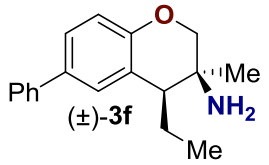
Compound **(±)-3c**, PDSP ID 52290, 5-HT_1 receptor:



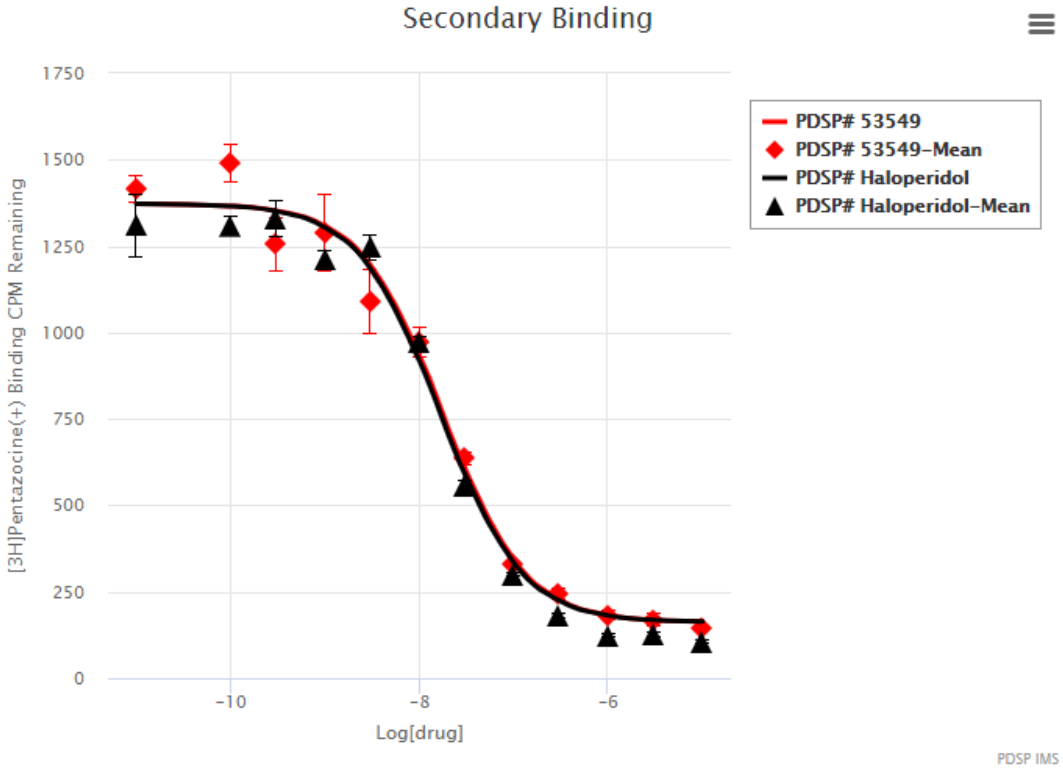


Compound: **3c**					pK_i	± pK_i	K_i (nM)
PDSP ID:	52290			**3c**	7.13	±0.1	74
Receptor	5-HT_1			8-OH-DPAT	9.5		
log[**3c**]	1	2	3	log[8-OH-DPAT]	1	2	3
-12	684	605	650	-12	674	609	594
-10	788	772	701	-11	693	697	657
-9.5	755	656	435	-10.5	681	509	589
-9	647	659	709	-10	620	539	465
-8.5	711	680	763	-9.5	505	521	418
-8	762	656	660	-9	415	358	281
-7.5	598	550	641	-8.5	310	309	234
-7	479	371	482	-8	220	218	170
-6.5	354	297	337	-7.5	165	153	149
-6	197	166	179	-7	112	98	92
-5.5	123	112	122	-6.5	68	75	72
-5	61	55	49	-6	53	64	37

Compound **(±)-3f**, PDSP ID 53549, σ_1 receptor:

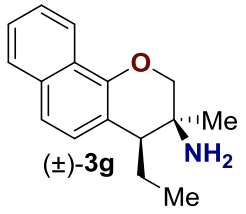


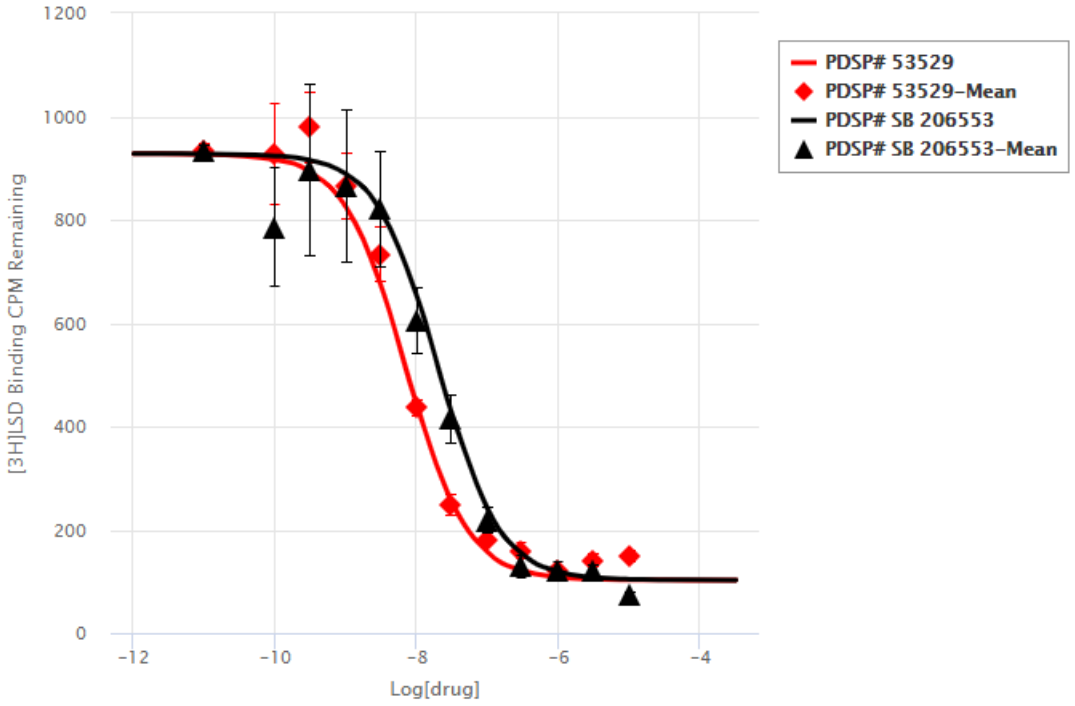
Triplicate trials: pK_i = 8.1 (shown), 7.7, 7.8; average 7.9 reported.



Compound:	**3f**					pK_i	± pK_i	K_i (nM)
PDSP ID:	53549			**3f**		8.1	±0.2	7.5
Receptor:	σ_1			Haloperidol		8.1		
log[**3f**]	1	2	3	log[Haloperidol]		1	2	3
-11	1364	1372	1512	-11		1089	1460	1380
-10	1485	1608	1378	-10		1276	1374	1275
-9.52	1392	1303	1072	-9.52		1211	1427	1349
-9	1393	1456	1022	-9		1150	1237	1251
-8.52	974	1318	980	-8.52		1167	1326	1246
-8	873	1036	1009	-8		942	965	1009
-7.52	653	593	664	-7.52		591	550	525
-7	313	331	341	-7		309	300	290
-6.52	282	219	230	-6.52		193	173	175
-6	194	149	202	-6		137	114	119
-5.52	166	134	207	-5.52		131	134	115
-5	158	143	129	-5		94	110	112

Compound **(±)-3g**, PDSP ID 53529, 5-HT_{2B} receptor:

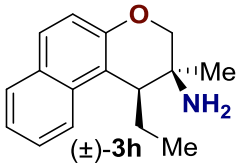




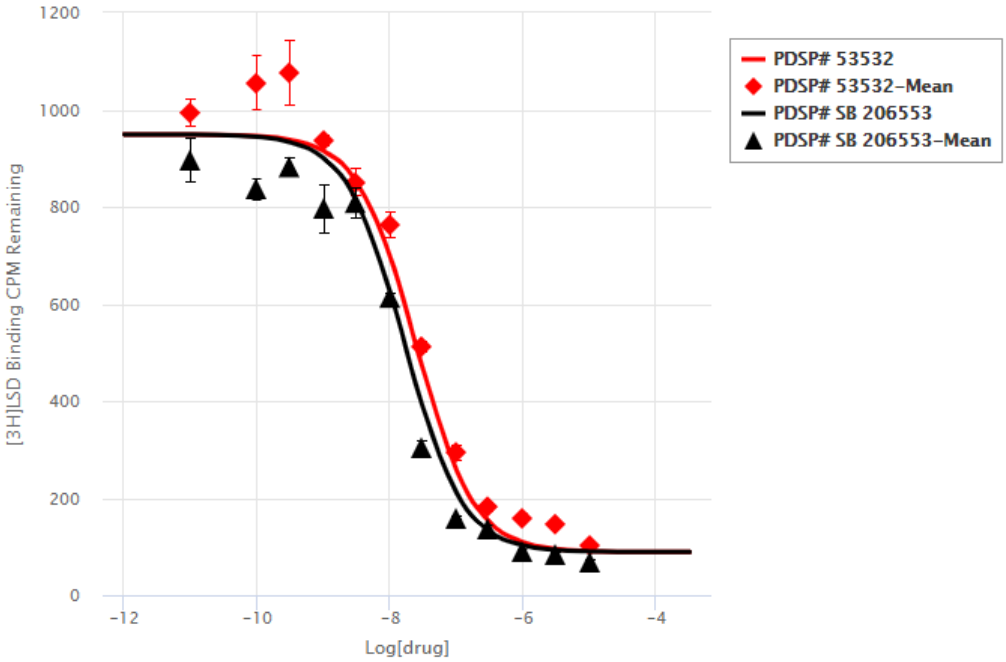
PDSP IMS

Compound: **3g**					pK_i	± pK_i	K_i (nM)
PDSP ID:	53529			**3g**	8.6	±0.2	3.4
Receptor	5-HT_{2B}			SB 206553	8.0		
log[3g]	1	2	3	log[SB 206553]	1	2	3
-11	922	966	914	-11	960	934	902
-10	1161	848	774	-10	1030	788	539
-9.52	1135	941	859	-9.52	1279	815	592
-9	1021	792	781	-9	1188	841	565
-8.52	844	732	622	-8.52	1072	792	598
-8	426	474	409	-8	748	586	478
-7.52	212	298	235	-7.52	524	389	330
-7	190	179	166	-7	279	179	196
-6.52	195	148	135	-6.52	182	109	96
-6	139	122	100	-6	154	121	92
-5.52	171	132	120	-5.52	140	96	130
-5	120	162	163	-5	73	65	87

Compound **(±)-3h**, PDSP ID 53532, 5-HT_{2B} receptor:



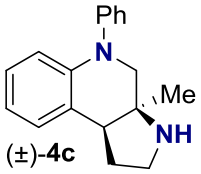
Duplicate trials: pK_i = 7.9 (shown), 7.5; average of 7.7 reported.



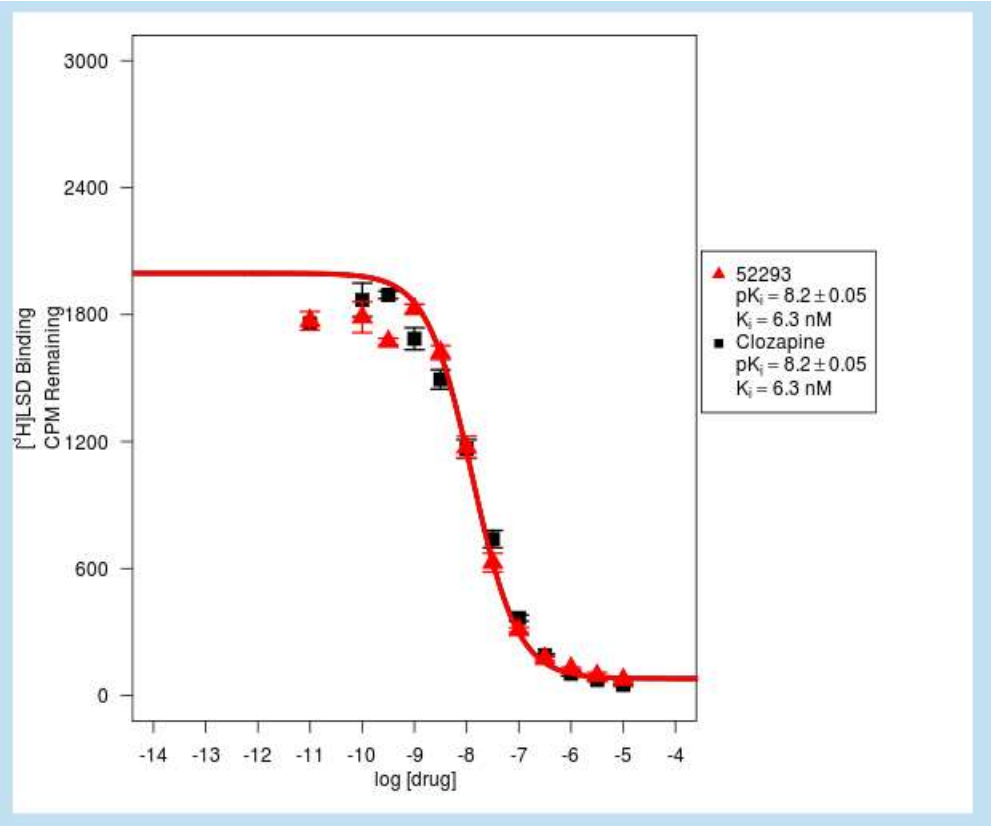
PDSP IMS

Compound: **3h**					pK_i	± pK_i	K_i (nM)
PDSP ID:	53532			**3h**	7.9	±0.2	12
Receptor:	5-HT_{2B}			SB 206553	8.1		
log[**3h**]	1	2	3	log[SB 206553]	1	2	3
-11	927	1018	1036	-11	1007	853	827
-10	1010	967	1188	-10	871	851	786
-9.52	934	1072	1221	-9.52	907	906	834
-9	955	913	943	-9	918	731	738
-8.52	806	829	918	-8.52	882	791	753
-8	731	733	826	-8	622	622	596
-7.52	491	505	540	-7.52	300	339	269
-7	258	324	300	-7	160	164	155
-6.52	161	189	196	-6.52	132	157	123
-6	150	150	179	-6	78	100	92
-5.52	148	151	140	-5.52	91	74	90
-5	92	108	111	-5	53	72	76
-5	92	108	111	-5	53	72	76

Compound **(±)-4c**, PDSP ID 52293, 5-HT_7 receptor:

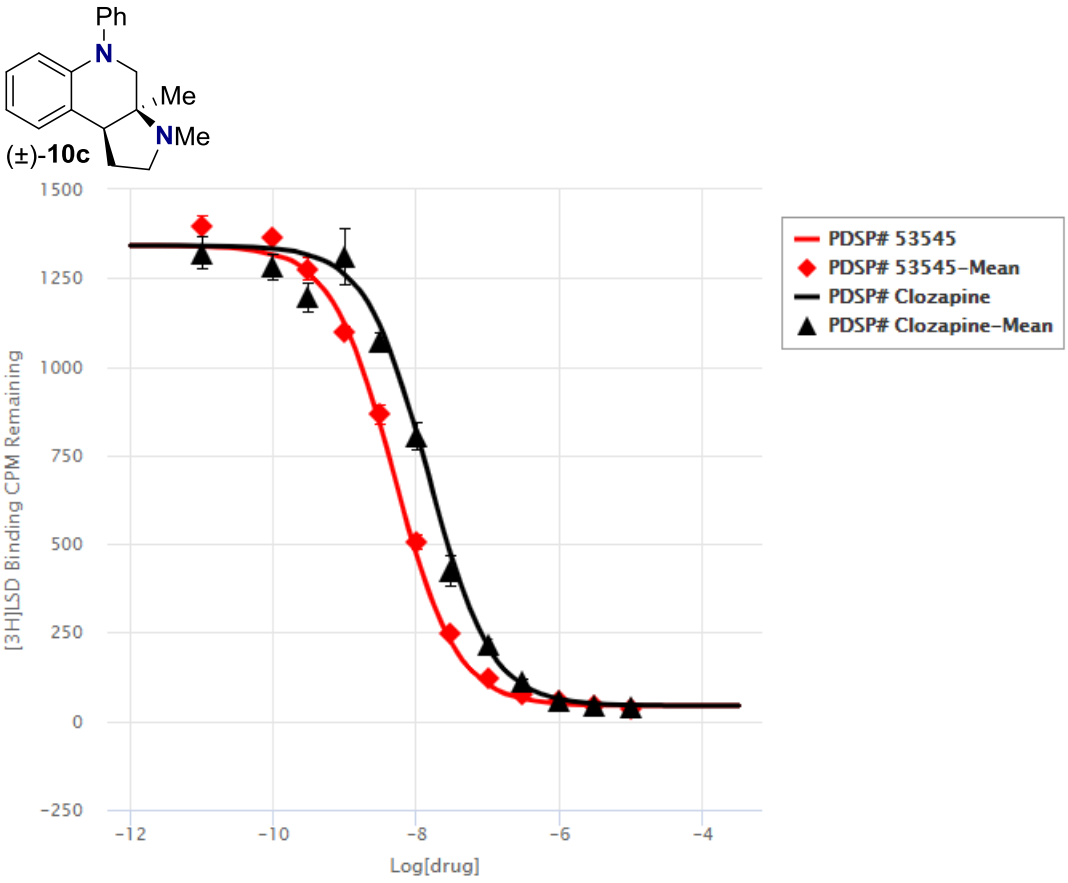


(±)-**4c**



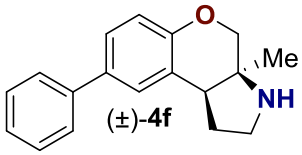
Compound: **4c**					pK_i	± pK_i	K_i (nM)
PDSP ID:	52293			**4c**	8.2	±0.1	6.3
Receptor:	5-HT_7			Clozapine	8.2		
log[**4c**]	1	2	3	Log[Clozapine]	1	2	3
-11	1606	1814	1727	-11	1416	1759	1583
-10	1661	1788	1914	-10	1801	2028	1780
-9.5	1652	1703	1662	-9.5	1916	1904	1859
-9	1802	1871	1806	-9	1585	1758	1715
-8.5	1585	1687	1589	-8.5	1564	1509	1408
-8	1252	1192	1074	-8	1248	1146	1102
-7.5	569	600	715	-7.5	663	752	803
-7	288	324	317	-7	342	364	392
-6.5	190	176	156	-6.5	202	186	184
-6	125	137	121	-6	125	93	90
-5.5	85	124	71	-5.5	63	72	84
-5	68	82	72	-5	53	59	38

Compound **(±)-10c**, PDSP ID 53545, 5-HT$_7$ receptor:

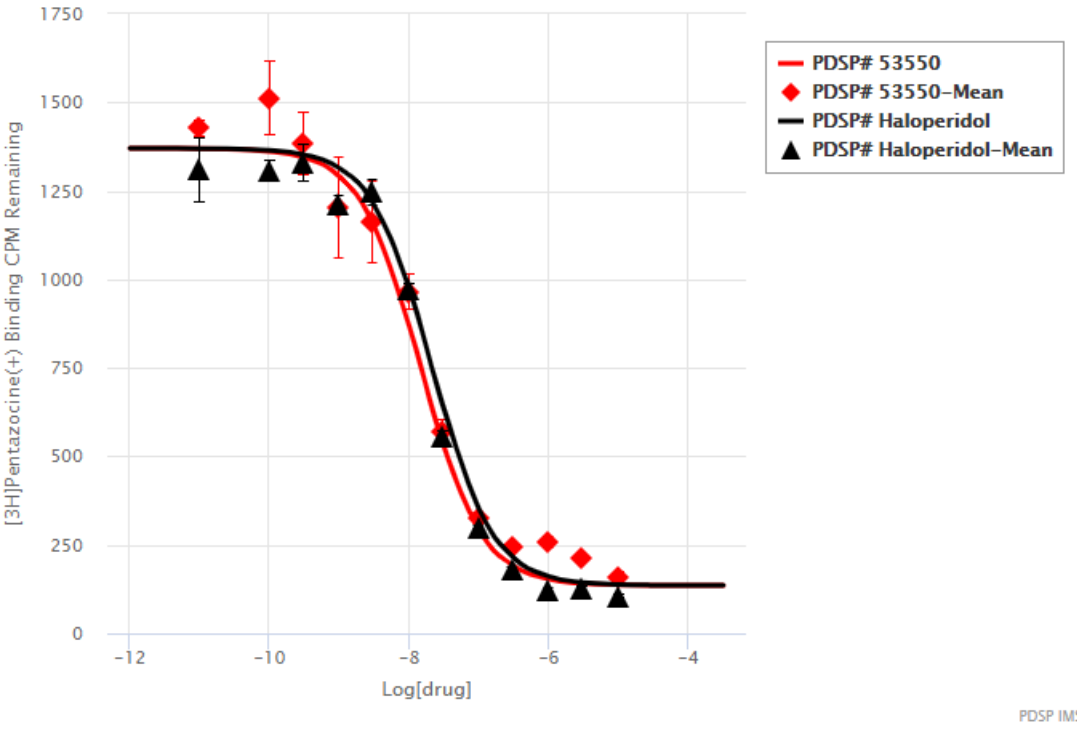


Compound:	**10c**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53545			**10c**	8.57	±0.04	2.4
Receptor:	5-HT$_7$			Clozapine	8.1		
log[**10c**]	1	2	3	log[Clozapine]	1	2	3
-11	1326	1428	1435	-11	1209	1376	1375
-10	1376	1360	1359	-10	1219	1261	1364
-9.52	1215	1270	1342	-9.52	1109	1283	1195
-9	1076	1126	1097	-9	746	1420	1196
-8.52	815	854	927	-8.52	1024	1126	1065
-8	453	533	532	-8	757	895	754
-7.52	224	264	250	-7.52	321	467	484
-7	104	136	124	-7	203	250	194
-6.52	71	79	70	-6.52	99	124	115
-6	65	53	48	-6	59	62	56
-5.52	49	32	53	-5.52	42	32	52
-5	27	28	48	-5	25	41	49

Compound **(±)-4f**, PDSP ID 53550, σ_1 receptor:

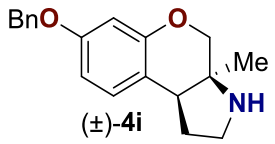


Triplicate trials: pK_i = 8.2 (shown), 7.8, 7.8; average of 7.9 reported.



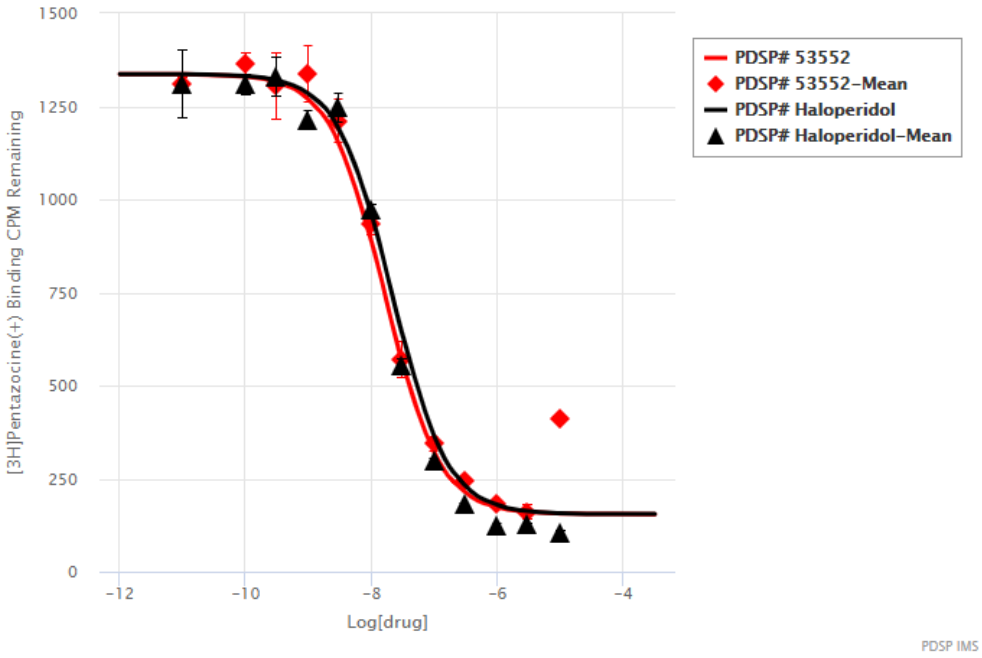
Compound:	**4f**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53550			**4f**	8.2	±0.1	6.1
Receptor:	σ_1			Haloperidol	8.1		
log[**4f**]	1	2	3	log[Haloperidol]	1	2	3
-11	1374	1444	1467	-11	1089	1460	1380
-10	1271	1694	1571	-10	1276	1374	1275
-9.52	1200	1575	1371	-9.52	1211	1427	1349
-9	1140	1529	941	-9	1150	1237	1251
-8.52	1233	1359	892	-8.52	1167	1326	1246
-8	943	1081	871	-8	942	965	1009
-7.52	567	641	503	-7.52	591	550	525
-7	369	302	306	-7	309	300	290
-6.52	268	229	229	-6.52	193	173	175
-6	296	245	231	-6	137	114	119
-5.52	229	206	208	-5.52	131	134	115
-5	188	134	156	-5	94	110	112

Compound **(±)-4i**, PDSP ID 53552, σ_1 receptor:



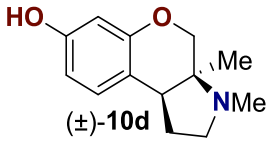
(±)-**4i**

Triplicate trials: pK_i = 8.2 (shown), 8.1, 8.0; average 8.1 reported.

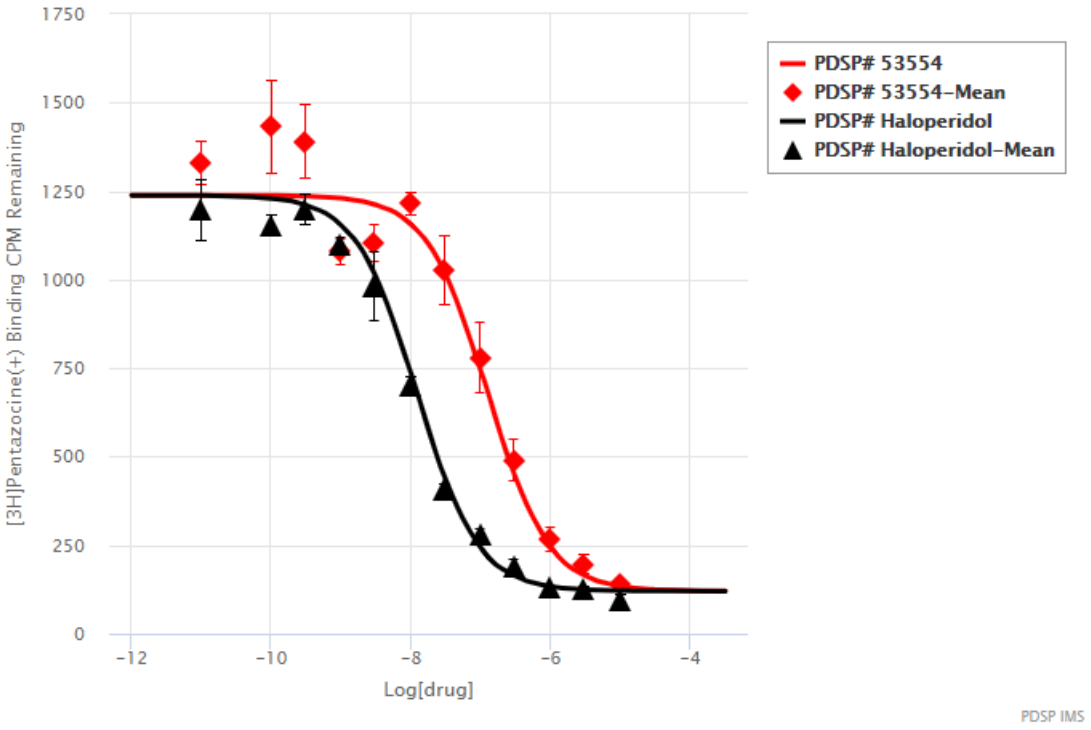


Compound:	**4i**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53552			**4i**	8.2	±0.1	6.3
Receptor:	σ_1			Haloperidol	8.1		
log[**4i**]	1	2	3	log[Haloperidol]	1	2	3
-11	1273	1342	1313	-11	1089	1460	1380
-10	1434	1350	1314	-10	1276	1374	1275
-9.52	1248	1518	1150	-9.52	1211	1427	1349
-9	1426	1430	1155	-9	1150	1237	1251
-8.52	1228	1323	1081	-8.52	1167	1326	1246
-8	941	989	871	-8	942	965	1009
-7.52	647	611	450	-7.52	591	550	525
-7	373	363	298	-7	309	300	290
-6.52	256	219	253	-6.52	193	173	175
-6	184	181	180	-6	137	114	119
-5.52	209	148	125	-5.52	131	134	115
-5	414	396	419	-5	94	110	112

Compound **(±)-10d**, PDSP ID 53554, σ_1 receptor:

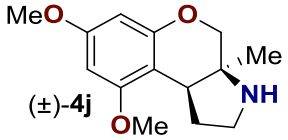


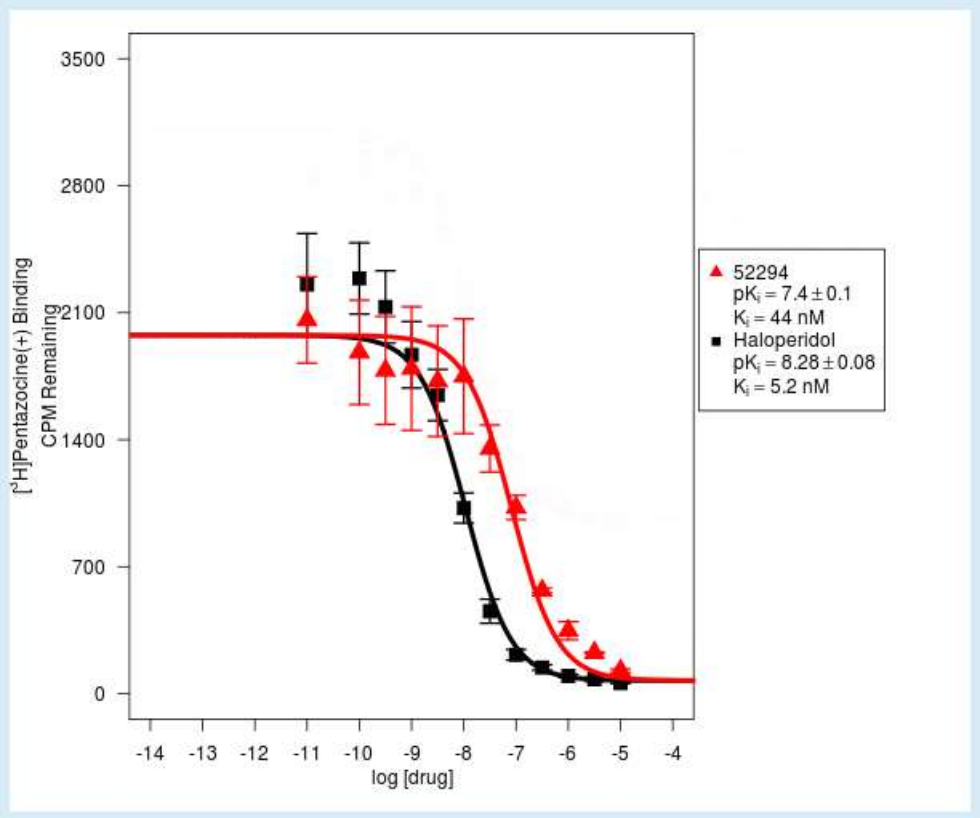
Triplicate trials: pK_i = 7.4 (shown), 7.3, 7.1; average of 7.3 reported.



Compound:	**10d**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53554			**10d**	7.4	±0.1	52
Receptor:	σ_1			Haloperidol	8.3		
log[53554]	1	2	3	log[Haloperidol]	1	2	3
-11	1449	1193	1345	-11	1187	1015	1387
-10	1696	1456	1143	-10	1225	1110	1129
-9.52	1532	1502	1137	-9.52	1134	1159	1300
-9	1023	1168	1048	-9	1038	1114	1138
-8.52	999	1212	1098	-8.52	874	848	1219
-8	1282	1203	1158	-8	718	644	741
-7.52	1268	887	925	-7.52	362	429	424
-7	877	539	922	-7	242	310	288
-6.52	572	345	549	-6.52	146	215	215
-6	318	183	302	-6	128	142	121
-5.52	214	130	244	-5.52	109	144	124
-5	128	131	155	-5	121	102	63

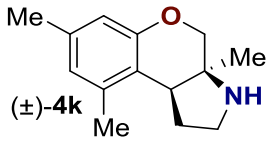
Compound **(±)-4j**, PDSP ID 52294, σ_1 receptor:



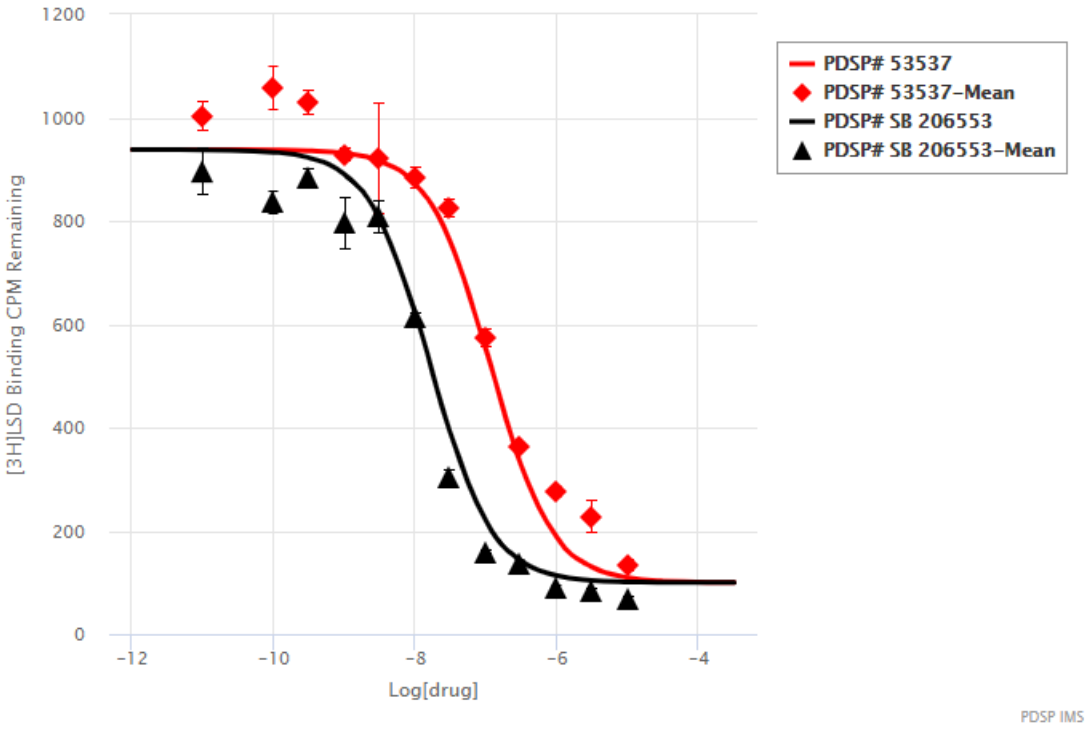


Compound:	**4j**				pK_i	± pK_i	K_i (nM)
PDSP ID:	52294			**4j**	7.4	±0.1	44
Receptor:	σ_1			Haloperidol	8.28		
Log[**4j**]	1	2	3	Log[Haloperidol]	1	2	3
-11	2529	1895	1756	-11	2795	1851	2120
-10	2408	1418	1818	-10	2681	2106	2079
-9.5	2246	1227	1873	-9.5	2491	1803	2101
-9	2266	1131	1979	-9	1984	1509	2111
-8.5	2154	1134	1880	-8.5	1859	1378	1701
-8	2251	1166	1832	-8	1189	935	945
-7.5	1470	1092	1491	-7.5	401	377	586
-7	1129	901	1049	-7	192	179	272
-6.5	564	549	592	-6.5	120	141	171
-6	432	349	260	-6	92	87	115
-5.5	221	225	232	-5.5	57	83	98
-5	134	108	139	-5	56	57	61

Compound **(±)-4k**, PDSP ID 53537, 5-HT$_{2B}$ receptor:

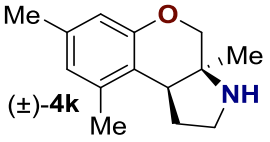


Duplicate trials: pK_i = 7.2 (shown) and 7.0; average of 7.1 reported.

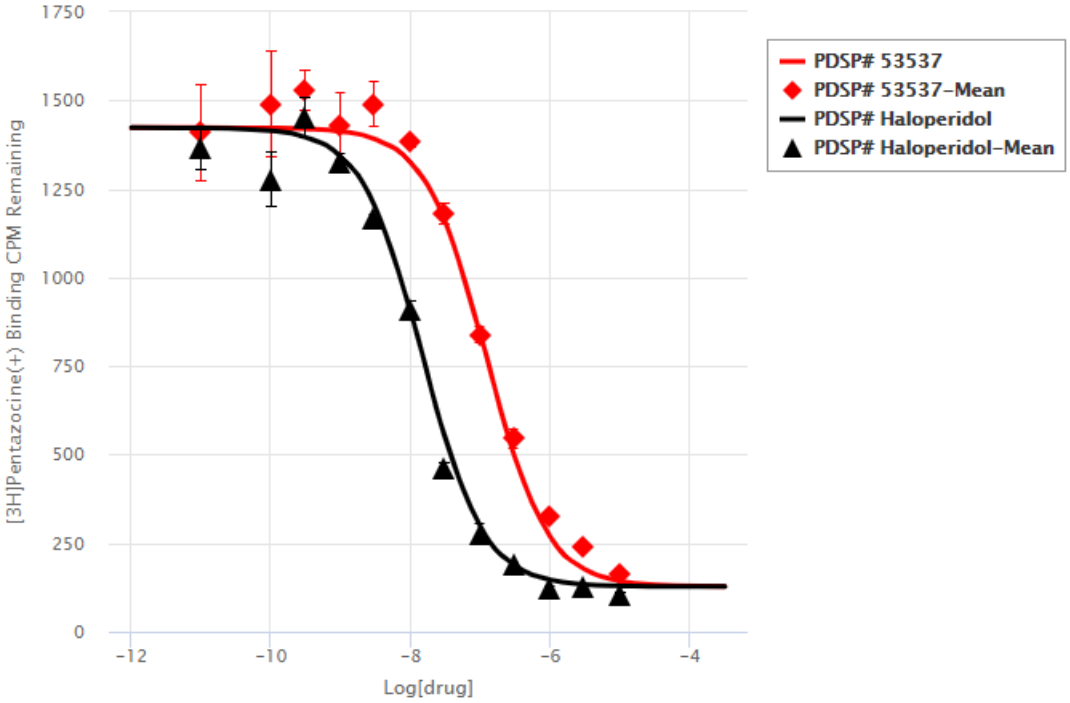


Compound:	4k				pKi	± pKi	Ki (nM)
PDSP ID:	53537			4k	7.2	±0.1	63
Receptor:	5-HT2B			SB 206553	8.1		
log[4k]	1	2	3	log[SB 206553]	1	2	3
-11	988	950	1069	-11	1007	853	827
-10	990	1027	1158	-10	871	851	786
-9.52	1008	994	1088	-9.52	907	906	834
-9	939	898	947	-9	918	731	738
-8.52	1129	678	955	-8.52	882	791	753
-8	840	880	931	-8	622	622	596
-7.52	841	853	783	-7.52	300	339	269
-7	539	568	614	-7	160	164	155
-6.52	363	367	357	-6.52	132	157	123
-6	275	253	302	-6	78	100	92
-5.52	166	219	297	-5.52	91	74	90
-5	109	146	146	-5	53	72	76

Compound **(±)-4k**, PDSP ID 53537, σ_1 receptor:



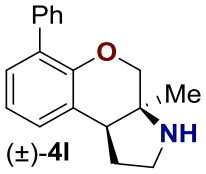
Triplicate trials: pK_i = 7.3 (shown), 7.1, 7.2; average of 7.2 reported.

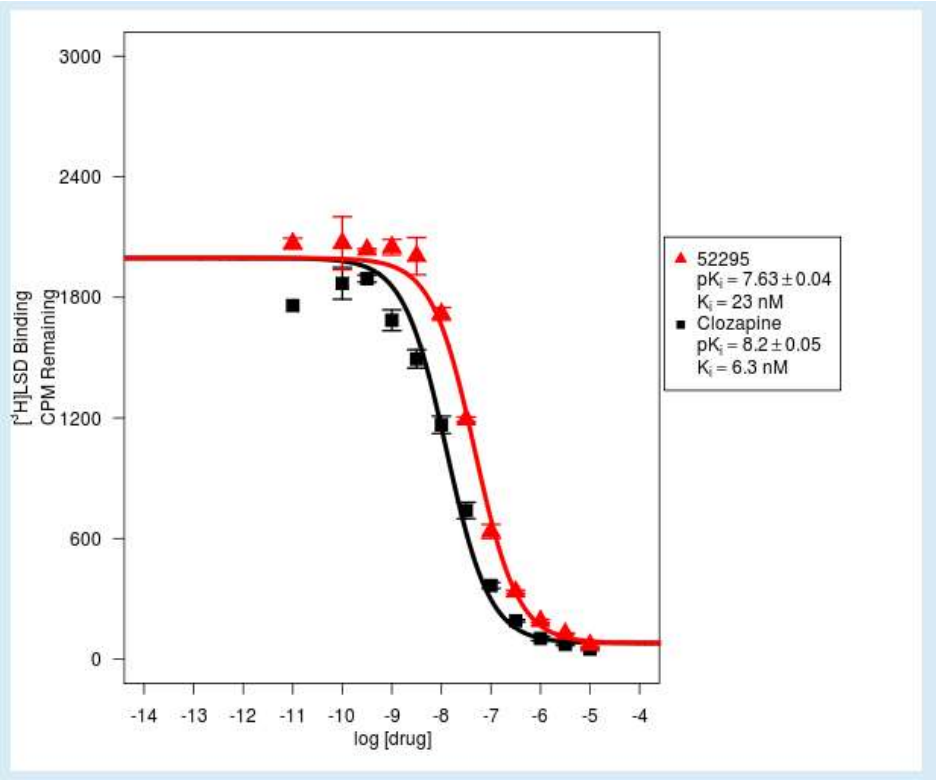


PDSP IMS

Compound:	**4k**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53537			**4k**	7.3	±0.1	50
Receptor:	σ_1			Haloperidol	8.2		
log[**4k**]	1	2	3	log[Haloperidol]	1	2	3
-11	1463	1097	1667	-11	1264	1328	1505
-10	1478	1176	1815	-10	1415	1094	1322
-9.52	1515	1414	1653	-9.52	1580	1351	1423
-9	1533	1195	1557	-9	1378	1273	1318
-8.52	1453	1374	1641	-8.52	1175	1147	1184
-8	1419	1358	1368	-8	929	954	842
-7.52	1145	1257	1139	-7.52	494	457	438
-7	792	841	882	-7	349	257	224
-6.52	480	588	568	-6.52	202	193	171
-6	301	342	334	-6	142	110	108
-5.52	244	226	249	-5.52	128	141	111
-5	166	153	175	-5	118	93	98

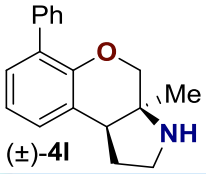
Compound **(±)-4l**, PDSP ID 52295, 5-HT$_7$ receptor:



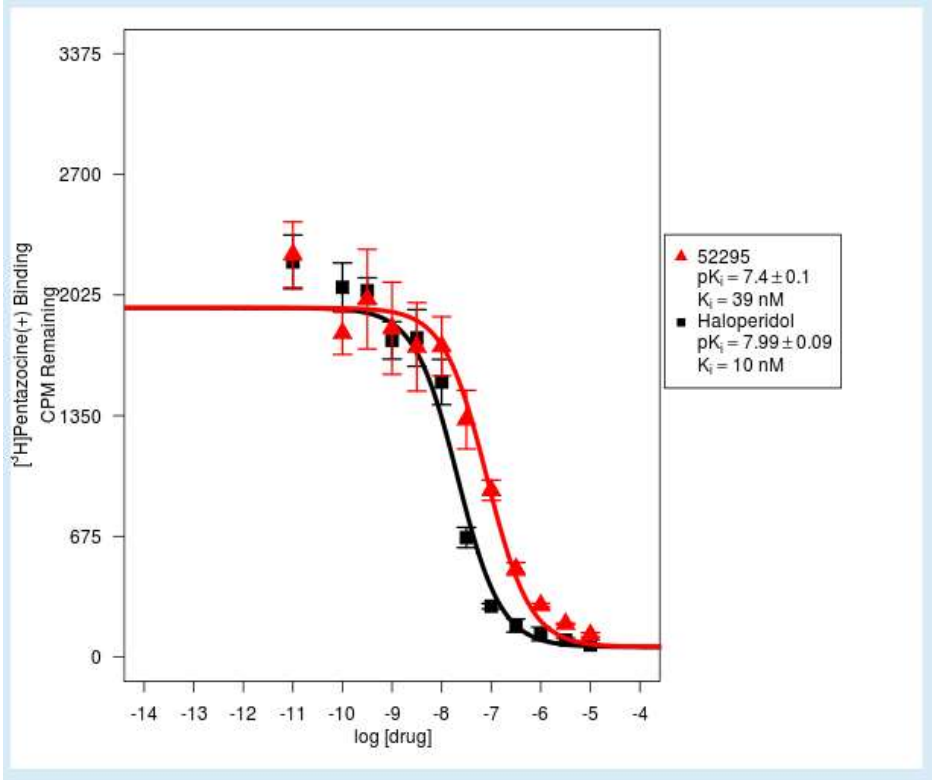


Compound:	**4l**						
PDSP ID:	52295				pK_i	± pK_i	K_i (nM)
Receptor:	5-HT$_7$			**4l**	7.63	±0.04	23
log[**4l**]	1	2	3	Clozapine	8.2		
-11	2063	2116	2025	log[Clozapine]	1	2	3
-10	1938	2201	2373	-11	1416	1759	1583
-9.5	2043	2032	2461	-10	1801	2028	1780
-9	1984	2046	2118	-9.5	1916	1904	1859
-8.5	1972	1864	2179	-9	1585	1758	1715
-8	1755	1743	1655	-8.5	1564	1509	1408
-7.5	1214	1190	1175	-8	1248	1146	1102
-7	606	705	594	-7.5	663	752	803
-6.5	327	328	351	-7	342	364	392
-6	193	173	201	-6.5	202	186	184
-5.5	132	122	126	-6	125	93	90
-5	56	76	80	-5.5	63	72	84
				-5	53	59	38

Compound **(±)-4l**, PDSP ID 52295, σ_1 receptor:

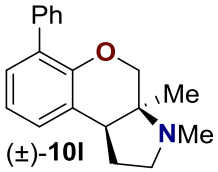


(±)-**4l**



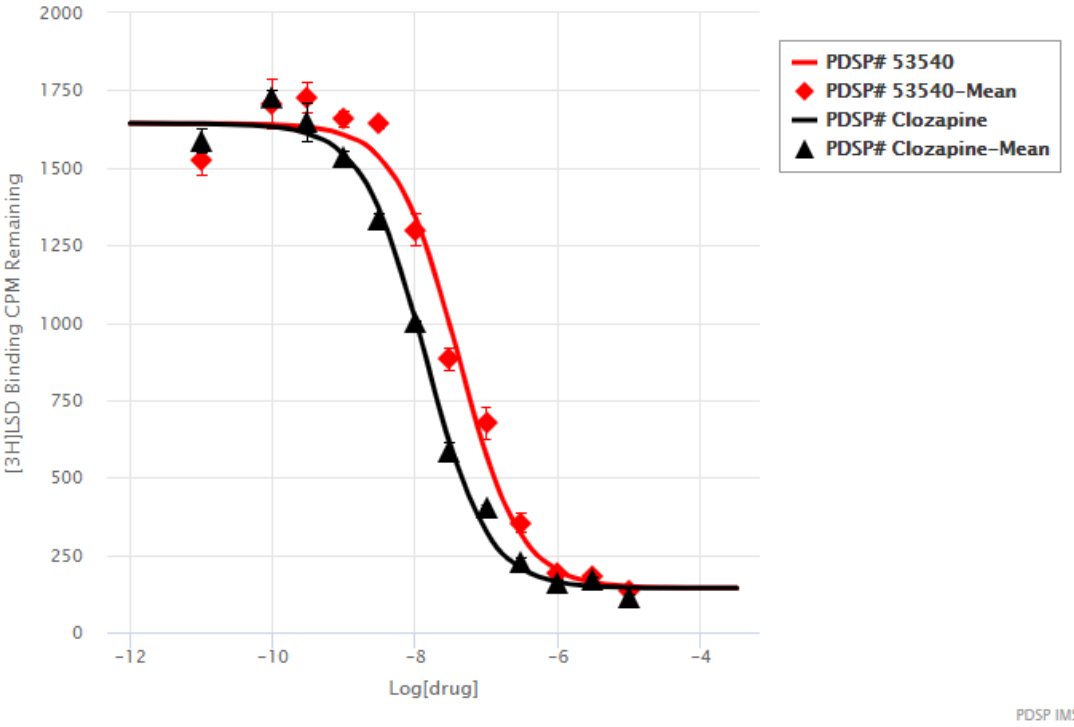
Compound:	**4l**					pK_i	± pK_i	K_i (nM)
PDSP ID:	52295			**4l**		7.4	±0.1	39
Receptor:	5-HT_7			Haloperidol		7.99		
log[**4l**]	1	2	3	log[Haloperidol]		1	2	3
-11	2159	1989	2604	-11		2313	1913	2404
-10	1957	1901	1576	-10		2063	1835	2307
-9.5	1925	1562	2518	-9.5		2054	1921	2171
-9	2070	1325	2122	-9		1824	1569	1919
-8.5	1765	1292	2148	-8.5		1835	1489	2030
-8	1772	1437	2006	-8		1593	1297	1724
-7.5	1445	1004	1535	-7.5		773	579	653
-7	973	821	1004	-7		274	264	314
-6.5	551	497	429	-6.5		132	146	249
-6	268	299	300	-6		80	103	203
-5.5	177	189	190	-5.5		80	82	119
-5	133	138	100	-5		62	58	81

Compound **(±)-10l**, PDSP ID 53540, 5-HT$_7$ receptor:



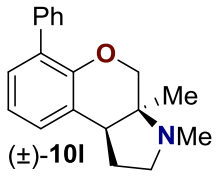
(±)-**10l**

Triplicate trials: pK_i = 7.8 (shown), 7.6, 7.7 ; average of 7.7 reported.



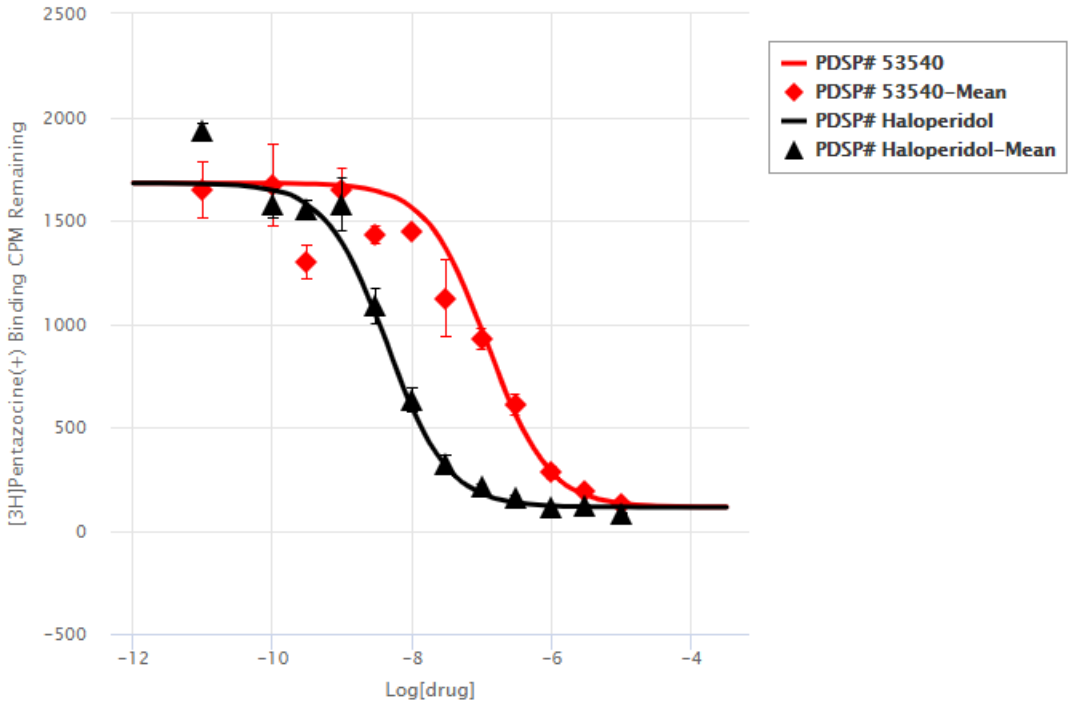
Compound:	**10l**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53540			**10l**	7.8	±0.1	16
Receptor:	5-HT$_7$			Clozapine	8.2		
log[**10l**]	1	2	3	log[Clozapine]	1	2	3
-11	1595	1581	1405	-11	1680	1566	1516
-10	1832	1510	1768	-10	1741	1675	1767
-9.52	1840	1638	1705	-9.52	1732	1496	1711
-9	1720	1629	1622	-9	1527	1576	1496
-8.52	1677	1611	1637	-8.52	1317	1299	1379
-8	1266	1213	1420	-8	998	1013	1001
-7.52	904	800	943	-7.52	541	656	552
-7	806	620	598	-7	404	398	415
-6.52	420	290	350	-6.52	206	211	259
-6	218	152	199	-6	133	176	169
-5.52	208	153	179	-5.52	157	168	190
-5	136	102	171	-5	90	127	120

Compound **(±)-10l**, PDSP ID 53540, σ_1 receptor:



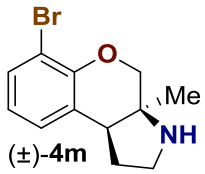
(±)-**10l**

Triplicate trials: pK_i = 7.4 (shown), 7.3, 7.2; average of 7.3 reported.

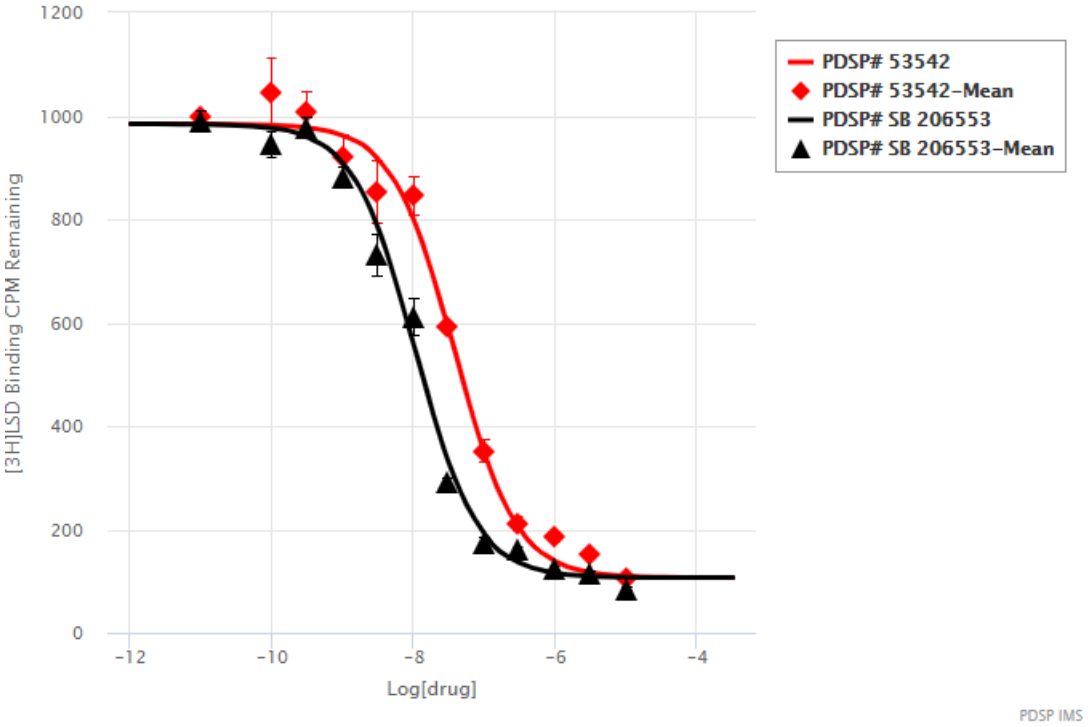


Compound:	**10l**				pK_i	± pK_i	K_i (nM)
PDSP ID:	53540			**10l**	7.4	±0.1	40
Receptor:	σ_1			Haloperidol	8.8		
log[**10l**]	1	2	3	log[Haloperidol]	1	2	3
-11	1326	1877	1743	-11	1944	1838	2012
-10	1210	1776	2029	-10	1449	1558	1734
-9.52	1106	1440	1353	-9.52	1472	1532	1651
-9	1592	1441	1899	-9	1552	1865	1314
-8.52	1335	1441	1514	-8.52	1012	1291	960
-8	1427	1465	1446	-8	740	656	499
-7.52	1151	716	1505	-7.52	428	267	278
-7	821	924	1031	-7	189	231	229
-6.52	491	639	692	-6.52	154	181	148
-6	294	211	337	-6	119	122	99
-5.52	202	203	162	-5.52	122	123	110
-5	134	98	154	-5	83	78	85

Compound **(±)-4m**, PDSP ID 53542, 5-HT_{2B} receptor:

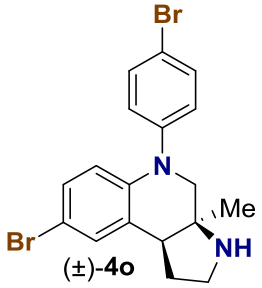


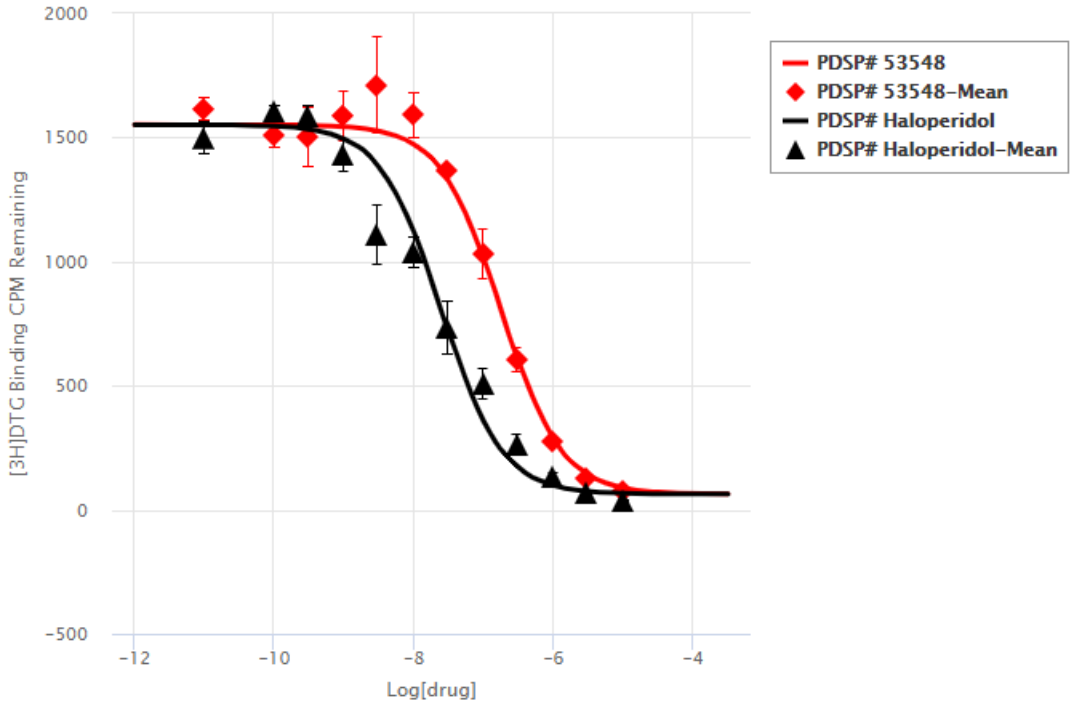
Triplicate trials: pK_i = 7.8 (shown), 7.5, 7.7; average of 7.7 reported.



Compound:	**4m**					pK_i	± pK_i	K_i (nM)
PDSP ID:	53542			**4m**		7.8	±0.1	16
Receptor:	5-HT_{2B}			SB 206553		8.29		
log[**4m**]	1	2	3	log[SB 206553]		1	2	3
-11	1018	971	1002	-11		941	1012	1017
-10	1148	1099	892	-10		889	954	993
-9.52	957	1099	971	-9.52		959	943	1028
-9	992	953	815	-9		879	842	924
-8.52	827	991	742	-8.52		711	655	825
-8	914	864	758	-8		547	593	695
-7.52	579	606	594	-7.52		274	298	301
-7	404	328	322	-7		153	164	202
-6.52	205	183	242	-6.52		165	150	166
-6	164	183	207	-6		133	121	120
-5.52	137	146	170	-5.52		99	115	128
-5	115	88	117	-5		81	91	83

Compound **(±)-4o**, PDSP ID 53548, σ_2 receptor:





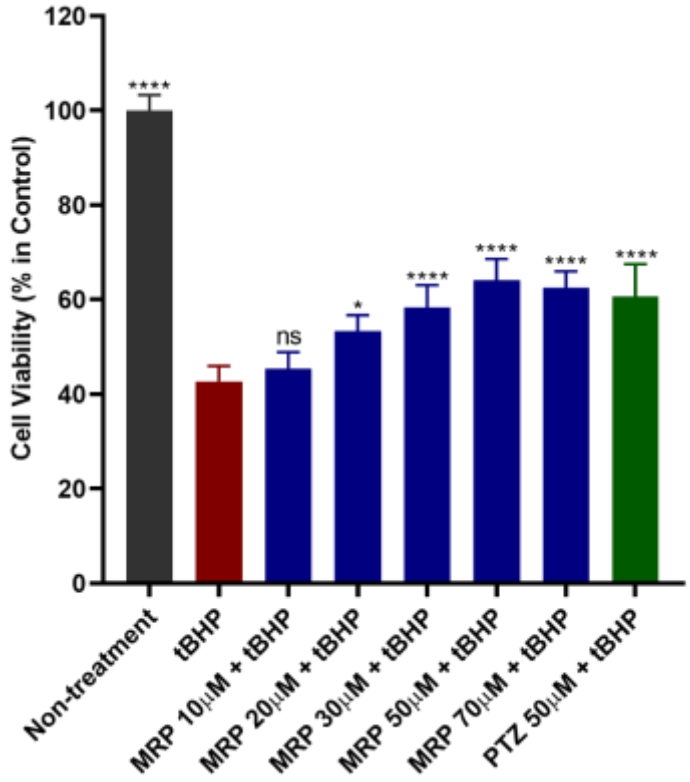
PDSP IMS

Compound:	**4o**					pK_i	± pK_i	K_i (nM)
PDSP ID:	53548			**4o**		7.1	±0.2	80
Receptor:	σ_2			Haloperidol		7.95		
log[53548]	1	2	3	log[Haloperidol]		1	2	3
-11	1651	1690	1503	-11		1604	1345	1544
-10	1496	1620	1418	-10		1645	1614	1557
-9.52	1331	1671	810	-9.52		1595	1666	1503
-9	1562	1811	1392	-9		1346	1348	1593
-8.52	2097	1754	1285	-8.52		1385	1044	899
-8	1619	1766	1385	-8		1064	1147	899
-7.52	1361	1374	1375	-7.52		861	871	470
-7	885	1177	1820	-7		542	621	368
-6.52	542	722	553	-6.52		319	301	174
-6	280	289	263	-6		165	113	122
-5.52	146	128	114	-5.52		69	67	65
-5	93	68	60	-5		48	36	31

Additional Cellular Assays

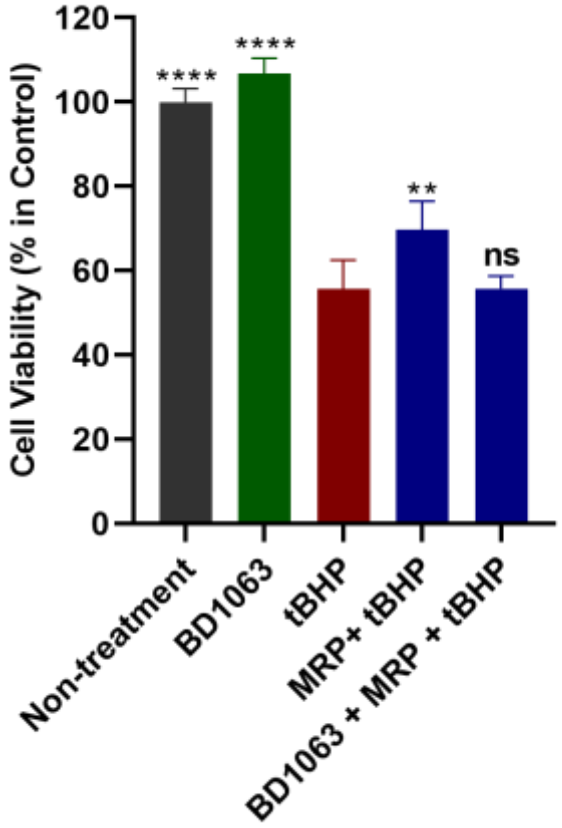
Two additional cellular assays were conducted to further investigate the activity of compound **4j** on 661W cells were treated with tBHP. They were (i) to demonstrate a dose responsive behavior of compound 4j and (ii) to demonstrate the the activity of 4j could be counteracted by the addition of a sigma 1 receptor antagonist.

Figure S1. Enhanced 661W Cell Viability with Compound 4j Upon tBHP Exposure

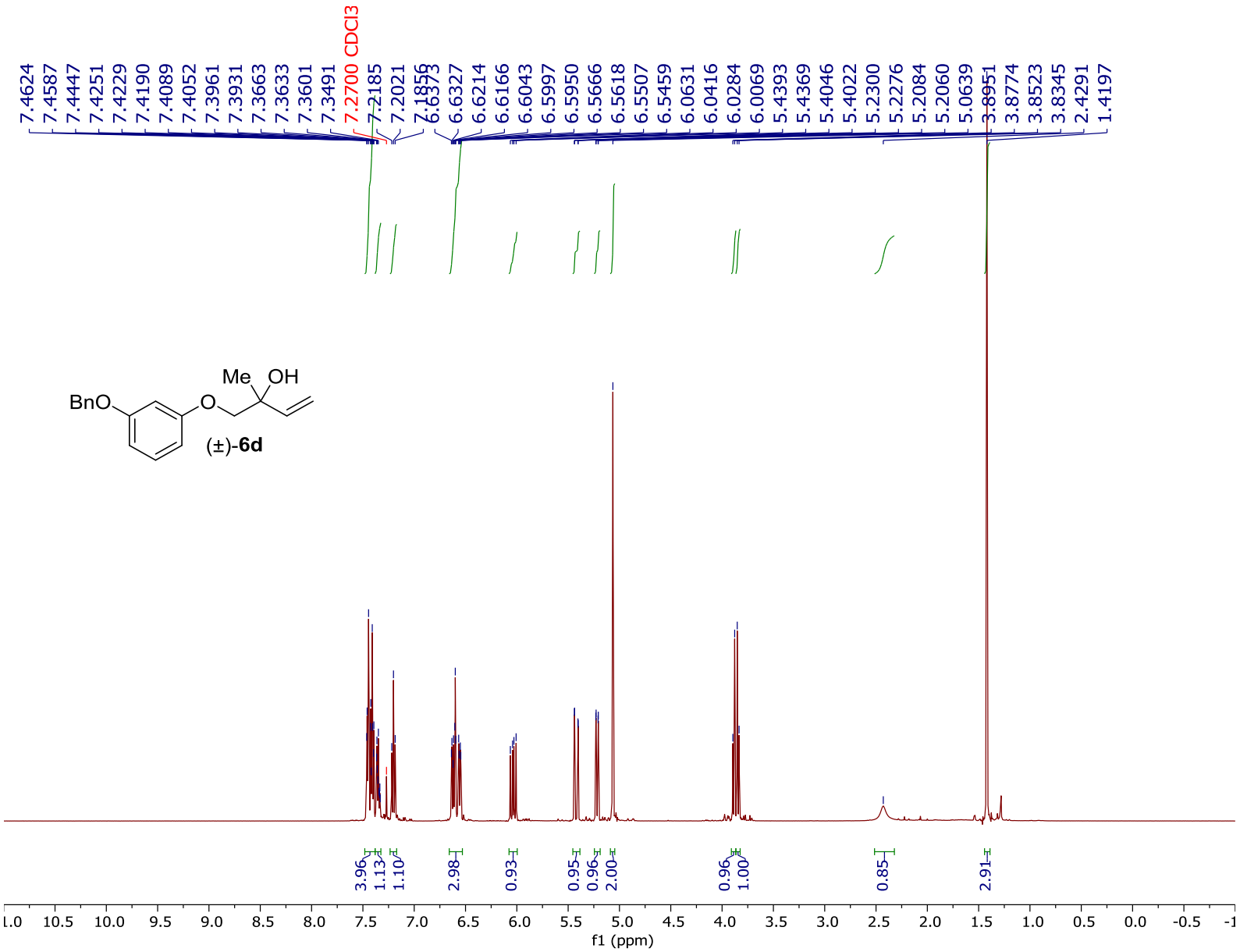


661W cells were treated with tBHP in the presence/absence of increasing concentrations of compound **4j** (10-70 μM) or the σ_1 receptor ligand PTZ (50 μM) for 24 h before cell viability assessment. Cell viability was assessed using the MTT assay. Data are presented as mean ± standard error of the mean (SEM) of triplicate measurements, *p< 0.05. ** p< 0.01; *** p< 0.001, **** p < 0.0001, ns = not significant as compared to the tBHP treatment. (tBHP = *tert*-butyl hydroperoxide; MRP = compound **4j**; PTZ = (+)-pentazocine).

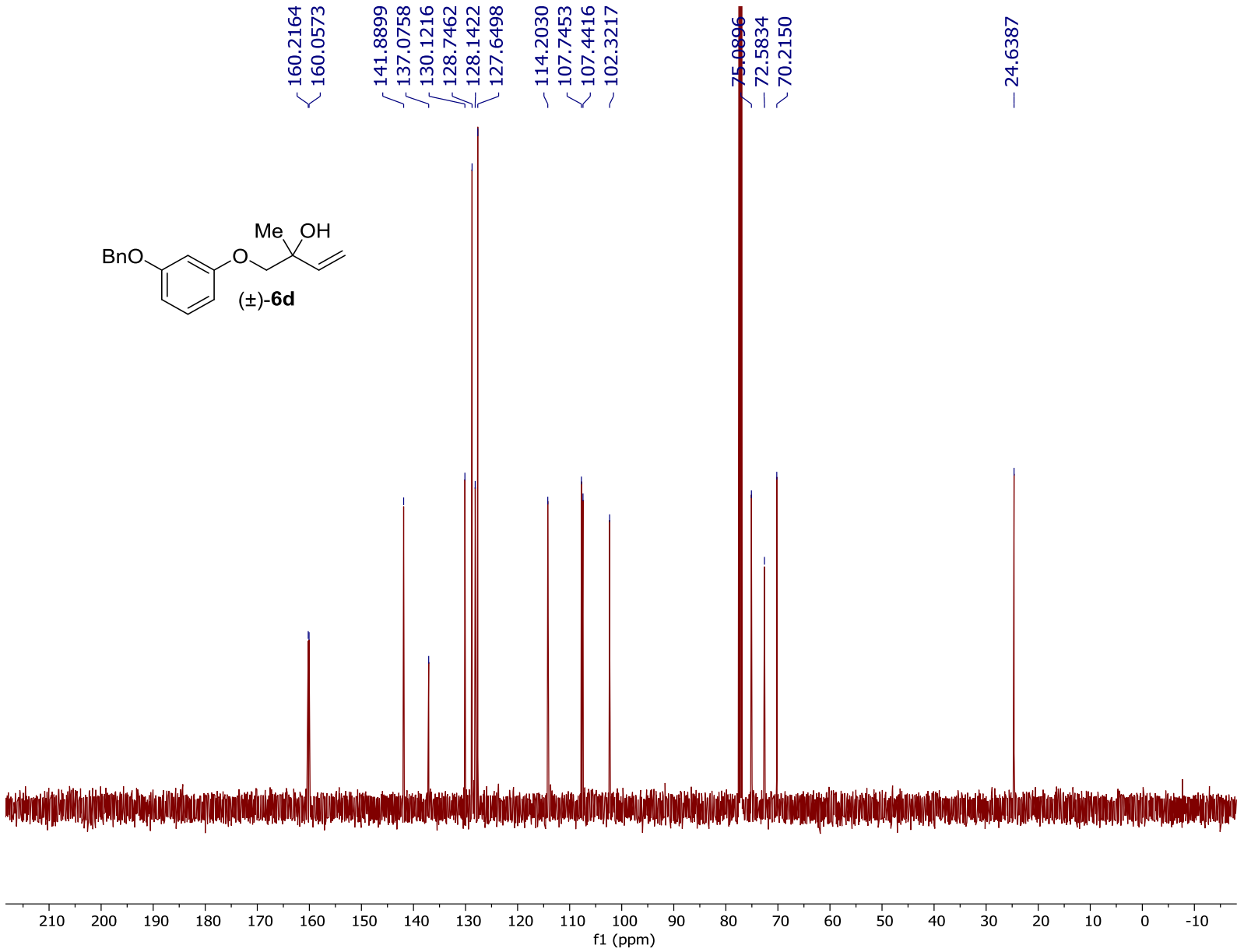
Figure S2. BD1063 blocked the protective effect of MRP3215 in 661W cells treated with tBHP.



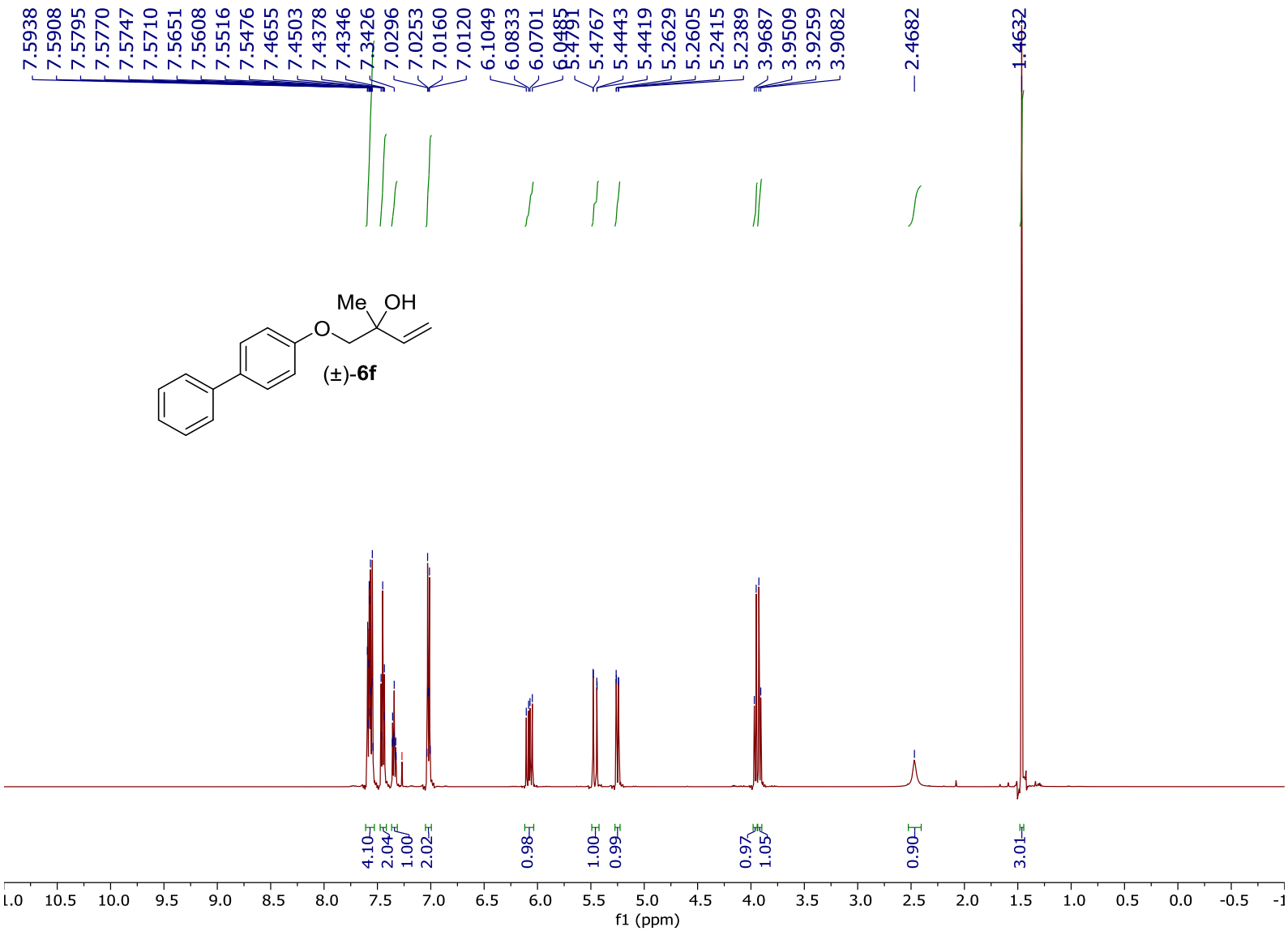
661W cells were pre-treated with/without BD1063 (10 μM) for 30 minutes. Then the cells were treated with tBHP alone or compound **4j** (30 μM) and tBHP in the presence/absence of BD1063 (10 μM) for 24 h before cell viability assessment. Cell viability was assessed using the MTT assay. Data are presented as mean ± standard error of the mean (SEM) of triplicate measurements. ** $p < 0.01$; **** $p < 0.0001$, ns = not significant as compared to the tBHP treatment. (tBHP = tert-butyl hydroperoxide; MRP = compound 4j).



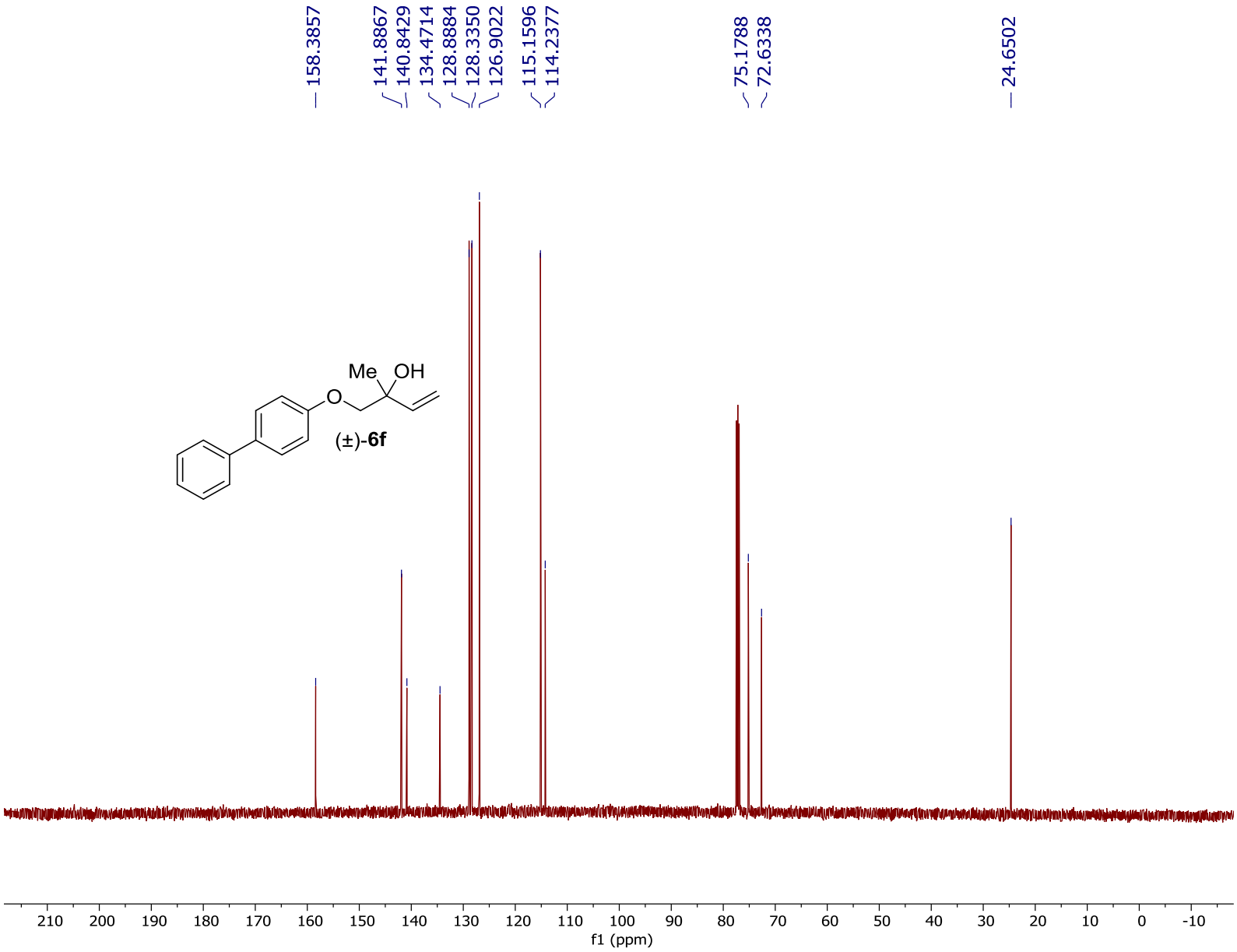
Compound 6d, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



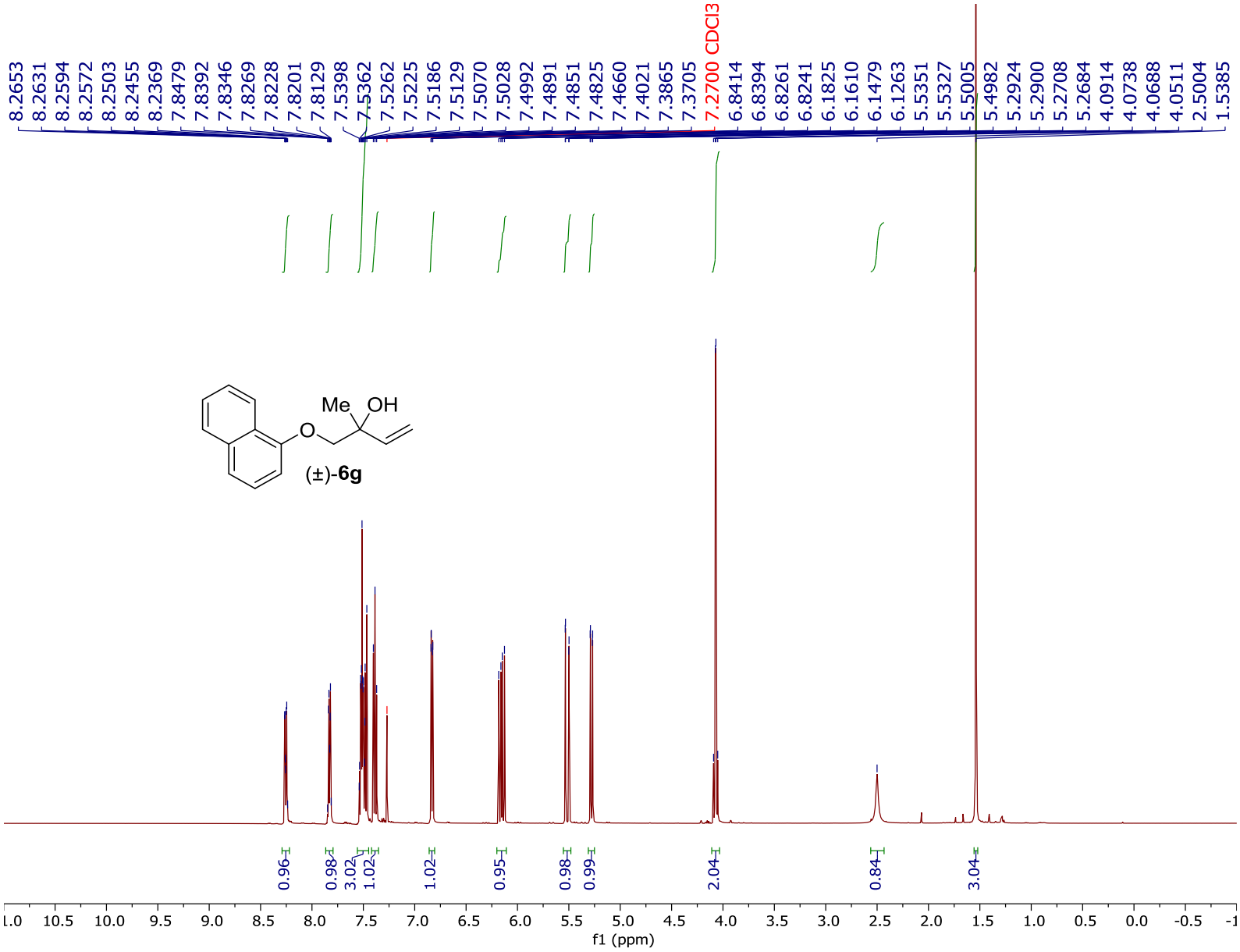
Compound 6d, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



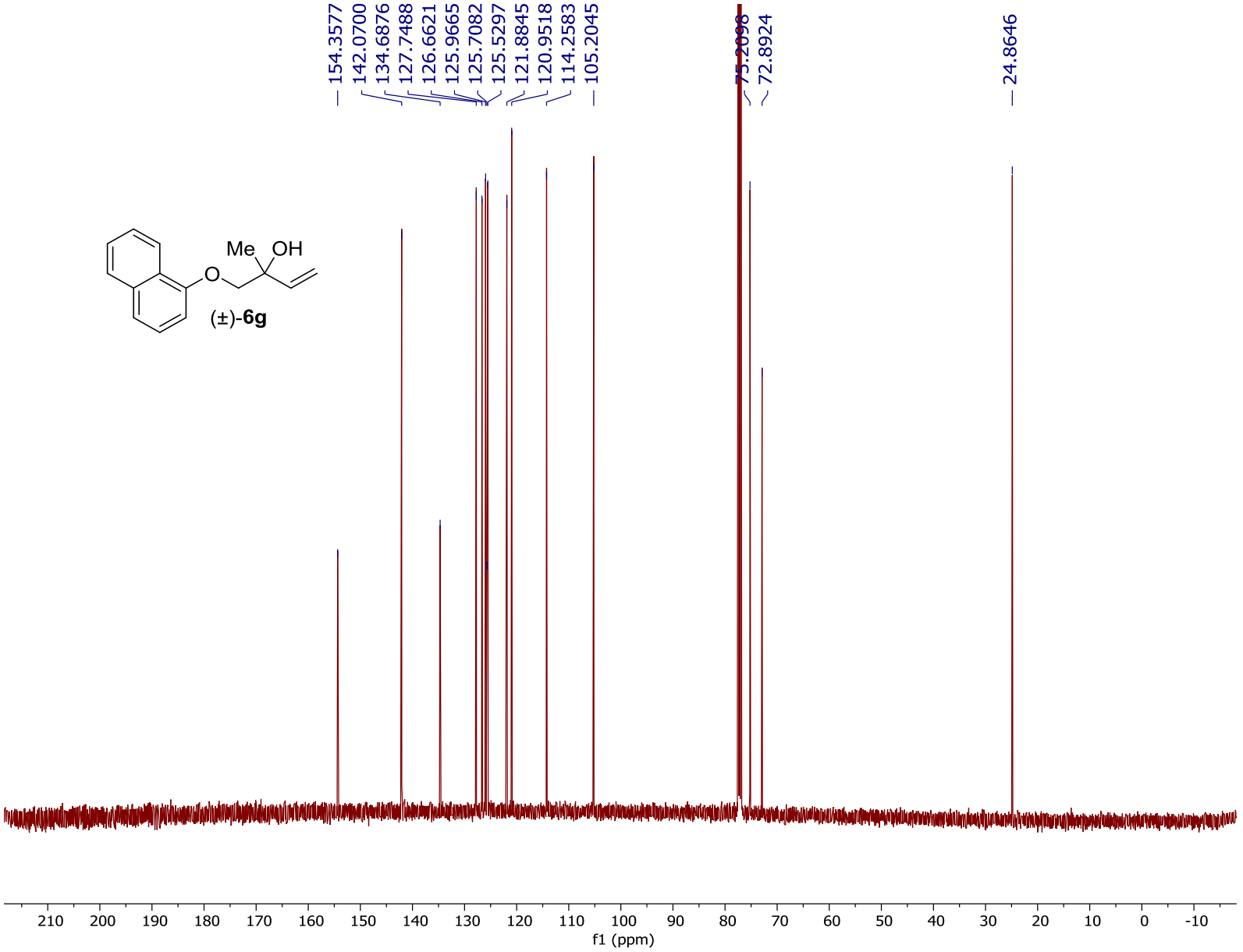
Compound 6f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



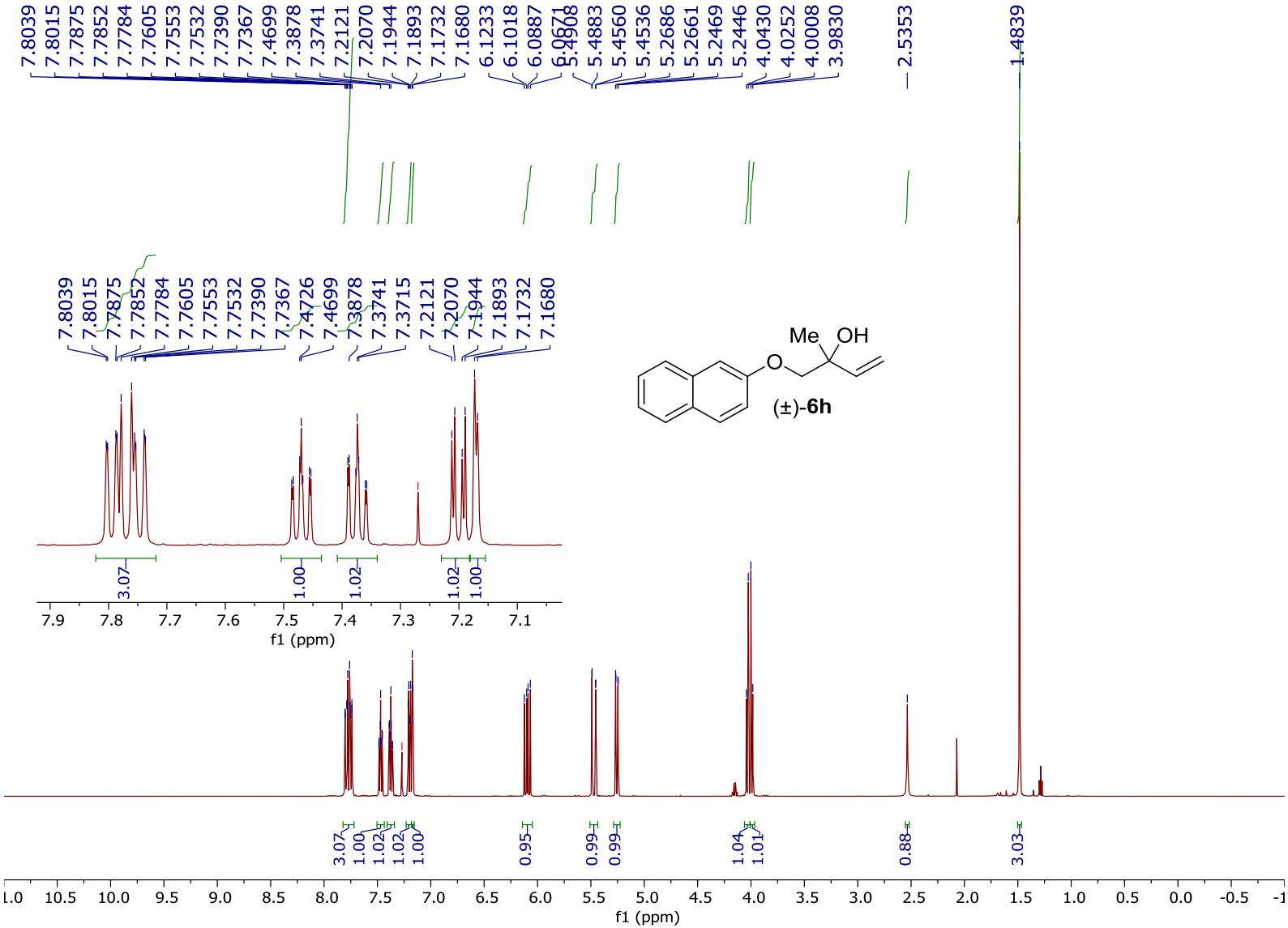
Compound 6f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



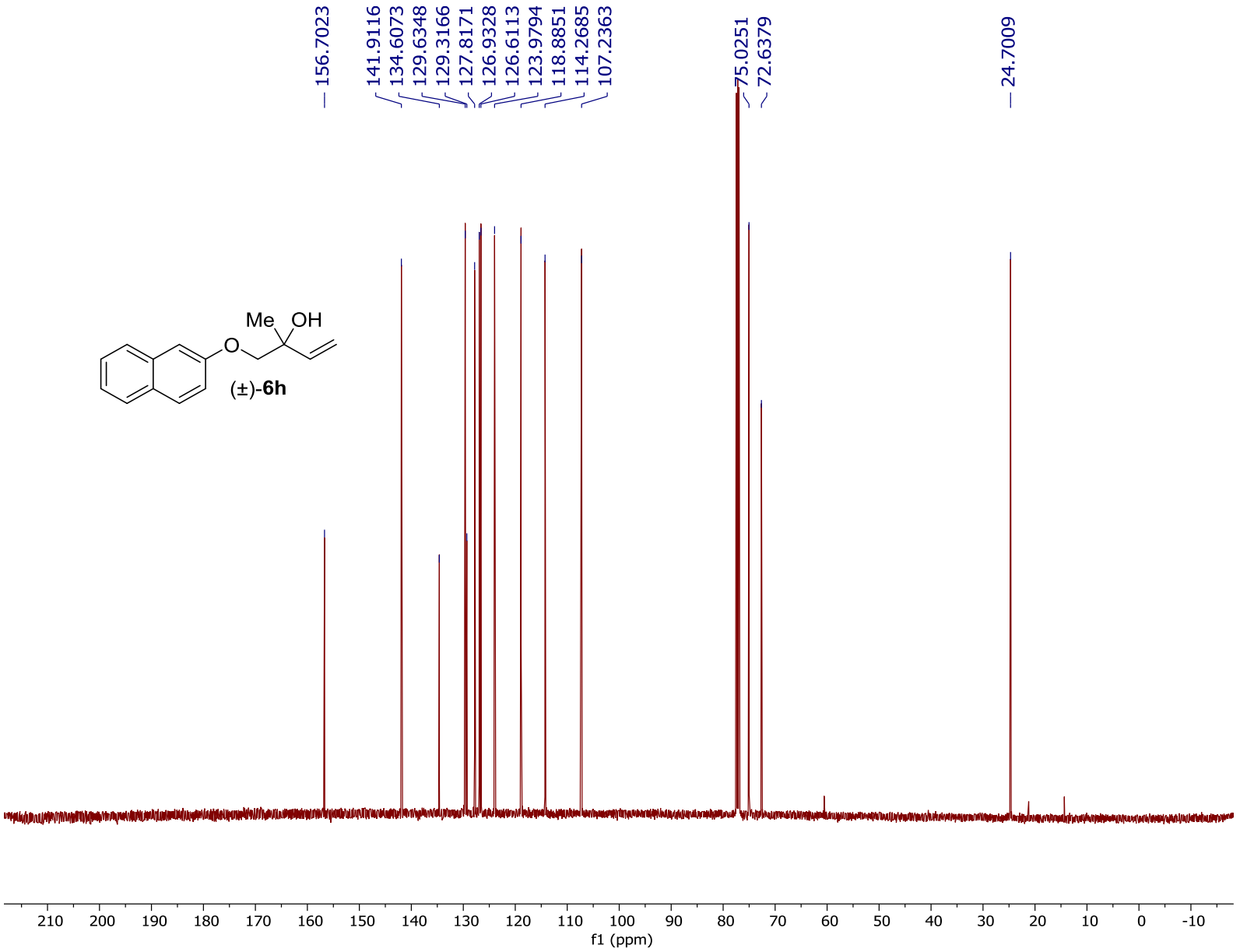
Compound 6g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



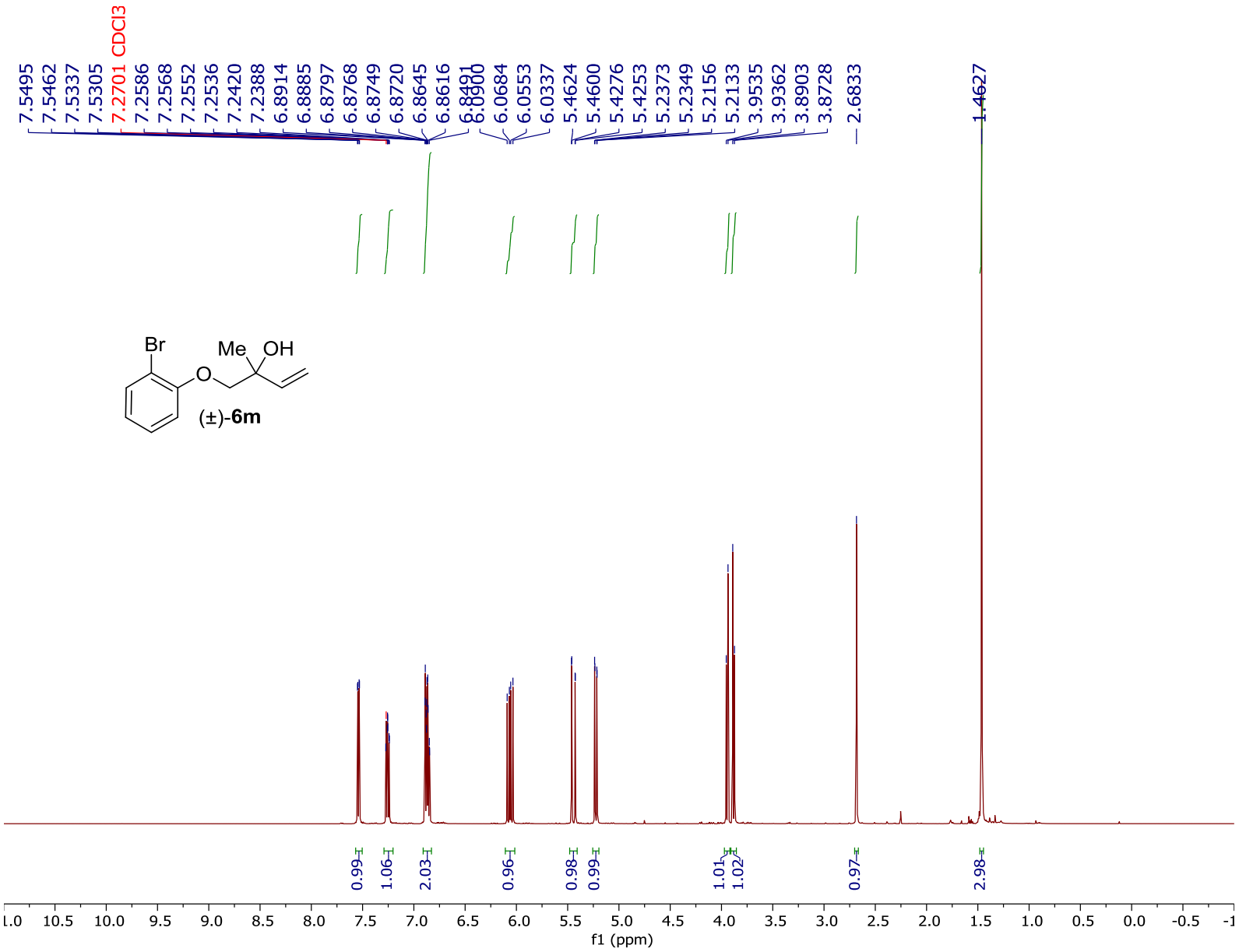
Compound 6g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



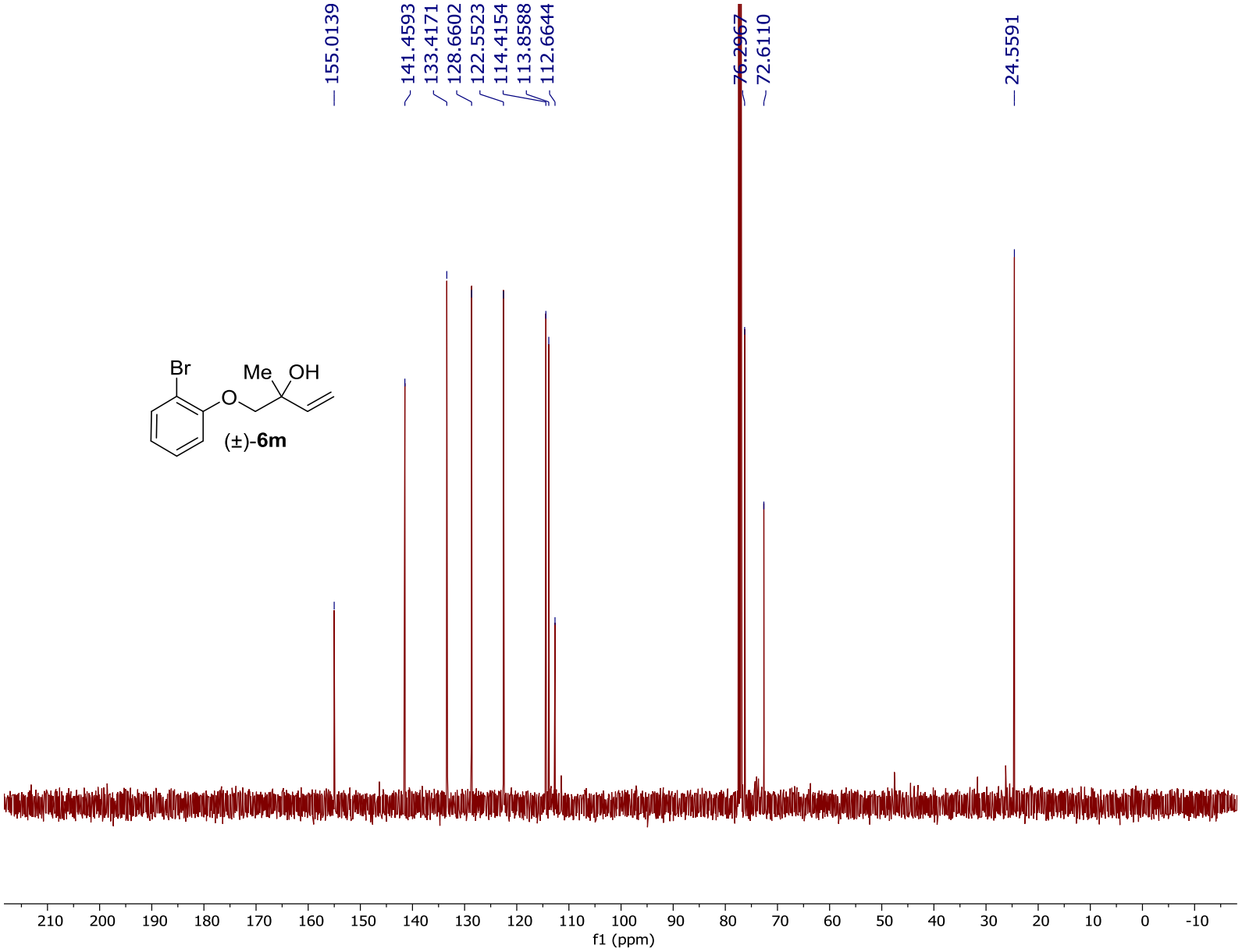
Compound 6h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



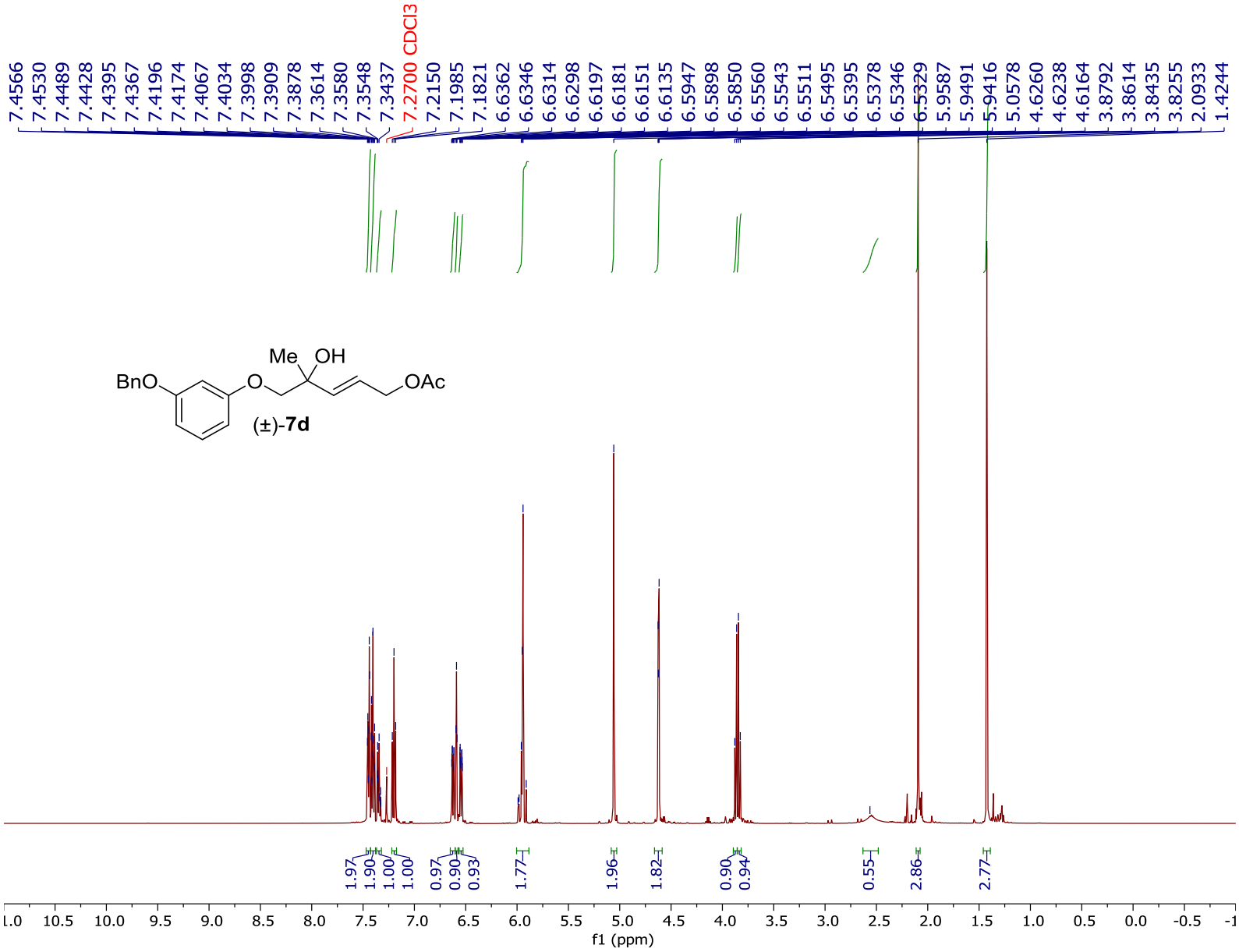
Compound 6h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



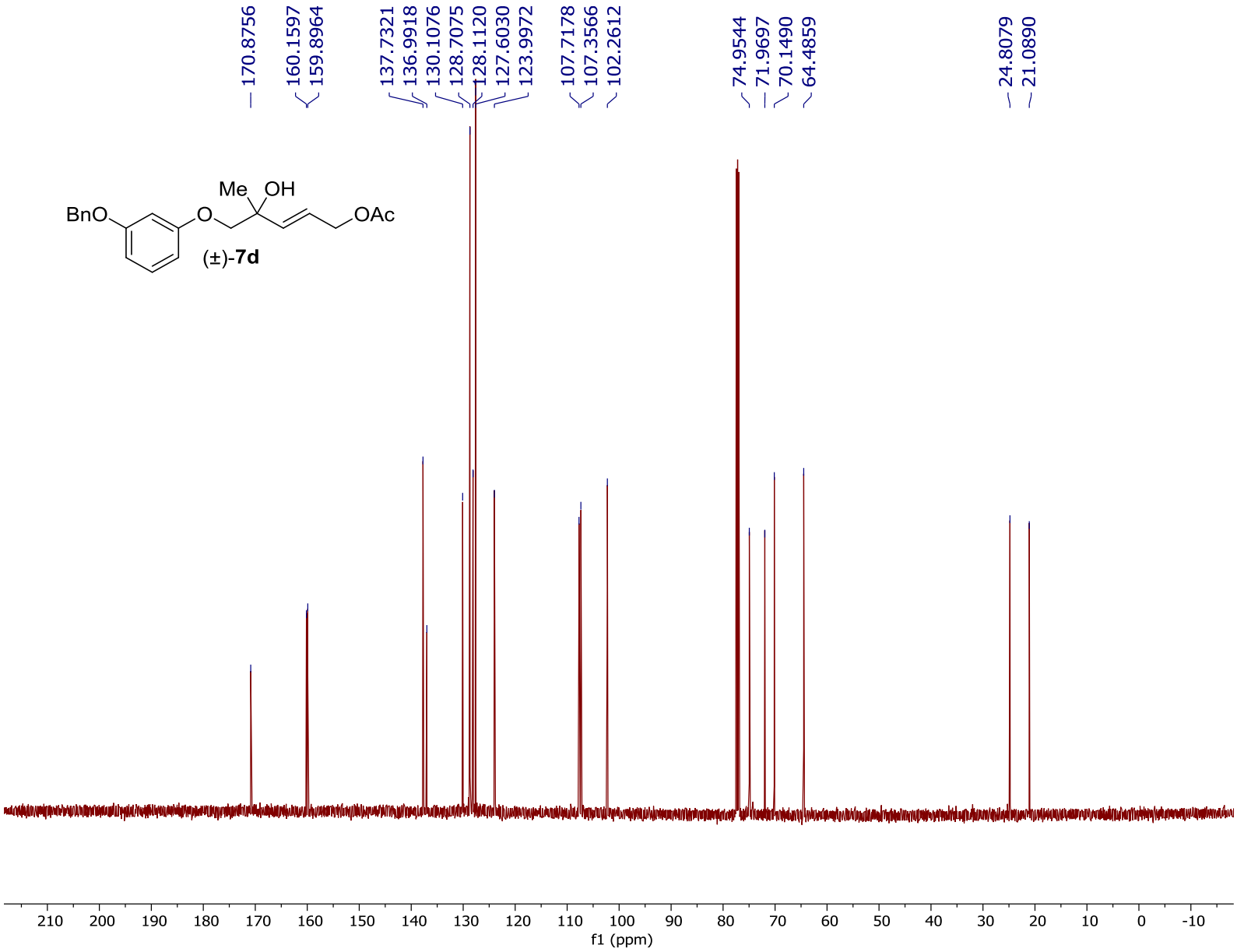
Compound 6m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



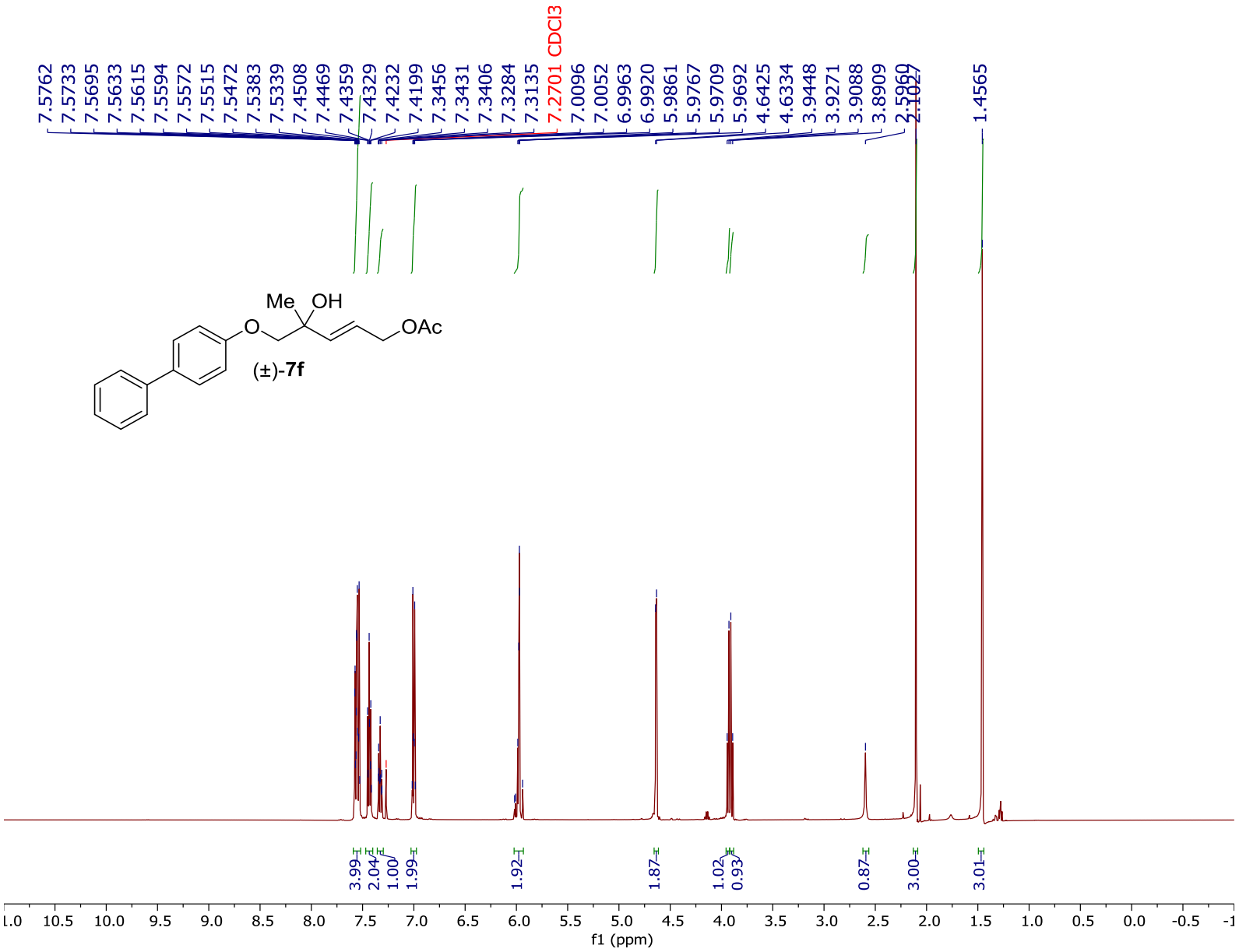
Compound 6m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



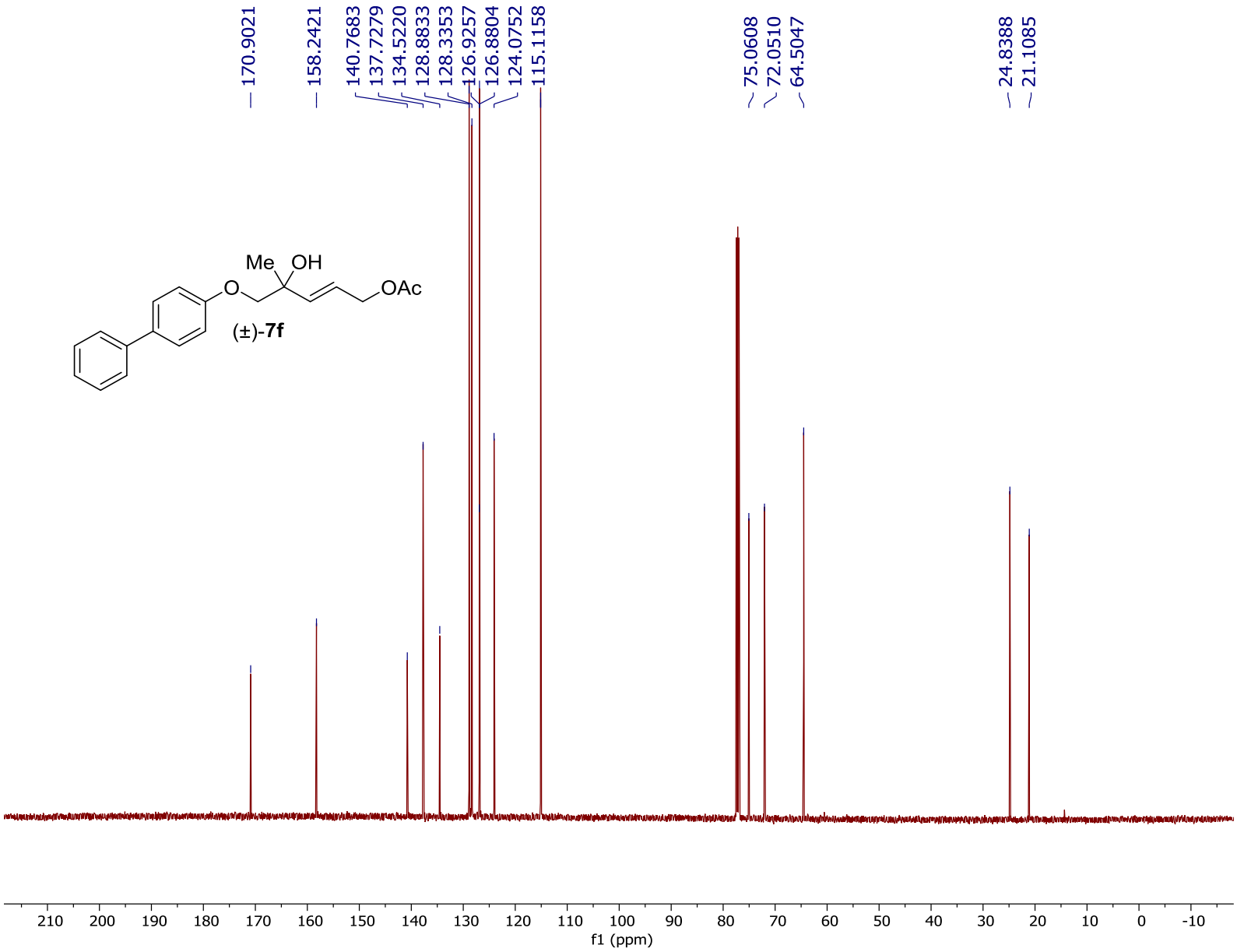
Compound 7d, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



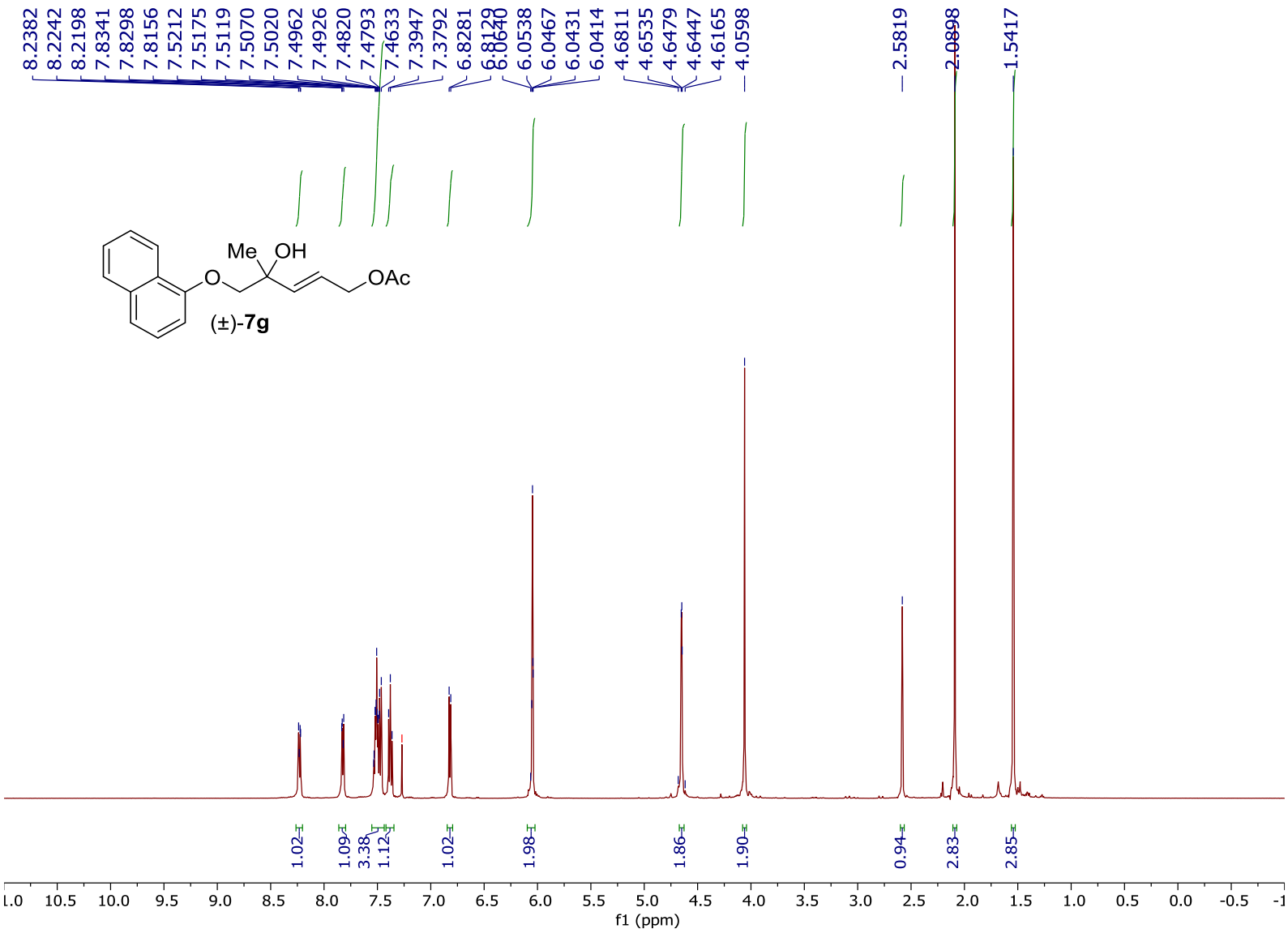
Compound 7d, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



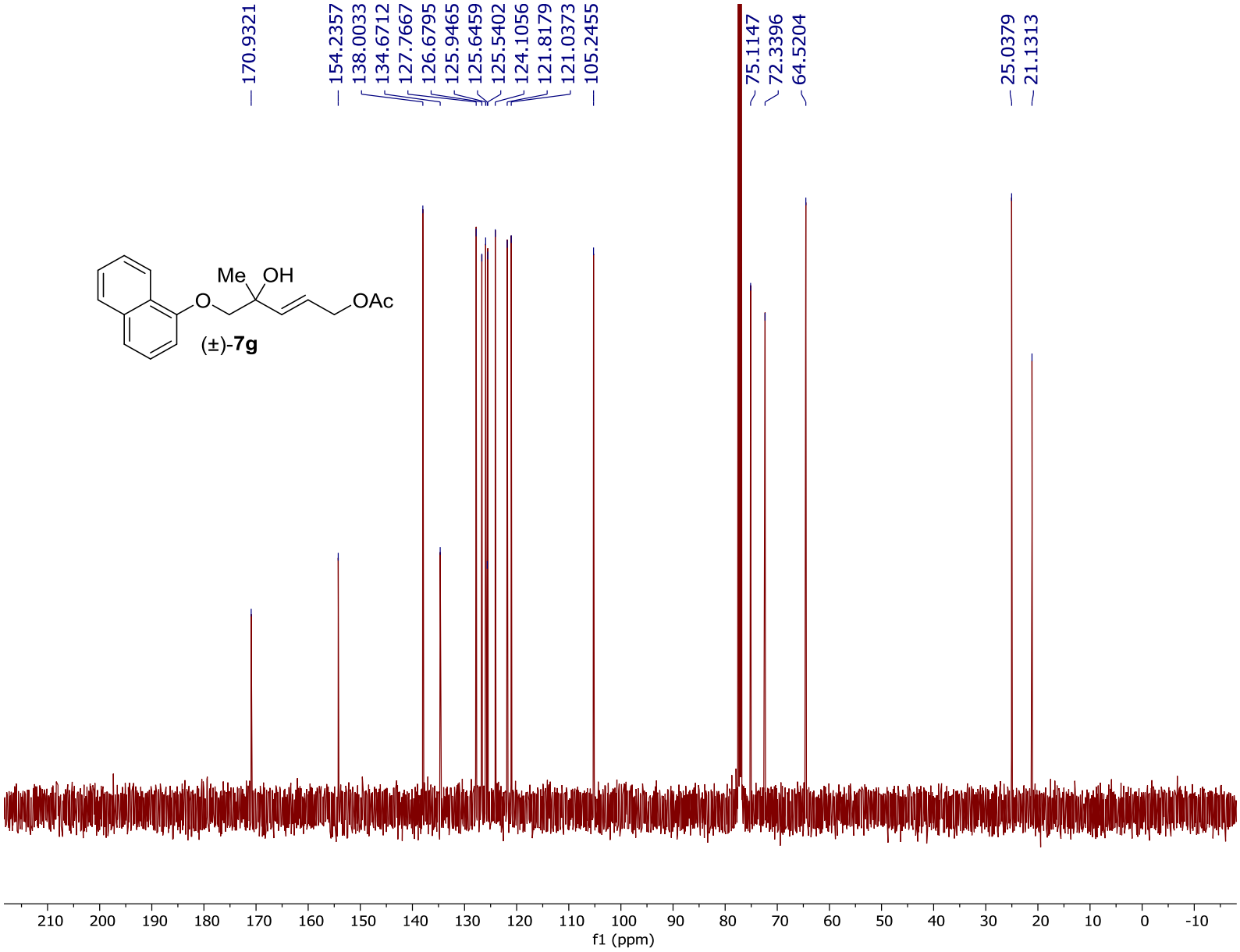
Compound 7f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



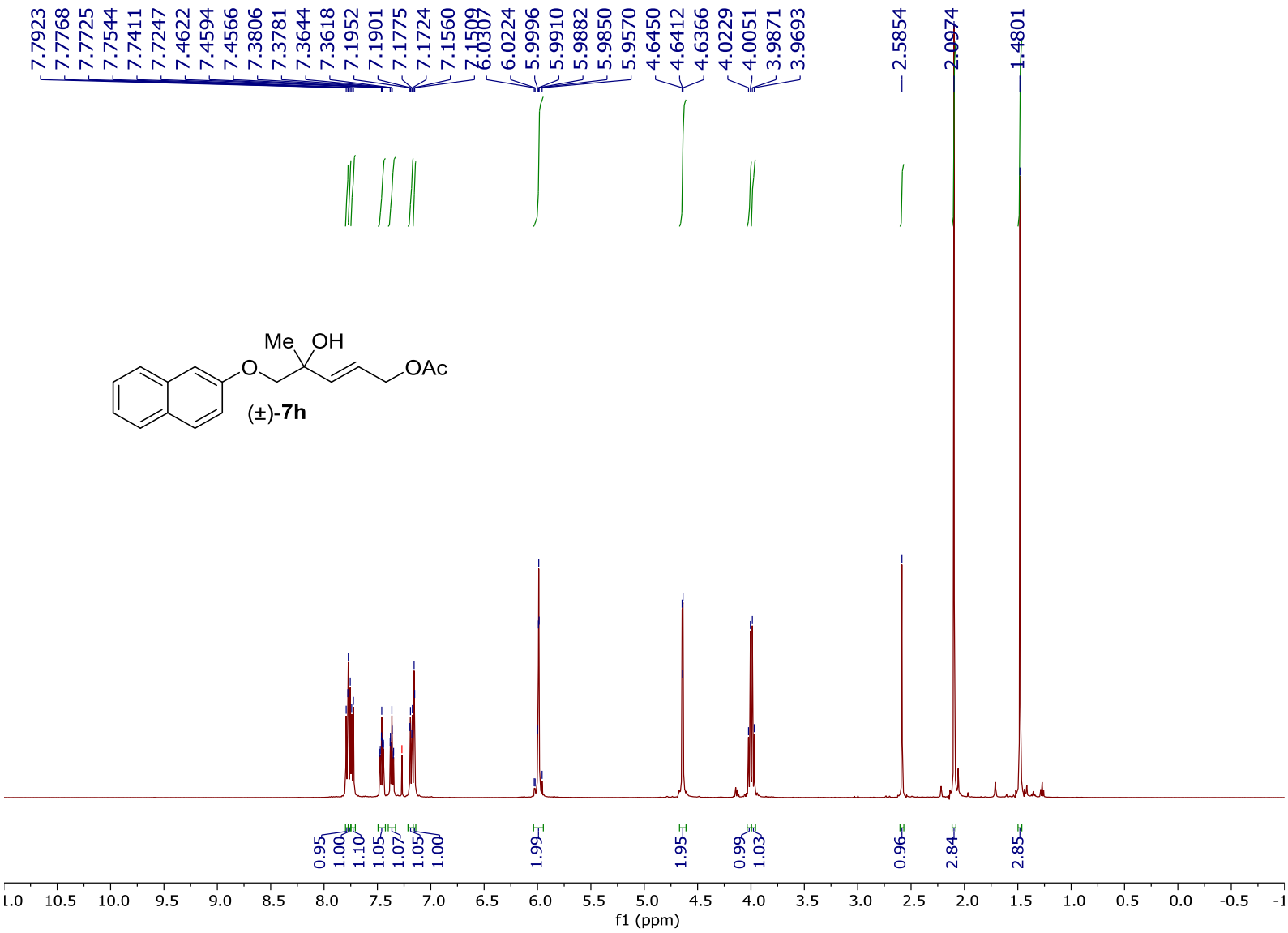
Compound 7f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



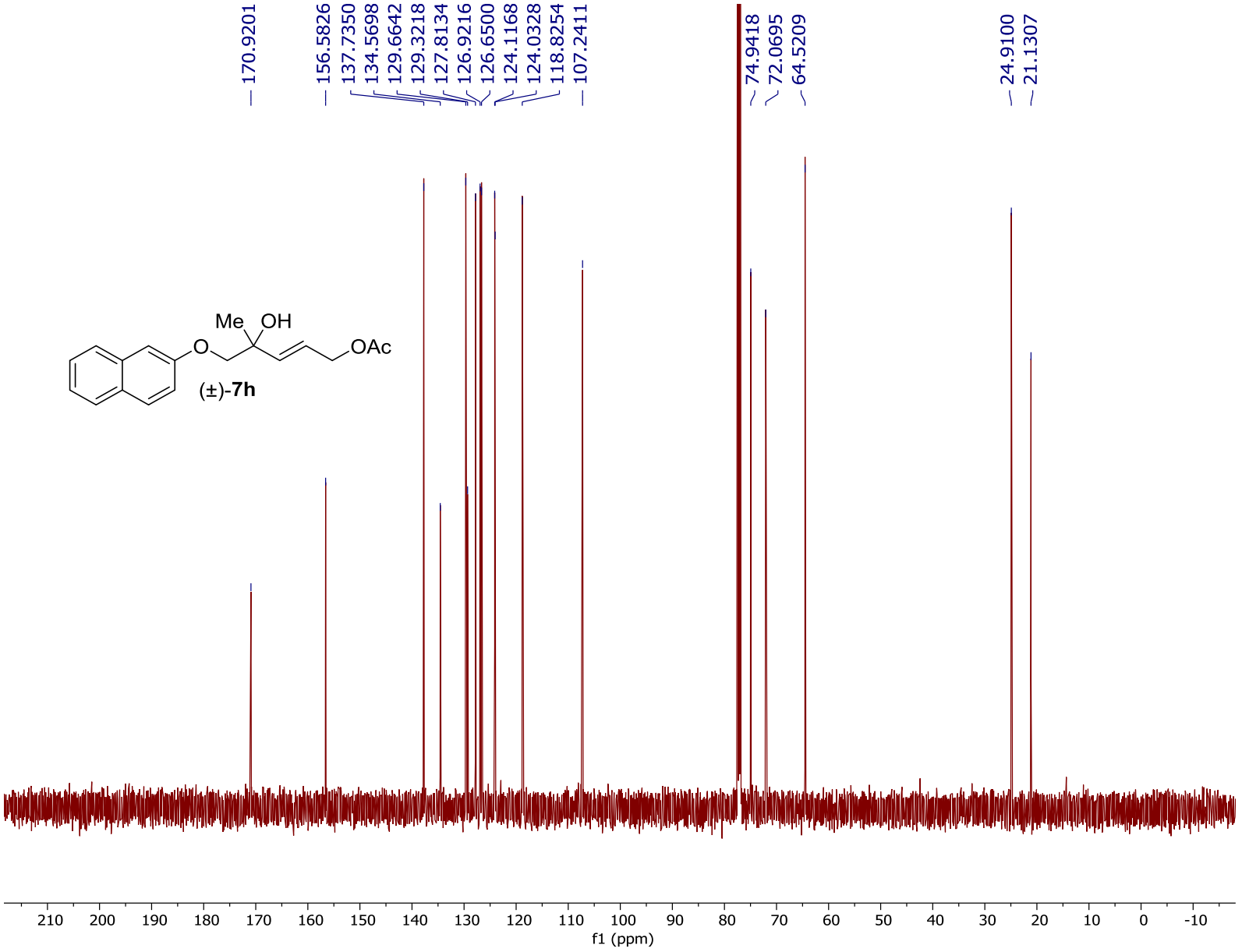
Compound 7g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



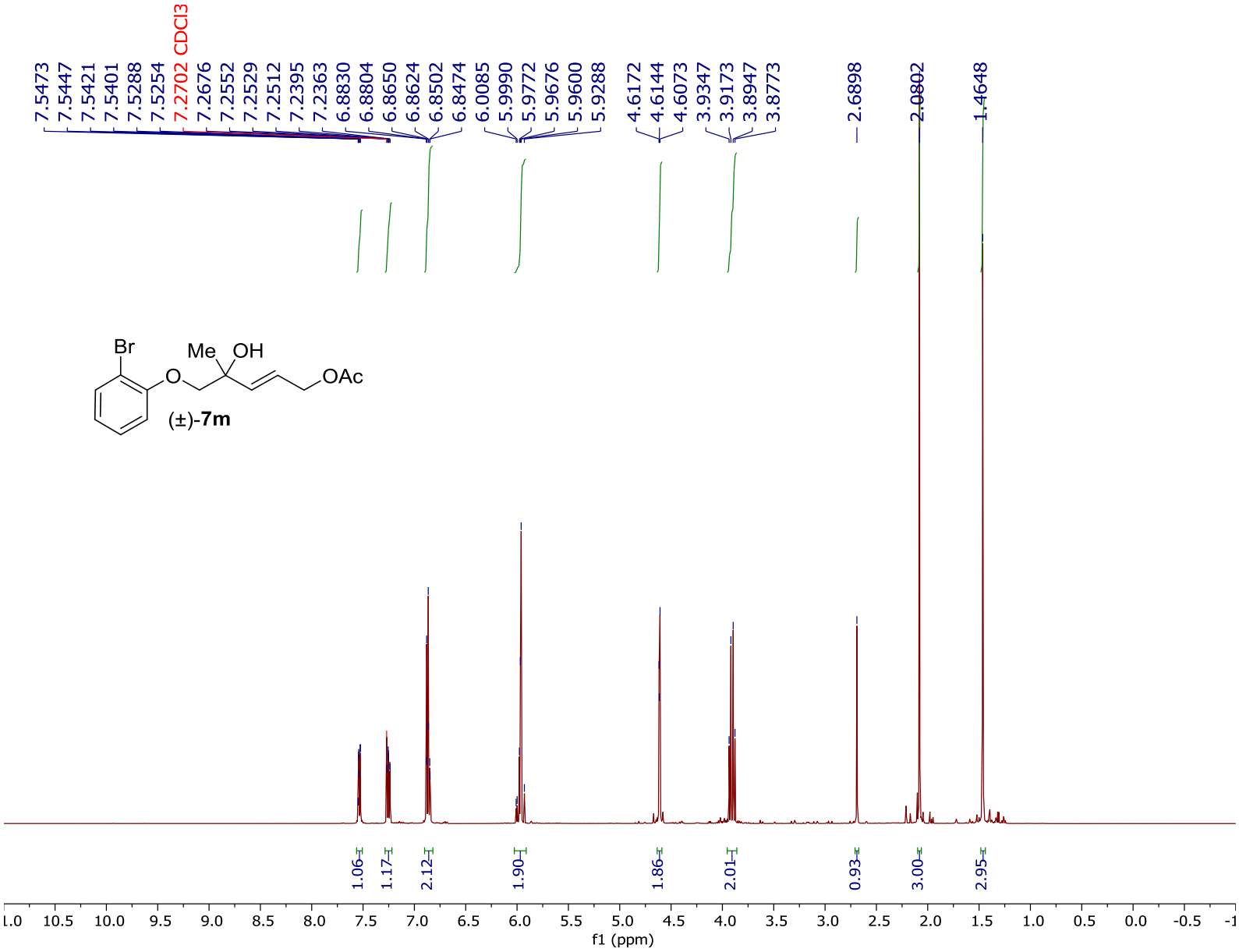
Compound 7g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



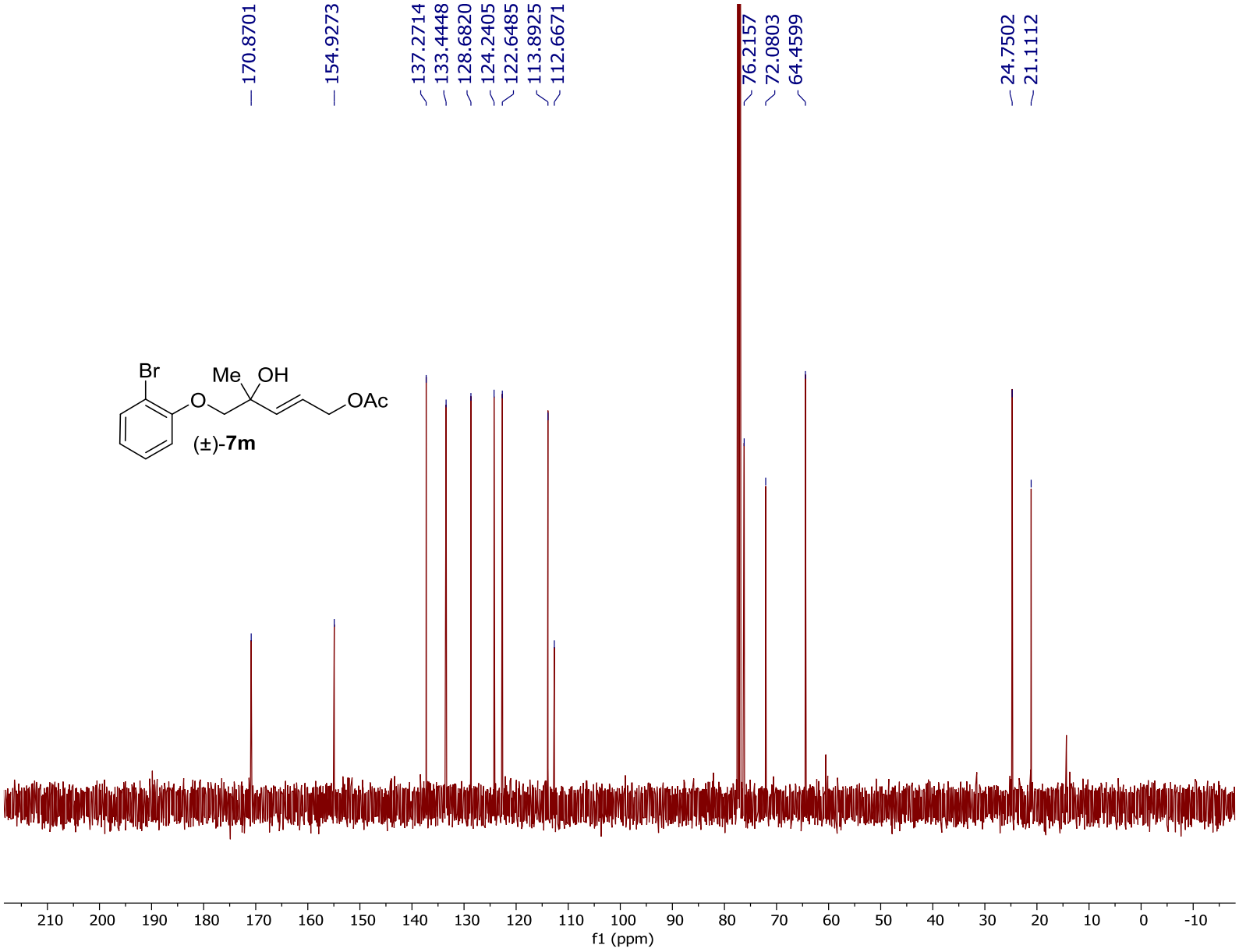
Compound 7h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



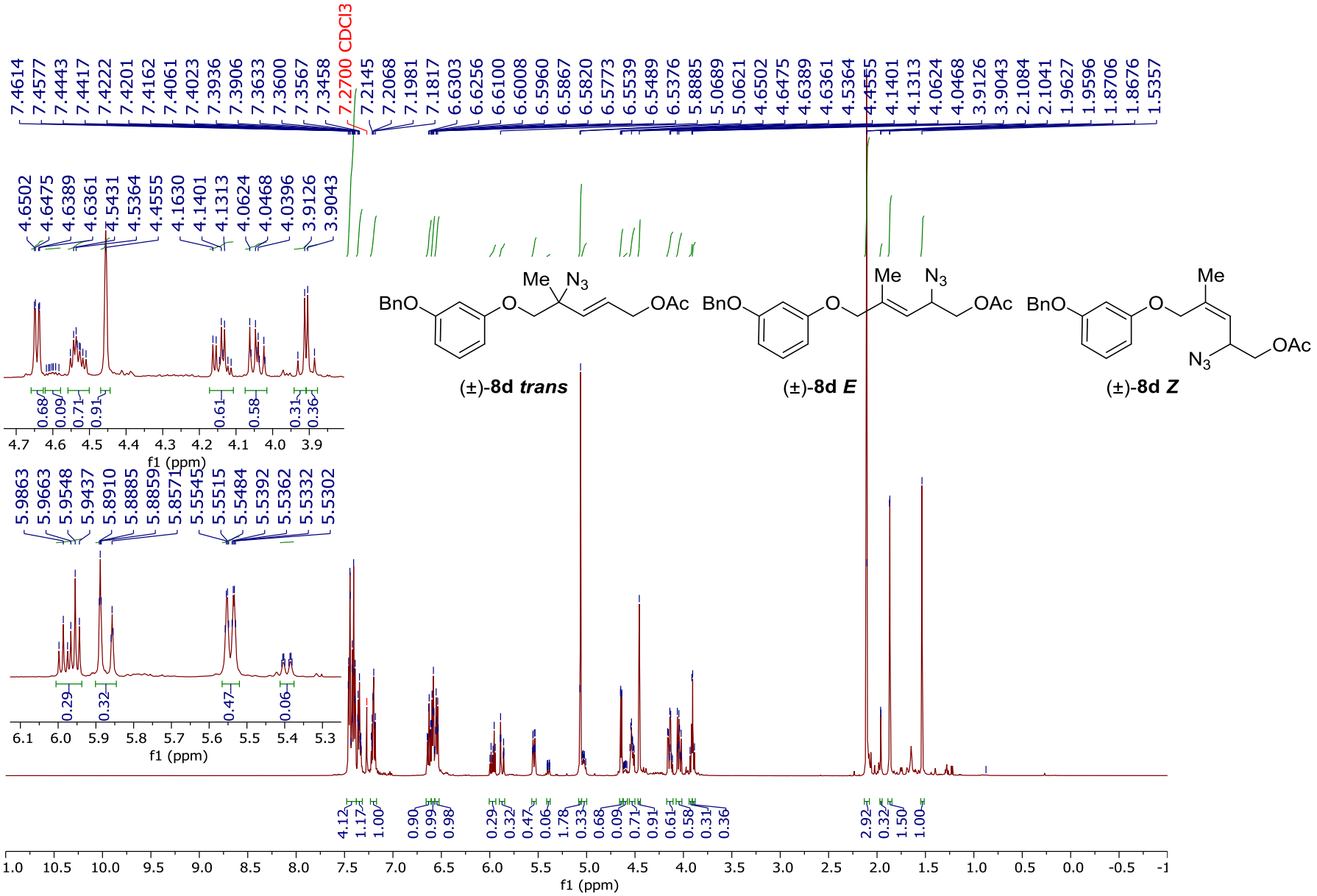
Compound 7h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



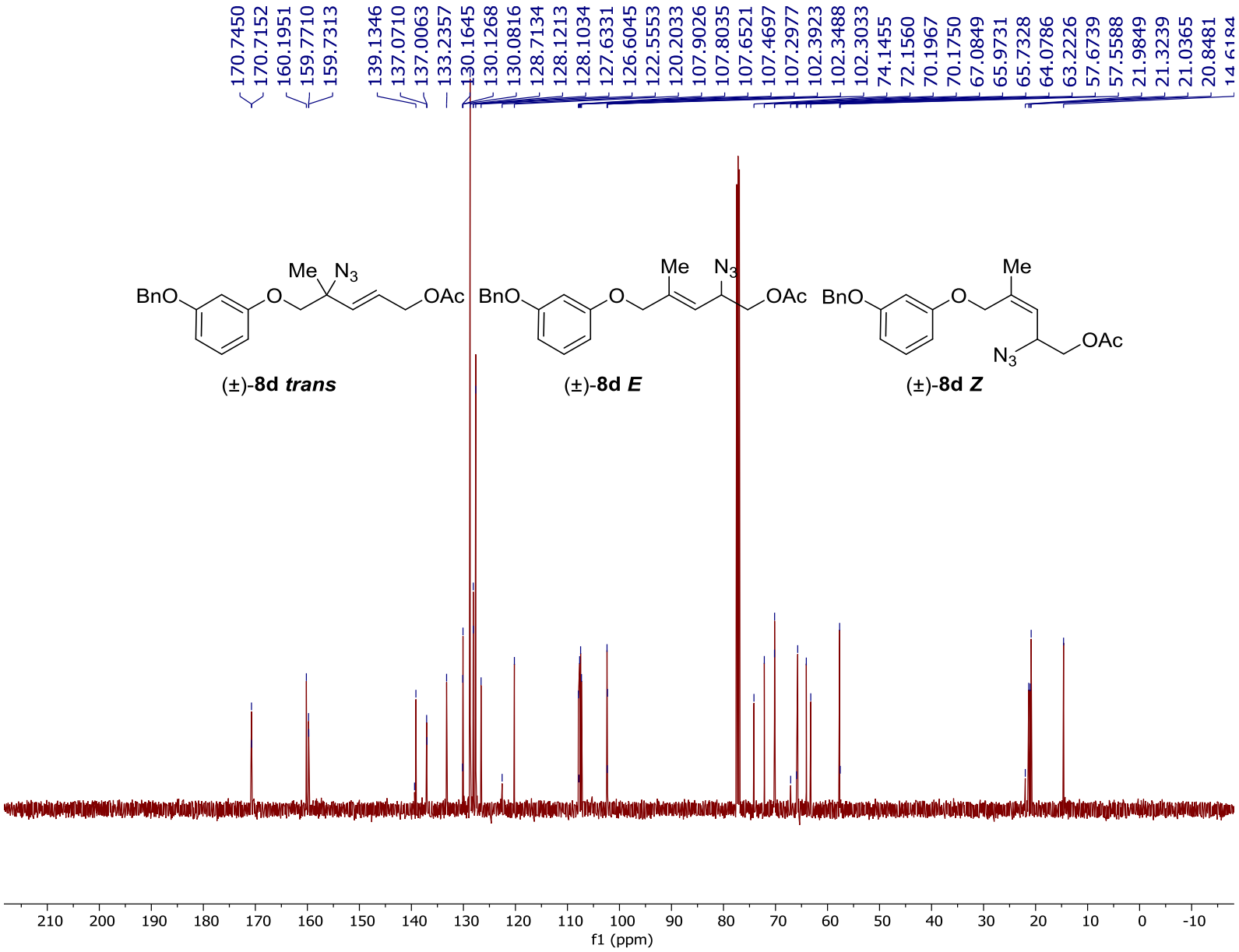
Compound 7m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



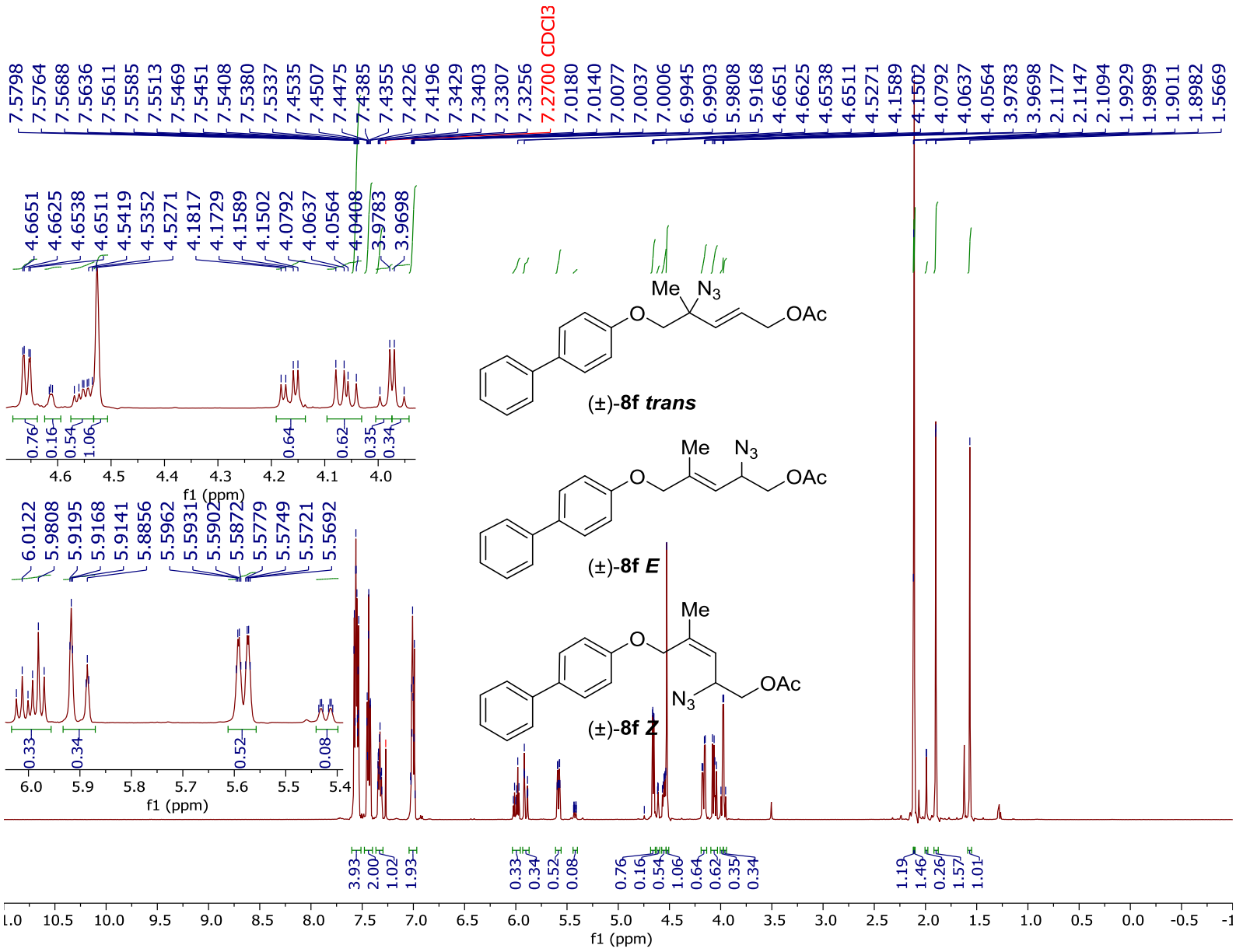
Compound 7m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



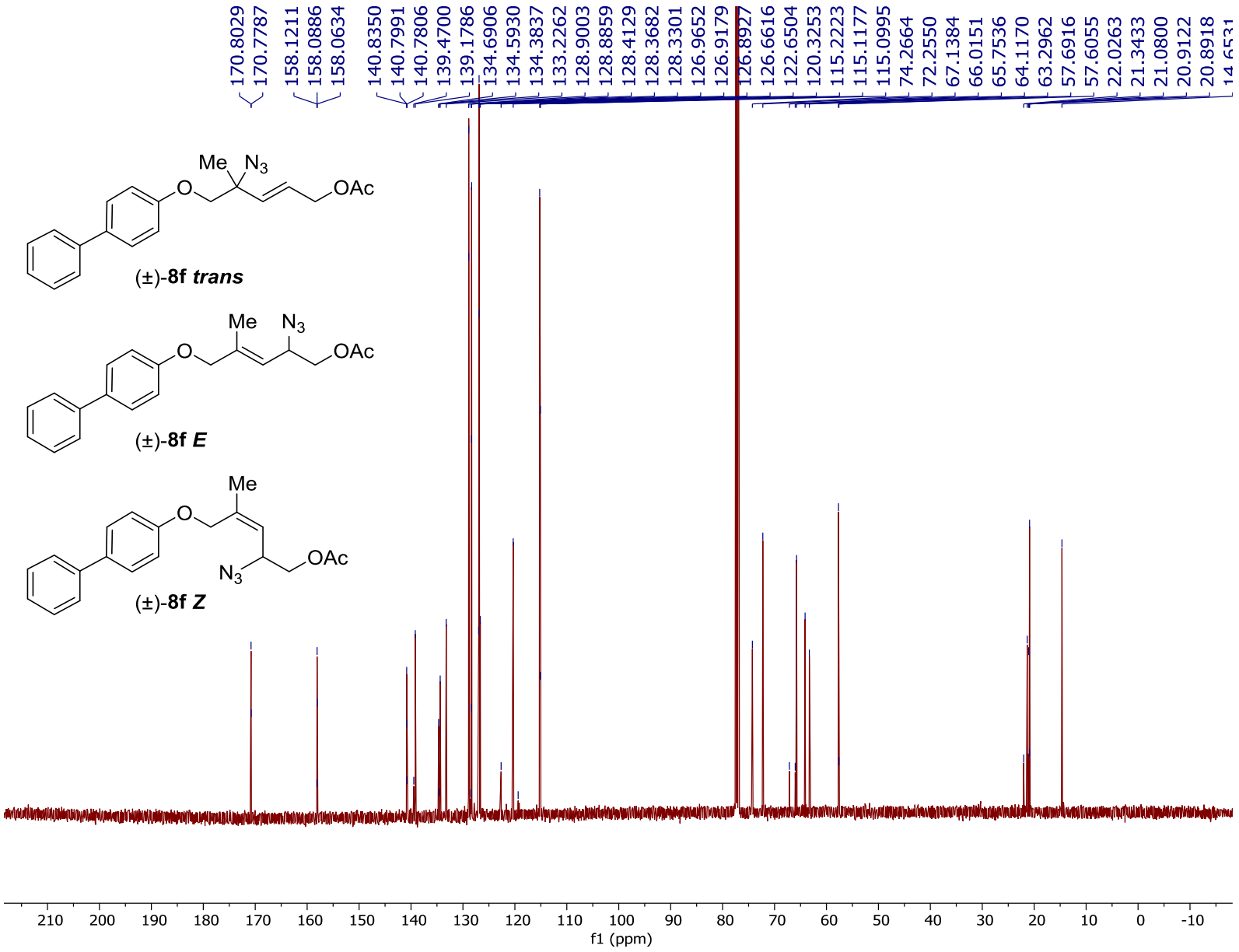
Compound 8d, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



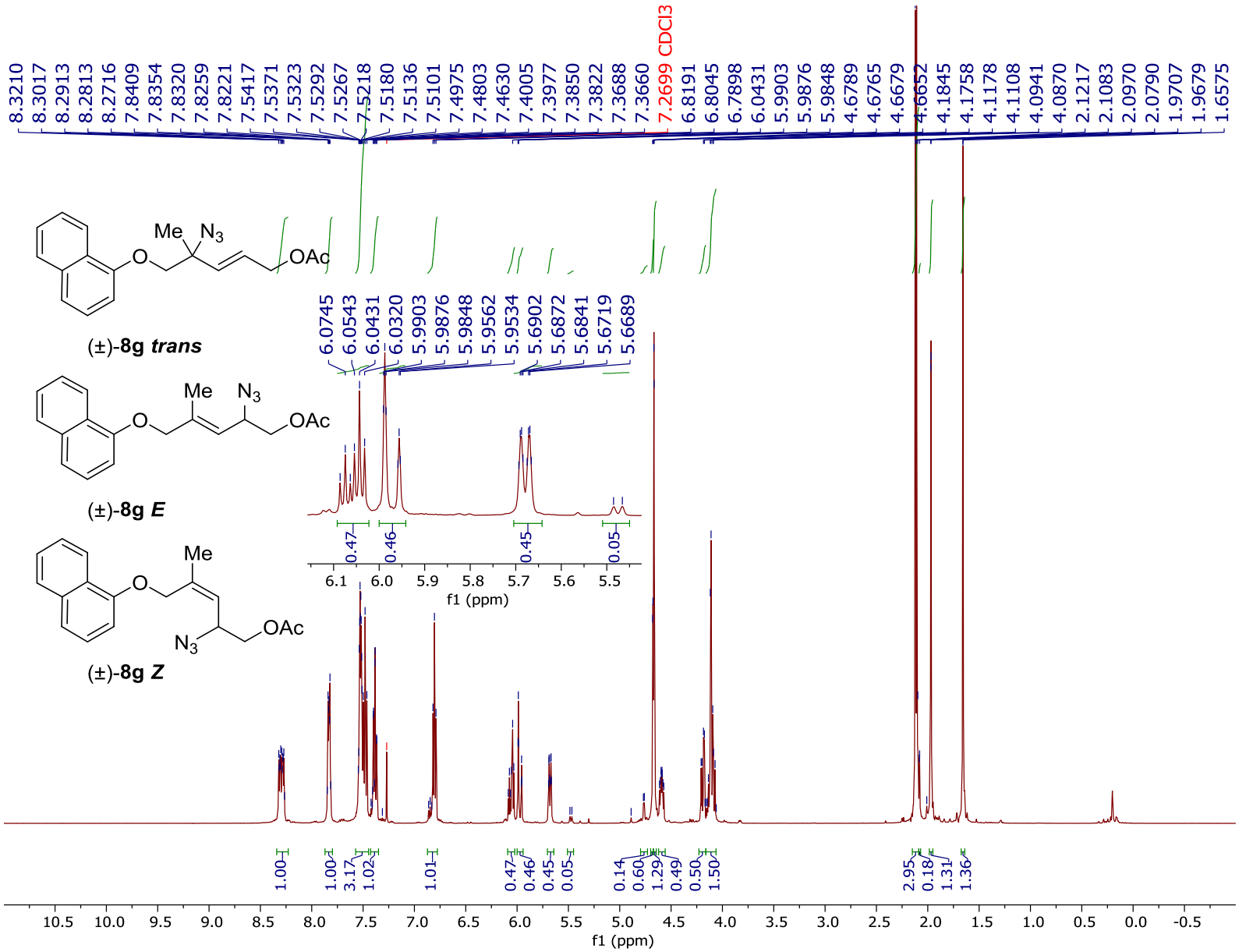
Compound 8d, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



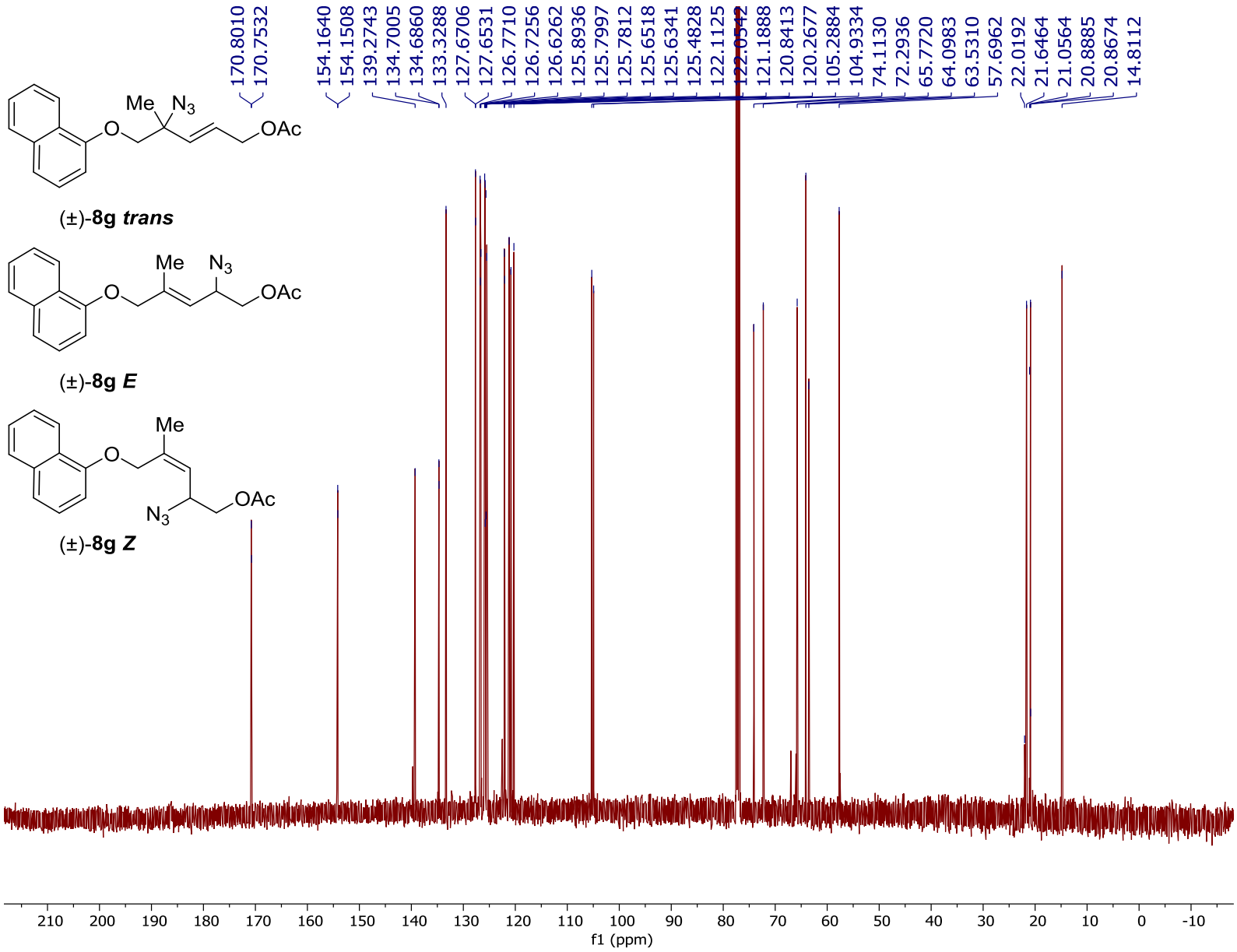
Compound 8f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



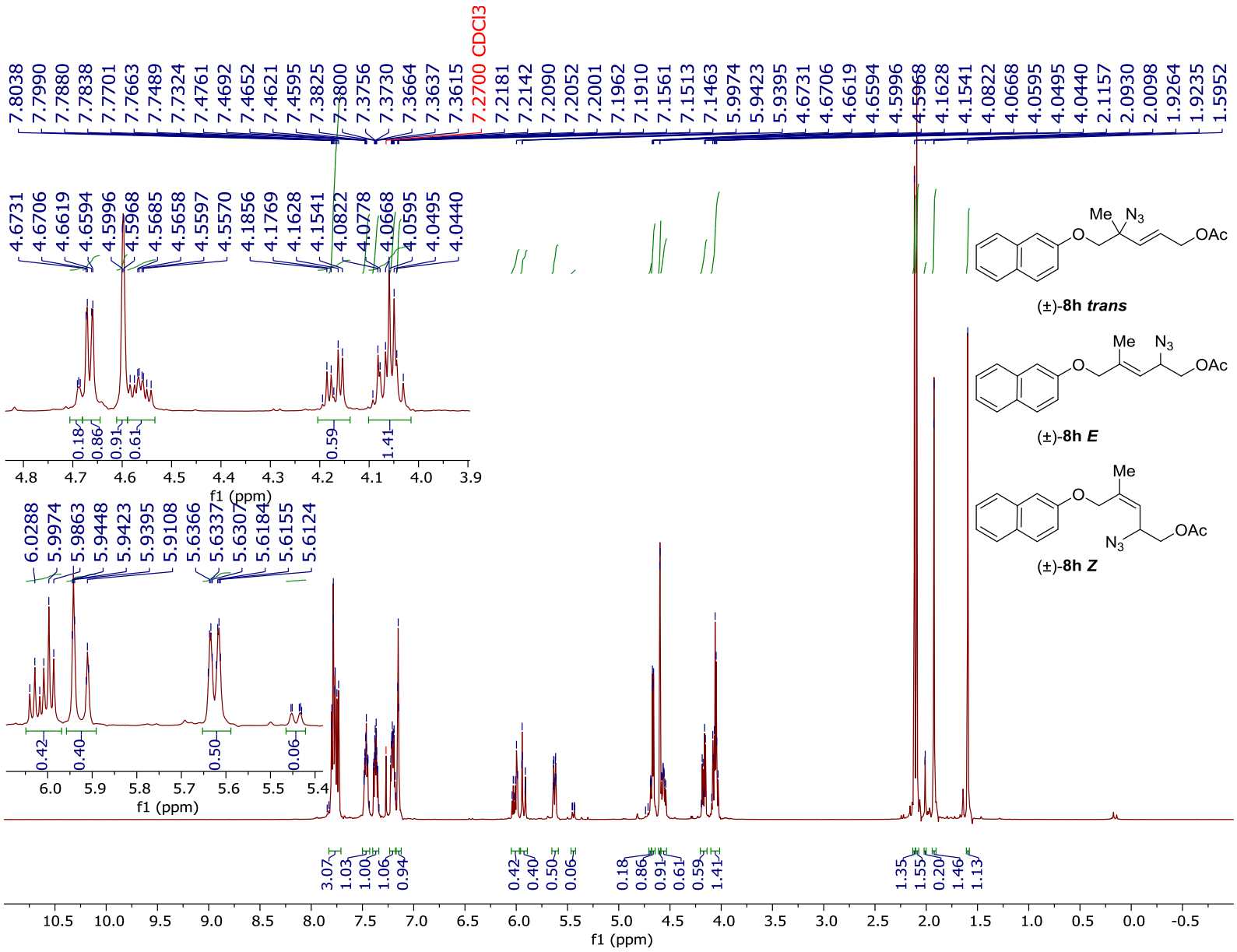
Compound 8f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



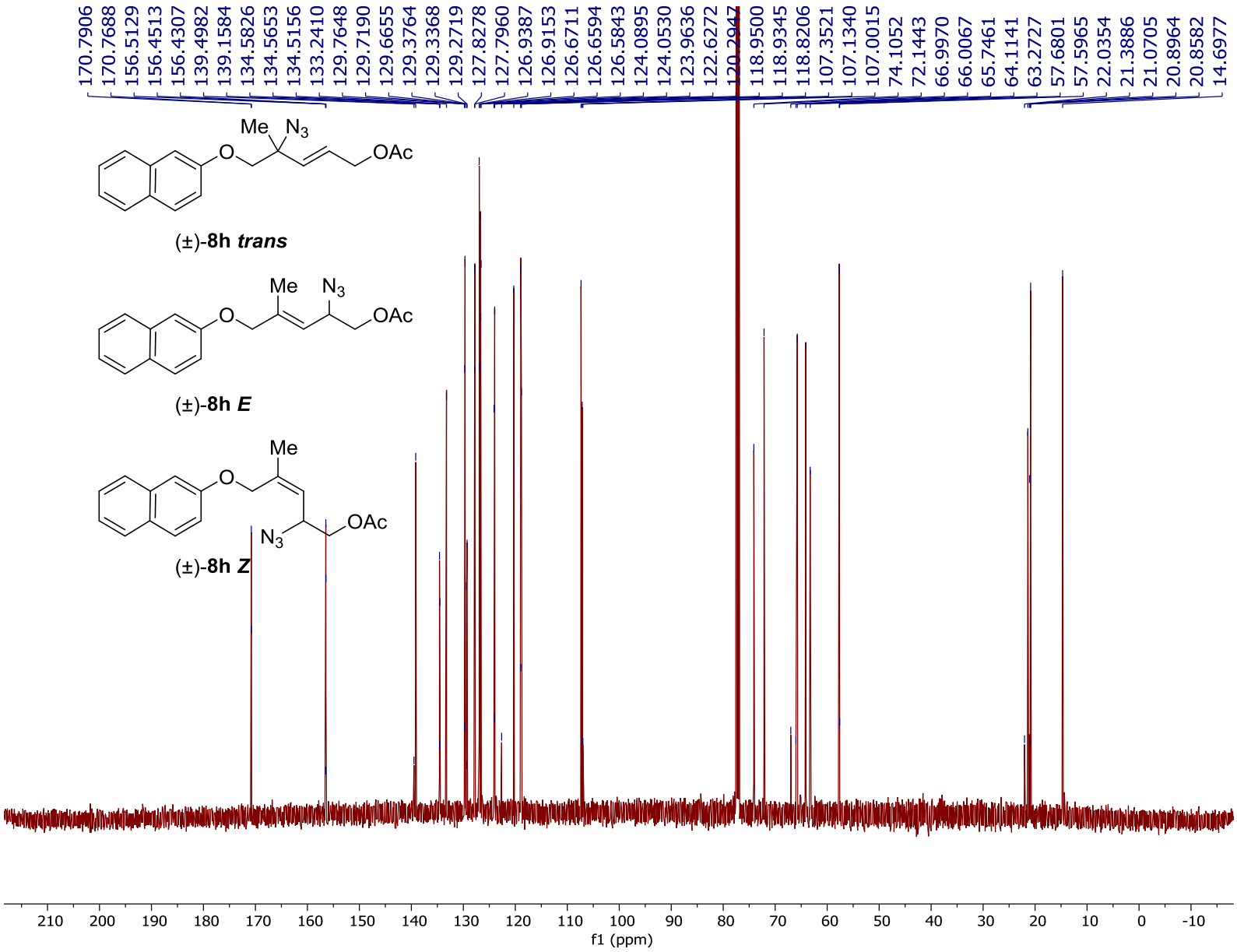
Compound 8g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



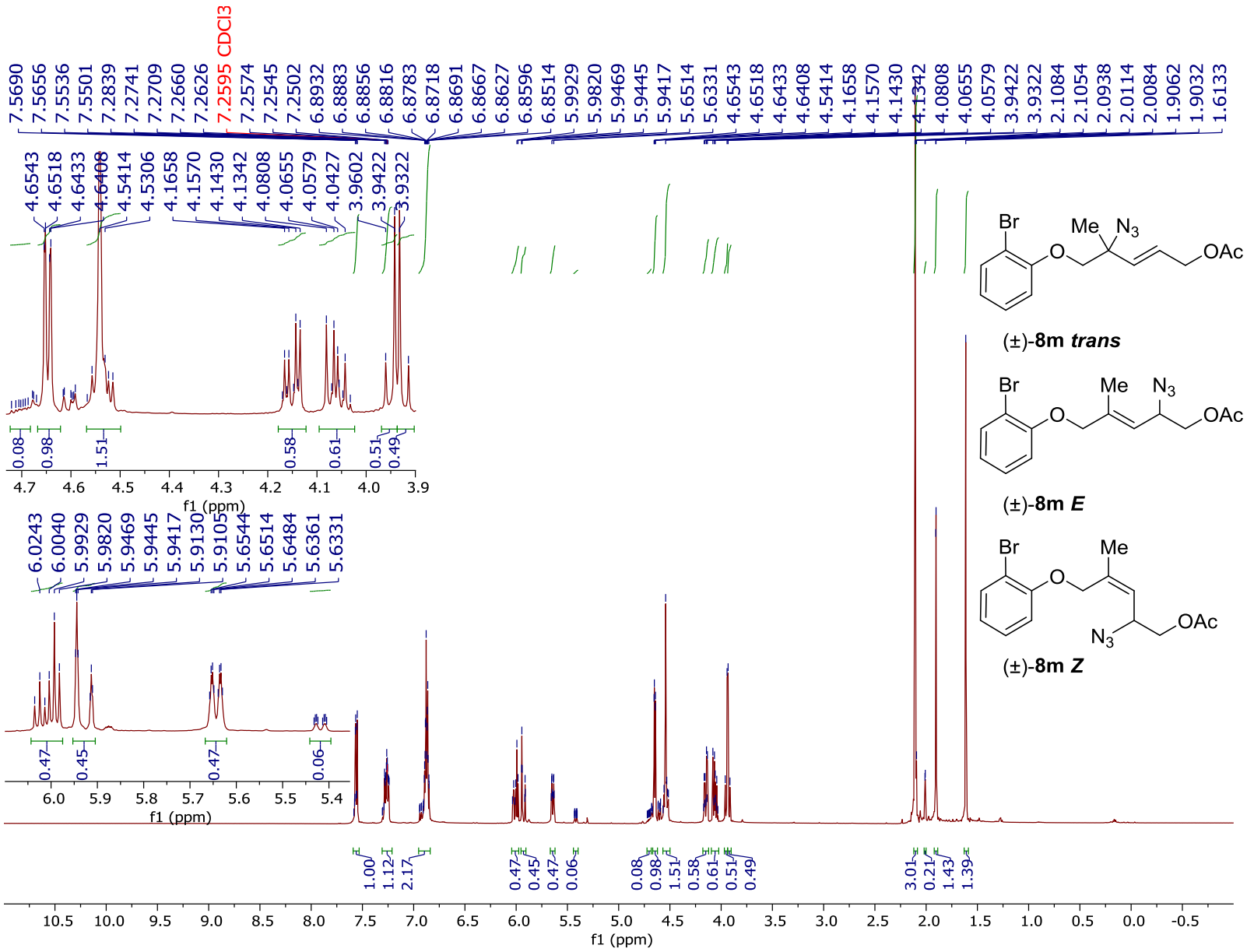
Compound 8g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



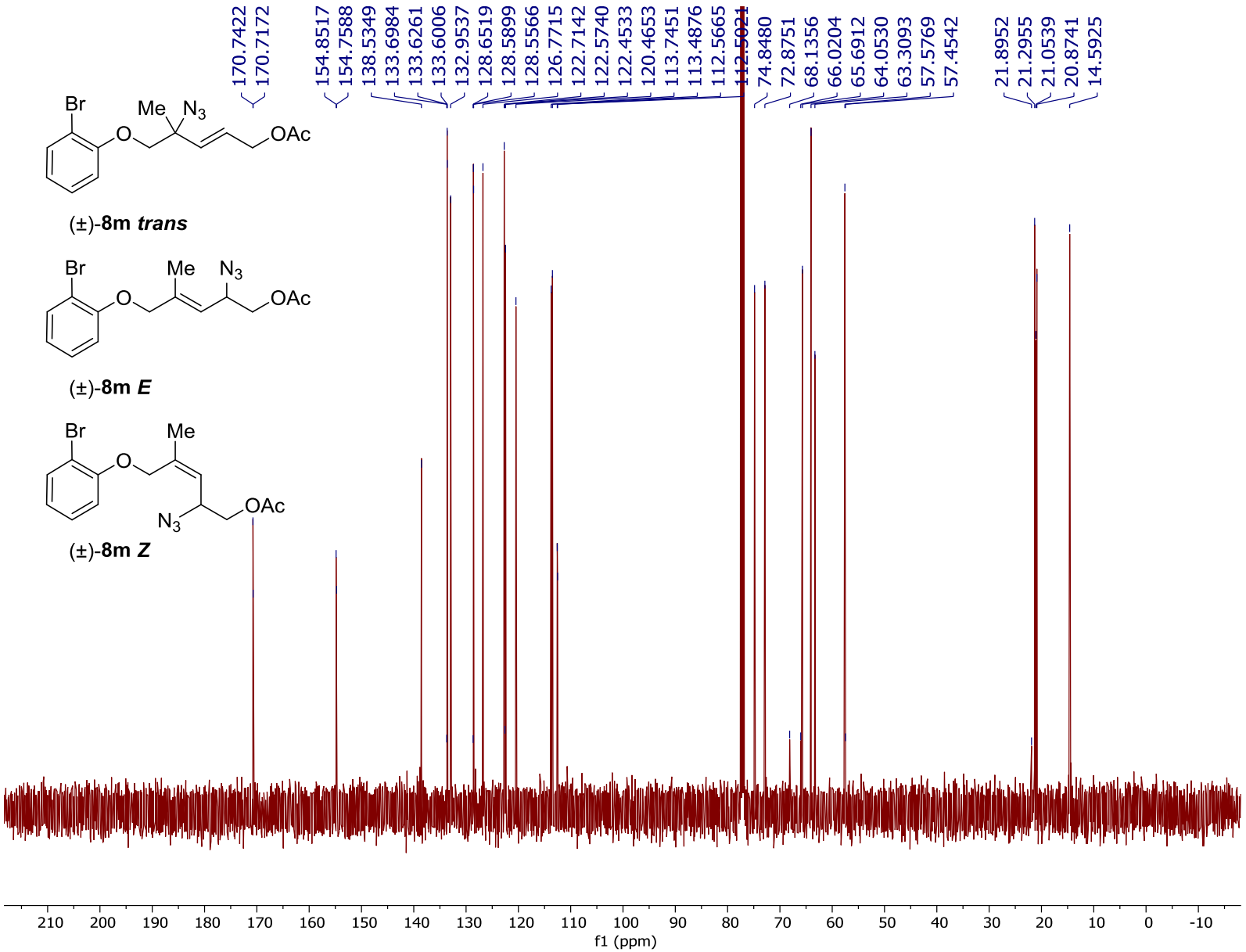
Compound 8h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



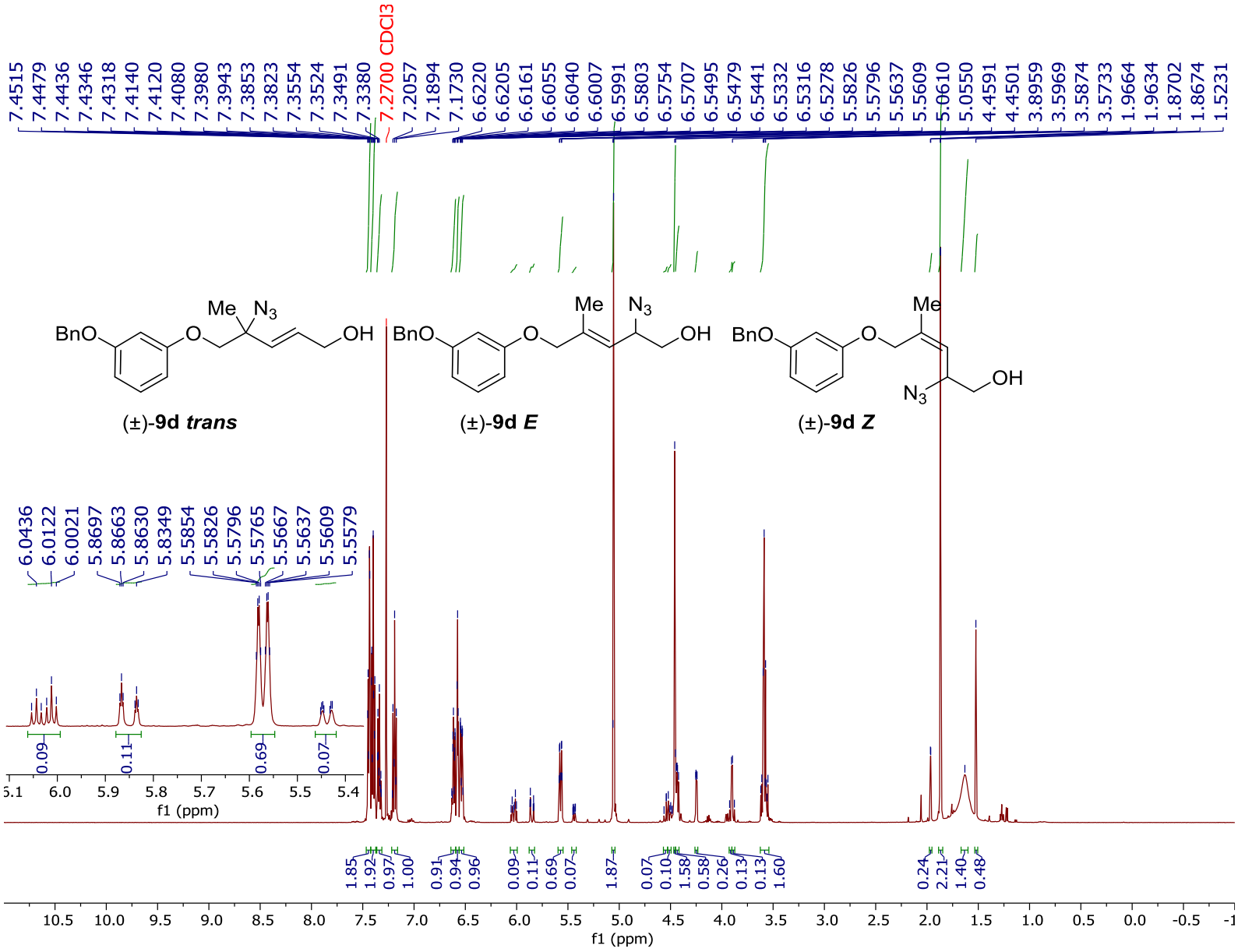
Compound 8h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



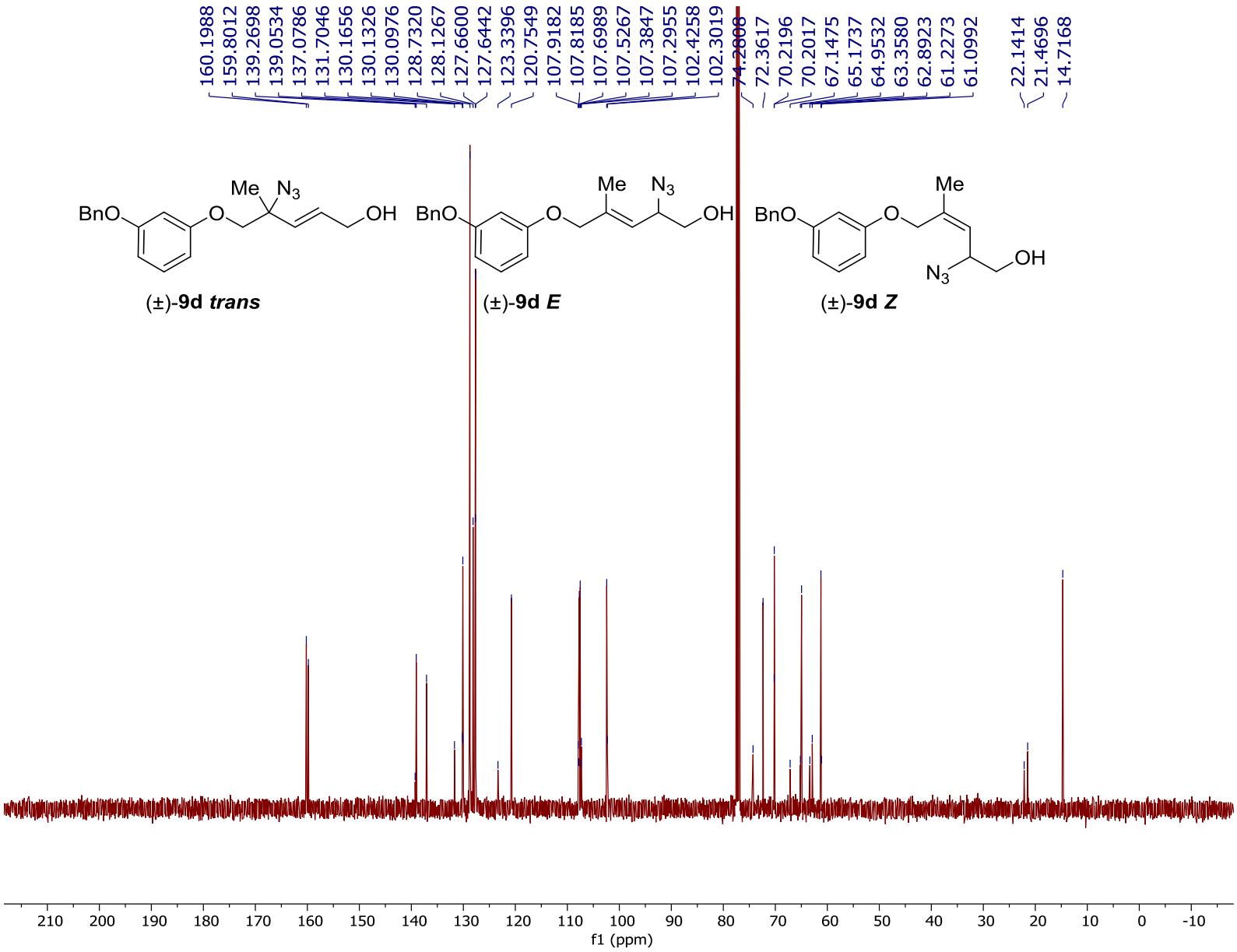
Compound 8m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



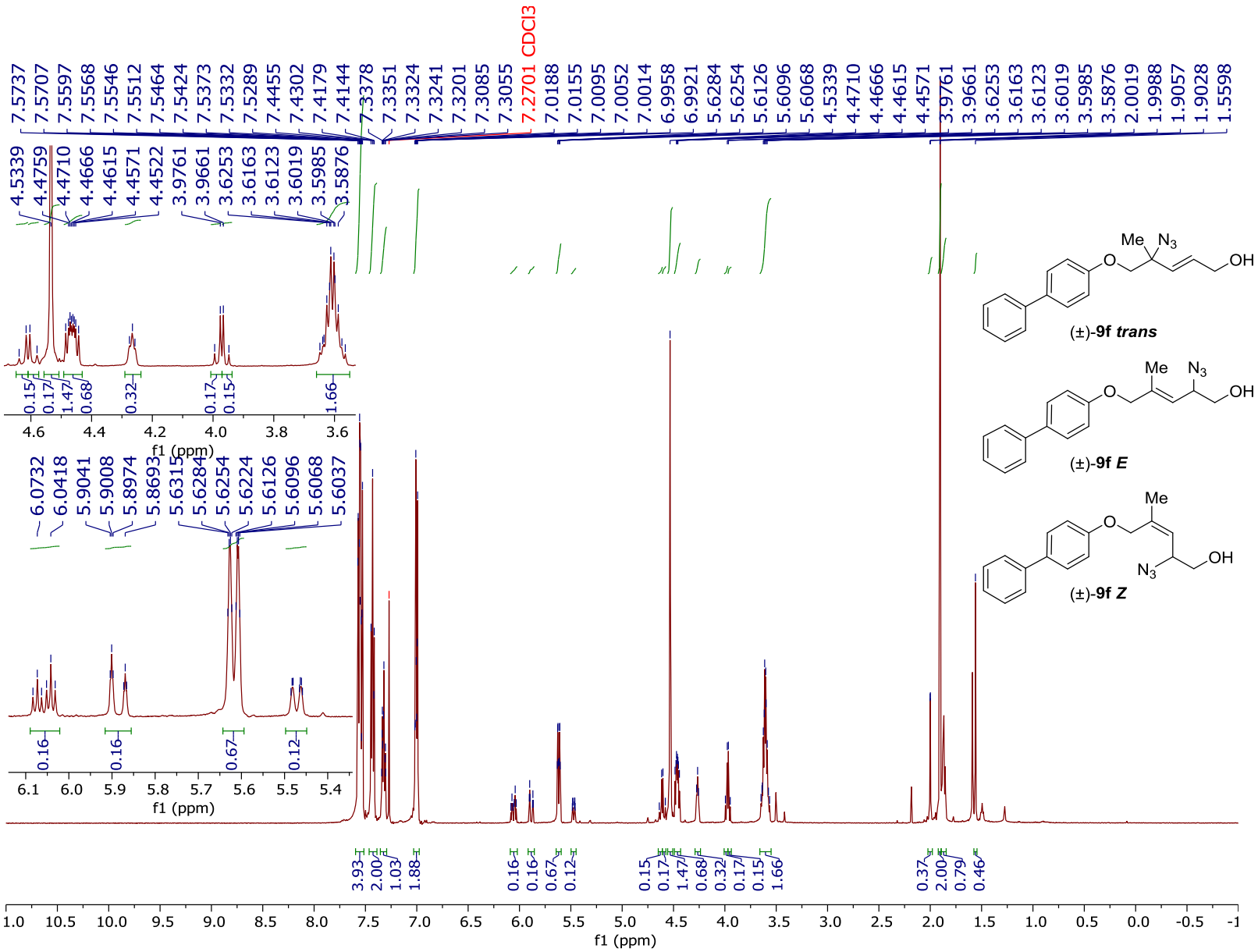
Compound 8m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



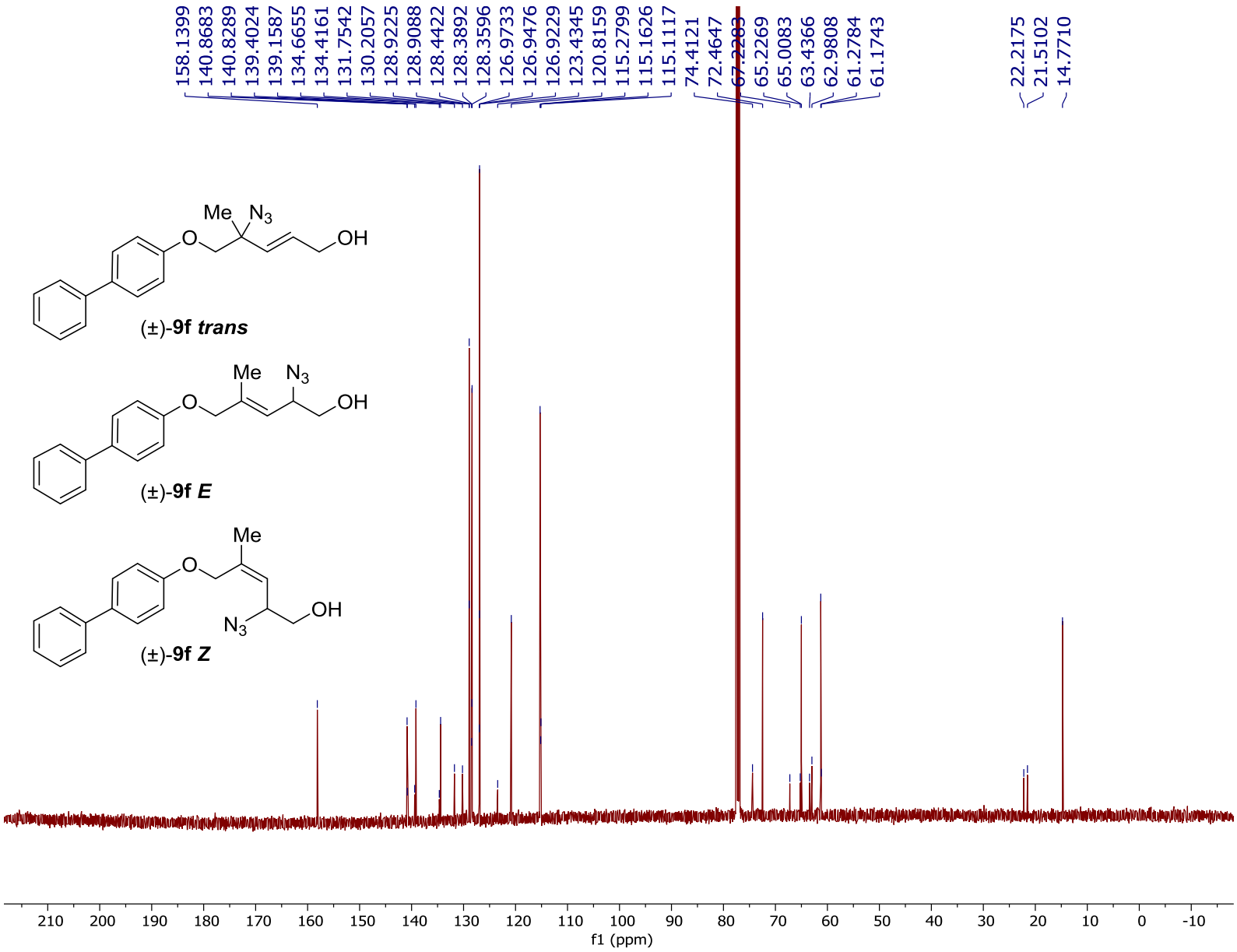
Compound 9d, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



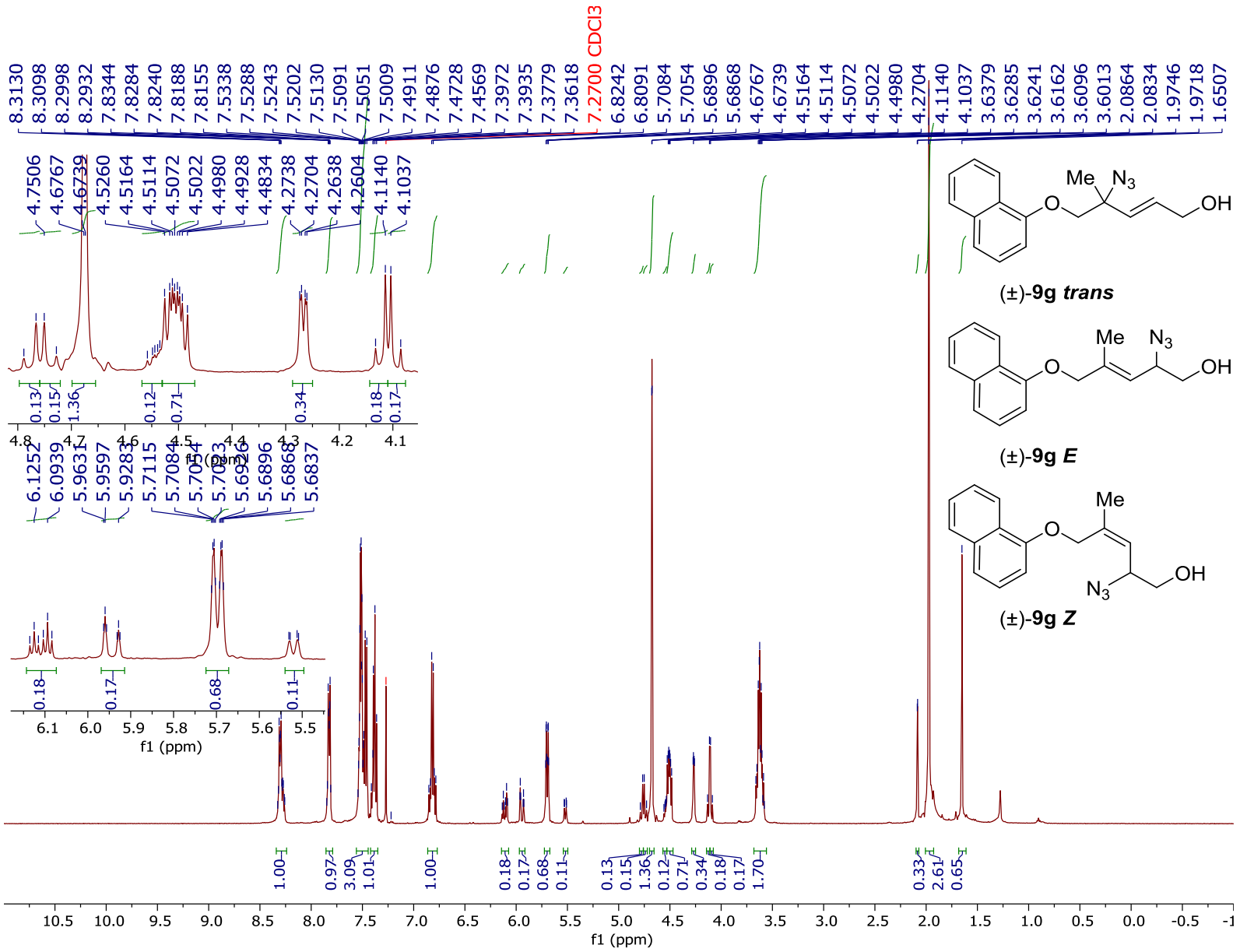
Compound 9d, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



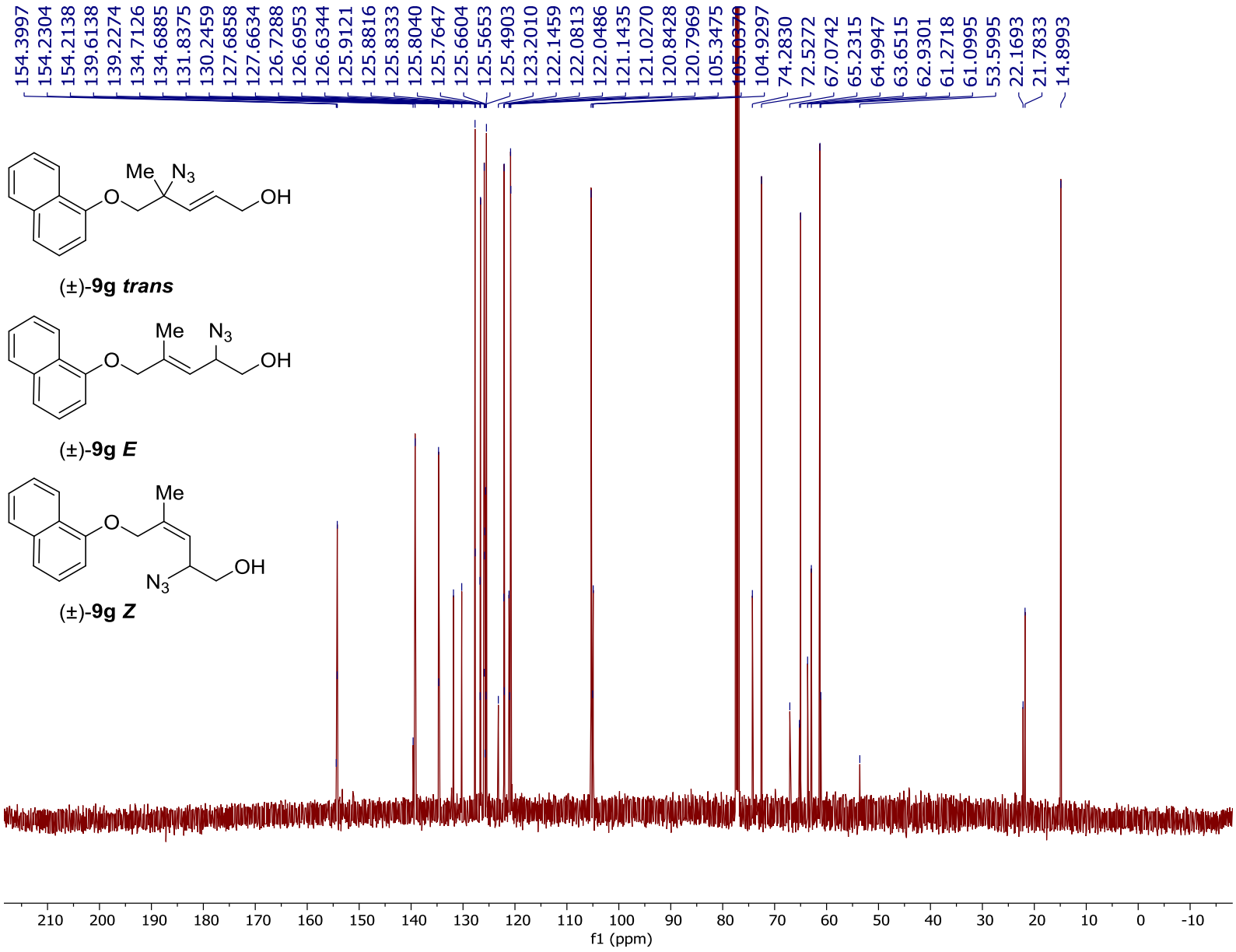
Compound 9f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



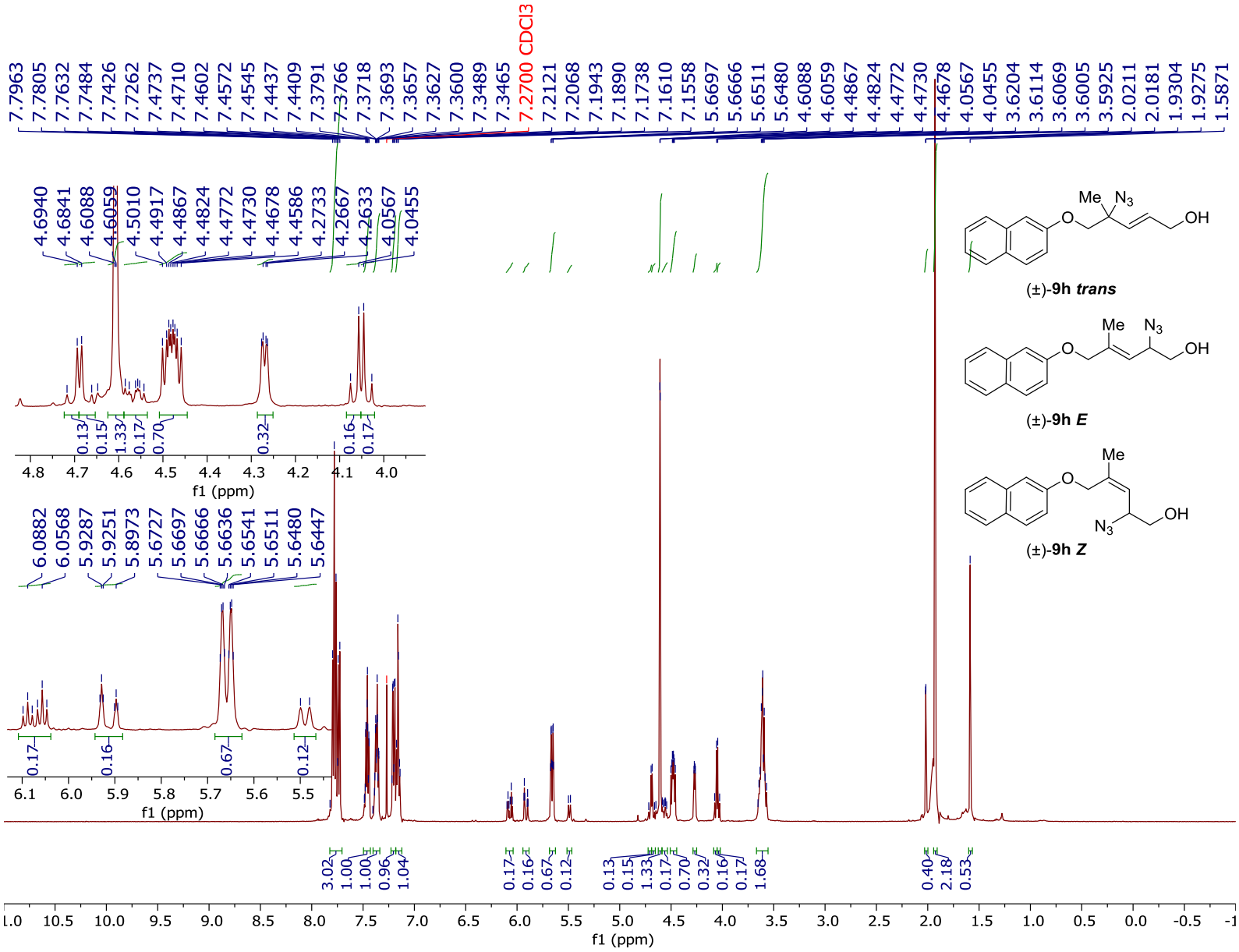
Compound 9f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



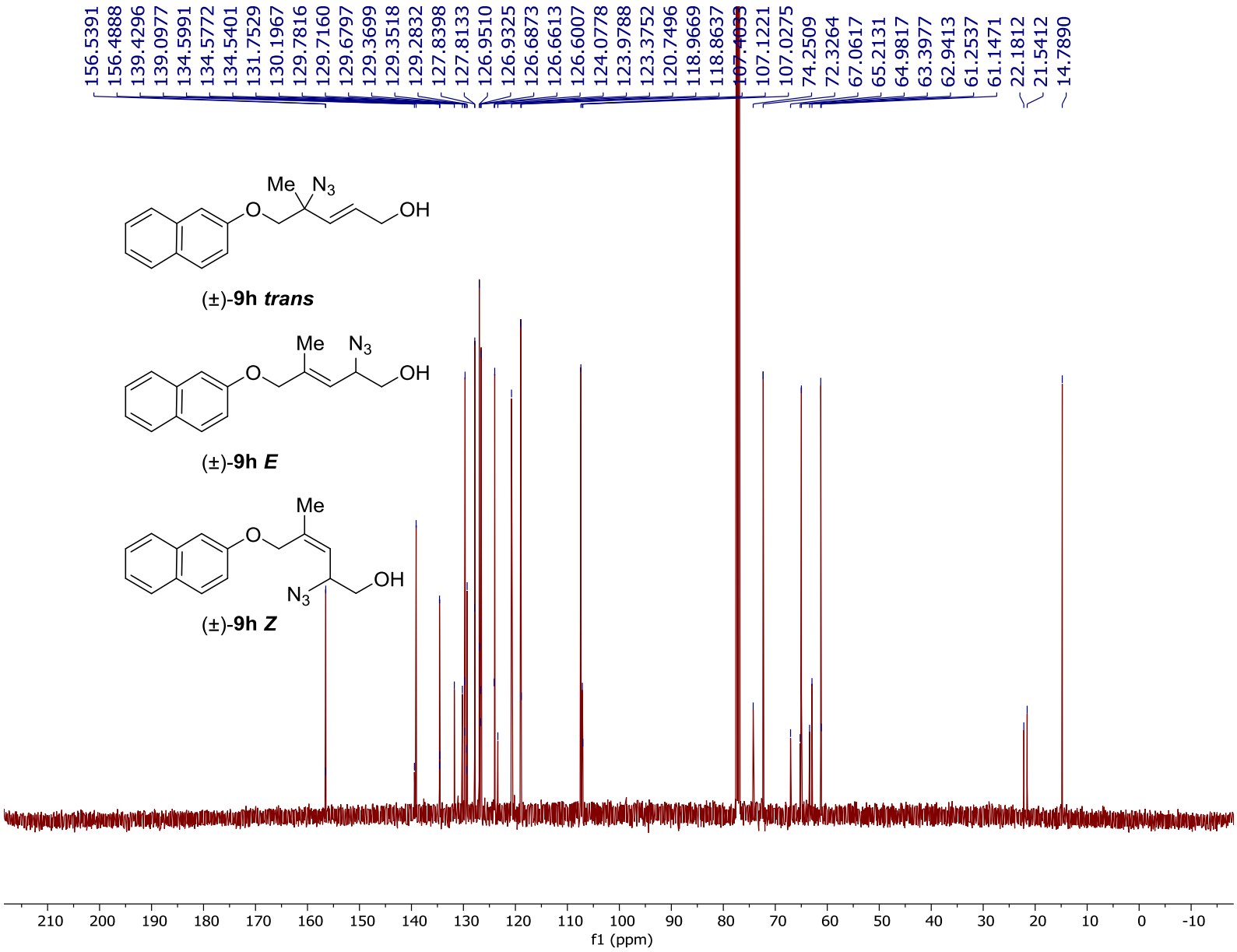
Compound 9g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



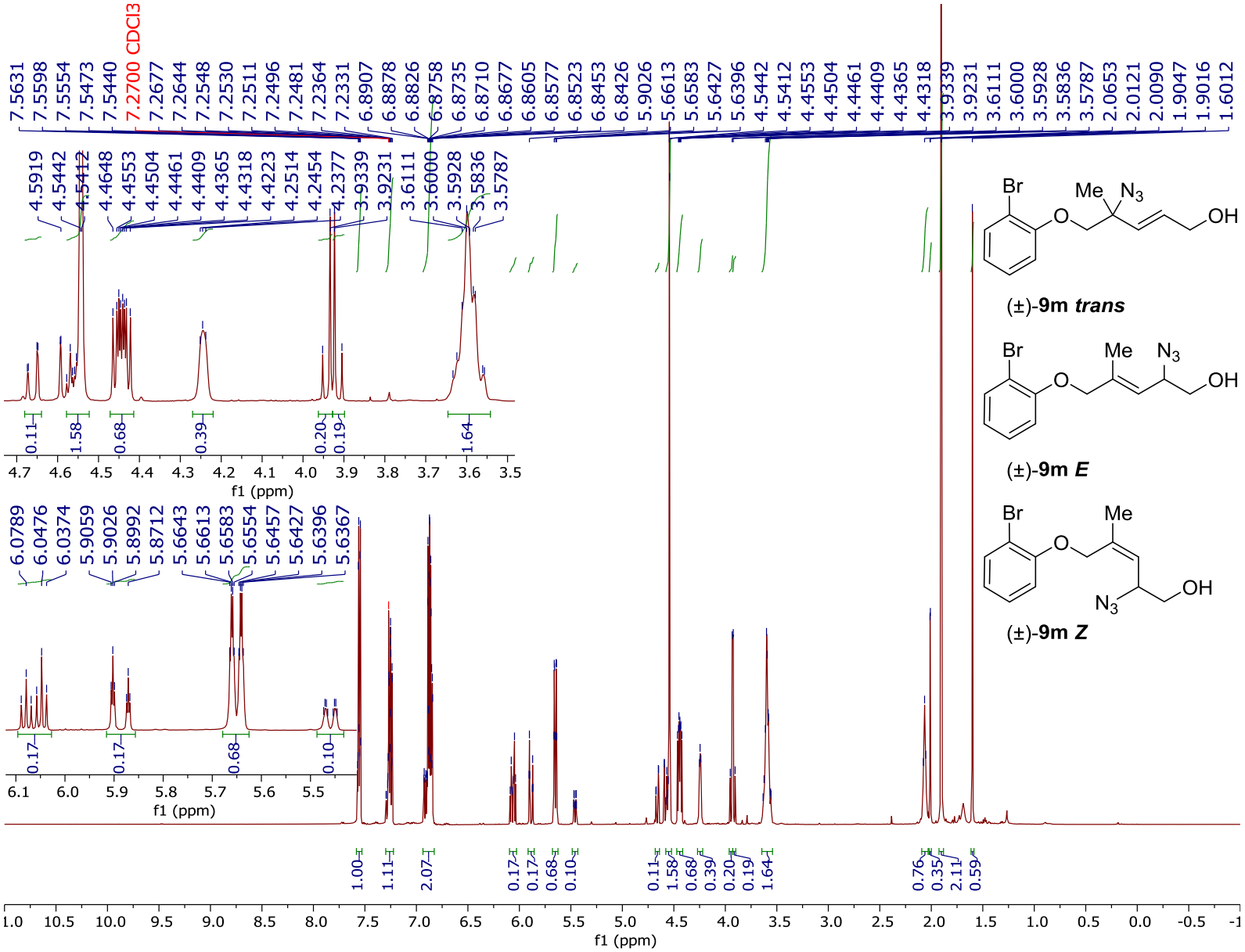
Compound 9g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



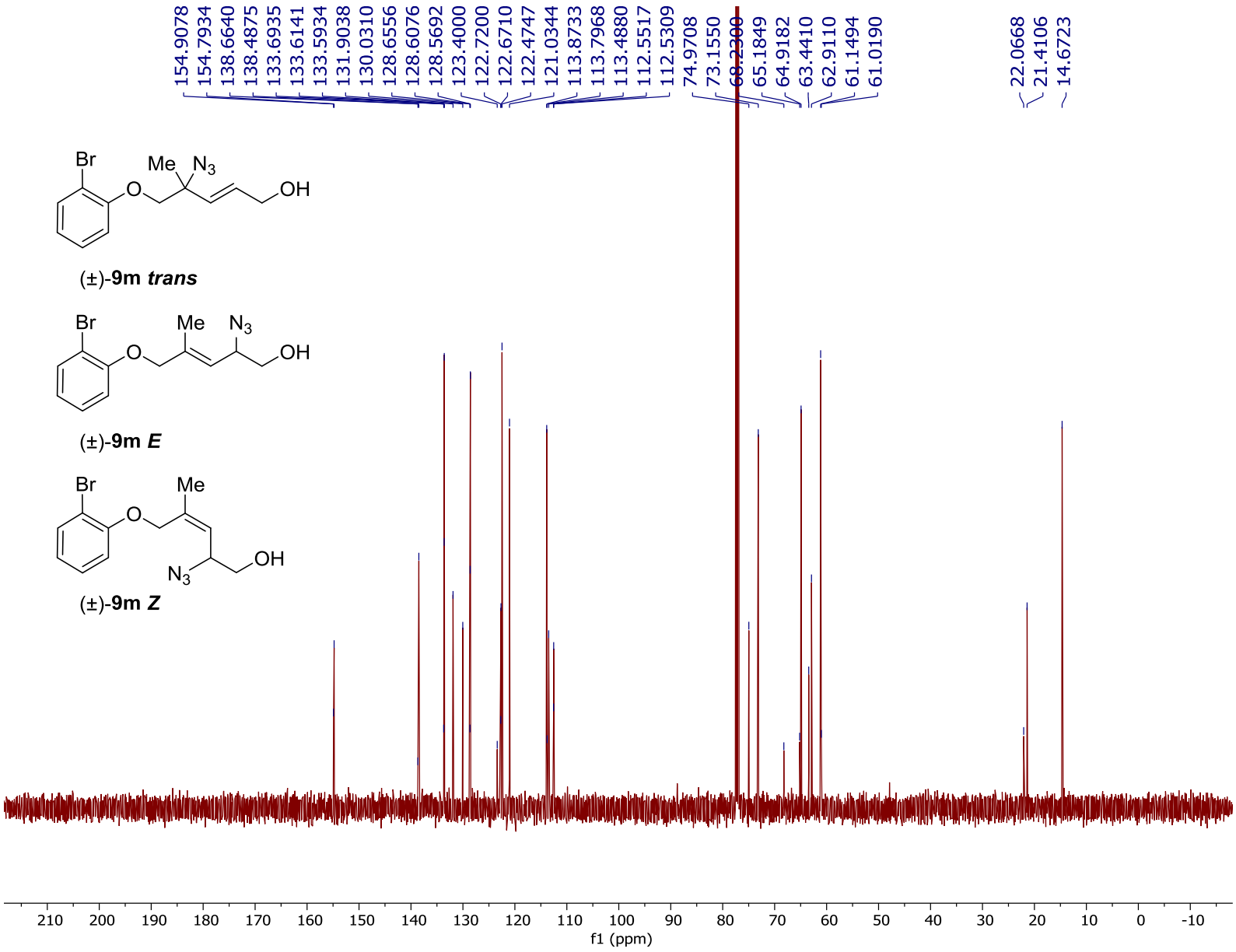
Compound 9h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



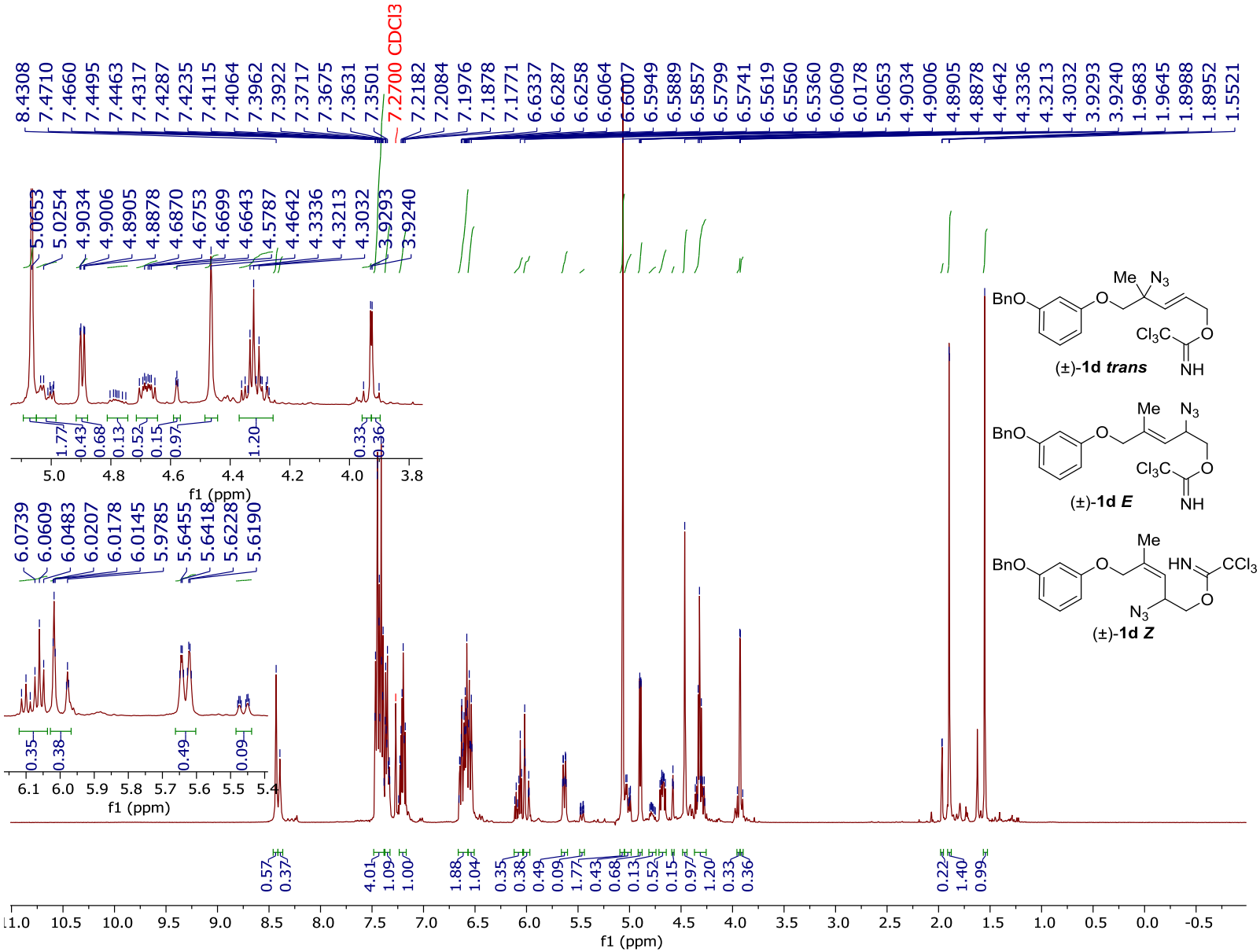
Compound 9h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



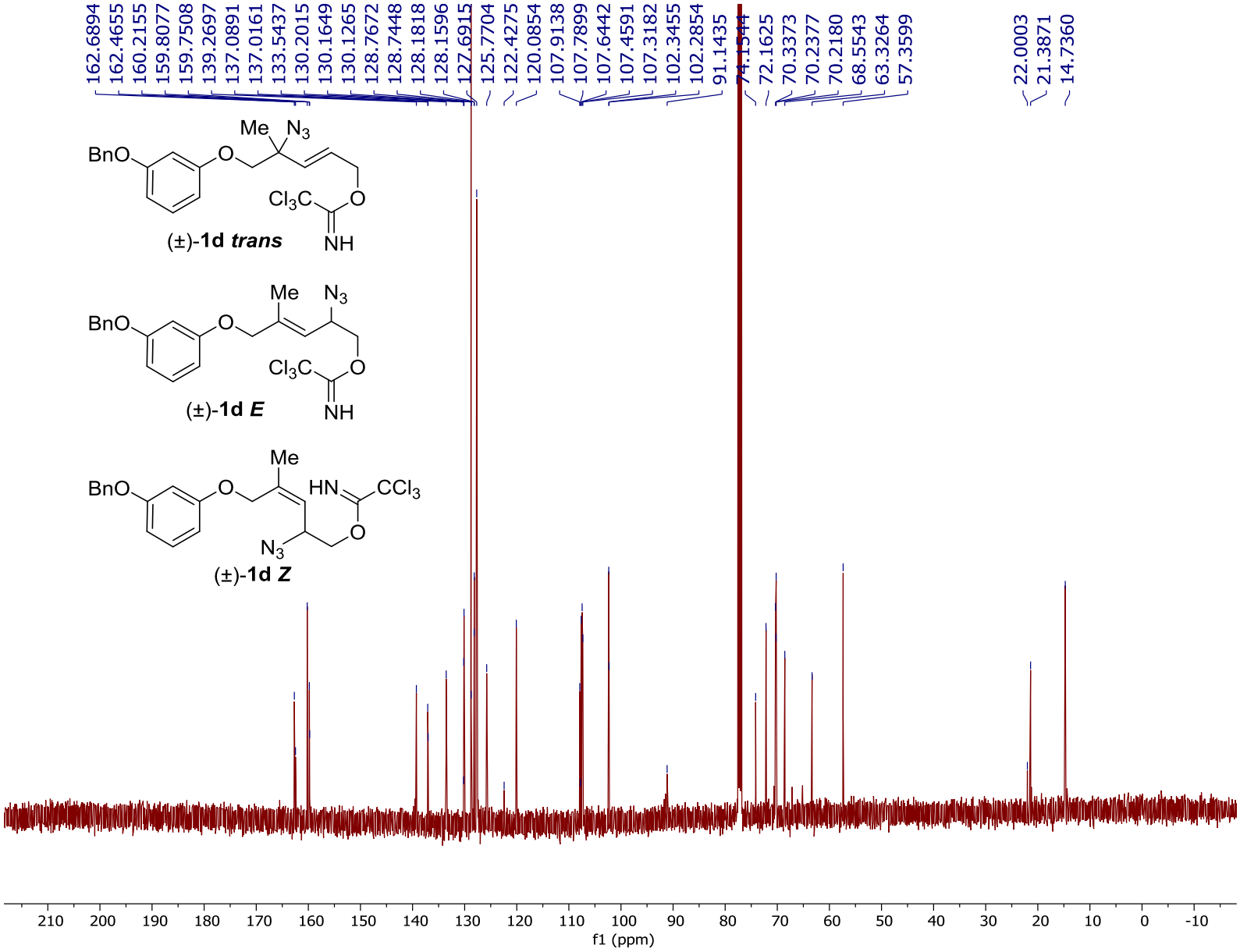
Compound 9m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



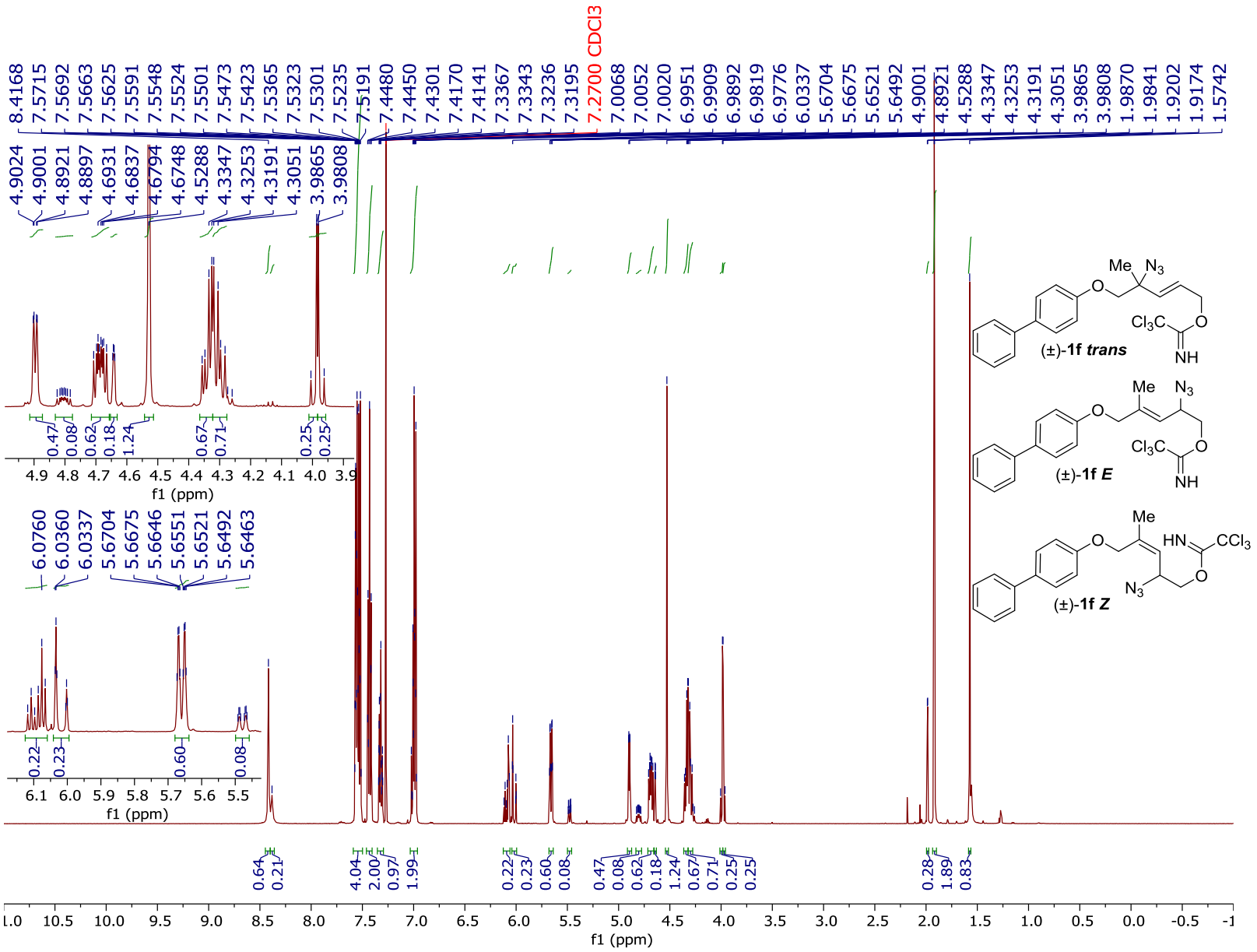
Compound 9m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



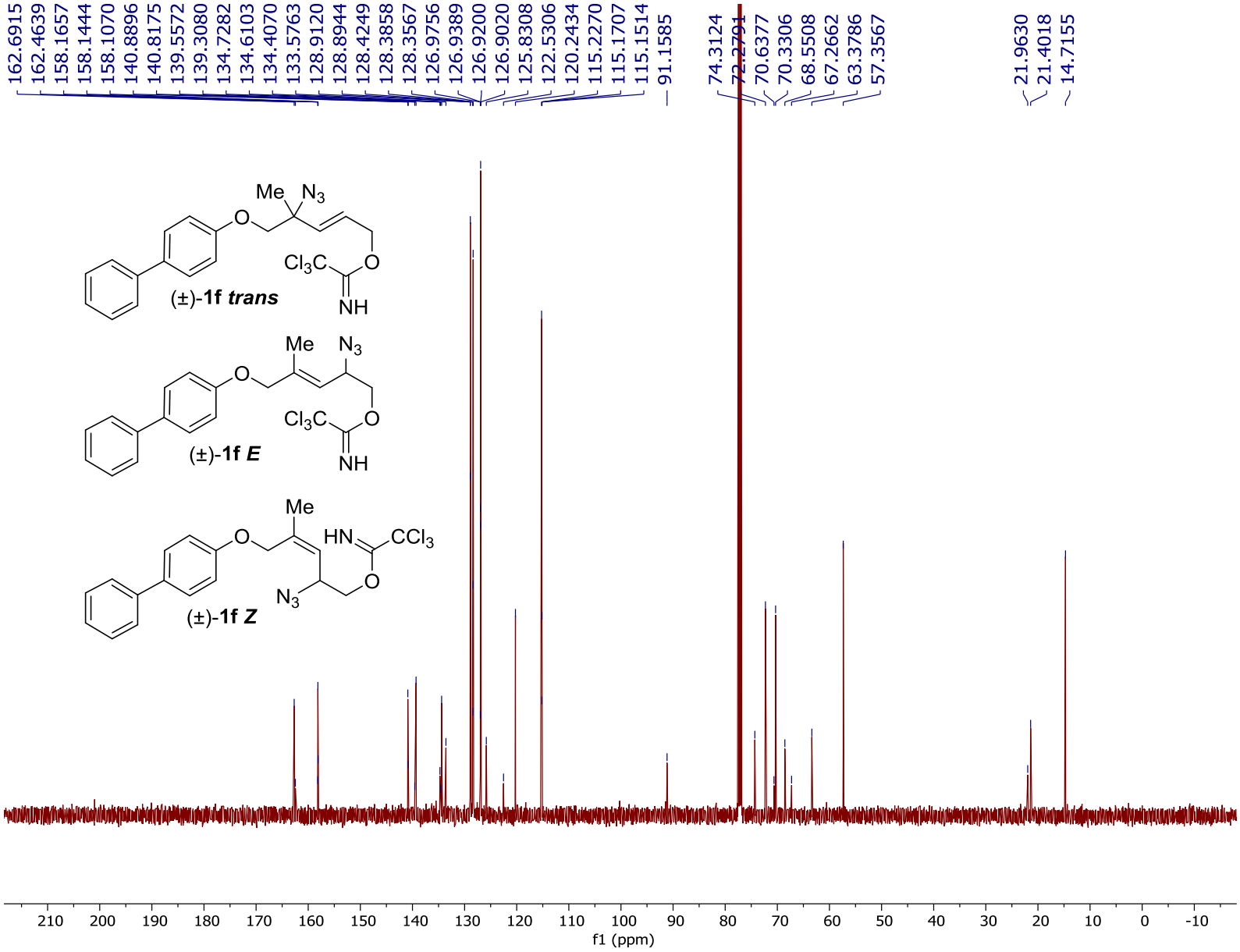
Compound 1d, 400 MHz ^{1}H NMR Spectrum in $CDCl_3$



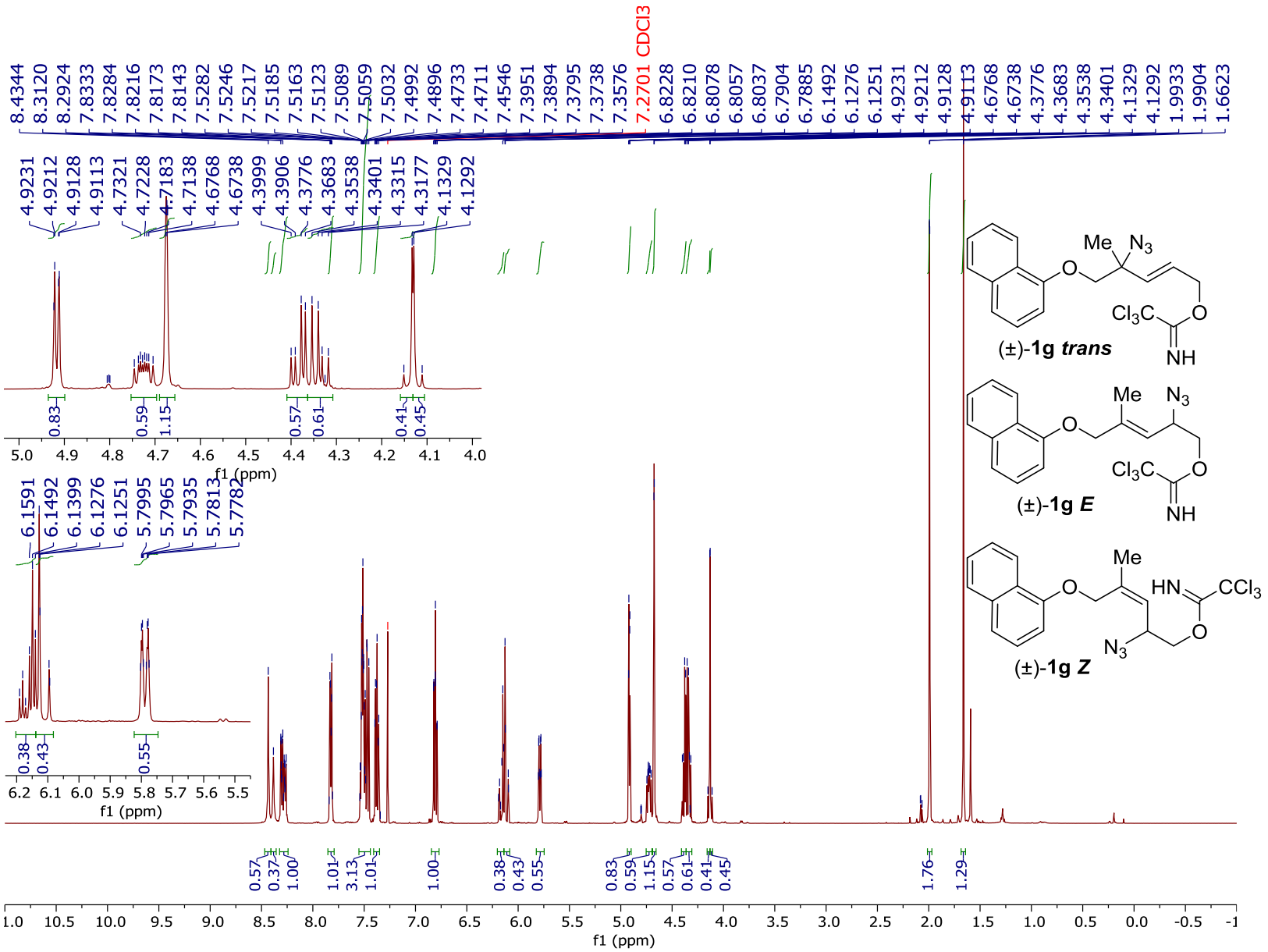
Compound 1d, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



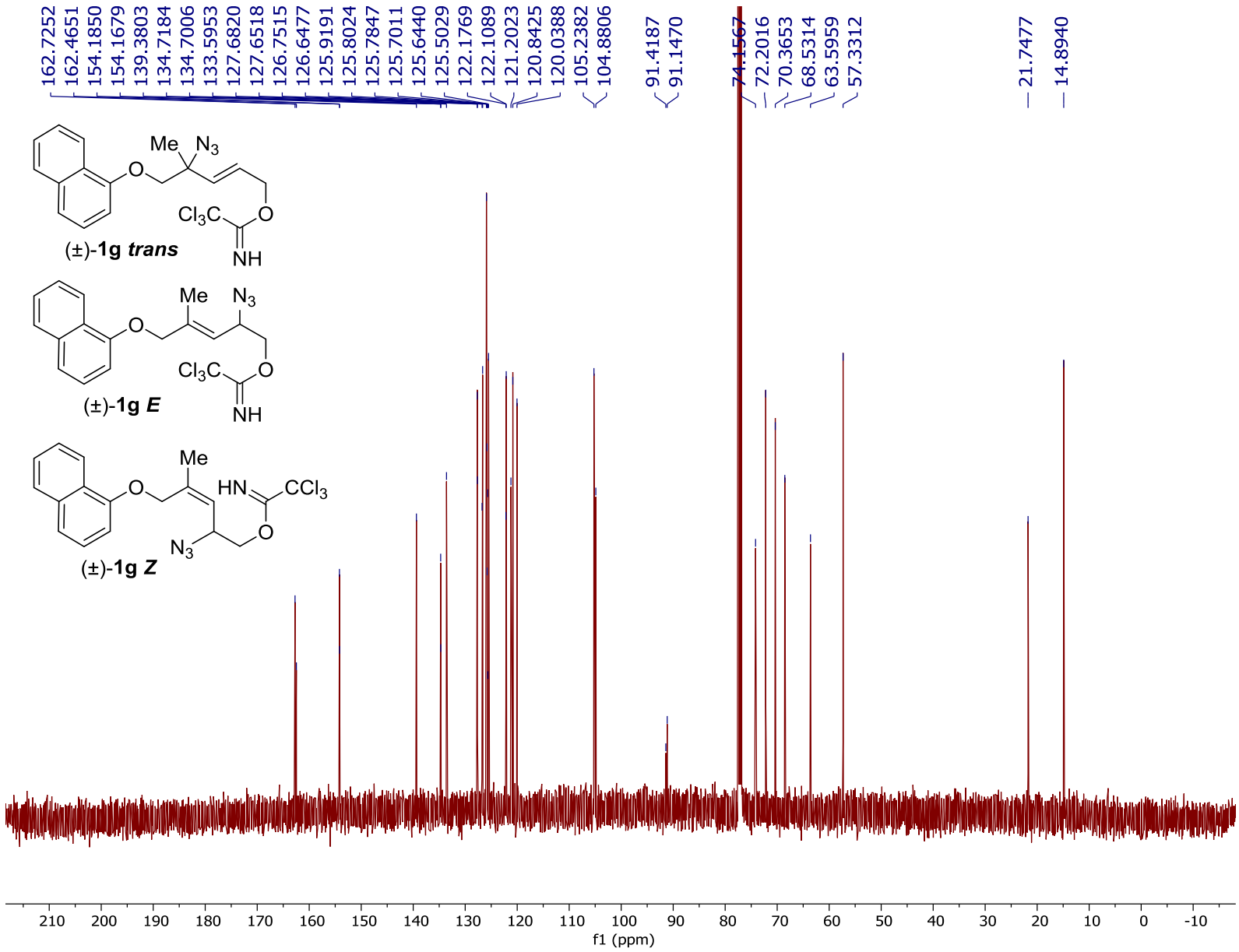
Compound 1f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



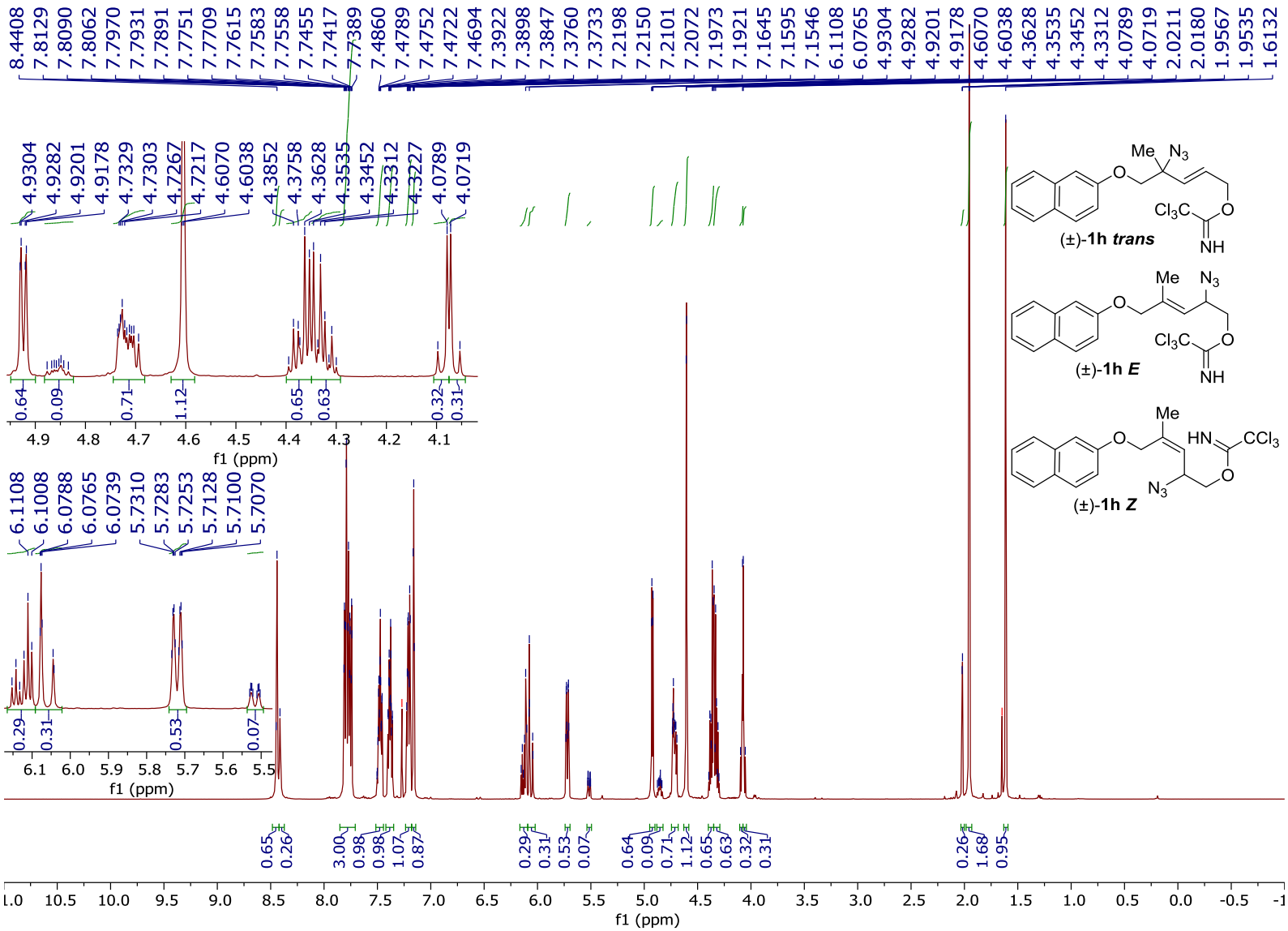
Compound 1f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



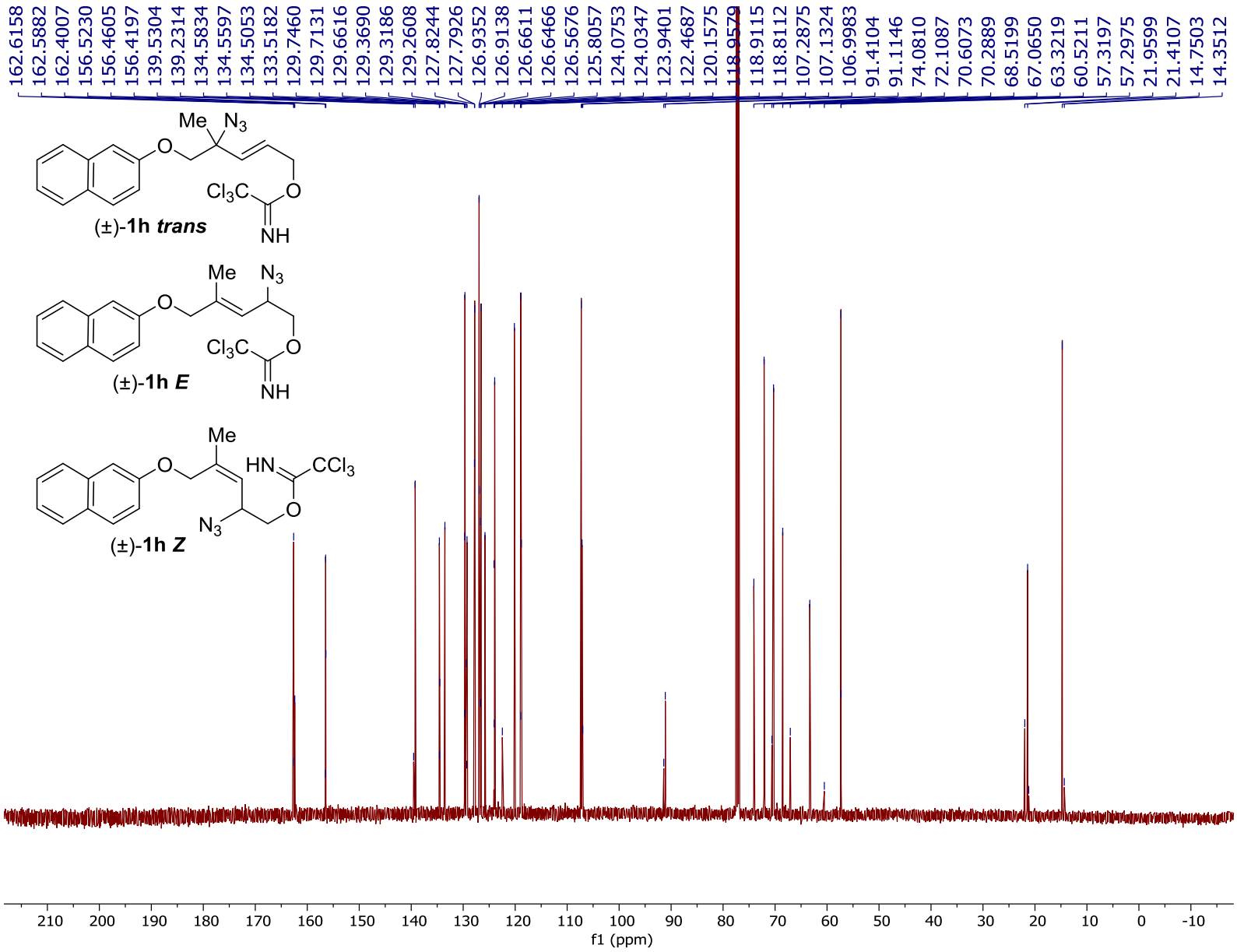
Compound 1g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



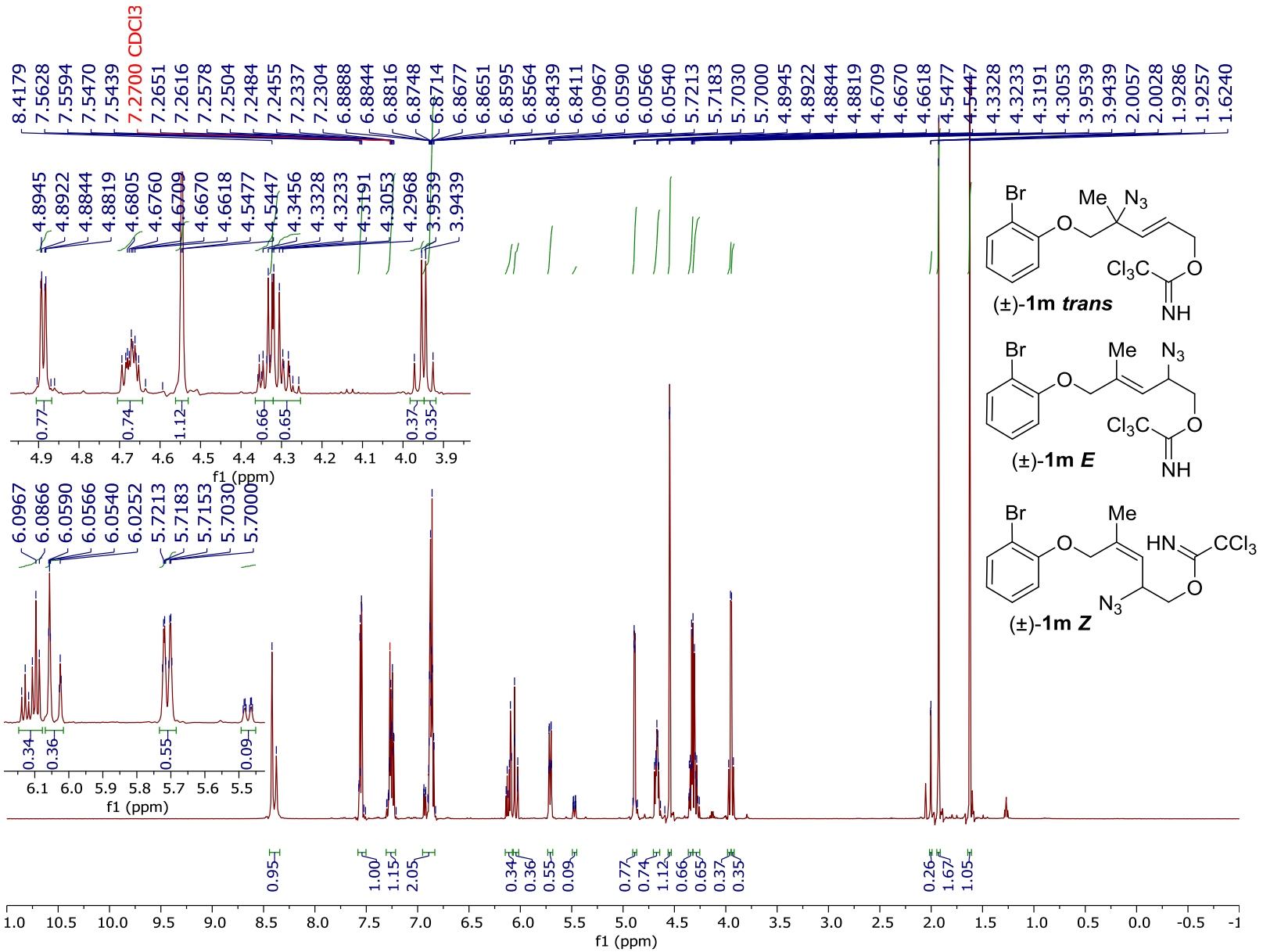
Compound 1g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



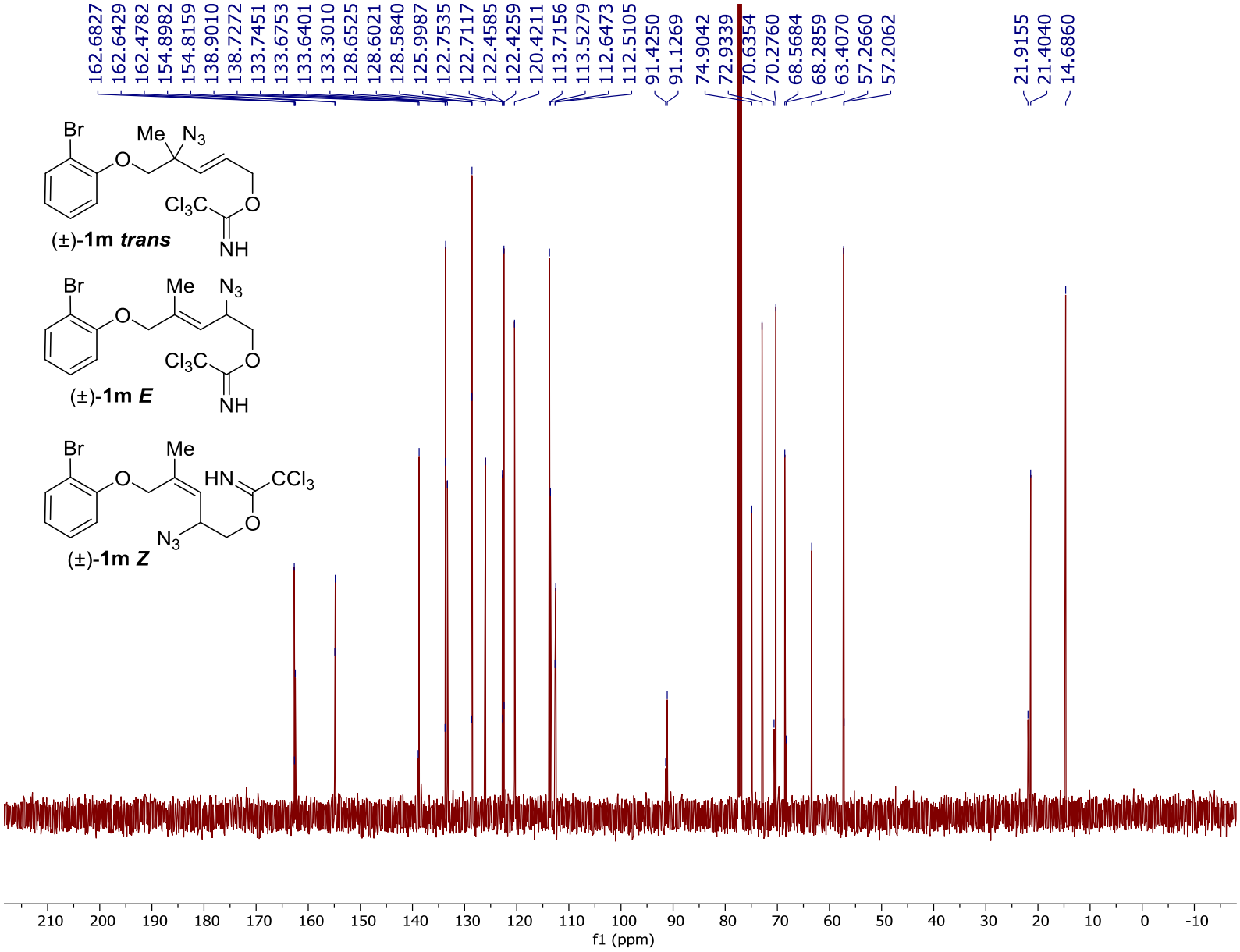
Compound 1h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



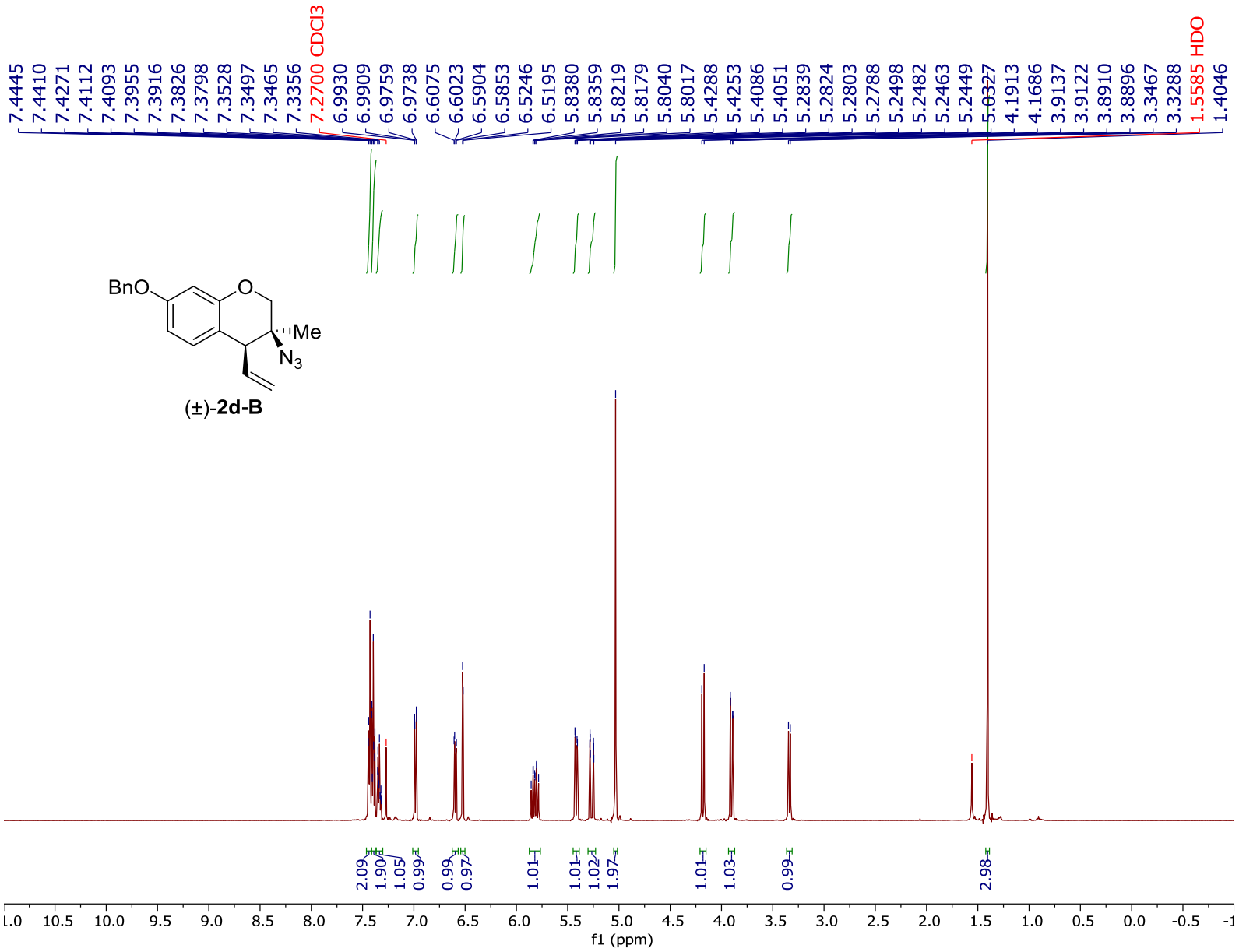
Compound 1h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



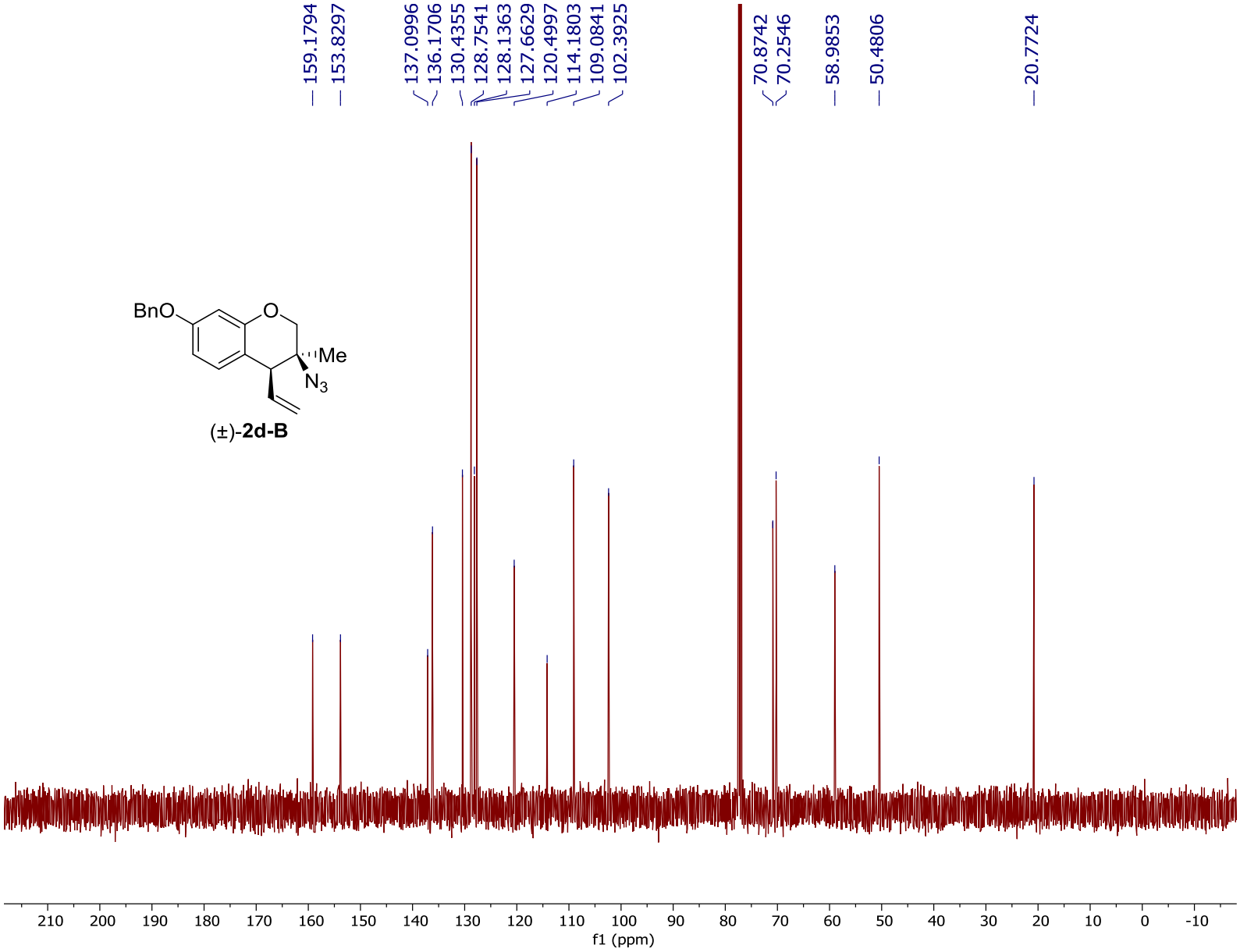
Compound 1m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



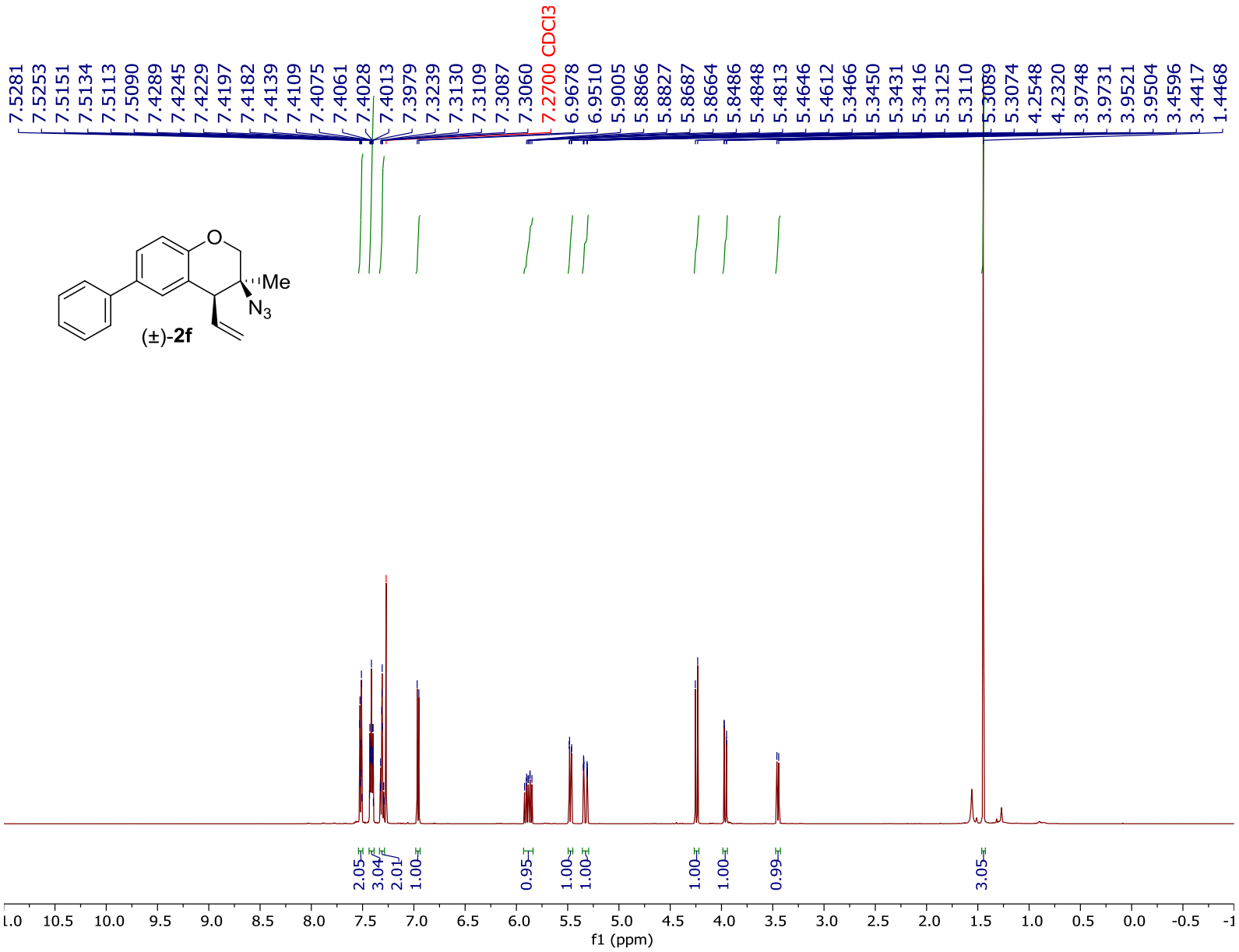
Compound 1m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



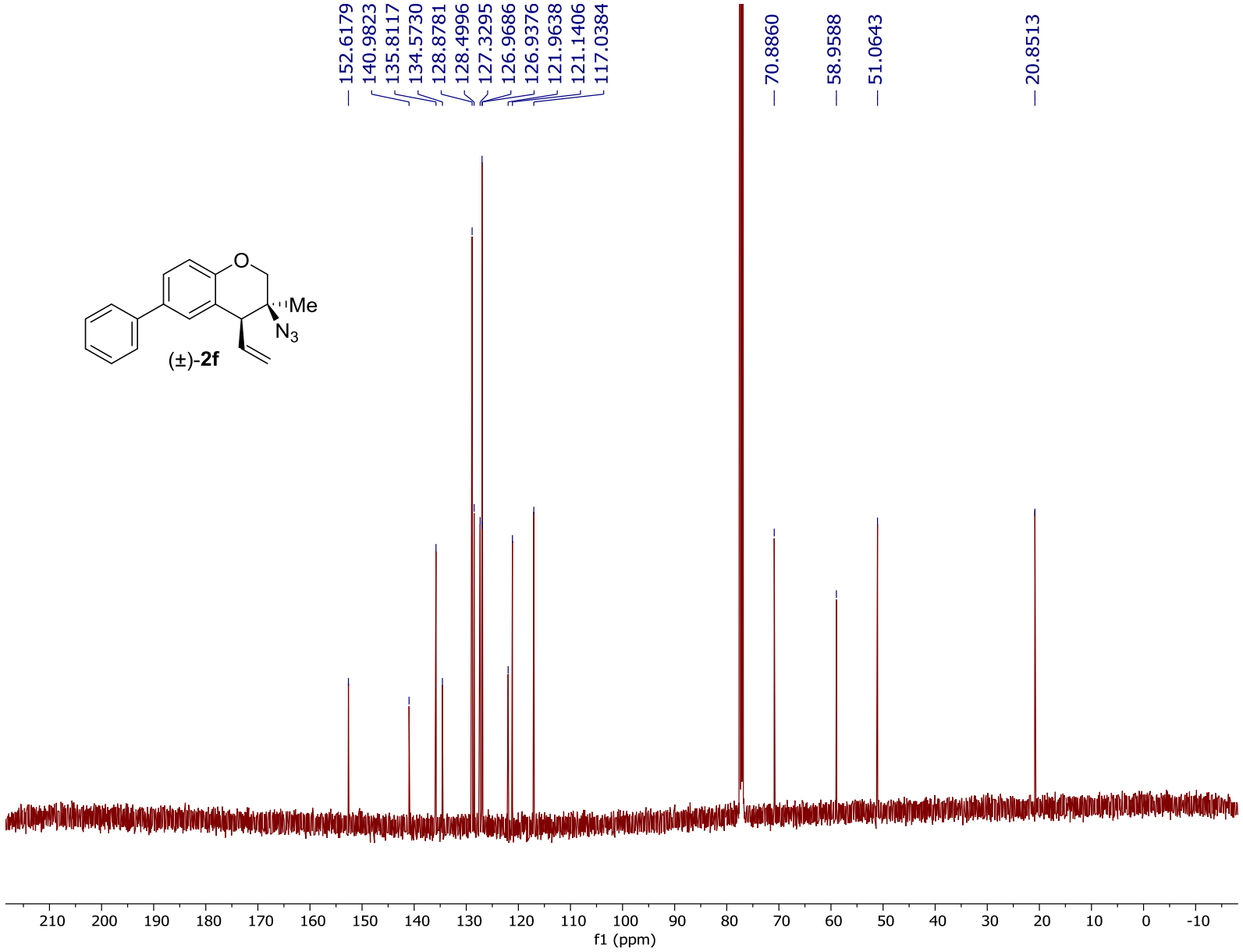
Compound 2d-B, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



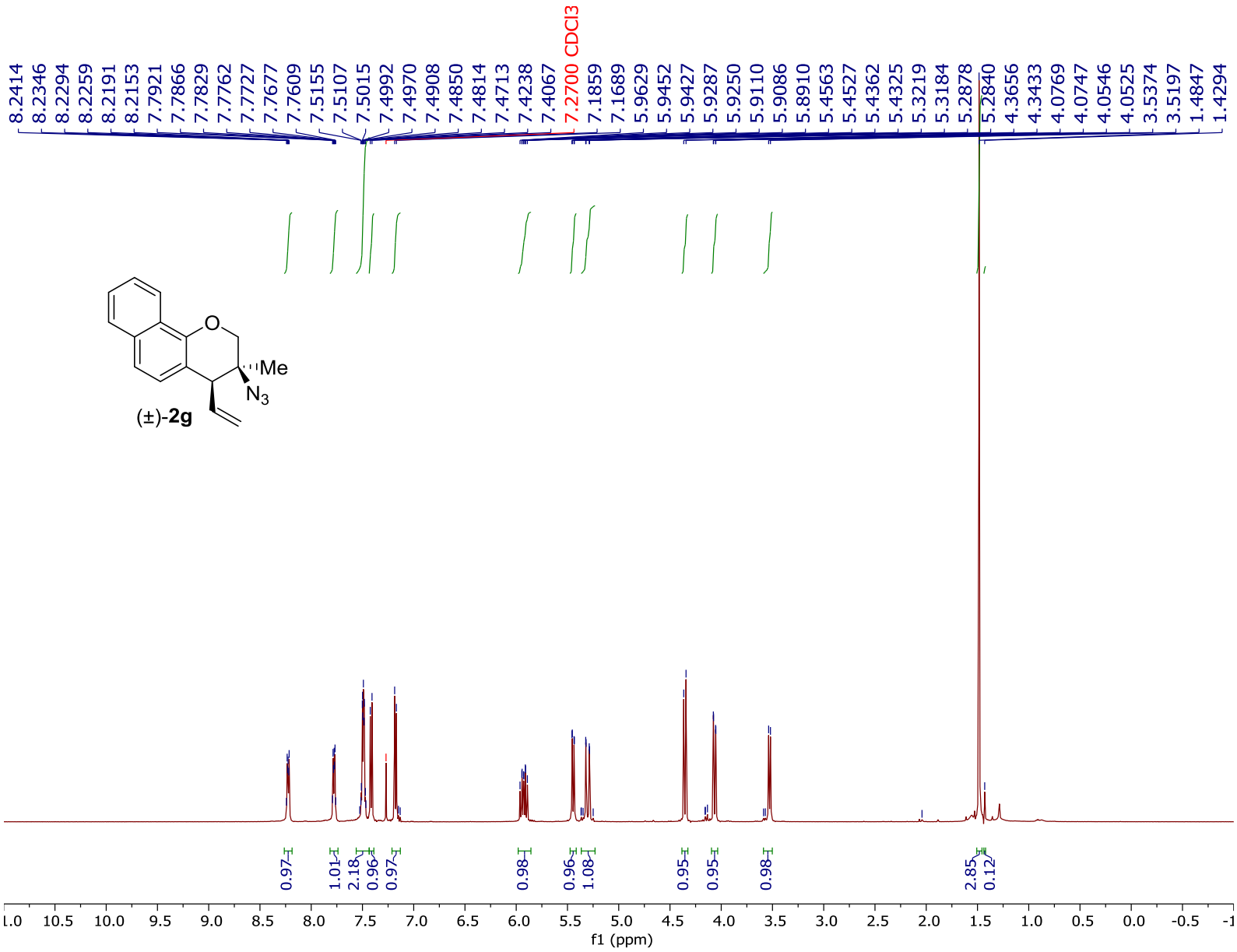
Compound 2d-B, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



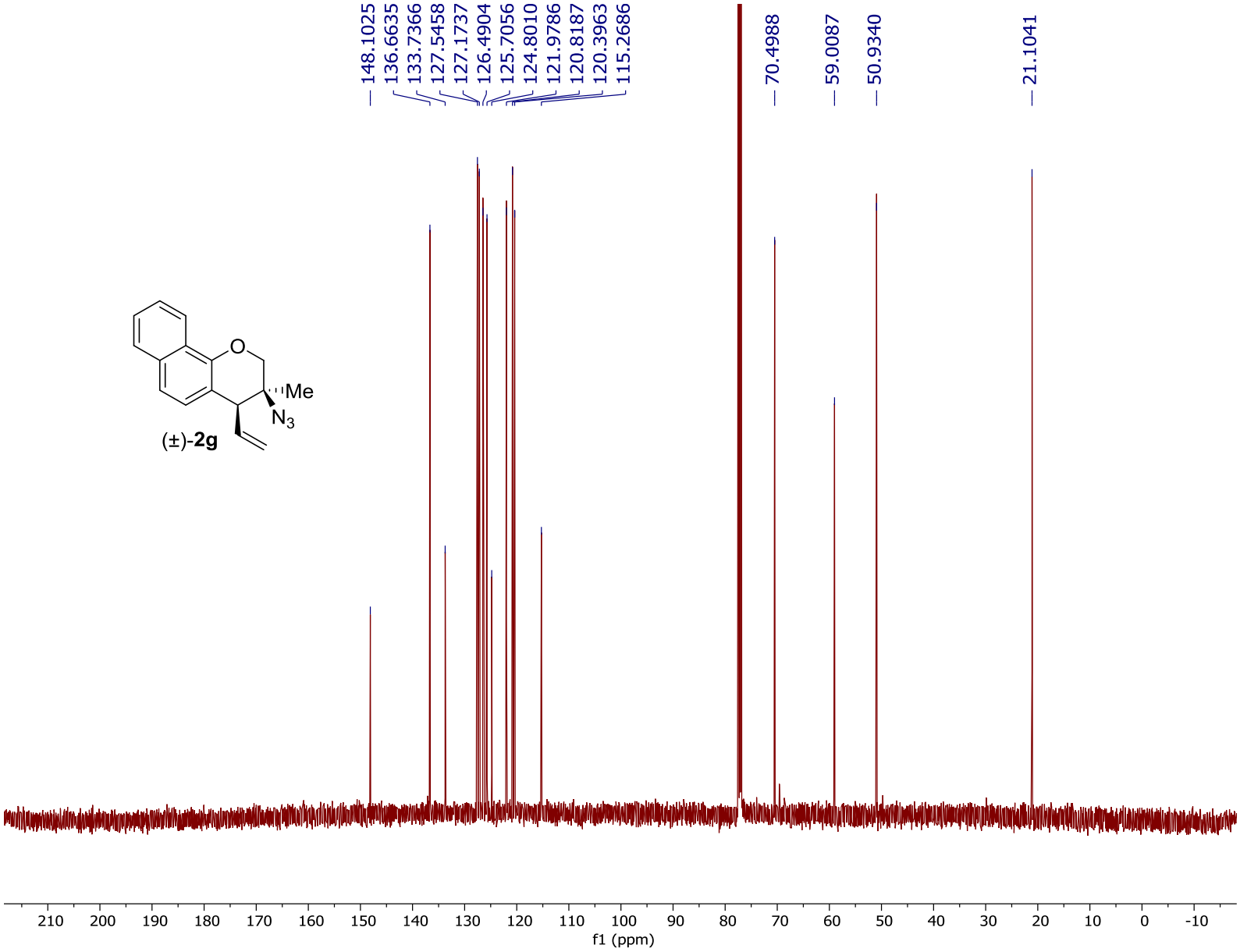
Compound 2f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



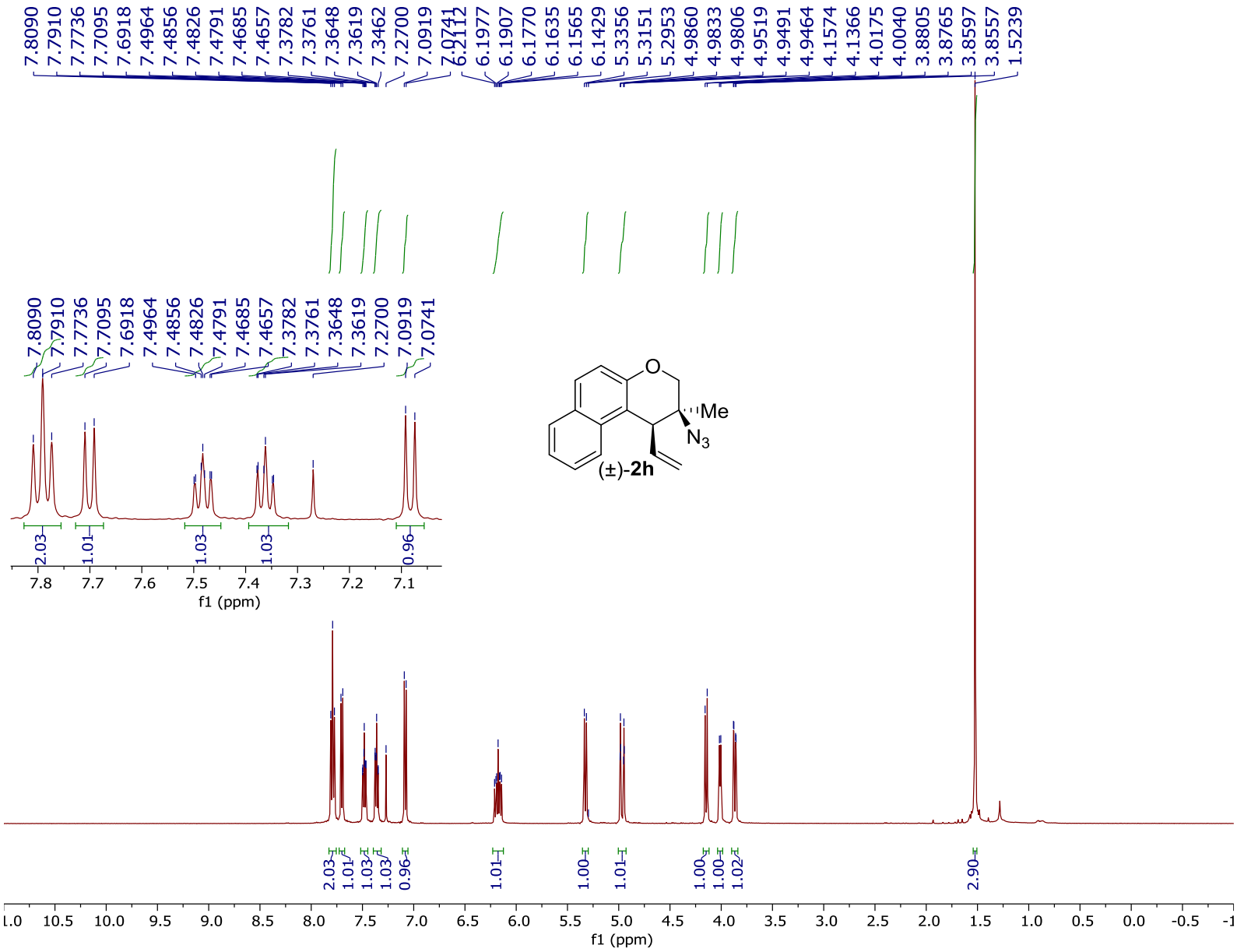
Compound 2f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



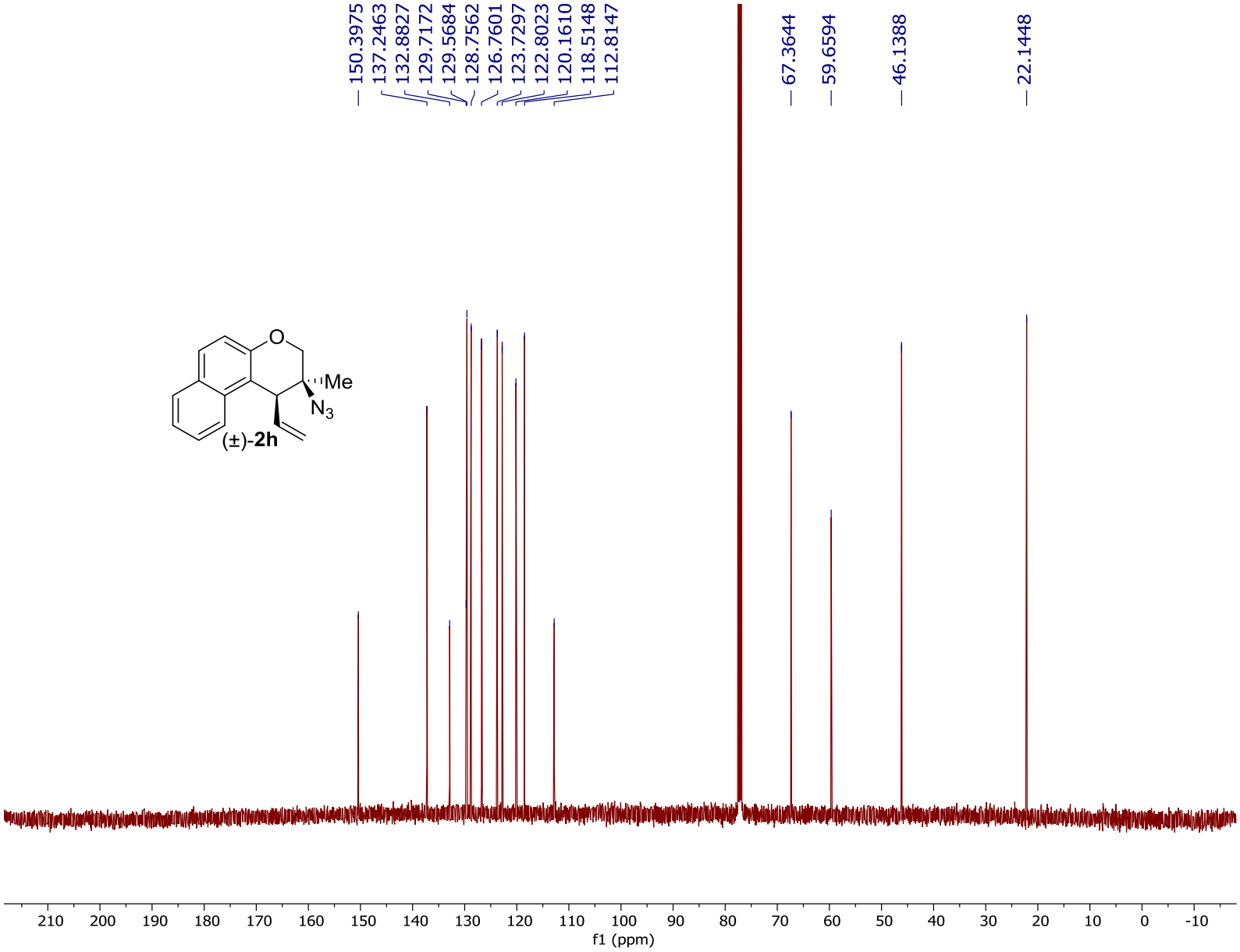
Compound 2g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



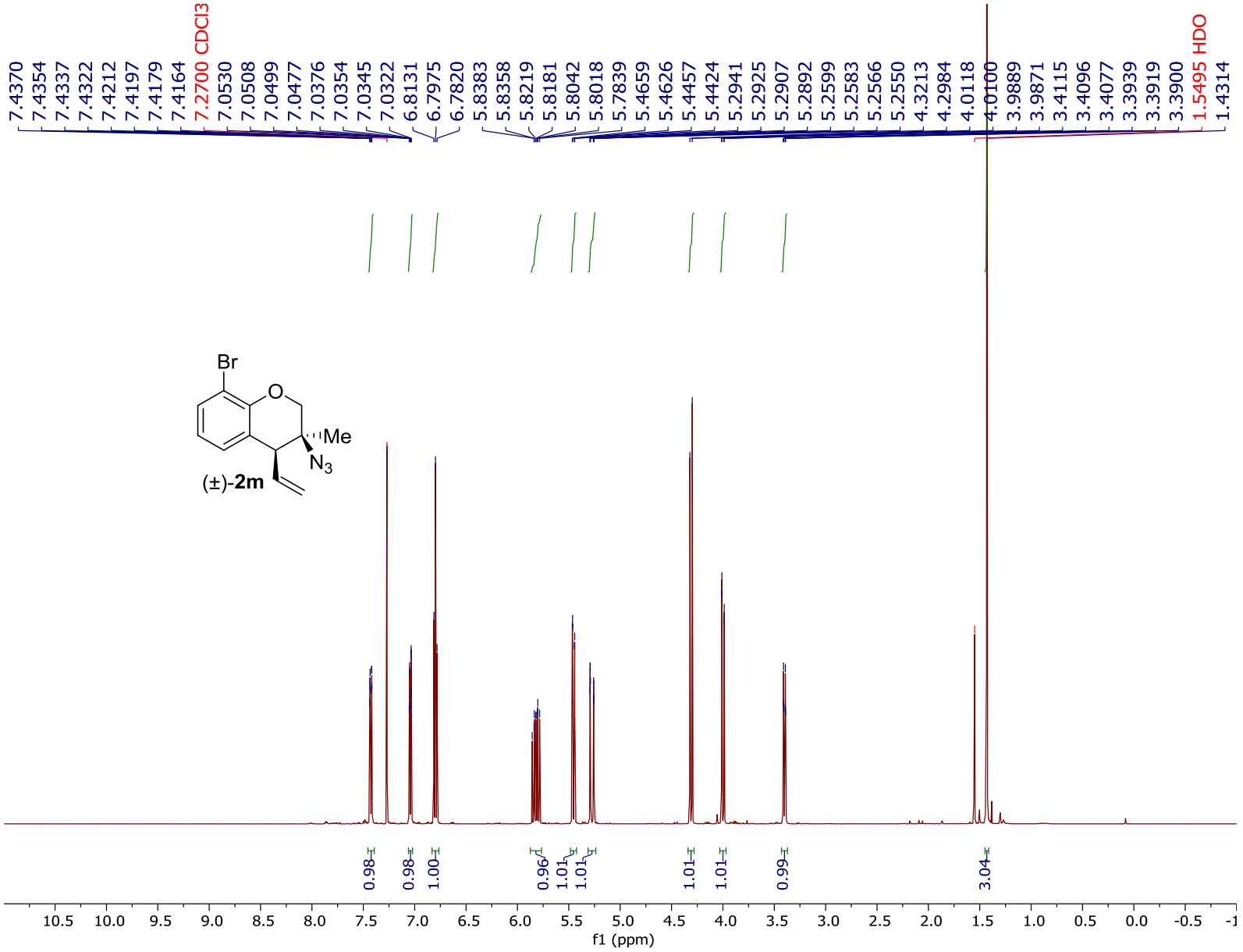
Compound 2g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



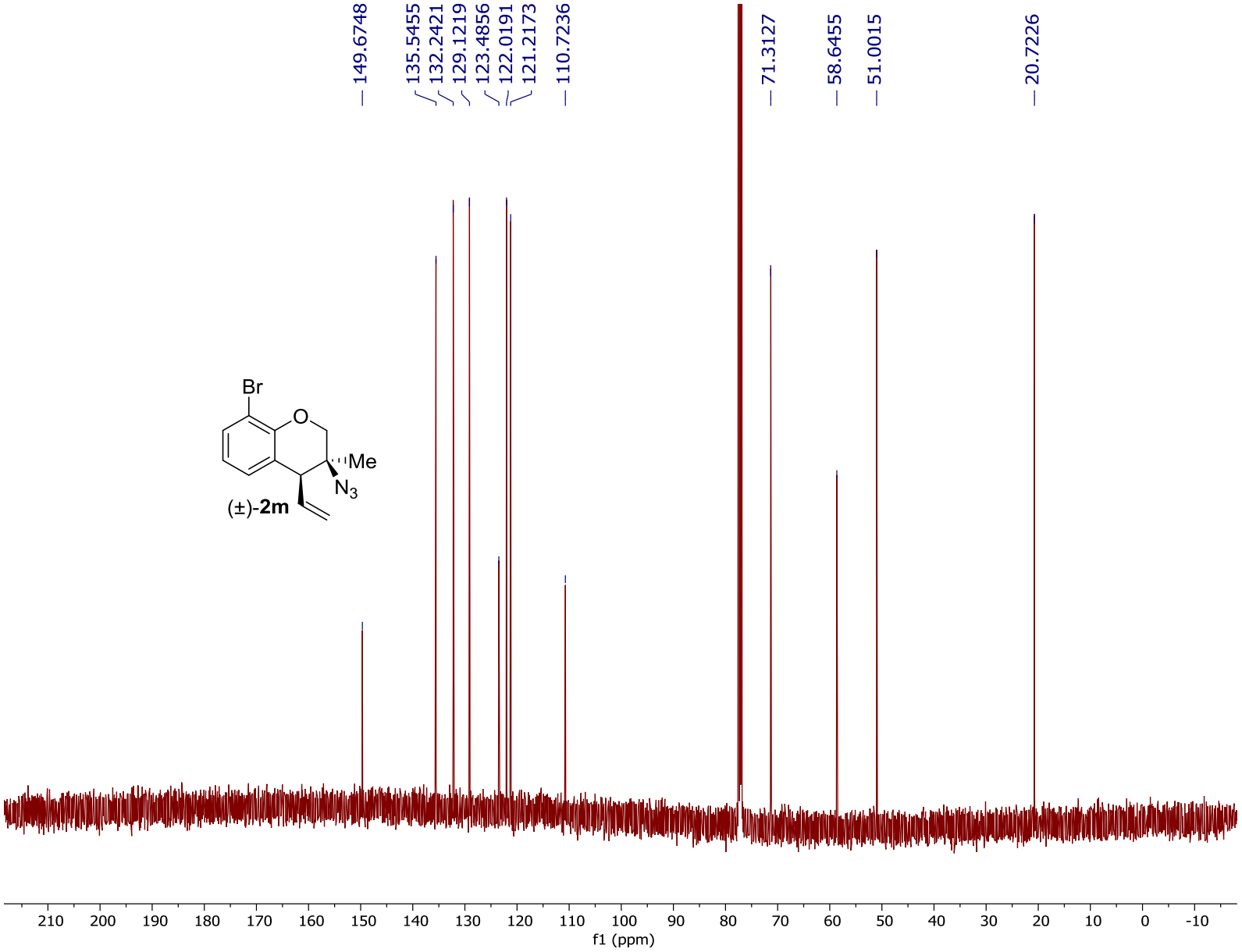
Compound 2h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



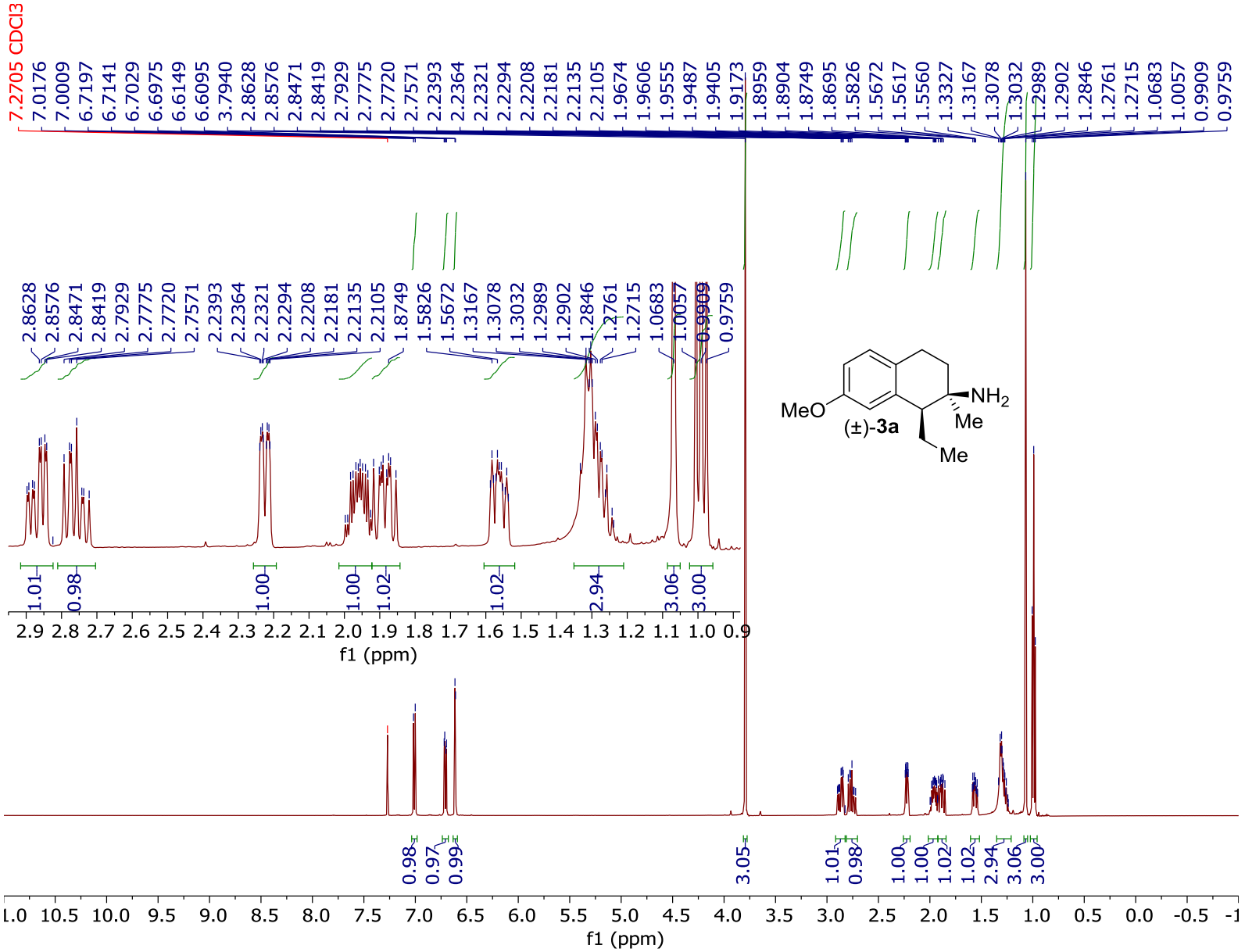
Compound 2h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



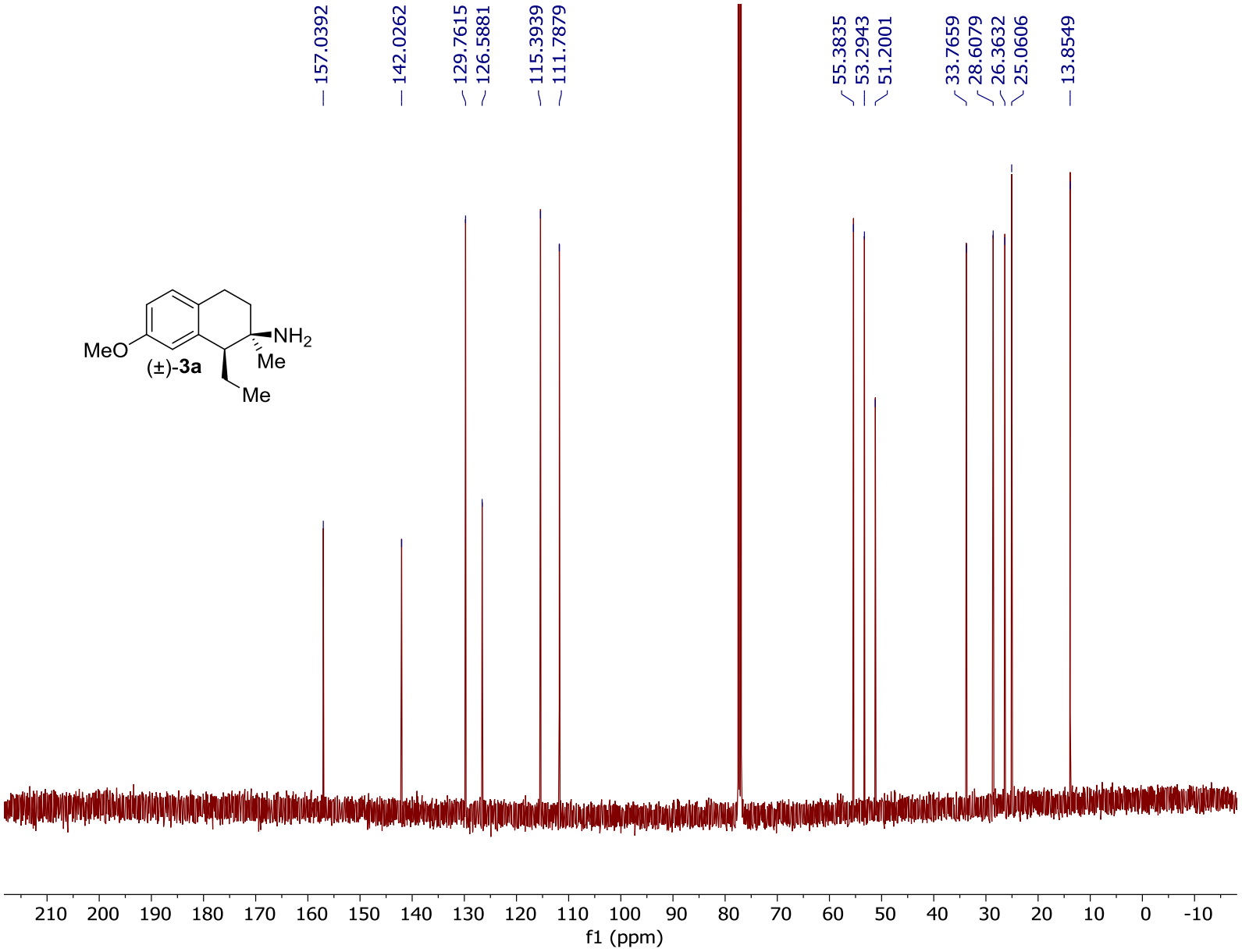
Compound 2m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



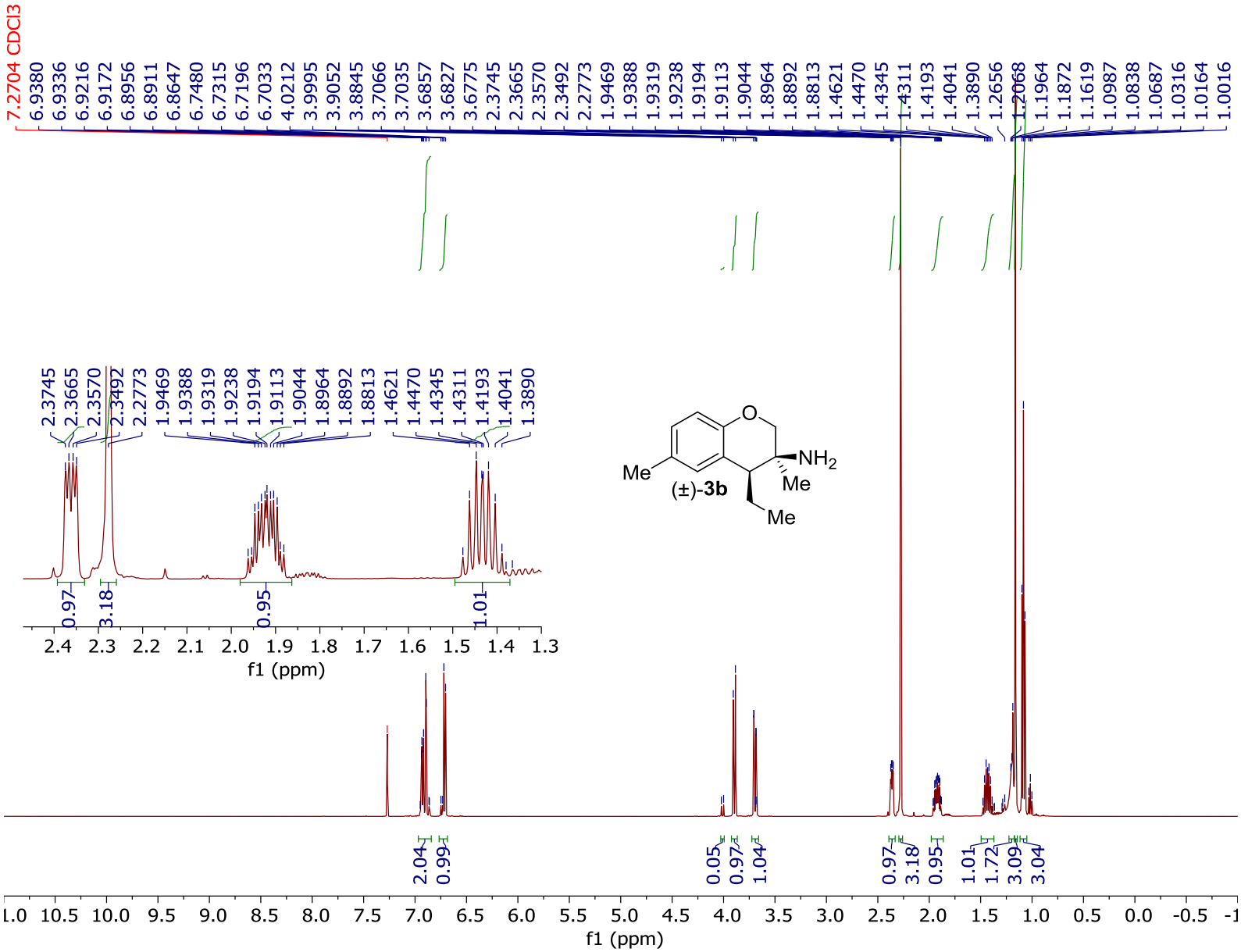
Compound 2m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



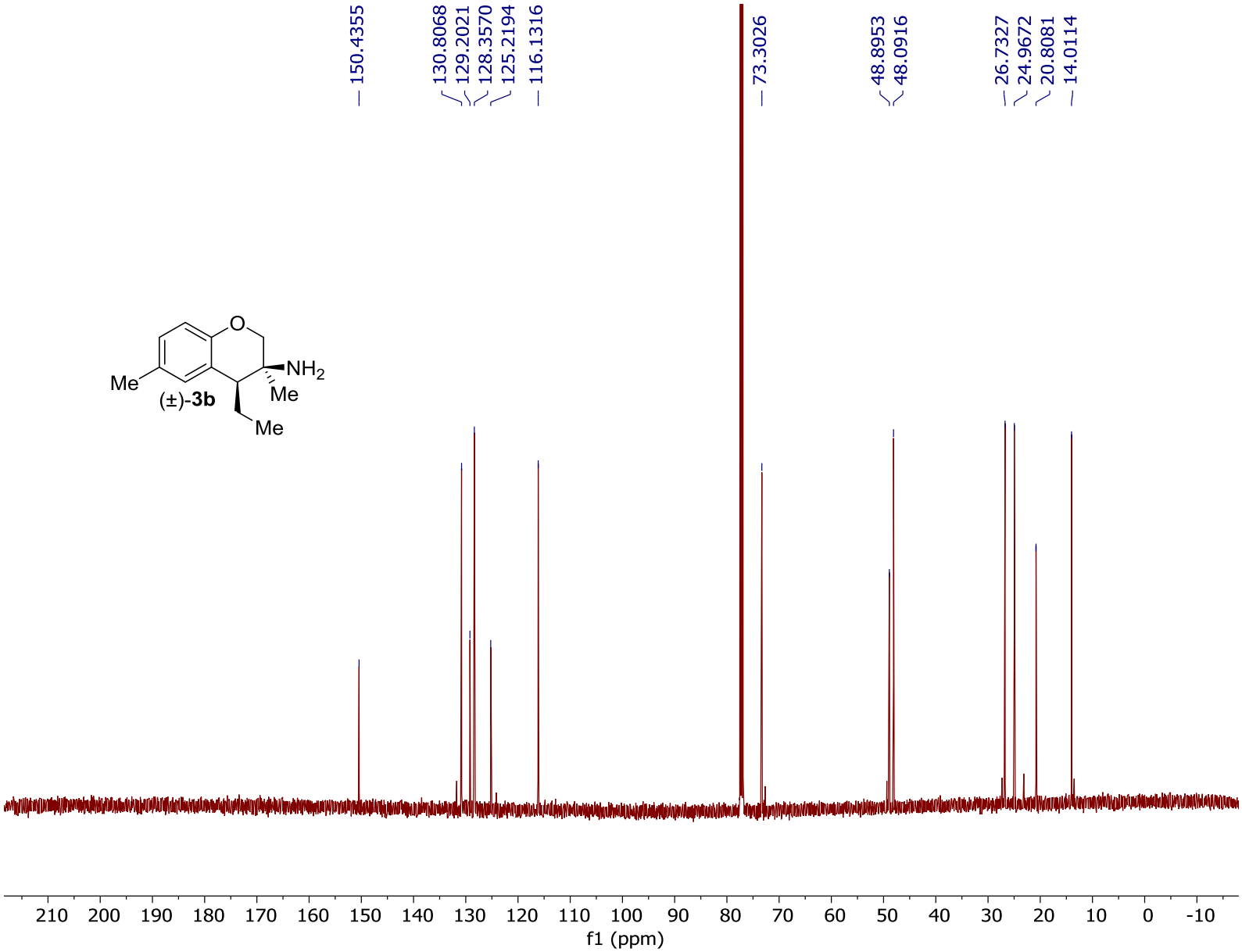
Compound 3a, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



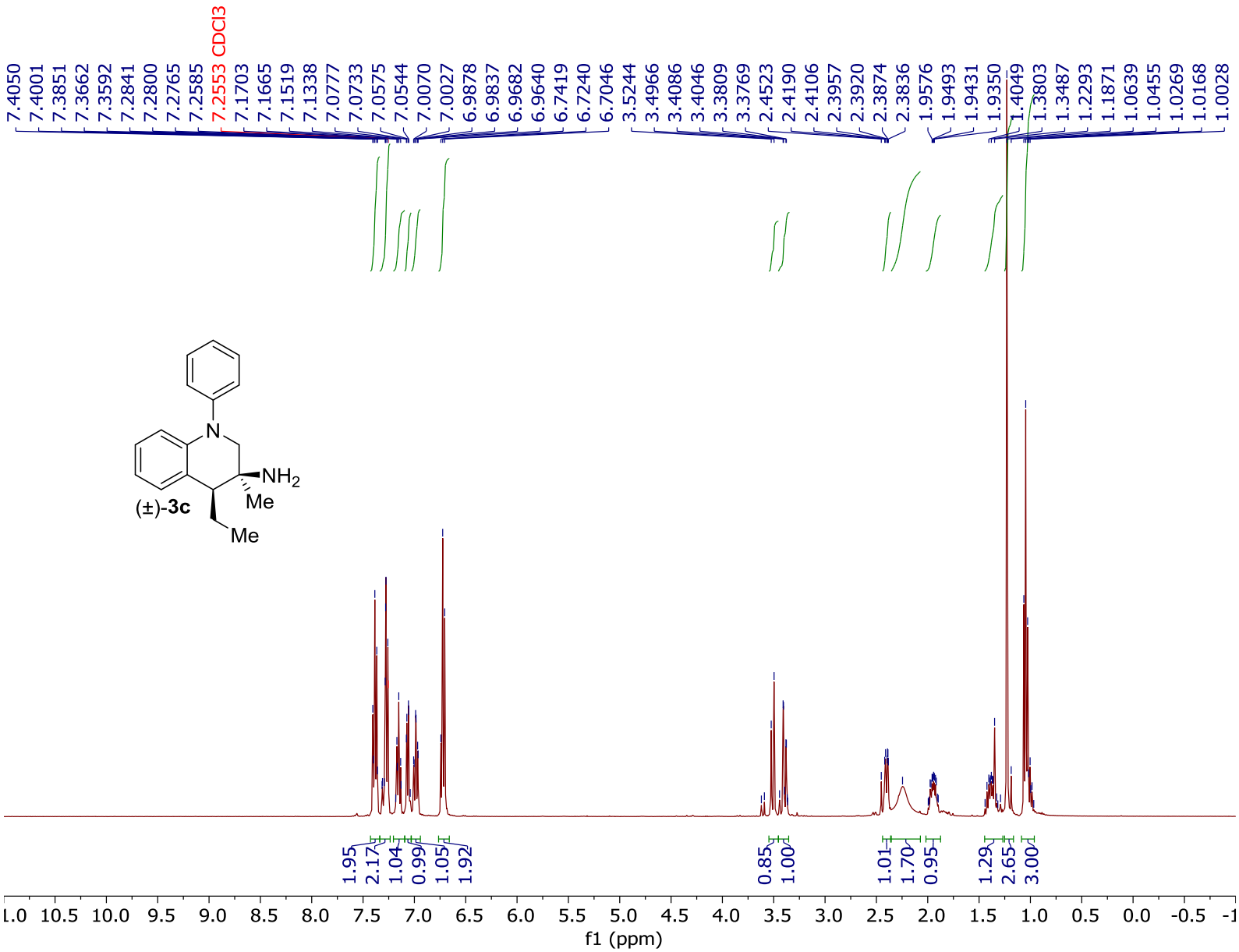
Compound 3a, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



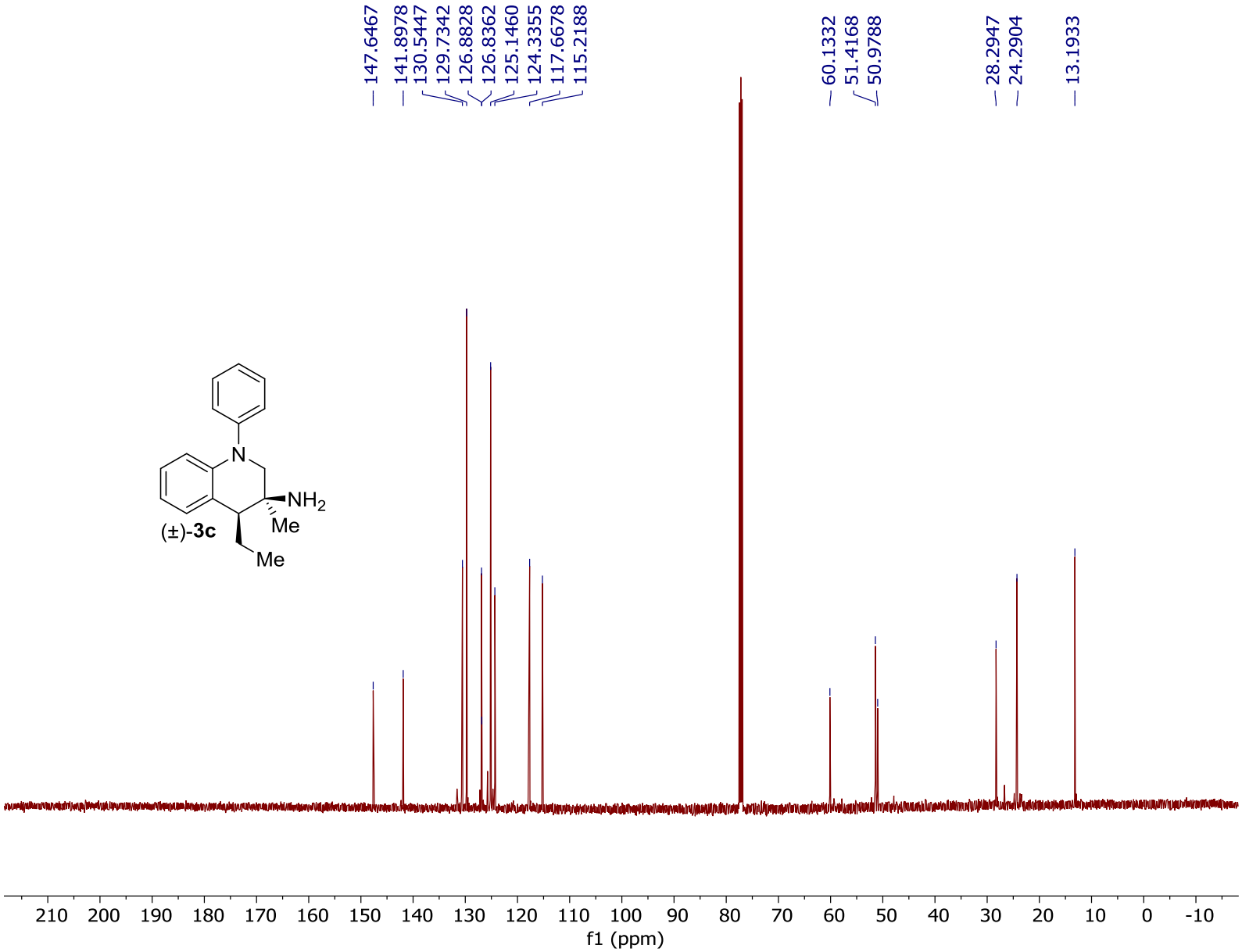
Compound 3b, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



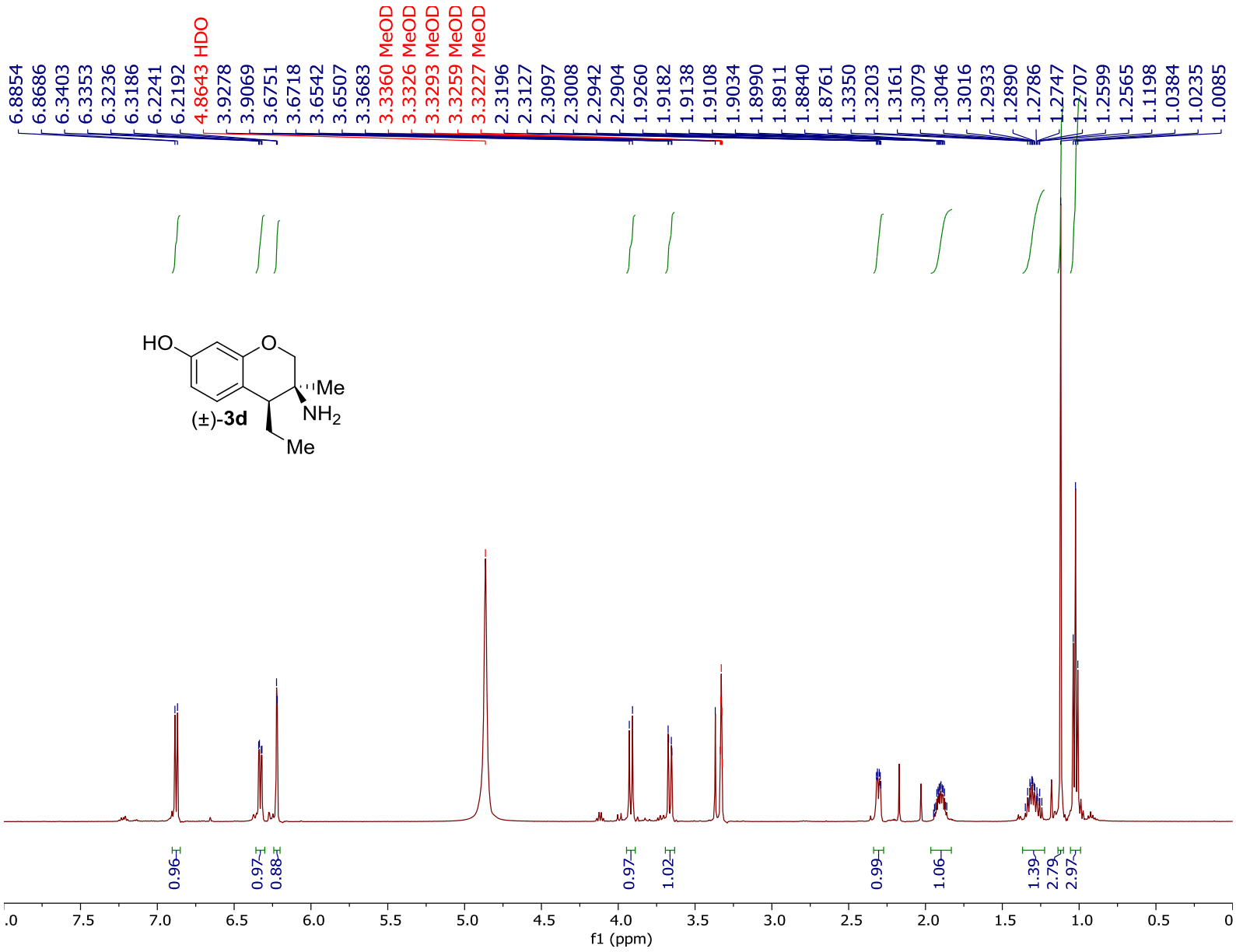
Compound 3b, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



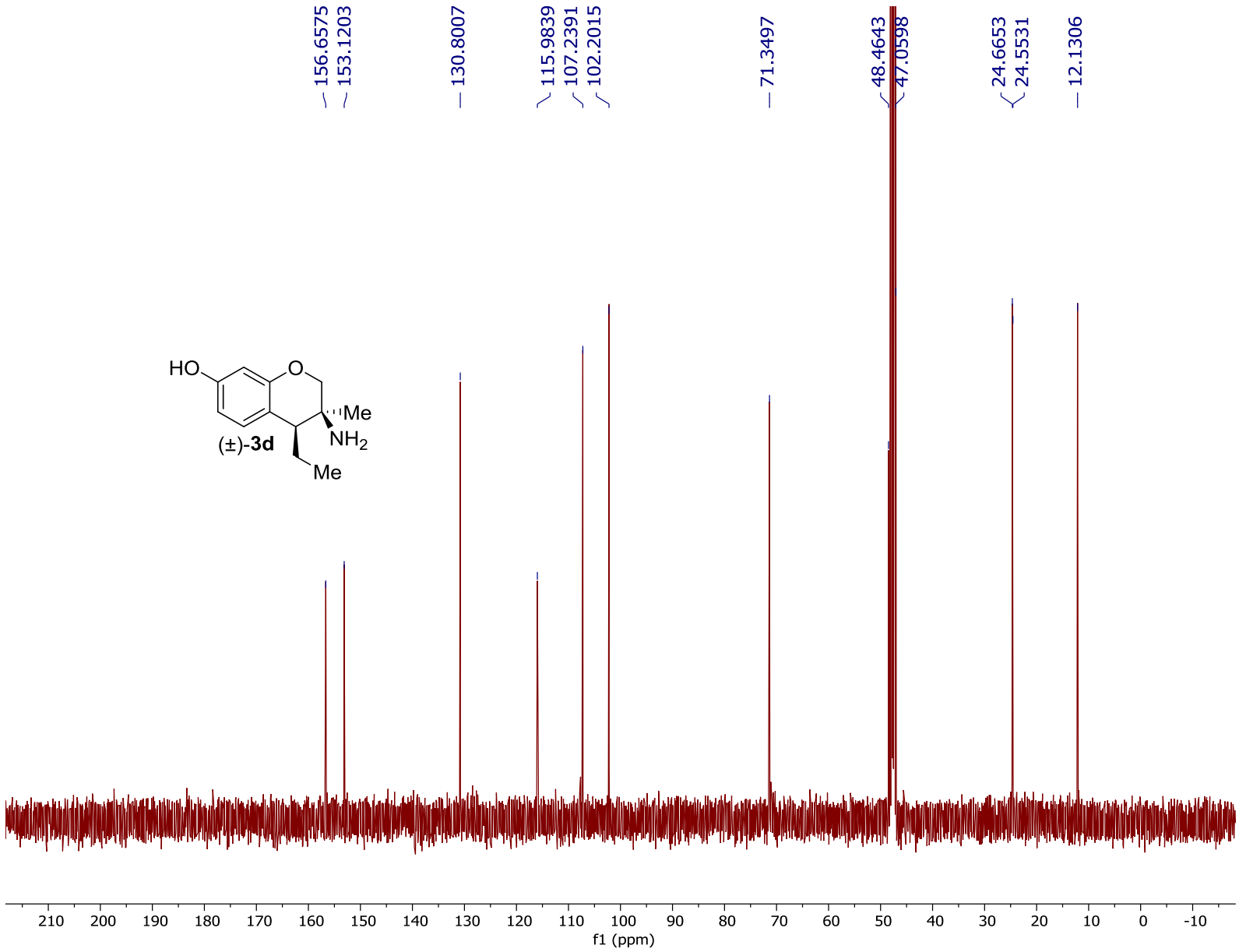
Compound 3c, 400 MHz ^{1}H NMR Spectrum in $CDCl_3$



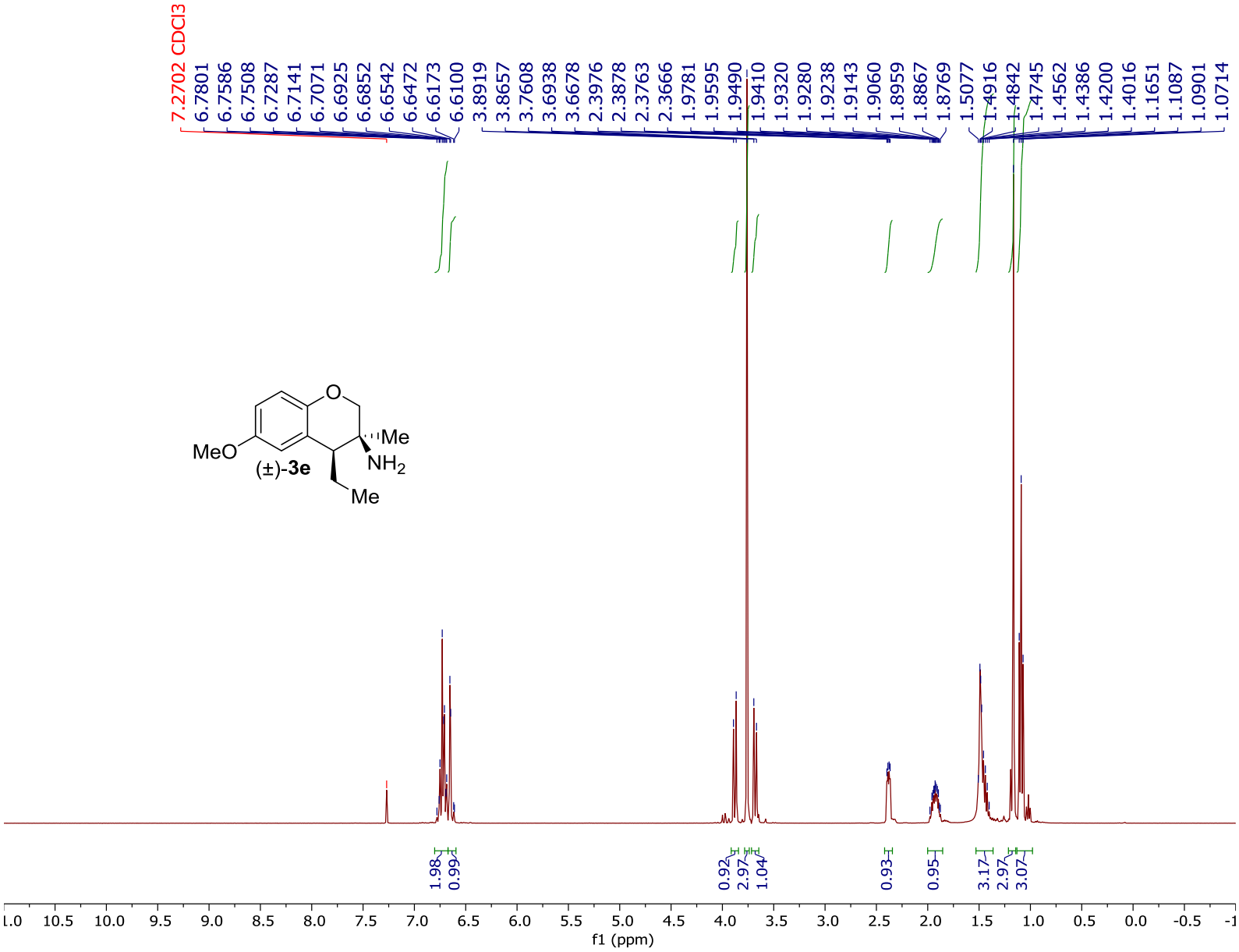
Compound 3c, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



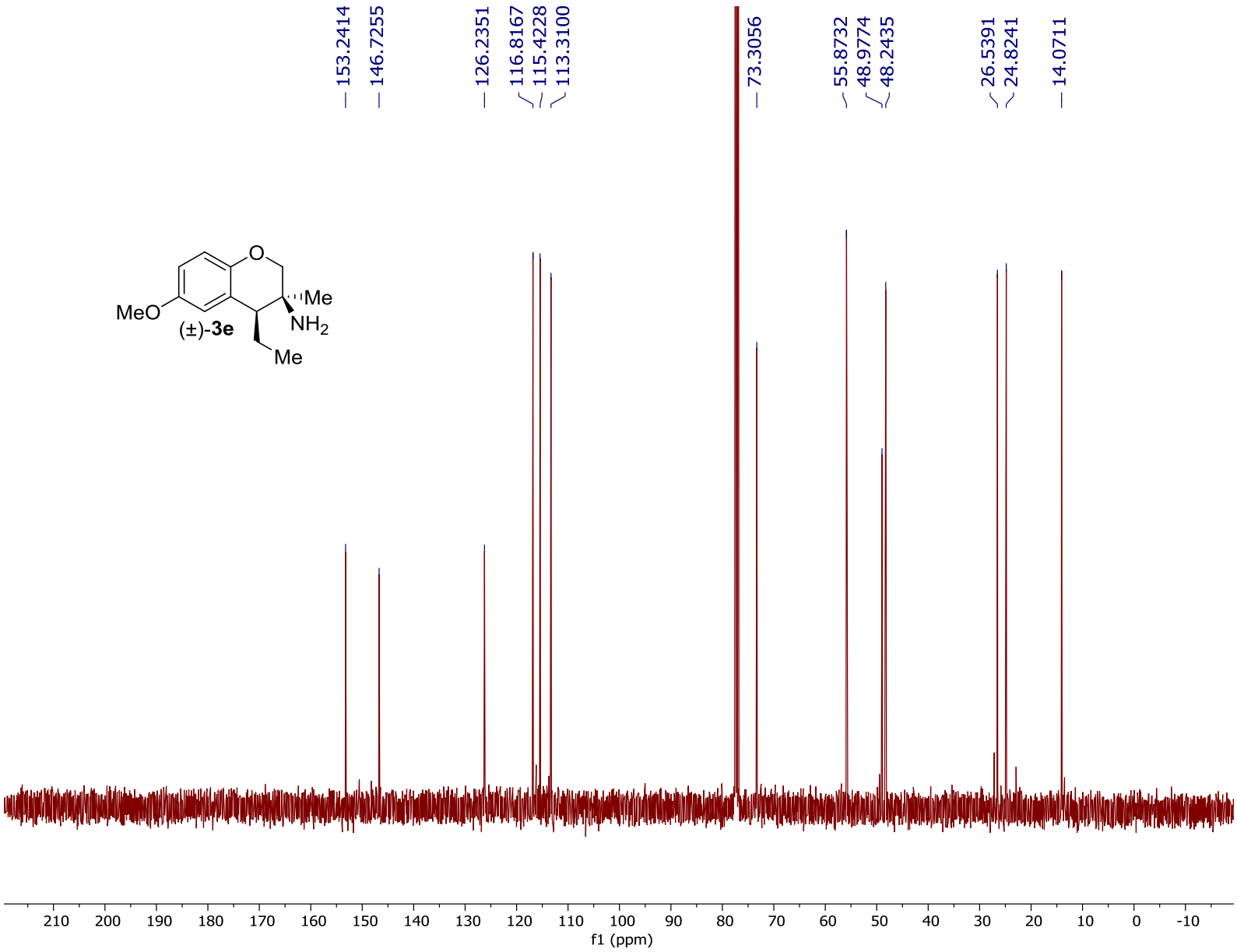
Compound 3d, 500 MHz ^{1}H NMR Spectrum in CD_3OD



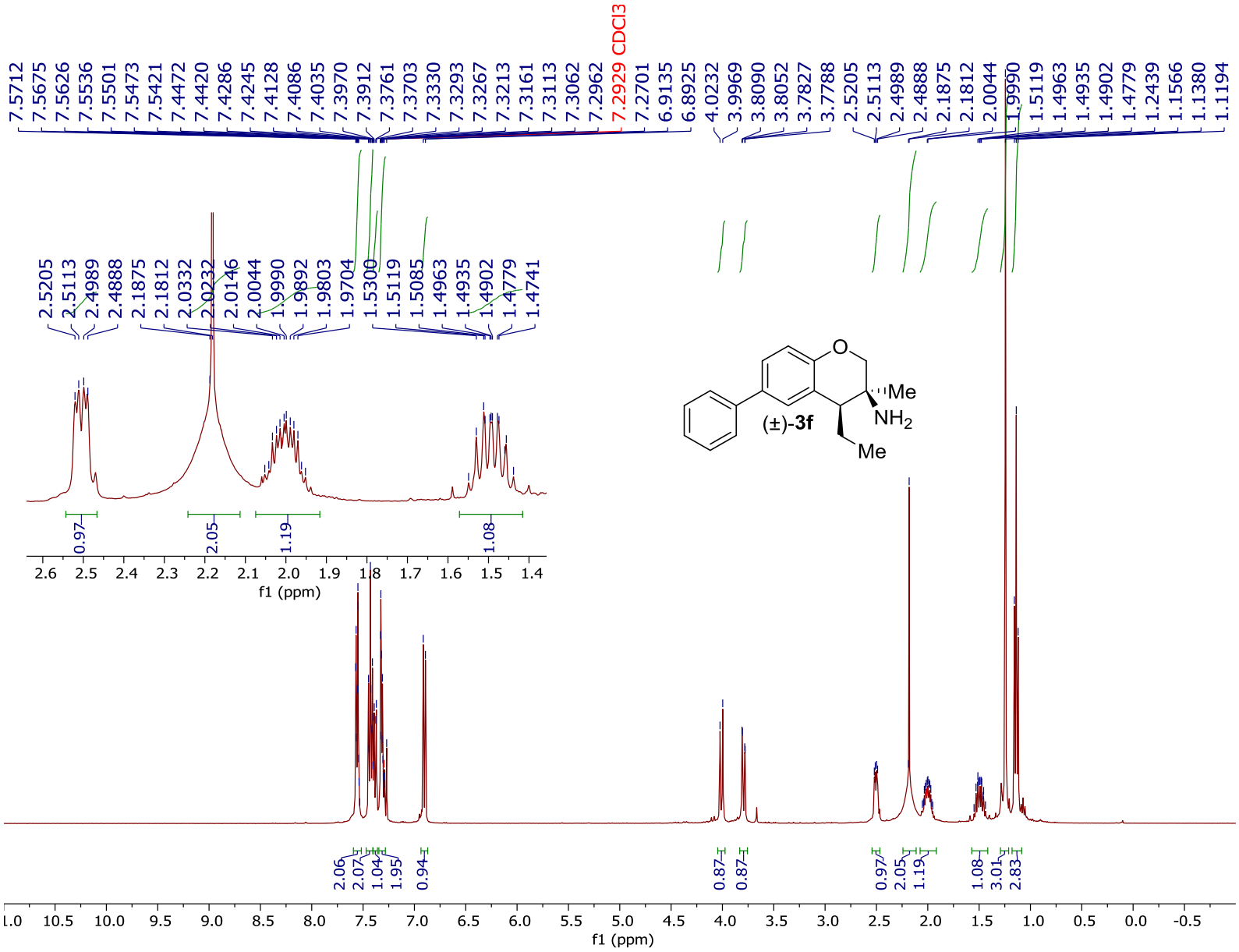
Compound 3d, 126 MHz ^{13}C NMR Spectrum in CD_3OD



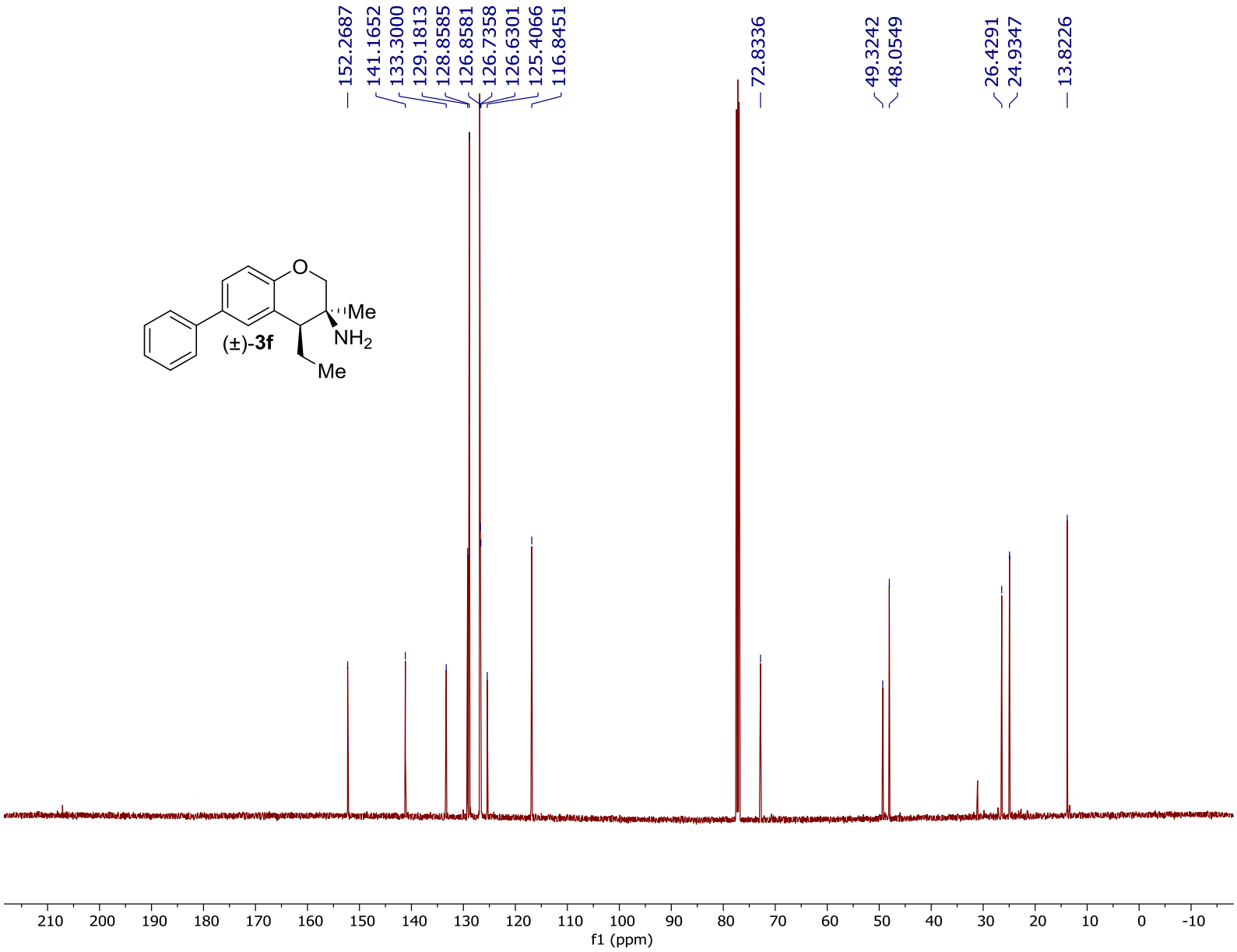
Compound 3e, 400 MHz ^{1}H NMR Spectrum in $CDCl_3$



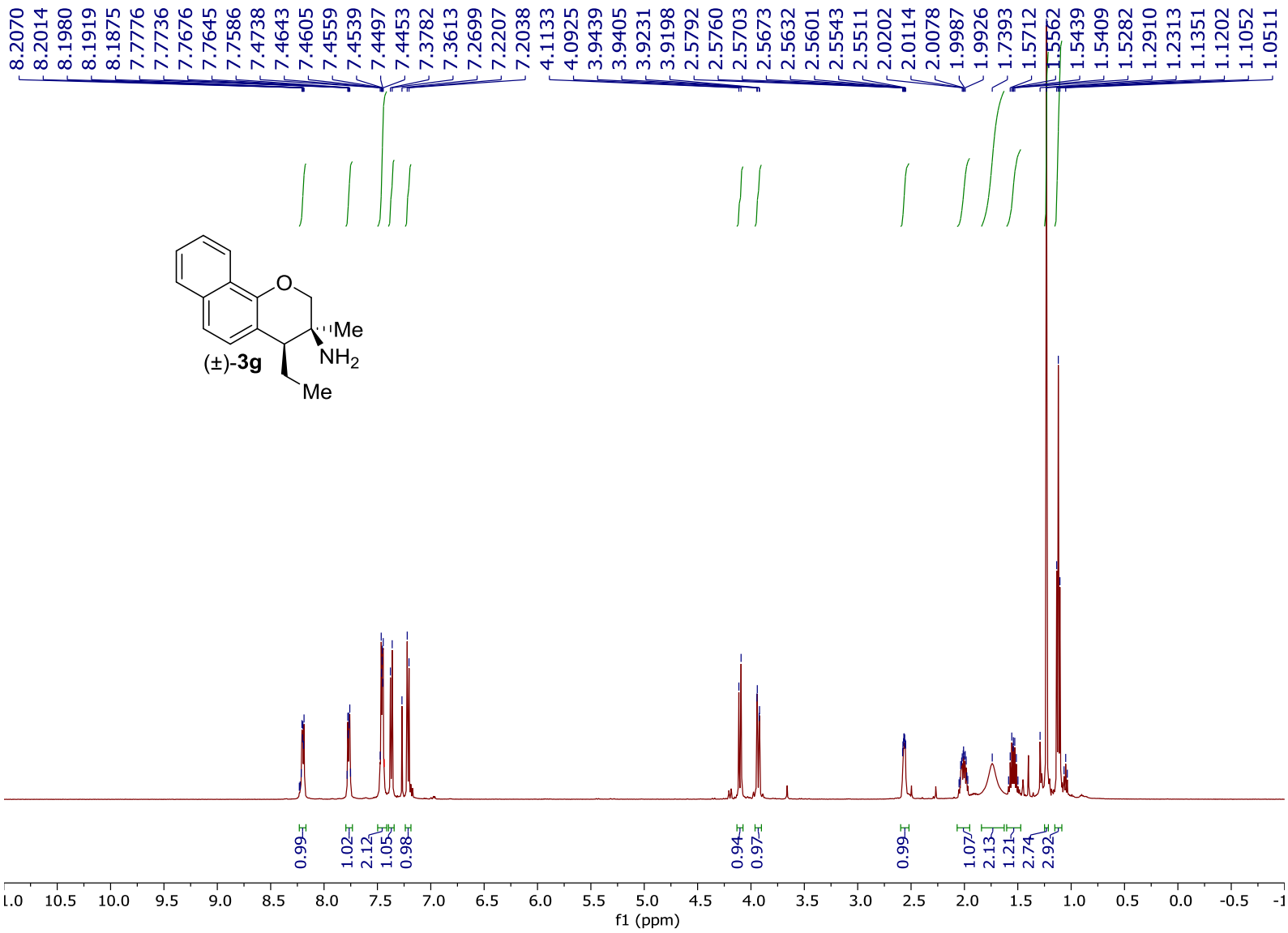
Compound 3e, 101 MHz ^{13}C NMR Spectrum in $CDCl_3$



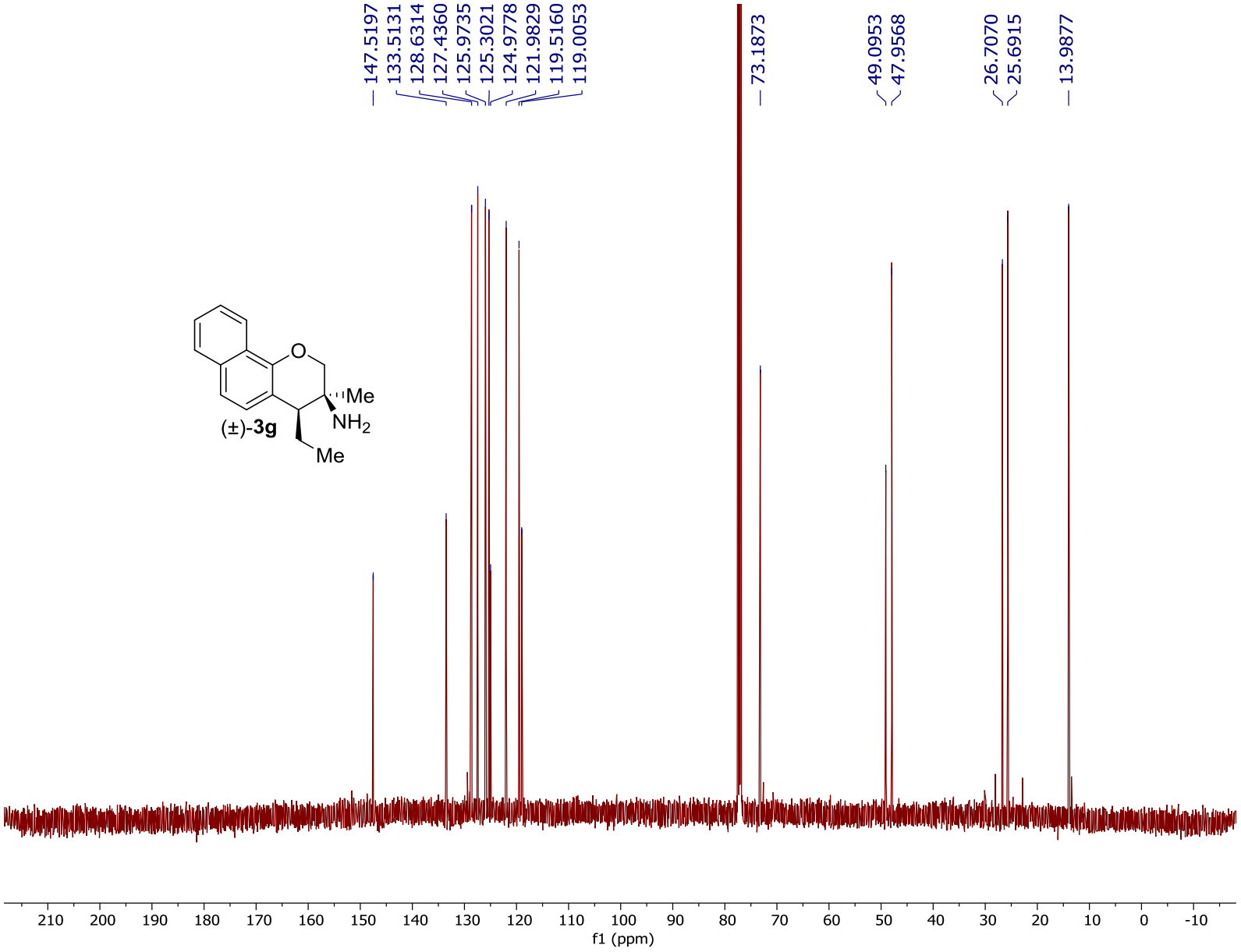
Compound 3f, 400 MHz ^{1}H NMR Spectrum in $CDCl_3$



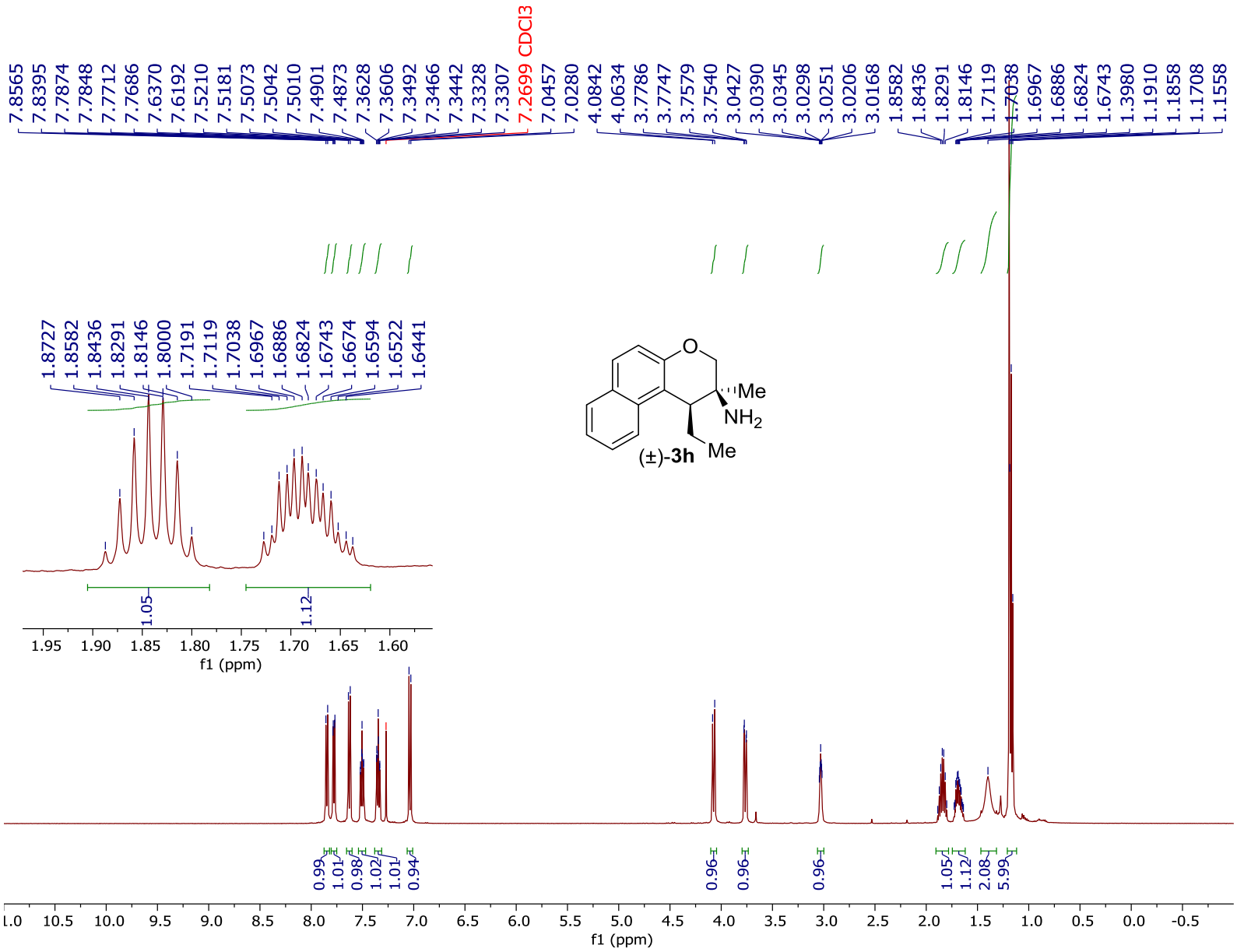
Compound 3f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



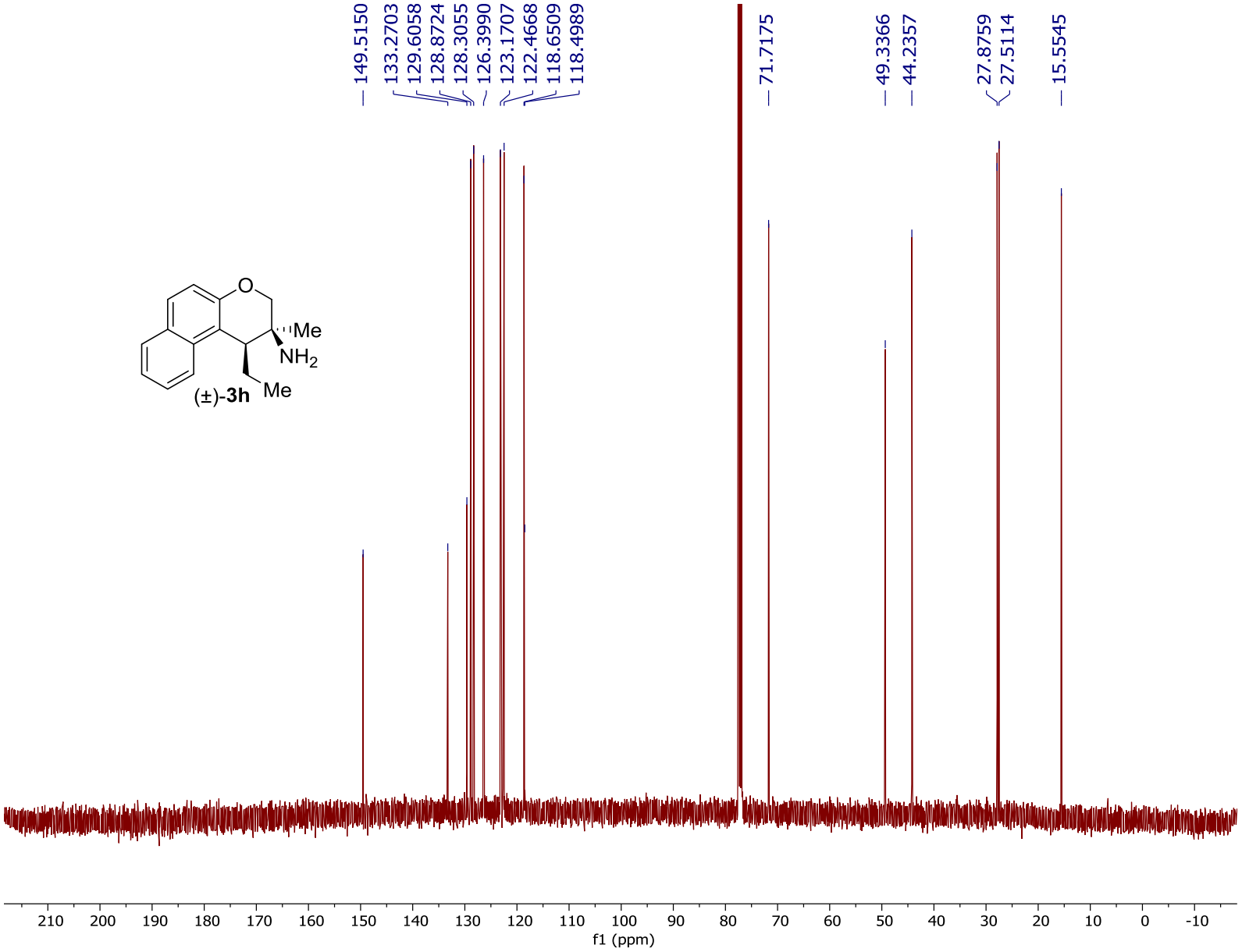
Compound 3g, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



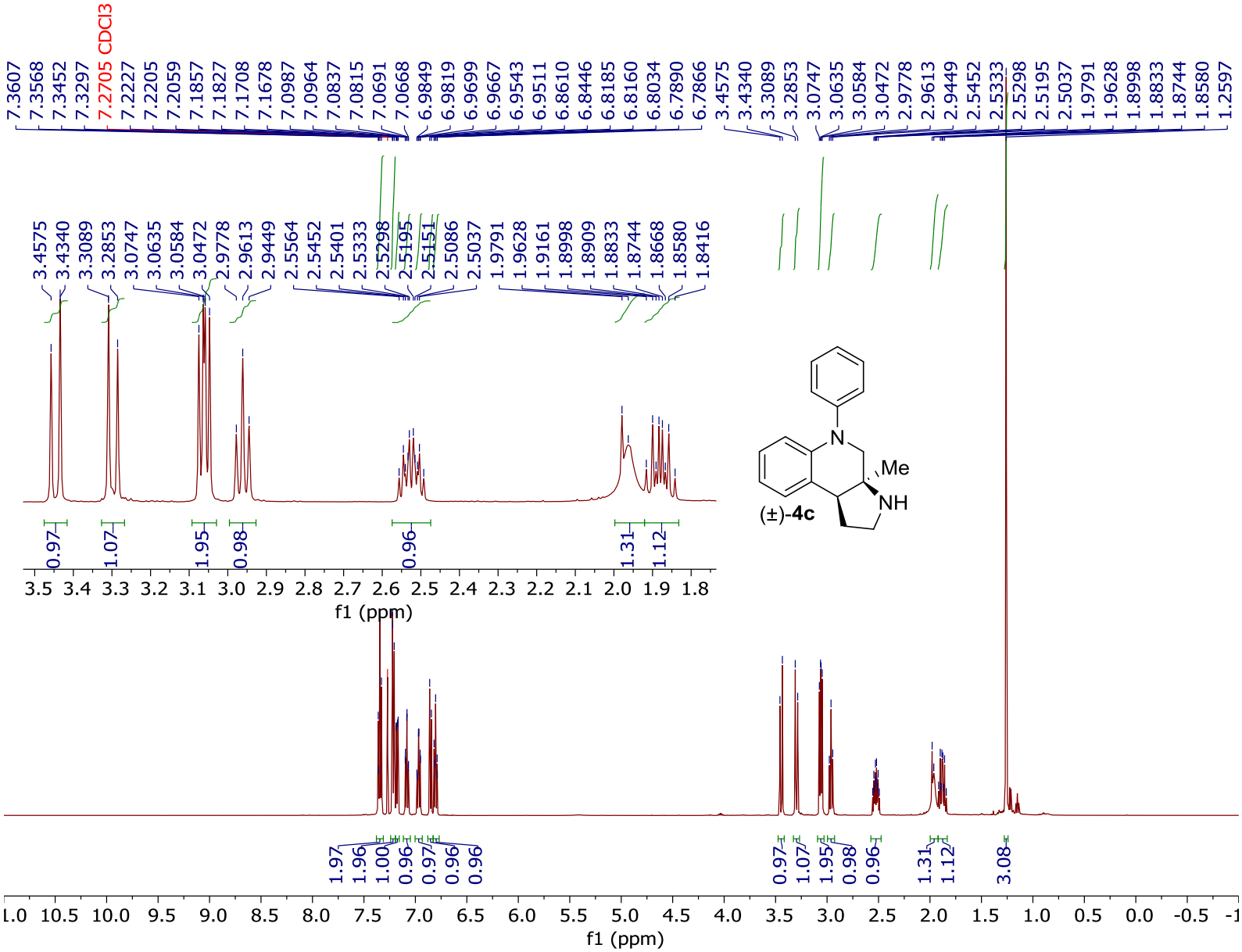
Compound 3g, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



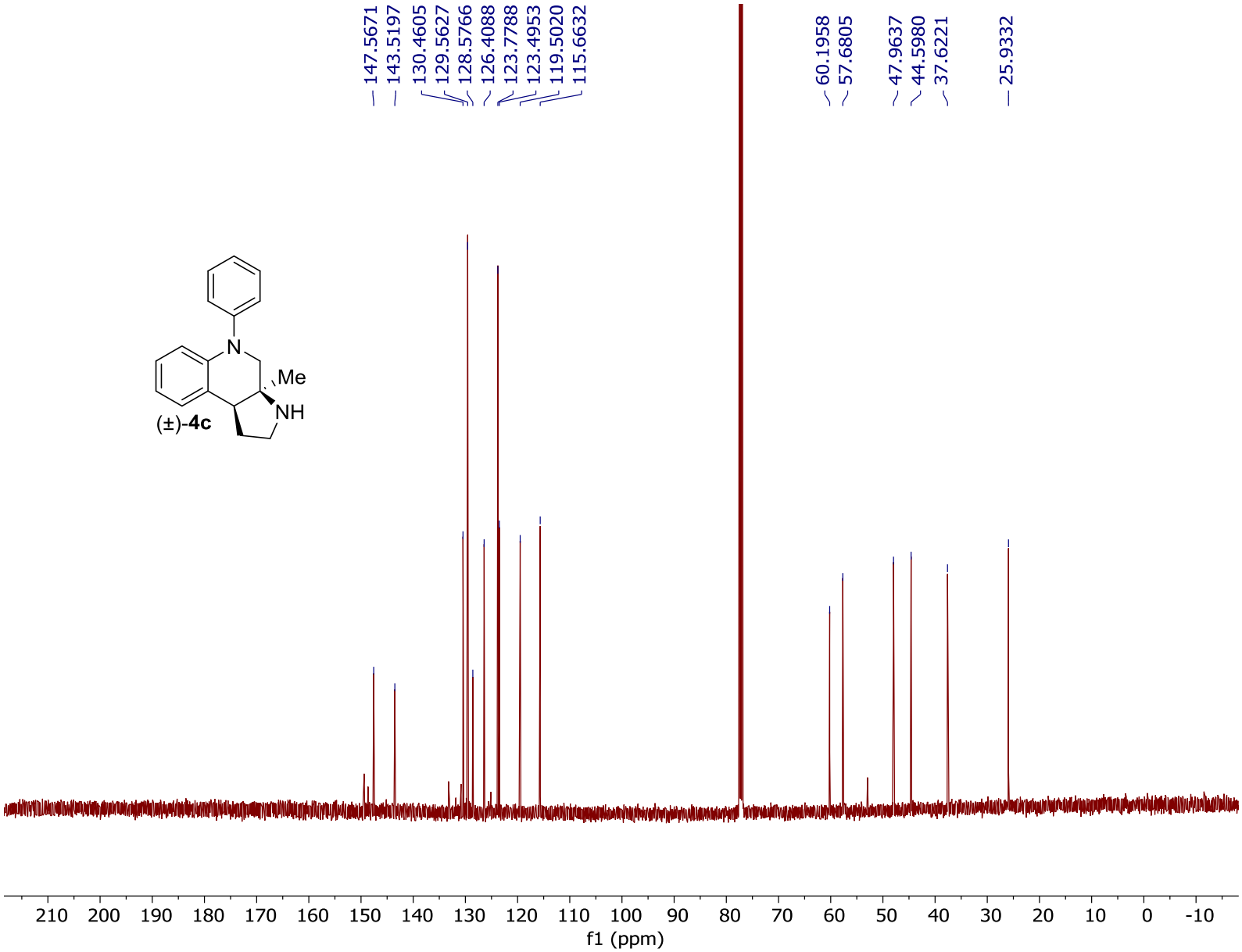
Compound 3h, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



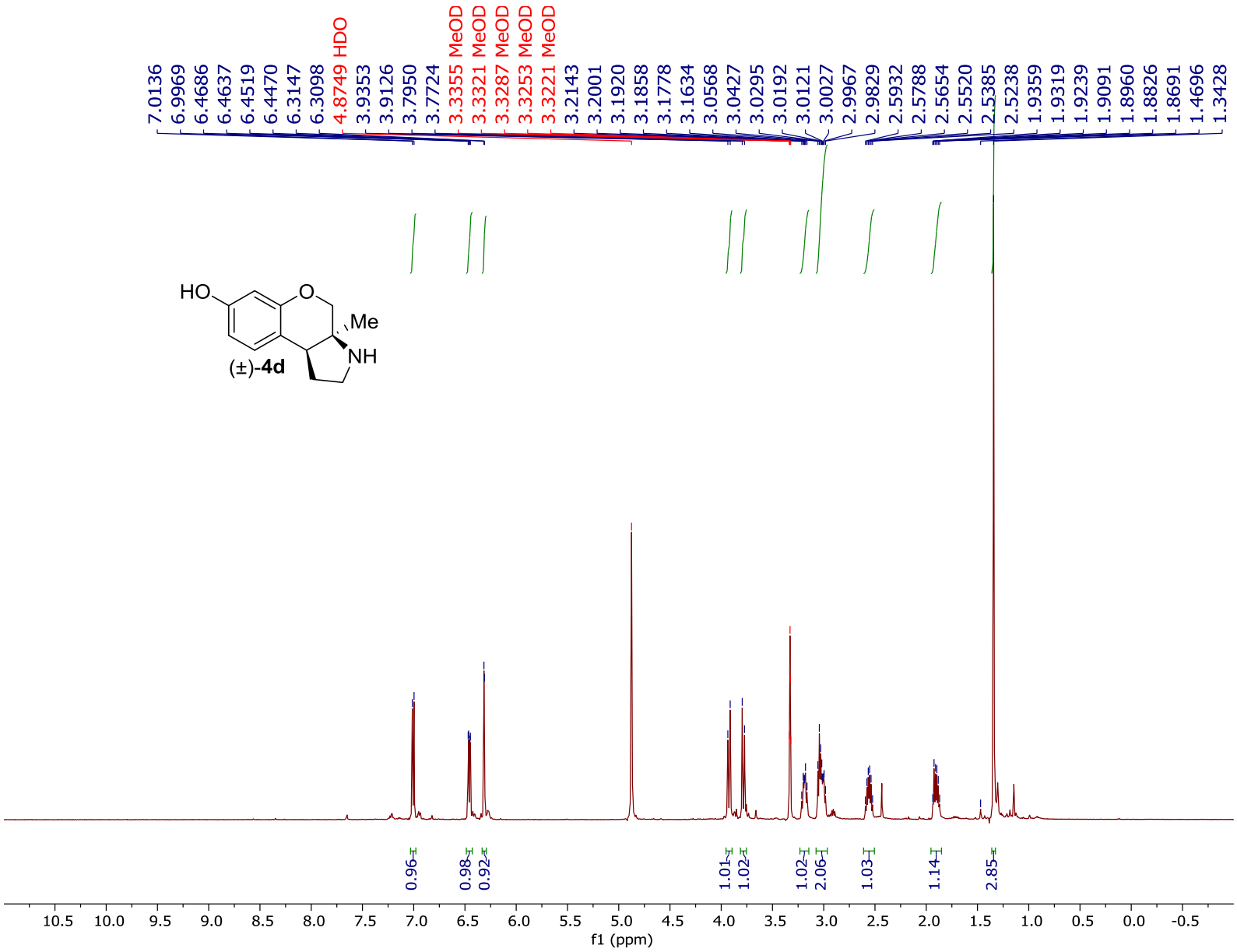
Compound 3h, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



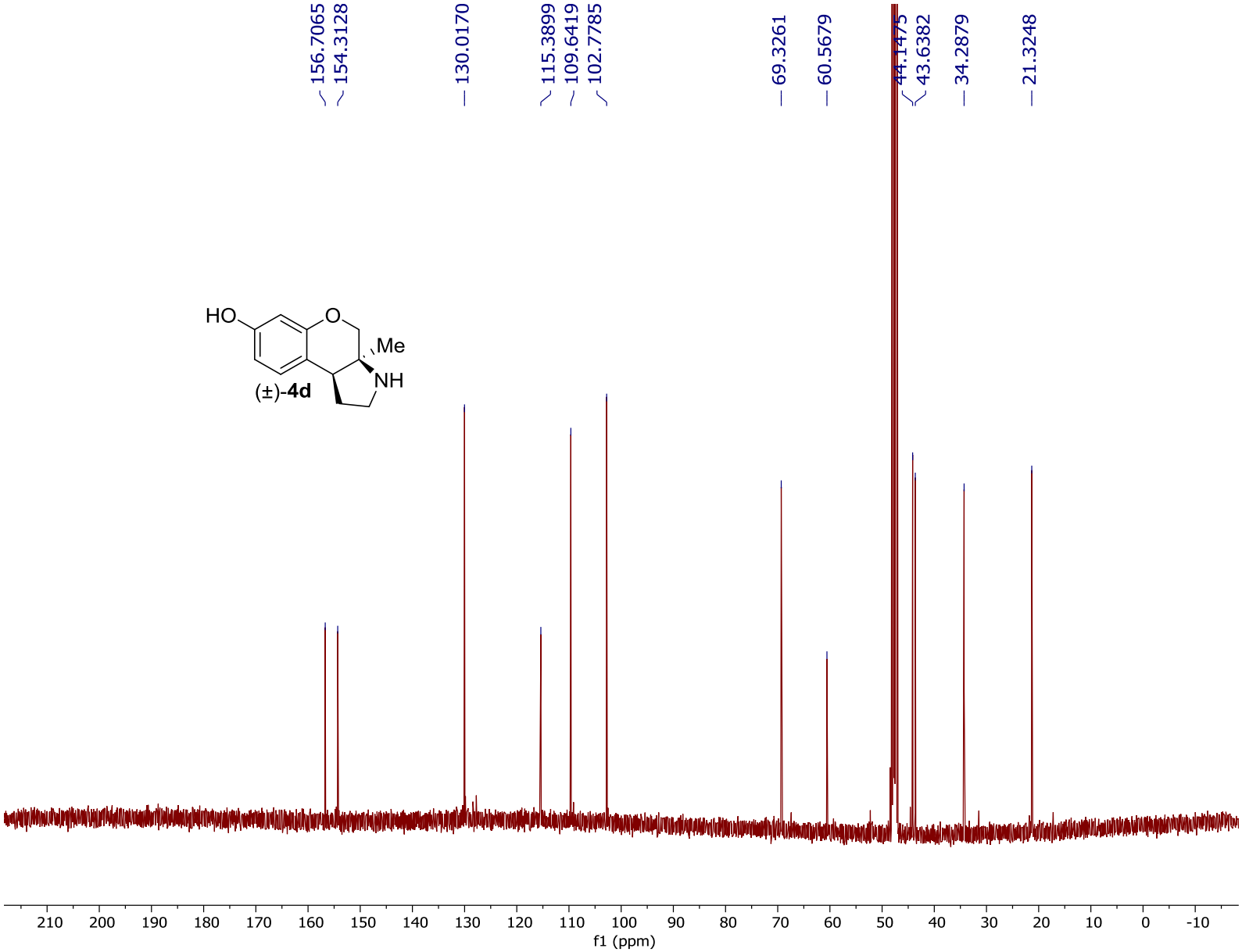
Compound 4c, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



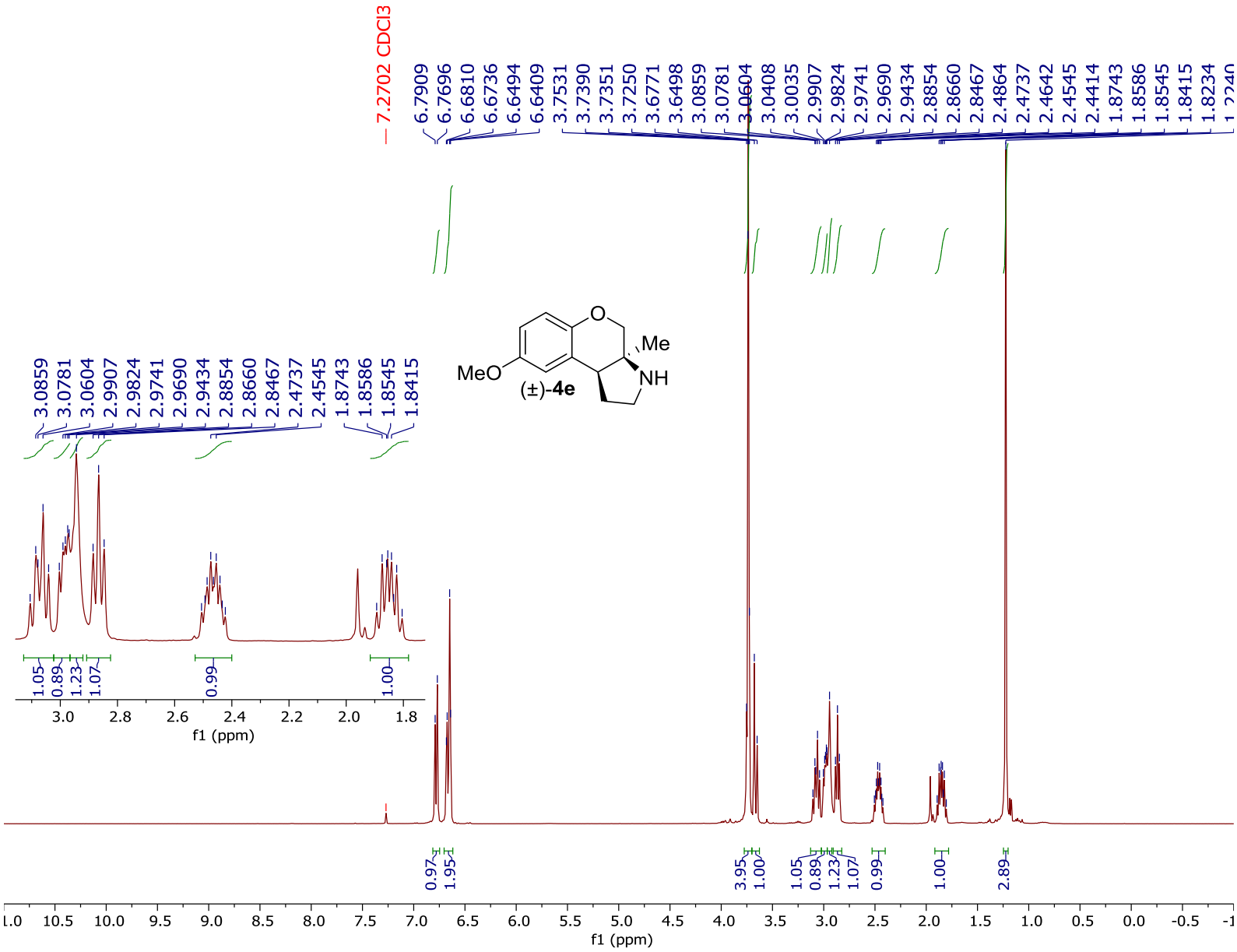
Compound 4c, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



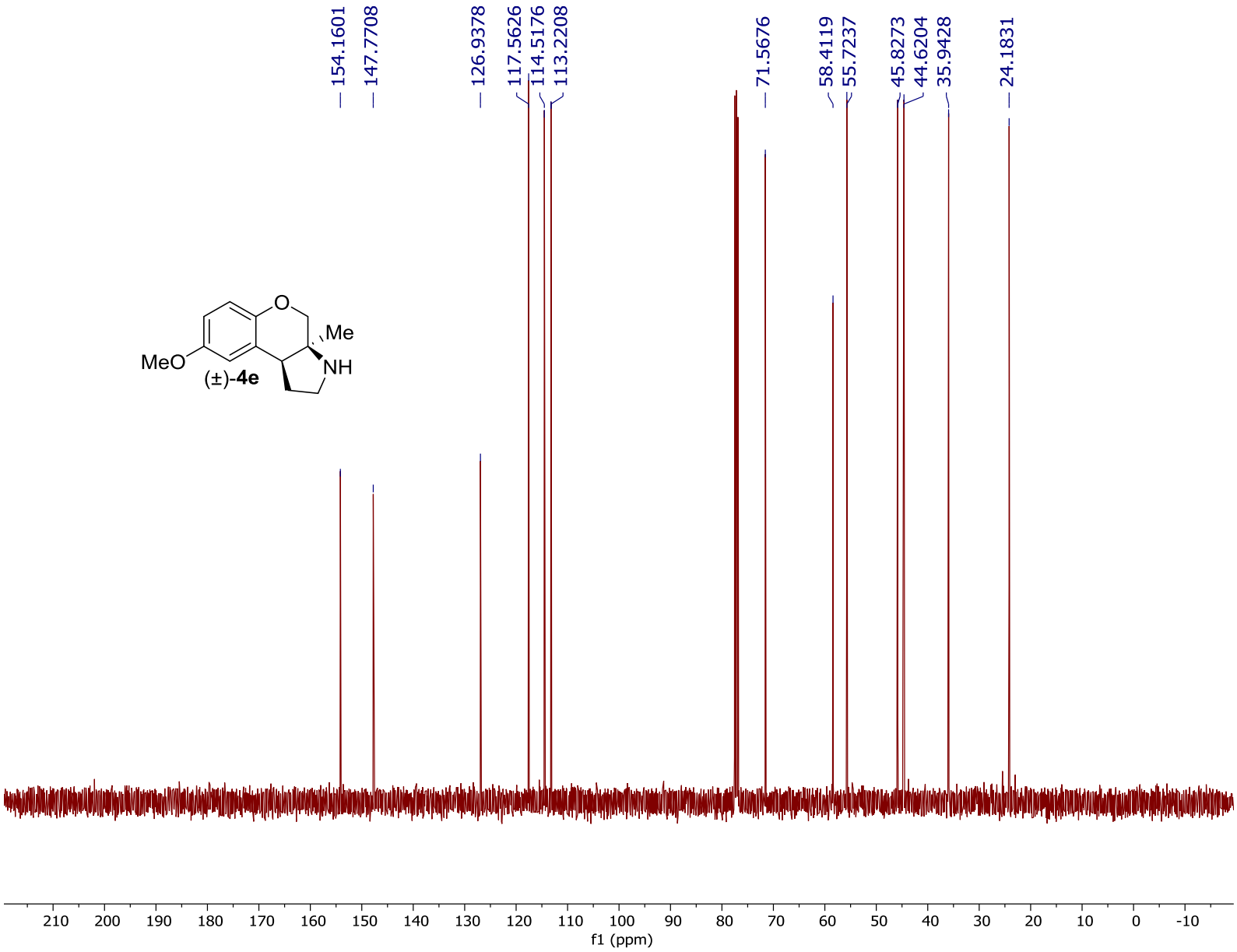
Compound 4d, 500 MHz ^{1}H NMR Spectrum in CD_3OD



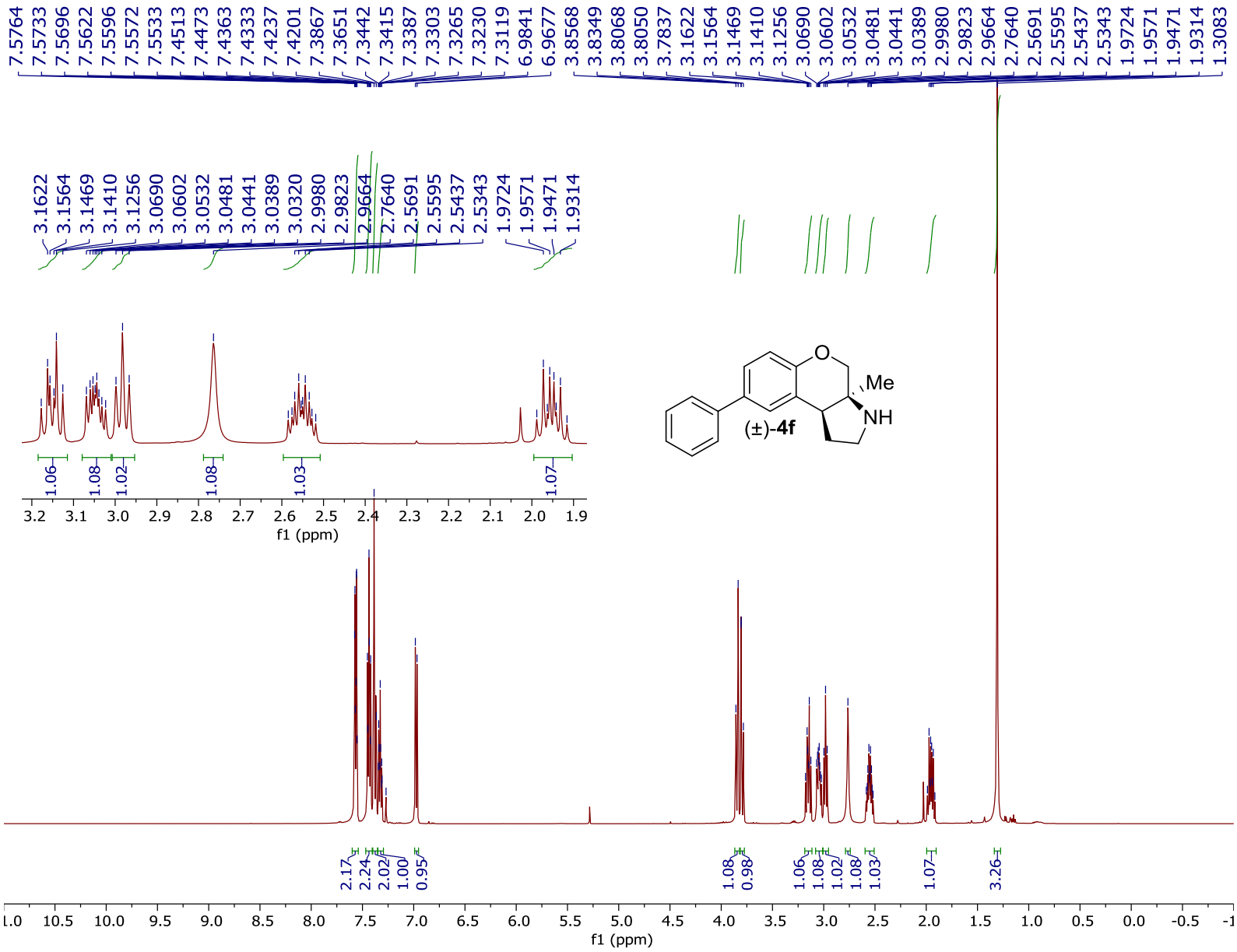
Compound 4d, 126 MHz ^{13}C NMR Spectrum in CD_3OD



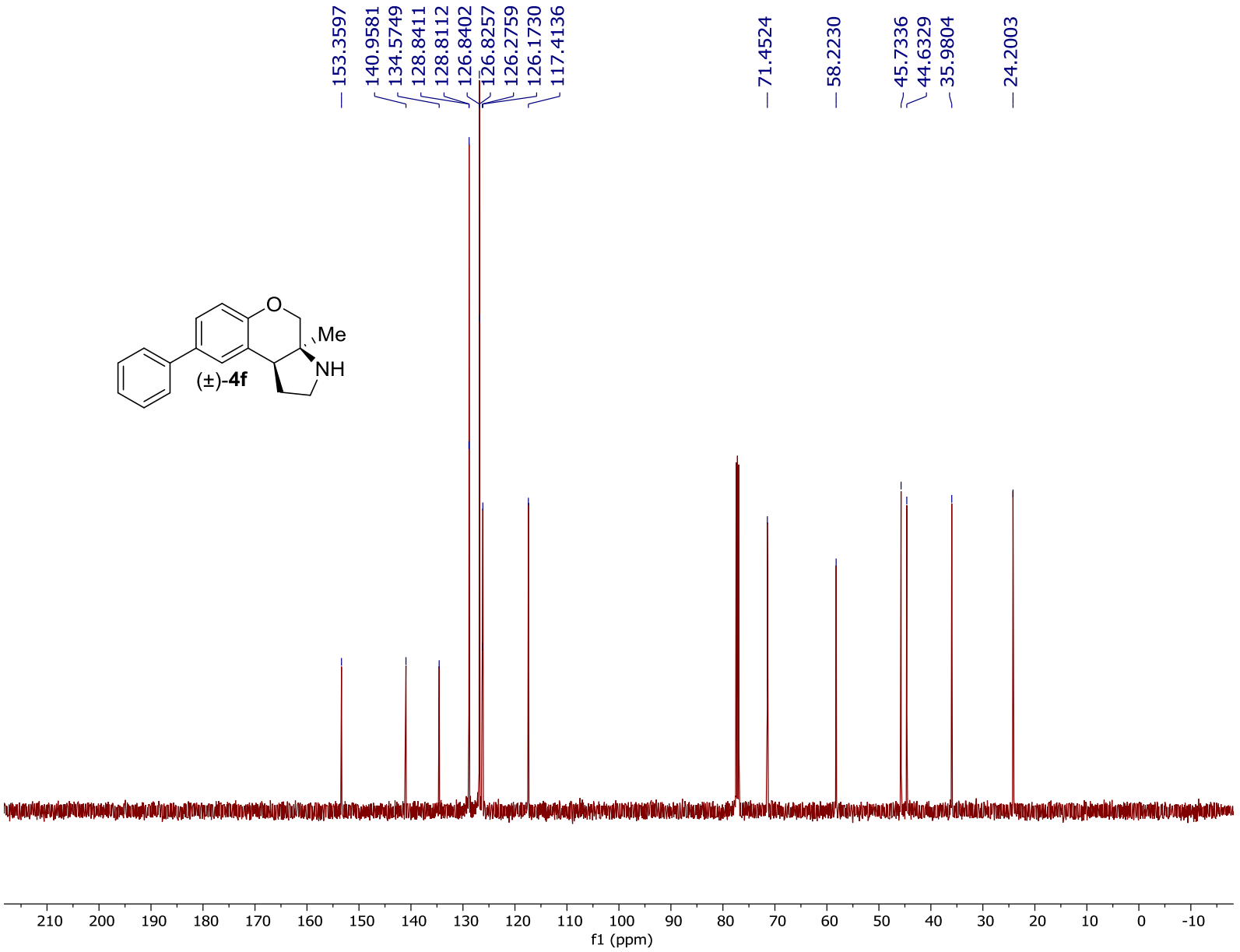
Compound 4e, 400 MHz ^{1}H NMR Spectrum in $CDCl_3$



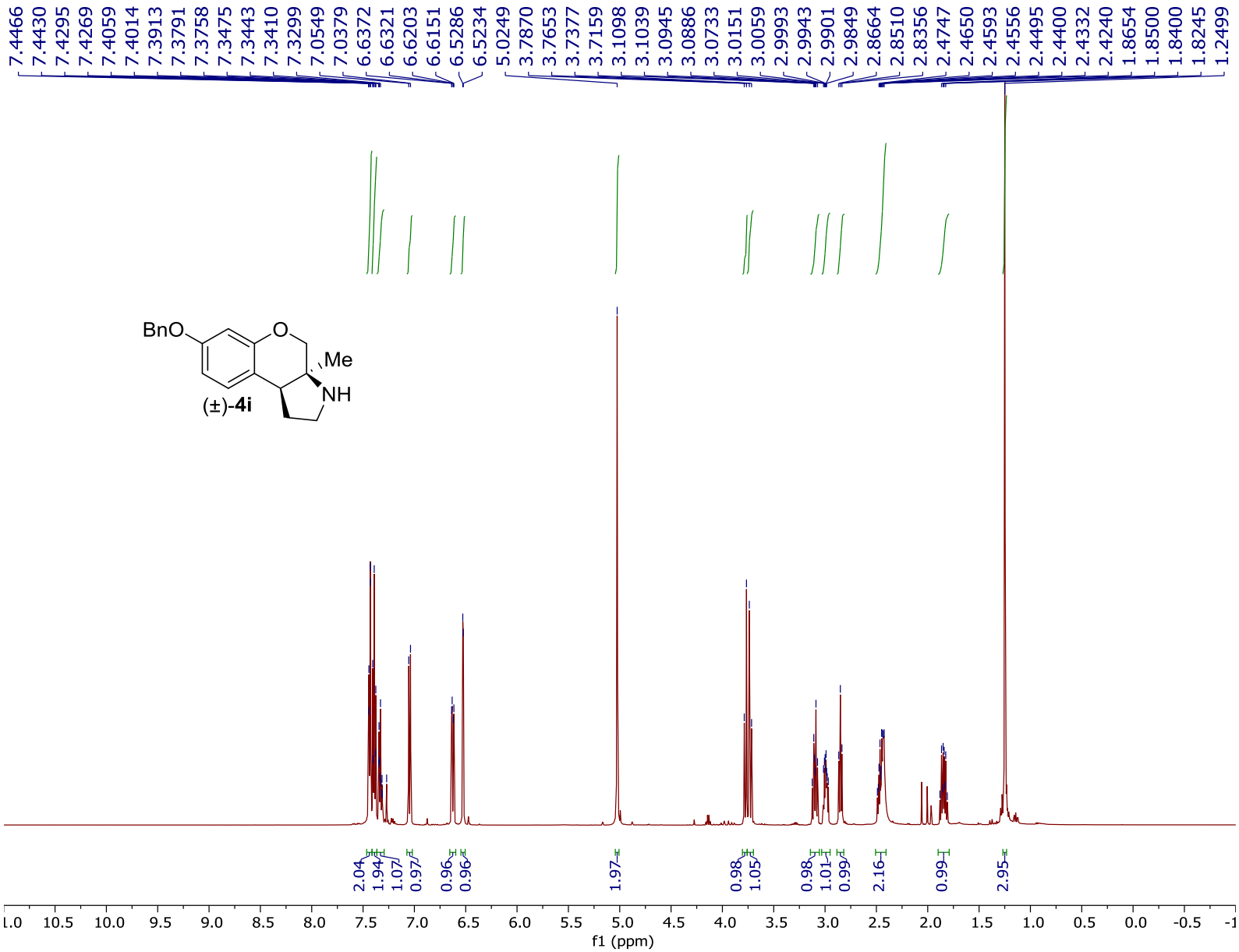
Compound 4e, 101 MHz ^{13}C NMR Spectrum in $CDCl_3$



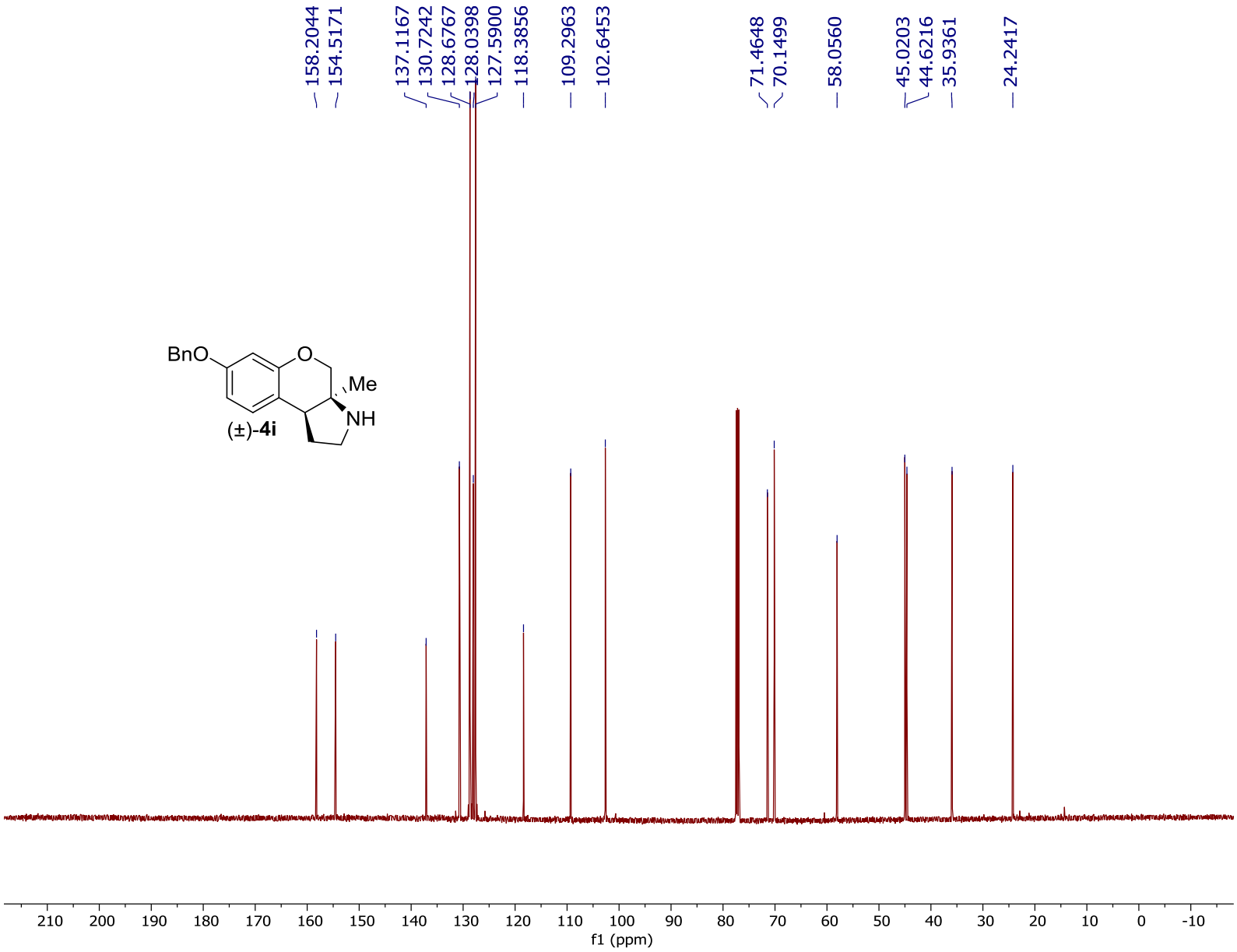
Compound 4f, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



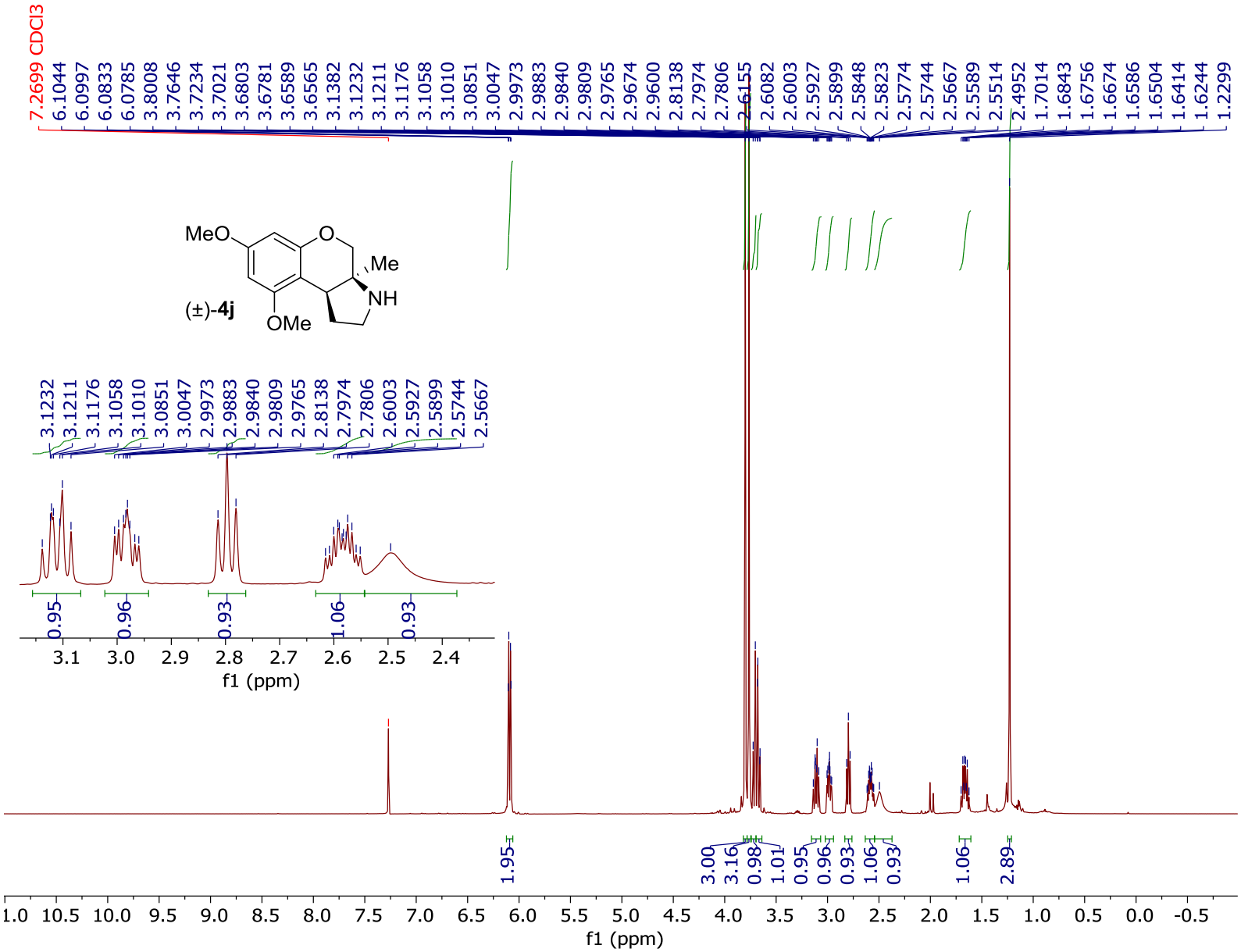
Compound 4f, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



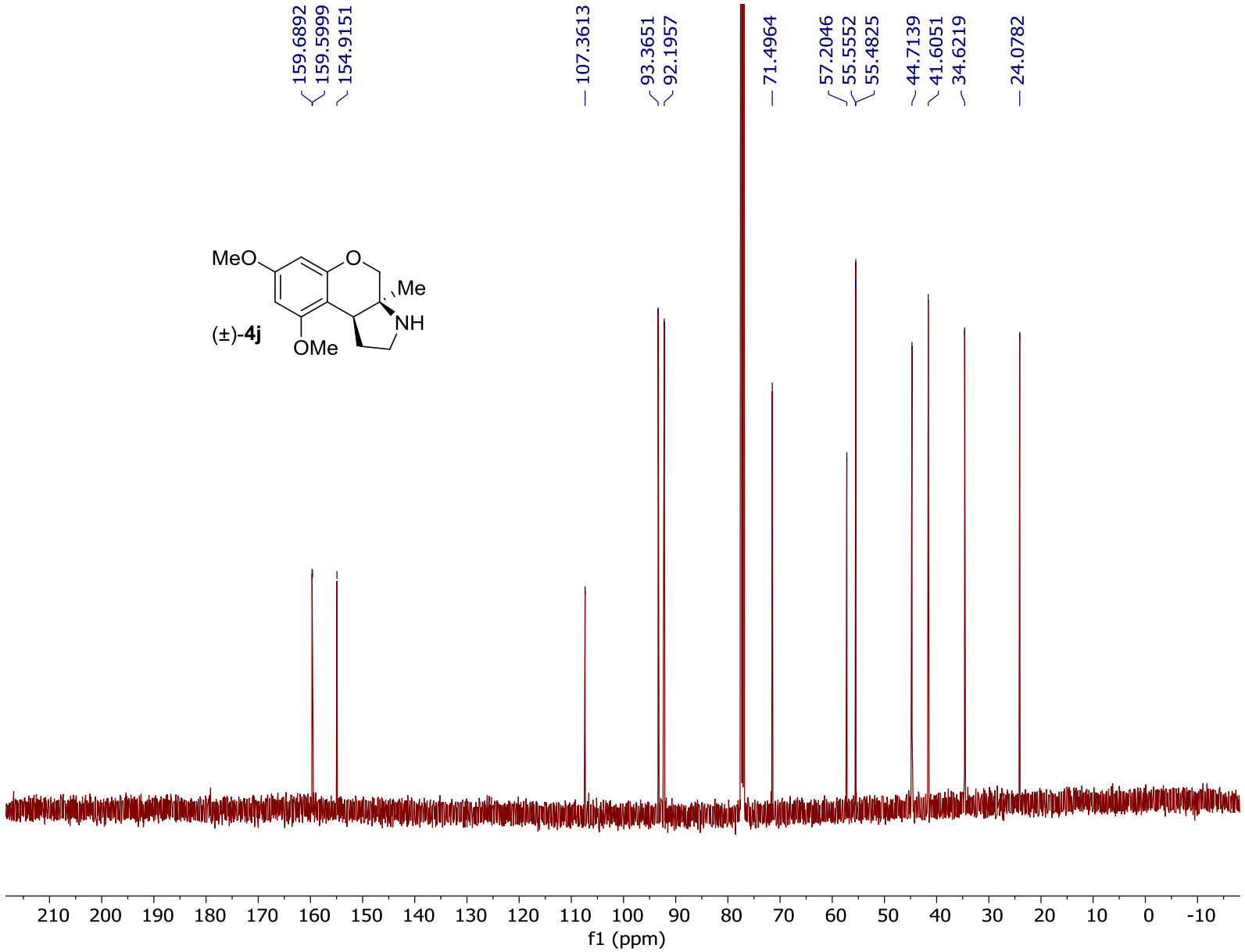
Compound 4i, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



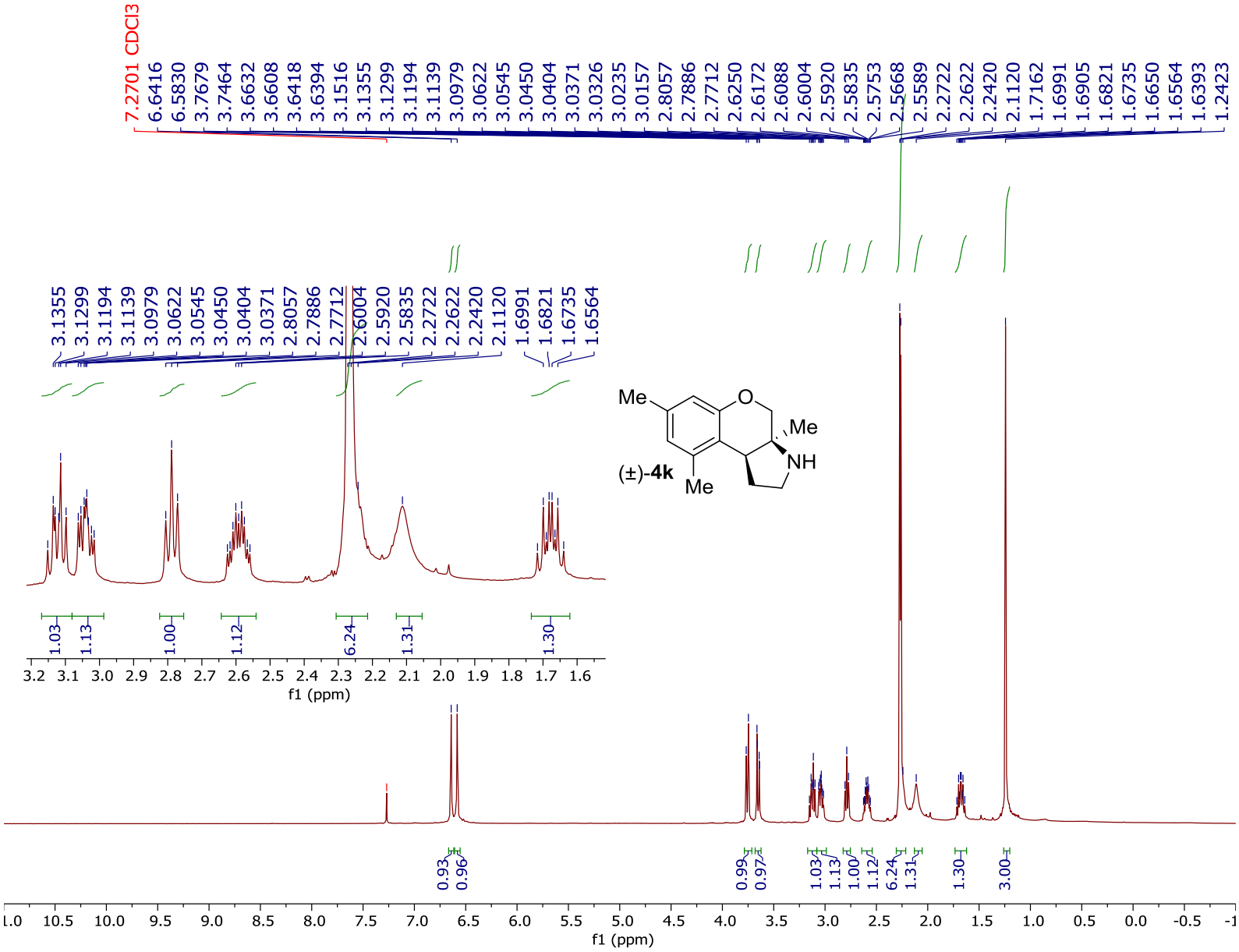
Compound 4i, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



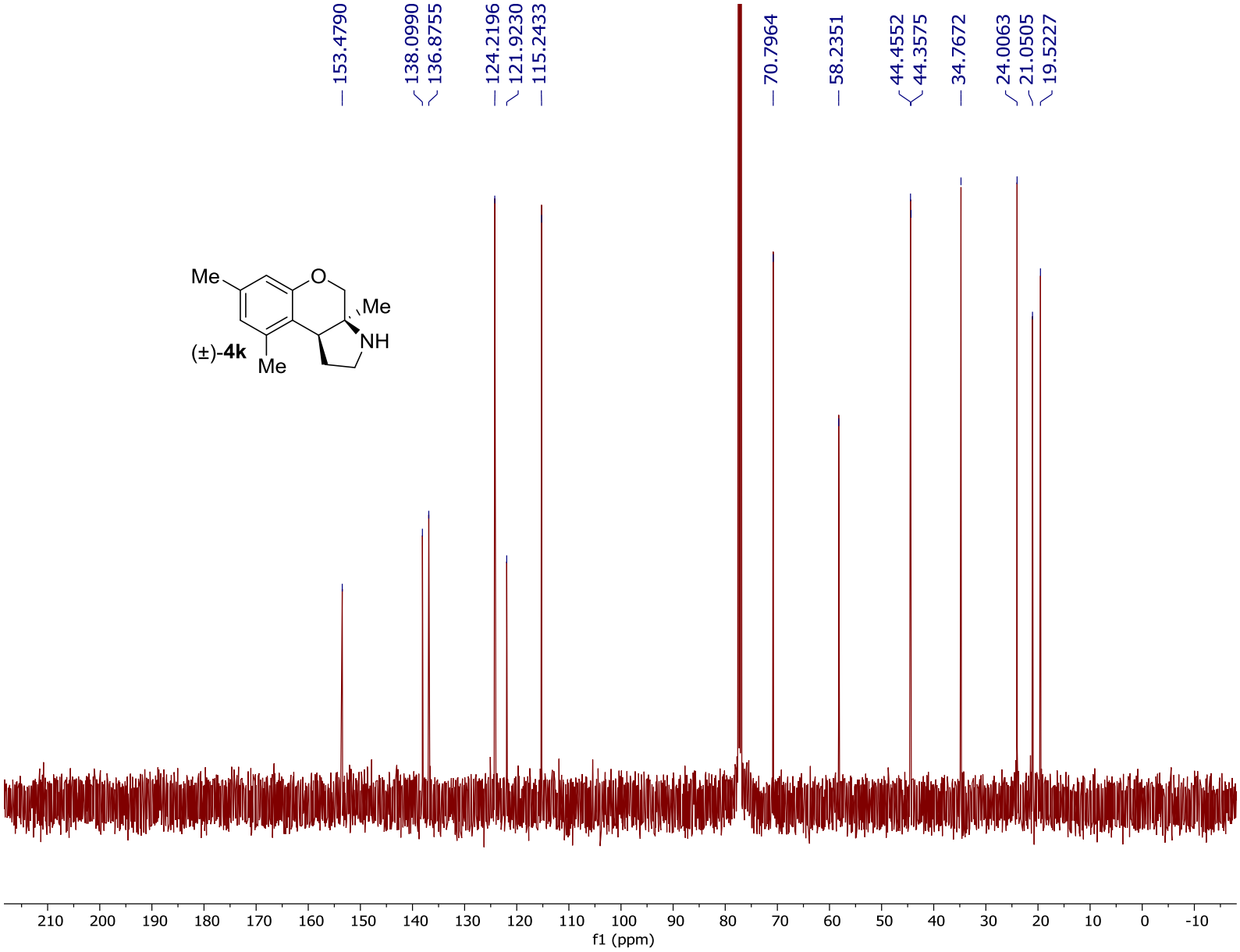
Compound 4j, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



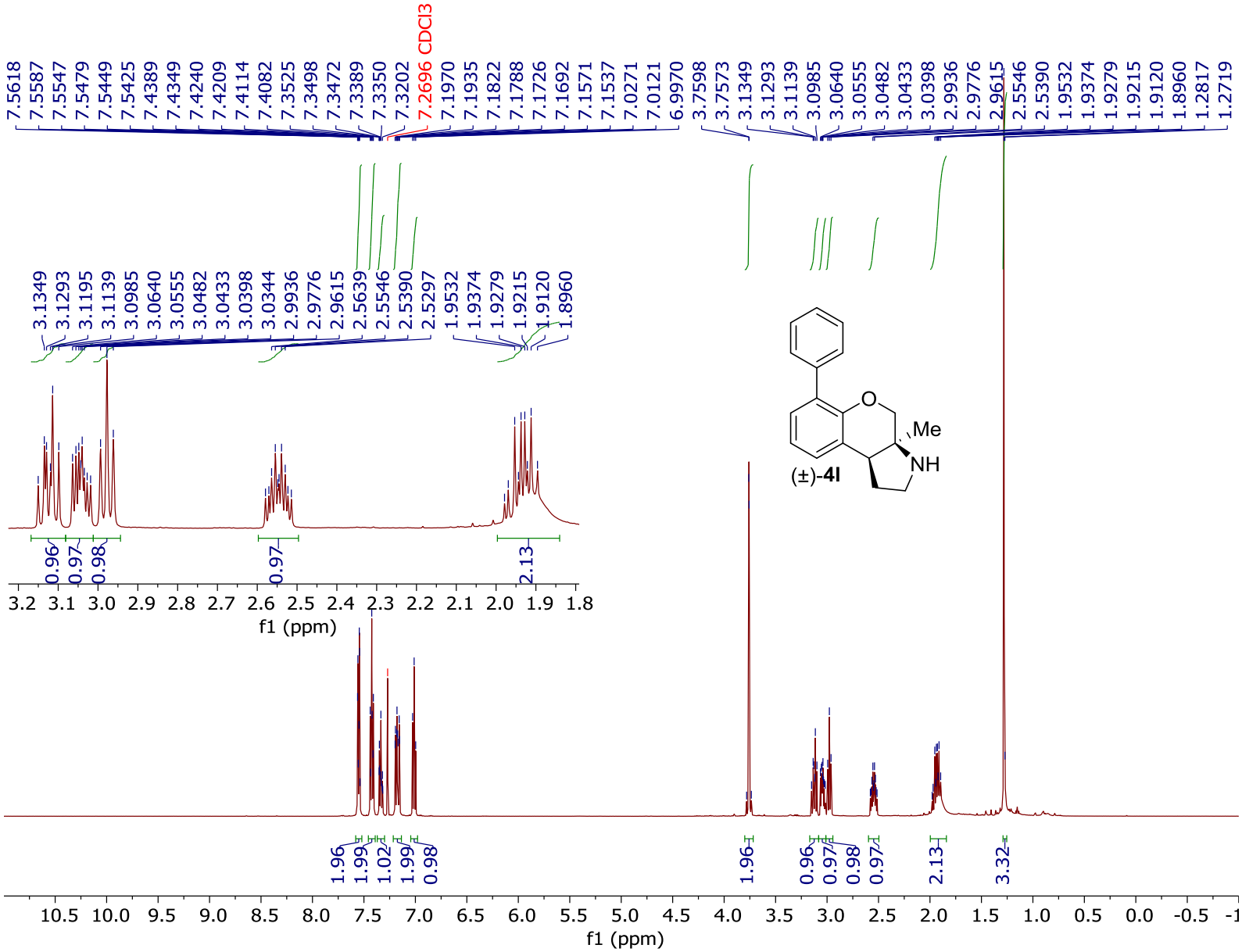
Compound 4j, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



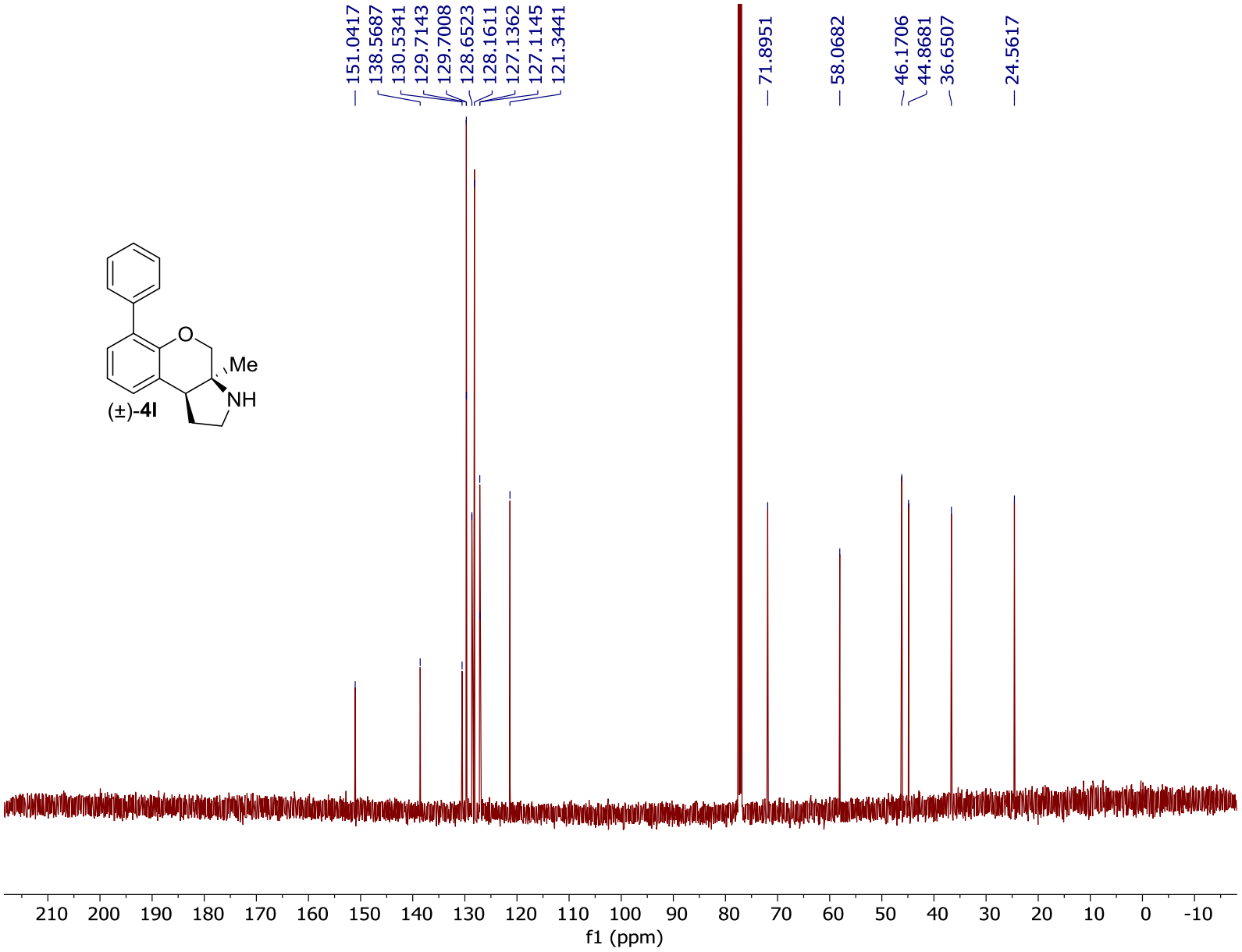
Compound 4k, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



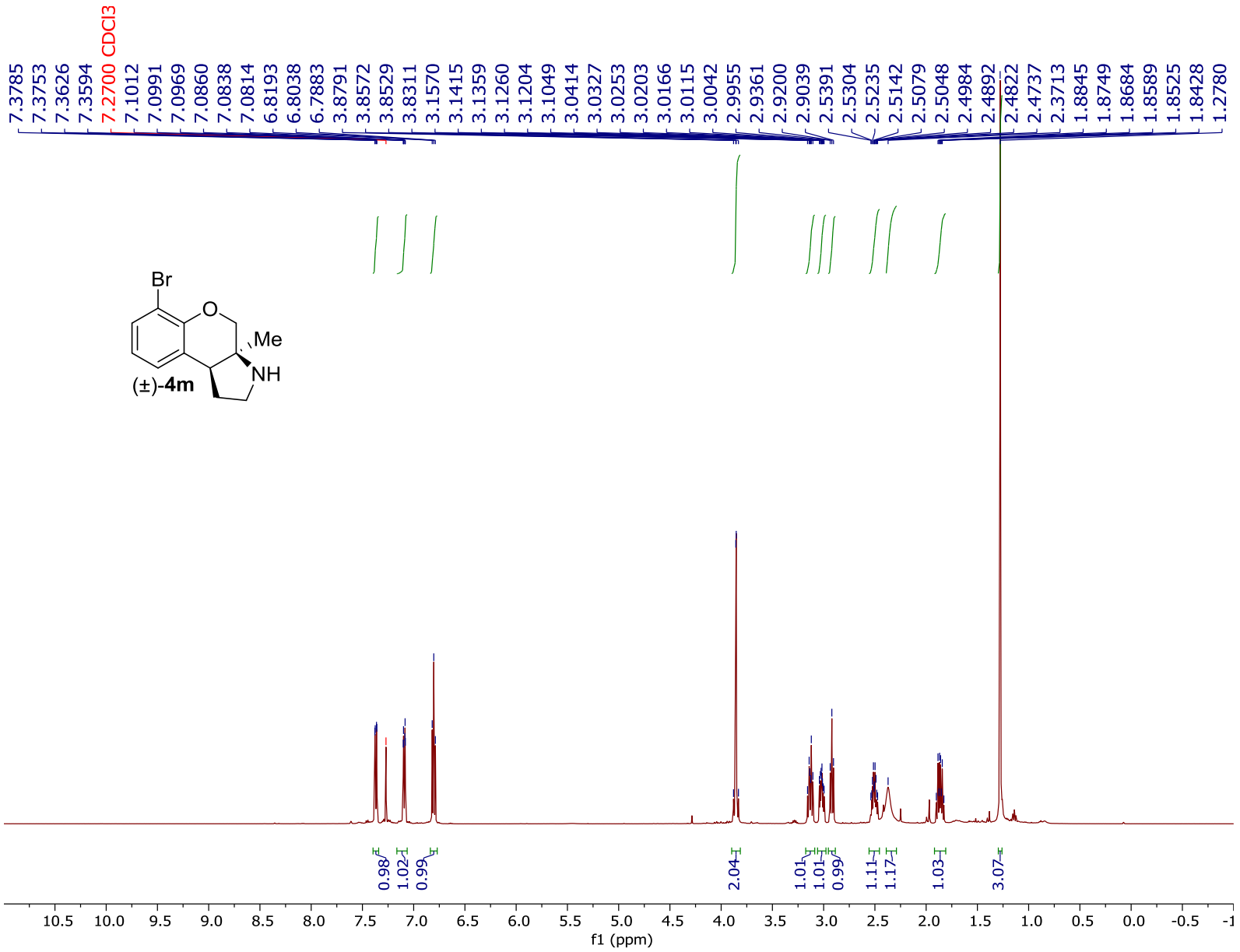
Compound 4k, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



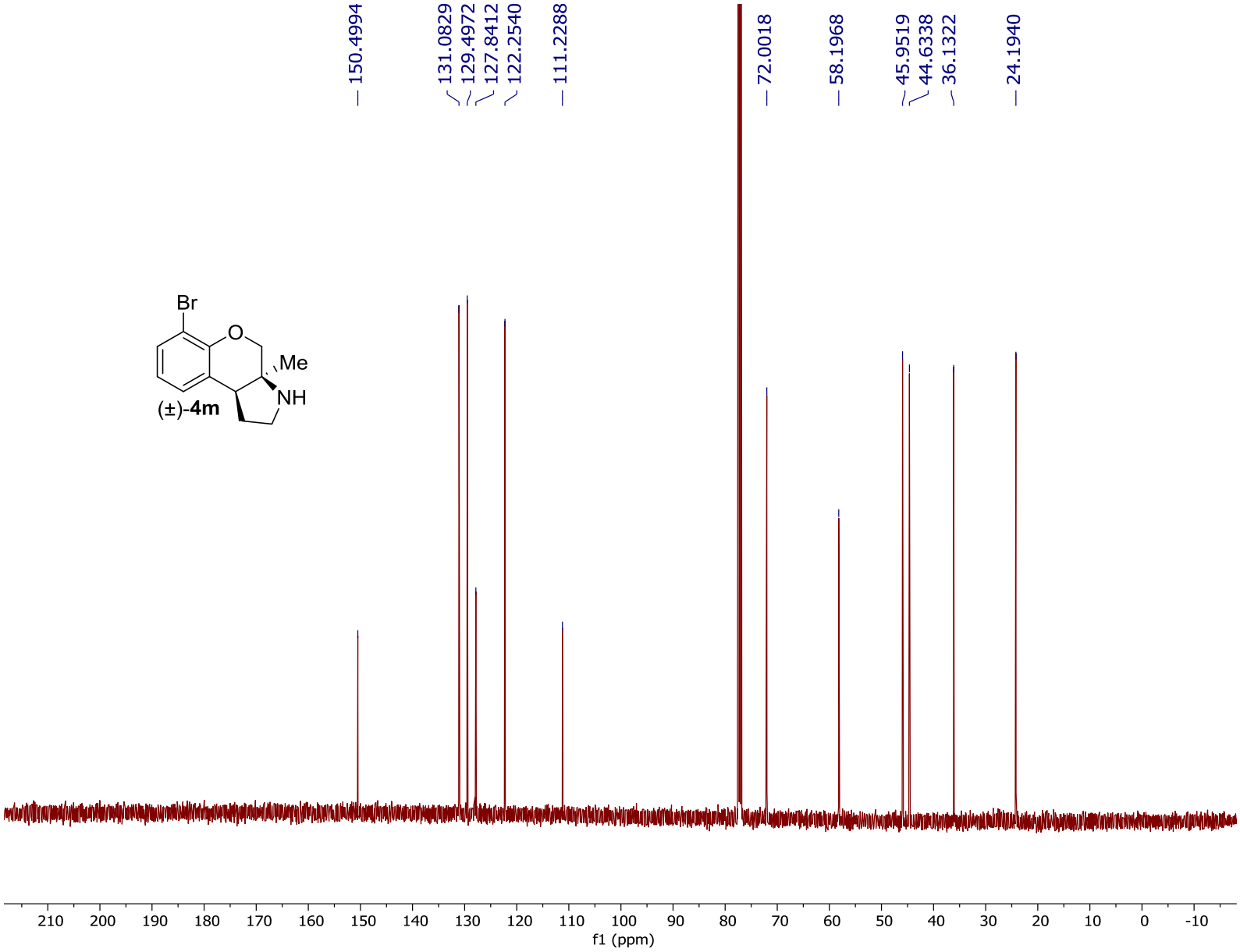
Compound 4l, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



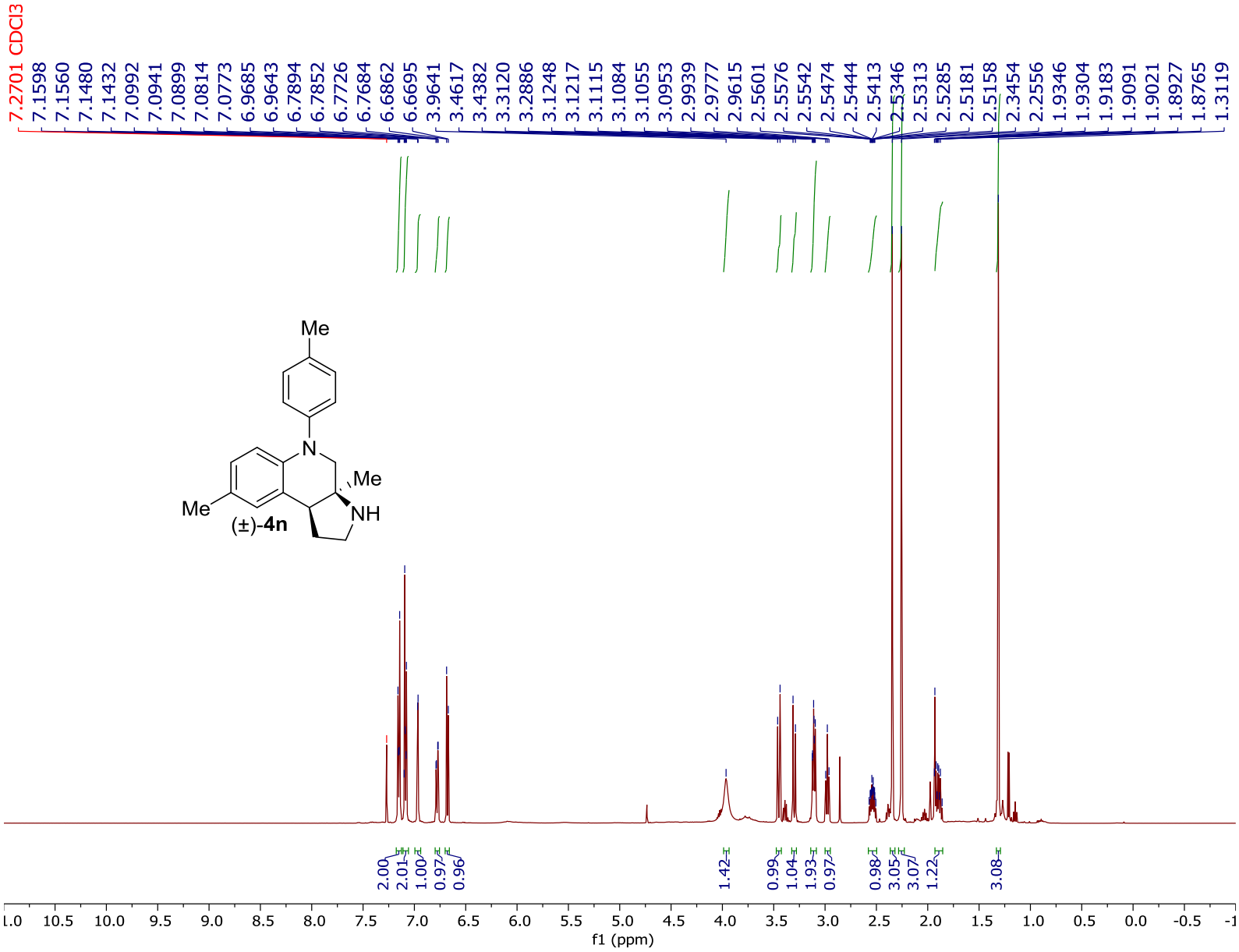
Compound 4l, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



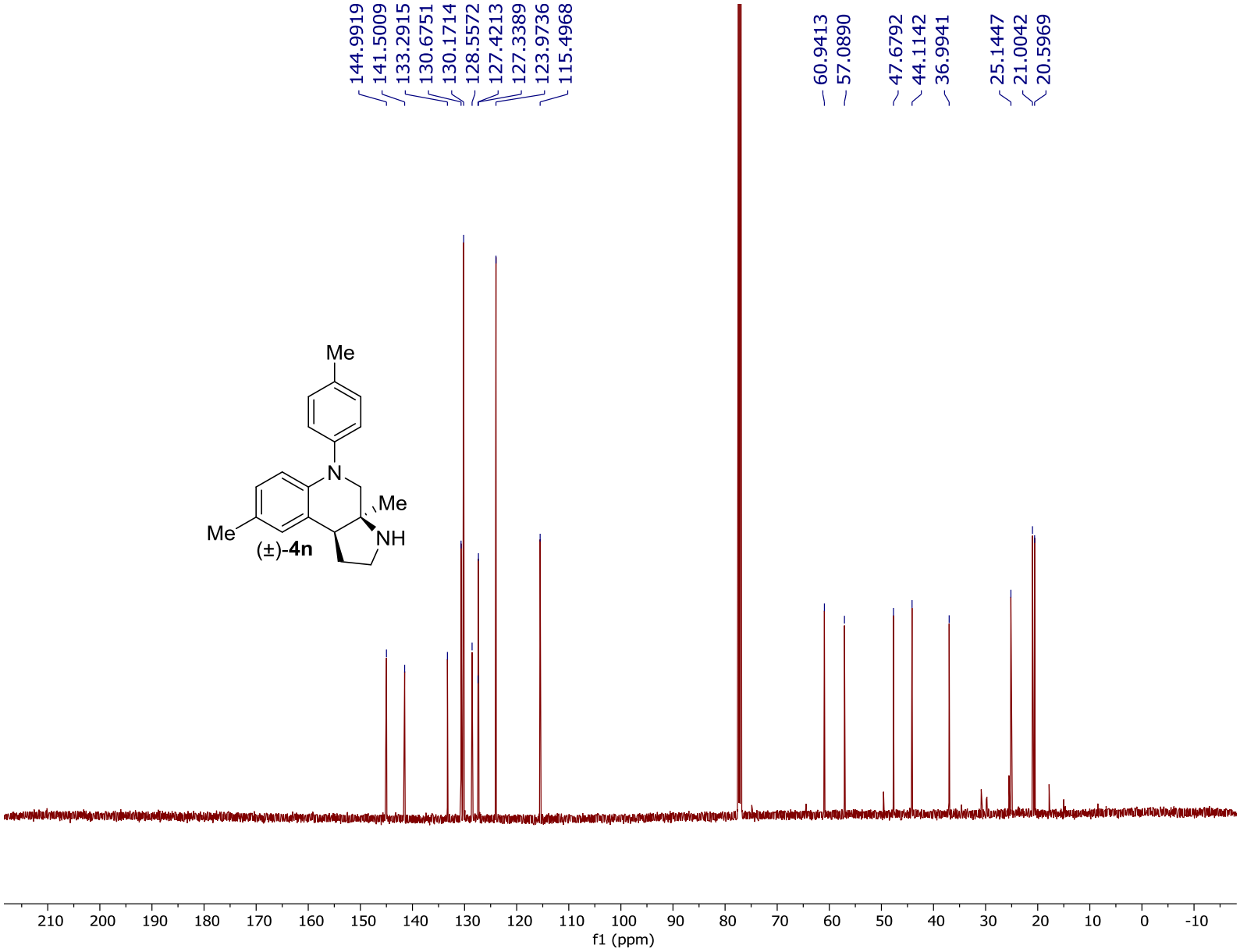
Compound 4m, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



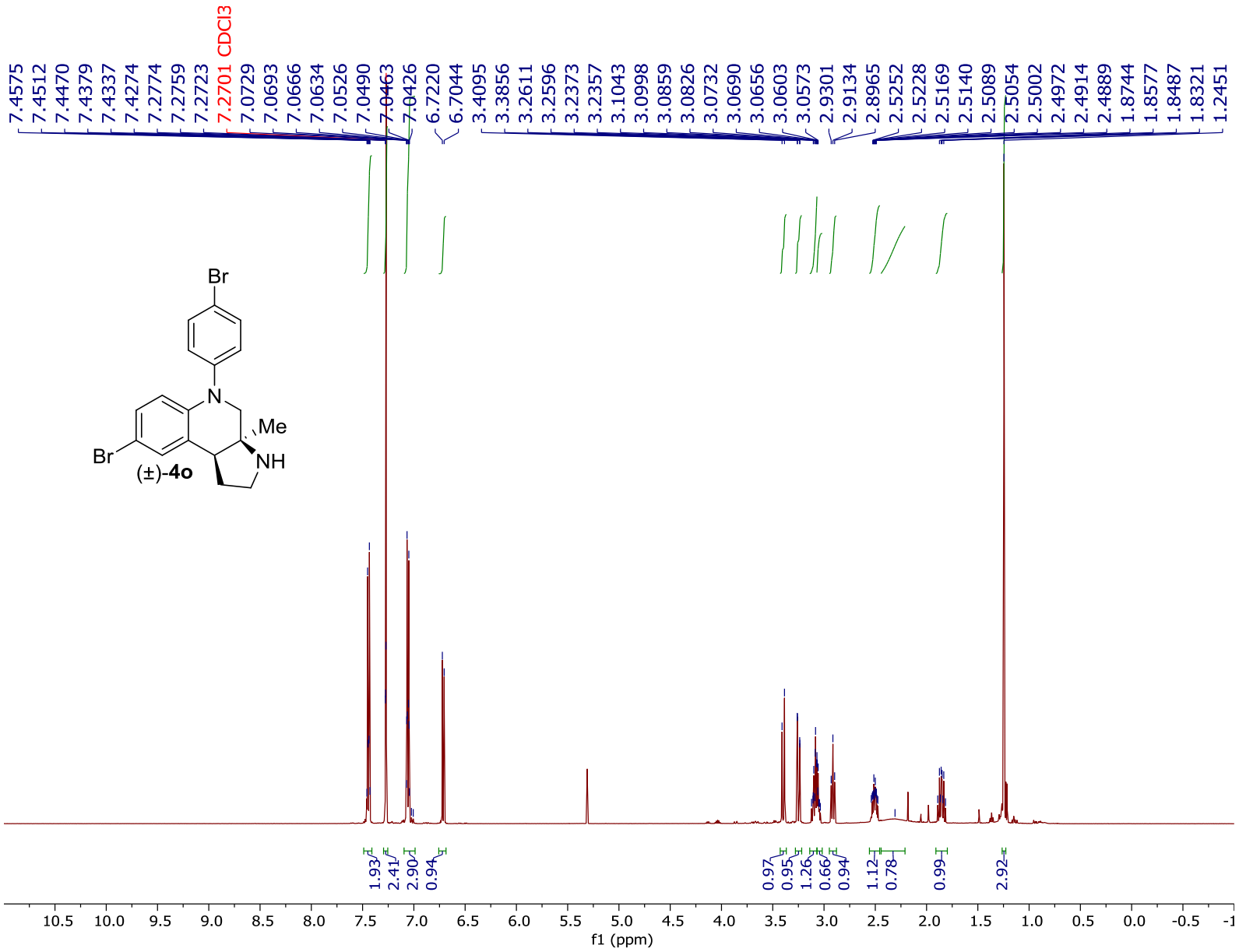
Compound 4m, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



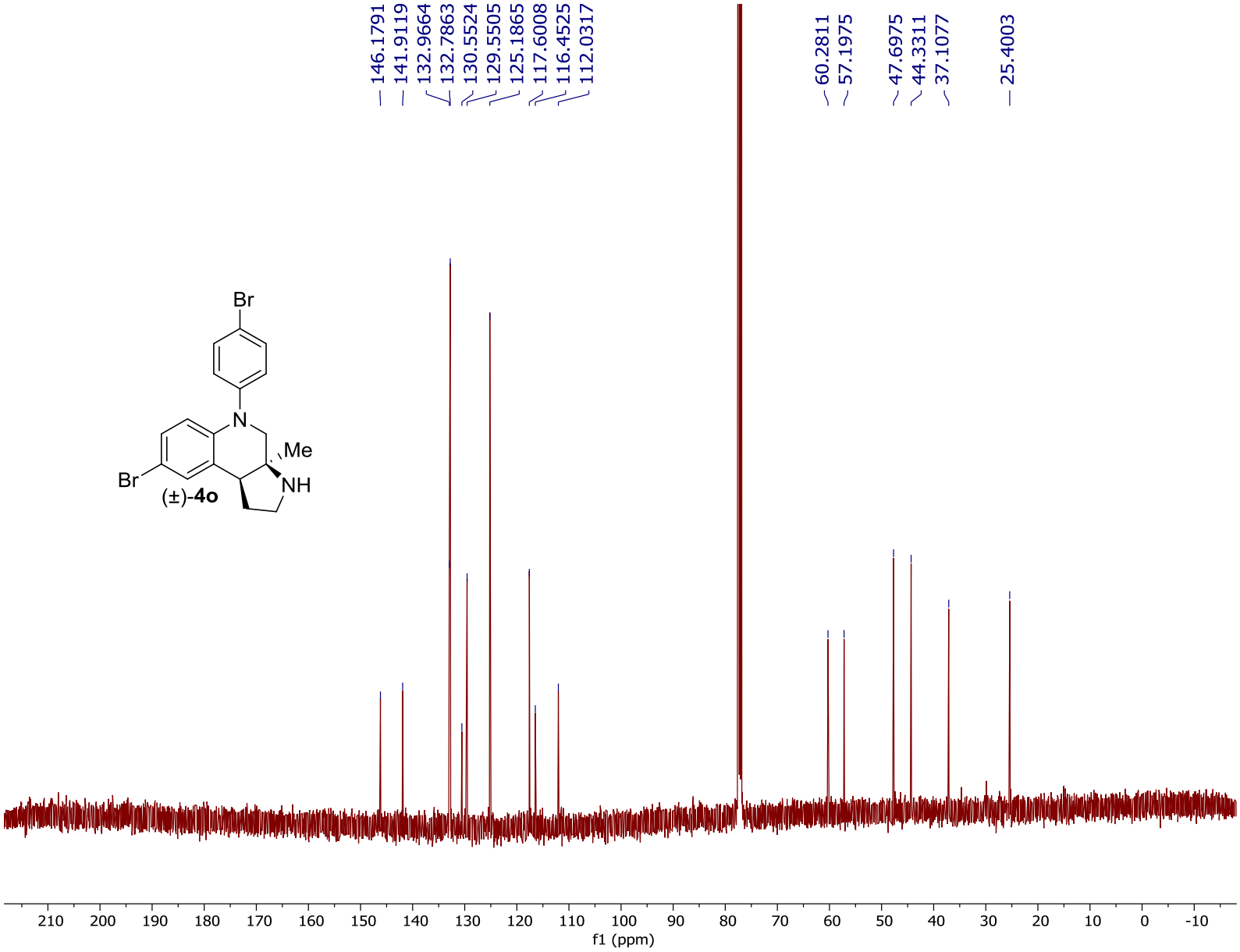
Compound 4n, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



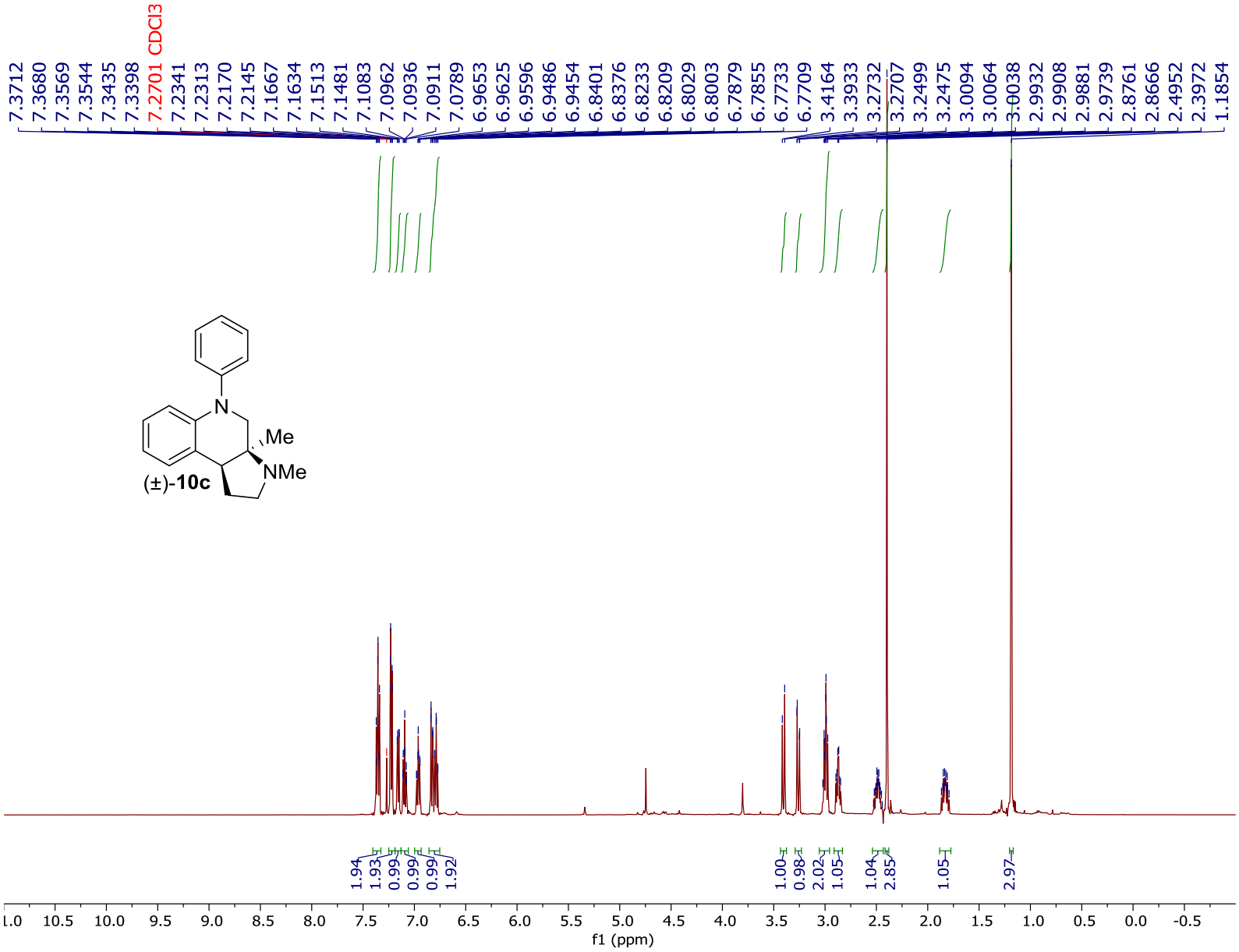
Compound 4n, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



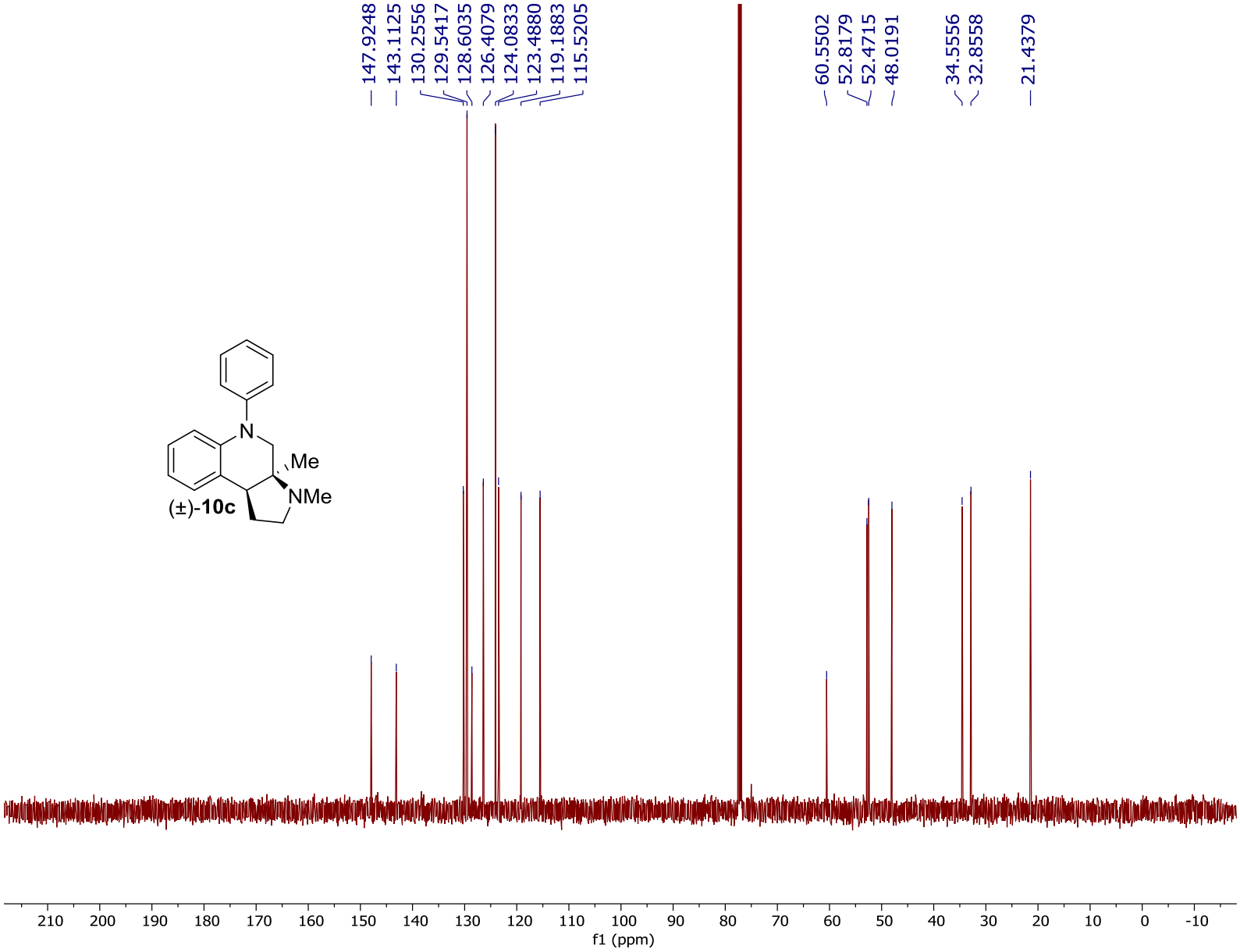
Compound 4o, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



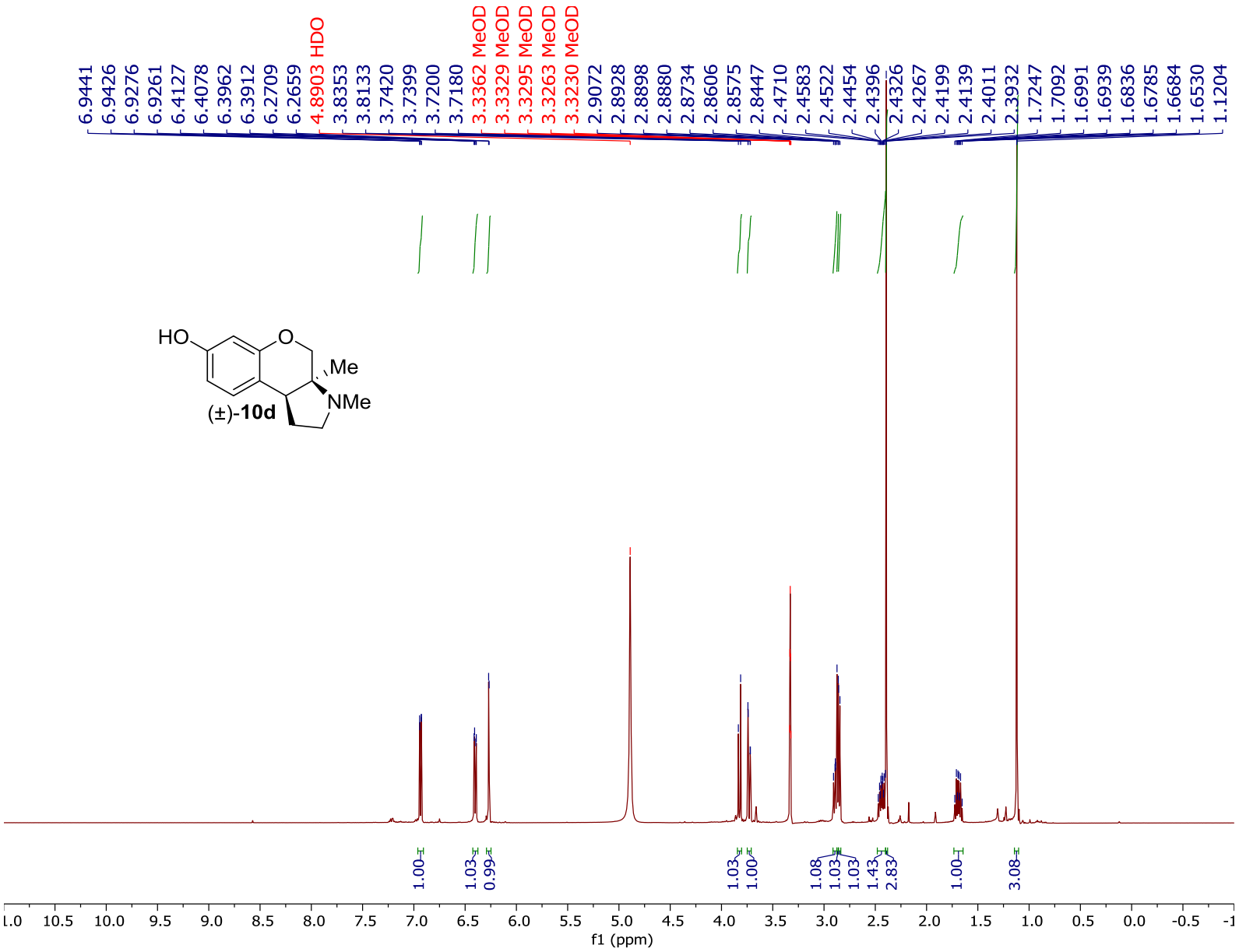
Compound 4o, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



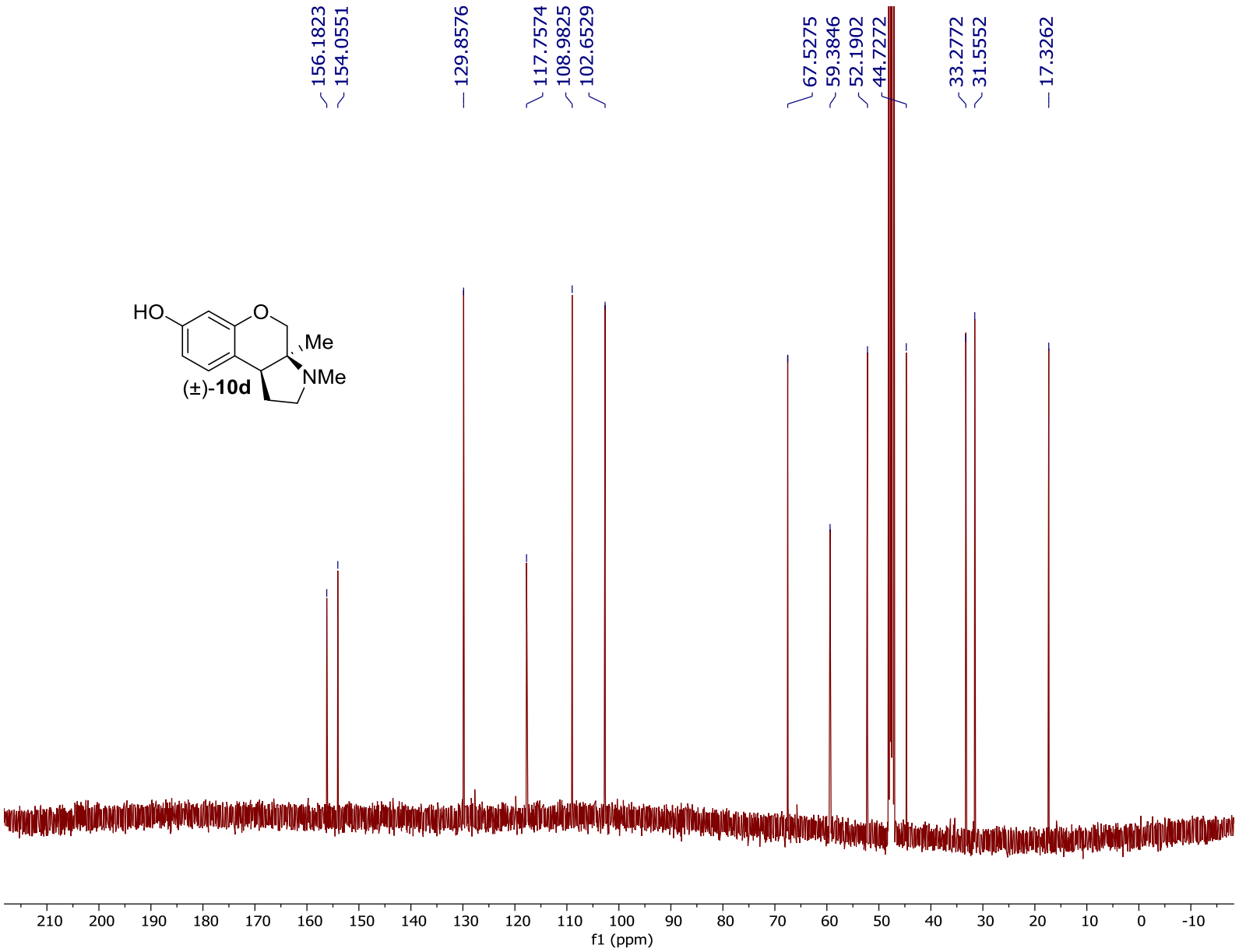
Compound 10c, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



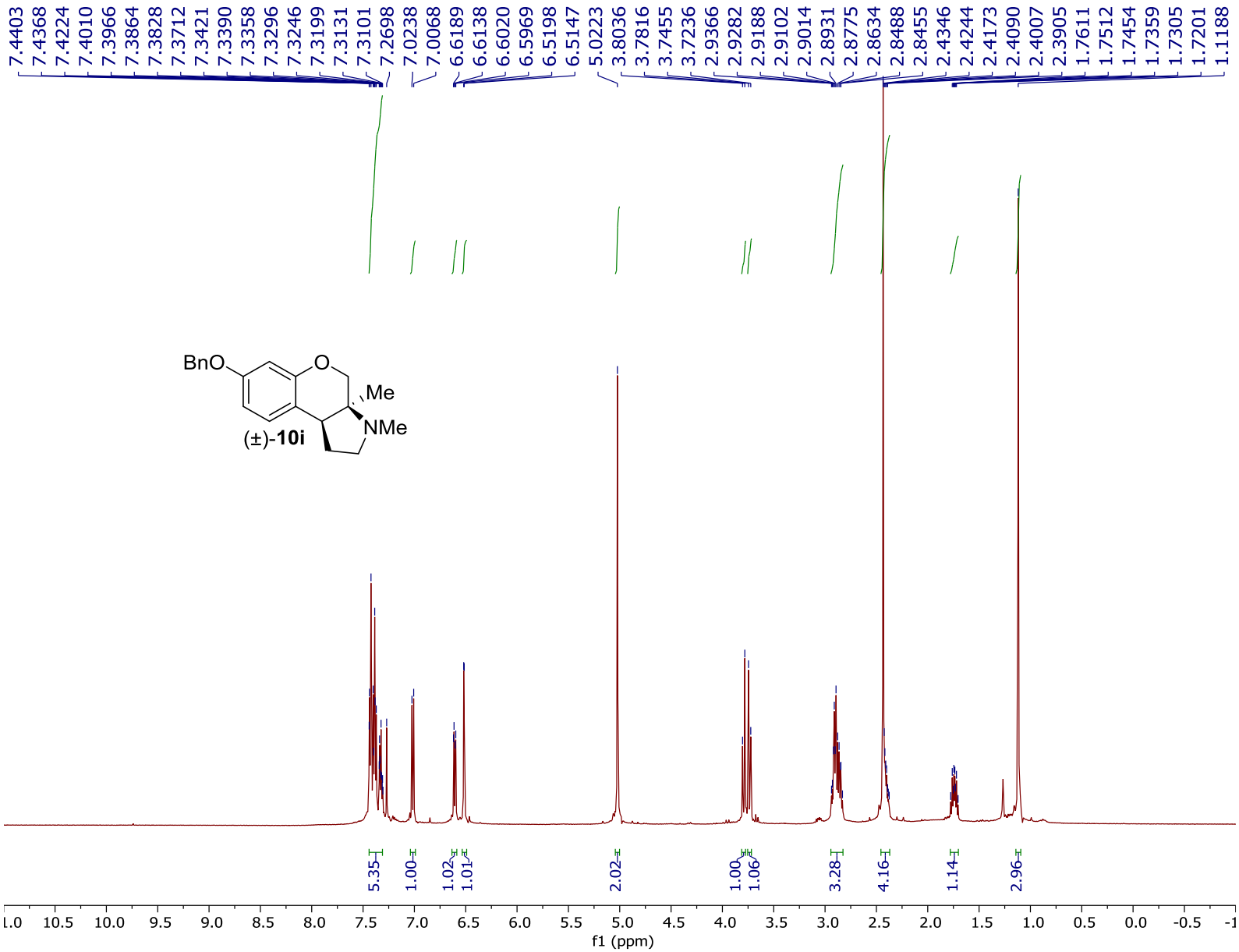
Compound 10c, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



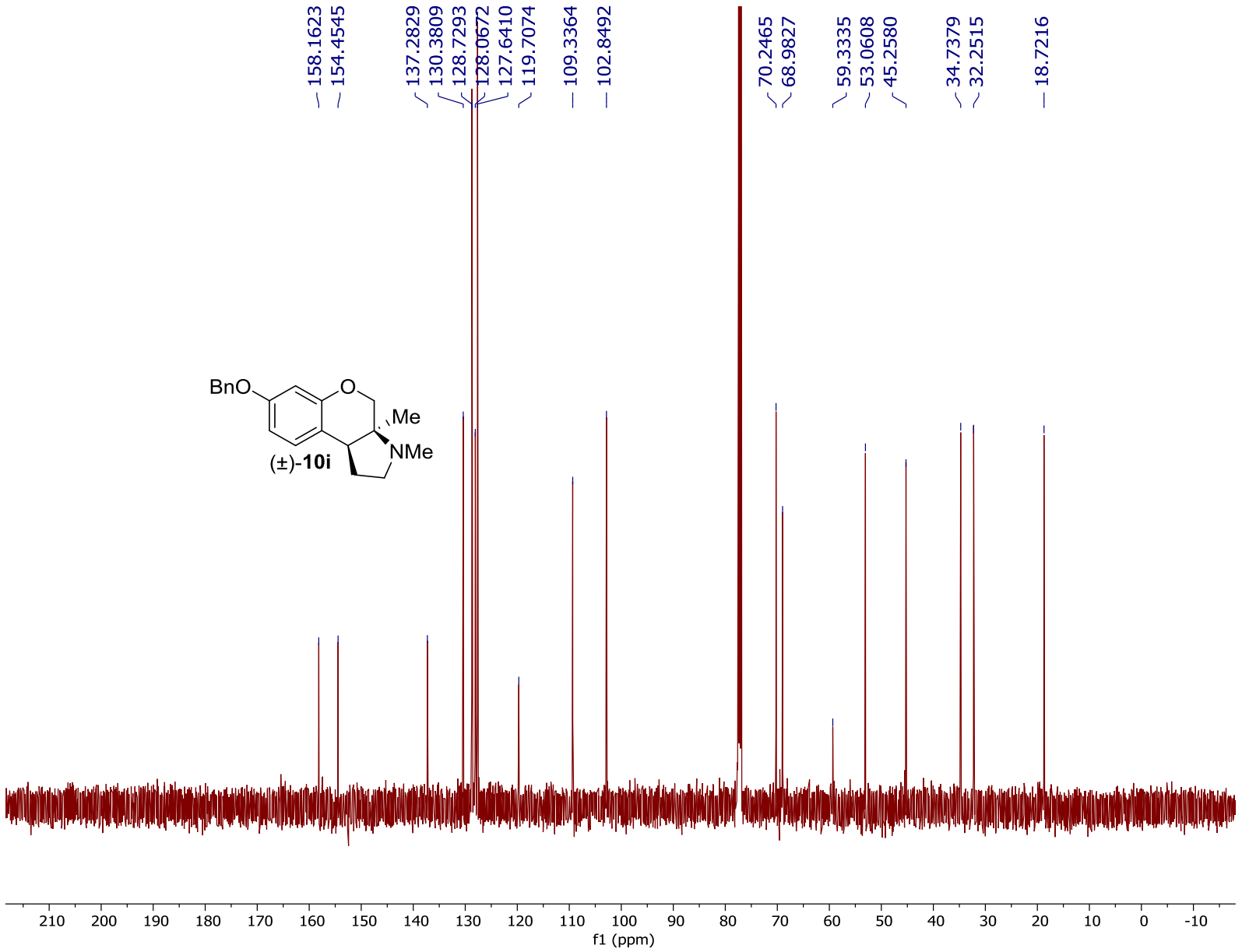
Compound 10d, 500 MHz ^{1}H NMR Spectrum in CD_3OD



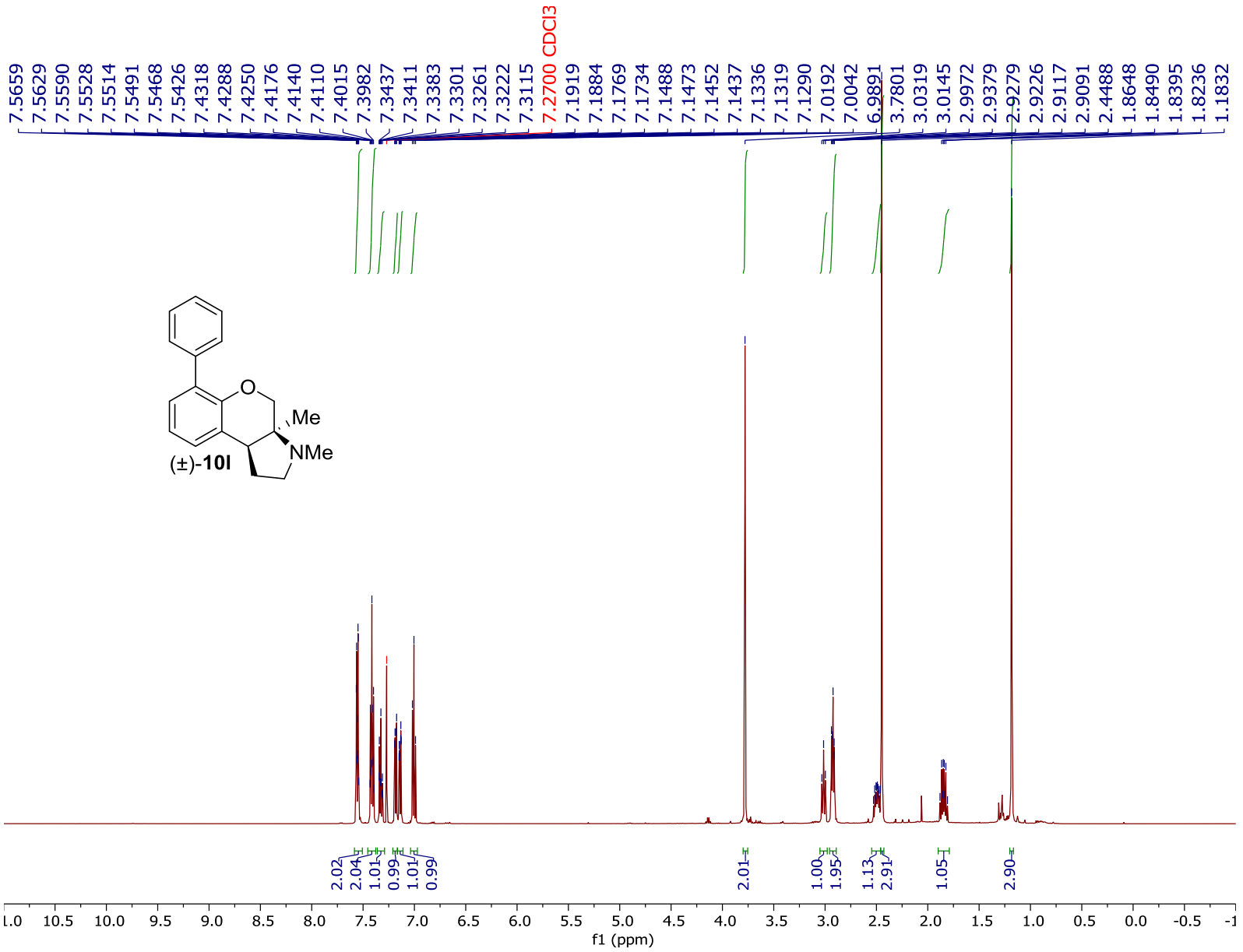
Compound 10d, 126 MHz ^{13}C NMR Spectrum in CD_3OD



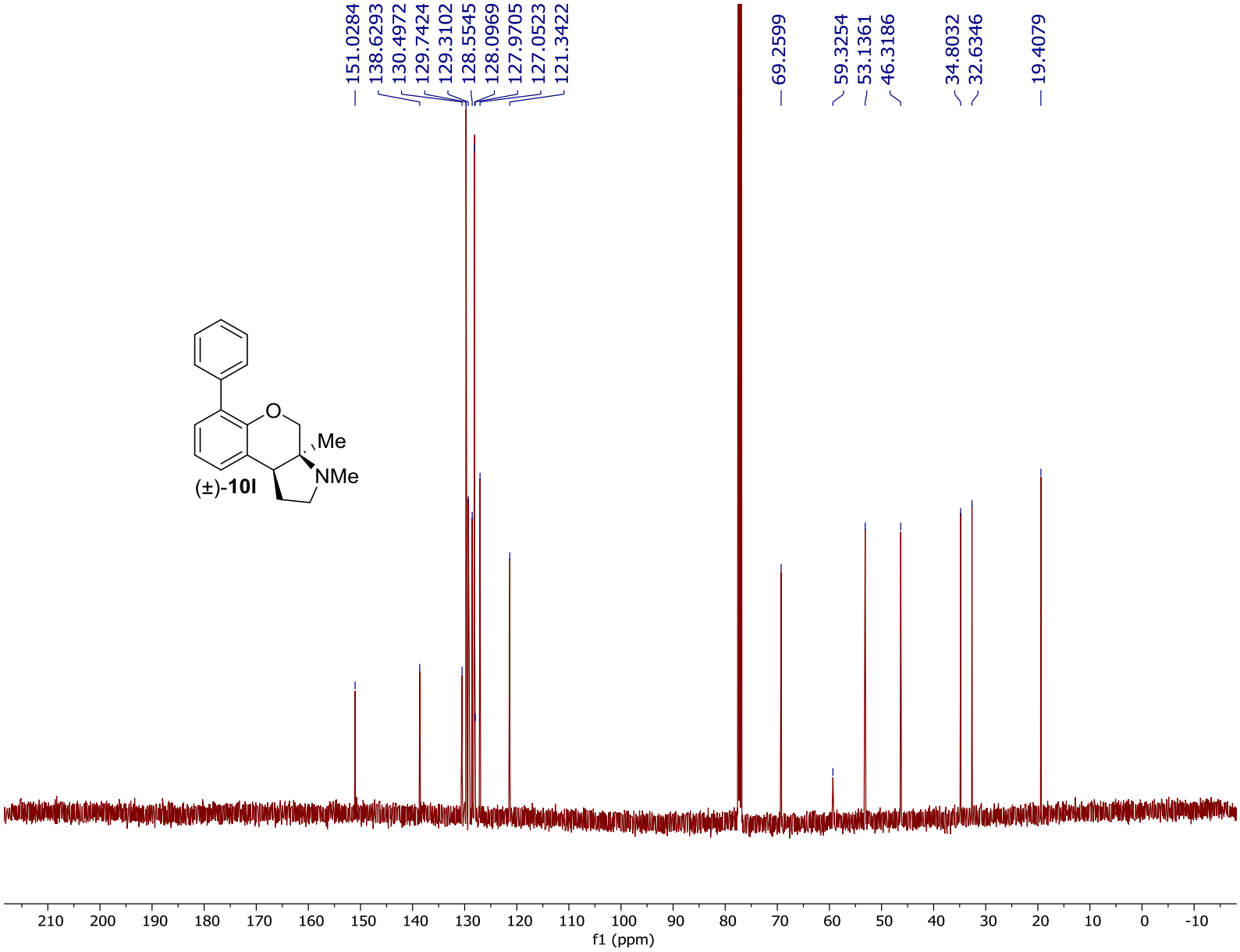
Compound 10i, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



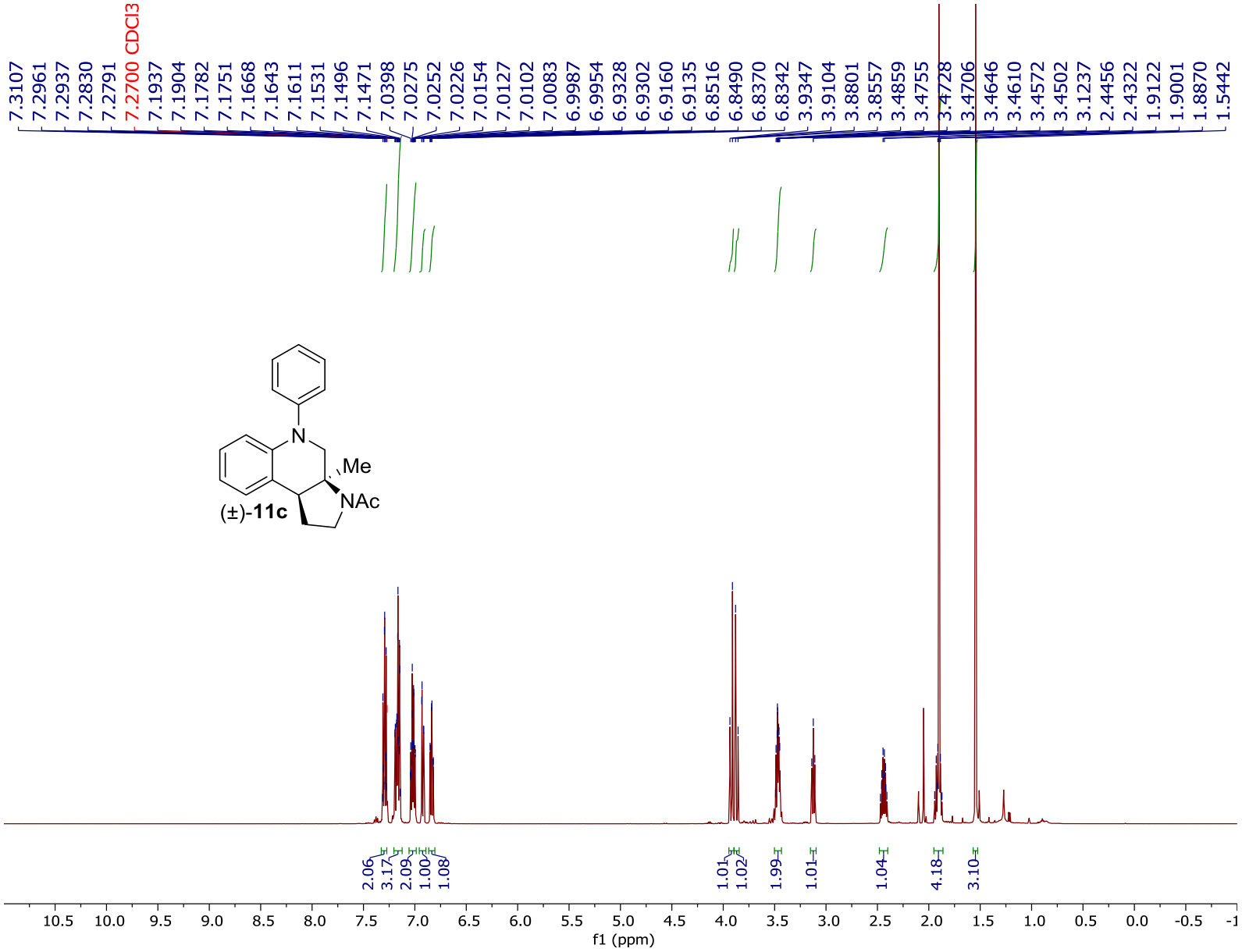
Compound 10i, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



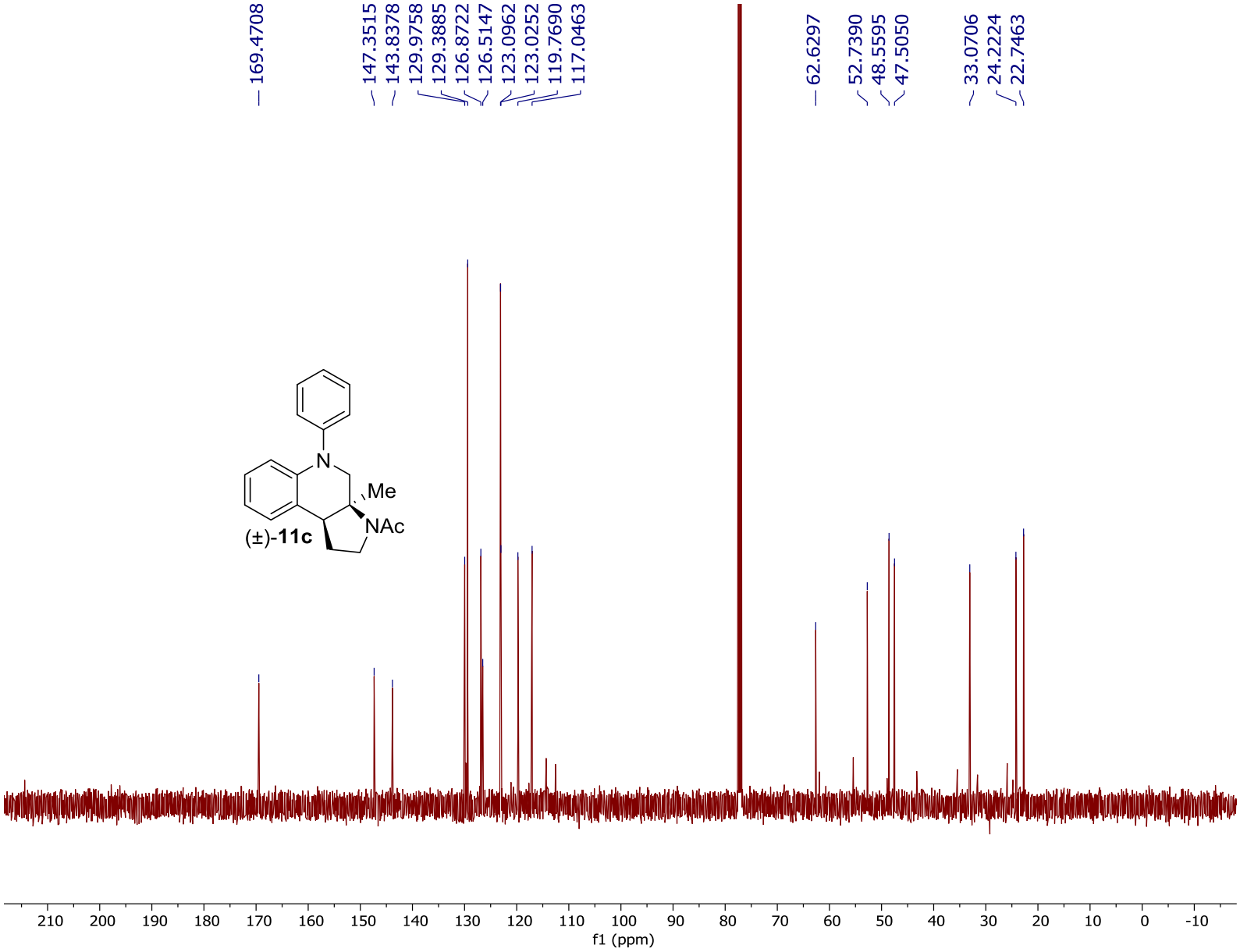
Compound 10l, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



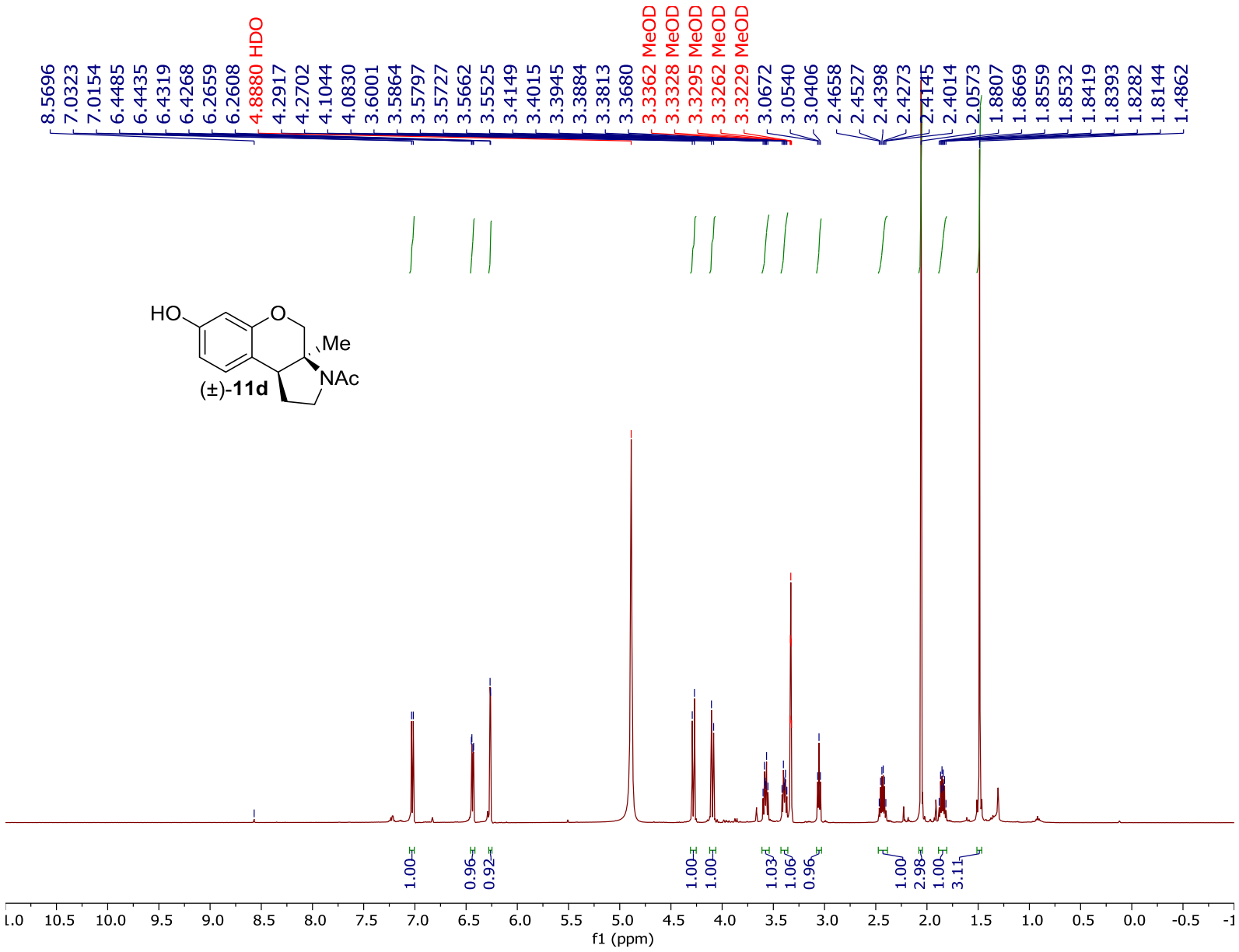
Compound 10l, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



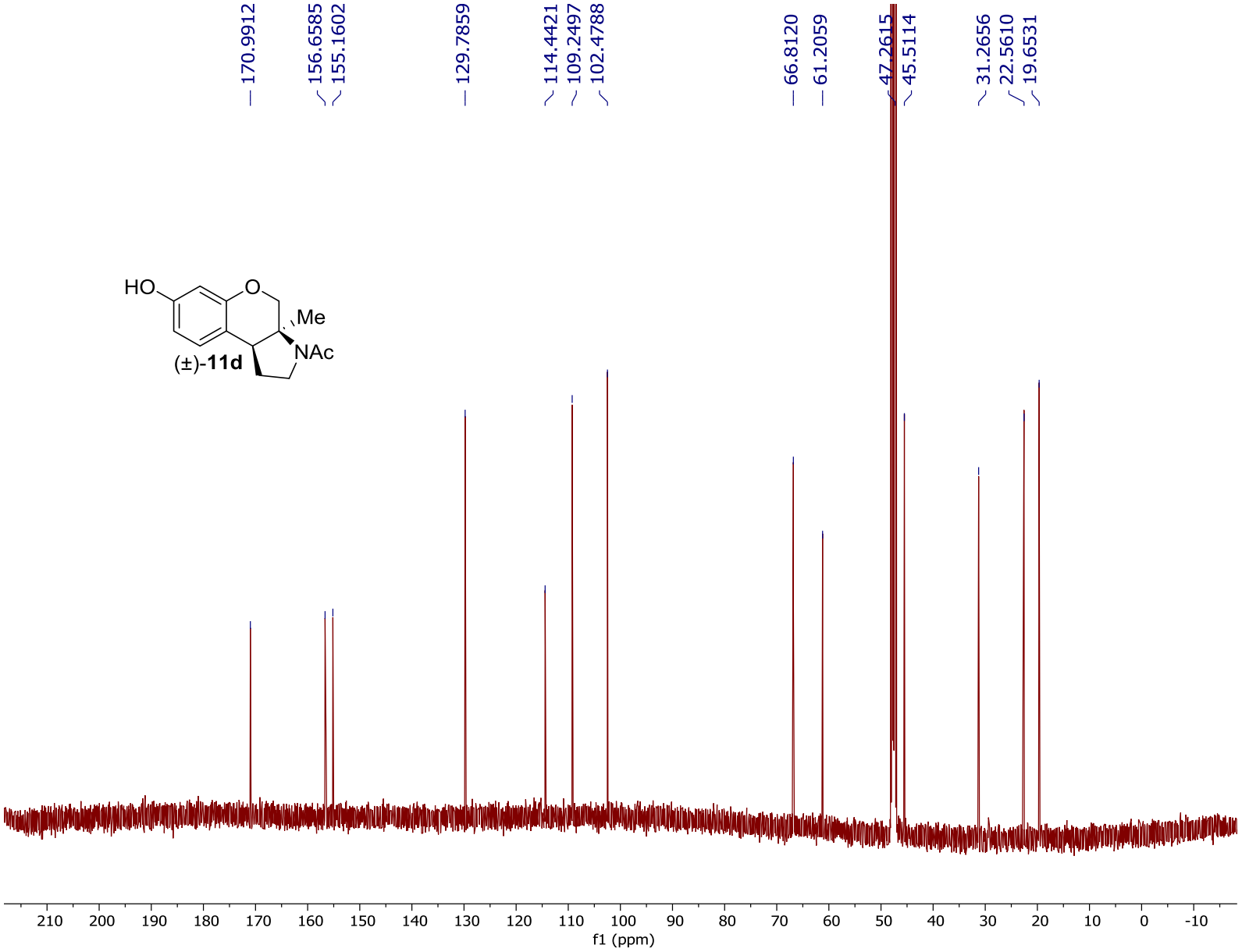
Compound 11c, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



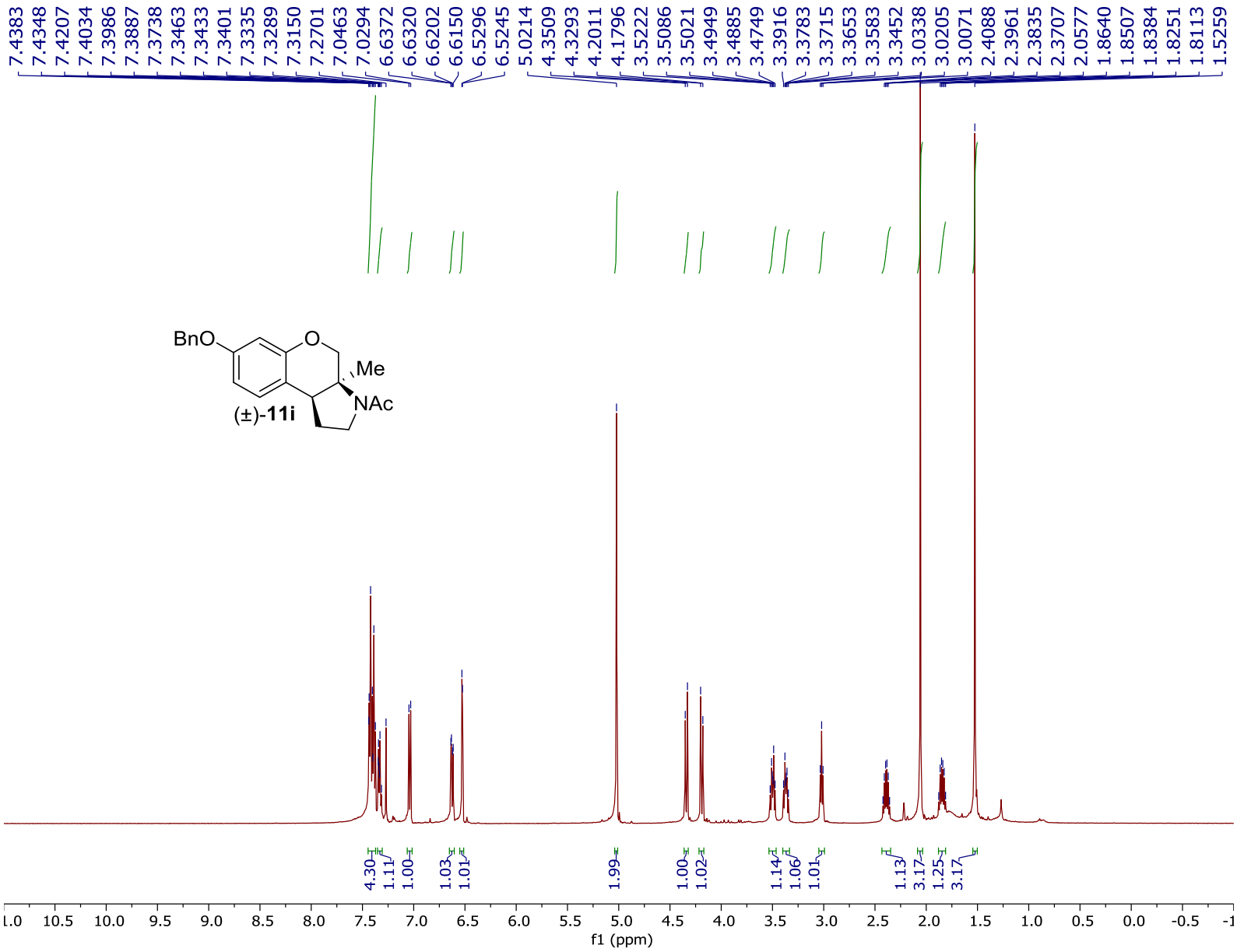
Compound 11c, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



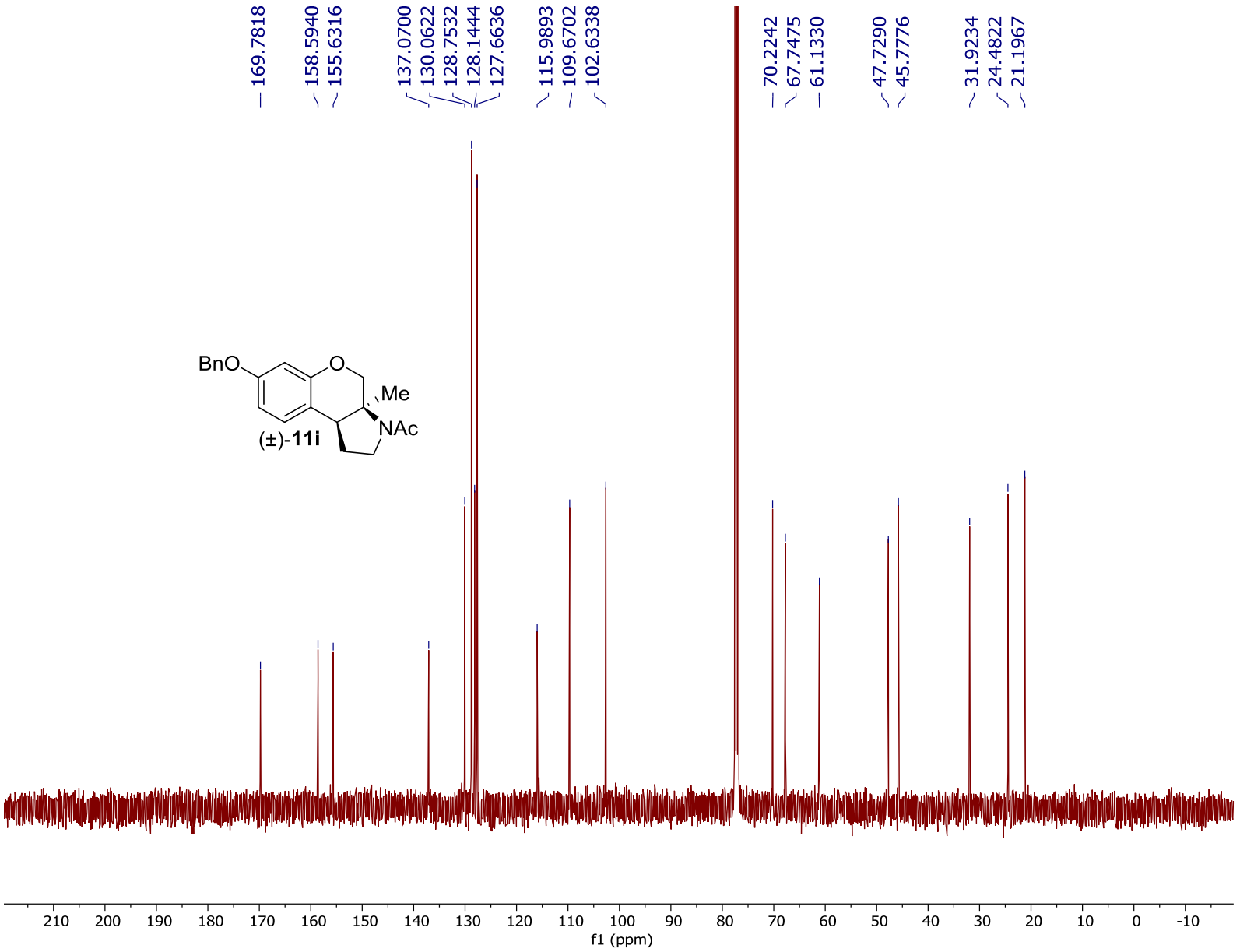
Compound 11d, 500 MHz ^{1}H NMR Spectrum in CD_3OD



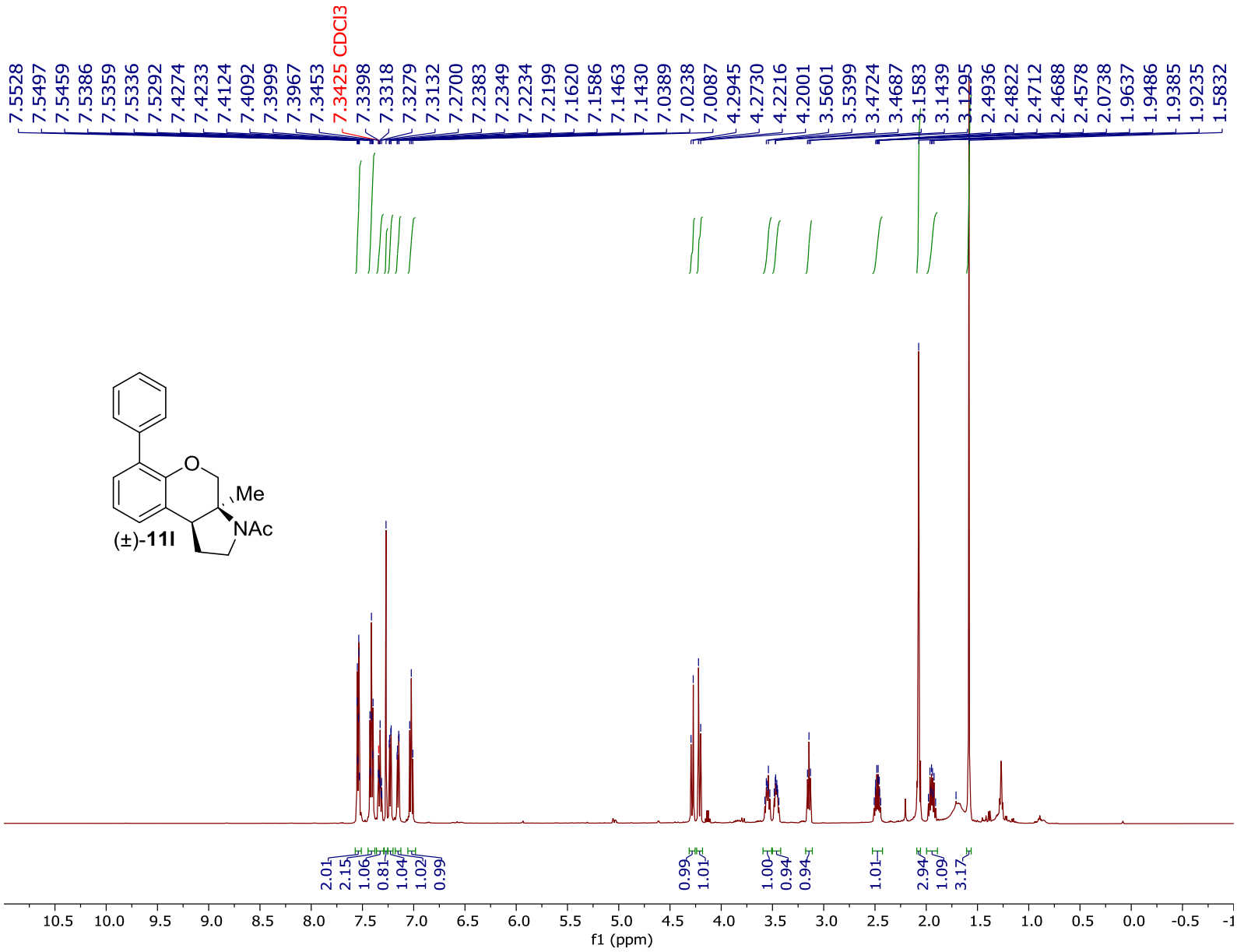
Compound 11d, 126 MHz ^{13}C NMR Spectrum in CD_3OD



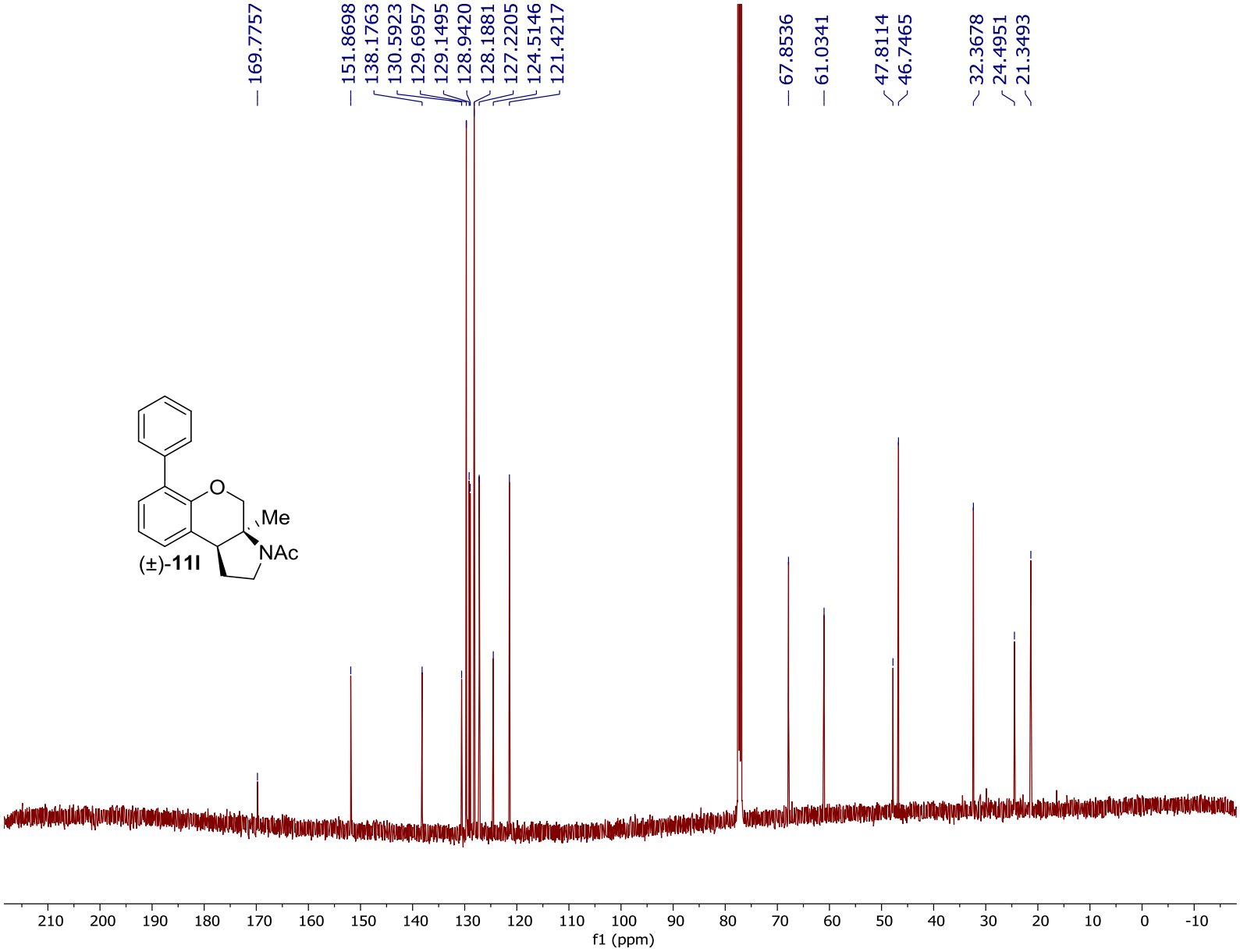
Compound 11i, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



Compound 11i, 126 MHz ^{13}C NMR Spectrum in $CDCl_3$



Compound 11l, 500 MHz ^{1}H NMR Spectrum in $CDCl_3$



Compound 11l, 101 MHz ^{13}C NMR Spectrum in $CDCl_3$