Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Nickel-Catalyzed Intramolecular C–O Bond Formation: Synthesis of Cyclic Enol Ethers

*Seo-Jung Han, Ryohei Doi, and Brian M. Stoltz**

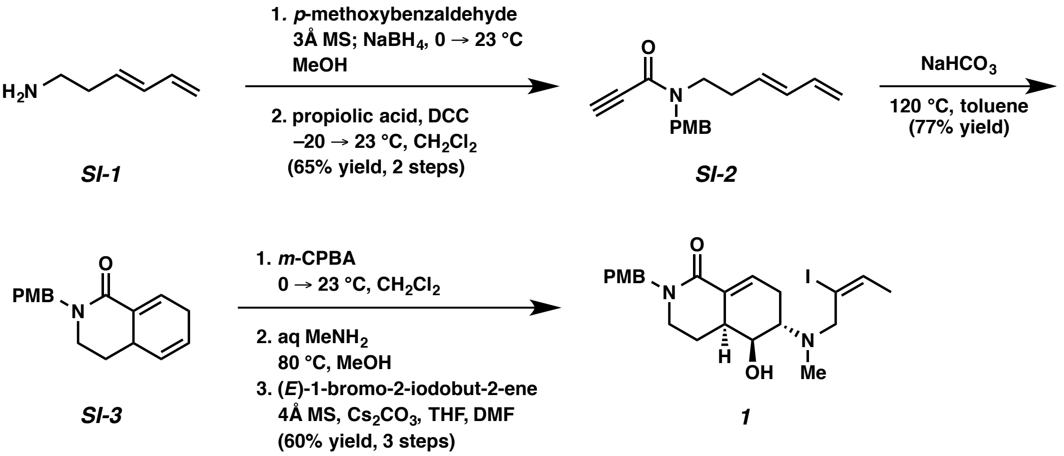
anie_201601991_sm_miscellaneous_information.pdf

Table of Contents:

Materials and Methods.

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. THF, Et_2O, CH_2Cl_2, toluene, benzene, CH_3CN, and dioxane were dried by passage through an activated alumina column under argon. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. Commercially available reagents were purchased from Sigma-Aldrich, Acros Organics, TCI, Oakwood chemicals, Strem, or Alfa Aesar and used as received unless otherwise stated. $Ni(COD)_2$ and NiI_2 were purchased from Strem. $NiBr_2$(dme) was purchases from Aldrich. Zinc dust or powder purchased from Aldrich worked well for the reaction but Zinc powder (99.999%) purchased from Strem gave poor conversion. Reaction temperatures were controlled by an IKAmag temperature modulator unless otherwise indicated. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, $KMnO_4$ or PMA (phosphomolybdic acid) staining. Silicycle Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.064 mm) was used for flash column chromatography. ^1H NMR spectra were recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm), $CHDCl_2$ (δ 5.32) or C_6HD_6 (δ 7.16 ppm). ^{13}C NMR spectra are recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers (75 MHz, 126 MHz, and 151 MHz, respectively) and are reported relative to $CHCl_3$ (δ 77.16 ppm), $CHDCl_2$ (δ 53.84) or C_6HD_5 (δ 128.06 ppm). ^{19}F NMR spectra are recorded on a Varian Mercury 300 MHz (at 282 MHz). ^{19}F NMR spectra are reported relative to $CFCl_3$(δ 0.0 ppm). Data for ^1H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d= broad doublet, app = apparent. Data for ^{13}C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode, or Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+).

Experimental Procedures and Spectroscopic Data



To a solution of amine **SI-1** (6.66 g, 68.5 mmol, 1.00 equiv), which was prepared by the literature procedure[1], in MeOH (171 mL) were added *p*-methoxybenzaldehyde (10.0 mL, 82.3 mmol, 1.20 equiv) and 3Å MS (18.8 g). The reaction mixture was stirred at 23 °C for 17 h. Then, $NaBH_4$ (5.20g, 0.137 mol, 2.00 equiv) was added to the solution at 0 °C. The solution was stirred at 23 °C for 12 h. After the reaction was done, water (40 mL) was added at 0 °C. The aqueous phase was extracted with EtOAc (3 x 80.0 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the PMB-amine, which was used without further purification.

A solution of propiolic acid (4.64 mL, 75.4 mmol, 1.10 equiv) in CH_2Cl_2 (343 mL) was cooled to 0 °C. DCC (15.6g, 75.4 mmol, 1.10 equiv) and the PMB-amine (68.5 mmol, 1.00 equiv) were added to the reaction mixture sequentially. The mixture was warmed to 23 °C and stirred for 30 min. The solvent was evaporated and the residue was purified by flash column chromatography (1:4 EtOAc:hexanes) on silica gel to give amide **SI-2** (12.0g, 65% yield, 2 steps).

To a stirred solution of amide **SI-2** (12.0 g, 44.6 mmol, 1.00 equiv) in toluene (558 mL) was added solid $NaHCO_3$ (4.50g, 53.5 mmol, 1.20 equiv). The reaction mixture was heated to 120 °C for 48 h. After the reaction was done, water (200 mL) was added. The aqueous phase was extracted with EtOAc (3 x 120 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo.* The residue was purified by flash column chromatography (1:4 EtOAc:hexanes) on silica gel to give lactam **SI-3** (9.25g, 77% yield).

To a stirred solution of lactam **SI-3** (339 mg, 1.26 mmol, 1.00 equiv) in CH_2Cl_2 (6.30 mL) at 0 °C was added *m*-CPBA ($\leq$77%, 1.89 mmol, 424 mg, 1.50 equiv), and the mixture was stirred for 3 h at 23 °C. The reaction mixture was quenched with sat.

---

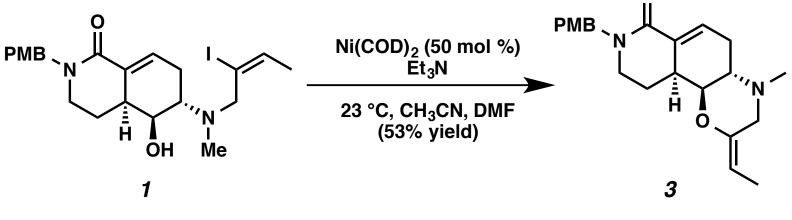
[1] (a) Miller, C. A.; Batey, R. A. *Org. Lett.* **2004**, *6*, 699–702. (b) Grieco, P. A.; Galatsis, P.; Spohn, R. F. *Tetrahedron* **1986**, *42*, 2847–2853. (c) Nieto-García, O.; Alonso, R. *J. Org. Chem.* **2013**, *78*, 2564–2570.

$NaHSO_3$ and sat. $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (3 x 6.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to furnish the epoxide, which was used without further purification.

To a solution of epoxide (1.26 mmol, 1.00 equiv) in MeOH (6.30 mL) was added aq $MeNH_2$ (40 wt.% in H_2O, 12.6 mmol, 10.9 mL, 10.0 equiv). The reaction mixture was stirred at 80 °C for 12 h. After the reaction was done, water (6.00 mL) was added. The aqueous phase was extracted with EtOAc (3 x 8.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to afford the aminoalcohol, which was used without further purification.

To a solution of the aminoalcohol (1.26 mmol, 1.00 equiv) in THF (3.15 mL) and DMF (3.15 mL) were added 4Å MS (443 mg), (*E*)-1-bromo-2-iodobut-2-ene (411 mg, 1.58 mmol, 1.25 equiv) and Cs_2CO_3 (415 mg, 1.27 mmol, 1.01 equiv) at 23 °C. The reaction mixture was stirred at 23 °C for 24 h. The resulting suspension was filtered and washed with EtOAc (5.00 mL). The combined organic phases were extracted with EtOAc (3 x 6.00 mL). The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (2:1 EtOAc:hexane) on silica gel to give vinyl iodide **1** (375 mg, 60% yield, 3 steps).

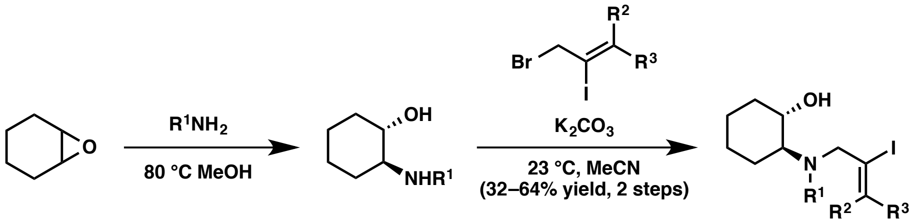
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.75 (dt, *J* = 6.7, 2.1 Hz, 1H), 6.47 – 6.41 (m, 1H), 4.71 (d, *J* = 14.4 Hz, 1H), 4.41 (d, *J* = 14.4 Hz, 1H), 3.96 – 3.89 (m, 2H), 3.80 (s, 3H), 3.35 – 3.27 (m, 2H), 3.20 (d, *J* = 13.6 Hz, 1H), 3.11 (d, *J* = 13.6 Hz, 1H), 2.99 – 2.91 (m, 1H), 2.61 (td, *J* = 10.7, 4.4 Hz, 1H), 2.39 – 2.26 (m, 2H), 2.22 (s, 3H), 2.20 – 2.14 (m, 1H), 1.74 (d, *J* = 7.1 Hz, 3H), 1.56 – 1.45 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 159.1, 139.0, 133.7, 130.3, 129.6, 129.5, 114.1, 103.3, 66.8, 60.1, 57.3, 55.4, 49.7, 46.9, 39.3, 35.6, 23.8, 22.3, 17.1; IR (Neat Film NaCl) 3416, 2927, 1663, 1613, 1512, 1454, 1246, 1175, 1034, 817, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{30}IN_2O_3$ $[M+H]^+$: 497.1296; found: 497.1296.



To a solution of vinyl iodide **1** (20.0 mg, 0.0402 mmol, 1.00 equiv) and Et_3N (56.0 μL, 0.402 mmol, 10.0 equiv) in CH_3CN (2.01 mL) and DMF (1.01 mL) in a scintillation vial at 23 °C was added $Ni(COD)_2$ (6.00 mg, 0.0201 mmol, 0.50 equiv) in a nitrogen-filled glove box. The reaction mixture was stirred at 23 °C for 120 min, and then, BHT (18.0 mg, 0.0804 mmol, 2.00 equiv) was added. After being stirred for 20 min, the vial was removed from the glovebox and uncapped. Saturated $NaHCO_3$ aqueous solution was added and the mixture was extracted with Et_2O (3 x 2.00 mL), the combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (1:20 MeOH:CH_2Cl_2) to give morpholine derivative **3** (7.85 mg, 53% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.66 (dt, *J* = 6.8, 1.9 Hz, 1H), 5.03 (qd, *J* = 7.1, 1.4 Hz, 1H), 4.63 (d, *J* = 14.4 Hz, 1H), 4.48 (d, *J* = 14.4 Hz, 1H), 3.78 (s, 3H), 3.76 (d, *J* = 7.1 Hz, 1H), 3.54 (d, *J* = 12.5 Hz, 1H), 3.29 – 3.24 (m, 2H), 2.86 – 2.74 (m, 1H), 2.68 – 2.60 (m, 2H), 2.32 (s, 3H), 2.30 – 2.24 (m, 1H), 2.12 – 1.96 (m, 2H), 1.58 (dd, *J* = 7.1, 1.3 Hz, 3H), 1.55 – 1.49 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.0, 158.9, 148.5, 133.5, 129.5, 129.0, 113.9, 103.5, 77.8, 58.4, 52.2, 49.5, 46.6, 42.4, 37.9, 28.9, 24.3, 11.0; IR (Neat Film NaCl) 3416, 2927, 1663, 1613, 1512, 1454, 1246, 1175, 1034, 817, 732 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{29}N_2O_3$ $[M+H]^+$: 369.2173; found: 369.2212.

Typical procedure for aminocyclohexanols 4

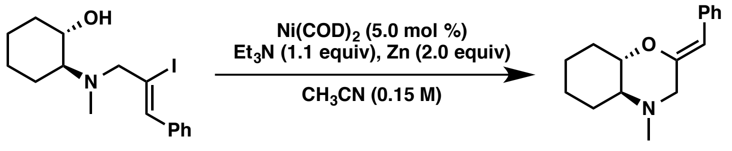


SI-4 ***SI-5*** ***4***

To a scintillation vial were added cyclohexene oxide **SI-4** (5.09 mmol, 1.00 equiv), R^1NH_2 (5.09 mmol, 1.00 equiv), and MeOH (2.50 mL). The reaction mixture was heated to 80 °C for 12 h. The solvent was evaporated to give the corresponding aminocyclohexanols **SI-5**, which were used without further purification.

To a solution of aminocyclohexanols **SI-5** (5.09 mmol, 1.00 equiv) in MeCN (25.0 mL) were added K_2CO_3 (25.5 mmol, 5.00 equiv) and allyl bromides (5.60 mmol, 1.10 equiv). The reaction mixture was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography, using mixture of hexanes and ethyl acetate as eluent to furnish the product **4**.

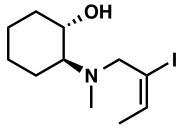
Representative procedure for cross-coupling of aminocyclohexanols 4



4c ***5c***

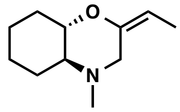
Ni-Catalyzed C–O bond formation experiments were performed in a nitrogen-filled glove box. To a solution of aminocyclohexanol **4c** (50.0 mg, 0.135 mmol, 1.00 equiv) in MeCN (0.900 mL) in a scintillation vial were added Et_3N (21.0 μL, 0.149 mmol, 1.10 equiv), Zn powder (17.7 mg, 0.270 mmol, 2.00 equiv), and $Ni(COD)_2$ (1.90 mg, 0.00673 mmol, 0.05 equiv). The reaction mixture was stirred at 23 °C for

24 h. After the reaction was done, the vial was removed from the glove box and uncapped. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (1:2 EtOAc:hexanes) to give **5c** (30.7 mg, 93% yield).



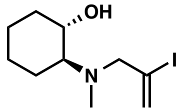
4a

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.41 (q, *J* = 7.1 Hz, 1H), 4.03 (s, 1H), 3.40 (td, *J* = 9.8, 4.5 Hz, 1H), 3.15 (d, *J* = 13.7 Hz, 1H), 3.08 (d, *J* = 13.9 Hz, 1H), 2.26 (ddd, *J* = 14.0, 10.2, 3.6 Hz, 1H), 2.18 (s, 3H), 2.15 – 2.11 (m, 1H), 1.79 (dt, *J* = 8.9, 2.0 Hz, 2H), 1.73 (d, *J* = 7.2 Hz, 3H), 1.31 – 1.17 (m, 4H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 138.3, 104.4, 69.3, 68.7, 57.3, 35.7, 33.3, 25.6, 24.2, 22.8, 17.0; IR (Neat Film NaCl) 3467, 2930, 2855, 1449, 1282, 1080, 1037 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{11}H_{21}NOI$ [M+H]$^+$: 310.0668; found: 310.0654.



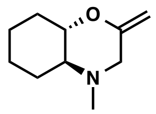
5a

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.02 (qd, *J* = 7.1, 1.6 Hz, 1H), 3.58 (d, *J* = 12.6 Hz, 1H), 3.35 – 3.23 (m, 1H), 2.62 (d, *J* = 12.6 Hz, 1H), 2.29 (s, 3H), 2.09 (dtd, *J* = 12.9, 3.7, 2.0 Hz, 1H), 1.94 (ddt, *J* = 11.9, 4.5, 2.6 Hz, 1H), 1.85 (s, br, 1H), 1.77 – 1.71 (m, 2H), 1.56 (dd, *J* = 7.1, 1.5 Hz, 3H), 1.42 – 1.33 (m, 1H), 1.33 – 1.22 (m, 2H), 1.14 – 1.02 (m, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 148.9, 103.3, 81.1, 67.4, 53.0, 42.0, 31.4, 28.1, 24.8, 24.4, 11.1; IR (Neat Film NaCl) 2934, 2861, 2779, 1682, 1451, 1192, 1108, 841 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{11}H_{20}NO$ [M+H]$^+$: 182.1545; found: 182.1538.



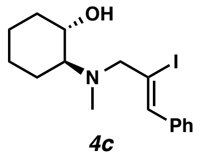
4b

^{1}H NMR (300 MHz, CDCl$_3$) δ 6.28 (q, *J* = 1.4 Hz, 1H), 5.86 (dt, *J* = 0.8, 1.6 Hz, 1H), 3.97 (s, 1H), 3.40 (m, 1H), 3.17 (d, *J* = 13.7 Hz, 1H), 2.96 (d, *J* = 13.7 Hz, 1H), 2.28 (m, 1H), 2.18 (s, 3H), 2.13 (m, 1H), 1.75 (m, 3H), 1.20 (m, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 126.8, 113.7, 69.3, 69.1, 64.8, 35.8, 33.1, 25.4, 24.0, 22.6; IR (neat film NaCl) 3470, 2930, 2855, 2796, 1616, 1448, 1079, 1036 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{10}H_{19}INO$, [M+H]$^+$: 296.0506; found: 296.0499.



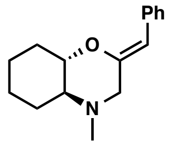
5b

^{1}H NMR (300 MHz, CDCl$_3$) δ 4.40 (s, 1H), 4.16 (s, 1H), 3.36 (ddd, *J* = 2.5, 5.4, 6.7 Hz, 1H), 3.25 (d, *J* = 7.5 Hz, 1H), 2.81 (7.5 Hz, 1H), 2.24 (s, 3H), 2.09 (m, 1H), 1.98 (m, 1H), 1.84 – 1.73 (m, 3H), 1.43 – 1.07 (m, m, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 156.1, 91.9, 81.1, 66.8, 57.9, 41.7, 31.3, 28.1, 24.3, 24.3; IR (neat film NaCl) 2929, 2858, 2770, 1747, 1653, 1277, 1229, 1074 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{10}H_{18}NO$, $[M+H]^+$: 168.1383; found: 168.1385.



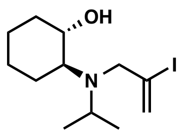
4c

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.57 – 7.50 (m, 2H), 7.40 – 7.29 (m, 3H), 6.97 (s, 1H), 4.04 (s, 1H), 3.52 – 3.41 (m, 2H), 3.27 (dd, *J* = 13.5, 1.1 Hz, 1H), 2.42 – 2.29 (m, 1H), 2.24 (s, 3H), 2.19 – 2.11 (m, 1H), 1.79 (dd, *J* = 6.9, 3.9 Hz, 2H), 1.75 – 1.64 (m, 1H), 1.35 – 1.15 (m, 4H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 137.4, 135.7, 128.8, 128.3, 128.2, 109.0, 69.5, 69.3, 66.8, 35.8, 33.3, 25.6, 24.2, 22.9; IR (neat film NaCl) 3467, 2930, 2855, 1446, 1079, 1058, 1033, 750, 695 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{23}INO$, $[M+H]^+$: 372.0819; found: 372.0859.



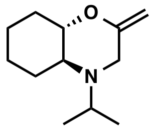
5c

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65 – 7.53 (m, 2H), 7.32 – 7.25 (m, 2H), 7.17 – 7.11 (m, 1H), 5.44 (d, *J* = 1.7 Hz, 1H), 3.53 (ddd, *J* = 11.5, 9.1, 4.3 Hz, 1H), 3.32 (d, *J* = 12.8 Hz, 1H), 3.00 (dd, *J* = 12.8, 1.6 Hz, 1H), 2.29 (s, 3H), 2.13 (ddtd, *J* = 12.5, 6.2, 4.3, 3.8, 2.1 Hz, 2H), 1.93 (td, *J* = 10.2, 9.1, 3.9 Hz, 1H), 1.79 (ddt, *J* = 13.0, 10.3, 2.9 Hz, 2H), 1.60 – 1.49 (m, 1H), 1.41 – 1.24 (m, 2H), 1.20 – 1.07 (m, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 150.4, 136.0, 128.5, 128.2, 126.0, 107.5, 80.8, 67.0, 59.2, 41.7, 31.4, 28.3, 24.7, 24.4; IR (neat film NaCl) 2935, 2860, 2774, 1664, 1449, 1342, 1179, 1060, 1032, 694 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{22}NO$, $[M+H]^+$: 244.1696; found: 244.1716.



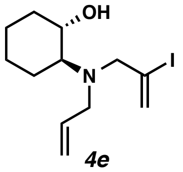
4d

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.29 (s, 1H), 5.87 (s, 1H), 3.90 (s, 1H), 3.36 – 3.21 (m, 2H), 3.02 (td, *J* = 13.7, 6.6 Hz, 2H), 2.39 (d, *J* = 10.5 Hz, 1H), 2.19 – 2.09 (m, 1H), 1.73 (q, *J* = 10.1 Hz, 3H), 1.35 – 1.17 (m, 4H), 1.14 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 127.2, 116.0, 69.3, 61.7, 57.4, 48.1, 33.2, 28.0, 26.1, 24.4, 22.9, 18.0; IR (neat film NaCl) 2930, 1614, 1173, 1080, 896 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{23}NOI$, $[M+H]^+$: 324.0819; found: 324.0845.



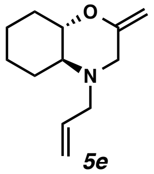
5d

^{1}H NMR (400 MHz, C_6D_6) δ 4.64 (d, *J* = 1.1 Hz, 1H), 4.12 (d, *J* = 1.5 Hz, 1H), 3.48 (ddd, *J* = 11.1, 8.9, 4.3 Hz, 1H), 3.23 (d, *J* = 12.7 Hz, 1H), 3.07 (p, *J* = 6.6 Hz, 1H), 2.89 (dt, *J* = 12.7, 1.4 Hz, 1H), 2.14 (ddd, *J* = 10.8, 8.9, 3.9 Hz, 1H), 2.02 – 1.93 (m, 1H), 1.75 (dq, *J* = 13.6, 2.9, 2.4 Hz, 1H), 1.48 – 1.33 (m, 4H), 0.99 (s, 3H), 0.96 – 0.79 (m, 2H), 0.65 (s, 3H). ^{13}C NMR (101 MHz, C_6D_6) δ 158.4, 89.6, 81.0, 62.1, 46.7, 45.8, 31.8, 28.1, 25.0, 24.4, 21.4, 12.4; IR (neat film NaCl) 2933, 1657, 1450, 1280, 1175, 1075, 800 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{22}NO$, $[M+H]^+$: 196.1696; found: 196.1697.



4e

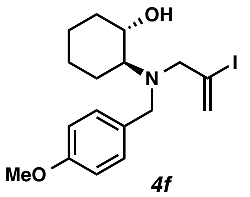
^{1}H NMR (500 MHz, CDCl$_3$) δ 6.29 (d, *J* = 1.8 Hz, 1H), 5.92 – 5.81 (m, 2H), 5.23 – 5.10 (m, 2H), 3.83 (s, 1H), 3.41 (td, *J* = 9.9, 4.5 Hz, 1H), 3.34 (d, *J* = 14.2 Hz, 1H), 3.31 – 3.23 (m, 1H), 2.94 (dd, *J* = 14.1, 8.4 Hz, 1H), 2.88 (d, *J* = 14.2 Hz, 1H), 2.41 (ddd, *J* = 12.7, 9.9, 3.4 Hz, 1H), 2.13 (ddq, *J* = 12.2, 4.6, 2.0 Hz, 1H), 1.85 – 1.74 (m, 2H), 1.71 – 1.68 (m, 1H), 1.32 – 1.16 (m, 3H), 1.15 – 1.03 (m, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 136.4, 127.6, 117.9, 113.9, 69.1, 64.9, 60.4, 52.4, 33.2, 25.7, 24.2, 23.5; IR (neat film NaCl) 2930, 2856, 1615, 1450, 1157, 1078, 917 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{21}NIO$, $[M+H]^+$: 322.0662; found: 322.0668.



5e

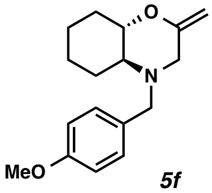
^{1}H NMR (500 MHz, CDCl$_3$) δ 5.86 (dddd, *J* = 17.1, 10.2, 8.0, 5.4 Hz, 1H), 5.24 – 5.16 (m, 2H), 4.38 (dt, *J* = 1.3, 0.7 Hz, 1H), 4.13 (dd, *J* = 1.6, 0.7 Hz, 1H), 3.48 (ddt, *J* = 13.6, 5.4, 1.6 Hz, 1H), 3.45 – 3.40 (m, 1H), 3.35 (d, *J* = 12.9 Hz, 1H), 2.88 – 2.79

(m, 2H), 2.17 – 2.04 (m, 2H), 1.99 (dddd, *J* = 10.2, 4.8, 3.9, 2.4 Hz, 1H), 1.79 – 1.69 (m, 2H), 1.46 – 1.37 (m, 1H), 1.35 – 1.21 (m, 2H), 1.12 (q, *J* = 12.3, 11.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 134.3, 118.8, 91.6, 80.8, 64.6, 56.0, 53.7, 31.5, 28.2, 24.8, 24.3; IR (neat film NaCl) 2935, 2862, 1657, 1280, 1075, 839 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{20}NO$, $[M+H]^+$: 194.1539; found: 194.1542.



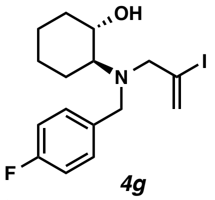
4f

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.32 (d, *J* = 1.7 Hz, 1H), 5.90 (t, *J* = 1.4 Hz, 1H), 3.80 (s, 3H), 3.81 – 3.74 (m, 2H), 3.44 (td, *J* = 9.8, 4.6 Hz, 1H), 3.36 (d, *J* = 13.9 Hz, 1H), 3.28 (d, *J* = 13.2 Hz, 1H), 2.92 (d, *J* = 14.0 Hz, 1H), 2.42 – 2.29 (m, 1H), 2.13 – 2.04 (m, 1H), 1.90 – 1.81 (m, 1H), 1.75 (ddd, *J* = 6.7, 4.4, 2.3 Hz, 1H), 1.70 – 1.63 (m, 1H), 1.25 – 1.04 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 130.6, 130.5, 128.1, 113.9, 113.5, 68.9, 63.6, 60.5, 55.4, 52.8, 33.3, 25.6, 24.2, 22.6; IR (neat film NaCl) 3483, 2931, 2855, 1612, 1511, 1247, 1036, 813 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{17}H_{25}INO_2$, $[M+H]^+$: 402.0924; found: 402.0934.



5f

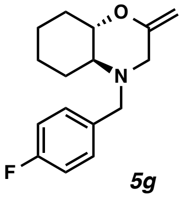
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.33 (s, 1H), 4.09 – 3.96 (m, 2H), 3.81 (s, 3H), 3.51 (s, br, 1H), 3.19 (d, *J* = 13.0 Hz, 1H), 3.09 (d, *J* = 12.9 Hz, 1H), 2.71 (d, *J* = 13.0 Hz, 1H), 2.21 (d, *J* = 12.9 Hz, 1H), 2.13 (s, br, 1H), 2.06 – 1.96 (m, 1H), 1.84 – 1.72 (m, 2H), 1.50 – 1.36 (m, 1H), 1.32 (qd, *J* = 11.1, 9.7, 5.6 Hz, 2H), 1.22 (d, *J* = 22.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 156.5, 130.4, 130.2, 113.8, 91.1, 80.4, 65.2, 56.5, 55.4, 53.4, 31.6, 28.7, 24.8, 24.4; IR (neat film NaCl) 2935, 2861, 1733, 1674, 1611, 1511, 1246, 1036, 843 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{17}H_{24}NO_2$, $[M+H]^+$: 274.1802; found: 274.1820.



4g

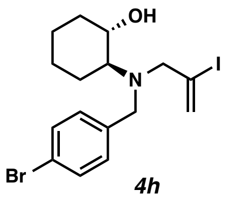
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 6.33 (s, 1H), 5.91 (t, *J* = 1.4 Hz, 1H), 3.80 (d, *J* = 13.3 Hz, 1H), 3.73 (s, br, 1H), 3.45

(td, J = 9.7, 4.6 Hz, 1H), 3.35 (t, J = 12.6 Hz, 2H), 2.95 (d, J = 13.9 Hz, 1H), 2.33 (d, J = 10.4 Hz, 1H), 2.14 – 2.04 (m, 1H), 1.92 – 1.83 (m, 1H), 1.81 – 1.72 (m, 1H), 1.67 (dt, J = 7.8, 2.8 Hz, 1H), 1.25 – 1.06 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (d, J = 245.2 Hz), 134.2, 131.1 (d, J = 8.0 Hz), 128.4, 115.5 (d, J = 21.3 Hz), 113.1, 68.9, 63.8, 60.6, 52.7, 33.3, 25.5, 24.2, 22.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ -115.5; IR (neat film NaCl) 3485, 2930, 2856, 1602, 1508, 1221, 1152, 1073, 818 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{22}FNOI$, $[M+H]^+$: 390.0725; found: 390.0732.



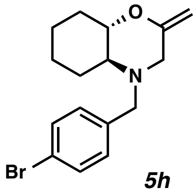
5g

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 2H), 7.08 – 6.93 (m, 2H), 4.34 (s, 1H), 4.04 (d, J = 13.1 Hz, 1H), 3.99 (d, J = 1.5 Hz, 1H), 3.50 (tt, J = 11.8, 10.9, 4.1 Hz, 2H), 3.16 (d, J = 13.0 Hz, 1H), 3.08 (d, J = 13.2 Hz, 1H), 2.72 (d, J = 12.9 Hz, 1H), 2.24 – 2.05 (m, 2H), 2.07 – 1.94 (m, 1H), 1.87 – 1.66 (m, 2H), 1.53 – 1.35 (m, 1H), 1.38 – 1.24 (m, 1H), 1.24 – 1.13 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1 (d, J = 244.7 Hz), 156.3, 134.3, 130.1 (d, J = 6.1 Hz), 115.3 (d, J = 20.9 Hz), 91.2, 80.5, 65.3, 56.4, 53.6, 31.6, 28.8, 24.8, 24.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -116.0; IR (neat film NaCl) 2936, 2862, 1736, 1673, 1604, 1508, 1222, 1075, 821 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{21}FNO$, $[M+H]^+$: 262.1602; found: 262.1629.



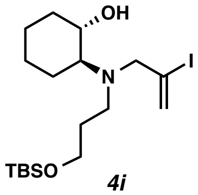
4h

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.7 Hz, 2H), 7.27 (d, J = 7.7 Hz, 2H), 6.33 (s, br, 1H), 5.91 (t, J = 1.6 Hz, 1H), 3.78 (d, J = 13.3 Hz, 1H), 3.71 (s, br, 1H), 3.53 – 3.41 (m, 1H), 3.42 – 3.26 (m, 2H), 2.95 (d, J = 14.0 Hz, 1H), 2.33 (s, br, 1H), 2.08 (dd, J = 9.6, 4.3 Hz, 1H), 1.94 – 1.54 (m, 3H), 1.27 – 1.03 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5, 131.7, 131.2, 128.6, 121.4, 112.9, 69.0, 63.9, 60.6, 52.9, 33.3, 25.5, 24.2, 22.6; IR (neat film NaCl) 3486, 2930, 2855, 1615, 1486, 1450, 1403, 1152, 1071, 1011, 799 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{22}BrNOI$, $[M+H]^+$: 449.9924; found: 449.9937.



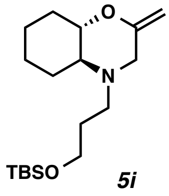
5h

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 4.24 (d, *J* = 1.1 Hz, 1H), 4.02 (d, *J* = 13.4 Hz, 1H), 3.93 (d, *J* = 1.5 Hz, 1H), 3.44 (ddd, *J* = 11.2, 8.7, 4.2 Hz, 1H), 3.13 (d, *J* = 12.9 Hz, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 2.69 (dt, *J* = 12.9, 1.5 Hz, 1H), 2.18 – 2.07 (m, 2H), 2.02 – 1.91 (m, 1H), 1.75 (tdd, *J* = 10.4, 5.5, 2.5 Hz, 2H), 1.47 – 1.34 (m, 1H), 1.36 – 1.22 (m, 2H), 1.19 – 1.06 (m, 1H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 157.1, 138.9, 131.8, 131.2, 121.0, 90.7, 81.0, 65.8, 56.9, 54.2, 31.9, 29.1, 25.2, 24.7; IR (neat film NaCl) 2935, 2861, 1654, 1486, 1280, 1074, 1012, 843, 802 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{16}H_{21}BrNO$, $[M+H]^+$: 322.0801; found: 322.0817.



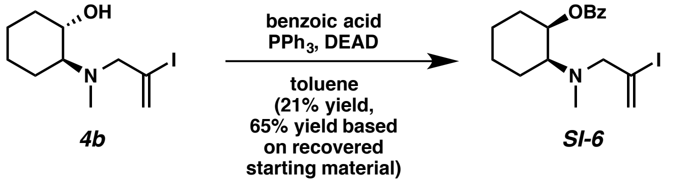
4i

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (s, 1H), 5.84 (s, 1H), 3.83 (s, 1H), 3.66 (td, *J* = 6.2, 2.2 Hz, 2H), 3.38 (td, *J* = 9.9, 4.4 Hz, 1H), 3.29 (d, *J* = 14.1 Hz, 1H), 2.91 (d, *J* = 14.2 Hz, 1H), 2.65 (dt, *J* = 13.0, 8.0 Hz, 1H), 2.43 (ddd, *J* = 13.1, 7.4, 5.8 Hz, 1H), 2.34 (ddd, *J* = 12.6, 9.8, 3.3 Hz, 1H), 2.17 – 2.08 (m, 1H), 1.82 – 1.72 (m, 2H), 1.71 (dt, *J* = 8.4, 6.0 Hz, 3H), 1.32 – 1.14 (m, 3H), 1.10 (tt, *J* = 12.2, 5.9 Hz, 1H), 0.89 (d, *J* = 0.9 Hz, 9H), 0.05 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 127.3, 114.2, 69.1, 65.6, 61.6, 61.4, 46.1, 33.3, 31.9, 26.1, 25.7, 24.3, 23.1, 18.4, -5.11, -5.13; IR (neat film NaCl) 3489, 2929, 2856, 1255, 1097, 835, 775 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{18}H_{37}INO_2Si$, $[M+H]^+$: 454.1633; found: 454.1658.



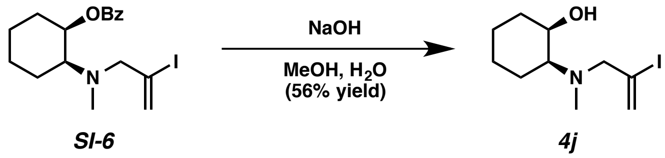
5i

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (s, 1H), 4.13 (s, 1H), 3.63 (td, *J* = 6.2, 2.2 Hz, 2H), 3.47 – 3.31 (m, 2H), 2.94 – 2.79 (m, 2H), 2.34 (s, br, 1H), 2.15 – 2.04 (m, 2H), 1.98 (ddq, *J* = 11.8, 4.4, 2.4, 1.9 Hz, 1H), 1.79 – 1.59 (m, 5H), 1.46 – 1.21 (m, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 91.4, 80.9, 64.6, 61.4, 53.8, 49.3, 31.5, 28.9, 28.3, 26.1, 24.8, 24.3, 18.4, -5.15, -5.17; IR (neat film NaCl) 2931, 2857, 1739, 1674, 1463, 1256, 1094, 838, 776 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{18}H_{36}NO_2Si$, $[M+H]^+$: 326.2510; found: 326.2544.



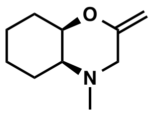
A solution of cyclohexanol **4b** (500 mg, 1.69 mmol, 1.00 equiv) in toluene (1.20 mL) was added to a cooled solution of PPh_3 (532 mg, 2.03 mmol, 1.20 equiv) and benzoic acid (248 mg, 2.03 mmol, 1.20 equiv) in toluene (8.45 mL) at –40 °C. Then, DEAD in toluene (40 wt% in toluene, 0.92 mL, 1.20 equiv) was added dropwise to a solution over 20 min at –40 °C. After stirring for 1.5 h at –40 °C, the solution was warm to 23 °C. After being stirred for 18 h, saturated $NaHCO_3$ aqueous solution was added and the mixture was extracted with EtOAc (3 x 7.00 mL). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (1:20 EtOAc:hexanes) to give benzoate **SI-6** (142 mg, 21% yield, 65% yield based on recovered starting material).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 6.25 (s, 1H), 5.73 (s, 1H), 5.10 (td, *J* = 10.4, 4.6 Hz, 1H), 3.29 (d, *J* = 15.1 Hz, 1H), 3.22 (d, *J* = 15.1 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.25 (s, 3H), 2.19 – 2.11 (m, 1H), 1.92 (d, *J* = 13.1 Hz, 1H), 1.83 – 1.72 (m, 2H), 1.40 (dddd, *J* = 17.5, 10.7, 8.0, 3.7 Hz, 2H), 1.35 – 1.23 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 132.9, 131.0, 129.9, 128.4, 125.5, 113.4, 73.5, 67.3, 65.8, 36.2, 32.2, 27.4, 25.3, 24.5; IR (Neat Film NaCl) 2934, 2858, 1714, 1450, 1317, 1273, 1175, 1106, 710 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{17}H_{23}INO_2$ $[M+H]^+$: 400.0768; found: 400.0769.



A solution of benzoate **SI-6** (140 mg, 0.351 mmol, 1.00 equiv) in MeOH (1.80 mL) and H_2O (0.20 mL) was treated with NaOH (28 mg, 0.701 mmol, 2.00 equiv) at 60 °C. After 1 h and 45 min, the solution was poured into H_2O and the mixture was extracted with CH_2Cl_2 (3 x 3.00 mL). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (1:8 EtOAc:hexanes) to give cyclohexanol **4j** (58 mg, 56% yield).

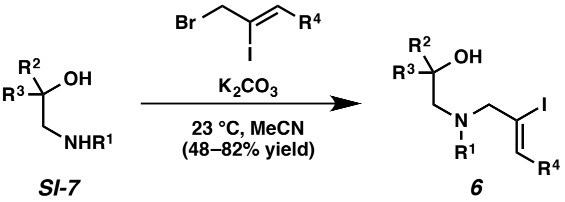
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.28 (q, *J* = 1.4 Hz, 1H), 5.86 (dt, *J* = 1.6, 0.8 Hz, 1H), 3.96 (s, 1H), 3.40 (td, *J* = 9.9, 4.5 Hz, 1H), 3.17 (d, *J* = 13.8 Hz, 1H), 2.95 (d, *J* = 13.8 Hz, 1H), 2.28 (ddd, *J* = 11.4, 9.7, 3.5 Hz, 1H), 2.18 (s, 3H), 2.18 – 2.09 (m, 1H), 1.83 – 1.65 (m, 3H), 1.35 – 1.07 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 127.0, 113.8, 69.4, 69.3, 65.0, 35.9, 33.3, 25.6, 24.2, 22.8; IR (Neat Film NaCl) 3468, 2930, 2855, 2796, 1615, 1449, 1282, 1080, 1036, 901 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{19}INO$ $[M+H]^+$: 296.0506; found: 296.0528.



5j

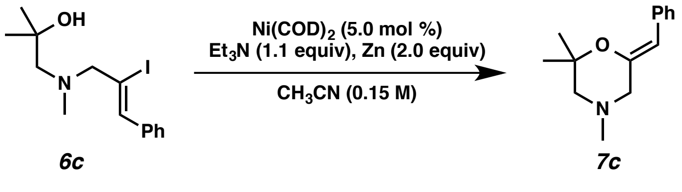
^{1}H NMR (400 MHz, CD_2Cl_2) δ 4.28 (dd, J = 1.4, 0.7 Hz, 1H), 4.09 (dd, J = 1.7, 0.5 Hz, 1H), 3.31 (ddd, J = 11.2, 9.0, 4.2 Hz, 1H), 3.21 (d, J = 12.7 Hz, 1H), 2.75 (dt, J = 12.7, 1.6 Hz, 1H), 2.18 (s, 3H), 2.12 – 2.01 (m, 1H), 1.90 (dtd, J = 13.3, 4.7, 2.7 Hz, 1H), 1.81 – 1.66 (m, 3H), 1.43 – 1.23 (m, 3H), 1.03 (tdd, J = 13.0, 11.2, 3.7 Hz, 1H); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 157.3, 91.0, 81.4, 67.2, 58.2, 41.9, 31.7, 28.5, 25.1, 24.8; IR (Neat Film NaCl) 2937, 2862, 2770, 1654, 1451, 1339, 1278, 1161, 1075, 1042, 900, 836 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{18}NO$ $[M+H]^+$: 168.1383; found: 168.1396.

Typical procedure for linear aminoalcohols 6

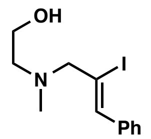


To a solution of aminoalcohols **SI-7** (1.12 mmol, 1.00 equiv) in MeCN (5.60 mL) were added K_2CO_3 (11.2 mmol, 10.0 equiv) and allyl bromides (1.23 mmol, 1.10 equiv). The reaction mixture was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography, using mixture of hexanes and ethyl acetate as eluent to give the product **6**.

Representative procedure for cross-coupling of linear aminoalcohols 6

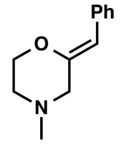


Ni-Catalyzed C–O bond formation experiments were performed in a nitrogen-filled glove box. To a solution of aminoalcohol **6c** (50.0 mg, 0.145 mmol, 1.00 equiv) in MeCN (0.97 mL) in a scintillation vial were added Et_3N (22.0 μL, 0.160 mmol, 1.10 equiv), Zn powder (19.0 mg, 0.290 mmol, 2.00 equiv), and $Ni(COD)_2$ (2.00 mg, 0.00724 mmol, 0.05 equiv). The reaction mixture was stirred at 23 °C for 24 h. After the reaction was done, the vial was removed from the glovebox and uncapped. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography, using mixture of hexanes and ethyl acetate as eluent to furnish the product **7c** (30.0 mg, 95% yield).



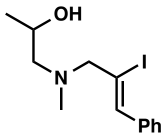
6a

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.54 (m, 2H), 7.36 (m, 3H), 6.98 (s, 1H), 3.65 (t, *J* = 5.4 Hz, 2H), 3.36 (s, 2H), 2.95 (br, 1H), 2.66 (t, *J* = 5.5 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 137.2, 136.1, 128.7, 128.1, 128.0, 107.1, 70.4, 58.5, 57.8, 40.7; IR (neat film NaCl) 3442, 2946, 2840, 2792, 1490, 1445, 1083, 1066, 1046, 748, 694 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{17}INO$, $[M+H]^+$: 318.0349; found: 318.0344.



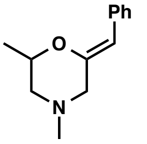
7a

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.56 (m, 2H), 7.28 (m, 2H), 7.14 (m, 1H), 5.45 (s, 1H), 4.06 (m, 2H), 3.03 (s, 2H), 2.59 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 149.6, 135.6, 128.4, 128.1, 125.9, 107.9, 67.4, 58.3, 54.1, 46.1; IR (neat film NaCl) 2939. 2790, 1738, 1668, 1452, 1339, 1170, 1051, 695; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{16}NO$, $[M+H]^+$: 190.1226; found: 190.1228.



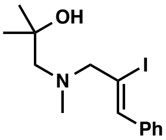
6b

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.59 – 7.50 (m, 2H), 7.41 – 7.30 (m, 3H), 6.98 (s, 1H), 3.90 (dqd, *J* = 9.4, 6.1, 3.0 Hz, 1H), 3.75 – 3.53 (m, 1H), 3.47 (d, *J* = 13.5 Hz, 1H), 3.29 (d, *J* = 13.5 Hz, 1H), 2.45 (dd, *J* = 12.3, 3.1 Hz, 1H), 2.41 – 2.36 (m, 1H), 2.32 (s, 3H), 1.16 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 137.4, 136.4, 128.8, 128.3, 128.3, 128.2, 107.1, 70.8, 64.6, 63.3, 41.3, 19.9; IR (neat film NaCl) 3459, 3054, 3023, 2968, 2930, 2843, 2795, 1598, 1491, 1446, 1408, 1361, 1324, 1291, 1209, 1161, 1135, 1065, 1029, 935, 841, 750, 695 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{13}H_{19}NIO$, $[M+H]^+$: 332.0506; found: 332.0519.



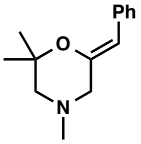
7b

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65 – 7.56 (m, 2H), 7.33 – 7.26 (m, 2H), 7.19 – 7.10 (m, 1H), 5.46 (d, *J* = 1.4 Hz, 1H), 4.06 (dqd, *J* = 9.9, 6.3, 2.6 Hz, 1H), 3.20 (dd, *J* = 12.5, 1.7 Hz, 1H), 2.85 – 2.72 (m, 2H), 2.31 (s, 3H), 2.06 (dd, *J* = 11.7, 9.8 Hz, 1H), 1.36 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 150.2, 136.0, 128.6, 128.2, 126.0, 107.8, 73.4, 60.9, 58.0, 46.1, 19.2; IR (neat film NaCl) 2973, 2936, 2788, 1666, 1448, 1328, 1154, 1070, 975, 755, 694 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{13}H_{18}NO$, [M+H]$^+$: 204.1383; found: 204.1386.



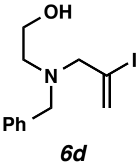
6c

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.57 – 7.48 (m, 2H), 7.33 (s, 3H), 6.99 (s, 1H), 3.46 (s, 2H), 3.26 (s, br, 1H), 2.51 (s, 2H), 2.37 (s, 3H), 1.23 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 137.5, 135.8, 129.2, 128.9, 128.2, 108.3, 73.0, 70.9, 68.1, 44.0, 28.0; IR (neat film NaCl) 2969, 2786, 2360, 1446, 1356, 1121, 1031, 970, 749, 695 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{14}H_{21}NIO$, [M+H]$^+$: 346.0662; found: 346.0664.



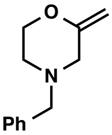
7c

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 – 7.59 (m, 2H), 7.29 – 7.25 (m, 2H), 7.17 – 7.09 (m, 1H), 5.47 (s, 1H), 2.94 (s, 2H), 2.38 (s, 2H), 2.28 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 149.2, 136.3, 128.3, 128.2, 125.8, 108.7, 76.8, 64.7, 58.3, 46.4, 26.3; IR (neat film NaCl) 2974, 2766, 1663, 1449, 1368, 1346, 1254, 1207, 1152, 1110, 968, 754, 694 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{14}H_{20}NO$, [M+H]$^+$: 218.1539; found: 218.1577.



6d

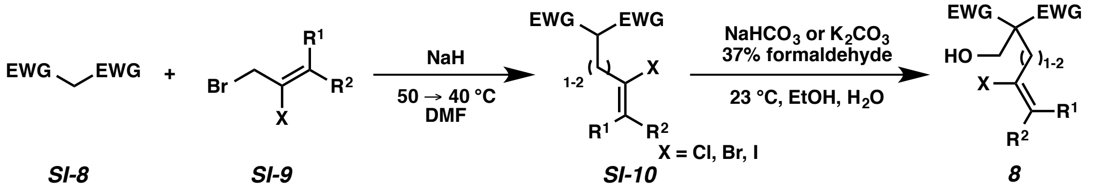
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.38 – 7.25 (m, 5H), 6.33 (q, J = 1.4 Hz, 1H), 5.92 (m, 1H), 3.63 (s, 2H), 3.56 (q, J = 5.4 Hz, 2H), 3.16 (s, 2H), 2.70 (t, J = 5.7 Hz, 1H), 2.65 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 137.8, 129.3, 128.4, 127.9, 127.4, 111.9, 64.8, 58.5, 57.5, 54.1; IR (neat film NaCl) 3435, 3024, 2808, 1616, 1493, 1452, 1257, 1151, 1027, 904, 739, 698 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{17}INO$, $[M+H]^+$: 318.0349; found: 318.0356.



7d

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.33 – 7.24 (m, 5H), 4.39 (s, 1H), 4.11 (s, 1H), 3.90 (m, 2H), 3.50 (s, 2H), 2.98 (s, 2H), 2.52 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 155.9, 137.4, 129.3, 128.5, 127.4, 92.2, 67.9, 63.2, 55.3, 52.1; IR (neat film NaCl) 2875, 2807, 1653, 1453, 1313, 1278, 1125, 1079, 1067, 851, 699 cm^{-1}; HRMS (MM: ESI-APCI+) m/z calc'd for $C_{12}H_{16}NO$, $[M+H]^+$: 190.1226; found: 190.1229.

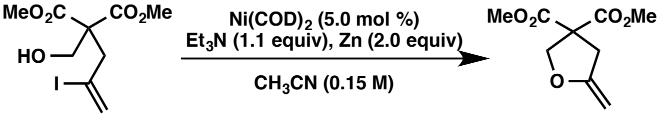
Typical procedure for malonate substrates 8



To a suspension of NaH (60% dispersion in mineral oil, 4.16 mmol, 1.10 equiv) in DMF (19.0 mL) at 0 °C was added malonate **SI-8** (3.78 mmol, 1.00 equiv) in portions. The reaction mixture was stirred at 50 °C for 1 h. The solution was cooled to 0 °C and allyl bromide (3.78 mmol, 1.00 equiv) in DMF (2 mL) was added in portions over 5 min. Then, the mixture was stirred at 40 °C for 1 h. The reaction was quenched by sat. NH_4Cl and the aqueous phase was extracted with Et_2O (3 x 10.0 mL). The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (1:20 EtOAc:hexanes) on silica gel to give vinyl halide **SI-10**.

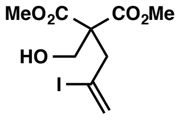
To a solution of vinyl halide **SI-10** (0.74 mmol, 1.00 equiv) in EtOH (0.50 mL) and H_2O (0.25 mL) were added solid $NaHCO_3$ or K_2CO_3 (0.15 mmol, 0.20 equiv) and formaldehyde (37wt.% in H_2O, 0.89 mmol, 1.20 equiv). The reaction mixture was stirred at 23 °C for 24 h. Then, water (0.40 mL) was added and the aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography, using mixture of hexanes and ethyl acetate as eluent to furnish the product **8**.

Representative procedure for cross-coupling of malonates 8



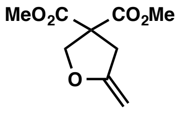
8a **9a**

Ni-Catalyzed C–O bond formation experiments were performed in a nitrogen-filled glove box. To a solution of vinyl iodide **8a** (83.9 mg, 0.256 mmol, 1.00 equiv) in MeCN (1.71 mL) in a scintillation vial were added Et_3N (39.0 μL, 0.282 mmol, 1.10 equiv), Zn powder (33.0 mg, 0.512 mmol, 2.00 equiv), and $Ni(COD)_2$ (3.50 mg, 0.013 mmol, 0.05 equiv). The reaction mixture was stirred at 23 °C for 1 h. After the reaction was done, the vial was removed from the glovebox and uncapped. Solids were removed via a filtration through a celite plug and the resulting solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (1:4 EtOAc:hexanes) to furnish the product **9a** (44.5 mg, 87% yield).



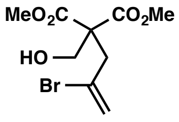
8a

^{1}H NMR (500 MHz, C_6D_6) δ 5.79 (q, J = 1.2 Hz, 1H), 5.61 (d, J = 1.4 Hz, 1H), 4.09 (d, J = 5.8 Hz, 2H), 3.33 (s, 6H), 3.32 (d, J = 1.1 Hz, 2H); ^{13}C NMR (126 MHz, C_6D_6) δ 169.9, 131.5, 101.2, 63.3, 59.3, 52.4, 45.4; IR (Neat Film NaCl) 3520, 2952, 1731, 1435, 1210, 1033 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_9H_{14}IO_5$ $[M+H]^+$: 328.9886; found: 328.9891.



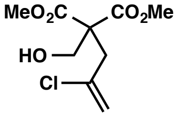
9a

^{1}H NMR (500 MHz, C_6D_6) δ 4.53 (q, J = 1.9 Hz, 1H), 4.44 (s, 2H), 3.91 (q, J = 1.7 Hz, 1H), 3.16 (s, 6H), 3.09 (t, J = 1.7 Hz, 2H); ^{13}C NMR (126 MHz, C_6D_6) δ 169.2, 160.2, 81.8, 74.3, 59.8, 52.6, 37.0; IR (Neat Film NaCl) 2957, 2358, 2340, 1737, 1436, 1280, 1046 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_9H_{13}O_5$ $[M+H]^+$: 201.0757; found: 201.0765.



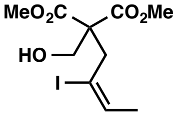
8b

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (dt, *J* = 1.7, 0.9 Hz, 1H), 5.59 (d, *J* = 1.7 Hz, 1H), 4.09 (s, 2H), 3.79 (s, 6H), 3.25 (d, *J* = 0.9 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 126.6, 122.4, 63.7, 59.0, 53.1, 42.4; IR (Neat Film NaCl) 2953, 1728, 1626, 1435, 1299, 1208, 1032, 902, 857 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_9H_{14}BrO_5$ $[M+H]^+$: 281.0024; found: 281.0036.



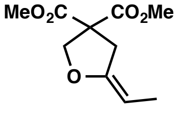
8c

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (d, *J* = 1.3 Hz, 1H), 5.30 – 5.28 (m, 1H), 4.07 (s, 2H), 3.78 (s, 6H), 3.13 (d, *J* = 0.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 136.6, 117.7, 63.8, 58.7, 53.0, 40.6; IR (Neat Film NaCl) 2955, 1735, 1632, 1437, 1212, 1035, 898 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_9H_{14}O_5Cl$ $[M+H]^+$: 237.0530; found: 237.0540.



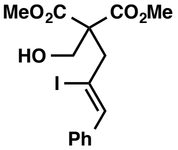
8d

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.50 (qt, *J* = 7.2, 0.8 Hz, 1H), 4.04 (d, *J* = 6.6 Hz, 2H), 3.80 (s, 6H), 3.30 (s, br, 2H), 2.36 (t, *J* = 6.7 Hz, 1H), 1.70 (dt, *J* = 7.2, 0.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 142.1, 91.5, 63.6, 59.2, 53.1, 38.7, 17.2; IR (Neat Film NaCl) 2952, 1733, 1436, 1299, 1223, 1040 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{10}H_{16}O_5I$ $[M+H]^+$: 343.0043; found: 343.0048.



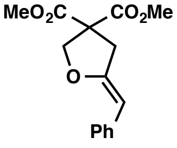
9d

^{1}H NMR (400 MHz, C_6D_6) δ 4.97 (qt, *J* = 7.0, 2.2 Hz, 1H), 4.44 (s, 2H), 3.18 (s, 6H), 3.11 (dq, *J* = 2.8, 1.5 Hz, 2H), 1.40 (dt, *J* = 7.1, 1.4 Hz, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 169.6, 153.8, 92.2, 73.6, 59.7, 52.6, 34.2, 12.2; IR (Neat Film NaCl) 2956, 1740, 1437, 1275, 1169, 1070, 803 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{10}H_{14}O_5$ $[M]^{+\bullet}$: 214.0841; found: 214.0836.



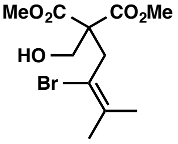
8e

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 5H), 6.88 (s, 1H), 4.15 (s, 2H), 3.81 (s, 6H), 3.57 (d, *J* = 0.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 140.1, 138.2, 128.7, 128.3, 128.3, 96.5, 63.6, 59.9, 53.1, 46.9; IR (Neat Film NaCl) 2951, 1727, 1437, 1215, 1032, 696 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_{15}H_{18}O_5I$ $[M+H]^+$: 405.0193; found: 405.0195.



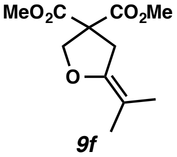
9e

^{1}H NMR (400 MHz, C_6D_6) δ 7.75 – 7.70 (m, 2H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.05 (ddt, *J* = 8.6, 7.2, 1.2 Hz, 1H), 5.21 – 5.18 (m, 1H), 4.54 (s, 2H), 3.20 (d, *J* = 1.6 Hz, 2H), 3.16 (s, 6H); ^{13}C NMR (101 MHz, C_6D_6) δ 168.8, 153.7, 136.4, 128.2, 127.8, 125.3, 99.4, 75.2, 58.5, 52.3, 38.3; IR (Neat Film NaCl) 2953, 1738, 1678, 1435, 1279, 1210, 1028, 695 cm^{-1}; HRMS (MM: EI +) *m/z* calc'd for $C_{15}H_{16}O_5$ $[M]^{+\bullet}$: 276.0998; found: 276.1012.



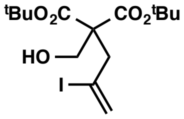
8f

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (s, 2H), 3.78 (s, 6H), 3.37 (s, 2H), 1.88 (d, *J* = 0.9 Hz, 3H), 1.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 136.4, 114.1, 63.7, 59.3, 53.0, 38.8, 25.9, 21.2; IR (Neat Film NaCl) 2952, 1734, 1437, 1209, 1043 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{11}H_{18}O_5Br$ $[M+H]^+$: 309.0338; found: 309.0325.



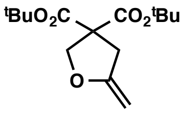
9f

^{1}H NMR (500 MHz, C_6D_6) δ 4.12 (d, *J* = 6.0 Hz, 2H), 3.57 (s, 2H), 3.38 (s, 6H), 1.66 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, C_6D_6) δ 170.6, 136.2, 115.0, 63.6, 59.5, 52.3, 39.0, 25.6, 20.8; IR (Neat Film NaCl) 2952, 1731, 1437, 1301, 1209, 1043 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{11}H_{17}O_5$ $[M+H]^+$: 229.1076; found: 229.1074.



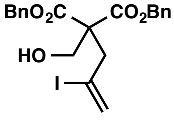
8g

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.18 (q, *J* = 1.3 Hz, 1H), 5.91 (d, *J* = 1.5 Hz, 1H), 4.06 (d, *J* = 3.6 Hz, 2H), 3.20 (d, *J* = 1.1 Hz, 2H), 2.32 (s, 1H), 1.50 (s, 18H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.1, 130.9, 101.6, 82.8, 63.9, 60.7, 45.4, 28.1; IR (Neat Film NaCl) 2978, 1728, 1369, 1256, 1148, 1020, 842 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{15}H_{26}O_5I$ [M+H]$^+$: 413.0825; found: 413.0821.



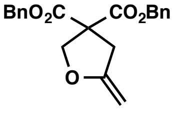
9g

^{1}H NMR (500 MHz, C$_6$D$_6$) δ 4.54 (q, *J* = 1.8 Hz, 1H), 4.51 (s, 2H), 3.94 (q, *J* = 1.6 Hz, 1H), 3.14 (t, *J* = 1.7 Hz, 2H), 1.27 (s, 18H); ^{13}C NMR (126 MHz, C$_6$D$_6$) δ 168.3, 160.9, 81.8, 81.3, 74.5, 61.2, 37.0, 27.7; IR (Neat Film NaCl) 2979, 1732, 1370, 1146, 1050, 844 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{15}H_{25}O_5$ [M+H]$^+$: 285.1702; found: 285.1693.



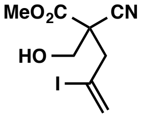
8h

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 – 7.29 (m, 6H), 7.29 – 7.26 (m, 4H), 6.12 (q, *J* = 1.1 Hz, 1H), 5.87 (d, *J* = 1.6 Hz, 1H), 5.17 (d, *J* = 3.2 Hz, 4H), 4.13 (s, 2H), 3.29 (d, *J* = 1.1 Hz, 2H), 2.27 (s, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.6, 135.1, 131.8, 128.7, 128.6, 128.4, 100.3, 67.8, 63.6, 59.5, 45.4; IR (Neat Film NaCl) 2952, 1725, 1455, 1214, 695 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_{21}H_{22}O_5I$ [M+H]$^+$: 481.0506; found: 481.0509.



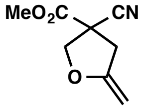
9h

^{1}H NMR (600 MHz, C$_6$D$_6$) δ 7.10 – 6.90 (m, 10H), 4.83 (d, *J* = 8.0 Hz, 4H), 4.50 (q, *J* = 1.8 Hz, 1H), 4.46 (s, 2H), 3.87 (q, *J* = 1.7 Hz, 1H), 3.11 (t, *J* = 1.7 Hz, 2H); ^{13}C NMR (151 MHz, C$_6$D$_6$) δ 168.7, 148.2, 135.6, 128.7, 128.5, 128.3, 81.9, 74.3, 67.7, 55.8, 37.0; IR (Neat Film NaCl) 2915, 1732, 1455, 1243, 1045, 901, 695 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_{21}H_{21}O_5$ [M+H]$^+$: 353.1384; found: 353.1394.



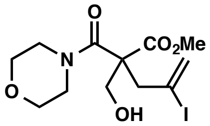
8i

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.35 (dt, *J* = 2.2, 1.1 Hz, 1H), 6.05 (d, *J* = 2.1 Hz, 1H), 4.04 (dd, *J* = 11.1, 7.6 Hz, 1H), 3.98 (dd, *J* = 11.1, 6.5 Hz, 1H), 3.90 (s, 3H), 3.13 (dd, *J* = 14.9, 1.1 Hz, 1H), 3.05 (dd, *J* = 14.9, 1.1 Hz, 1H), 2.45 (dd, *J* = 7.6, 6.5 Hz, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.6, 132.6, 117.2, 97.2, 66.0, 54.2, 52.1, 46.9; IR (Neat Film NaCl) 2952, 2359, 1738, 1611, 1434, 1224, 1144, 1060, 910 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_8H_{11}O_3NI$ [M+H]$^+$: 295.9784; found: 295.9775.



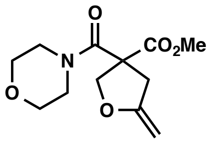
9i

^{1}H NMR (500 MHz, C_6D_6) δ 4.44 (q, *J* = 2.0 Hz, 1H), 3.84 (d, *J* = 8.9 Hz, 1H), 3.79 – 3.75 (m, 2H), 3.02 (d, *J* = 0.7 Hz, 3H), 2.69 (dt, *J* = 15.9, 1.9 Hz, 1H), 2.42 (dt, *J* = 15.9, 1.6 Hz, 1H); ^{13}C NMR (126 MHz, C_6D_6) δ 166.1, 158.0, 117.3, 83.6, 75.1, 53.3, 46.9, 38.7; IR (Neat Film NaCl) 2959, 2249, 1747, 1682, 1435, 1231, 1046, 819 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_8H_{10}O_3N$ [M+H]$^+$: 168.0661; found: 168.0666.



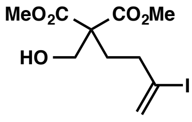
8j

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.22 (q, *J* = 1.2 Hz, 1H), 5.97 (d, *J* = 1.6 Hz, 1H), 4.25 (d, *J* = 11.2 Hz, 1H), 3.88 (d, *J* = 11.2 Hz, 1H), 3.81 (s, 3H), 3.79 – 3.55 (m, 6H), 3.39 (s, br, 2H), 3.30 (dd, *J* = 15.5, 1.0 Hz, 1H), 3.06 (dd, *J* = 15.4, 1.1 Hz, 1H), 2.60 (s, br, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 171.9, 167.7, 132.2, 99.9, 66.3, 66.1, 57.4, 53.1, 45.6, 37.2; IR (Neat Film NaCl) 2955, 2859, 1733, 1627, 1436, 1272, 1228, 1115, 1064, 999, 851 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_{12}H_{19}NO_5I$ [M+H]$^+$: 384.0302; found: 384.0315.



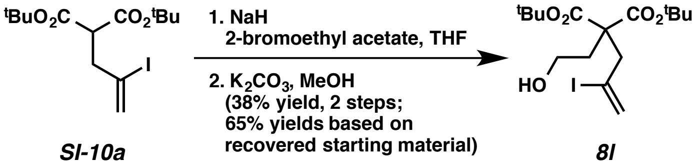
9j

^{1}H NMR (500 MHz, C_6D_6) δ 4.60 (d, *J* = 9.0 Hz, 1H), 4.55 (q, *J* = 1.8 Hz, 1H), 4.41 (d, *J* = 9.0 Hz, 1H), 3.94 (q, *J* = 1.7 Hz, 1H), 3.22 (s, br, 2H), 3.15 – 2.97 (m, 9H), 2.71 (s, br, 2H); ^{13}C NMR (101 MHz, C_6D_6) δ 171.6, 165.8, 160.7, 81.4, 75.2, 66.4, 66.0, 58.8, 52.5, 46.0, 43.5, 37.5; IR (Neat Film NaCl) 2857, 1733, 1651, 1435, 1274, 1115, 1018, 804 cm^{-1}; HRMS (MM: ESI-APCI +) *m/z* calc'd for $C_{12}H_{18}NO_5$ [M+H]$^+$: 256.1179; found: 256.1196.



8k

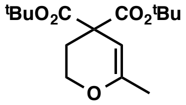
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (q, *J* = 1.4 Hz, 1H), 5.72 (d, *J* = 1.7 Hz, 1H), 3.96 (s, 2H), 3.79 (d, *J* = 0.6 Hz, 6H), 2.49 – 2.43 (m, 2H), 2.20 – 2.13 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 126.4, 109.9, 64.9, 59.0, 52.9, 40.8, 31.5; IR (Neat Film NaCl) 2952, 1729, 1617, 1436, 1205, 1043, 898 cm^{-1}; HRMS (MM: FAB+) *m/z* calc'd for $C_{10}H_{16}IO_5$ [M+H]$^+$: 343.0043; found: 343.0031.



To a solution of NaH (60% dispersion in mineral oil, 78.0 mg, 1.95 mmol, 2.00 equiv) in THF (3.26 mL) was added vinyl iodide **SI-10a** (374 mg, 0.977 mmol, 1.00 equiv), and the solution was stirred until gas evolution was complete. 2-Bromoethyl acetate (0.27 mL, 2.44 mmol, 2.50 equiv) was added to the reaction mixture at 0 °C and then, the solution was stirred at 23 °C for 24 h. The reaction was quenched with sat. NH_4Cl at 0 °C and the mixture was extracted with EtOAc (3 x 3.00 mL), the combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (1:20 EtOAc:hexanes) to give dialkylated malonate and recovered **SI-10a**.

To a solution of dialkylated malonate intermediate (344 mg, 0.735 mmol, 1.00 equiv) in MeOH (2.50 mL) was added K_2CO_3 (203 mg, 1.47 mmol, 2.00 equiv) and the solution was stirred at 23 °C for 24 h. The reaction mixture was diluted with CH_2Cl_2 (3.00 mL) and the mixture was extracted with CH_2Cl_2 (3 x 2.00 mL), the combined organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (1:20 → 1:8 → 1:4 EtOAc:hexanes) to give malonate **8l** (159 mg, 38% yield, 2 steps).

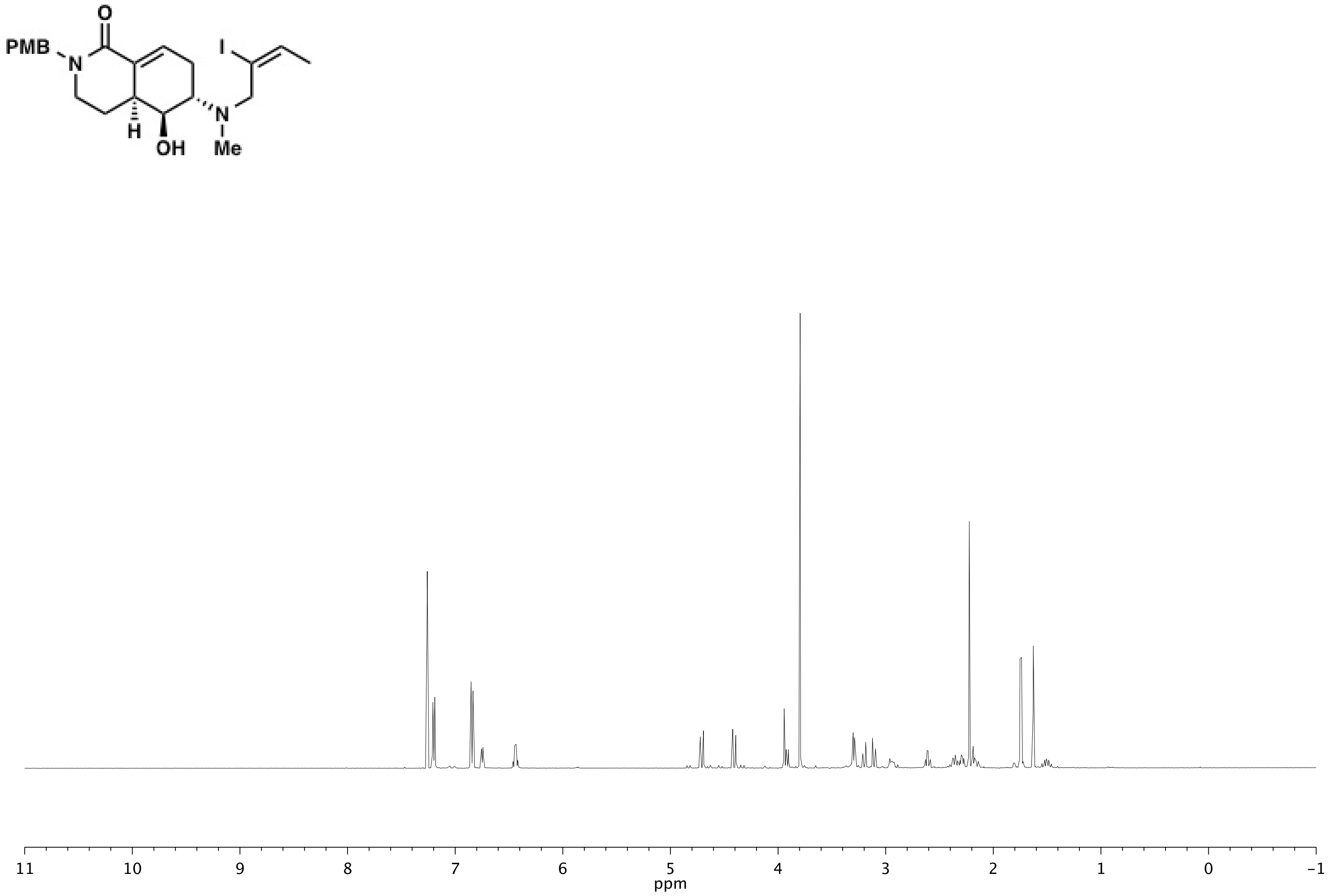
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (q, *J* = 1.4 Hz, 1H), 5.91 (d, *J* = 1.7 Hz, 1H), 3.72 (t, *J* = 6.7 Hz, 2H), 3.17 (d, *J* = 1.2 Hz, 2H), 2.28 (t, *J* = 6.7 Hz, 2H), 1.65 (s, br, 1H), 1.47 (s, 18H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 130.5, 102.2, 82.5, 59.2, 57.7, 46.9, 34.7, 28.1; IR (Neat Film NaCl) 3447, 2977, 1726, 1368, 1250, 1145, 843 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{16}H_{28}IO_5$ [M+H]$^+$: 427.0982; found: 427.0985.



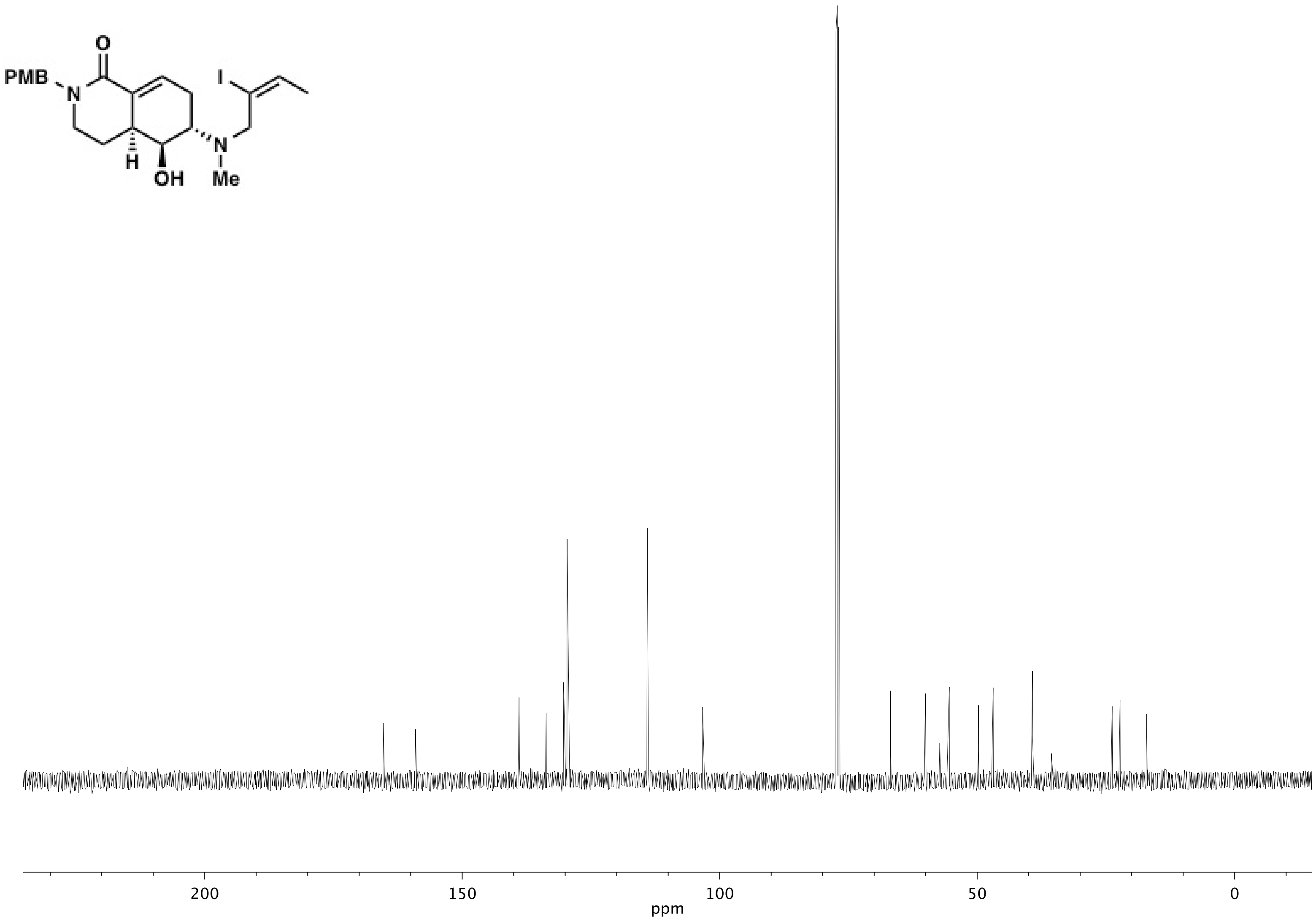
9l

^{1}H NMR (500 MHz, CD_2Cl_2) δ 4.68 (h, *J* = 0.9 Hz, 1H), 4.02 – 3.96 (m, 2H), 2.10 – 2.04 (m, 2H), 1.76 (d, *J* = 1.0 Hz, 3H), 1.43 (s, 18H); ^{13}C NMR (126 MHz, CD_2Cl_2) δ

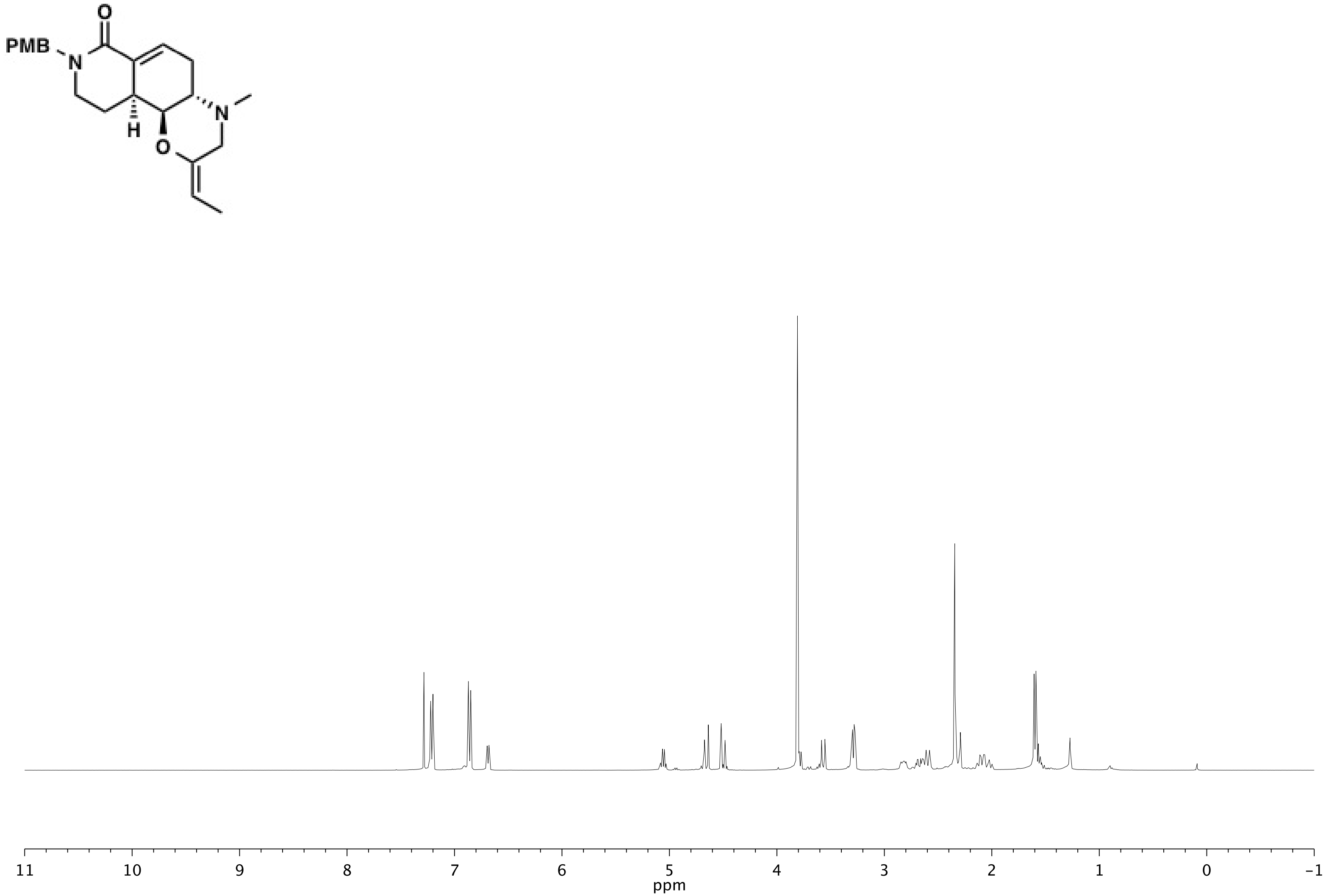
170.6, 153.8, 94.6, 81.7, 64.1, 52.5, 28.7, 28.1, 20.6; IR (Neat Film NaCl) 2977, 2933, 1728, 1369, 1266, 1146, 1108, 1088, 847 cm^{-1}; HRMS (MM: FAB +) *m/z* calc'd for $C_{16}H_{27}O_5$ $[M+H]^+$: 299.1858; found: 299.1835.



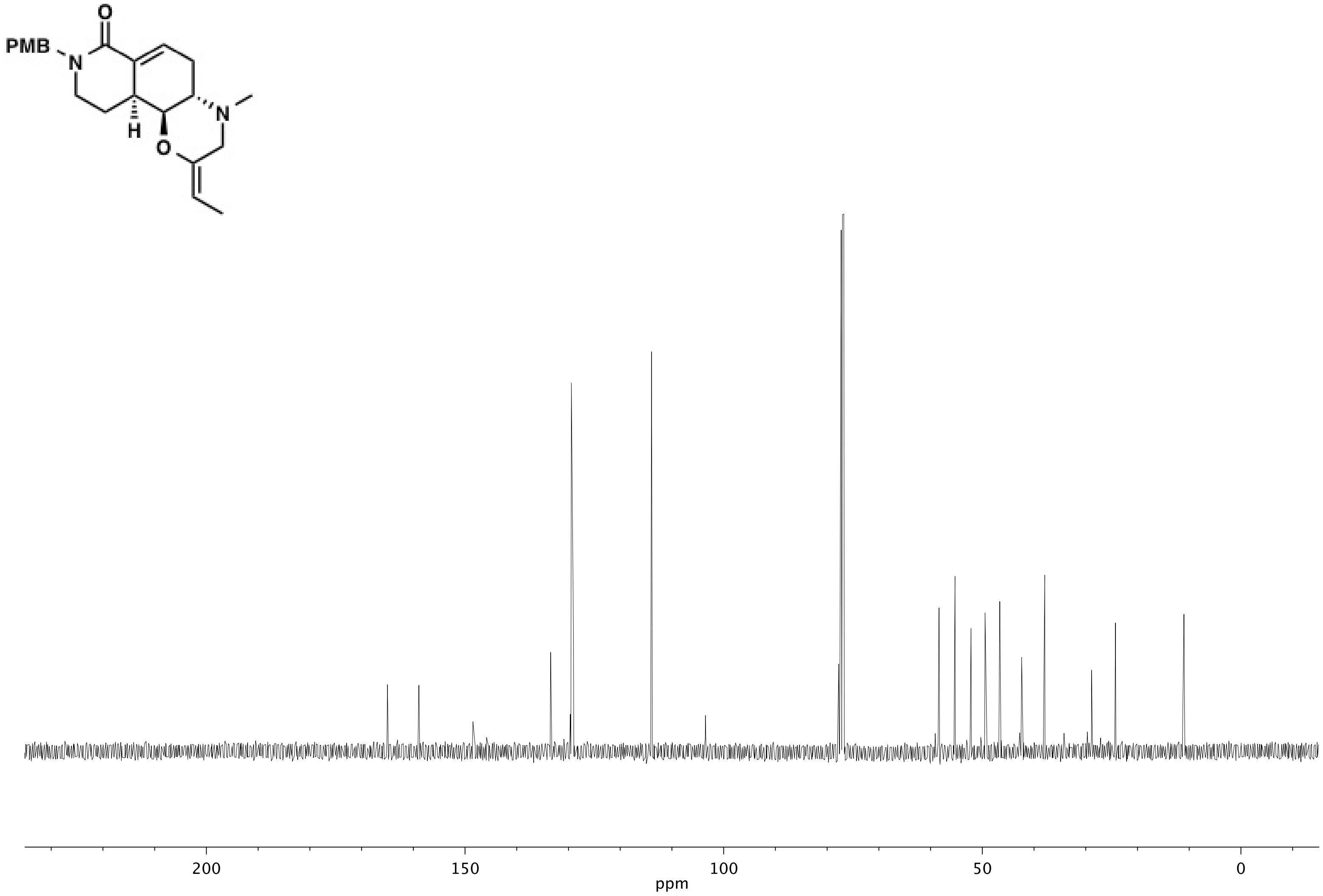
^{1}H NMR (500 MHz, CDCl$_3$) of compound **1**.



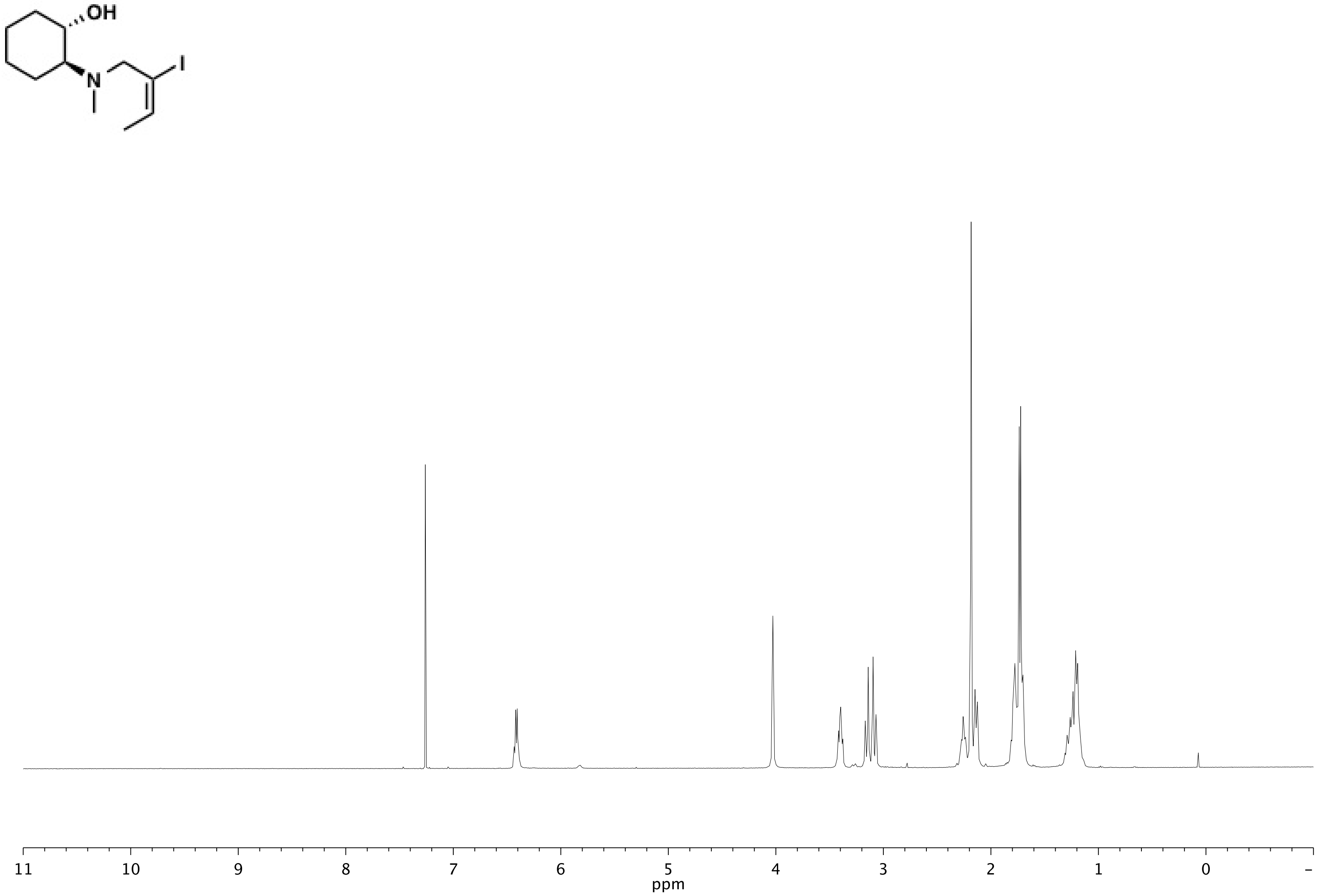
^{13}C NMR (126 MHz, CDCl$_3$) of compound **1**.



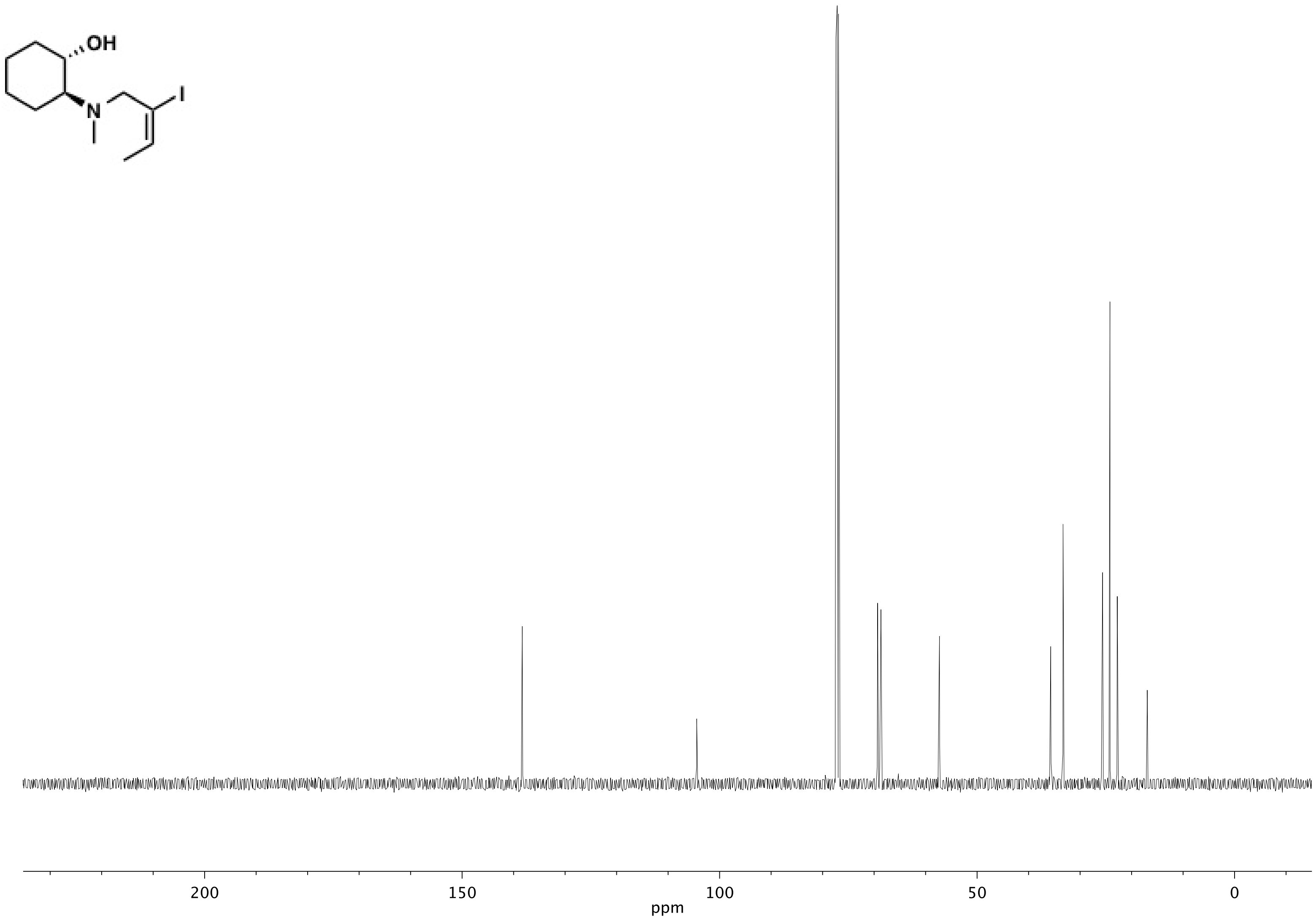
^{1}H NMR (400 MHz, CDCl$_3$) of compound **3**.



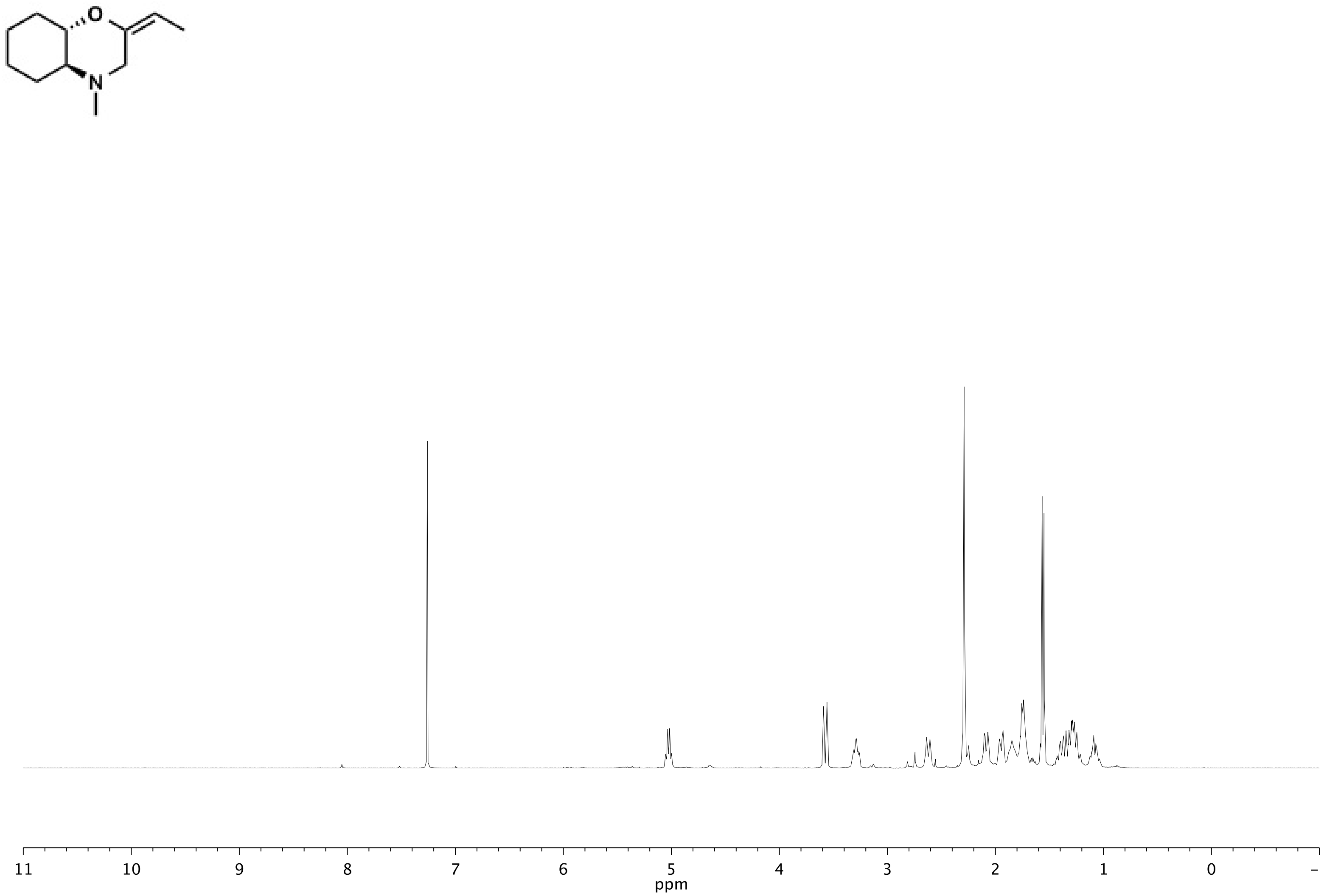
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3**.



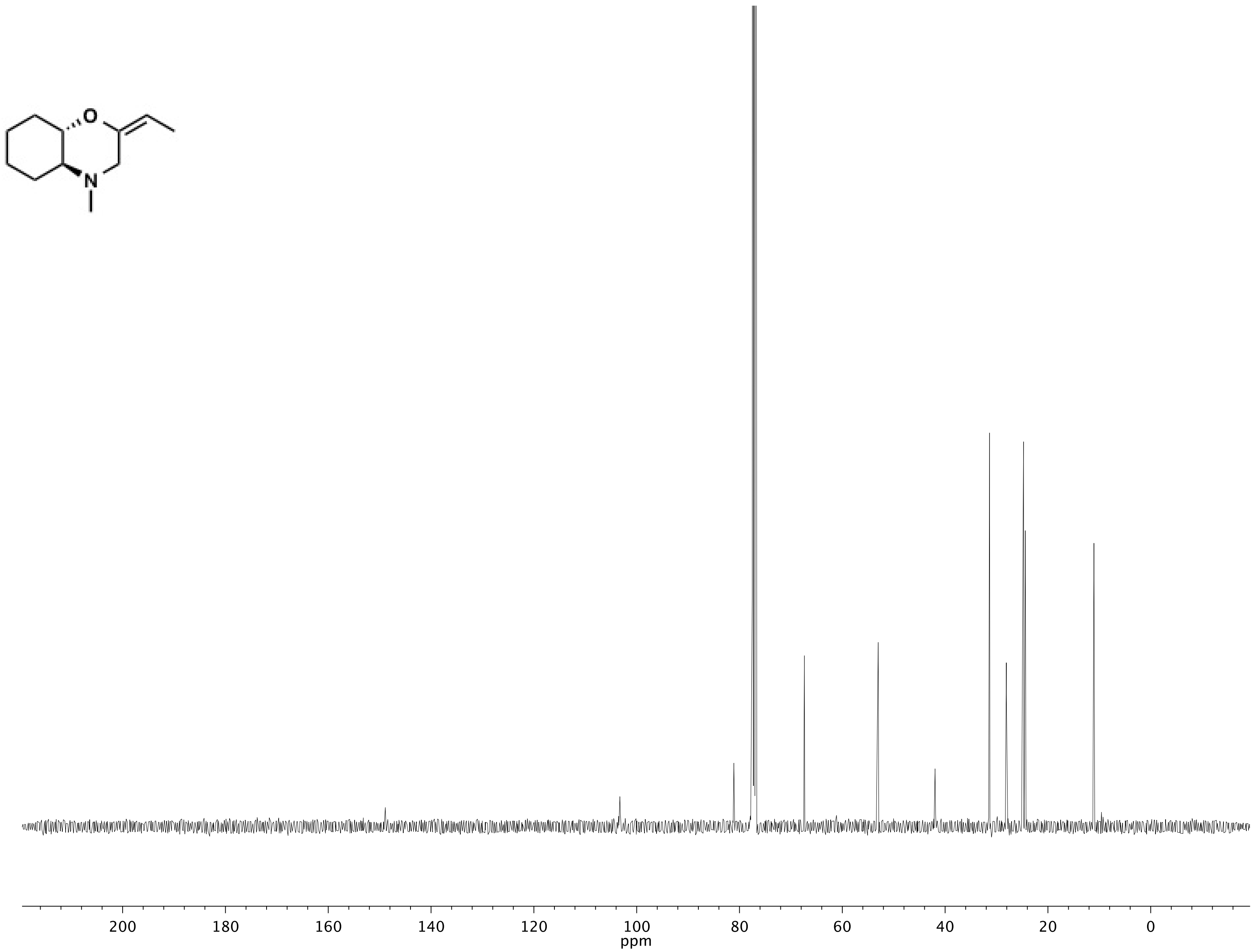
^{1}H NMR (500 MHz, CDCl$_3$) of compound **4a**.



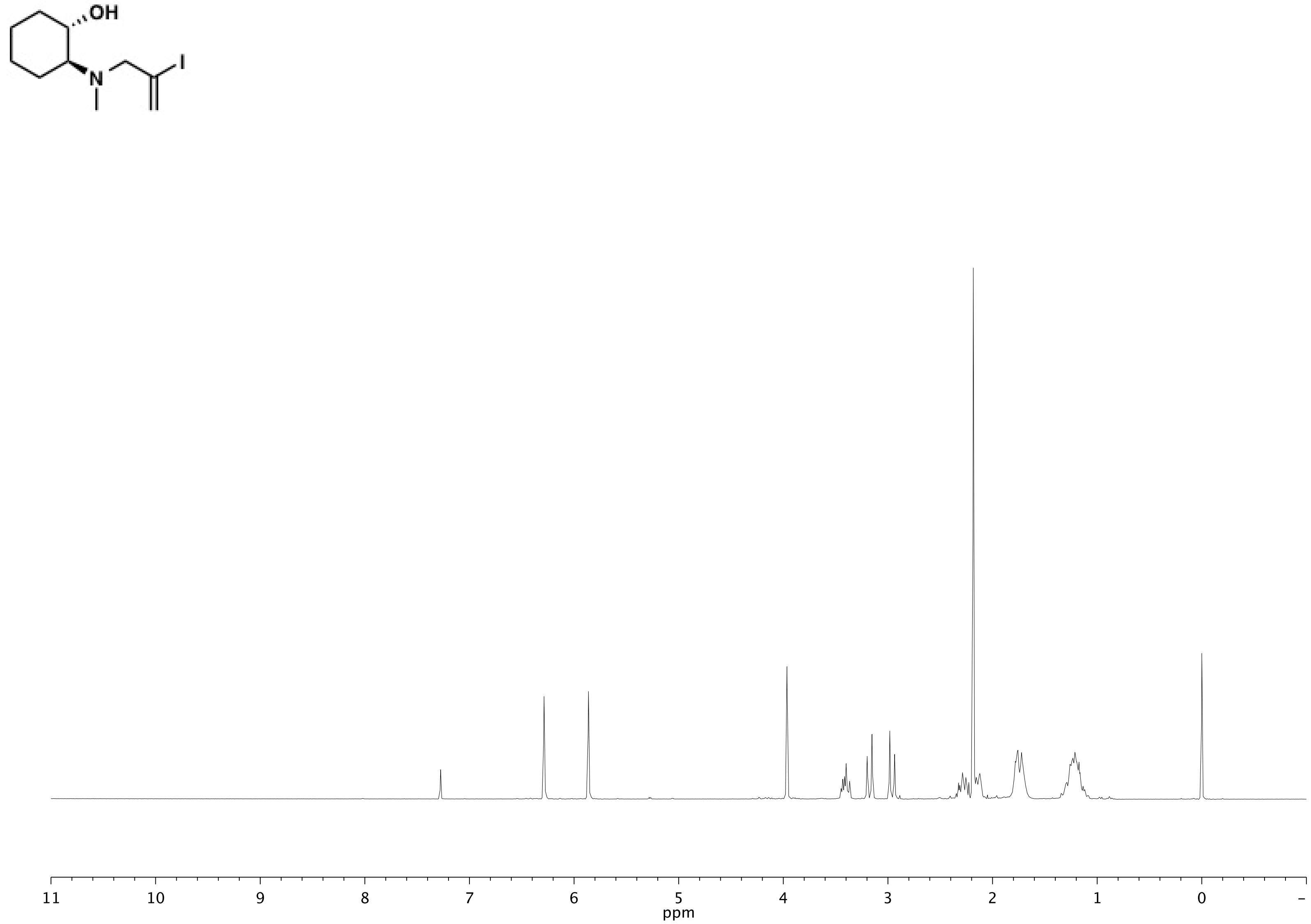
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4a**.



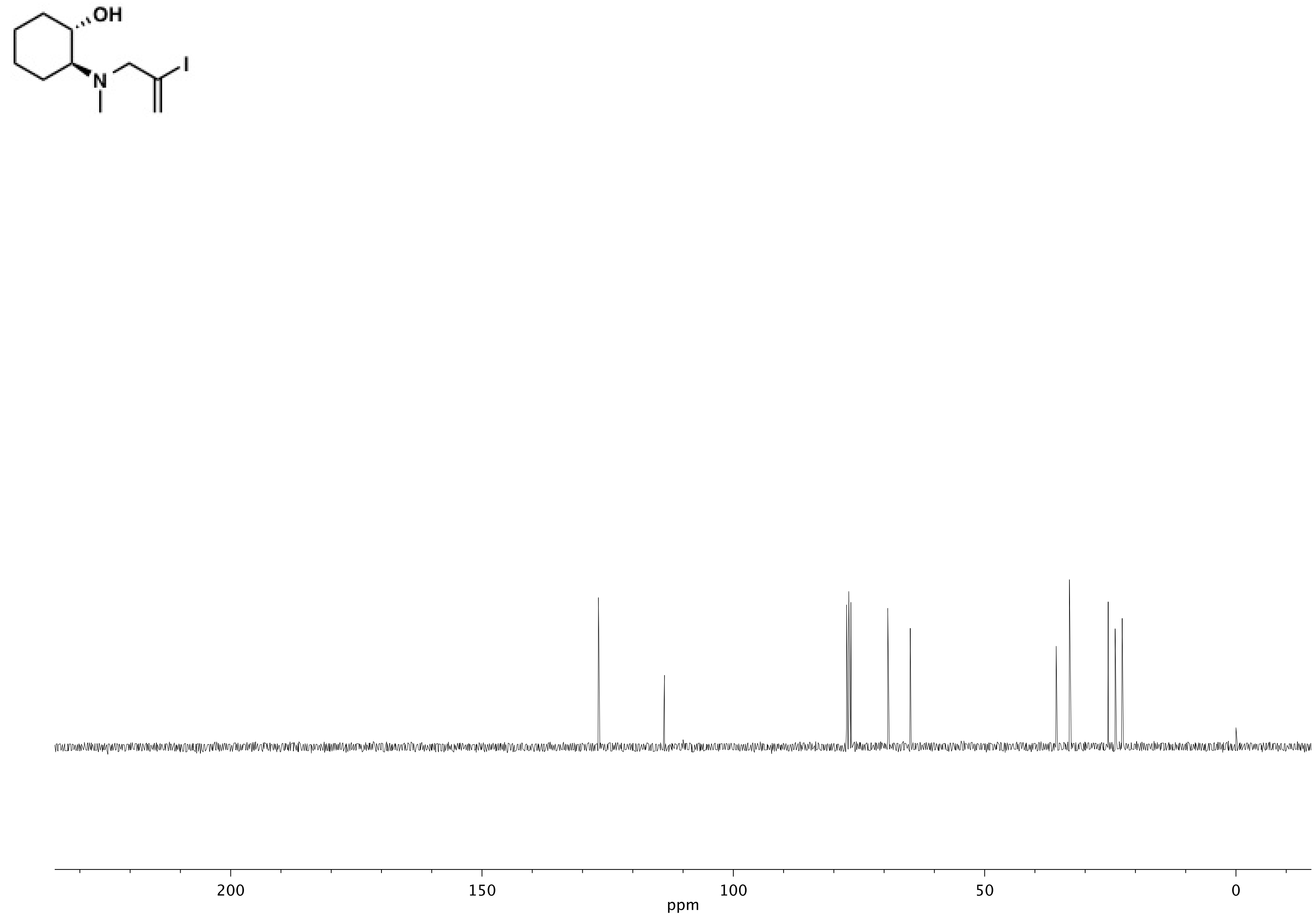
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5a**.



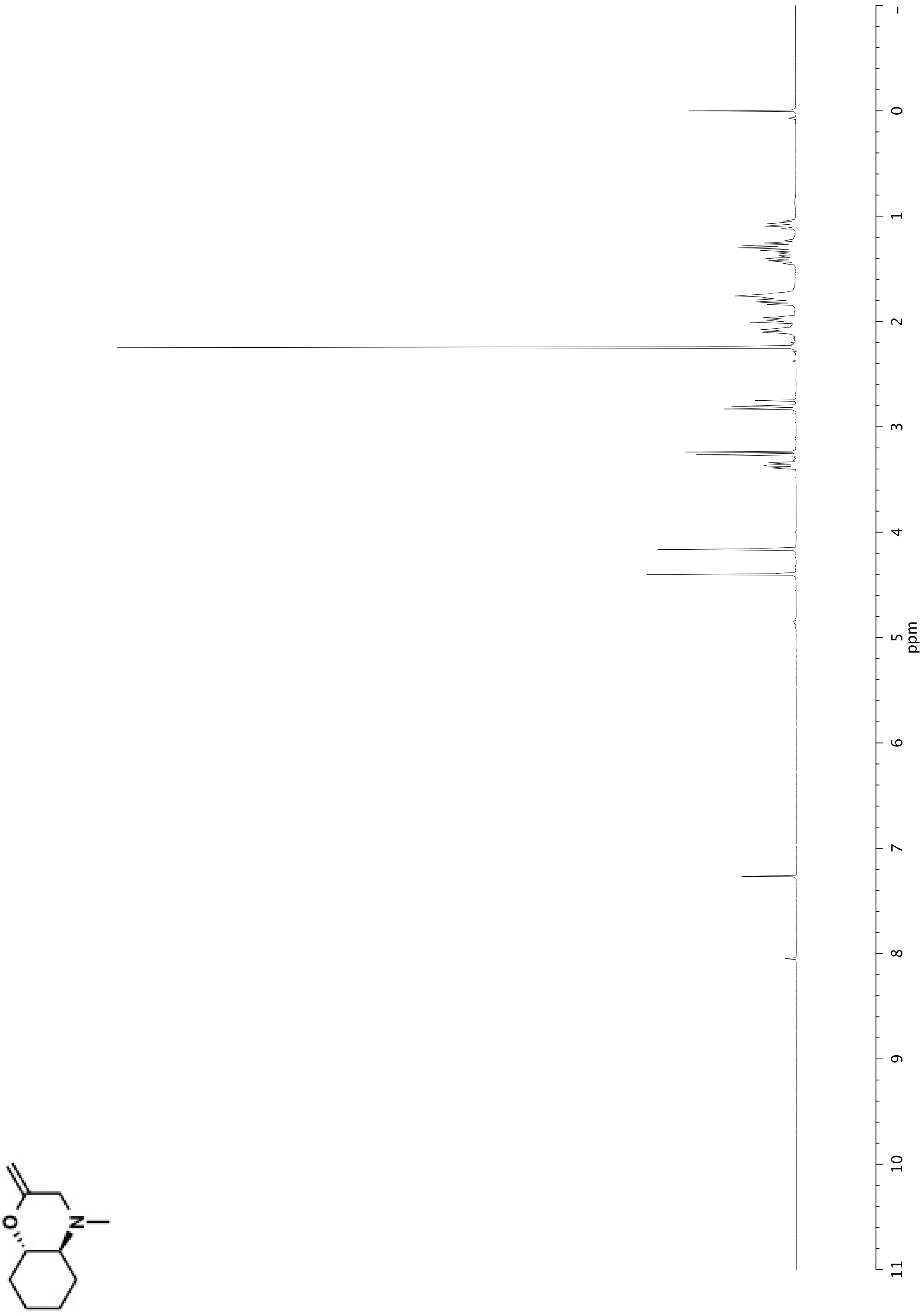
^{13}C NMR (101 MHz, CDCl$_3$) of compound **5a**.



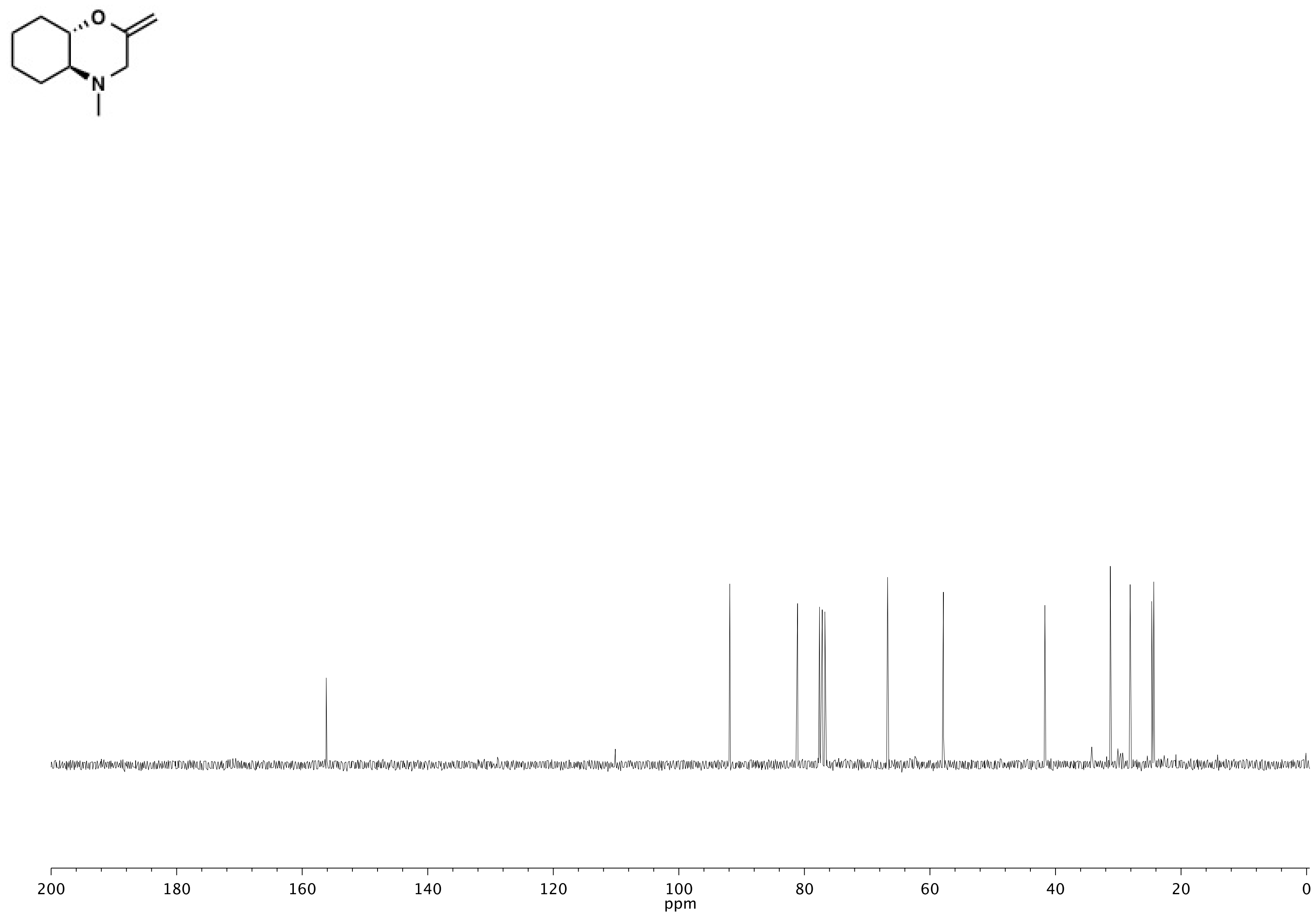
^{1}H NMR (300 MHz, $CDCl_3$) of compound **4b**.



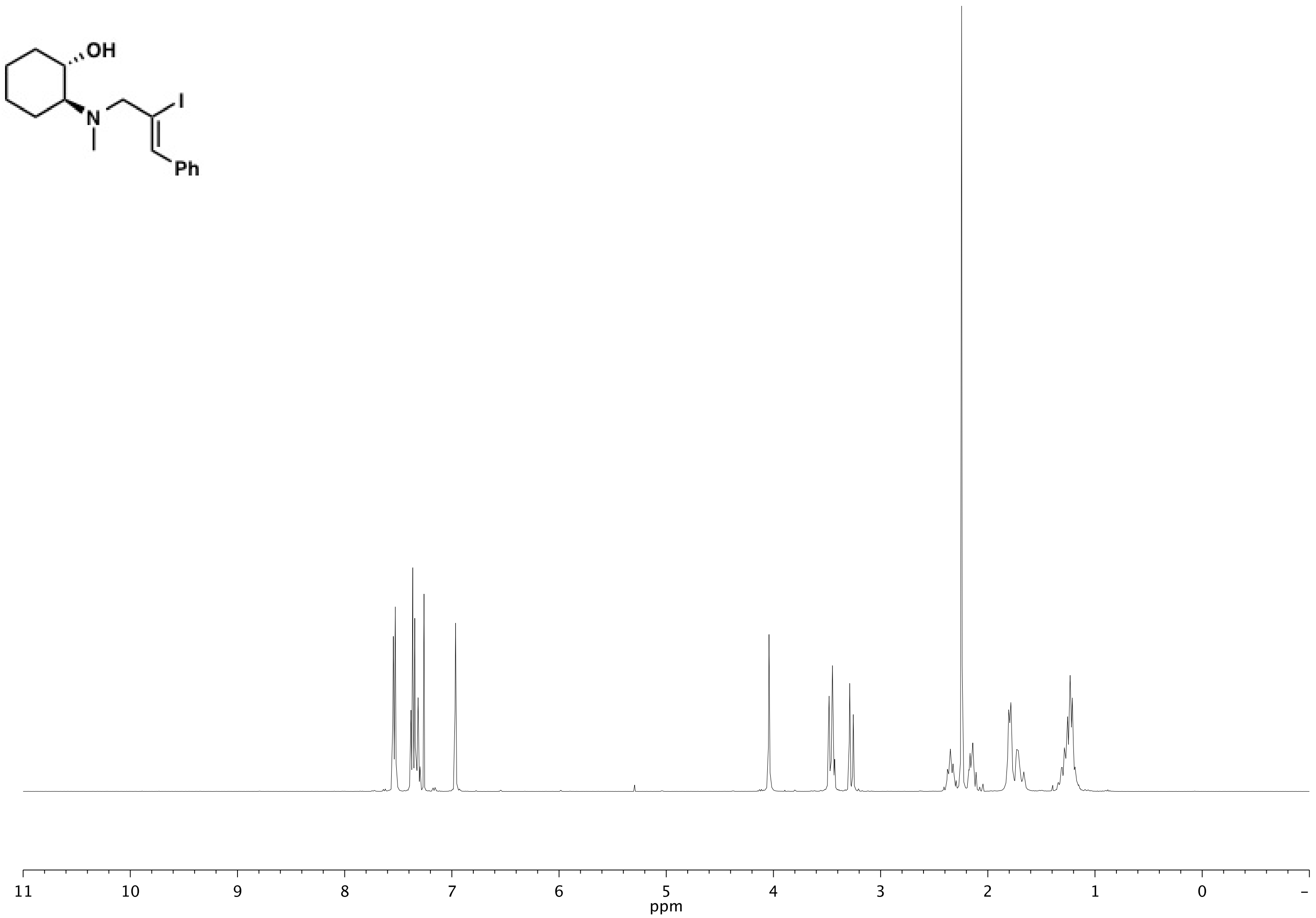
^{13}C NMR (75 MHz, $CDCl_3$) of compound **4b**.



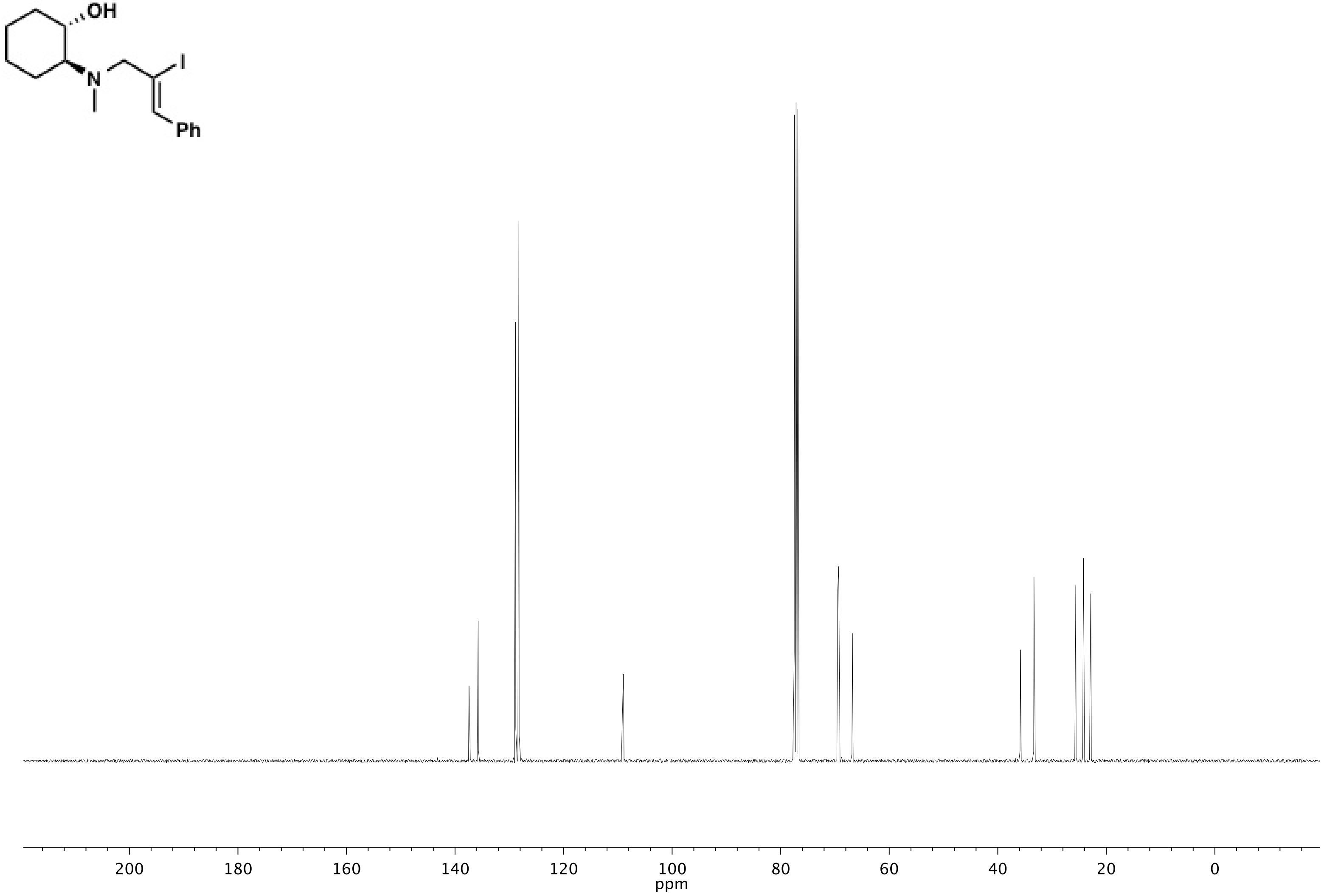
^{1}H NMR (300 MHz, CDCl$_3$) of compound **5b**.



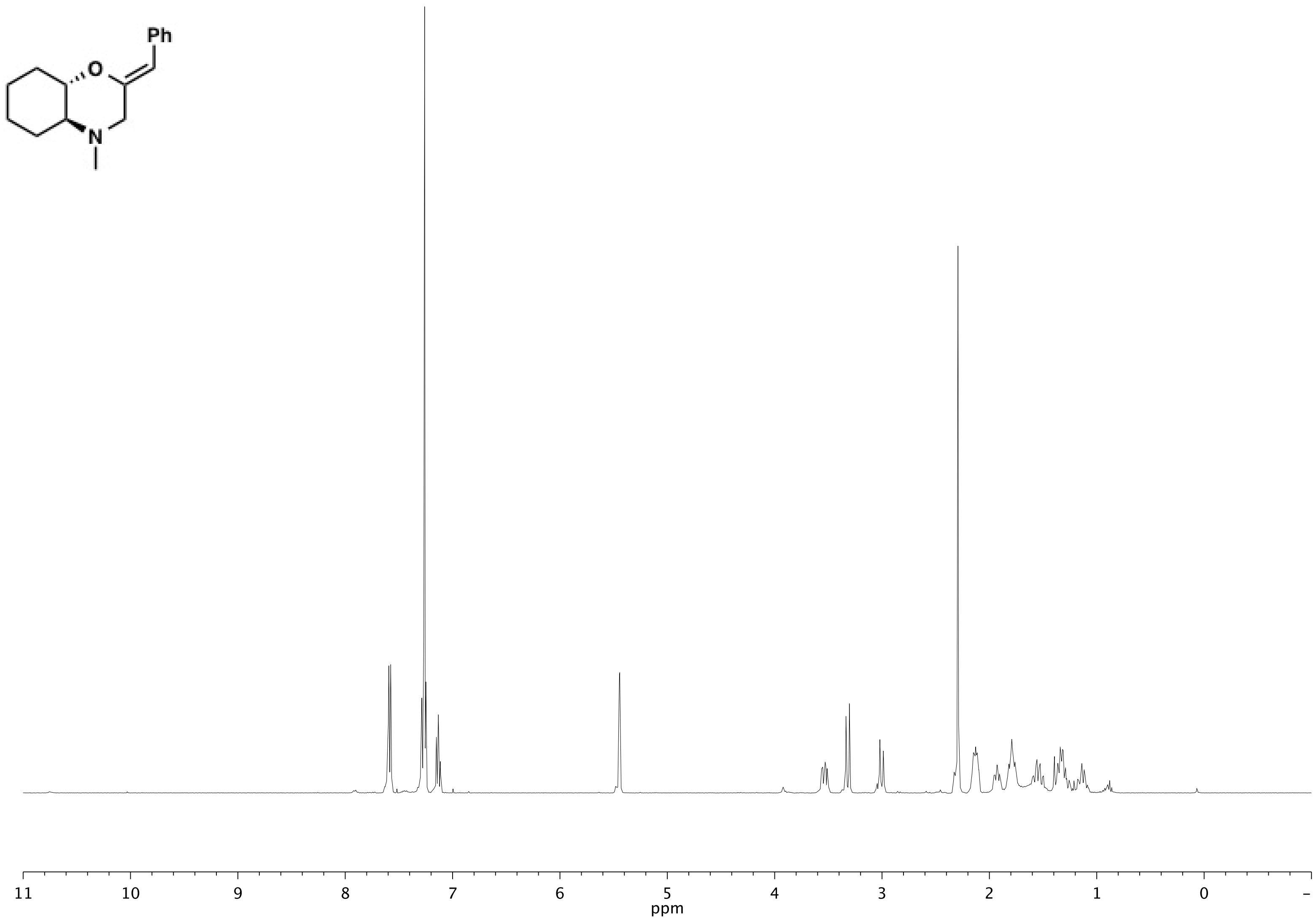
^{13}C NMR (75 MHz, CDCl$_3$) of compound **5b**.



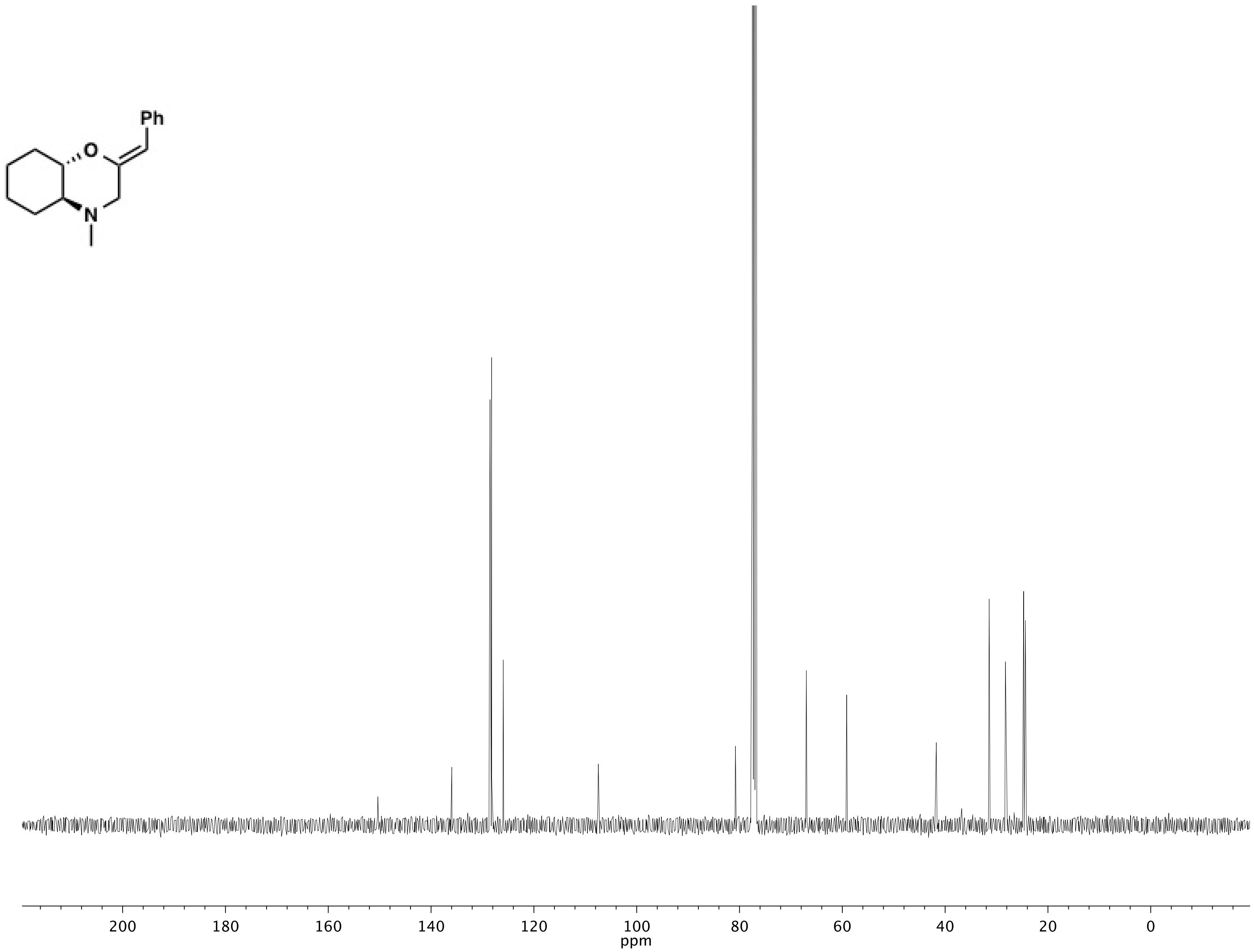
^{1}H NMR (400 MHz, CDCl$_3$) of compound **4c**.



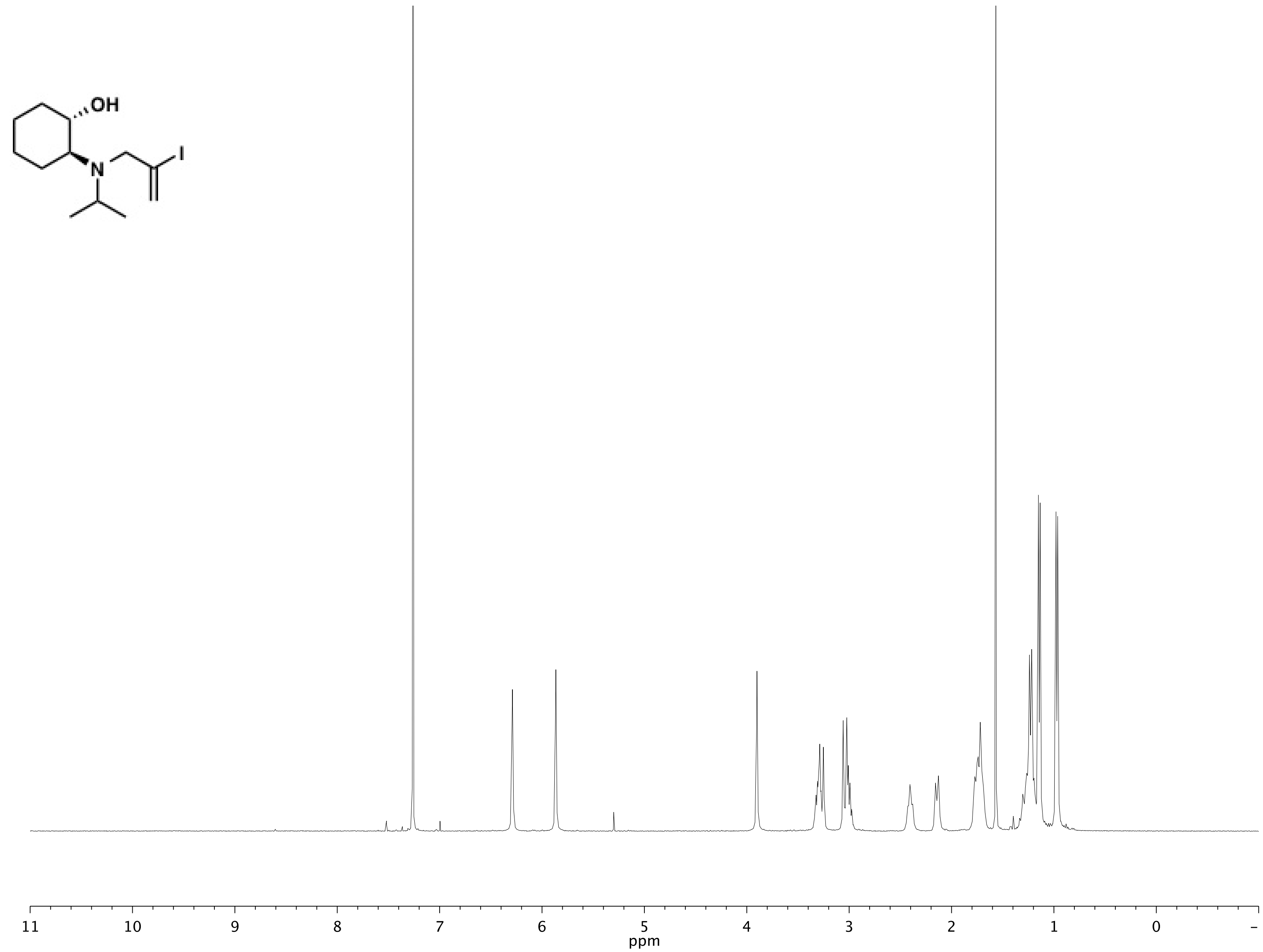
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4c**.



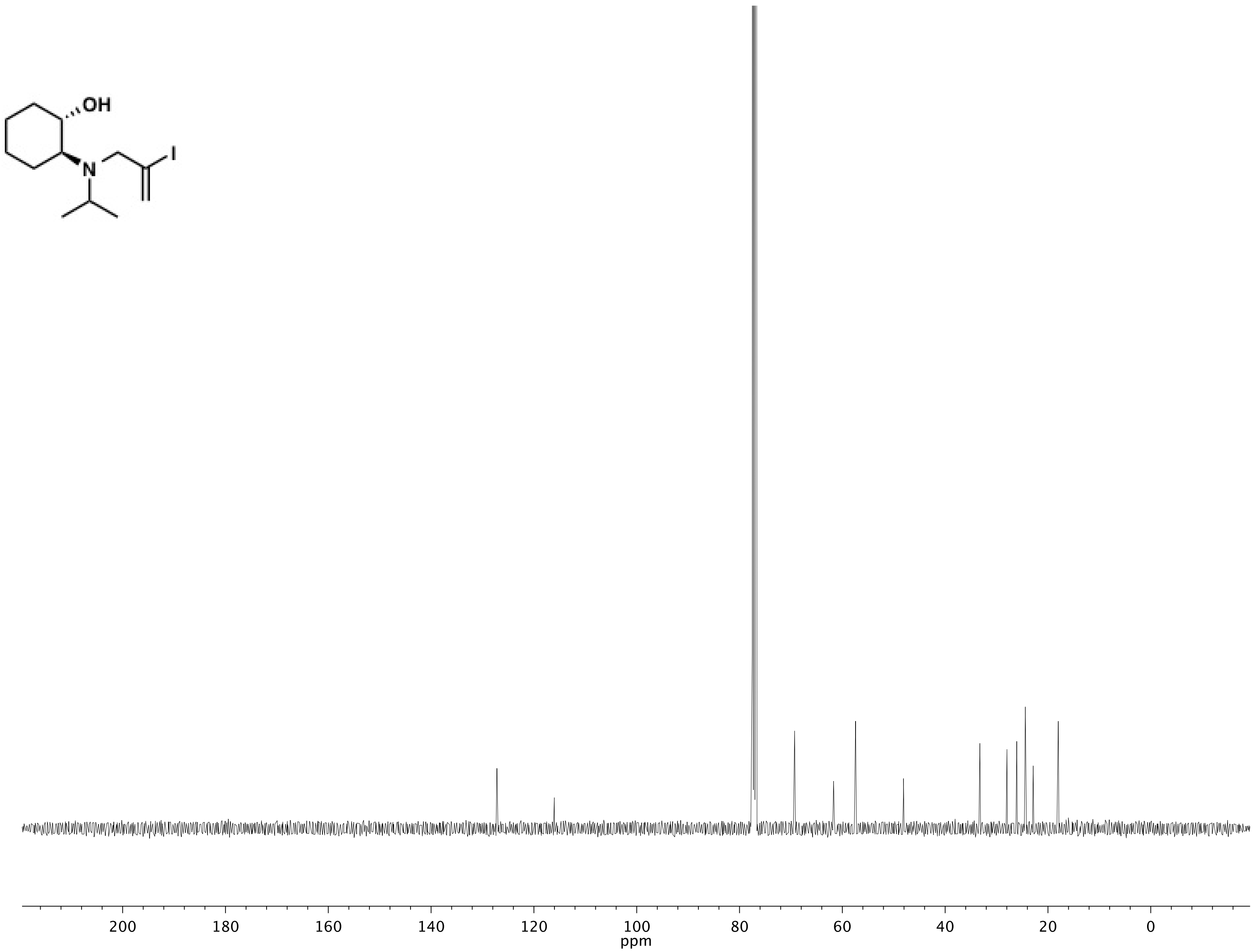
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5c**.



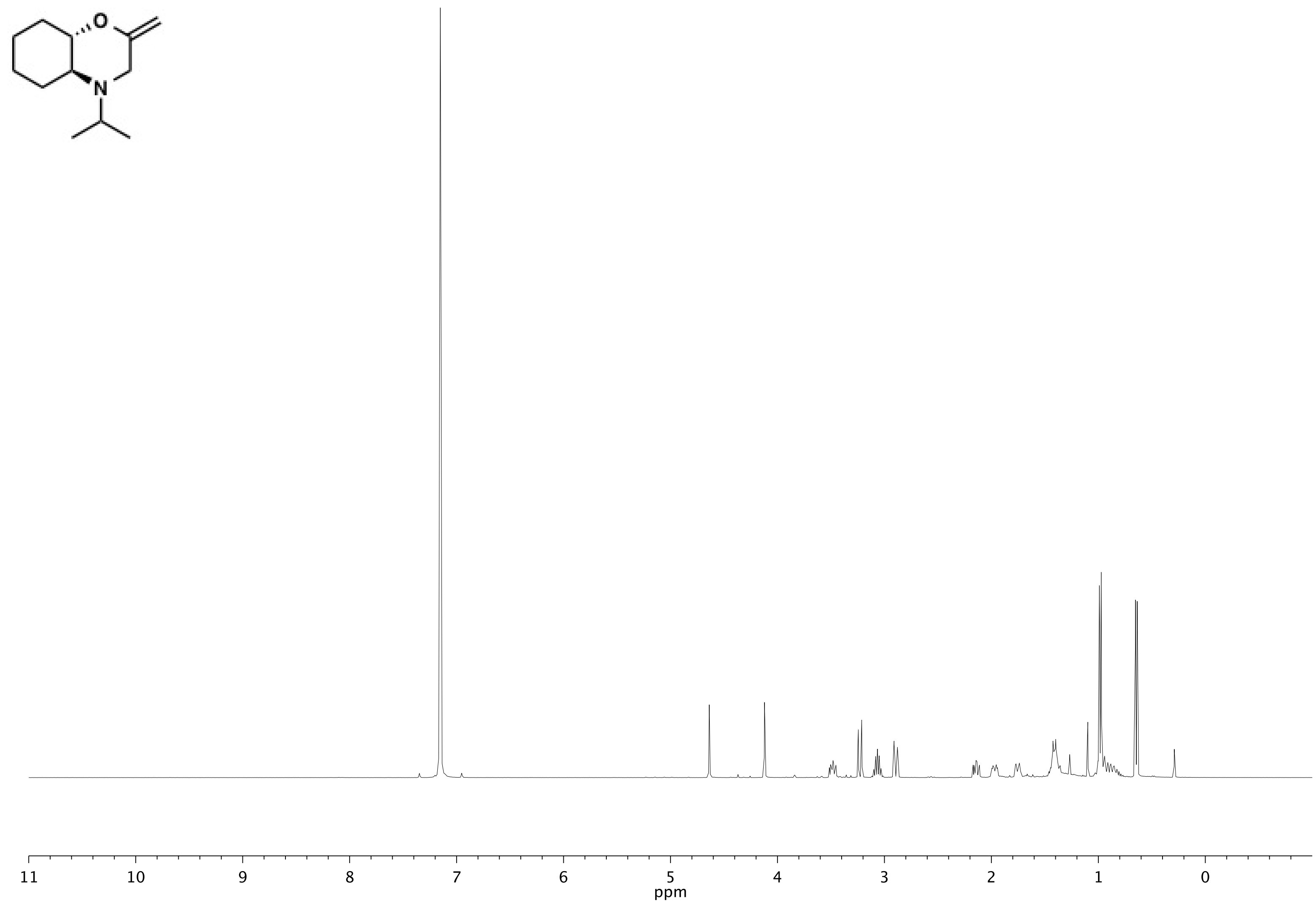
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5c**.



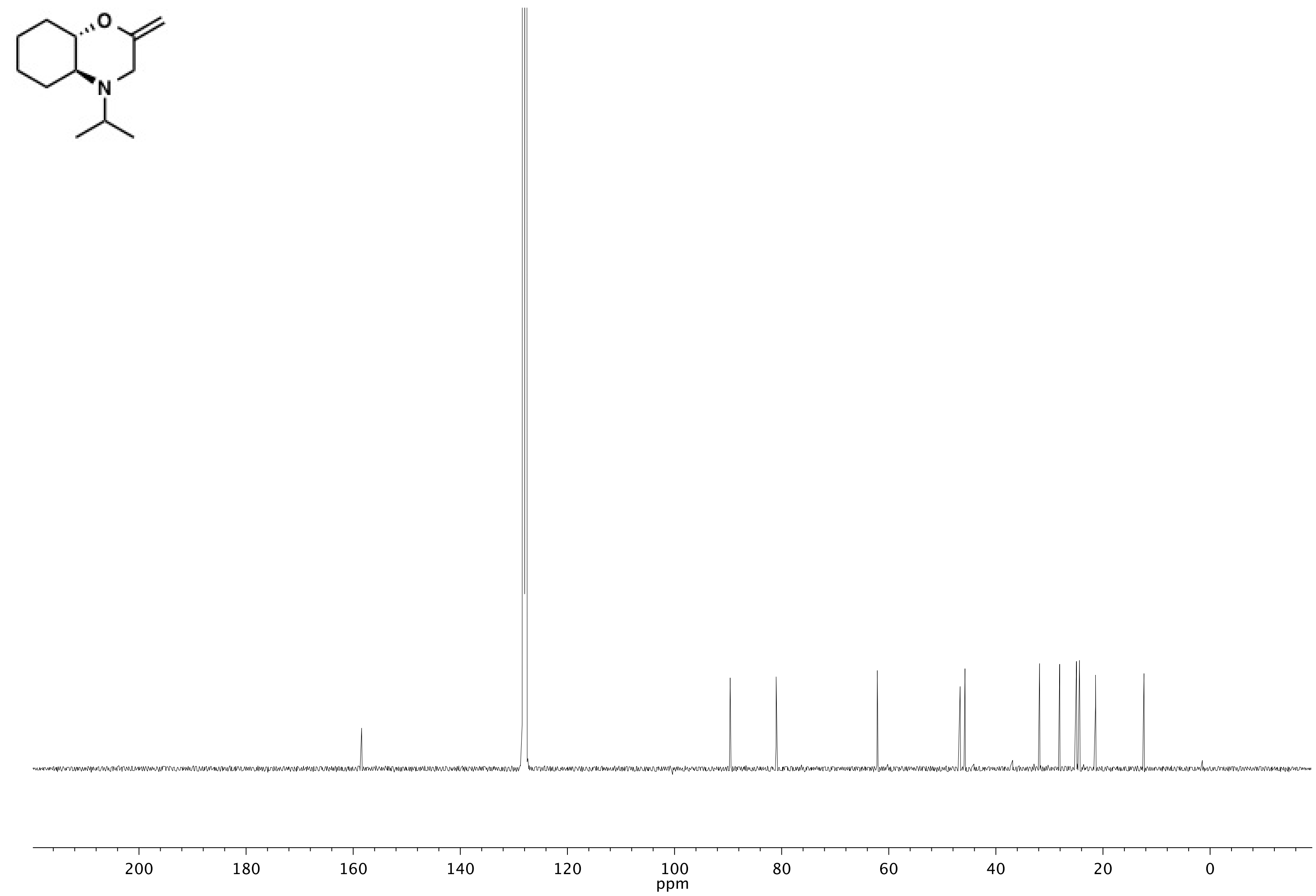
^{1}H NMR (400 MHz, CDCl$_3$) of compound **4d**.



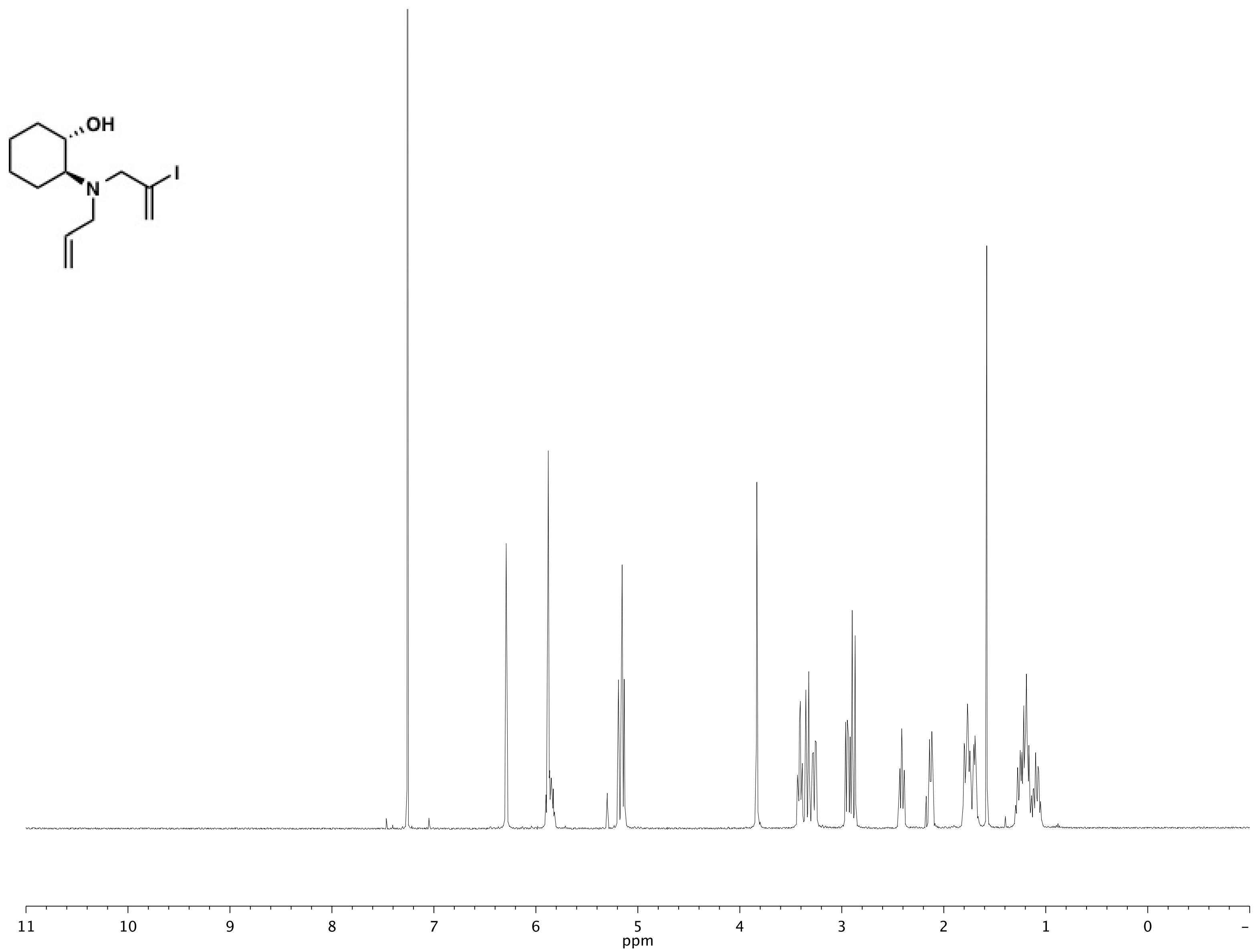
^{13}C NMR (101 MHz, CDCl$_3$) of compound **4d**.



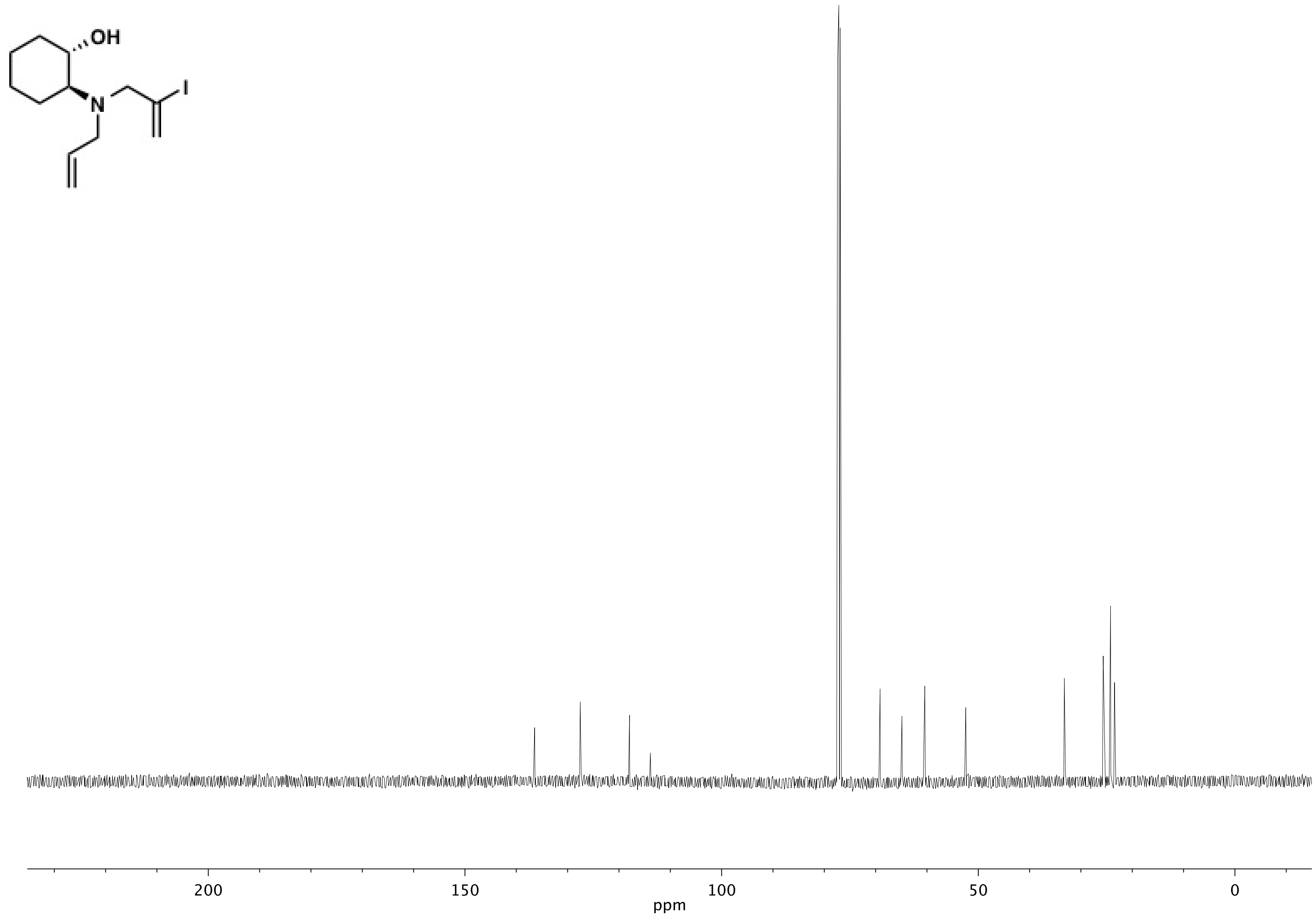
^{1}H NMR (400 MHz, C_6D_6) of compound **5d**.



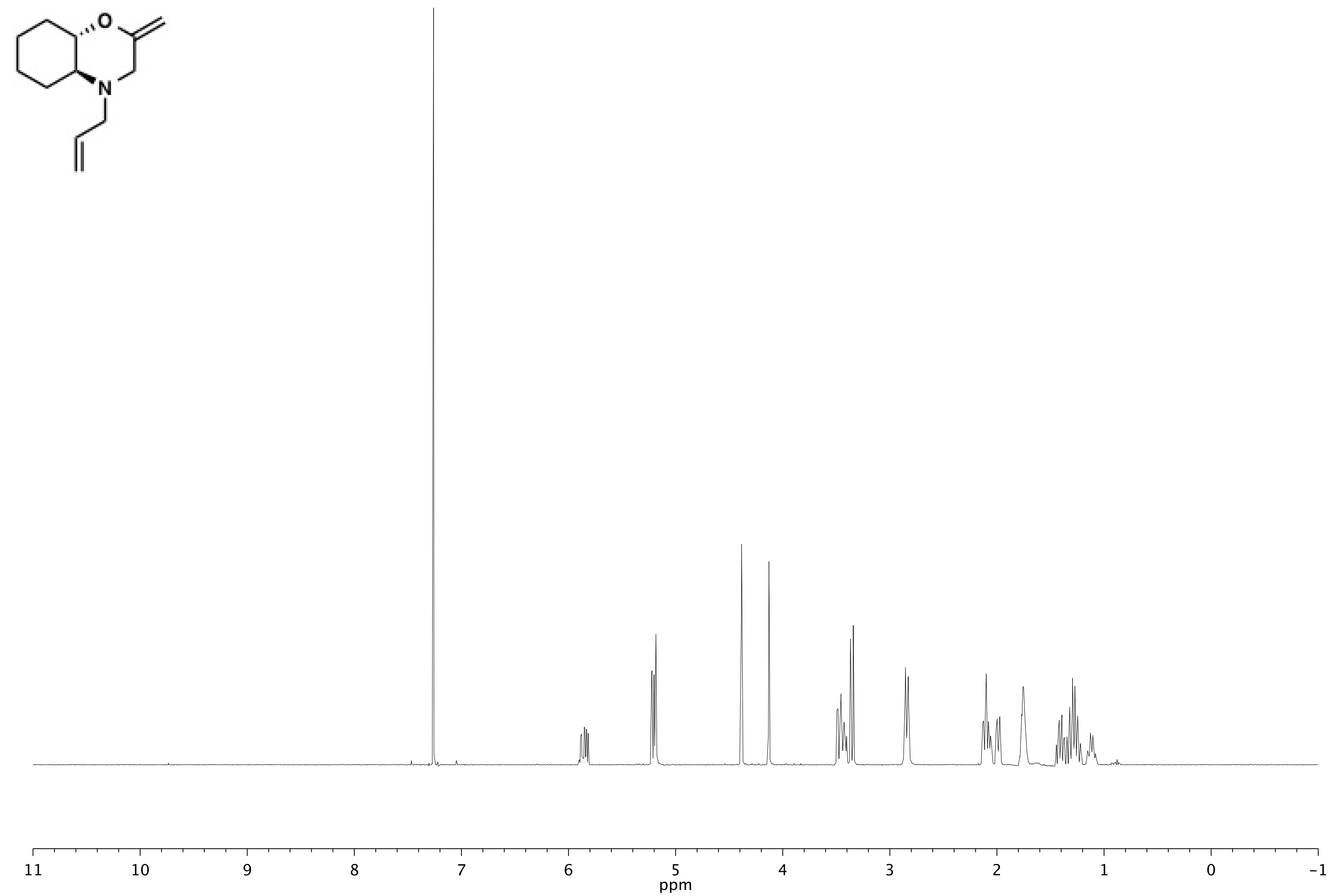
^{13}C NMR (101 MHz, C_6D_6) of compound **5d**.



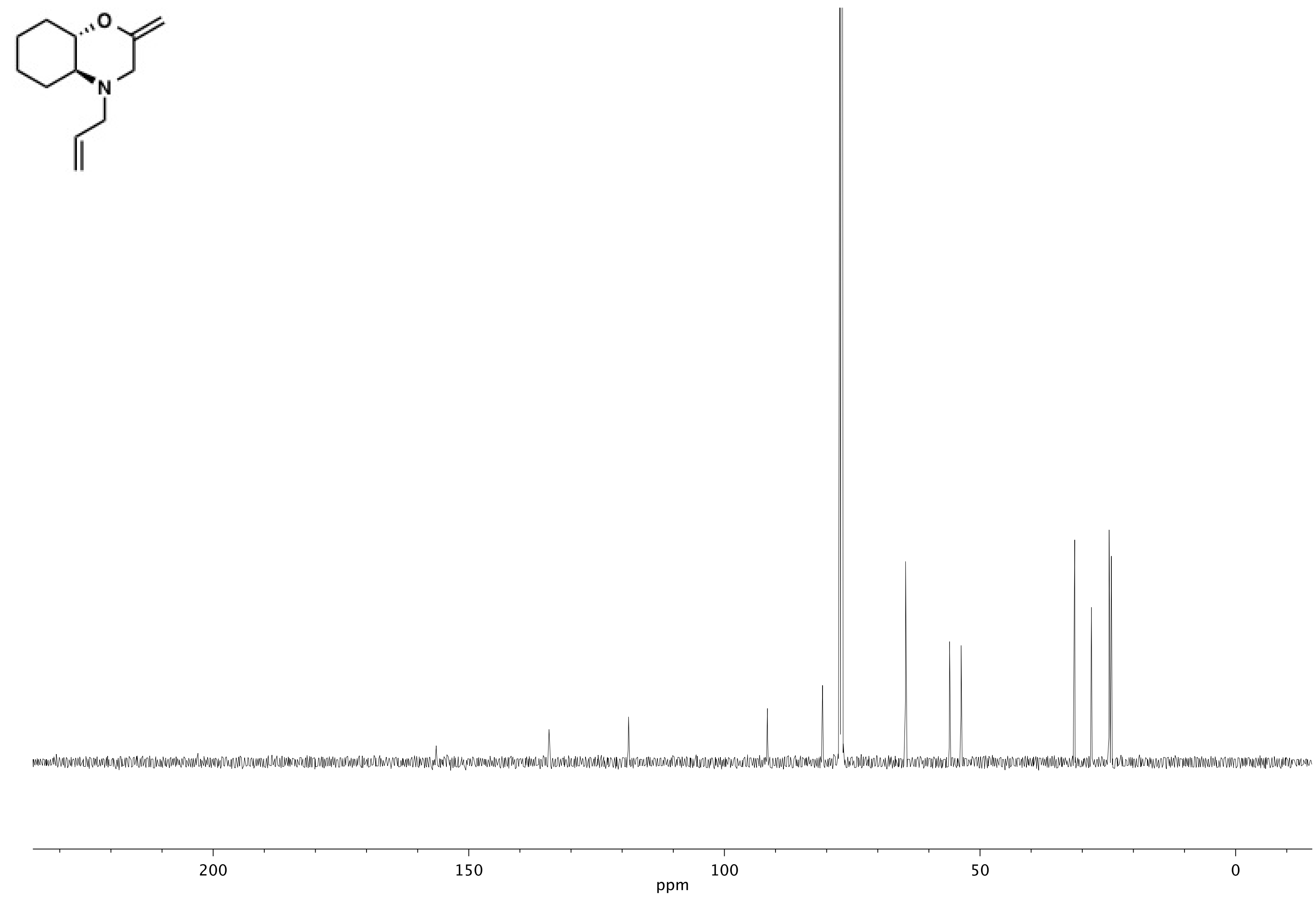
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4e**.



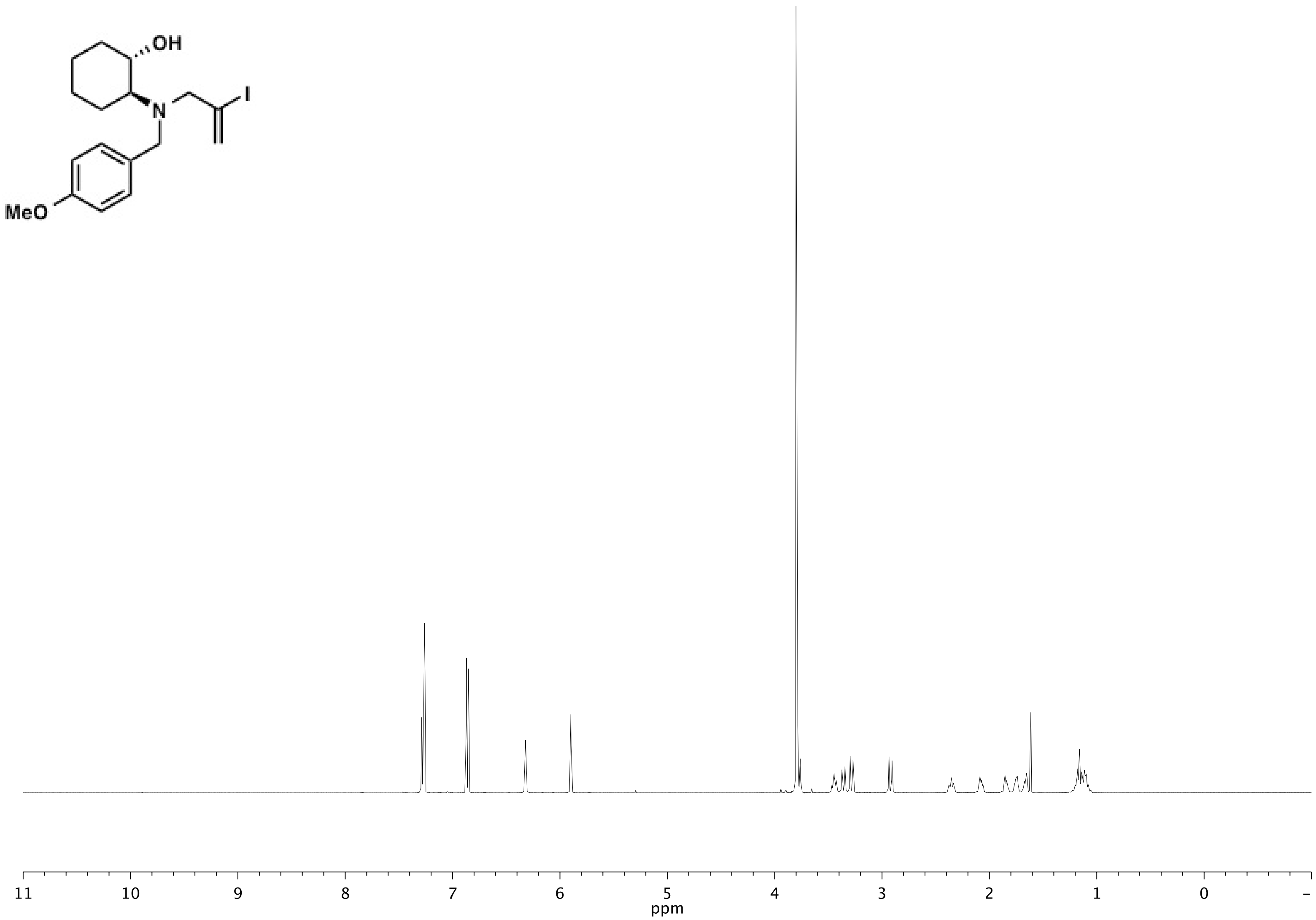
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4e**.



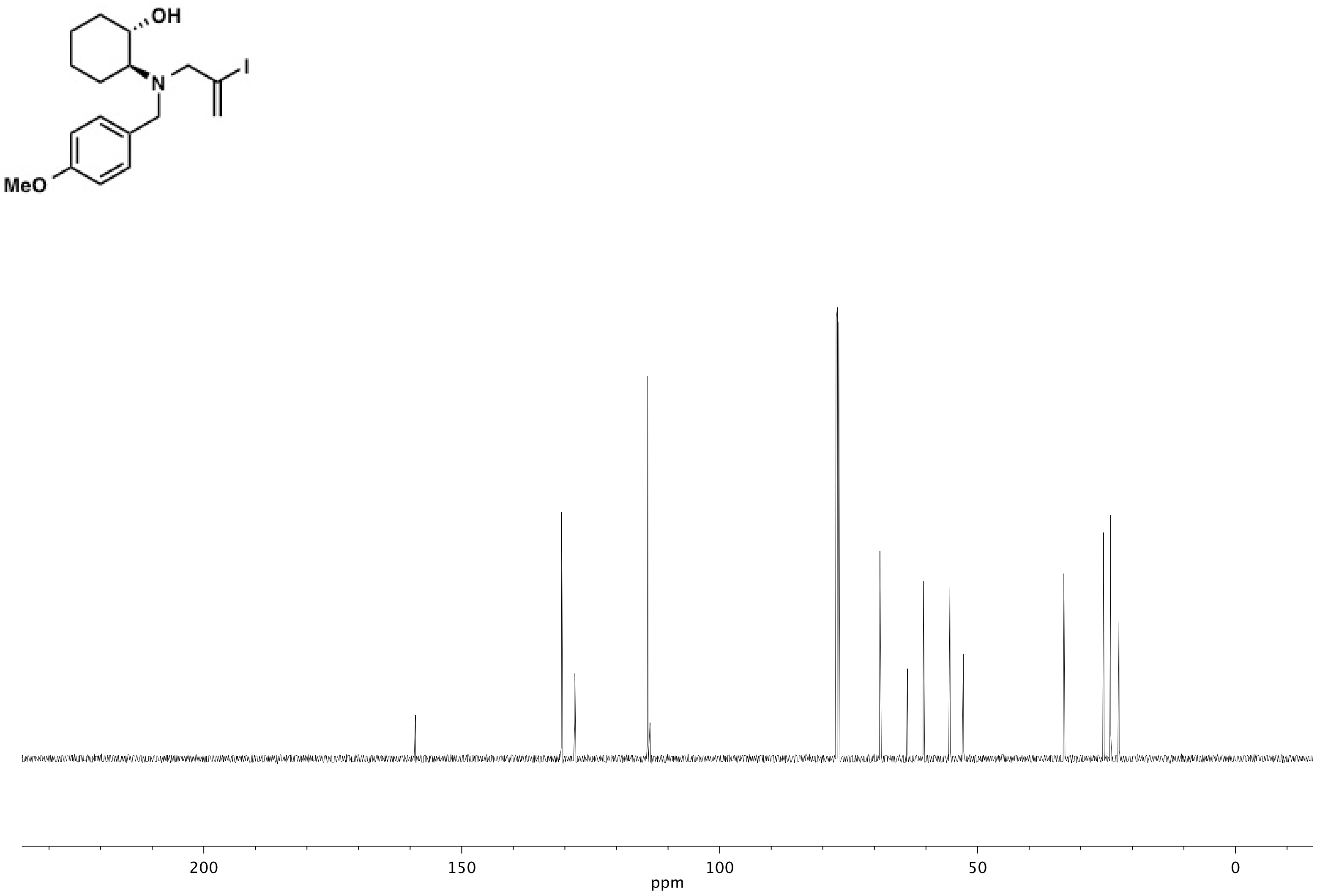
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5e**.



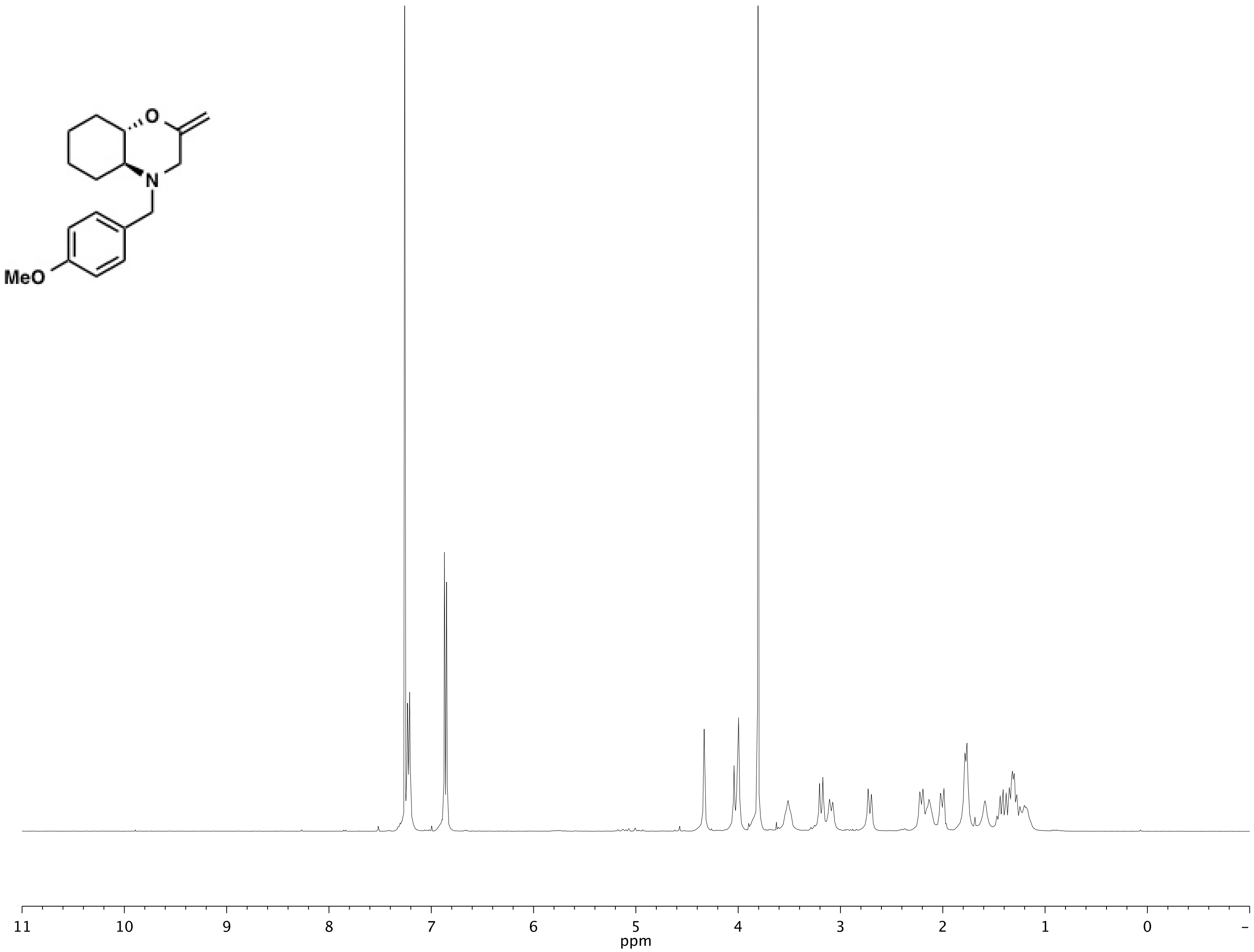
^{13}C NMR (126 MHz, $CDCl_3$) of compound **5e**.



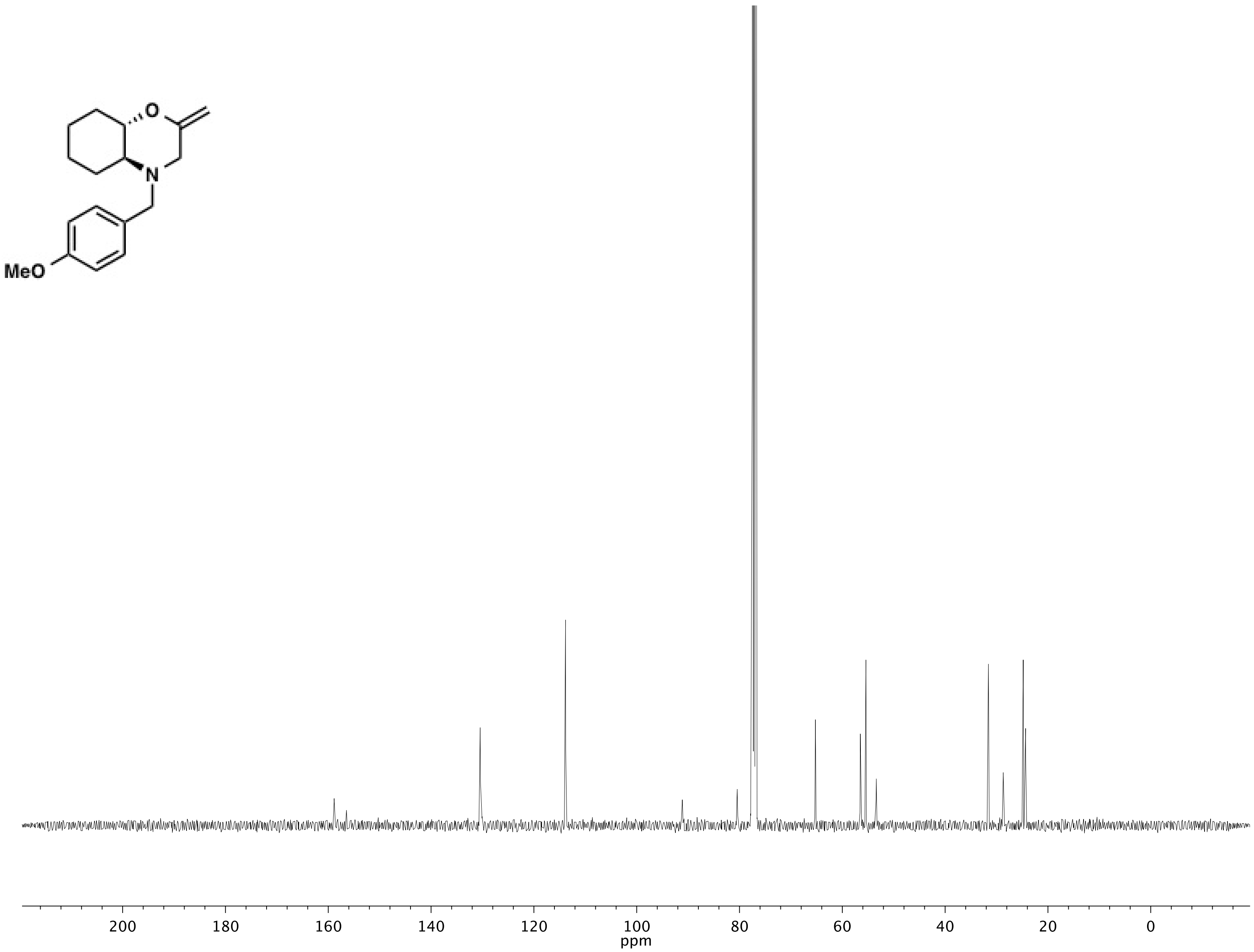
^{1}H NMR (500 MHz, CDCl$_3$) of compound **4f**.



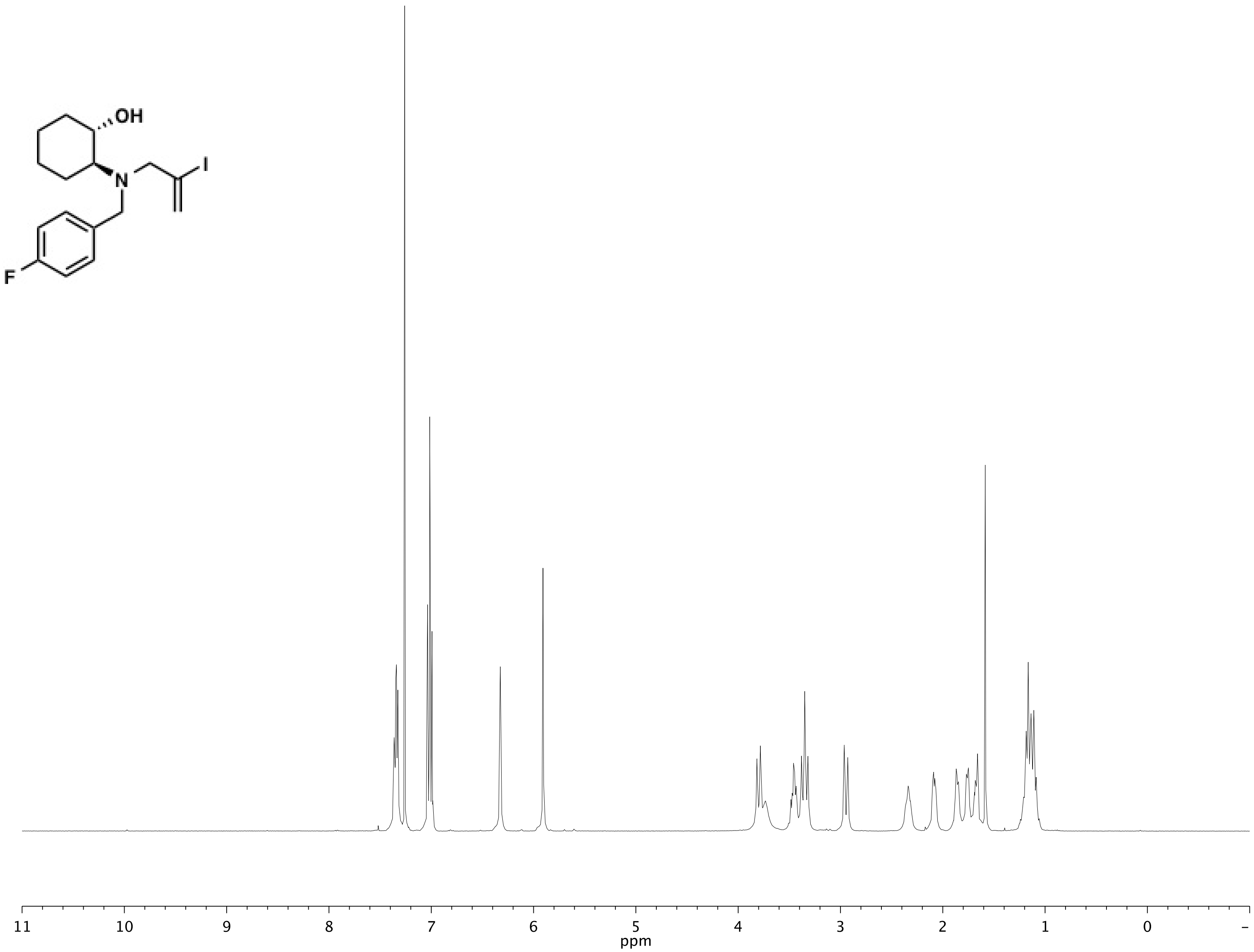
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4f**.



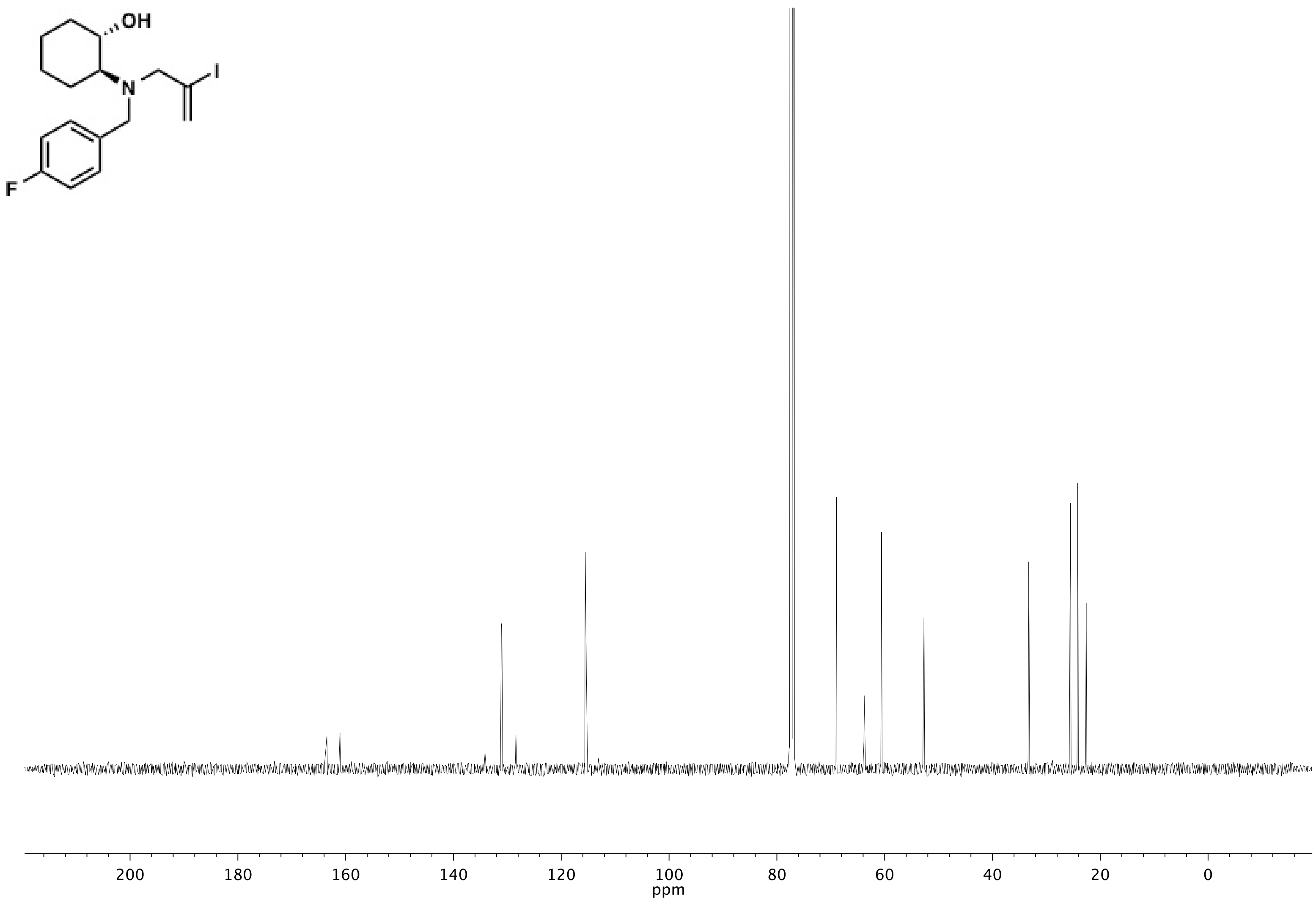
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5f**.



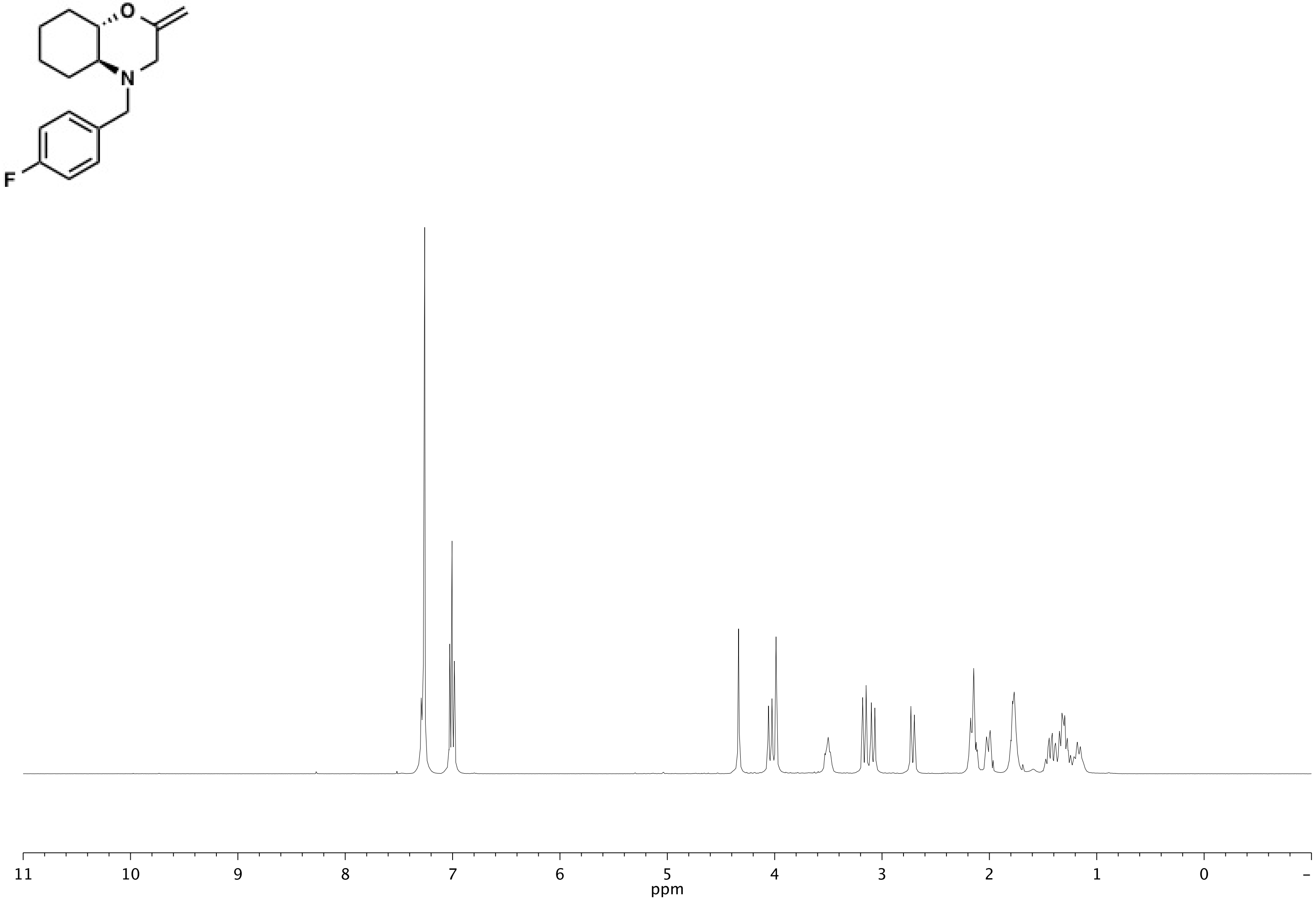
^{13}C NMR (101 MHz, CDCl$_3$) of compound **5f**.



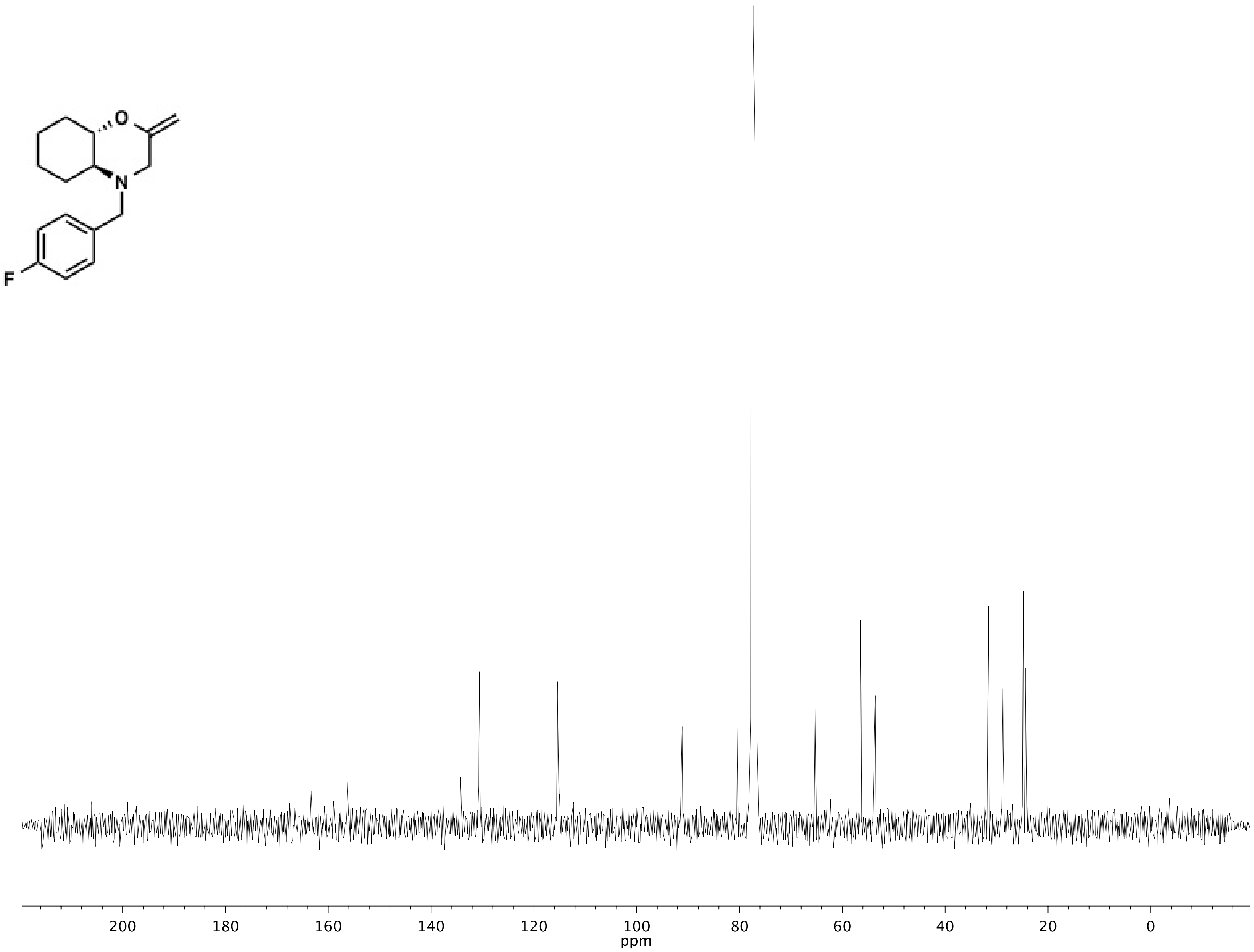
^{1}H NMR (400 MHz, CDCl$_3$) of compound **4g**.



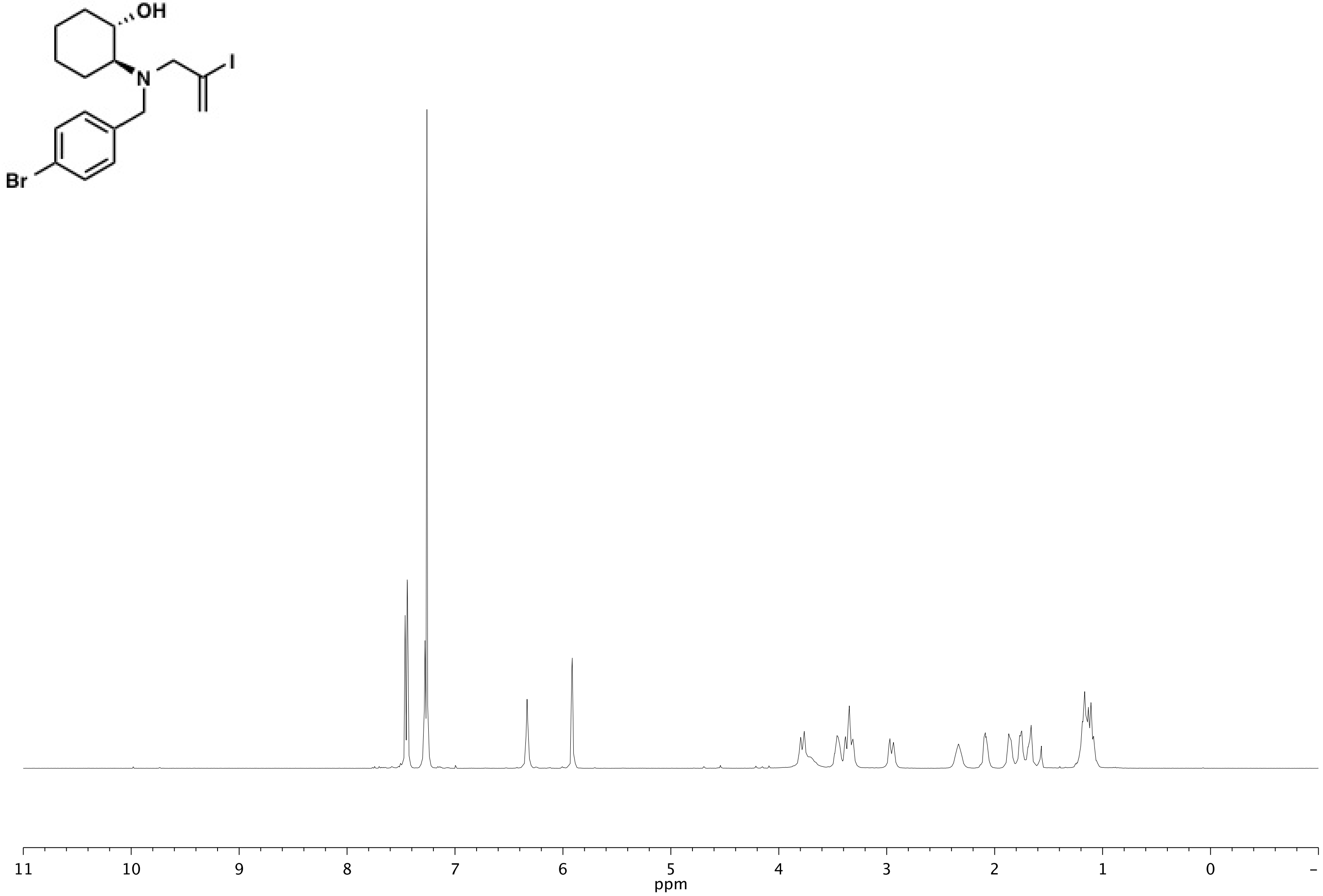
^{13}C NMR (101 MHz, CDCl$_3$) of compound **4g**.



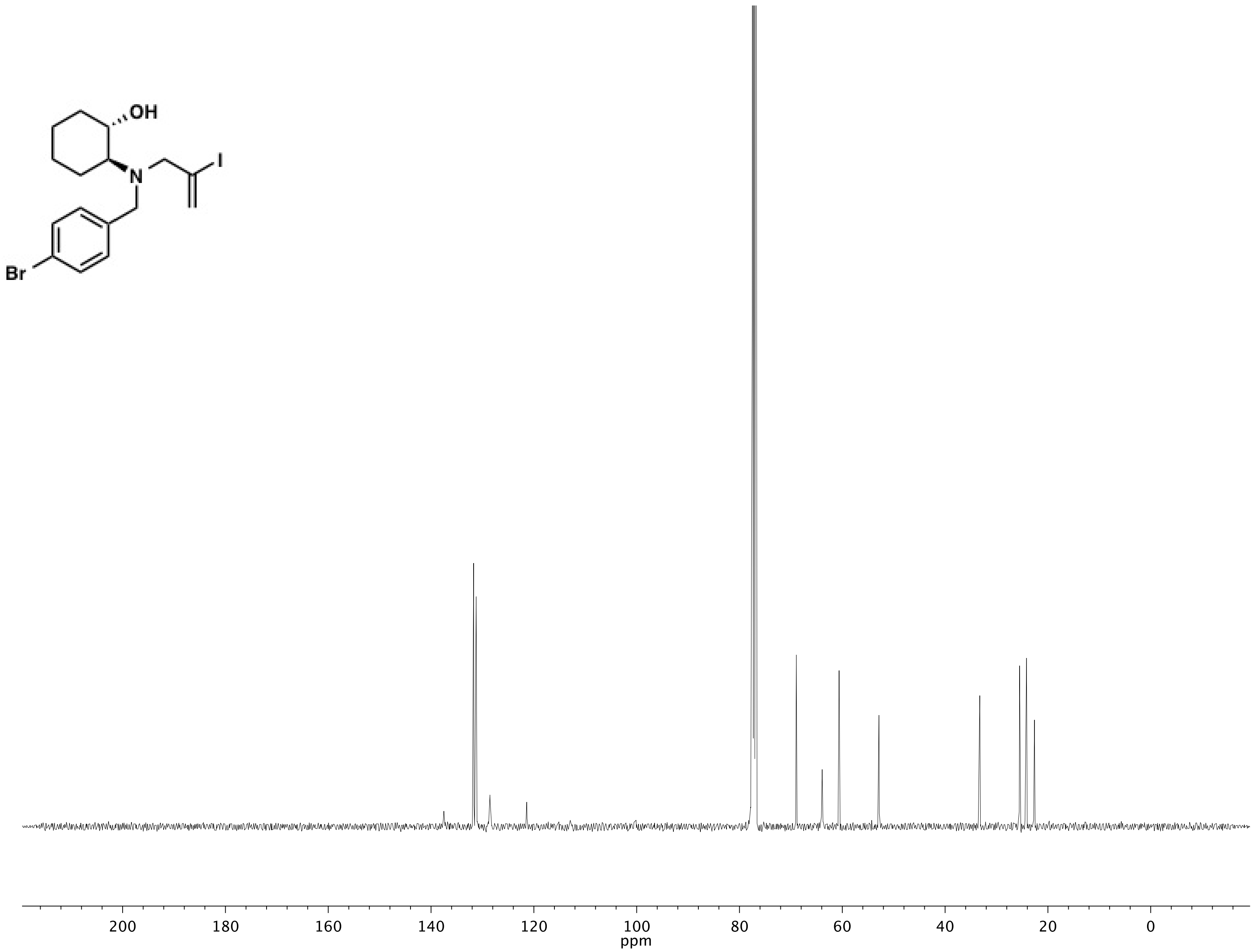
^{1}H NMR (400 MHz, CDCl$_3$) of compound **5g**.



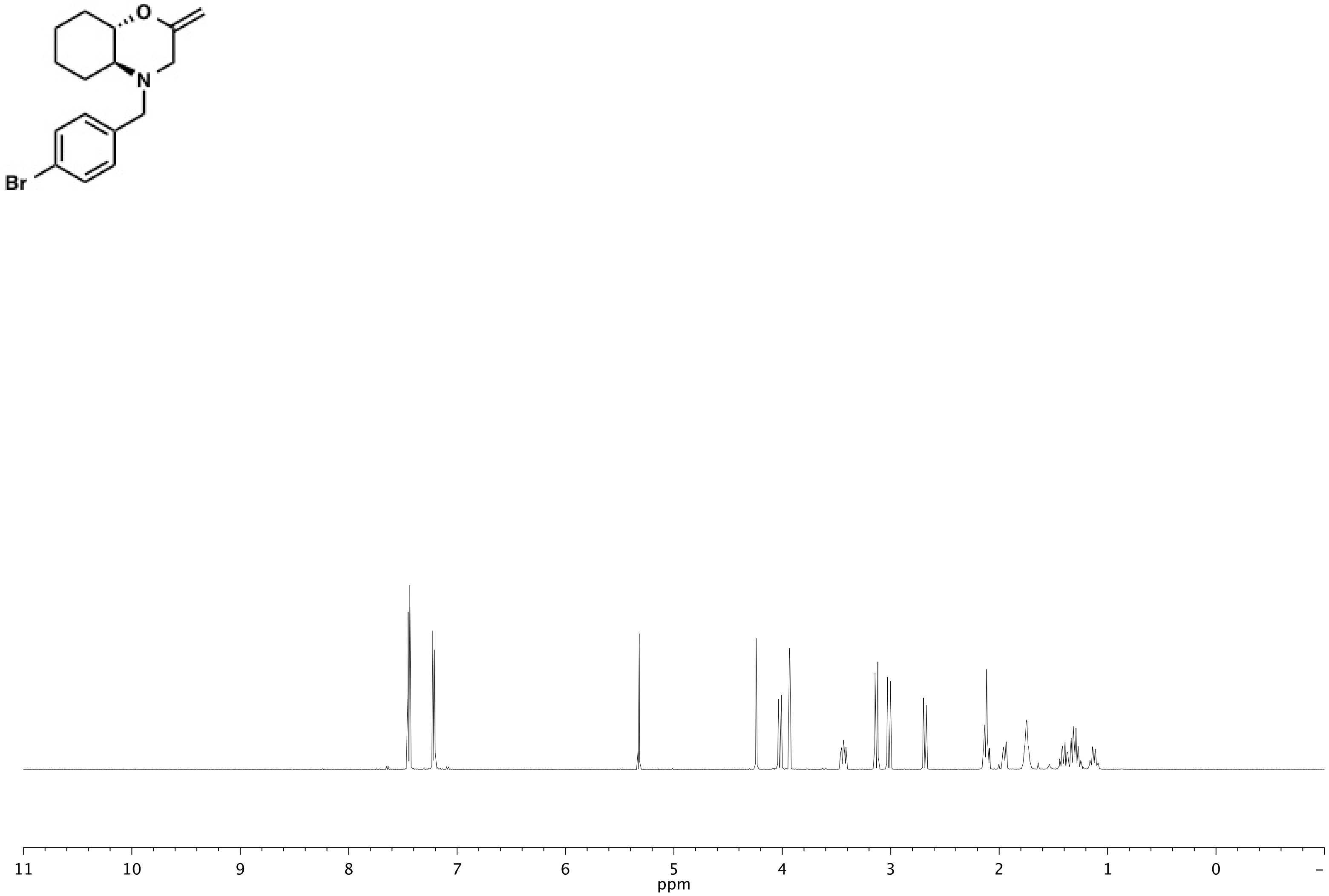
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5g**.



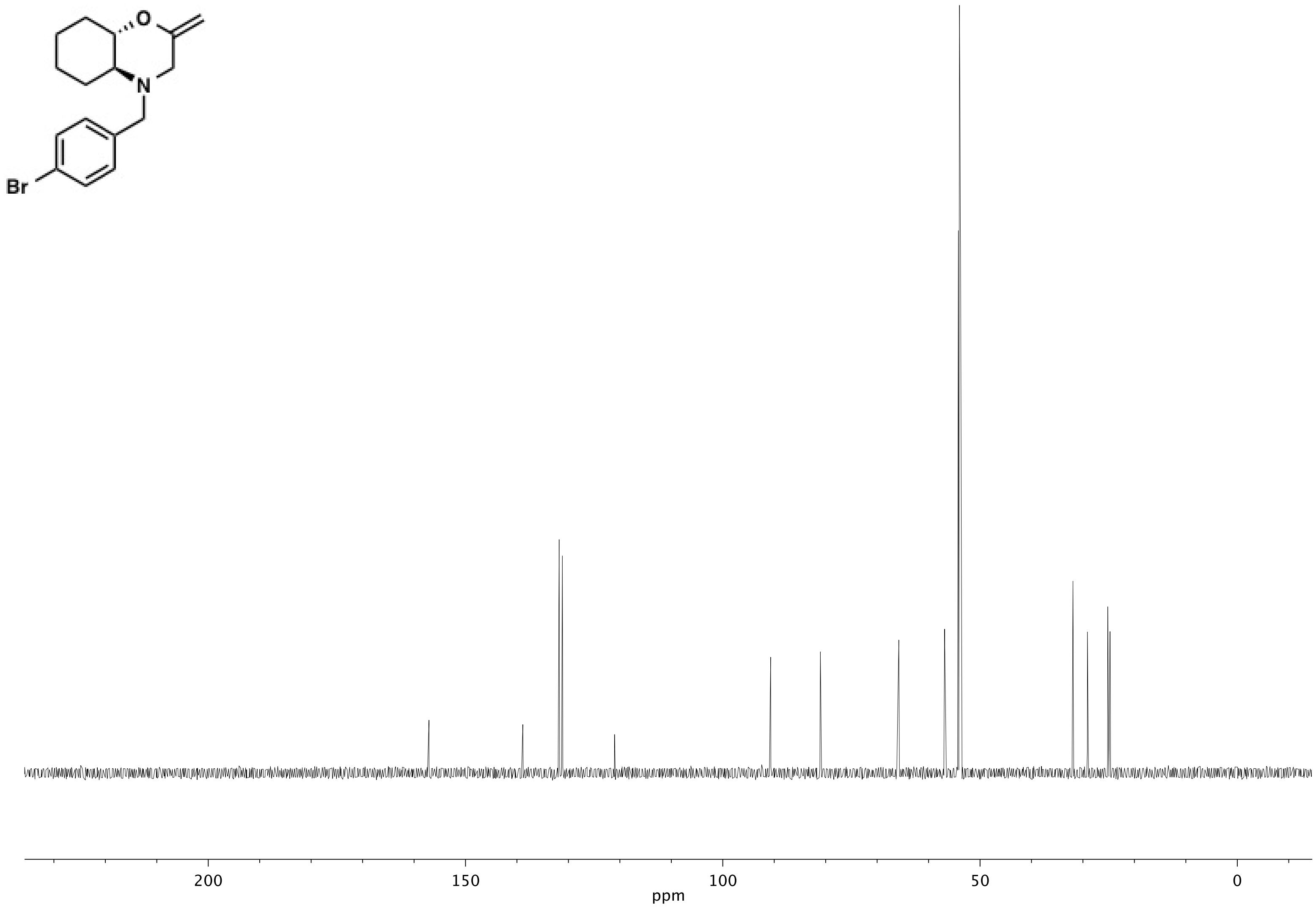
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4h**.



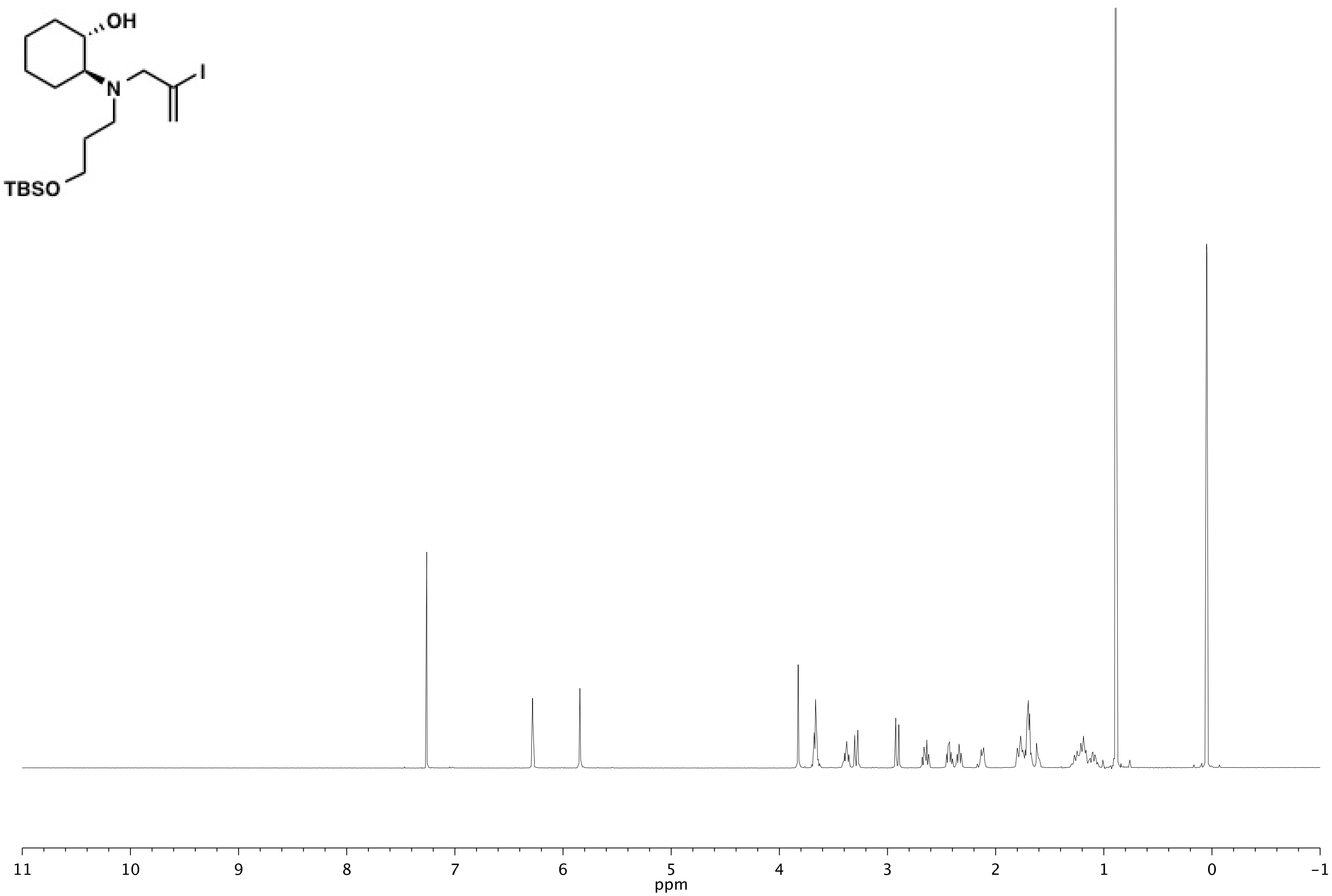
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4h**.



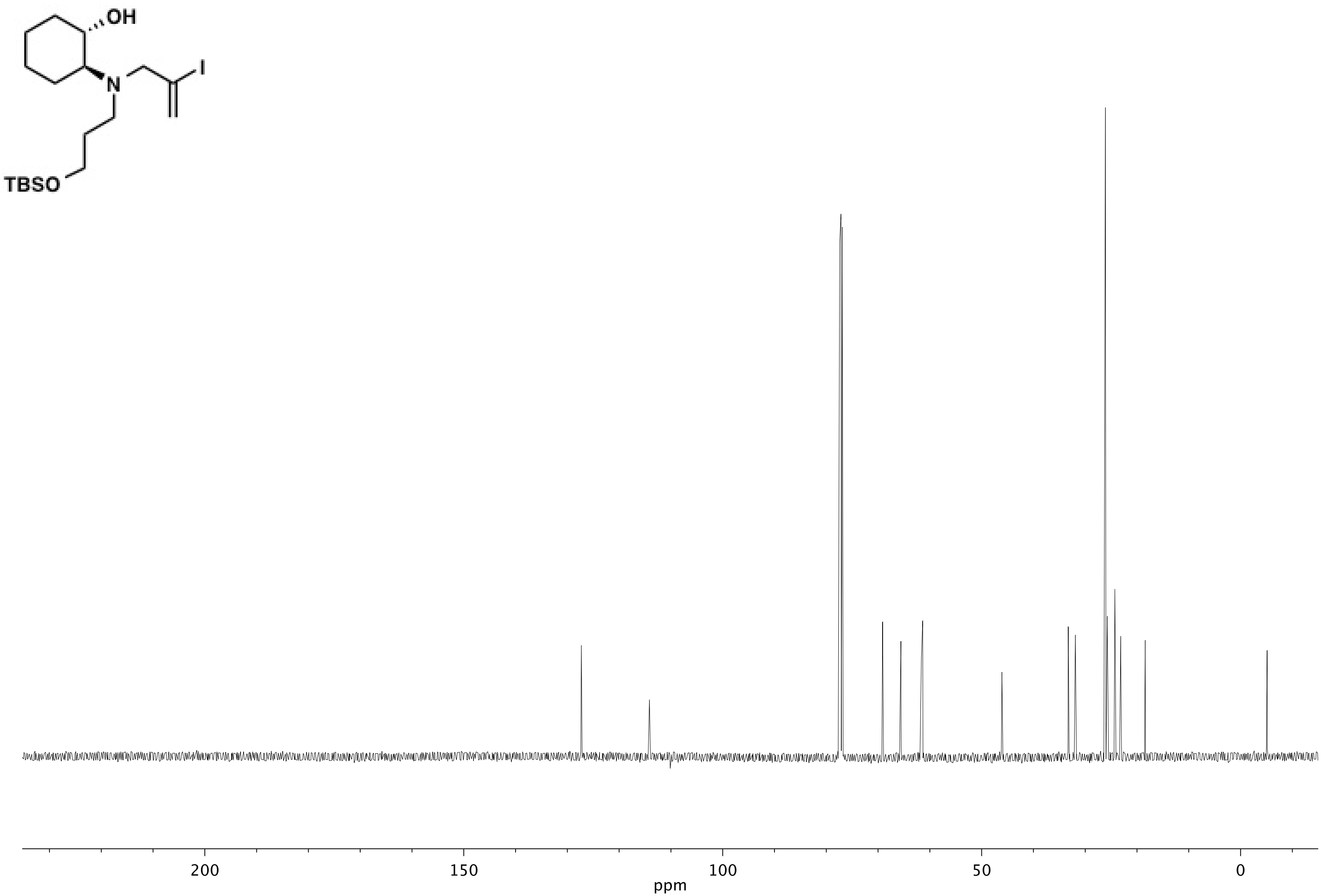
^{1}H NMR (500 MHz, CD_2Cl_2) of compound **5h**.



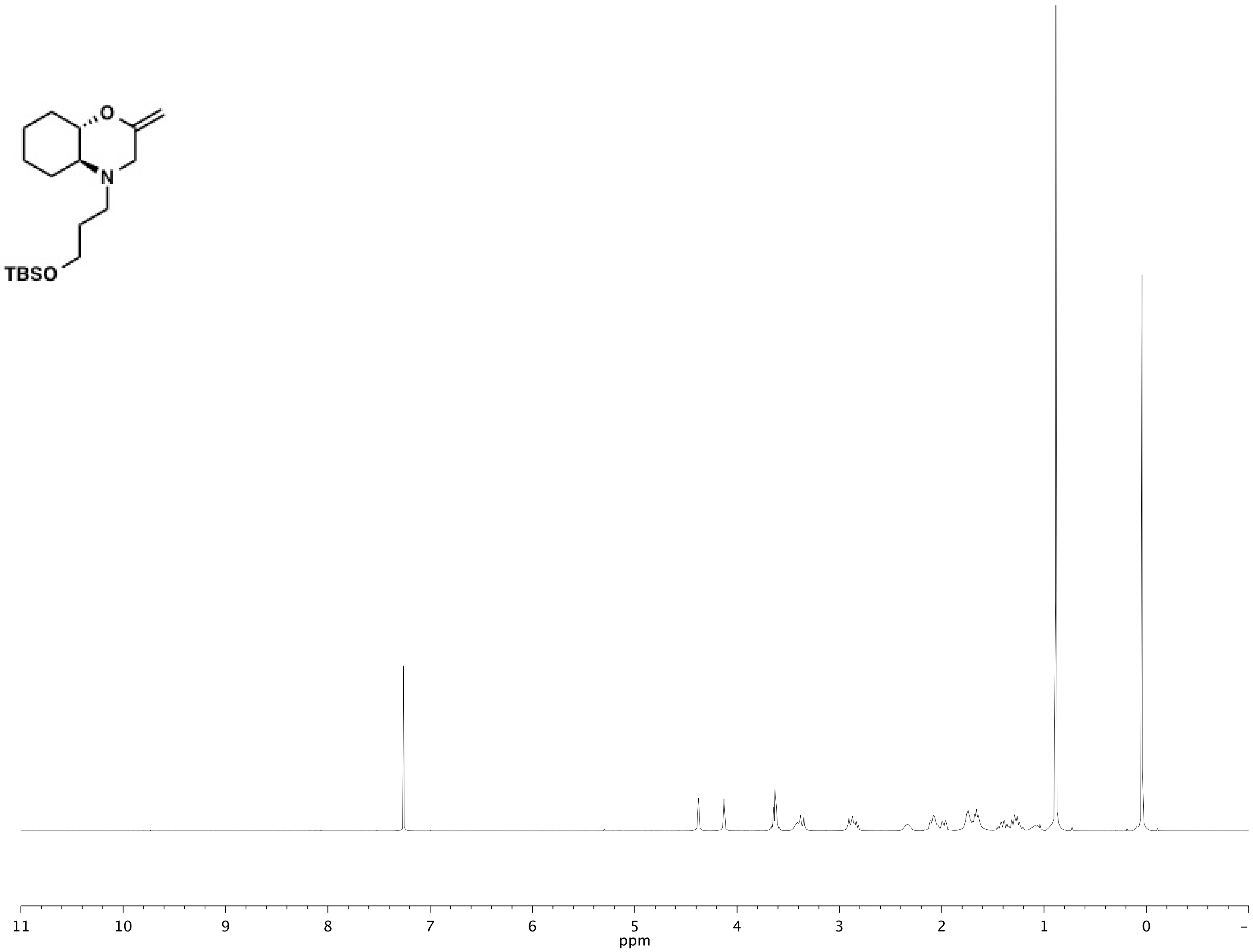
^{13}C NMR (126 MHz, CD_2Cl_2) of compound **5h**.



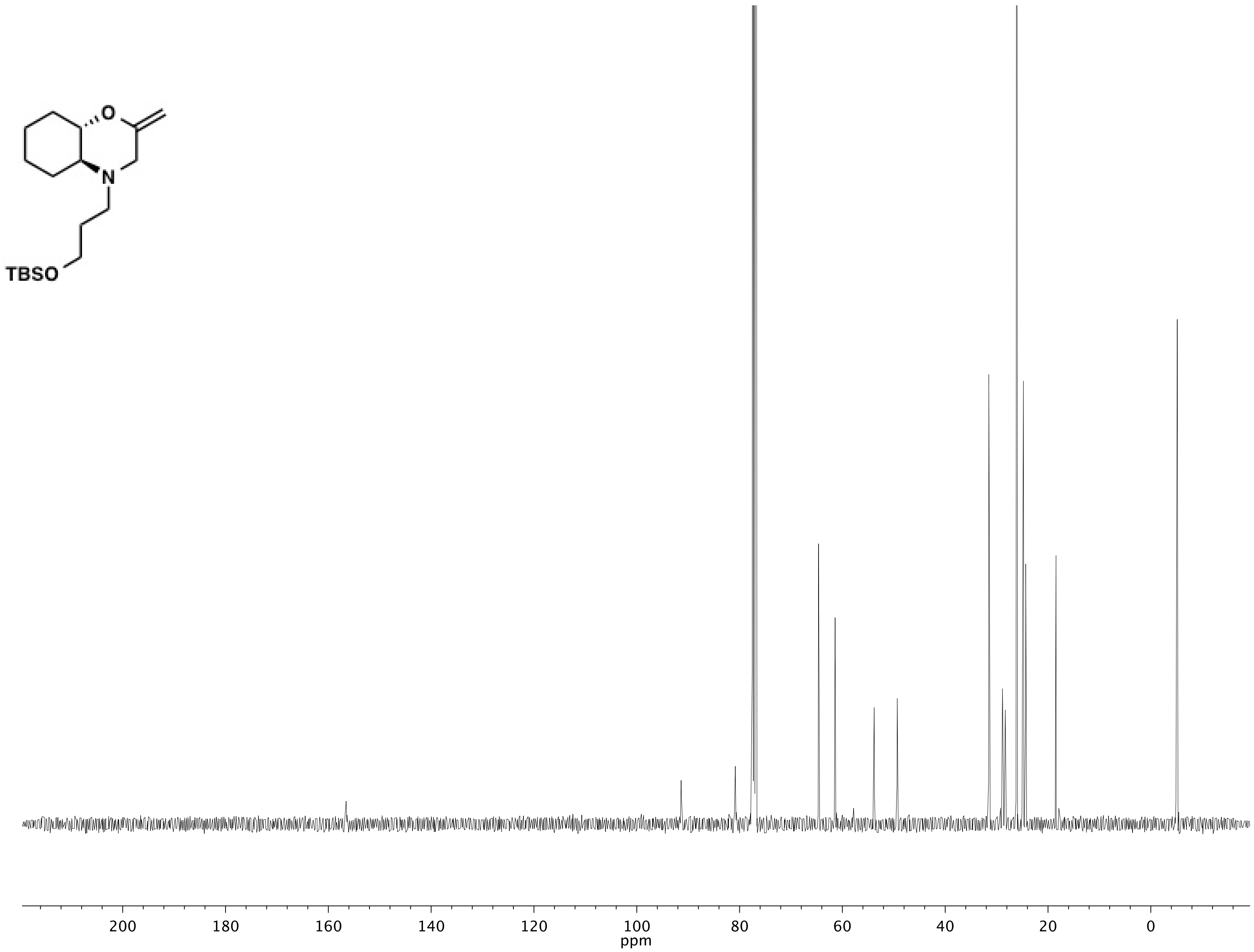
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4i**.



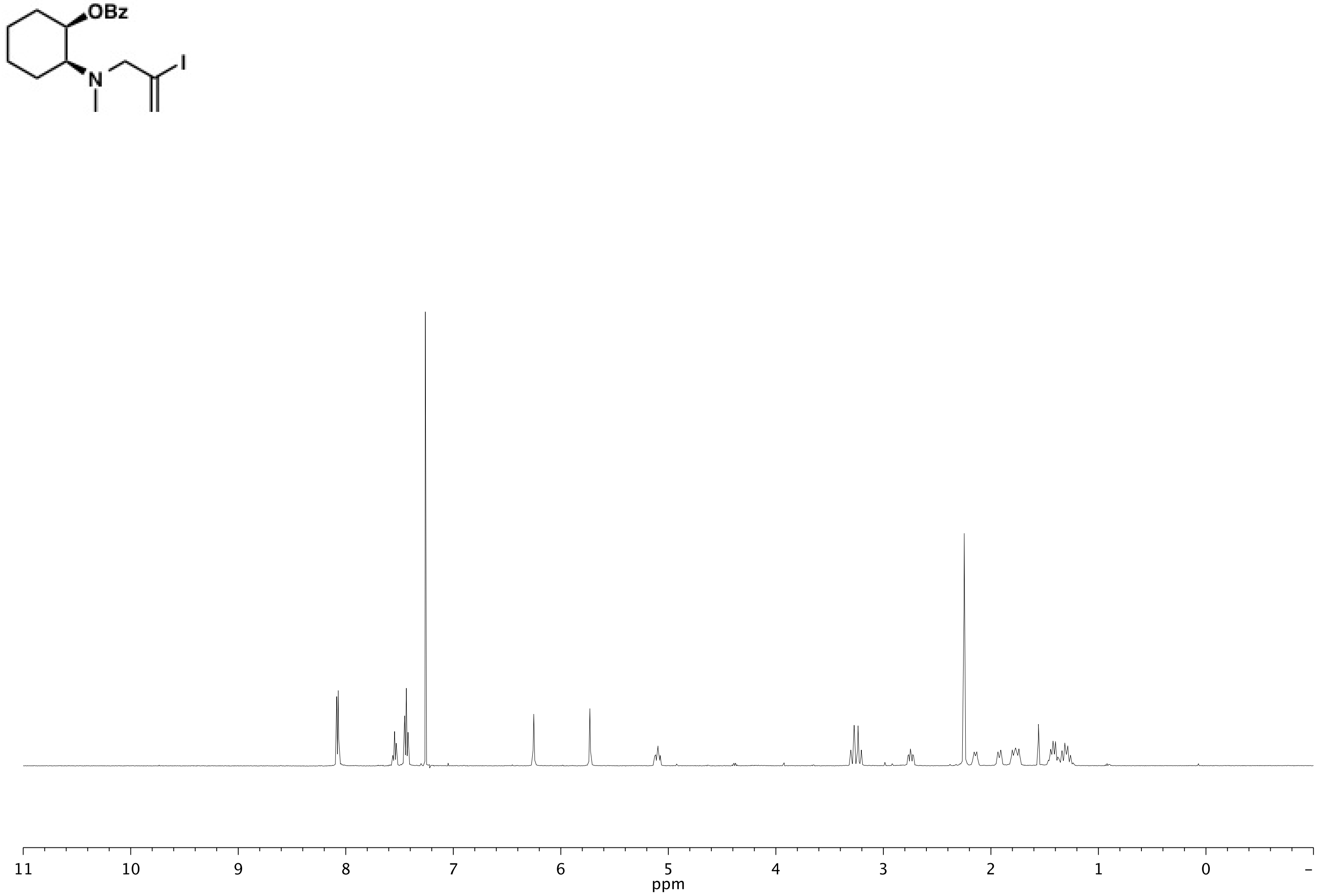
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4i**.



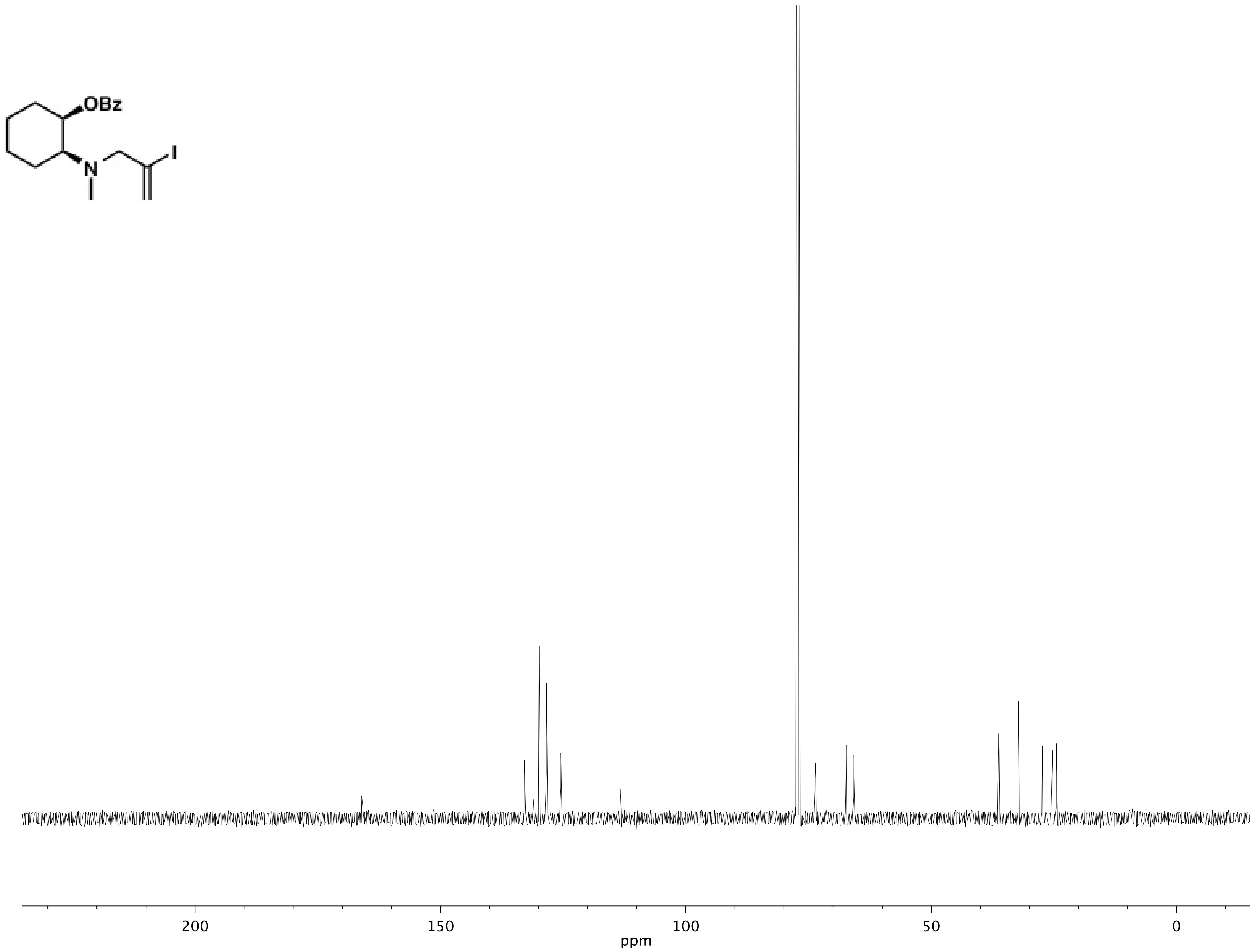
^{1}H NMR (400 MHz, CDCl$_3$) of compound **5i**.



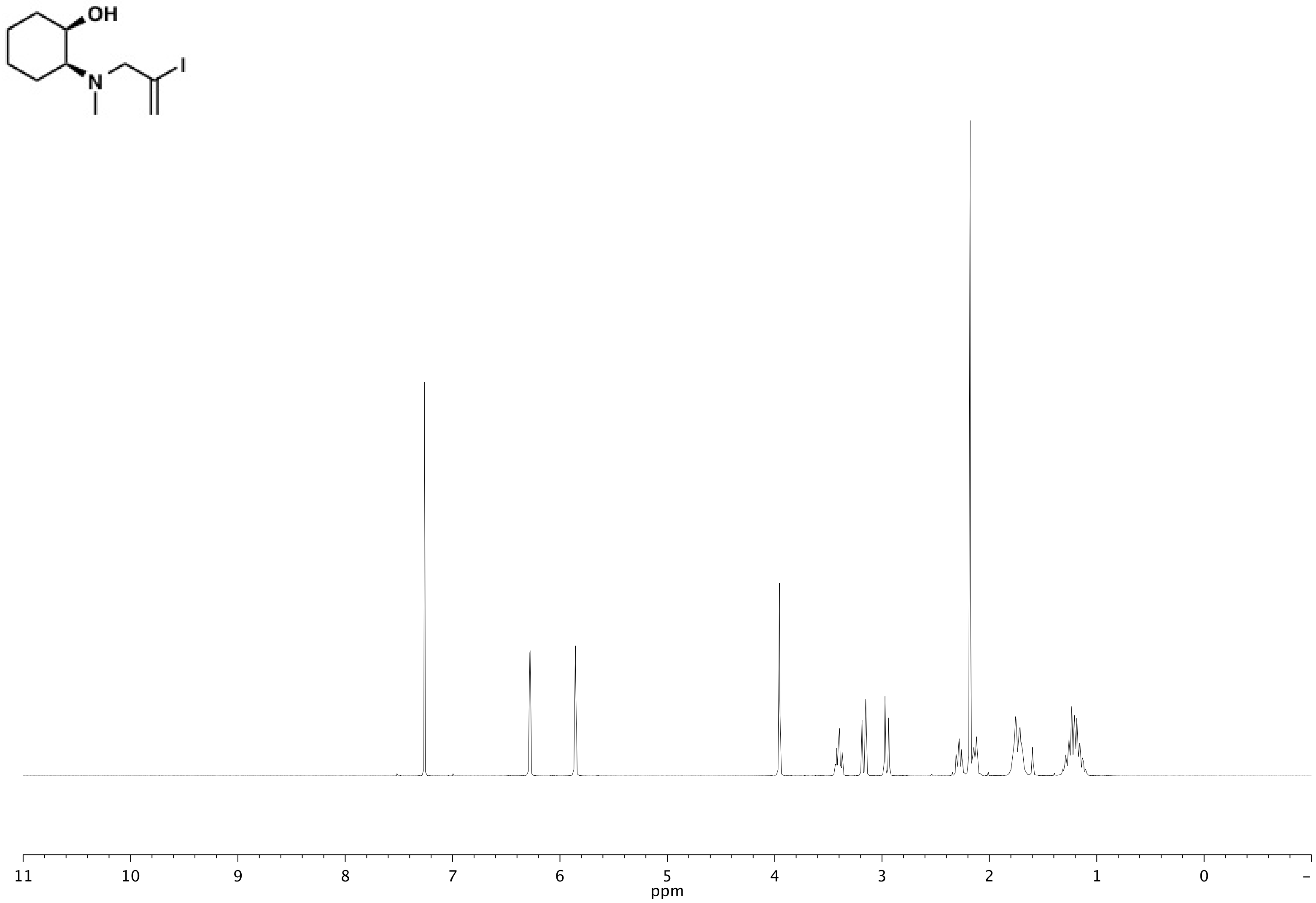
^{13}C NMR (101 MHz, CDCl$_3$) of compound **5i**.



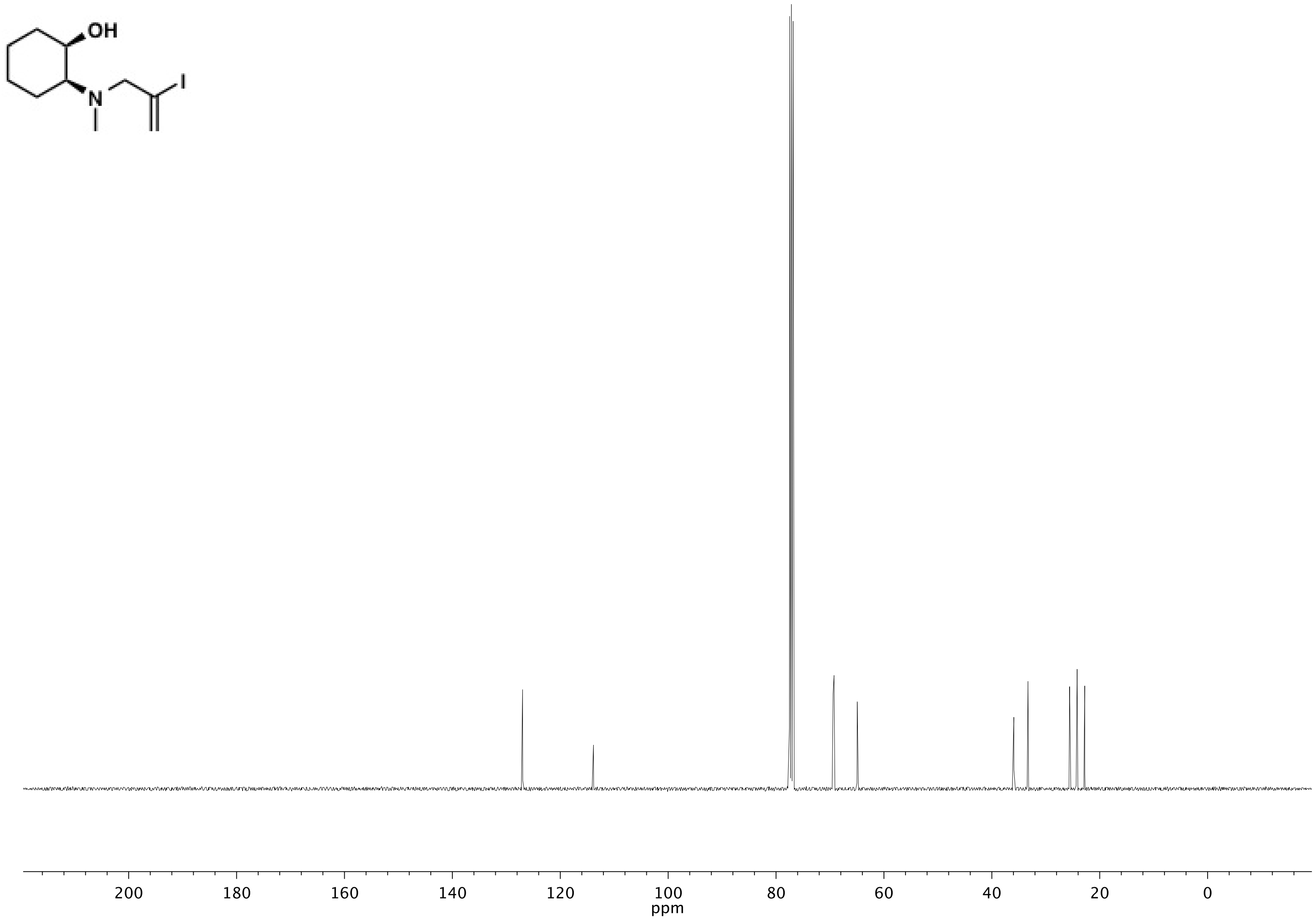
^{1}H NMR (500 MHz, $CDCl_3$) of compound **SI-6**.



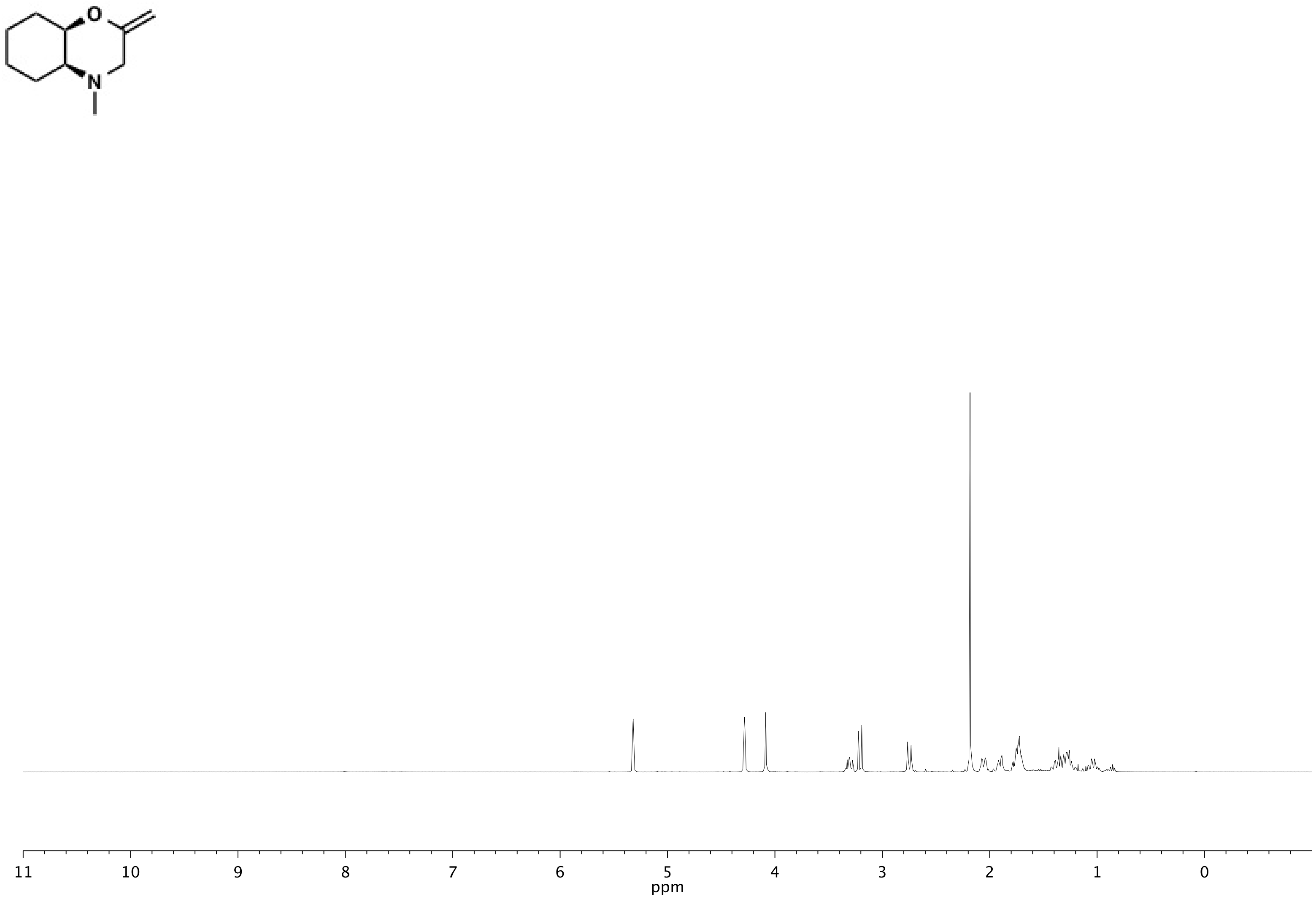
^{13}C NMR (126 MHz, CDCl$_3$) of compound **SI-6**.



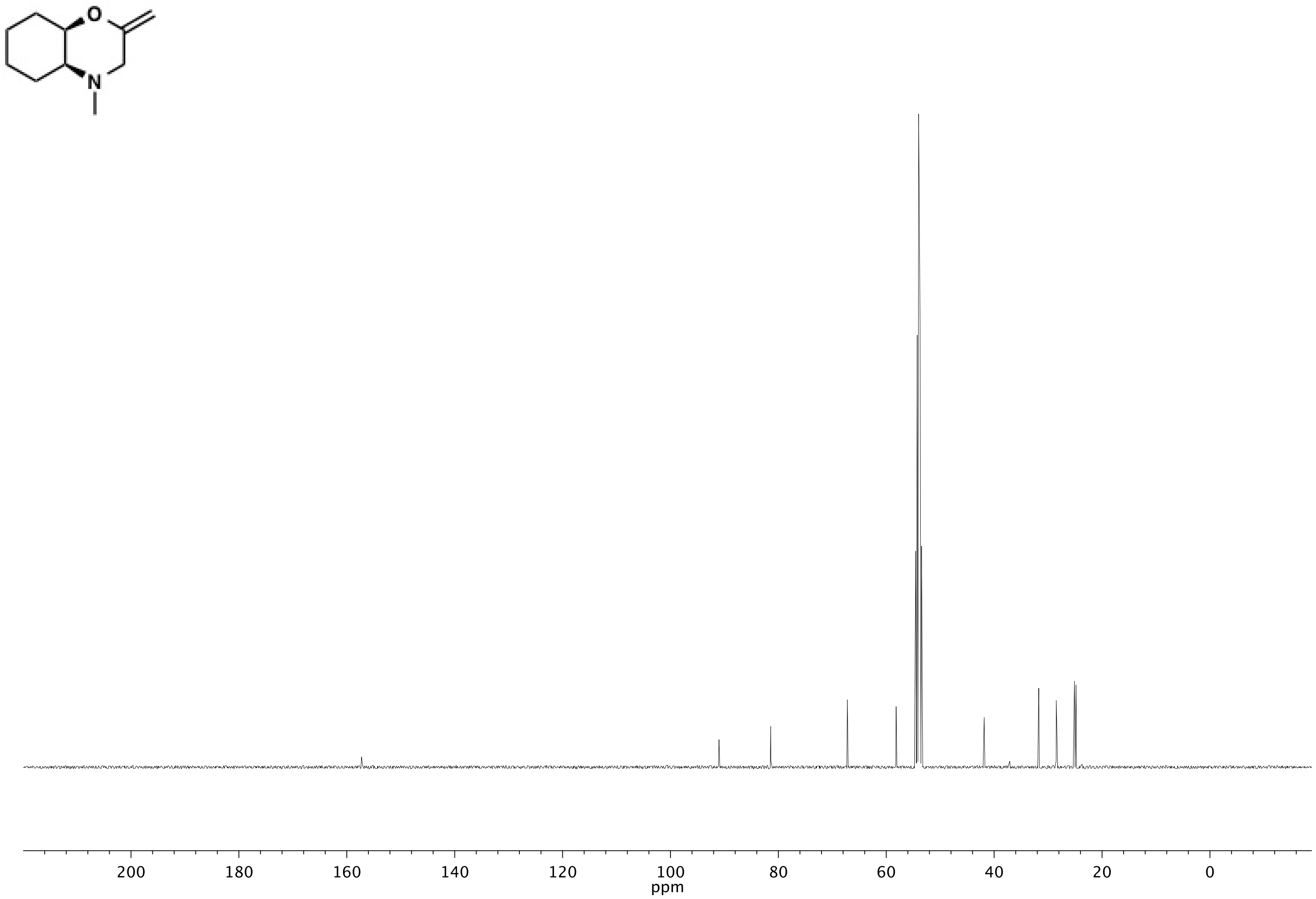
^{1}H NMR (400 MHz, CDCl$_3$) of compound **4j**.



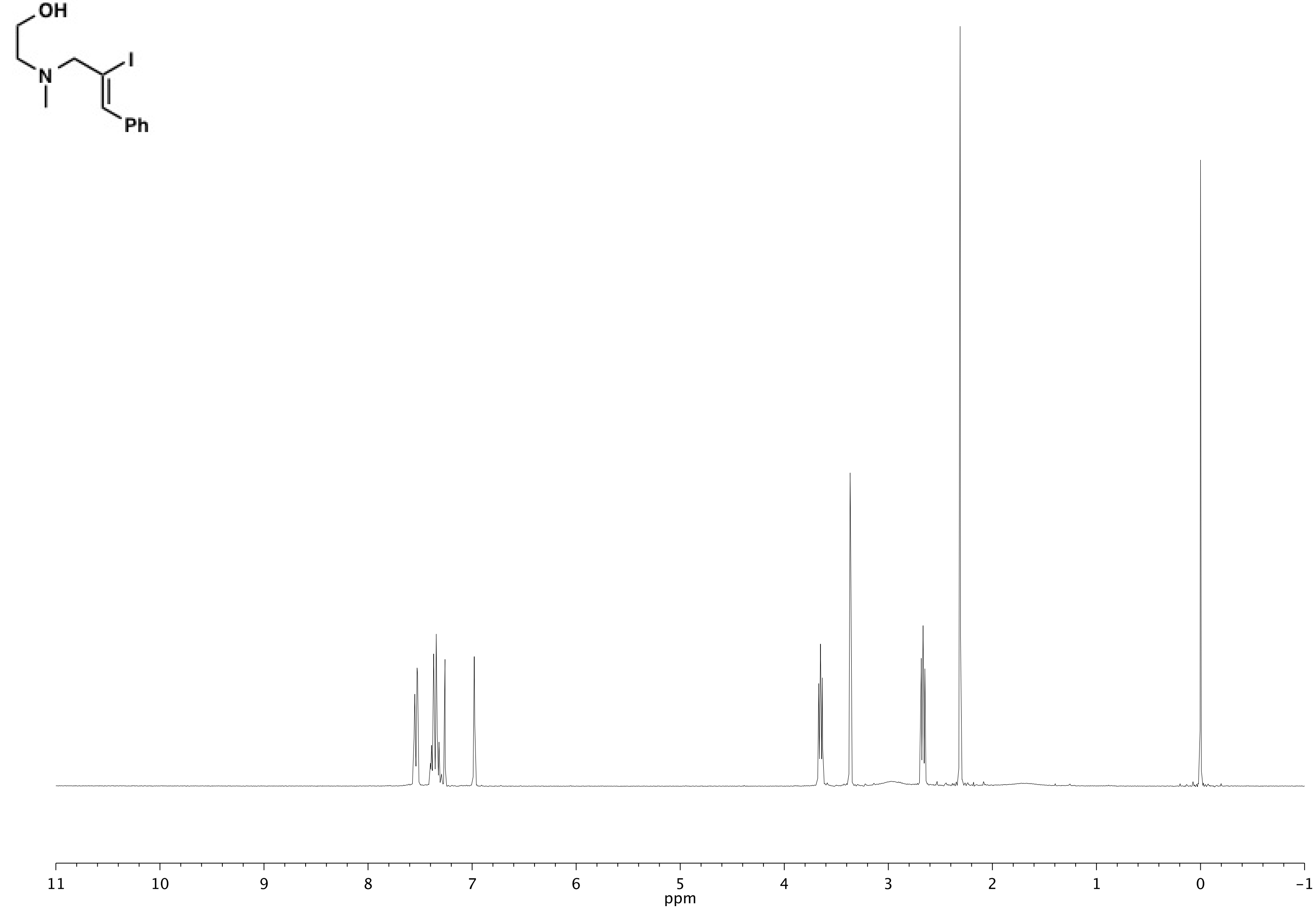
^{13}C NMR (101 MHz, CDCl$_3$) of compound **4j**.



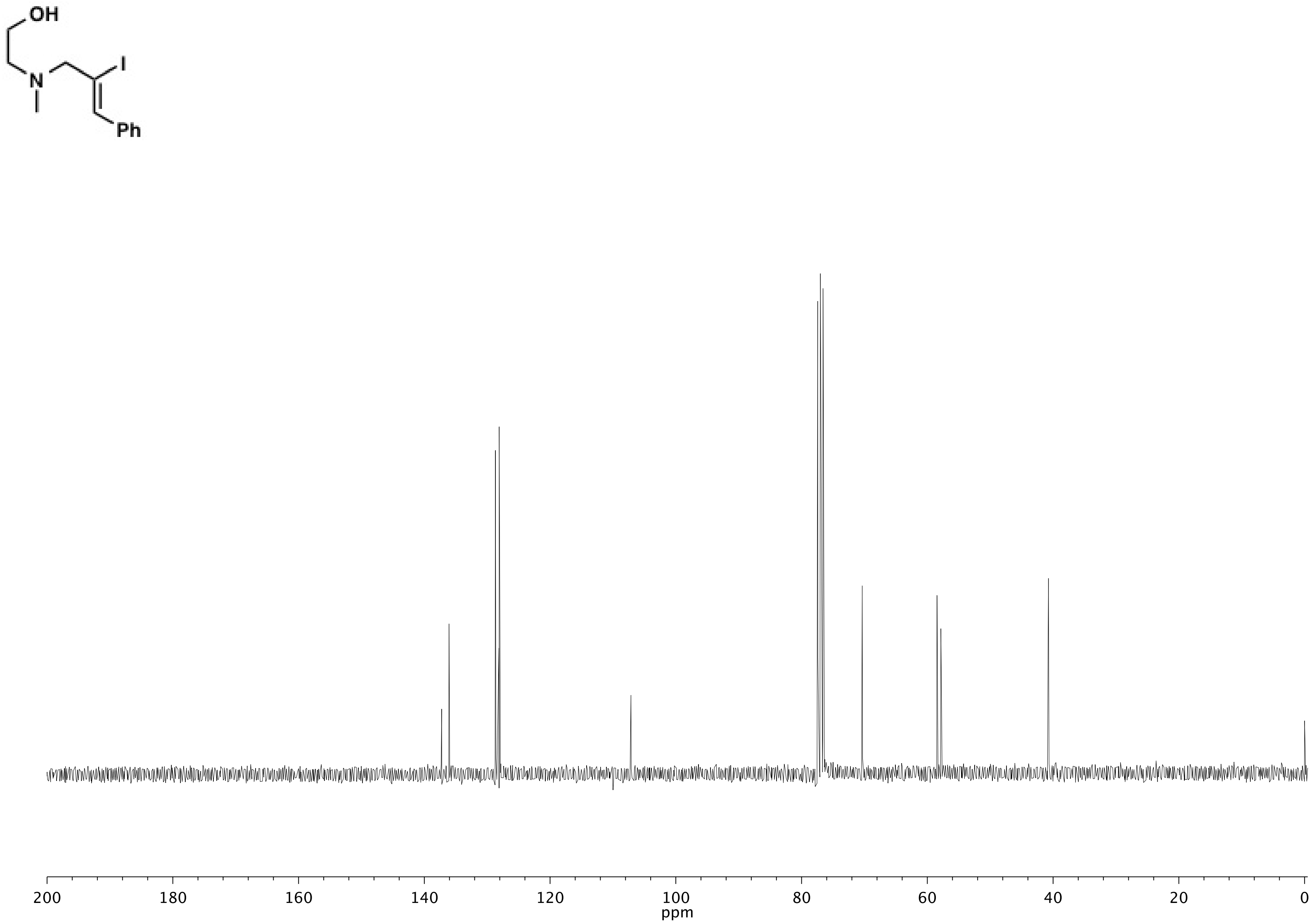
^{1}H NMR (400 MHz, CD_2Cl_2) of compound **5j**.



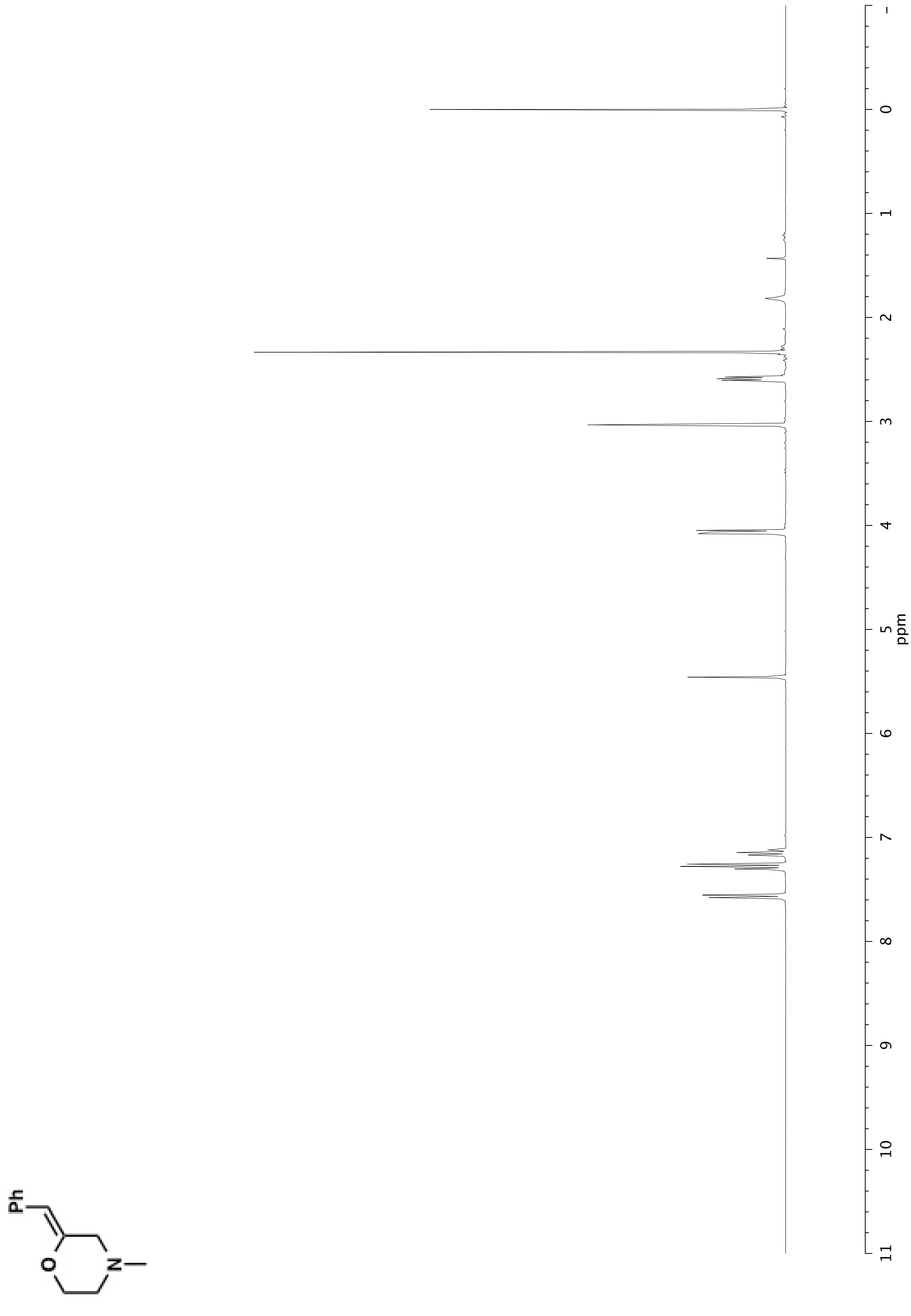
^{13}C NMR (101 MHz, CD_2Cl_2) of compound **5j**.



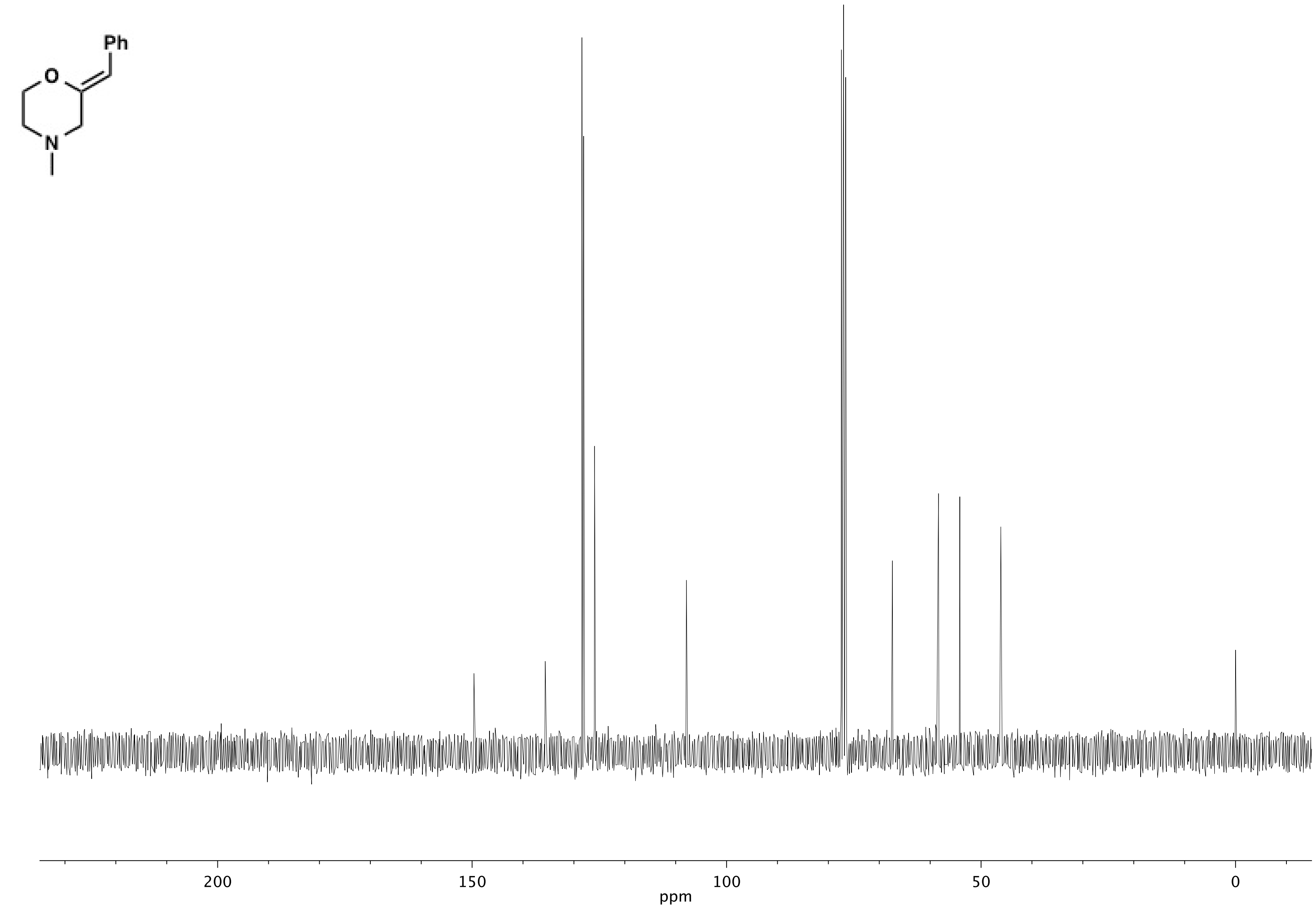
^{1}H NMR (300 MHz, $CDCl_3$) of compound **6a**.



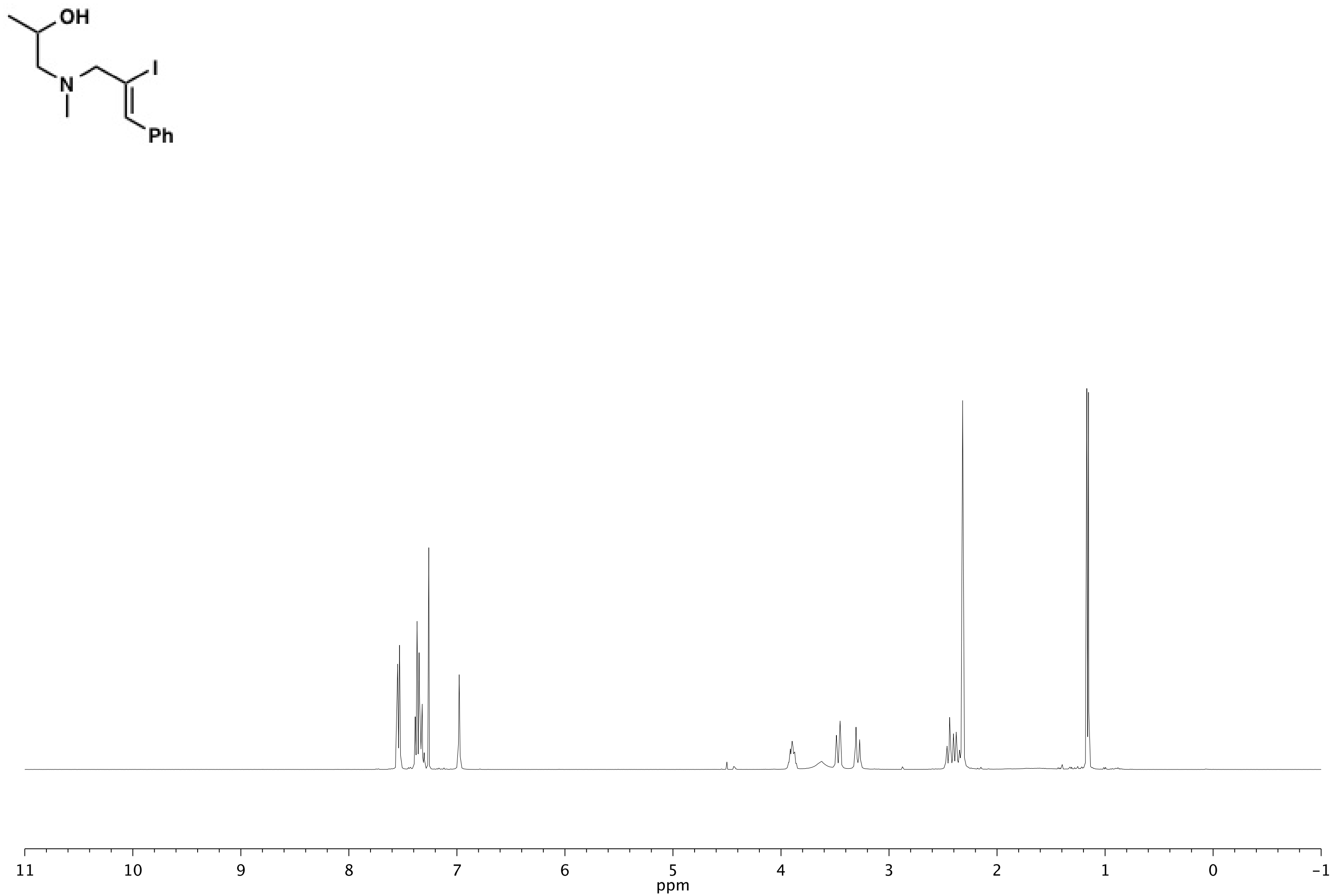
^{13}C NMR (75 MHz, CDCl$_3$) of compound **6a**.



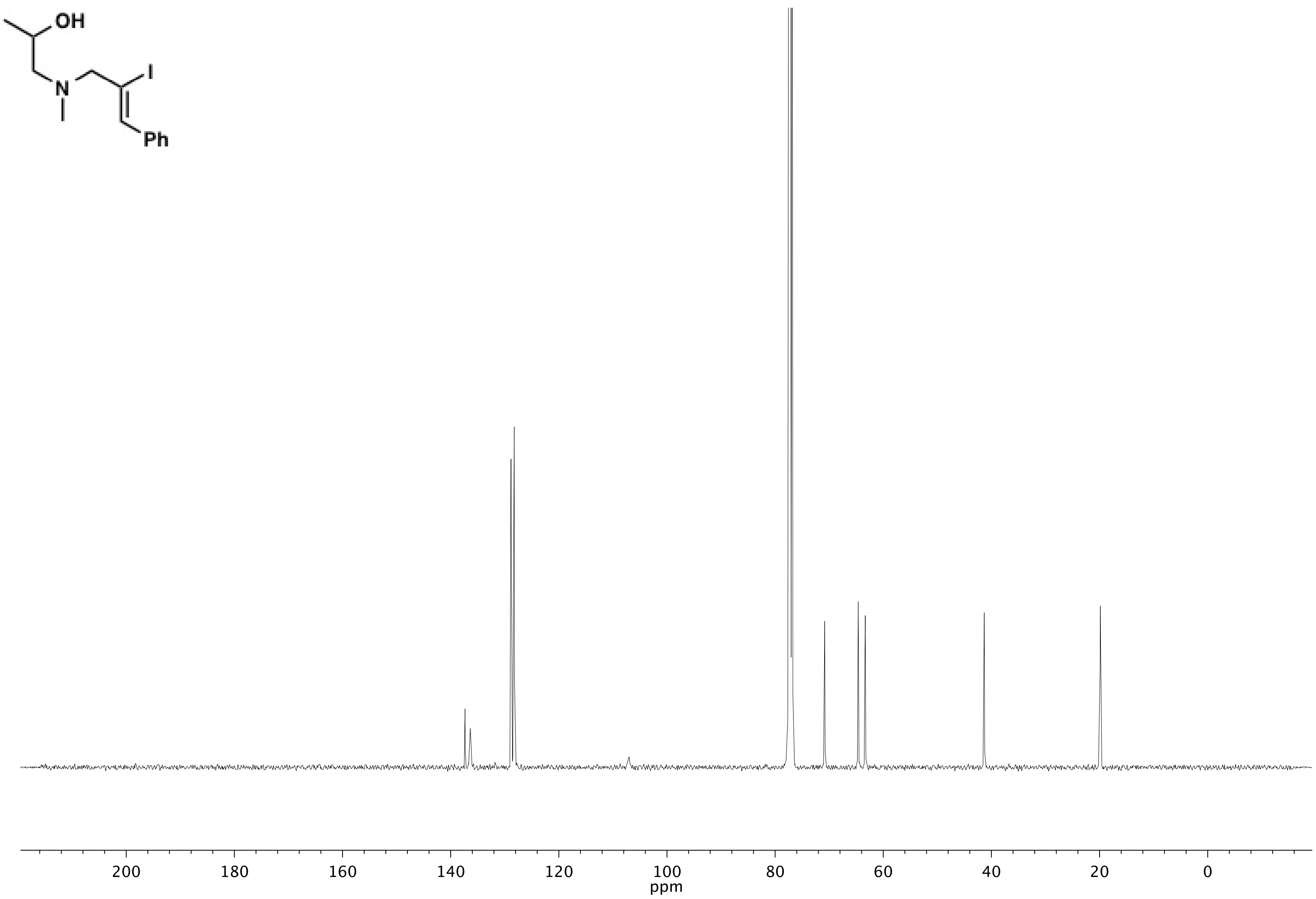
^{1}H NMR (300 MHz, $CDCl_3$) of compound **7a**.



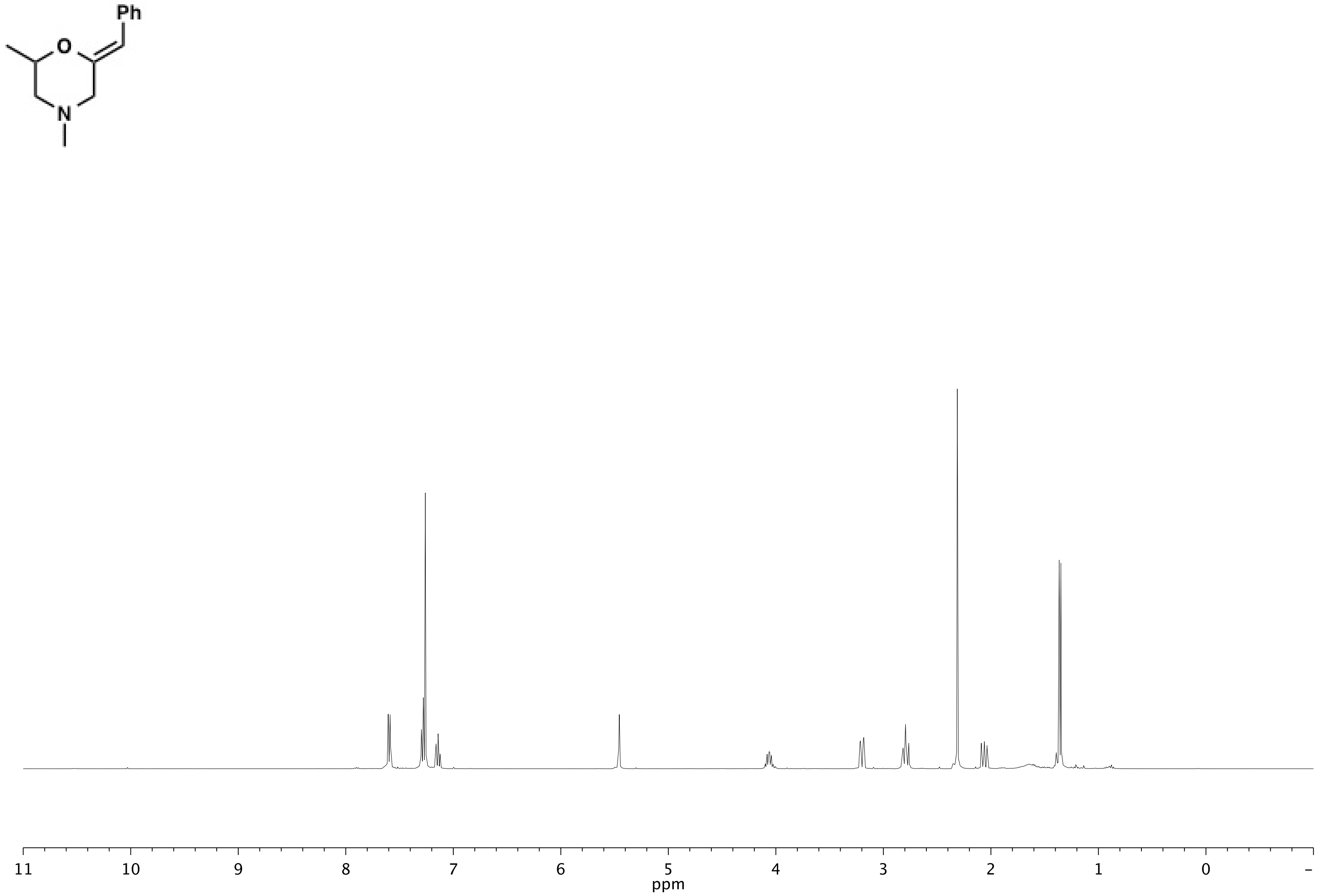
^{13}C NMR (75 MHz, CDCl$_3$) of compound **7a**.



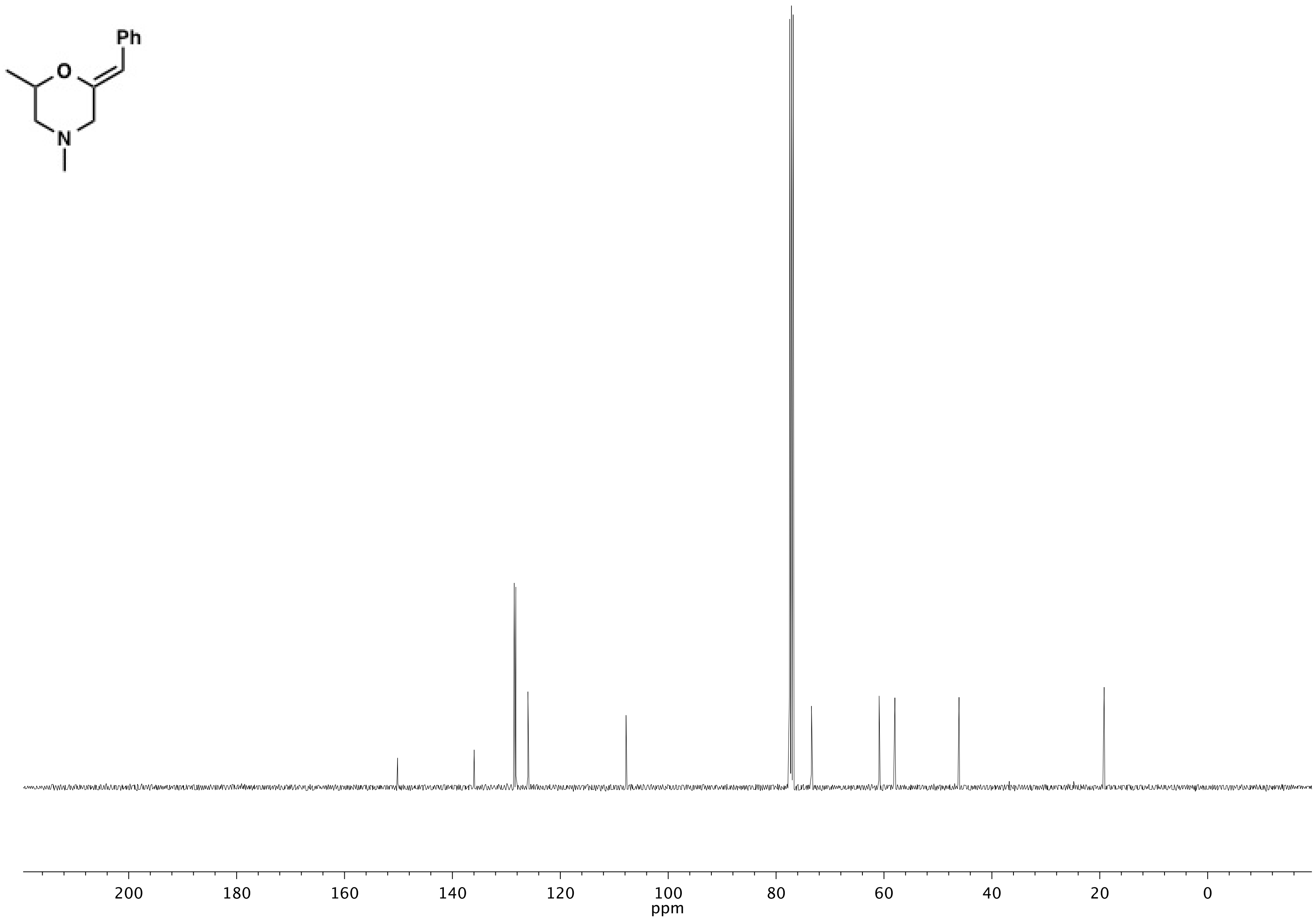
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6b**.



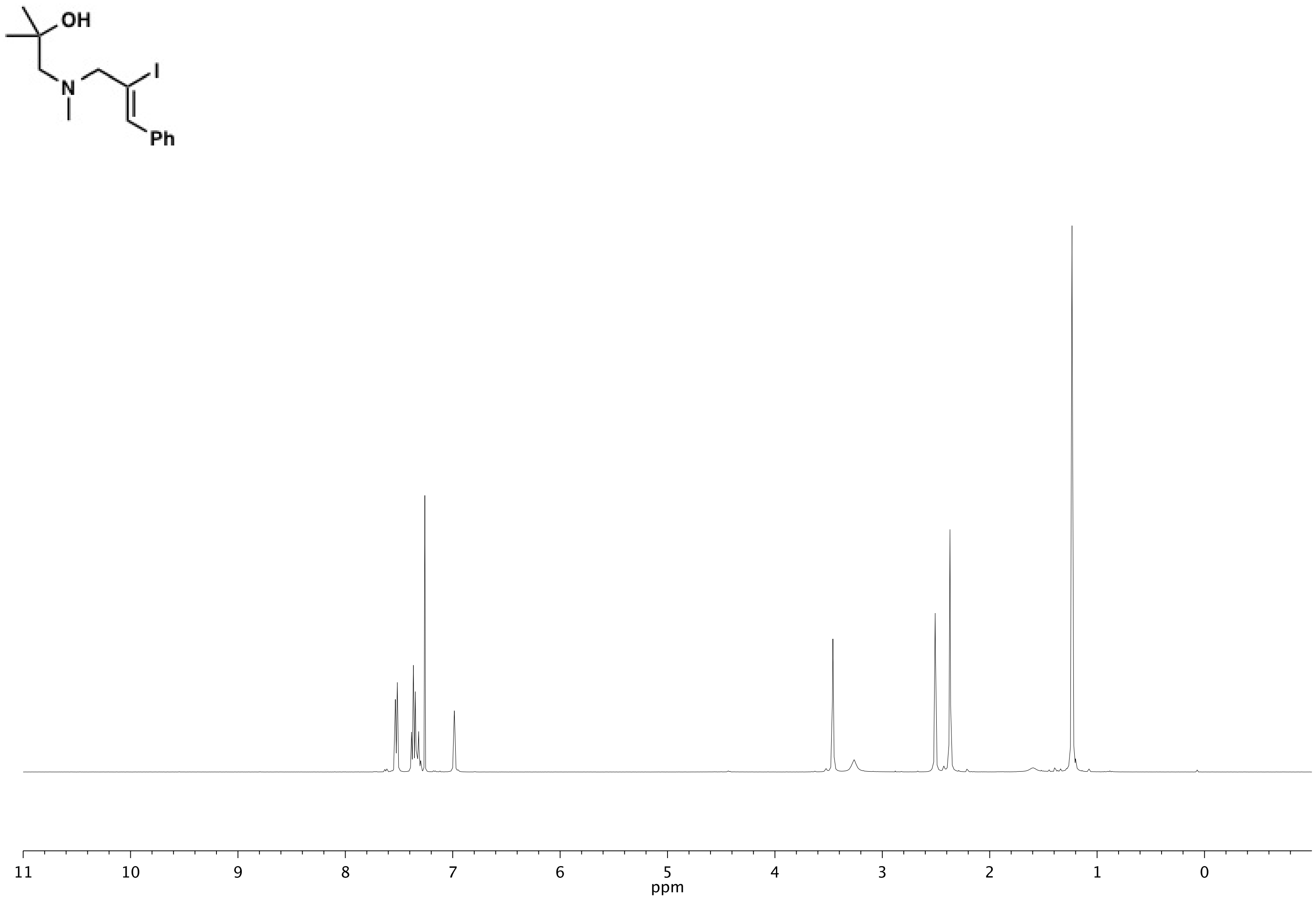
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6b**.



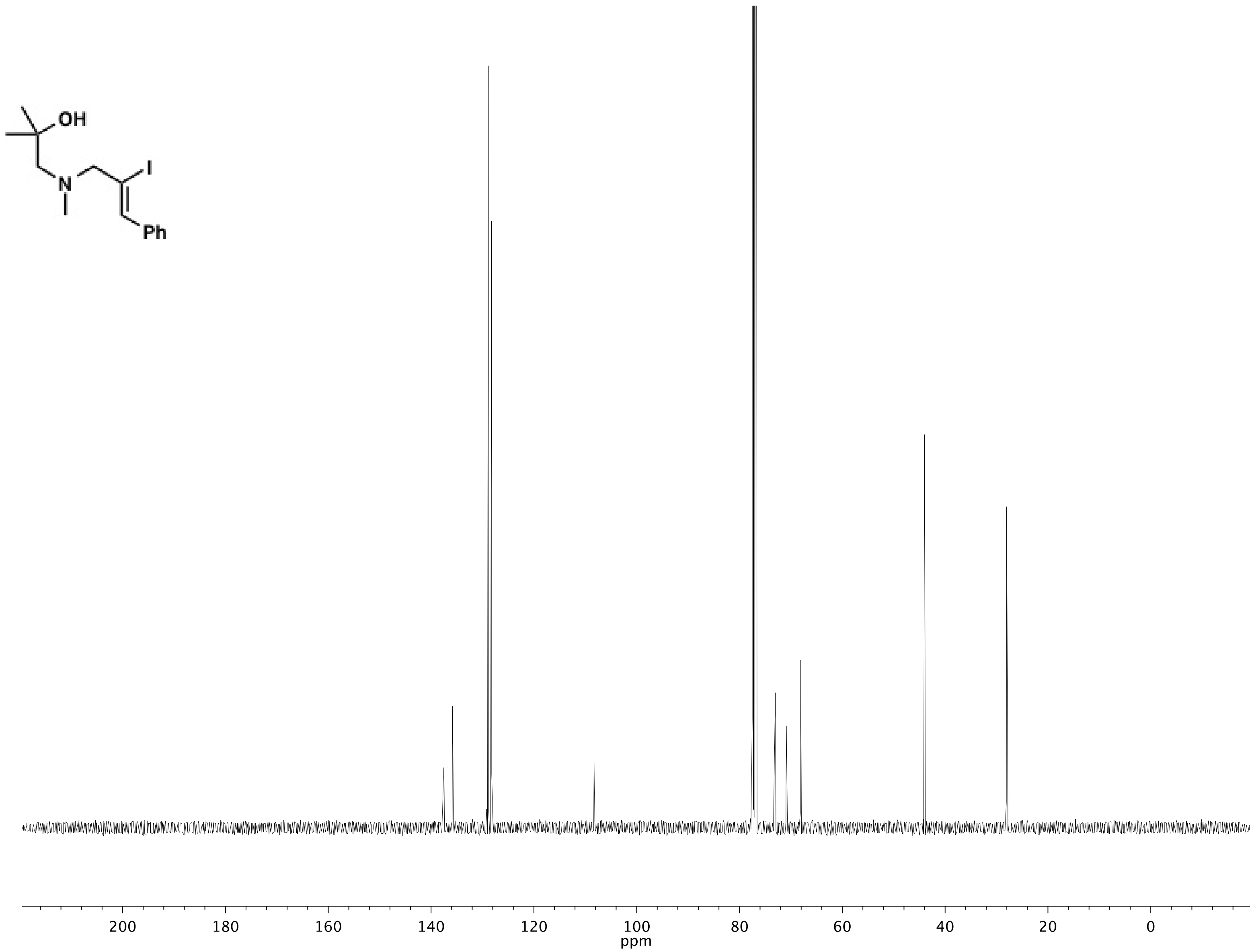
^{1}H NMR (400 MHz, CDCl$_3$) of compound **7b**.



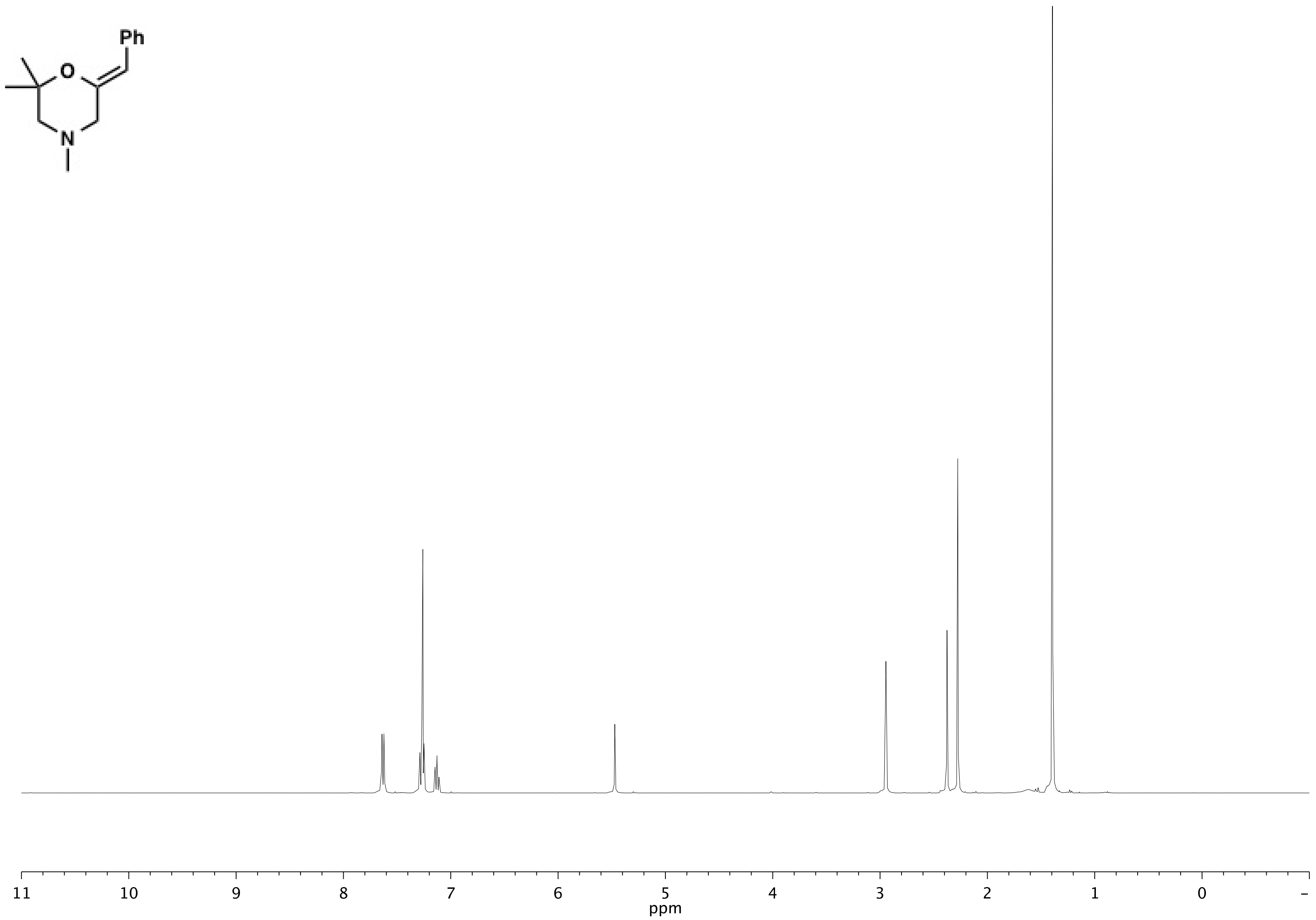
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7b**.



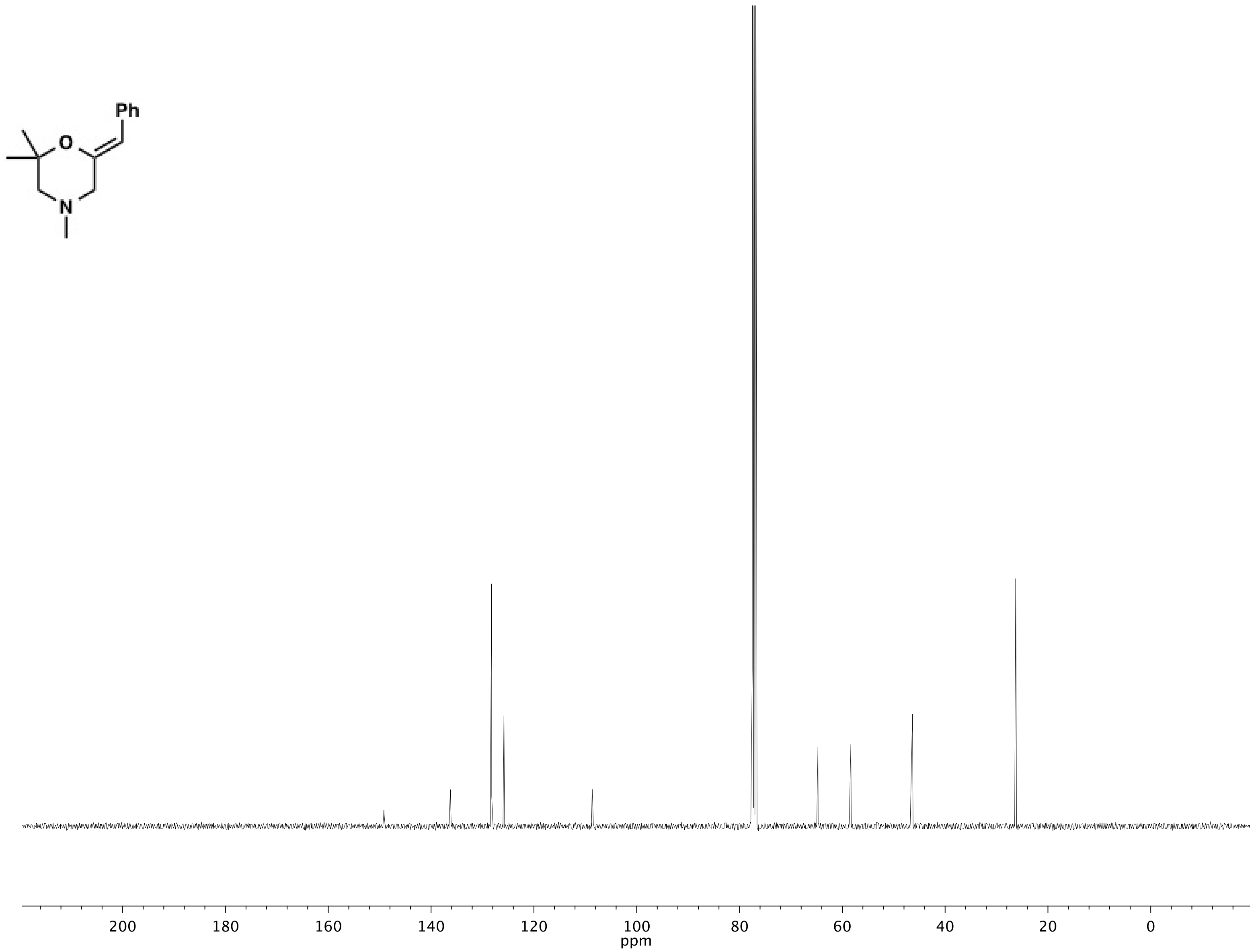
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6c**.



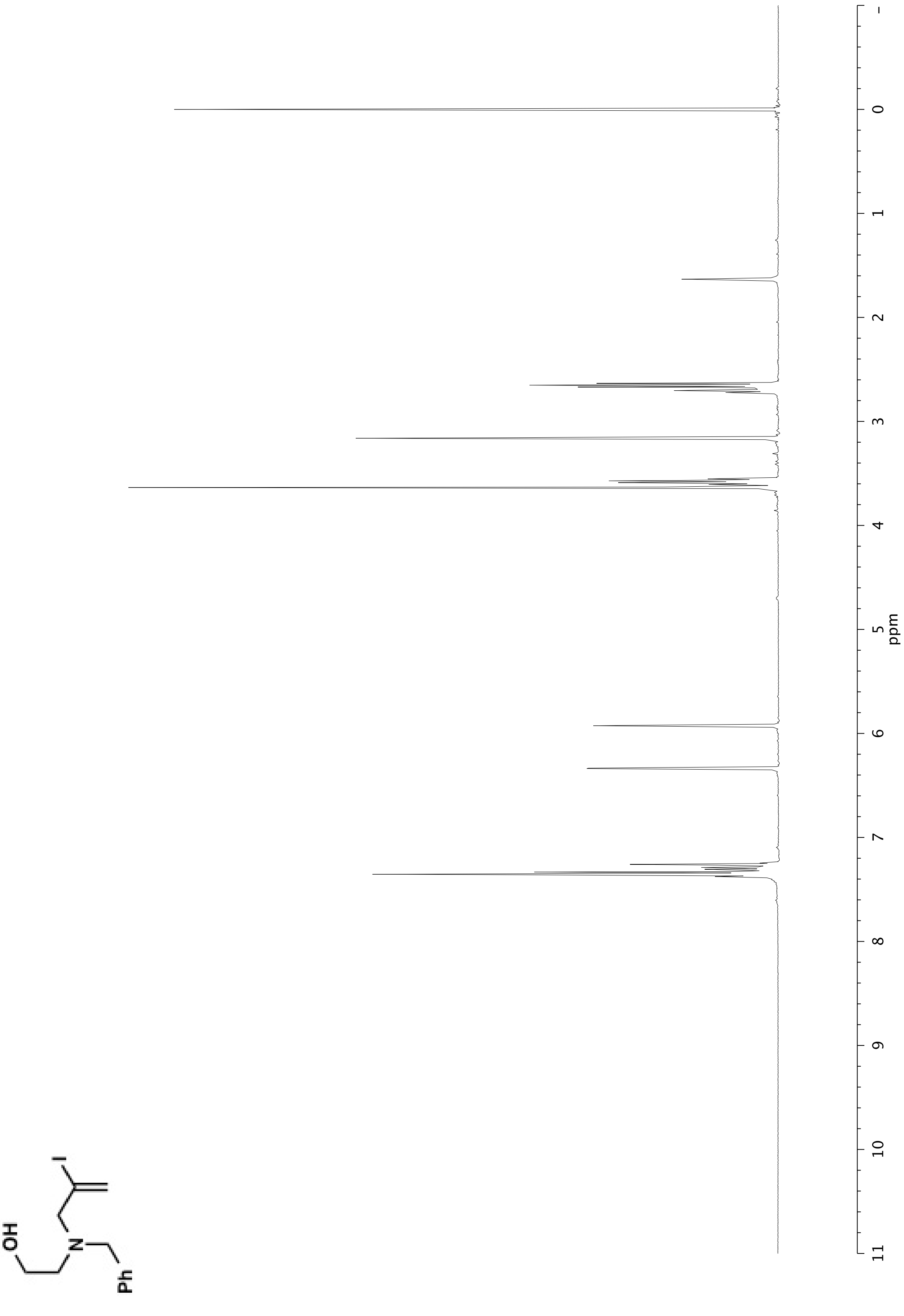
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6c**.



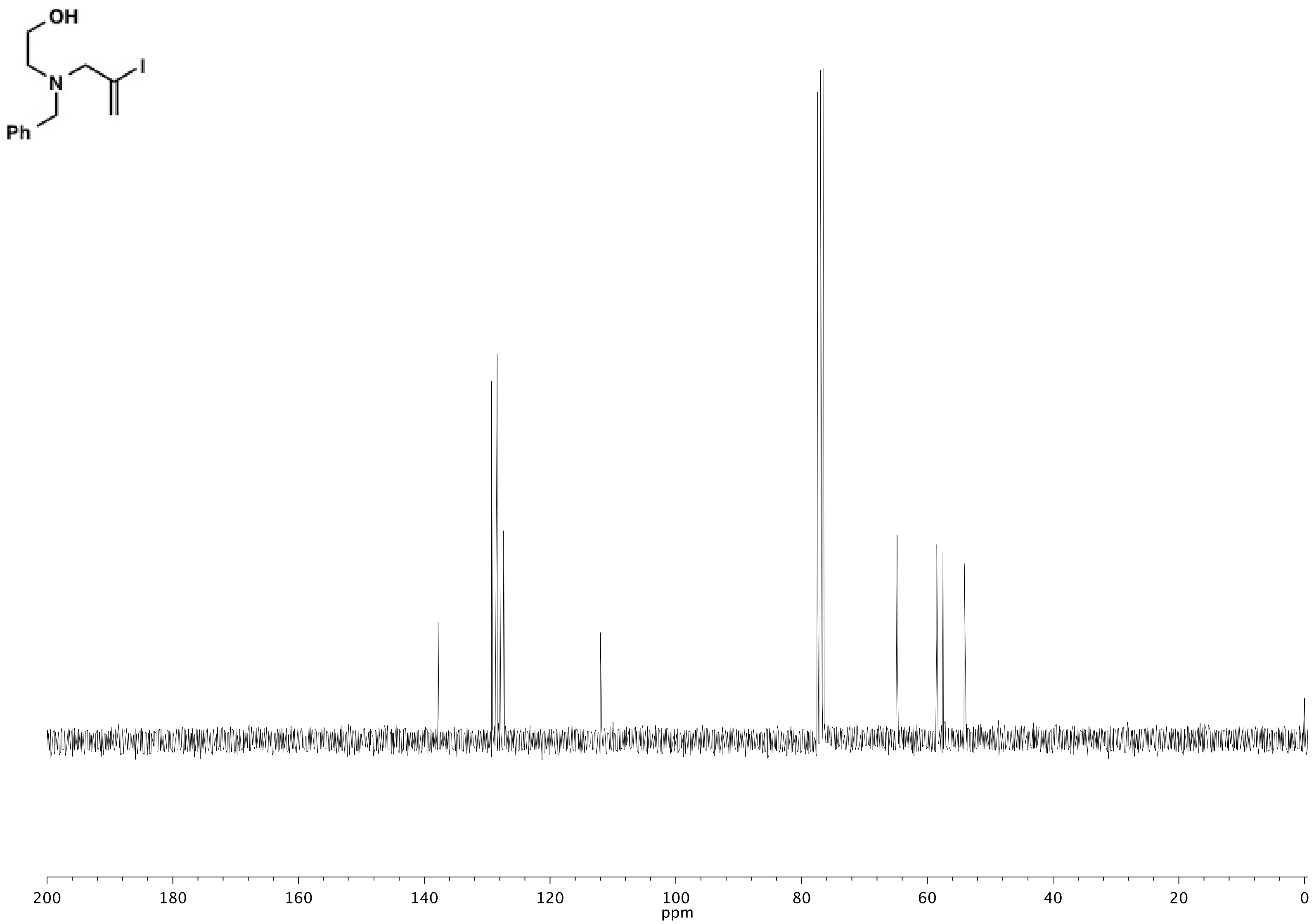
^{1}H NMR (400 MHz, CDCl$_3$) of compound **7c**.



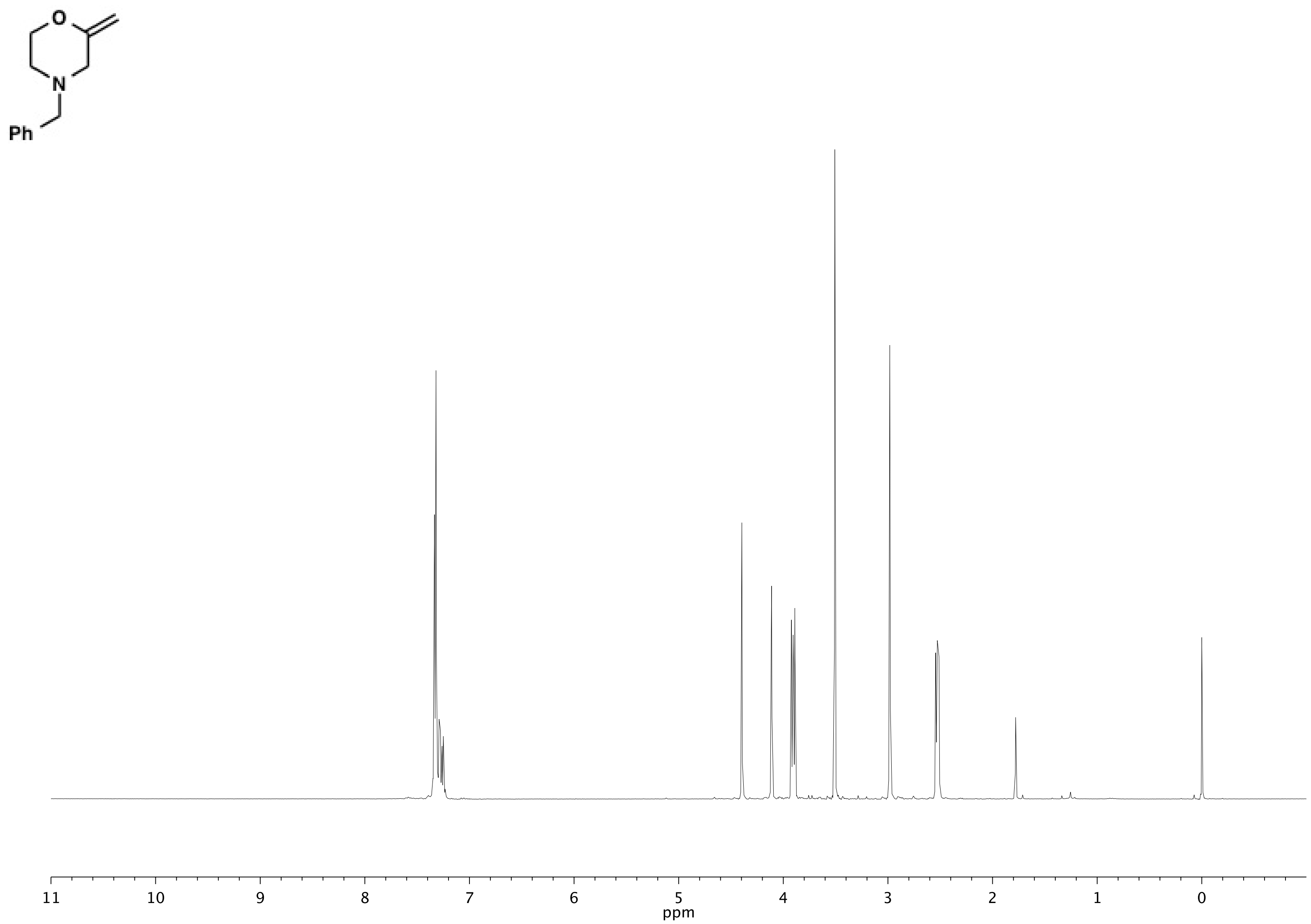
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7c**.



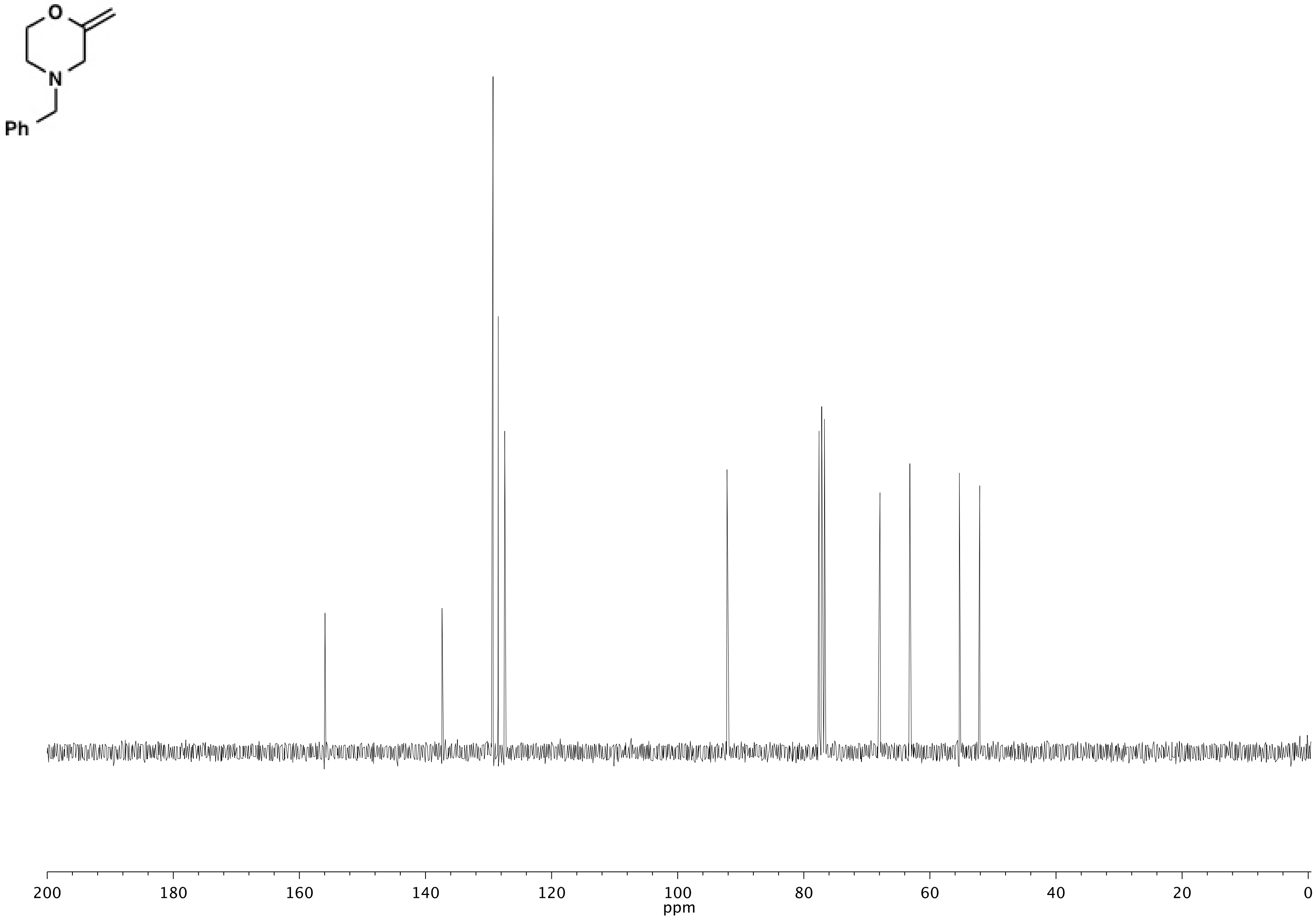
^{1}H NMR (300 MHz, $CDCl_3$) of compound **6d**.



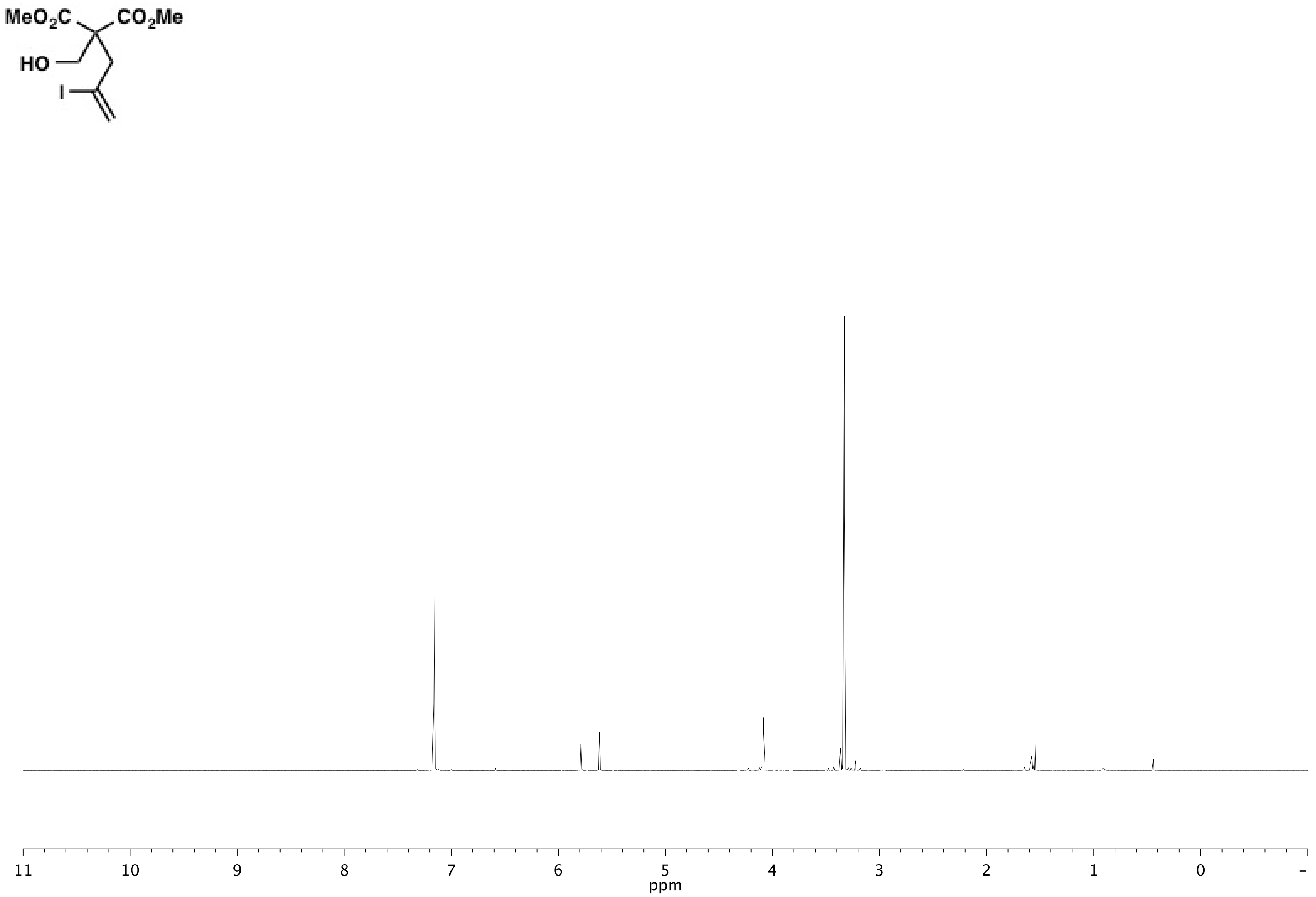
^{13}C NMR (75 MHz, CDCl$_3$) of compound **6d**.



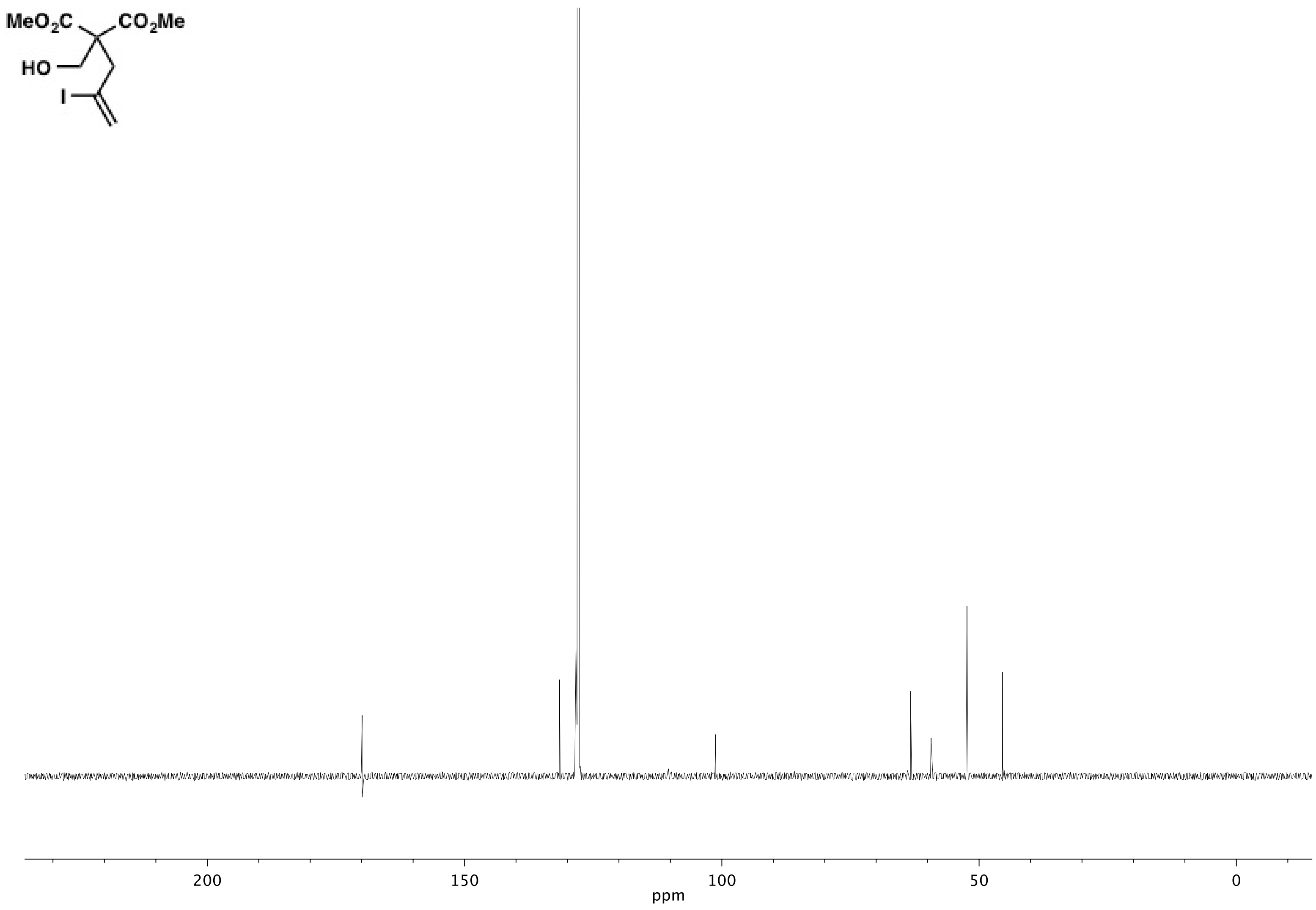
^{1}H NMR (300 MHz, $CDCl_3$) of compound **7d**.



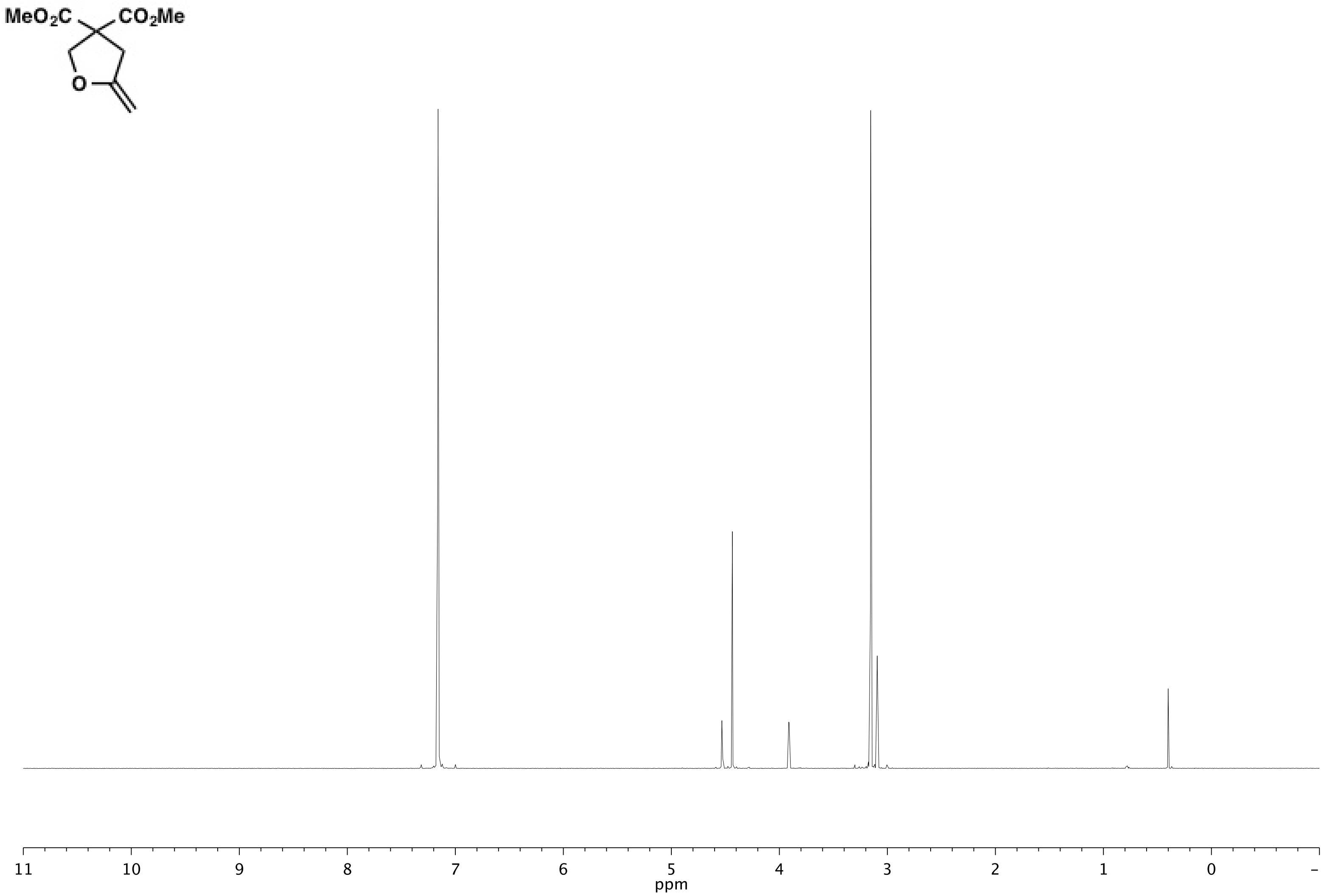
^{13}C NMR (75 MHz, CDCl$_3$) of compound **7d**.



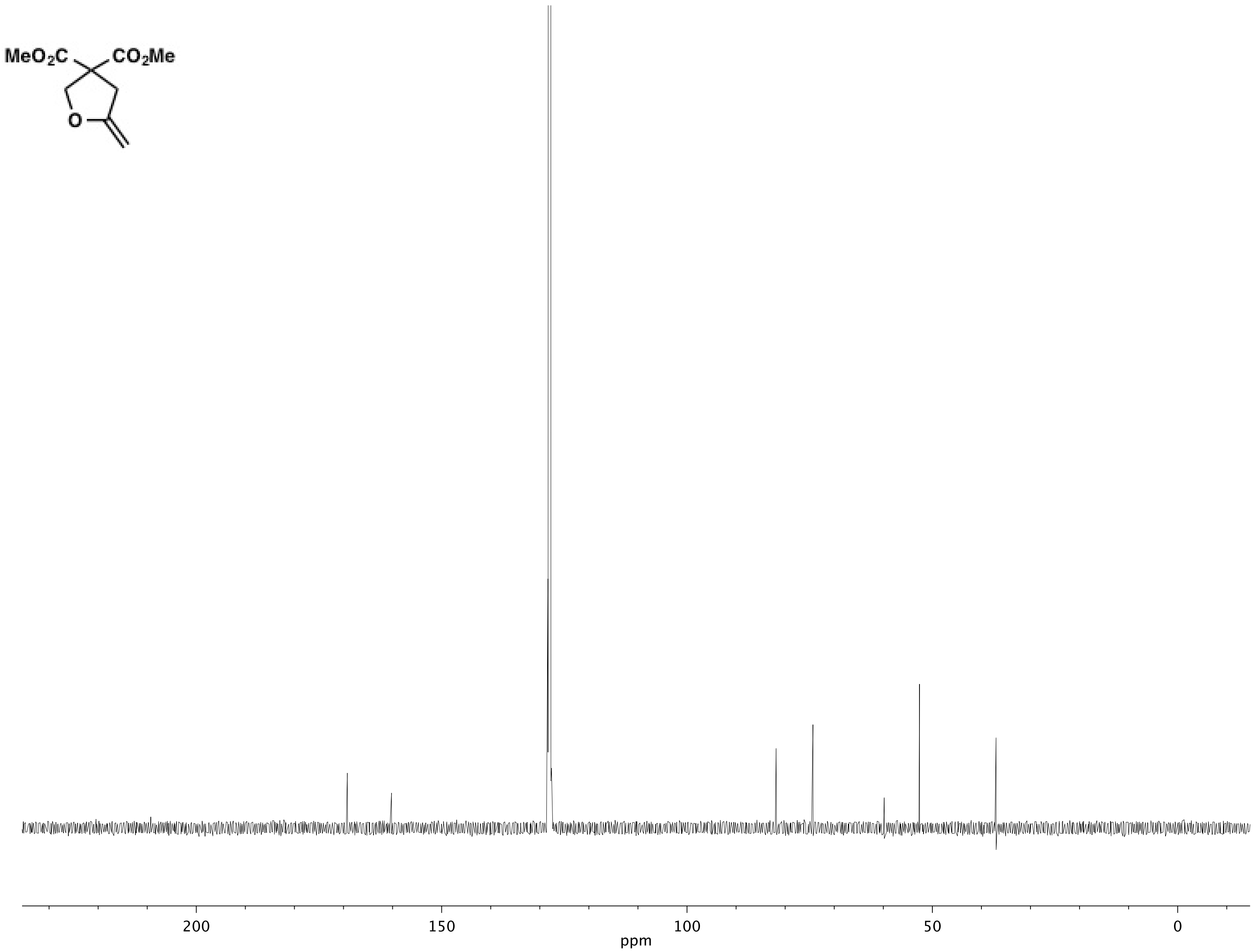
^{1}H NMR (500 MHz, C_6D_6) of compound **8a**.



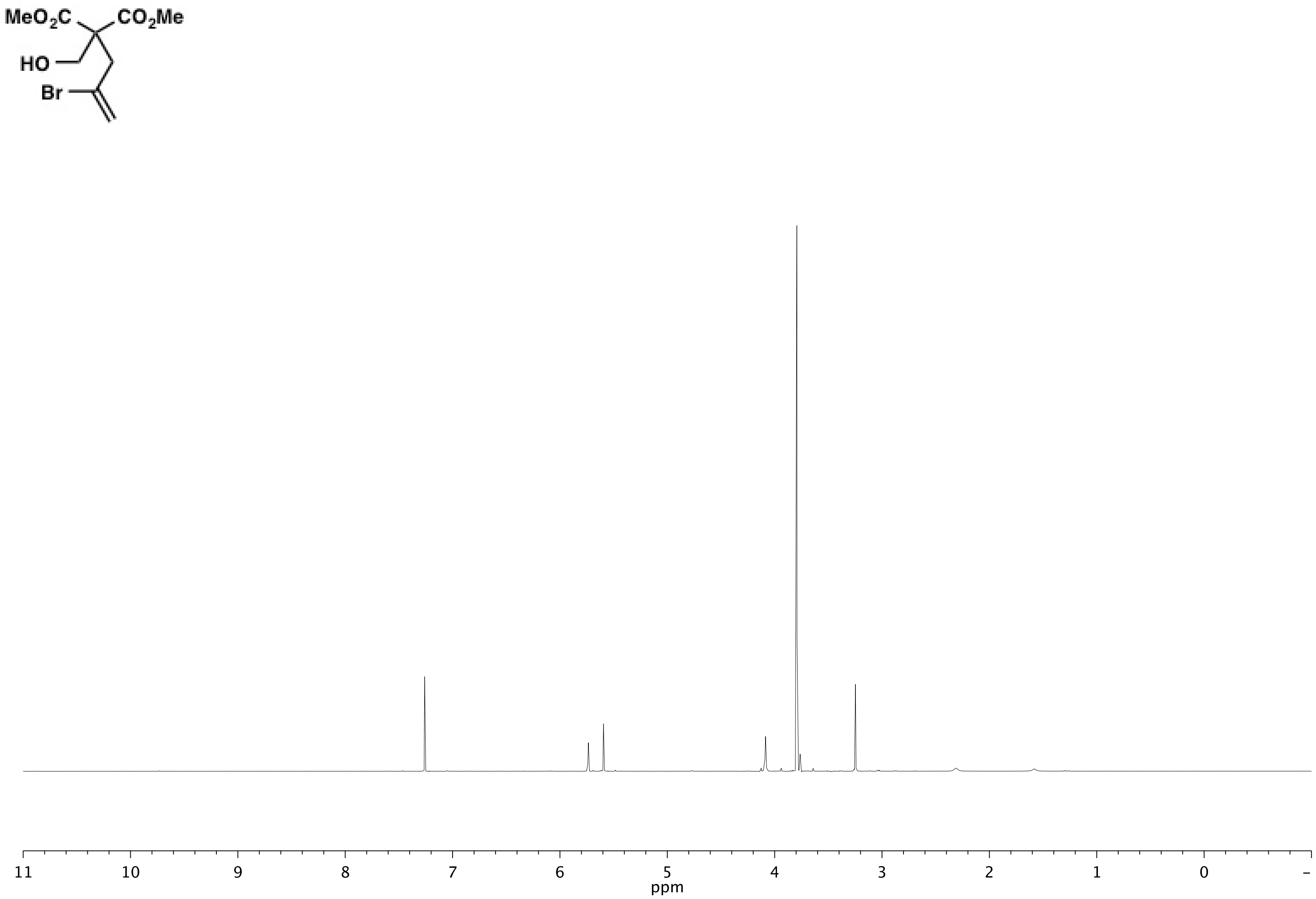
^{13}C NMR (126 MHz, C_6D_6) of compound **8a**.



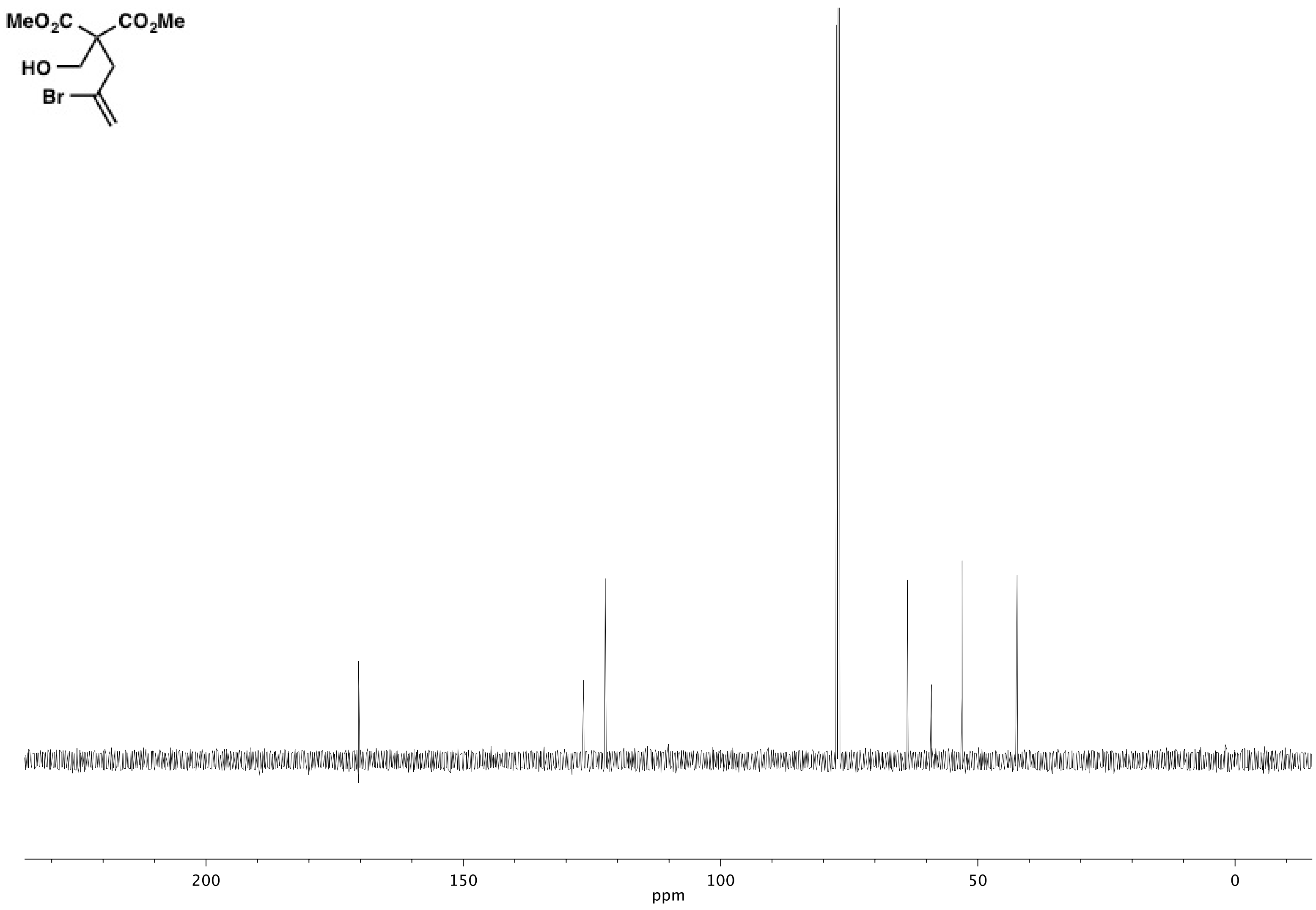
^{1}H NMR (500 MHz, C_6D_6) of compound **9a**.



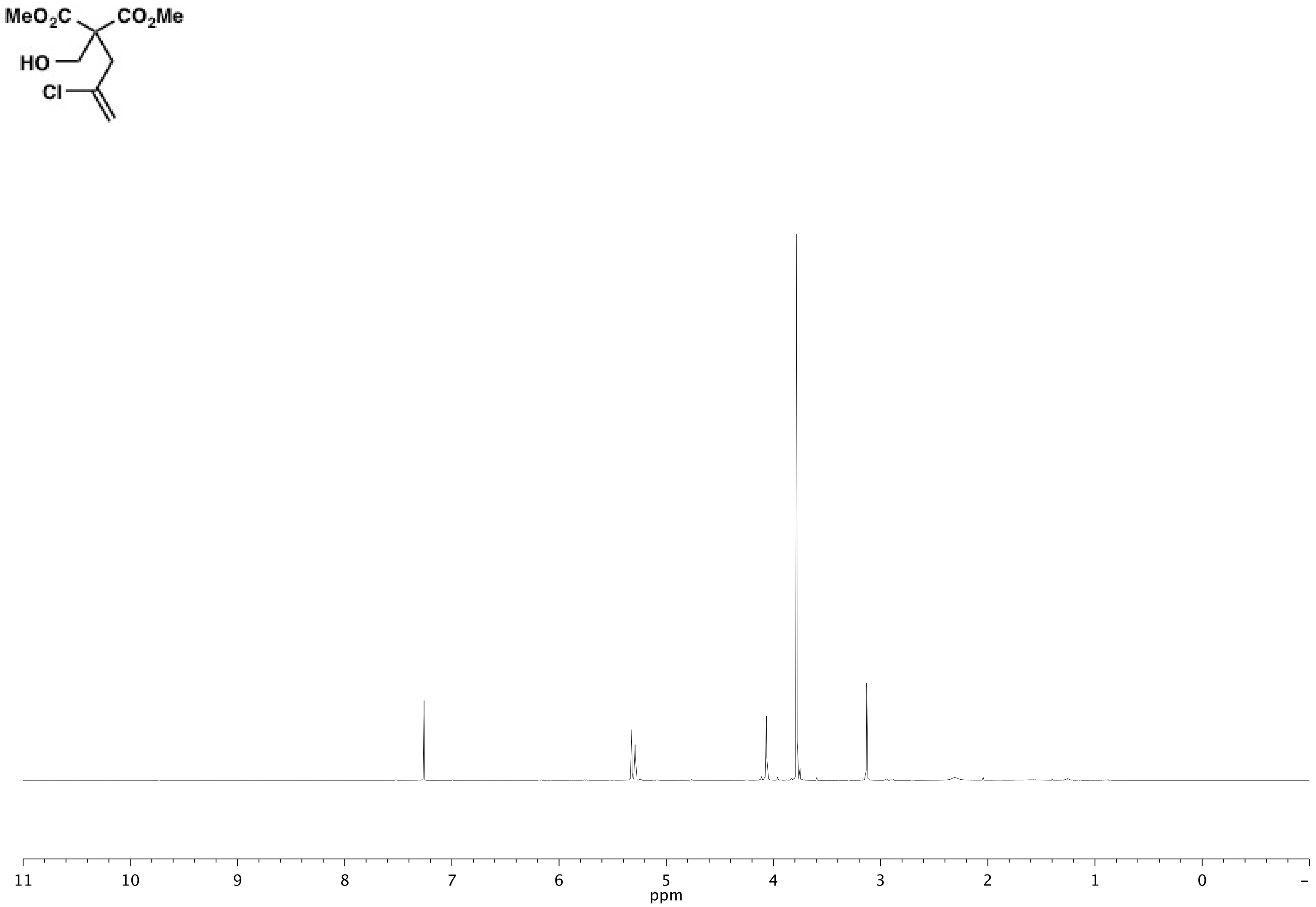
^{13}C NMR (126 MHz, C_6D_6) of compound **9a**.



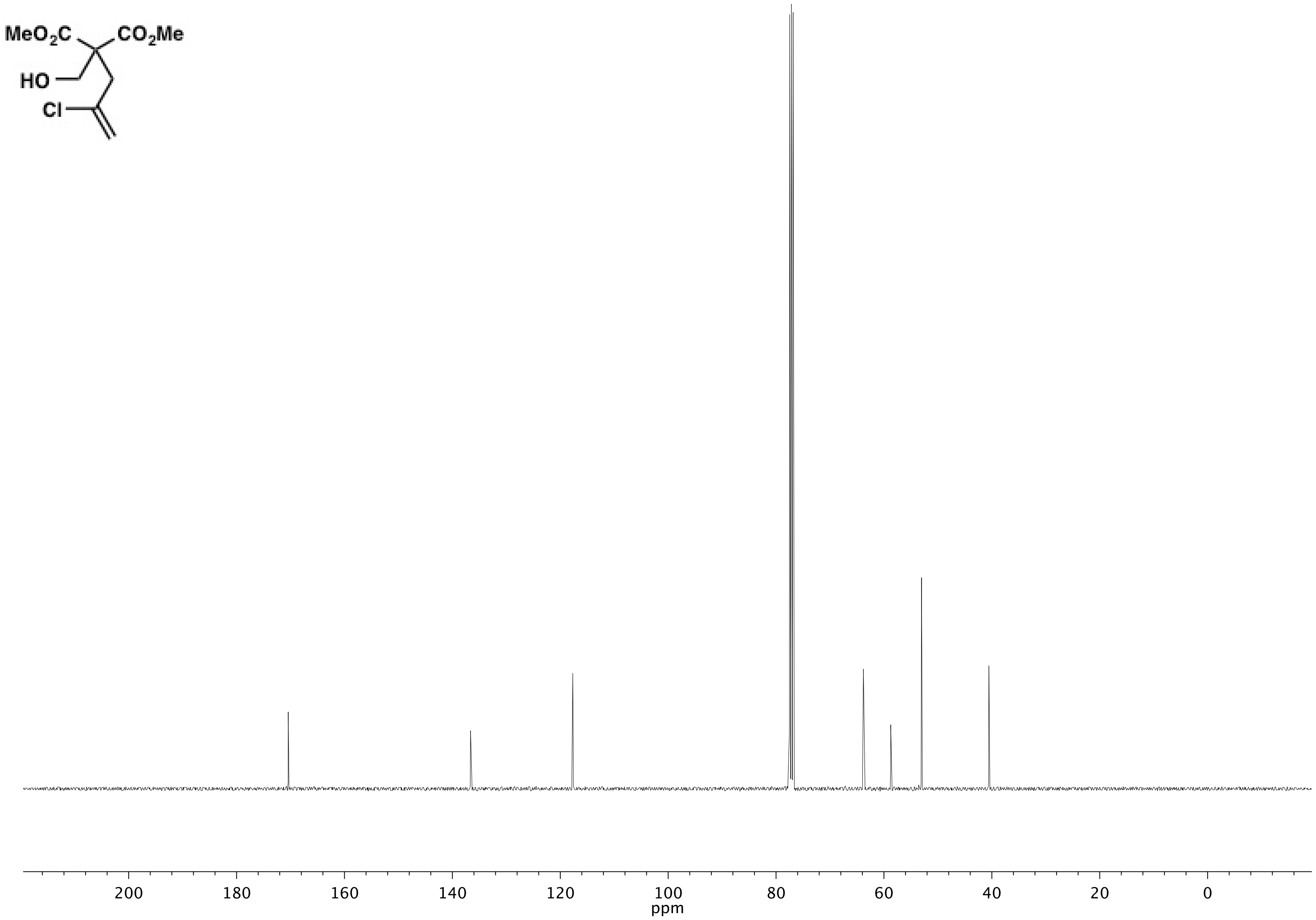
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8b**.



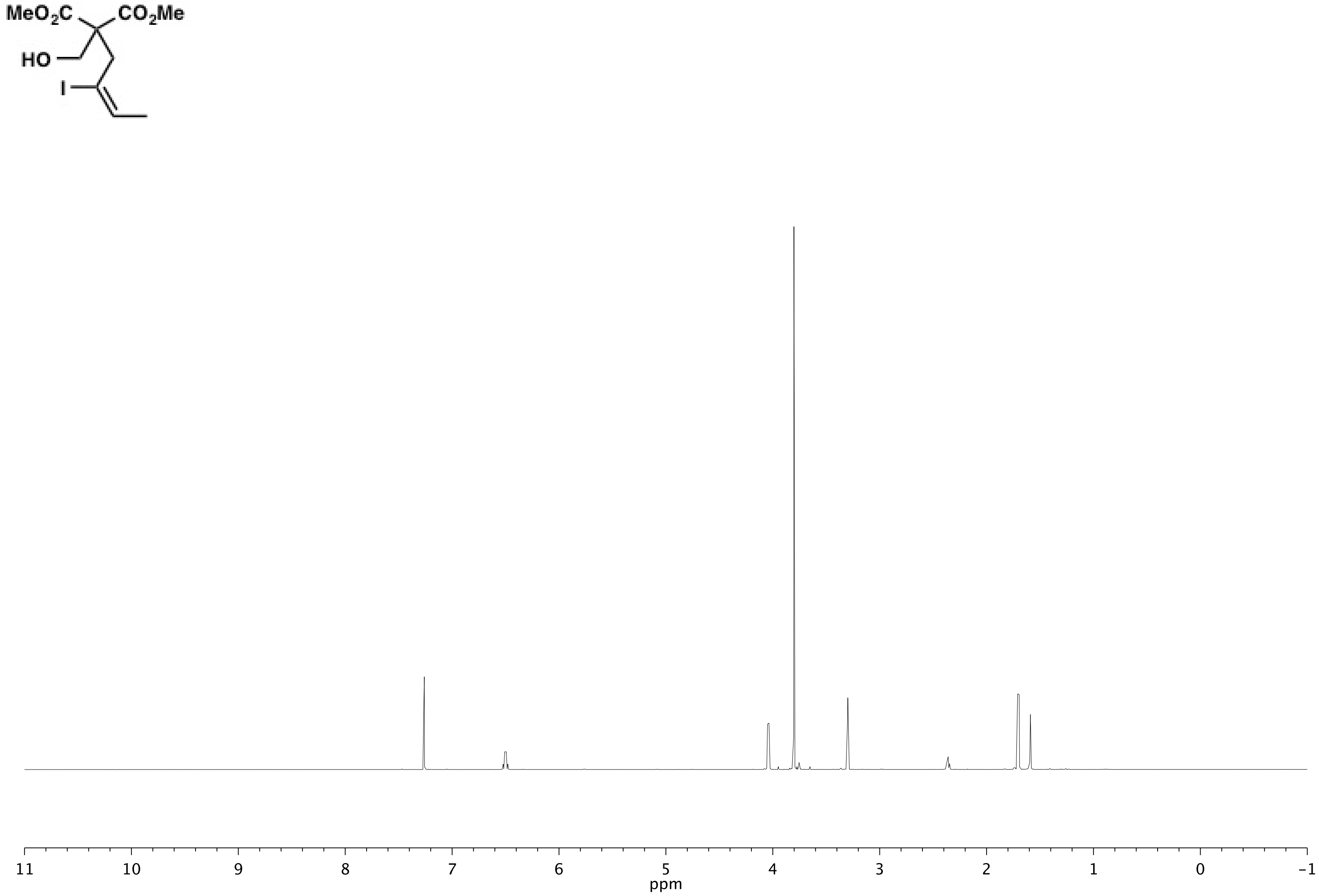
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8b**.



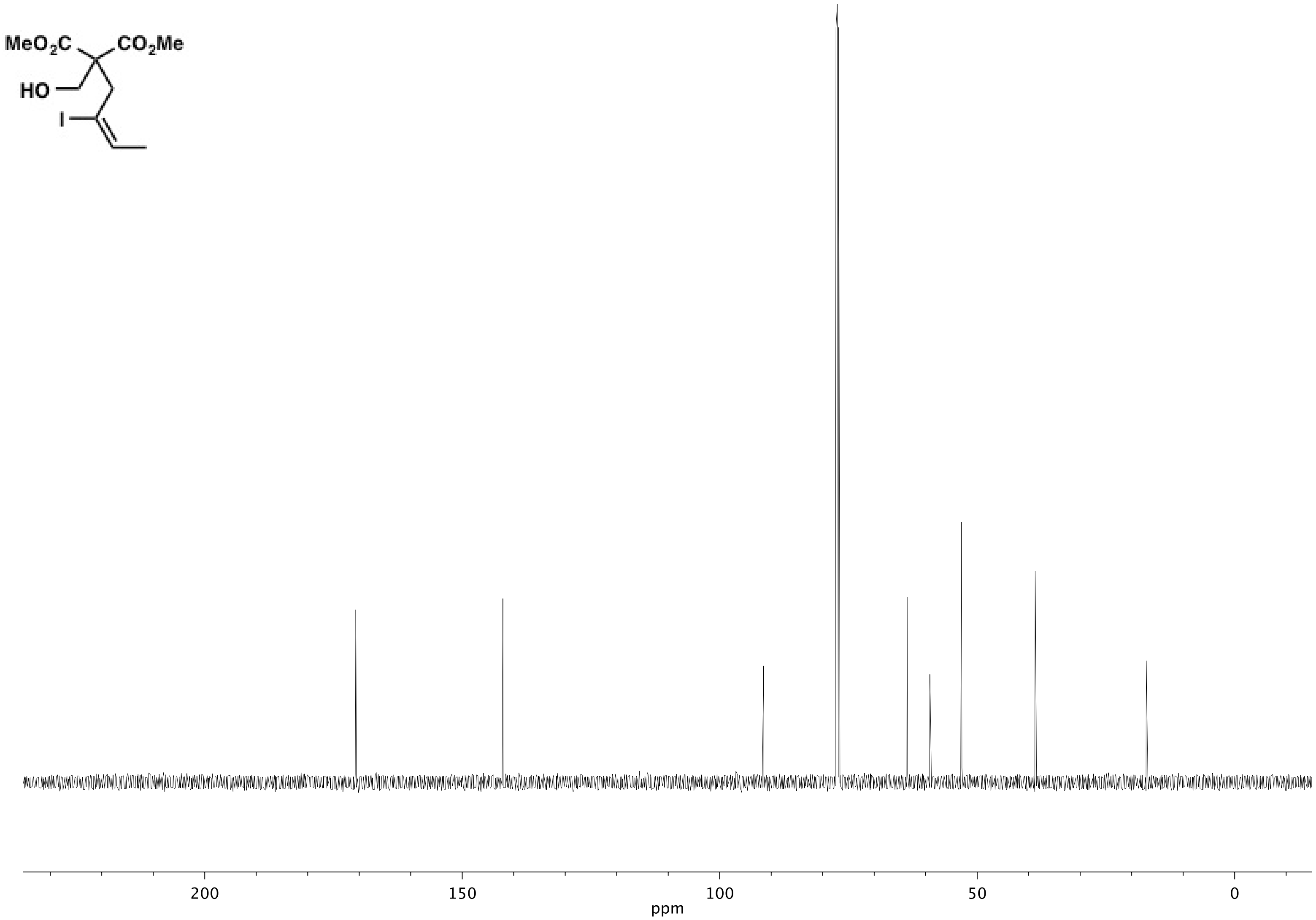
^{1}H NMR (400 MHz, CDCl$_3$) of compound **8c**.



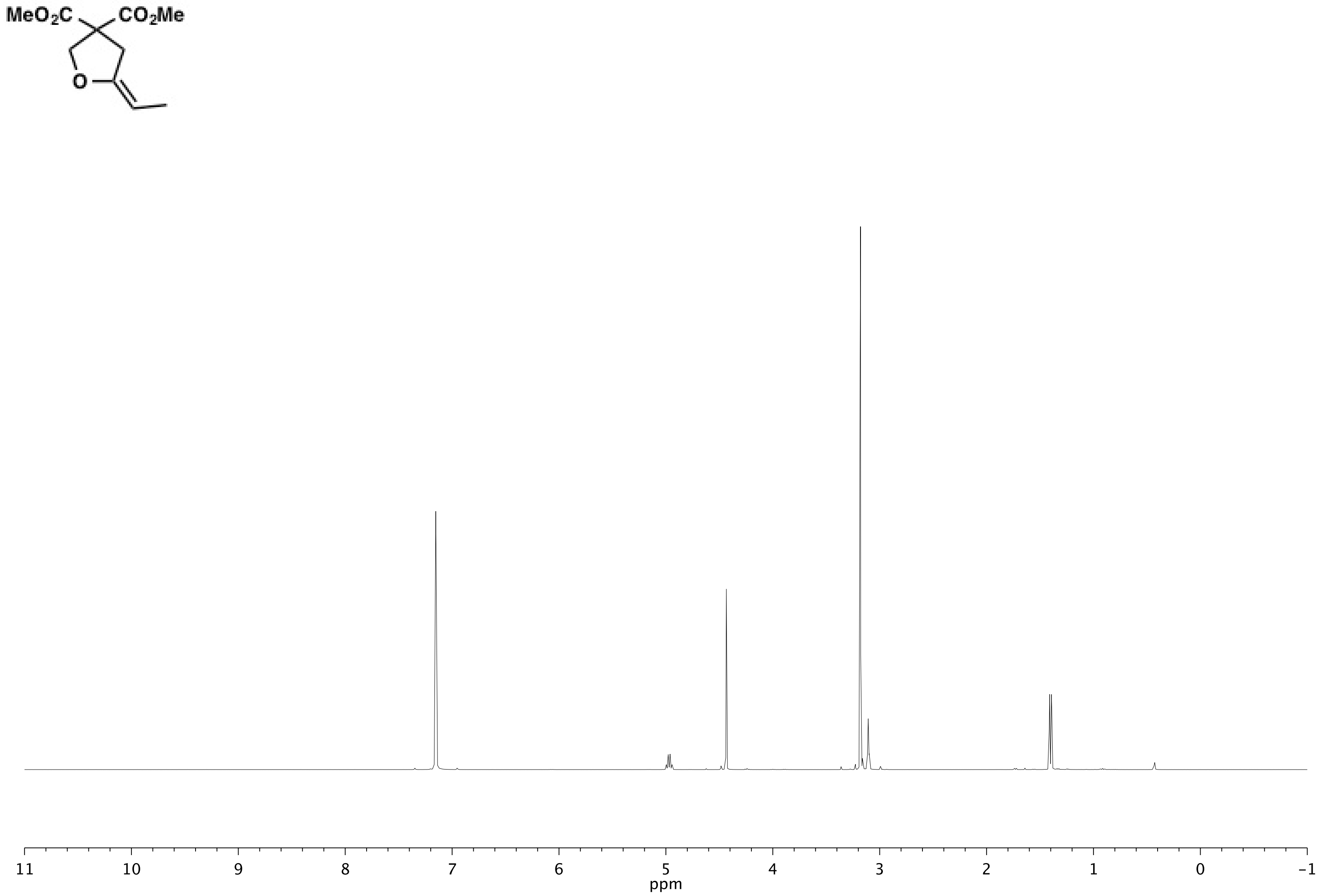
^{13}C NMR (101 MHz, CDCl$_3$) of compound **8c**.



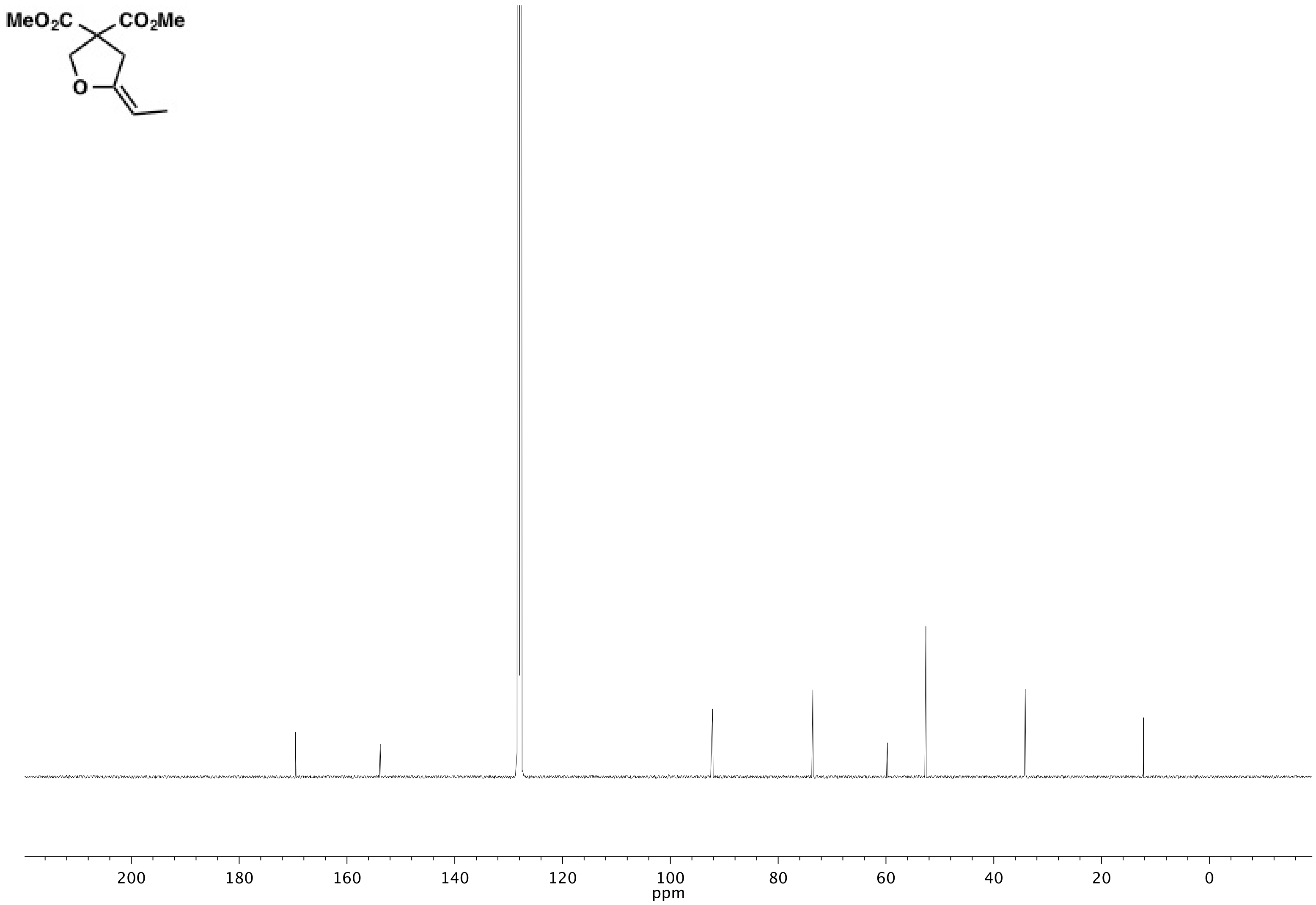
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8d**.



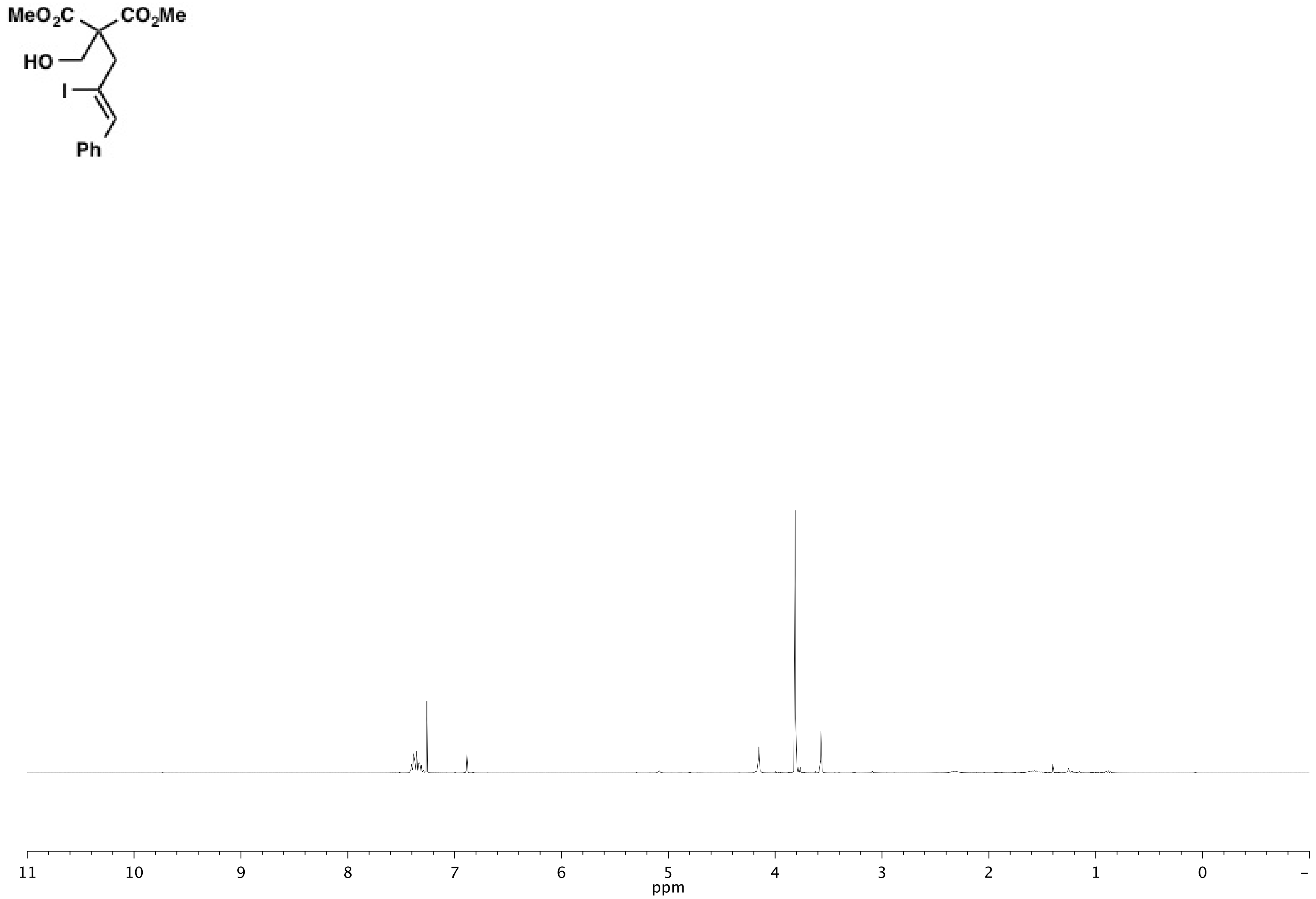
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8d**.



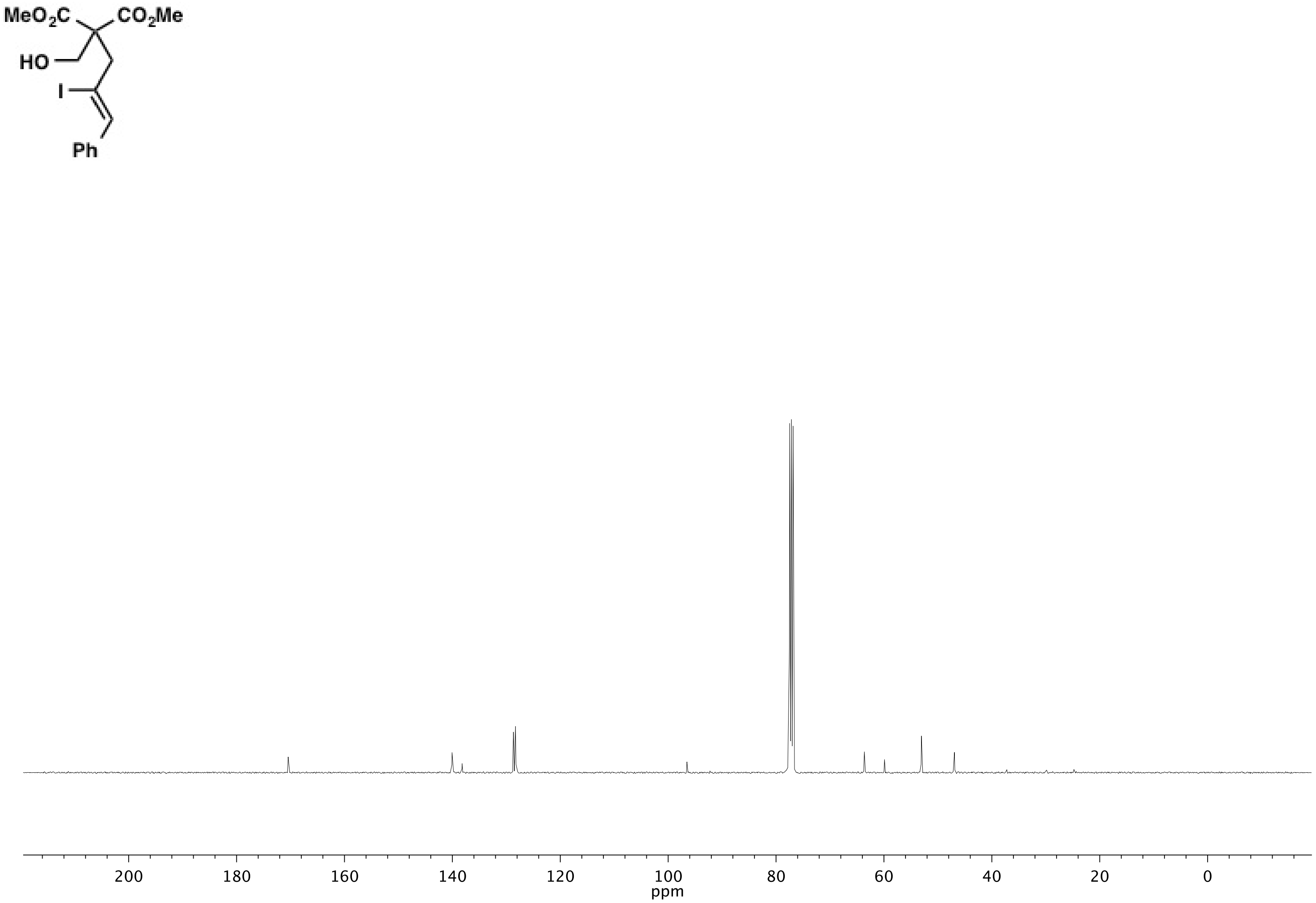
^{1}H NMR (400 MHz, C_6D_6) of compound **9d**.



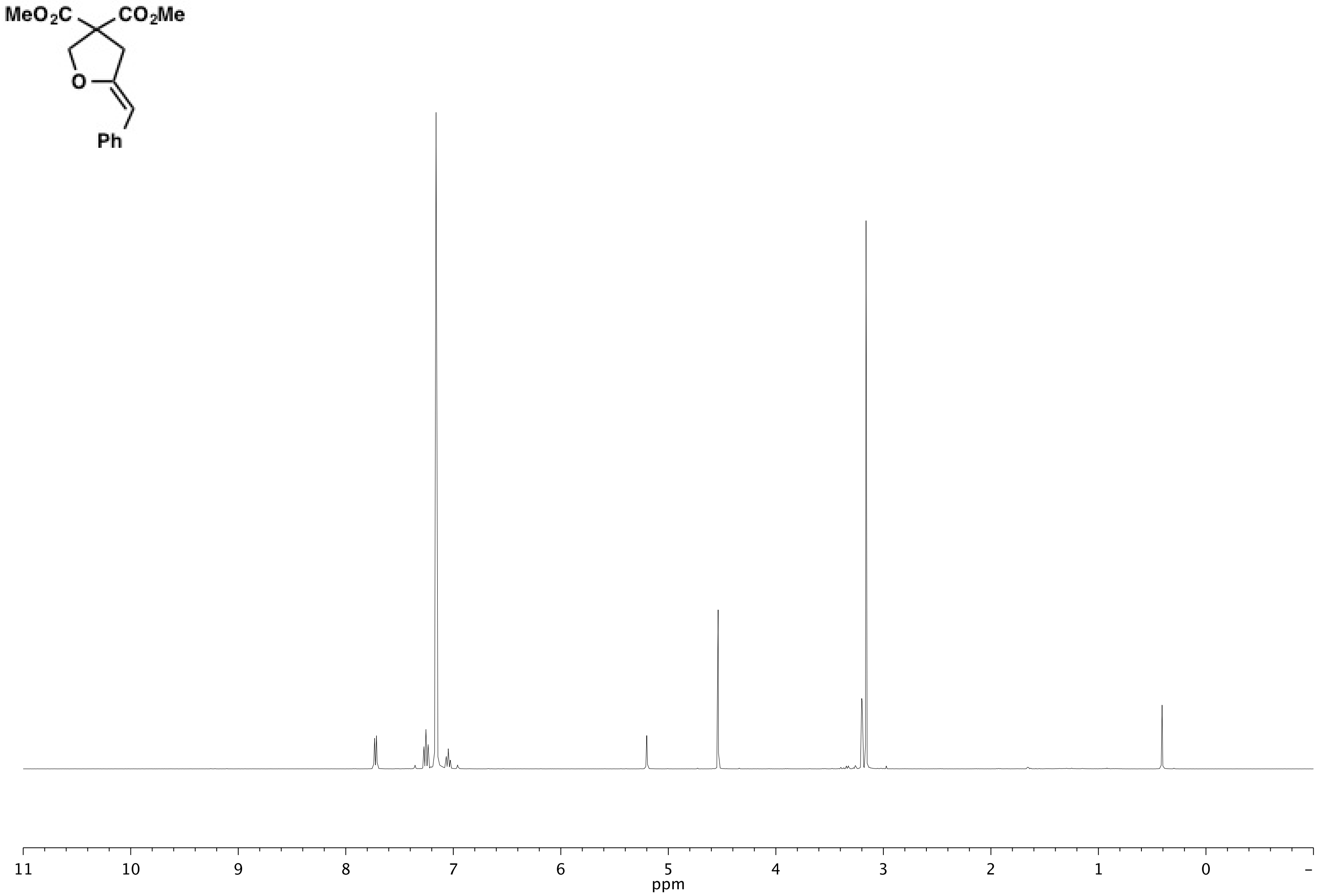
^{13}C NMR (101 MHz, C_6D_6) of compound **9d**.



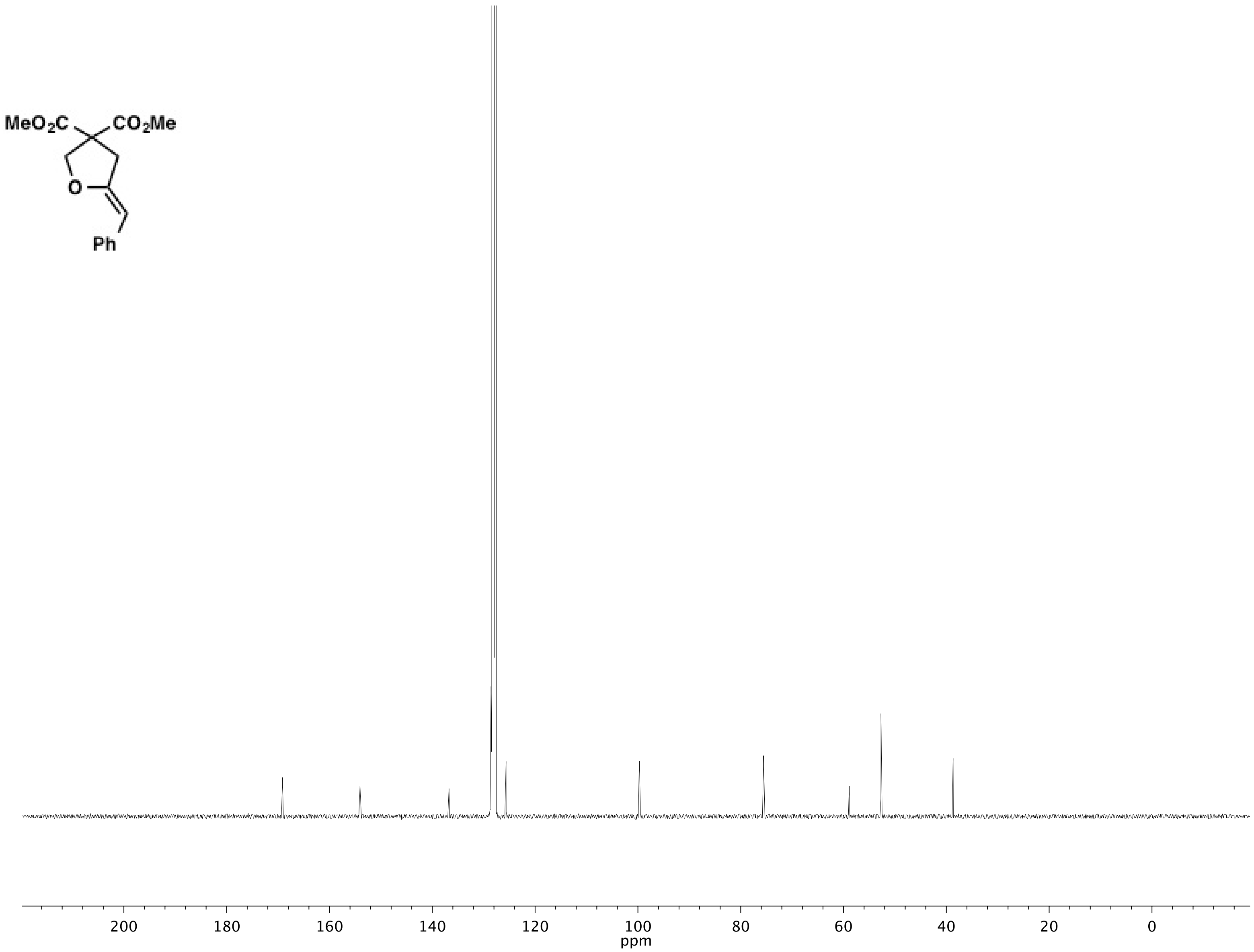
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8e**.



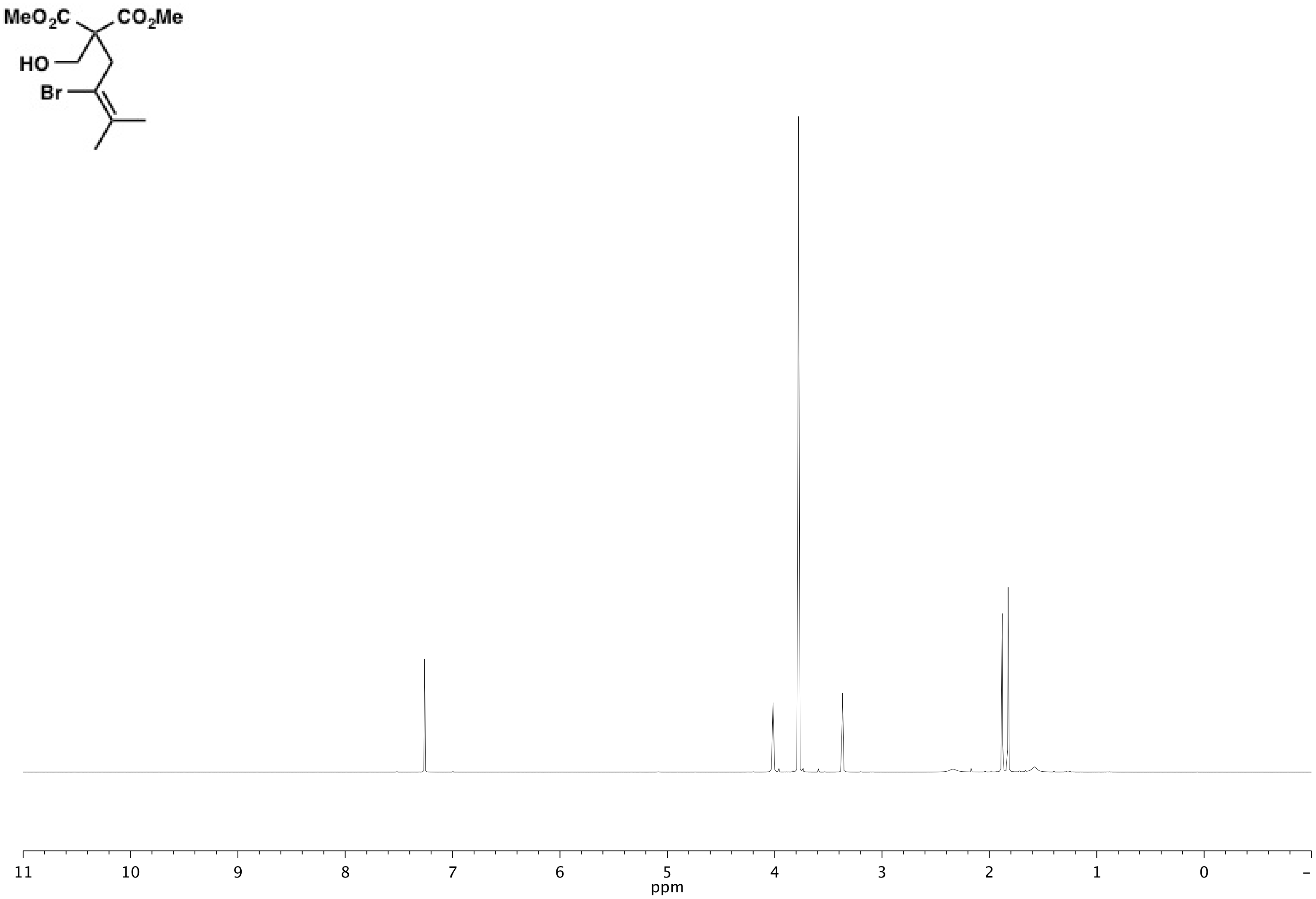
^{13}C NMR (101 MHz, CDCl$_3$) of compound **8e**.



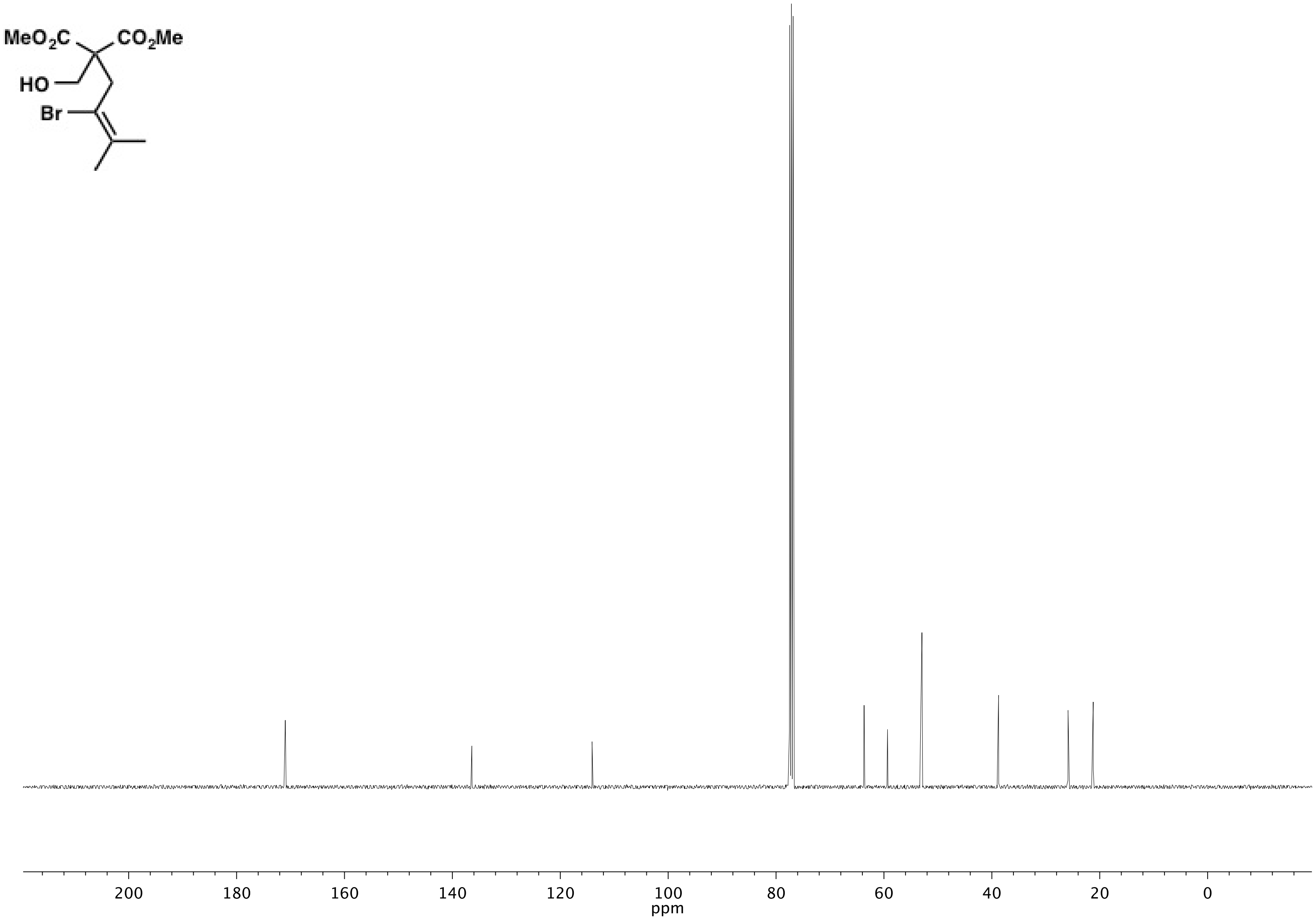
^{1}H NMR (400 MHz, C_6D_6) of compound **9e**.



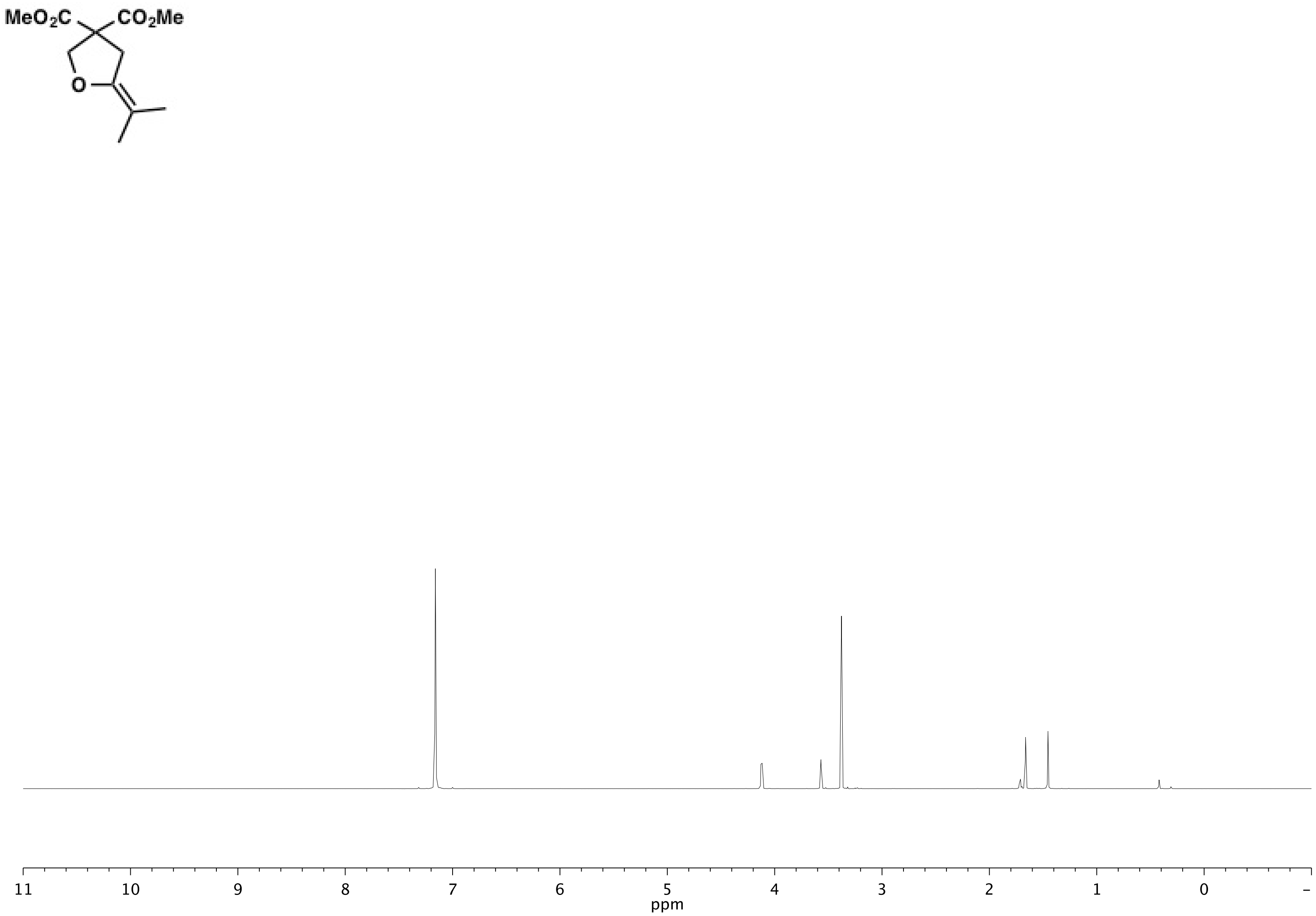
^{13}C NMR (101 MHz, C_6D_6) of compound **9e**.



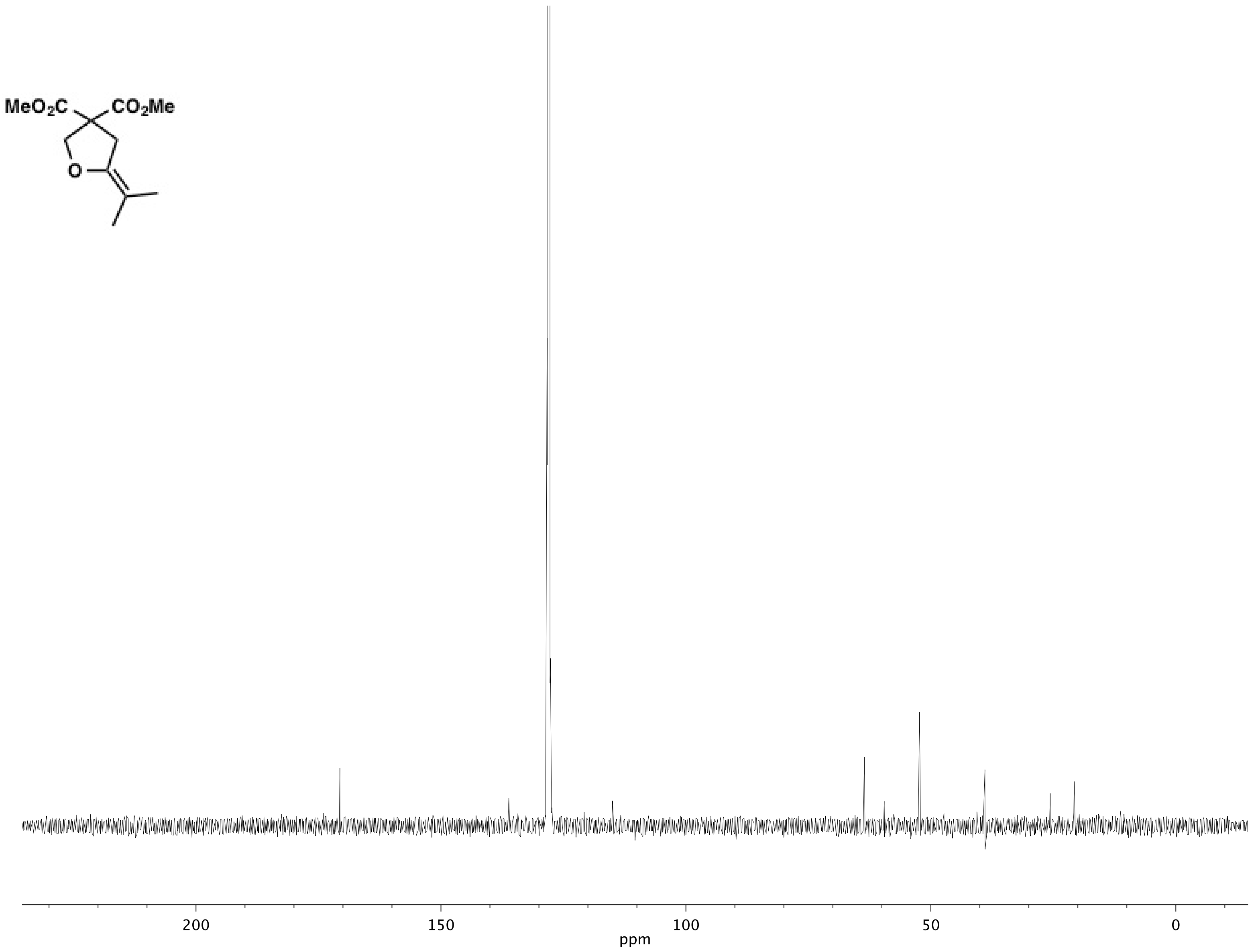
^{1}H NMR (400 MHz, CDCl$_3$) of compound **8f**.



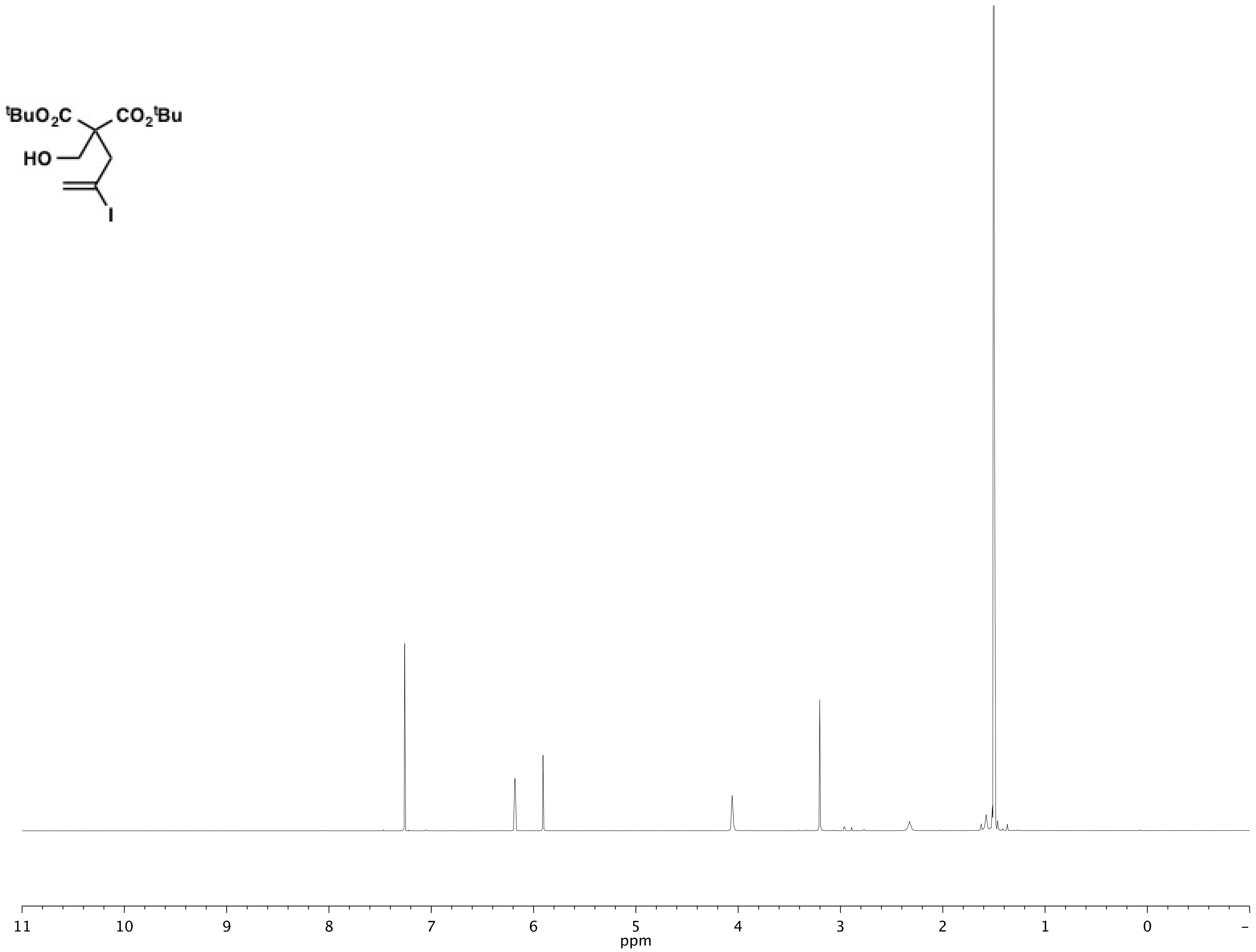
^{13}C NMR (101 MHz, CDCl$_3$) of compound **8f**.



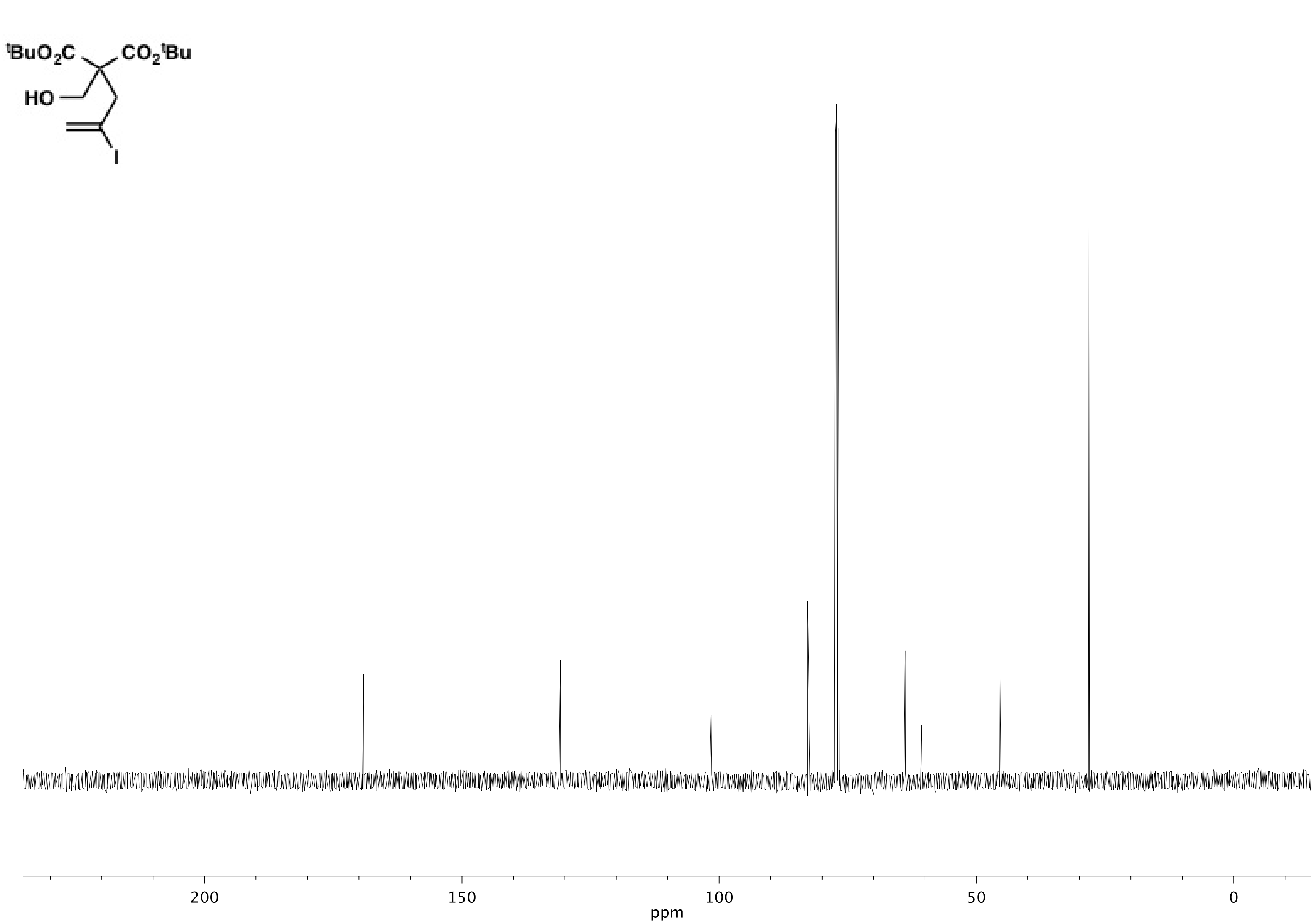
^{1}H NMR (500 MHz, C_6D_6) of compound **9f**.



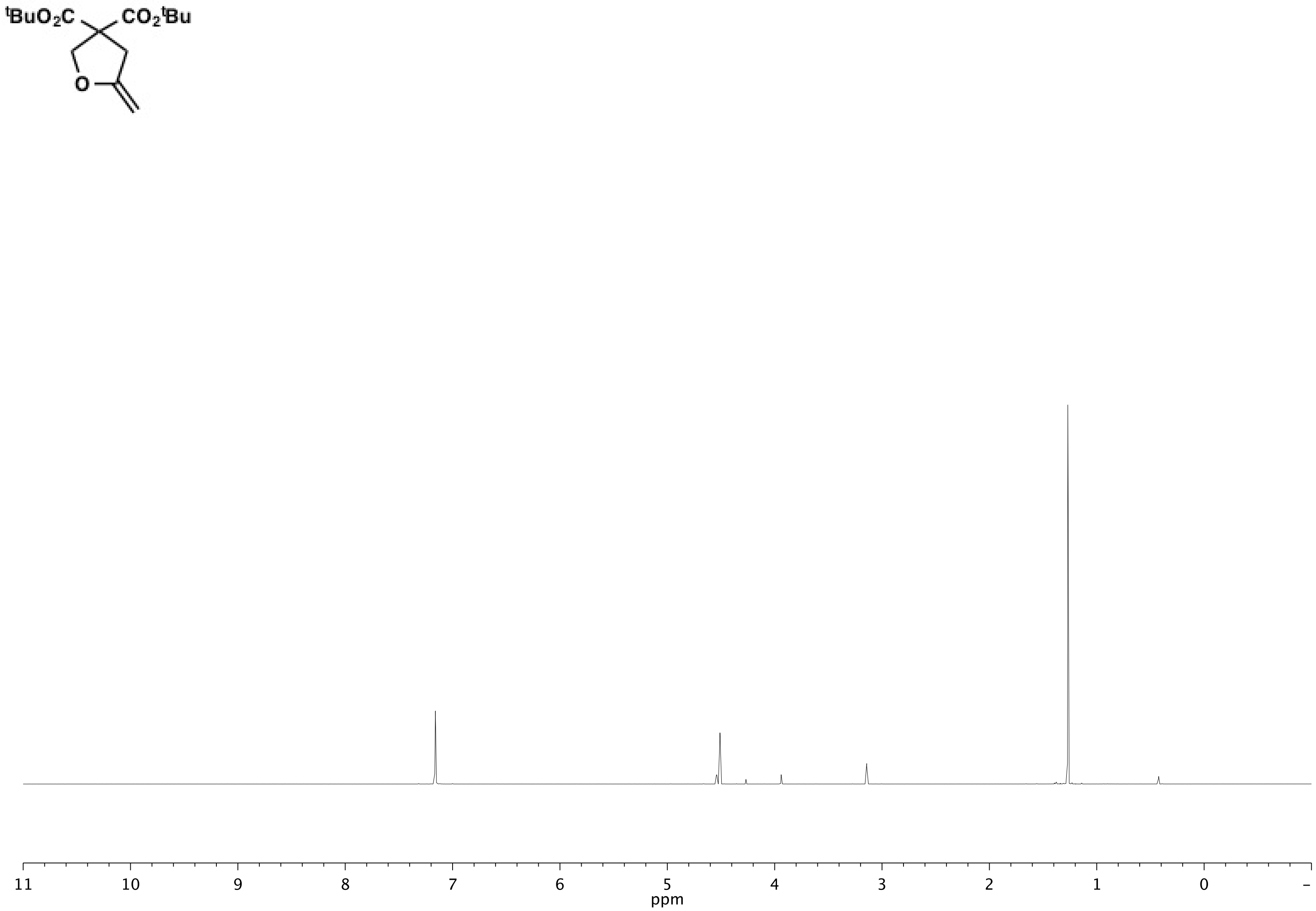
^{13}C NMR (126 MHz, C_6D_6) of compound **9f**.



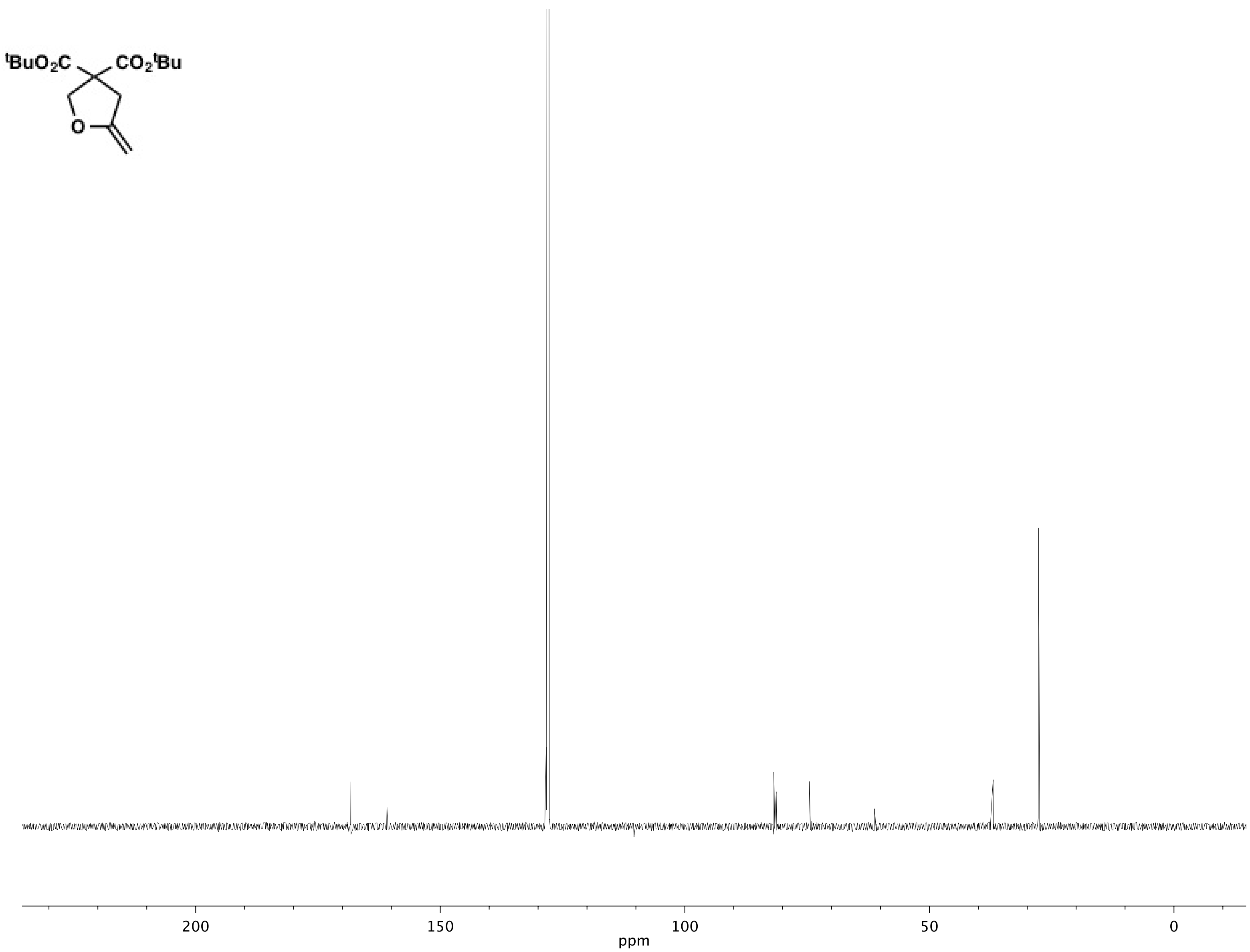
^{1}H NMR (500 MHz, $CDCl_3$) of compound **8g**.



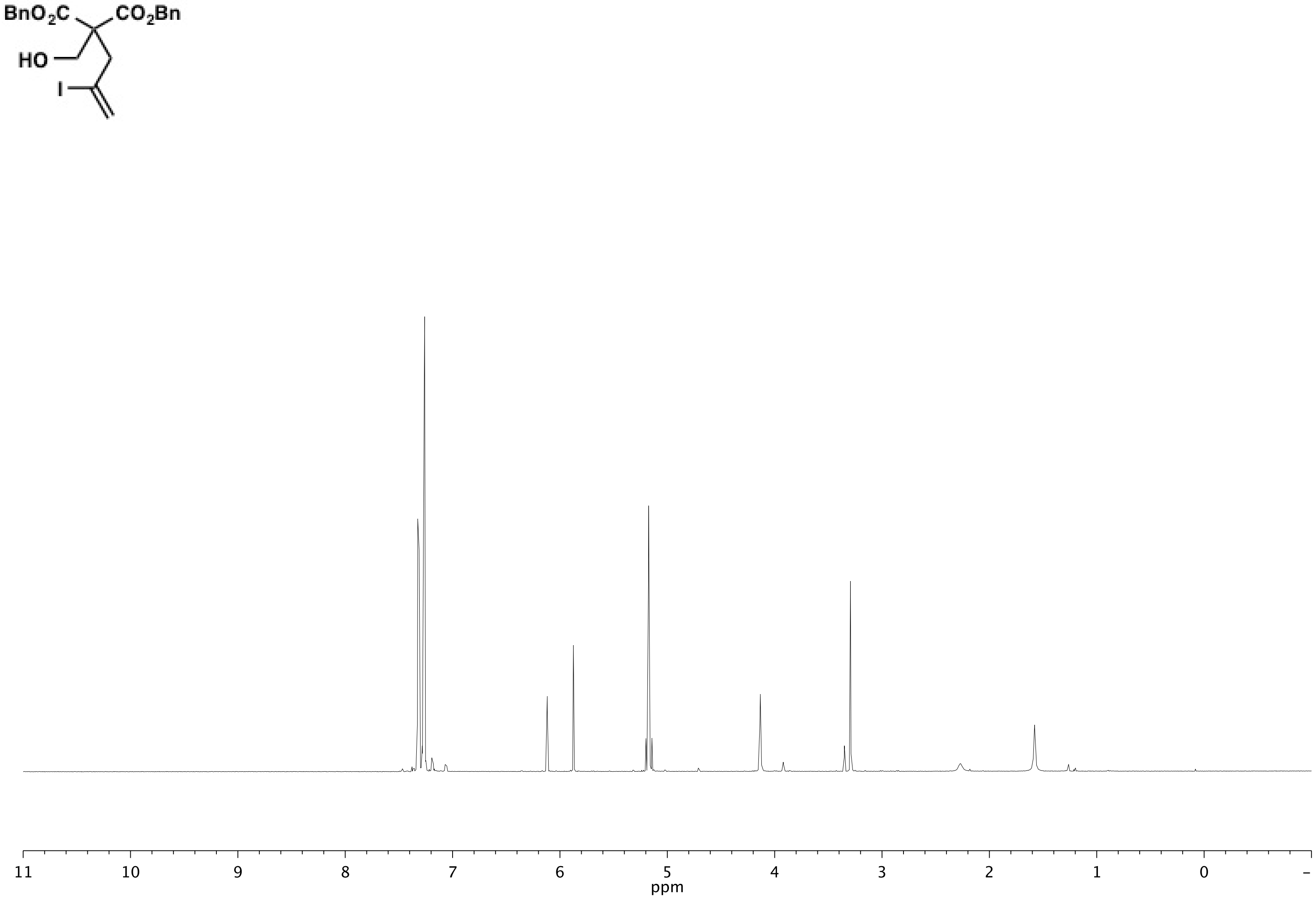
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8g**.



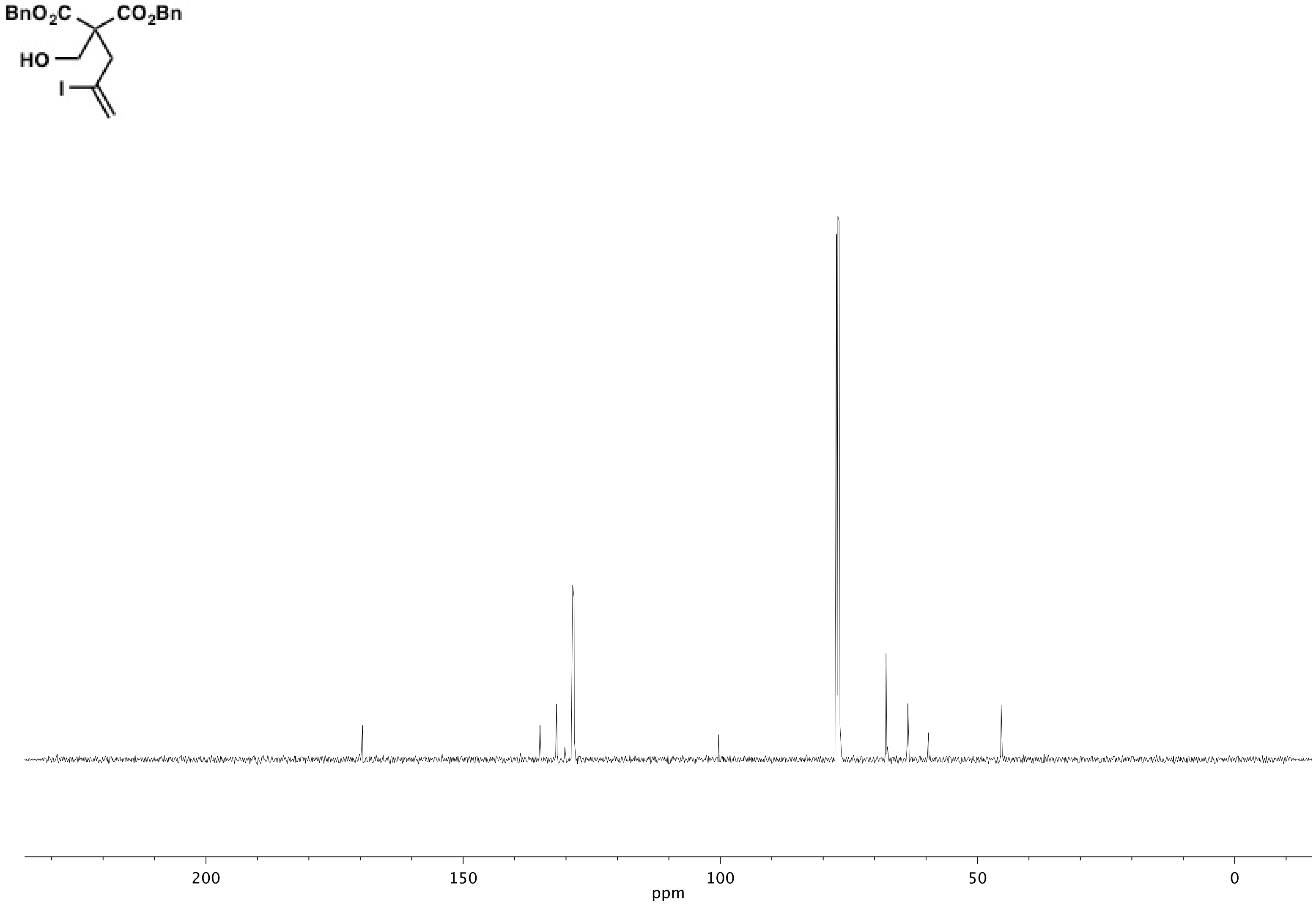
^1H NMR (500 MHz, C_6D_6) of compound **9g**.



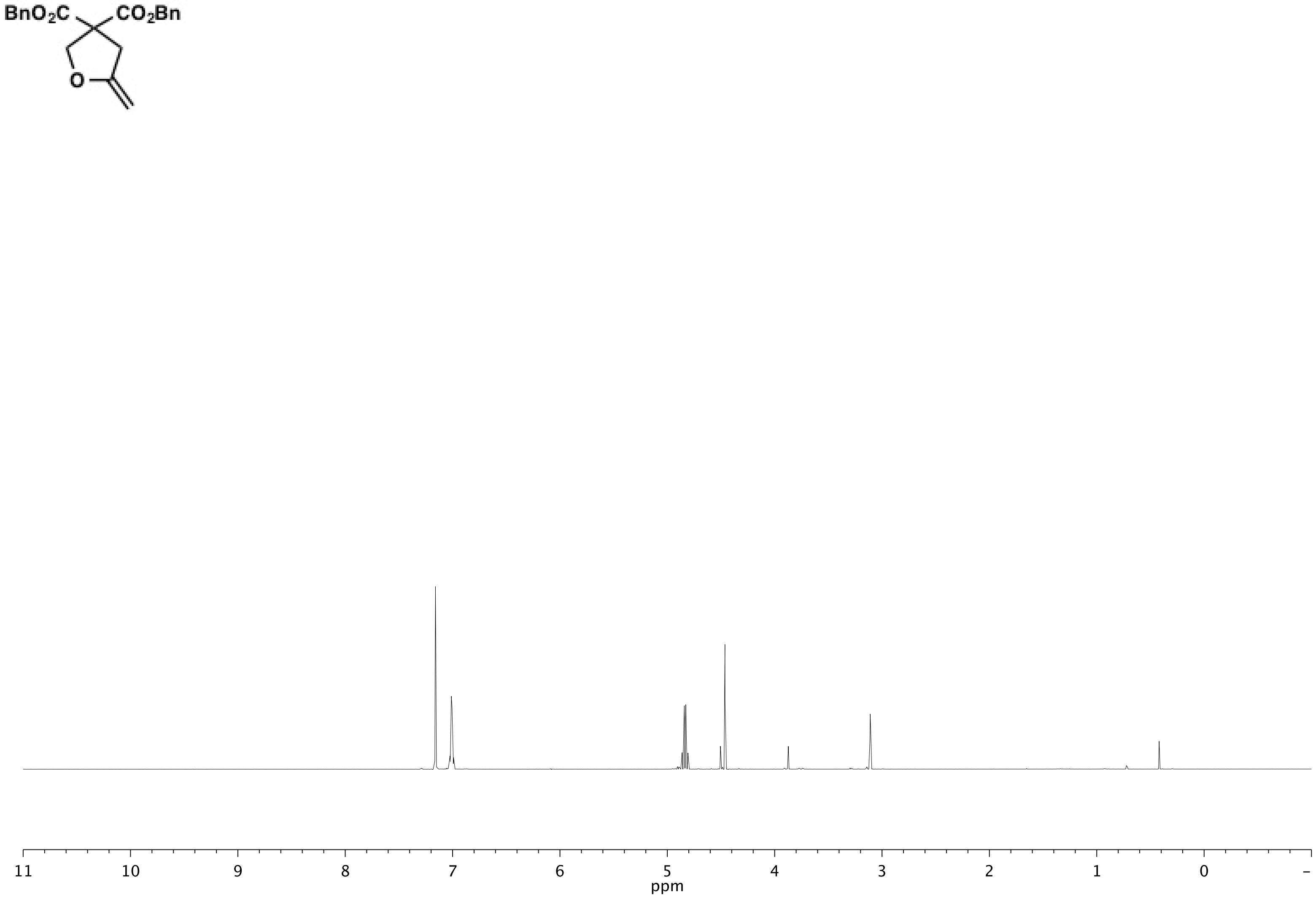
^{13}C NMR (126 MHz, C_6D_6) of compound **9g**.



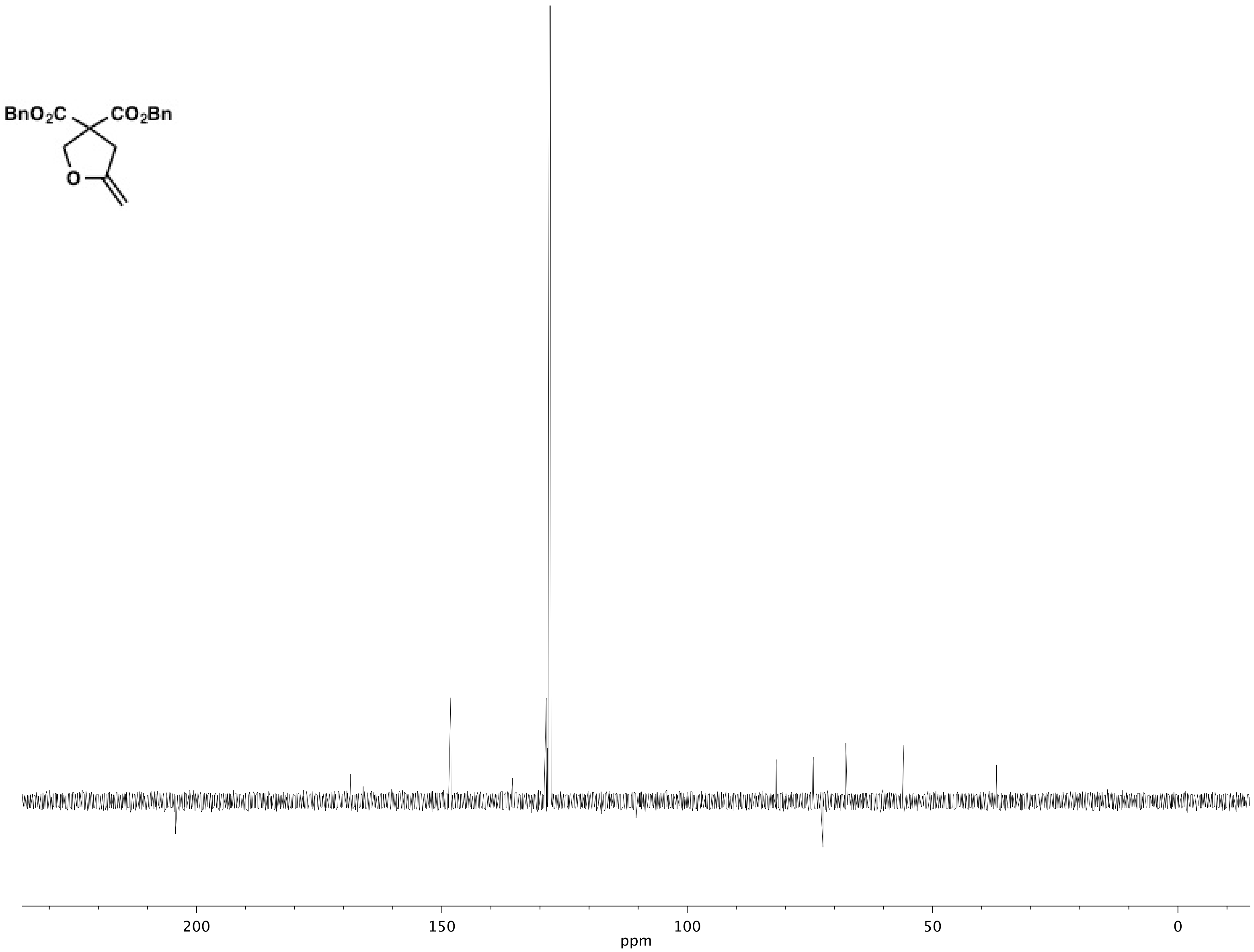
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8h**.



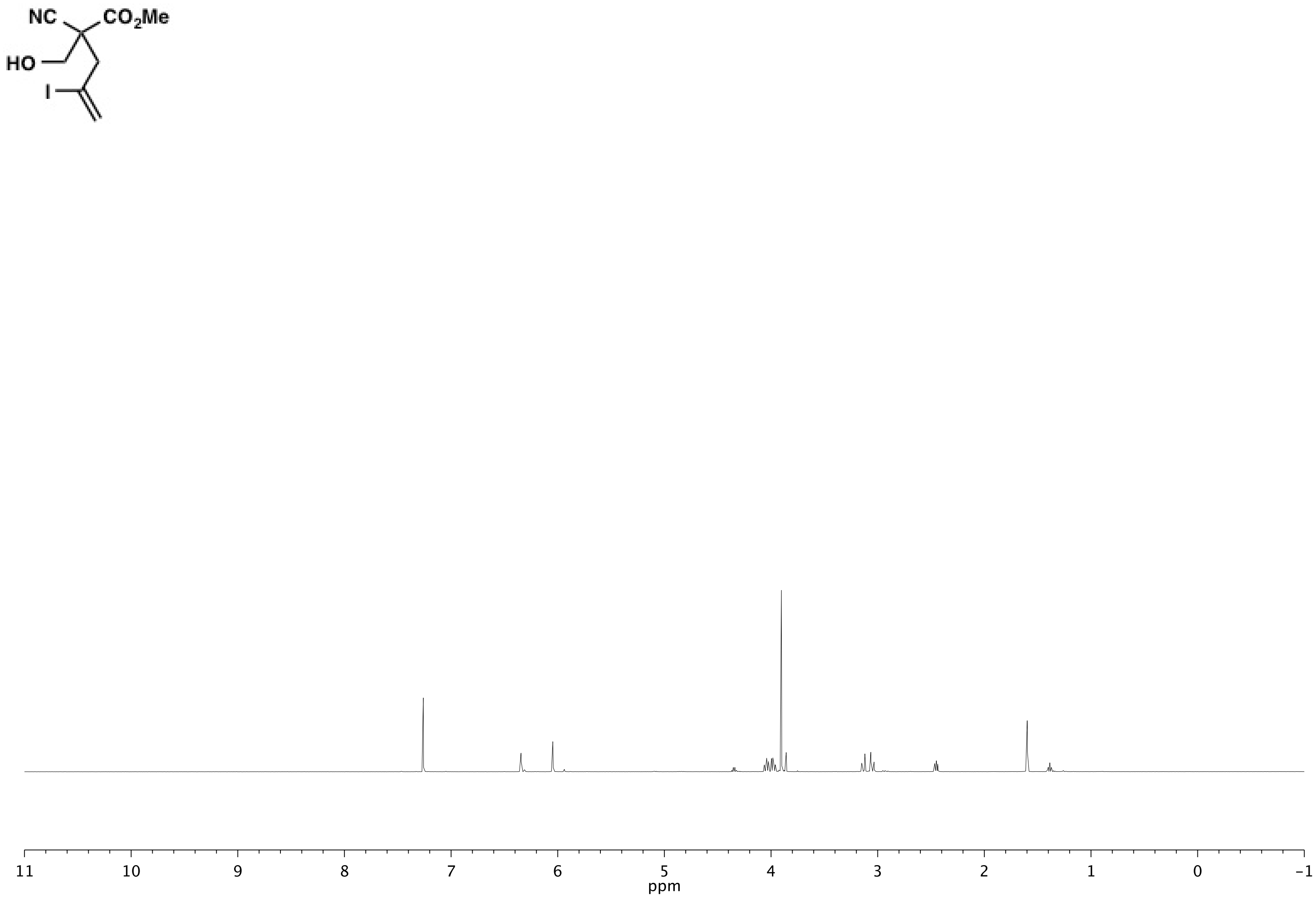
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8h**.



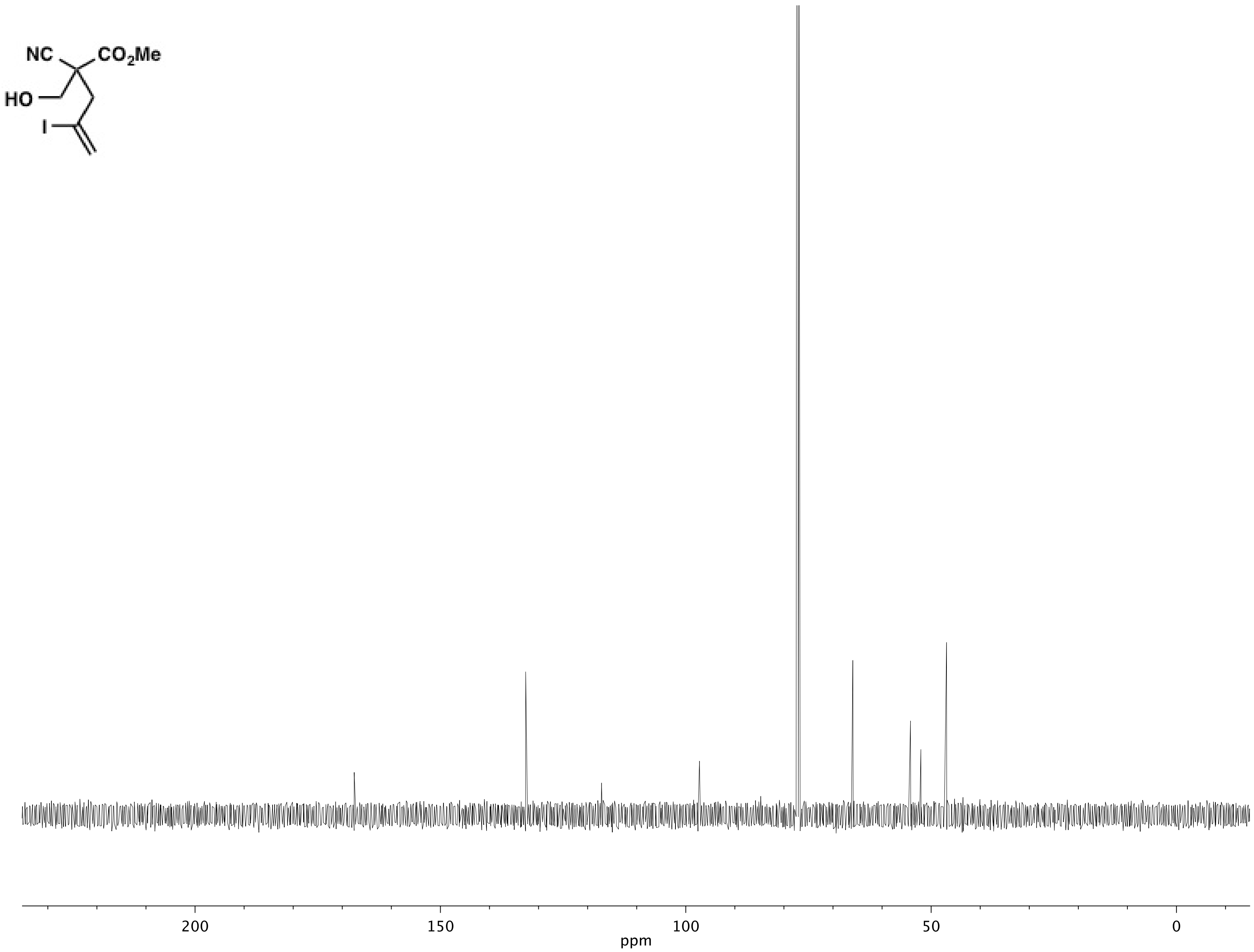
^{1}H NMR (600 MHz, C_6D_6) of compound **9h**.



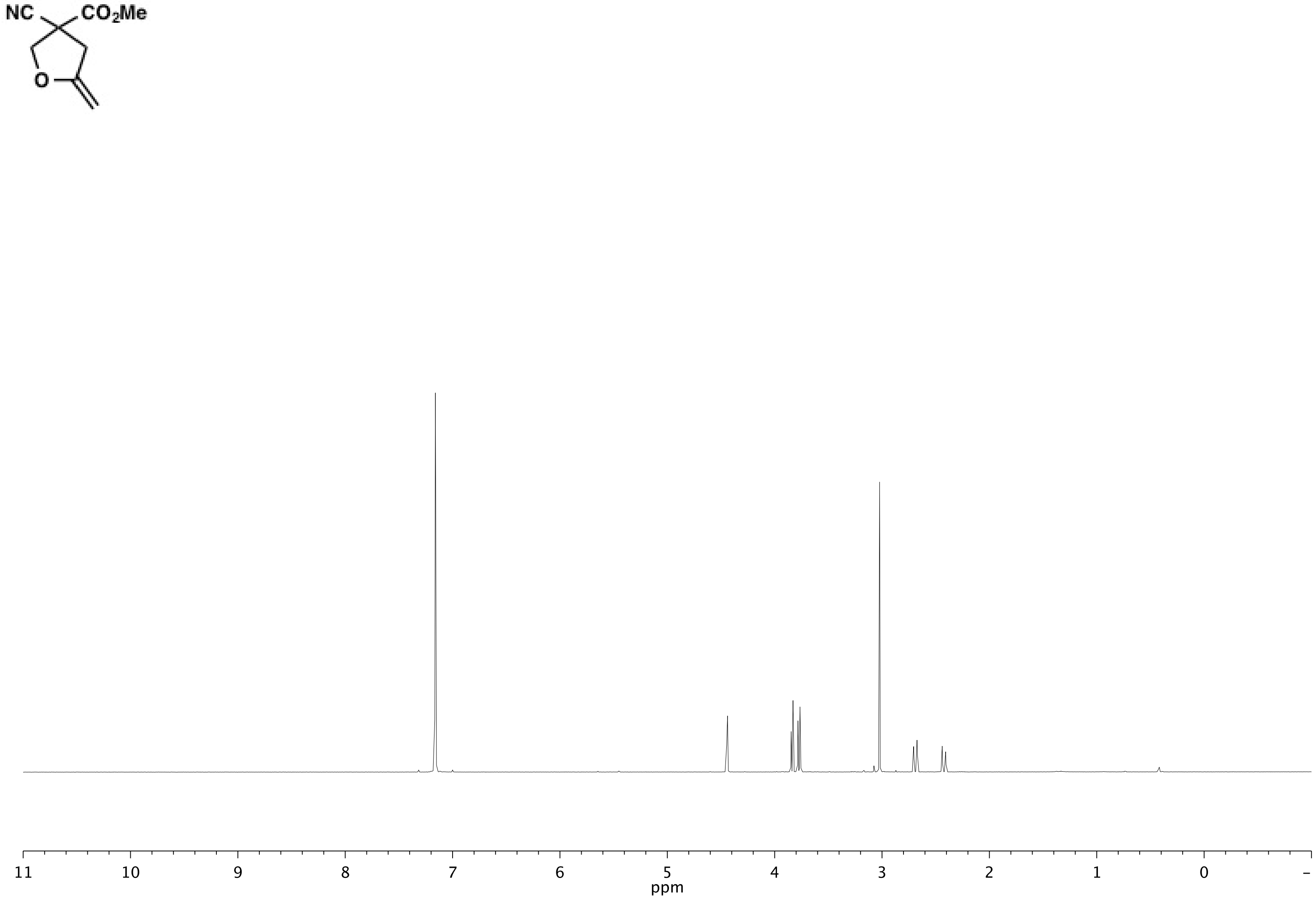
^{13}C NMR (151 MHz, C_6D_6) of compound **9h**.



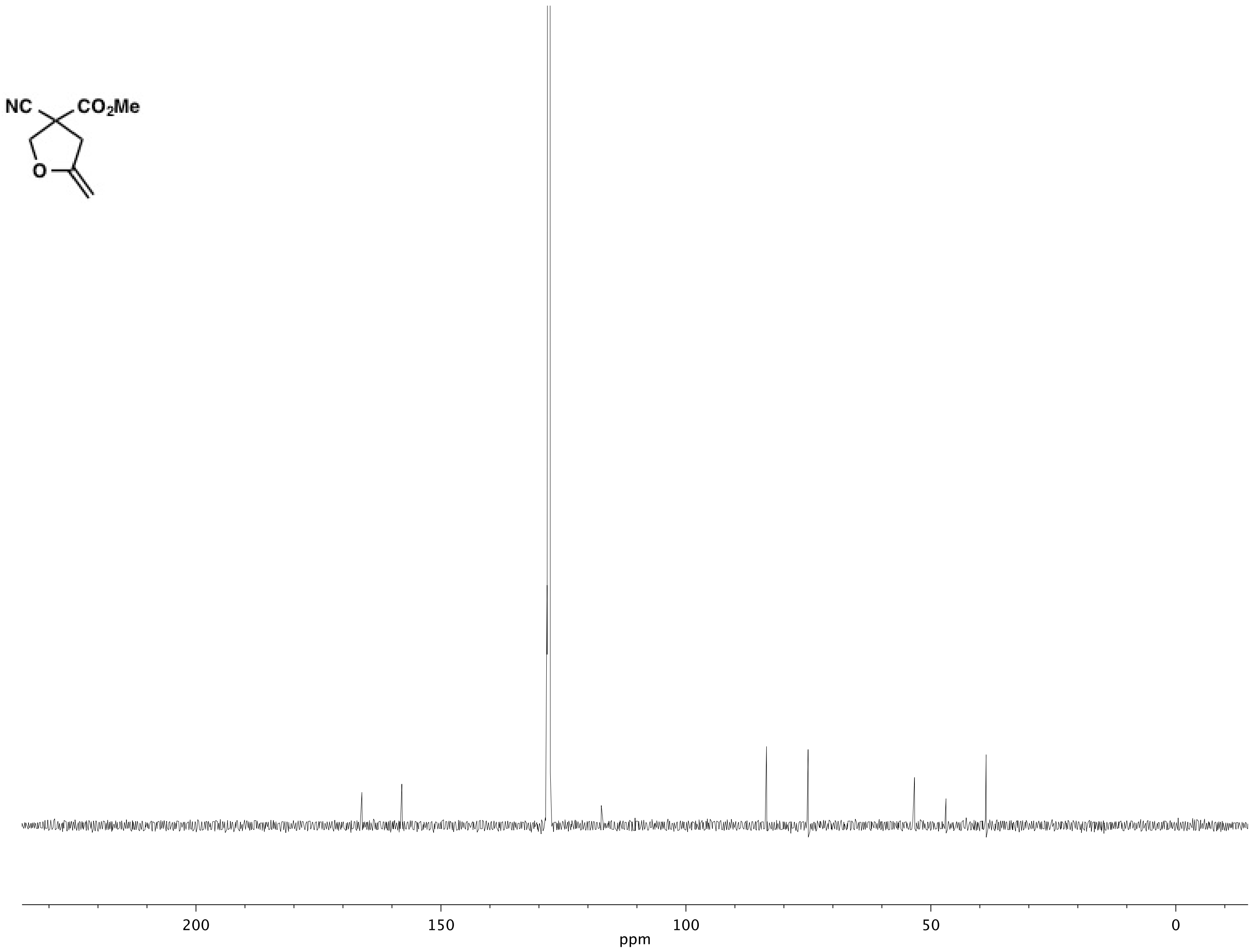
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8i**.



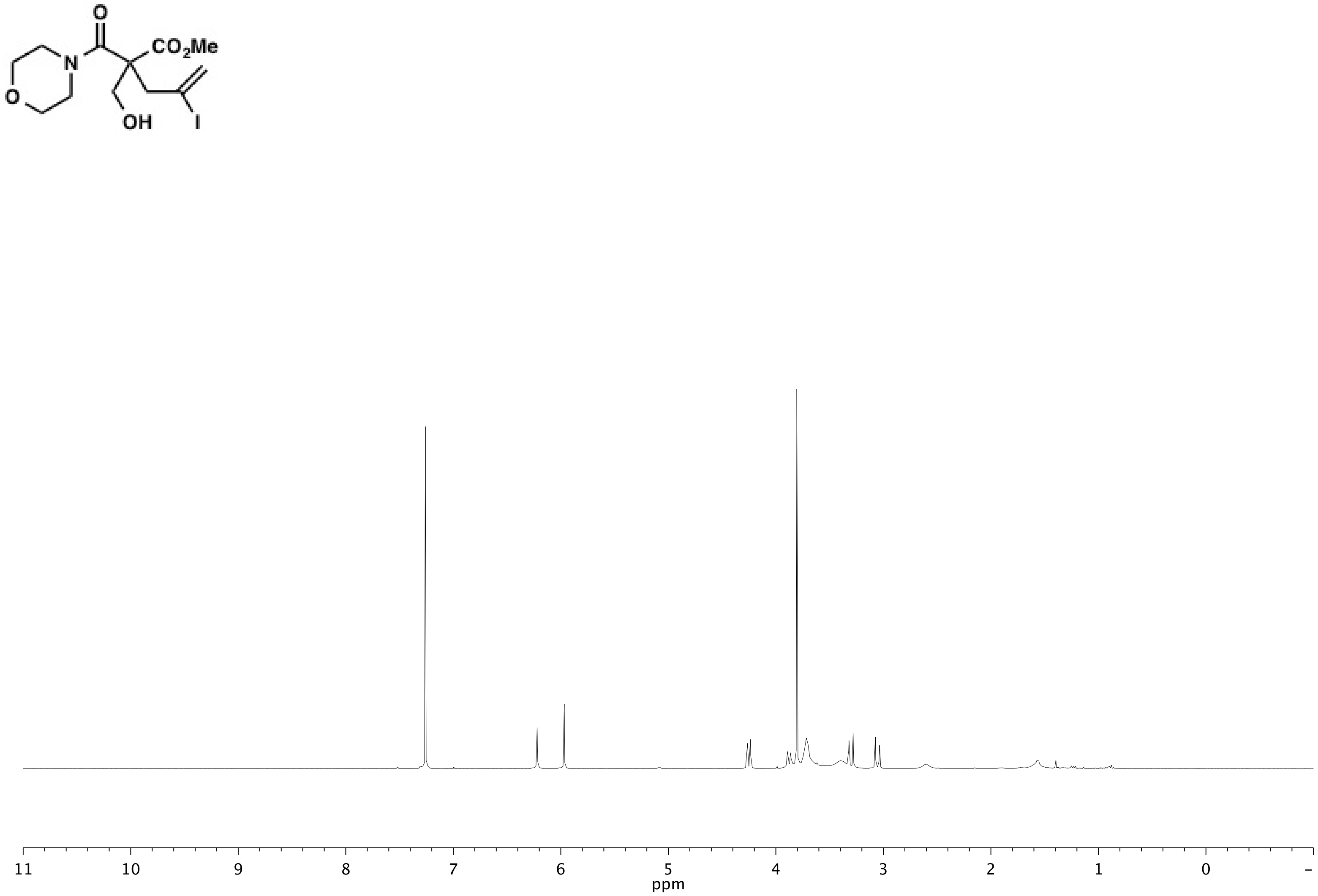
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8i**.



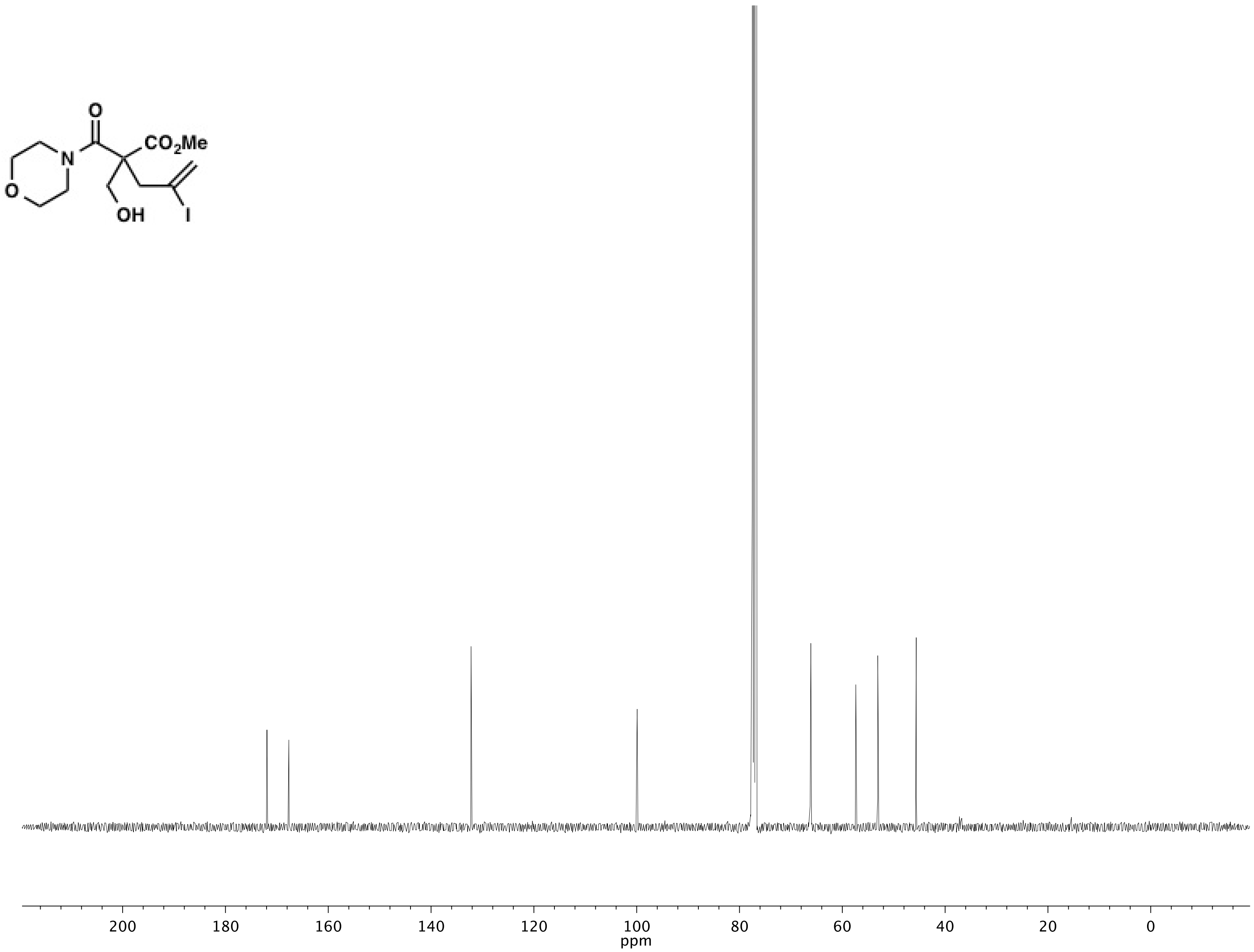
^{1}H NMR (500 MHz, C_6D_6) of compound **9i**.



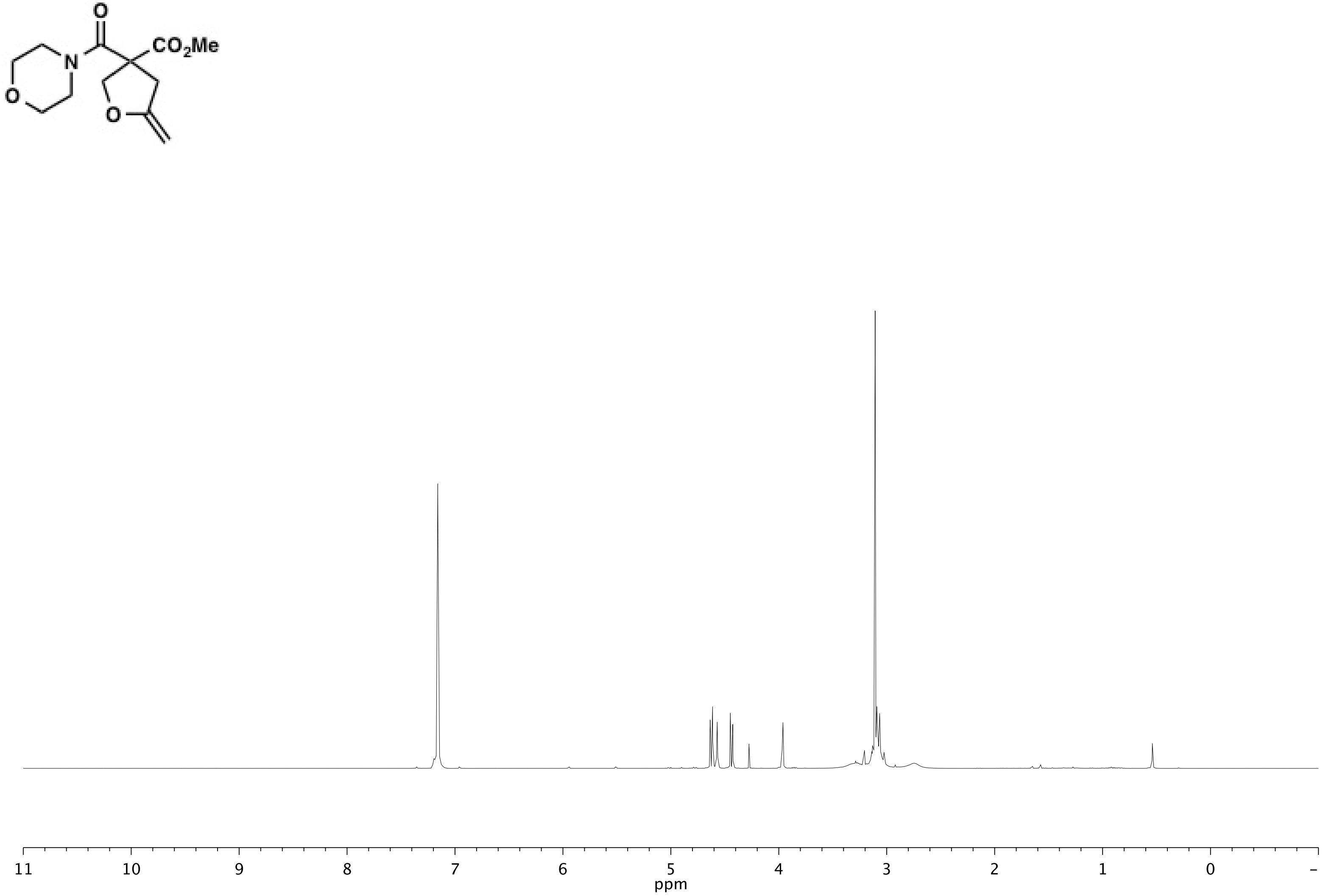
^{13}C NMR (126 MHz, C_6D_6) of compound **9i**.



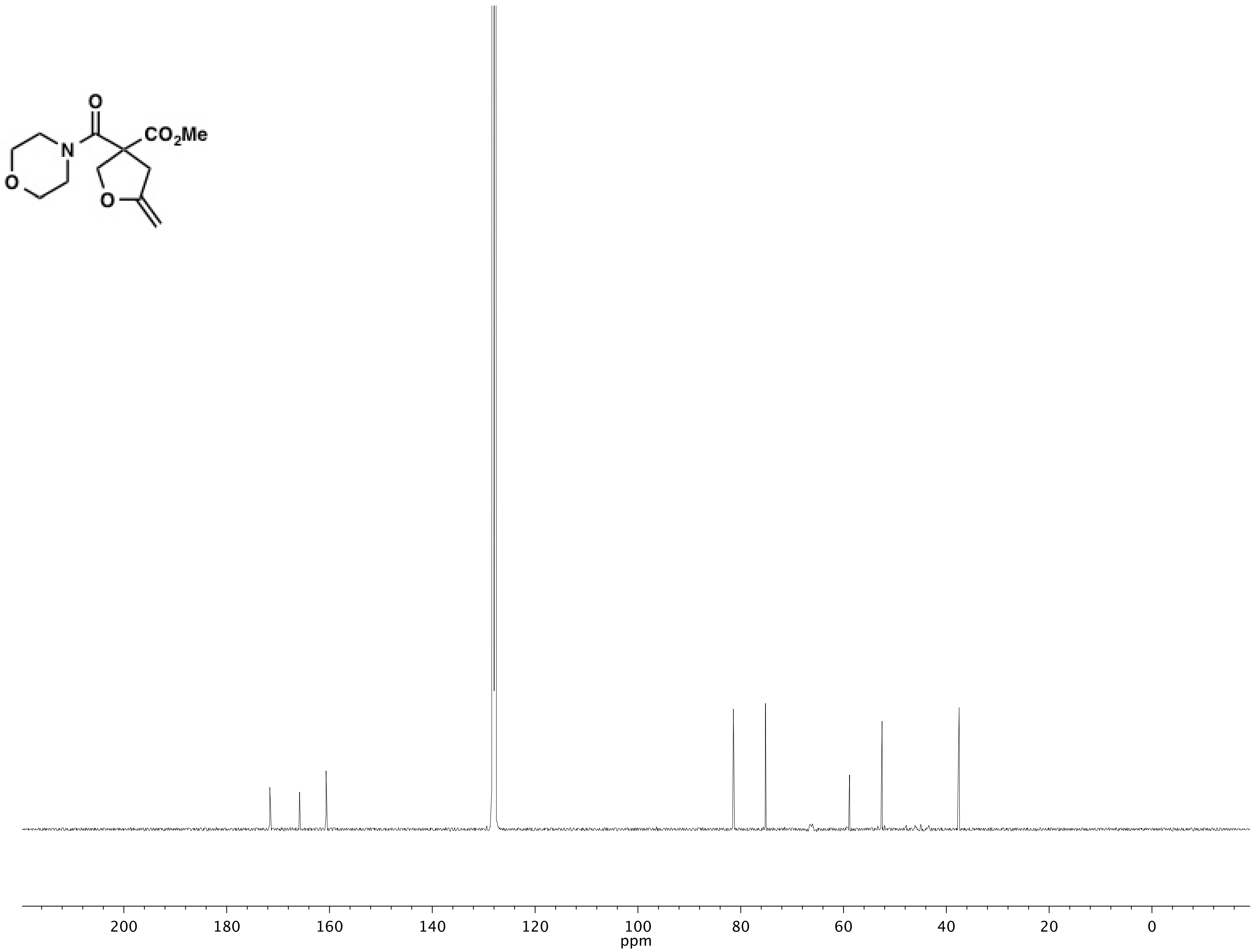
^{1}H NMR (400 MHz, CDCl$_3$) of compound **8j**.



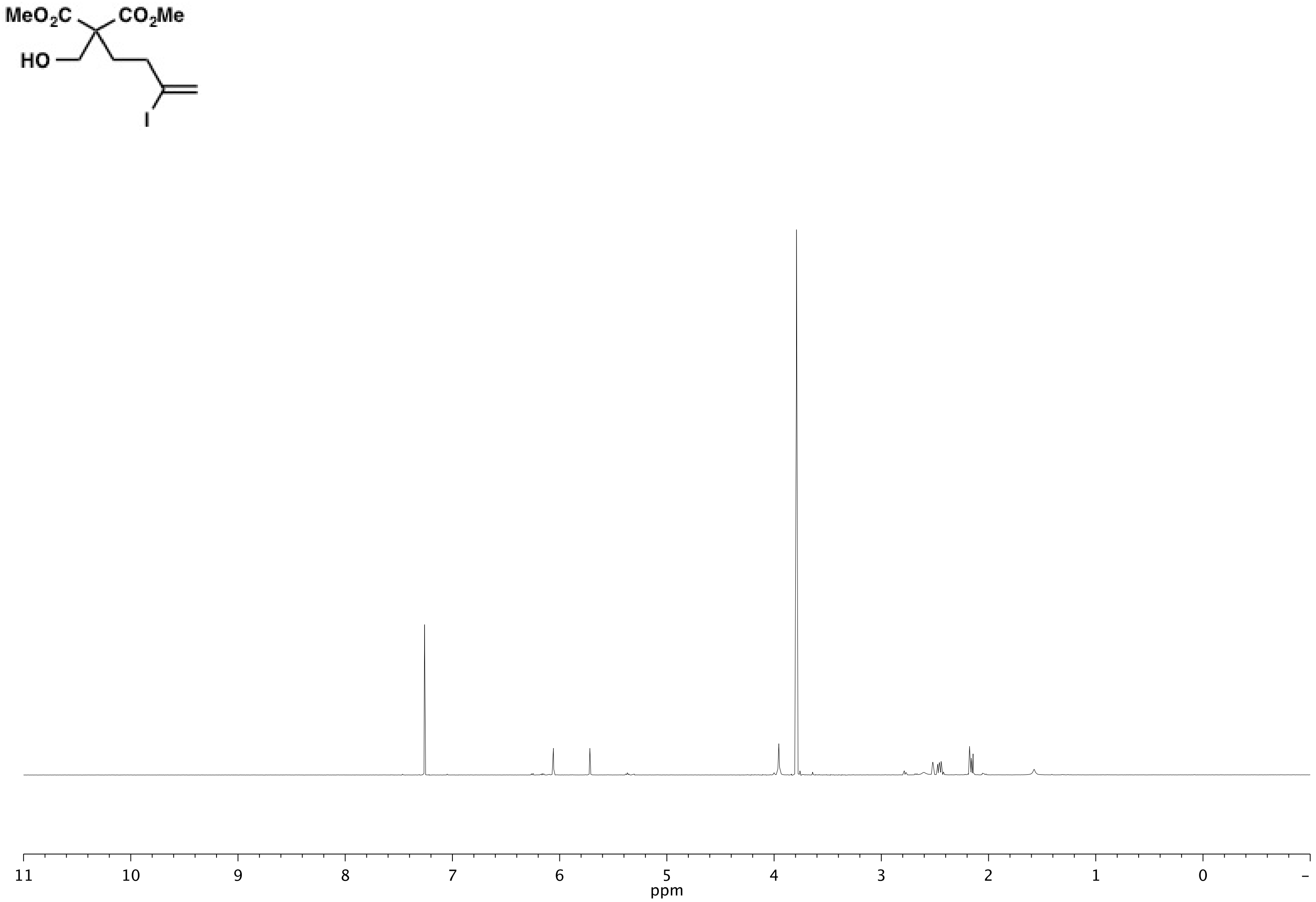
^{13}C NMR (101 MHz, CDCl$_3$) of compound **8j**.



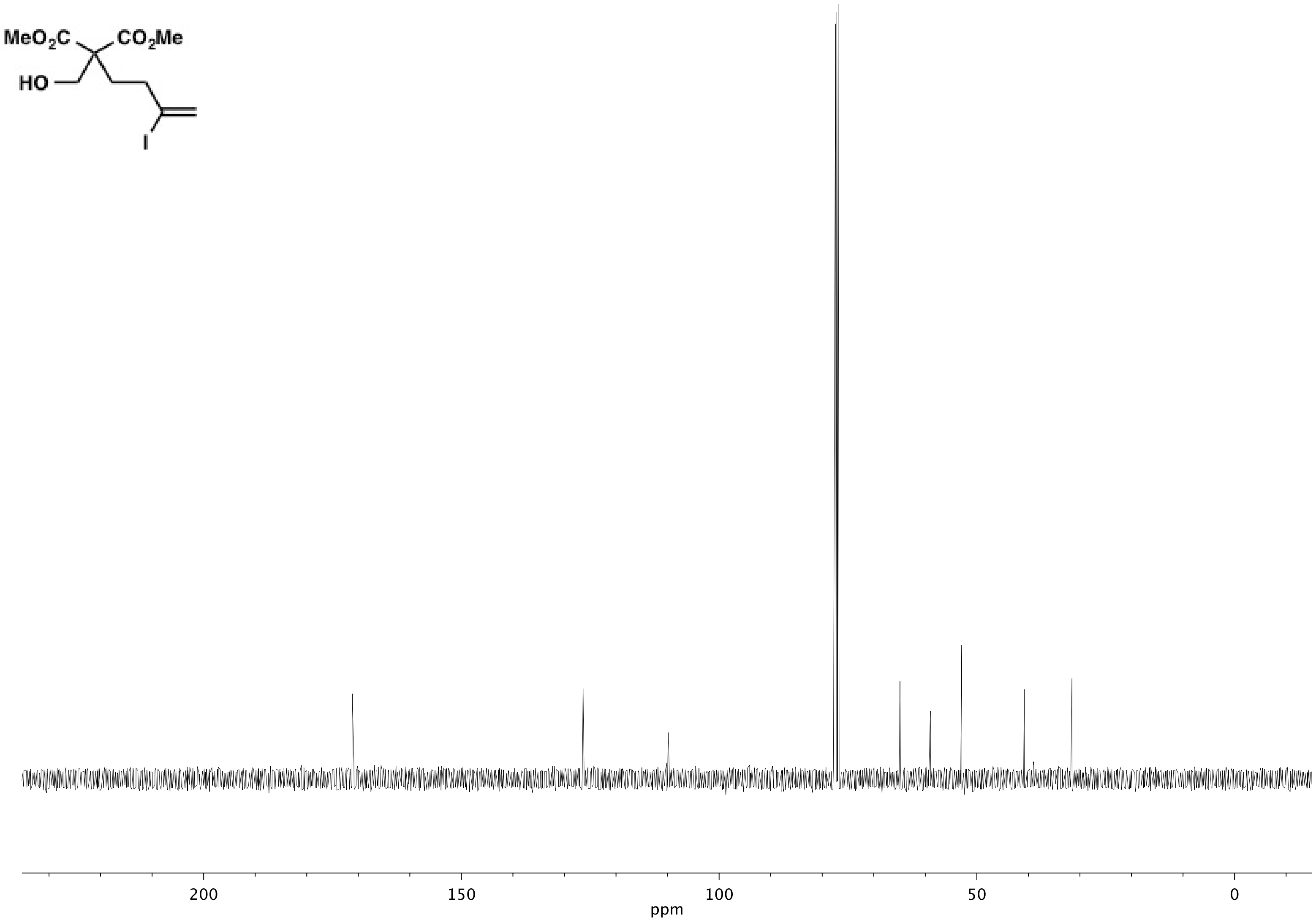
^{1}H NMR (500 MHz, C_6D_6) of compound **9j**.



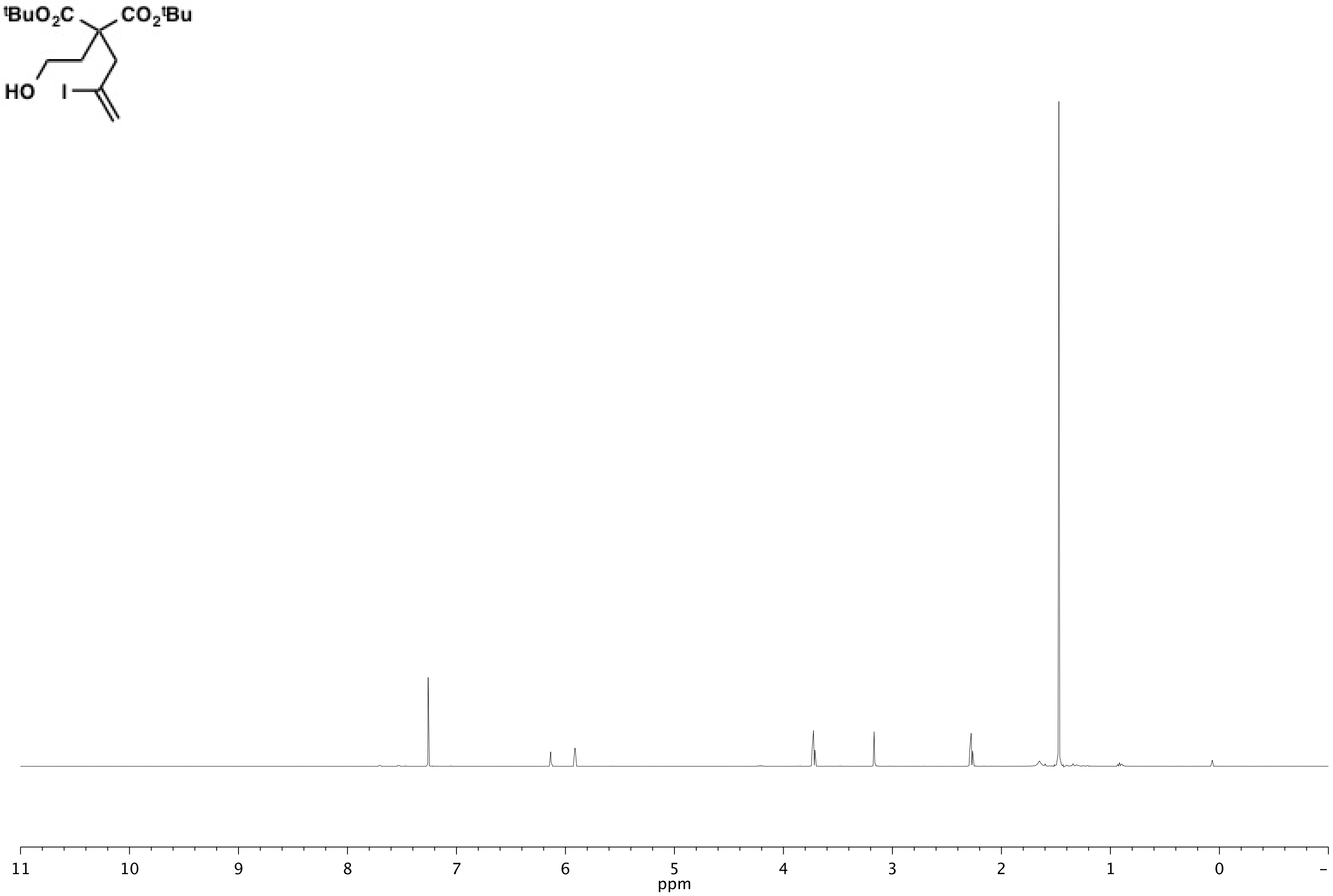
^{13}C NMR (101 MHz, C_6D_6) of compound **9j**.



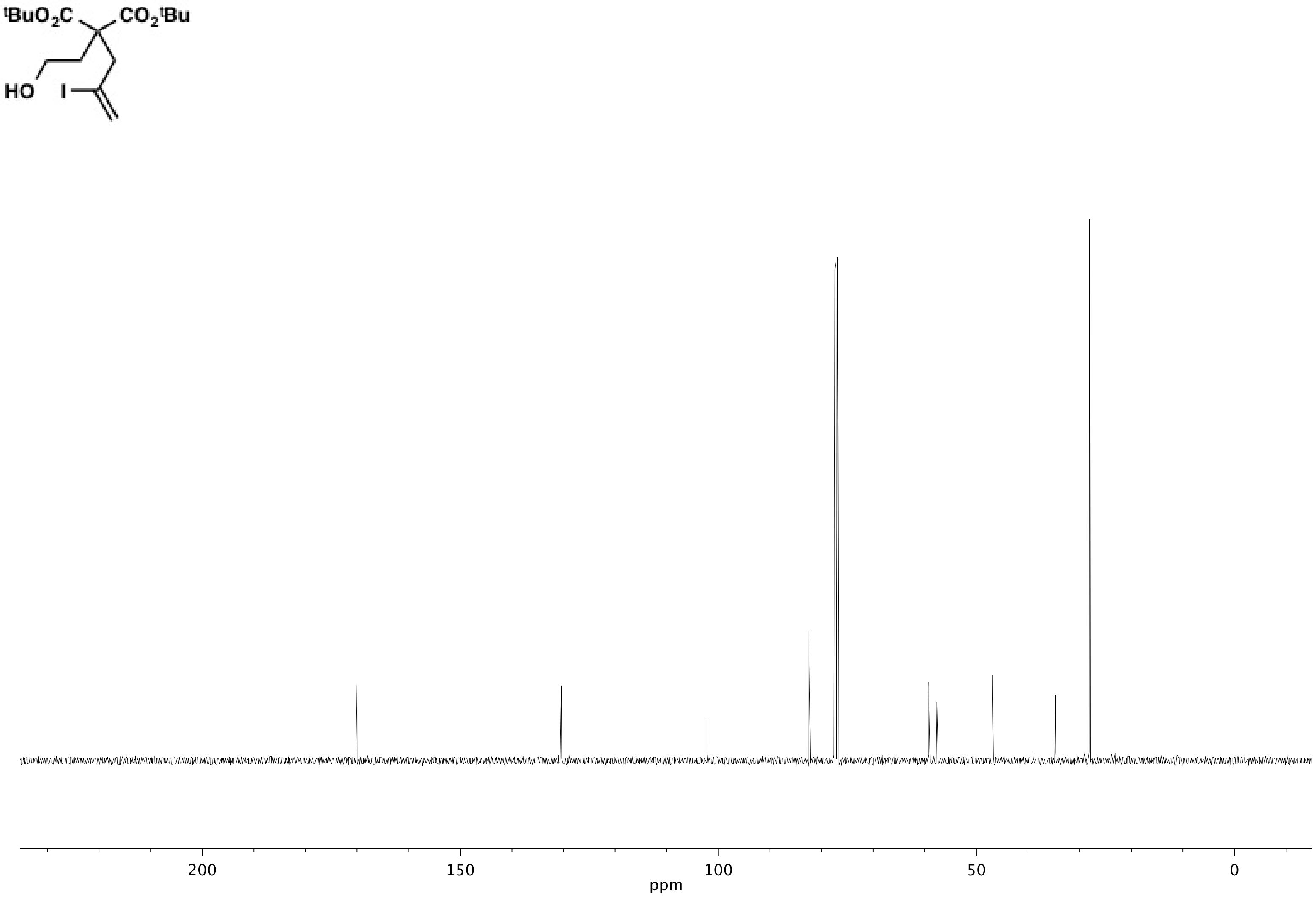
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8k**.



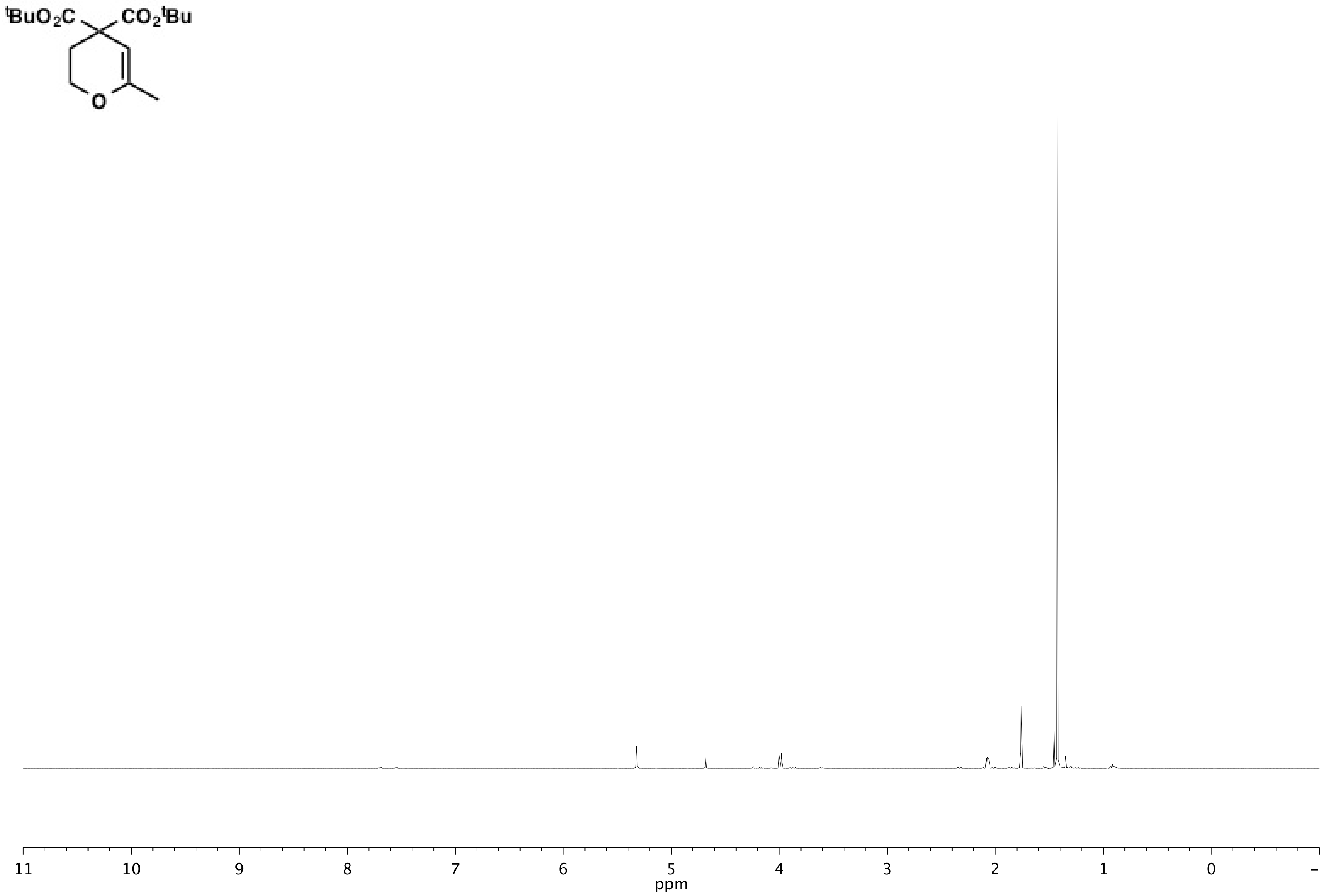
^{13}C NMR (126 MHz, CDCl$_3$) of compound **8k**.



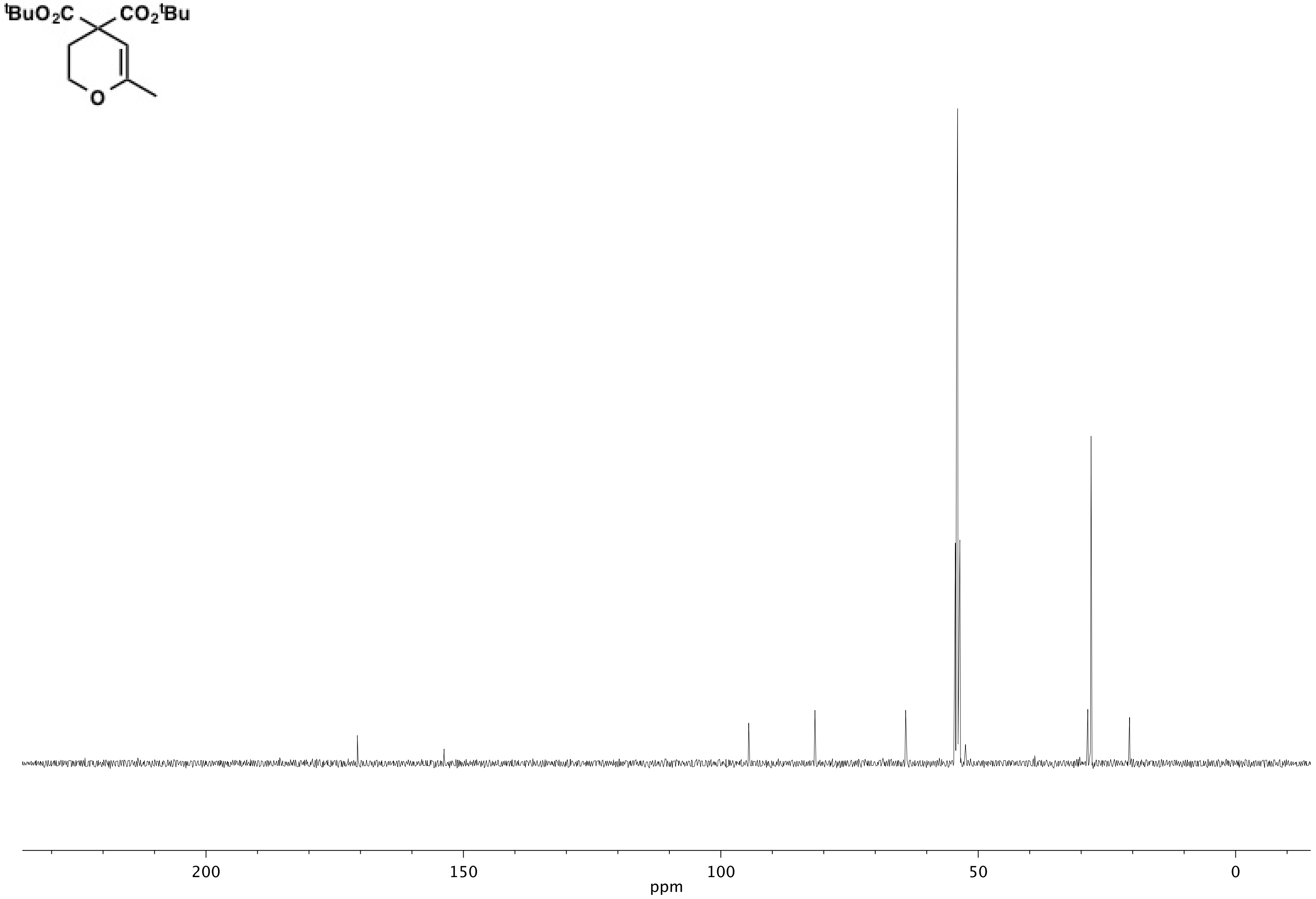
^{1}H NMR (500 MHz, CDCl$_3$) of compound **8l**.



^{13}C NMR (126 MHz, CDCl$_3$) of compound **8l**.



^{1}H NMR (500 MHz, CD_2Cl_2) of compound **9l**.



^{13}C NMR (126 MHz, CD_2Cl_2) of compound **9l**.