Iridium-Catalyzed Enantioselective and Diastereoselective Hydrogenation of 1,3-Disubstituted Isoquinolines

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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.[1] Solvents were dried by passage through an activated alumina column under argon. Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Bruker 400 MHz or Varian Mercury 300 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on Bruker 400 MHz spectrometer (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). ^{19}F NMR spectra were recorded on Varian Mercury 300 MHz spectrometer (282 MHz). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities 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 NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in 10 mg/1 mL, solvent). Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from 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+), or obtained from Caltech mass spectrometry laboratory.

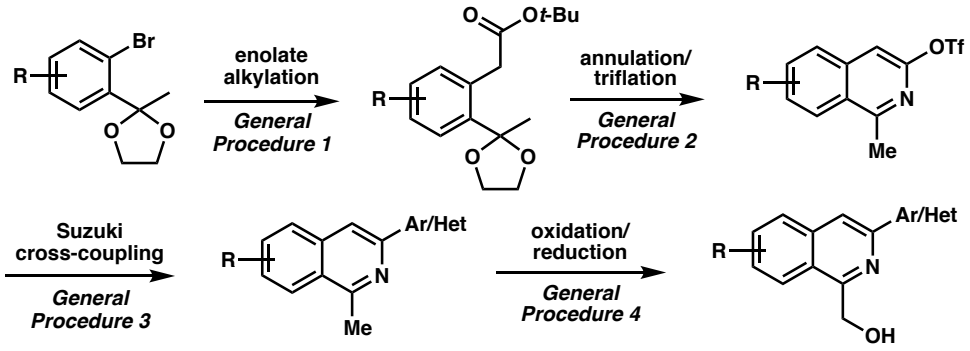
A crystal was mounted on a polyimide MiTeGen loop with STP Oil Treatment and placed under a nitrogen stream. Low temperature (100K) X-ray data were collected with a Bruker AXS KAPPA APEX II diffractometer diffractometer running at 50 kV and 30 mA (Mo K_α = 0.71073 Å; PHOTON 100 CMOS detector with TRIUMPH graphite monochromator). All diffractometer manipulations, including data collection, integration, and scaling were carried out using the Bruker APEX3 software. An absorption correction was applied using SADABS in point group 2. The space group was determined and the structure solved by intrinsic phasing using XT. Refinement was full-matrix least squares on F^2 using XL. All non-hydrogen atoms were refined using anisotropic displacement parameters. Hydrogen atoms were placed in idealized positions and the coordinates refined (each of the two disordered pairs were constrained to the same position). The isotropic displacement parameters of all hydrogen atoms were fixed at 1.2 times (1.5 times for methyl groups and alcohol) the U_{eq} value of the bonded atom.

Reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated.

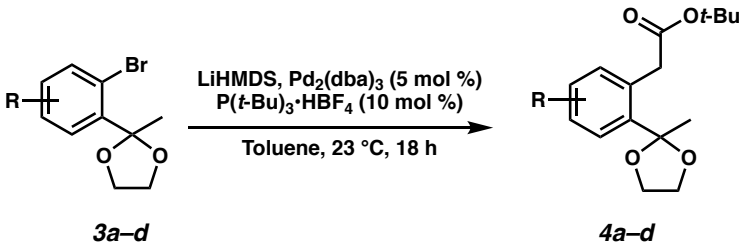
List of Abbreviations:
ee – enantiomeric excess, SFC – supercritical fluid chromatography, TLC – thin-layer chromatography, IPA – isopropanol, LiHMDS – lithium bis(trimethylsilyl)amide, dba – dibenzylideneacetone, RBF – round-bottom flask, TFA – trifluoroacetic acid, TBAI – tetrabutylammonium iodide, Boc_2O – di-*tert*-butyl dicarbonate, HPLC – high-performance liquid chromatography, DMAP – 4-dimethylaminopyridine, THF – tetrahydrofuran, BnBr – benzyl bromide, CDI – 1,1'-carbonyldiimidazole

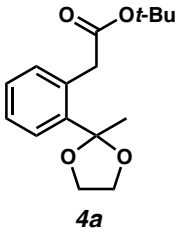
Syntheses of Hydroxymethyl 1,3-Disubstituted Isoquinolines

General sequence:



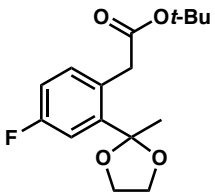
General procedure 1: Enolate alkylation of aryl bromide





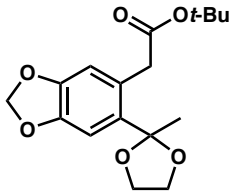
***tert*-butyl 2-(2-(2-methyl-1,3-dioxolan-2-yl)phenyl)acetate (4a):** This procedure has been adapted from a previous report.[2] In a Schlenk flask was added $P(t\text{-}Bu)_3{\bullet}HBF_4$ (119 mg, 0.41 mmol), $Pd_2(dba)_3$ (188 mg, 0.21 mmol), a solution of 2-(2-bromophenyl)-2-methyl-1,3-dioxolane

(**3a)** (1.0 g, 4.1 mmol, 0.42 M), and *tert*-Butyl acetate (0.95 g, 8.2 mmol), respectively. The reaction mixture was cooled to –78 °C and sparged with nitrogen for 15 minutes. A degassed solution of LiHMDS (1.72 g, 10.25 mmol, 1 M in toluene) was then added via syringe. The reaction mixture was degassed for an additional 15 minutes at –78 °C, and allowed to slowly warm to room temperature. The reaction was stirred at room temperature for 18 hours, and then quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O twice. The combined organic phases were dried over $MgSO_4$, filtered, and the solvent was removed in vacuo. The crude product was purified by silica gel flash chromatography (5% EtOAc in hexanes) to afford **4a** as a yellow oil (1.05 g, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.45 (m, 1H), 7.20 – 7.06 (m, 3H), 3.96 – 3.83 (m, 2H), 3.71 (s, 2H), 3.68 – 3.55 (m, 2H), 1.60 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 141.1, 132.6, 132.3, 128.2, 127.1, 126.4, 109.2, 80.4, 64.3, 40.4, 28.2, 28.2, 27.6; IR (Neat Film, NaCl) 3454, 3062, 2977, 2936, 2893, 1731, 1484, 1455, 1392, 1368, 1218, 1196, 1168, 1037, 952, 869, 763, 706 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{23}O_4$ $[M+H]^+$: 279.1591, found 279.1589.



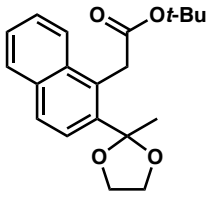
4b

***tert*-butyl 2-(4-fluoro-2-(2-methyl-1,3-dioxolan-2-yl)phenyl)acetate (4b):** Compound **4b** was prepared from aryl bromide (2-(2-bromo-5-fluorophenyl)-2-methyl-1,3-dioxolane) (**3b**) using general procedure 1, and purified by column chromatography (10% EtOAc in hexanes) to afford **4b** with impurities. The compound was then subjected to the second column chromatography (15% Et_2O in hexanes) to obtain **4b** as a colorless solid (74 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 10.3, 2.8 Hz, 1H), 7.15 (dd, *J* = 8.4, 5.7 Hz, 1H), 6.94 (td, *J* = 8.2, 2.9 Hz, 1H), 4.06 – 3.90 (m, 2H), 3.74 (s, 2H), 3.72 – 3.69 (m, 2H), 1.65 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 161.9 (d, *J* = 245.1 Hz), 143.9 (d, *J* = 6.2 Hz), 134.2 (d, *J* = 7.8 Hz), 127.9 (d, *J* = 3.3 Hz), 114.9 (d, *J* = 21.1 Hz), 113.5 (d, *J* = 23.0 Hz), 108.6, 80.6, 64.4, 39.6, 28.2, 27.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ –115.6 (ddd, *J* = 10.3, 8.0, 5.8 Hz); IR (Neat Film, NaCl) 2980, 1732, 1613, 1493, 1412, 1392, 1368, 1340, 1256, 1200, 1179, 1147, 1037, 947, 878 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{22}FO_4$ $[M+H]^+$: 297.1497, found 297.1494.



4c

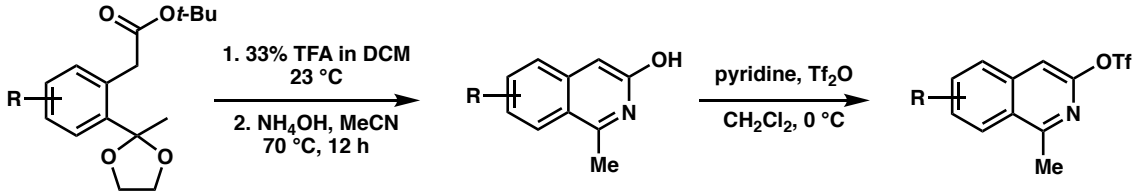
***tert*-butyl 2-(6-(2-methyl-1,3-dioxolan-2-yl)benzo[*d*][1,3]dioxol-5-yl)acetate (4c):** Compound **4c** was prepared from aryl bromide (5-bromo-6-(2-methyl-1,3-dioxolan-2-yl)benzo[*d*][1,3]dioxole) (**3c**) using general procedure 1, and purified by column chromatography (5% to 15% EtOAc in hexanes) to afford **4c** as a pale yellow oil (83.4 mg, 63% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (s, 1H), 6.66 (s, 1H), 5.93 (s, 2H), 3.95 – 3.93 (m, 2H), 3.72 – 3.69 (m, 2H), 3.62 (s, 2H), 1.64 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 147.2, 146.7, 135.2, 125.9, 112.3, 109.1, 107.0, 101.3, 80.6, 64.3, 40.0, 28.3, 27.6; IR (Neat Film, NaCl) 2978, 2897, 1732, 1504, 1486, 1369, 1332, 1259, 1197, 1166, 1142, 1041, 929, 869, 935 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{23}O_6$ $[M+H]^+$: 323.1489, found 323.1501.



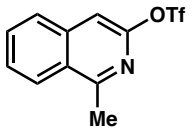
4d

***tert*-butyl 2-(2-(2-methyl-1,3-dioxolan-2-yl)naphthalen-1-yl)acetate (4d):** Compound **4d** was prepared from aryl bromide (2-(1-bromonaphthalen-2-yl)-2-methyl-1,3-dioxolane) (**3d**) using general procedure 1, and purified by column chromatography (0% to 5% EtOAc in hexanes) to afford **4d** as a pale yellow oil (2.15 g, 98% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.76 (s, 2H), 7.48 (ddd, J = 7.9, 6.7, 1.4 Hz, 2H), 4.38 (s, 2H), 4.04 – 4.00 (m, 2H), 3.79 – 3.73 (m, 2H), 1.78 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 139.3, 133.6, 128.7, 128.6, 127.8, 126.5, 125.8, 124.3, 124.1, 109.7, 80.7, 64.4, 36.2, 28.2, 27.8. IR (Neat Film, NaCl) 2980, 2890, 1732, 1454, 1368, 1336, 1142, 1100, 1037, 951, 884, 870, 822, 750 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{25}O_4$ $[M+H]^+$: 329.1747, found 329.1739.

General procedure 2: Isoquinoline annulation and triflation



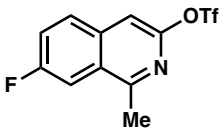
4a–d ***5a–d***



5a

1-methylisoquinolin-3-yl trifluoromethanesulfonate (5a): This procedure has been adapted from a previous report.[3] In a RBF were added ester **4a** (2.78 g, 10.0 mmol), anhydrous CH_2Cl_2 (75 mL, 0.13 M), and TFA (25 mL, 33% volume of CH_2Cl_2), respectively. The reaction was stirred at room temperature for 2 hours, and then concentrated in vacuo. The crude was transferred to a Schlenk tube, dissolved in MeCN (10 mL, 1 M), and aqueous NH_4OH (28–30%, 20 mL, 200% volume of MeCN). The tube was sealed with Kontes valve to prevent loss of gaseous ammonia and stirred at 70 °C. Within 1 hour, the yellow solid of the 3-hydroxyisoquinoline began to precipitate from the reaction solution. After stirring for 18 hours at 70 °C, the reaction was cooled to room temperature, then placed in a –20 °C freezer, and the yellow solid was collected via vacuum filtration. This yellow powder was then washed with cold MeCN and dried at high vacuum to provide 3-hydroxyisoquinoline intermediate (0.70 g, 4.39 mmol). If any starting material remains, the filtrate could be transferred to a flask and concentrated in vacuo to undergo a second condensation reaction.

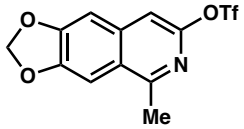
To a separate flame-dried RBF containing CH_2Cl_2 (22 mL, 0.2 M) and distilled pyridine (3.6 mL, 44 mmol), the collected yellow powder (0.70 g, 4.39 mmol) was added, and the resulting mixture was cooled to 0 °C. Trifluoromethanesulfonic anhydride (1.5 mL, 8.8 mmol) was then added dropwise at 0 °C, and the reaction was stirred at 0 °C for 1 hour. The reaction was then quenched with saturated aqueous $NaHCO_3$ at 0 °C, and then slowly warmed to room temperature. The reaction was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography (10% EtOAc in hexanes) to afford **5a** as a pale yellow oil (1.11 g, 38% yield over 3 steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 8.5, 1.0 Hz, 1H), 7.88 (dt, J = 8.3, 1.0 Hz, 1H), 7.76 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H), 7.67 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 7.42 (s, 1H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 151.3, 138.6, 131.5, 128.1, 127.8, 127.6, 126.1, 118.9 (q, J = 320.5 Hz), 109.0, 22.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ –73.0 IR (Neat Film, NaCl) 1624, 1600, 1563, 1422, 1327, 1213, 1138, 1116, 987, 958, 891, 832, 742, 616 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{11}H_9F_3NO_3S$ $[M+H]^+$: 292.0250, found 292.0253.



5b

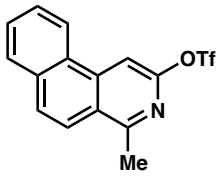
7-fluoro-1-methylisoquinolin-3-yl trifluoromethanesulfonate (5b): Compound **5b** was prepared from ester **4b** using general procedure 2 and purified by column chromatography (10% EtOAc in hexanes) to provide a pale brown oil (384 mg, 31% yield over 3 steps): ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.90 (dd, *J* = 9.0, 5.3 Hz, 1H), 7.76 (dd, *J* = 9.6, 2.5 Hz, 1H), 7.56 (ddd, *J* = 8.9, 8.0, 2.5 Hz, 1H), 7.43 (s, 1H), 2.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, *J* = 251.1 Hz), 159.4 (d, *J* = 6.1 Hz), 151.1 (d, *J* = 3.3 Hz), 135.5, 130.3 (d, *J* = 8.7 Hz), 128.5 (d, *J* = 8.3 Hz), 122.2 (d, *J* = 25.6 Hz), 118.9 (q, *J* = 320.5 Hz), 109.8 (d, *J* = 21.8 Hz), 108.9, 22.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ –73.0, –109.0 (ddd, *J* = 9.5, 8.0, 5.4 Hz); IR (Neat Film, NaCl) 1598, 1573, 1516, 1416, 1209, 1136, 1114, 986, 960, 933, 875, 805, 764 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{11}H_8F_4NO_3S$ $[M+H]^+$: 310.0156, found 310.0149.



5c

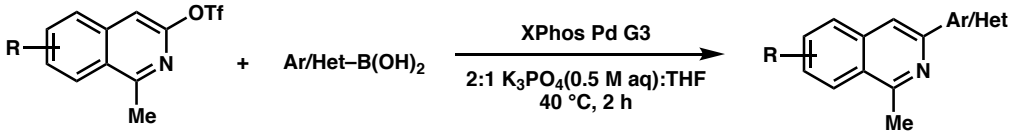
5-methyl-[1,3]dioxolo[4,5-*g*]isoquinolin-7-yl trifluoromethanesulfonate (5c): Compound **5c** was prepared from ester **4c** using general procedure 2 and purified by column chromatography (10 to 20% EtOAc in hexanes) to provide a white solid (608 mg, 58% yield over 3 steps): ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.23 (s, 1H), 7.10 (s, 1H), 6.15 (s, 2H), 2.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 151.9, 150.9, 149.2, 137.3, 124.8, 118.8 (q, *J* = 321.2 Hz), 108.4, 103.3, 102.2, 101.8, 22.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –73.0; IR (Neat Film, NaCl) 2918, 1584, 1504, 1464, 1416, 1223, 1134, 1038, 964, 940, 873, 840 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{12}H_9F_3NO_5S$ $[M+H]^+$: 336.0148, found 336.0146.



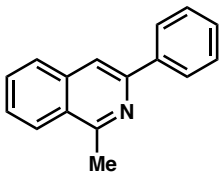
5d

4-methylbenzo[*f*]isoquinolin-2-yl trifluoromethanesulfonate (5d): Compound **5d** was prepared from ester **4d** using general procedure 2 and purified by column chromatography (5 to 10% EtOAc in hexanes) to provide a white solid (497 mg, 65% yield over 3 steps): ^1H NMR (400 MHz, $CDCl_3$) δ 8.63 – 8.57 (m, 1H), 8.15 (s, 1H), 8.01 – 7.95 (m, 2H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.81 – 7.73 (m, 2H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 152.5, 138.6, 133.3, 129.6, 129.1, 128.9, 128.6, 127.8, 125.8, 123.6, 122.2, 118.8 (q, *J* = 321.2 Hz), 105.1, 22.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ –78.3; IR (Neat Film, NaCl) 1588, 1416, 1377, 1207, 1180, 1138, 972, 878, 846, 817, 754 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{15}H_{11}F_3NO_3S$ $[M+H]^+$: 342.0406, found 342.0399.

General procedure 3: Suzuki cross-coupling

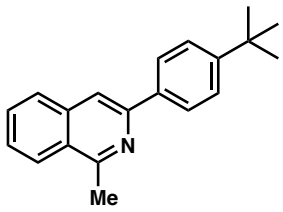


5a–d ***6a–q, S1a–f***



6a

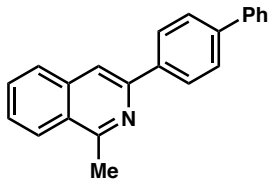
1-methyl-3-phenylisoquinoline (6a): This procedure has been adapted from a previous report.[4] To a flame-dried 20-mL scintillation vial capped with a PTFE-lined septum was added XPhos Pd G3 (11.63 mg, 0.014 mmol) and phenyl boronic acid (126 mg, 1.03 mmol). The reaction vial was then evacuated and backfilled with N_2 three times. The isoquinoline triflate **5a** (200 mg, 0.687 mmol) in degassed THF (2 mL, 0.3 M) was then added to the vial, followed by degassed 0.5 M K_3PO_4 solution (4 mL, 0.2 M). The reaction was then stirred at 40 °C for 2 hours. Afterwards, the reaction was diluted with water and the aqueous layer was extracted with Et_2O. The combined organic phases were dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography (5% EtOAc in hexanes) to afford **6a** as a white solid (138 mg, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.13 (m, 3H), 7.93 (s, 1H), 7.86 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.67 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.42 – 7.38 (m, 1H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 150.2, 140.0, 136.9, 130.2, 128.9, 128.4, 127.8, 127.1, 126.9, 126.7, 125.8, 115.4, 22.9; IR (Neat Film, NaCl) 3060, 1621, 1589, 1571, 1501, 1440, 1390, 1332, 1030, 902, 880, 786, 765, 692 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{14}N$ $[M+H]^+$: 220.1121, found 220.1129.



6b

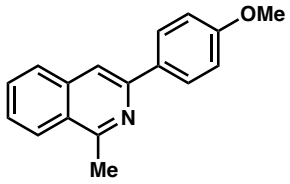
3-(4-(*tert*-butyl)phenyl)-1-methylisoquinoline (6b): Compound **6b** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a pale yellow oil (177 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 1H) 8.06 (d, *J* = 8.5 Hz, 2H), 7.90 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.66 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.57 – 7.52 (m, 3H), 3.04 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 151.5, 150.3, 137.3, 136.9, 130.1, 127.7, 126.8, 126.7, 126.6, 125.8, 125.8, 115.0, 34.8,

31.5, 22.8; IR (Neat Film, NaCl) 2961, 1622, 1591, 1568, 1515, 1442, 1390, 1362, 1333, 1268, 1112, 1017, 837, 754, 743, 685 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}N$ $[M+H]^+$: 276.1747, found 276.1749.



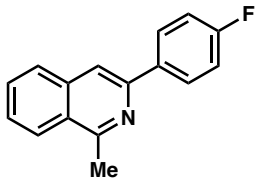
6c

3-([1,1'-biphenyl]-4-yl)-1-methylisoquinoline (6c): Compound **6c** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a colorless solid (191 mg, 94% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.22 (m, 2H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.98 (s, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.73 (m, 2H), 7.70 – 7.67 (m, 3H), 7.58 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.39 – 7.37 (m, 1H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 149.7, 141.2, 141.0, 138.9, 136.9, 130.2, 128.9, 127.8, 127.6, 127.5, 127.5, 127.2, 126.9, 126.8, 125.8, 115.2, 22.9; IR (Neat Film, NaCl) 3028, 1621, 1568, 1488, 1440, 1389, 1334, 842, 766, 730, 696 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{22}H_{18}N$ $[M+H]^+$: 296.1434, found 296.1426.



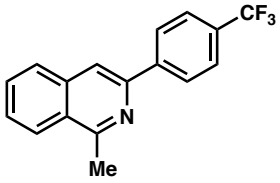
6d

3-(4-methoxyphenyl)-1-methylisoquinoline (6d): Compound **6d** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to afford a white solid (79 mg, 93% yield): ^1H NMR (400 MHz, $CDCl_3$) ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.07 (m, 3H), 7.84 (s, 1H), 7.81 (d, *J* = 8.5, 1H), 7.64 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.53 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.06 – 7.01 (m, 2H), 3.88 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 158.4, 149.8, 136.9, 132.6, 130.0, 128.2, 127.5, 126.4, 126.3, 125.7, 114.1, 114.1, 55.4, 22.7; IR (Neat Film, NaCl) 3060, 2955, 2835, 1608, 1568, 1514, 1439, 1390, 1290, 1249, 1174, 1034, 833, 751, 730 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}NO$ $[M+H]^+$: 250.1226, found 250.1220.



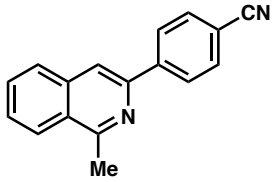
6e

3-(4-fluorophenyl)-1-methylisoquinoline (6e): Compound **6e** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (155 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.07 (m, 3H), 7.89 – 7.81 (m, 2H), 7.68 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.20 – 7.16 (m, 2H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, *J* = 247.3 Hz), 162.1, 158.8, 149.1, 136.9, 136.0 (d, *J* = 3.3 Hz), 130.3, 128.8 (d, *J* = 8.2 Hz), 127.7, 127.0, 126.6, 125.8, 115.8, 115.6, 115.1, 22.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –114.2; IR (Neat Film, NaCl) 1605, 1570, 1510, 1440, 1390, 1332, 1231, 1156, 836, 749, 723 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}FN$ $[M+H]^+$: 238.1027, found 238.1030.



6f

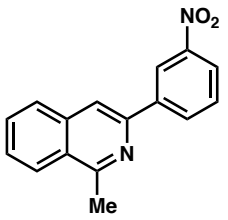
1-methyl-3-(4-(trifluoromethyl)phenyl)isoquinoline (6f): Compound **6f** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (2% to 3% EtOAc in hexanes) to afford a white solid (89 mg, 91% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.1 Hz, 2H), 8.15 (d, *J* = 8.4, 1H), 7.96 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.73 (m, 2H), 7.73 – 7.67 (m, 1H), 7.63 – 7.59 (m, 1H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.5, 143.3, 136.7, 130.4, 130.2 (q, *J* = 32.5 Hz), 127.9, 127.5, 127.3, 127.1, 125.8, 125.7 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 271.9 Hz), 116.1, 22.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.4; IR (Neat Film, NaCl) 3070, 2357, 1622, 1573, 1418, 1390, 1324, 1162, 1122, 1066, 1015, 842, 754, 742, 682 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{13}F_3N$ $[M+H]^+$: 288.0995, found 288.0988.



6g

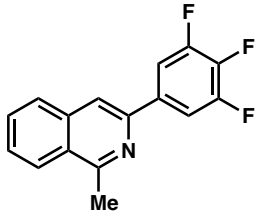
4-(1-methylisoquinolin-3-yl)benzonitrile (6g): Compound **6g** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (10% to 20% EtOAc in hexanes) to provide a white solid (144 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 –

8.22 (m, 2H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.89 (d, *J* = 8.3, 1H), 7.82 – 7.75 (m, 2H), 7.73 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.64 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 147.6, 144.0, 136.6, 132.7, 130.7, 128.0, 127.9, 127.6, 127.3, 125.9, 119.3, 116.6, 111.8, 22.8; IR (Neat Film, NaCl) 2224, 1618, 1570, 1508, 1441, 1390, 1334, 878, 844, 748, 731 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{13}N_2$ $[M+H]^+$: 245.1073, found 245.1070.



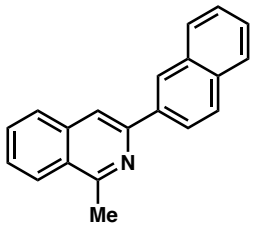
6h

1-methyl-3-(3-nitrophenyl)isoquinoline (6h): Compound **6h** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (139 mg, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (t, *J* = 2.0 Hz, 1H), 8.51 (ddd, *J* = 7.8, 1.8, 1.1 Hz, 1H), 8.24 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.0 Hz, 1H), 8.01 (s, 1H), 7.90 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.72 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.72 – 7.59 (m, 2H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 149.0, 147.3, 141.7, 136.6, 132.8, 130.6, 129.7, 127.9, 127.8, 127.2, 125.9, 123.0, 121.9, 116.0, 22.8; IR (Neat Film, NaCl) 1619, 1568, 1524, 1442, 1390, 1350, 880, 806, 749, 692 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}N_2O_2$ $[M+H]^+$: 265.0972, found 265.0974.



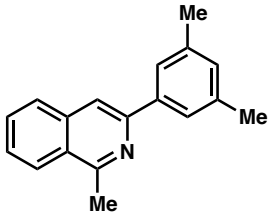
6i

1-methyl-3-(3,4,5-trifluorophenyl)isoquinoline (6i): Compound **6i** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to afford a white solid (103 mg, 87% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4, 1H), 7.86 – 7.78 (m, 4H), 7.72 – 7.68 (m, 1H), 7.65 – 7.58 (m, 1H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 151.6 (ddd, *J* = 248.4, 10.1, 4.1 Hz), 146.5, 140.0 (dt, *J* = 252.6, 15.7 Hz), 136.6, 136.0 (td, *J* = 7.5, 4.5 Hz), 130.6, 127.8, 127.7, 127.1, 125.8, 115.4, 110.9 – 110.7 (m), 22.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ –134.4 (dd, *J* = 20.5, 9.2 Hz), –161.1 – –161.3 (m); IR (Neat Film, NaCl) 1619, 1570, 1526, 1446, 1392, 1352, 1237, 1034, 879, 847, 753 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{11}F_3N$ $[M+H]^+$: 274.0838, found 274.0841.



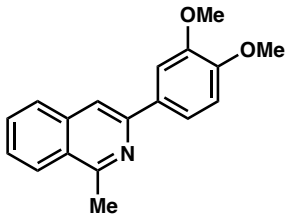
6j

1-methyl-3-(naphthalen-2-yl)isoquinoline (6j): Compound **6j** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (159 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.27 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.16 (dq, *J* = 8.3, 1.0 Hz, 1H), 8.07 (s, 1H), 8.00 – 7.96 (m, 2H), 7.91 – 7.86 (m, 2H), 7.70 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.56 – 7.46 (m, 2H), 3.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 149.9, 137.2, 137.0, 133.9, 133.5, 130.2, 128.9, 128.5, 127.8, 127.8, 127.0, 126.8, 126.3, 126.3, 125.8, 124.9, 115.7, 22.9; IR (Neat Film, NaCl) 3059, 1621, 1585, 1567, 1508, 1439, 1390, 879, 848, 816, 744 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{16}N$ $[M+H]^+$: 270.1277, found 270.1270.



6k

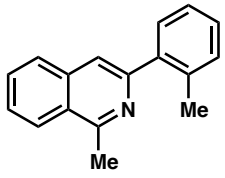
3-(3,5-dimethylphenyl)-1-methylisoquinoline (6k): Compound **6k** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography to provide a white solid (156 mg, 92% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.90 (s, 1H), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.75 (s, 2H), 7.66 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.05 (s, 1H), 3.05 (s, 3H), 2.43 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 150.5, 139.9, 138.3, 136.9, 130.2, 130.1, 127.7, 126.8, 126.7, 125.8, 125.0, 115.4, 22.8, 21.7; IR (Neat Film, NaCl) 2919, 2358, 1622, 1582, 1568, 1443, 1391, 1335, 874, 846, 786, 750, 711 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{18}N$ $[M+H]^+$: 248.1434, found 248.1434.



6l

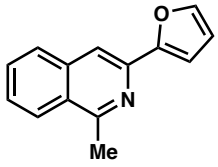
3-(3,4-dimethoxyphenyl)-1-methylisoquinoline (6l): Compound **6l** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (20% EtOAc in hexanes)

to provide a white solid (195 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4, 1H), 7.89 – 7.81 (m, 2H), 7.77 (d, *J* = 2.1 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.55 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 4.04 (s, 3H), 3.95 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 149.8, 149.6, 149.3, 137.0, 132.9, 130.2, 127.6, 126.7, 126.5, 125.8, 119.5, 114.5, 111.4, 110.3, 56.1, 22.8; IR (Neat Film, NaCl) 2936, 2833, 1568, 1516, 1454, 1436, 1317, 1259, 1236, 1170, 1026, 874, 817, 751 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{18}NO_2$ $[M+H]^+$: 280.1332, found 280.1337.



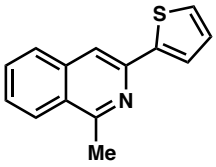
6m

1-methyl-3-(*o*-tolyl)isoquinoline (6m): Compound **6m** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (153 mg, 96% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.4, 1H), 7.84 (d, *J* = 8.3, 1H), 7.70 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.53 – 7.45 (m, 1H), 7.32 – 7.30 (m, 3H), 3.04 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 152.7, 140.9, 136.5, 136.3, 130.9, 130.1, 130.1, 128.1, 127.5, 127.0, 126.2, 126.0, 125.7, 118.9, 22.6, 20.6; IR (Neat Film, NaCl) 3053, 2950, 2920, 2355, 1622, 1584, 1567, 1498, 1446, 1392, 1360, 1330, 1144, 1033, 969, 906, 884, 763, 752, 726 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}N$ $[M+H]^+$: 234.1277, found 234.1286.



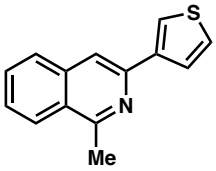
6n

3-(furan-2-yl)-1-methylisoquinoline (6n): Compound **6n** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (106 mg, 99% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.80 (dd, *J* = 8.4 Hz, 1H), 7.67 – 7.59 (m, 1H), 7.57 – 7.49 (m, 2H), 7.13 (dd, *J* = 3.4, 0.8 Hz, 1H), 6.56 (dd, *J* = 3.4, 1.8 Hz, 1H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 154.4, 142.9, 142.3, 136.5, 130.2, 127.6, 126.7, 126.6, 125.8, 113.0, 112.0, 108.1, 22.6; IR (Neat Film, NaCl) 3067, 1622, 1568, 1488, 1447, 1390, 1325, 1288, 1216, 1157, 1007, 970, 883, 814, 736 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NO$ $[M+H]^+$: 210.0913, found 210.0910.



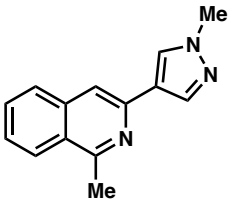
6o

1-methyl-3-(thiophen-2-yl)isoquinoline (6o): Compound **6o** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (3% EtOAc in hexanes) to provide a white solid (103 mg, 92% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dt, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 7.79 (dd, *J* = 8.2 Hz, 1H), 7.69 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.64 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.52 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.38 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.14 (dd, *J* = 5.0, 3.6 Hz, 1H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 145.5, 145.4, 136.6, 130.2, 128.1, 127.4, 126.7, 126.6, 125.8, 123.8, 113.1, 22.5; IR (Neat Film, NaCl) 3068, 1620, 1586, 1568, 1446, 1387, 1330, 1238, 1194, 1036, 876, 820, 748, 704 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NS$ $[M+H]^+$: 226.0685, found 226.0680.



6p

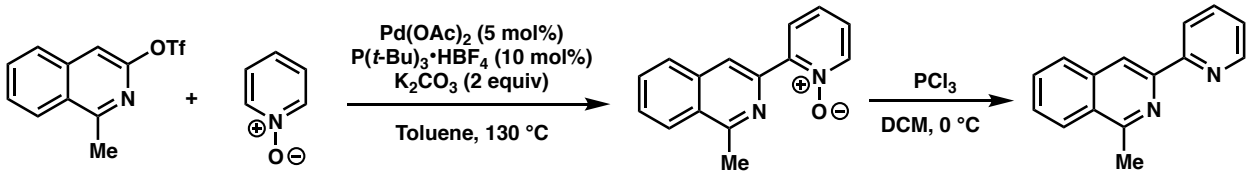
1-methyl-3-(thiophen-3-yl)isoquinoline (6p): Compound **6p** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (148 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 8.4, 1.0 Hz, 1H), 8.04 (dd, *J* = 3.1, 1.3 Hz, 1H), 7.81 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.79 (s, 1H), 7.73 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.65 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.54 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.42 (dd, *J* = 5.0, 3.1 Hz, 1H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 146.4, 142.7, 136.9, 130.2, 127.6, 126.7, 126.6, 126.3, 126.2, 125.8, 123.2, 114.7, 22.8; IR (Neat Film, NaCl) 3056, 2920, 1622, 1591, 1568, 1496, 1446, 1388, 1317, 874, 842, 795, 749, 696 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NS$ $[M+H]^+$: 226.0685, found 226.0687.



6q

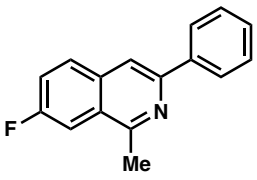
1-methyl-3-(1-methyl-1*H*-pyrazol-4-yl)isoquinoline (6q): Compound **6q** was prepared from triflate **5a** using general procedure 3 and purified by column chromatography (50% to 60% EtOAc in hexanes) to provide a white solid (112 mg, 99% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H), 8.04 – 8.00 (m, 2H), 7.77 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.67 – 7.60 (m, 2H),

7.54 – 7.47 (m, 1H), 3.98 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 137.4, 136.8, 130.1, 128.9, 127.1, 126.2, 126.1, 125.7, 113.3, 39.1, 22.6; IR (Neat Film, NaCl) 2940, 2351, 1620, 1601, 1568, 1556, 1493, 1416, 1182, 983, 840, 750, 702 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{14}N_3$ $[M+H]^+$: 224.1182, found 224.1176.



5a ***6r***

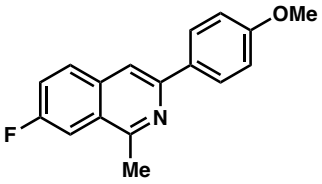
1-methyl-3-(pyridin-2-yl)isoquinoline (6r): Compound **6r** was prepared from triflate **5a** using a procedure adapted from a previous report.[5] To a microwave vial was added flame-dried K_2CO_3 (142 mg, 1.03 mmol), $Pd(OAc)_2$ (5.8 mg, 0.026 mmol), P(*t*-Bu)$_3$•HBF_4 (15 mg, 0.052 mmol), and the *N*-oxide (147 mg, 1.55 mmol). The vial was then evacuated and backfilled with argon three times. A solution of **5a** (150 mg, 0.52 mmol) in toluene (2 mL, 0.3 M) was then added, and the reaction was stirred at 130 °C overnight. The reaction was then cooled to room temperature, filtered through celite, and dissolved in CH_2Cl_2 (10 mL, 0.05 M). The reaction flask was then cooled to 0 °C and PCl_3 (0.27 mL, 3.1 mmol) was added dropwise, then the reaction stirred for 30 minutes at 0 °C. The reaction was then quenched with saturated aqueous K_2CO_3, extracted with EtOAc, and dried over Na_2SO_4. The crude product was purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid (56 mg, 50% yield over 2 steps); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.62 (s, 1H), 8.56 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.95 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.84 (td, *J* = 7.7, 1.8 Hz, 1H), 7.68 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.29 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 3.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 156.9, 149.4, 148.7, 137.1, 136.9, 130.2, 128.6, 127.7, 127.5, 125.8, 123.3, 121.4, 116.5, 22.9; IR (Neat Film, NaCl) 3053, 3004, 2916, 1621, 1580, 1568, 1474, 1443, 1426, 1391, 1335, 1142, 891, 796, 742, 681, 624 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{15}H_{13}N_2$ $[M+H]^+$: 221.1073, found 221.1076.



S1a

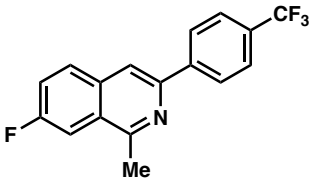
7-fluoro-1-methyl-3-phenylisoquinoline (S1a): Compound **S1a** was prepared from triflate **5b** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (110 mg, 93% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.11 (m, 2H), 7.90 (s, 1H), 7.85 (dd, *J* = 9.2, 5.7 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.54 – 7.48 (m, 2H), 7.48 – 7.38 (m, 2H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (d, *J* = 248.3 Hz), 158.0 (d, *J* = 5.8

Hz), 149.8 (d, *J* = 2.8 Hz), 139.7, 133.9, 130.3 (d, *J* = 8.5 Hz), 128.9, 128.5, 127.3 (d, *J* = 7.8 Hz), 127.0, 120.6 (d, *J* = 25.3 Hz), 114.9 (d, *J* = 1.7 Hz), 109.4 (d, *J* = 21.0 Hz), 22.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –109.7 – –111.8 (m); IR (Neat Film, NaCl) 3031, 2358, 1576, 1506, 1446, 1393, 1372, 1313, 1230, 1183, 1028, 972, 922, 904, 881, 822, 777, 764, 704 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}FN$ $[M+H]^+$: 238.1027, found 238.1027.



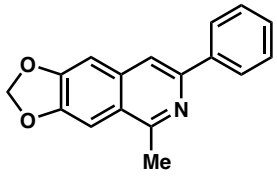
S1b

7-fluoro-3-(4-methoxyphenyl)-1-methylisoquinoline (S1b): Compound **S1b** was prepared from triflate **5b** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (110 mg, 99% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 2H), 7.87 – 7.81 (m, 2H), 7.70 (dd, *J* = 9.9, 2.6 Hz, 1H), 7.44 (ddd, *J* = 9.0, 8.3, 2.5 Hz, 1H), 7.06 – 6.99 (m, 2H), 3.88 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4 (d, *J* = 248.5 Hz), 160.1, 157.7 (d, *J* = 5.7 Hz), 149.4 (d, *J* = 2.8 Hz), 133.9, 132.2, 130.0 (d, *J* = 8.5 Hz), 128.1, 126.7 (d, *J* = 7.7 Hz), 120.5 (d, *J* = 25.3 Hz), 114.2, 113.7 (d, *J* = 1.8 Hz), 109.3 (d, *J* = 20.9 Hz), 55.4, 22.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ –111.9 (ddd, *J* = 9.3, 9.1, 5.7 Hz); IR (Neat Film, NaCl) 1608, 1514, 1443, 1393, 1288, 1252, 1186, 1029, 878, 863, 836, 821 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{15}FNO$ $[M+H]^+$: 268.1132, found 268.1133.



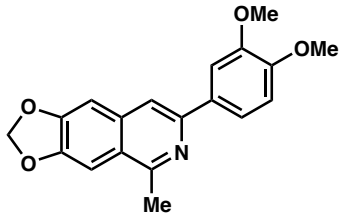
S1c

7-fluoro-1-methyl-3-(4-(trifluoromethyl)phenyl)isoquinoline (S1c): Compound **S1c** was prepared from triflate **5b** using general procedure 3 and purified by column chromatography (5% EtOAc in hexanes) to provide a white solid (150 mg, 98% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.0 Hz, 2H), 7.94 (s, 1H), 7.90 – 7.85 (m, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.71 – 7.69 (m, 1H), 7.53 – 7.43 (m, 1H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1 (d, *J* = 249.4 Hz), 158.4 (d, *J* = 6.2 Hz), 148.1, 143.0, 133.7, 130.4 (d, *J* = 8.5 Hz), 130.2 (q, *J* = 32.4 Hz), 127.8 (d, *J* = 8.1 Hz), 127.2, 125.8 (q, *J* = 3.8 Hz), 124.5 (q, *J* = 272.7 Hz), 120.9 (d, *J* = 24.9 Hz), 115.6, 109.5 (d, *J* = 21.4 Hz), 22.8 ; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5, –110.2 (ddd, *J* = 9.9, 8.2, 5.5 Hz); IR (Neat Film, NaCl) 1592, 1418, 1393, 1330, 1157, 1126, 1107, 1067, 880, 868, 847, 816 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{12}NF_4$ $[M+H]^+$: 306.0900, found 306.0895.



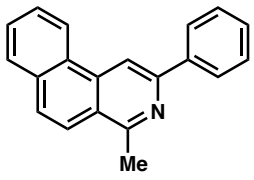
S1d

5-methyl-7-phenyl-[1,3]dioxolo[4,5-*g*]isoquinoline (S1d): Compound **S1d** was prepared from triflate **5c** using general procedure 3 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (153 mg, 97% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.2 Hz, 2H), 7.77 (s, 1H), 7.52 – 7.44 (m, 2H), 7.41 – 7.32 (m, 2H), 7.11 (s, 1H), 6.10 (s, 2H), 2.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 150.5, 149.5 148.1, 140.0, 135.1, 128.7, 128.1, 126.8, 123.5, 115.1, 103.4, 101.9, 101.6, 23.0; IR (Neat Film, NaCl) 2914, 1591, 1486, 1462, 1232, 1189, 1039, 945, 878, 846, 695, 684 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{14}NO_2$ $[M+H]^+$: 264.1019, found 264.1021.



S1e

7-(3,4-dimethoxyphenyl)-5-methyl-[1,3]dioxolo[4,5-*g*]isoquinoline (S1e): Compound **S1e** was prepared from triflate **5c** using general procedure 3 at 65 °C and purified by column chromatography via dry loading (40% EtOAc in hexanes) to provide a white solid (202 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 2.1 Hz, 1H), 7.69 (s, 1H), 7.60 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.34 (s, 1H), 7.09 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.09 (s, 2H), 4.02 (s, 3H), 3.94 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 150.5, 149.3, 149.2, 147.9, 135.2, 134.3, 133.0, 123.2, 119.1, 114.3, 111.2, 110.0, 103.3, 101.8, 101.5, 56.0, 56.0, 23.0; IR (Neat Film, NaCl) 2935, 1591, 1517, 1462, 1267, 1230, 1165, 1143, 1024, 872, 731 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{18}NO_4$ $[M+H]^+$: 324.1230, found 324.1229.

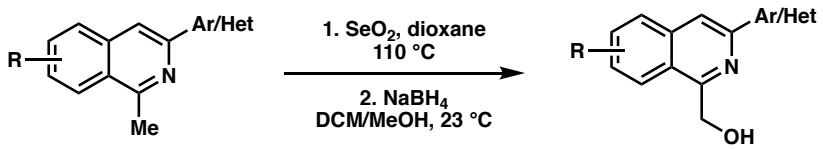


S1f

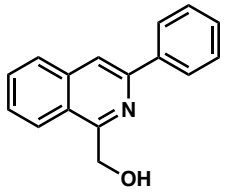
4-methyl-2-phenylbenzo[*f*]isoquinoline (S1f): Compound **S1f** was prepared from triflate **5d** using general procedure 3 and the product was collected via vacuum filtration to provide a white solid (246 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 – 8.40 (m, 2H), 7.96 – 7.88 (m, 2H), 7.73 (t, *J* = 8.7 Hz, 1H), 7.69 – 7.61 (m, 1H), 7.54 (t, *J* = 8.3 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.26 (td, *J* = 7.6, 1.7 Hz, 2H), 7.16 (td, *J* = 7.3, 1.7 Hz, 1H), 2.81 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 157.9, 152.0, 140.3, 135.6, 133.4, 129.3, 128.8, 128.7, 128.5, 128.4, 127.7, 127.2, 127.1, 124.4, 123.4, 122.9, 111.0, 23.1; IR (Neat Film, NaCl) 2342, 1574, 1506, 1483, 1444, 1386, 1242, 1028, 876, 824, 760, 725, 692 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{16}N$ $[M+H]^+$: 270.1277, found 270.1289.

General procedure 4: Oxidation and reduction to hydroxymethyl isoquinoline



6a–r, S1a–f ***7a–r, 9a–f***

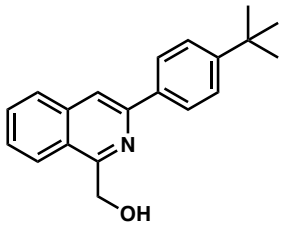


7a

(3-phenylisoquinolin-1-yl)methanol (7a): This procedure has been adapted from a previous report.[4] To a 20-mL microwave vial containing a stir bar was added SeO_2 (140 mg, 1.26 mmol), isoquinoline **6a** (138 mg, 0.63 mmol), and 1,4-dioxane (13 mL, 0.05 M). The reaction vial was then sealed and heated to 110 °C while stirring for 2 hours. The reaction was then cooled to room temperature, filtered through celite, and rinsed with EtOAc. The filtrate was then concentrated in vacuo to afford the aldehyde intermediate, which was used in the next step without further purification.

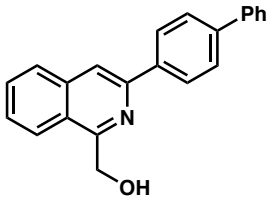
A scintillation vial containing the crude in 4:1 DCM:MeOH (0.1 M) was added sodium borohydride (24 mg, 0.63 mmol) at room temperature. The reaction was stirred until no starting material remained by TLC, and then quenched by the addition of citric acid monohydrate (132 mg, 0.63 mmol). The reaction was stirred for an additional 10 minutes then basified by the addition of saturated aqueous $NaHCO_3$. The layers were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (20% acetone in hexanes) to afford **7a** as a white solid (100 mg, 68% yield over 2 steps): ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.15 (d, *J* = 7.0 Hz, 2H), 8.03 (s, 1H), 7.94 – 7.92 (m, 2H), 7.73 (ddd, *J* = 8.3, 6.9, 1.1 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.46 – 7.42 (m, 1H), 5.31 (s, 2H), 5.26 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 148.7, 138.9, 137.1, 130.9, 129.0, 128.9, 128.0, 127.5, 127.0, 124.2, 123.3, 116.3, 61.6; IR (Neat Film, NaCl) 3378, 3060, 2867, 1624, 1574, 1502, 1461, 1443, 1370, 1331, 1304, 1088, 1072, 1024, 1009, 882, 782, 766,

693 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{14}NO$ $[M+H]^+$: 236.1070, found 236.1078.



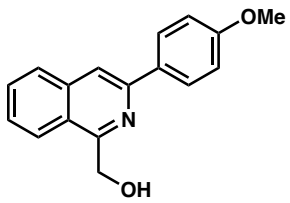
7b

((3-(4-(*tert*-butyl)phenyl)isoquinolin-1-yl)methanol (7b): Compound **7b** was prepared from isoquinoline **6b** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (162 mg, 95% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.06 (m, 2H), 8.00 (s, 1H), 7.97 – 7.85 (m, 2H), 7.72 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.58 – 7.52 (m, 2H), 5.30 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 152.1, 148.7, 137.1, 136.2, 130.8, 127.9, 127.3, 126.7, 125.9, 124.1, 123.3, 115.9, 61.5, 34.9, 31.5; IR (Neat Film, NaCl) 3385, 2958, 1626, 1574, 1514, 1446, 1416, 1360, 1333, 1265, 1088, 1014, 841, 744, 680 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1696, found 292.1696.



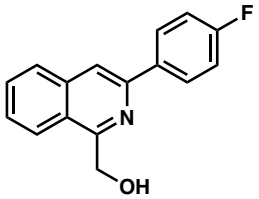
7c

(3-([1,1'-biphenyl]-4-yl)isoquinolin-1-yl)methanol (7c): Compound **7c** was prepared from isoquinoline **6c** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a colorless solid (181 mg, 92% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.20 (m, 2H), 8.07 (s, 1H), 7.98 – 7.88 (m, 2H), 7.81 – 7.66 (m, 5H), 7.62 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.49 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.43 – 7.34 (m, 1H), 5.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 148.3, 141.7, 140.7, 137.8, 137.1, 130.9, 129.0, 128.0, 127.7, 127.7, 127.6, 127.3, 127.2, 124.2, 123.3, 116.2, 61.6; IR (Neat Film, NaCl) 3382, 3060, 2359, 1623, 1574, 1488, 1445, 1412, 1374, 1334, 1088, 1006, 840, 766, 729, 697 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{22}H_{18}NO$ $[M+H]^+$: 312.1382, found 312.1383.



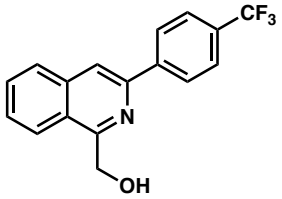
7d

(3-(4-methoxyphenyl)isoquinolin-1-yl)methanol (7d): Compound **7d** was prepared from isoquinoline **6d** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (48 mg, 73% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.07 (m, 2H), 7.93 (s, 1H), 7.91 – 7.85 (m, 2H), 7.69 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.06 – 7.03 (m, 2H), 5.28 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 157.0, 148.3, 137.1, 131.4, 130.7, 128.1, 127.7, 127.0, 123.7, 123.1, 115.0, 114.2, 61.4, 55.4; IR (Neat Film, NaCl) 3376, 2928, 2836, 1608, 1573, 1515, 1442, 1372, 1334, 1287, 1250, 1175, 1087, 1032, 1010, 832, 750, 730 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}NO_2$ $[M+H]^+$: 266.1176, found 266.1185.



7e

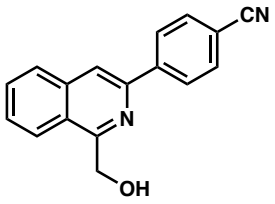
(3-(4-fluorophenyl)isoquinolin-1-yl)methanol (7e): Compound **7e** was prepared from isoquinoline **6e** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a colorless solid (149 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.96 (s, 1H), 7.95 – 7.89 (m, 2H), 7.73 (ddd, *J* = 8.3, 6.9, 1.1 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.21 (dd, *J* = 8.9, 8.5 Hz, 2H), 5.30 (s, 2H), 5.17 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, *J* = 248.3 Hz), 157.5, 147.8, 137.0, 135.1 (d, *J* = 3.2 Hz), 131.0, 128.7 (d, *J* = 8.2 Hz), 127.9, 127.6, 124.1, 123.3, 116.0, 115.8, 61.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ –113.3 – –113.4 (m); IR (Neat Film, NaCl) 3382, 3059, 2354, 1622, 1604, 1574, 1512, 1446, 1331, 1230, 1157, 1087, 1011, 837, 750, 725 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}FNO$ $[M+H]^+$: 254.0974, found 254.0976.



7f

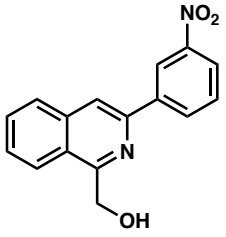
(3-(4-(trifluoromethyl)phenyl)isoquinolin-1-yl)methanol (7f): Compound **7f** was prepared from isoquinoline **6f** using general procedure 4 and purified by column chromatography (10% to 20% EtOAc in hexanes) to provide a white solid (23 mg, 25% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.8 Hz, 2H), 8.07 (s, 1H), 8.00 – 7.92 (m, 2H), 7.82 – 7.73 (m, 3H), 7.70 – 7.61 (m, 1H), 5.32 (s, 2H), 5.10 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 147.1, 142.3, 136.8, 131.2, 130.7 (q, *J* = 32.5 Hz), 128.2, 128.1, 127.2, 125.9 (q, *J* = 3.8 Hz), 124.6, 124.4 (q, *J* = 273.7 Hz), 123.4, 117.2, 61.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5; IR (Neat Film,

NaCl) 3408, 1623, 1574, 1418, 1324, 1166, 1111, 1075, 1014, 842, 753, 682 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{13}F_3NO$ $[M+H]^+$: 304.0944, found 304.0934.



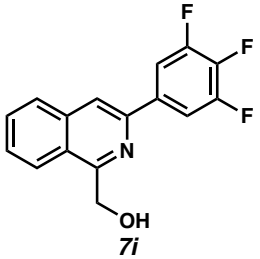
7g

4-(1-(hydroxymethyl)isoquinolin-3-yl)benzonitrile (7g): Compound **7g** was prepared from isoquinoline **6g** using general procedure 4 and purified by column chromatography (30% EtOAc in hexanes) to provide a white solid (138 mg, 92% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.18 (m, 2H), 8.09 (s, 1H), 7.97 (m, 2H), 7.86 – 7.74 (m, 3H), 7.68 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 5.32 (s, 2H), 4.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 146.5, 143.2, 136.7, 132.8, 131.4, 128.5, 128.2, 127.4, 124.7, 123.5, 119.0, 117.7, 112.3, 61.7; IR (Neat Film, NaCl) 3404, 2895, 2358, 2224, 1416, 1332, 1303, 1085, 1006, 840, 764, 682 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{13}N_2O$ $[M+H]^+$: 261.1022, found 261.1032.



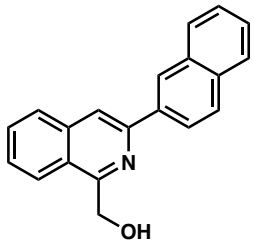
7h

(3-(3-nitrophenyl)isoquinolin-1-yl)methanol (7h): Compound **7h** was prepared from isoquinoline **6h** using general procedure 4 and purified by column chromatography (20% EtOAc in CH_2Cl_2) to provide a white solid (67 mg, 38% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (t, *J* = 2.0 Hz, 1H), 8.52 (dt, *J* = 7.9, 1.3 Hz, 1H), 8.27 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 8.11 (s, 1H), 8.04 – 7.90 (m, 2H), 7.78 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H), 7.73 – 7.60 (m, 2H), 5.33 (s, 2H), 4.96 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 149.0, 146.1, 140.7, 136.8, 132.7, 131.4, 129.9, 128.4, 128.2, 124.7, 123.5, 123.4, 121.6, 117.2, 61.7; IR (Neat Film, NaCl) 3389, 2614, 1538, 1520, 1505, 1353, 1333, 1088, 1007, 892, 751, 690 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}N_2O_3$ $[M+H]^+$: 281.0921, found 281.0930.



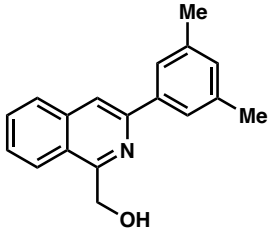
7i

(3-(3,4,5-trifluorophenyl)isoquinolin-1-yl)methanol (7i): Compound **7i** was prepared from isoquinoline **6i** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (90 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.89 (m, 3H), 7.84 – 7.71 (m, 3H), 7.65 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 5.30 (s, 2H), 4.89 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 151.7 (ddd, *J* = 249.3, 10.2, 4.1 Hz), 145.4 (d, *J* = 2.5 Hz), 140.2 (dt, *J* = 253.9, 15.7 Hz), 136.7, 135.1 (td, *J* = 7.6, 4.5 Hz), 131.4, 128.3, 128.0, 124.5, 123.4, 116.6 (d, *J* = 1.4 Hz), 110.9 – 110.7 (m), 61.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ –133.8 – –133.9 (m), –160.1 – –160.3 (m); IR (Neat Film, NaCl) 3351, 2882, 1557, 1531, 1451, 1350, 1326, 1080, 1039, 1008, 864, 848, 778, 747, 706 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{11}F_3NO$ $[M+H]^+$: 290.0787, found 290.0795.



7j

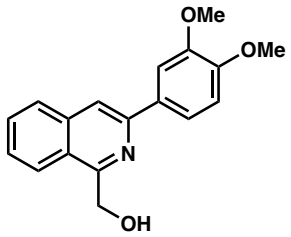
(3-(naphthalen-2-yl)isoquinolin-1-yl)methanol (7j): Compound **7j** was prepared from isoquinoline **6j** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (158 mg, 97% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.27 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.16 (s, 1H), 8.05 – 7.93 (m, 4H), 7.91 – 7.89 (m, 1H), 7.75 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.62 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.58 – 7.47 (m, 2H), 5.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 148.5, 137.1, 136.2, 133.7, 133.7, 130.9, 128.8, 128.6, 128.0, 127.8, 127.6, 126.7, 126.6, 126.3, 124.6, 124.2, 123.3, 116.6, 61.6; IR (Neat Film, NaCl) 3393, 3056, 1622, 1573, 1506, 1445, 1410, 1375, 1344, 1314, 1086, 1008, 856, 817, 744 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{16}NO$ $[M+H]^+$: 286.1231, found 286.1226.



7k

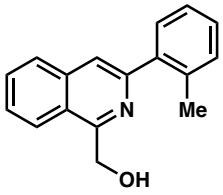
(3-(3,5-dimethylphenyl)isoquinolin-1-yl)methanol (7k): Compound **7k** was prepared from isoquinoline **6k** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (155 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.94 – 7.91 (m, 2H), 7.78 – 7.76 (m, 2H), 7.72 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.09 (s, 1H), 5.30 (s, 3H), 2.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 149.0, 138.9, 138.5, 137.1, 130.8, 130.6, 127.9, 127.4, 124.8, 124.1, 123.3, 116.3, 61.6, 21.7; IR (Neat Film, NaCl) 3382, 2913, 2338, 1622, 1574, 1503, 1444, 1379, 1332, 1084, 1011,

882, 849, 824, 750, 709 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{18}NO$ $[M+H]^+$: 264.1382, found 264.1383.



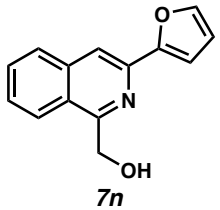
7l

(3-(3,4-dimethoxyphenyl)isoquinolin-1-yl)methanol (7l): Compound **7l** was prepared from isoquinoline **6l** using general procedure 4 and purified by column chromatography (40% EtOAc in hexanes) to provide a white solid (180 mg, 91% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.93 – 7.90 (m, 2H), 7.77 – 7.67 (m, 3H), 7.58 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.03 – 7.01 (m, 1H), 5.30 (s, 2H), 5.26 (br s, 1H, OH), 4.03 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 149.8, 149.3, 148.3, 137.0, 131.8, 130.7, 127.7, 127.1, 123.8, 123.2, 119.5, 115.3, 111.3, 110.0, 61.4, 56.1, 56.0; IR (Neat Film, NaCl) 3372, 2936, 2838, 1623, 1604, 1573, 1518, 1456, 1438, 1314, 1260, 1237, 1134, 1027, 1008 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{18}NO_3$ $[M+H]^+$: 296.1284, found 296.1283.



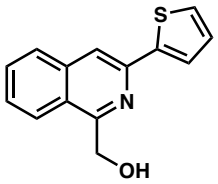
7m

(3-(*o*-tolyl)isoquinolin-1-yl)methanol (7m): Compound **7m** was prepared from isoquinoline **6m** using general procedure 4 and purified by column chromatography (15% EtOAc in hexanes) to provide a white solid (130 mg, 79% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.91 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.75 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.71 (s, 1H), 7.64 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.53 (d, *J* = 6.6 Hz, 1H), 7.39 – 7.29 (m, 3H), 5.30 (s, 2H), 5.14 (s, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 151.4, 140.1, 136.7, 136.5, 131.0, 130.8, 130.2, 128.4, 127.8, 127.6, 126.1, 123.7, 123.3, 120.0, 61.6, 20.9; IR (Neat Film, NaCl) 3389, 3057, 2932, 1626, 1573, 1502, 1455, 1402, 1377, 1330, 1087, 1069, 1008, 884, 786, 757, 727 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}NO$ $[M+H]^+$: 250.1226, found 250.1232.



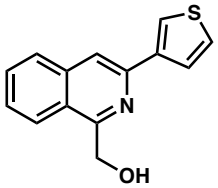
7n

(3-(furan-2-yl)isoquinolin-1-yl)methanol (7n): Compound **7n** was prepared from isoquinoline **6n** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (56 mg, 52% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.92 (m, 1H), 7.90 – 7.82 (m, 2H), 7.70 – 7.66 (m, 1H), 7.60 – 7.50 (m, 2H), 7.16 – 7.14 (m, 1H), 6.58 – 6.56 (m, 1H), 5.23 (s, 2H), 5.05 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 153.7, 143.1, 140.9, 136.6, 130.9, 127.8, 127.2, 124.0, 123.3, 113.6, 112.1, 108.6, 61.3; IR (Neat Film, NaCl) 3390, 3118, 2886, 1624, 1574, 1492, 1372, 1323, 1306, 1157, 1092, 1079, 1006, 884, 836, 743 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NO_2$ $[M+H]^+$: 226.0863, found 226.0871.



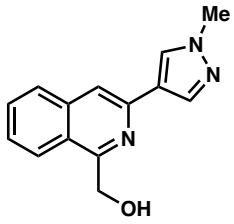
7o

(3-(thiophen-2-yl)isoquinolin-1-yl)methanol (7o): Compound **7o** was prepared from isoquinoline **6o** (0.5 mmol) using general procedure 4 and purified by column chromatography (10% to 20% EtOAc in hexanes) to provide a white solid (46 mg, 38% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.88 – 7.83 (m, 2H), 7.75 – 7.65 (m, 2H), 7.55 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.41 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.16 (dd, *J* = 5.0, 3.6 Hz, 1H), 5.25 (s, 2H), 5.02 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 144.4, 144.1, 136.8, 131.0, 128.2, 127.6, 127.2, 127.0, 124.1, 124.0, 123.3, 114.0, 61.3; IR (Neat Film, NaCl) 3382, 3066, 2868, 1621, 1589, 1573, 1501, 1452, 1402, 1329, 1084, 1006, 878, 822, 748, 701 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NOS$ $[M+H]^+$: 242.0634, found 242.0637.



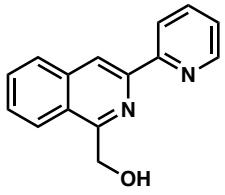
7p

(3-(thiophen-3-yl)isoquinolin-1-yl)methanol (7p): Compound **7p** was prepared from isoquinoline **6p** (0.58 mmol) using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (127 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 3.1, 1.3 Hz, 1H), 7.94 – 7.84 (m, 3H), 7.76 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.71 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.45 (dd, *J* = 5.1, 3.0 Hz, 1H), 5.27 (s, 2H), 5.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 145.0, 141.7, 137.0, 130.9, 127.8, 127.3, 126.6, 126.0, 124.1, 123.4, 123.4, 115.6, 61.5; IR (Neat Film, NaCl) 3372, 3098, 2888, 2363, 1622, 1594, 1573, 1456, 1350, 1318, 1299, 1086, 1008, 880, 842, 793, 748, 697 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{12}NOS$ $[M+H]^+$: 242.0634, found 242.0631.



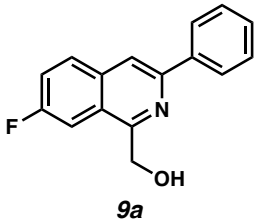
7q

(3-(1-methyl-1*H*-pyrazol-4-yl)isoquinolin-1-yl)methanol (7q): Compound **7q** was prepared from isoquinoline **6q** using general procedure 4 and purified by column chromatography (70% to 80% EtOAc in hexanes + 1% NEt_3) to provide a pale beige solid (72 mg, 62% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.95 (m, 2H), 7.85 – 7.79 (m, 2H), 7.71 – 7.59 (m, 2H), 7.53 – 7.49 (m, 1H), 5.21 (s, 2H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 143.2, 137.3, 136.9, 130.8, 128.8, 127.2, 126.7, 123.5, 123.2, 114.1 61.2, 39.2; IR (Neat Film, NaCl) 3370, 3068, 2937, 1626, 1603, 1573, 1503, 1416, 1321, 1278, 1186, 1092, 1011, 845, 753, 702 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{14}N_3O$ $[M+H]^+$: 240.1131, found 240.1123.



7r

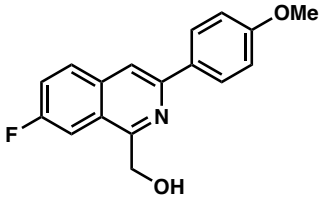
(3-(pyridin-2-yl)isoquinolin-1-yl)methanol (7r): Compound **7r** was prepared from isoquinoline **6r** using general procedure 4 and purified by column chromatography (10% to 20% acetone in CH_2Cl_2 + 1% NEt_3) to provide a pale cream solid (52 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 – 8.72 (m, 2H), 8.52 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.86 (td, *J* = 7.8, 1.8 Hz, 1H), 7.78 – 7.69 (m, 1H), 7.63 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.33 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 5.31 (s, 2H), 5.13 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 155.8, 149.5, 147.3, 137.2, 137.0, 130.9, 128.7, 128.1, 125.1, 123.6, 123.3, 121.1, 117.6, 61.6; IR (Neat Film, NaCl) 3390, 3048, 2359, 1622, 1583, 1474, 1428, 1333, 1309, 1166, 1087, 1009, 897, 793, 747, 681 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{15}H_{13}N_2O$ $[M+H]^+$: 237.1022, found 237.1020.



9a

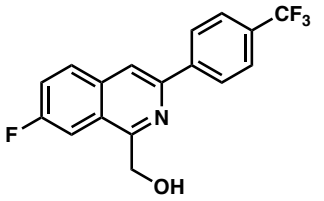
(7-fluoro-3-phenylisoquinolin-1-yl)methanol (9a): Compound **9a** was prepared from isoquinoline **S1a** using general procedure 4 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (94 mg, 81% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ

8.13 (d, *J* = 8.0 Hz, 2H), 8.00 (s, 1H), 7.96 – 7.87 (m, 1H), 7.57 – 7.47 (m, 4H), 7.44 (td, *J* = 6.9, 6.4, 1.4 Hz, 1H), 5.21 (s, 2H), 5.11 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (d, *J* = 250.3 Hz), 156.8 (d, *J* = 5.9 Hz), 148.4, 138.6, 134.1, 130.5 (d, *J* = 8.6 Hz), 129.0, 126.8, 124.7 (d, *J* = 8.5 Hz), 121.4 (d, *J* = 25.2 Hz), 115.9 (d, *J* = 2.0 Hz), 107.2 (d, *J* = 21.3 Hz), 61.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ –109.5 – –109.6 (m); IR (Neat Film, NaCl) 3393, 3063, 2878, 1594, 1579, 1506, 1417, 1392, 1321, 1232, 1185, 1085, 1015, 930, 777, 694 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{13}FNO$ $[M+H]^+$: 254.0976, found 254.0968.



9b

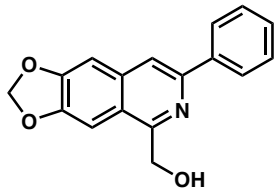
(7-fluoro-3-(4-methoxyphenyl)isoquinolin-1-yl)methanol (9b): Compound **9b** was prepared from isoquinoline **S1b** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (116 mg, 99% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.08 (m, 2H), 7.93 (s, 1H), 7.92 – 7.88 (m, 1H), 7.52 – 7.45 (m, 2H), 7.07 – 7.02 (m, 2H), 5.21 (s, 2H), 5.14 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8 (d, *J* = 249.0 Hz), 160.5, 156.6 (d, *J* = 5.9 Hz), 148.3 (d, *J* = 2.9 Hz), 134.3, 131.3, 130.4 (d, *J* = 8.6 Hz), 128.1, 124.3 (d, *J* = 8.2 Hz), 121.4 (d, *J* = 25.3 Hz), 114.8 (d, *J* = 1.7 Hz), 114.4, 107.2 (d, *J* = 21.3 Hz), 61.6, 55.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ –110.2 (ddd, *J* = 8.9, 8.8, 5.5 Hz); IR (Neat Film, NaCl) 3388, 2936, 1608, 1593, 1516, 1389, 1289, 1251, 1180, 1069, 1032, 1015, 929, 835 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{15}FNO_2$ $[M+H]^+$: 284.1081, found 284.1074.



9c

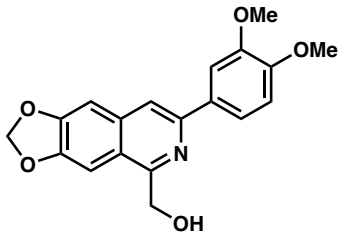
(7-fluoro-3-(4-(trifluoromethyl)phenyl)isoquinolin-1-yl)methanol (9c): Compound **9c** was prepared from isoquinoline **S1c** using general procedure 4 and purified by column chromatography (10% EtOAc in hexanes) to provide a white solid (80 mg, 60% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.1 Hz, 2H), 8.02 (s, 1H), 7.95 (dd, *J* = 9.8, 5.4 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.58 – 7.47 (m, 2H), 5.21 (s, 2H), 4.94 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3 (d, *J* = 251.5 Hz), 157.3 (d, *J* = 5.9 Hz), 146.8 (d, *J* = 2.9 Hz), 141.8 (d, *J* = 1.5 Hz), 133.8, 130.7 (d, *J* = 8.7 Hz), 130.7 (q, *J* = 33.3 Hz), 127.0, 125.9 (q, *J* = 3.8 Hz), 125.2 (d, *J* = 8.4 Hz), 124.3 (q, *J* = 272.7 Hz), 121.7 (d, *J* = 25.3 Hz), 116.8 (d, *J* = 1.7 Hz), 107.4 (d, *J* = 21.5 Hz), 61.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5, –108.4 (ddd, *J* = 8.7, 8.7, 5.4 Hz); IR (Neat Film, NaCl) 3410, 2886, 1619, 1597, 1504, 1416, 1391, 1328, 1233, 1165, 1124, 1111, 1074,

1016, 931, 847, 680 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{12}F_4NO$ $[M+H]^+$: 322.0850, found 322.0839.



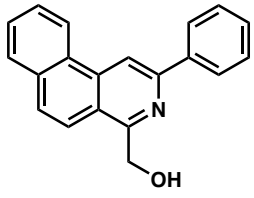
9d

(7-phenyl-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)methanol (9d): Compound **9d** was prepared from isoquinoline **S1d** using general procedure 4 and purified by column chromatography (30% to 40% EtOAc in hexanes) to provide a white solid (135 mg, 83% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.05 (m, 2H), 7.82 (s, 1H), 7.50 (m, 2H), 7.44 – 7.37 (m, 1H), 7.15 – 7.06 (m, 2H), 6.10 (s, 2H), 5.28 (br s, 1H, OH), 5.10 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 151.1, 148.6, 147.8, 138.9, 135.4, 128.8, 128.5, 126.6, 120.9, 115.9, 103.6, 101.9, 99.3, 61.4; IR (Neat Film, NaCl) 3324, 2914, 2355, 1597, 1497, 1463, 1436, 1422, 1236, 1066, 1036, 995, 940, 877, 775, 692 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{14}NO_3$ $[M+H]^+$: 280.0968, found 280.0975.



9e

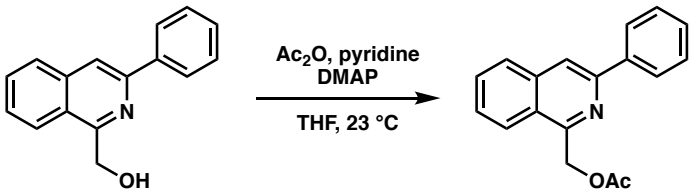
(7-(3,4-dimethoxyphenyl)-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)methanol (9e): Compound **9e** was prepared from isoquinoline **S1e** using general procedure 4 and purified by column chromatography (40% EtOAc in hexanes) via dry-loading to provide a pale pink solid (126 mg, 65% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.69 – 7.60 (m, 2H), 7.16 – 7.07 (m, 2H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.11 (s, 2H), 5.26 (br s, 1H, OH), 5.11 (s, 2H), 4.01 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 151.1, 149.7, 149.2, 148.4, 147.7, 135.5, 131.9, 120.6, 119.2, 115.1, 111.3, 109.7, 103.5, 101.8, 99.3, 61.4, 56.0, 56.0; IR (Neat Film, NaCl) 3378, 2912, 2353, 1595, 1519, 1496, 1463, 1456, 1435, 1258, 1234, 1034, 862, 730 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{18}NO_5$ $[M+H]^+$: 340.1179, found 340.1172.



9f

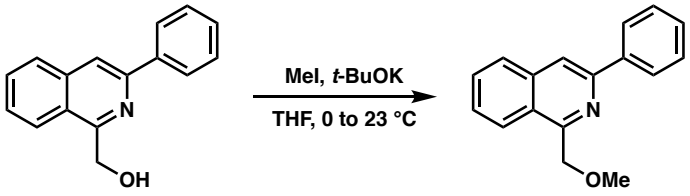
(2-phenylbenzo[*f*]isoquinolin-4-yl)methanol (9f): Compound **9f** was prepared from isoquinoline **S1f** using general procedure 4 and purified by column chromatography (20% EtOAc in hexanes) to provide a white solid (51 mg, 62% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 – 8.76 (m, 2H), 8.23 – 8.20 (m, 2H), 7.94 – 7.92 (m, 1H), 7.88 – 7.78 (m, 1H), 7.78 – 7.62 (m, 3H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 5.46 – 5.19 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 150.4, 139.2, 135.9, 133.5, 129.0, 129.0, 129.0, 128.8, 128.6, 127.5, 127.1, 123.5, 122.1, 120.0, 120.0, 111.7, 61.7; IR (Neat Film, NaCl) 3322, 3064, 2890, 1589, 1494, 1428, 1386, 1304, 1242, 1081, 1050, 814, 747 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{16}NO$ $[M+H]^+$: 286.1226, found 286.1235.

Syntheses of 1,3-Disubstituted Isoquinolines with Different Directing Groups



7a ***11a***

(3-phenylisoquinolin-1-yl)methyl acetate (11a): To a scintillation vial containing a stir bar and isoquinoline **7a** (165 mg, 0.70 mmol) in THF (7 mL, 0.1 M) was added DMAP (8.6 mg, 0.07 mmol) and pyridine (0.14 mL, 1.75 mmol). Acetic anhydride (0.1 mL, 1.05 mmol) was then added dropwise. The reaction was stirred overnight at room temperature then diluted with Et_2O and washed with saturated aqueous NH_4Cl. The organic phase was collected, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (10% EtOAc in hexanes) to afford **11a** as a colorless viscous oil (194 mg, >99% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.13 (m, 2H), 8.11 (dd, *J* = 8.4, 1.0 Hz, 1H), 8.07 (s, 1H), 7.92 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.71 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.45 – 7.38 (m, 1H), 5.79 (s, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 154.4, 150.2, 139.3, 137.5, 130.5, 128.9, 128.7, 128.0, 127.6, 127.1, 126.0, 124.8, 117.2, 66.1, 21.1; IR (Neat Film, NaCl) 2826, 2364, 1704, 1574, 1455, 1333, 1054, 904, 783, 764, 748, 719, 678 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{16}NO_2$ $[M+H]^+$: 278.1176, found 278.1178.



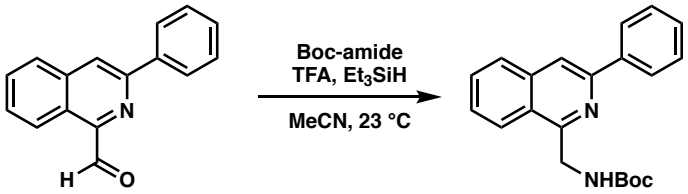
7a ***11b***

1-(methoxymethyl)-3-phenylisoquinoline (11b): To a scintillation vial containing a stir bar and isoquinoline **7a** (165 mg, 0.70 mmol) in THF (7 mL, 0.1 M) was added KO*t*-Bu (86 mg, 0.77

mmol) at room temperature. The resulting mixture was stirred for 5 minutes, then cooled to 0 °C, and MeI (0.05 mL, 0.77 mmol) was added. The reaction was allowed to slowly warm to room temperature overnight and then was quenched with saturated aqueous NH_4Cl. The organic phase was collected and the aqueous phase was extracted with EtOAc. The organic phases were combined, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (5% EtOAc in hexanes) to afford **11b** as a white solid (79 mg, 45% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 8.4, 1.1 Hz, 1H), 8.20 – 8.13 (m, 2H), 8.04 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.69 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.51 (td, *J* = 7.3, 6.5, 1.2 Hz, 2H), 7.45 – 7.37 (m, 1H), 5.14 (s, 2H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 149.9, 139.7, 137.5, 130.4, 128.9, 128.6, 127.7, 127.3, 127.1, 126.5, 125.9, 117.1, 75.8, 58.7; IR (Neat Film, NaCl) 3058, 2918, 2817, 1622, 1590, 1500, 1455, 1338, 1188, 1104, 885, 770, 752, 695, 668 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}NO$ $[M+H]^+$: 250.1226, found 250.1236.

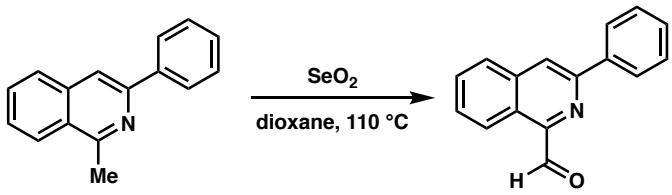
7a ***11c***

1-((benzyloxy)methyl)-3-phenylisoquinoline (11c): This procedure has been adapted from a previous report.[6] To a flame-dried RBF equipped with a stir bar was added NaH (36.4 mg, 60% w/w in oil, 0.91 mmol) and THF (7 mL, 0.1 M). To this suspension, isoquinoline **7a** (165 mg, 0.70 mmol) was added. After 5 minutes of stirring at room temperature, the reaction mixture was cooled to 0 °C and BnBr (0.91 mL, 0.91 mmol) was added. The reaction was allowed to slowly warm to room temperature overnight. Silica (1 g) was then added and the solvent was evaporated under vacuum. The crude product was purified by column chromatography (5% EtOAc in hexanes) to afford **11c** as a colorless viscous oil (153 mg, 67% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 8.4, 1.1 Hz, 1H), 8.21 – 8.14 (m, 2H), 8.04 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.69 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.58 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.51 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.45 – 7.27 (m, 6H), 5.24 (s, 2H), 4.67 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 149.9, 139.7, 138.2, 137.6, 130.4, 128.9, 128.6, 128.5, 128.3, 127.9, 127.7, 127.3, 127.1, 126.6, 126.1, 117.1, 73.6, 72.8; IR (Neat Film, NaCl) 3062, 2858, 1622, 1574, 1496, 1454, 1384, 1337, 1207, 1094, 1030, 885, 796, 768, 737, 696 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{23}H_{20}NO$ $[M+H]^+$: 326.1539, found 326.1544.



11f ***11d***

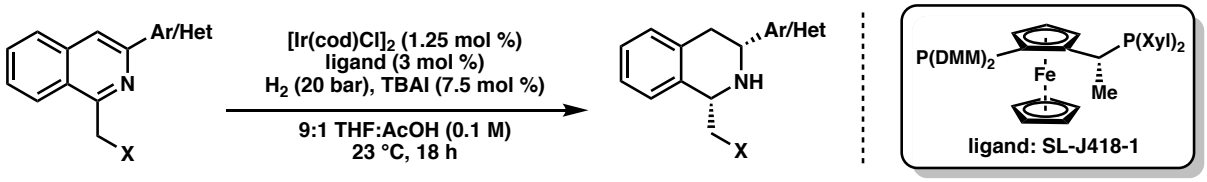
***tert*-butyl ((3-phenylisoquinolin-1-yl)methyl)carbamate (11d):** This procedure has been adapted from a previous report.[7] To a solution of aldehyde **11f** (150 mg, 0.64 mmol) and *t*-butyl carbamate (150 mg, 1.28 mmol) in MeCN (6.5 mL, 0.1 M) were added trifluoroacetic acid (0.15 mL, 1.92 mmol) and triethylsilane (1.0 mL, 6.4 mmol). The reaction was stirred at room temperature overnight and then quenched with saturated aqueous Na_2CO_3 and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (15% EtOAc in hexanes) to afford **11d** as a white solid (160 mg, 75% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.7 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.00 (s, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.70 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.48 – 7.40 (m, 1H), 6.43 (br s, 1H), 5.03 (d, *J* = 4.4 Hz, 2H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 155.0, 149.3, 139.4, 137.1, 130.6, 128.9, 128.8, 127.9, 127.6, 127.0, 125.1, 124.0, 116.3, 79.6, 43.5, 28.7; IR (Neat Film, NaCl) 3418, 2976, 1713, 1622, 1574, 1487, 1367, 1251, 1167, 1056, 882, 765, 695 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$: 335.1754, found 335.1760.



6a ***11f***

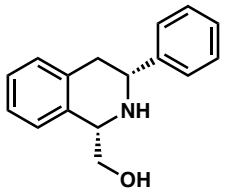
3-phenylisoquinoline-1-carbaldehyde (11f): To a Schlenk flask containing a stir bar was added SeO_2 (140 mg, 1.26 mmol) and isoquinoline **6a** (138 mg, 0.63 mmol) in 1,4-dioxane (13 mL, 0.05 M). The reaction vial was then sealed and heated to 110 °C while stirring for 2 hours. The reaction was then cooled to room temperature and filtered through celite rinsing with EtOAc. The crude product was then purified by column chromatography (5% EtOAc in hexanes) to afford **11f** as a pale yellow solid (1.32 g, 96% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 9.32 (d, *J* = 8.2 Hz, 1H), 8.31 (s, 1H), 8.24 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 7.3 Hz, 1H), 7.84 – 7.67 (m, 2H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 150.8, 149.7, 138.5, 138.1, 131.0, 129.9, 129.3, 129.1, 127.5, 127.1, 125.9, 125.5, 121.3; IR (Neat Film, NaCl) 2826, 2364, 1704, 1574, 1455, 1333, 1054, 904, 783, 764, 748, 719, 678 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{12}NO$ $[M+H]^+$: 234.0913, found 234.0914.

General Procedure 5: Hydrogenation Reactions



To an oven-dried 20-mL scintillation vial equipped with a stir bar and isoquinoline (0.2 mmol) was capped with a PTFE-lined septum and pierced with two 21 gauge green needles. The vials were then placed in a Parr bomb and brought into the glovebox, with the exception of the pressure gauge. A layer of plastic wrap and a rubber band were also brought in to seal the top of the bomb. In a nitrogen-filled glovebox, a solution of the ligand (SL-J418-1) (4.53 mg, 0.006 mmol per reaction) and $[Ir(cod)Cl]_2$ (1.68 mg, 0.0025 mmol per reaction) in THF (1.8 mL per reaction) was prepared and allowed to stand for 10 minutes. Meanwhile, a solution of TBAI (5.54 mg, 0.015 mmol per reaction) in AcOH (0.2 mL per reaction) was prepared in a 1-dram vial, and 0.2 mL of the solution was added to each reaction vial via a syringe. Afterwards, 1.8 mL of the homogeneous iridium catalyst solution was added to each reaction vial via a syringe. After re-capping the vials with caps equipped with needles, the reactions were placed in the bomb and the top was covered tightly with plastic wrap secured by a rubber band. The bomb was then removed from the glovebox, and the pressure gauge was quickly screwed in place and tightened. The bomb was charged to 5-10 bar H_2 and slowly released. This process was repeated two more times, before charging the bomb to 20 bar of H_2 (or 60 bar H_2). The bomb was then left stirring at 200 rpm at room temperature (or placed in an oil bath and heated to 60 °C) for 18 hours. Then, the bomb was removed from the stir plate and the hydrogen pressure was vented. The reaction vials were removed from the bomb and each solution was basified by the addition of saturated aqueous K_2CO_3. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organics layers were then dried over Na_2SO_4, and concentrated in vacuo. The product was then purified by column chromatography to furnish the product as an inseparable mixture of diastereomers.

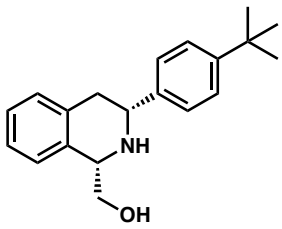
Please note that the NMR data listed is for the major diastereomer, and that the provided spectra for the following compounds reflect the inseparable mixture of *cis*- and *trans*-products. The enantiomeric excess was determined by chiral SFC analysis of the Cbz-protected amine (see Table S3). The absolute configuration was determined for compound **8p** via x-ray crystallographic analysis. Absolute configuration of compound **12e** were determined using vibrational circular dichroism (VCD), *vide infra*. The absolute configuration for all other products has been inferred by analogy.



8a

((1*S*,3*R*)-3-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8a): Compound **8a** was prepared from isoquinoline **7a** using general procedure 5 and purified by column chromatography (5% MeOH in CH_2Cl_2) to provide a tan solid as a mixture of diastereomers (47 mg, 98% yield) (dr = 15.7:1); 92% ee for major diastereomer; $[\alpha]_D^{25}$ +110.2 (*c* 1.02, $CHCl_3$); *Cis*-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 2H), 7.34 – 7.28 (m, 1H), 7.25 – 7.17 (m, 3H), 7.15 – 7.10 (m, 1H), 4.43 – 4.41 (m, 1H), 4.10 (dd, *J* = 11.1, 3.5 Hz, 1H), 4.02 (dd, *J* = 10.8, 3.3 Hz, 1H), 3.90 (dd, *J* = 10.9, 5.4 Hz, 1H), 3.02 (ddt, *J* = 15.9, 11.1, 1.4 Hz, 1H), 2.90 (dd, *J* = 15.7, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 136.7, 134.9, 129.3, 128.8, 127.7, 126.8, 126.7, 126.5, 125.5, 66.7, 58.7, 57.7, 39.0; IR (Neat Film, NaCl) 3296, 3060, 2910, 2360, 1494, 1455, 1314, 1116, 1036, 909, 742, 700 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1383, found 240.1385; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.34, minor = 4.02.

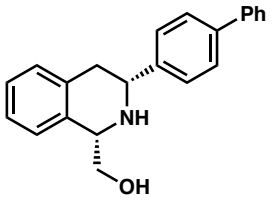
Trans-diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.27 (m, 1H), 7.26 – 7.10 (m, 4H), 4.23 (dd, *J* = 10.5, 4.8 Hz, 1H), 4.16 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.80 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.71 (t, *J* = 10.7 Hz, 1H), 3.07 (dd, *J* = 16.4, 3.9 Hz, 1H), 2.95 (dd, *J* = 15.9, 11.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 135.5, 134.7, 129.5, 128.8, 127.5, 127.0, 126.7, 126.6, 126.4, 63.8, 57.4, 50.7, 36.8.



8b

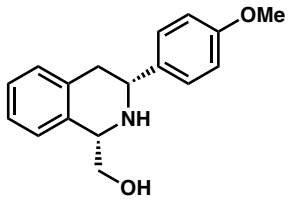
((1*S*,3*R*)-3-(4-(*tert*-butyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8b): Compound **8b** was prepared from isoquinoline **7b** using general procedure 5 and purified by column chromatography (50% EtOAc in hexanes) to provide a tan solid as a mixture of diastereomers (51 mg, 87% yield) (dr = 13.3:1); 91% ee for major diastereomer; $[\alpha]_D^{25}$ +78.8 (*c* 1.03, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 4H), 7.26 – 7.21 (m, 2H), 7.21 – 7.17 (m, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 4.42 – 4.40 (m, 1H), 4.08 (dd, *J* = 11.2, 3.4 Hz, 1H), 4.01 (dd, *J* = 10.8, 3.3 Hz, 1H), 3.89 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.03 (dd, *J* = 15.8, 11.2 Hz, 1H), 2.89 (dd, *J* = 15.7, 3.4 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

150.7, 141.2, 136.7, 135.0, 129.3, 126.7, 126.5, 126.5, 125.7, 125.5, 66.6, 58.7, 57.3, 38.8, 34.7, 31.5; IR (Neat Film, NaCl) 3318, 2961, 2868, 1494, 1454, 1362, 1312, 1270, 1116, 1038, 820, 743 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{26}NO$ $[M+H]^+$: 296.2009, found 296.2005; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 1.81, minor = 2.73.



8c

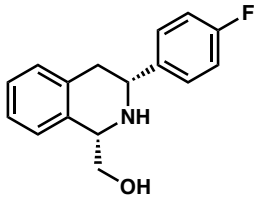
((1*S*,3*R*)-3-([1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8c):
Compound **8c** was prepared from isoquinoline **7c** using general procedure 5 and purified by column chromatography (50% EtOAc in hexanes) to provide a tan solid as a mixture of diastereomers (50 mg, 79% yield) (dr = 9.0:1); 92% ee for major diastereomer; $[\alpha]_D^{25}$ +73.2 (*c* 1.03, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 4H), 7.55 – 7.53 (m, 2H), 7.47 – 7.44 (m, 2H), 7.39 – 7.32 (m, 1H), 7.28 – 7.16 (m, 3H), 7.15 (d, *J* = 6.2 Hz, 1H), 4.46 – 4.44 (m, 1H), 4.15 (dd, *J* = 11.2, 3.4 Hz, 1H), 4.04 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.91 (dd, *J* = 10.9, 5.5 Hz, 1H), 3.12 – 3.00 (m, 1H), 2.94 (dd, *J* = 15.6, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 141.0, 140.7, 136.5, 134.9, 129.3, 128.9, 127.5, 127.4, 127.3, 127.2, 126.8, 126.6, 125.5, 66.6, 58.7, 57.4, 38.9; IR (Neat Film, NaCl) 3318, 3029, 2924, 2365, 1487, 1455, 1312, 1218, 1112, 1038, 833, 763, 748, 699 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{22}H_{22}NO$ $[M+H]^+$: 316.1696, found 316.1686; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 4.08, minor = 5.18.



8d

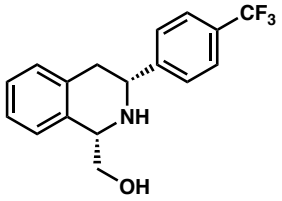
((1*S*,3*R*)-3-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8d): Compound **8d** was prepared from isoquinoline **7d** using general procedure 5 and purified by column chromatography (50% to 60% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (40 mg, 75% yield) (dr = 13.3:1); 92% ee for major diastereomer; $[\alpha]_D^{25}$ +69.3 (*c* 1.01, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.24 – 7.15 (m, 3H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.94 – 6.90 (m, 2H), 4.41 – 4.39 (m, 1H), 4.07 – 3.97 (m, 2H), 3.86 (dd, *J* = 10.9, 5.9 Hz, 1H), 3.83 (s, 3H), 3.06 – 2.95 (m, 1H), 2.86 (dd, *J* = 15.7, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 136.6, 136.3, 134.8, 129.2, 127.8,

126.6, 126.3, 125.3, 114.0, 66.5, 58.6, 57.0, 55.4, 38.8; IR (Neat Film, NaCl) 3342, 2929, 2835, 1612, 1514, 1494, 1453, 1302, 1250, 1176, 1108, 1036, 824, 801, 743 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{20}NO_2$ $[M+H]^+$: 270.1489, found 270.1486; SFC Conditions: 45% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.59, minor = 3.61.



8e

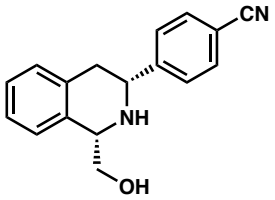
((1*S*,3*R*)-3-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8e): Compound **8e** was prepared from isoquinoline **7e** using general procedure 5 and purified by column chromatography (40% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (51 mg, 99% yield) (dr = 10.1:1); 93% ee for major diastereomer; $[\alpha]_D^{25}$ +79.2 (*c* 1.00, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 2H), 7.24 – 7.18 (m, 3H), 7.12 (d, *J* = 6.9 Hz, 1H), 7.08 – 7.04 (m, 2H), 4.42 – 4.40 (m, 1H), 4.08 (dd, *J* = 11.0, 3.5 Hz, 1H), 4.02 (dd, *J* = 10.8, 3.3 Hz, 1H), 3.88 (dd, *J* = 10.9, 5.5 Hz, 1H), 3.03 – 2.91 (m, 1H), 2.87 (dd, *J* = 15.7, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (d, *J* = 245.5 Hz), 140.0 (d, *J* = 3.0 Hz), 136.4, 134.8, 129.3, 128.4 (d, *J* = 7.9 Hz), 126.6 (d, *J* = 19.9 Hz), 125.5, 115.5 (d, *J* = 21.2 Hz), 66.7, 58.6, 57.1, 39.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ –115.0 – –115.1 (m); IR (Neat Film, NaCl) 3310, 3069, 2924, 2828, 1605, 1511, 1494, 1454, 1225, 1158, 1063, 1040, 844, 826, 744 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{17}FNO$ $[M+H]^+$: 258.1289, found 258.1286; SFC Conditions: 45% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 1.93, minor = 2.87.



8f

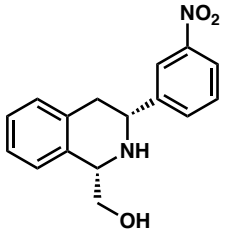
((1*S*,3*R*)-3-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8f): Compound **8f** was prepared from isoquinoline **7f** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a yellow solid as a mixture of diastereomers (49 mg, 80% yield) (dr = 4.6:1); 92% ee for major diastereomer; $[\alpha]_D^{25}$ +35.5 (*c* 1.01, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.55 (m, 2H, integration overlapped with minor diastereomer), 7.51 (d, *J* = 8.3 Hz, 2H), 7.18 – 7.10 (m, 3H), 7.10 – 7.03 (m, 1H), 4.36 – 4.34 (m, 1H), 4.08 (dd, *J* = 10.6, 4.0 Hz, 1H), 3.97 (dd, *J* = 10.8, 3.3 Hz, 1H), 3.81 (dd, *J* = 10.9, 5.8 Hz, 1H), 2.95 – 2.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

148.1, 135.9, 134.6, 129.1, 127.1, 127.0, 126.9, 126.7, 126.7, 126.6, 126.5, 125.7 – 125.5 (m), 125.4, 66.6, 58.4, 57.3, 38.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –115.1 (qd, *J* = 8.7, 5.6 Hz); IR (Neat Film, NaCl) 3304, 2917, 1621, 1418, 1325, 1166, 1123, 1068, 1018, 844, 745 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{17}F_3NO$ $[M+H]^+$: 308.1257, found 308.1265; SFC Conditions: 25% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.11 minor = 5.54.



8g

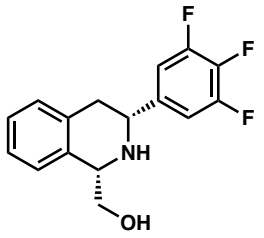
4-((1*S*,3*R*)-1-(hydroxymethyl)-1,2,3,4-tetrahydroisoquinolin-3-yl)benzonitrile (8g): Compound **8g** was prepared from isoquinoline **7g** using general procedure 5 and purified by column chromatography (30% EtOAc in CH_2Cl_2 + 1% NEt_3) to provide a pale tan solid as a mixture of diastereomers (44 mg, 83% yield) (dr = 2.4:1); 82% ee for major diastereomer; $[\alpha]_D^{25}$ +57.4 (*c* 1.00, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.66 (m, 2H), 7.60 – 7.57 (m, 2H), 7.26 – 7.17 (m, 3H, integration overlapped with minor diastereomer), 7.16 – 7.12 (m, 1H), 4.43 – 4.41 (m, 1H), 4.16 (dd, *J* = 10.0, 4.6 Hz, 1H), 4.06 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.89 (dd, *J* = 10.9, 5.8 Hz, 1H), 2.99 – 2.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 135.7, 134.5, 132.6, 129.2, 127.6, 126.9, 126.8, 125.5, 118.9, 111.5, 66.7, 58.5, 57.4, 38.8; IR (Neat Film, NaCl) 3314, 3060, 2925, 2227, 1608, 1494, 1454, 1311, 1115, 1040, 910, 846, 826, 780, 740 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{17}N_2O$ $[M+H]^+$: 265.1335, found 265.1336; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.03, minor = 3.33.



8h

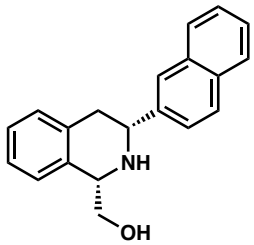
((1*S*,3*R*)-3-(3-nitrophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8h): Compound **8h** was prepared from isoquinoline **7h** using general procedure 5 and purified by column chromatography (0% to 2% MeOH in CH_2Cl_2) to provide a pale yellow solid as a mixture of diastereomers (44 mg, 78% yield) (dr = 3.2:1); 86% ee for major diastereomer; $[\alpha]_D^{25}$ +54.4 (*c* 1.02, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.62 – 7.47 (m, 1H), 7.25 – 7.07 (m, 4H, integration overlapped with minor diastereomer), 4.43 – 4.41 (m, 1H), 4.20 (dd, *J* = 9.2, 5.4 Hz, 1H), 4.07

(dd, *J* = 10.9, 3.2 Hz, 1H), 3.91 – 3.83 (m, 1H), 3.15 – 3.02 (m, 1H), 2.98 – 2.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 146.5, 135.7, 134.6, 133.2, 129.8, 129.4, 127.0, 126.9, 125.6, 122.9, 122.0, 66.8, 58.7, 57.2, 38.9; IR (Neat Film, NaCl) 3388, 2924, 1635, 1531, 1495, 1454, 1350, 1220, 1117, 1038, 802, 781, 748, 738, 682 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{17}N_2O_3$ $[M+H]^+$: 285.1234, found 285.1234; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.45, minor = 3.23.



8i

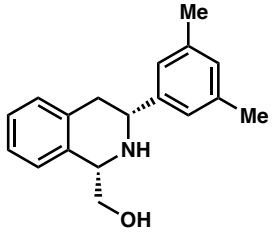
((1*S*,3*R*)-3-(3,4,5-trifluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8i): Compound **8i** was prepared from isoquinoline **7i** using general procedure 5 and purified by column chromatography (5% to 10% EtOAc in CH_2Cl_2 + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (55 mg, 94% yield) (dr = 3.5:1); 89% ee for major diastereomer; $[\alpha]_D^{25}$ +61.6 (*c* 1.02, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 2H, integration overlapped with minor diastereomer), 7.16 – 7.08 (m, 4H), 4.40 – 4.38 (m, 1H), 4.09 – 4.00 (m, 2H), 3.87 (dd, *J* = 10.9, 5.9 Hz, 1H), 2.88 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 151.4 (ddd, *J* = 250.1, 9.8, 3.6 Hz), 139.0 (dt, *J* = 250.9, 15.6 Hz), 135.5, 134.4, 129.2, 127.0, 126.8, 125.5, 110.9 – 110.6 (m), 66.7, 58.5, 56.2, 38.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –133.6 – –134.4 (m), –161.8 – –162.0 (m); IR (Neat Film, NaCl) 3307, 2928, 1621, 1532, 1454, 1372, 1340, 1235, 1043, 866, 804, 748, 698 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{15}F_3NO$ $[M+H]^+$: 294.1100, found 294.1095; SFC Conditions: 40% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 1.67, minor = 2.20.



8j

((1*S*,3*R*)-3-(naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8j): Compound **8j** was prepared from isoquinoline **7j** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a single diastereomer (49 mg, 80% yield); 95% ee; $[\alpha]_D^{25}$ +90.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.88 – 7.84 (m, 3H), 7.60 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.28 – 7.20 (m, 3H), 7.15 (d, *J* = 6.8 Hz, 1H), 4.48 – 4.46 (m, 1H), 4.27 (dd, *J* = 11.1, 3.5 Hz,

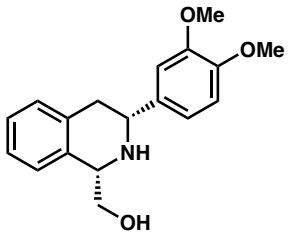
1H), 4.06 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.94 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.14 – 3.07 (m, 1H), 2.98 (dd, *J* = 15.7, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 136.7, 135.1, 133.7, 133.2, 129.4, 128.6, 128.1, 127.9, 126.9, 126.7, 126.4, 126.1, 125.6, 125.3, 66.8, 58.8, 57.9, 39.1; IR (Neat Film, NaCl) 3056, 2917, 2356, 1602, 1494, 1454, 1425, 1366, 1314, 1276, 1112, 1047, 862, 820, 743 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{20}NO$ $[M+H]^+$: 290.1539, found 290.1540; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.61, minor = 5.81.



8k

((1*S*,3*R*)-3-(3,5-dimethylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8k):

Compound **8k** was prepared from isoquinoline **7k** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a single diastereomer (49 mg, 80% yield); 92% ee; $[\alpha]_D^{25}$ +93.5 (*c* 0.98, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.16 (m, 3H), 7.12 (d, *J* = 6.5 Hz, 1H), 7.07 (s, 2H), 6.95 (s, 1H), 4.41 – 4.39 (m, 1H), 4.02 (dd, *J* = 10.9, 3.3 Hz, 2H), 3.90 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.04 – 3.00 (m, 1H), 2.88 (dd, *J* = 15.8, 3.4 Hz, 1H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 138.3, 136.8, 135.0, 129.3, 126.7, 126.4, 125.4, 124.6, 66.6, 58.7, 57.6, 38.9, 21.5; IR (Neat Film, NaCl) 3318, 3014, 2916, 1607, 1494, 1454, 1313, 1117, 1038, 854, 782, 746, 725 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{22}NO$ $[M+H]^+$: 268.1696, found 268.1702; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 1.95, minor = 3.02.

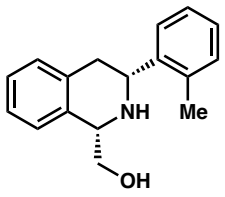


8l

((1*S*,3*R*)-3-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8l):

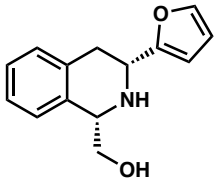
Compound **8l** was prepared from isoquinoline **7l** using general procedure 5 and purified by column chromatography (1% MeOH in CH_2Cl_2 + 1% NEt_3) to provide a pale yellow solid as a single diastereomer (49 mg, 80% yield); 88% ee; $[\alpha]_D^{25}$ +62.4 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 3H), 7.12 (d, *J* = 6.7 Hz, 1H), 7.04 – 6.94 (m, 2H), 6.87 – 6.84 (m, 1H), 4.38 – 4.36 (m, 1H), 4.01 (dt, *J* = 11.2, 4.0 Hz, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.84 (dd,

J = 11.0, 6.0 Hz, 1H), 3.08 – 3.00 (m, 1H), 2.87 (dd, *J* = 15.8, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 148.5, 136.5, 136.4, 134.6, 129.3, 126.7, 126.4, 125.3, 119.0, 111.2, 110.0, 66.3, 58.8, 57.6, 56.1, 38.7; IR (Neat Film, NaCl) 3332, 2934, 2832, 1593, 1518, 1494, 1454, 1264, 1238, 1141, 1028, 745, 720 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{22}NO_3$ $[M+H]^+$: 300.1594, found 300.1600; SFC Conditions: 45% IPA, 3.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.28, minor = 2.93.



8m

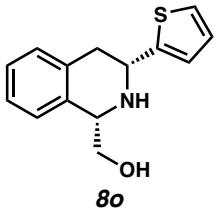
((1*S*,3*R*)-3-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8m): Compound **8m** was prepared from isoquinoline **7m** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale beige solid as a mixture of diastereomers (49 mg, 80% yield) (dr = 10.1:1); 49% ee from major diastereomer; $[\alpha]_D^{25}$ +53.7 (*c* 1.01, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.1 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.26 – 7.17 (m, 5H), 7.14 (d, *J* = 7.3 Hz, 1H), 4.44 – 4.42 (m, 1H), 4.32 (dd, *J* = 10.9, 3.5 Hz, 1H), 4.04 (dd, *J* = 10.8, 3.2 Hz, 1H), 3.92 (dd, *J* = 10.8, 5.3 Hz, 1H), 3.03 – 2.92 (m, 1H), 2.88 (dd, *J* = 15.8, 3.5 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 136.9, 135.2, 135.0, 130.6, 129.4, 127.3, 126.7, 126.5, 125.6, 125.5, 66.6, 58.9, 53.4, 37.7, 19.5; IR (Neat Film, NaCl) 3318, 3022, 2925, 2354, 1492, 1454, 1316, 1117, 1037, 864, 751, 743, 727 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{20}NO$ $[M+H]^+$: 254.1539, found 254.1539; SFC Conditions: 30% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 5.91, minor = 6.39.



8n

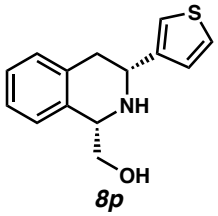
((1*S*,3*R*)-3-(furan-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8n): Compound **8n** was prepared from isoquinoline **7n** using general procedure 5 and purified by column chromatography (40% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (34 mg, 74% yield) (dr = 3.3:1); 92% ee for major diastereomer; $[\alpha]_D^{25}$ +35.5 (*c* 1.00, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.39 (m, 1H), 7.24 – 7.14 (m, 4H, integration overlapped with minor diastereomer), 6.37 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.28 (d, *J* = 3.2 Hz, 1H), 4.37 – 4.35 (m, 1H), 4.20 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.03 (dd, *J* = 11.0, 3.3 Hz, 1H), 3.86 – 3.75 (m, 1H), 3.18 – 3.05 (m, 1H), 3.05 – 2.95 (m, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 141.8, 135.5, 134.7, 129.4, 126.9, 126.7, 126.5, 125.3, 110.2, 105.3, 66.2, 57.9, 50.7, 34.5; IR (Neat Film, NaCl) 3304, 2920, 1495, 1454, 1316, 1146, 1114, 1062, 1037, 1009, 883, 740 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{16}NO_2$ $[M+H]^+$: 230.1176, found 230.1181; SFC Conditions: 35% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 1.52, minor = 1.82.



8o

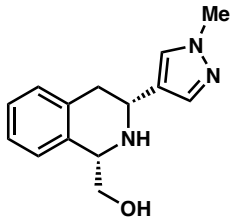
((1*S*,3*R*)-3-(thiophen-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8o): Compound **8o** was prepared from isoquinoline **7o** using general procedure 5 and purified by column chromatography (40% EtOAc in hexanes + 1% NEt_3) to provide a pale beige solid as a mixture of diastereomers (46 mg, 94% yield) (dr = 3.6:1); 90% ee for major diastereomer; $[\alpha]_D^{25}$ +57.4 (*c* 1.04, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 1H), 7.28 – 7.21 (m, 3H, integration overlapped with minor diastereomer), 7.19 – 7.15 (m, 1H), 7.11 – 7.09 (m, 1H), 7.07 – 7.04 (m, 1H), 4.47 – 4.42 (m, 2H), 4.06 (dd, *J* = 10.9, 3.4 Hz, 1H), 3.87 (dd, *J* = 11.0, 5.9 Hz, 1H), 3.19 – 2.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 135.8, 134.7, 129.1, 126.7, 126.7, 126.6, 125.3, 124.2, 123.5, 66.4, 58.5, 53.1, 39.3; IR (Neat Film, NaCl) 3312, 2923, 2360, 1494, 1454, 1424, 1310, 1280, 1112, 1038, 850, 830, 744, 704 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{16}NOS$ $[M+H]^+$: 246.0947, found 246.0941; SFC Conditions: 35% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 2.86, minor = 6.02.



8p

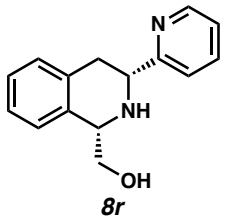
((1*S*,3*R*)-3-(thiophen-3-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8p): Compound **8p** was prepared from isoquinoline **7p** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale beige solid as a mixture of diastereomers (25.5 mg, 52% yield) (dr = 7.3:1). The isolated product contained long-chain hydrocarbon impurities, so it was repurified by partitioning between acetonitrile and hexanes. The acetonitrile layer was collected and concentrated to afford **8p** as a pale yellow solid (24.0 mg, 49% yield); 89% ee for major diastereomer; $[\alpha]_D^{25}$ +86.8 (*c* 0.99, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.18 – 7.16 (m, 1H), 7.13 – 7.07 (m, 4H), 7.05 – 7.02 (m, 1H), 4.28 – 4.26 (m, 1H), 4.10 (dd, *J* = 10.8, 3.8 Hz, 1H), 3.93 (dd, *J* = 10.9, 3.4 Hz, 1H), 3.73 (dd, *J* = 11.0, 6.1 Hz, 1H), 2.99 – 2.90 (m, 1H), 2.86 (dd, *J* = 15.8, 3.8 Hz, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 145.3, 136.2, 134.9, 129.3, 126.7, 126.5, 126.5, 126.2, 125.3, 120.9, 66.3, 58.5, 53.3, 38.1; IR (Neat Film, NaCl) 3318, 2924, 2366, 1494, 1454, 1424, 1313, 1279, 1218, 1116, 1038, 854, 782, 748 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{16}NOS$ $[M+H]^+$: 246.0947, found 246.0952; SFC Conditions: 35% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.19, minor = 4.05.



8q

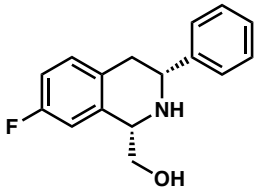
((1*S*,3*R*)-3-(1-methyl-1*H*-pyrazol-4-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8q): Compound **8q** was prepared from isoquinoline **7q** using general procedure 5 and purified by column chromatography (5% to 10% MeOH in EtOAc + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (48 mg, 98% yield) (dr = 2.9:1); 87% ee for major diastereomer; $[\alpha]_D^{25}$ +37.1 (*c* 1.021, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.61 (m, 2H), 7.26 – 7.16 (m, 2H, integration overlapped with minor diastereomer), 7.19 – 7.06 (m, 2H), 4.50 – 4.98 (m, 1H), 4.20 (dd, *J* = 11.8, 3.3 Hz, 1H), 4.02 (dd, *J* = 11.6, 3.3 Hz, 1H), 3.84 (s, 3H), 3.34 – 3.22 (m, 1H), 3.13 – 2.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 134.7, 132.2, 129.3, 129.2, 127.2, 126.9, 125.4, 121.5, 64.6, 58.6, 49.1, 39.0, 36.1; IR (Neat Film, NaCl) 3315, 2931, 2371, 1560, 1494, 1455, 1408, 1295, 1169, 1031, 1008, 986, 748, 724 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{14}H_{18}N_3O$ $[M+H]^+$: 244.1444, found 244.1448; SFC Conditions: 25% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): minor = 1.84, major = 2.60.



8r

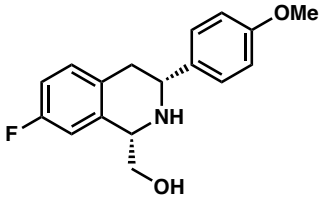
((1*S*,3*R*)-3-(pyridin-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (8r): Compound **8r** was prepared from isoquinoline **7r** using general procedure 5 and purified using reverse-phase (C_{18}) preparative-HPLC (MeCN/0.4% acetic acid in water, 5.0 mL/min, monitor wavelength = 255 nm, 5–23% MeCN over 6 min, ramp to 95% MeCN over 0.5 min, and hold at 95% for 3.5 min) to provide a tan solid as a mixture of diastereomers (49 mg, 80% yield) (dr = 2.5:1). This compound appears to be unstable and significant decomposition was observed under prolonged storage; 85% ee for major diastereomer; $[\alpha]_D^{25}$ +49.0 (*c* 1.01, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 – 8.57 (m, 1H), 7.72 – 7.67 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.11 (m, 4H, integration overlapped with minor diastereomer), 4.41 – 4.39 (m, 1H), 4.23 –

4.20 (m, 1H, integration overlapped with minor diastereomer), 4.07 (dd, *J* = 11.1, 3.4 Hz, 1H), 3.85 (dd, *J* = 11.0, 6.4 Hz, 1H), 3.08 – 3.00 (m, 2H, integration overlapped with minor diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 149.4, 137.0, 136.0, 135.3, 129.4, 126.7, 126.5, 125.4, 122.6, 121.1, 66.4, 58.6, 58.0, 36.5; IR (Neat Film, NaCl) 3300, 3056, 2934, 1592, 1574, 1473, 1454, 1435, 1316, 1142, 1060, 910, 744 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{15}H_{17}N_2O$ $[M+H]^+$: 241.1335, found 241.1334; SFC Conditions: 30% IPA, 2.5 mL/min, Chiralpak OD-H column, λ = 210 nm, t_R (min): minor = 2.52, major = 2.79.



10a

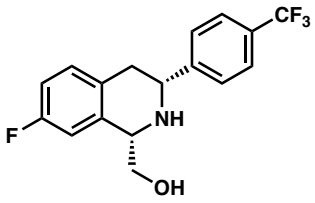
((1*S*,3*R*)-7-fluoro-3-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (10a): Compound **10a** was prepared from isoquinoline **9a** using general procedure 5 and purified by column chromatography (30% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (49 mg, 94% yield) (dr = 11.5:1); 93% ee for major diastereomer; $[\alpha]_D^{25}$ +76.9 (*c* 1.04, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.40 – 7.36 (m, 2H), 7.33 – 7.30 (m, 1H), 7.08 (dd, *J* = 8.4, 5.8 Hz, 1H), 6.97 – 6.87 (m, 2H), 4.38 – 4.36 (m, 1H), 4.06 (dd, *J* = 10.8, 3.7 Hz, 1H), 3.99 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.86 (dd, *J* = 10.9, 5.2 Hz, 1H), 3.00 – 2.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 (d, J = 243.8 Hz), 144.0, 136.9 (d, *J* = 6.8 Hz), 132.2 (d, *J* = 3.0 Hz), 130.6 (d, *J* = 7.9 Hz), 128.8, 127.8, 126.8, 113.9 (d, *J* = 21.3 Hz), 112.1 (d, *J* = 21.8 Hz), 66.4, 58.6 (d, *J* = 2.1 Hz), 57.7, 38.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –116.2 – –116.4 (m); IR (Neat Film, NaCl) 3309, 2918, 1614, 1498, 1455, 1428, 1255, 1221, 1031, 911, 868, 808, 758, 745, 700 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{17}FNO$ $[M+H]^+$: 258.1289, found 258.1281; SFC Conditions: 40% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 2.56, minor = 3.04.



10b

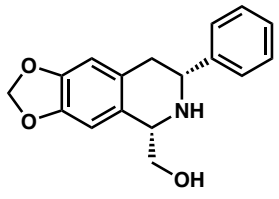
((1*S*,3*R*)-7-fluoro-3-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (10b): Compound **10b** was prepared from isoquinoline **9b** using general procedure 5 and purified by column chromatography (30% to 40% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a single diastereomer (57 mg, 99% yield); 90% ee; $[\alpha]_D^{25}$ +57.8 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 2H), 7.07 (dd, *J* = 8.4, 5.8 Hz, 1H), 6.97 – 6.84 (m, 4H), 4.36 – 4.34 (m, 1H), 3.99 (ddd, *J* = 12.3, 10.9, 3.4 Hz, 2H), 3.86 – 3.84 (m, 1H), 3.82 (s,

3H), 2.99 – 2.87 (m, 1H), 2.83 (dd, *J* = 15.6, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 (d, *J* = 243.7 Hz), 159.2, 136.9 (d, *J* = 6.7 Hz), 136.2, 132.3, 130.6 (d, *J* = 7.9 Hz), 127.9, 114.1, 113.8 (d, *J* = 21.3 Hz), 112.1 (d, *J* = 21.8 Hz), 66.4, 58.7 (d, *J* = 2.0 Hz), 57.1, 55.5, 38.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ –116.3 – –116.4 (m); IR (Neat Film, NaCl) 3305, 2930, 2838, 1614, 1591, 1514, 1498, 1304, 1249, 1178, 1111, 1034, 912, 868, 830, 816, 736 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{19}FNO_2$ $[M+H]^+$: 288.1394, found 288.1404; SFC Conditions: 30% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 1.93, minor = 2.42.



10c

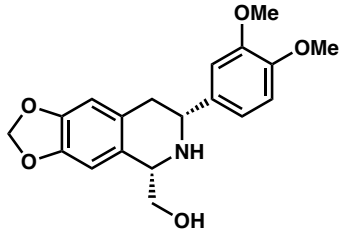
((1*S*,3*R*)-7-fluoro-3-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (10c): Compound **10c** was prepared from isoquinoline **9c** using general procedure 5 and purified by column chromatography (20% to 30% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (50 mg, 77% yield) (dr = 6.7:1); 94% ee for major diastereomer; $[\alpha]_D^{25}$ +44.2 (*c* 1.002, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.09 (dd, *J* = 8.4, 5.7 Hz, 1H), 7.00 – 6.87 (m, 2H), 4.39 – 4.37 (m, 1H), 4.13 (dd, *J* = 8.9, 5.7 Hz, 1H), 4.02 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.88 (dd, *J* = 10.9, 5.4 Hz, 1H), 2.94 – 2.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (d, *J* = 244.2 Hz), 148.0, 136.7 (d, *J* = 6.7 Hz), 131.5 (d, *J* = 3.1 Hz), 130.6 (d, *J* = 7.9 Hz), 130.1 (q, *J* = 32.5 Hz), 127.2, 125.7 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 272.1 Hz), 114.0 (d, J = 21.3 Hz), 112.1 (d, *J* = 21.9 Hz) 66.4, 58.5 (d, *J* = 2.0 Hz), 57.4, 38.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –62.5, –115.8 – –115.9 (m); IR (Neat Film, NaCl) 3304, 2922, 1620, 1593, 1500, 1428, 1326, 1255, 1222, 1165, 1125, 1068, 1018, 868, 836, 816 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{16}F_4NO$ $[M+H]^+$: 326.1163, found 326.1175; SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.93, minor = 4.46.



10d

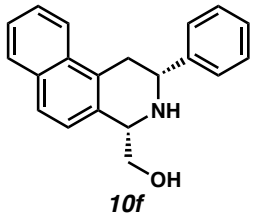
((5*S*,7*R*)-7-phenyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)methanol (10d): Compound **10d** was prepared from isoquinoline **9d** using general procedure 5 and purified by column chromatography (75% EtOAc in hexanes + 1% NEt_3) to provide a pale beige solid as a mixture of diastereomers (17 mg, 30% yield) (dr = 4.9:1); 58% ee for major diastereomer; $[\alpha]_D^{25}$

+29.2 (*c* 0.940, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H), 7.39 – 7.37 (m, 2H), 7.33 – 7.27 (m, 1H), 6.71 (s, 1H), 6.60 – 6.58 (m, 1H), 5.95 – 5.89 (m, 2H), 4.32 – 4.30 (m, 1H), 4.04 (dd, *J* = 11.1, 3.4 Hz, 1H), 3.93 (dd, *J* = 10.9, 3.2 Hz, 1H), 3.82 (dd, *J* = 10.9, 5.1 Hz, 1H), 2.97 – 2.88 (m, 1H), 2.78 (dd, *J* = 15.5, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 146.4, 144.2, 130.0, 128.8, 127.9, 127.7, 126.8, 109.0, 105.5, 101.0, 66.7, 58.6, 57.7, 39.0; IR (Neat Film, NaCl) 3324, 3028, 2897, 1504, 1486, 1454, 1434, 1384, 1306, 1279, 1231, 1128, 1038, 936, 910, 858, 750, 733, 701 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{18}NO_3$ $[M+H]^+$: 284.1281, found 284.1276; SFC Conditions: 45% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 5.00, minor = 7.22.



10e

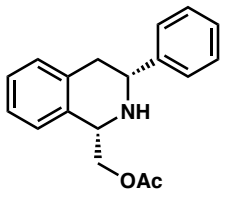
((5*S*,7*R*)-7-(3,4-dimethoxyphenyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)methanol (10e): Compound **10e** was prepared from isoquinoline **9e** using general procedure 5 and purified by column chromatography (100% EtOAc to 10% MeOH in EtOAc + 1% NEt_3) to provide a pale yellow solid as a single diastereomer (28 mg, 41% yield); 54% ee; $[\alpha]_D^{25}$ +25.5 (*c* 0.197, CH_3OH); ^1H NMR (400 MHz, $CDCl_3$) δ 6.99 – 6.96 (m, 2H), 6.87 – 6.85 (m, 1H), 6.71 (s, 1H), 6.60 – 6.58 (m, 1H), 5.94 – 5.91 (m, 2H), 4.32 – 4.30 (m, 1H), 3.99 (dd, *J* = 11.1, 3.4 Hz, 1H), 3.94 (dd, *J* = 11.1, 3.4 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.83 (dd, *J* = 11.0, 5.0 Hz, 1H), 2.97 – 2.85 (m, 1H), 2.76 (dd, *J* = 15.6, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 148.7, 146.7, 146.5, 136.9, 130.1, 127.8, 119.0, 111.4, 110.0, 109.1, 105.6, 101.1, 66.7, 58.8, 57.7, 56.2, 39.1; IR (Neat Film, NaCl) 3374, 2890, 2360, 1505, 1487, 1268, 1260, 1237, 1140, 1076, 1024, 971, 932, 918, 730 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{22}NO_5$ $[M+H]^+$: 344.1492, found 344.1483; SFC Conditions: 45% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.89, minor = 5.16.



10f

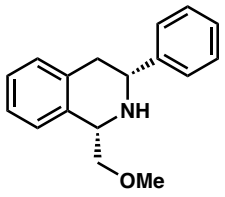
((2*R*,4*S*)-2-phenyl-1,2,3,4-tetrahydrobenzo[*f*]isoquinolin-4-yl)methanol (10f): Compound **10f** was prepared from isoquinoline **9f** using general procedure 5 and purified by column chromatography (40% to 60% EtOAc in hexanes + 1% NEt_3) to provide a pale yellow solid as a mixture of diastereomers (25 mg, 43% yield) (dr = 15.7:1); 82% ee for major diastereomer; $[\alpha]_D^{25}$ +85.7 (*c* 1.01, $CHCl_3$); Major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.91 (m,

1H), 7.85 – 7.82 (m, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.50 – 7.47 (m, 2H), 7.45 – 7.34 (m, 4H), 4.61 – 4.59 (m, 1H), 4.20 (dd, *J* = 11.0, 3.4 Hz, 1H), 4.09 (dd, *J* = 10.9, 3.2 Hz, 1H), 4.01 (dd, *J* = 10.9, 4.8 Hz, 1H), 3.50 – 3.39 (m, 1H), 3.23 – 3.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 132.2, 132.1, 132.0, 131.9, 128.8, 128.4, 127.7, 126.8, 126.7, 126.3, 125.5, 123.4, 122.9, 66.4, 59.1, 57.6, 35.4; IR (Neat Film, NaCl) 3306, 3056, 2918, 1417, 1308, 1034, 910, 884, 813, 762, 700, 736, 682 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{20}NO$ $[M+H]^+$: 290.1539, found 290.1534; SFC Conditions: 45% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 5.31, minor = 10.01.



12a

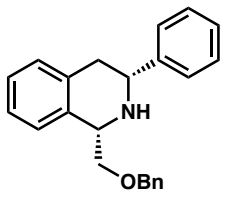
((1*S*,3*R*)-3-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl acetate (12a): Compound **12a** was prepared from isoquinoline **11a** using general procedure 5 and purified by column chromatography (5% EtOAc in CH_2Cl_2 + 1% NEt_3) to provide a yellow oil as a single diastereomer (32 mg, 56% yield); 86% ee; $[\alpha]_D^{25}$ +103.8 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 2H), 7.41 – 7.37 (m, 2H), 7.34 – 7.30 (m, 1H), 7.27 – 7.24 (m, 1H), 7.23 – 7.18 (m, 2H), 7.16 – 7.10 (m, 1H), 4.78 (dd, *J* = 10.8, 3.5 Hz, 1H), 4.54 – 4.51 (m, 1H), 4.14 (dd, *J* = 10.8, 8.7 Hz, 1H), 4.05 (dd, *J* = 11.1, 3.4 Hz, 1H), 3.08 – 3.01 (m, 1H), 2.90 (dd, *J* = 15.5, 3.6 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 144.4, 136.3, 134.1, 129.5, 128.8, 127.7, 126.9, 126.9, 126.3, 125.3, 69.1, 57.9, 56.4, 39.2, 21.2; IR (Neat Film, NaCl) 3024, 2926, 2802, 1741, 1494, 1454, 1386, 1366, 1314, 1229, 1118, 1034, 754, 701 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{18}H_{20}NO_2$ $[M+H]^+$: 282.1489, found 282.1492; SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 3.32, major = 3.93.



12b

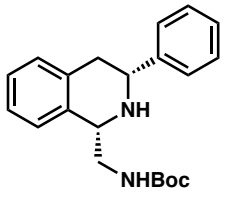
(1*S*,3*R*)-1-(methoxymethyl)-3-phenyl-1,2,3,4-tetrahydroisoquinoline (12b): Compound **12b** was prepared from isoquinoline **11b** using general procedure 5 and purified by column chromatography (10% EtOAc in CH_2Cl_2+ 1% NEt_3) to provide a viscous yellow oil as a single diastereomer (40 mg, 80% yield); 89% ee; $[\alpha]_D^{25}$ +94.3 (*c* 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 2H), 7.39 – 7.35 (m, 2H), 7.32 – 7.27 (m, 1H), 7.25 – 7.20 (m, 1H), 7.20 – 7.15 (m, 2H), 7.16 – 7.10 (m, 1H), 4.45 – 4.42 (m, 1H), 4.07 – 3.94 (m, 2H), 3.59 (t, *J* =

8.7 Hz, 1H), 3.43 (s, 3H), 3.06 (dd, *J* = 16.0, 11.1 Hz, 1H), 2.92 (dd, *J* = 16.0, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 136.3, 135.4, 129.5, 128.7, 127.5, 126.9, 126.6, 126.1, 124.8, 59.3, 58.1, 57.4, 39.0; IR (Neat Film, NaCl) 3028, 2895, 2812, 1604, 1494, 1454, 1313, 1194, 1112, 1072, 1030, 958, 923, 840, 744, 700 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{17}H_{20}NO$ $[M+H]^+$: 254.1539, found 254.1531; SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak OD-H column, λ = 210 nm, t_R (min): major = 4.82, major = 5.25.



12c

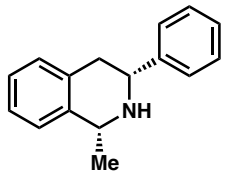
(1*S*,3*R*)-1-((benzyloxy)methyl)-3-phenyl-1,2,3,4-tetrahydroisoquinoline (12c): Compound **12c** was prepared from isoquinoline **11c** using general procedure 5 and purified by column chromatography (5% EtOAc in CH_2Cl_2 + 1% NEt_3) to provide a pale yellow oil as a single diastereomer (60 mg, 90% yield); 88% ee; $[\alpha]_D^{25}$ +80.4 (*c* 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 2H), 7.40 – 7.34 (m, 6H), 7.32 – 7.28 (m, 2H), 7.22 – 7.16 (m, 3H), 7.14 – 7.11 (m, 1H), 4.61 (s, 2H), 4.48 (dd, *J* = 8.7, 3.4 Hz, 1H), 4.12 (dd, *J* = 9.0, 3.6 Hz, 1H), 4.04 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.67 (t, *J* = 8.7 Hz, 1H), 3.05 (dd, *J* = 15.9, 11.1 Hz, 1H), 2.91 (dd, *J* = 15.8, 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 138.3, 136.3, 135.3, 129.5, 128.7, 128.6, 127.9, 127.8, 127.5, 126.9, 126.6, 126.1, 124.9, 74.8, 73.6, 58.1, 57.5, 39.2; IR (Neat Film, NaCl) 3060, 3028, 2862, 1494, 1454, 1366, 1312, 1098, 1028, 742, 698 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{23}H_{24}NO$ $[M+H]^+$: 330.1852, found 330.1857; SFC Conditions: 25% IPA, 2.5 mL/min, Chiralpak OD-H column, λ = 210 nm, t_R (min): major = 5.66, major = 6.38.



12d

***tert*-butyl (((1*S*,3*R*)-3-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl)carbamate (12d):** Compound **12d** was prepared from isoquinoline **11d** using general procedure 5 and purified by column chromatography (15% EtOAc in hexanes + 1% NEt_3) to provide a white solid as a mixture of diastereomers (44 mg, 71% yield) (dr = 9.0:1); 90% ee for major diastereomer; $[\alpha]_D^{25}$ +50.4 (*c* 0.99, $CHCl_3$); Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.1 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.36 – 7.26 (m, 2H), 7.26 – 7.14 (m, 2H), 7.11 (d, *J* = 6.7 Hz, 1H), 5.02 (s, 1H), 4.44 (s, 1H), 4.04 (dd, *J* = 11.0, 3.5 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.49 (dt, *J* = 13.2, 6.3 Hz, 1H), 3.00 (dd, *J* = 15.8, 10.9 Hz, 1H), 2.89 (dd, *J* = 15.8, 3.5 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 144.4, 136.4, 135.2, 129.2, 128.7, 127.7, 126.8, 126.6, 126.4,

125.7, 79.4, 58.0, 57.1, 46.3, 39.1, 28.5; IR (Neat Film, NaCl) 3352, 2978, 2932, 1704, 1495, 1455, 1392, 1366, 1247, 1171, 752, 701 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{21}H_{27}N_2O_2$ $[M+H]^+$: 339.2067, found 339.2063; SFC Conditions: 40% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 1.41, major = 1.76.

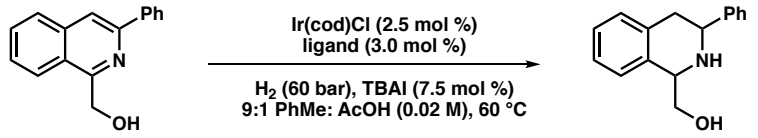


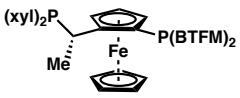
12e

(1*R*,3*R*)-1-methyl-3-phenyl-1,2,3,4-tetrahydroisoquinoline (12e): Compound **12e** was prepared from 1-methyl-3-phenylisoquinoline using general procedure 5 and purified by column chromatography (10% to 20% EtOAc in hexanes + 1% NEt_3) to provide a colorless oil as a single diastereomer (29 mg, 64% yield); 90% ee; $[\alpha]_D^{25}$ +133.3 (*c* 0.79, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.46 (m, 2H), 7.41 – 7.37 (m, 2H), 7.33 – 7.29 (m, 1H), 7.28 – 7.23 (m, 1H), 7.23 – 7.14 (m, 2H), 7.11 (d, *J* = 6.9 Hz, 1H), 4.34 (q, *J* = 6.6 Hz, 1H), 4.08 (dd, *J* = 11.1, 3.9 Hz, 1H), 3.12 – 3.01 (m, 1H), 2.96 (dd, *J* = 16.2, 4.1 Hz, 1H), 1.55 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 139.9, 135.2, 129.1, 128.7, 127.5, 126.7, 126.2, 126.2, 125.4, 58.8, 53.6, 38.9, 22.4; IR (Neat Film, NaCl) 3024, 2962, 2926, 2792, 1602, 1494, 1453, 1372, 1352, 1306, 1140, 1118, 1031, 790, 753, 733, 700 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{16}H_{18}N$ $[M+H]^+$: 224.1434, found 224.1426; SFC Conditions: 20% IPA, 3.5 mL/min, Chiralpak AS-H column, λ = 210 nm, t_R (min): major = 2.16, minor = 2.62.

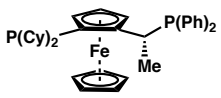
Additional Optimization Results

Table S1. Additional Ligand Screen

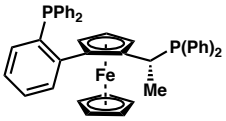




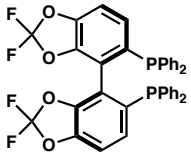
SL-J008-2
> 95% conversion
86% yield, 49% ee



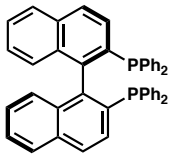
SL-J004-1
56% conversion
37% yield, –61% ee



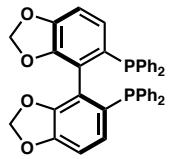
Walphos (SL-002-1)
23% conversion
9% yield, ee ND



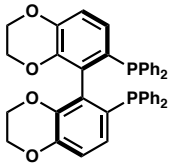
59% conversion
59% yield, –61% ee



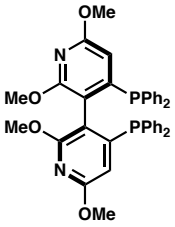
36% conversion
23% yield, 19% ee



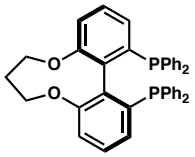
50% conversion
20% yield, ee ND



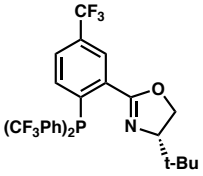
15% conversion
16% yield, ee ND



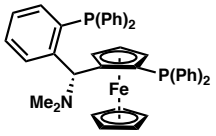
59% conversion
46% yield, –41% ee



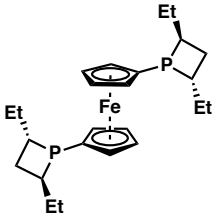
50% conversion
20% yield, ee ND



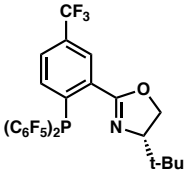
65% conversion
71% yield, 2% ee



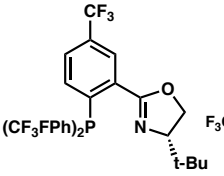
>95% conversion
80% yield, –40% ee



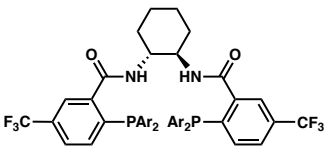
>62% conversion
48% yield, –44% ee



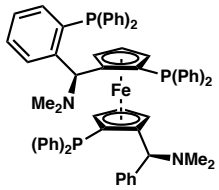
55% conversion
39% yield, –4% ee



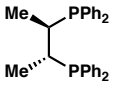
74% conversion
46% yield, 5% ee



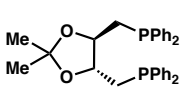
0% conversion
0% yield, ee ND



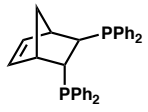
SL-M001-2
> 61% conversion
51% yield, 49% ee



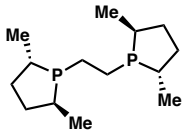
(R, R)-chiralphos
78% conversion
57% yield, –37% ee



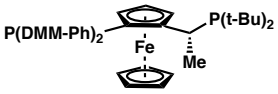
(R, R)-DIOP
37% conversion
28% yield, 5% ee



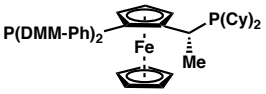
Norphos
31% conversion
20% yield, ee ND



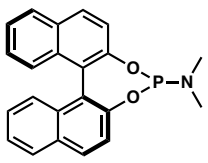
Me-BPE
22% conversion
10% yield, ee ND



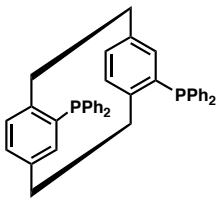
SL-J013-1
0% conversion
0% yield



SL-J007-1
16% conversion
6% yield, ee ND

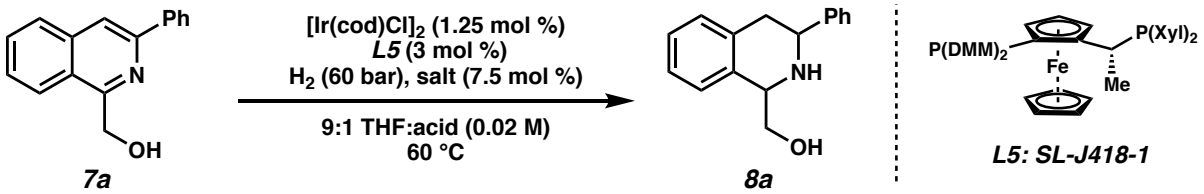


Monophos
42% conversion
29% yield, 5% ee



PhanePhos
67% conversion
74% yield, –19% ee

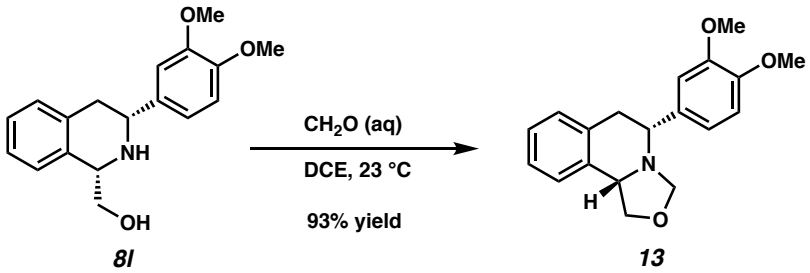
Table S2. Additive Effects[a]



entry	salt additive	acid	% conversion[b]	cis:trans[b]	% ee of cis[c]
1	TBAI	AcOH	>95	10:1	89
2	LiI	AcOH	>95	10:1	89
3	NaI	AcOH	>95	10:1	90
4	KI	AcOH	92	10:1	87
5	TBACl	AcOH	>95	1:1.2	31
6	TBABr	AcOH	>95	1.2:1	63
7	none	AcOH	50	1:1	27
8	TBAI	none	31	ND	67
9	TBAI	TFA	>95	10:1	90
10	TBAI	$(n\text{-BuO})_2PO_2H$	>95	7:1	84

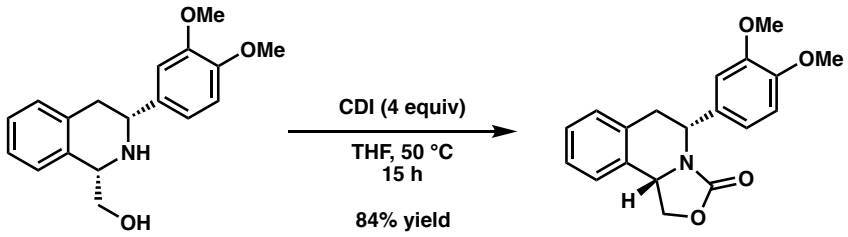
[a]Conditions: 0.04 mmol *1*, 1.25 mol % $[Ir(COD)Cl]_2$, 3 mol % ligand, 7.5 mol % salt additive, 60 bar H_2 in 2.0 mL 9:1 THF:acid. [b]Determined from crude 1H NMR using trimethoxybenzene as a standard. [c]Determined by chiral SFC analysis of Cbz-protected product.

Experimental Procedure for Product Transformations:



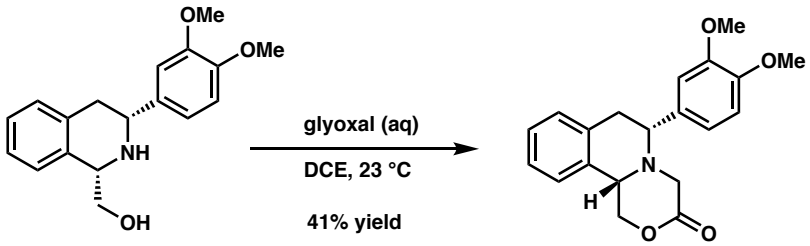
To a 1-dram vial equipped with a stir bar was added tetrahydroisoquinoline **8l** (20.0 mg, 0.067 mmol) in 1,2-dichloroethane (1.3 mL, 0.05 M). Formaldehyde solution (37 wt% in H_2O, 9.2 µL, 0.124 mmol) was then added and the reaction was stirred for 15 minutes at room temperature. The reaction was then basified with K_2CO_3, and extracted with CH_2Cl_2. The collected organic layers were dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by column chromatography (50% EtOAc in hexanes + 1% NEt_3) to afford **13** as a white solid (19.3 mg, 93% yield): $[\alpha]_D^{25}$ +134.8 (*c* 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.14 (m, 3H), 7.04 (d, *J* = 2.0 Hz, 1H), 7.02 – 6.90 (m, 2H), 6.83 (d, *J* = 8.2 Hz, 1H), 4.58 – 4.43 (m, 2H), 3.97 (t, *J* = 7.6 Hz, 1H), 3.94 – 3.87 (m, 2H), 3.89 (s, 6H), 3.83 (dd, *J* = 10.6, 4.8 Hz, 1H), 3.23 (dd, *J* = 16.8, 10.6 Hz, 1H), 3.11 (dd, *J* = 16.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

149.4, 148.7, 135.1, 134.7, 134.6, 128.6, 127.2, 126.3, 125.0, 119.6, 110.9, 110.2, 84.2, 71.5, 62.9, 61.3, 56.1, 56.0, 37.3; IR (Neat Film, NaCl) 2930, 1592, 1513, 1454, 1263, 1237, 1167, 1060, 1027, 918, 752, 680 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{22}NO_3$ $[M+H]^+$: 312.1594, found 312.1594.



8l ***14***

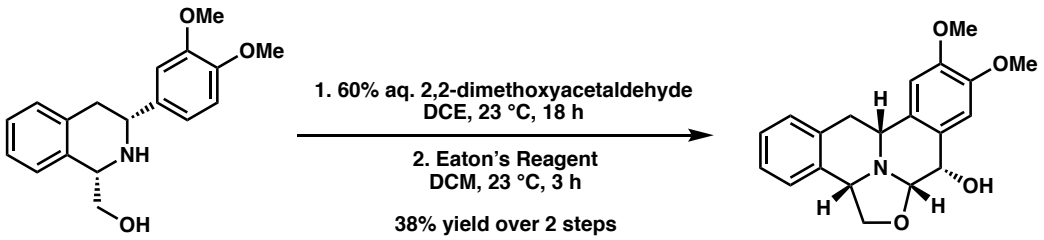
To a 1-dram vial equipped with a stir bar was added tetrahydroisoquinoline **8l** (10.0 mg, 0.033 mmol), THF (0.7 mL, 0.05 M), and CDI (21.7 mg, 0.134 mmol). The solution was stirred at 50 °C for 15 h. After complete conversion of the starting material monitored by TLC, the reaction concentrated and the crude product was purified by preparative-TLC (100% EtOAc) to afford **14** as a white solid (9.2 mg, 84% yield): $[\alpha]_D^{25}$ +71.4 (*c* 0.76, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.3, 7.0 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.08 (t, *J* = 6.6 Hz, 2H), 6.66 (d, *J* = 8.2 Hz, 1H), 6.52 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.33 (d, *J* = 2.1 Hz, 1H), 5.14 – 5.02 (m, 2H), 4.92 (t, *J* = 7.9 Hz, 1H), 4.49 (dd, *J* = 10.1, 8.2 Hz, 1H), 3.78 (s, 3H), 3.60 (s, 3H), 3.36 (dd, *J* = 14.9, 6.4 Hz, 1H), 2.99 (dd, *J* = 14.9, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 148.7, 148.3, 136.0, 134.2, 133.9, 129.4, 128.5, 127.5, 122.4, 118.5, 110.9, 109.3, 67.5, 55.9, 55.6, 54.6, 53.4, 36.8; IR (Neat Film, NaCl) 2933, 1756, 1515, 1464, 1396, 1260, 1234, 1139, 1025, 779, 762, 748 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1387, found 326.1386.



8l ***15***

To a 1-dram vial equipped with a stir bar was added tetrahydroisoquinoline **8l** (20.0 mg, 0.067 mmol) in 1,2-dichloroethane (1.3 mL, 0.05 M). Glyoxal solution (40 wt% in H_2O, 0.15 mL, 1.336 mmol) was then added, and the reaction was stirred at room temperature overnight. After complete conversion of the starting material monitored by TLC, the reaction was diluted with H_2O, and extracted with CH_2Cl_2. The collected organic layers were dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by preparative-TLC (50% EtOAc in hexanes) to afford **15** as a white solid (9.2 mg, 41% yield): $[\alpha]_D^{25}$ +187.8 (*c* 0.61, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 2H), 7.20 – 7.10 (m, 2H), 6.95 – 6.81 (m, 3H), 4.84

(dd, *J* = 10.5, 3.4 Hz, 1H), 4.33 (t, *J* = 10.7 Hz, 1H), 4.04 – 3.94 (m, 1H), 3.90 (s, 6H), 3.62 (d, *J* = 17.7 Hz, 1H), 3.43 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.32 – 3.19 (m, 1H), 2.98 – 2.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 149.8, 149.1, 135.0, 132.8, 130.6, 129.1, 127.7, 126.7, 124.7, 120.5, 111.4, 110.2, 73.3, 63.8, 59.5, 56.1, 56.1, 54.9, 38.9; IR (Neat Film, NaCl) 2932, 1745, 1511, 1463, 1421, 1263, 1242, 1137, 1028, 809, 746 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_4$ $[M+H]^+$: 340.1543, found 340.1545.

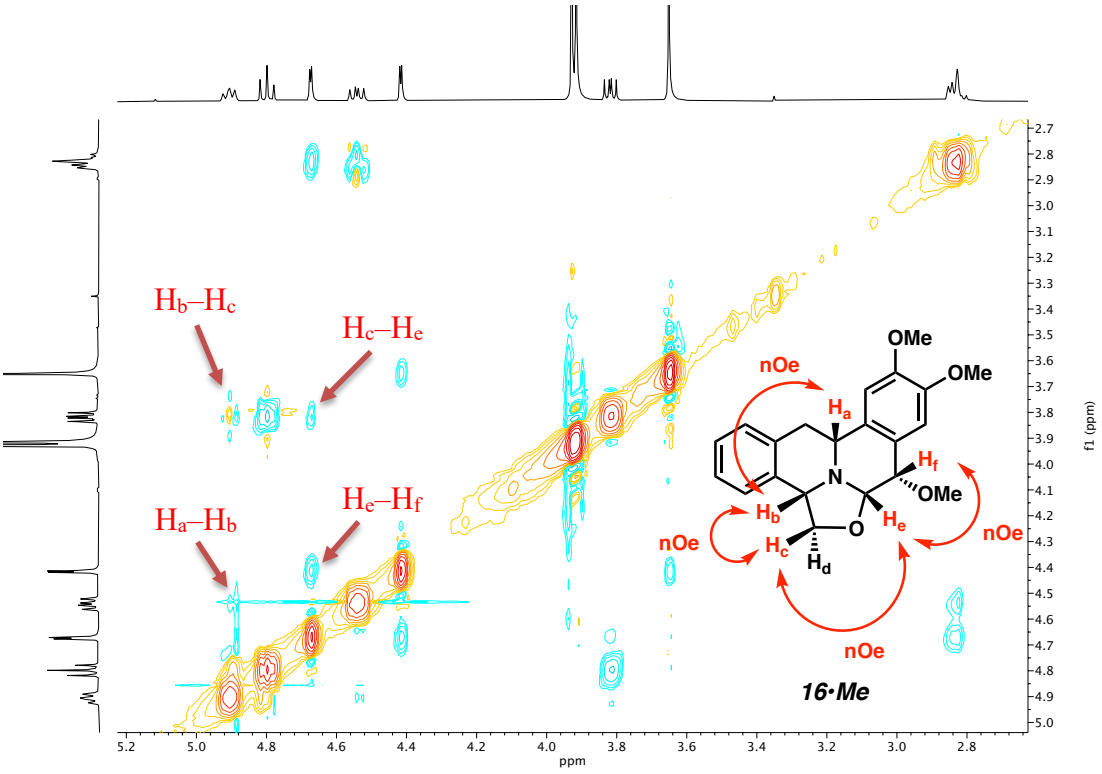


8l ***16***

To a 1-dram vial equipped with a stir bar was added tetrahydroisoquinoline **8l** (10.0 mg, 0.033 mmol) in 1,2-dichloroethane (0.5 mL, 0.07 M). 2,2-Dimethoxyacetaldehyde solution (60 wt% in H_2O, 9.2 μL, 0.061 mmol) was then added and the reaction stirred at room temperature overnight. The reaction was then concentrated under vacuum to afford a yellow oil, which was then used in the next step without further purification.

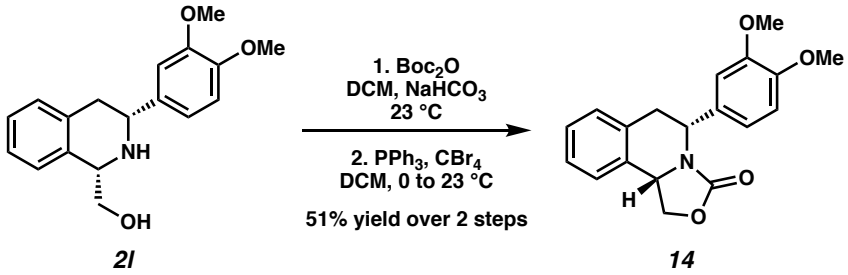
To a 1-dram vial was added the crude product and CH_2Cl_2 (0.5 mL, 0.07 M). Eaton's reagent (0.28 mL, 0.134 mmol) was then added dropwise, and the reaction was stirred for 3 hours. The reaction was then quenched by slow addition of saturated aqueous $NaHCO_3$, diluted with H_2O and extracted with CH_2Cl_2. The collected organic phases were dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by preparative-TLC (100% EtOAc) twice to afford **16** as a white solid as a single diastereomer (4.3 mg, 38% yield over 2 steps): $[\alpha]_D^{25}$ +32.0 (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H), 7.24 – 7.20 (m, 1H), 7.16 (d, *J* = 6.0 Hz, 1H), 7.08 (d, *J* = 6.8 Hz, 1H), 6.97 (s, 1H), 6.69 (s, 1H), 4.89 – 4.82 (m, 1H), 4.79 (t, *J* = 7.8 Hz, 1H), 4.71 (dd, *J* = 8.3, 2.1 Hz, 1H), 4.65 (d, *J* = 2.1 Hz, 1H), 4.47 (dd, *J* = 9.1, 7.0 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.86 (dd, *J* = 7.9, 5.3 Hz, 1H), 2.89 – 2.87 (m, 2H), 2.79 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 148.6, 136.5, 133.1, 130.9, 129.3, 127.3, 127.3, 126.8, 126.6, 113.6, 109.2, 86.7, 74.4, 67.9, 57.3, 56.2, 56.1, 54.2, 31.1; IR (Neat Film, NaCl) 3442, 2918, 1610, 1515, 1464, 1380, 1353, 1270, 1242, 1160, 1117, 1074, 1010, 868, 762, 732, 642 cm^{-1}; HRMS (MM:ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_4$ $[M+H]^+$: 340.1543, found 340.1548.

The stereochemistry of **16** was assigned using diagnostic nOe correlations (highlighted arrows, *vide infra*). Due to the ambiguous nOe correlations observed in **16**, the stereochemistry was determined by derivatizing the hydroxyl group of **16** to the methoxy group.



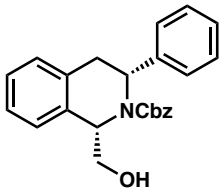
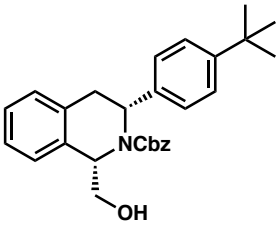
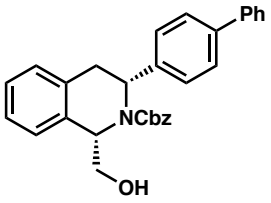
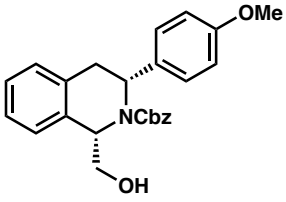
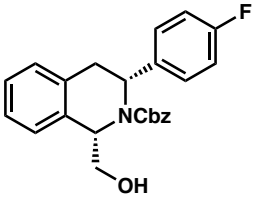
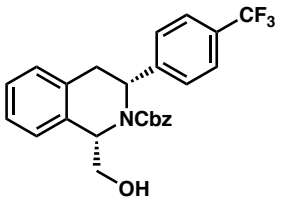
2D NOESY NMR of compound **16•Me**.

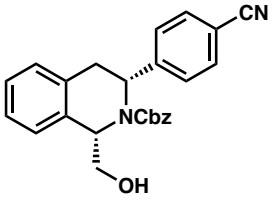
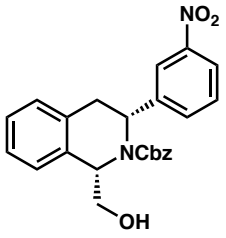
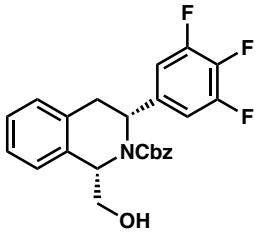
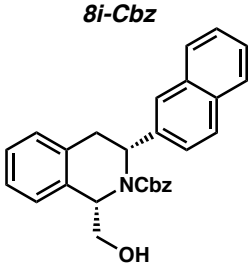
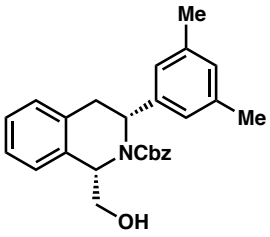
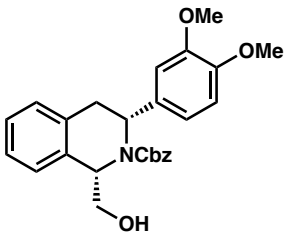
Alternative route to access oxazolidinone 14:

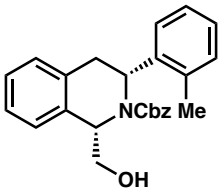
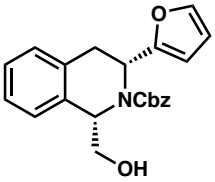
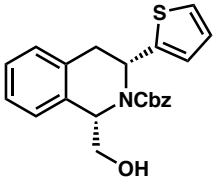
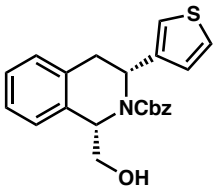
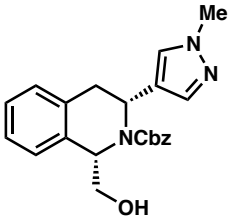
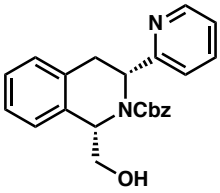


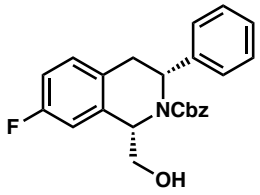
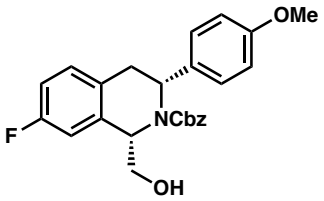
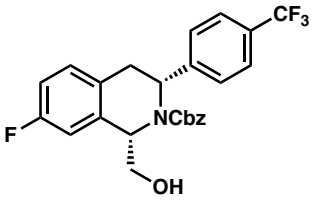
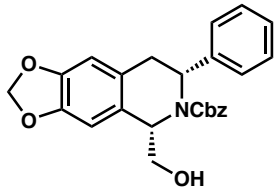
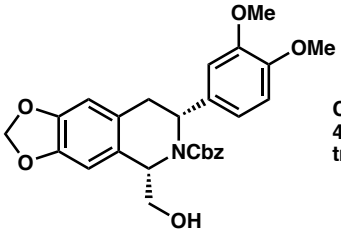
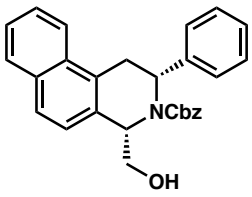
To a 1-dram vial equipped with a stir bar was added Boc_2O (30.0 mg, 0.10 mmol) in CH_2Cl_2 (0.05 mL, 2.5 M). A solution of tetrahydroisoquinoline **2l** (20 mg, 0.07 mmol) in CH_2Cl_2 (0.95 mL, 0.11 M) was then added, followed by 0.1 mL of saturated solution of $NaHCO_3$. The reaction was stirred at room temperature overnight, then concentrated under vacuum to afford an orange oil, which was used in the next step without purification. To a scintillation vial was added the crude product, CBr_4 (50 mg, 0.15 mmol), and CH_2Cl_2 (1.0 mL, 0.1 M), and the reaction was cooled to 0 °C. PPh_3 (39 mg, 0.15 mmol) was then added to the solution, and the reaction was warmed to room temperature. After stirring overnight, the crude reaction was filtered over celite, and rinsed with EtOAc and CH_2Cl_2. The crude product was purified by column chromatography (10% EtOAc in CH_2Cl_2) to afford **14** as a white solid (16.6 mg, 51% yield over 2 steps).

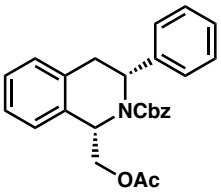
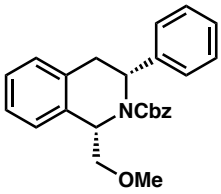
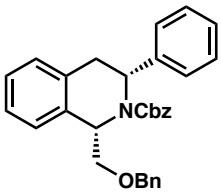
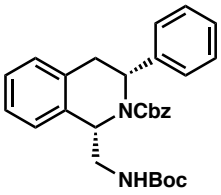
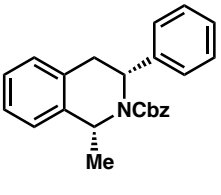
Table S3. Determination of Enantiomeric Excess

entry	compound	SFC analytic conditions	ee (%)
1	 ***8a-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 2.34, minor 4.02**	**92**
2	 ***8b-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 1.81, minor 2.73**	**91**
3	 ***8c-Cbz***	**Chiracel AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 4.08, minor 5.18**	**92**
4	 ***8d-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 2.5 mL/min t_R (min) major 2.59, minor 3.61**	**92**
5	 ***8e-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 2.5 mL/min t_R (min) major 1.93, minor 2.87**	**93**
6	 ***8f-Cbz***	**Chiralpak AD-H, λ = 210 nm 25% IPA/CO_2, 2.5 mL/min t_R (min) major 3.11, minor 5.54**	**92**

entry	compound	SFC analytic conditions	ee (%)
7	 ***8g-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 2.03, minor 3.33**	**82**
8	 ***8h-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 2.45, minor 3.23**	**86**
9	 ***8i-Cbz***	**Chiracel AD-H, λ = 210 nm 40% IPA/CO_2, 2.5 mL/min t_R (min) major 1.67, minor 2.20**	**89**
10	 ***8j-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 3.61, minor 5.81**	**95**
11	 ***8k-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 1.95, minor 3.02**	**92**
12	 ***8l-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 2.28, minor 2.93**	**88**

entry	compound	SFC analytic conditions	ee (%)
13	 ***8m-Cbz***	**Chiralpak AD-H, λ = 210 nm 30% IPA/CO_2, 2.5 mL/min t_R (min) major 5.91, minor 6.39**	**49**
14	 ***8n-Cbz***	**Chiralpak OJ-H, λ = 210 nm 35% IPA/CO_2, 2.5 mL/min t_R (min) major 1.52, minor 1.82**	**92**
15	 ***8o-Cbz***	**Chiracel OJ-H, λ = 210 nm 35% IPA/CO_2, 2.5 mL/min t_R (min) major 2.86, minor 6.02**	**90**
16	 ***8p-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 3.5 mL/min t_R (min) major 3.19, minor 4.05**	**89**
17	 ***8q-Cbz***	**Chiralpak OJ-H, λ = 210 nm 25% IPA/CO_2, 2.5 mL/min t_R (min) minor 1.84, major 2.60**	**87**
18	 ***8r-Cbz***	**Chiralpak OD-H, λ = 210 nm 30% IPA/CO_2, 2.5 mL/min t_R (min) major 2.52, minor 2.79**	**85**

entry	compound	SFC analytic conditions	ee (%)
19	 ***10a-Cbz***	**Chiralpak AD-H, λ = 210 nm 40% IPA/CO_2, 2.5 mL/min t_R (min) major 2.56, minor 3.04**	**93**
20	 ***10b-Cbz***	**Chiralpak OJ-H, λ = 210 nm 30% IPA/CO_2, 2.5 mL/min t_R (min) major 1.93, minor 2.42**	**90**
21	 ***10c-Cbz***	**Chiracel AD-H, λ = 210 nm 20% IPA/CO_2, 2.5 mL/min t_R (min) major 3.93, minor 4.46**	**94**
22	 ***10d-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 2.5 mL/min t_R (min) major 5.00, minor 7.22**	**58**
23	 ***10e-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 2.5 mL/min t_R (min) major 3.89, minor 5.16**	**54**
24	 ***10f-Cbz***	**Chiralpak AD-H, λ = 210 nm 45% IPA/CO_2, 2.5 mL/min t_R (min) major 5.31, minor 10.01**	**82**

entry	compound	SFC analytic conditions	ee (%)
25	 ***12a-Cbz***	**Chiralpak OJ-H, λ = 210 nm 20% IPA/CO_2, 2.5 mL/min t_R (min) major 3.32, minor 3.93**	**86**
26	 ***12b-Cbz***	**Chiracel OD-H, λ = 210 nm 20% IPA/CO_2, 2.5 mL/min t_R (min) major 4.82, minor 5.25**	**89**
27	 ***12c-Cbz***	**Chiralpak OD-H, λ = 210 nm 25% IPA/CO_2, 2.5 mL/min t_R (min) major 5.66, minor 6.38**	**88**
28	 ***12d-Cbz***	**Chiralpak AD-H, λ = 210 nm 40% IPA/CO_2, 2.5 mL/min t_R (min) major 1.41, minor 1.76**	**90**
29	 ***12e-Cbz***	**Chiralpak AS-H, λ = 210 nm 20% IPA/CO_2, 3.5 mL/min t_R (min) major 2.16, minor 2.62**	**90**

X-Ray Crystal Structure Data for Hydrogenated Product 8p

The tetrahydroisoquinoline product **8p** (87% ee) was crystallized by slow evaporation from chloroform at 23 °C to provide crystals suitable for X-ray analysis.

Compound d19110 crystallizes in the monoclinic space group $P2_1$(#4) with one molecule in the asymmetric unit. The S atom and one C atom were disordered 60:40; the anisotropic displacement parameters of each of the C S bonded pairs were constrained to be the same

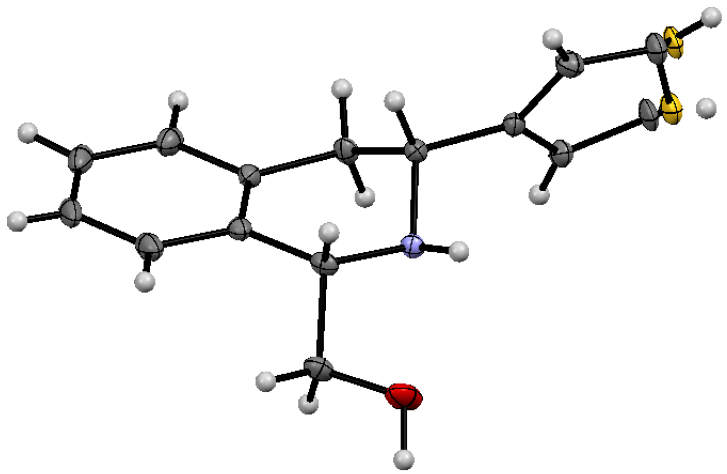


Table S4. Crystal data and structure refinement for d19110.

Identification code	d19110	
Empirical formula	C14 H15 N O S	
Formula weight	245.33	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.3309(19) Å	a= 90°
	b = 6.6556(18) Å	b= 96.337(8)°
	c = 10.916(3) Å	g = 90°
Volume	601.6(3) Å^3	
Z	2	
Density (calculated)	1.354 g/cm^3	
Absorption coefficient	0.251 mm^{-1}	
F(000)	260	
Crystal size	0.38 x 0.17 x 0.08 mm^3	
Theta range for data collection	1.877 to 35.613°.	
Index ranges	-13 £ h £ 13, -10 £ k £ 10, -17 £ l £ 17	

Reflections collected	25734
Independent reflections	5228 [R(int) = 0.0337]
Completeness to theta = 25.242°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.9299
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5228 / 1 / 209
Goodness-of-fit on F^2	1.058
Final R indices [I>2sigma(I)]	R1 = 0.0383, wR2 = 0.0909
R indices (all data)	R1 = 0.0484, wR2 = 0.0960
Absolute structure parameter [Flack]	0.04(2)
Absolute structure parameter [Hooft]	0.03(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.457 and -0.227 e.$Å^{-3}$

Table S5. Atomic coordinates (x 10^5), equivalent isotropic displacement parameters ($Å^2$x 10^4), and population for d19110. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)	pop
S(1)	-1782(9)	10112(13)	8554(8)	192(2)	0.61(1)
S(1A)	-12835(17)	26880(20)	15351(16)	200(4)	0.40(1)
O(1)	46731(15)	90530(20)	2239(13)	250(3)	1
N(1)	38190(14)	60130(20)	16462(10)	126(2)	1
C(1)	31520(15)	47500(20)	25761(12)	119(2)	1
C(2)	45361(17)	34360(20)	31317(14)	146(2)	1
C(3)	59104(16)	47440(20)	36870(12)	135(2)	1
C(4)	69583(19)	40430(30)	46858(14)	193(3)	1
C(5)	81732(19)	52630(30)	52519(15)	236(3)	1
C(6)	83610(20)	71900(30)	48189(15)	243(4)	1
C(7)	73300(20)	79110(30)	38302(15)	210(3)	1
C(8)	60916(17)	66970(20)	32554(13)	140(2)	1
C(9)	49394(17)	75610(20)	22155(13)	133(2)	1
C(10)	58373(18)	84320(30)	11976(14)	174(3)	1
C(11)	16954(16)	36170(20)	20222(13)	127(2)	1
C(12)	17083(17)	18760(20)	13110(13)	147(2)	1
C(13)	-10370(60)	29940(90)	16190(50)	192(2)	0.61(1)
C(13A)	1840(80)	11730(130)	9760(70)	200(4)	0.40(1)

C(14)	1166(19)	42160(30)	21889(15)	177(3)	1

Table S6. Bond lengths [Å] and angles [°] for d19110.

S(1)-C(12)	1.6959(16)
S(1)-C(13)	1.755(6)
S(1A)-C(13A)	1.746(9)
S(1A)-C(14)	1.6492(19)
O(1)-H(1)	0.93(3)
O(1)-C(10)	1.419(2)
N(1)-H(1A)	0.90(2)
N(1)-C(1)	1.4732(18)
N(1)-C(9)	1.4799(19)
C(1)-H(1B)	1.03(2)
C(1)-C(2)	1.5193(19)
C(1)-C(11)	1.4985(19)
C(2)-H(2A)	0.98(2)
C(2)-H(2B)	1.00(2)
C(2)-C(3)	1.511(2)
C(3)-C(4)	1.400(2)
C(3)-C(8)	1.396(2)
C(4)-H(4)	0.91(3)
C(4)-C(5)	1.389(2)
C(5)-H(5)	0.93(3)
C(5)-C(6)	1.382(3)
C(6)-H(6)	0.85(3)
C(6)-C(7)	1.388(3)
C(7)-H(7)	0.99(3)
C(7)-C(8)	1.403(2)
C(8)-C(9)	1.517(2)
C(9)-H(9)	0.99(2)
C(9)-C(10)	1.521(2)
C(10)-H(10A)	0.96(3)
C(10)-H(10B)	1.01(3)
C(11)-C(12)	1.395(2)
C(11)-C(14)	1.405(2)
C(12)-C(13A)	1.365(6)
C(12)-H(12)	0.94(2)
C(12)-H(12A)	0.94(2)
C(13)-H(13)	0.91(5)

C(13)-C(14)	1.357(5)
C(13A)-H(13A)	1.04(8)
C(14)-H(14A)	0.90(3)
C(14)-H(14)	0.90(3)

C(12)-S(1)-C(13)	91.08(18)
C(14)-S(1A)-C(13A)	91.0(2)
C(10)-O(1)-H(1)	112.9(17)
C(1)-N(1)-H(1A)	108.6(14)
C(1)-N(1)-C(9)	112.10(10)
C(9)-N(1)-H(1A)	106.4(15)
N(1)-C(1)-H(1B)	110.5(13)
N(1)-C(1)-C(2)	106.04(11)
N(1)-C(1)-C(11)	111.07(11)
C(2)-C(1)-H(1B)	108.3(12)
C(11)-C(1)-H(1B)	106.3(12)
C(11)-C(1)-C(2)	114.61(12)
C(1)-C(2)-H(2A)	112.8(13)
C(1)-C(2)-H(2B)	110.8(13)
H(2A)-C(2)-H(2B)	106(2)
C(3)-C(2)-C(1)	109.66(12)
C(3)-C(2)-H(2A)	108.2(13)
C(3)-C(2)-H(2B)	109.0(13)
C(4)-C(3)-C(2)	120.00(14)
C(8)-C(3)-C(2)	120.42(12)
C(8)-C(3)-C(4)	119.48(14)
C(3)-C(4)-H(4)	117.4(15)
C(5)-C(4)-C(3)	120.85(16)
C(5)-C(4)-H(4)	121.3(15)
C(4)-C(5)-H(5)	120.5(18)
C(6)-C(5)-C(4)	119.70(16)
C(6)-C(5)-H(5)	119.6(18)
C(5)-C(6)-H(6)	122.3(19)
C(5)-C(6)-C(7)	120.17(15)
C(7)-C(6)-H(6)	117.3(19)
C(6)-C(7)-H(7)	122.1(15)
C(6)-C(7)-C(8)	120.68(17)
C(8)-C(7)-H(7)	117.2(15)
C(3)-C(8)-C(7)	119.12(14)
C(3)-C(8)-C(9)	121.50(12)

C(7)-C(8)-C(9)	119.33(14)
N(1)-C(9)-C(8)	111.60(12)
N(1)-C(9)-H(9)	108.5(13)
N(1)-C(9)-C(10)	107.26(12)
C(8)-C(9)-H(9)	111.2(13)
C(8)-C(9)-C(10)	111.69(12)
C(10)-C(9)-H(9)	106.4(14)
O(1)-C(10)-C(9)	107.91(12)
O(1)-C(10)-H(10A)	111.9(15)
O(1)-C(10)-H(10B)	111.6(13)
C(9)-C(10)-H(10A)	109.0(14)
C(9)-C(10)-H(10B)	110.1(14)
H(10A)-C(10)-H(10B)	106(2)
C(12)-C(11)-C(1)	125.94(13)
C(12)-C(11)-C(14)	111.87(13)
C(14)-C(11)-C(1)	122.19(13)
S(1)-C(12)-H(12)	119.9(15)
C(11)-C(12)-S(1)	112.40(11)
C(11)-C(12)-H(12)	127.7(16)
C(11)-C(12)-H(12A)	127.7(16)
C(13A)-C(12)-C(11)	111.7(4)
C(13A)-C(12)-H(12A)	120.6(16)
S(1)-C(13)-H(13)	105(3)
C(14)-C(13)-S(1)	111.3(4)
C(14)-C(13)-H(13)	143(3)
S(1A)-C(13A)-H(13A)	105(3)
C(12)-C(13A)-S(1A)	112.0(5)
C(12)-C(13A)-H(13A)	143(4)
S(1A)-C(14)-H(14A)	120.7(15)
C(11)-C(14)-S(1A)	113.35(14)
C(11)-C(14)-H(14A)	125.9(15)
C(11)-C(14)-H(14)	125.9(15)
C(13)-C(14)-C(11)	113.4(3)
C(13)-C(14)-H(14)	120.7(15)

Symmetry transformations used to generate equivalent atoms:

Table S7. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for d19110. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	146(4)	220(4)	204(4)	-44(3)	-7(3)	-76(3)
S(1A)	121(7)	246(7)	223(6)	-49(5)	-15(4)	-92(4)
O(1)	205(6)	302(7)	251(6)	151(5)	60(4)	14(5)
N(1)	133(5)	113(5)	131(5)	14(4)	8(4)	-15(4)
C(1)	109(5)	126(5)	121(5)	0(4)	13(4)	-11(4)
C(2)	129(6)	135(6)	168(6)	39(5)	-7(4)	-20(5)
C(3)	101(5)	182(6)	123(5)	1(5)	14(4)	5(5)
C(4)	157(6)	274(8)	144(6)	12(6)	2(5)	45(5)
C(5)	127(6)	437(10)	143(6)	-57(6)	2(5)	35(6)
C(6)	148(6)	416(11)	167(6)	-123(7)	23(5)	-95(6)
C(7)	191(7)	255(8)	193(6)	-75(6)	54(5)	-94(6)
C(8)	125(5)	173(6)	126(5)	-31(5)	35(4)	-21(5)
C(9)	150(6)	94(5)	161(6)	-5(5)	45(4)	-16(4)
C(10)	171(6)	166(6)	191(6)	30(5)	53(5)	-35(5)
C(11)	124(5)	138(6)	114(5)	5(4)	-2(4)	-20(4)
C(12)	150(6)	141(6)	147(6)	-16(5)	10(4)	-27(5)
C(13)	146(4)	220(4)	204(4)	-44(3)	-7(3)	-76(3)
C(13A)	121(7)	246(7)	223(6)	-49(5)	-15(4)	-92(4)
C(14)	153(6)	197(7)	186(6)	-13(5)	45(5)	-5(5)

Table S8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for d19110.

	x	y	z	U(eq)
H(1)	5130(30)	9700(50)	-410(30)	38
H(1A)	3010(30)	6680(40)	1220(20)	15
H(1B)	2770(20)	5620(40)	3270(20)	14
H(2A)	4220(30)	2540(40)	3780(20)	18
H(2B)	4930(30)	2550(40)	2490(20)	18
H(4)	6740(30)	2820(40)	5010(20)	23
H(5)	8820(30)	4820(50)	5950(20)	28
H(6)	9050(30)	8010(40)	5180(20)	29
H(7)	7390(30)	9310(40)	3530(20)	25
H(9)	4290(30)	8670(40)	2510(20)	16
H(10A)	6490(30)	9530(40)	1520(20)	21
H(10B)	6600(30)	7400(40)	910(20)	21
H(13)	-2130(60)	2800(70)	1480(40)	23
H(13A)	-450(70)	-40(120)	550(60)	24
H(12)	2610(30)	1210(40)	1060(20)	21
H(12A)	2610(30)	1210(40)	1060(20)	21
H(14A)	-150(30)	5310(40)	2600(20)	21
H(14)	-150(30)	5310(40)	2600(20)	21

Table S9. Torsion angles [°] for d19110.

S(1)-C(13)-C(14)-C(11)	0.6(4)
N(1)-C(1)-C(2)-C(3)	58.56(14)
N(1)-C(1)-C(11)-C(12)	78.77(18)
N(1)-C(1)-C(11)-C(14)	-102.09(16)
N(1)-C(9)-C(10)-O(1)	52.73(16)
C(1)-N(1)-C(9)-C(8)	44.46(15)
C(1)-N(1)-C(9)-C(10)	167.09(12)
C(1)-C(2)-C(3)-C(4)	151.33(13)
C(1)-C(2)-C(3)-C(8)	-25.09(17)
C(1)-C(11)-C(12)-S(1)	179.50(12)
C(1)-C(11)-C(12)-C(13A)	178.1(4)
C(1)-C(11)-C(14)-S(1A)	-177.87(13)
C(1)-C(11)-C(14)-C(13)	-179.8(3)
C(2)-C(1)-C(11)-C(12)	-41.36(19)

C(2)-C(1)-C(11)-C(14)	137.77(14)
C(2)-C(3)-C(4)-C(5)	-176.42(14)
C(2)-C(3)-C(8)-C(7)	176.81(13)
C(2)-C(3)-C(8)-C(9)	-0.66(19)
C(3)-C(4)-C(5)-C(6)	-0.5(2)
C(3)-C(8)-C(9)-N(1)	-7.99(18)
C(3)-C(8)-C(9)-C(10)	-128.05(14)
C(4)-C(3)-C(8)-C(7)	0.4(2)
C(4)-C(3)-C(8)-C(9)	-177.09(13)
C(4)-C(5)-C(6)-C(7)	0.7(2)
C(5)-C(6)-C(7)-C(8)	-0.3(2)
C(6)-C(7)-C(8)-C(3)	-0.3(2)
C(6)-C(7)-C(8)-C(9)	177.26(14)
C(7)-C(8)-C(9)-N(1)	174.55(12)
C(7)-C(8)-C(9)-C(10)	54.49(17)
C(8)-C(3)-C(4)-C(5)	0.0(2)
C(8)-C(9)-C(10)-O(1)	175.30(13)
C(9)-N(1)-C(1)-C(2)	-71.23(14)
C(9)-N(1)-C(1)-C(11)	163.67(12)
C(11)-C(1)-C(2)-C(3)	-178.55(11)
C(11)-C(12)-C(13A)-S(1A)	0.4(6)
C(12)-S(1)-C(13)-C(14)	-0.3(4)
C(12)-C(11)-C(14)-S(1A)	1.37(18)
C(12)-C(11)-C(14)-C(13)	-0.6(3)
C(13)-S(1)-C(12)-C(11)	0.0(2)
C(13A)-S(1A)-C(14)-C(11)	-0.9(3)
C(14)-S(1A)-C(13A)-C(12)	0.3(5)
C(14)-C(11)-C(12)-S(1)	0.29(16)
C(14)-C(11)-C(12)-C(13A)	-1.1(4)

Symmetry transformations used to generate equivalent atoms:

Table S10. Hydrogen bonds for d19110 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...N(1)#1	0.93(3)	1.90(3)	2.8310(18)	177(2)

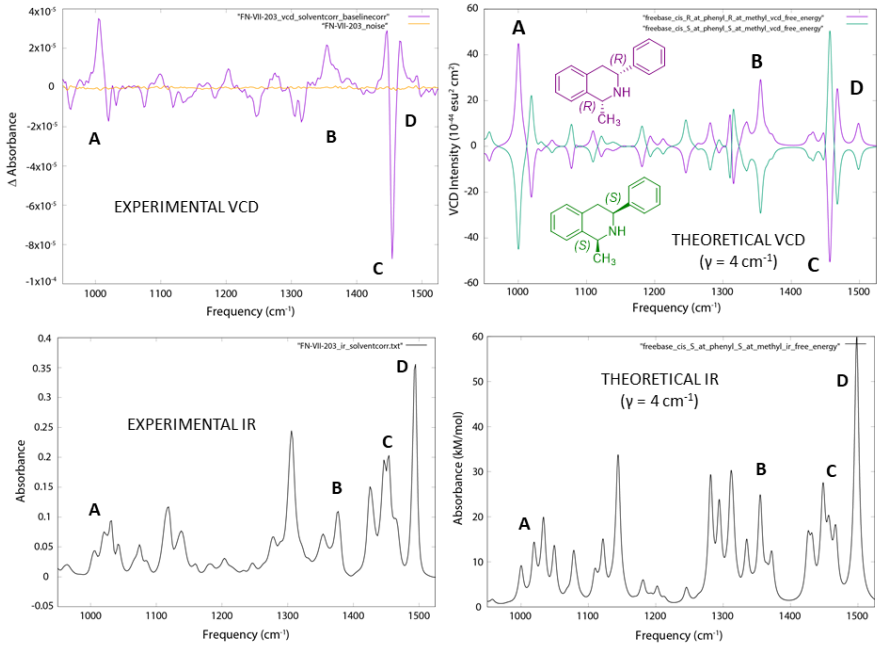
Symmetry transformations used to generate equivalent atoms: #1 -x+1,y+1/2,-z

Determination of Relative and Absolute Configuration of 12e

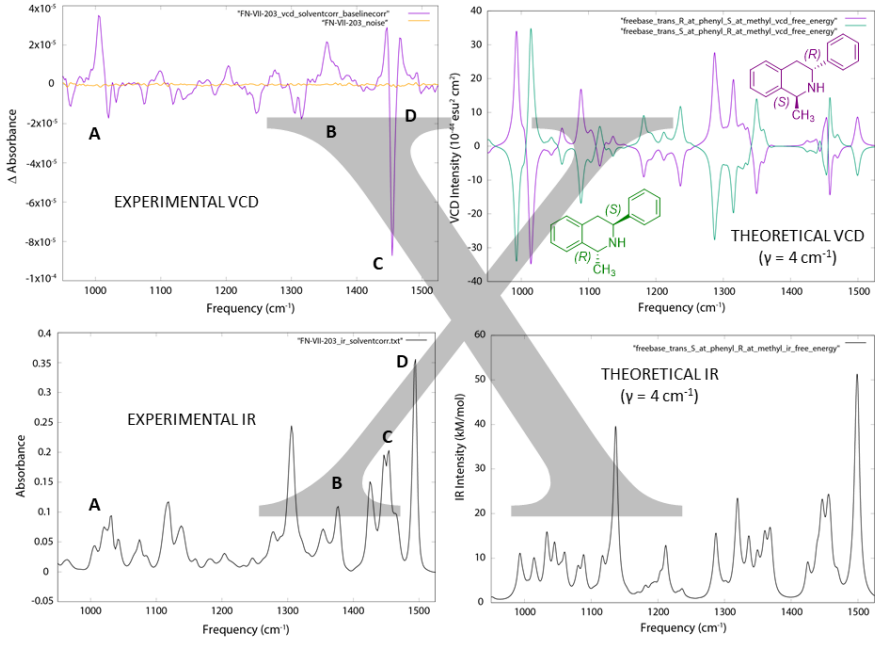
Method 1 – Vibrational Circular Dichroism (VCD)

Experimental Protocol. A solution of **12e** (60 mg/mL) was prepared in $CDCl_3$ and loaded into a front-loading SL-4 cell (International Crystal Laboratories) possessing BaF_2 windows and 100 μm path length. Infrared (IR) and VCD spectra were acquired on a BioTools ChiralIR-2X VCD spectrometer as a set of set of 27 one-hour blocks (27 blocks, 3120 scans per block) in dual PEM mode. A 15-minute acquisition of neat (-)-α-pinene control (separate 75 μm BaF_2 cell) yielded a VCD spectrum in agreement with literature spectra. IR and VCD spectra were background-corrected using a 30-minute block IR acquisition of the empty instrument chamber under gentle N_2 purge, and were solvent corrected using an 8-hour (8 blocks, 3120 scans per block) IR/VCD acquisition of $CDCl_3$ in the same 100 μm BaF_2 cell as used for **12e**. The reported spectra represent the result of block averaging.

Computational Protocol. The arbitrarily chosen (*S*,*S*) stereoisomer of compound **12e** (*(S)* at methyl, *(S)* at phenyl; thus *cis*) was subjected to an exhaustive initial molecular mechanics-based conformational search (MMFF94 force field, 0.08 Å geometric RMSD cutoff, and 30 kcal/mol energy window) as implemented in MOE 2019.0102 (Chemical Computing Group, Montreal, CA). All conformers retained the (*S*) configuration at both centers. Separately, a study involving the *trans* stereoisomer possessing the *(R)* configuration at the methyl group and *(S)* configuration at phenyl was performed in identical fashion, with stereochemical integrity again retained throughout the stochastic conformational search. All MMFF94 conformers within a 10 kcal/mol energy window were then subjected to geometry optimization, harmonic frequency calculation, and VCD rotational strength evaluation using density functional theory. All quantum mechanical calculations first utilized the B3LYP functional, small 6-31G* basis, and IEFPCM model (chloroform solvent) as an initial filter, followed by subsequent optimization using B3PW91 functional, cc-pVTZ basis, and implicit IEFPCM chloroform solvation model on all IEFPCM-B3LYP/6-31G* conformers below 5 kcal/mol. All calculations were performed with the *Gaussian 16* program system (Rev. C.01; Frisch *et al*., Gaussian, Inc., Wallingford, CT). Resultant IEFPCM-B3PW91/cc-pVTZ harmonic frequencies were scaled by 0.98. All structurally unique conformers possessing all positive Hessian eigenvalues were Boltzmann weighted by relative free energy at 298.15 K. The predicted IR and VCD frequencies and intensities of the retained conformers were convolved using Lorentzian line shapes (γ = 4 cm^{-1}) and summed using the respective Boltzmann weights to yield the final predicted IR and VCD spectra of the species described above. The predicted VCD of the corresponding enantiomers were generated by inversion of sign. From a combination of (a) the best overall agreement of (*R,R*)-**12e** with experiment among all of the theoretical spectra in the useful range of the VCD (~ 1000-1450 cm^{-1}, regions **A-D**; see below) coupled with (b) support of this assignment by the agreement between predicted versus measured optical rotation (see Method 2) the absolute configuration of **6e** was established as *cis* and (*R,R*).



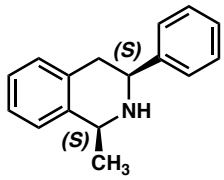
Experimental (left) and computed (right) IR and VCD spectra for the *cis* isomers of **12e**. The better agreement with the *(R,R)* stereoisomer, upon alignment of the achiral IR spectra and correlation to VCD signals, is readily evident.



Experimental (left) and computed (right) IR and VCD spectra for the *trans* isomers of **12e**. The worse agreement with experiment between either of the predicted *trans* stereoisomers, compared to the *cis*- and *(R,R)* stereoisomer above, can be seen. This assertion is further supported to an extent by the optical rotation data below.

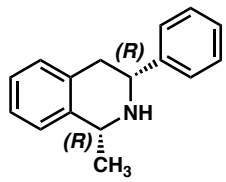
Method 2 – Optical Rotation (OR)

Computational Protocol. The ensemble of unique IEFPCM-B3PW91/cc-pVTZ conformers of **12e** generated in Method 1 above were subjected to optical rotation calculation at 589.0 nm using the B3LYP hybrid density functional, the large and diffuse 6-311++G(2df,2pd) basis set, and the IEFPCM implicit chloroform solvent model. The computed IEFPCM-B3LYP/6-311++G(2df,2pd) optical rotations (weighted by IEFPCM-B3PW91/cc-pVTZ free energies at 298.15 K) along with those resulting from alternatively weighting by either the IEFPCM-B3PW91/cc-pVTZ total energies or IEFPCM-B3LYP/6-311++G(2df,2pd)//IEFPCM-B3PW91/cc-pVTZ total energies are reported in (a)-(d) below.



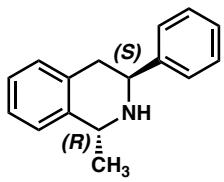
(a)

Predicted optical rotation, weighted by IEFPCM-B3PW91/cc-pVTZ free energies: **-144.5°**
Predicted optical rotations, weighted by IEFPCM-B3PW91/cc-pVTZ total energies: **-144.6°**
Predicted optical rotations, weighted by IEFPCM-B3LYP/6-311++G(2df,2pd)//IEFPCM-B3PW91/cc-pVTZ total energies: **-147.0°**



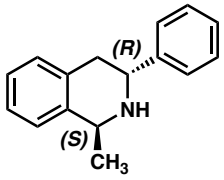
(b)

Predicted optical rotation, weighted by IEFPCM-B3PW91/cc-pVTZ free energies: **+144.5°**
Predicted optical rotations, weighted by IEFPCM-B3PW91/cc-pVTZ total energies: **+144.6°**
Predicted optical rotations, weighted by IEFPCM-B3LYP/6-311++G(2df,2pd)//IEFPCM-B3PW91/cc-pVTZ total energies: **+147.0°**



(c)

Predicted optical rotation, weighted by IEFPCM-B3PW91/cc-pVTZ free energies: **-94.5°**
Predicted optical rotations, weighted by IEFPCM-B3PW91/cc-pVTZ total energies: **-101.0°**
Predicted optical rotations, weighted by IEFPCM-B3LYP/6-311++G(2df,2pd)//IEFPCM-B3PW91/cc-pVTZ total energies: **-100.1°**



(d)

Predicted optical rotation, weighted by IEFPCM-B3PW91/cc-pVTZ free energies: **+94.5°**
Predicted optical rotations, weighted by IEFPCM-B3PW91/cc-pVTZ total energies: **+101.0°**
Predicted optical rotations, weighted by IEFPCM-B3LYP/6-311++G(2df,2pd)//IEFPCM-B3PW91/cc-pVTZ total energies: **+100.1°**

Measured optical rotation: $[\alpha]_D^{25}$ +133.3 (*c* 0.79, $CHCl_3$)

Assuming only that the *sign* of the optical rotation is correctly predicted by theory, given the experimentally measured value of +133.3°, the absolute configuration of **12e** must either be: (i) *(R)* at both chiral centers (and therefore *cis*); or (b) *(S)* at phenyl and *(R)* at methyl (*trans*). Scenario (b) is unlikely, given the wrong (opposite) directionality of the VCD signals in regions **C** and **D** of the experimental spectrum. Scenario (a) also gives rise to the best agreement between the predicted and measured VCD spectra.

The individual relative energies, free energies, and optical rotational signatures of each conformer of the cis and trans stereoisomers are separately provided in the accompanying Microsoft Excel files.

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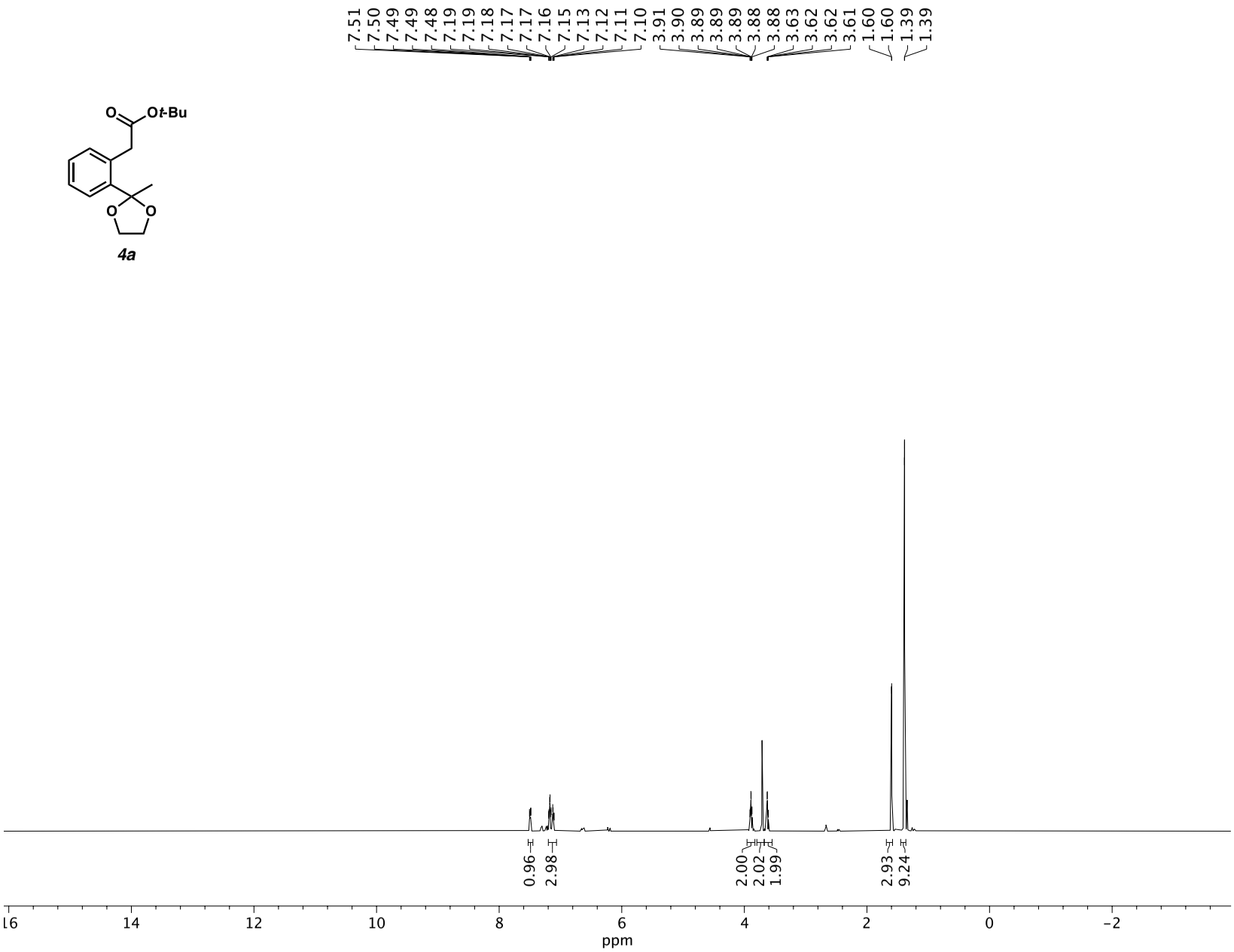
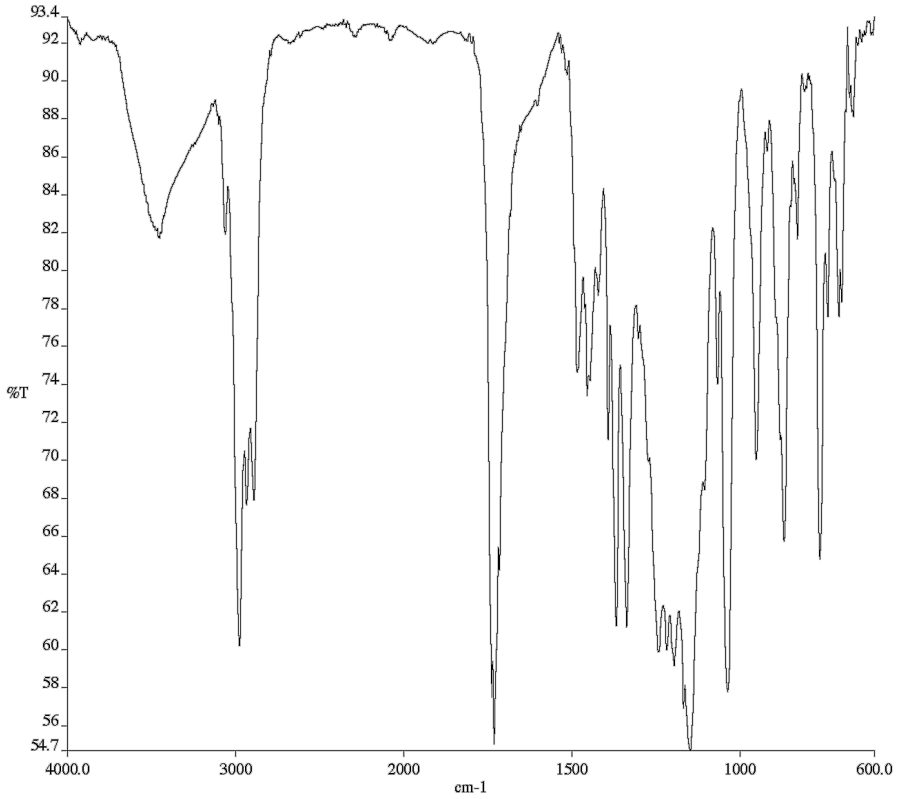
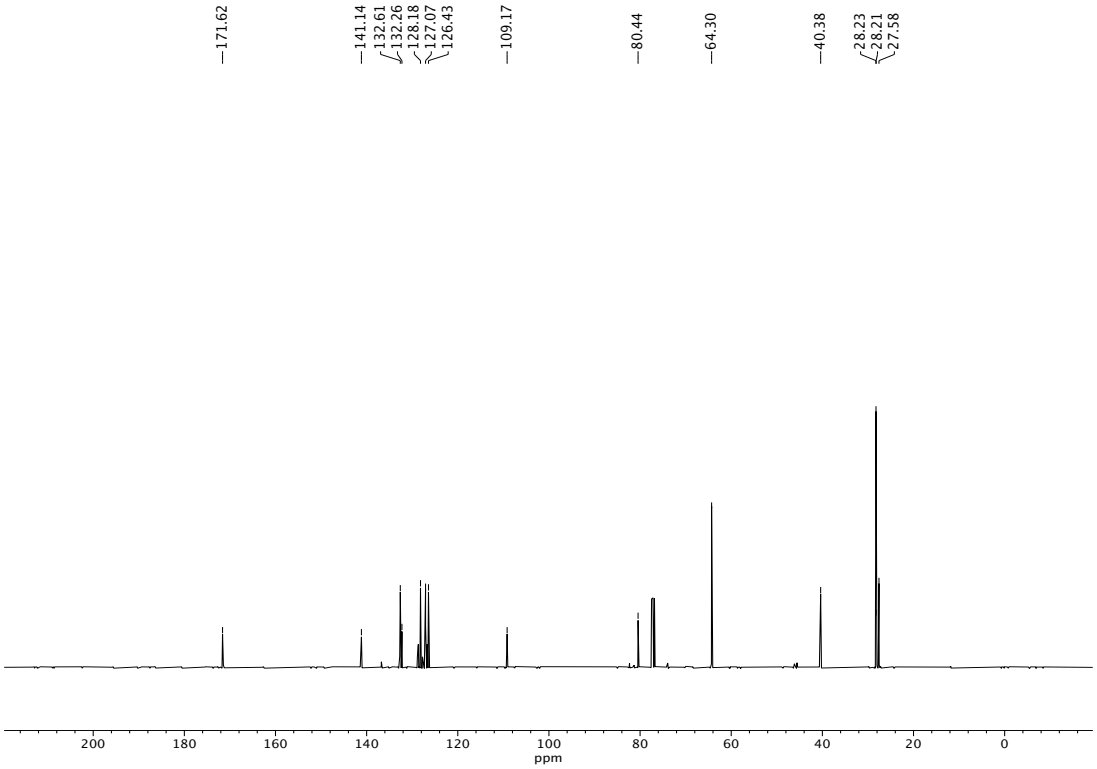


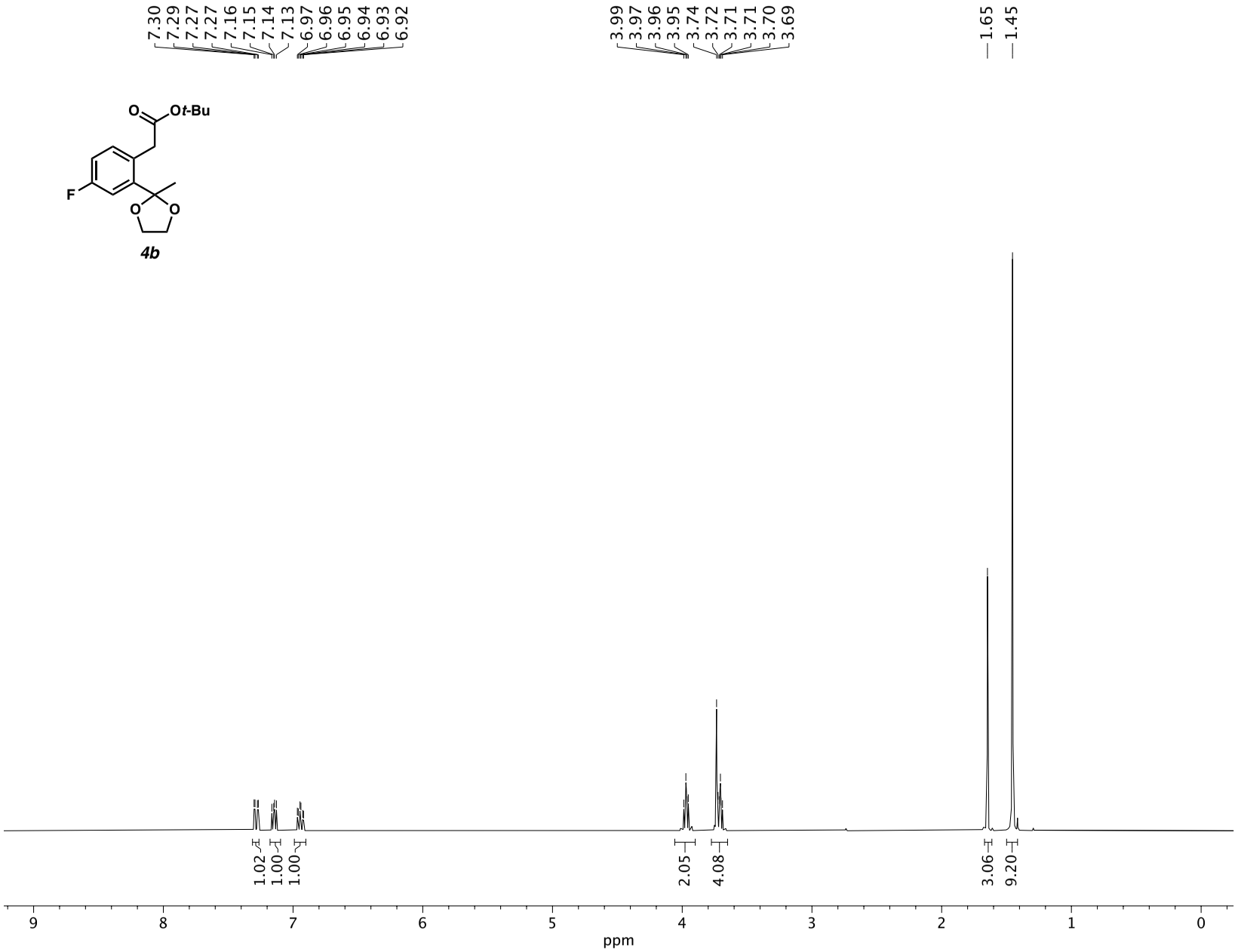
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4a**.



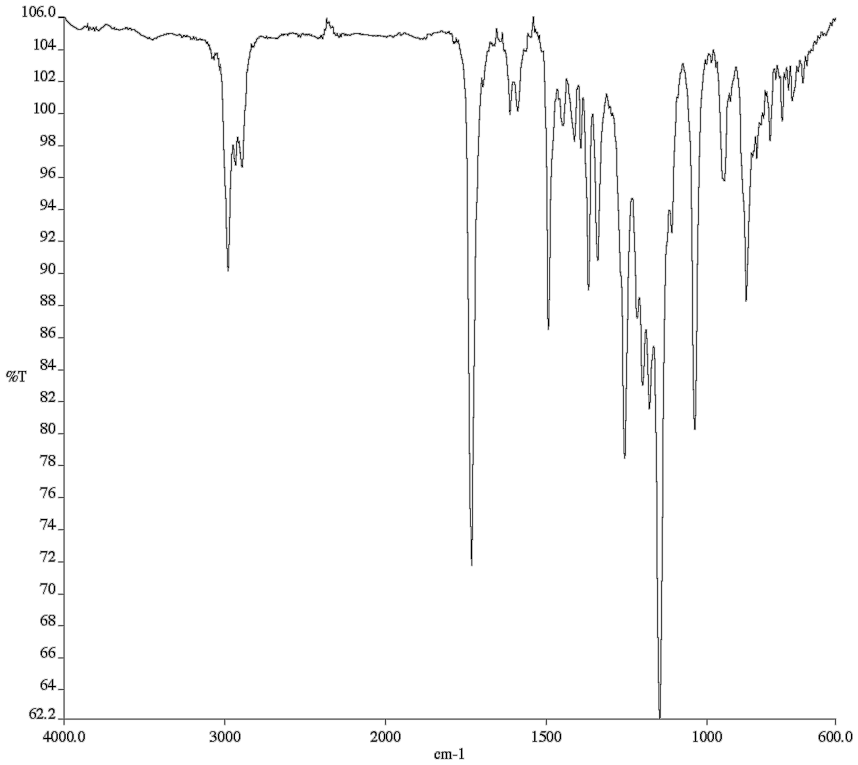
Infrared spectrum (Thin Film, NaCl) of compound **4a**.



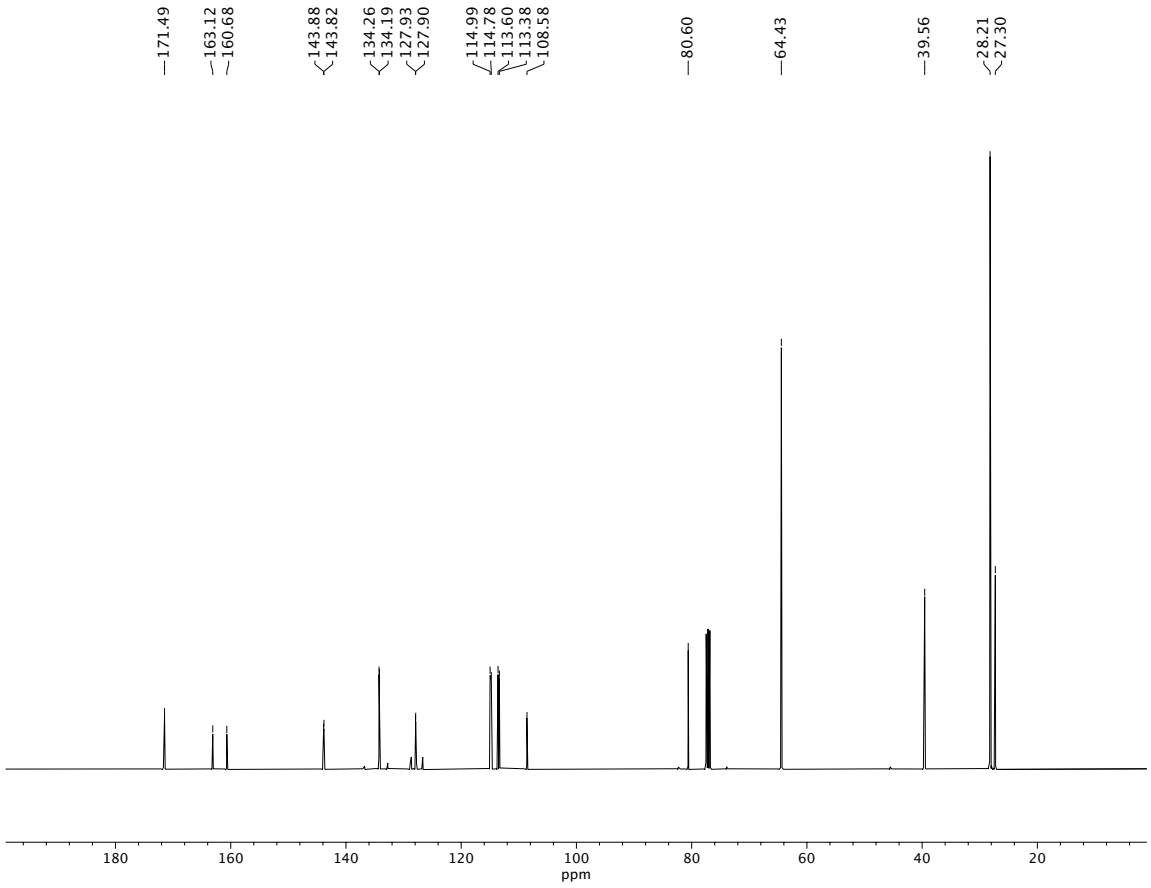
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4a**.



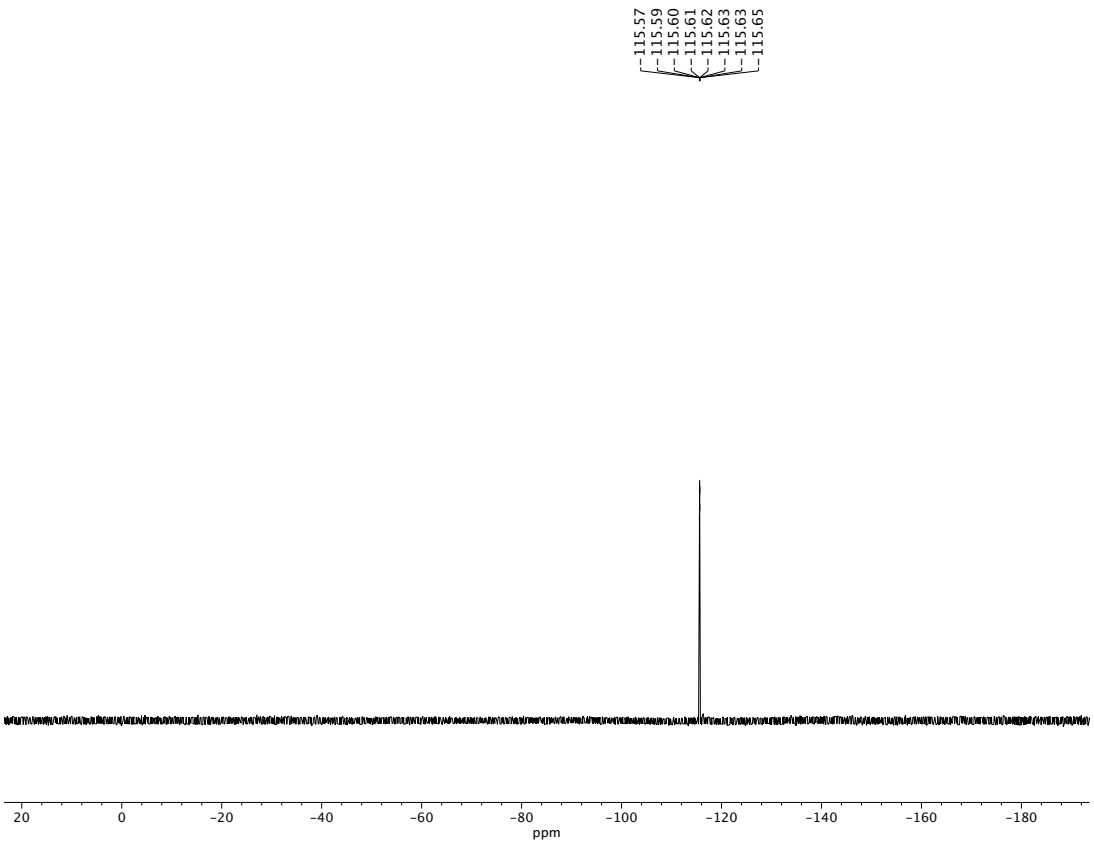
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4b**.



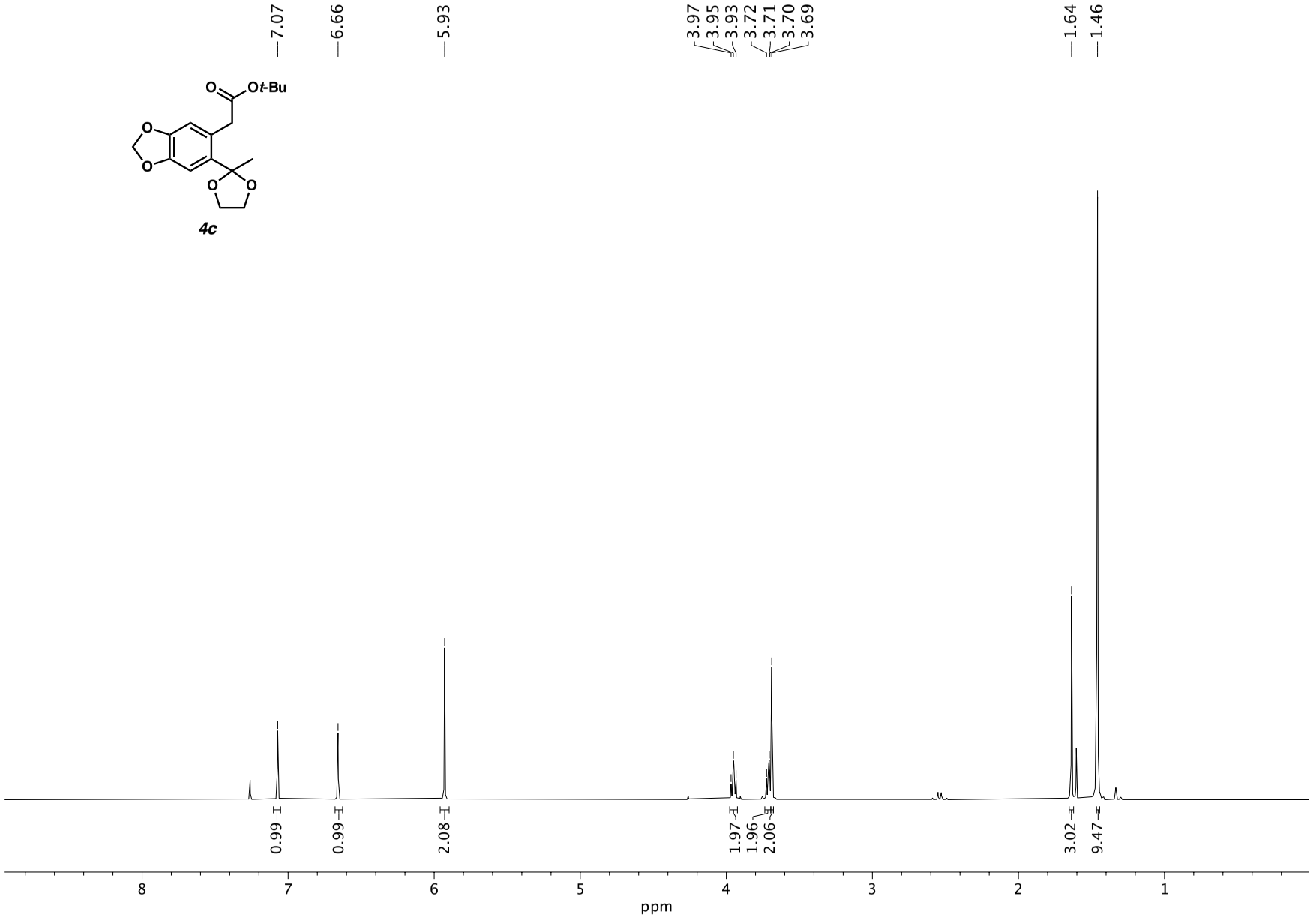
Infrared spectrum (Thin Film, NaCl) of compound **4b**.



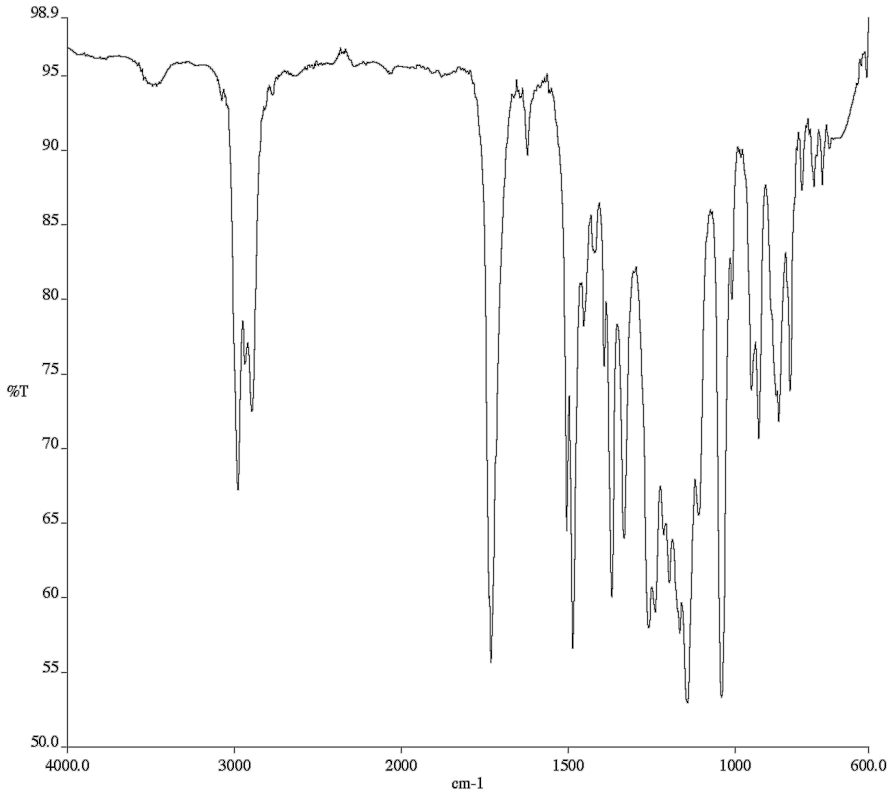
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4b**.



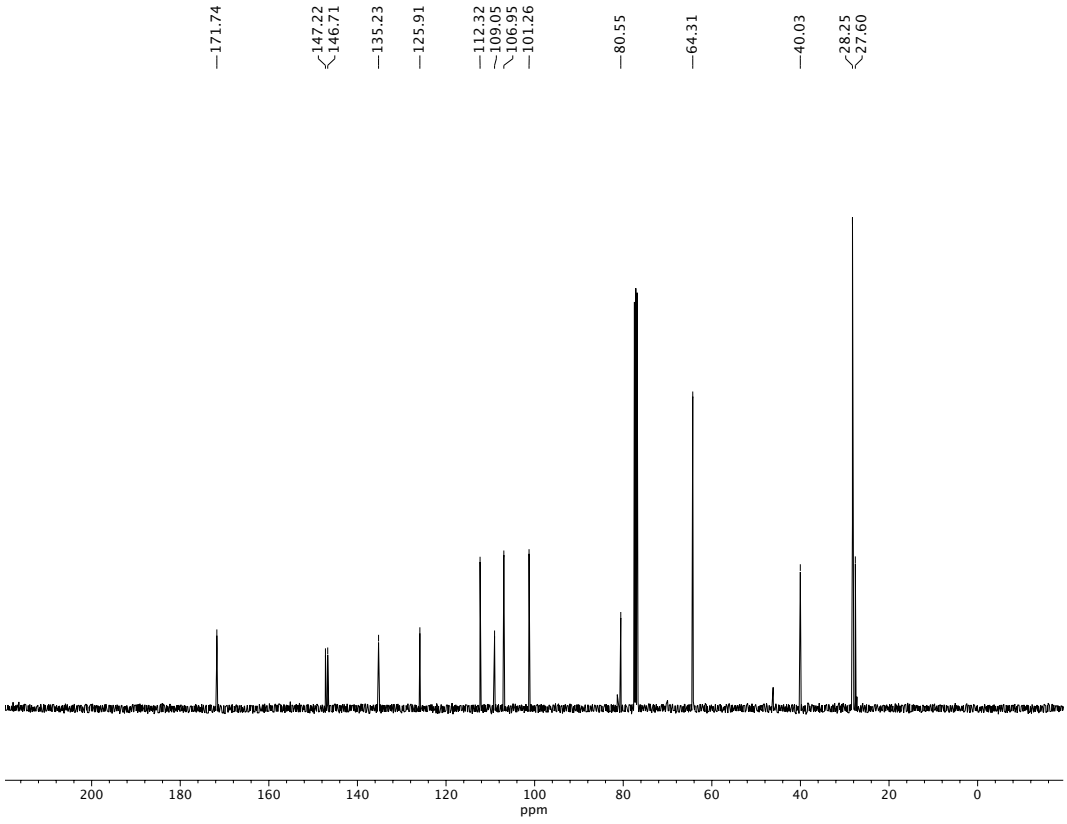
^{19}F NMR (282 MHz, $CDCl_3$) of **4b**.



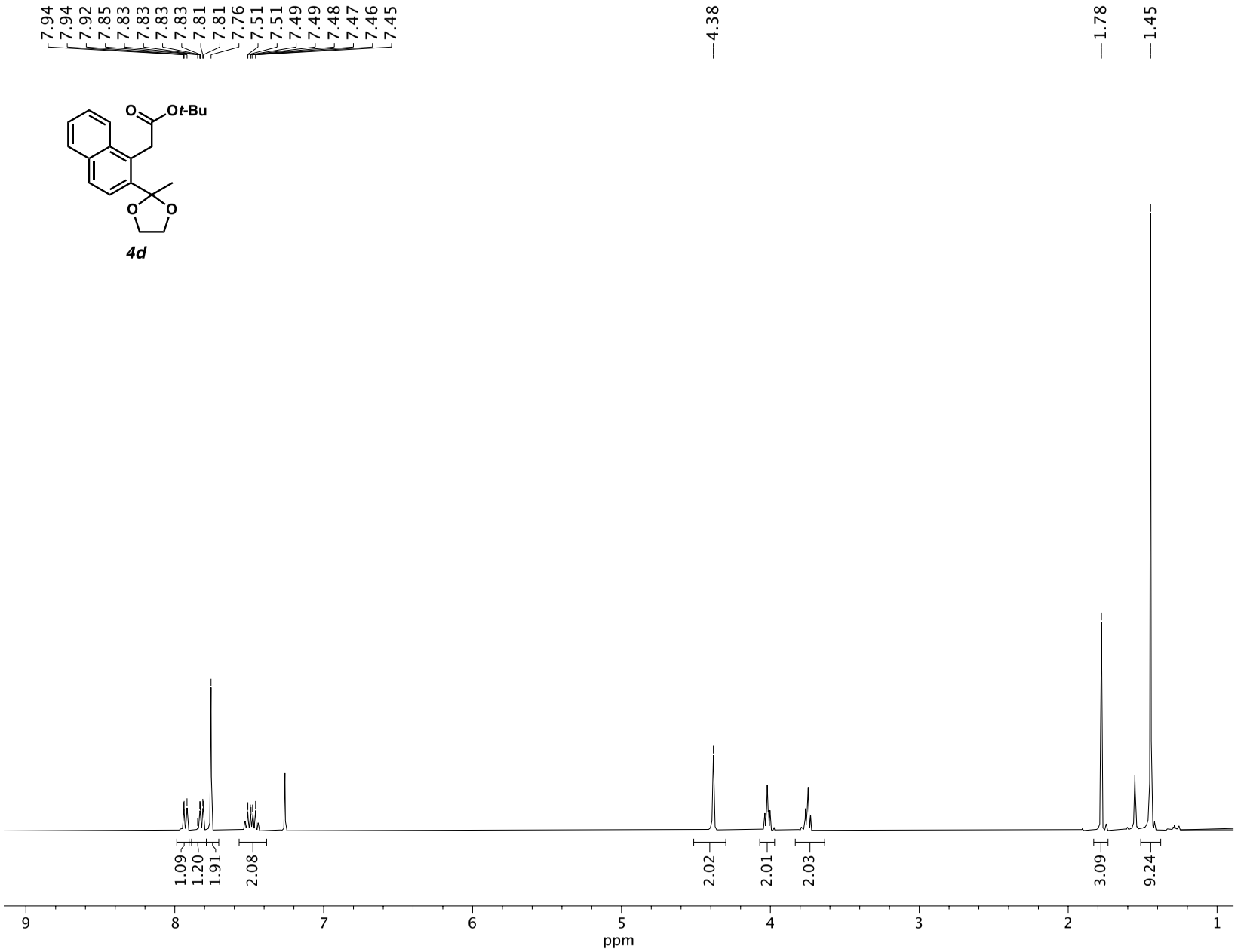
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4c**.



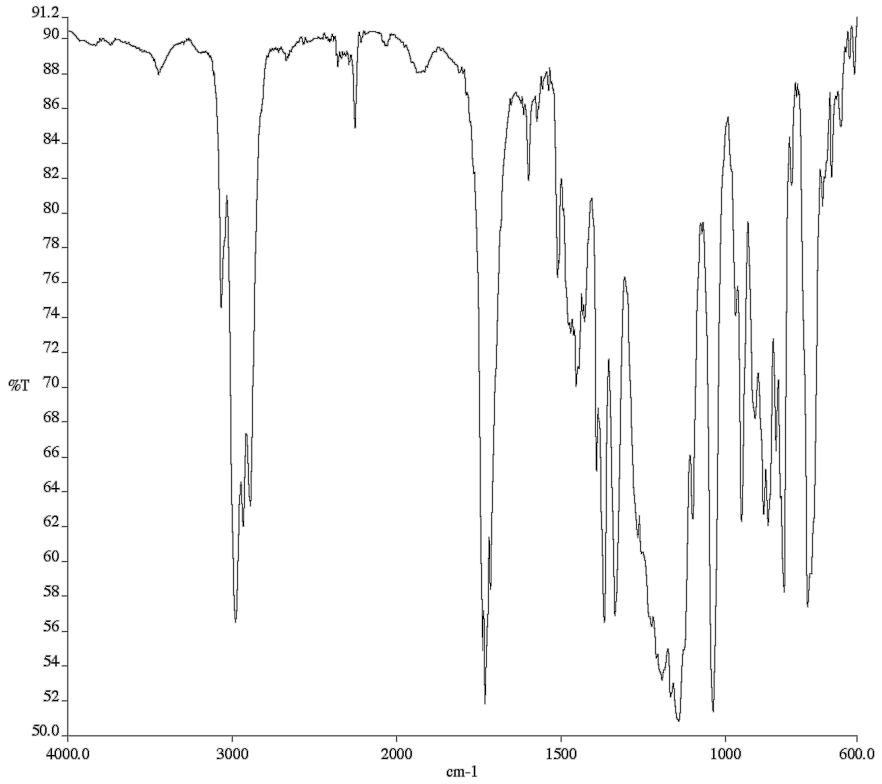
Infrared spectrum (Thin Film, NaCl) of compound **4c**.



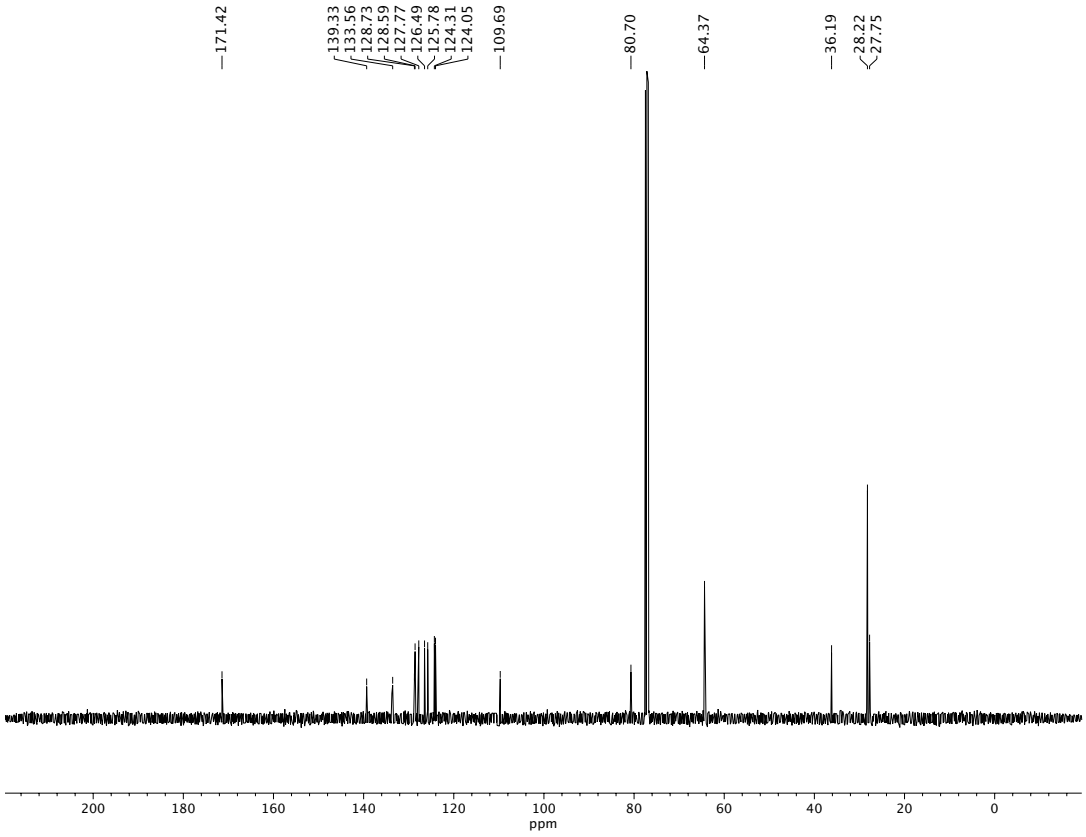
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4c**.



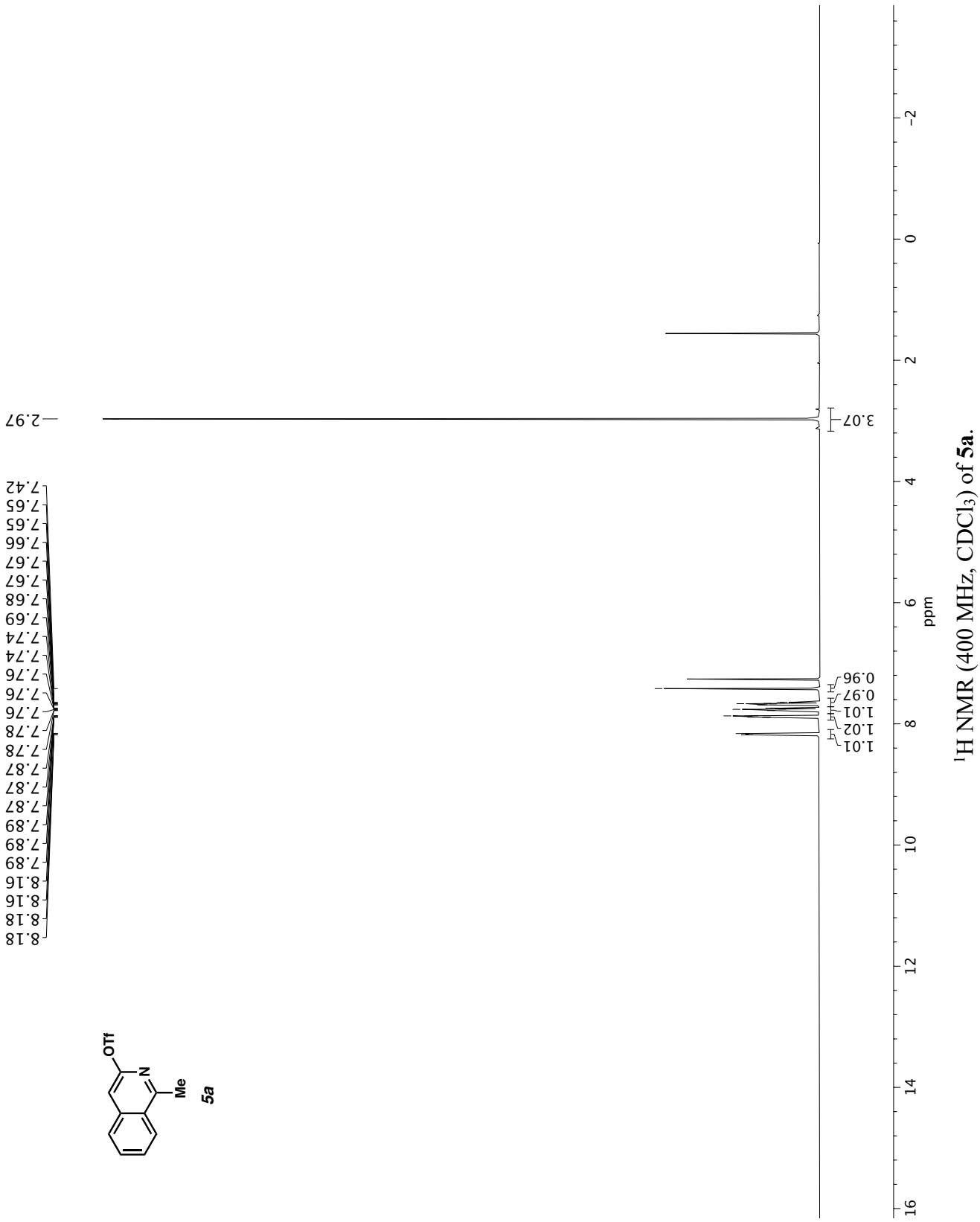
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4d**.



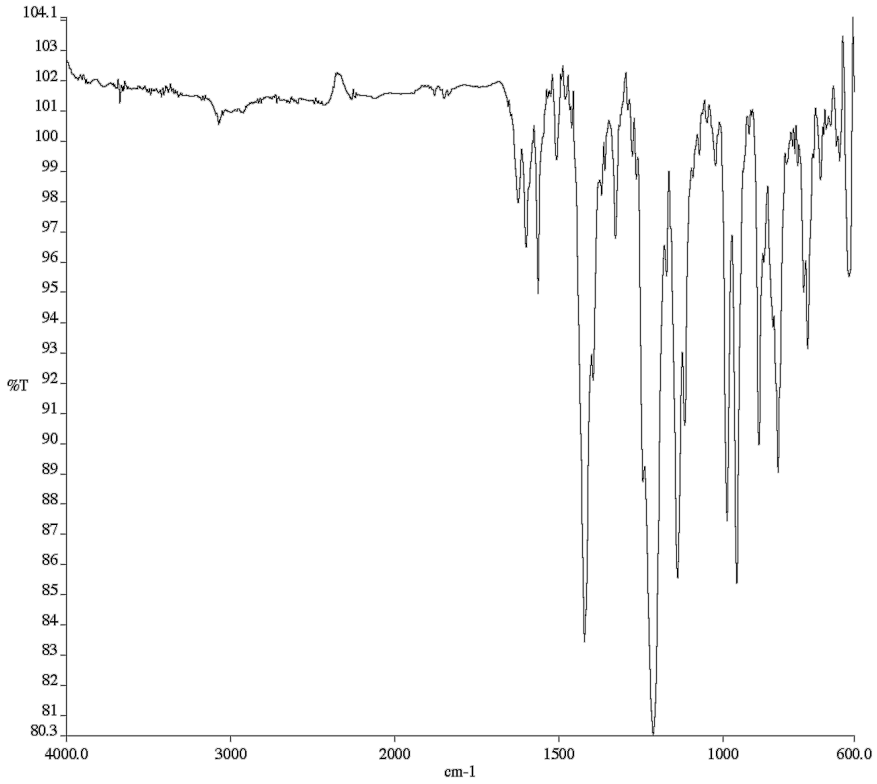
Infrared spectrum (Thin Film, NaCl) of compound **4d**.



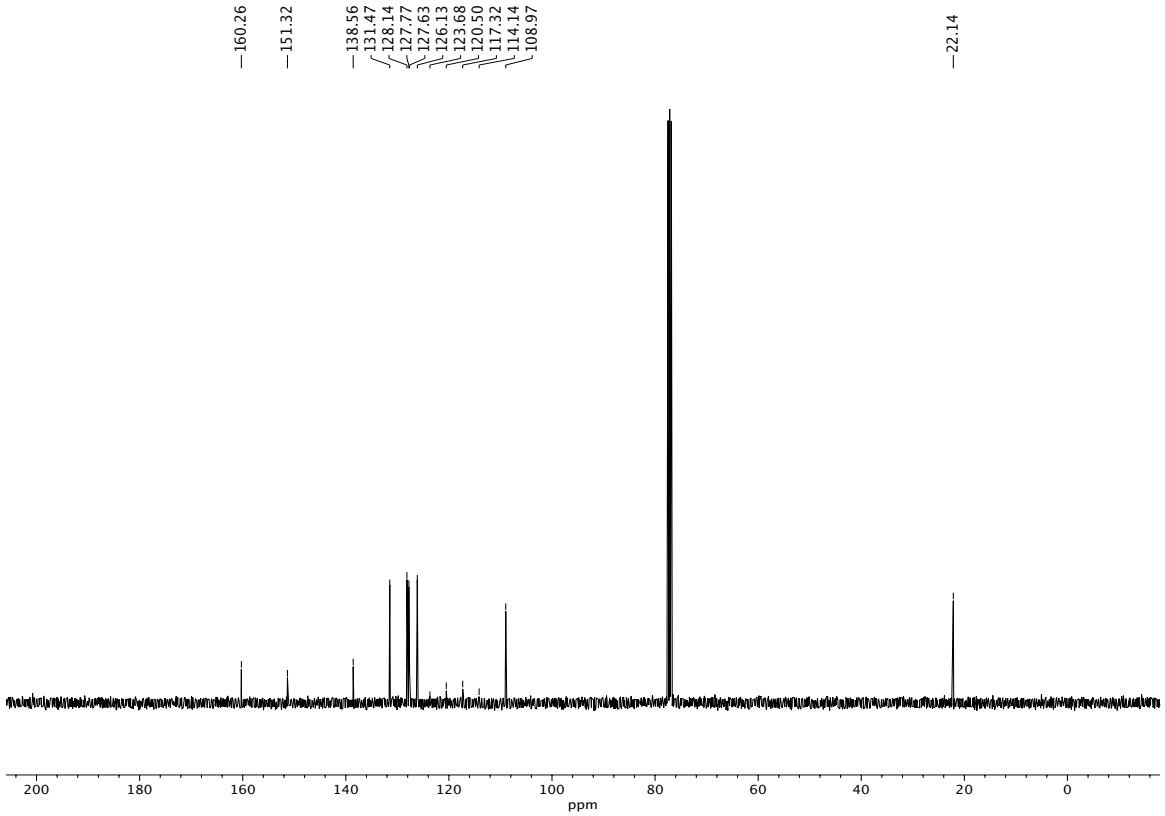
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4d**.



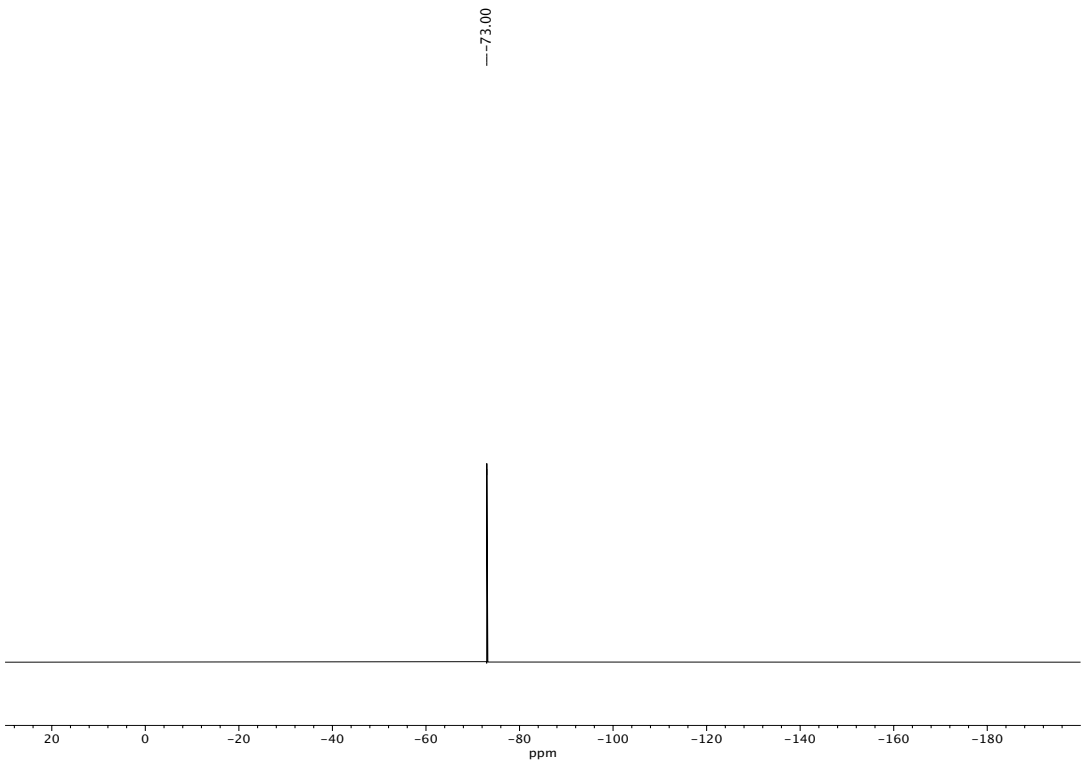
^{1}H NMR (400 MHz, $CDCl_3$) of **5a**.



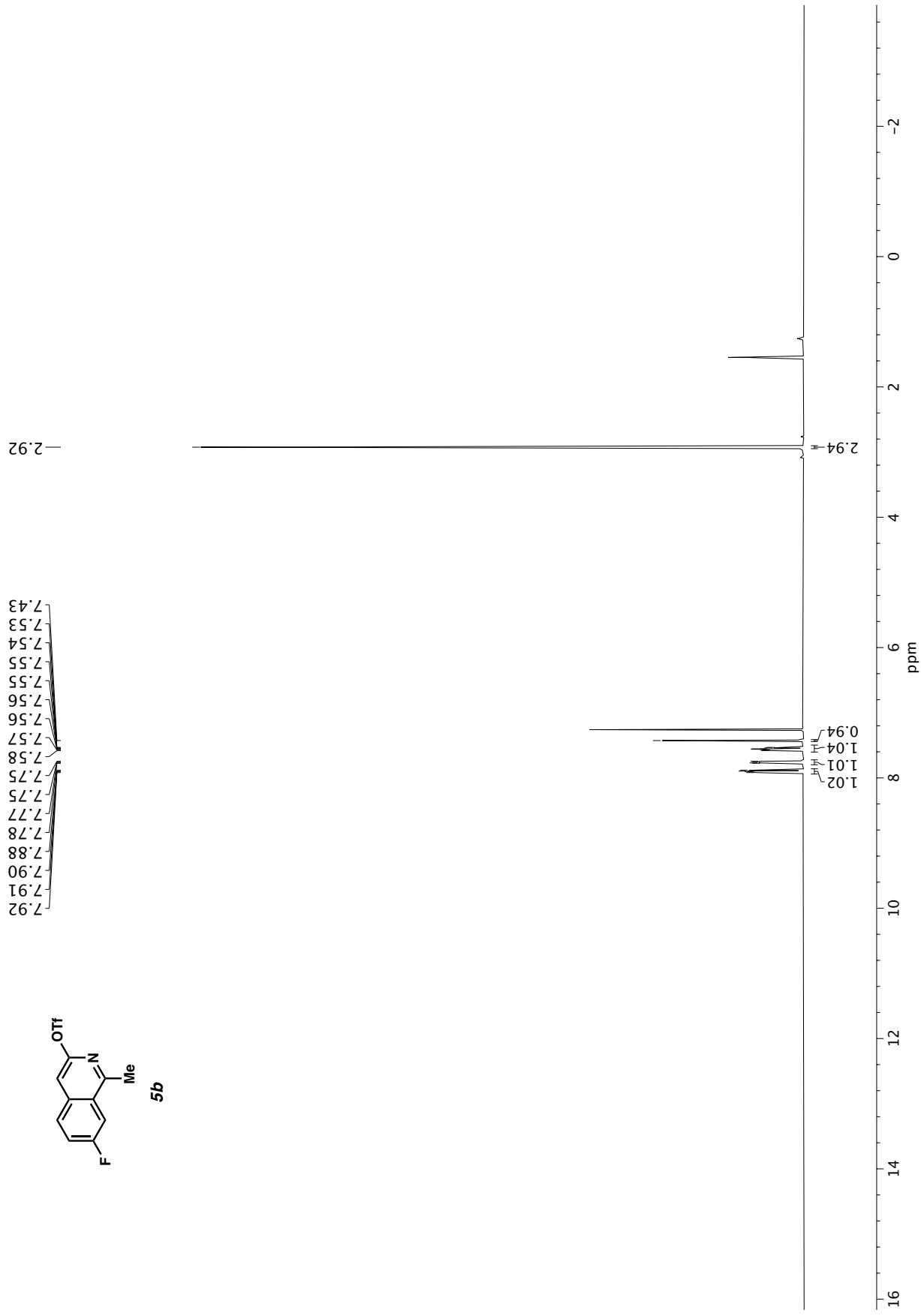
Infrared spectrum (Thin Film, NaCl) of **5a**.



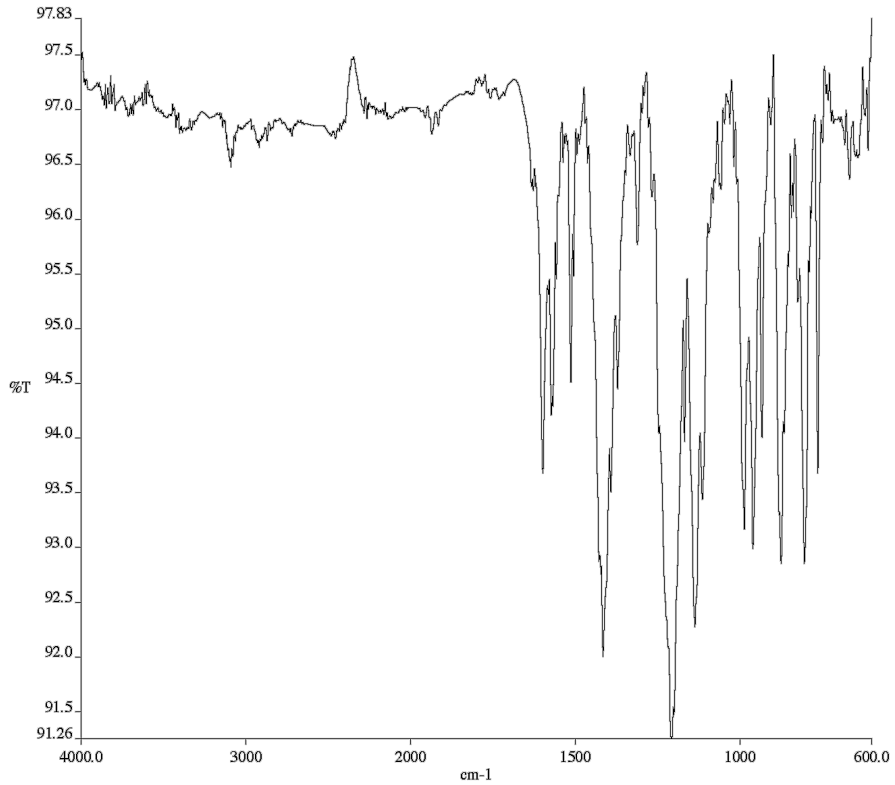
^{13}C NMR (100 MHz, $CDCl_3$) of **5a**.



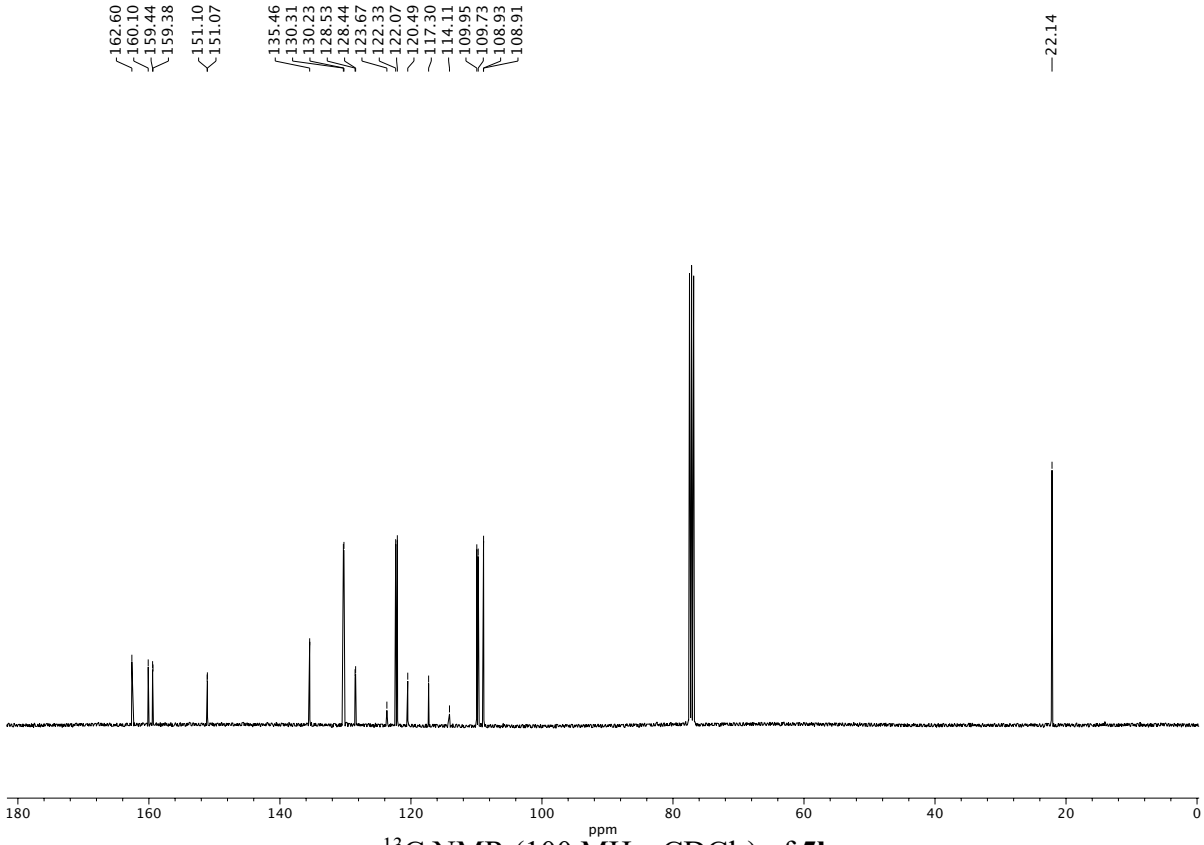
^{19}F NMR (282 MHz, $CDCl_3$) of **5a**.



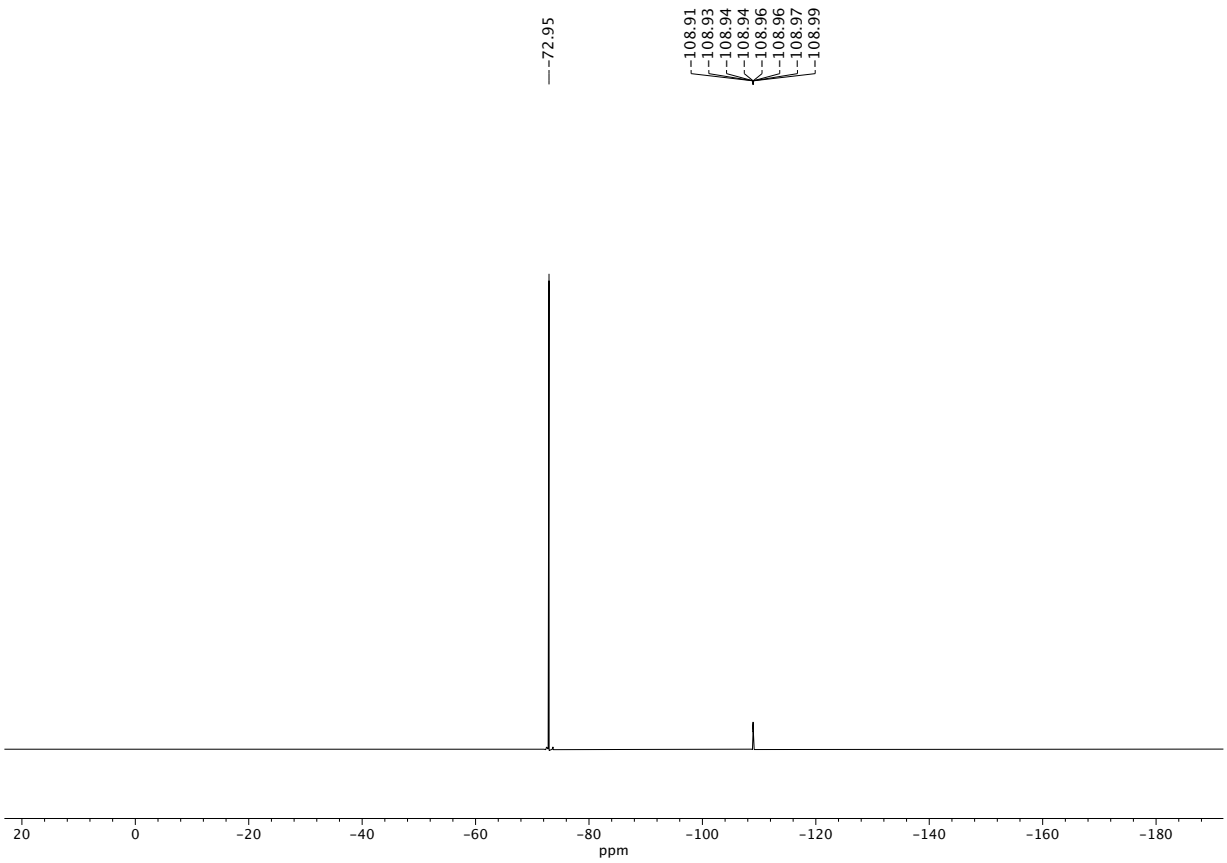
^{1}H NMR (400 MHz, $CDCl_3$) of **5b**.



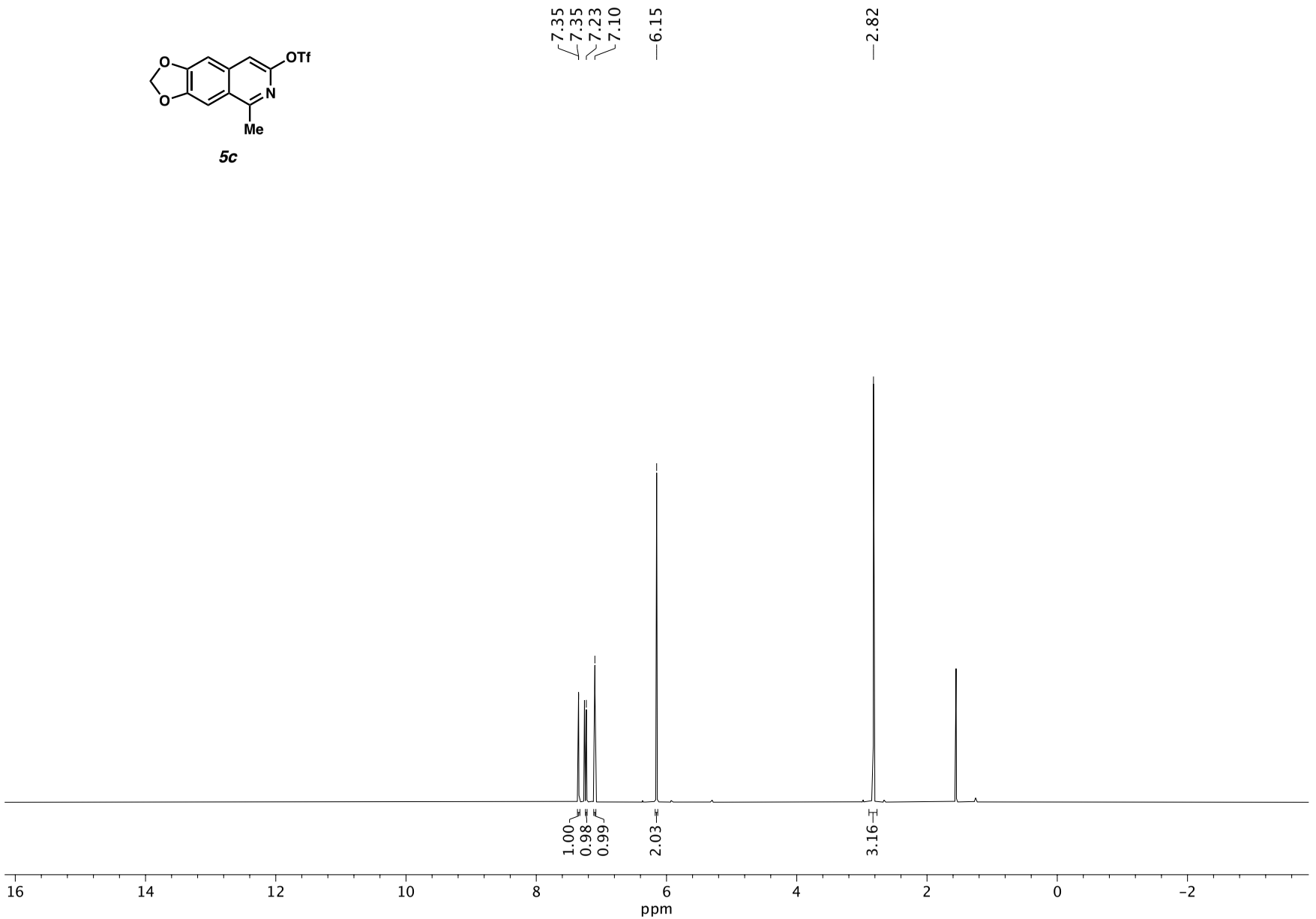
Infrared spectrum (Thin Film, NaCl) of **5b**.



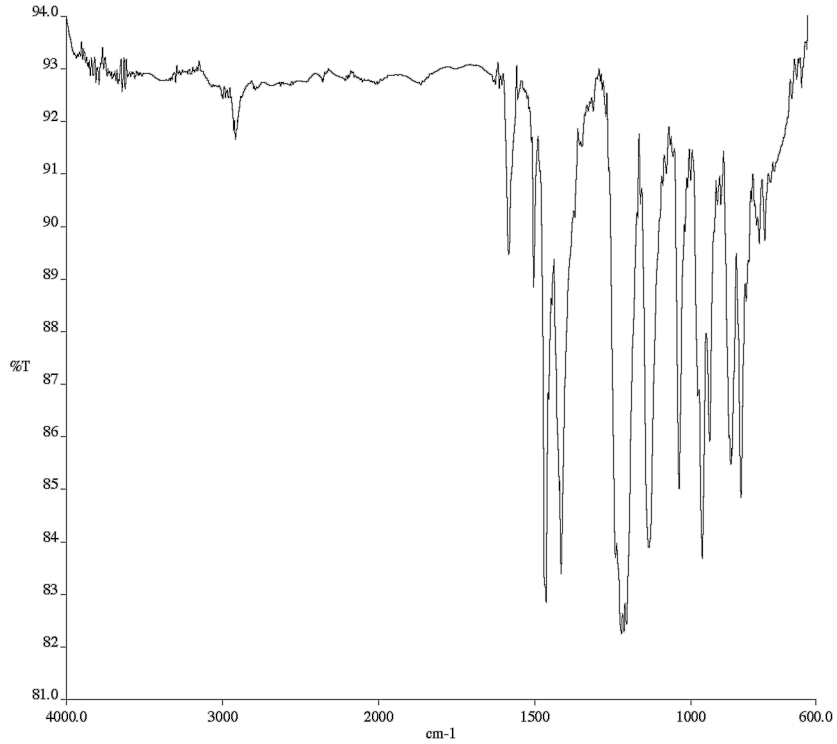
^{13}C NMR (100 MHz, $CDCl_3$) of **5b**.



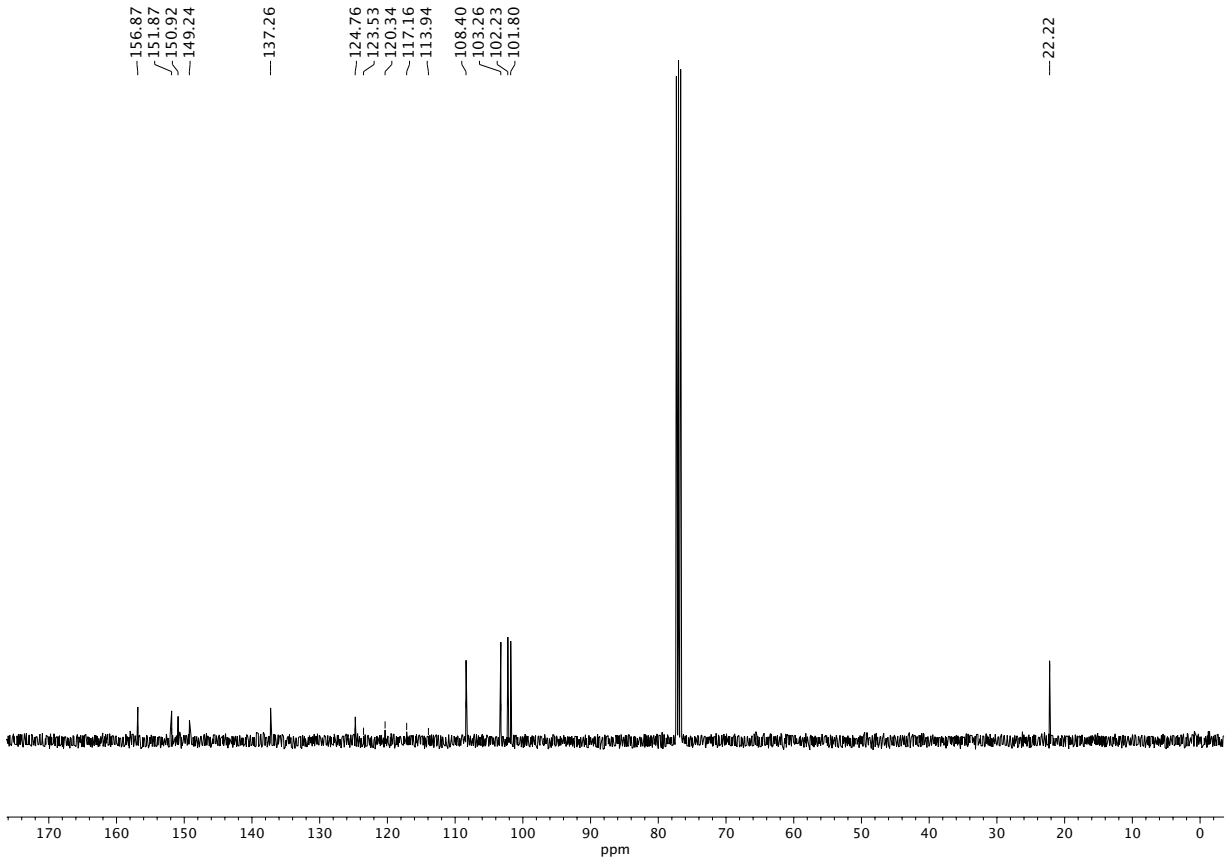
^{19}F NMR (282 MHz, $CDCl_3$) of **5b**.



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



Infrared spectrum (Thin Film, NaCl) of **5c**.



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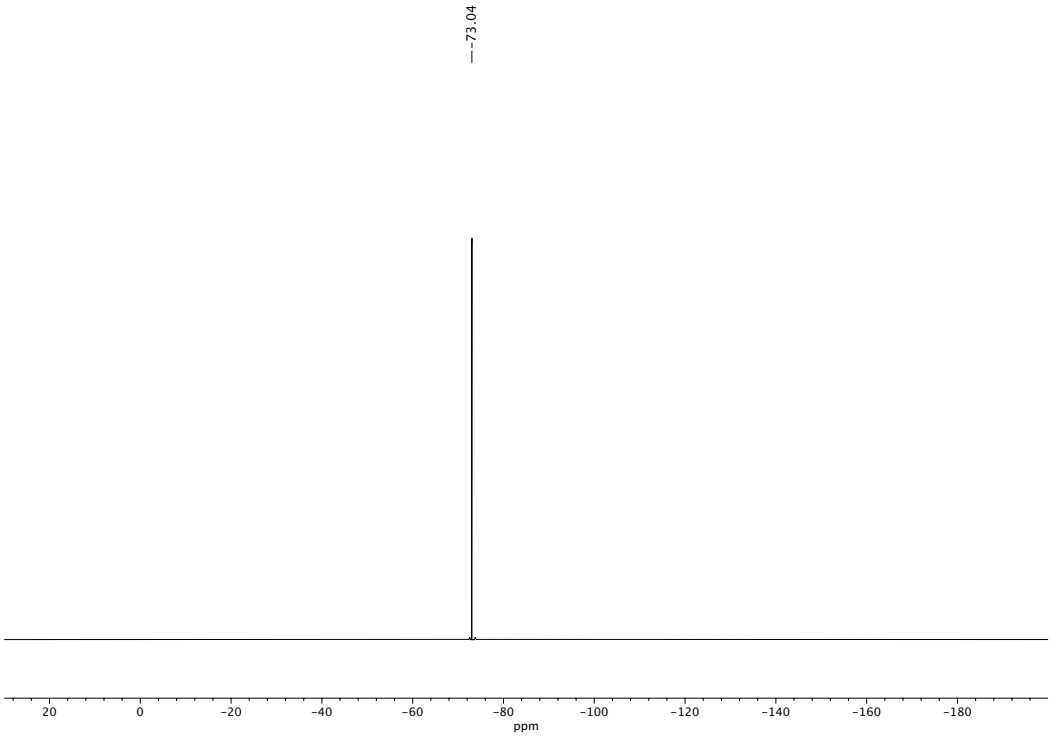

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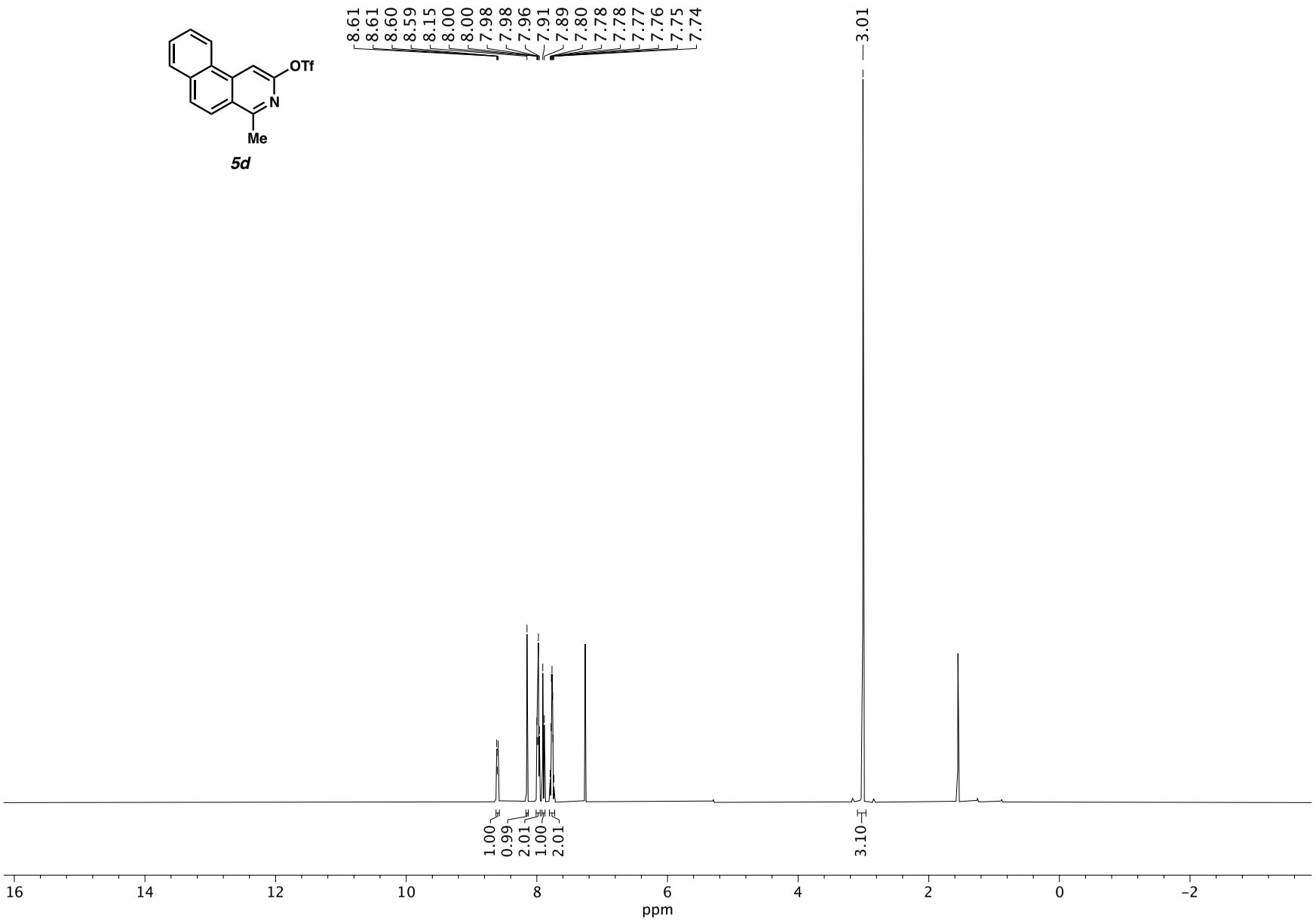
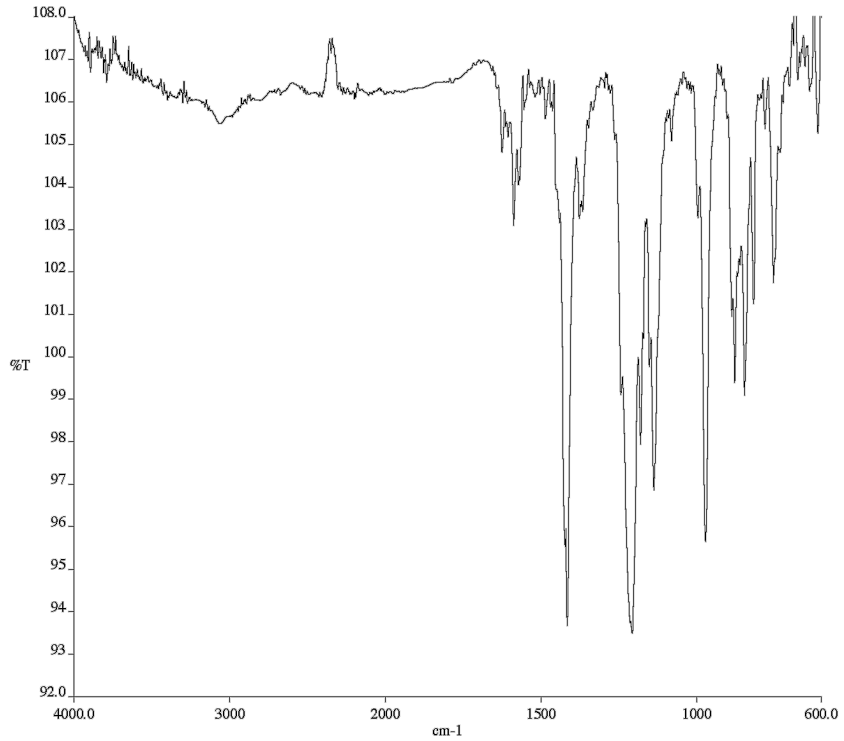
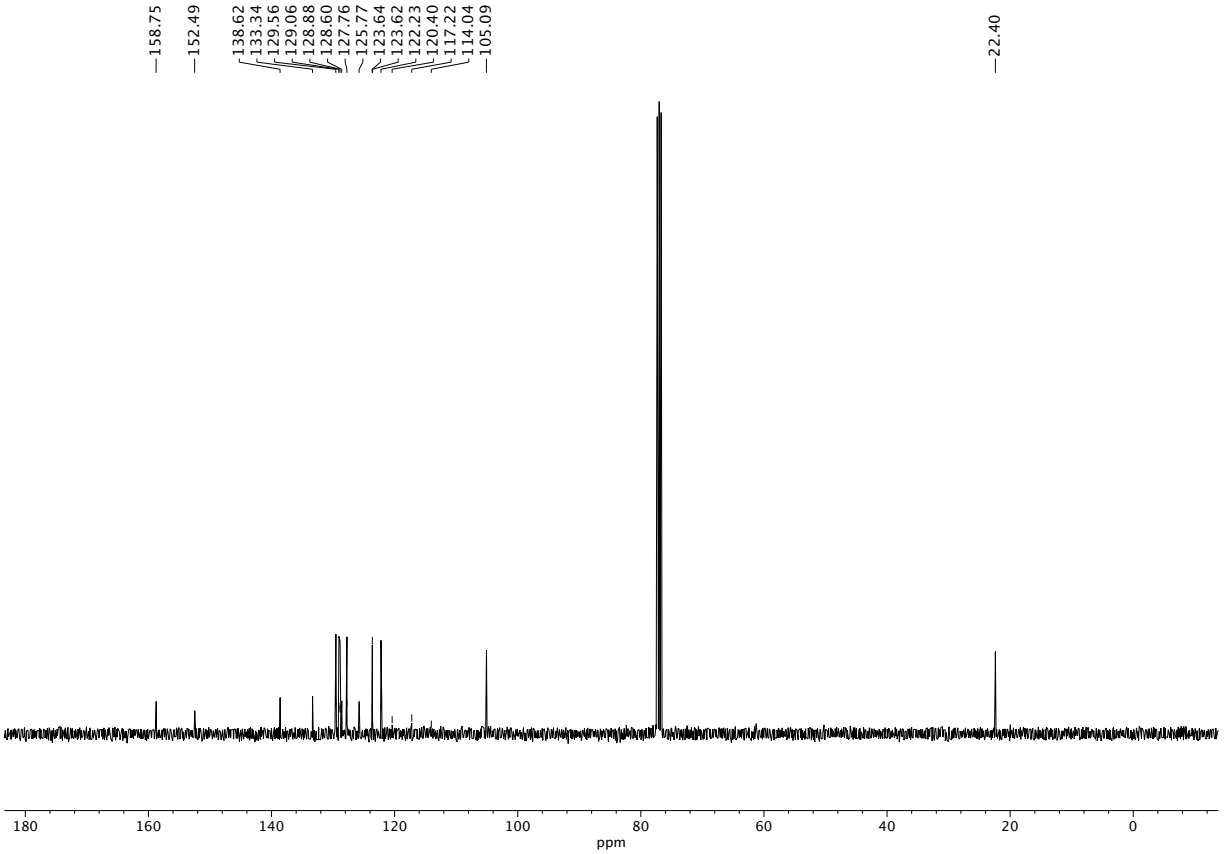


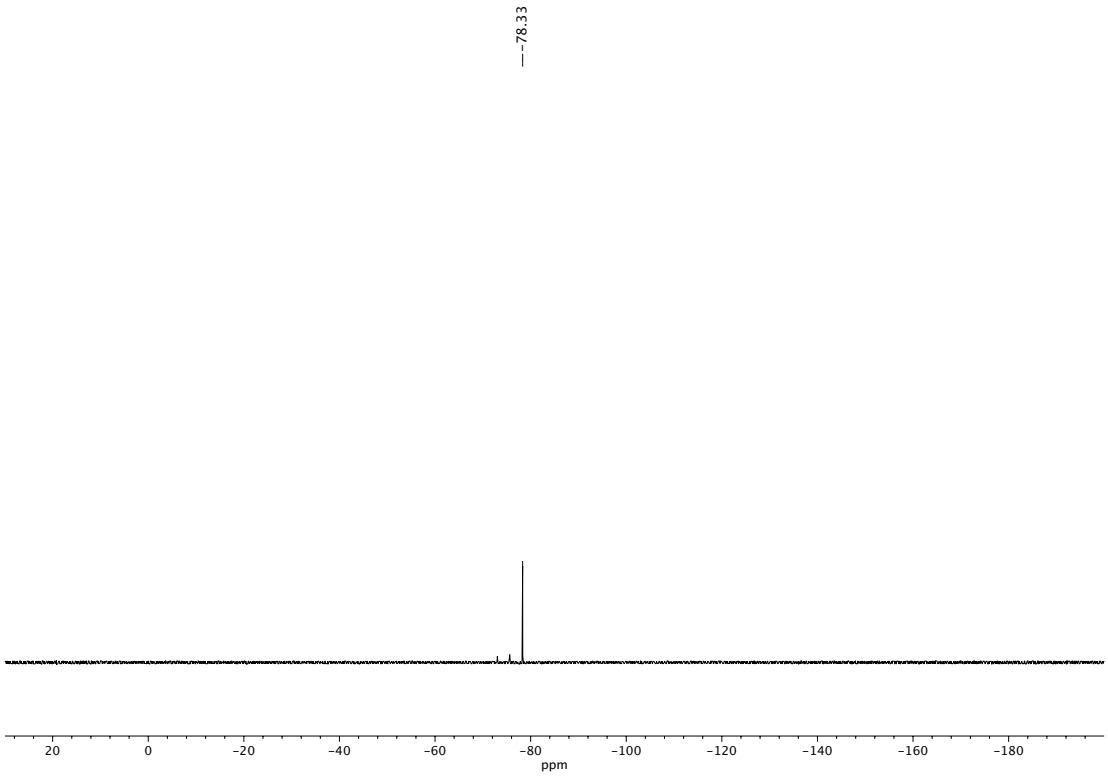
^{1}H NMR (400 MHz, $CDCl_3$) of **5d**.



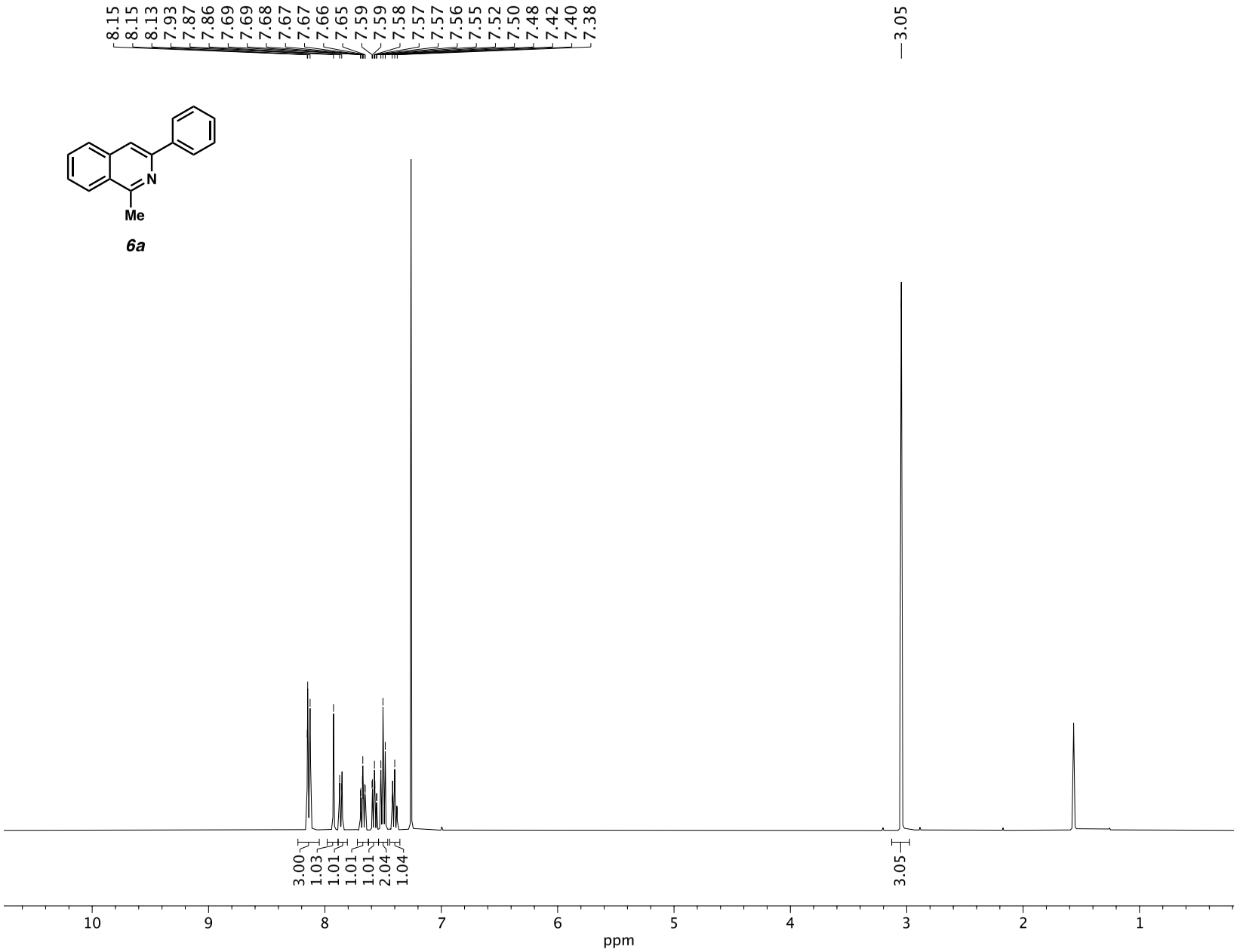
Infrared spectrum (Thin Film, NaCl) of **5d**.



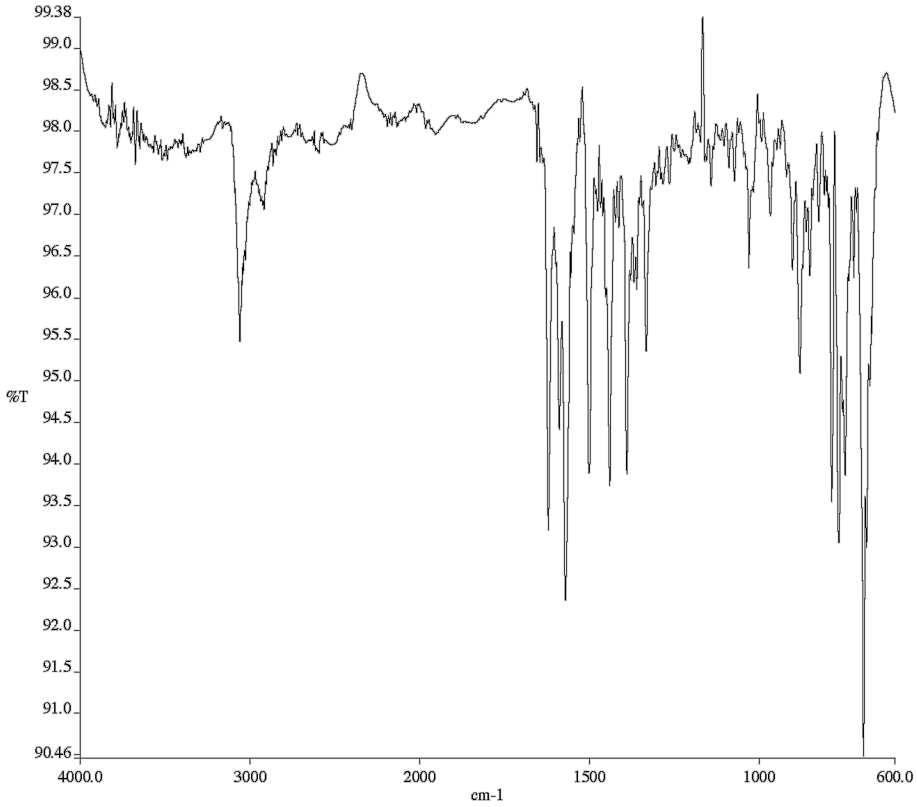
^{13}C NMR (100 MHz, $CDCl_3$) of **5d**.



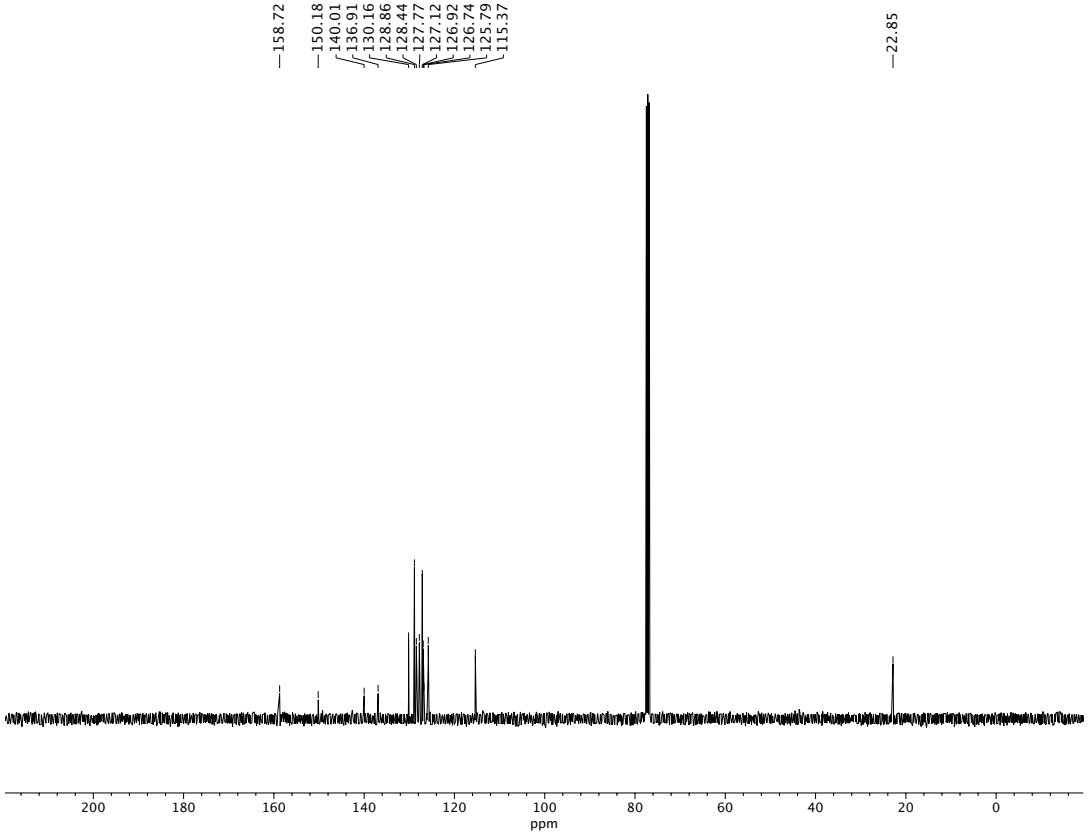
^{19}F NMR (282 MHz, $CDCl_3$) of **5d**.



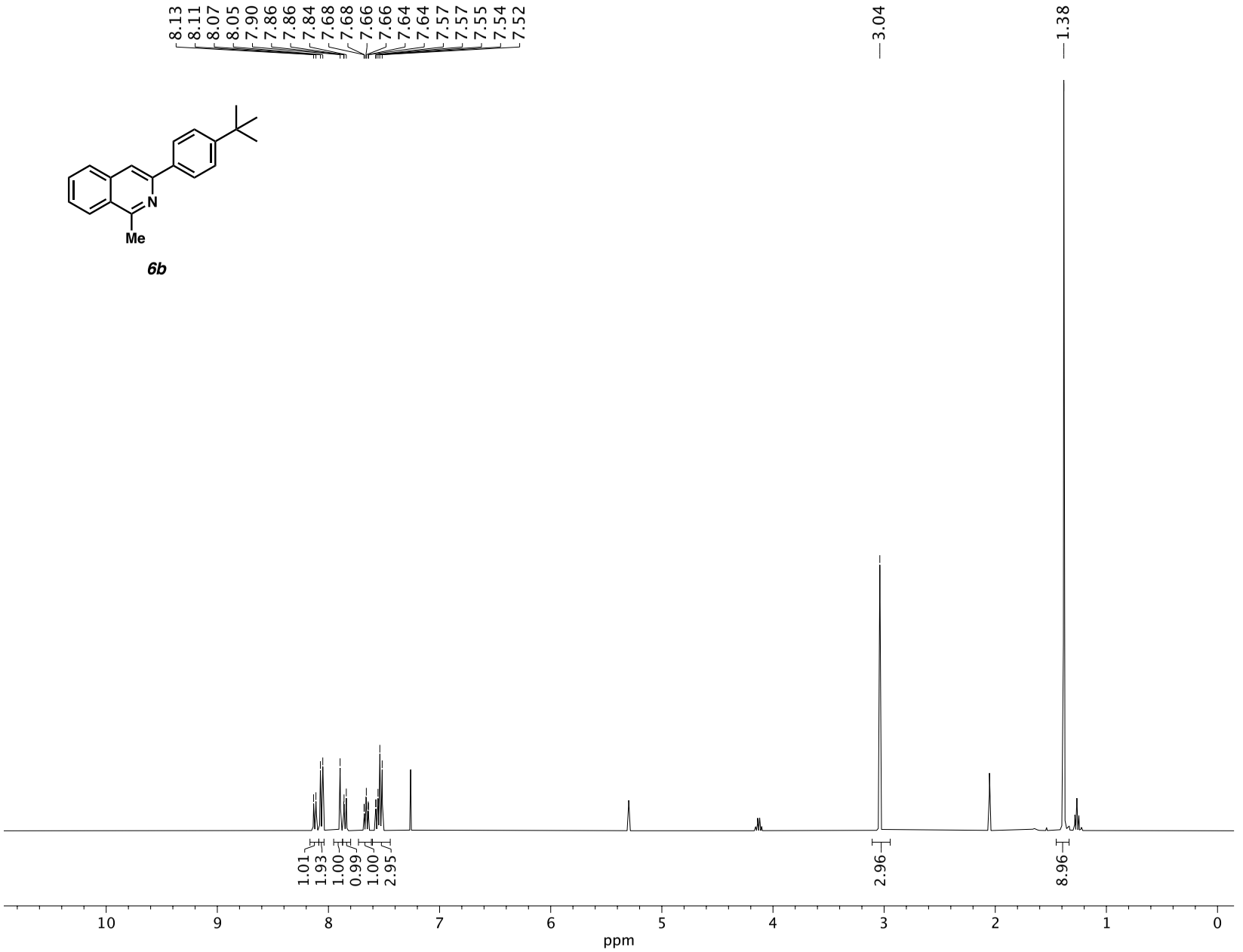
^{1}H NMR (400 MHz, $CDCl_3$) of **6a**.



Infrared spectrum (Thin Film, NaCl) of **6a**.



^{13}C NMR (100 MHz, $CDCl_3$) of **6a**.



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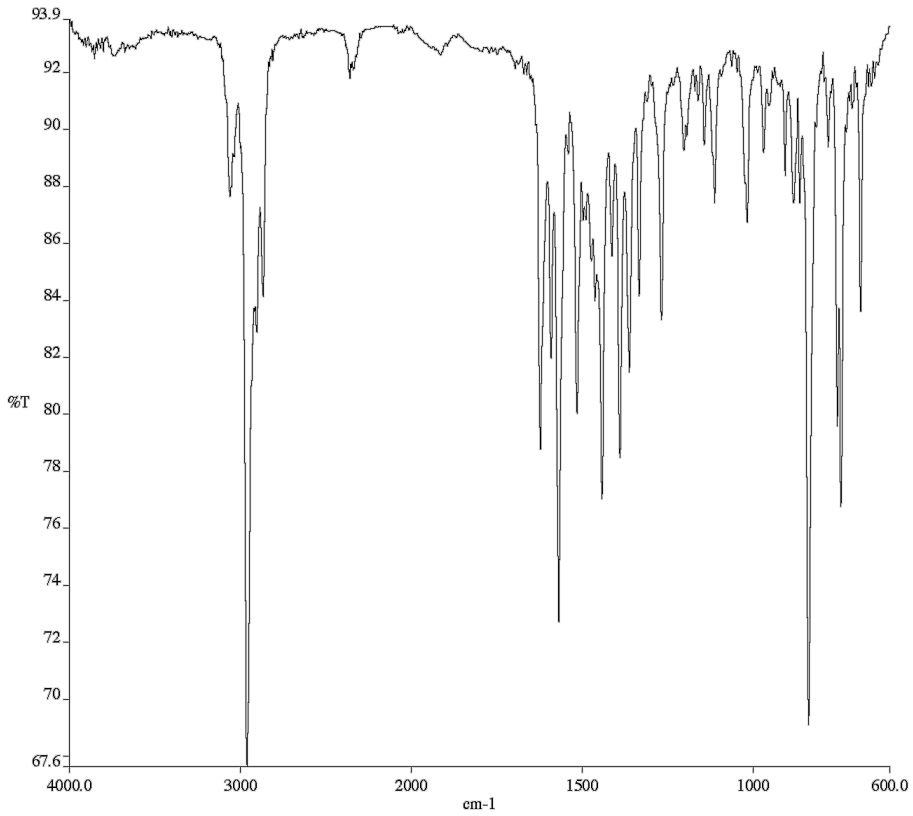
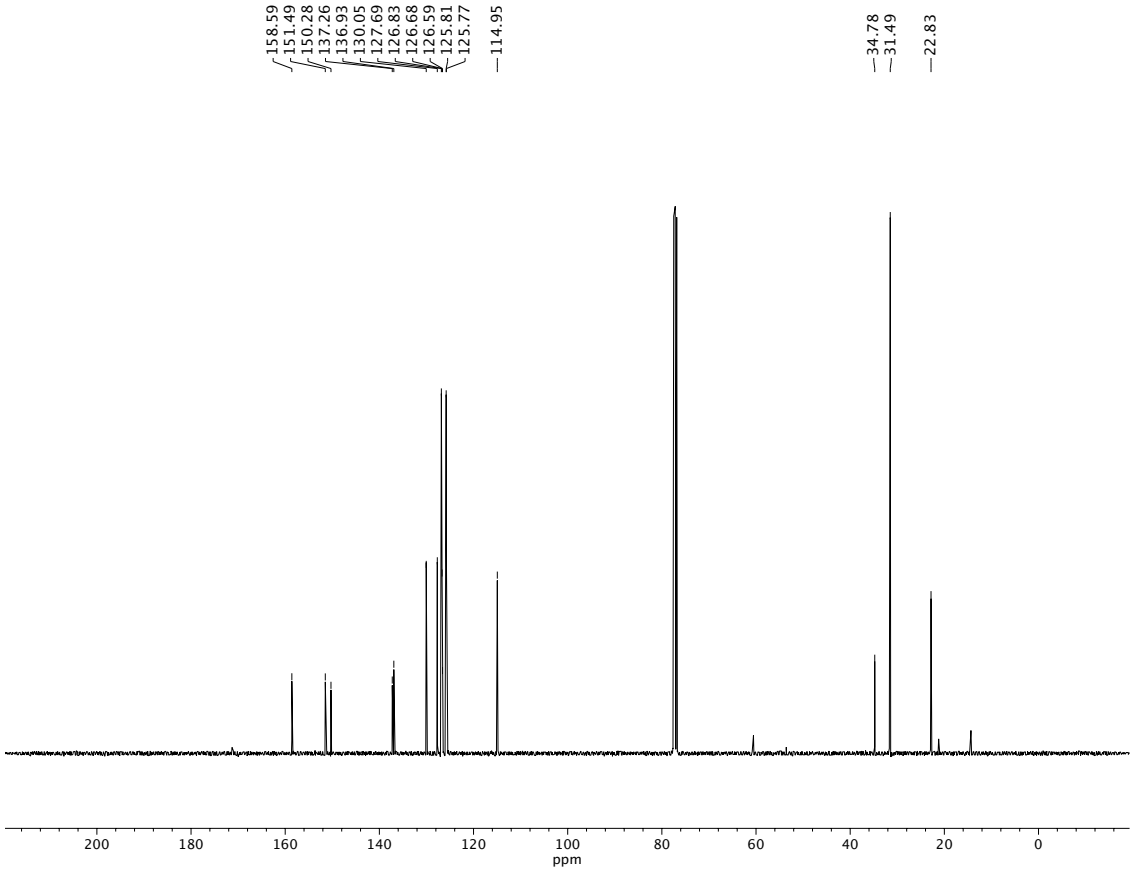
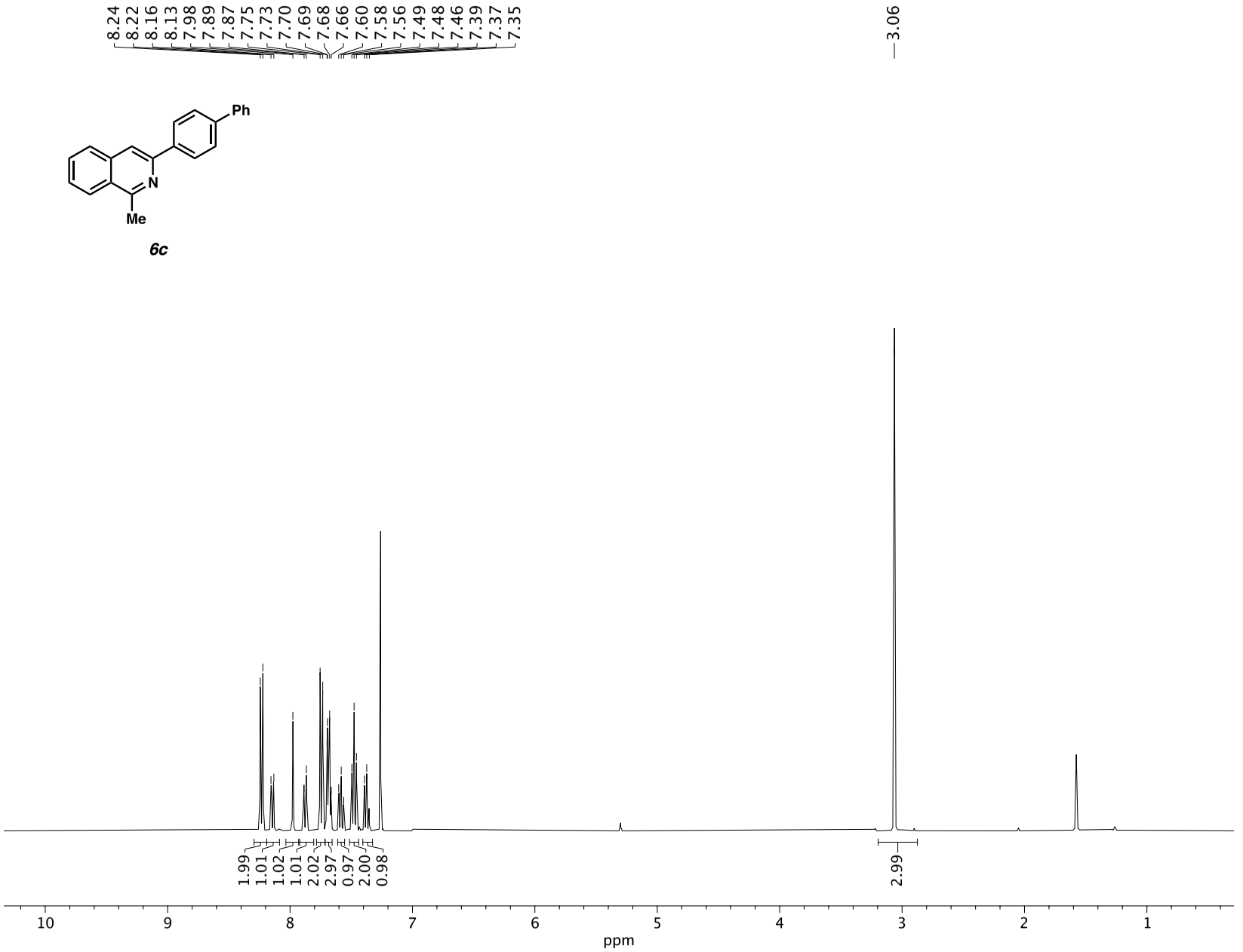


Infrared spectrum (Thin Film, NaCl) of **6b**.



^{13}C NMR (100 MHz, $CDCl_3$) of **6b**.



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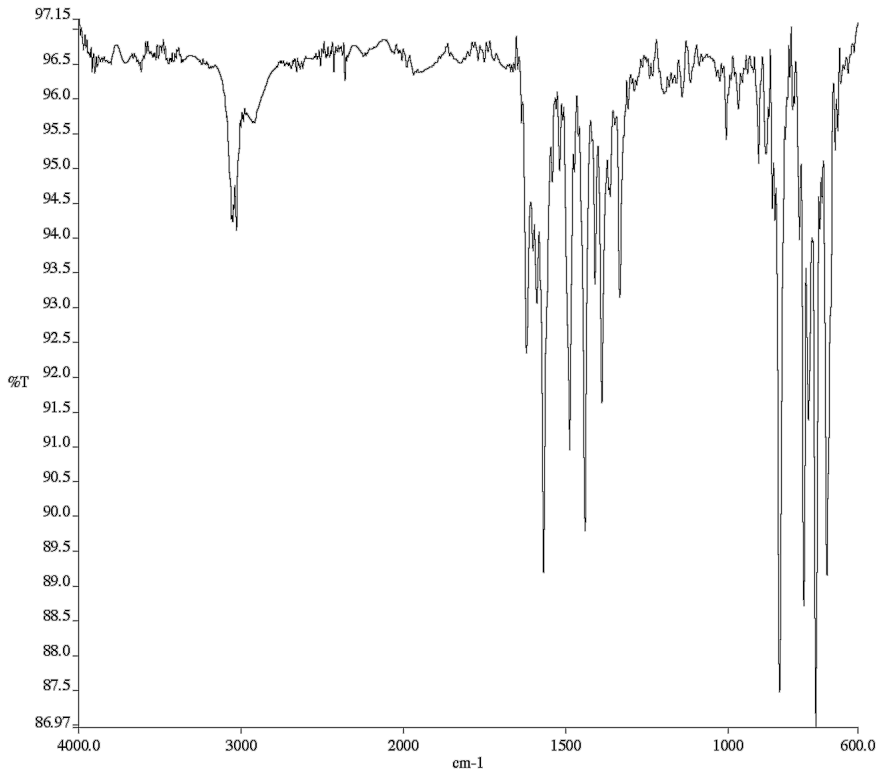
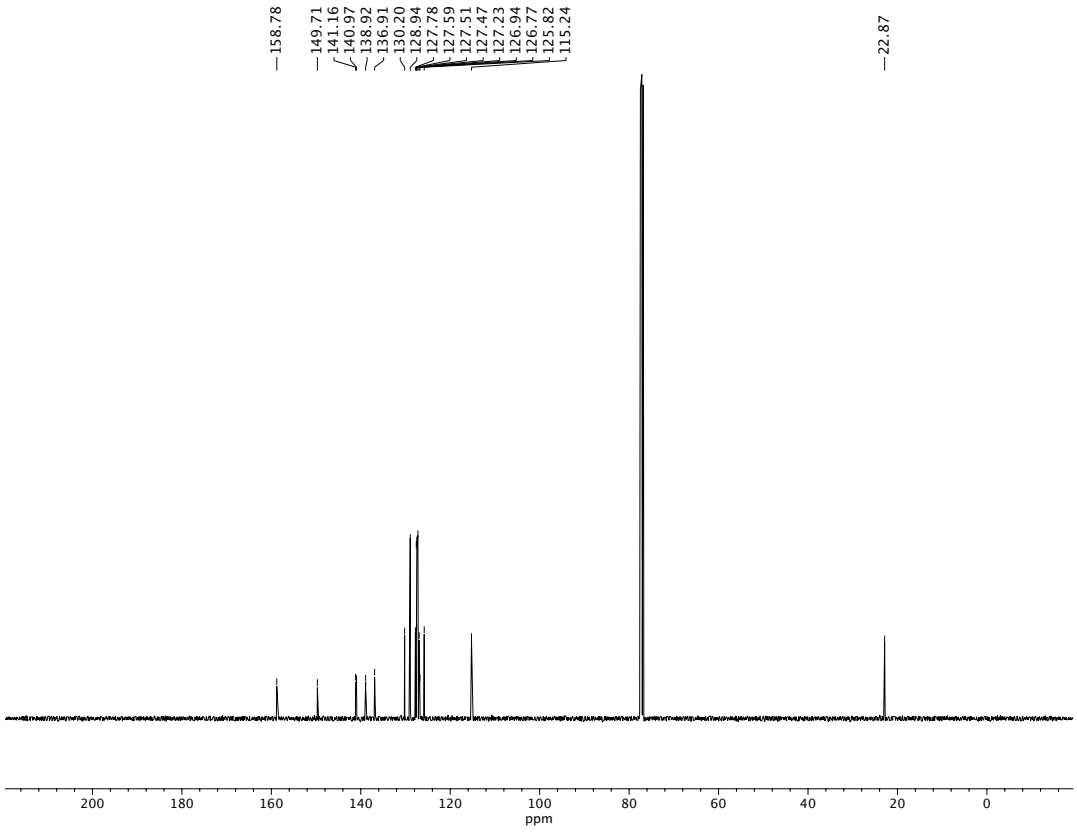
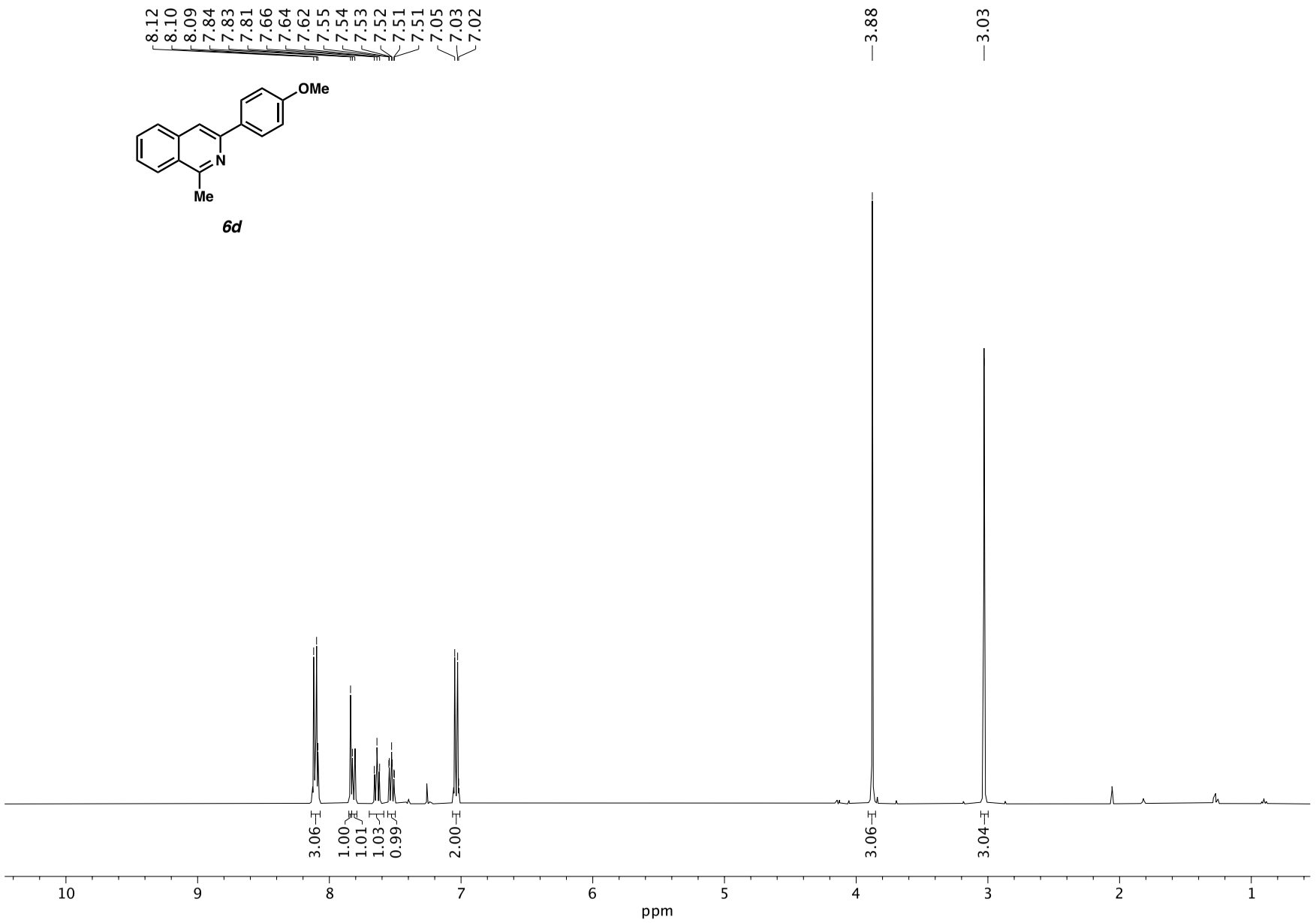


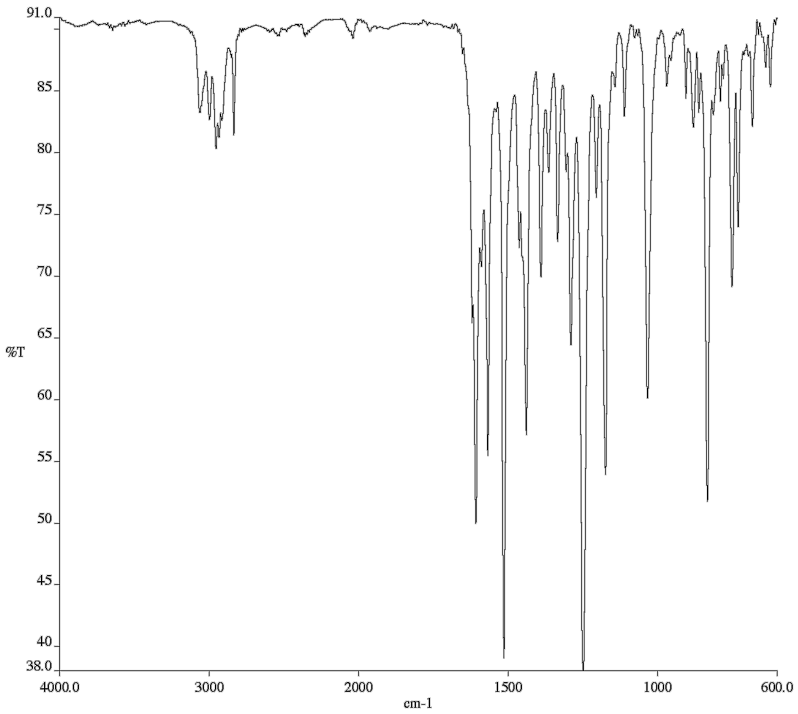
Infrared spectrum (Thin Film, NaCl) of **6c**.



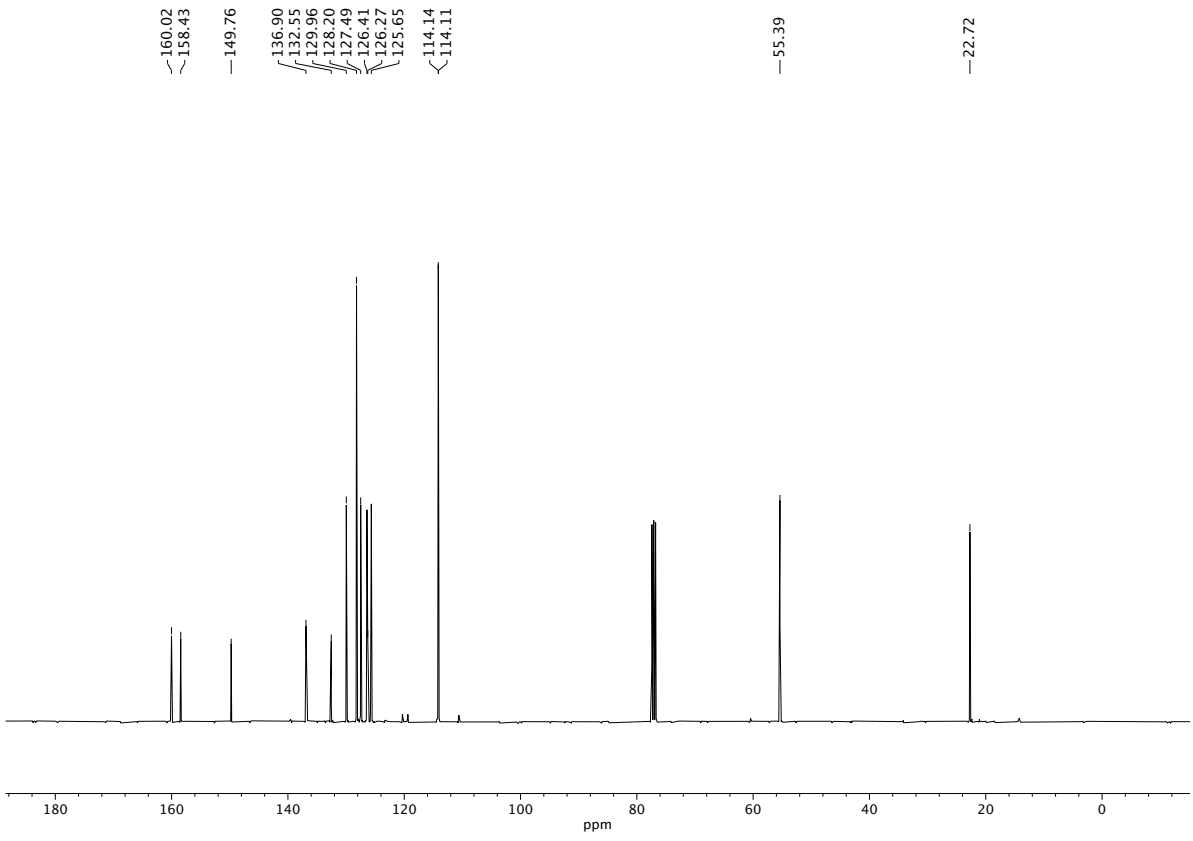
^{13}C NMR (100 MHz, $CDCl_3$) of **6c**.



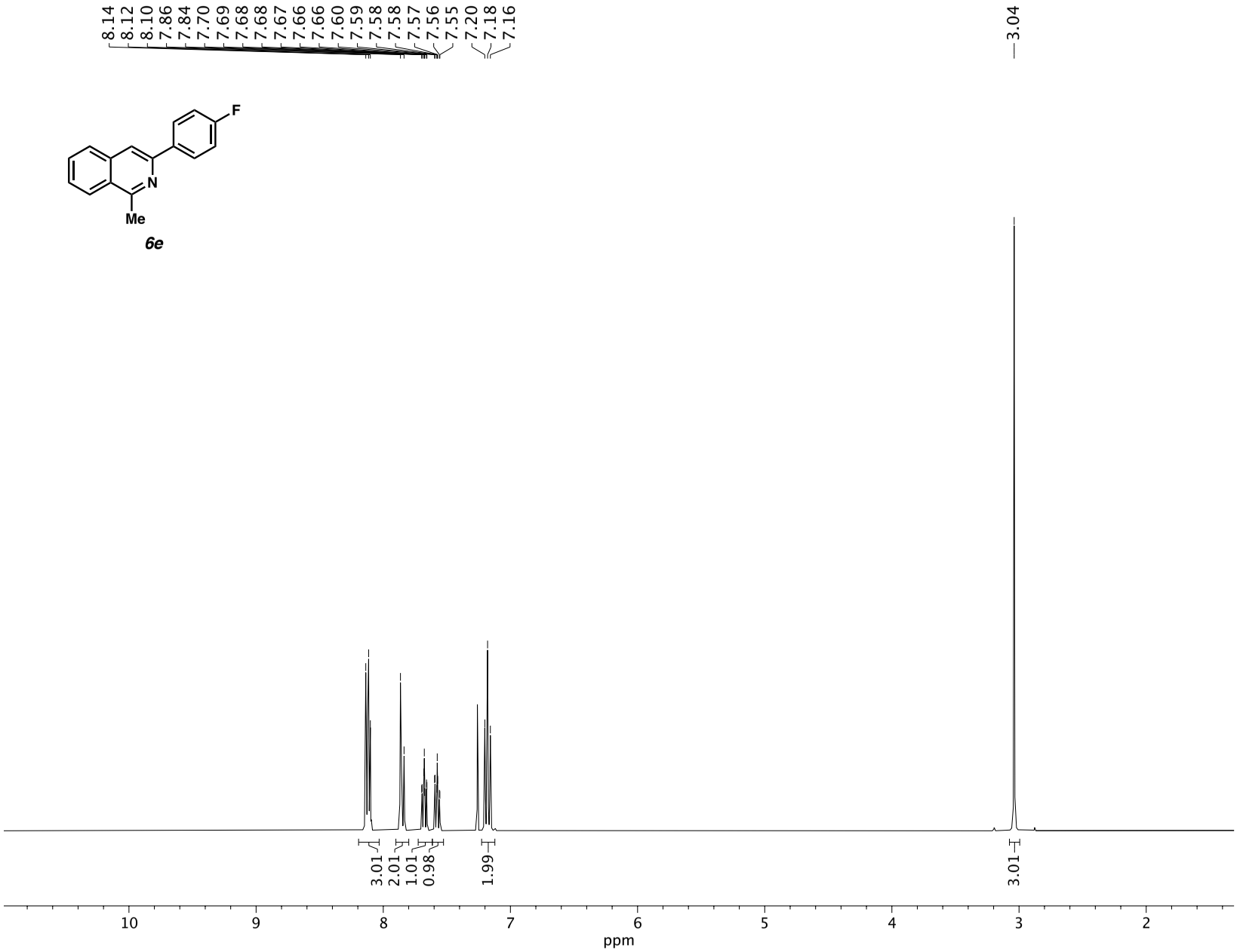
^{1}H NMR (400 MHz, $CDCl_3$) of **6d**.



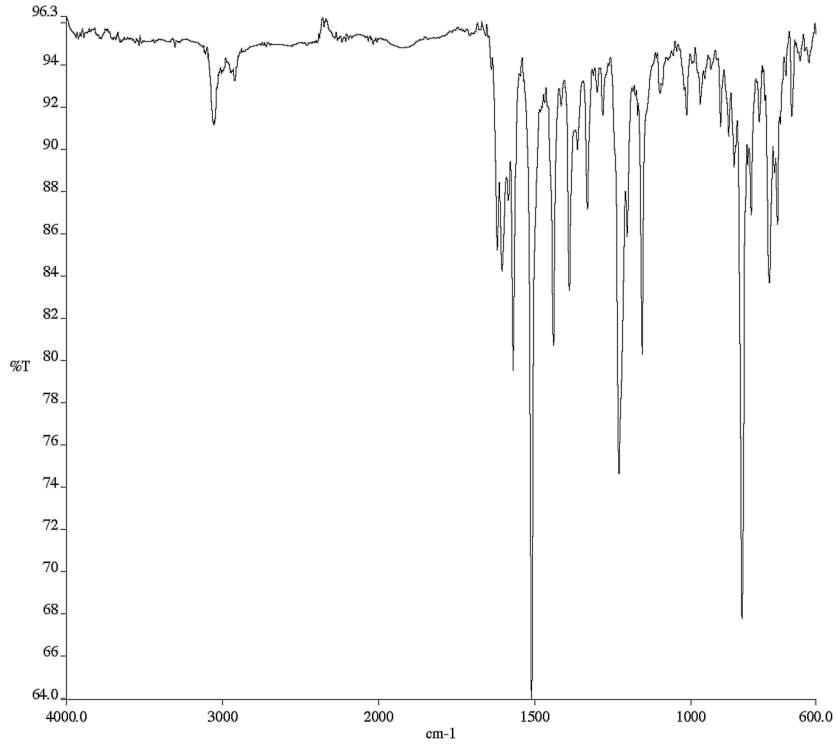
Infrared spectrum (Thin Film, NaCl) of **6d**.



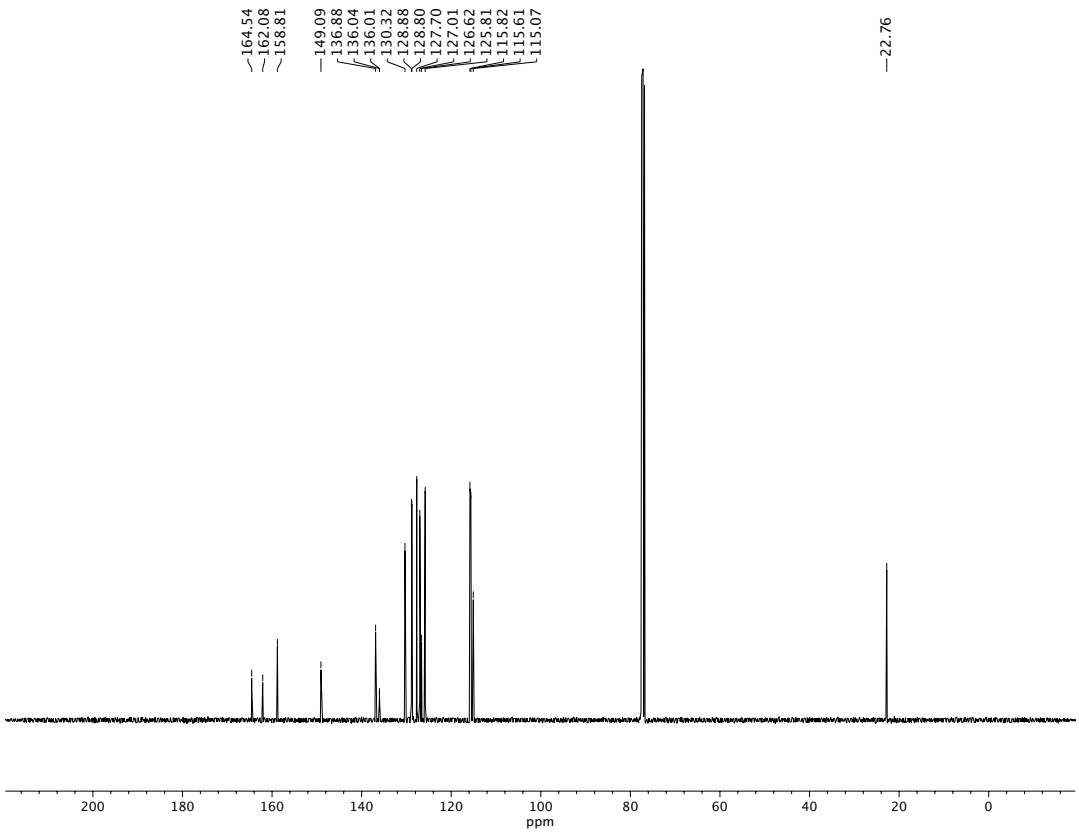
^{13}C NMR (100 MHz, $CDCl_3$) of **6d**.



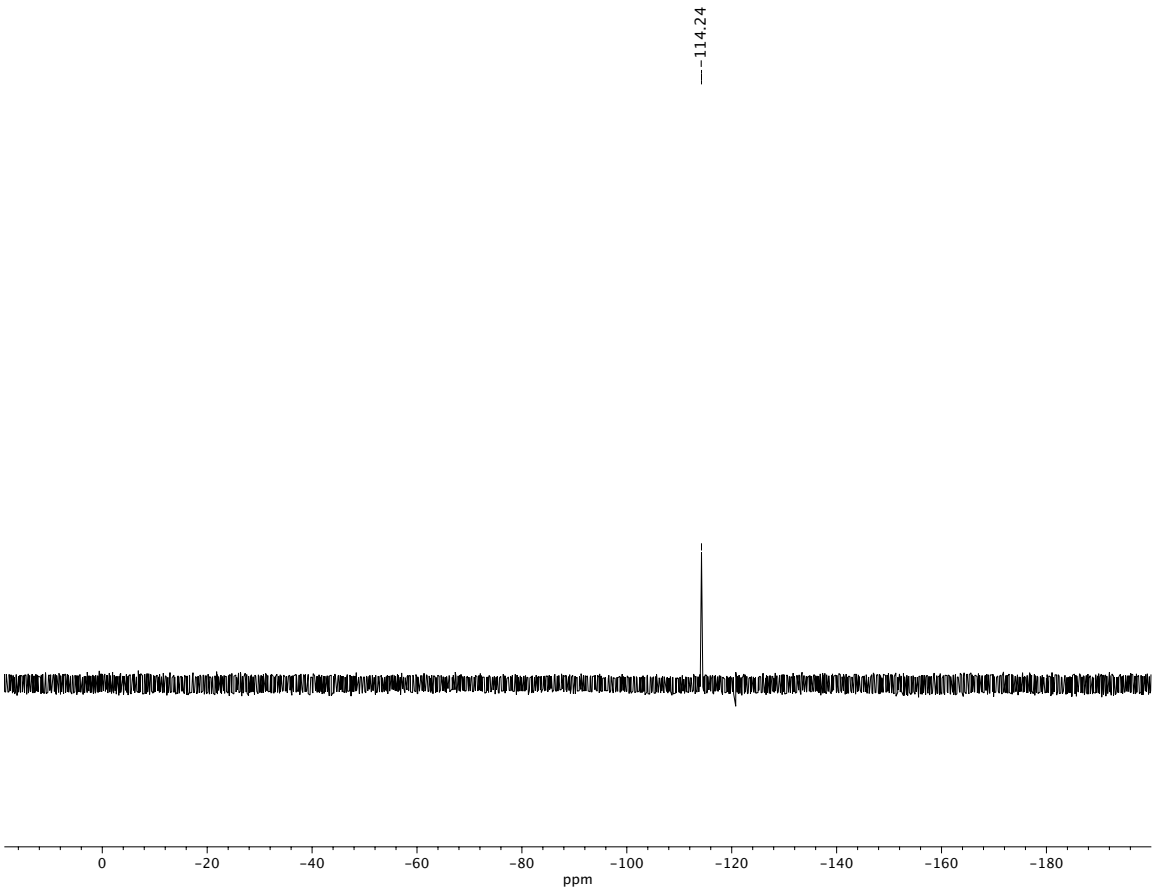
^{1}H NMR (400 MHz, $CDCl_3$) of **6e**.



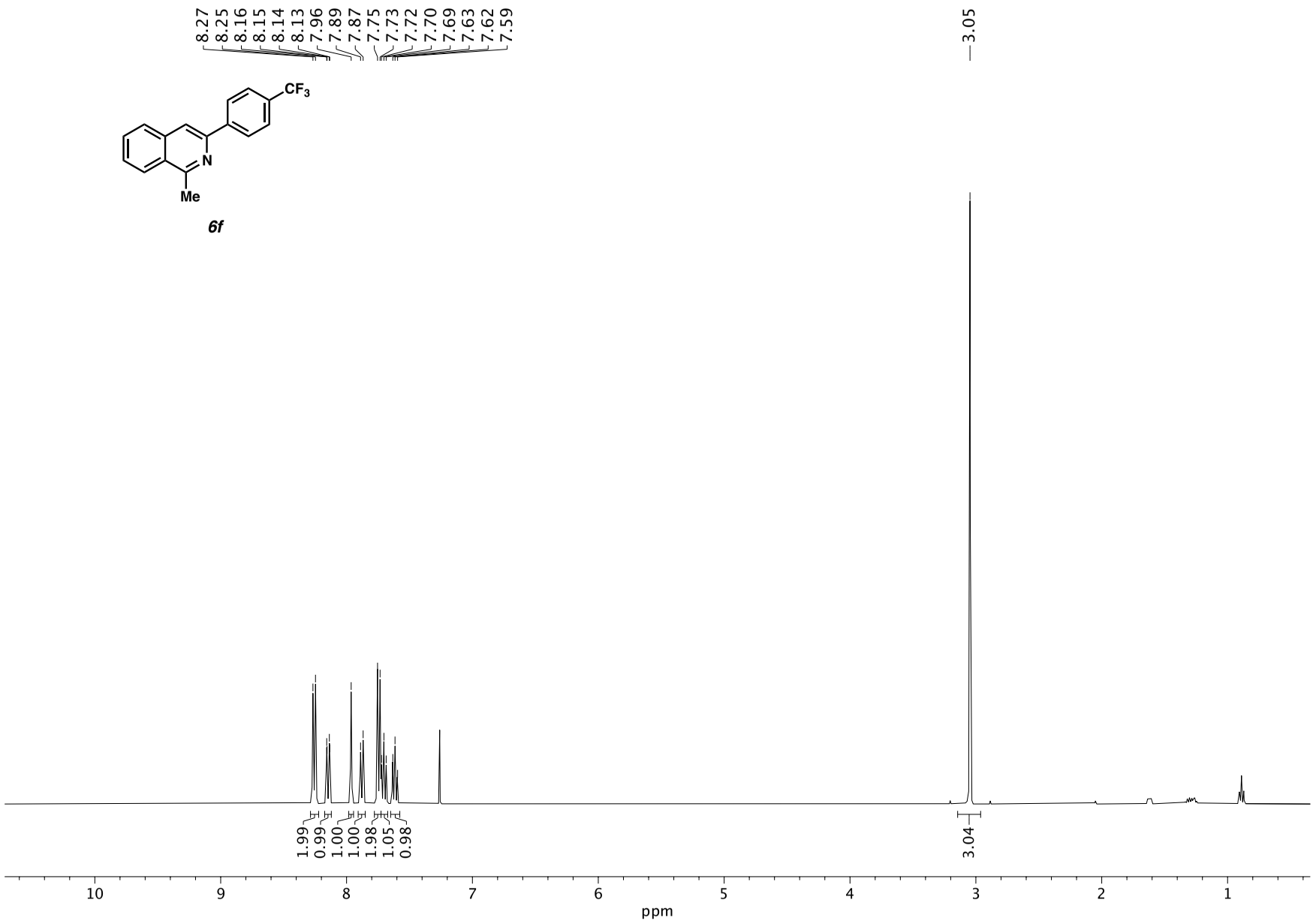
Infrared spectrum (Thin Film, NaCl) of **6e**.



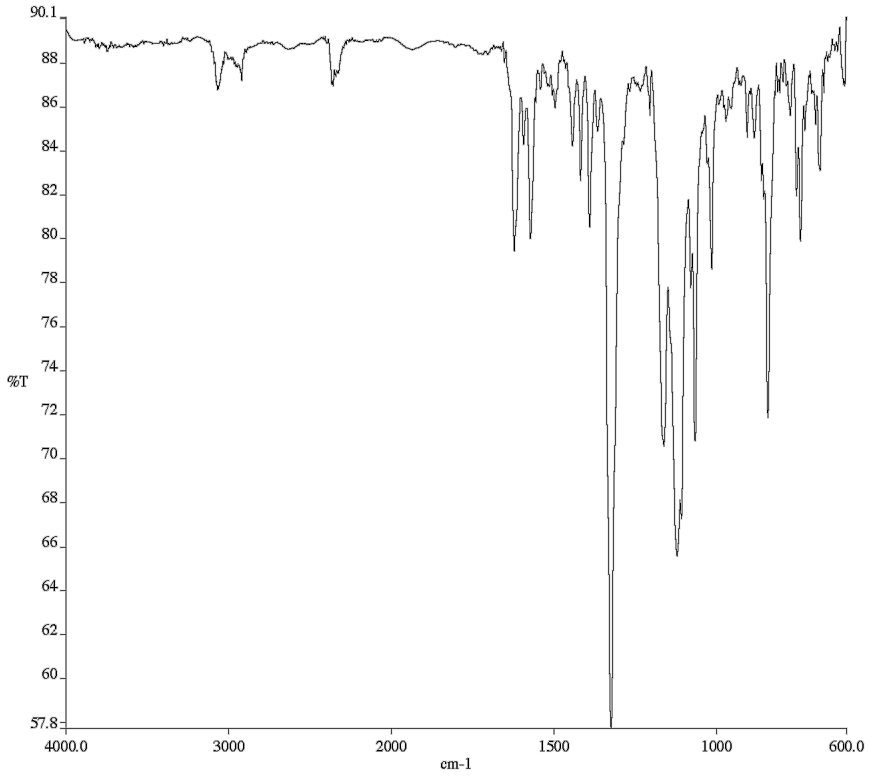
^{13}C NMR (100 MHz, $CDCl_3$) of **6e**.



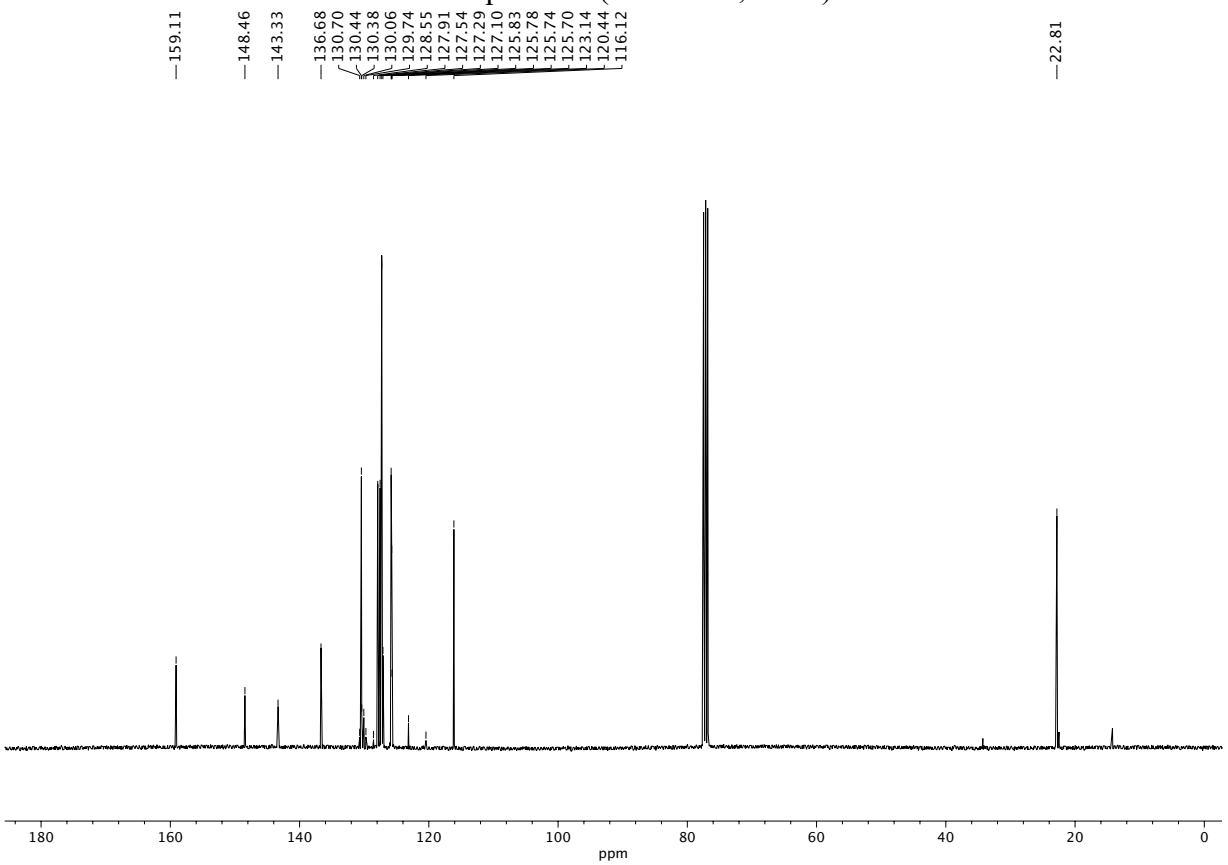
^{19}F NMR (282 MHz, $CDCl_3$) of **6e**.



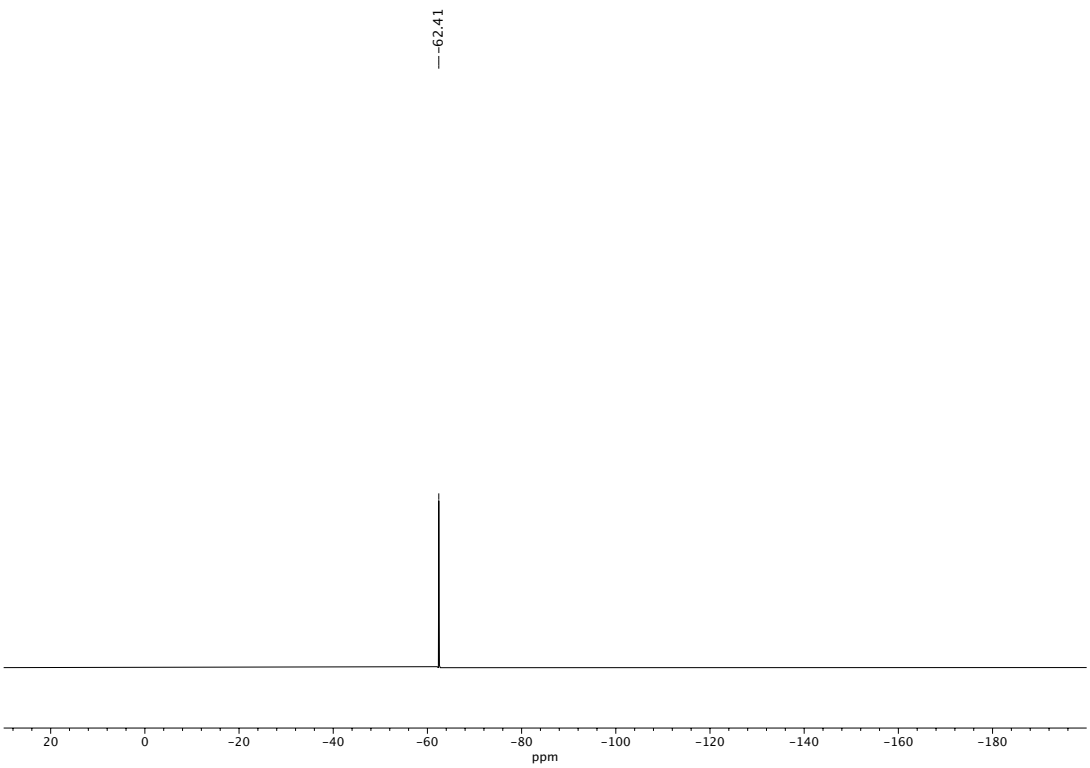
^{1}H NMR (400 MHz, $CDCl_3$) of **6f**.



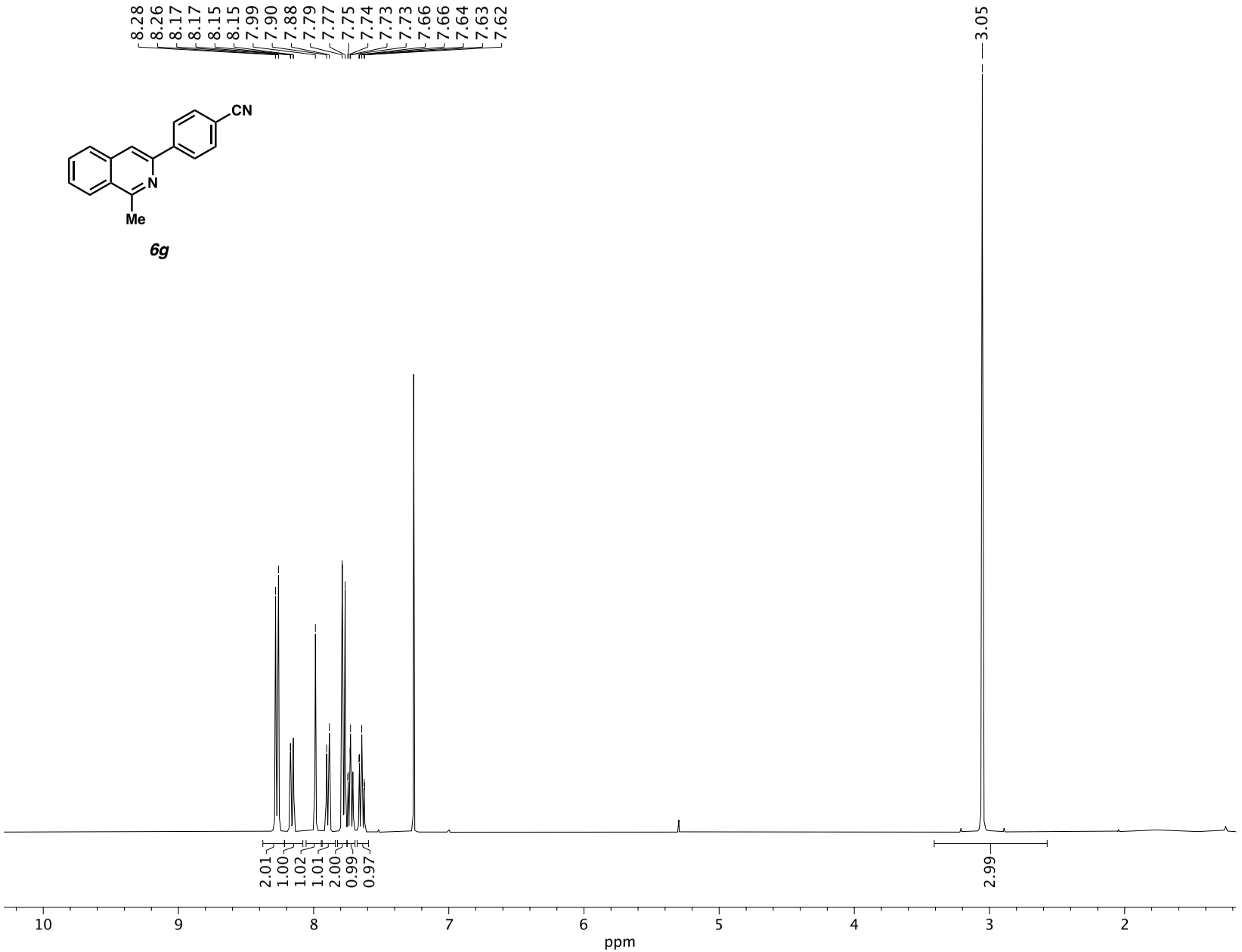
Infrared spectrum (Thin Film, NaCl) of **6f**.



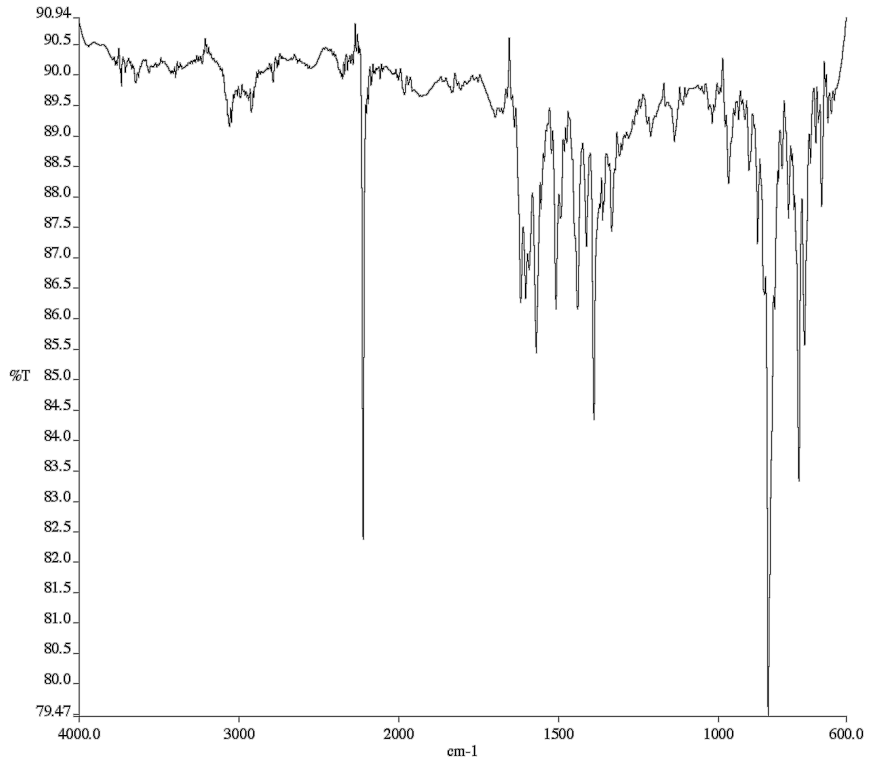
^{13}C NMR (100 MHz, $CDCl_3$) of **6f**.



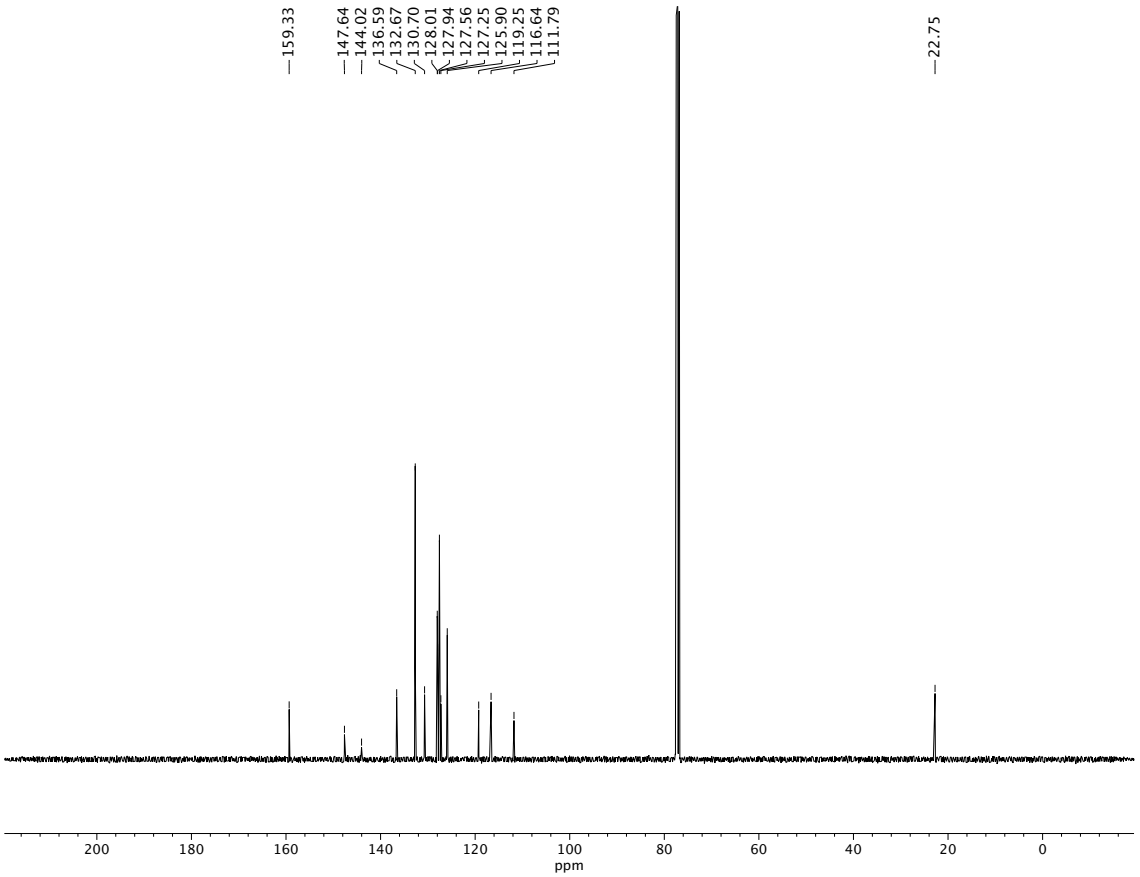
^{19}F NMR (282 MHz, $CDCl_3$) of **6f**.



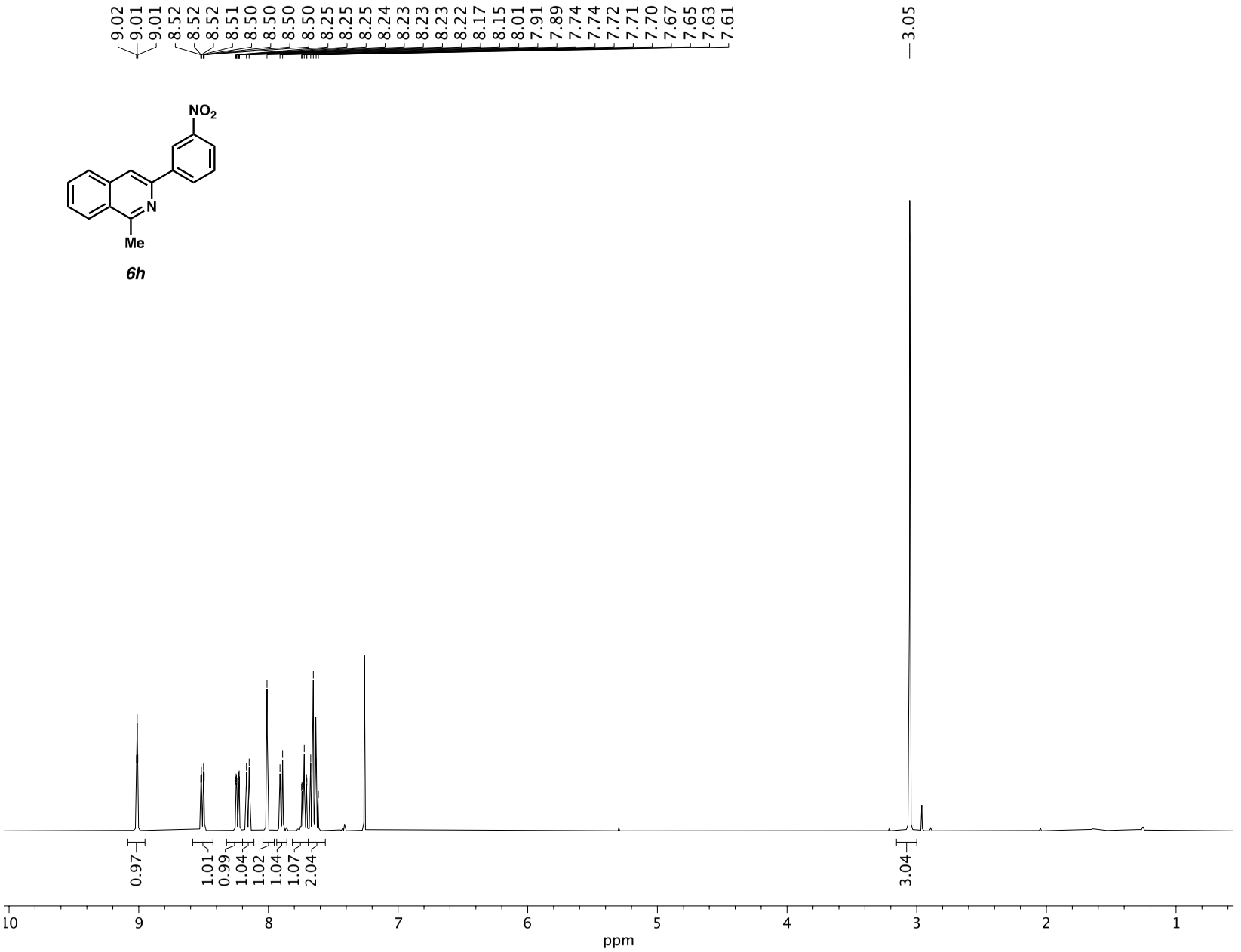
^{1}H NMR (400 MHz, $CDCl_3$) of **6g**.



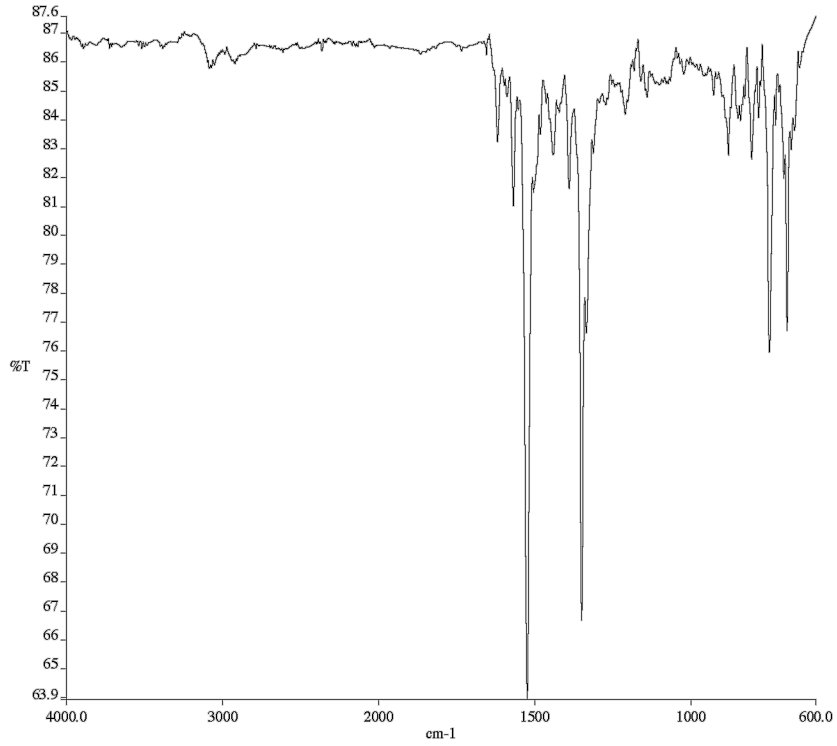
Infrared spectrum (Thin Film, NaCl) of **6g**.



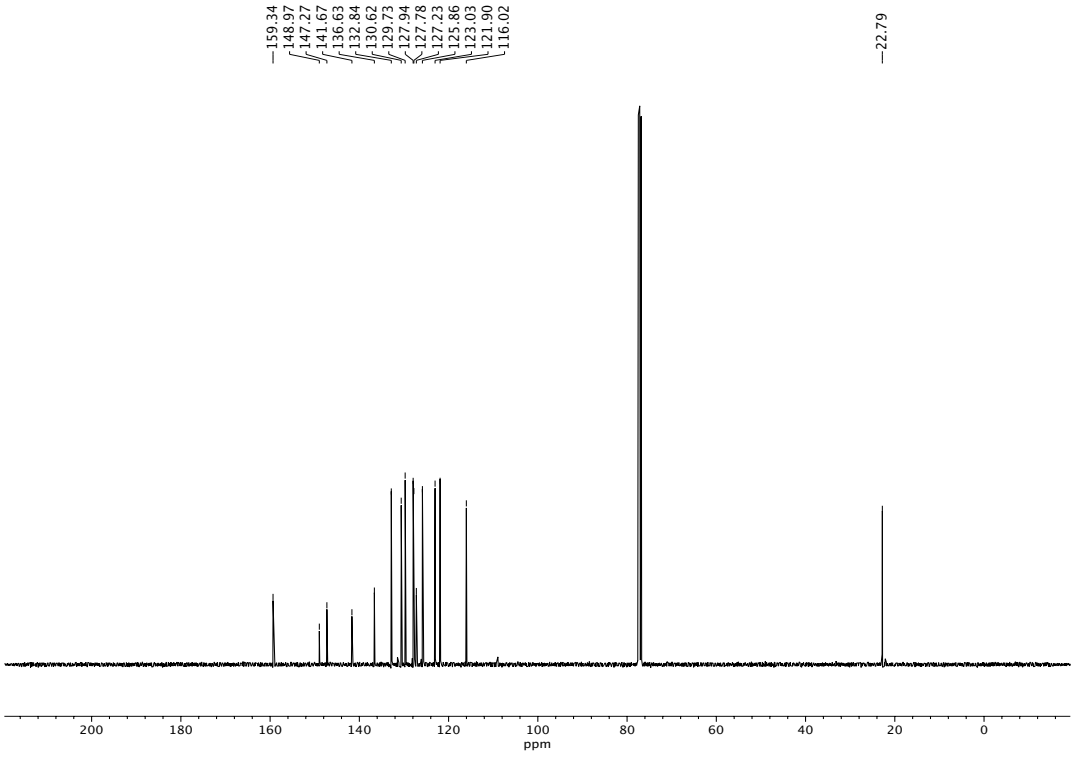
^{13}C NMR (100 MHz, $CDCl_3$) of **6g**.



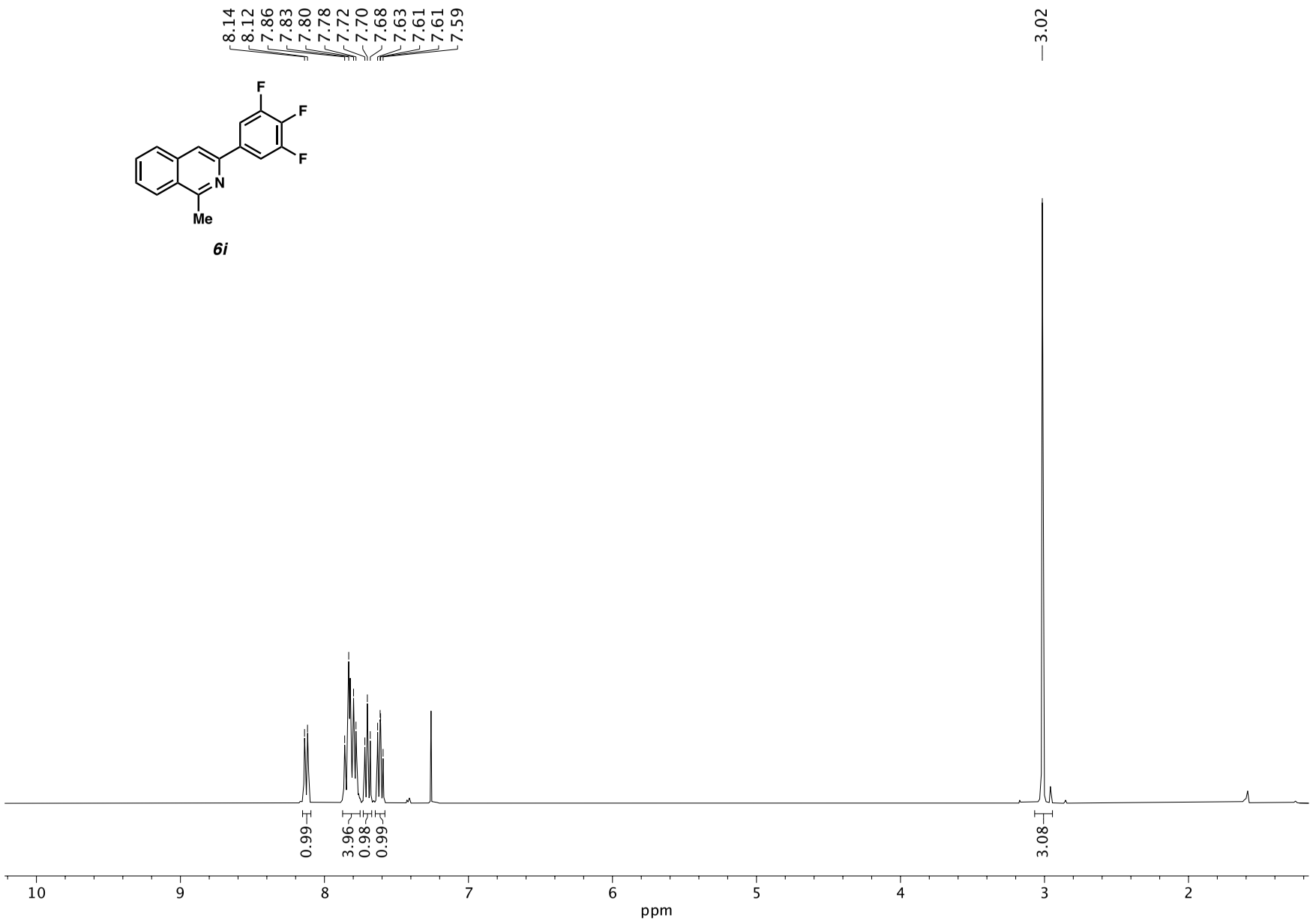
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6h**.



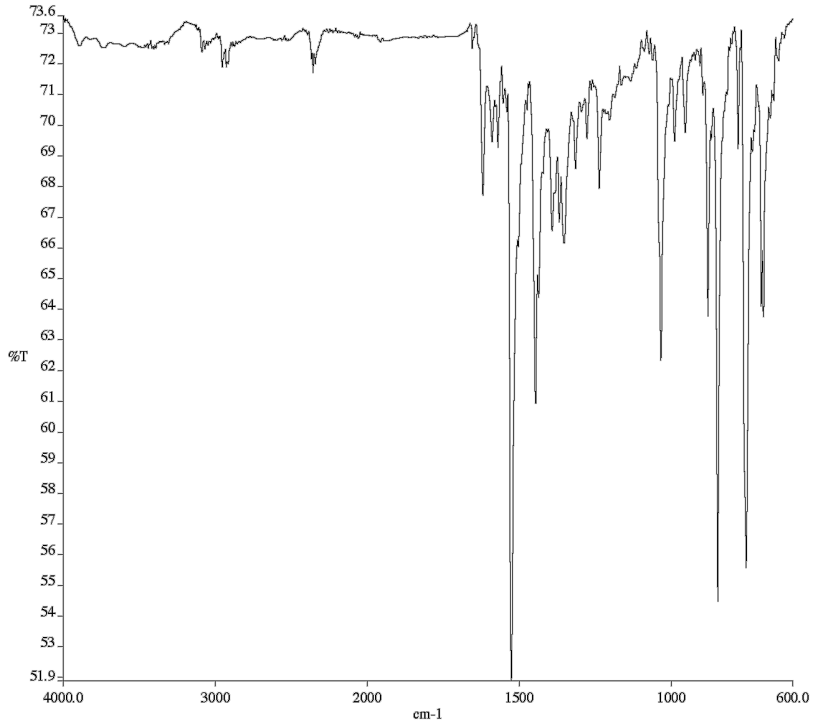
Infrared spectrum (Thin Film, NaCl) of **6h**.



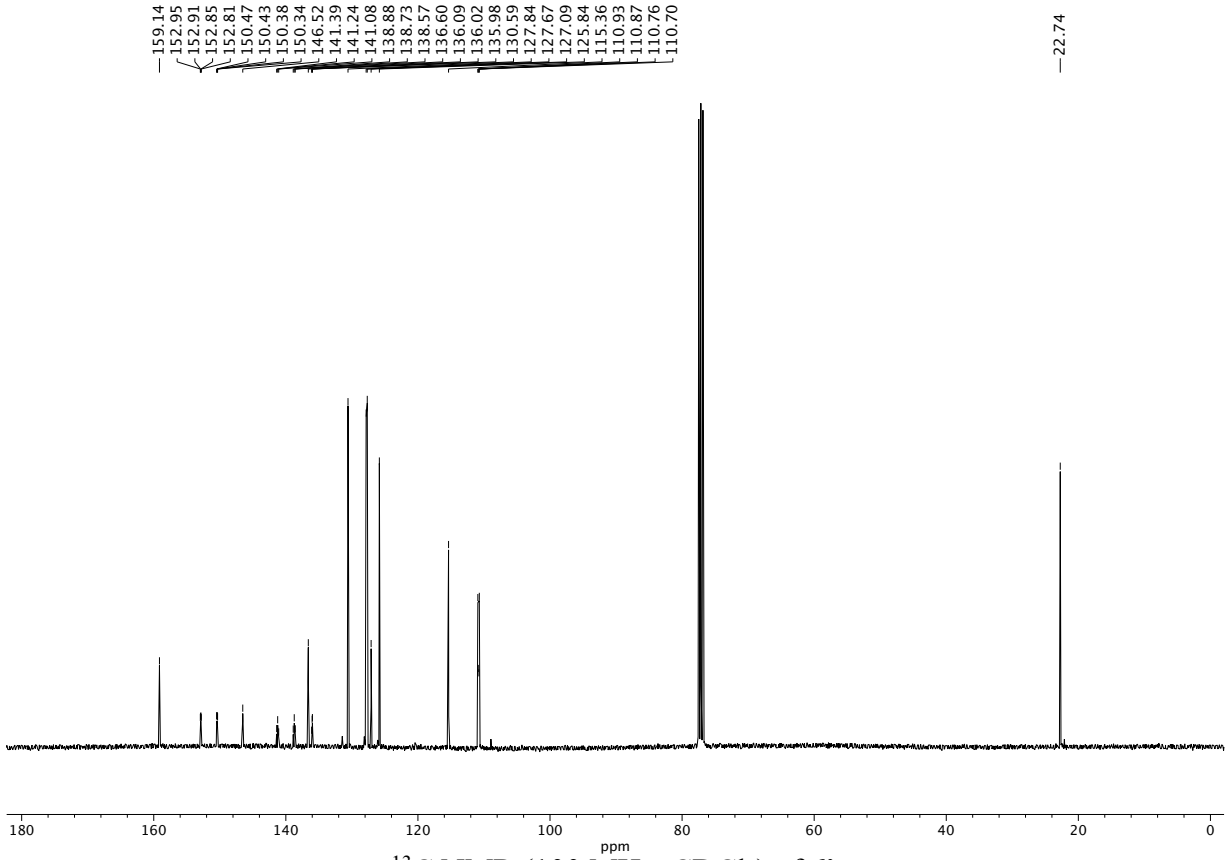
^{13}C NMR (100 MHz, $CDCl_3$) of **6h**.



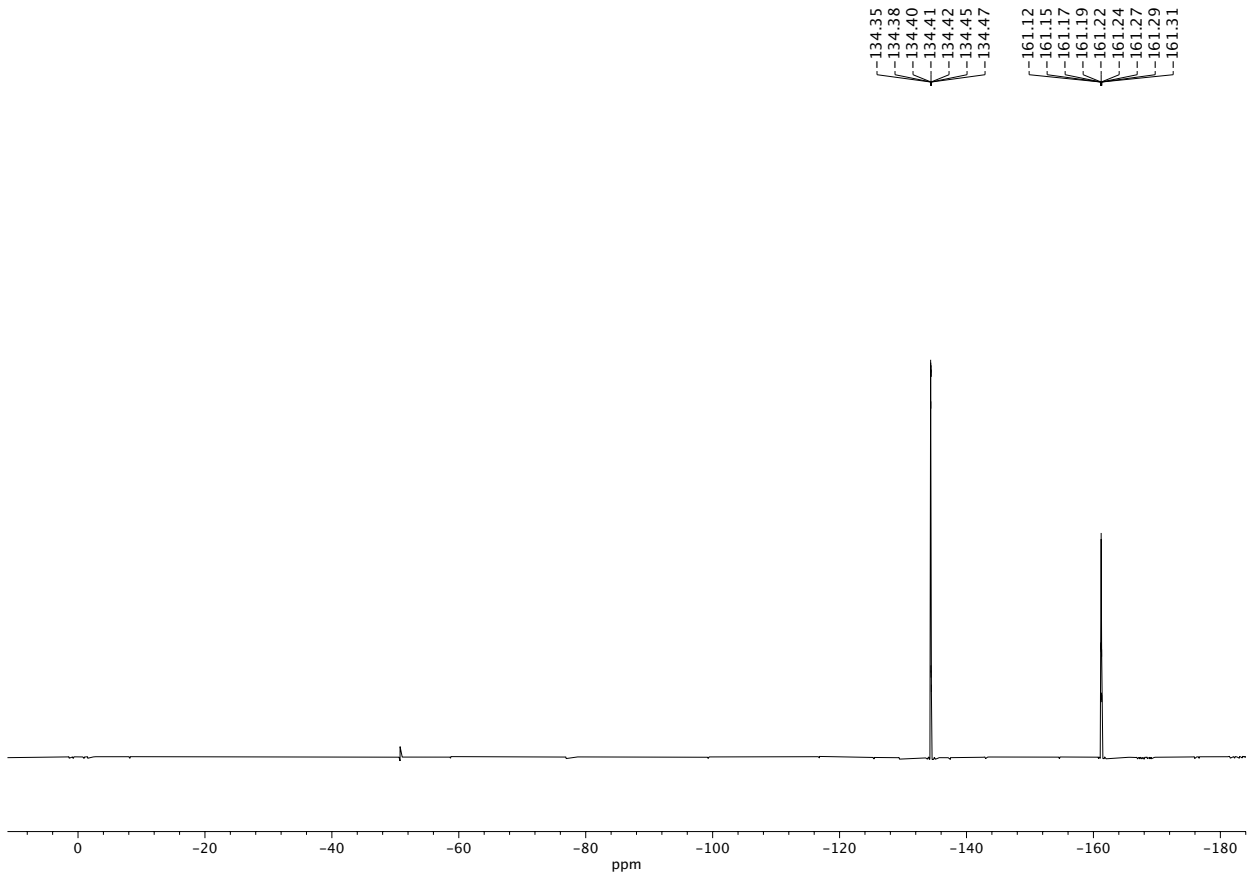
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6i**.



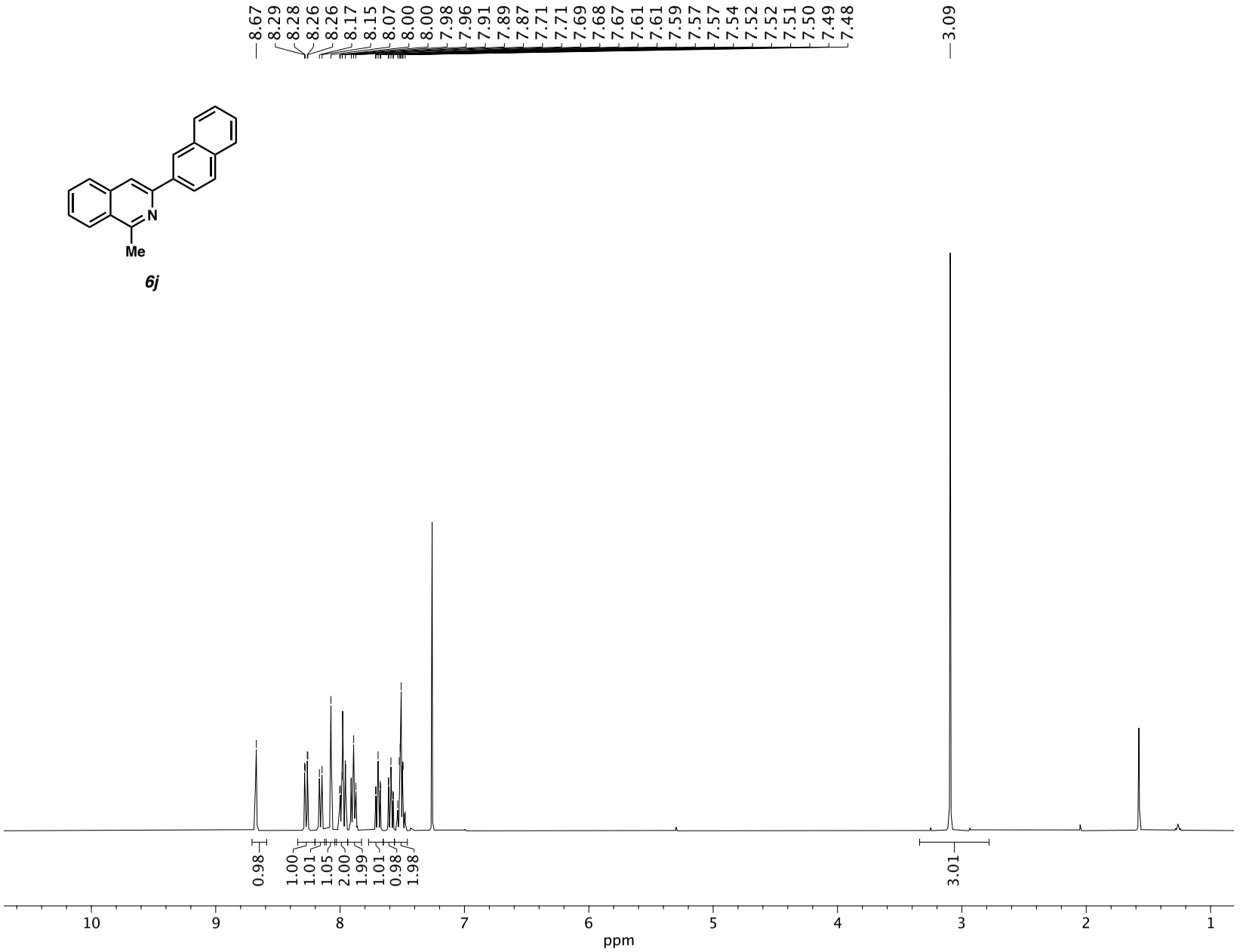
Infrared spectrum (Thin Film, NaCl) of **6i**.



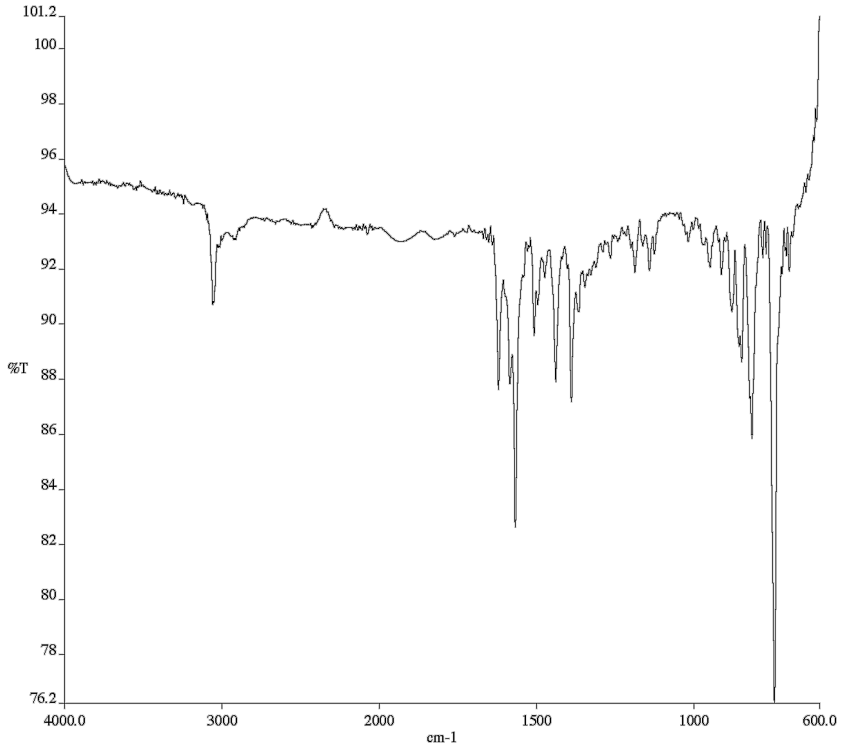
^{13}C NMR (100 MHz, $CDCl_3$) of **6i**.



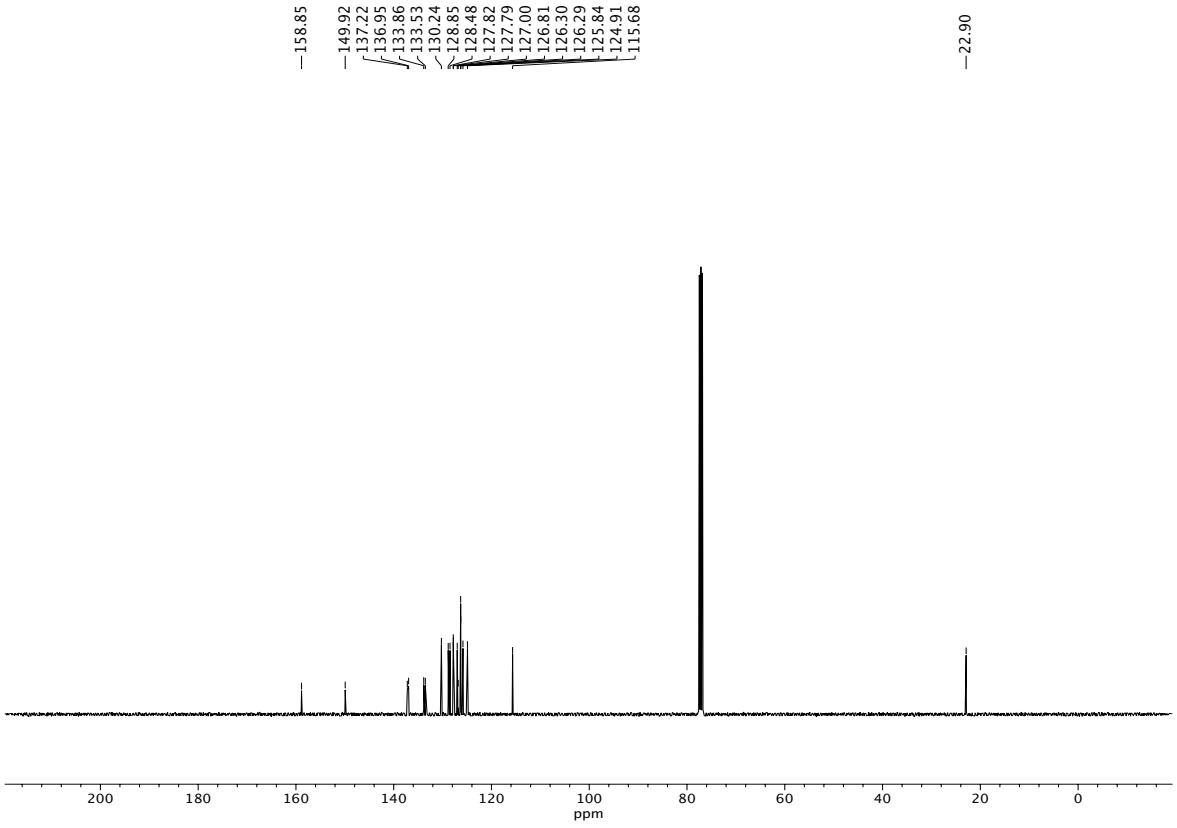
^{19}F NMR (282 MHz, $CDCl_3$) of **6i**.



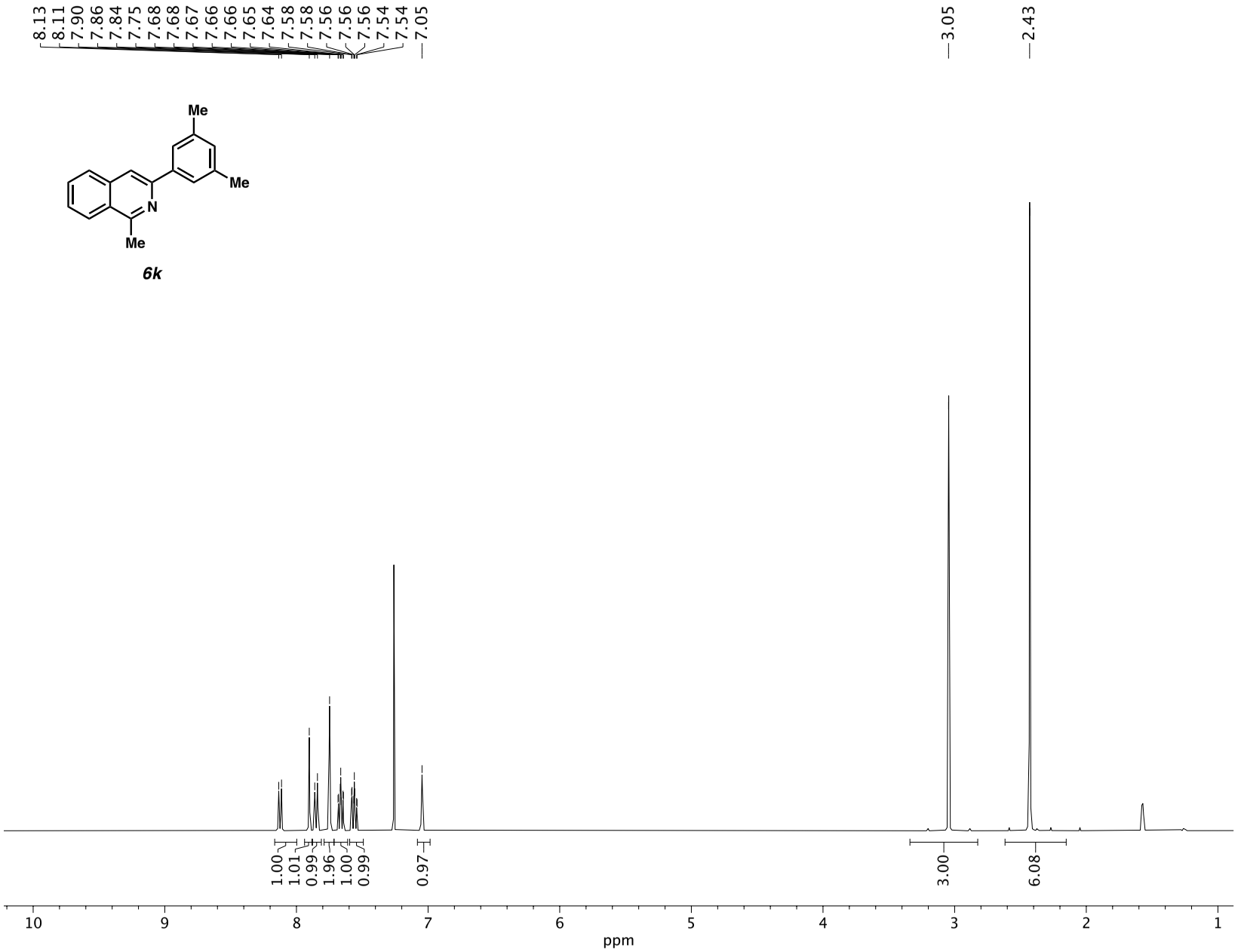
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6j**.



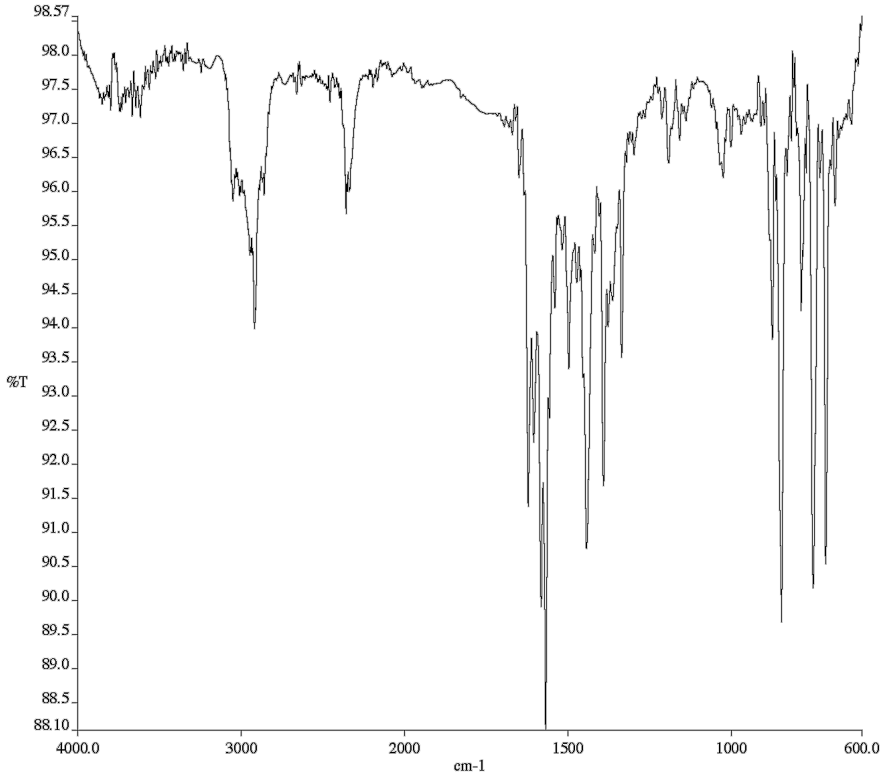
Infrared spectrum (Thin Film, NaCl) of **6j**.



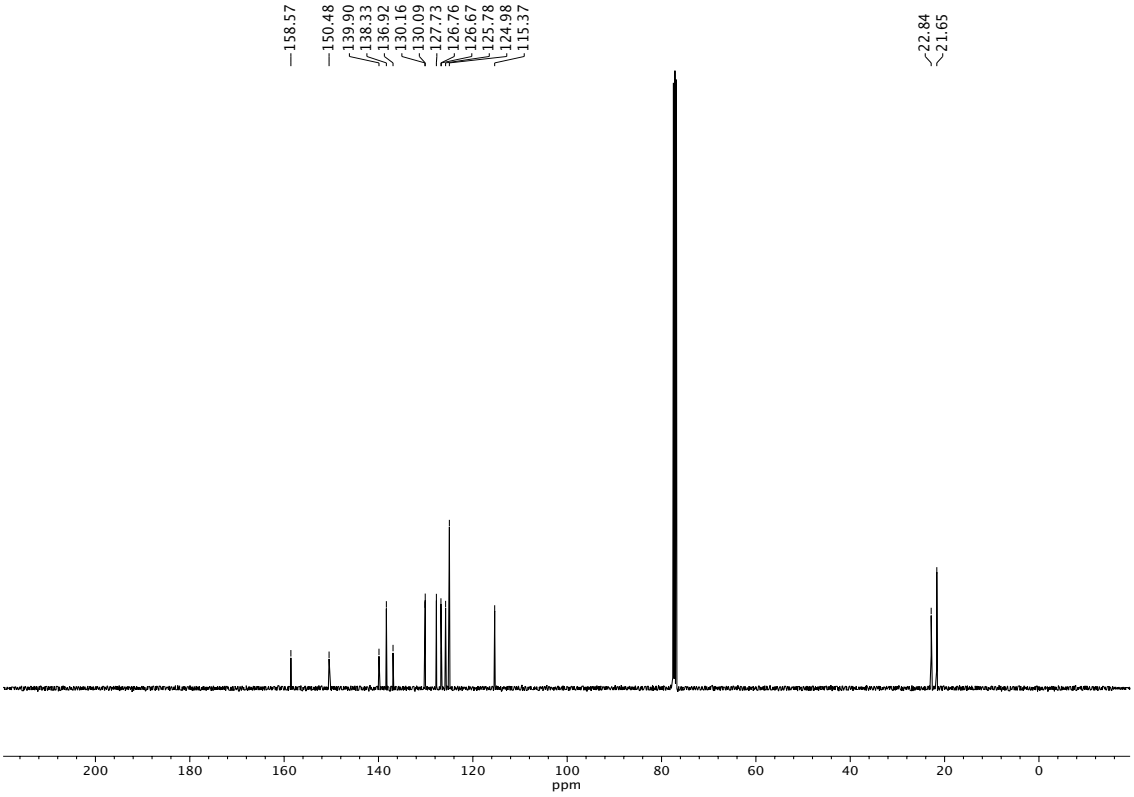
^{13}C NMR (100 MHz, $CDCl_3$) of **6j**.



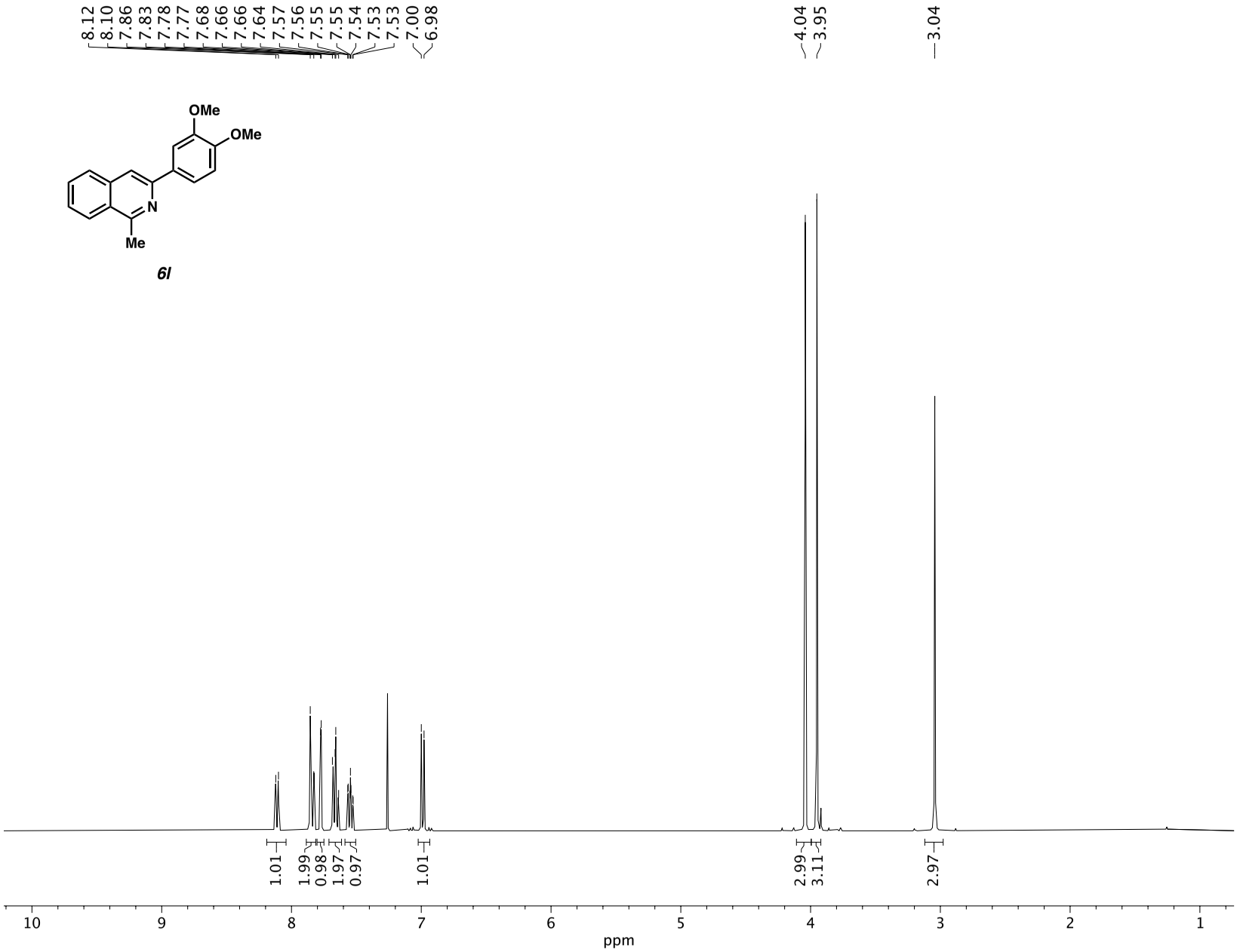
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6k**.



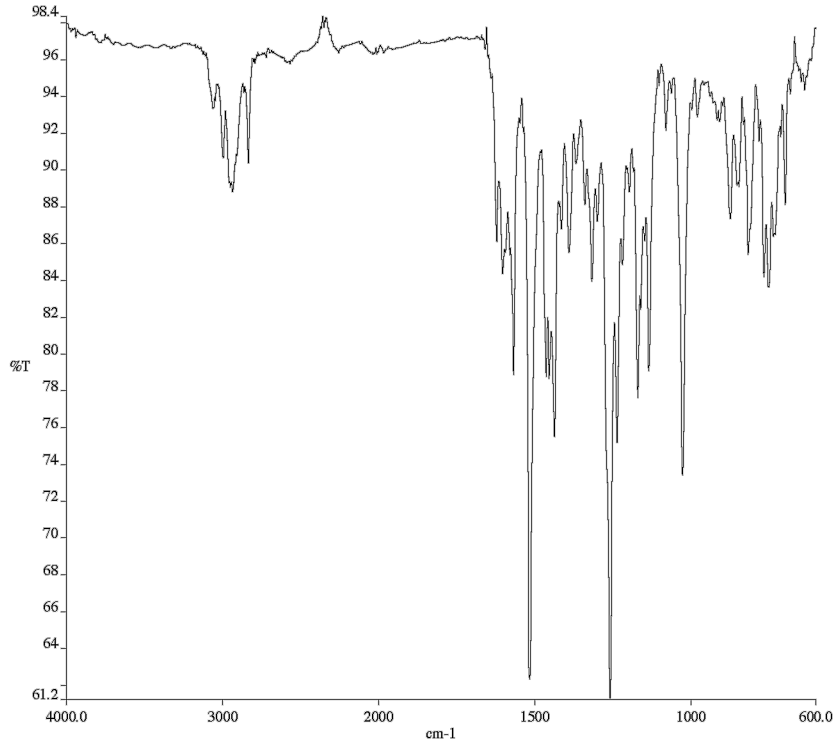
Infrared spectrum (Thin Film, NaCl) of **6k**.



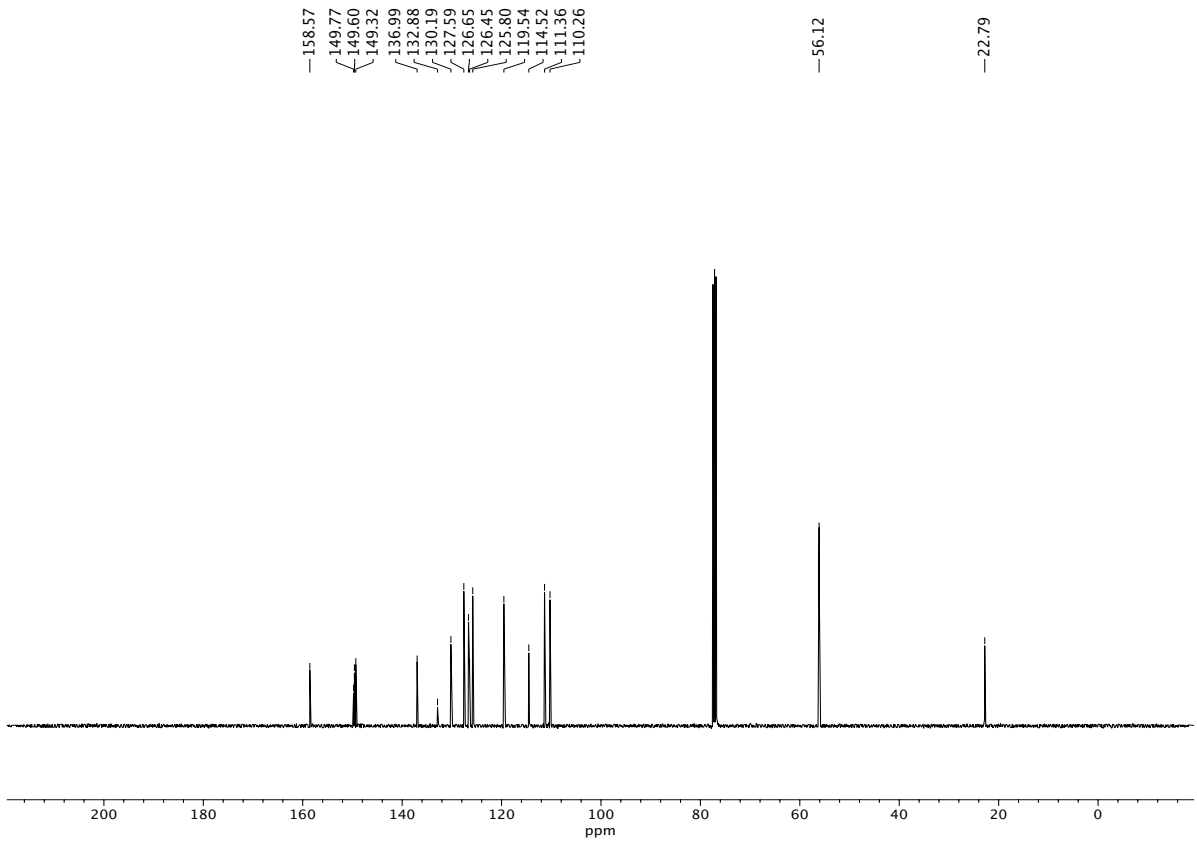
^{13}C NMR (100 MHz, $CDCl_3$) of **6k**.



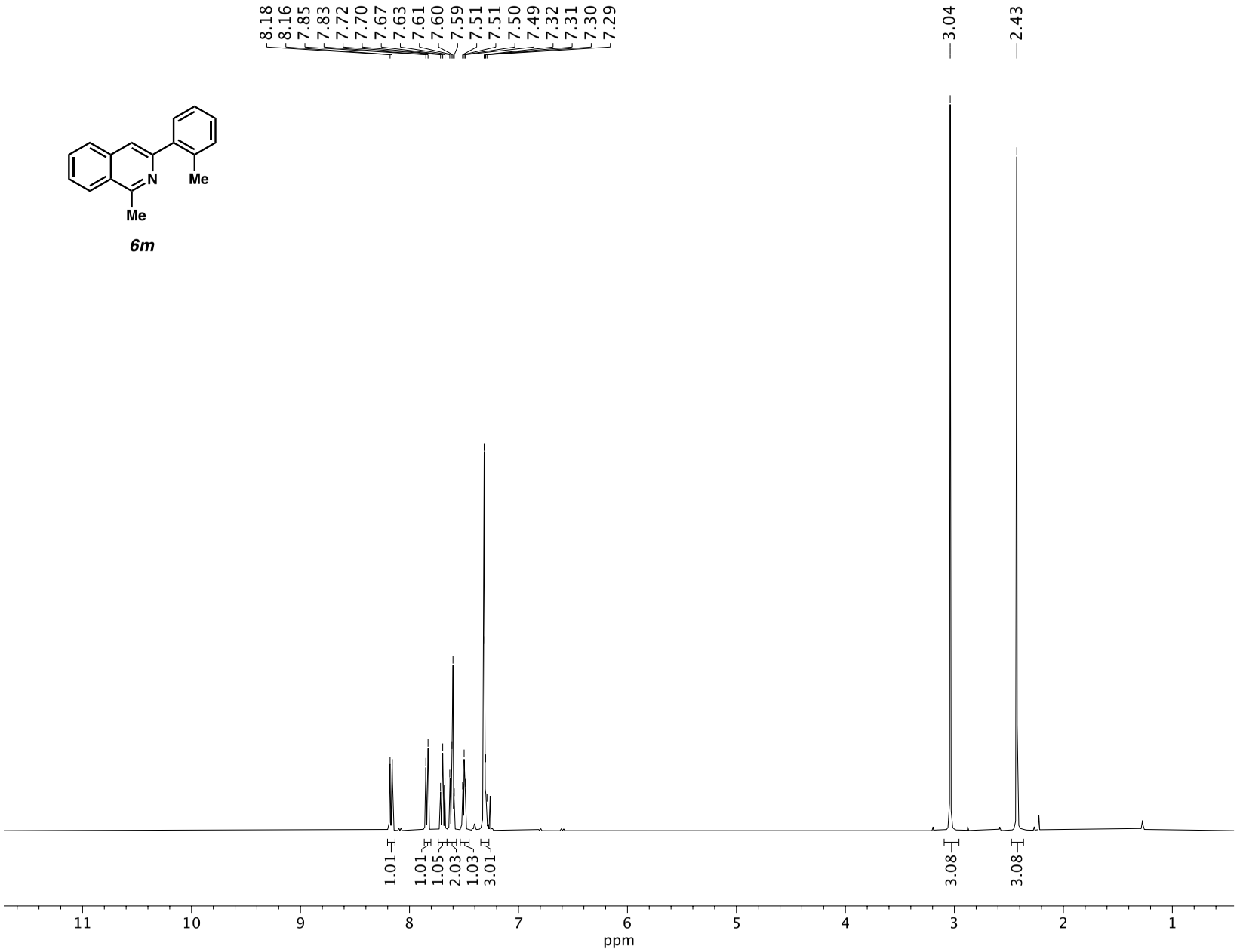
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6l**.



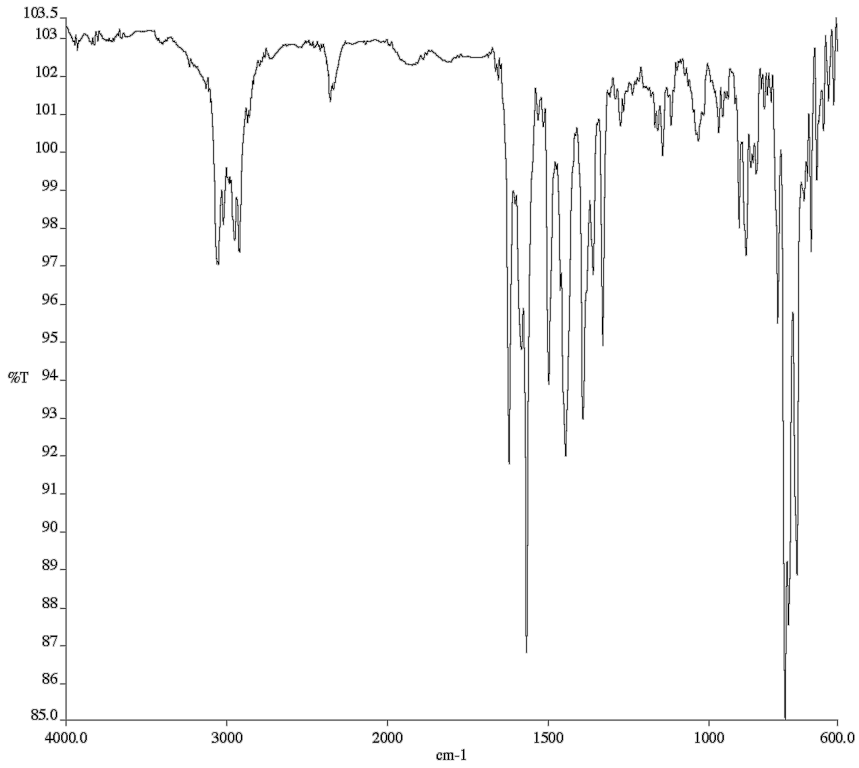
Infrared spectrum (Thin Film, NaCl) of **6l**.



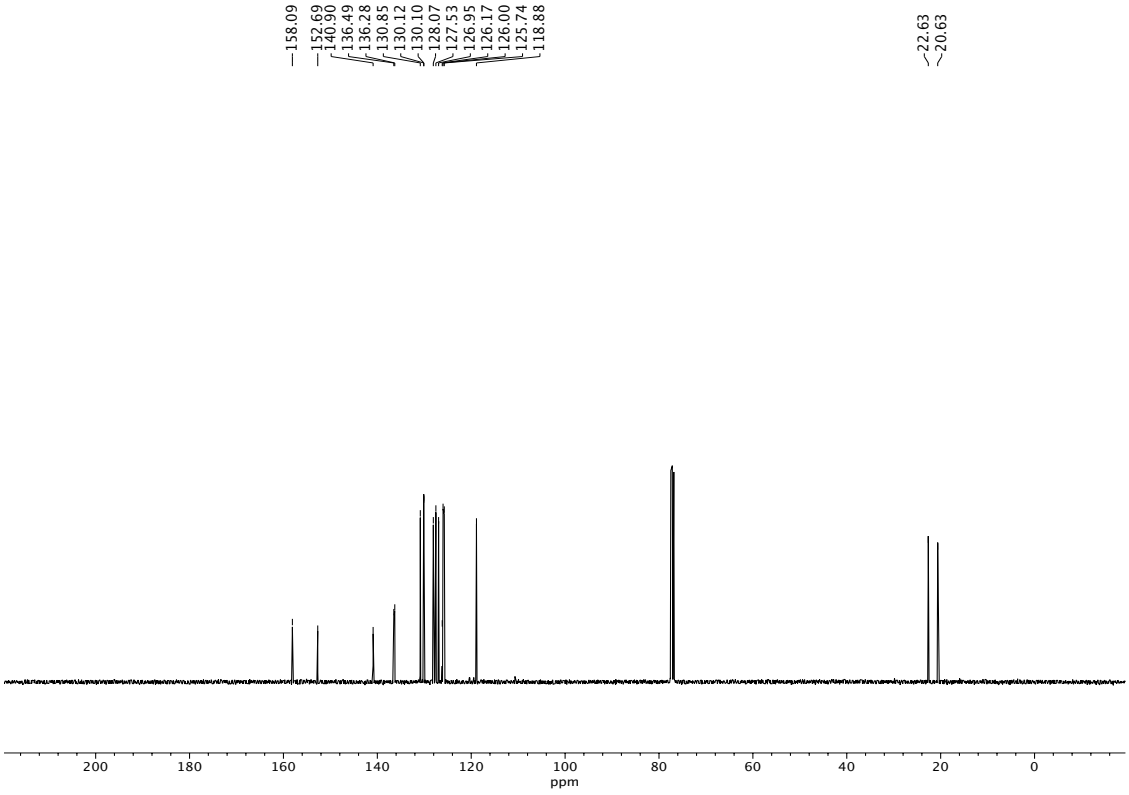
^{13}C NMR (100 MHz, $CDCl_3$) of **6l**.



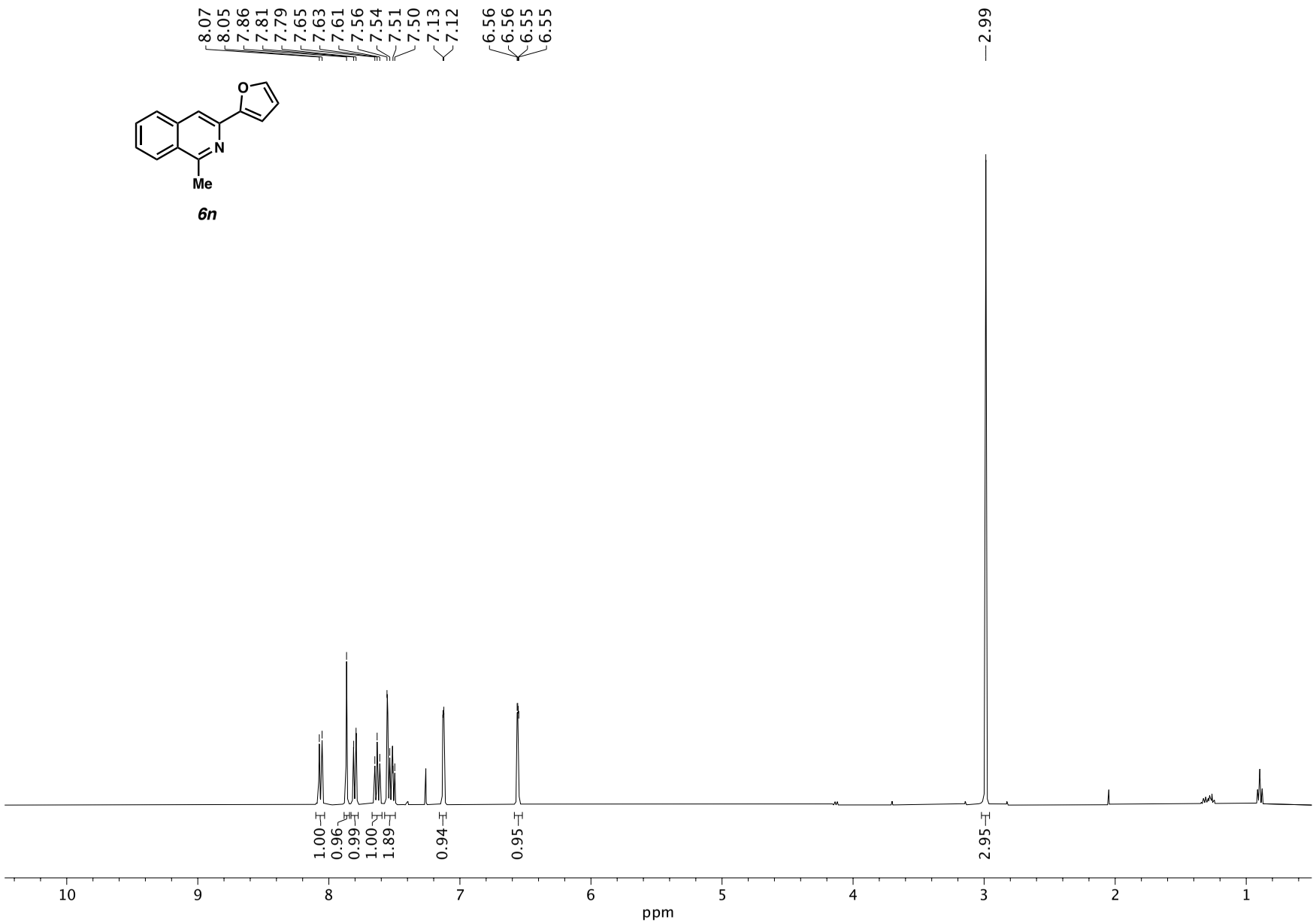
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6m**.



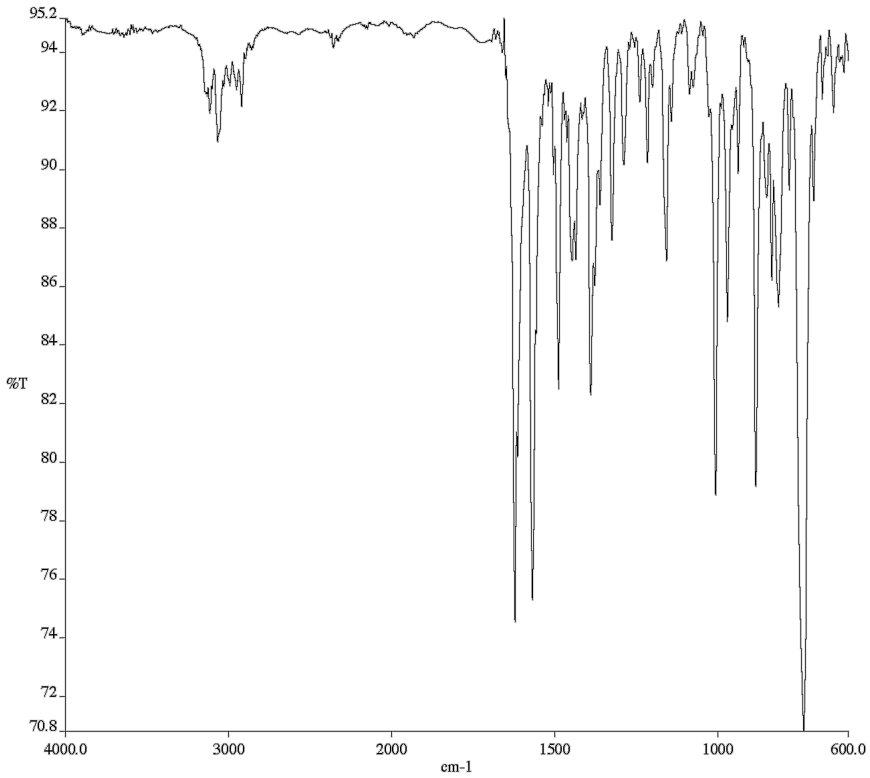
Infrared spectrum (Thin Film, NaCl) of **6m**.



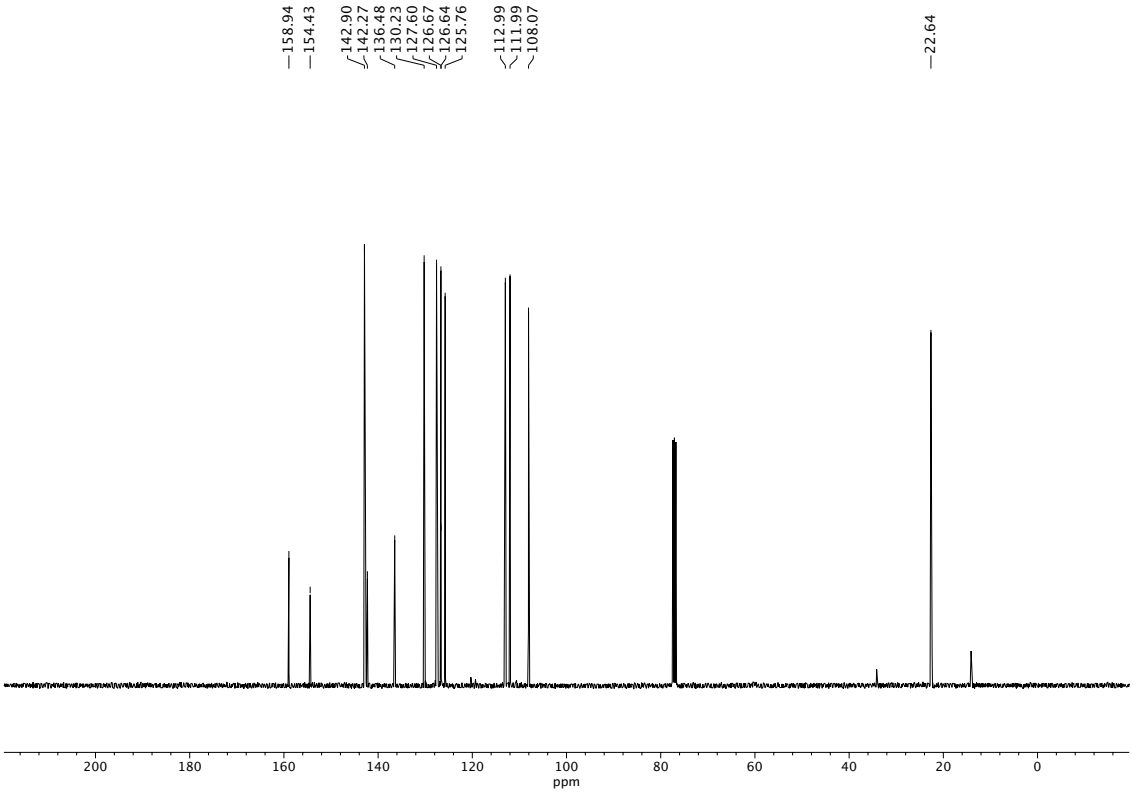
^{13}C NMR (100 MHz, $CDCl_3$) of **6m**.



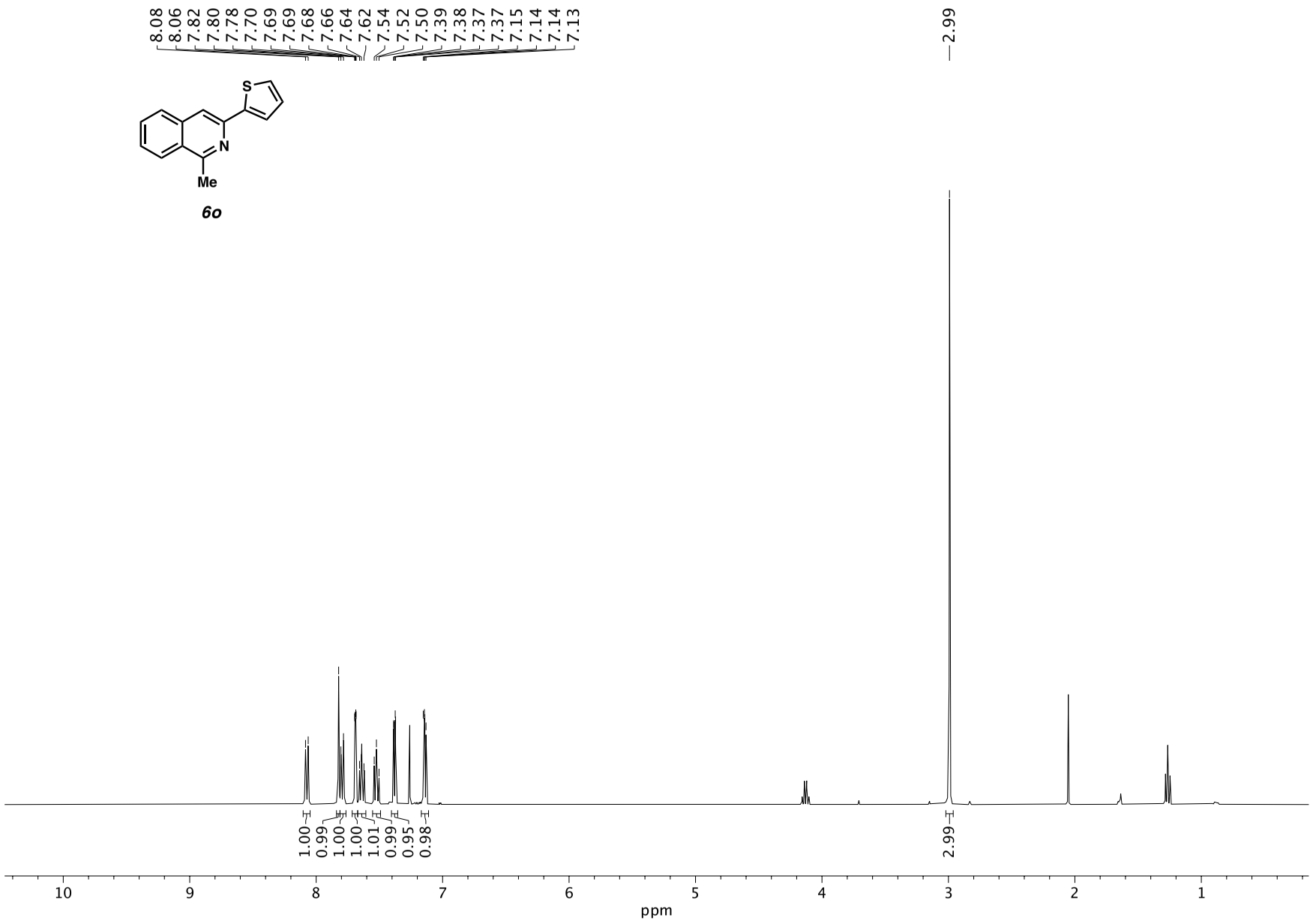
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6n**.



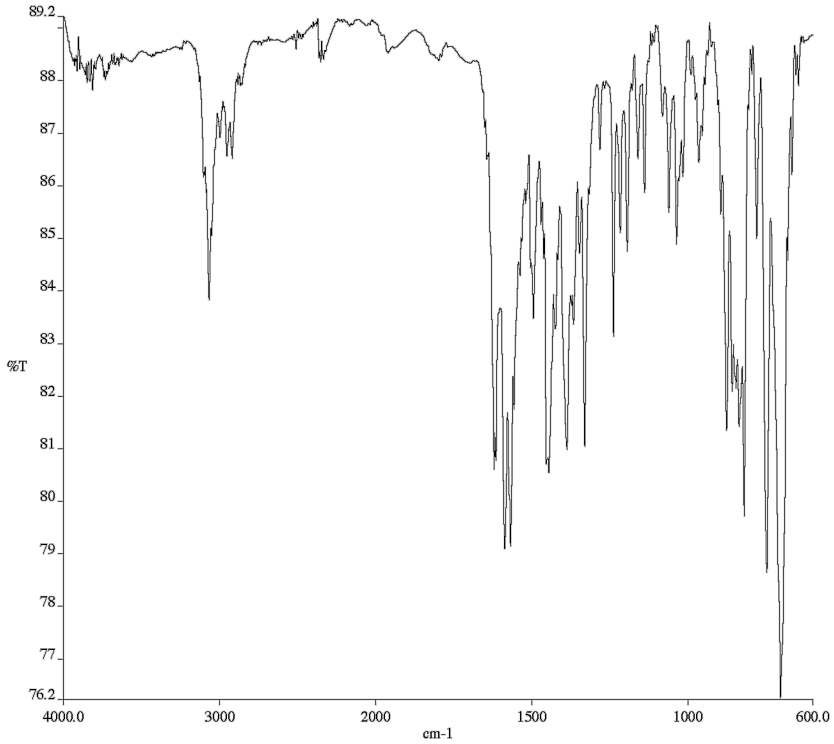
Infrared spectrum (Thin Film, NaCl) of **6n**.



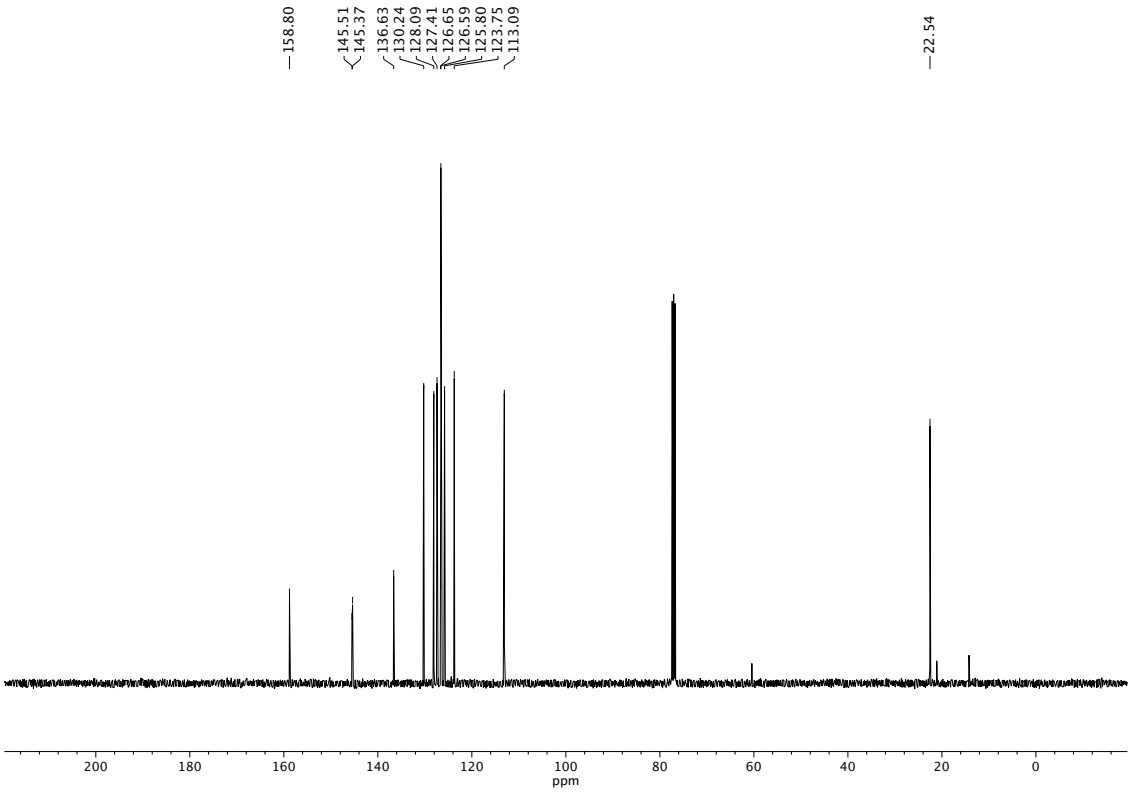
^{13}C NMR (100 MHz, $CDCl_3$) of **6n**.



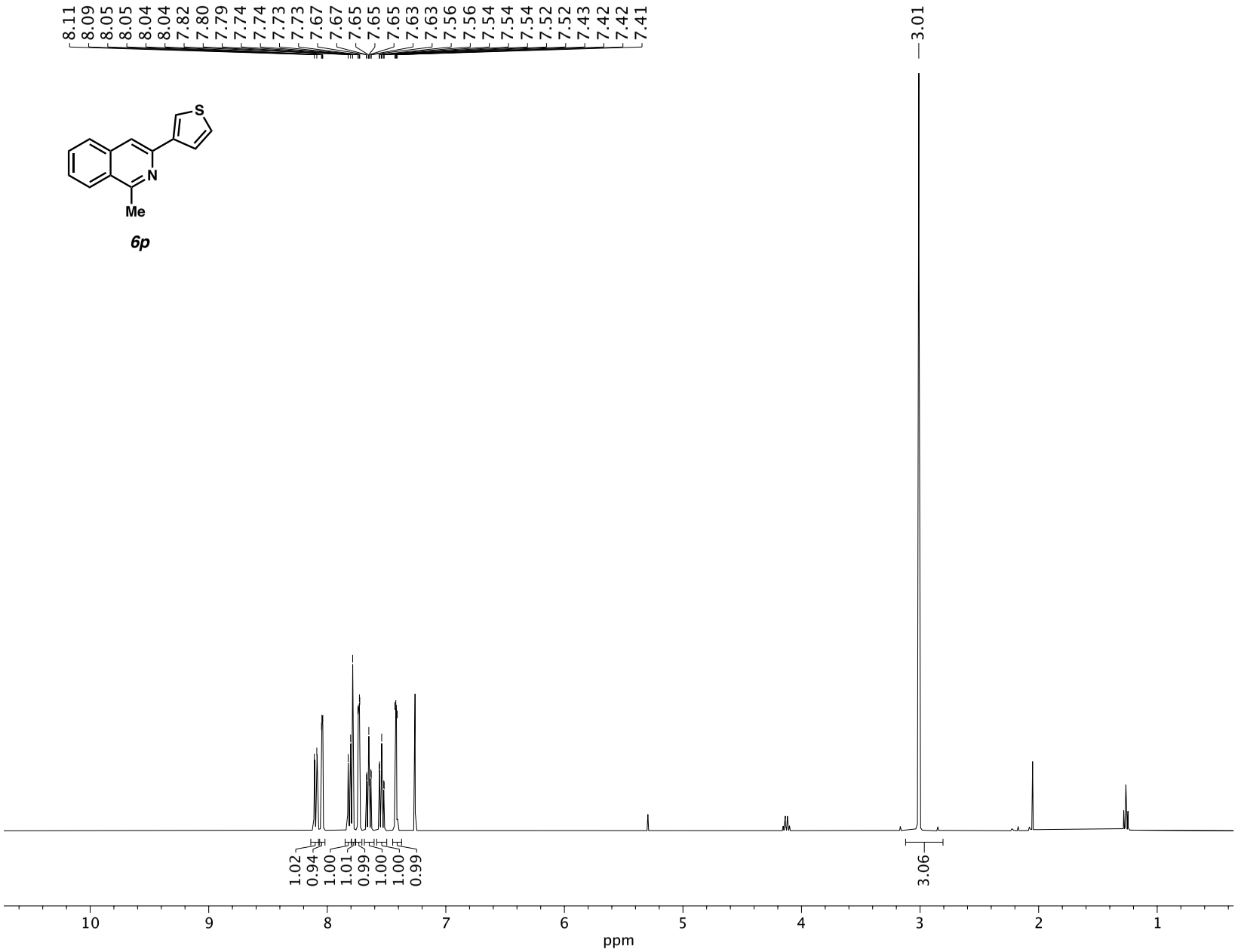
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6o**.



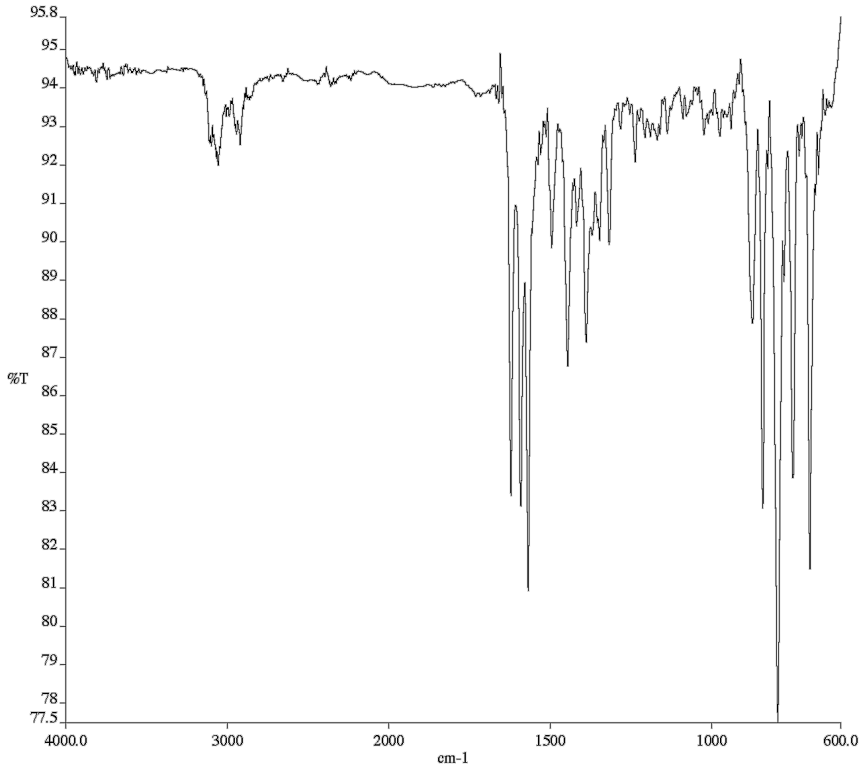
Infrared spectrum (Thin Film, NaCl) of **6o**.



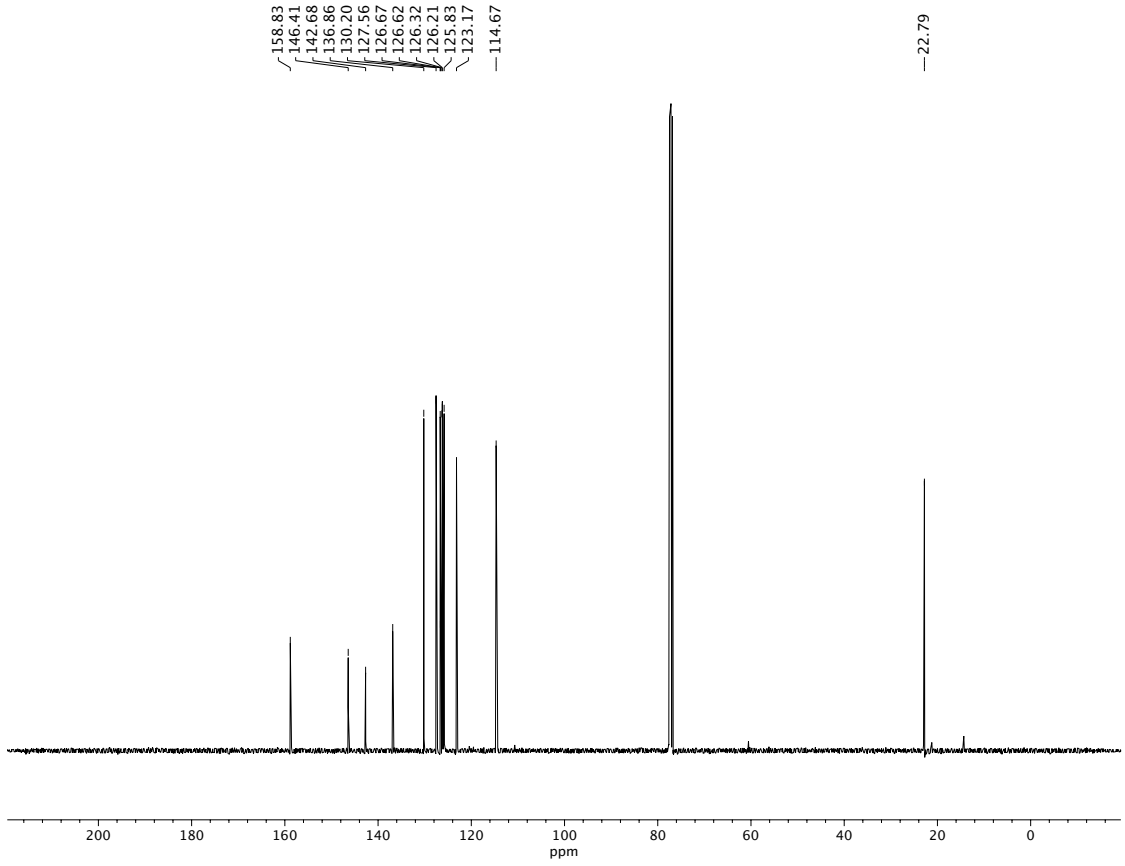
^{13}C NMR (100 MHz, $CDCl_3$) of **6o**.



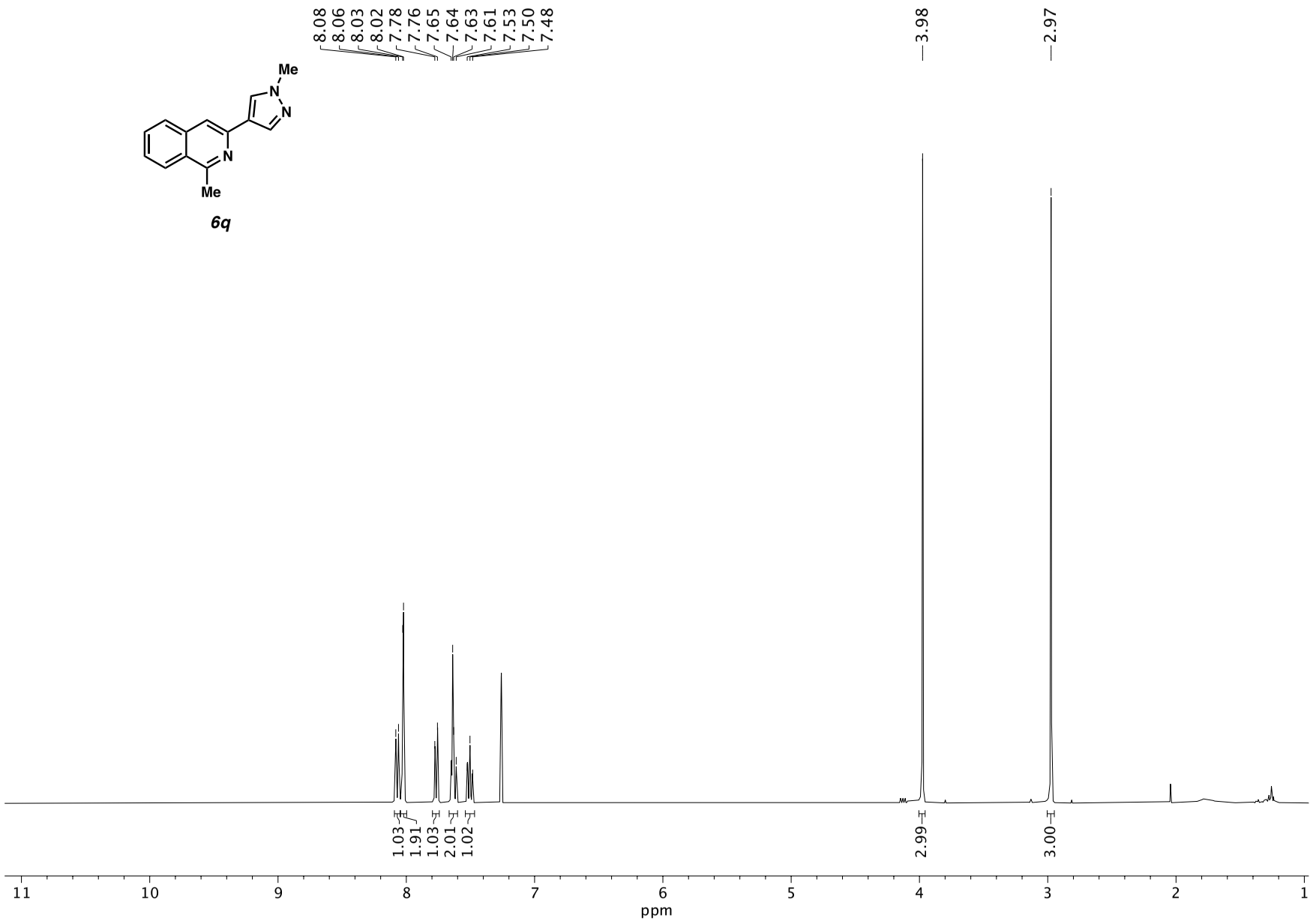
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6p**.



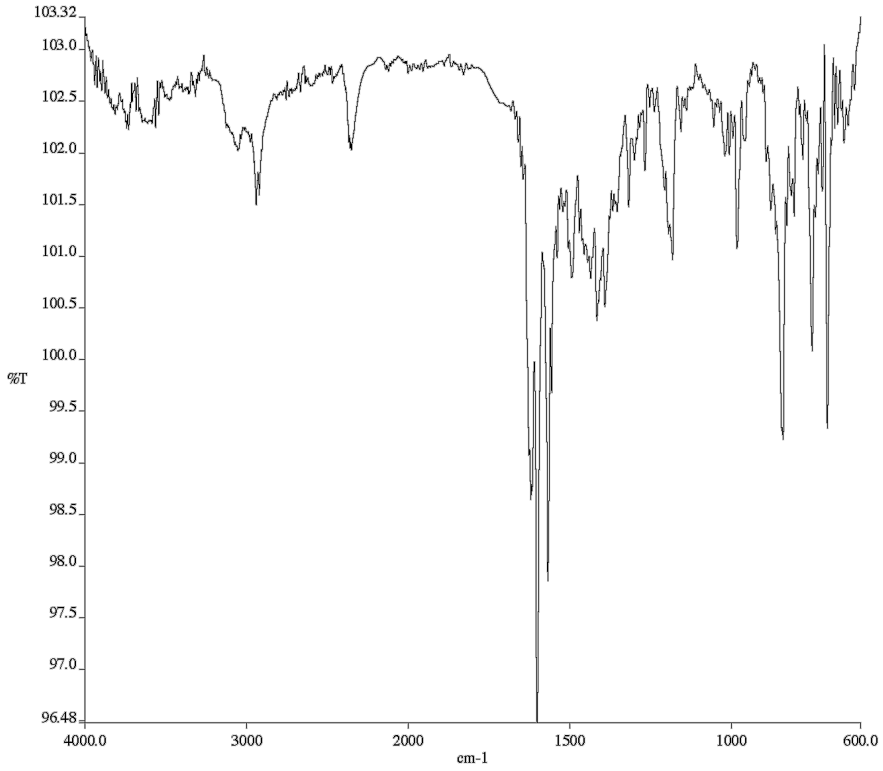
Infrared spectrum (Thin Film, NaCl) of **6p**.



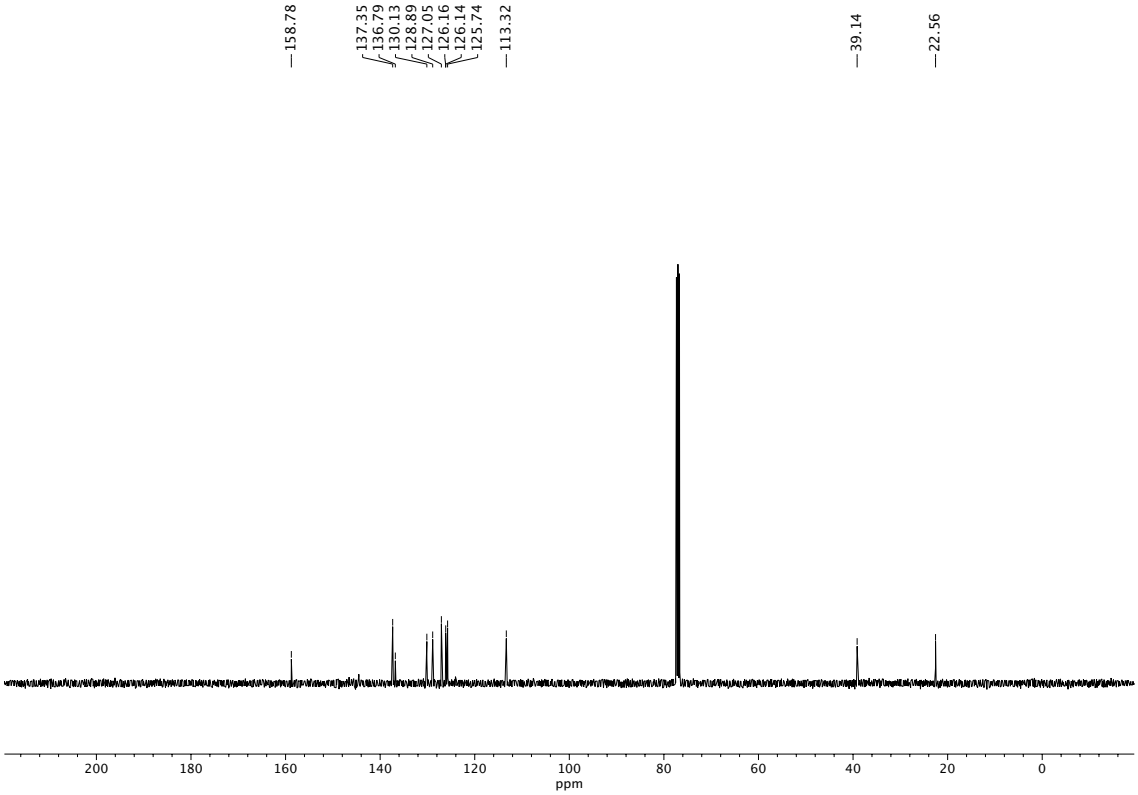
^{13}C NMR (100 MHz, $CDCl_3$) of **6p**.



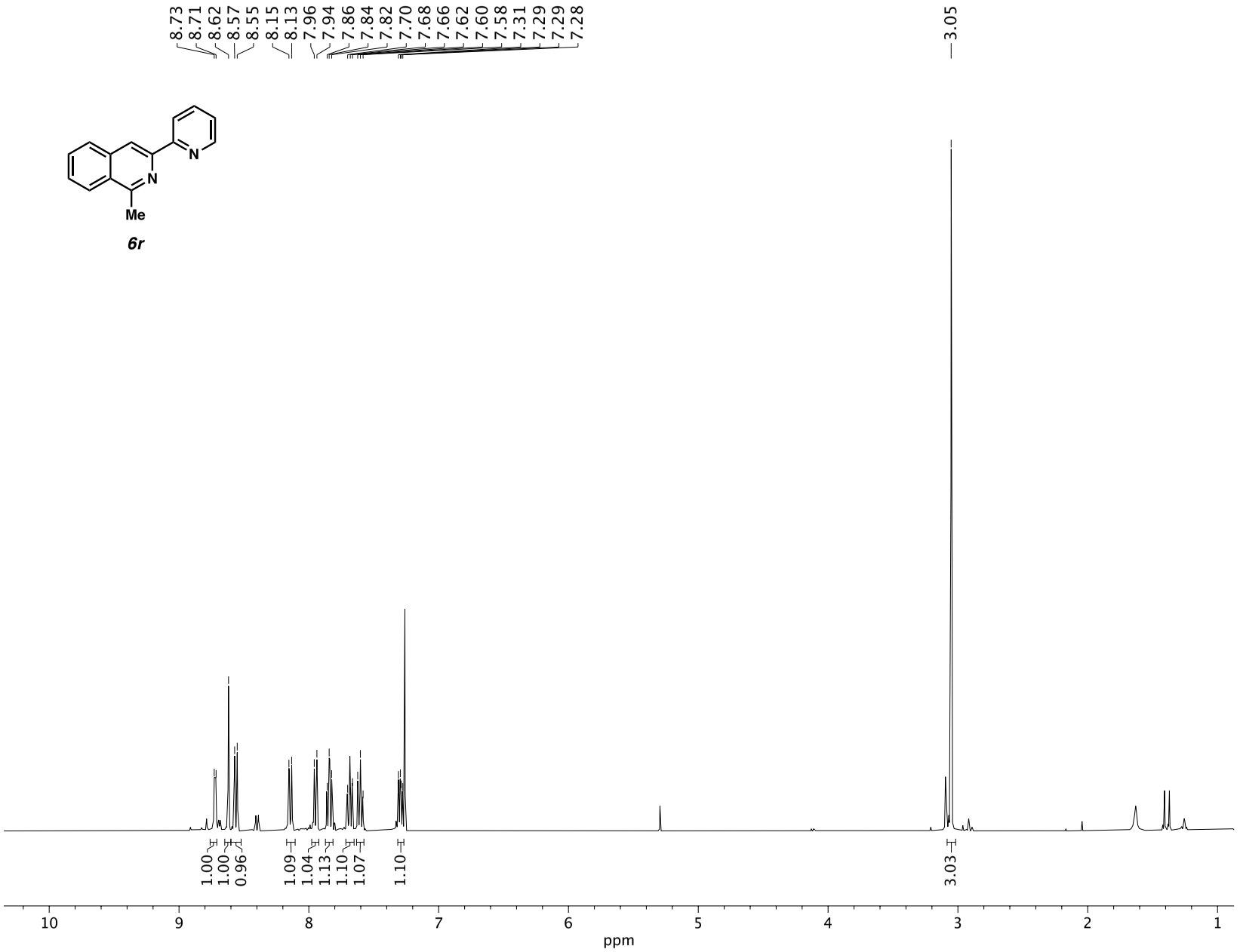
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6q**.



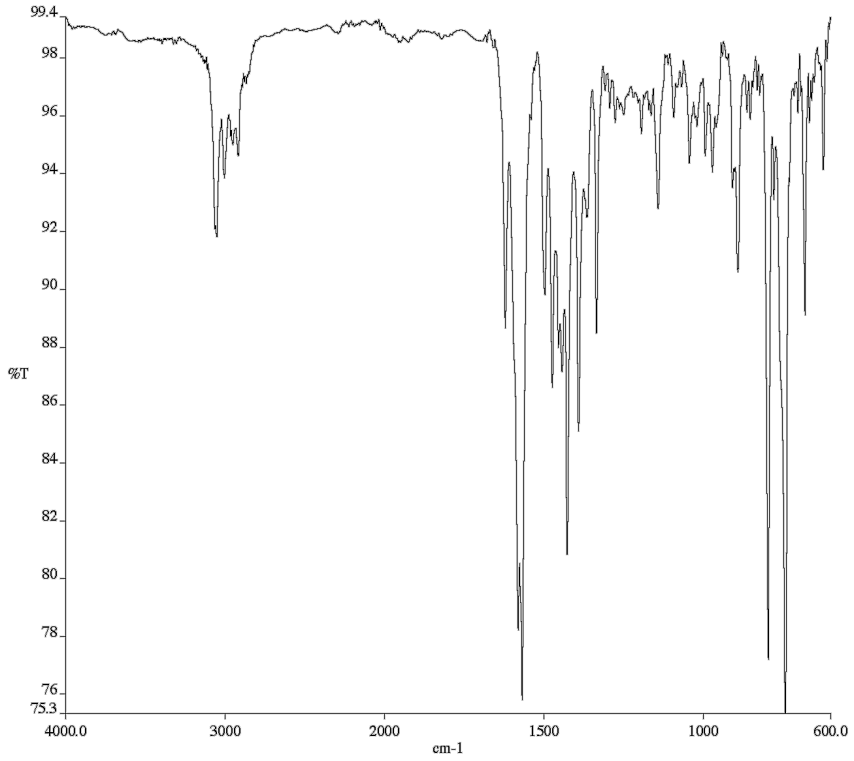
Infrared spectrum (Thin Film, NaCl) of **6q**.



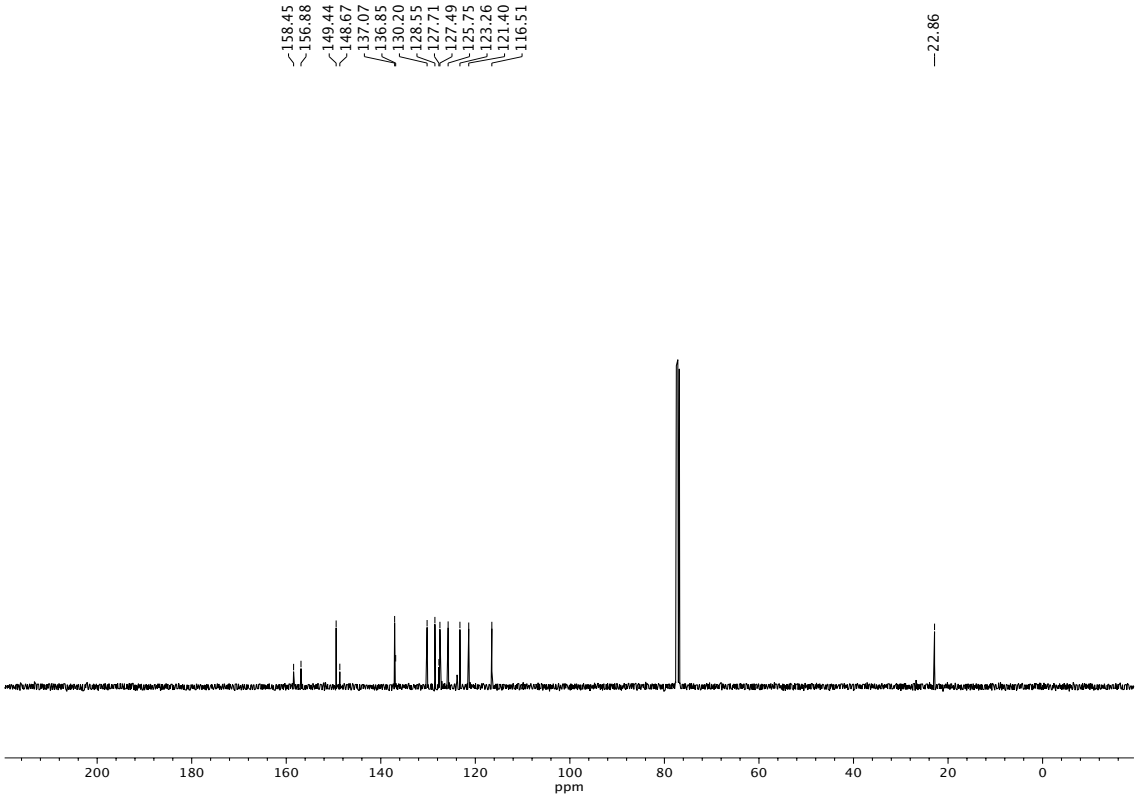
^{13}C NMR (100 MHz, $CDCl_3$) of **6q**.



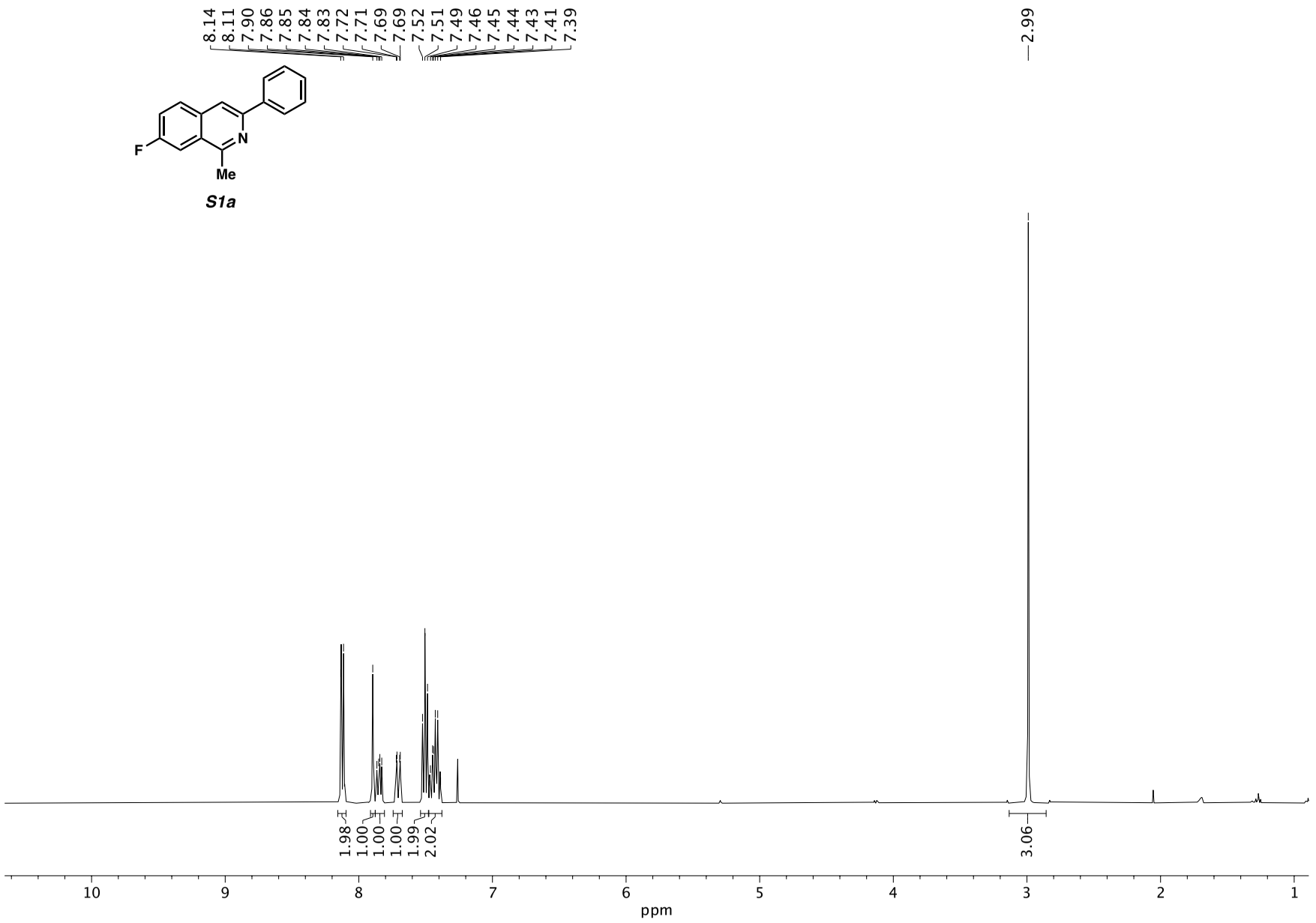
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6r**.



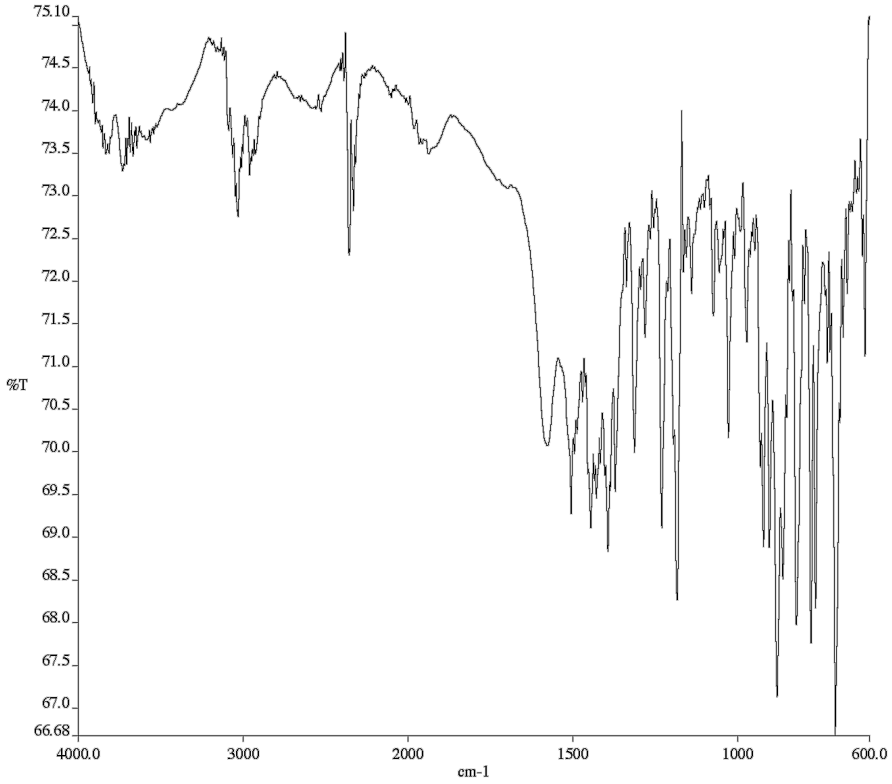
Infrared spectrum (Thin Film, NaCl) of **6r**.



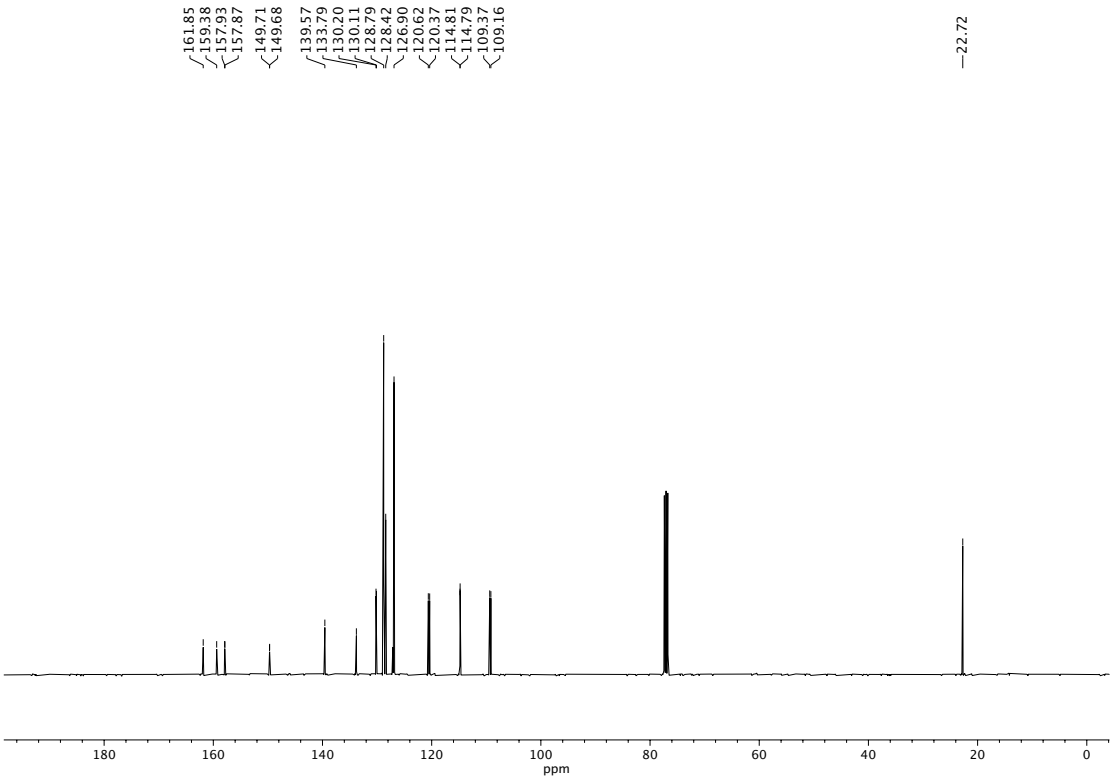
^{13}C NMR (100 MHz, $CDCl_3$) of **6r**.



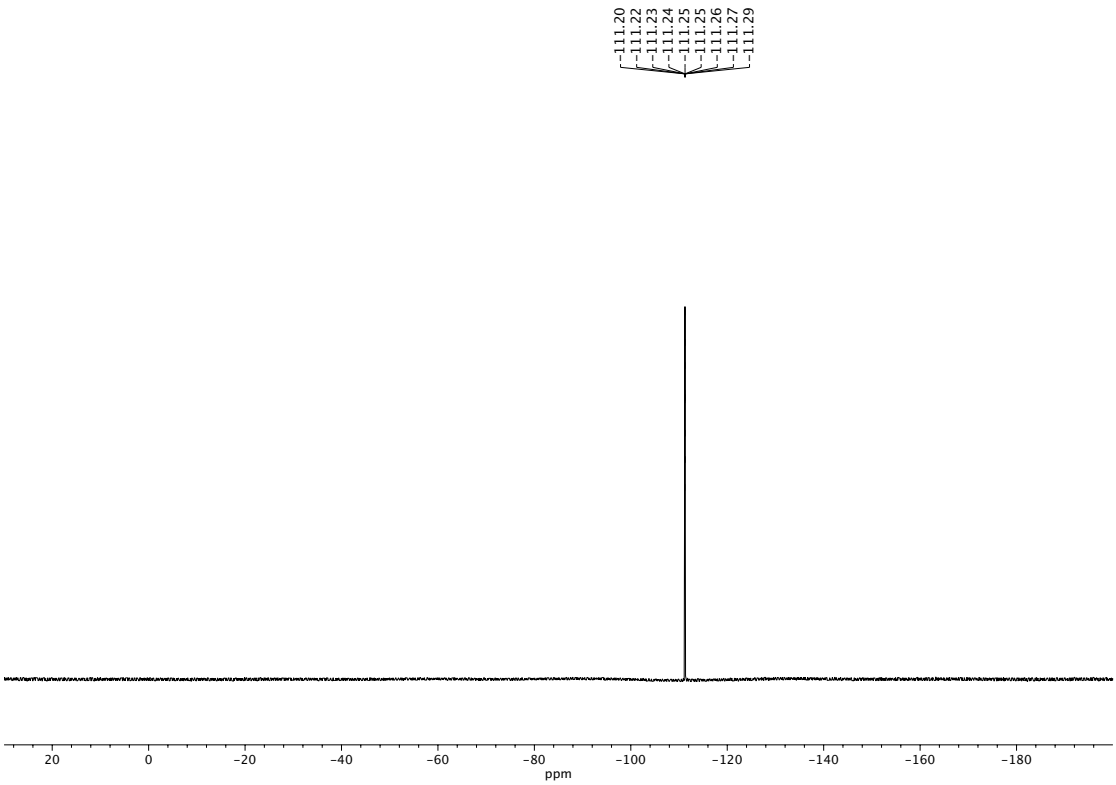
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1a**.



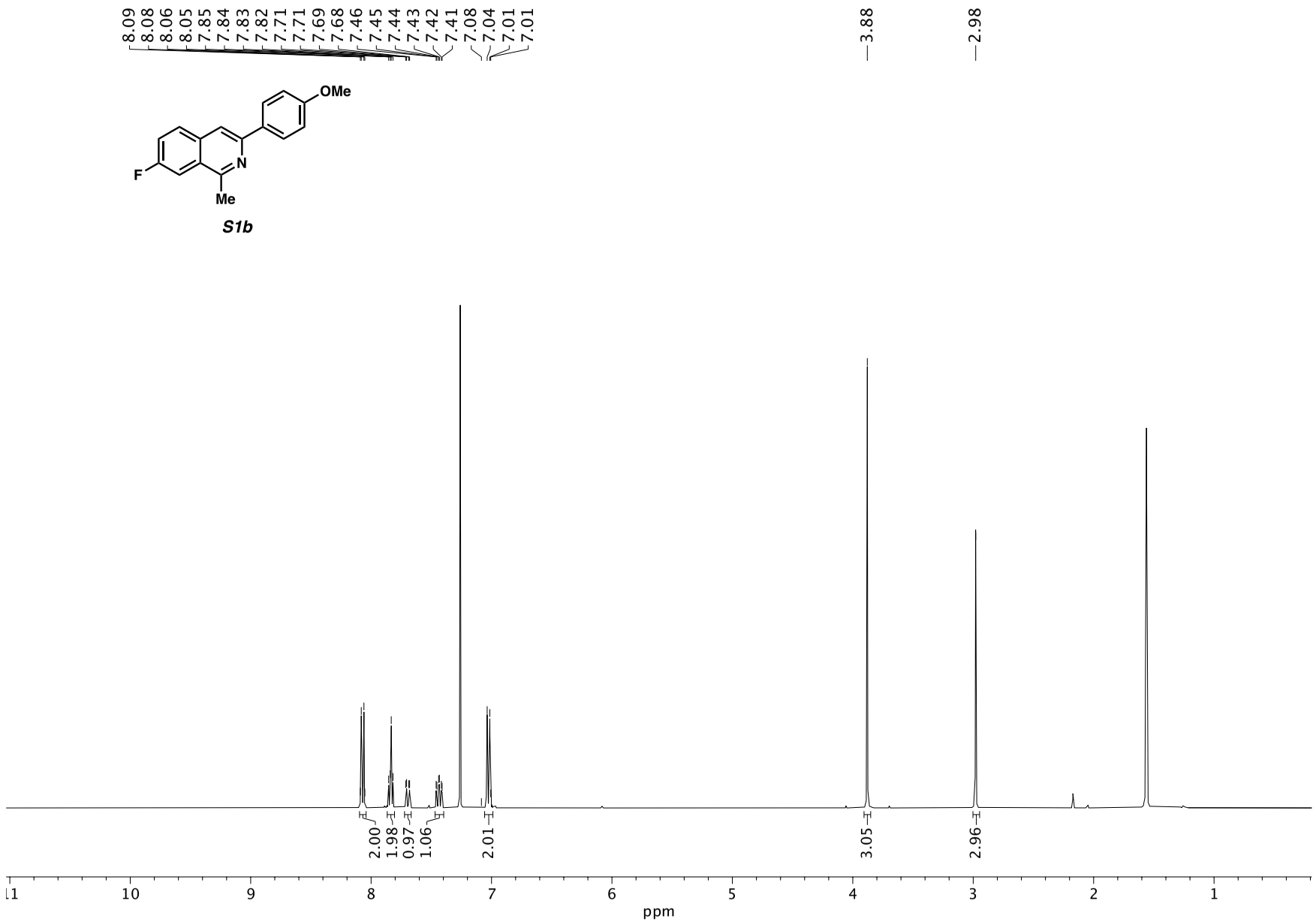
Infrared spectrum (Thin Film, NaCl) of **S1a**.



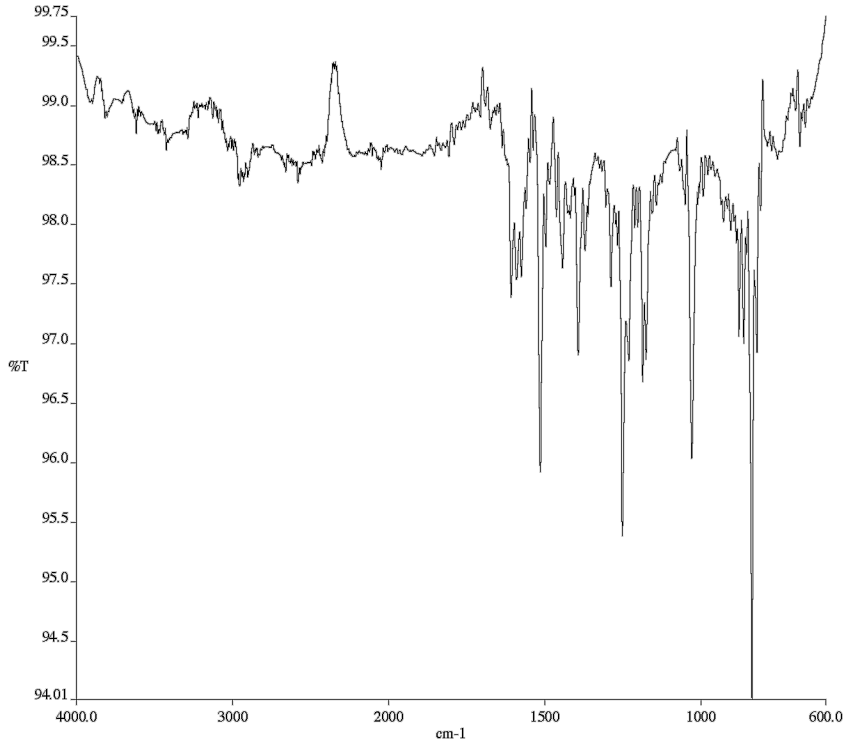
^{13}C NMR (100 MHz, $CDCl_3$) of **S1a**.



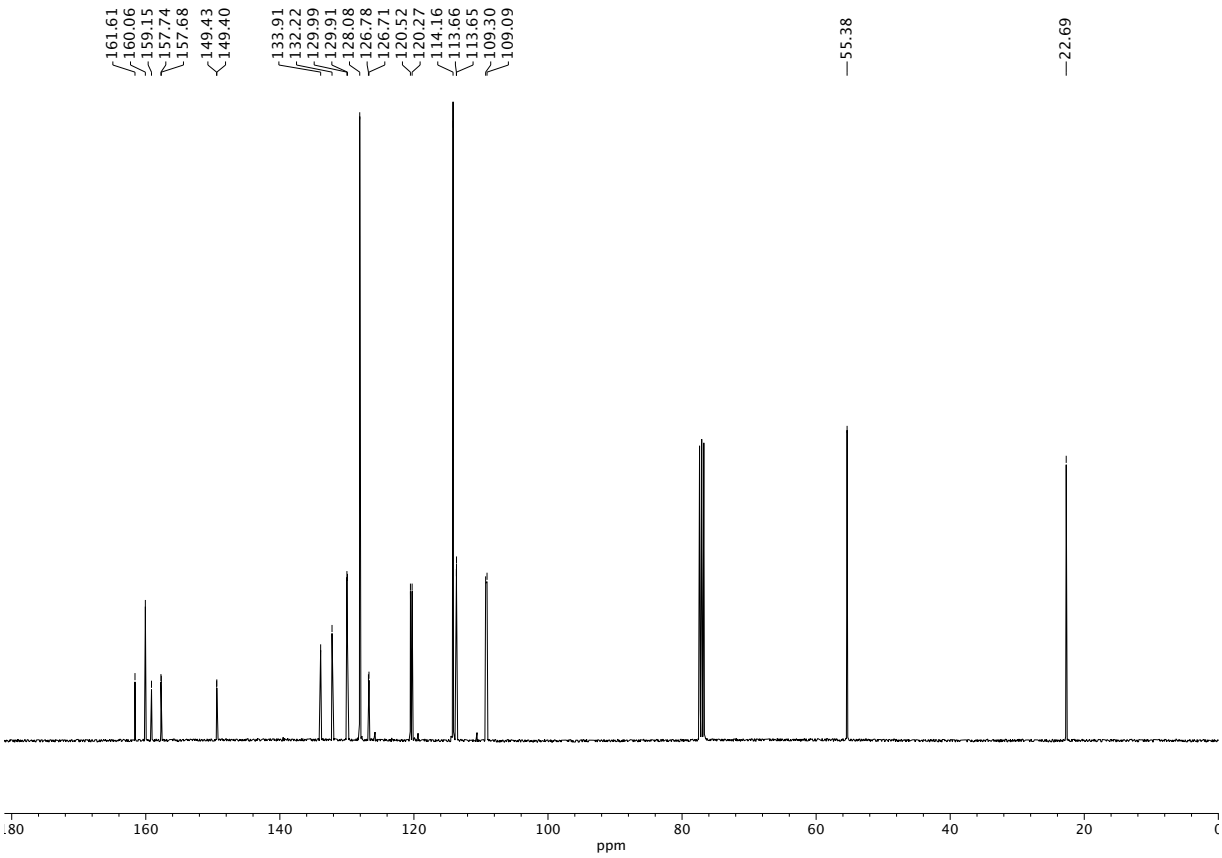
^{19}F NMR (282 MHz, $CDCl_3$) of **S1a**.



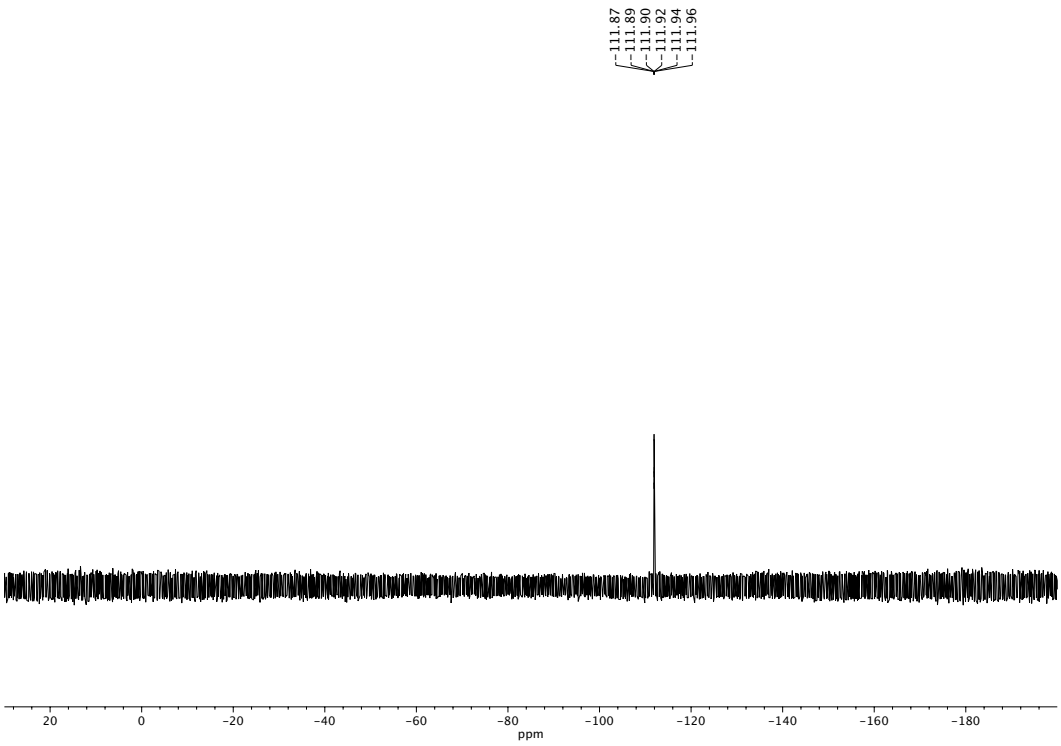
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1b**.



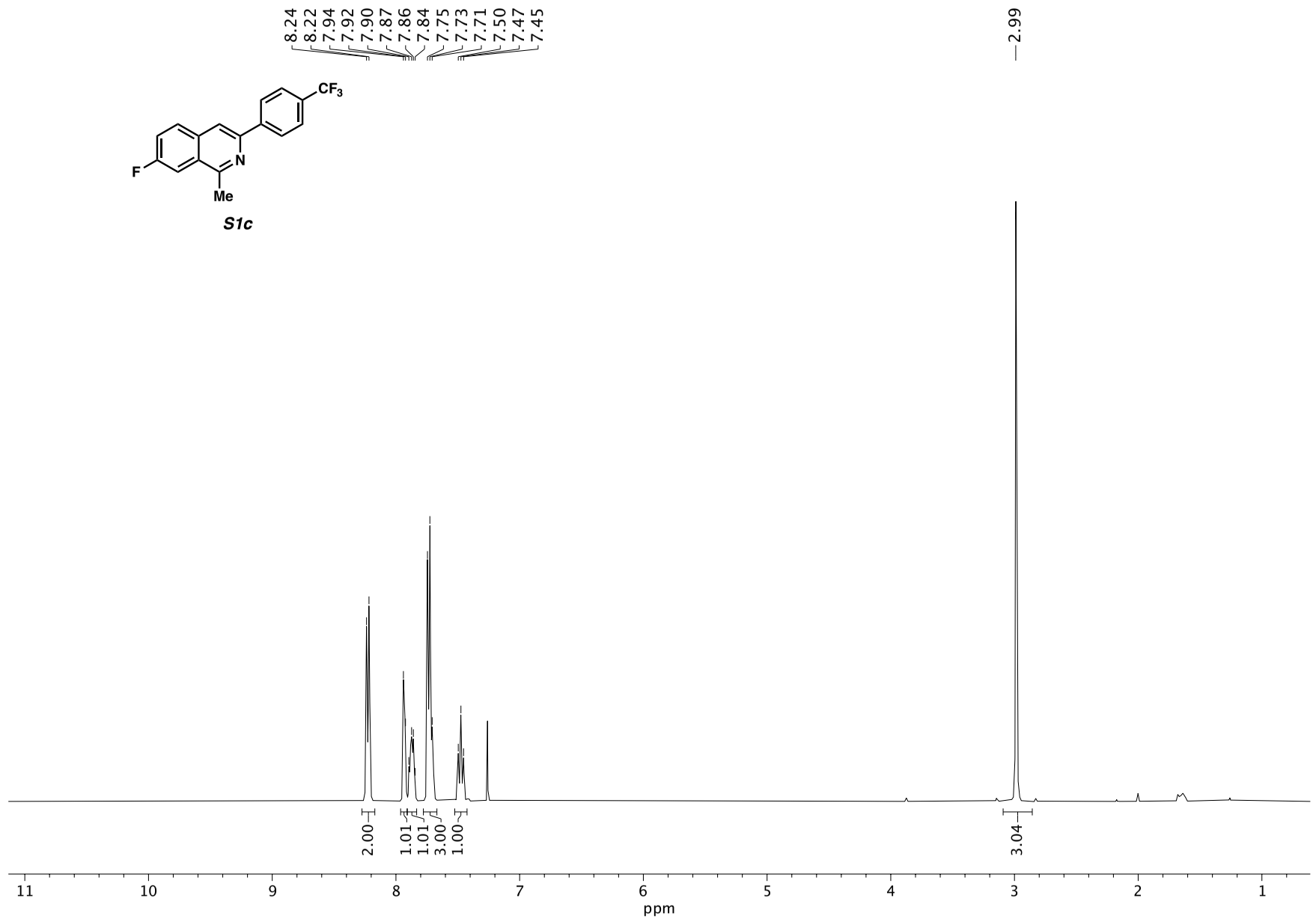
Infrared spectrum (Thin Film, NaCl) of compound **S1b**.



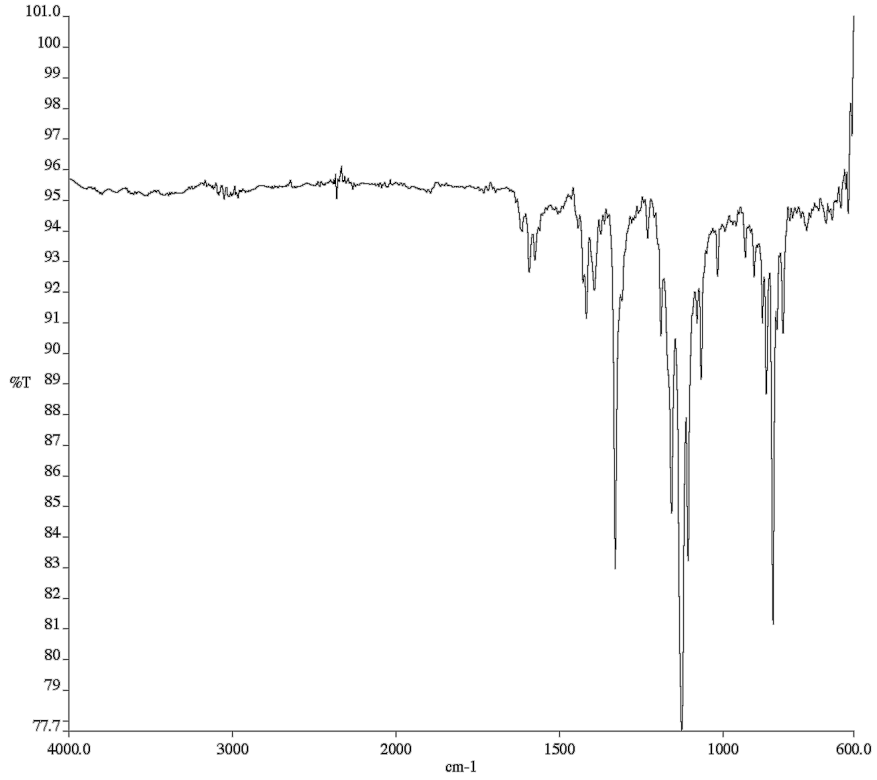
^{13}C NMR (100 MHz, $CDCl_3$) of **S1b**.



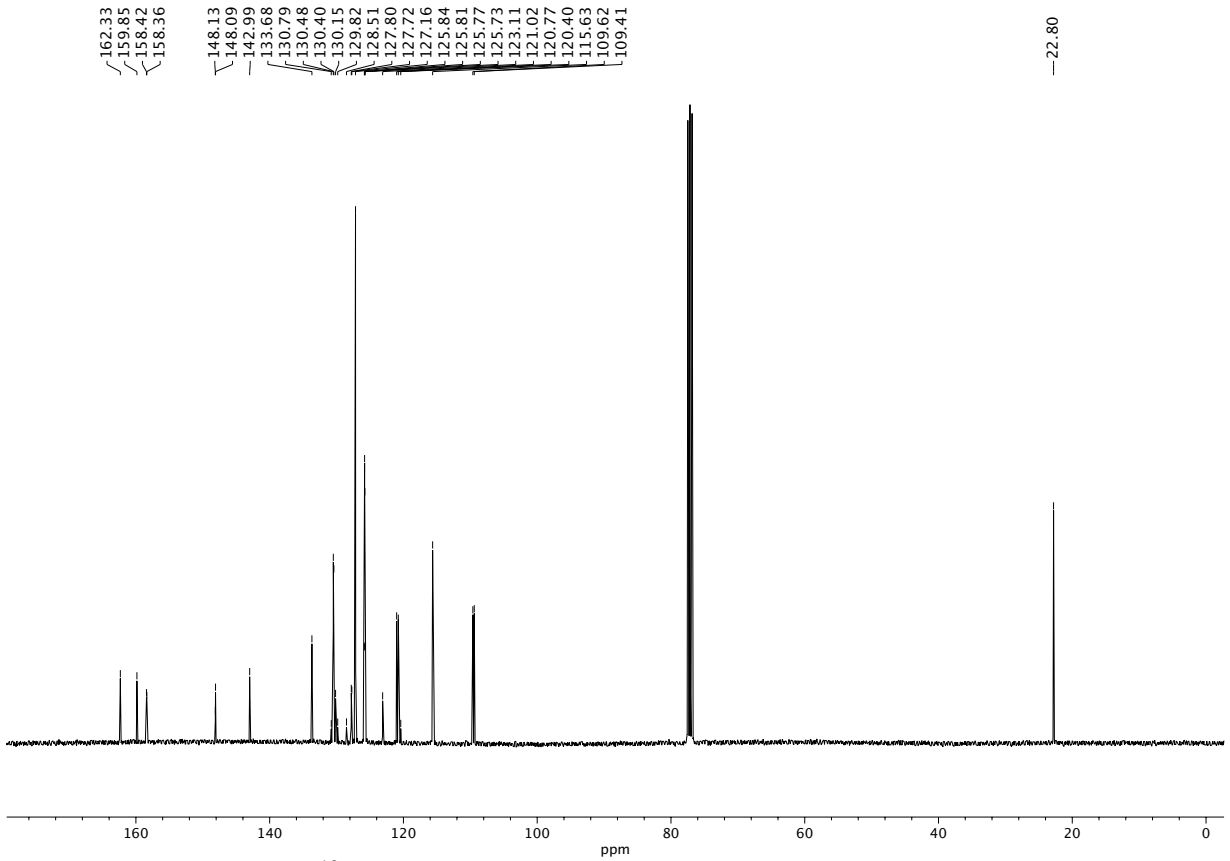
^{19}F NMR (282 MHz, $CDCl_3$) of **S1b**.



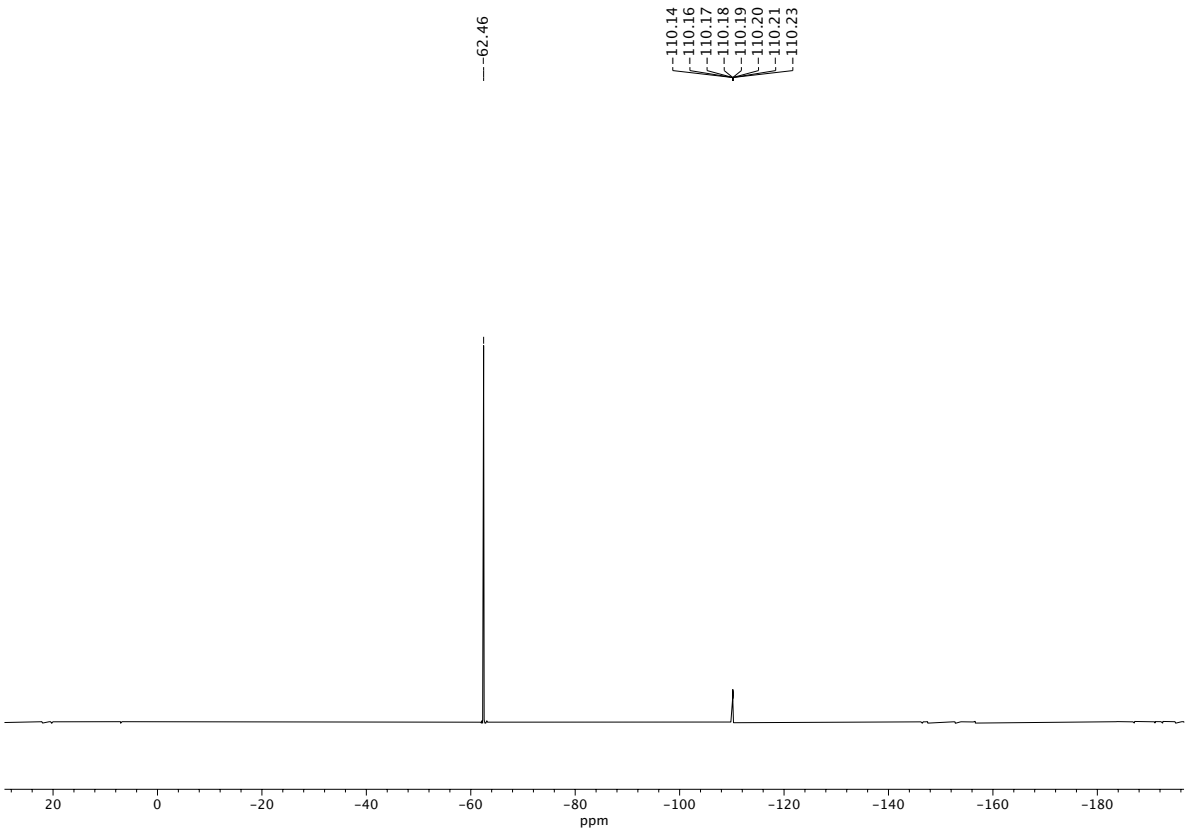
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1c**.



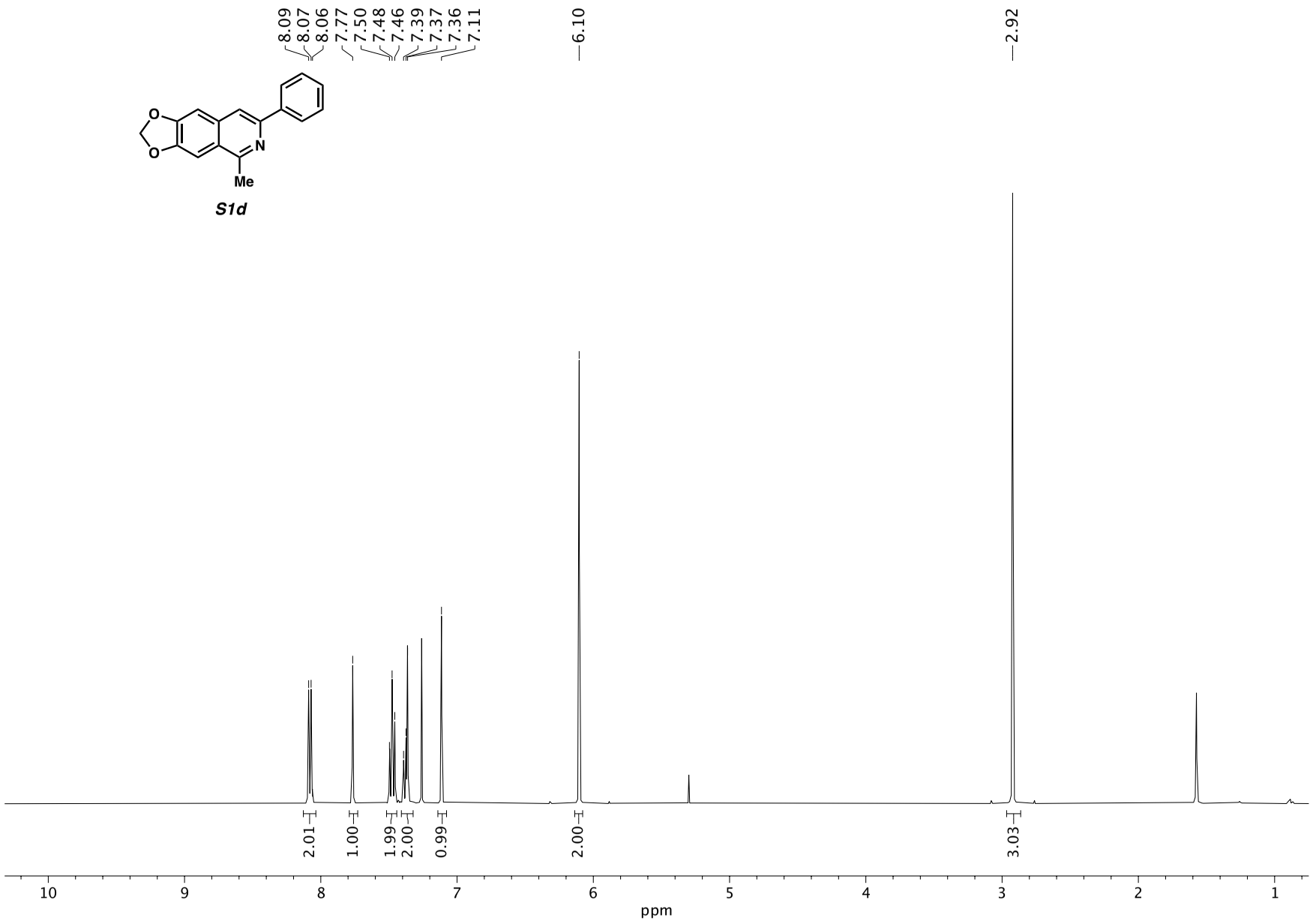
Infrared spectrum (Thin Film, NaCl) of compound **S1c**.



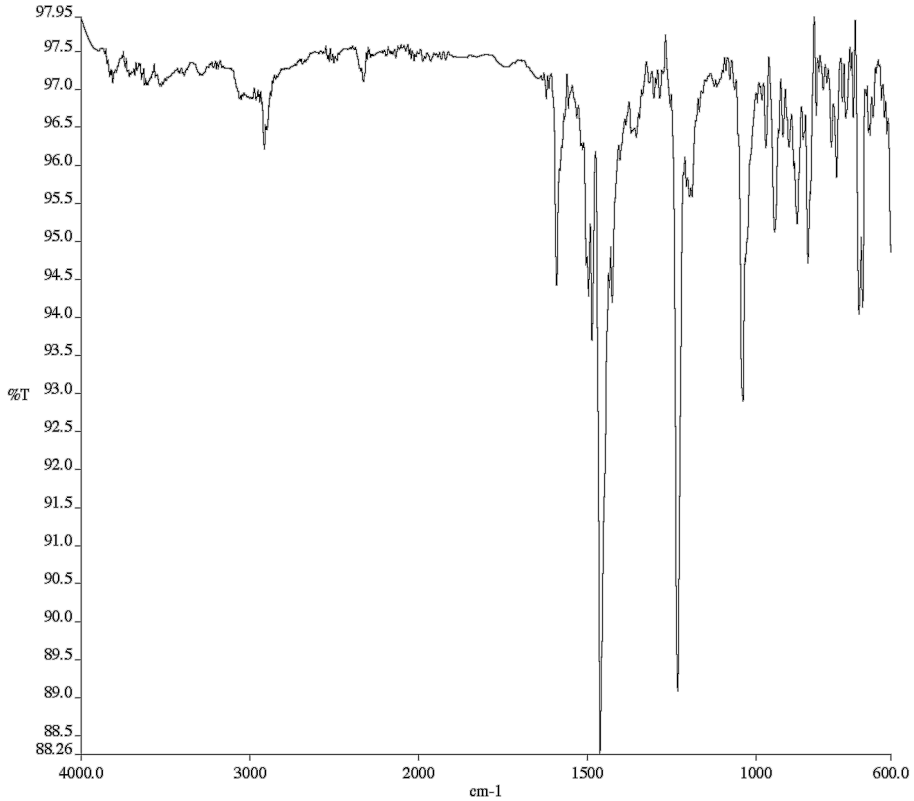
^{13}C NMR (100 MHz, $CDCl_3$) of compound **S1c**.



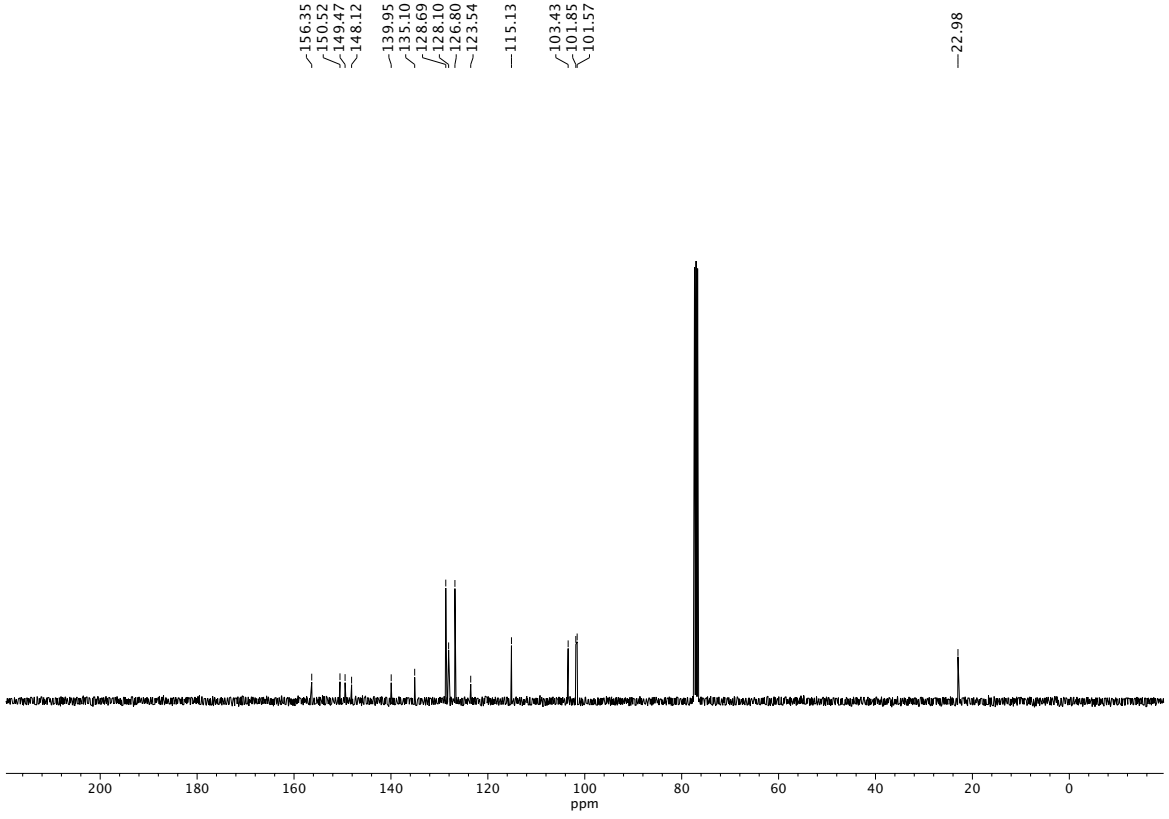
^{19}F NMR (282 MHz, $CDCl_3$) of **S1c**.



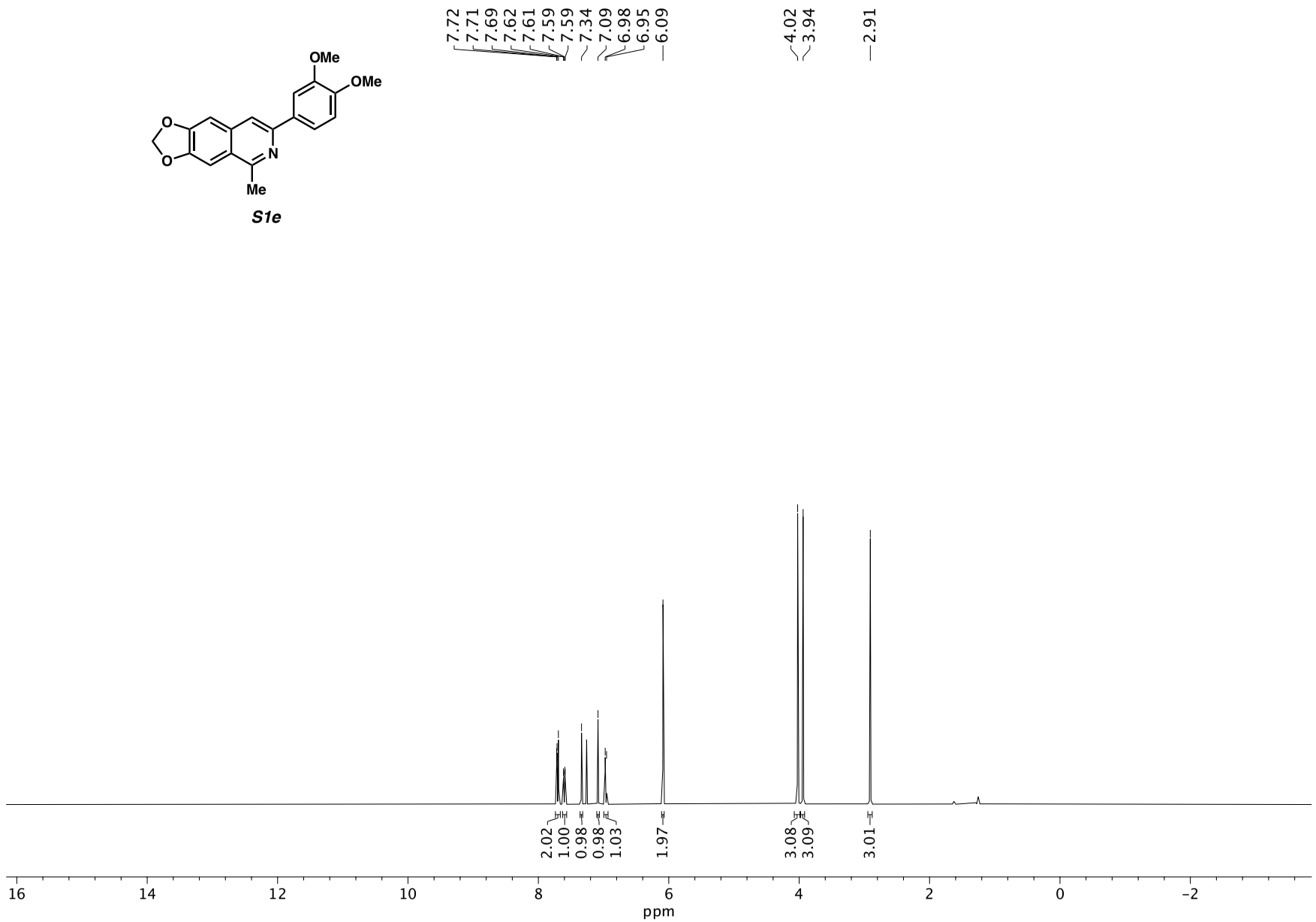
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1d**.



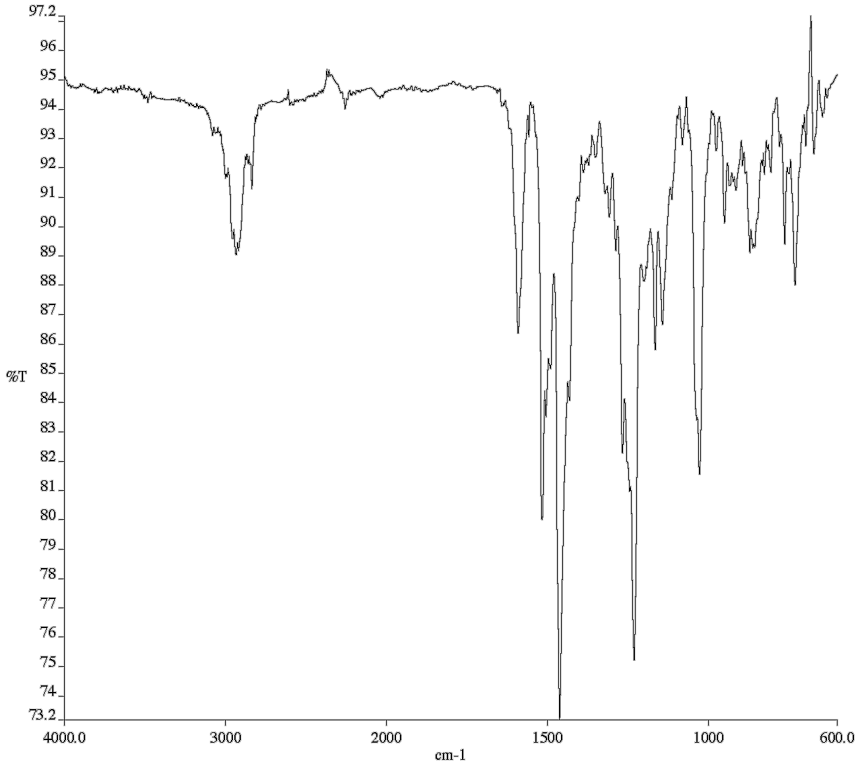
Infrared spectrum (Thin Film, NaCl) of compound **S1d**.



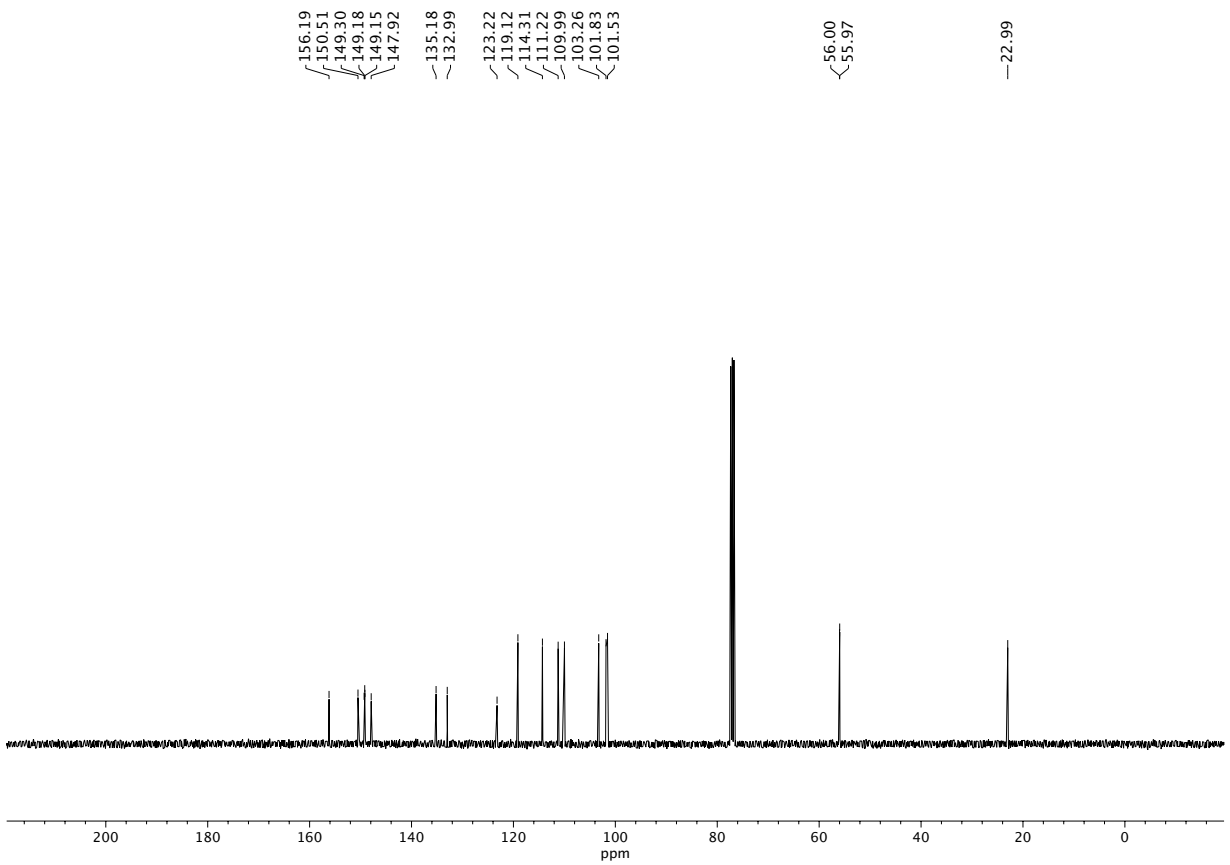
^{13}C NMR (100 MHz, $CDCl_3$) of compound **S1d**.



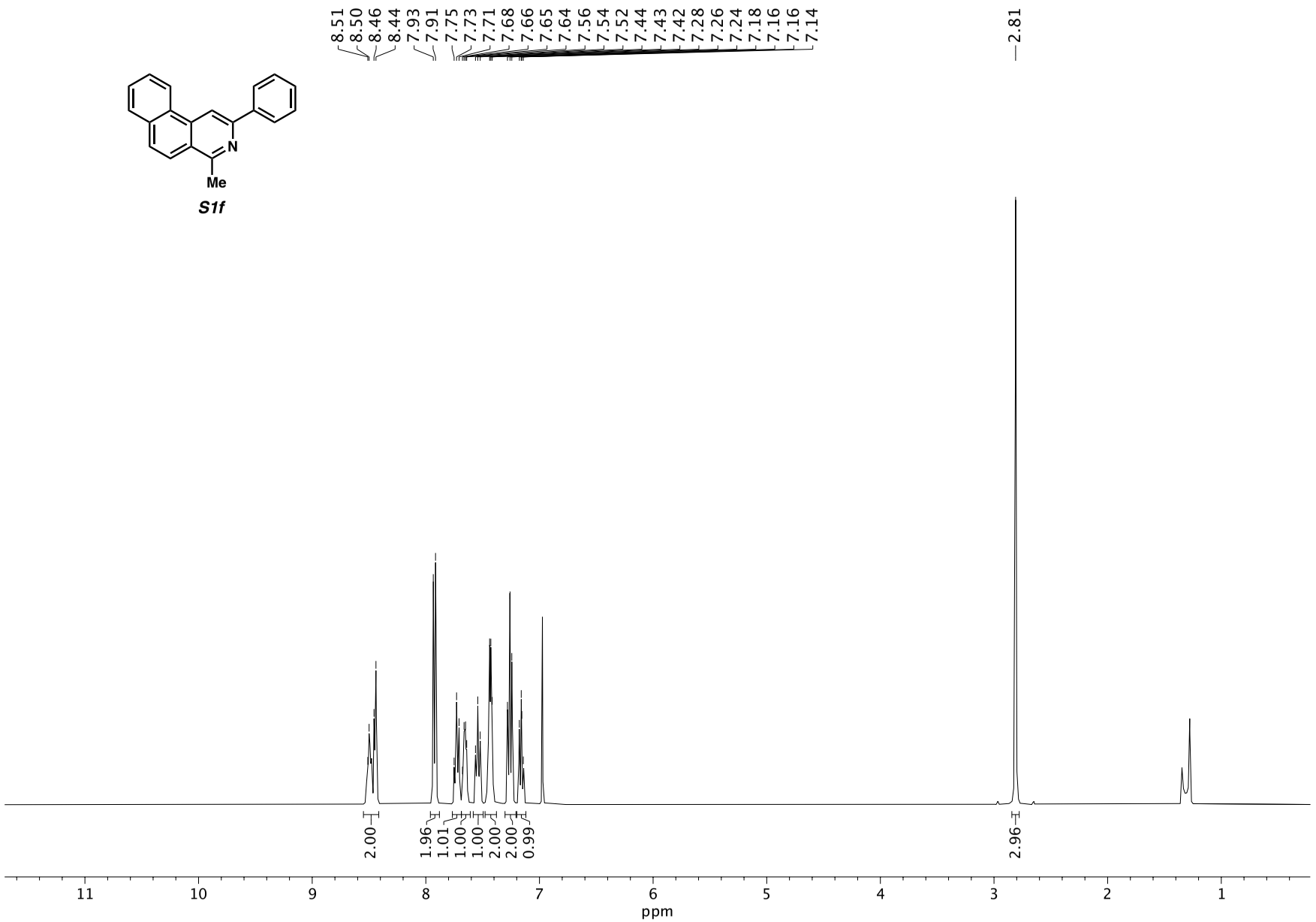
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1e**.



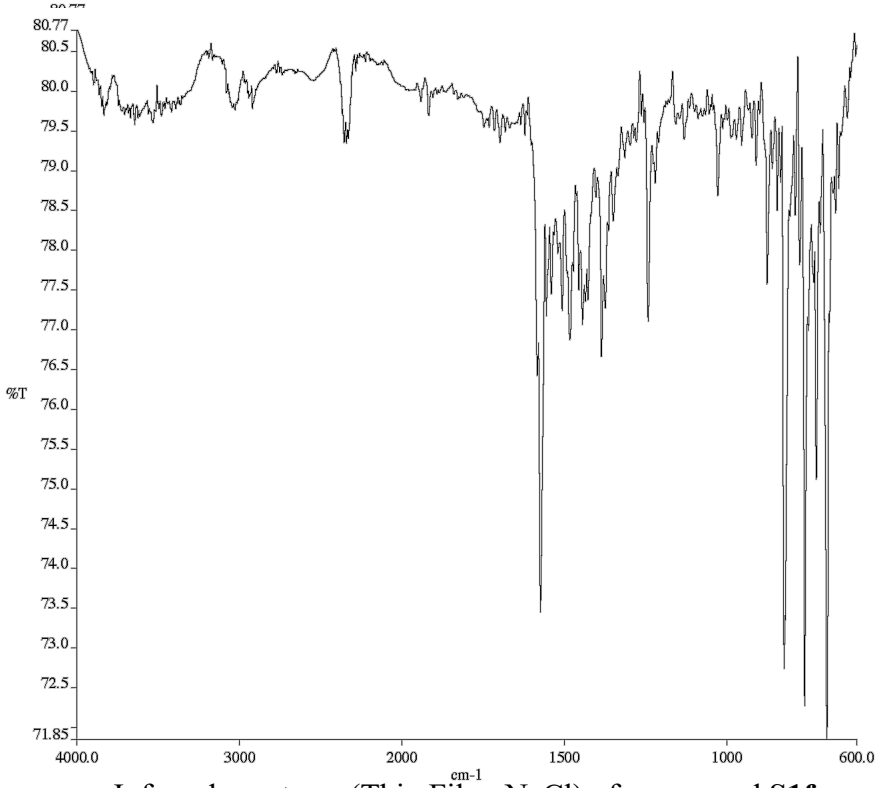
Infrared spectrum (Thin Film, NaCl) of compound **S1e**.



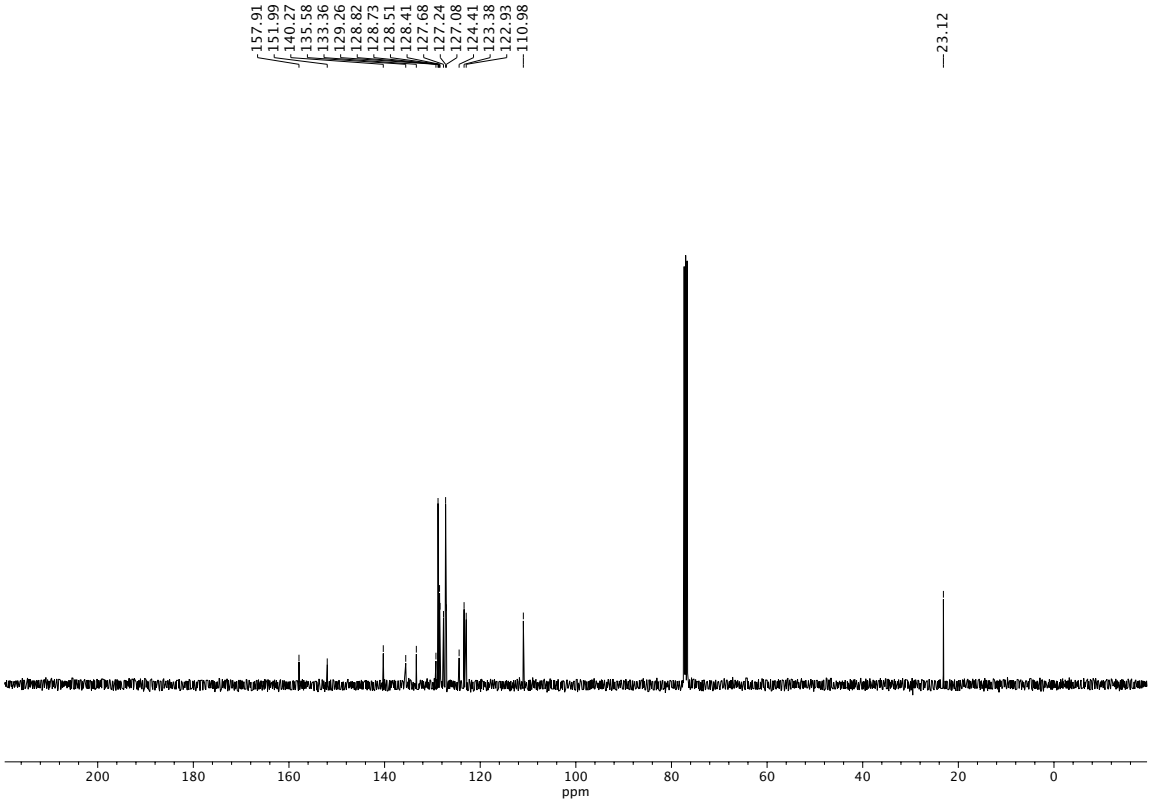
^{13}C NMR (100 MHz, $CDCl_3$) of compound **S1e**.



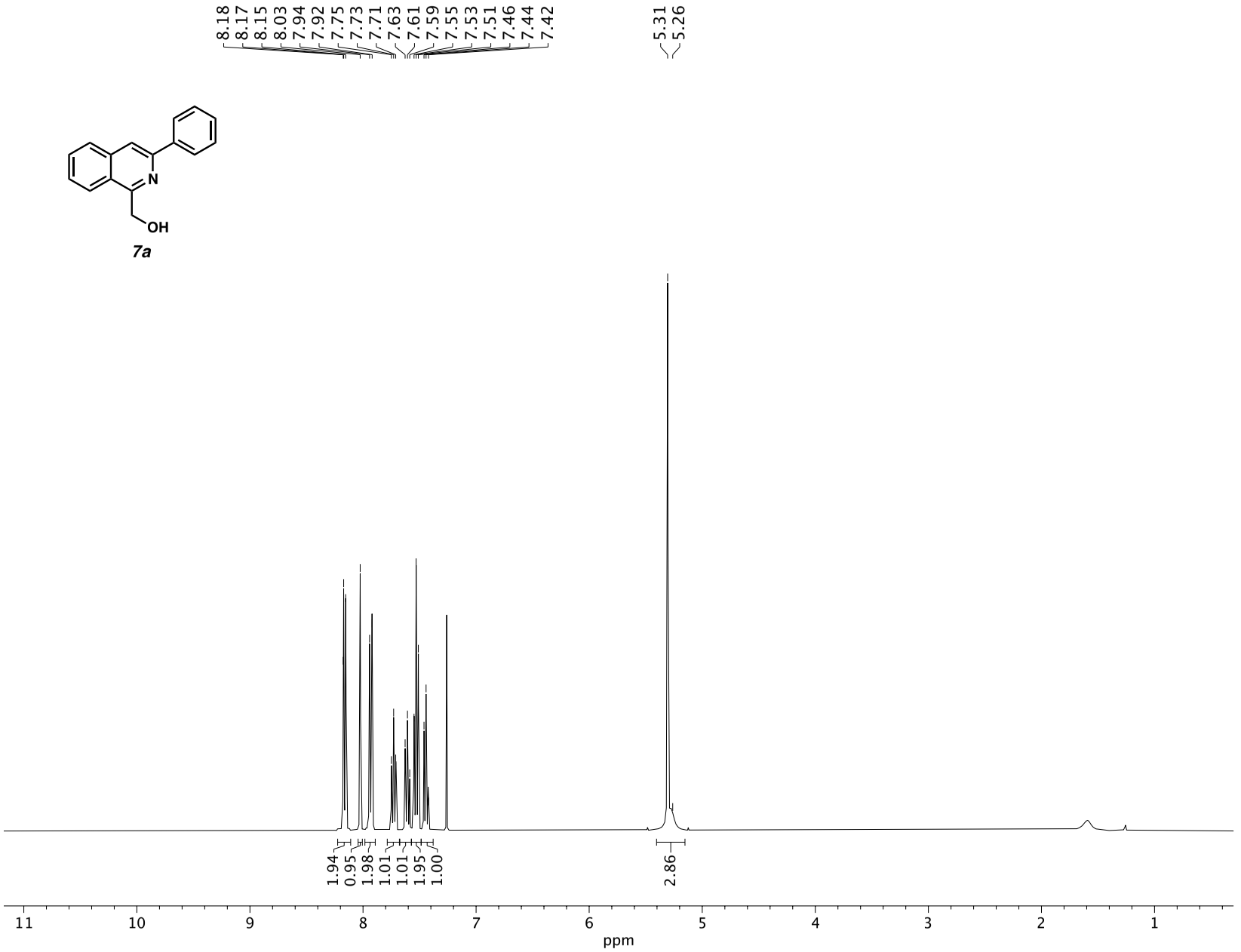
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S1f**.



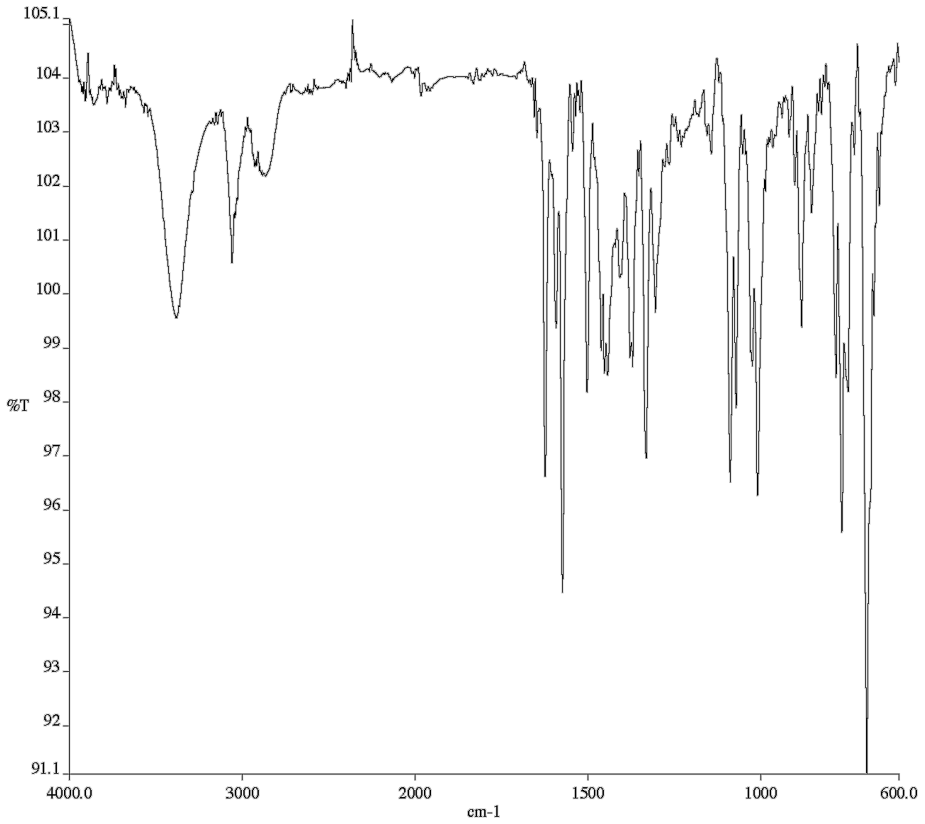
Infrared spectrum (Thin Film, NaCl) of compound **S1f**.



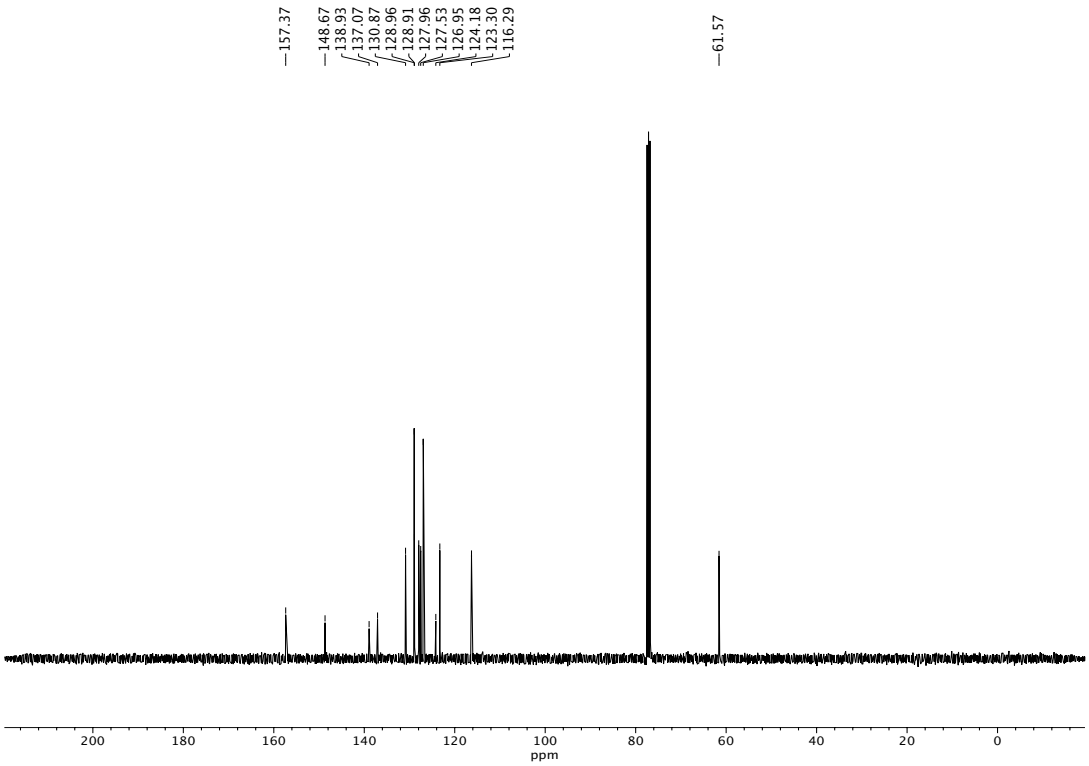
^{13}C NMR (100 MHz, $CDCl_3$) of compound **S1f**.



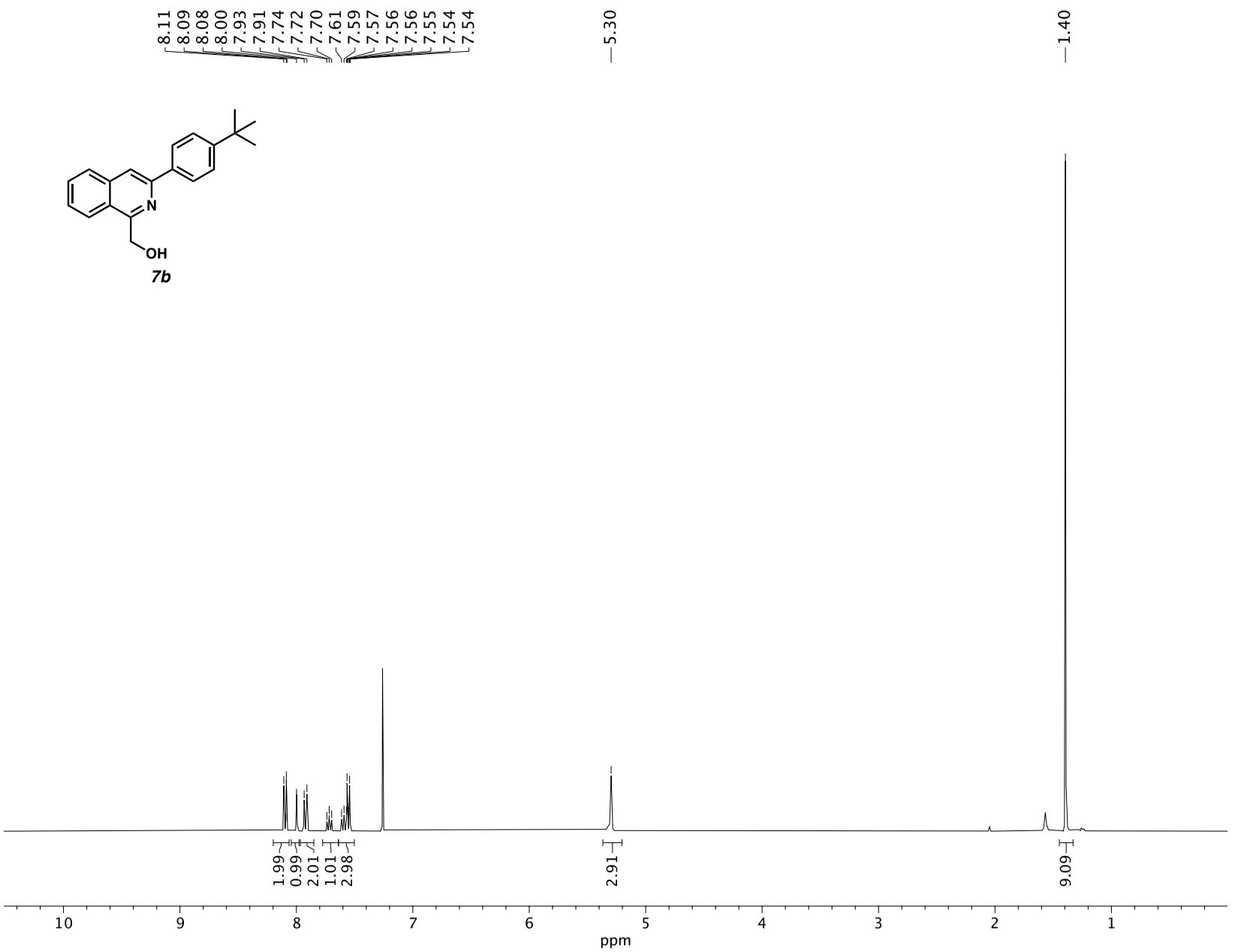
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7a**.



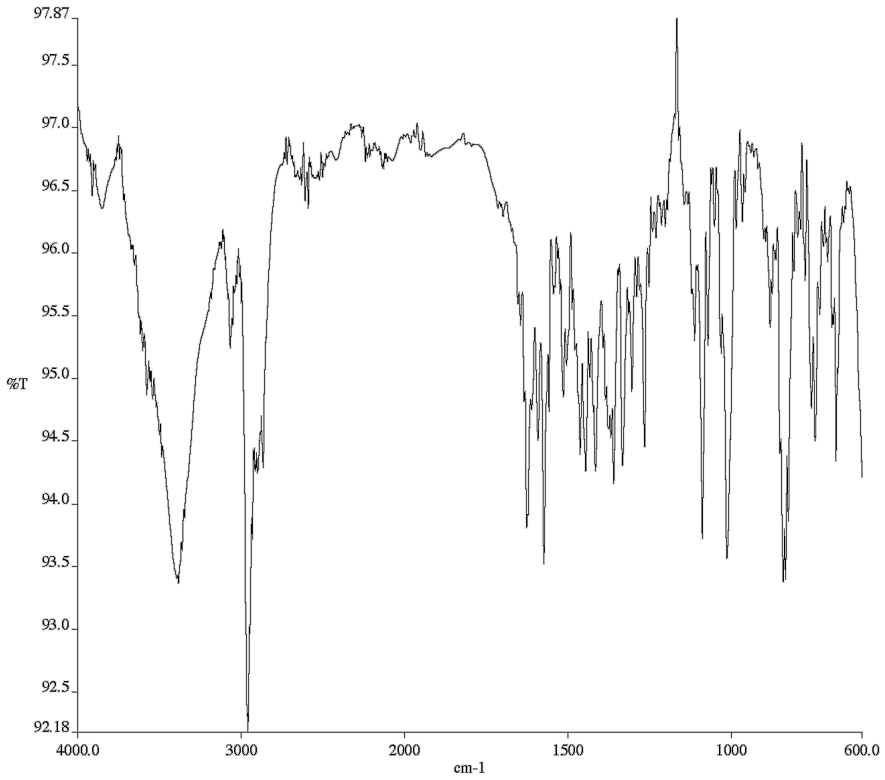
Infrared spectrum (Thin Film, NaCl) of compound **7a**.



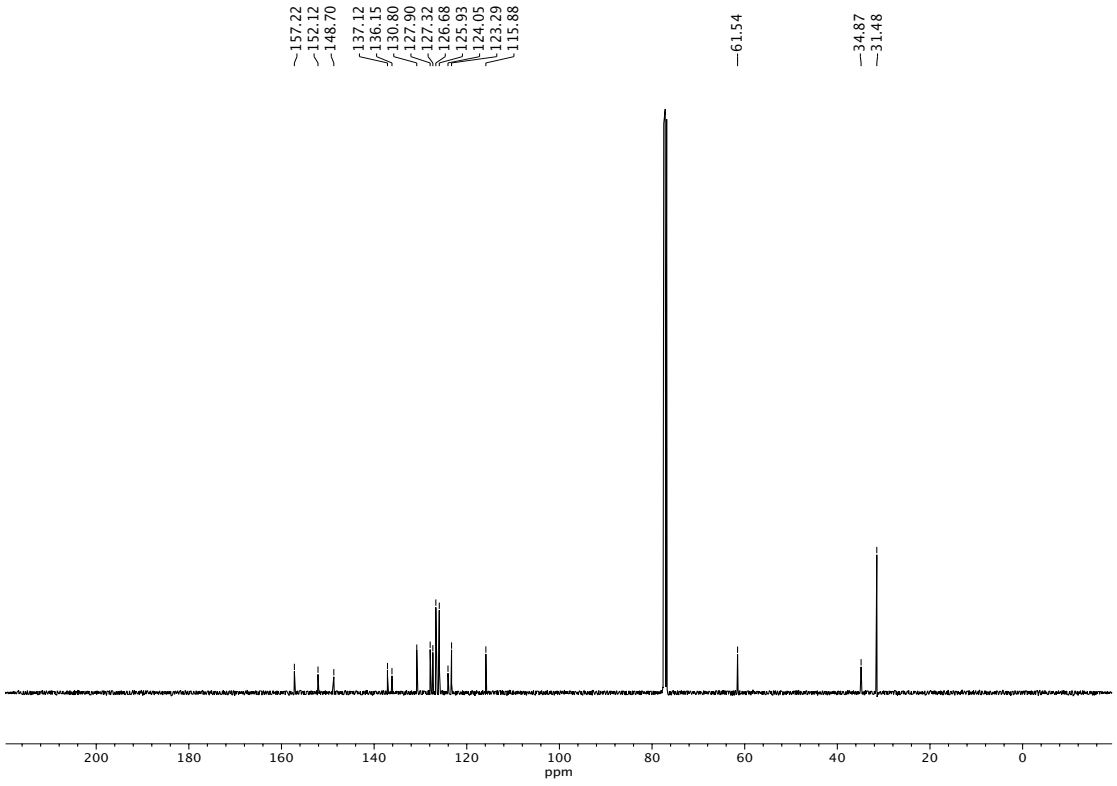
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7a**.



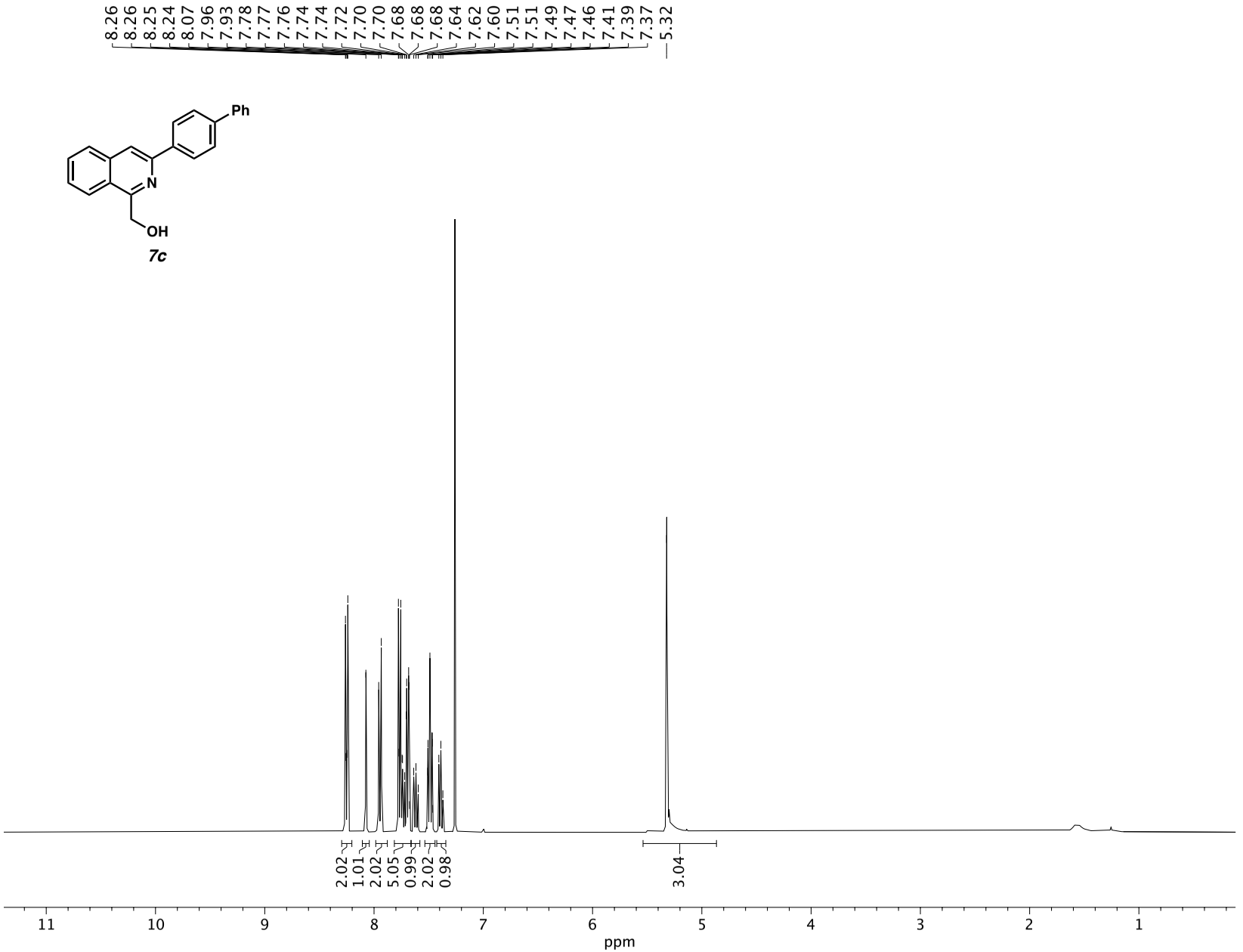
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7b**.



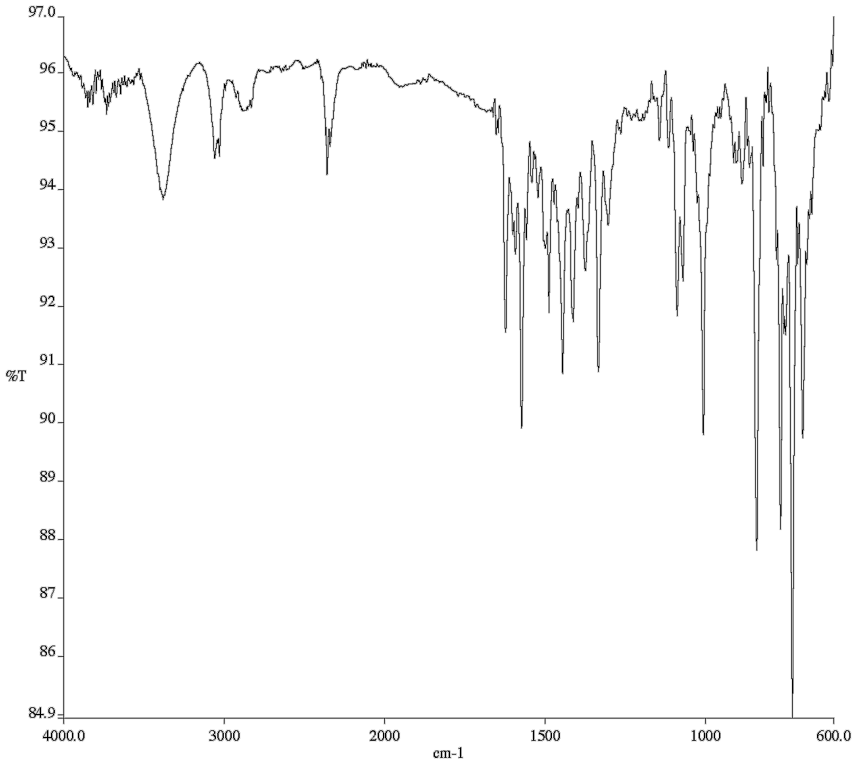
Infrared spectrum (Thin Film, NaCl) of compound **7b**.



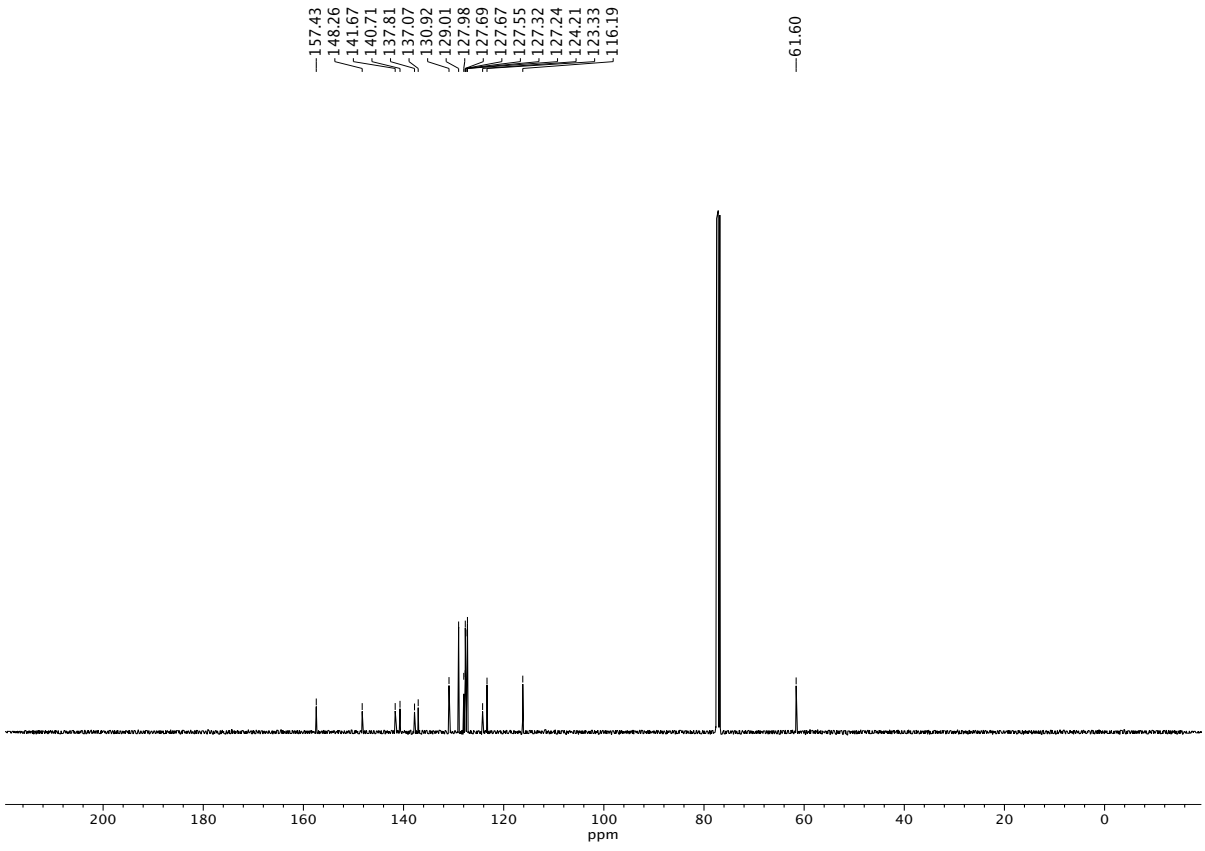
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7b**.



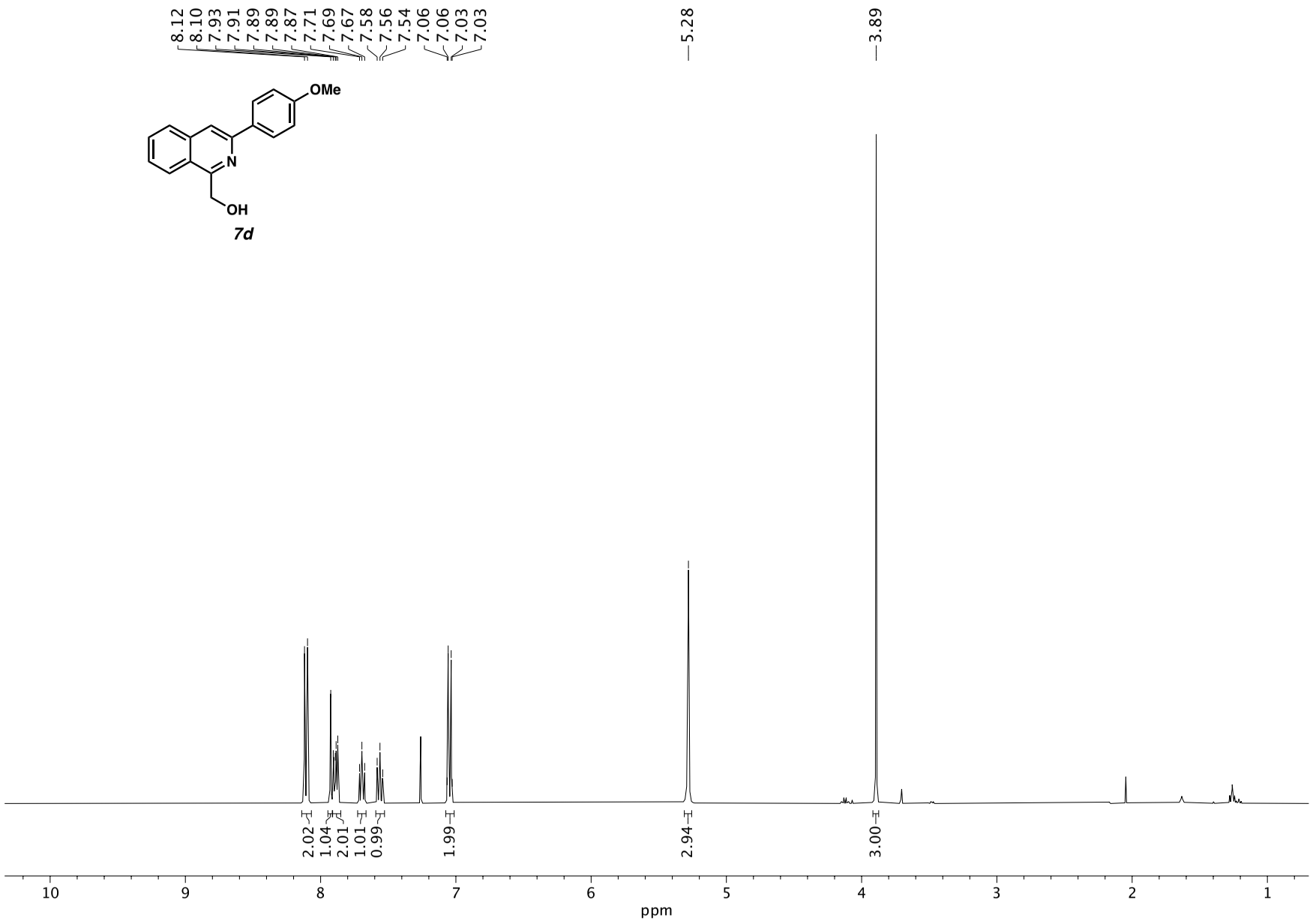
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7c**.



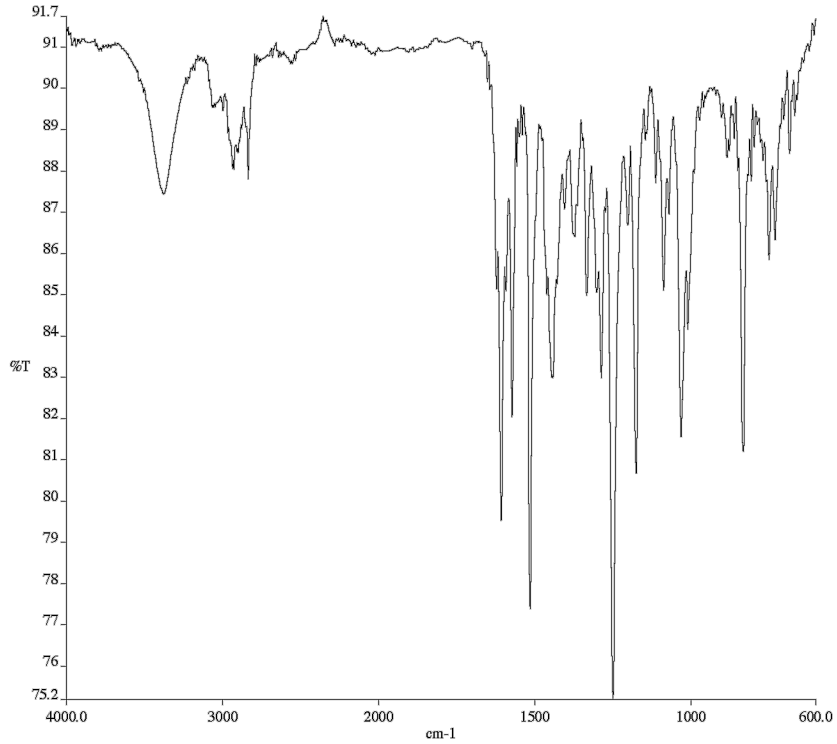
Infrared spectrum (Thin Film, NaCl) of compound **7c**.



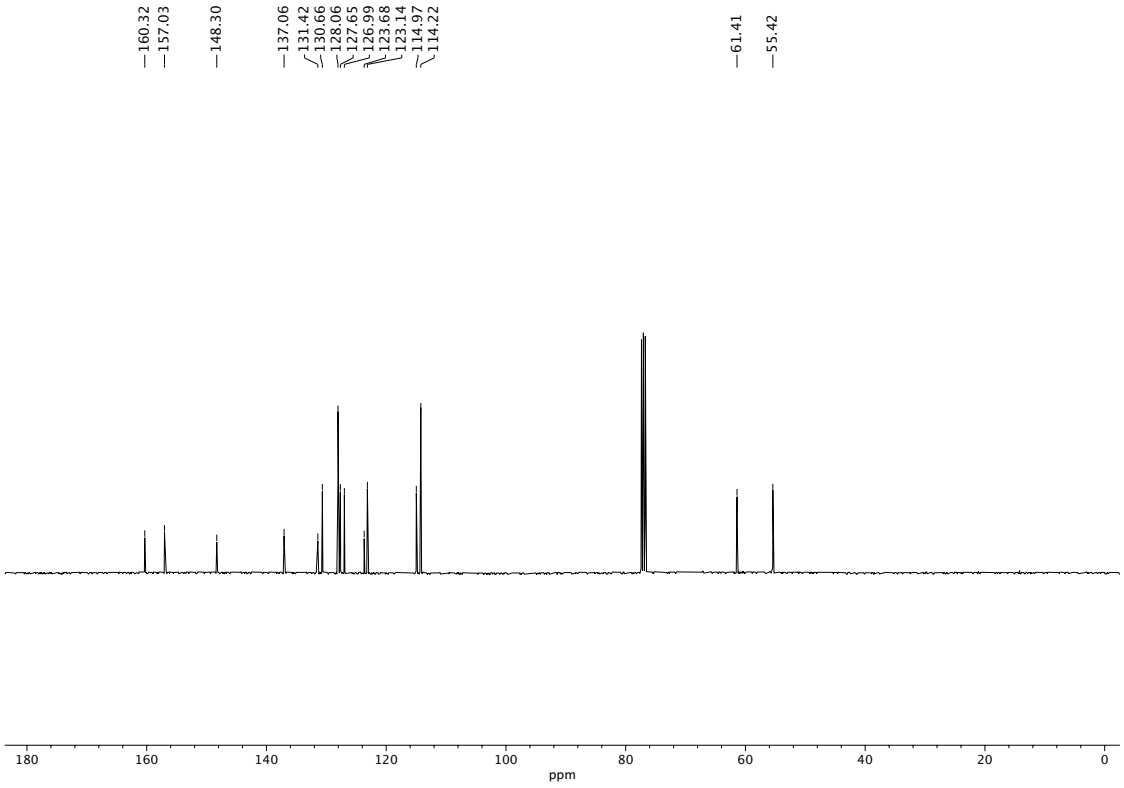
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7c**.



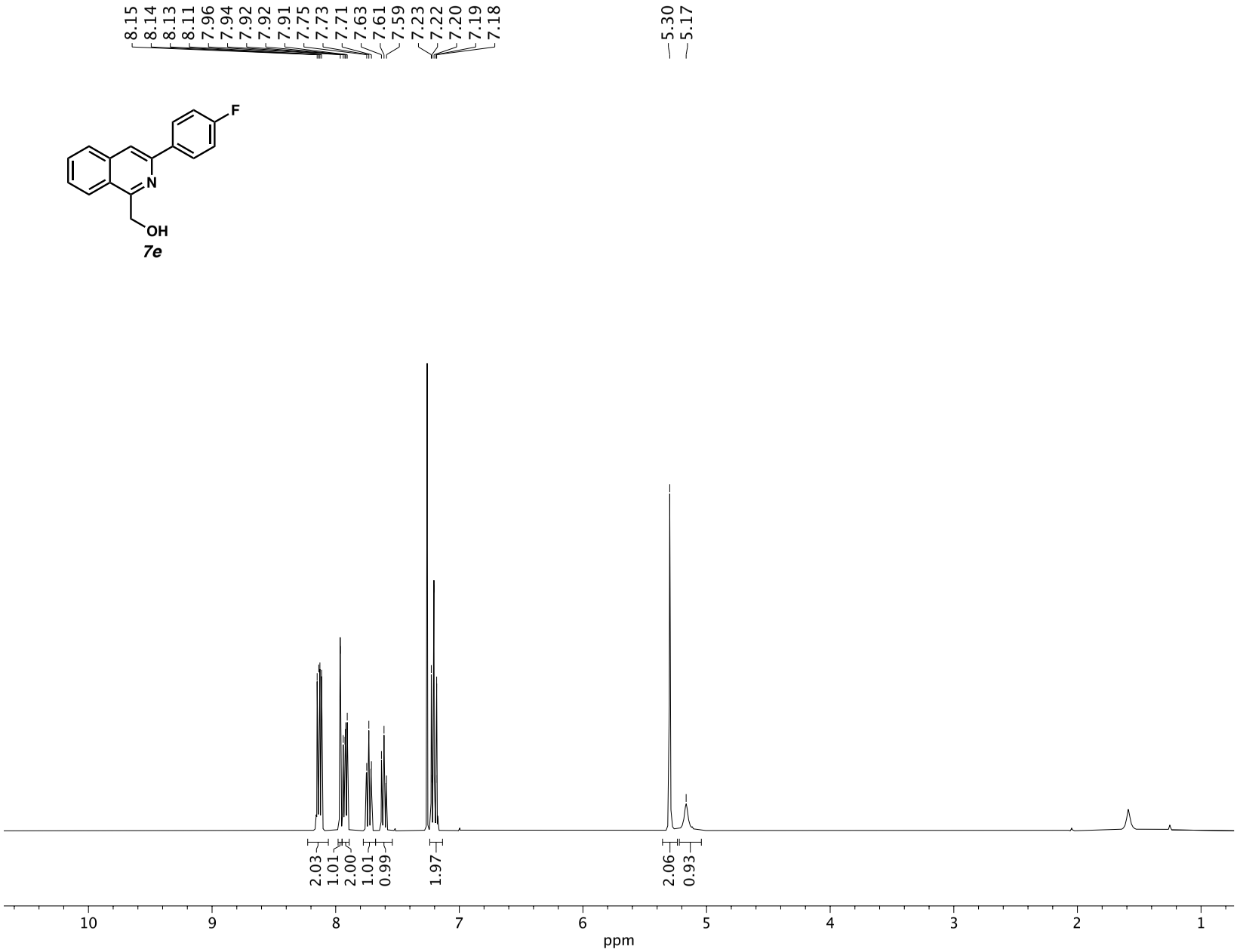
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7d**.



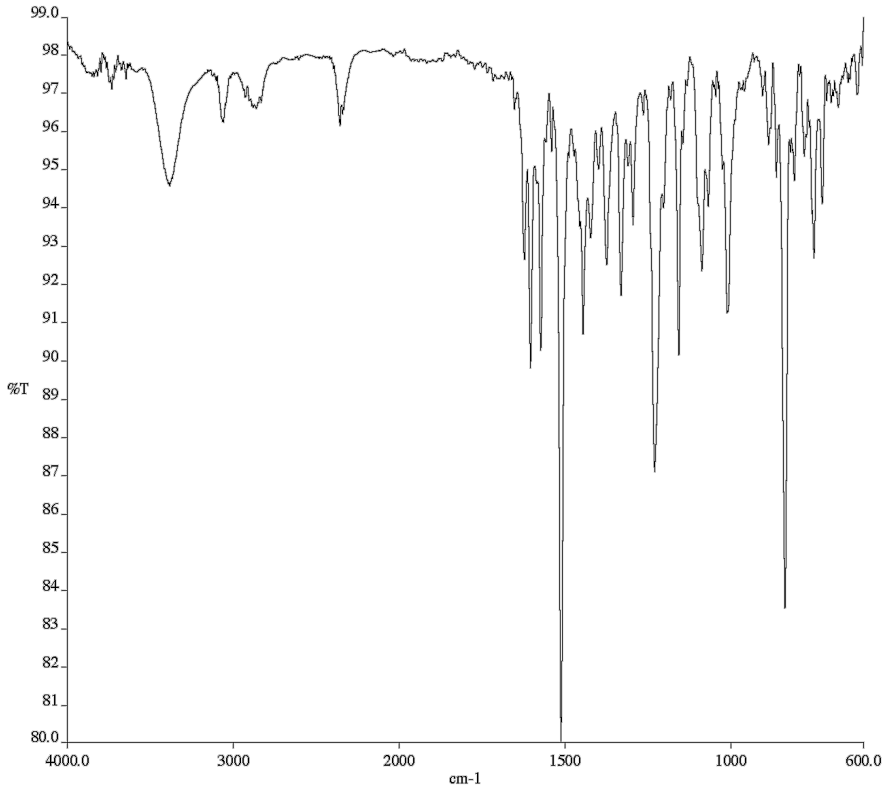
Infrared spectrum (Thin Film, NaCl) of compound **7d**.



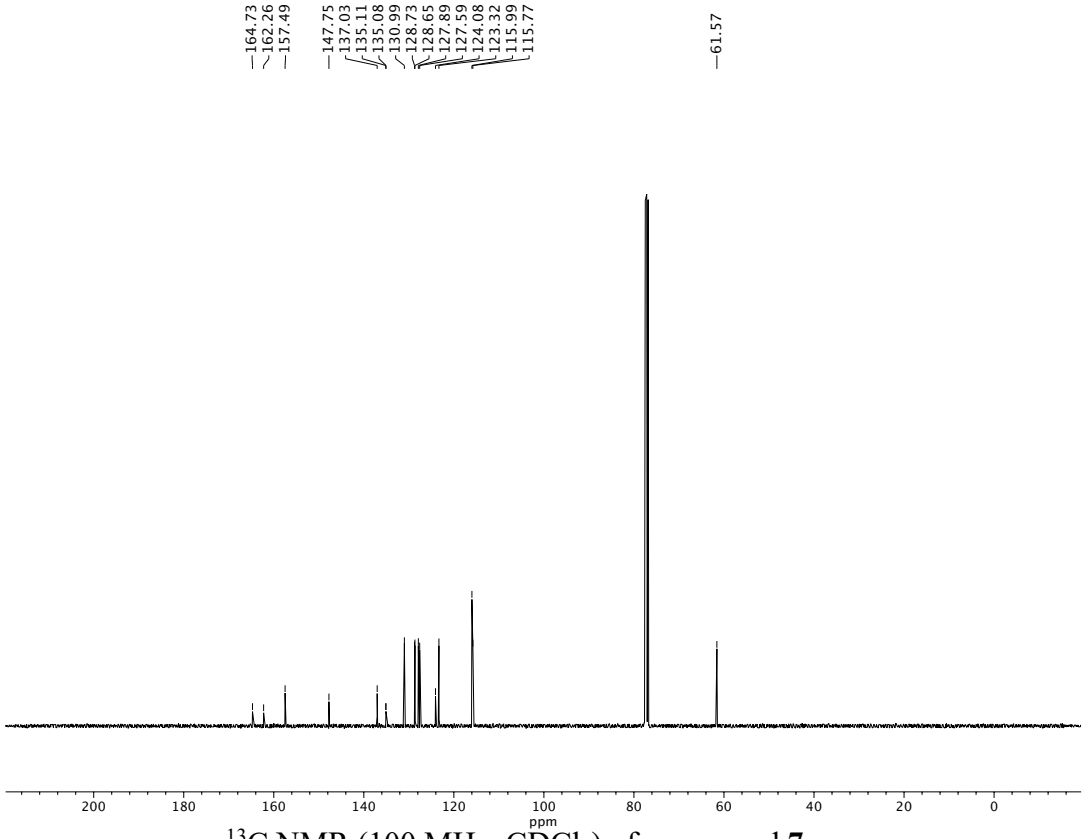
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7d**.



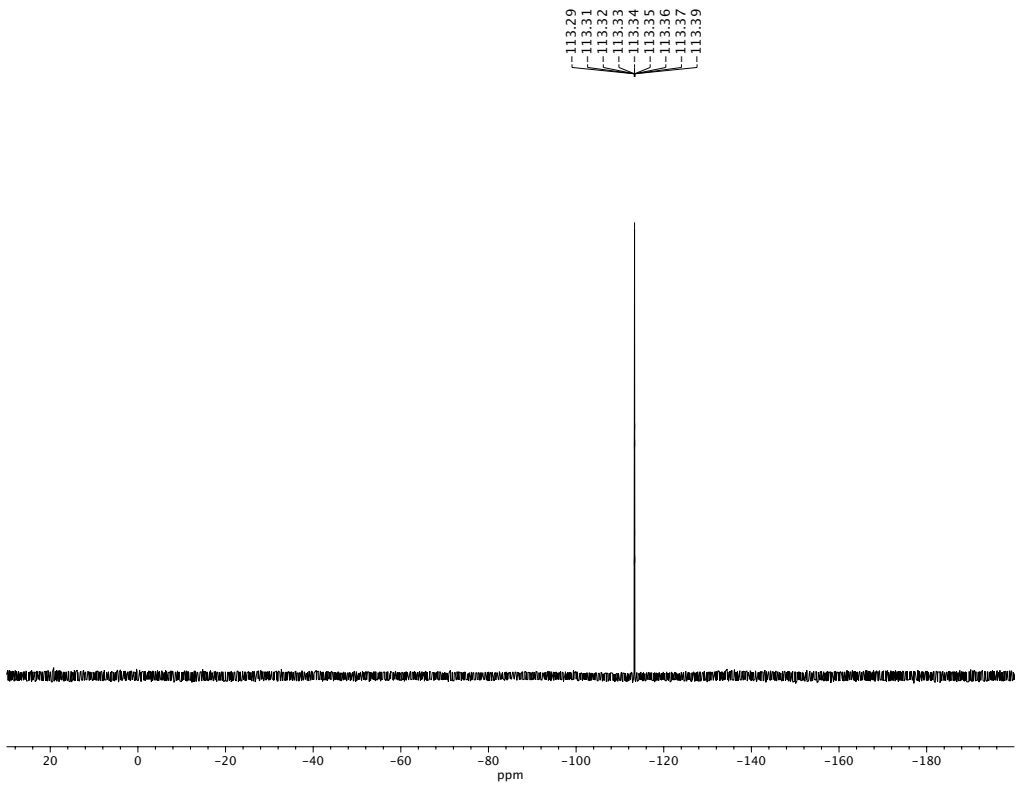
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7e**.



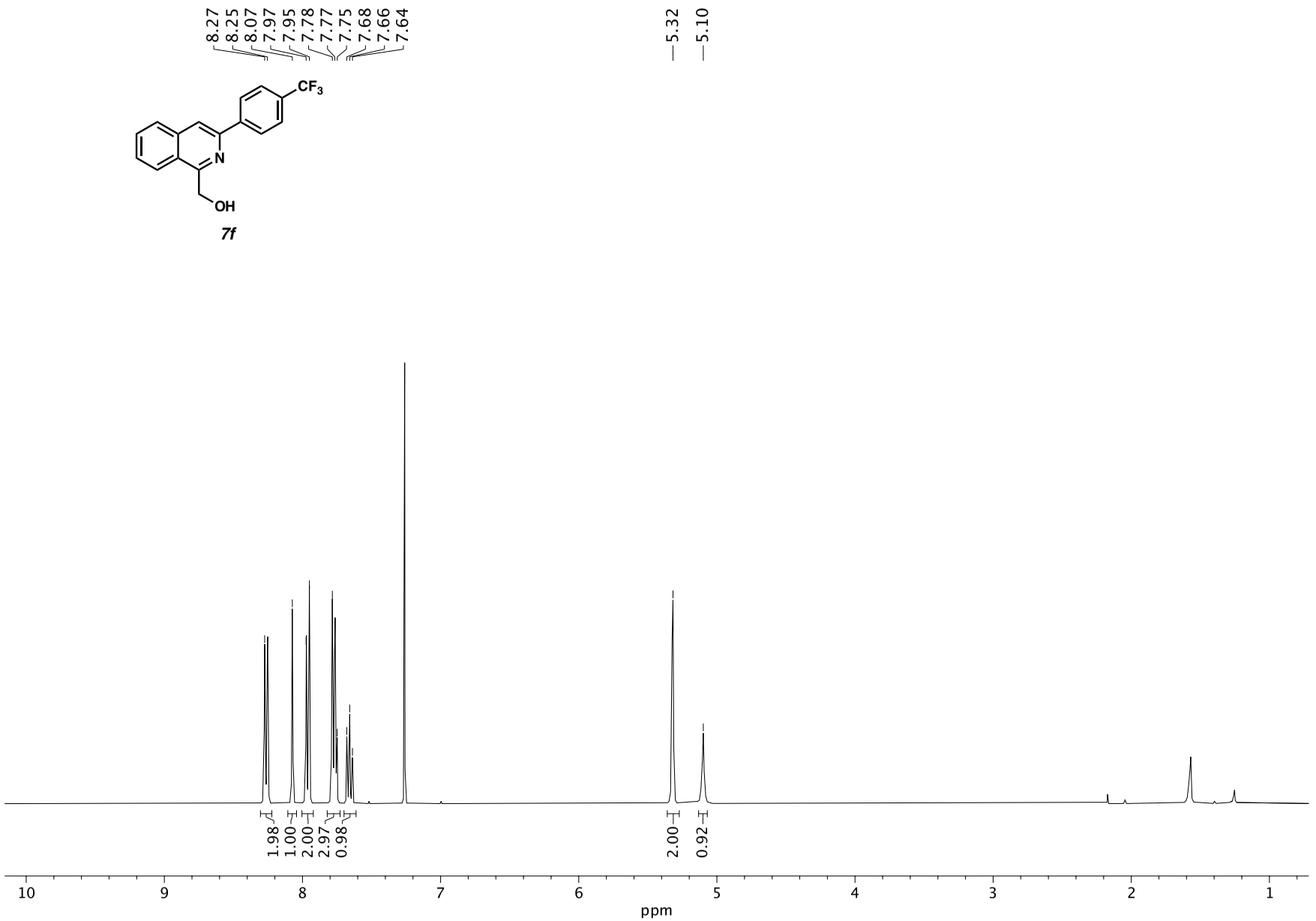
Infrared spectrum (Thin Film, NaCl) of compound **7e**.



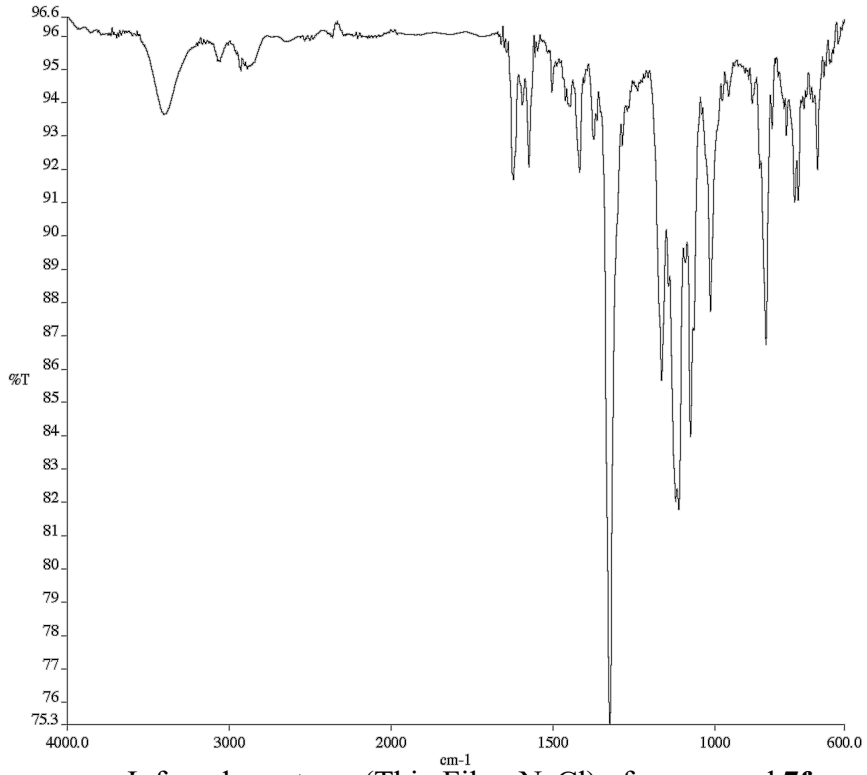
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7e**.



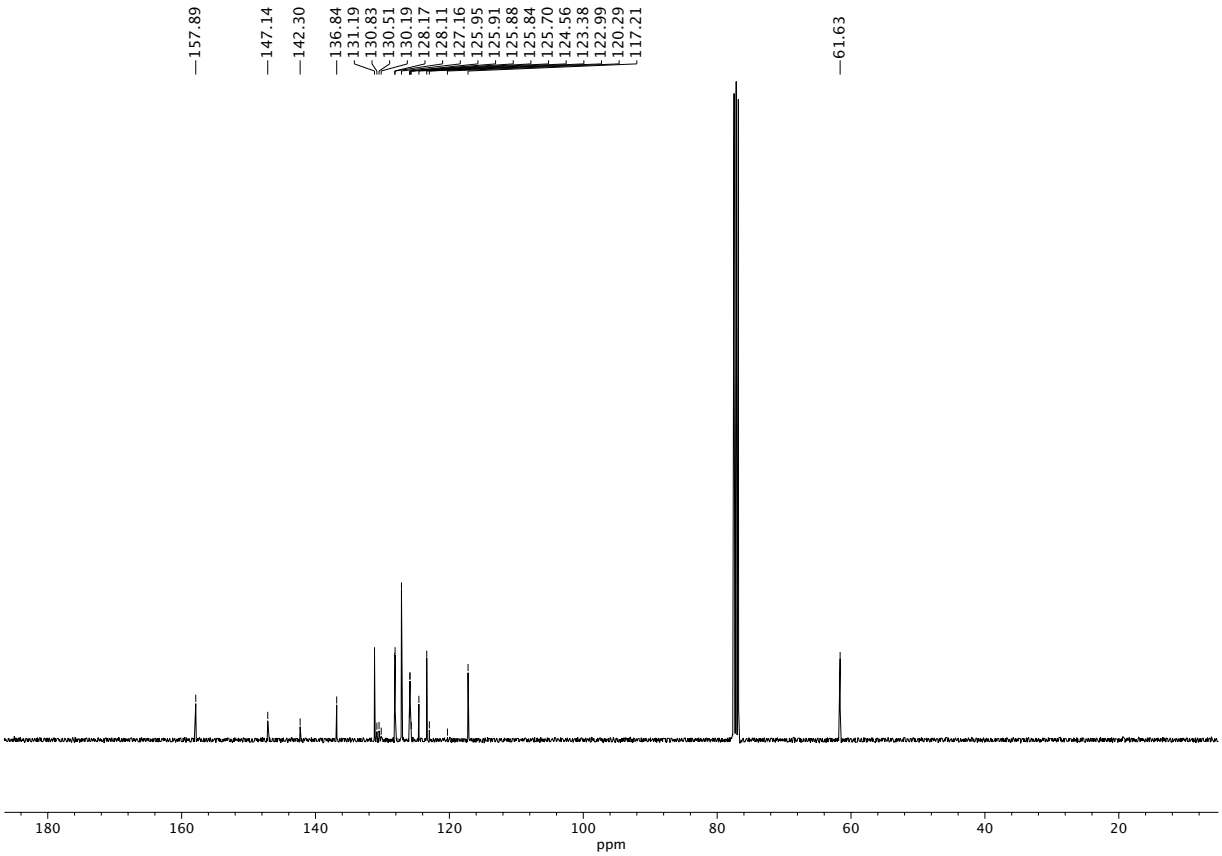
^{19}F NMR (282 MHz, $CDCl_3$) of **7e**.



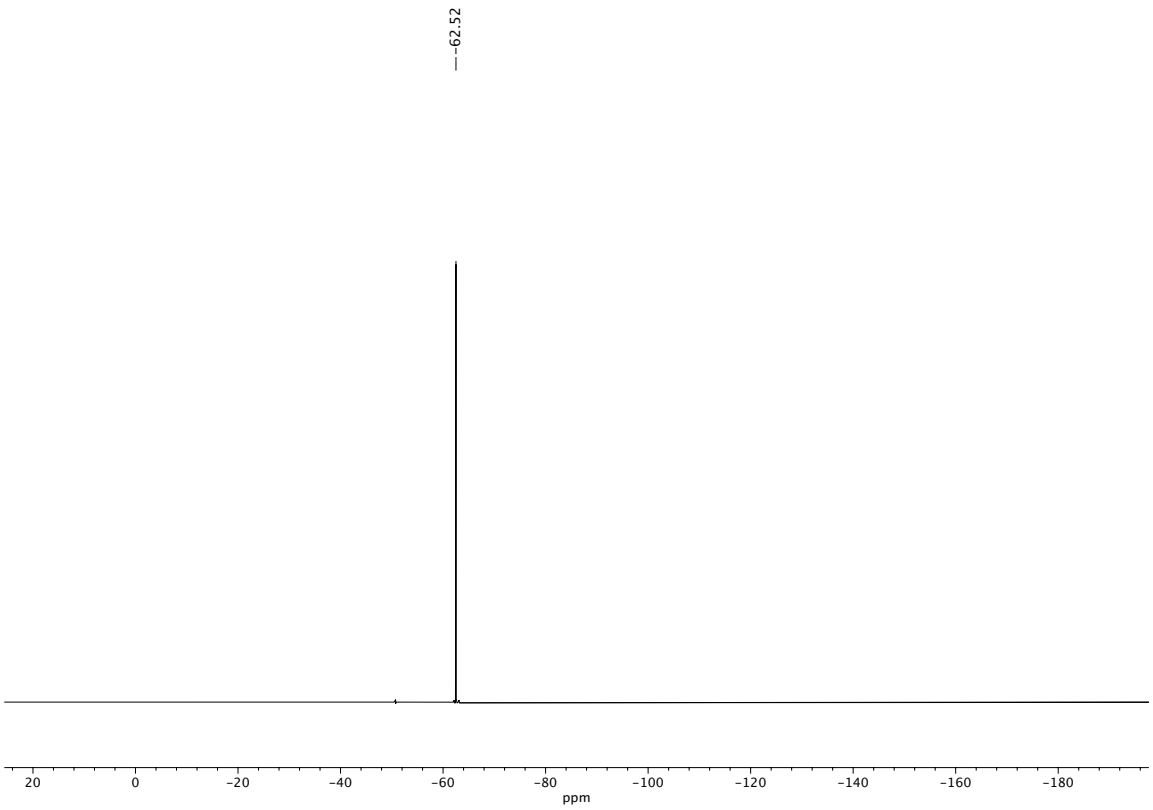
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7f**.



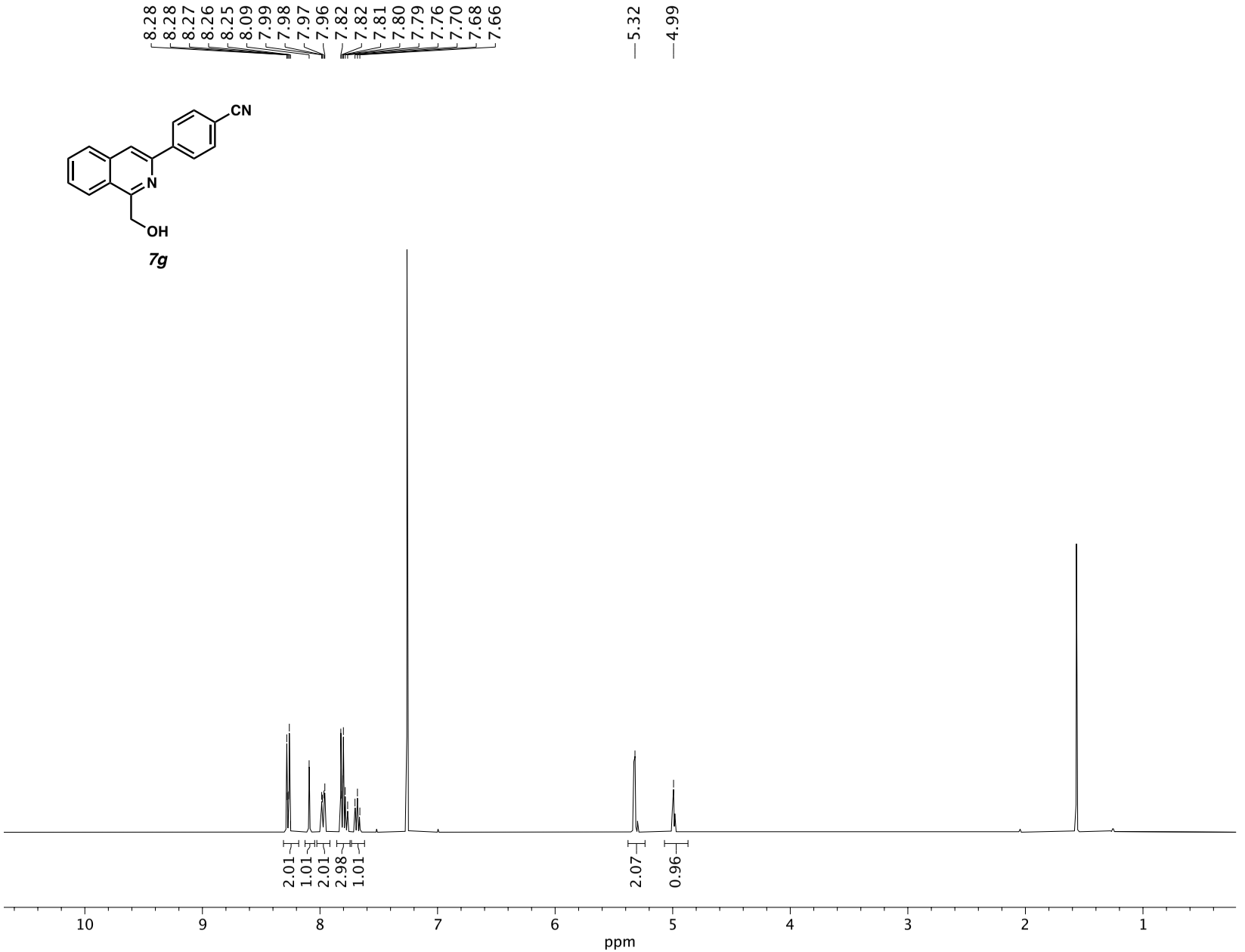
Infrared spectrum (Thin Film, NaCl) of compound **7f**.



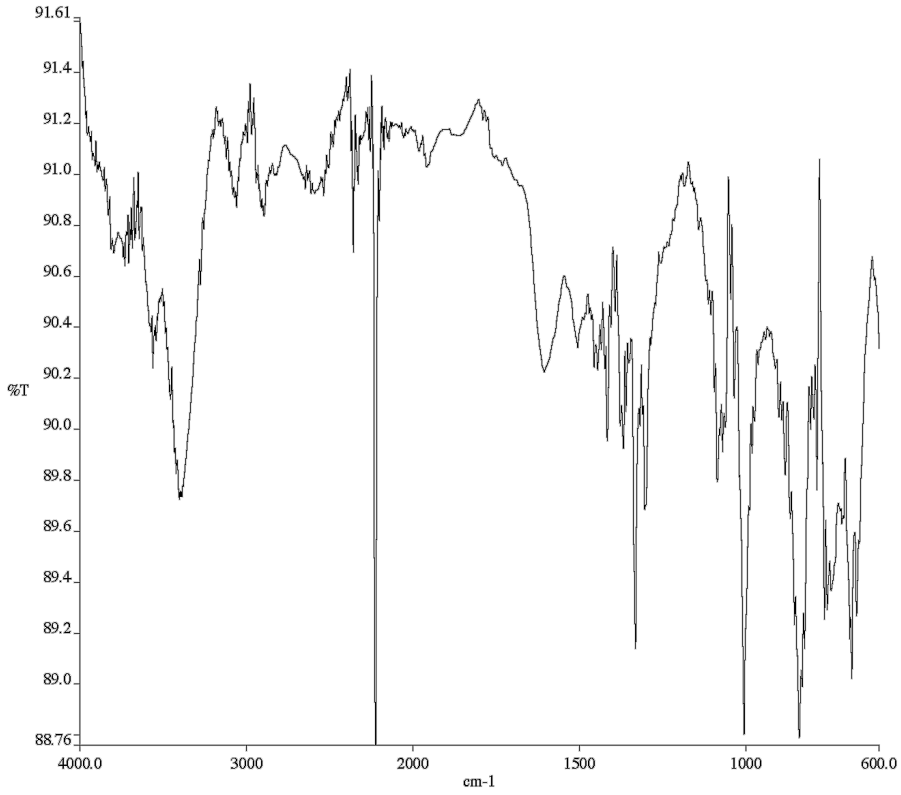
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7f**.



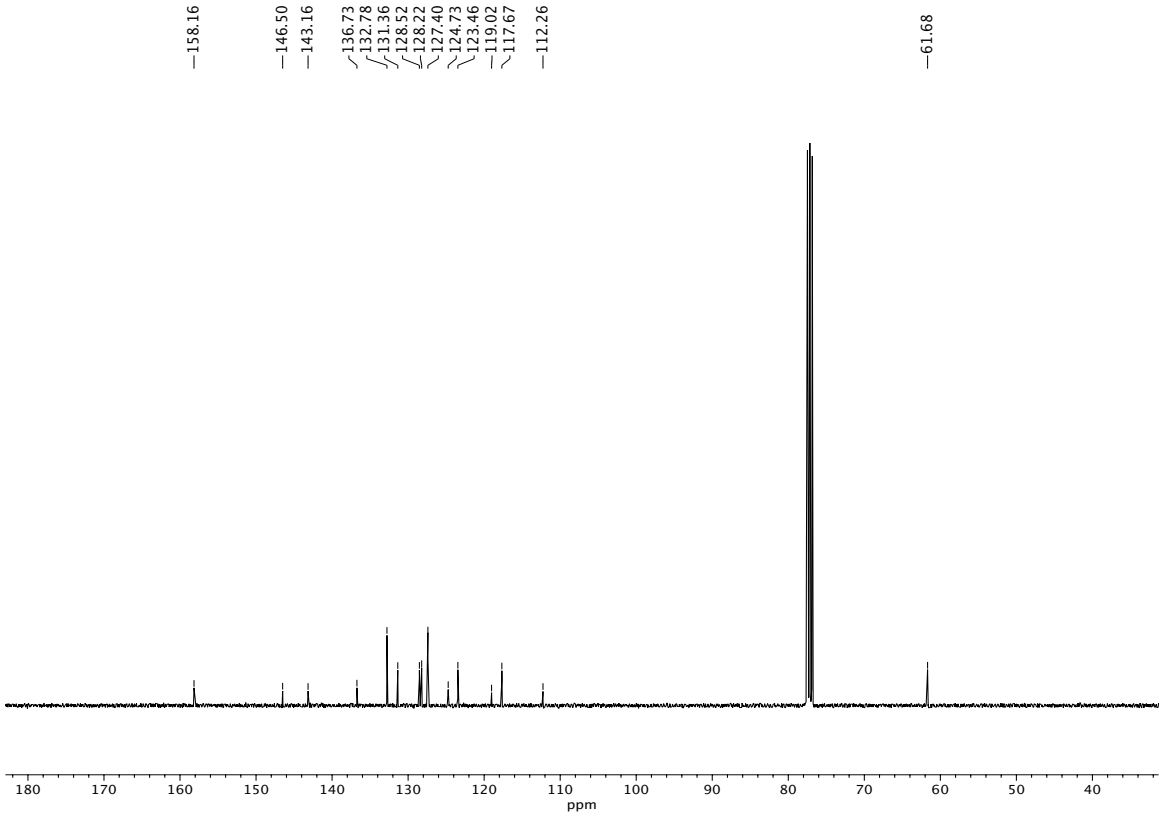
^{19}F NMR (282 MHz, $CDCl_3$) of **7f**.



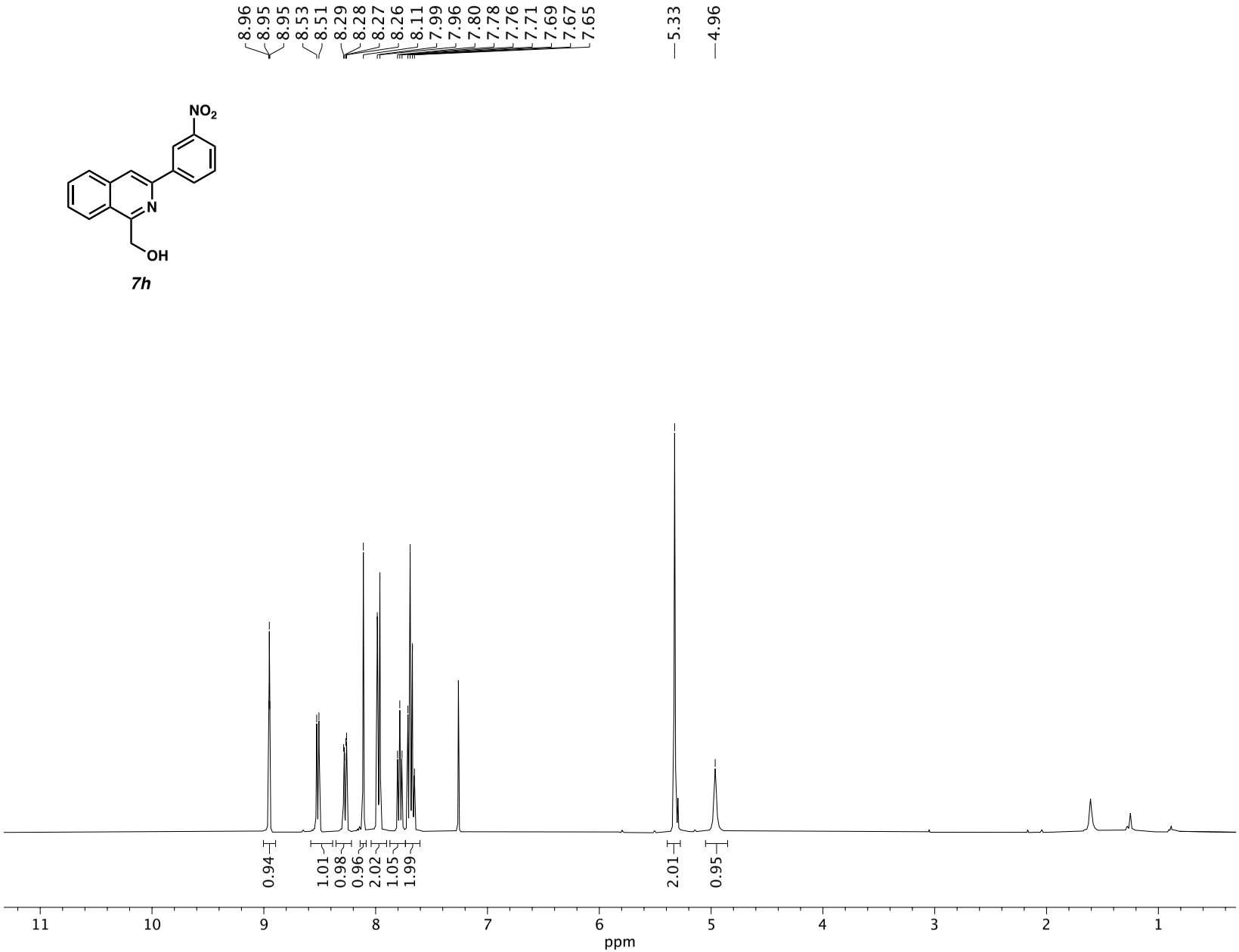
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7g**.



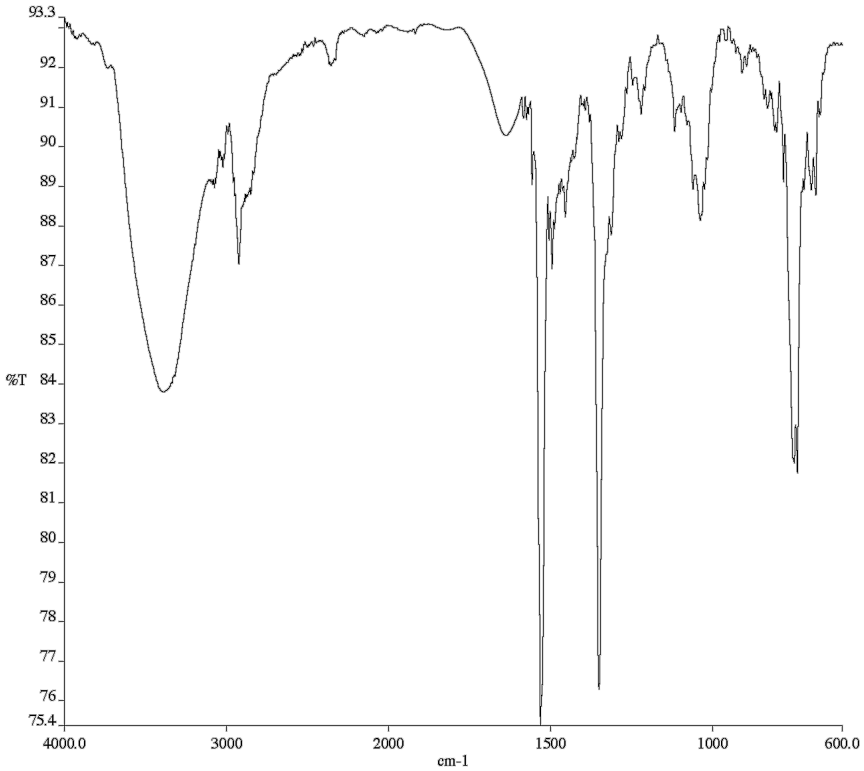
Infrared spectrum (Thin Film, NaCl) of compound **7g**.



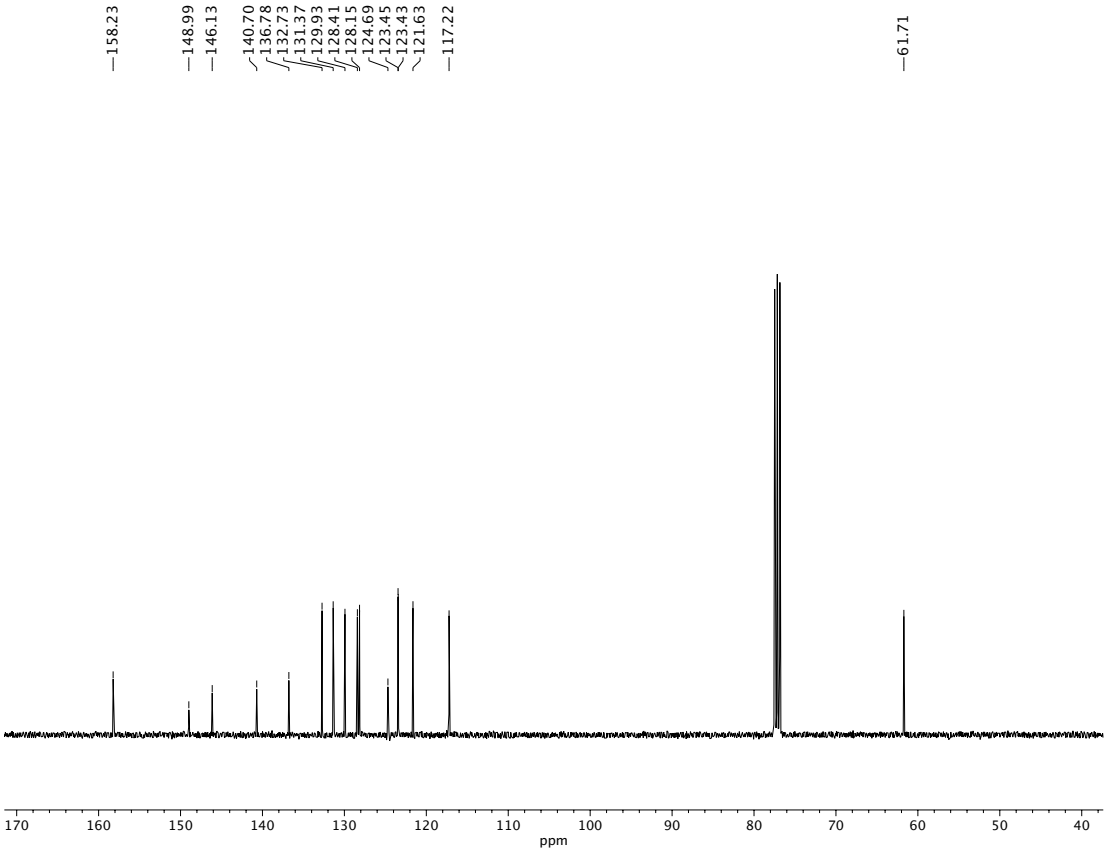
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7g**.



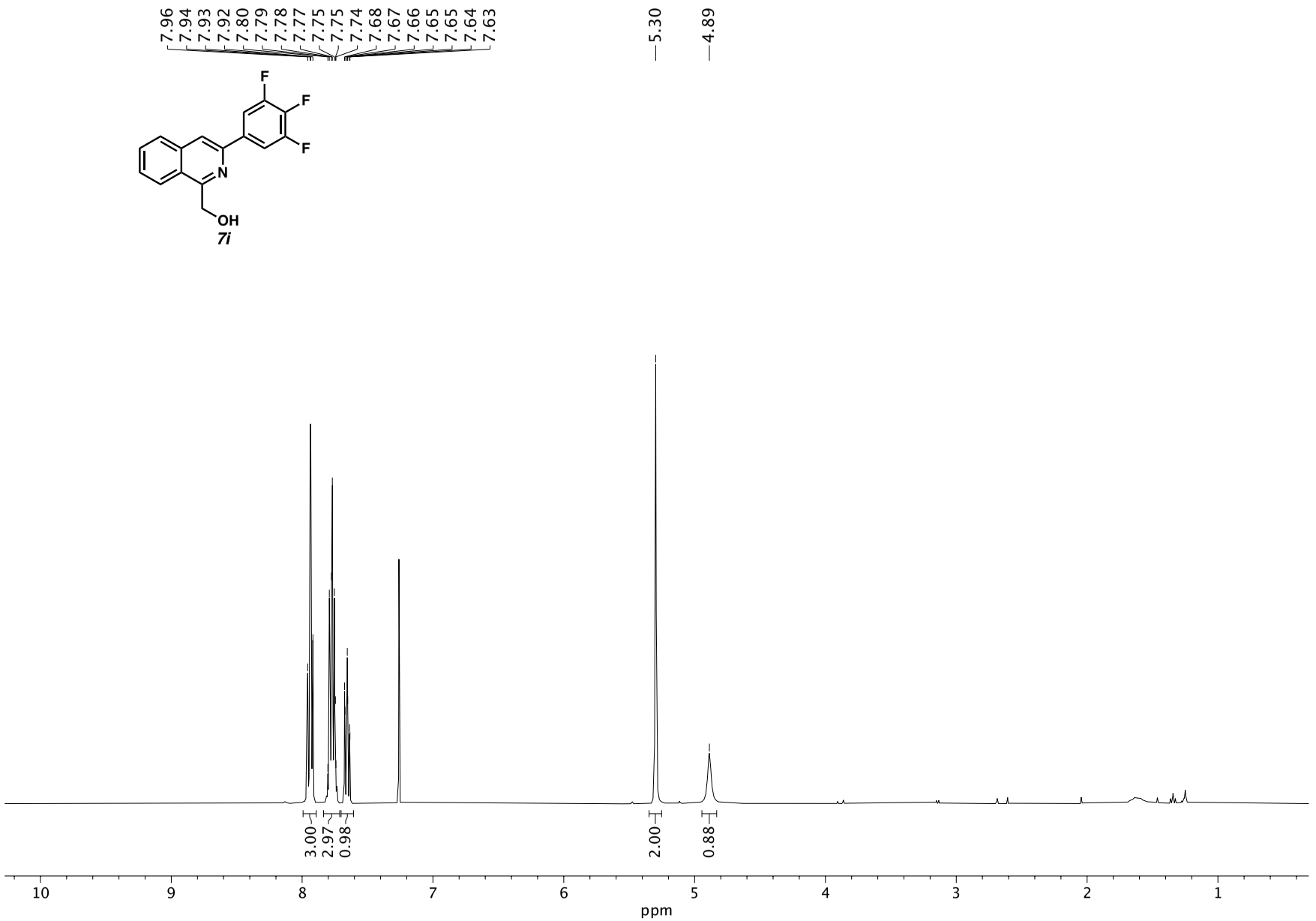
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7h**.



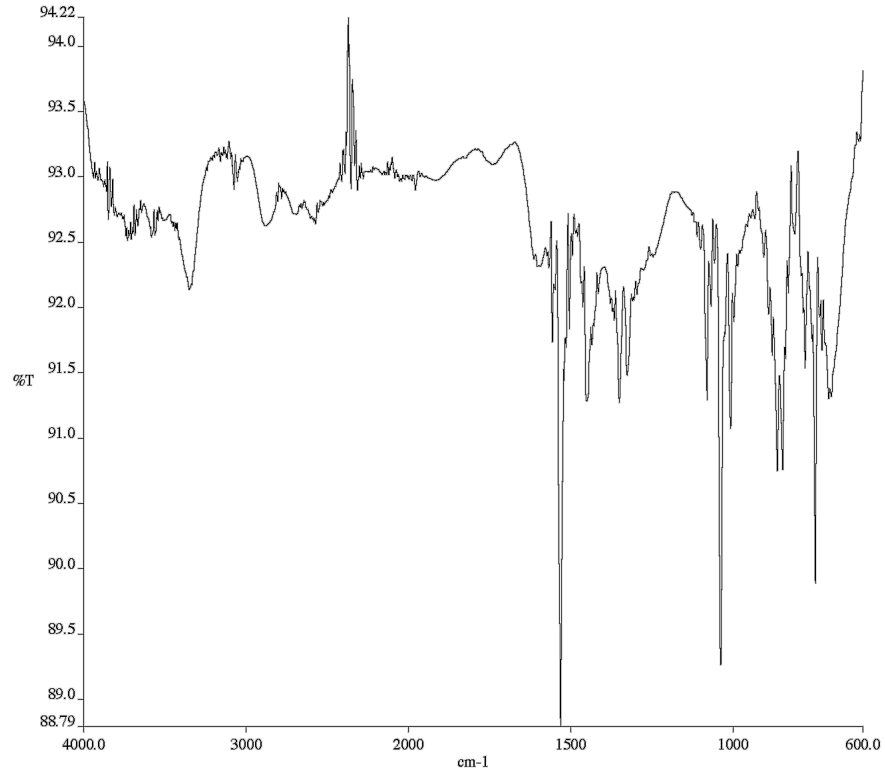
Infrared spectrum (Thin Film, NaCl) of compound **7h**.



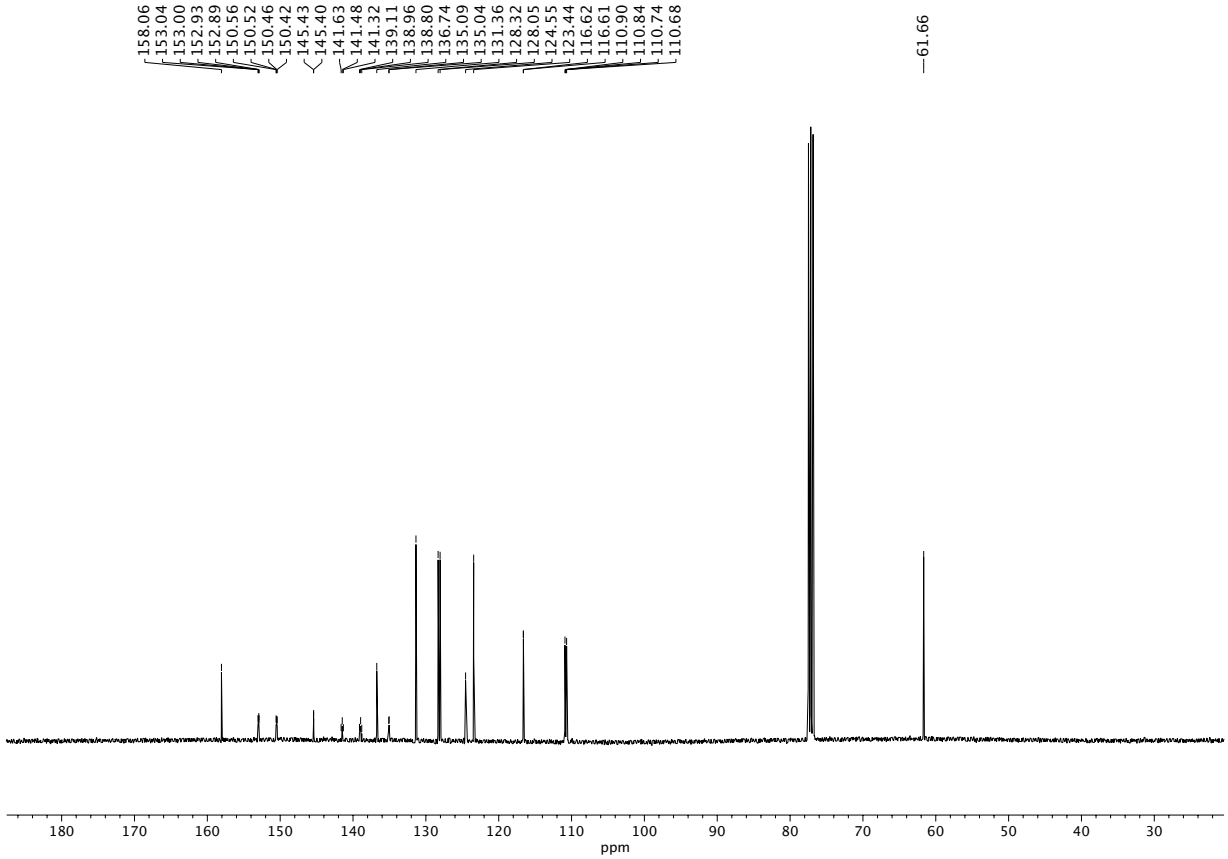
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7h**.



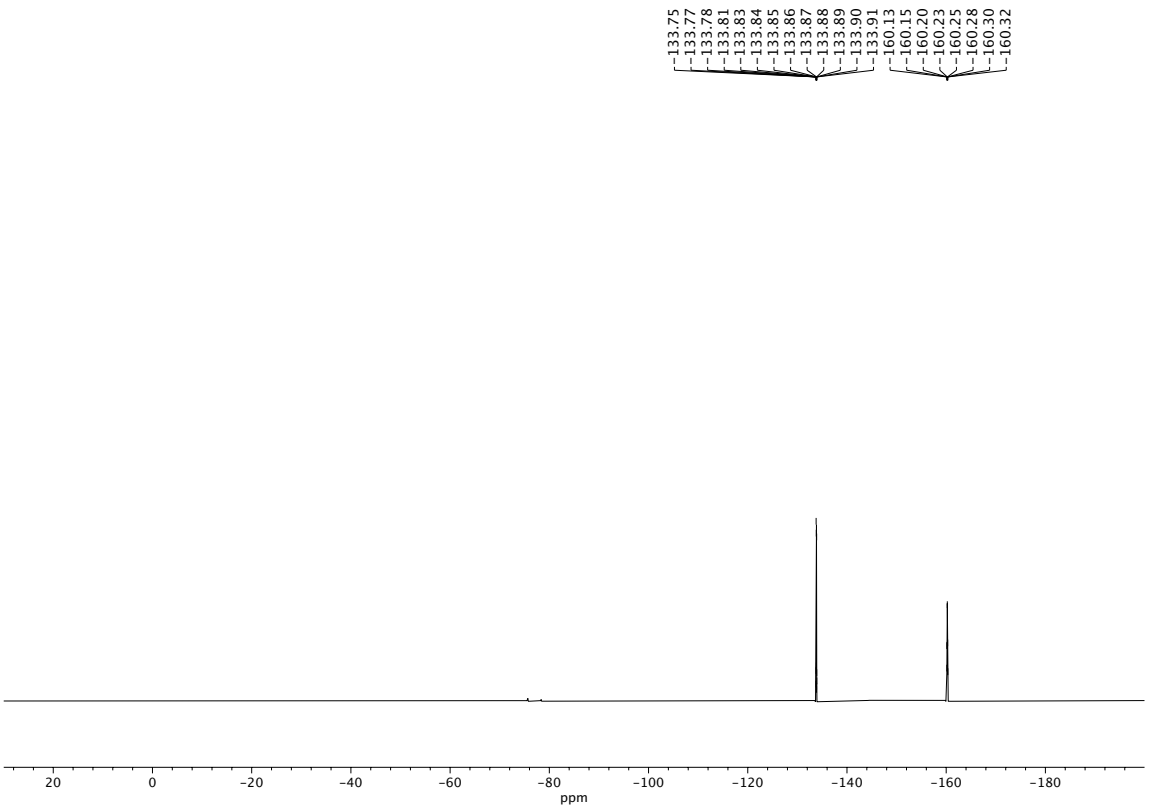
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7i**.



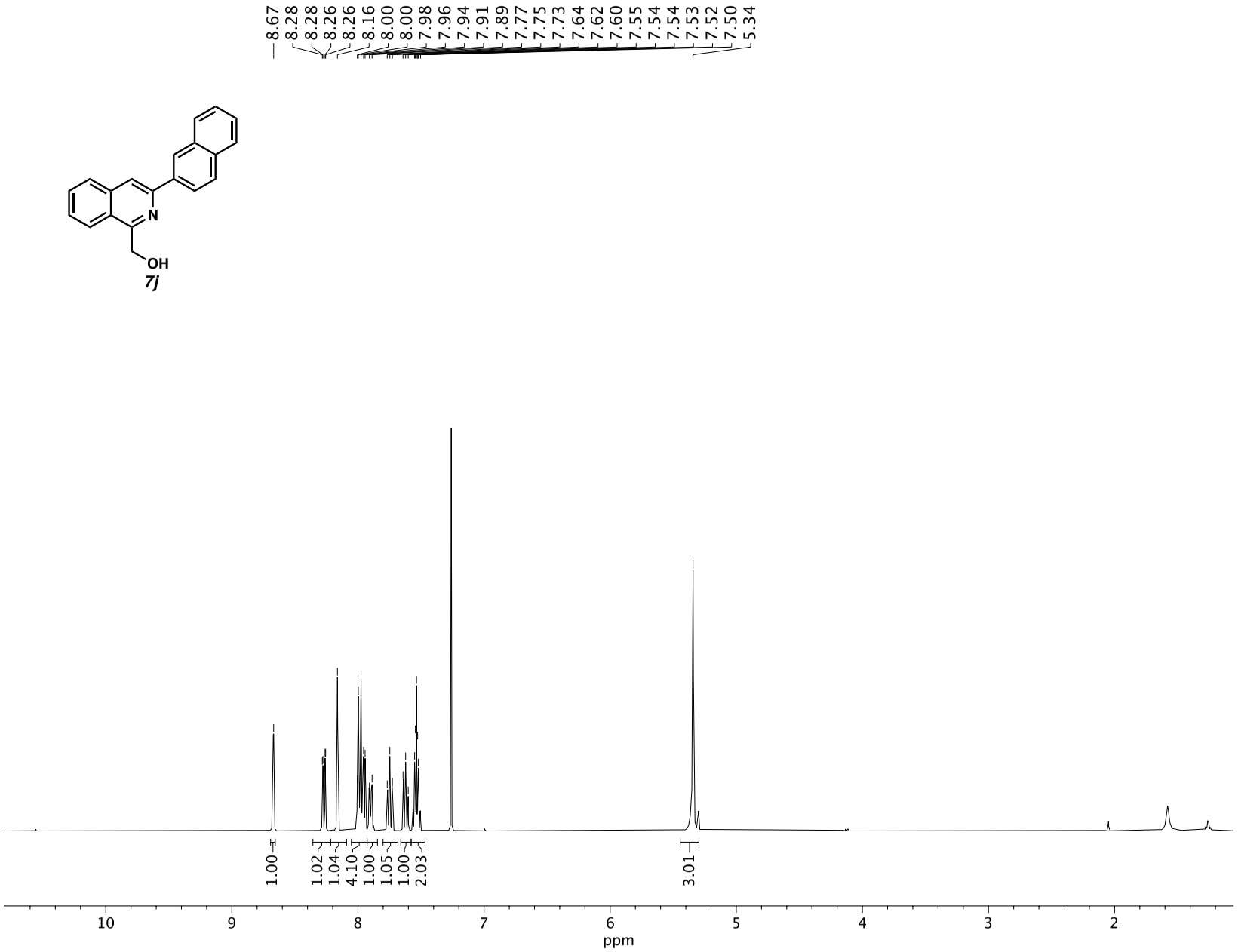
Infrared spectrum (Thin Film, NaCl) of compound **7i**.



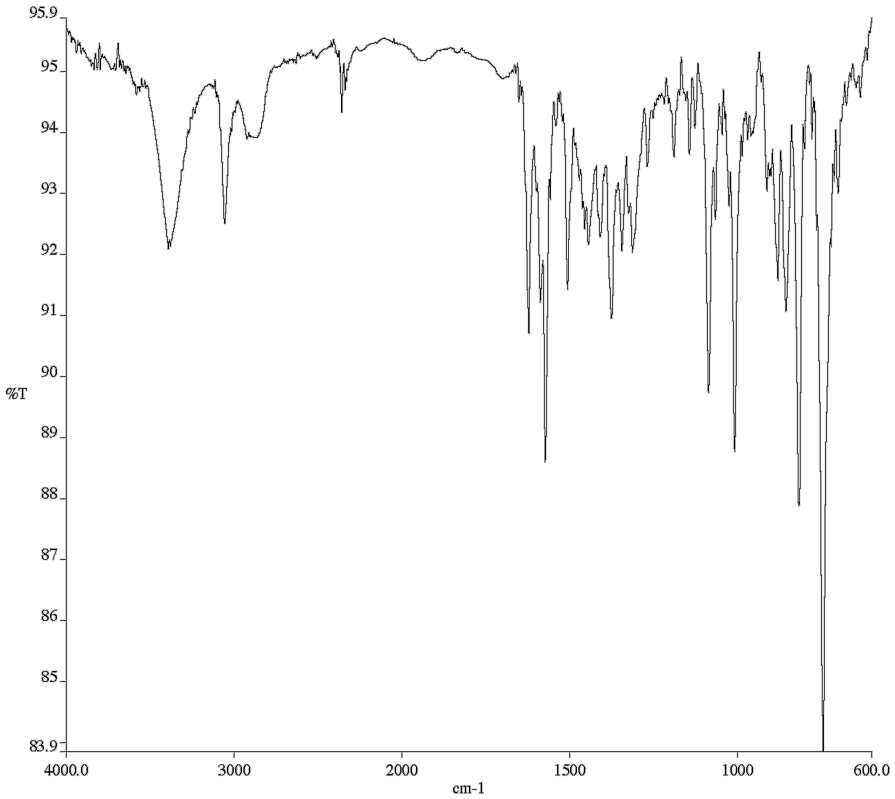
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7i**.



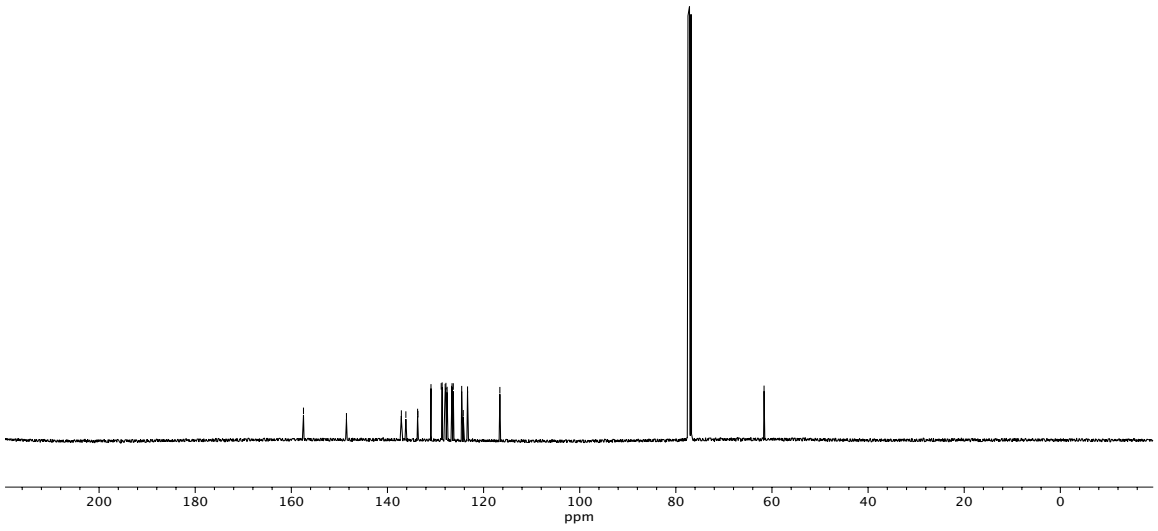
^{19}F NMR (282 MHz, $CDCl_3$) of **7i**.



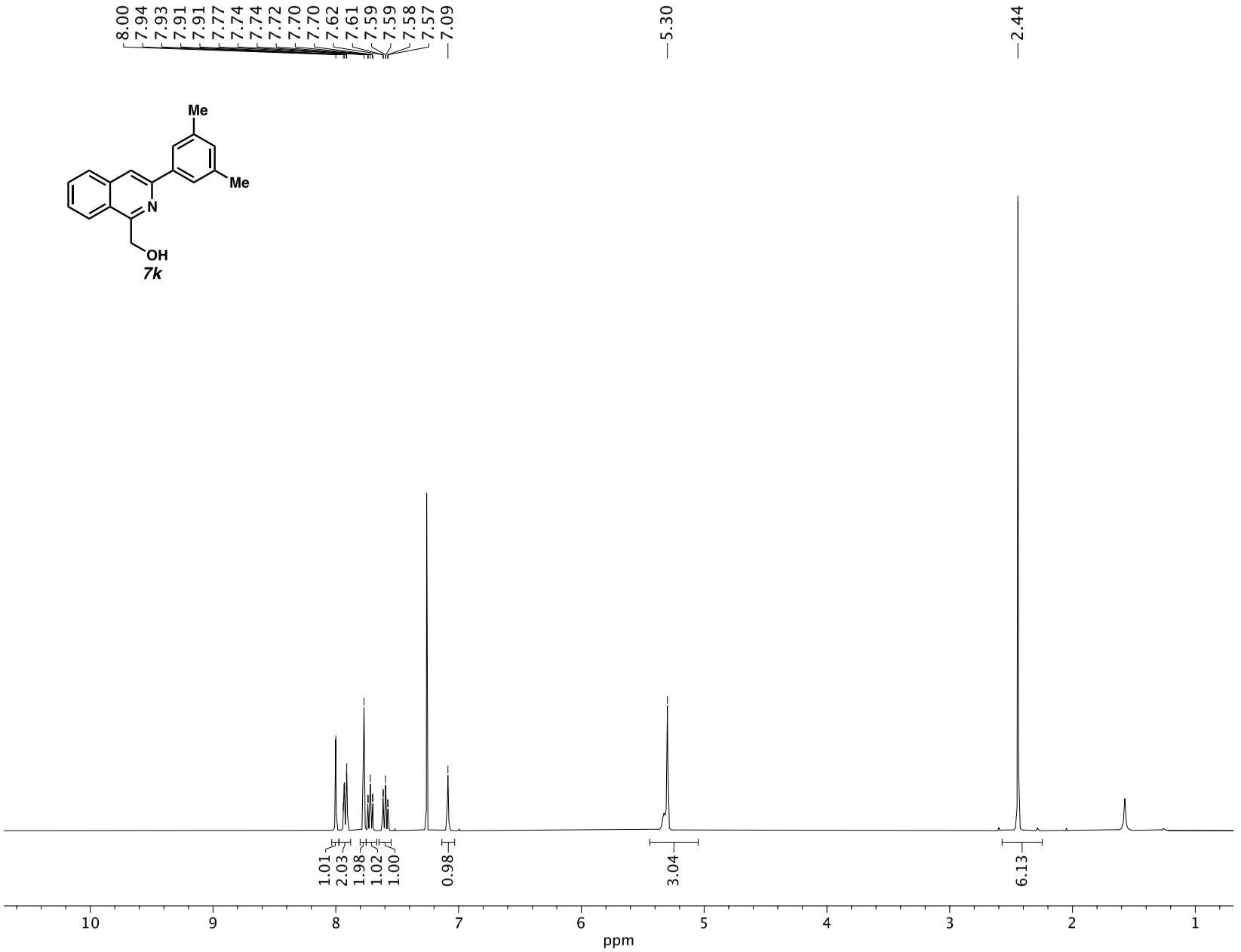
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7j**.



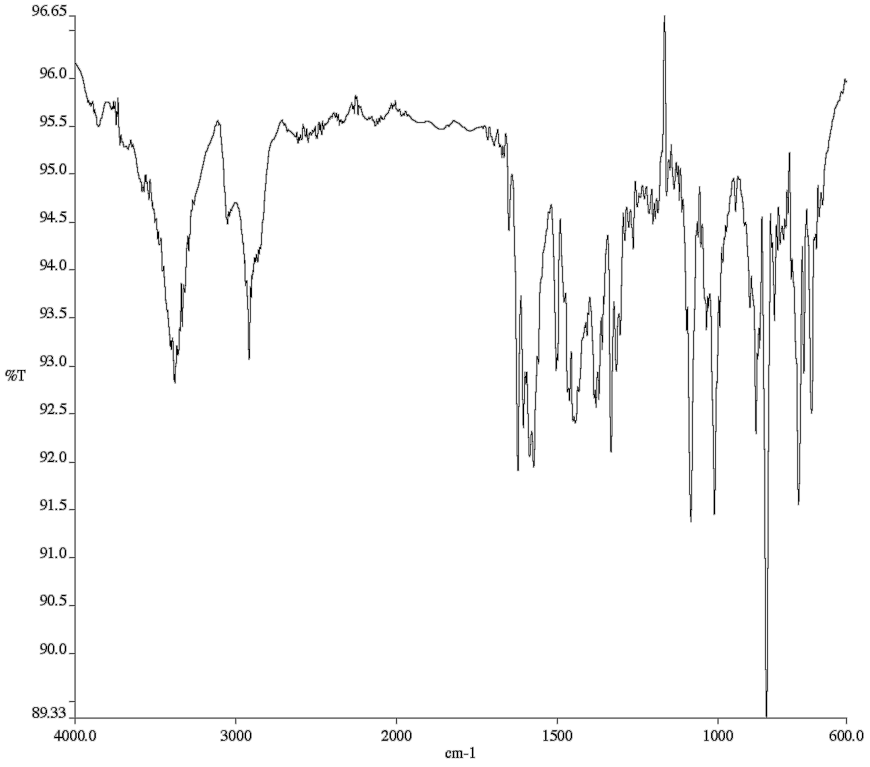
Infrared spectrum (Thin Film, NaCl) of compound **7j**.



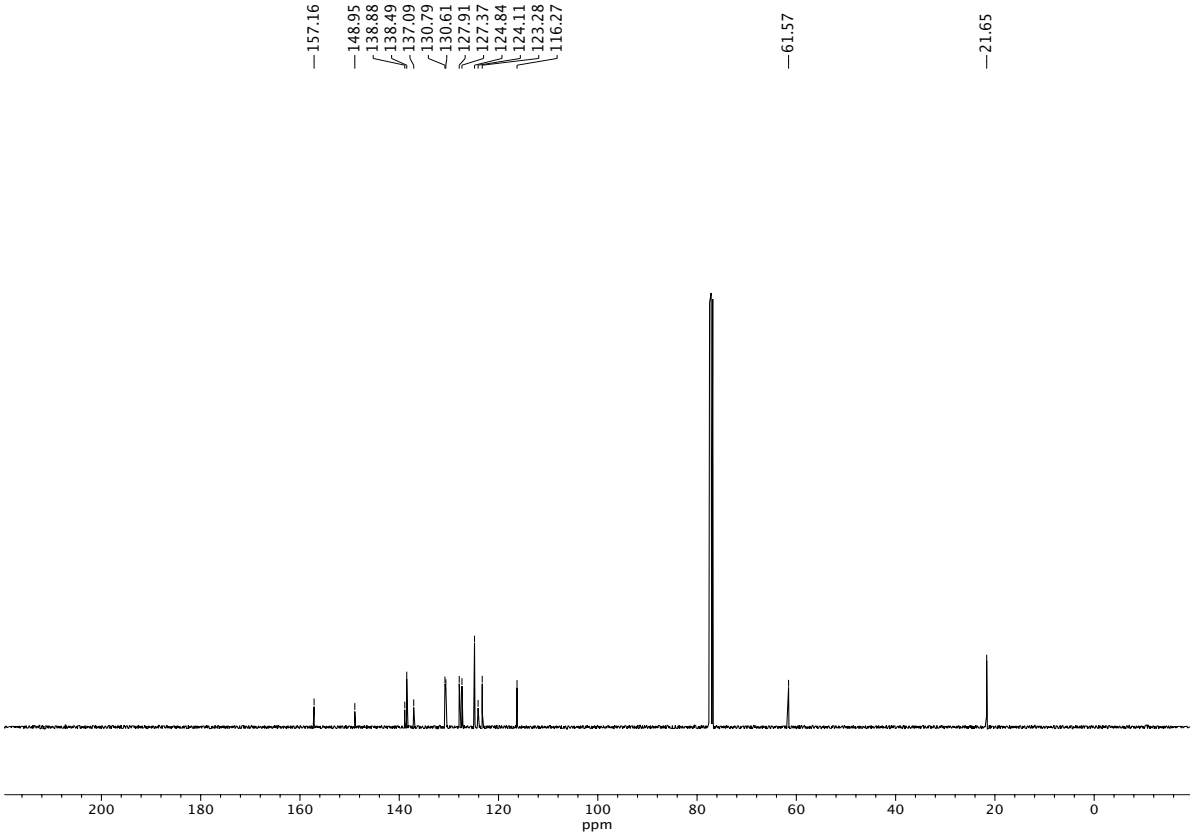
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7j**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **7k**.

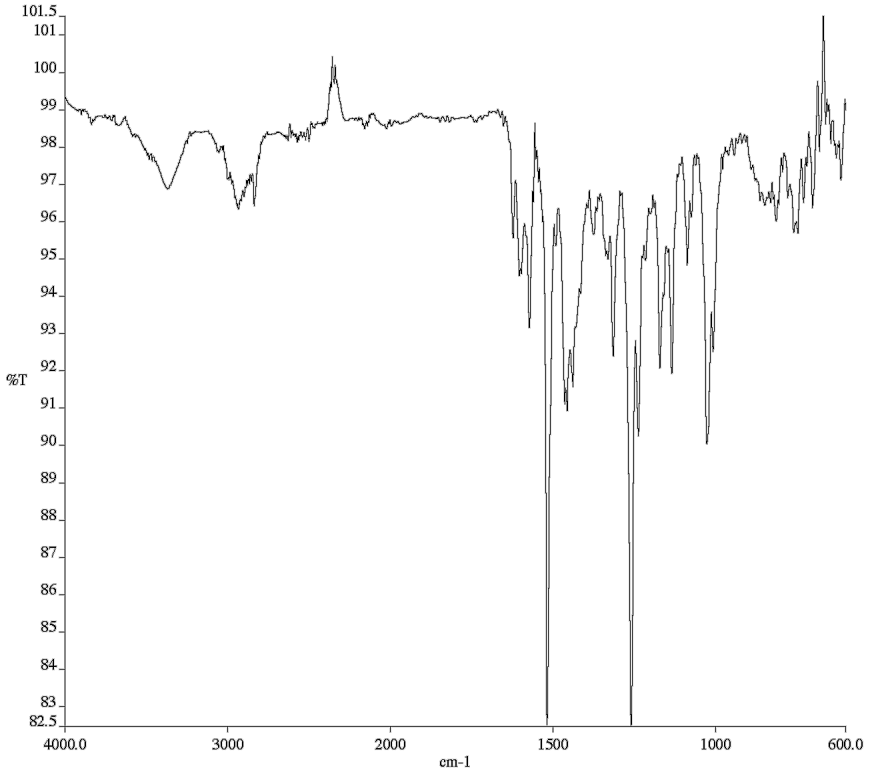


Infrared spectrum (Thin Film, NaCl) of compound **7k**.

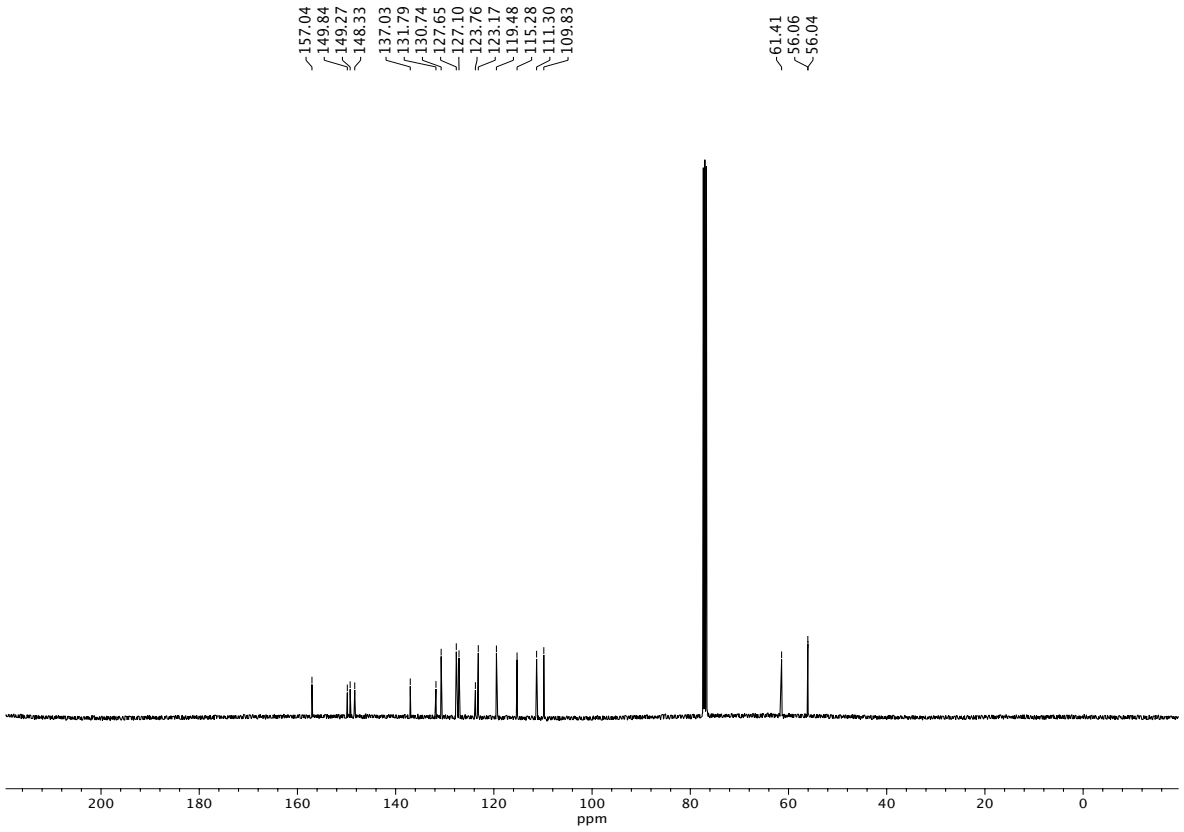


^{13}C NMR (100 MHz, $CDCl_3$) of compound **7k**.

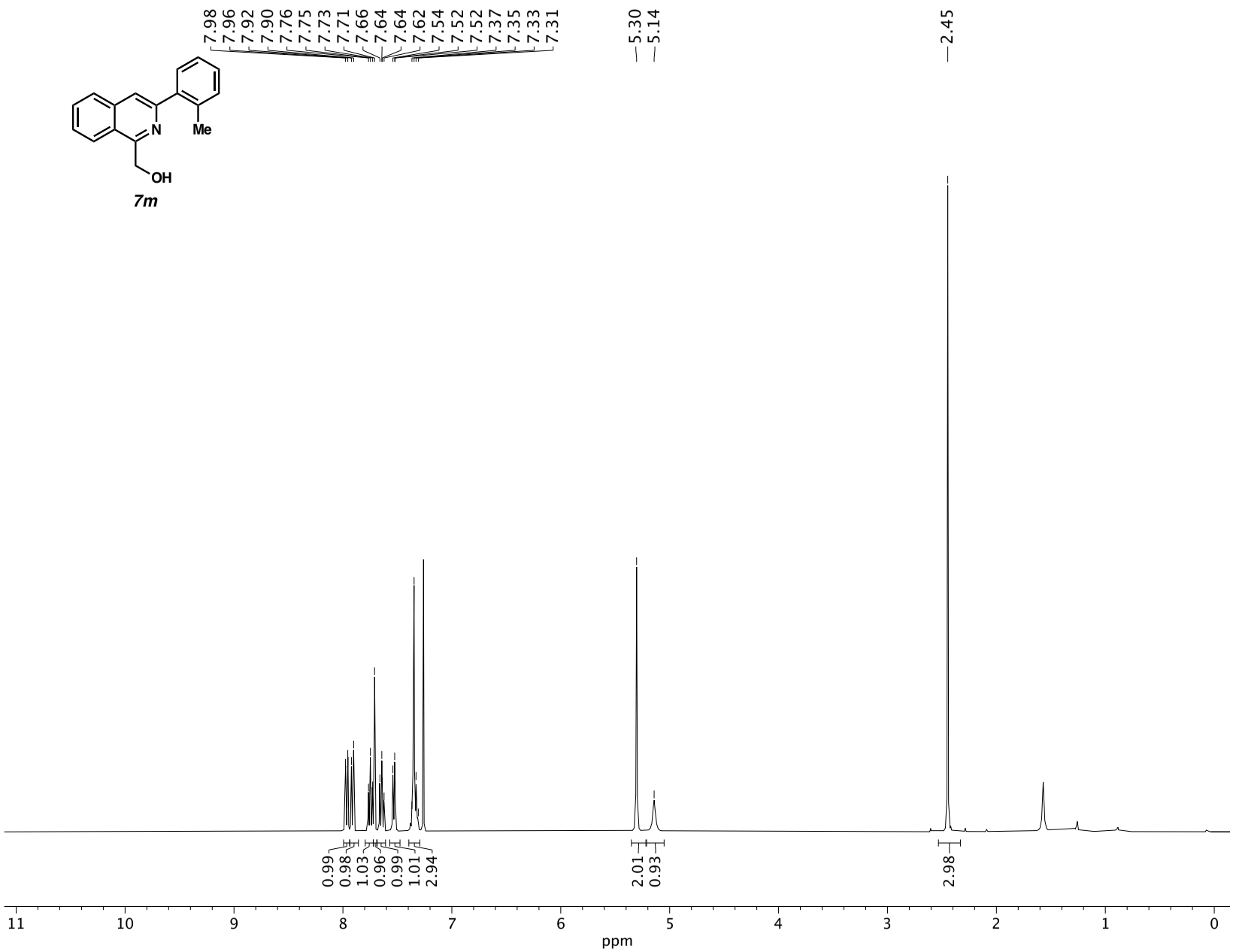
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7l**.



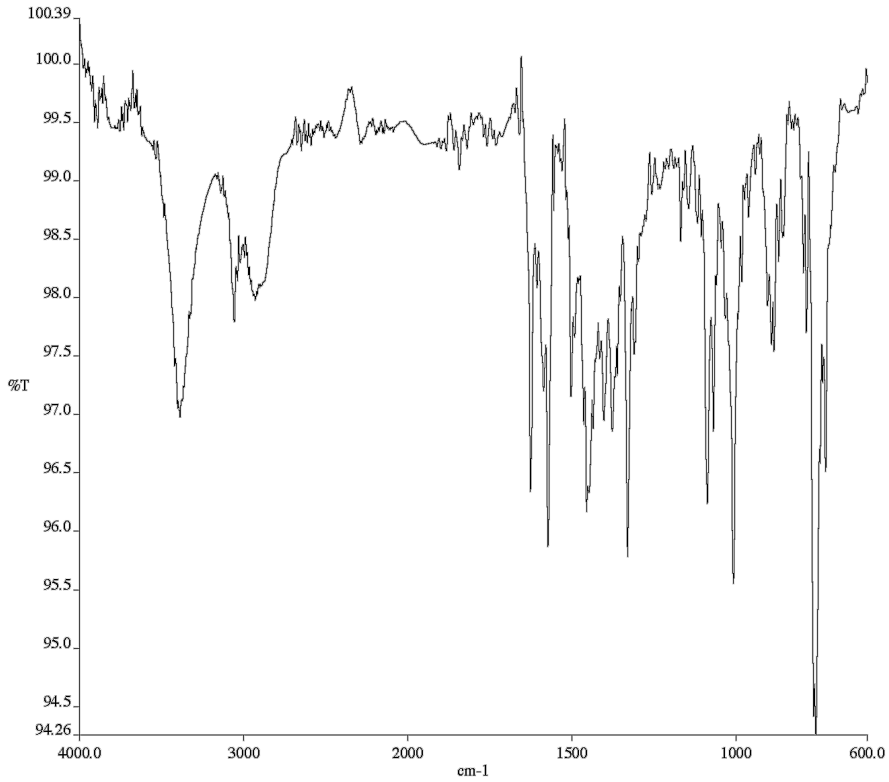
Infrared spectrum (Thin Film, NaCl) of compound **7l**.



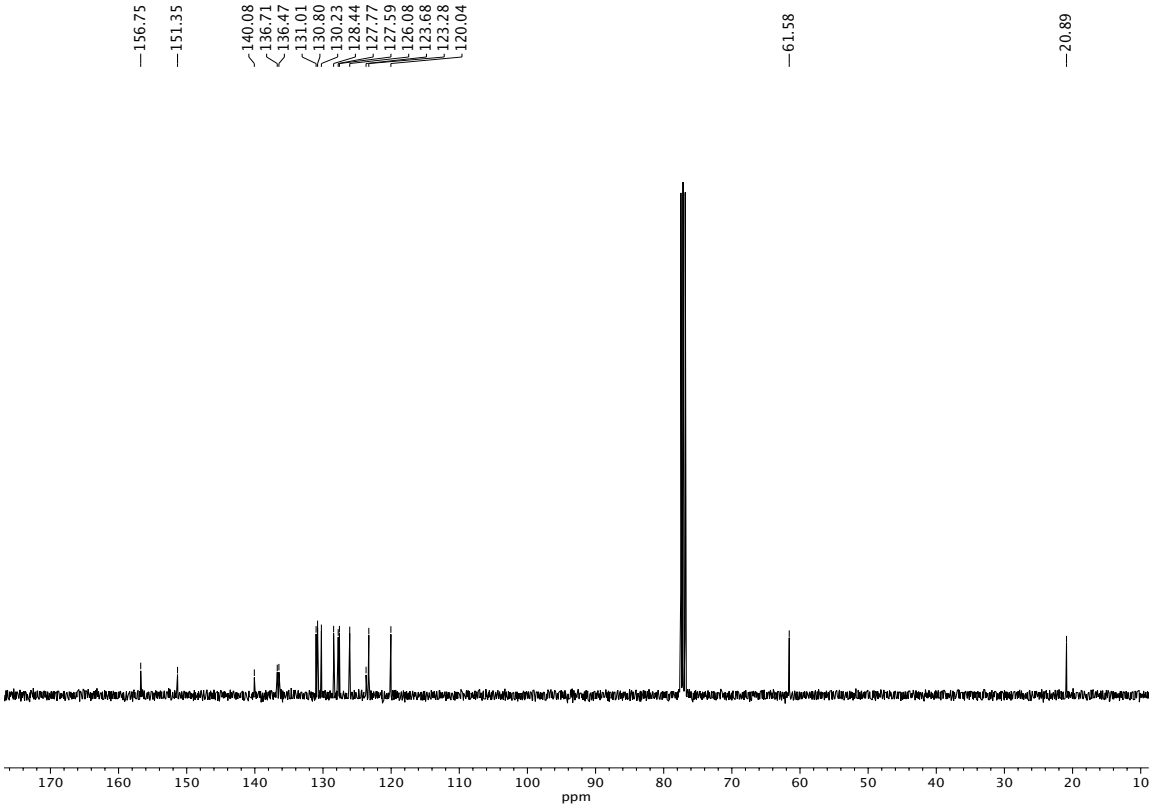
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7l**.



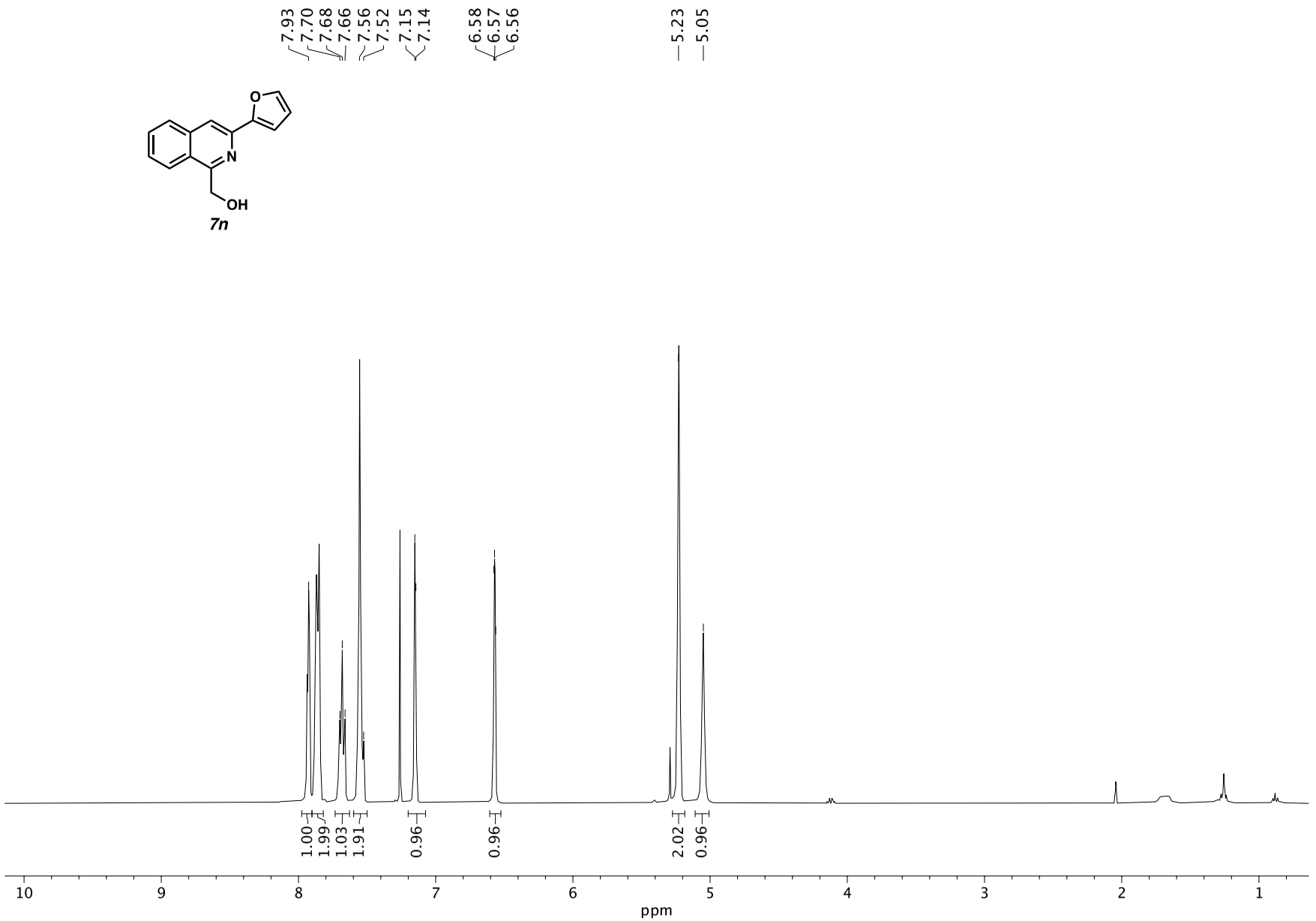
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7m**.



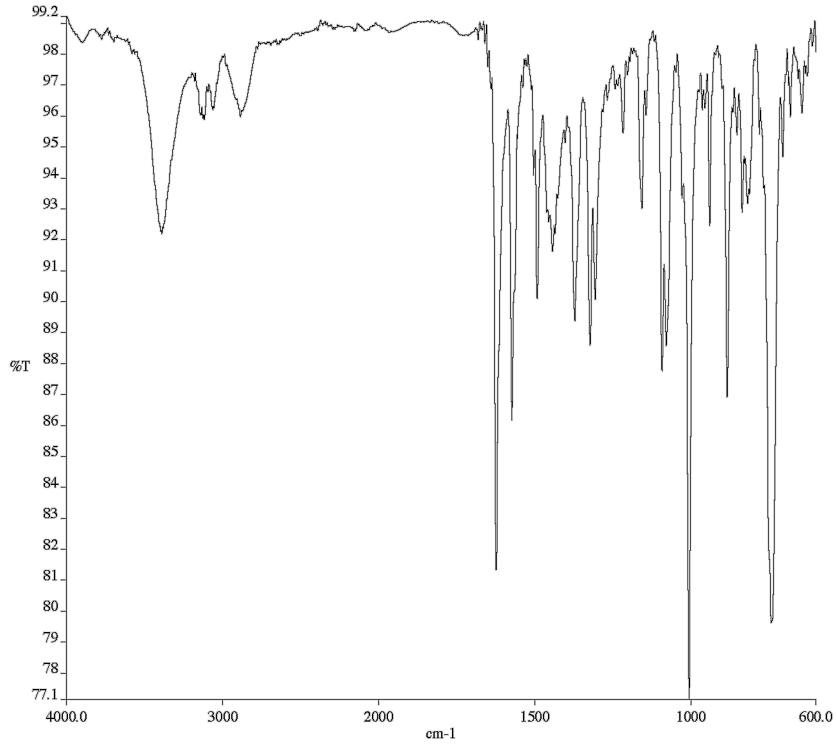
Infrared spectrum (Thin Film, NaCl) of compound **7m**.



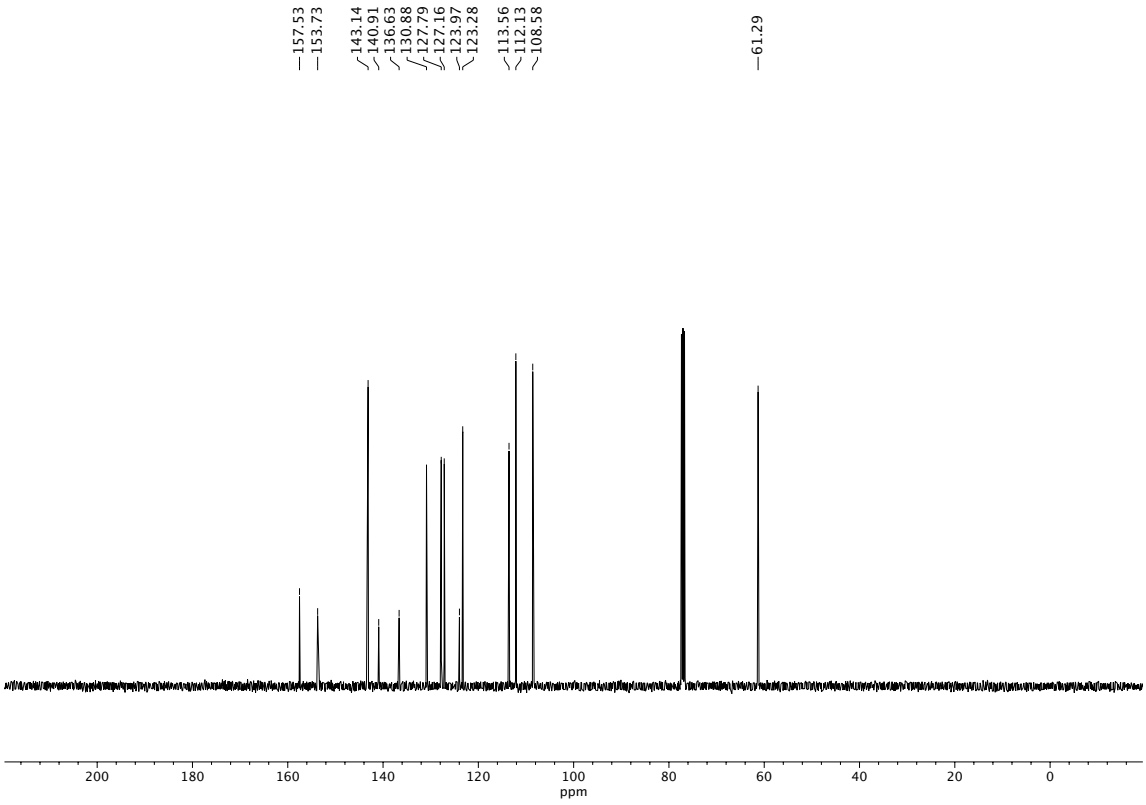
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7m**.



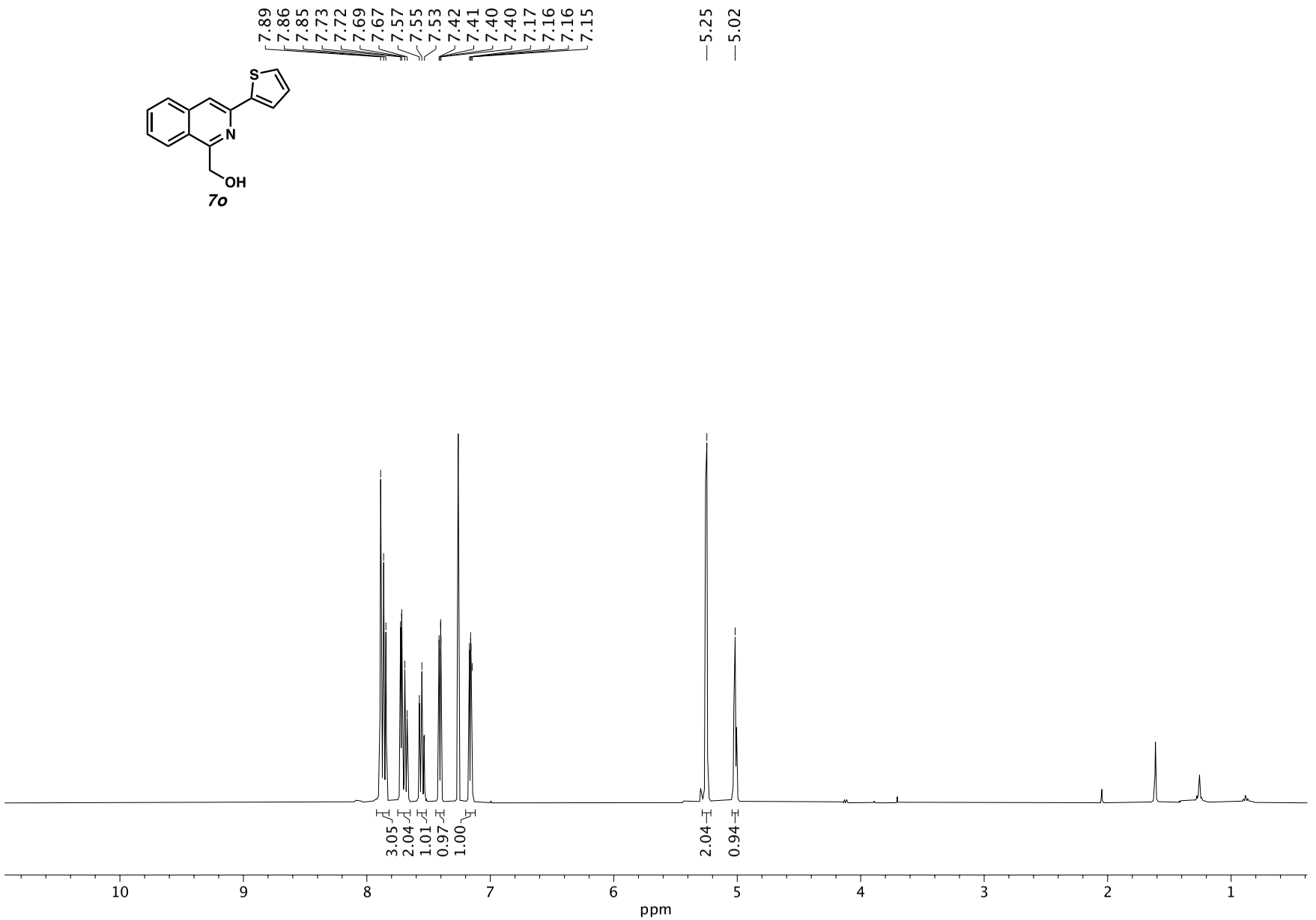
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7n**.



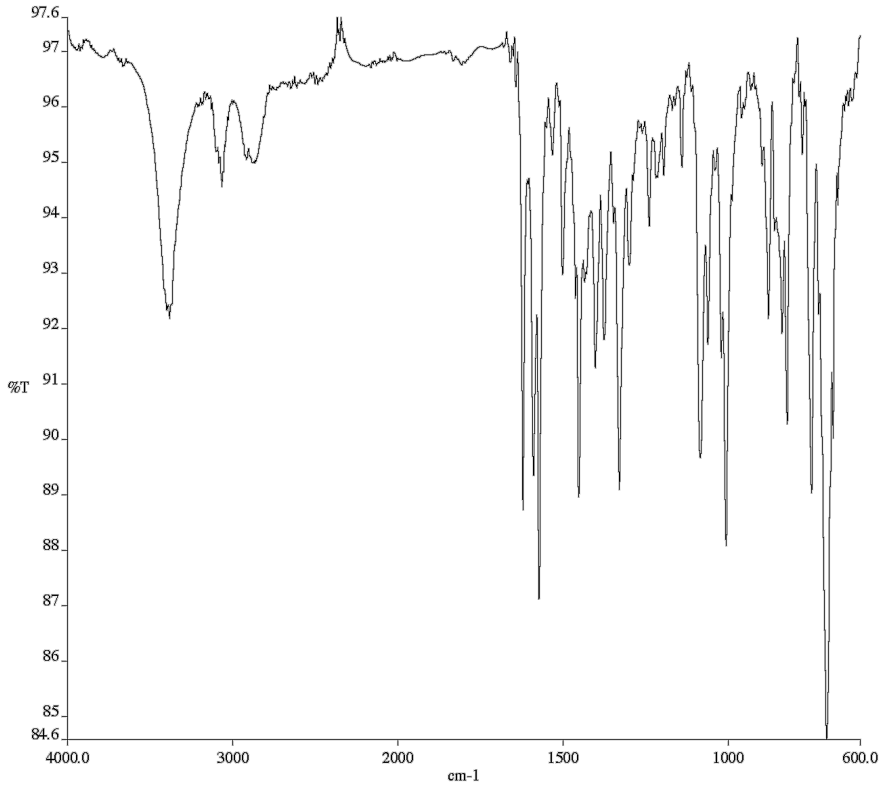
Infrared spectrum (Thin Film, NaCl) of compound **7n**.



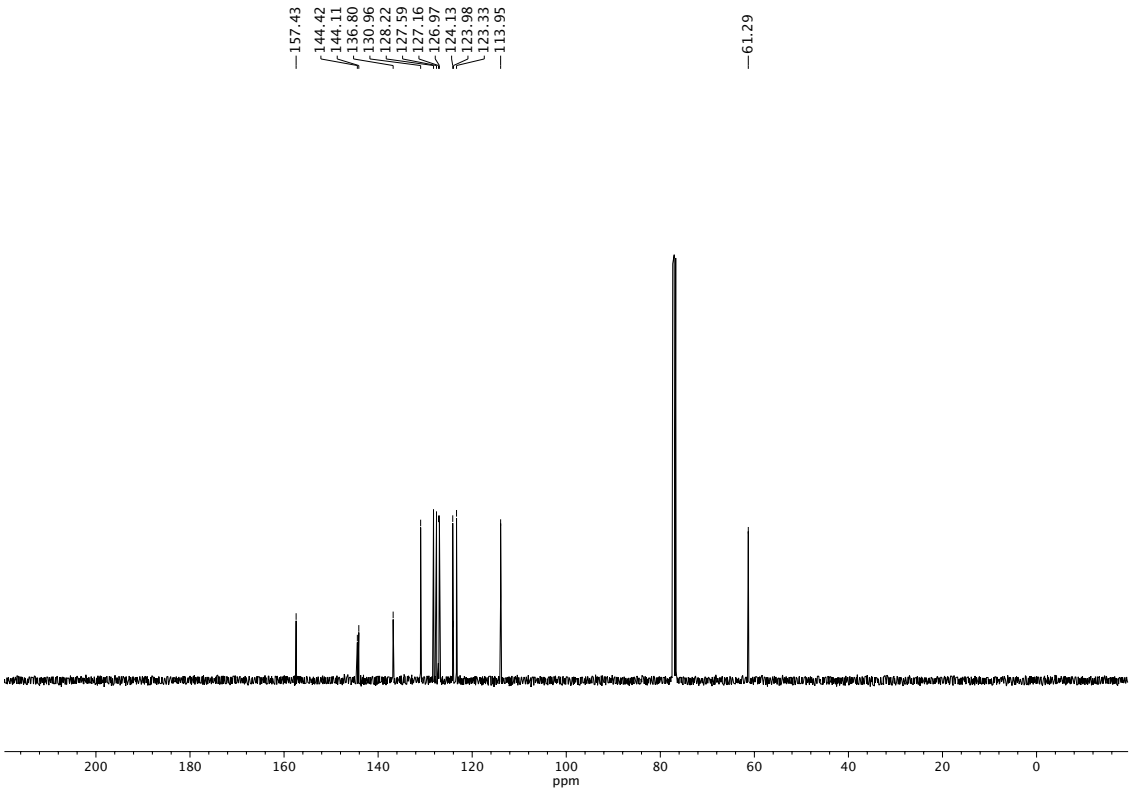
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7n**.



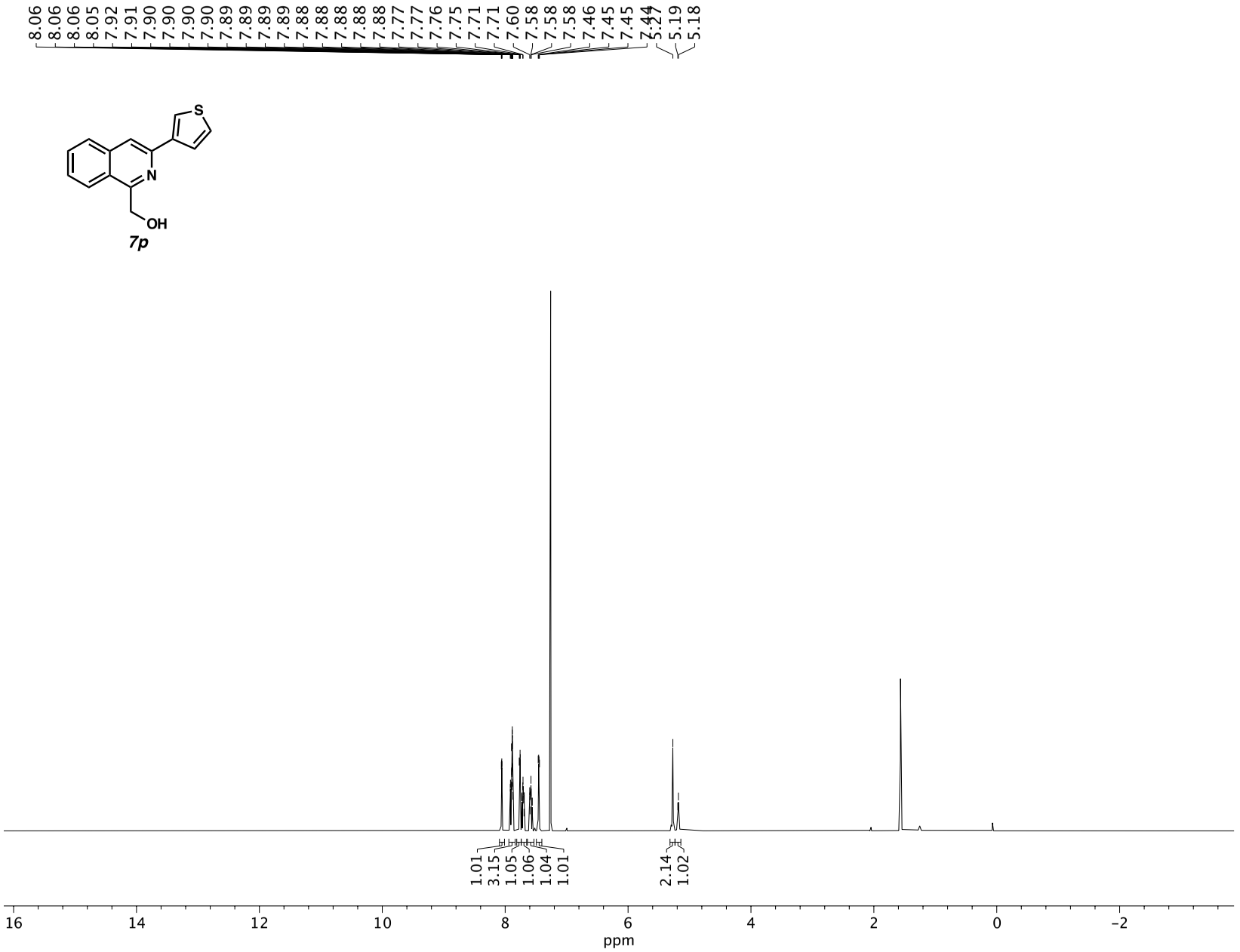
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7o**.



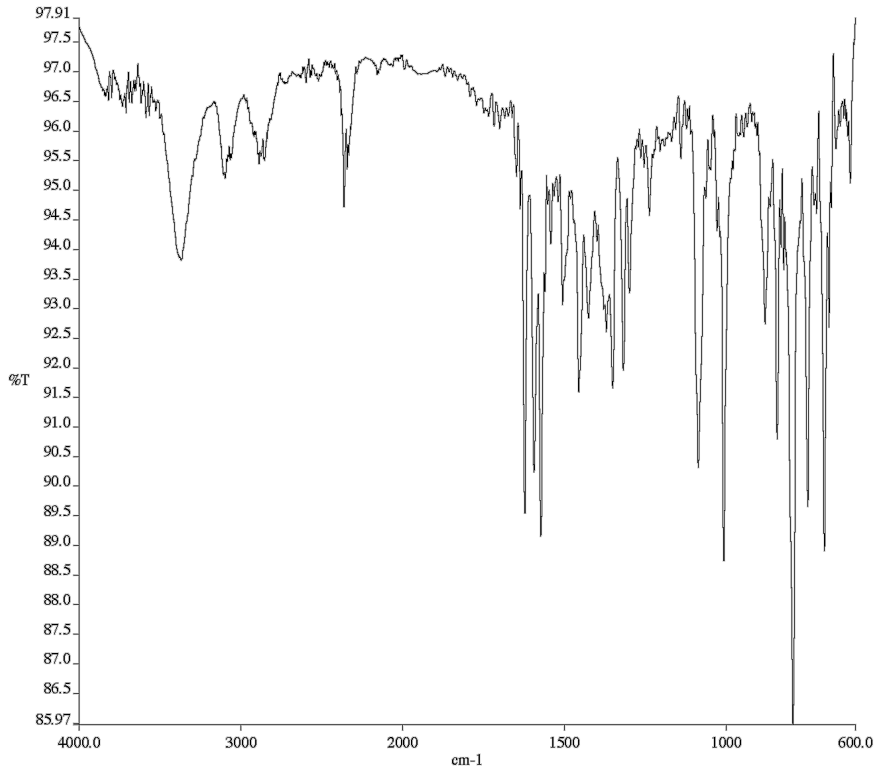
Infrared spectrum (Thin Film, NaCl) of compound **7o**.



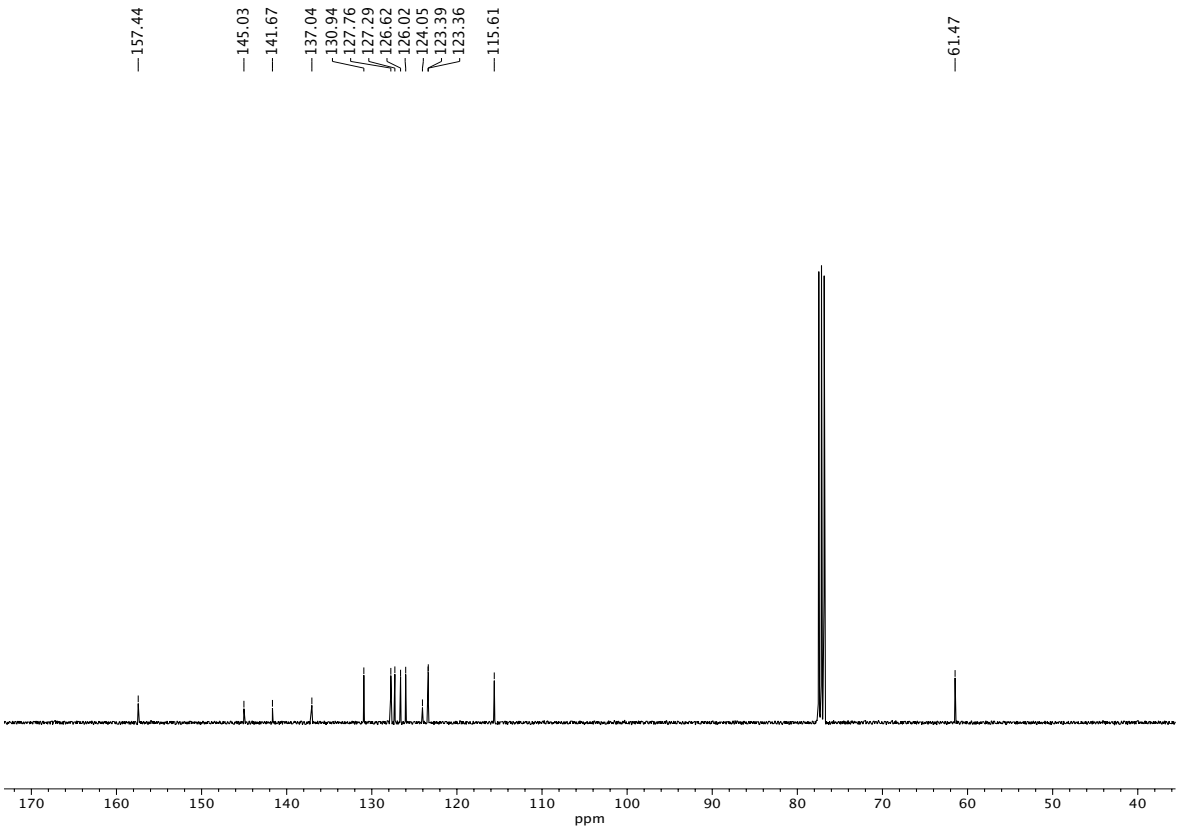
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7o**.



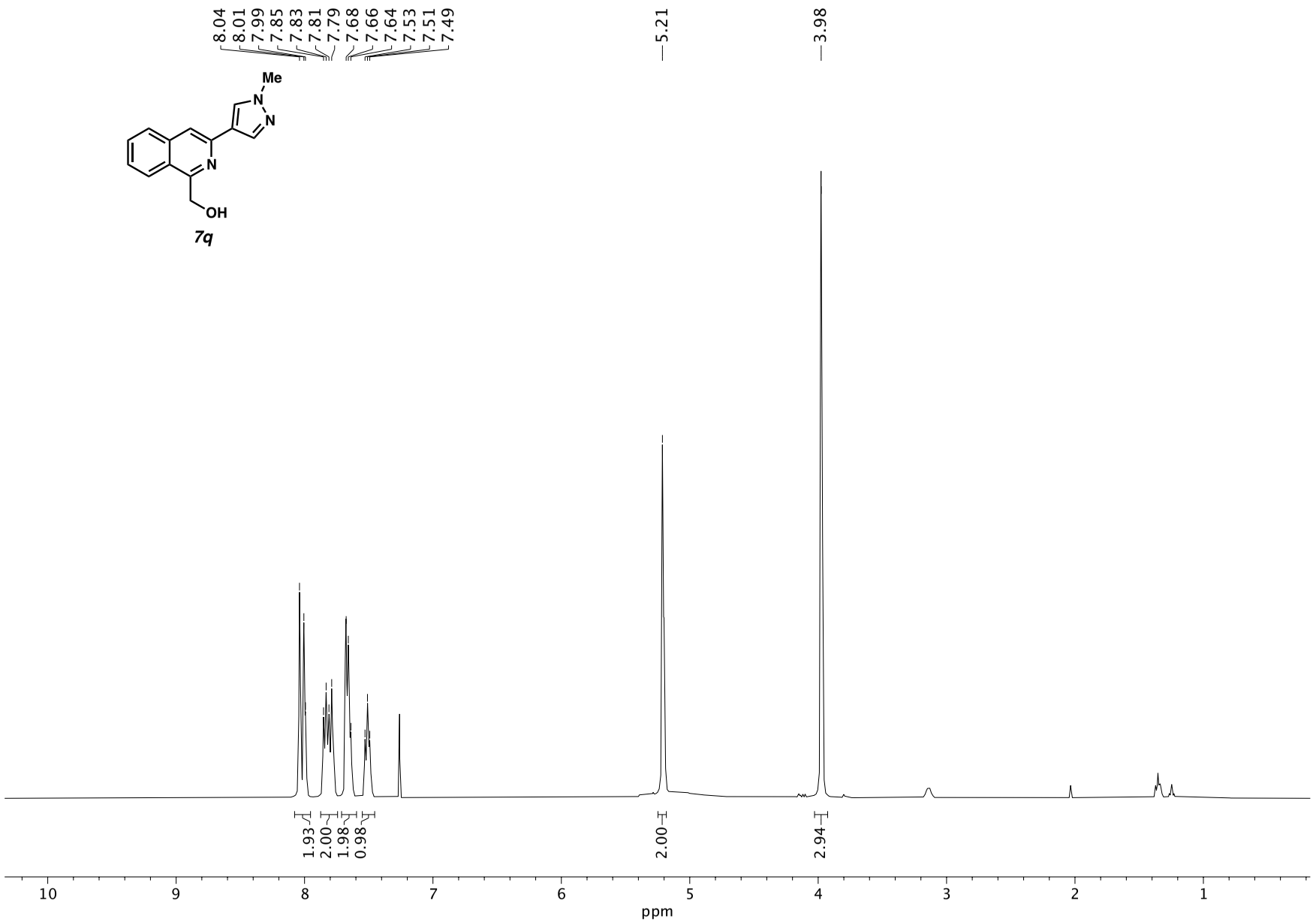
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7p**.



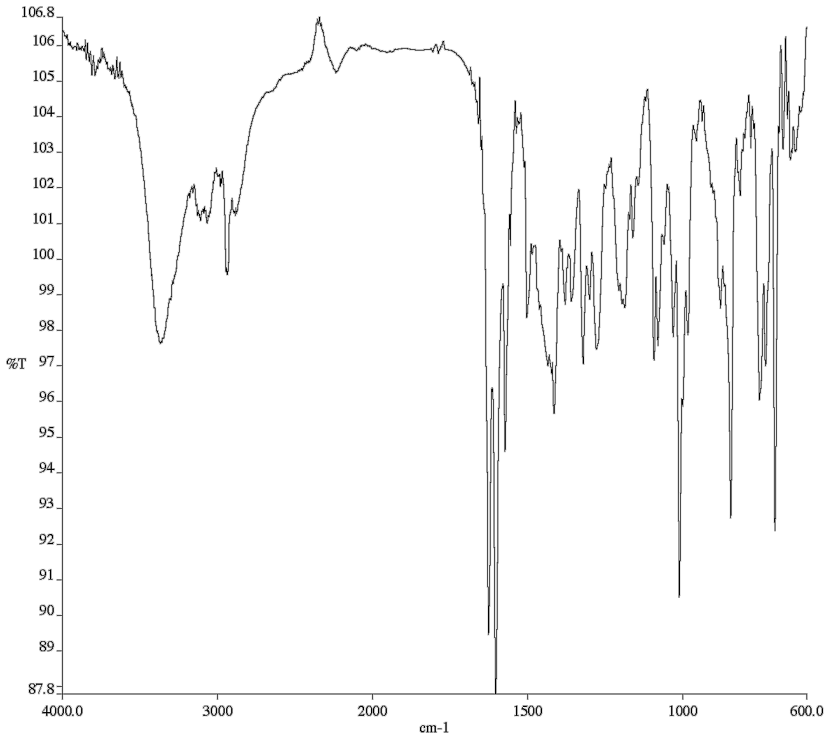
Infrared spectrum (Thin Film, NaCl) of compound **7p**.



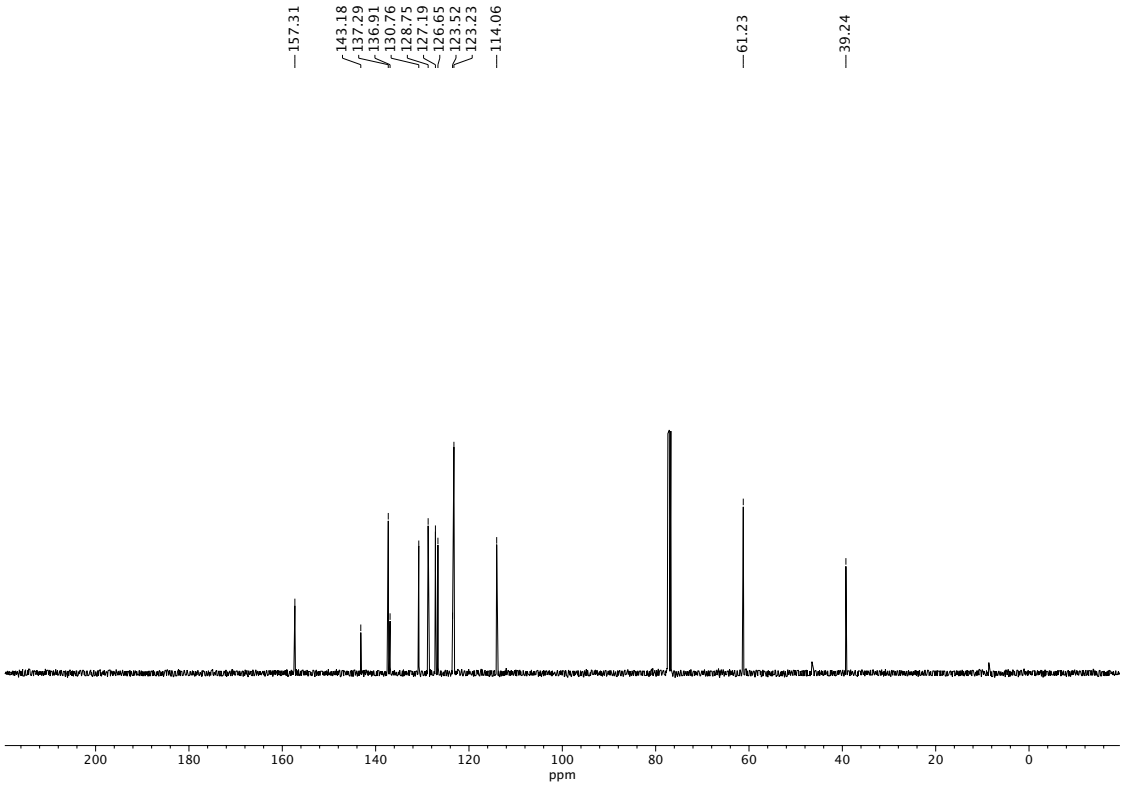
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7p**.



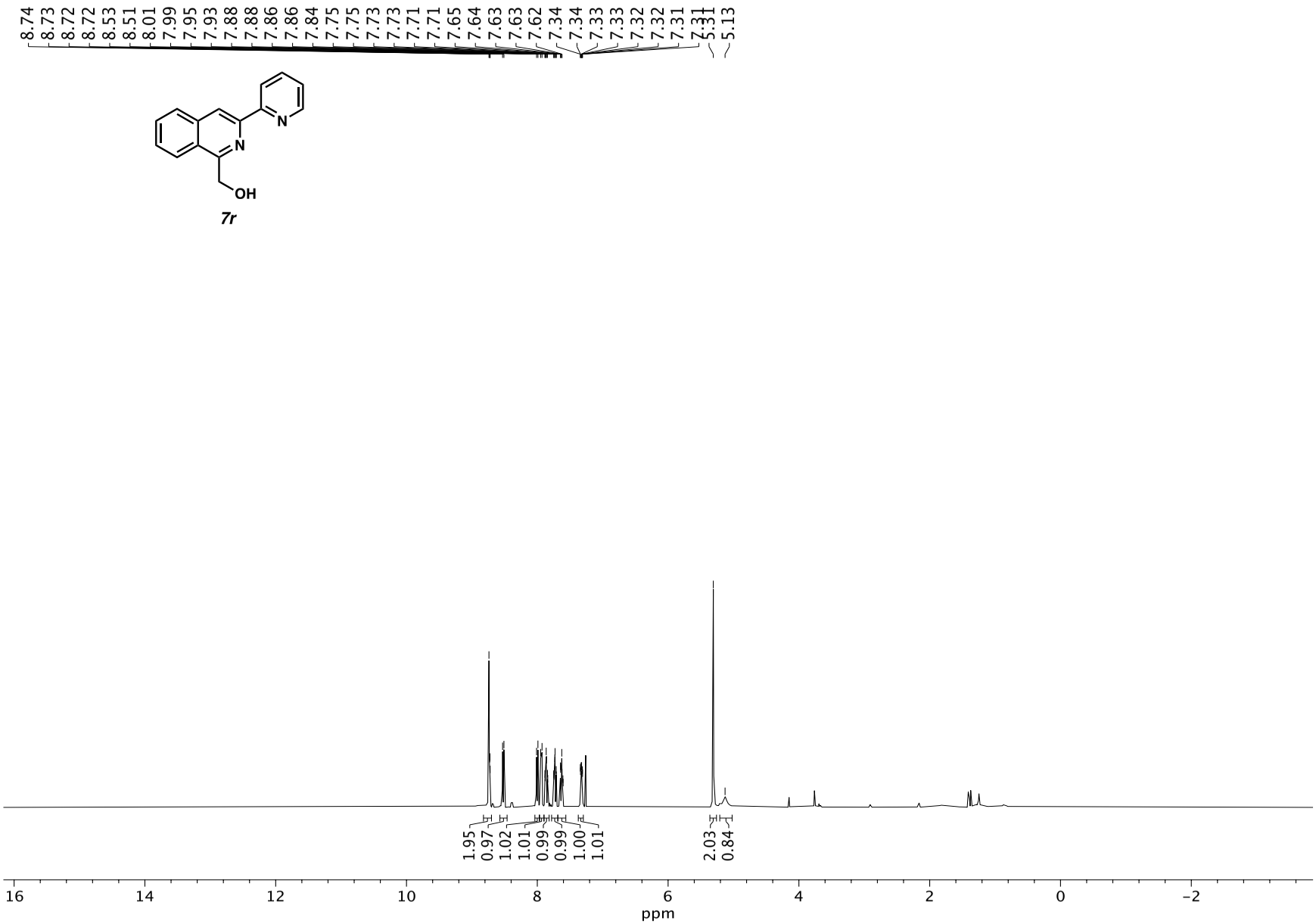
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7q**.



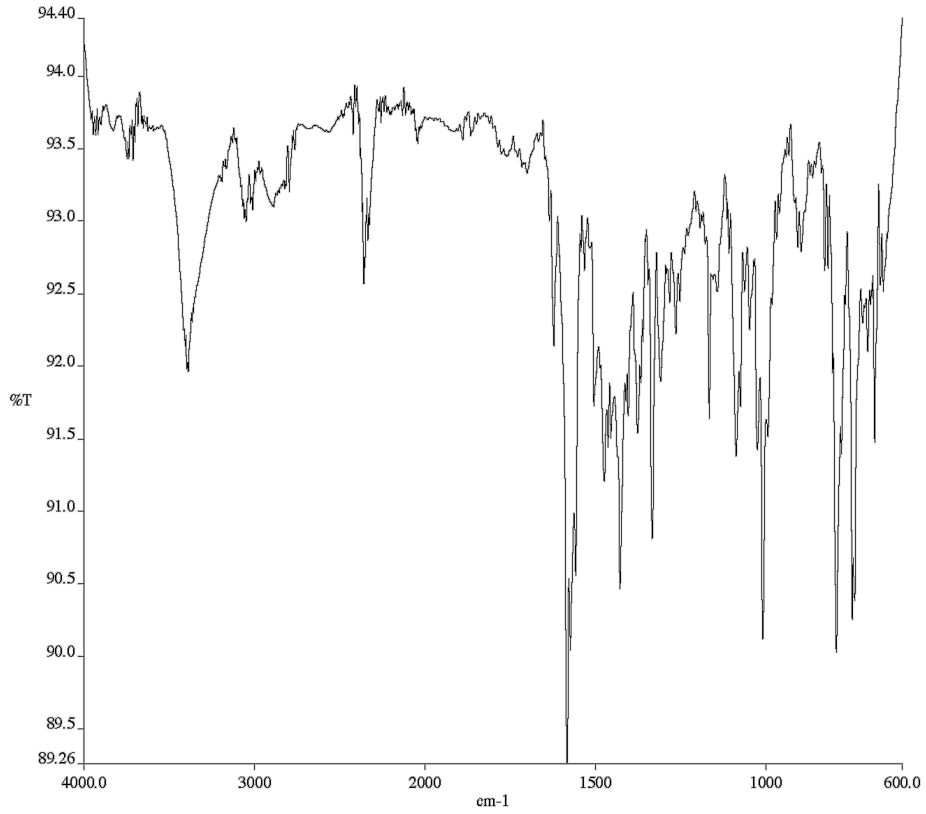
Infrared spectrum (Thin Film, NaCl) of compound **7q**.



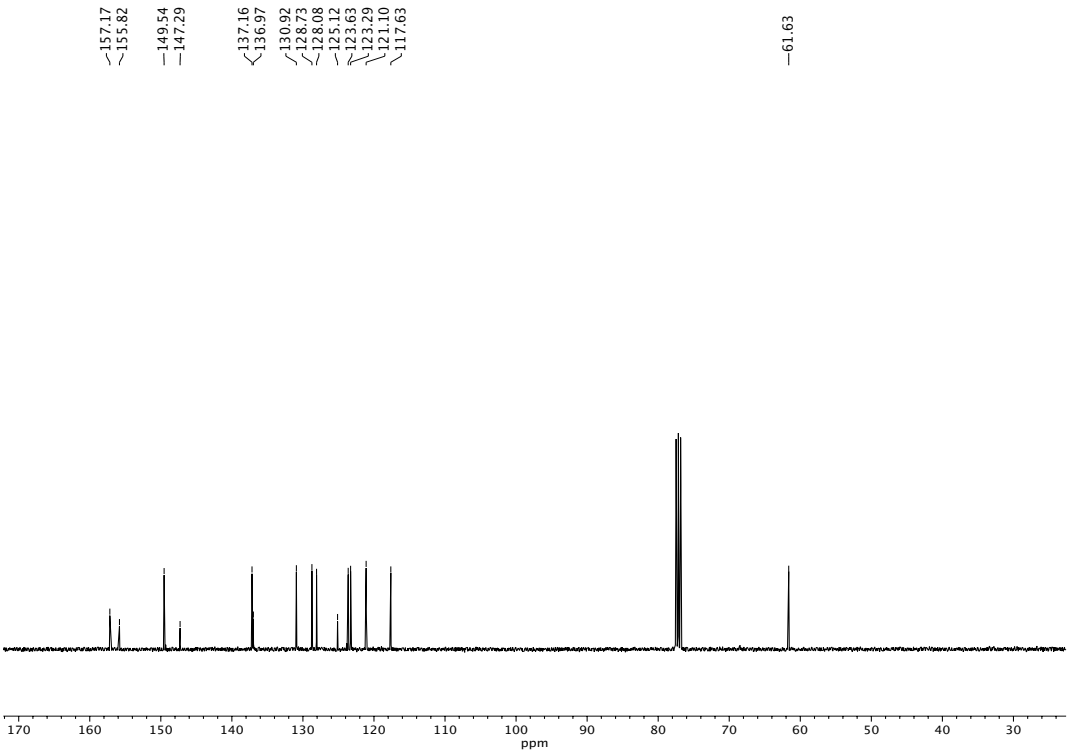
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7q**.



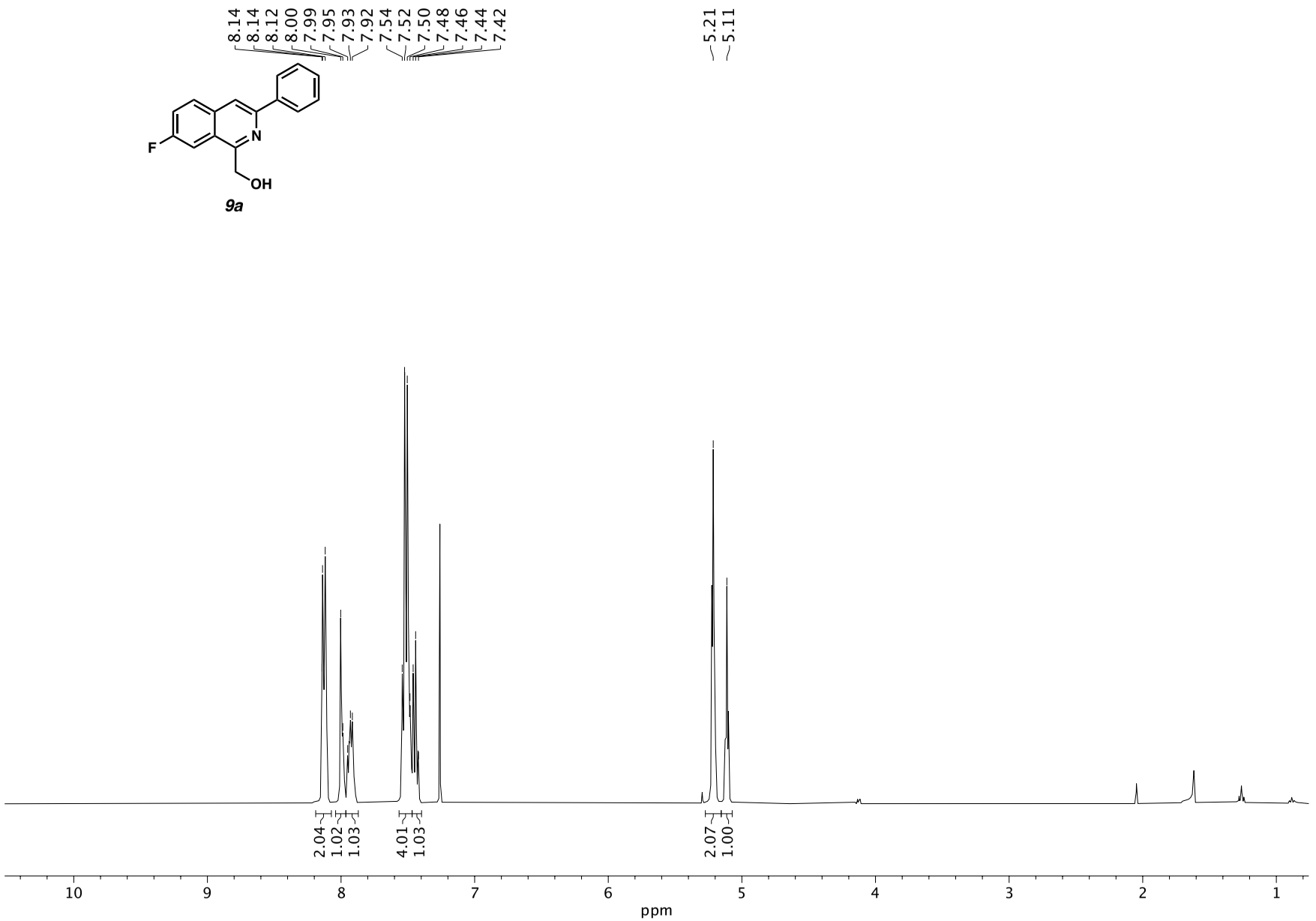
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7r**.



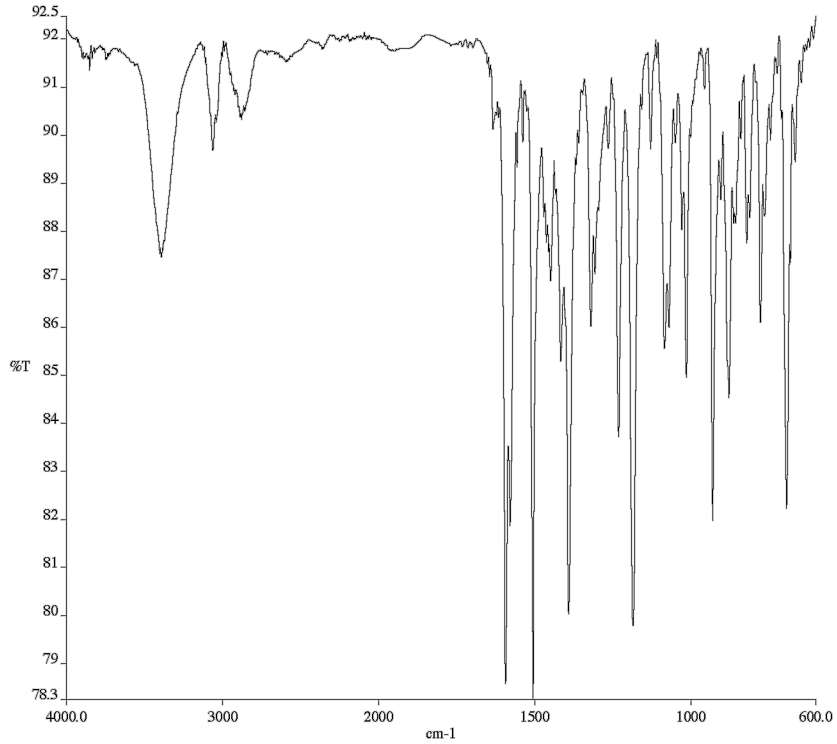
Infrared spectrum (Thin Film, NaCl) of compound **7r**.



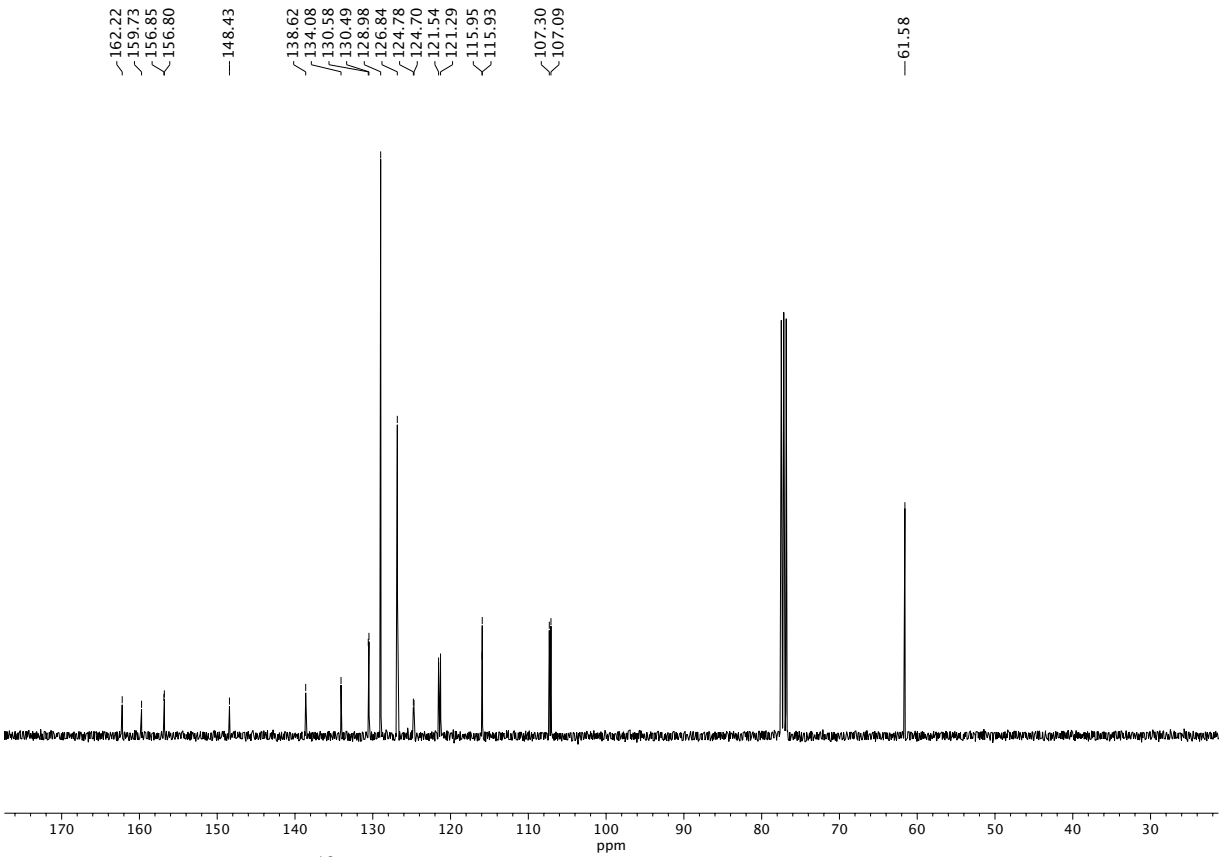
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7r**.



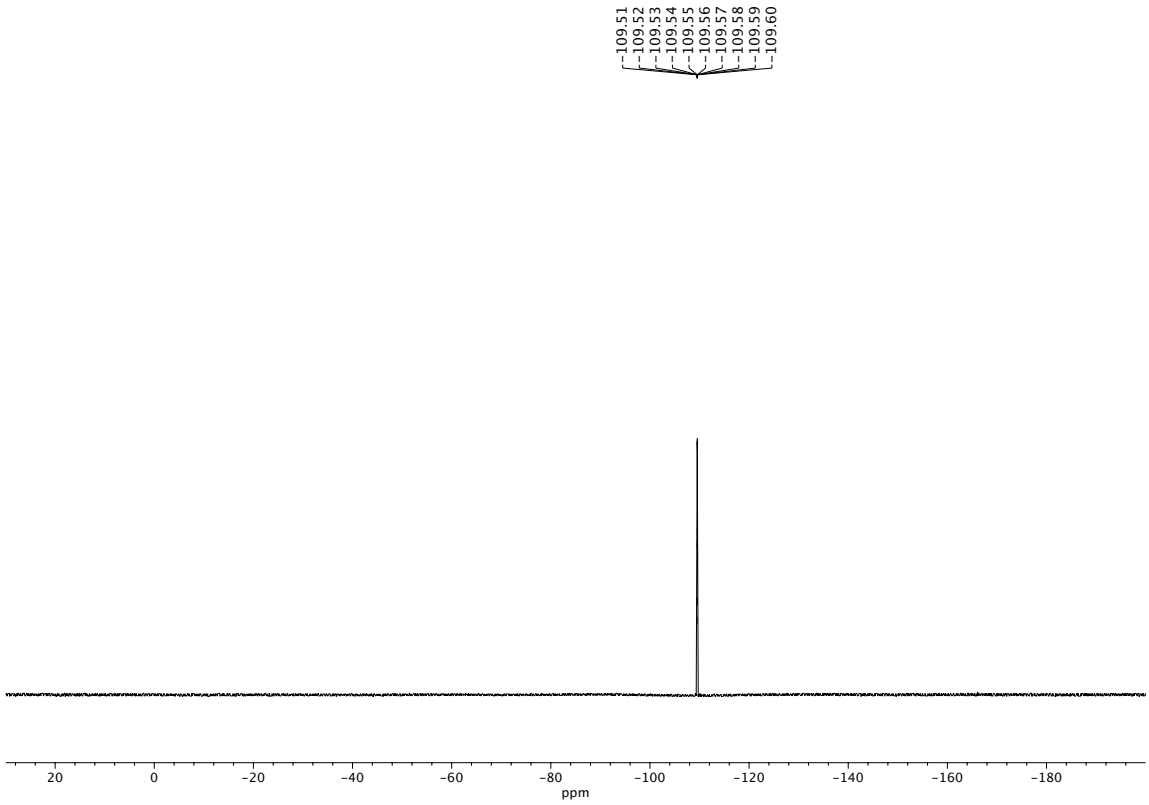
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9a**.



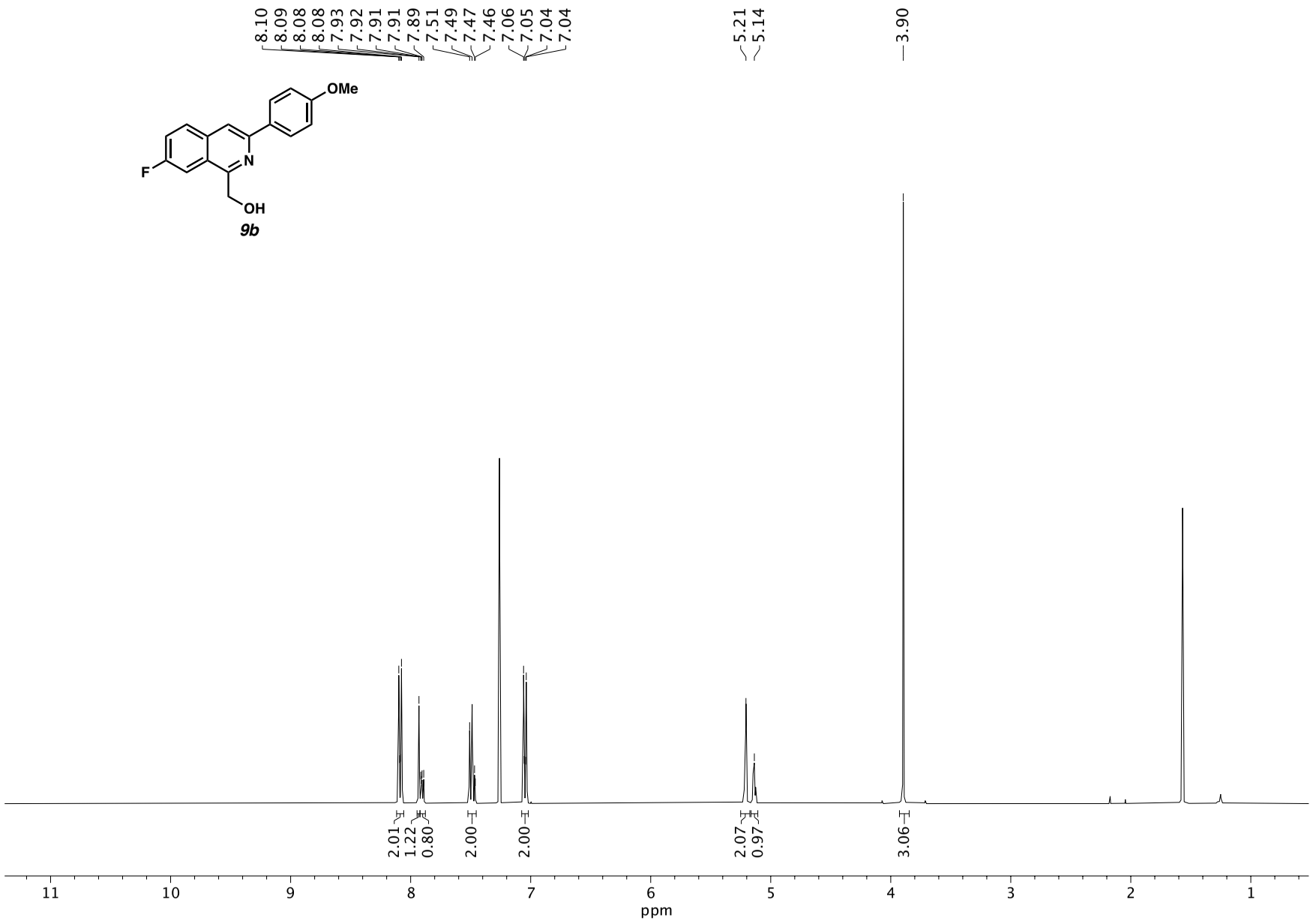
Infrared spectrum (Thin Film, NaCl) of compound **9a**.



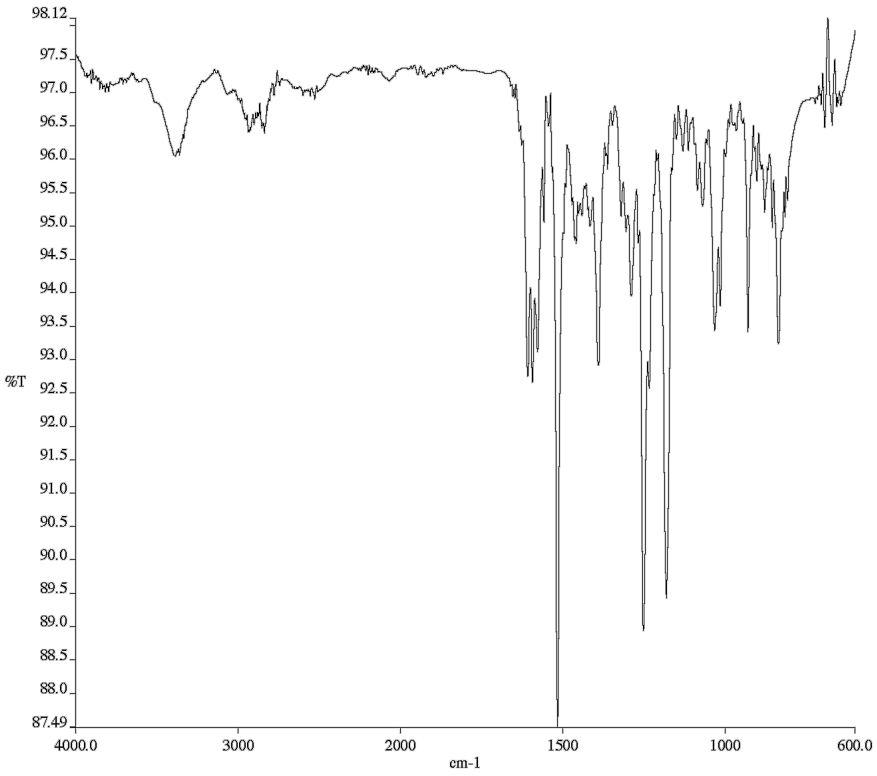
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9a**.



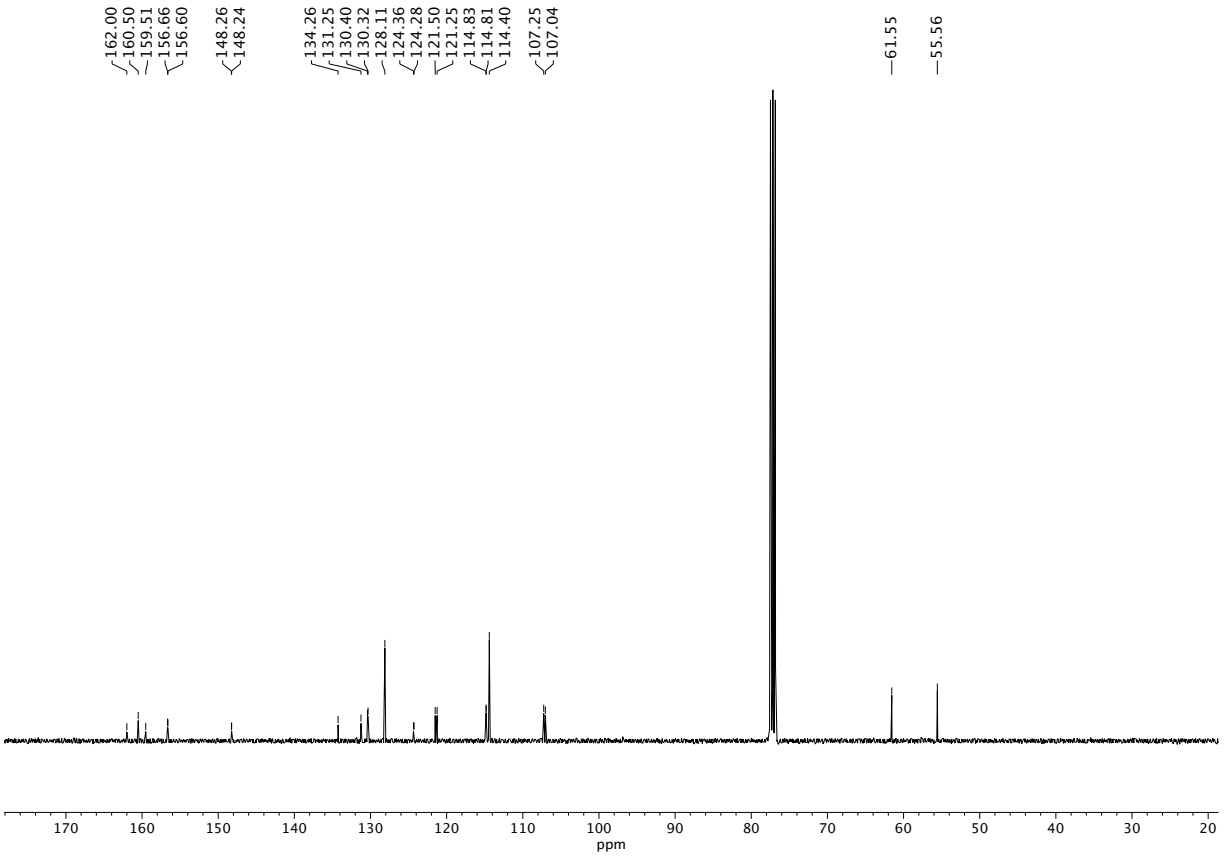
^{19}F NMR (282 MHz, $CDCl_3$) of **9a**.



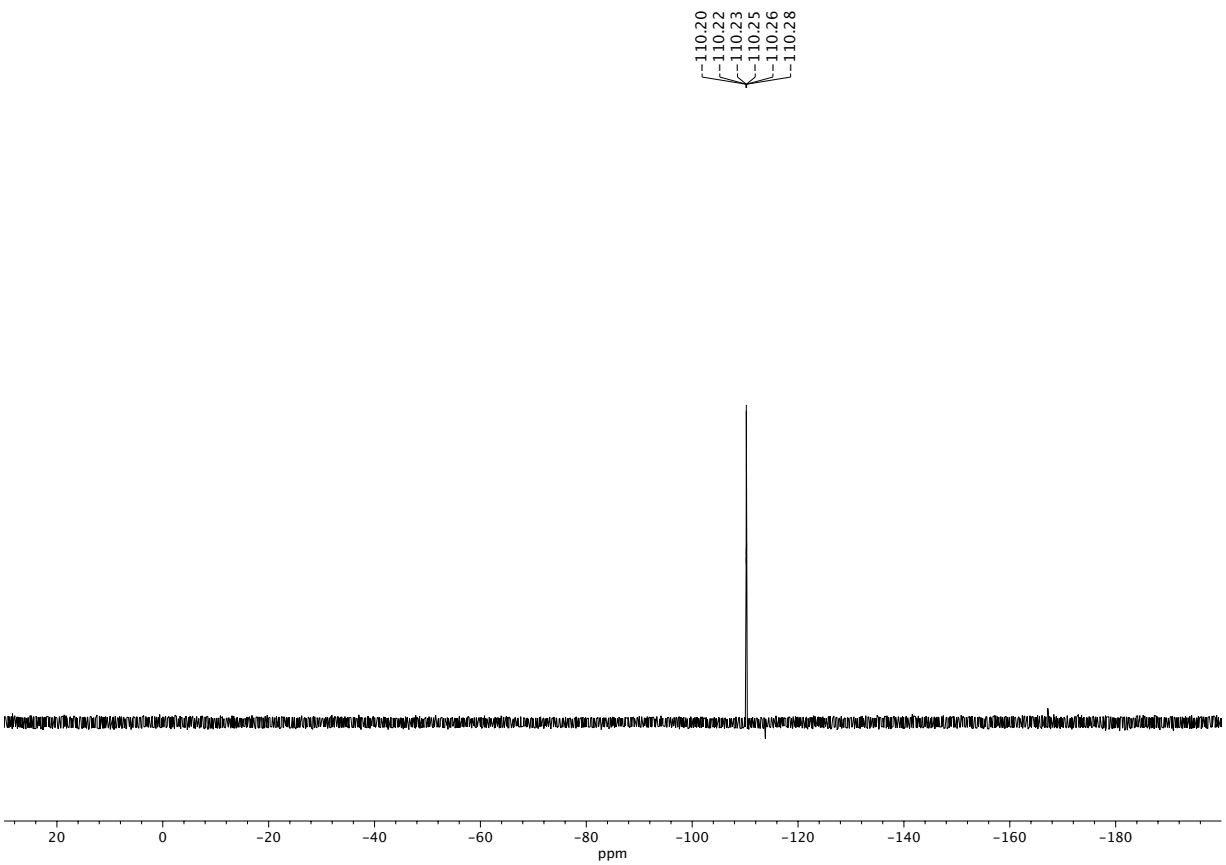
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9b**.



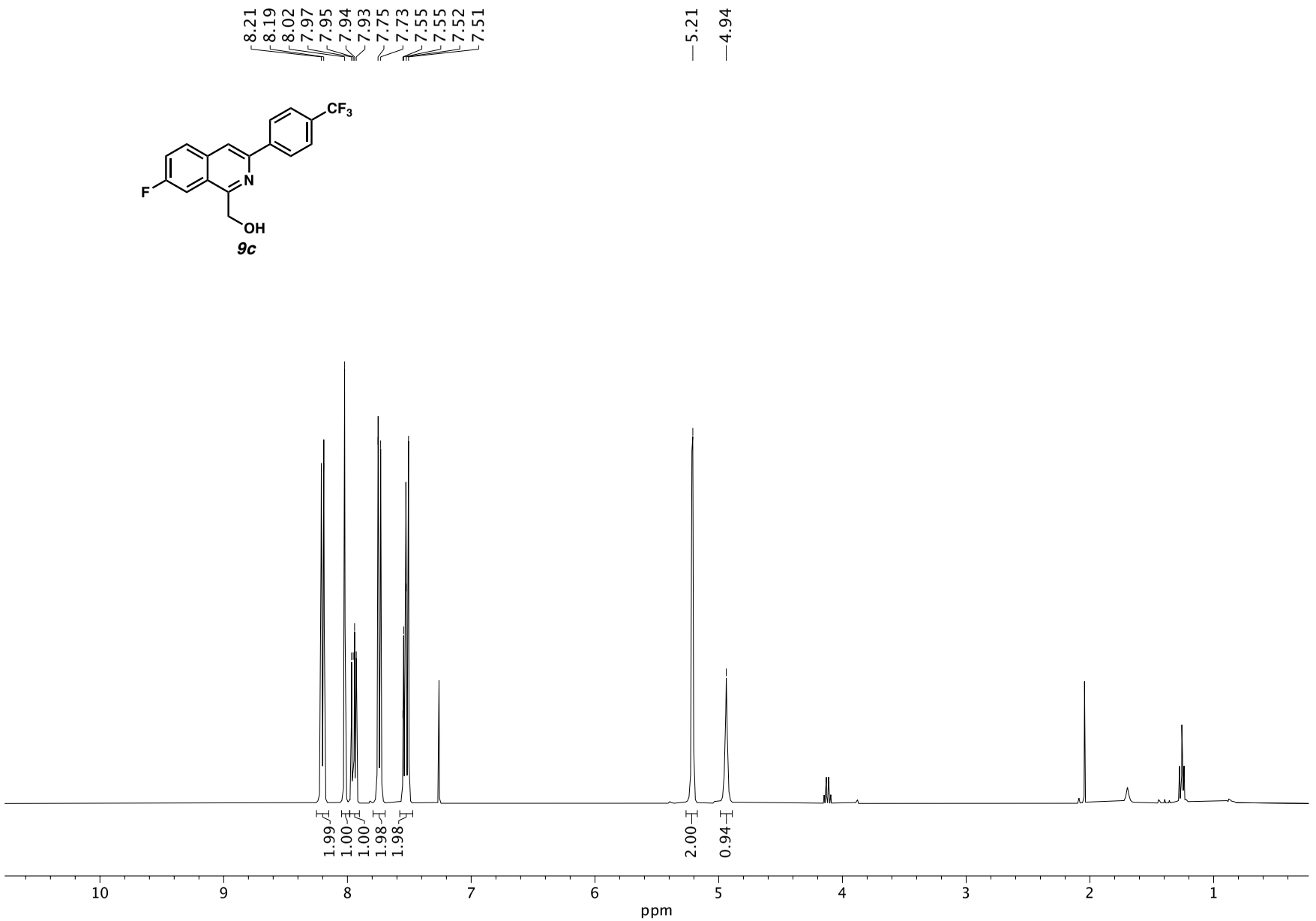
Infrared spectrum (Thin Film, NaCl) of compound **9b**.



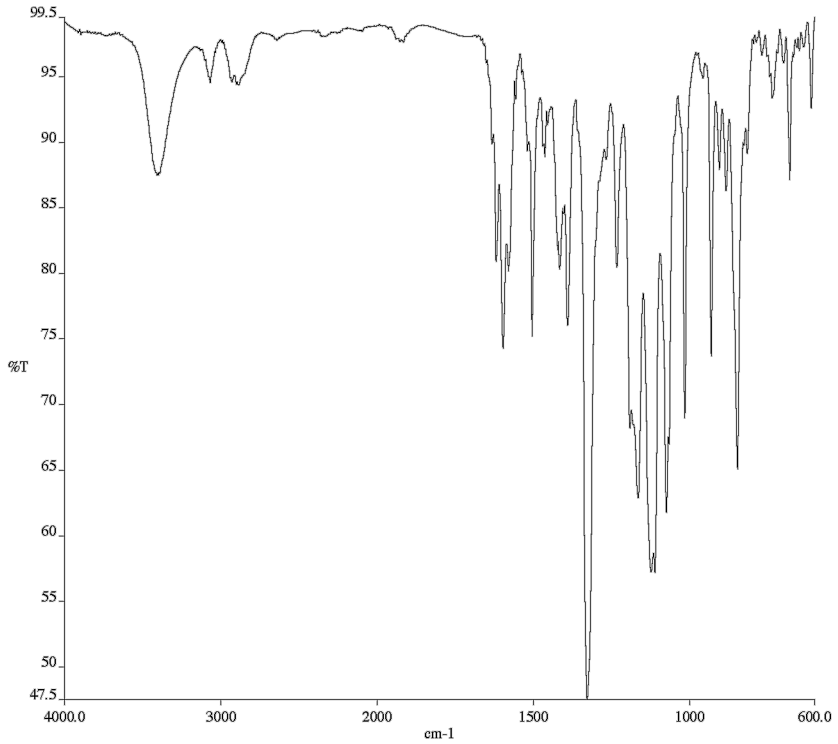
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9b**.



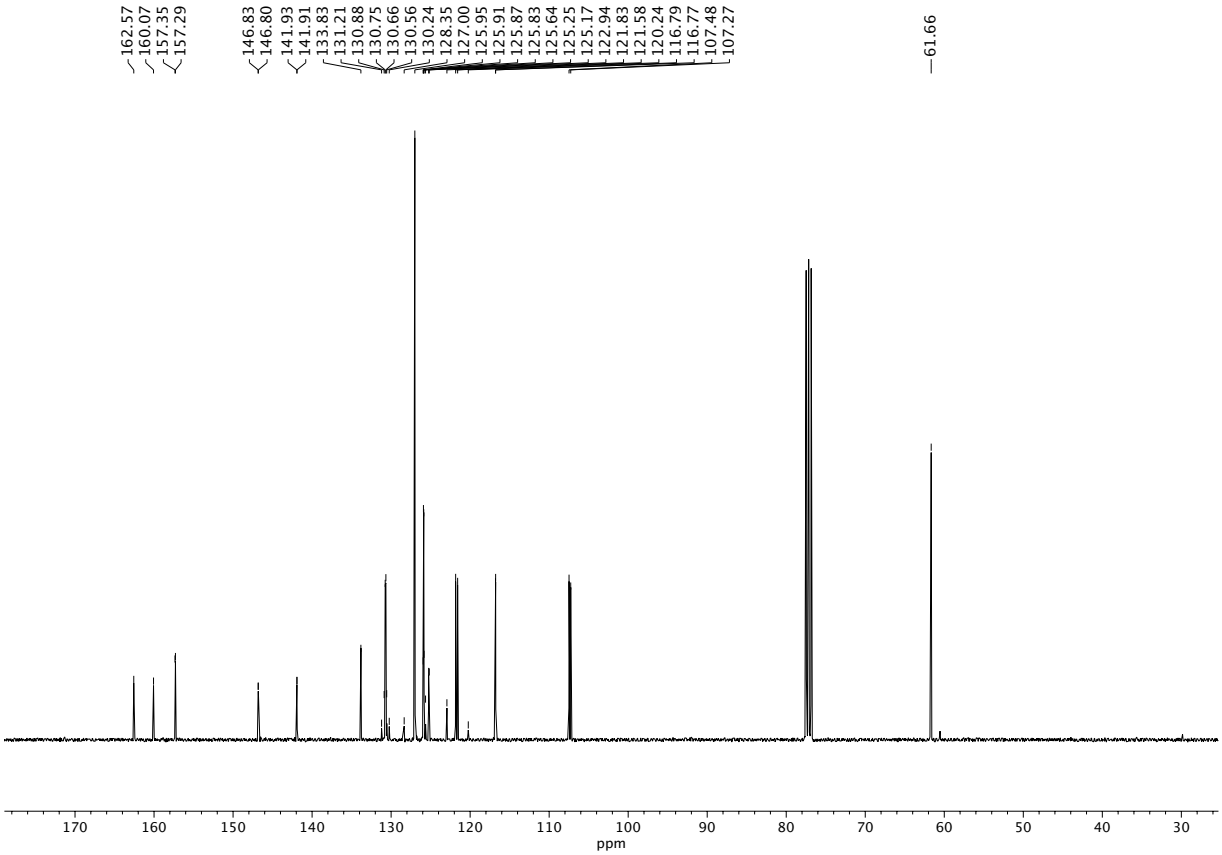
^{19}F NMR (282 MHz, $CDCl_3$) of **9b**.



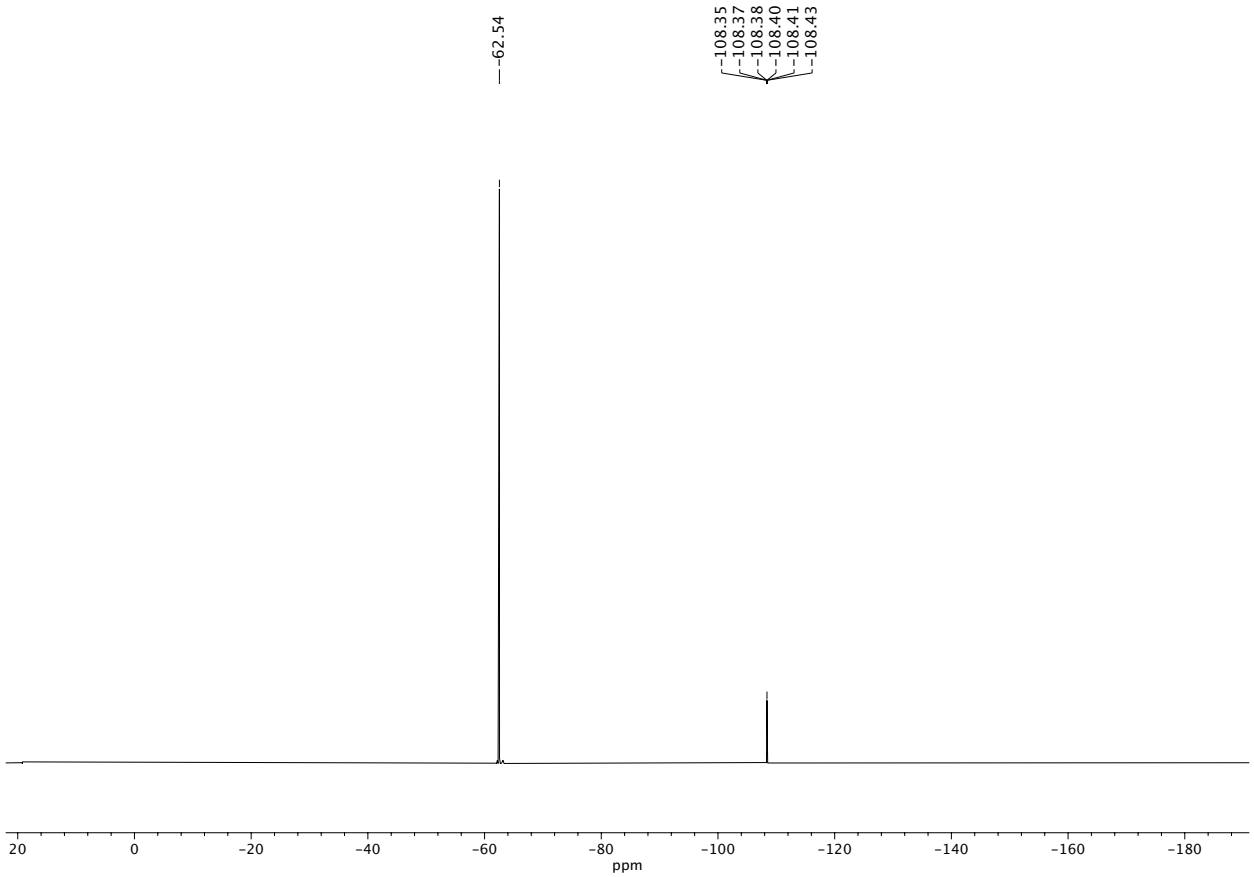
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9c**.



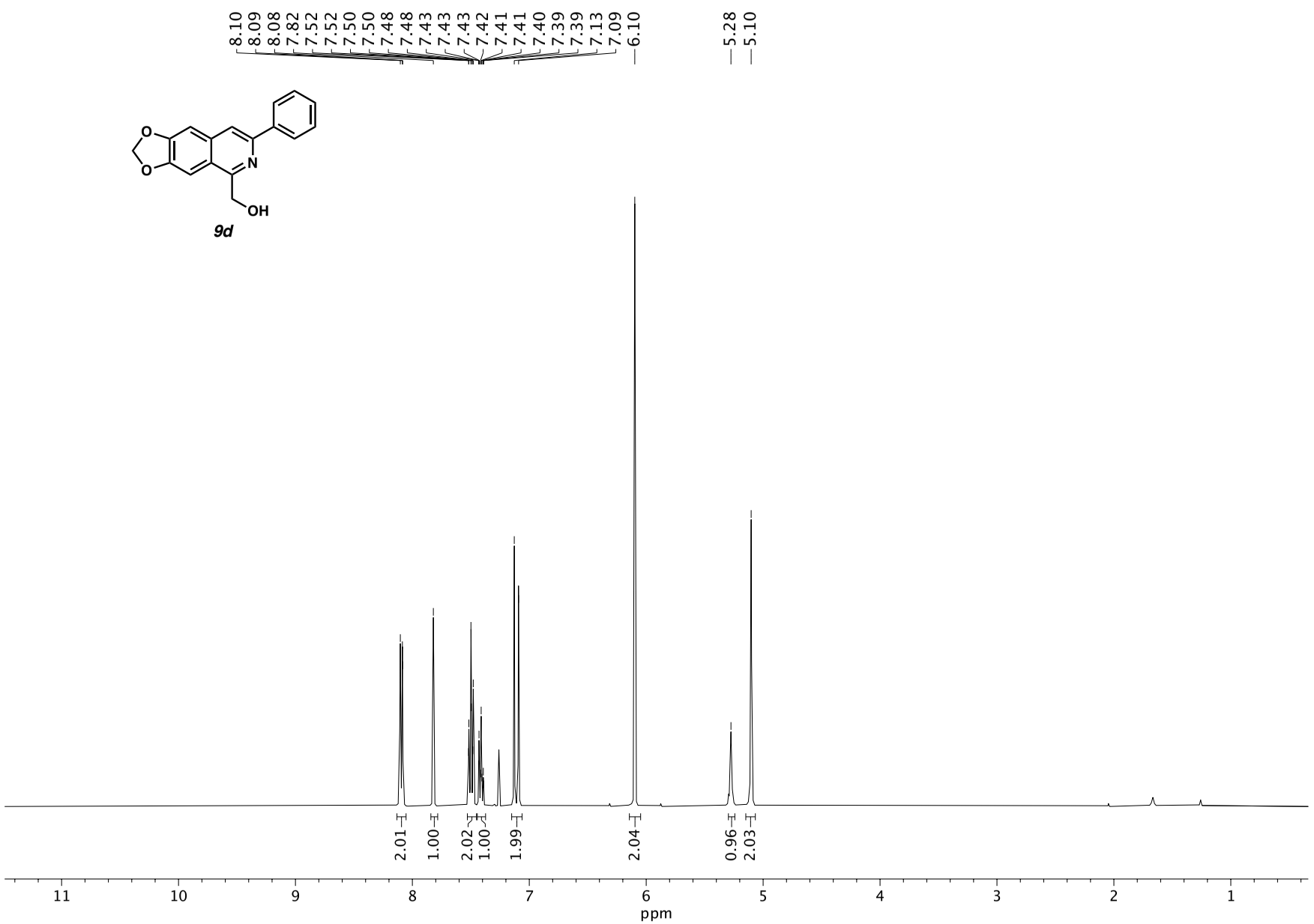
Infrared spectrum (Thin Film, NaCl) of compound **9c**.



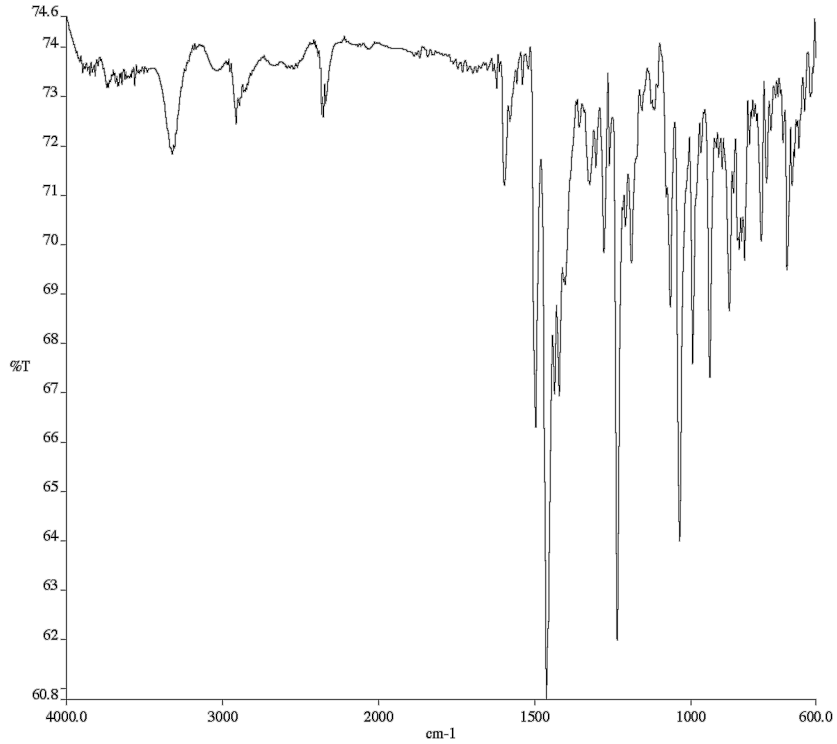
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9c**.



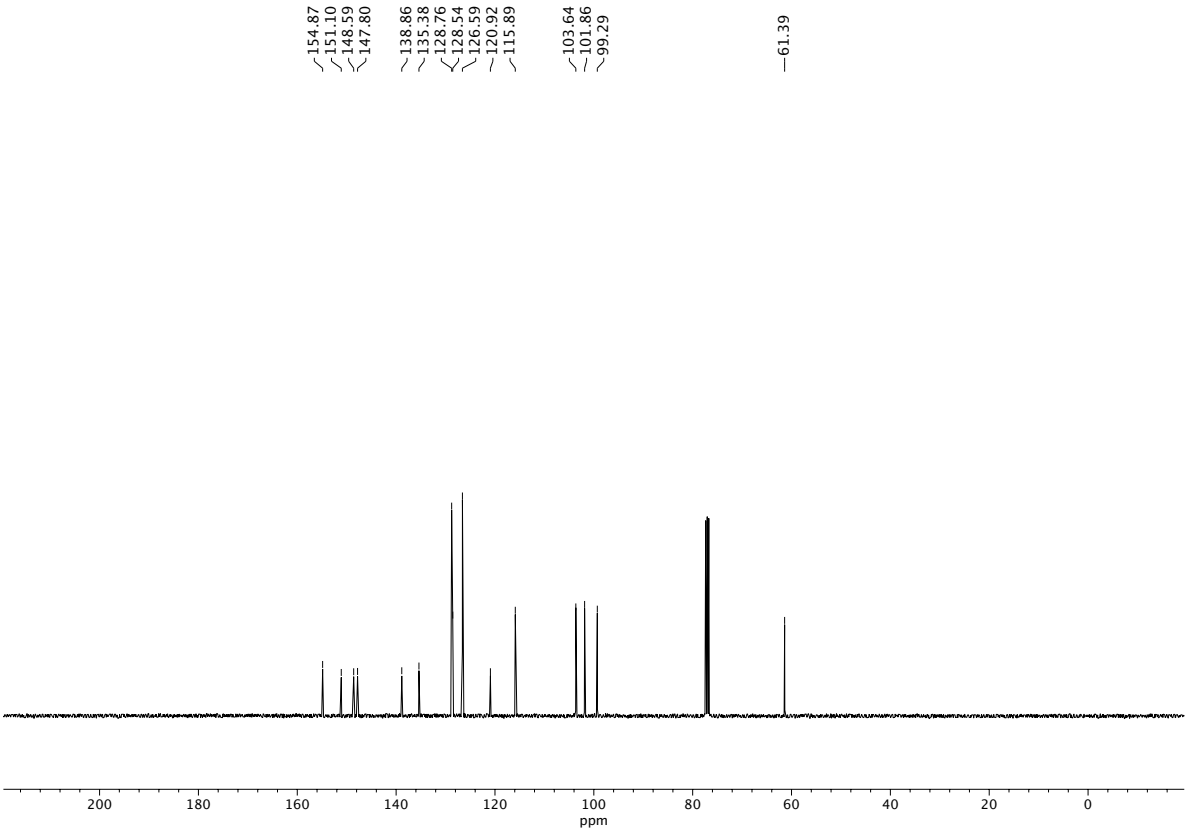
^{19}F NMR (282 MHz, $CDCl_3$) of **9c**.



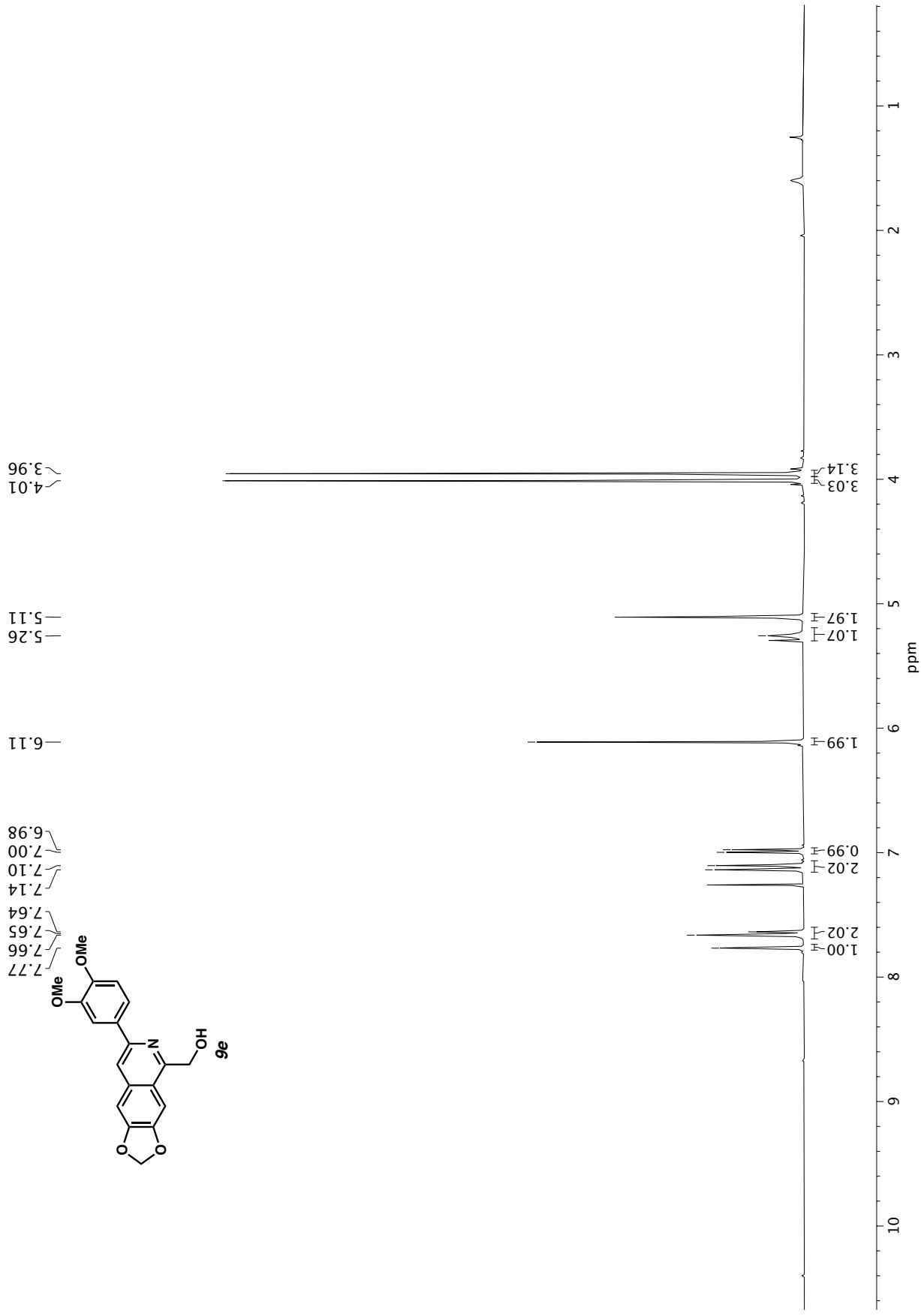
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9d**.



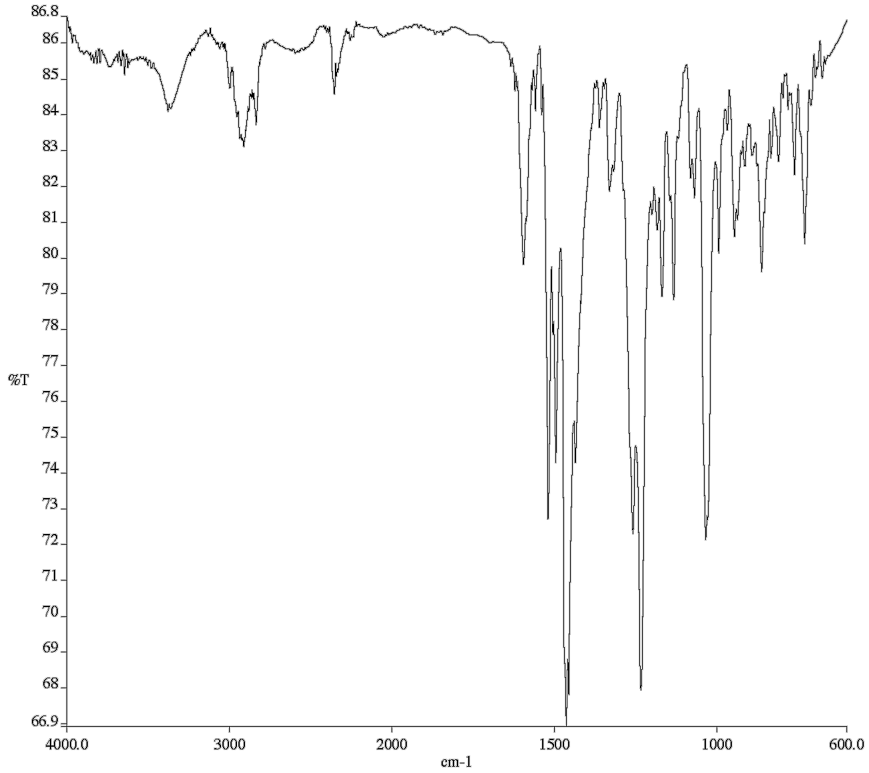
Infrared spectrum (Thin Film, NaCl) of compound **9d**.



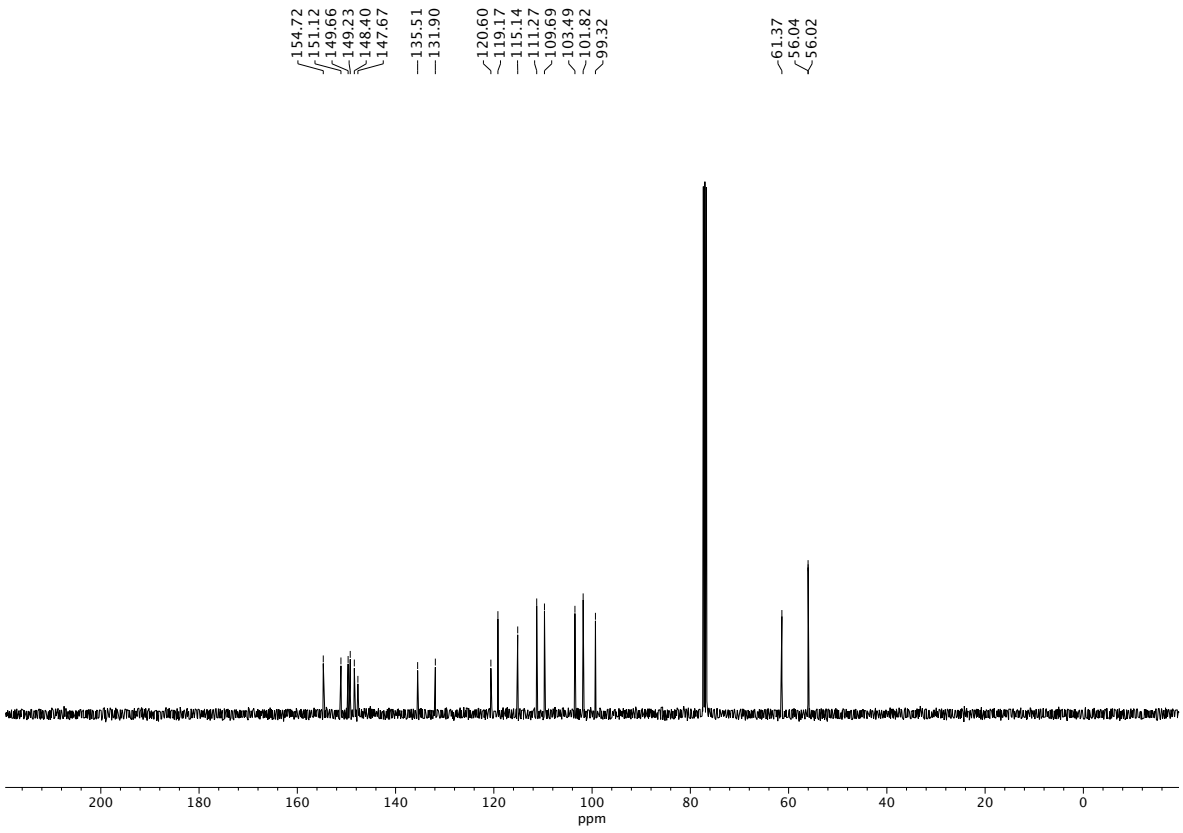
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9d**.



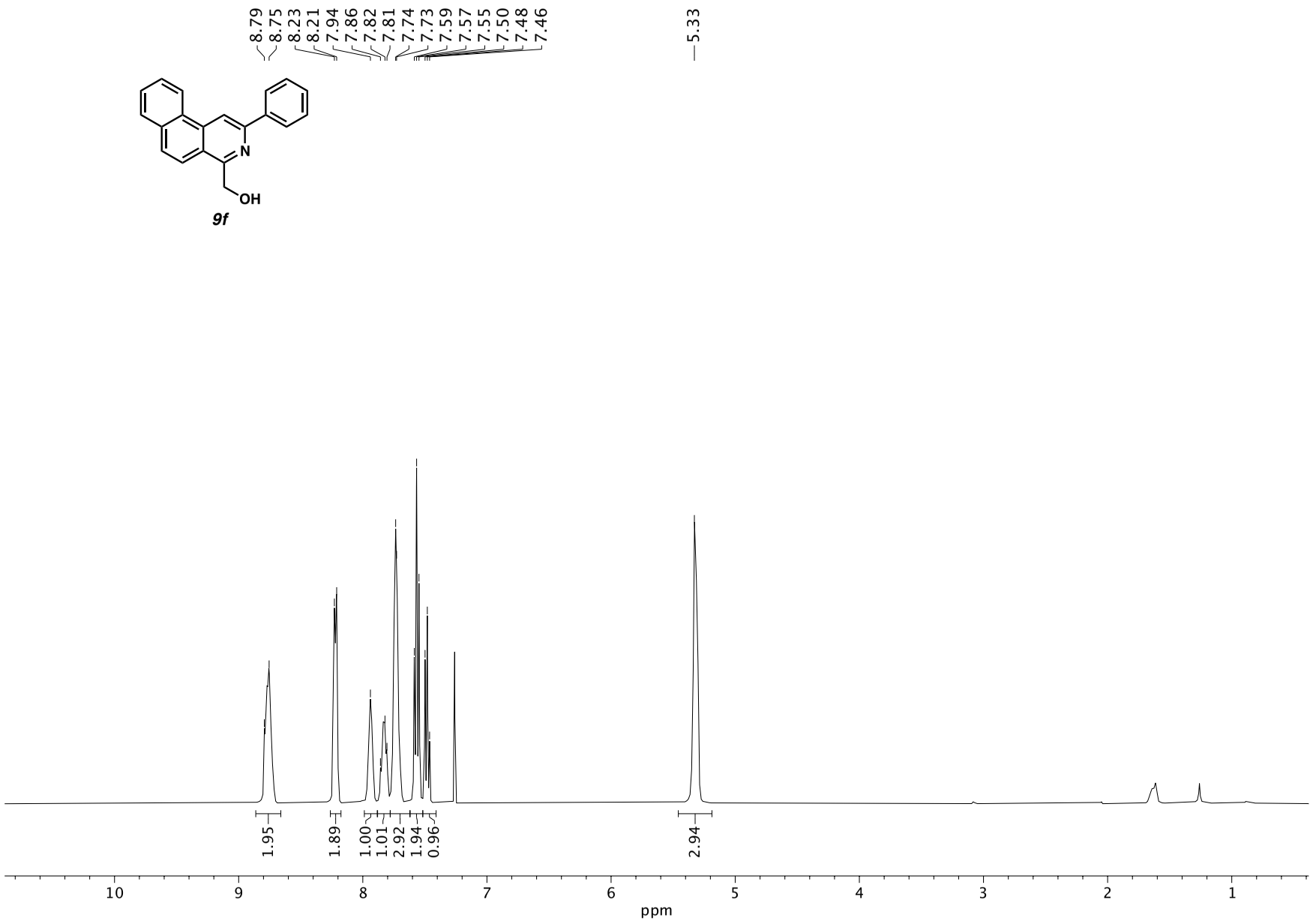
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9e**.



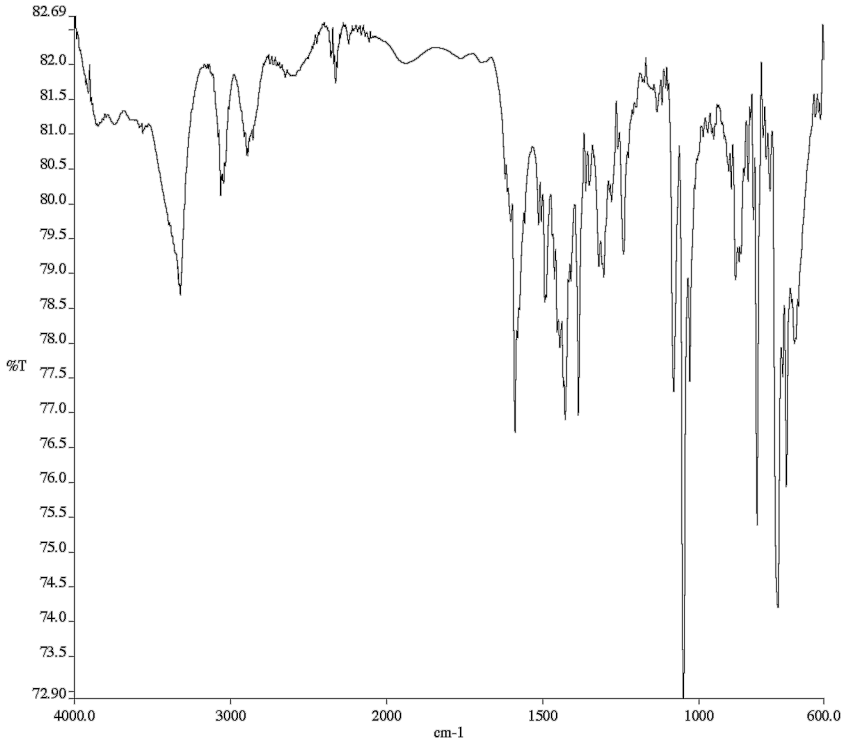
Infrared spectrum (Thin Film, NaCl) of compound **9e**.



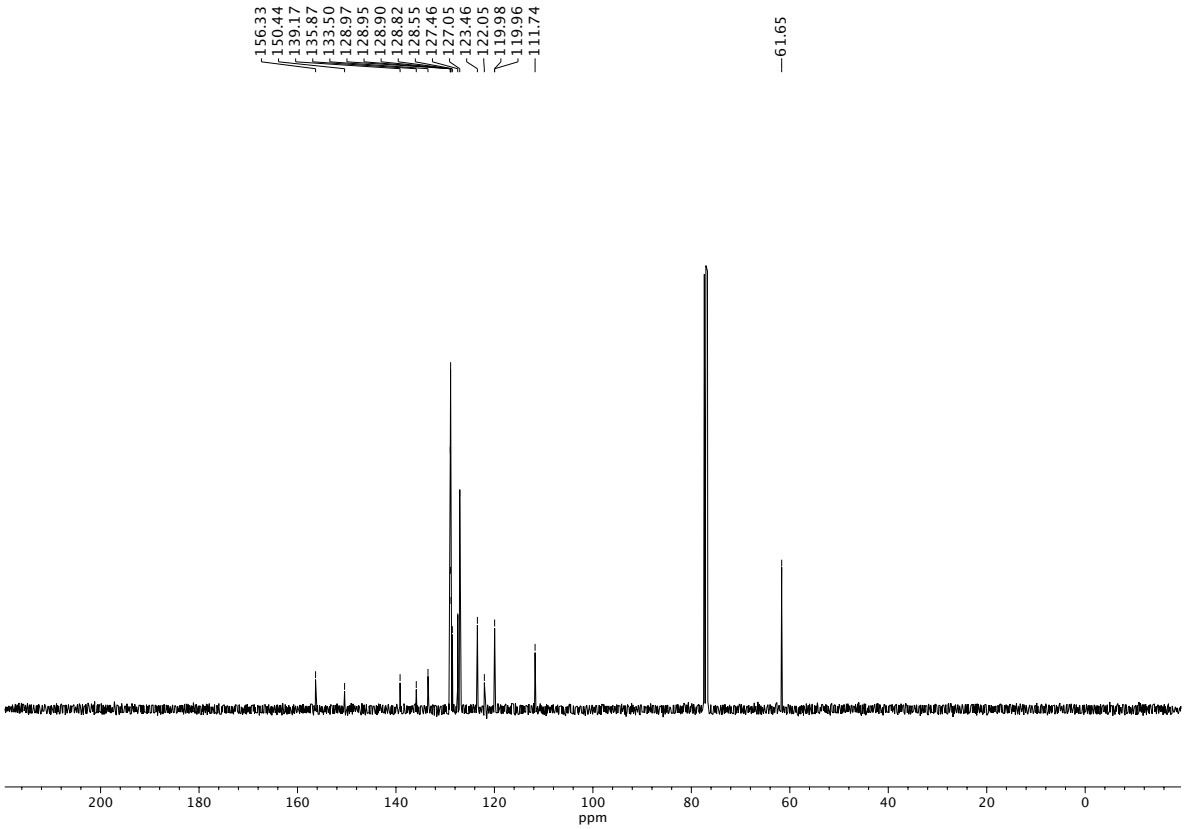
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9e**.



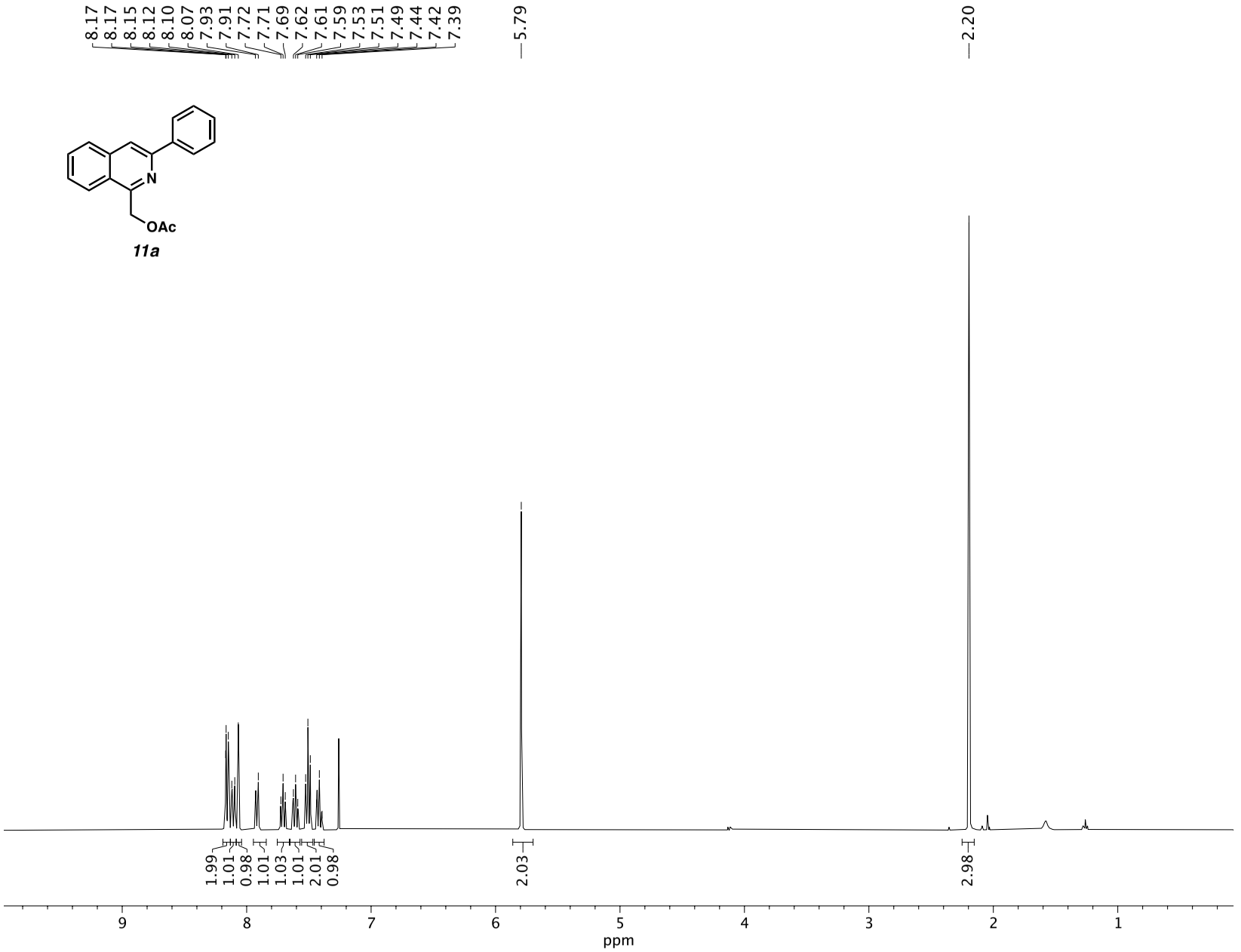
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9f**.



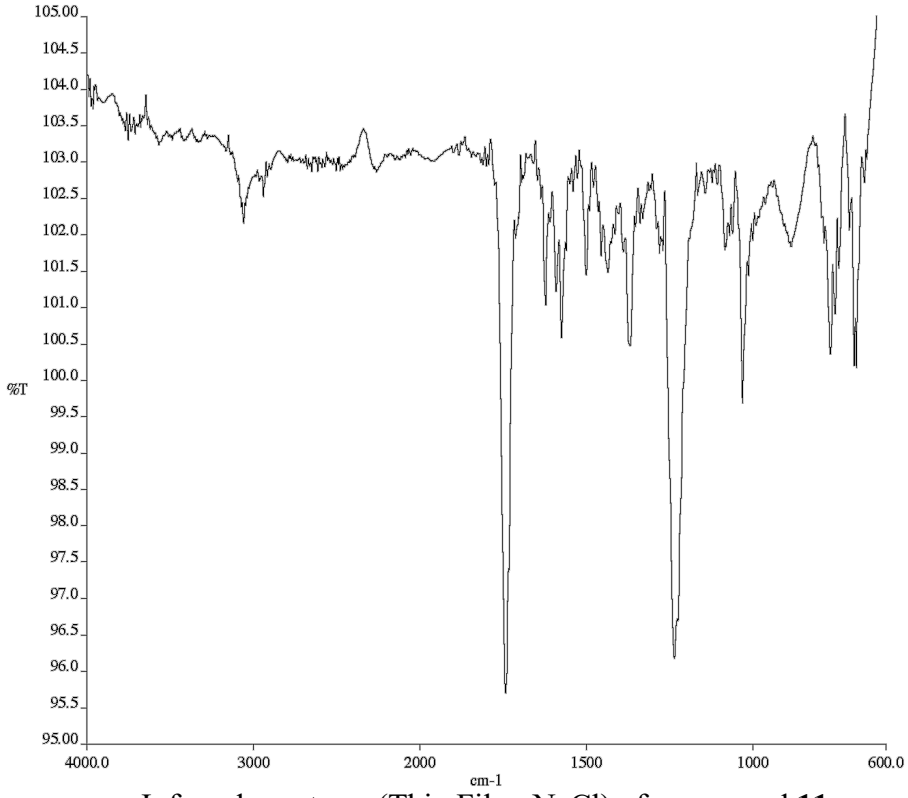
Infrared spectrum (Thin Film, NaCl) of compound **9f**.



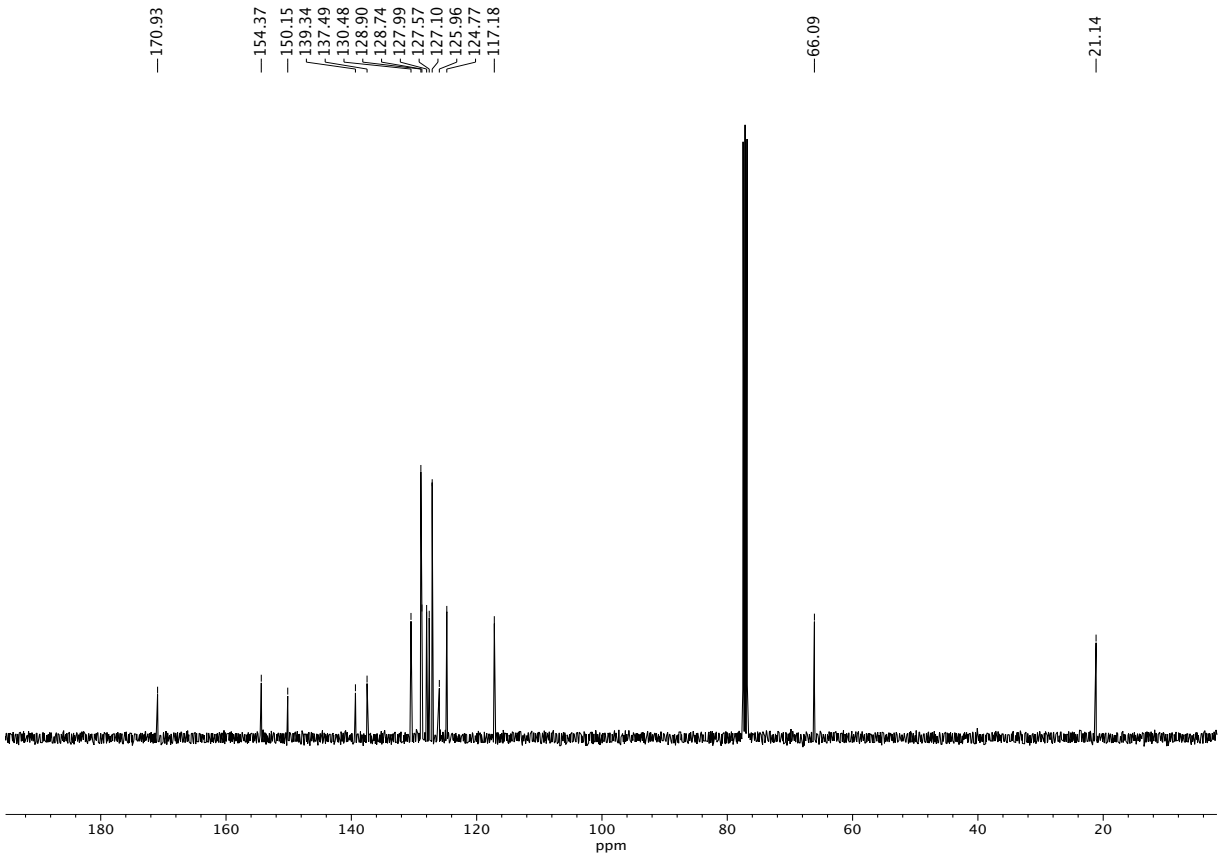
^{13}C NMR (100 MHz, $CDCl_3$) of compound **9f**.



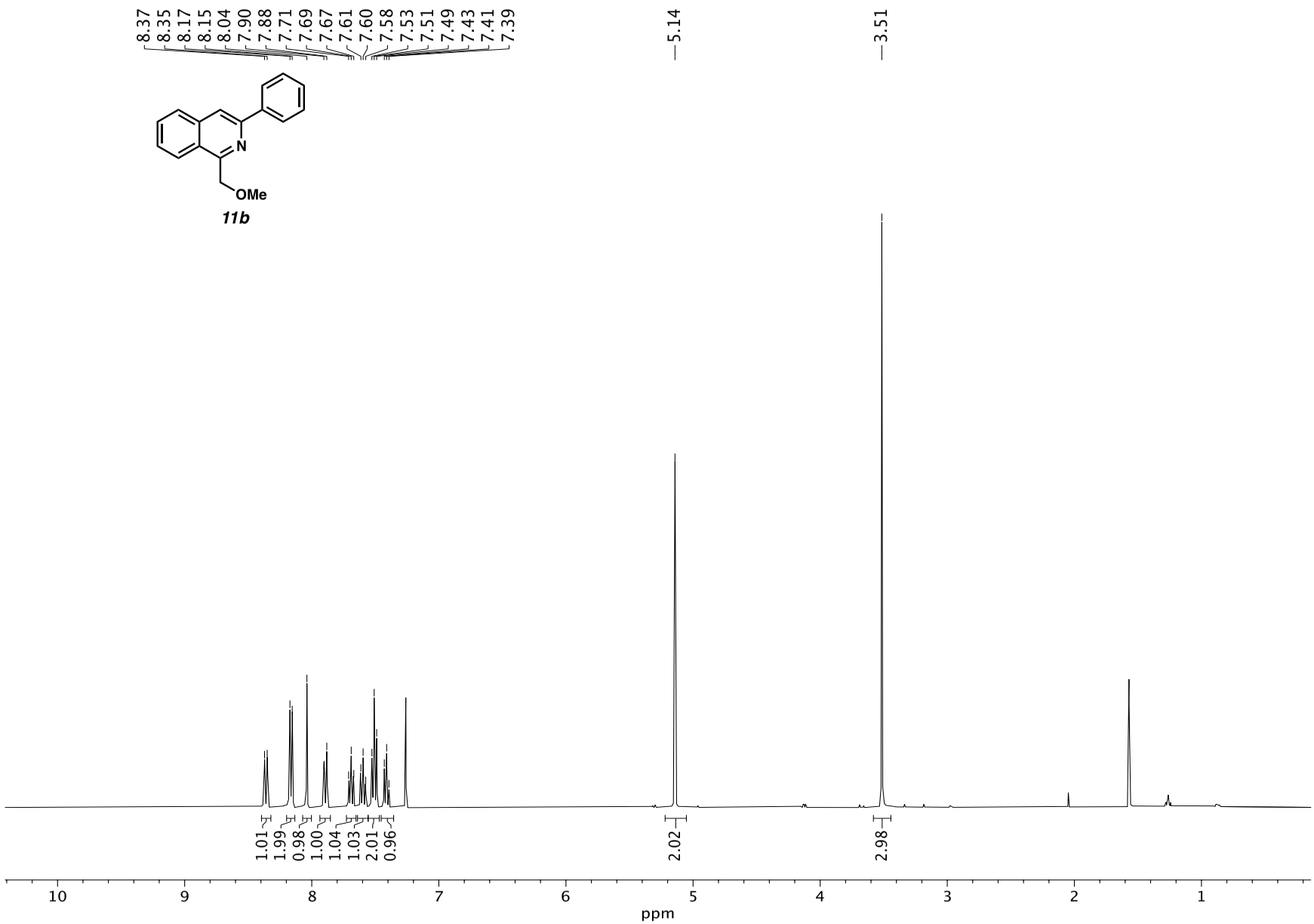
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11a.**



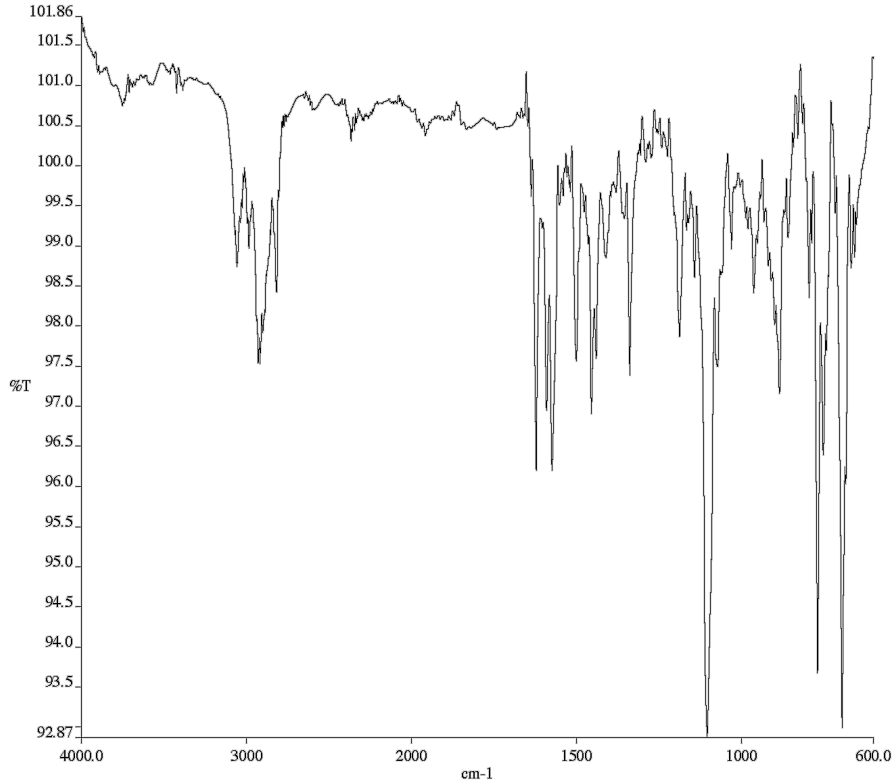
Infrared spectrum (Thin Film, NaCl) of compound **11a**.



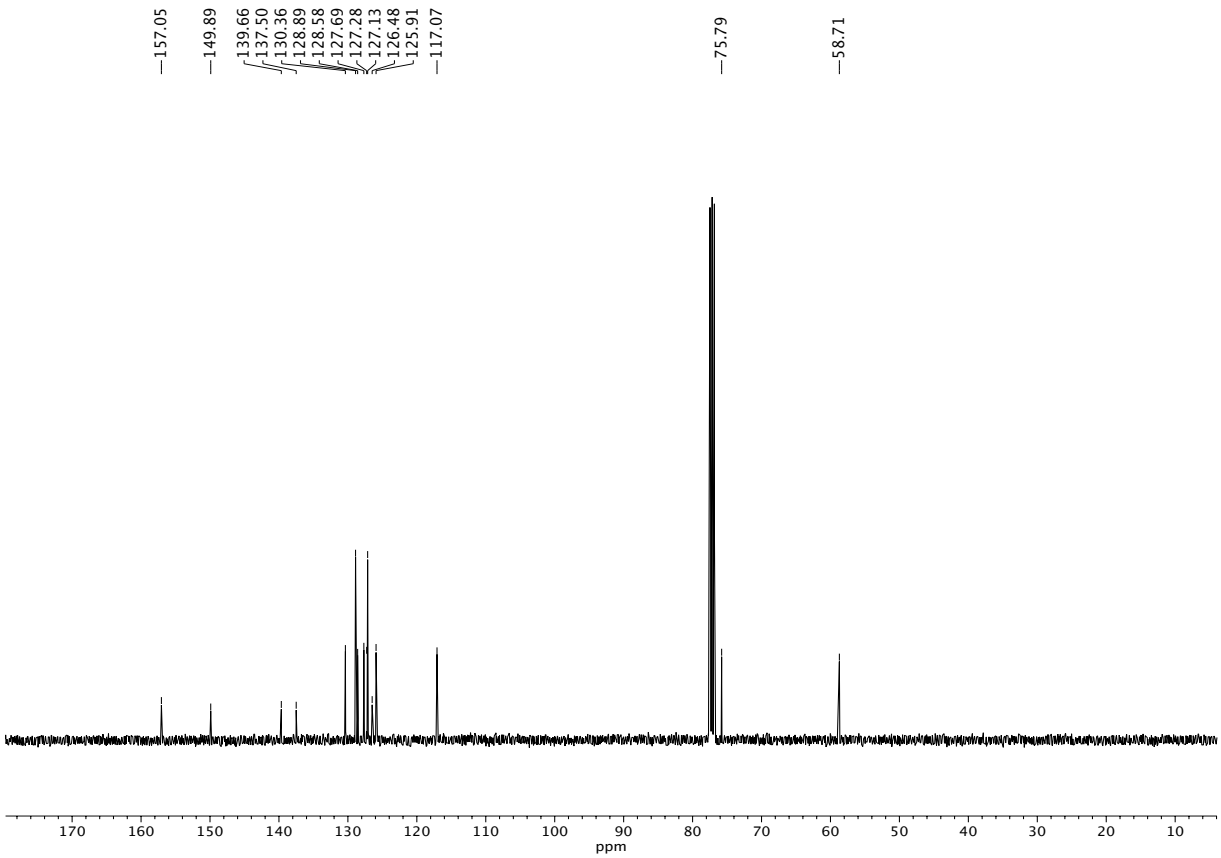
^{13}C NMR (100 MHz, $CDCl_3$) of compound **11a**.



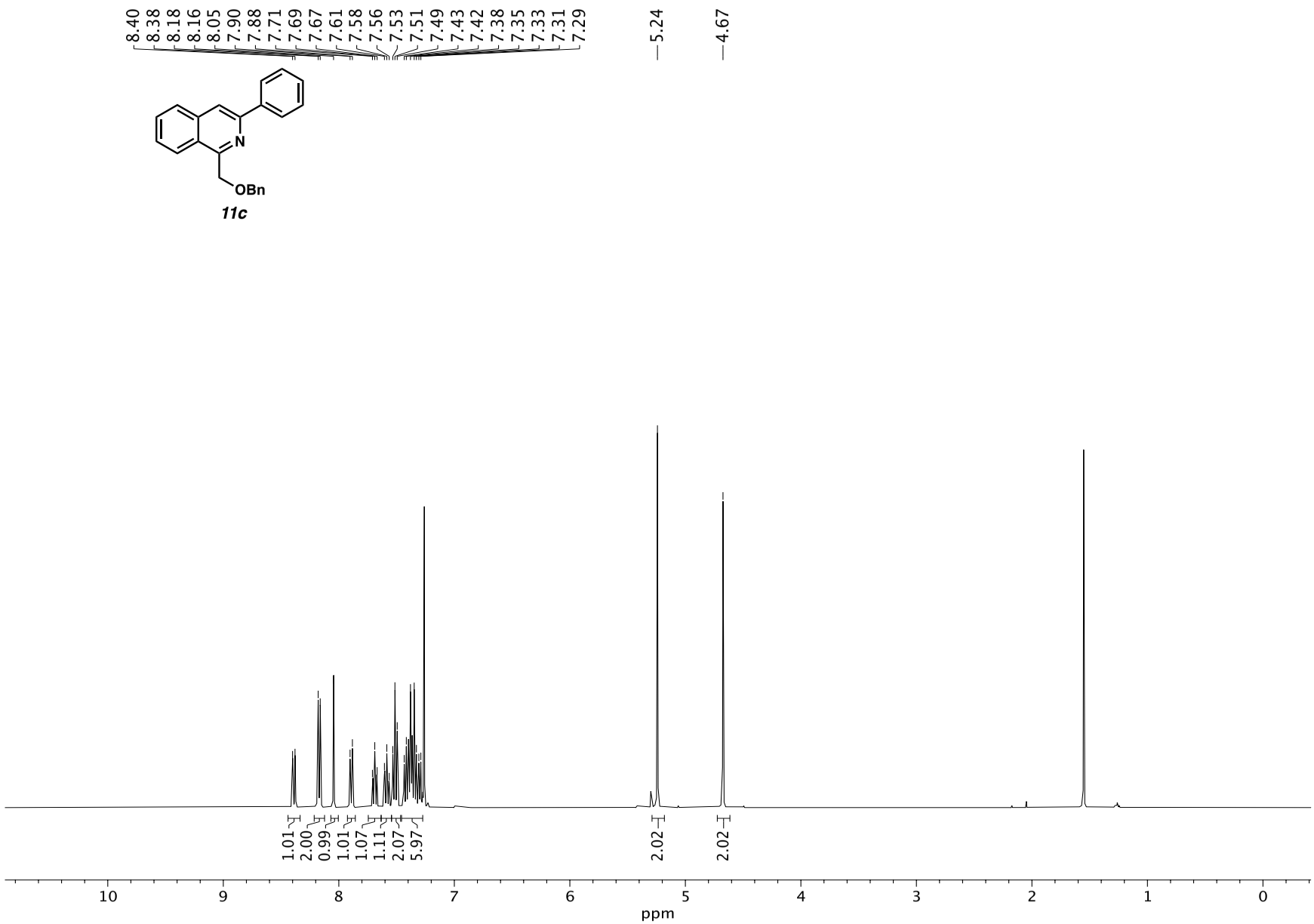
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11b**.



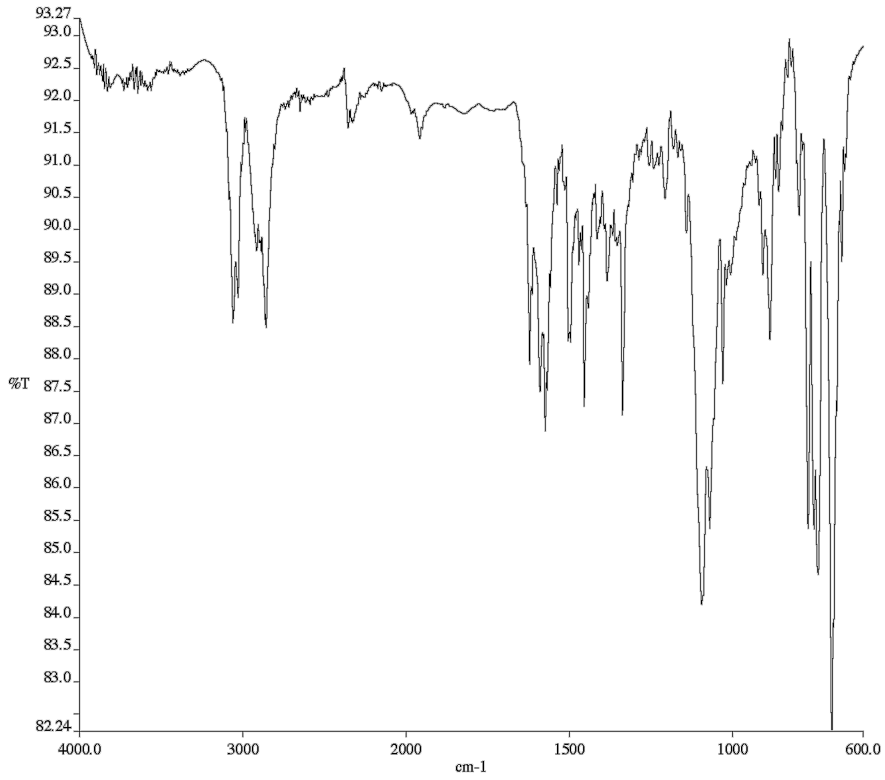
Infrared spectrum (Thin Film, NaCl) of compound **11b**.



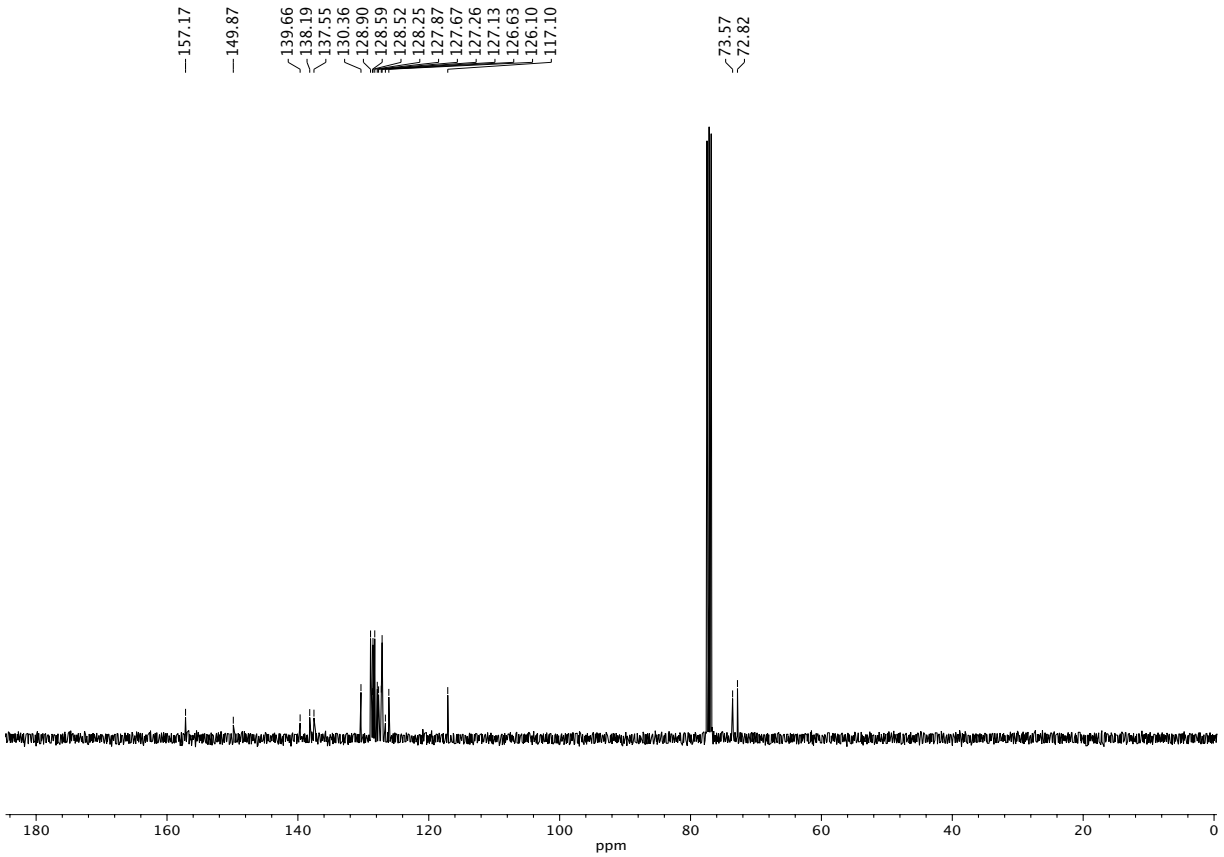
^{13}C NMR (100 MHz, $CDCl_3$) of compound **11b**.



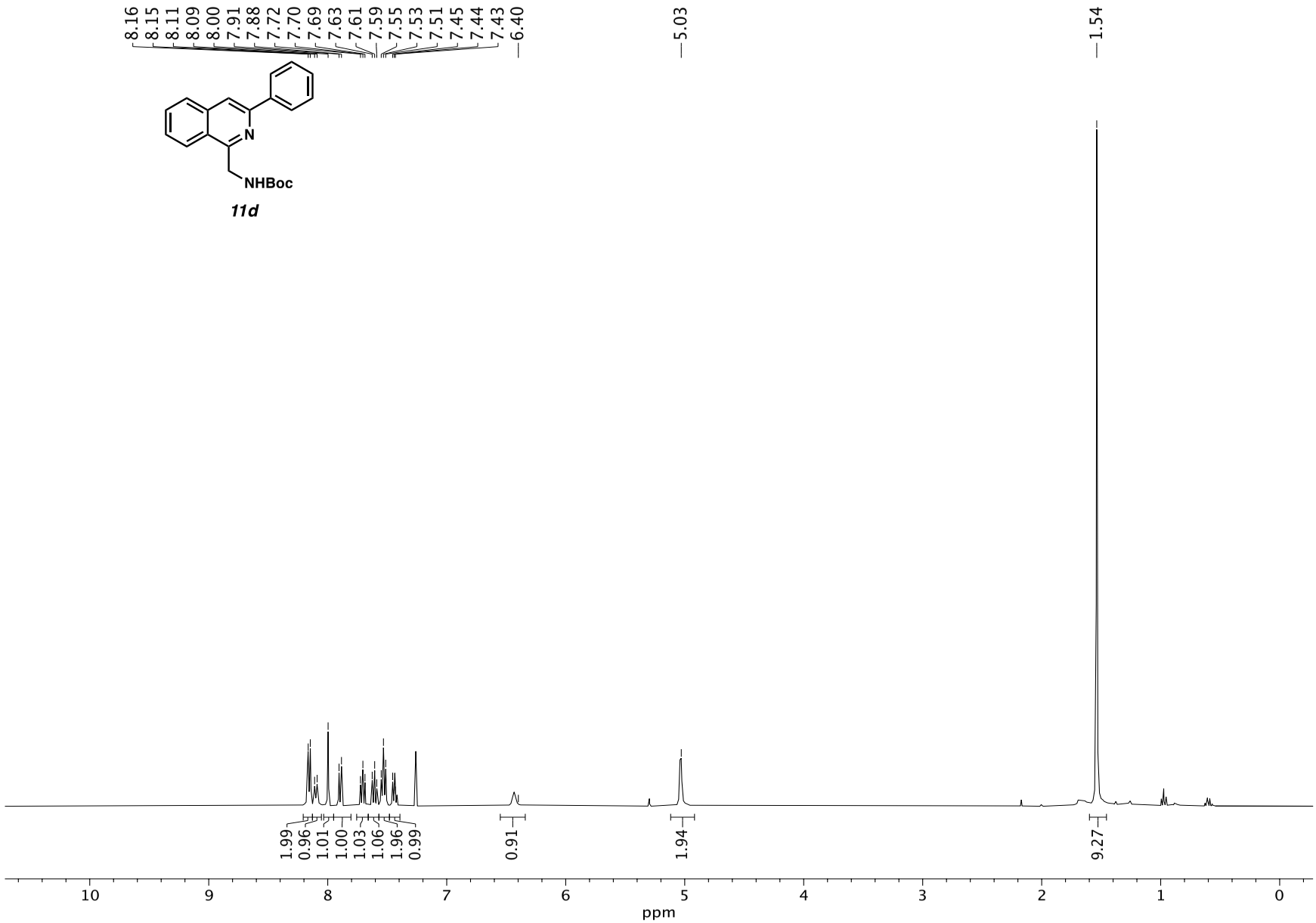
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11c**.



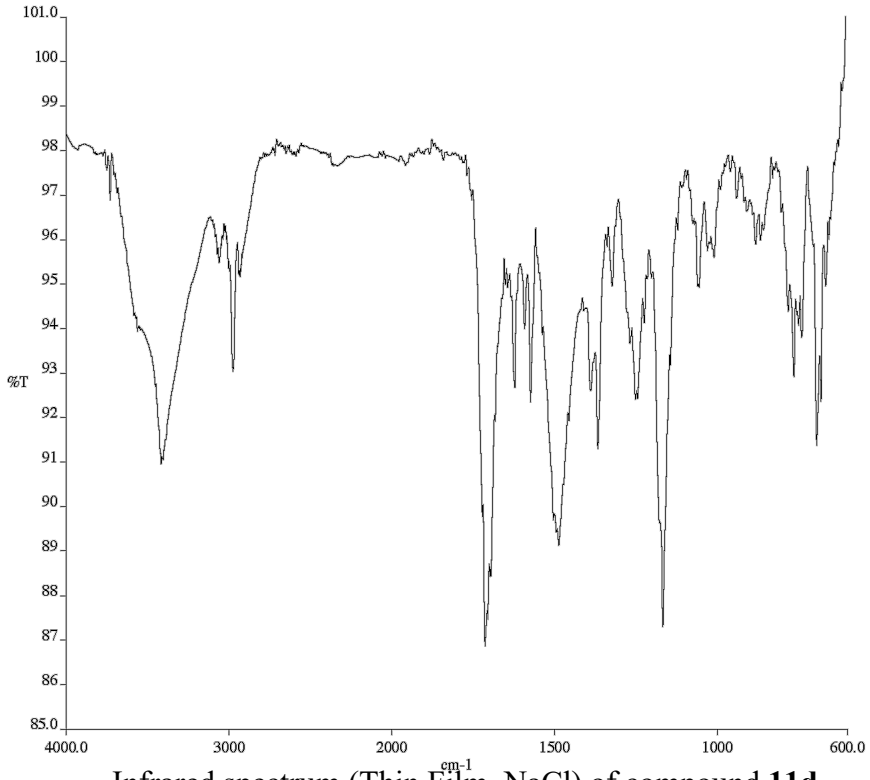
Infrared spectrum (Thin Film, NaCl) of compound **11c**.



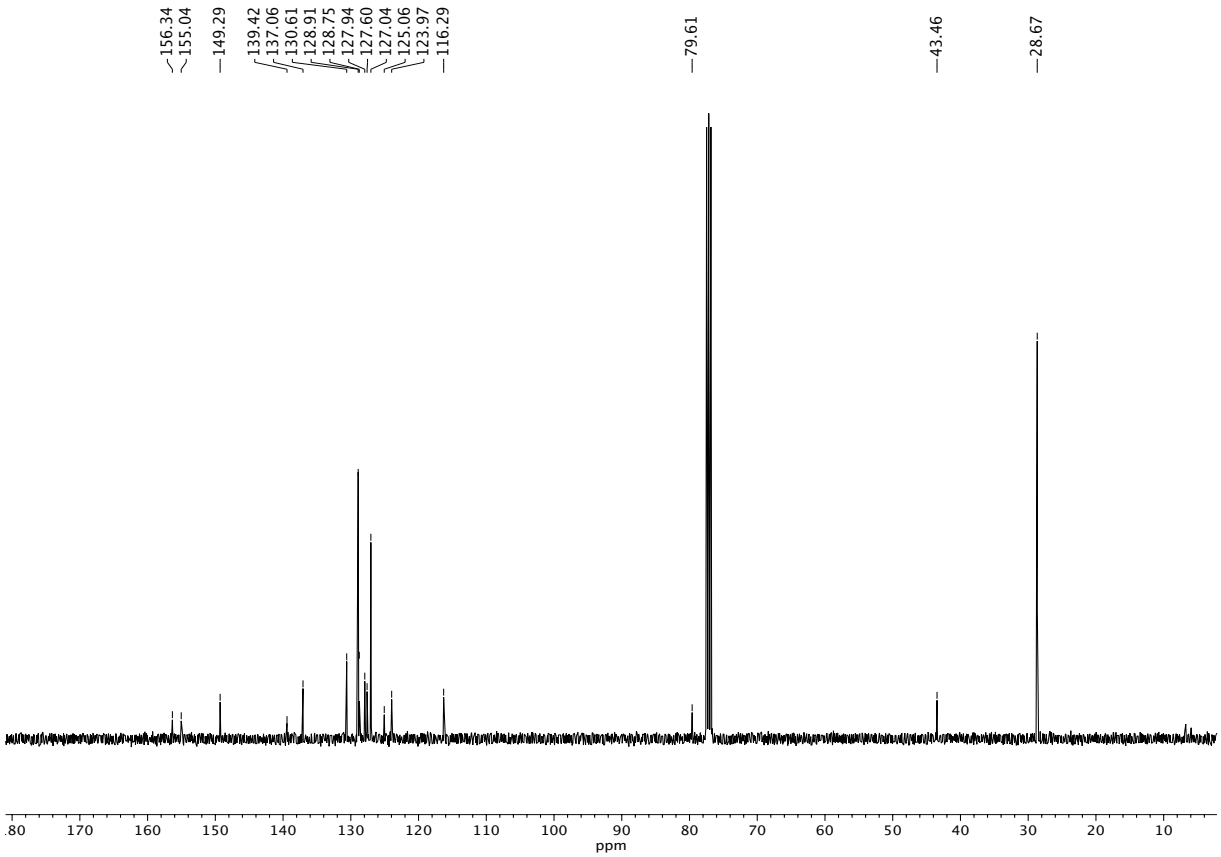
^{13}C NMR (100 MHz, $CDCl_3$) of compound **11c**.



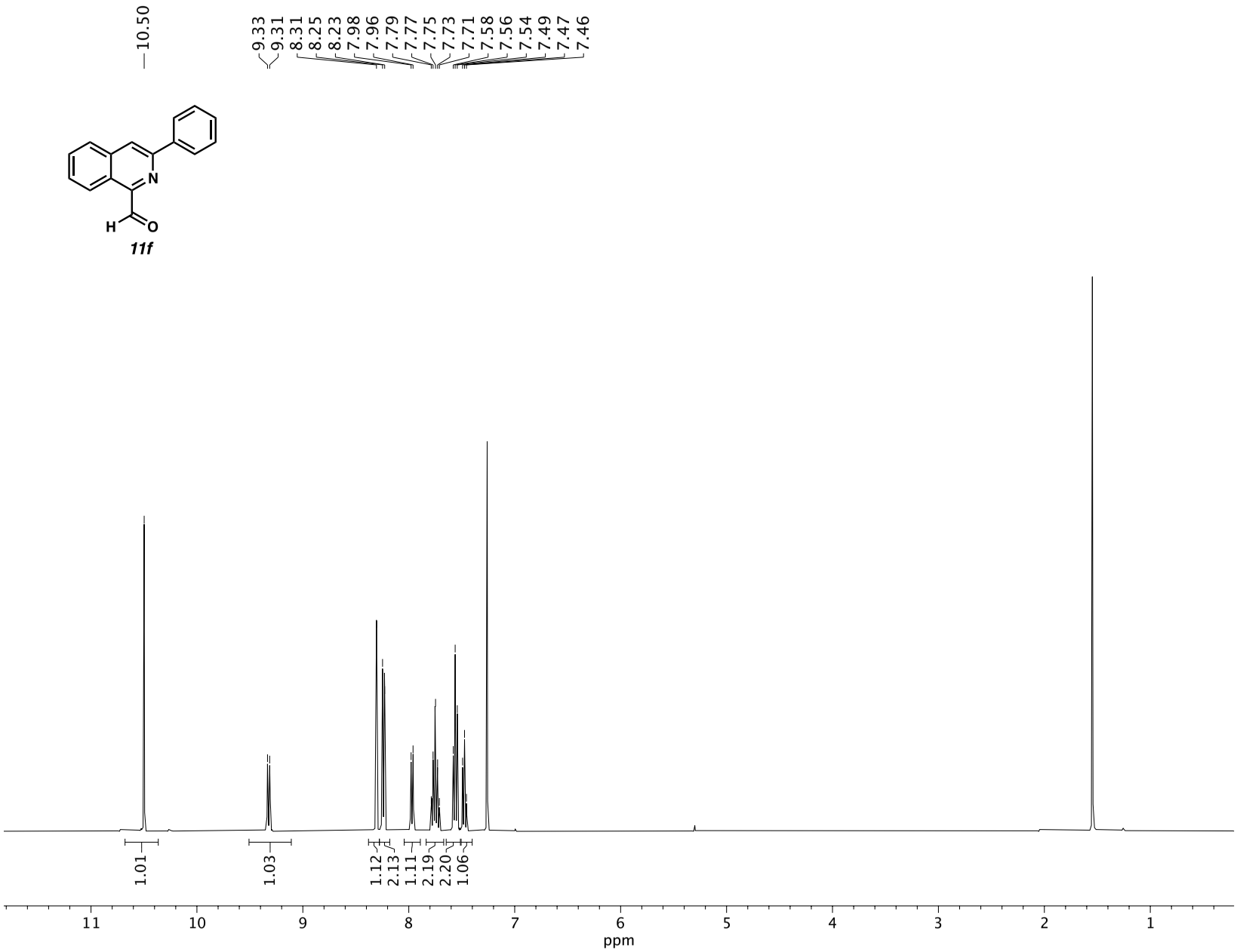
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11d**.



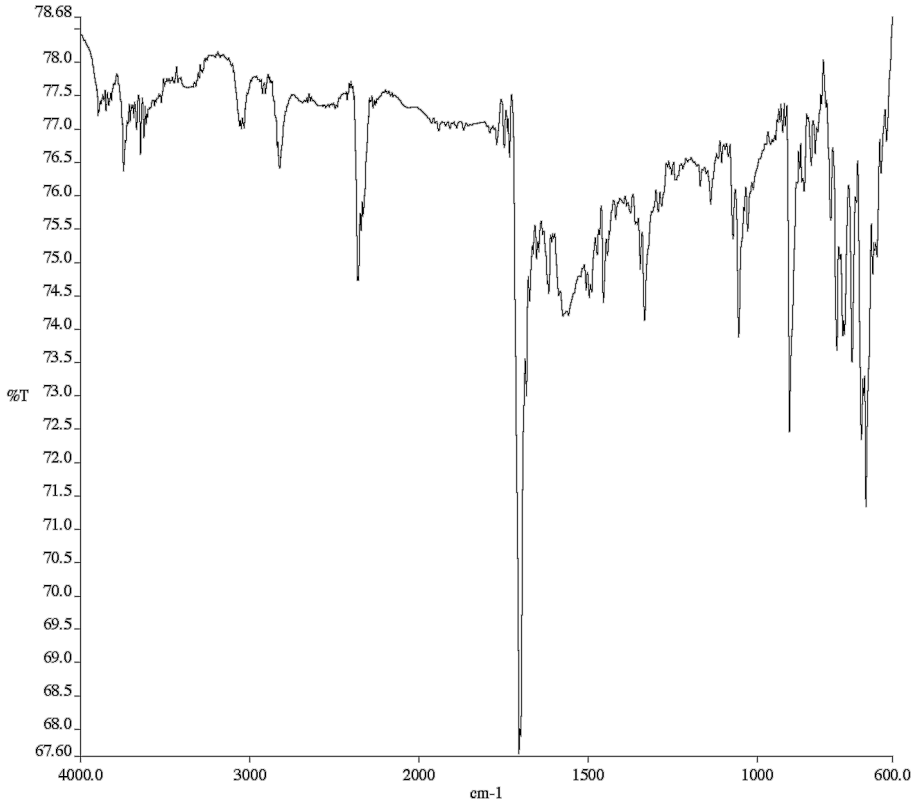
Infrared spectrum (Thin Film, NaCl) of compound **11d**.



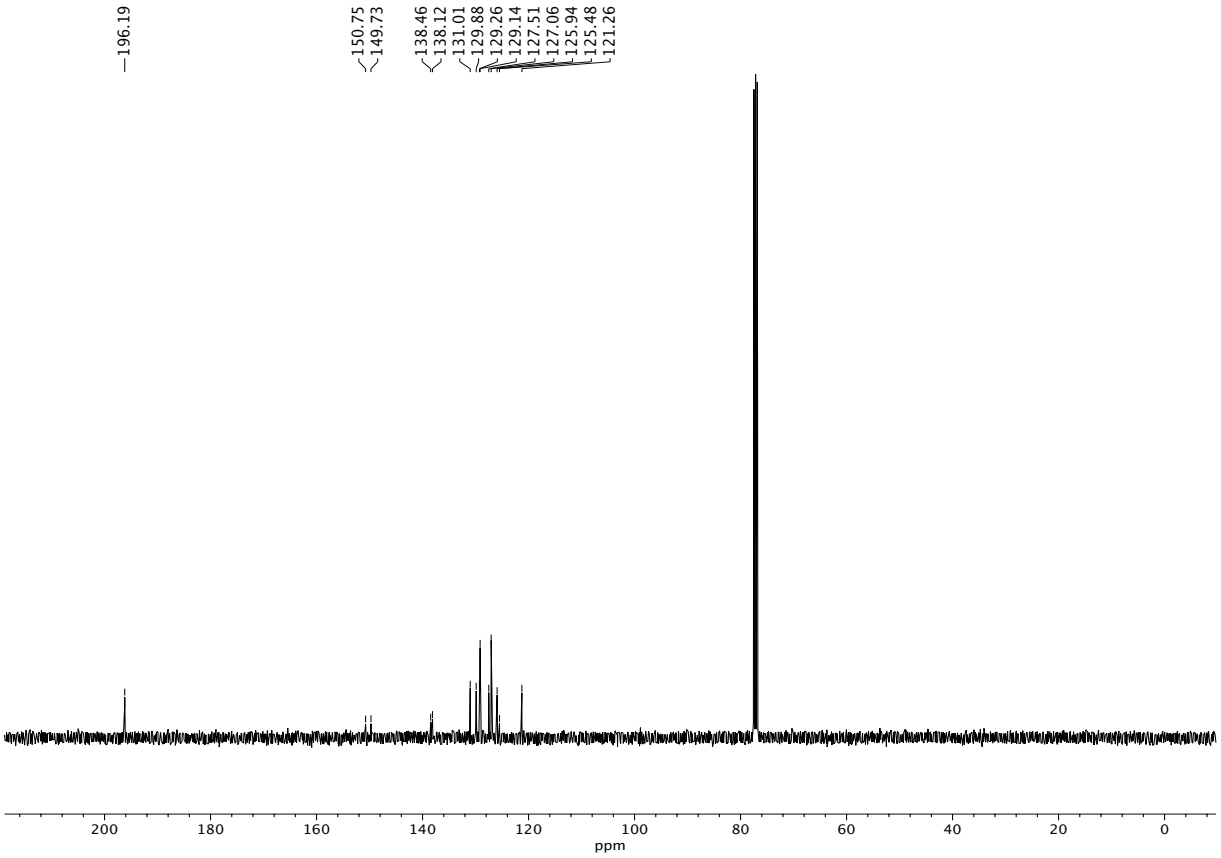
^{13}C NMR (100 MHz, $CDCl_3$) of compound **11d**.



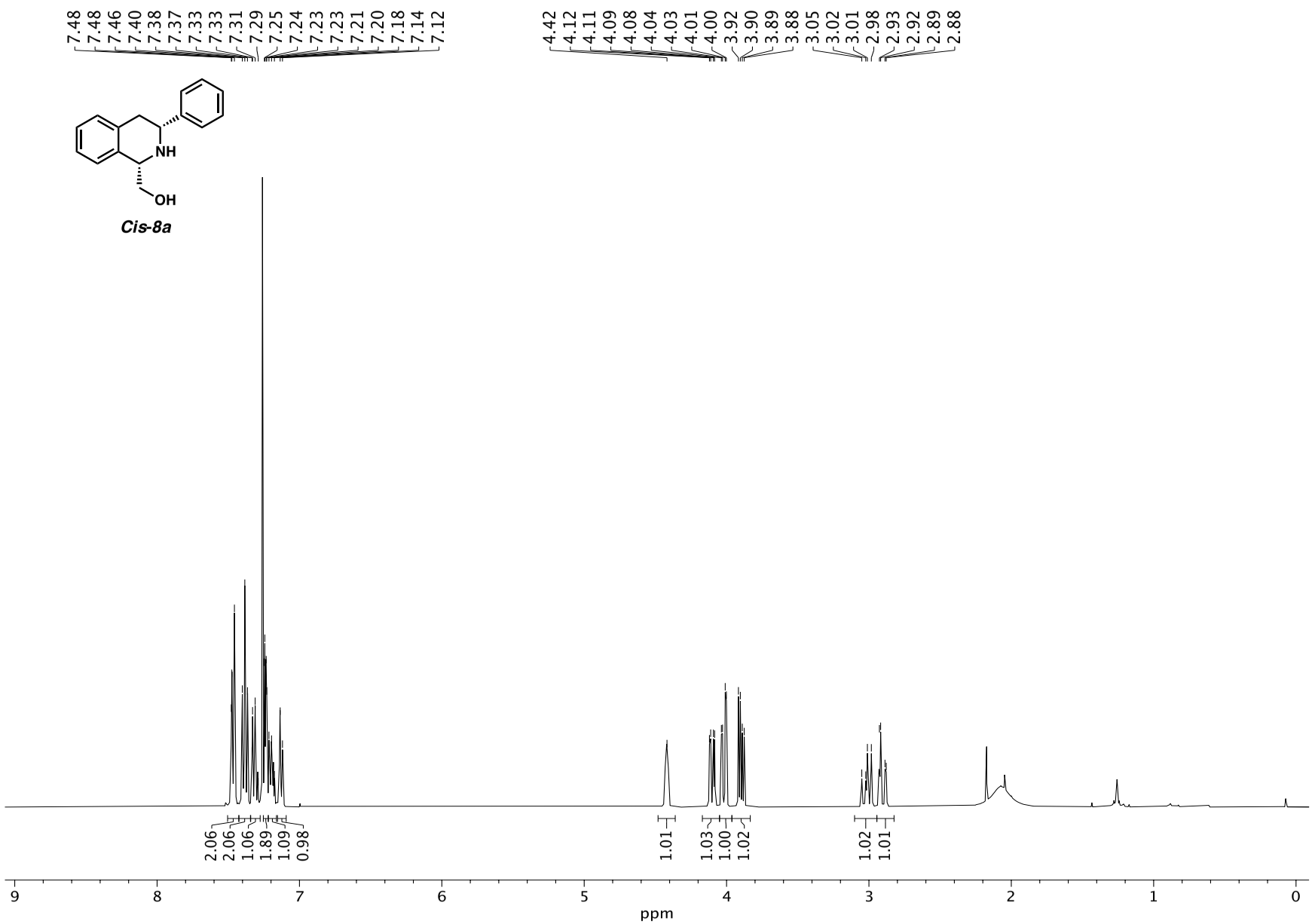
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11f**.



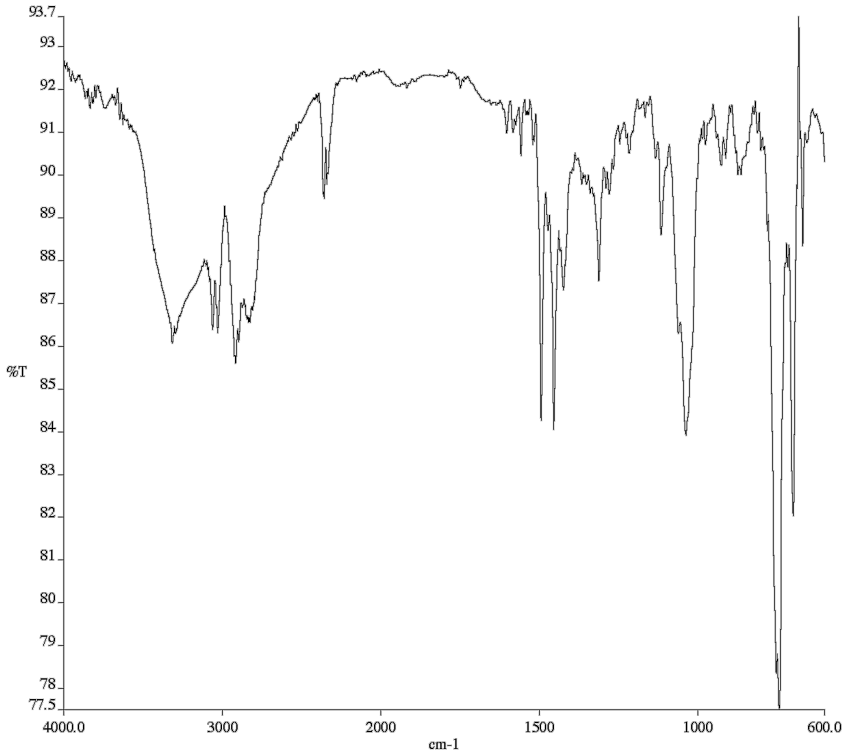
Infrared spectrum (Thin Film, NaCl) of compound **11f**.



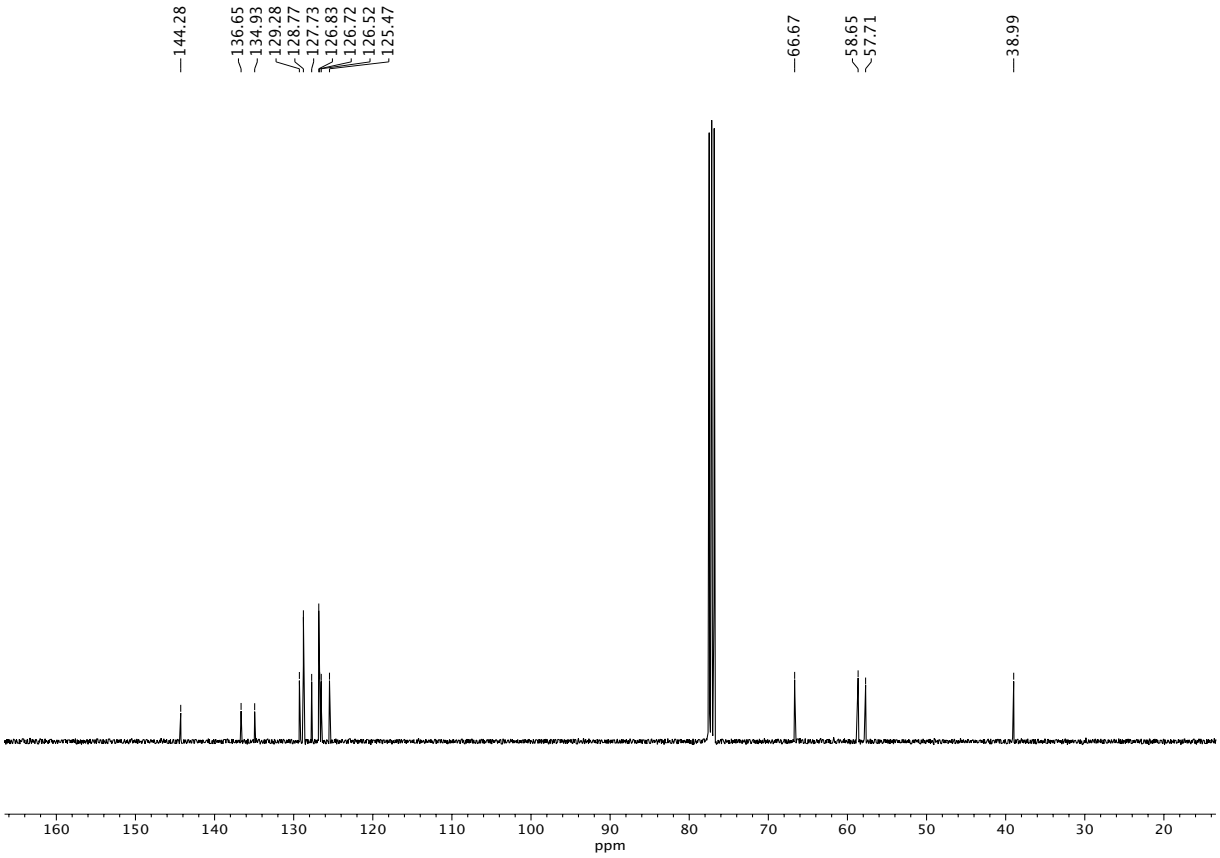
^{13}C NMR (100 MHz, $CDCl_3$) of compound **11f.**



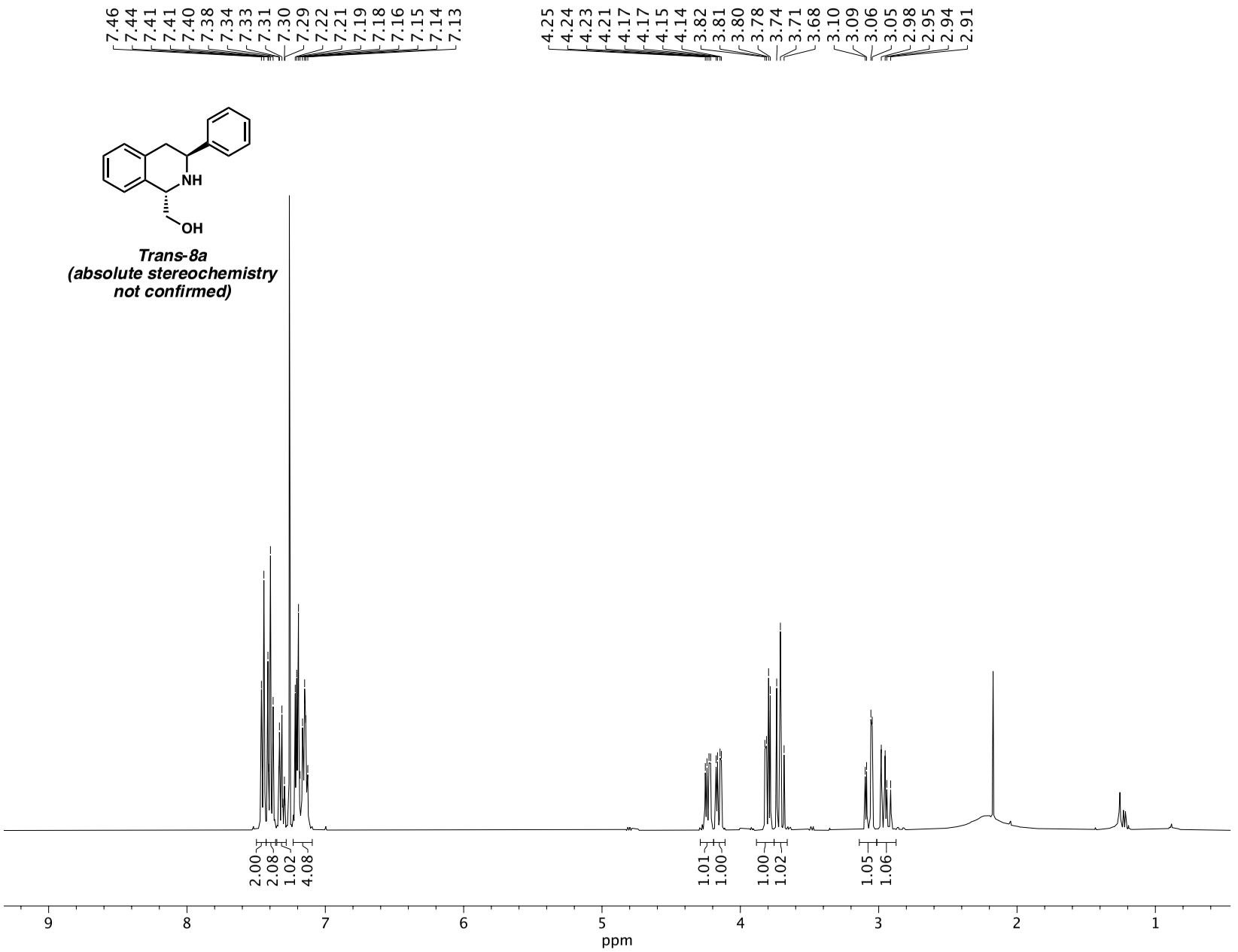
^{1}H NMR (400 MHz, $CDCl_3$) of compound ***Cis*-8a**.



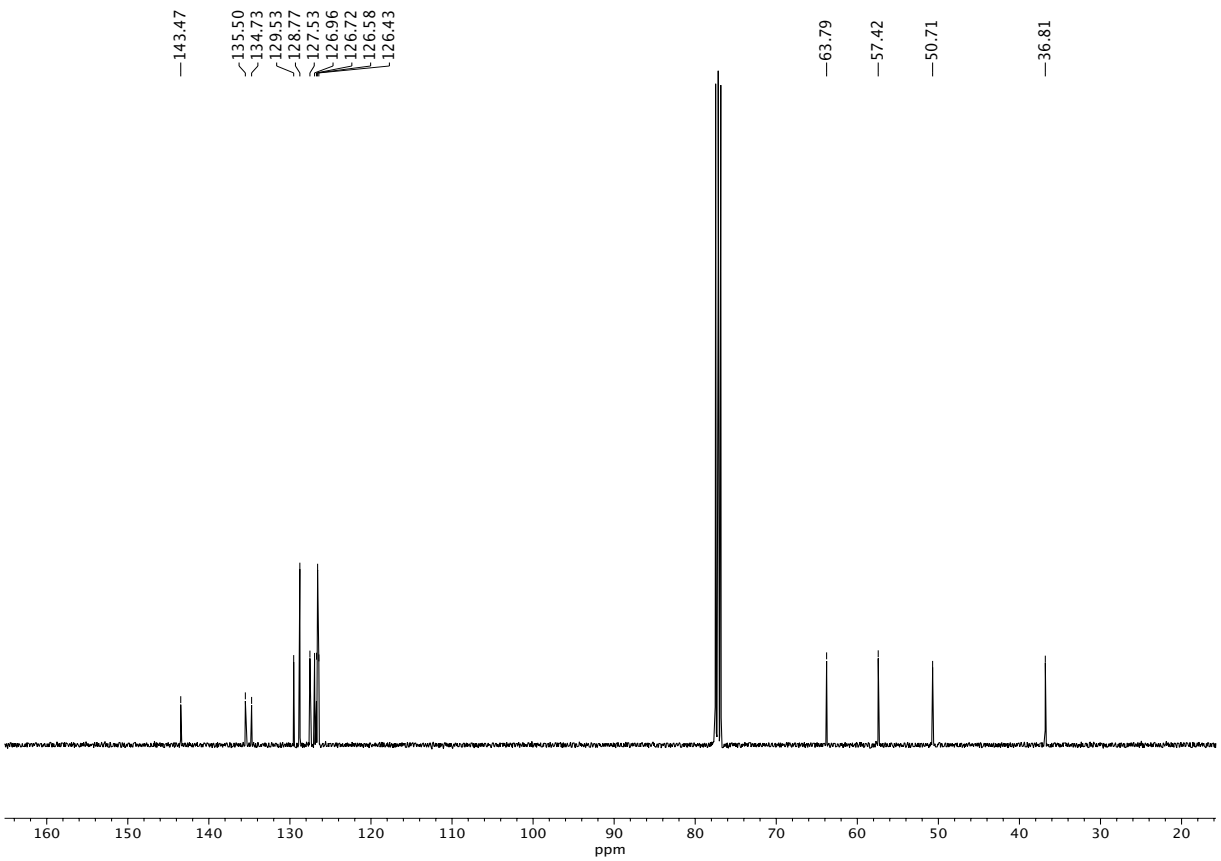
Infrared spectrum (Thin Film, NaCl) of compound **8a**.



^{13}C NMR (100 MHz, $CDCl_3$) of compound ***Cis*-8a**.

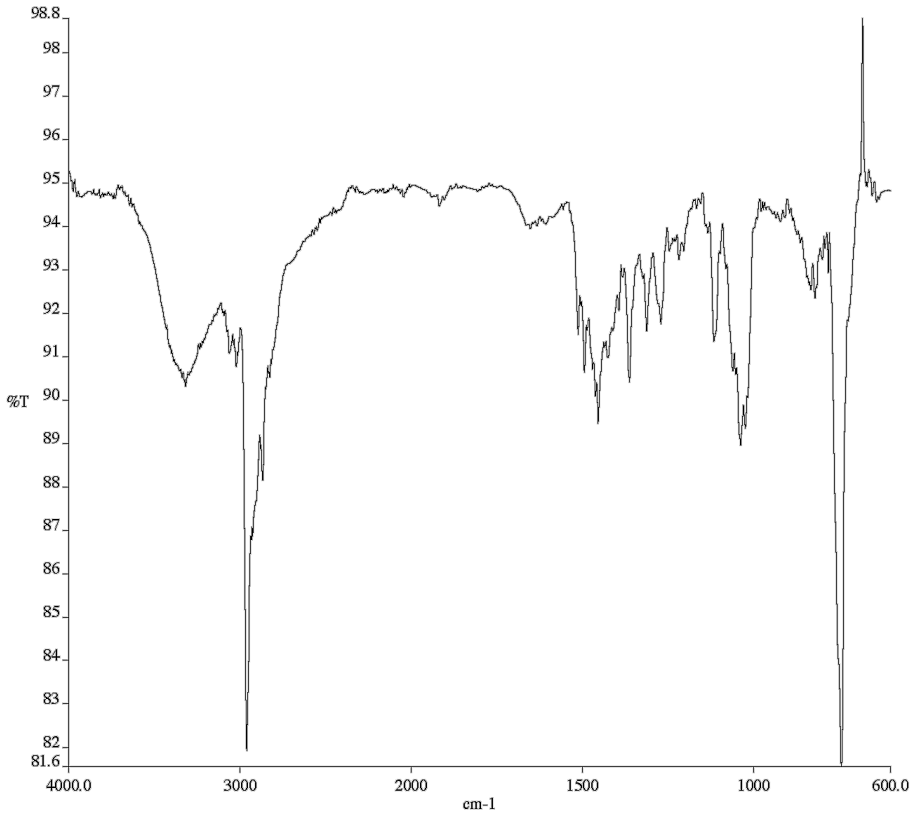


^{1}H NMR (400 MHz, $CDCl_3$) of compound ***Trans*-8a**.

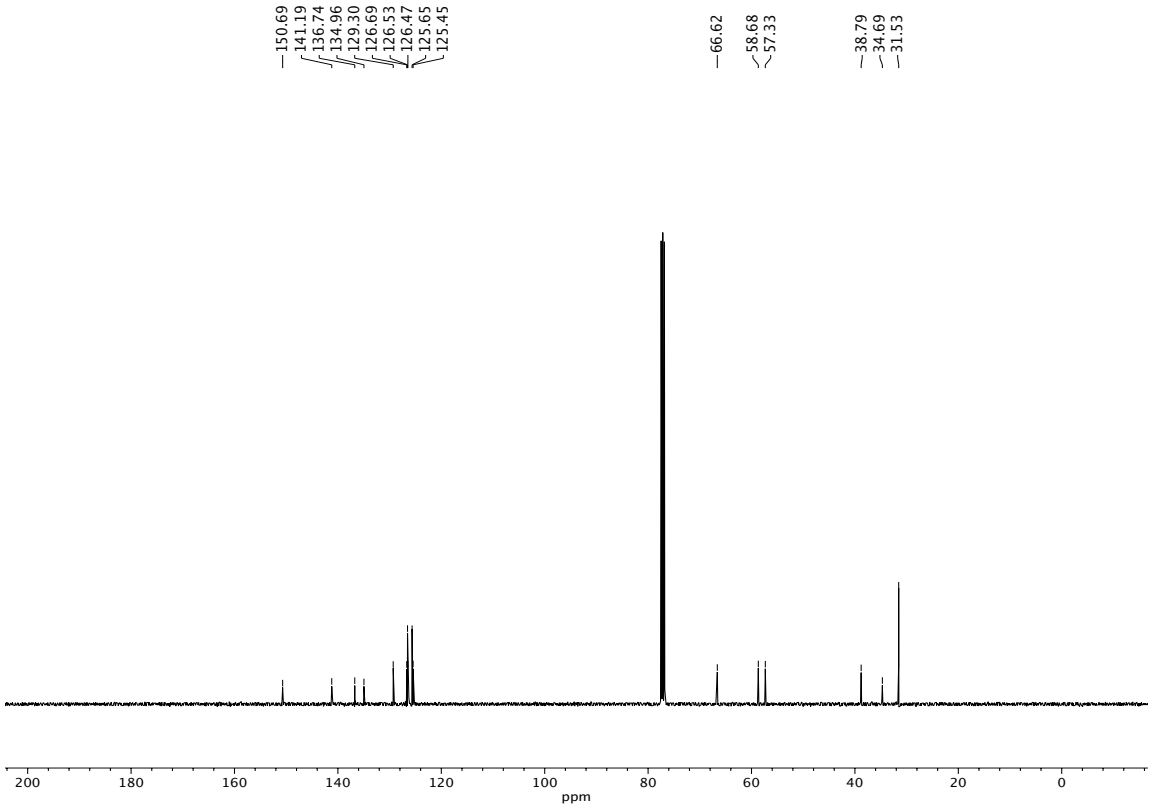


^{13}C NMR (100 MHz, $CDCl_3$) of compound ***Trans*-8a**.

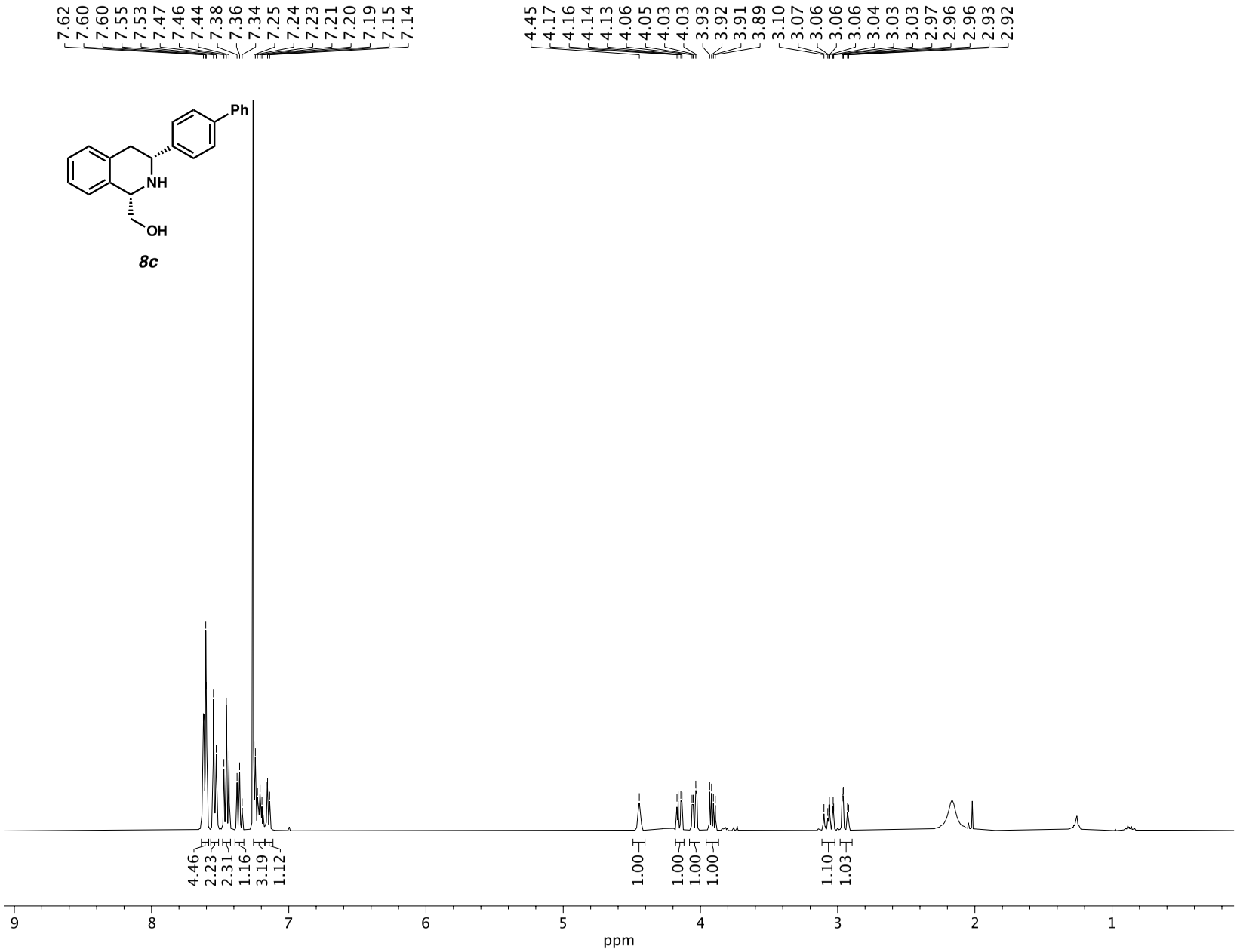
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8b**.



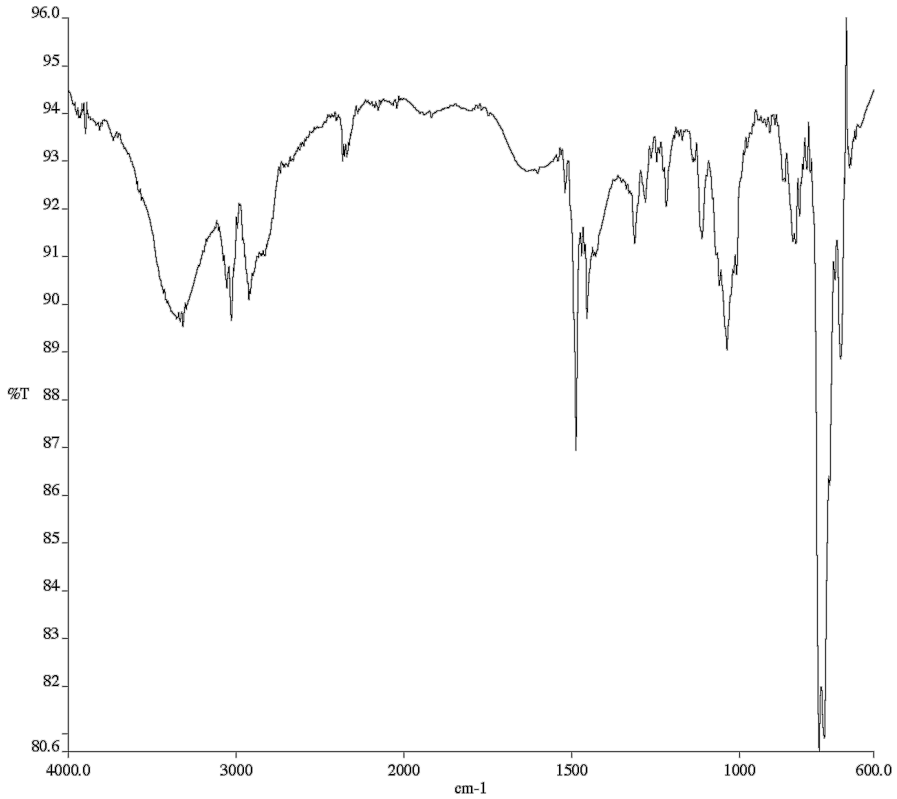
Infrared spectrum (Thin Film, NaCl) of compound **8b**.



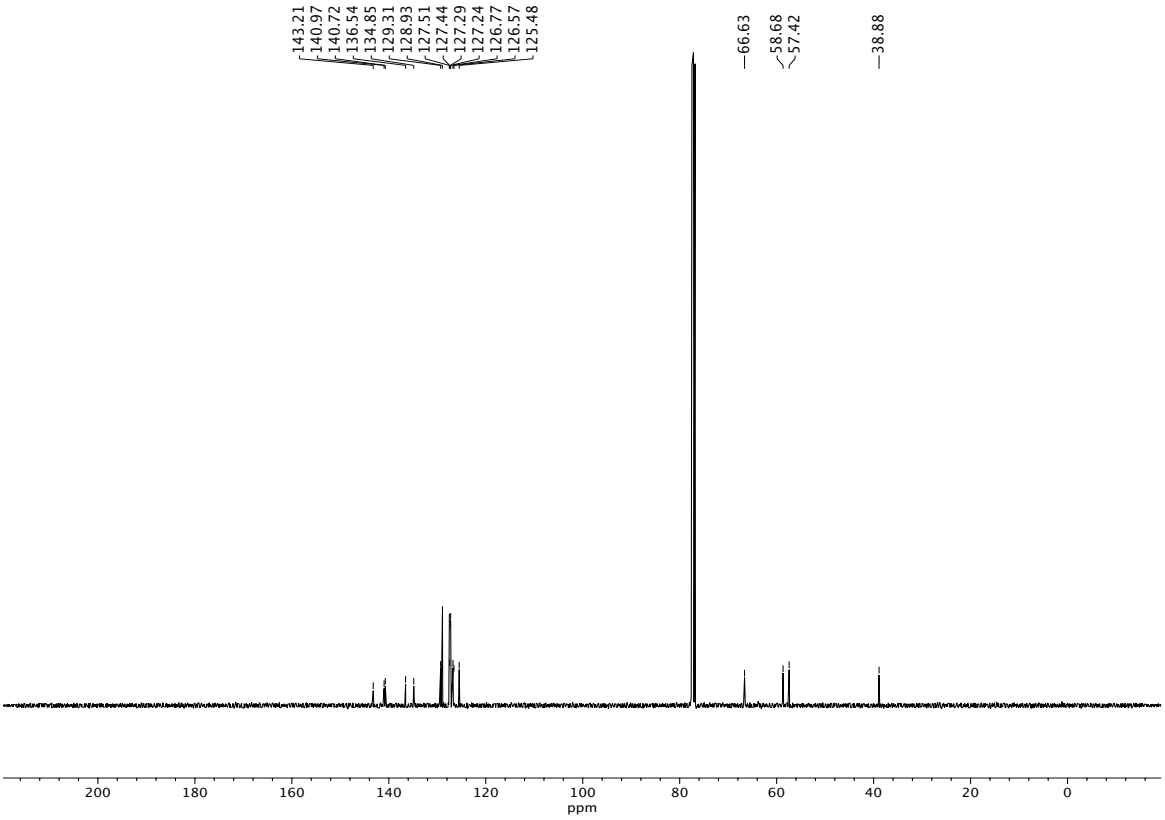
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8b**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **8c**.

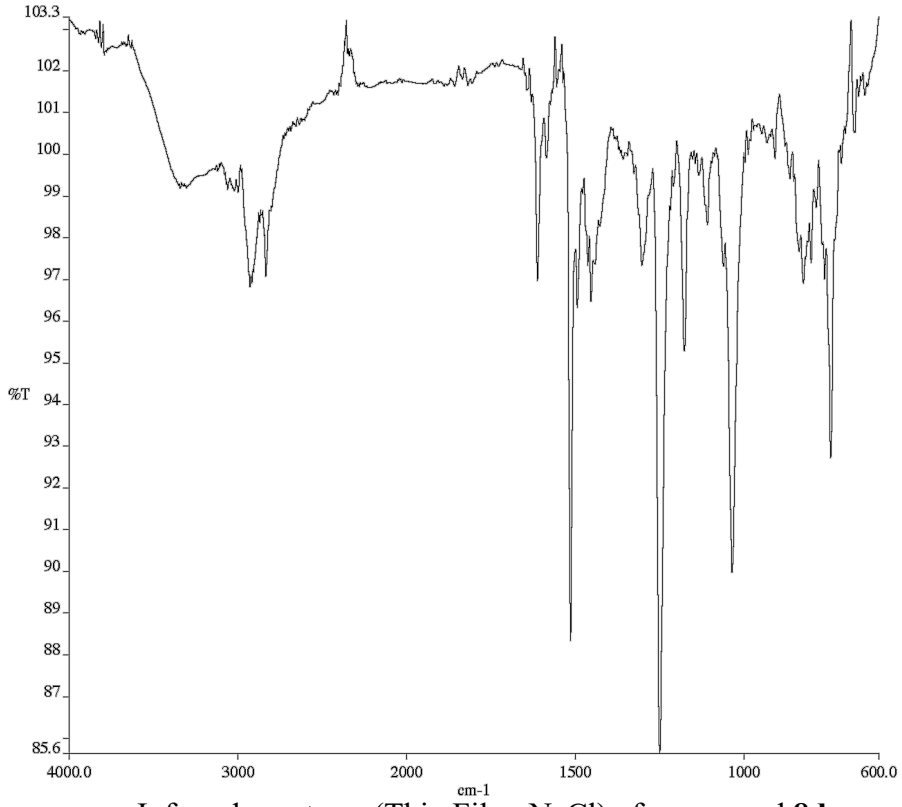


Infrared spectrum (Thin Film, NaCl) of compound **8c**.

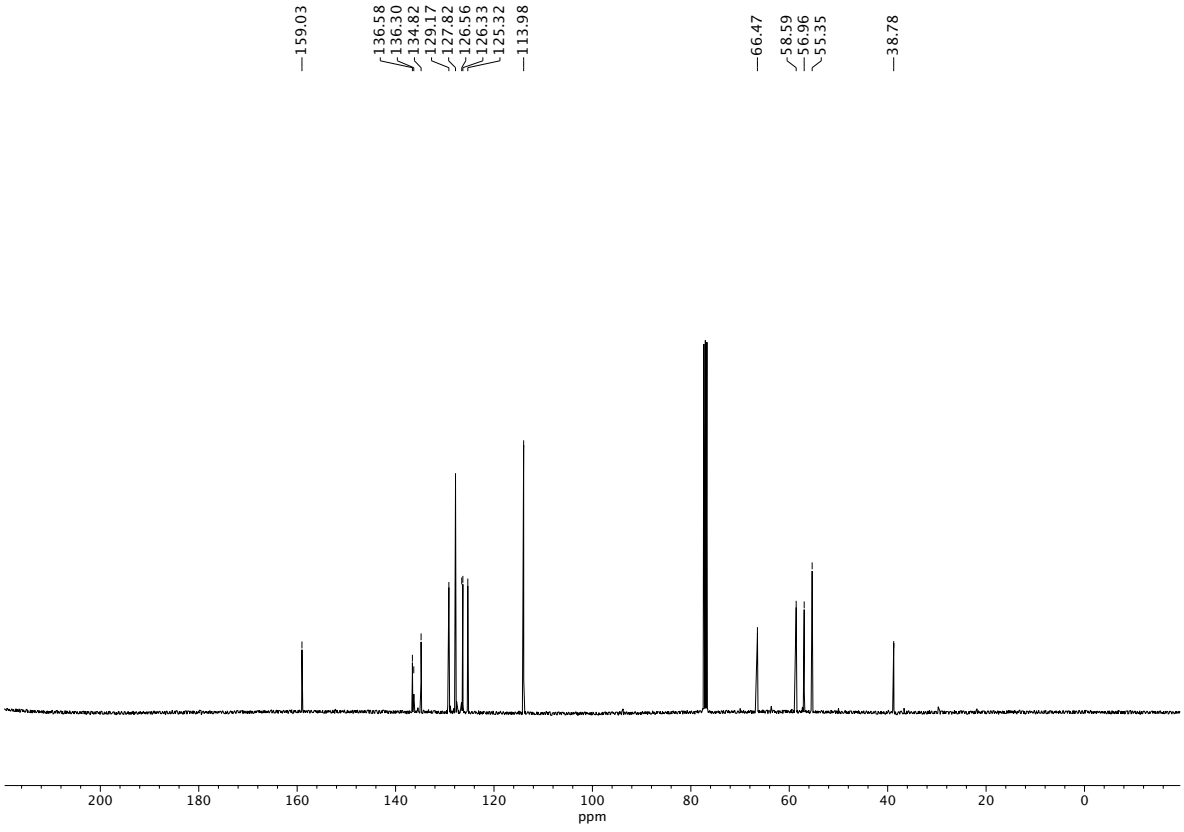


^{13}C NMR (100 MHz, $CDCl_3$) of compound **8c**.

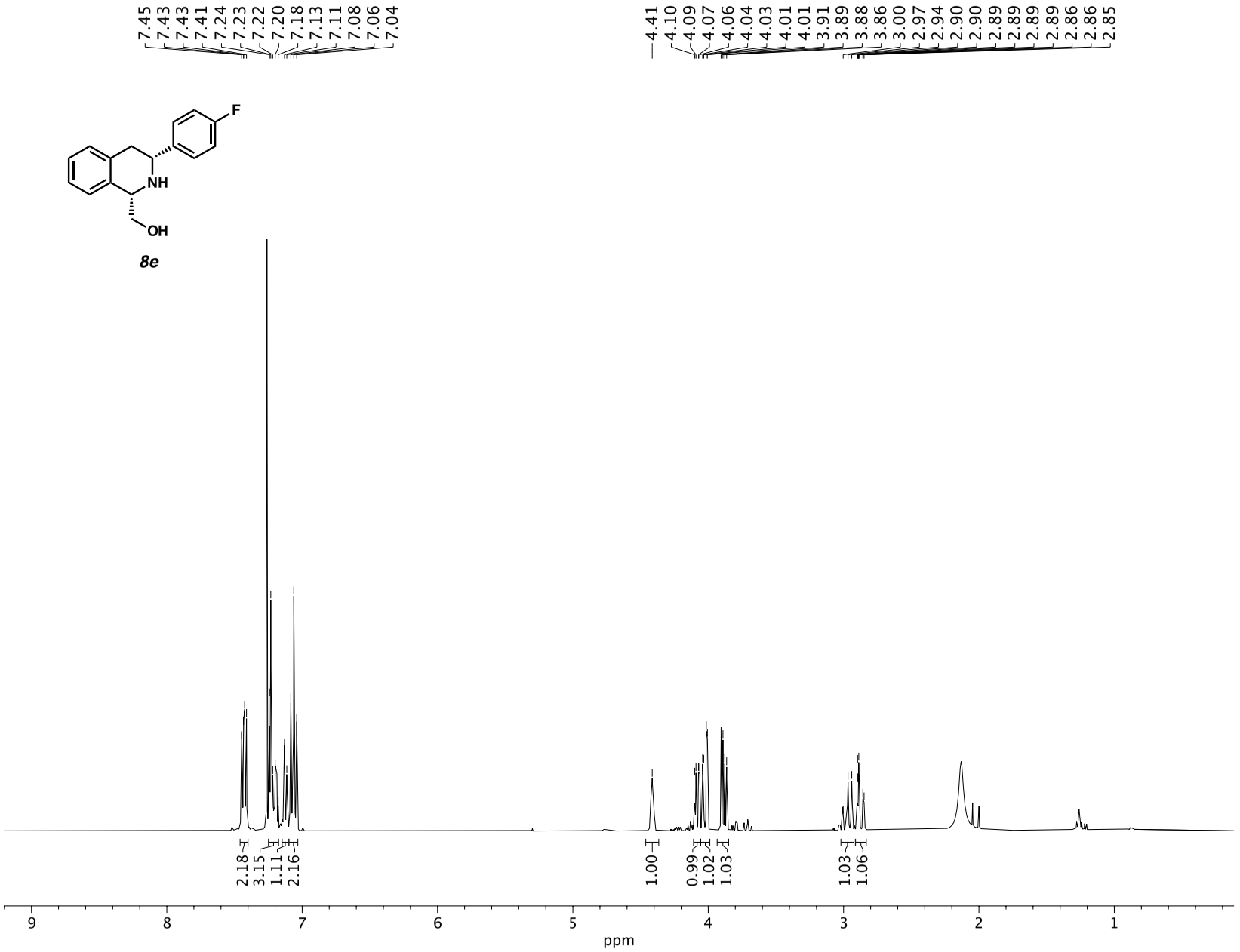
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8d**.



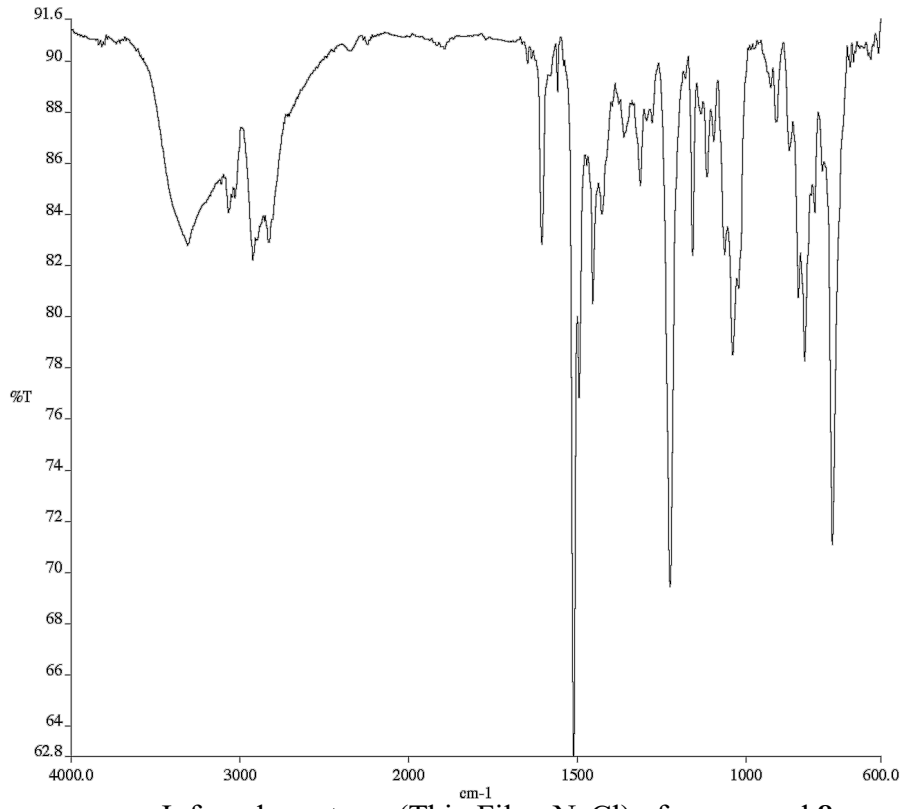
Infrared spectrum (Thin Film, NaCl) of compound **8d**.



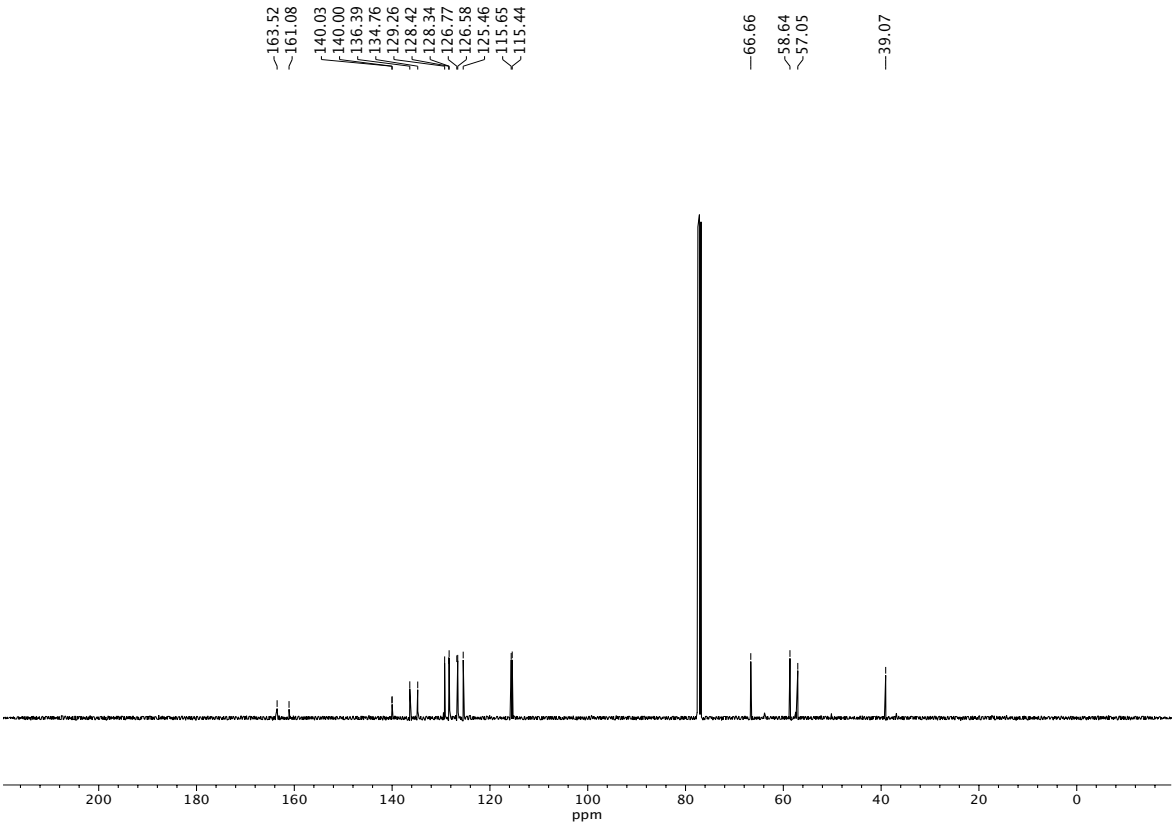
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8d**.



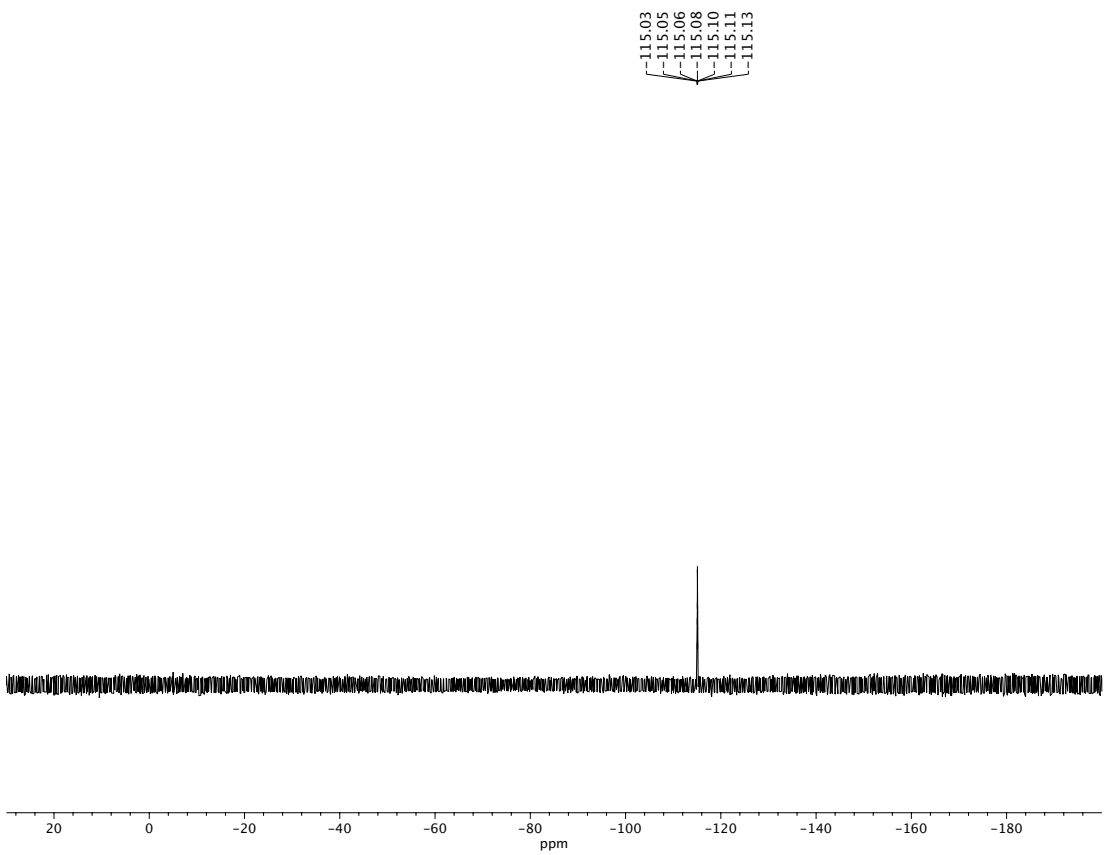
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8e**.



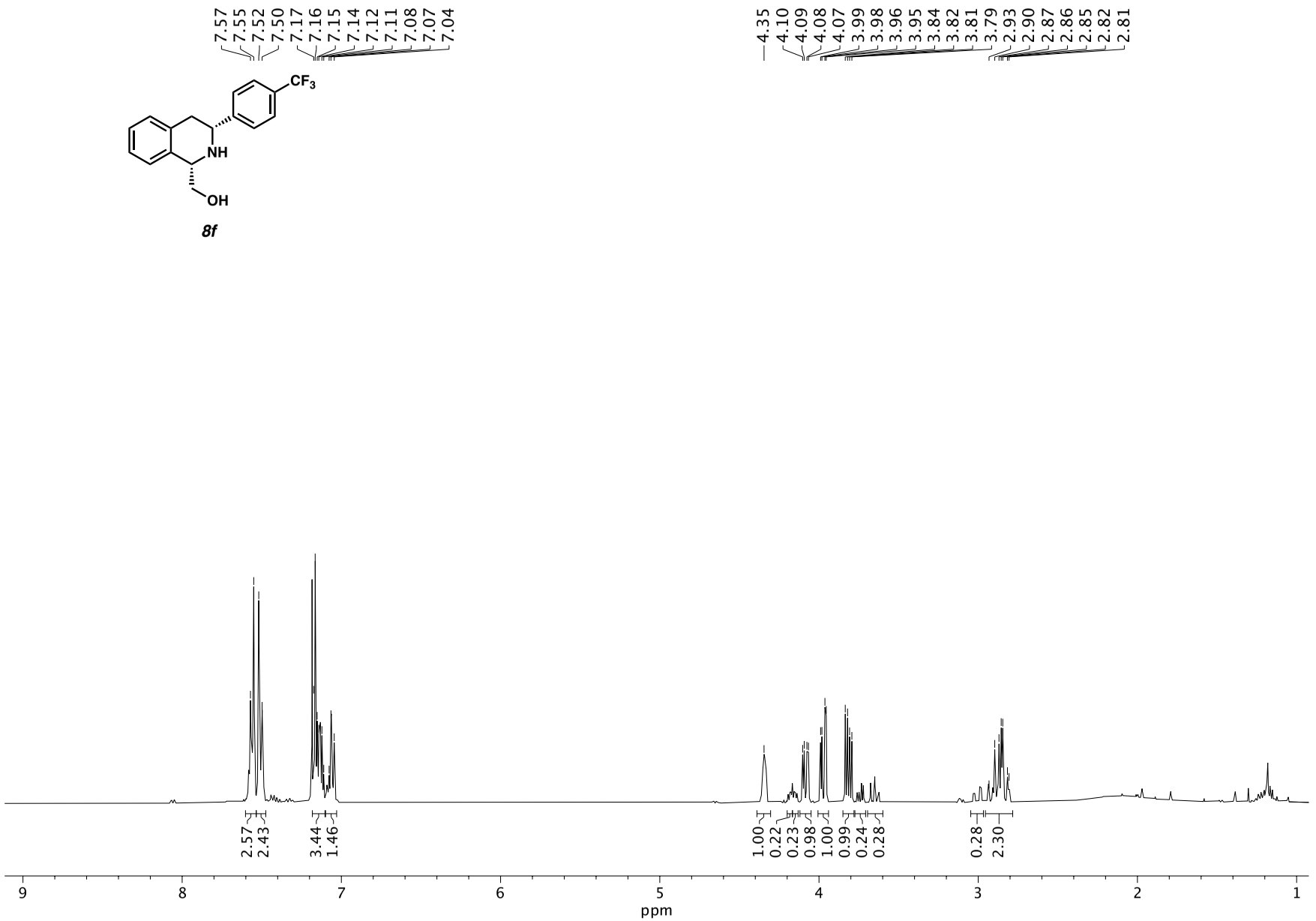
Infrared spectrum (Thin Film, NaCl) of compound **8e**.



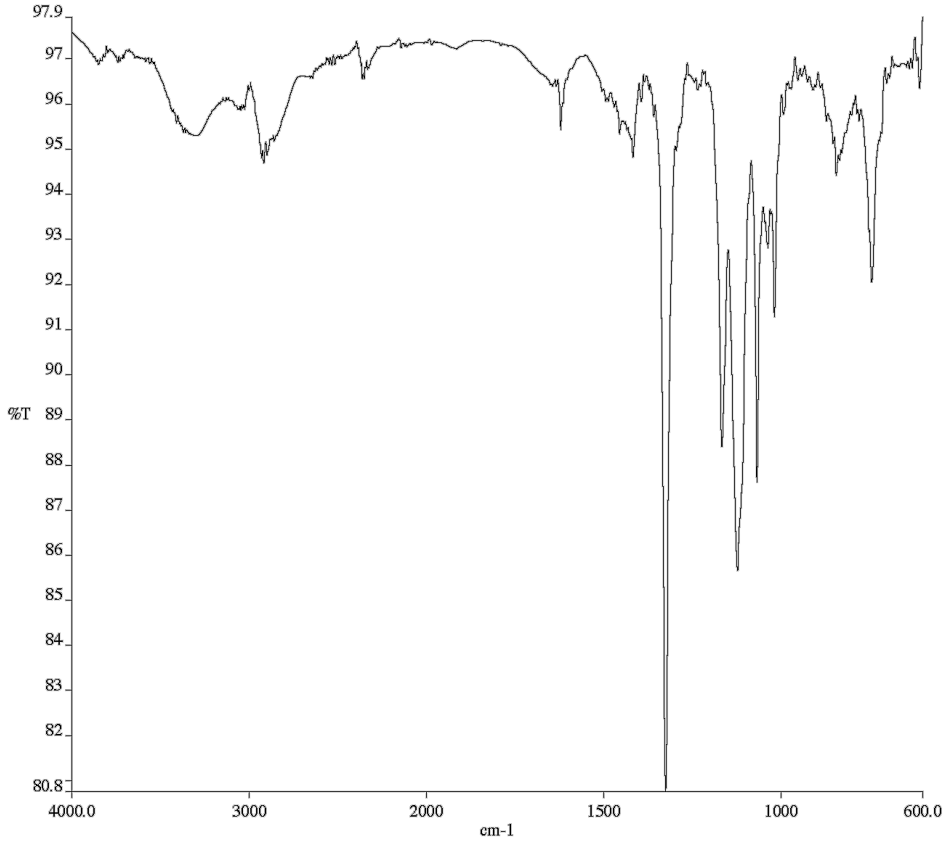
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8e**.



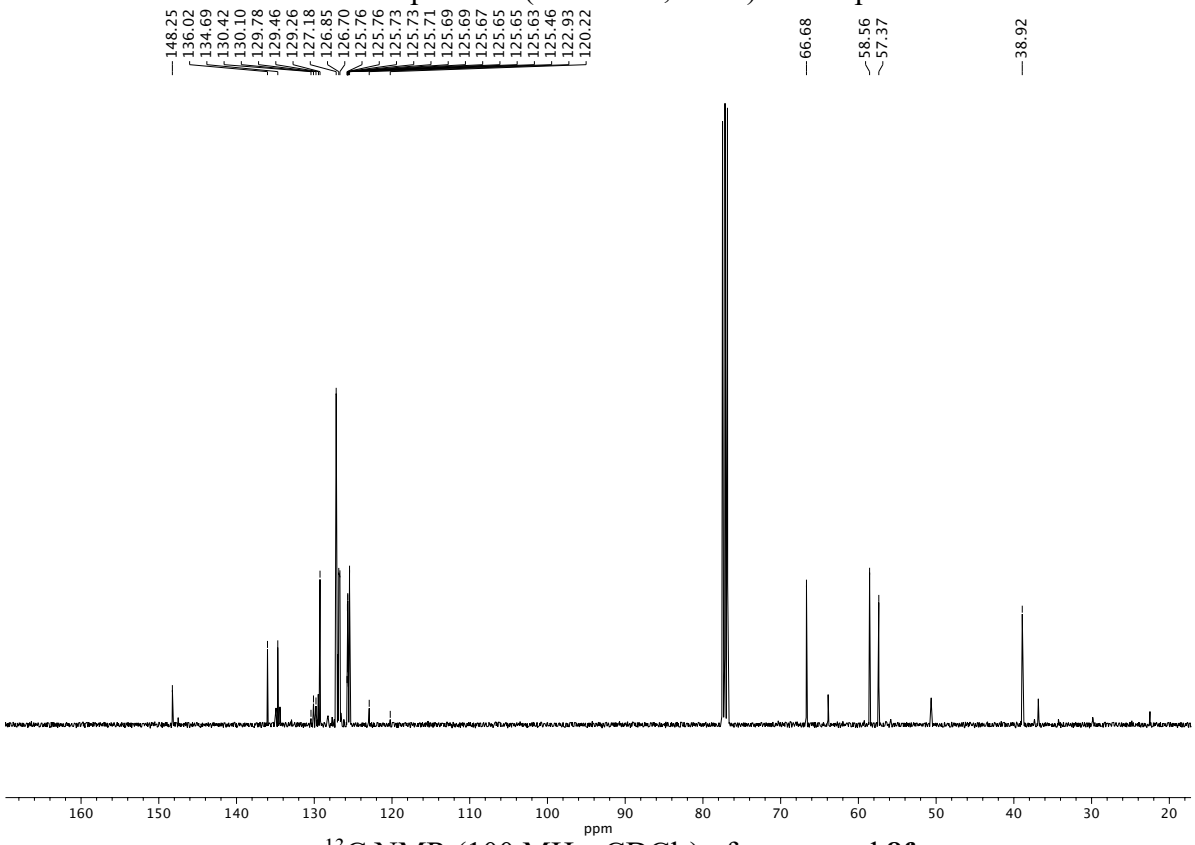
^{19}F NMR (282 MHz, $CDCl_3$) of **8e**.



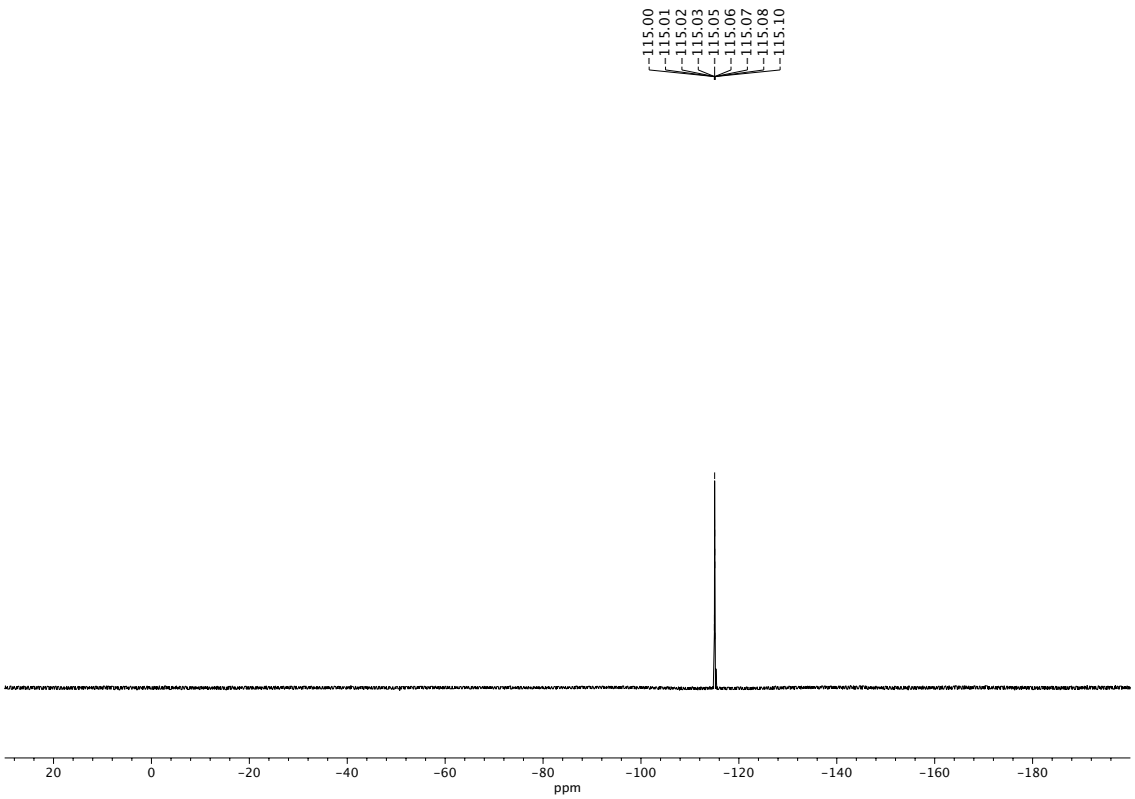
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8f**.



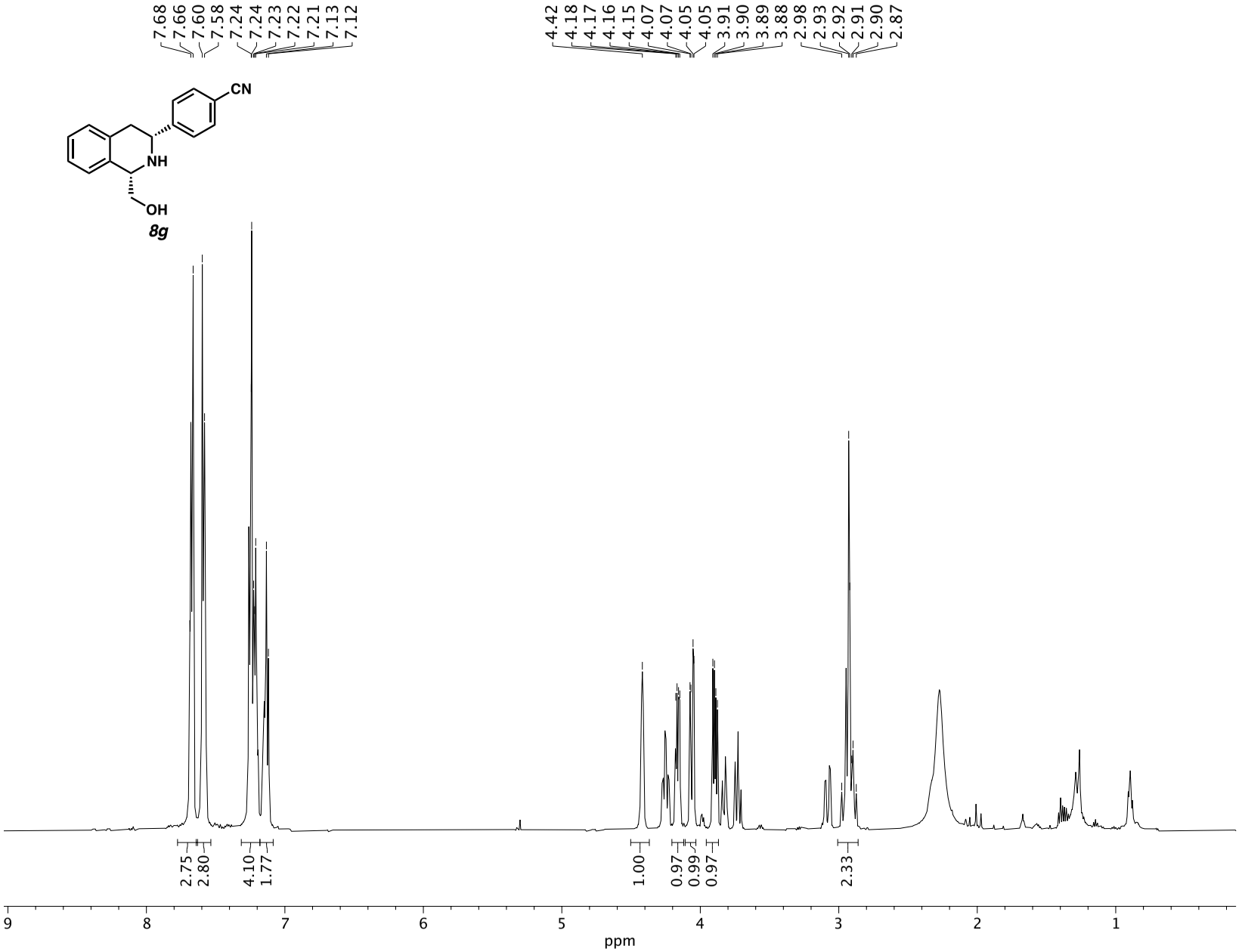
Infrared spectrum (Thin Film, NaCl) of compound **8f**.



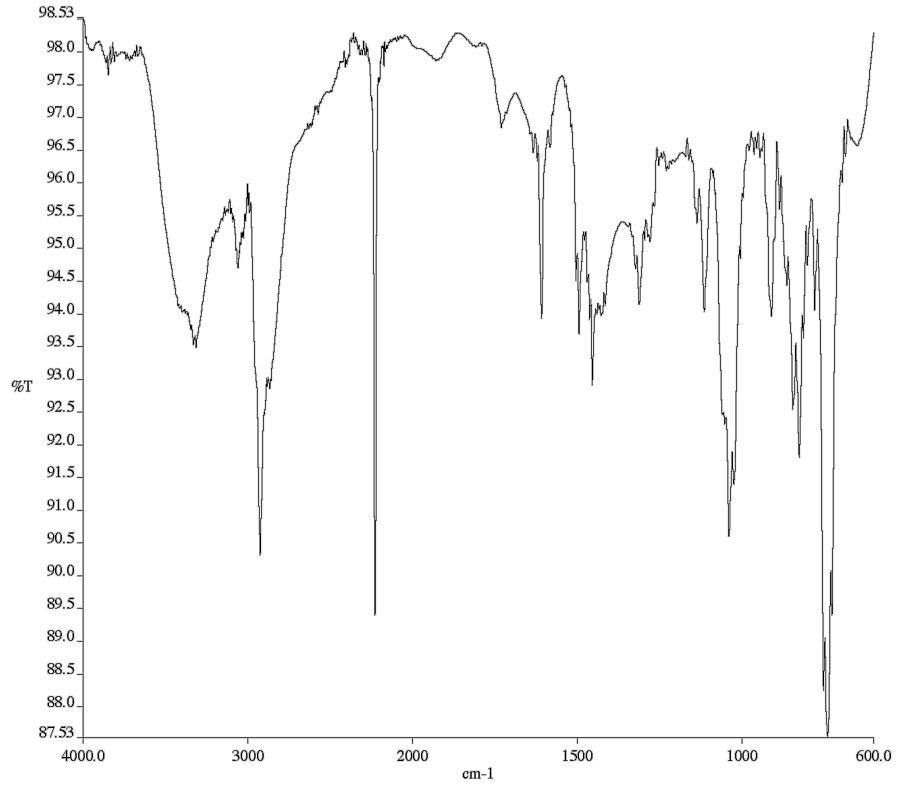
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8f**.



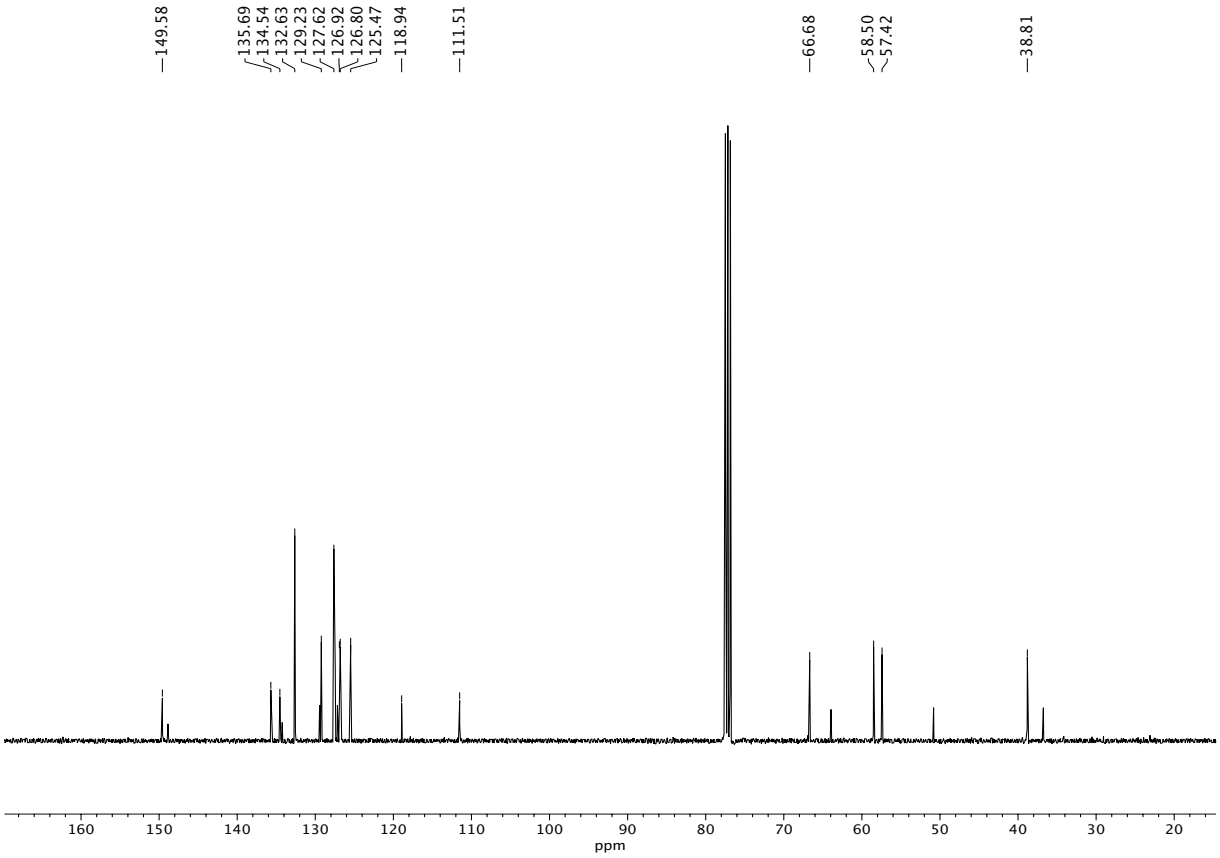
^{19}F NMR (282 MHz, $CDCl_3$) of **8f**.



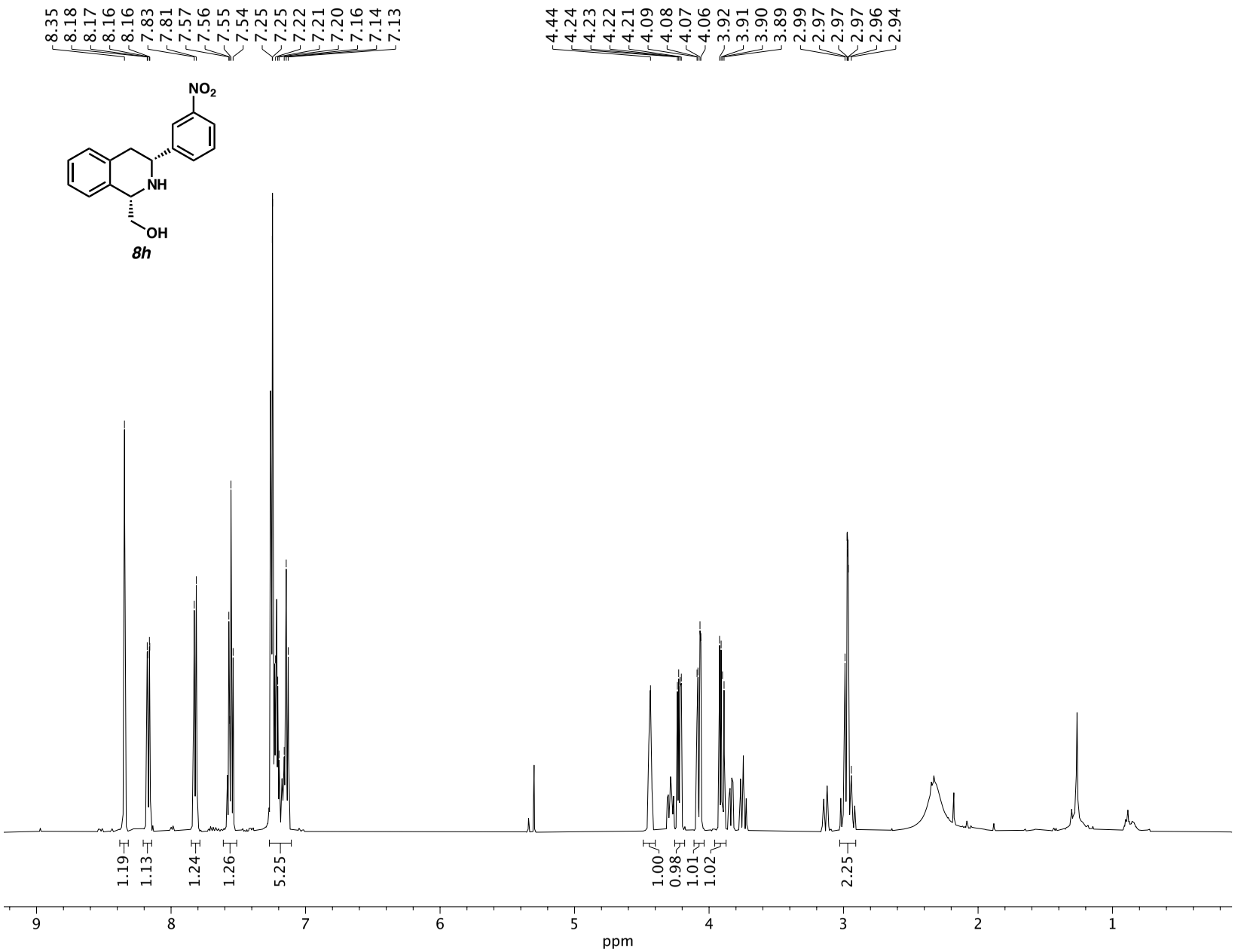
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8g**.



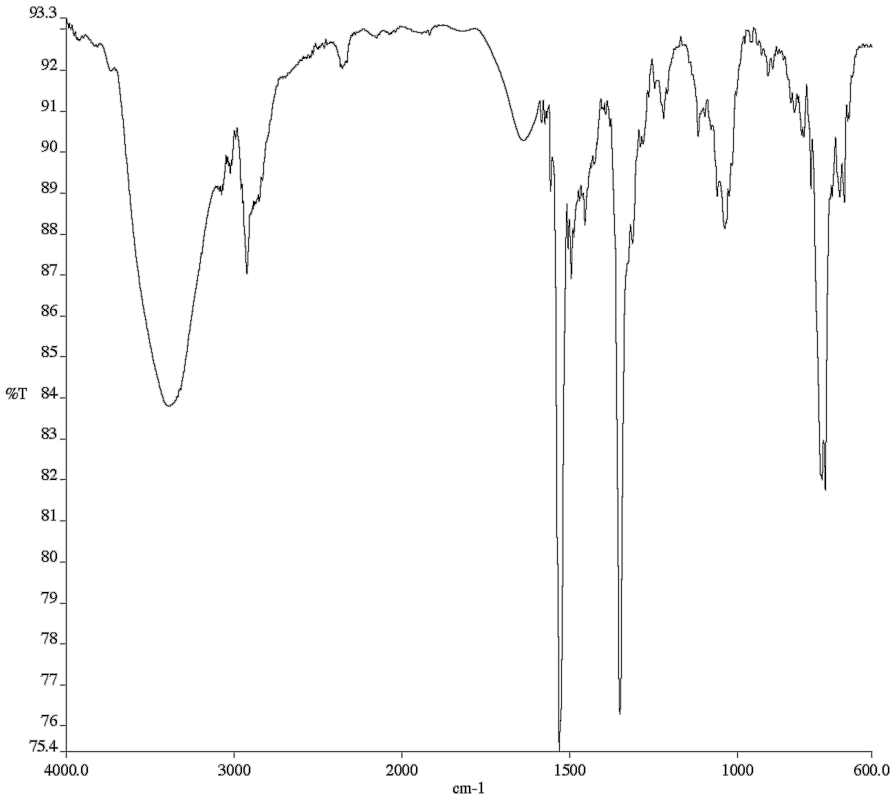
Infrared spectrum (Thin Film, NaCl) of compound **8g**.



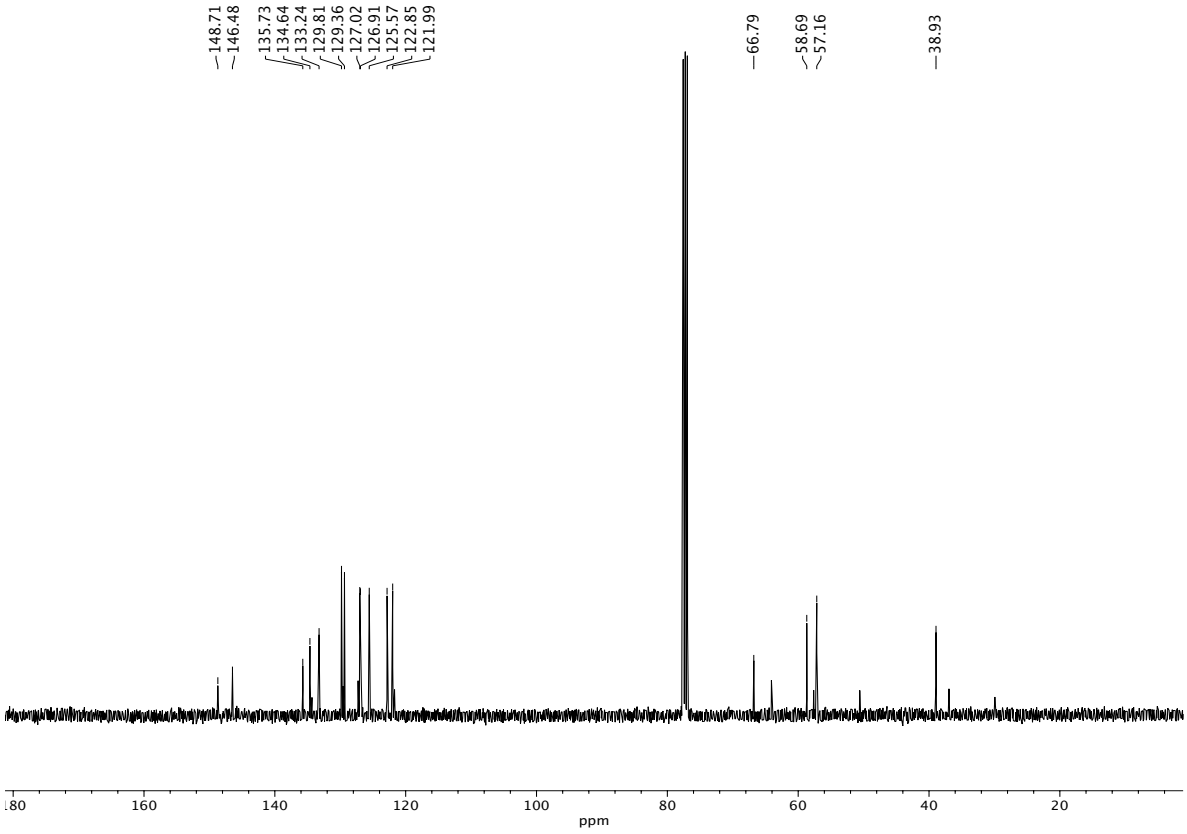
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8g**.



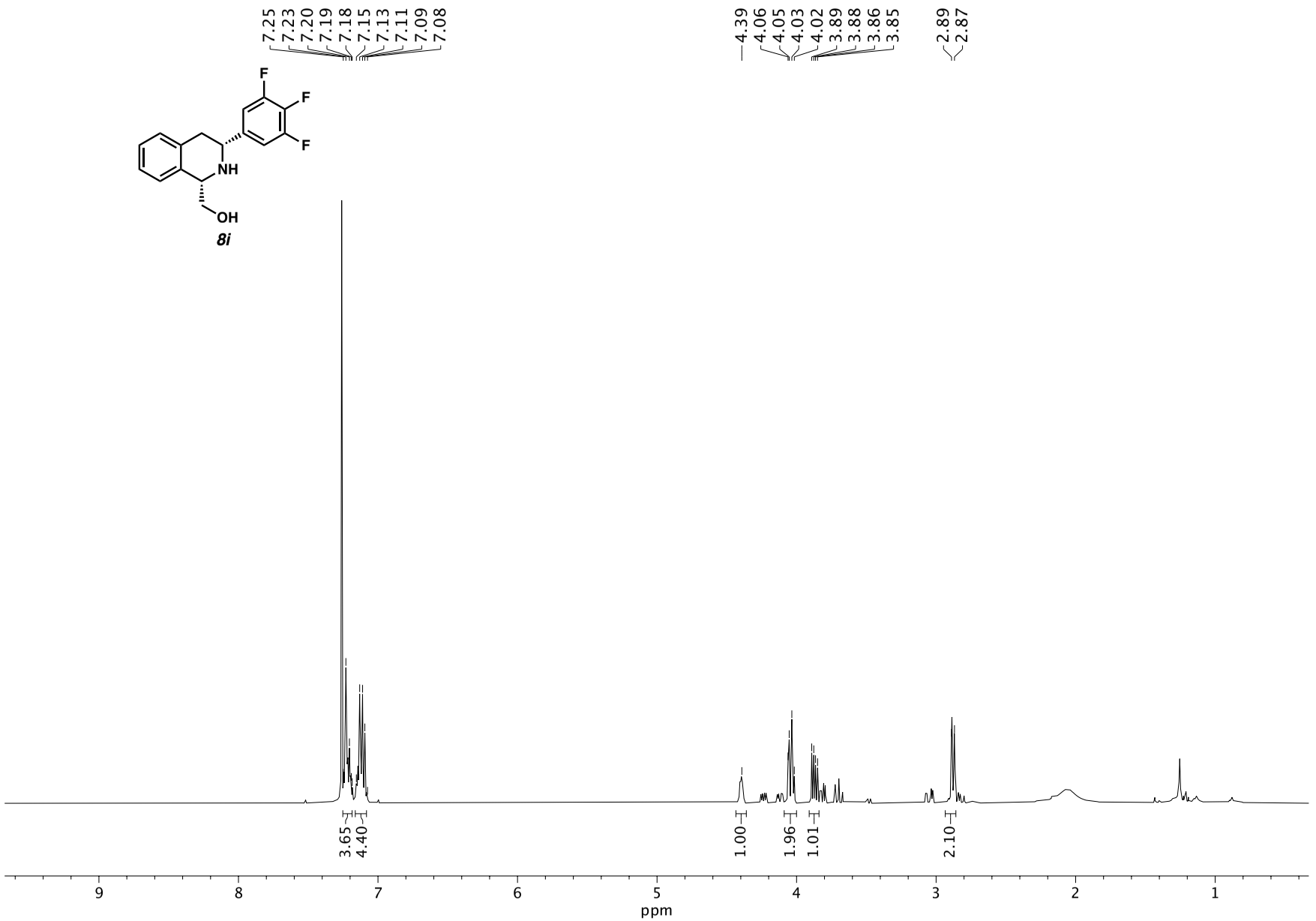
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8h**.



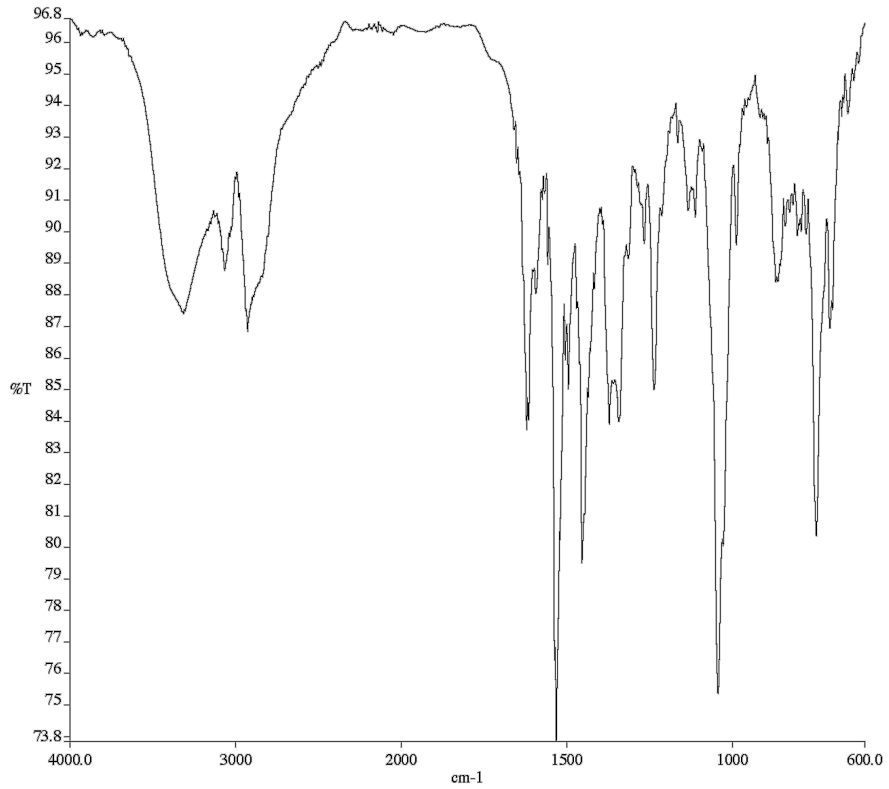
Infrared spectrum (Thin Film, NaCl) of compound **8h**.



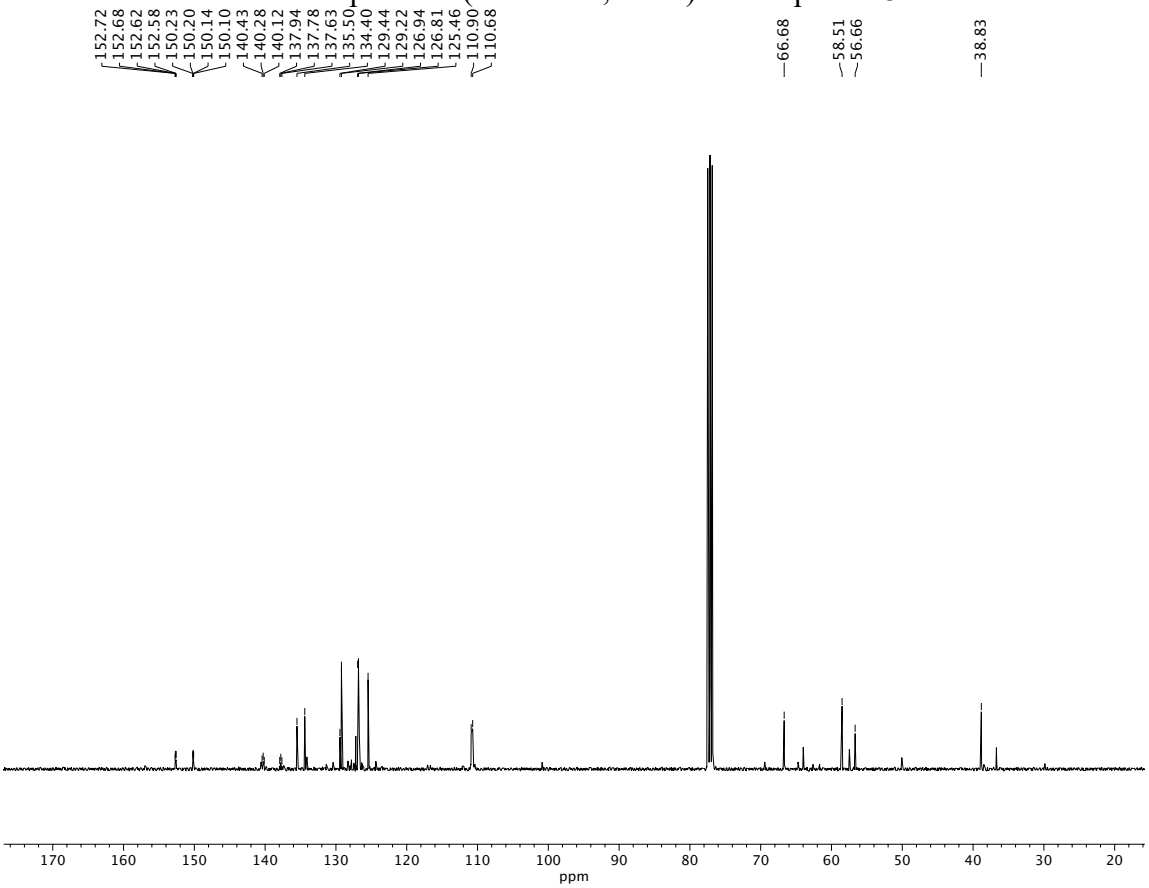
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8h**.



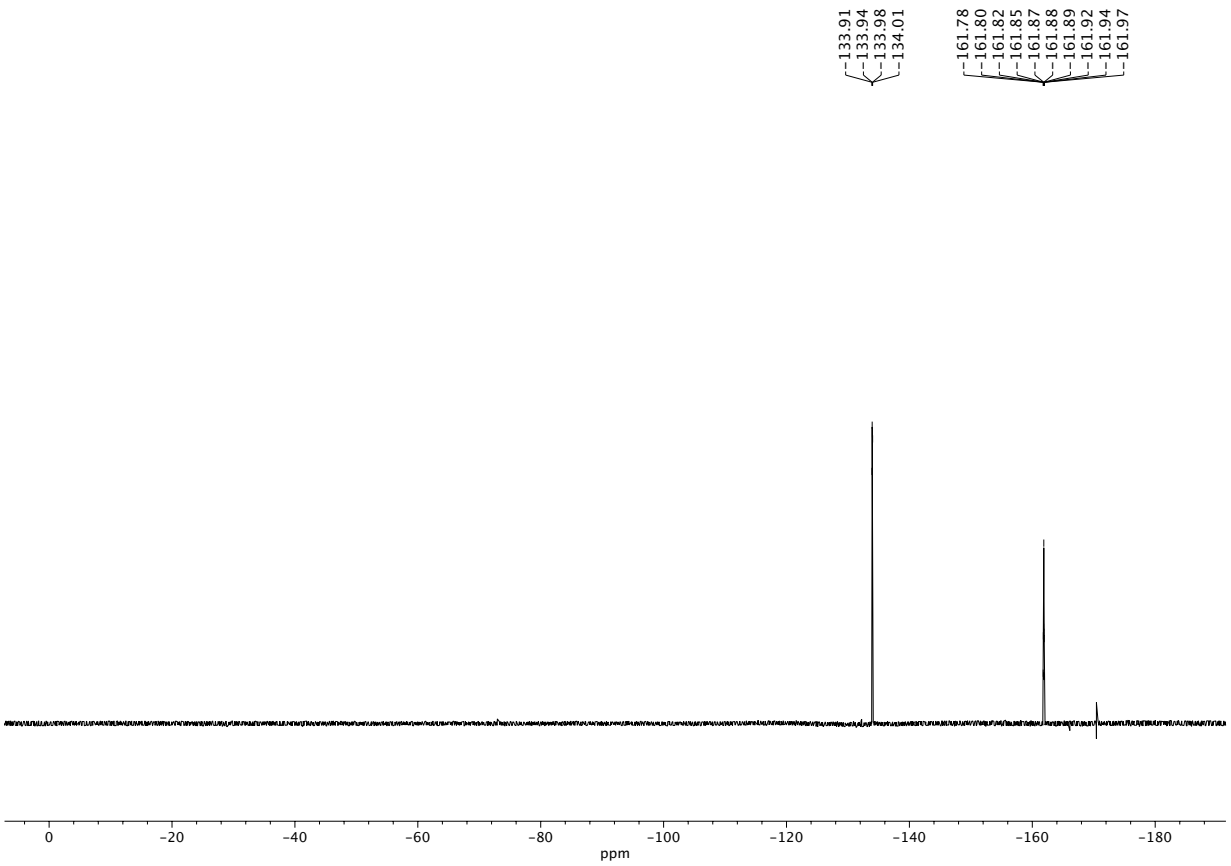
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8i**.



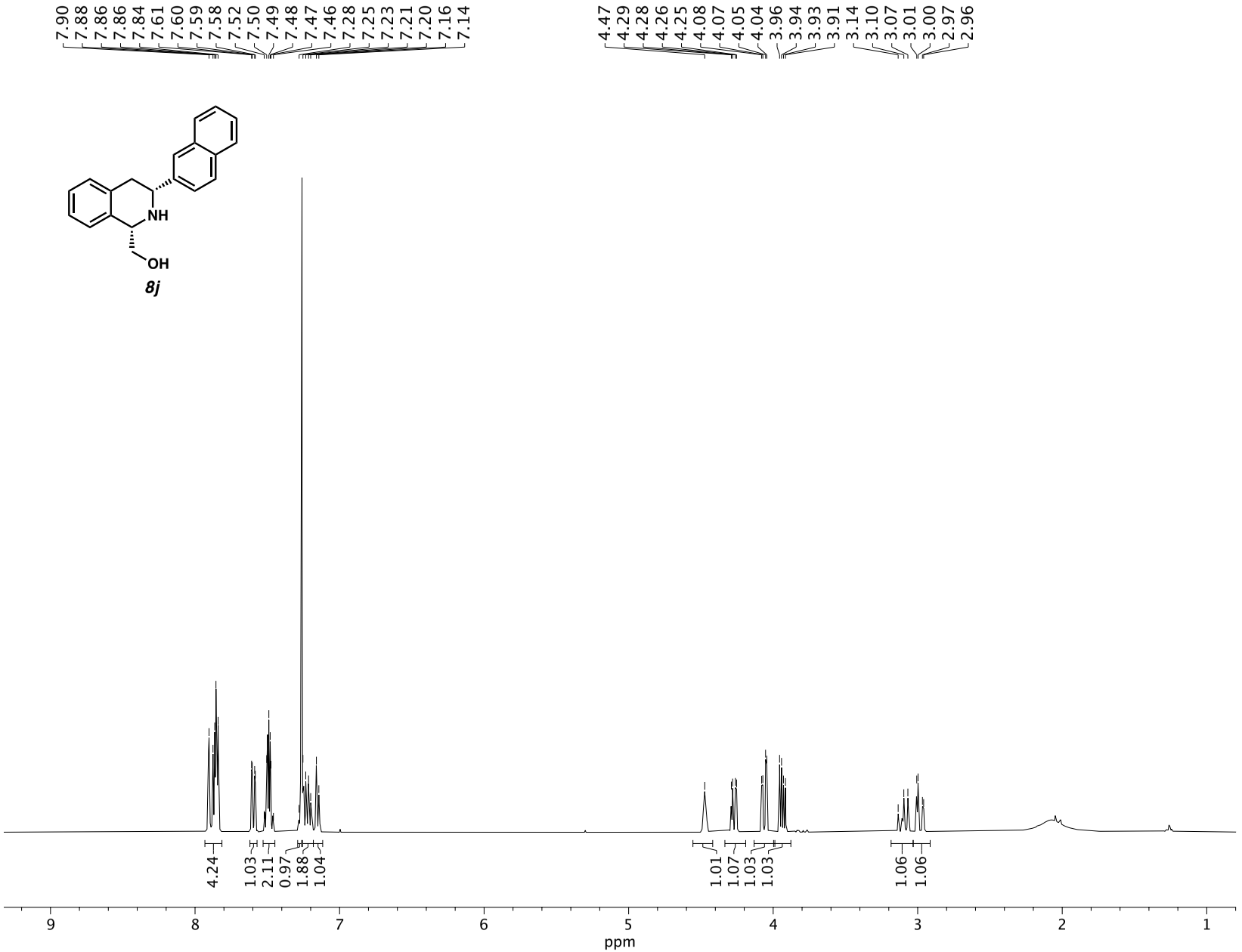
Infrared spectrum (Thin Film, NaCl) of compound **8i**.



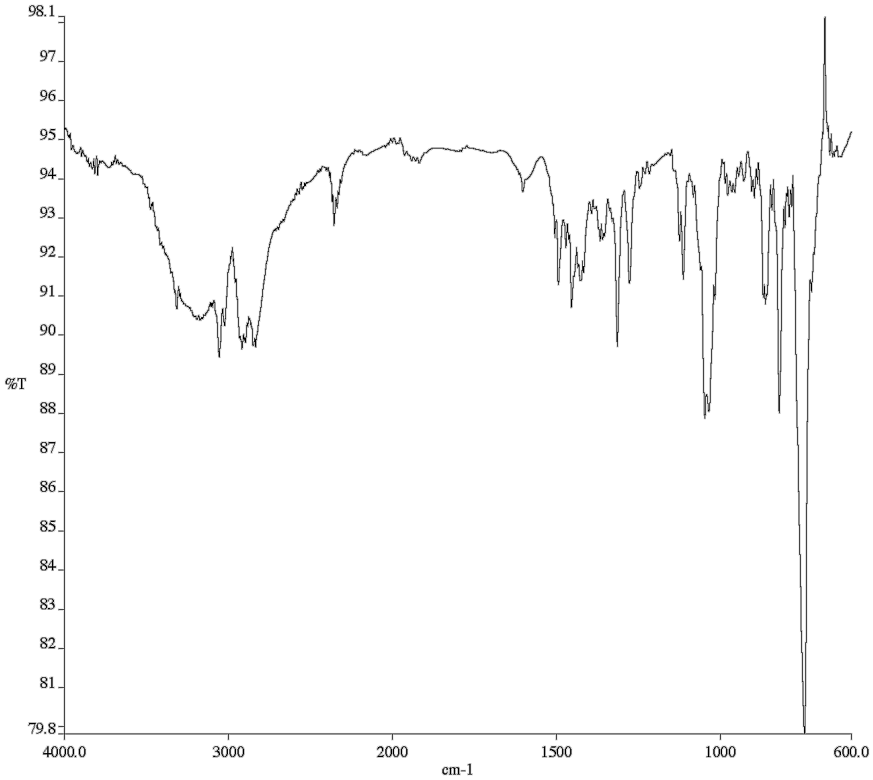
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8i**.



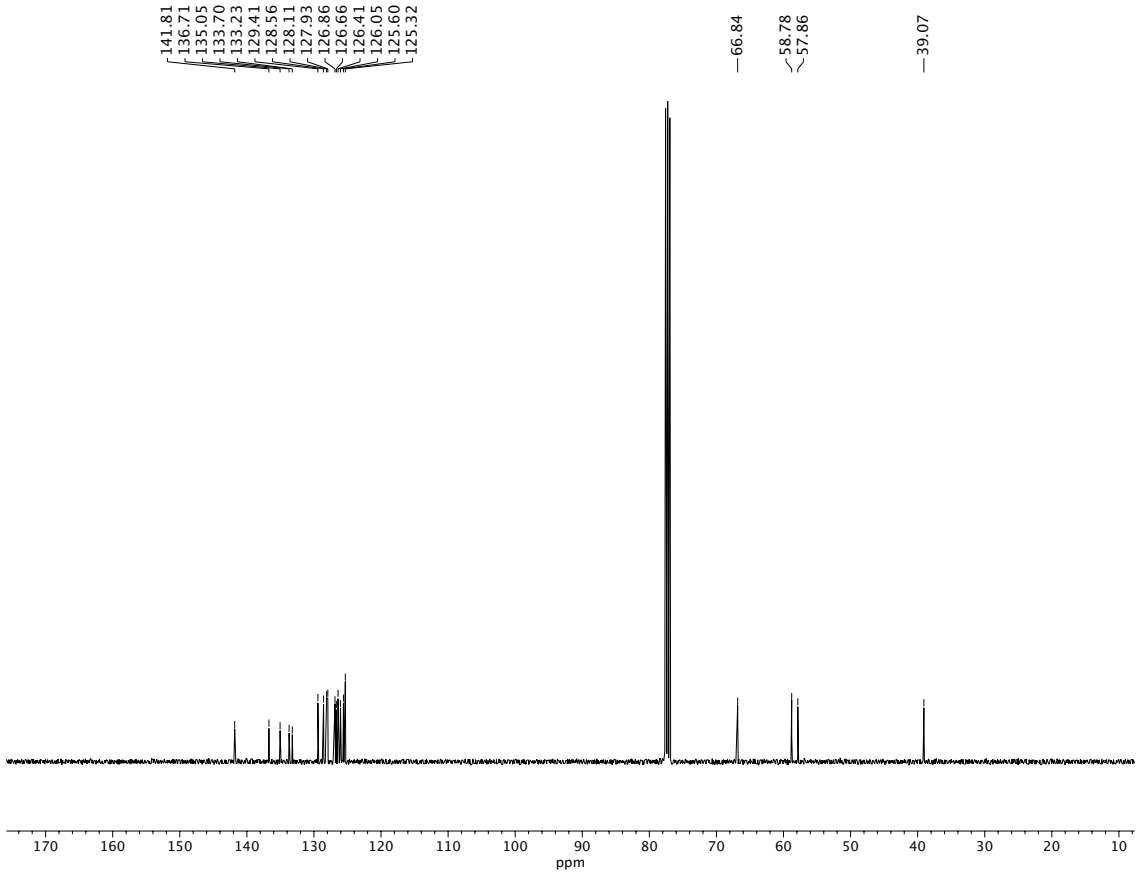
^{19}F NMR (282 MHz, $CDCl_3$) of **8i**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **8j**.

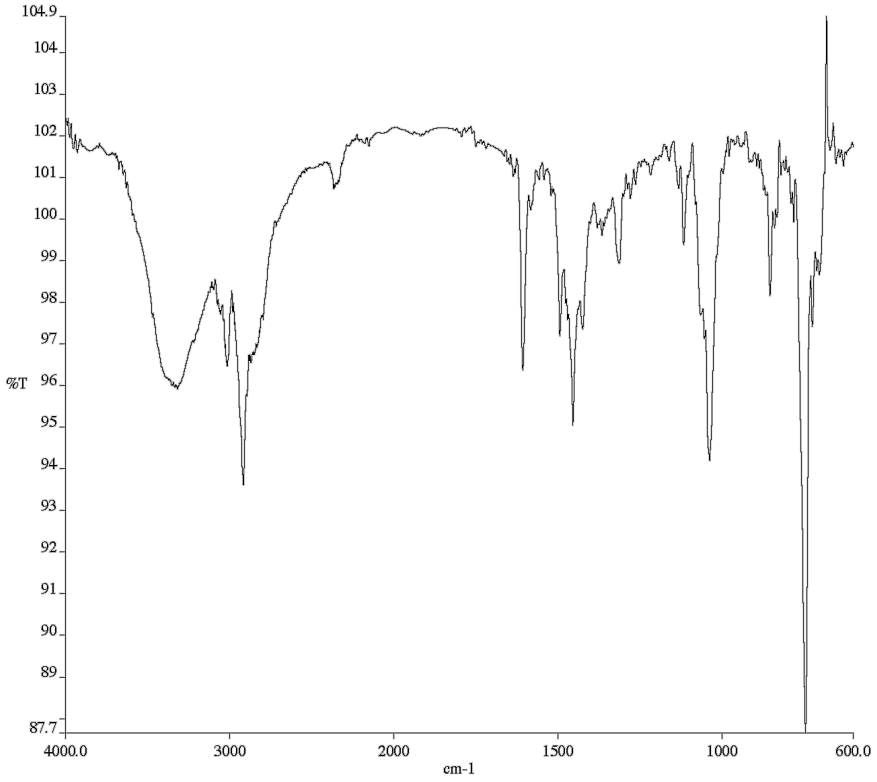


Infrared spectrum (Thin Film, NaCl) of compound **8j**.

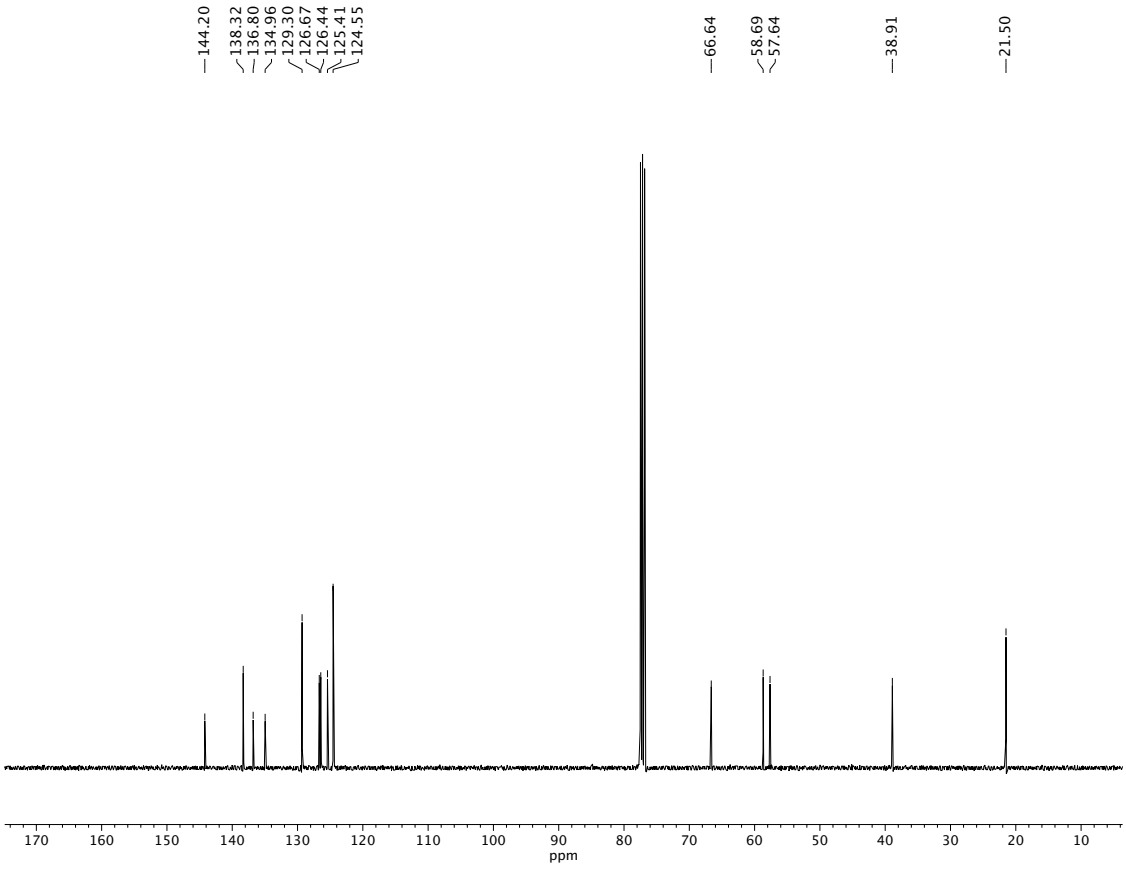


^{13}C NMR (100 MHz, $CDCl_3$) of compound **8j**.

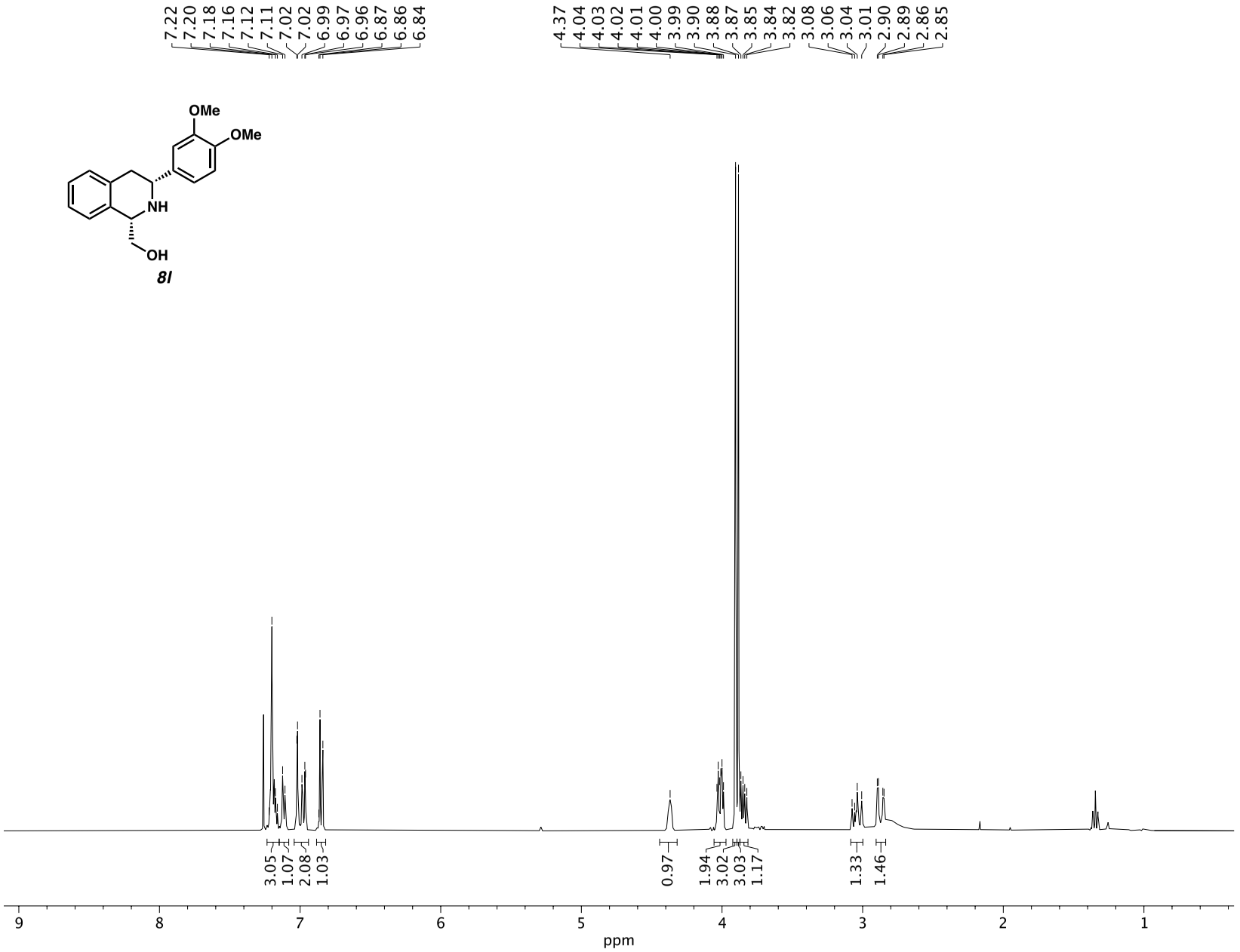
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8k**.



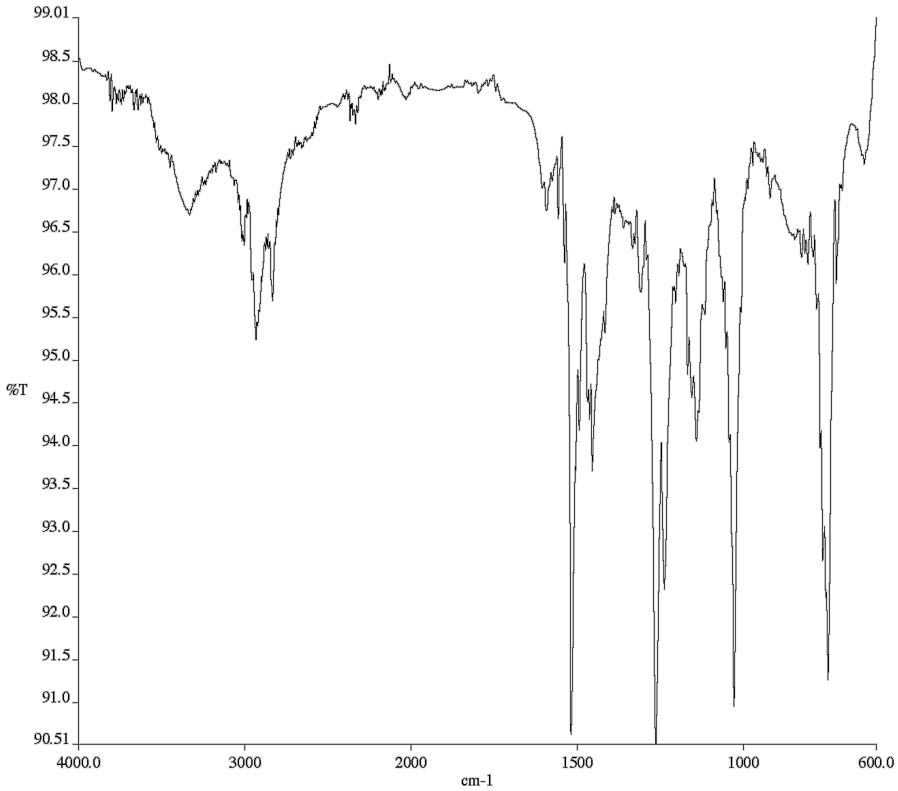
Infrared spectrum (Thin Film, NaCl) of compound **8k**.



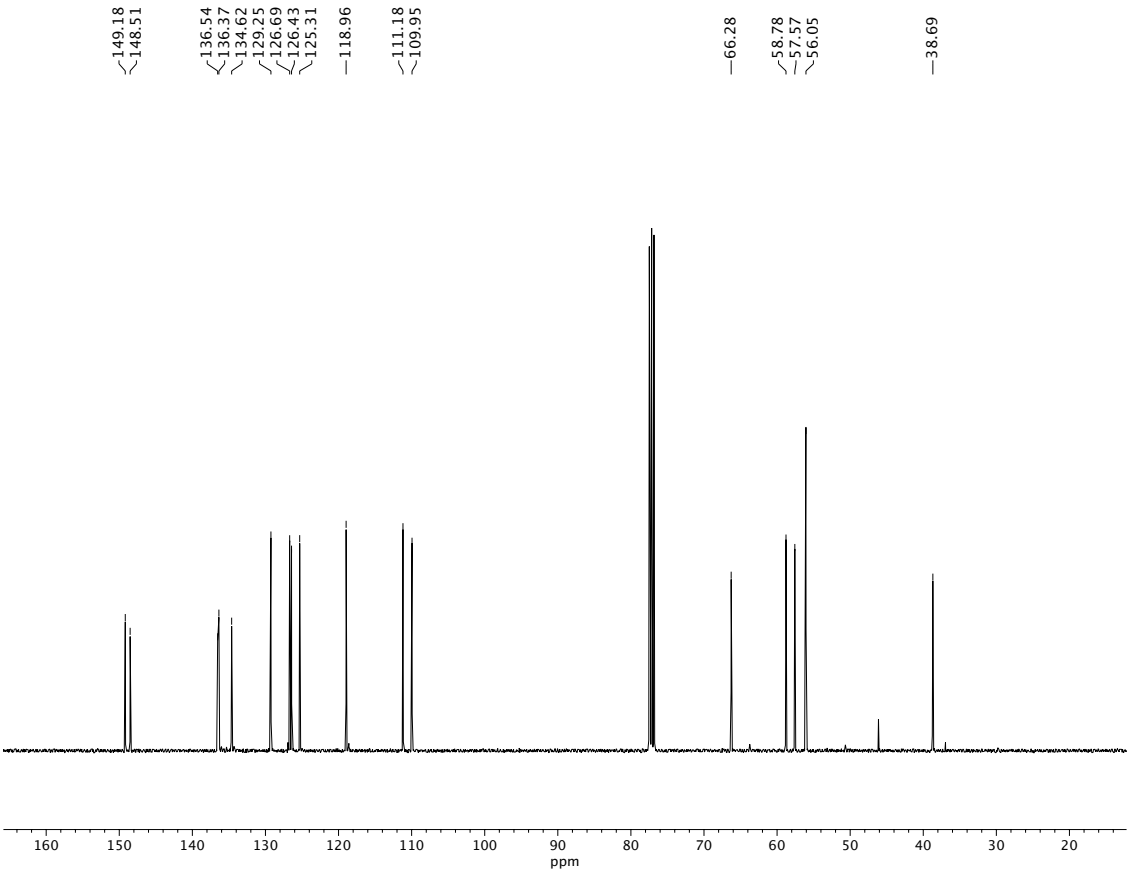
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8k**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **8l**.

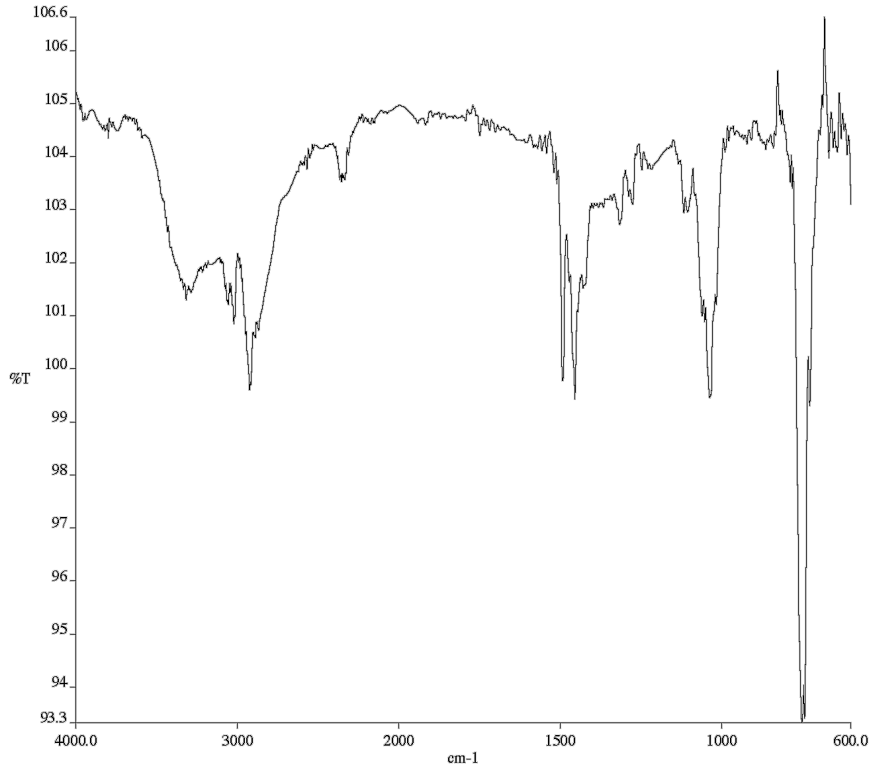


Infrared spectrum (Thin Film, NaCl) of compound **8l**.

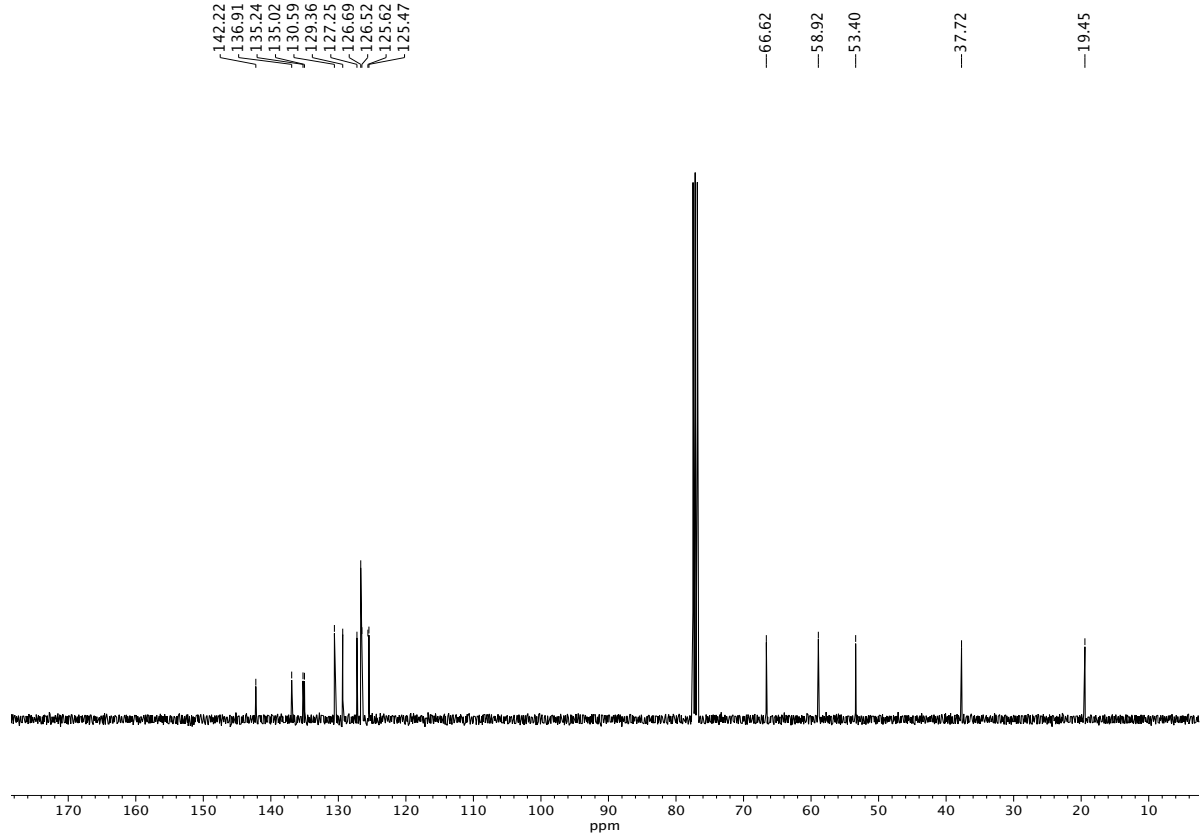


^{13}C NMR (100 MHz, $CDCl_3$) of compound **8l**.

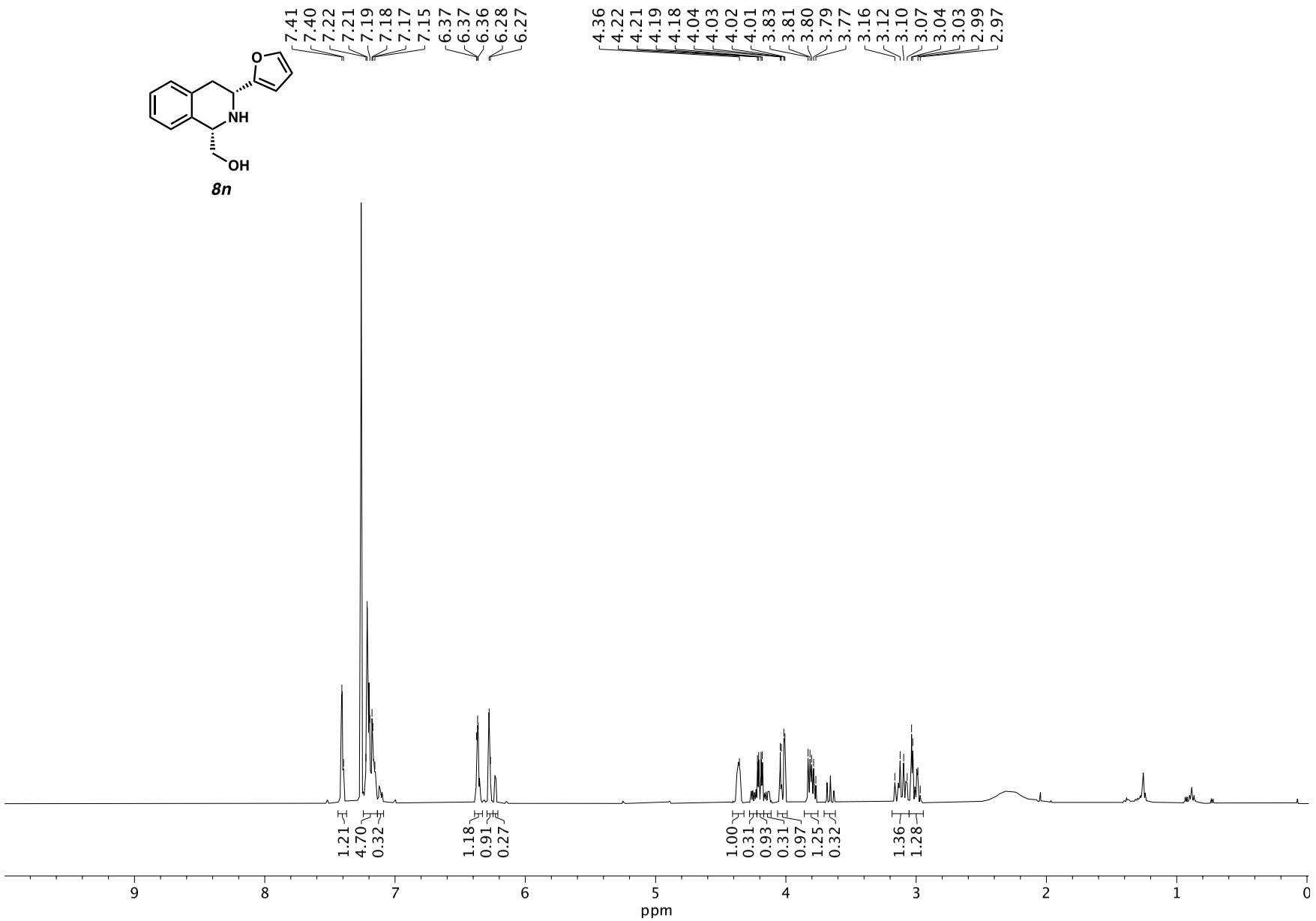
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8m**.



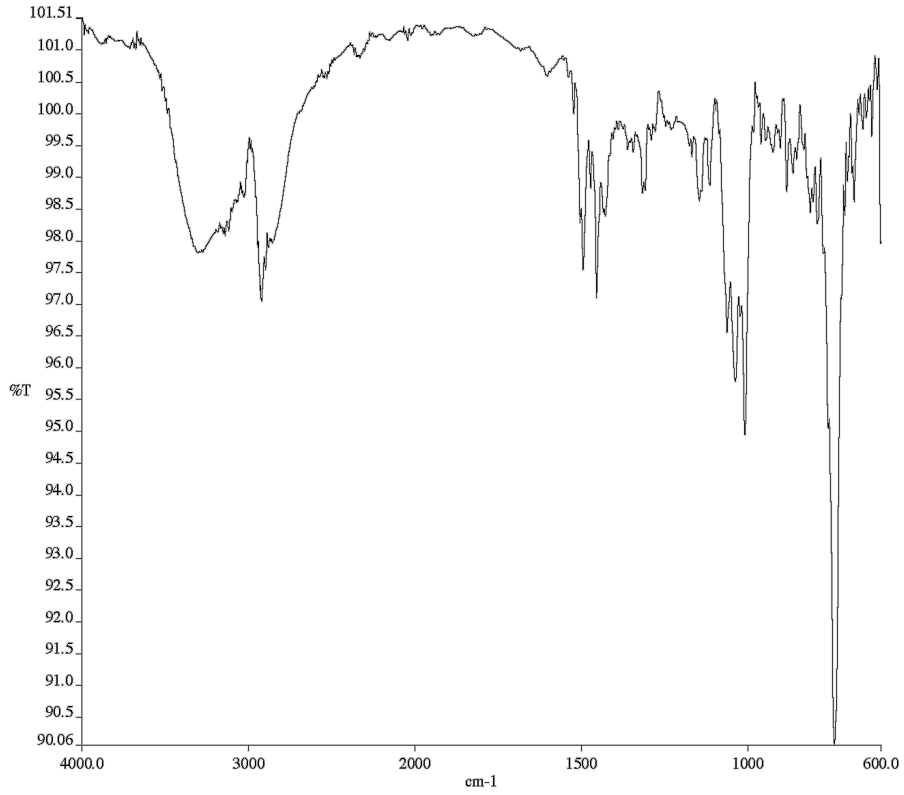
Infrared spectrum (Thin Film, NaCl) of compound **8m**.



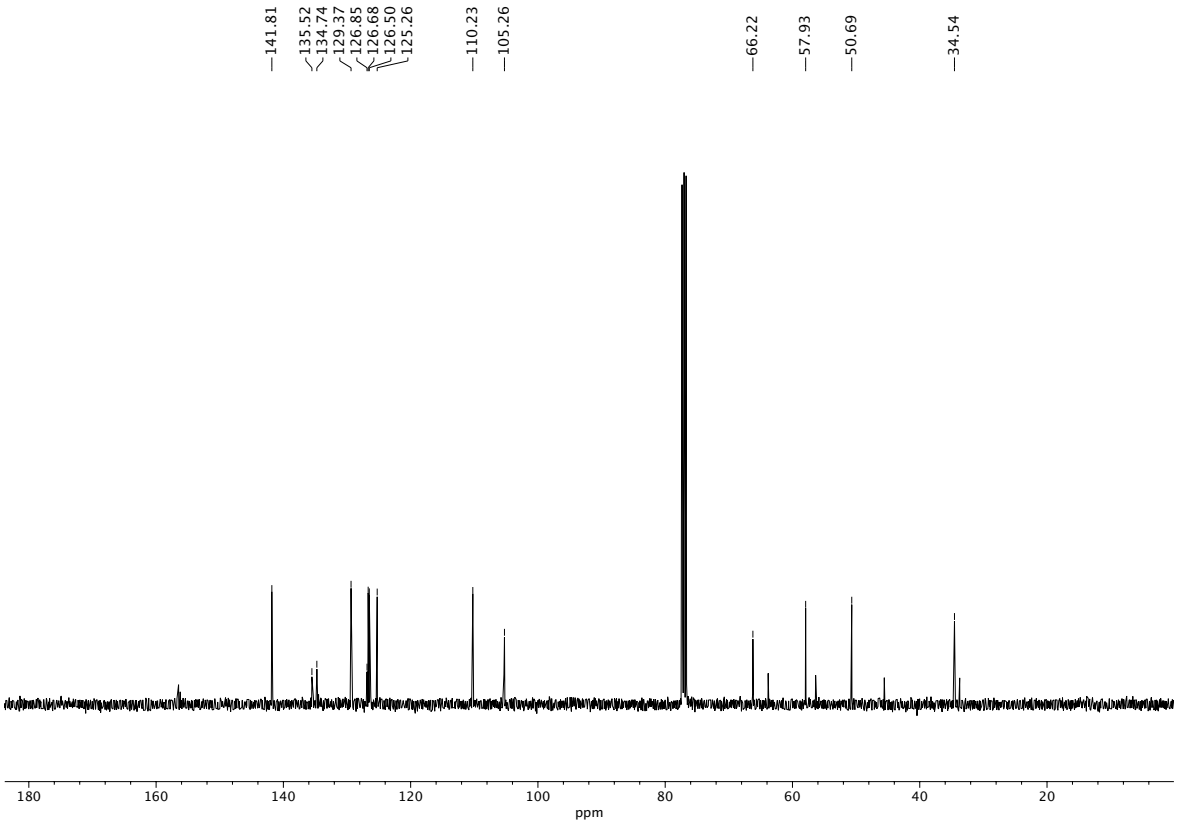
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8m**.



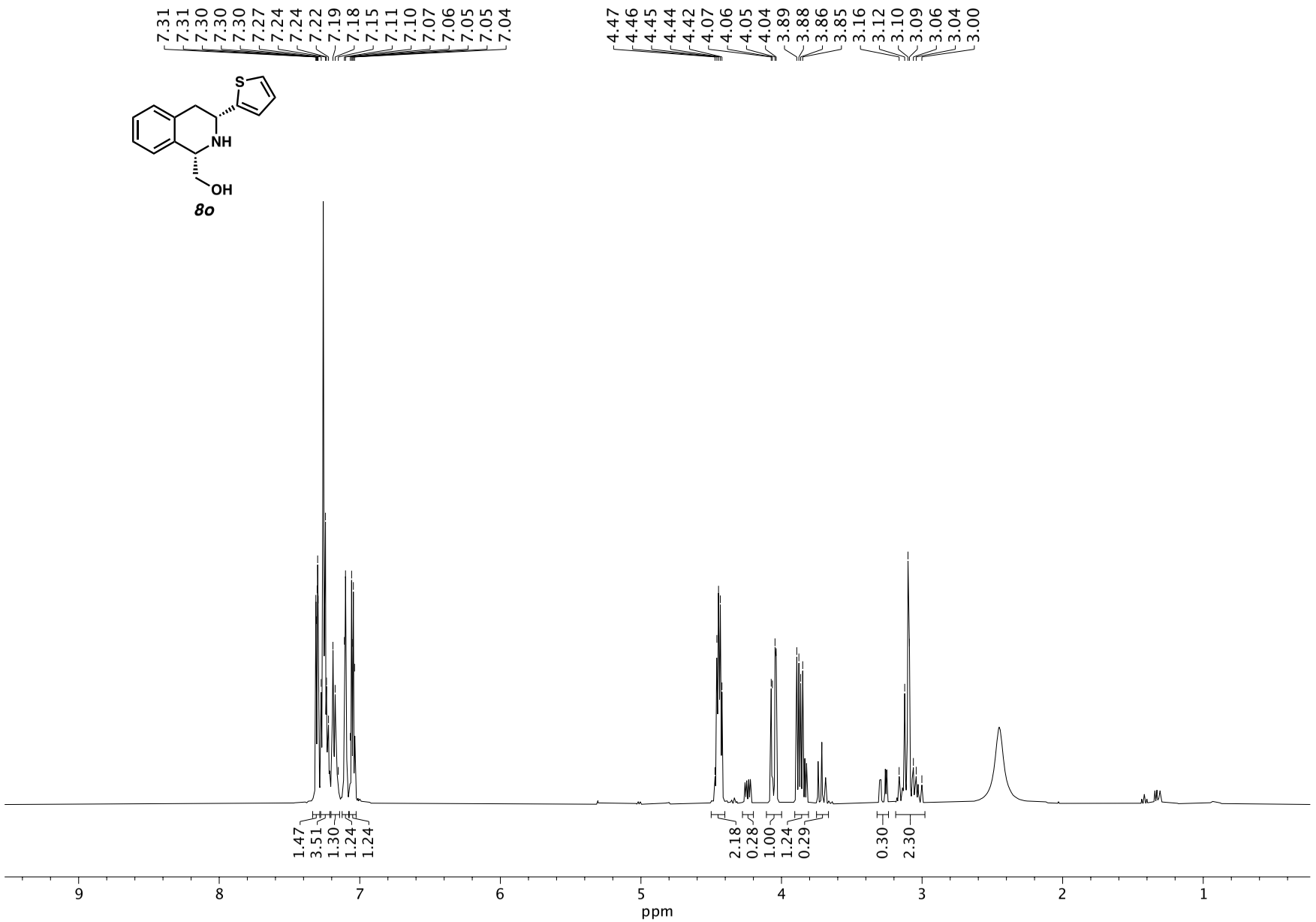
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8n**.



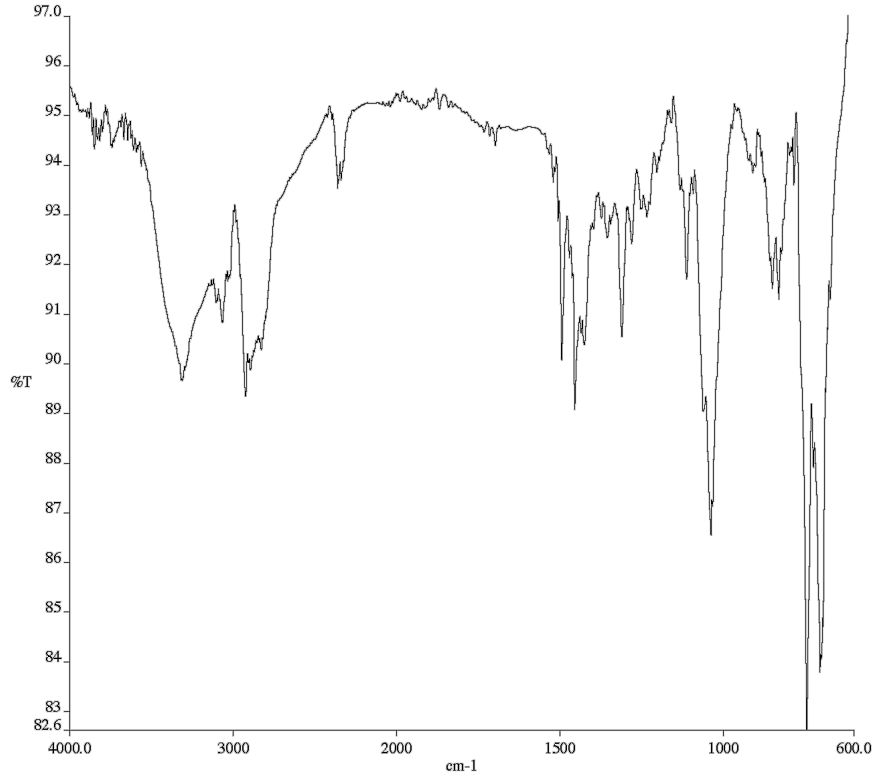
Infrared spectrum (Thin Film, NaCl) of compound **8n**.



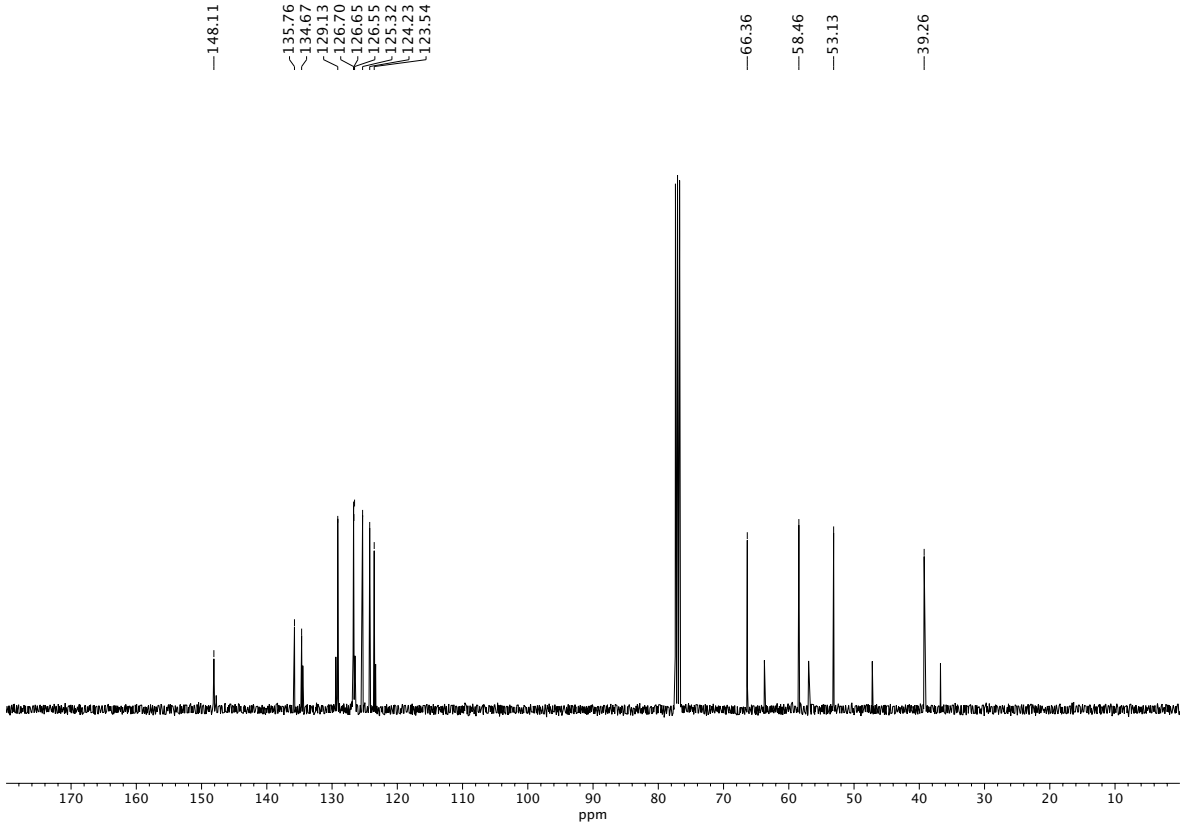
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8n**.



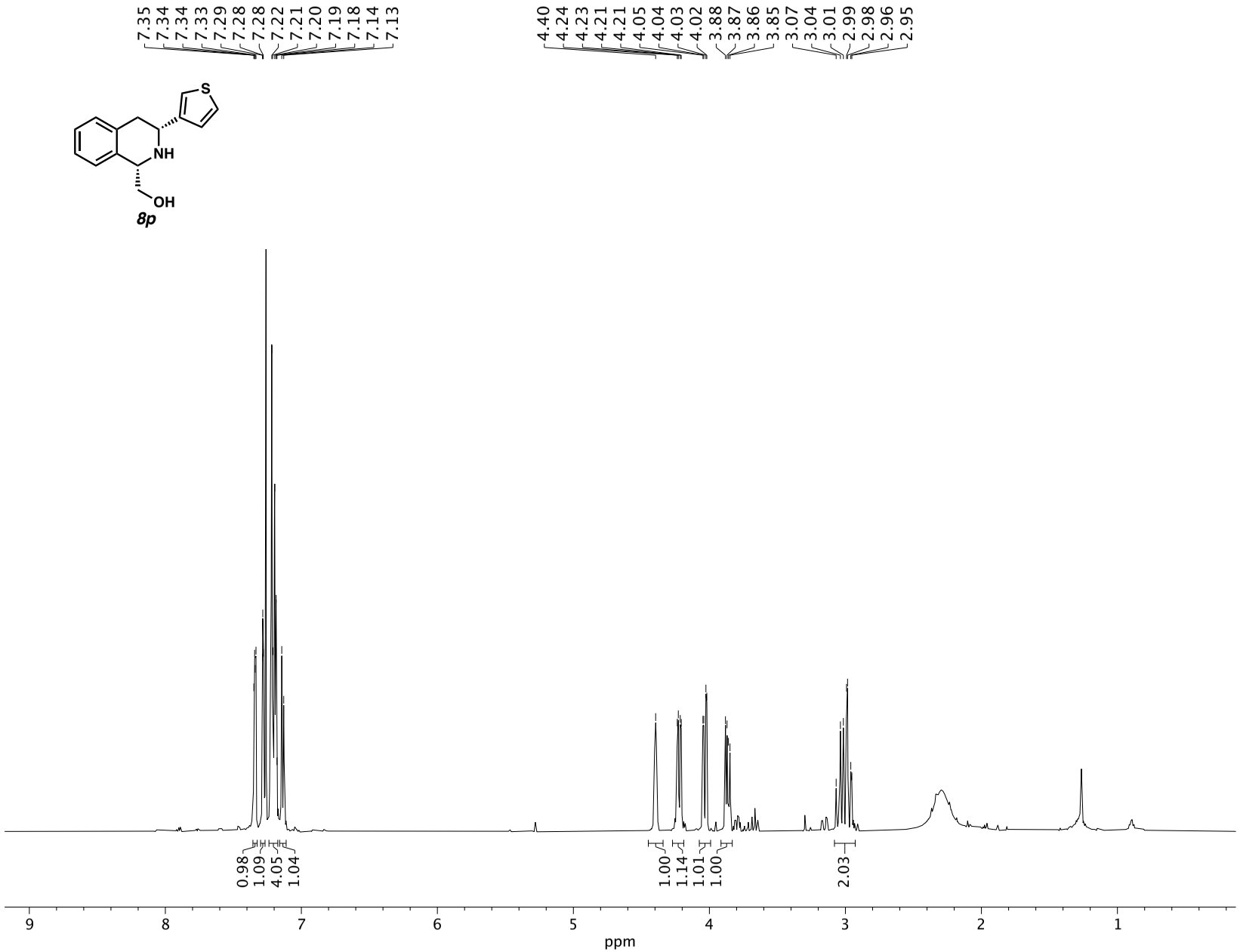
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8o**.



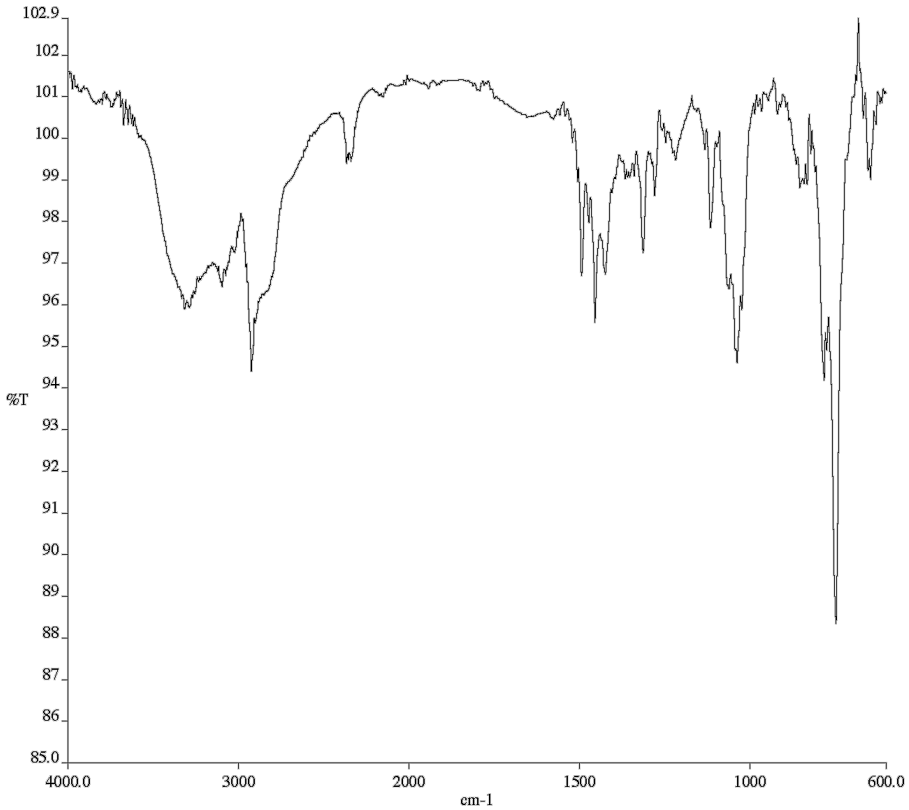
Infrared spectrum (Thin Film, NaCl) of compound **8o**.



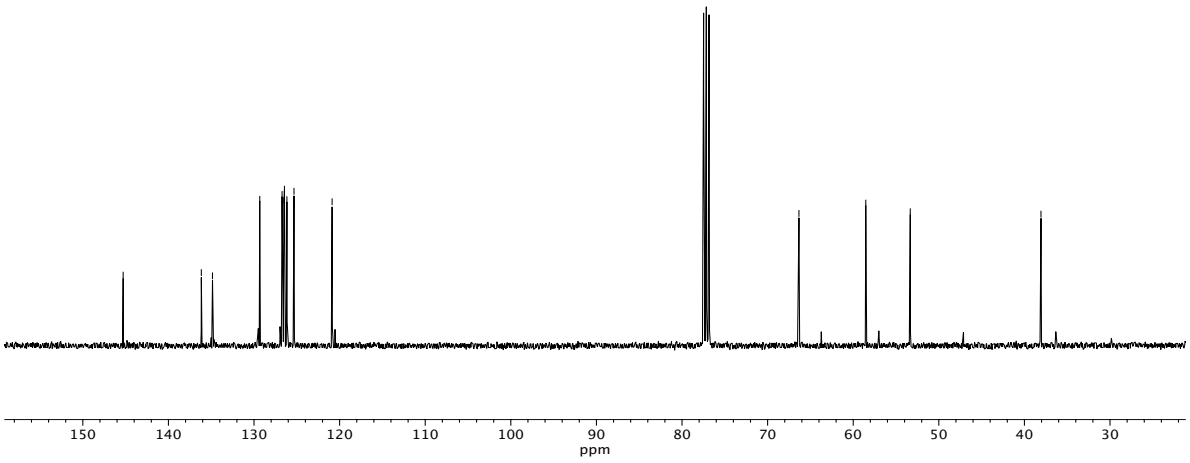
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8o**.



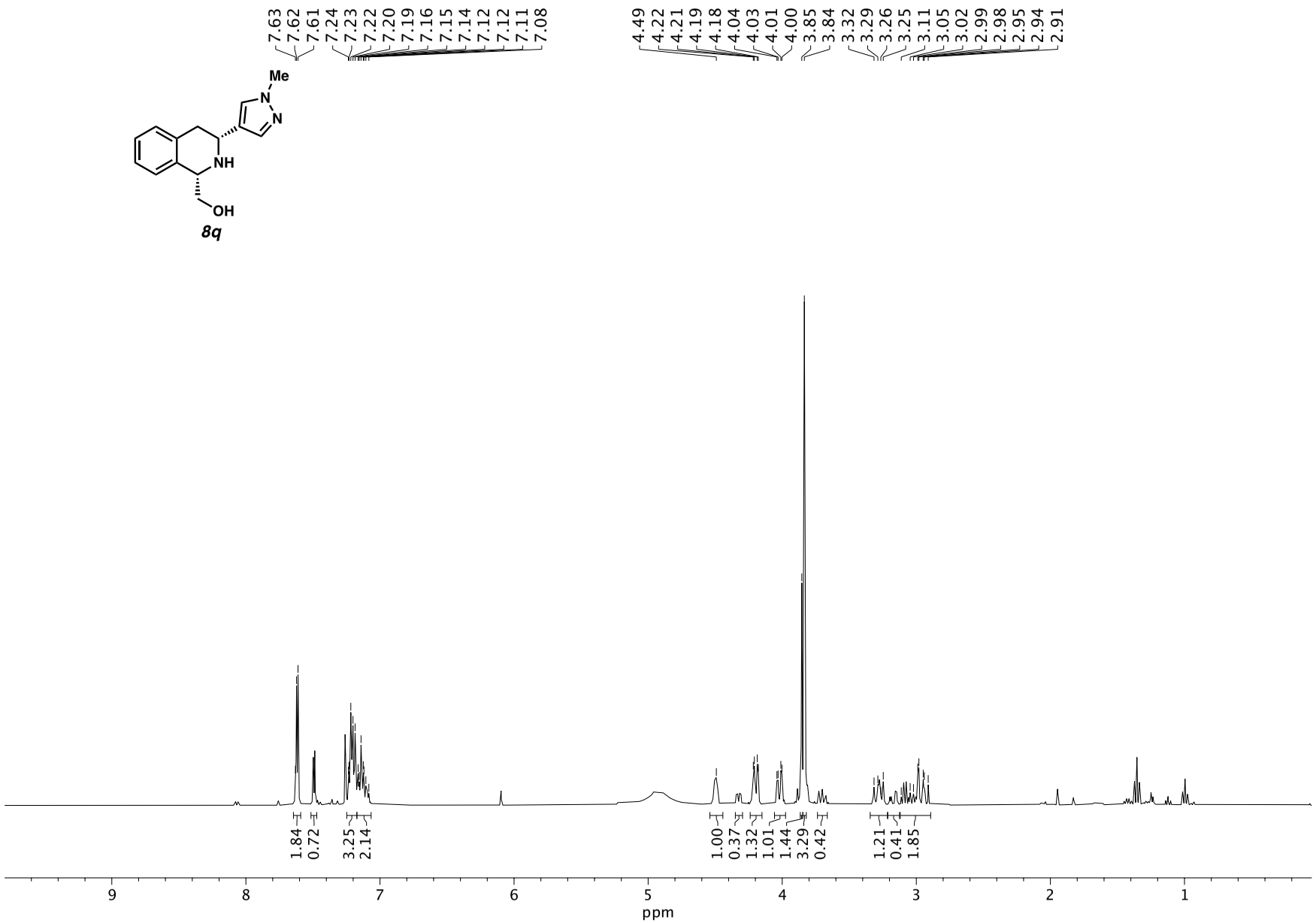
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8p**.



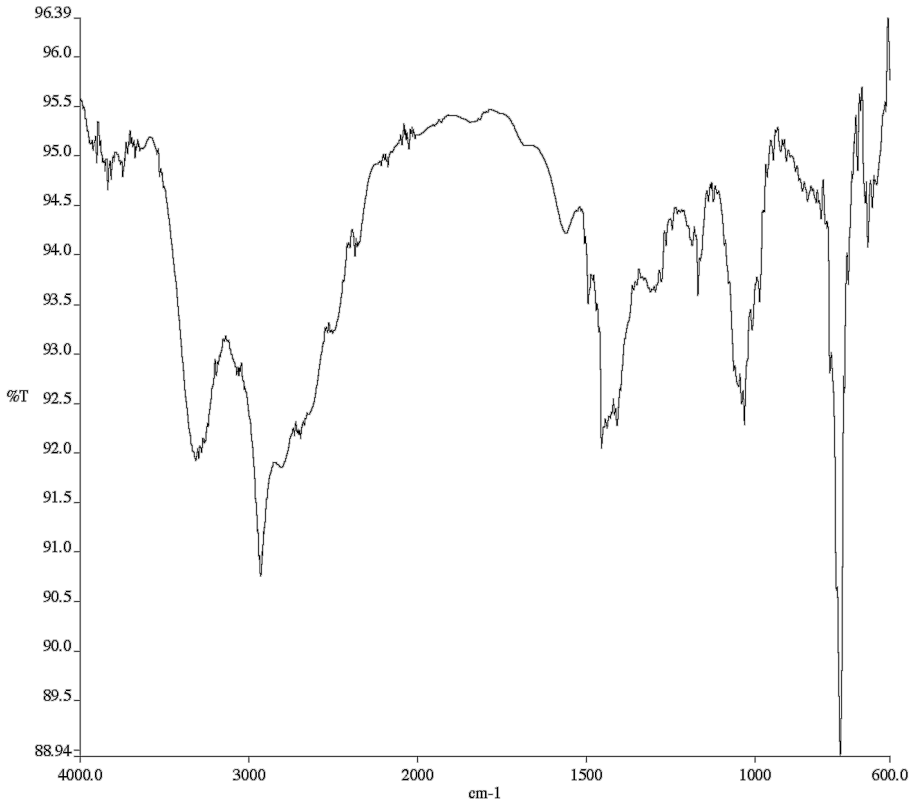
Infrared spectrum (Thin Film, NaCl) of compound **8p**.



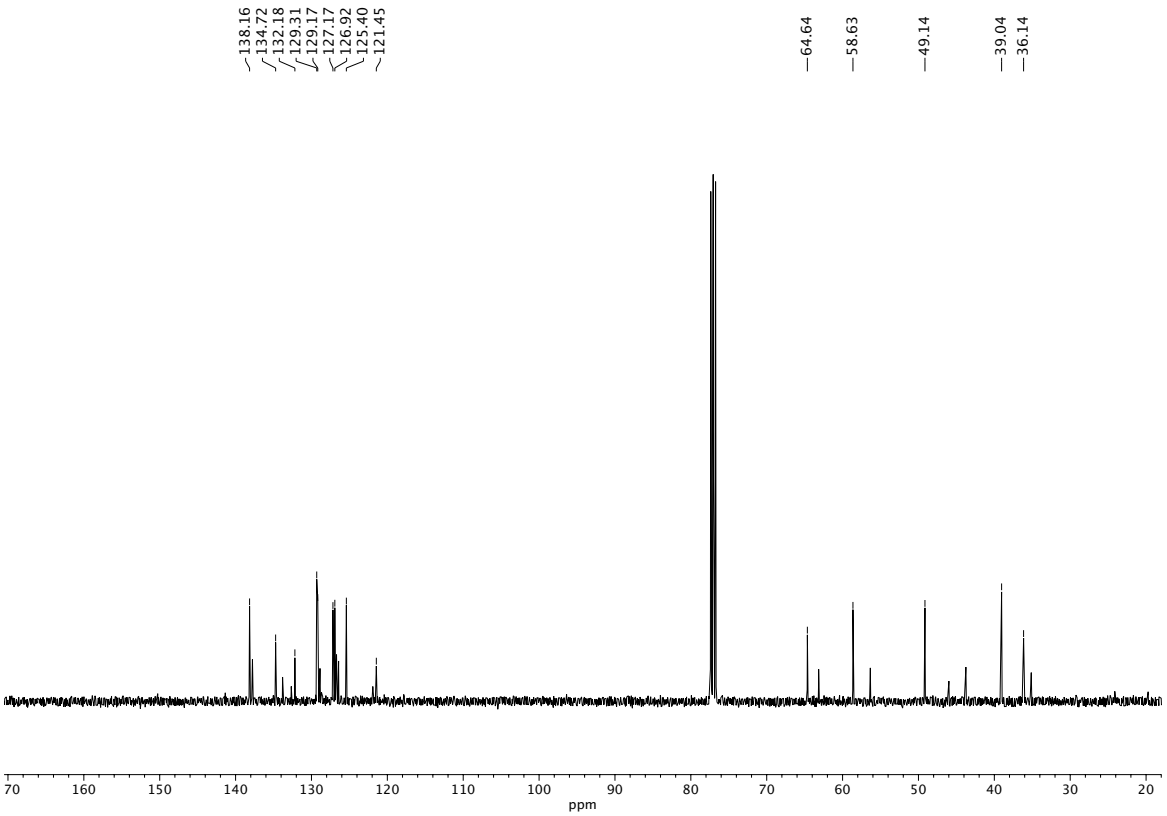
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8p**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **8q**.

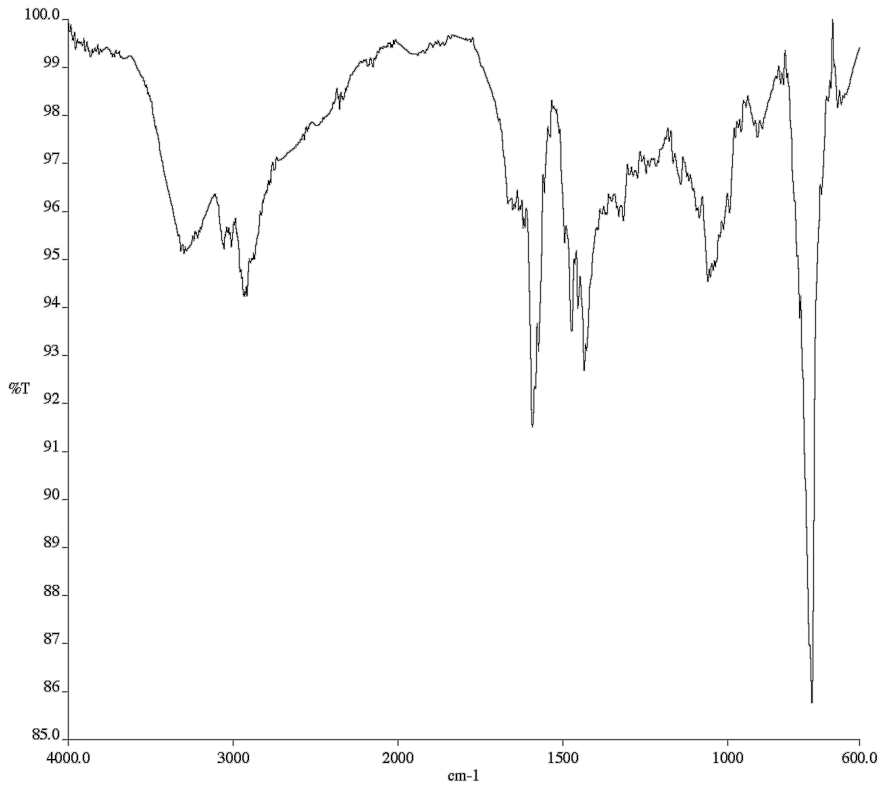


Infrared spectrum (Thin Film, NaCl) of compound **8q**.

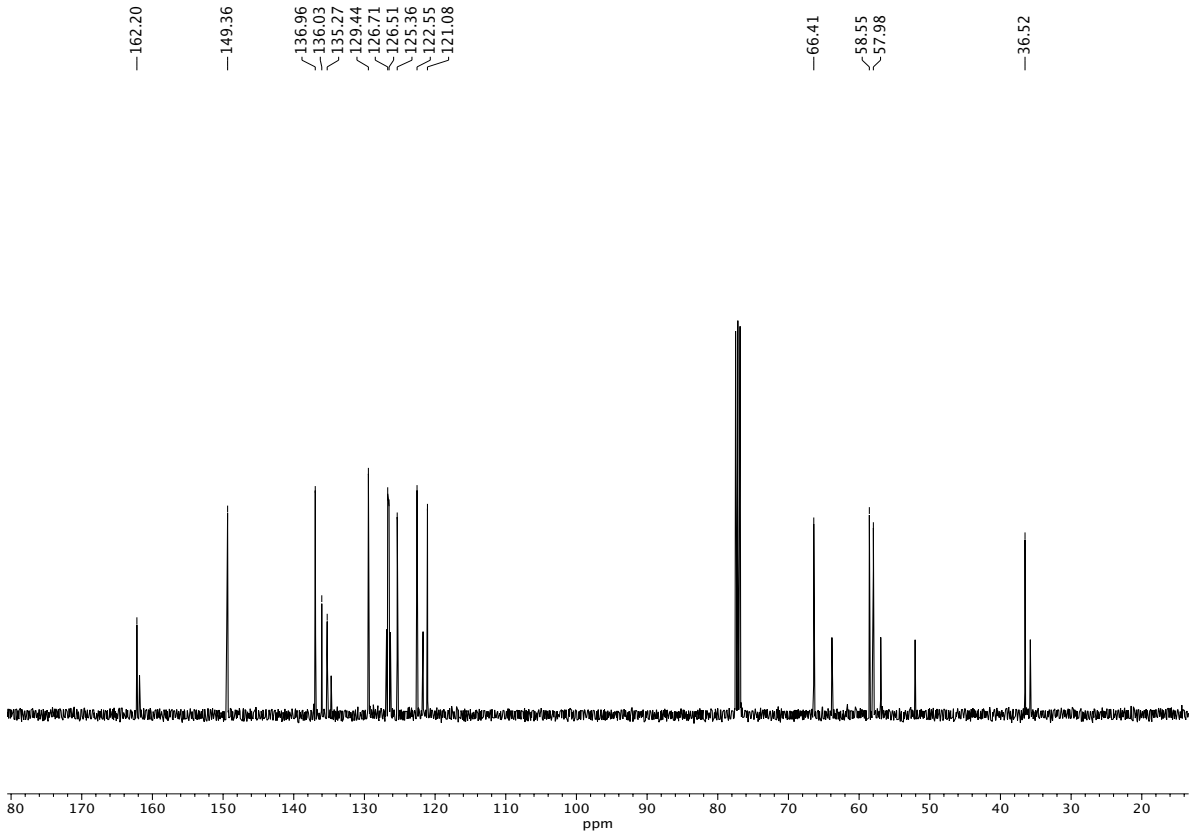


^{13}C NMR (100 MHz, $CDCl_3$) of compound **8q**.

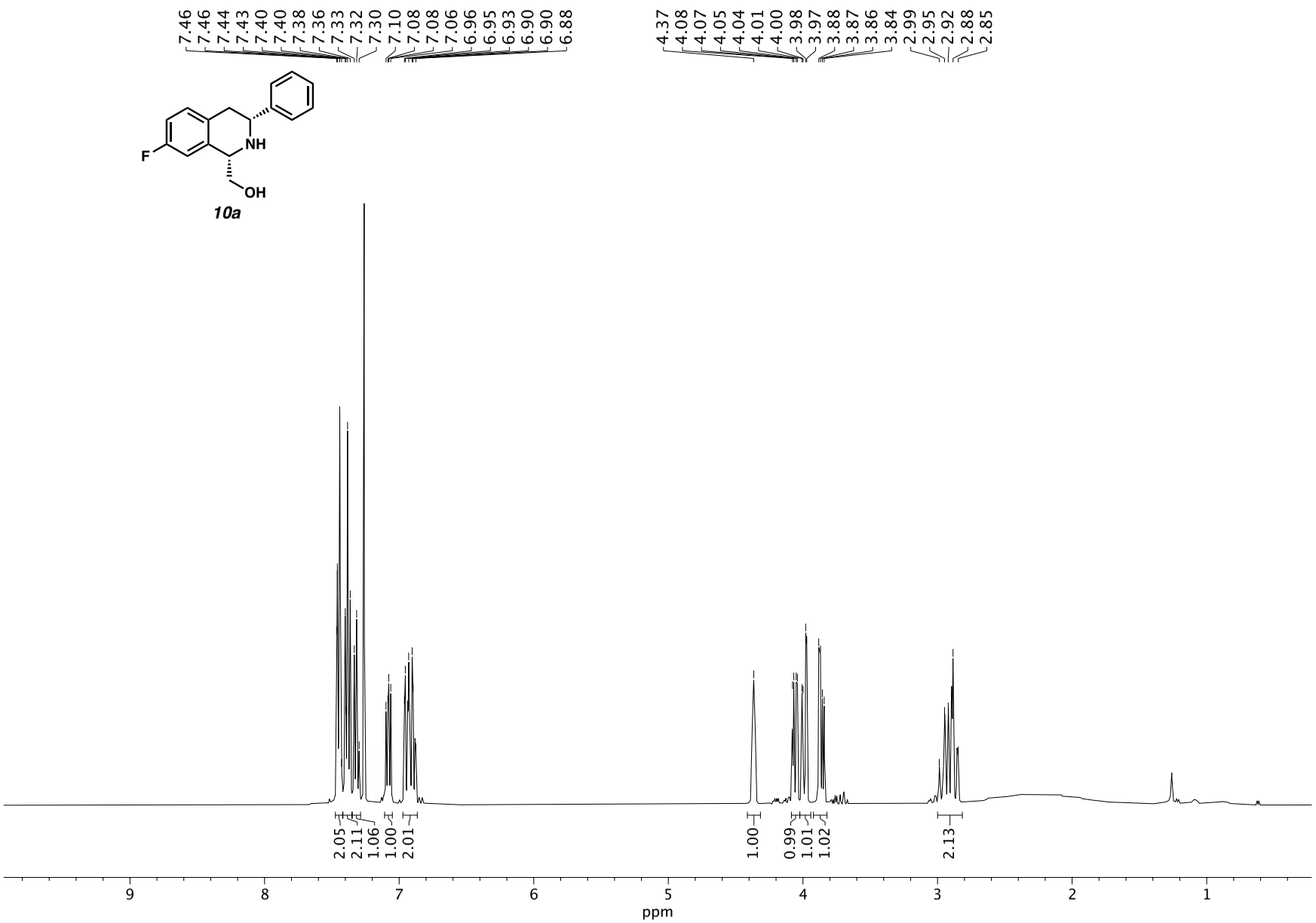
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8r**.



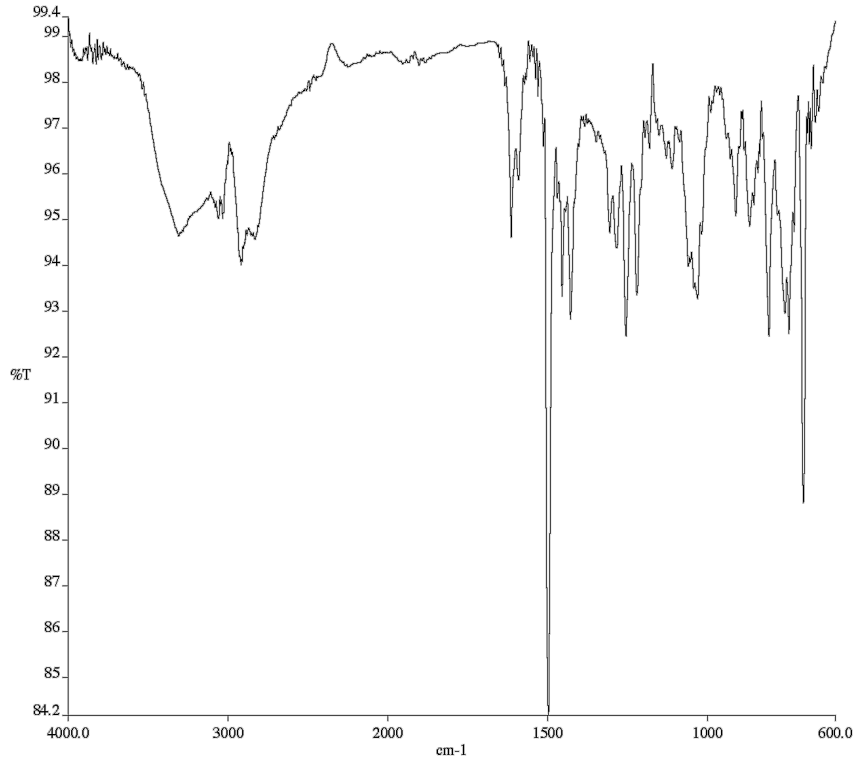
Infrared spectrum (Thin Film, NaCl) of compound **8r**.



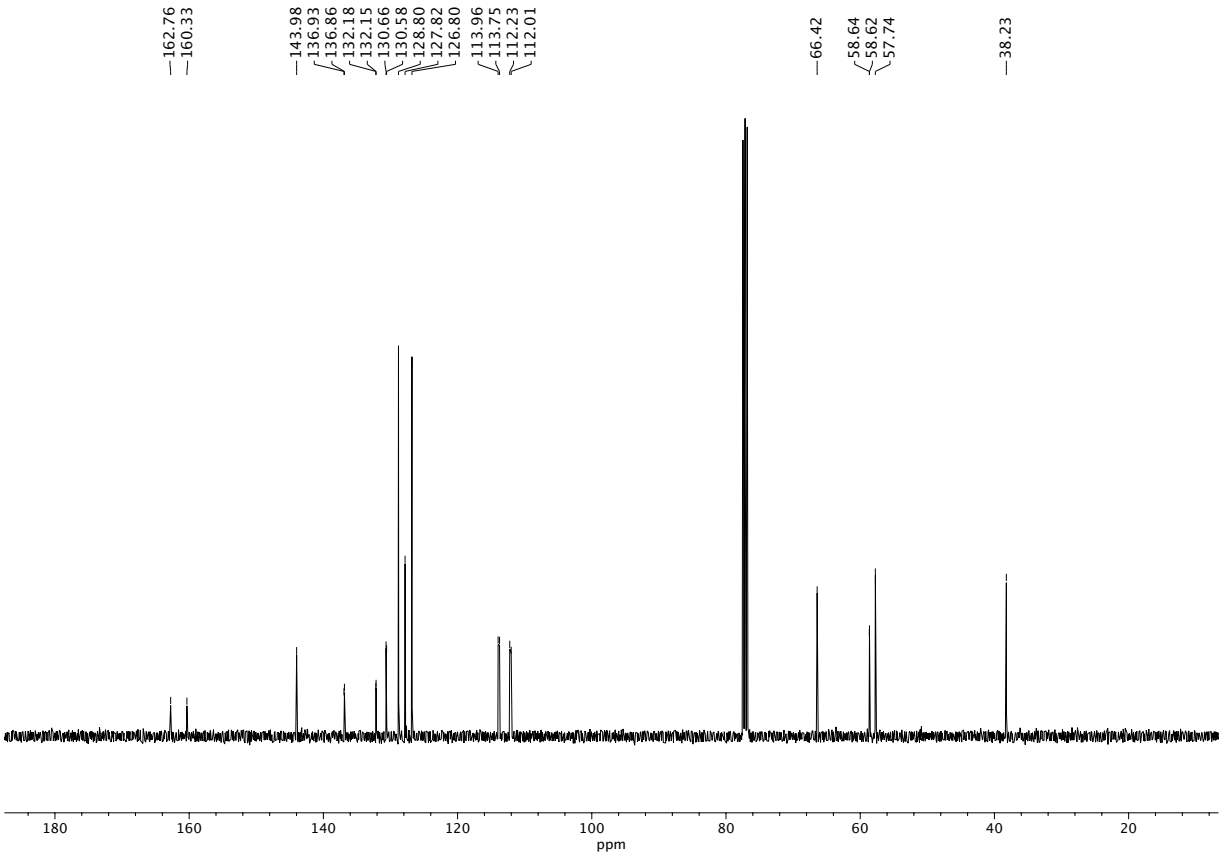
^{13}C NMR (100 MHz, $CDCl_3$) of compound **8r**.



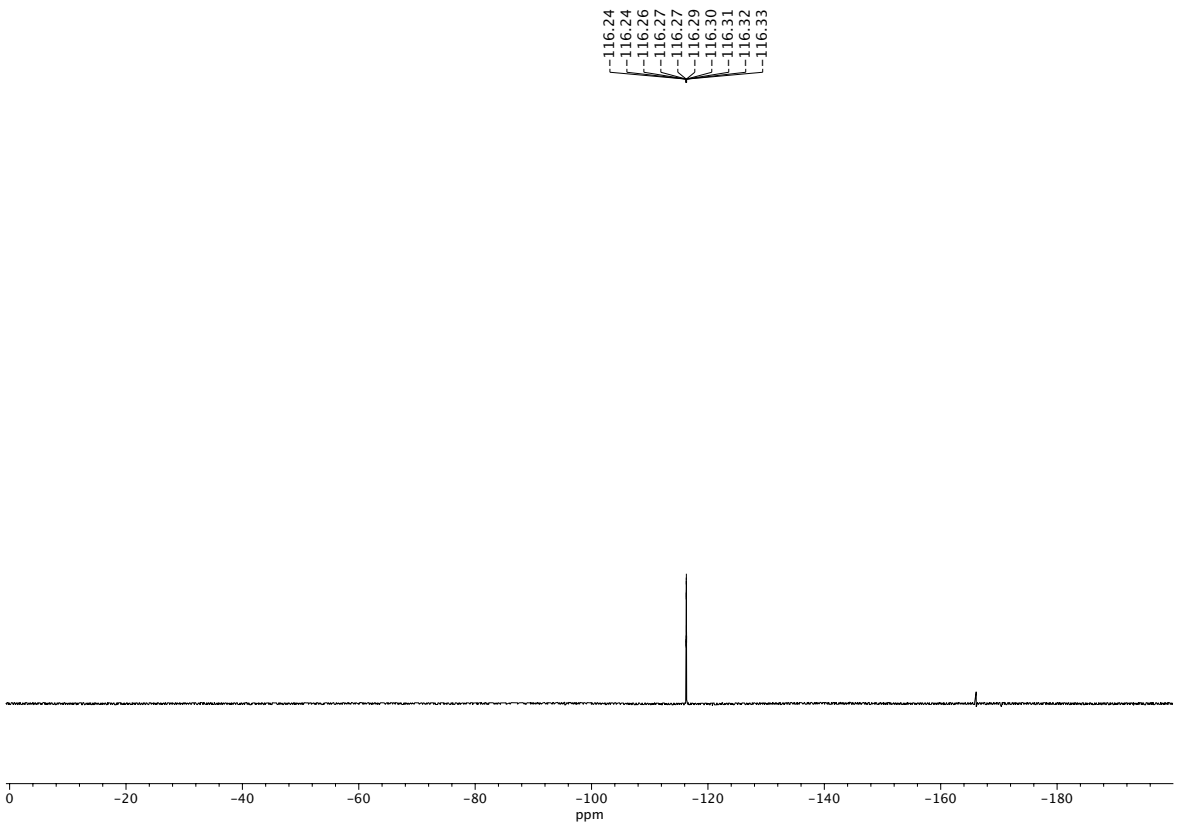
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10a**.



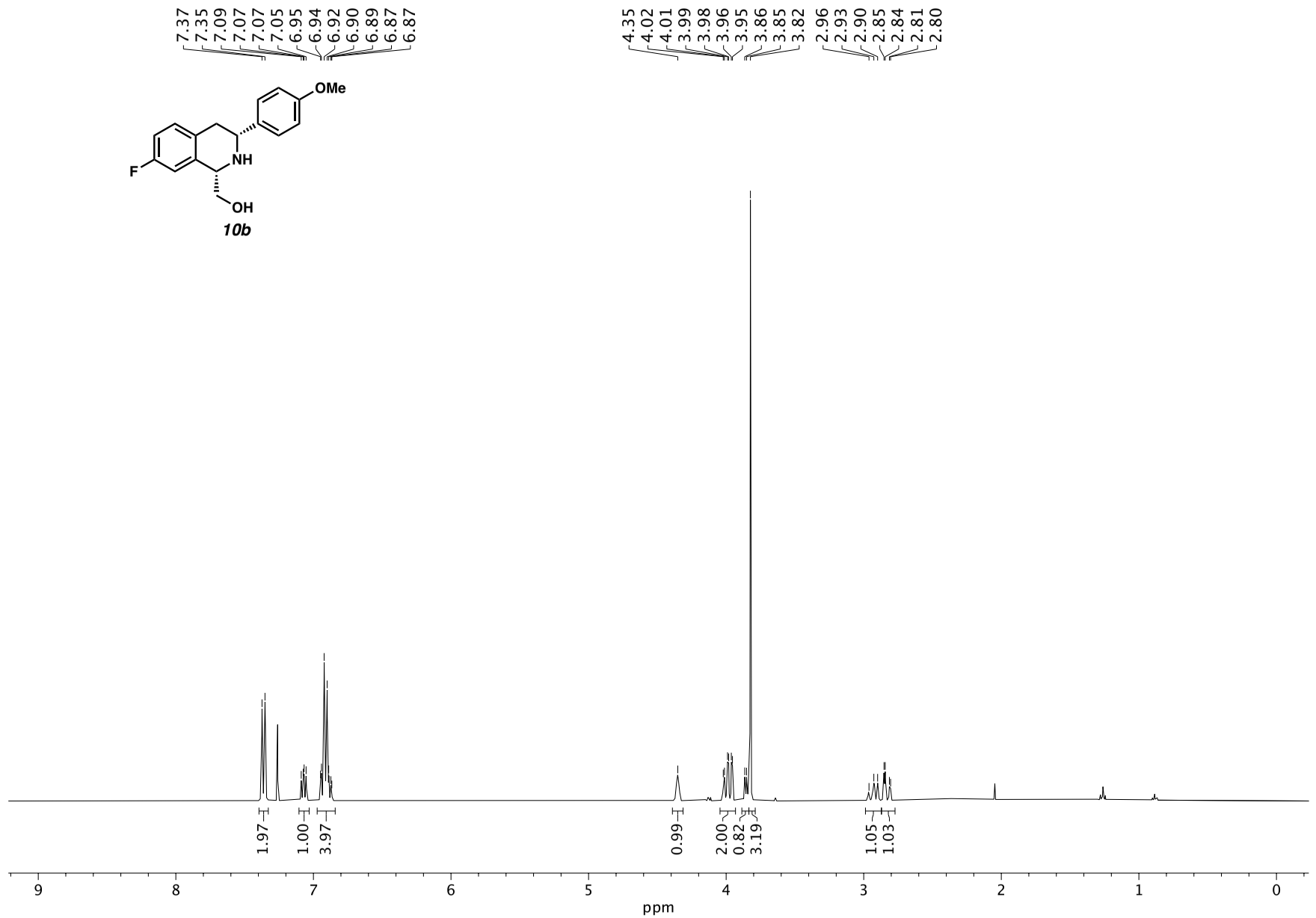
Infrared spectrum (Thin Film, NaCl) of compound **10a**.



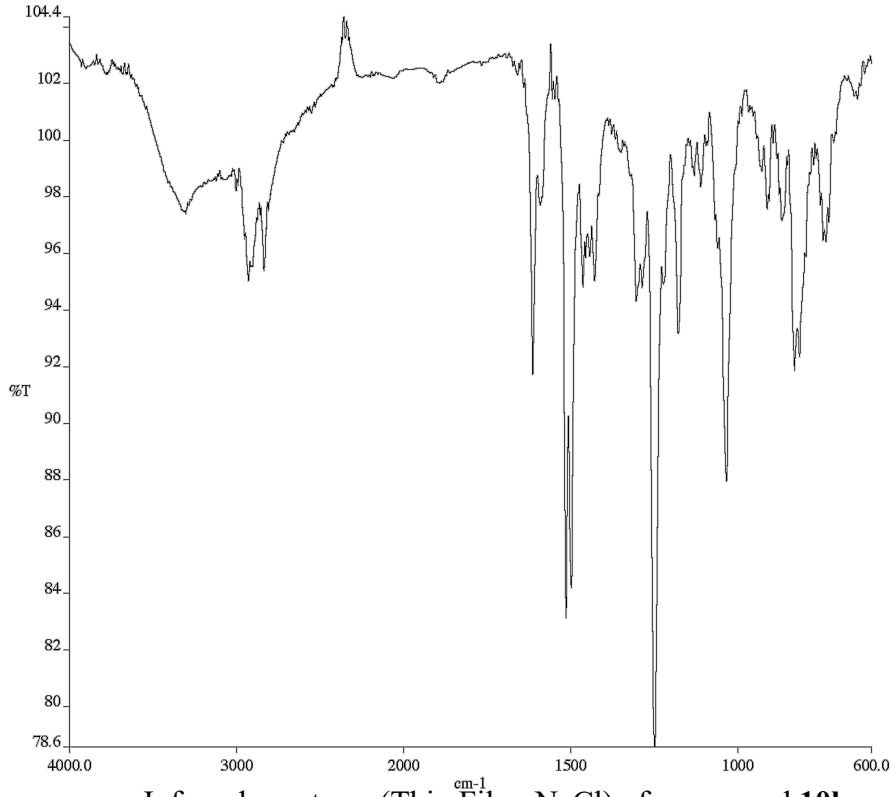
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10a**.



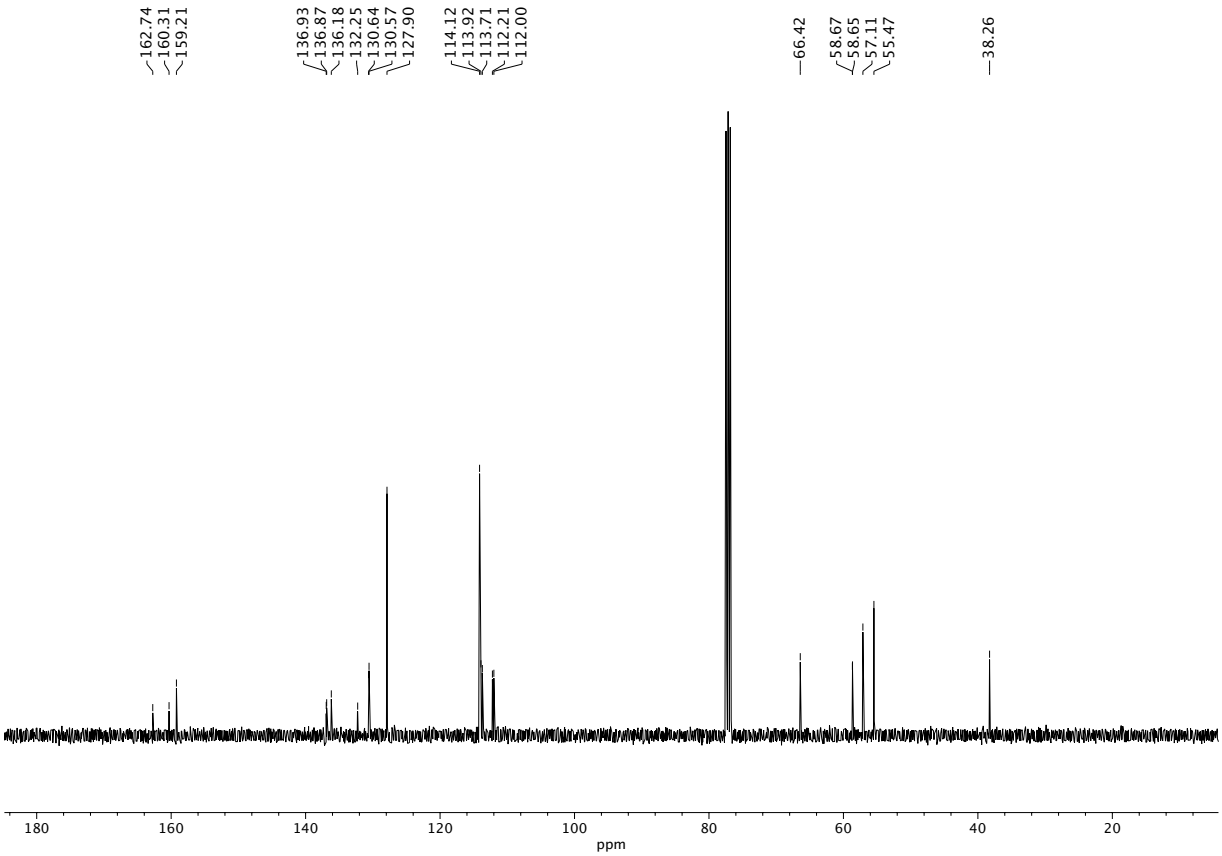
^{19}F NMR (282 MHz, $CDCl_3$) of **10a**.



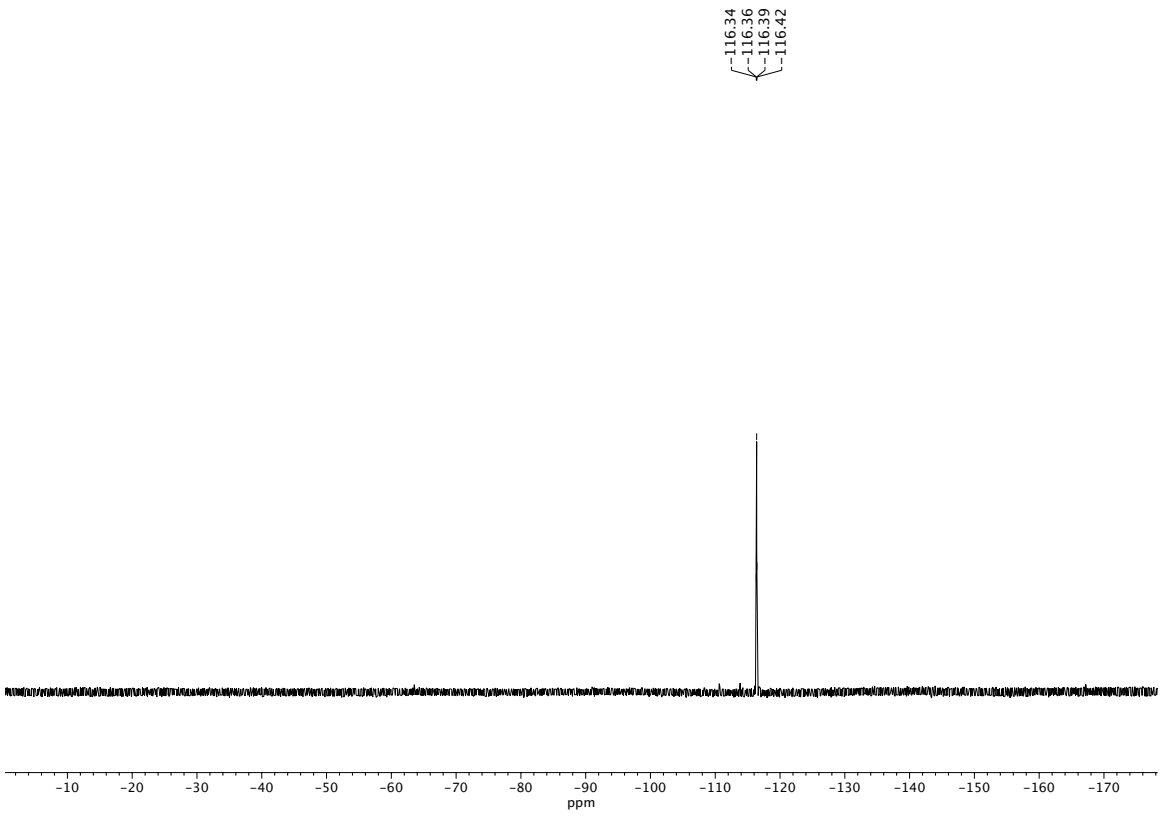
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10b**.



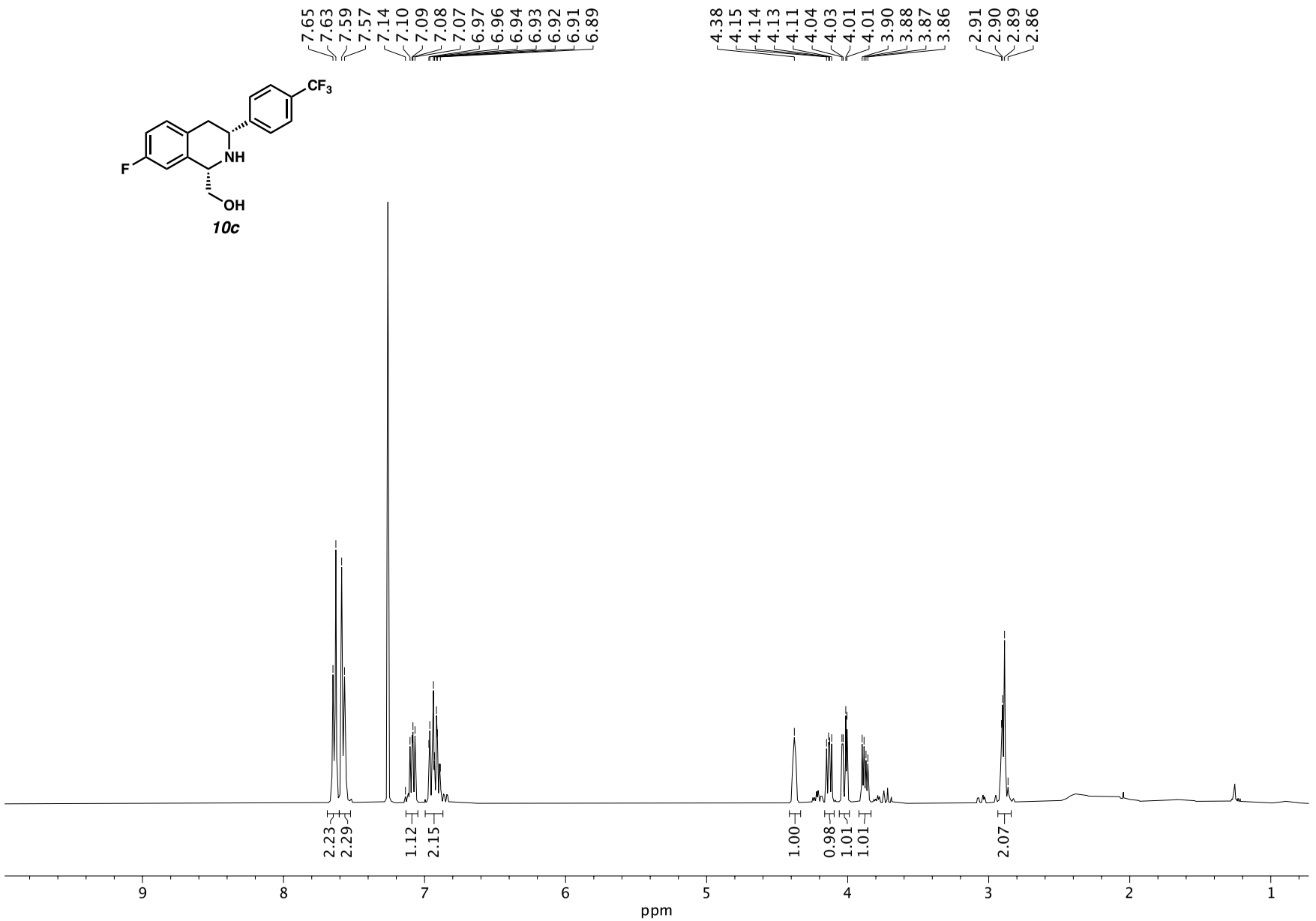
Infrared spectrum (Thin Film, NaCl) of compound **10b**.



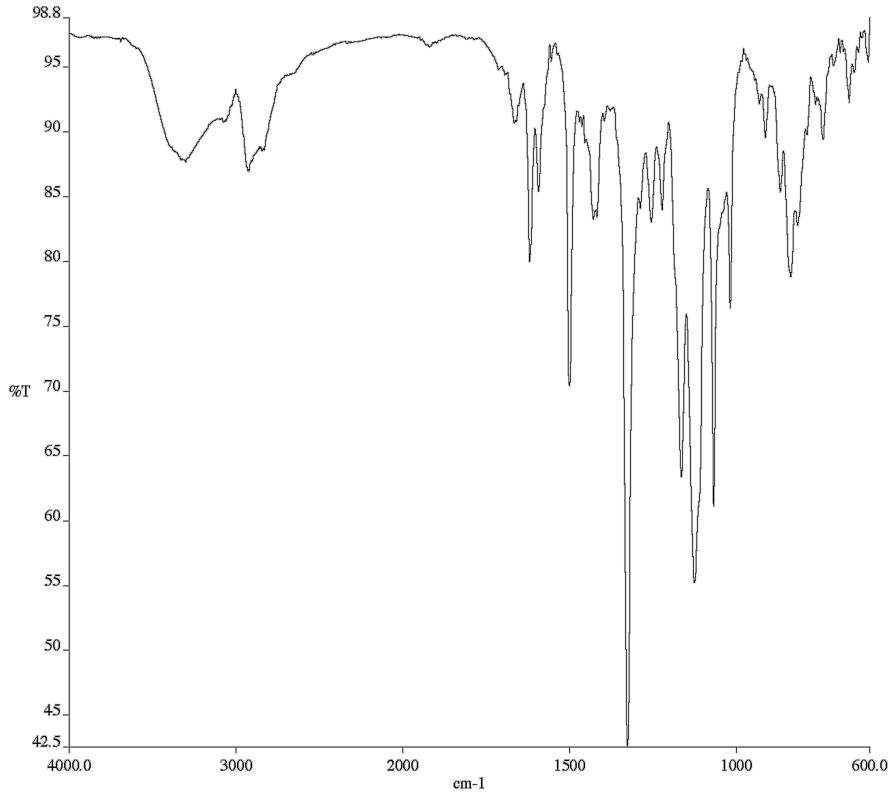
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10b**.



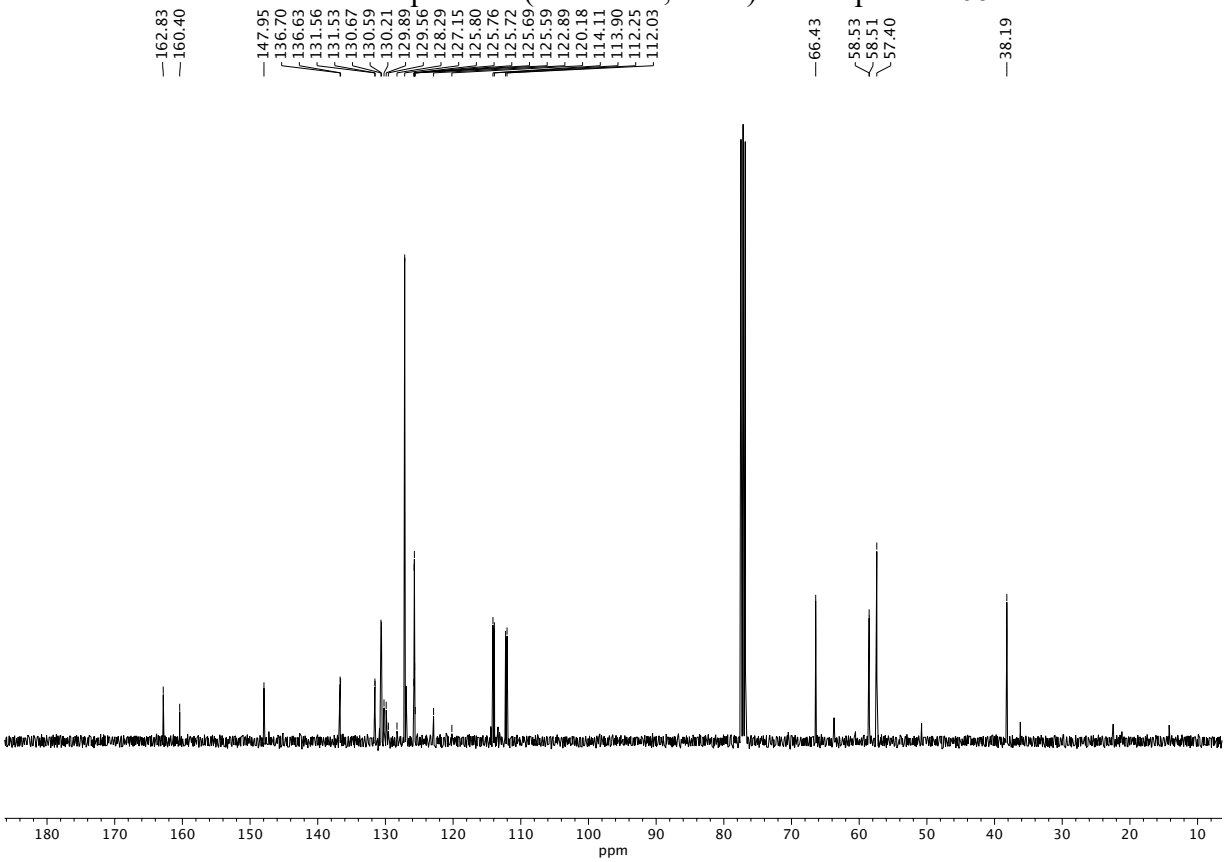
^{19}F NMR (282 MHz, $CDCl_3$) of **10b**.



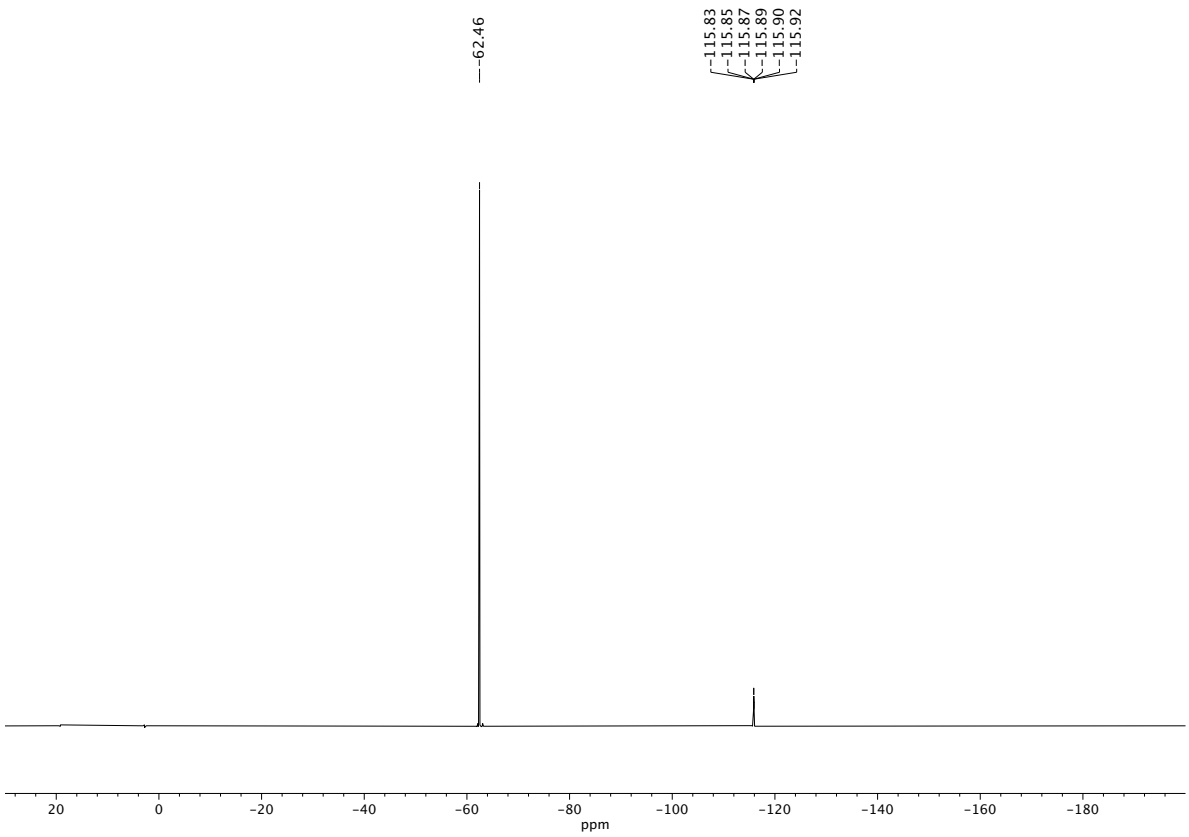
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10c**.



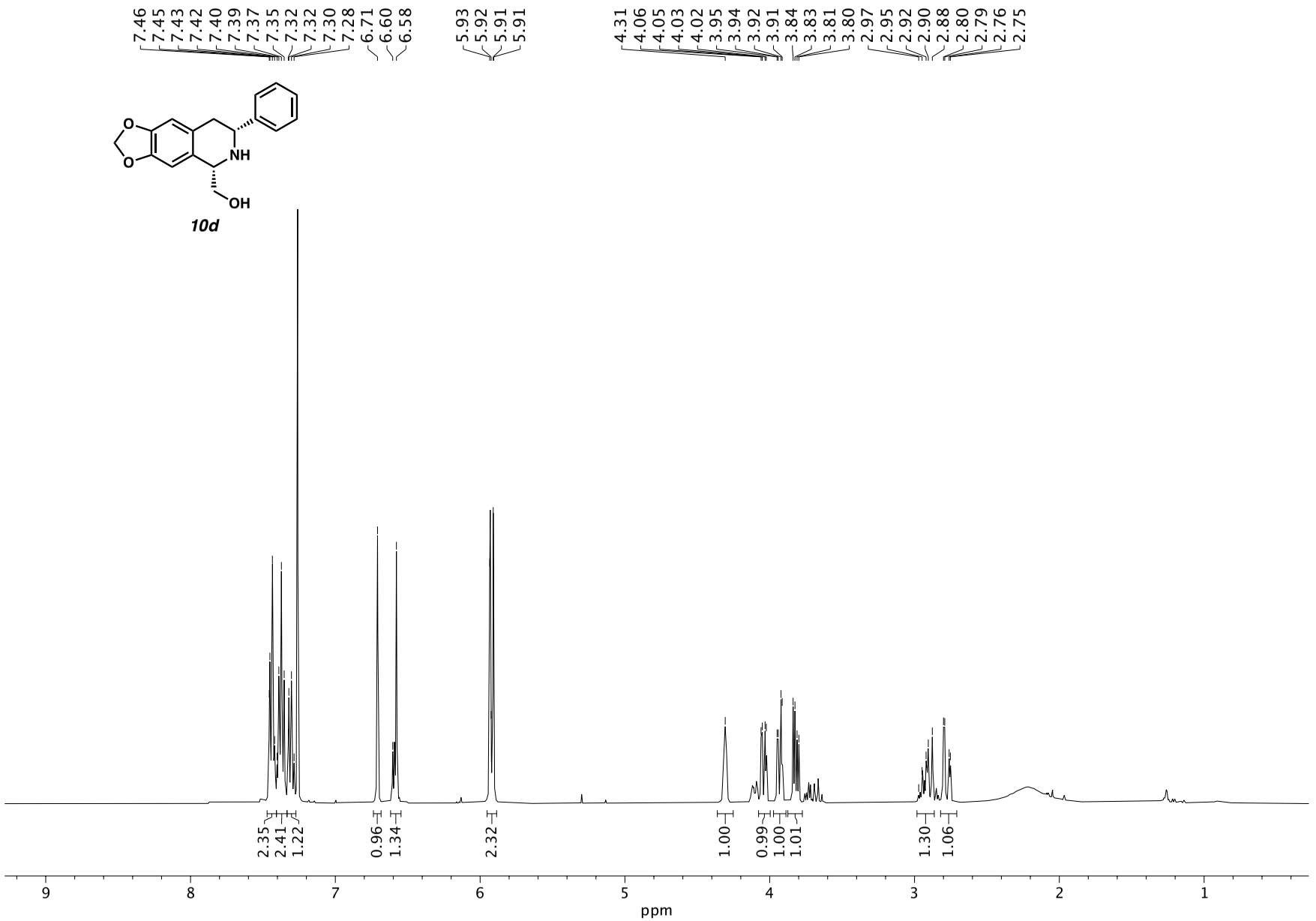
Infrared spectrum (Thin Film, NaCl) of compound **10c**.



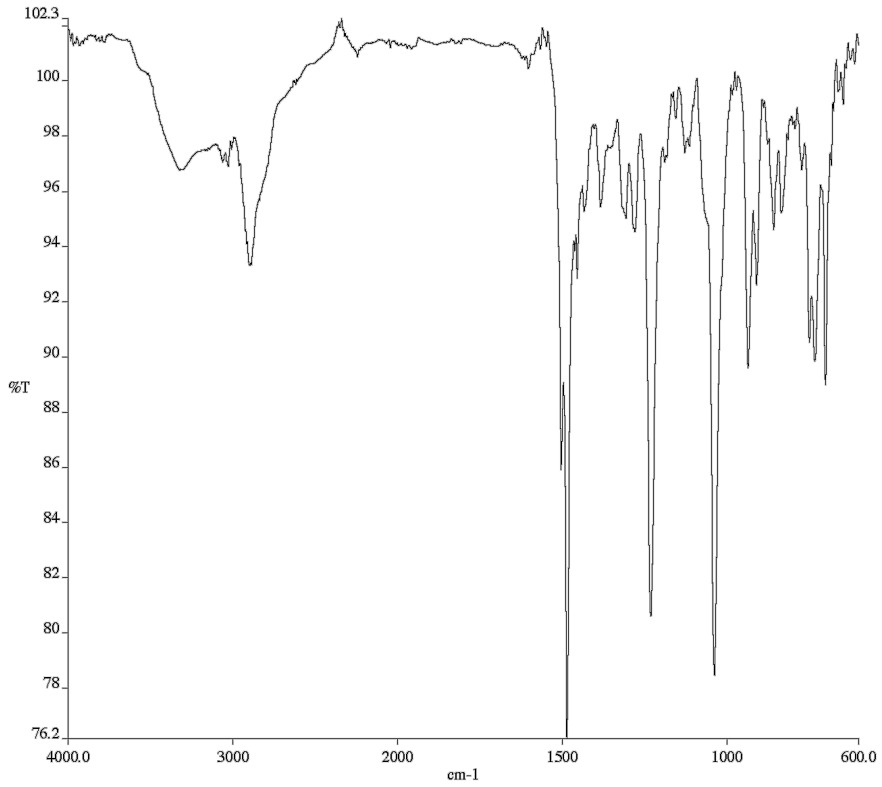
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10c**.



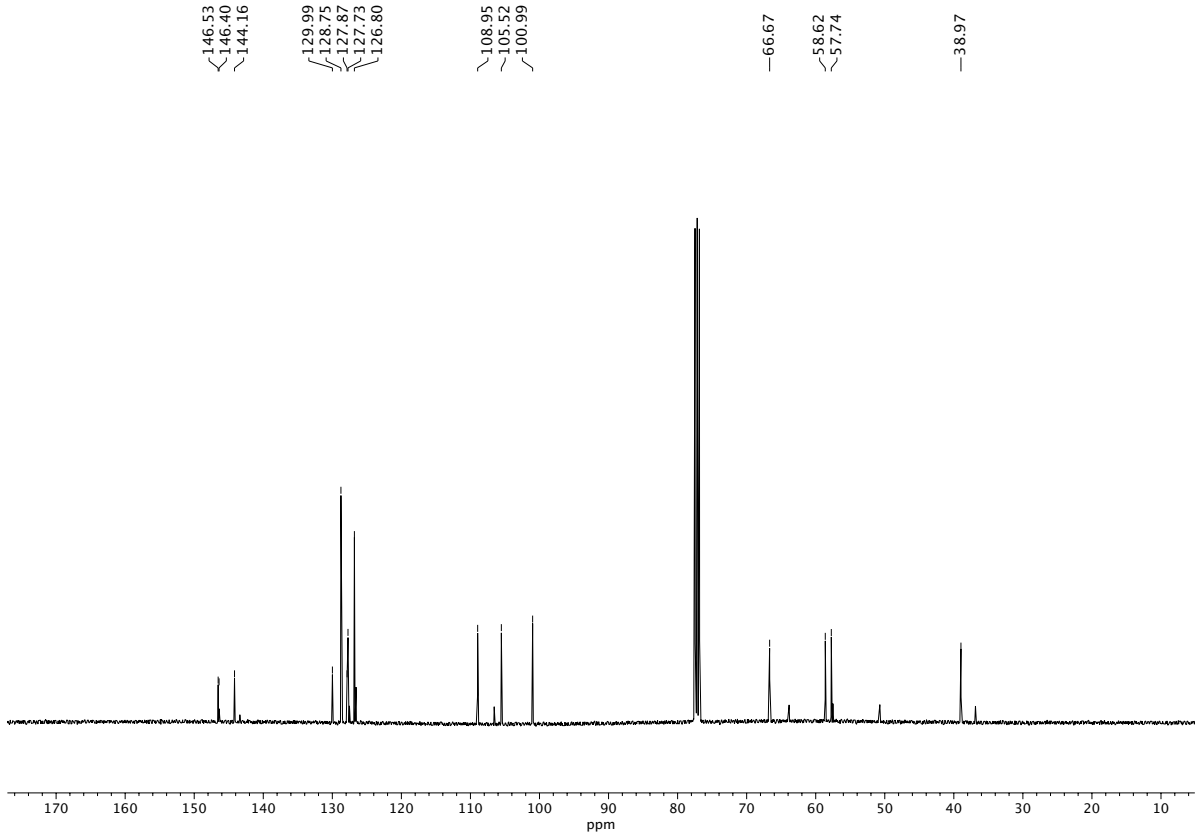
^{19}F NMR (282 MHz, $CDCl_3$) of **10c**.



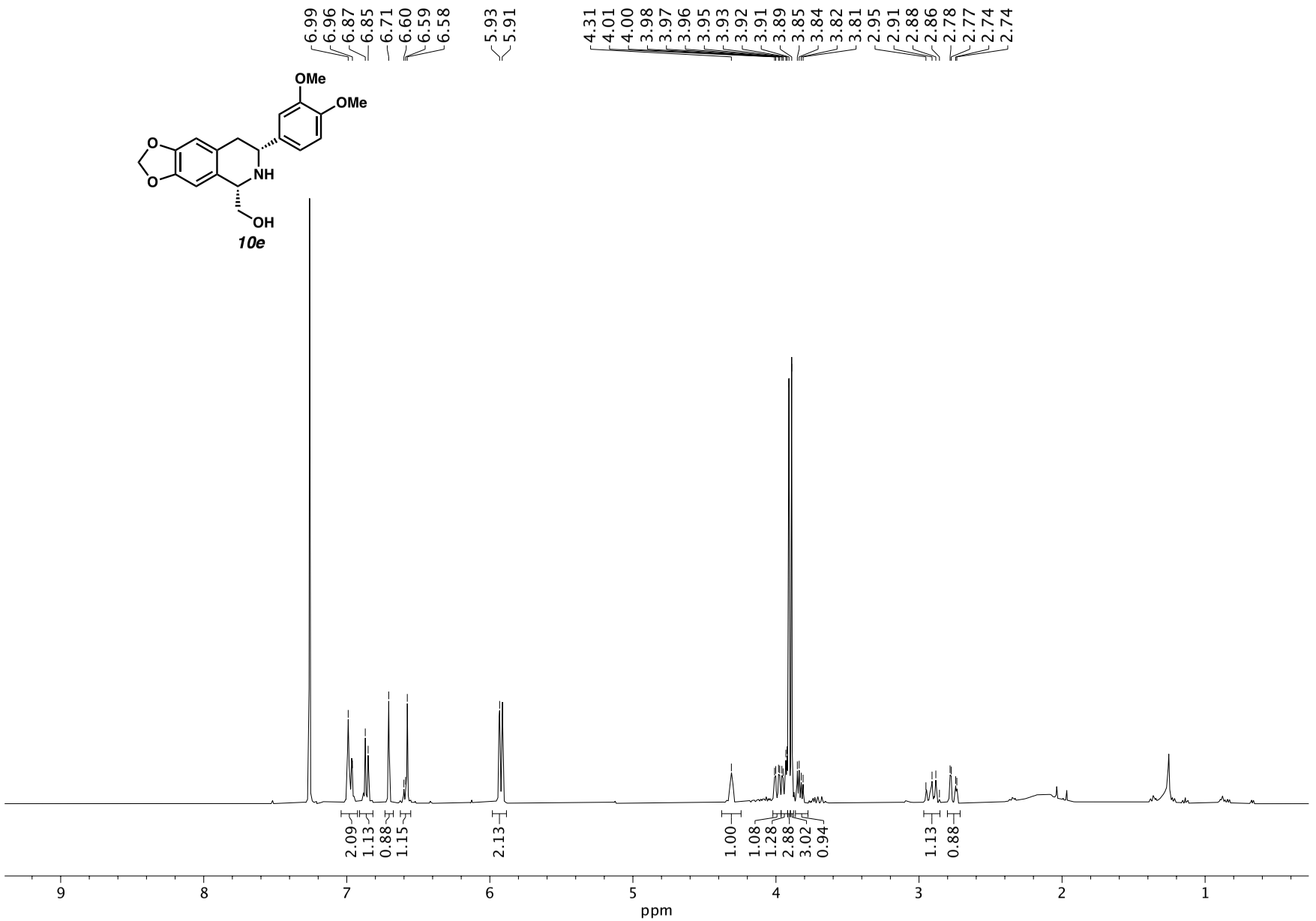
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10d**.



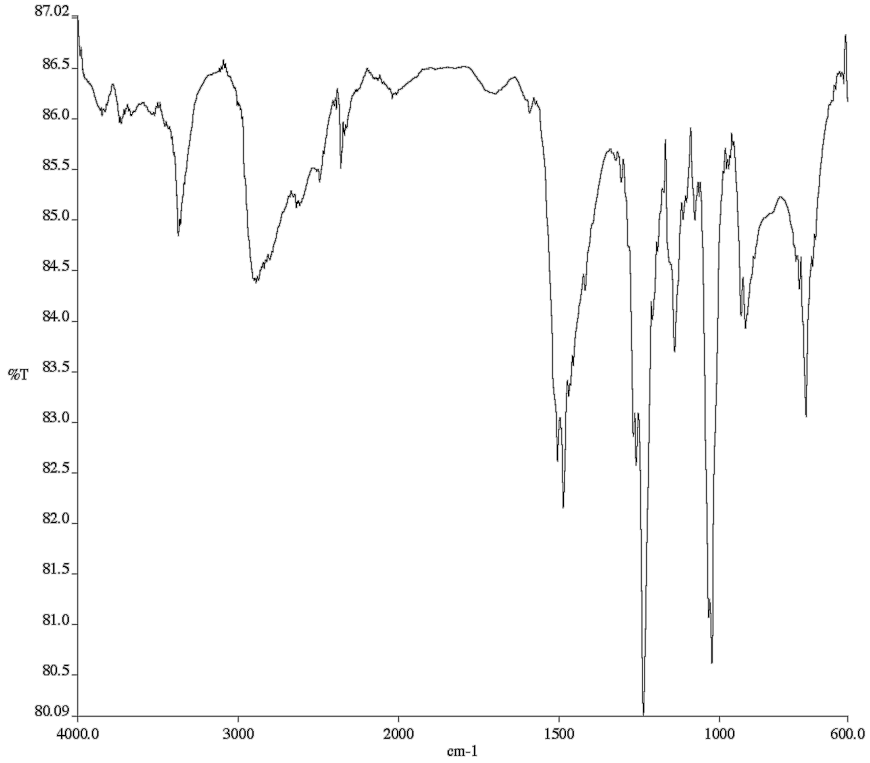
Infrared spectrum (Thin Film, NaCl) of compound **10d**.



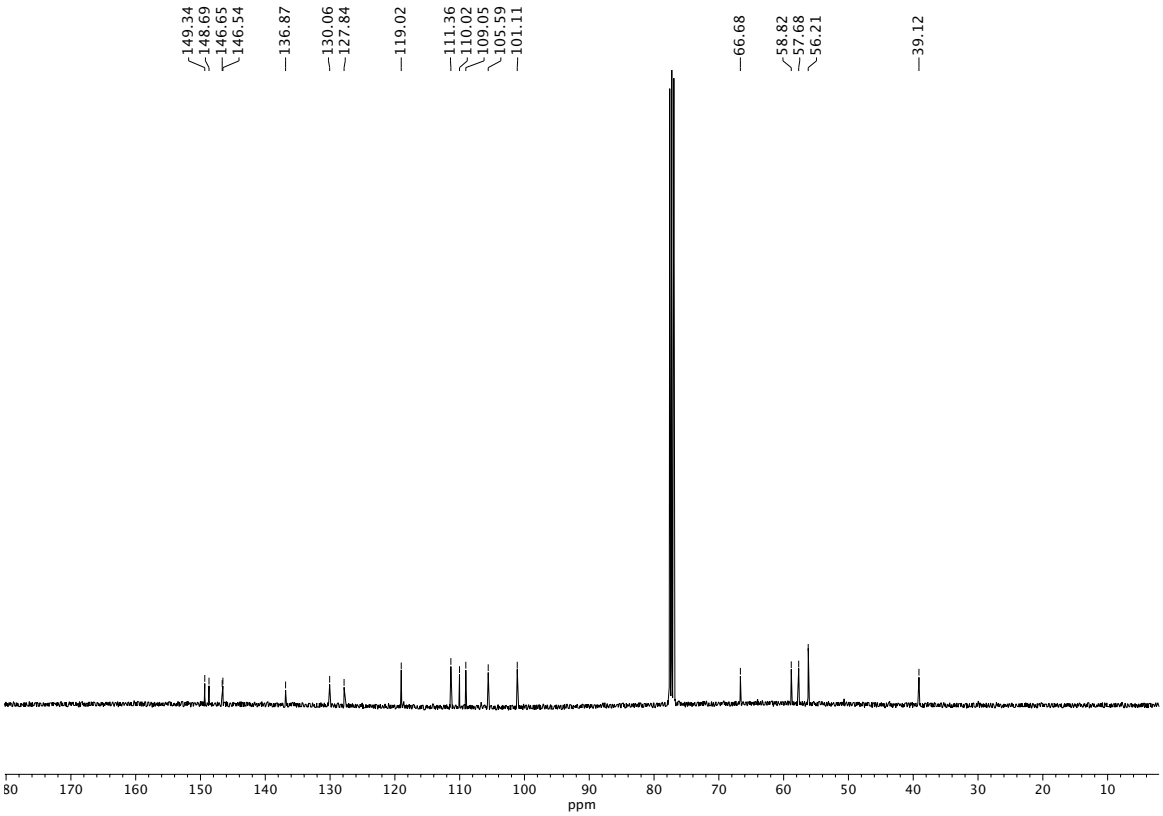
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10d**.



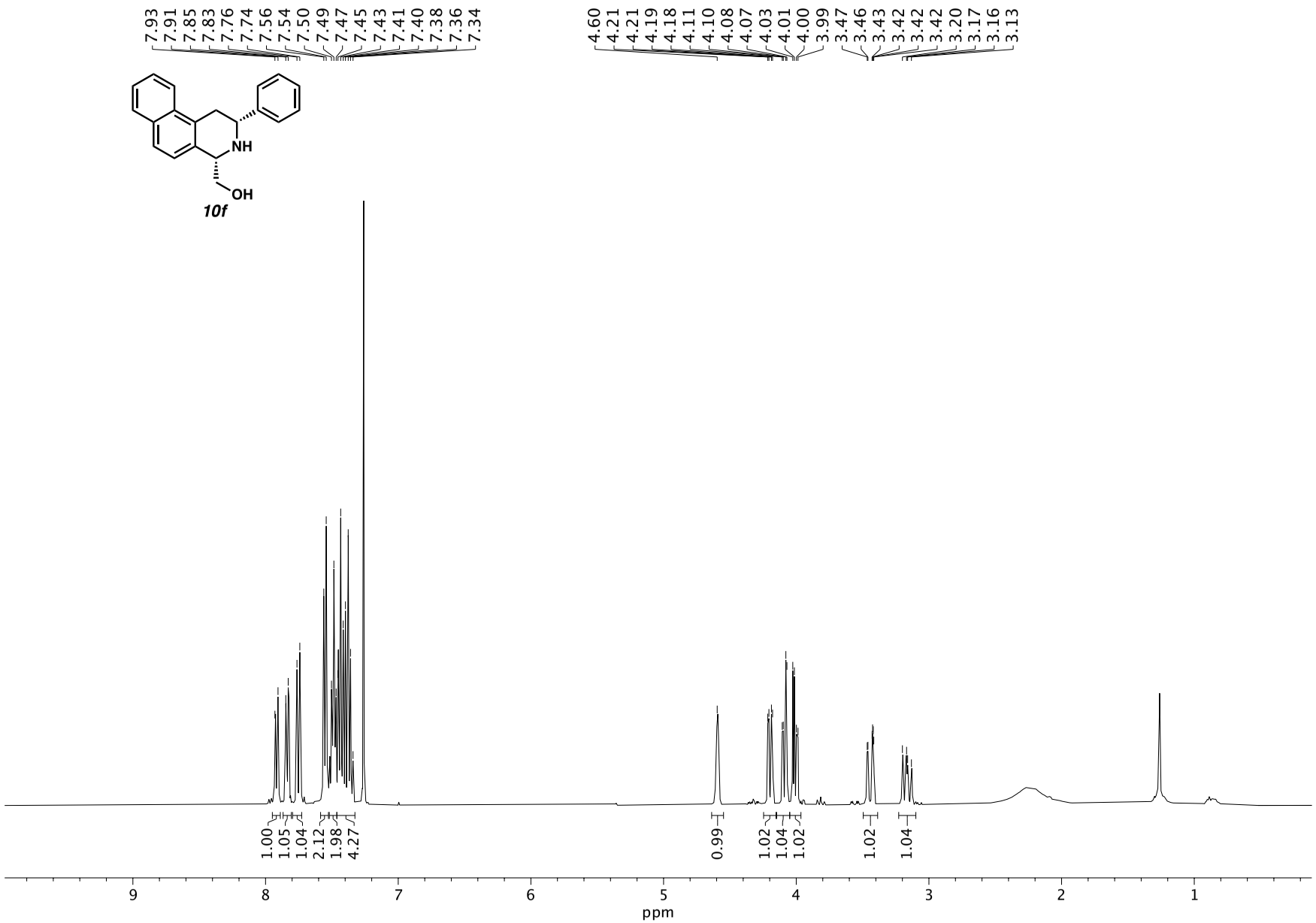
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10e**.



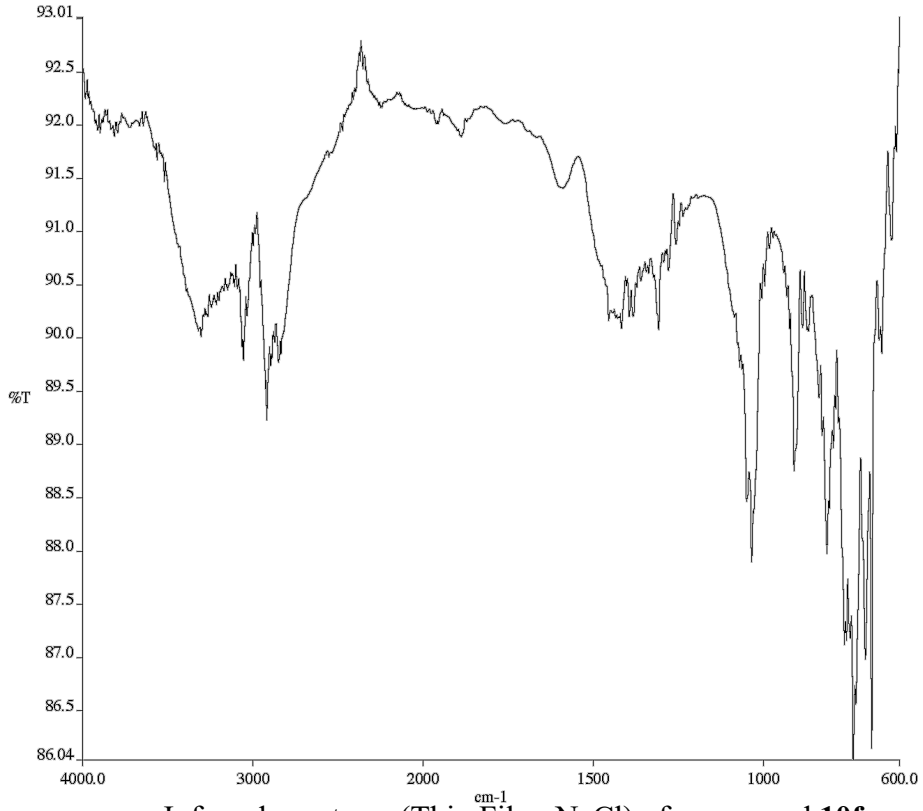
Infrared spectrum (Thin Film, NaCl) of compound **10e**.



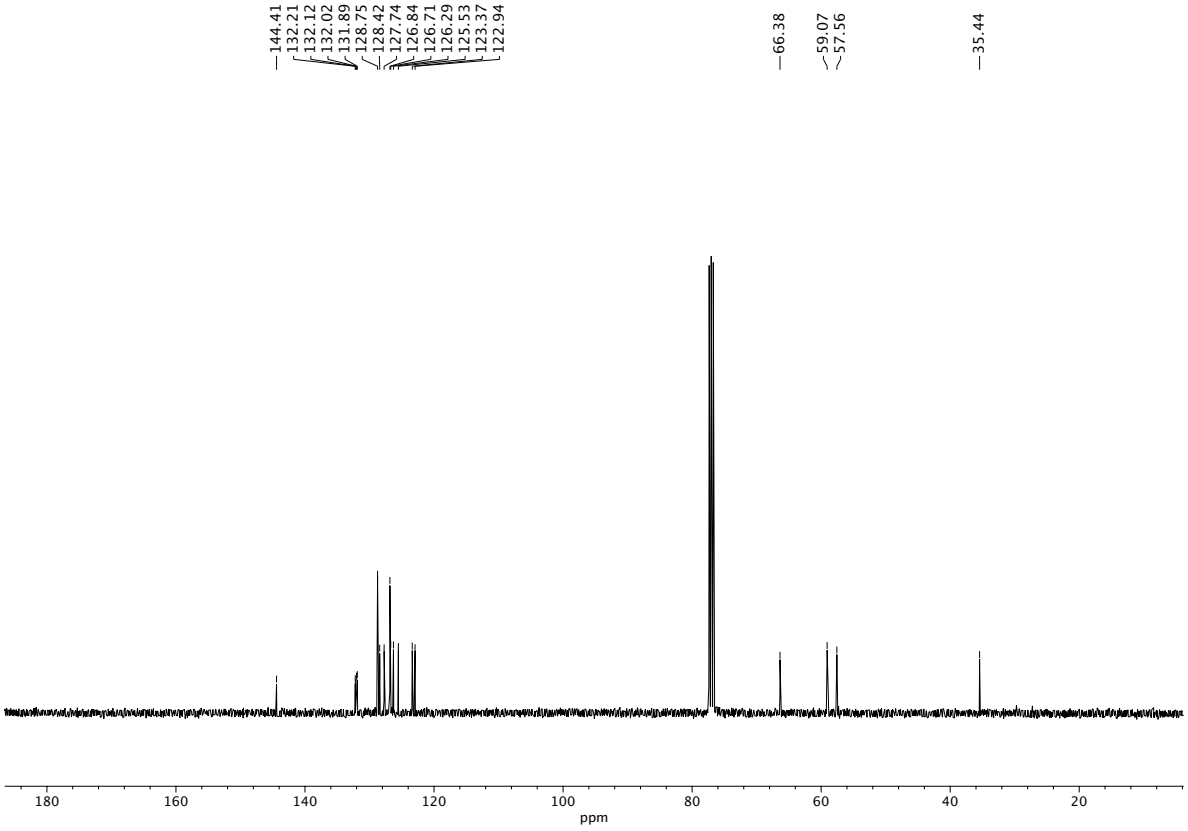
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10e**.



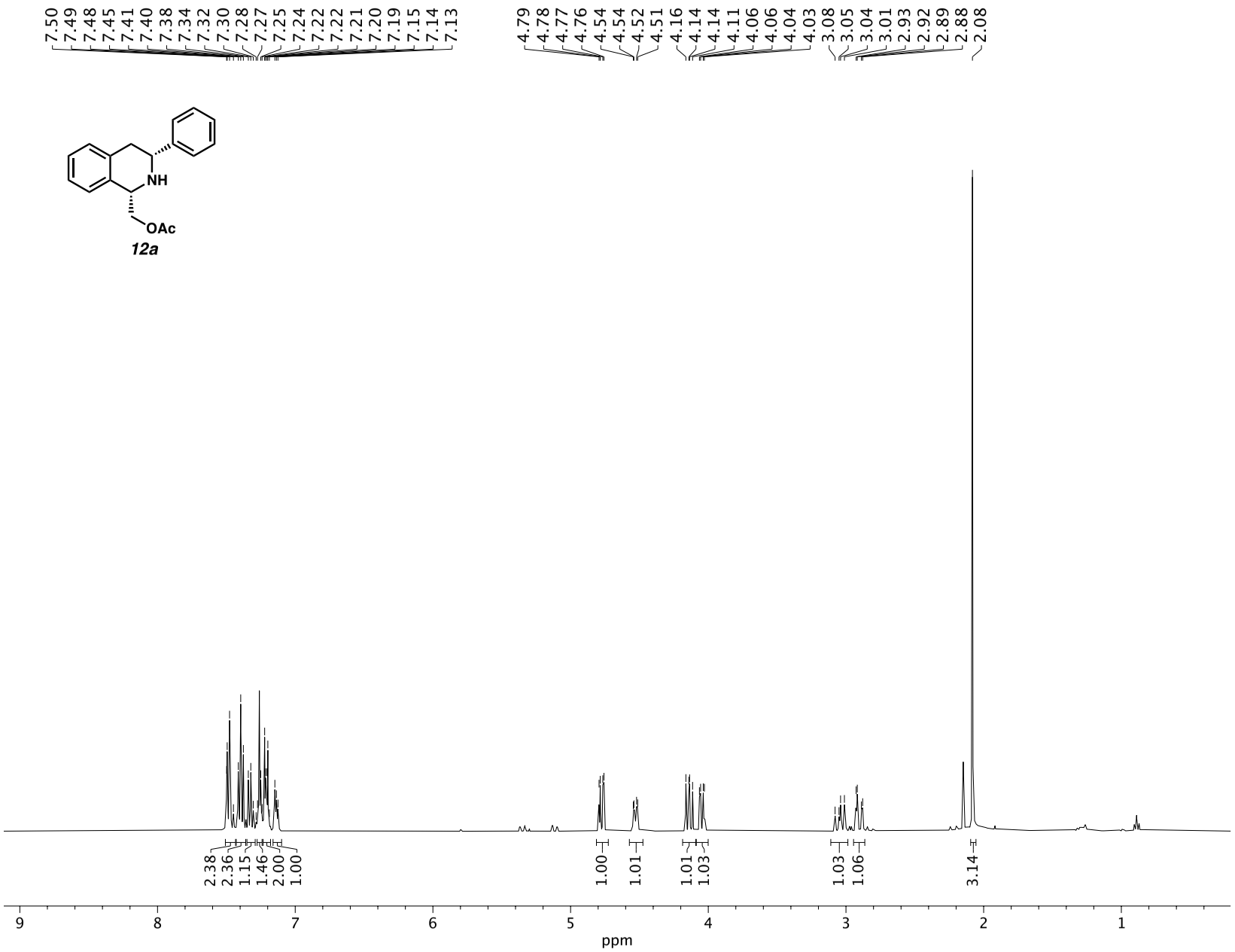
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10f**.



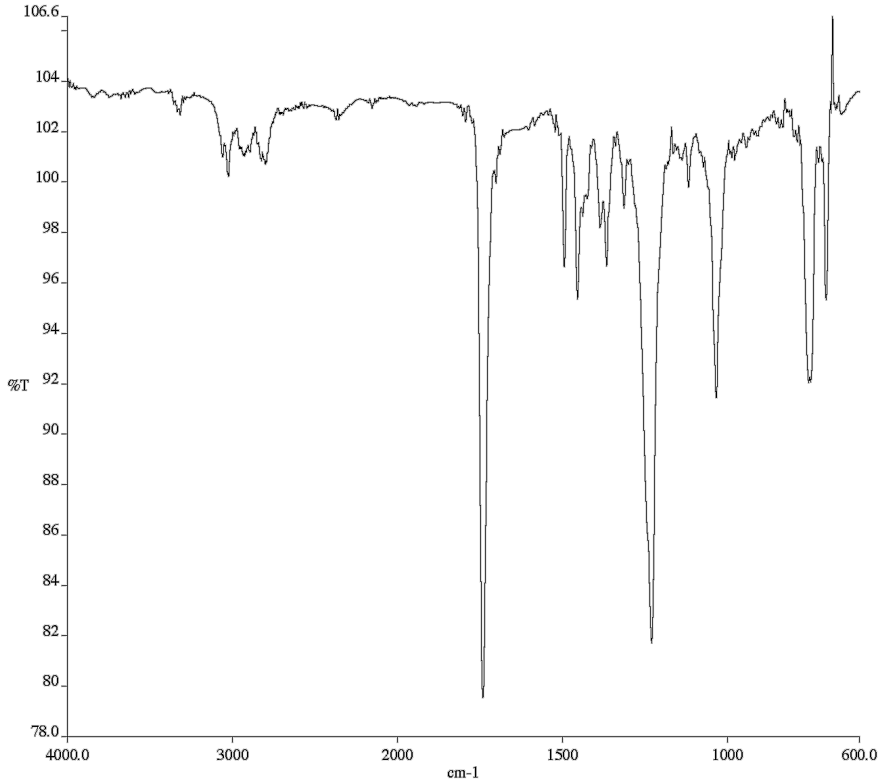
Infrared spectrum (Thin Film, NaCl) of compound **10f**.



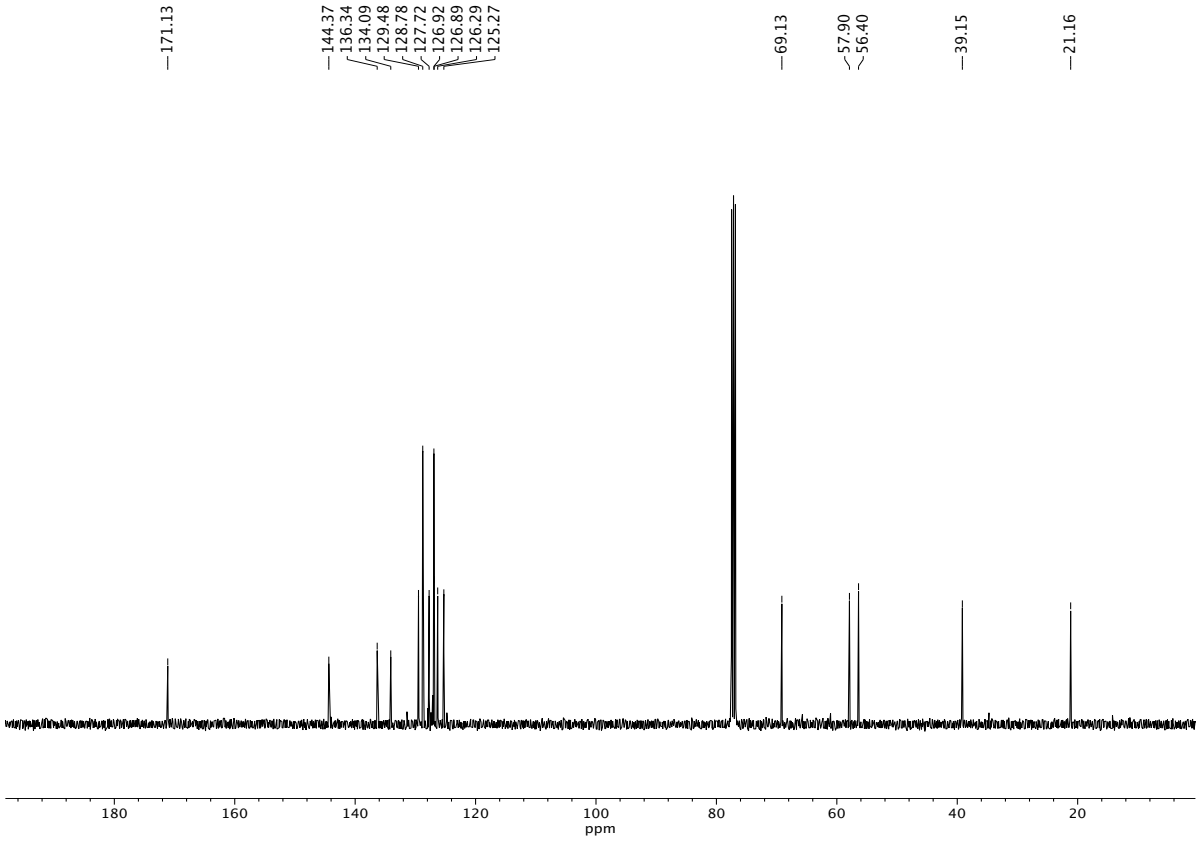
^{13}C NMR (100 MHz, $CDCl_3$) of compound **10f**.



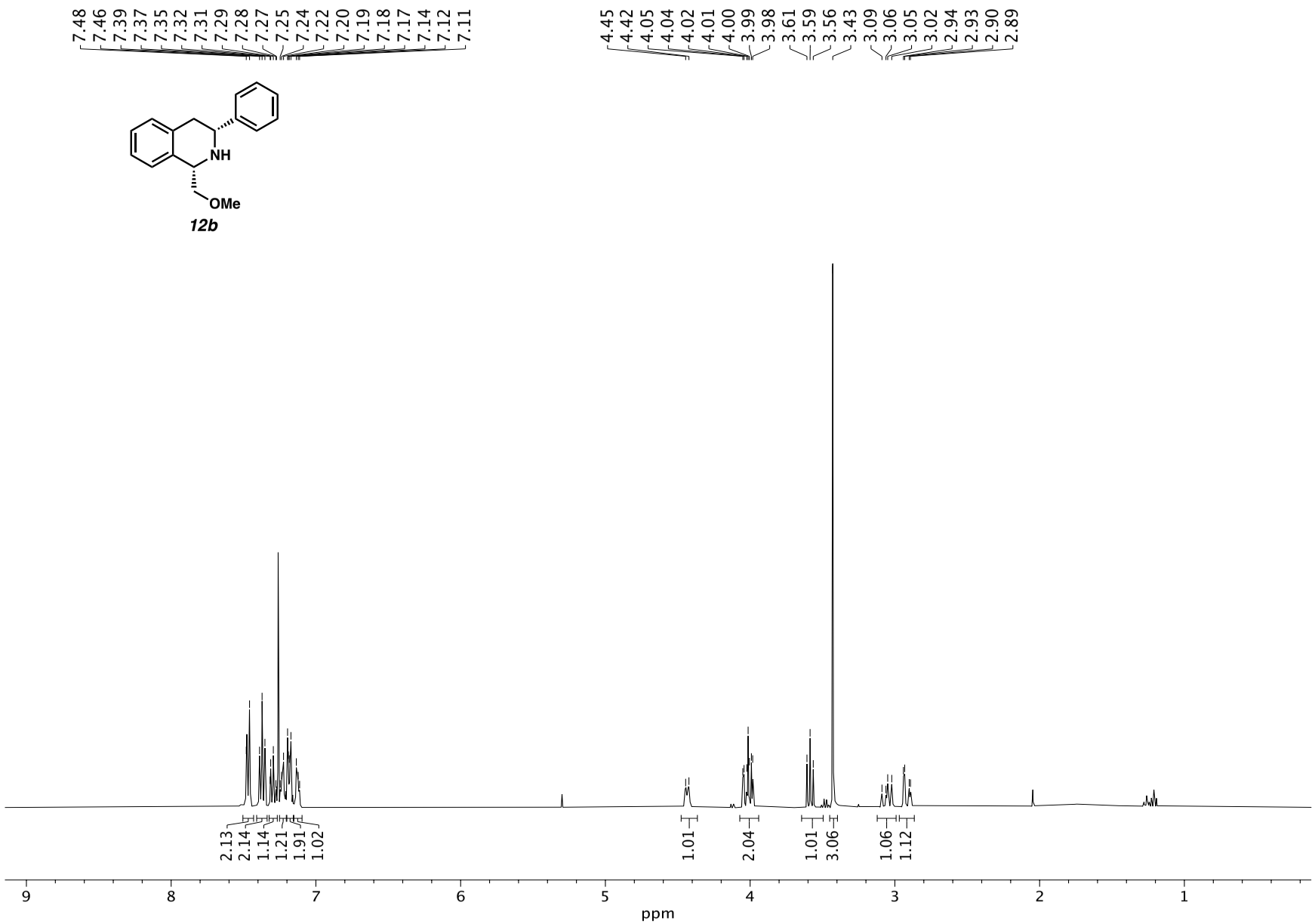
^{1}H NMR (400 MHz, $CDCl_3$) of compound **12a**.



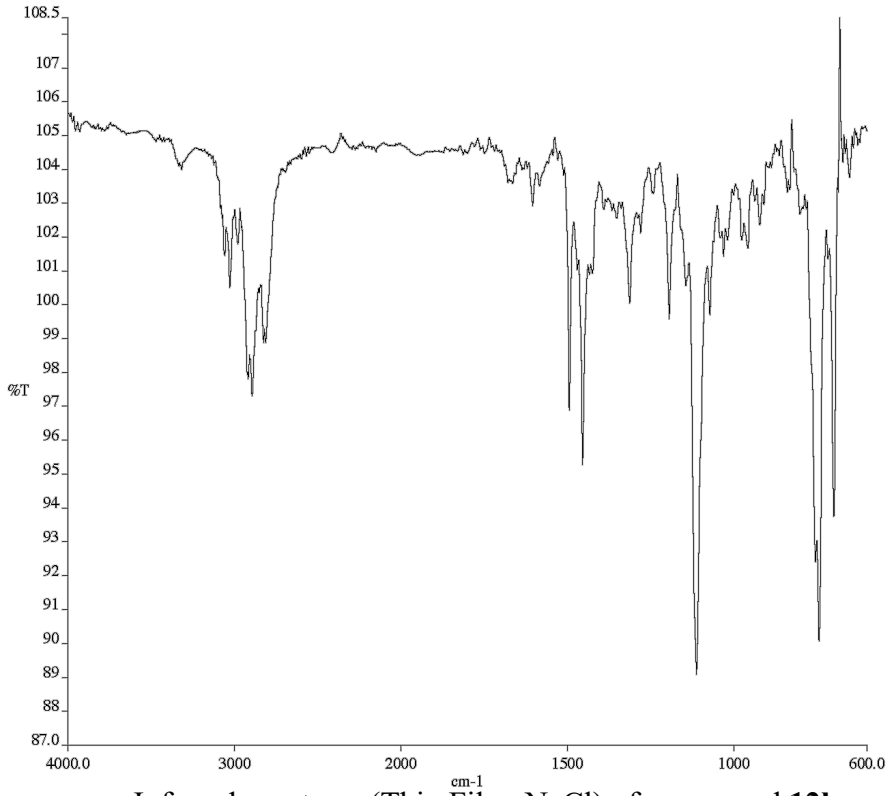
Infrared spectrum (Thin Film, NaCl) of compound **12a**.



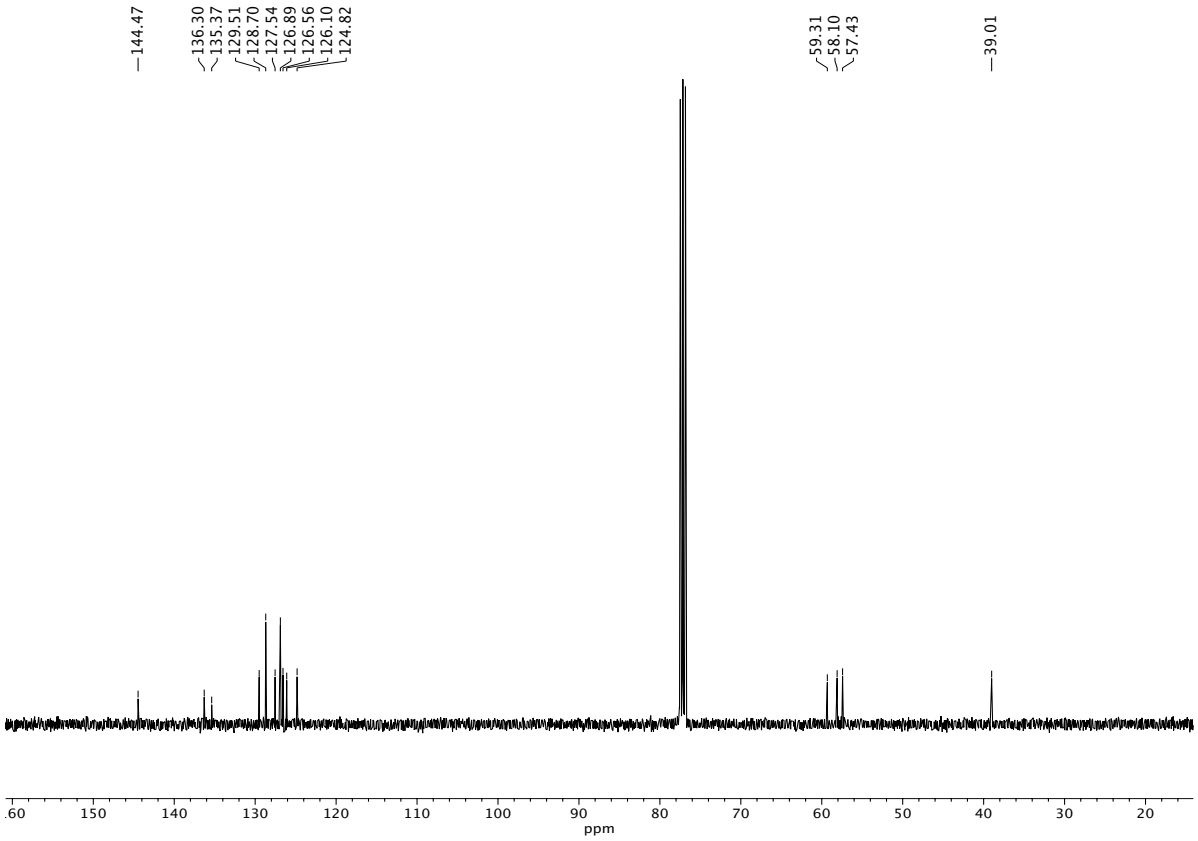
^{13}C NMR (100 MHz, $CDCl_3$) of compound **12a**.



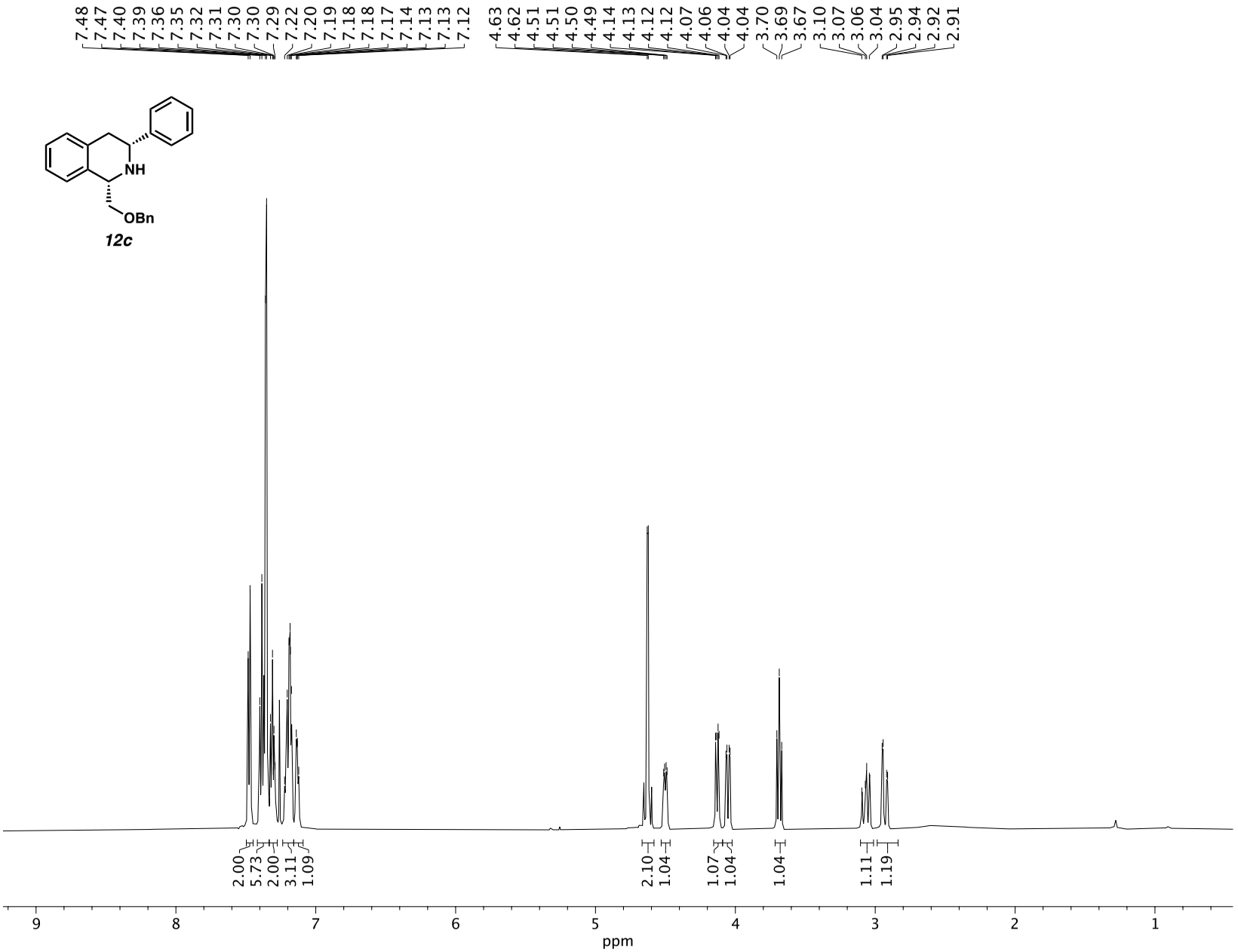
^{1}H NMR (400 MHz, $CDCl_3$) of compound **12b**.



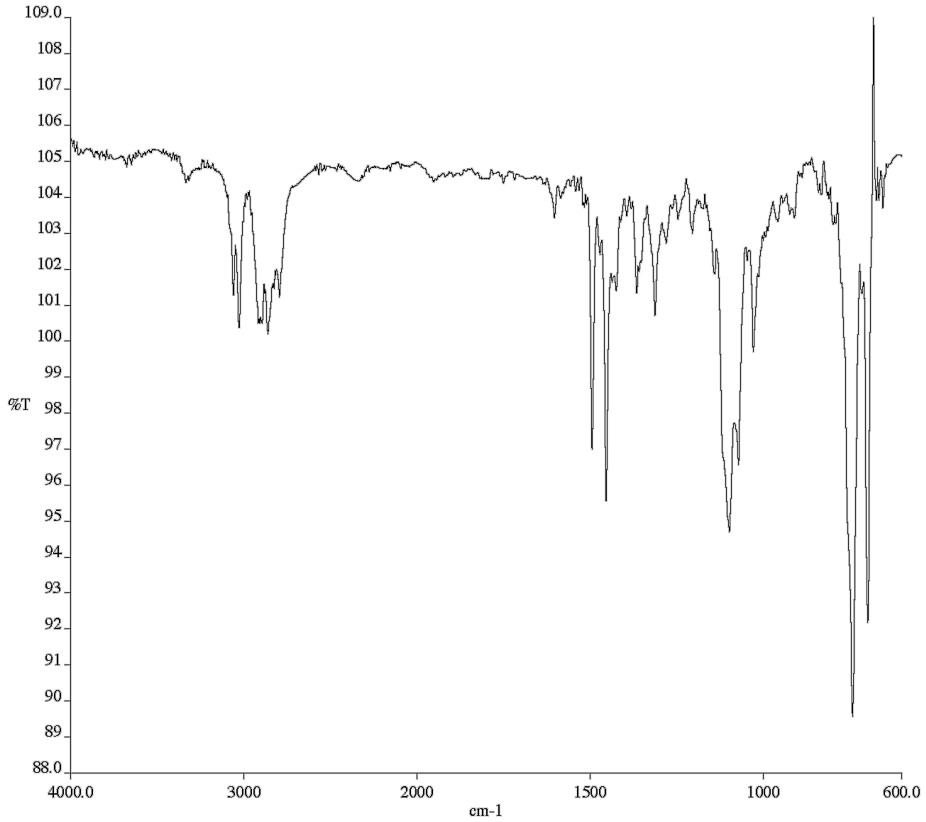
Infrared spectrum (Thin Film, NaCl) of compound **12b**.



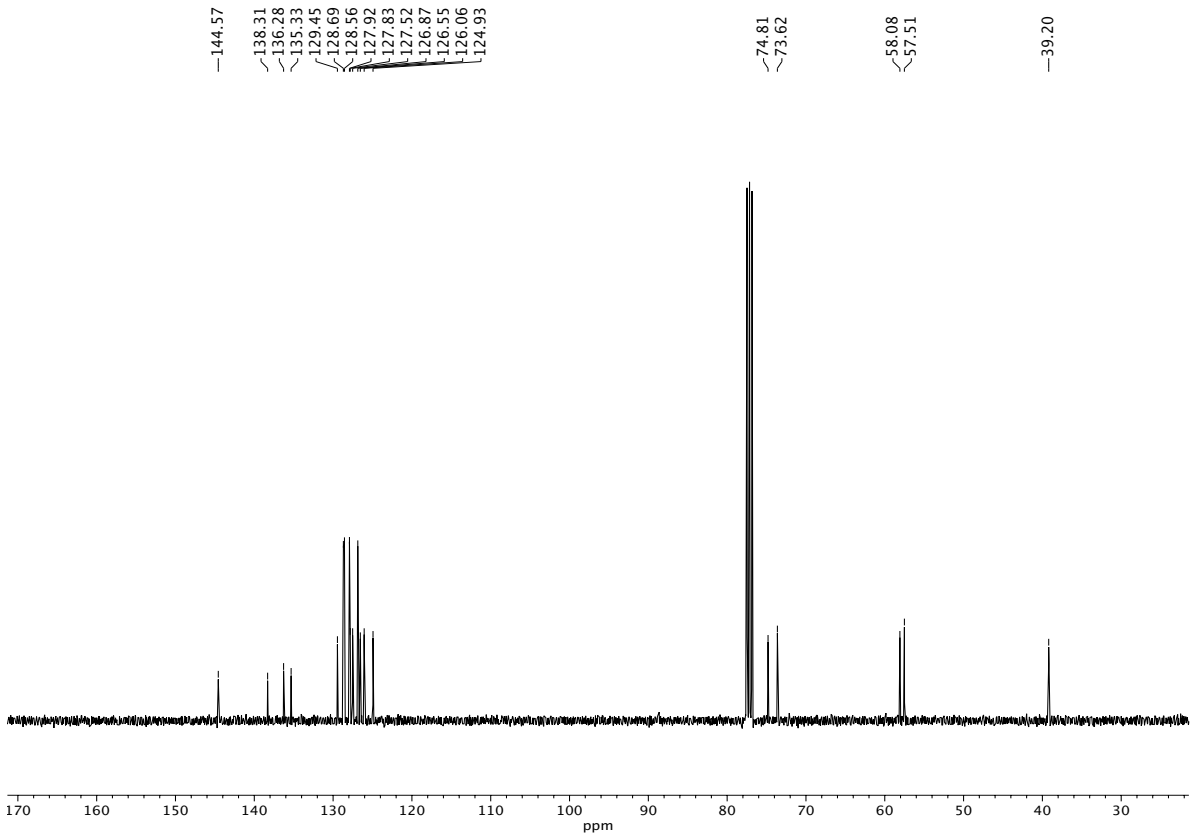
^{13}C NMR (100 MHz, $CDCl_3$) of compound **12b**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **12c**.

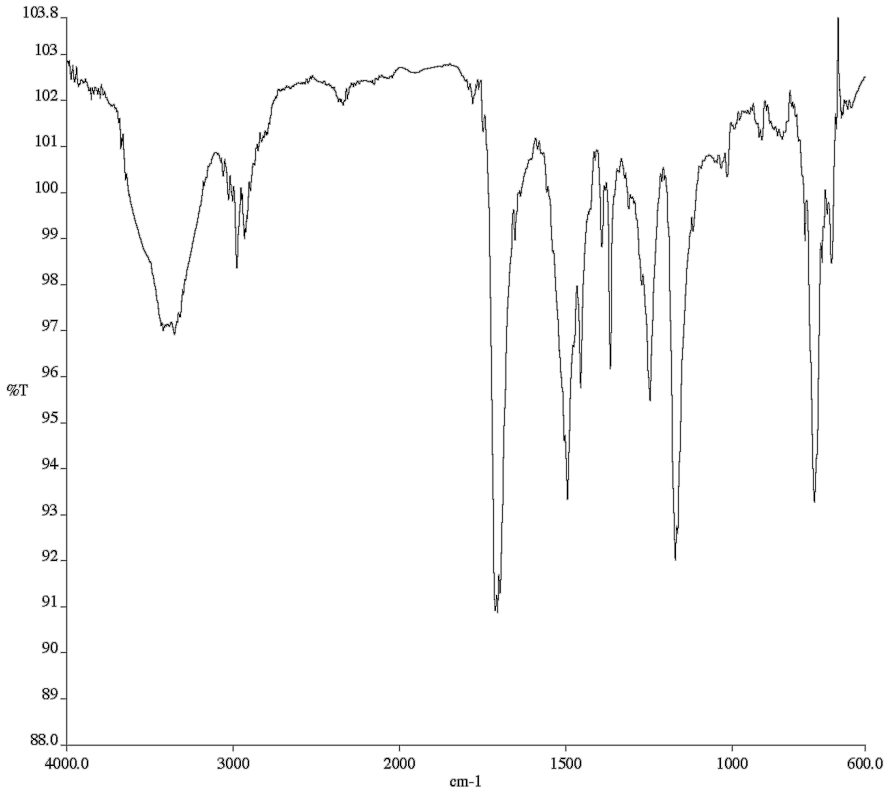


Infrared spectrum (Thin Film, NaCl) of compound **12c**.

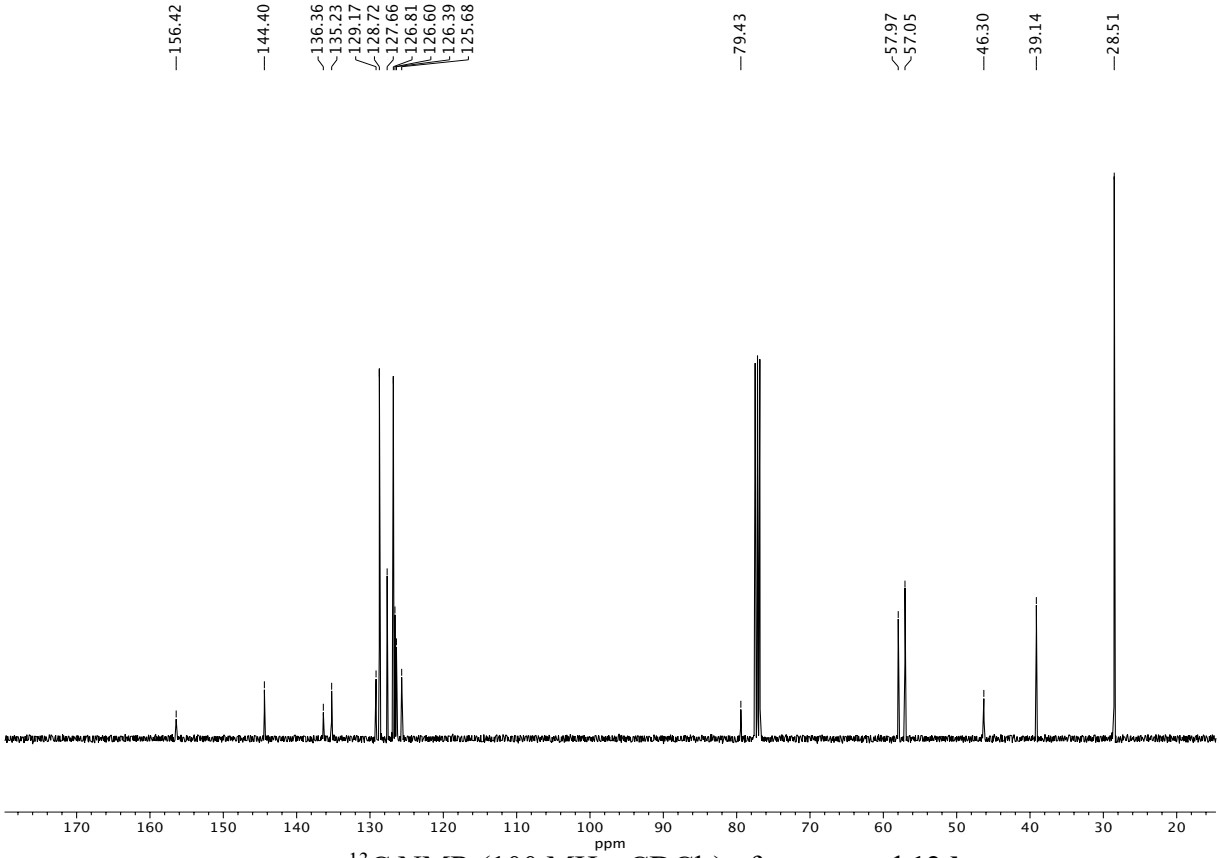


^{13}C NMR (100 MHz, $CDCl_3$) of compound **12c**.

^{1}H NMR (400 MHz, $CDCl_3$) of compound **12d**.

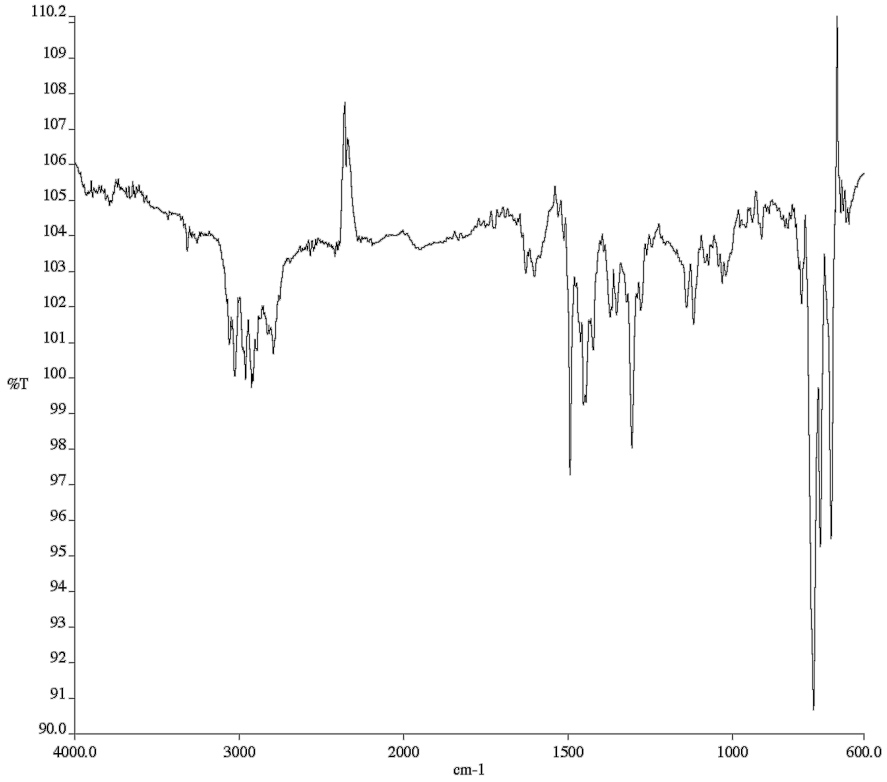


Infrared spectrum (Thin Film, NaCl) of compound **12d**.

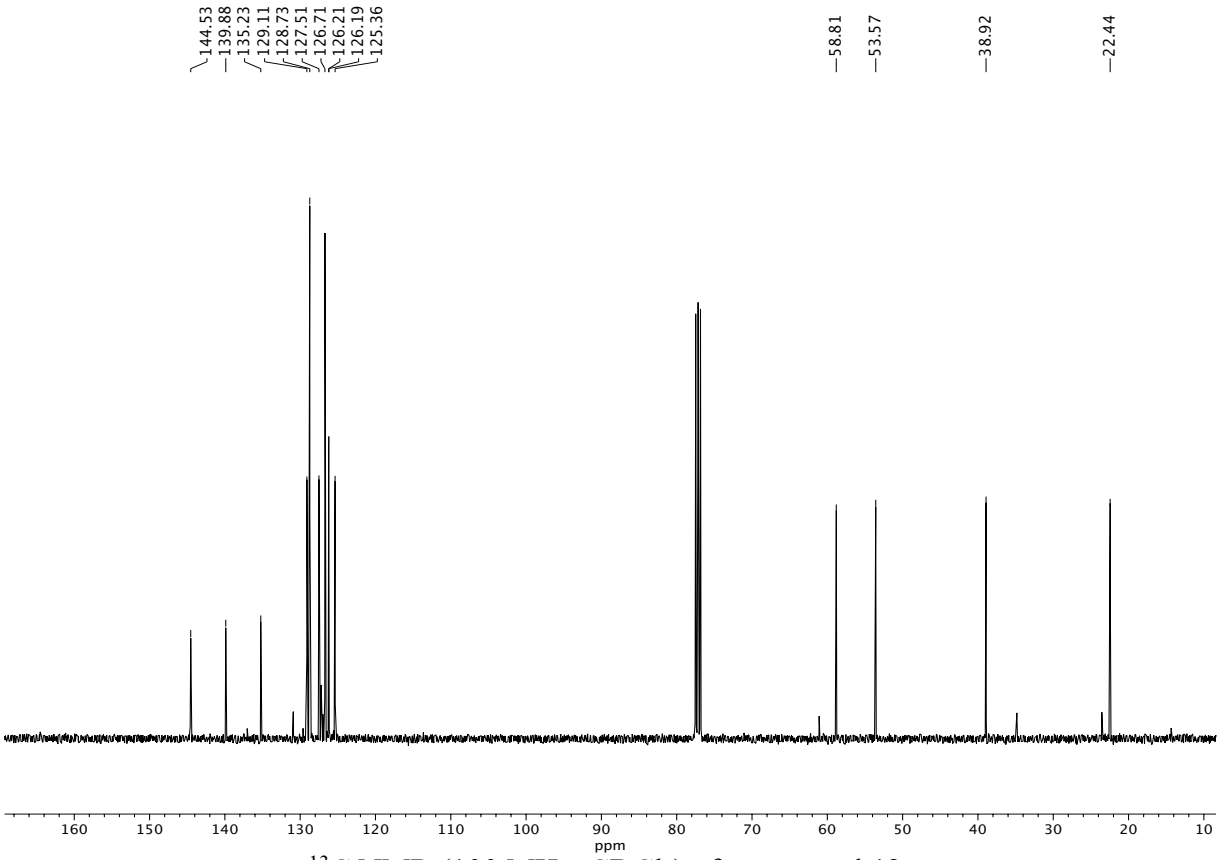


^{13}C NMR (100 MHz, $CDCl_3$) of compound **12d**.

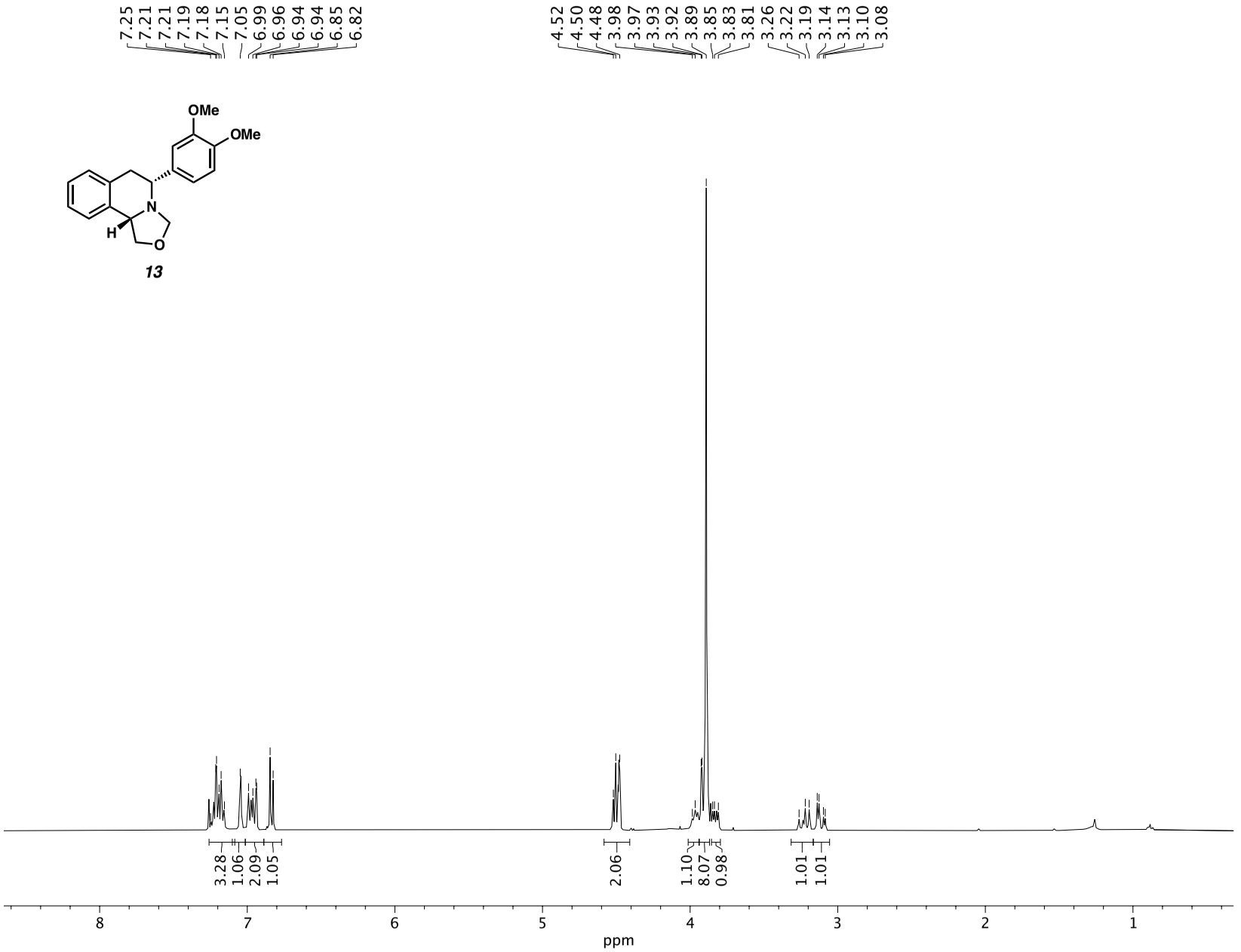
^{1}H NMR (400 MHz, $CDCl_3$) of compound **12e**.



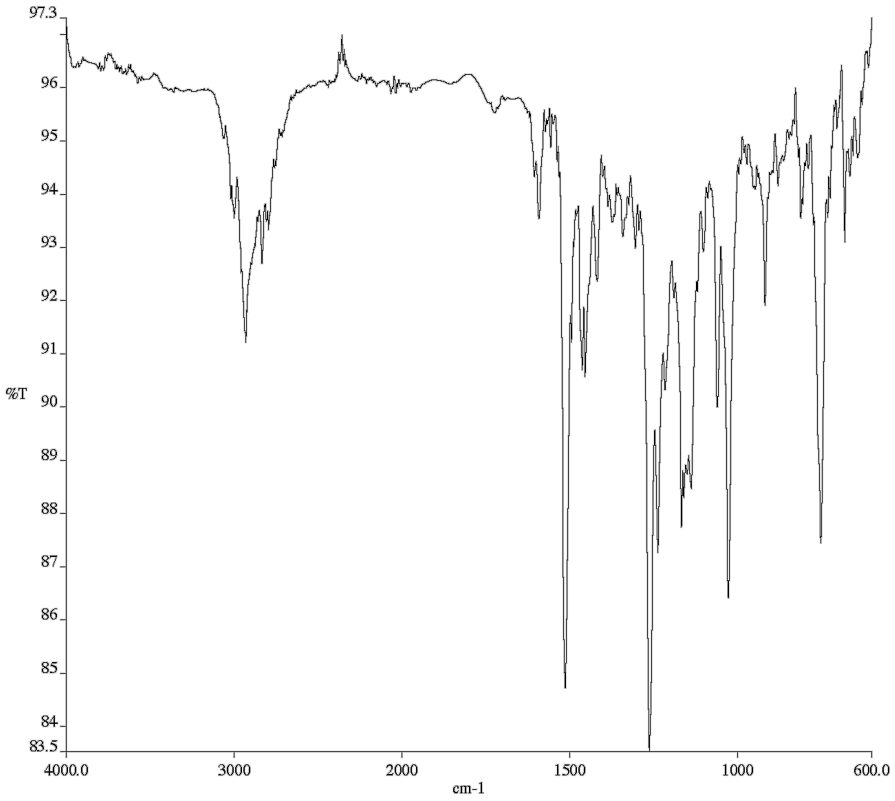
Infrared spectrum (Thin Film, NaCl) of compound **12e**.



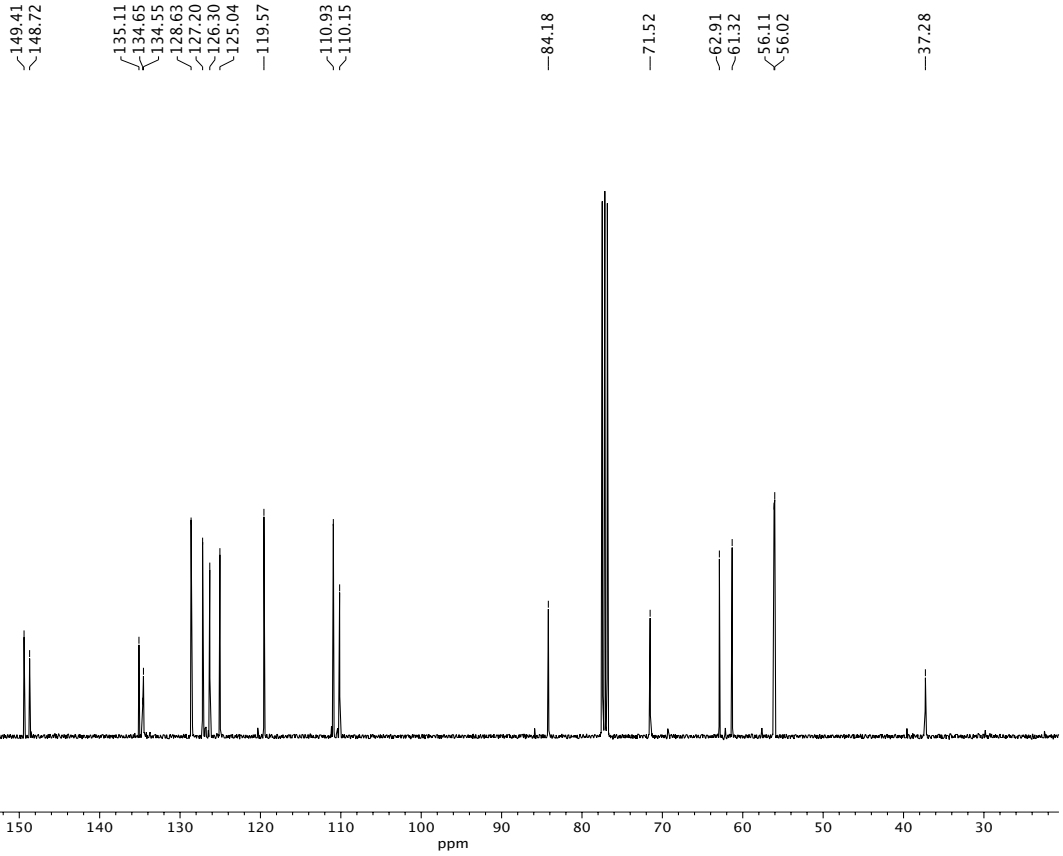
^{13}C NMR (100 MHz, $CDCl_3$) of compound **12e**.



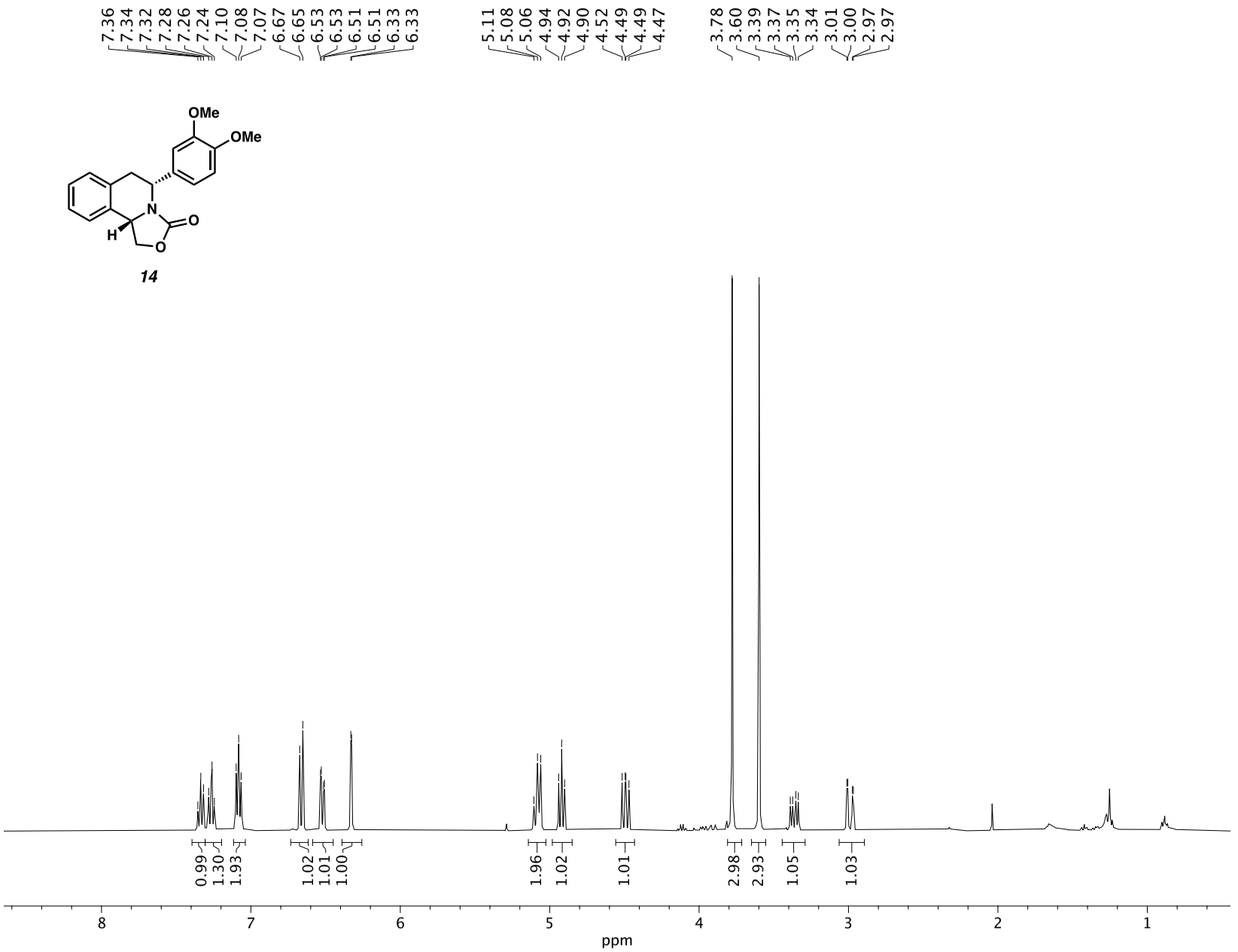
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13**.



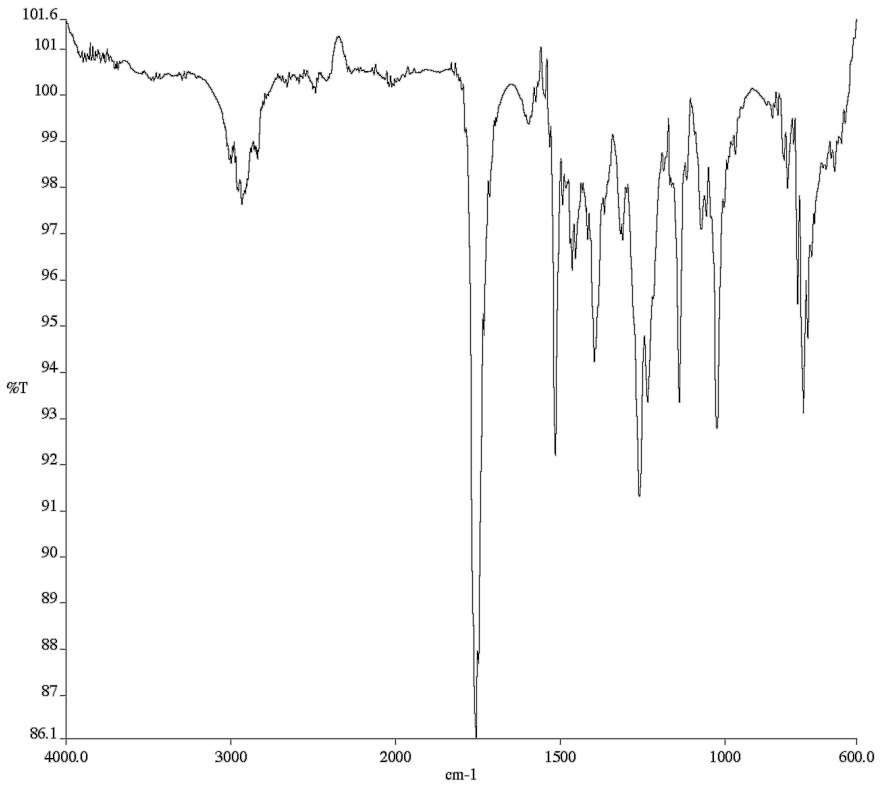
Infrared spectrum (Thin Film, NaCl) of compound **13**.



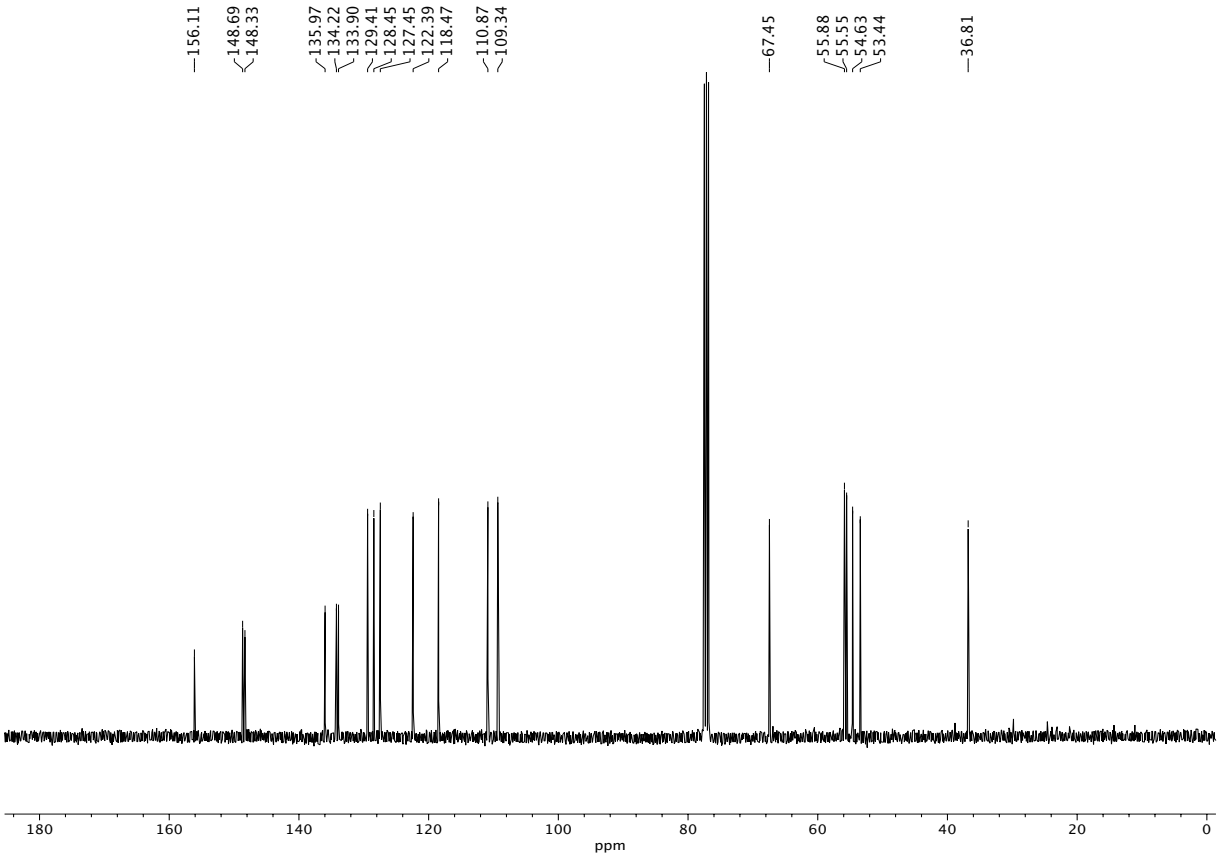
^{13}C NMR (100 MHz, $CDCl_3$) of compound **13**.



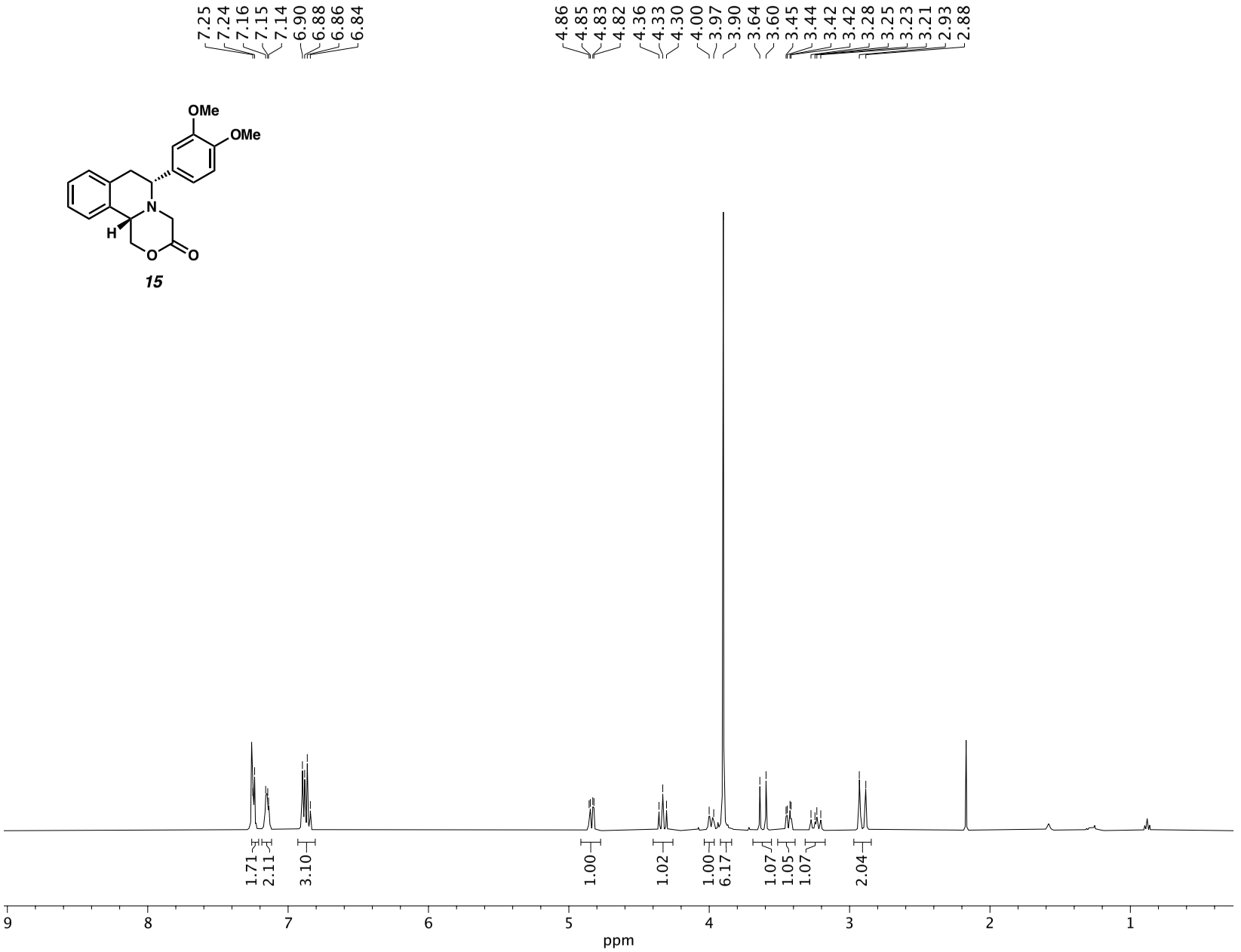
^{1}H NMR (400 MHz, $CDCl_3$) of compound **14**.



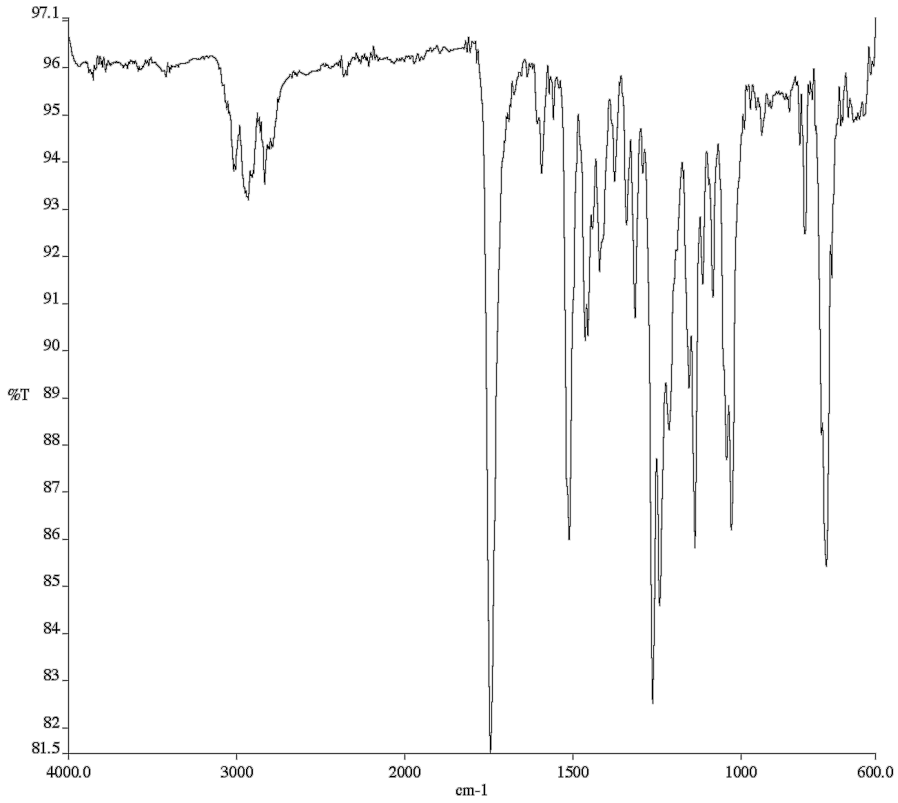
Infrared spectrum (Thin Film, NaCl) of compound **14**.



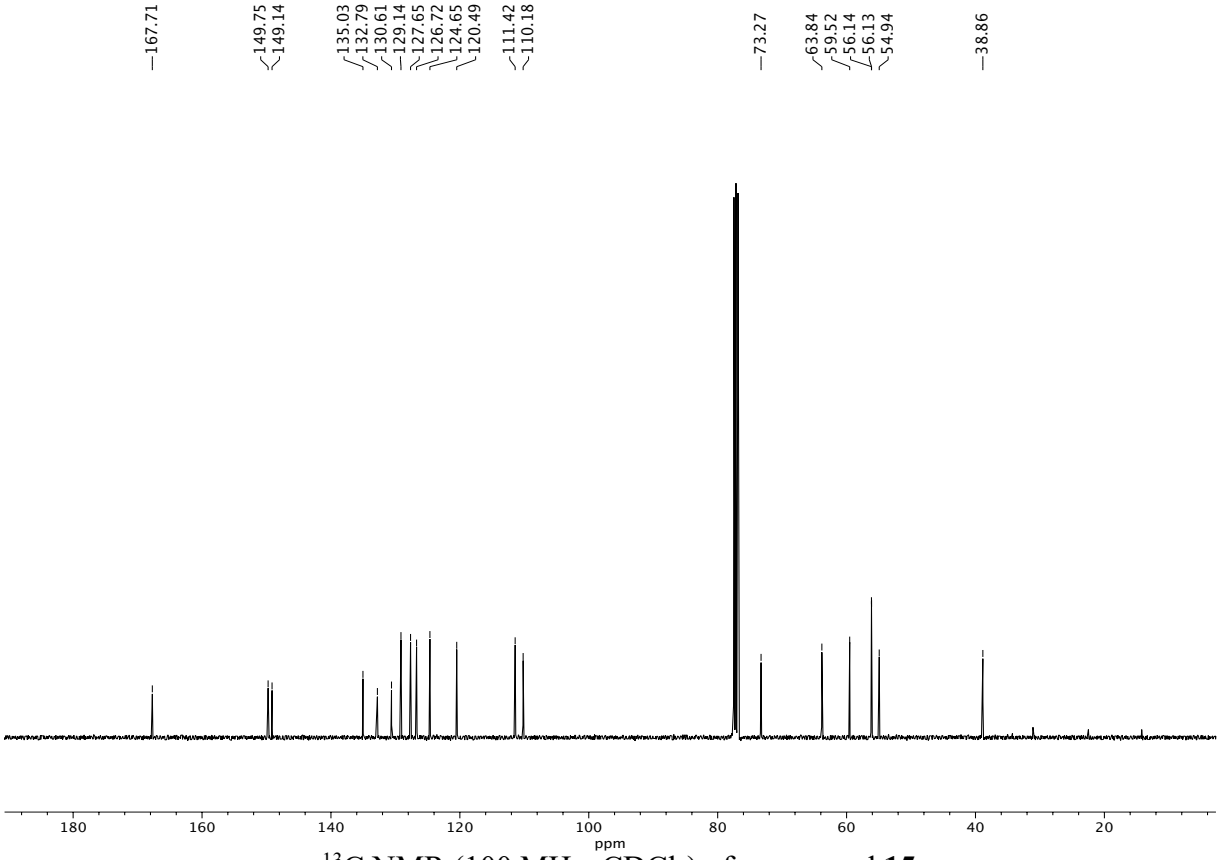
^{13}C NMR (100 MHz, $CDCl_3$) of compound **14**.



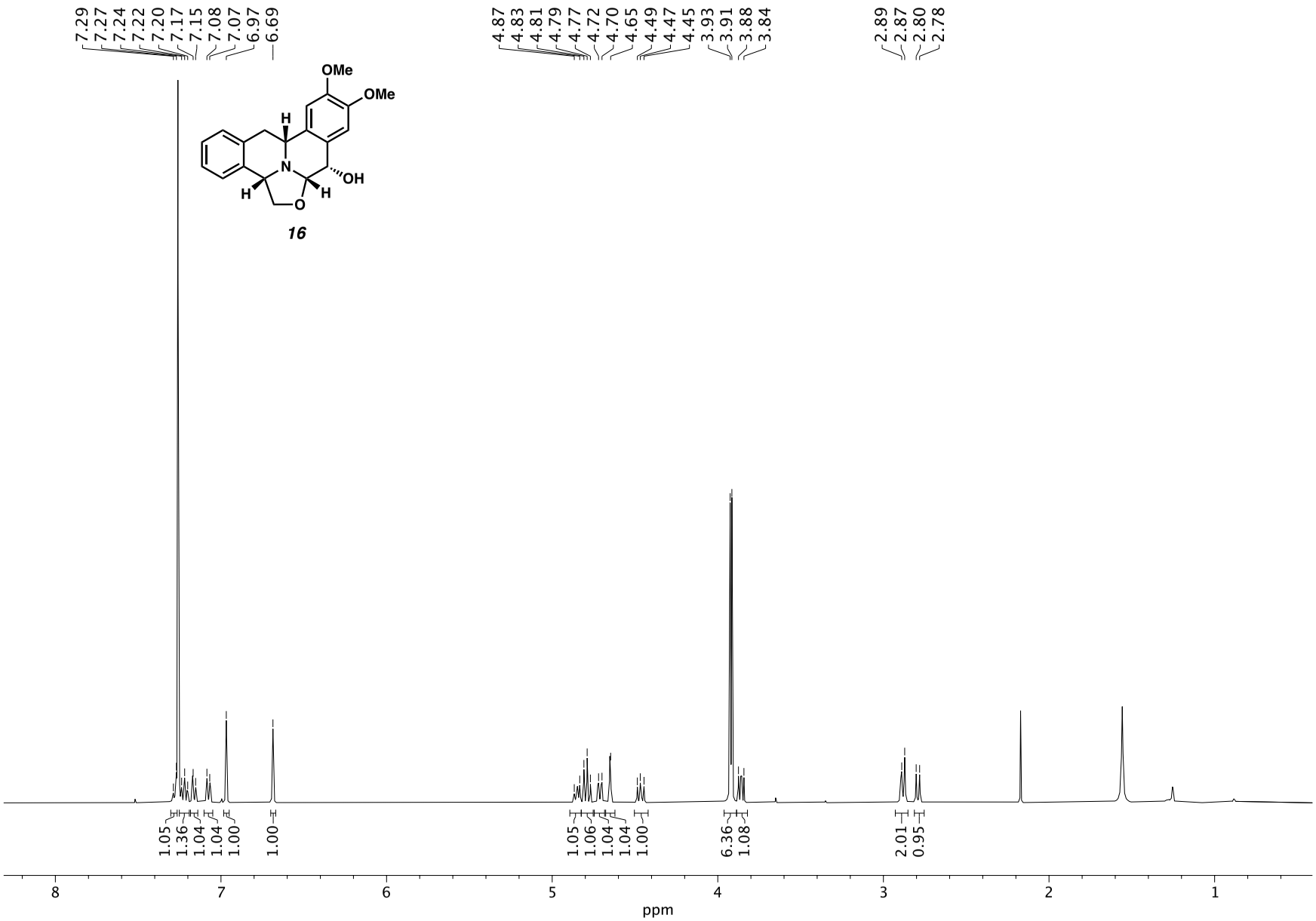
^{1}H NMR (400 MHz, $CDCl_3$) of compound **15**.



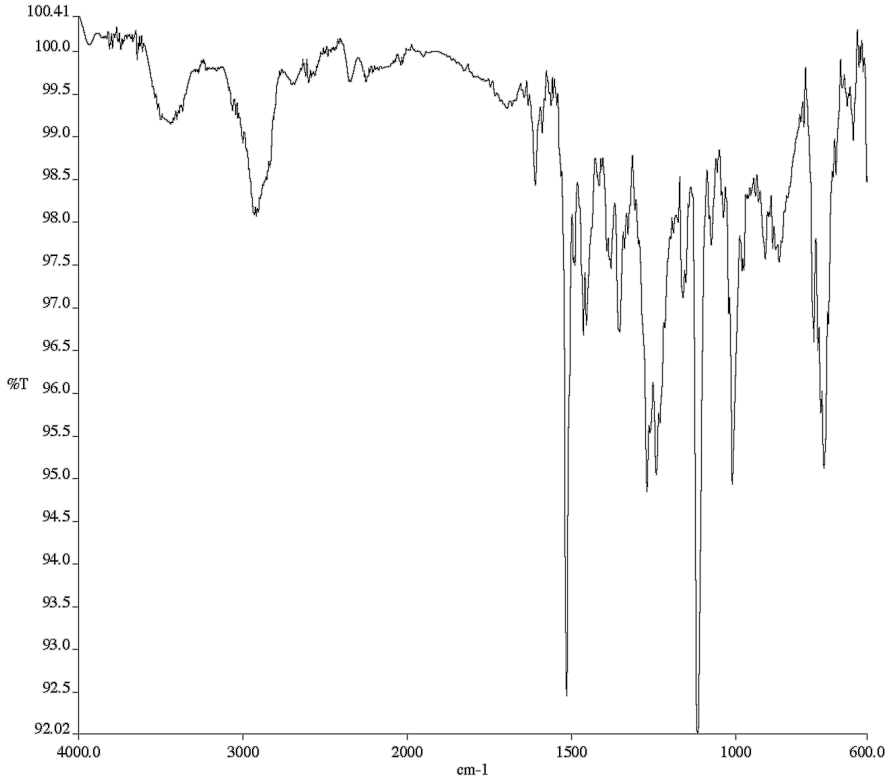
Infrared spectrum (Thin Film, NaCl) of compound **15**.



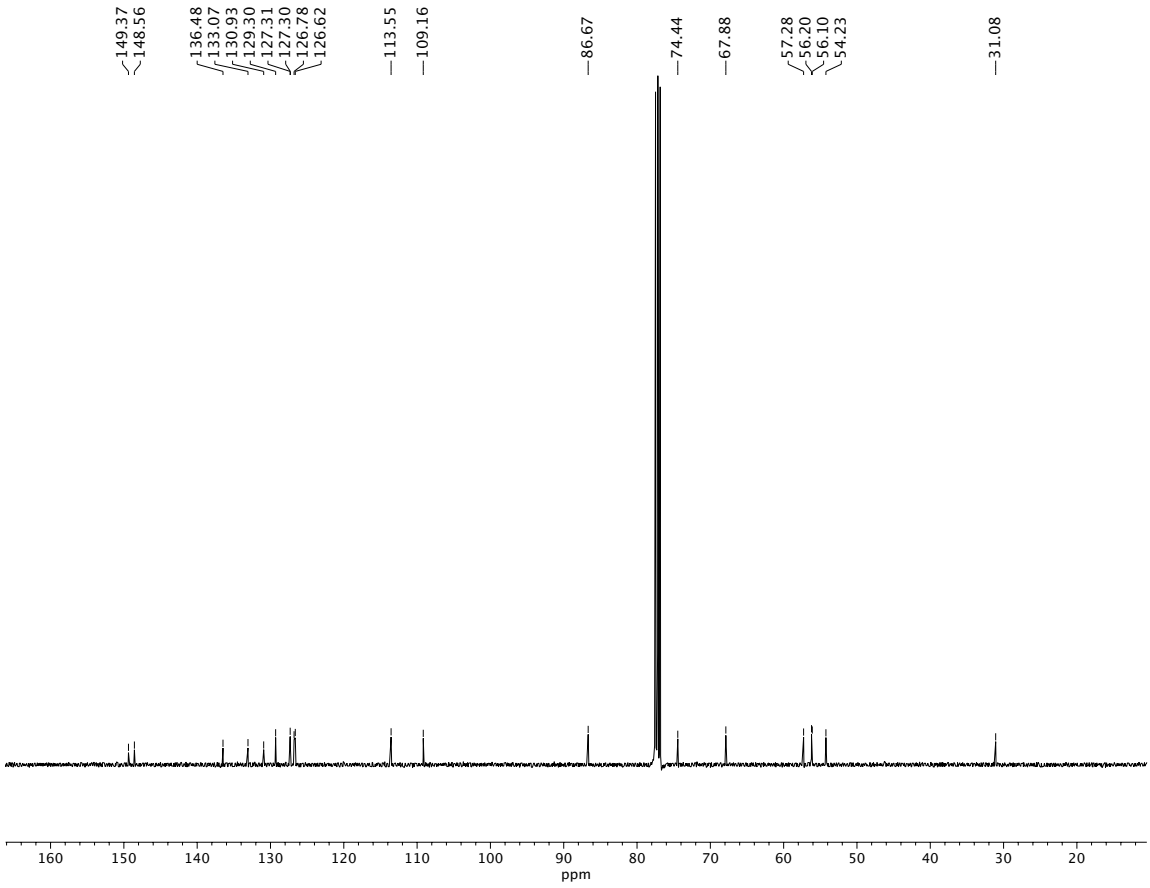
^{13}C NMR (100 MHz, $CDCl_3$) of compound **15**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **16**.



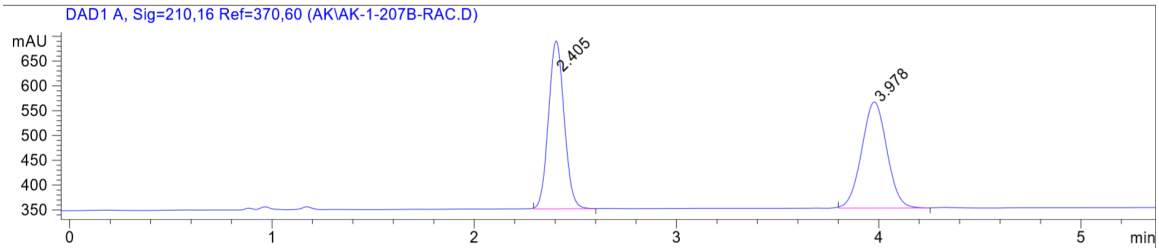
Infrared spectrum (Thin Film, NaCl) of compound **16**.



^{13}C NMR (100 MHz, $CDCl_3$) of compound **16**.

SFC Traces of Racemic and Enantioenriched Compounds

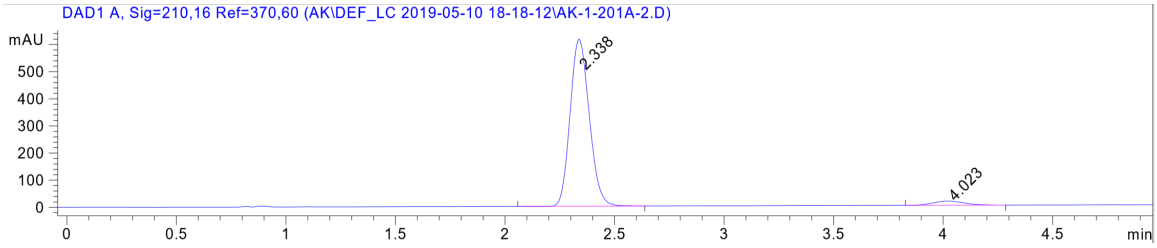
Racemic **8a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.405	BB	0.0872	1827.17725	337.16122	49.6720
2	3.978	BB	0.1331	1851.30725	213.68279	50.3280

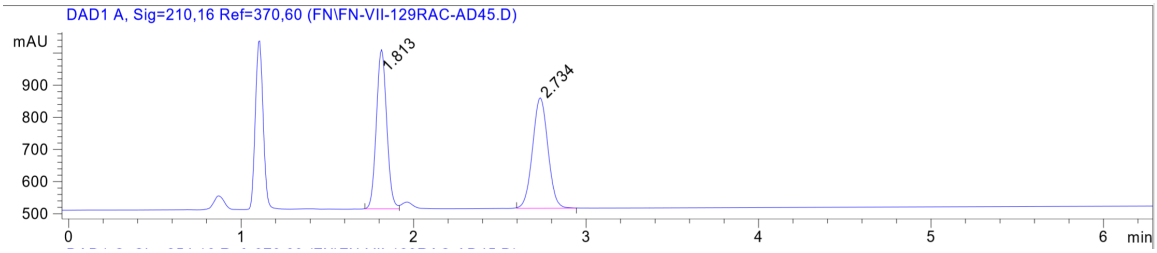
Enantioenriched **8a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.338	BB	0.0970	3750.96460	616.63293	96.1873
2	4.023	BB	0.1508	148.68077	15.37459	3.8127

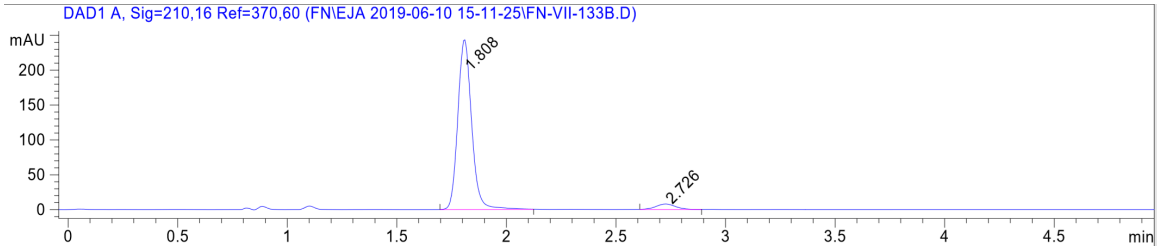
Racemic **8b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.813	BV	0.0691	2070.81763	492.04037	49.2789
2	2.734	BB	0.0966	2131.41943	342.59348	50.7211

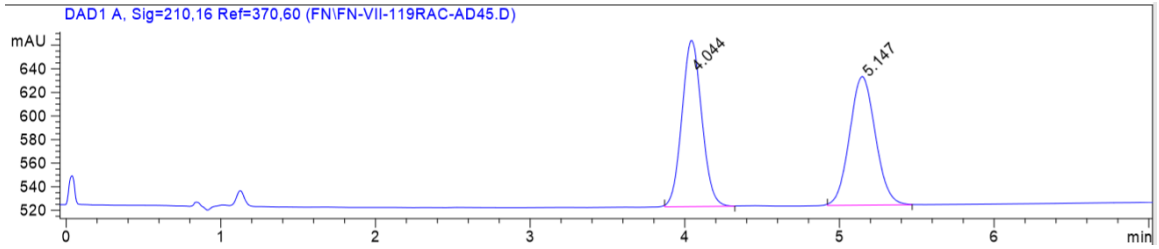
Enantioenriched **8b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.808	BB	0.0670	1068.41528	244.38884	95.6879
2	2.726	BB	0.0959	48.14769	7.81482	4.3121

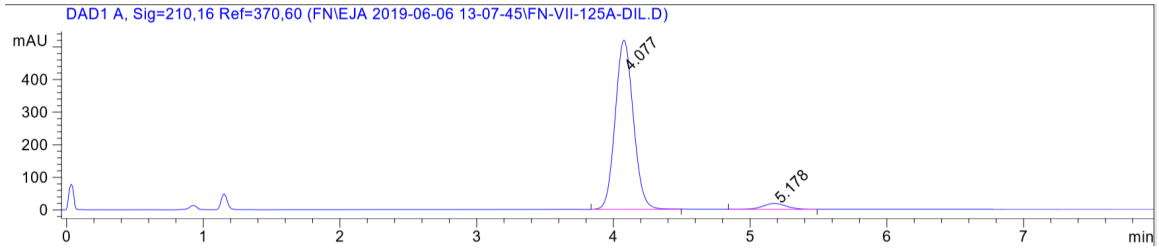
Racemic **8c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.044	BB	0.1403	1258.43604	140.79761	49.8928
2	5.147	BB	0.1793	1263.84558	109.00304	50.1072

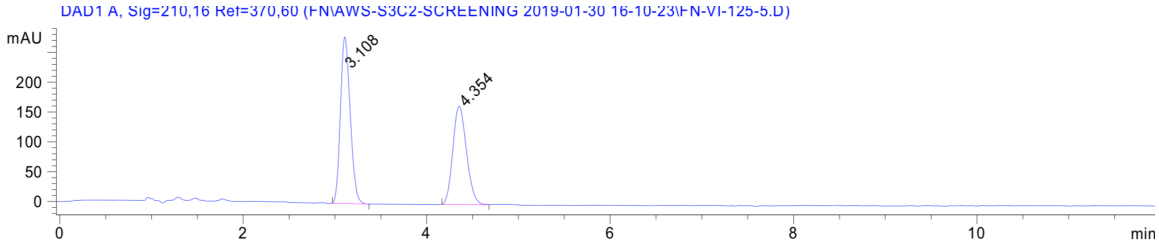
Enantioenriched **8c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.077	BB	0.1435	4781.52539	519.04926	95.7798
2	5.178	VB	0.1778	210.68056	18.09942	4.2202

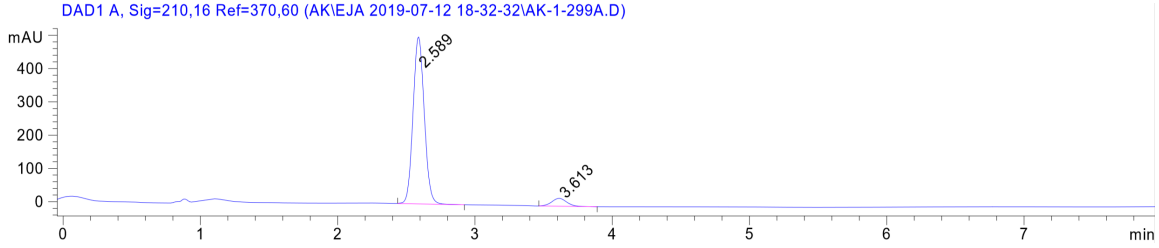
Racemic **8d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.108	BB	0.1143	2061.14478	278.61850	54.7029
2	4.354	BB	0.1608	1706.74719	164.80942	45.2971

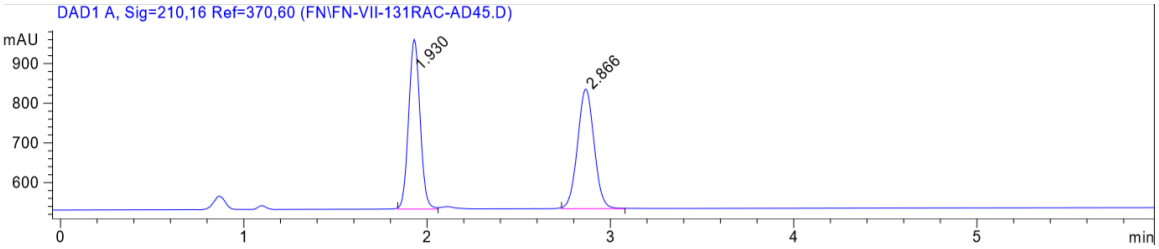
Enantioenriched **8d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.589	BB	0.0881	2843.16016	502.08252	94.1881
2	3.613	BB	0.1167	175.43710	23.59426	5.8119

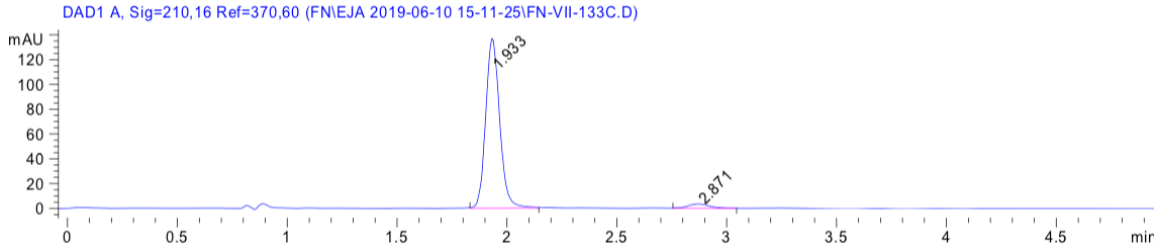
Racemic **8e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.930	BV	0.0708	1849.34583	424.51587	49.3594
2	2.866	BB	0.1015	1897.34631	301.09756	50.6406

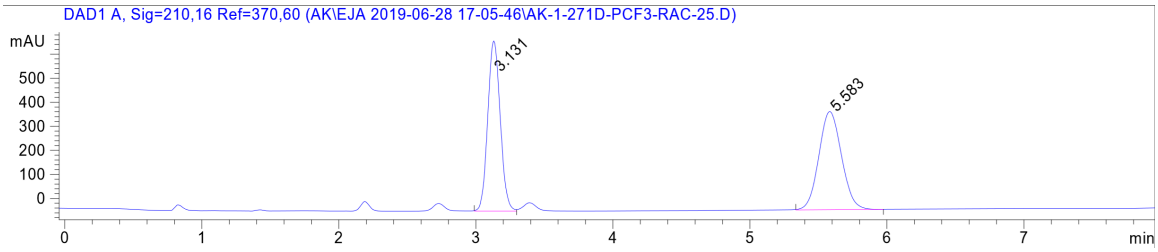
Enantioenriched **8e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.933	BB	0.0676	606.81042	137.18159	96.4113
2	2.871	BB	0.0969	22.58703	3.51686	3.5887

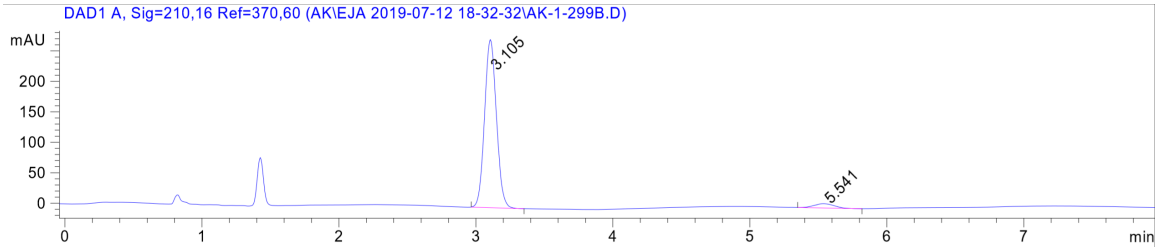
Racemic **8f•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.131	BV	0.0980	4470.82178	704.84247	48.8296
2	5.583	BB	0.1821	4685.14355	407.61465	51.1704

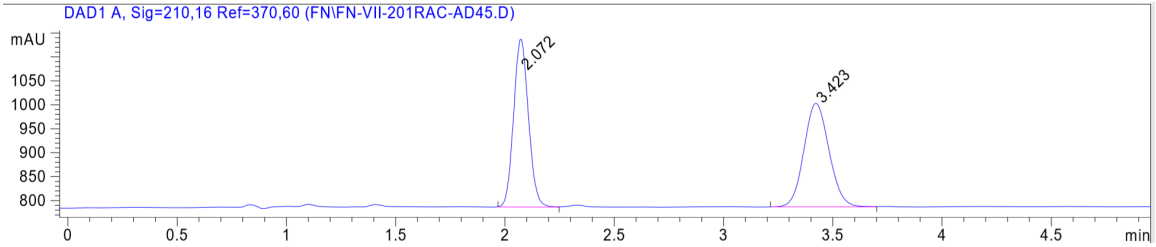
Enantioenriched **8f•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.105	BB	0.0920	1656.91443	276.13840	95.9298
2	5.541	BB	0.1475	70.30067	7.09913	4.0702

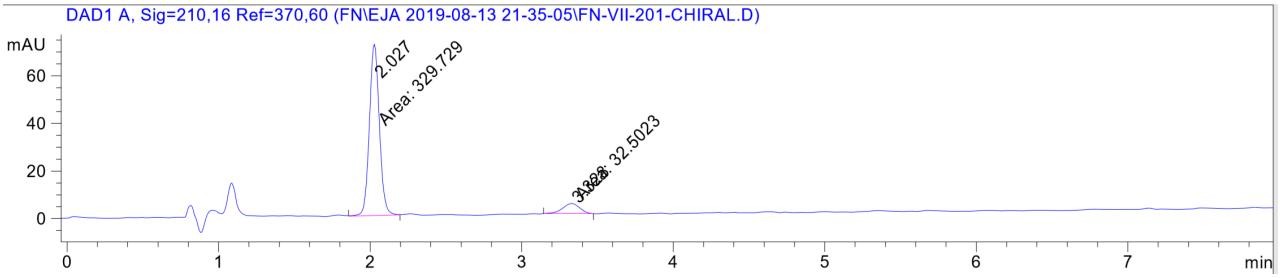
Racemic **8g•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.072	BV	0.0750	1656.99988	351.78995	48.9589
2	3.423	BB	0.1251	1727.47400	216.40314	51.0411

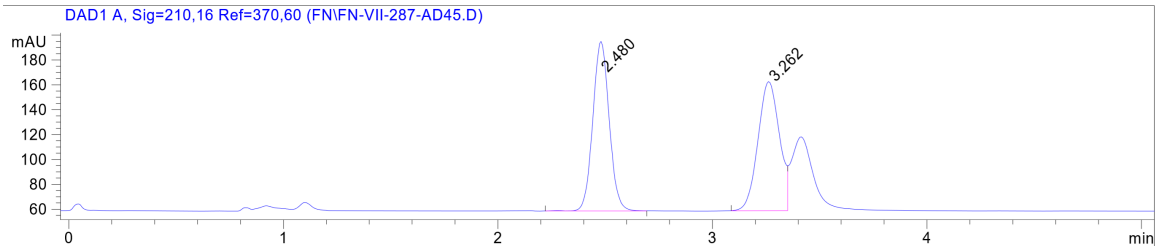
Enantioenriched **8g•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.027	MM	0.0761	329.72919	72.18623	91.0272
2	3.328	MM	0.1273	32.50227	4.25578	8.9728

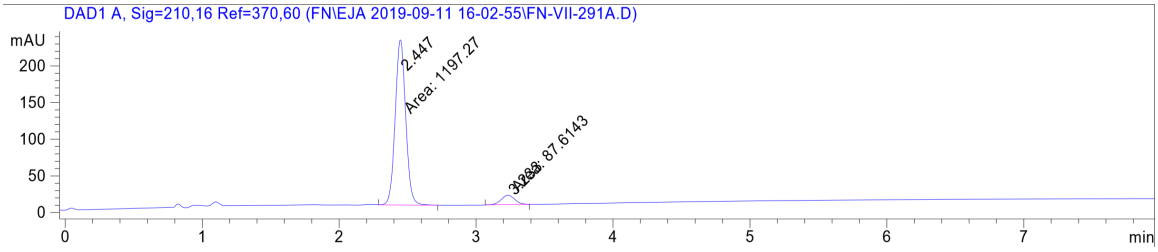
Racemic **8h•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.480	BB	0.0820	725.99445	136.52641	50.0536
2	3.262	BV	0.1073	724.44000	103.92244	49.9464

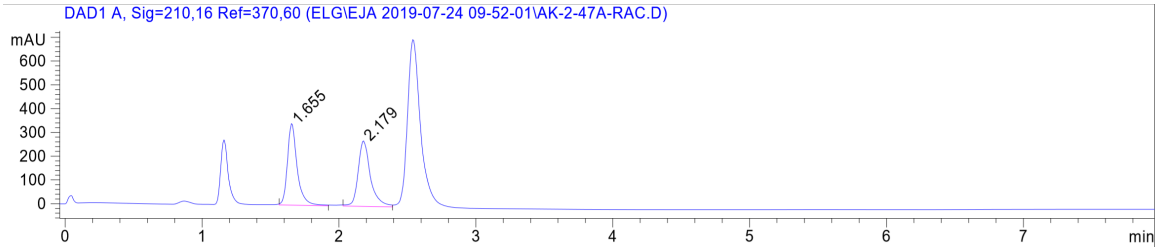
Enantioenriched **8h•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.447	MM	0.0881	1197.27063	226.37776	93.1812
2	3.233	MM	0.1138	87.61434	12.83208	6.8188

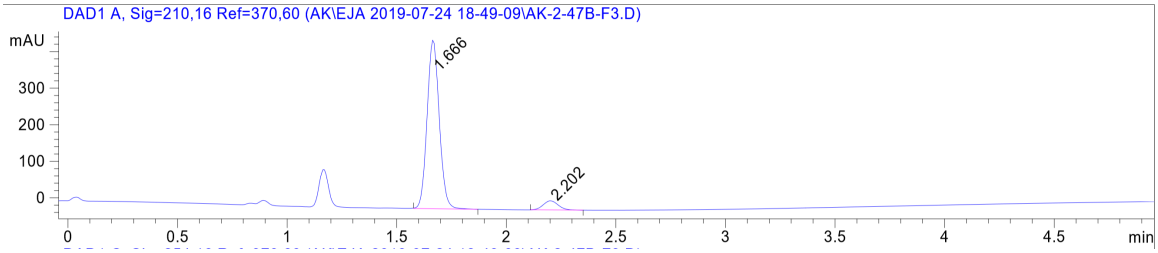
Racemic **8i•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.655	BB	0.0780	1695.18689	340.95029	49.6001
2	2.179	BV	0.0931	1722.52197	275.01672	50.3999

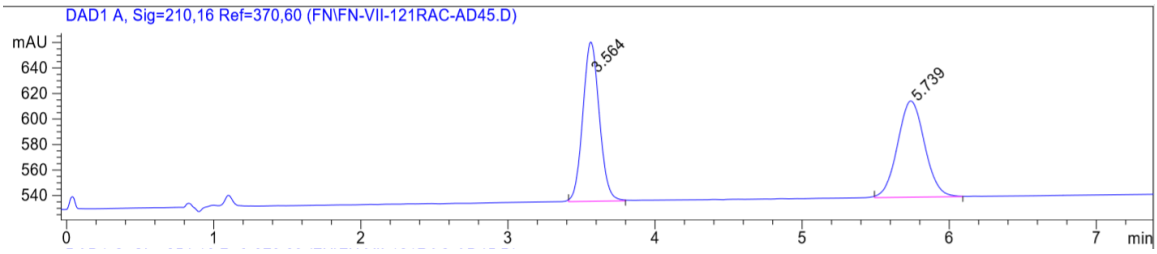
Enantioenriched **8i•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.666	BB	0.0609	1779.05176	461.77499	93.7135
2	2.202	BB	0.0729	119.34183	25.36208	6.2865

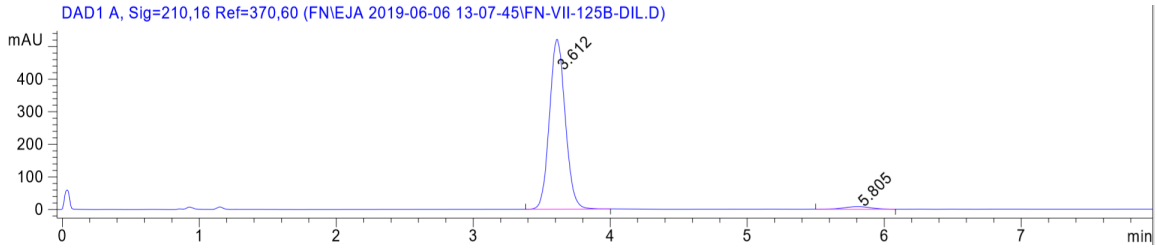
Racemic **8j•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.564	BB	0.1231	973.81842	124.71865	50.1687
2	5.739	BB	0.1977	967.27094	75.39081	49.8313

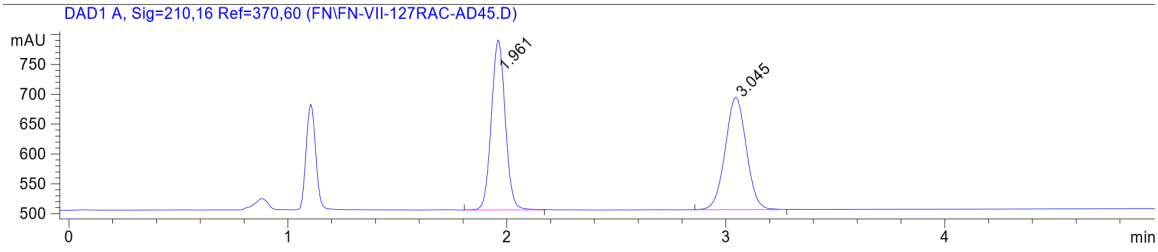
Enantioenriched **8j•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.612	BB	0.1254	4178.18115	521.86456	97.4007
2	5.805	BV	0.1948	111.50051	8.29716	2.5993

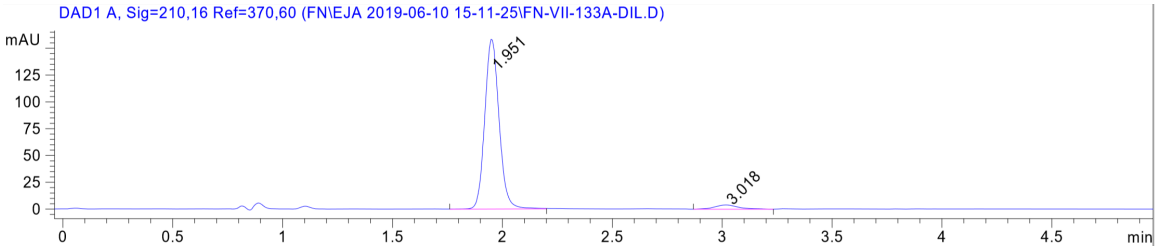
Racemic **8k•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.961	VB	0.0674	1257.14734	285.41742	49.8960
2	3.045	BB	0.1042	1262.38831	188.33221	50.1040

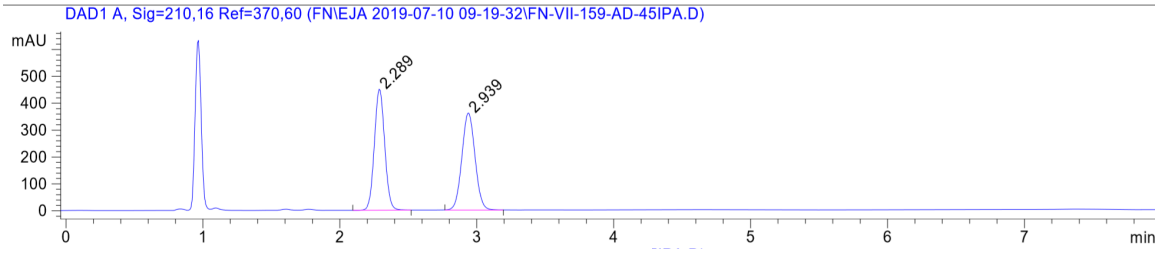
Enantioenriched **8k•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.951	VB	0.0687	718.81940	159.04907	95.9575
2	3.018	BV	0.1136	30.28240	4.03425	4.0425

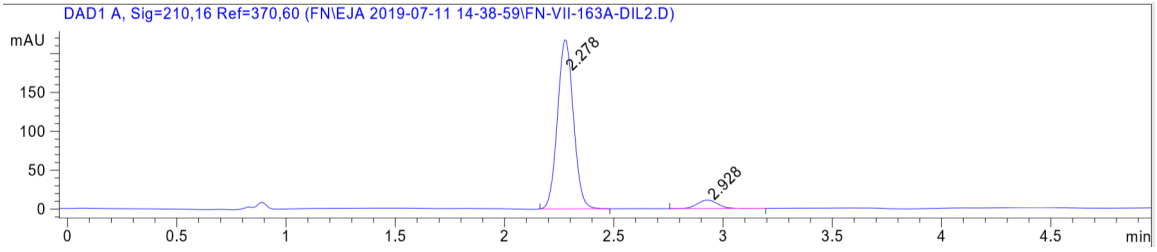
Racemic **8l•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.289	BB	0.0811	2358.96533	450.59644	49.5114
2	2.939	BB	0.1037	2405.52295	361.37506	50.4886

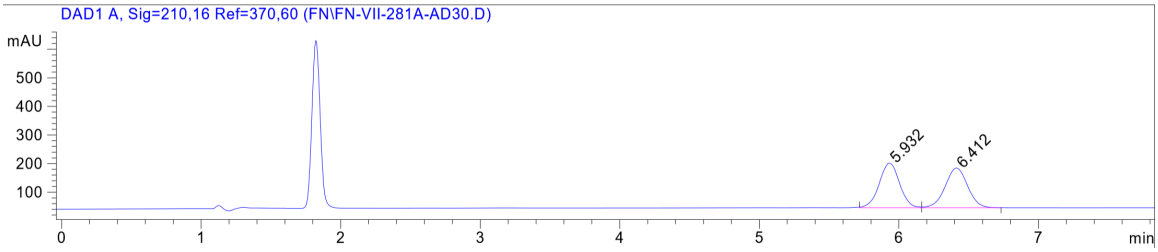
Enantioenriched **8l•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.278	BB	0.0790	1102.16956	218.12439	94.1062
2	2.928	BB	0.0994	69.02821	10.96723	5.8938

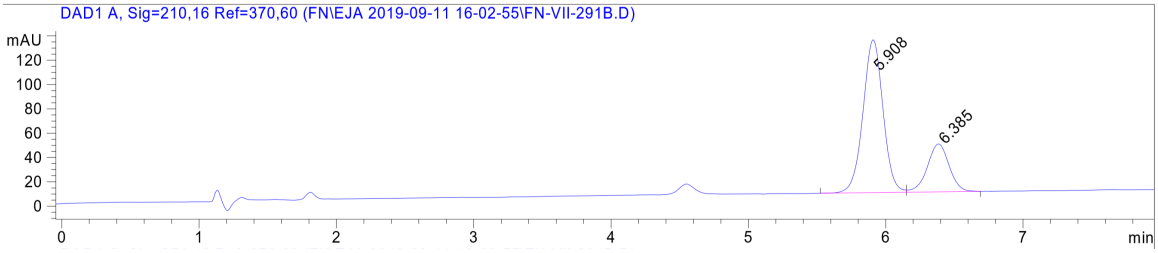
Racemic **8m•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.932	BV	0.1541	1584.34717	156.53989	50.4165
2	6.412	VB	0.1748	1558.16772	139.03162	49.5835

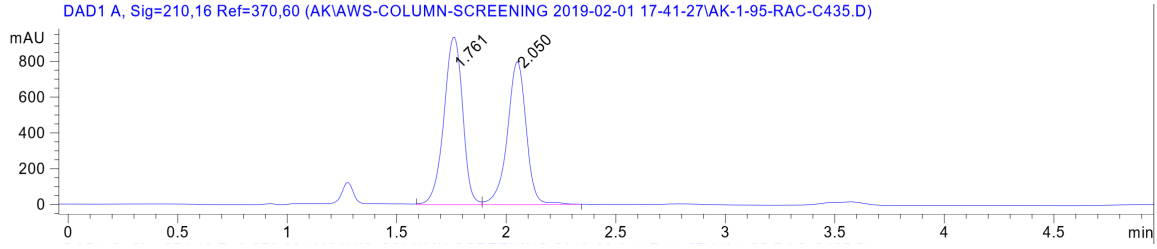
Enantioenriched **8m•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.908	BV	0.1561	1272.85767	125.74207	74.5442
2	6.385	VB	0.1686	434.66418	39.41822	25.4558

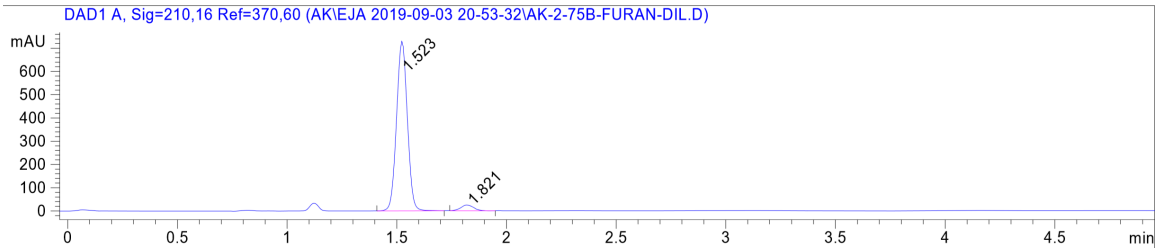
Racemic **8n•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.761	BV	0.0933	5567.44824	937.00757	53.7908
2	2.050	VB	0.0918	4782.73486	799.48718	46.2092

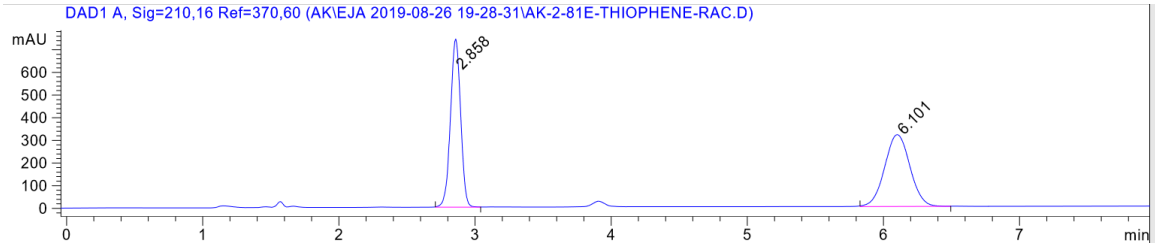
Enantioenriched **8n•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.523	BB	0.0540	2507.61743	731.10217	95.9818
2	1.821	BB	0.0641	104.97870	25.48206	4.0182

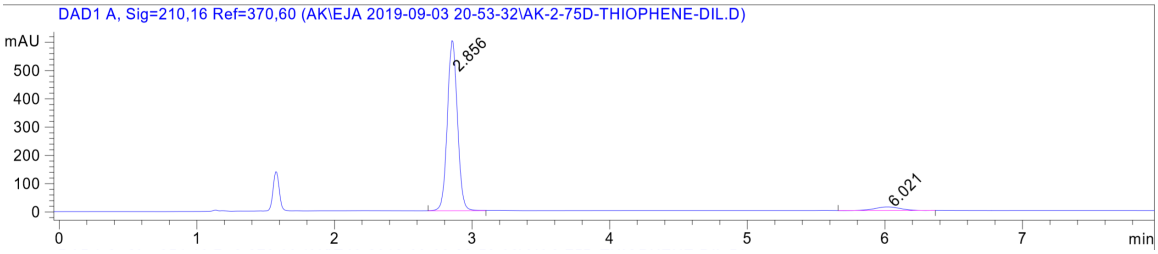
Racemic **8o•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.858	BB	0.0809	3854.20142	738.73291	48.5294
2	6.101	BB	0.1985	4087.78906	316.89798	51.4706

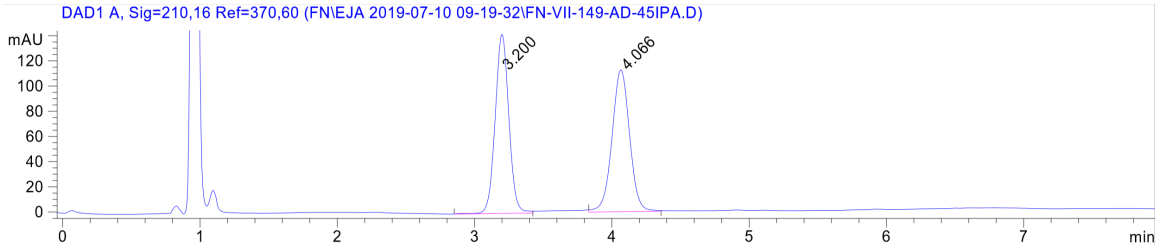
Enantioenriched **8o•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.856	BB	0.0794	3073.72705	603.51361	95.1667
2	6.021	BB	0.1866	156.10904	12.59354	4.8333

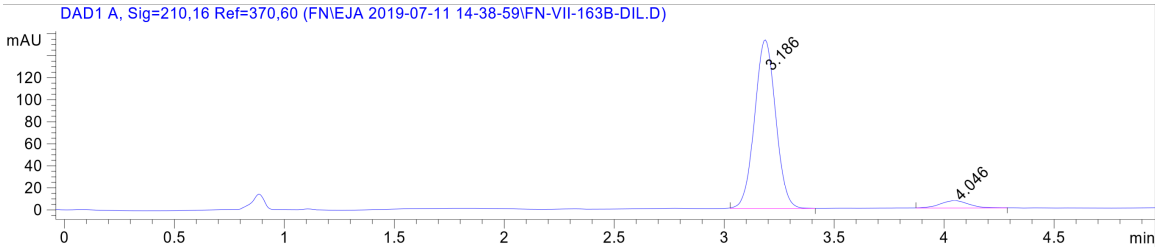
Racemic **8p•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.200	BB	0.1065	981.89862	142.25697	49.4769
2	4.066	BB	0.1378	1002.66058	112.71777	50.5231

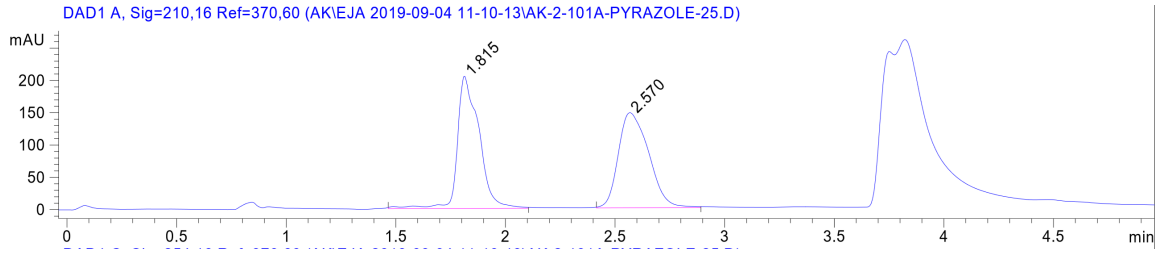
Enantioenriched **8p•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.186	BB	0.1037	1020.52930	153.26720	94.3455
2	4.046	BB	0.1415	61.16384	6.76278	5.6545

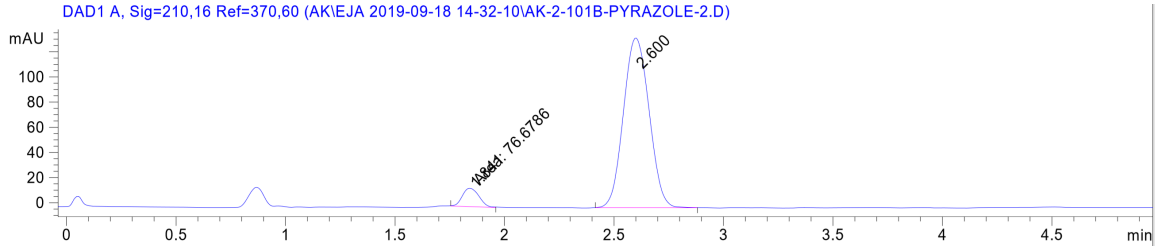
Racemic **8q•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.815	BB	0.0964	1416.28662	205.47318	50.0412
2	2.570	BB	0.1604	1413.95361	146.76917	49.9588

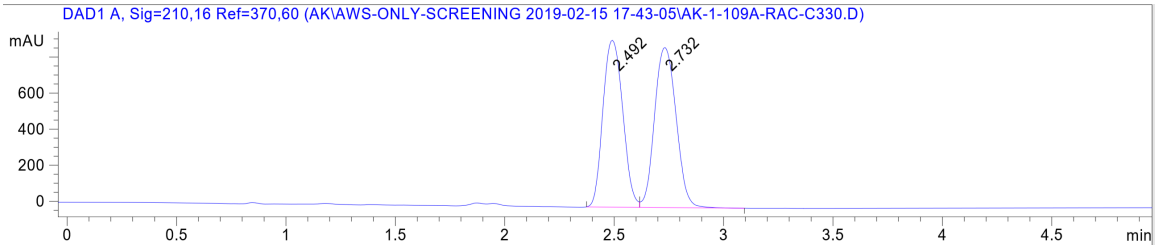
Enantioenriched **8q•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.841	MM	0.0872	76.67860	14.65488	6.5141
2	2.600	BB	0.1291	1100.44189	135.06032	93.4859

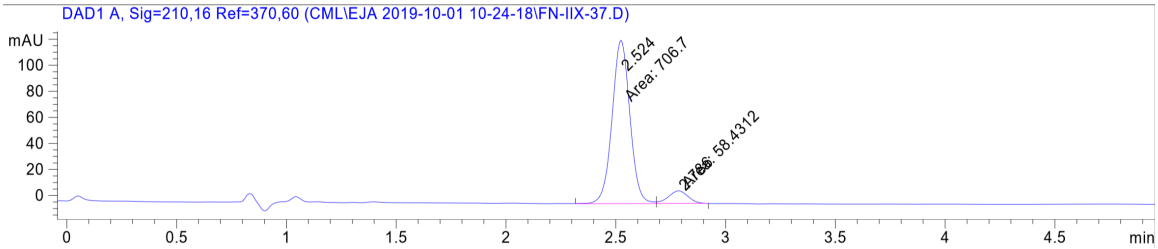
Racemic **8r•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.492	BV	0.1016	5821.55029	922.38538	48.8926
2	2.732	VB	0.1082	6085.25879	885.50177	51.1074

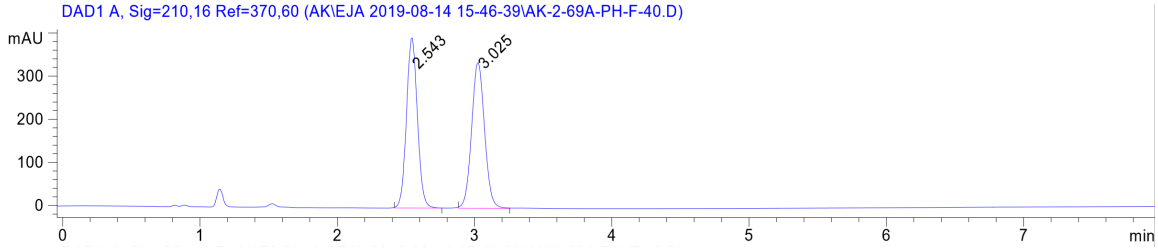
Enantioenriched **8r•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.524	MF	0.0937	706.70044	125.69700	92.3632
2	2.786	FM	0.1009	58.43125	9.65216	7.6368

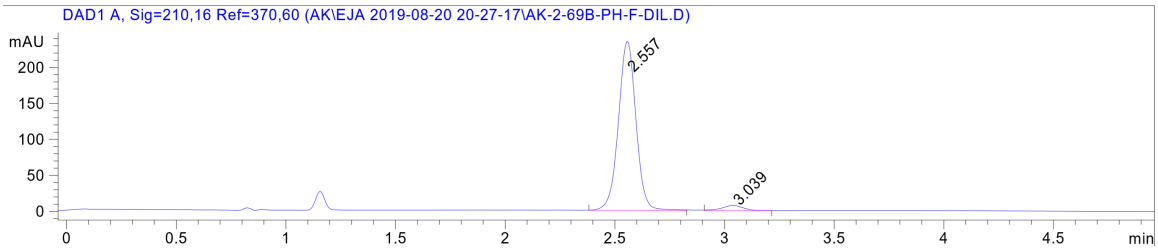
Racemic **10a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.543	BB	0.0891	2190.28516	392.62985	49.6934
2	3.025	BB	0.1008	2217.31665	336.81812	50.3066

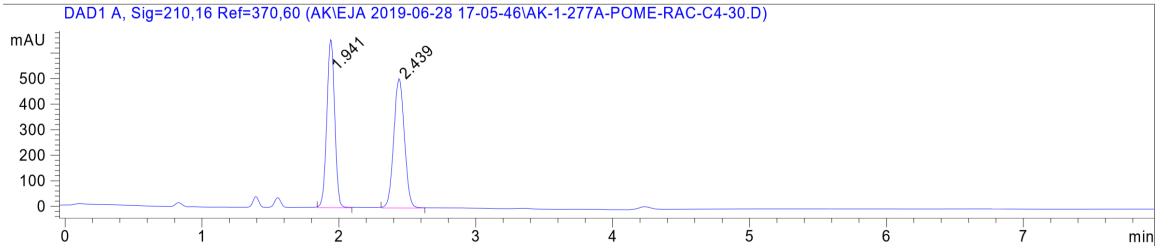
Enantioenriched **10a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.557	BB	0.0848	1307.88232	235.36581	96.4332
2	3.039	BB	0.1029	48.37504	7.15398	3.5668

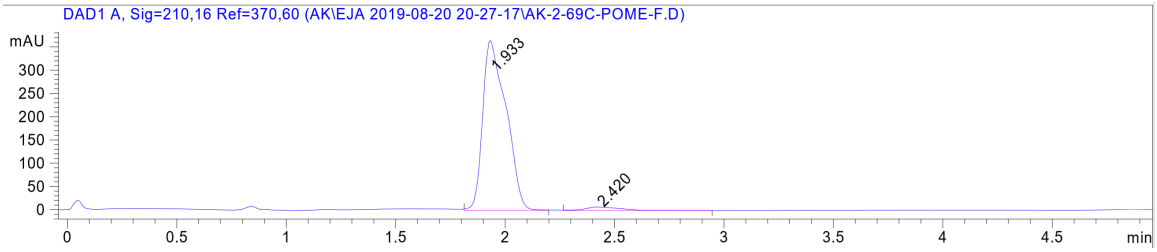
Racemic **10b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.941	BB	0.0632	2637.20605	652.49164	48.9944
2	2.439	BB	0.0835	2745.45801	504.47842	51.0056

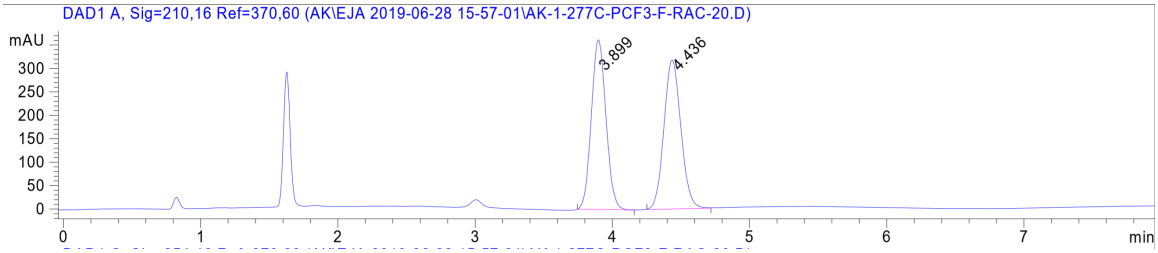
Enantioenriched **10b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.933	BB	0.1048	2717.86035	365.49832	96.9924
2	2.420	BB	0.1516	84.27748	7.58419	3.0076

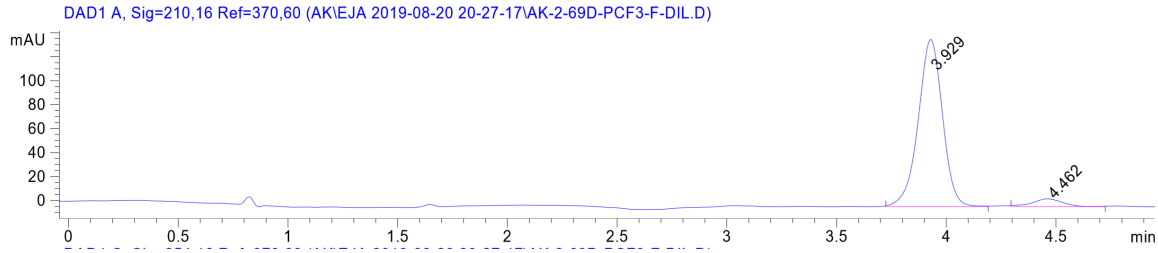
Racemic **10c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.899	BB	0.1183	2674.89038	361.63055	49.4474
2	4.436	BB	0.1364	2734.68140	317.63568	50.5526

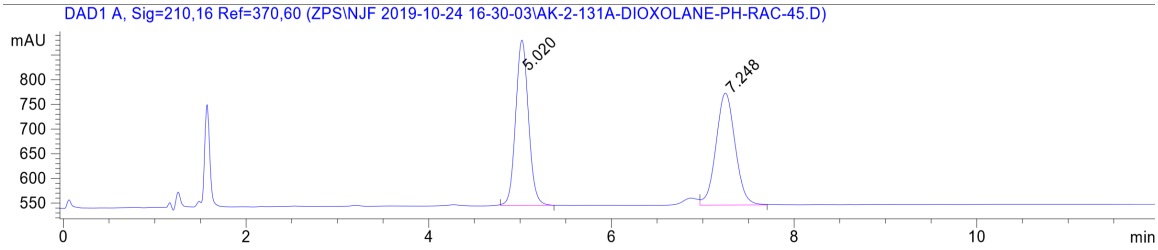
Enantioenriched **10c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.929	BB	0.1179	1076.24158	139.70760	94.6188
2	4.462	BB	0.1424	61.20900	6.46822	5.3812

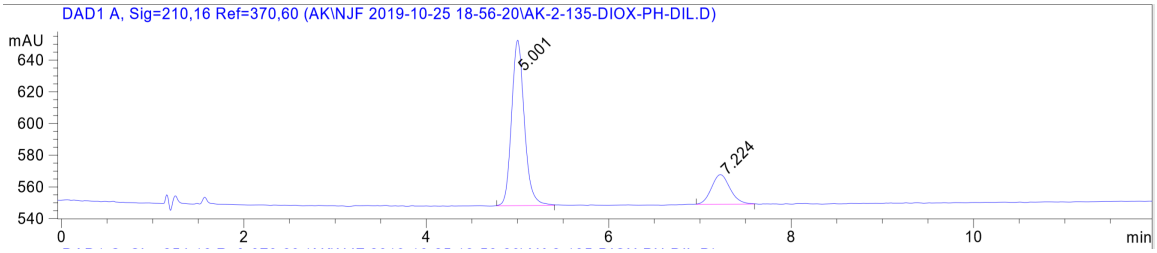
Racemic **10d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.020	BB	0.1540	3273.37476	334.94397	49.7505
2	7.248	VB	0.2260	3306.21167	226.86429	50.2495

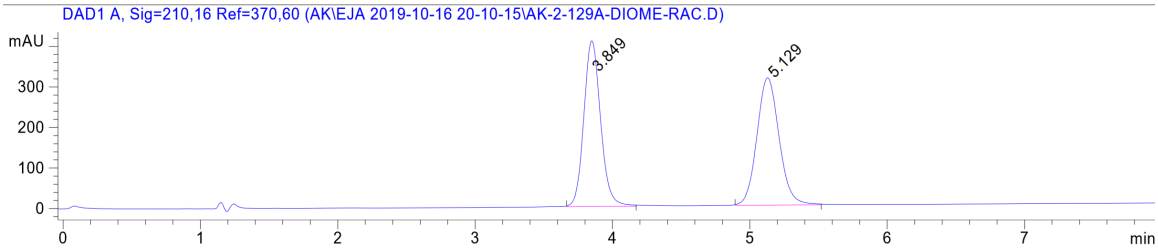
Enantioenriched **10d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.001	BB	0.1472	1013.64154	104.43392	79.2472
2	7.224	BB	0.2156	265.44623	18.70652	20.7528

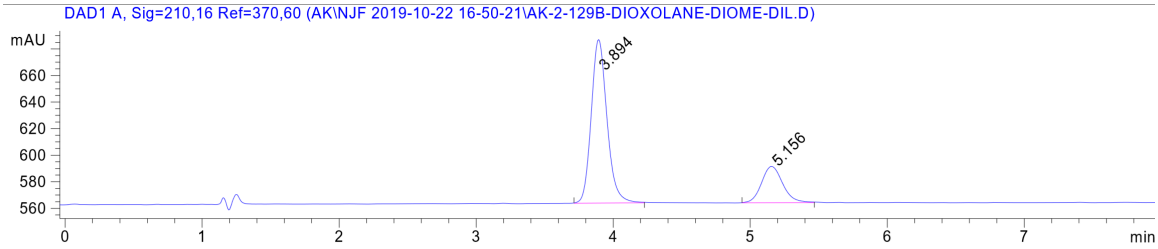
Racemic **10e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.849	BB	0.1310	3464.39844	408.41620	49.5651
2	5.129	BB	0.1749	3525.19043	314.15067	50.4349

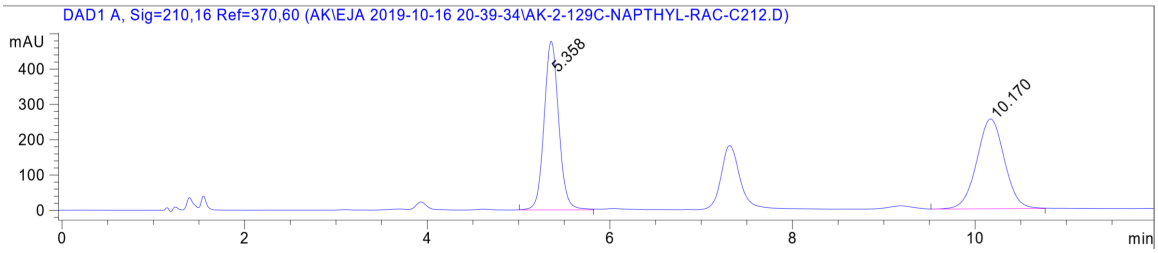
Enantioenriched **10e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.894	BB	0.1232	984.75873	123.21400	77.0345
2	5.156	BB	0.1627	293.57529	27.45859	22.9655

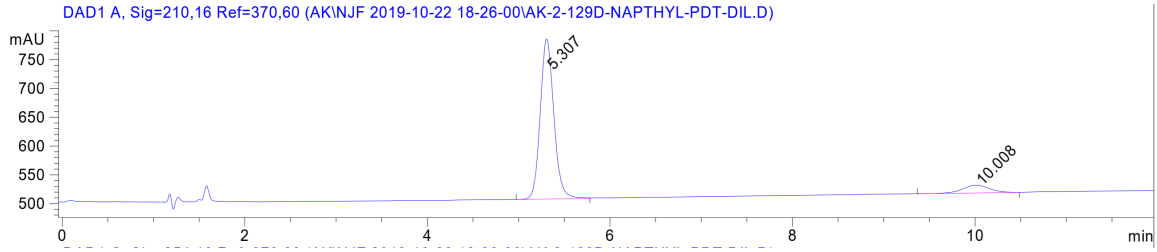
Racemic **10f•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.358	BB	0.1693	5294.22119	477.65454	49.7768
2	10.170	VB	0.3231	5341.70605	254.29431	50.2232

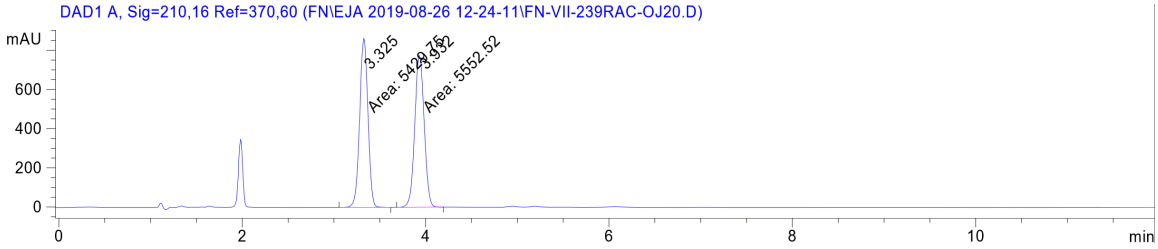
Enantioenriched **10f•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.307	BB	0.1589	2883.06396	278.23975	91.1323
2	10.008	BV	0.3114	280.54007	13.55918	8.8677

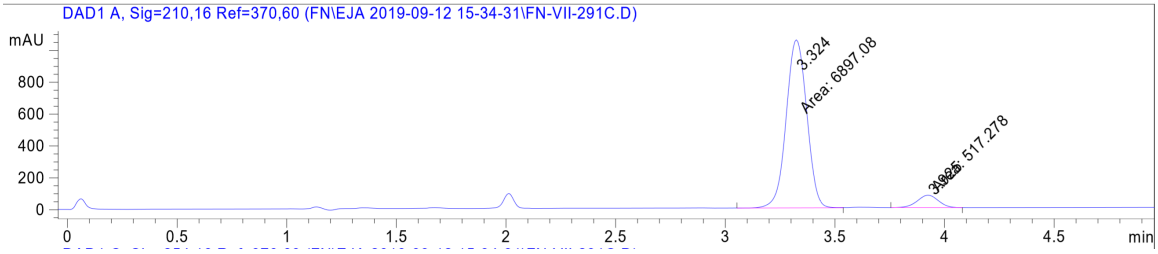
Racemic **12a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.325	MM	0.1045	5429.74902	866.15106	49.4411
2	3.932	MM	0.1190	5552.51855	777.85889	50.5589

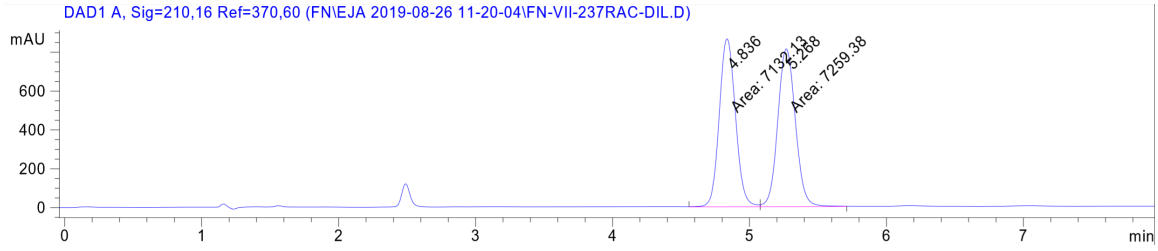
Enantioenriched **12a•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.324	MM	0.1085	6897.07910	1059.70032	93.0233
2	3.925	MM	0.1103	517.27832	78.12787	6.9767

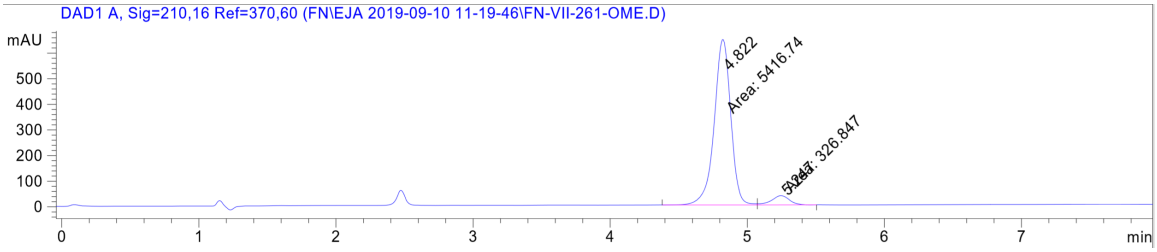
Racemic **12b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.836	MF	0.1369	7132.13086	868.20764	49.5579
2	5.268	FM	0.1484	7259.37549	815.35889	50.4421

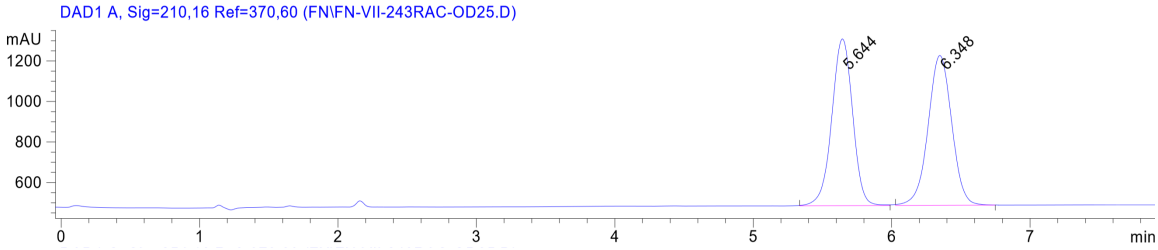
Enantioenriched **12b•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.822	MF	0.1393	5416.73535	648.23450	94.3094
2	5.247	FM	0.1491	326.84689	36.52797	5.6906

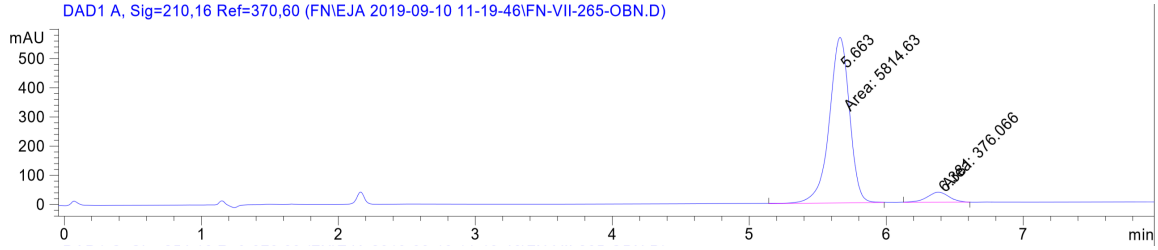
Racemic **10c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.644	BB	0.1623	8622.24121	822.63135	49.5394
2	6.348	BB	0.1826	8782.58984	739.38312	50.4606

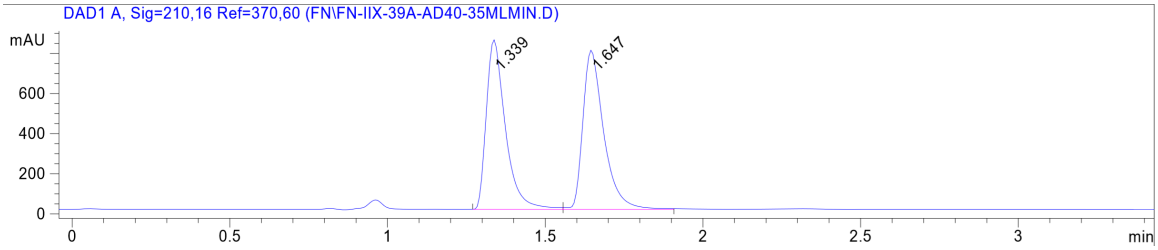
Enantioenriched **10c•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.663	MM	0.1704	5814.63037	568.69189	93.9253
2	6.381	MM	0.1822	376.06619	34.40401	6.0747

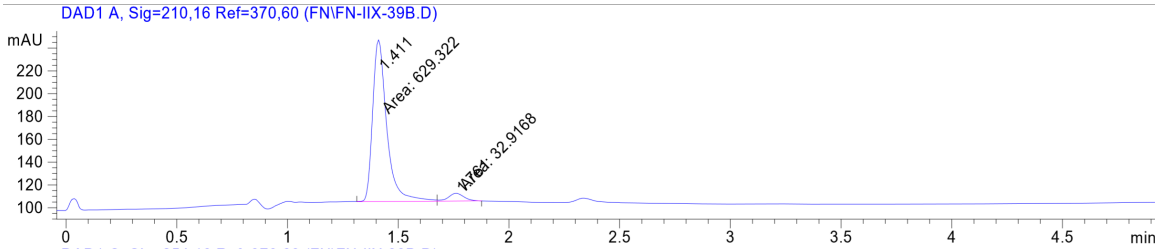
Racemic **10d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.339	BV	0.0654	3562.84033	841.34003	49.4402
2	1.647	VB	0.0697	3643.52856	791.14252	50.5598

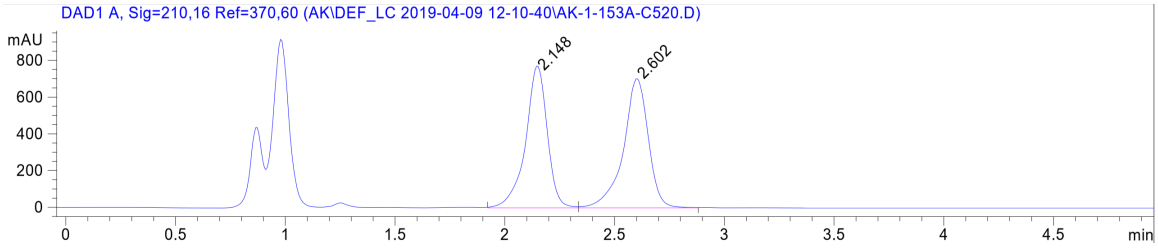
Enantioenriched **10d•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.411	MF	0.0737	629.32190	142.36954	95.0295
2	1.761	FM	0.0794	32.91683	6.91080	4.9705

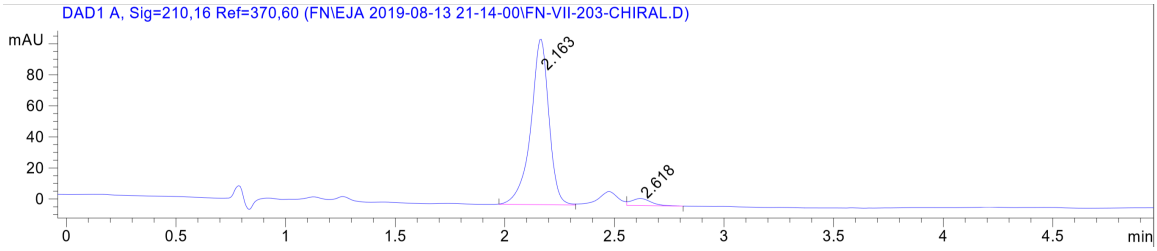
Racemic **12e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.148	BV	0.1044	5318.58984	771.45270	48.8723
2	2.602	VB	0.1204	5564.02832	702.45618	51.1277

Enantioenriched **12e•Cbz**



Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.163	BV	0.0868	612.66595	106.95222	95.4794
2	2.618	VB	0.0928	29.00750	4.64774	4.5206