Expedient Synthesis of 3-Hydroxyisoquinolines and 2-Hydroxy-1,4-naphthoquinones *via* One-Pot Aryne Acyl-Alkylation and Condensation

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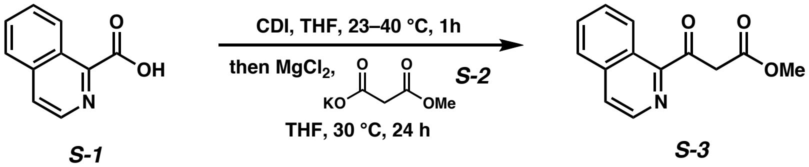
Materials and Methods

Unless stated otherwise, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents (distilled or passed over a column of activated alumina). Commercially obtained reagents were used as received. 3-methoxy-2-(trimethylsilyl)phenyl triflate (Table 1, entry 1),[1] 4,5-dimethoxy-2-(trimethylsilyl)phenyl triflate (Table 1, entry 3),[2] 6-(trimethylsilyl)benzo[*d*][1,3]dioxol-5-yl triflate (Table 1, entry 4),[3] 4,5-difluoro-2-(trimethylsilyl)phenyl triflate (Table 1, entry 5),[4] and 2-(trimethylsilyl)cyclohexene triflate (Table 1, entry 6)[5] were prepared according to literature procedures. Reaction temperatures were controlled by an IKAmag temperature modulator. Brine solutions are saturated aqueous sodium chloride solutions. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or ceric ammonium molybdate staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz, respectively) and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Data for ^{13}C NMR spectra are reported in terms of chemical shift relative to Me_4Si (δ 0.0). IR spectra were recorded on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or mixed (MM) ionization mode, or obtained from the Caltech Mass Spectral Facility (FAB+).

Representative procedure for the synthesis of β-ketoesters from carboxylic acids:



This procedure is based on the method of Masamune, *et al.*[6] A flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar was charged with magnesium chloride (0.469 g, 4.93 mmol, 1.0 equiv) and potassium monomethyl malonate (**S-2**) (1.02 g, 6.53 mmol, 1.3 equiv). A reflux condenser was attached and the flask was subsequently evacuated and back-filled with argon. Tetrahydrofuran (7.5 mL) was added and the suspension was heated to 65 °C for 3 h. After the above reaction had proceeded for 2 h, a separate flame-dried 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with isoquinoline-1-carboxylic acid (**S-1**) (0.852 g, 4.92 mmol, 1.0 equiv) and tetrahydrofuran (5 mL). To this solution was added carbonyl diimidazole (0.957 g, 5.90 mmol, 1.2 equiv) in portions, allowing for effervescence to subside between additions. **Warning:** vigorous gas evolution. The reaction was stirred at 23 °C until bubbling ceased (30 min), and then heated to 40 °C (at which point bubbling renewed) for an additional 30 min. The magnesium malonate suspension was cooled to 30 °C and the acyl-imidazole solution was added dropwise via syringe (NOTE: a white precipitate forms rapidly during this addition; vigorous stirring is necessary to avoid clumping). The resulting milky white suspension was stirred at 30 °C for 24 h. The reaction was cooled to 0 °C when TLC analysis showed complete consumption of the intermediate acyl imidazole. The reaction was quenched by the addition of 1.0 N HCl (15 mL) and extracted with EtOAc (3 x 40 mL). The combined organic layers were sequentially washed with water (80 mL), saturated aqueous sodium bicarbonate (80 mL), and brine (80 mL). The organic layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography over silica gel.

Spectroscopic Data for β-Ketoesters[7]:

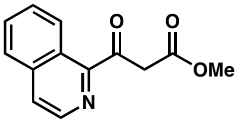


Table 2, Entry 10

Purified via flash chromatography (SiO_2, 10:90 EtOAc/hexanes) to yield a clear colorless oil (64% yield). $R_f = 0.70$ (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14–9.11 (m, 1H), 8.59 (d, *J* = 5.4 Hz, 1H), 7.89 (dd, *J* = 5.9, 2.4 Hz, 1H), 7.86 (dd, *J* = 5.9, 1.0 Hz, 1H), 7.76–7.70 (comp m, 2H), 4.38 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 169.0, 150.5, 141.0, 137.1, 130.5, 129.6, 127.0, 126.7, 126.3, 125.4, 52.2, 46.8; IR (Neat Film, NaCl) 3055, 2952, 1744, 1698, 1580, 1436, 1323, 1104, 1089 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{13}H_{11}NO_3$ $[M+H]^+$: 230.0812, found 230.0815.

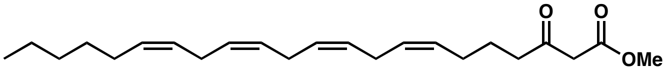


Table 2, Entry 11

Purified via flash chromatography (SiO_2, 5:95 → 8:92 EtOAc/hexanes) to yield a waxy white solid (90% yield). $R_f = 0.64$ (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45–5.32 (comp m, 8H), 3.75 (s, 3H), 3.45 (s, 2H), 2.84 (comp m, 6H), 2.56 (t, *J* = 7.3 Hz, 2H), 2.10 (dt, *J* = 7.3, 6.6 Hz, 2H), 2.07 (dt, *J* = 7.1, 7.1 Hz, 2H), 1.69 (tt, *J* = 7.6, 7.3 Hz, 2H), 1.41–1.26 (comp m, 6H), 0.90 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 167.6, 130.5, 129.0, 128.9, 128.6, 128.3, 128.1, 127.8, 127.5, 52.3, 49.0, 42.3, 31.5, 29.3, 27.2, 26.3, 25.7, 25.6, 25.6, 23.2, 22.6, 14.1; IR (Neat Film, NaCl) 3434, 2928, 2858, 1743, 1716, 1438, 1321, 1175, 1083, 1002 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{23}H_{36}O_3$ $[M+H]^+$: 361.2737, found 361.2735.

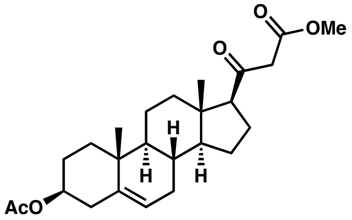


Table 2, Entry 12

Purified via flash chromatography (SiO_2, 5:95 → 10:90 EtOAc/hexanes) to yield a white solid (96% yield). R_f = 0.42 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.37 (d, *J* = 5.1 Hz, 1H), 4.64–4.57 (m, 1H), 3.73 (s, 3H), 3.45 (s, 2H), 2.62 (t, *J* = 9.0 Hz, 1H), 2.33 (dd, *J* = 3.7, 1.5 Hz, 1H), 2.31 (dd, *J* = 2.7, 2.2 Hz, 1H), 2.22–2.15 (m, 1H), 2.05–2.00 (comp m, 2H), 2.03 (s, 3H), 1.98 (td, *J* = 5.4, 2.0 Hz, 1H), 1.87 (app dd, *J* = 9.3, 2.4 Hz, 2H), 1.76–1.67 (comp m, 2H), 1.66–1.54 (comp m, 4H), 1.54–1.44 (comp m, 2H), 1.28–1.12 (comp m, 3H), 1.02 (s, 3H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5, 170.5, 167.7, 139.7, 122.2, 73.8, 63.1, 56.8, 52.2, 50.4, 49.8, 44.5, 38.6, 38.1, 37.0, 36.6, 31.9, 31.7, 27.7, 24.4, 23.1, 21.4, 21.0, 19.3, 13.4; IR (Neat Film, NaCl) 2945, 2903, 1748, 1732, 1709, 1438, 1374, 1310, 1245, 1032 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{25}H_{36}O_5$ $[M–H]^-$: 415.2490, found 415.2516.

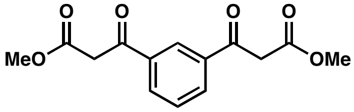
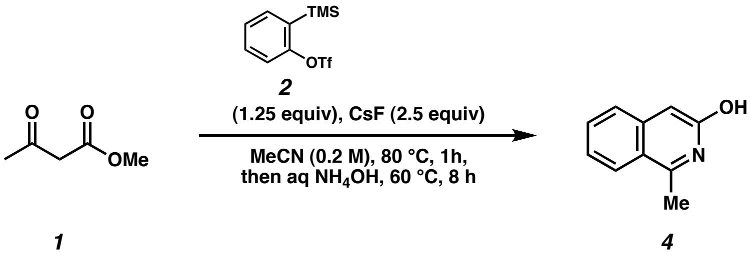


Table 2, Entry 13[8]

Purified via flash chromatography (SiO_2, 15:85 → 25:75 EtOAc/hexanes) to yield a clear colorless oil (92% yield). R_f = 0.20 (25:75 EtOAc/hexanes); product is isolated as a 1:0.8:0.3 mixture of bis(β-ketoester), *E*-mono-enolized, and *Z*-mono-enolized tautomers, respectively. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.54 (s, 0.8H), 12.52 (s, 0.3H), 8.50 (t, *J* = 1.8 Hz, 1H), 8.35 (t, *J* = 1.8 Hz, 0.8H), 8.19 (dd, *J* = 7.5, 1.8 Hz, 2H), 8.03 (tt, *J* = 7.5, 1.8 Hz, 1H), 8.02 (tt, *J* = 7.5, 1.8 Hz, 0.8H), 7.88 (dd, *J* = 7.5, 1.8

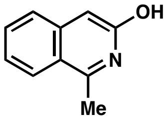
Hz, 0.3H), 7.65 (t, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 0.8H), 7.49 (t, *J* = 7.8 Hz, 0.3H), 5.75 (s, 0.8H), 5.74 (s, 0.3H), 4.06 (s, 4H), 4.05 (s, 1.6H), 3.83 (s, 2.4H), 3.83 (s, 0.9H), 3.78 (s, 6H), 3.77 (s, 2.4H), 3.77 (s, 0.9H); ^{13}C NMR (125 MHz, $CDCl_3$) bis(β-ketoester): δ 191.5, 167.5, 133.3, 131.0, 129.6, 128.5, 52.6, 45.7; combination of *E*- and *Z*-mono-enolized tautomers: δ 191.8, 173.3, 170.5, 169.8, 167.7, 167.1, 136.5, 136.3, 134.2, 133.9, 130.9, 129.2, 128.9, 128.7, 126.1, 123.8, 88.1, 87.7, 52.6, 52.5, 51.6, 51.5, 48.7, 45.7; IR (Neat Film, NaCl) 2955, 1742, 1689, 1654, 1625, 1438, 1327, 1268, 1199, 1150, 1012 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{14}H_{14}O_6$ [M+H]$^+$: 279.0863, found 279.0863.

Representative procedure for the synthesis of 3-hydroxyisoquinolines from *β*-ketoesters:



A flame-dried 10 mL Schlenk flask with a septum-covered side arm equipped with a magnetic stir bar was charged with cesium fluoride (0.152 g, 1.00 mmol, 2.5 equiv). The flask was evacuated and back-filled with argon (x2). Acetonitrile (2 mL), methyl acetoacetate (**1**) (0.043 mL, 0.4 mmol, 1.0 equiv) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**) (0.121 mL, 0.498 mmol, 1.25 equiv) were sequentially added. The screw valve was sealed and the reaction was heated to 80 °C while stirring for 1 h. The reaction was cooled to room temperature when TLC analysis showed complete consumption of methyl acetoacetate (**1**) (NOTE: at this point, the major component of the reaction is the acyl-alkylated arene). The screw valve was removed under positive argon pressure and aqueous ammonium hydroxide (28% w/w, 2 mL) was added via syringe. The screw valve was replaced and tightened, and the reaction was heated to 60 °C while stirring for 8 h. The reaction was cooled to room temperature when TLC analysis showed complete consumption of the intermediate acyl-alkylated arene. The mixture was diluted with brine (5 mL) and extracted with EtOAc (2 x 15 mL). The aqueous layer was neutralized to pH 7 with 2.0 N HCl and extracted again with EtOAc (2 x 15 mL). The aqueous layers were discarded and the combined organic layers were extracted with 2.0 N HCl (3 x 20 mL) (NOTE: this process separates nitrogen containing products capable of forming HCl salts (in aqueous phase) from other organic products (in organic phase)). The organic layers were discarded and the combined aqueous layers were neutralized to pH 7 with 2.0 N NaOH and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified either by recrystallization or flash chromatography over silica gel.

Spectroscopic Data for 3-Hydroxyisoquinolines:



1-Methyl-3-hydroxyisoquinoline (4)[9]

Purified via recrystallization from boiling EtOAc to yield a yellow solid (84% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.18 (br s, 1H), 7.99 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.51 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.26 (ddd, *J* = 8.3, 6.8, 1.0 Hz, 1H), 6.67 (s, 1H), 2.77 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.8, 157.2, 140.4, 130.6, 126.3, 126.1, 123.5, 122.1, 99.2, 21.3; IR (Neat Film, NaCl) 3384, 3244, 2641, 1668, 1627, 1454, 1382, 1234 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{10}H_9NO$ $[M+H]^+$: 160.0757, found 160.0765.

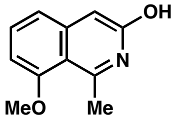


Table 1, Entry 1

Purified via recrystallization from boiling EtOAc to yield a yellow solid (70% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.94 (br s, 1H), 7.33 (dd, *J* = 8.1, 7.6 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 6.52 (s, 1H), 3.88 (s, 3H), 2.87 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.7, 158.6, 155.5, 143.7, 131.2, 118.4, 114.1, 102.4, 100.2, 56.0, 26.6; IR (Neat Film, NaCl) 2590, 1651, 1627, 1587, 1502, 1438, 1388 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{11}H_{11}NO_2$ $[M+H]^+$: 190.0863, found 190.0886.

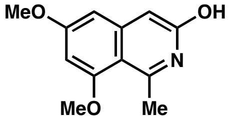


Table 1, Entry 2[10]

Purified via recrystallization from boiling EtOAc to yield a yellow solid (81% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.40 (s, 1H), 6.29 (s, 1H), 6.10 (s, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.8, 160.2, 160.0, 159.9, 157.9, 140.8, 122.2, 106.7, 98.8, 56.1, 55.7, 20.1; IR (Neat Film, NaCl) 2921, 2719, 1666, 1641, 1624, 1560, 1497, 1430, 1178 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{12}H_{13}NO_3$ $[M+H]^+$: 220.0968, found 220.0963.

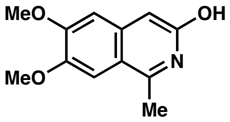


Table 1, Entry 3[11]

Purified via recrystallization from boiling EtOAc to yield a yellow solid (75% yield). ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.83 (s, 1H), 6.64 (s, 1H), 6.58 (s, 1H), 4.00 (s, 3H), 3.95 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.2, 155.1, 147.7, 146.4, 142.0, 113.5, 104.8, 102.9, 102.5, 56.3, 56.1, 17.5; IR (Neat Film, NaCl) 3251, 2939, 2836, 1645, 1488, 1433, 1245, 1161, 1029 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{12}H_{13}NO_3$ $[M^{\bullet}]^-$: 219.0895, found 219.0884.

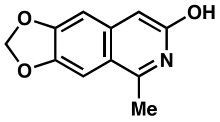


Table 1, Entry 4[12]

Purified via recrystallization from boiling EtOAc to yield a yellow solid (77% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.25 (s, 1H), 6.96 (s, 1H), 6.50 (s, 1H), 6.08 (s, 2H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.6, 151.3, 145.7, 139.9, 131.6, 106.9, 105.0, 101.8, 101.4, 101.1, 20.8; IR (Neat Film, NaCl) 3306, 2918, 1658, 1651, 1620, 1478, 1433, 1231 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{11}H_9NO_3$ $[M+H]^+$: 204.0655, found 204.0656.

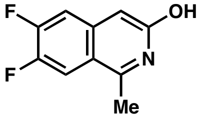


Table 1, Entry 5

Purified via recrystallization from boiling EtOAc to yield a pale yellow solid (73% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.86 (br s, 1H), 8.04 (dd, J = 12.0, 8.3 Hz, 1H), 7.71 (dd, J = 12.0, 8.1 Hz, 1H), 6.73 (s, 1H), 2.74 (s, 3H); ^{13}C NMR (125 MHz, DMSO-*d*$_6$) δ 160.3 (d, $J_{C–F}$ = 2.3 Hz), 153.5 (d, $J_{C–F}$ = 16.6 Hz), 151.5 (d, $J_{C–F}$ = 16.6 Hz), 148.0 (d, $J_{C–F}$ = 16.6 Hz), 146.1 (d, $J_{C–F}$ = 16.6 Hz), 138.3 (d, $J_{C–F}$ = 9.7 Hz), 113.1 (d, $J_{C–F}$ = 15.2 Hz), 111.8 (d, $J_{C–F}$ = 17.5 Hz), 99.2, 21.7; ^{19}F NMR (282 MHz, DMSO-*d*$_6$) δ –132.5 (app quintet, *J* = 11.0 Hz), –140.5 (app q, *J* = 11.0 Hz); IR (Neat Film, NaCl) 2613, 1679, 1656, 1516, 1488, 1454, 1336 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{10}H_7F_2NO$ [M+H]$^+$: 196.0568, found 196.0573.

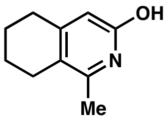


Table 1, Entry 6[13]

Purified via flash chromatography (SiO_2, 20:80 EtOAc/hexanes) to yield a white solid (54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (s, 1H), 2.64 (t, *J* = 6.1 Hz, 2H), 2.44 (t, *J* = 6.5 Hz, 2H), 2.27 (s, 3H), 1.80–1.74 (comp m, 2H), 1.73–1.67 (comp m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 154.3, 142.3, 114.3, 114.2, 30.2, 24.2, 23.0, 22.2, 16.5; IR (Neat Film, NaCl) 2942, 1651, 1609, 1536, 1450, 1251, 1172, 1103 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{10}H_{13}NO$ [M+H]$^+$: 164.1070, found 164.1065.

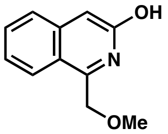


Table 2, Entry 1

Purified via flash chromatography (SiO_2, 40:60 → 50:50 EtOAc/hexanes) to yield a yellow solid (82% yield). R_f = 0.20 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.53 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 1H), 7.29 (ddd, *J* = 8.8, 6.8, 1.2 Hz, 1H), 6.99

(s, 1H), 5.02 (s, 2H), 3.51 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.8, 153.3, 141.8, 131.0, 126.1, 125.6, 123.9, 121.2, 104.0, 71.5, 58.7; IR (Neat Film, NaCl) 2929, 2670, 2595, 1629, 1562, 1514, 1457, 1326, 1103 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{11}H_{11}NO_2$ [M+H]$^+$: 190.0863, found 190.0860.

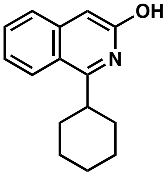


Table 2, Entry 2

Purified via flash chromatography (SiO$_2$, 15:85 EtOAc/hexanes) to yield a yellow solid (81% yield). R_f = 0.20 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.37 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 7.09 (ddd, *J* = 8.8, 6.6, 1.0 Hz, 1H), 6.73 (s, 1H), 3.46 (tt, *J* = 11.8, 3.4 Hz, 1H), 2.04–1.76 (comp m, 7H), 1.54–1.42 (comp m, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 160.7, 159.8, 143.2, 131.0, 126.3, 125.1, 122.5, 117.5, 104.4, 39.8, 31.5, 26.7, 25.6; IR (Neat Film, NaCl) 3208, 2930, 2855, 1694, 1651, 1602, 1452, 1374, 1258, 1066 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{15}H_{17}NO$ [M+H]$^+$: 228.1383, found 228.1382.

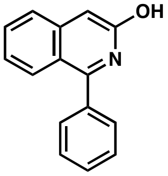


Table 2, Entry 3[14]

Purified via flash chromatography (SiO$_2$, 40:60 EtOAc/hexanes) to yield a yellow solid (79% yield). R_f = 0.27 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.81 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.61–7.58 (m, 2H), 7.56–7.52 (comp m, 3H), 7.49 (ddd, *J* = 8.8, 6.6, 1.2 Hz, 1H), 7.18

(ddd, *J* = 8.8, 6.6, 1.2 Hz, 1H), 6.93 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 157.1, 142.0, 136.4, 130.7, 130.0, 129.2, 128.4, 127.8, 125.9, 123.7, 121.2, 103.1; IR (Neat Film, NaCl) 3151, 3058, 2883, 1662, 1639, 1552, 1450 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{15}H_{11}NO$ $[M+H]^+$: 222.0913, found 222.0917.

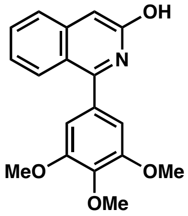


Table 2, Entry 4

Purified via flash chromatography (SiO_2, 30:70 EtOAc/hexanes) to yield a yellow solid (68% yield). R_f = 0.14 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.50 (ddd, *J* = 8.5, 6.6, 1.2 Hz, 1H), 7.19 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 6.93 (s, 1H), 6.80 (s, 2H), 3.95 (s, 3H), 3.83 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 156.0, 153.0, 142.4, 138.8, 131.1, 130.9, 127.7, 126.0, 123.7, 120.5, 107.3, 103.5, 60.9, 56.1; IR (Neat Film, NaCl) 3191, 2940, 1711, 1694, 1679, 1640, 1585, 1505, 1454, 1414, 1354, 1335, 1236, 1127 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{18}H_{17}NO_4$ $[M+H]^+$: 312.1230, found 312.1249.

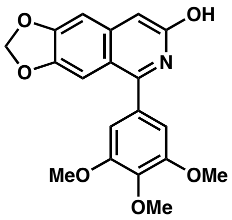


Table 2, Entry 5

Purified via flash chromatography (SiO_2, 40:60 → 80:20 EtOAc/hexanes) to yield a yellow-orange solid (73% yield). R_f = 0.15 (70:30 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (s, 1H), 6.80 (s, 1H), 6.72 (app s, 3H), 6.01 (s, 2H), 3.92 (s, 3H), 3.82 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 153.1, 152.1, 150.5, 146.4, 142.6, 138.7, 130.2, 115.7, 106.9, 105.5, 101.8, 101.5, 100.6, 60.9, 56.1; IR (Neat Film, NaCl) 3181, 2938, 1643, 1612, 1584, 1455, 1236, 1126 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{19}H_{17}NO_6$ $[M+H]^+$: 356.1129, found356.1126.

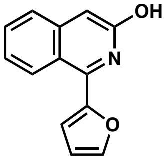


Table 2, Entry 6

Purified via flash chromatography (SiO_2, 25:75 → 35:65 EtOAc/hexanes) to yield a red-orange solid (85% yield). R_f = 0.13 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.8 Hz, 1H), 7.66 (s, 1H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 3.4 Hz, 1H), 6.97 (s, 1H), 6.60 (dd, *J* = 3.4, 1.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 150.3, 144.4, 144.1, 142.5, 130.8, 126.9, 126.1, 124.4, 119.7, 114.0, 112.1, 104.6; IR (Neat Film, NaCl) 3057, 2893, 1634, 1551, 1444, 1300, 1152 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{13}H_9NO_2$ $[M+H]^+$: 212.0706, found 212.0717.

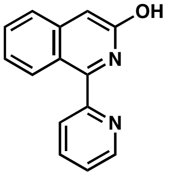


Table 2, Entry 7

Purified via flash chromatography (SiO_2, 40:60 → 70:30 EtOAc/hexanes) to yield a yellow solid (72% yield). R_f = 0.20 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (ddd, *J* = 4.9, 1.0, 0.7 Hz, 1H), 8.22 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.90 (td, *J* = 7.6, 1.7 Hz, 1H), 7.85 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.51 (ddd, *J* = 8.6, 6.6, 1.0 Hz, 1H), 7.44 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.27 (ddd, *J* = 8.9, 6.6, 1.0 Hz, 1H), 7.03 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 155.2, 154.0, 149.3, 142.1, 136.8, 130.7, 127.4, 125.9, 125.4, 124.5, 123.7, 121.4, 104.3; IR (Neat Film, NaCl) 3056, 2665, 1626, 1587, 1555, 1445, 1312, 1132 cm^{-1}; HRMS (MM: ESI–APCI) *m*/*z* calc'd for $C_{14}H_{10}N_2O$ $[M+H]^+$: 223.0866, found 223.0870.

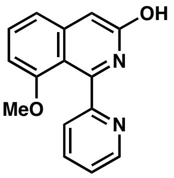


Table 2, Entry 8

Purified via flash chromatography (SiO_2, 60:40 EtOAc/hexanes → 80:15:5 EtOAc/hexanes/CH_2Cl_2) to yield a yellow solid (94% yield). R_f = 0.13 (70:30 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 5.1, 0.7 Hz, 1H), 7.73 (td, *J* = 7.6, 1.7 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.30 (ddd, *J* = 7.3, 4.9, 1.0 Hz, 1H), 7.06 (d, *J* = 8.5 Hz, 1H), 6.70 (br s, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 3.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 156.9, 148.3, 144.2, 135.3, 131.6, 130.1, 124.0, 122.8, 121.6, 118.4, 115.0, 113.0, 102.3, 55.2; IR (Neat Film, NaCl) 3062, 2937, 1643, 1638, 1556, 1434, 1390, 1281, 1147 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{15}H_{12}N_2O_2$ $[M+H]^+$: 253.0972, found 253.0843.

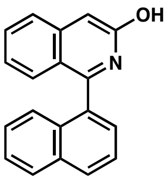


Table 2, Entry 9

Purified via flash chromatography (SiO_2, 20:80 EtOAc/hexanes → 80:10:10 EtOAc/hexanes/CH_2Cl_2) to yield a yellow solid (69% yield). R_f = 0.15 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.6 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.64 (dd, *J* = 8.5, 7.1 Hz, 1H), 7.58 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.52 (ddd, *J* = 8.3, 6.6, 1.5 Hz, 1H), 7.48 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 7.41 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.37 (dd, *J* = 6.6, 1.2 Hz, 1H), 7.35 (dd, *J* = 8.1, 0.5 Hz, 1H), 7.05 (ddd, *J* = 8.6, 6.6, 1.2 Hz, 1H), 6.96 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 156.4, 141.5, 134.2, 133.6, 132.0, 130.9, 129.5, 128.4, 127.8, 126.7, 126.2, 125.8, 125.7, 125.1, 123.8, 122.8, 105.0, 103.0; IR (Neat Film, NaCl) 2968, 2665, 2582, 1626, 1601, 1558, 1449, 1317 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{19}H_{13}NO$ $[M+H]^+$: 272.1070, found 272.1082.

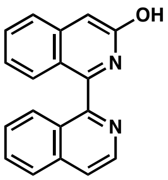


Table 2, Entry 10

Purified via flash chromatography (SiO_2, 50:50 → 60:40 EtOAc/hexanes) to yield a yellow solid (68% yield). R_f = 0.30 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 5.9 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.85 (dd, *J* = 5.9, 1.0 Hz, 1H), 7.72 (ddd, *J* = 8.3, 6.6, 1.0 Hz, 1H), 7.70 (d, *J* = 8.6

Hz, 1H), 7.64 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.52 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 7.47 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 1H), 7.44 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.15 (ddd, *J* = 8.6, 6.8, 1.2), 7.02 (d, *J* = 0.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 156.4, 155.4, 142.2, 141.2, 136.6, 130.7, 130.5, 127.7, 127.6, 127.2, 127.0, 126.9, 125.9, 124.4, 123.4, 121.4, 102.7; IR (Neat Film, NaCl) 3053, 2665, 2586, 1624, 1554, 1448, 1318, 1136 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{18}H_{12}N_2O$ [M+H]$^+$: 273.1022, found 273.1033.

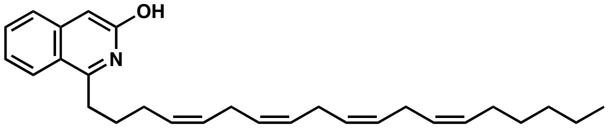


Table 2, Entry 11

Purified via flash chromatography (SiO_2, 15:85 EtOAc/hexanes) to yield a pale yellow oil (81% yield). R_f = 0.16 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.40 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 7.12 (ddd, *J* = 8.8, 6.6, 1.0 Hz, 1H), 6.76 (s, 1H), 5.49–5.31 (comp m, 8H), 3.26 (dd, *J* = 8.1, 7.8 Hz, 2H), 2.86–2.78 (comp m, 6H), 2.28 (dd, *J* = 7.1, 6.8 Hz, 2H), 2.05 (dd, *J* = 7.1, 7.1 Hz, 2H), 1.92 (tt, *J* = 7.8, 7.6 Hz, 2H), 1.38–1.24 (comp m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 156.4, 143.1, 131.3, 130.5, 129.1, 129.0, 128.6, 128.2, 128.1, 127.9, 127.6, 126.1, 125.7, 122.7, 118.3, 104.6, 31.5, 31.3, 30.4, 29.4, 27.2, 27.1, 25.7, 25.6, 25.5, 22.6, 14.1; IR (Neat Film, NaCl) 3265, 2930, 1697, 1602, 1458, 1284 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{28}H_{37}NO$ [M+H]$^+$: 404.2948, found 404.2951.

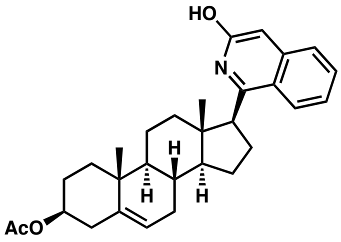


Table 2, Entry 12

Purified via flash chromatography (SiO_2, 15:85 → 50:50 EtOAc/hexanes) to yield a yellow oil (62% yield). $R_f = 0.20$ (25:75 EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.36 (ddd, *J* = 8.5, 6.6, 1.0 Hz, 1H), 7.05 (ddd, *J* = 8.8, 6.6, 1.2 Hz, 1H), 6.72 (s, 1H), 5.42 (d, *J* = 5.1 Hz, 1H), 4.62 (dddd, *J* = 5.9, 5.6, 5.4, 4.1 Hz, 1H), 3.72 (app t, *J* = 9.5 Hz, 1H), 2.67 (ddd, *J* = 11.2, 9.5, 2.5 Hz, 1H), 2.38–2.28 (comp m, 2H), 2.14–2.02 (comp m, 2H), 2.05 (s, 3H), 1.96–1.81 (comp m, 3H), 1.71–1.40 (comp m, 8H), 1.32 (app qd, *J* = 12.5, 4.8 Hz, 1H), 1.14 (app td, *J* = 13.4, 3.9 Hz, 1H), 1.06 (app td, *J* = 12.0, 4.8 Hz, 1H), 0.99 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 170.6, 159.9, 154.9, 143.0, 139.7, 130.9, 126.1, 122.4, 122.3, 119.9, 104.7, 73.8, 57.2, 50.5, 50.1, 47.0, 38.6, 38.1, 37.0, 36.7, 32.2, 31.9, 27.7, 26.4, 25.0, 21.5, 21.0, 19.3, 13.5; IR (Neat Film, NaCl) 3221, 2943, 1729, 1711, 1600, 1438, 1375, 1365, 1249, 1033 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{30}H_{37}NO_3$ $[M+H]^+$: 460.2846, found 460.2845.

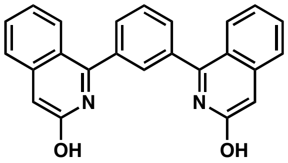
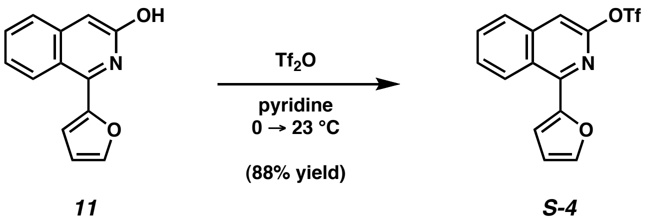


Table 2, Entry 13[15]

Purified via flash chromatography (SiO_2, 50:50 → 75:25 EtOAc/hexanes) to yield a yellow solid (66% yield). $R_f = 0.46$ (70:30 EtOAc/hexanes); ^1H NMR (500 MHz, CD_3OD) δ 7.93 (t, *J* = 8.5 Hz, 2H), 7.91 (t, *J* = 1.2 Hz, 1H), 7.85 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.79 (dd, *J* = 8.5, 7.1 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.56 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 2H), 7.27 (ddd, *J* = 8.5, 6.6, 1.2 Hz, 2H), 6.95 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 167.9, 160.0, 141.1, 139.1, 131.5, 130.6, 130.4, 128.6, 127.2, 126.4, 124.6, 122.0, 100.5; IR (Neat Film, NaCl) 3181, 3063, 2958, 1671, 1639, 1624, 1555, 1446, 1343, 1281, 1152, 1024 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{24}H_{16}N_2O_2$ [M+H]$^+$: 365.1285, found 365.1293.

Synthesis of a 1,3-diarylisoquinoline *via* Suzuki coupling:

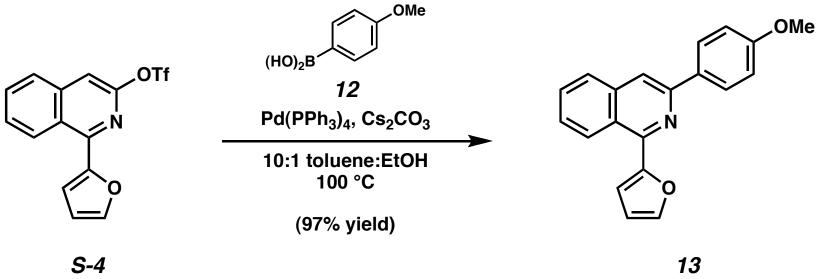


11 *S-4*

Isoquinoline triflate S-4

A flame-dried 1 dram vial equipped with a magnetic stir bar and a screw cap with PTFE septum was charged with 3-hydroxyisoquinoline **11** (0.028 g, 0.133 mmol) and pyridine (0.7 mL). The mixture was cooled to 0 °C in an ice bath while stirring, and Tf_2O (0.033 mL, 0.196 mmol, 1.5 equiv) was then added dropwise via syringe. The reaction was stirred at 0 °C for 5 minutes, after which the ice bath was removed. The resulting brown solution was allowed to warm to room temperature while stirring for 11 hours. When TLC analysis showed complete consumption of the 3-hydroxyisoquinoline **11**, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate (1 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography over silica gel (SiO_2, 10:90 EtOAc/hexanes) to yield triflate **S-4** as a pale yellow oil (0.040 g, 88% yield). R_f = 0.70 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (dd, *J* = 8.6, 0.7 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.77 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.75 (d, *J* = 0.73 Hz, 1H), 7.70 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 1H), 7.44 (s, 1H), 7.40 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.67 (dd, *J* = 3.4, 1.7

Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 151.0, 148.2, 144.9, 140.3, 131.3, 128.5, 127.5, 127.4, 124.8, 118.8 (q, J_{C-F} = 320.8 Hz), 115.0, 112.4, 109.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ –72.8; IR (Neat Film, NaCl) 3141, 3077, 2923, 1593, 1547, 1484, 1420, 1321, 1224, 1212, 1139, 1109, 1016 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{14}H_8F_3NO_4S$ [M$^•$]$^+$: 343.0126, found 343.0131.

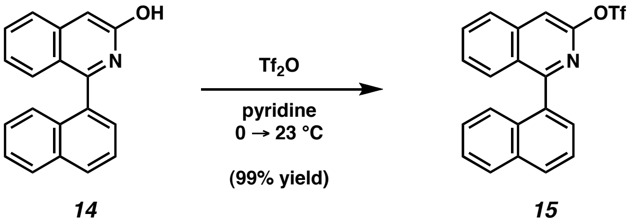


Diarylisoquinoline 13

A flame-dried 1 dram vial equipped with a magnetic stir bar and a screw cap with a PTFE septum was charged with $Pd(PPh_3)_4$ (0.0035 g, 0.003 mmol, 0.05 equiv), caesium carbonate (0.0220 g, 0.068 mmol, 1.2 equiv), and 4-methoxyphenylboronic acid (**12**) (0.0142 g, 0.093 mmol, 1.6 equiv). The vial was evacuated and backfilled with argon (x2). Isoquinoline triflate **S-4** (0.020 g, 0.058 mmol) in toluene (0.6 mL) was added *via* syringe followed by ethanol (0.06 mL). The vial was sealed and heated to 100 °C. After stirring for 18 h, the reaction was cooled to room temperature and filtered through a plug of silica under EtOAc elution. The solvents were removed under vacuum and the crude yellow residue was purified via flash chromatography (SiO_2, 3:97 EtOAc/hexanes) to yield 1,3-diarylisoquinoline **13** as a colorless oil (0.0169 g, 97% yield). R_f = 0.37 (15:85 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 8.5, 1.0 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 2H), 7.94 (s, 1H), 7.87 (ddd, *J* = 8.1, 0.7, 0.5 Hz, 1H), 7.74 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.67 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.58 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1H), 7.37 (dd, *J* = 3.4, 0.7 Hz, 1H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.67 (dd, *J* = 3.4, 2.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 155.0, 149.8, 148.4, 143.7, 138.3, 132.0, 130.0, 128.2, 127.4, 127.0, 126.9, 124.2, 114.9, 114.1, 112.6, 111.8, 55.4; IR (Neat Film, NaCl) 3052, 2958, 2933, 2835, 1607, 1554, 1514, 1487, 1439, 1334, 1289, 1249, 1173, 1033, 1012 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{20}H_{15}NO_2$ [M$^{•}$]$^{+}$: 301.1103, found 301.1099.

Synthesis of QUINAP:

Spectroscopic data is provided only for those compounds that have not been previously reported in the literature (i.e., **15**). Spectroscopic data for compounds **16**,[16] **17**,[17] and QUINAP (**18**)[18] match those previously reported in all respects.

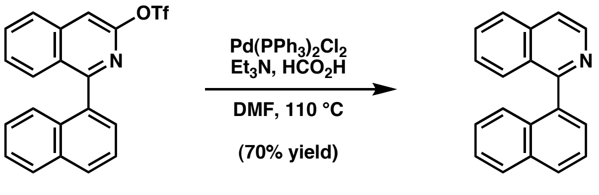


14 ***15***

Isoquinoline triflate 15

A flame-dried 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with 3-hydroxyisoquinoline **14** (0.053 g, 0.195 mmol) and pyridine (1.2 mL). The mixture was cooled to 0 °C in an ice bath while stirring, and Tf_2O (0.056 mL, 0.333 mmol, 1.7 equiv) was then added dropwise via syringe. The reaction was stirred at 0 °C for 5 minutes, after which the ice bath was removed. The resulting orange brown solution was allowed to warm to room temperature while stirring for 12 hours. When TLC analysis showed complete consumption of the 3-hydroxyisoquinoline **14**, the reaction was quenched by the addition of water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography over silica gel (SiO_2, 5:95 → 10:90 EtOAc/hexanes) to yield triflate **15** as a colorless oil (0.0782 g, 99% yield). $R_f = 0.70$ (25:75 EtOAc/hexanes); ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.78 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.72 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.69 (d, *J* = 0.7 Hz, 1H), 7.63 (dd, *J* = 7.0, 8.1 Hz, 1H), 7.58 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.52 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.49 (ddd, *J* = 8.5, 6.8, 1.0 Hz, 1H), 7.45 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.38 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 151.3, 139.2, 134.7, 133.7, 131.9, 131.6, 129.7, 128.4, 128.3, 128.2, 128.2, 127.3, 126.7, 126.2, 125.6, 125.0, 118.8 (q, *J* = 320.8 Hz), 110.4; ^{19}F (282 MHz, $CDCl_3$) δ –72.9; IR (Neat Film, NaCl) 3066, 1622, 1594, 1553, 1509, 1504, 1422, 1321, 1244, 1227, 1212, 1138, 1110 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{20}H_{12}F_3NO_3S$ $[M^{\bullet}]^+$: 403.0490, found 403.0504.

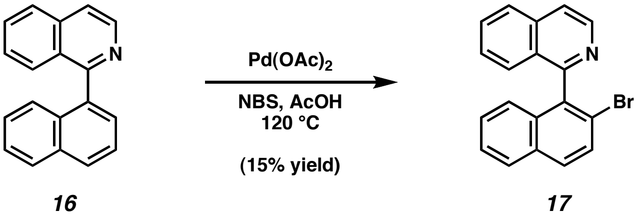


15 ***16***

Naphthyl isoquinoline 16

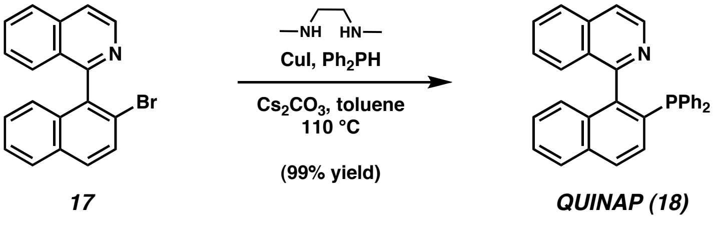
A flame-dried 1 dram vial equipped with a magnetic stir bar and a screw cap with a PTFE septum was charged with 1-(1'-naphthyl)-3-(trifluoromethanesulfonyloxy)isoquinoline **15** (0.020 g, 0.0496 mmol) and DMF (0.6 mL). The mixture was stirred for approximately 5 minutes at room temperature, after which $Pd(PPh_3)_2Cl_2$ (0.075 g, 0.0107 mmol, 20 mol%), Et_3N (0.040 mL, 0.287 mmol, 5.8 equiv), and formic acid (0.020 mL, 0.530 mmol, 10.6 equiv) were added sequentially. The resulting mixture was heated to 110 °C for 90 minutes. The reaction was then cooled to room temperature when TLC analysis showed complete consumption of triflate **15**, diluted with water (2 mL), and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography over silica gel (SiO_2, 5:95 → 20:80

EtOAc/hexanes) to yield napthyl isoquinoline **16** as a white solid (0.0087 g, 70% yield). Spectroscopic data matched those reported in the literature.[16]



1-(2'-bromo-1'-naphthyl)isoquinoline 17

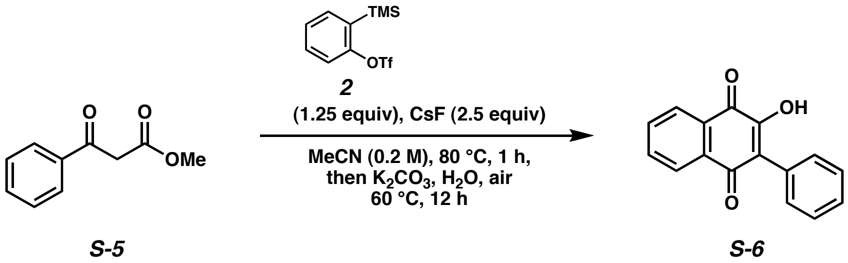
This procedure is based on the method of Sanford, *et al.*[19] A flame-dried 1 dram vial equipped with a magnetic stir bar and a screw cap with a PTFE septum was charged with naphthyl isoquinoline **16** (0.021 mg, 0.081 mmol), Pd(OAc)$_2$ (0.063 g, 0.028 mmol, 35 mol%), NBS (0.016 g, 0.090 mmol, 1.1 equiv), and AcOH (0.8 mL). The vial was sealed with a Teflon-lined screw cap, and the mixture was heated to 120 °C while stirring for 17 hours. The solvent was then evaporated under reduced pressure and the crude residue was purified by flash chromatography over silica gel (SiO$_2$, 5:95 → 20:80 EtOAc/hexanes) to yield bromonaphthyl isoquinoline **17** as a colorless film (0.0039 g, 15% yield). Spectroscopic data matched those reported in the literature.[17]



1-(2'-diphenylphosphino-1'-naphthyl)isoquinoline (QUINAP, 18)

This procedure is based on our previously reported variant of Buchwald's copper-catalyzed phosphine–aryl halide coupling reaction.[20] A flame-dried 1 dram vial equipped with a magnetic stir bar and a screw cap with a PTFE septum was charged with copper(I) iodide (0.0022 g, 0.012 mmol, 70 mol%), diphenylphosphine (0.0061 mL, 0.035 mmol, 2.1 equiv), *N,N'*-dimethylethylenediamine (0.002 mL, 0.019 mmol, 1.1 equiv), and toluene (0.1 mL). The mixture was stirred for 30 minutes at room temperature. Following this, cesium carbonate (0.0221 g, 0.068 mmol, 4 equiv), 1-(2-bromo-1-naphthyl)isoquinoline (**17**) (0.0055 g, 0.017 mmol, 1 equiv), and toluene (0.15 mL) were added, and the vial was sealed and heated to 110 °C. After stirring for 14 hours, the reaction mixture was allowed to cool to room temperature and filtered through celite under dichloromethane elution (20 mL). The solution was concentrated under reduced pressure and the crude residue was purified via flash chromatography (SiO_2, 5:95 → 10:90 EtOAc/hexanes) to yield QUINAP (**18**) as a colorless film (0.0075 g, 99% yield). Spectroscopic data matched those reported in the literature.[18]

Representative procedure for the synthesis of 2-hydroxy-1,4-naphthoquinones from *β*-ketoesters:



A flame-dried 15 mL reaction tube equipped with a magnetic stir bar was charged with cesium fluoride (0.152 g, 1.00 mmol, 2.5 equiv). The reaction tube was sealed with a rubber septum, evacuated, and back-filled with argon (x2). Acetonitrile (2 mL), methyl 3-oxo-4-phenylbutanoate (**S-5**) (0.077 g, 0.4 mmol, 1.0 equiv) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**) (0.121 mL, 0.498 mmol, 1.25 equiv) were sequentially added. The reaction was then heated to 80 °C while stirring for 1 h. The reaction was cooled to room temperature when TLC analysis showed complete consumption of methyl 3-oxo-4-phenylbutanoate (**S-5**) (NOTE: at this point, the major component of the reaction is the acyl-alkylated arene). Potassium carbonate (0.276 g, 5.0 equiv) in water (2 mL) was added via syringe and the biphasic mixture was vigorously stirred at room temperature for 30 min. The septum was then removed and the reaction was heated to 60 °C while open to air for 12 h. The reaction was cooled to room temperature when TLC analysis showed complete consumption of the acyl-alkylated arene intermediate. The reaction was diluted with EtOAc (10 mL) and extracted with 1.0 N K_2CO_3 (5 x 15 mL). The organic layer was discarded. The combined aqueous layers were acidified to pH 1 with 2.0 N HCl (**Warning:** vigorous gas evolution) and extracted with EtOAc (3 x 40 mL). The combined organic layers were washed with brine (50 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the residue was purified via flash chromatography over silica gel.

Spectroscopic Data for 2-Hydroxy-1,4-naphthoquinones:

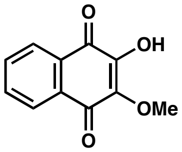


Table 3, Entry 1[21]

Purified via flash chromatography (SiO_2, 40:60 EtOAc/hexanes) to yield an orange solid (86% yield). R_f = 0.11 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 8.06 (ddd, *J* = 7.6, 1.2, 0.5 Hz, 1H), 7.74 (td, *J* = 7.6, 1.5 Hz, 1H), 7.69 (td, *J* = 7.6, 1.5 Hz, 1H), 6.91 (br s, 1H), 4.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.2, 181.1, 142.5, 140.5, 134.7, 133.4, 131.3, 129.1, 126.8, 126.1, 60.7; IR (Neat Film, NaCl) 3370, 2967, 1673, 1639, 1592, 1461, 1276, 1203 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{11}H_8O_4$ $[M+H]^+$: 205.0495, found 205.0498.

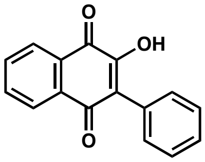


Table 3, Entry 2 (S-6)[22]

Purified via flash chromatography (SiO_2, 10:90 EtOAc/hexanes) to yield a bright yellow solid (92% yield). R_f = 0.37 (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.17 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.83 (td, *J* = 7.6, 1.5 Hz, 1H), 7.76 (td, *J* = 7.6, 1.5 Hz, 1H), 7.60 (br s, 1H), 7.52 (d, *J* = 7.1 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.42 (tt, *J* = 7.3, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.9, 182.1, 152.4, 135.5, 133.4, 133.1, 130.9, 130.2, 129.5, 128.9, 128.2, 127.5, 126.4, 122.4; IR (Neat Film, NaCl) 3345, 3057, 1651, 1594, 1365, 1332, 1282, 1000 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{16}H_{10}O_3$ $[M+H]^+$: 251.0703, found 251.0705.

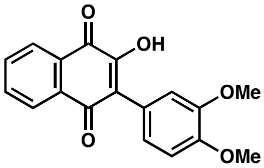


Table 3, Entry 3[23]

Purified via flash chromatography (SiO_2, 15:85 → 25:75 EtOAc/hexanes) to yield a dark red solid (78% yield). R_f = 0.45 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (ddd, *J* = 7.6, 1.2, 0.5 Hz, 1H), 8.16 (ddd, *J* = 7.6, 1.2, 0.5 Hz, 1H), 7.82 (td, *J* = 7.6, 1.2 Hz, 1H), 7.74 (td, *J* = 7.6, 1.2 Hz, 1H), 7.61 (br s, 1H), 7.17 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.0, 181.8, 151.9, 149.4, 148.4, 135.2, 133.1, 132.9, 129.3, 127.3, 126.1, 124.0, 122.4, 121.9, 114.0, 110.6, 56.0, 55.9; IR (Neat Film, NaCl) 3363, 2938, 1712, 1655, 1594, 1516, 1364, 1260, 1145, 1026 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{18}H_{14}O_5$ $[M+H]^+$: 311.0914, found 311.0914.

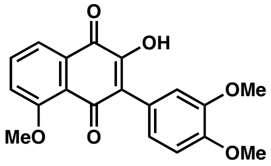


Table 3, Entry 4

Purified via flash chromatography (SiO_2, 30:70 → 70:30 EtOAc/hexanes) to yield a dark red solid (84% yield). R_f = 0.10 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.67 (dd, *J* = 8.6, 7.6 Hz, 1H), 7.39 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.13 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.11 (d, *J* = 1.5 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 4.01 (s, 3H), 3.93 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.7, 182.2, 159.9, 150.5, 149.3, 148.2, 134.1, 131.6, 124.1, 123.4, 122.9, 120.1, 119.9, 119.0, 114.2, 110.5, 56.6, 56.0, 55.9; IR (Neat Film, NaCl) 3347, 2937, 2838, 1650, 1585, 1516, 1472, 1369, 1280, 1256, 1016 cm^{-1}; HRMS (MM: ESI–APCI) *m*/*z* calc'd for $C_{19}H_{16}O_6$ $[M+H]^+$: 341.1020, found 341.1022.

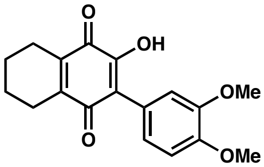


Table 3, Entry 5

Purified via flash chromatography (SiO_2, 20:80 EtOAc/hexanes) to yield a red solid (61% yield). R_f = 0.53 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (br s, 1H), 7.07 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 2.52 (ddd, *J* = 12.5, 4.4, 2.0 Hz, 4H), 1.75 (comp m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.6, 183.6, 149.5, 149.2, 148.3, 145.3, 138.1, 123.7, 122.4, 118.7, 113.9, 110.6, 55.9, 55.8, 23.4, 22.1, 21.2, 21.0; IR (Neat Film, NaCl) 3347, 2937, 1639, 1516, 1346, 1257, 1143, 1026 cm^{-1}; HRMS (MM: ESI–APCI) *m*/*z* calc'd for $C_{18}H_{18}O_5$ $[M+H]^+$: 315.1227, found 315.1228.

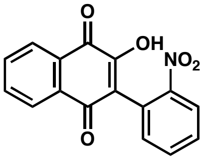


Table 3, Entry 6[24]

Purified via flash chromatography (SiO_2, 50:50 → 70:30 EtOAc/hexanes) to yield a red-orange solid (70% yield). $R_f = 0.37$ (70:30 EtOAc/hexanes); ^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (dd, *J* = 7.3, 1.5 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.0 Hz, 1H), 8.07 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.83 (td, *J* = 7.5, 1.5 Hz, 1H), 7.79 (td, *J* = 7.5, 1.5 Hz, 1H), 7.74 (td, *J* = 7.6, 1.2 Hz, 1H), 7.60 (td, *J* = 7.6, 1.5 Hz, 1H), 7.57 (dd, *J* = 7.6, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 183.0, 181.5, 151.3, 149.3, 135.5, 134.2, 133.7, 133.5, 132.2, 130.5, 129.9, 127.0, 126.6, 126.5, 124.6, 105.0; IR (Neat Film, NaCl) 3325, 2923, 1674, 1639, 1523, 1363, 1303, 1286, 1263 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_9NO_5$ $[M+H]^+$: 296.0553, found 296.0564.

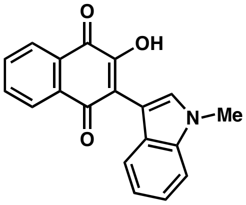


Table 3, Entry 7[25]

Purified via flash chromatography (SiO_2, 5:95 → 15:85 EtOAc/hexanes) to yield a dark blue solid (84% yield). $R_f = 0.17$ (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 8.16 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 7.79 (td, *J* = 7.6, 1.5 Hz, 1H), 7.73 (td, *J* = 7.6, 1.2 Hz, 1H), 7.68 (br s, 1H), 7.65 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.64 (s, 1H), 7.38 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.29 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.20 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.4, 181.2, 150.4, 136.9, 134.7, 133.2, 133.1, 133.0, 129.8, 127.2, 126.8, 125.9, 122.4, 122.1, 120.1, 118.1, 109.6, 104.2, 33.3; IR (Neat Film, NaCl) 3350, 3052, 2928, 1651, 1627, 1525, 1474, 1362, 1332, 1287, 1240, 1104 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{19}H_{13}NO_3$ $[M+H]^+$: 304.0968, found 304.0968.

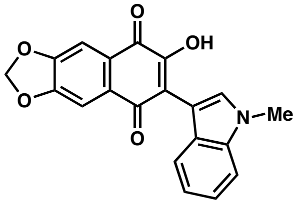


Table 3, Entry 8

Purified via flash chromatography (SiO_2, 15:85 → 20:80 EtOAc/hexanes) to yield a dark blue solid (88% yield). $R_f = 0.60$ (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (br s, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.61 (s, 1H), 7.58 (s, 1H), 7.53 (s, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.28 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.19 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 6.17 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.5, 180.1, 153.1, 151.6, 150.1, 136.8, 132.8, 130.6, 126.8, 126.0, 122.3, 122.0, 120.0, 116.9, 109.5, 107.2, 105.4, 104.1, 102.7, 33.2; IR (Neat Film, NaCl) 3346, 2911, 1706, 1647, 1595, 1478, 1330, 1306, 1239, 1035 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{20}H_{13}NO_5$ $[M^{\bullet}]^+$: 347.0794, found 347.0804.

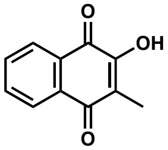


Table 3, Entry 9 (Phthiocol)[26,27]

Purified via flash chromatography (SiO_2, 10:90 → 15:85 EtOAc/hexanes) to yield a yellow solid (80% yield). $R_f = 0.37$ (25:75 EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (ddd, *J* = 7.8, 1.2, 0.5 Hz, 1H), 8.09 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 7.76 (td, *J* = 7.8, 1.5 Hz, 1H), 7.69 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (br s, 1H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 185.0, 181.2, 153.1, 134.8, 133.0, 132.9, 129.4, 126.7, 126.1, 120.5, 8.9; IR (Neat Film, NaCl) 3336, 1658, 1592, 1395, 1349, 1305, 1278, 1208, 1181, 1072 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{11}H_8O_3$ [M+H]$^+$: 189.0546, found 189.0539.

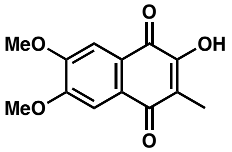


Table 3, Entry 10 (*O*-des-methyl-Stoechadone)[26,28]

Purified via flash chromatography (SiO$_2$, 15:85 → 25:75 EtOAc/hexanes) to yield a yellow-orange solid (63% yield). R_f = 0.63 (50:50 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.56 (s, 1H), 7.48 (s, 1H), 7.28 (br s, 1H), 4.03 (s, 3H), 4.01 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 184.8, 180.5, 154.3, 152.9, 152.5, 128.1, 123.5, 119.2, 108.7, 107.6, 56.6, 56.5, 8.6; IR (Neat Film, NaCl) 3371, 2964, 1638, 1579, 1375, 1321, 1126, 1018 cm^{-1}; HRMS (MM: ESI–APCI) *m/z* calc'd for $C_{13}H_{12}O_5$ [M+H]$^+$: 249.0757, found 249.0764.

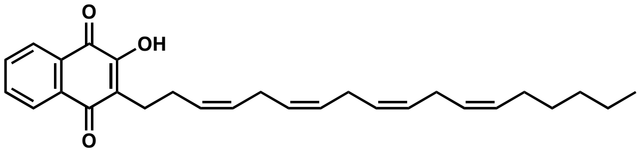


Table 3, Entry 11[26]

Purified via flash chromatography (SiO$_2$, 5:95 EtOAc/hexanes) to yield a yellow oil (66% yield). R_f = 0.33 (15:85 EtOAc/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.13 (ddd, *J* = 7.6, 1.5, 0.5 Hz, 1H), 8.09 (ddd, *J* = 7.6, 1.2, 0.5 Hz, 1H), 7.76 (td, *J* = 7.6, 1.2 Hz, 1H), 7.69 (td, *J* = 7.6, 1.5 Hz, 1H), 7.35 (br s, 1H), 5.50 (ddt, *J* = 18, 7.5, 1.5 Hz, 1H), 5.45–5.27 (comp m, 7H), 2.85–2.77 (comp m, 6H), 2.70 (app t, *J* = 7.5 Hz, 2H), 2.36 (dt, *J* = 7.3, 7.1 Hz, 2H), 2.05 (dt, *J* = 7.3, 6.8 Hz, 2H), 1.38–1.24 (comp m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 184.6, 181.4, 153.2, 134.9, 132.9, 132.8, 130.5, 129.4, 128.9, 128.8, 128.5, 128.2, 128.1, 127.9, 127.6, 126.8, 126.1, 123.8, 31.5, 29.3, 27.2, 25.9, 25.6, 25.6, 25.5, 23.3, 22.6, 14.1; IR (Neat Film, NaCl) 3377, 3012, 2928, 2857, 1774, 1664, 1648, 1594, 1371, 1348, 1276, 1216 cm^{-1}; HRMS (MM: ESI–APCI) *m*/*z* calc'd for $C_{28}H_{34}O_3$ $[M+H]^+$: 419.2581, found 419.2580.

Notes and references

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7 Spectroscopic data is only reported for those *β*-ketoesters that have not been previously reported in the literature.

8 The molar equivalents of carbonyl diimidazole, magnesium chloride, and potassium monomethyl malonate (**S-2**) were doubled for this substrate (i.e., 2.4 equiv carbonyl diimidazole, 2.0 equiv magnesium chloride, and 2.6 equiv potassium monomethyl malonate (**S-2**)).

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15 The molar equivalents of 2-(trimethylsilyl)phenyl triflate (**2**) and cesium fluoride were doubled for this substrate (i.e., 2.5 equiv silyl aryl triflate **2** and 5.0 equiv cesium fluoride).

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26 For the first preparation of this compound, see: R. J. Anderson and M. S. Newman, *J. Biol. Chem.*, 1933, **103**, 405–412.

27 NaOMe (5 equiv) in MeOH (2 mL) was used in place of K_2CO_3 in H_2O.

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Expedient Synthesis of 3-Hydroxyisoquinolines and 2-Hydroxy-1,4-naphthoquinones *via* One-Pot Aryne Acyl-Alkylation and Condensation

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The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA

Experimental Spectra

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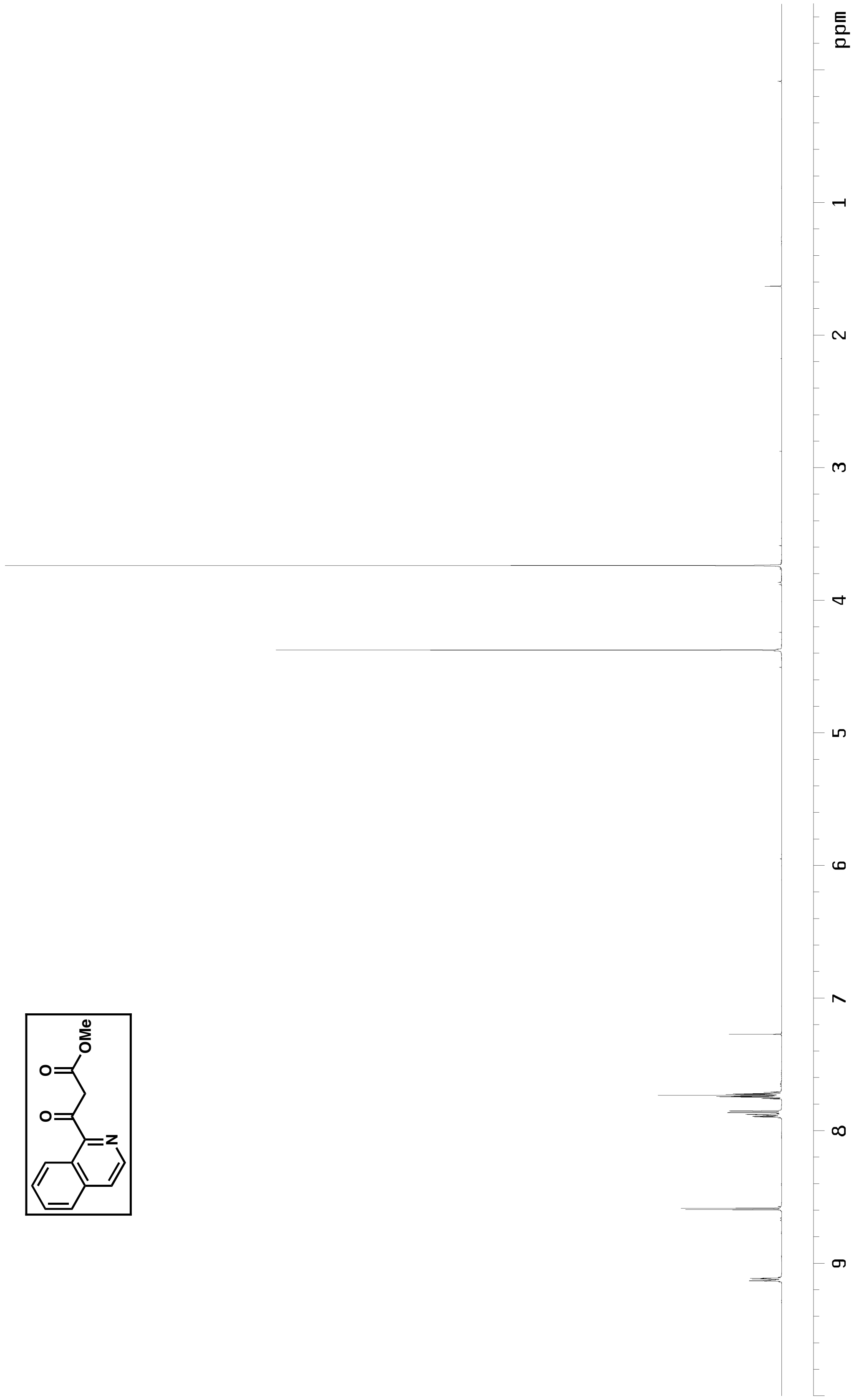


Figure 1.1 ^{1}H NMR (500 MHz, $CDCl_3$) of β-ketoester Table 2, entry 10.

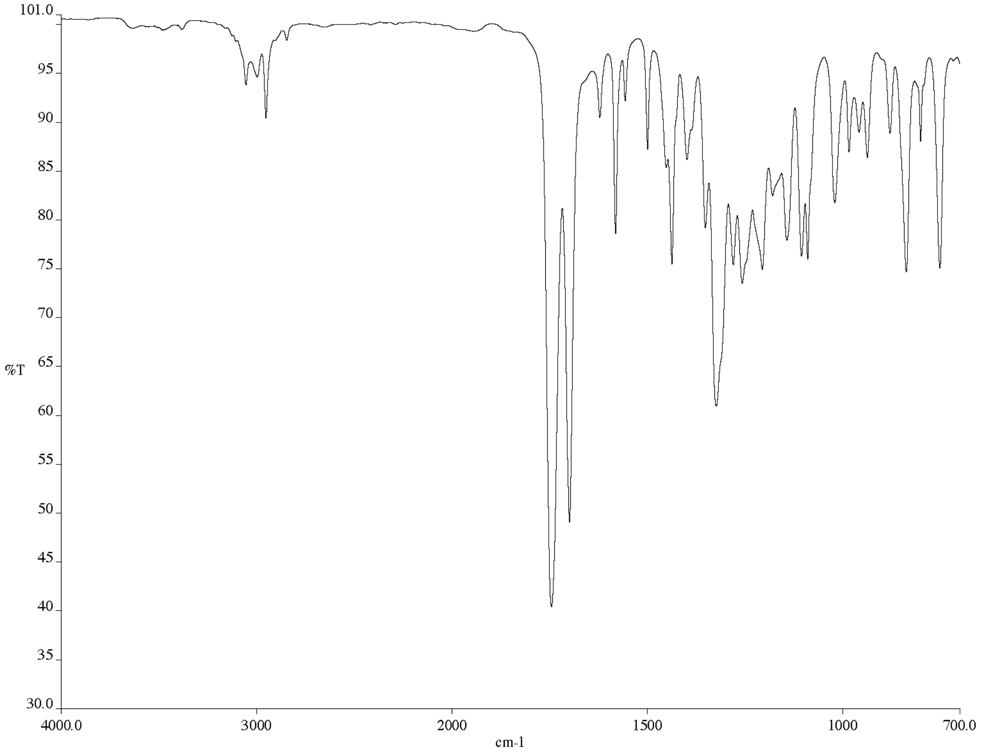


Figure 1.2 Infrared spectrum (thin film/NaCl) of *β*-ketoester Table 2, entry 10.

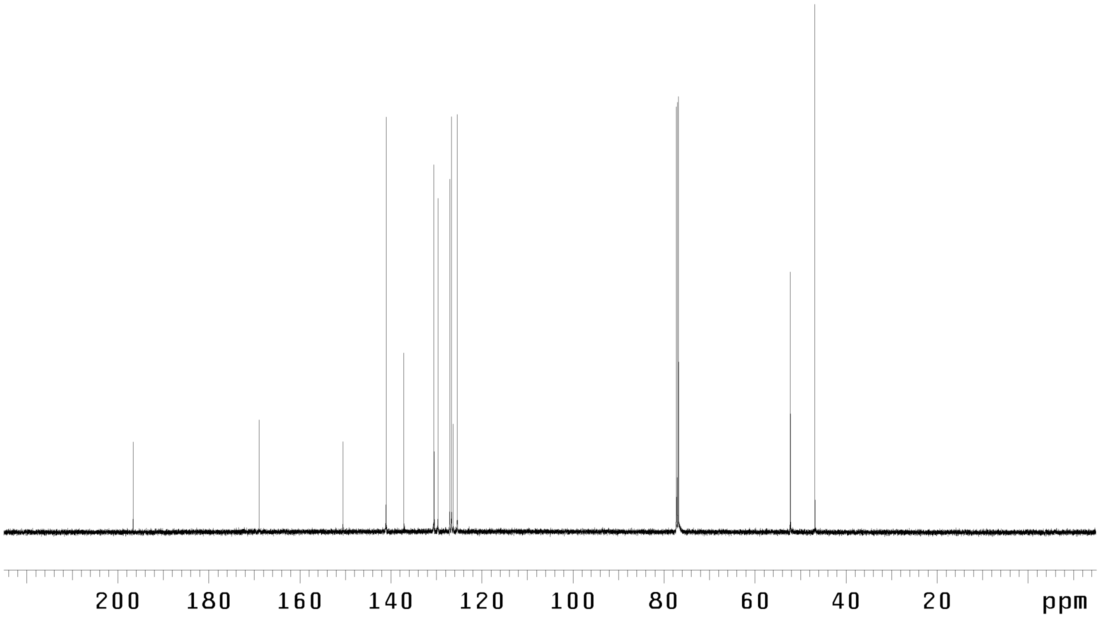
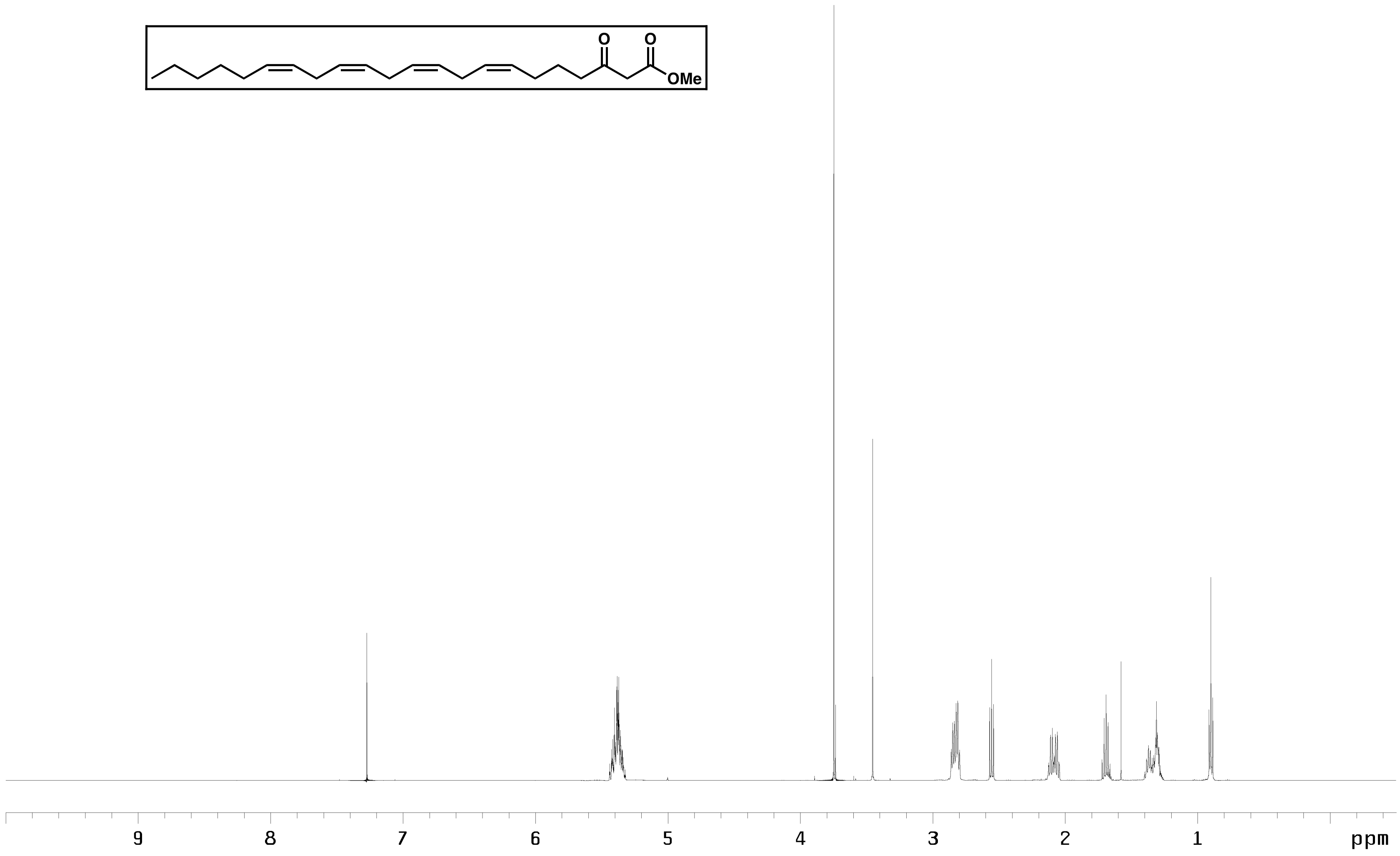


Figure 1.3 ^{13}C NMR (125 MHz, CDCl$_3$) of *β*-ketoester Table 2, entry 10.



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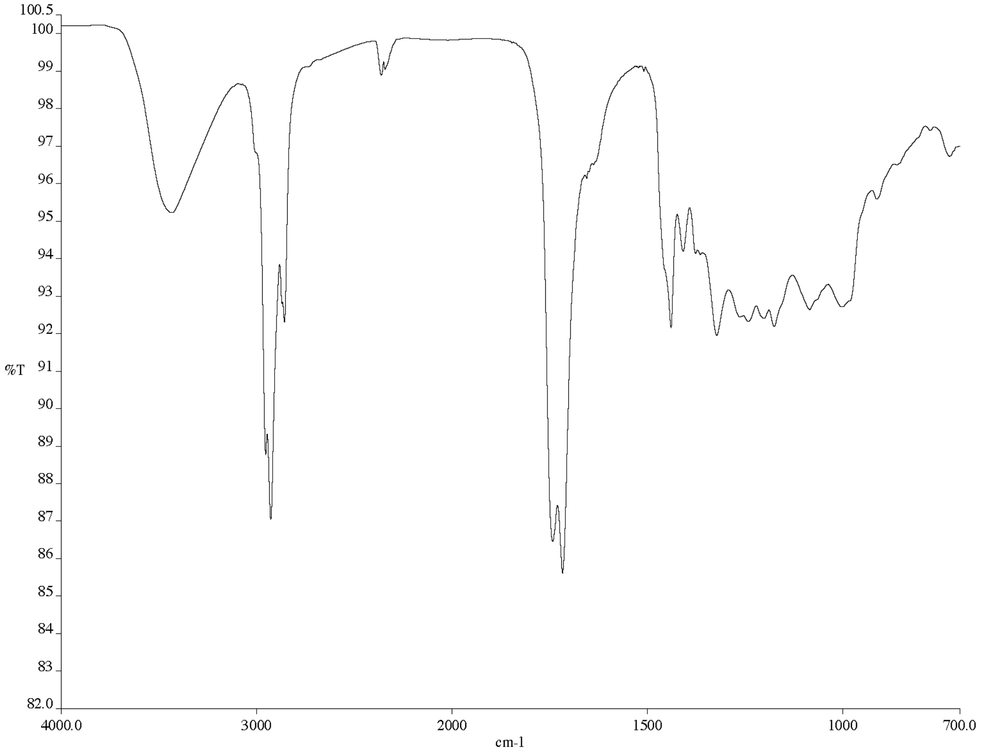

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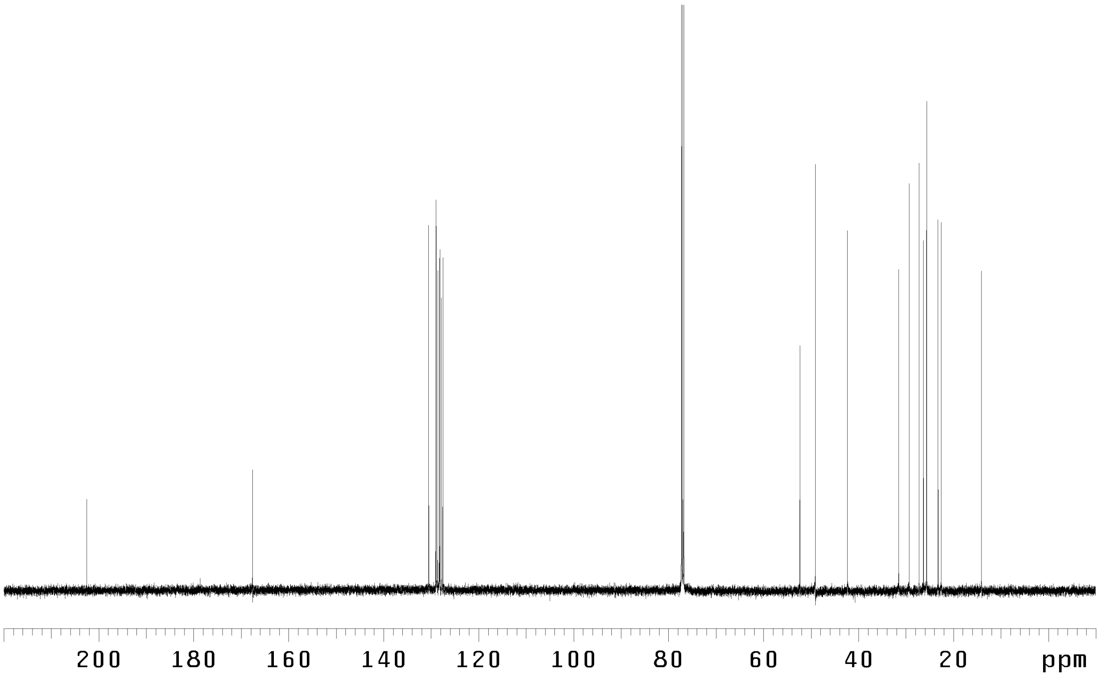

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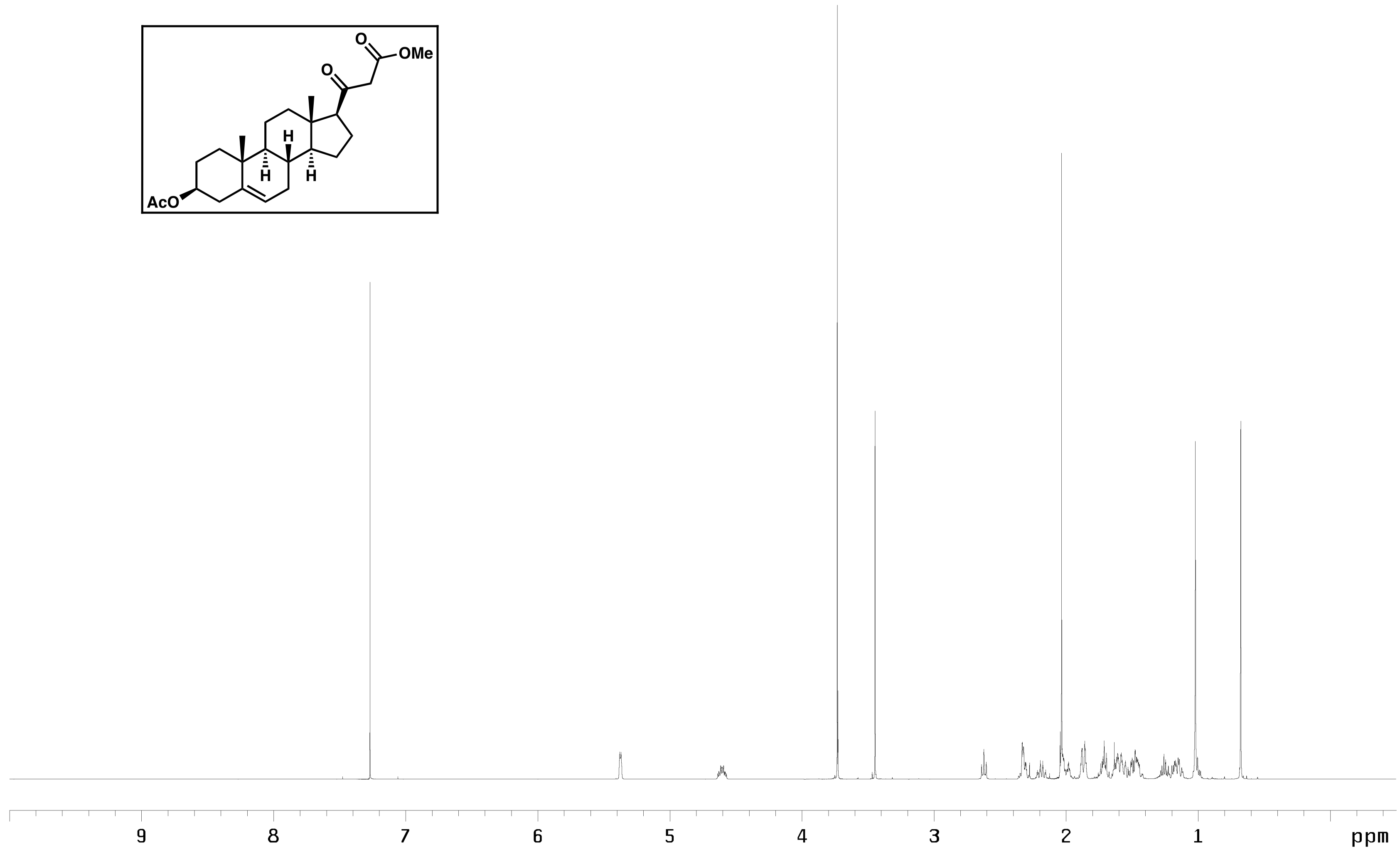

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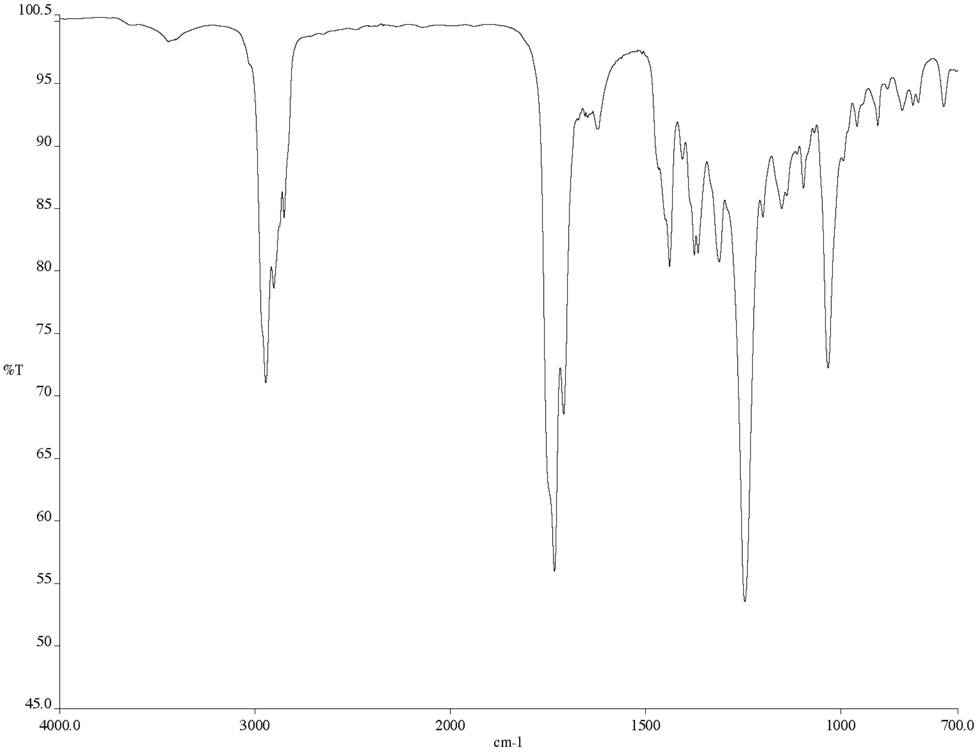

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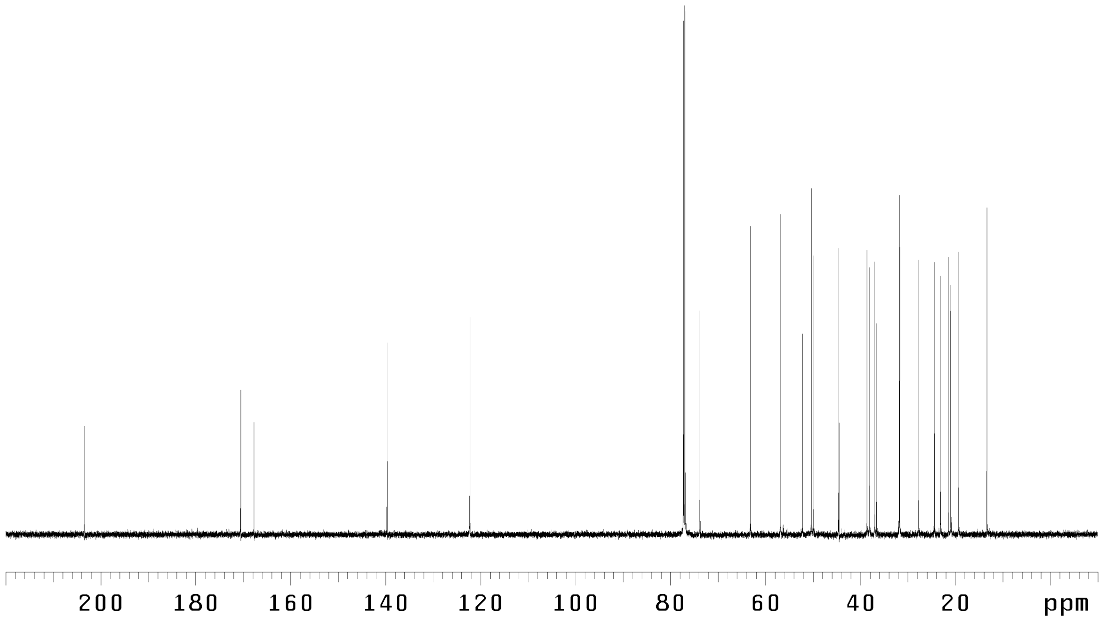

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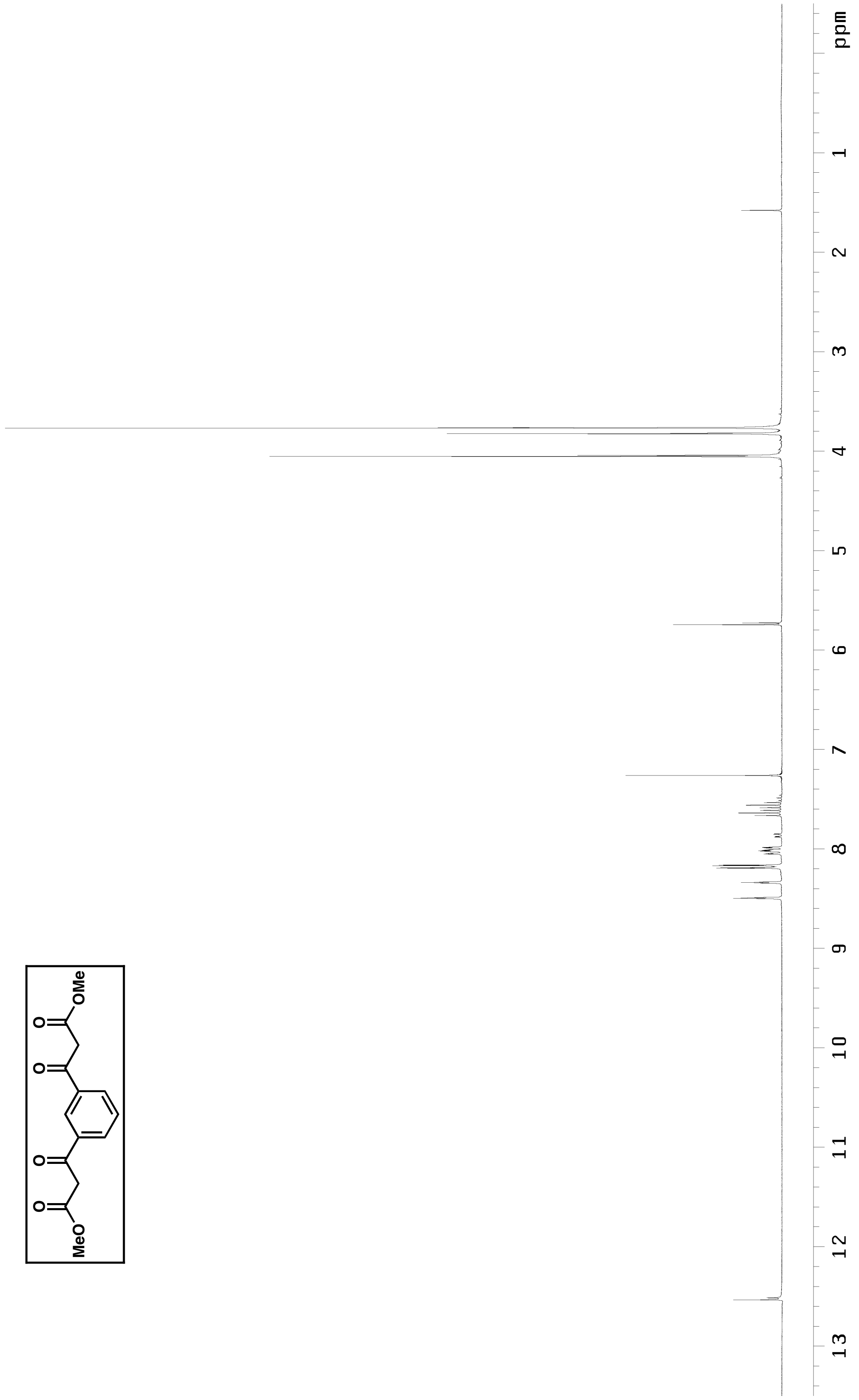

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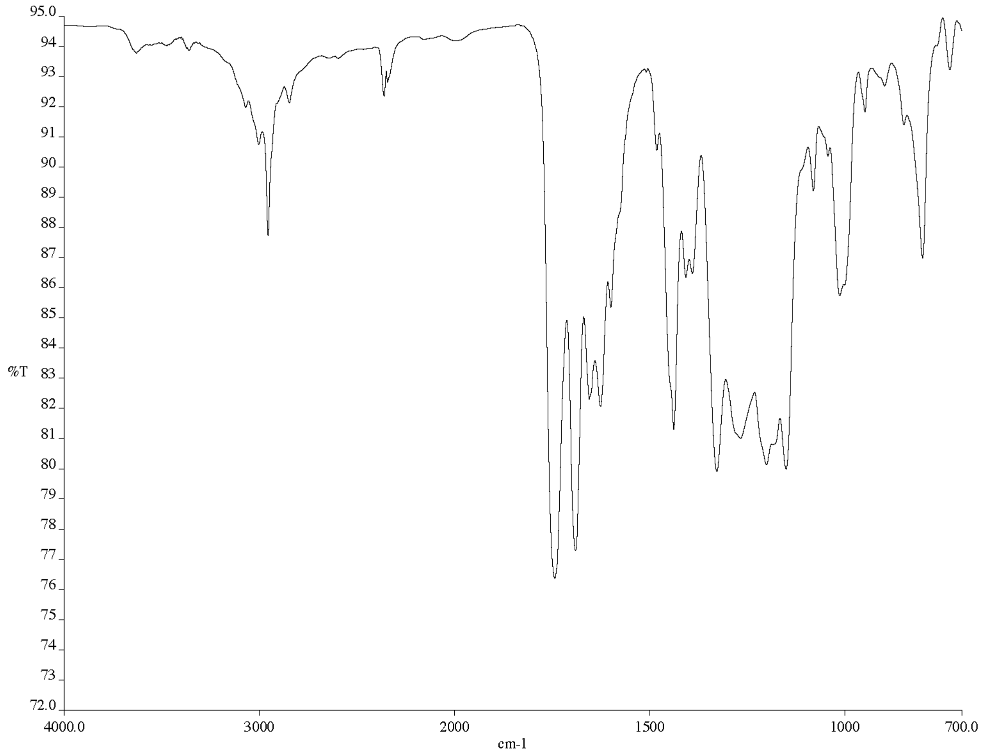

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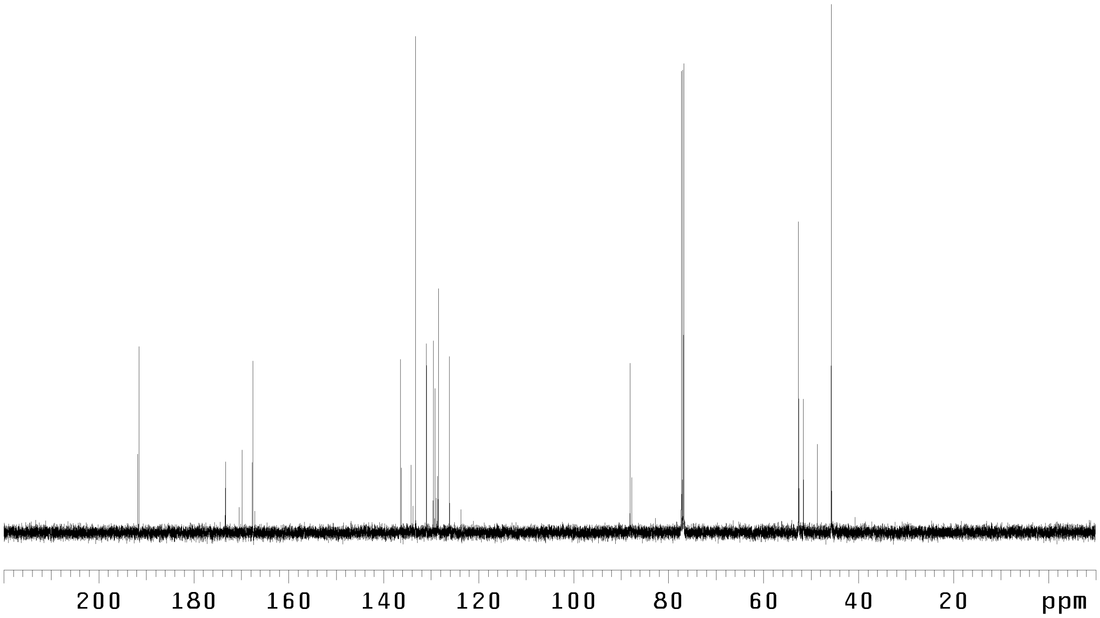

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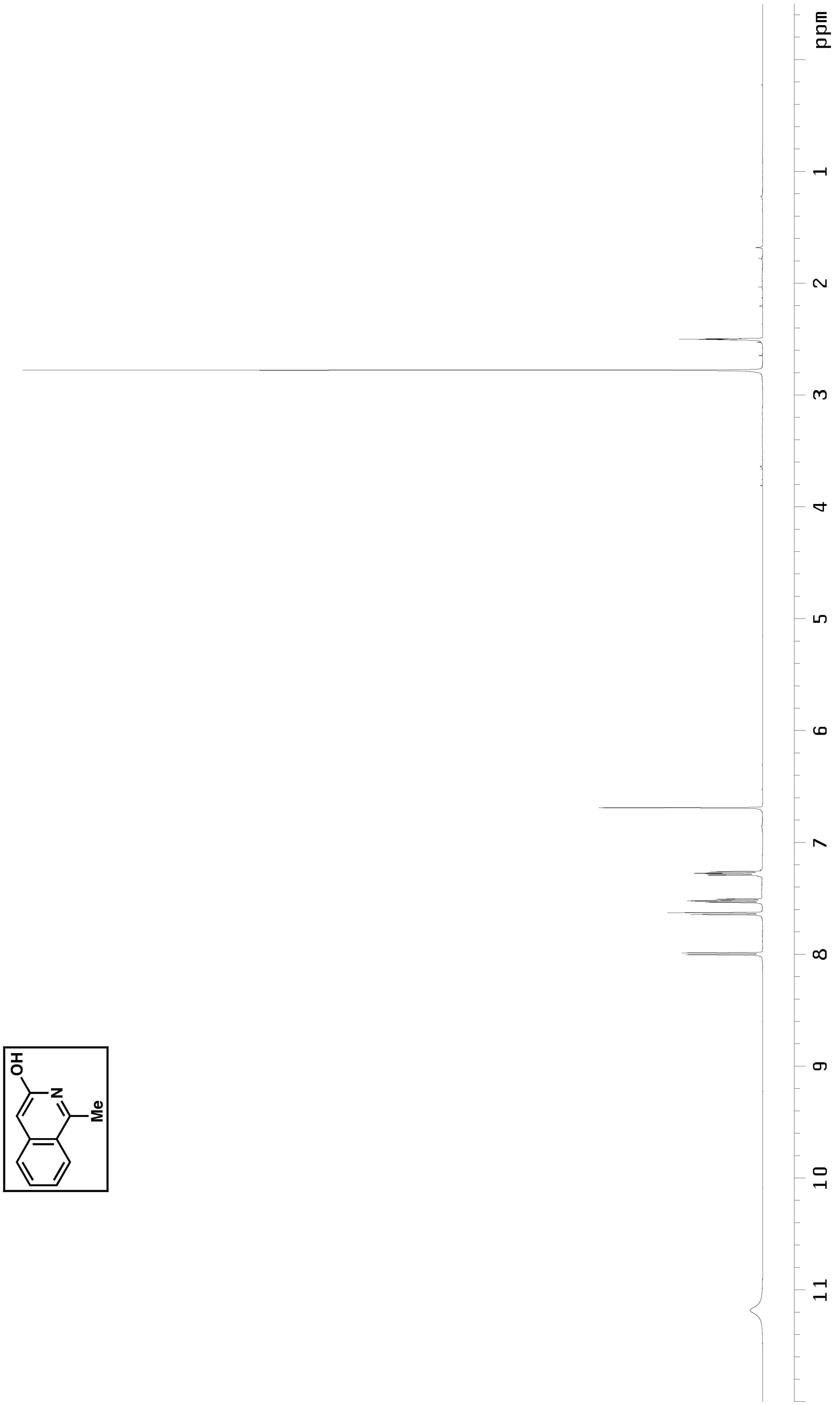
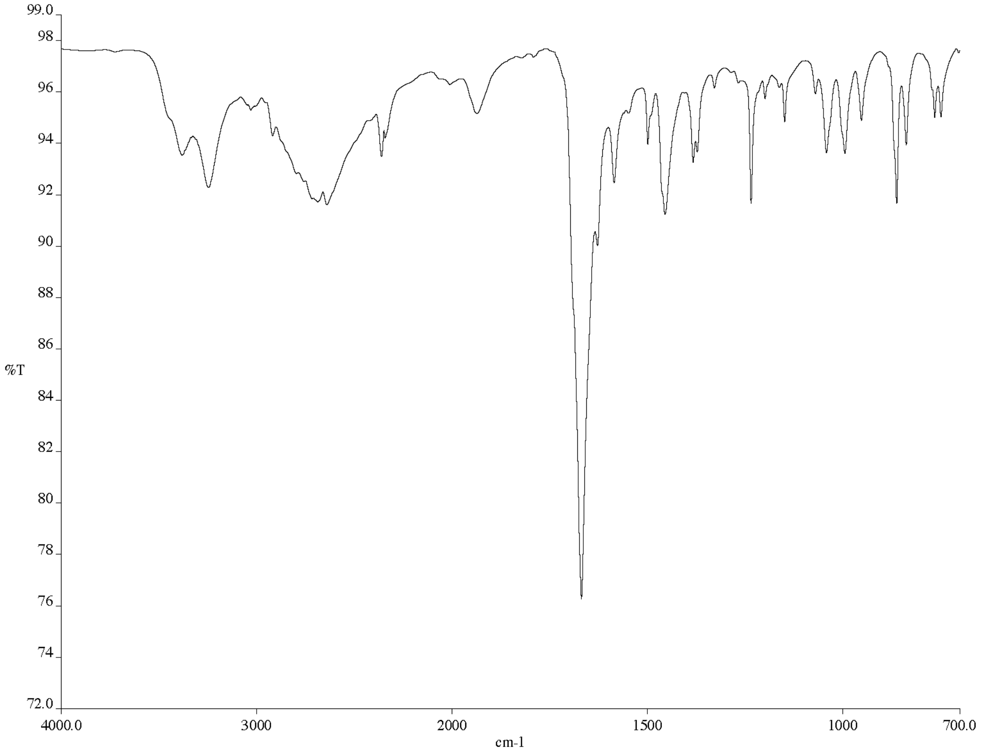


Figure 5.1 ^{1}H NMR (500 MHz, DMSO-d_6) of 1-methyl-3-hydroxyisoquinoline (**4**).



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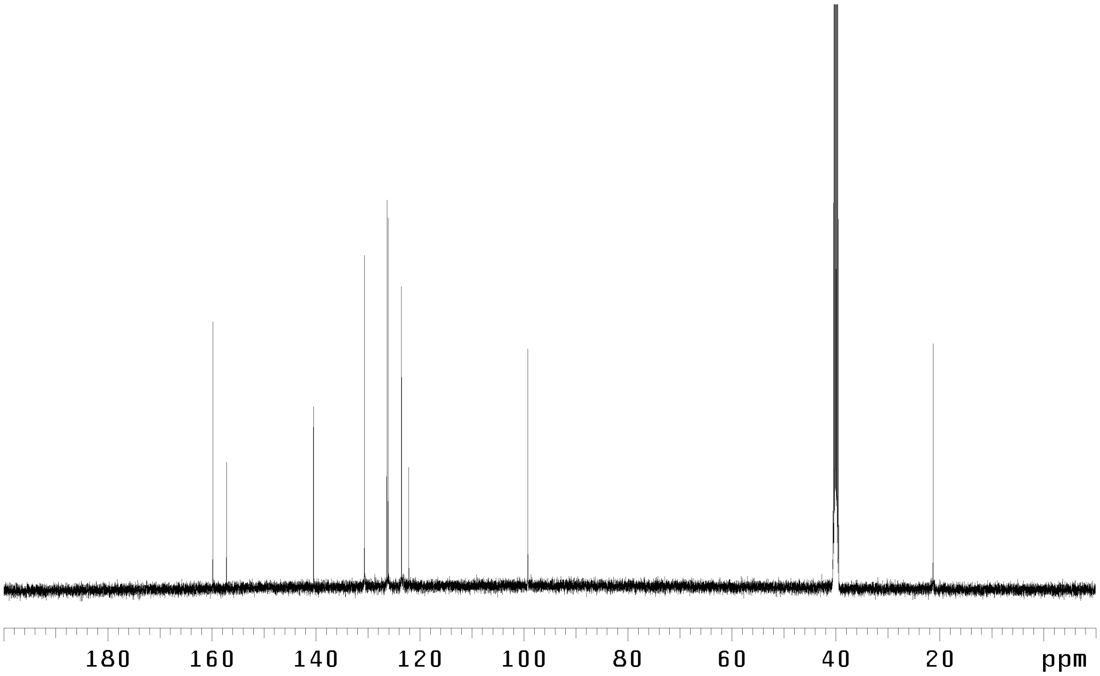

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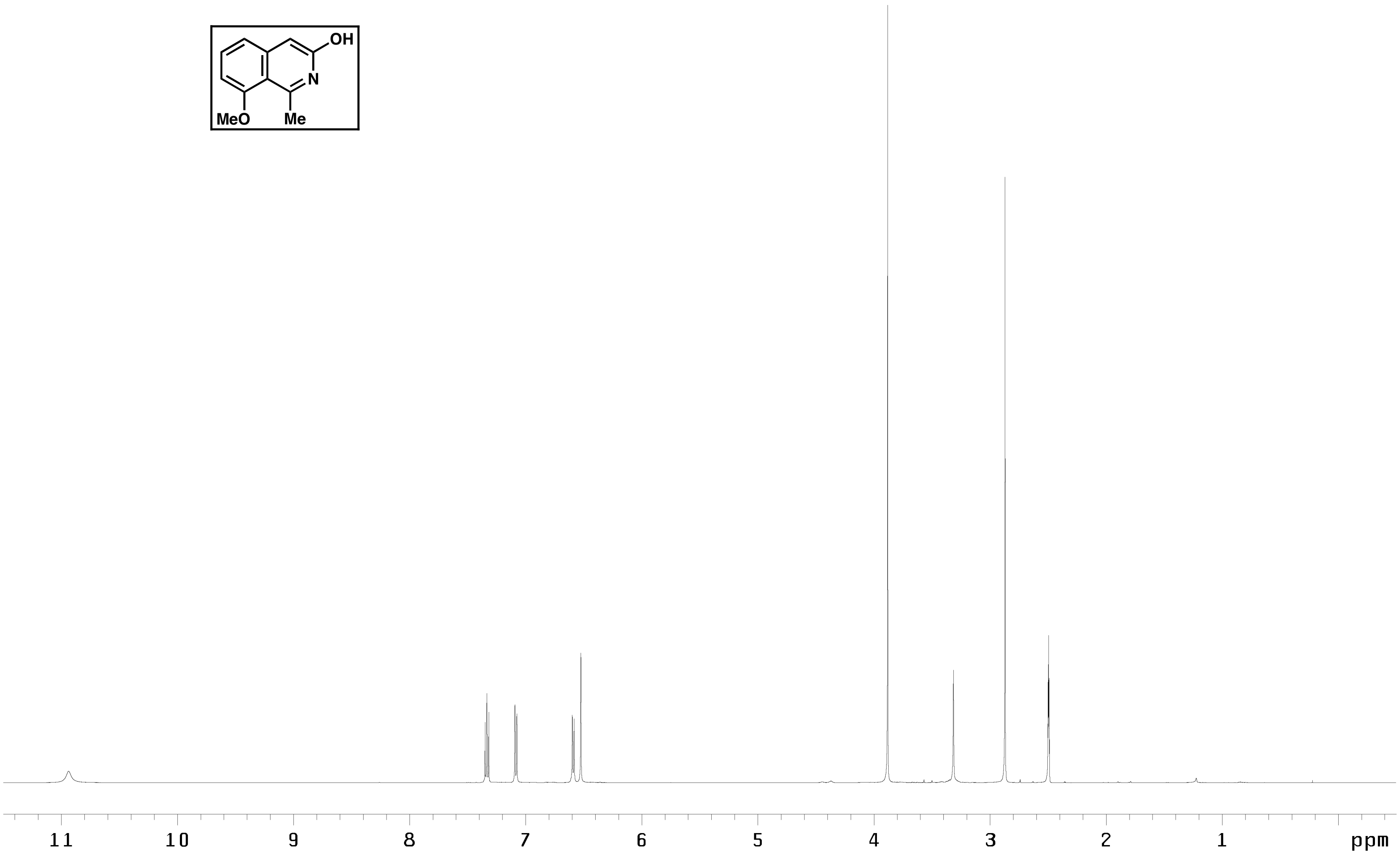
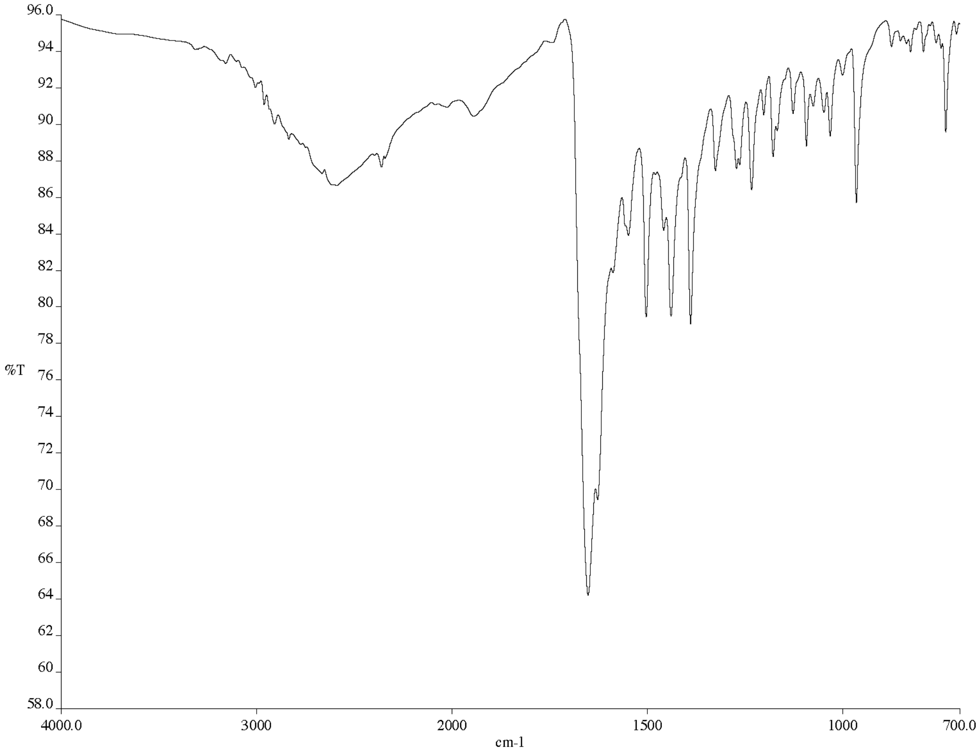


Figure 6.1 ^{1}H NMR (500 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 1, entry 1.



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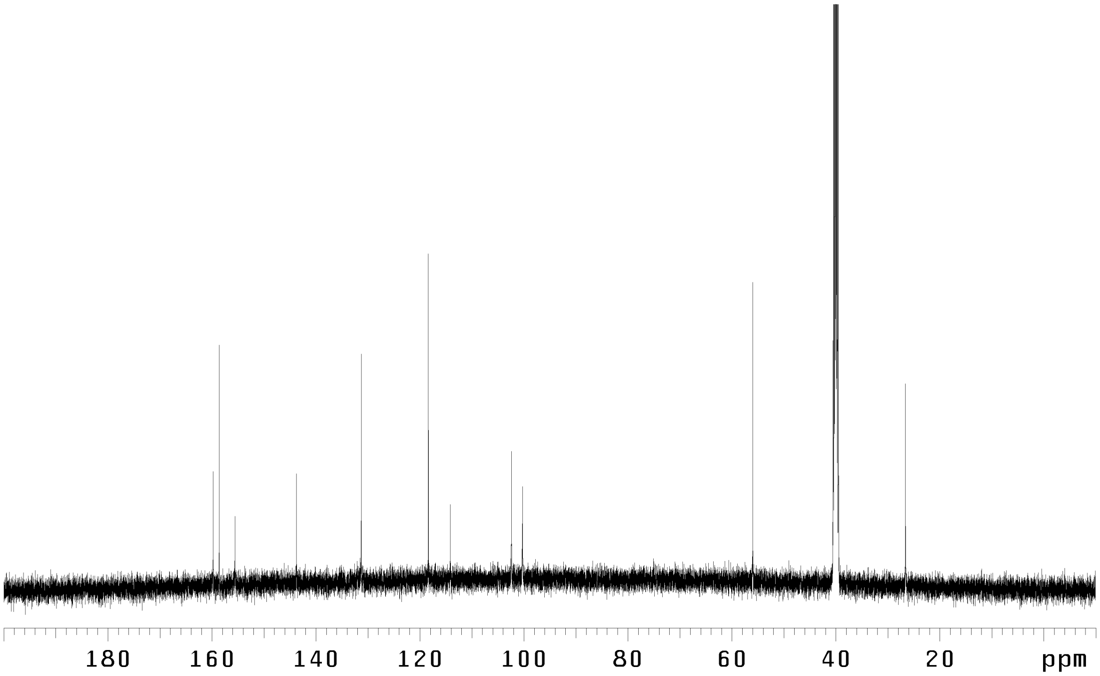

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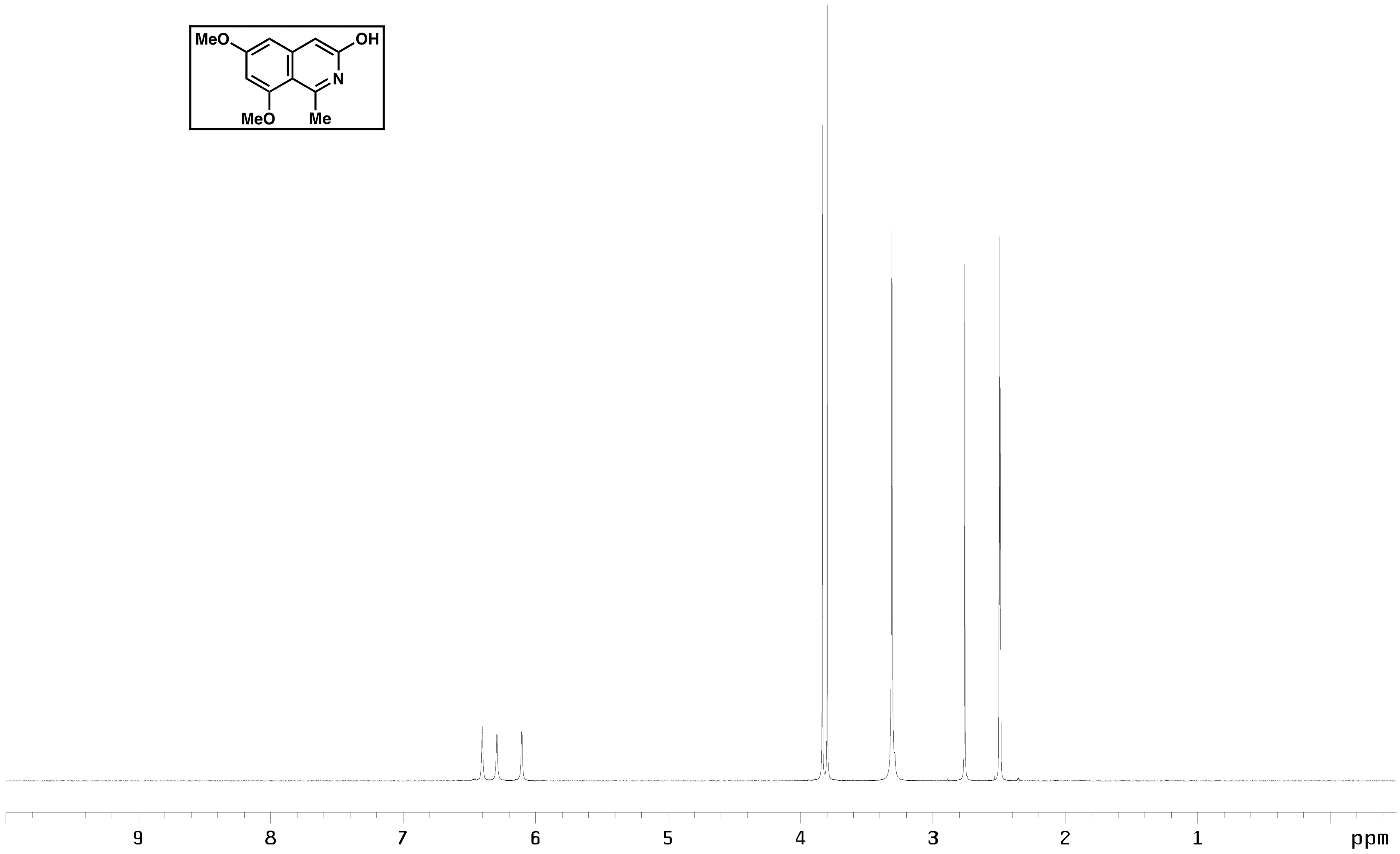

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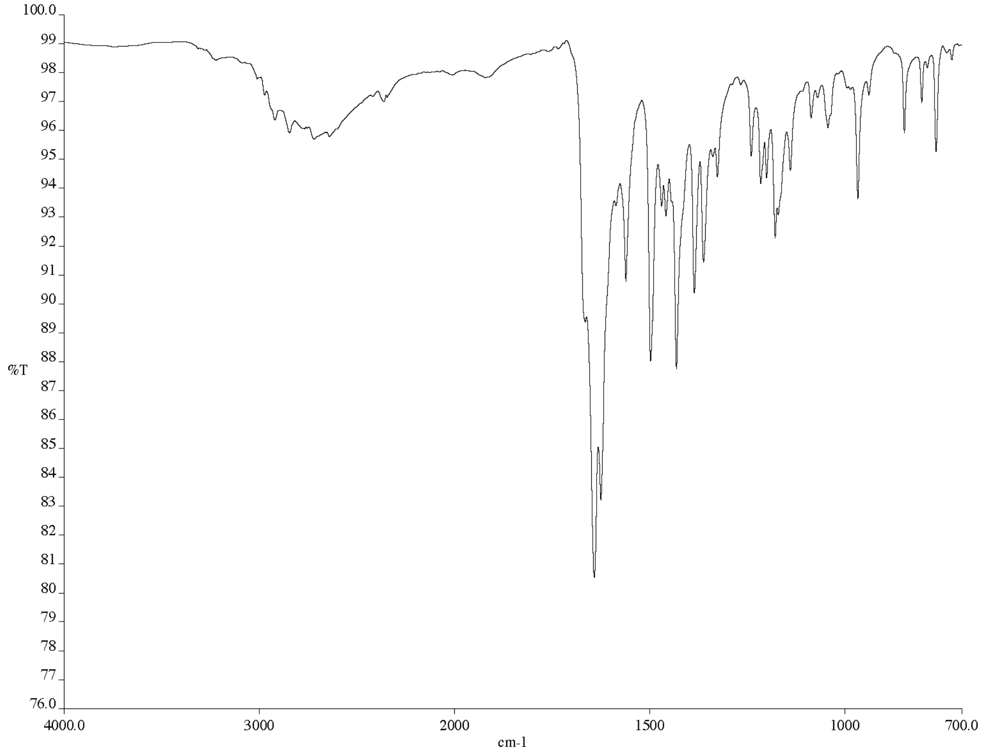

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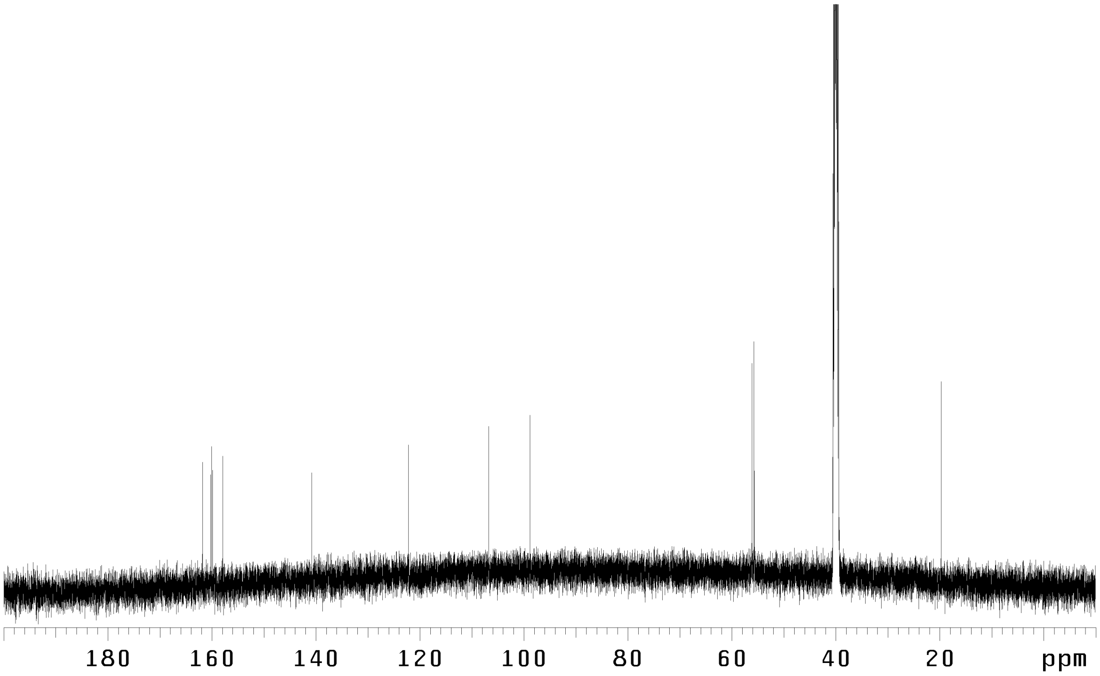
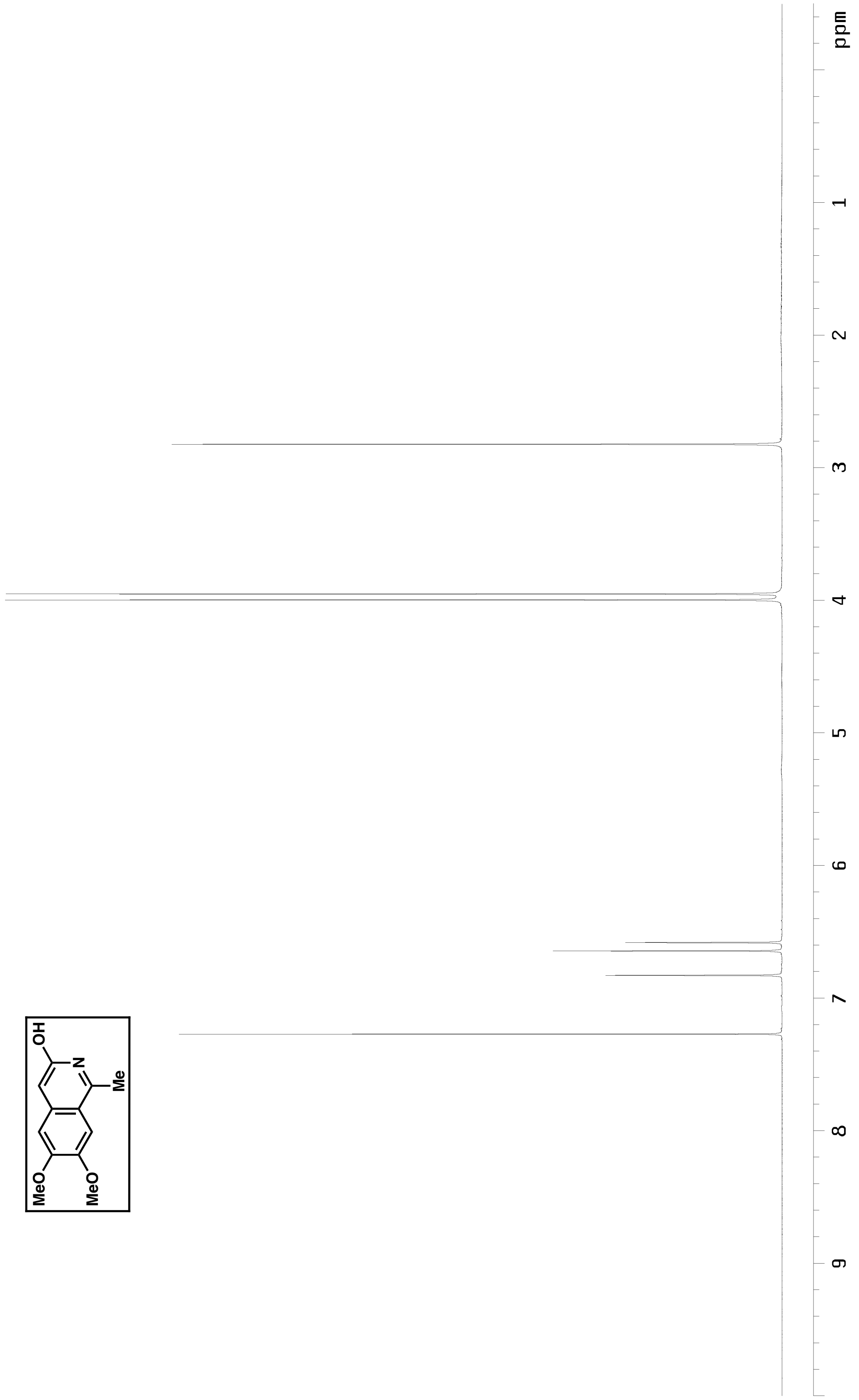


Figure 7.3 ^{13}C NMR (125 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 1, entry 2.



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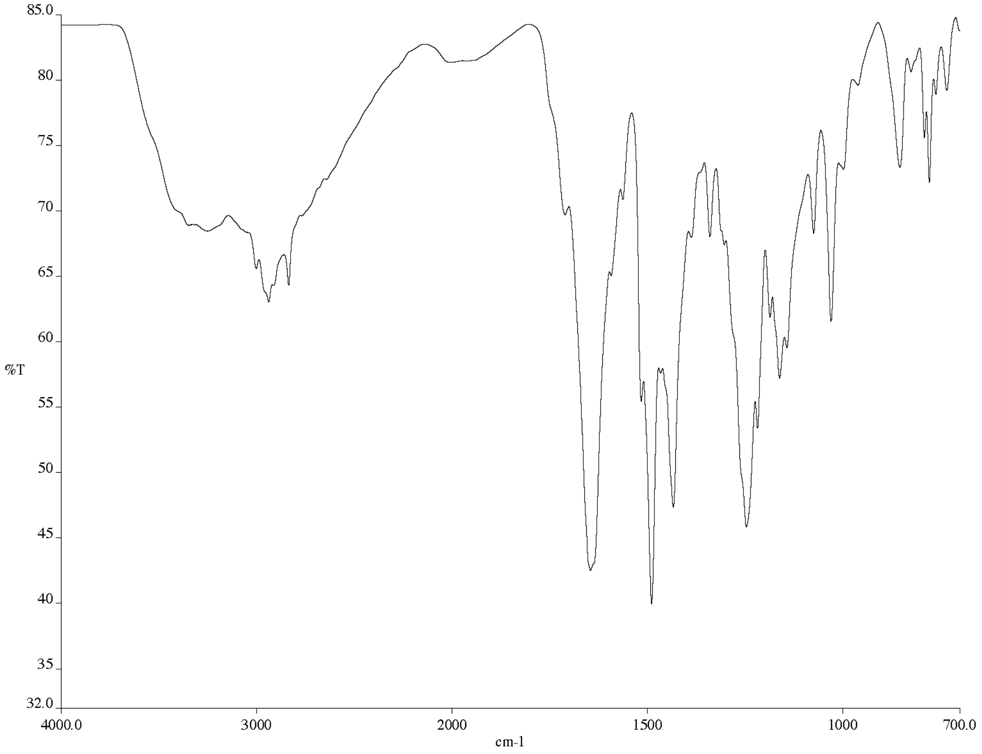

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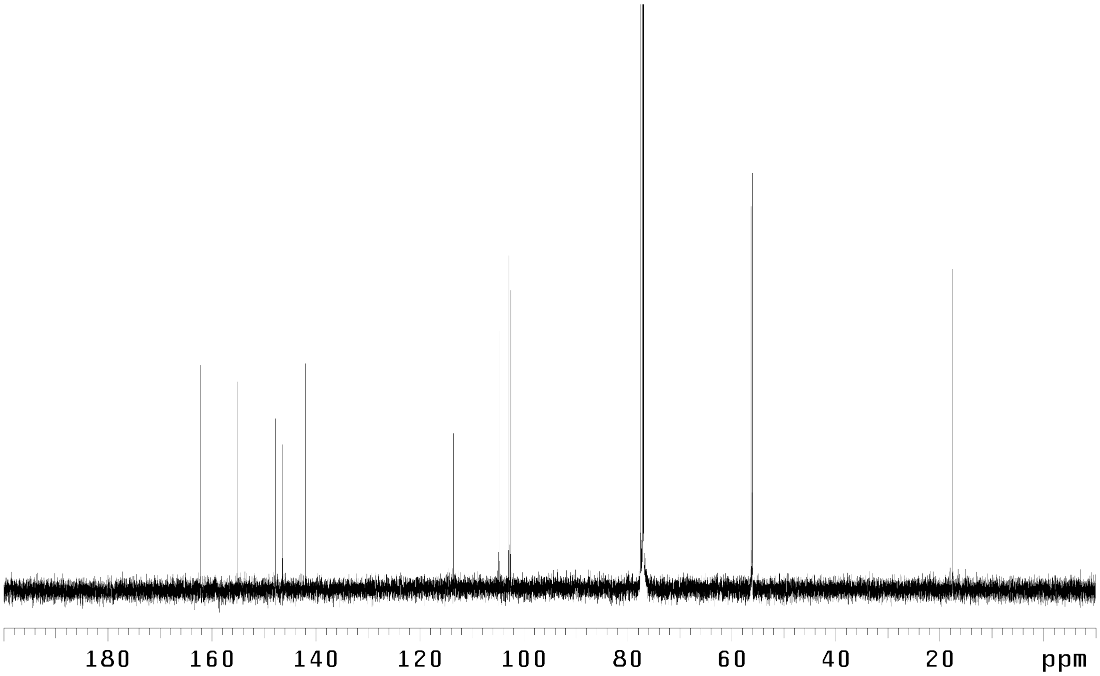
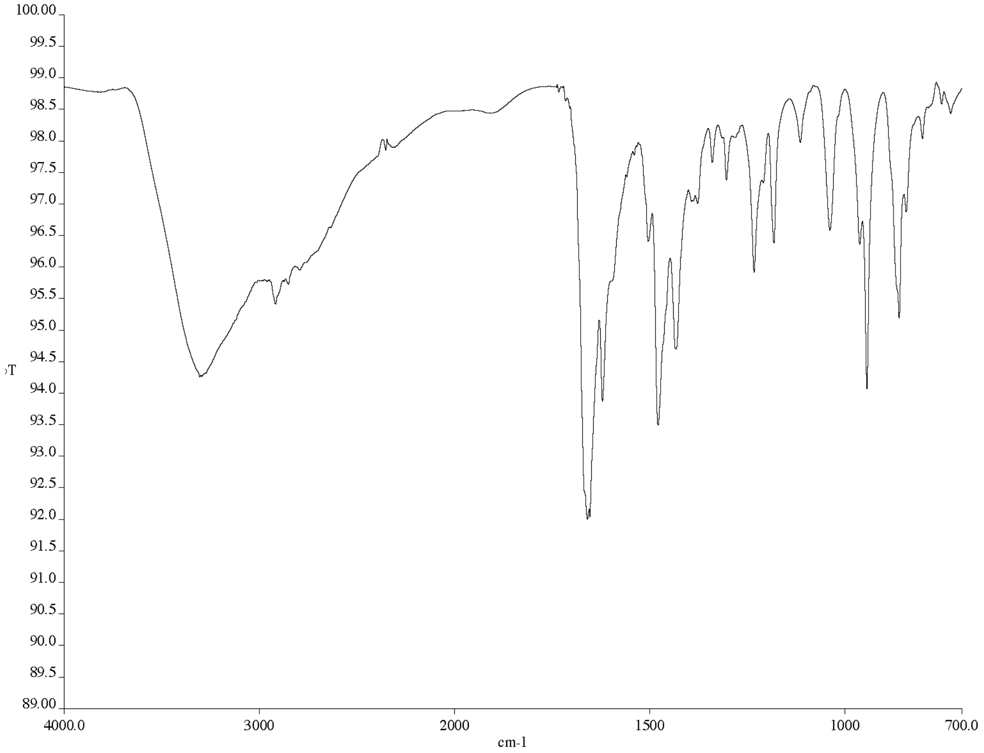


Figure 8.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 1, entry 3.

Figure 9.1 ^{1}H NMR (500 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 1, entry 4.



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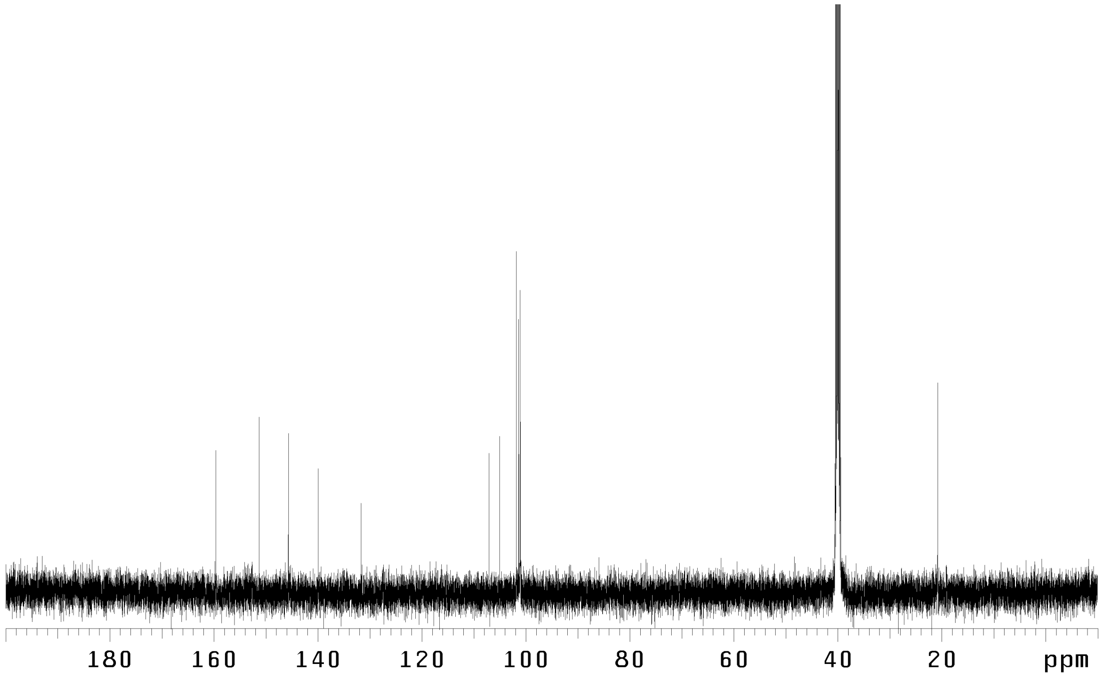


Figure 9.3 ^{13}C NMR (125 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 1, entry 4.

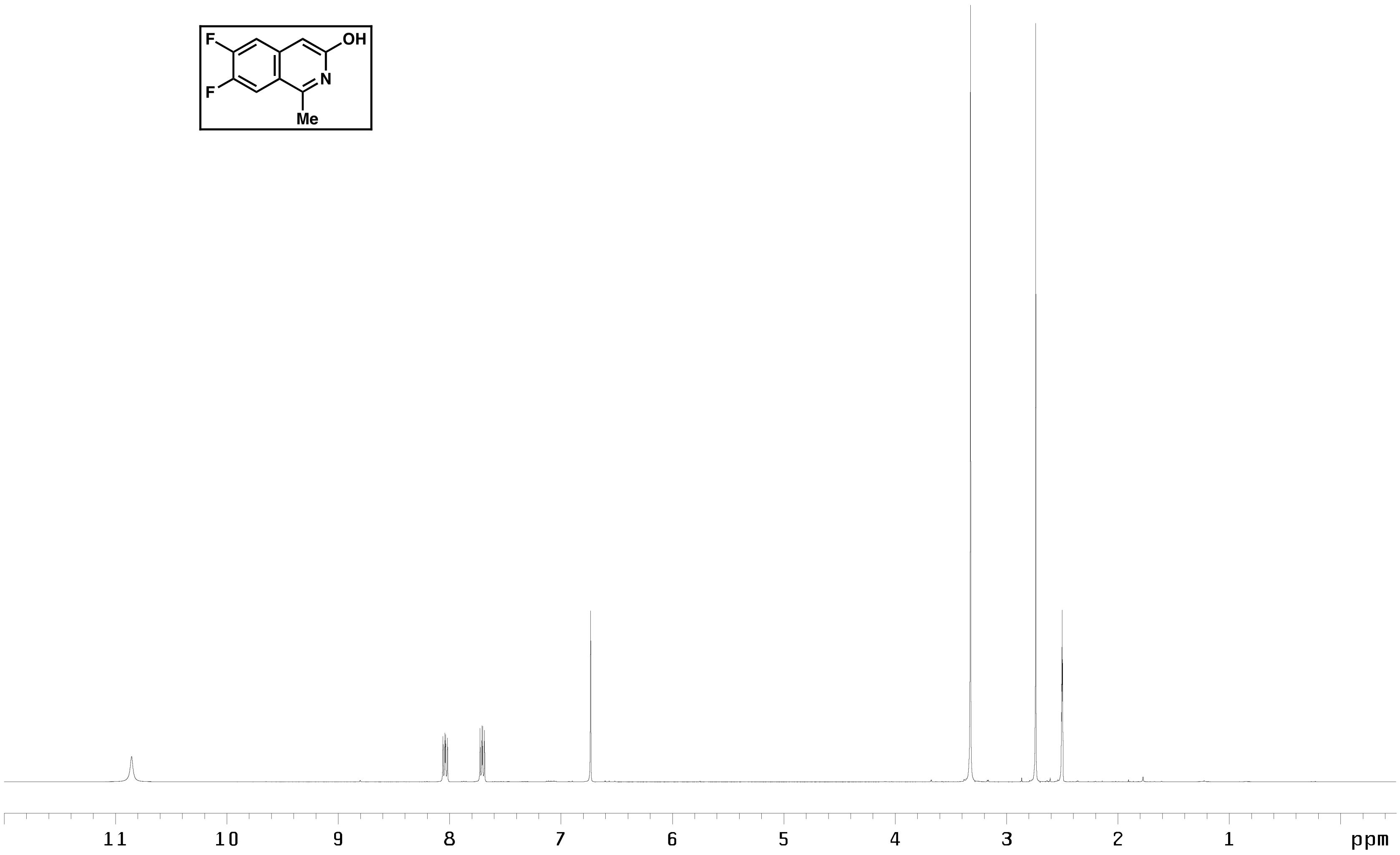
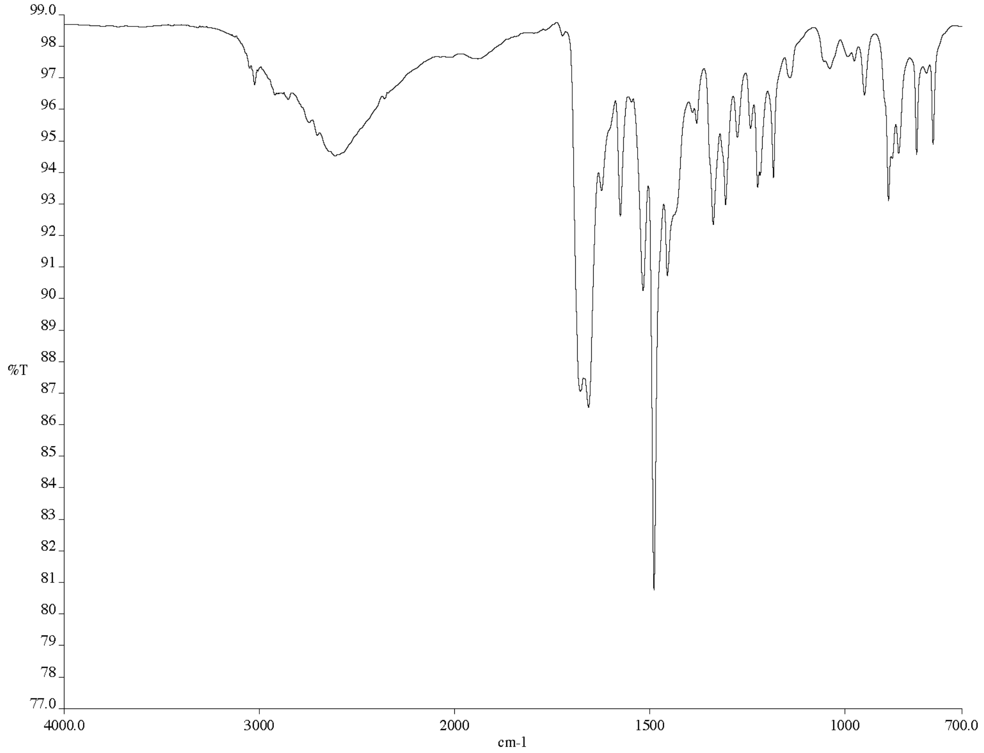


Figure 10.1 ^{1}H NMR (500 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 1, entry 5.



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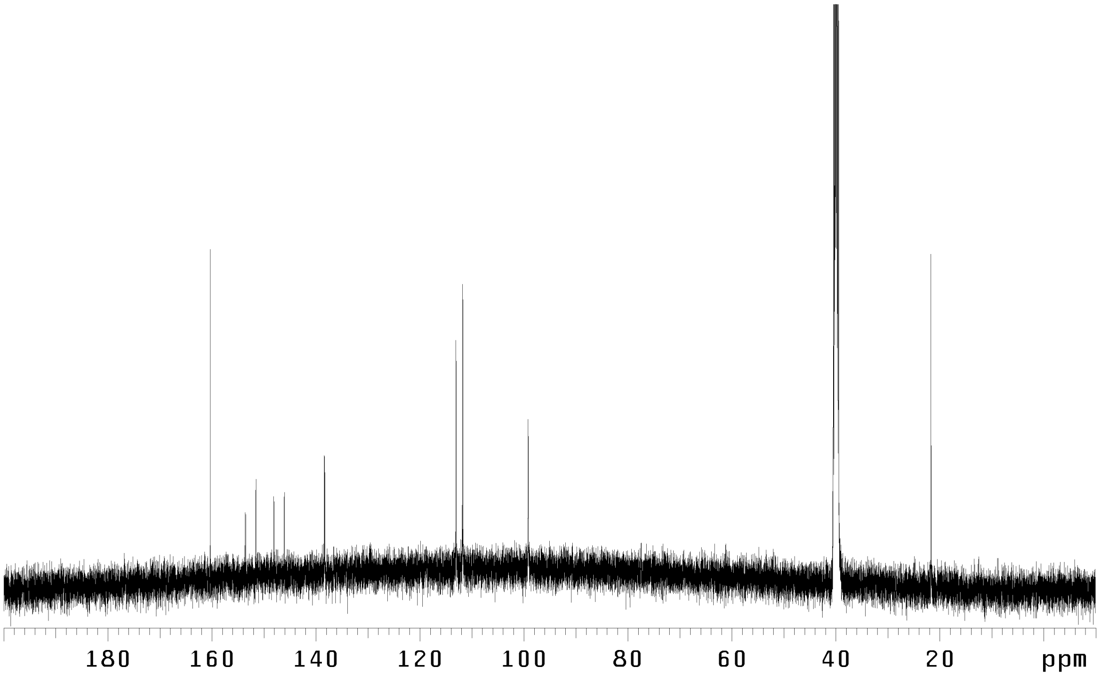

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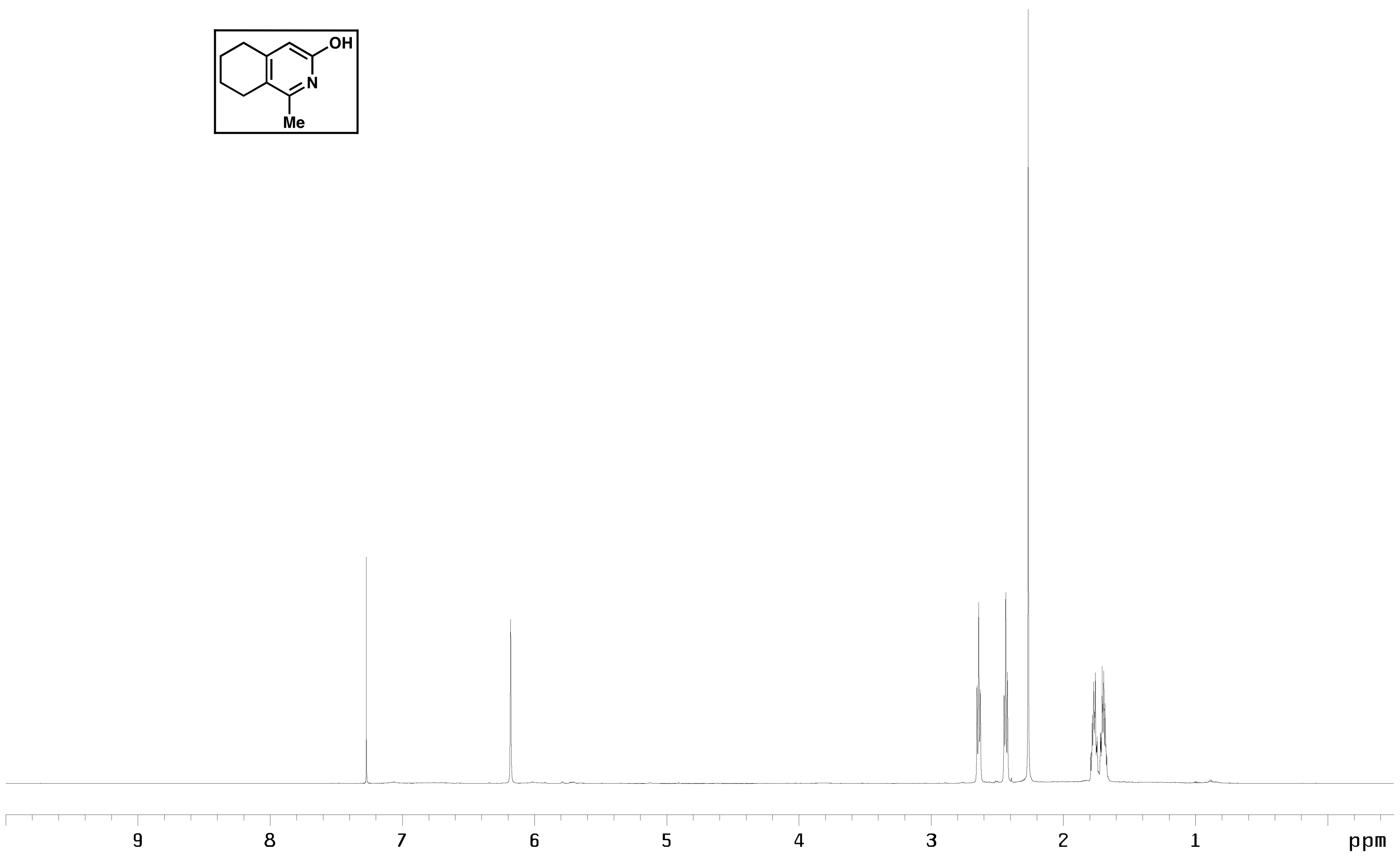
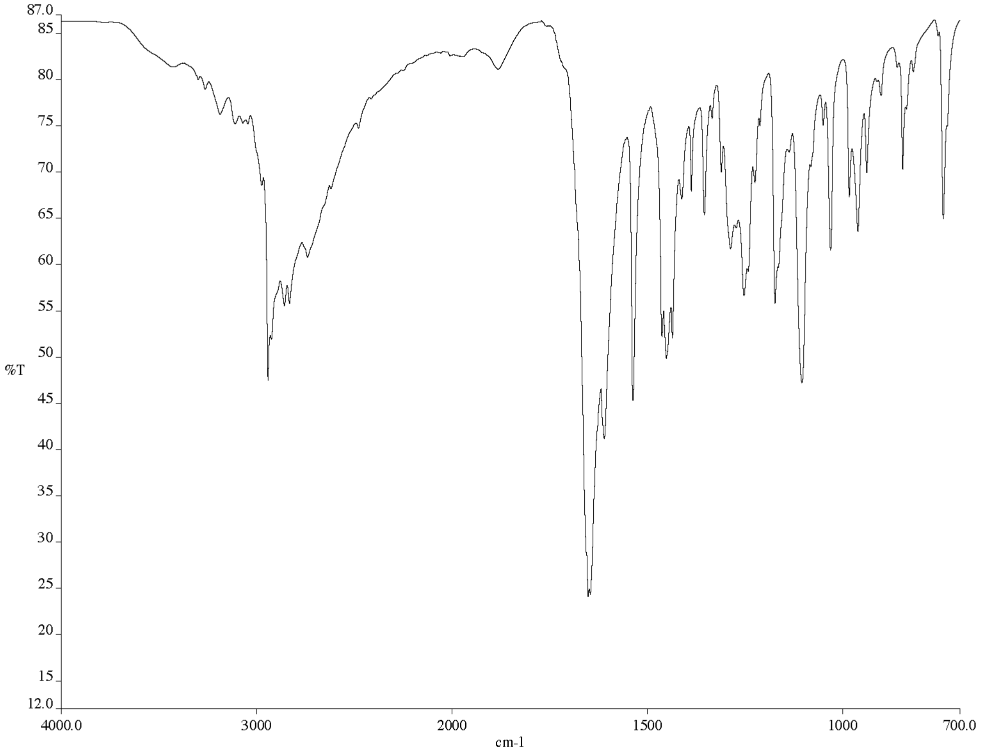


Figure 11.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxy-5,6,7,8-tetrahydroisoquinoline
Table 1, entry 6.



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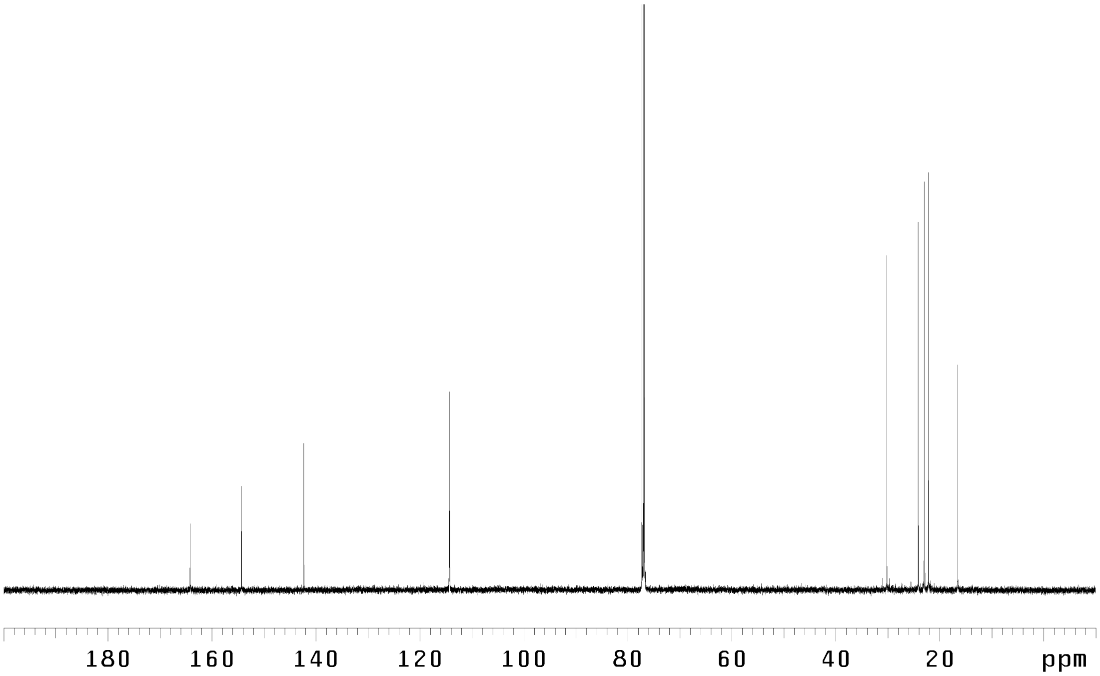

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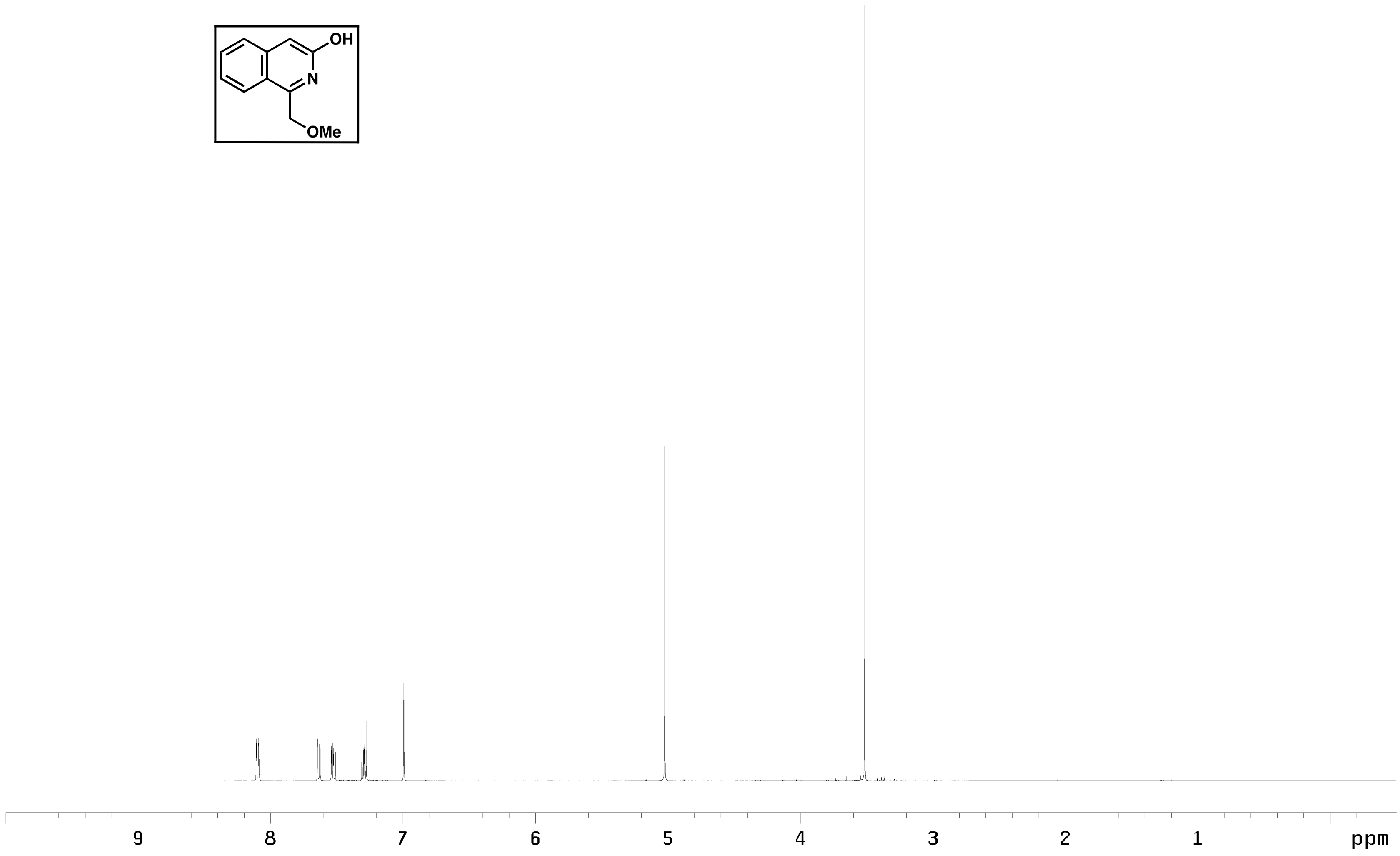

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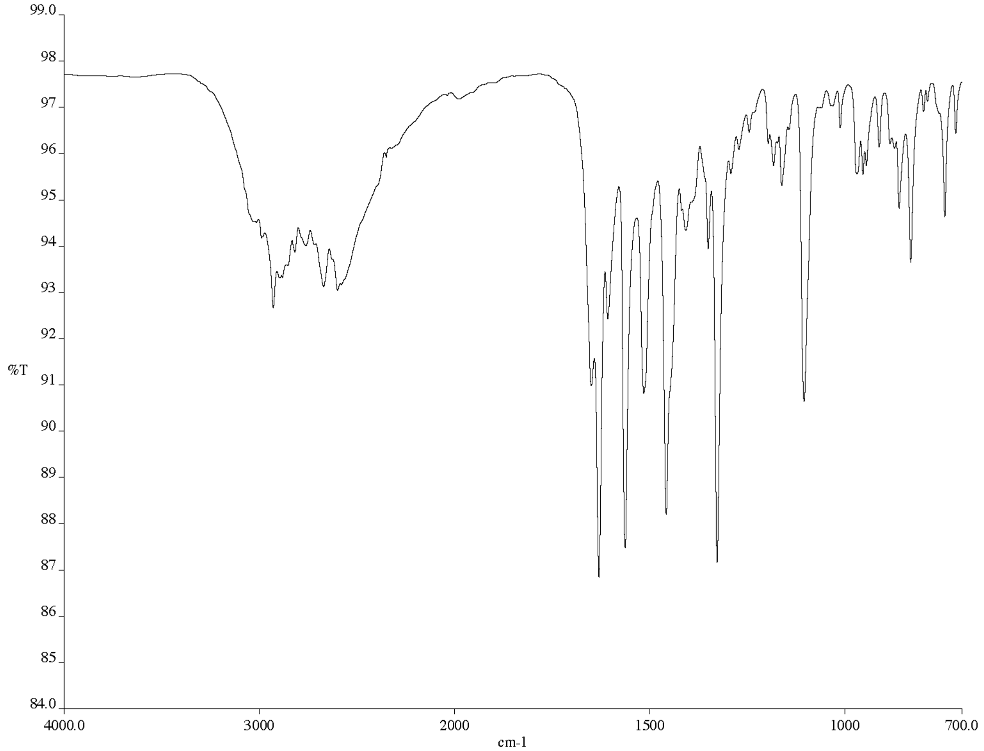
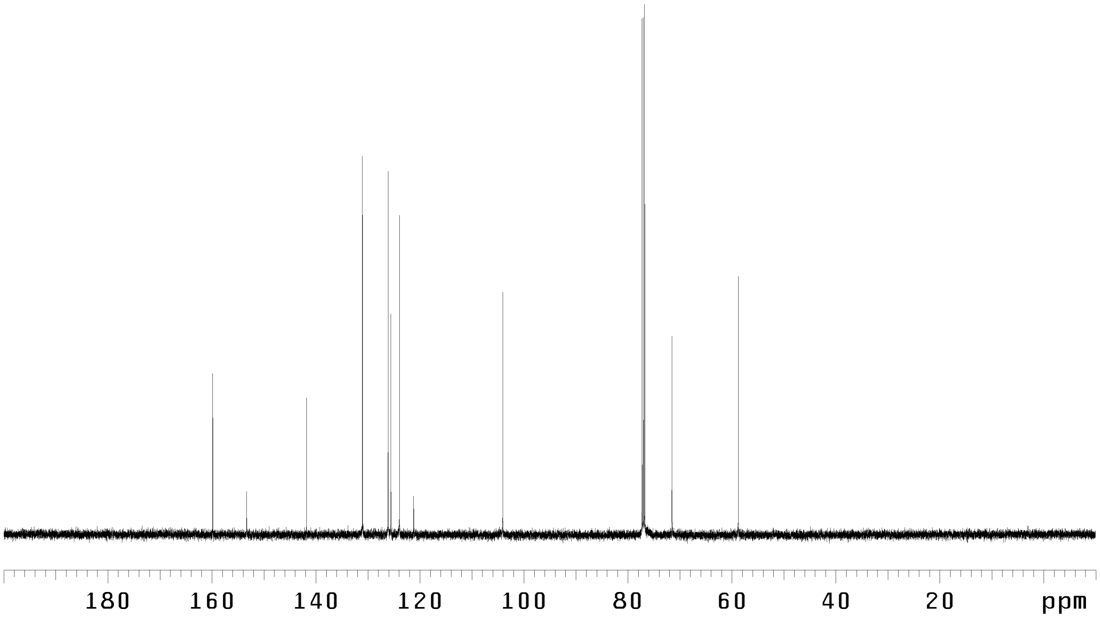


Figure 12.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 1.



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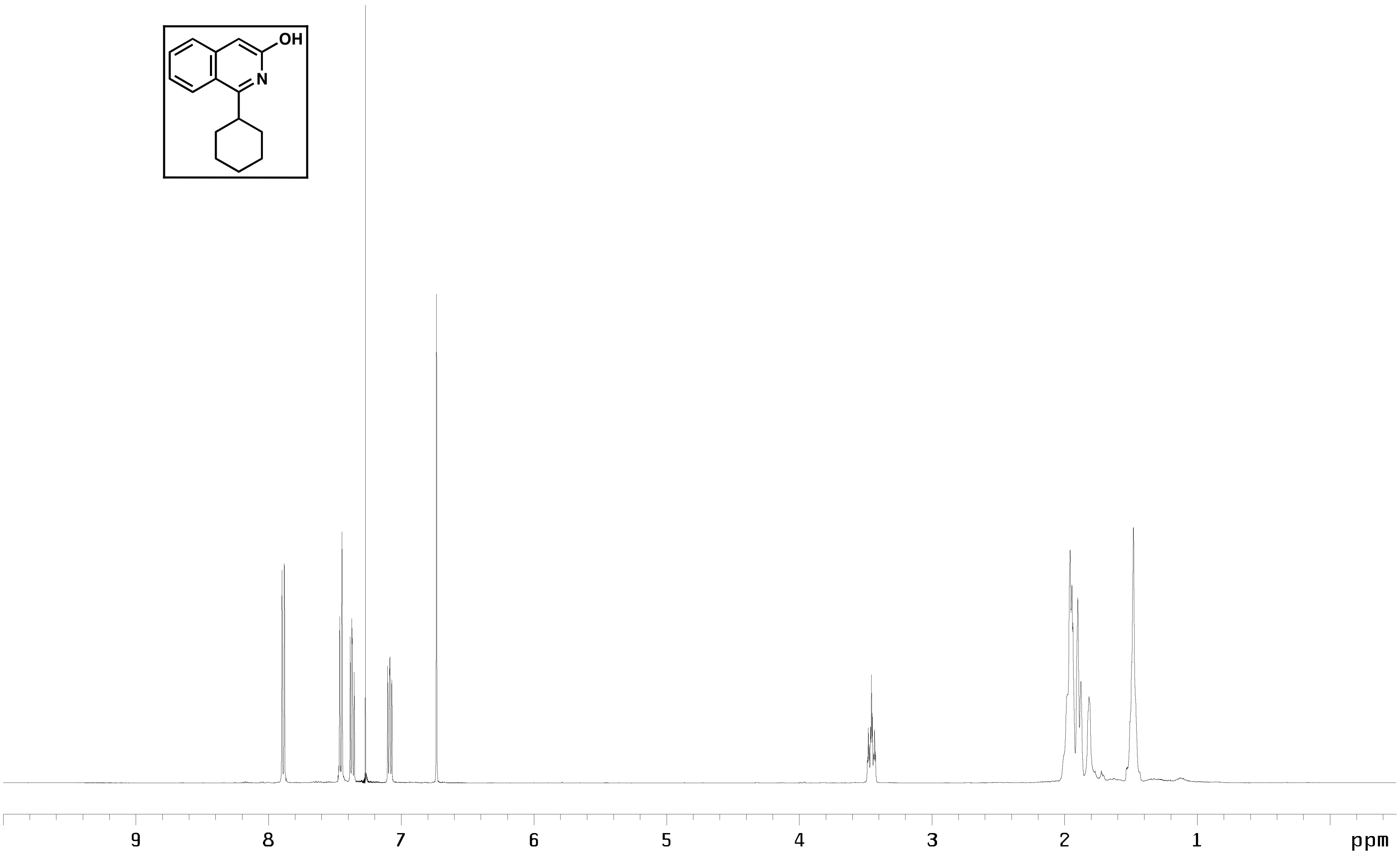

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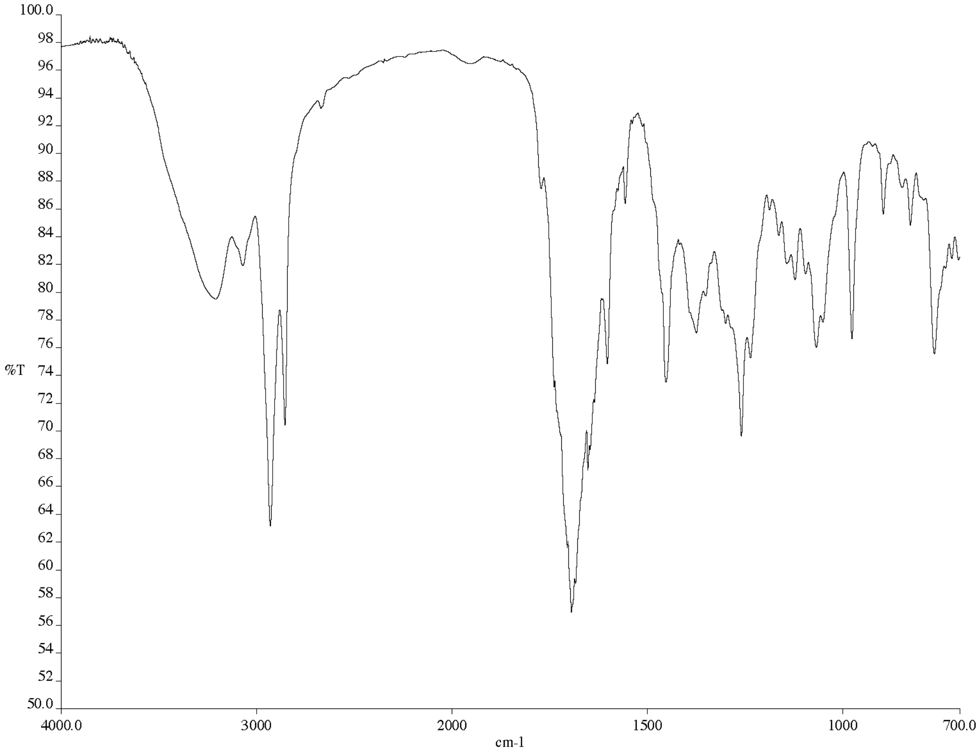

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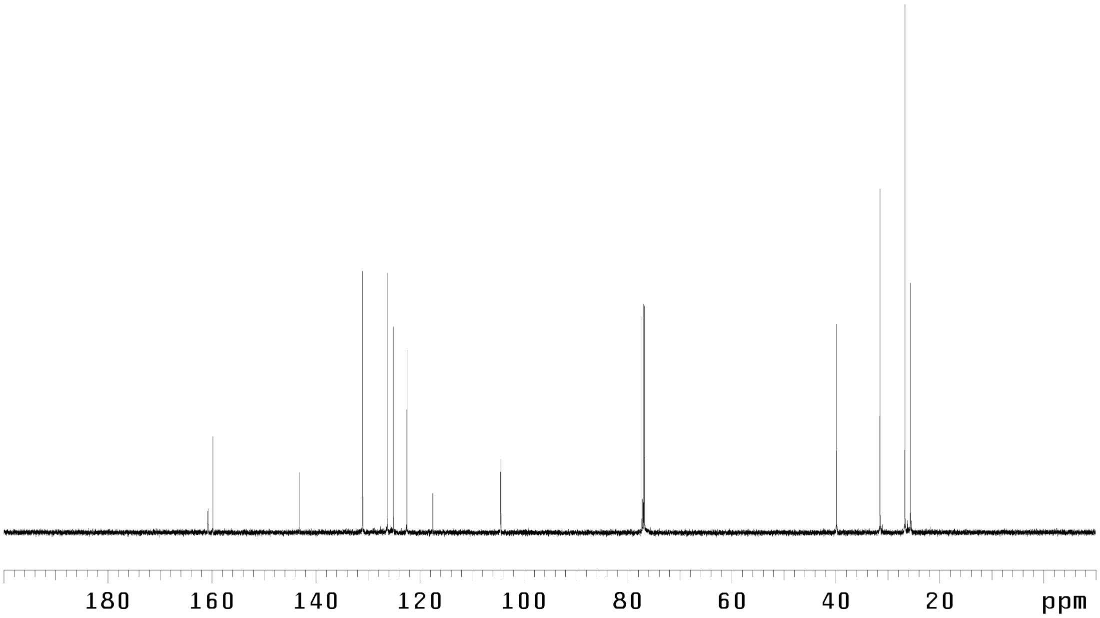

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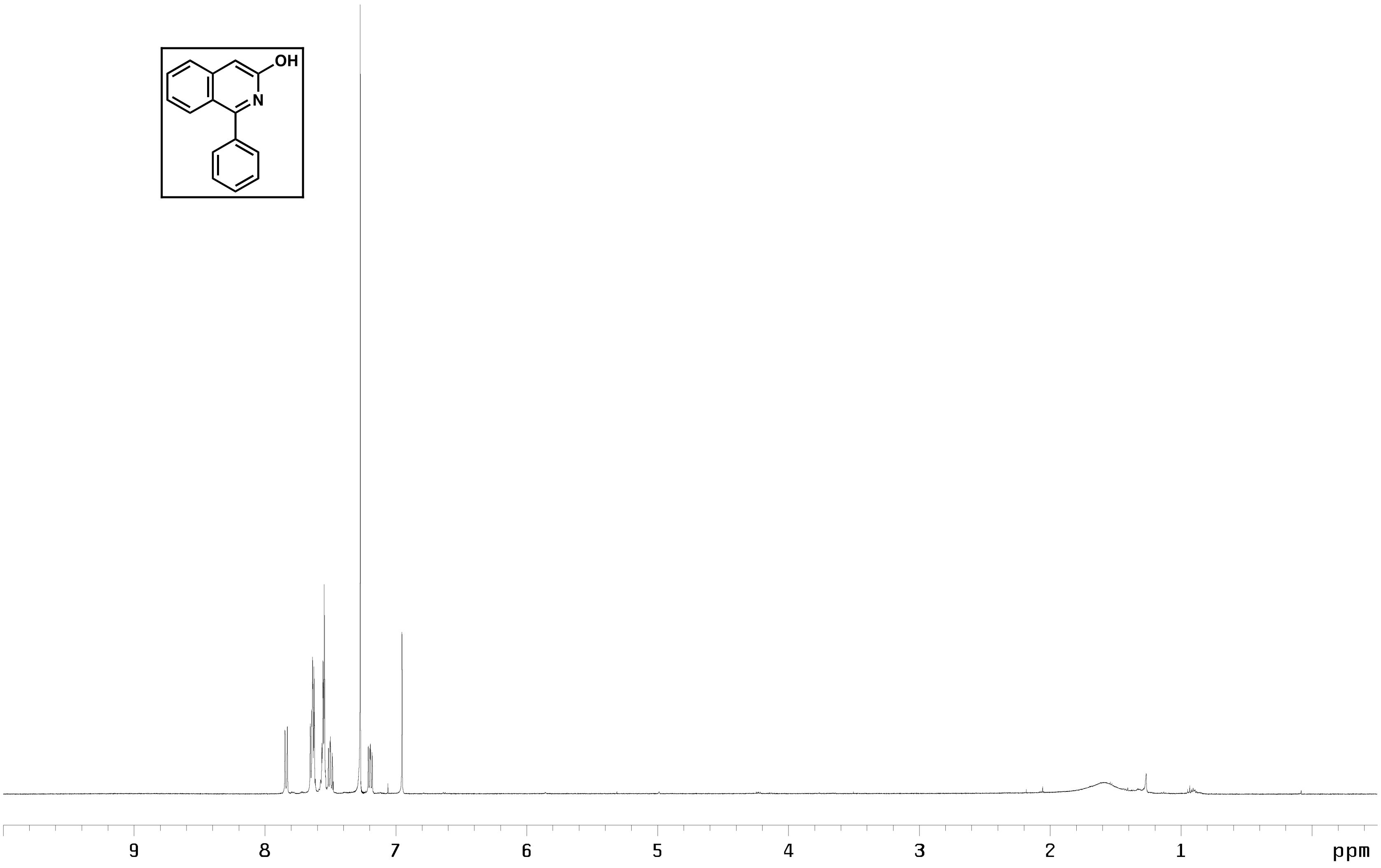

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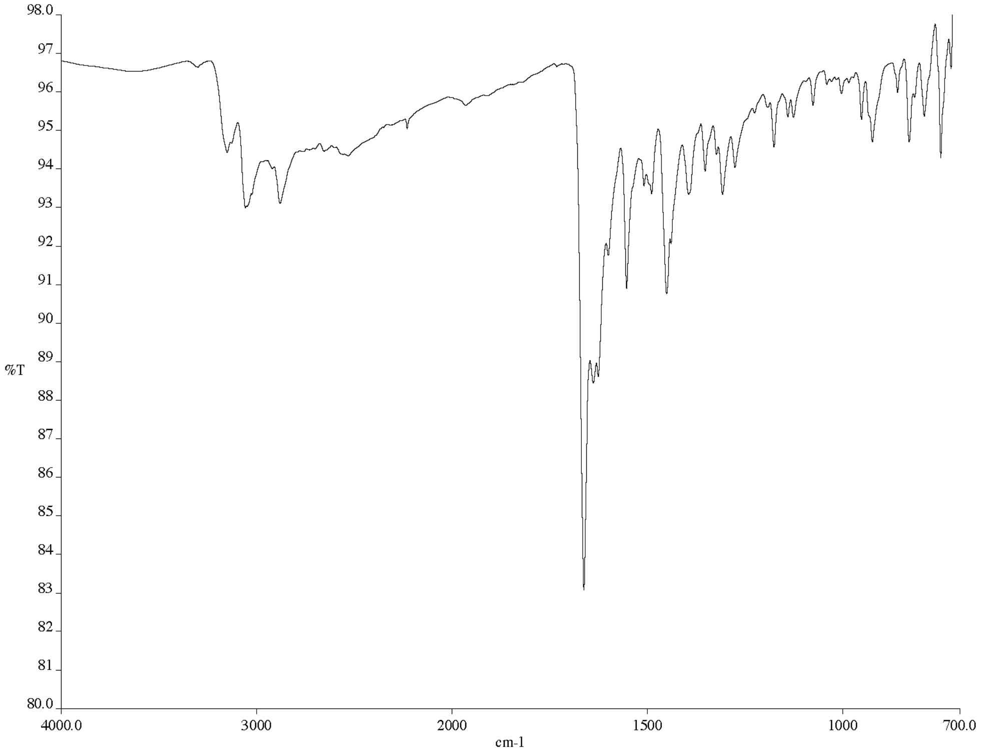
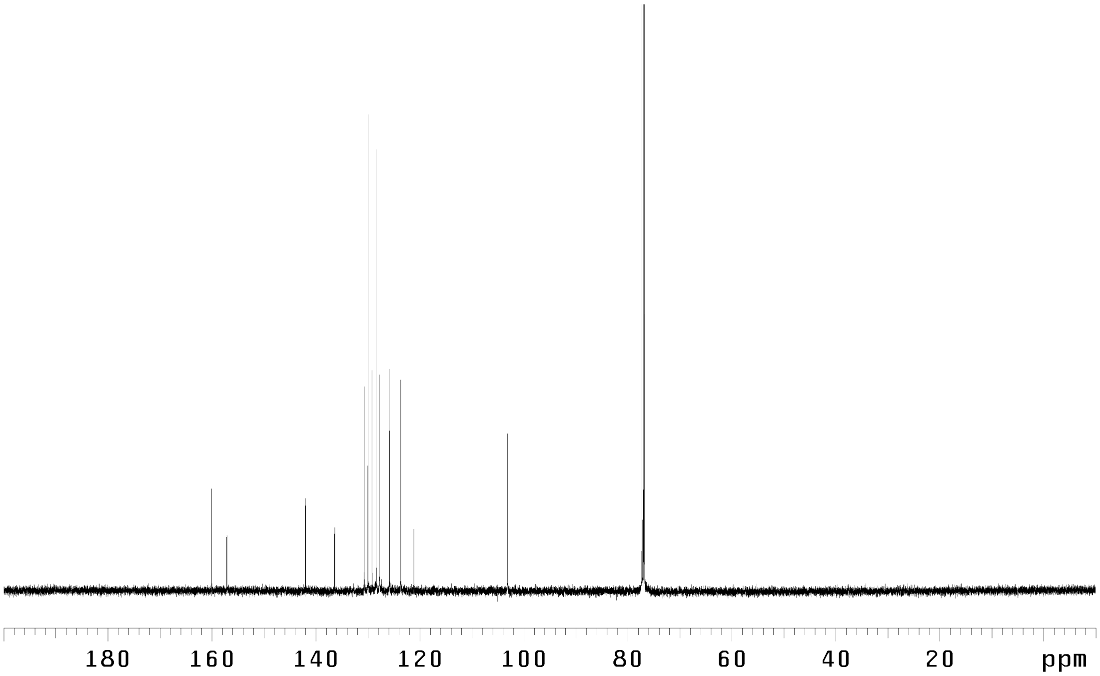


Figure 14.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 3.



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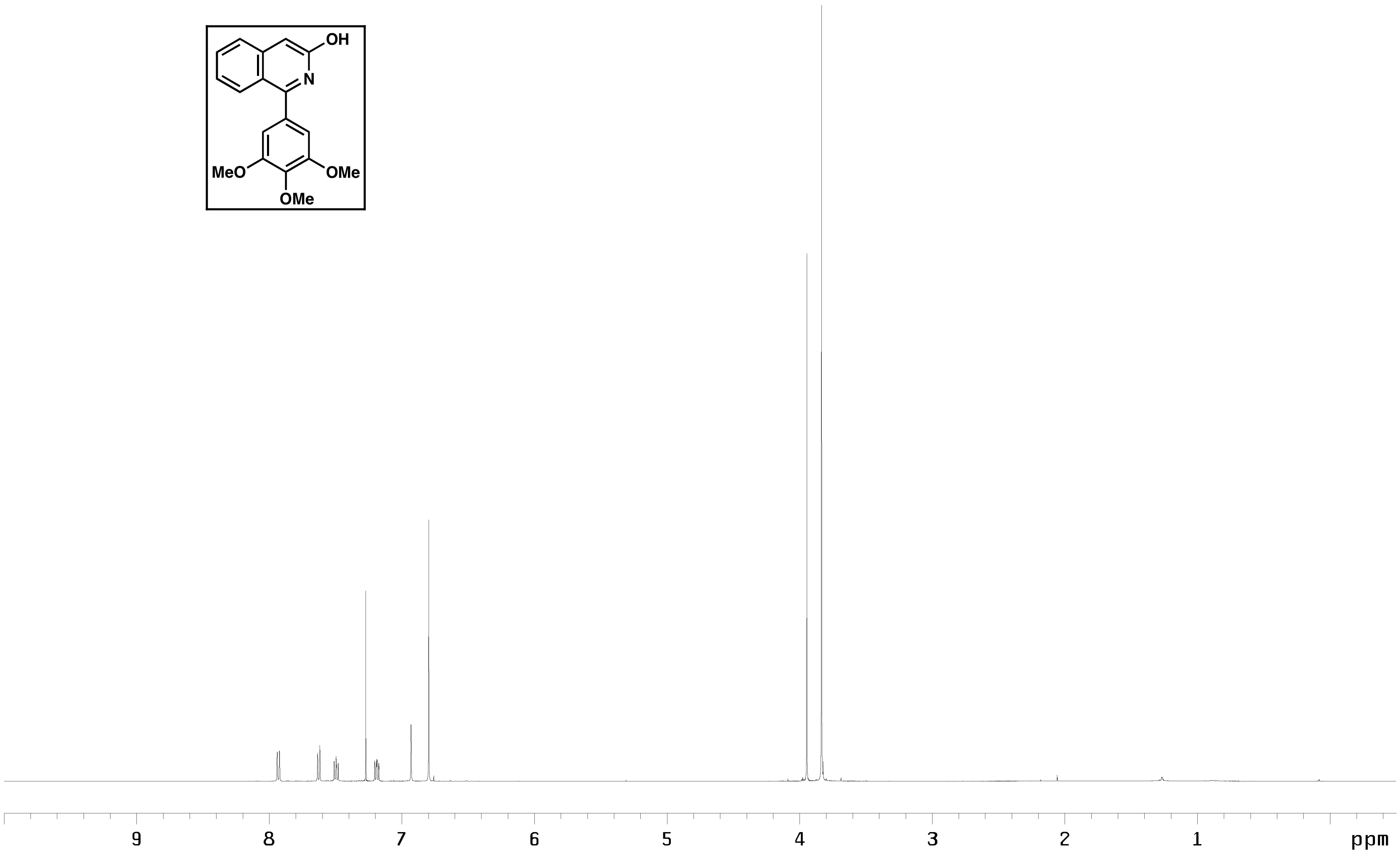

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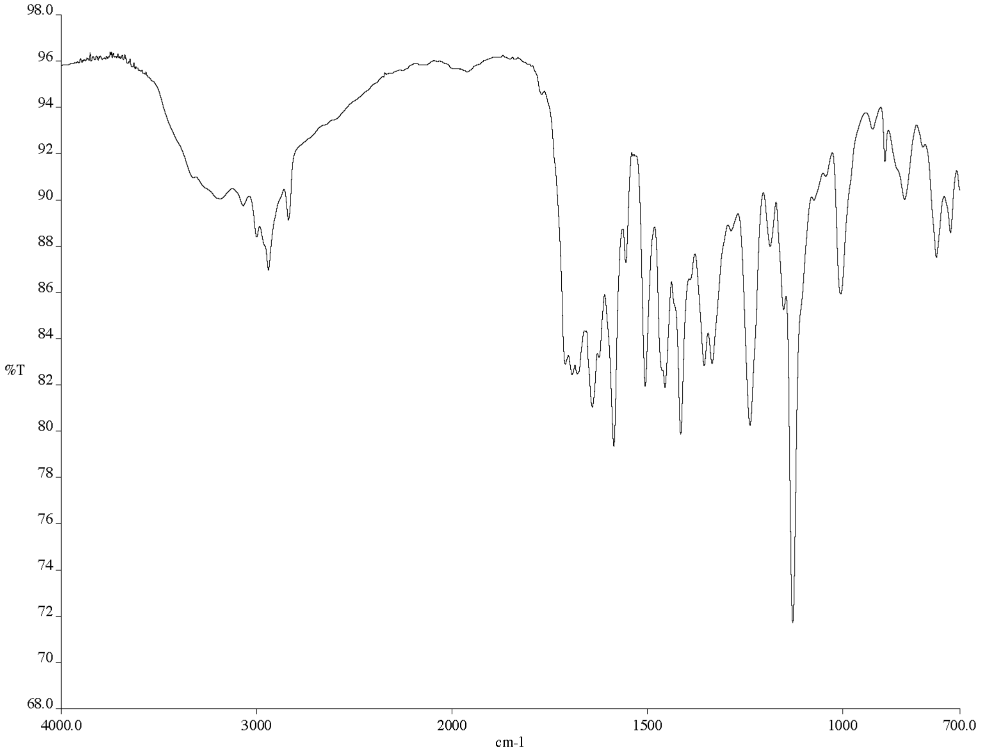

Figure 15.2 Infrared spectrum (thin film/NaCl) of of 3-hydroxyisoquinoline Table 2, entry 4.

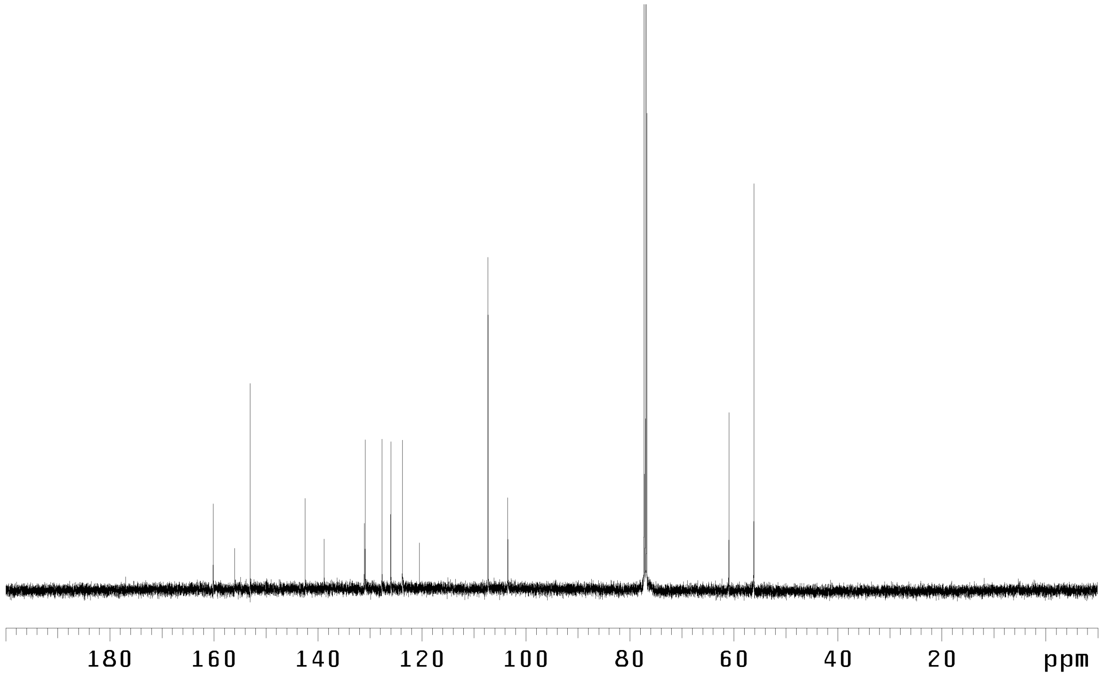

Figure 15.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 4.

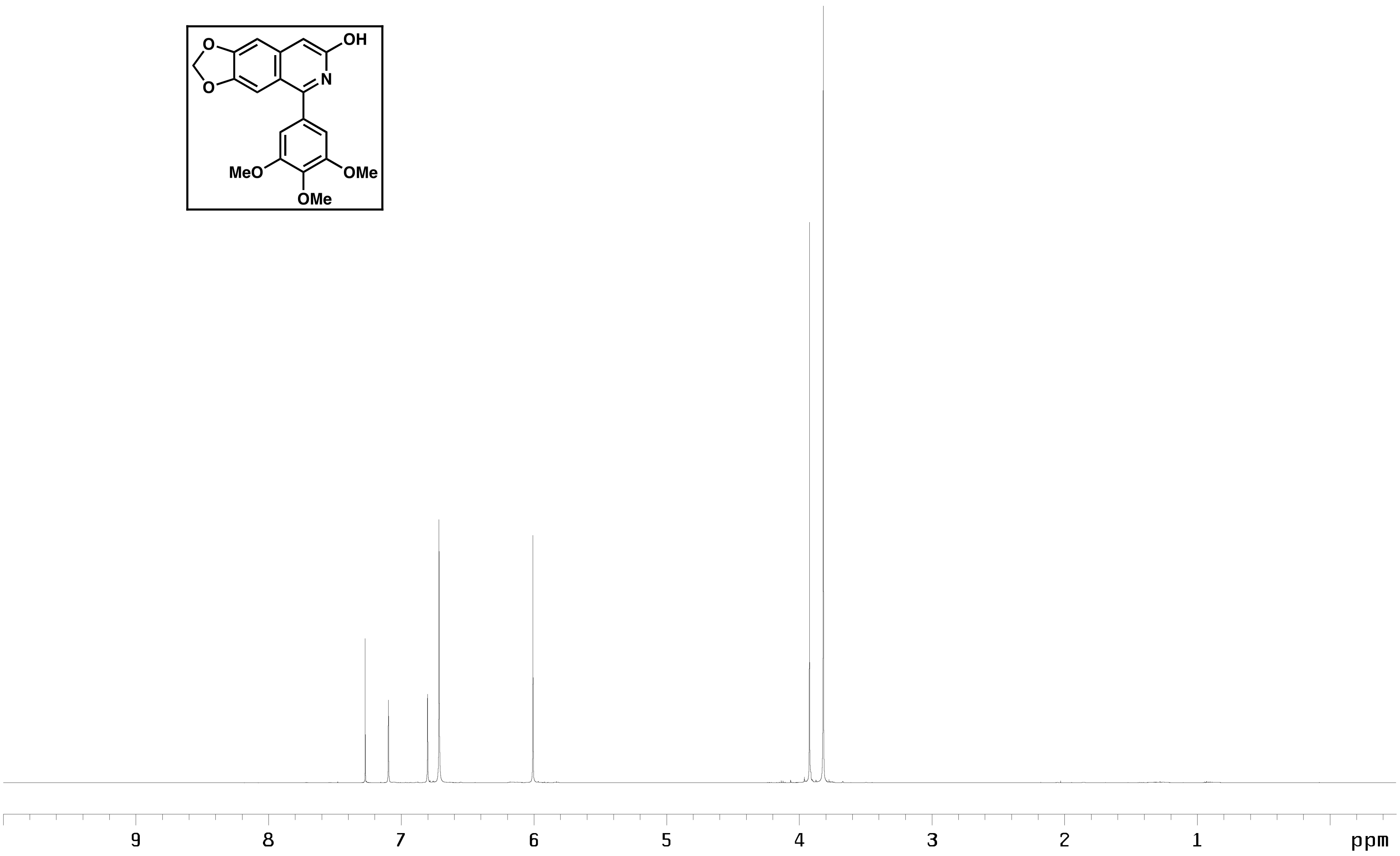

Figure 16.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 5.

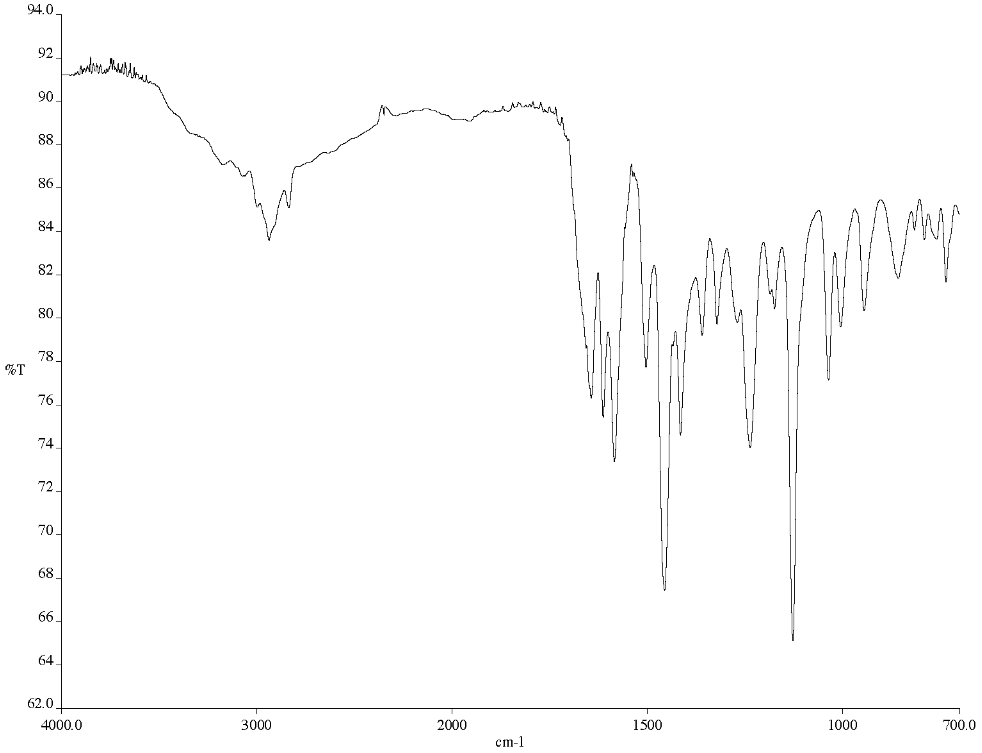

Figure 16.2 Infrared spectrum (thin film/NaCl) of of 3-hydroxyisoquinoline Table 2, entry 5.

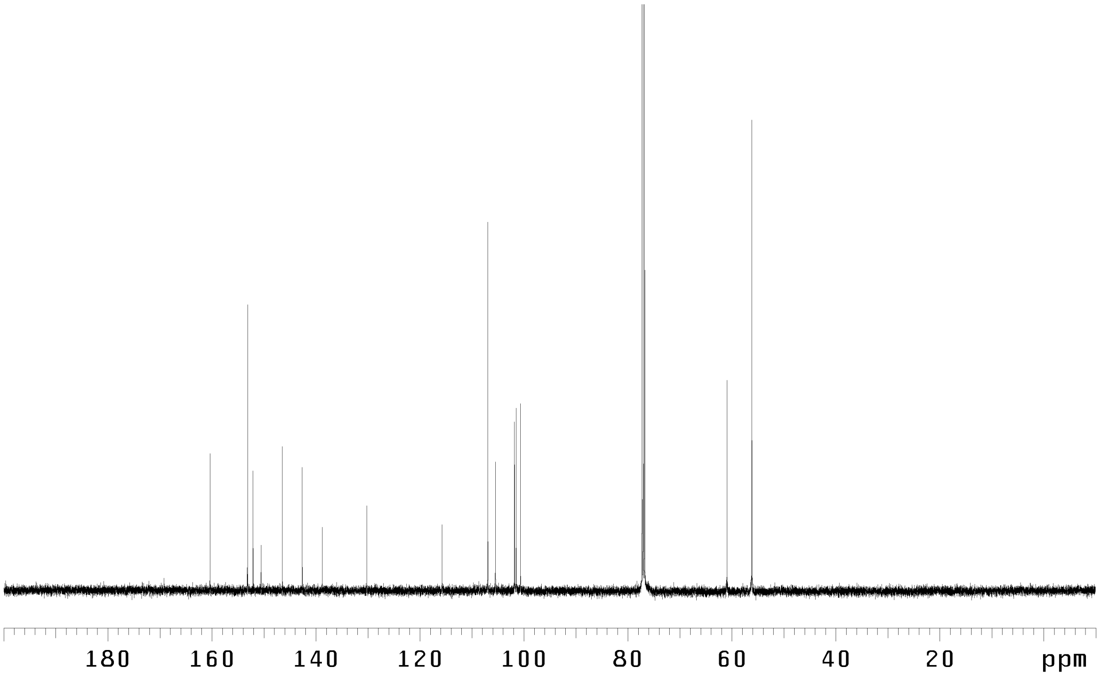

Figure 16.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 5.

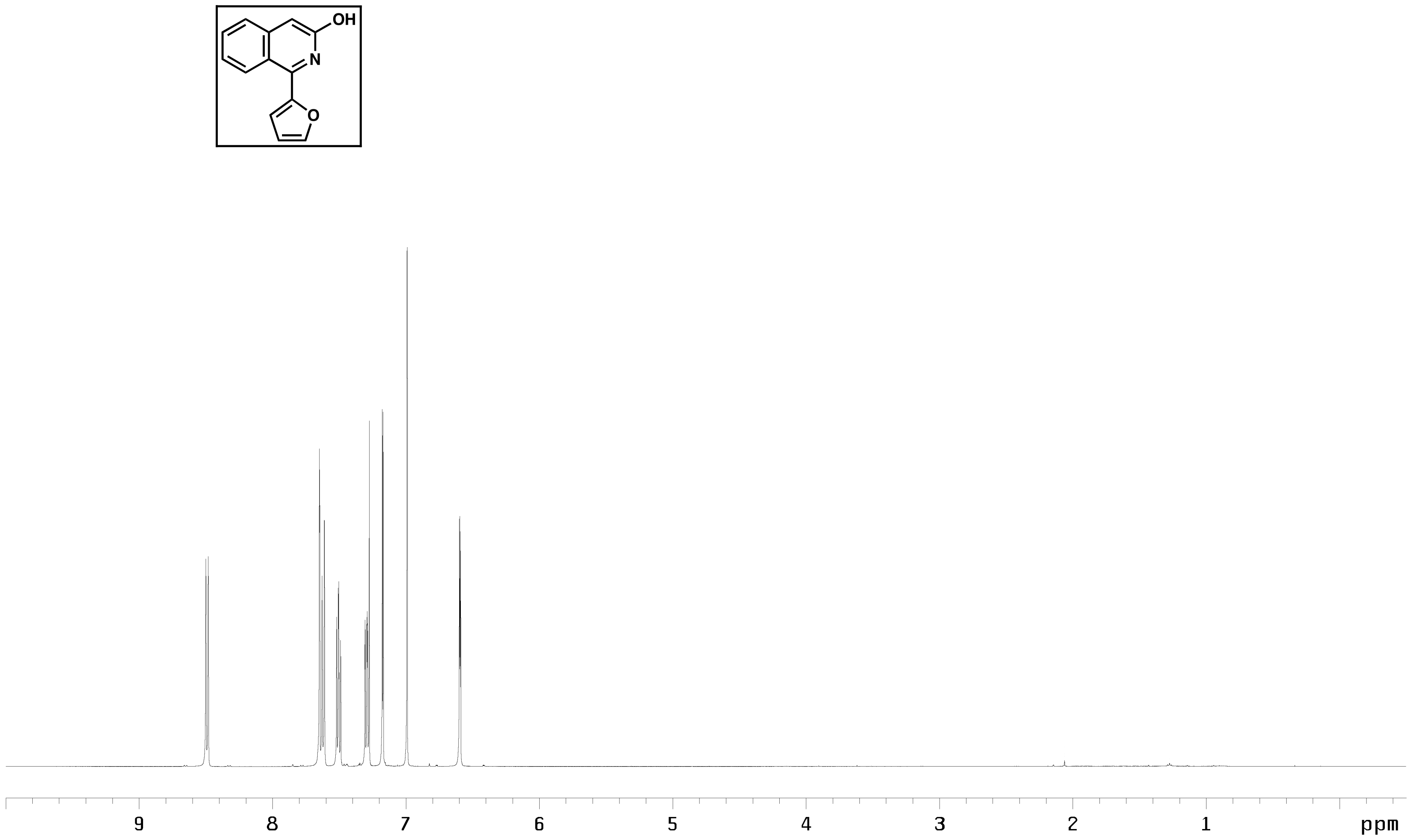

Figure 17.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 6.

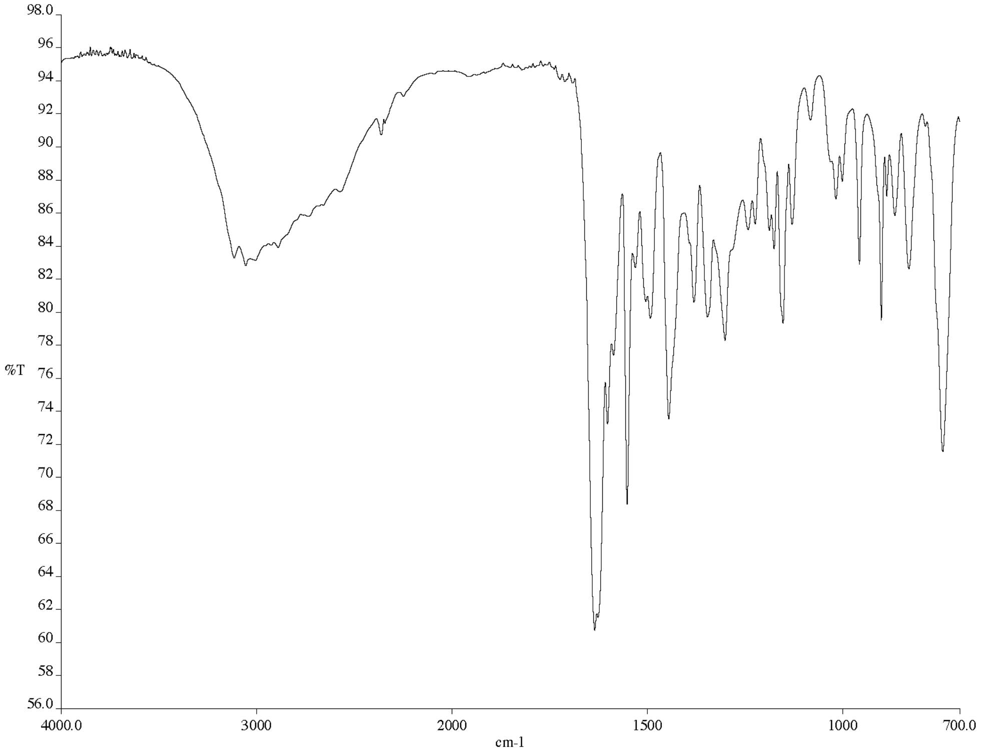

Figure 17.2 Infrared spectrum (thin film/NaCl) 3-hydroxyisoquinoline Table 2, entry 6.

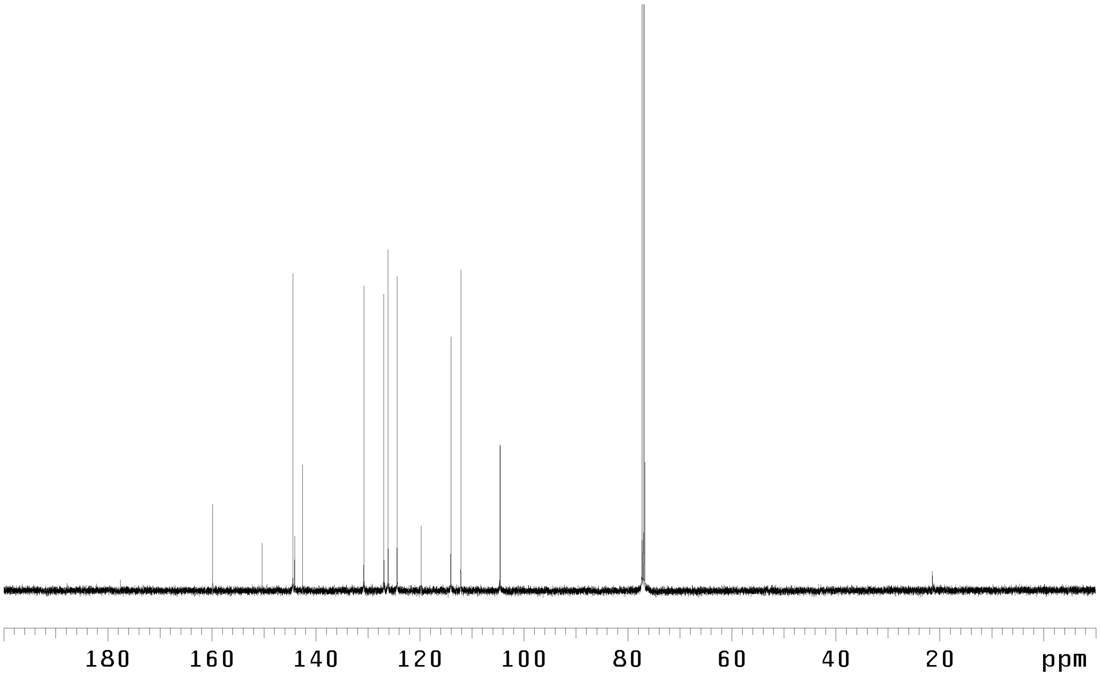

Figure 17.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 6.

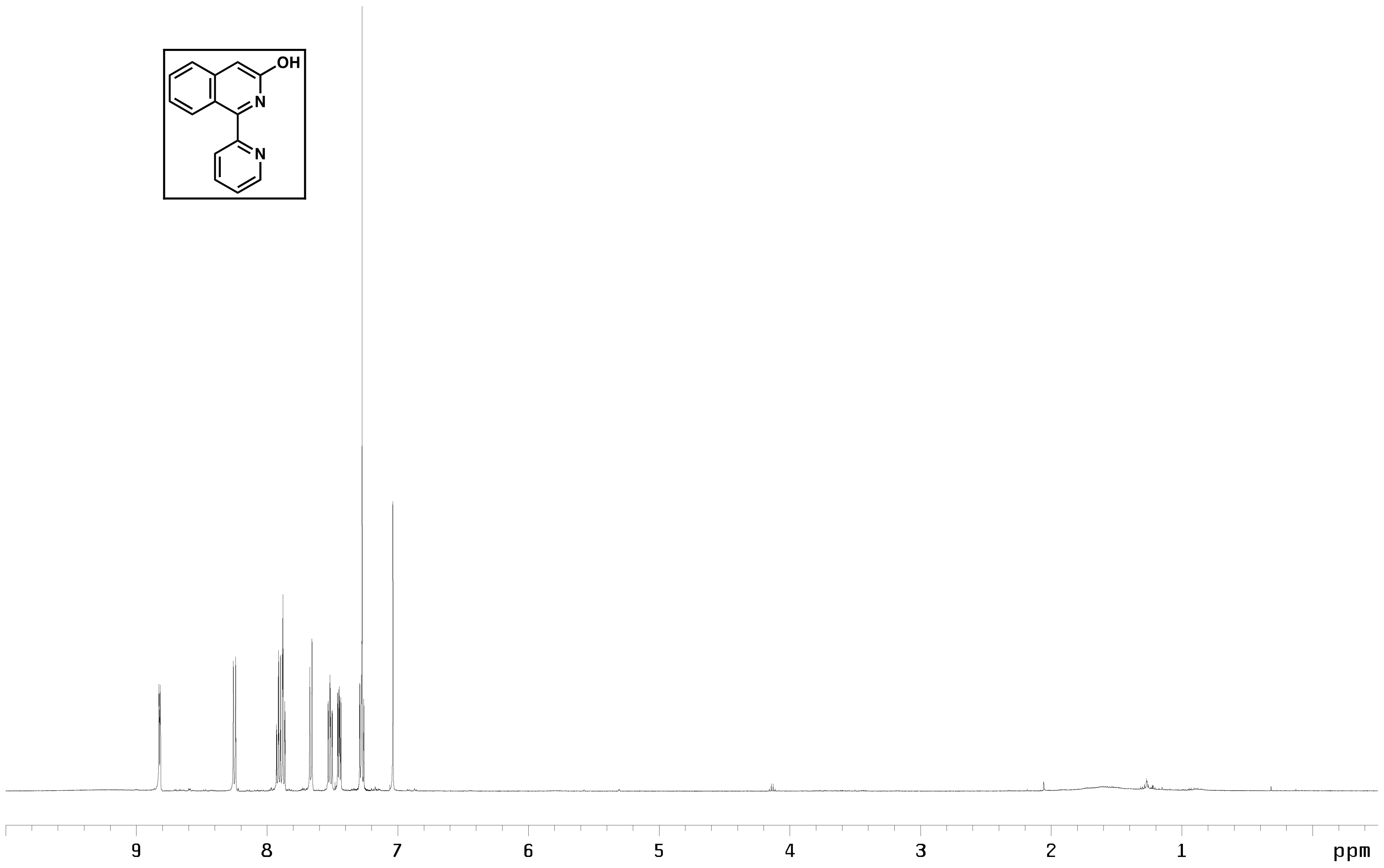

Figure 18.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 7.

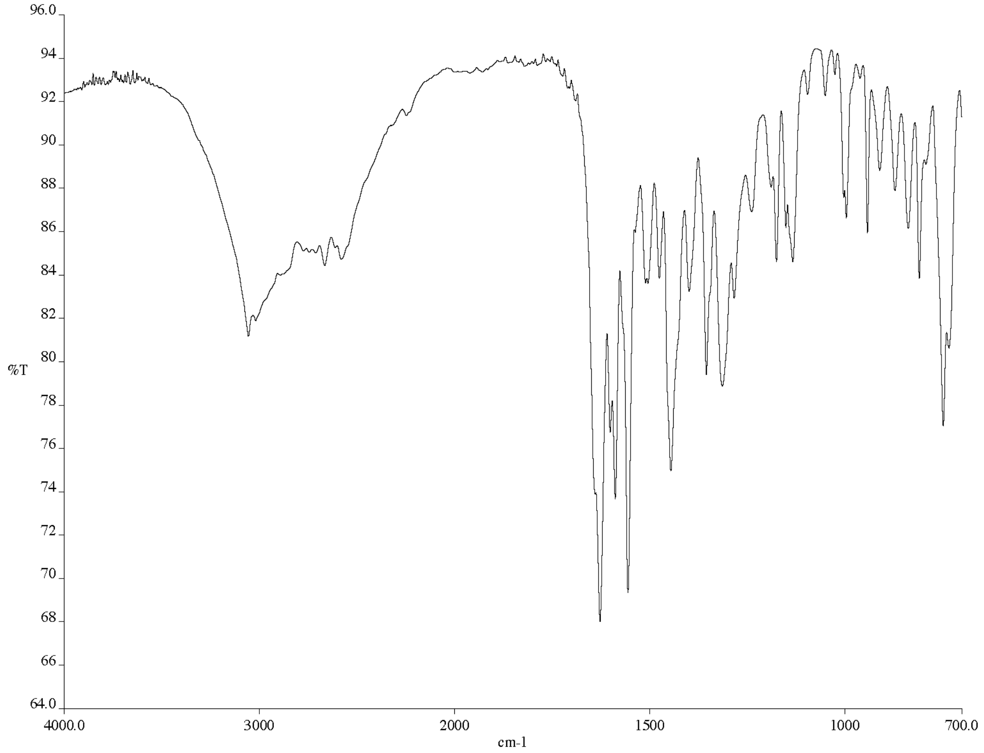

Figure 18.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 7.

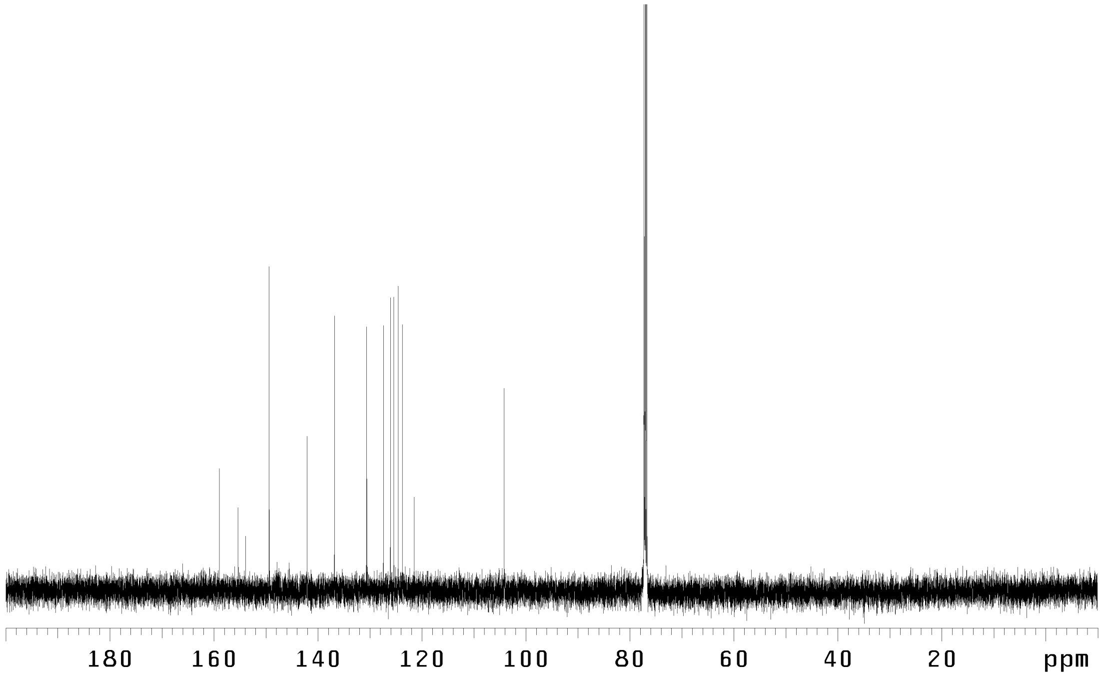

Figure 18.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 7.

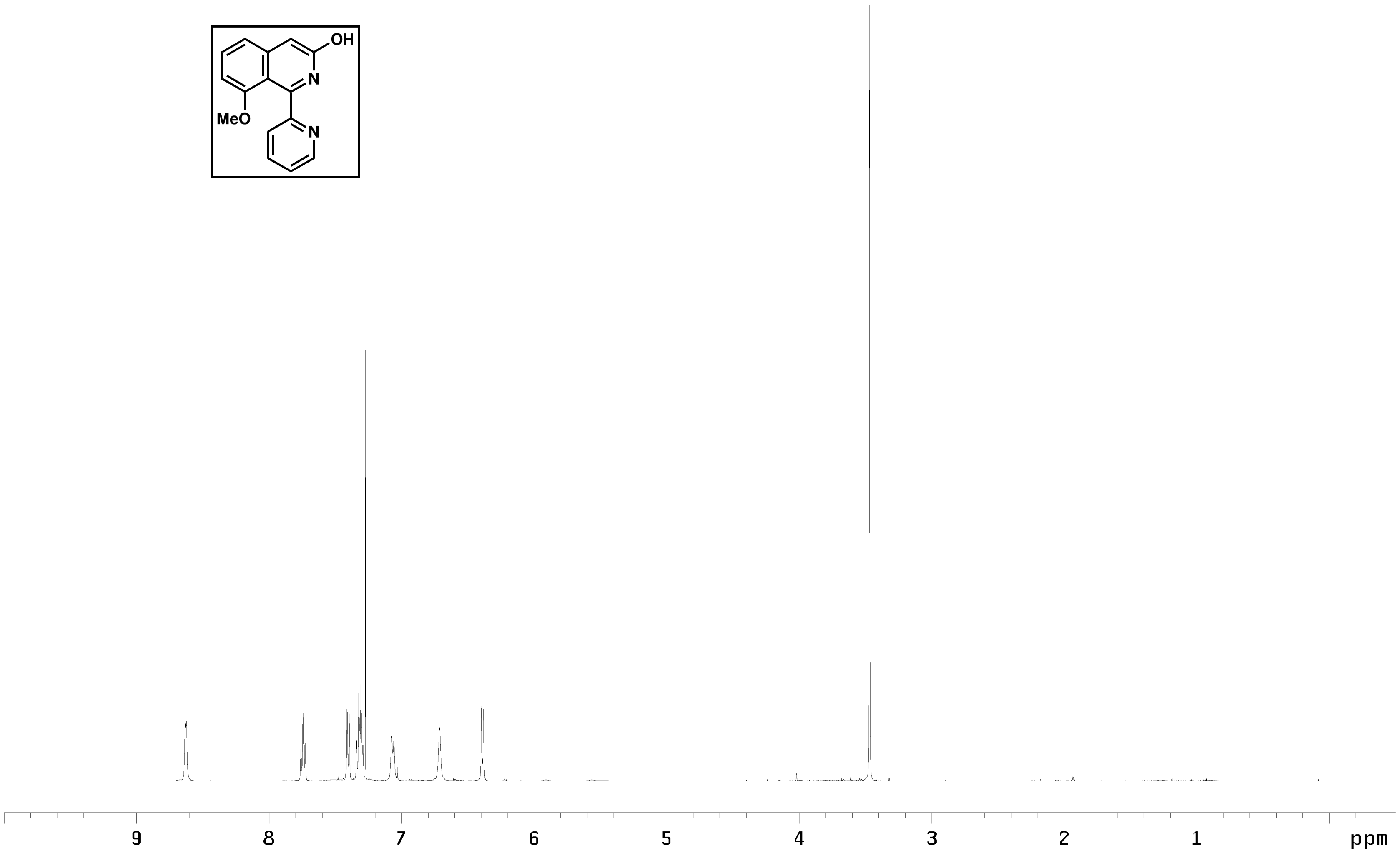

Figure 19.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 8.

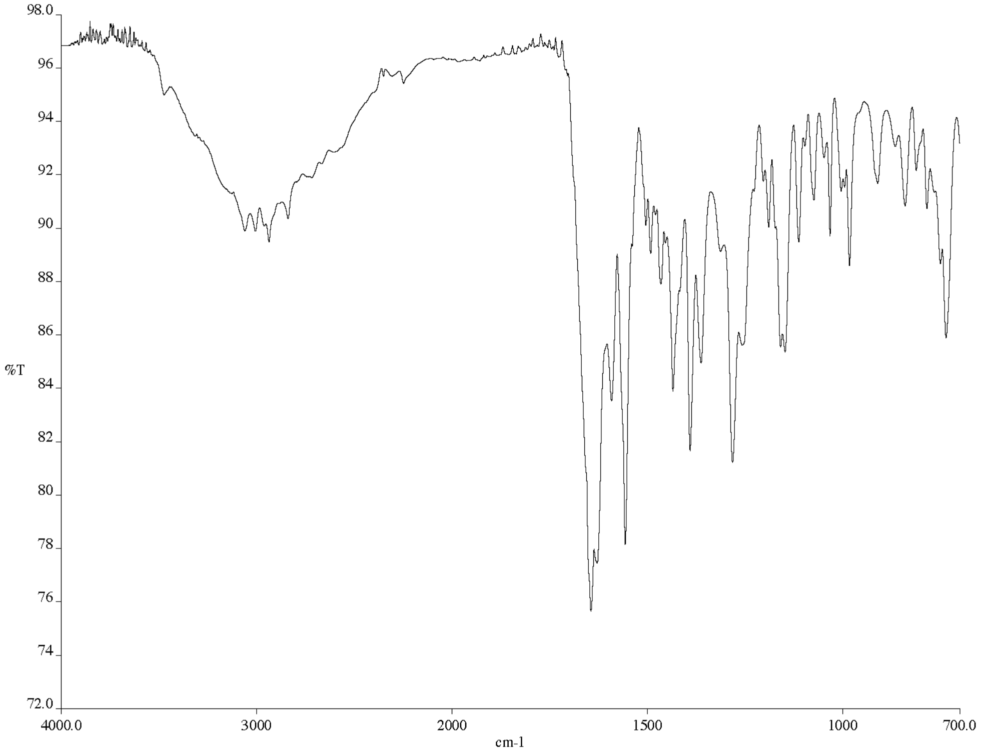

Figure 19.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 8.

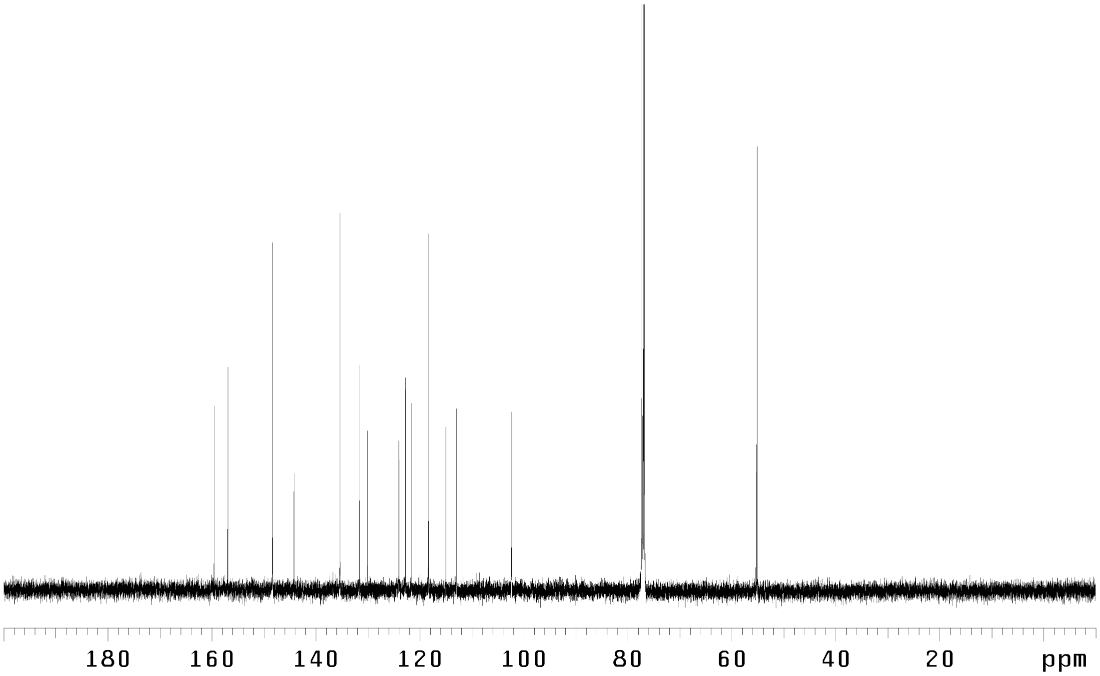

Figure 19.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 8.

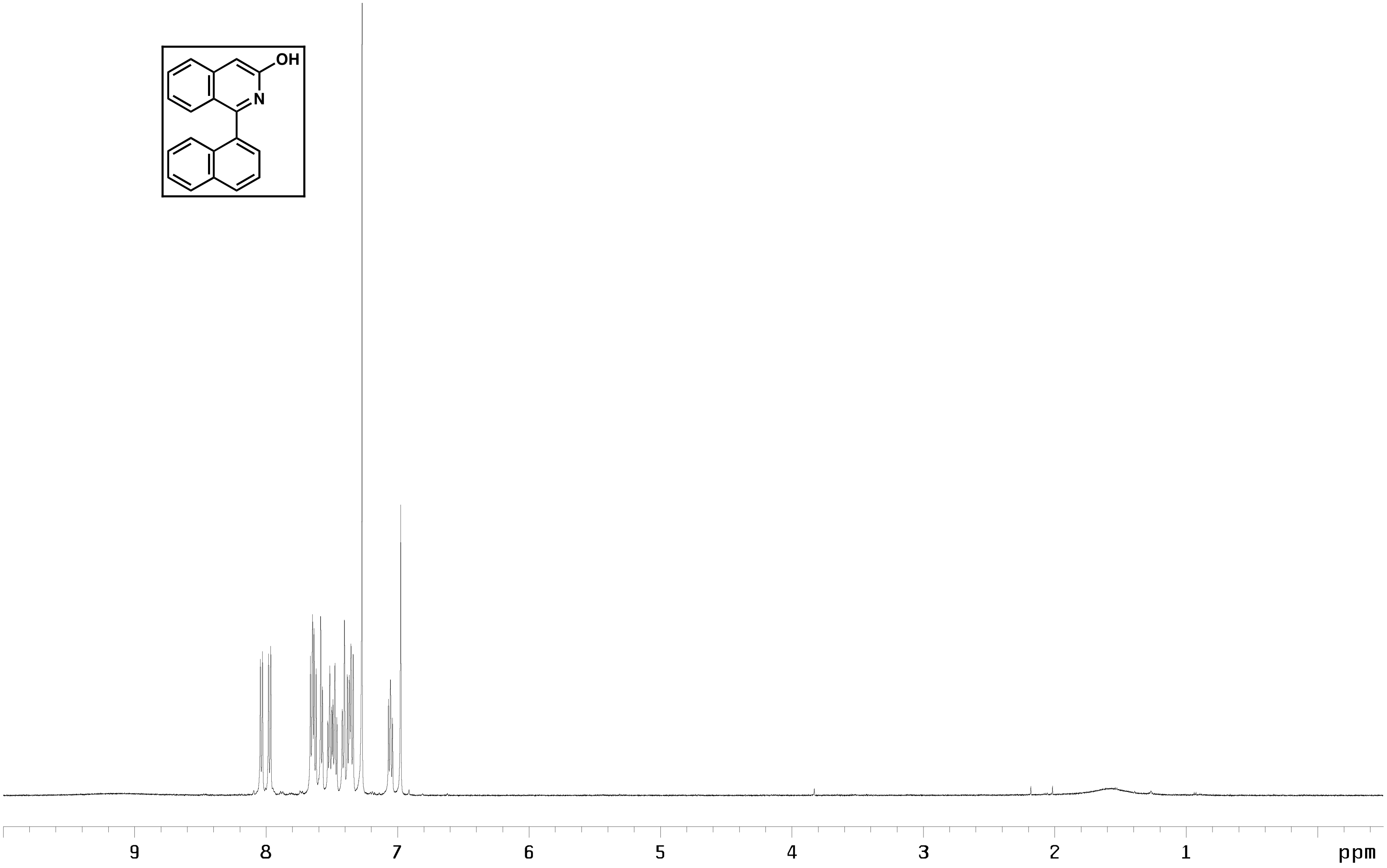

Figure 20.1 ^{1}H NMR (500 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 9.

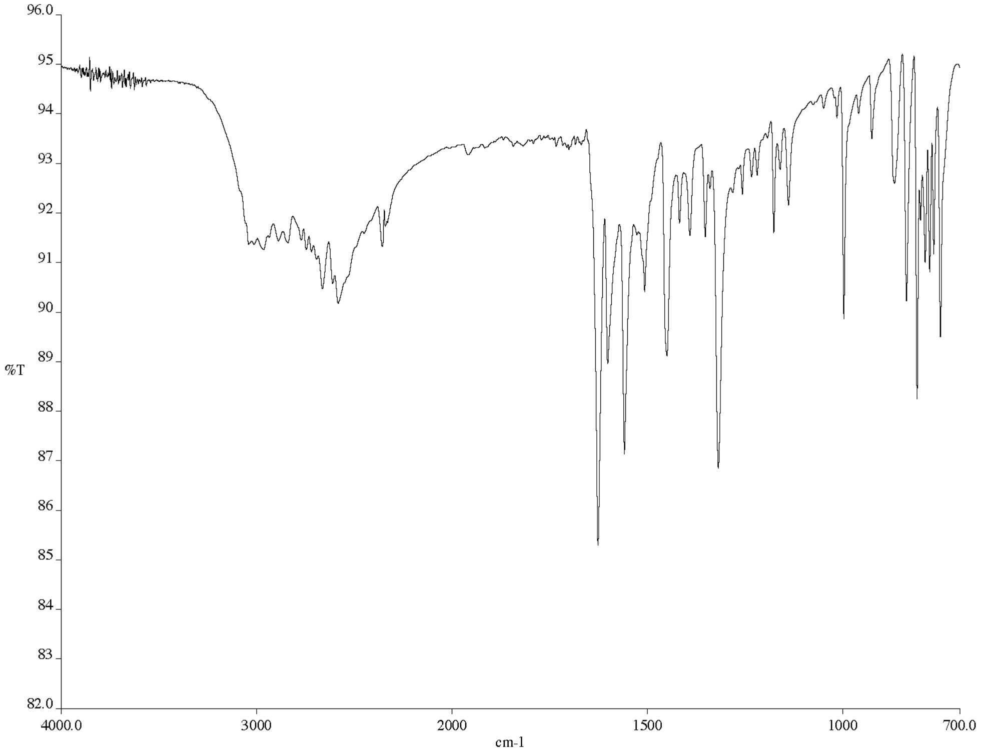

Figure 20.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 9.

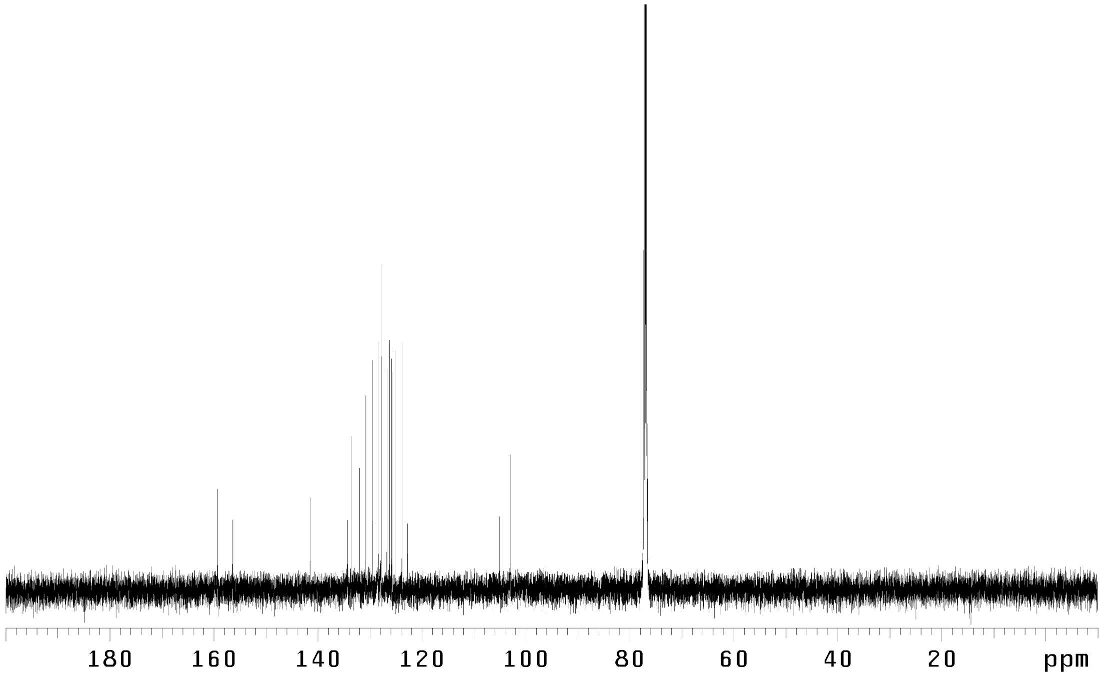

Figure 20.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 9.

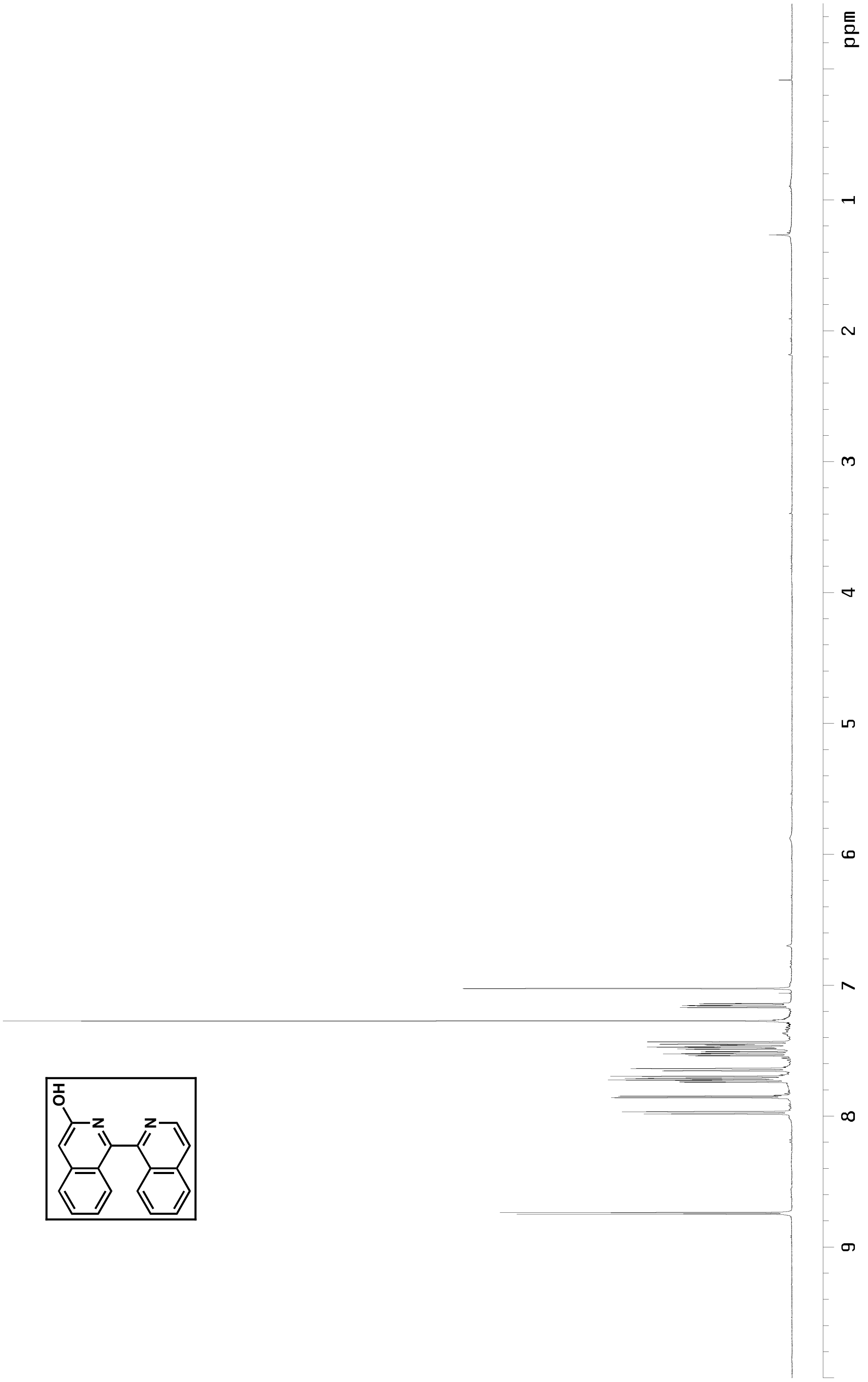

Figure 21.1 ^{1}H NMR (500 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 10.

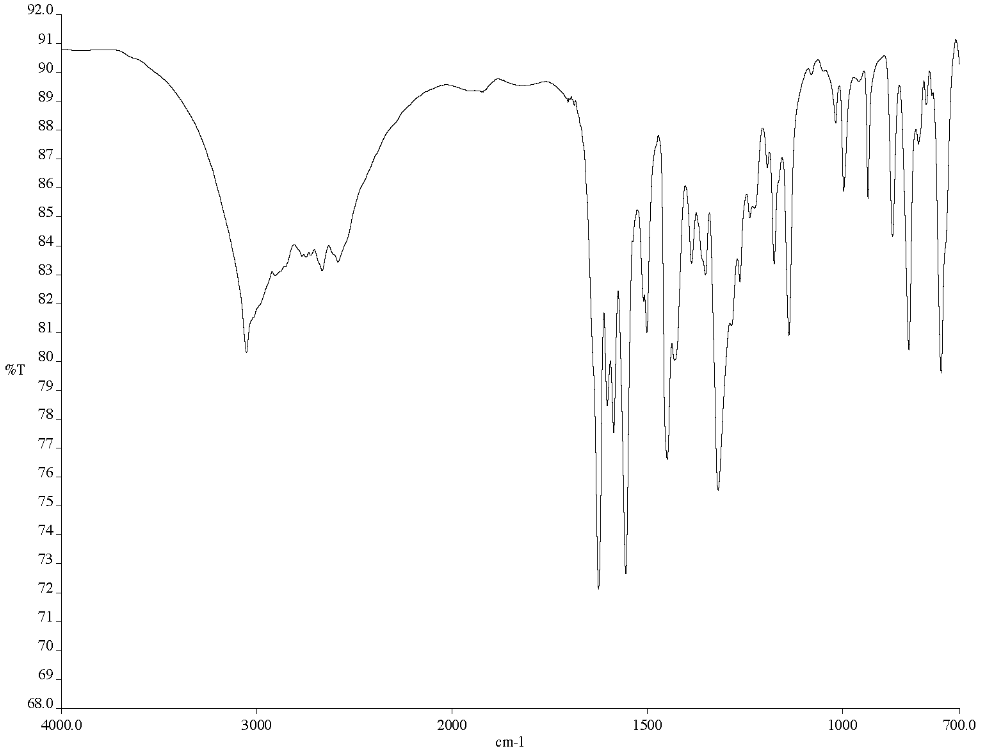

Figure 21.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 10.

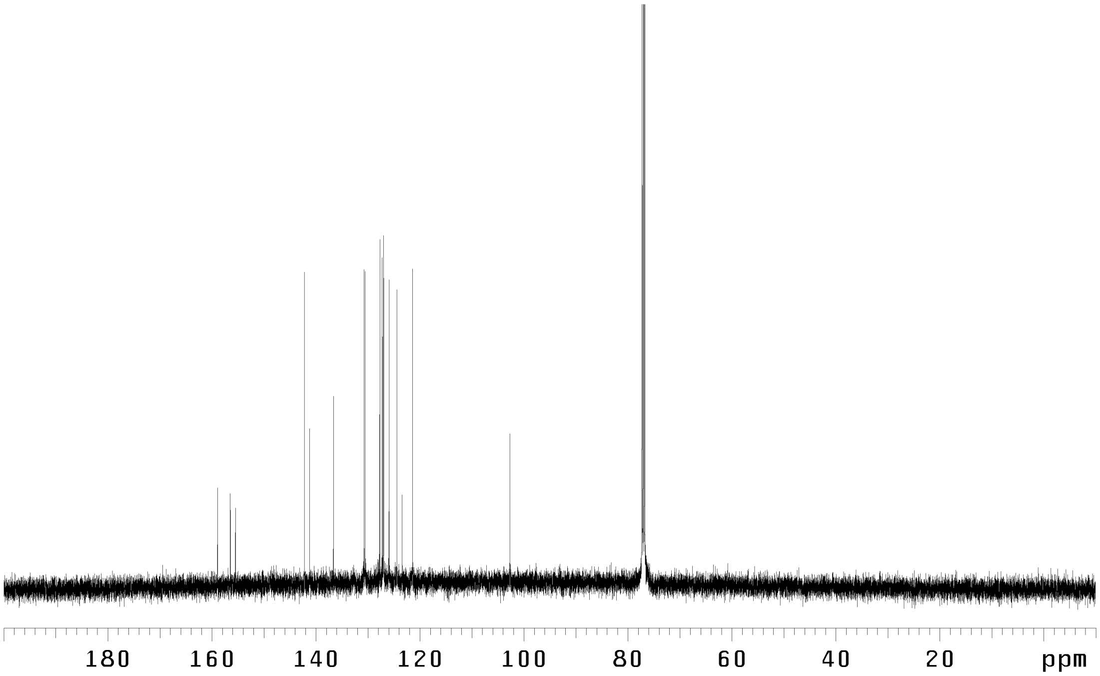

Figure 21.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 10.

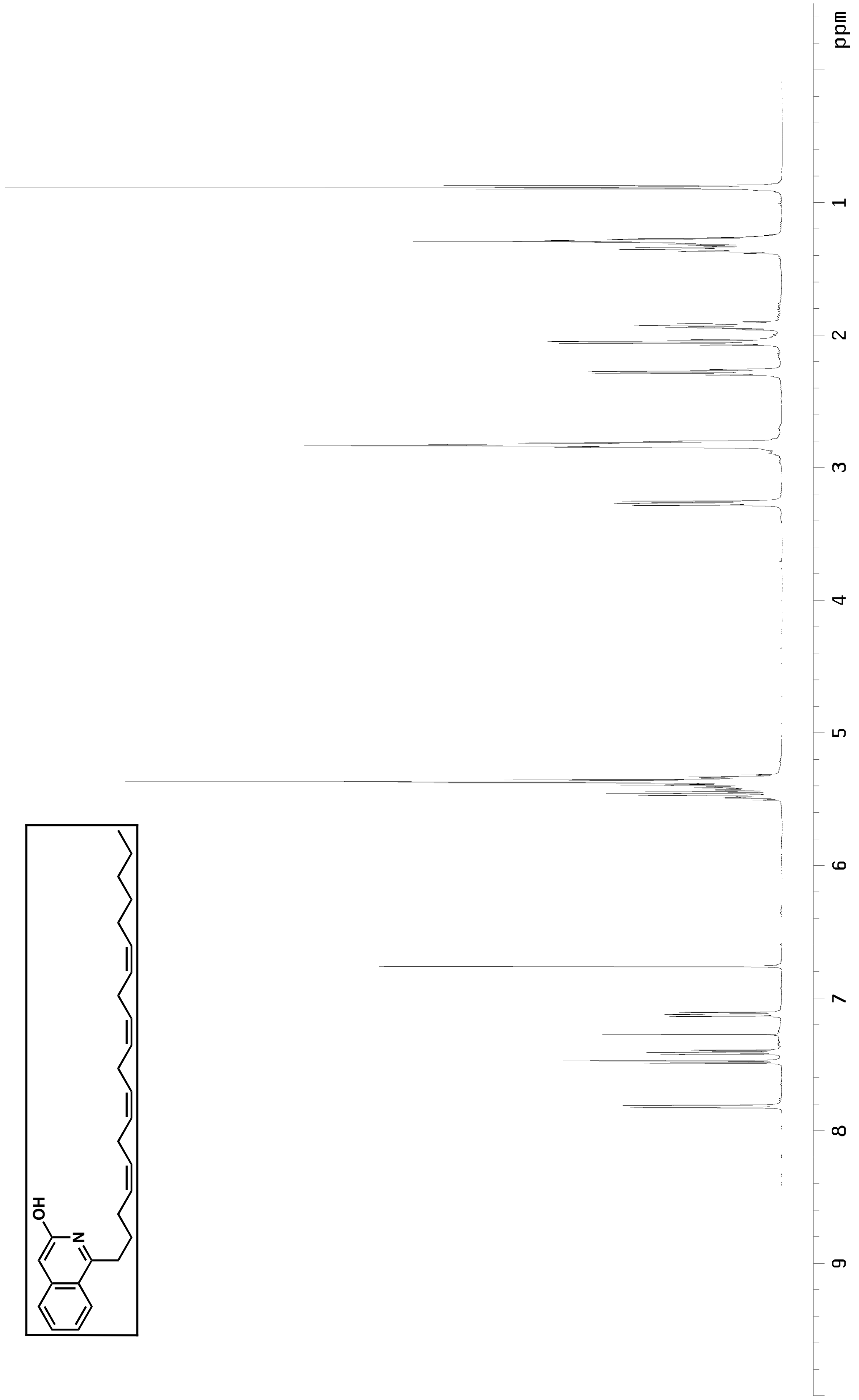

Figure 22.1 ^{1}H NMR (500 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 11.

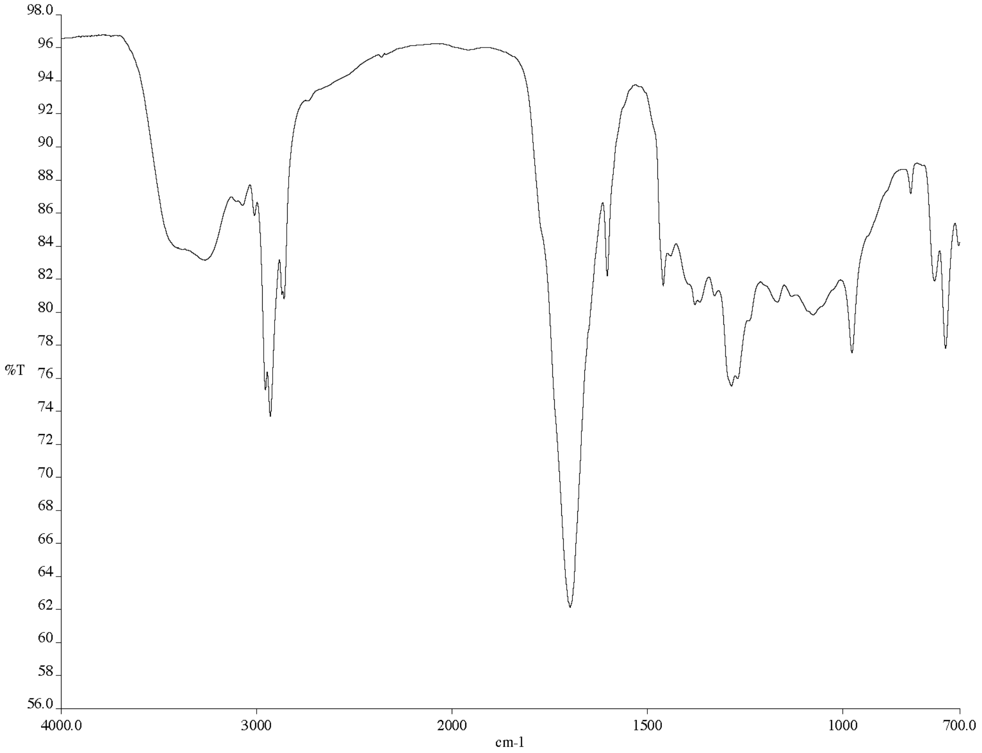

Figure 22.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 11.

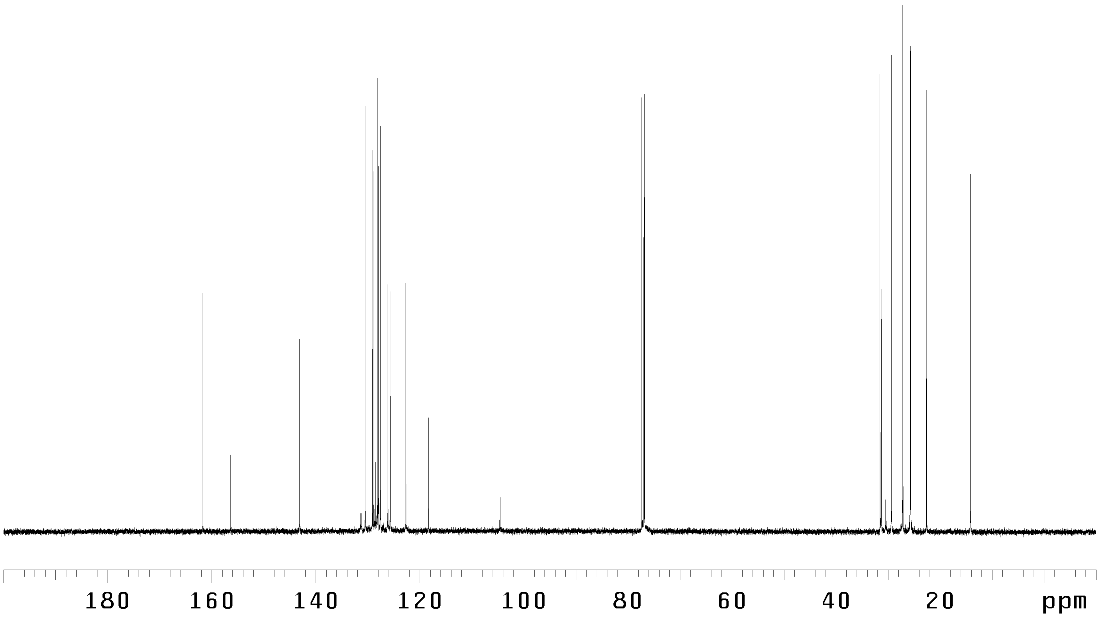

Figure 22.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 3-hydroxyisoquinoline Table 2, entry 11.

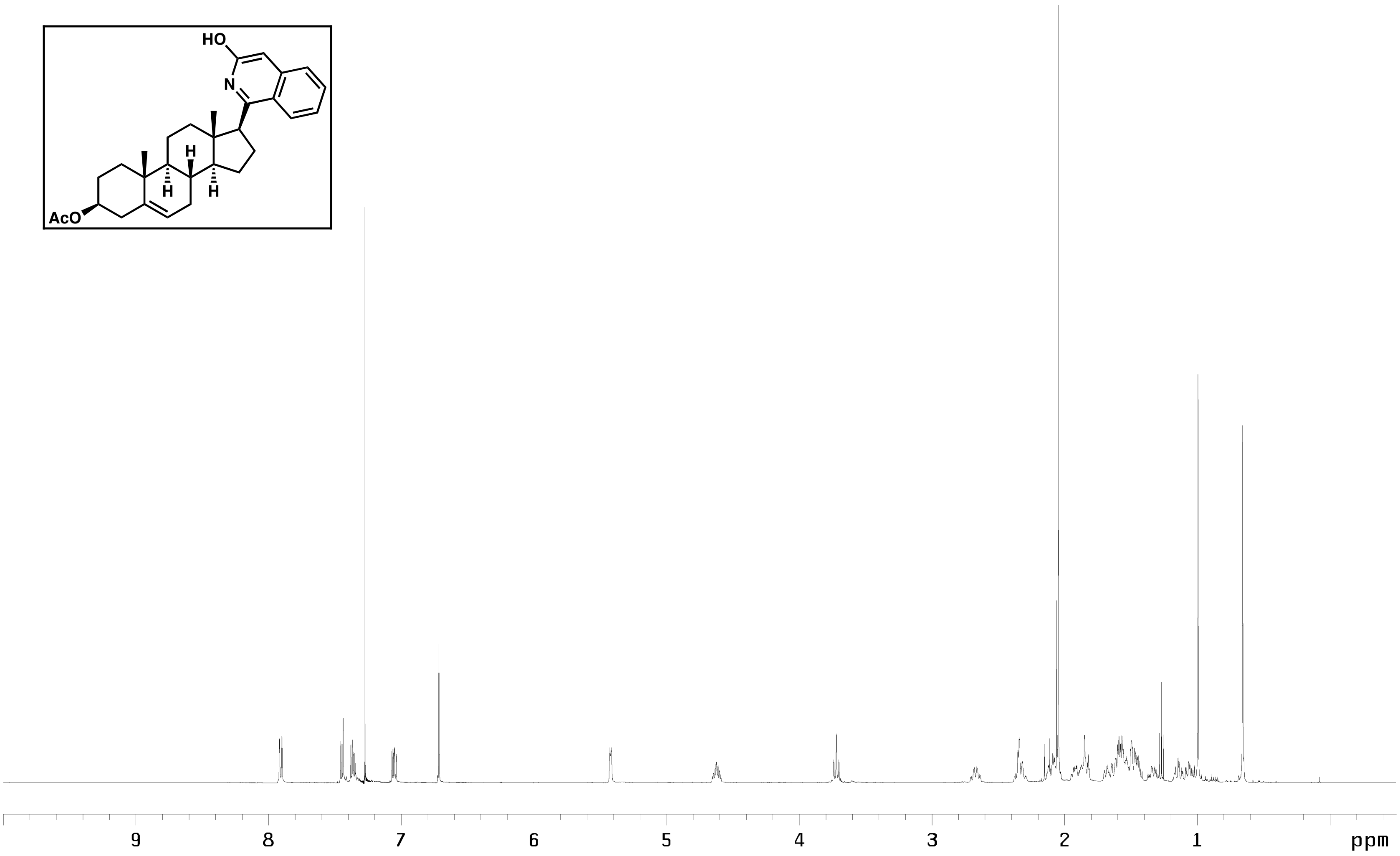

Figure 23.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 12.

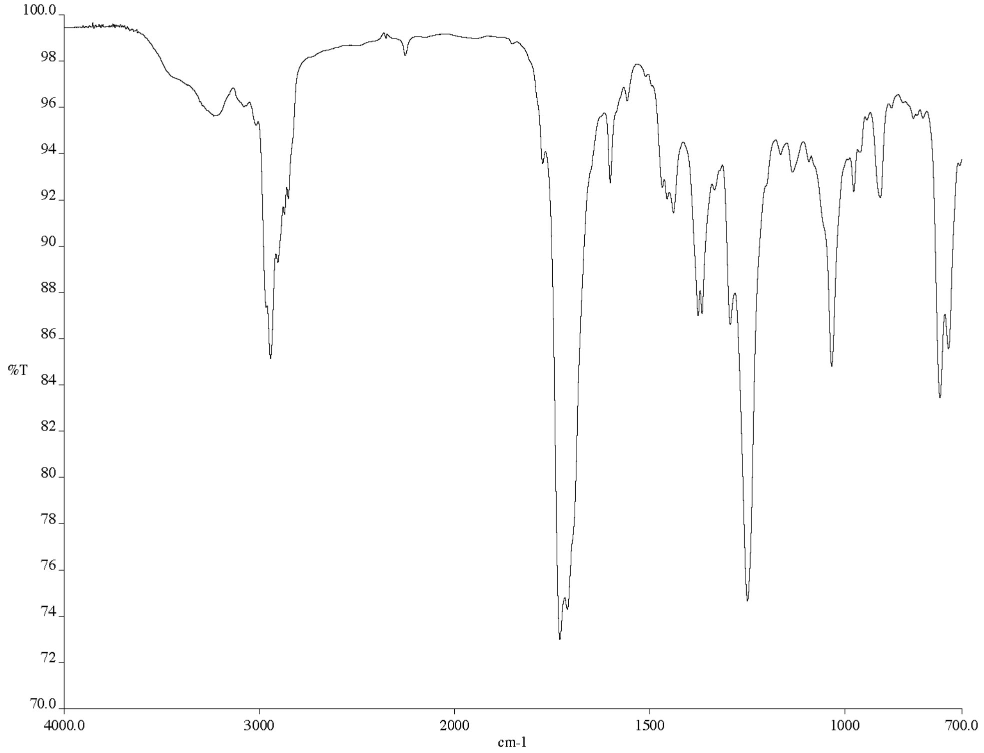

Figure 23.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 12.

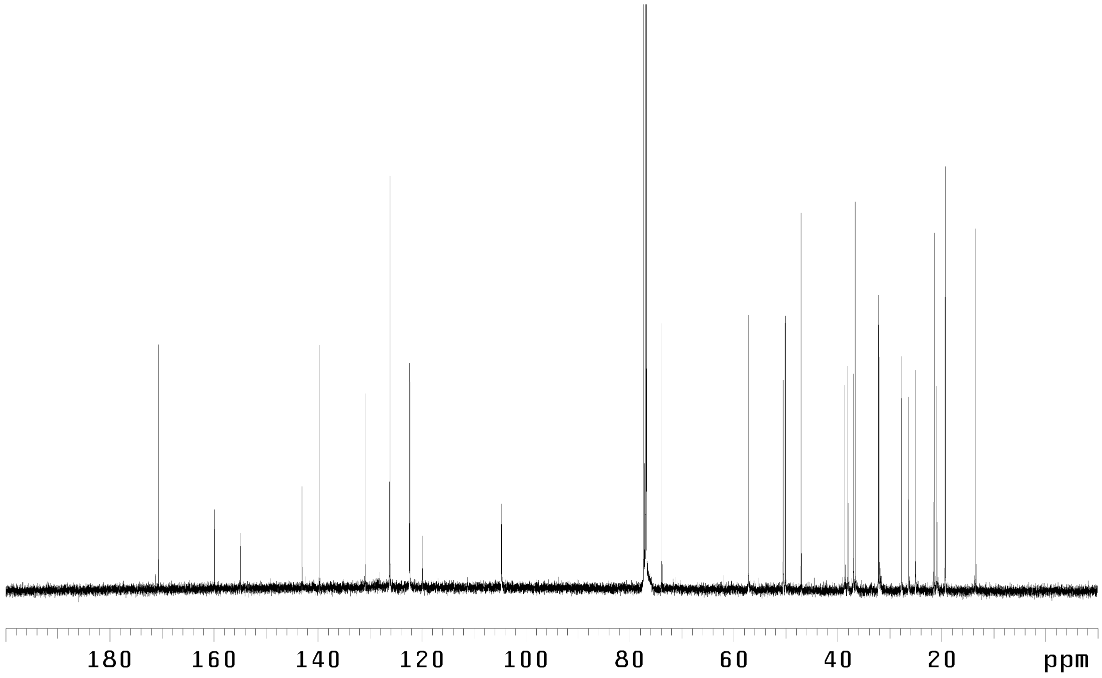

Figure 23.3 ^{13}C NMR (125 MHz, $CDCl_3$) of 3-hydroxyisoquinoline Table 2, entry 12.

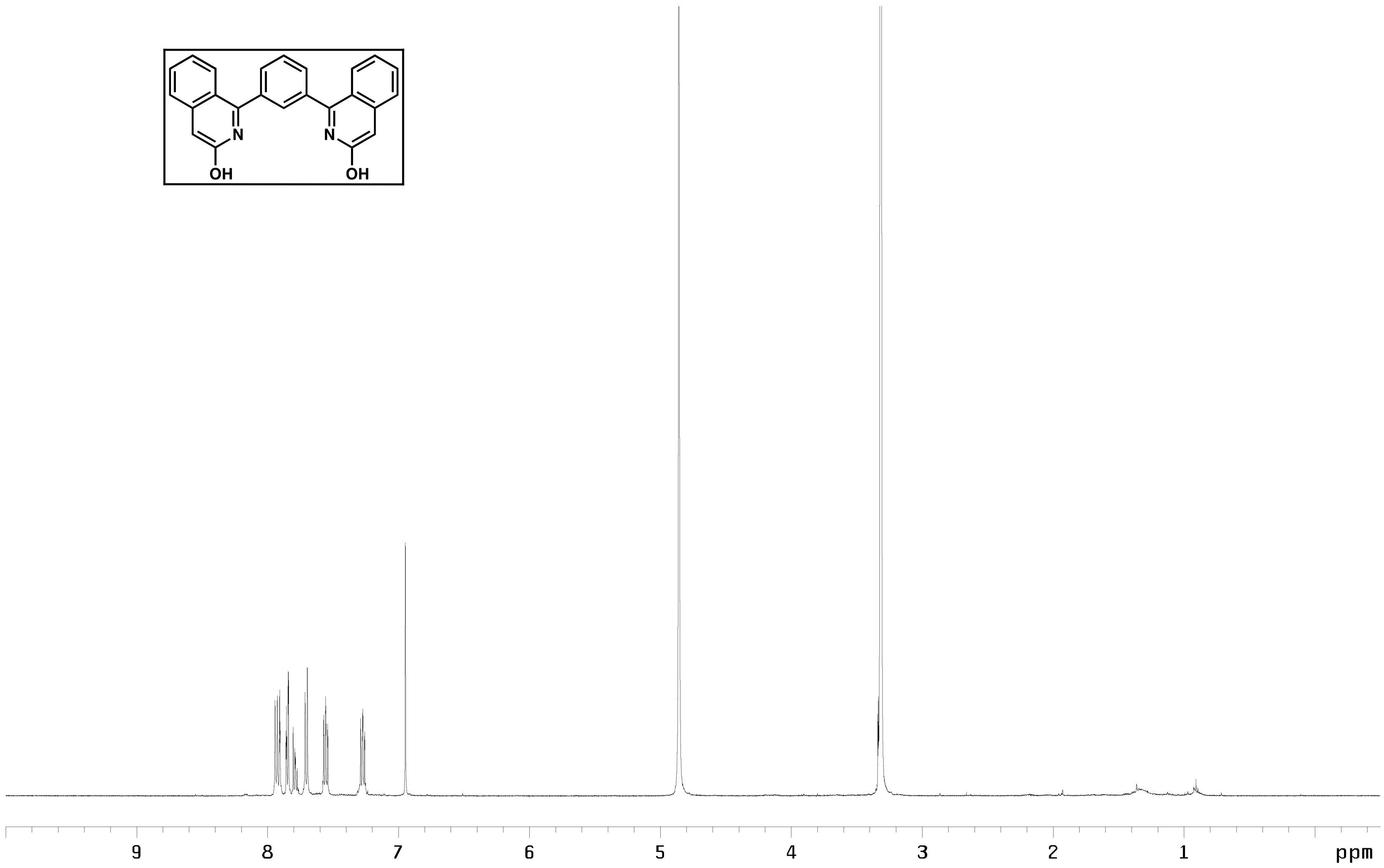

Figure 24.1 ^{1}H NMR (500 MHz, CD_3OD) of 3-hydroxyisoquinoline Table 2, entry 13.

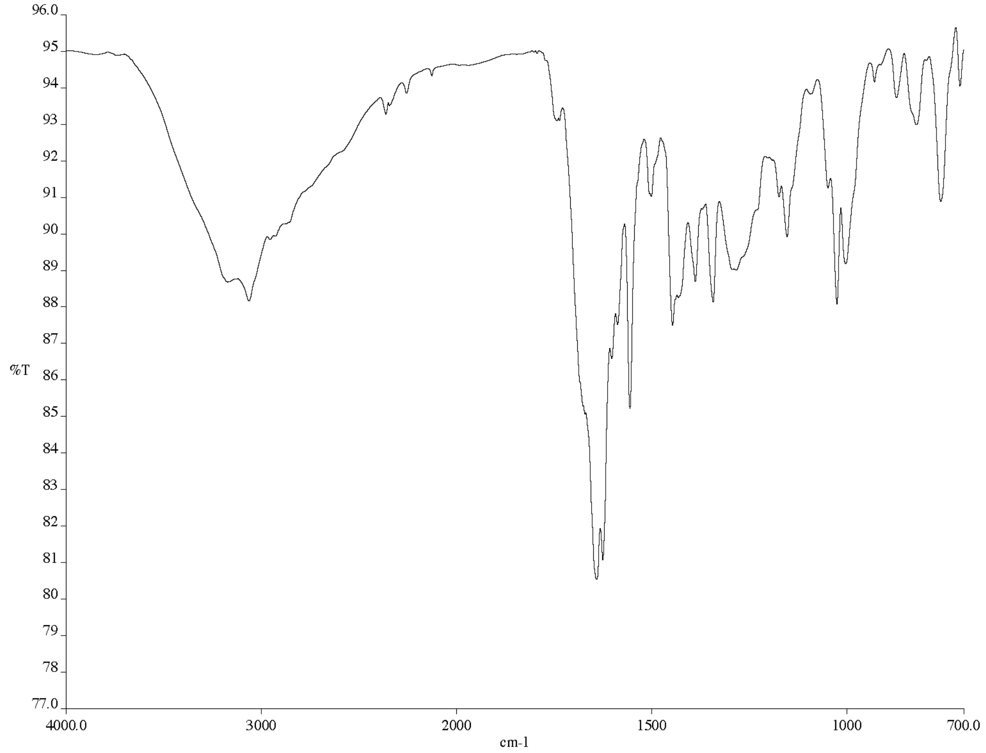

Figure 24.2 Infrared spectrum (thin film/NaCl) of 3-hydroxyisoquinoline Table 2, entry 13.

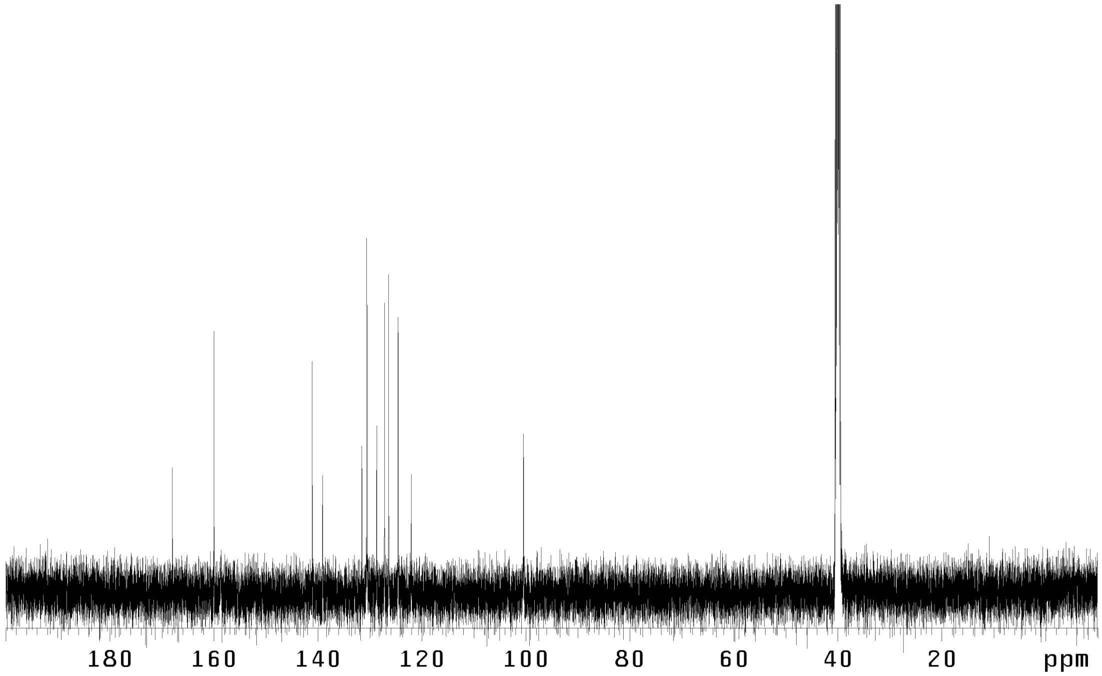

Figure 24.3 ^{13}C NMR (125 MHz, DMSO-d_6) of 3-hydroxyisoquinoline Table 2, entry 13.

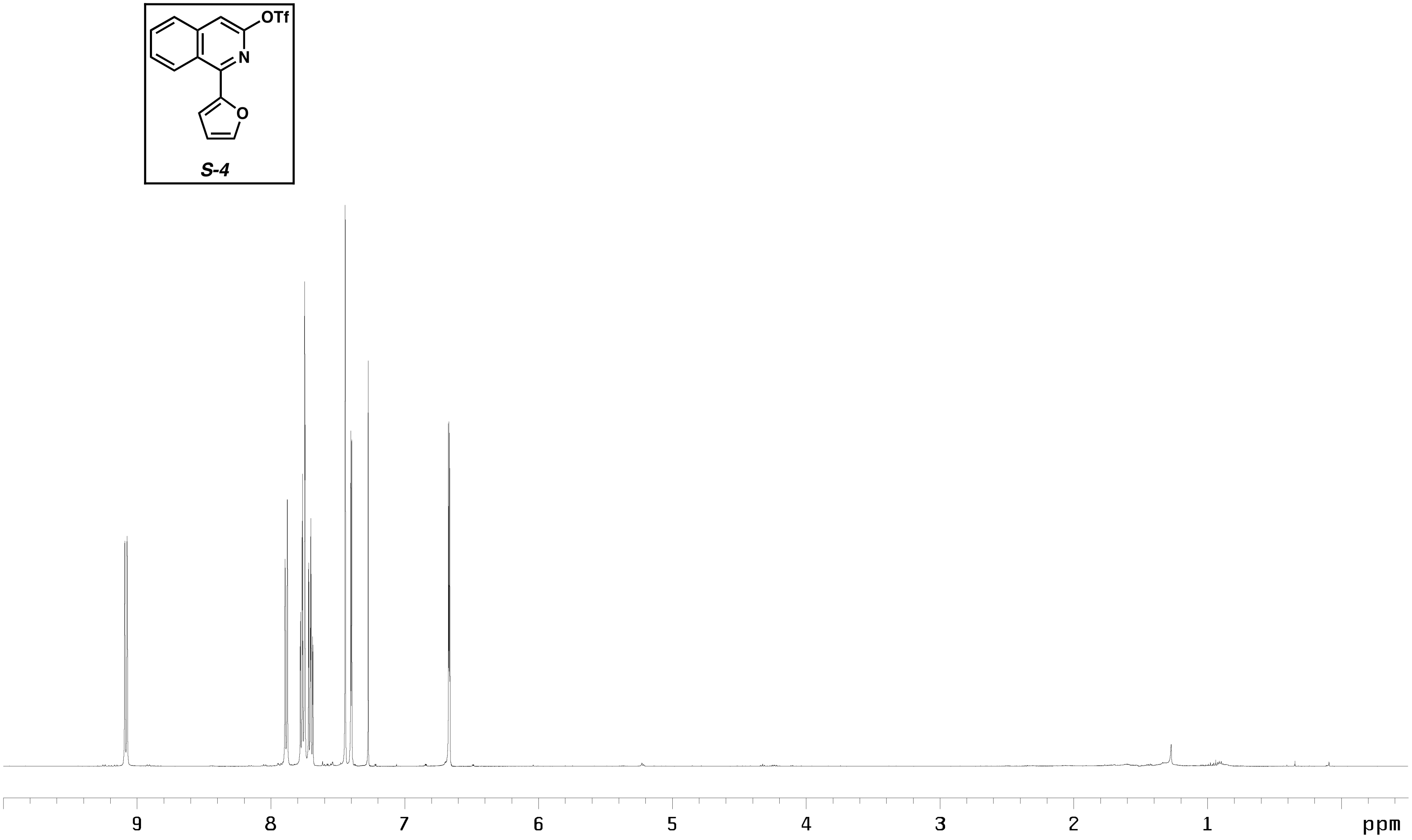

Figure 25.1 ^{1}H NMR (500 MHz, $CDCl_3$) of isoquinoline triflate **S-4**.

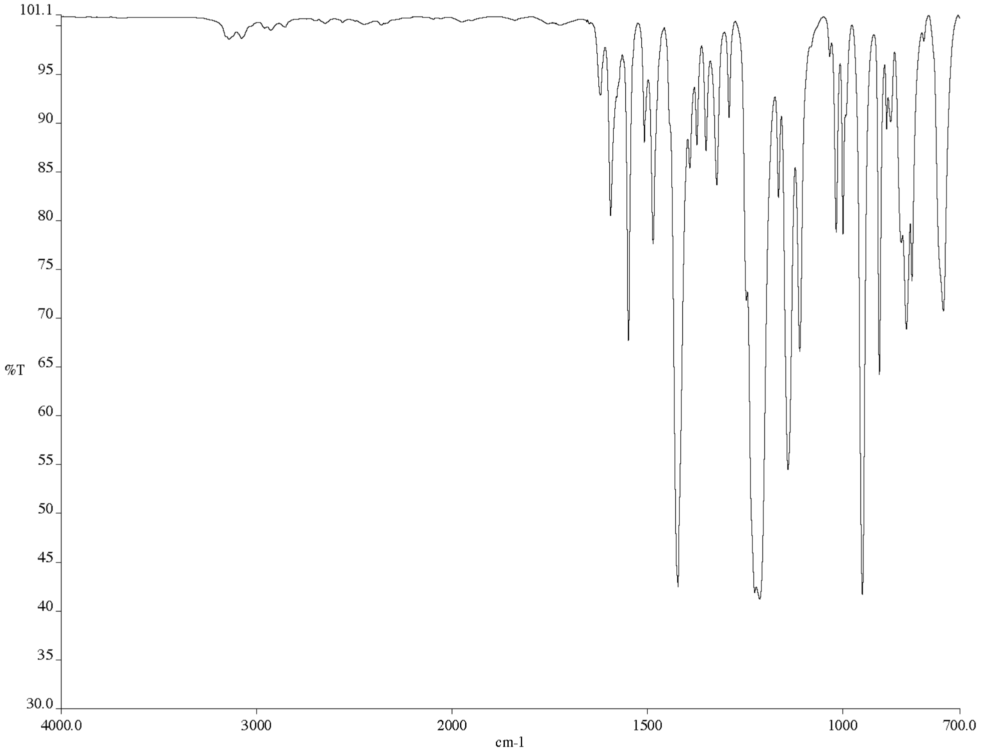

Figure 25.2 Infrared spectrum (thin film/NaCl) of isoquinoline triflate **S-4**.

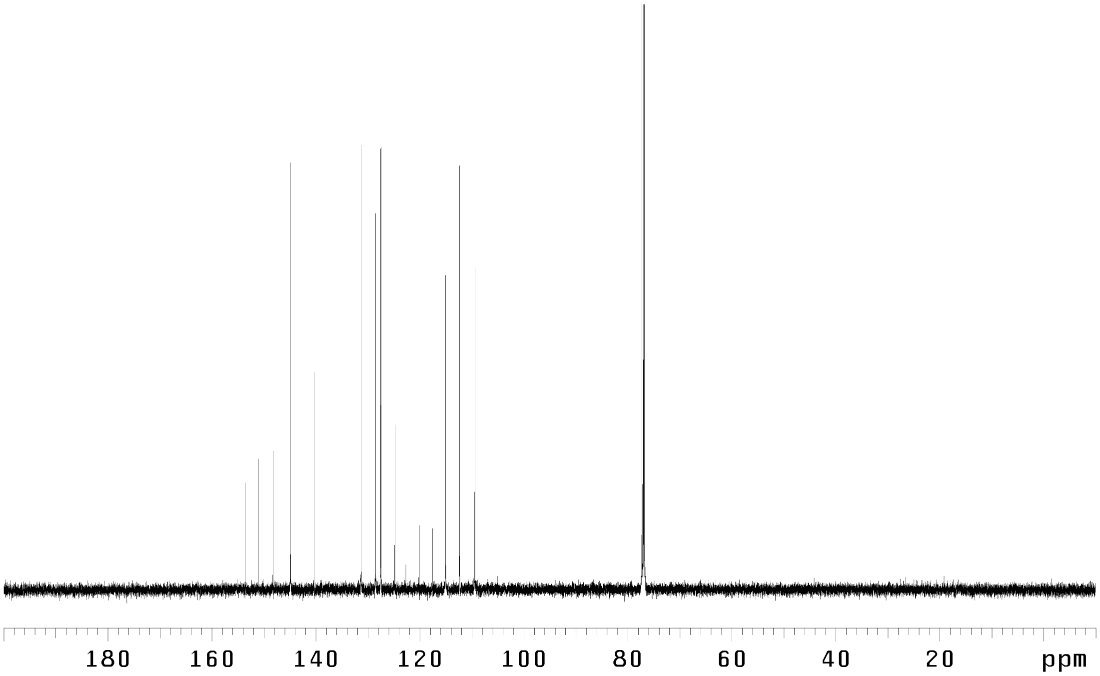

Figure 25.3 ^{13}C NMR (125 MHz, CDCl$_3$) of isoquinoline triflate **S-4**.

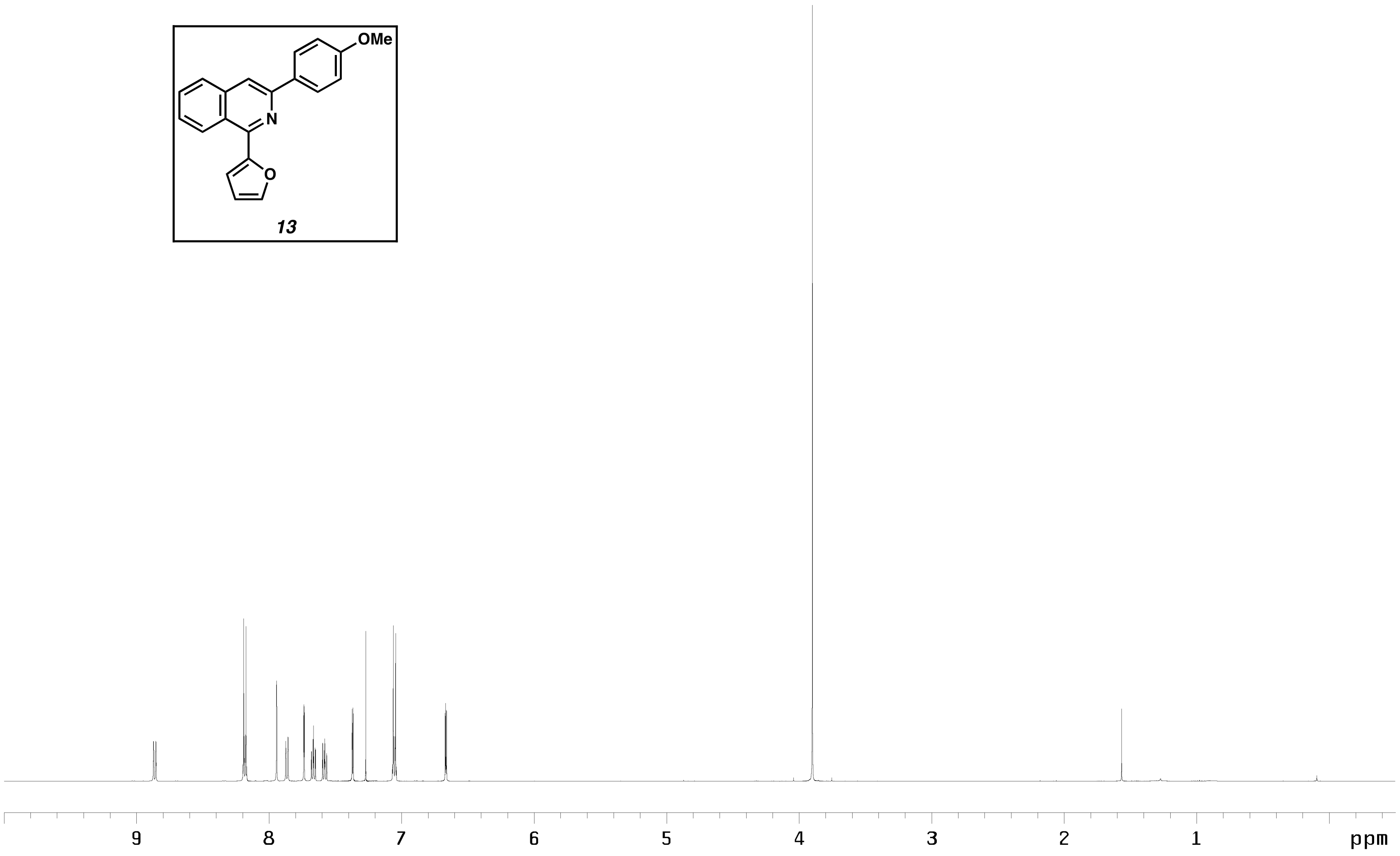

Figure 26.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 1,3-diarylisoquinoline **13**.

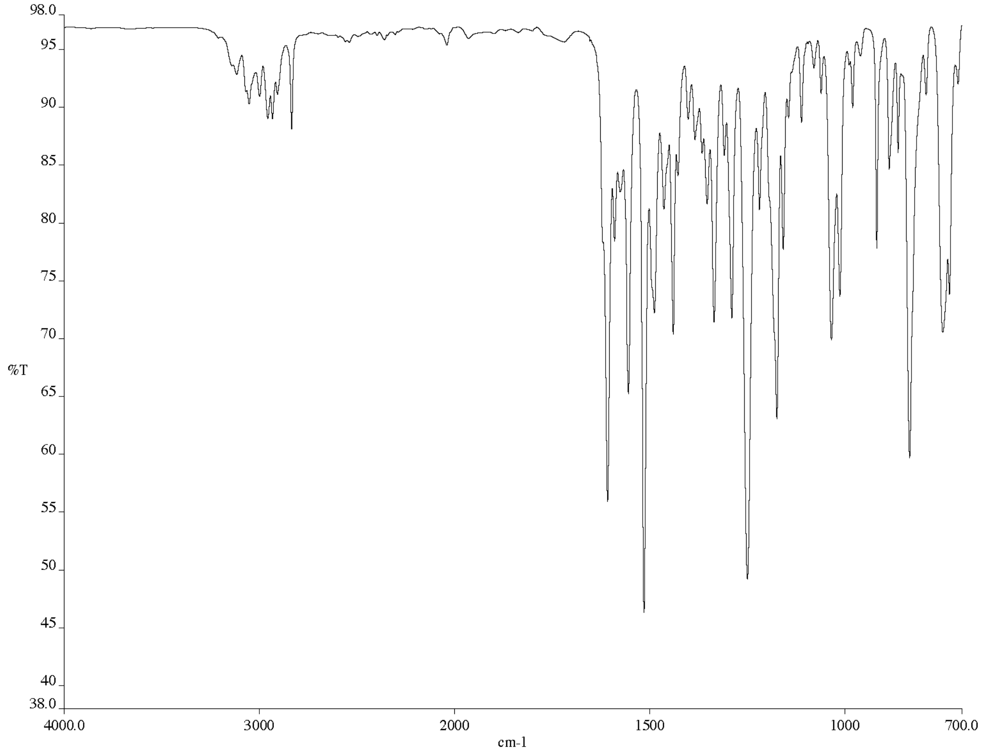

Figure 26.2 Infrared spectrum (thin film/NaCl) of 1,3-diarylisoquinoline **13**.

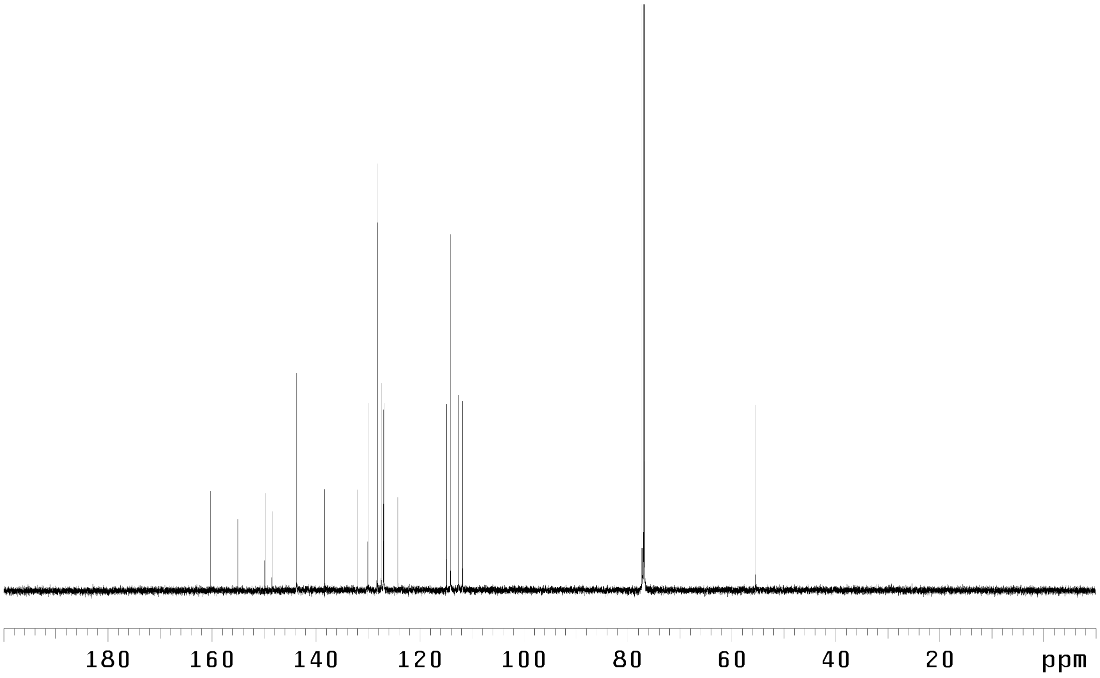

Figure 26.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 1,3-diarylisoquinoline **13**.

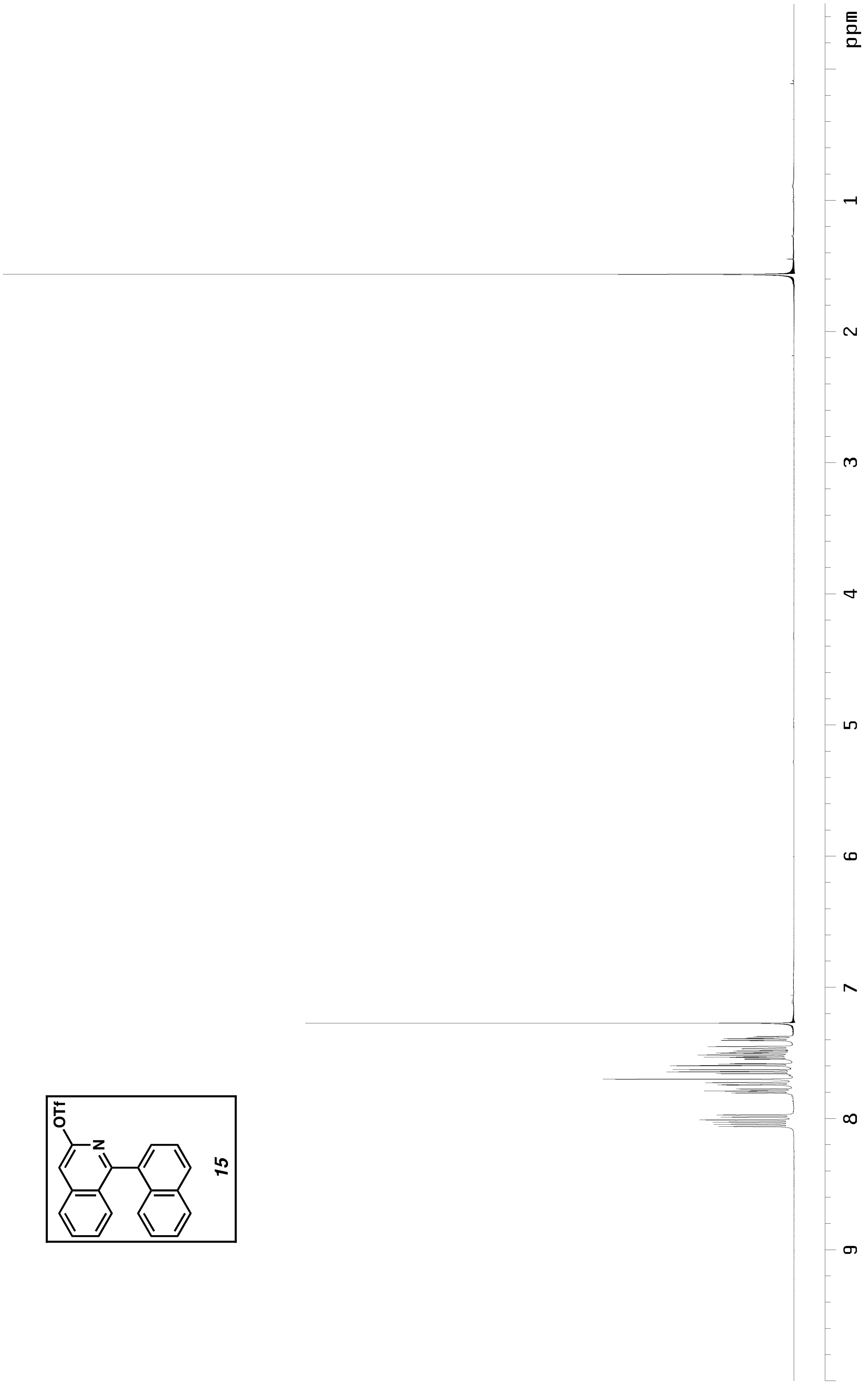

Figure 27.1 ^{1}H NMR (500 MHz, CDCl$_3$) of isoquinoline triflate **15**.

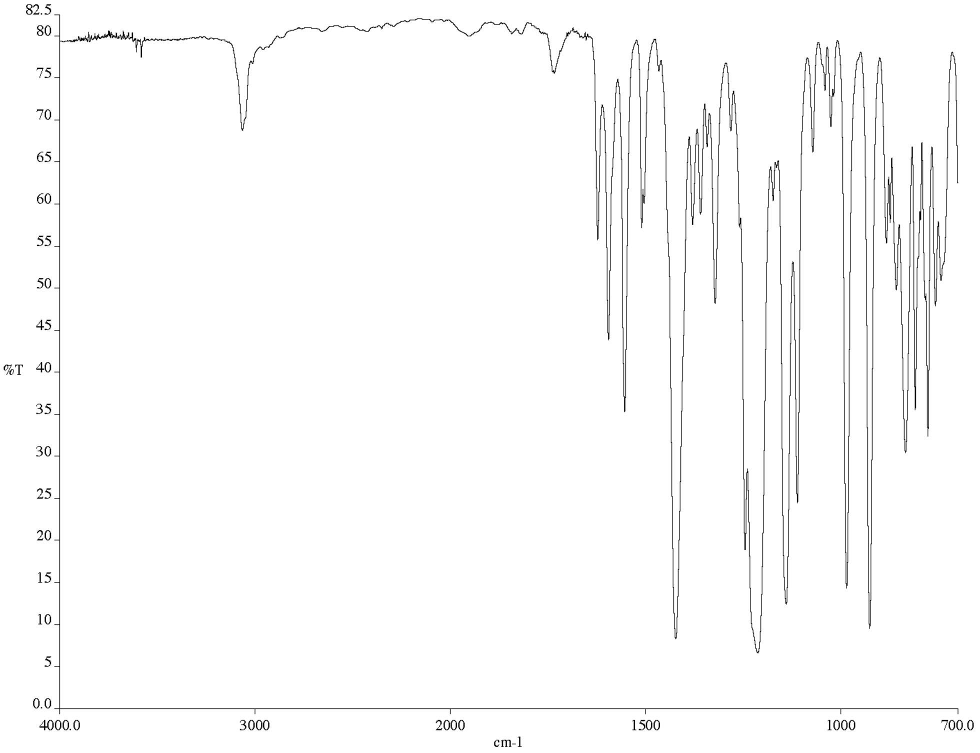

Figure 27.2 Infrared spectrum (thin film/NaCl) of isoquinoline triflate **15**.

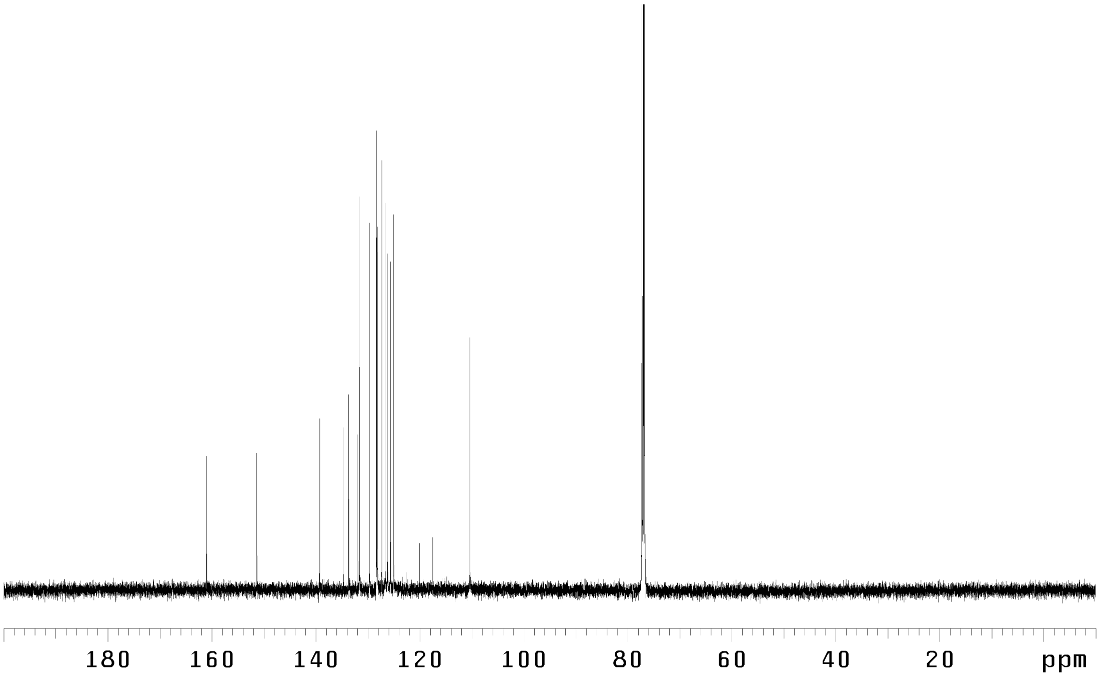

Figure 27.3 ^{13}C NMR (125 MHz, $CDCl_3$) of isoquinoline triflate **15**.

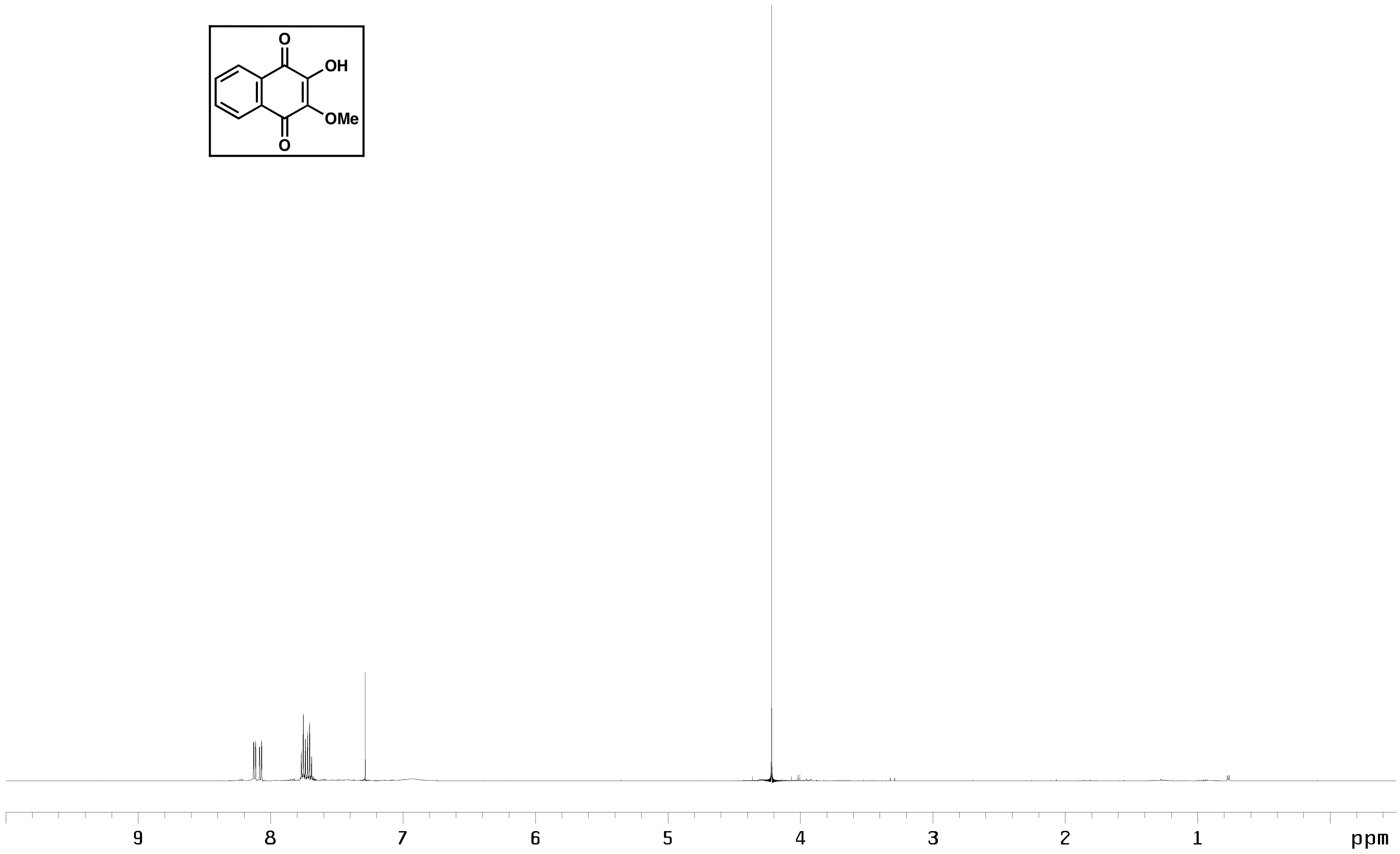

Figure 28.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 1.

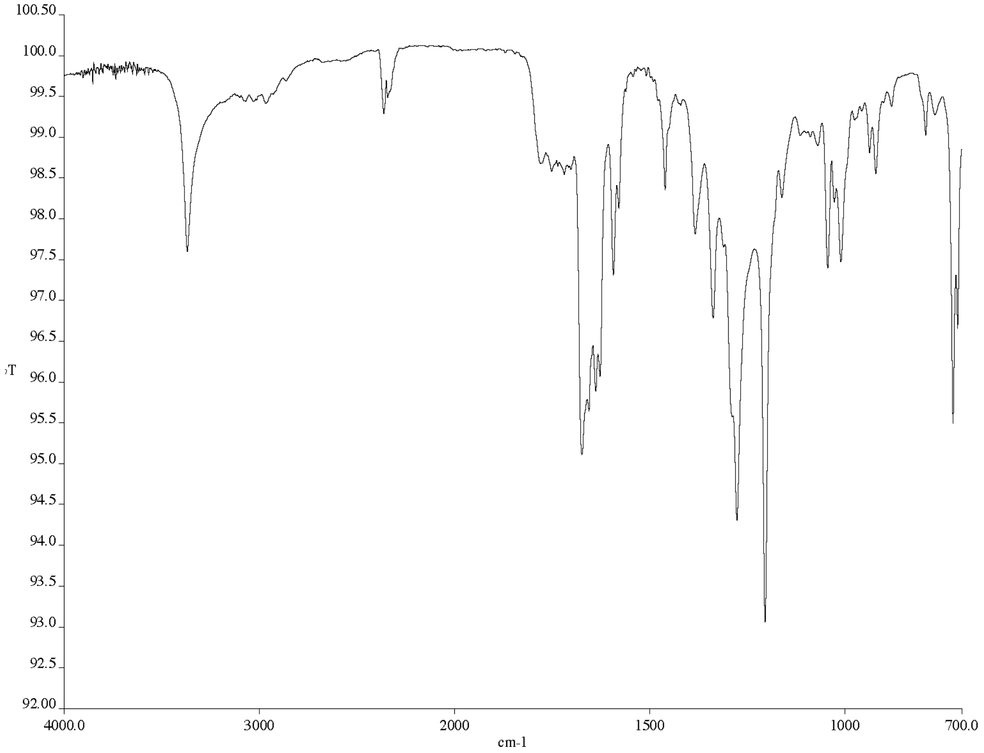

Figure 28.2 Infrared spectrum (thin film/NaCl) 2-hydroxy-1,4-naphthaquinone Table 3, entry 1.

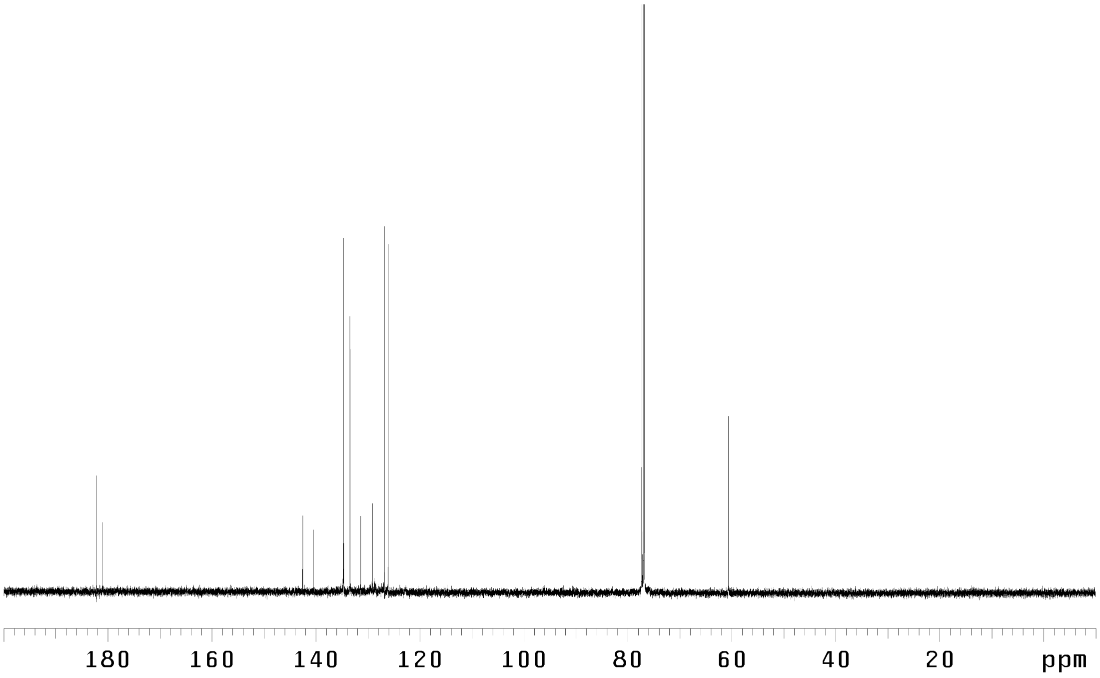

Figure 28.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 1.

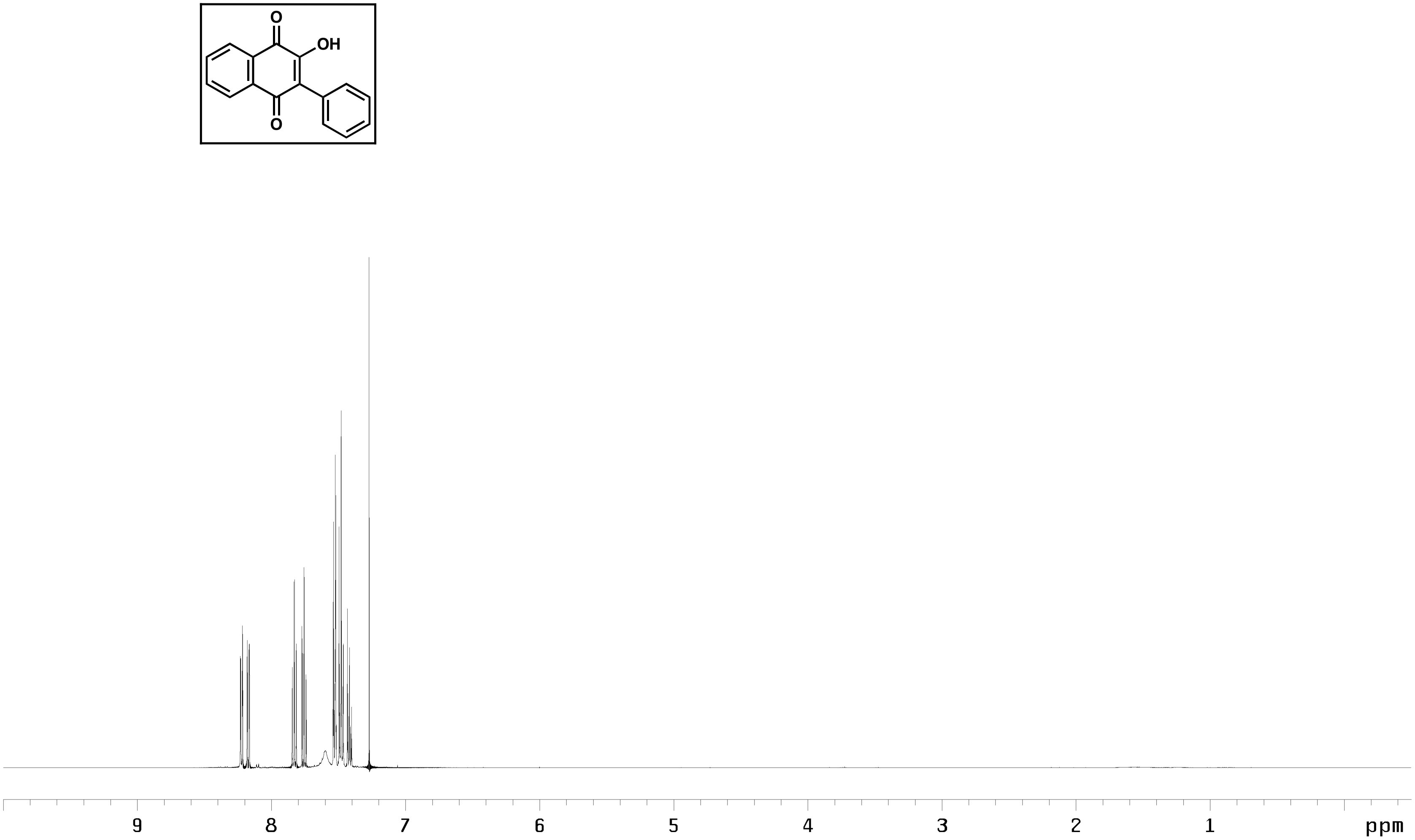

Figure 29.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 2.

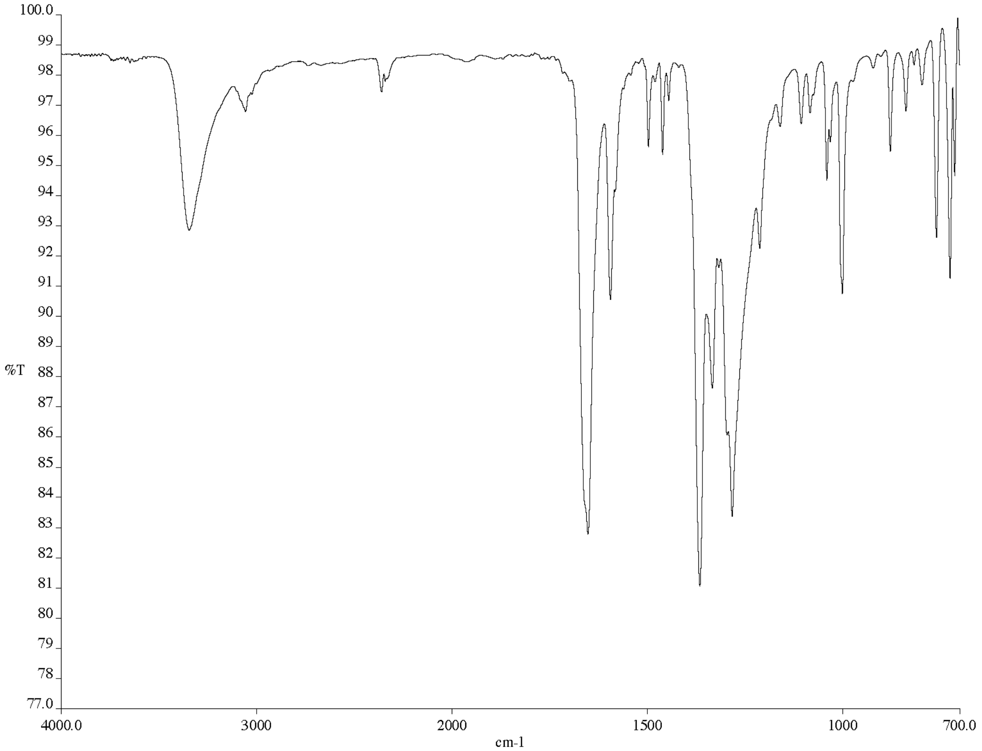

Figure 29.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 2.

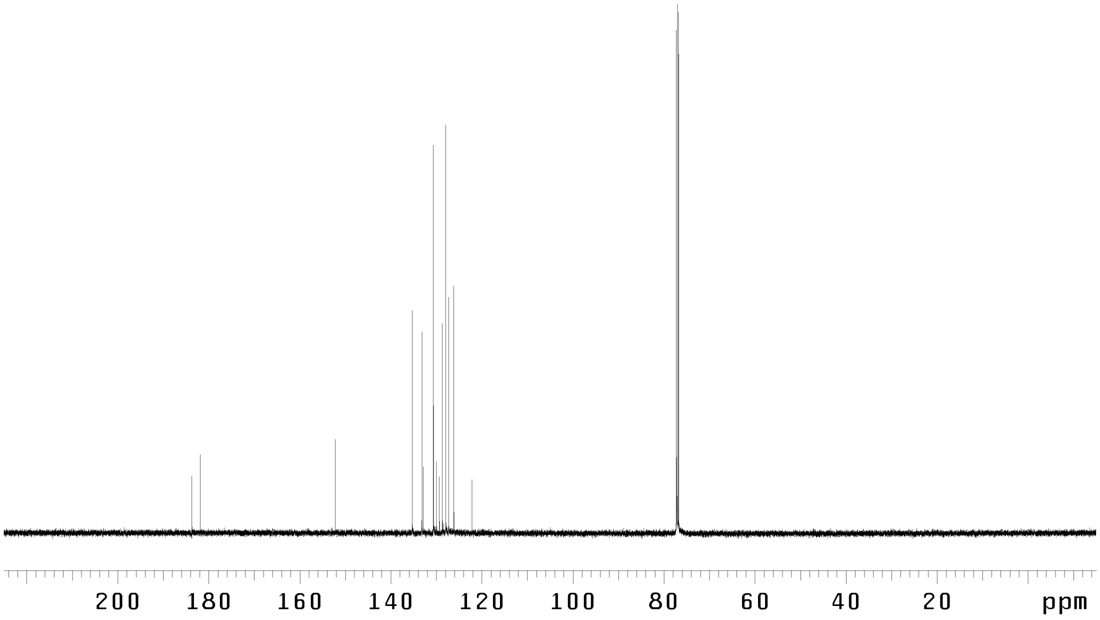

Figure 29.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 2.

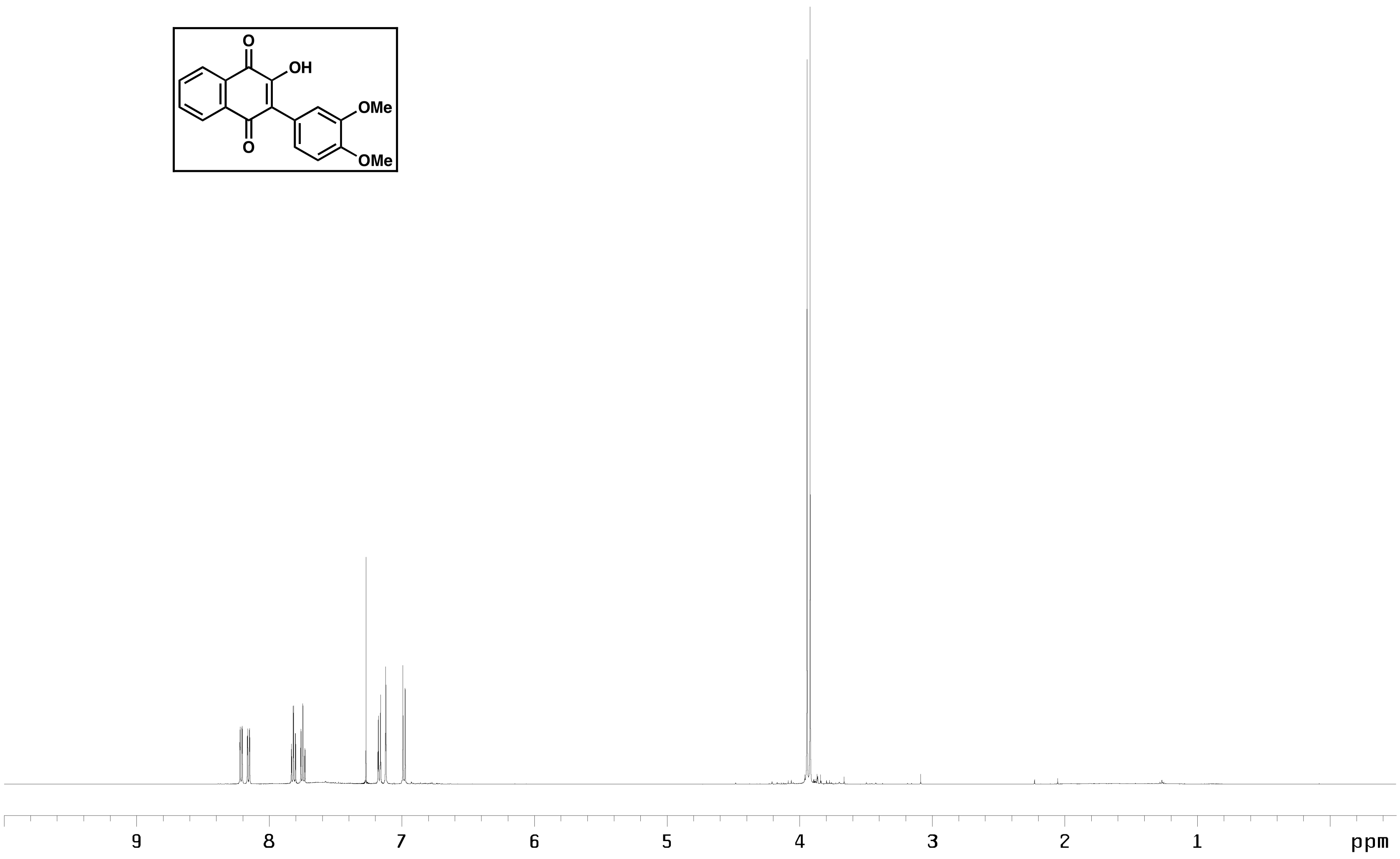

Figure 30.1 ^{1}H NMR (500 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 3.

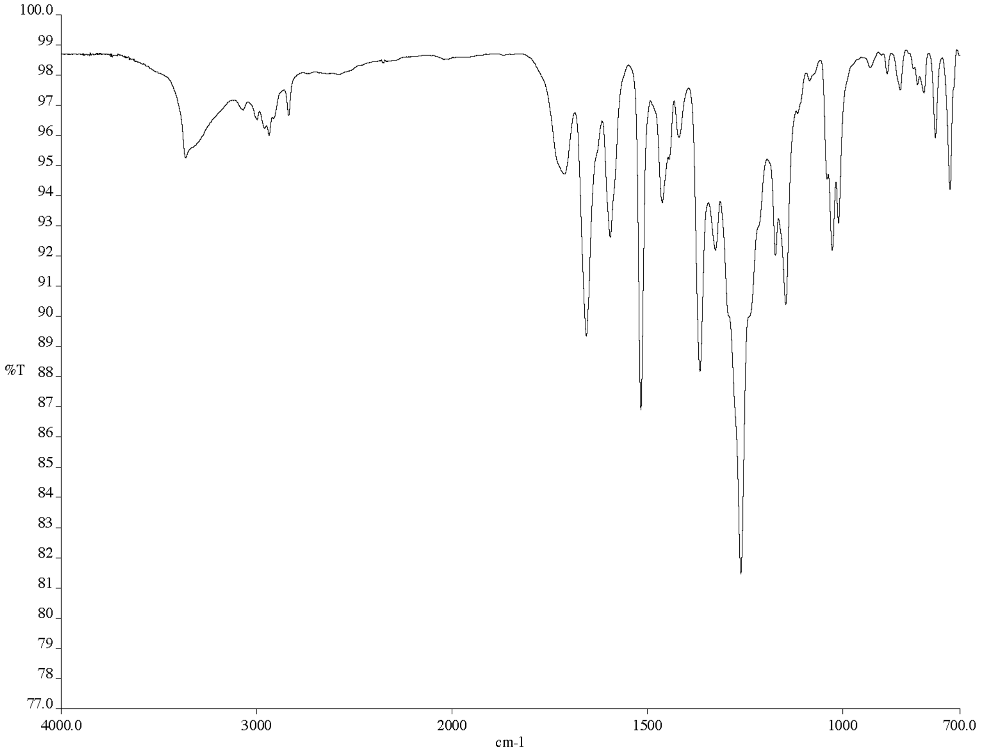

Figure 30.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 3.

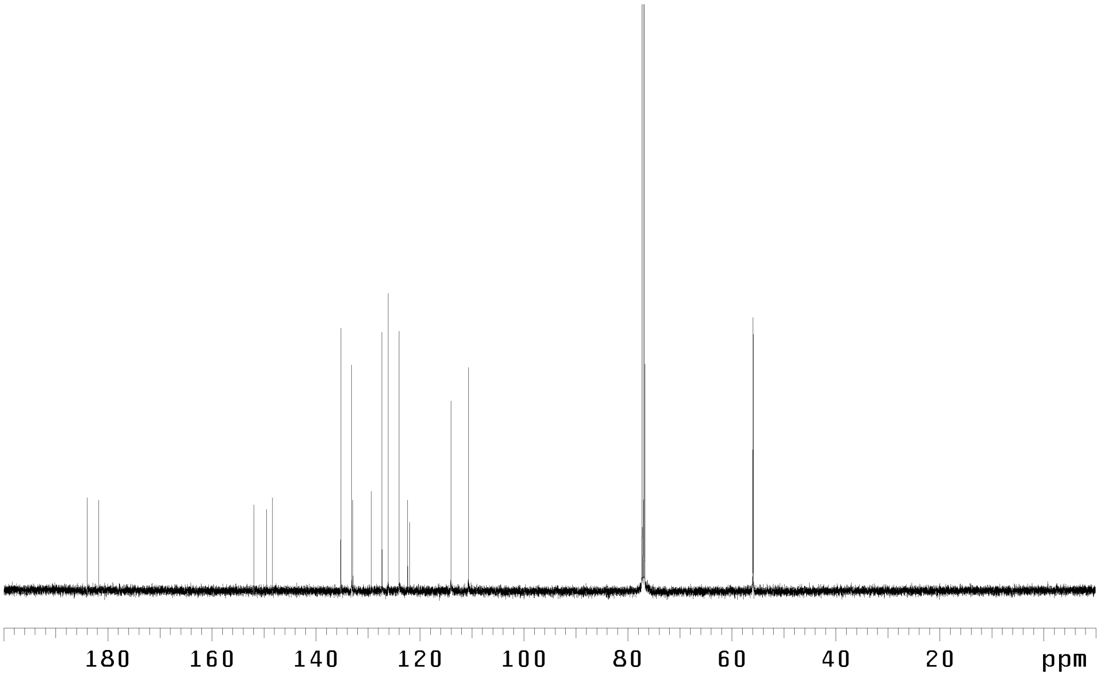

Figure 30.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 3.

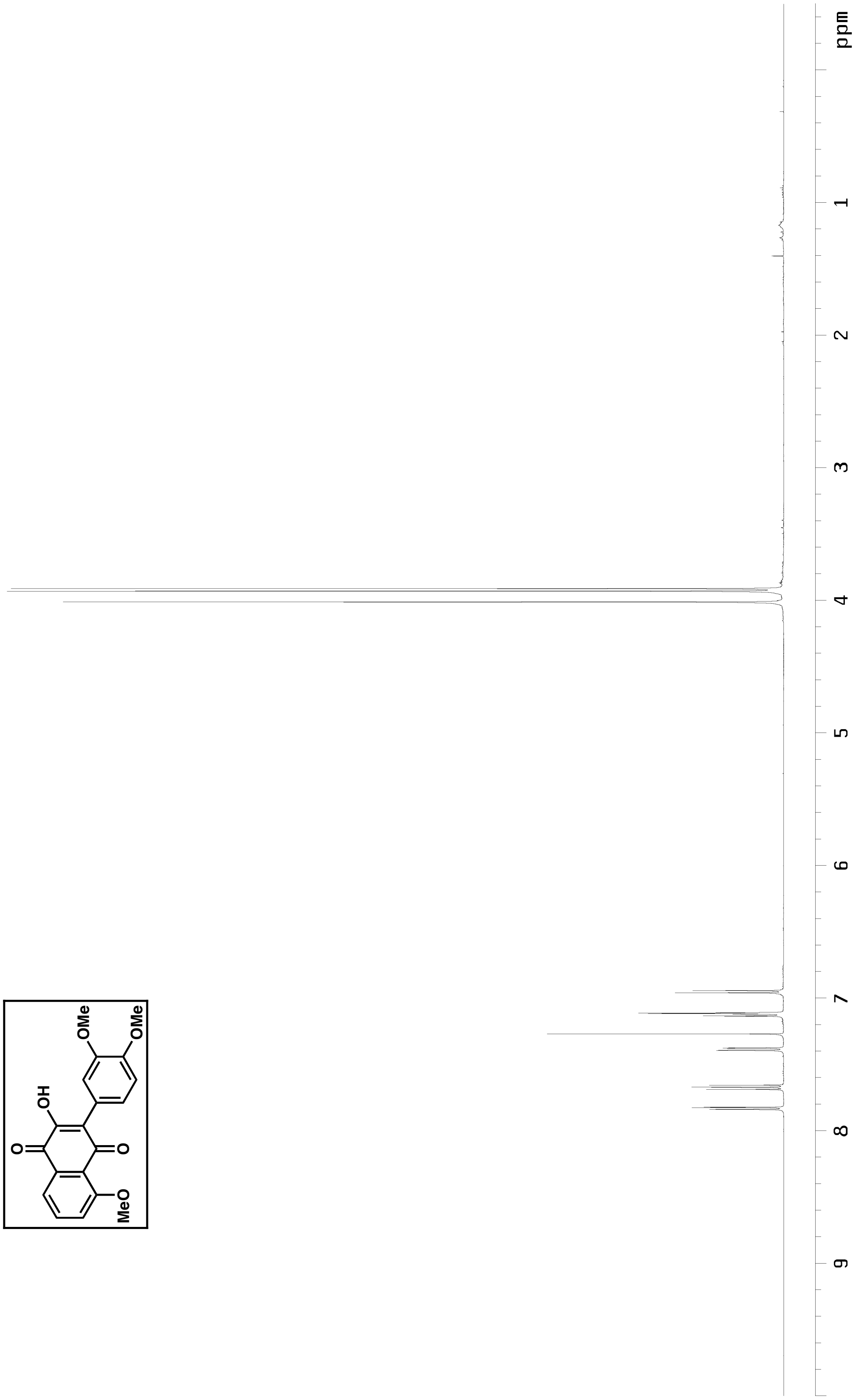

Figure 31.1 ^{1}H NMR (500 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 4.

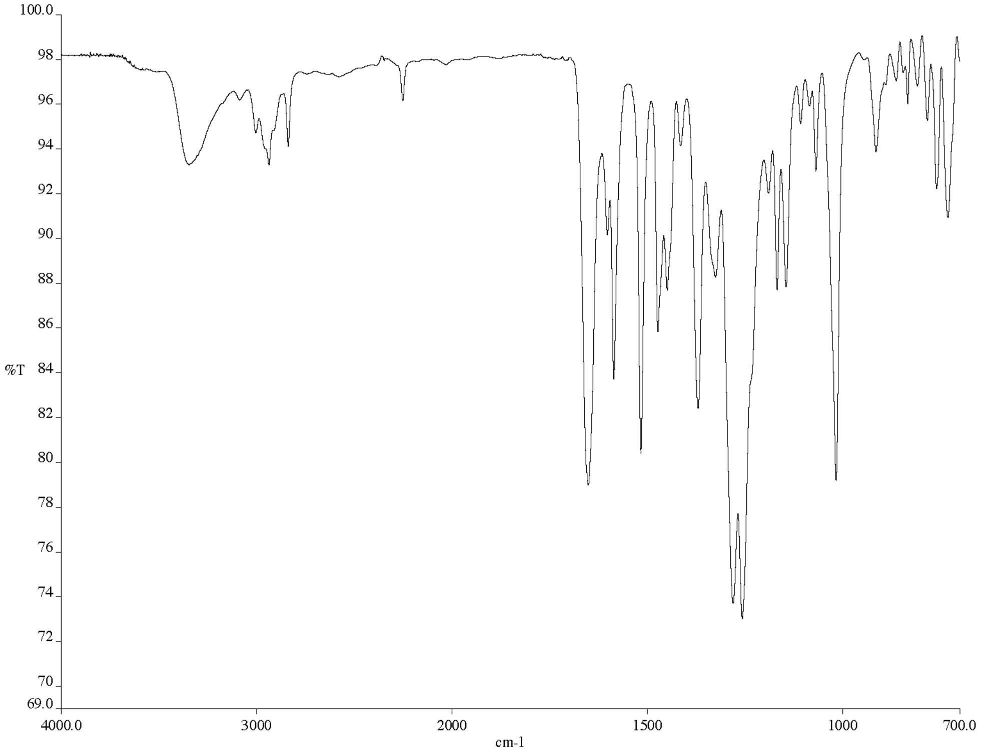

Figure 31.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 4.

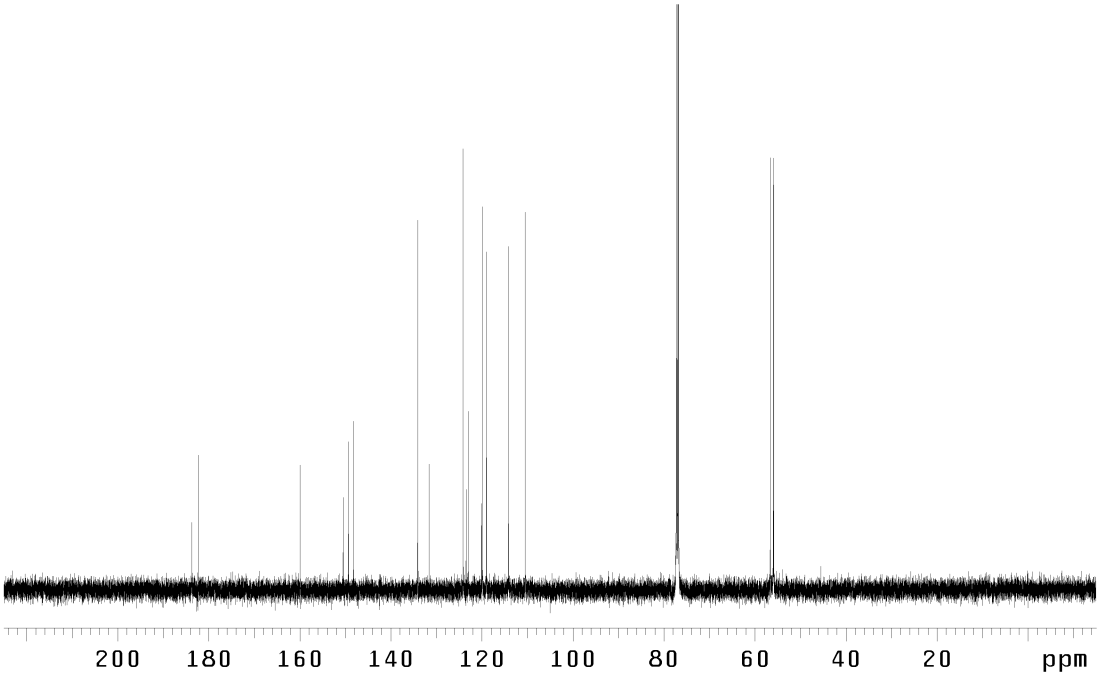

Figure 31.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 4.

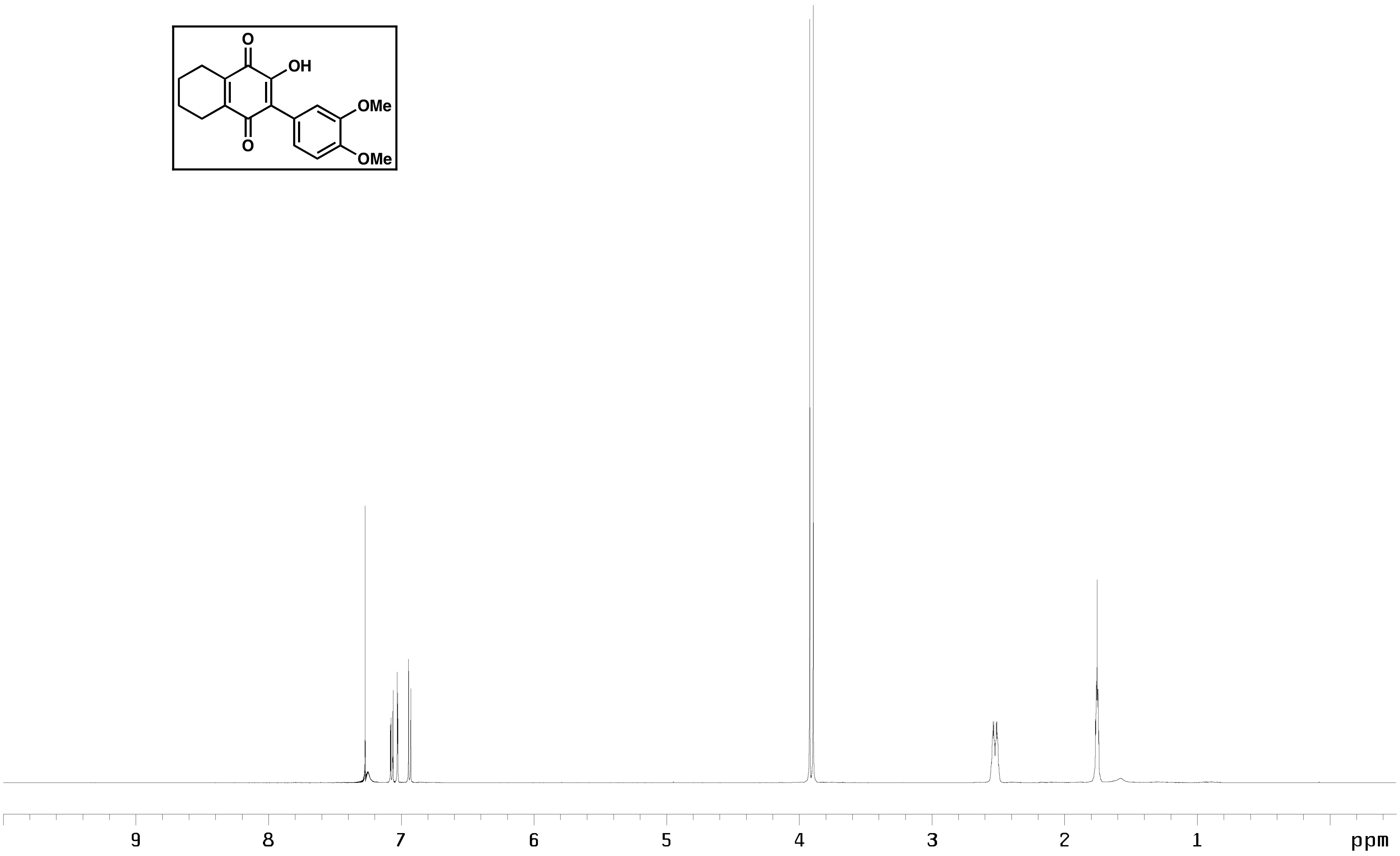

Figure 32.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-5,6,7,8-tetrahydronaphtha-1,4-quinone Table 3, entry 5.

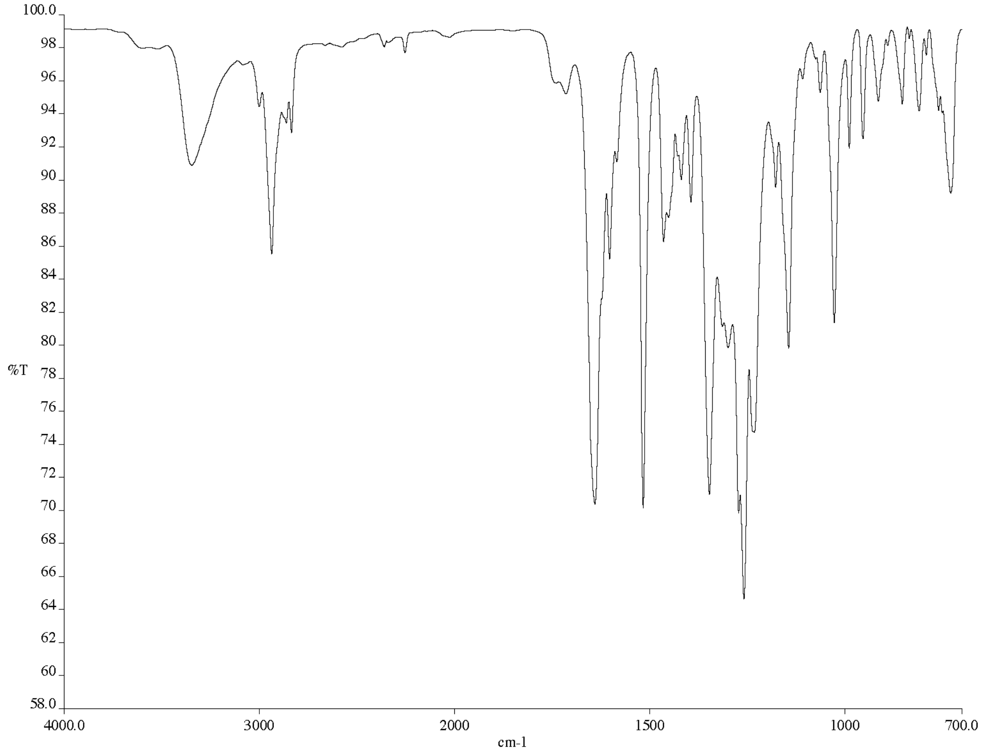

Figure 32.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-5,6,7,8-tetrahydronaphtha-1,4-quinone Table 3, entry 5.

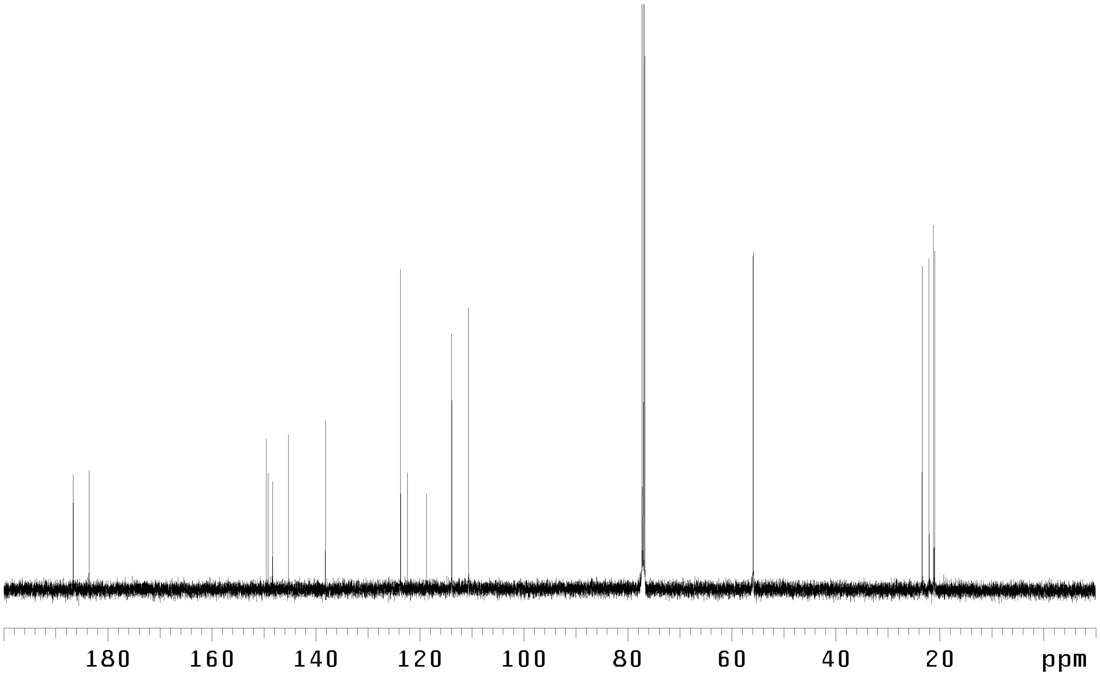

Figure 32.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-5,6,7,8-tetrahydronaphtha-1,4-quinone Table 3, entry 5.

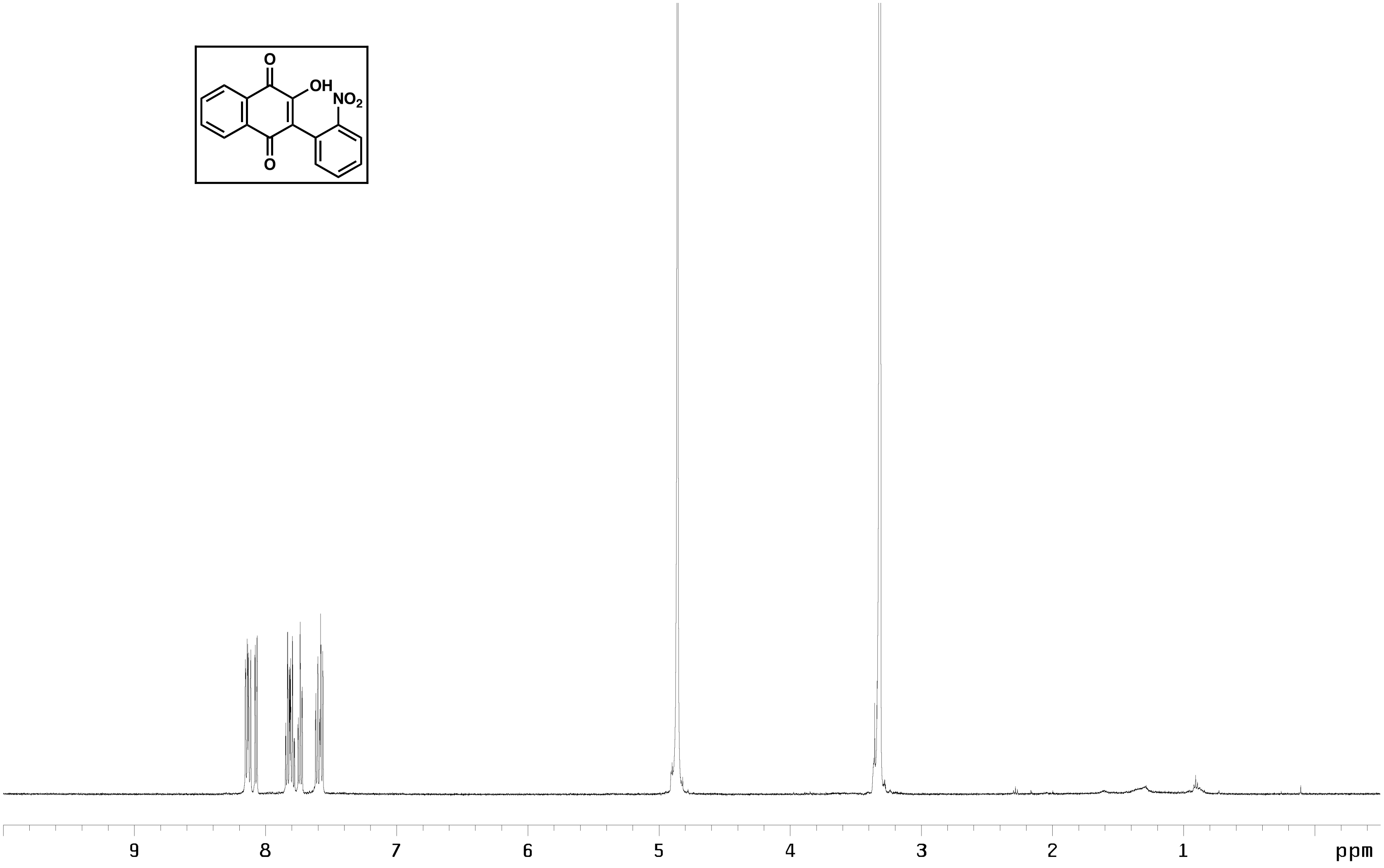

Figure 33.1 ^{1}H NMR (500 MHz, CD_3OD) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 6.

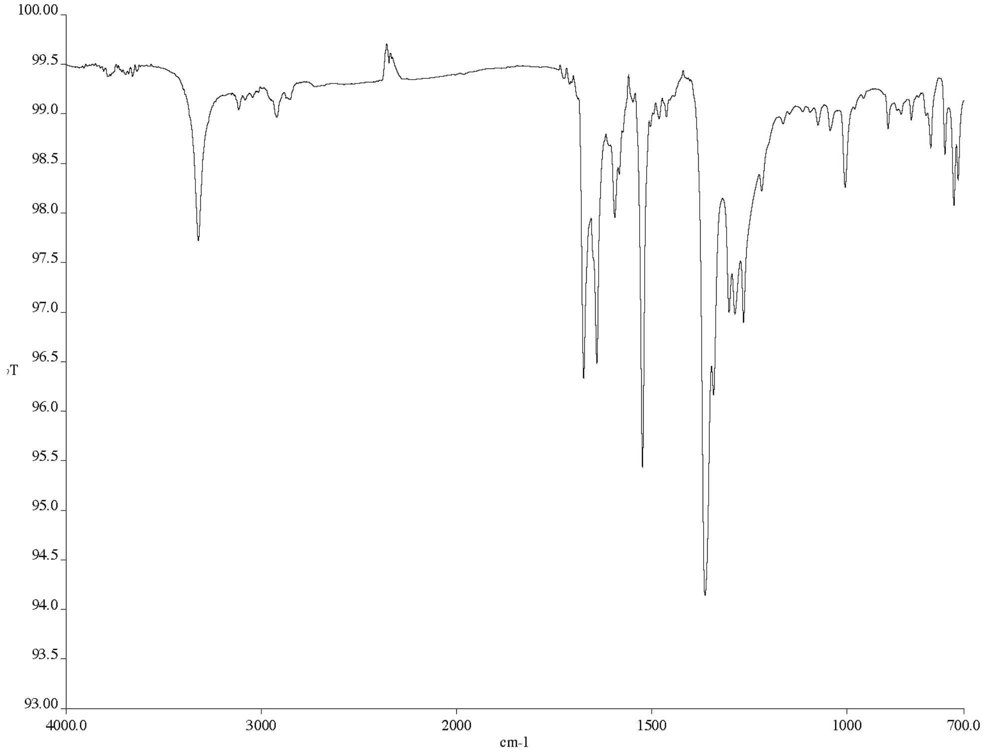

Figure 33.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 6.

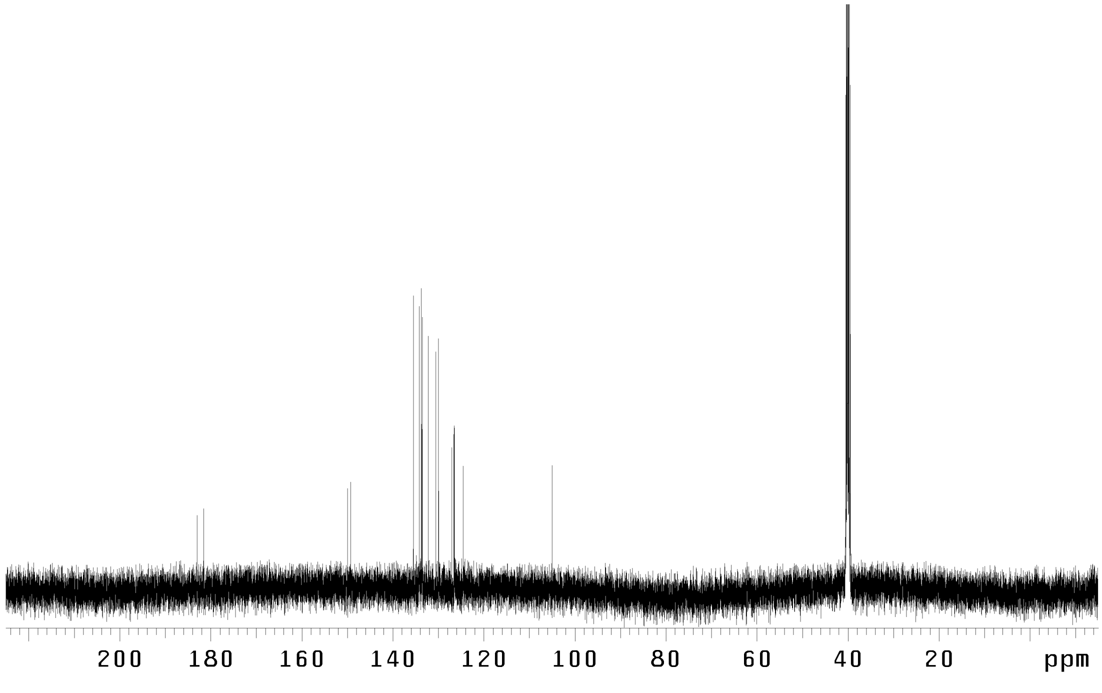

Figure 33.3 ^{13}C NMR (125 MHz, DMSO-d_6) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 6.

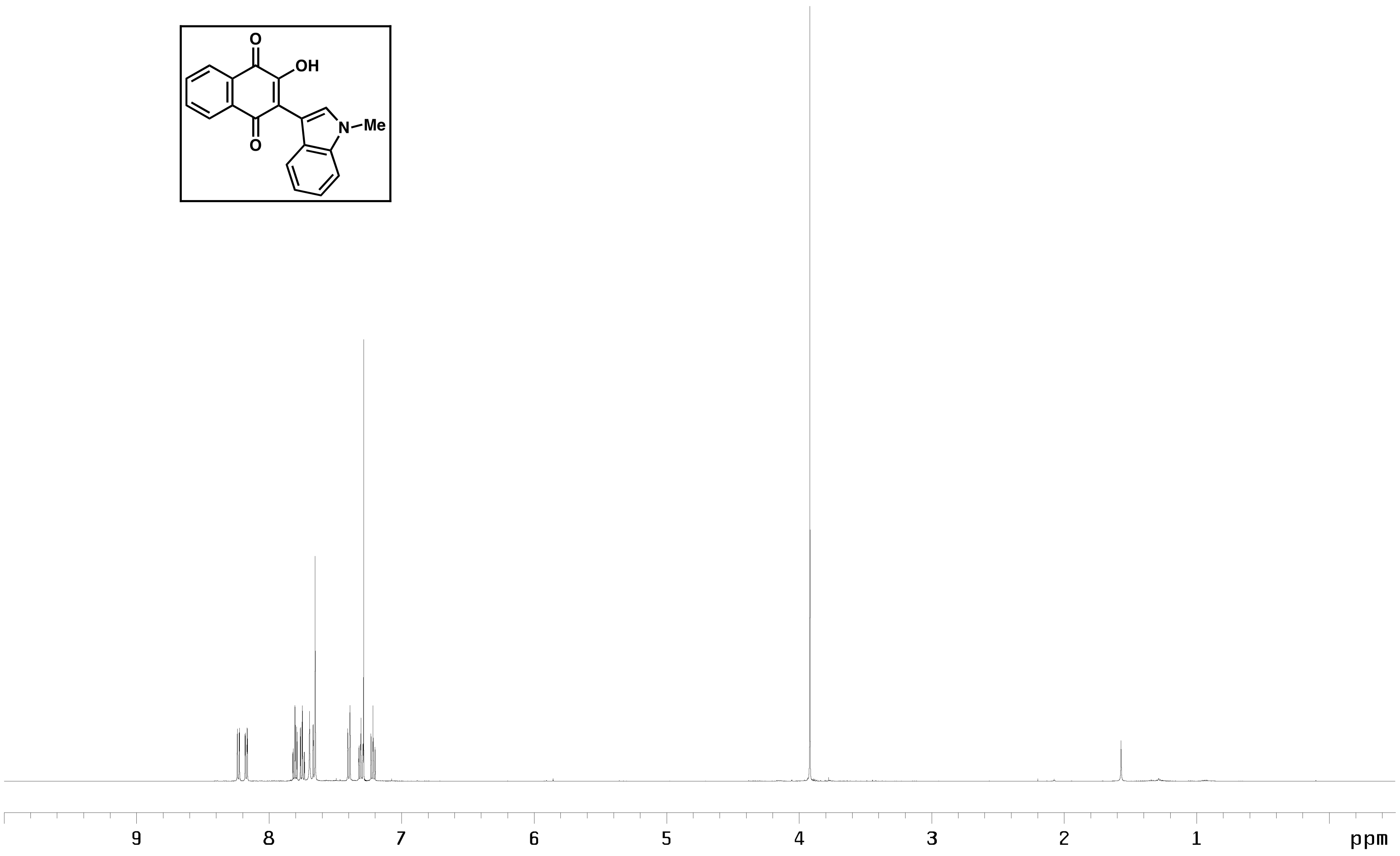

Figure 34.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 7.

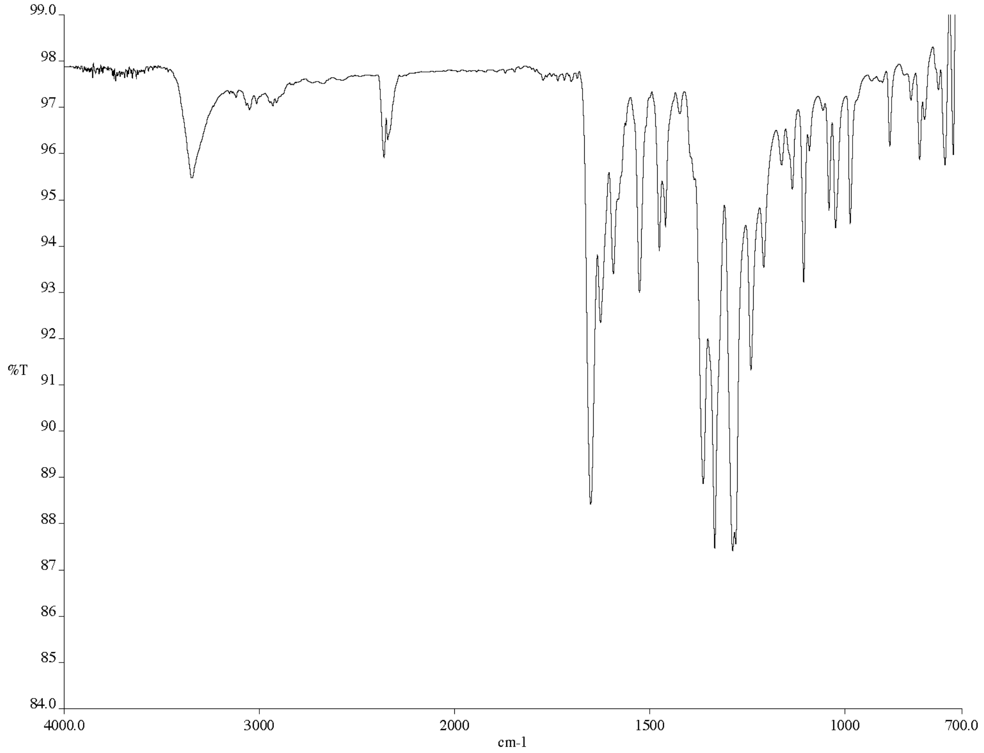

Figure 34.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 7.

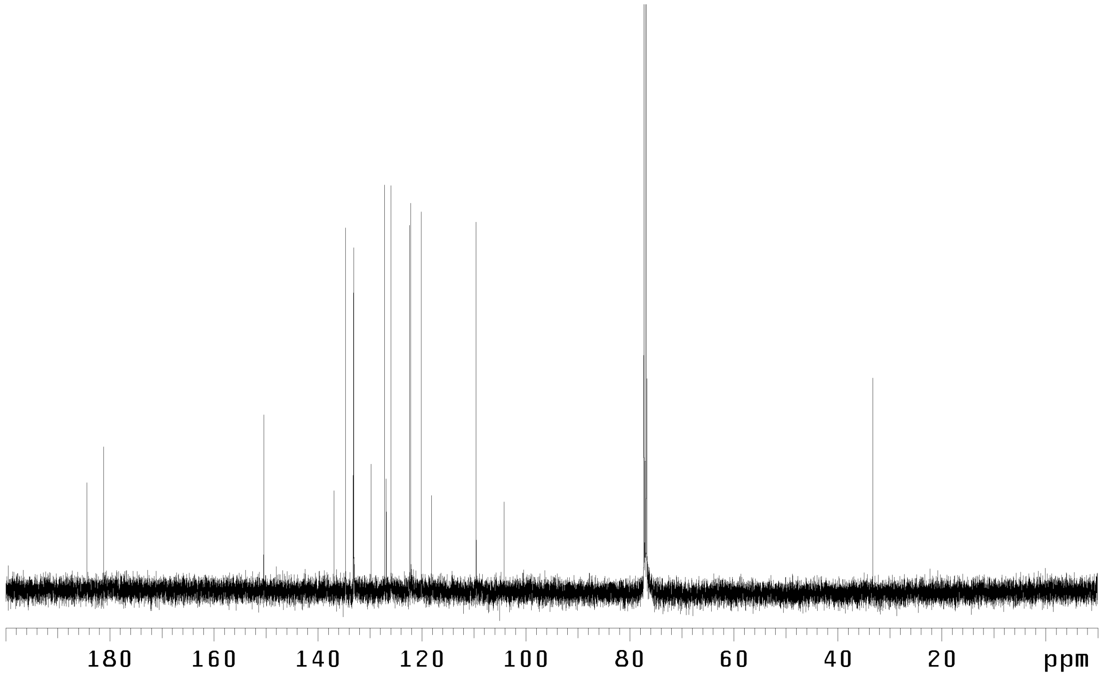

Figure 35.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 7.

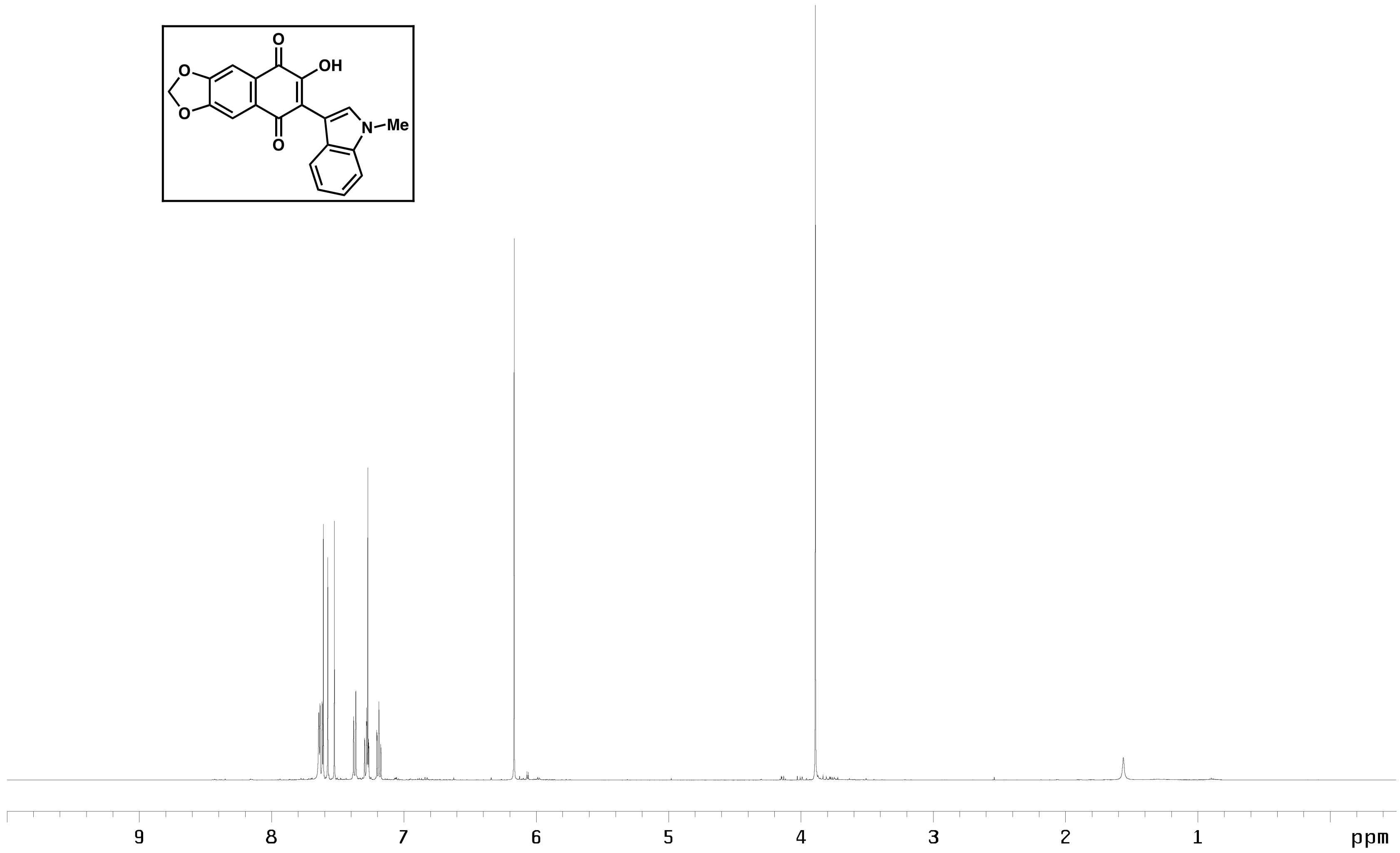

Figure 35.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 8.

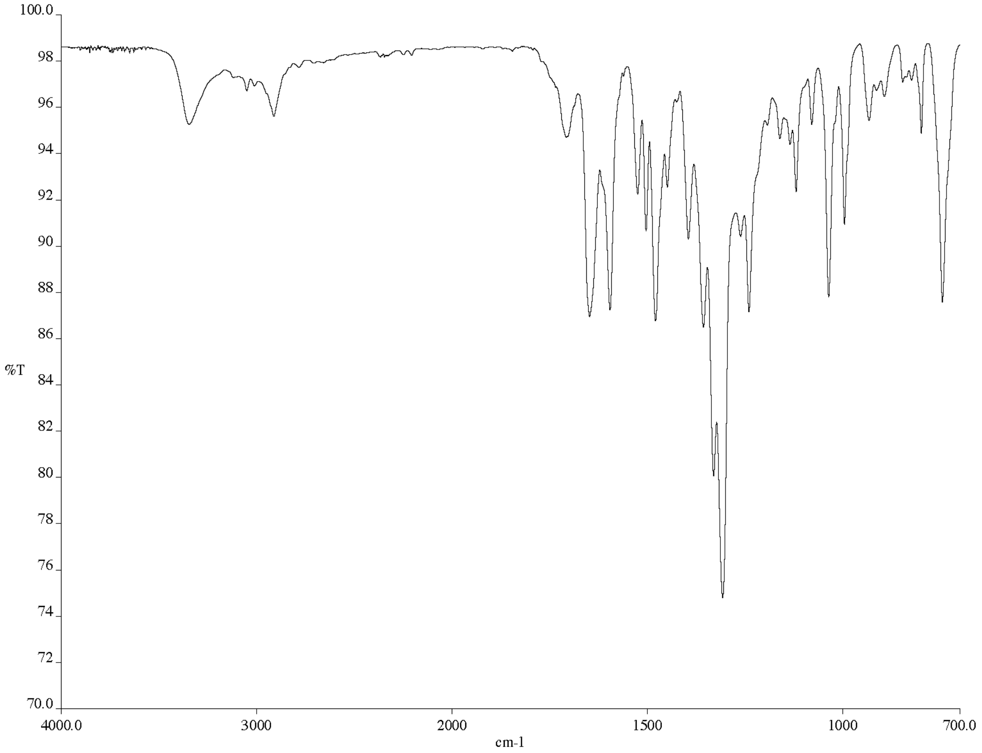

Figure 35.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 8.

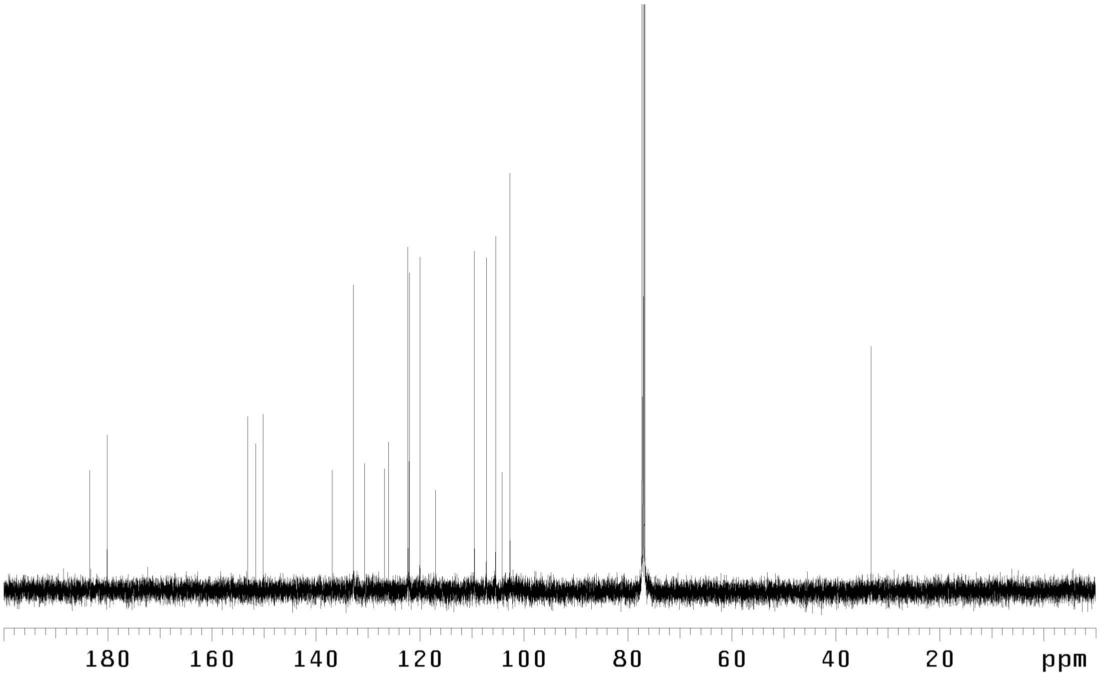

Figure 35.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 8.

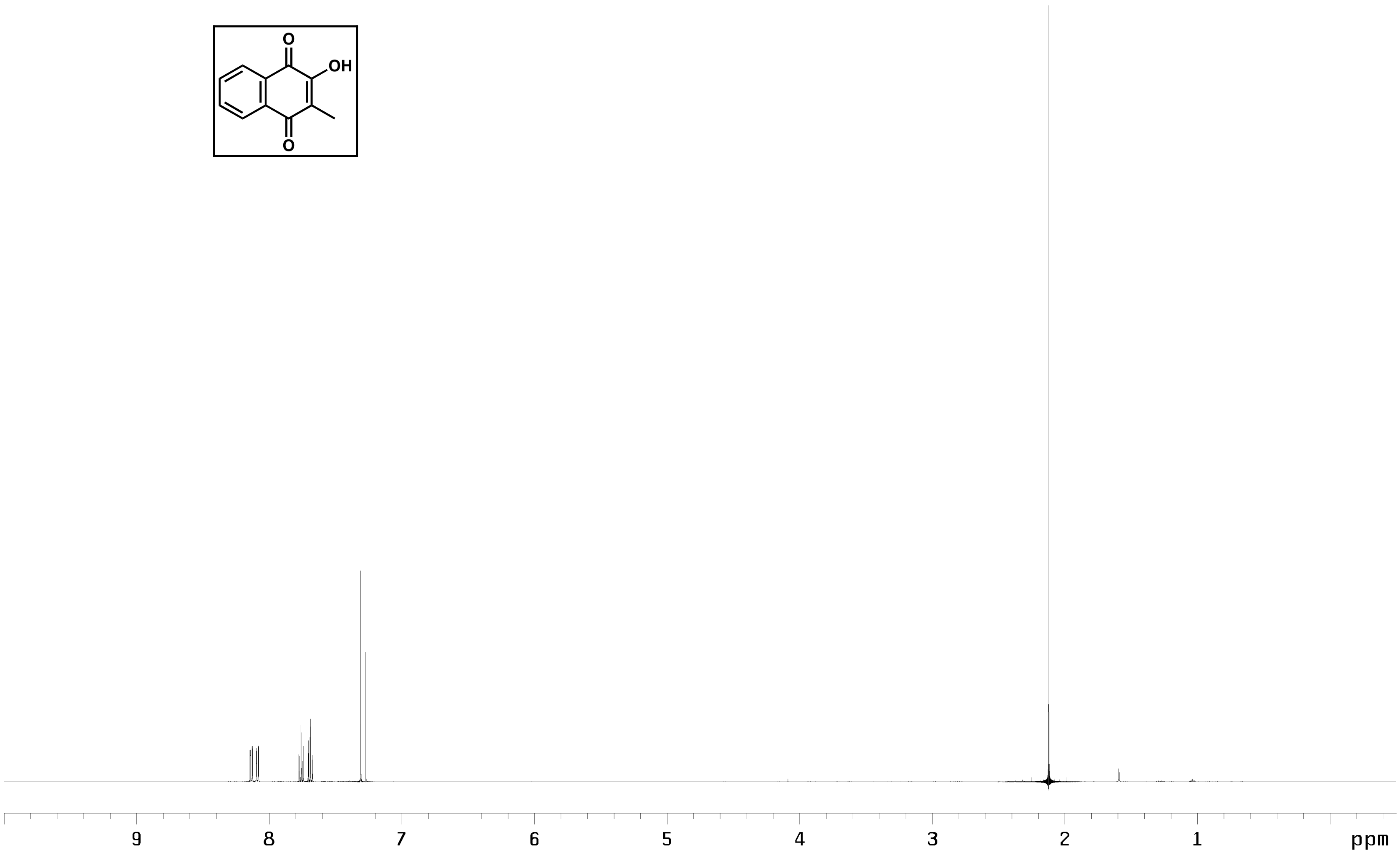

Figure 36.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 9.

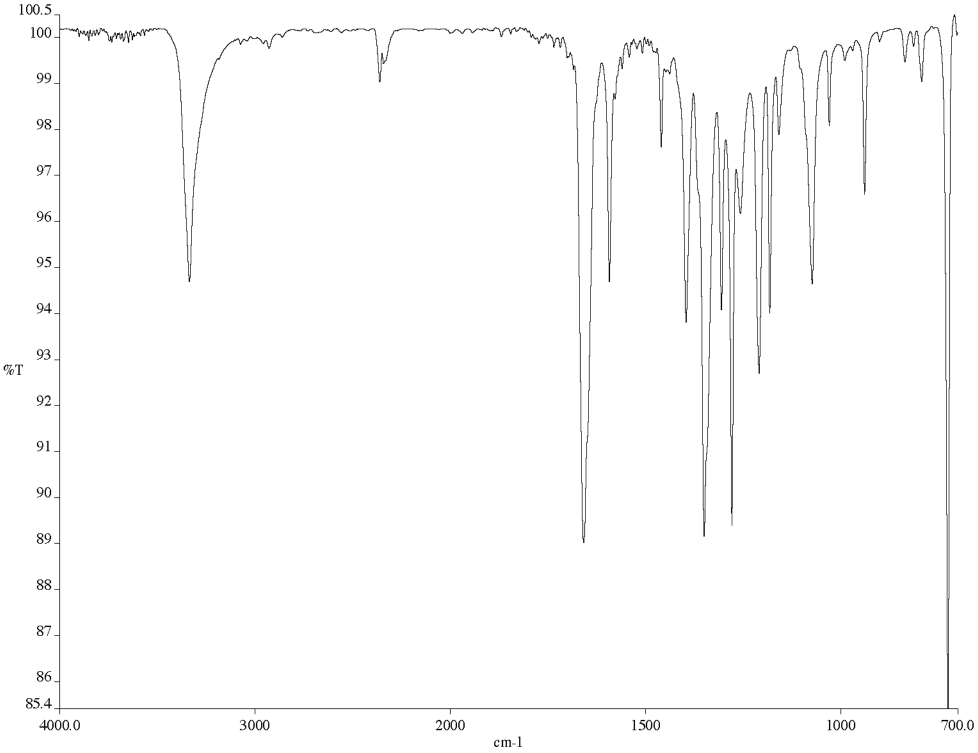

Figure 36.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 9.

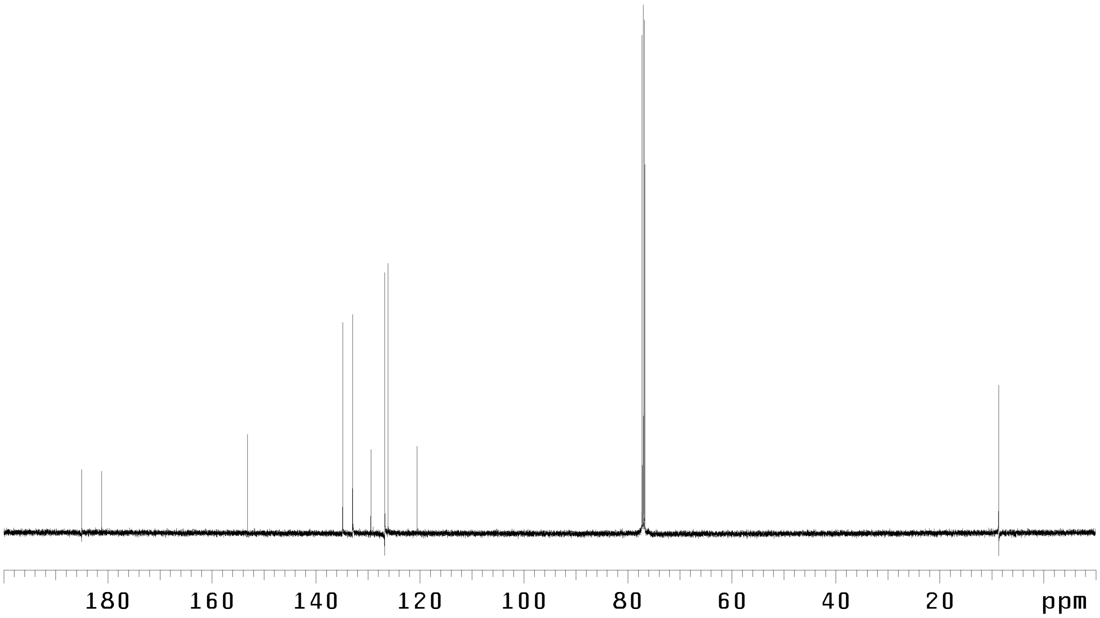

Figure 36.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 9.

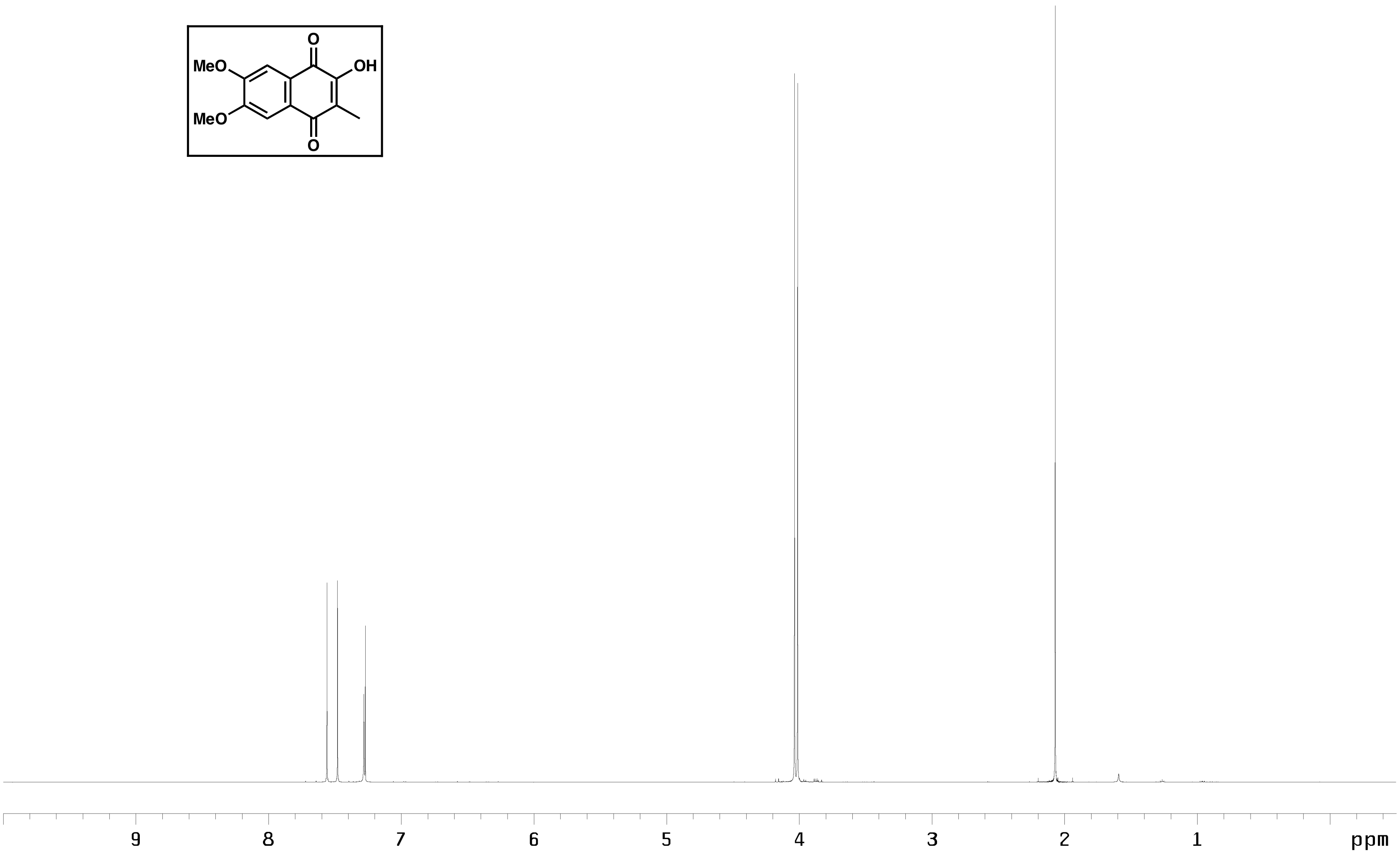

Figure 37.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 10.

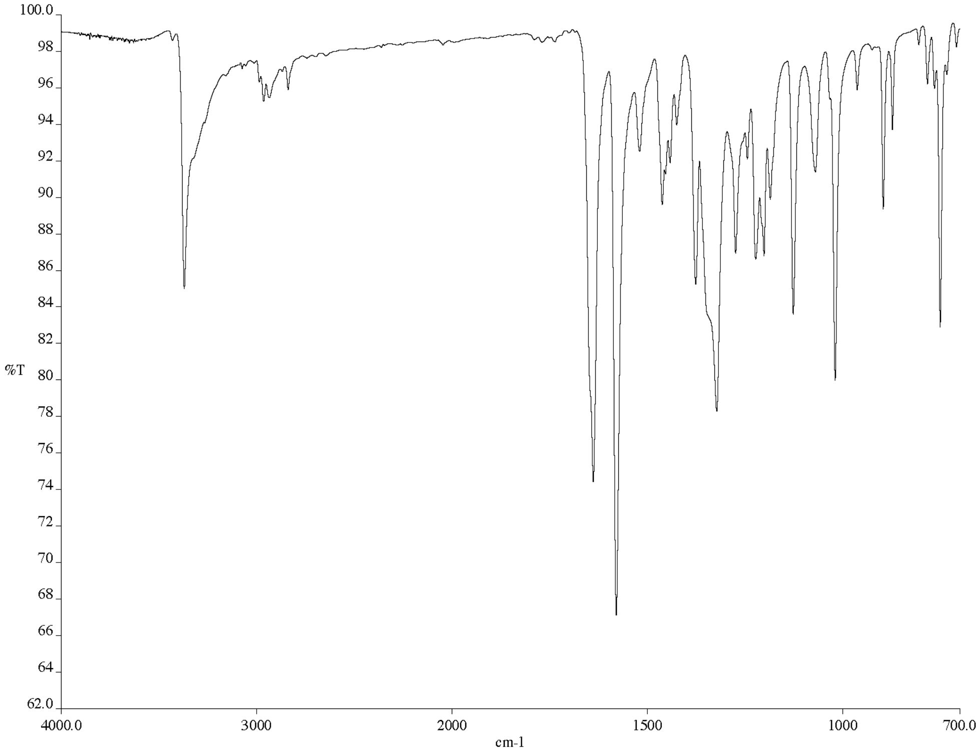

Figure 37.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 10.

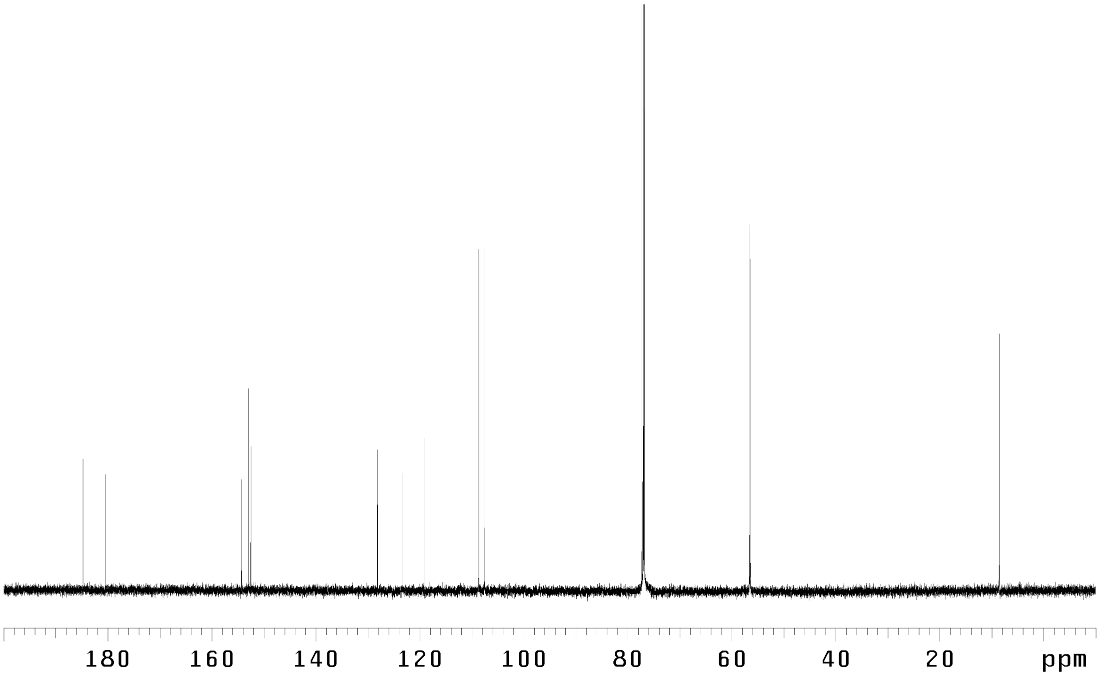

Figure 37.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 10.

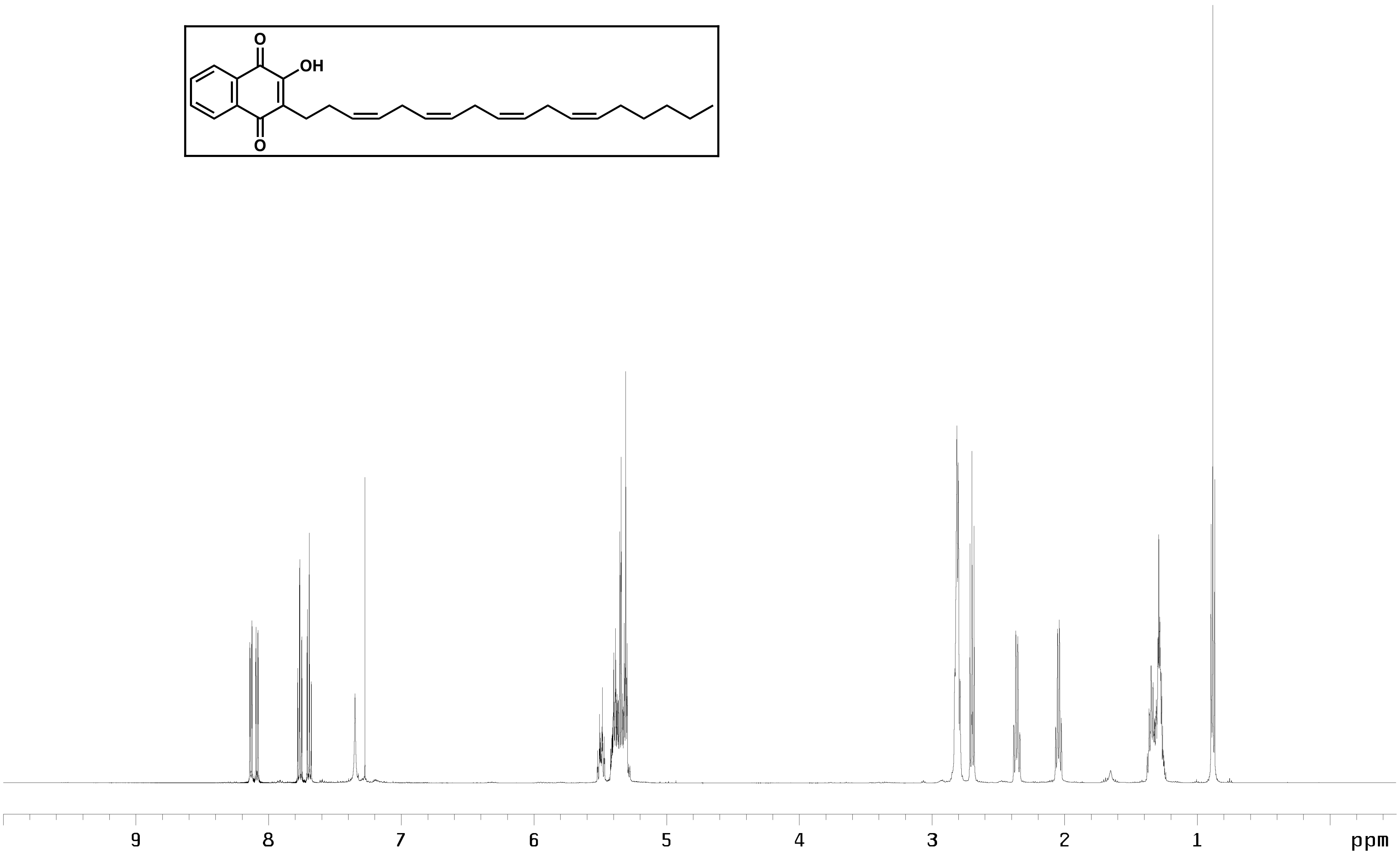

Figure 38.1 ^{1}H NMR (500 MHz, $CDCl_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 11.

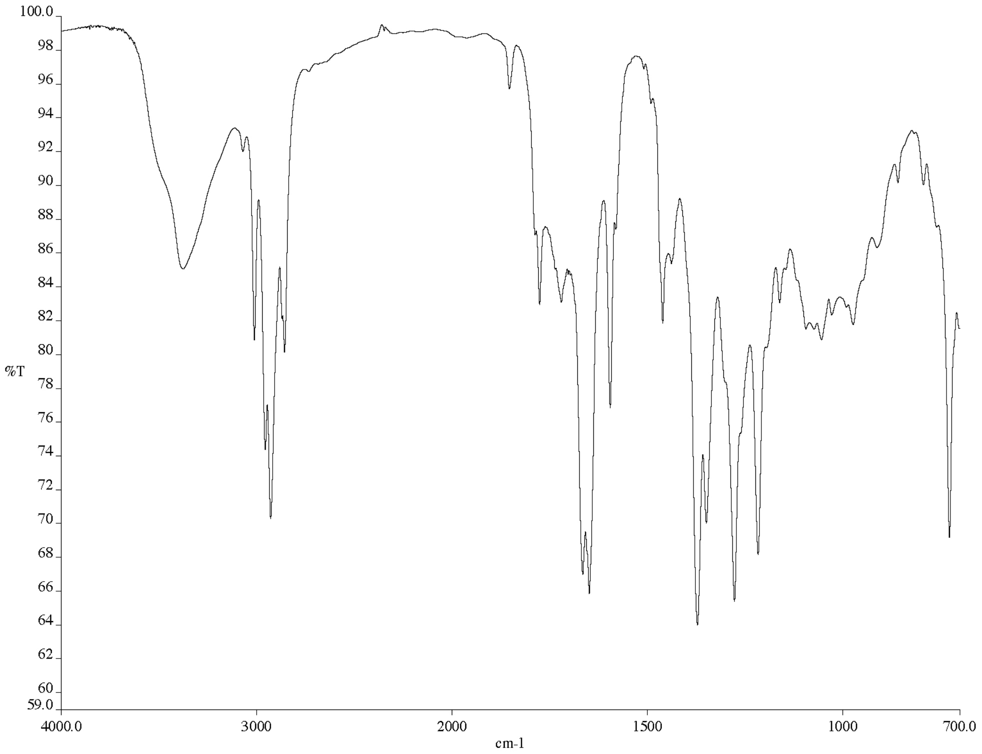

Figure 38.2 Infrared spectrum (thin film/NaCl) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 11.

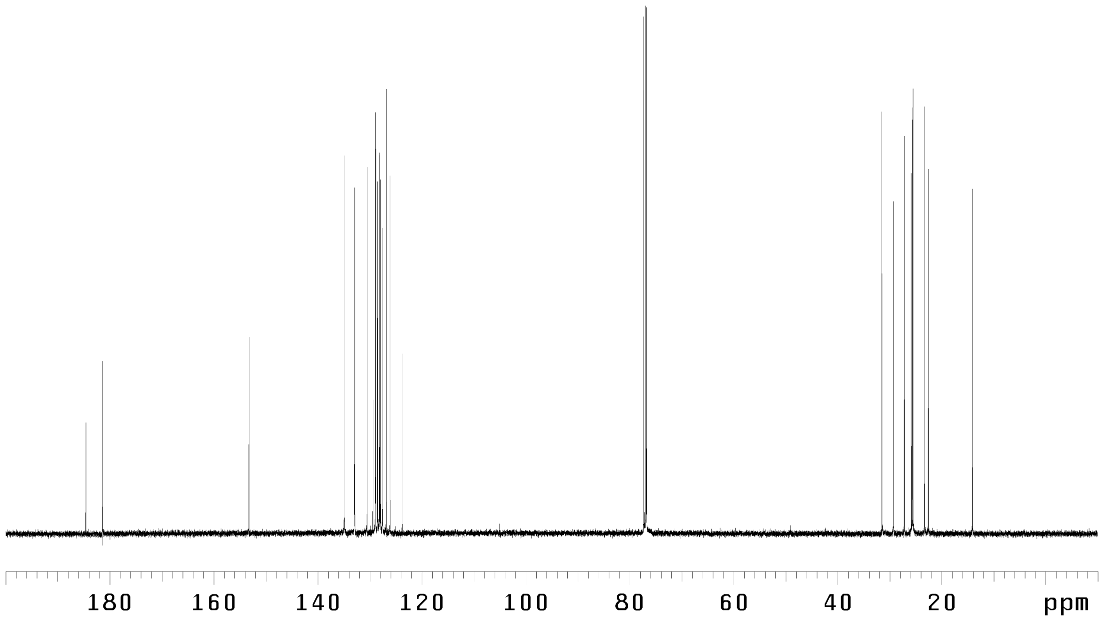

Figure 38.3 ^{13}C NMR (125 MHz, CDCl$_3$) of 2-hydroxy-1,4-naphthaquinone Table 3, entry 11.