A Catalytic, Enantioselective Formal Synthesis of (+)-Dichroanone and (+)-Taiwaniaquinone H

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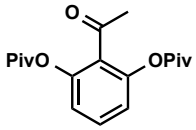
Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Triethylamine was distilled over CaH_2 prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Commercially obtained reagents were used as received. Previously reported methods were used to prepare (*S*)-*t*-BuPyOx;[1] all other chemicals were purchased from Sigma Aldrich/Strem/Alfa Aesar and used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Microwave-assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor. Glove box manipulaitons were performed under a nitrogen atmosphere. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching or *p*-anisaldehyde staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040–0.063 mm) was used for flash chromatography. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer or a Bruker Avance HD 400 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm) or $(CH_3)_2SO$ (δ 2.50 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and are reported relative to residual $CDCl_3$ (δ 77.16 ppm), $(CD_3)_2SO$ (δ 39.52 ppm) or $(CD_3)_2CO$ (δ 29.84 ppm). Data for ^{1}H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, app = apparent. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a Perkin

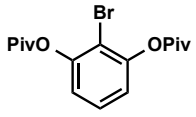
Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from an Agilent 6200 Series TOF with Agilent G1978A Multimode source in mixed ionization mode (MultiMode ESI/APCI) or from a JEOL JMS-600H in fast atom bombardment (FAB+).

Experimental Procedures and Tabulated Spectroscopic Data

General Procedure for the Synthesis of Resorcinol Pivaloyl Esters

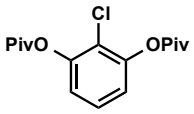


2-acetyl-1,3-phenylene bis(2,2-dimethylpropanoate) (17). An oven-dried 1 L round-bottom flask was charged with a magnetic stir bar, 2,6-dihydroxyacetophenone (10 g, 65.7 mmol, 1 equiv) and DMAP (800 mg, 6.57 mmol, 10 mol %). The flask was evacuated under vacuum and back-filled three times with argon. The solids were suspended in CH_2Cl_2 (450 mL), and NEt_3 (23 mL, 165 mmol, 2.5 equiv) was added, at which time the solution became homogenous and a transparent, pale yellow color was observed. The reaction solution was cooled to 0 °C in an ice/water bath and pivaloyl chloride (17 mL, 138 mmol, 2.1 equiv) was added *via* mechanical syringe pump addition over the course of 2 h. Slow addition is essential to maintain an internal temperature of less than 5 °C and minimize formation of side products. Upon complete addition, the ice/water bath was removed and the reaction mixture was allowed to warm to ambient temperature. After 1 h, the starting material was consumed by TLC analysis (30% acetone/hexanes, stain *p*-anisaldehyde), and the reaction mixture was quenched with sat. NH_4Cl (aq, 300 mL). The mixture was diluted with CH_2Cl_2 (400 mL) and transferred to a separatory funnel. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic extracts were washed with 1M HCl (3 x 100 mL) and brine (1 x 100 mL), dried over Mg_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by silica gel flash column chromatography (150 g silica gel, eluent: 20% acetone/hexanes) to afford the title compound as a white, crystalline solid (19.73 g, 61.58 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (t, J = 8.3 Hz, 1H), 6.99 (d, J = 8.2 Hz, 2H), 2.45 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 176.4, 147.9, 130.4, 128.6, 120.1, 39.2, 31.7, 27.1; IR (Neat Film, NaCl): 3487, 3395, 2976, 2936, 2874, 1755, 1705, 1611, 1576, 1478, 1457, 1397, 1368, 1274, 1251, 1233, 1117, 1101 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{18}H_{23}O_5$ $[M-H]^-$: 319.1551, found 319.1542.

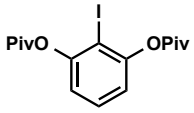


2-bromo-1,3-phenylene bis(2,2-dimethylpropanoate) (31). White, crystalline solid (3.77 g, 10.55 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, J = 8.2 Hz, 1H), 7.00 (d, J = 8.2 Hz, 2H), 1.40 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 149.9,

128.0, 120.9, 111.4, 39.6, 27.4; IR (Neat Film, NaCl): 2971, 2934, 2972, 1762, 1586, 1479, 1460, 1396, 1365, 1274, 1254, 1233, 1093, 1031, 884 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{16}H_{25}BrNO_4$ $[M+NH_4]^+$: 374.0961, found 374.0960.

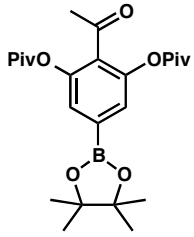


2-chloro-1,3-phenylene bis(2,2-dimethylpropanoate) (S-1). White, crystalline solid (7.57 g, 24.1 mmol, 98% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 2H), 1.40 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 148.4, 127.0, 121.0, 121.0, 39.3, 27.1; IR (Neat Film, NaCl): 2970, 2935, 2874, 1765, 1749, 1583, 1478, 1463, 14552, 1397, 1368, 1273, 1259, 1235, 1112, 1033 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{16}H_{25}ClNO_4$ $[M+NH_4]^+$: 330.1467, found 330.1472.



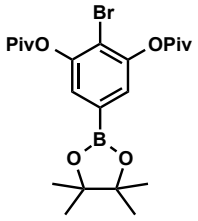
2-iodo-1,3-phenylene bis(2,2-dimethylpropanoate) (S-2). White, crystalline solid (14.0 g, 34.6 mmol, 96% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, *J* = 8.1 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 2H), 1.42 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 152.9, 129.5, 120.0, 88.0, 39.5, 27.5; IR (Neat Film, NaCl): 2972, 2873, 1755, 1583, 1479, 1451, 1396, 1367, 1274, 1244, 1218, 1095, 1029, 967, 941, 886 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{16}H_{20}IO_4$ $[M-H]^-$: 403.0412, found 403.0413.

General Procedure for the Synthesis of Borylated Arenes

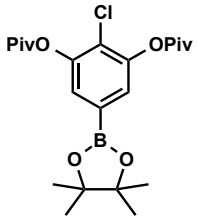


2-acetyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-phenylene bis(2,2-dimethylpropanoate) (18). In a nitrogen-filled glovebox, a 500 mL round-bottom flask with a Kontes valve was charged with a stir bar, arene **17** (16.02 g, 50.0 mmol, 1.0 equiv), B_2Pin_2 (9.5 g, 37.5 mmol, 0.75 equiv), $[Ir(cod)(OMe)]_2$ (33 mg, 0.05 mmol, 0.1 mol %), and tetramethylphenanthroline (24 mg, 0.10 mmol, 0.2 mol %). The solids were suspended in THF (50 mL), and the flask was sealed and removed from the glove box. The reaction mixture was stirred in an oil bath heated at 60 °C for 45 h, at which time the reaction was complete by TLC analysis (20% acetone/hexanes, *p*-anisaldehyde stain). The reaction mixture was cooled to ambient temperature and filtered through a silica gel plug (50 g silica gel, eluent: acetone), and concentrated *in vacuo*. The crude reaction

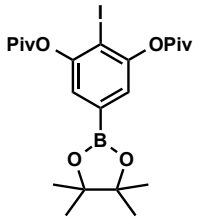
mixture was further purified by silica gel flash chromatography (200 g silica gel, eluent: 20% acetone/hexanes) to afford the title compound as an amorphous off-white solid (19.85 g, 44.47 mmol, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 2H), 2.43 (s, 3H), 1.33 (s, 12H), 1.32 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 176.5, 147.3, 131.0, 126.0, 120.1, 84.6, 39.2, 31.5, 27.2, 25.0; IR (Neat Film, NaCl): 3509, 2981, 2935, 1766, 1707, 1482, 1459, 1405, 1396, 1354, 1331, 1259, 1212, 1147 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m/z* calc'd for $C_{24}H_{39}BNO_7$ $[M+NH_4]^+$: 463.2850, found 463.2852.



2-bromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-phenylene bis(2,2-dimethylpropanoate) (32). Amorphous off-white solid (2.04 g, 5.72 mmol, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 2H), 1.39 (s, 18H), 1.32 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 149.5, 129.8, 126.6, 114.9, 84.6, 39.5, 27.4, 25.0; IR (Neat Film, NaCl): 2977, 1764, 1600, 1479, 1397, 1389, 1364, 1329, 1274, 1211, 1141, 1094, 1036 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m/z* calc'd for $C_{22}H_{36}BBrNO_6$ $[M+NH_4]^+$: 499.1850, found 499.1834.

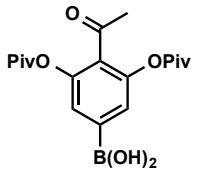


2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-phenylene bis(2,2-dimethylpropanoate) (S-3). Amorphous off-white solid (9.01 g, 20.5 mmol, 99% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 2H), 1.38 (s, 18H), 1.33 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 148.1, 128.6, 126.8, 124.1, 84.6, 39.4, 27.3, 23.0; IR (Neat Film, NaCl): 2977, 2935, 2873, 1763, 1605, 1480, 1404, 1365, 1326, 1270, 1213, 1145, 1121, 1094, 1036 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m/z* calc'd for $C_{22}H_{36}BClNO_6$ $[M+NH_4]^+$: 455.2355, found 455.2358.

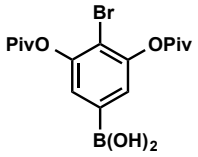


2-iodo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-phenylene bis(2,2-dimethylpropanoate) (S-4). Amorphous off-white solid (12.5 g, 23.5 mmol, 95% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (s, 2H), 1.41 (s, 18H), 1.32 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 152.6, 131.2, 125.7, 92.3, 84.6, 39.5, 27.5, 25.0; IR (Neat Film, NaCl): 2974, 2935, 2873, 1761, 1598, 1549, 1480, 1463, 1395, 1360, 1330, 1274, 1209, 1142, 1094, 1034, 965, 900, 848 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{22}H_{32}BFIO_6$ $[M+F]^-$: 549.1321, found 549.1337.

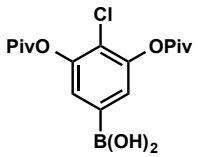
General Procedure for the Synthesis of Boronic Acid Analogues



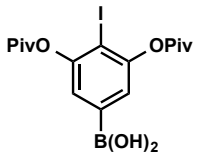
(4-acetyl-3,5-bis(pivaloyloxy)phenyl)boronic acid (**19**). A 250 mL round-bottom flask was charged with a stir bar and pinacol boronate ester **18** (8.65 g, 19.27 mmol, 1.0 equiv). The solid was dissolved in EtOAc (250 mL), and diethanolamine (2.35 mL, 24.10 mmol, 1.25 equiv) was added with vigorous stirring. (Note: a glass pipette was cut to have a wide bore, and this wide-bored pipet was used to add the viscous diethanolamine.) Upon addition of diethanolamine, a white precipitate formed. This suspension was stirred vigorously for a further 4 h at ambient temperature, at which time the mixture was concentrated *in vacuo*. The crude white semi-solid reaction residue was suspended in Et_2O (300 mL) and stirred vigorously for 30 min. The suspension was then cooled to –20 °C in a freezer overnight. The white solid was collected by vacuum filtration, and the compound was washed with additional portions of Et_2O (3 x 50 mL). The collected white solid (7.38 g) was suspended in 0.5 M HCl (200 mL) and stirred vigorously. CH_2Cl_2 (ca. 50 mL) was added until the solid fully dissolved. The biphasic mixture was stirred for 12 h with extreme vigor. The mixture was then subjected to continuous extraction with boiling CH_2Cl_2 (300 mL) for 6 h. The combined organic extracts were concentrated *in vacuo* and dried under high vacuum to afford the title compound as an off-white, flaky solid (6.45 g, 17.71 mmol, 92% yield over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (s, 2H), 2.19 (s, 3H), 1.08 (s, 18H); ^{13}C NMR (125 MHz, acetone-d_6) δ 198.5, 176.7, 148.1, 138.0, 131.2, 126.2, 39.5, 31.7, 27.2; IR (Neat Film, NaCl): 3446, 2975, 2359, 1751, 1700, 1653, 1635, 1558, 1540, 1480, 1456, 1407, 1340, 1247, 1100, 1038 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{18}H_{29}BNO_7$ $[M+NH_4]^+$: 381.2068, found 381.2061.



(4-bromo-3,5-bis(pivaloyloxy)phenyl)boronic acid (33). Note: 2 M H_2SO_4 and THF were used in place of 0.5 M HCl and CH_2Cl_2, a continuous extraction was not required. Off-white, flaky solid (11.0 g, 27.50 mmol, 82% yield over two steps). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.50 (s, 2H), 1.40 (s, 18H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 175.3, 148.6, 135.6, 126.3, 112.8, 38.8, 26.8; IR (Neat Film, NaCl): 3454, 3364, 2976, 2937, 2874, 1755, 1733, 1736, 1480, 1454, 1426, 1365, 1342, 1271, 1218, 1137, 1108, 1038 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{16}H_{22}BBr_2O_6$ [M+Br]$^-$: 477.9918, found 477.9923.

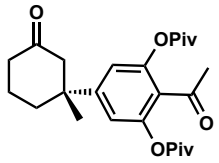


(4-chloro-3,5-bis(pivaloyloxy)phenyl)boronic acid (S-5). Note: 2 M H_2SO_4 and THF were used in place of 0.5 M HCl and CH_2Cl_2, a continuous extraction was not required. Off-white, flaky solid (3.50 g, 9.81 mmol, 86% yield over two steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 (s, 2H), 1.34 (s, 18H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.3, 147.2, 134.8, 126.3, 121.5, 38.8, 26.7; IR (Neat Film, NaCl): 3377, 2980, 1753, 1735, 1639, 1480, 1463, 1428, 1366, 1342, 1280, 1139, 1113, 1089 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{16}H_{22}BCl_2O_6$ [M+Cl]$^-$: 390.0928, found 390.0936.

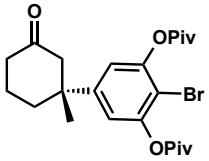


(4-iodo-3,5-bis(pivaloyloxy)phenyl)boronic acid (S-6). Note: 2 M H_2SO_4 and THF were used in place of 0.5 M HCl and CH_2Cl_2, a continuous extraction was not required. Off-white, flaky solid (4.82 g, 10.76 mmol, 94% yield over two steps). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.37 (s, 2H), 1.37 (s, 18H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 175.4, 152.0, 136.5, 125.2, 92.0, 38.8, 27.0; IR (Neat Film, NaCl): 3369, 2975, 1759, 1735, 1395, 1360, 1277, 1095, 1034, 904 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{16}H_{22}BClIO_6$ [M+Cl]$^-$: 482.0284, found 482.0296.

General Procedure for Asymmetric Conjugate Addition of Arylboronic Acis to 3-methylcyclohexenone

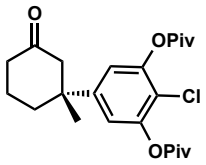


(*R*)-2-acetyl-5-(1-methyl-3-oxocyclohexyl)-1,3-phenylene bis(2,2-dimethylpropanoate) (20). A 20 mL screw-top vial was charged with a stir bar, $Pd(OCOCF_3)_2$ (25 mg, 0.075 mmol, 2.5 mol %), (*S*)-*t*-BuPyOx (18 mg, 0.099 mmol, 3 mol %), NH_4PF_6 (145 mg, 0.99 mmol, 30 mol %), and the solids were dissolved in 1,2-dichloroethane (2 mL) and stirred at ambient temperature for 5 min. Not all solids dissolved at this time. A 100 mL round bottom flask was charged with a stir bar, boronic acid **19** (1.20 g, 3.30 mmol, 1.1 equiv), and 1,2-dichloroethane (10 mL), and stirred at ambient temperature. The catalyst solution was filtered through a pipet plugged with a Kimwipe and added to the suspension of boronic acid in one portion. 3-methylcyclohexen-2-one (340 µL, 3.00 mmol, 1.0 equiv) and water (270 µL, 15 mmol, 5 equiv) were added by syringe and the flask was stirred in an oil bath heated to 50 °C for 72 h. When the starting material was consumed as determined by TLC analysis (10% acetone/hexanes, *p*-anisaldehyde stain), the mixture was cooled to ambient temperature and filtered through a plug of silica gel (eluent: CH_2Cl_2) and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (200 g silica gel, eluent gradient: 5% acetone/hexanes to 10% acetone/hexanes) to afford the title compound as a colorless oil (1.19 g, 2.77 mmol, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (s, 2H), 2.77 (d, J = 14.1 Hz, 1H), 2.42 (s, 4H), 2.33 (t, J = 6.8 Hz, 2H), 2.12 (s, 1H), 1.99 – 1.84 (m, 2H), 1.82 – 1.71 (m, 1H), 1.32 (s, 21H);^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4, 198.5, 176.4, 151.3, 148.0, 126.5, 117.5, 52.8, 43.0, 40.8, 39.2, 37.6, 31.5, 28.9, 27.2, 27.1, 27.1, 22.0; IR (Neat Film, NaCl): 3404, 2973, 2937, 2874, 1758, 1708, 1620, 1562, 1480, 1408, 1397, 1257, 1095 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{25}H_{34}NaO_6$ $[M+Na]^+$: 453.2248, found 453.2234; $[\alpha]^{25}_D$ –36.1° (*c* 1.85, $CHCl_3$, 94% ee).

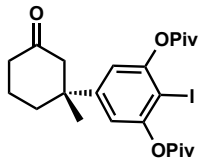


(*R*)-2-bromo-5-(1-methyl-3-oxocyclohexyl)-1,3-phenylene bis(2,2-dimethylpropanoate) (27). Note: 1.5 equiv of boronic acid were employed. Colorless solid (4.57 g, 9.78 mmol, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.93 (s, 2H), 2.76 (d, J = 14.1 Hz, 1H), 2.44 (d, 14.1 Hz, 1H), 2.33 (t, J = 6.7 Hz, 2H), 2.19 – 2.06 (m, 1H), 1.98 – 1.85 (m, 2H), 1.80 – 1.74 (m, 1H), 1.40 (s, 18H), 1.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 175.8, 149.8, 149.0, 118.4, 108.9, 53.0, 42.8, 40.8, 39.6, 37.7, 28.8, 27.4, 22.1; IR (Neat Film, NaCl): 2973, 2936, 2874, 1763, 1713, 1601, 1571, 1480, 1463, 1408, 1397, 1365, 1272, 1227, 1096, 1037, 894 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{23}H_{35}BrNO_5$ $[M+NH_4]^+$: 484.1693, found 484.1693; $[\alpha]^{25}_D$ –

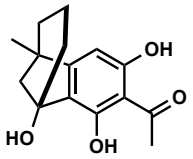
34.5° (*c* 1.41, $CHCl_3$, >99% ee).



(*R*)-2-chloro-5-(1-methyl-3-oxocyclohexyl)-1,3-phenylene bis(2,2-dimethylpropanoate) (28). Note: 1.5 equiv of boronic acid were employed. Colorless solid (0.74 g, 1.75 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (s, 2H), 2.76 (d, *J* = 14.1 Hz, 1H), 2.43 (d, *J* = 14.1 Hz, 1H), 2.32 (t, *J* = 6.7 Hz, 2H), 2.15 – 2.06 (m, 1H), 1.98 – 1.84 (m, 2H), 1.82 – 1.71 (m, 1H), 1.38 (s, 18H), 1.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.3, 175.7, 148.2, 147.8, 118.4, 118.3, 52.8, 42.6, 40.6, 39.3, 37.5, 28.7, 27.2, 21.9; IR (Neat Film, NaCl): 2972, 2936, 2874, 2256, 1763, 1713, 1607, 1574, 1479, 1413, 1397, 1352, 1316, 1272, 1227, 1050, 1038, 895, 734 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{23}H_{35}ClNO_5$ $[M+NH_4]^+$: 440.2198, found 440.2197; $[\alpha]^{25}_D$ –38.9° (*c* 2.59, $CHCl_3$, >99% ee).

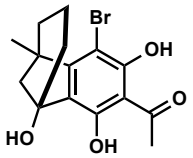


(*R*)-2-iodo-5-(1-methyl-3-oxocyclohexyl)-1,3-phenylene bis(2,2-dimethylpropanoate) (26). Note: 1.5 equiv of boronic acid were employed. Colorless solid (0.40 g, 0.78 mmol, 42% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 2H), 2.75 (d, *J* = 14.1 Hz, 1H), 2.42 (d, 14.1 Hz, 1H), 2.30 (t, *J* = 6.8 Hz, 2H), 2.12 – 2.06 (m, 1H), 1.92 – 1.85 (m, 2H), 1.77 – 1.72 (m, 1H), 1.40 (s, 18H), 1.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4, 175.9, 152.7, 150.4, 117.6, 85.0, 52.8, 42.7, 40.7, 39.4, 37.5, 28.7, 27.4, 22.0; IR (Neat Film, NaCl): 2972, 2936, 2873, 1759, 1711, 1598, 1560, 1480, 1461, 1396, 1368, 1314, 1271, 1226, 1098, 1036, 938, 914, 894, 754, 733 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{23}H_{35}INO_5$ $[M+NH_4]^+$: 532.1554, found 532.1567; $[\alpha]^{25}_D$ –29.2° (*c* 4.47, $CHCl_3$, 92% ee).



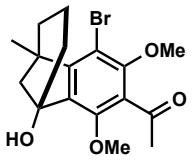
(*R*)-1-(1,3,9-trihydroxy-5-methyl-6,7,8,9-tetrahydro-5*H*-5,9-methanobenzo[7]annulen-2-yl)ethanone (23). A 250 mL round-bottom flask was charged with a stir bar, flame-dried under vacuum, back-filled with argon, and charged with THF (25 mL). The solution was cooled to 0 °C in an ice/water bath and ethanethiol (0.890 mL, 12.5 mmol, 2.7 equiv) was added *via* syringe. *n*-BuLi (2.5 M solution in hexanes, 5.5 mL, 13.75 mmol, 2.97 equiv) was added dropwise, and a white precipitate was observed at the completion of the addition. DMF (ca. 25 mL) was added until the

solution became homogenous and clear. The solution was allowed to stir at 0 °C for 30 min. A flame-dried, 25 mL conical flask was charged with ketone **20** (1.99 g, 4.62 mmol, 1 equiv) and DMF (10 mL). The ketone solution was transferred *via* cannula to the cooled, freshly-prepared solution of LiSEt dropwise over 10 min. The ice/water bath was removed and the reaction was allowed to stir and warm to ambient temperature over 30 min, at which time the starting material was consumed as determined by TLC analysis (20% EtOAc/hexanes, *p*-anisaldehyde stain). The reaction was quenched by addition of sat. NH_4Cl solution (aq, 50 mL), diluted with CH_2Cl_2 (200 mL) and water (200 mL) and transferred to a separatory funnel. 1M HCl (aq) was added until the aqueous layer was pH 2–4. The aqueous layer was extracted with CH_2Cl_2 (5 x 50 mL) and the combined organic extracts were washed with water (7 x 50 mL), brine (1 x 50 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified *via* silica gel flash chromatography (90 g silica gel, eluent gradient: 10% EtOAc/hexanes to 20% EtOAc/hexanes) to afford the title compound as a pale yellow oil (1.15 g, 4.39 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.30 (s, 1H), 8.30 (s, 1H), 6.23 (d, *J* = 1.9 Hz, 1H), 2.71 (s, 3H), 2.58 (bs, 1H), 2.12 (ddd, *J* = 9.5, 2.9, 2.2 Hz, 1H), 2.01–1.89 (m, 1H), 1.76 – 1.59 (m, 3H), 1.48 – 1.32 (m, 2H), 1.31 (s, 3H), 1.03 – 0.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.9, 165.8, 156.1, 154.4, 118.8, 109.1, 102.4, 82.3, 59.0, 45.7, 35.4, 34.5, 33.2, 22.9, 21.4; IR (Neat Film, NaCl): 3338, 2934, 2867, 1641, 1588, 1435, 1375, 1324, 1270, 1243, 1124, 1055, 1027, 973, 839 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{15}H_{19}O_4$ $[M+H]^+$: 263.1278, found 263.1272; $[\alpha]^{25}_D$ –19.0° (*c* 0.26, $CHCl_3$).

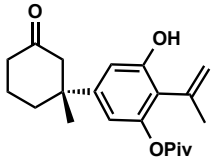


(*R*)-1-(4-bromo-1,3,9-trihydroxy-5-methyl-6,7,8,9-tetrahydro-5*H*-5,9-methanobenzo[7]annulen-2-yl)ethanone (S-7). A 50 mL, flame-dried, round-bottom flask was charged with a stir bar, tricycle **23** (110 mg, 0.419 mmol, 1 equiv) and dibromodimethylhydantoin (151 mg, 0.461 mmol, 1.1 equiv). The flask was evacuated under vacuum and back-filled with argon, and the solids were dissolved in CH_2Cl_2 (5 mL) and stirred at ambient temperature. After 30 min, an aliquot was partitioned between EtOAc (1 mL) and sat. $Na_2S_2O_3$ (aq, 1 mL), and the organic layer was subjected to LCMS analysis, where no starting material was observed. The red-colored reaction was quenched by the addition of 20% $Na_2S_2O_3$ solution (aq, 20 mL) and stirred vigorously for 3 h, until the orange/red color was no longer observed. The mixture was partitioned between CH_2Cl_2 (20 mL) and water (20 mL) and transferred to a separatory funnel. 1M HCl was added until the aqueous layer was pH 3. The aqueous layer was extracted with CH_2Cl_2 (5 x 25 mL) and the combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by silica gel column chromatography (12 g silica gel, eluent gradient: 10% EtOAc/hexanes to 25% EtOAc/hexanes) to afford the title compound as a yellow, semi-crystalline solid (92 mg, 0.273 mmol, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.37 (s, 1H), 9.10 (s, 1H), 2.74 (s, 3H), 2.55 (s, 1H), 2.22 (ddd, *J* = 9.7, 3.0, 2.2 Hz, 1H), 1.93 (ddd, *J* = 11.2, 6.2, 3.0 Hz, 1H), 1.75 – 1.64 (m, 4H), 1.61 (s, 3H), 1.35 (td, J = 13.0, 5.5 Hz, 1H), 0.96 – 0.80 (m,

1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 154.3, 151.9, 120.2, 110.2, 109.9, 97.9, 81.4, 59.1, 48.8, 34.4, 33.1, 33.0, 24.6, 21.6; IR (Neat Film, NaCl): 3381, 2936, 2852, 1631, 1566, 1415, 1373, 1326, 1274, 1233 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m*/*z* calc'd for $C_{15}H_{16}BrO_4$ $[M-H]^-$: 339.0237, found 339.0230; $[\alpha]^{25}_D$ –20.8° (*c* 1.26, $CHCl_3$).



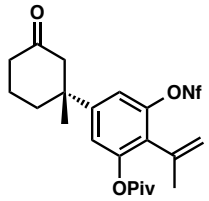
(*R*)-1-(4-bromo-9-hydroxy-1,3-dimethoxy-5-methyl-6,7,8,9-tetrahydro-5*H*-5,9-methanobenzo[7]annulen-2-yl)ethanone (24). A flame-dried 20 mL vial was charged with a stir bar, bromo-diphenol **S-7** (92 mg, 0.270 mmol, 1 equiv), Cs_2CO_3 (194 mg, 0.595 mmol, 2.2 equiv), and acetone (5 mL). The vial was stirred under argon atmosphere at ambient temperature, and MeI (0.037 mL, 0.595 mmol, 2.2 equiv) was added in one portion. The yellow reaction slurry was stirred for 40 h at ambient temperature, at which time the color had faded to a white slurry and the starting material was consumed as determined by TLC analysis (20% EtOAc/hexanes, *p*-anisaldehyde stain). The reaction was quenched with sat. NH_4Cl solution (aq, 5 mL) and stirred for 12 h at ambient temperature. The reaction was diluted with EtOAc (10 mL) and water (10 mL), and the mixture was transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organic extracts were washed with water (2 x 10 mL) and brine (1 x 10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (12 g silica gel, eluent gradient 10% EtOAc/hexanes to 20% EtOAC/hexanes) to afford the title compound as a clear oil that solidified to an amorphous white solid upon standing (62 mg, 63% yield). Crystals of sufficient quality for single crystal X-ray diffraction analysis were grown by recrystallization from dichloromethane and hexanes. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H), 3.80 (s, 3H), 2.56 (s, 3H), 2.24 (dt, *J* = 10.1, 2.5 Hz, 1H), 1.84 – 1.71 (m, 2H), 1.71 – 1.61 (m, 4H), 1.60 (s, 3H), 1.35 (td, *J* = 12.9, 5.8 Hz, 1H), 0.81 – 0.67 (m, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 153.9, 151.0, 148.1, 135.9, 130.5, 108.9, 79.7, 63.9, 63.1, 58.6, 48.0, 36.7, 33.2, 32.6, 25.1, 21.6; IR (Neat Film, NaCl): 3429, 2938, 2853, 1704, 1642, 1590, 1450, 1382, 1323, 1237, 1120, 1077 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m*/*z* calc'd for $C_{17}H_{22}BrO_4$ $[M+H]^+$: 369.0696, found 369.0690; $[\alpha]^{25}_D$ –5.8° (*c* 0.73, $CHCl_3$).



(*R*)-3-hydroxy-5-(1-methyl-3-oxocyclohexyl)-2-(prop-1-en-2-yl)phenyl pivalate (34). Four 20 mL microwave vials were each charged with a stir bar, ketone **27** (0.594 g, 1.27 mmol, 1 equiv), potassium isopropenyltrifluoroborate (281 mg, 1.91 mmol, 1.25 equiv), K_2CO_3 (263 g, 1.91 mmol, 1.5 equiv), PPh_3 (33 mg, 0.127 mmol, 10 mol %), and $Pd(OAc)_2$ (14 mg, 0.0635 mmol, 5 mol %), and capped with a microwave septum top.

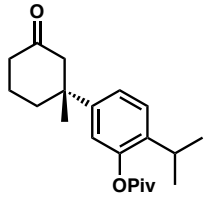
The vials were evacuated with vacuum and back-filled with argon three times. The solids were suspended in degassed dioxane/H_2O (9:1 ratio, 20 mL) before the reaction was stirred in the microwave reactor for 1 h at 170 °C on very high absorbance mode. The mixture was cooled to ambient temperature and filtered through a plug of silica gel (eluent: EtOAc) and concentrated *in vacuo* to afford a brown oil.

A 100 mL round-bottom flask was charged with the combined crude reaction residues, a stir bar, Bu_4NOH (4.7 mL, 7.15 mmol, 2.4 equiv), and dioxane/H_2O (9:1 ratio, 50 mL). The reaction was stirred at ambient temperature for 10 h, at which point the starting material was consumed as determined by TLC analysis (20% EtOAc/hexanes, *p*-anisaldehyde stain). The reaction was quenched with sat. NH_4Cl (aq, 25 mL) and transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (3 x 100 mL), and the combined organic extracts were washed with brine (1 x 100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (50 g silica gel, eluent gradient: 10% EtOAc/hexanes to 20% EtOAc/hexanes) to afford the title compound as a yellow oil (1.23 g, 3.57 mmol, 70% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, J = 1.8 Hz, 1H), 6.53 (d, J = 1.8 Hz, 1H), 5.52 (s, 1H), 5.43 (s, 1H), 5.04 (s, 1H), 2.79 (d, J = 14.1 Hz, 1H), 2.41 (d, J = 14.1 Hz, 1H), 2.32 (t, J = 6.7 Hz, 2H), 2.14 – 2.08 (m, 1H), 2.00 (s, 3H), 1.91 – 1.84 (m, 2H), 1.83 – 1.73 (m, 1H), 1.31 (s, 9H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.0, 176.8, 152.9, 149.1, 148.7, 138.1, 121.3, 119.3, 111.9, 110.3, 53.2, 42.8, 40.9, 39.2, 37.8, 29.0, 27.3, 23.6, 22.2; IR (Neat Film, NaCl): 3418, 3083, 2970, 2874, 1712, 1620, 1480, 1414, 1368, 1316, 1278, 1230, 1122, 1073, 1035, 1017, 943, 901, 758 cm^{-1}; HRMS (MultiMode ESI/APCI-) *m/z* calc'd for $C_{21}H_{27}O_4$ $[M-H]^-$: 343.1915, found 343.1926; $[\alpha]^{25}_D$ –37.4° (*c* 1.26, $CHCl_3$).

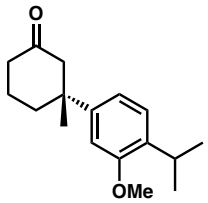


(*R*)-5-(1-methyl-3-oxocyclohexyl)-3-(perfluorobutoxy)-2-(prop-1-en-2-yl)phenyl pivalate (35). A 15 mL, flame-dried, round-bottom flask was charged with a stir bar, phenol **34** (165 mg, 0.479 mmol, 1 equiv) and DMAP (3 mg, 0.024 mmol, 5 mol%). The flask was evacuated under vacuum and back-filled with argon three times. The solids were dissolved in CH_2Cl_2 (5 mL), and NEt_3 (1.34 mL, 9.58 mmol, 20 equiv) was added. Perfluorobutanesulfonyl fluoride (1.72 mL, 9.58 mmol, 20 equiv) was then added dropwise and the resulting solution was stirred at ambient temperature for 18 h, at which time the starting material was consumed as determined by TLC analysis (30% EtOAc/hexanes, *p*-anisaldehyde stain). The mixture was washed with water (10 mL) and brine (10 mL), and the organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by silica gel column chromatography (9 g silica gel, gradient: 10% EtOAc/hexanes) to afford the title compound as a colorless oil (0.2694 g, 0.479 mmol, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 1.8 Hz, 1H), 7.00 (d, J = 1.9 Hz, 1H), 5.39 (t, J = 1.2 Hz, 1H), 5.00 (t, J = 1.2 Hz, 1H), 2.76 (d, J = 14.0 Hz,

1H), 2.47 (d, *J* = 14.0 Hz, 1H), 2.35 (t, *J* = 6.8 Hz, 2H), 2.19 – 2.05 (m, 1H), 2.00 (s, 3H), 1.99 – 1.87 (m, 2H), 1.86 – 1.74 (m, 1H), 1.32 (s, 9H), 1.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1, 176.7, 149.5, 149.5, 147.3, 135.1, 129.6, 120.3, 120.3, 117.0, 116.4, 114.3, 109.9, 108.0, 52.9, 42.9, 40.8, 39.2, 37.6, 28.8, 27.2, 23.1, 22.0; ^{19}F (376 MHz, $CDCl_3$) δ -80.94 (t, *J* = 9.9 Hz, 3F), -109.86 (t, *J* = 14.0 Hz, 2F), -121.04 – -120.86 (m, 2F), -126.04 (dt, *J* = 13.9, 13.5, 4.9 Hz, 2F). IR (Neat Film, NaCl): 2971, 2877, 1759, 1720, 1649, 1623, 1553, 1482, 1427, 1353, 1240, 1200, 1145, 1107, 1032, 1011, 985, 944, 922 cm^{-1}. HRMS (FAB+) *m/z* calc'd for $C_{25}H_{28}F_9O_6S$ $[M+H]^+$: 627.1457, found 627.2216; $[\alpha]^{25}_D$ –22.1° (*c* 1.31, $CHCl_3$).



(*R*)-2-isopropyl-5-(1-methyl-3-oxocyclohexyl)phenyl pivalate (36). A 25 mL Schlenk flask was charged with a stir bar, nonaflate **35** (62.1 mg, 0.110 mmol, 1 equiv), 10% Pd/C (62.1 mg, equal weight to that of the nonaflate), Et_3N (38 μL, 0.276 mmol, 2.5 equiv), and MeOH (5 mL). The reaction mixture was degassed then back-filled with H_2 gas (1 atm) using Schlenk technique. The flask was sealed and stirred in an oil bath heated to 65 °C for 11 h. The mixture was cooled to ambient temperature, filtered through a silica gel plug (10 g silica gel, eluent: EtOAc) and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (9 g silica gel, eluent: 5% EtOAc/hexanes) to afford the title compound as a colorless oil (26.4 mg, 0.080 mmol, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 2.4 Hz, 1H), 7.16 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.90 (d, *J* = 2.1 Hz, 1H), 3.13 (p, *J* = 6.9 Hz, 1H), 2.84 (d, *J* = 14.1 Hz, 1H), 2.45 (d, *J* = 14.2 Hz, 1H), 2.33 (t, *J* = 6.7 Hz, 2H), 2.19 – 2.12 (m, 1H), 1.99 – 1.84 (m, 2H), 1.84 – 1.70 (m, 1H), 1.41 (s, 9H), 1.32 (s, 3H), 1.21 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 177.2, 148.6, 146.5, 138.0, 126.5, 123.3, 119.5, 53.2, 42.6, 40.9, 39.3, 37.9, 29.3, 27.4, 27.1, 23.0, 22.9, 22.2; IR (Neat Film, NaCl): 2963, 2872, 1750, 1714, 1619, 1504, 1462, 1410, 1365, 1276, 1229, 1160, 1120, 1055, 1030, 932, 904 cm^{-1}; HRMS (MultiMode ESI/APCI+) *m/z* calc'd for $C_{21}H_{34}NO_3$ $[M+NH_4]^+$: 348.2533, found 348.2518; $[\alpha]^{25}_D$ –41.4° (*c* 1.30, $CHCl_3$).

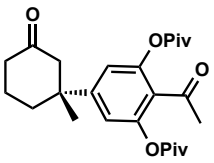
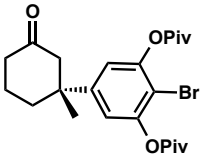
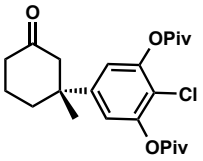
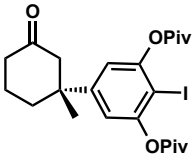


(*R*)-3-(4-isopropyl-3-methoxyphenyl)-3-methylcyclohexane-1-one (29). A 25 mL round bottom flask was charged with a stir bar, flame-dried under vacuum, back-filled with argon and charged with THF (2 mL). The solution was cooled to 0 °C in an ice/water bath and ethanethiol (57 μL, 0.787 mmol, 10 equiv) was added *via* syringe. *n*-BuLi (2.5 M solution in hexanes, 322 μL, 0.802 mmol, 10.2 equiv) was added dropwise,

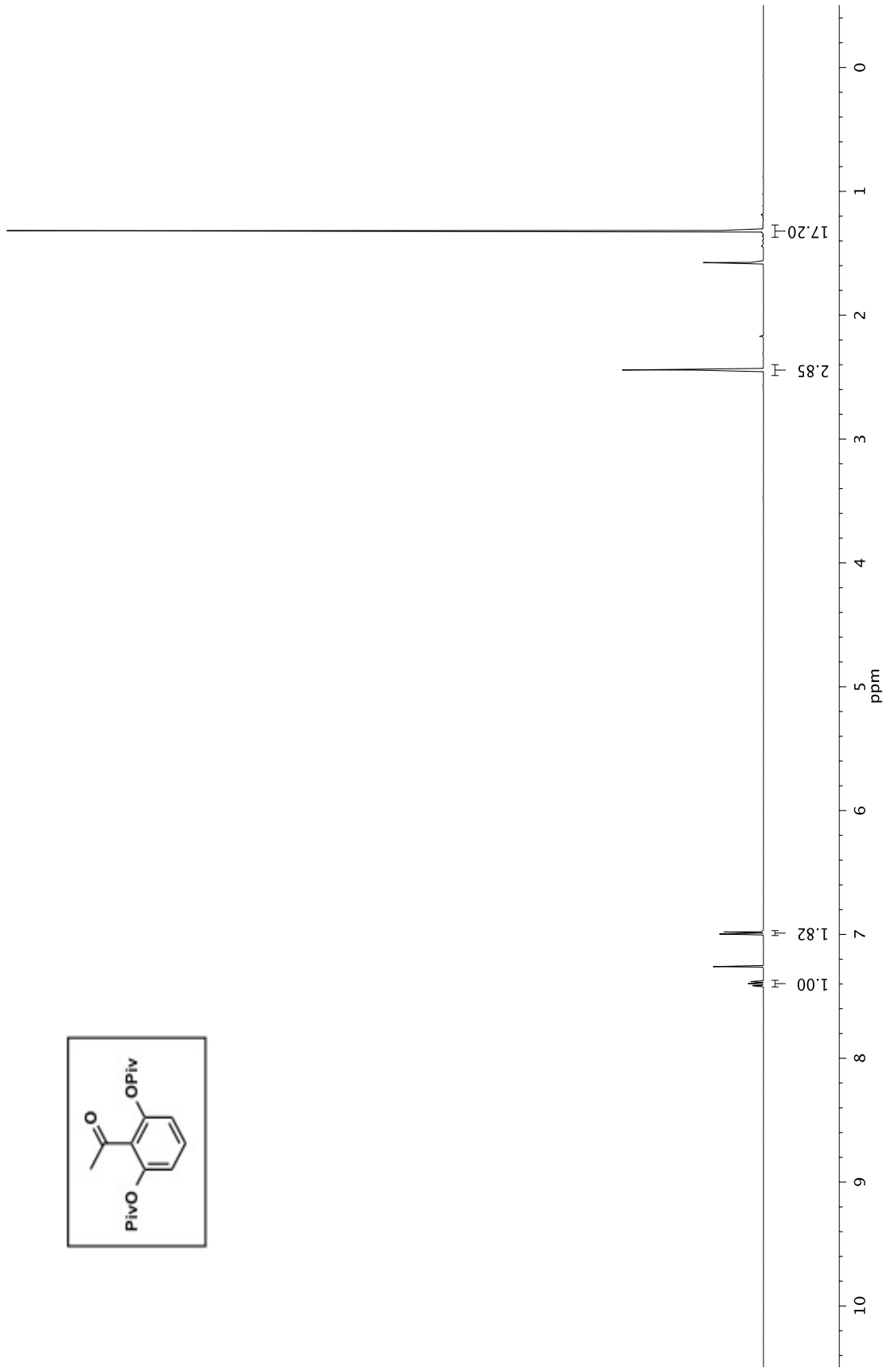
and a white precipitate was observed at the completion of the addition. The solution was allowed to stir at 0 °C for 1 h. A flame-dried 15 mL conical flask was charged with ketone **36** (26.0 mg, 0.079 mmol, 1 equiv) and DMF (1 mL). The ketone solution was transferred *via* cannula to the cooled, freshly-prepared solution of LiSEt dropwise over 5 min. The ice/water bath was removed and the reaction was stirred in an oil bath heated to 45 °C for 6 h, at which time the starting material was consumed as determined by TLC analysis (30% EtOAc/hexanes, *p*-anisaldehyde stain). Me_2SO_4 (112 μL, 1.185 mmol, 15 equiv) was added to the reaction mixture and stirred at 45 °C for an additional 15 min, at which time the reaction was complete as determined by TLC analysis (30% EtOAc/hexanes, *p*-anisaldehyde stain). The reaction was quenched with NH_4OH (aq, 5 mL) and stirred at 45 °C for another 15 min then diluted with H_2O (10 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), dried with $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified *via* silica gel flash chromatography (9 g silica gel, eluent: 2.5% EtOAc/hexanes) to afford the title compound as a colorless oil (17.0 mg, 0.065 mmol, 83 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.0 Hz, 1H), 6.86 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.78 (d, *J* = 1.9 Hz, 1H) 3.82 (s, 3H), 3.26 (p, *J* = 6.9 Hz, 1H), 2.87 (d, *J* = 14.2 Hz, 1H), 2.43 (d, *J* = 14.1 Hz, 1H), 2.31 (t, *J* = 6.8 Hz, 2H), 2.20 – 2.14 (m, 1H), 1.93 – 1.82 (m, 2H), 1.72 – 1.62 (m, 1H), 1.33 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.8, 156.8, 146.1, 134.9, 126.1, 117.8, 108.3, 55.5, 53.4, 43.0, 41.0, 38.3, 30.1, 26.6, 22.8, 22.2; IR (Neat Film, NaCl): 2958, 2869, 1713, 1611, 1573, 1504, 1462, 1409, 1350, 1305, 1254, 1240, 1164, 1092, 1038, 920 cm^{-1}; HRMS (FAB+) *m*/*z* calc'd for $C_{17}H_{24}O_2$ $[M]^+$: 260.1776, found 260.1782; $[\alpha]^{25}_D$ –60.4° (*c* 1.49, $CHCl_3$).

Chiral HPLC and SFC Data

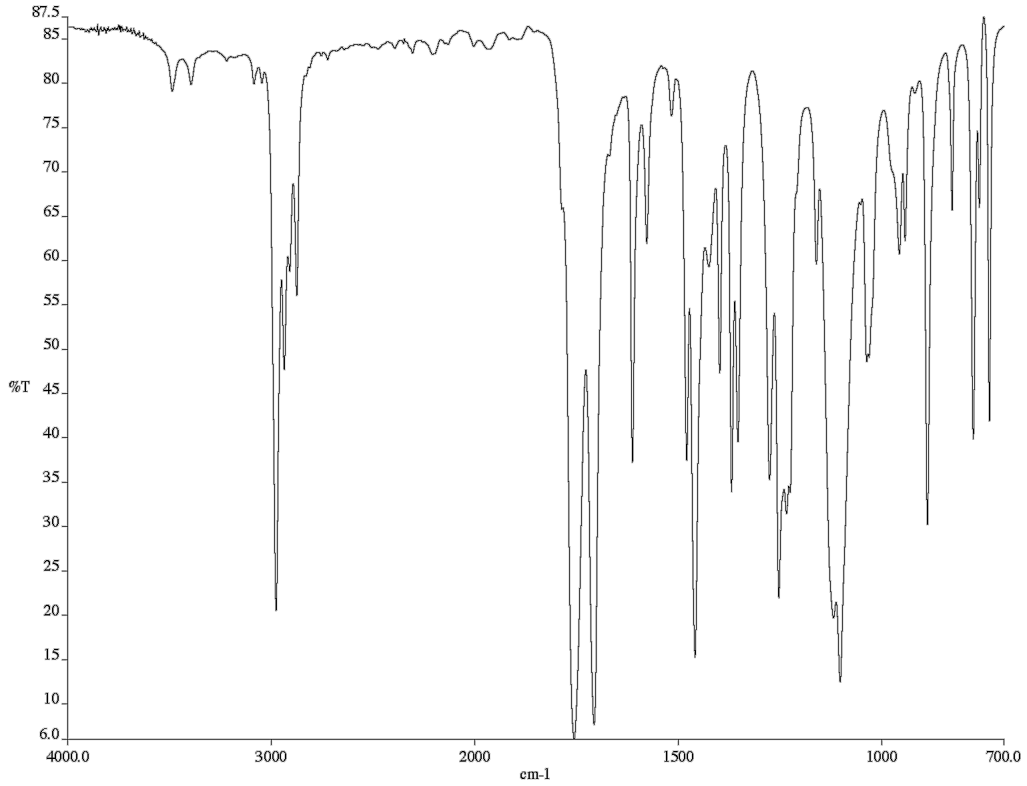
Table 1. Methods for the determination of enantiomeric excess.

Entry	Product	Assay Conditions	Retention time of major isomer (min)	Retention time of minor isomer (min)	%ee
1		HPLC Chiralpak AD-H 5% IPA in hexanes isocratic, 1.0 mL/min	6.454	6.227	94
2		HPLC Chiralpak IC 20% IPA in hexanes isocratic, 1.0 mL/min	5.795	6.232	>99
3		SFC Chiralpak AS-H 3% IPA in hexanes isocratic, 2.5 mL/min	5.3931	6.285	>99
4		HPLC Chiralpak IC 20% IPA in hexanes isocratic, 1.0 mL/min	6.130	7.008	92

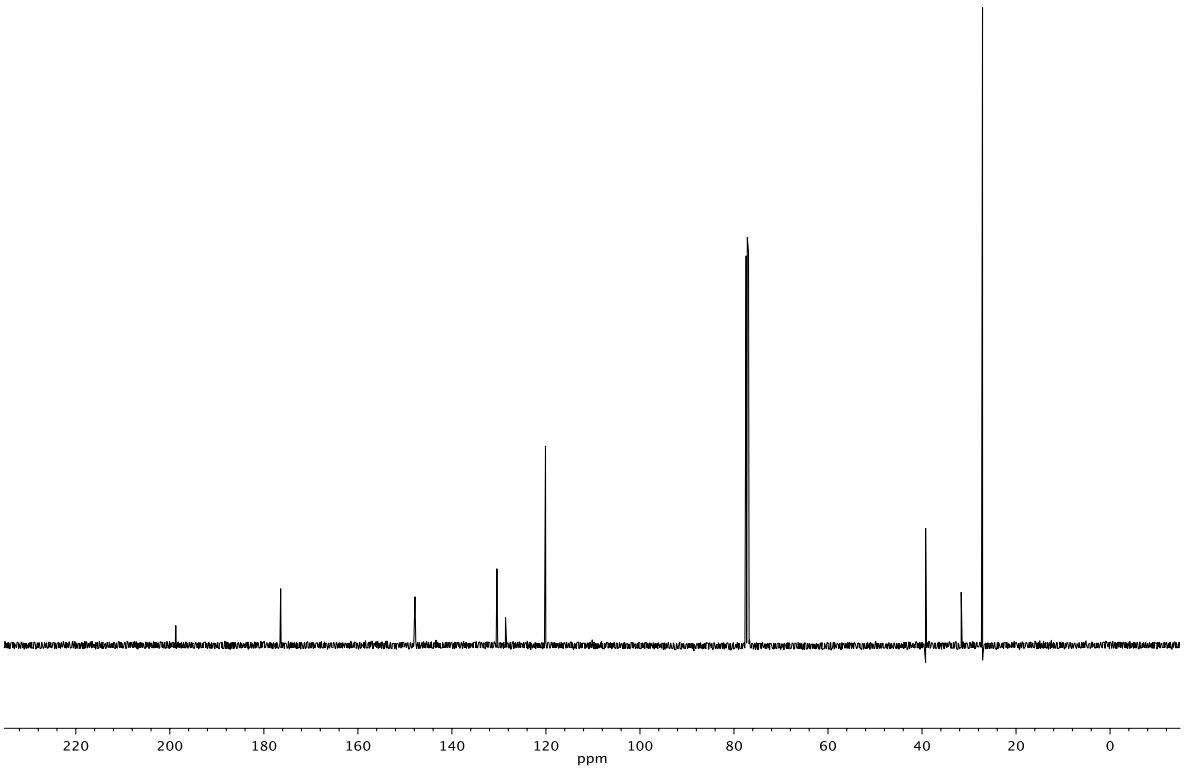
Note: racemic products were made using the same general method for conjugate addition, except substituting racemic *i*-Pr-PyOx for (*S*)-*t*-BuPyOx.



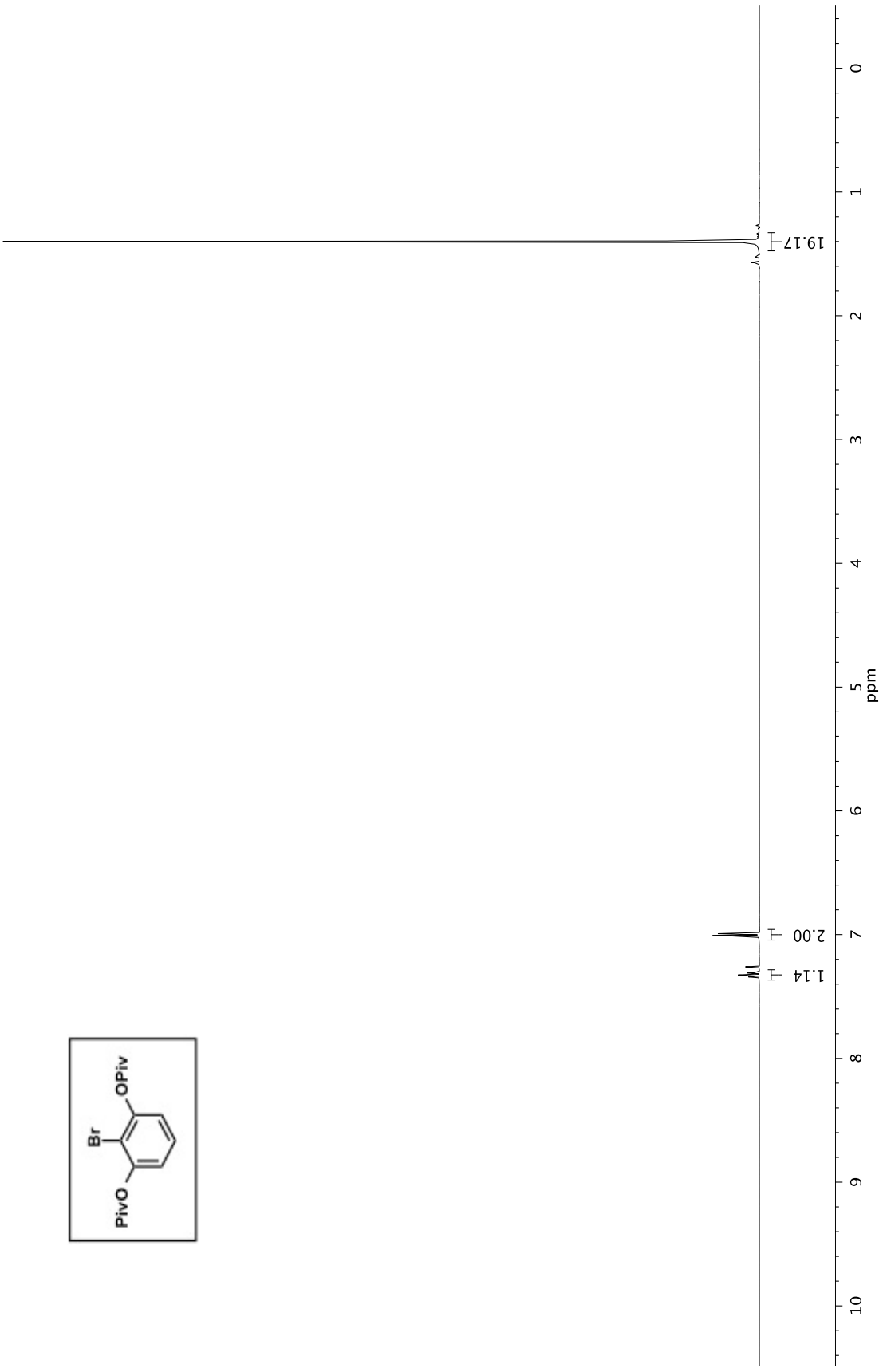
^{1}H NMR (500 MHz, $CDCl_3$) of compound **17**.



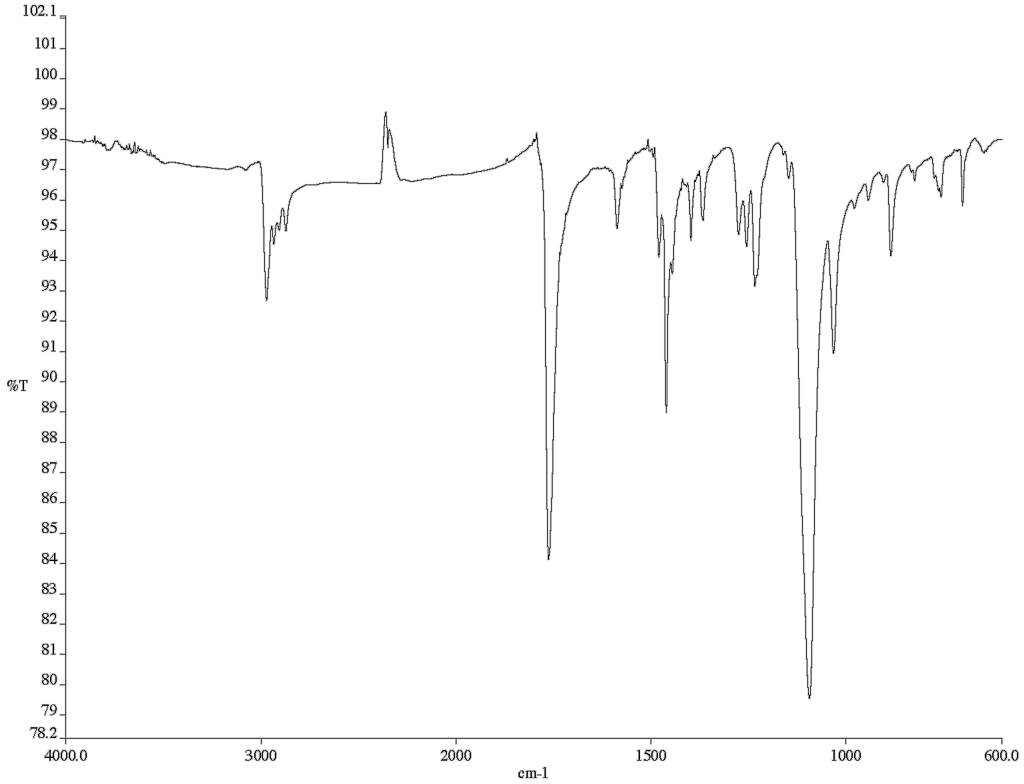
Infrared spectrum (Thin Film, NaCl) of compound **17**.



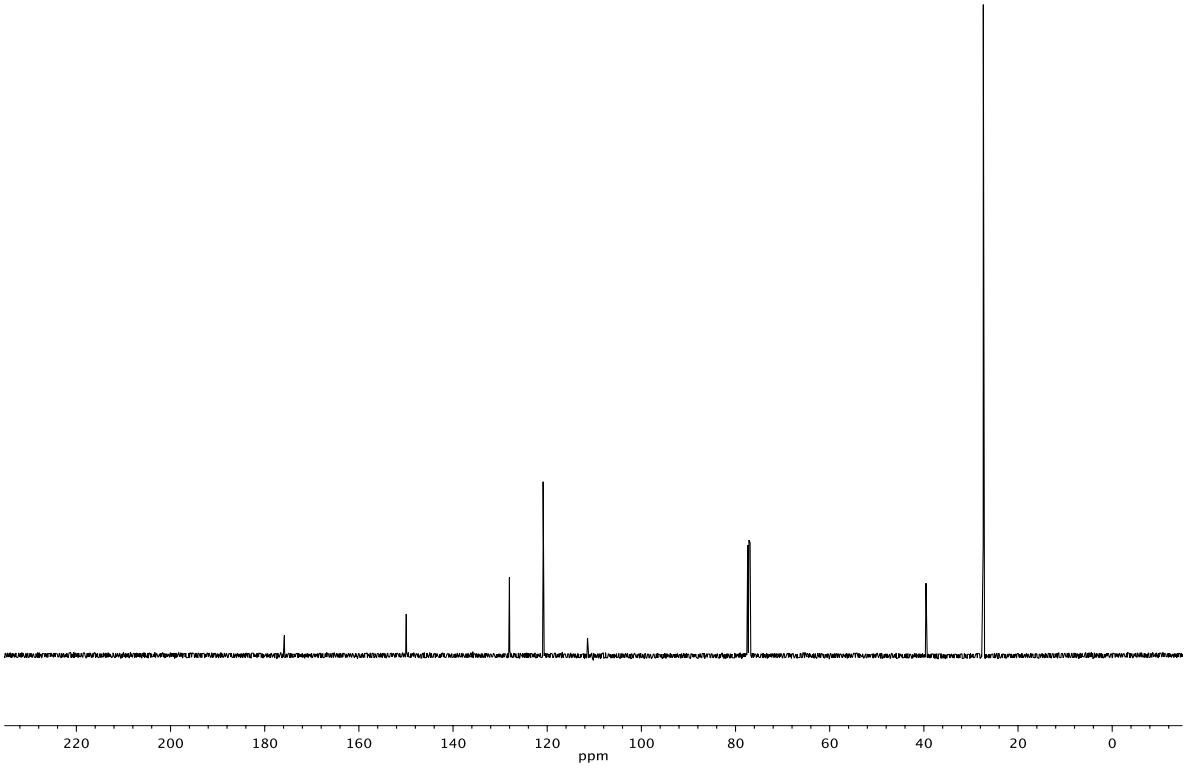
^{13}C NMR (126 MHz, $CDCl_3$) of compound **17**.



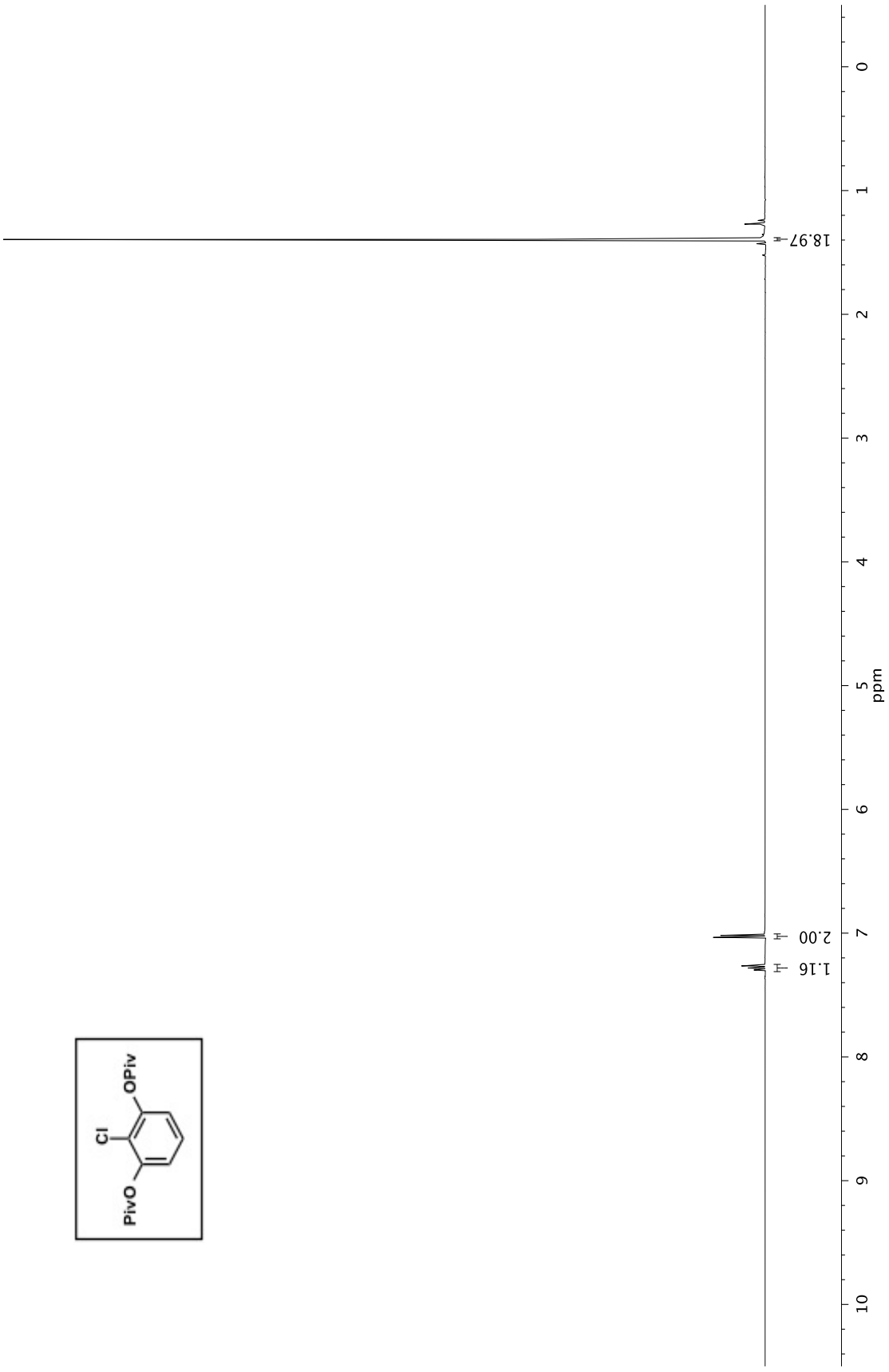
^{1}H NMR (500 MHz, $CDCl_3$) of compound **31**.



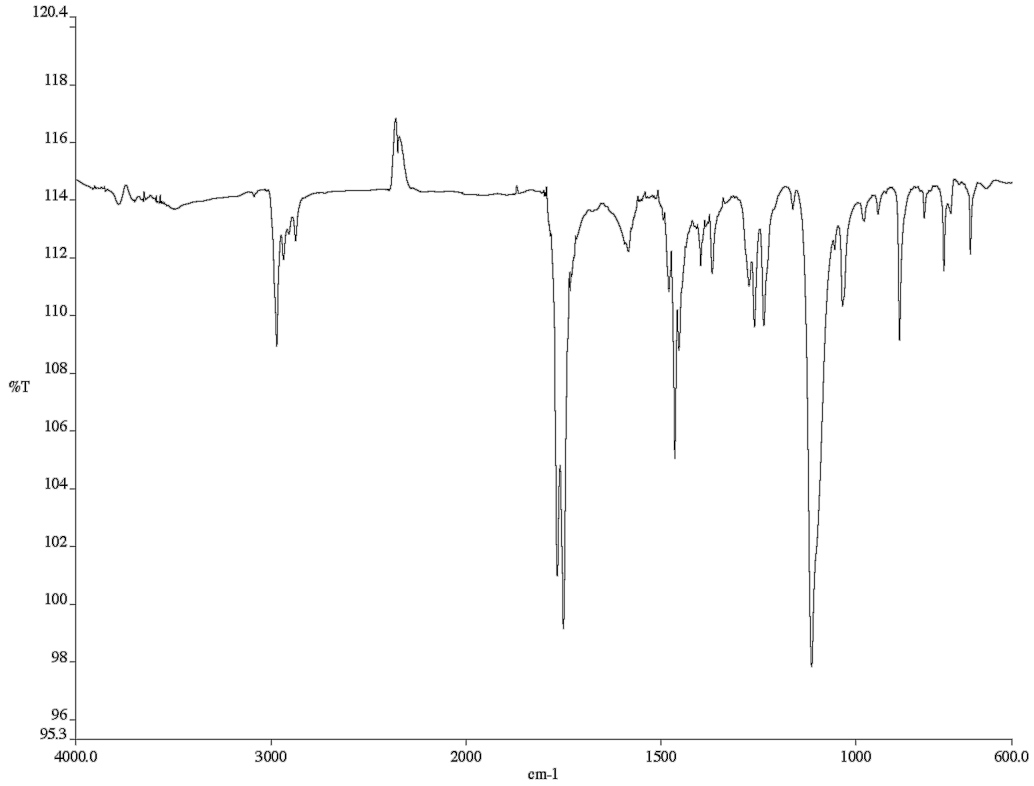
Infrared spectrum (Thin Film, NaCl) of compound **31**.



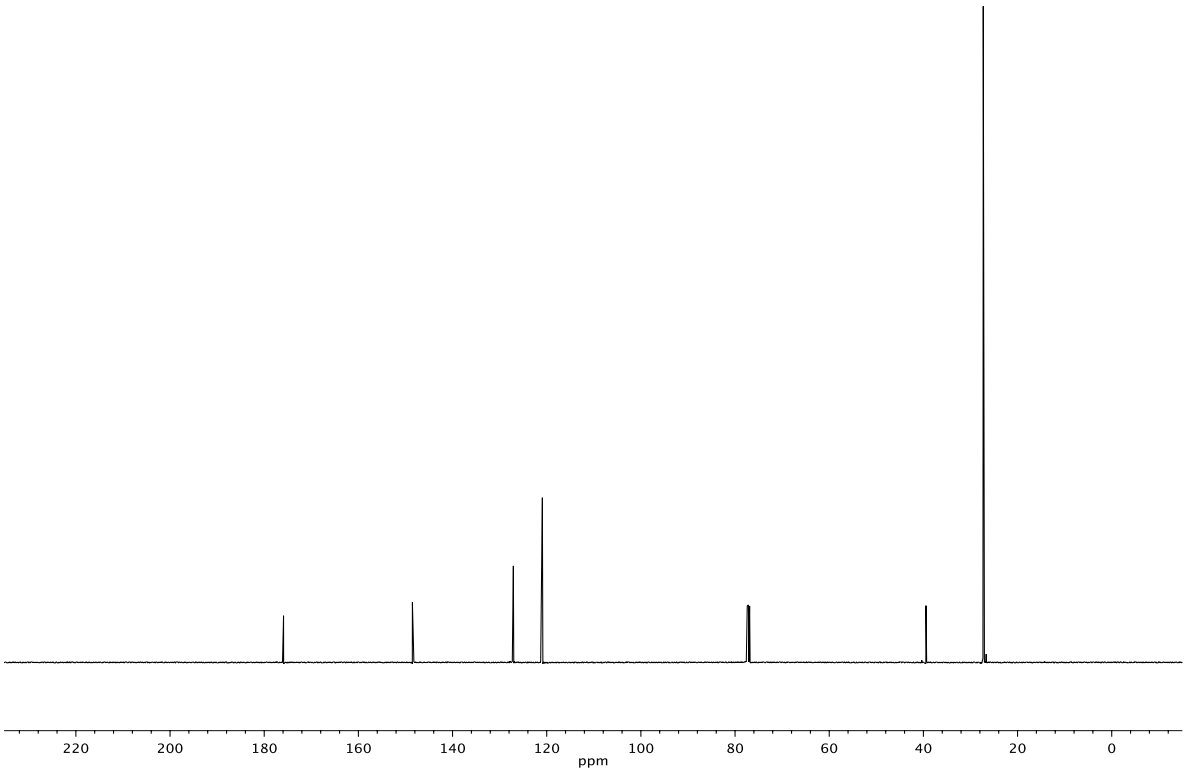
^{13}C NMR (126 MHz, $CDCl_3$) of compound **31**.



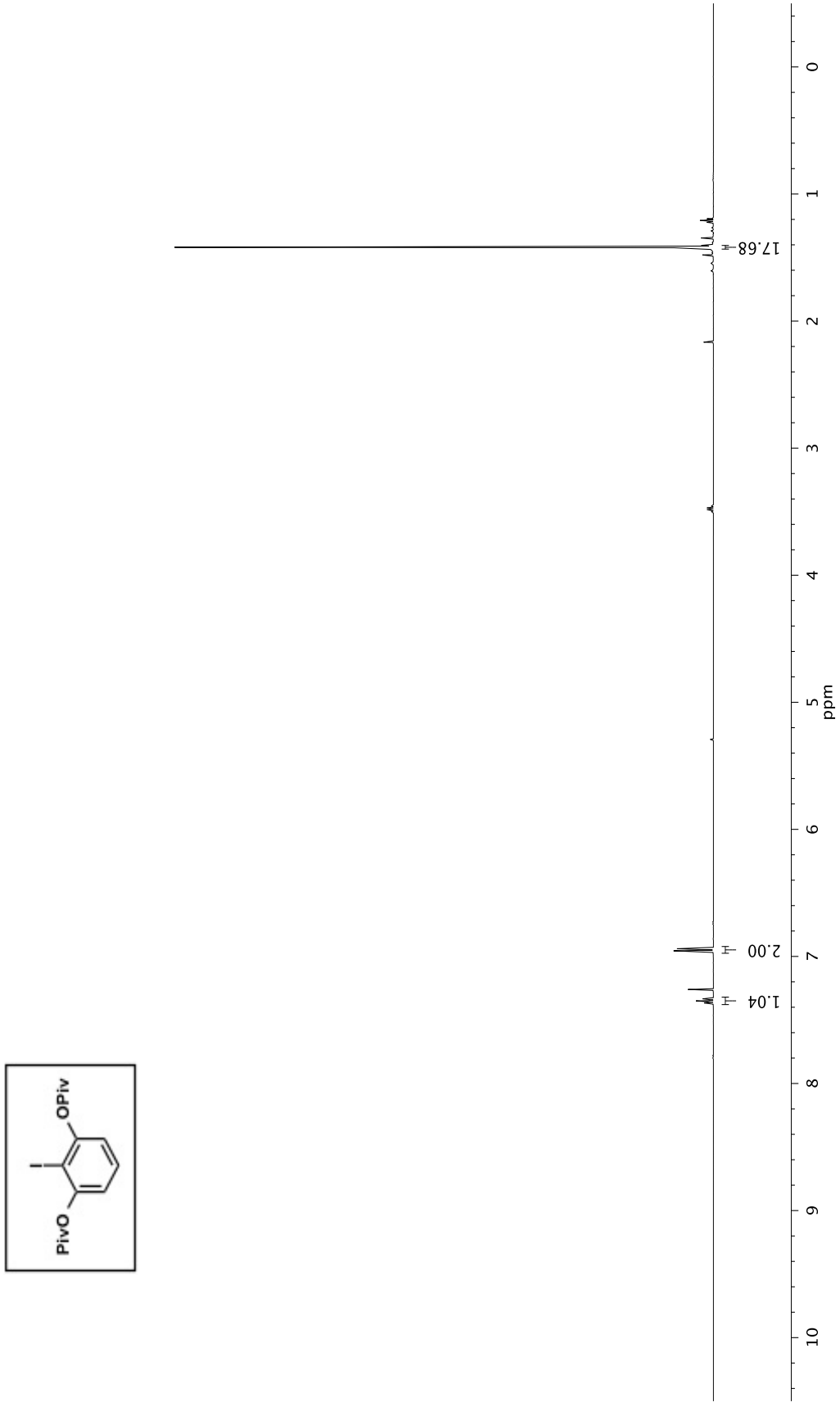
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S-1**.



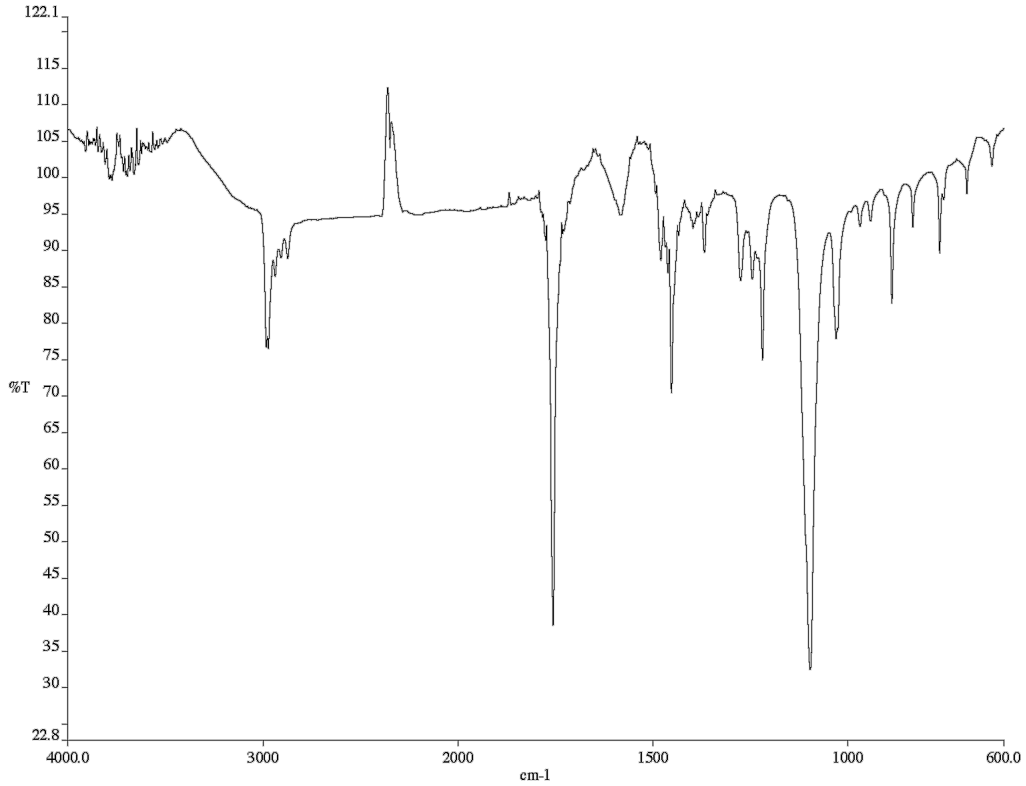
Infrared spectrum (Thin Film, NaCl) of compound **S-1**.



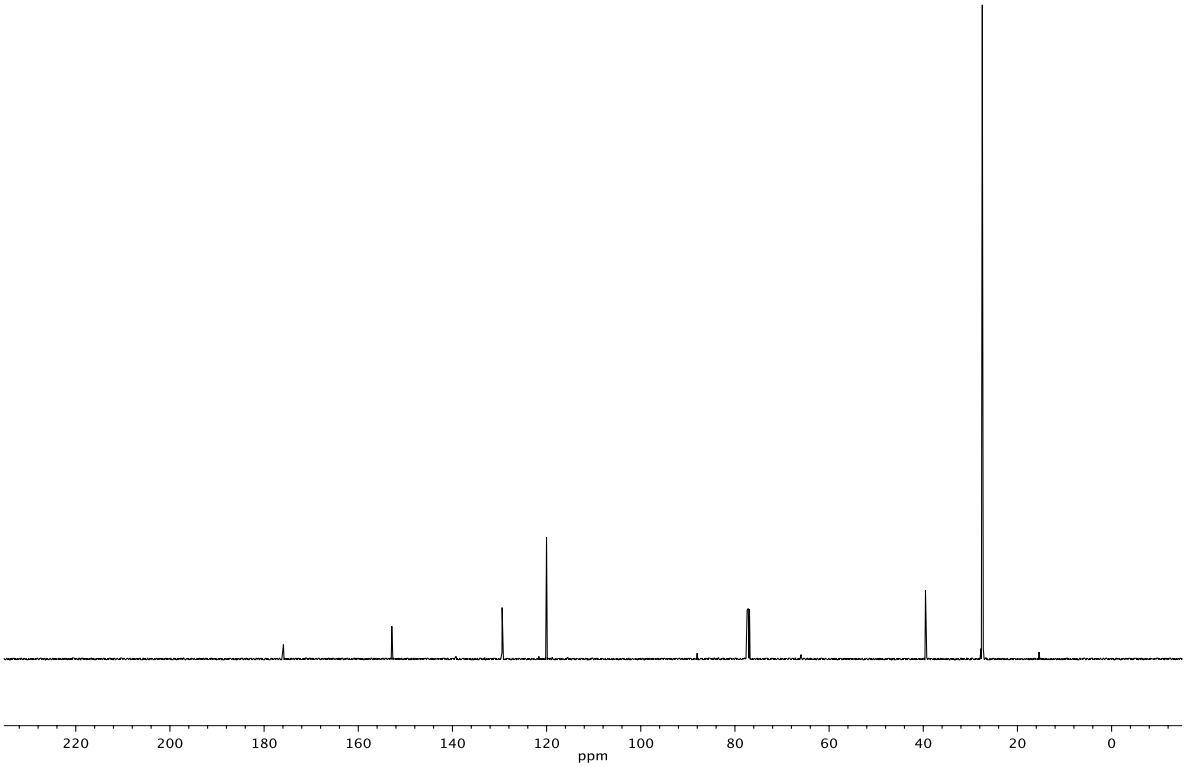
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S-1**.



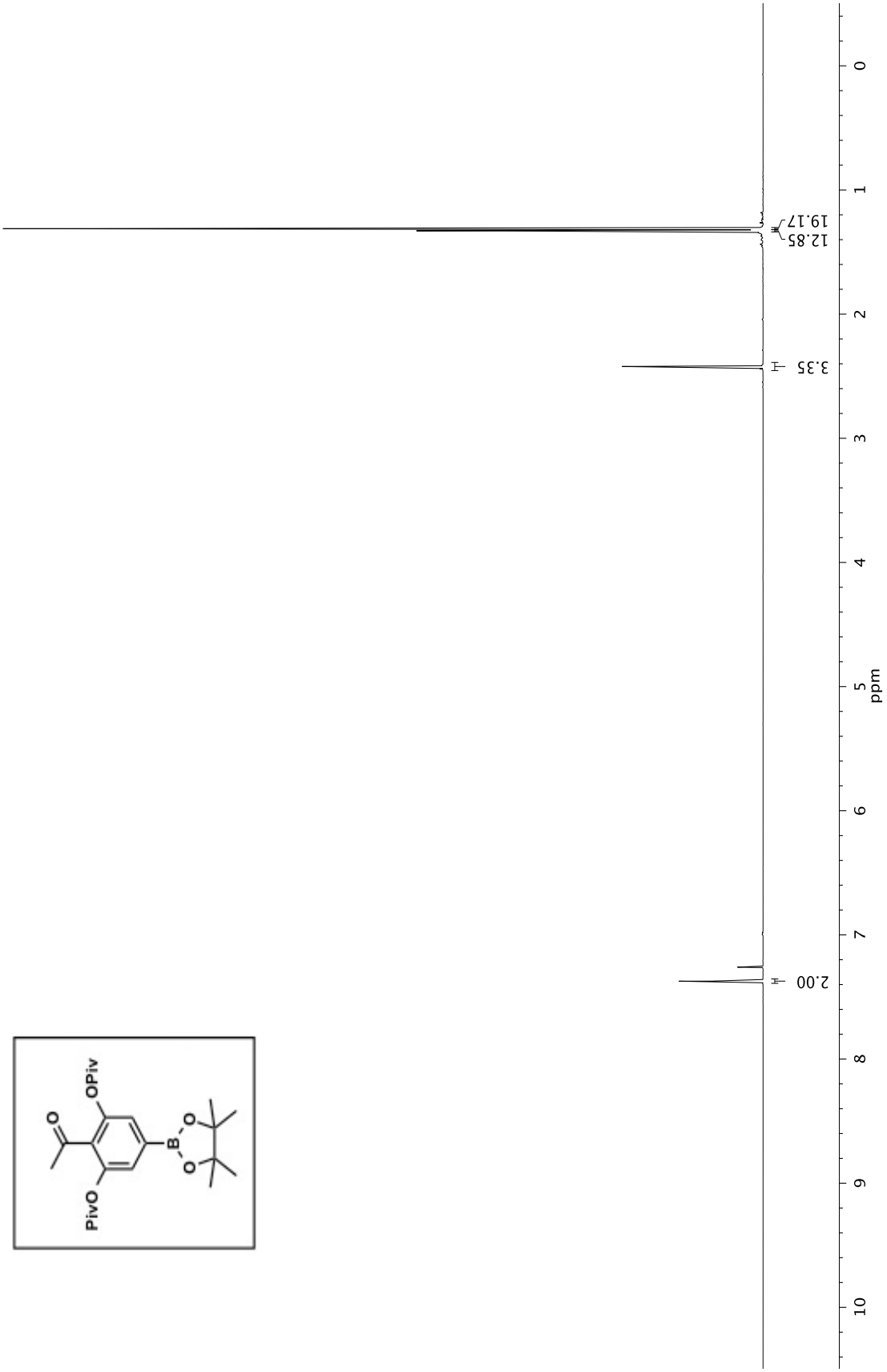
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S-2**.



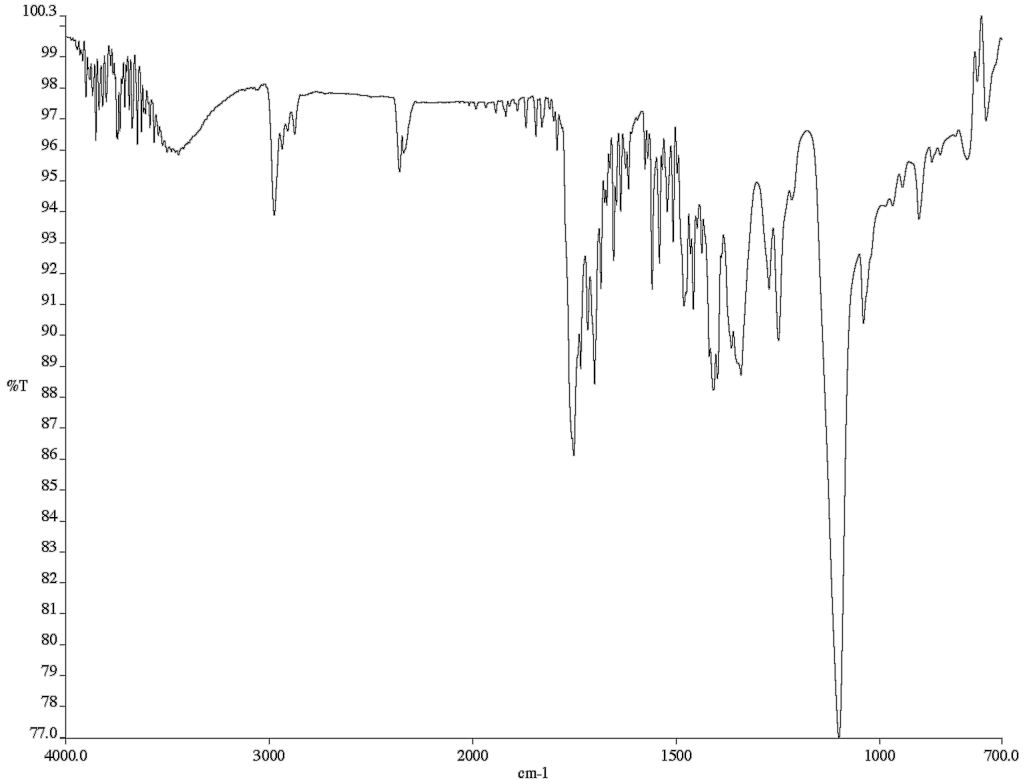
Infrared spectrum (Thin Film, NaCl) of compound **S-2**.



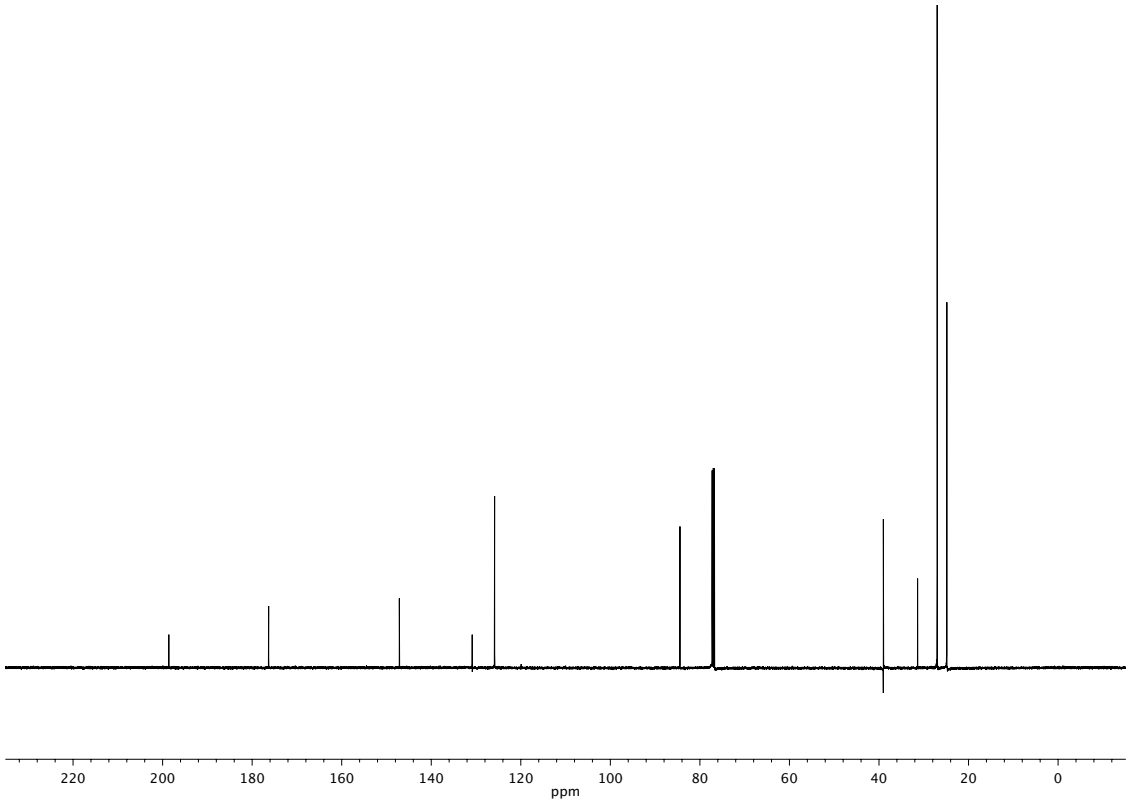
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S-2**.



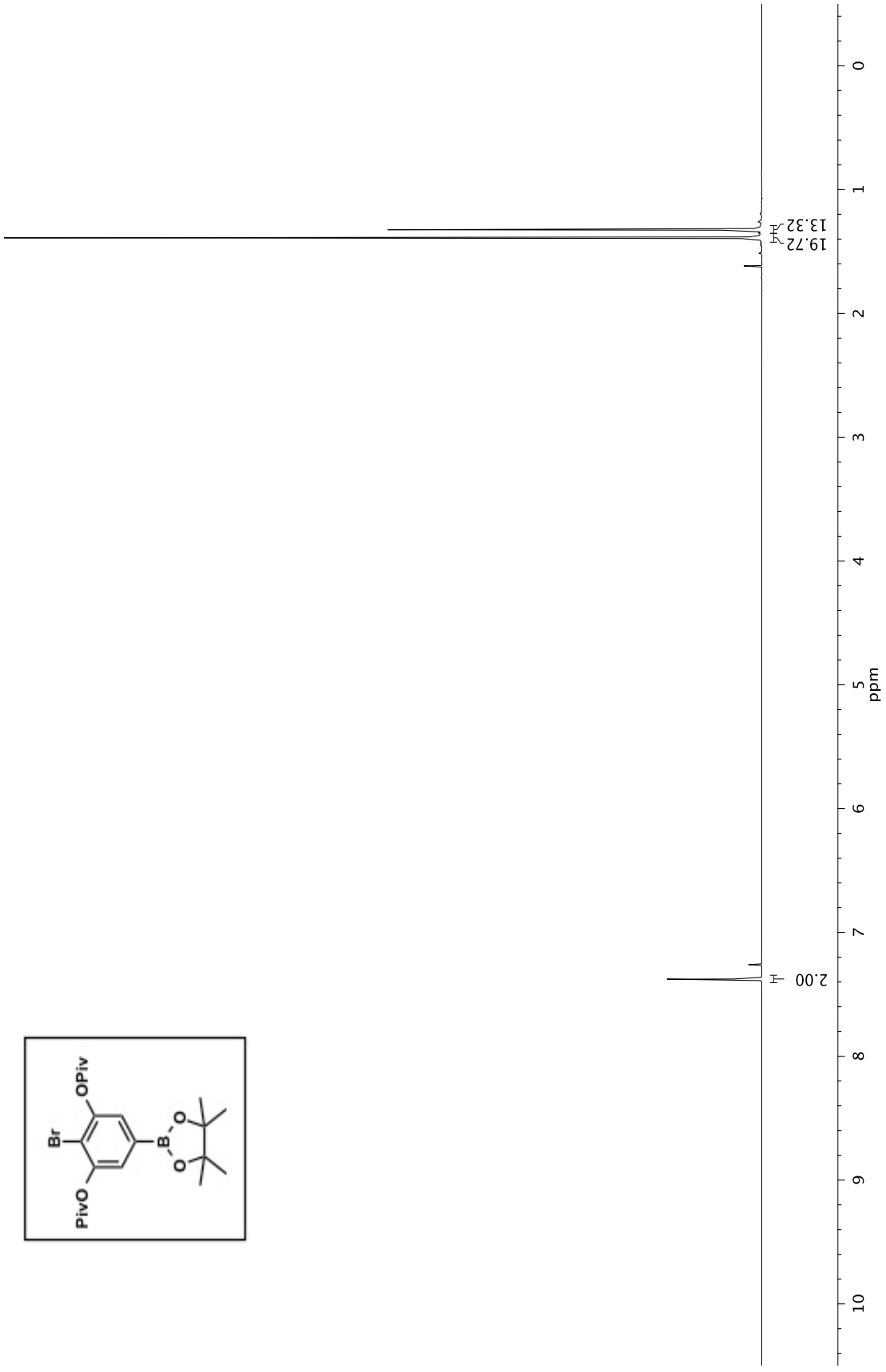
^{1}H NMR (500 MHz, $CDCl_3$) of compound **18**.



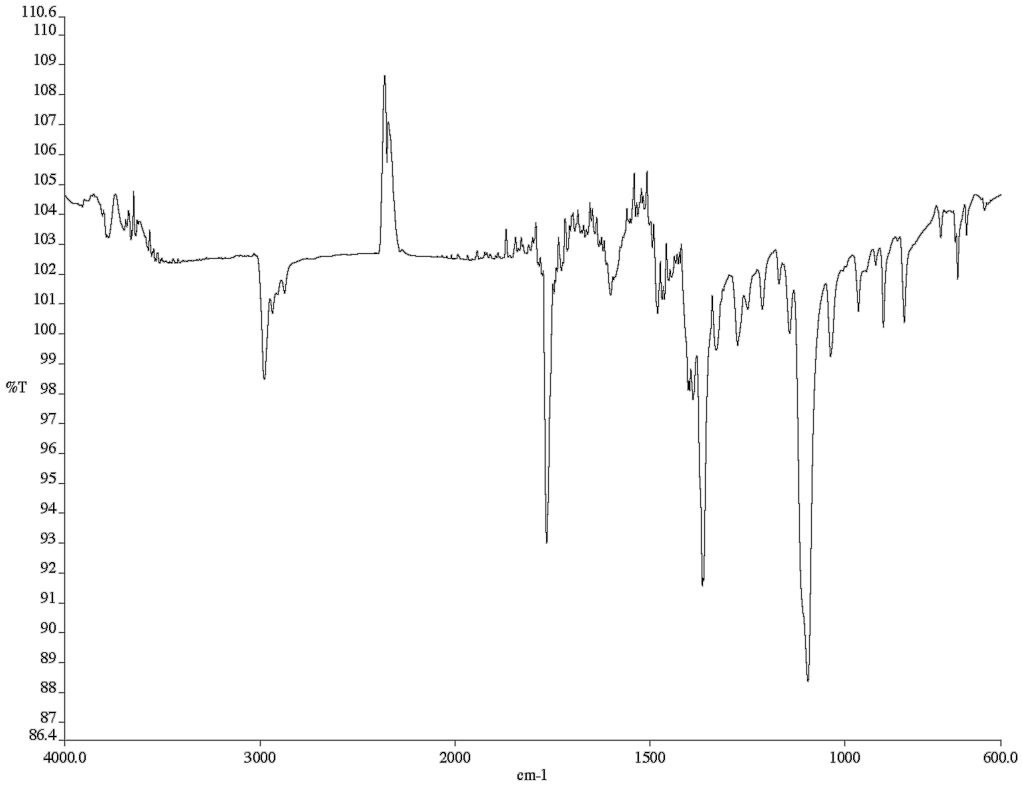
Infrared spectrum (Thin Film, NaCl) of compound **18**.



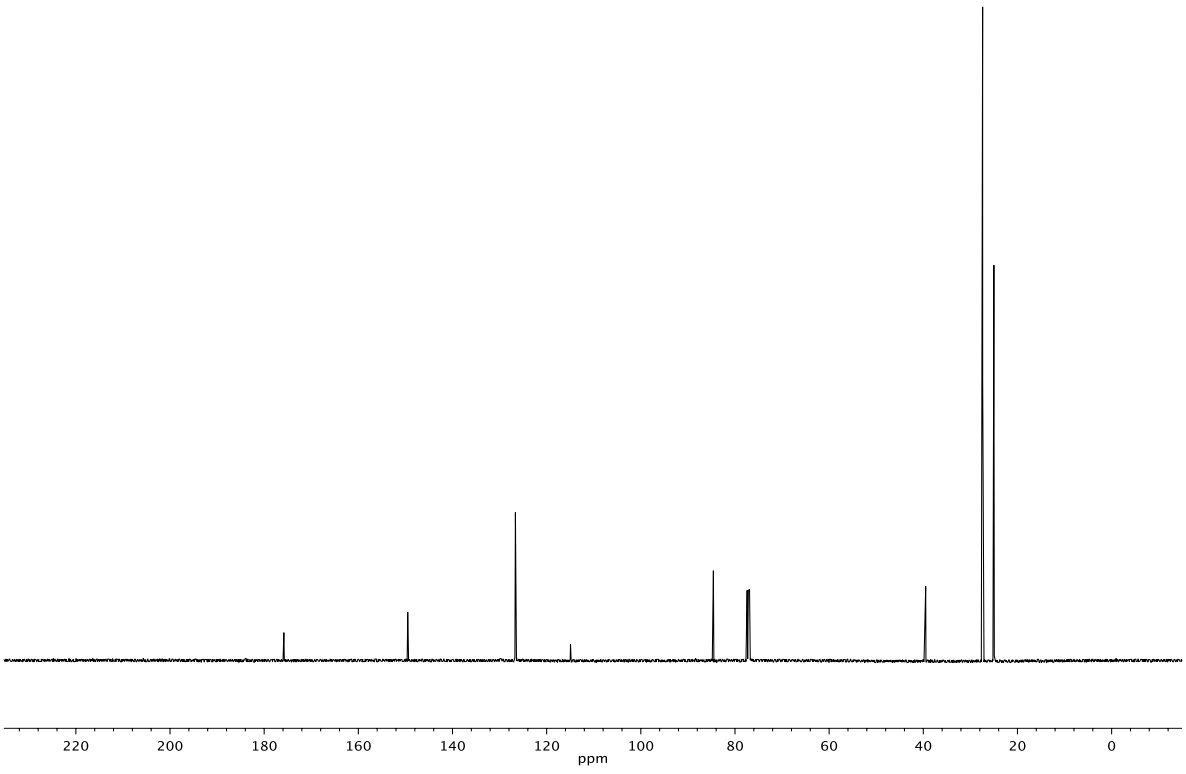
^{13}C NMR (126 MHz, $CDCl_3$) of compound **18**.



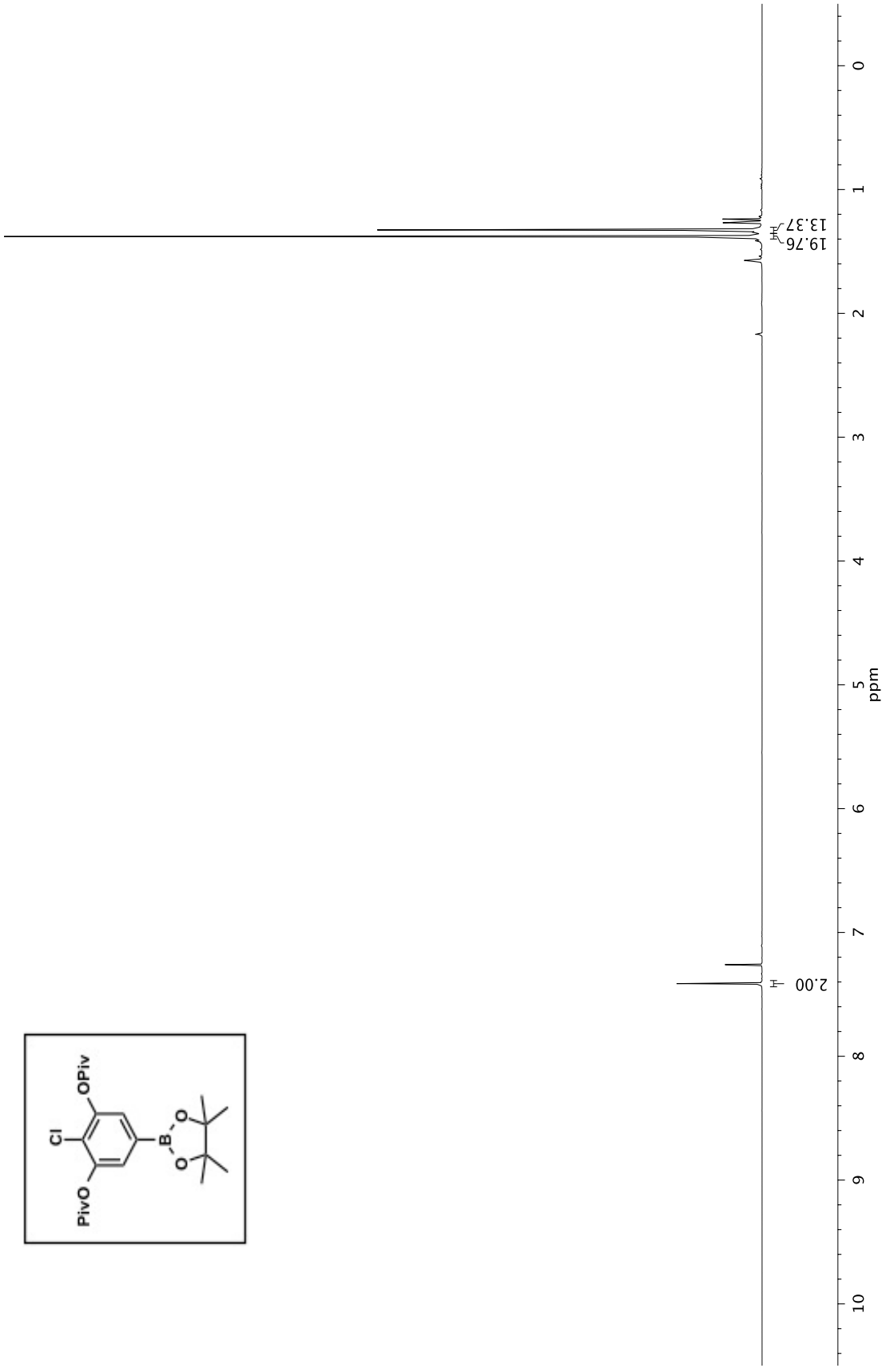
^{1}H NMR (500 MHz, $CDCl_3$) of compound **32**.



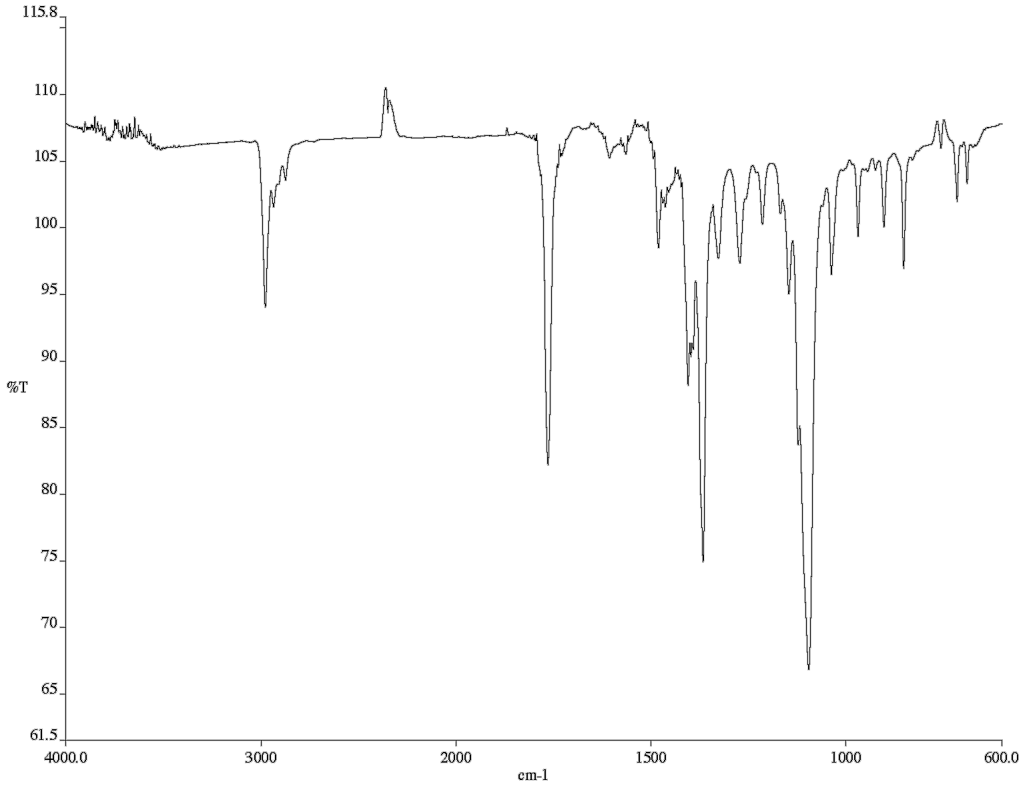
Infrared spectrum (Thin Film, NaCl) of compound **32**.



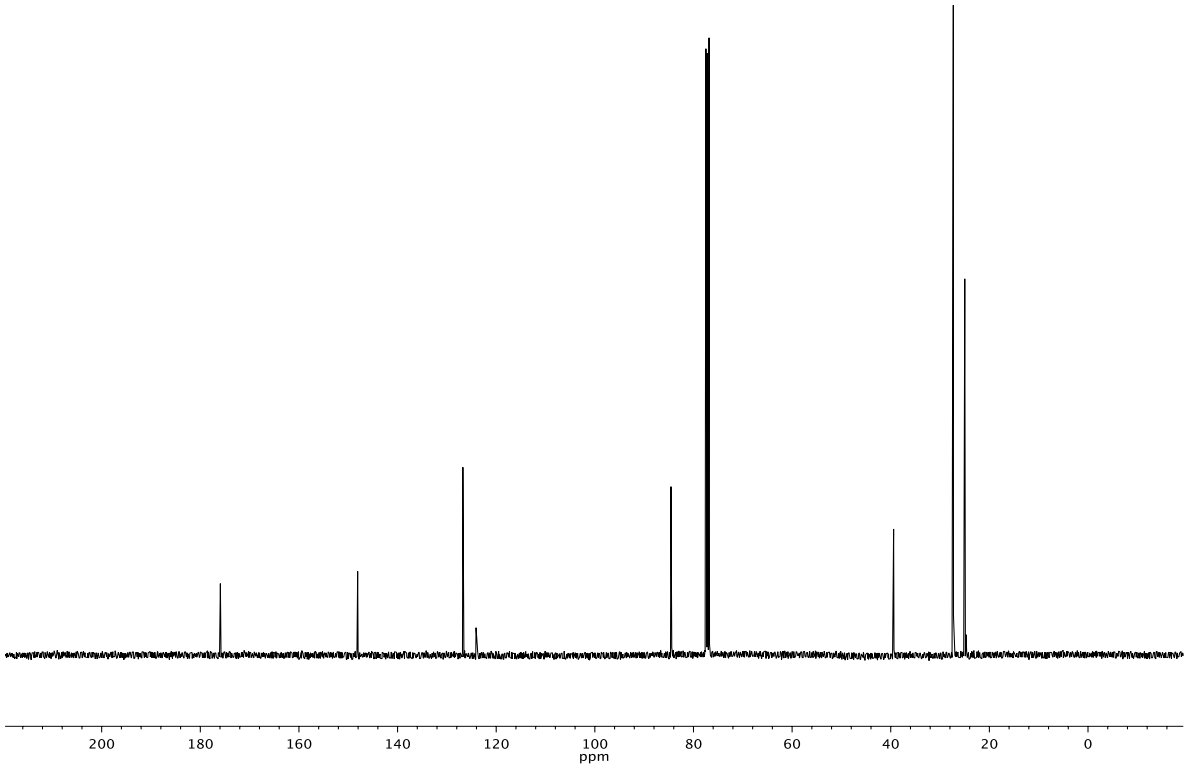
^{13}C NMR (126 MHz, $CDCl_3$) of compound **32**.



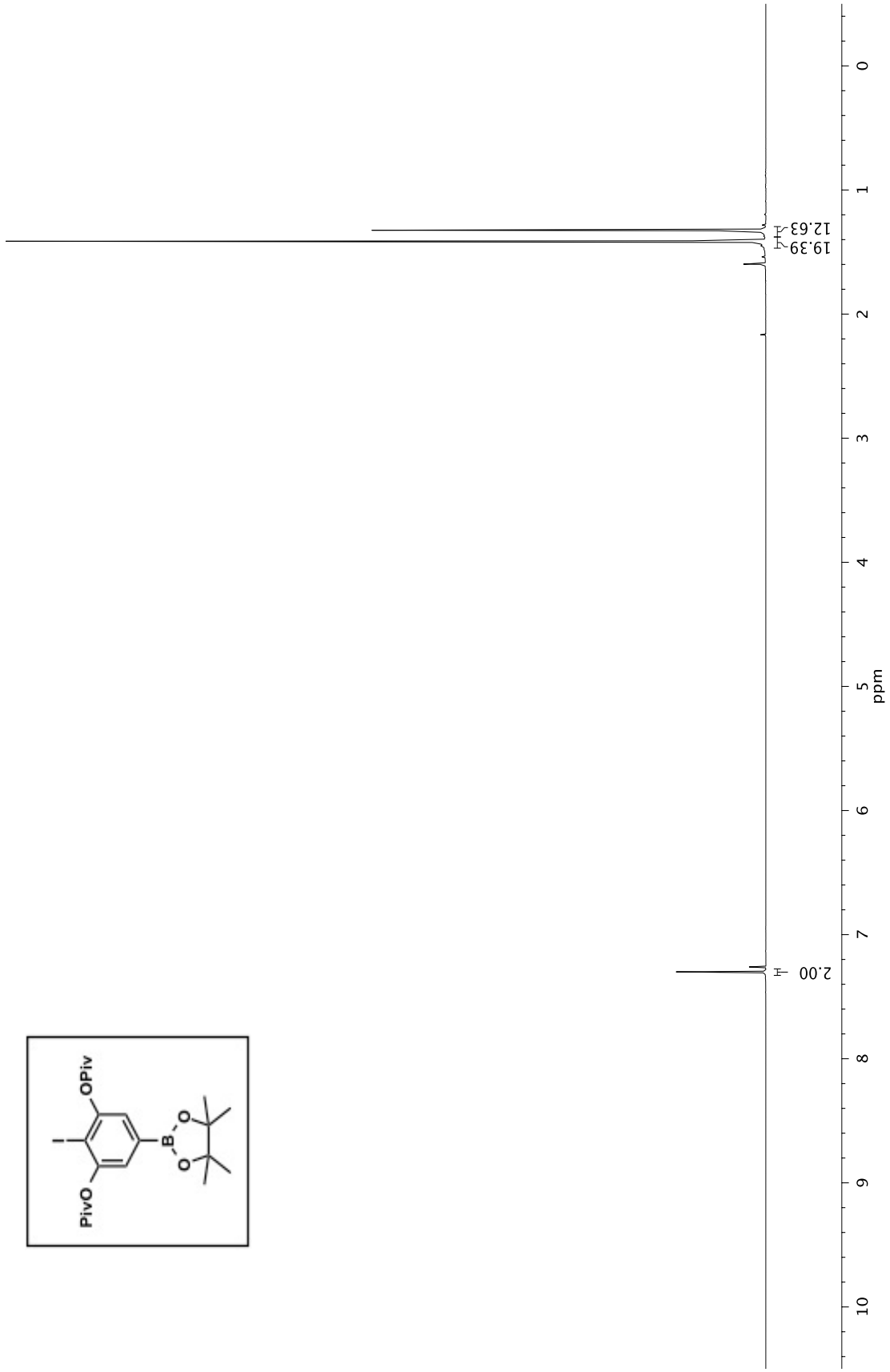
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S-3**.



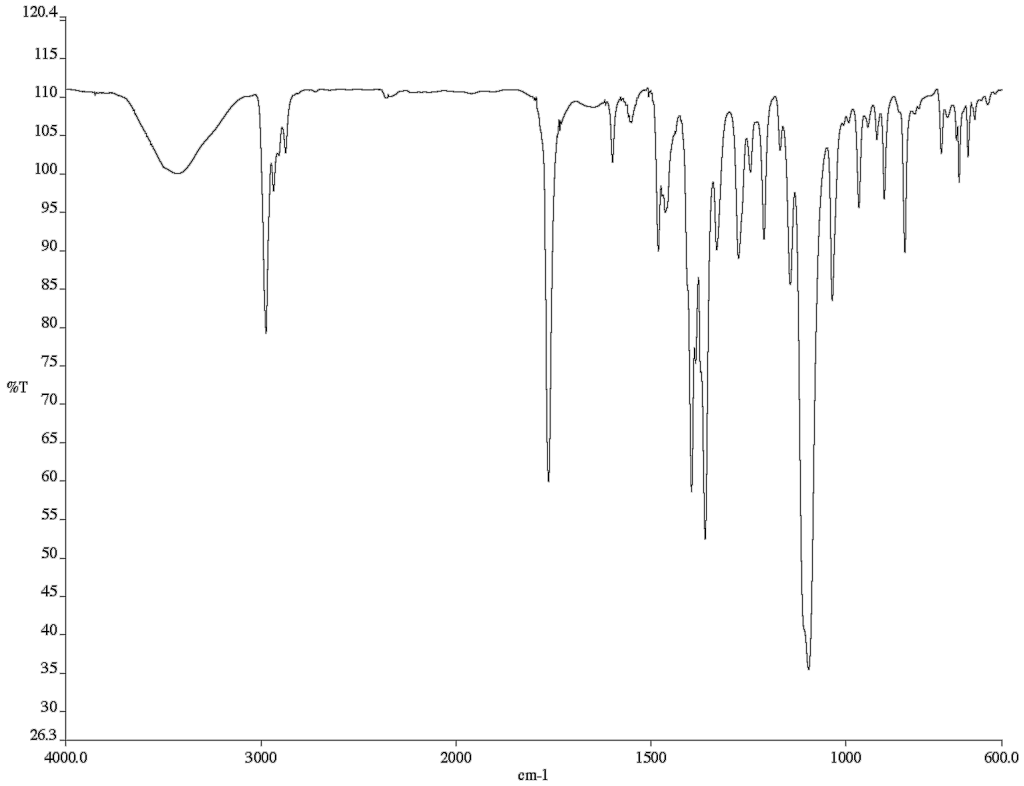
Infrared spectrum (Thin Film, NaCl) of compound **S-3**.



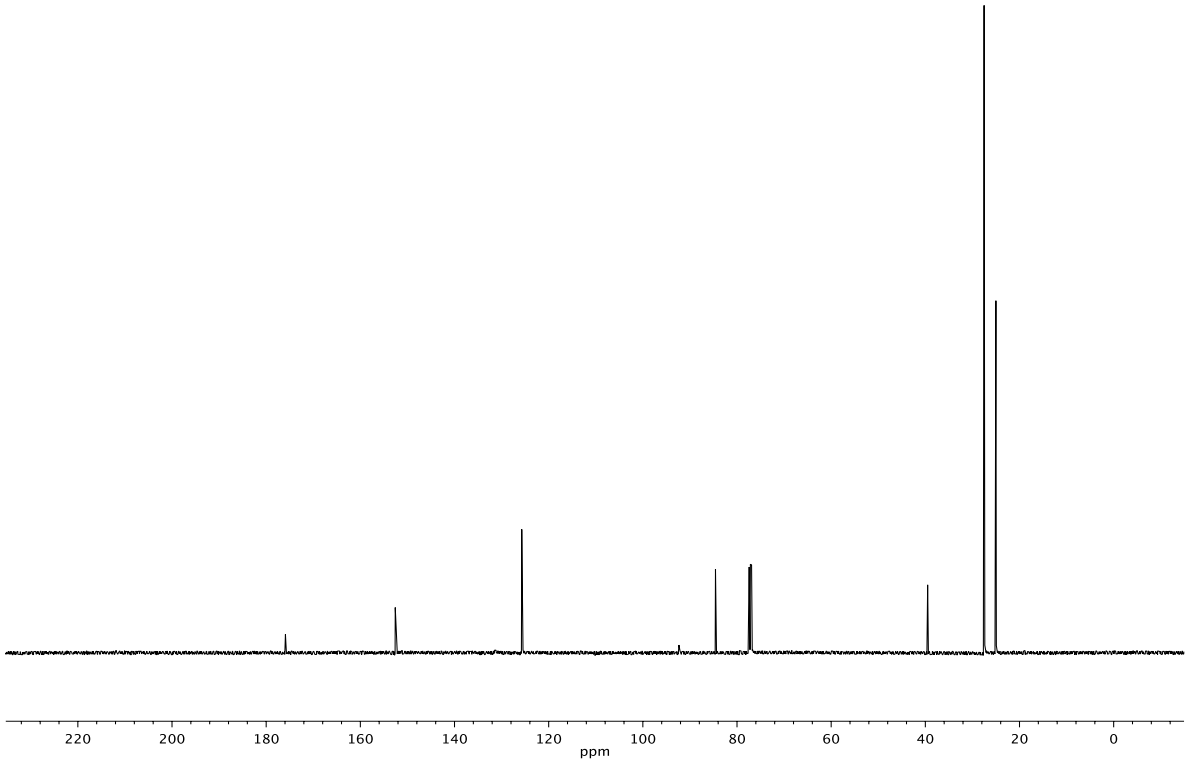
^{13}C NMR (100 MHz, $CDCl_3$) of compound **S-3**.



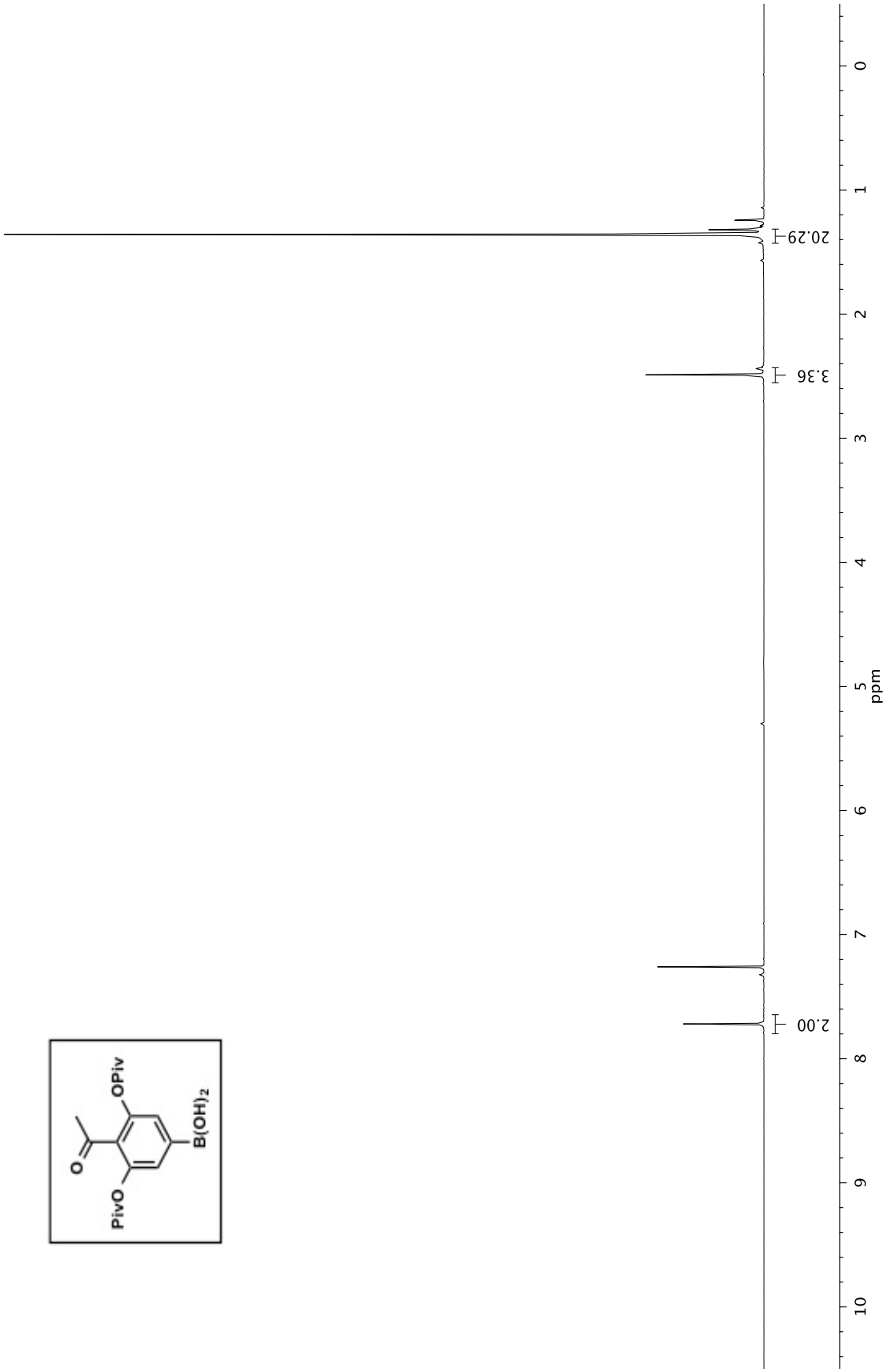
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S-4**.



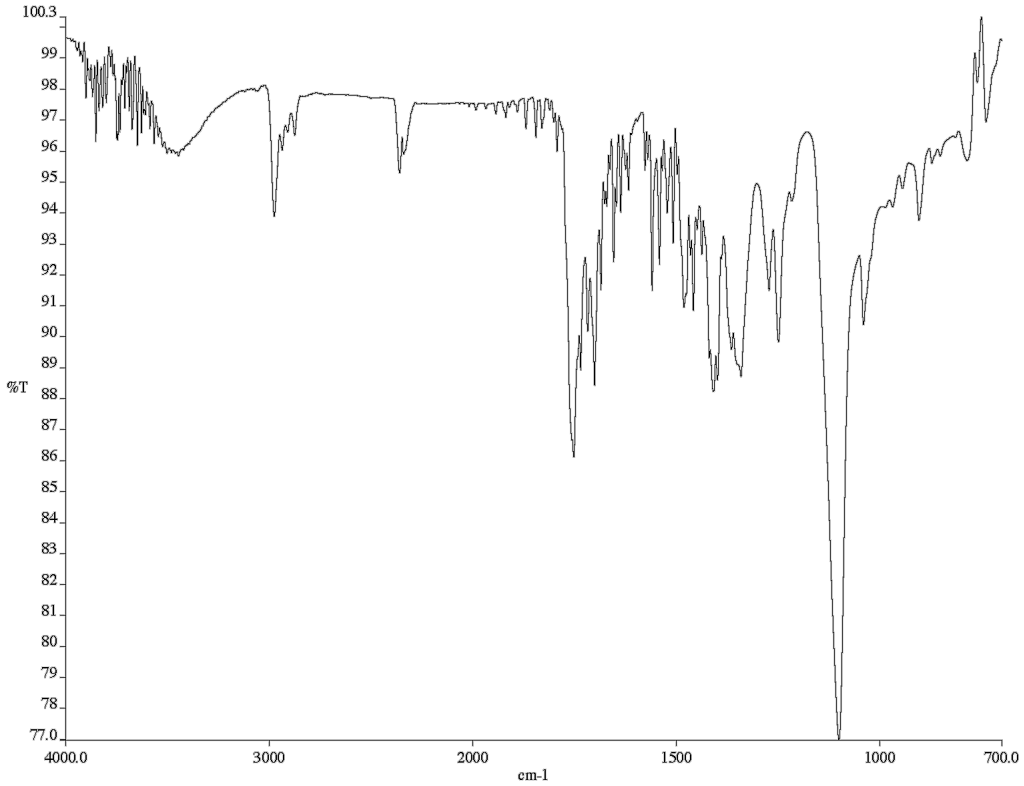
Infrared spectrum (Thin Film, NaCl) of compound **S-4**.



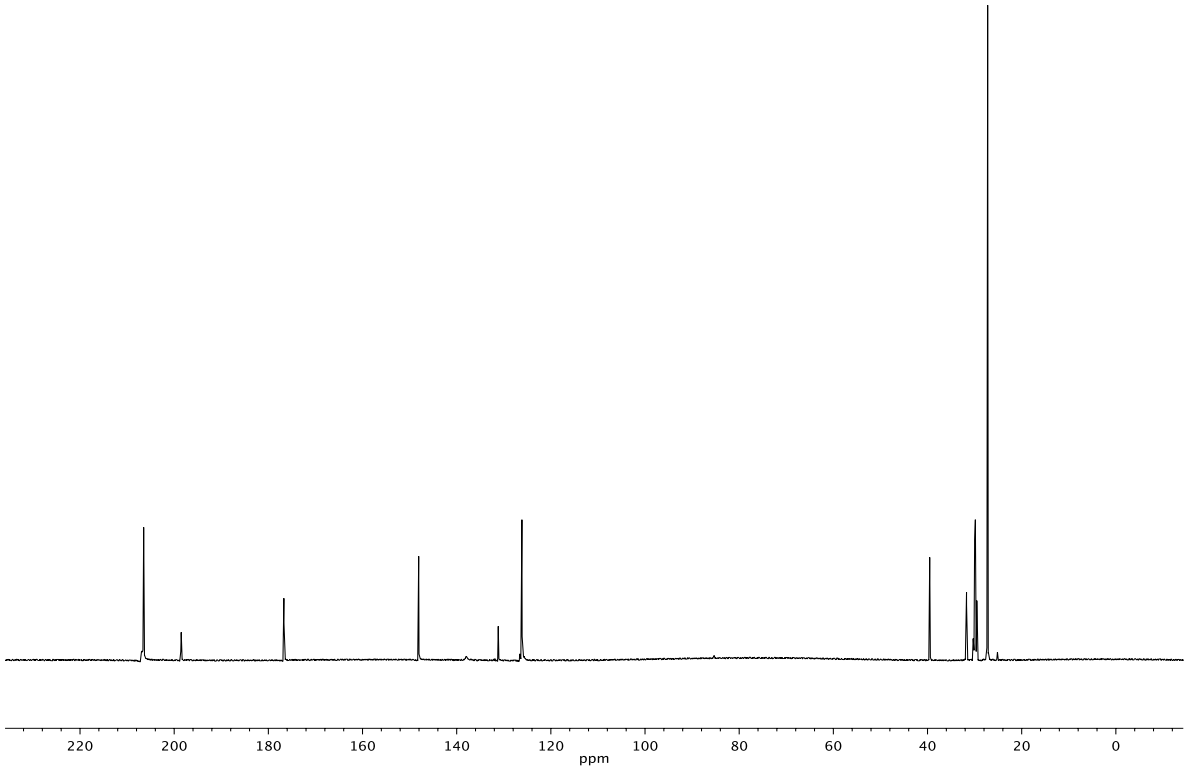
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S-4**.



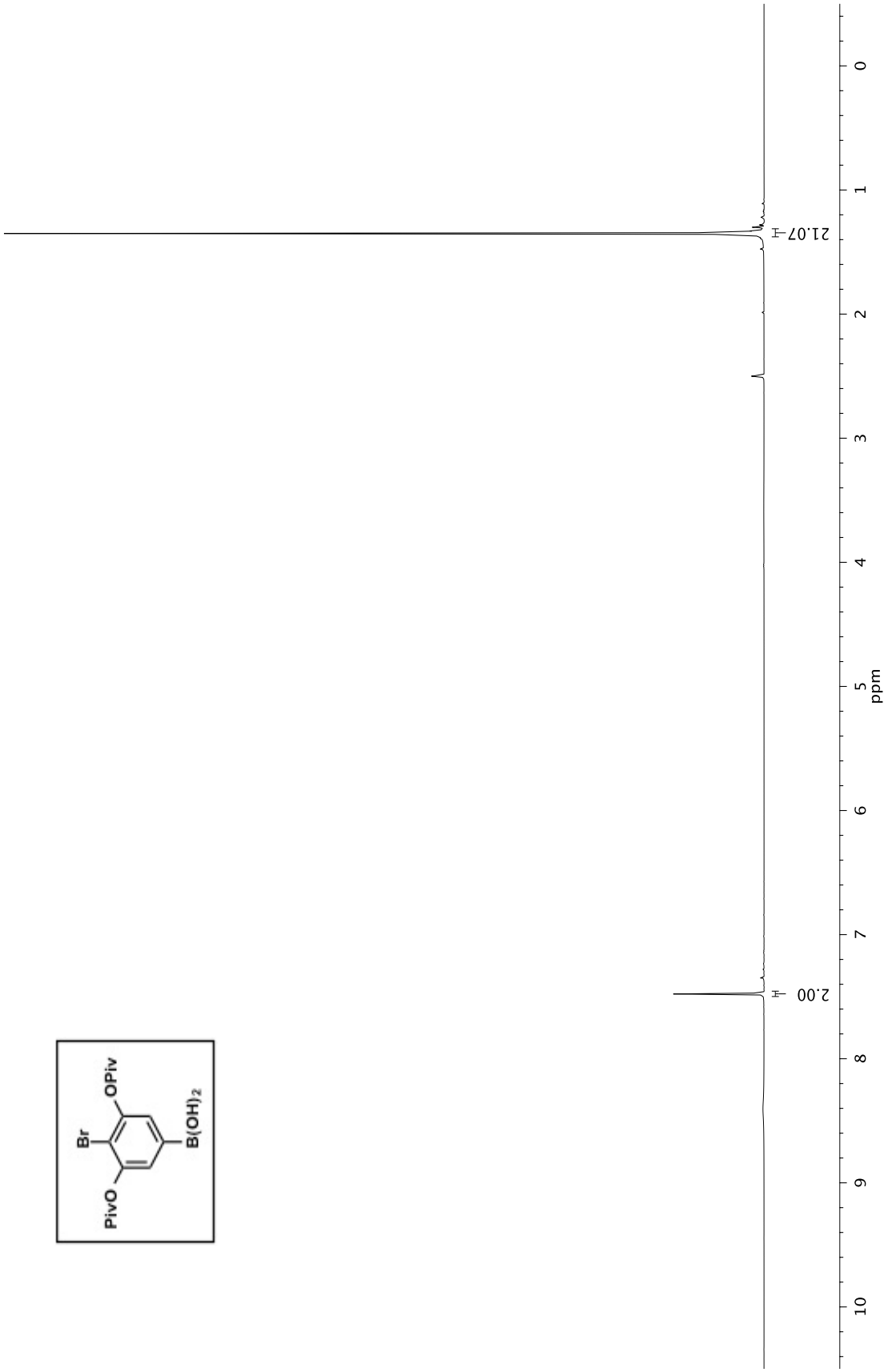
^{1}H NMR (300 MHz, $CDCl_3$) of compound **19**.



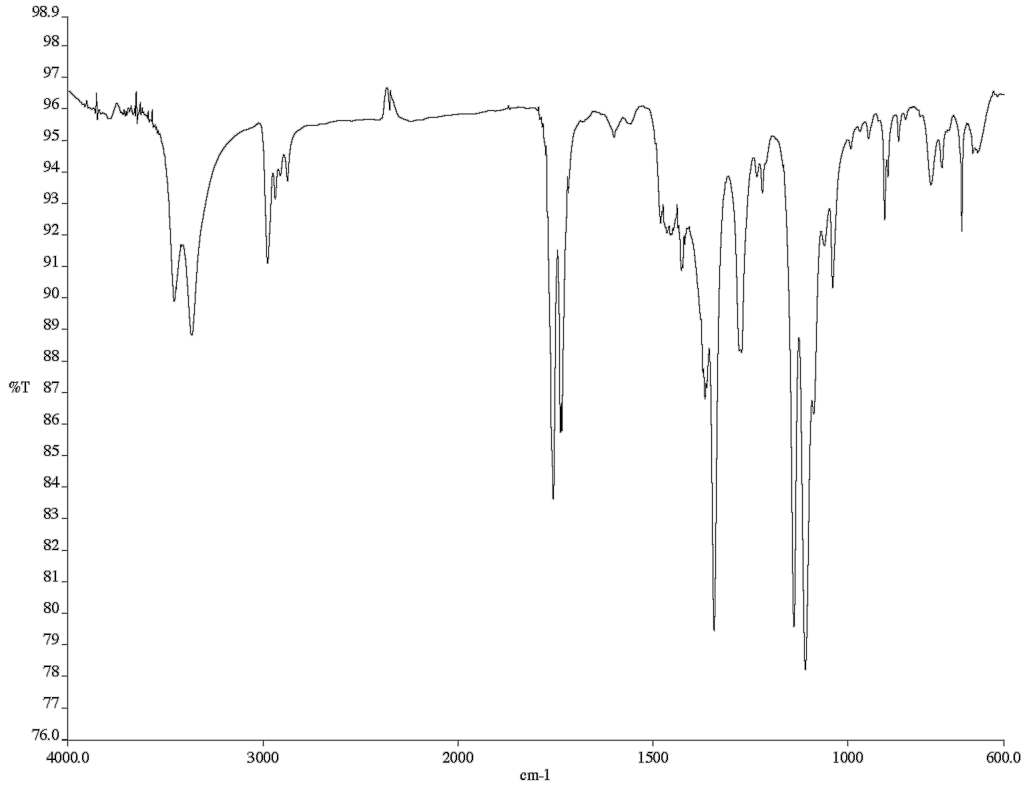
Infrared spectrum (Thin Film, NaCl) of compound **19**.



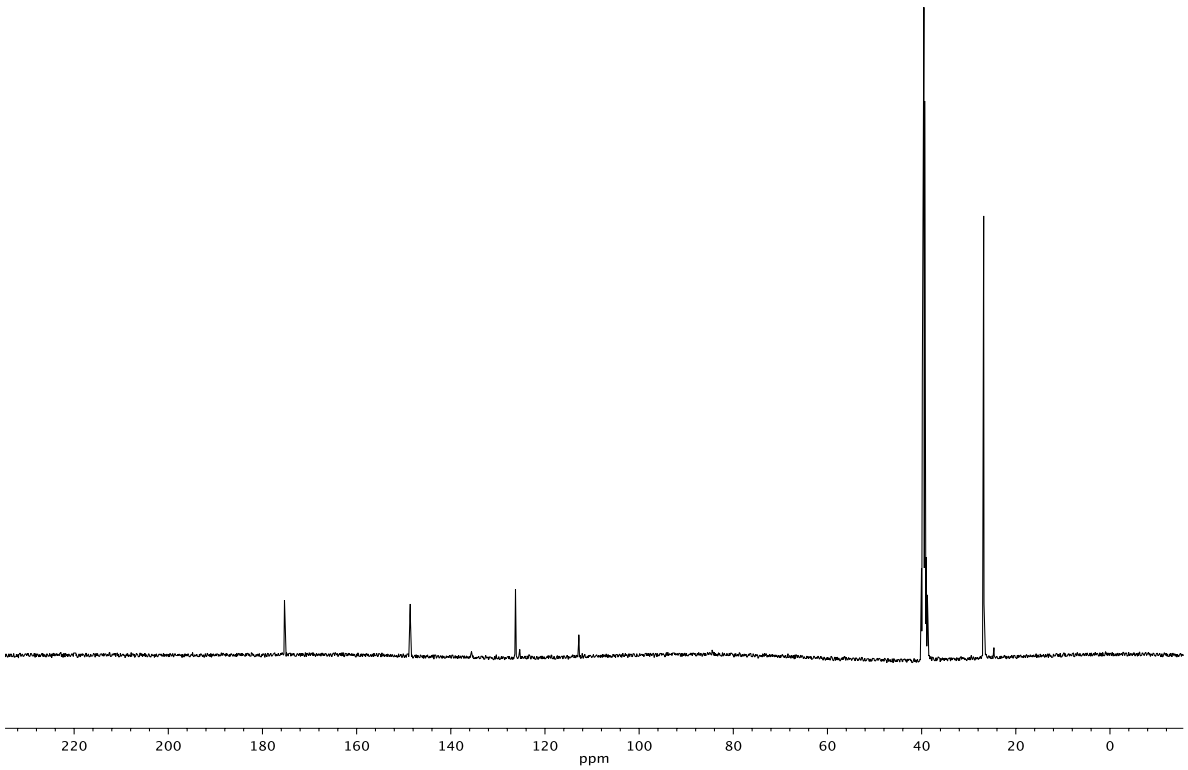
^{13}C NMR (126 MHz, $(CD_3)_2CO$) of compound **19**.



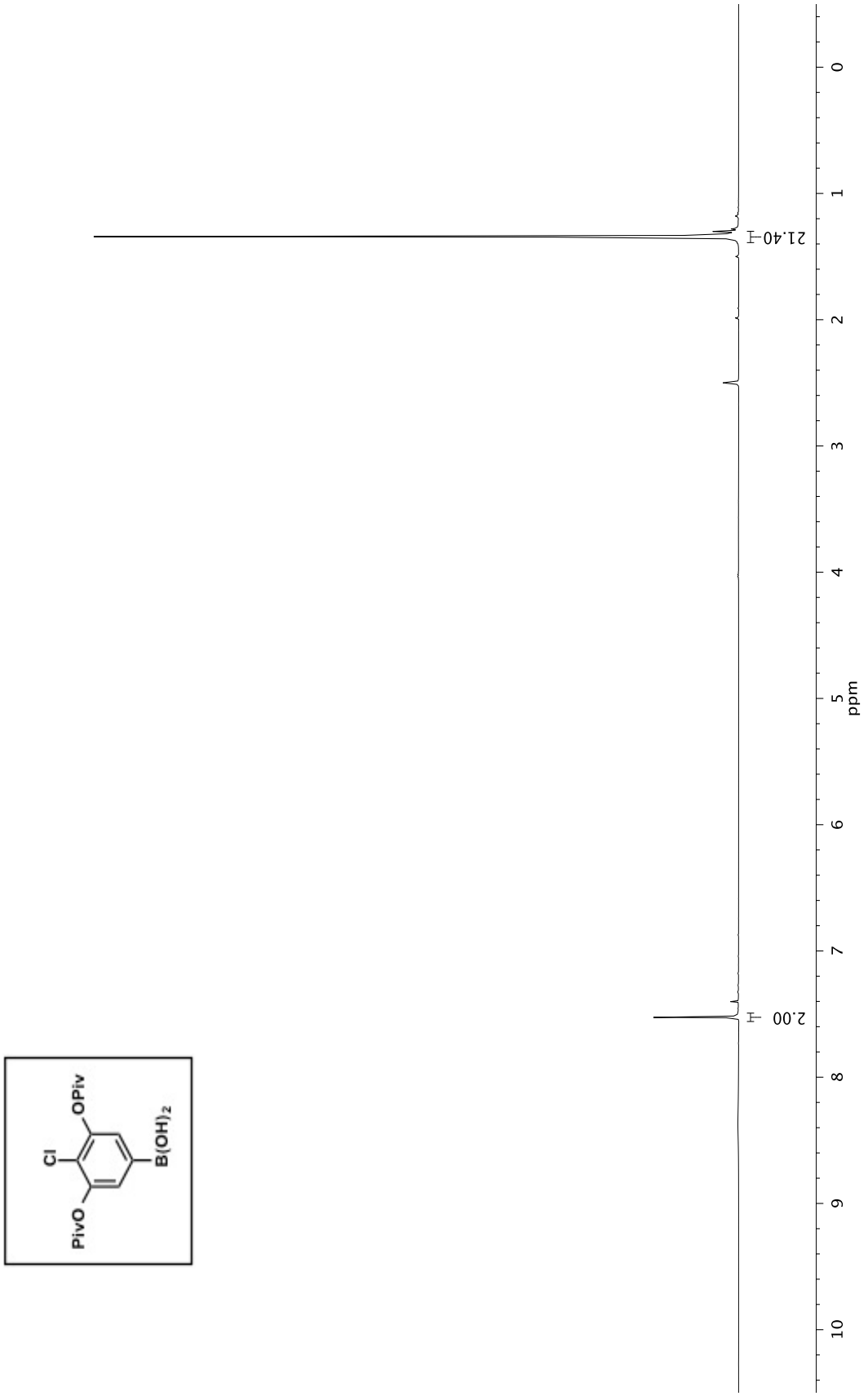
^{1}H NMR (500 MHz, $(CD_3)_2SO$) of compound **33**.



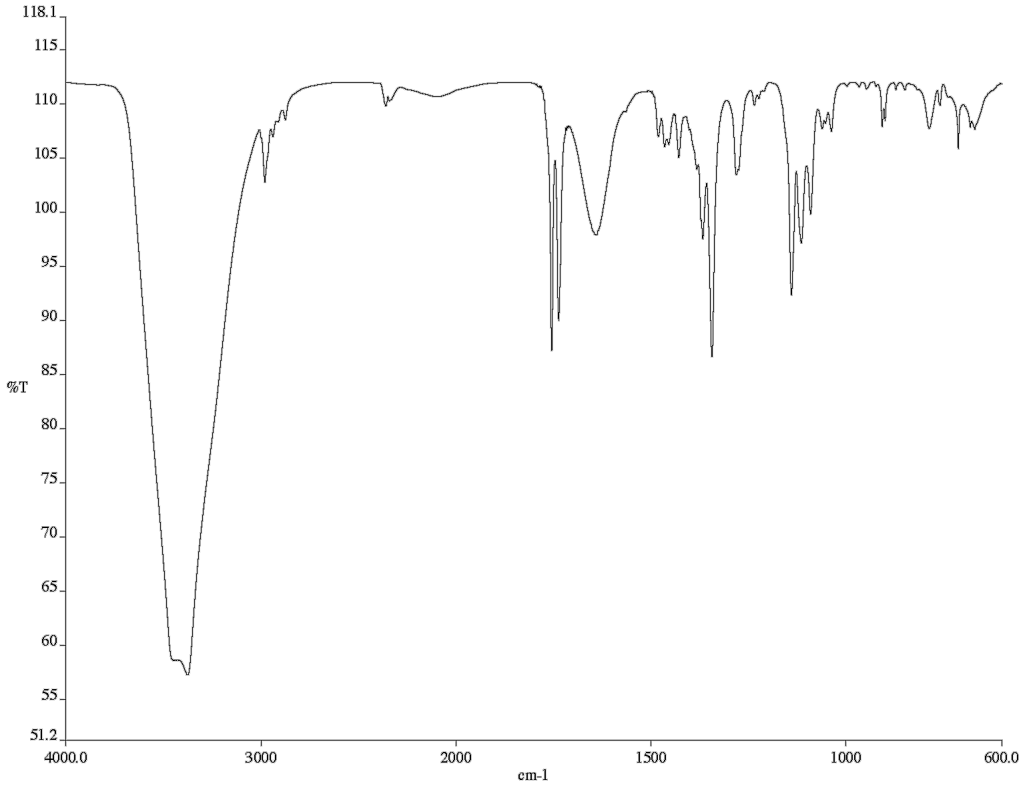
Infrared spectrum (Thin Film, NaCl) of compound **33**.



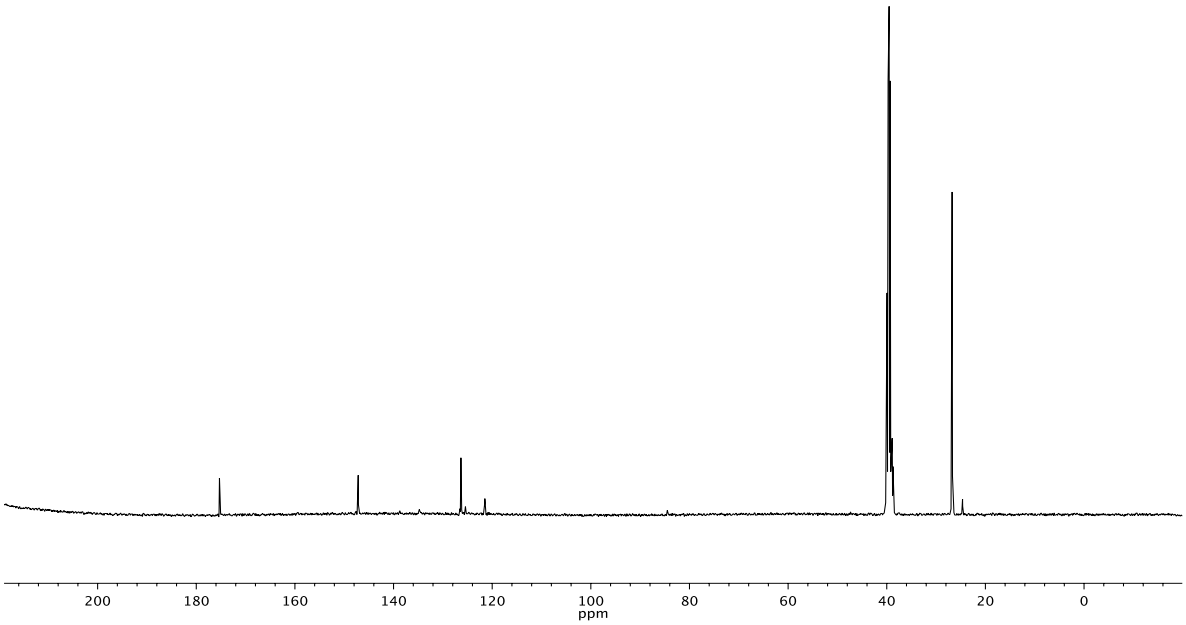
^{13}C NMR (126 MHz, $(CD_3)_2SO$) of compound **33**.



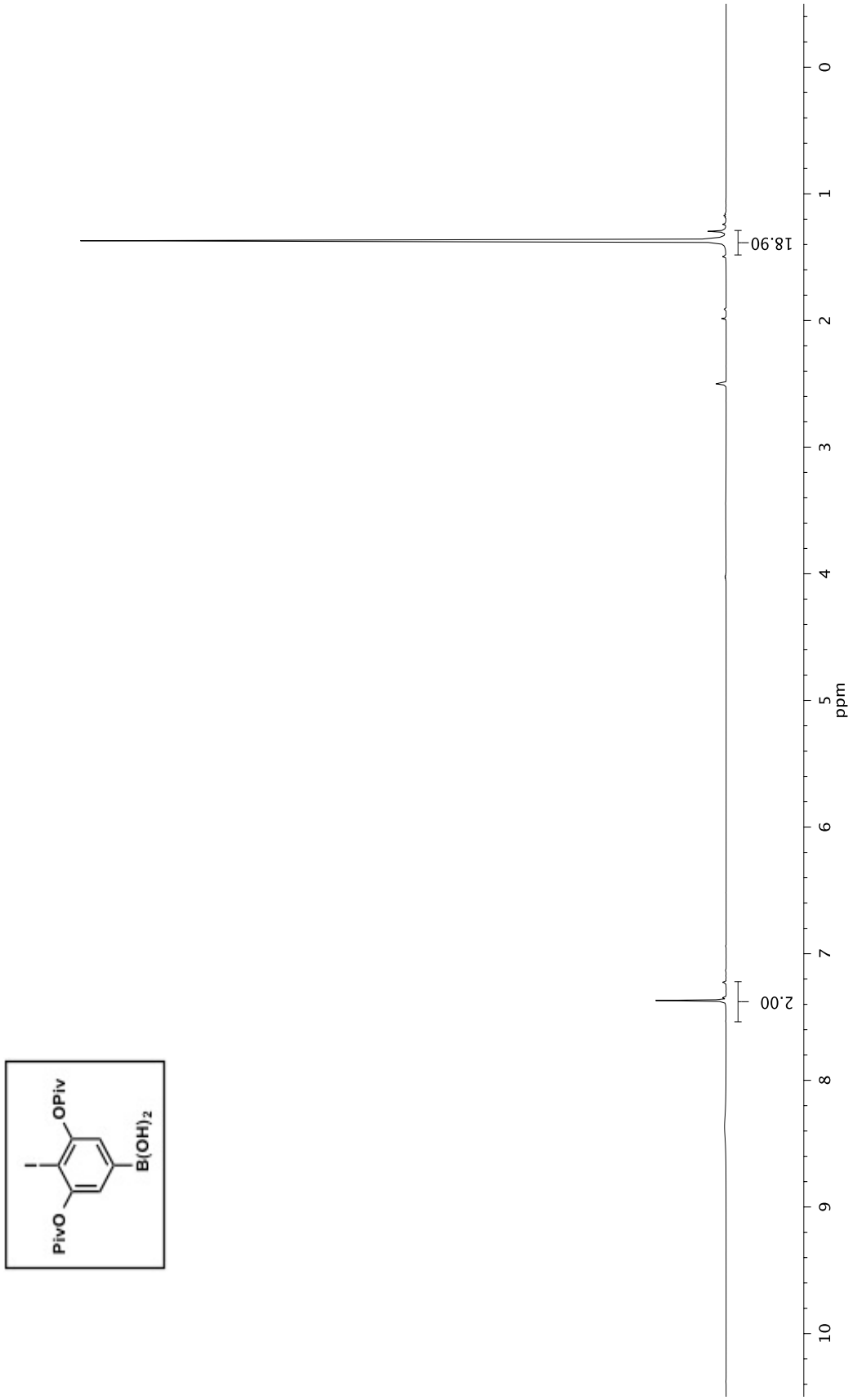
^{1}H NMR (400 MHz, $(CD_3)_2SO$) of compound **S-5**.



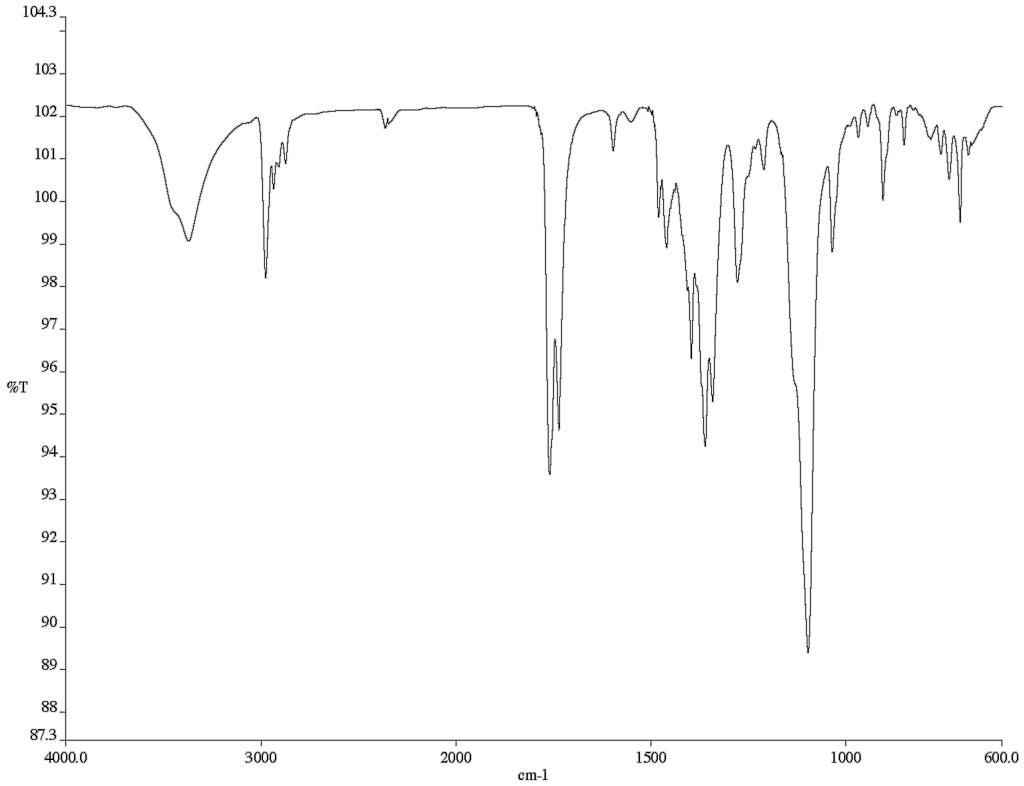
Infrared spectrum (Thin Film, NaCl) of compound **S-5**.



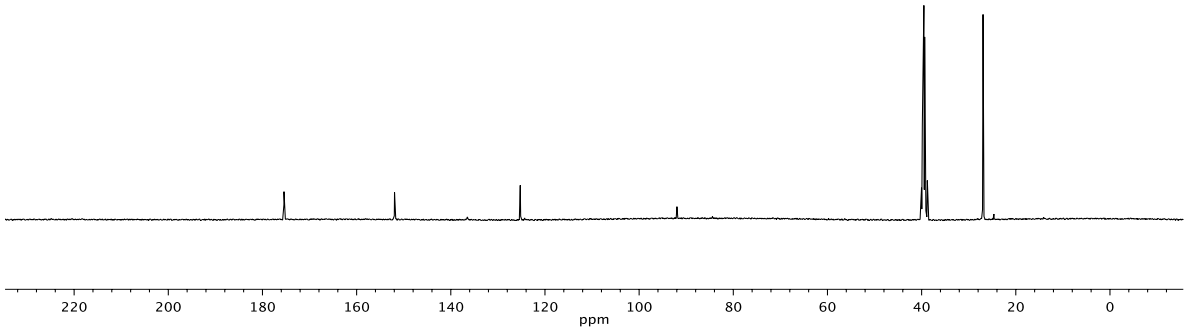
^{13}C NMR (100 MHz, $(CD_3)_2SO$) of compound **S-5**.



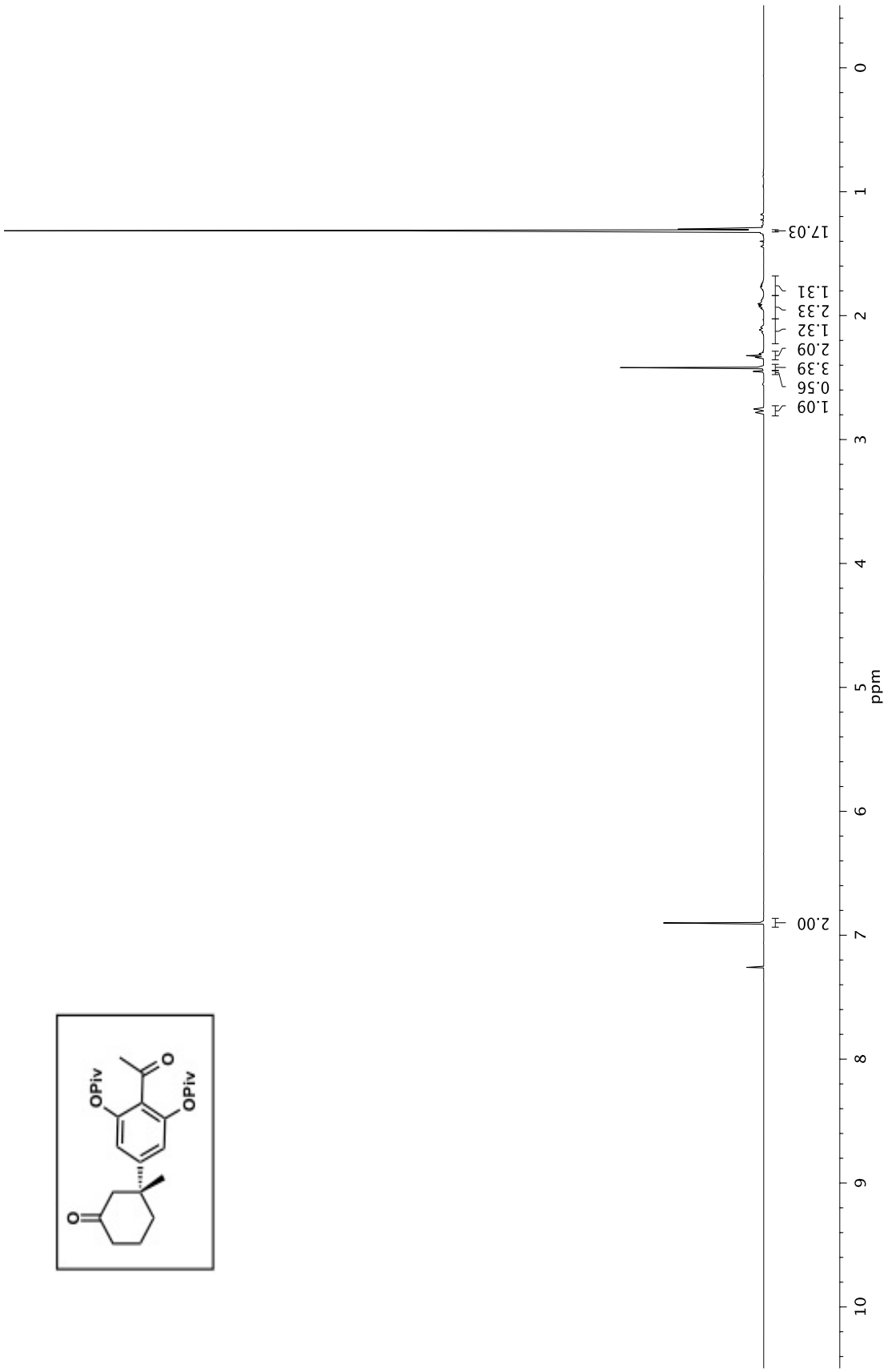
^{1}H NMR (500 MHz, $(CD_3)_2SO$) of compound **S-6**.



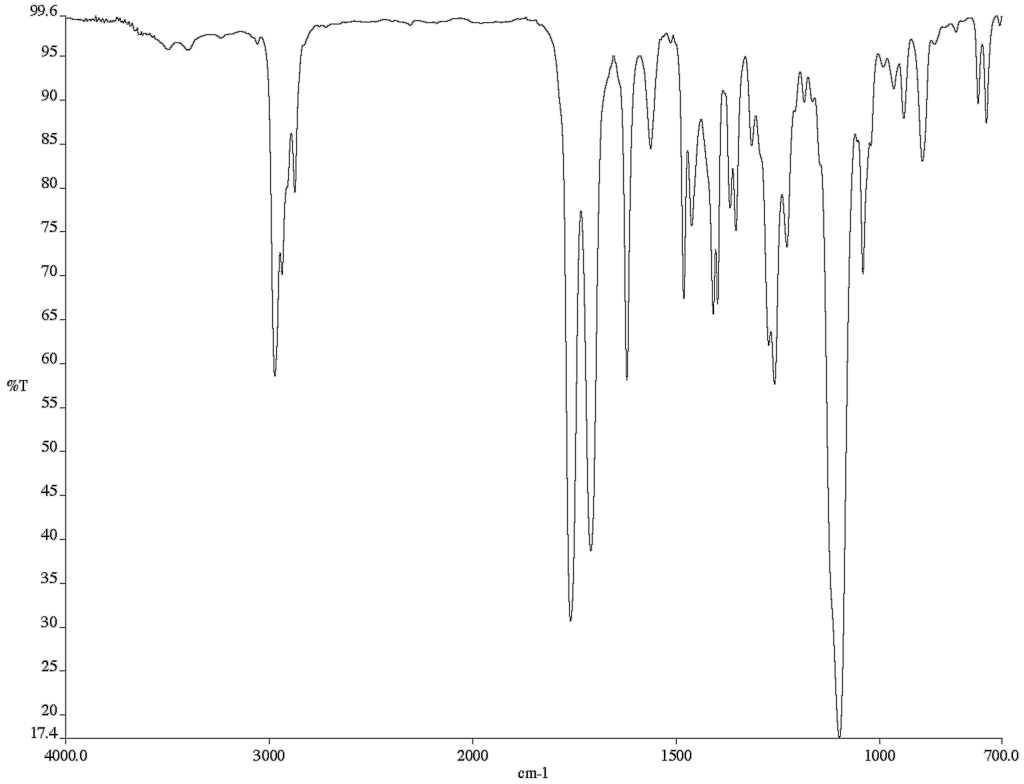
Infrared spectrum (Thin Film, NaCl) of compound **S-6**.



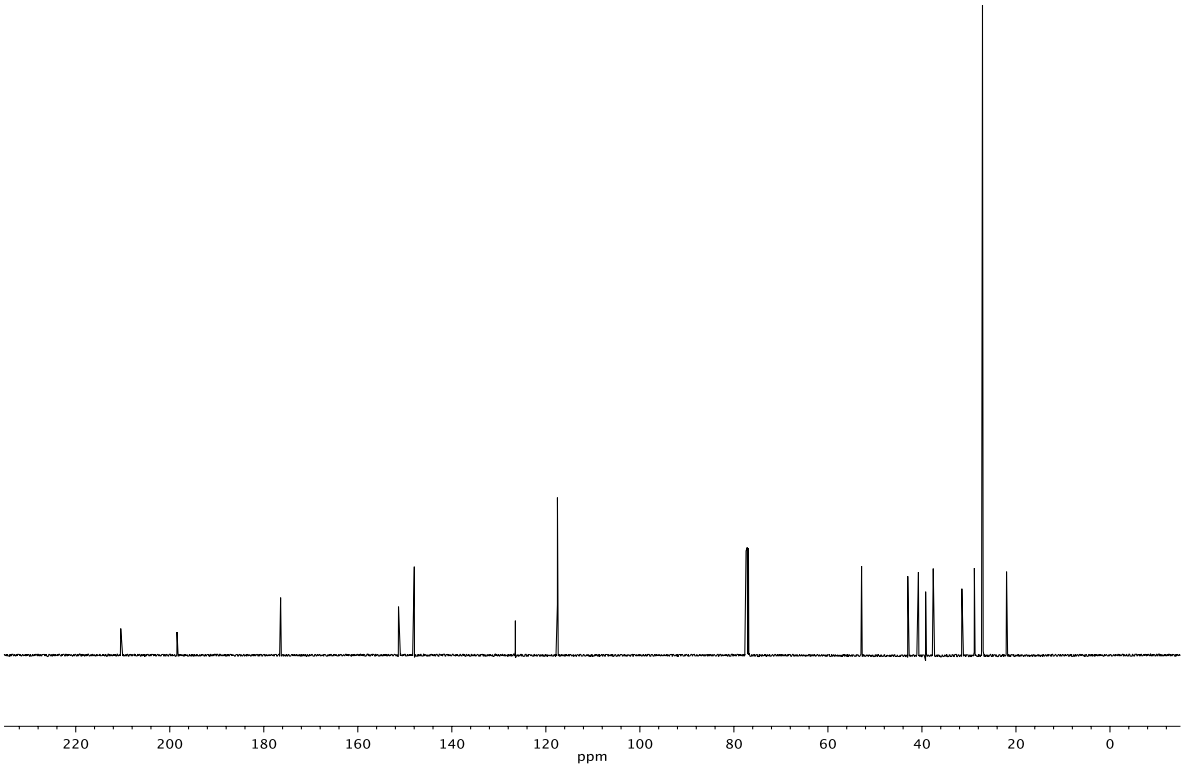
^{13}C NMR (126 MHz, $(CD_3)_2SO$) of compound **S-6**.



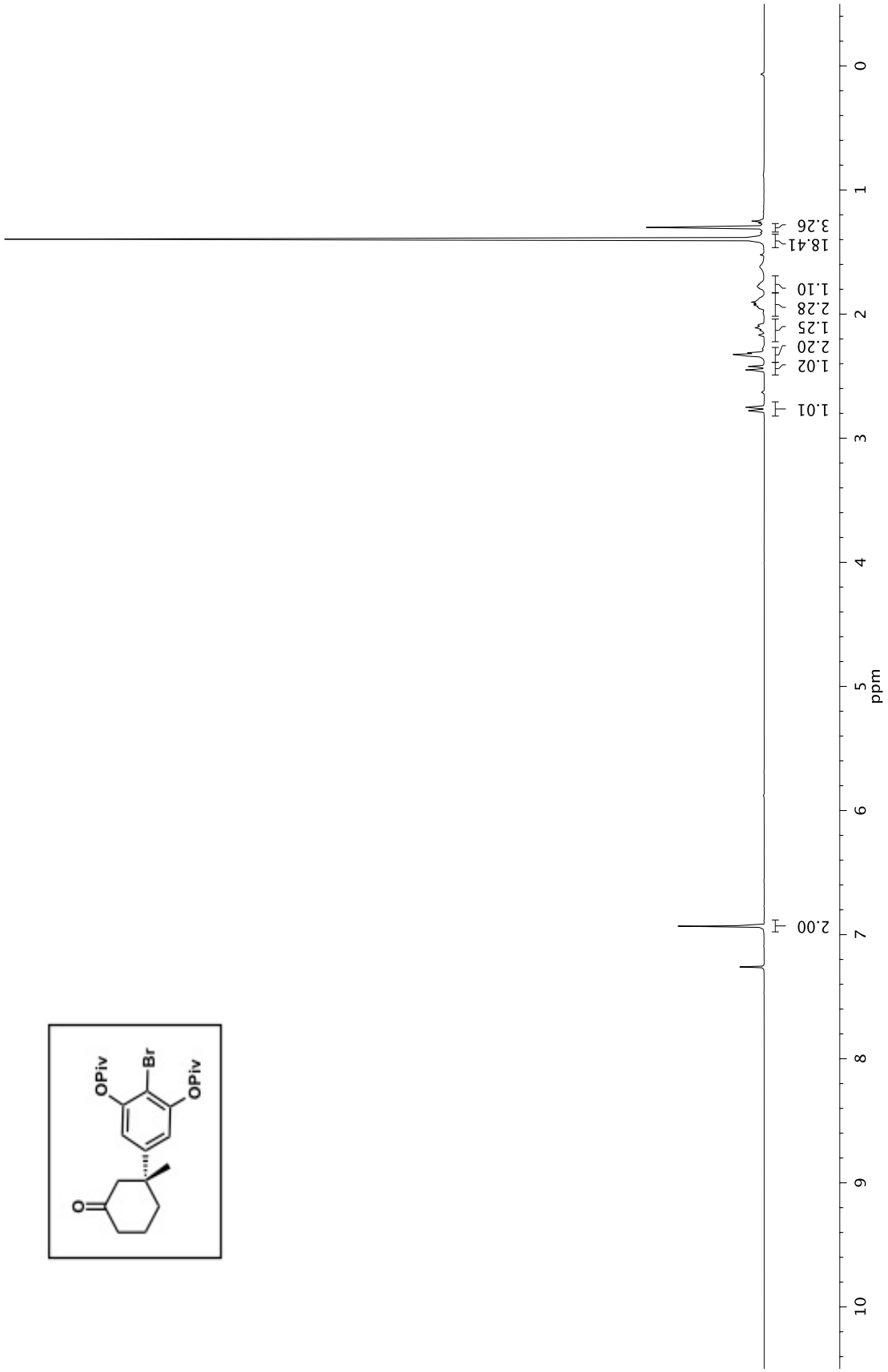
^{1}H NMR (500 MHz, $CDCl_3$) of compound **20**.



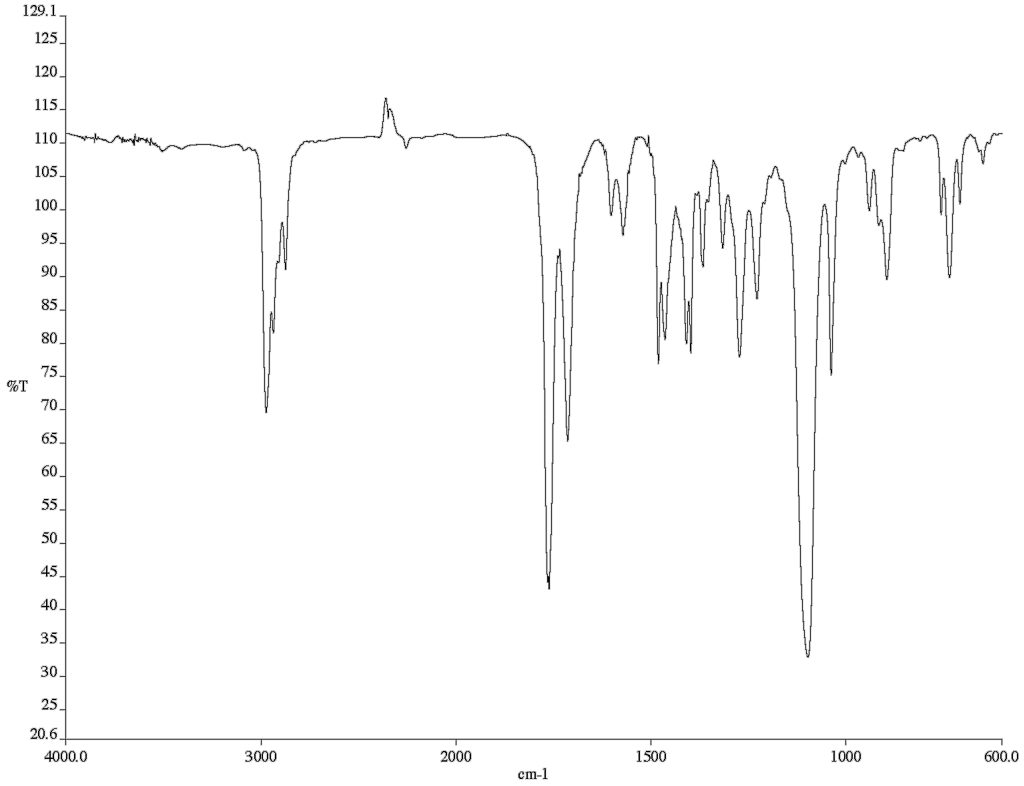
Infrared spectrum (Thin Film, NaCl) of compound **20**.



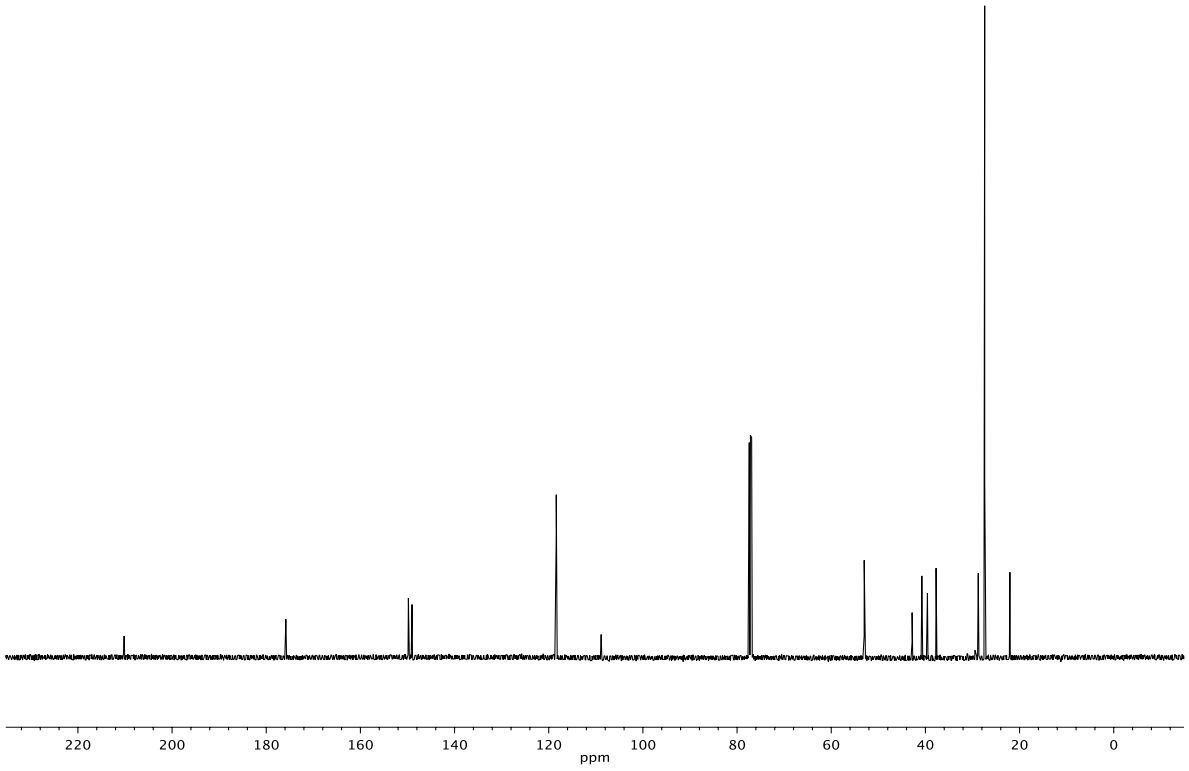
^{13}C NMR (126 MHz, $CDCl_3$) of compound **20**.



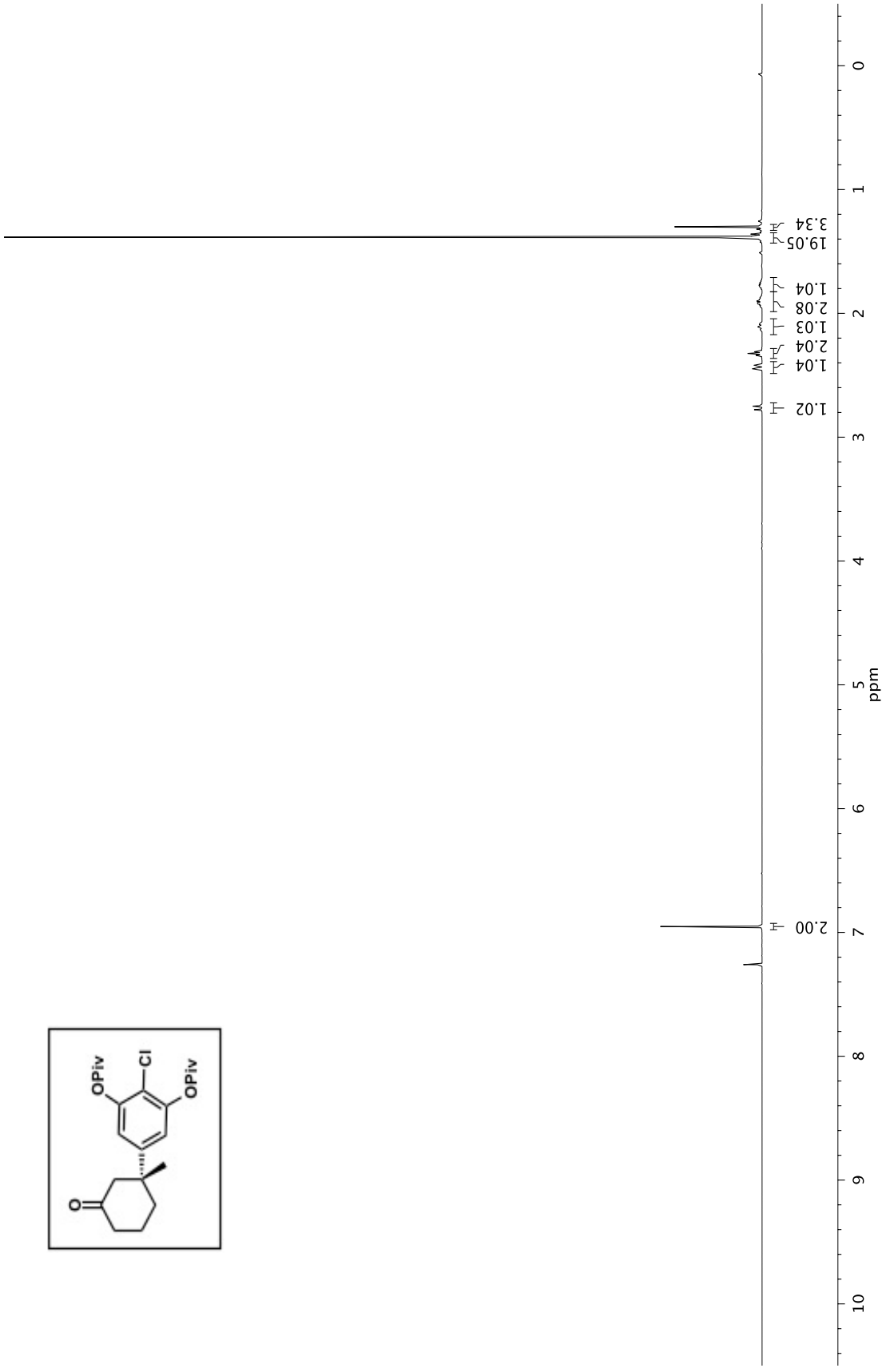
^{1}H NMR (500 MHz, $CDCl_3$) of compound **27**.



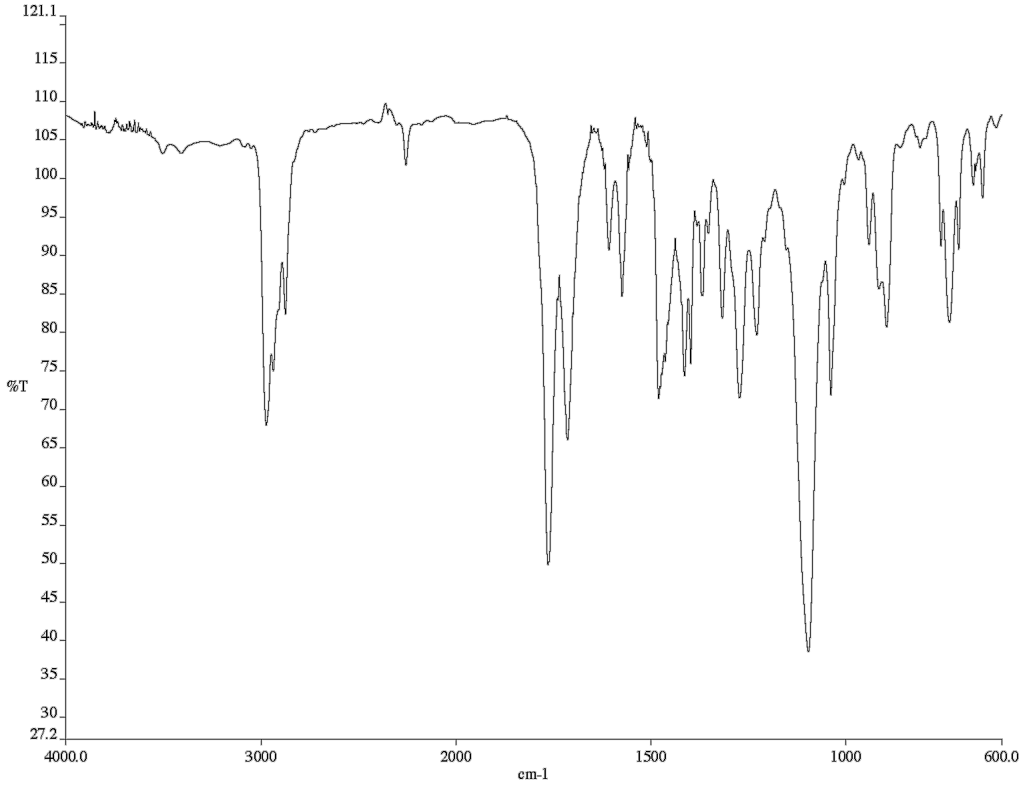
Infrared spectrum (Thin Film, NaCl) of compound **27**.



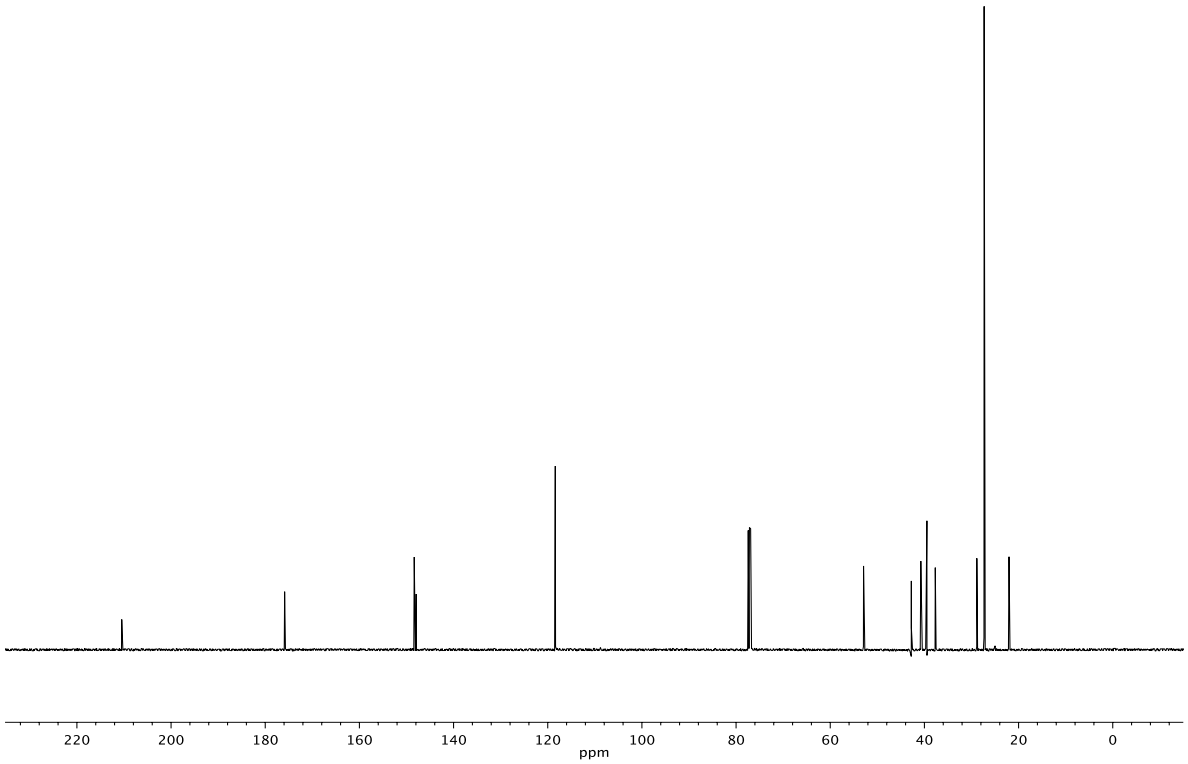
^{13}C NMR (126 MHz, $CDCl_3$) of compound **27**.



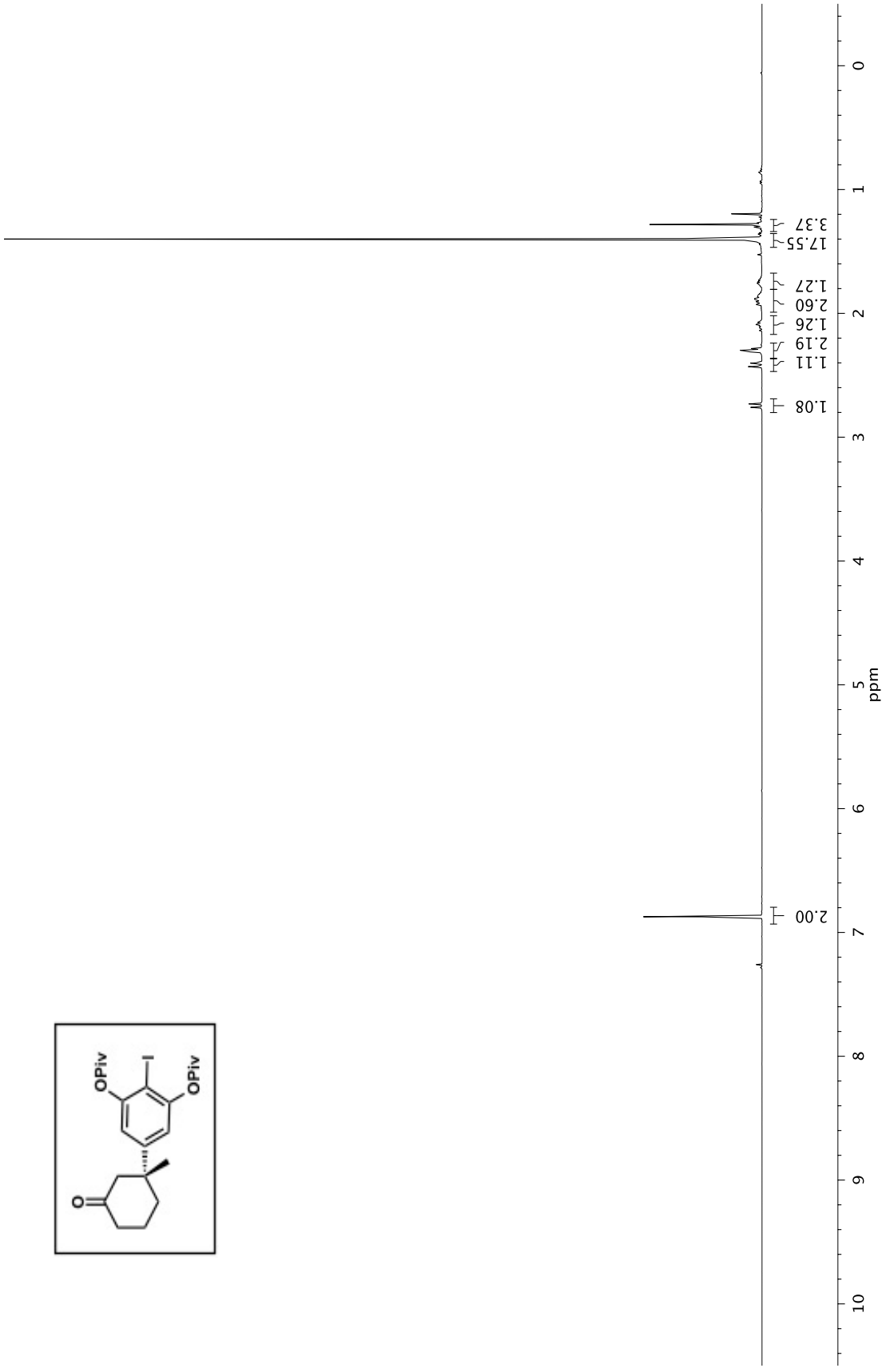
^{1}H NMR (500 MHz, $CDCl_3$) of compound **28**.



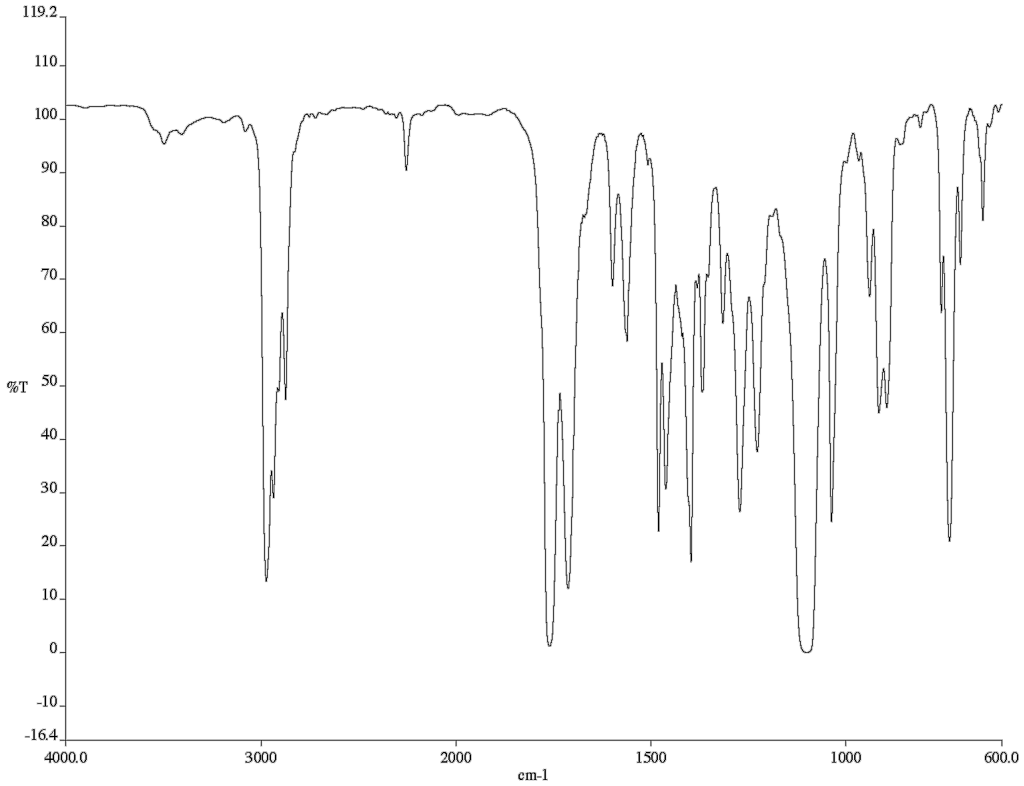
Infrared spectrum (Thin Film, NaCl) of compound **28**.



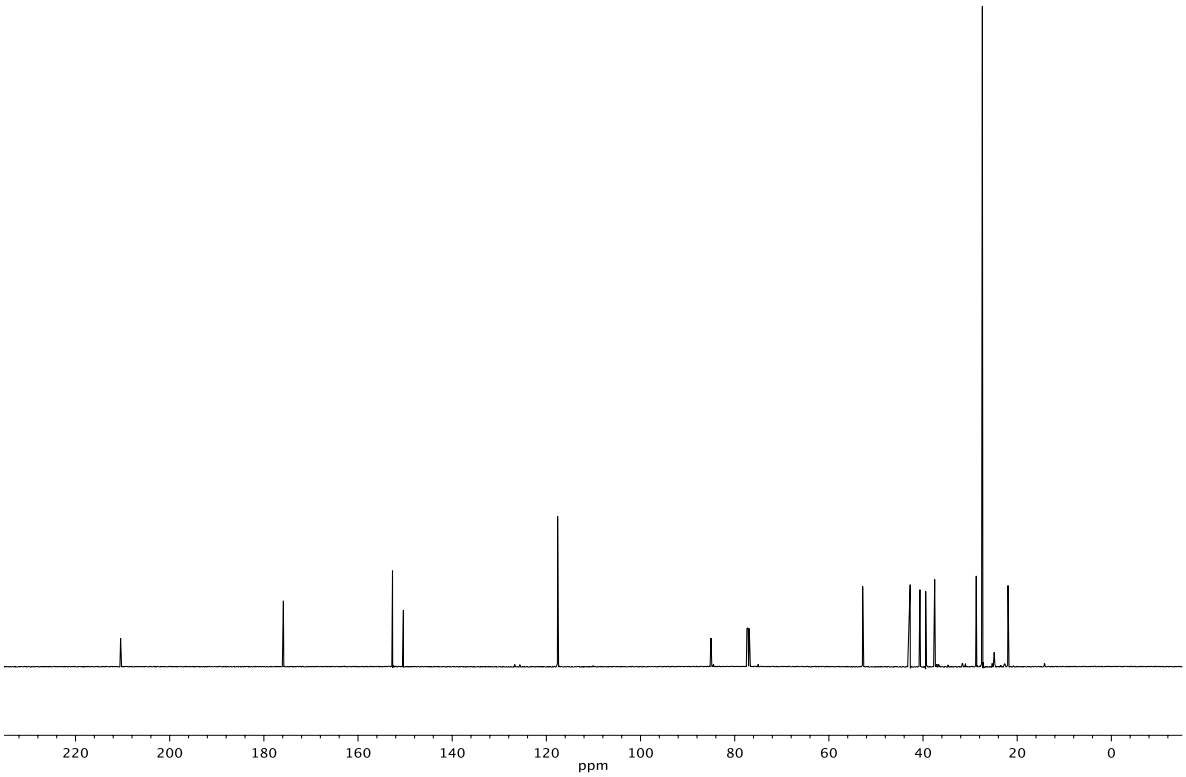
^{13}C NMR (126 MHz, $CDCl_3$) of compound **28**.



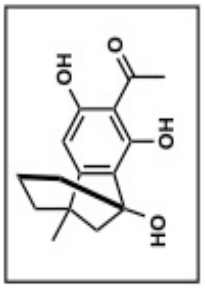
^{1}H NMR (500 MHz, $CDCl_3$) of compound **26**.

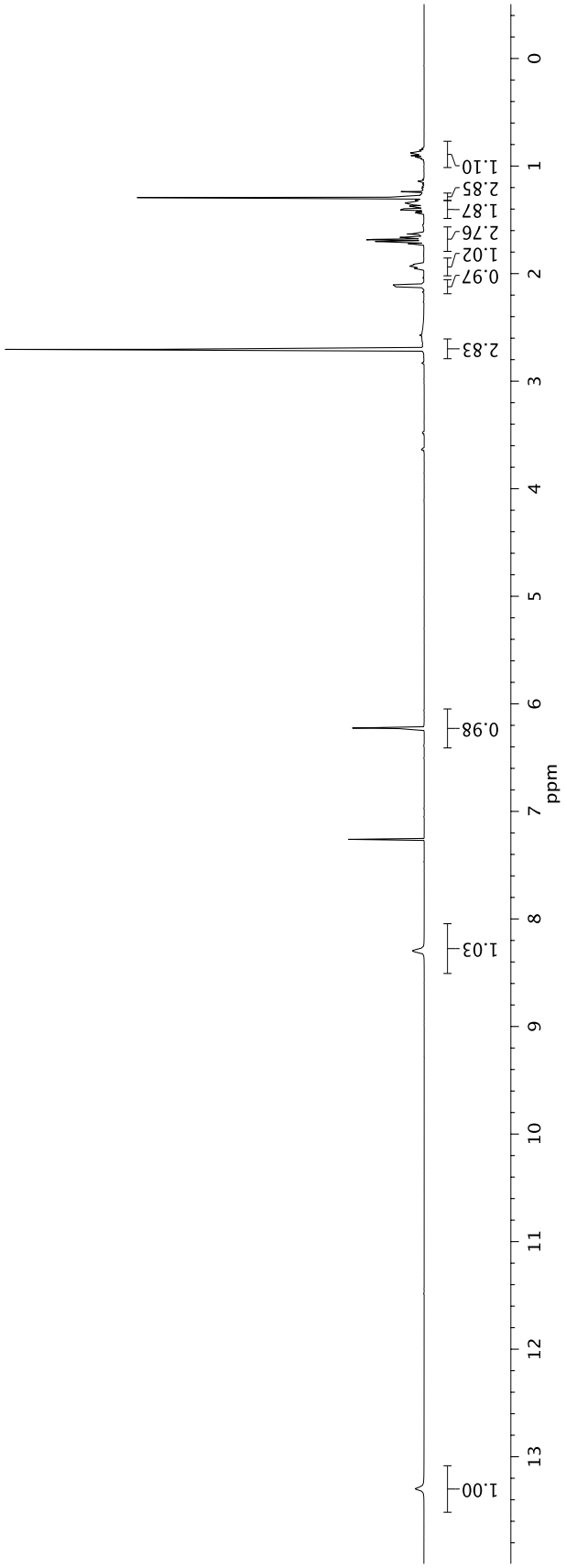


Infrared spectrum (Thin Film, NaCl) of compound **26**.

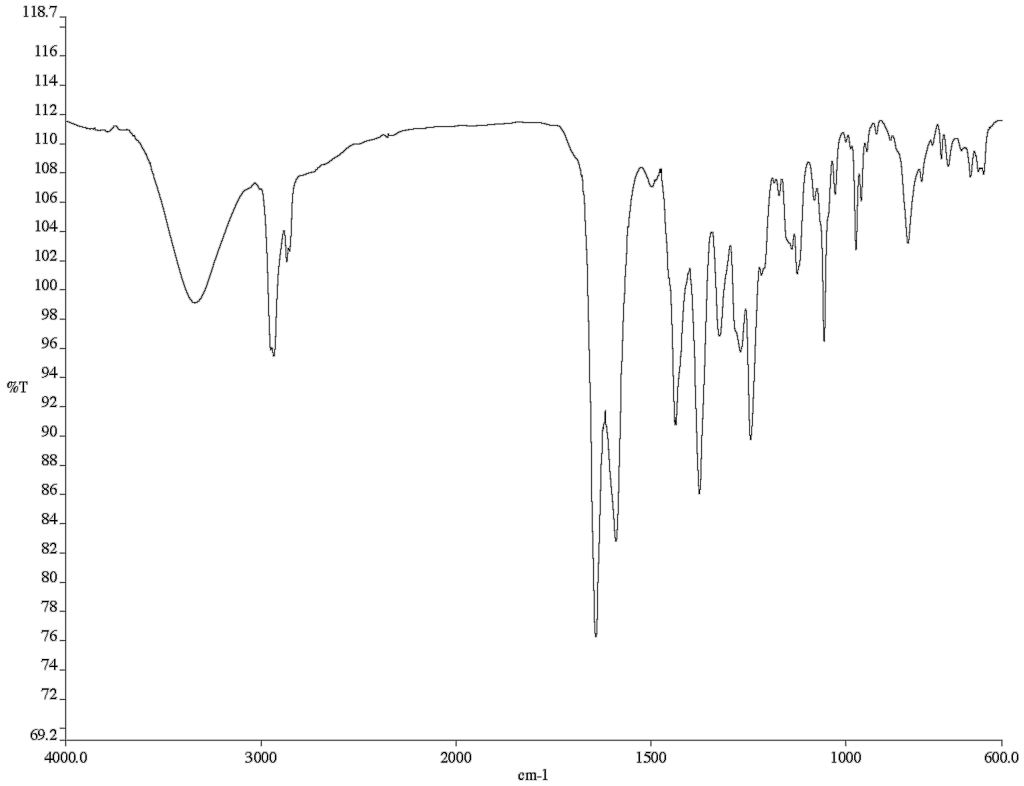


^{13}C NMR (126 MHz, $CDCl_3$) of compound **26**.

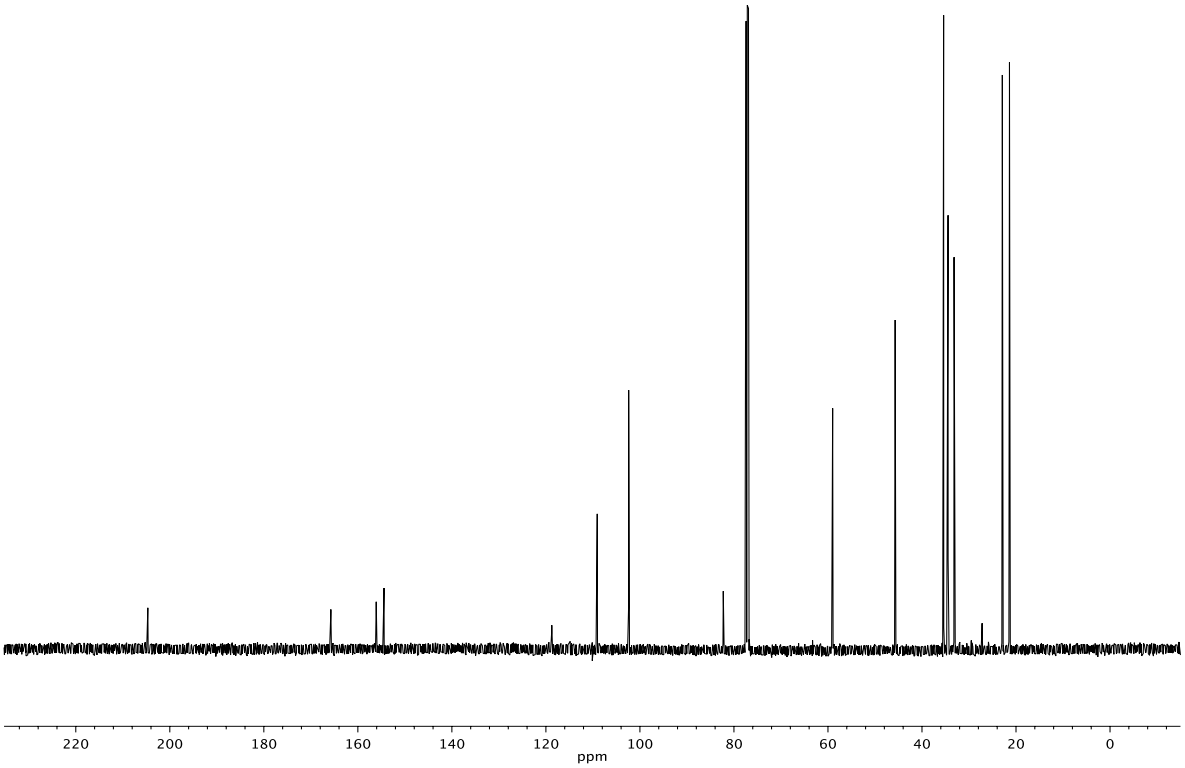




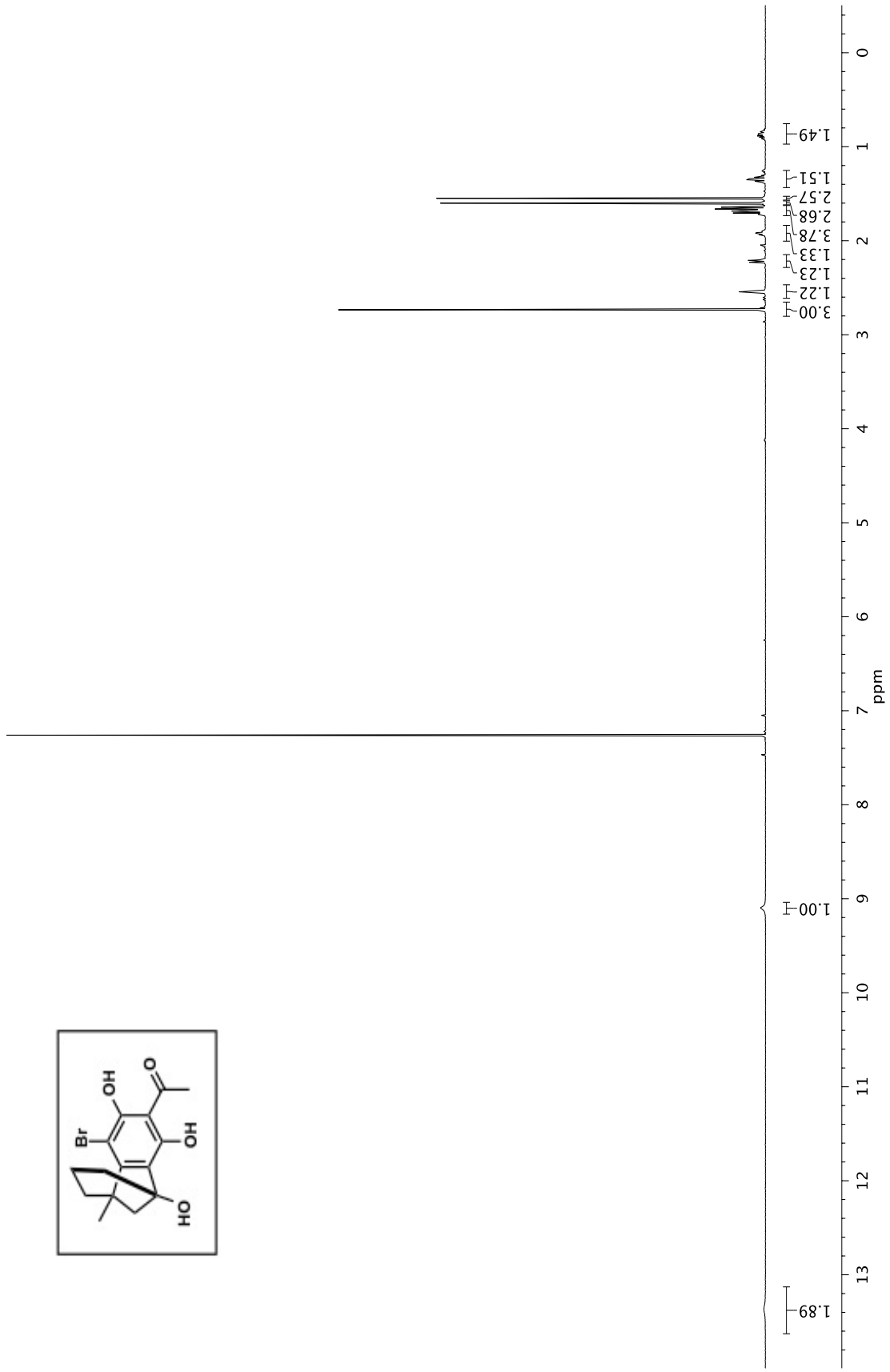
^{1}H NMR (500 MHz, $CDCl_3$) of compound **23**.



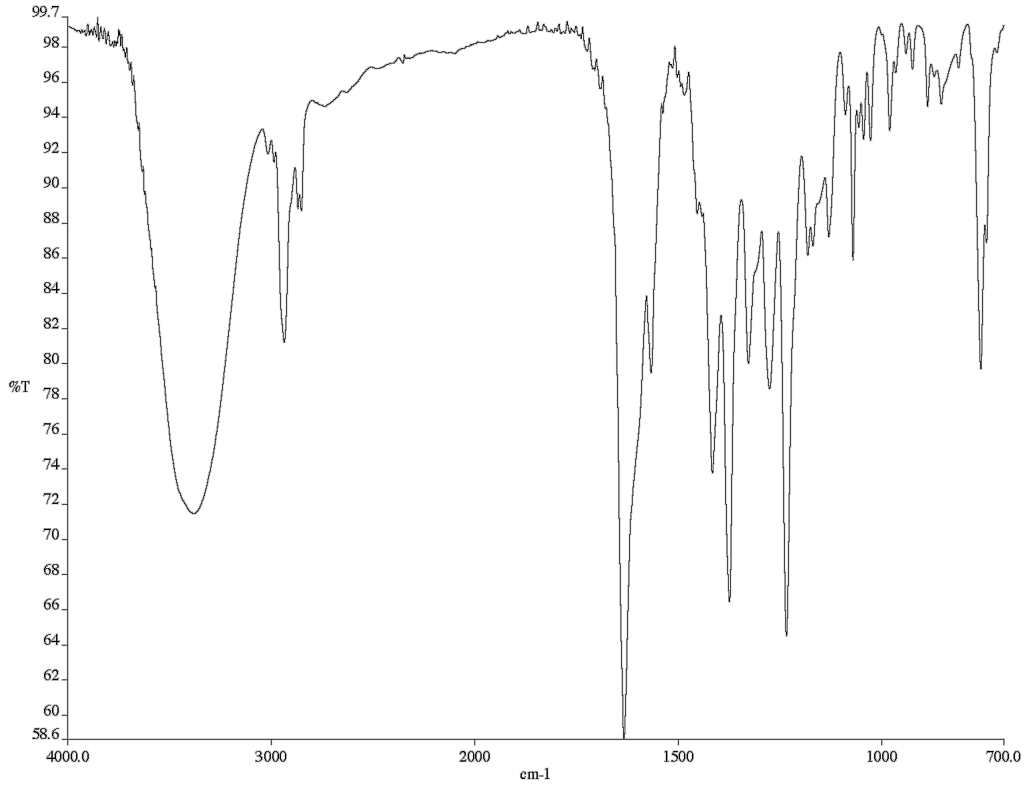
Infrared spectrum (Thin Film, NaCl) of compound **23**.



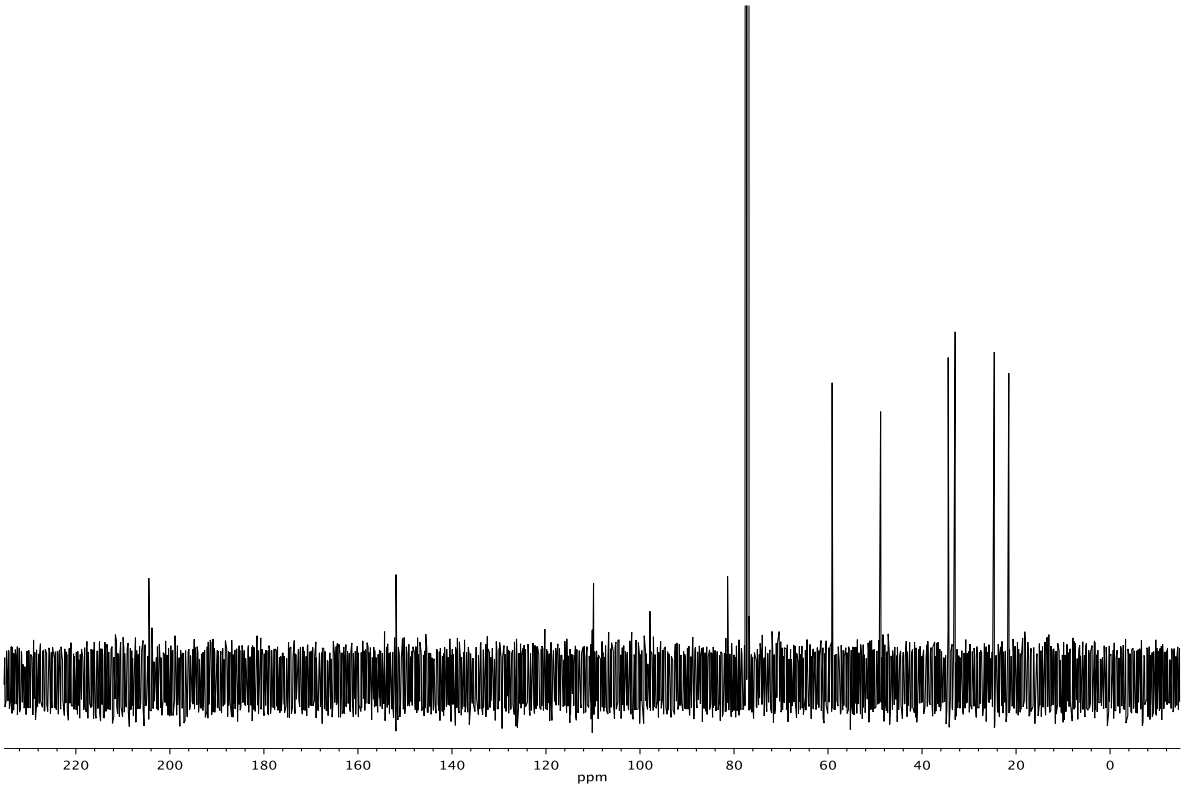
^{13}C NMR (126 MHz, $CDCl_3$) of compound **23**.



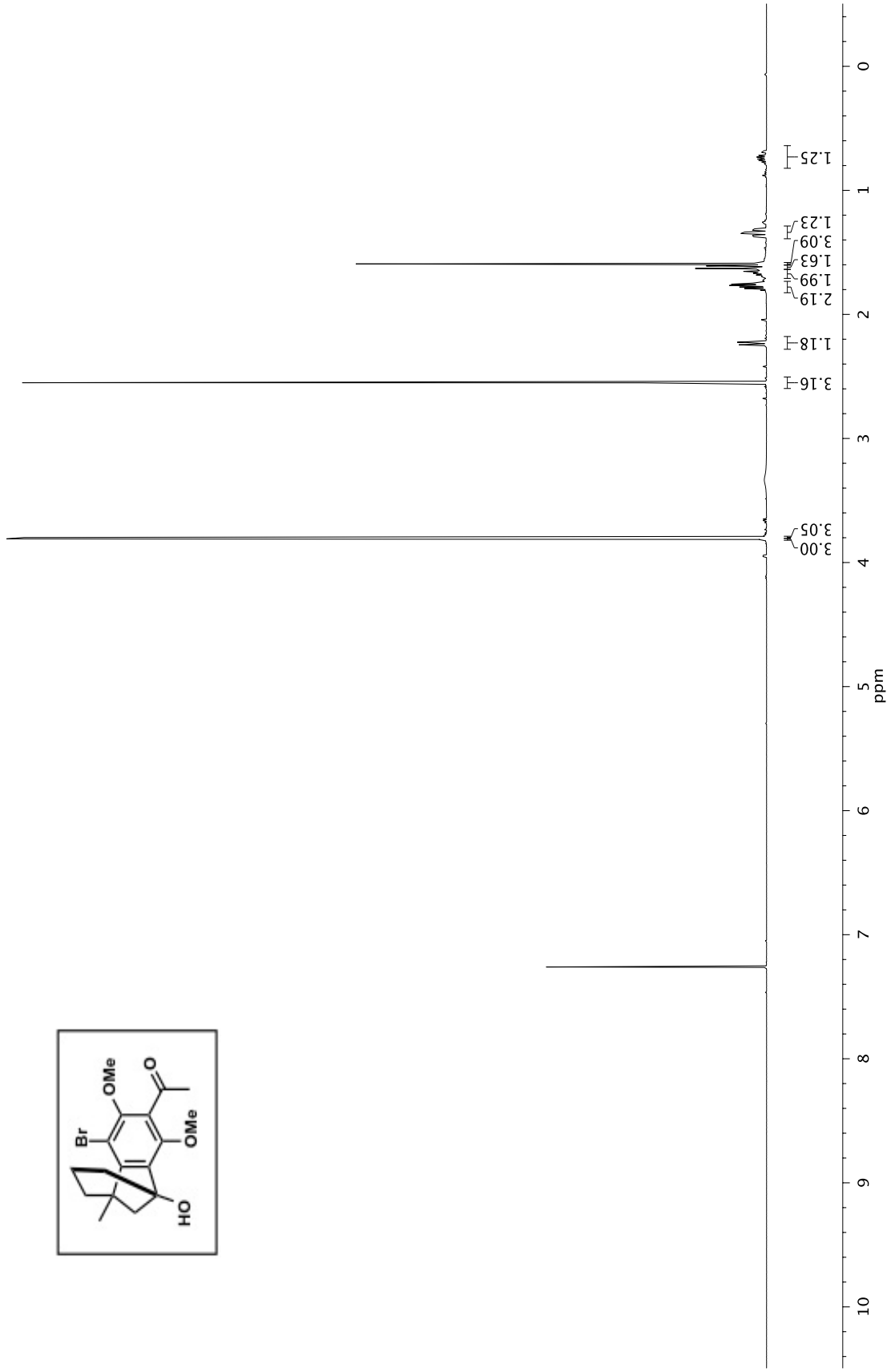
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S-7**.



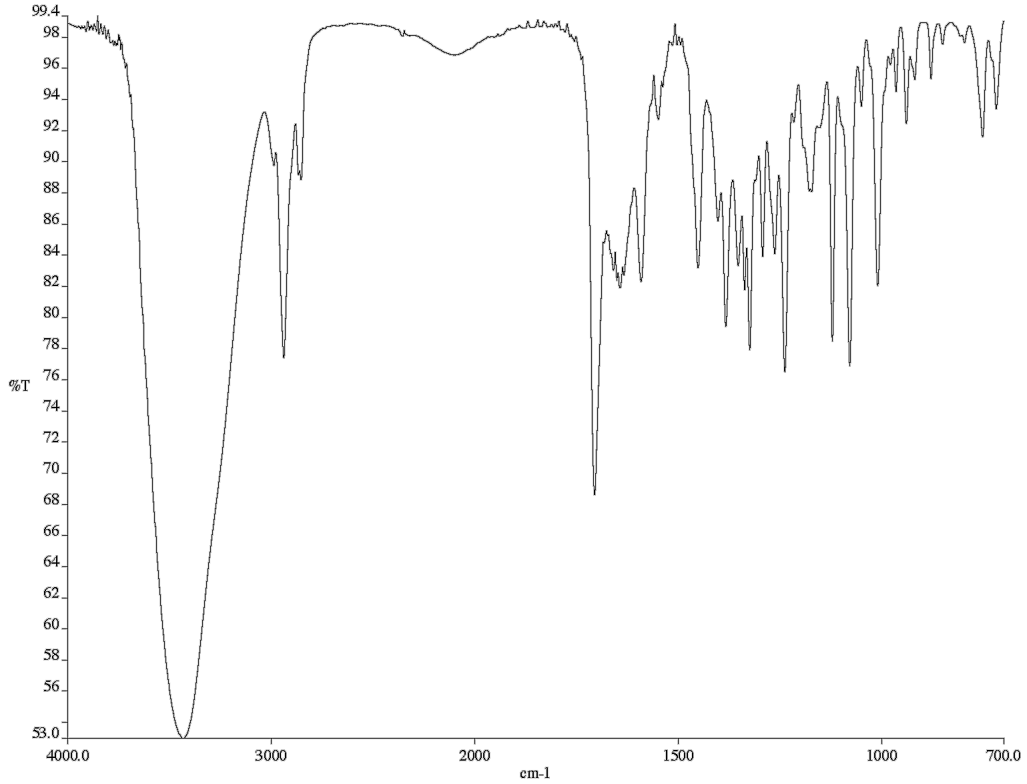
Infrared spectrum (Thin Film, NaCl) of compound **S-7**.



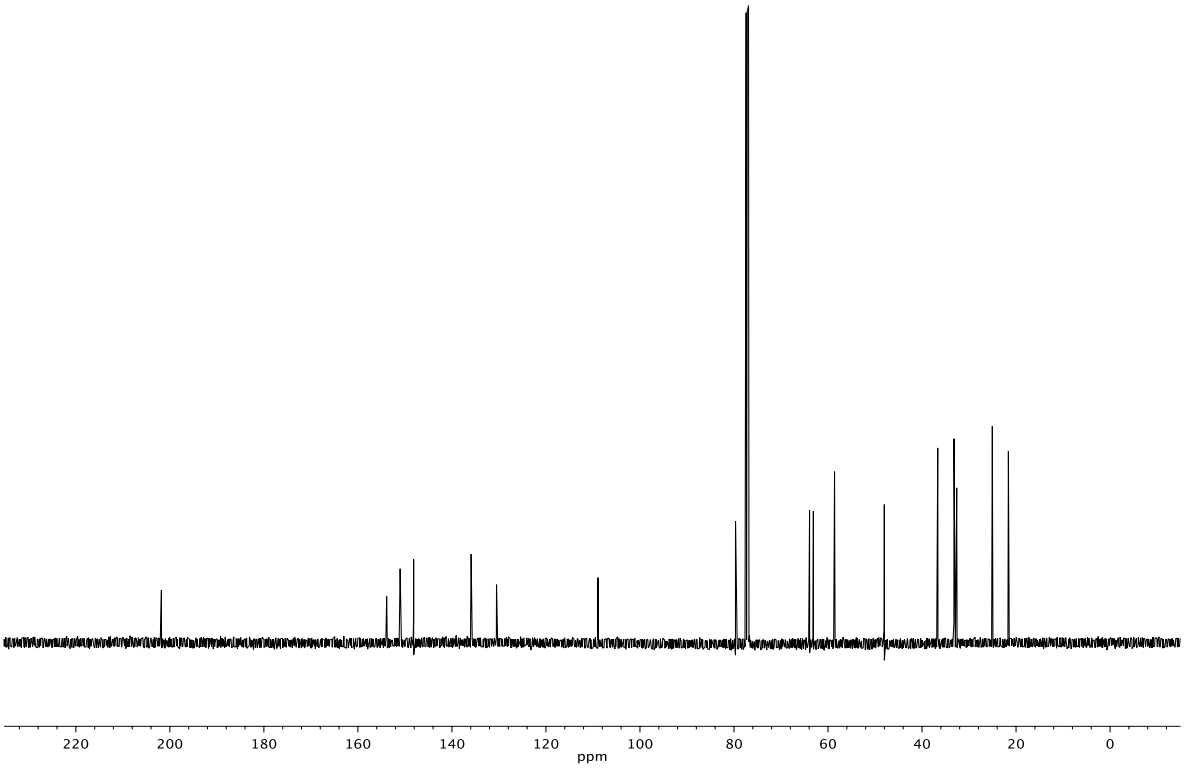
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S-7**.



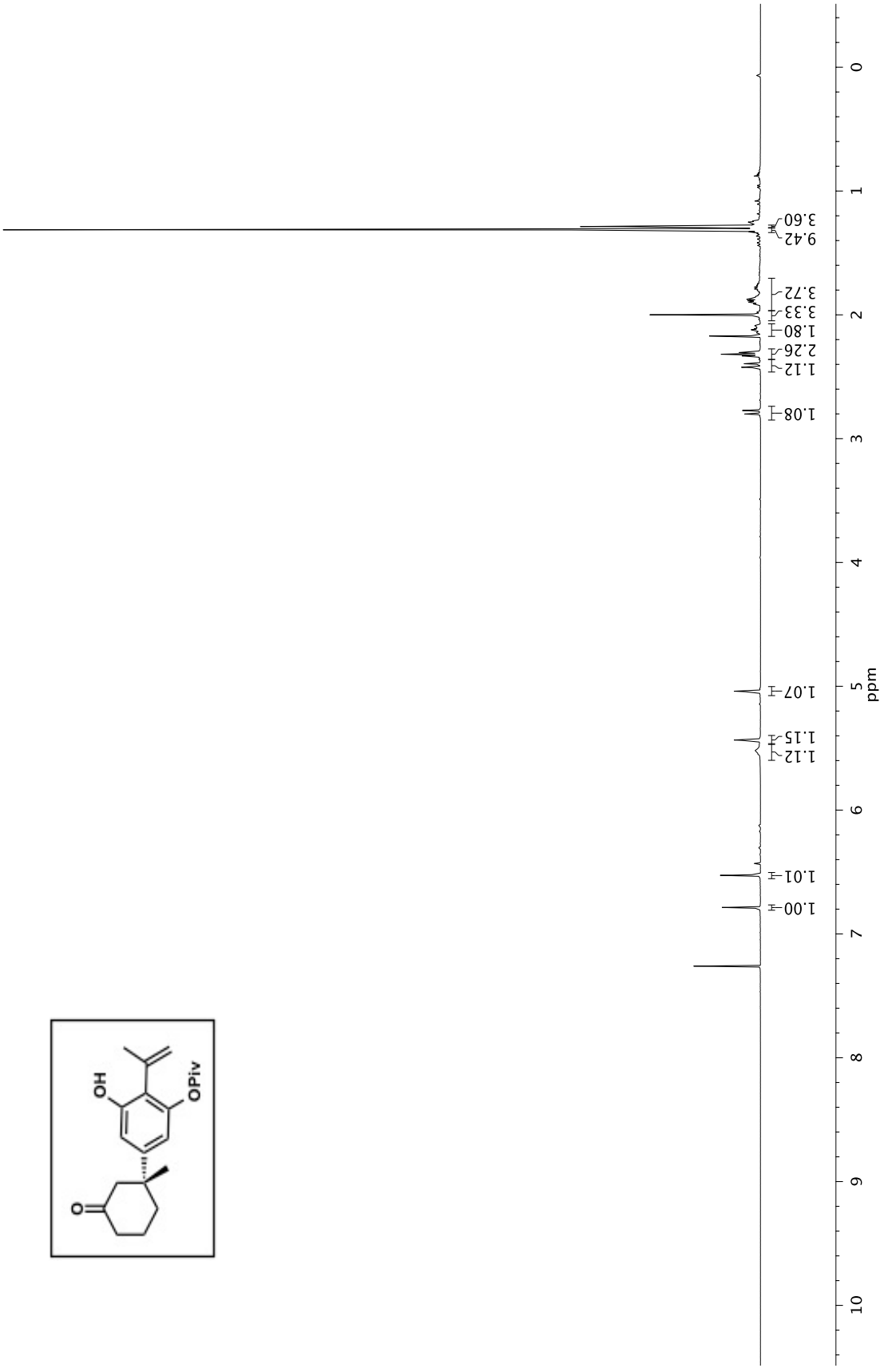
^{1}H NMR (500 MHz, $CDCl_3$) of compound **24**.



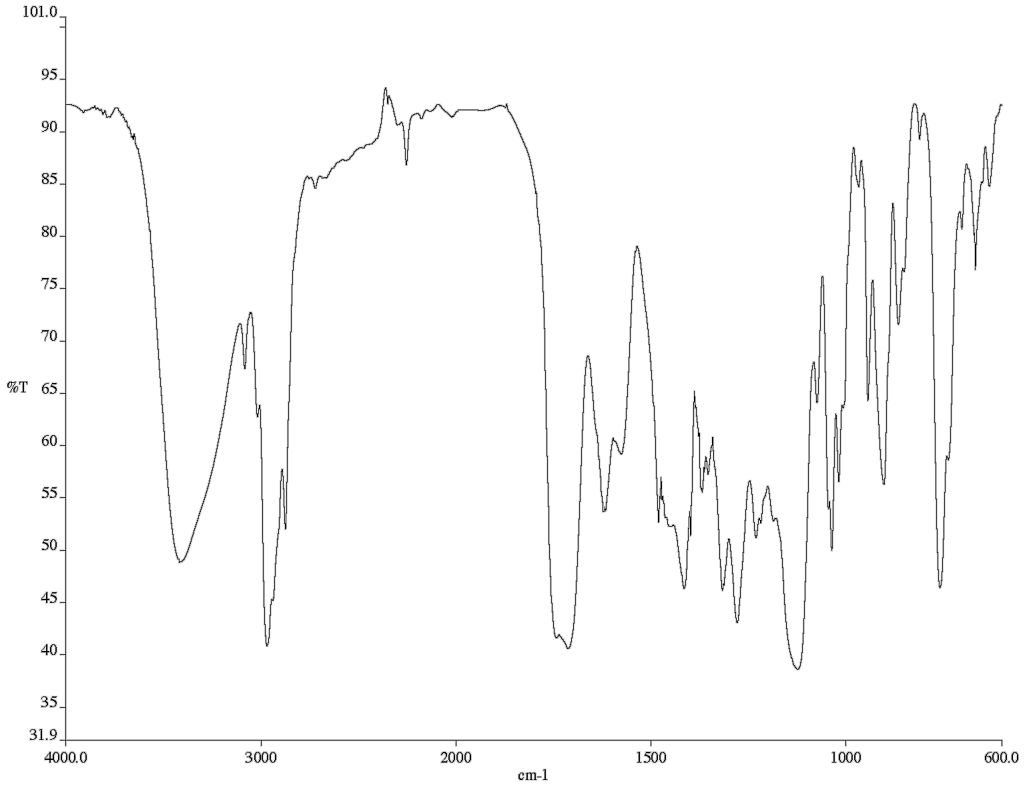
Infrared spectrum (Thin Film, NaCl) of compound **24**.



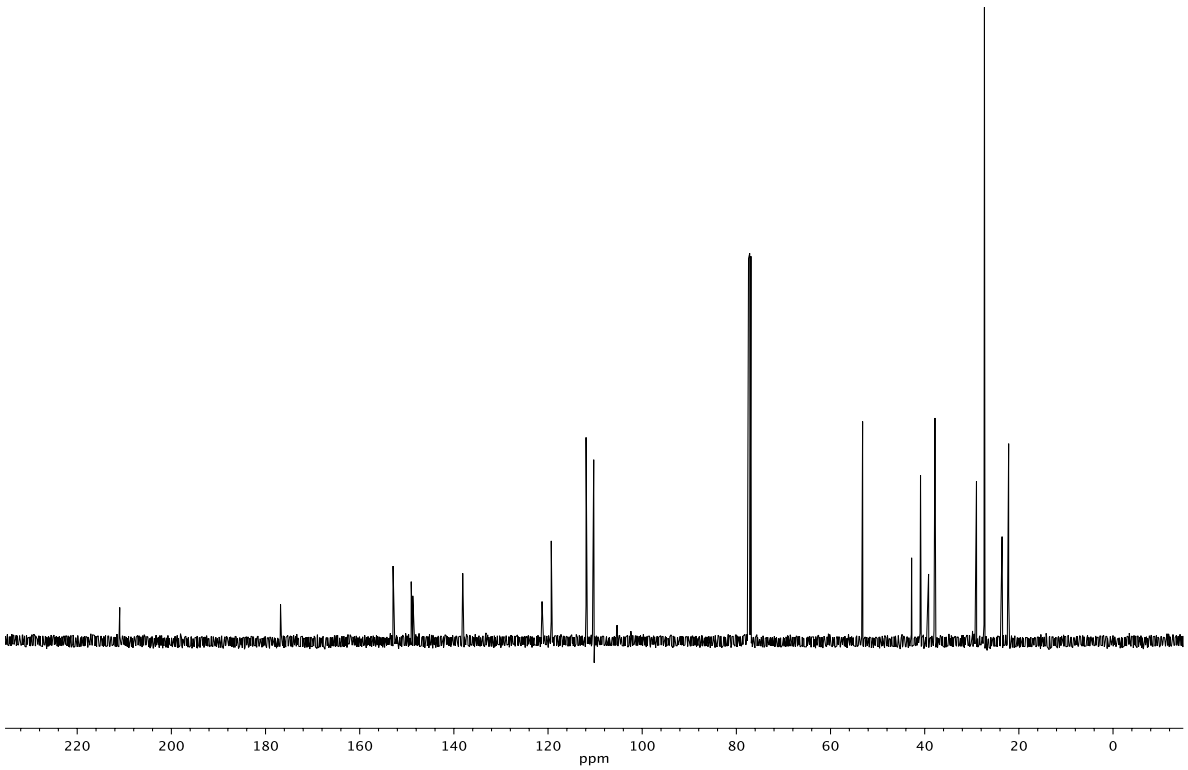
^{13}C NMR (126 MHz, $CDCl_3$) of compound **24**.



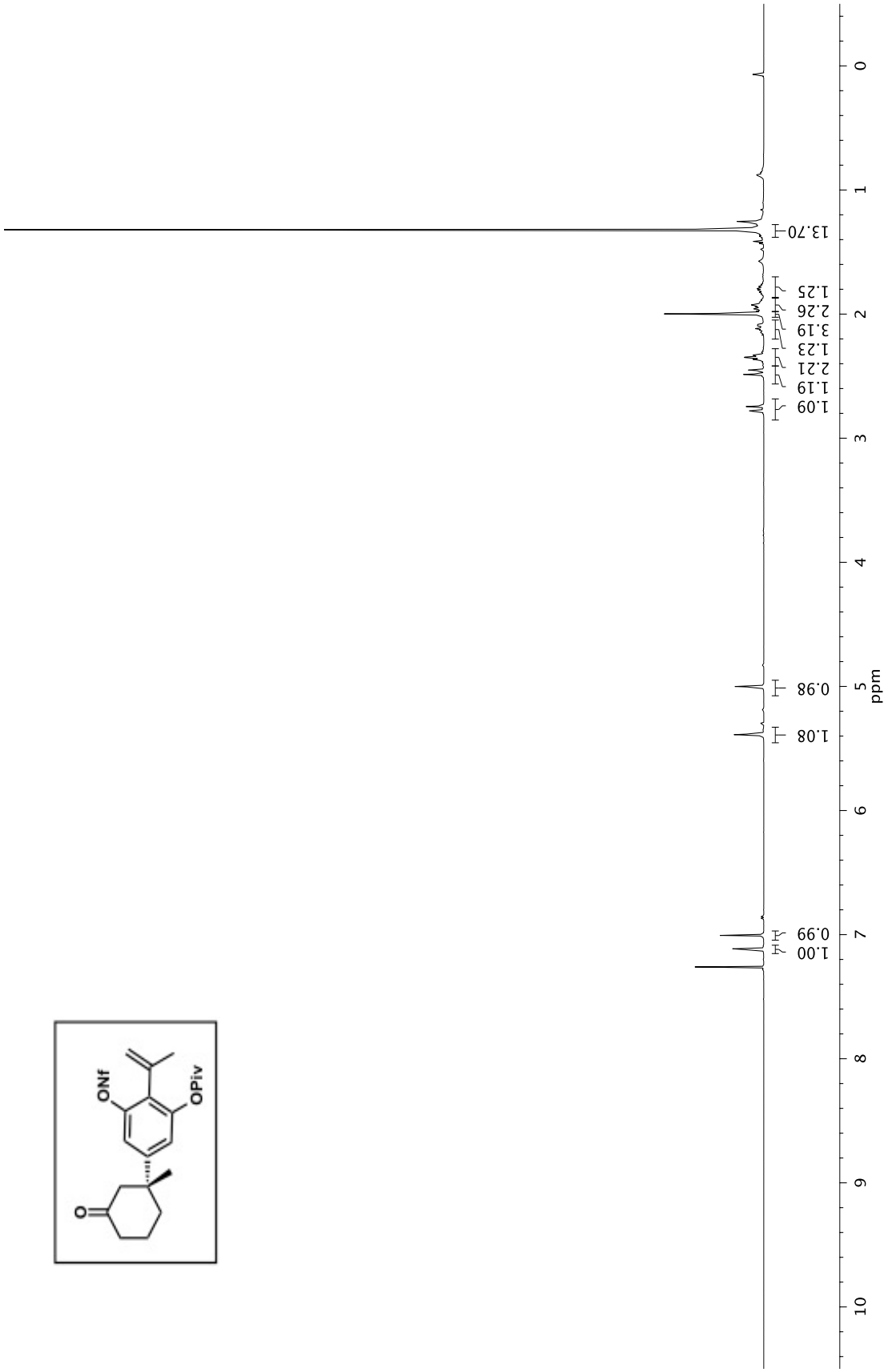
^{1}H NMR (500 MHz, $CDCl_3$) of compound **34**.



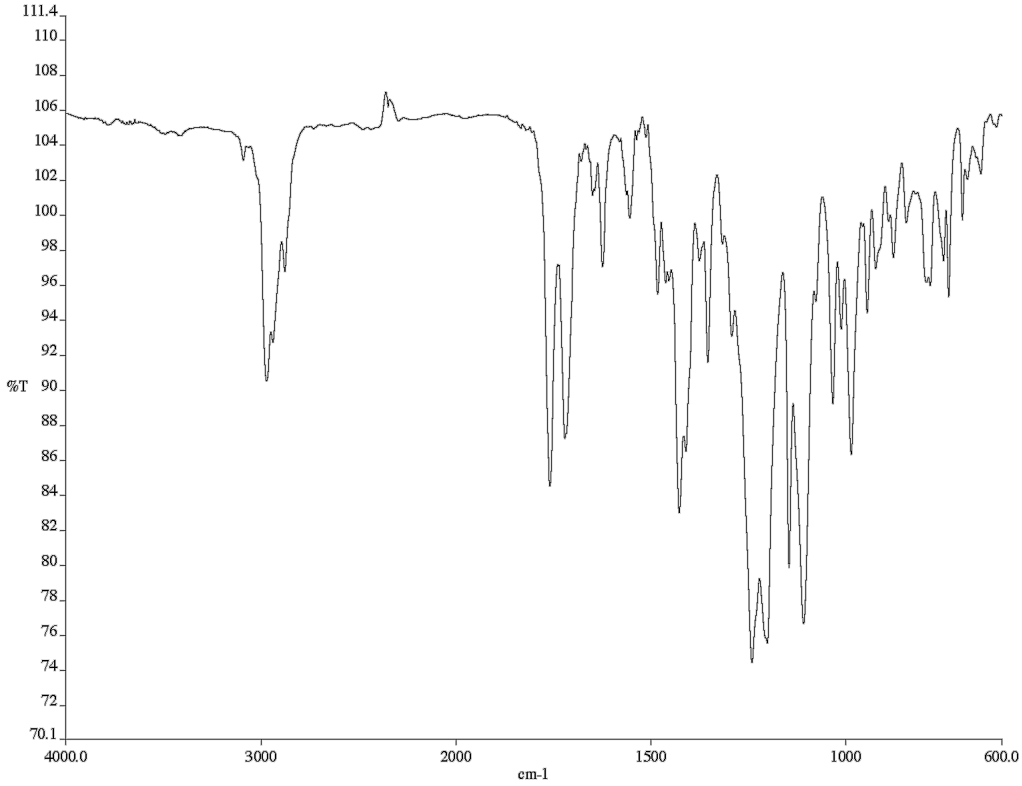
Infrared spectrum (Thin Film, NaCl) of compound **34**.



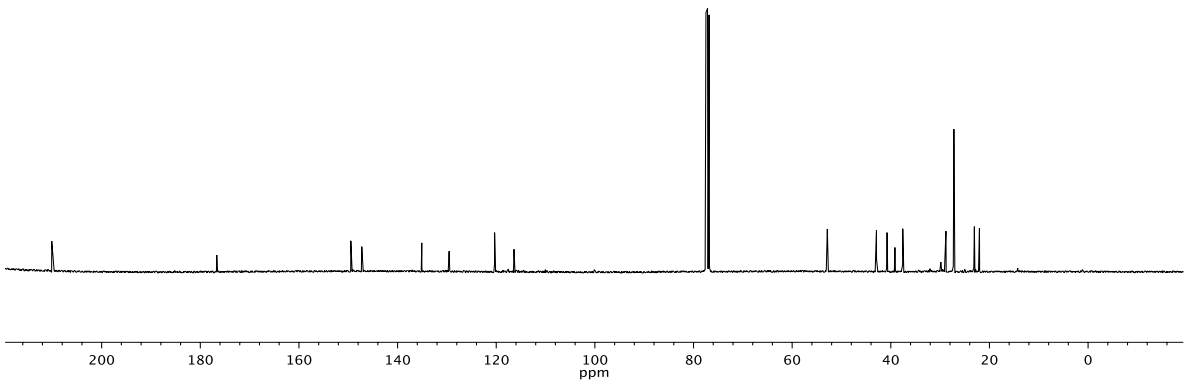
^{13}C NMR (126 MHz, $CDCl_3$) of compound **34**.



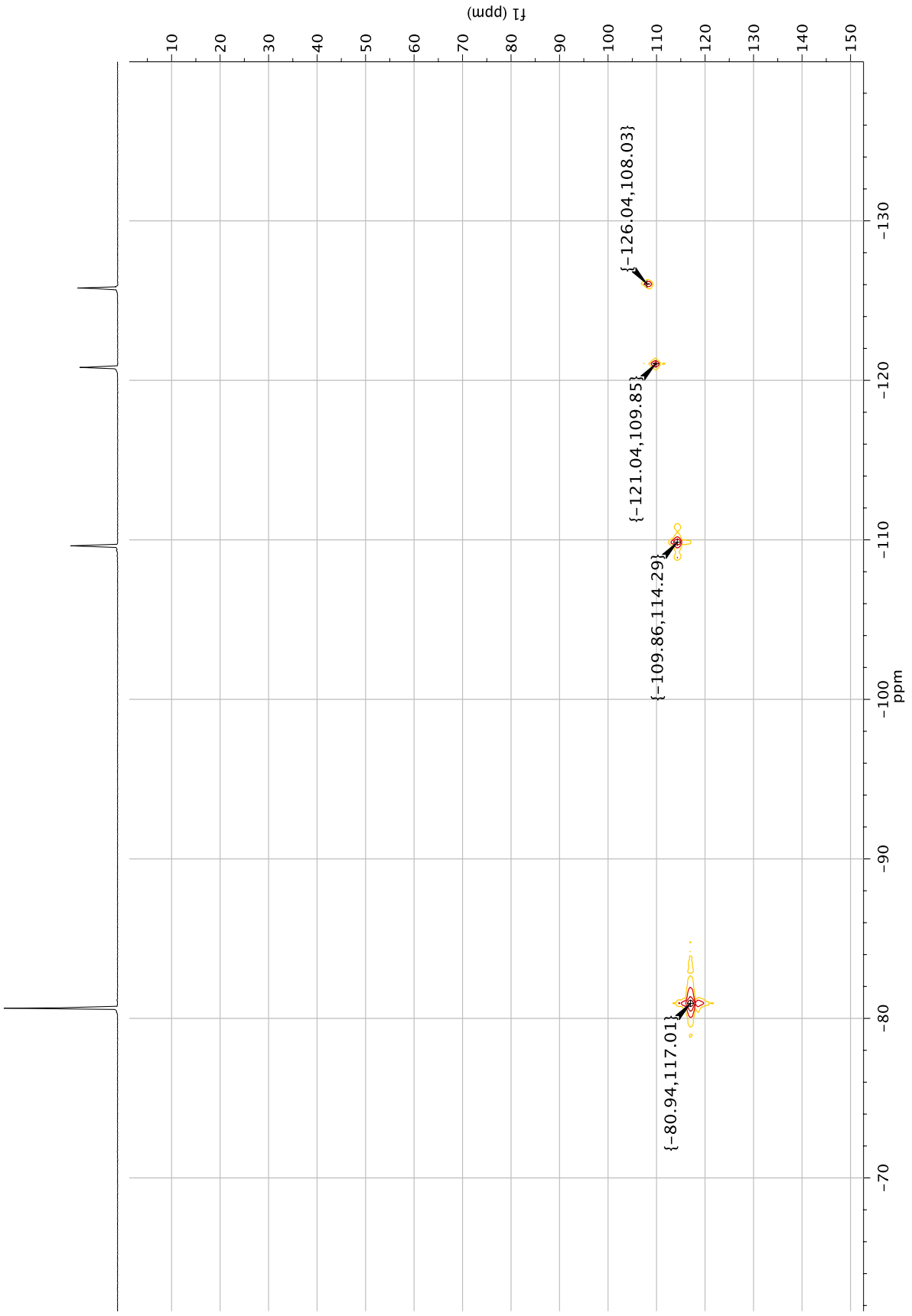
^{1}H NMR (400 MHz, $CDCl_3$) of compound **35**.



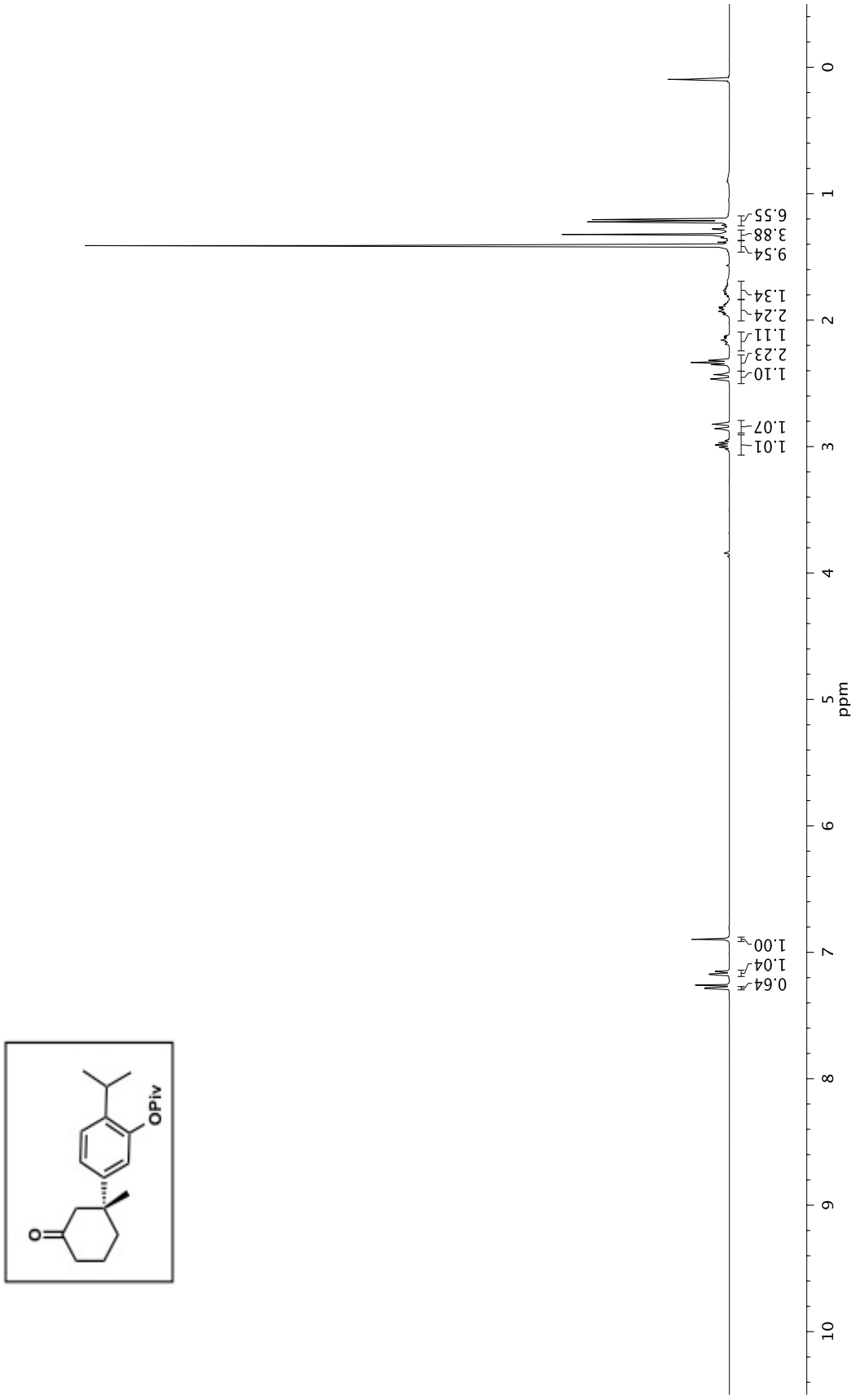
Infrared spectrum (Thin Film, NaCl) of compound **35**.



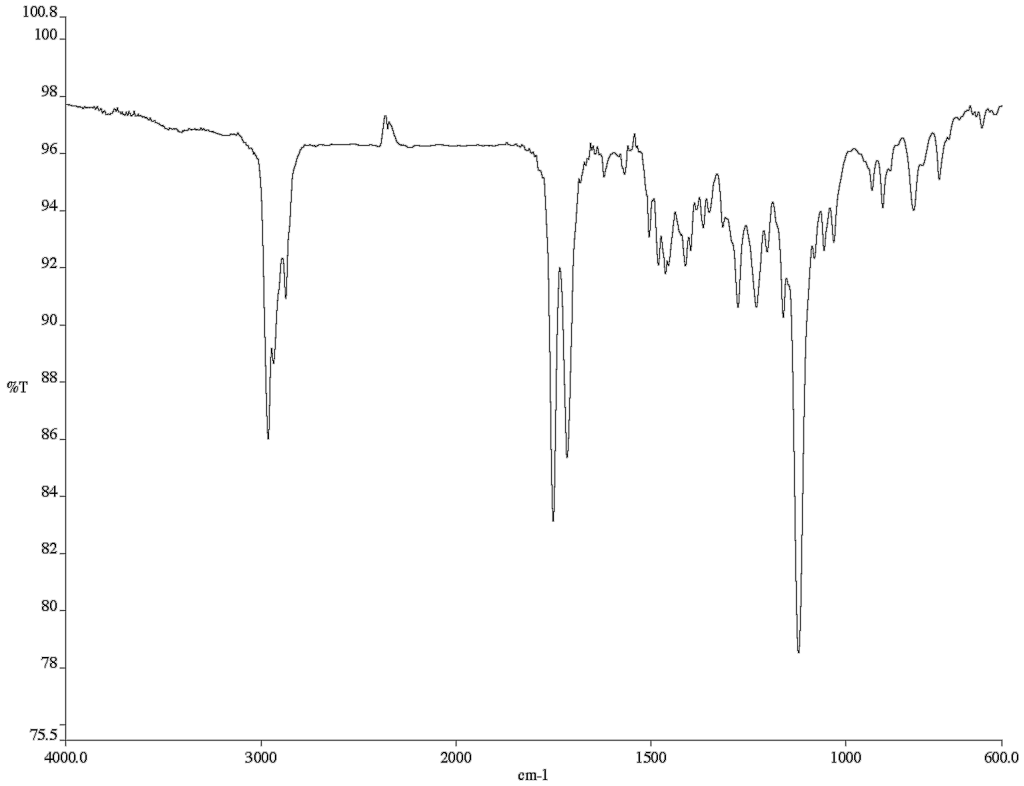
^{13}C NMR (100 MHz, $CDCl_3$) of compound **35**.



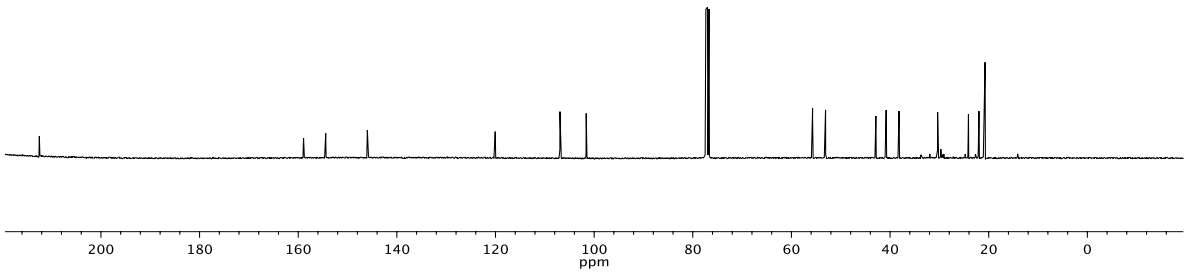
^{19}F vs ^{13}C HSQC NMR (376 MHz, $CDCl_3$) of compound **35**.



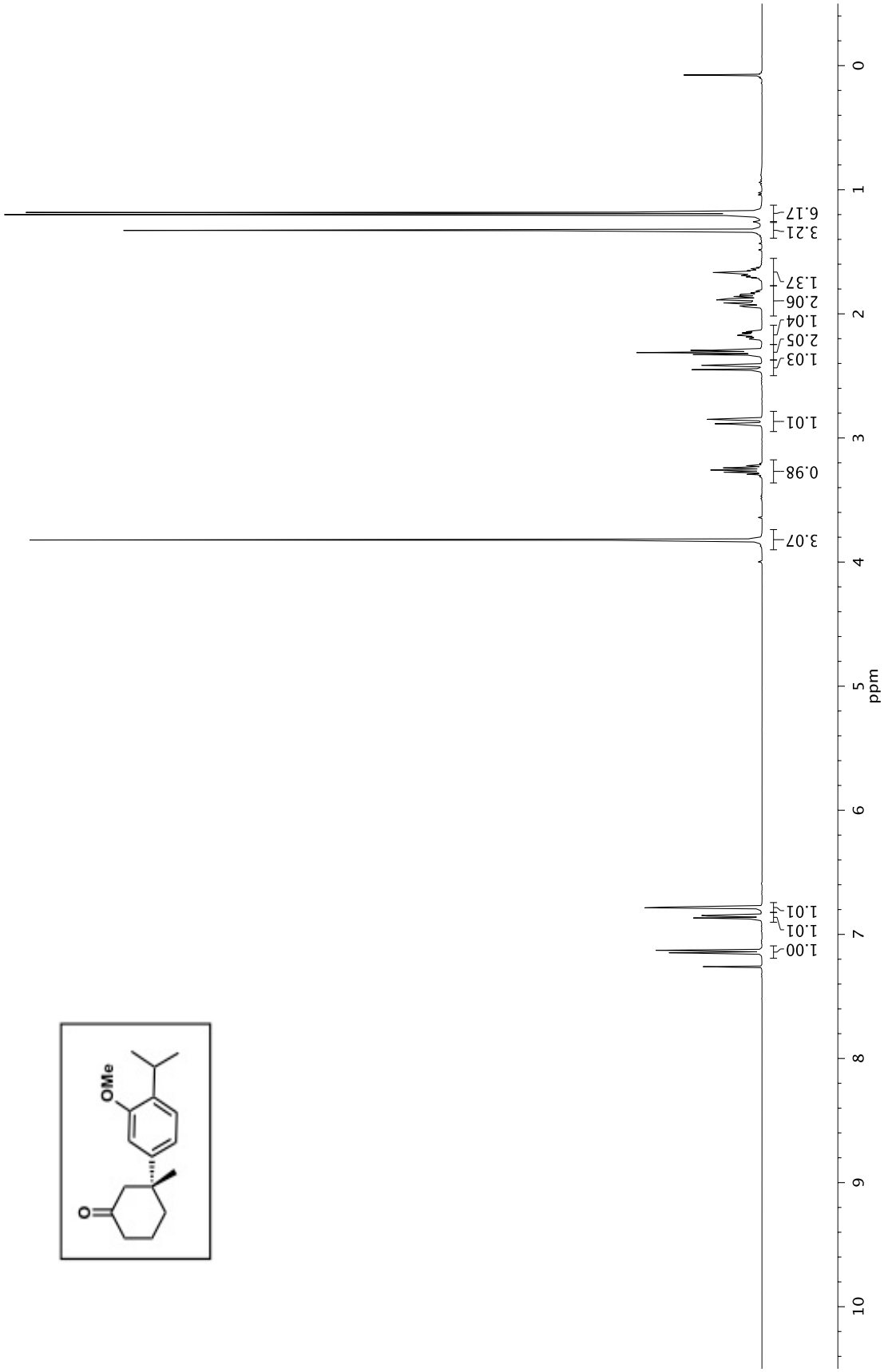
^{1}H NMR (400 MHz, $CDCl_3$) of compound **36**.



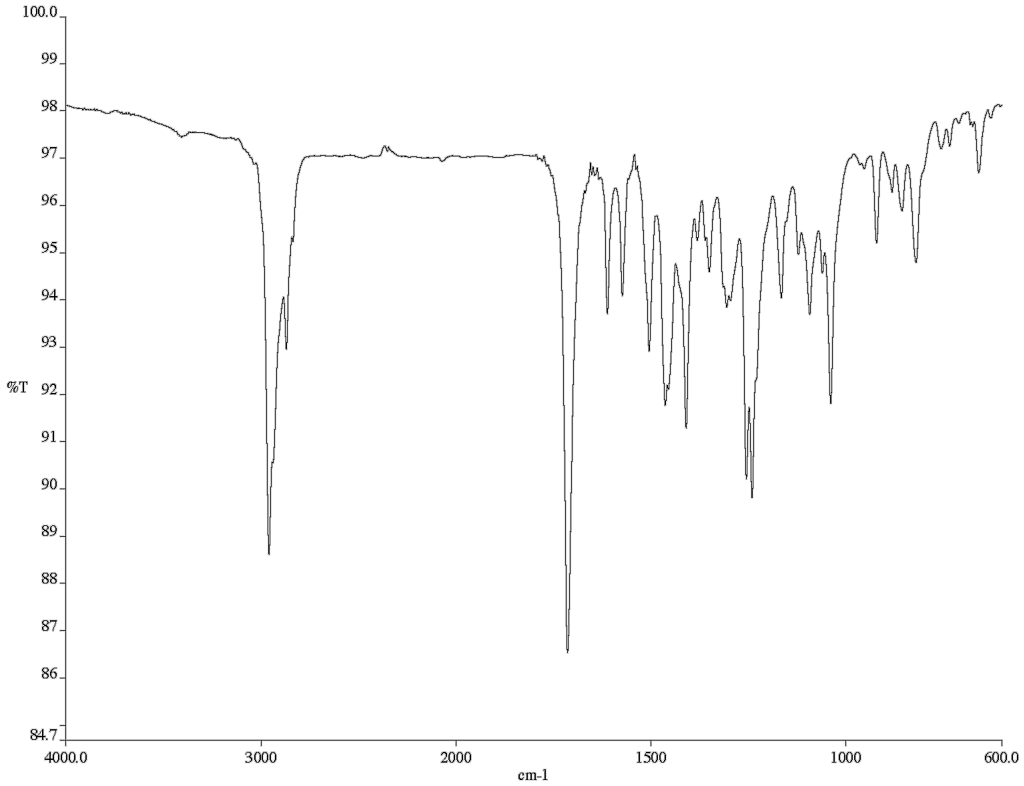
Infrared spectrum (Thin Film, NaCl) of compound **36**.



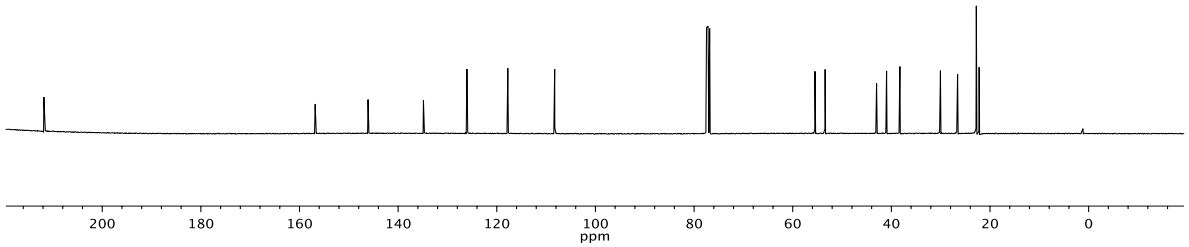
^{13}C NMR (100 MHz, $CDCl_3$) of compound **36**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **29**.

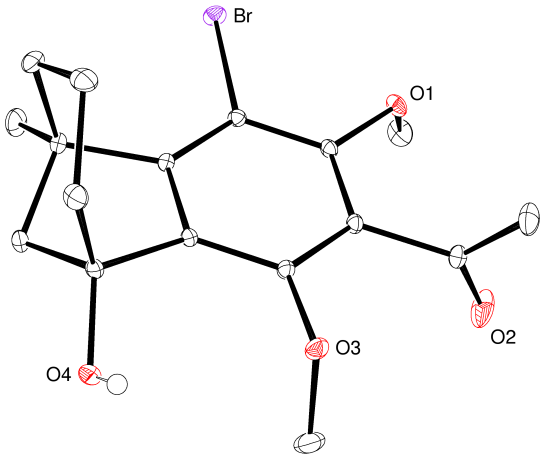


Infrared spectrum (Thin Film, NaCl) of compound **29**.



^{13}C NMR (100 MHz, $CDCl_3$) of compound **29**.

Crystal Structure for 24



A14105

Note: The crystallographic data have been deposited in the Cambridge Database (CCDC). The deposition number is 1024141.

Table 2. Crystal data and structure refinement for A14105 (CCDC 1024141).

Empirical formula	$C_{17}H_{21}BrO_4 \bullet H_2O$
Formula weight	387.26
Crystallization solvent	Dichloromethane/hexanes
Crystal Habit	Chunk
Crystal color	Colorless
Crystal size (mm)	0.43 x 0.42 x 0.29 mm^3

Data Collection

Type of diffractometer	Bruker *APEX*-II CCD
Wavelength	0.71073 Å MoKα
Data collection temperature	100 K
θ range for 9869 reflections used in lattice determination	2.8 to 45.7°

Unit cell dimensions	a = 18.8295(9) Å b = 7.8451(4) Å c = 11.4443(5) Å β = 95.208(2)°
Volume	1683.56(14) $Å^3$
Z	4
Crystal system	Monoclinic
Space group	C2
Density (calculated)	1.528 Mg/m^3
F(000)	800
Data collection program	APEX2 2014.1-1 (Bruker-AXS, 2007)
θ range for data collection	1.8 to 48.8°
Completeness to θ = 48.8°	99.6%
Index ranges	$-39 \leq h \geq 39$, $-16 \leq k \geq 16$, $-22 \leq l \geq 24$
Data collection scan type	ω scans at 5 ϕ settings
Data reduction program	SAINT v8.34A (Bruker-AXS, 2007)
Reflections collected	78240
Independent reflections	16574
Absorption coefficient	2.464 mm^{-1}
Absorption correction	Multiscan
Max. and min. transmission	0.4462 and 0.5777

Hammett Plot Data

Table 3. Data for Hammett analysis of enantioselectivity for select boronic acids.

phenylboronic acid	σ_p[2]	ee[3]	er	$\log_{10}$(er)
p-Et	-0.15	85	12	1.1
p-Me	-0.17	87	14	1.2
p-H	0	92	24	1.4
p-F	0.06	92	24	1.4
p-Cl	0.23	95	39	1.6
p-Ac	0.50	96	49	1.7
p-CF_3	0.54	96	49	1.7
p-Br	0.23			
p-iPr	-0.15			

References

[1] Shimizu, H.; Holder, J. C.; Stoltz, B. M. *Beilstein J. Org. Chem.* **2013**, *9*, 1637–1642.

[2] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.

[3] Kikushima, K; Holder, J. C.; Gatti, M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2011**, *133*, 6902–6905.