Supplementary Material (ESI) for Dalton Transactions

Solvent-free aromatic C-H functionalisation/halogenation reactions

Robin B. Bedford, Jens U. Engelhart, Mairi F. Haddow, Charlotte J. Mitchell and Ruth L. Webster

Supporting Information

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General experimental conditions. All reagents were used as supplied, without further purification. Acetanilides were purchased from commercials sources, pivanilides were synthesised using the method described. Benzamides were synthesised using a literature method[1] and were analytically comparable to the reported substrates. Two previously unreported benzamides were synthesised using the same method (2-methoxy-*N*-isopropylbenzamide and 3-fluoro-*N*-isopropylbenzamide), analytical data is provided. Carbamates were prepared following literature methods[2,3] and compared with the previously reported compounds. Reactions were performed in Biotage microwave vials, heating in an oil bath at the stated temperature for the specified reaction time. Thin layer chromatography was carried out on Polygram 0.2 mm silica gel TLC plates visualising with 254 nm UV light. Palladium-free reactions were carried out with 99.999% copper salts (Sigma Aldrich), which were determined to contain < 2 ppm Pd by Varian 730-ES axially viewed ICP-OES (with a detection limit of 2ppm). Regiochemistry for all compounds was confirmed by HMBC and NOE NMR spectroscopy techniques.

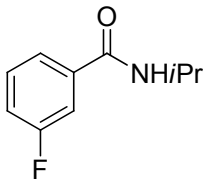
General procedure for the synthesis of anilides. Aniline (13.8 mmol) was dissolved in DCM followed by the addition of NEt_3 (2.5 ml, 18.0 mmol). The solution was cooled to 0 °C and the appropriate acetyl chloride (18.0 mmol) was added drop wise over the course of 5 minutes. The solution was allowed to warm to room temperature and stirred for a further 4 hours. The solution was then further diluted with Et_2O and washed with water, 1M HCl, $NaHCO_3$ (sat.) and then brine. The organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was then recrystallised (EtOAc/ hexanes) to provide the analytically pure product.

Large scale synthesis of *N*-(2-chloro-4-methylphenyl)acetamide (2a). 4-methylacetanilide (14.9 g, 100 mmol), $CuCl_2$ (26.9 g, 200 mmol) and $Pd(OAc)_2$ (1.12 g, 5 mmol) were ground with a pestle and mortar (approx. 2 mins) until homogeneous. The powder was transferred to a beaker (70 mm diameter) with a long-stemmed filter funnel placed over the top. The reaction mixture was heated at 120 °C for 24 hours, without stirring. The reaction mixture was allowed to cool to room temperature then extracted with 800 ml Et_2O. The organic extracts were washed with 3 x 150 ml 2M HCl followed by 2 x 100 ml H_2O. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The resulting pale orange solid

was recrystallised (EtOAc/ hexanes) and air dried to provide the microanalytically pure product, **2a**, as an off-white solid (13.47 g, 73%).

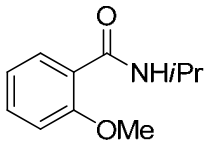
Product characterisation data

3-Fluoro-*N*-isopropylbenzamide (3e)



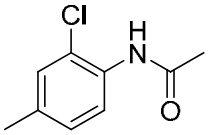
White crystalline solid, 1.70 g (68 %); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.53-7.47 (m, 2H), 7.41-7.36 (m, 1H), 7.18 (dddd, *J* 8.5, 8.2, 1.5, 1.1 Hz, 1H), 6.12 (br. s, 1H), 4.32-4.24 (br. m, 1H), 1.27 (d, *J* 6.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 165.5, 164.1 (d, *J* 248 Hz), 137.4 (d, *J* 7 Hz), 130.3 (d, *J* 8 Hz), 122.4 (d, *J* 3 Hz), 118.4 (d, *J* 22 Hz), 114.5 (d, *J* 23 Hz), 42.2, 22.9; IR neat, ν (cm^{-1}) 3255, 3072, 2973, 1631, 1582, 1545, 1289, 1226; m.p. 84.0-85.4 °C; HRMS (CI) calcd. for $C_{10}H_{12}FNO$ $(M+H)^+$ 182.0981, found 182.0980; Anal. calcd. for $C_{10}H_{12}FNO$: C, 66.3; H, 6.7; N, 7.7. Found: C, 66.3; H, 6.6; N, 7.7.

2-Methoxy-*N*-isopropylbenzamide (3g)



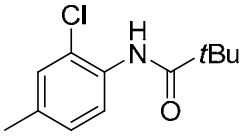
Colourless oil, 1.31 g (68 %); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.15 (m, 1H), 7.70 (br. s, 1H), 7.38 (m, 1H), 7.02 (m, 2H), 4.30-4.22 (m, 1H), 3.91 (s, 3H), 1.23 (d, *J* 6.4 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 164.4, 157.5, 132.6, 121.3, 111.5, 56.0, 41.6, 22.9; IR neat, ν (cm^{-1}) 3393, 2971, 1644, 1528, 1464, 1290, 1236; HRMS (CI) calcd. for $C_{11}H_{16}NO_2$ $(M+H)^+$ 194.1181, found 194.1190; Anal. calcd. for $C_{11}H_{15}NO_2$: C, 68.4; H, 7.8; N, 7.3. Found: C, 68.7; H, 8.1; N, 7.1.

Table 1, Entry 1 (2a)



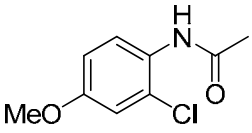
White solid, 171 mg (93 %); R*f* 0.4 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.20 (d, *J* 8.3 Hz, 1H), 7.54 (br. s, 1H), 7.19 (s, 1H), 7.08 (d, *J* 8.3 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.1, 134.7, 132.0, 129.2, 128.3, 121.6, 119.6, 24.8, 20.6; IR neat, ν (cm^{-1}) 3277, 2922, 1659, 1527, 1364, 1294, 1059; m.p. 115.4- 116.0 °C; HRMS (EI) calcd. for $C_9H_{11}ClNO$ $(M+H)^+$ 184.0529, found 184.0525; Anal. calcd. for $C_9H_{10}ClNO$: C, 58.9; H, 5.5; N, 7.6. Found: C, 59.1; H, 5.1; N, 7.8.

Table 1, Entry 2 (2b)



White solid, 190 mg (84 %); R*f* 0.32 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.22 (d, *J* 8.4 Hz, 1H), 7.90 (br. s, 1H), 7.13 (d, *J* 2.6 Hz, 1H), 7.02 (dd, *J* 8.4, 2.6 Hz, 1H), 2.25 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.5, 134.5, 132.3, 129.2, 128.4, 122.9, 121.4, 40.1, 27.6, 20.7; IR neat, ν (cm^{-1}) 3308, 2955, 2868, 1654, 1509, 1492, 1398, 1174; m.p. 68.0 °C; HRMS (EI) calcd. for $C_{12}H_{17}ClNO$ $(M+H)^+$ 226.0999, found 226.0990; Anal. calcd. for $C_{12}H_{16}ClNO$: C, 63.9; H, 7.1; N, 6.2. Found: C, 63.8; H, 7.3; N, 6.2.

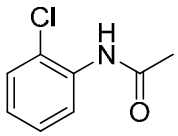
Table 1, Entry 3 (2c)



White solid, 64 mg (32 %); R*f* 0.29 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.16 (d, *J* 9.0 Hz, 1H), 7.39 (br. s, 1H), 6.94 (d, *J* 3.0 Hz, 1H), 6.83 (dd, *J* 9.0, 3.0 Hz, 1H), 3.79 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.0, 156.2, 127.9, 124.0, 123.3, 114.4, 113.2,

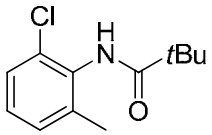
55.7, 24.6; IR neat, ν (cm^{-1}) 3293, 2933, 2839, 1655, 1529, 1490, 1364, 1277, 1037; m.p. 113-114 °C; HRMS (CI) calcd. for $C_9H_{11}ClNO_2$ $(M+H)^+$ 200.0478, found 200.0486; Anal. calcd. for $C_9H_{10}ClNO_2$: C, 54.2; H, 5.1; N, 7.0. Found: C, 54.5; H, 5.2; N, 6.6.

Table 1, Entry 4 (2d)



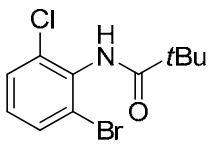
White solid, 96 mg (57 %); R*f* 0.50 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.32 (d, *J* 8.0 Hz, 1H), 7.69 (br. s, 1H), 7.35 (d, *J* 8.0 Hz, 1H), 7.24 (dd, *J* 7.3, 1.2 Hz, 1H), 7.03 (t, *J* 7.3 Hz, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.7, 134.6, 129.1, 127.8, 124.9, 122.0, 24.7; IR neat, ν (cm^{-1}) 3232, 3038, 1661, 1583, 1526, 1436, 1369, 1300, 1059; m.p. 87.9- 88.5 °C; MS (EI) m/z 170.0 (100%).

Table 1, Entry 8 (2e)



White solid, 221 mg (98 %); R*f* 0.62 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.31-7.10 (br. m, 4H), 2.25 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.6, 138.1, 132.8, 129.0, 127.5, 126.8, 124.9, 39.3, 27.6, 18.7; IR neat, ν (cm^{-1}) 3282, 2962, 1651, 1496, 1366, 1226, 1173; m.p. 164.2- 165.1 °C; HRMS (EI) calcd. for $C_{12}H_{17}ClNO$ $(M+H)^+$ 226.0999, found 226.0998; Anal. calcd. for $C_{12}H_{16}ClNO$: C, 63.9; H, 7.1; N, 6.2. Found: C, 64.1; H, 7.3; N, 6.1.

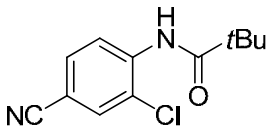
Table 1, Entry 9 (2f)



White solid, 190 mg (66 %); R*f* 0.66 (EtOAc/cyclohexane, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.51 (dd, *J* 8.1, 1.4 Hz, 1H), 7.38 (dd, *J* 8.1, 1.4 Hz, 1H), 7.21 (br. s, 1H), 7.07 (t, *J* 8.1 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.2, 133.8, 132.2, 131.4, 129.1, 128.7, 123.8,

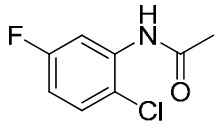
39.5, 27.8; IR neat, ν (cm^{-1}) 3268, 2968, 1656, 1500, 1446, 1432, 1171; m.p. 162.0- 164.0 °C; HRMS (ESI) calcd. for $C_{11}H_{14}BrClNO$ $(M+H)^+$ 289.9951, found 289.9947; Anal. calcd. for $C_{11}H_{13}BrClNO$: C, 45.5; H, 4.5; N, 4.8. Found: C, 45.8; H, 4.6; N, 4.7.

Table 1, Entry 10 (2g)



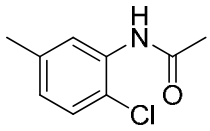
Off-white solid, 62 mg (26 %); R*f* 0.67 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.66 (d, *J* 8.8 Hz, 1H), 8.23 (br. s, 1H), 7.70 (d, *J* 1.8 Hz, 1H), 7.59 (dd, *J* 8.8, 1.8 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.9, 138.9, 132.3, 132.0, 122.7, 120.8, 117.6, 107.3, 40.5, 27.4; IR neat, ν (cm^{-1}) 3419, 2961, 1694, 1596, 1500, 1485, 1393, 1301; m.p. 108.1-109.5 °C; HRMS (CI) calcd. for $C_{12}H_{12}ClNO_2$ $(M+H)^+$ 237.0557, found 237.0566; Anal. calcd. for $C_{12}H_{11}ClNO_2$: C, 60.9; H, 5.5; N, 11.8. Found: C, 60.8; H, 5.2; N, 11.8.

Table 1, Entry 11 (2h)



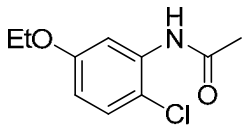
White solid, 120 mg (64 %); R*f* 0.33 (EtOAc/hexanes, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.26 (dd, *J* 10.3, 2.4 Hz, 1H), 7.66 (br. s, 1H), 7.32 (dd, *J* 8.8, 5.6 Hz, 1H), 6.77 (ddd, *J* 10.5, 8.8, 2.4 Hz, 1H), 2.30 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.3, 162.7 (d, *J* 245 Hz), 135.7 (d, *J* 13 Hz), 129.6 (d, *J* 9 Hz), 116.9 (d, *J* 2 Hz), 111.4 (d, *J* 23 Hz), 108.9 (d, *J* 30 Hz), 24.9; IR neat, ν (cm^{-1}) 3268, 3084, 1667, 1593, 1534, 1422, 1287, 1255; m.p. 89.5 °C; MS (ESI) calcd. for C_8H_8ClFNO $(M+H)^+$ 188.03, found 188.03; Anal. calcd. for C_8H_7ClFNO: C, 51.2; H, 3.8; N, 7.5. Found: C, 50.9; H, 3.9; N, 7.2.

Table 1, Entry 12 (2j)



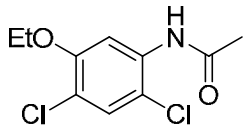
White solid, 116 mg (63 %); R*f* 0.36 (EtOAc/cyclohexane, 3:7); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.16 (app. s, 1H), 7.59 (br. s, 1H), 7.21 (d, *J* 8.3 Hz, 1H), 6.84 (app. d, *J* 8.3 Hz, 1H), 2.32 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 137.8, 134.1, 128.5, 125.4, 122.2, 119.6, 24.8, 21.3; IR neat, ν (cm^{-1}) 3263, 2988, 1666, 1576, 1517, 1413, 1374, 1251, 1056; m.p. 90.5-91.5 °C; MS (ESI) calcd. for $C_9H_{10}ClNNaO$ $(M+Na)^+$ 206.04, found 206.04; Anal. calcd. for $C_9H_{10}ClNO$: C, 58.9; H, 5.5; N, 7.6. Found: C, 58.9; H, 5.5; N, 7.2.

Table 1, Entry 13 (2l)



White solid, 117 mg (55 %); R*f* 0.27 (EtOAc/hexanes, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.07 (s, 1H), 7.59 (br. s, 1H), 7.22 (d, *J* 8.8 Hz, 1H), 6.60 (dd, *J* 8.8, 3.0 Hz, 1H), 4.04 (q, *J* 7.0 Hz, 2H), 2.24 (s, 3H), 1.40 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 158.3, 135.2, 129.1, 113.4, 111.5, 107.1, 63.9, 25.0, 14.7; IR neat, ν (cm^{-1}) 3243, 2973, 1656, 1581, 1532, 1438, 1269; m.p. 106 °C; HRMS (ESI) calcd. for $C_{10}H_{13}ClNO_2$ $(M+H)^+$ 214.0629, found 214.0635; Anal. calcd. for $C_{10}H_{12}ClNO_2$: C, 56.2; H, 5.7; N, 6.6. Found: C, 55.8; H, 5.6; N, 6.3.

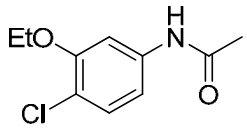
Table 1, Entry 13 (2m)



White solid, 63 mg (25 %); R*f* 0.11 (EtOAc/hexanes, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.18 (s, 1H), 7.57 (br. s, 1H), 7.34 (s, 1H), 4.12 (q, *J* 7.1 Hz, 2H), 2.24 (s, 3H), 1.46 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.3, 153.6, 134.0, 129.5, 117.5, 121.6, 113.0, 106.1, 65.1, 14.6,

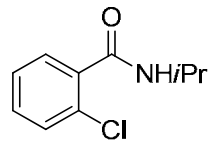
14.4; IR neat, ν (cm^{-1}) 3284, 2977, 2933, 1668, 1514, 1467, 1390, 1245, 1190; m.p. 144.0 °C; MS (CI) calcd. for $C_{10}H_{12}Cl_2NO_2$ $(M+H)^+$ 248.0, found 248.0.

Table 1, Entry 13 (2n)



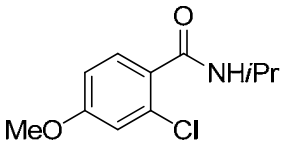
White solid, 29 mg (14 %); R*f* 0.05 (EtOAc/hexanes, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.51 (d, *J* 2.2 Hz, 1H), 7.25 (d, *J* 8.4 Hz, 1H), 7.21 (br. s, 1H), 6.78 (dd, *J* 8.4, 2.2 Hz, 1H), 4.12 (q, *J* 7.0 Hz, 2H), 2.18 (s, 3H), 1.47 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 154.7, 137.6, 130.0, 117.8, 111.8, 105.5, 64.8, 24.7, 14.6; IR neat, ν (cm^{-1}) 3282, 2935, 1695, 1659, 1597, 1495, 1389, 1263, 1064; m.p. 99.0 °C; MS (CI) calcd. for $C_{10}H_{12}ClNO_2$ $(M+H)^+$ 214.1, found 214.1.

Table 2, Entry 2 (4b)



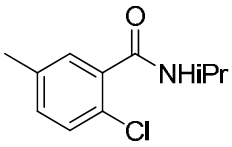
White solid, 135 mg (69 %); R*f* 0.37 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.60 (dd, *J* 7.3, 1.7 Hz, 1H), 7.36-7.29 (m, 3H), 6.03 (br. s, 1H), 4.28 (septet, *J* 6.6 Hz, 1H), 2.32 (s, 3H), 1.27 (d, *J* 6.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ165.7, 135.6, 131.0, 130.5, 130.1, 130.0, 127.0, 42.2, 22.7; IR neat, ν (cm^{-1}) 3247, 3077, 2980, 1631, 1552, 1430, 1299, 1051; m.p. 139.8- 140.9°C; MS (ESI) calcd. for $C_{10}H_{12}ClNaNO$ $(M+Na)^+$ 220.05, found 220.05; Anal. calcd. for $C_{10}H_{12}ClNO$: C, 60.8; H, 6.1; N, 7.1. Found: C, 60.8; H, 6.4; N, 7.1.

Table 2, Entry 3 (4c)



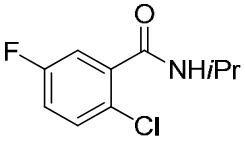
White solid, 129 mg (57 %); R*f* 0.33 (EtOAc/cyclohexane, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.687 (d, *J* 8.8 Hz, 1H), 6.89 (d, *J* 2.5 Hz 1H), 6.84 (dd, *J* 8.8, 2.5 Hz, 1H), 6.17 (br. s, 1H), 4.32-4.23 (br. m, 1H), 3.82 (s, 3H), 1.27 (d, *J* 6.3 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 165.1, 161.2, 131.9, 131.5, 127.3, 115.4, 112.9, 55.5, 42.1, 22.6; IR neat, ν (cm^{-1}) 3284, 2970, 1631, 1535, 1287, 1233, 1045; m.p. 117.0 °C; HRMS (CI) calcd. for $C_{11}H_{15}ClNO_2$ $(M+H)^+$ 228.0791, found 228.0801.

Table 2, Entry 4 (4d)



White solid, 160 mg (76 %); R*f* 0.44 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.42 (app. s, 1H), 7.24 (d, *J* 8.1 Hz, 1H), 7.13 (dd, *J* 8.1, 2.2 Hz, 1H), 6.05 (br. s, 1H), 4.28 (septet, *J* 6.6 Hz, 1H), 2.32 (s, 3H), 1.26 (d, *J* 6.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 165.9, 137.2, 135.2, 131.9, 130.6, 129.9, 127.4, 42.2, 22.7, 20.8; IR neat, ν (cm^{-1}) 3294, 2974, 1639, 1528, 1451, 1326; m.p. 126.0 °C; HRMS (CI) calcd. for $C_{11}H_{15}ClNO$ $(M+H)^+$ 212.0842, found 212.0834; Anal. calcd. for $C_{11}H_{14}ClNO$: C, 62.4; H, 6.7; N, 6.6. Found: C, 62.2; H, 6.7; N, 6.6.

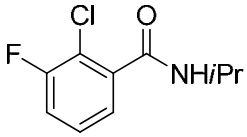
Table 2, Entry 5 (4e)



White solid, 22 mg (10 %); R*f* 0.40 (EtOAc/cyclohexane, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.38-7.33 (m, 2H), 7.06 (ddd, *J* 10.5, 7.6, 1.8 Hz, 1H), 6.08 (br. s, 1H), 4.32-4.24 (br. m, 1H), 1.28 (d, *J* 6.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 164.2, 162.4 (d, *J* 248 Hz), 136.9 (d, *J* 7

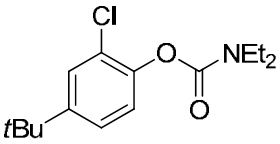
Hz), 131.7 (d, *J* 8 Hz), 125.4 (d, *J* 3 Hz), 118.4 (d, *J* 23 Hz), 117.3 (d, *J* 24 Hz), 42.4, 22.6; IR neat, ν (cm^{-1}) 3240, 3076, 2978, 1632, 1556, 1467, 1253; m.p. 131.0 °C; HRMS (CI) calcd. for $C_{10}H_{12}ClFNO$ $(M+H)^+$ 216.0591, found 216.0584.

Table 2, Entry 5 (4f)



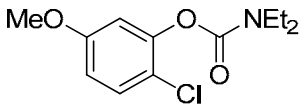
White solid, 59 mg (27 %); R*f* 0.21 (EtOAc/cyclohexane, 1:2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.38 (app. dt, *J* 7.6, 1.4 Hz, 1H), 7.30-7.25 (m, 1H), 7.19 (ddd, *J* 17.1, 7.6, 1.7 Hz, 1H), 5.97 (br. s, 1H), 4.29 (br. m, 1H), 1.28 (d, *J* 6.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 164.6, 159.4 (d, *J* 250 Hz), 137.8, 128.1 (d, *J* 8 Hz), 124.9 (d, *J* 4 Hz), 118.4 (d, *J* 20 Hz), 117.9 (d, *J* 22 Hz), 42.4, 22.6; IR neat, ν (cm^{-1}) 3267, 2977, 1637, 1541, 1440, 1259; m.p. 91.0 °C; HRMS (CI) calcd. for $C_{10}H_{12}ClFNO$ $(M+H)^+$ 216.0591, found 216.0599.

Table 2, Entry 8 (6a)



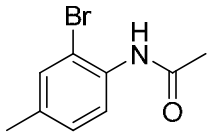
White solid, 170 mg (60 %); R*f* 0.7 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.41 (d, *J* 2.2 Hz, 1H), 7.28 (dd, *J* 8.6, 2.2 Hz, 1H), 7.13 (d, *J* 8.6 Hz, 1H), 3.51-3.37 (br. m, 4H), 1.30-1.20 (br. m, 15H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 153.4, 149.6, 145.2, 127.1, 126.4, 124.6, 123.4, 42.4, 42.1, 34.6, 31.3, 14.1, 13.3; IR neat, ν (cm^{-1}) 2967, 2872, 1706, 1423, 1265, 1160, 1058; m.p. 78.5- 78.8 °C; HRMS (EI) calcd. for $C_{15}H_{23}ClNO_2$ $(M+H)^+$ 284.1417, found 284.1412; Anal. calcd. for $C_{15}H_{12}ClNO_2$: C, 63.5; H, 7.8; N, 4.9. Found: C, 63.4; H, 7.7; N, 4.7.

Table 2, Entry 9 (6b)



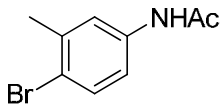
Colourless oil, 125 mg (48 %); R*f* 0.21 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.27 (d, *J* 8.8 Hz, 1H), 6.79 (d, *J* 2.7 Hz, 1H), 6.70 (dd, *J* 8.8, 2.7 Hz, 1H), 3.77 (s, 3H), 3.48 (quartet, *J* 7.1 Hz, 2H), 3.39 (quartet, *J* 6.9 Hz, 2H), 1.29 (t, *J* 7.1 Hz, 3H), 1.21 (t, *J* 6.9 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.9, 153.0, 148.2, 130.0, 118.5, 112.5, 109.8, 55.6, 42.4, 42.0, 14.1, 13.3; IR neat, ν (cm^{-1}) 2974, 2936, 1720, 1603, 1488, 1410, 1266, 1154, 1069; HRMS (CI) calcd. for $C_{12}H_{17}ClNO_3$ $(M+H)^+$ 258.0897, found 258.0899; Anal. calcd. for $C_{12}H_{16}ClNO_3$: C, 55.9; H, 6.3; N, 5.4. Found: C, 56.3; H, 6.6; N, 5.4.

Table 3 (7a)



White solid, 226 mg; R*f* 0.4 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.17 (d, *J* 8.3 Hz, 1H), 7.52 (br. s, 1H), 7.36 (s, 1H), 7.12 (d, *J* 8.3 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.1, 135.3, 133.1, 132.4, 129.0, 121.9, 119.6, 24.8, 20.5; IR neat, ν (cm^{-1}) 3276, 2921, 1658, 1522, 1363, 1277, 1047; m.p. 117.1- 118.2 °C; HRMS (EI) calcd. for $C_9H_{11}BrNO$ $(M+H)^+$ 228.0024, found 228.0023; Anal. calcd. for $C_9H_{10}BrNO$: C, 47.4; H, 4.4; N, 6.1. Found: C, 47.0; H, 4.8; N, 6.2.

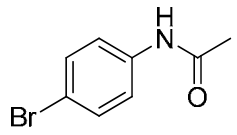
Table 4, Entry 1 (7b)



Reaction carried out using general procedure for bromination of anilides, but on a 0.5 mmol scale. White solid, 94 mg (82 %); R*f* 0.2 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.87 (br. s, 1H), 7.42-7.39 (m, 2H), 7.19 (dd, *J* 8.6, 2.6 Hz, 1H), 2.33 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.7, 138.4, 137.1, 132.5, 122.2, 119.4, 119.0, 24.4, 22.9; IR neat, ν (cm^{-1}) 3270, 2923, 1666, 1587, 1542, 1398, 1275, 1024; m.p. 105.4- 105.8 °C; HRMS (ESI)

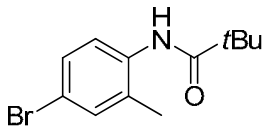
calcd. for $C_9H_{10}BrNNaO$ $(M+Na)^+$ 249.9838, found 249.9841; Anal. calcd. for $C_9H_{10}BrNO$: C, 47.4; H, 4.4; N, 6.1. Found: C, 47.3; H, 4.4; N, 6.0.

Table 4, Entry 2 (7c)



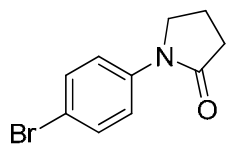
White solid, 209 mg (98 %); R*f* 0.17 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.44-7.39 (m, 4H), 7.32 (br. s, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.3, 136.9, 132.0, 121.4, 116.9, 24.6; m.p. 167.9-168.3 °C; HRMS (EI) calcd. for C_8H_9BrNO $(M+H)^+$ 213.9868, found 213.9860; Anal. calcd. for C_8H_8BrNO: C, 44.9; H, 3.8; N, 6.5. Found: C, 45.2; H, 3.7; N, 6.5.

Table 4, Entry 3 (7d)



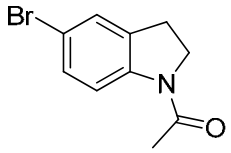
White solid, 226 mg (84 %); R*f* 0.63 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.71 (d, *J* 9.2 Hz, 1H), 7.31-7.22 (br. m, 2H), 7.21 (br. s, 1H), 2.319 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.7, 135.0, 132.9, 129.4, 125.0, 117.8, 39.6, 27.6, 17.4; IR neat, ν (cm^{-1}) 3338, 2957, 1648, 1510, 1479, 1183; m.p. 115.2 °C; HRMS (ESI) calcd. for $C_{12}H_{17}BrNO$ $(M+H)^+$ 270.0488, found 270.0498; Anal. calcd. for $C_{12}H_{16}BrNO$: C, 53.4; H, 6.0; N, 5.2. Found: C, 53.6; H, 6.1; N, 5.1.

Table 4, Entry 4 (7e)



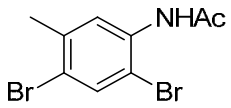
White solid, 220 mg (92 %); R*f* 0.14 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.52 (app. dt, *J* 9.0, 2.4 Hz, 2H), 7.45 (app. dt, *J* 9.0, 2.4 Hz, 2H), 3.81 (t, *J* 7.0 Hz, 2H), 2.60 (t, *J* 7.9 Hz, 2H), 2.15 (app. quintet, *J* 7.9 Hz, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 174.4, 138.6, 131.8, 121.3, 117.3, 48.7, 32.8, 18.0; IR neat, ν (cm^{-1}) 2890, 1683, 1481, 1385, 1305, 1223; m.p. 97.2- 99.1 °C; HRMS (ESI) calcd. for $C_{10}H_{11}BrNO$ $(M+H)^+$ 240.0019, found 240.0028; Anal. calcd. for $C_{10}H_{10}BrNO$: C, 50.0; H, 4.2; N, 5.8. Found: C, 50.0; H, 4.3; N, 5.6.

Table 4, Entry 5 (7f)



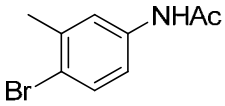
White solid, 180 mg (75 %); R*f* 0.11 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.08 (d, *J* 8.5 Hz, 1H), 7.30-7.27 (m, 2H), 4.04 (t, *J* 8.3 Hz, 2H), 3.16 (t, *J* 8.3 Hz, 2H), 2.21 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.9, 142.2, 133.6, 130.4, 127.7, 118.3, 116.0, 48.9, 27.8, 24.2; IR neat, ν (cm^{-1}) 2962, 1652, 1591, 1466, 1389, 1330, 1245; m.p. 118.2- 119.7 °C; HRMS (ESI) calcd. for $C_{10}H_{11}BrNO$ $(M+H)^+$ 240.0019, found 240.0029; Anal. calcd. for $C_{10}H_{10}BrNO$: C, 50.0; H, 4.2; N, 5.8. Found: C, 50.4; H, 4.2; N, 5.4.

Table 7, Entry 6 (7i)



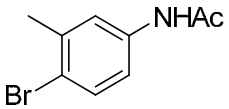
Reaction carried out using general procedure for bromination of anilides, but on a 0.5 mmol scale. White solid, 65 mg (21 %); R*f* 0.4 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.27 (br. s, 1H), 7.69 (s, 2H), 2.24 (s, 3H) 2.23 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 138.4, 134.6, 131.7, 123.4, 120.3, 119.3, 24.6, 22.9; IR neat, ν (cm^{-1}) 3266, 1663, 1565, 1515, 1370, 1281, 1256; m.p. 167.1- 168.0 °C; MS (EI) m/z 305.9 (100%), 307.9 (54%); Anal. calcd. for $C_9H_9Br_2NO$: C, 35.2; H, 3.0; N, 4.6. Found: C, 35.1; H, 3.1; N, 4.6.

Table 5, Entry 7 (7b)



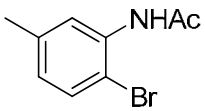
Reaction carried out on a 0.5 mmol scale. White solid, 91 mg (80 %); R*f* 0.2 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.70 (br. s, 1H), 7.43-7.41 (m, 2H), 7.20 (dd, *J* 8.6, 2.5 Hz, 1H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.6, 138.5, 137.0, 132.5, 122.1, 119.4, 118.9, 24.5, 23.0; IR neat, ν (cm^{-1}) 3270, 2923, 1666, 1587, 1542, 1398, 1275, 1024; m.p. 105.4- 105.8 °C; HRMS (ESI) calcd. for $C_9H_{10}BrNNaO$ $(M+Na)^+$ 249.9838, found 249.9844; Anal. calcd. for $C_9H_{10}BrNO$: C, 47.4; H, 4.4; N, 6.1. Found: C, 47.7; H, 4.3; N, 6.1.

***N*-(4-Bromo-3-methylphenyl)acetamide, 7b**



Synthesised using the general method for the preparartion of anilides using 4-bromo-3-methylaniline and acetyl chloride (*see* S2 for method & S80-81 for NMR spectra). ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.78 (br. s, 1H), 7.42-7.40 (m, 2H), 7.20 (dd, *J* 8.6, 2.5 Hz, 1H), 2.33 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.6, 138.5, 137.1, 132.5, 122.2, 119.4, 119.0, 24.5, 23.0; m.p. 105.0 °C.

***N*-(2-Bromo-5-methylphenyl)acetamide, 7j**



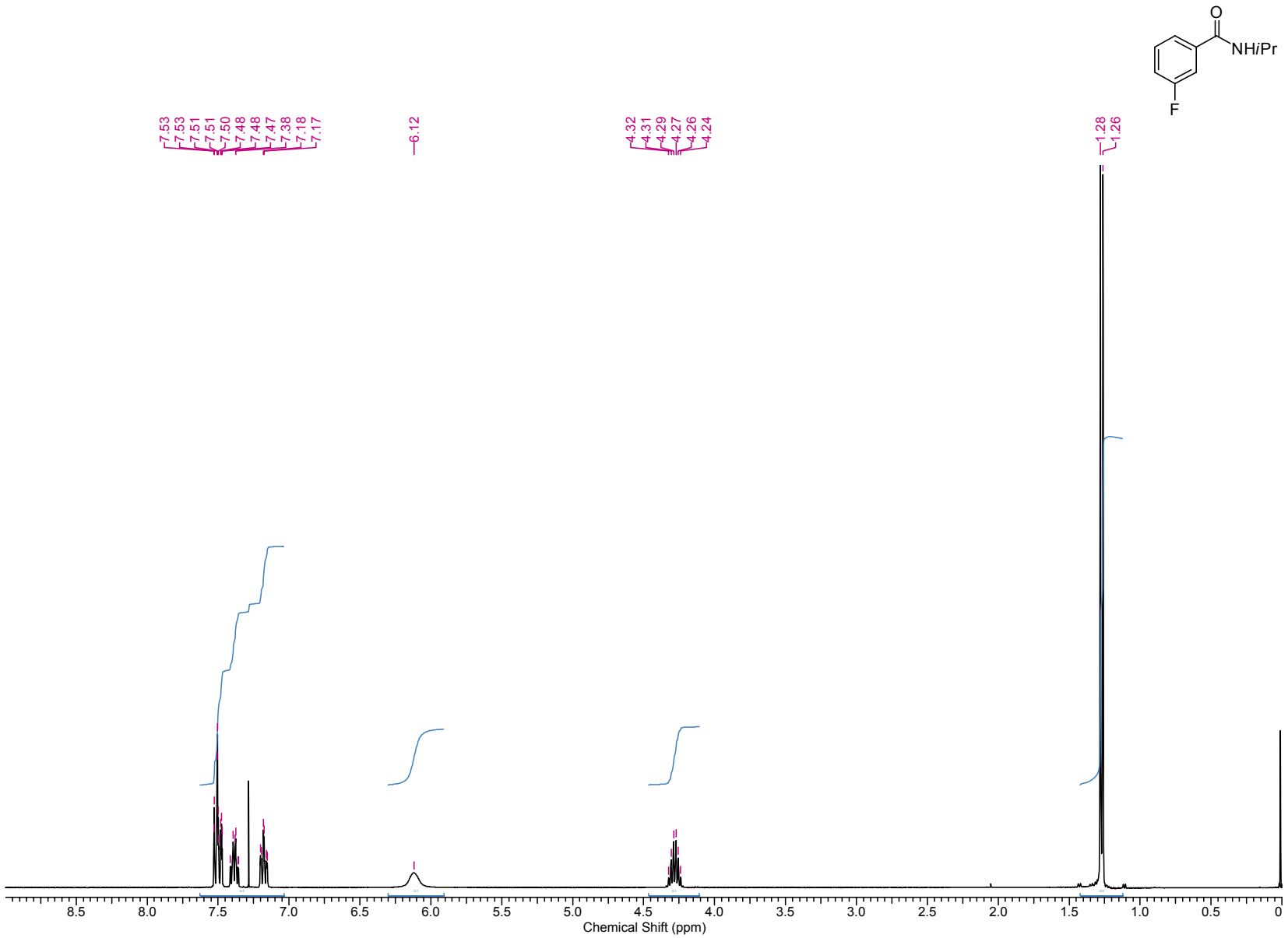
Synthesised using the general method for the preparartion of anilides using 2-bromo-5-methylaniline and acetyl chloride (*see* S2 for method & S80-81 for NMR spectra). ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.16 (app. s, 1H), 7.55 (br. s, 1H), 7.40 (d, *J* 8.3 Hz, 1H), 6.80 (dd, *J* 8.3, 1.0 Hz, 1H), 2.33 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.3, 138.8, 135.4, 131.9, 126.2, 122.6, 110.1, 25.0, 21.4; m.p. 122.5- 123.3 °C.

References

1. J. Clayden, C. C. Stimson and M. Keenan, *Chem. Commun.*, 2006, 1393

2. C.A. James and V. Snieckus, *J. Org. Chem.*, 2009, **74**, 4080

3. R. B. Bedford, R. L. Webster and C. J. Mitchell, *Org. Biomol. Chem.*, 2009, **7**, 4853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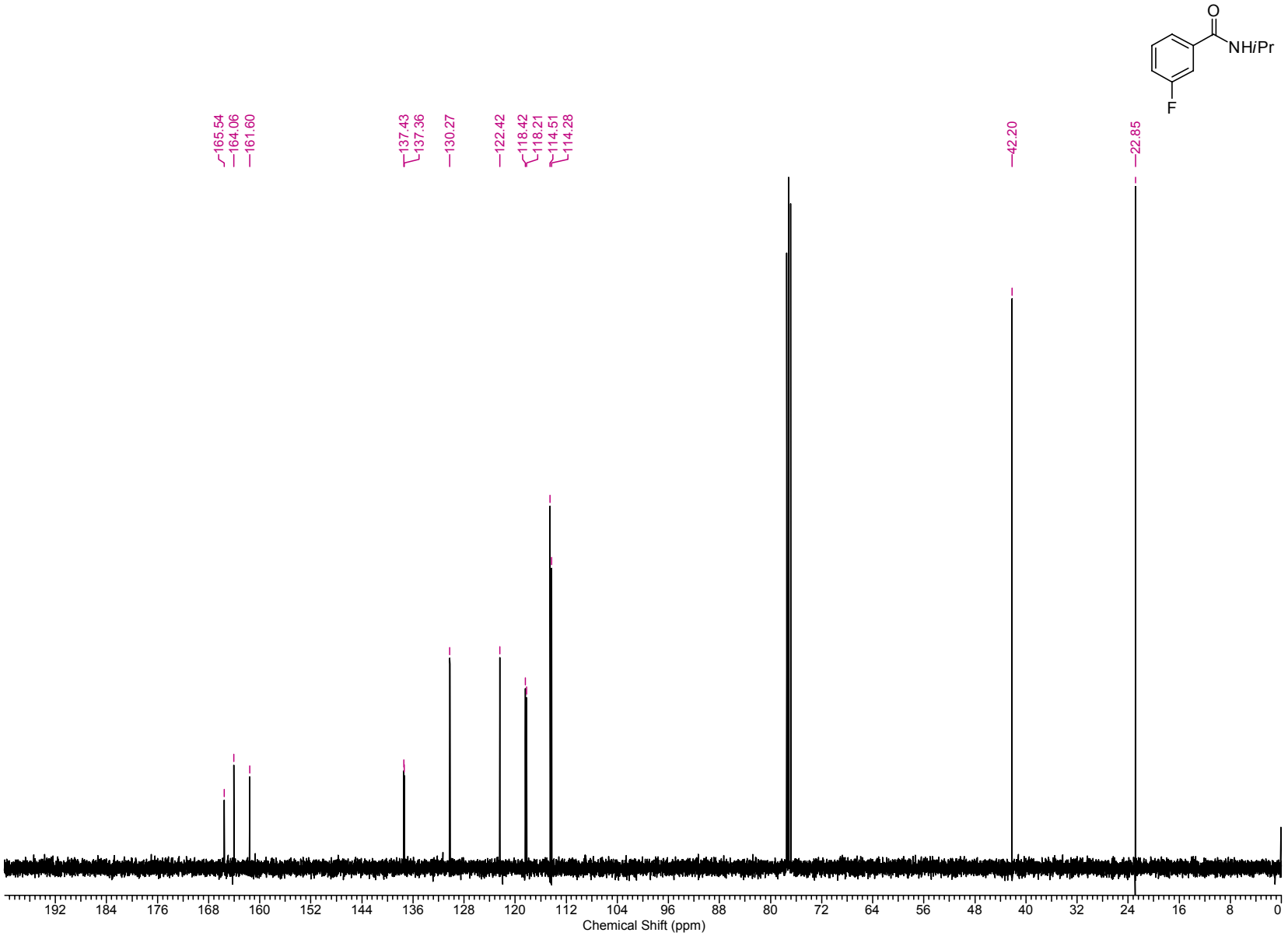
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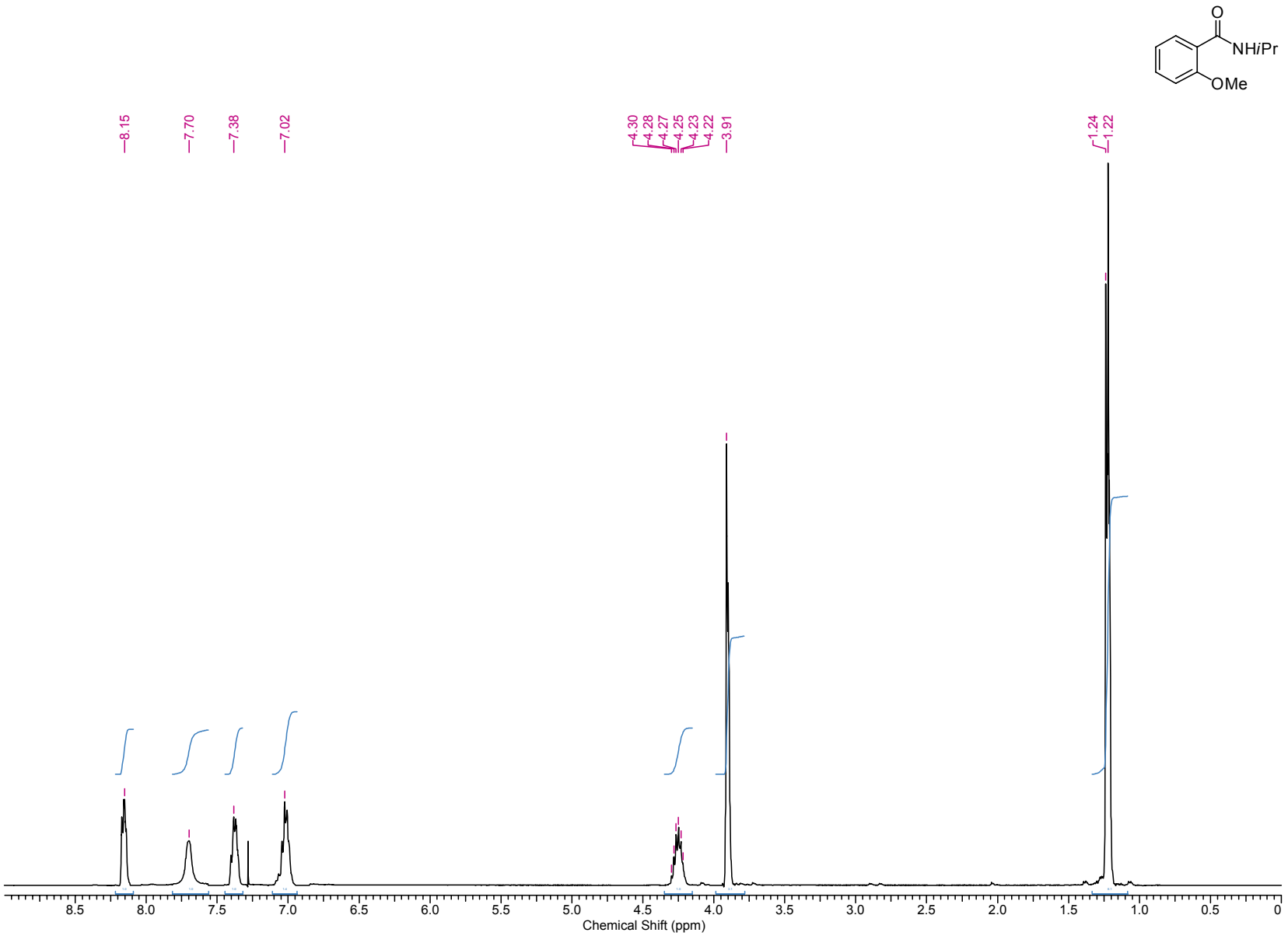
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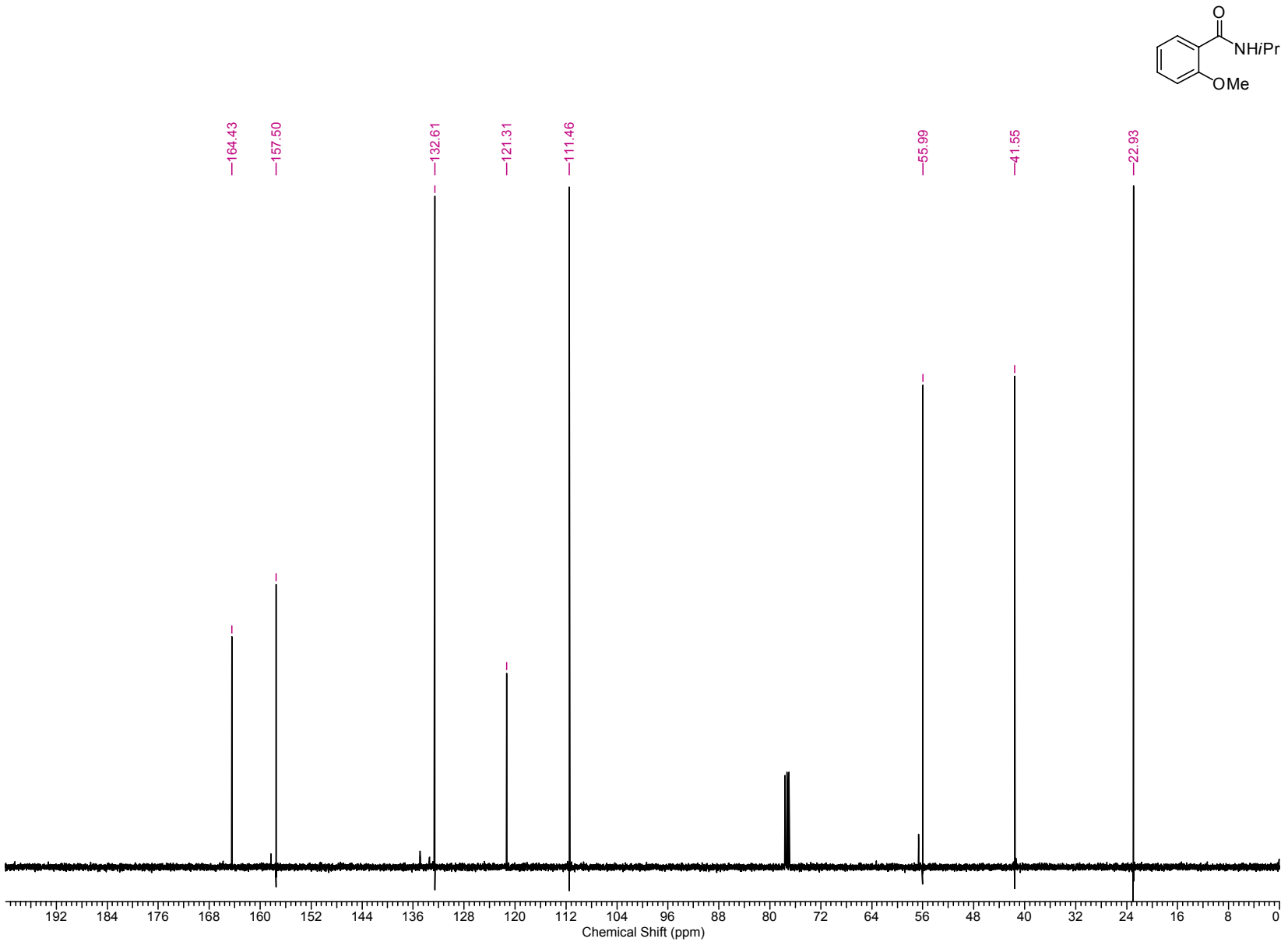
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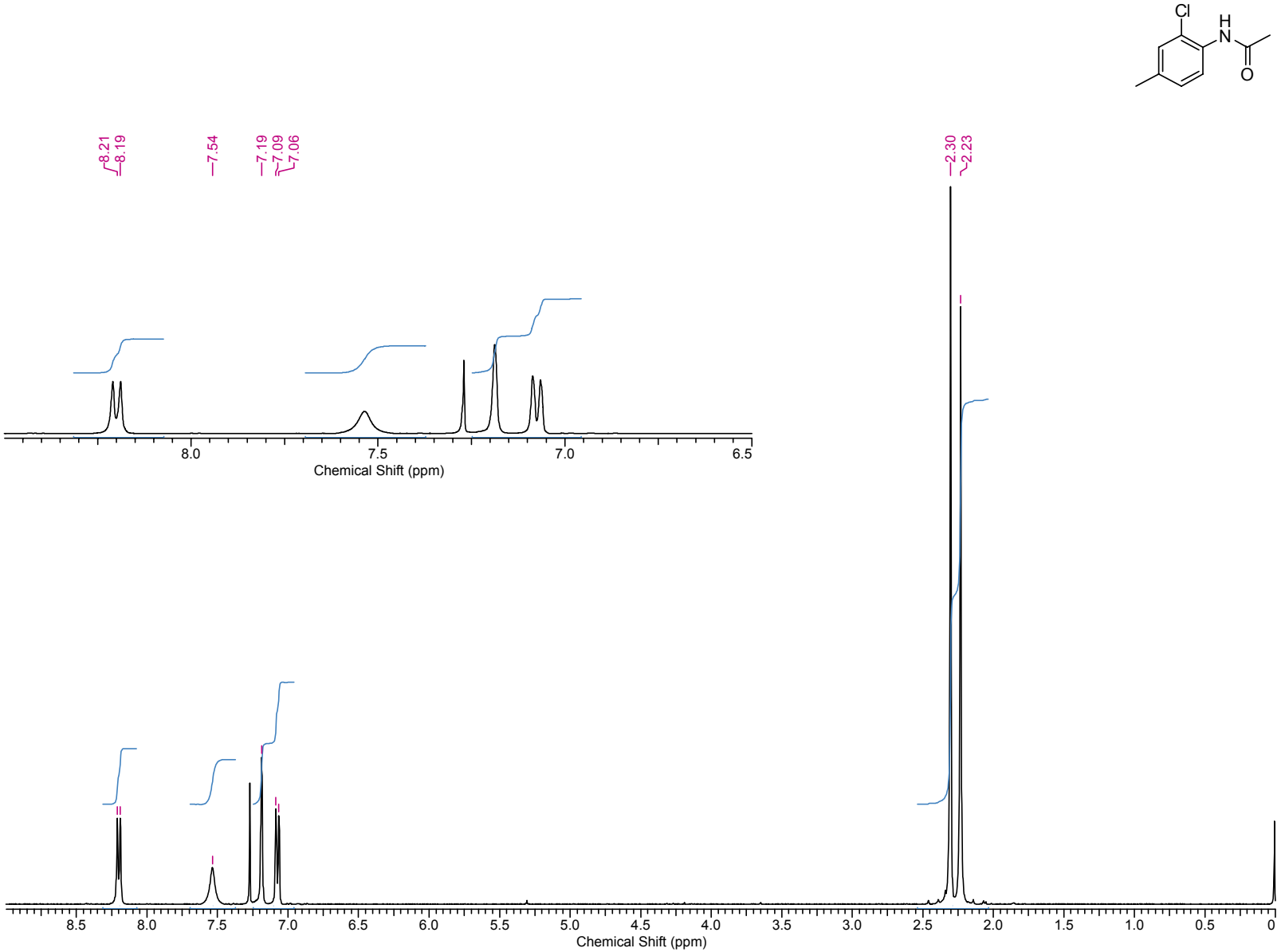
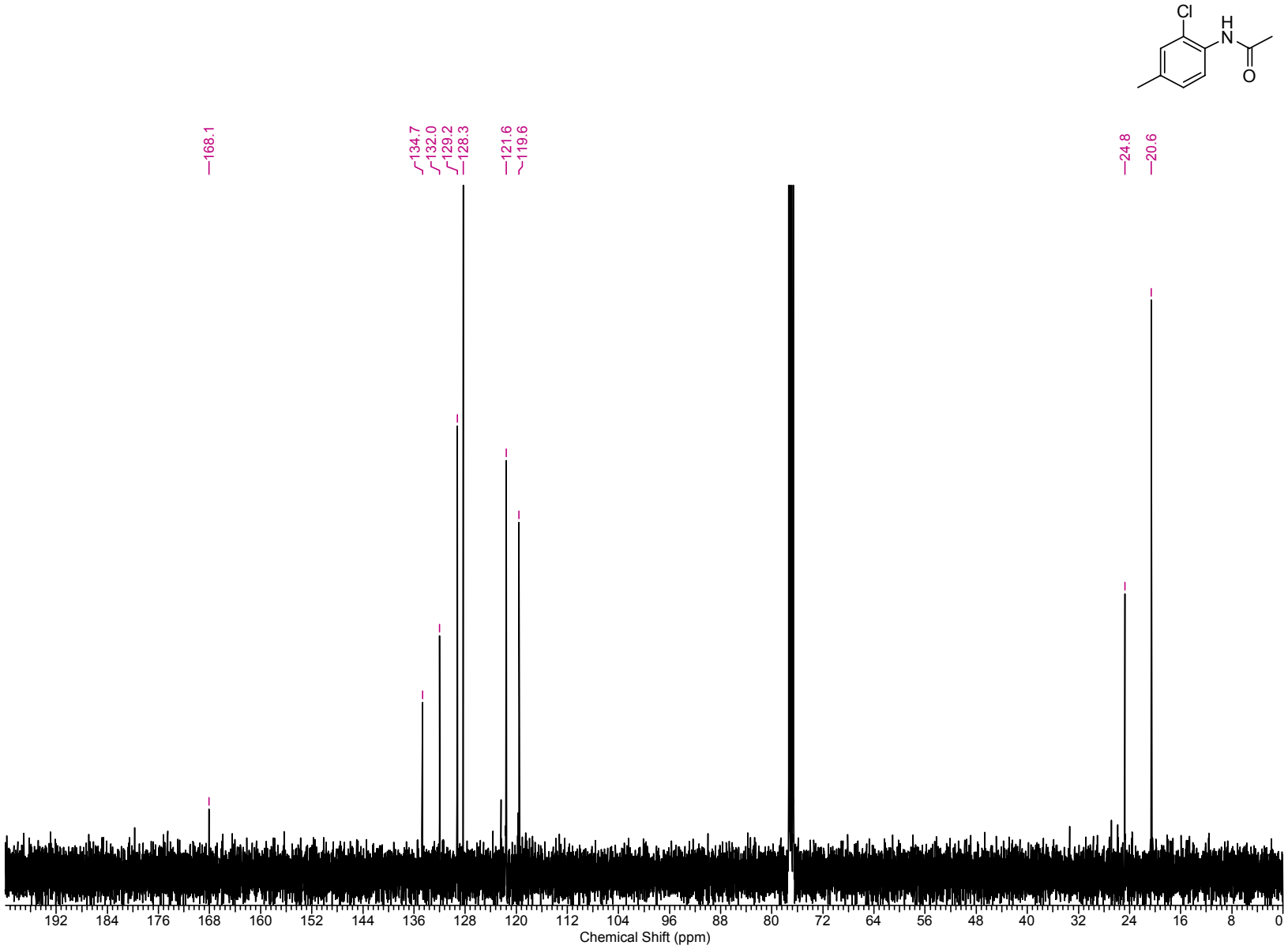
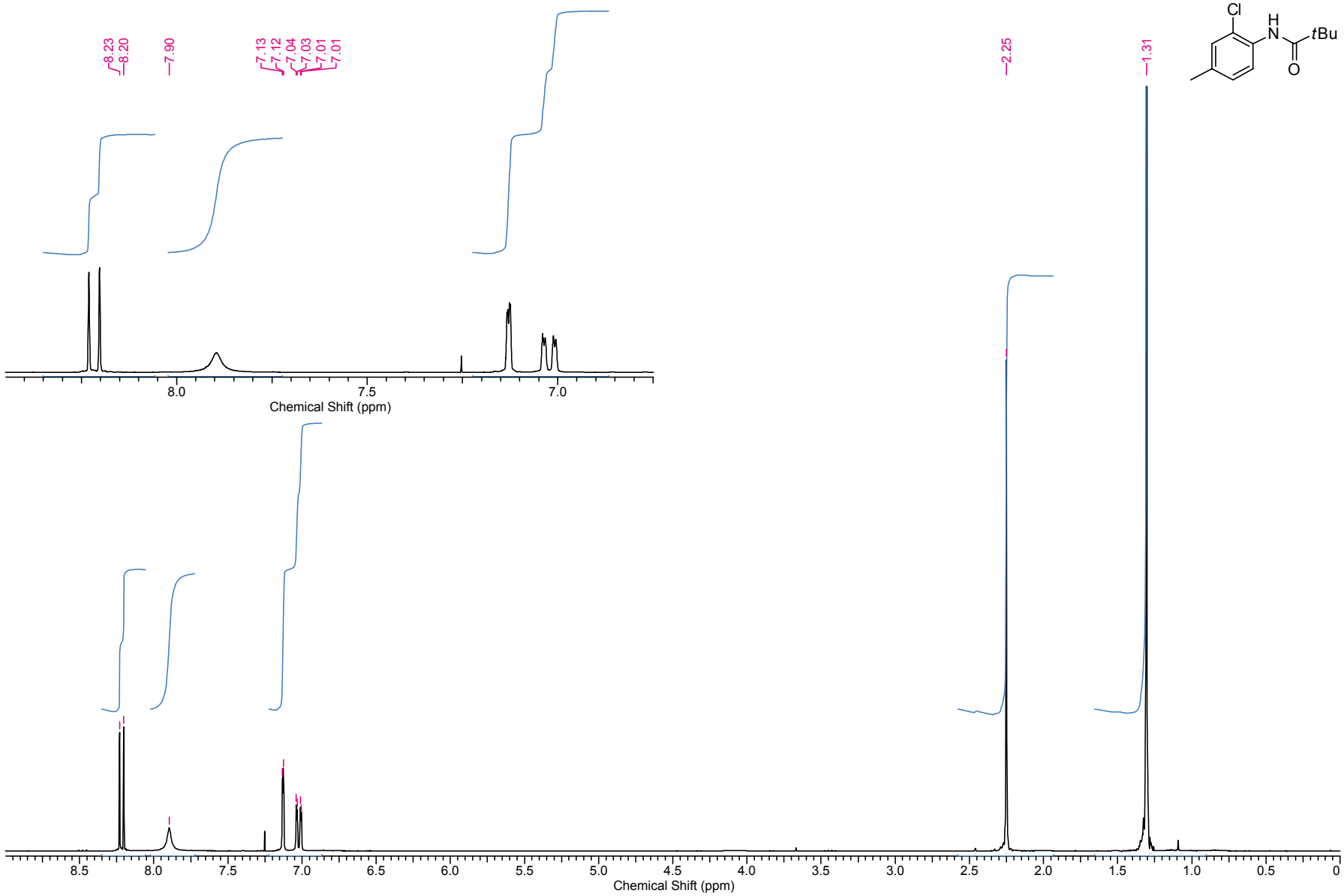
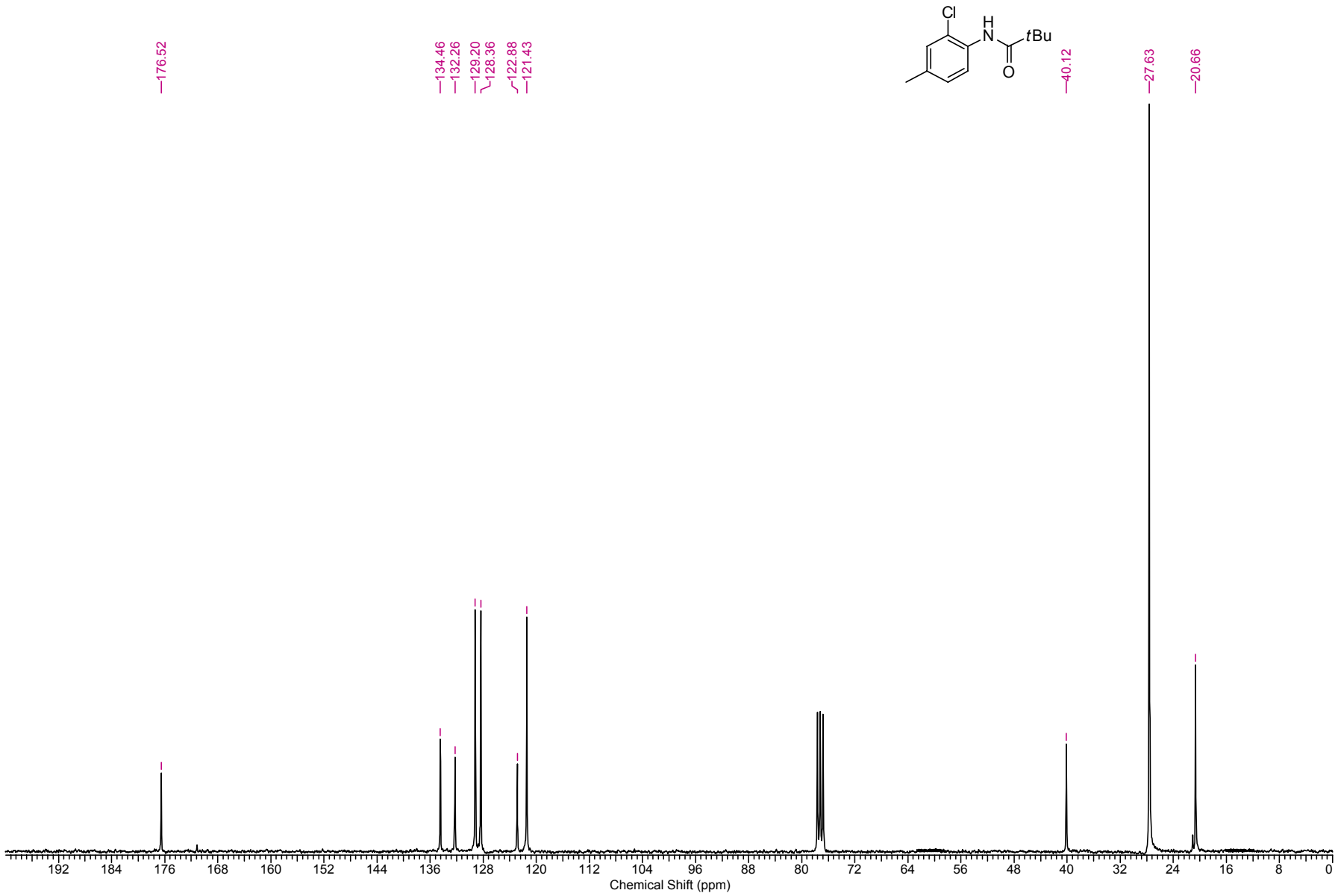
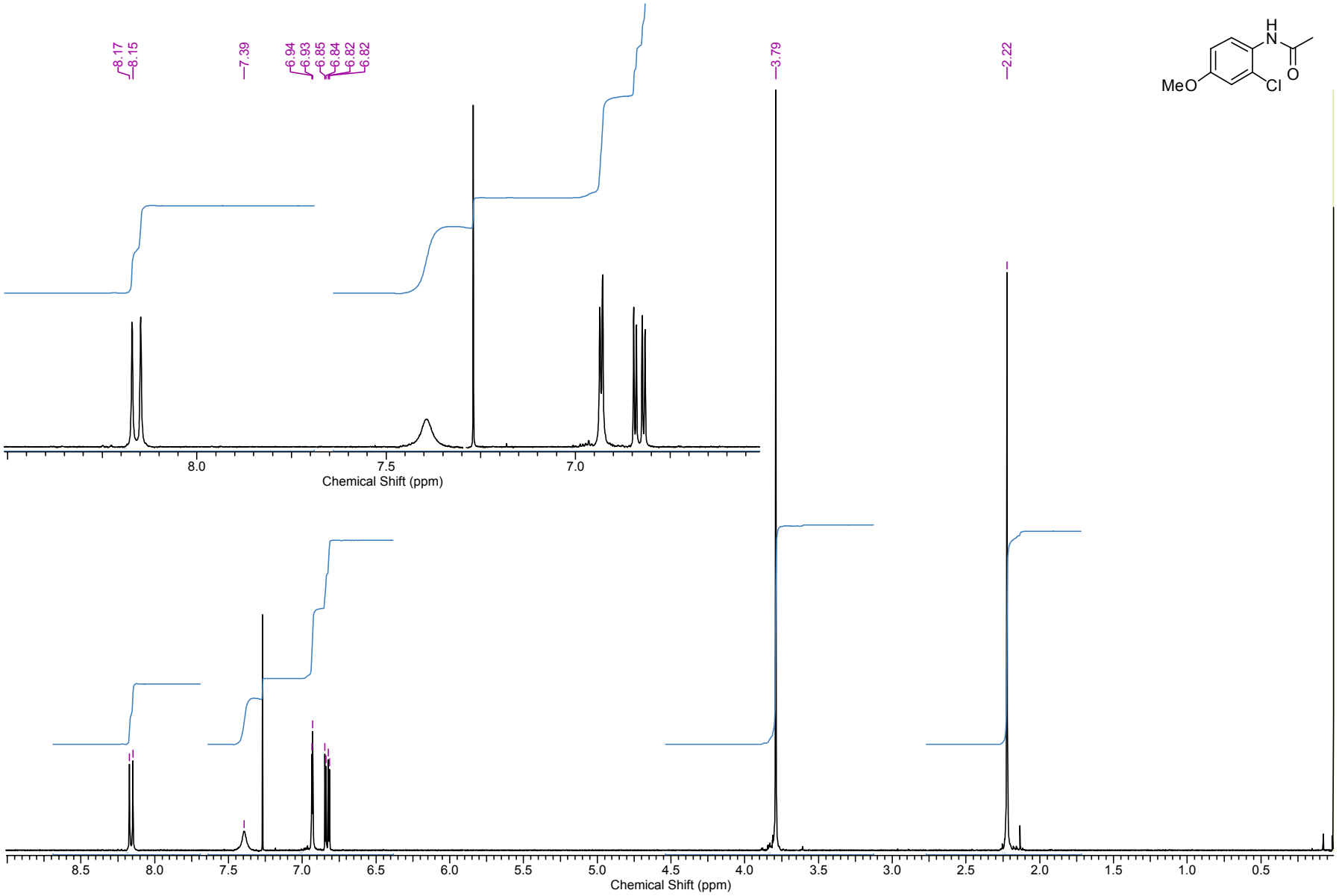
Chemical Shift (ppm)

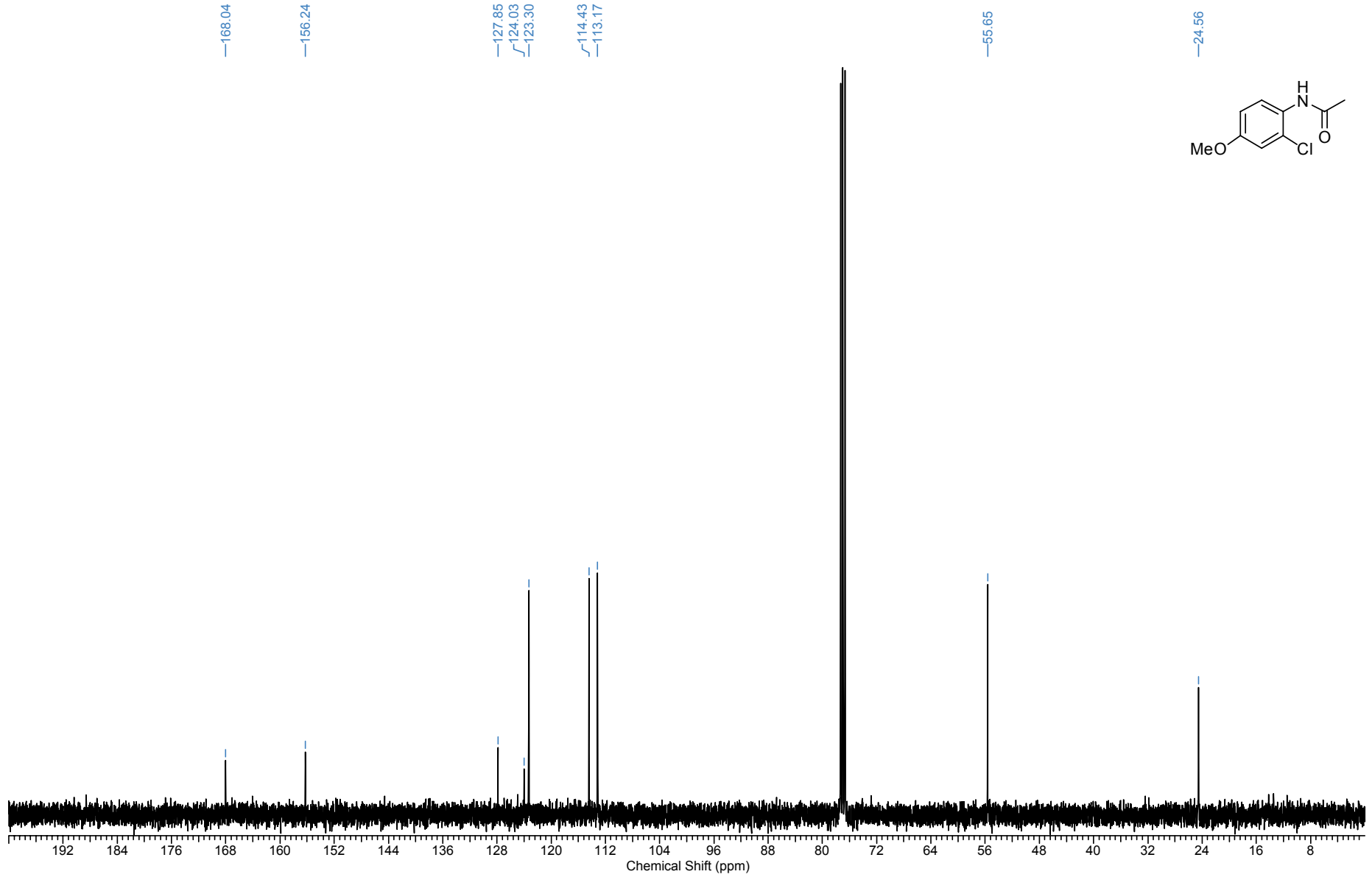

Cl
H
N
O
8.21
8.19
7.54
7.19
7.09
7.06
2.30
2.23
8.0
7.5
7.0
6.5
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

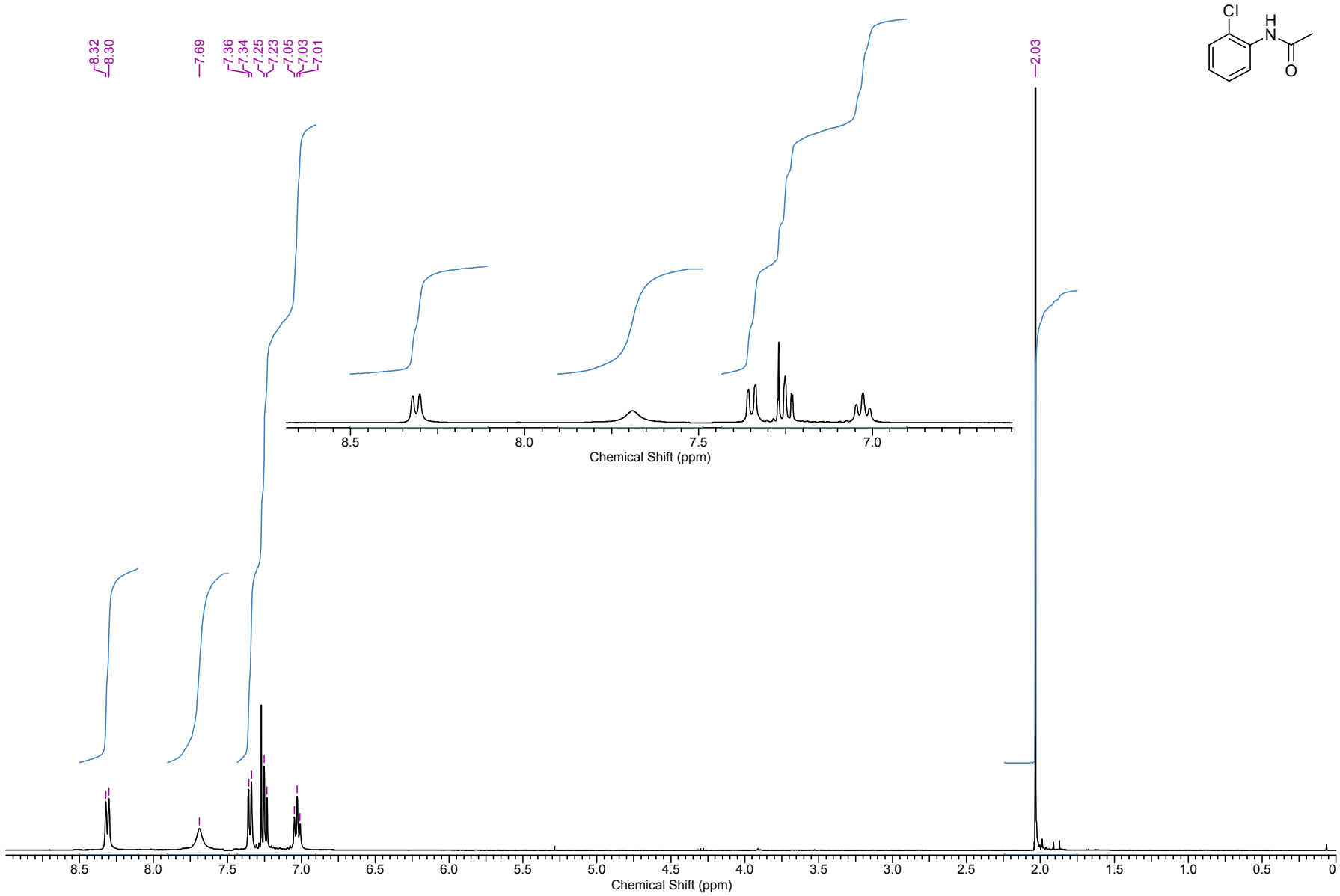

Cl
H
N
O
168.1
134.7
132.0
129.2
128.3
121.6
119.6
24.8
20.6
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

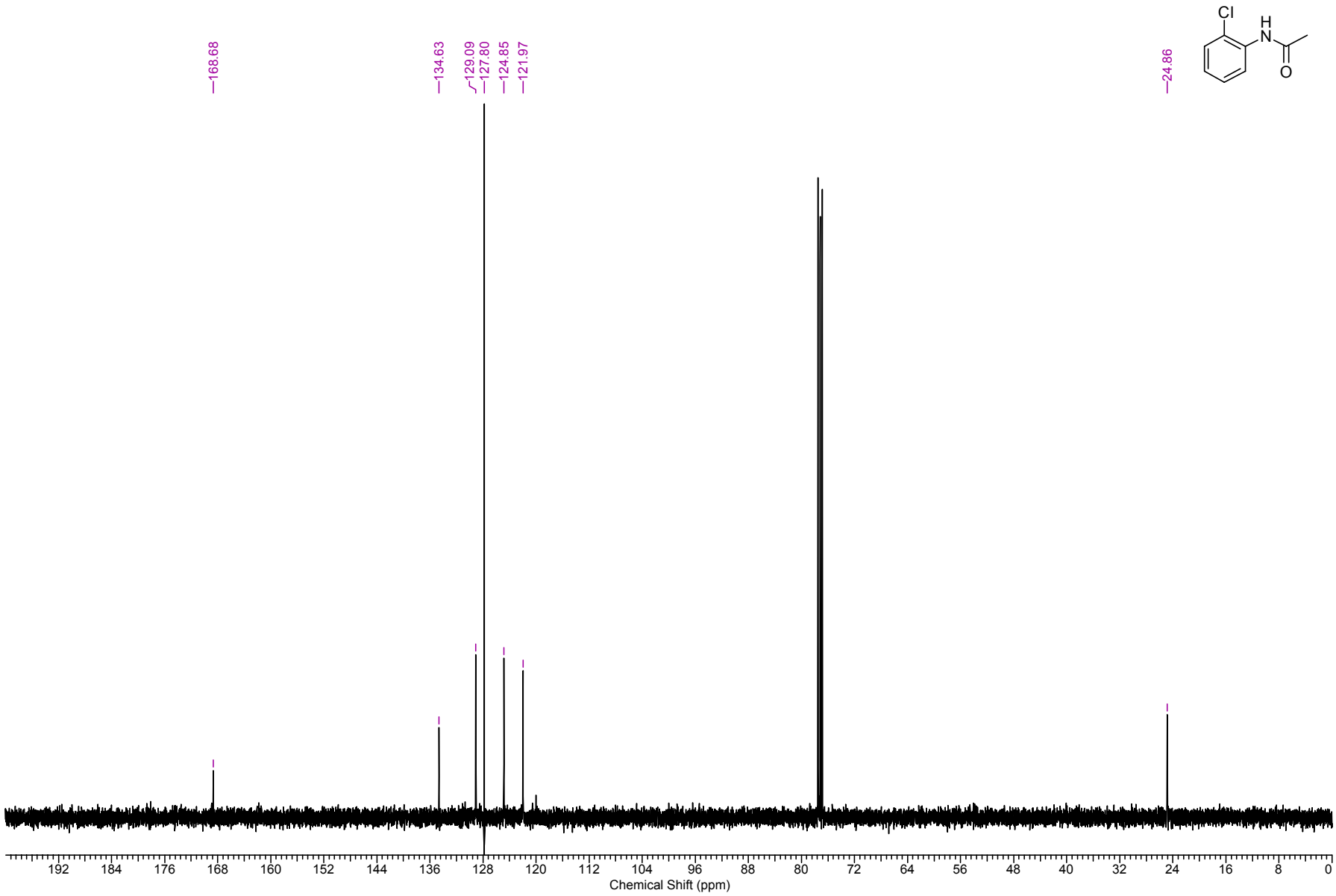

8.23
8.20
7.90
7.13
7.12
7.04
7.03
7.01
7.01
2.25
1.31
Cl
H
N
tBu
O
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

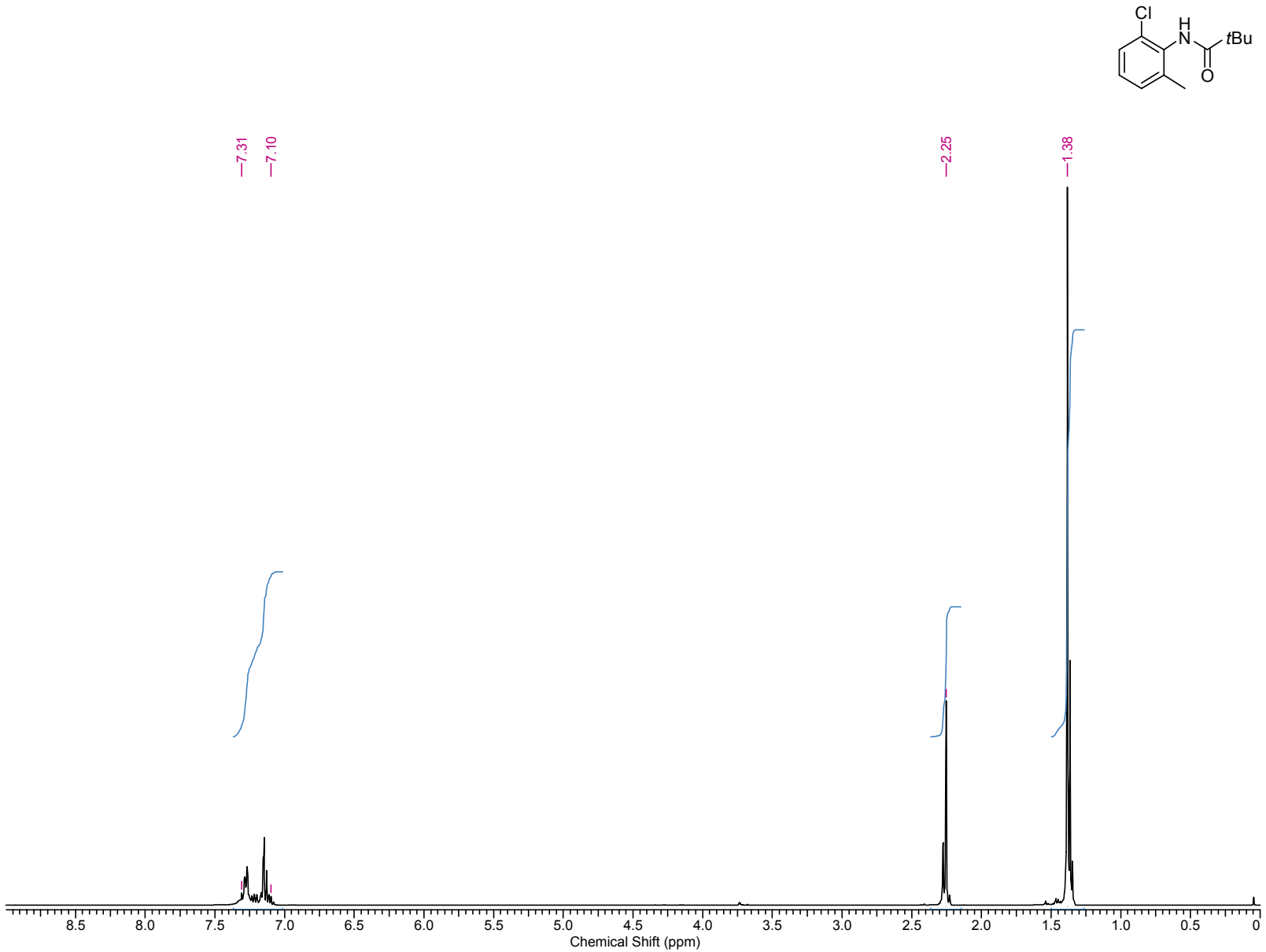

176.52
134.46
132.26
129.20
128.36
122.88
121.43
40.12
27.63
20.66
Cl
H
N
O
tBu
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

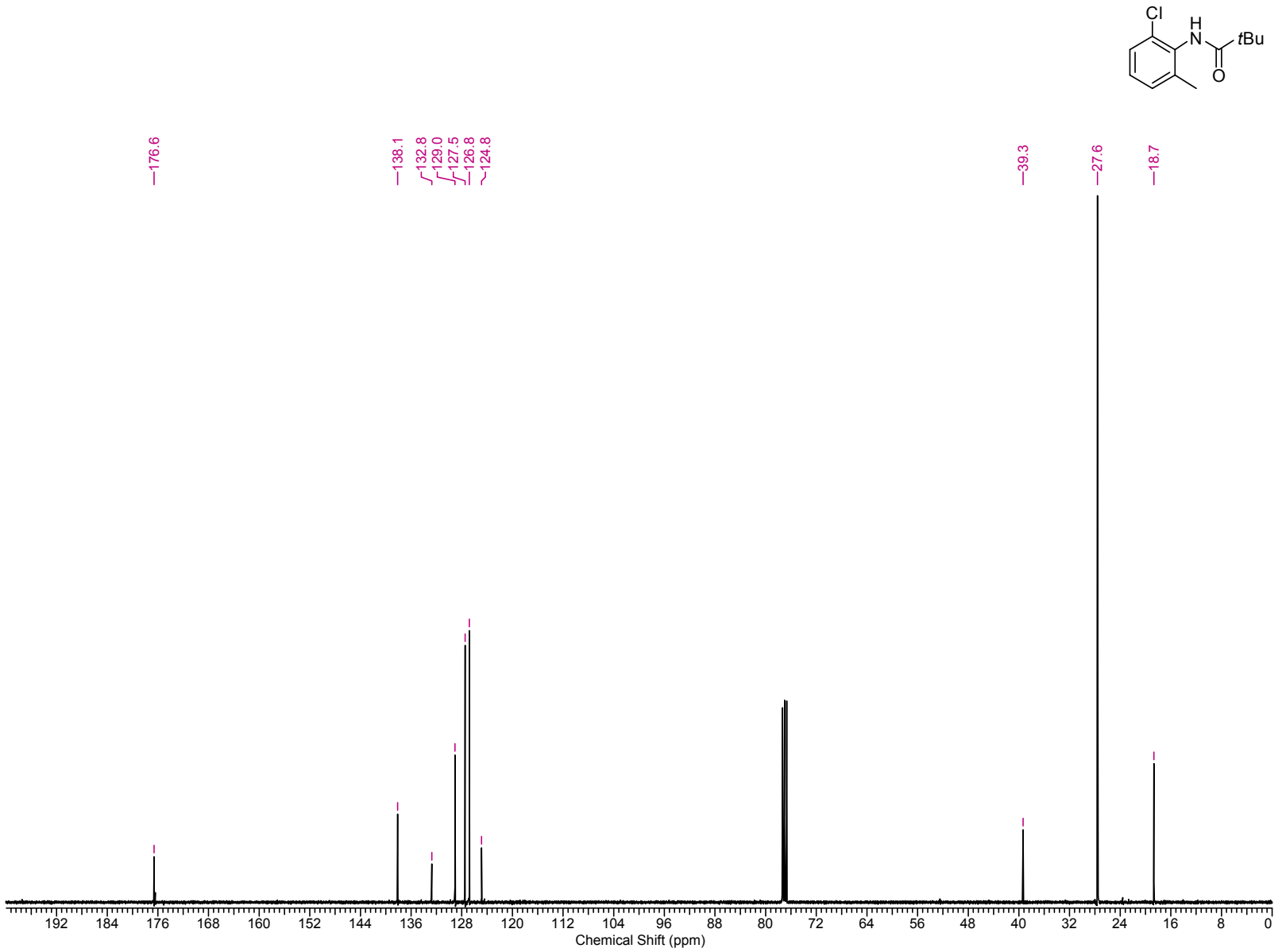

8.17
8.15
7.39
6.94
6.93
6.85
6.84
6.82
6.82
3.79
2.22
H
N
O
MeO
Cl
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


168.04
156.24
127.85
124.03
123.30
114.43
113.17
55.65
24.56
H
N
O
MeO
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

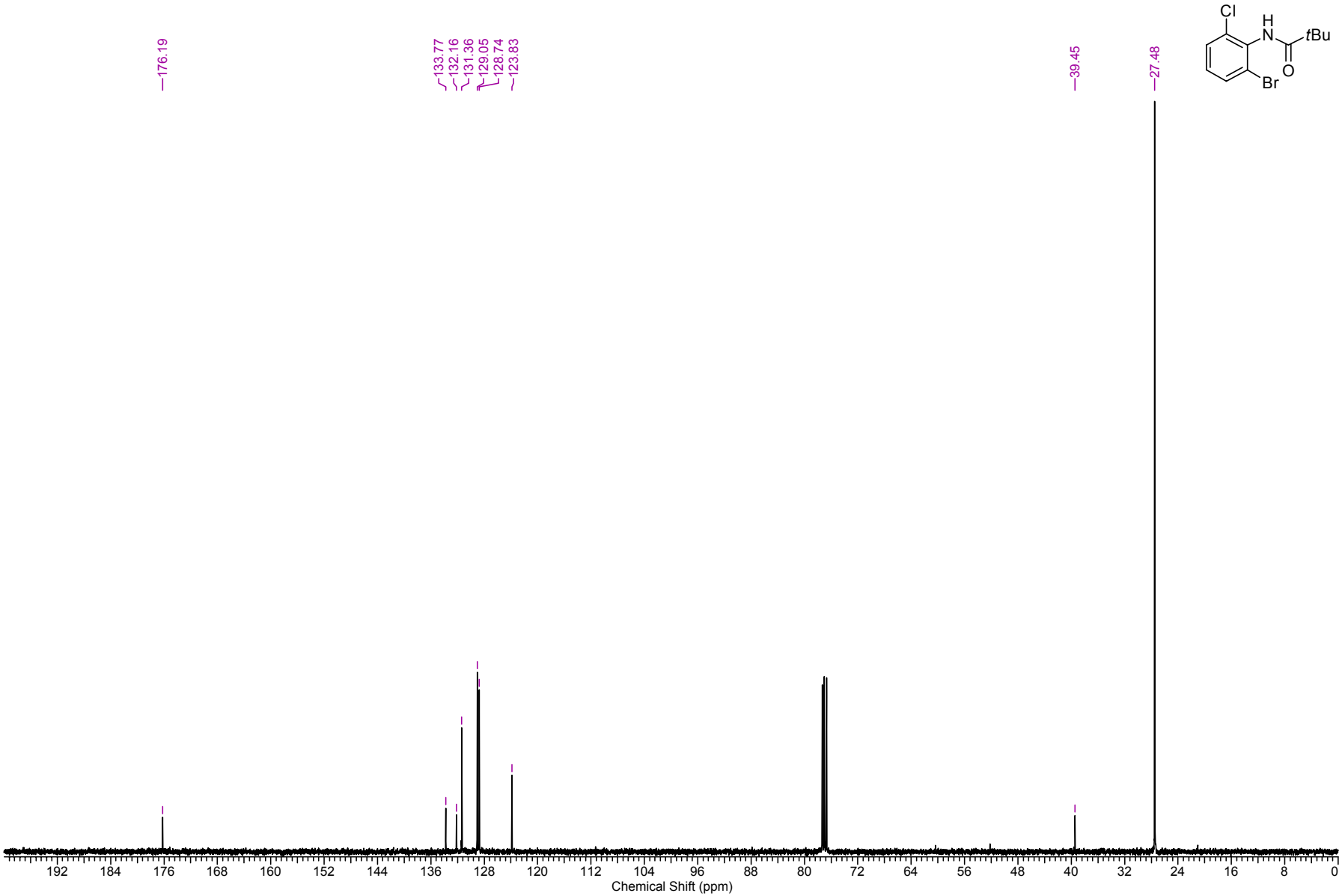

8.32
8.30
7.69
7.36
7.34
7.25
7.23
7.05
7.03
7.01
2.03
Cl
H
N
O
8.5
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

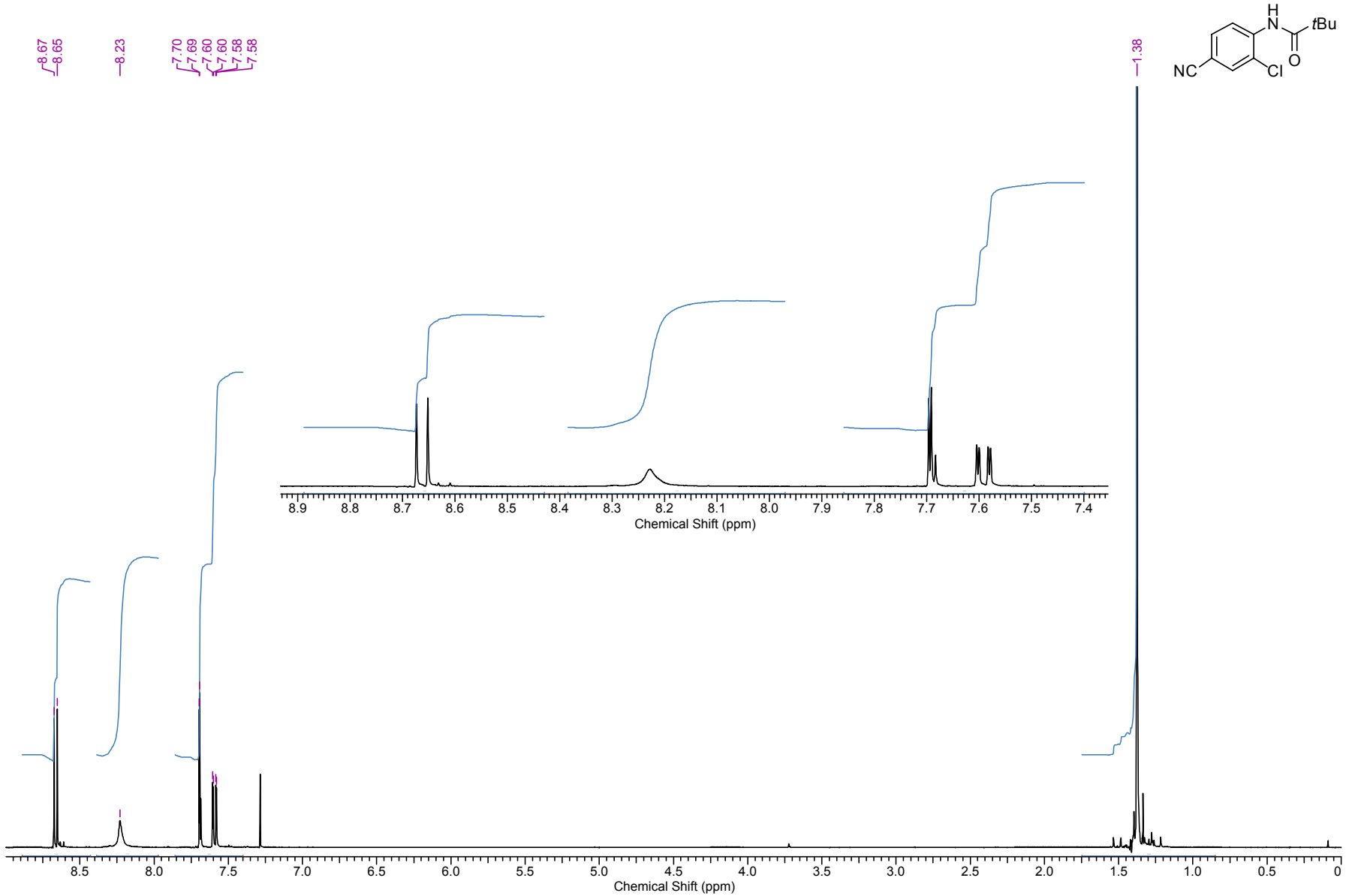

168.68
134.63
129.09
127.80
124.85
121.97
24.86
Cl
H
N
O
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

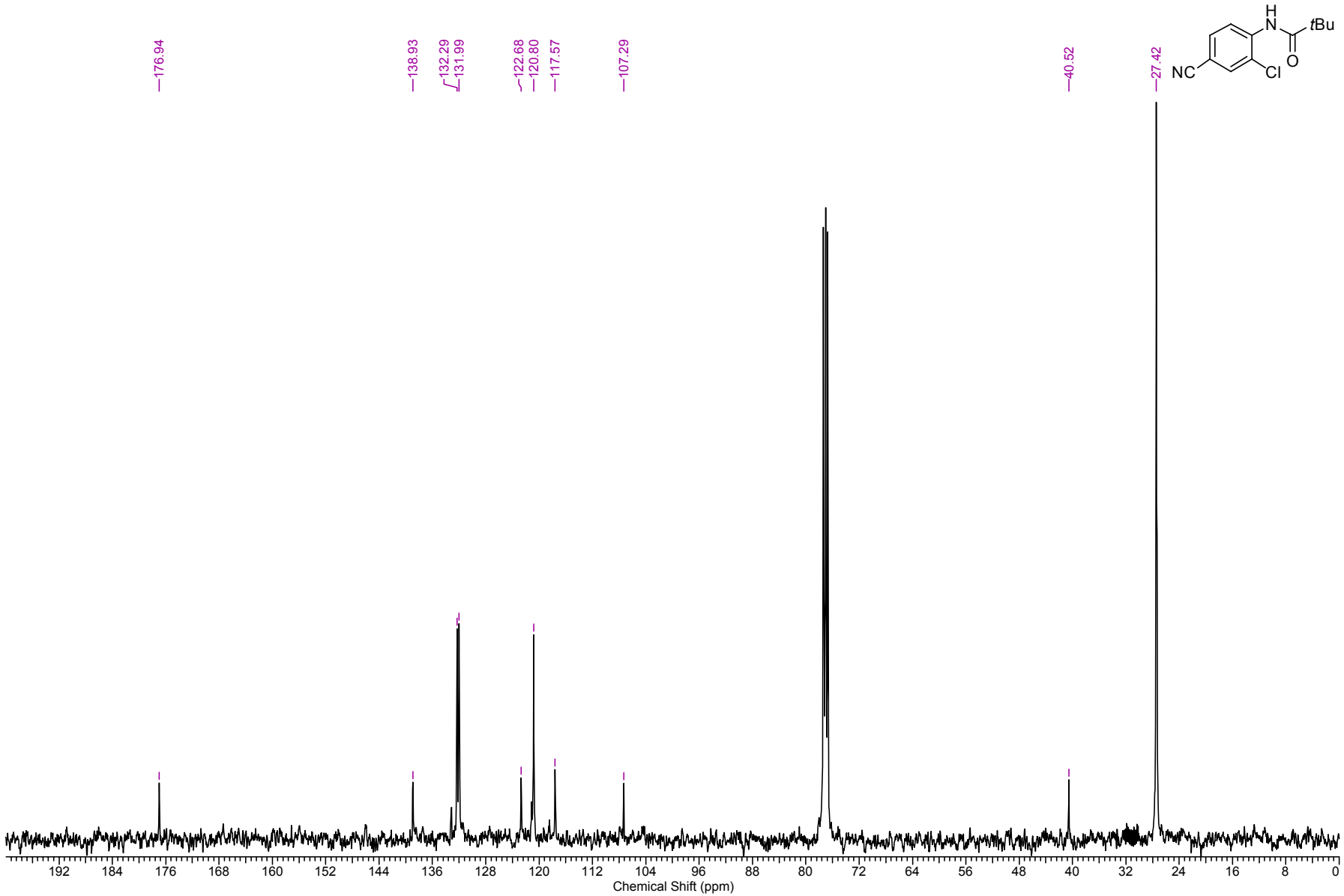

Cl
H
N
tBu
O
7.31
7.10
2.25
1.38
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

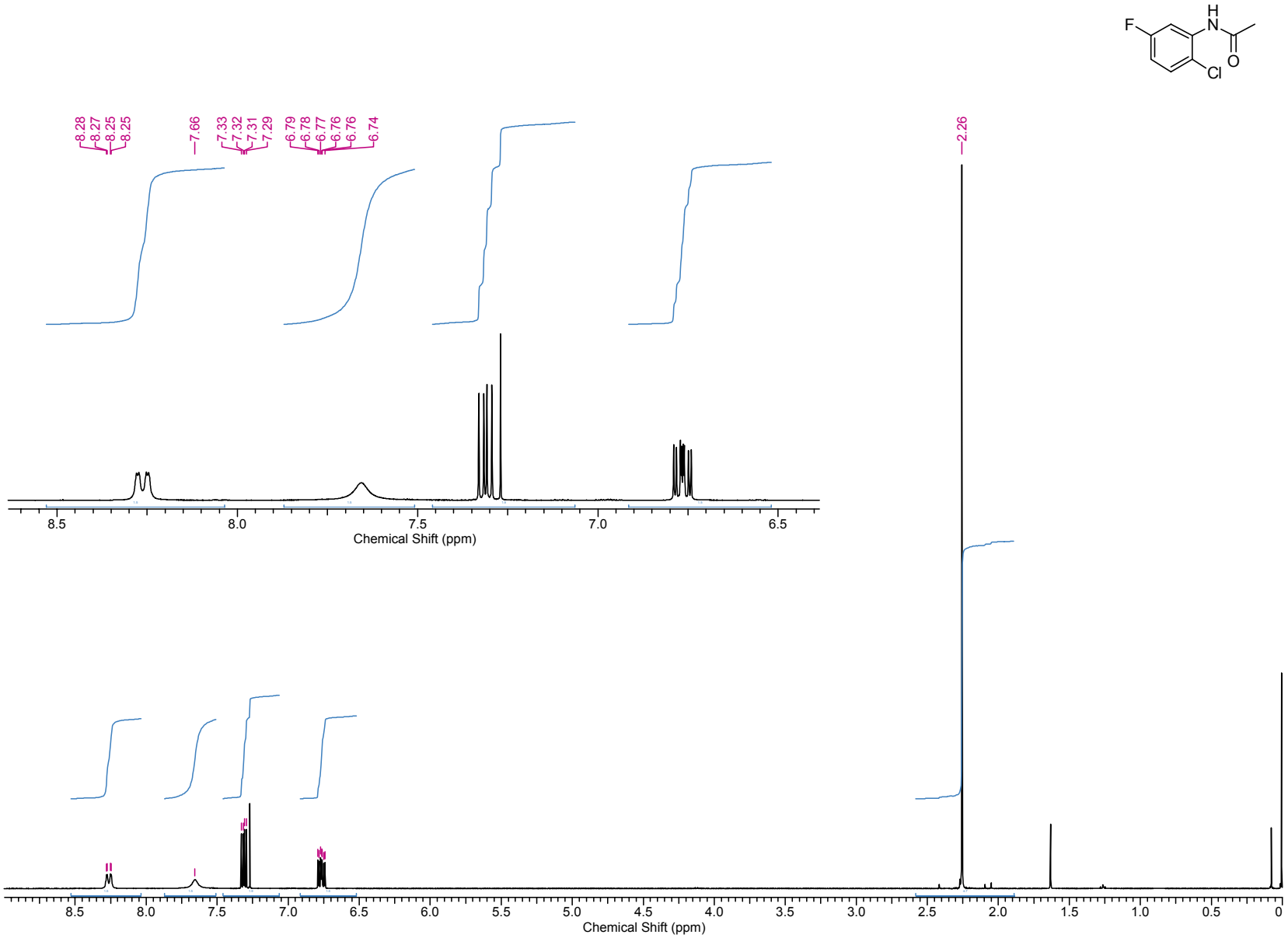

Cl
H
N
tBu
O
176.6
138.1
132.8
129.0
127.5
126.8
124.8
39.3
27.6
18.7
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

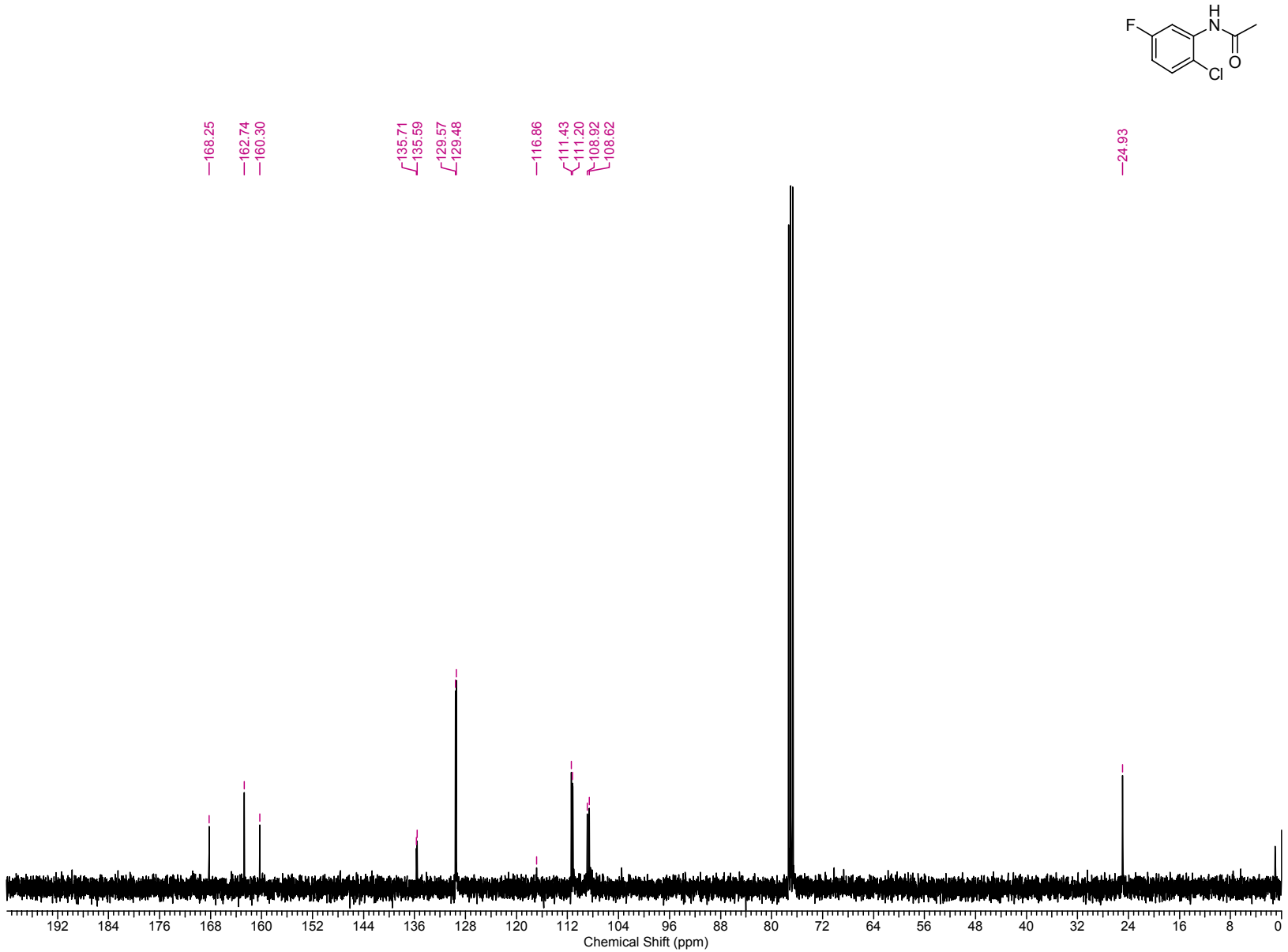

7.52
7.52
7.50
7.40
7.38
7.37
7.21
7.10
7.07
7.05
1.36
Cl
H
N
tBu
O
Br
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

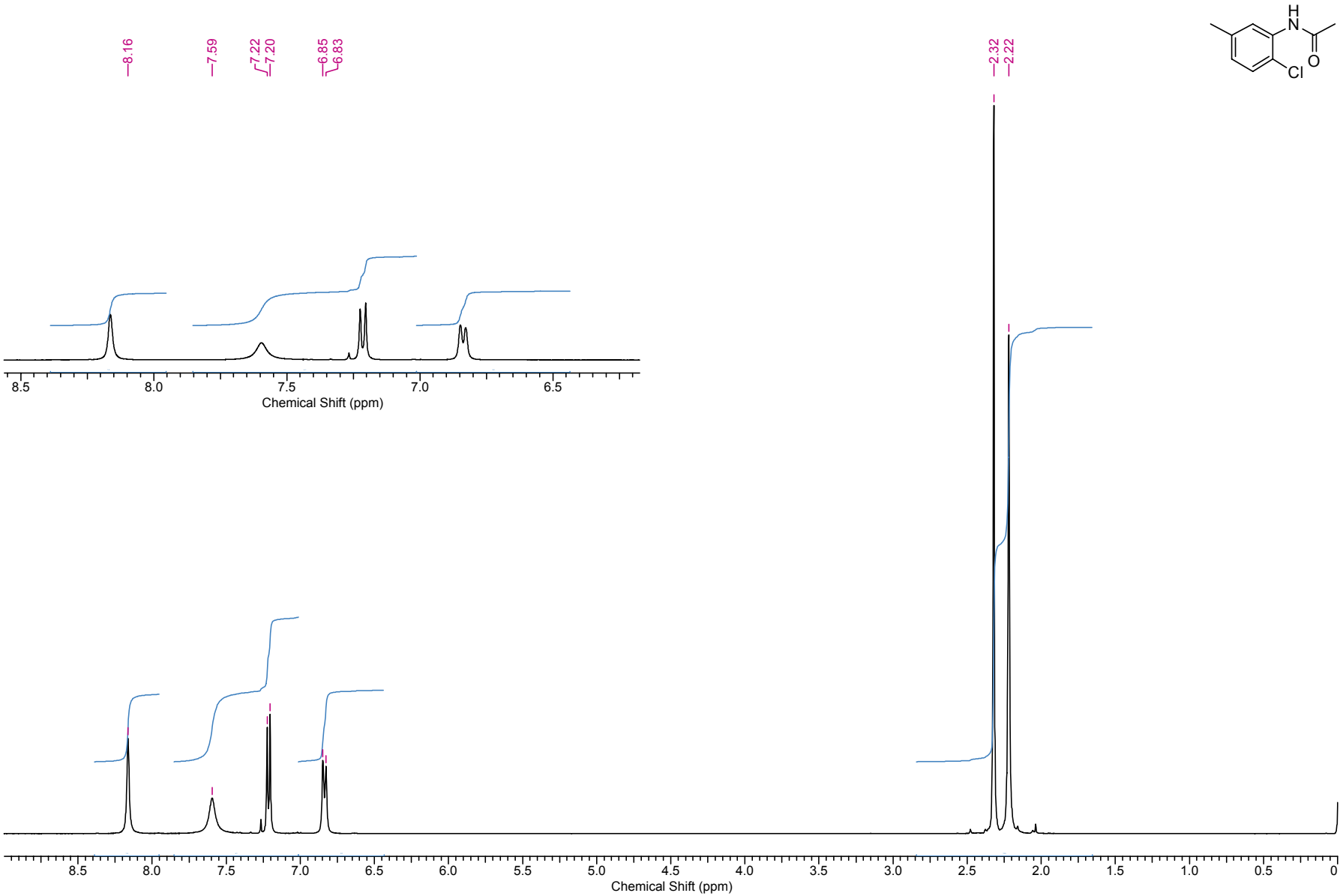

176.19
133.77
132.16
131.36
129.05
128.74
123.83
39.45
27.48
Cl
H
N
tBu
O
Br
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

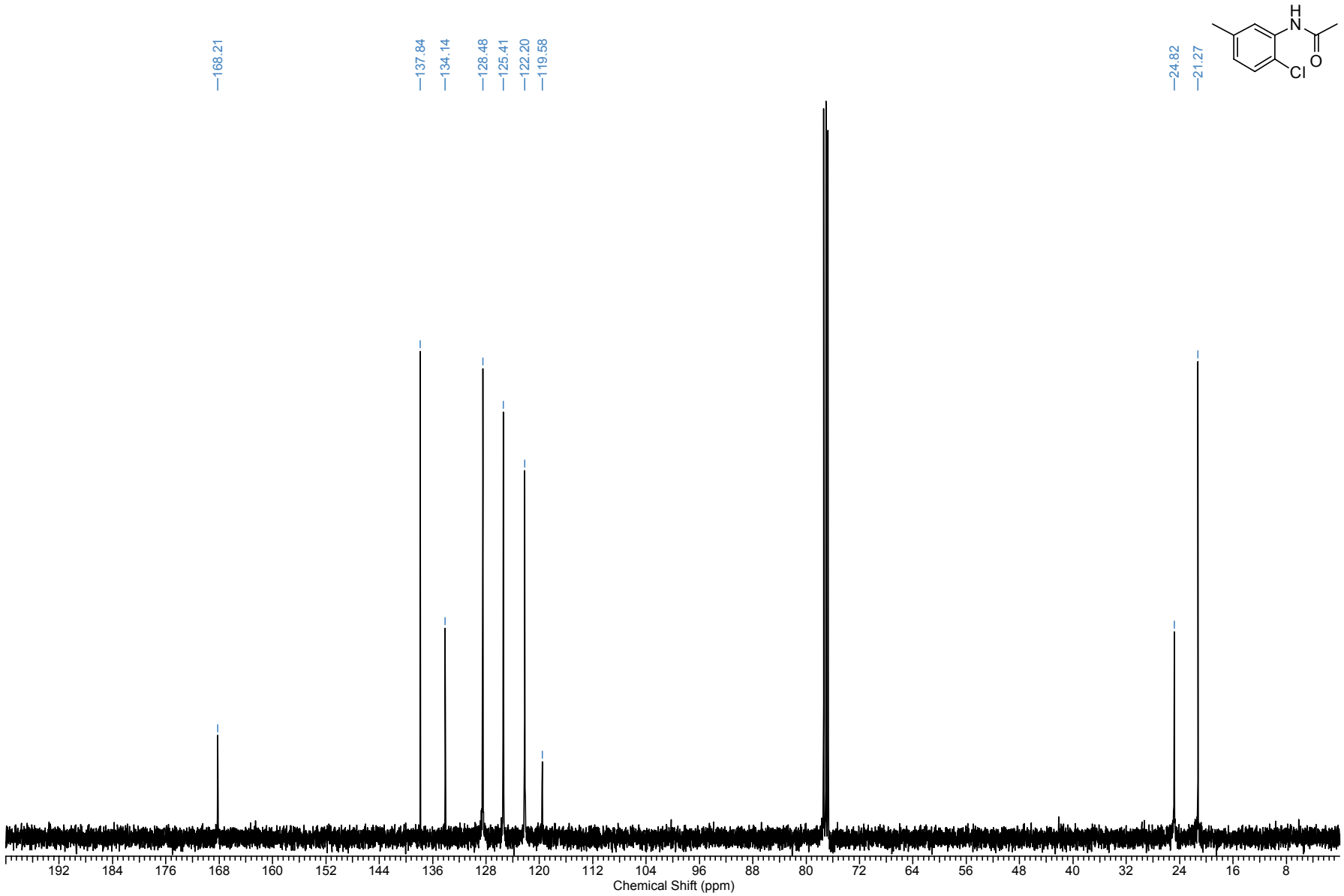

8.67
8.65
8.23
7.70
7.69
7.60
7.60
7.58
7.58
1.38
H
N
tBu
O
NC
Cl
8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4
Chemical Shift (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

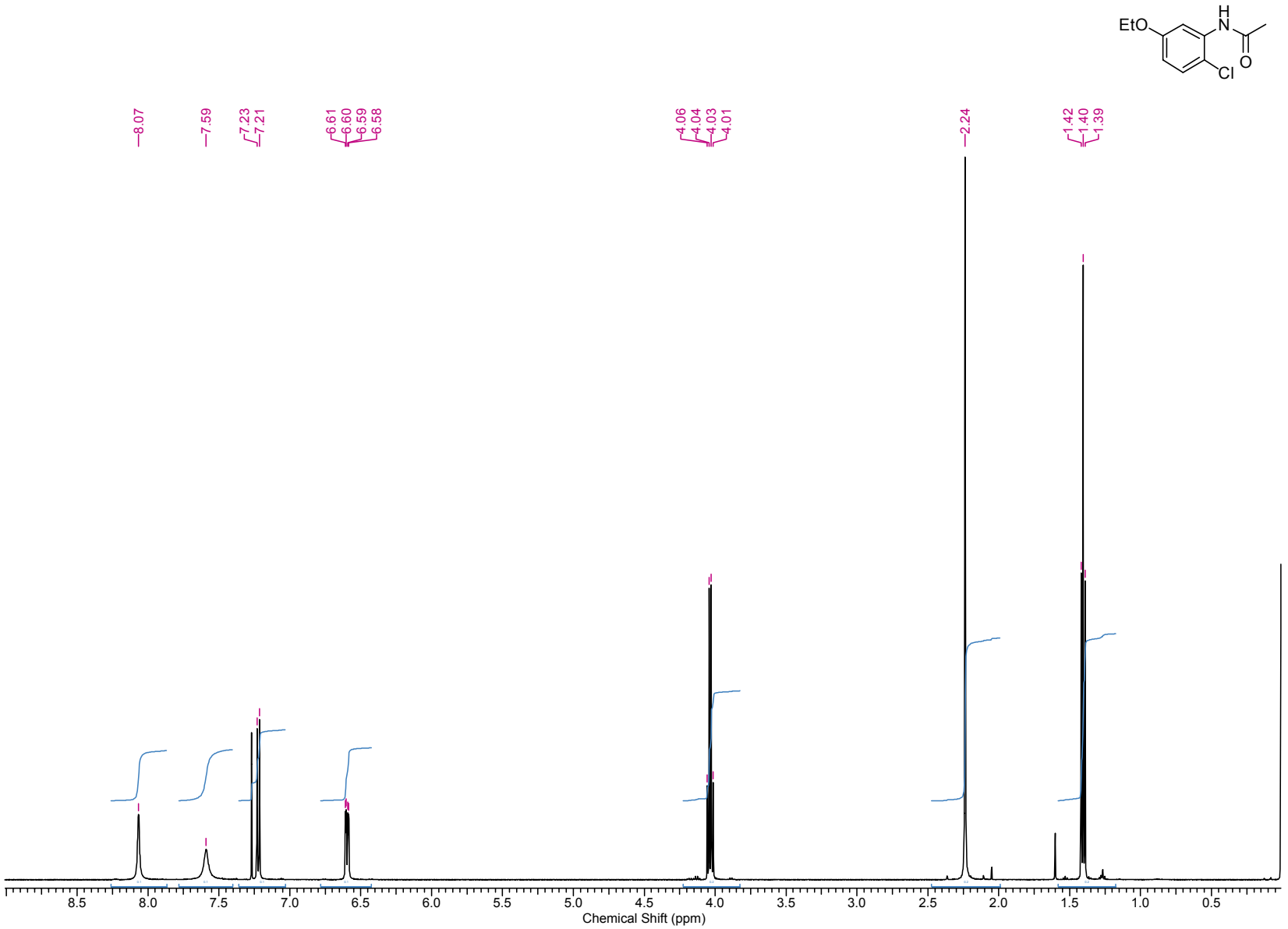

176.94
138.93
132.29
131.99
122.68
120.80
117.57
107.29
40.52
27.42
H
N
tBu
O
NC
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

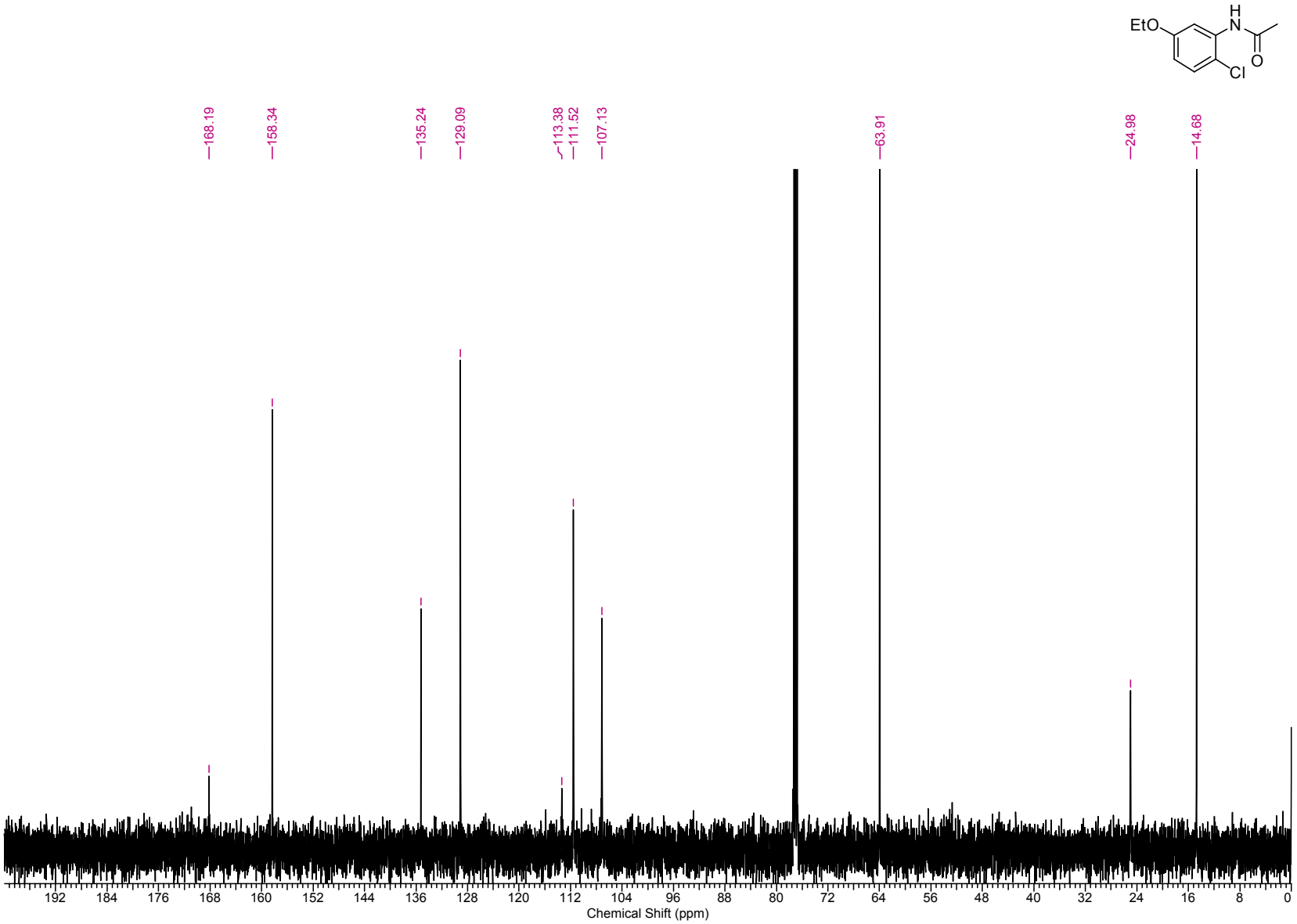

F
H
N
O
Cl
8.28
8.27
8.25
8.25
7.66
7.33
7.32
7.31
7.29
6.79
6.78
6.77
6.76
6.76
6.74
2.26
Chemical Shift (ppm)
Chemical Shift (ppm)

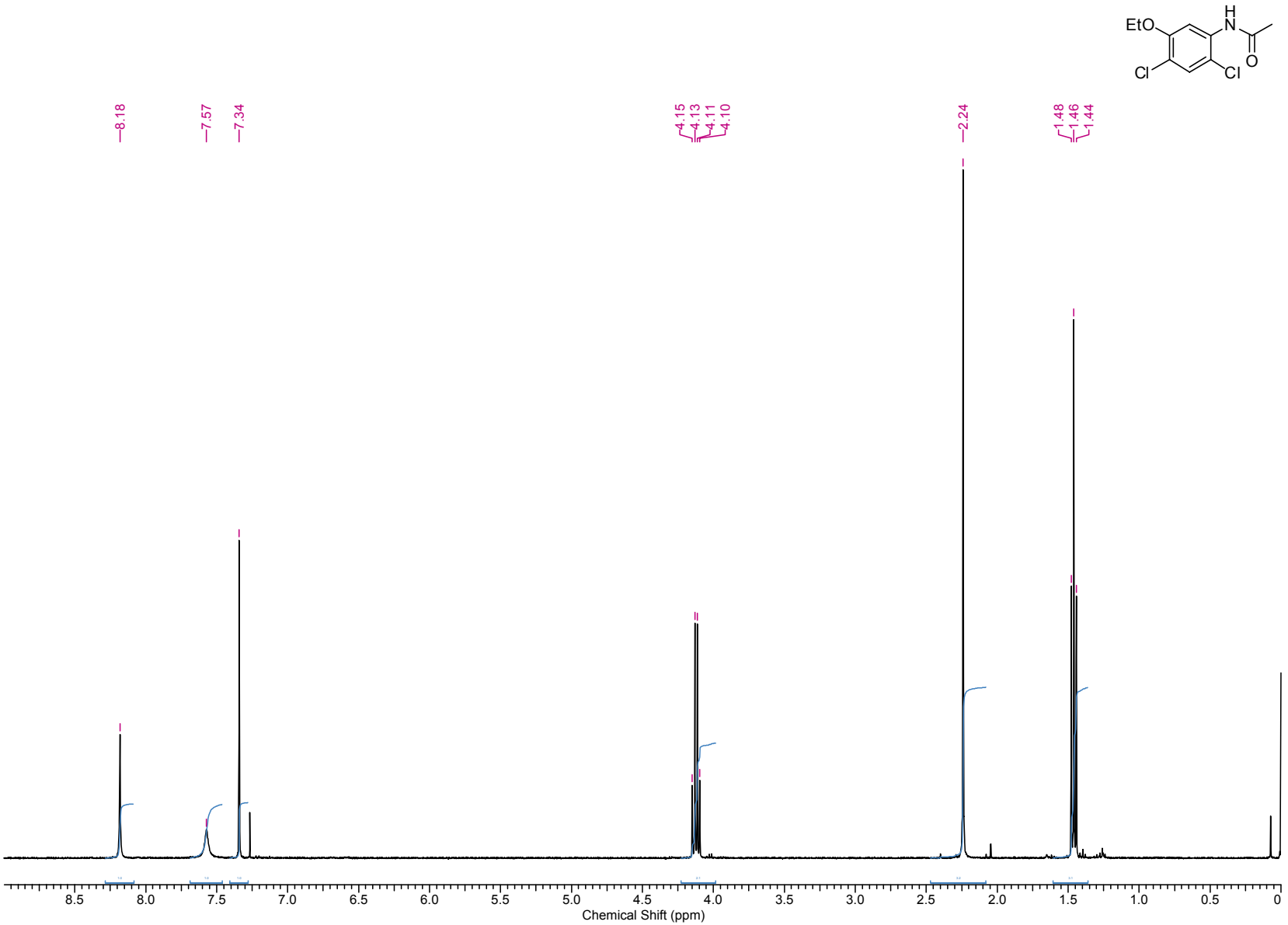

F
H
N
O
Cl
168.25
162.74
160.30
135.71
135.59
129.57
129.48
116.86
111.43
111.20
108.92
108.62
24.93
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

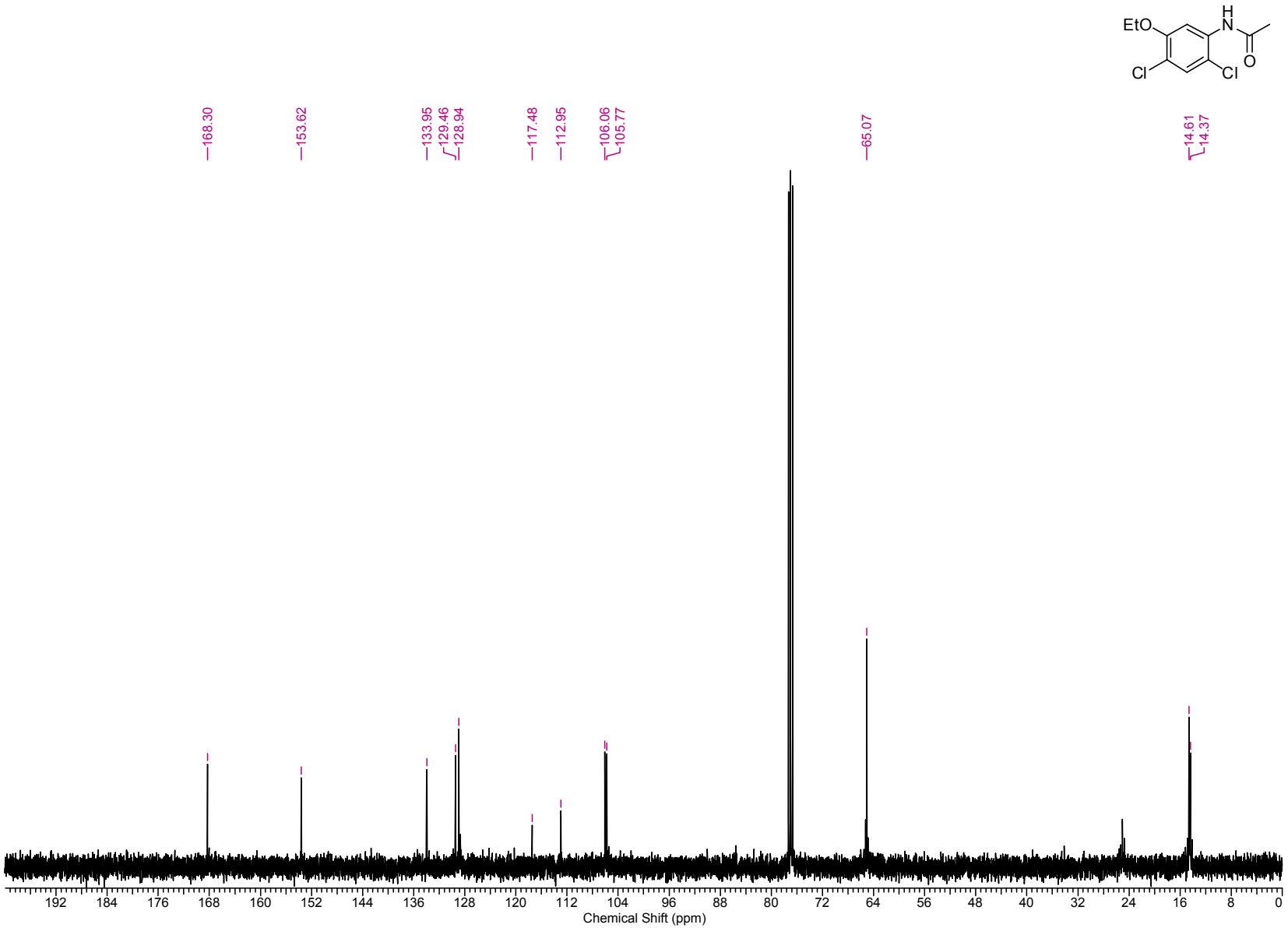

8.16
7.59
7.22
7.20
6.85
6.83
2.32
2.22
H
N
O
Cl
8.5
8.0
7.5
7.0
6.5
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

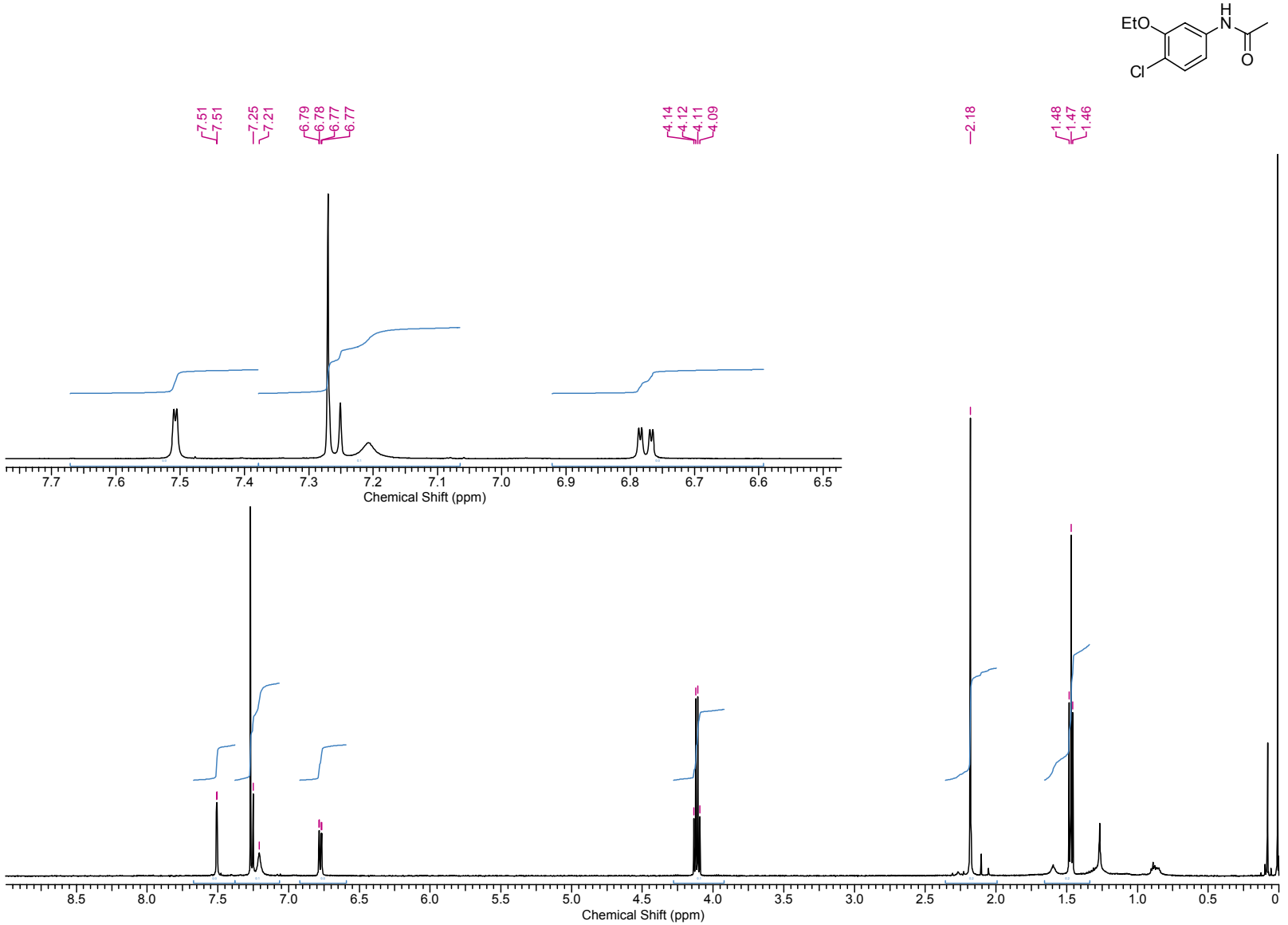

168.21
137.84
134.14
128.48
125.41
122.20
119.58
24.82
21.27
H
N
O
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

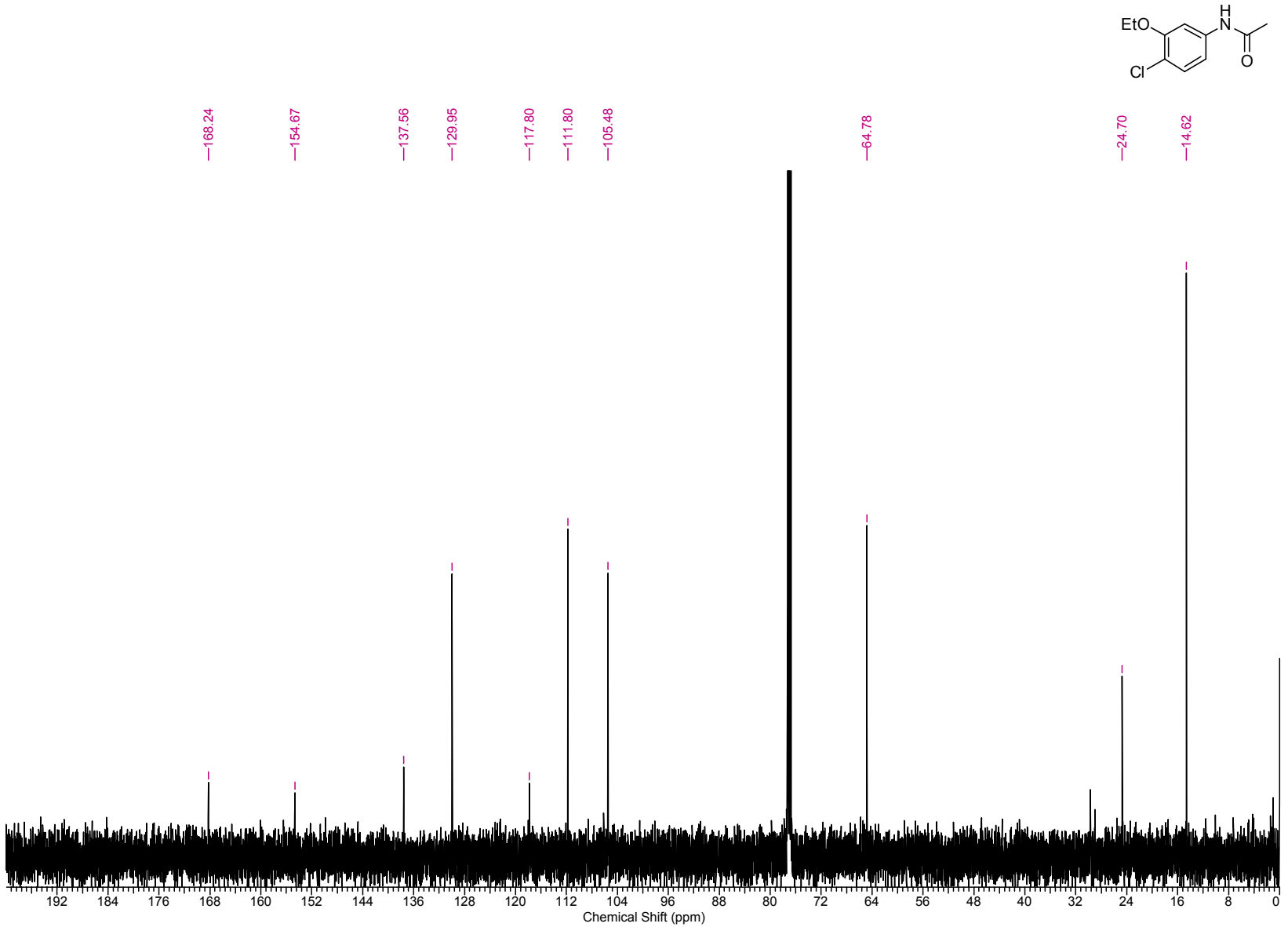

EtO
H
N
O
Cl
8.07
7.59
7.23
7.21
6.61
6.60
6.59
6.58
4.06
4.04
4.03
4.01
2.24
1.42
1.40
1.39
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

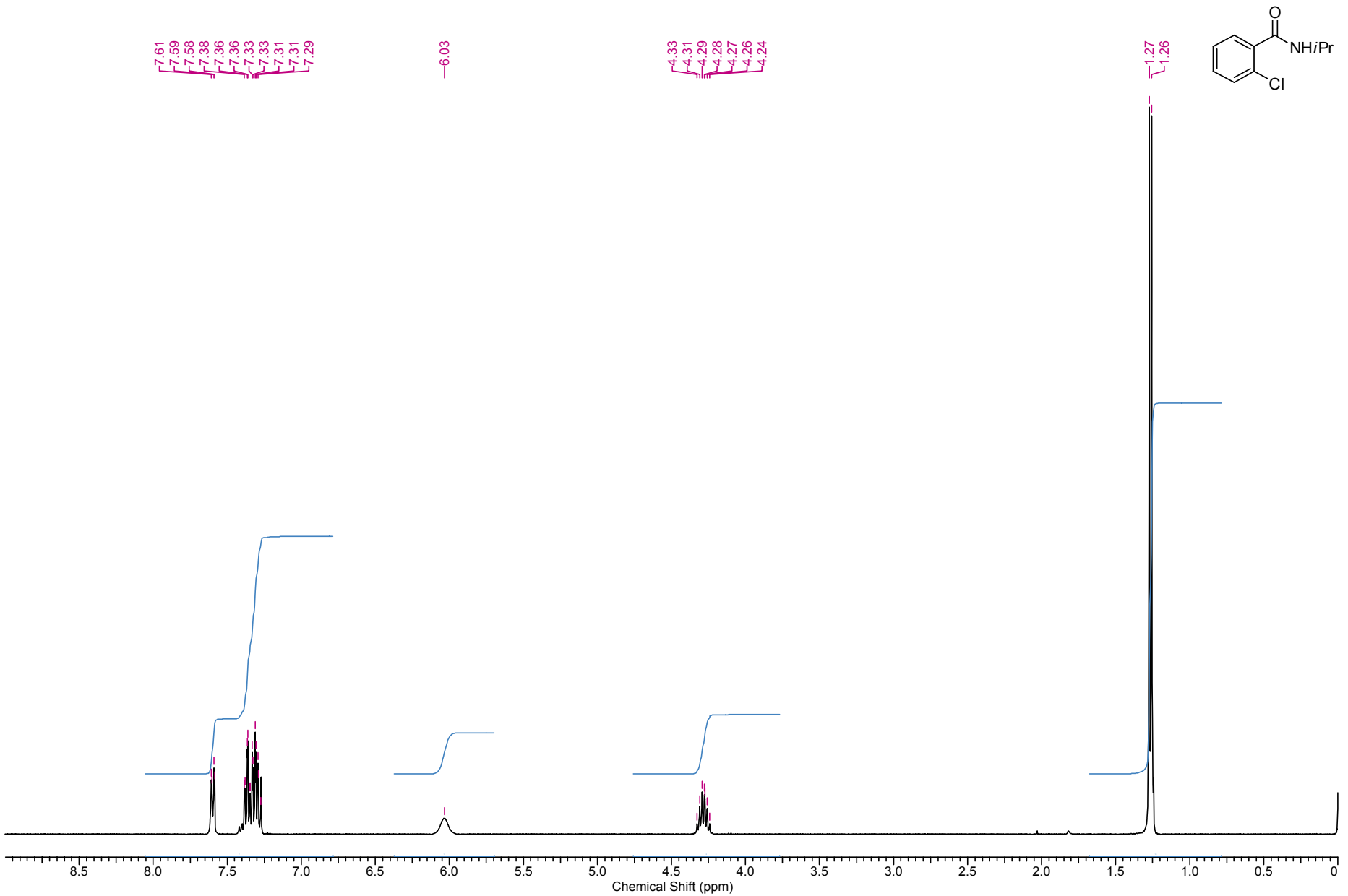

EtO
H
N
O
Cl
168.19
158.34
135.24
129.09
113.38
111.52
107.13
63.91
24.98
14.68
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

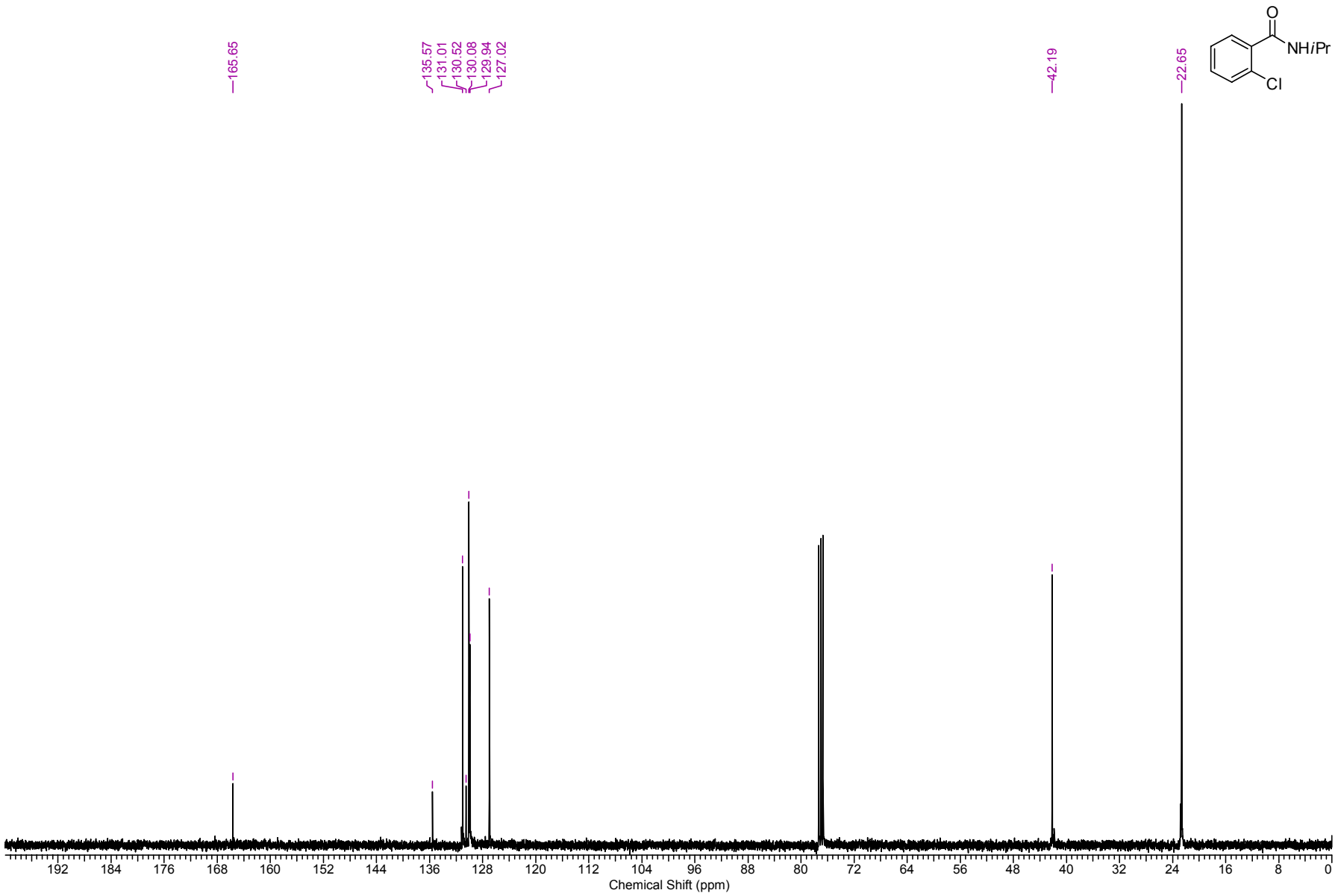

EtO
H
N
O
Cl
Cl
8.18
7.57
7.34
4.15
4.13
4.11
4.10
2.24
1.48
1.46
1.44
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

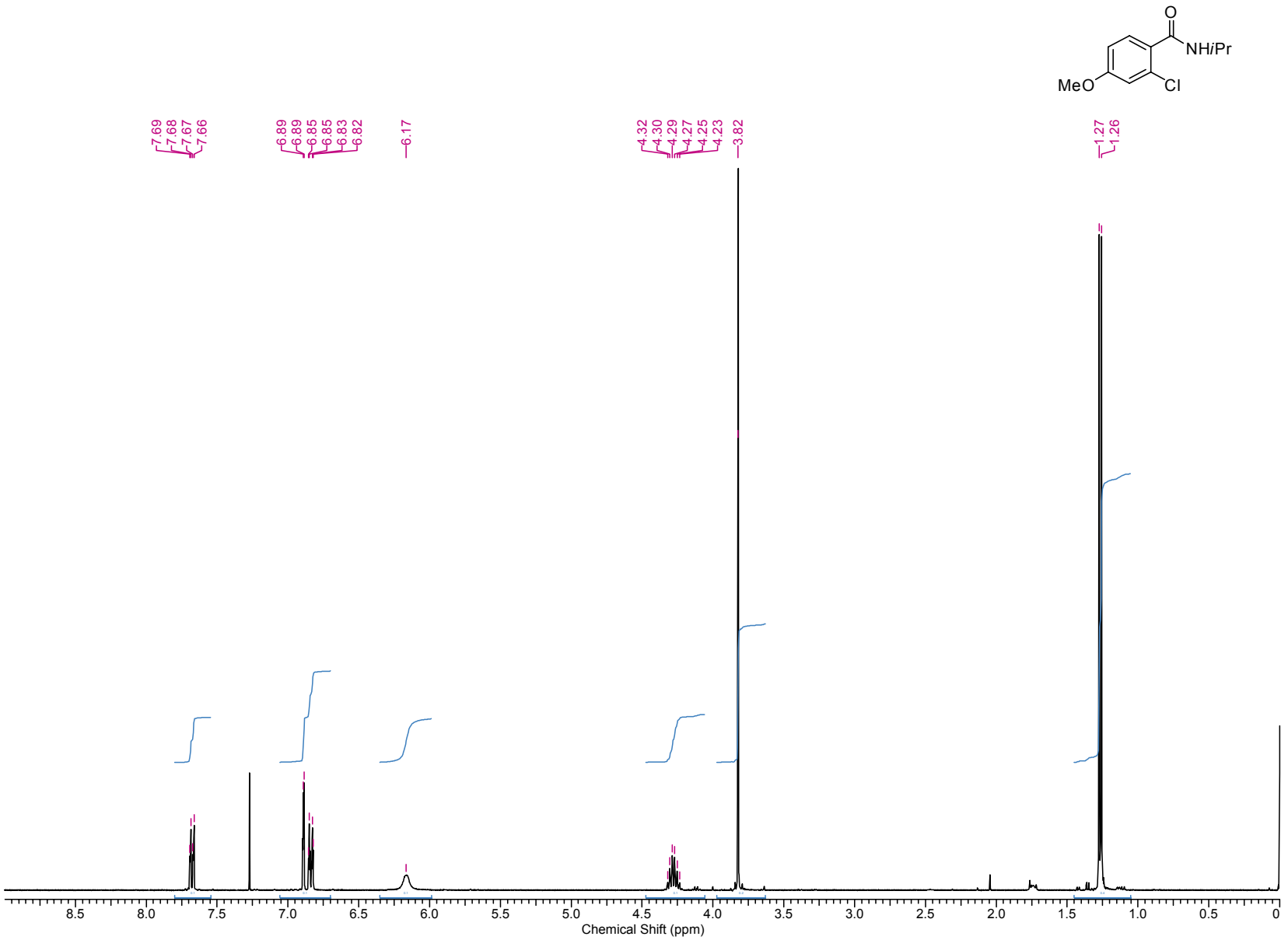

EtO
H
N
O
Cl
Cl
168.30
153.62
133.95
129.46
128.94
117.48
112.95
106.06
105.77
65.07
14.61
14.37
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

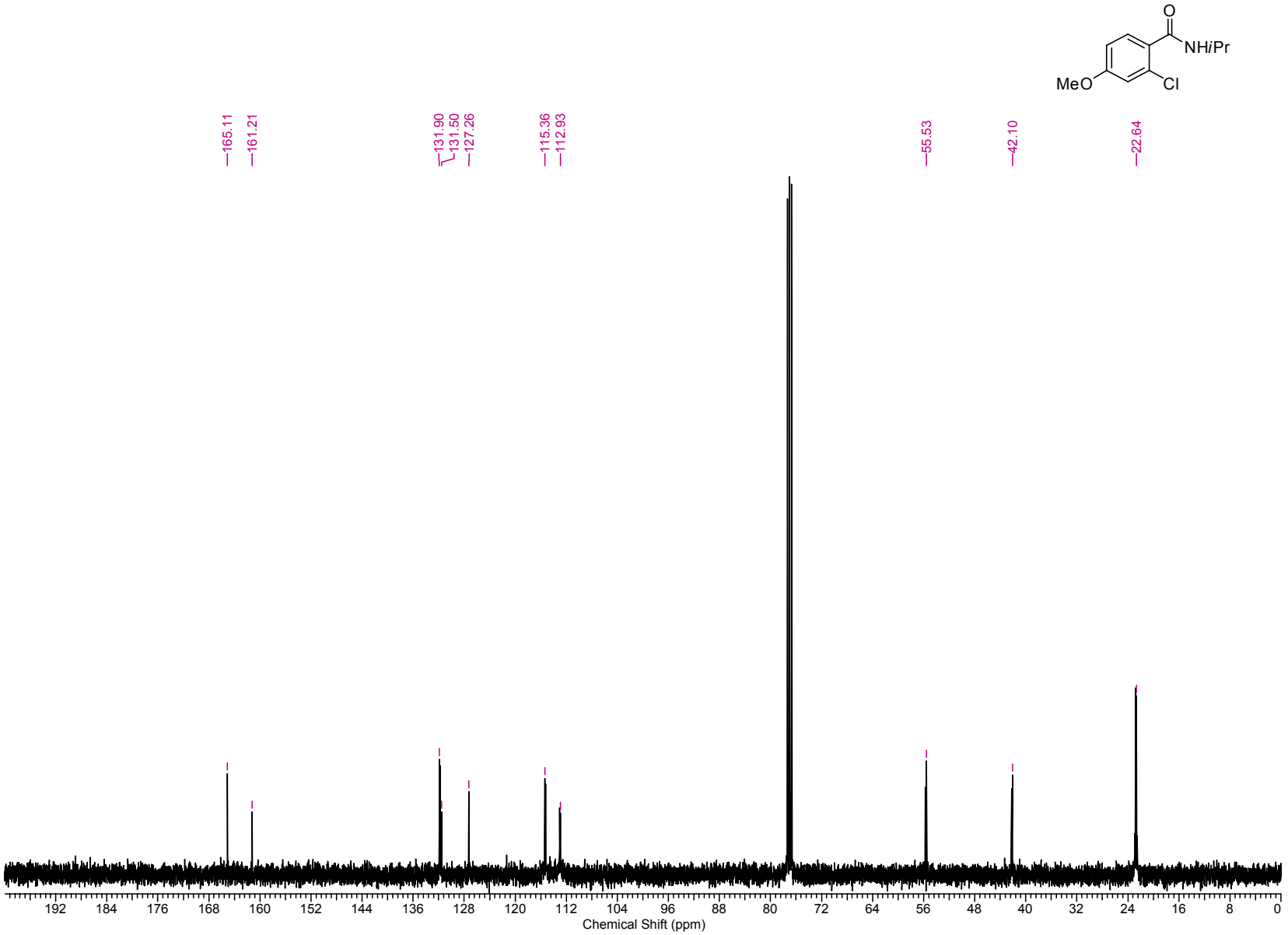

EtO
H
N
O
Cl
7.51
7.51
7.25
7.21
6.79
6.78
6.77
6.77
4.14
4.12
4.11
4.09
2.18
1.48
1.47
1.46
Chemical Shift (ppm)
Chemical Shift (ppm)

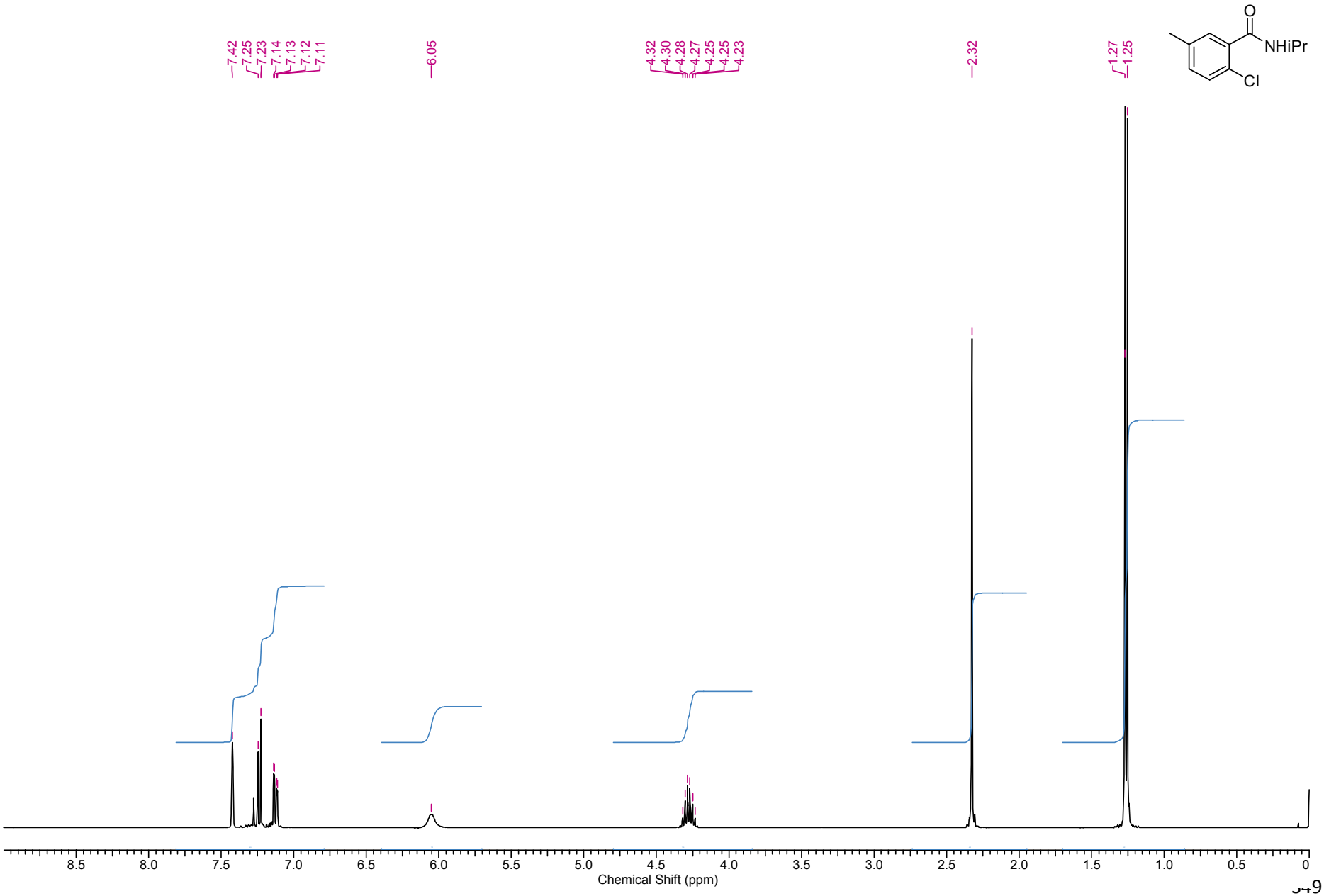

EtO
Cl
H
N
O
168.24
154.67
137.56
129.95
117.80
111.80
105.48
64.78
24.70
14.62
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

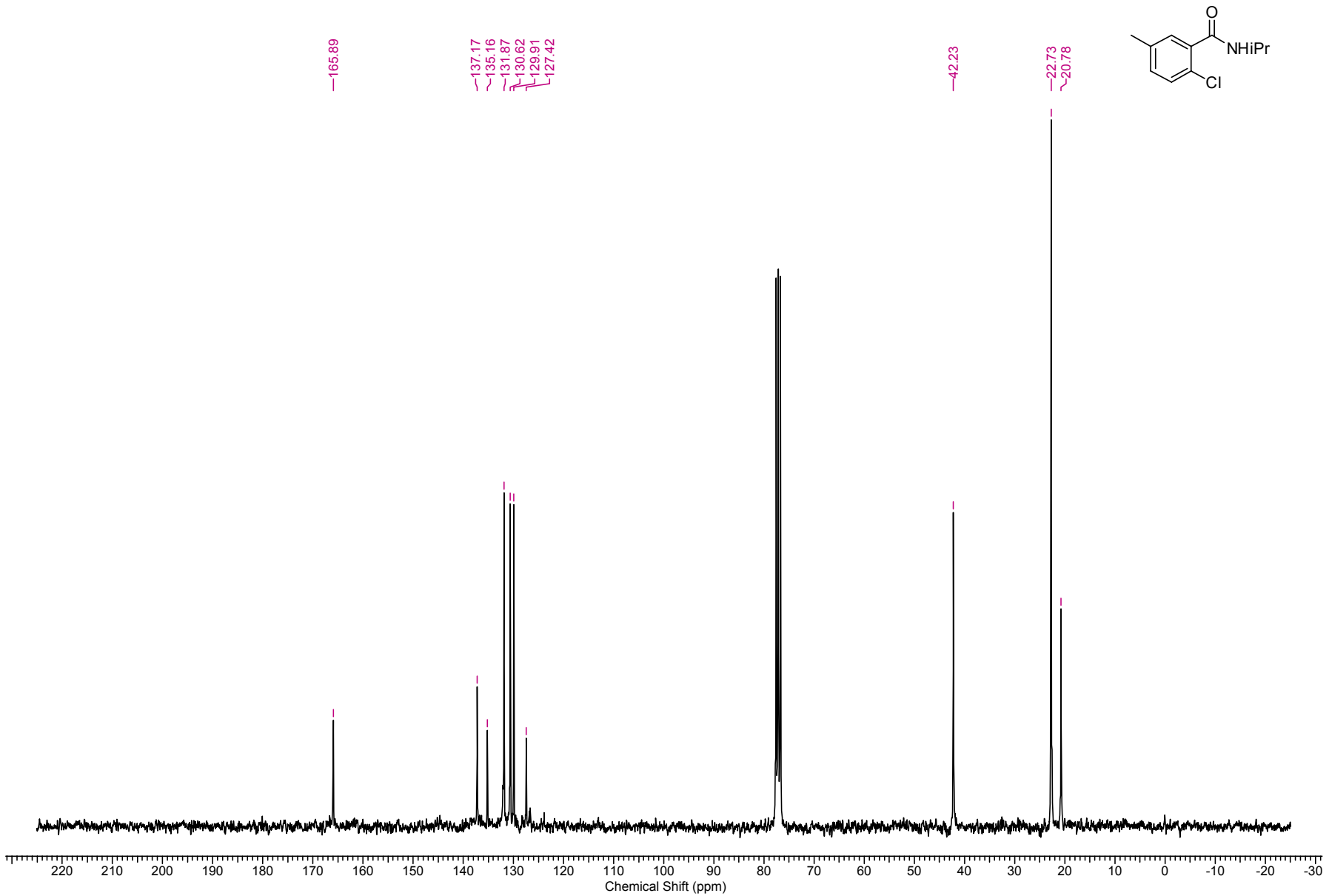

7.61
7.59
7.58
7.38
7.36
7.36
7.33
7.33
7.31
7.31
7.29
6.03
4.33
4.31
4.29
4.28
4.27
4.26
4.24
1.27
1.26
O
NHiPr
Cl
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

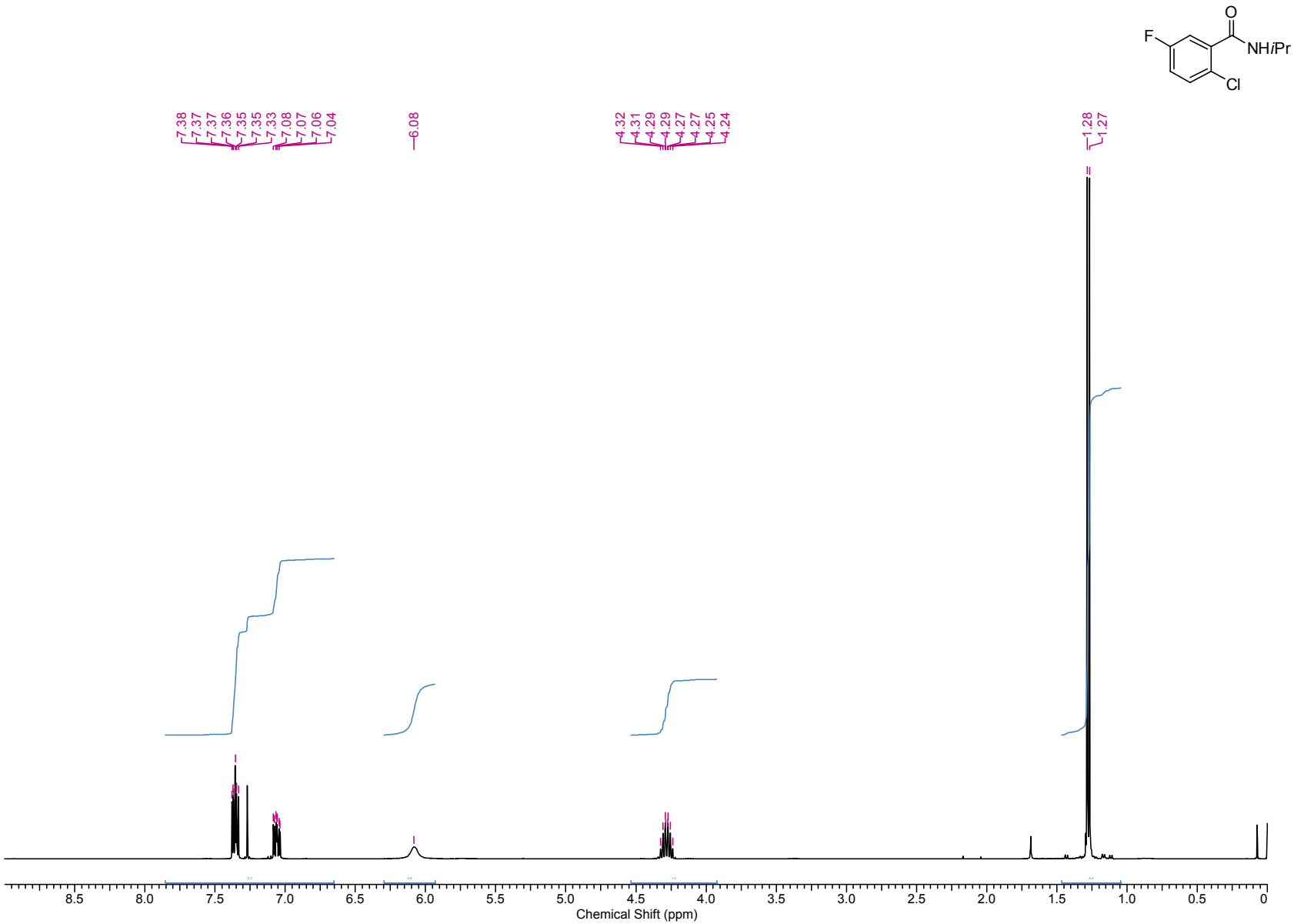

165.65
135.57
131.01
130.52
130.08
129.94
127.02
42.19
22.65
O
NH*i*Pr
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

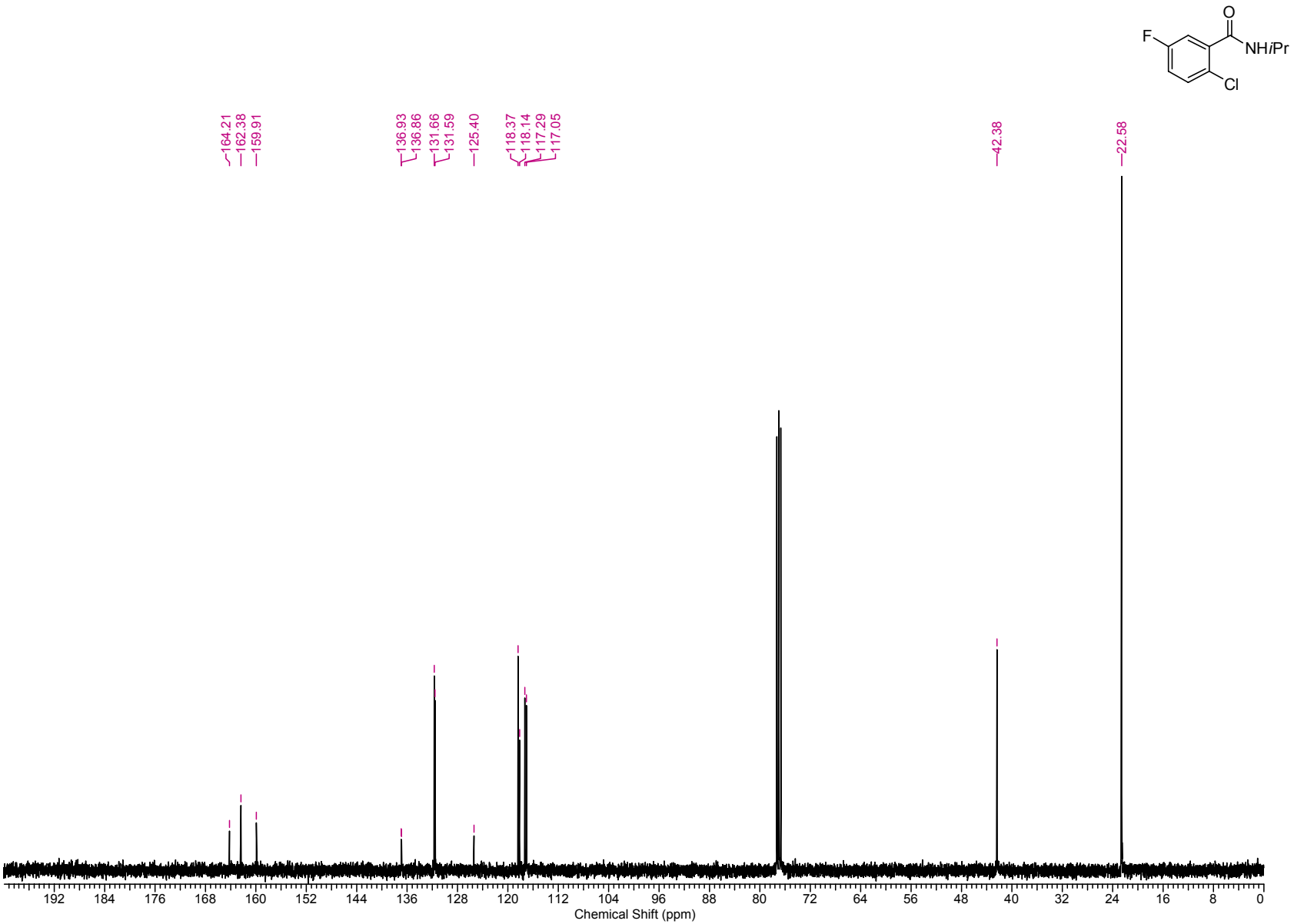

O
NHiPr
MeO
Cl
7.69
7.68
7.67
7.66
6.89
6.89
6.85
6.85
6.83
6.82
6.17
4.32
4.30
4.29
4.27
4.25
4.23
3.82
1.27
1.26
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

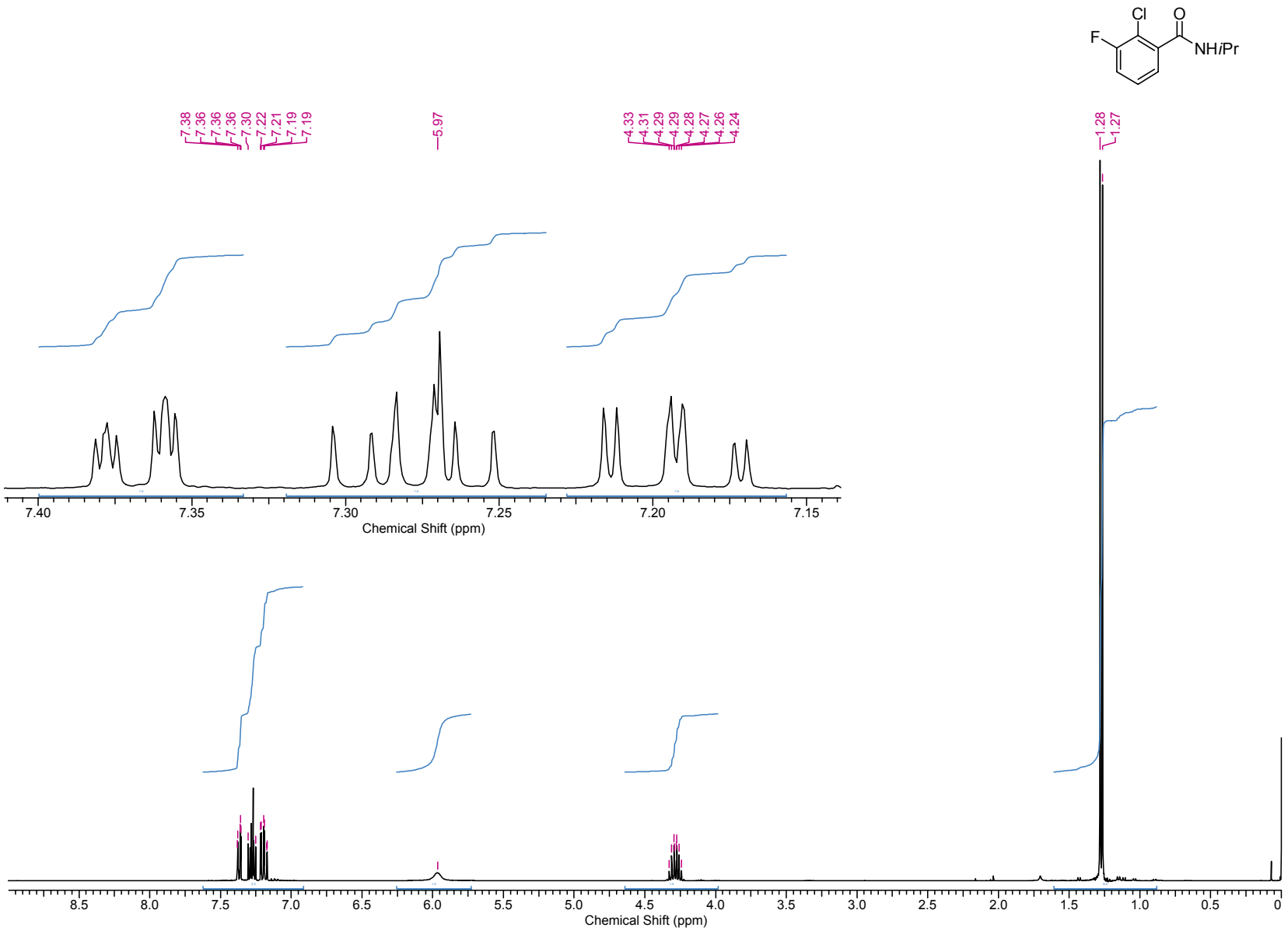

O
NHiPr
MeO
Cl
165.11
161.21
131.90
131.50
127.26
115.36
112.93
55.53
42.10
22.64
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

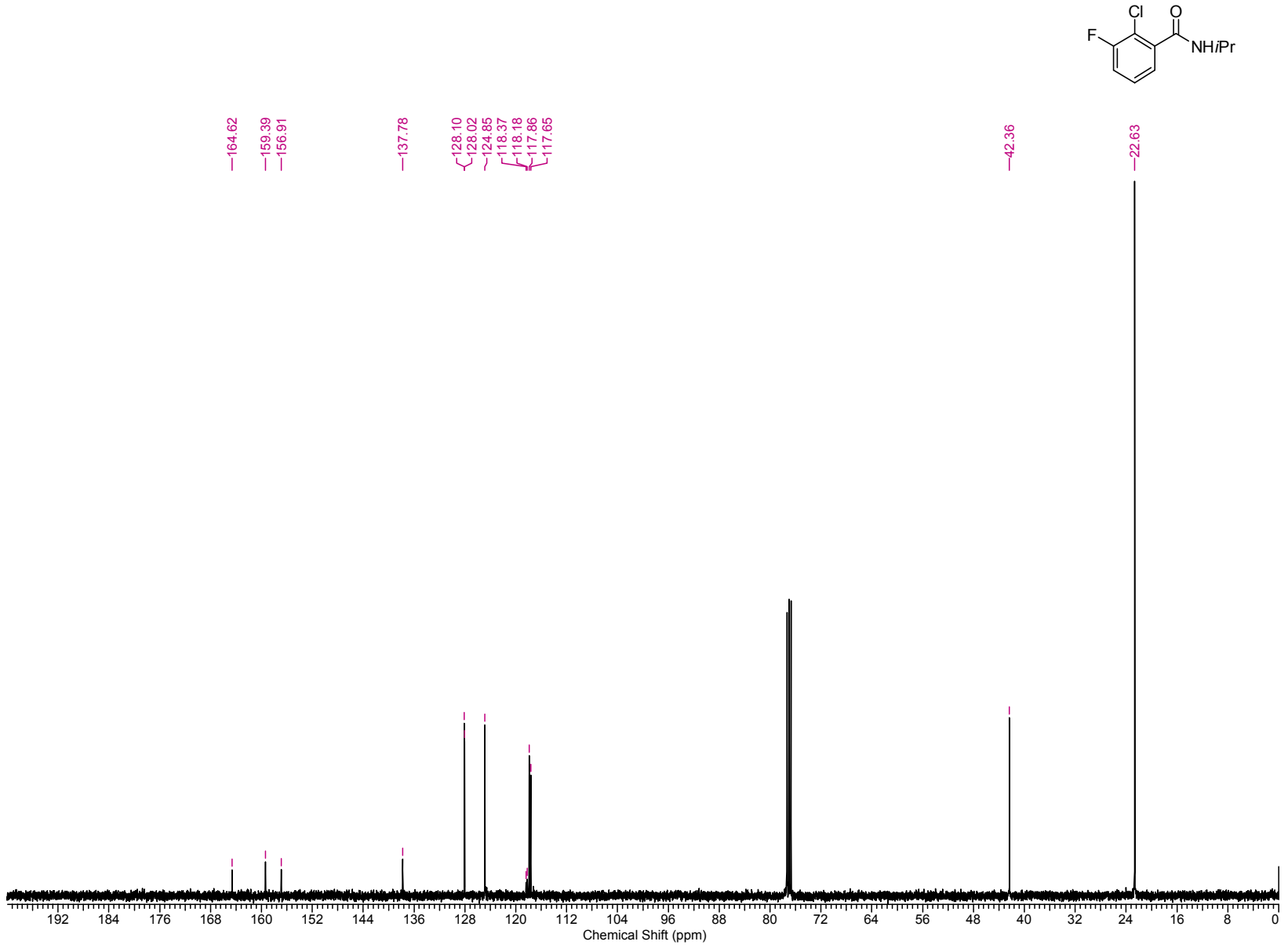

7.42
7.25
7.23
7.14
7.13
7.12
7.11
6.05
4.32
4.30
4.28
4.27
4.25
4.25
4.23
2.32
1.27
1.25
O
NHiPr
Cl
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

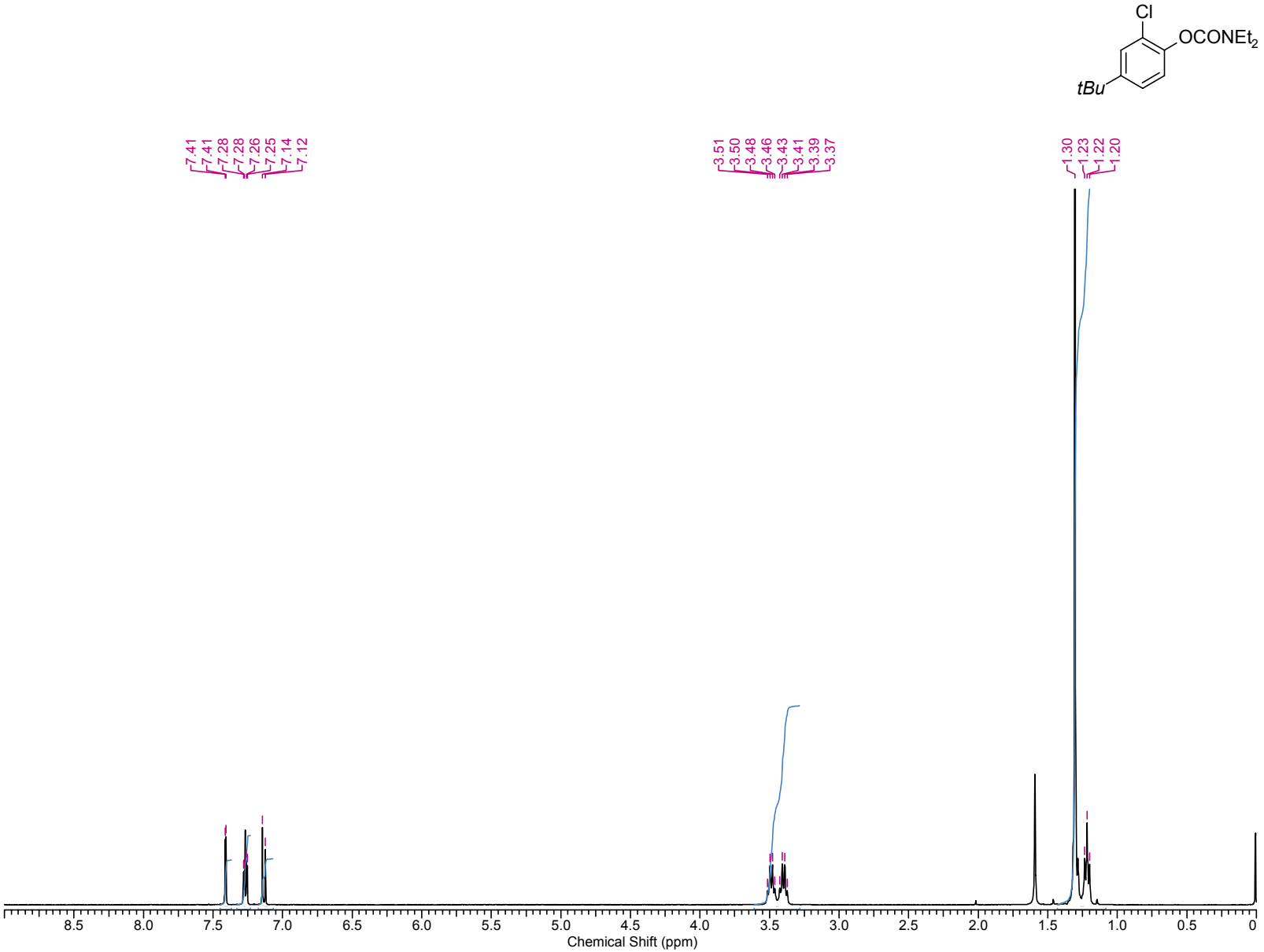


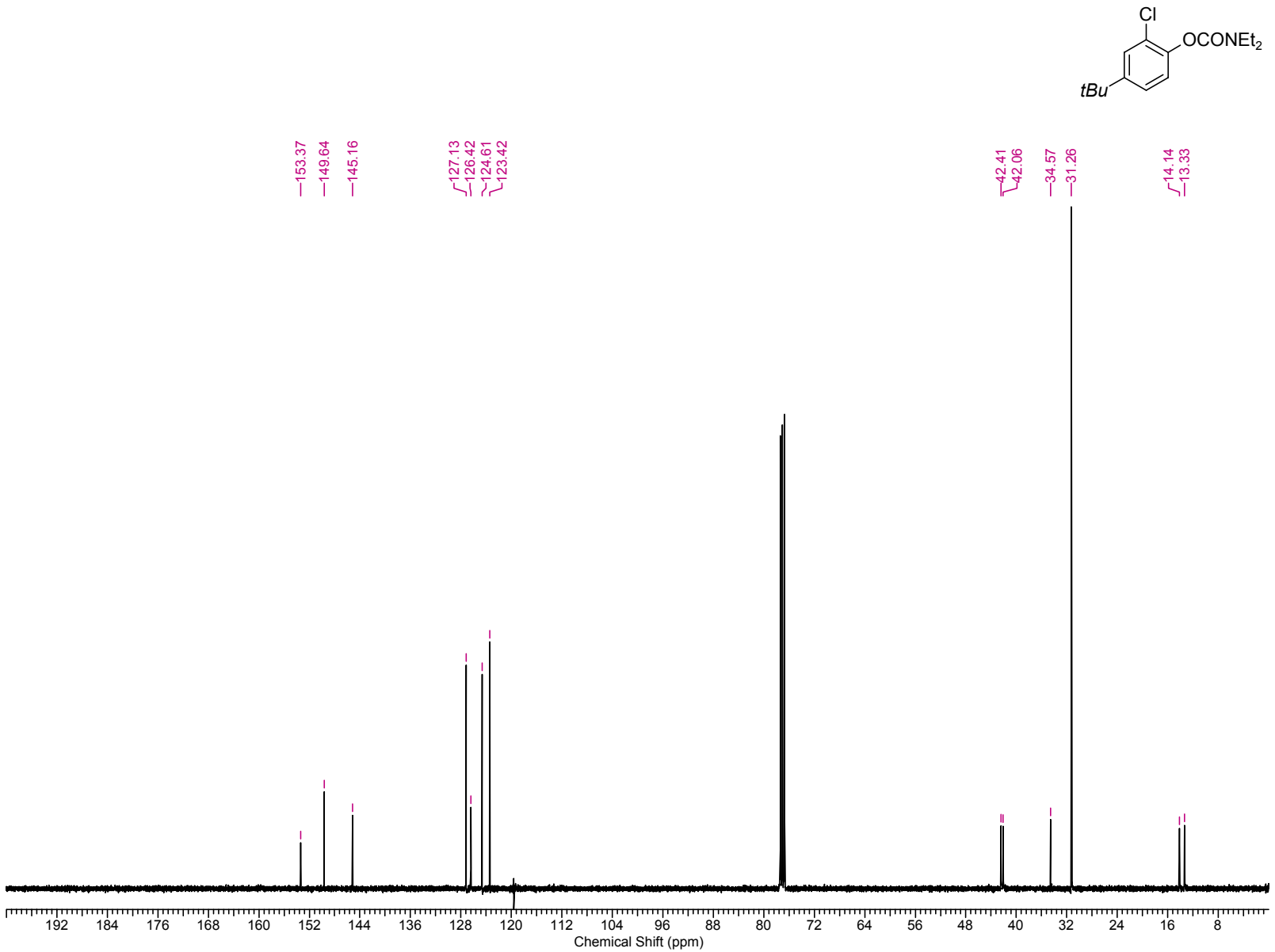

F
O
NH*i*Pr
Cl
7.38
7.37
7.37
7.36
7.35
7.35
7.33
7.08
7.07
7.06
7.04
6.08
4.32
4.31
4.29
4.29
4.27
4.27
4.25
4.24
1.28
1.27
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

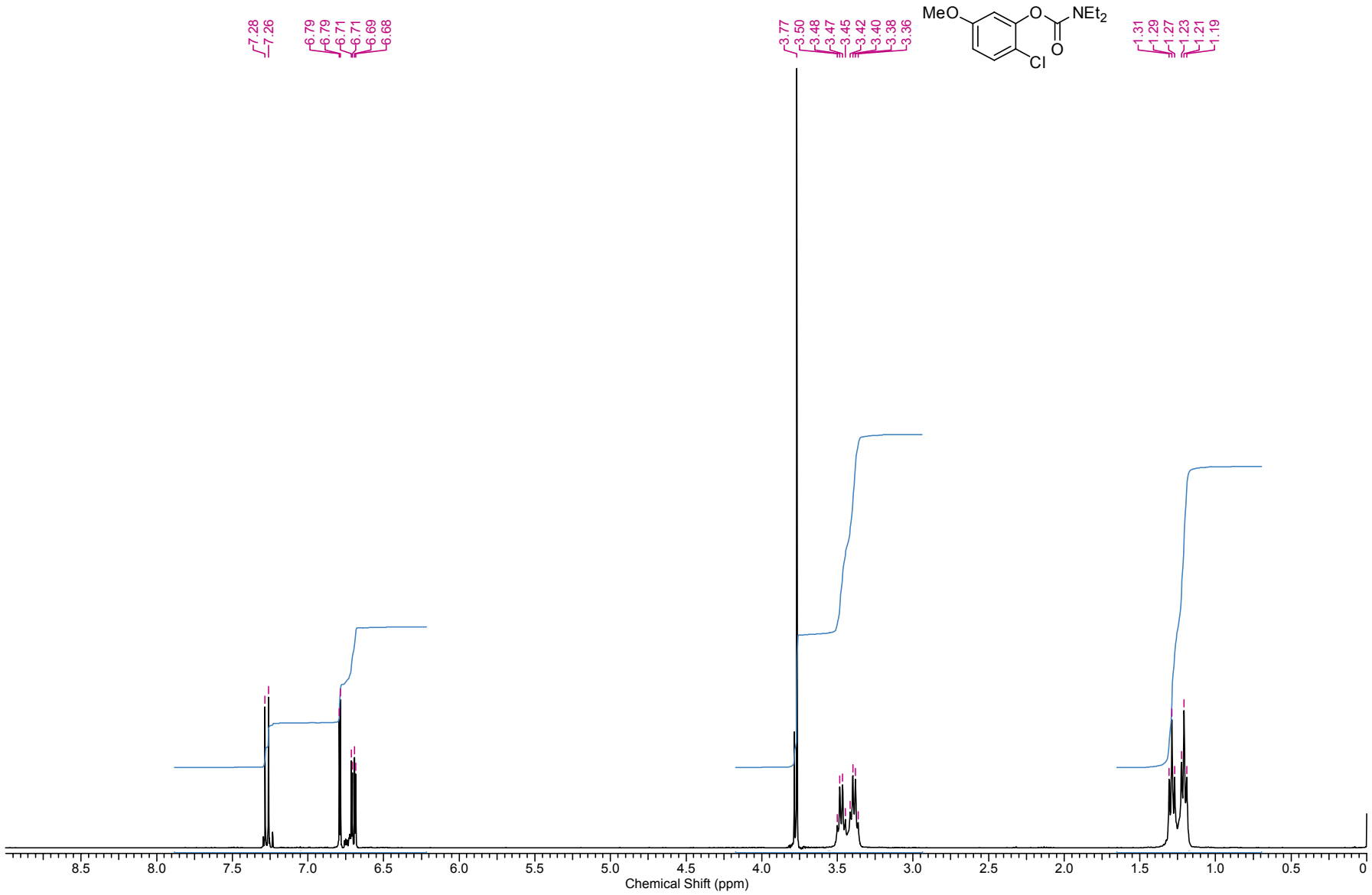

O
F
NH*i*Pr
Cl
164.21
162.38
159.91
136.93
136.86
131.66
131.59
125.40
118.37
118.14
117.29
117.05
42.38
22.58
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

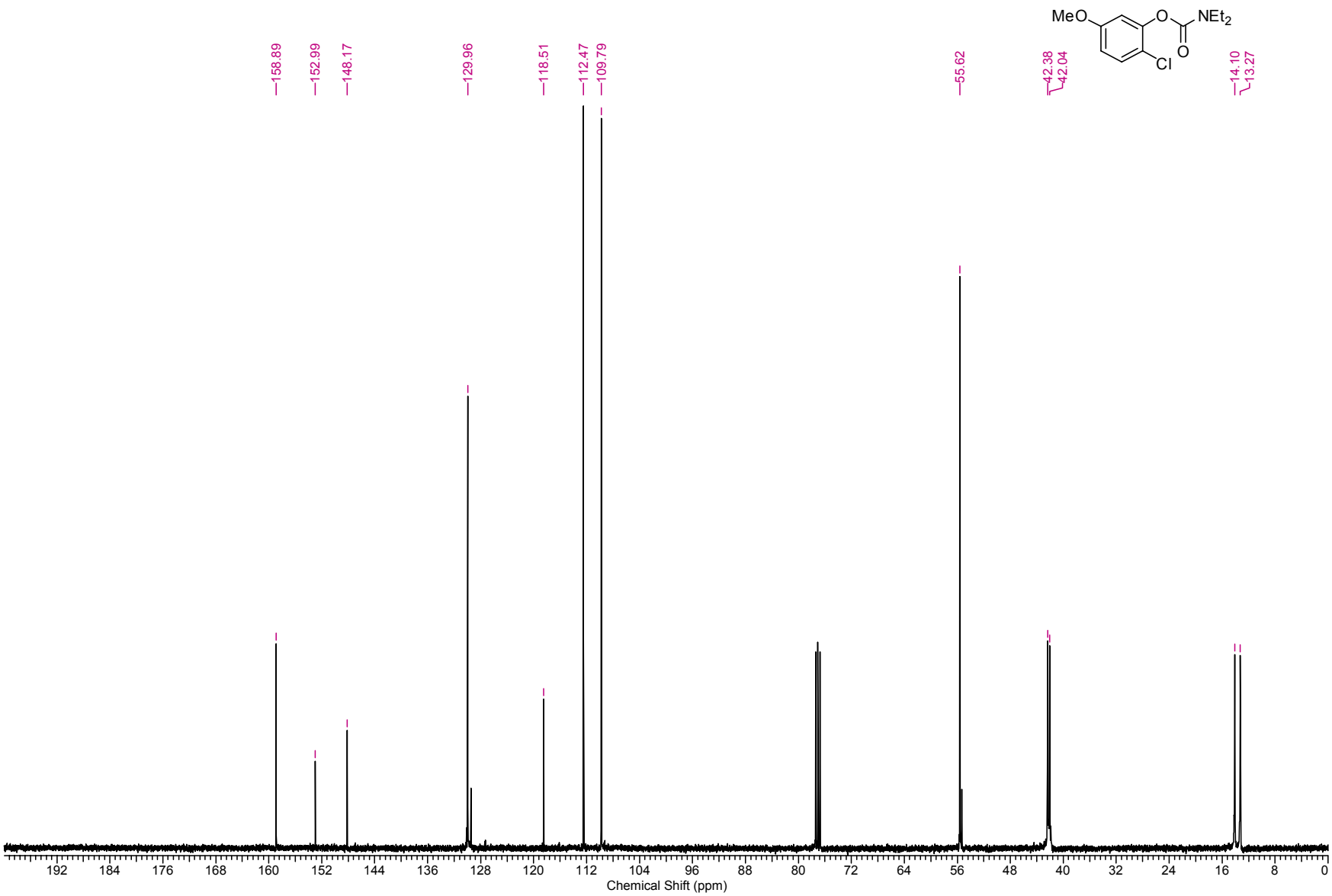

Cl
O
F
NHiPr
7.38
7.36
7.36
7.36
7.30
7.22
7.21
7.19
7.19
5.97
4.33
4.31
4.29
4.29
4.28
4.27
4.26
4.24
1.28
1.27
7.40
7.35
7.30
7.25
7.20
7.15
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

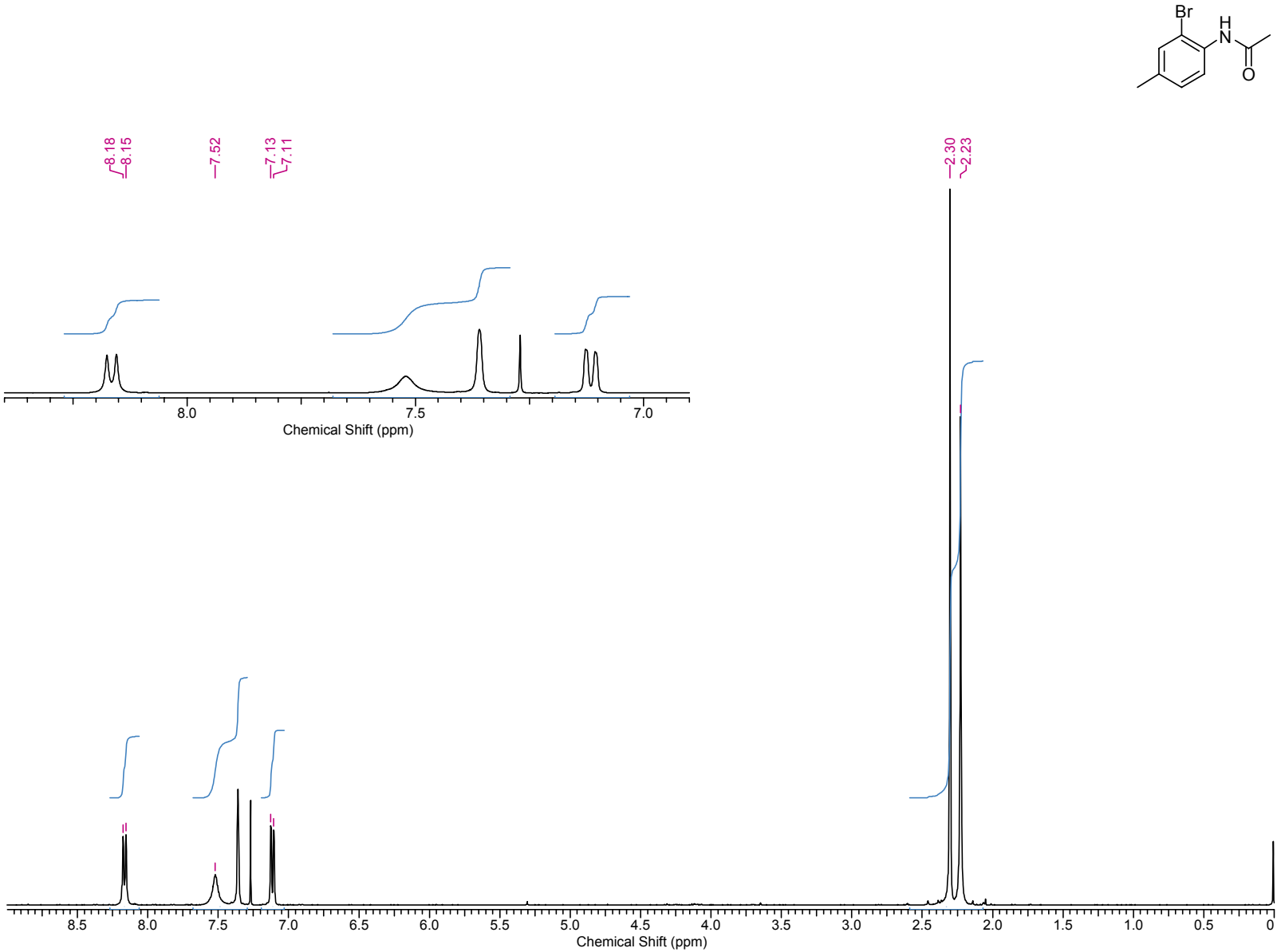

Cl
O
F
NH*i*Pr
164.62
159.39
156.91
137.78
128.10
128.02
124.85
118.37
118.18
117.86
117.65
42.36
22.63
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


Cl
OCONEt2
tBu
7.41
7.41
7.28
7.28
7.26
7.25
7.14
7.12
3.51
3.50
3.48
3.46
3.43
3.41
3.39
3.37
1.30
1.23
1.22
1.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Cl
OCONEt2
tBu
153.37
149.64
145.16
127.13
126.42
124.61
123.42
42.41
42.06
34.57
31.26
14.14
13.33
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)


7.28
7.26
6.79
6.79
6.71
6.71
6.69
6.68
3.77
3.50
3.48
3.47
3.45
3.42
3.40
3.38
3.36
1.31
1.29
1.27
1.23
1.21
1.19
MeO
O
NEt2
O
Cl
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


MeO
O
NEt2
O
Cl
158.89
152.99
148.17
129.96
118.51
112.47
109.79
55.62
42.38
42.04
14.10
13.27
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


Br
H
N
O
8.18
8.15
7.52
7.13
7.11
2.30
2.23
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

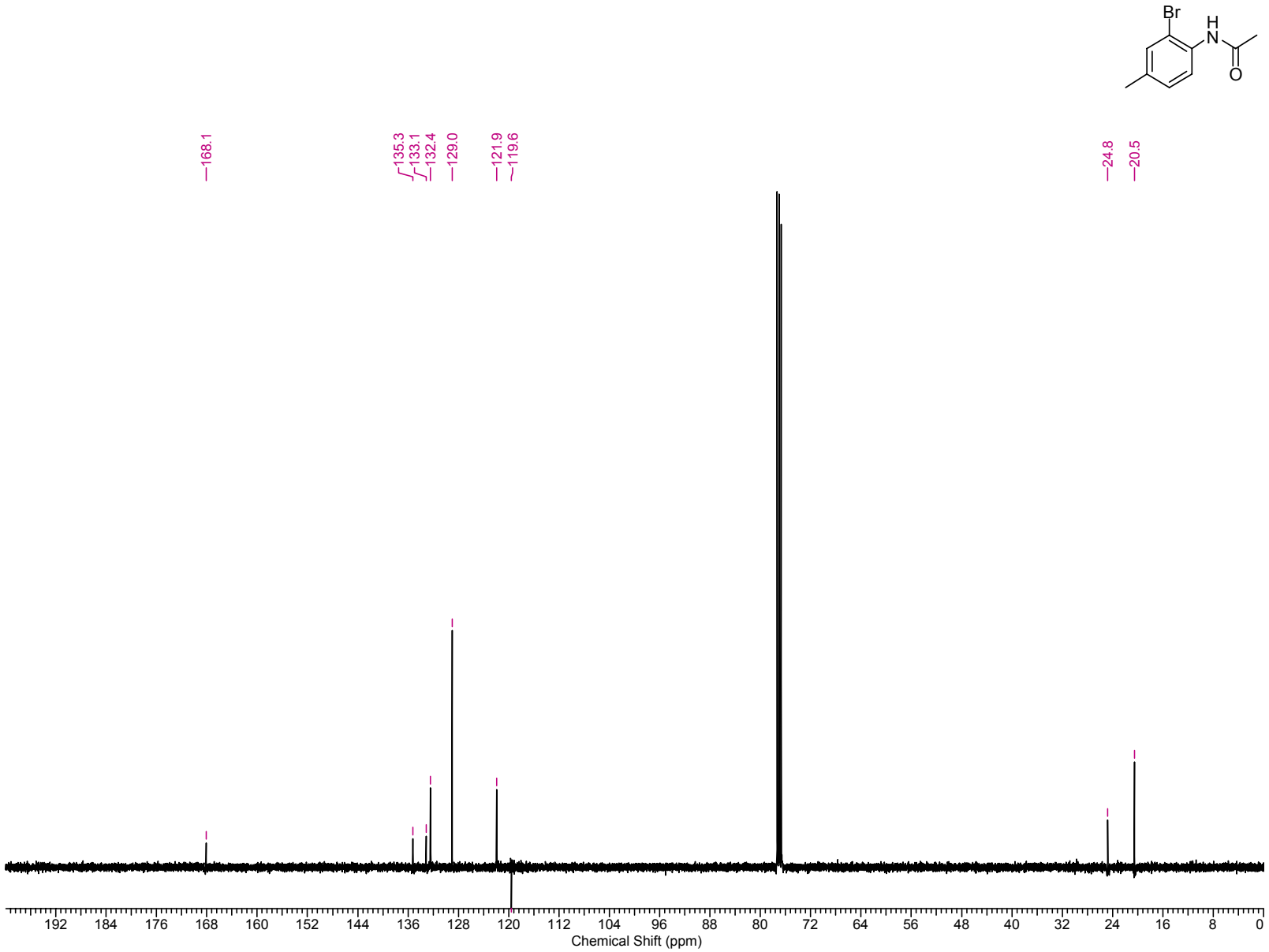

Br
H
N
O
168.1
135.3
133.1
132.4
129.0
121.9
119.6
24.8
20.5
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

Table 4, Entry 1 (7b)

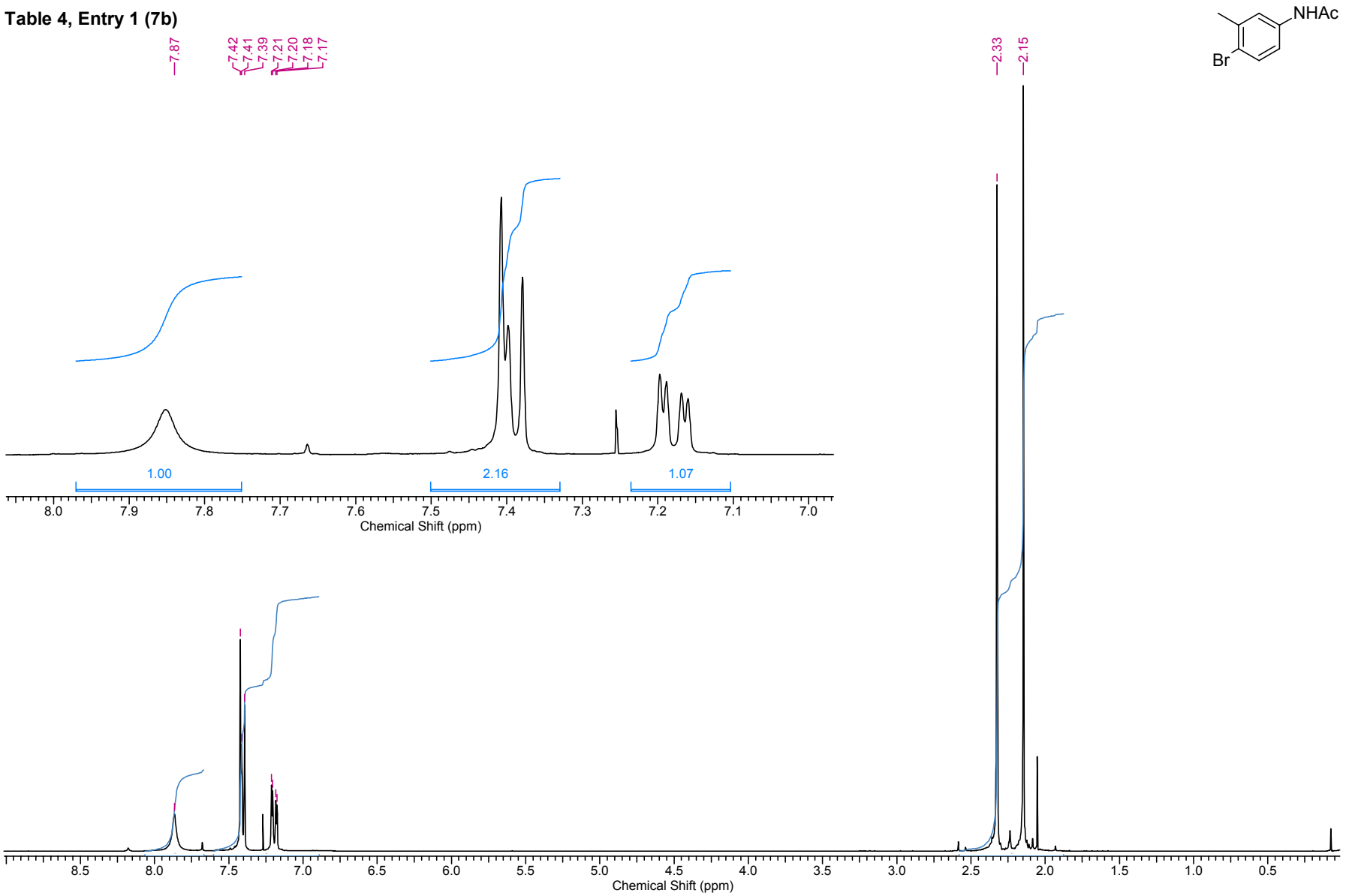


Table 4, Entry 1 (7b)

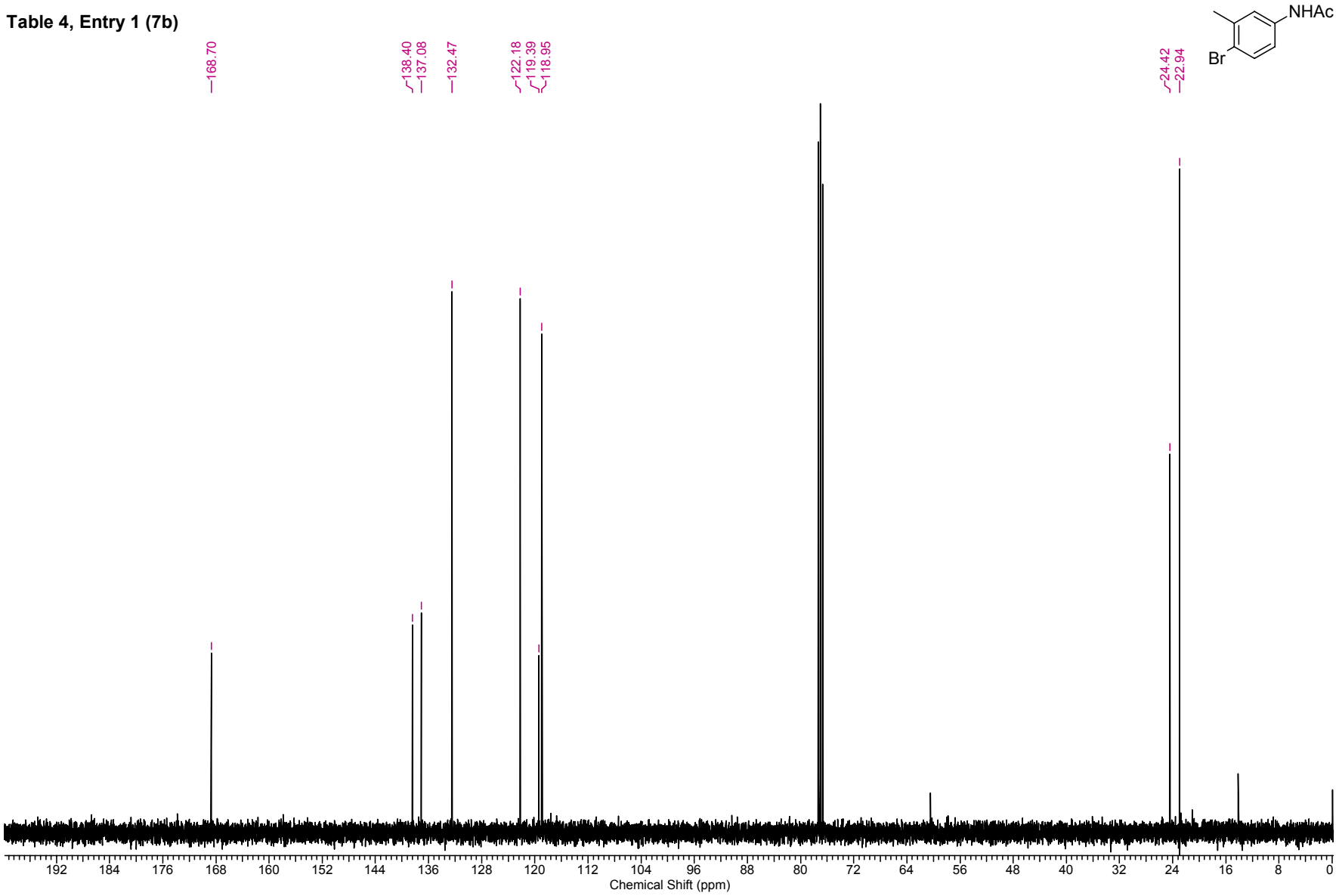


Table 4, Entry 1 (7b) HMQC

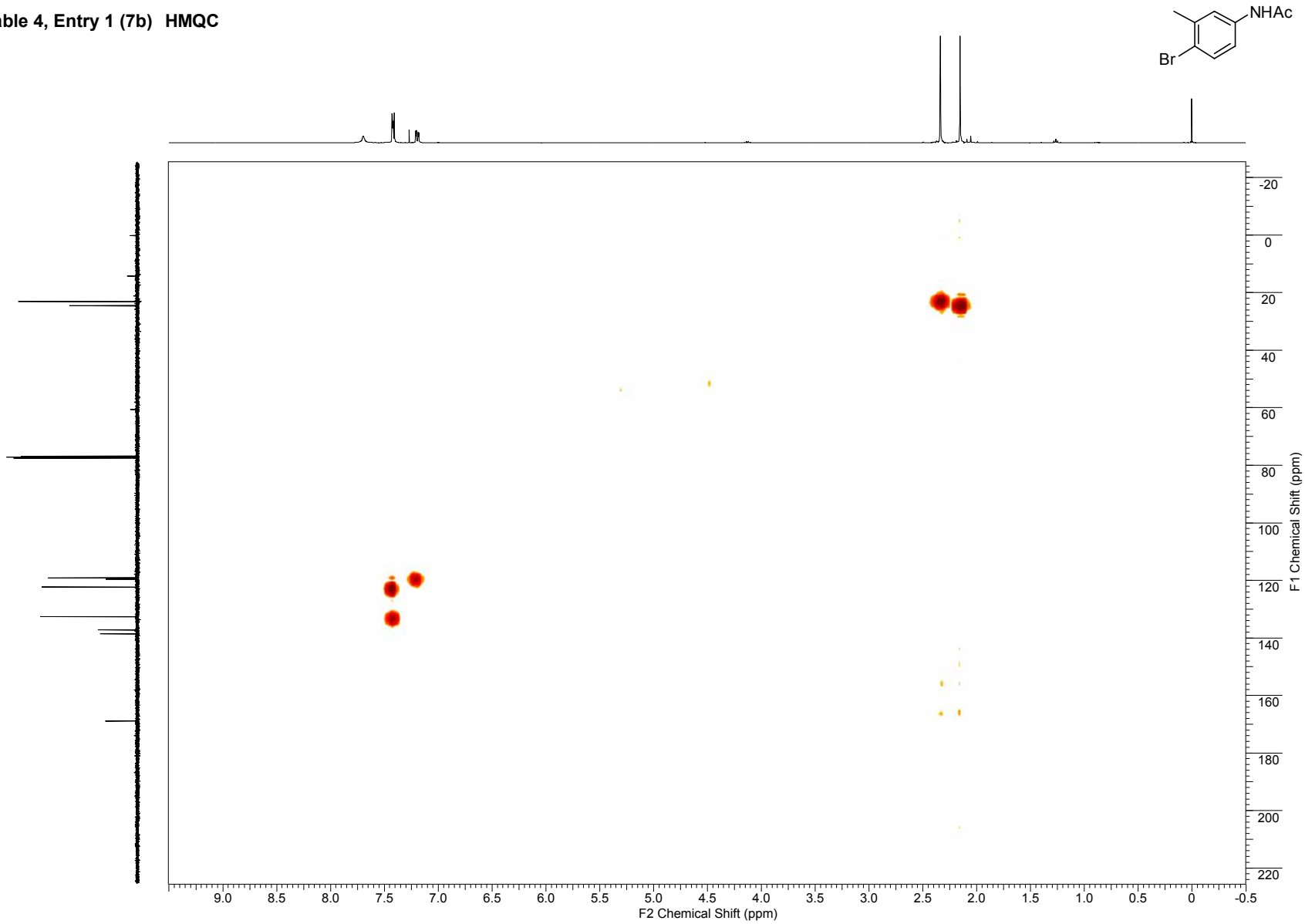


Table 4, Entry 1 (7b) HMBC

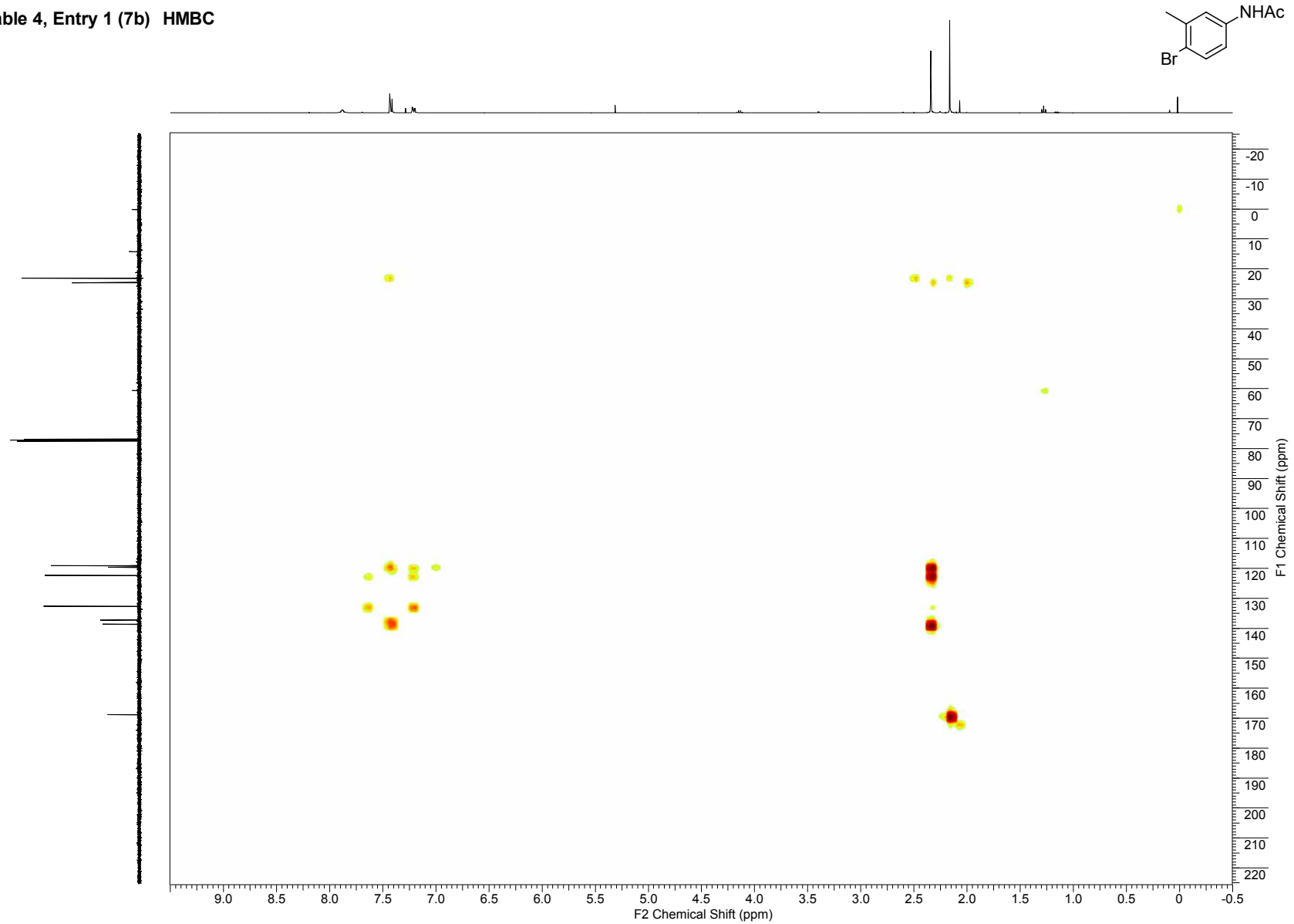
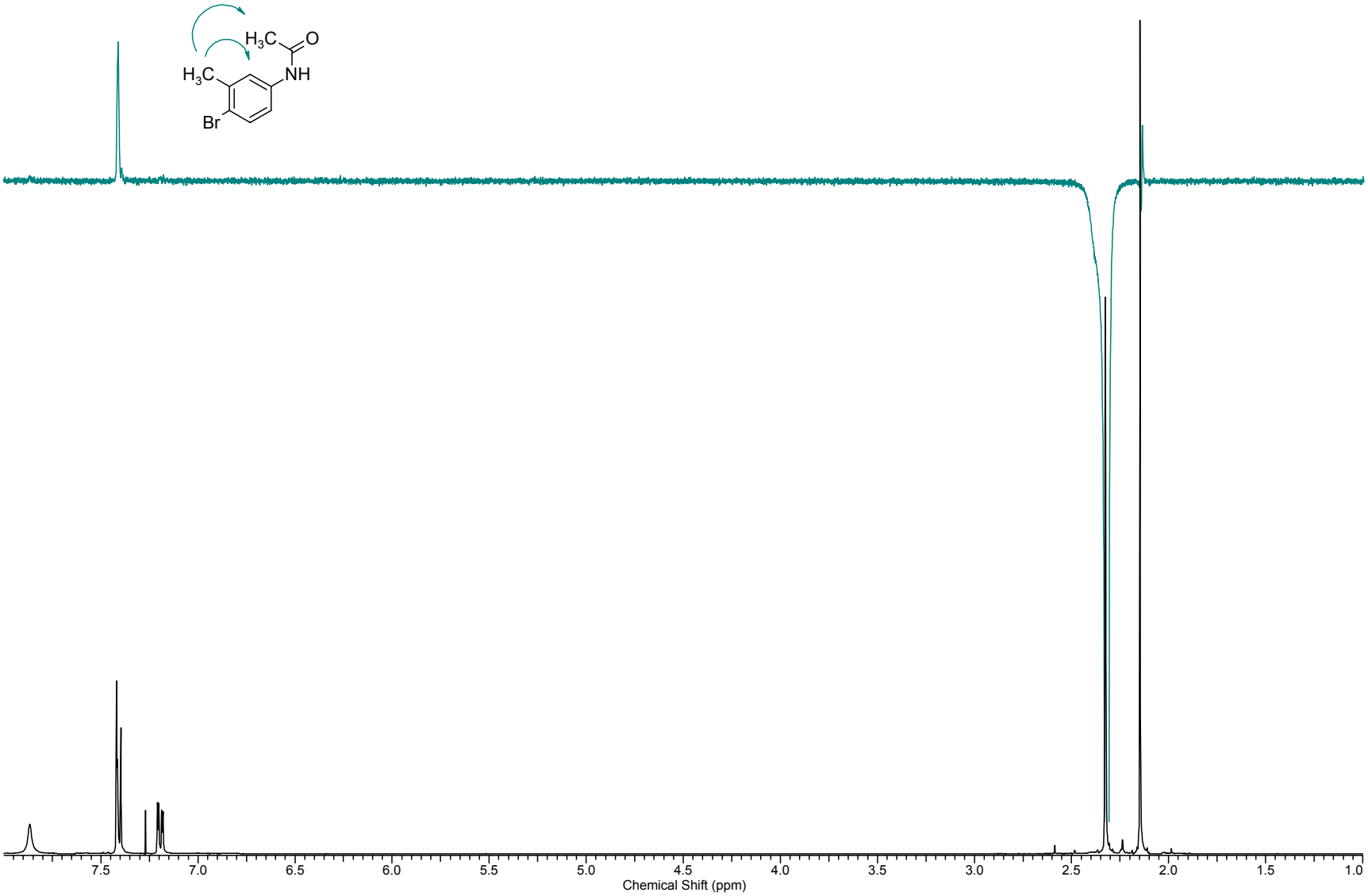
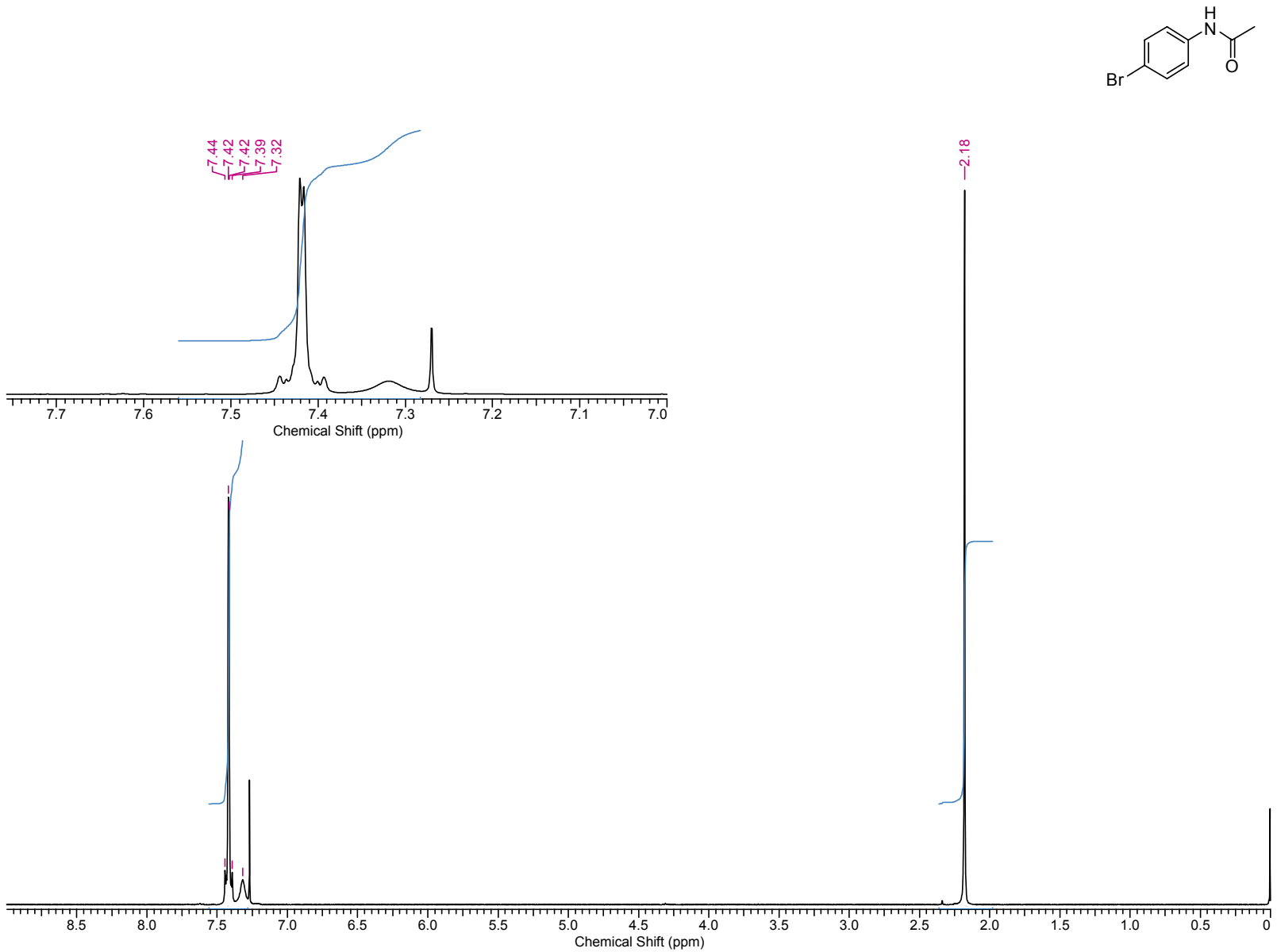
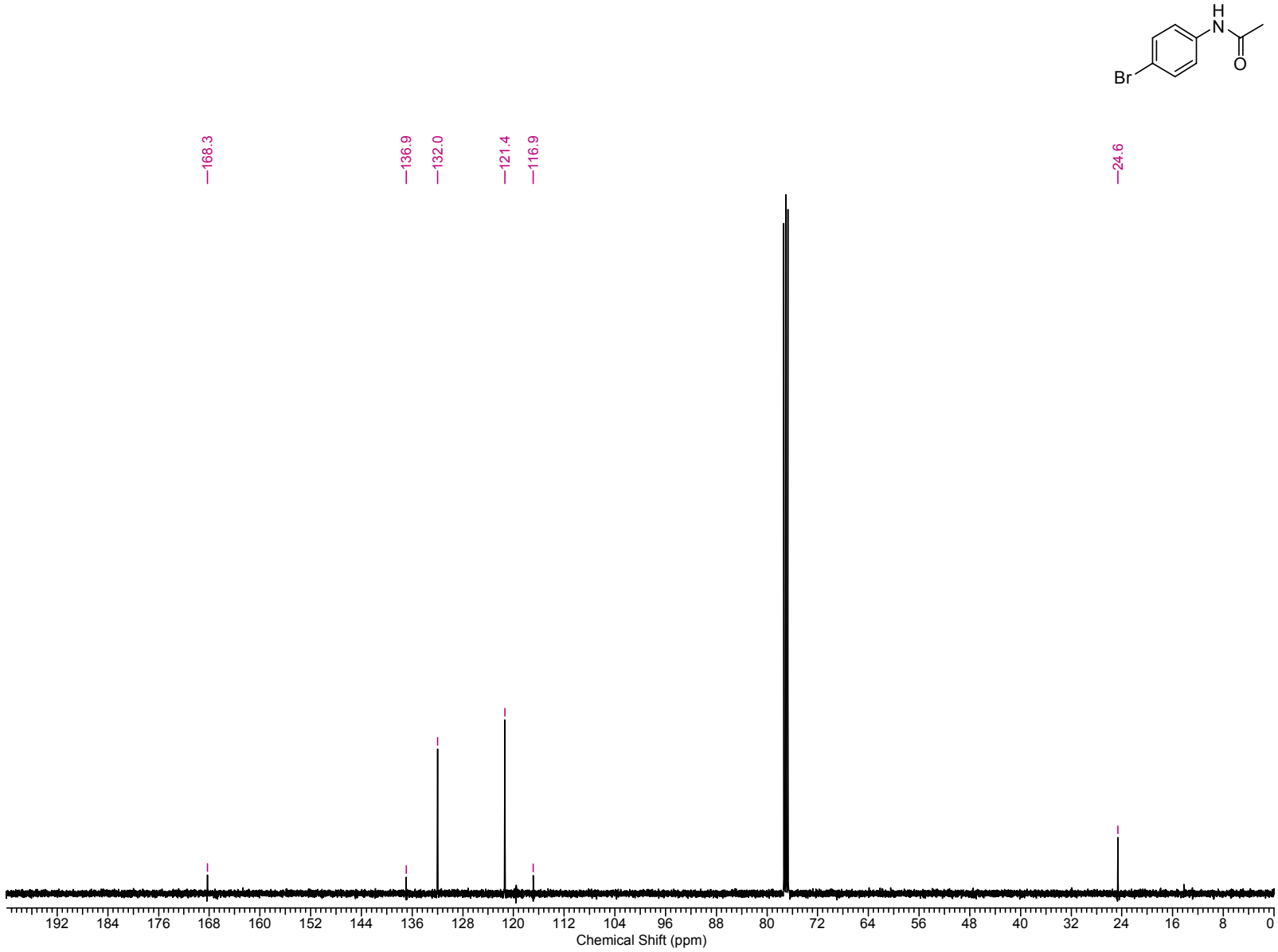
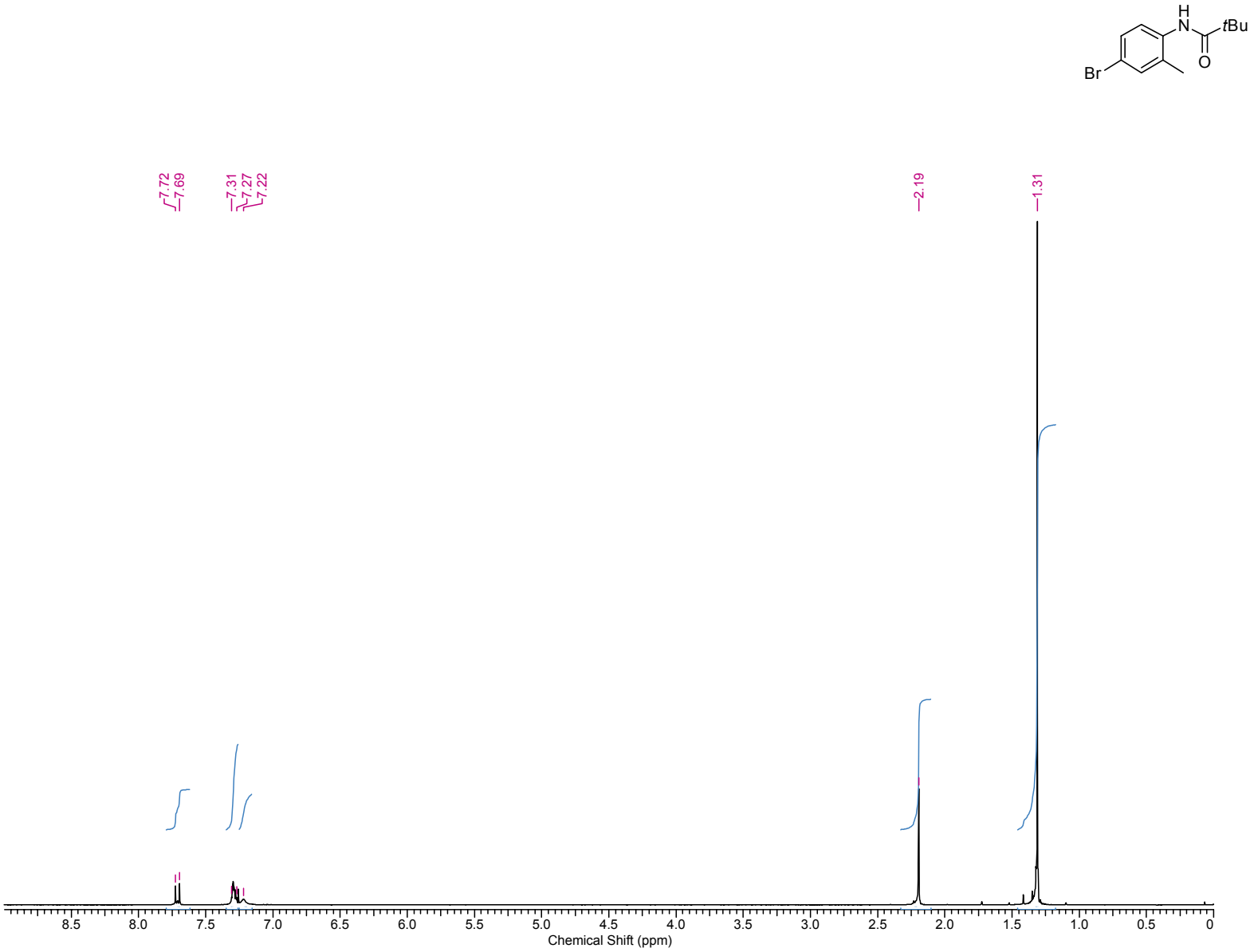


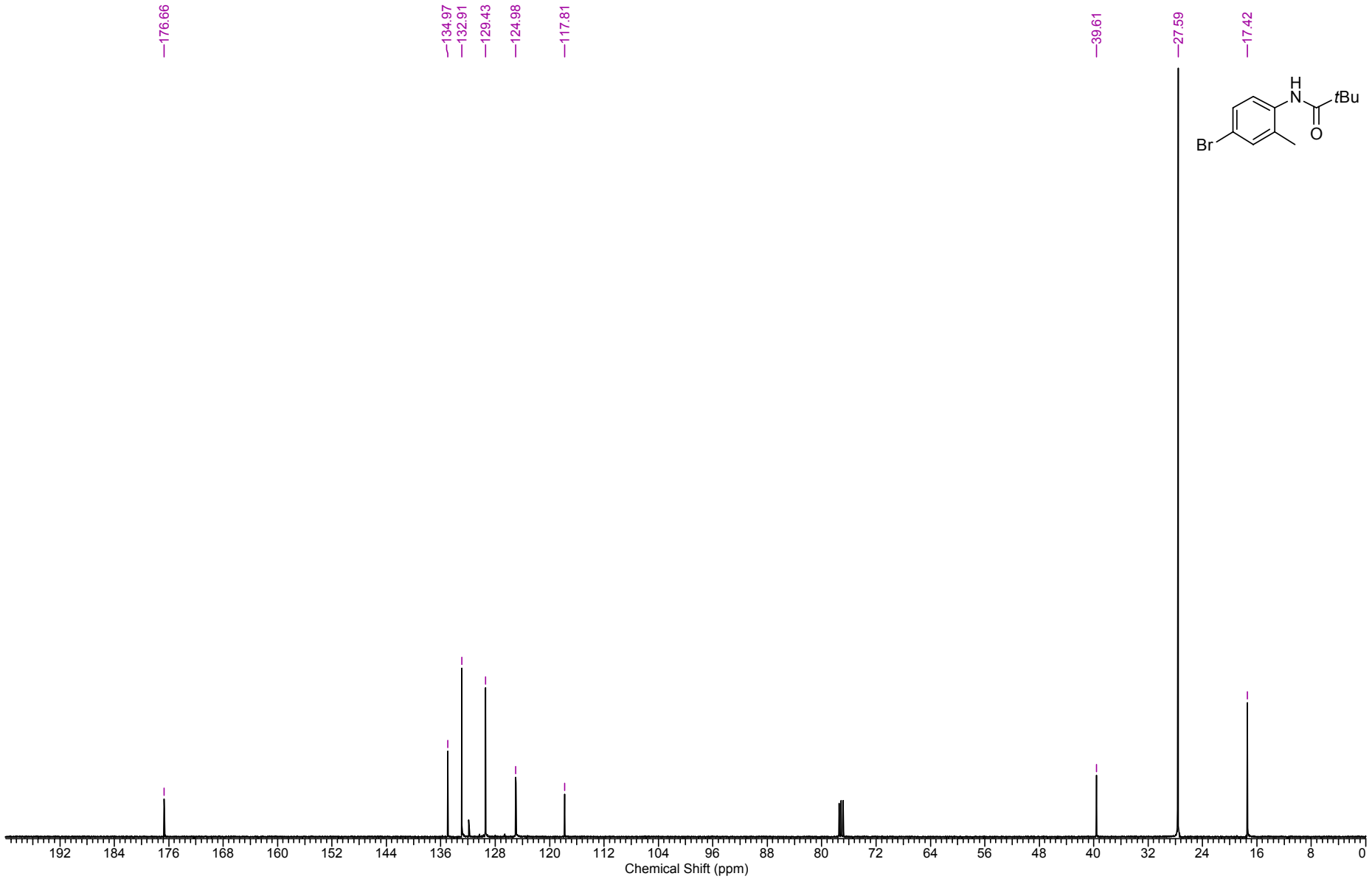
Table 4, Entry 1 (7b) NOE

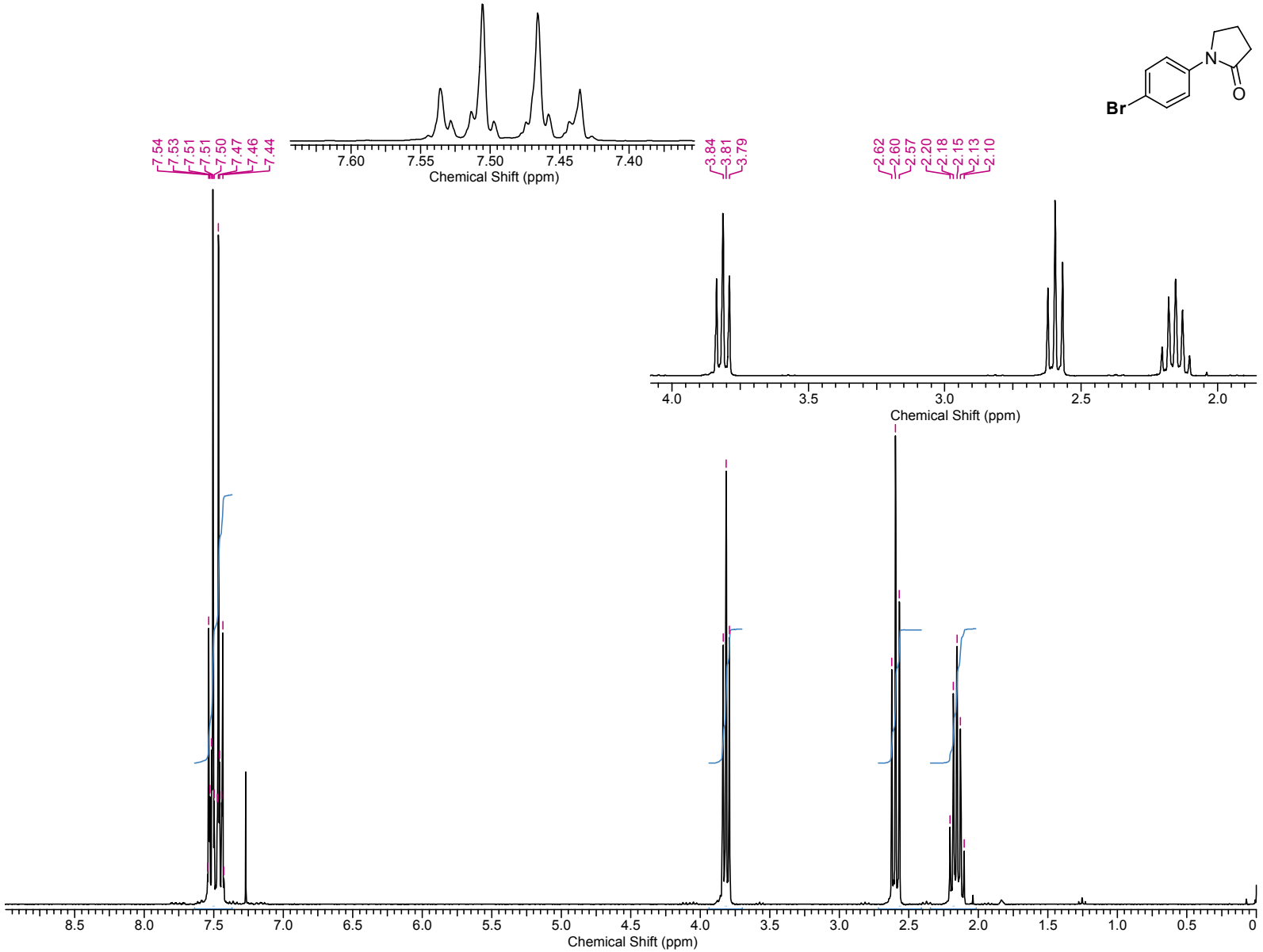


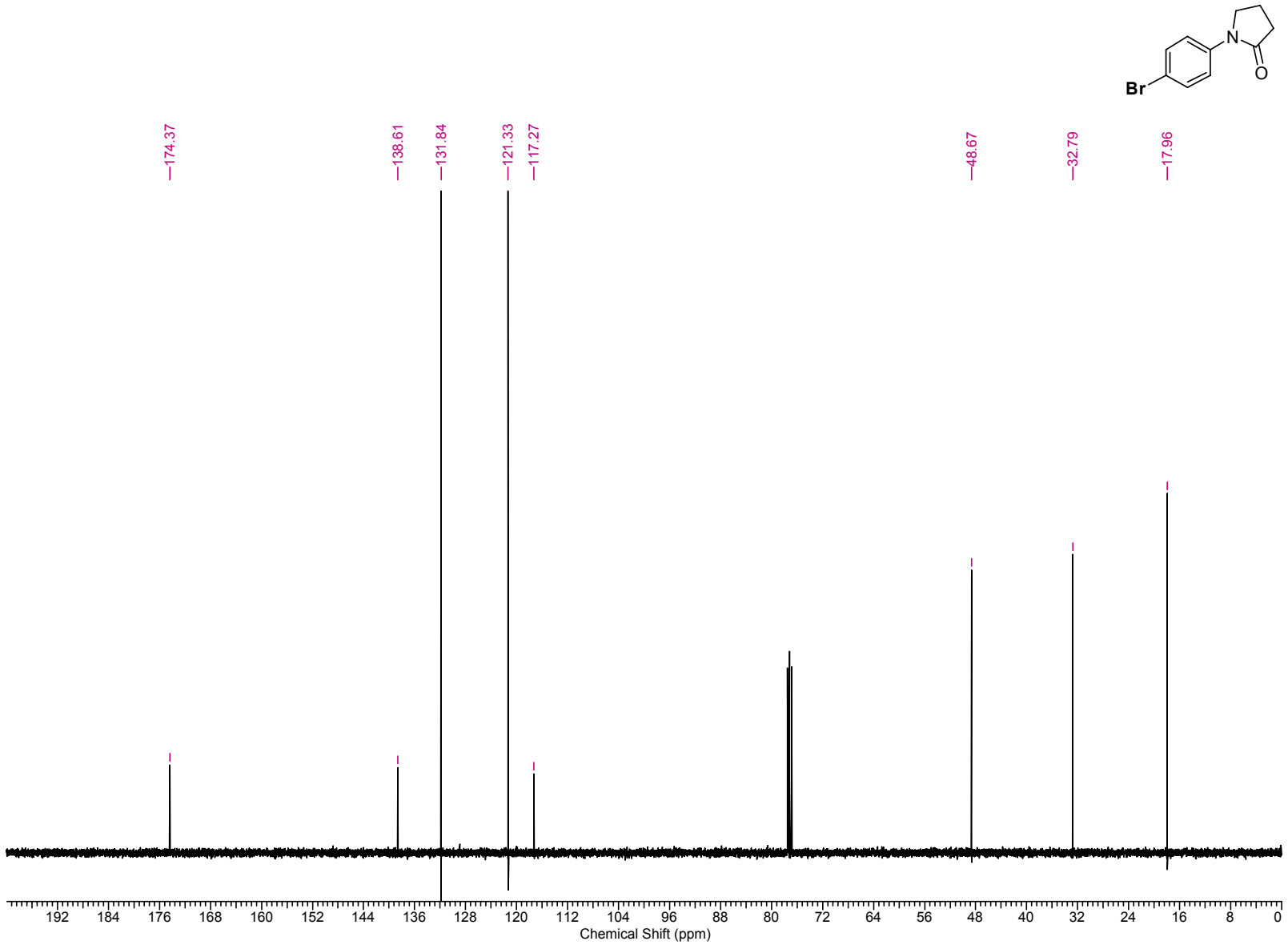

H
N
O
Br
7.44
7.42
7.42
7.39
7.32
2.18
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

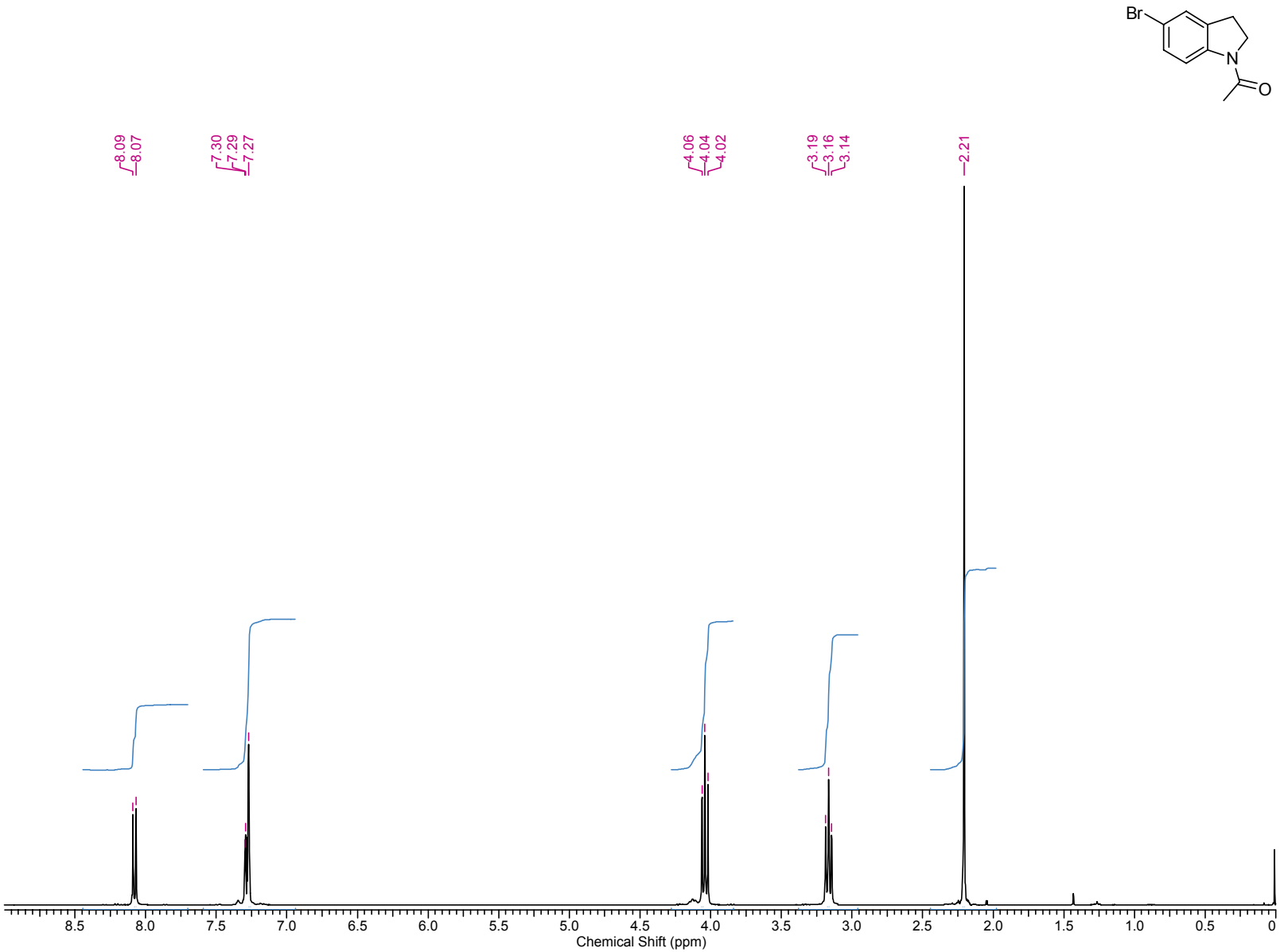


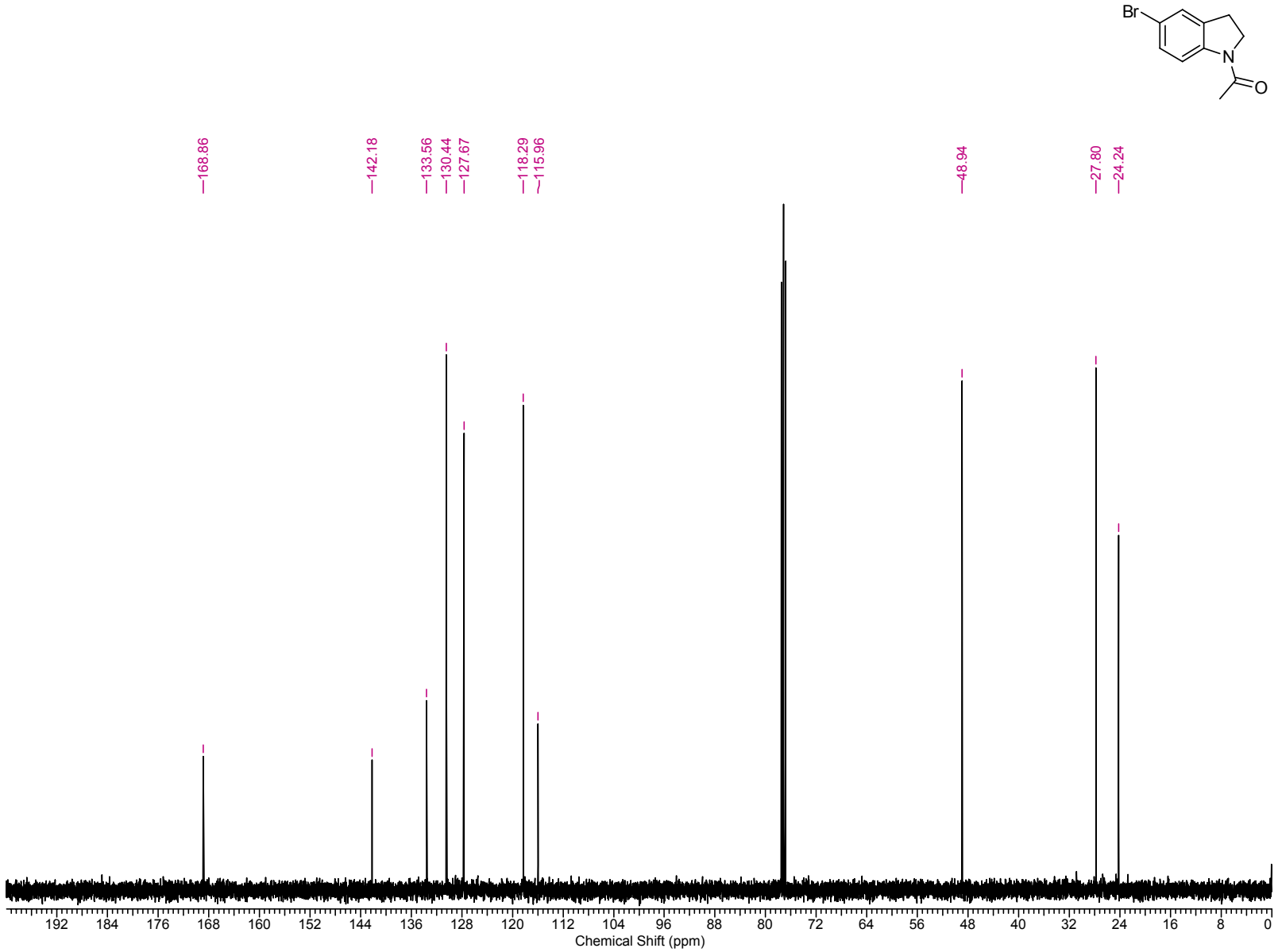

H
N
tBu
O
Br
7.72
7.69
7.31
7.27
7.22
2.19
1.31
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

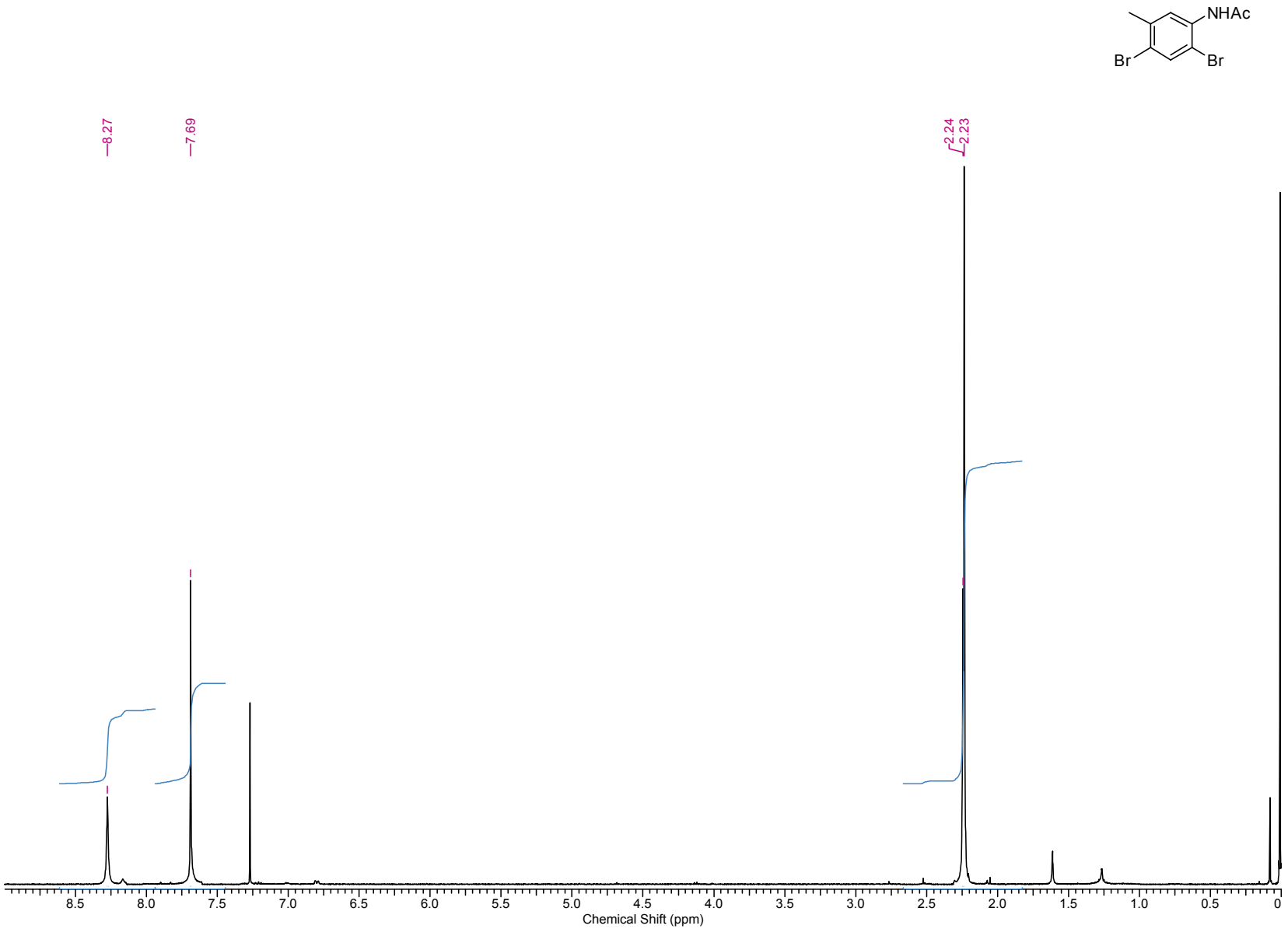

176.66
134.97
132.91
129.43
124.98
117.81
39.61
27.59
17.42
H
N
tBu
O
Br
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


7.54
7.53
7.51
7.51
7.50
7.47
7.46
7.44
7.60
7.55
7.50
7.45
7.40
Chemical Shift (ppm)
3.84
3.81
3.79
2.62
2.60
2.57
2.20
2.18
2.15
2.13
2.10
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)
Br
N
O
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Br
N
O
174.37
138.61
131.84
121.33
117.27
48.67
32.79
17.96
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


Br
N
O
8.09
8.07
7.30
7.29
7.27
4.06
4.04
4.02
3.19
3.16
3.14
2.21
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Br
N
O
168.86
142.18
133.56
130.44
127.67
118.29
115.96
48.94
27.80
24.24
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


NHAc
Br
Br
8.27
7.69
2.24
2.23
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

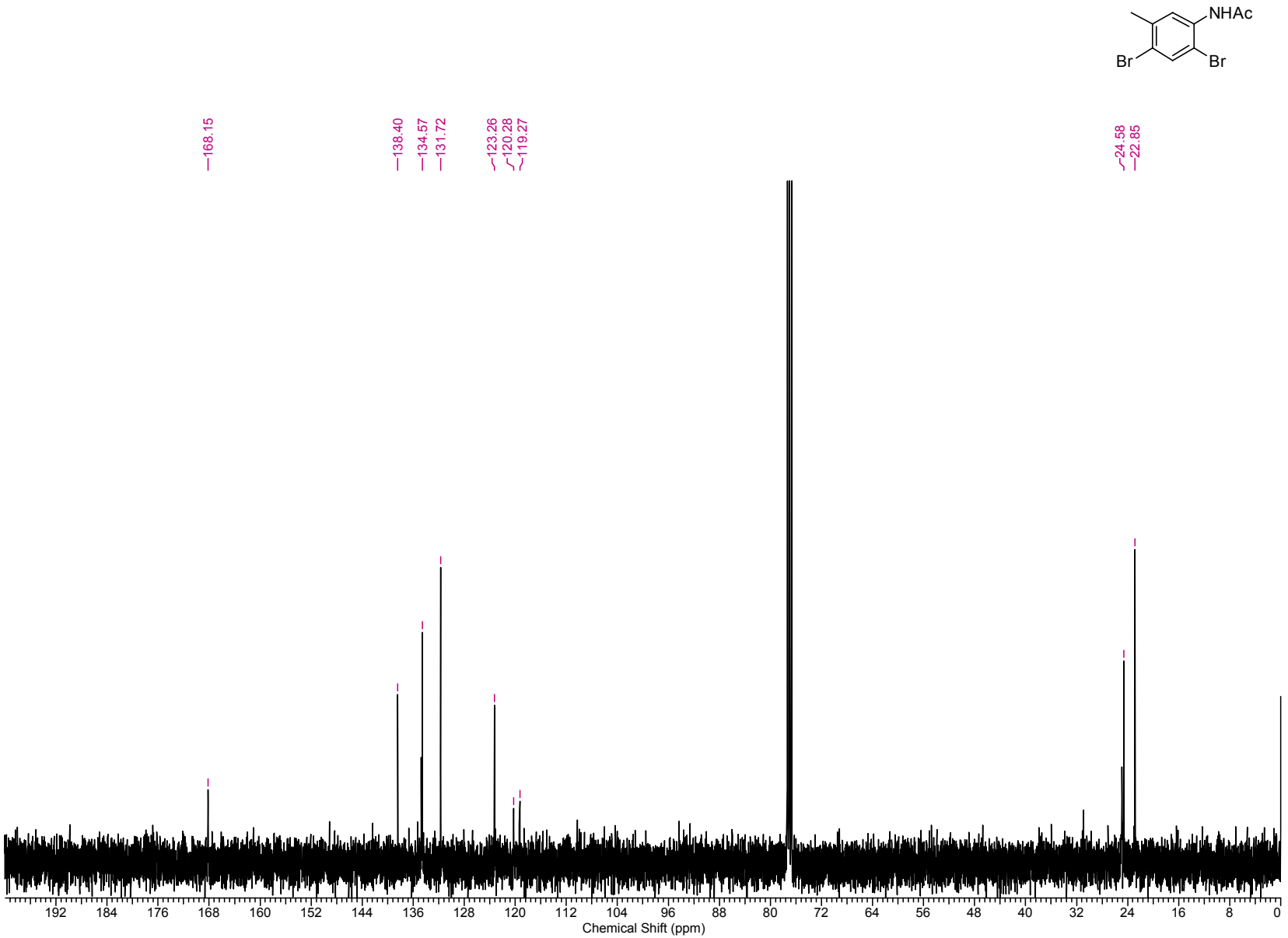


Table 5, Entry 7 (7b)

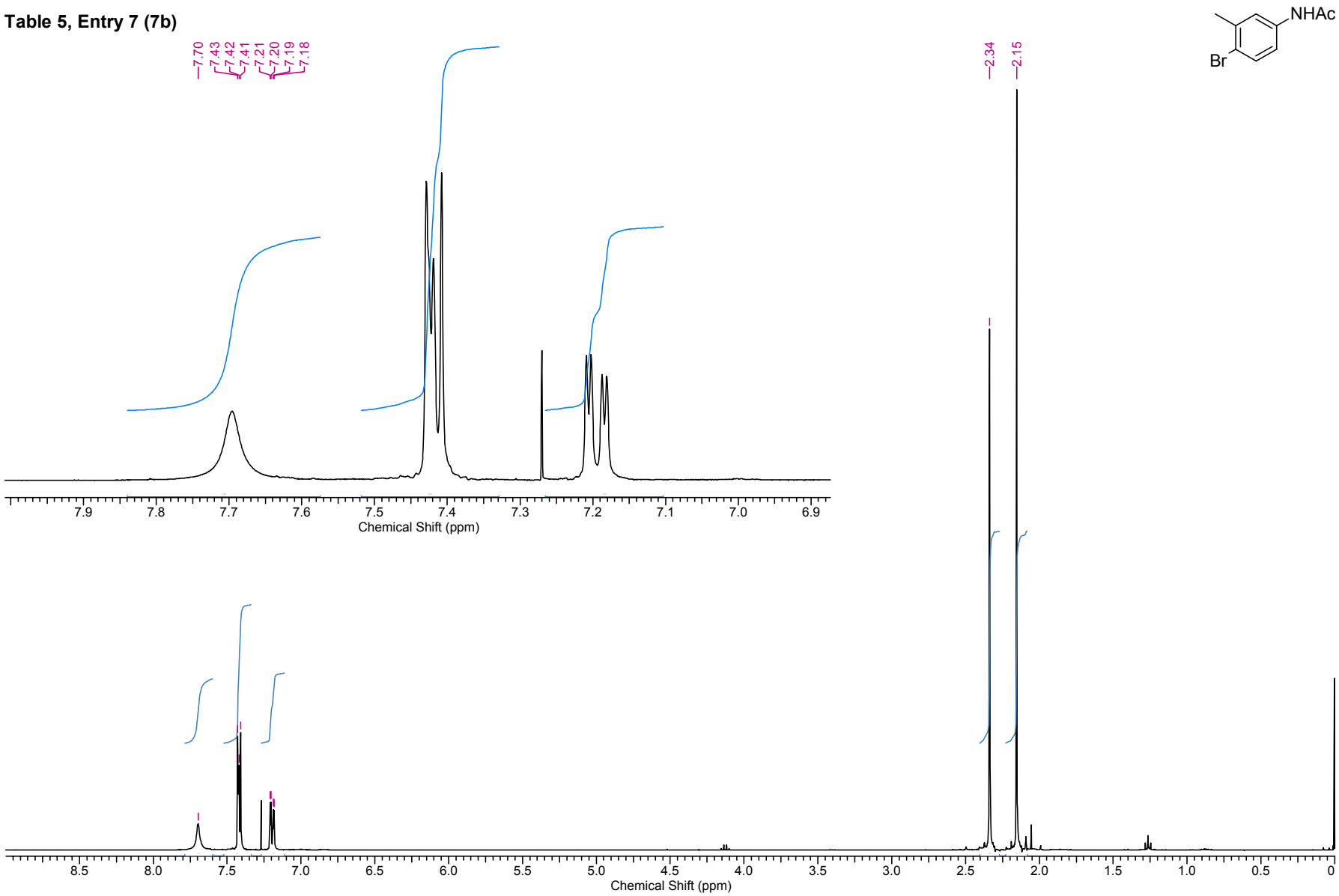


Table 5, Entry 7 (7b)

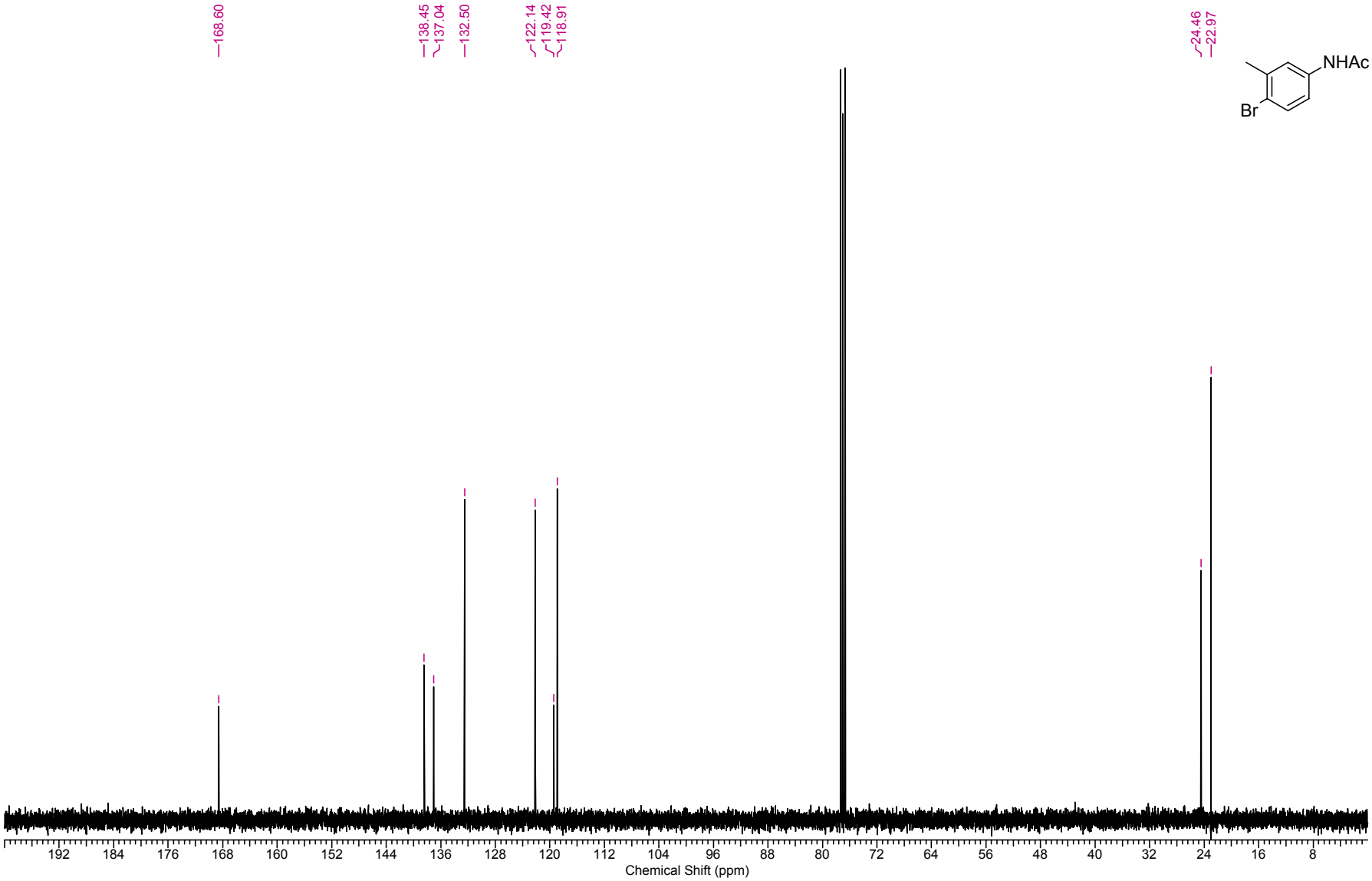


Table 5, Entry 7 (7b) HMQC

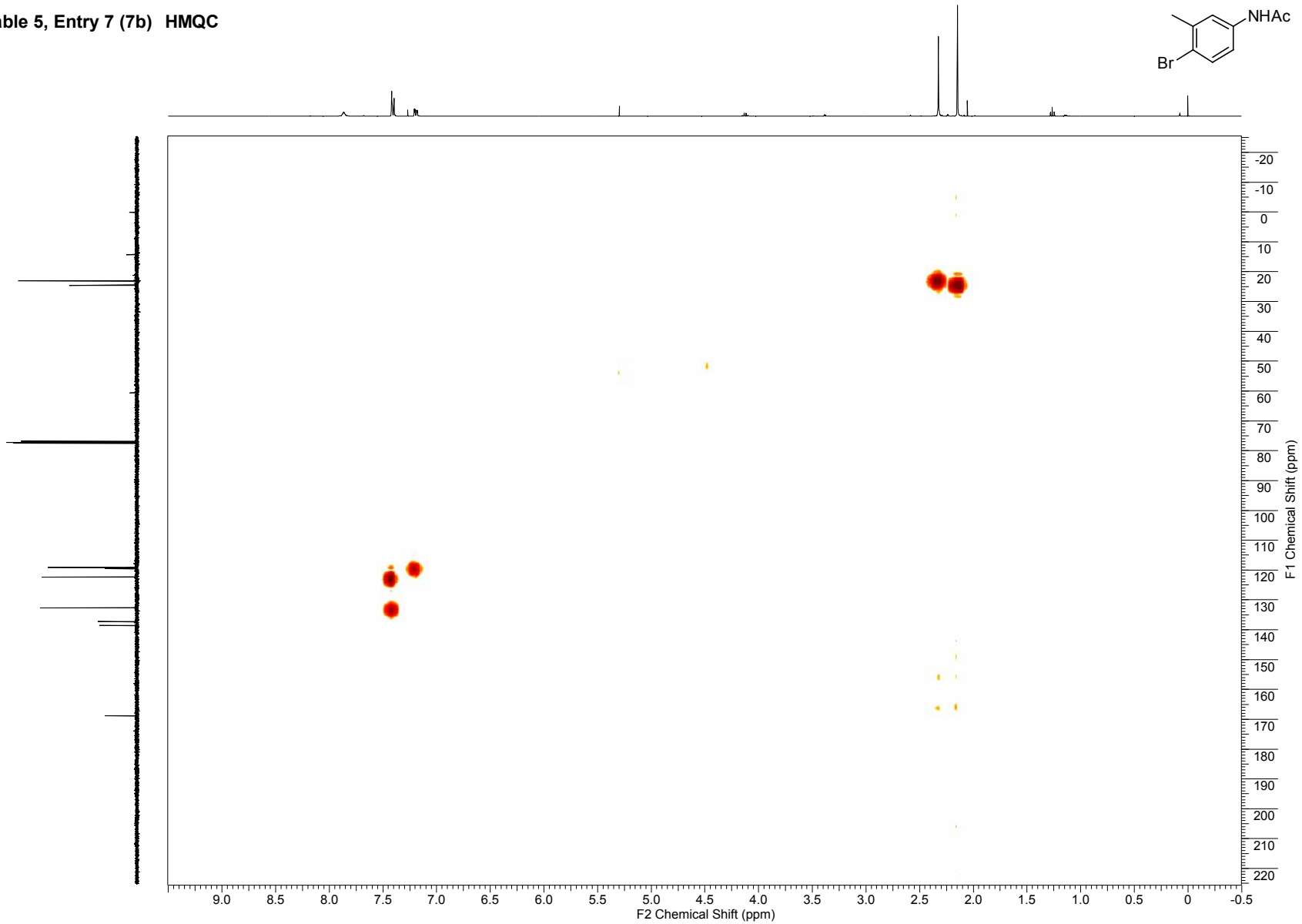


Table 5, Entry 7 (7b) HMBC

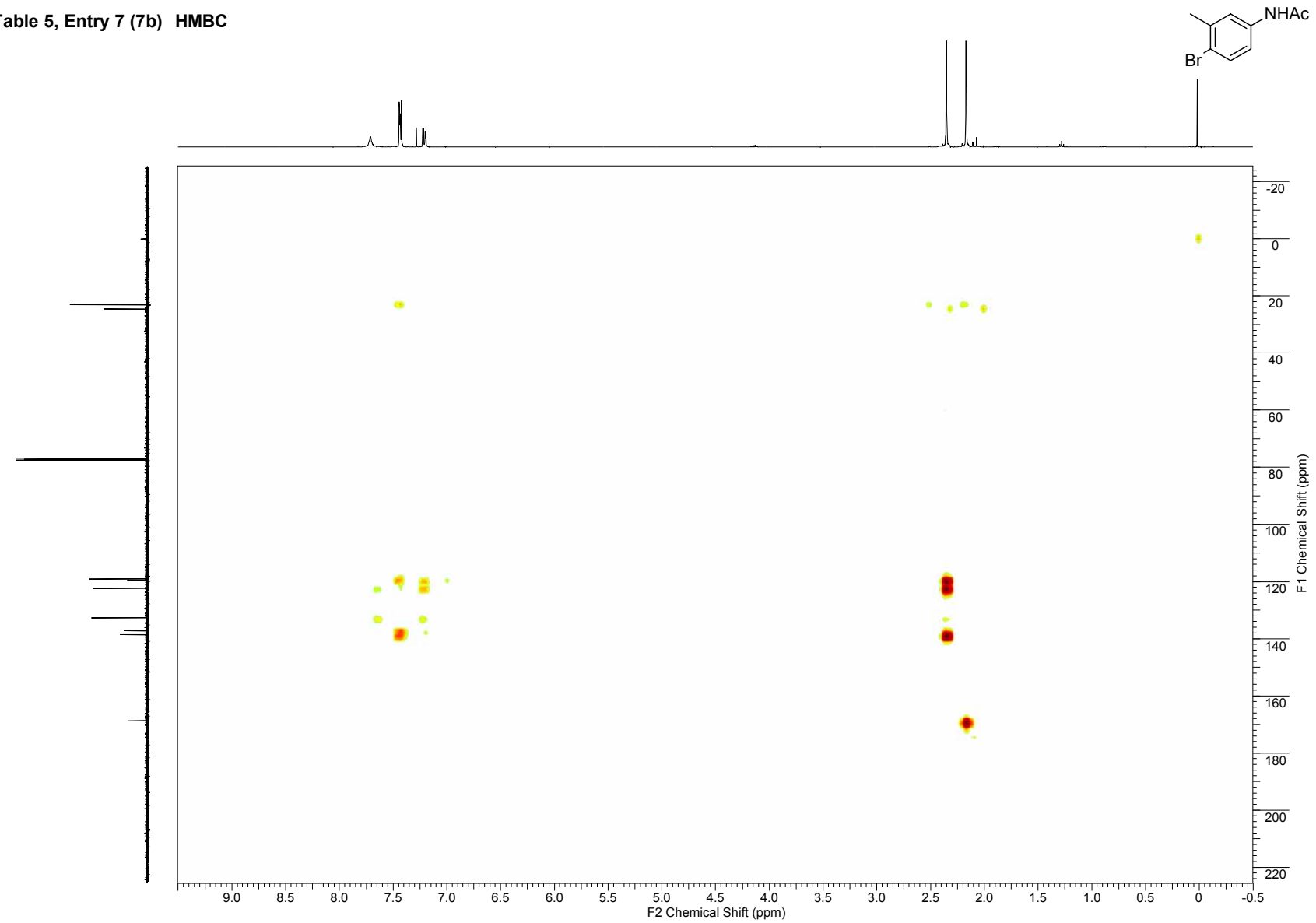
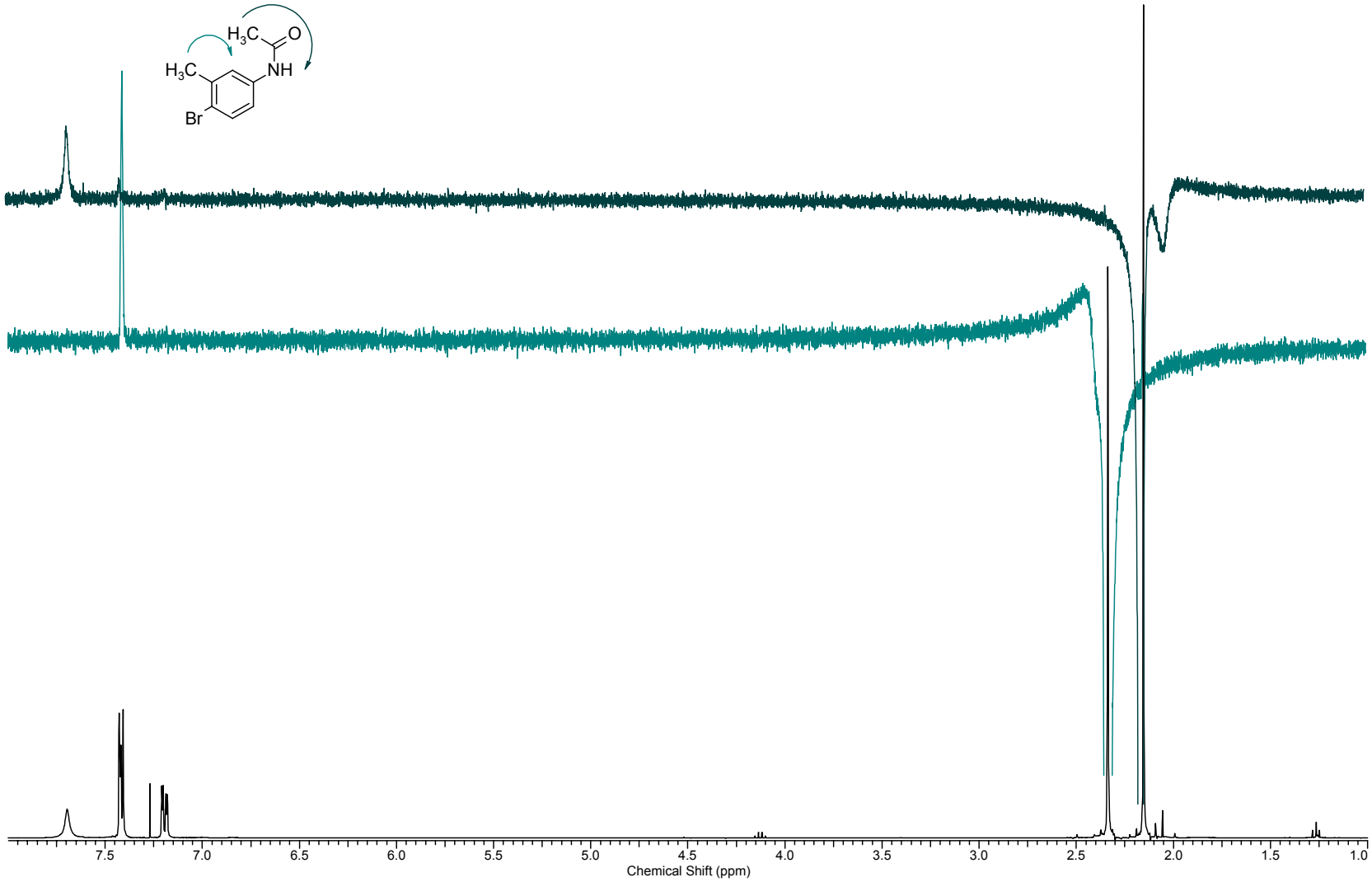
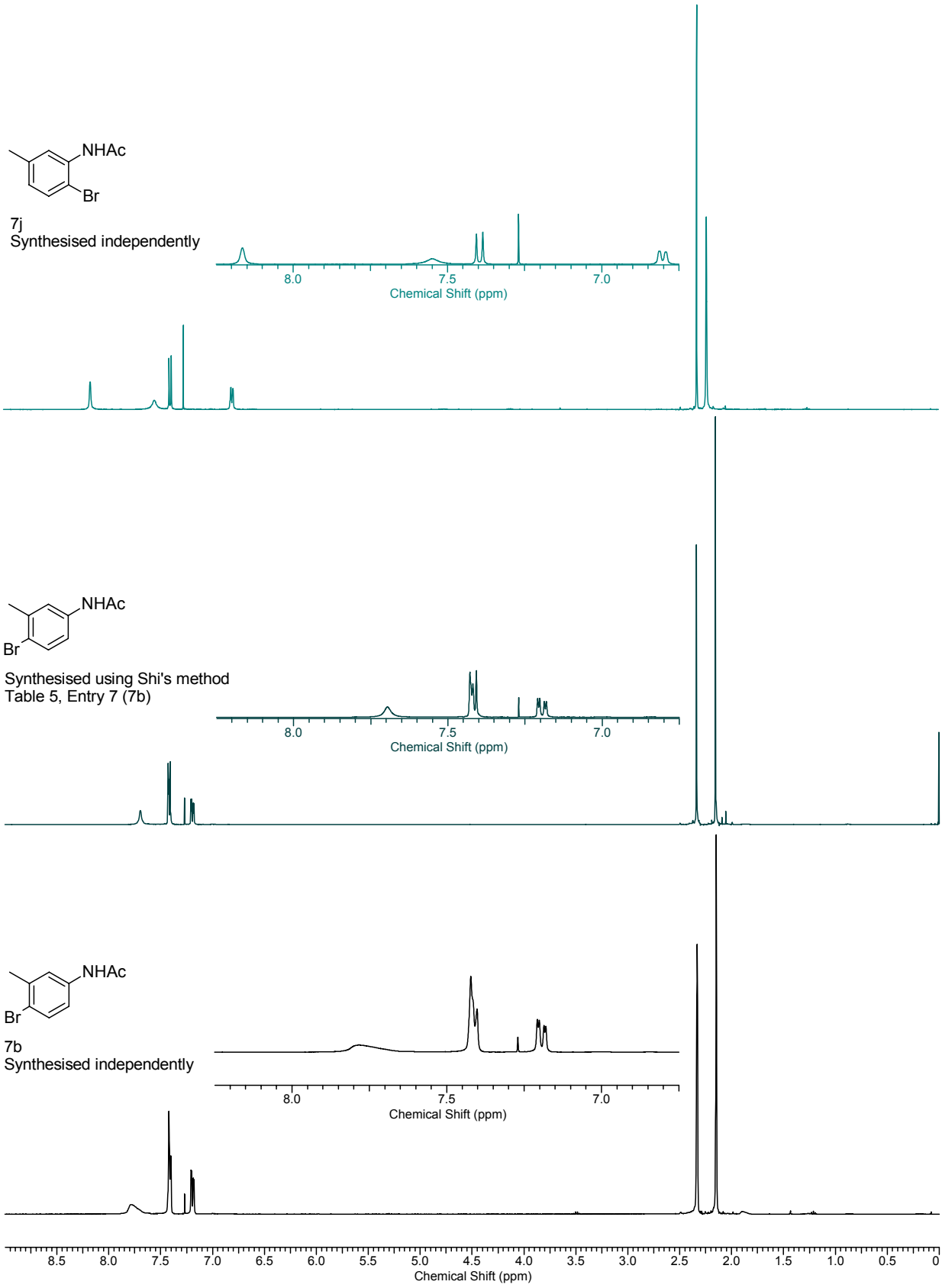
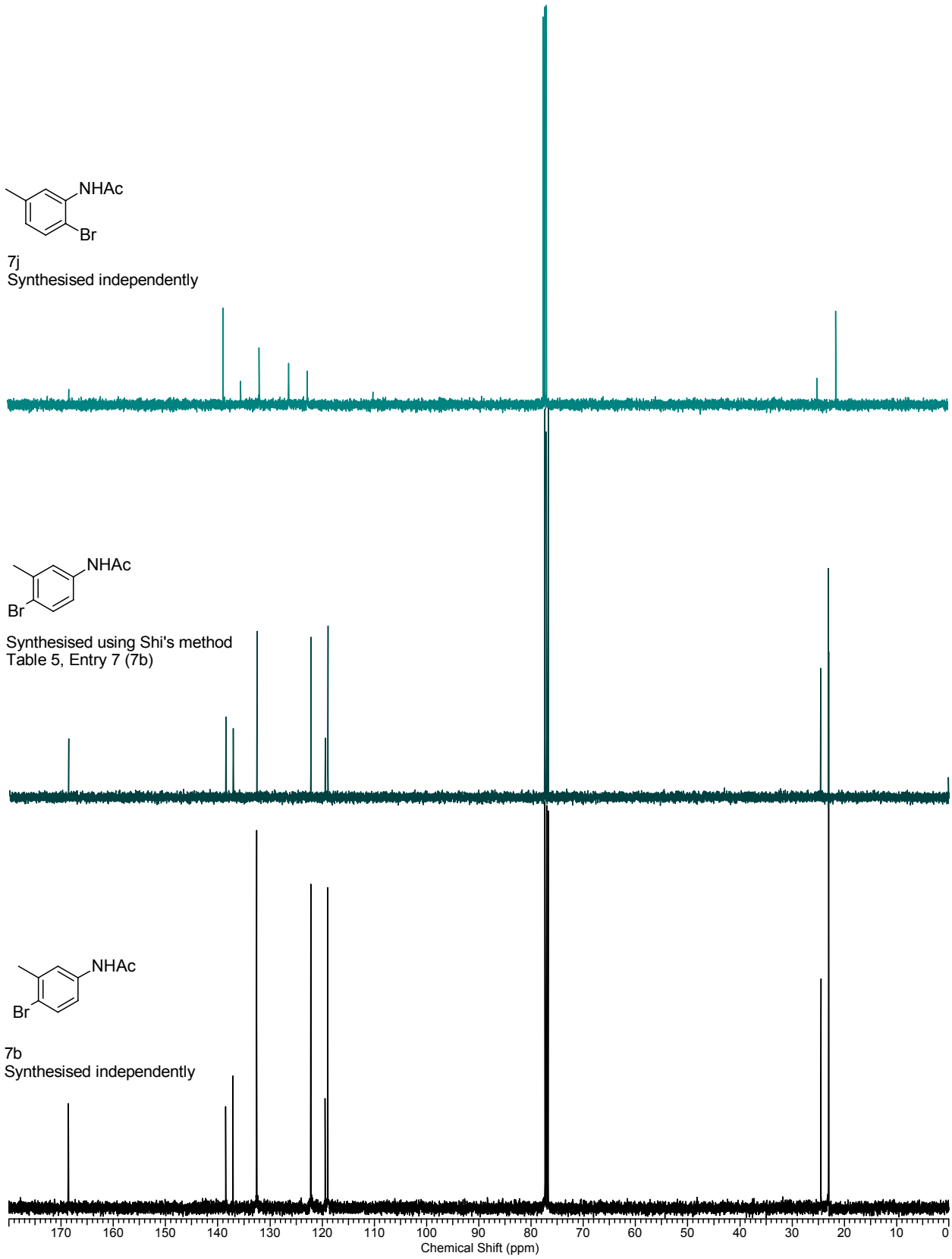
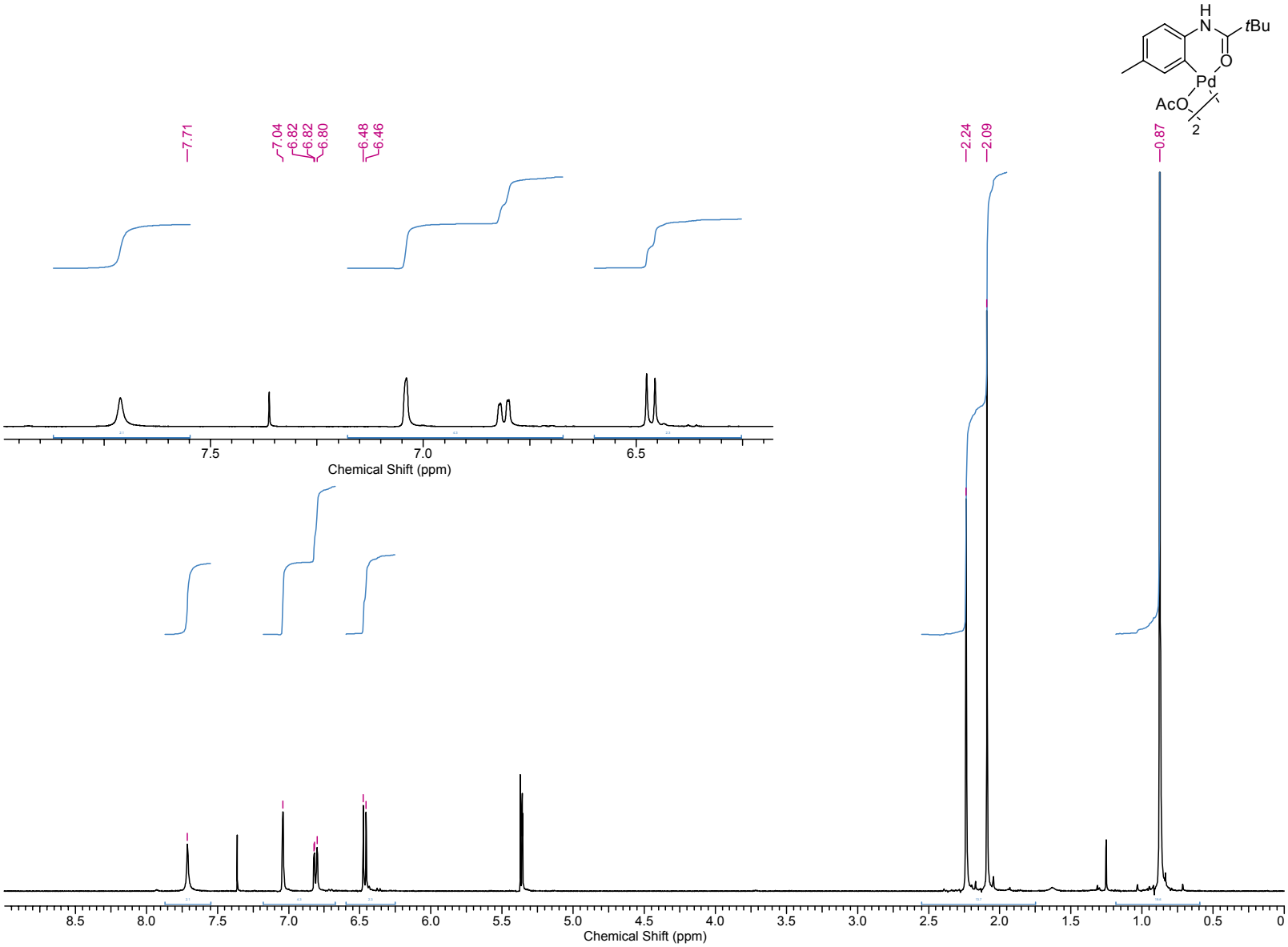


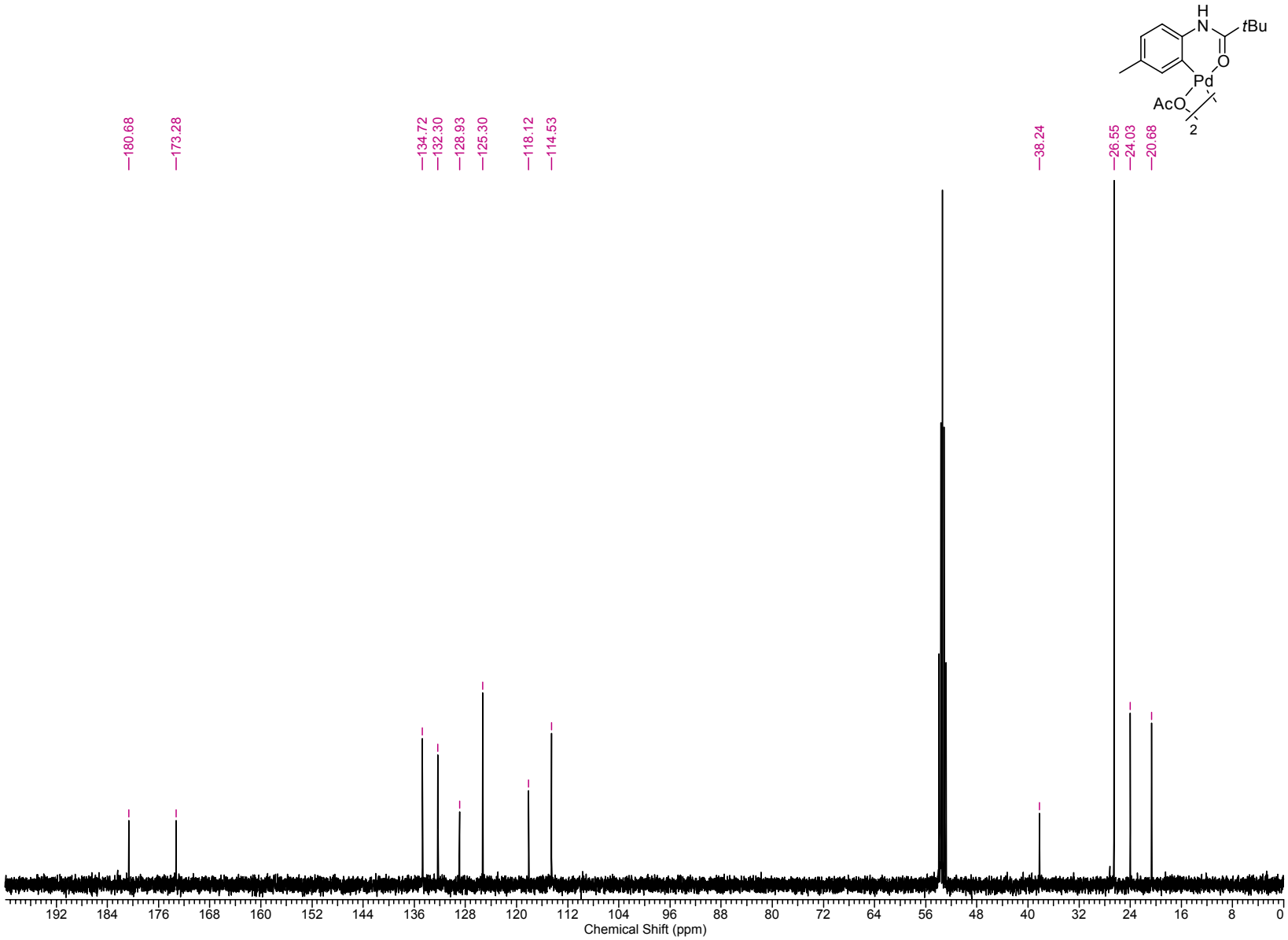
Table 5, Entry 7 (7b) NOE




NHAc
Br
7j
Synthesised independently
8.0
7.5
7.0
Chemical Shift (ppm)
NHAc
Br
Synthesised using Shi's method
Table 5, Entry 7 (7b)
8.0
7.5
7.0
Chemical Shift (ppm)
NHAc
Br
7b
Synthesised independently
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


NHAc
Br
7j
Synthesised independently
NHAc
Br
Synthesised using Shi's method
Table 5, Entry 7 (7b)
NHAc
Br
7b
Synthesised independently
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)


H
N
tBu
O
Pd
AcO
2
7.71
7.04
6.82
6.82
6.80
6.48
6.46
2.24
2.09
0.87
7.5
7.0
6.5
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


H
N
tBu
O
Pd
AcO
2
180.68
173.28
134.72
132.30
128.93
125.30
118.12
114.53
38.24
26.55
24.03
20.68
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

Sample spectra from kinetic studies (1 mmol anilide, 2 mmol $CuCl_2$ and $Cu(OAc)_2$, 5 mol% $Pd(OAc)_2$, 120 °C, solvent-free)