Supplementary Material (ESI) for Chemical Communications

Solvent-Free Catalytic C-H Functionalization

Robin B. Bedford, Charlotte J. Mitchell and Ruth L. Webster
School of Chemistry, University of Bristol, Cantock's Close, Bristol,UK
GlaxoSmithKline, Stevenage, SG1 2NY, UK

Electronic Supporting Information

Contents

General Experimental Conditions. All reagents were used as supplied, without further purification. Carbamates were prepared following literature methods[1] and their data compared with the known compounds.[2] Diaryl iodonium triflate reagents were prepared following literature methods.[3] Reactions were performed in Biotage microwave vials, heating in an oil bath at the stated temperature and 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).

General procedure for the attempted palladium-catalyzed *ortho*-arylation of carbamates on water. To a mortar was added carbamate (0.181 mmol), diaryliodonium triflate (0.362 mmol) and $Pd(OAc)_2$ (0.009 mmol). The reagents were ground with a pestle to form a homogenous powder. The reaction mixture was suspended in deionised water (2 ml) and heated for 18h at 80 °C. The reaction was monitored by TLC. No new species were observed to form during the course of the reaction.

Alternatively, to a mortar was added carbamate (0.181 mmol), 4-iodoanisole (0.724 mmol), AgOAc (0.362 mmol), PPh_3 (0.036 mmol) and $Pd(OAc)_2$ (0.018 mmol). The reagents were ground with a pestle to form a homogenous powder. The reaction mixture was suspended in deionised water (2 ml) and heated for 18h at 80 °C. The reaction was monitored by TLC. No new species were observed to form during the course of the reaction.

General procedure for the palladium-catalyzed *ortho*-arylation of carbamates (Table 1, entries 1 – 8). To a mortar was added carbamate (0.181 mmol), diaryliodonium triflate (0.362 mmol) and $Pd(OAc)_2$ (0.009 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was then transferred to a thick walled glass vial. The vessel was then heated at 120 °C for 4 hours, under an atmosphere of air without stirring. The vessel was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder (if a gum or oil formed during the reaction a small quantity of silica was added to form a powder), and added directly to the

top of a chromatography column. The product was purified by flash chromatography, eluting with ethyl acetate in hexanes.

For the preparation of **1f** and **2** (where the starting material was a liquid), the carbamate was added directly to a vial followed by a homogenous mixture of diaryliodonium triflate and $Pd(OAc)_2$ (prepared by the same procedure described above). The vessel was heated for 4 h at 120 °C under an atmosphere of air without stirring.

General procedure for the palladium-catalyzed *ortho*-arylation of anilides (Table 1, entries 9 – 17). To a mortar was added anilide (0.5 mmol), diaryliodonium triflate (1.0 mmol) and $Pd(OAc)_2$ (0.025 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 120 °C for 18 hours, under an atmosphere of air without stirring. The vessel was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder (if a gum or oil formed during the reaction a small quantity of silica was added to form a powder), and added directly to the top of a chromatography column. The product was purified by flash chromatography, eluting with a gradient of 0-50% ethylacetate in cyclohexane or with the specified ratio of ethylacetate in hexanes.

General procedure for the copper-mediated *meta*-arylation of anilides (Table 1, entries 18 – 24). To a mortar was added anilide (0.5 mmol), diaryliodonium triflate (1.0 mmol) and $Pd(OAc)_2$ (0.05 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 100 °C for 18 hours, under an atmosphere of air without stirring. The vessel was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder (if a gum or oil formed during the reaction a small quantity of silica was added to form a powder), and added directly to the top of a chromatography column. The reaction was purified by flash chromatography, eluting with a

gradient of 0-50% ethylacetate in cyclohexane or with the specified ratio of ethylacetate in hexanes.

General procedure for the halogenations of pyridines and pyrrolidinones using NXS (Table 2, entries 1 – 3). To a mortar was added pyrrolidinone (1 mmol), NXS (X = Br or Cl)(1.2 mmol) and $Pd(OAc)_2$ (0.05 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 120 °C for the appropriate length of time, under an atmosphere of air without stirring. The vial was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder (if a gum or oil formed during the reaction a small quantity of silica was added to form a powder), and added directly to the top of a chromatography column. The reaction was purified by flash chromatography, eluting with a gradient of 0-50% ethylacetate in cyclohexane.

For the preparation of **6a** and **6b** (where the starting material was a liquid), the aryl species was added directly to a vial followed by a homogenous mixture of NXS and $Pd(OAc)_2$ (prepared by the same procedure described above). The vessel was heated for 2 h at 120 °C under an atmosphere of air without stirring.

General procedure for the preparation of 2-chloroarenes using $CuCl_2$ (Table 2, entries 4 – 7). To a mortar was added anilide (1 mmol), copper (II) acetate (363 mg, 2 mmol), copper (II) chloride (266 mg, 2 mmol) and $Pd(OAc)_2$ (0.05 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 120 °C for the appropriate length of time, under an atmosphere of air without stirring. The vial was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder, and added to the top of a chromatography column directly. The reaction was purified by flash chromatography, eluting with a gradient of 0-50% ethylacetate in cyclohexane.

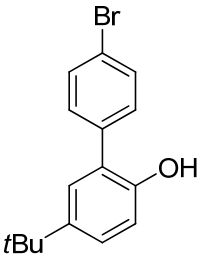
General procedure for the preparation of bromoanilides using $CuBr_2$ (Table 2, entries 8 – 10). To a mortar was added anilide (1 mmol), copper (II) acetate (363 mg, 2 mmol) and

copper (II) bromide (447 mg, 2 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 120 °C for the appropriate length of time, under an atmosphere of air without stirring. The vial was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder, and added to the top of a chromatography column directly. The reaction was purified by flash chromatography, eluting with a gradient of 0-50% ethylacetate in cyclohexane.

Large scale synthesis of *N*-(2-bromo-4-tolyl)acetamide, 11 (Table 2, Entry 8). *N*-(4-tolyl)acetamide (0.89 mmol), copper (II) acetate (1.78 mmol) and copper (II) bromide (1.78 mmol) were ground with a pestle and mortar (2 – 3 mins) until homogenous. The mixture was transferred to 250 ml beaker and heated at 120 °C for 18 hours, without stirring. The reaction mixture was allowed to cool to room temperature, added to the top of a pad of Celite on a sintered funnel and the product extracted through the celite with acetonitrile until the eluent was colourless. The solvent was removed from the filtrate and the resulting solid triturated under diethyl ether (~100 ml) and this process repeated four times to give microanalytical pure **11** as an off-white solid (78%).

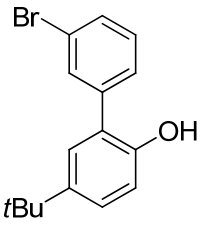
General procedure for the sequential bromination/ Suzuki-coupling reaction. To a mortar were added anilide (1 mmol), copper acetate (363 mg, 2 mmol) and copper bromide (447 mg, 2 mmol). The reagents were ground with a pestle to form a homogenous powder (30 – 60s). The reaction mixture was transferred to a thick walled glass vial. The vessel was then heated at 120 °C for 1 hour, under an atmosphere of air without stirring. The reaction mixture was transferred to a mortar, K_3PO_4 (425 mg, 2 mmol), $Pd(OAc)_2$ (4.5 mg, 2 mol%) and aryl boronic acid (1.4 mmol) were added, and the mixture ground to form a fine, free-flowing homogenous powder. The mixture was returned to the vial, where it was heated at 120 °C, under air without stirring for a further 3 hours. The vial was then allowed to cool to room temperature, mixed with a spatula to form a free-flowing homogenous powder, and added to the top of a chromatography column directly. The reaction was purified by flash chromatography, eluting with a gradient of 0-50% ethylacetate in cyclohexane.

Table 1, Entry 1 (1a)



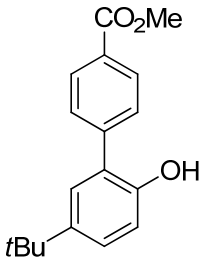
White solid, 32 mg (59%); R*f* 0.38 (EtOAc/hexanes, 1:9); ^{1}H NMR (300 MHz; $CDCl_3$) δ 7.56 (app. dt, *J* 8.4, 1.8 Hz, 2H), 7.41 (dd, *J* 8.5, 2.6 Hz, 1H), 7.37 (d, *J* 2.6 Hz, 1H), 7.32 (app. dt, *J* 8.5, 1.9 Hz, 2H), 7.07 (d, *J* 8.4 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 149.5, 145.4, 137.2, 133.0, 131.6, 130.7, 129.3, 127.7, 126.1, 122.4, 34.7, 31.5; IR neat, ν (cm^{-1}) 2966 (s), 2867 (w), 1584 (w), 1501 (m), 1479 (s), 1371 (s), 1196 (s); m.p. 96.2-97.0 °C; MS (EI) m/z 289.1 (100%), 291.1 (100 %), 304.2 (55%), 306.2 (100%); Anal. Calcd. for $C_{16}H_{17}BrO$: C, 63.0; H, 5.6. Found: C, 63.4; H, 5.4.

Table 1, Entry 2 (1b)



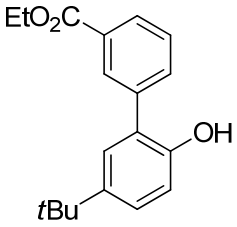
White solid, 35 mg (63%); R*f* 0.38 (EtOAc/hexanes, 1:9); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.62 (t, *J* 1.7 Hz, 1H), 7.51 (dt, *J* 7.7, 1.7 Hz, 1H), 7.44 (dd, *J* 8.4, 2.4 Hz, 1H), 7.40-7.37 (m, 2H), 7.32 (d, *J* 7.7 Hz, 1H), 7.09 (d, *J* 8.5 Hz, 1H), 1.38 (9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 149.5, 145.4, 140.3, 132.6, 132.0, 130.5, 130.0, 127.7, 126.3, 122.4, 34.7, 31.5; IR neat, ν (cm^{-1}) 2963 (s), 1594 (w), 1560 (m), 1472 (br), 1366 (s), 1188 (s); m.p. 85.0-86.7 °C; MS (EI) m/z 289.1 (100%), 291.1 (100%), 304.2 (58%), 306.2 (58%); Anal. Calcd. for $C_{16}H_{17}BrO$: C, 63.0; H, 5.6. Found: C, 63.1; H, 5.9.

Table 1, Entry 3 (1c)



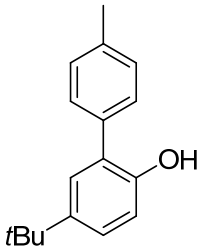
White solid, 31 mg (60 %); R*f* 0.25 (EtOAc/hexanes, 3:17); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.14 (app. dt, *J* 8.3, 1.8 Hz, 2H), 7.60 (app. dt, *J* 8.3, 1.8 Hz, 2H), 7.31 (dd, *J* 8.6, 2.4 Hz, 1H), 7.26 (d, *J* 2.4 Hz, 1H), 6.91 (d, *J* 8.3 Hz, 1H), 3.95 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 169.6, 149.5, 143.1, 129.7, 129.1, 127.8, 126.5, 122.4, 52.3, 34.7, 31.5; IR neat, ν (cm^{-1}) 3676 (w), 2962 (m), 1713 (s), 1607 (m), 1491 (m), 1441 (m), 1364 (m); m.p. 101.2-102.9 °C; HRMS (ESI) calcd for $C_{18}H_{19}O_3$ $(M-H)^-$ 283.1340, found 283.1342; Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.0; H, 7.1. Found: C, 77.1; H, 7.2.

Table 1, Entry 4 (1d)



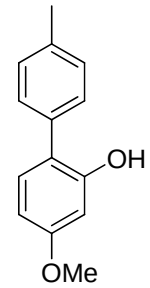
White gum, 28 mg (51%); R*f* 0.08 (EtOAc/hexanes, 1:9); ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.18 (t, *J* 1.7 Hz, 1H), 8.07 (dt, *J* 7.7, 1.7 Hz, 1H), 7.69 (dt, *J* 7.7, 1.6 Hz, 1H), 7.55 (t, *J* 7.7 Hz, 1H), 7.30 (dd, *J* 8.5, 2.4 Hz, 1H), 7.25 (d, *J* 2.5 Hz, 1H), 6.92 (d, *J* 8.4 Hz, 1H), 4.40 (quartet, *J* 7.2 Hz, 2H), 1.40 (t, *J* 7.2 Hz, 3H), 1.32 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 169.5, 166.4, 149.3, 145.4, 138.4, 133.3, 132.9, 130.0, 128.5, 128.3, 127.7, 126.0, 122.3, 61.1, 34.6, 31.4, 14.3; IR neat, ν (cm^{-1}) 2964 (m), 2906 (w), 1717 (s), 1587 (w), 1477 (w), 1366 (s), 1189 (s); HRMS (EI) calcd for $C_{19}H_{22}O_3$ $(M)^+$ 298.1569, found 298.1563.

Table 1, Entry 5 (1e)



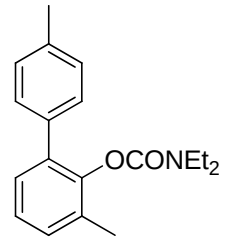
White solid, 29 mg (66 %); R*f* 0.27 (EtOAc/cyclohexane, 16:23); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.37 (d, *J* 8.1 Hz, 2H), 7.31-7.22 (m, 4H), 6.91 (d, *J* 8.6 Hz, 1H), 2.41 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 161.5, 150.1, 143.4, 137.5, 134.6, 129.9, 129.0, 127.1, 125.8, 115.2, 34.1, 31.5, 21.2; IR neat, ν (cm^{-1}) 3075, 2963, 2839, 1591, 1459, 1195, 1148, 1063; m.p. 54.6- 56.0 °C; MS (EI) m/z 241.2 (100%); Anal. Calcd. for $C_{17}H_{20}N$: C, 85.0; H, 8.4; N. Found: C, 84.7; H, 8.4.

Table 1, Entry 6 (1g)



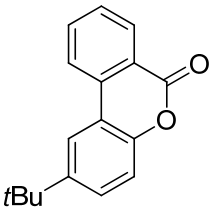
White solid, 15 mg (38 %); R*f* 0.21 (EtOAc/hexanes, 3:17); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.33-7.27 (m, 4H), 7.13 (d, *J* 8.8 Hz, 1H), 6.57-6.54 (m, 2H), 3.82 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 160.4, 153.4, 137.3, 133.8, 130.7, 130.0, 128.9, 120.7, 106.9, 101.1, 55.6, 21.2; IR neat, ν (cm^{-1}) 3402, 2921, 1693, 1617, 1496, 1441, 1203, 1043; MS (EI) m/z 215.1 (100%); Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.5; H, 6.6. Found: C, 78.4; H, 6.9.

Table 1, Entry 7 (2)



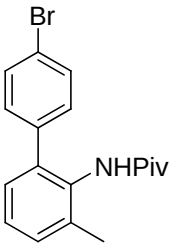
White solid, 27 mg (50 %); R*f* 0.17 (EtOAc/cyclohexane, 1:9); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.30 (d, *J* 8.0 Hz, 2H), 7.20-7.14 (m, 5H), 3.25 (q, *J* 6.9 Hz, 4H), 2.36 (s, 3H), 2.25 (s, 3H), 1.05-1.00 (m, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 153.5, 147.2, 136.6, 135.5, 131.6, 129.9, 128.9, 128.6, 128.3, 125.4, 125.3, 42.0, 41.6, 21.1, 16.6, 14.0, 13.1; IR neat, ν (cm^{-1}) 2973, 2875, 1713, 1415, 1190, 1154; HRMS (ESI) calcd for $C_{19}H_{24}NO_2$ $(M+H)^+$ 298.1802, found 298.1812; Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.7; H, 7.8; N, 4.7. Found: C, 76.6; H, 8.1; N, 4.6.

Table 1, Entry 8 (3)



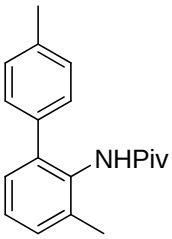
White solid, 26 mg (58 %); R*f* 0.08 (EtOAc/hexanes, 1:9); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.42 (dd, *J* 8.1, 1.5 Hz, 1H), 8.19 (d, *J* 8.1 Hz, 1H), 8.07 (d, 2.2 Hz, 1H), 7.85 (td, *J* 8.2, 1.5 Hz, 1H), 7.59 (td, *J* 8.2, 1.5 Hz, 1H), 7.55 (dd, *J* 8.6, 2.2 Hz, 1H), 7.33 (d, *J* 8.6 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 161.7, 149.4, 147.6, 135.3, 134.8, 130.8, 128.8, 128.2, 121.7, 121.4, 119.0, 117.5, 117.3, 34.9, 31.6; IR neat, ν (cm^{-1}) 3669 (w), 2961 (m), 2902 (m), 2838 (w), 1729 (s), 1594 (s), 1478 (m), 1459 (m), 1410 (m), 1204 (s); m.p. 106.9-107.4°C; HRMS (CI) calcd for $C_{17}H_{17}O_2$ $(M+H)^+$ 253.1229, found 253.1231; Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.4. Found: C, 80.8; H, 6.4.

Table 1, Entry 9 (4a)



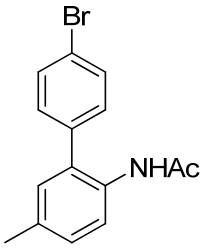
White solid, 44 mg (70 %); R*f* 0.69 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.54 (app. dt, *J* 8.3, 1.8 Hz, 2H), 7.29-7.25 (m, 2H), 7.21 (app. dt, *J* 8.3, 1.8 Hz, 2H), 7.16 (dd, *J* 6.6, 2.6 Hz, 1H), 6.79 (br. s, 1H), 2.28 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.8, 138.7, 136.8, 132.6, 131.3, 130.7, 130.4, 127.6, 127.3, 121.6, 119.6, 39.1, 27.6, 18.4 ; IR neat, ν (cm^{-1}) 3267, 2954, 2870, 1727, 1648, 1509, 1459, 1272, 1009; m.p. 223.6- 224.1 °C; HRMS (ESI) calcd for $C_{18}H_{21}BrNO$ $(M+H)^+$ 346.0807, found 346.0806; Anal. Calcd. for $C_{18}H_{20}BrNO$: C, 62.4; H, 5.8; N, 4.1. Found: C, 62.5; H, 5.8; N, 4.1.

Table 1, Entry 10 (4b)



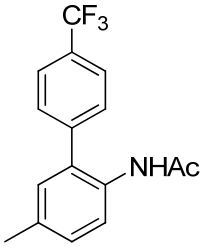
White solid, 107 mg (76 %); R*f* 0.32 (EtOAc/hexanes, 1:4); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.24-7.14 (m, 7H), 7.80 (br. s, 1H), 2.39 (s, 3H), 2.27 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.6, 139.3, 137.0, 136.6, 136.5, 132.9, 129.8, 128.9, 128.8, 127.7, 126.9, 39.1, 27.5, 21.2, 18.5; IR neat, ν (cm^{-1}) 3296, 2963, 1643, 1505, 1221, 1175; m.p. 183.7- 184.4 °C; HRMS (ESI) calcd for $C_{19}H_{23}NNaO$ $(M+Na)^+$ 304.1672, found 304.1679.

Table 1, Entry 11 (4c)



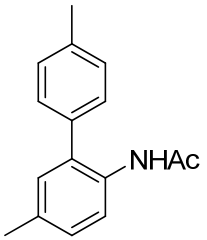
White solid, 33 mg (61 %); R*f* 0.39 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.01 (d, *J* 8.3, 1H), 7.61 (d, *J* 8.3 Hz, 2H), 7.25 (d, *J* 8.3 Hz, 2H), 7.20 (dd, *J* 8.3, 1.5 Hz, 1H), 7.04 (s, 1H), 6.91 (br. s, 1H), 2.35 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.7, 137.7, 134.5, 132.4, 132.2, 131.2, 130.8, 129.6, 123.1, 122.4, 119.9, 24.8, 21.2; IR neat, ν (cm^{-1}) 3256, 2919, 1640, 1520, 1369, 1283, 1008; m.p. 122.2- 123.7 °C; HRMS (ESI) calcd for $C_{15}H_{15}BrNO$ $(M+H)^+$ 304.0337, found 304.0331; Anal. Calcd. for $C_{15}H_{14}BrNO$: C, 59.2; H, 4.6; N, 4.6. Found: C, 59.1; H, 4.9; N, 4.6.

Table 1, Entry 12 (4d)



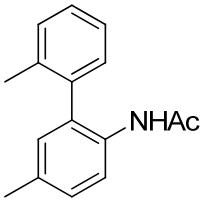
White solid, 70 mg (48 %); R*f* 0.28 (EtOAc/hexanes, 9:11); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.97 (d, *J* 8.3 Hz, 1H), 7.72 (d, *J* 8.0 Hz, 2H), 7.49 (d, *J* 8.0 Hz, 2H), 7.22 (dd, *J* 8.3, 1.2 Hz, 1H) 7.06 (s, 1H), 6.87 (br. s, 1H), 2.36 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.4, 142.3, 134.9, 131.9, 131.8, 130.5, 130.1, 129.7, 129.6, 125.8, 123.3, 24.3, 20.9; IR neat, ν (cm^{-1}) 3224, 3030, 1658, 1524, 1323, 1156, 1108, 1067; m.p. 129.0- 129.4 °C; HRMS (ESI) calcd for $C_{16}H_{14}F_3NNaO$ $(M+H)^+$ 316.0920, found 316.0926.

Table 1, Entry 13 (4e)



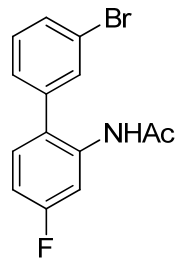
White solid, 72 mg (60 %); R*f* 0.32 (EtOAc/cyclohexane, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.09 (d, *J* 8.2 Hz, 1H), 7.29-7.22 (m, 4H), 7.15 (dd, *J* 8.2, 2.0 Hz, 1H), 7.07 (br. s, 1H), 7.04 (s, 1H), 2.41 (s, 3H), 2.33 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 137.6, 135.3, 134.0, 132.2, 130.6, 129.7, 129.2, 129.0, 128.7, 121.8, 24.5, 21.2, 20.9; IR neat, ν (cm^{-1}) 3255, 3024, 1660, 1510, 1368, 1293; HRMS (ESI) calcd for $C_{16}H_{18}NO$ $(M+H)^+$ 240.1383, found 240.1392; Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.3; H, 7.2; N, 5.9. Found: C, 80.0; H, 6.9; N, 6.1.

Table 1, Entry 14 (4f)



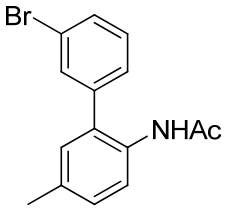
White solid, 43 mg (36 %); R*f* 0.42 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.10 (d, *J* 8.3 Hz, 1H), 7.36 (t, *J* 7.4 Hz, 1H), 7.23-7.16 (m, 4H), 7.11 (br. s, 1H), 7.06 (s, 1H), 2.42 (s, 3H), 2.35 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.1, 138.8, 133.9, 132.1, 130.5, 129.9, 128.7, 128.5, 126.1, 121.8, 24.4, 21.4, 20.8; IR neat, ν (cm^{-1}) 3339, 2921, 1667, 1595, 1516, 1367, 1293, 1241; m.p. 118.9- 120.0 °C; HRMS (EI) calcd for $C_{16}H_{18}NO$ $(M+H)^+$ 240.1388, found 240.1381; Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.3; H, 7.2; N, 5.9. Found: C, 80.3; H, 7.4; N, 5.8.

Table 1, Entry 15 (4g)



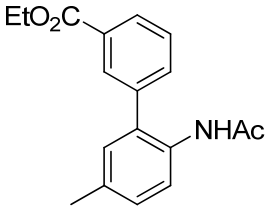
White solid, 60 mg (39 %); R*f* 0.41 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.14 (d, *J* 10.2 Hz, 1H), 7.58 (app. dq, *J* 8.0, 1.0Hz, 1H), 7.52 (t, *J* 1.5 Hz, 1H), 7.37 (t, *J* 8.0 Hz, 1H), 7.29 (dt, *J* 8.0, 1.5 Hz, 1H), 7.17 (dd, *J* 8.3, 6.1 Hz, 1H), 7.09 (br. s, 1H), 6.89 (dt, *J* 8.3, 2.7 Hz, 1H), 2.06 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 163.8 (d, *J* 246 Hz), 139.4, 136.1 (d, *J* 12 Hz), 132.4, 131.3, 131.0 (d, *J* 9 Hz), 130.7, 129.1, 127.9, 123.3, 111.2 (d, *J* 22 Hz), 108.9 (d, *J* 28 Hz), 24.7; IR neat, ν (cm^{-1}) 3260, 1692, 1667, 1596, 1523, 1428, 1238; HRMS (ESI) calcd for $C_{14}H_{12}BrFNO$ $(M+H)^+$ 308.0080, found 308.0089; Anal. Calcd. for $C_{14}H_{11}BrFNO$: C, 54.5; H, 3.6; N, 4.6. Found: C, 54.5; H, 3.7; N, 4.6.

Table 1, Entry 16 (4h)



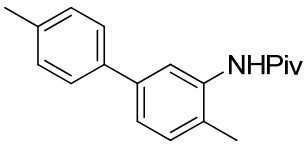
White solid, 114 mg (75 %); R*f* 0.37 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.49-7.44 (m, 3H), 7.31-7.21 (br. m, 4H), 7.18 (br. s, 2H), 2.22 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.6, 143.8, 141.2, 136.0, 132.4, 131.7, 131.3, 130.3, 130.0, 128.1, 122.5, 121.4, 119.8, 24.9, 20.1; IR neat, ν (cm^{-1}) 3286, 2918, 1656, 1614, 1593, 1551, 1469, 1376, 1319, 1259, 1042; m.p. 157.6- 158.1 °C; HRMS (ESI) calcd for $C_{15}H_{15}BrNO$ $(M+H)^+$ 304.0337, found 304.0330; Anal. Calcd. for $C_{15}H_{14}BrNO$: C, 59.2; H, 4.6; N, 4.6. Found: C, 59.2; H, 4.7; N, 4.6.

Table 1, Entry 17 (4i)



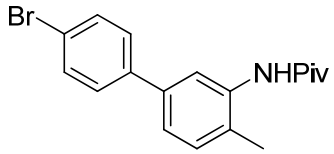
White solid, 22 mg (41 %); R*f* 0.26 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.11-8.08 (m, 1H), 8.06 (s, 1H), 8.02 (d, *J* 8.3 Hz, 1H), 7.57-7.55 (m, 2H), 7.22 (dd, *J* 8.3, 1.2 Hz, 1H), 7.09 (s, 1H), 6.91 (br. s, 1H), 4.41 (q, *J* 7.1 Hz, 2H), 2.37 (s, 3H), 2.02 (s, 3H), 1.41 (t, *J* 7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.3, 166.6, 141.6, 141.4, 135.7, 133.5, 131.4, 131.0, 130.4, 130.1, 128.2, 121.2, 119.4, 61.1, 24.6, 19.8, 14.4; IR neat, ν (cm^{-1}) 3290, 2982, 1716, 1659, 1596, 1551, 1276, 1231, 1106; m.p. 139.2- 139.4 °C; HRMS (ESI) calcd for $C_{18}H_{20}NO_3$ $(M+H)^+$ 298.1443, found 298.1440.

Table 1, Entry 18 (5a)



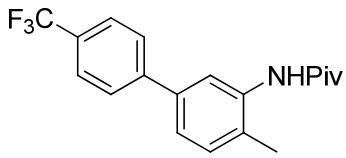
White solid, 128 mg (91 %); R*f* 0.39 (EtOAc/hexanes, 1:4); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.19 (d, *J* 2.0 Hz, 1H), 7.53 (app. dt, *J* 8.1, 2.0 Hz, 2H), 7.32 (br. s, 1H), 7.32 (dd, *J* 7.9, 2.2 Hz, 1H), 7.25-7.20 (m, 3H), 2.39 (s, 3H), 2.30 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.7, 140.0, 137.9, 137.0, 136.3, 130.8, 129.5, 127.0, 125.0, 123.4, 121.3, 40.0, 27.9, 21.2, 17.4; IR neat, ν (cm^{-1}) 3305, 2965, 1650, 1495, 1288, 1168; m.p. 163.4- 164.1 °C; MS (ESI) m/z 282.2 (100%), 304.2 (80%); Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.1; H, 8.2; N, 5.0. Found: C, 80.8; H, 8.2; N, 5.1.

Table 1, Entry 19 (5b)



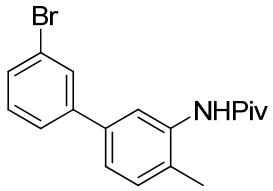
White solid, 53 mg (85 %); R*f* 0.71 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.14 (d, *J* 1.5 Hz, 1H), 7.51 (app. dt, *J* 6.8, 2.0 Hz, 2H), 7.46 (dd, *J* 6.8, 2.0 Hz, 2H), 7.35 (br. s, 1H), 7.25-7.22 (m, 2H), 2.29 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.9, 139.5, 138.7, 136.2, 132.2, 131.7, 130.9, 128.6, 128.0, 123.3, 121.2, 39.9, 27.7, 17.3; IR neat, ν (cm^{-1}) 3310, 2922, 1650, 1478, 1380, 1072, 1008, 806; HRMS (ESI) calcd for $C_{18}H_{21}BrNO$ $(M+H)^+$ 346.0807, found 346.0809; Anal. Calcd. for $C_{19}H_{23}BrNO$: C, 62.4; H, 5.8; N, 4.1. Found: C, 62.4; H, 5.8; N, 4.1.

Table 1, Entry 20 (5c)



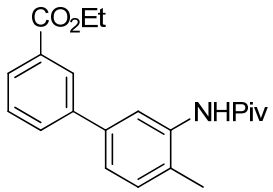
Gum that solidified slowly, 101 mg (57 %); R*f* 0.48 (EtOAc/hexanes, 1:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.24 (d, *J* 2.0 Hz, 1H), 7.84 (dd, *J* 8.1, 1.0 Hz, 1H), 7.72 (d, *J* 8.1 Hz, 1H), 7.65 (d, *J* 8.1 Hz, 1H), 7.40 (br. s, 1H), 7.28 (d, *J* 8.1 Hz, 1H), 2.31 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.7, 144.2, 138.4, 136.5, 135.9, 130.9 (d, *J* 59 Hz), 128.7 (d, *J* 42 Hz), 127.3, 125.6 (q, *J* 4 Hz), 124.9, 123.3 (d, *J* 51 Hz), 121.3, 39.9, 27.7, 17.3; IR neat, ν (cm^{-1}) 3295, 2965, 1651, 1510, 1489, 1324, 1123, 1071; HRMS (ESI) calcd for $C_{19}H_{20}F_3NNaO$ $(M+Na)^+$ 358.1389, found 358.1390.

Table 1, Entry 21 (5d)



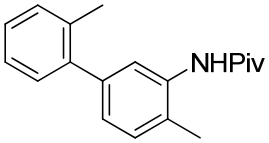
White solid, 46 mg (73 %); R*f* 0.73 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; DMSO) δ 8.98 (s, 1H), 7.80 (t, *J* 1.8 Hz, 1H), 7.64 (d, *J* 7.9 Hz, 1H), 7.55 (app. dt, *J* 7.8, 1.0 Hz, 1H), 7.50 (d, *J* 1.8 Hz, 1H), 7.46 (dd, *J* 7.9, 1.8 Hz, 1H), 7.41 (t, *J* 7.8 Hz, 1H), 7.32 (d, *J* 7.8 Hz, 1H), 2.19 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.9, 142.8, 138.5, 136.3, 130.9, 130.21, 130.17, 130.0, 128.4, 125.8, 123.6, 122.8, 121.5, 39.9, 27.8, 17.4; IR neat, ν (cm^{-1}) 3338, 2960, 2865, 1651, 1556, 1523, 1469, 1387, 1194; m.p. 92.1- 93.5 °C; HRMS (ESI) calcd for $C_{18}H_{21}BrNO$ $(M+H)^+$ 346.0807, found 346.0802.

Table 1, Entry 22 (5e)



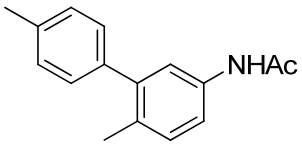
White solid, 36 mg (59 %); R*f* 0.48 (EtOAc/hexanes, 3:7); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.25 (t, *J* 1.2 Hz, 1H), 8.14 (d, *J* 1.8 Hz, 1H), 7.99 (dt, *J* 7.8, 1.2, 1H), 7.79 (dt, *J* 7.8, 1.2 Hz, 1H), 7.46 (t, *J* 7.8 Hz, 1H), 7.37 (br. s, 2H), 7.33 (dd, *J* 7.8, 1.8 Hz, 1H), 7.25 (d, *J* 7.8 Hz, 1H), 4.40 (q, *J* 7.1 Hz, 2H), 2.28 (s, 3H), 1.40 (t, *J* 7.1 Hz, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.7, 166.6, 141.0, 138.9, 136.3, 131.6, 130.87, 130.85, 128.7, 128.5, 128.2, 128.0, 123.6, 121.6, 61.0, 39.8, 27.7, 17.4, 14.4; IR neat, ν (cm^{-1}) 3294, 2963, 1717, 1651, 1479, 1450, 1251, 1107; HRMS (ESI) calcd for $C_{21}H_{25}NNaO_3$ $(M+Na)^+$ 362.1727, found 362.1729; Anal. Calcd. for $C_{21}H_{25}NO_3$: C, 74.3; H, 7.4; N, 4.1. Found: C, 73.9; H, 7.6; N, 4.4.

Table 1, Entry 23 (5f)



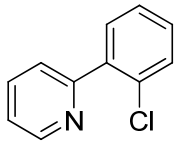
White solid, 66 mg (47 %); R*f* 0.39 (EtOAc/hexanes, 1:4); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.87 (d, *J* 1.8 Hz, 1H), 7.25-7.20 (m, 6H), 7.06 (dd, *J* 7.8, 1.8 Hz, 1H), 2.31 (s, 3H), 2.31 (s, 3H) 1.36 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.1, 141.5, 140.8, 139.5, 135.9, 135.5, 130.4, 130.2, 130.0, 127.3, 125.8, 124.0, 39.9, 27.9, 20.7, 17.5; IR neat, ν (cm^{-1}) 3307, 2961, 1649, 1481, 1400, 1270, 1120; m.p. 114.8- 116.1 °C; MS (ESI) m/z 282.2 (100%), 304.2 (70%); Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.1; H, 8.2; N, 5.0. Found: C, 81.1; H, 8.3; N, 5.1.

Table 1, Entry 24 (5g)



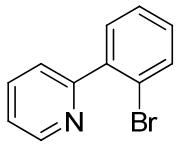
White solid, 45 mg (38 %); R*f* 0.21 (EtOAc/hexanes, 2:3); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.49 (dd, *J* 8.0, 2.4 Hz, 1H), 7.36 (br. s, 1H), 7.28 (d, *J* 2.4 Hz, 1H), 7.25-7.20 (m, 5H), 2.42 (s, 3H), 2.25 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.5, 142.5, 138.6, 136.7, 135.7, 131.6, 130.9, 129.1, 128.9, 121.5, 119.1, 24.6, 21.3, 20.0; IR neat, ν (cm^{-1}) 3292, 2919, 1660, 1612, 1542, 1493, 1367, 1315, 1013; HRMS (ESI) calcd for $C_{16}H_{18}NO$ $(M+H)^+$ 1240.1383, found 240.1394; Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.3; H, 7.2; N, 5.9. Found: C, 80.2; H, 7.5; N, 6.0.

Table 2, Entry 1 (6a)



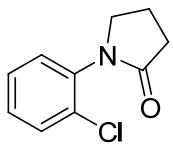
Colourless oil, 66 mg (35 %); R*f* 0.09 (EtOAc/cyclohexane, 1:4); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.73 (d, *J* 4.8 Hz, 1H), 7.77 (td, *J* 7.8, 1.7 Hz, 1H), 7.65 (d, *J* 8.0 Hz, 1H), 7.60 (dd, *J* 7.8, 1.7 Hz, 1H), 7.49 (dd, *J* 7.8, 1.7 Hz, 1H), 7.39-7.28 (m, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 156.9, 149.5, 139.2, 135.8, 132.1, 131.5, 130.1, 129.6, 127.0, 124.8, 122.4; IR neat, ν (cm^{-1}) 3068, 2924, 1585, 1459, 1421; HRMS (EI) calcd for $C_{11}H_9ClN$ $(M+H)^+$ 190.0424, found 190.0419.

Table 2, Entry 2 (6b)



Pale yellow oil, 77 mg (33 %); R*f* 0.48 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.73 (d, *J* 4.8 Hz, 1H), 7.78 (td, *J* 7.8, 1.8 Hz, 1H), 7.69 (d, *J* 8.1 Hz, 1H), 7.60 (d, *J* 7.3 Hz, 1H), 7.55 (d, *J* 7.5 Hz, 1H), 7.42 (t, *J* 7.5 Hz, 1H), 7.33-7.25 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.3, 149.4, 141.2, 135.8, 133.3, 131.4, 129.7, 127.5, 124.7, 122.4, 121.7; IR neat, ν (cm^{-1}) 2920, 2850, 1583, 1458; HRMS (EI) calcd for $C_{11}H_9BrN$ $(M+H)^+$ 233.9918, found 233.9921.

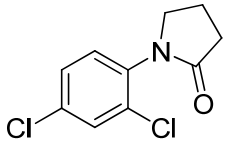
Table 2, Entry 3 (7)



White solid, 109 mg (56 %); R*f* 0.32 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.43 (d, *J* 7.5 Hz, 1H), 7.31-7.22 (m, 3H), 3.74 (t, *J* 7.1 Hz, 2H), 2.56 (t, *J* 8.3 Hz, 2H), 2.21 (quintet, *J* 7.1 Hz, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 175.0, 136.1, 132.0, 130.3, 129.3, 129.0, 127.7,

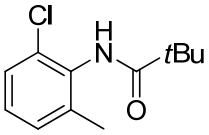
49.9, 30.9, 19.0; IR neat, ν (cm^{-1}) 2919, 1774, 1698, 1481, 1403, 1307, 1059; m.p. 42.8- 43.0 °C; HRMS (EI) calcd for $C_{10}H_{11}ClNO$ $(M+H)^+$ 196.0529, found 196.0529.

Table 2, Entry 3 (8)



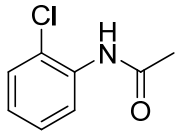
White solid, 23 mg (10 %); R*f* 0.17 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.49 (d, *J* 2.3 Hz, 1H), 7.30 (dd, *J* 8.3, 2.3 Hz, 1H), 7.24 (d, *J* 8.3 Hz, 1H), 3.76 (t, *J* 7.4 Hz, 2H), 2.58 (t, *J* 8.2 Hz, 2H), 2.25 (quintet, *J* 7.4 Hz, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 175.1, 135.0, 134.2, 133.0, 130.4, 130.2, 128.1, 49.9, 30.9, 19.1; IR neat, ν (cm^{-1}) 3030, 2882, 1691, 1485, 1409, 1264, 1236, 1121, 1061; m.p. 59.6- 59.8 °C; HRMS (EI) calcd for $C_{10}H_{10}Cl_2NO$ $(M+H)^+$ 230.0139, found 230.0139; Anal. Calcd. for $C_{10}H_9Cl_2NO$: C, 52.2; H, 3.9; N, 6.1. Found: C, 51.8; H, 4.2; N, 5.7.

Table 2, Entry 4 (9a)



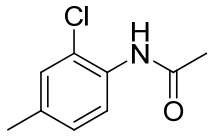
White solid, 221 mg (98 %); R*f* 0.62 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.31-7.10 (br. m, 4H), 2.25 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.6, 138.1, 132.8, 129.0, 127.5, 126.8, 124.9, 39.3, 27.6, 18.7; IR neat, ν (cm^{-1}) 3282, 2962, 1651, 1496, 1366, 1226, 1173; 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 2, Entry 5 (9b)



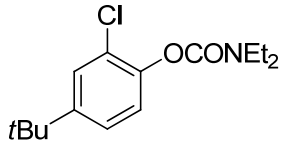
White solid, 96 mg (57 %); R*f* 0.50 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.32 (d, *J* 8.0 Hz, 1H), 7.69 (br. s, 1H), 7.35 (d, *J* 8.0 Hz, 1H), 7.24 (dd, *J* 7.3, 1.2 Hz, 1H), 7.03 (t, *J* 7.3 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.7, 134.6, 129.1, 127.8, 124.9, 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 2, Entry 6 (9c)



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.

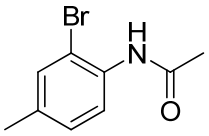
Table 2, Entry 7 (10)



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,

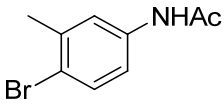
123.4, 42.4, 42.1, 34.6, 31.3, 14.1, 13.3; IR neat, ν (cm^{-1}) 2967, 2872, 1706, 1423, 1265, 1160, 1058; m.p. 78.5- 78.8 °C; HRMS (EI) calcd for $C_{15}H_{23}ClNO_2$ $(M+H)^+$ 284.1417, found 284.1412; Anal. Calcd. for $C_{15}H_{12}ClNO_2$: C, 63.5; H, 7.8; N, 4.9. Found: C, 63.4; H, 7.7; N, 4.7.

Table 2, Entry 8 (11)



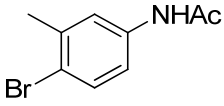
White solid, 226 mg; R*f* 0.4 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.17 (d, *J* 8.3 Hz, 1H), 7.52 (br. s, 1H), 7.36 (s, 1H), 7.12 (d, *J* 8.3 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.1, 135.3, 133.1, 132.4, 129.0, 121.9, 119.6, 24.8, 20.5; IR neat, ν (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 2, Entries 9 & 10 (12)



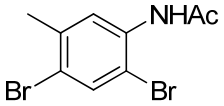
White solid, 94 mg (82 %); R*f* 0.2 (EtOAc/hexanes, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.87 (br. s, 1H), 7.42-7.39 (m, 2H), 7.19 (dd, *J* 8.6, 2.6 Hz, 1H), 2.33 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.7, 138.4, 137.1, 132.5, 122.2, 119.4, 119.0, 24.4, 22.9; IR neat, ν (cm^{-1}) 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 2, Entries 11 & 12 (12)



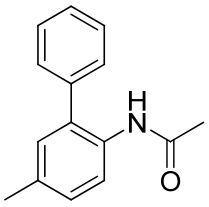
White solid, 91 mg (80 %); R*f* 0.2 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.70 (br. s, 1H), 7.43-7.41 (m, 2H), 7.20 (dd, *J* 8.6, 2.5 Hz, 1H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.6, 138.5, 137.0, 132.5, 122.1, 119.4, 118.9, 24.5, 23.0; IR neat, ν (cm^{-1}) 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.

Table 2, Entries 9 & 10 (13)



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.

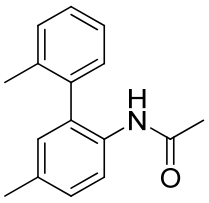
14a (Scheme 1)



Off-white solid, 122 mg (54 %); R*f* 0.3 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.10 (d, *J* 8.3 Hz, 1H), 7.51-7.37 (br. m, 5H), 7.20 (dd, *J* 8.3, 1.8 Hz, 1H), 7.08 (br. s, 2H), 2.37 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.9, 142.2, 133.6, 130.4, 127.7, 118.3, 116.0, 49.0, 27.8, 24.2; IR neat, ν (cm^{-1}) 3277, 3023, 1655, 1524, 1488, 1297; m.p. 121.4-

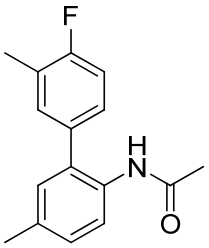
122.8 °C; HRMS (ESI) calcd for $C_{15}H_{16}NO$ $(M+H)^+$ 226.1226, found 226.1234; Anal. Calcd. for $C_{15}H_{15}NO$: C, 80.0; H, 6.7; N, 6.2. Found: C, 80.1; H, 6.7; N, 6.2.

14b (Scheme 1)



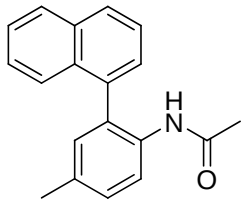
White solid, 160 mg (67 %); see **4f** (Table 1, Entry 14) for data.

14c (Scheme 1)



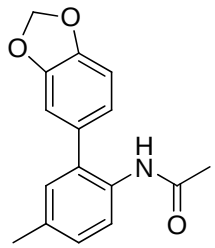
White solid, 103 mg (40 %); R*f* 0.42 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.02 (d, *J* 8.3 Hz, 1H), 7.18-7.03 (br. m, 6H), 2.34 (s, 3H), 2.33 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 162.1 (d, *J* 246 Hz), 134.1, 134.0 (d, *J* 6 Hz), 132.3 (d, *J* 6 Hz), 132.0, 131.9, 130.5, 128.9, 128.0 (d, *J* 28 Hz), 125.6 (d, *J* 18 Hz), 122.3, 115.5 (d, *J* 23 Hz), 24.3, 20.8, 14.6 (d, *J* 3 Hz); IR neat, ν (cm^{-1}) 3257, 2923, 1645, 1527, 1495, 1368, 1294, 1229, 1121; m.p. 106.4- 106.7 °C; HRMS (ESI) calcd for $C_{16}H_{17}FNO$ $(M+H)^+$ 258.1289, found 258.1297; Anal. Calcd. for $C_{16}H_{16}FNO$: C, 74.7; H, 6.3; N, 5.4. Found: C, 74.9; H, 6.3; N, 5.1.

14d (Scheme 1)



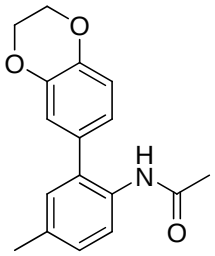
White solid, 138 mg (50 %); R*f* 0.47 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.22 (d, *J* 8.3 Hz, 1H), 7.94 (d, *J* 8.5 Hz, 2H), 7.60-7.52 (br. m, 3H), 7.47-7.42 (br. m, 2H), 7.29 (dd, *J* 8.3 Hz, 1.8 Hz, 1H), 7.11 (s, 1H), 6.67 (br. s, 1H), 2.38 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 135.5, 133.8, 133.7, 133.3, 131.6, 131.4, 130.2, 129.3, 128.7, 128.5, 127.8, 126.7, 126.3, 125.7, 121.4, 119.6, 24.4, 20.9; IR neat, ν (cm^{-1}) 3353, 3044, 1669, 1514, 1368, 1290, 1236, 1018; m.p. 134.0- 134.2 °C; HRMS (ESI) calcd for $C_{19}H_{18}NO$ $(M+H)^+$ 276.1383, found 276.1394; Anal. Calcd. for $C_{19}H_{17}NO$: C, 88.9; H, 6.2; N, 5.1. Found: C, 89.0; H, 6.3; N, 5.3.

14e (Scheme 1)



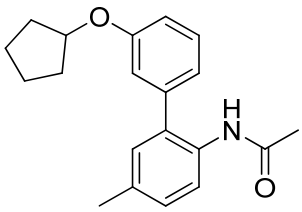
Off-white solid, 143 mg (53 %); R*f* 0.34 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.07 (d, *J* 8.3 Hz, 1H), 7.16 (dd, *J* 8.3, 1.8 Hz, 1H), 7.14 (br. s, 1H), 7.02 (s, 1H), 6.90 (d, *J* 8.1 Hz, 1H), 6.83-6.79 (br. m, 2H), 6.03 (s, 2H), 2.33 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 148.1, 147.3, 133.9, 132.2, 132.0, 130.6, 128.8, 122.5, 121.8, 109.7, 108.7, 101.3, 26.9, 24.5, 20.8; IR neat, ν (cm^{-1}) 3247, 2921, 1736, 1659, 1520, 1479, 1294, 1229, 1028; m.p. 122.6- 123.3 °C; HRMS (ESI) calcd for $C_{16}H_{15}NO_3$ $(M+H)^+$ 270.1125, found 270.1134.

14f (Scheme 1)



Off-white solid, 150 mg (53 %); R*f* 0.26 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.08 (d, *J* 8.3 Hz, 1H), 7.18 (br. s, 1H), 7.14 (dd, *J* 8.3, 1.8 Hz, 1H), 7.03 (s, 1H), 6.95 (d, *J* 8.1 Hz, 1H), 6.88 (d, *J* 2.0 Hz, 1H), 6.82 (dd, *J* 8.1, 2.0 Hz, 1H), 4.31 (s, 4H), 2.33 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 143.9, 130.6, 129.4, 128.6, 122.1, 121.7, 118.0, 117.7, 64.4, 24.5, 20.8; IR neat, ν (cm^{-1}) 3290, 2921, 1662, 1589, 1508, 1489, 1276, 1252, 1241, 1067; m.p. 175.3- 176.2 °C; HRMS (ESI) calcd for $C_{17}H_{18}NO_3$ $(M+H)^+$ 284.1281, found 284.1292; Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.1; H, 6.1; N, 4.9. Found: C, 71.7; H, 5.2; N, 4.7.

14g (Scheme 1)



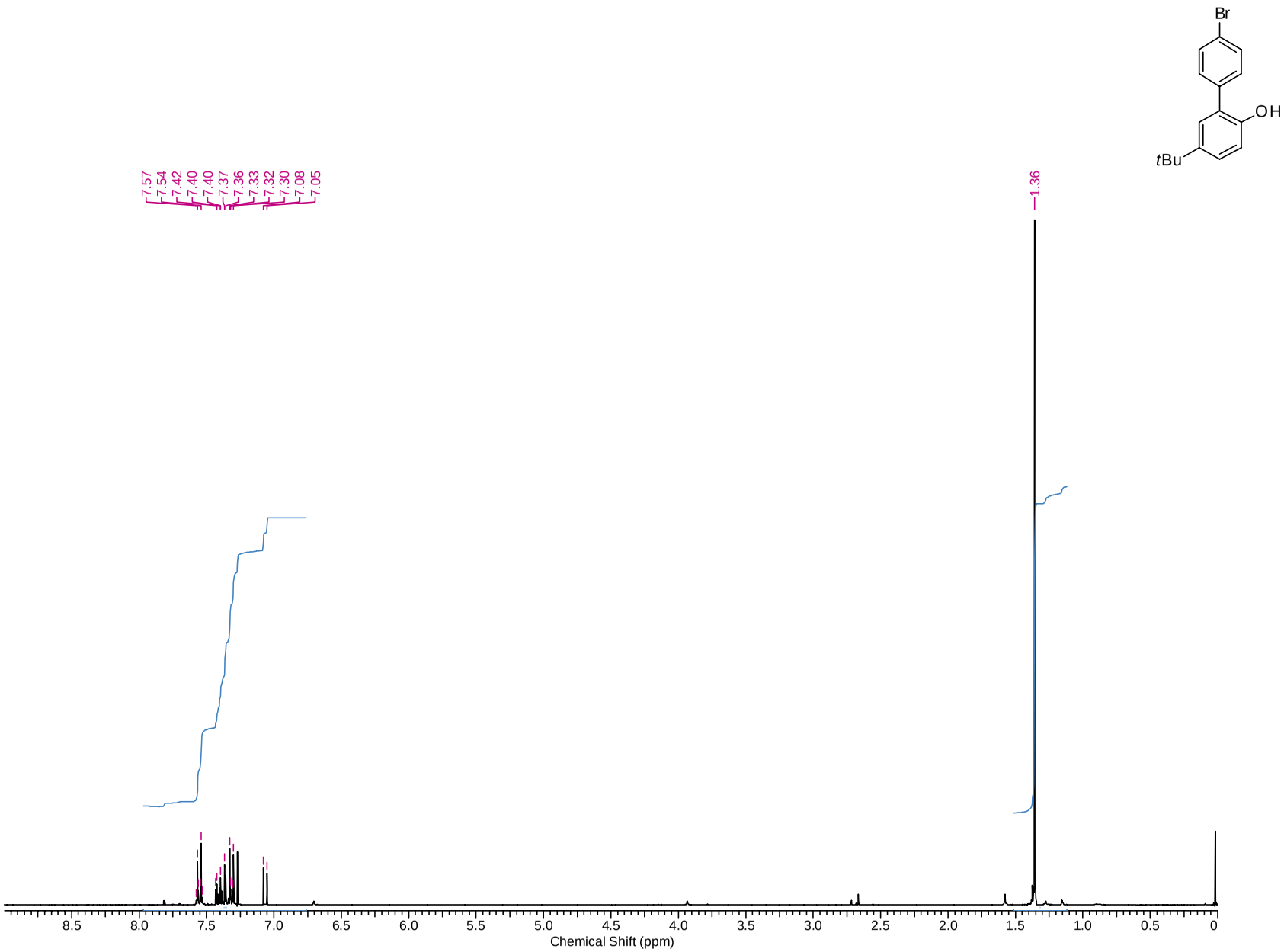
Light orange solid, 155 mg (50 %); R*f* 0.48 (EtOAc/cyclohexane, 1:1); ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.13 (d, *J* 8.3 Hz, 1H), 7.36 (t, *J* 7.8 Hz, 1H), 7.18 (dd, *J* 8.3, 1.8 Hz, 1H), 7.17 (br. s, 1H), 7.07 (s, 1H), 6.93-6.86 (m, 3H), 4.80-4.77 (m, 1H), 2.35 (s, 3H), 2.03 (s, 3H), 1.94-1.78 (br. m, 6H), 1.68-1.60 (br. m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 168.2, 158.6, 139.5, 133.8, 132.1, 130.5, 129.9, 128.9, 121.6, 120.8, 119.6, 116.1, 115.2, 79.3, 32.8, 24.6, 24.0, 20.8; IR neat, ν (cm^{-1}) 3340, 2956, 1667, 1595, 1516, 1369, 1294, 1223, 1160; m.p. 138.4- 138.8 °C; HRMS (ESI) calcd for $C_{20}H_{24}NO_2$ $(M+H)^+$ 310.1802, found 310.1813; Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.6; H, 7.5; N, 4.5. Found: C, 77.5; H, 7.4; N, 4.9.

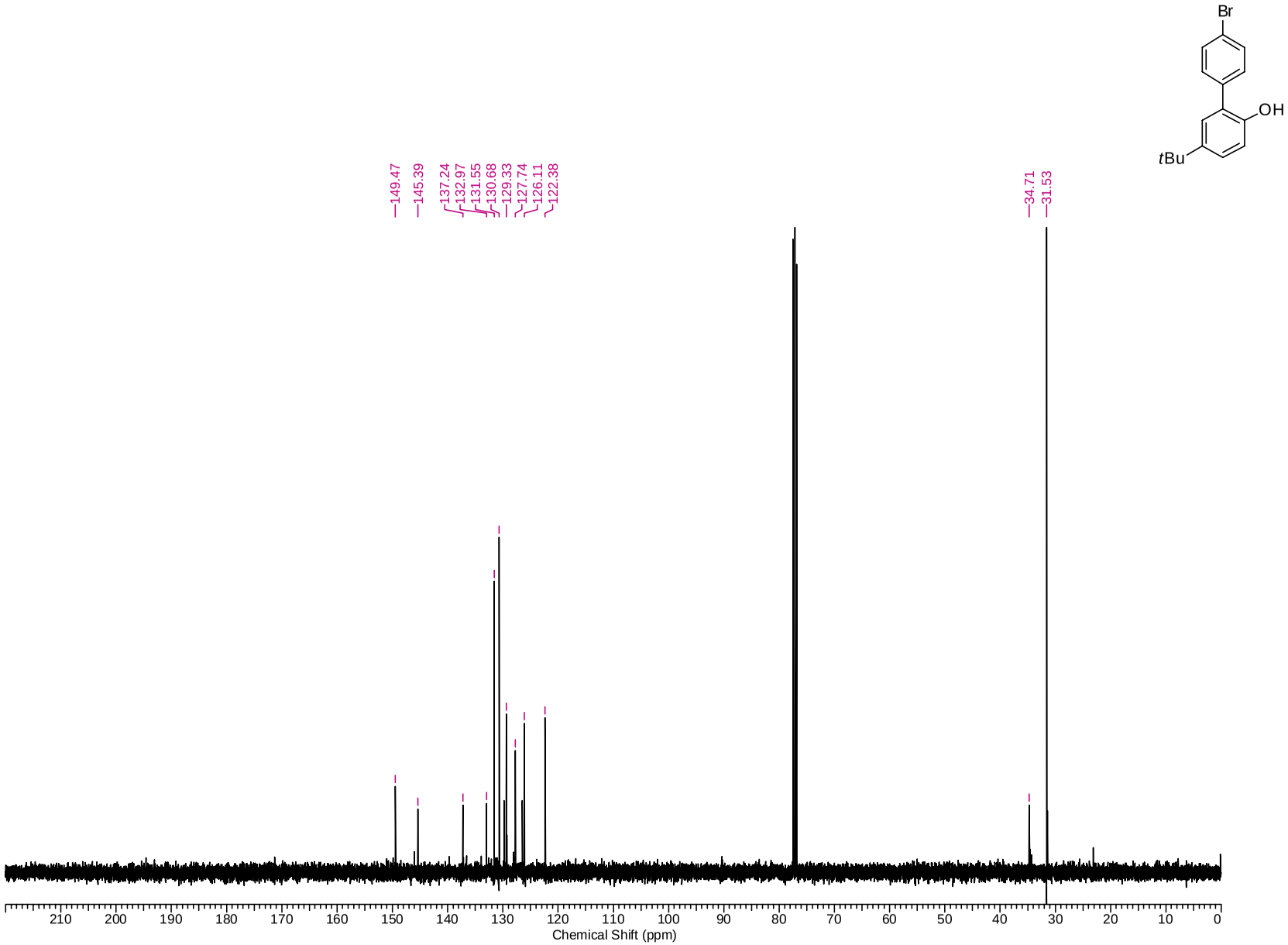
References

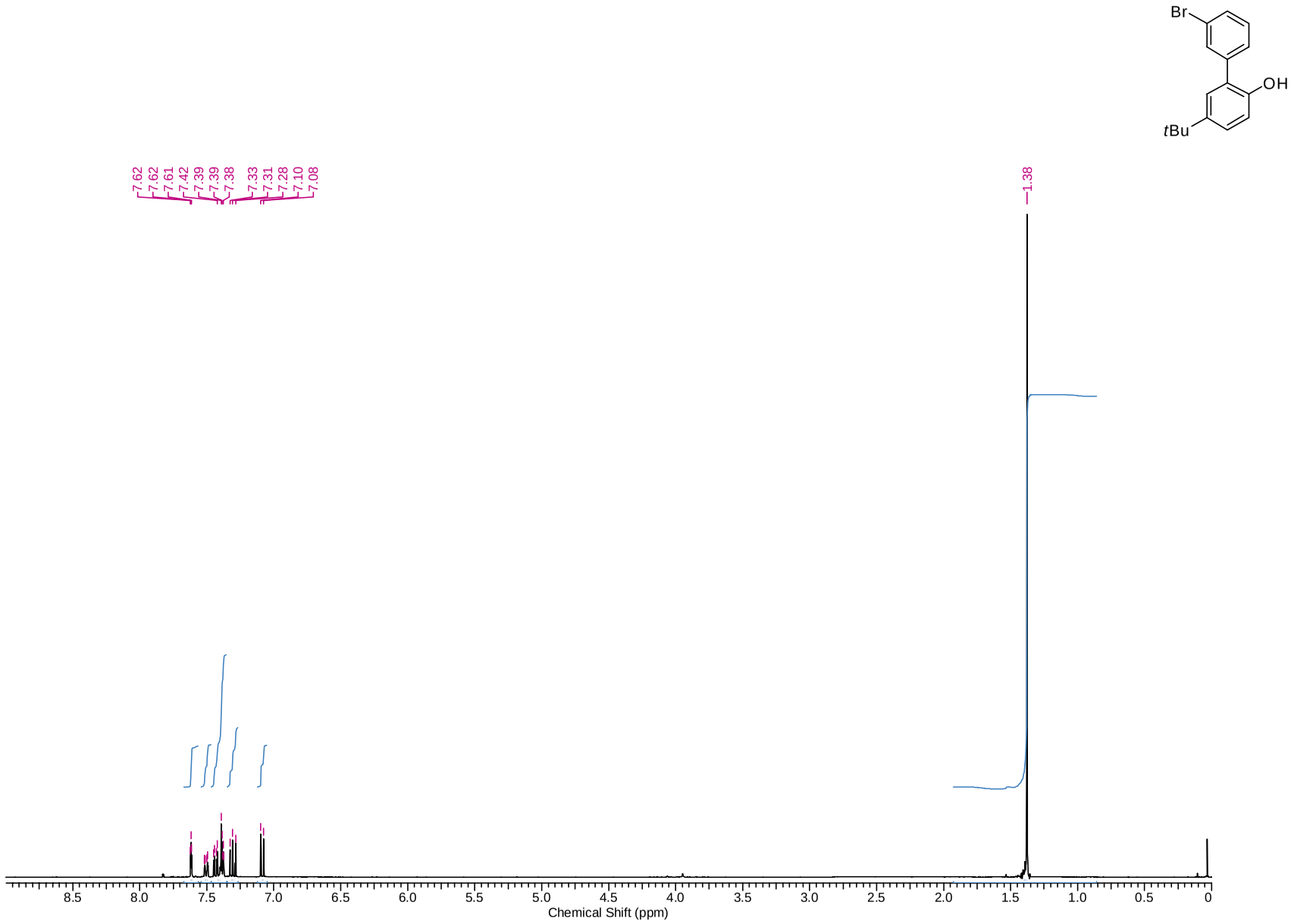
1. C. A. James and V. Snieckus, . *J. Org. Chem.*, 2009, **74**, 4080

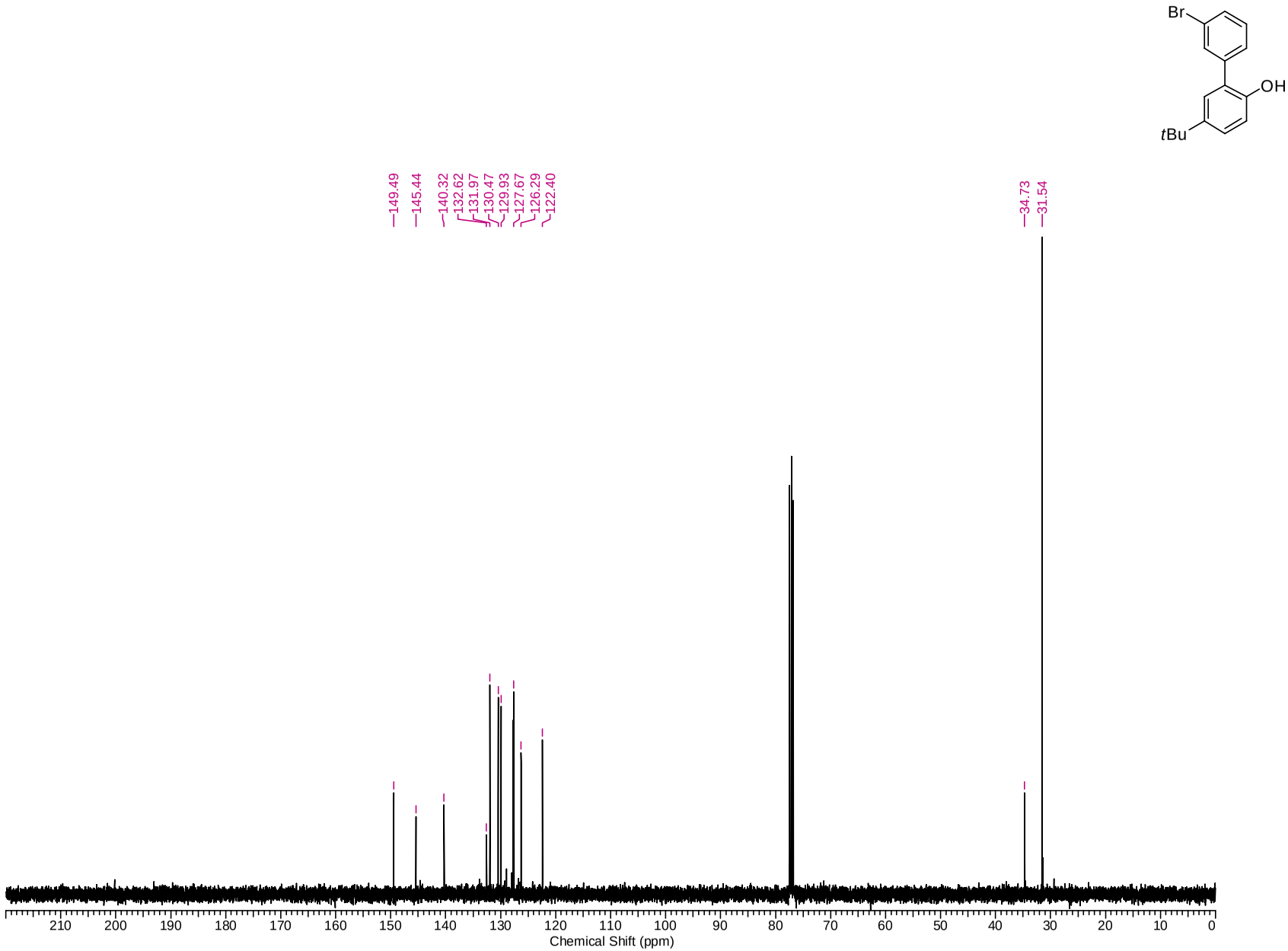
2. R. B. Bedford, R. L. Webster and C. J. Mitchell, *Org. Biomol. Chem*., 2009, **7**, 4853

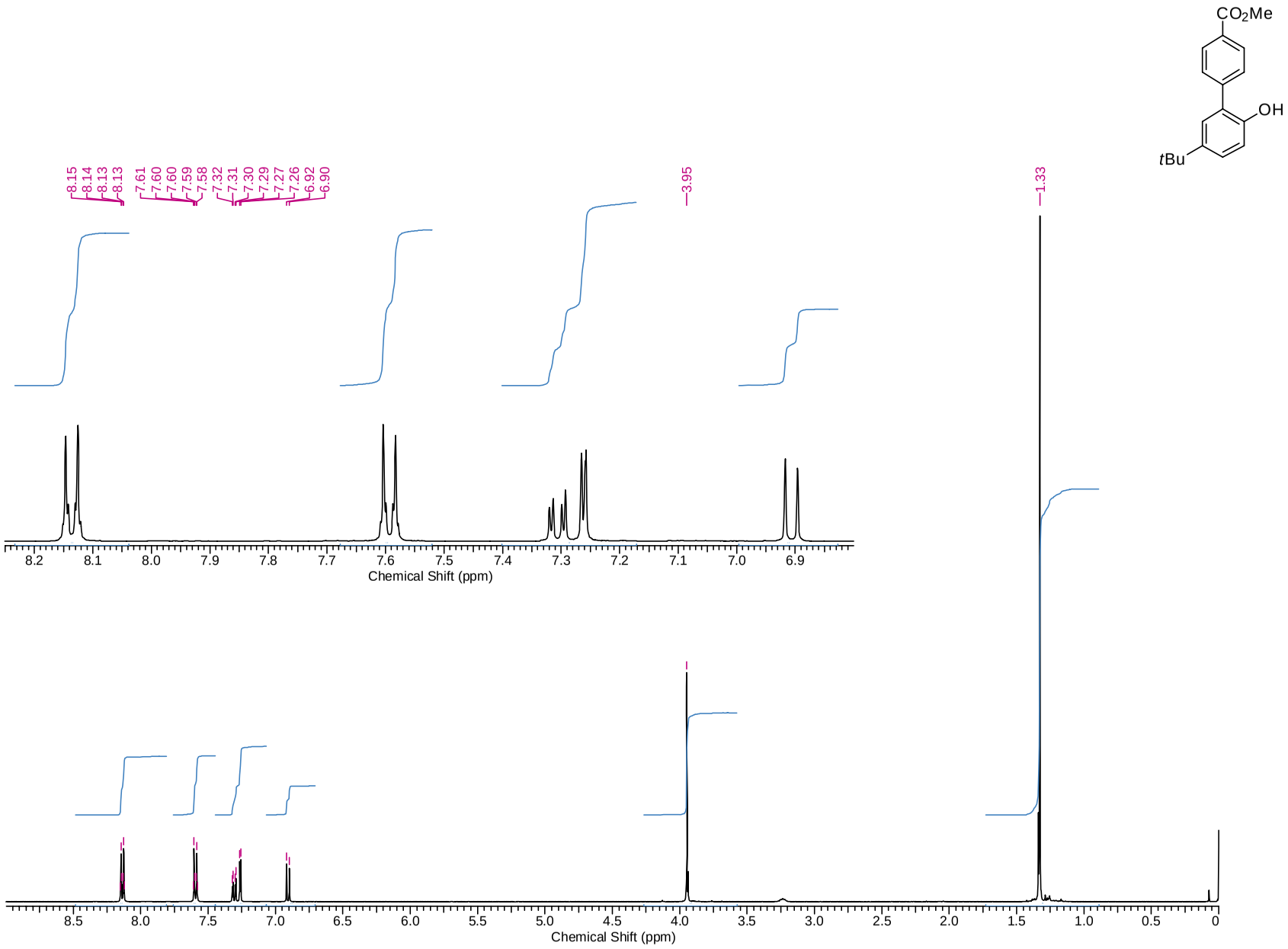
3. M. Bielawski, M. Zhu and B. Olofsson, *Adv. Synth. Catal.*, 2007, **349**, 2610

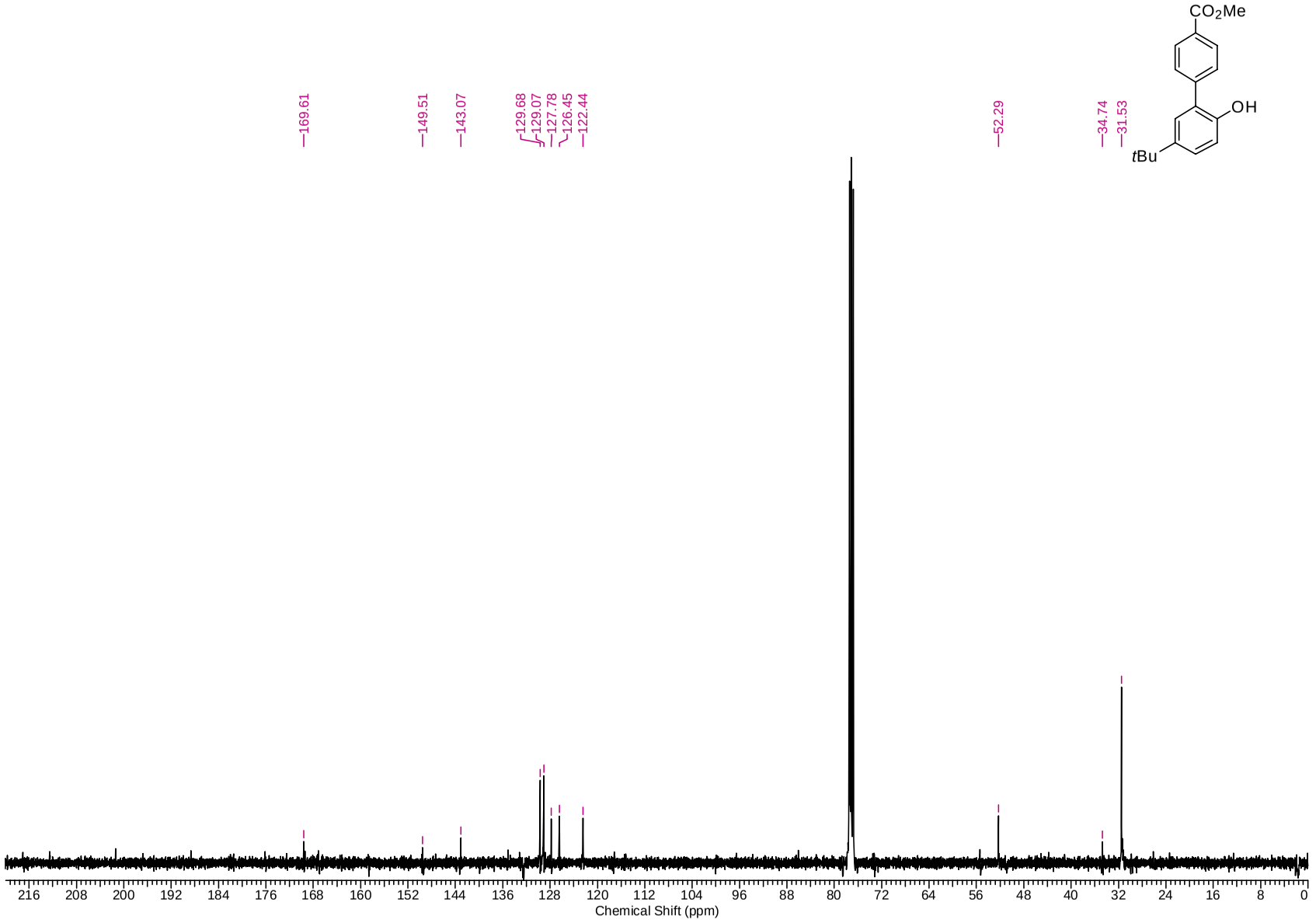

Br
OH
tBu
7.57
7.54
7.42
7.40
7.40
7.37
7.36
7.33
7.32
7.30
7.08
7.05
1.36
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

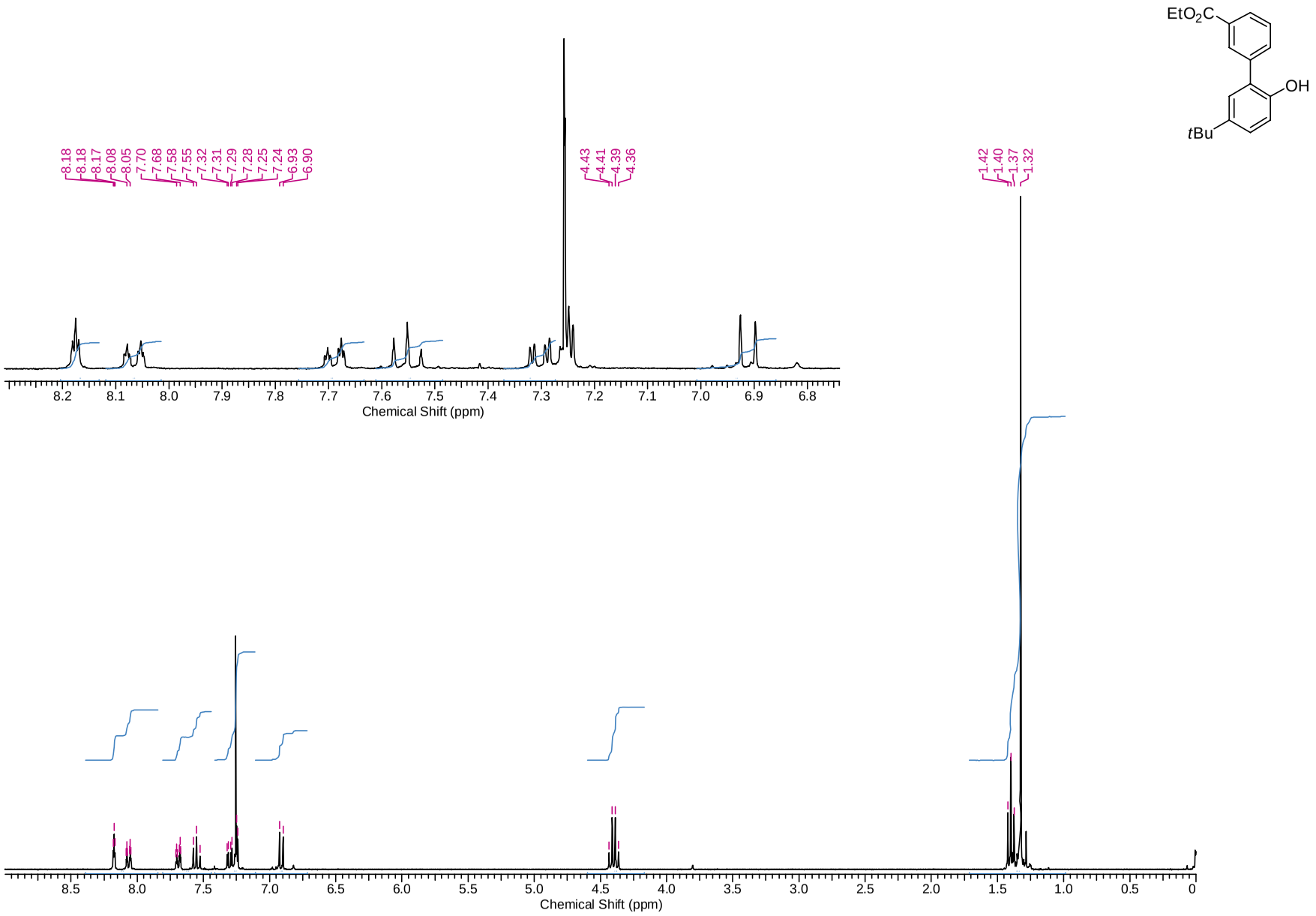

Br
OH
tBu
149.47
145.39
137.24
132.97
131.55
130.68
129.33
127.74
126.11
122.38
34.71
31.53
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

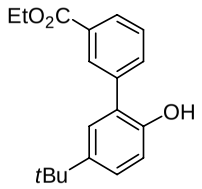

Br
OH
tBu
7.62
7.62
7.61
7.42
7.39
7.39
7.38
7.33
7.31
7.28
7.10
7.08
1.38
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

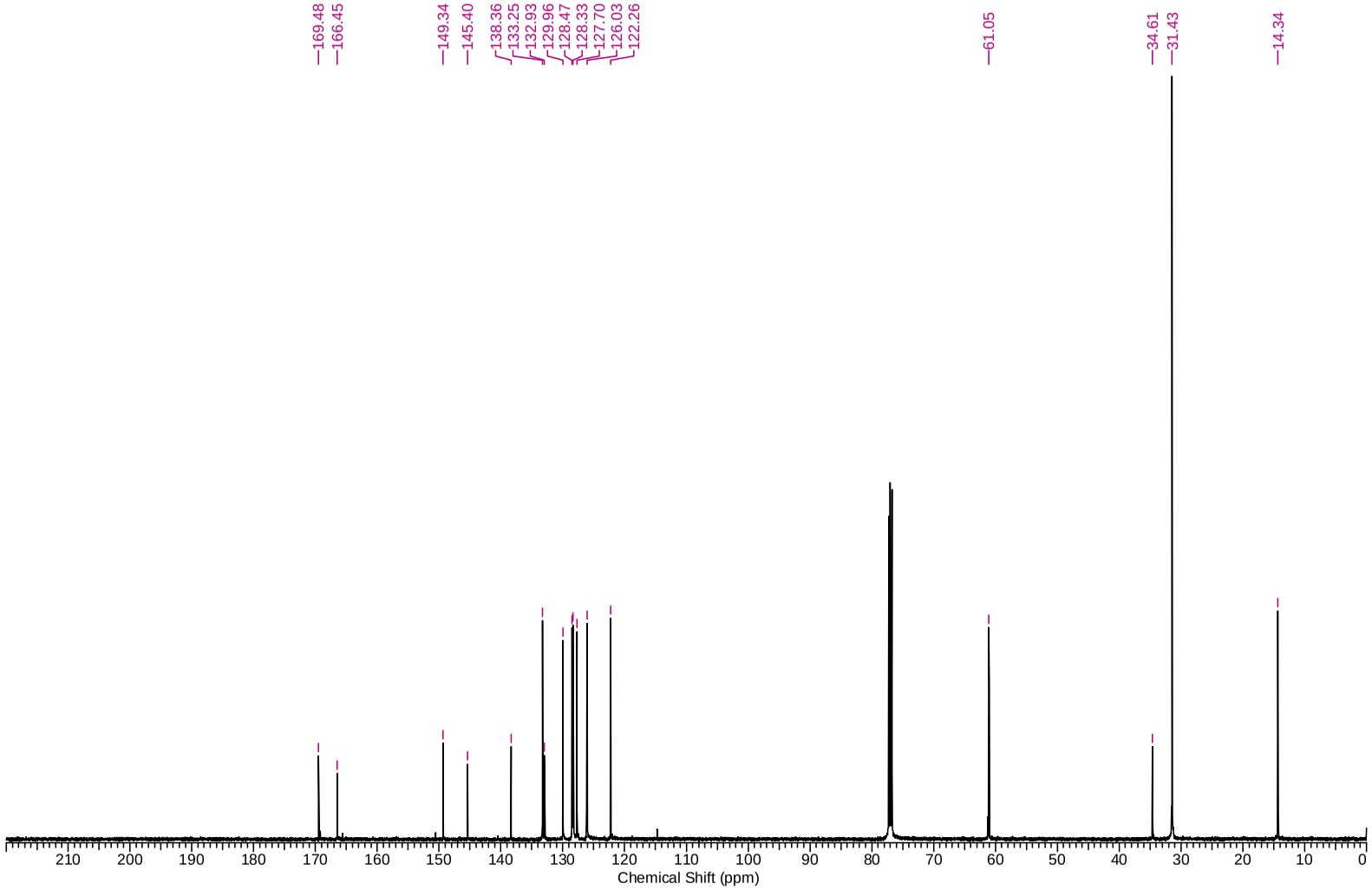

Br
OH
tBu
149.49
145.44
140.32
132.62
131.97
130.47
129.93
127.67
126.29
122.40
34.73
31.54
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical Shift (ppm)

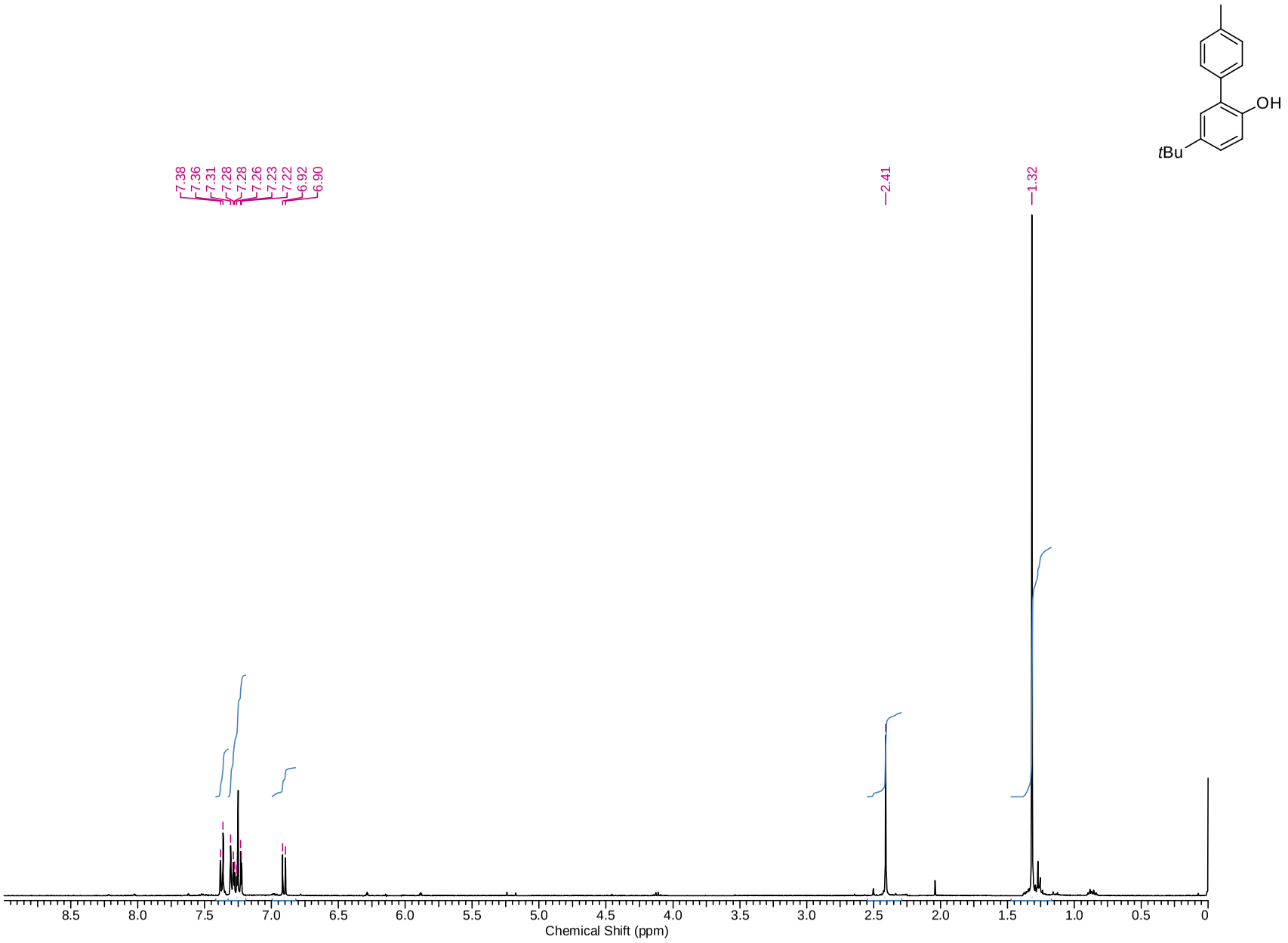

CO2Me
OH
tBu
8.15
8.14
8.13
8.13
7.61
7.60
7.60
7.59
7.58
7.32
7.31
7.30
7.29
7.27
7.26
6.92
6.90
3.95
1.33
Chemical Shift (ppm)
Chemical Shift (ppm)

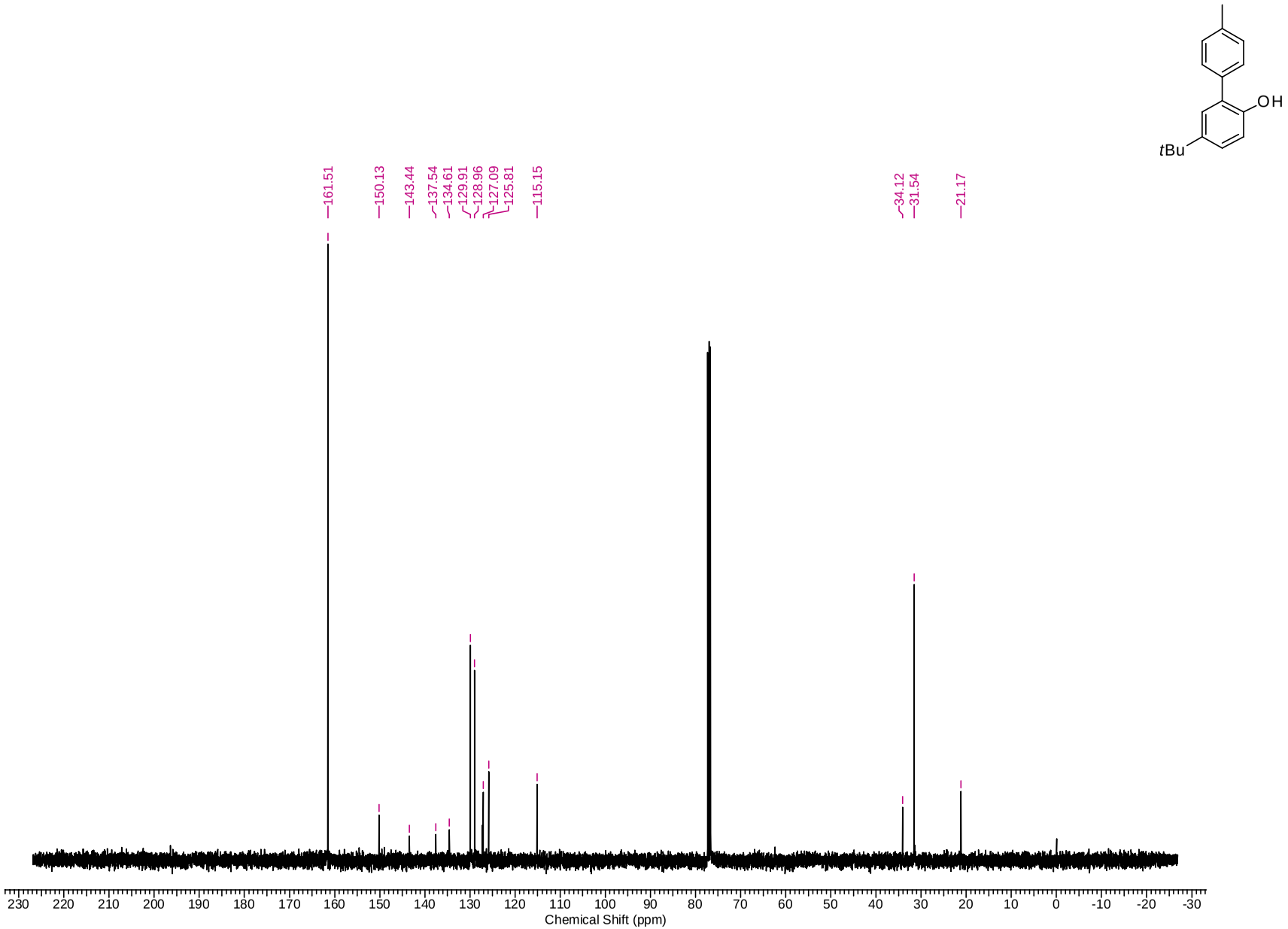

169.61
149.51
143.07
129.68
129.07
127.78
126.45
122.44
52.29
34.74
31.53
CO2Me
OH
tBu
216 208 200 192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

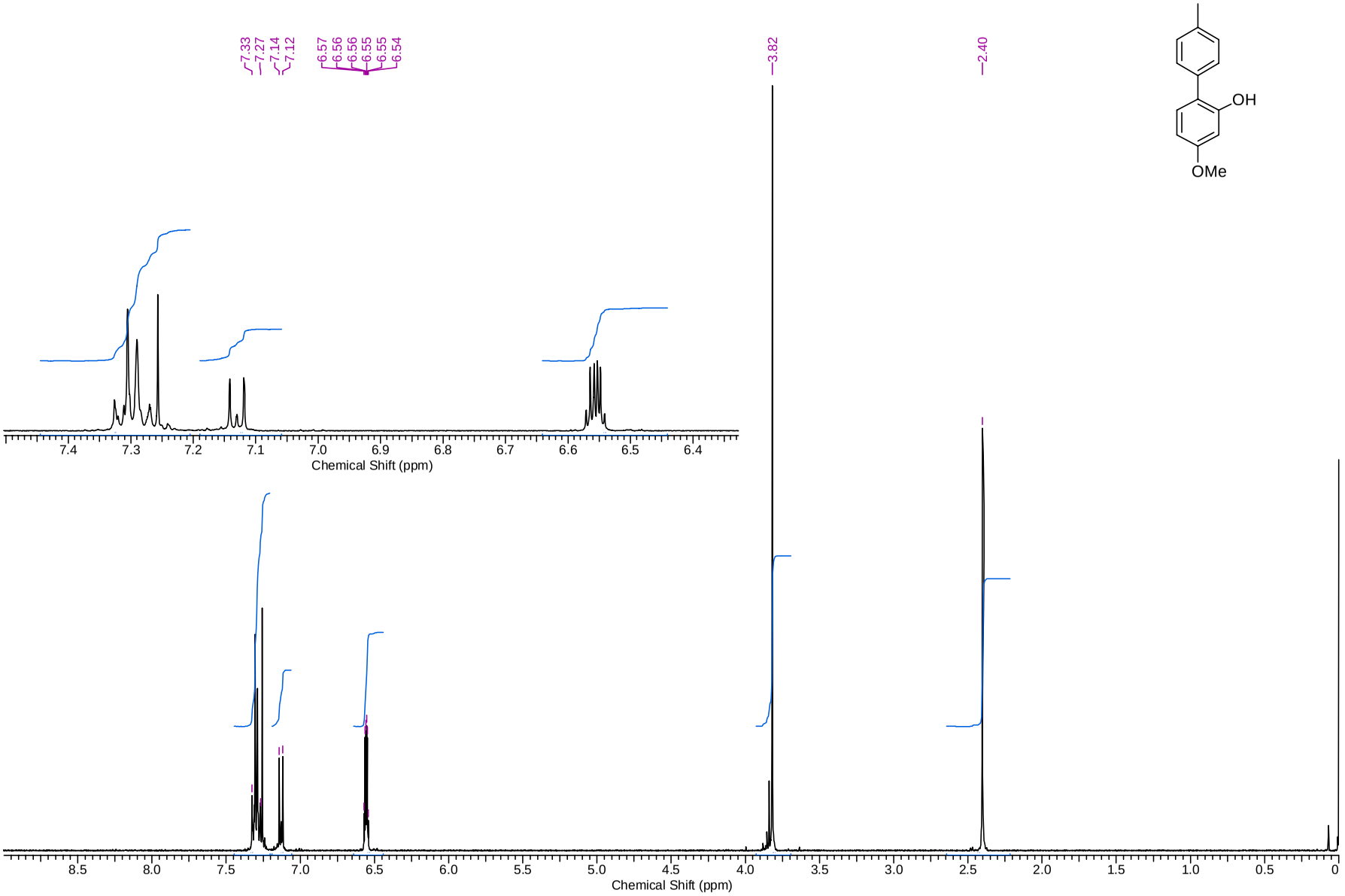

EtO2C
OH
tBu
8.18
8.18
8.17
8.08
8.05
7.70
7.68
7.58
7.55
7.32
7.31
7.29
7.28
7.25
7.24
6.93
6.90
4.43
4.41
4.39
4.36
1.42
1.40
1.37
1.32
Chemical Shift (ppm)
Chemical Shift (ppm)

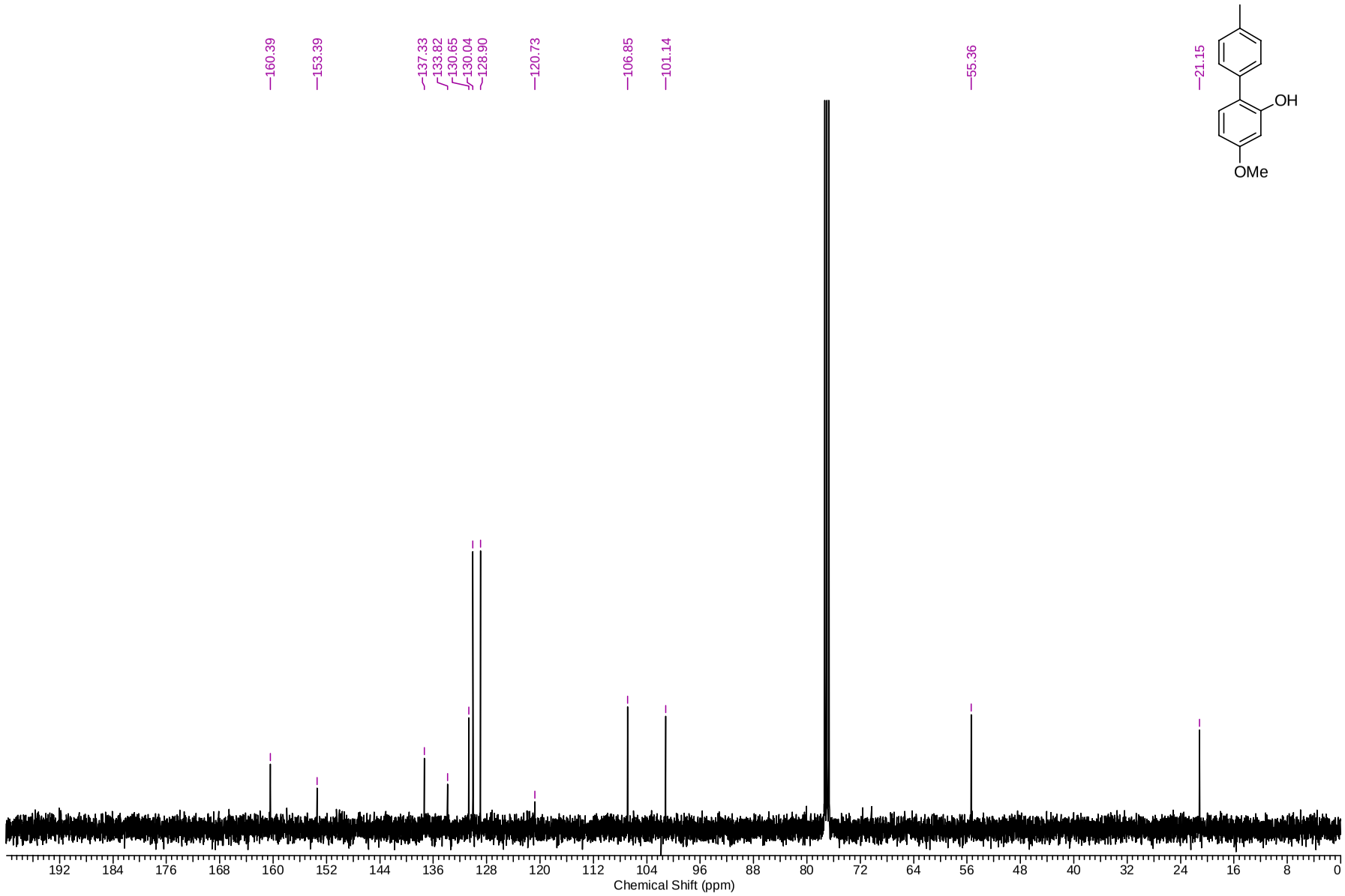

EtO2C
OH
tBu

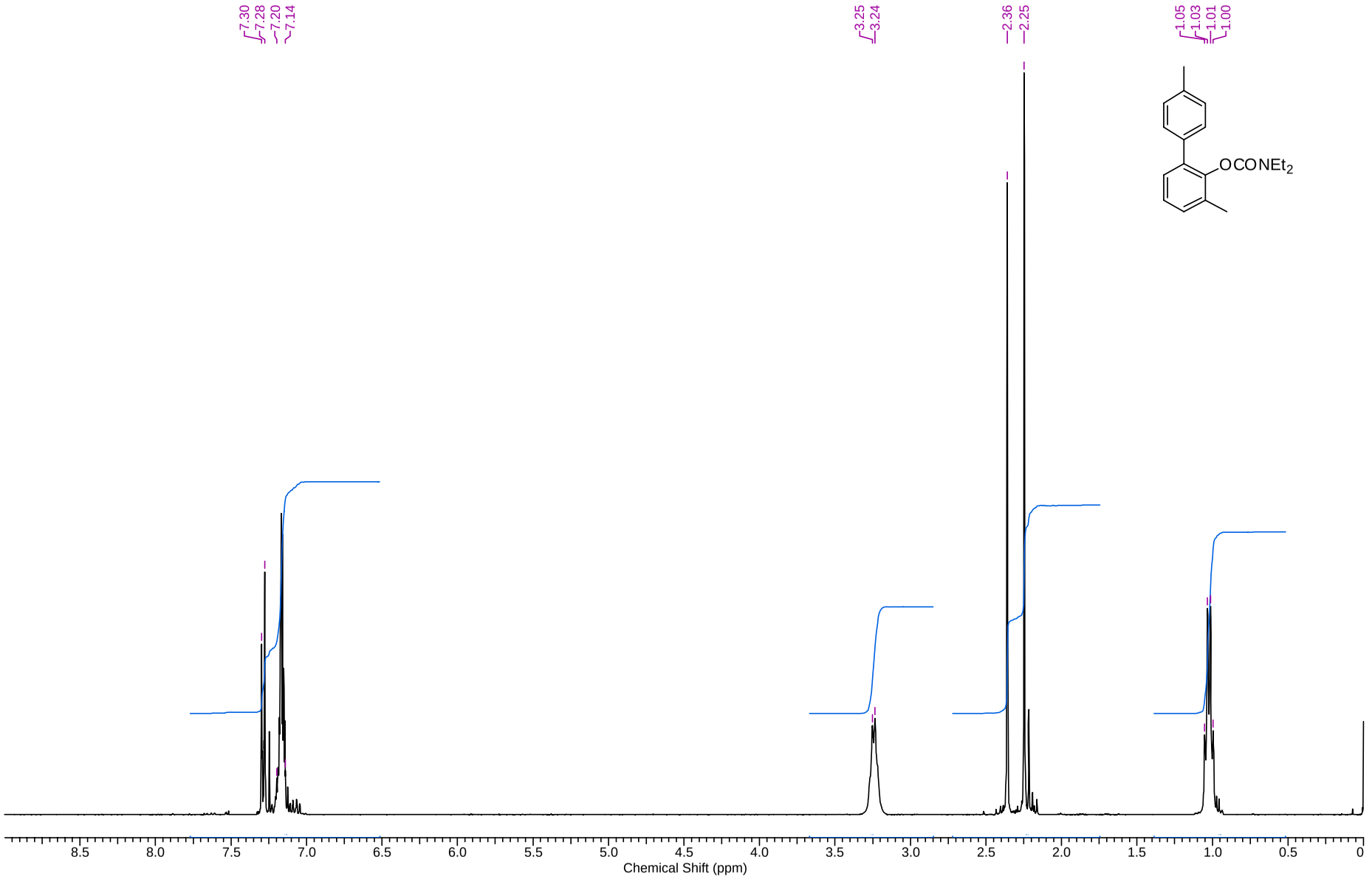

169.48
166.45
149.34
145.40
138.36
133.25
132.93
129.96
128.47
128.33
127.70
126.03
122.26
61.05
34.61
31.43
14.34
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

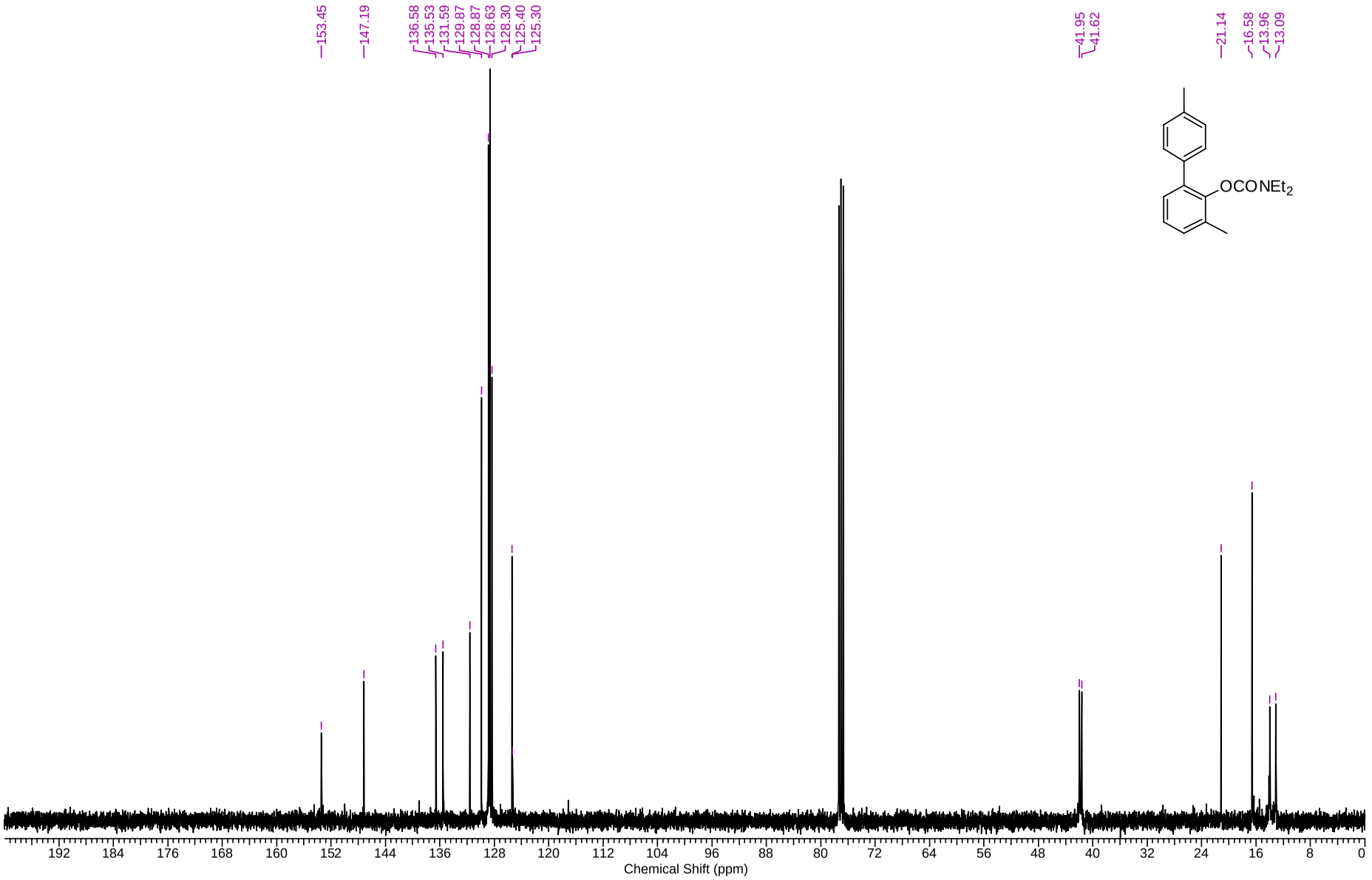

OH
tBu
7.38
7.36
7.31
7.28
7.28
7.26
7.23
7.22
6.92
6.90
2.41
1.32
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

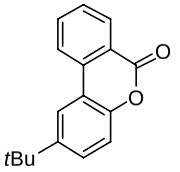

OH
tBu
161.51
150.13
143.44
137.54
134.61
129.91
128.96
127.09
125.81
115.15
34.12
31.54
21.17
Chemical Shift (ppm)

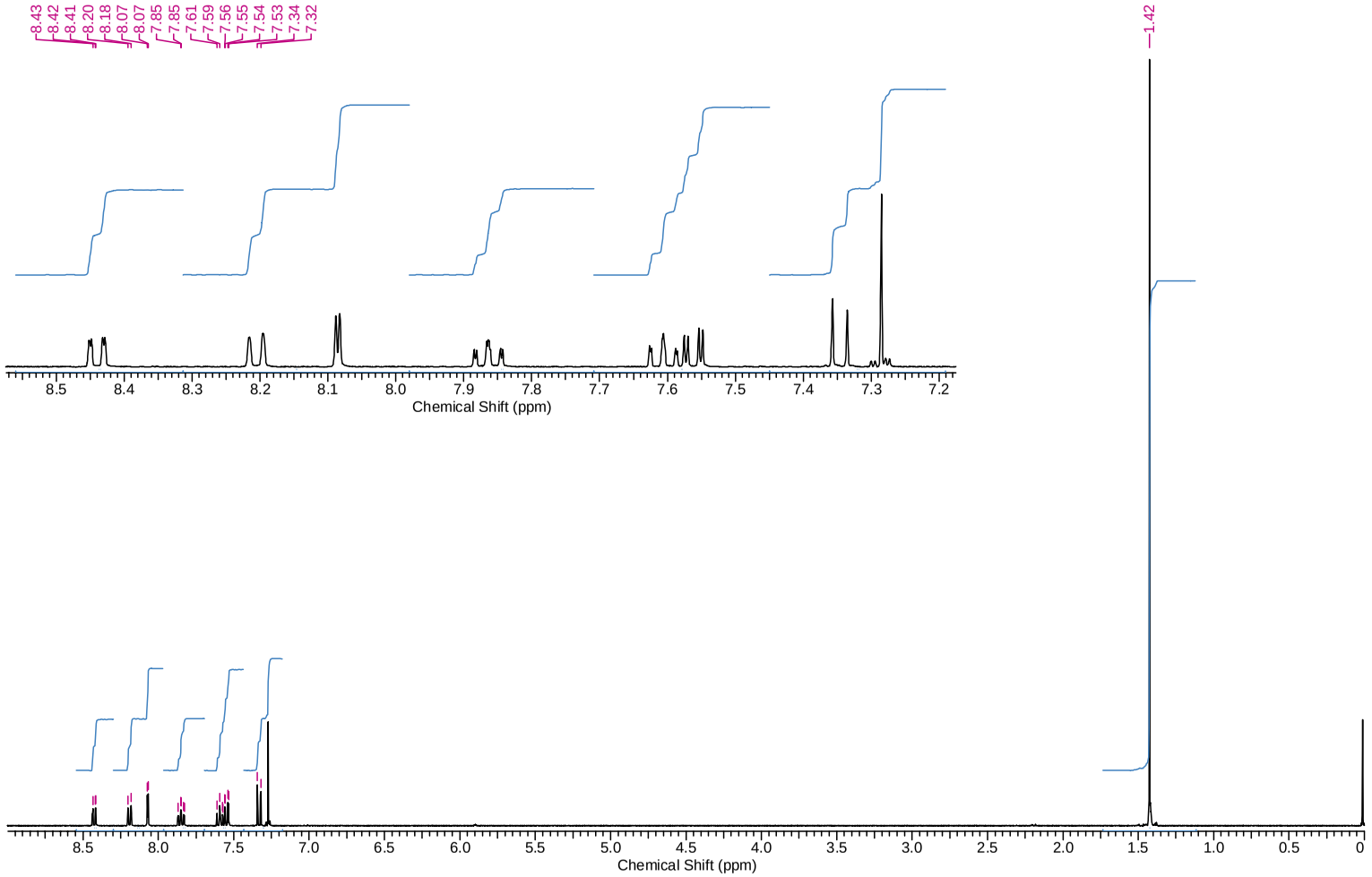

7.33
7.27
7.14
7.12
6.57
6.56
6.56
6.55
6.55
6.54
3.82
2.40
OH
OMe
Chemical Shift (ppm)
Chemical Shift (ppm)

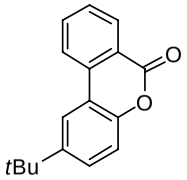

160.39
153.39
137.33
133.82
130.65
130.04
128.90
120.73
106.85
101.14
55.36
21.15
OH
OMe
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

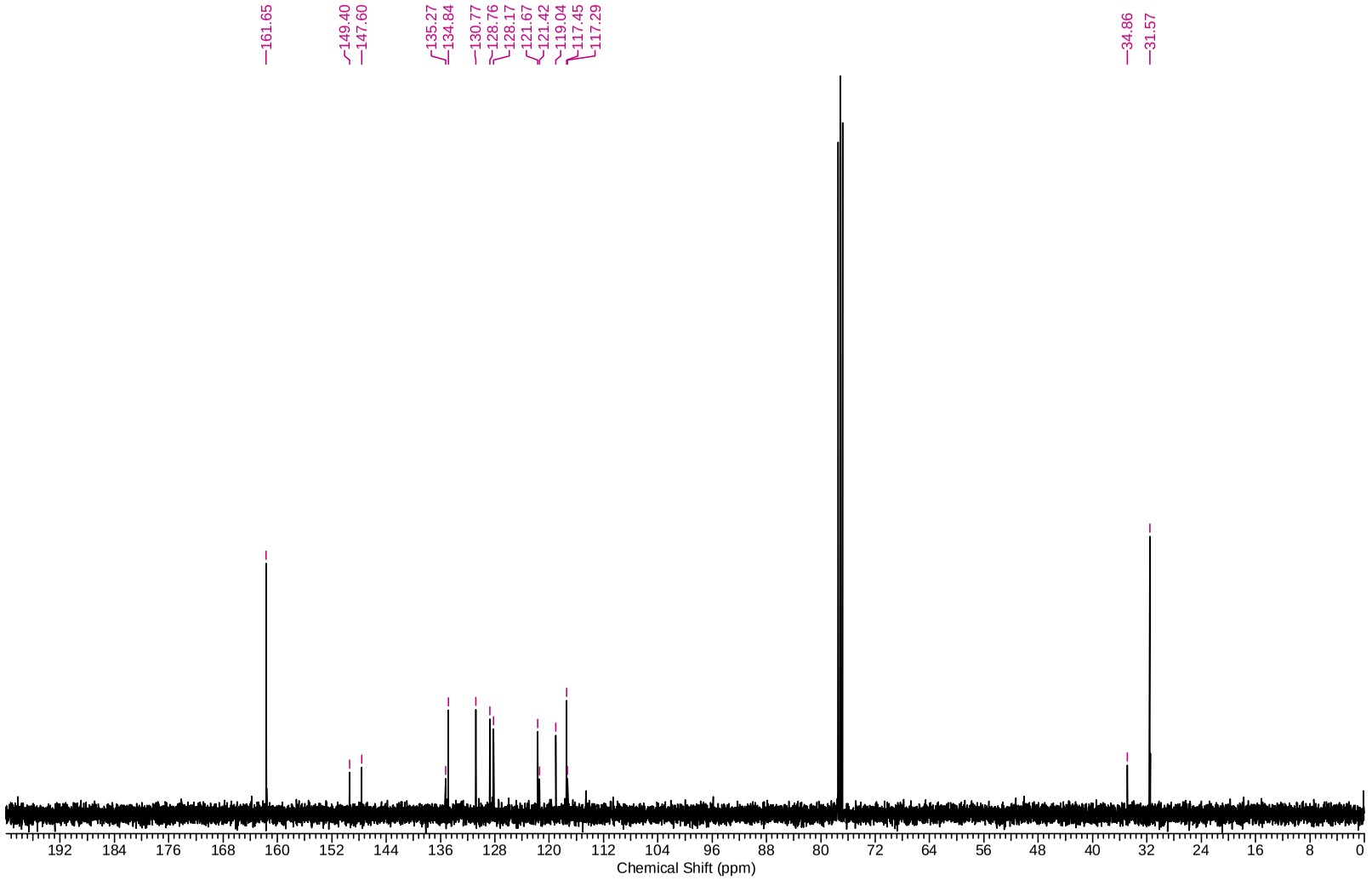

7.30
7.28
7.20
7.14
3.25
3.24
2.36
2.25
1.05
1.03
1.01
1.00
OCONEt2
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

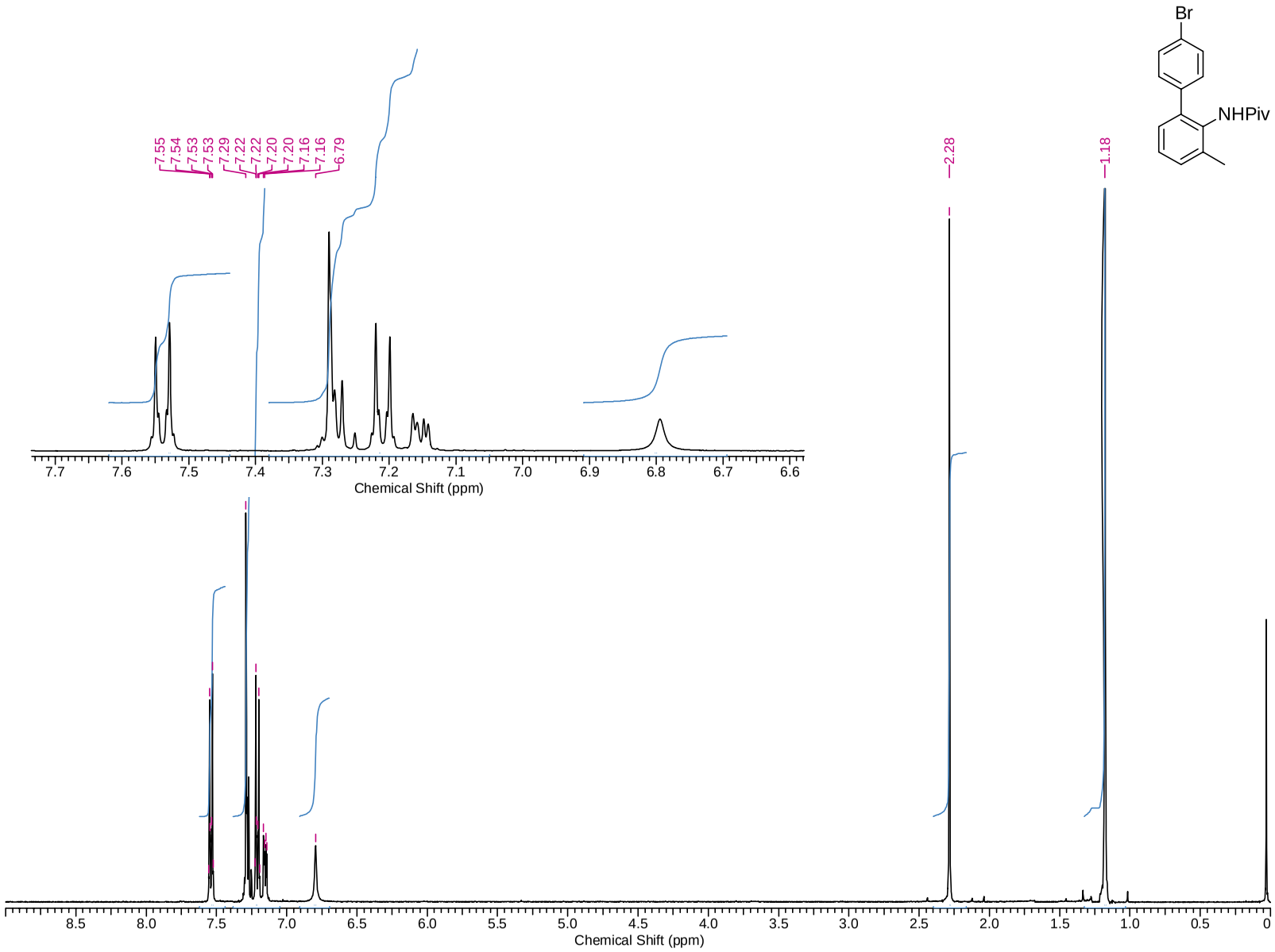

153.45
147.19
136.58
135.53
131.59
129.87
128.87
128.63
128.30
125.40
125.30
41.95
41.62
21.14
16.58
13.96
13.09
OCONEt2
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

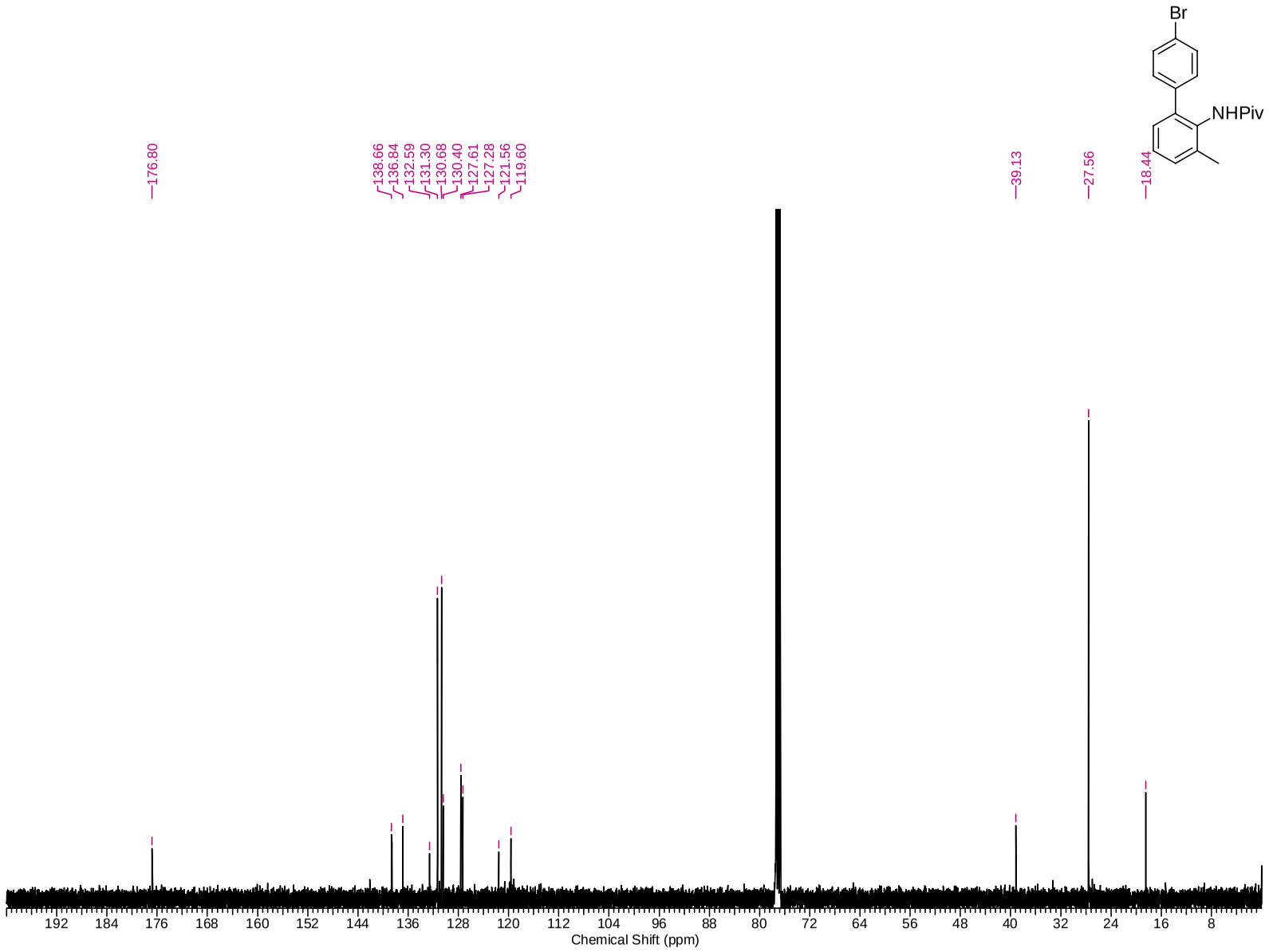

O
O
tBu

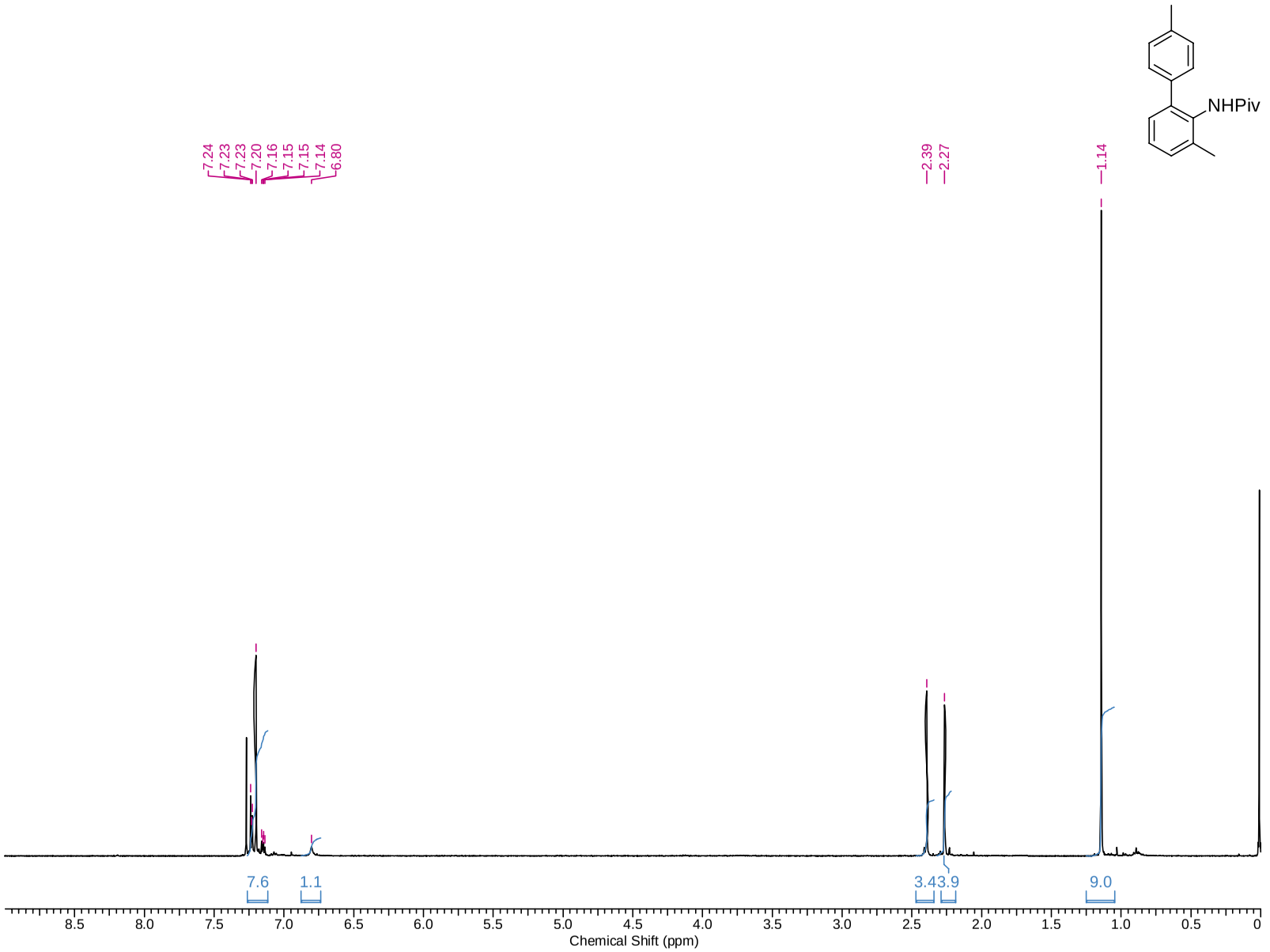

8.43
8.42
8.41
8.20
8.18
8.07
8.07
7.85
7.85
7.61
7.59
7.56
7.55
7.54
7.53
7.34
7.32
1.42
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
Chemical Shift (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

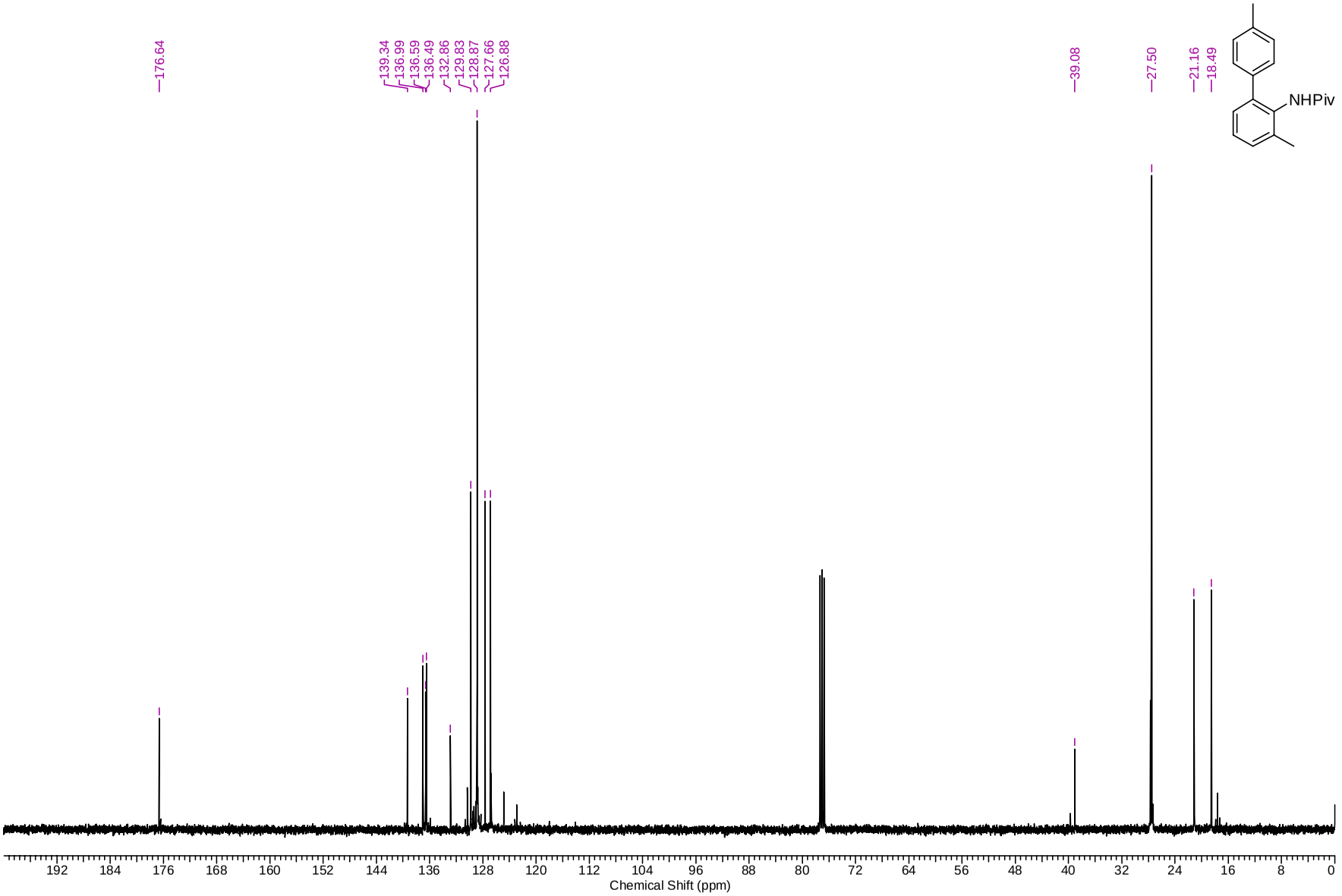

O
O
tBu

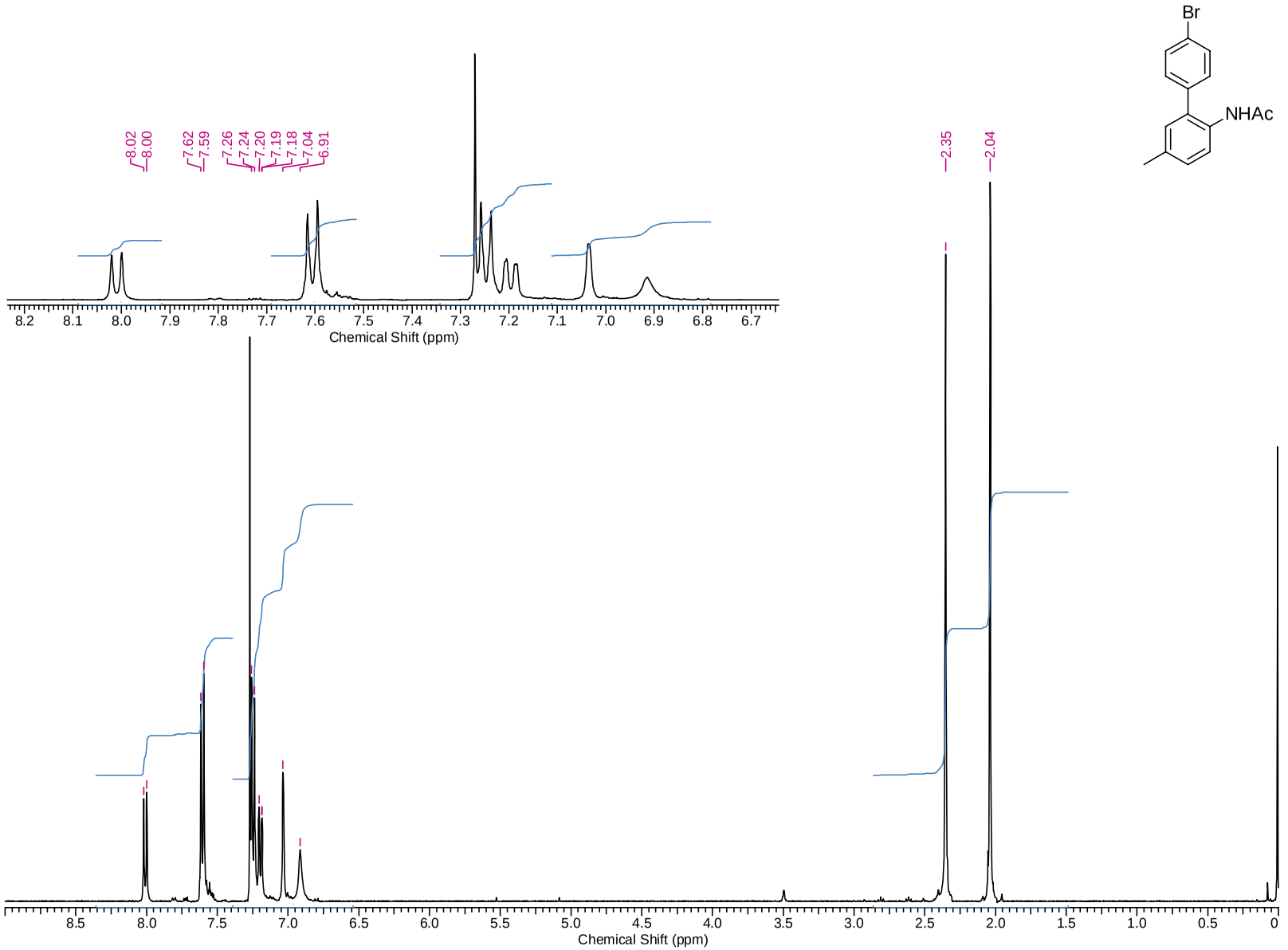

161.65
149.40
147.60
135.27
134.84
130.77
128.76
128.17
121.67
121.42
119.04
117.45
117.29
34.86
31.57
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

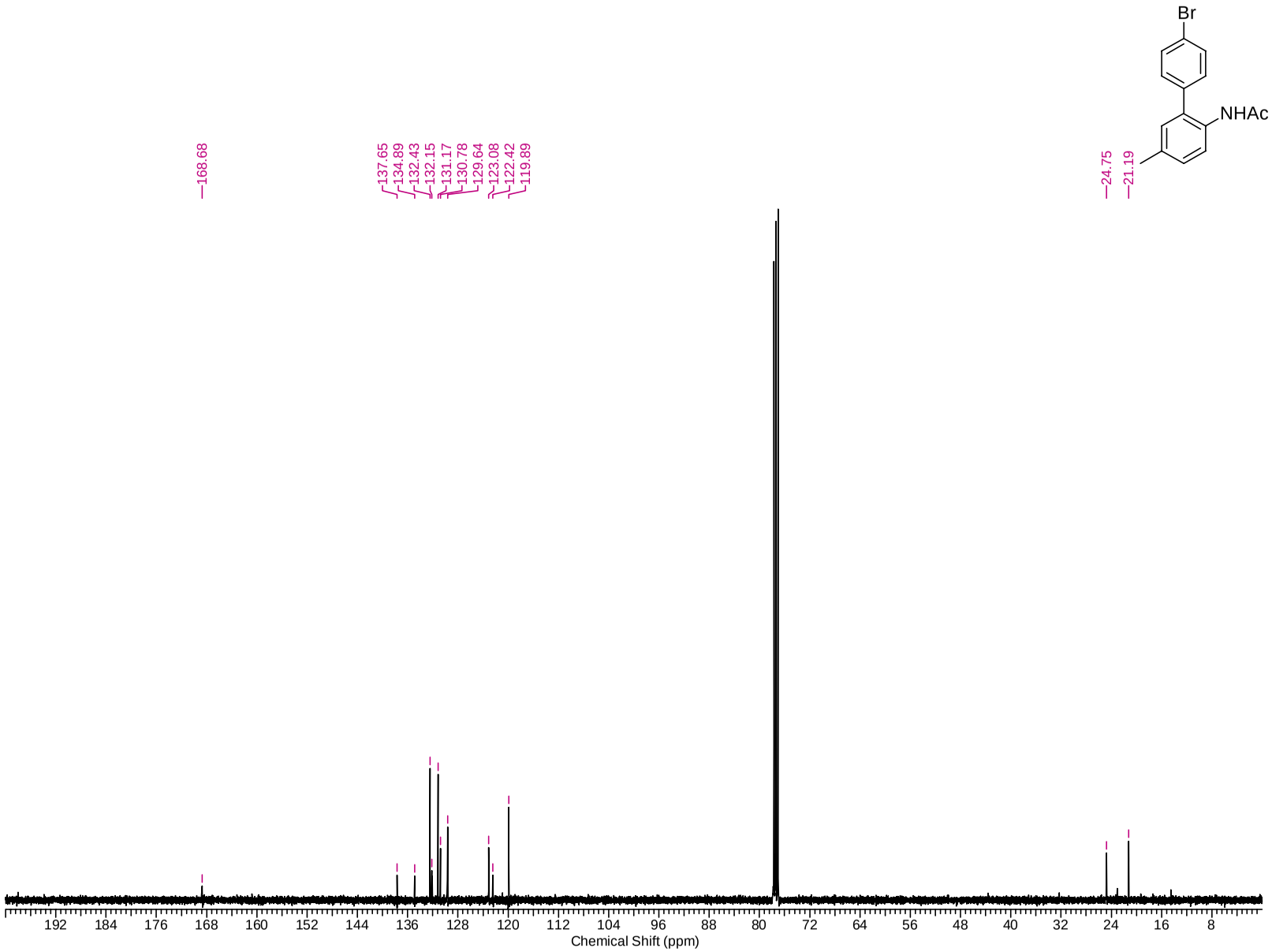

Br
NHPiv
7.55
7.54
7.53
7.53
7.29
7.22
7.22
7.20
7.20
7.16
7.16
6.79
2.28
1.18
Chemical Shift (ppm)
Chemical Shift (ppm)

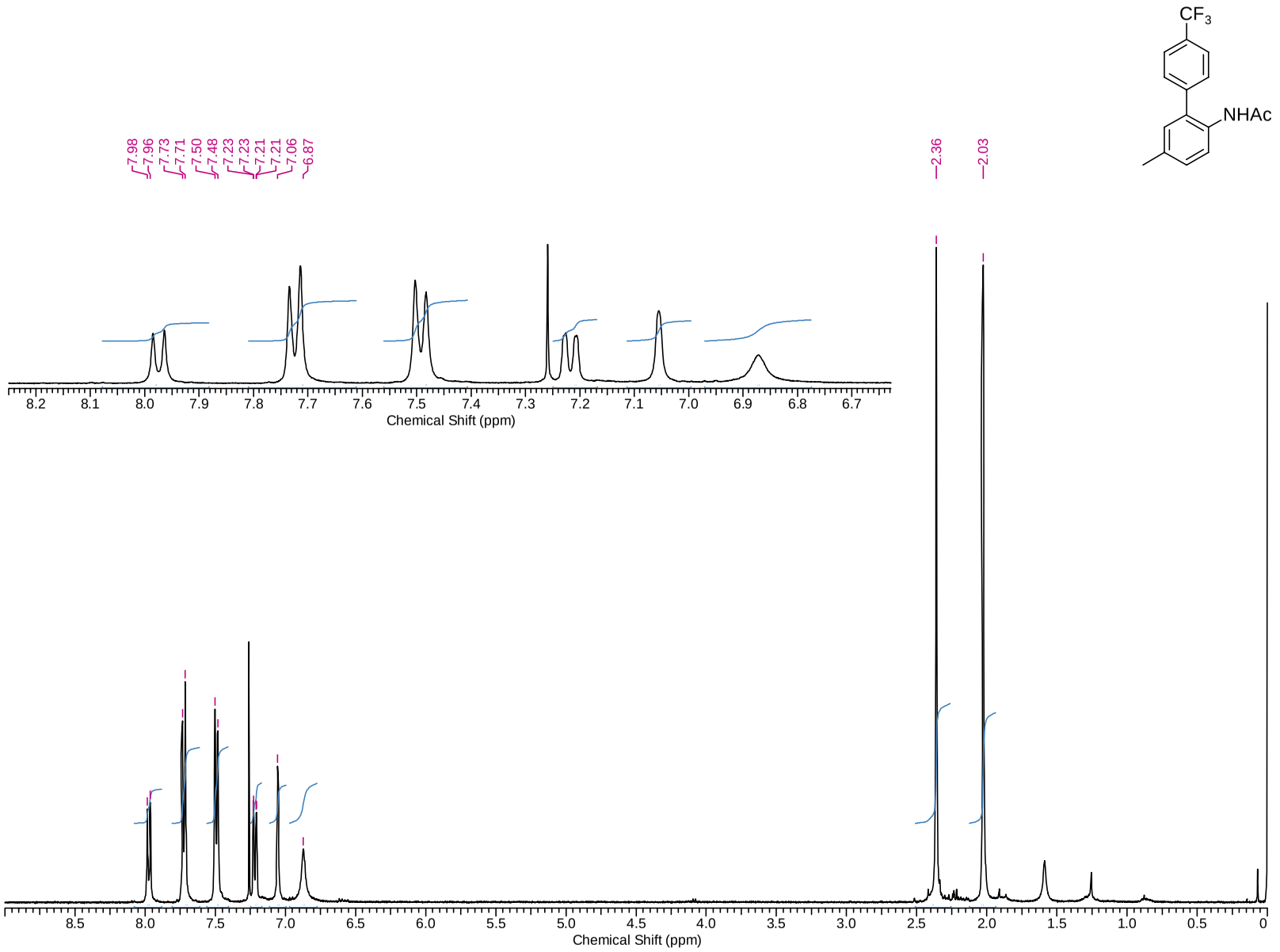

Br
NHPiv
176.80
138.66
136.84
132.59
131.30
130.68
130.40
127.61
127.28
121.56
119.60
39.13
27.56
18.44
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

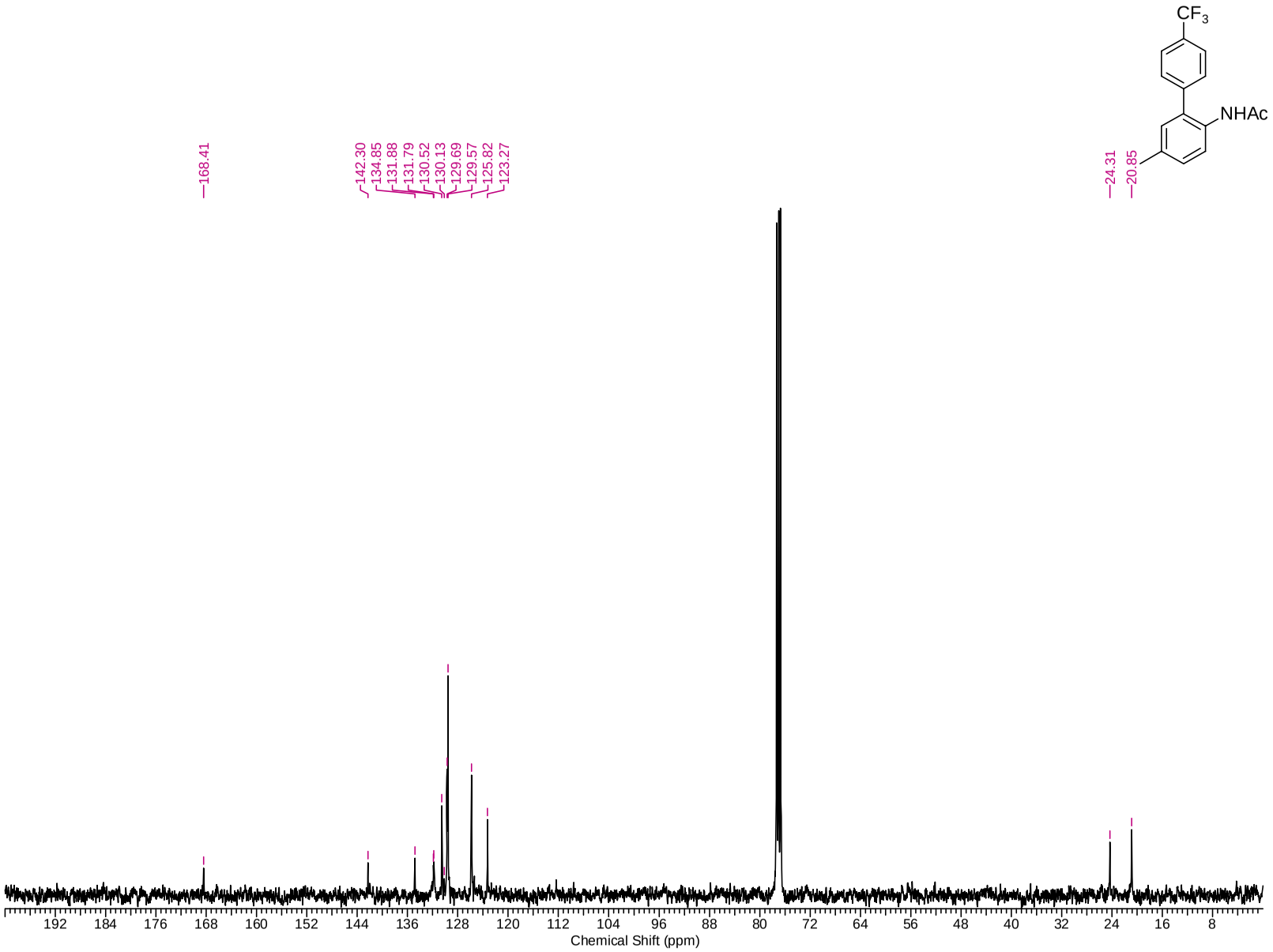

NHPiv
7.24
7.23
7.23
7.20
7.16
7.15
7.15
7.14
6.80
2.39
2.27
1.14
7.6
1.1
3.4
3.9
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

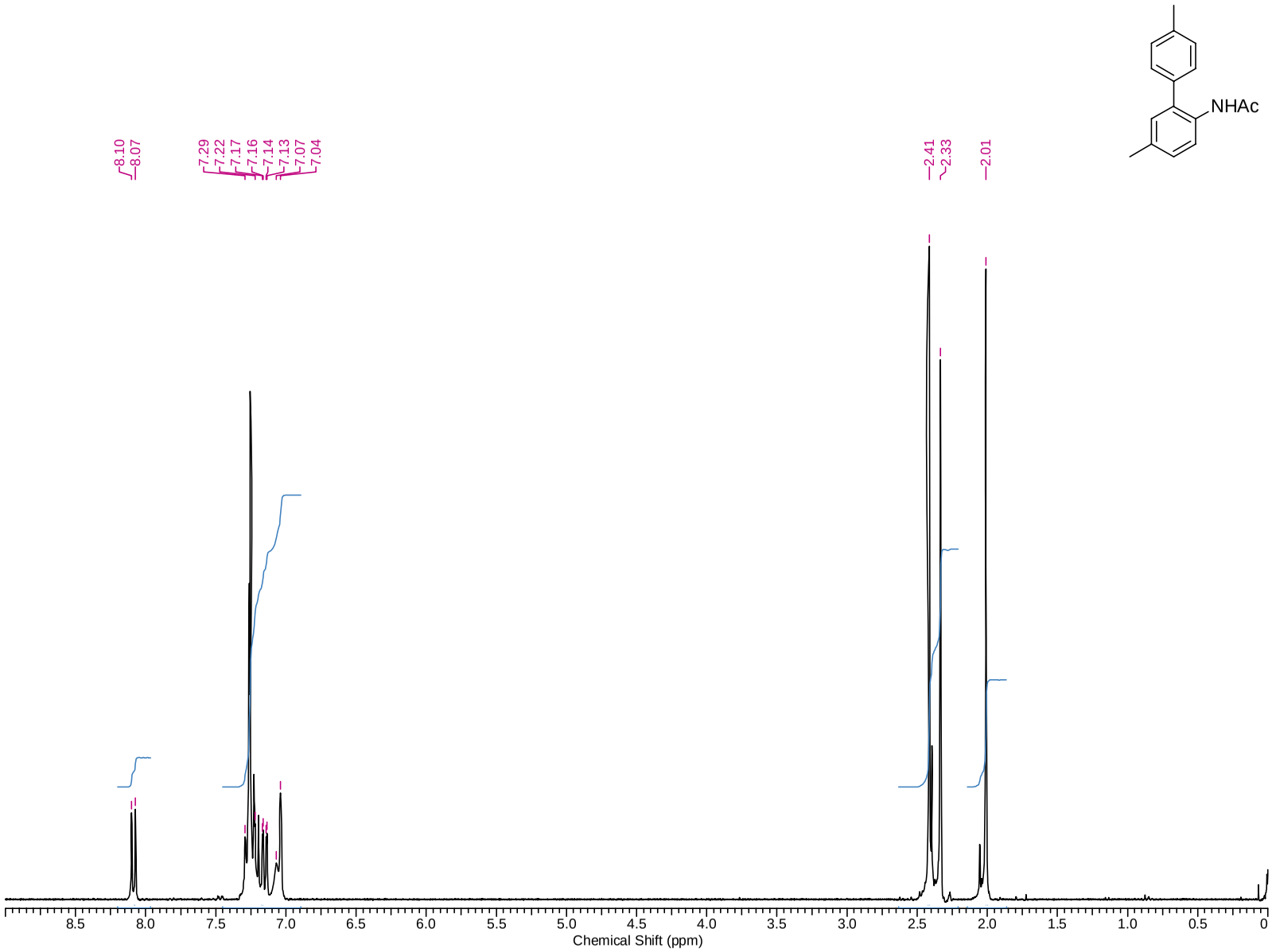

176.64
139.34
136.99
136.59
136.49
132.86
129.83
128.87
127.66
126.88
39.08
27.50
21.16
18.49
NHPiv
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

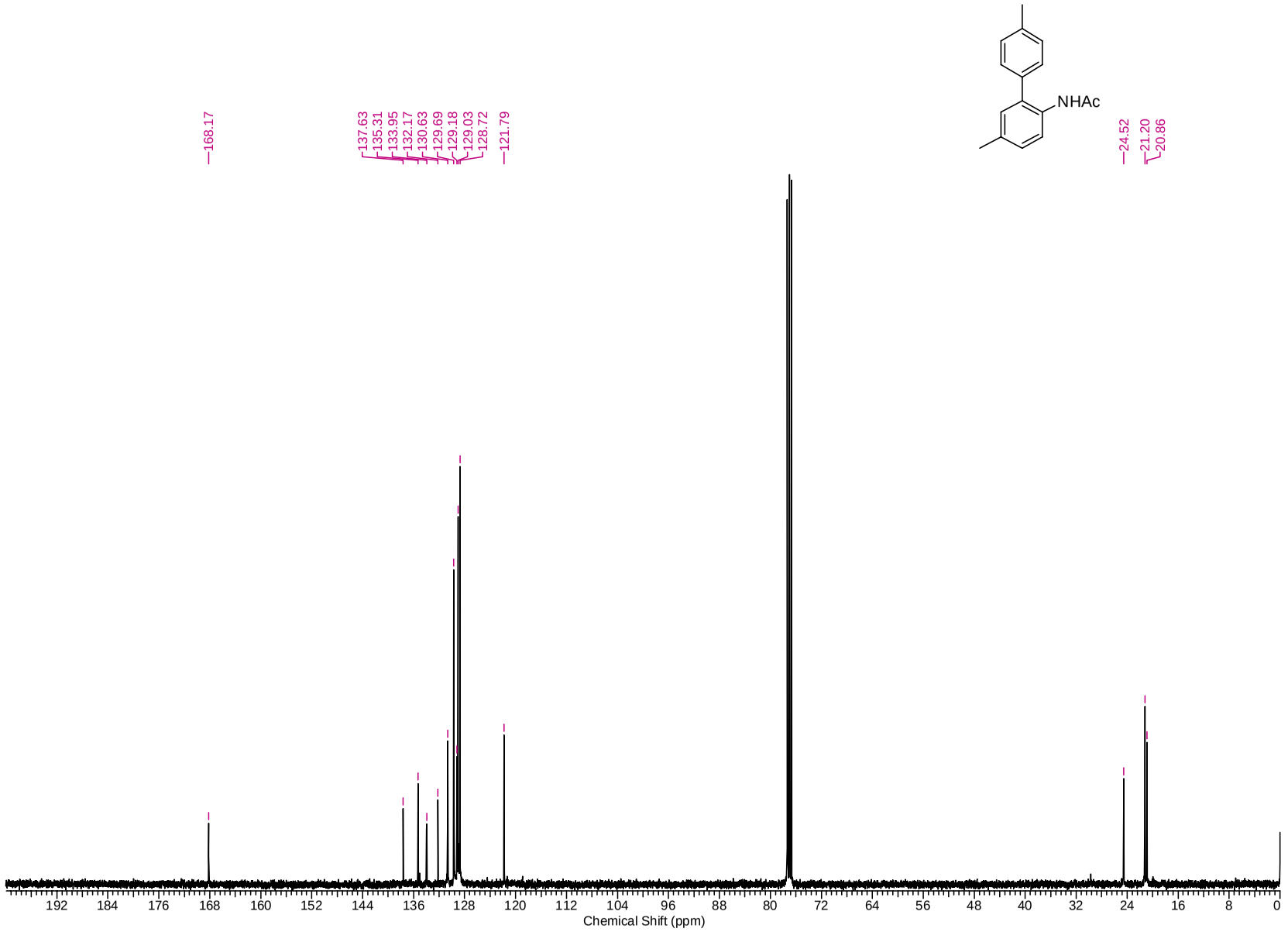

Br
NHAc
8.02
8.00
7.62
7.59
7.26
7.24
7.20
7.19
7.18
7.04
6.91
2.35
2.04
Chemical Shift (ppm)
Chemical Shift (ppm)

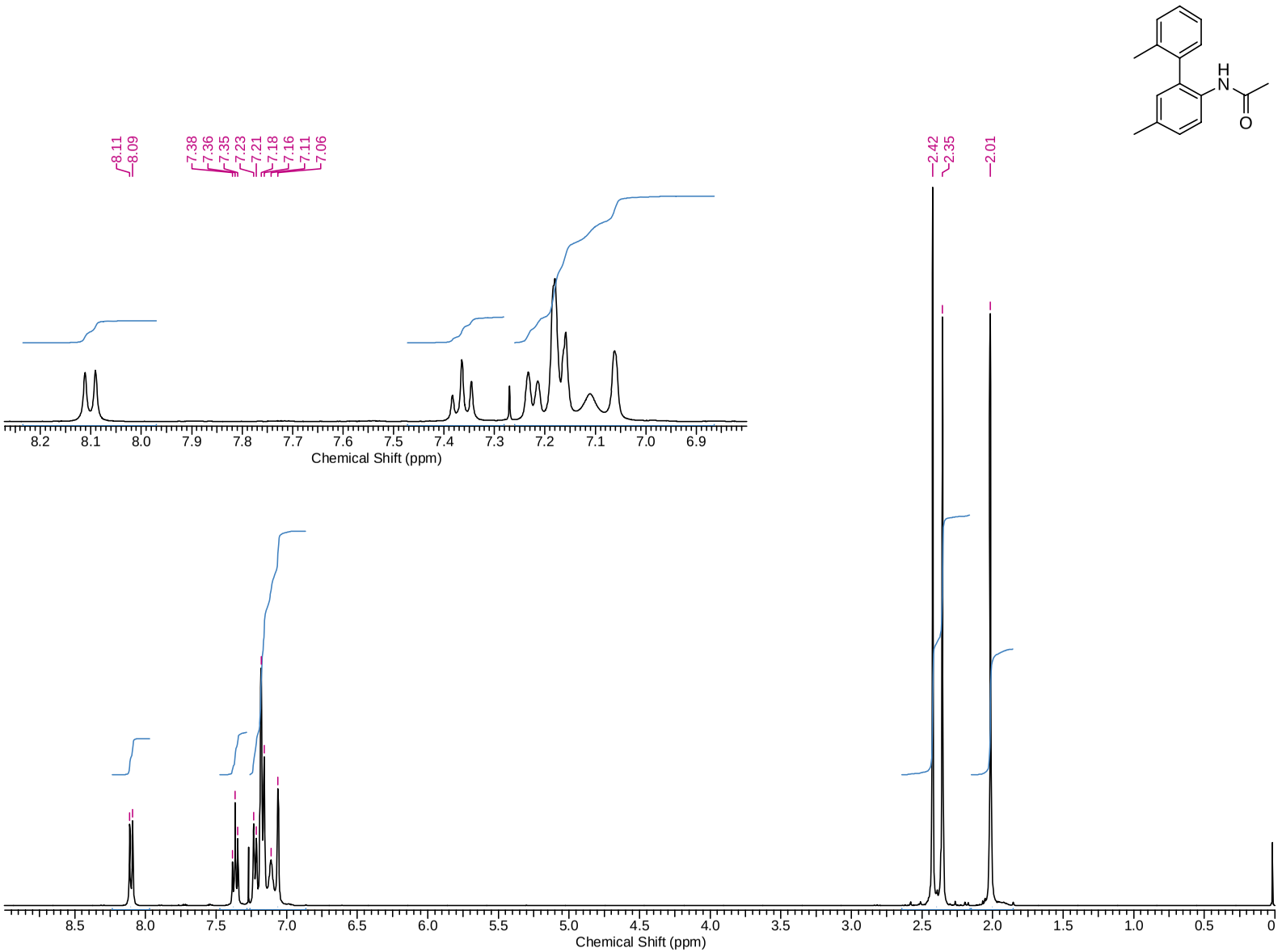

Br
NHAc
168.68
137.65
134.89
132.43
132.15
131.17
130.78
129.64
123.08
122.42
119.89
24.75
21.19
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

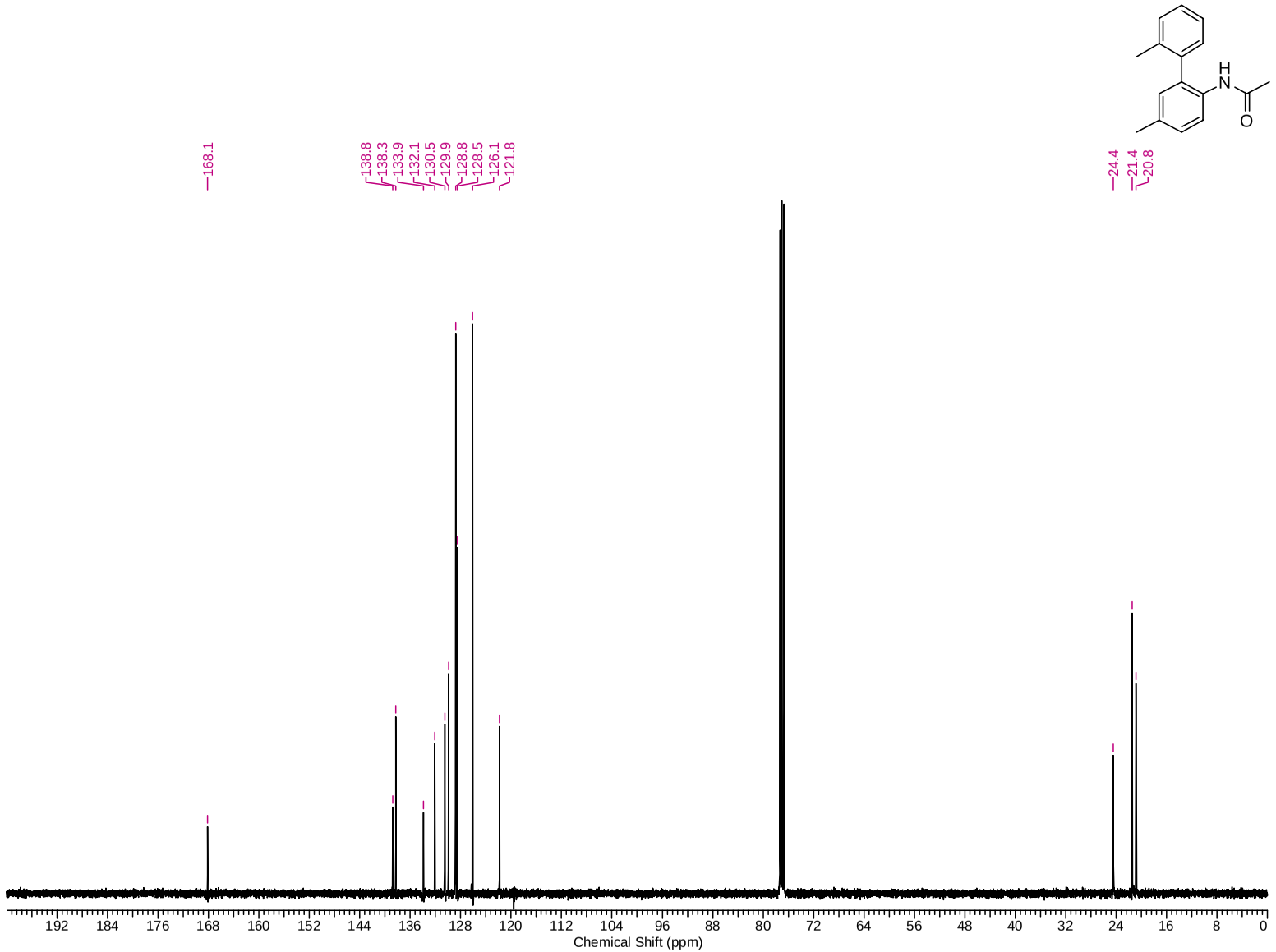

CF3
NHAc
7.98
7.96
7.73
7.71
7.50
7.48
7.23
7.23
7.21
7.21
7.06
6.87
2.36
2.03
Chemical Shift (ppm)
Chemical Shift (ppm)

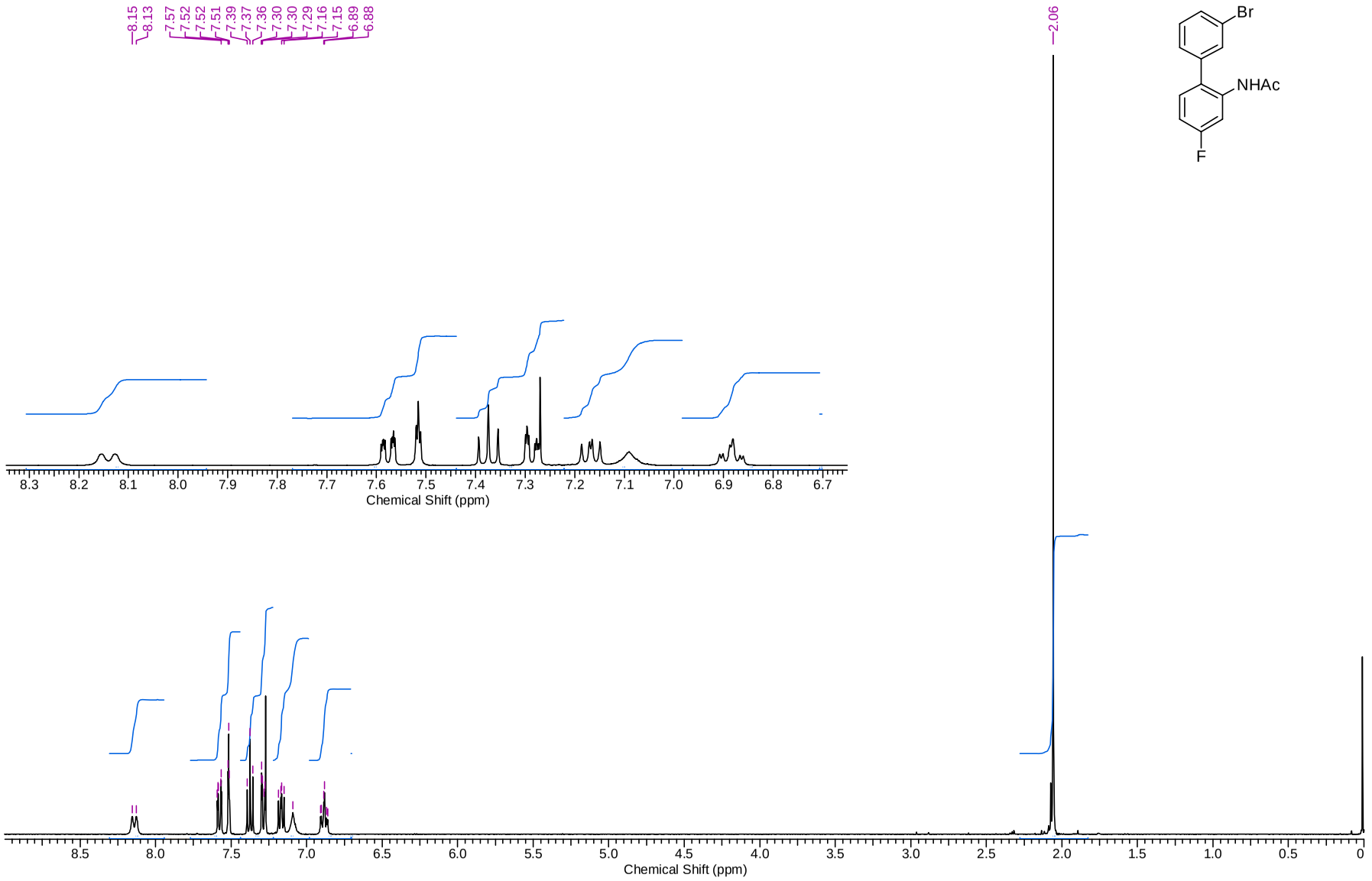

CF3
NHAc
168.41
142.30
134.85
131.88
131.79
130.52
130.13
129.69
129.57
125.82
123.27
24.31
20.85
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

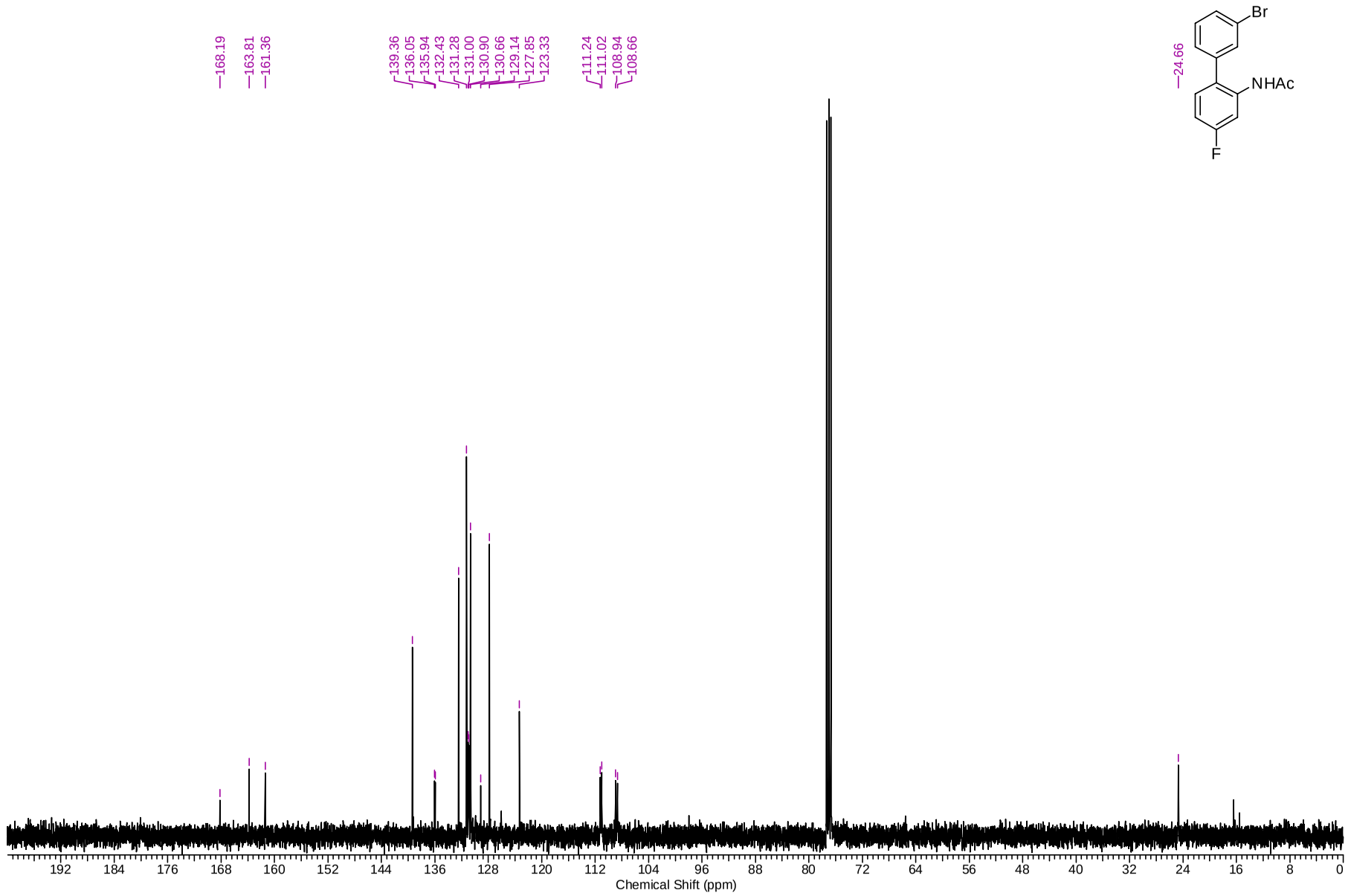

NHAc
8.10
8.07
7.29
7.22
7.17
7.16
7.14
7.13
7.07
7.04
2.41
2.33
2.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

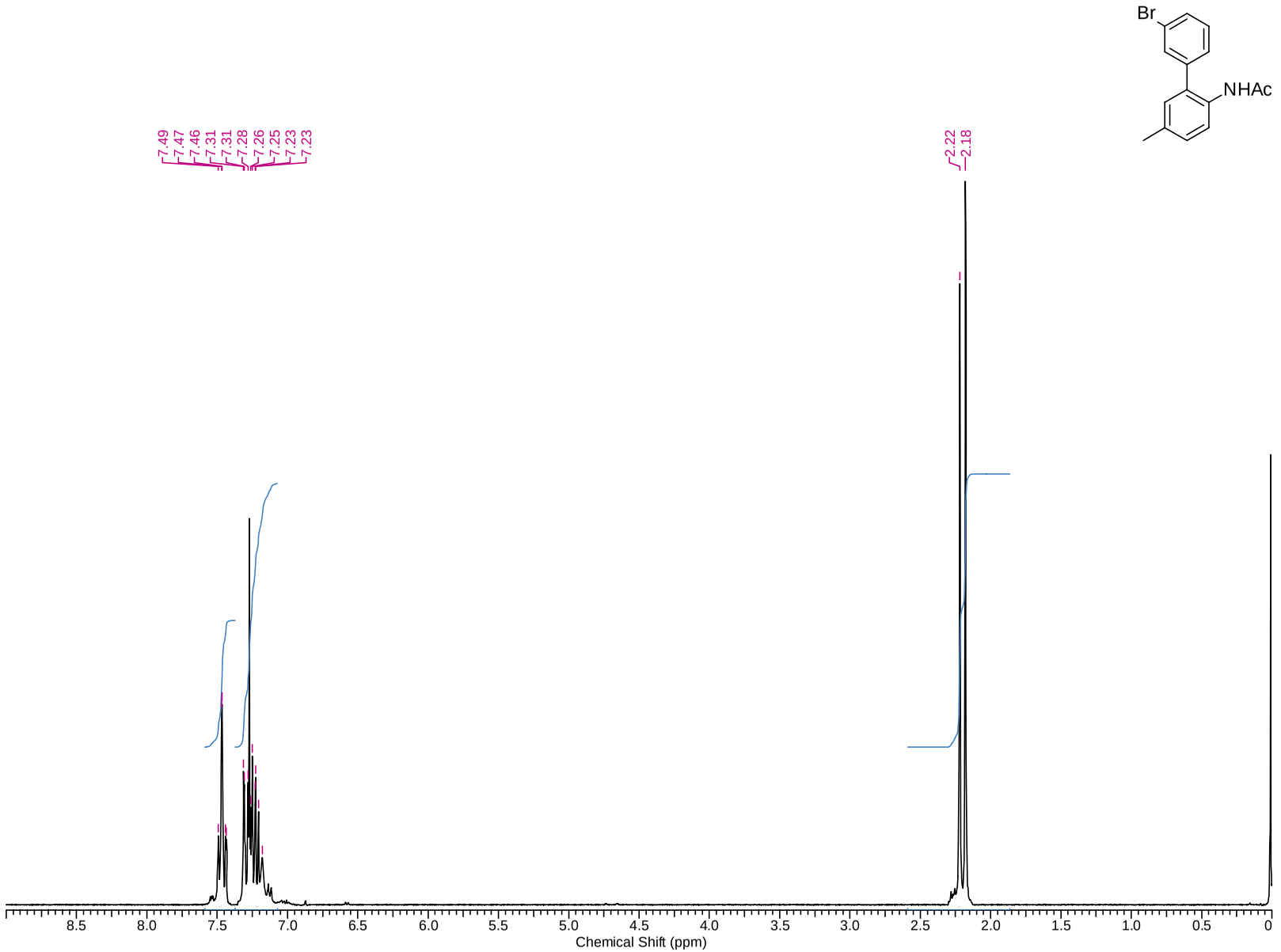

NHAc
168.17
137.63
135.31
133.95
132.17
130.63
129.69
129.18
129.03
128.72
121.79
24.52
21.20
20.86
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

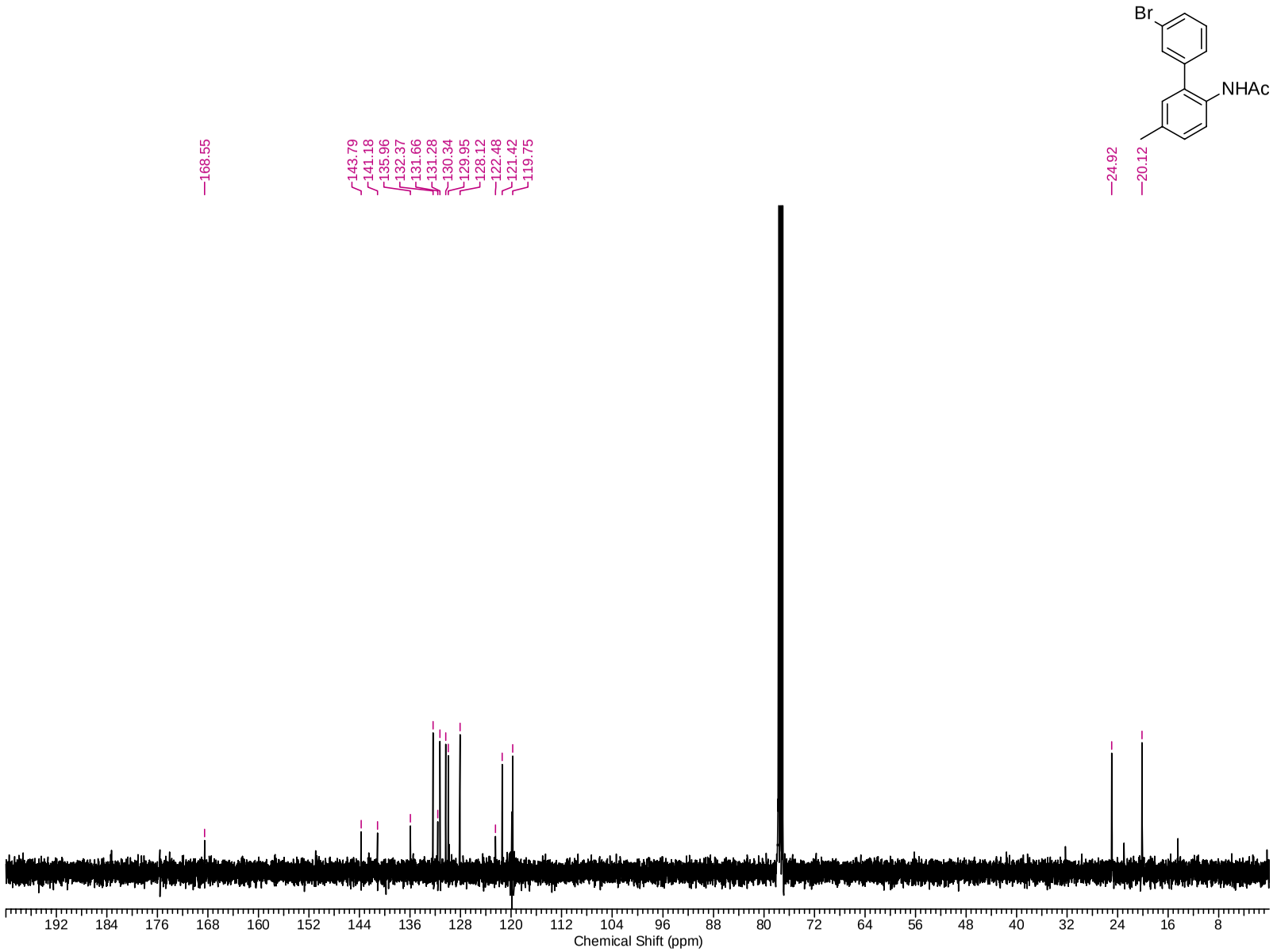

8.11
8.09
7.38
7.36
7.35
7.23
7.21
7.18
7.16
7.11
7.06
2.42
2.35
2.01
H
N
O
Chemical Shift (ppm)
Chemical Shift (ppm)

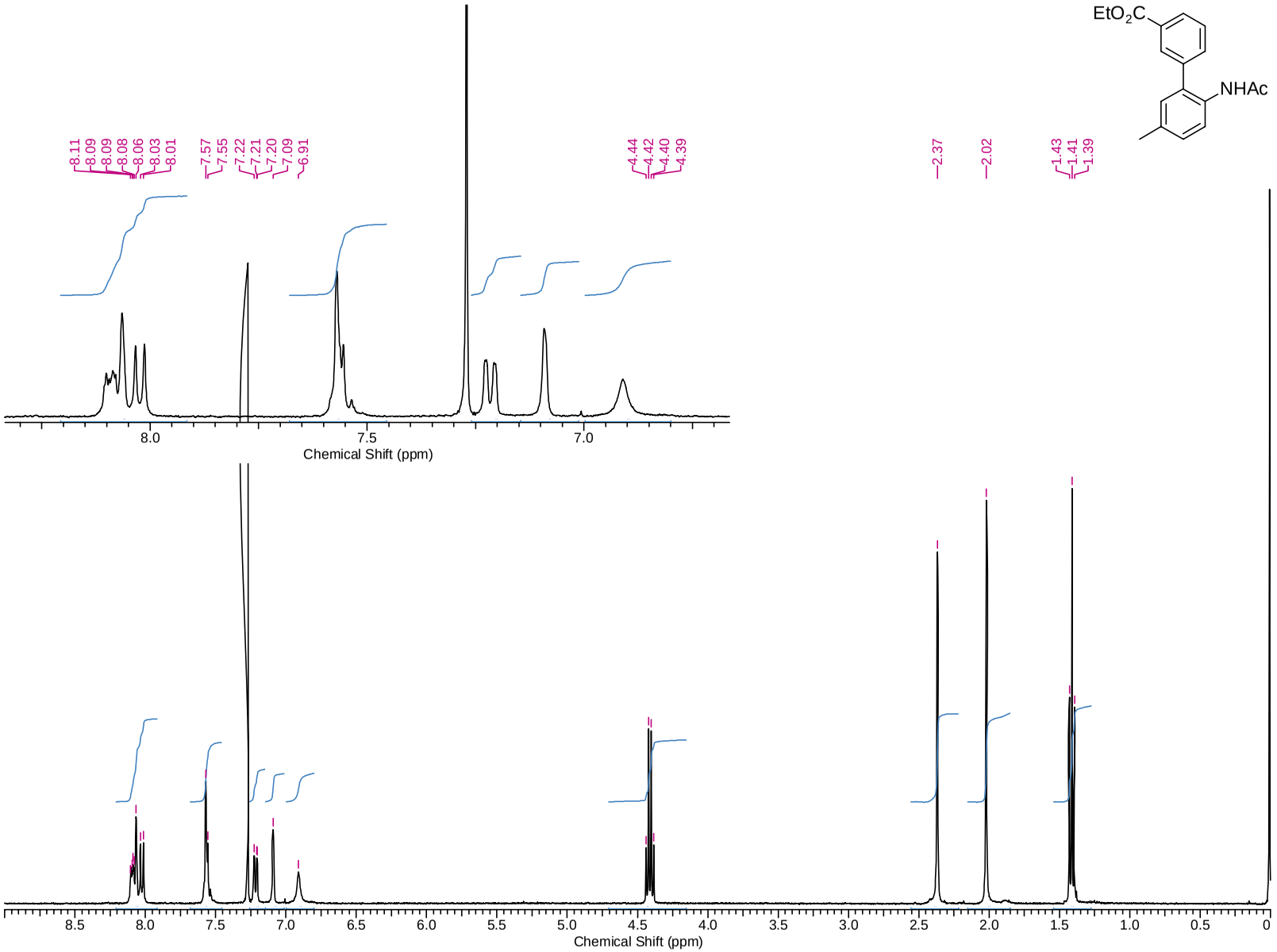

168.1
138.8
138.3
133.9
132.1
130.5
129.9
128.8
128.5
126.1
121.8
24.4
21.4
20.8
H
N
O
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

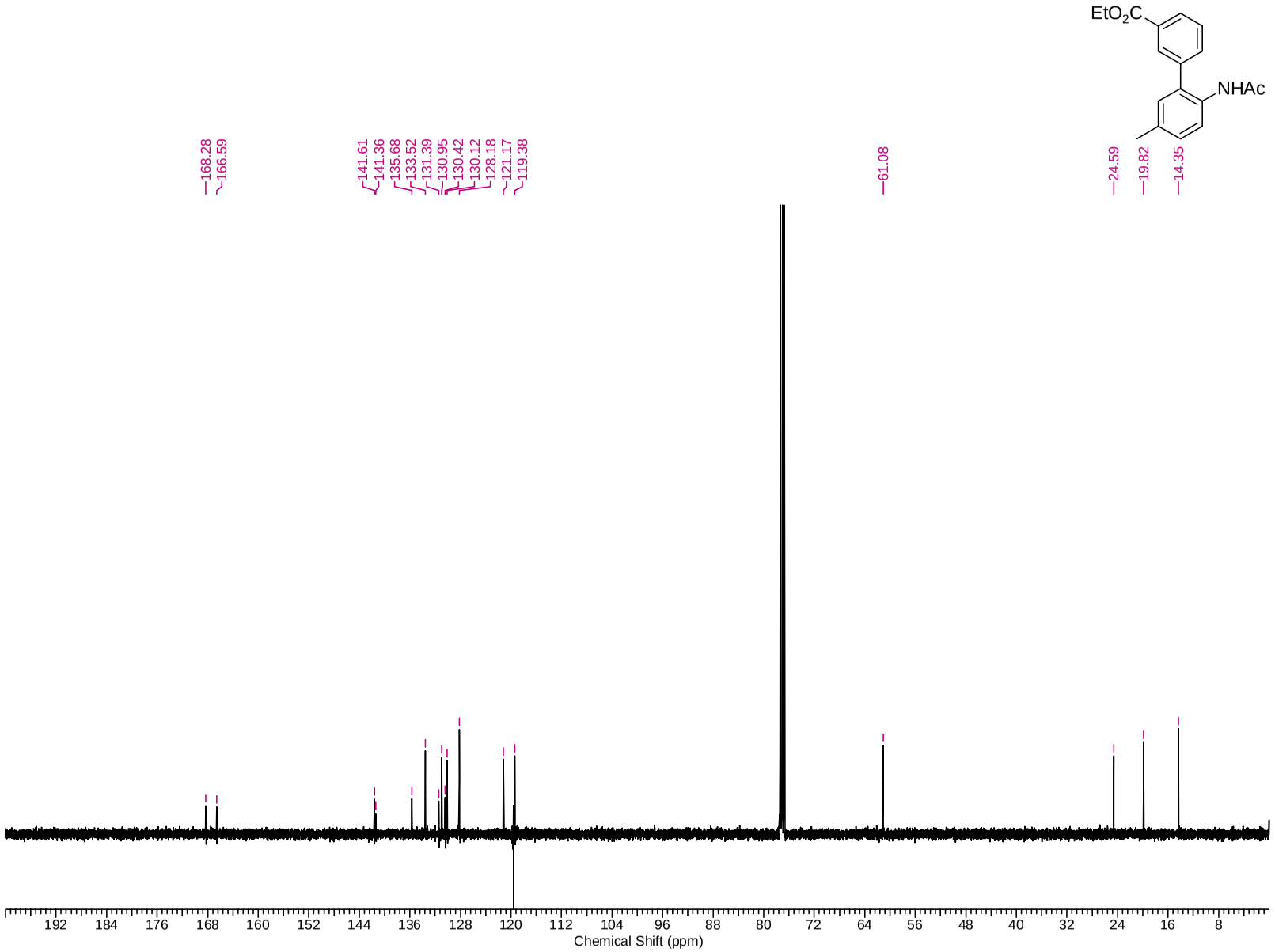

8.15
8.13
7.57
7.52
7.52
7.51
7.39
7.37
7.36
7.30
7.30
7.29
7.16
7.15
6.89
6.88
2.06
Br
NHAc
F
Chemical Shift (ppm)
Chemical Shift (ppm)

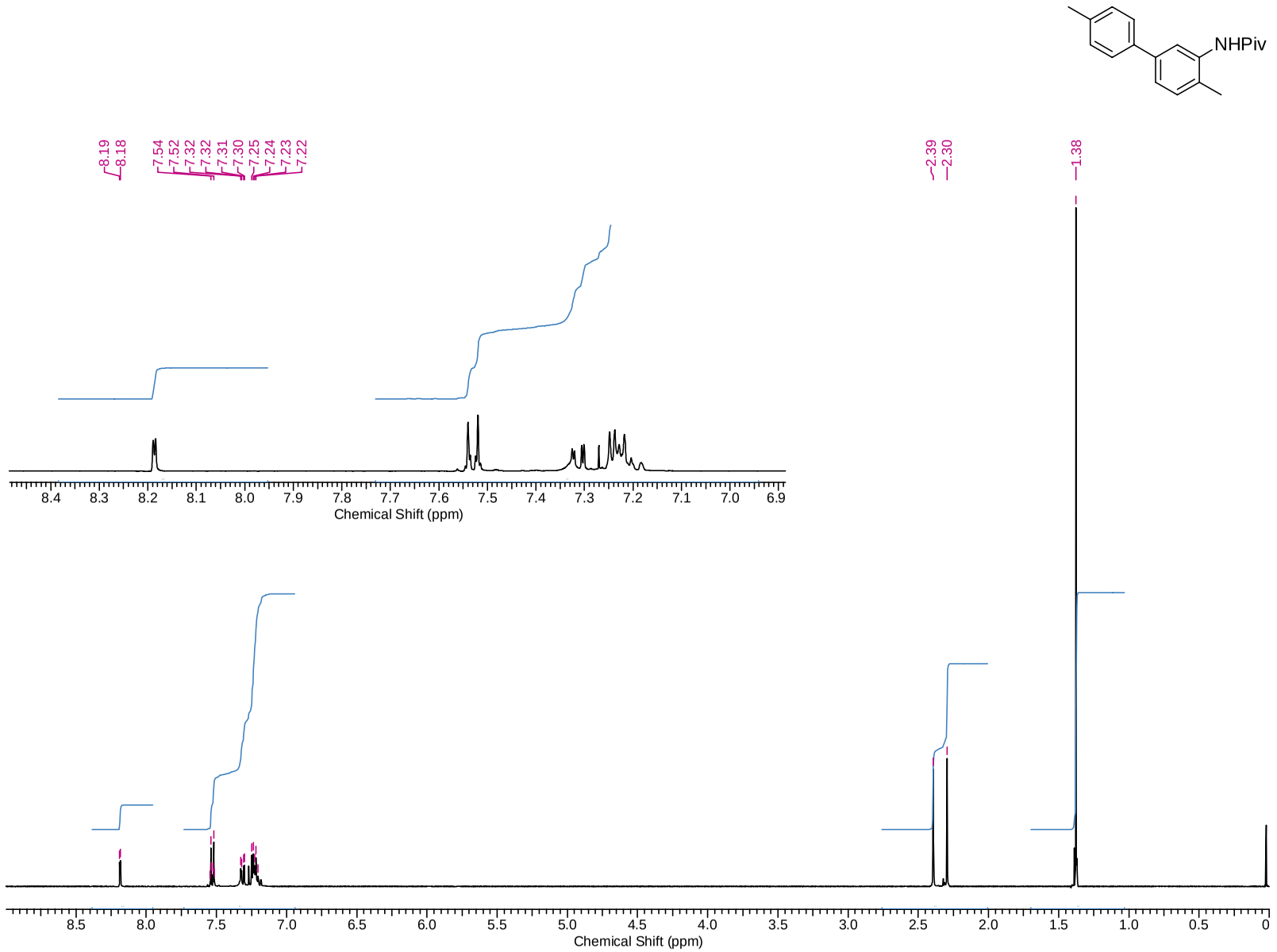

168.19
163.81
161.36
139.36
136.05
135.94
132.43
131.28
131.00
130.90
130.66
129.14
127.85
123.33
111.24
111.02
108.94
108.66
24.66
Br
NHAc
F
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

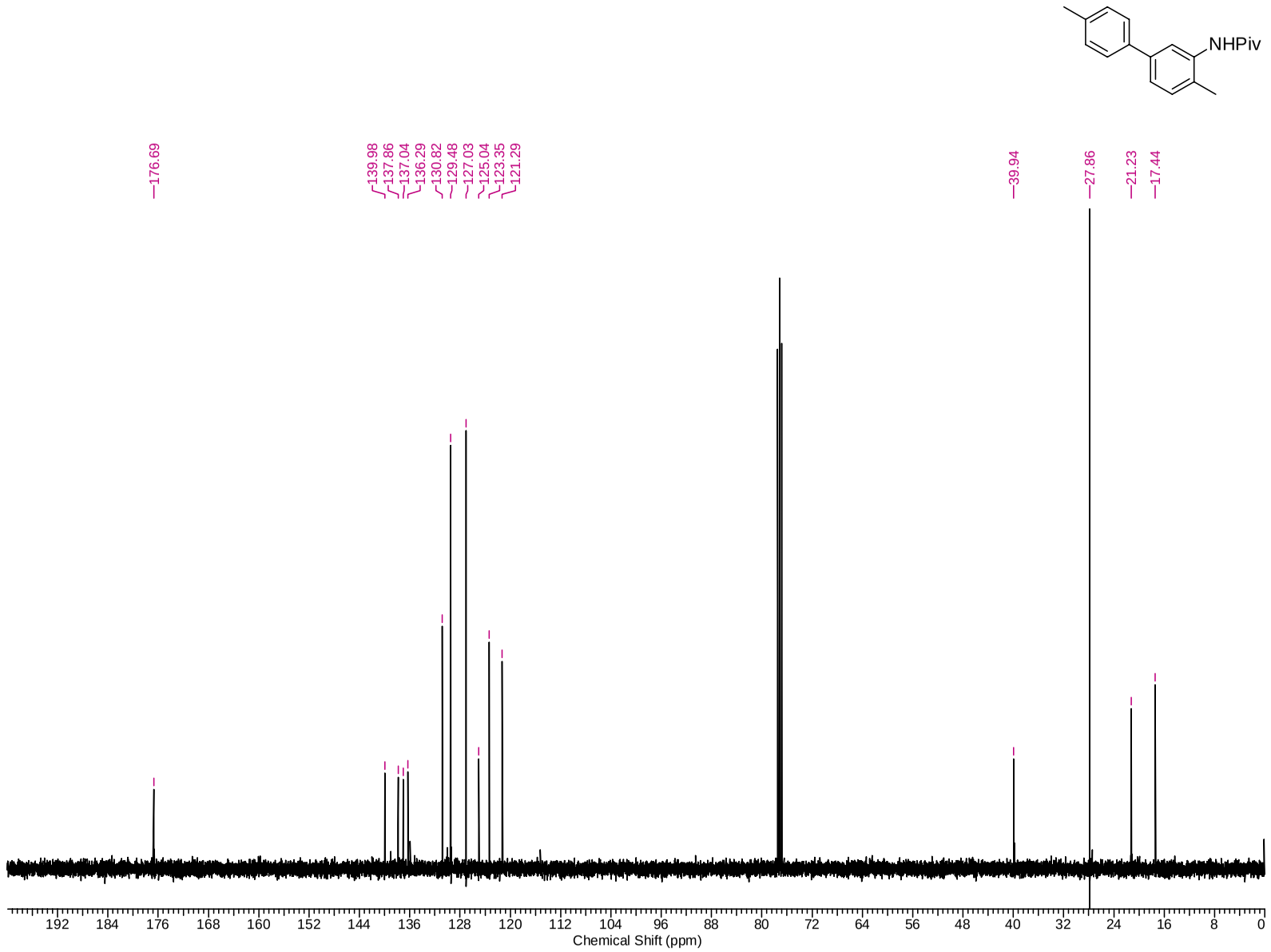

Br
NHAc
7.49
7.47
7.46
7.31
7.31
7.28
7.26
7.25
7.23
7.23
2.22
2.18
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

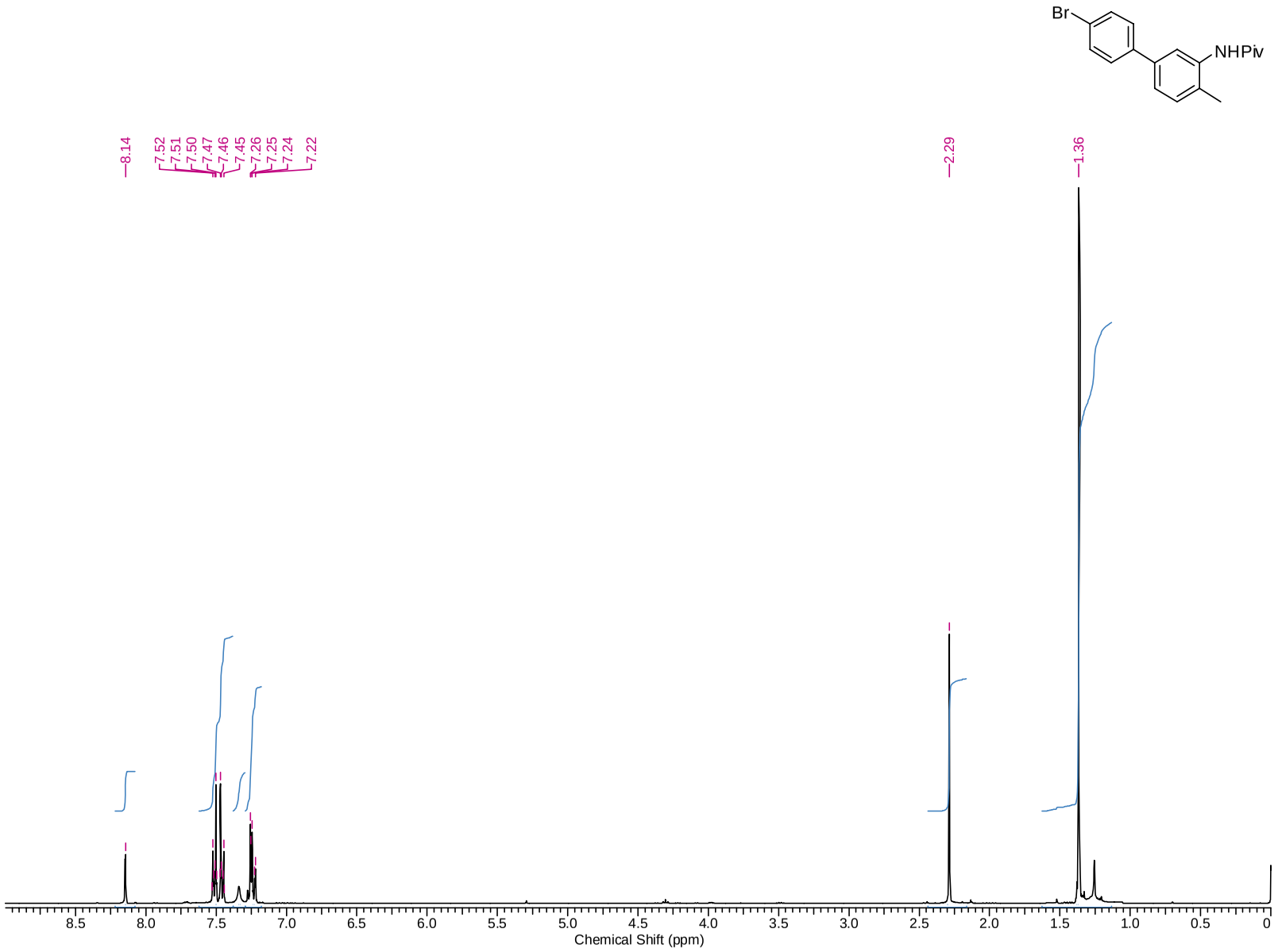

Br
NHAc
168.55
143.79
141.18
135.96
132.37
131.66
131.28
130.34
129.95
128.12
122.48
121.42
119.75
24.92
20.12
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

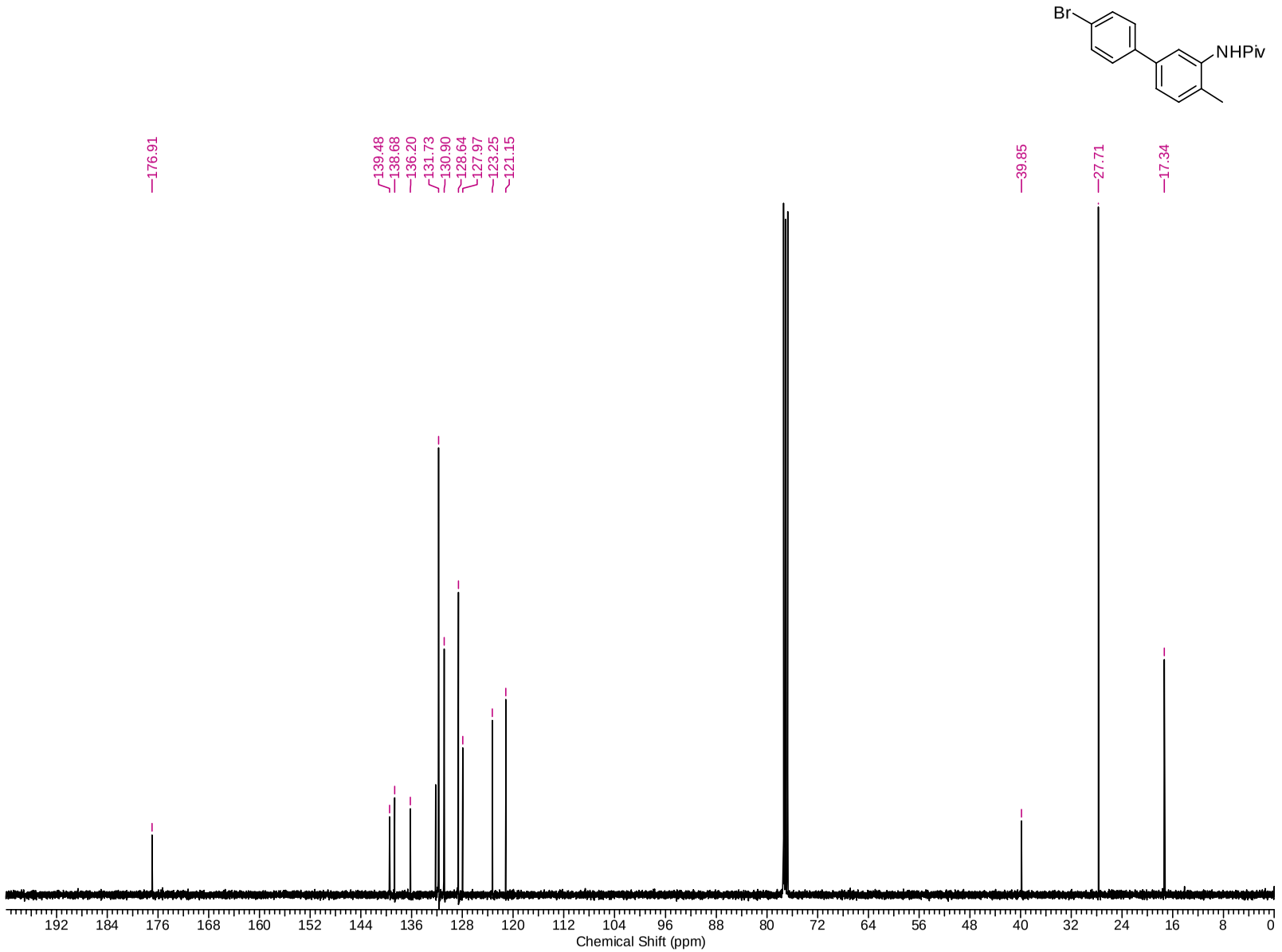

EtO2C
NHAc
8.11
8.09
8.09
8.08
8.06
8.03
8.01
7.57
7.55
7.22
7.21
7.20
7.09
6.91
4.44
4.42
4.40
4.39
2.37
2.02
1.43
1.41
1.39
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

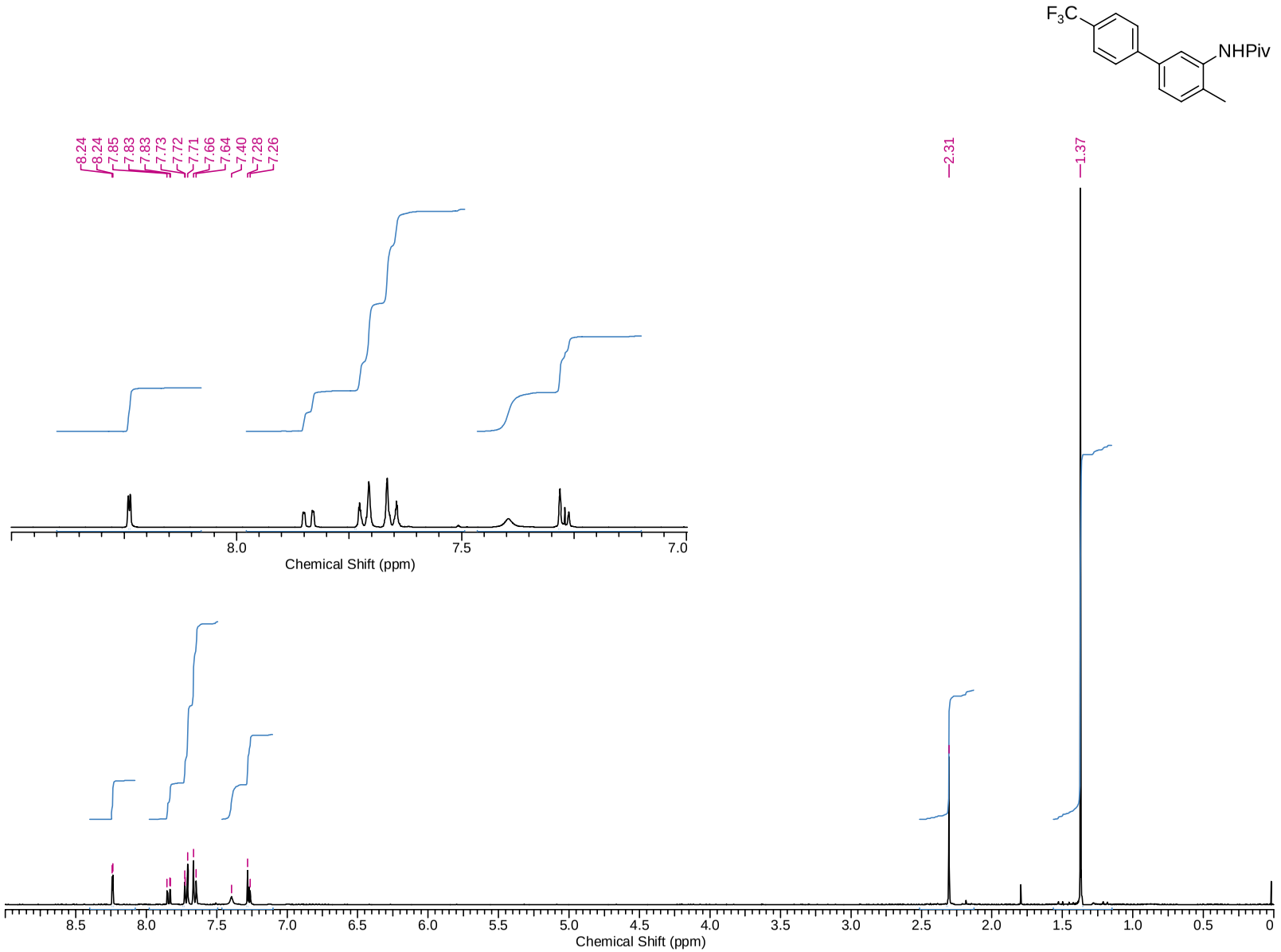

EtO2C
NHAc
168.28
166.59
141.61
141.36
135.68
133.52
131.39
130.95
130.42
130.12
128.18
121.17
119.38
61.08
24.59
19.82
14.35
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

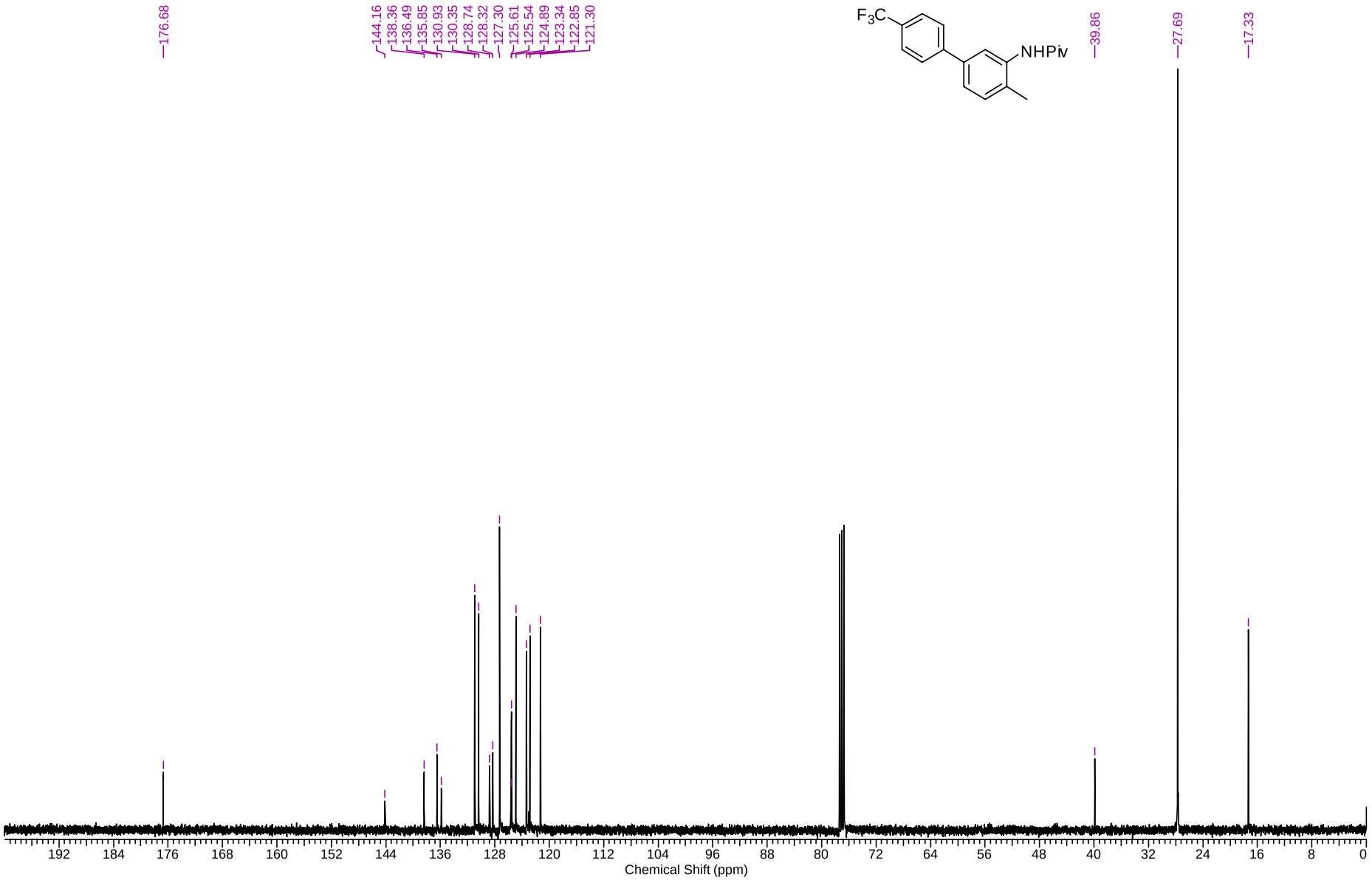

NHPiv
8.19
8.18
7.54
7.52
7.32
7.32
7.31
7.30
7.25
7.24
7.23
7.22
2.39
2.30
1.38
Chemical Shift (ppm)
Chemical Shift (ppm)

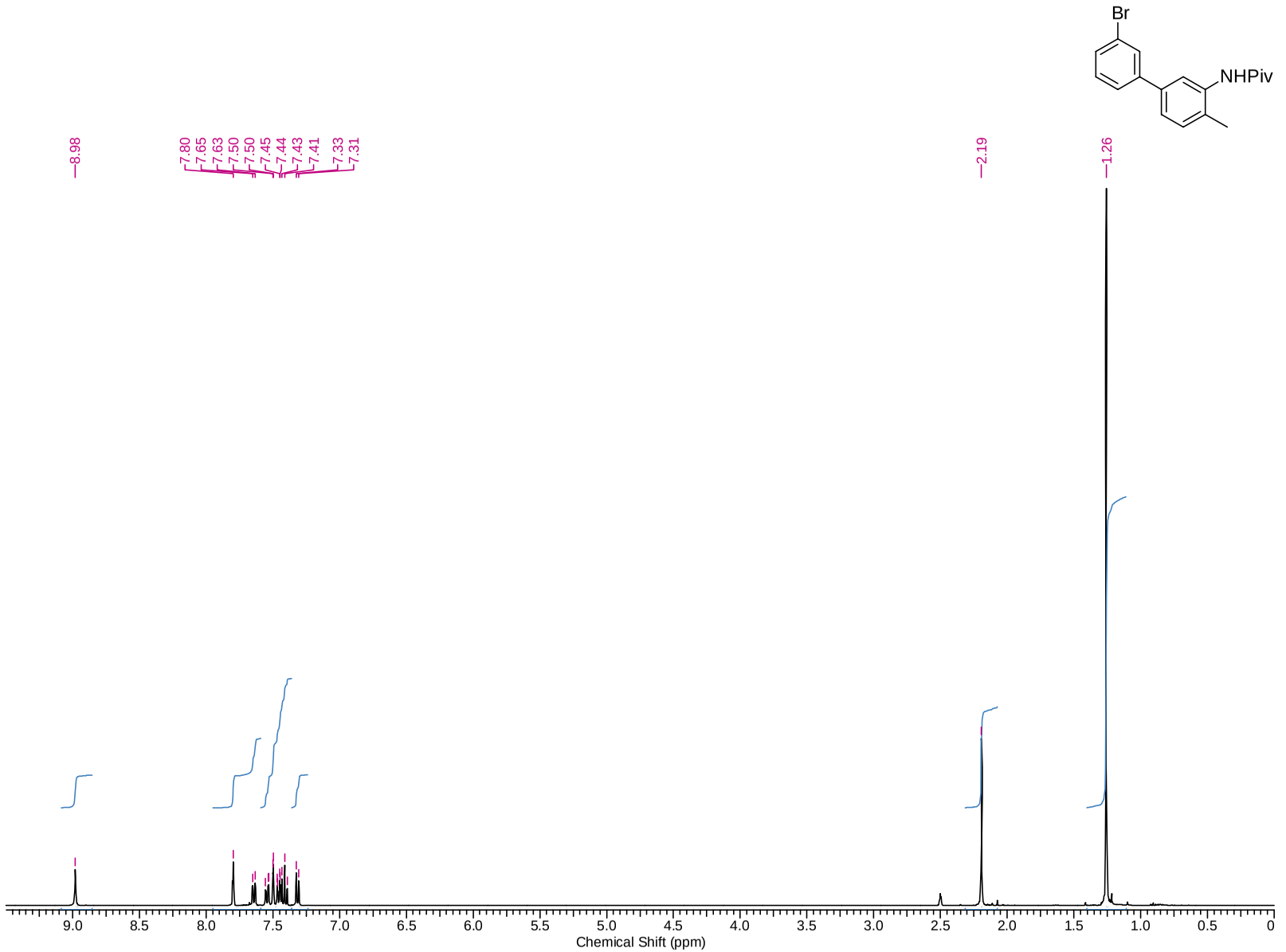

NHPiv
176.69
139.98
137.86
137.04
136.29
130.82
129.48
127.03
125.04
123.35
121.29
39.94
27.86
21.23
17.44
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

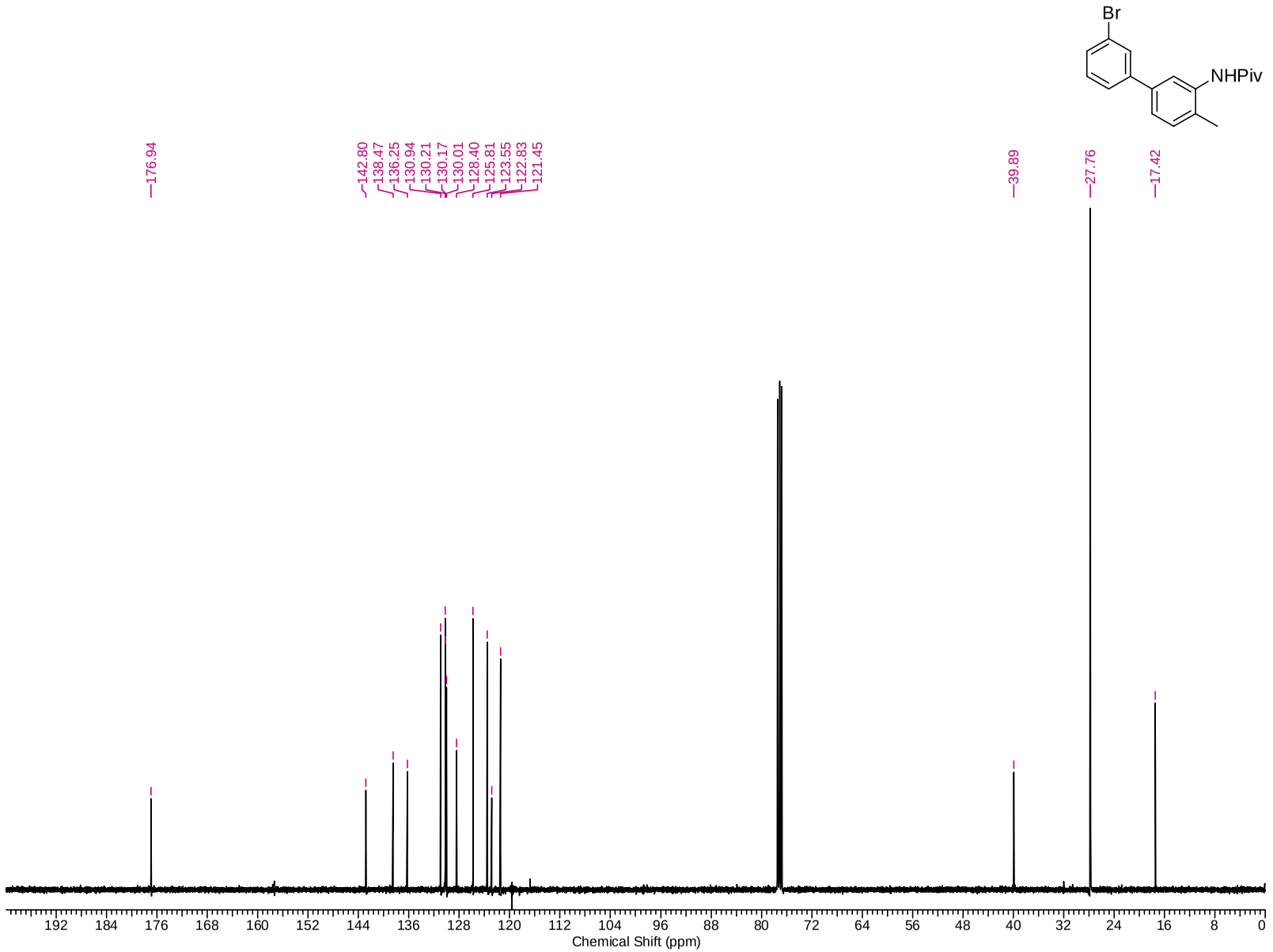

Br
NHPiv
8.14
7.52
7.51
7.50
7.47
7.46
7.45
7.26
7.25
7.24
7.22
2.29
1.36
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

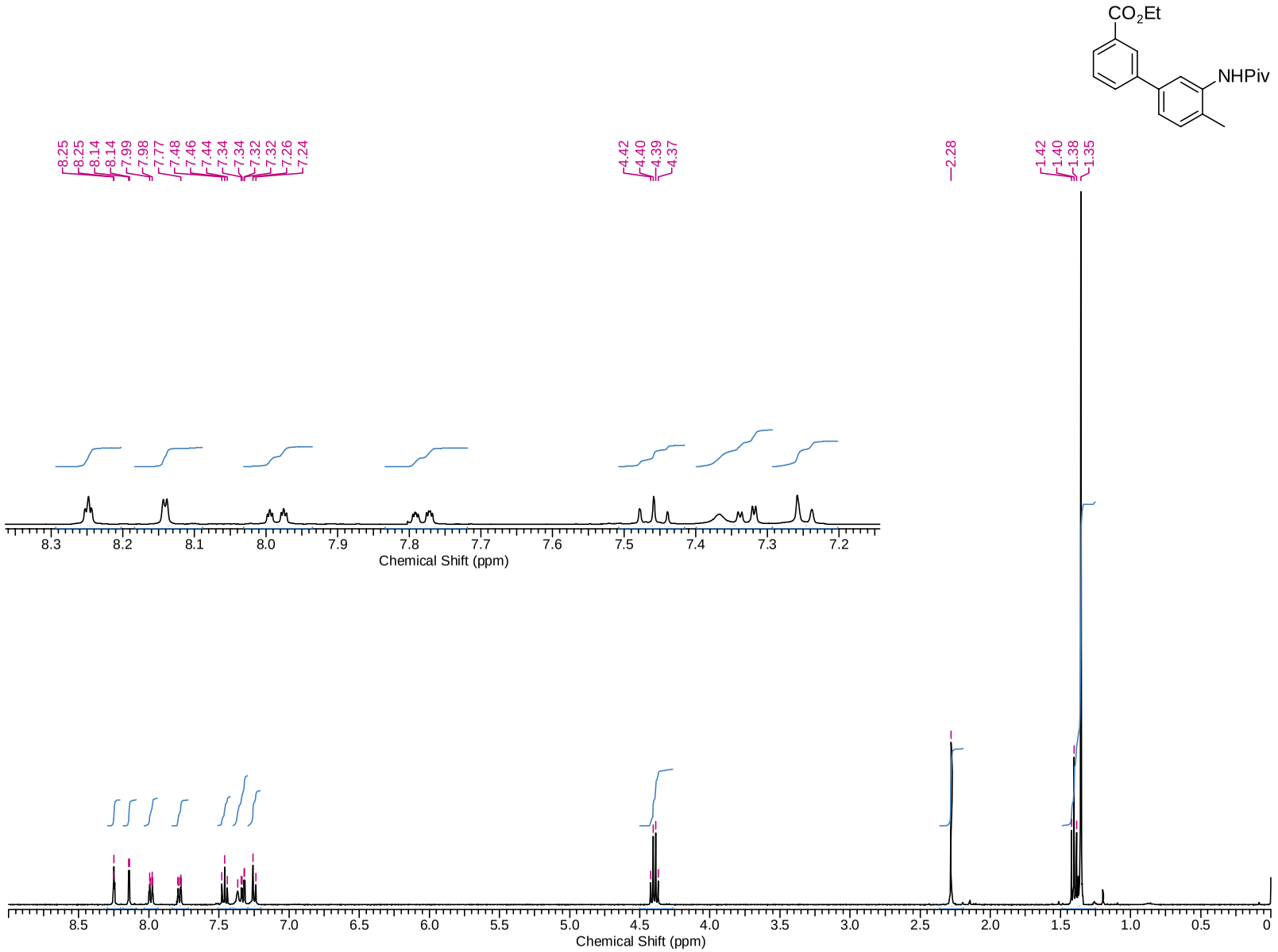

Br
NHPiv
176.91
139.48
138.68
136.20
131.73
130.90
128.64
127.97
123.25
121.15
39.85
27.71
17.34
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

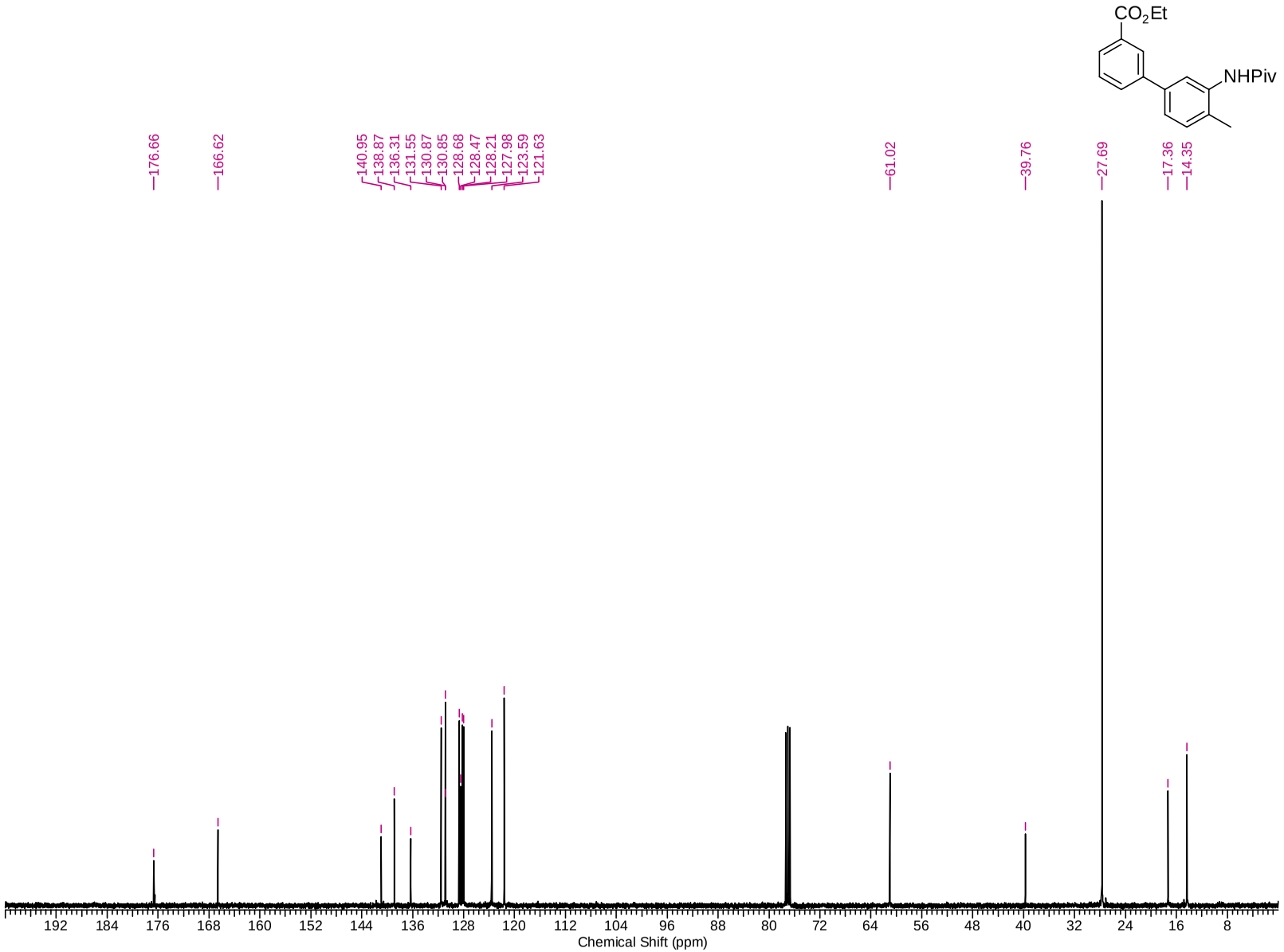

F3C
NHPiv
8.24
8.24
7.85
7.83
7.83
7.73
7.72
7.71
7.66
7.64
7.40
7.28
7.26
2.31
1.37
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

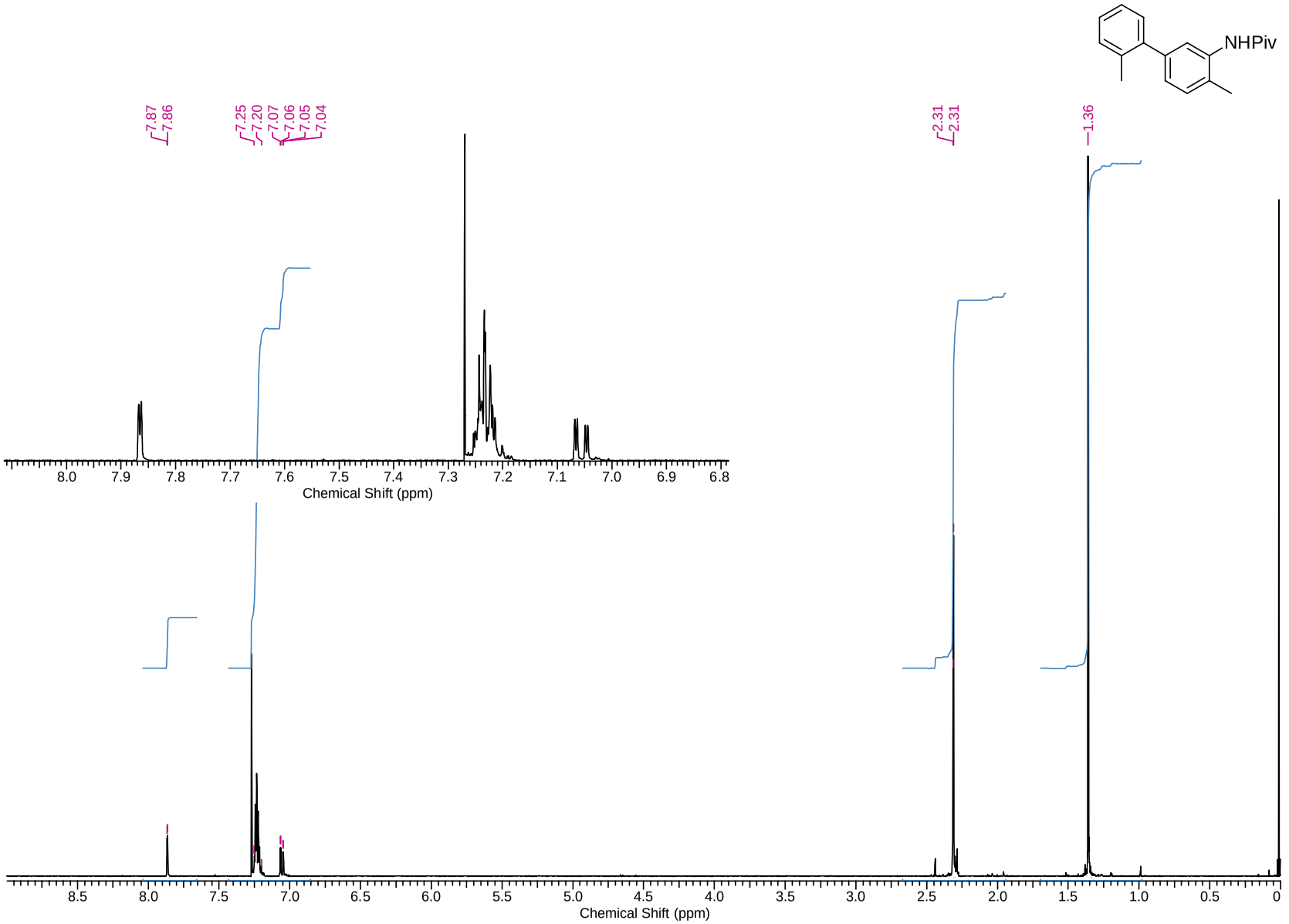

176.68
144.16
138.36
136.49
135.85
130.93
130.35
128.74
128.32
127.30
125.61
125.54
124.89
123.34
122.85
121.30
F3C
NHPiv
39.86
27.69
17.33
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

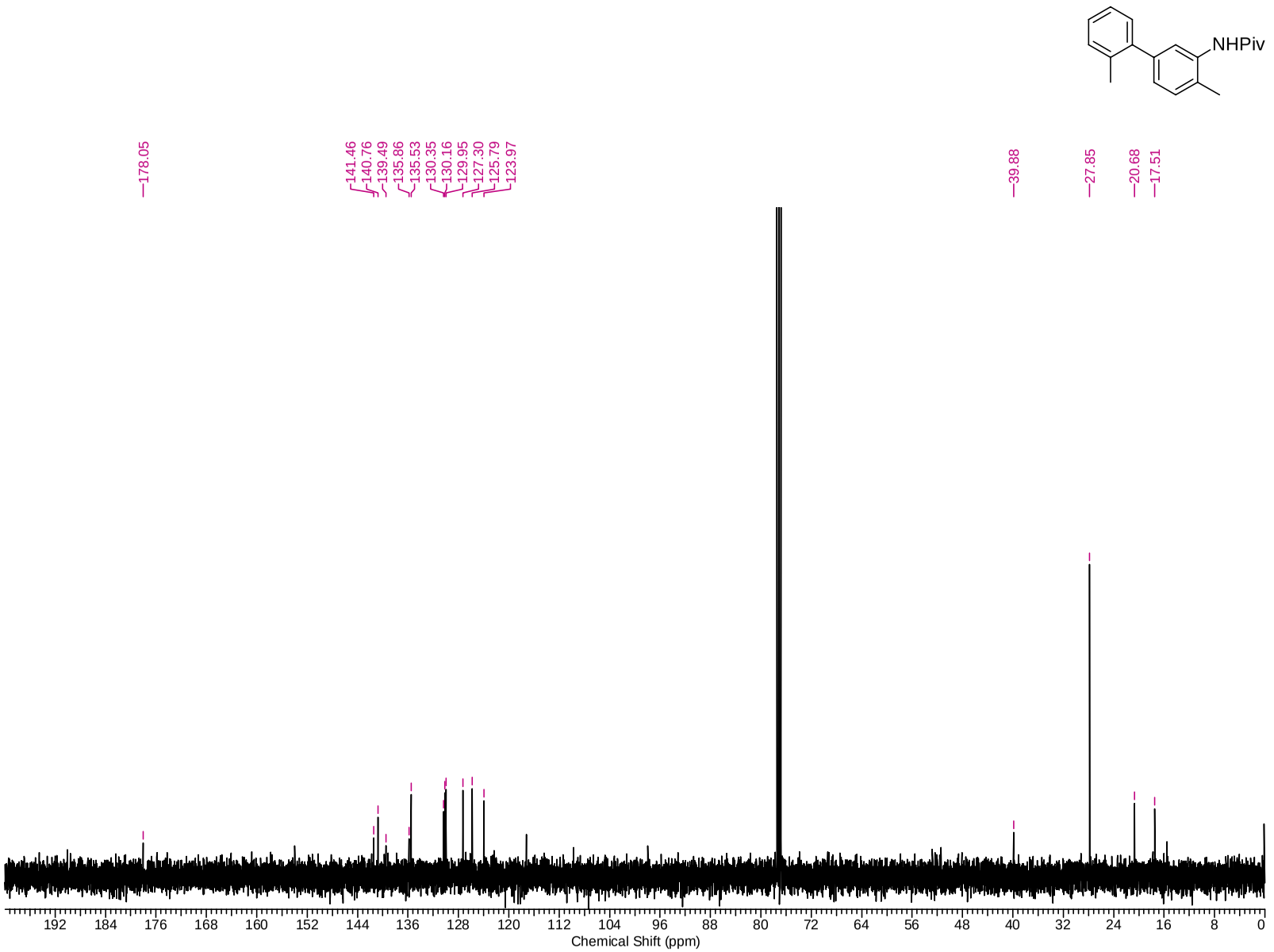

Br
NHPiv
8.98
7.80
7.65
7.63
7.50
7.50
7.45
7.44
7.43
7.41
7.33
7.31
2.19
1.26
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

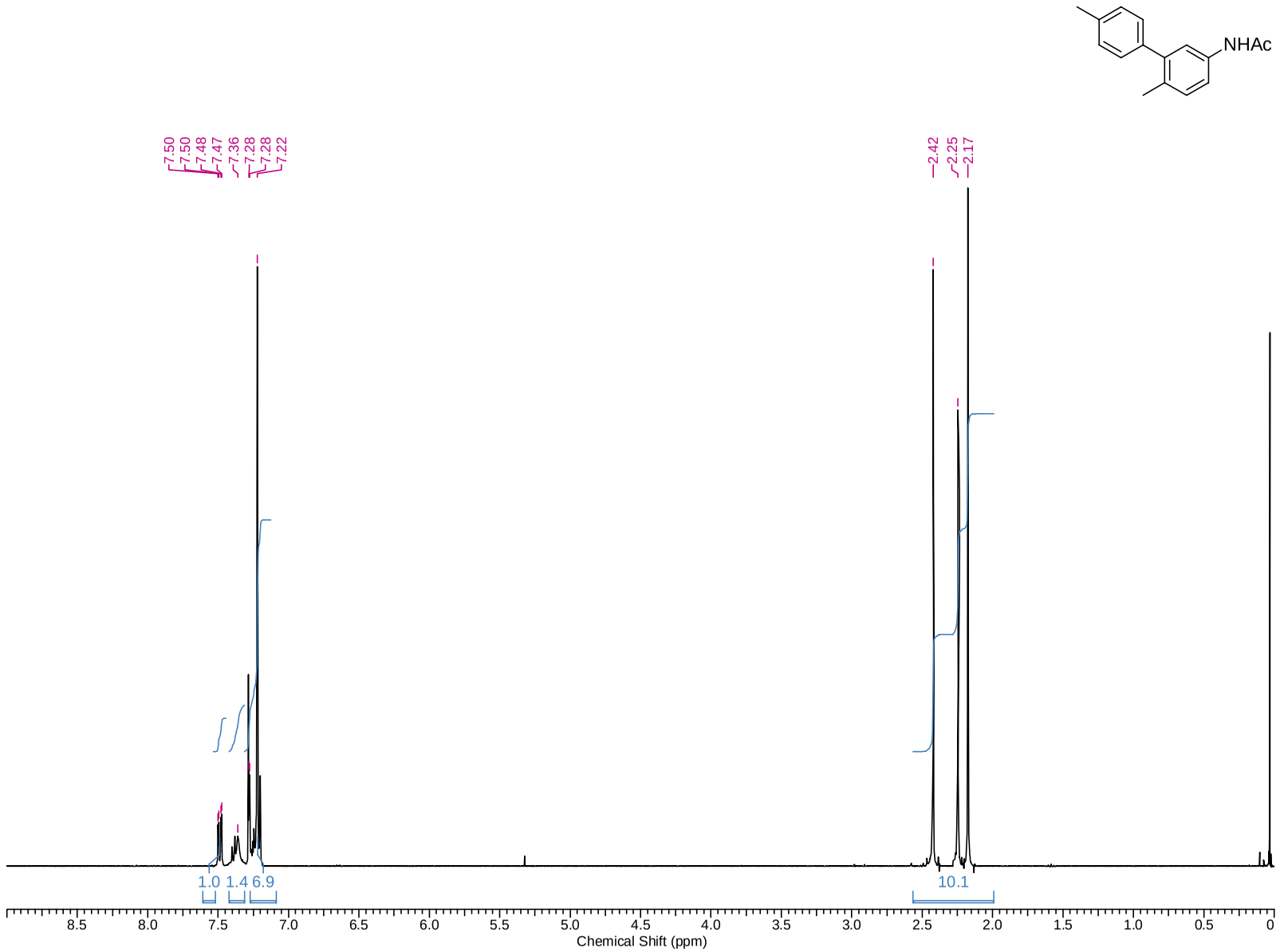

Br
NHPiv
176.94
142.80
138.47
136.25
130.94
130.21
130.17
130.01
128.40
125.81
123.55
122.83
121.45
39.89
27.76
17.42
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

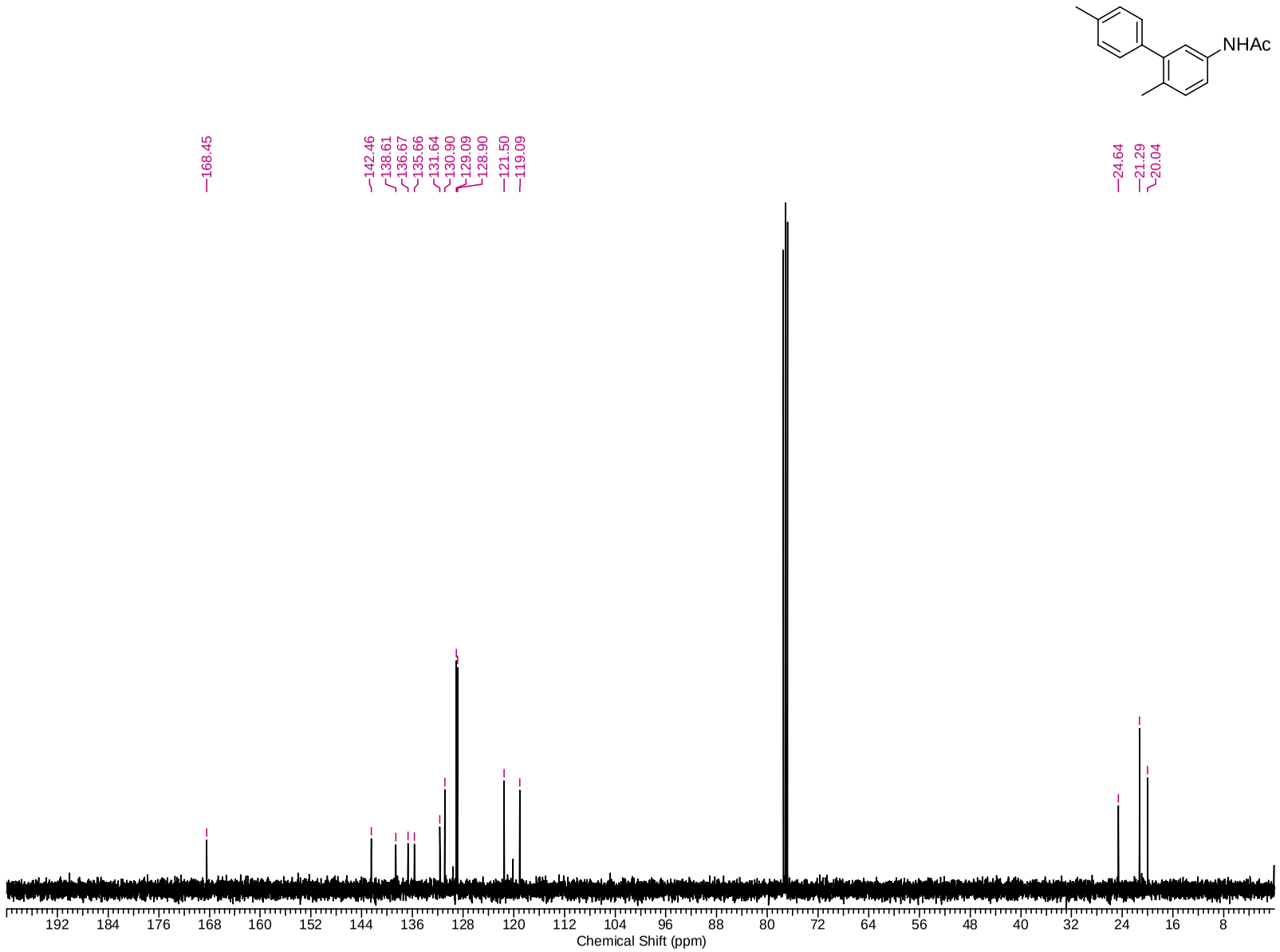

CO2Et
NHPiv
8.25
8.25
8.14
8.14
7.99
7.98
7.77
7.48
7.46
7.44
7.34
7.34
7.32
7.32
7.26
7.24
4.42
4.40
4.39
4.37
2.28
1.42
1.40
1.38
1.35
Chemical Shift (ppm)
Chemical Shift (ppm)

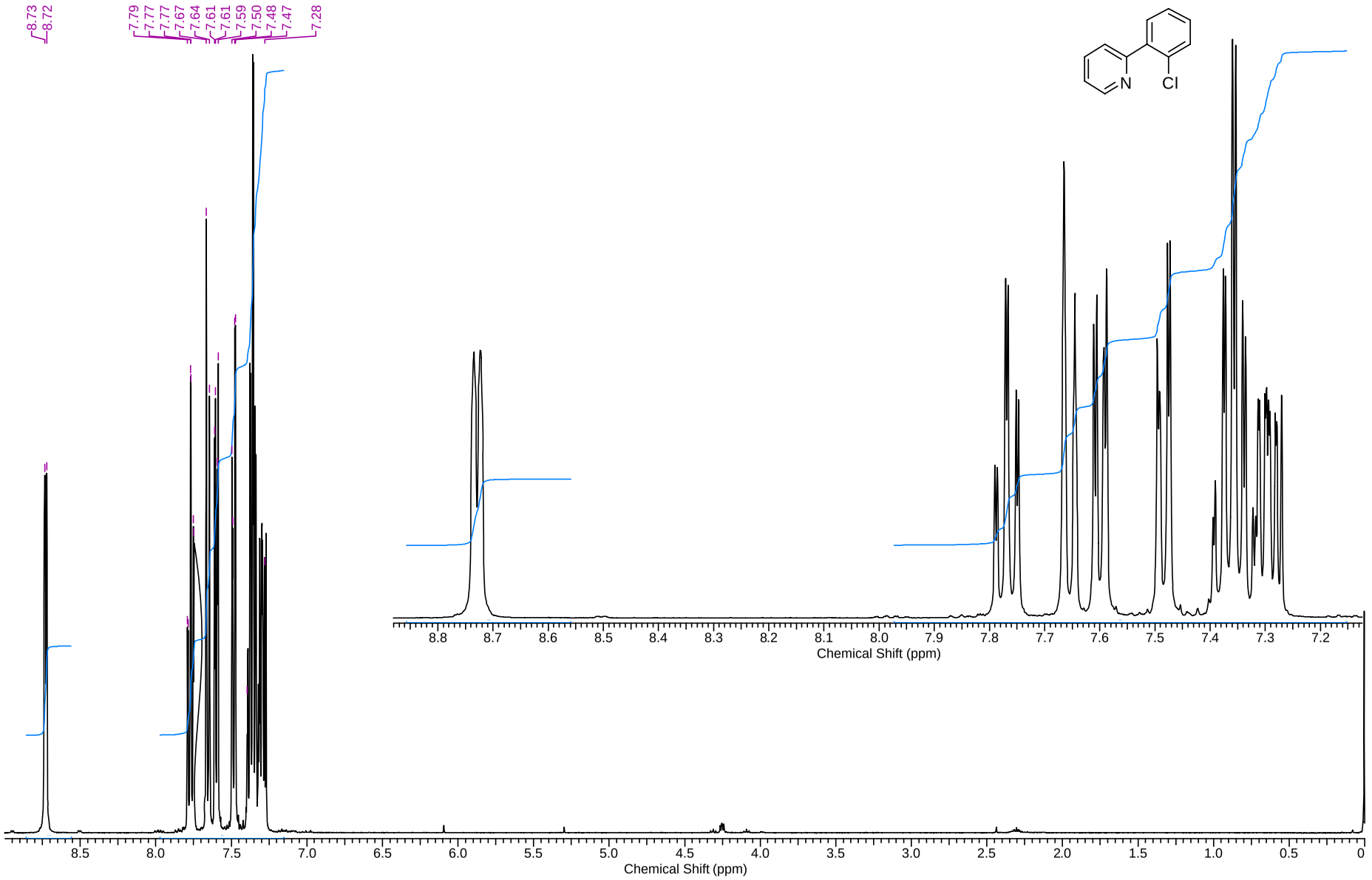

CO2Et
NHPiv
176.66
166.62
140.95
138.87
136.31
131.55
130.87
130.85
128.68
128.47
128.21
127.98
123.59
121.63
61.02
39.76
27.69
17.36
14.35
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

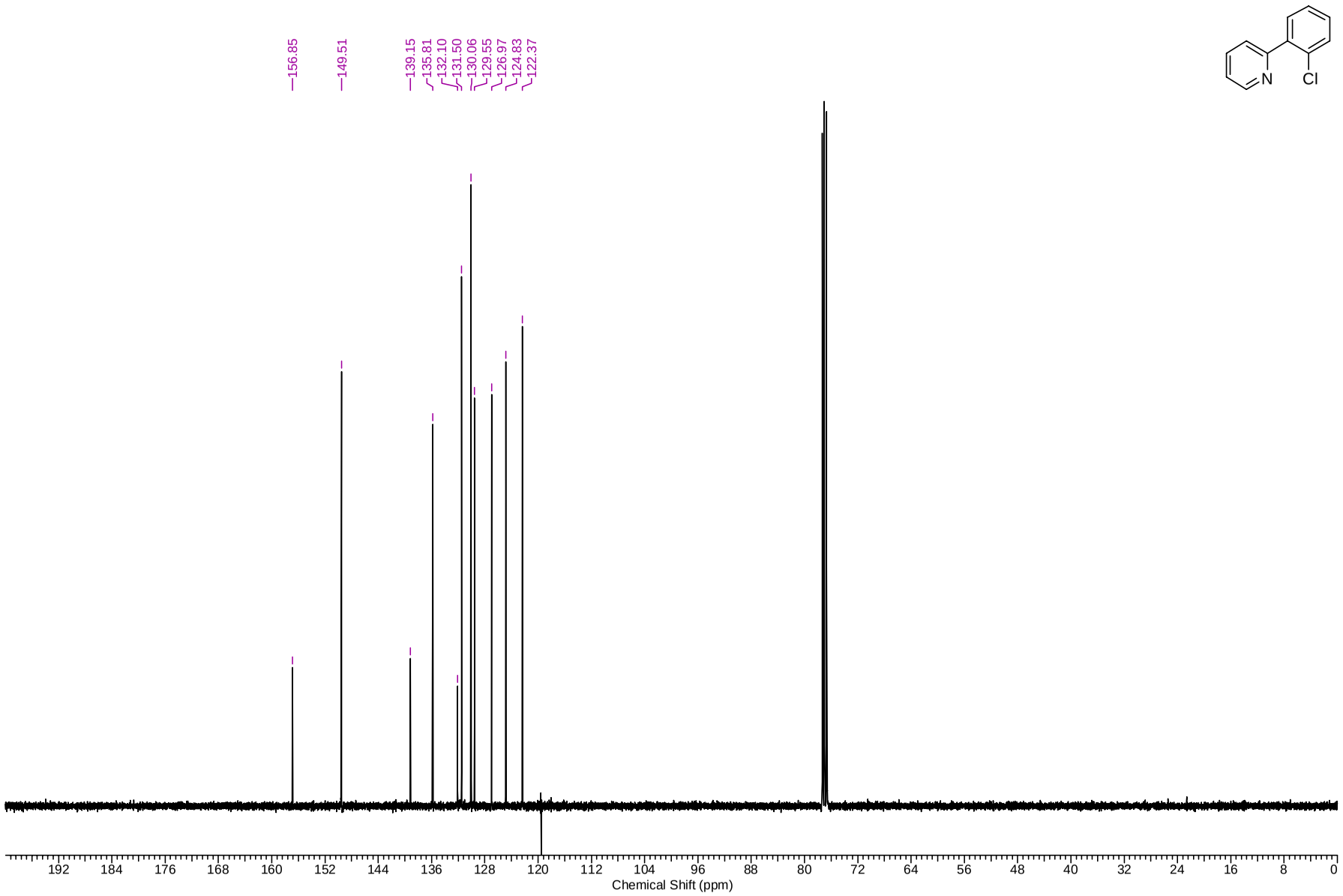

NHPiv
7.87
7.86
7.25
7.20
7.07
7.06
7.05
7.04
2.31
2.31
1.36
Chemical Shift (ppm)
Chemical Shift (ppm)

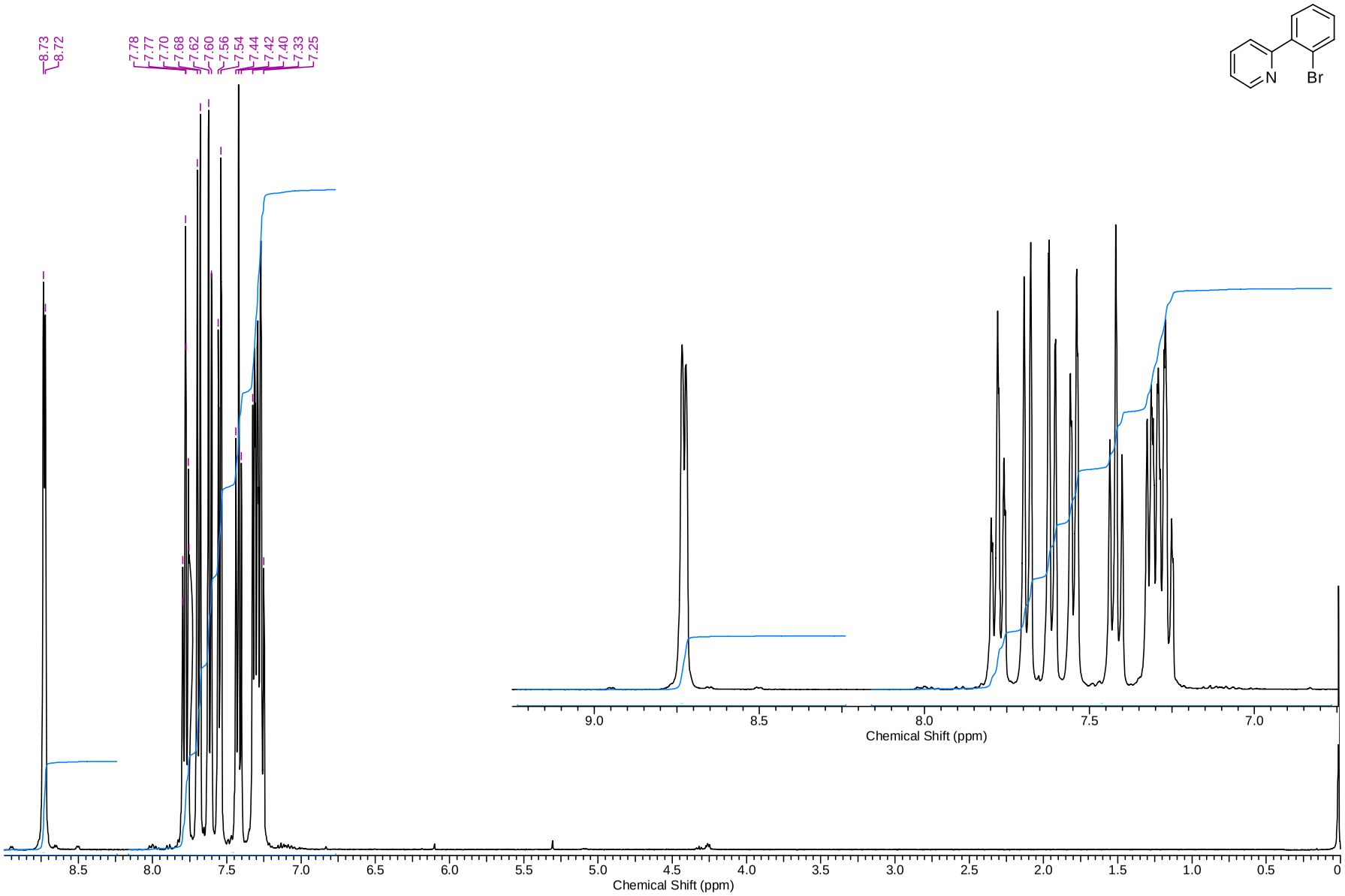

NHPiv
178.05
141.46
140.76
139.49
135.86
135.53
130.35
130.16
129.95
127.30
125.79
123.97
39.88
27.85
20.68
17.51
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

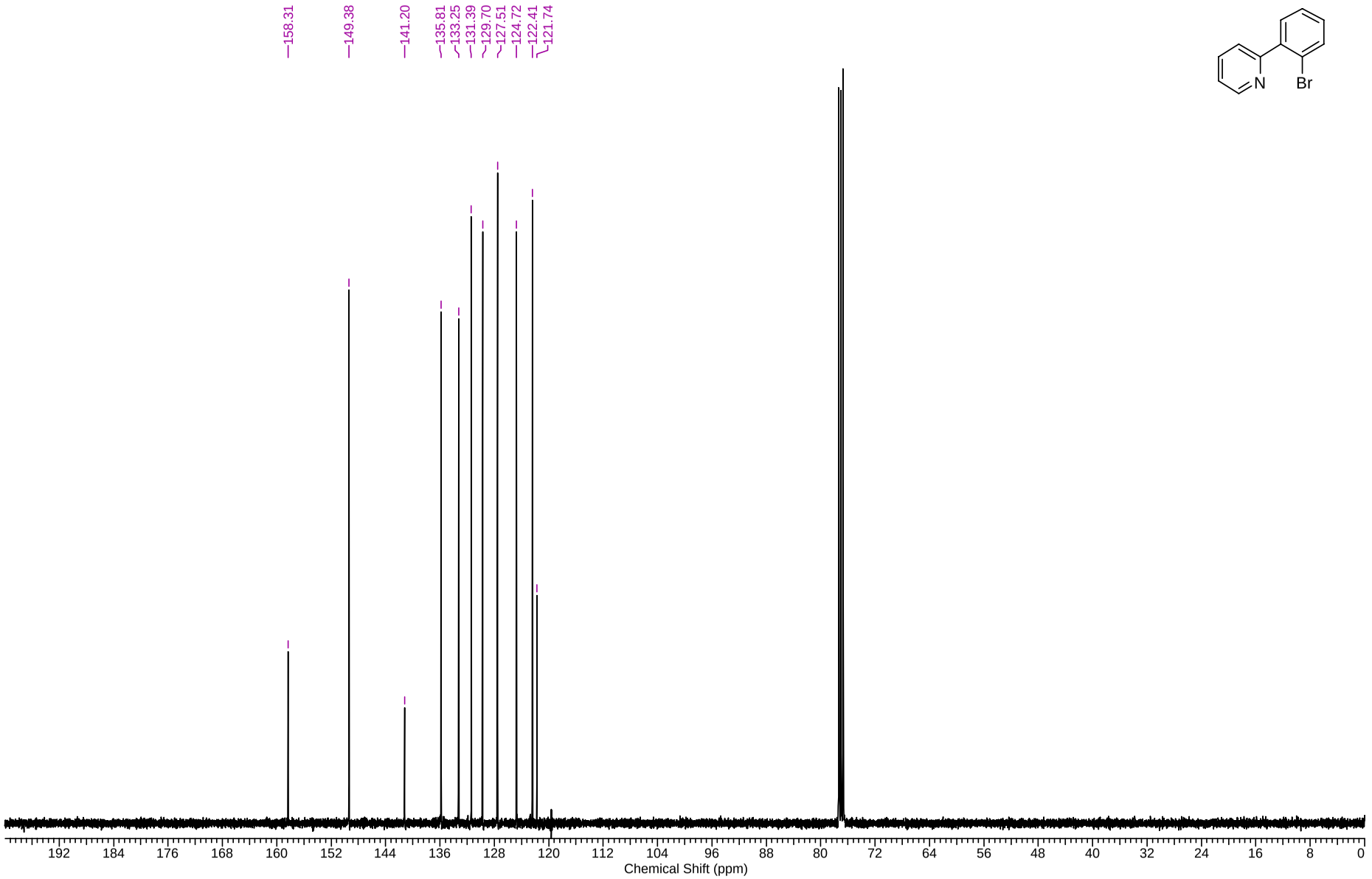

NHAc
7.50
7.50
7.48
7.47
7.36
7.28
7.28
7.22
2.42
2.25
2.17
1.0
1.4
6.9
10.1
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

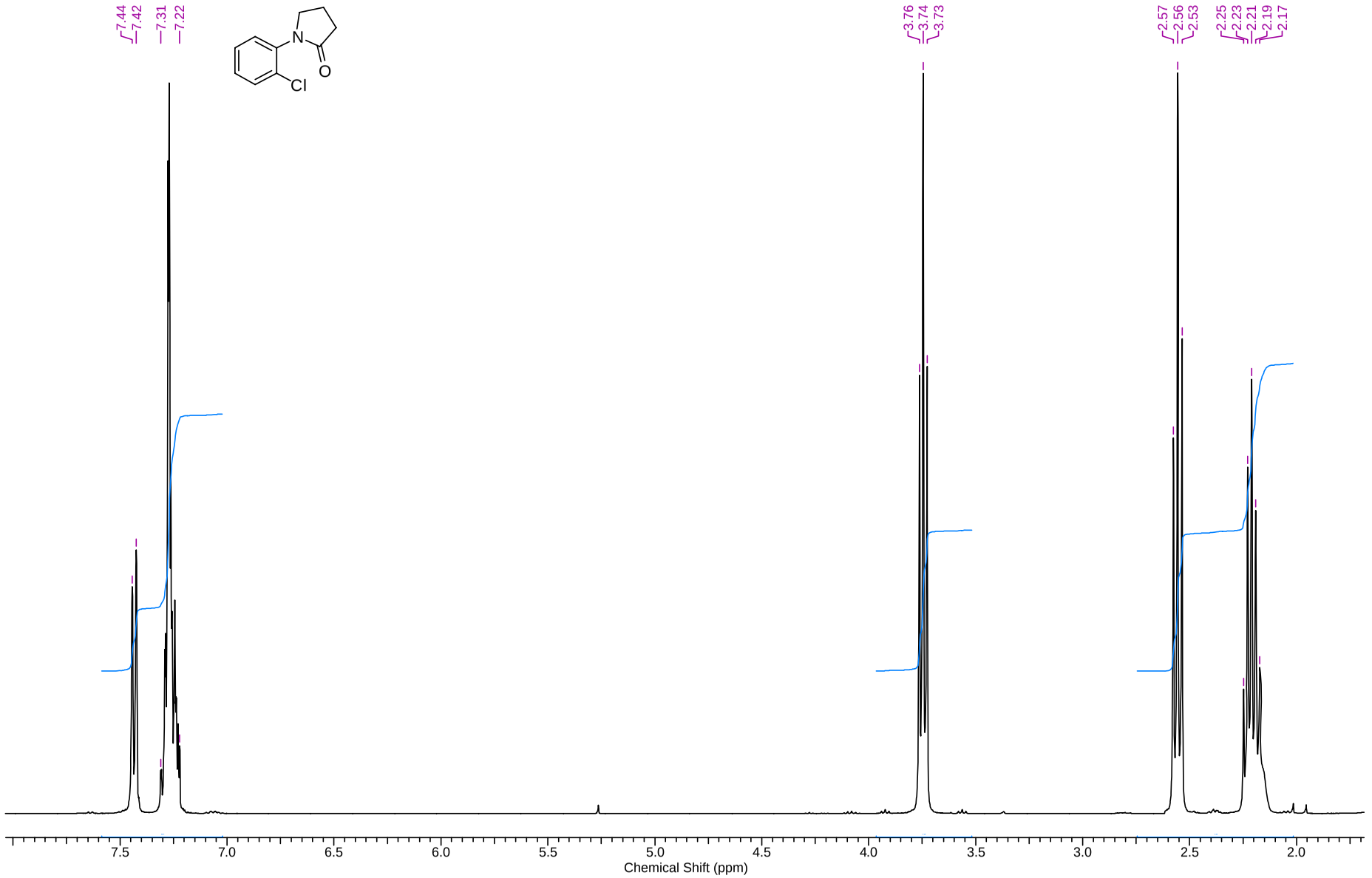

NHAc
168.45
142.46
138.61
136.67
135.66
131.64
130.90
129.09
128.90
121.50
119.09
24.64
21.29
20.04
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8
Chemical Shift (ppm)

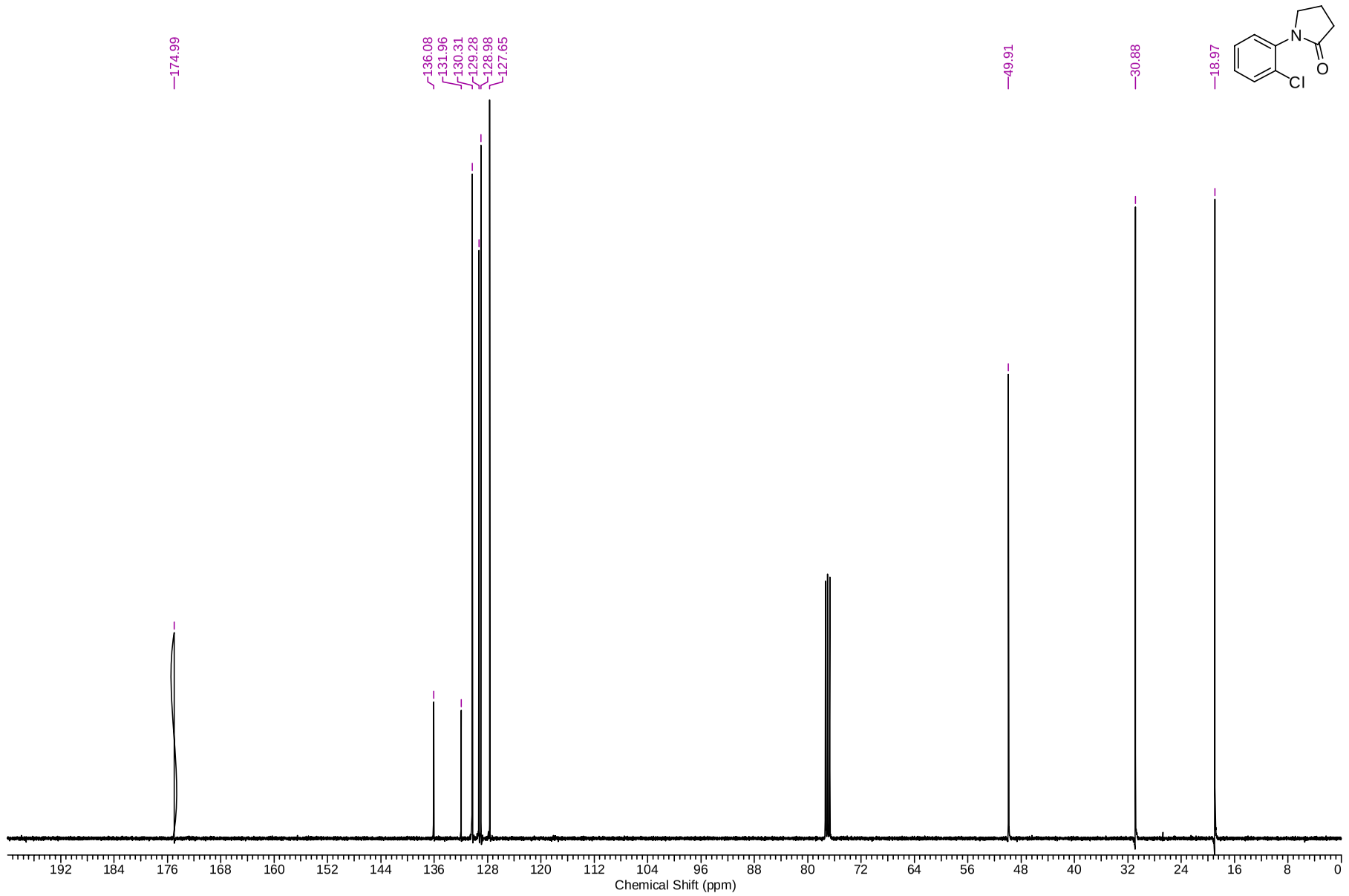

8.73
8.72
7.79
7.77
7.77
7.67
7.64
7.61
7.61
7.59
7.50
7.48
7.47
7.28
N
Cl
Chemical Shift (ppm)
Chemical Shift (ppm)

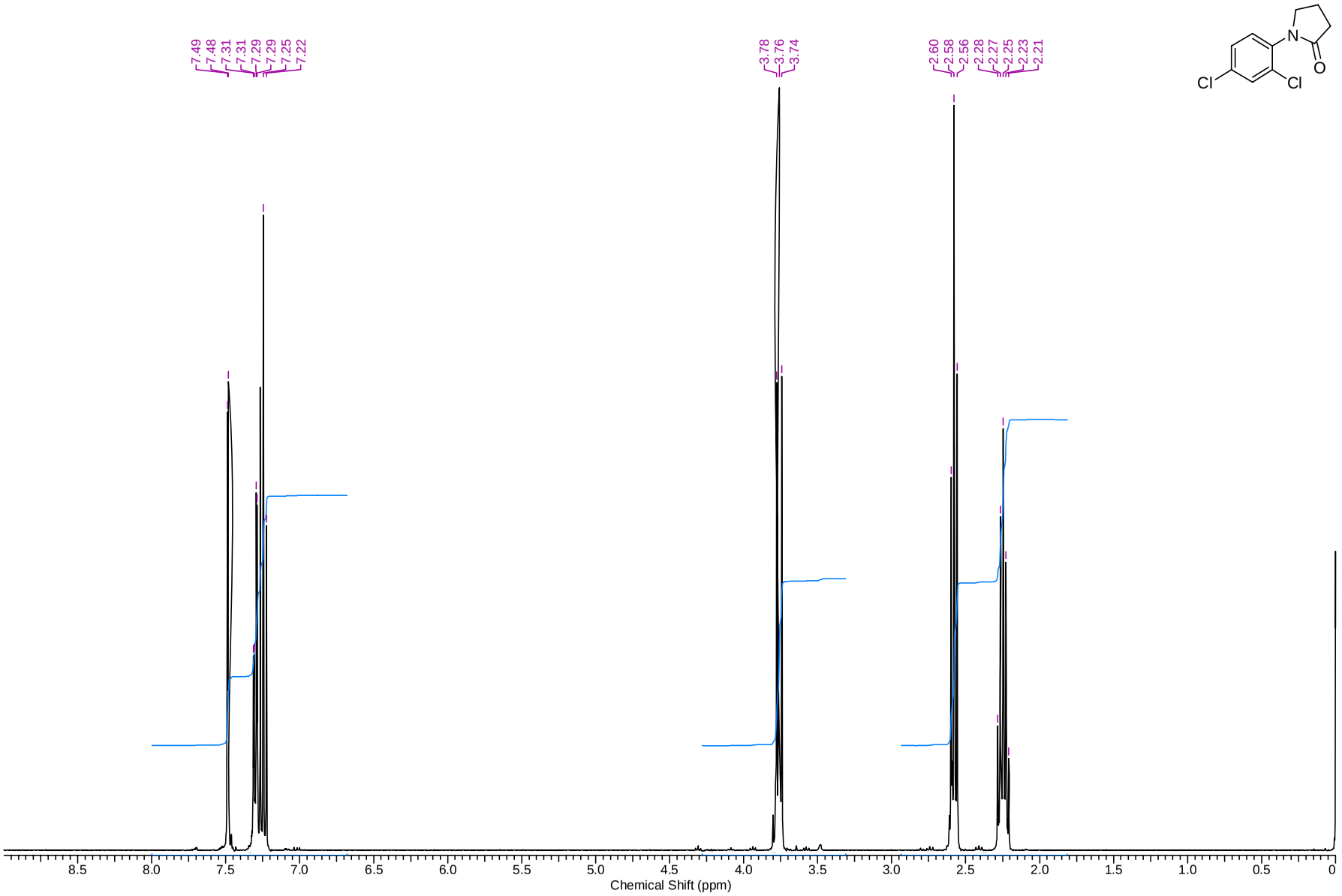

156.85
149.51
139.15
135.81
132.10
131.50
130.06
129.55
126.97
124.83
122.37
N
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

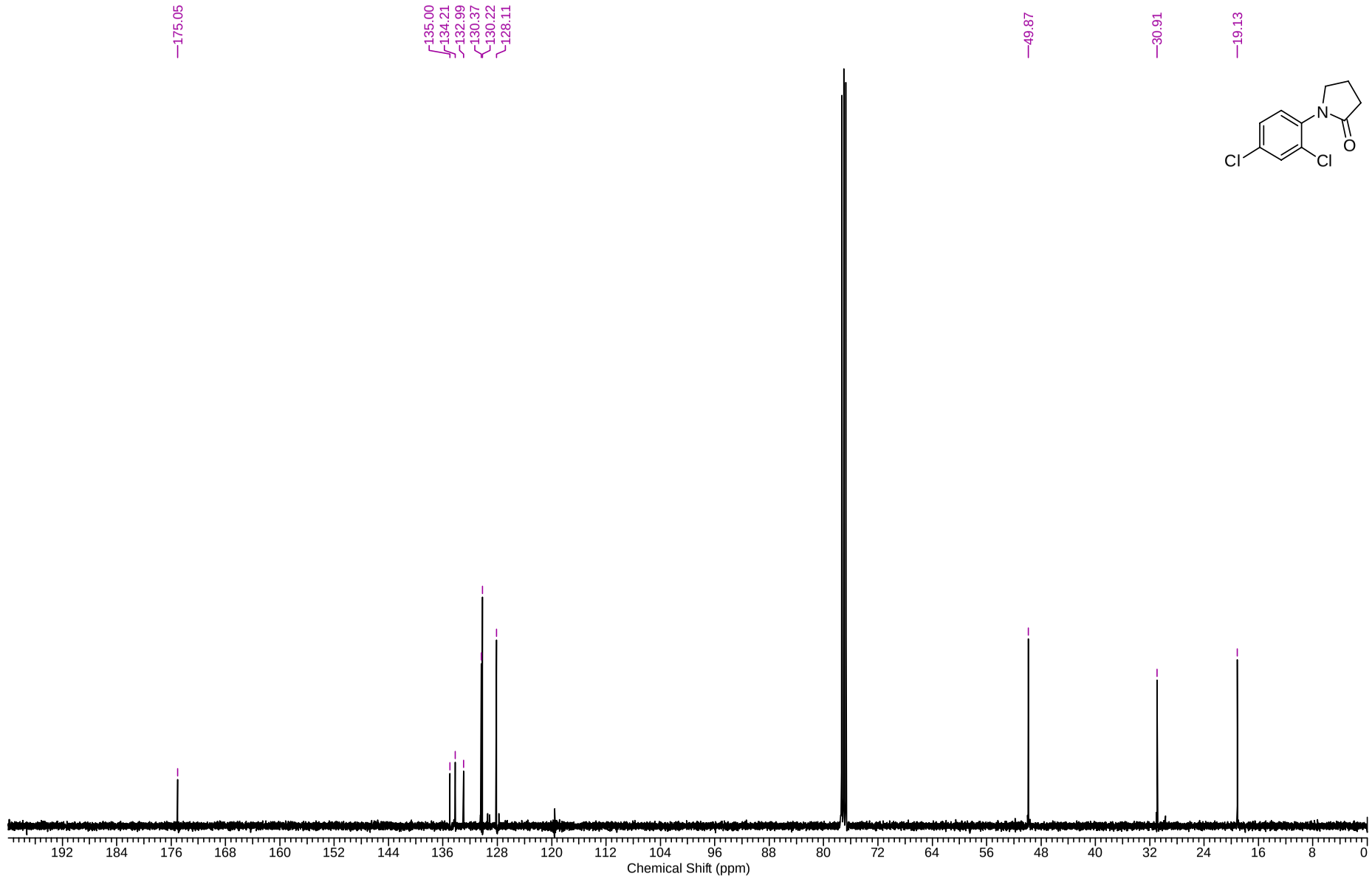

8.73
8.72
7.78
7.77
7.70
7.68
7.62
7.60
7.56
7.54
7.44
7.42
7.40
7.33
7.25
N
Br
9.0
8.5
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

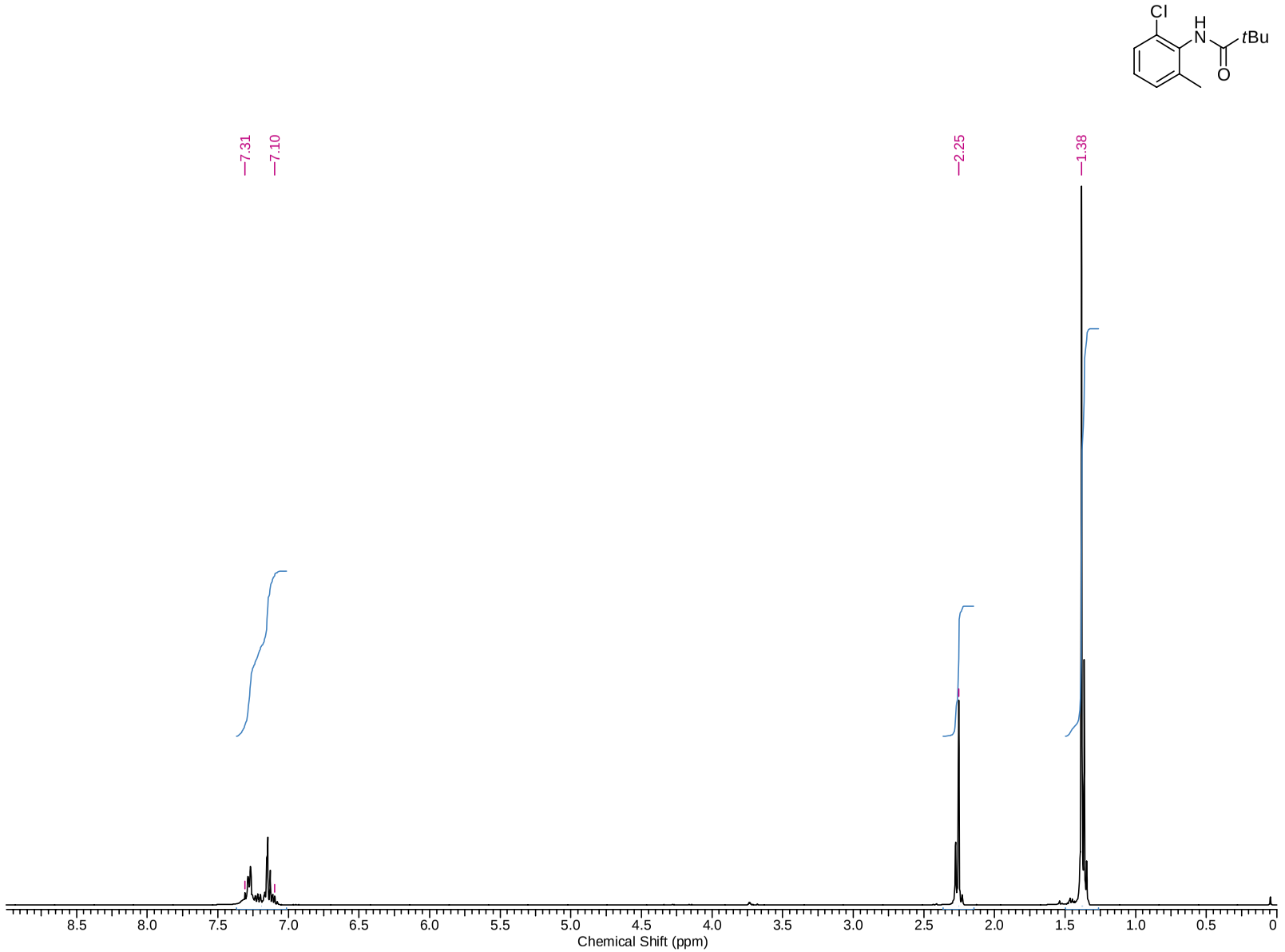

158.31
149.38
141.20
135.81
133.25
131.39
129.70
127.51
124.72
122.41
121.74
N
Br
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

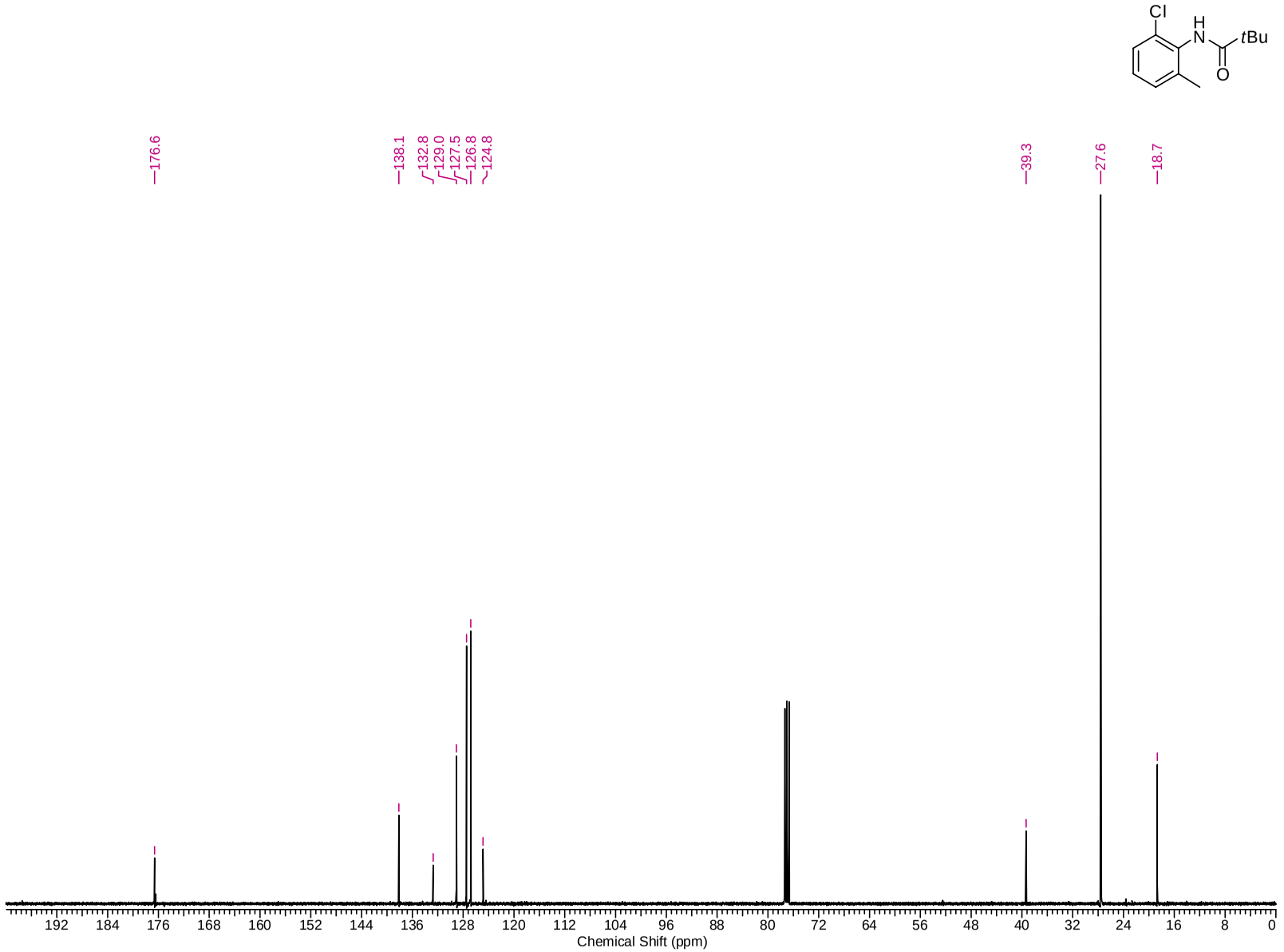

7.44
7.42
7.31
7.22
3.76
3.74
3.73
2.57
2.56
2.53
2.25
2.23
2.21
2.19
2.17
N
O
Cl
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)

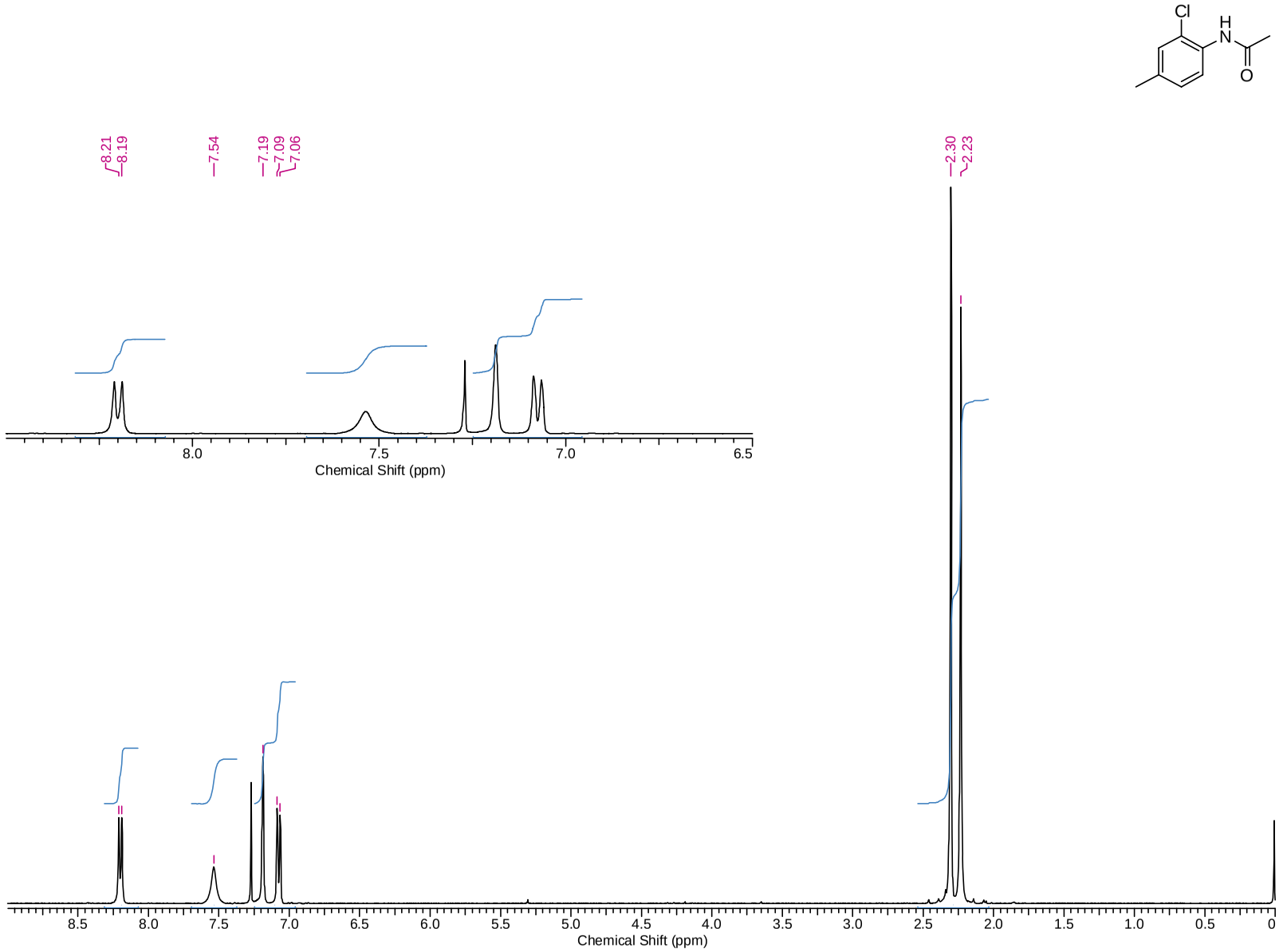

174.99
136.08
131.96
130.31
129.28
128.98
127.65
49.91
30.88
18.97
N
O
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

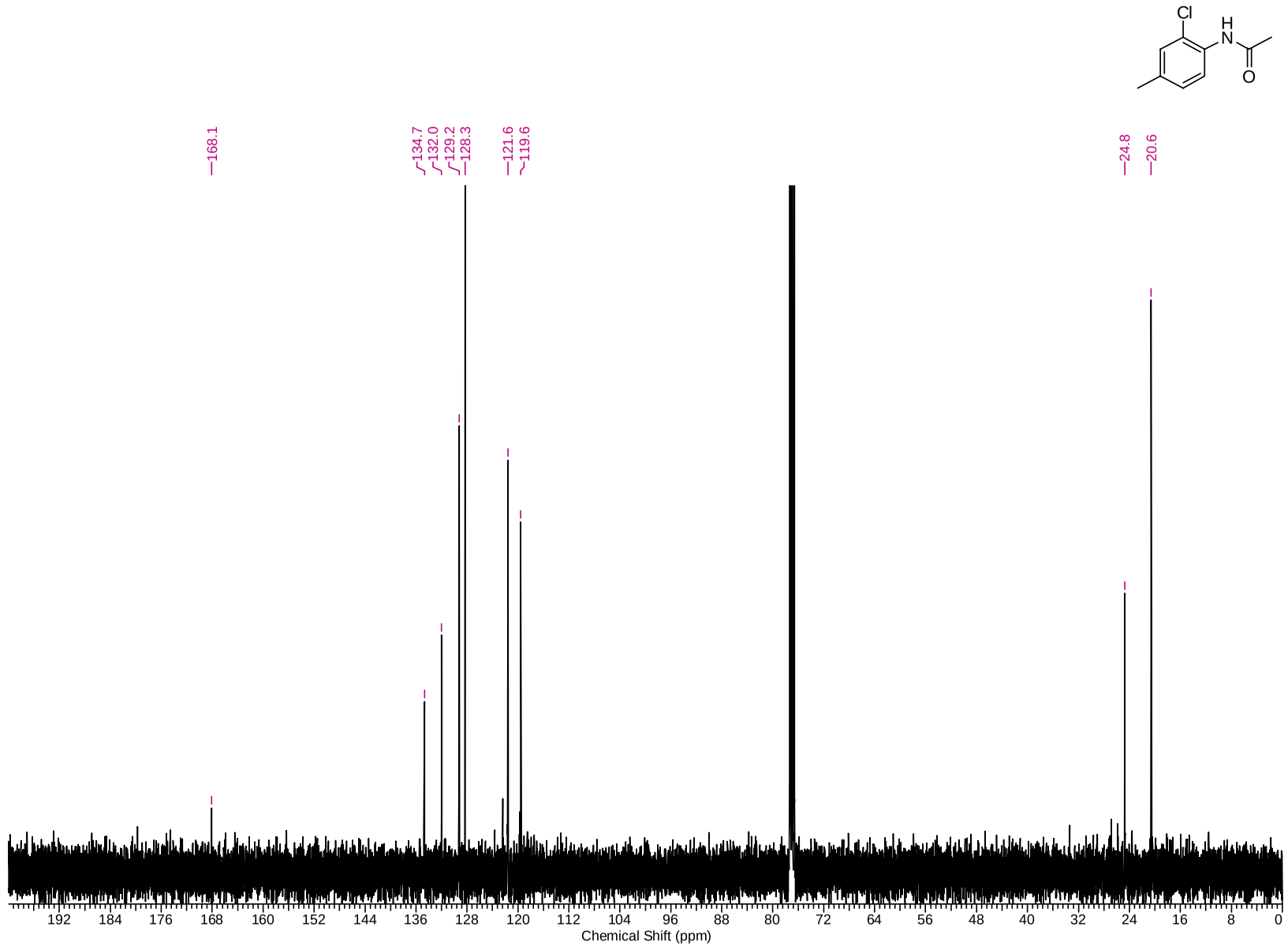

7.49
7.48
7.31
7.31
7.29
7.29
7.25
7.22
3.78
3.76
3.74
2.60
2.58
2.56
2.28
2.27
2.25
2.23
2.21
N
O
Cl
Cl
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

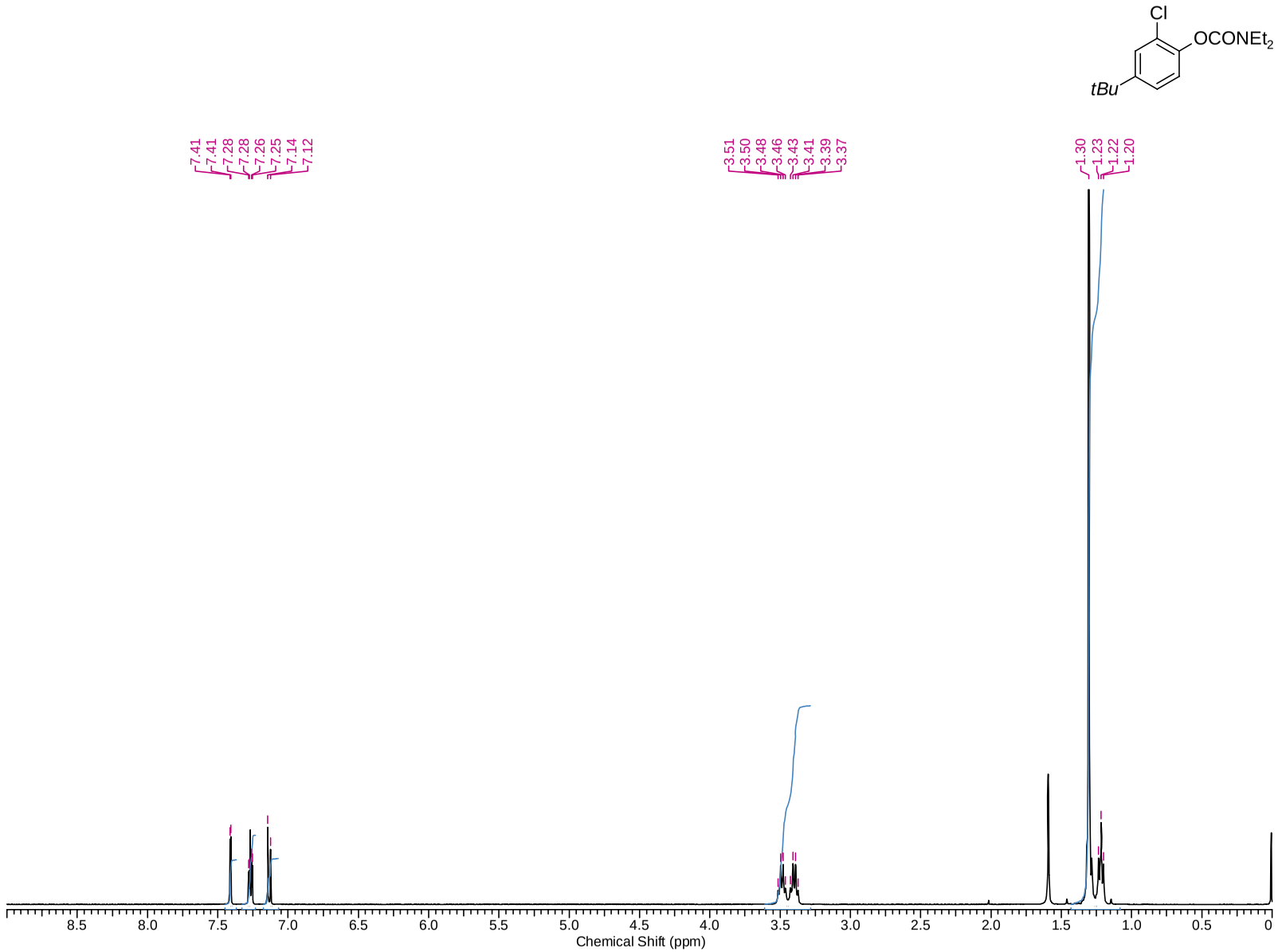

175.05
135.00
134.21
132.99
130.37
130.22
128.11
49.87
30.91
19.13
N
O
Cl
Cl
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

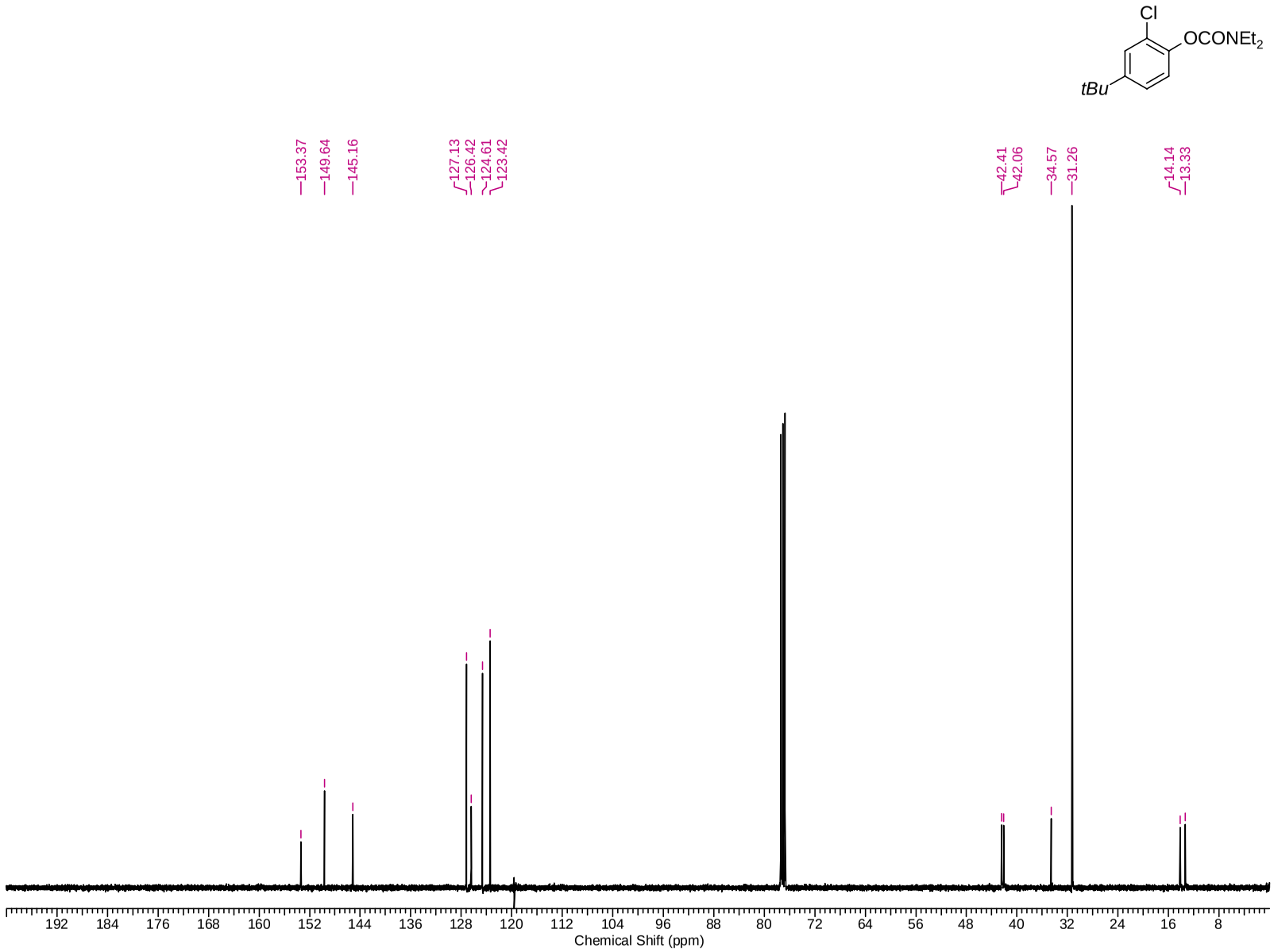

Cl
H
N
tBu
O
7.31
7.10
2.25
1.38
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

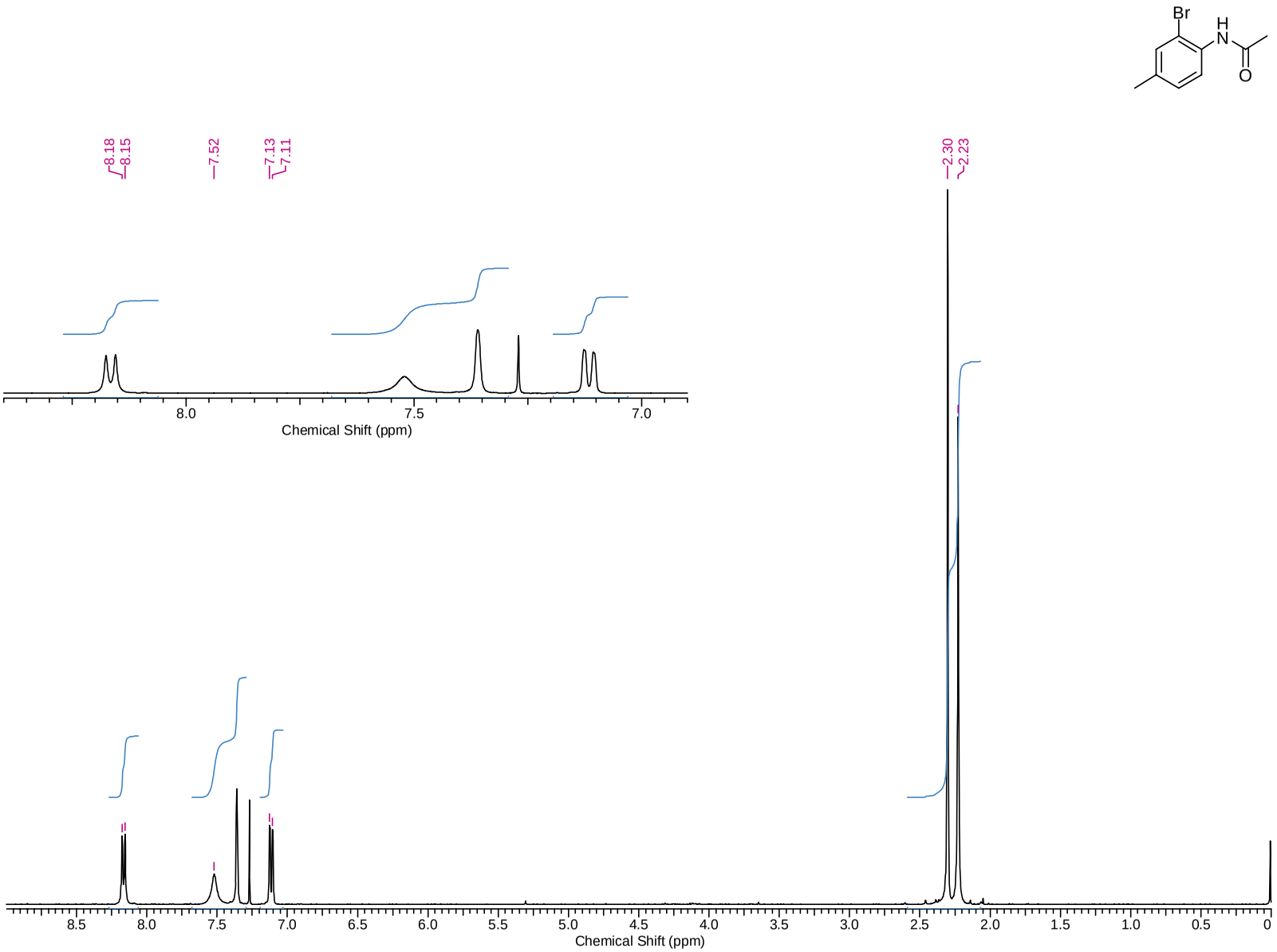

Cl
H
N
tBu
O
176.6
138.1
132.8
129.0
127.5
126.8
124.8
39.3
27.6
18.7
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


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)


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)


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)

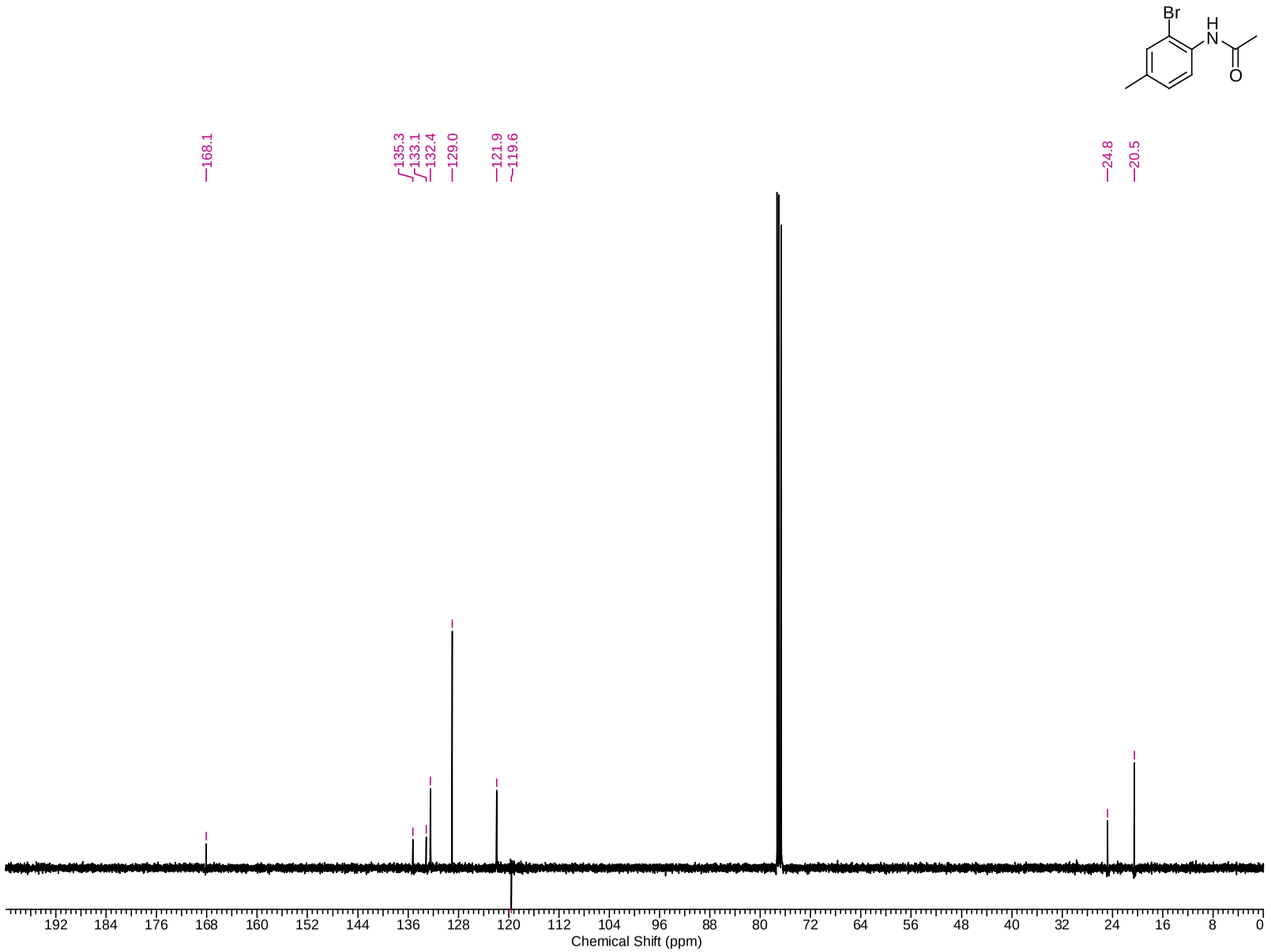

Br
H
N
O
168.1
135.3
133.1
132.4
129.0
121.9
119.6
24.8
20.5
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

Table 2, Entries 9 & 10

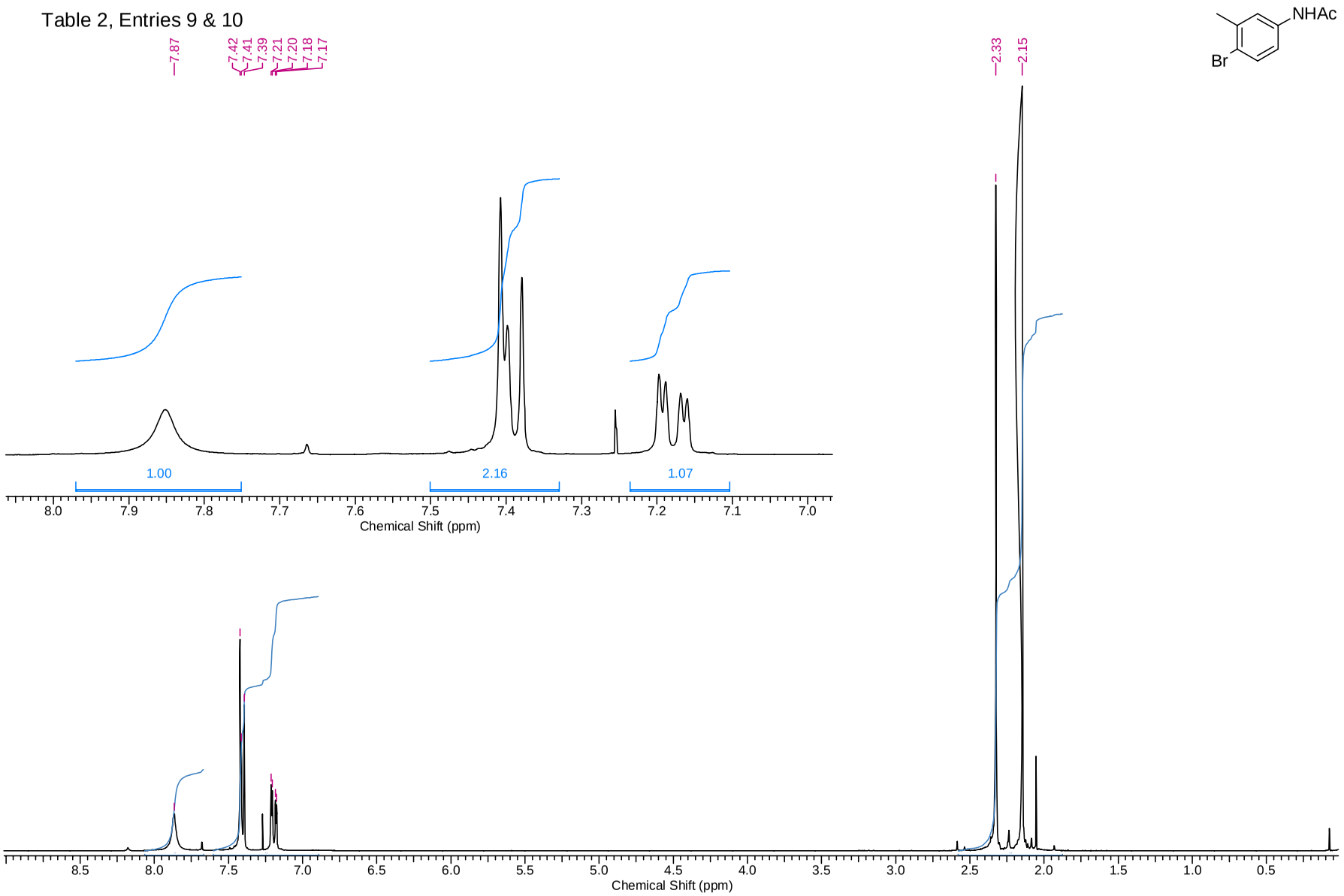


Table 2, Entries 9 & 10

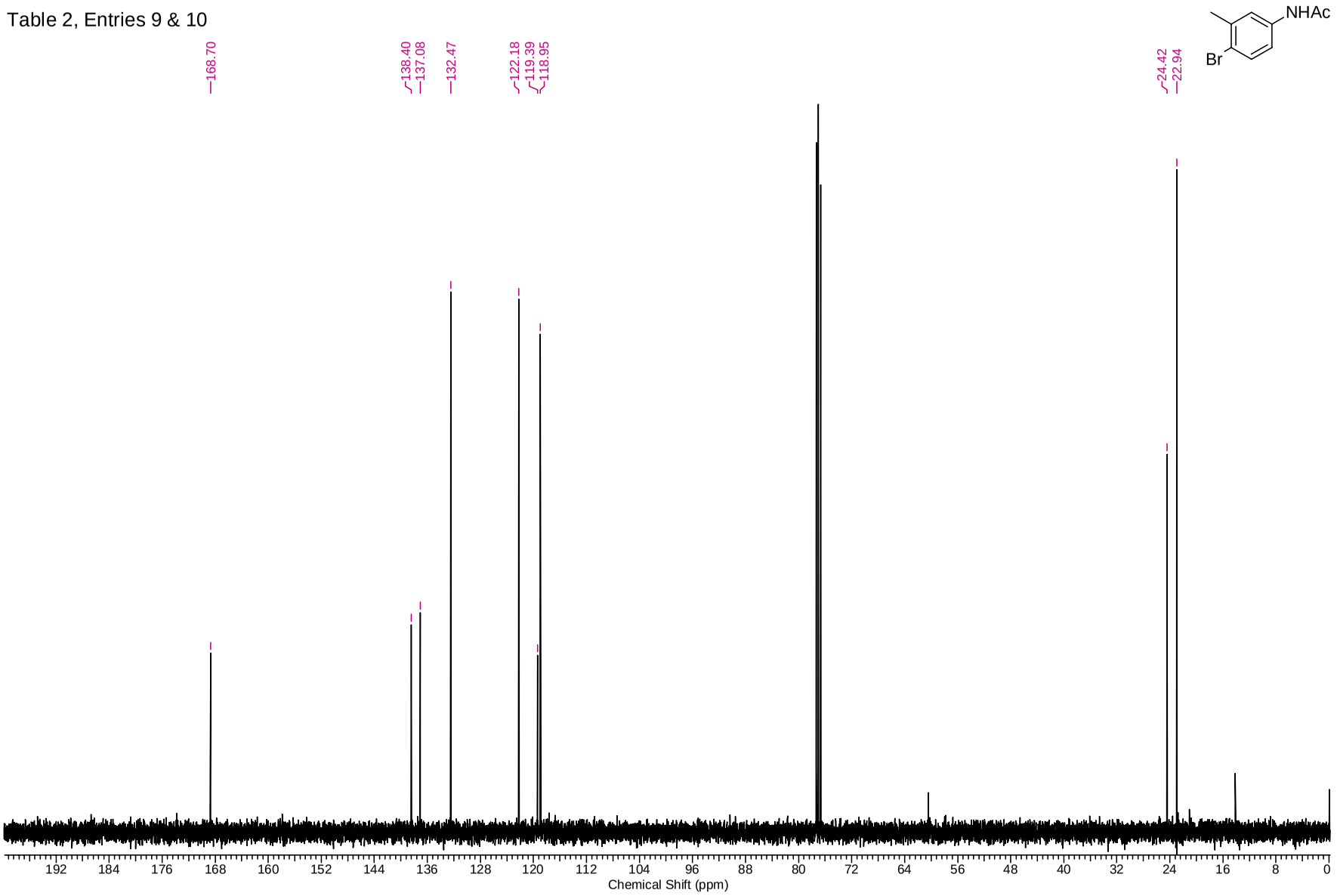


Table 2, Entries 9 & 10
HMQC

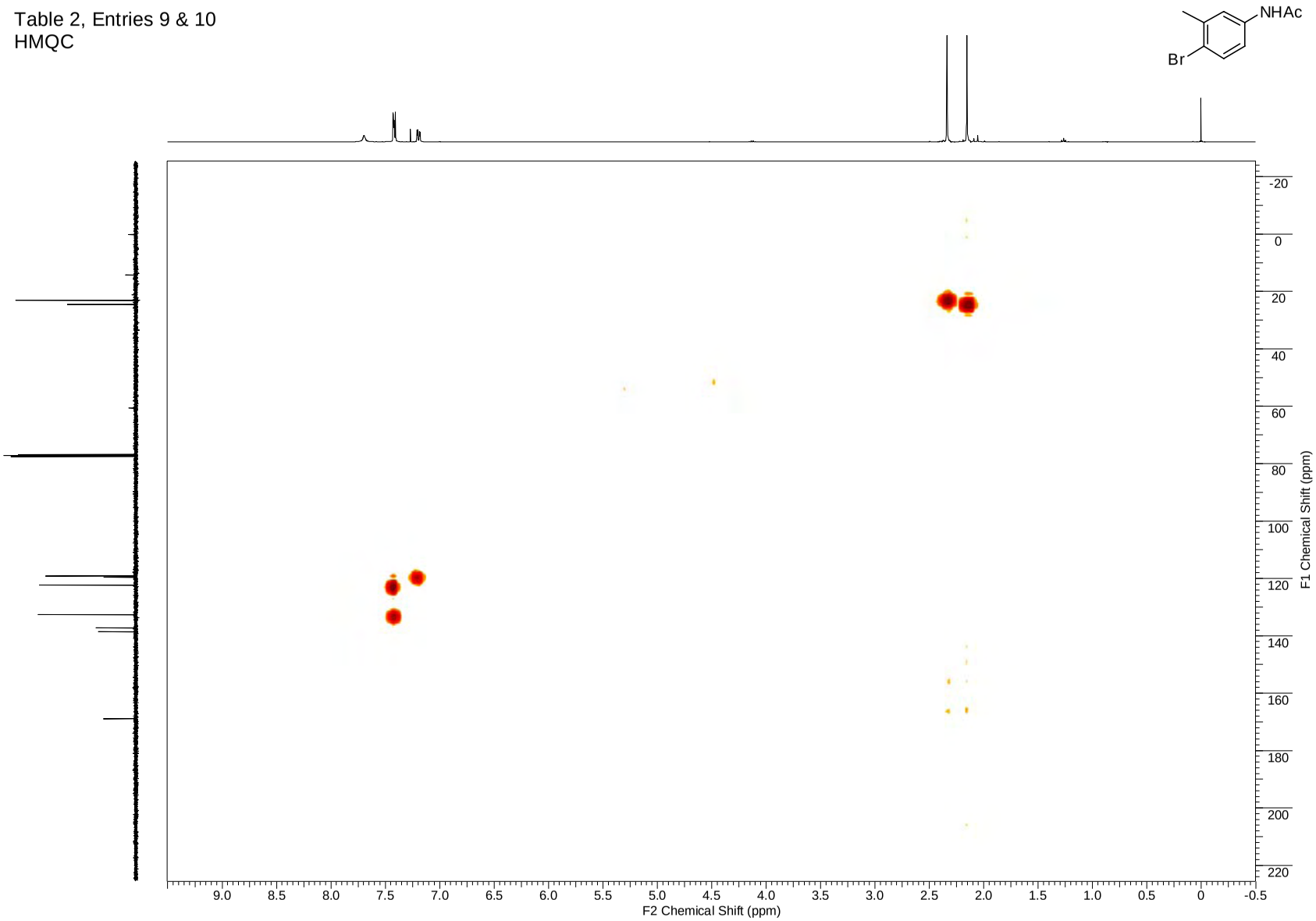


Table 2, Entries 9 & 10
(HMBC)

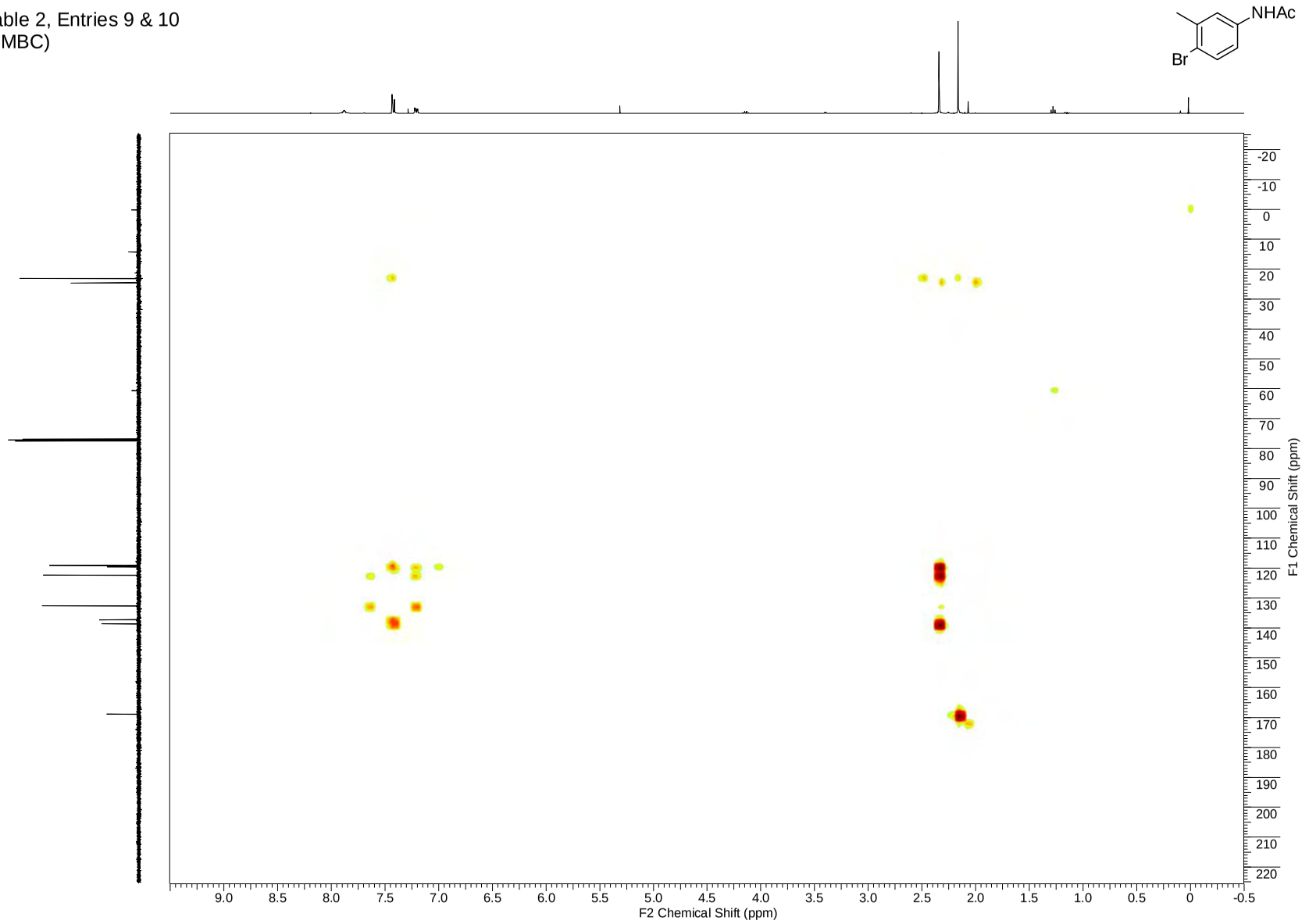


Table 2, Entries 9 & 10 NOE

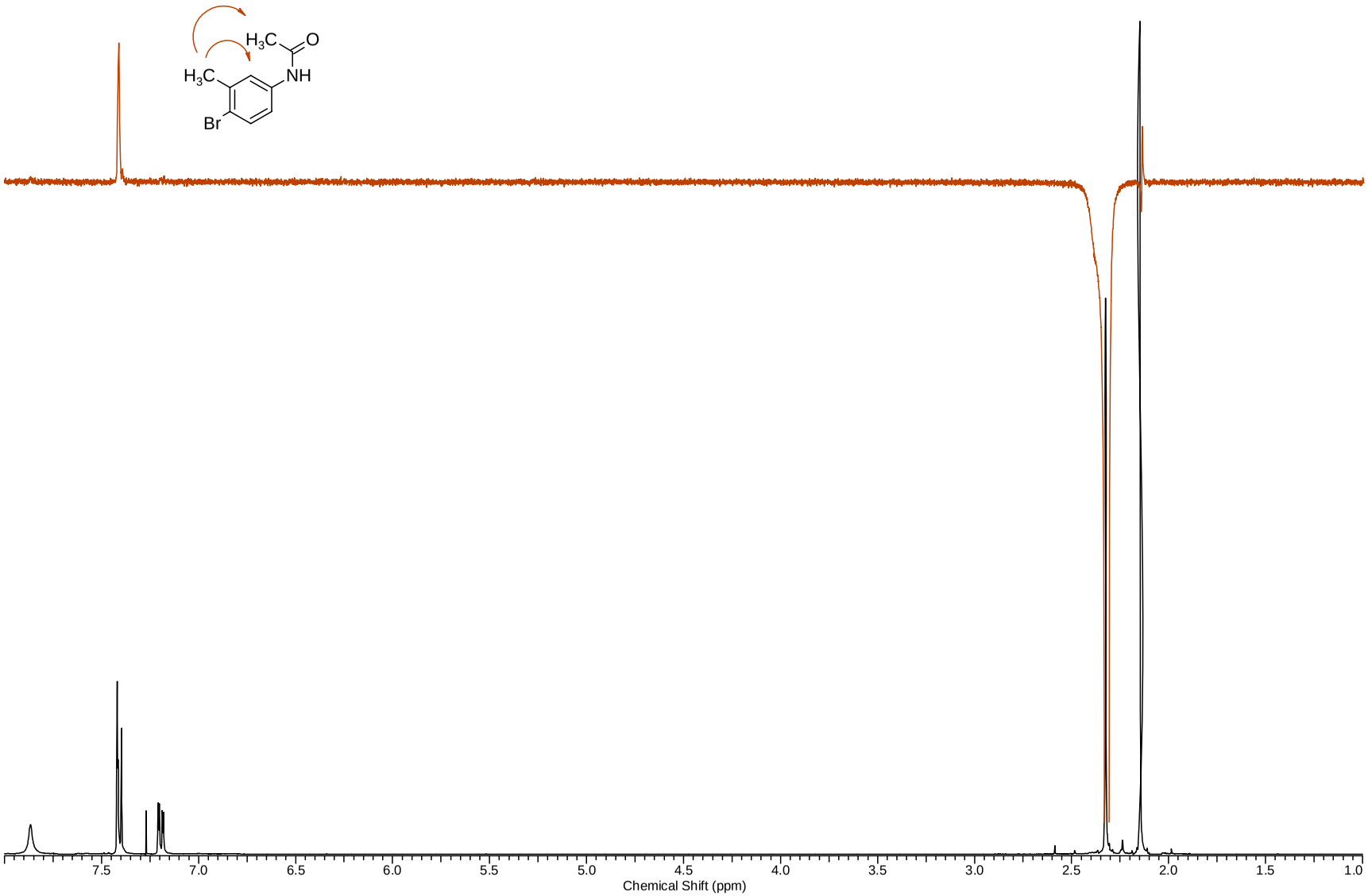


Table 2, Entries 11 & 12

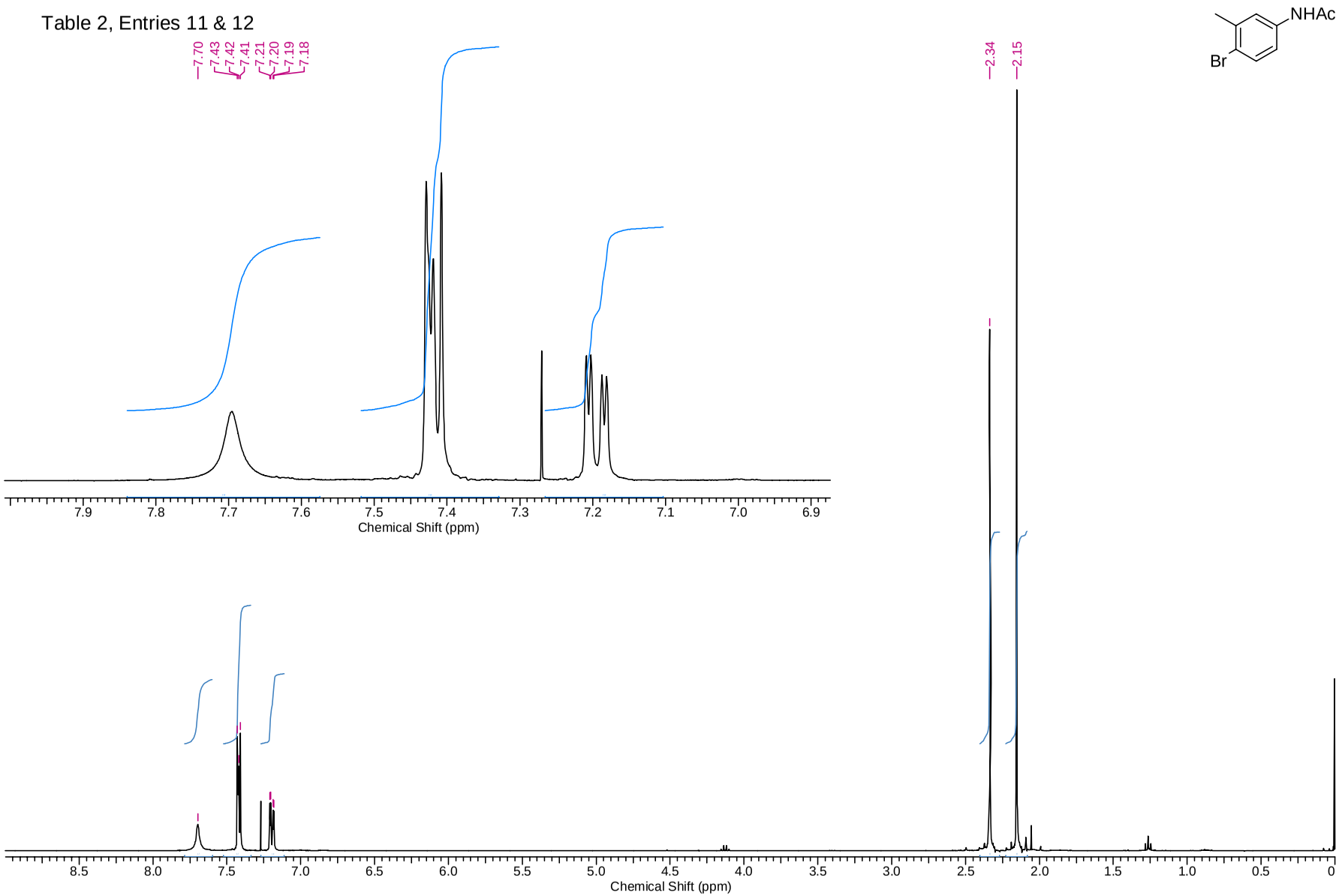


Table 2, Entries 11 & 12

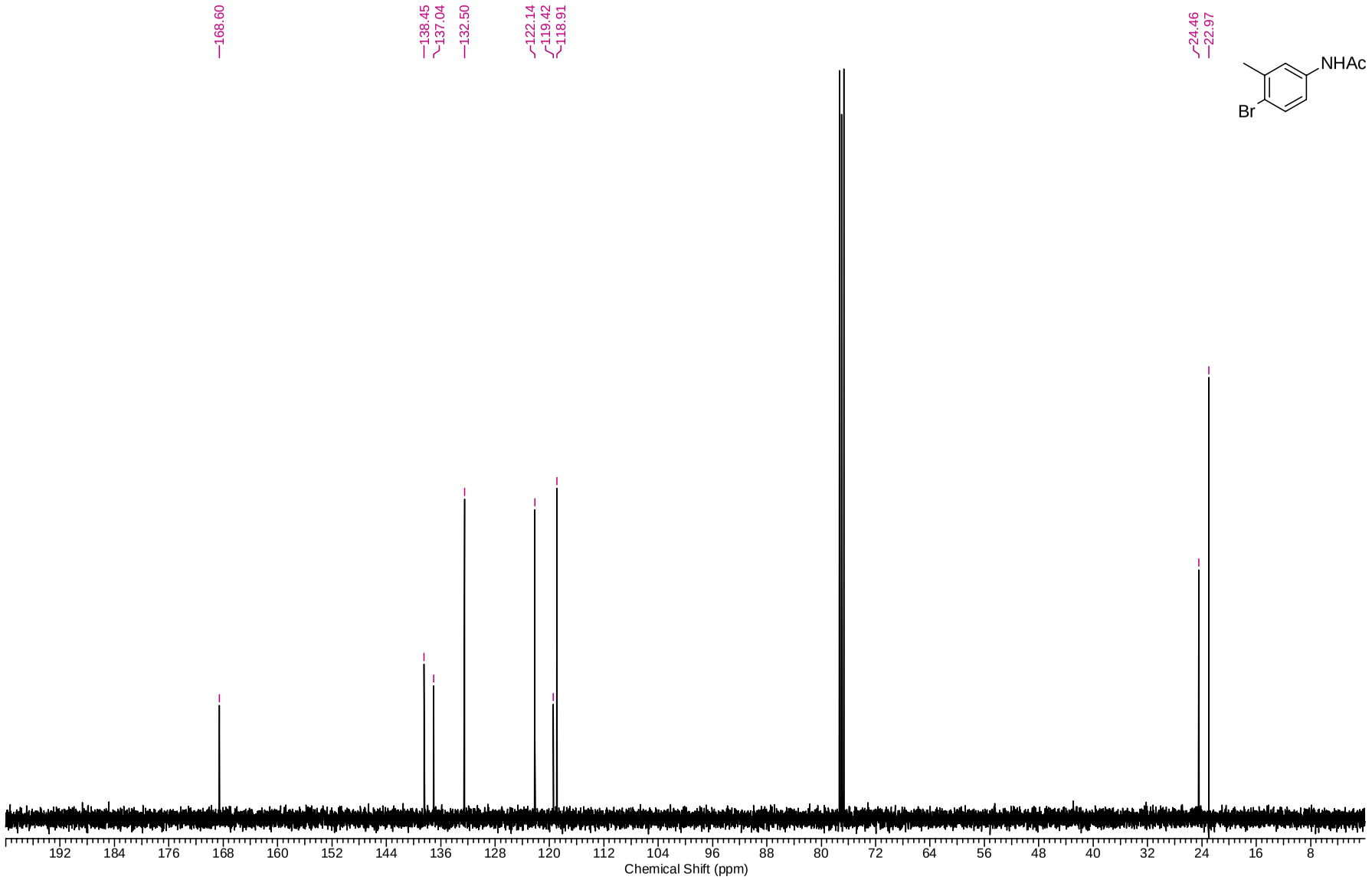


Table 2, Entries 11 & 12
HMQC

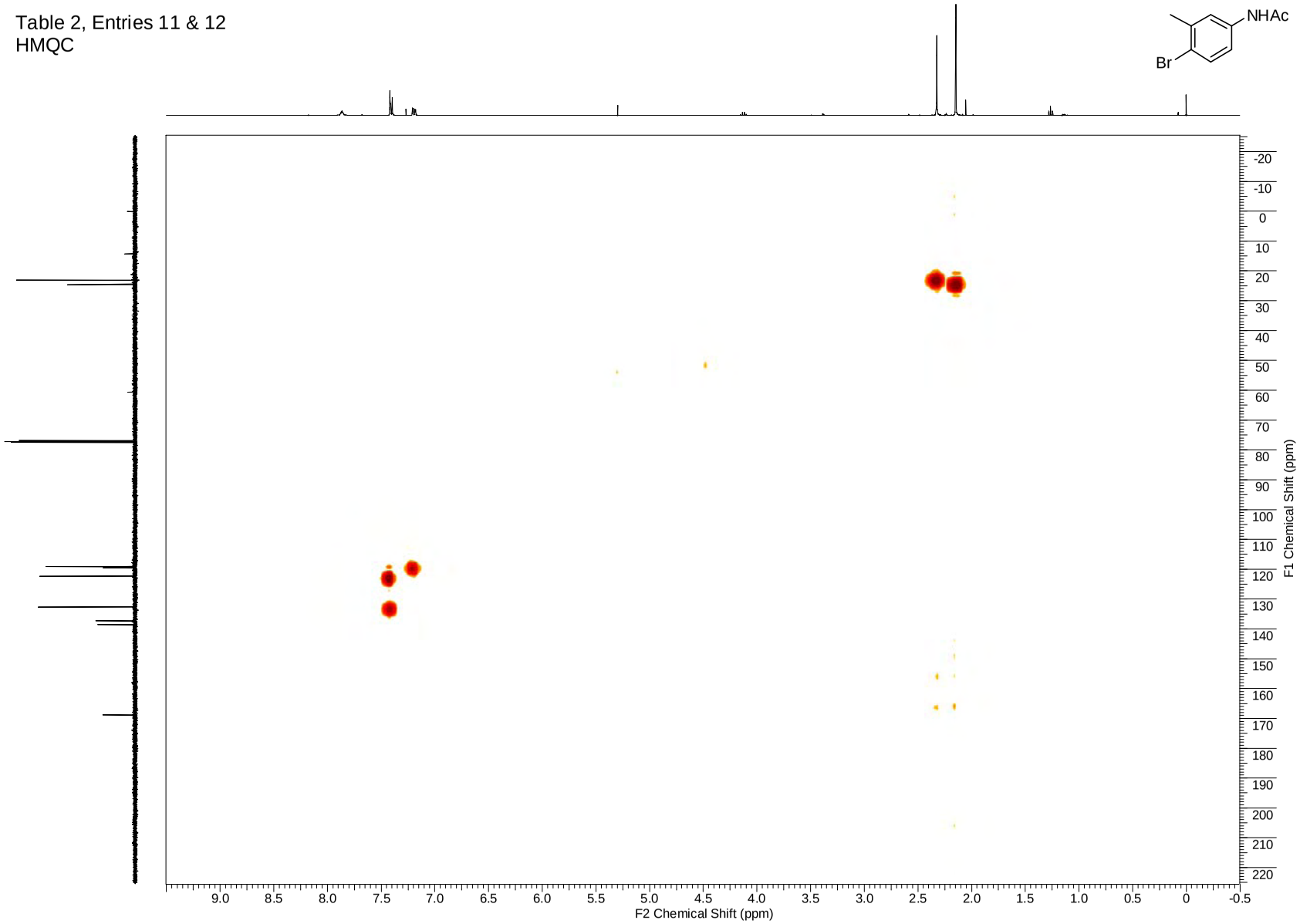


Table 2, Entries 11 & 12
HMBC

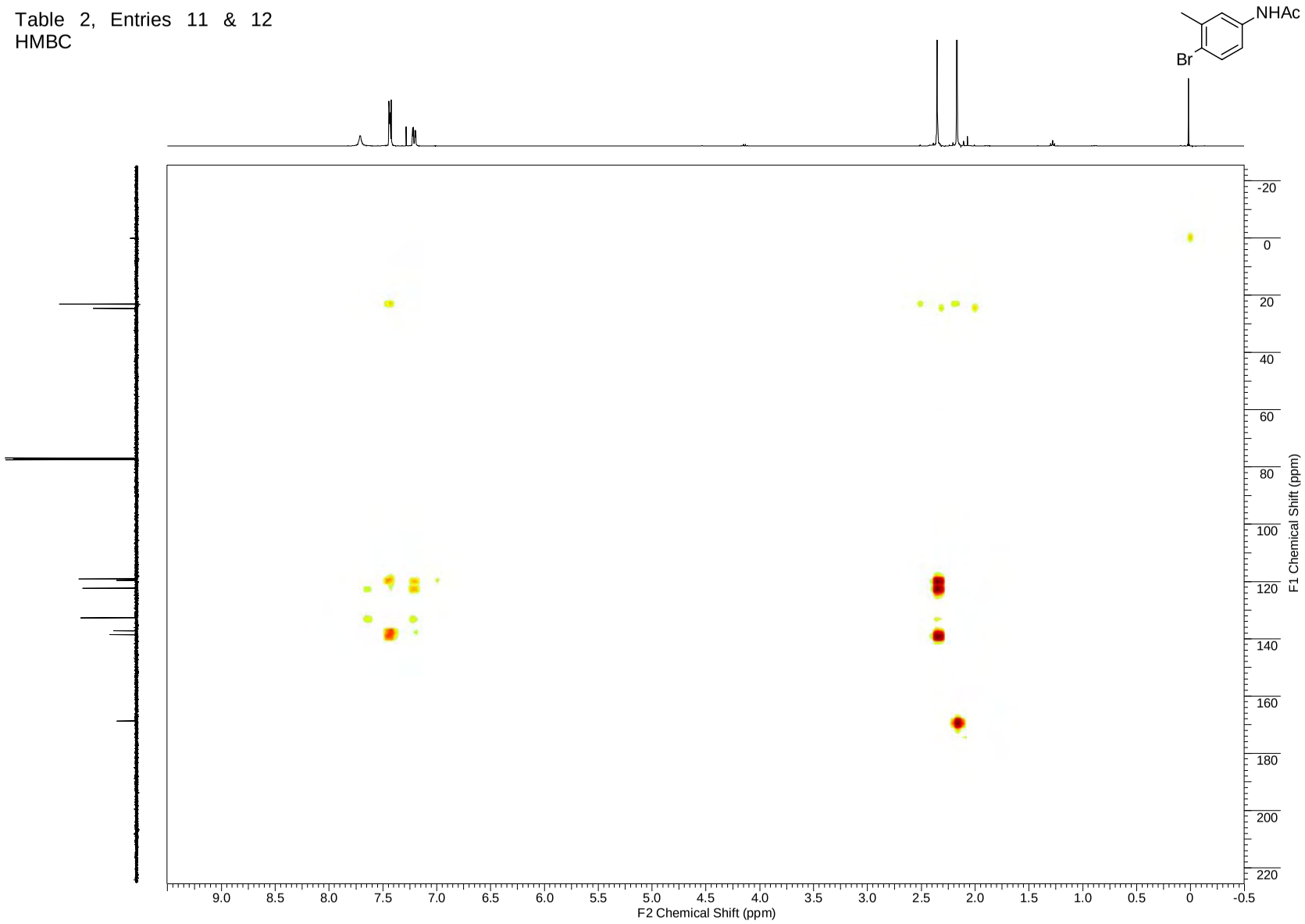
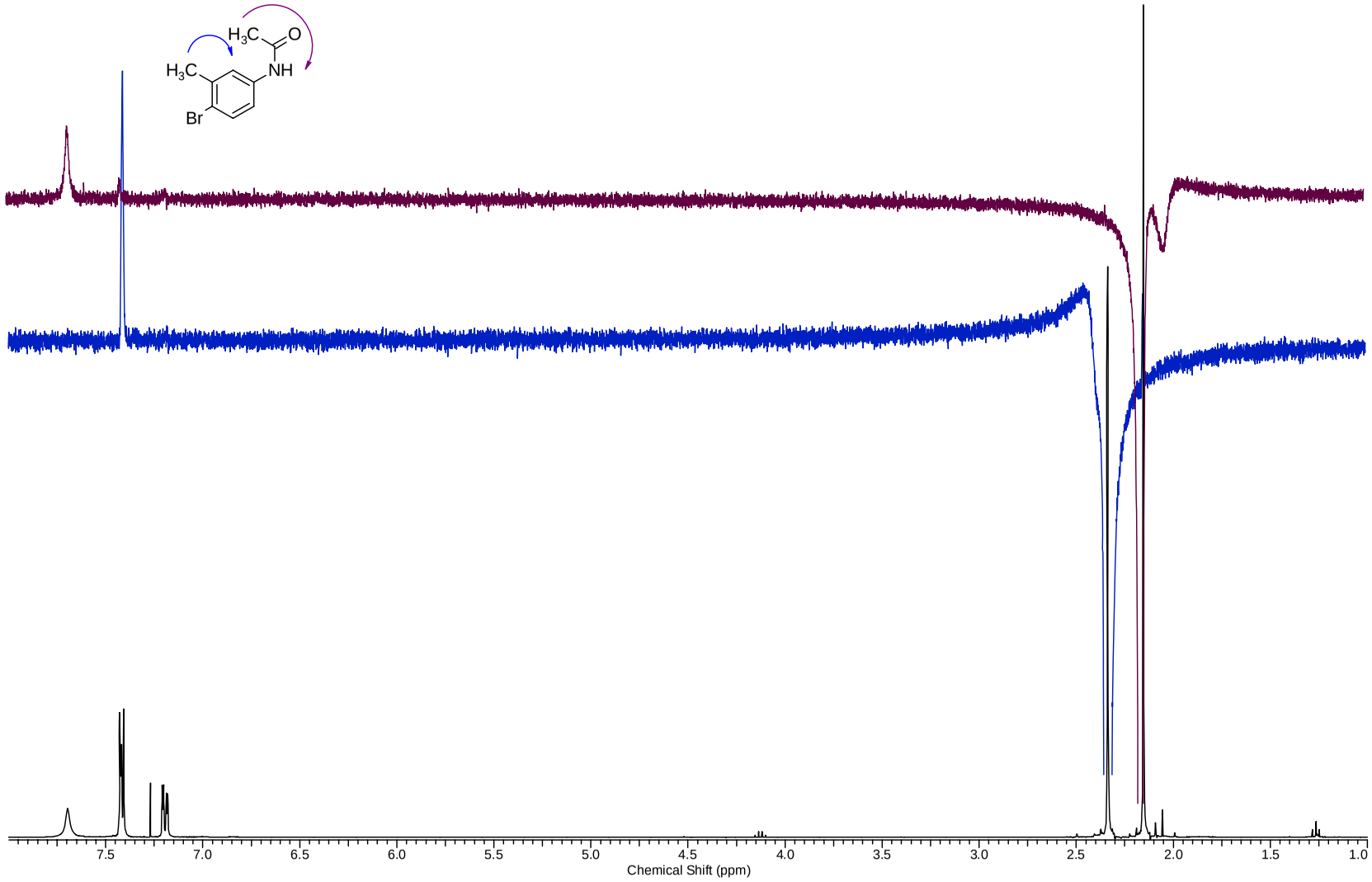
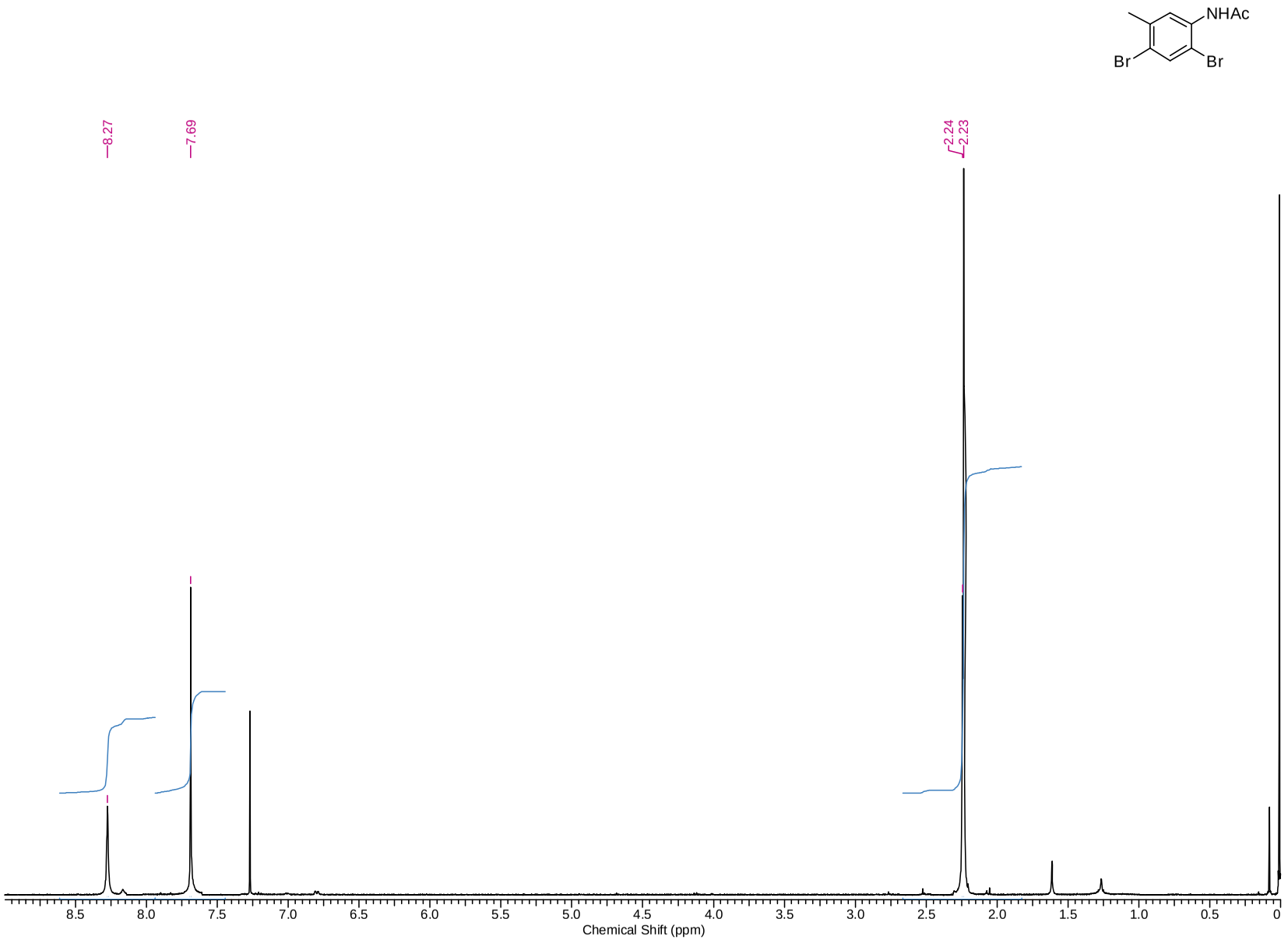
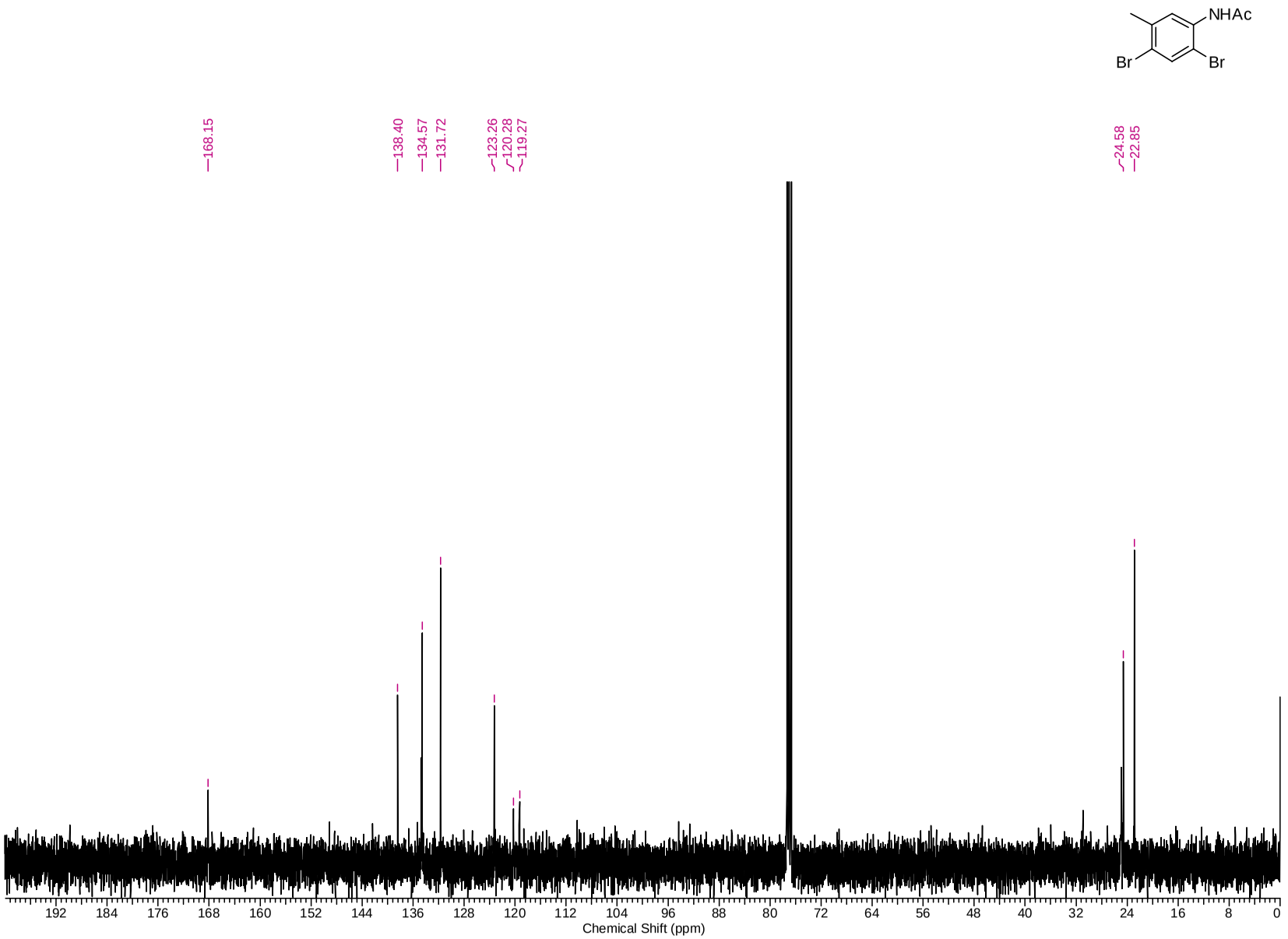
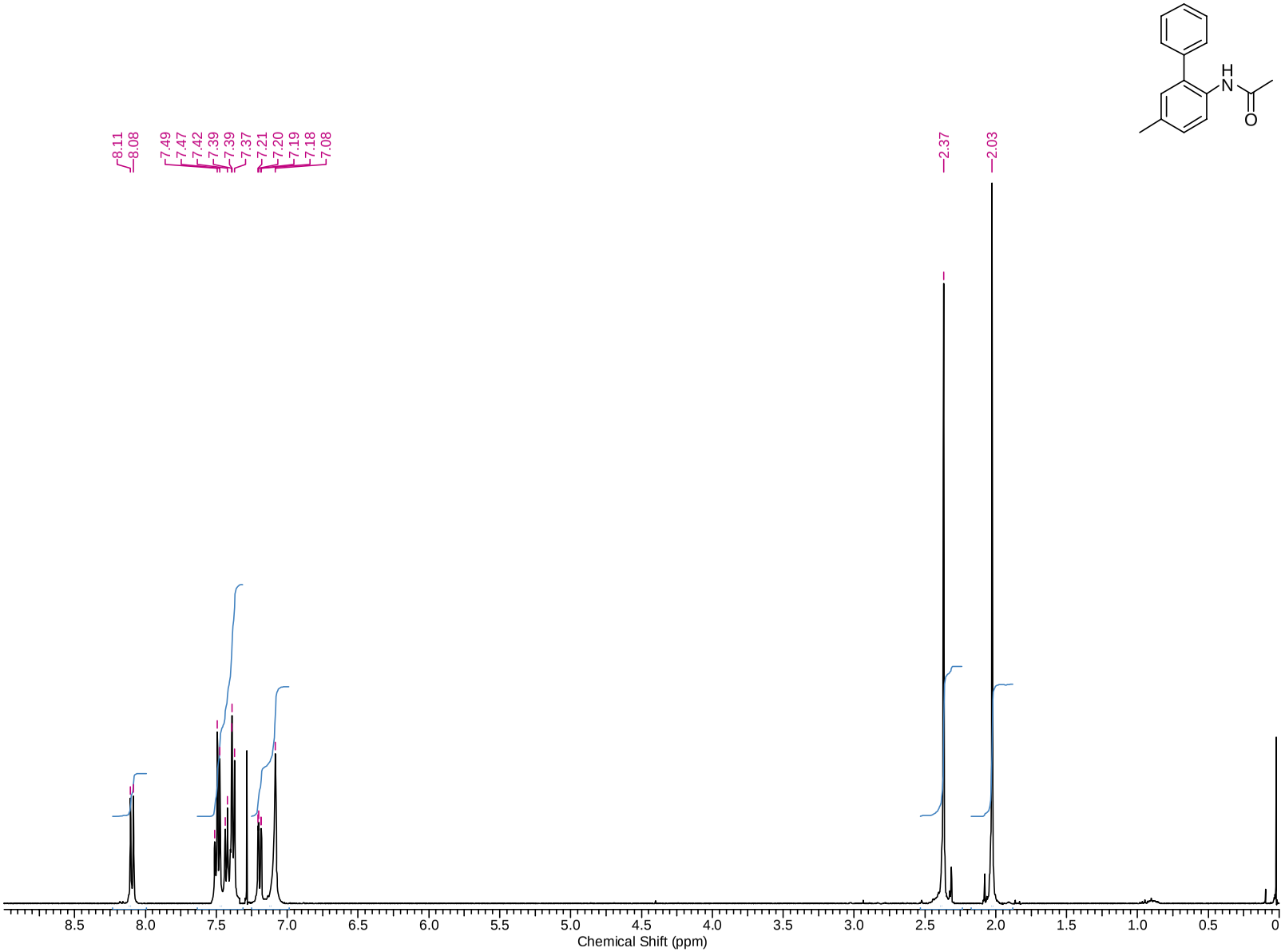


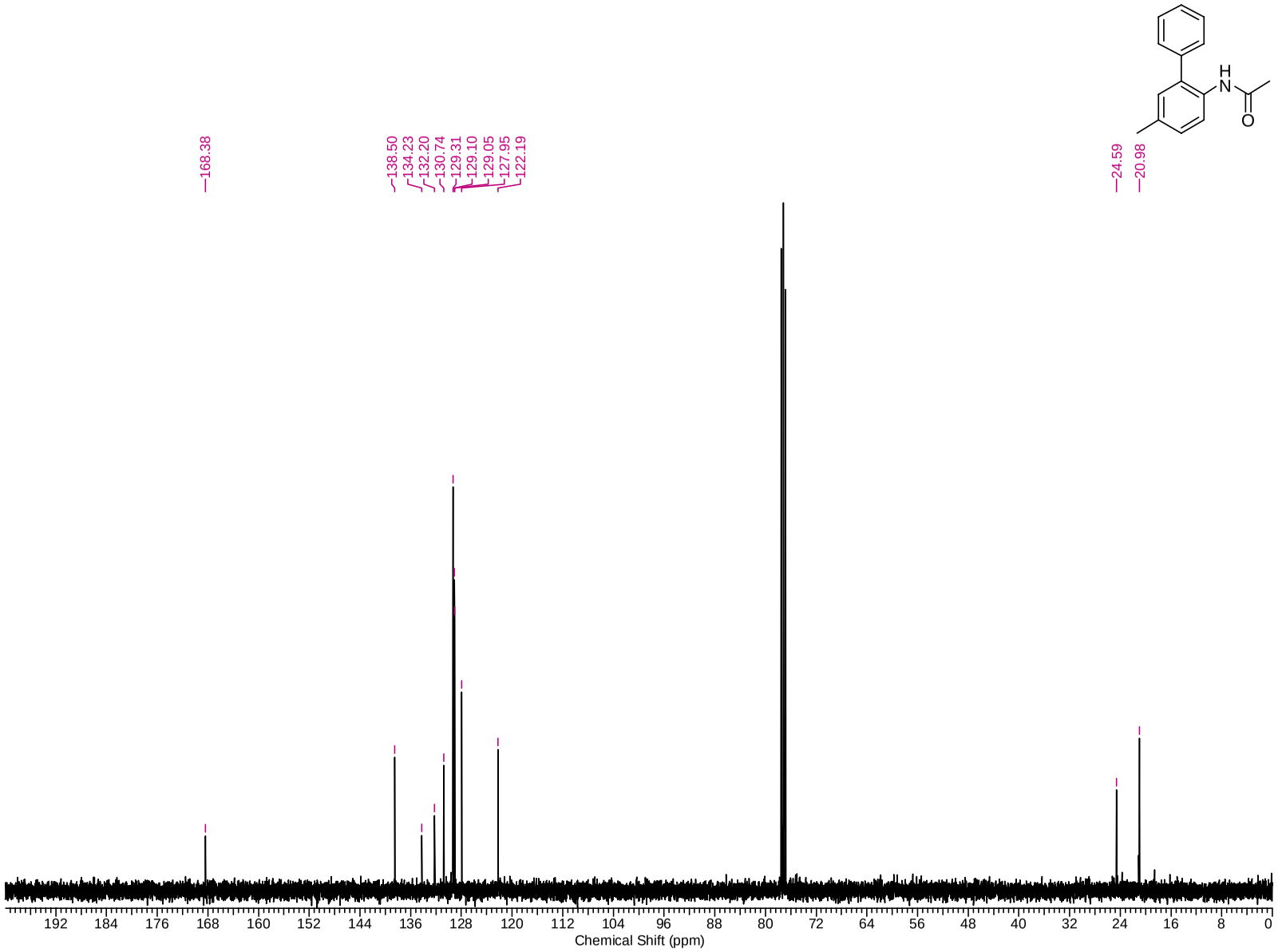
Table 2, Entries 11 & 12
NOE

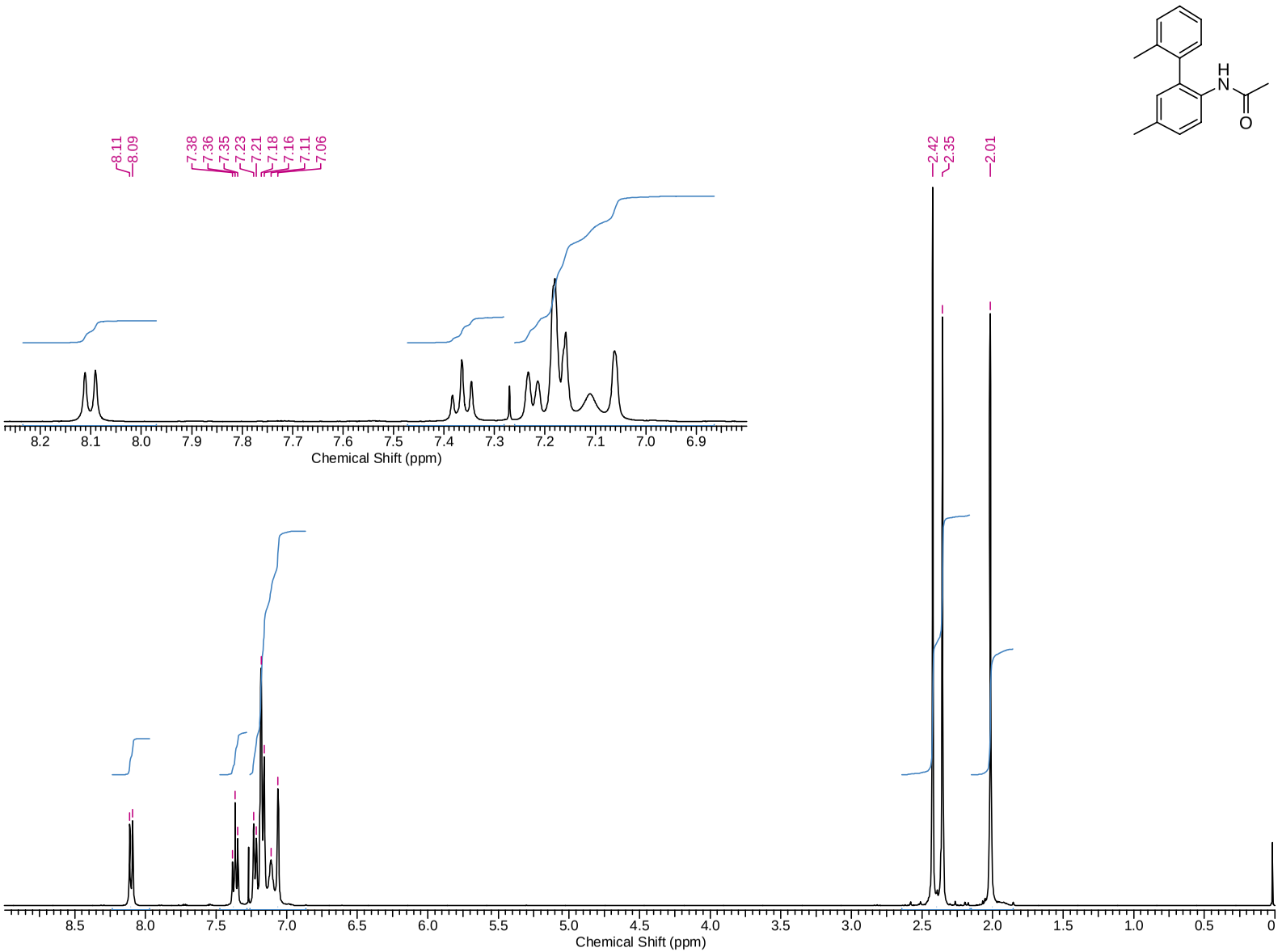


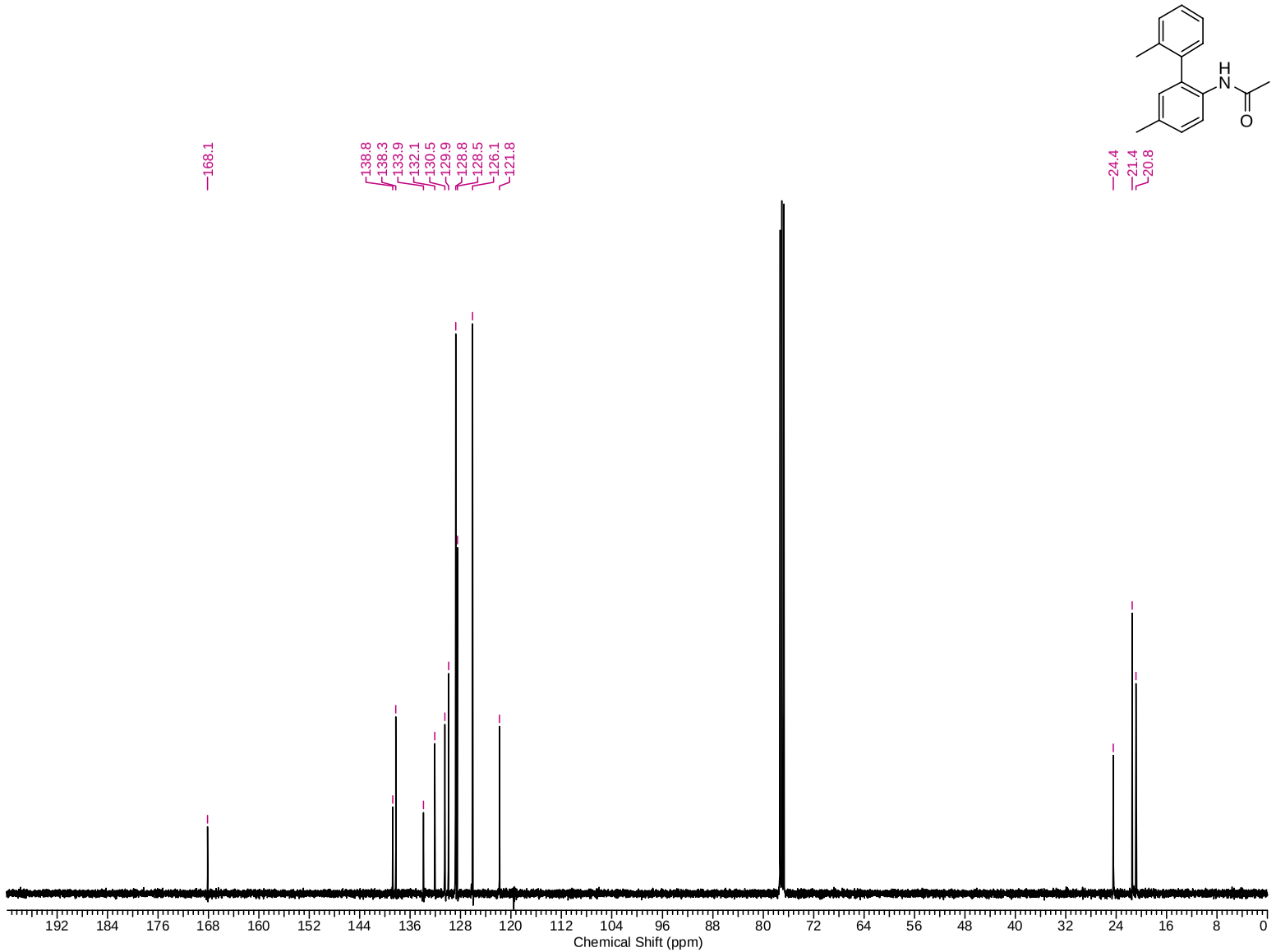

NHAc
Br
Br
8.27
7.69
2.24
2.23
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

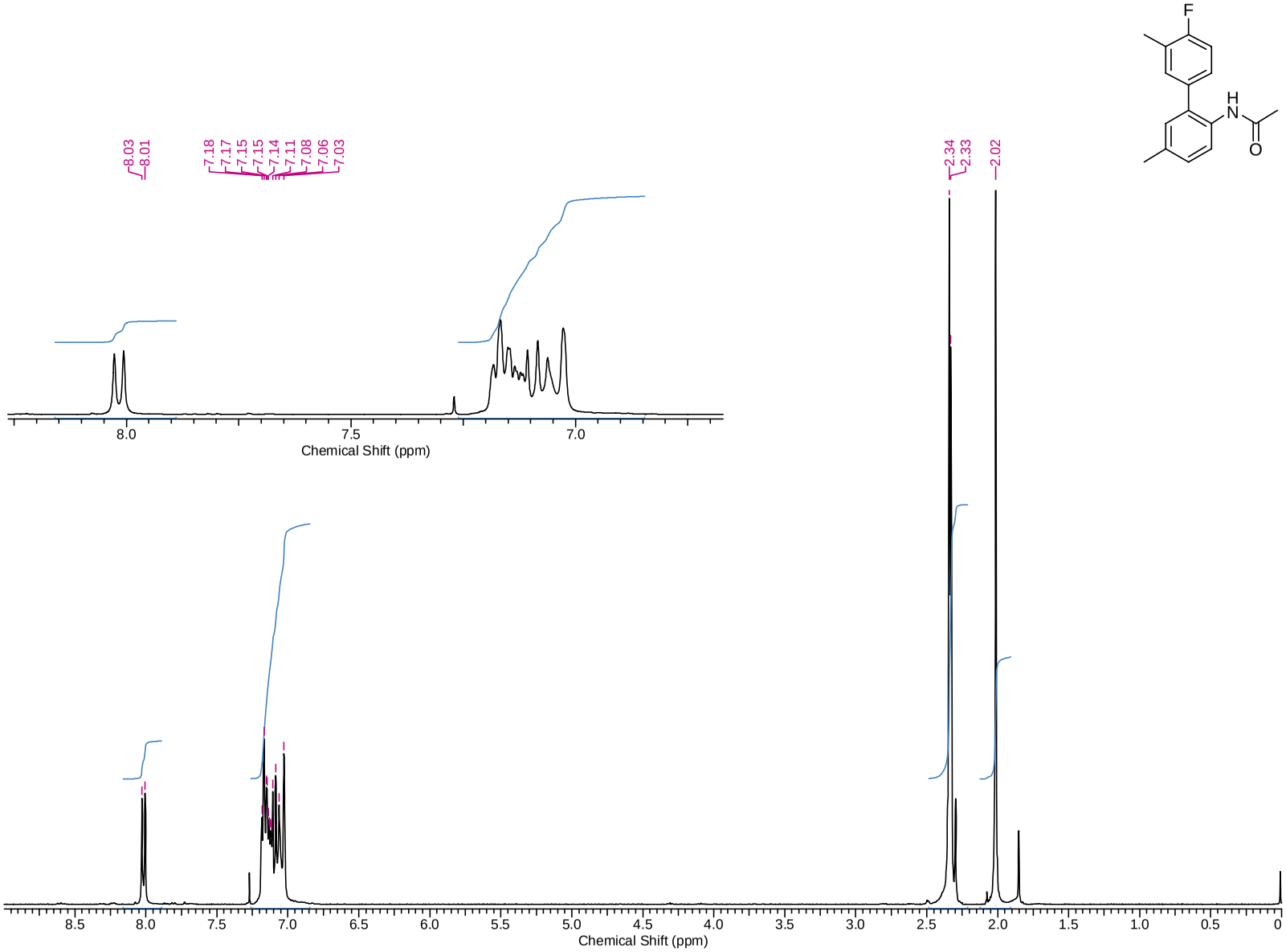

NHAc
Br
Br
168.15
138.40
134.57
131.72
123.26
120.28
119.27
24.58
22.85
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

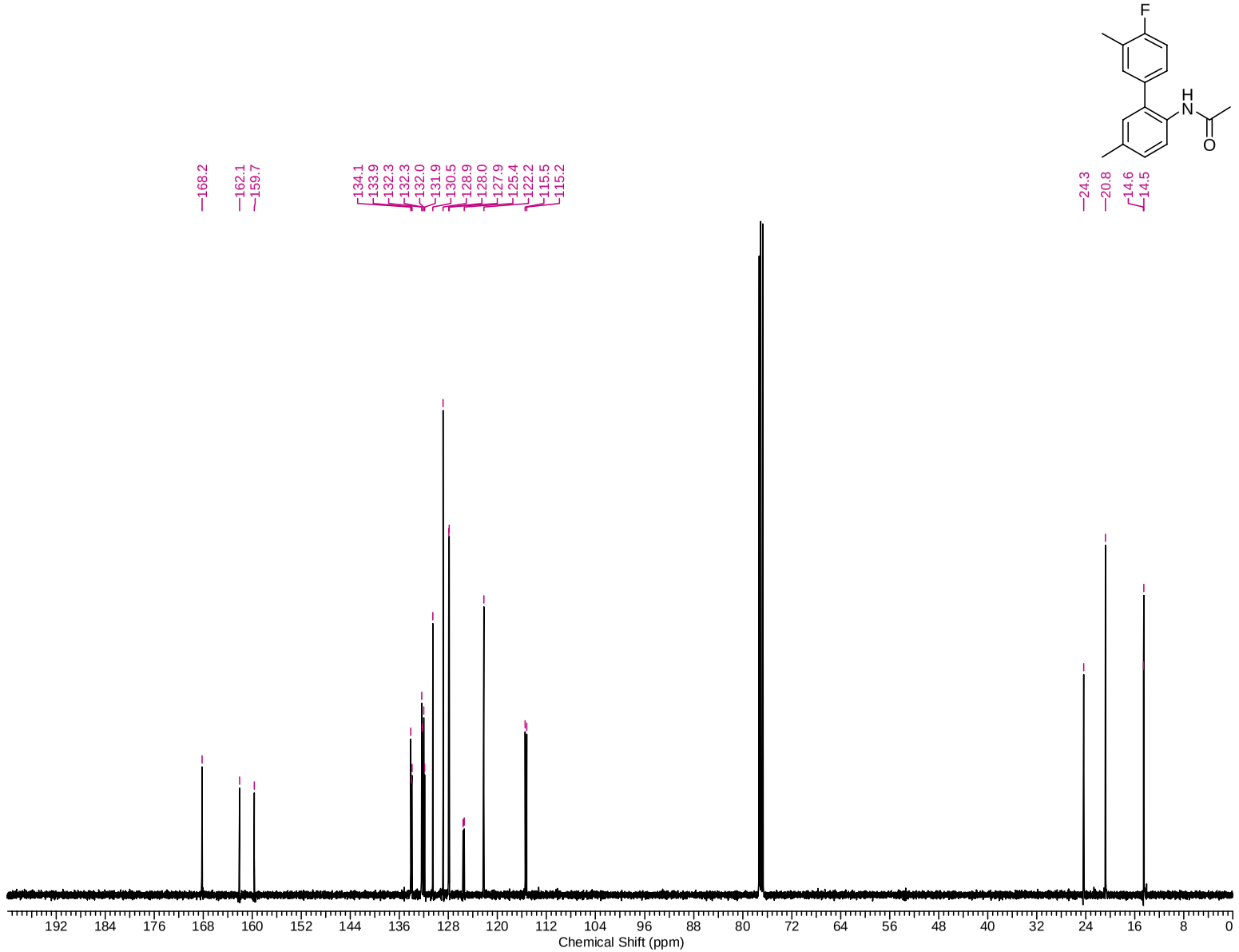

8.11
8.08
7.49
7.47
7.42
7.39
7.39
7.37
7.21
7.20
7.19
7.18
7.08
2.37
2.03
H
N
O
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

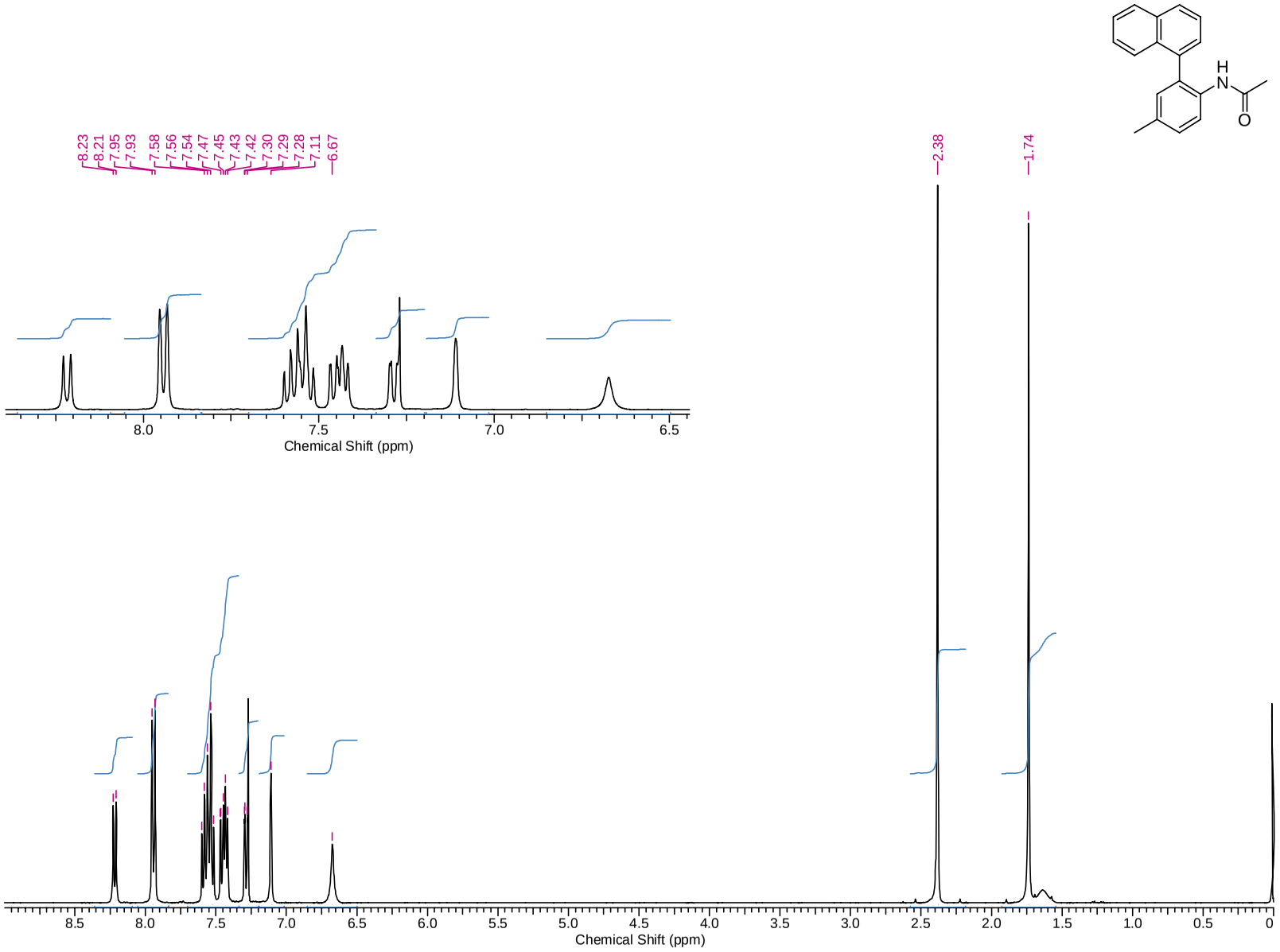

168.38
138.50
134.23
132.20
130.74
129.31
129.10
129.05
127.95
122.19
24.59
20.98
H
N
O
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

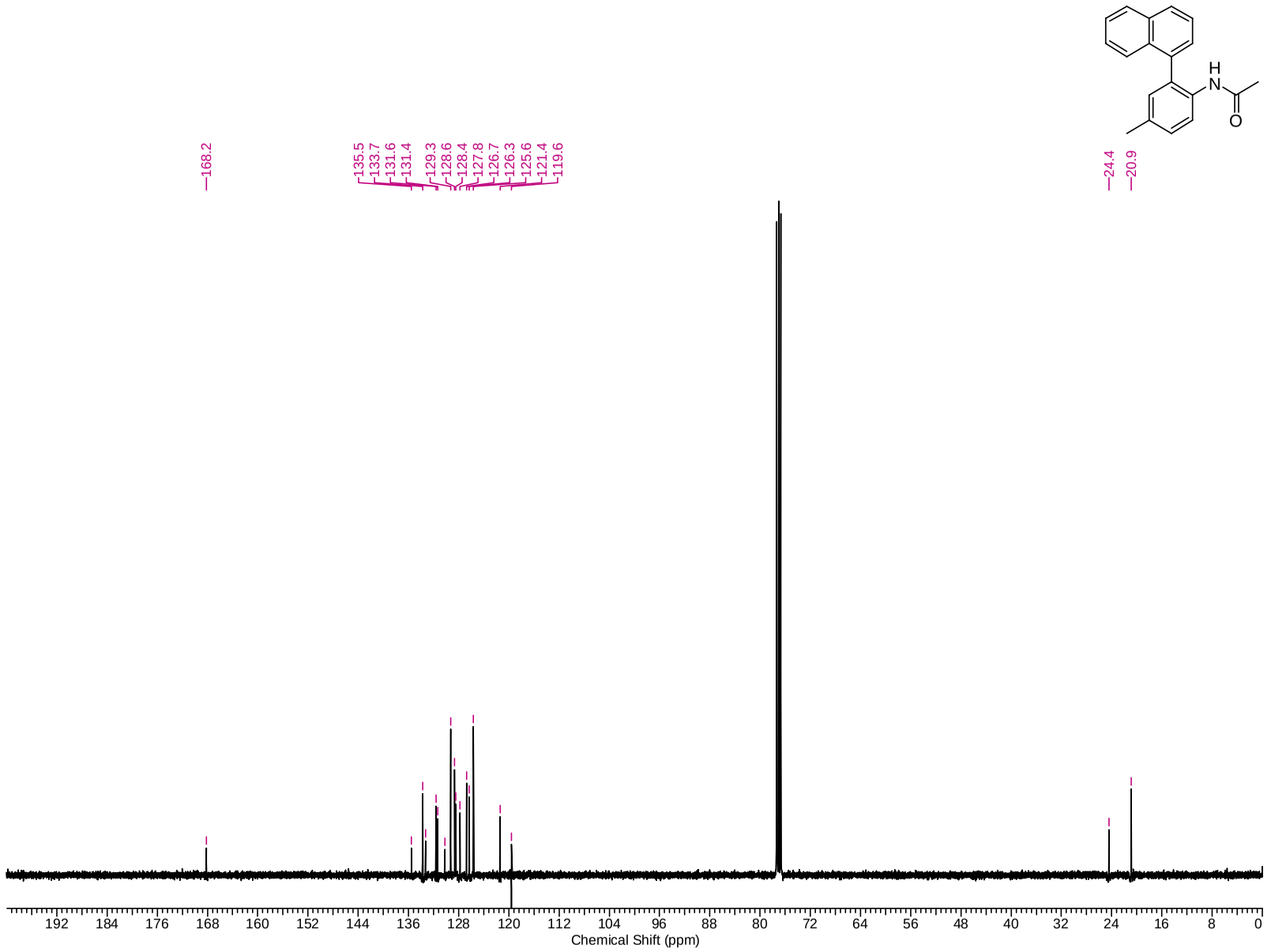

8.11
8.09
7.38
7.36
7.35
7.23
7.21
7.18
7.16
7.11
7.06
2.42
2.35
2.01
H
N
O
Chemical Shift (ppm)
Chemical Shift (ppm)

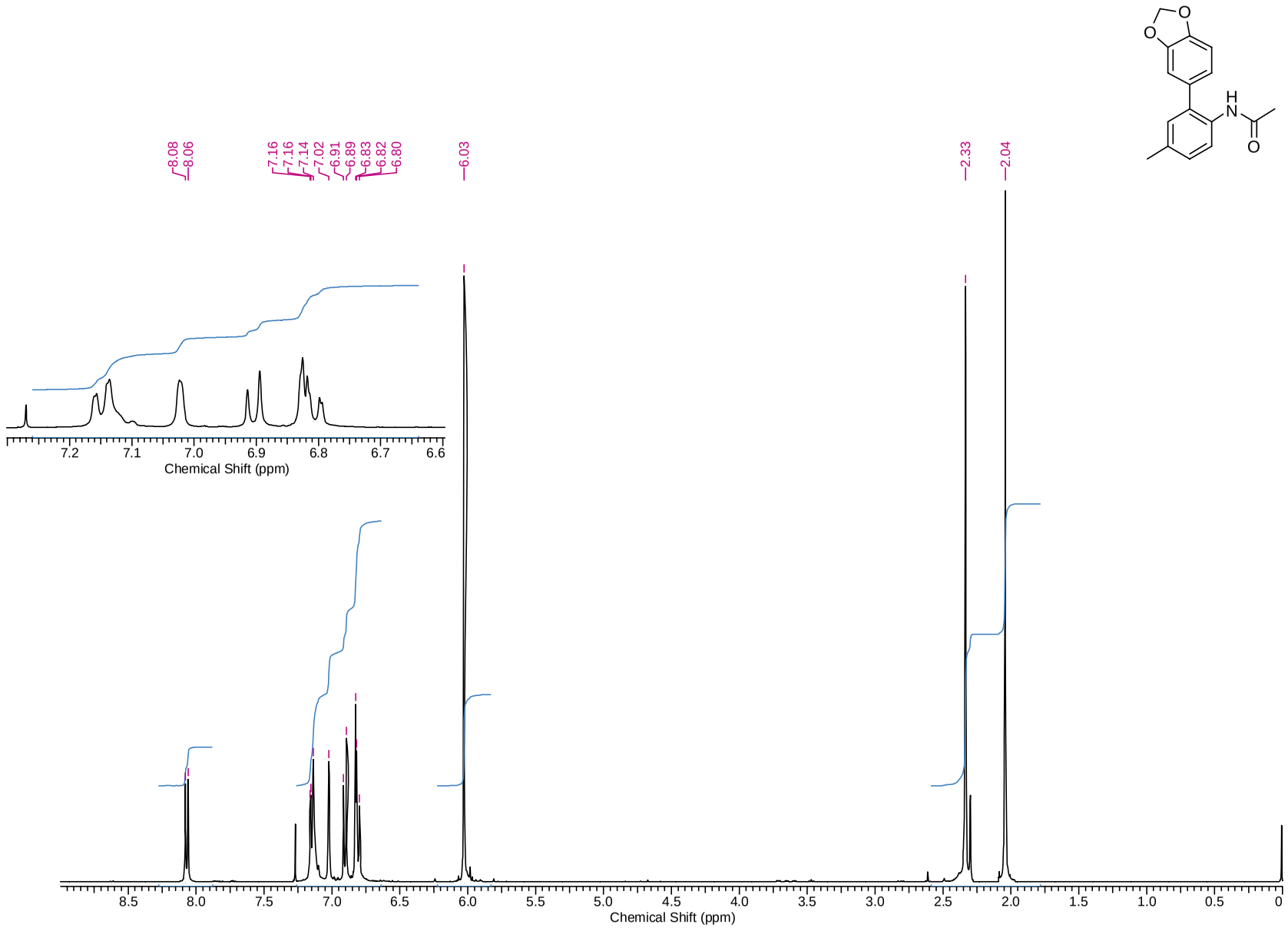

168.1
138.8
138.3
133.9
132.1
130.5
129.9
128.8
128.5
126.1
121.8
24.4
21.4
20.8
H
N
O
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

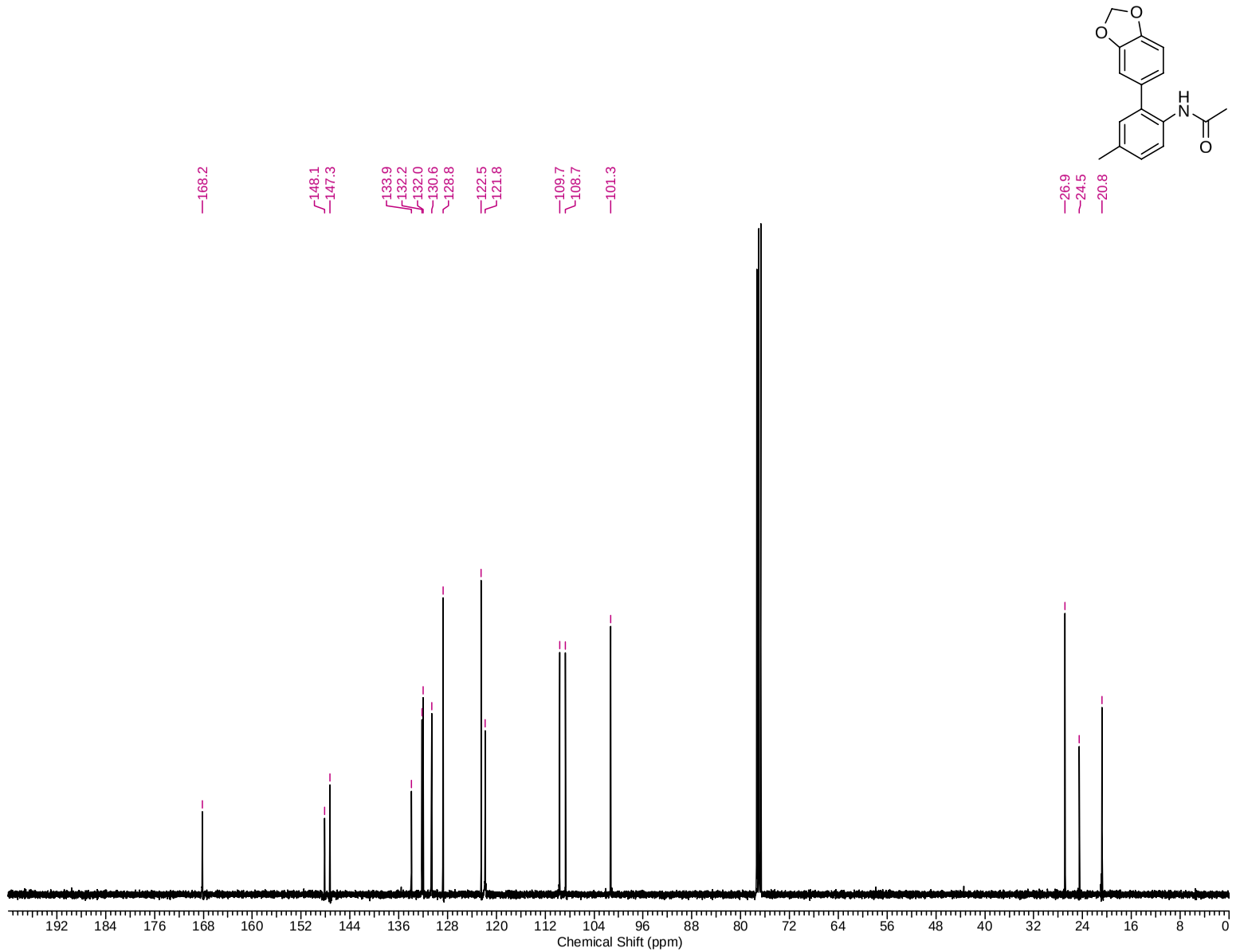

F
H
N
O
8.03
8.01
7.18
7.17
7.15
7.15
7.14
7.11
7.08
7.06
7.03
2.34
2.33
2.02
8.0
7.5
7.0
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

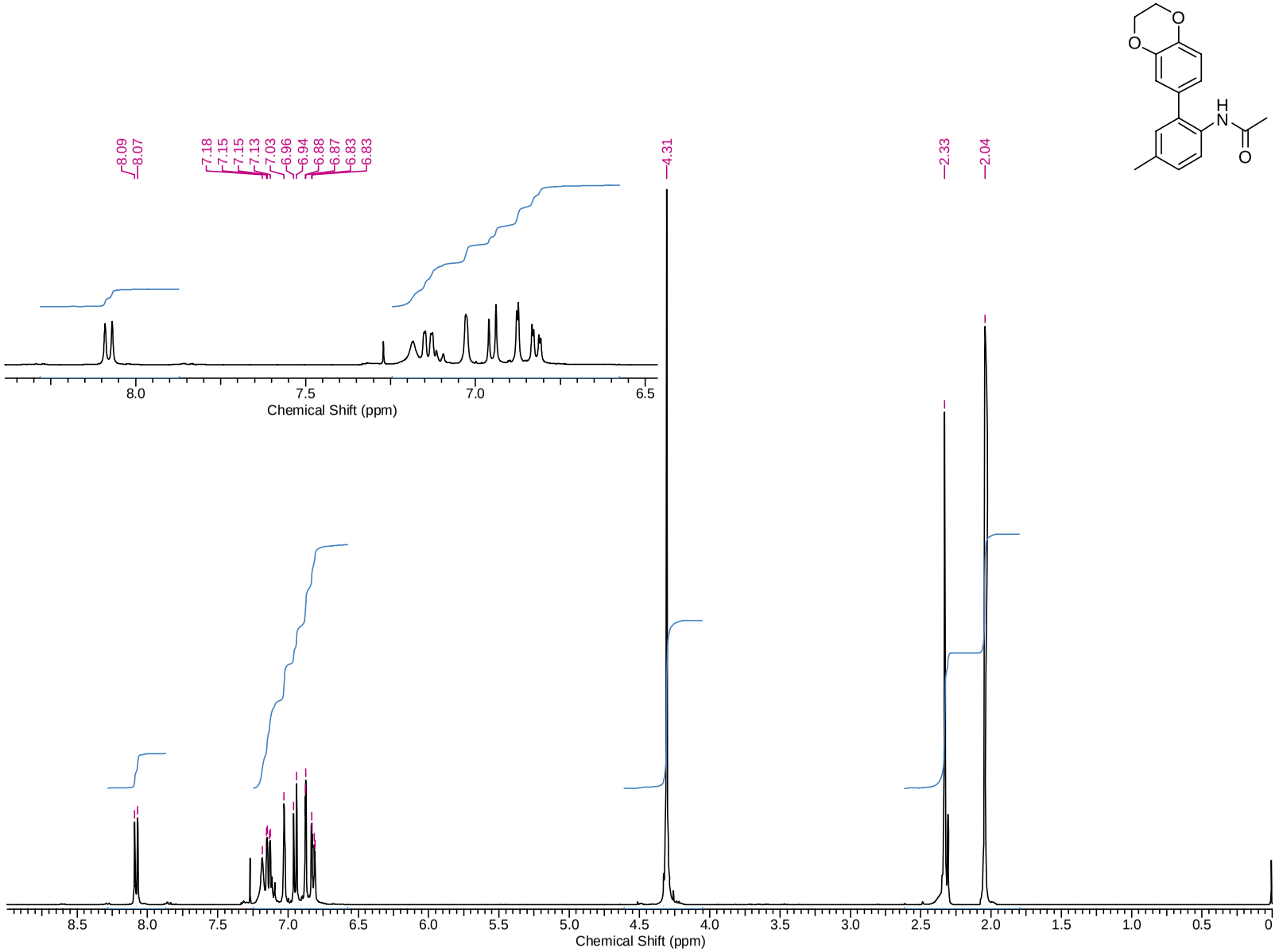

F
H
N
O
168.2
162.1
159.7
134.1
133.9
132.3
132.3
132.0
131.9
130.5
128.9
128.0
127.9
125.4
122.2
115.5
115.2
24.3
20.8
14.6
14.5
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

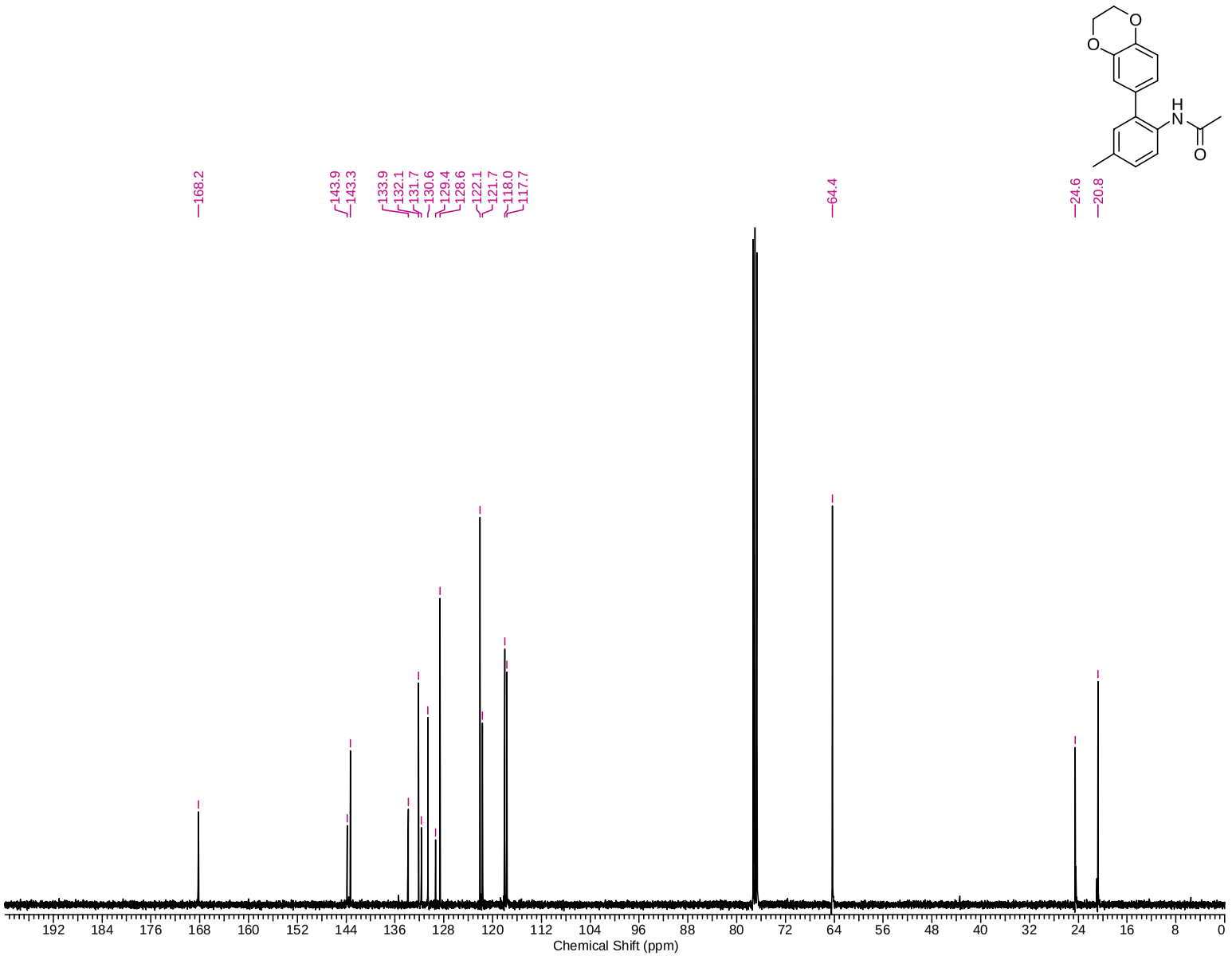

8.23
8.21
7.95
7.93
7.58
7.56
7.54
7.47
7.45
7.43
7.42
7.30
7.29
7.28
7.11
6.67
2.38
1.74
H
N
O
8.0
7.5
7.0
6.5
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

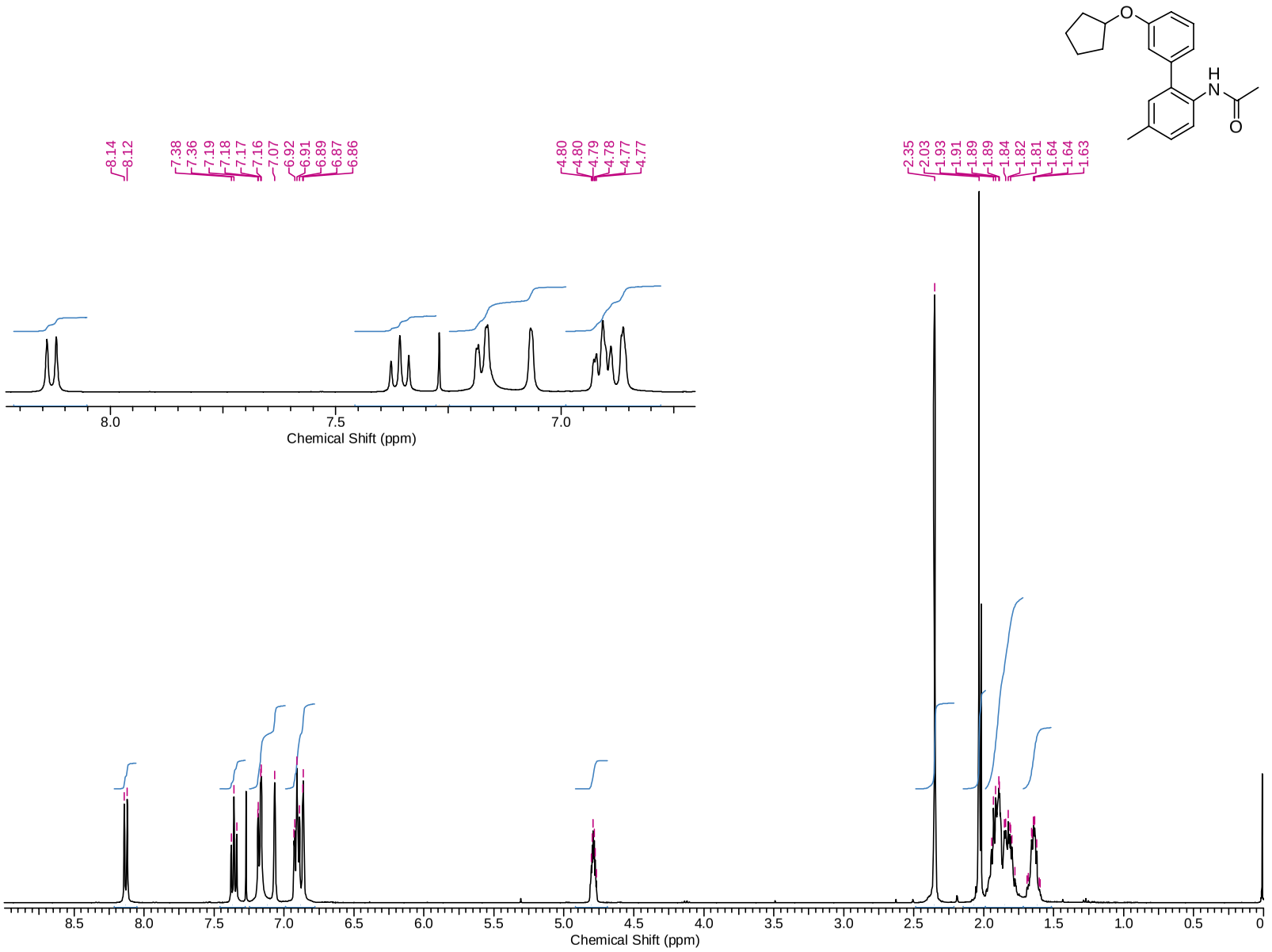

168.2
135.5
133.7
131.6
131.4
129.3
128.6
128.4
127.8
126.7
126.3
125.6
121.4
119.6
24.4
20.9
H
N
O
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

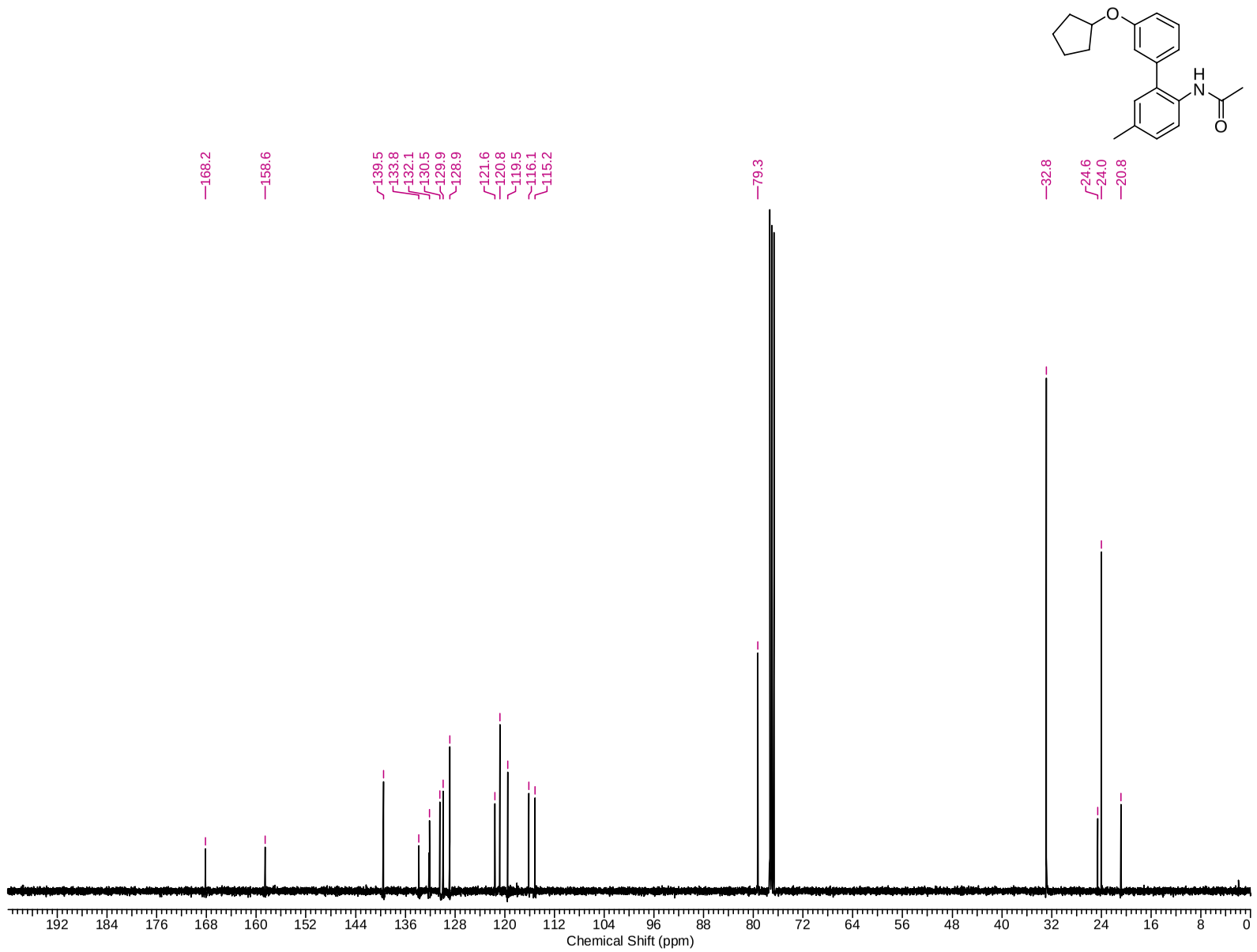

8.08
8.06
7.16
7.16
7.14
7.02
6.91
6.89
6.83
6.82
6.80
6.03
2.33
2.04
7.2
7.1
7.0
6.9
6.8
6.7
6.6
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)
O
O
H
N
O


O
O
H
N
O
168.2
148.1
147.3
133.9
132.2
132.0
130.6
128.8
122.5
121.8
109.7
108.7
101.3
26.9
24.5
20.8
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)


8.09
8.07
7.18
7.15
7.15
7.13
7.03
6.96
6.94
6.88
6.87
6.83
6.83
4.31
2.33
2.04
O
O
H
N
O
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)


168.2
143.9
143.3
133.9
132.1
131.7
130.6
129.4
128.6
122.1
121.7
118.0
117.7
64.4
24.6
20.8
O
O
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)


8.14
8.12
7.38
7.36
7.19
7.18
7.17
7.16
7.07
6.92
6.91
6.89
6.87
6.86
4.80
4.80
4.79
4.78
4.77
4.77
2.35
2.03
1.93
1.91
1.89
1.89
1.84
1.82
1.81
1.64
1.64
1.63
O
H
N
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)


O
H
N
O
168.2
158.6
139.5
133.8
132.1
130.5
129.9
128.9
121.6
120.8
119.5
116.1
115.2
79.3
32.8
24.6
24.0
20.8
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)