Supplementary information

Novel 2-phenyloxypyrimidine derivative induces apoptosis and autophagy via inhibiting PI3K pathway and activating MAPK/ERK signaling in hepatocellular carcinoma cells

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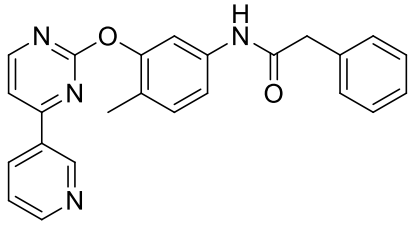
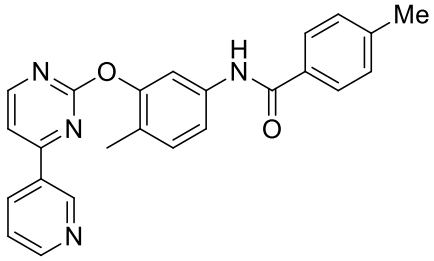
Materials & Methods

Chemical synthesis



A2

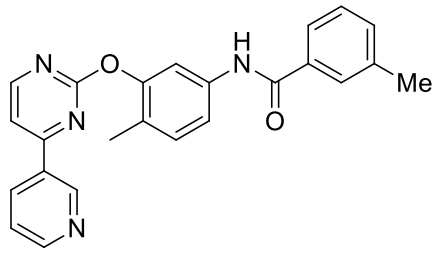
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)-2-phenylacetamide: A round bottom flask was charged with 0.28 g of **8**, 0.13 g of benzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.38 g of **A2** was obtained in the yield of 96%. HPLC R_t = 13.3 min, purity: 99%; ^{1}H NMR(300 MHz, $CDCl_3$) δ 9.18 (d, J = 1.8 Hz, 1H), 8.69 – 8.68 (m, 1H), 8.32 (d, J = 8.0 Hz, 1H), 7.99 (s, 1H), 7.51 (s, 1H), 7.42 – 7.38 (m, 2H), 7.36 – 7.27 (m, 5H), 7.25 – 7.16 (m, 2H), 3.64 (s, 2H), 2.12 (s, 3H) ppm; ^{13}C NMR(75 MHz, $CDCl_3$) δ 169.2, 164.0, 165.3, 164.6, 160.6, 151.9, 151.3, 148.5, 136.9, 134.9, 134.5, 131.8, 131.2, 127.5, 126.4, 123.8, 117.0, 113.6, 111.6, 44.6, 15.9 ppm; HRMS (ESI) calcd for $[C_{24}H_{20}N_4O_2+H]+$ 397.1586, found 397.1465.



A3

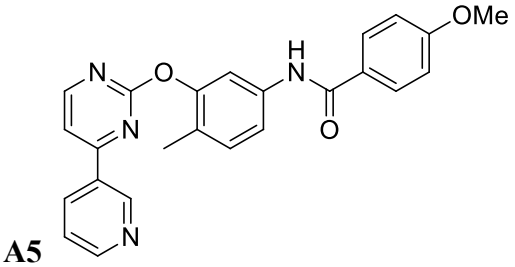
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)-2-phenylacetamide: A round bottom flask was charged with 0.28 g of **8**, 0.13 g of 4-methylbenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.33 g of **A3** was obtained in the yield of 85%. HPLC R_t = 11.8 min, purity: 99%; ^{1}H NMR(300 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.70 (d, J = 3.4 Hz, 1H), 8.68 – 8.58 (m, 1H), 8.37 – 8.34 (m, 1H), 7.98 (d, J = 8.1 Hz 1H), 7.73 – 7.67 (m, 3H), 7.45 – 7.40 (m, 3H), 7.39 – 7.18 (m, 3H), 2.36 (s, 3H), 2.17 (s, 3H) ppm; ^{13}C NMR(75 MHz, $CDCl_3$) δ 165.6, 165.4, 164.6, 160.6, 151.8, 151.4, 148.4, 142.3, 137.2, 135.0, 132.0, 131.8, 130.0, 129.4, 129.0, 127.0, 126.4, 123.9,

117.4, 114.0, 111.6, 21.5, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{20}N_4O_2+H]+$ 397.1586, found 397.1665.



A4

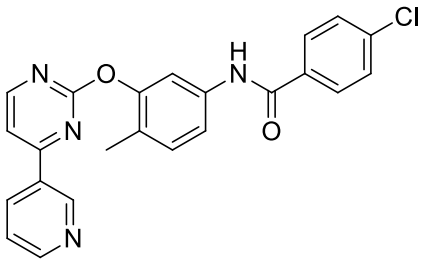
3-methyl-N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g of **8**, 0.13 g of 3-methylbenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.35 g of **A4** was obtained in the yield of 90%. HPLC R_t = 12.0 min, purity: 99%; ^{1}H NMR(300 MHz, $CDCl_3$) δ 9.12 (d, J = 1.2 Hz 1H), 8.61 (d, J = 3.5 Hz, 1H), 8.50 (d, J = 5.2 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.1 Hz 1H), 7.73 – 7.67 (m, 1H), 7.45 – 7.40 (m, 1H), 8.21 (s, 1H), 7.60 – 7.50 (s, 3H), 7.37 – 7.30 (m, 3H), 7.20 – 7.14 (m, 3H), 2.26 (s, 3H), 2.09 (s, 3H) ppm; ^{13}C NMR(75 MHz, $CDCl_3$) δ 166.2, 165.3, 164.5, 160.6, 151.7, 151.4, 148.4, 138.4, 137.4, 135.0, 134.8, 132.4, 131.8, 131.3, 128.4, 127.9, 126.3, 124.2, 123.8, 117.6, 114.1, 111.6, 21.2, 15.9 ppm; HRMS (ESI) calcd for $[C_{24}H_{20}N_4O_2+H]+$ 397.1586, found 397.1664.



A5

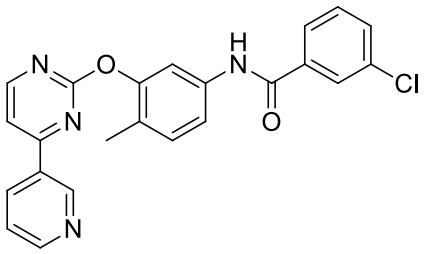
4-methoxy-N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)benzamid e: A round bottom flask was charged with 0.28 g of **8**, 0.17 g of 4-methoxybenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.37 g of **A5** was obtained in the yield of 90%. HPLC R_t = 14.2 min, purity: 99%; ^{1}H NMR(300 MHz, $CDCl_3$) δ 9.12 (d, J = 1.2 Hz 1H), 8.61 (d, J = 3.5 Hz, 1H), 8.50 (d, J = 5.2 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.1 Hz 1H), 7.73 – 7.67 (m, 1H), 7.45 – 7.40 (m, 1H), 8.21 (s, 1H), 7.60 – 7.50 (s, 3H), 7.37 – 7.30 (m, 3H), 7.20 – 7.14 (m, 3H), 2.26 (s, 3H), 2.09 (s, 3H) ppm; ^{13}C

NMR(75 MHz, $CDCl_3$) δ 165.4, 164.7, 162.4, 160.6, 151.9, 151.4, 148.5, 137.3, 134.9, 131.8, 129.0, 127.0, 126.3, 123.8, 117.5, 114.0, 113.8, 111.6, 55.4, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{20}N_4O_3+H]^+$ 413.1535, found 413.1614.



A6

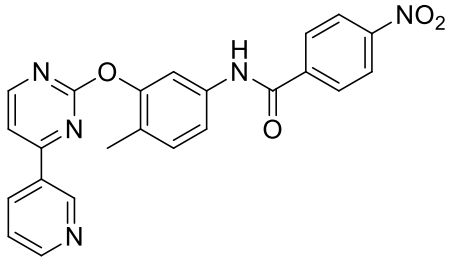
4-chloro-N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g of **8**, 0.17 g of 4-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.36 g of **A6** was obtained in the yield of 87%. HPLC R_t = 13.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.68 (d, J = 3.5 Hz, 1H), 8.57– 8.54 (m, 2H), 8.32 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.65 (s, 1H), 7.44 – 7.31 (m, 5H), 7.22 (d, J = 8.0 Hz, 1H), 2.16 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 164.9, 160.6, 151.9, 151.4, 148.5, 137.9, 137.0, 134.9, 133.2, 131.7, 131.4, 128.8, 128.6, 126.8, 123.8, 117.6, 114.2, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{17}N_4O_2Cl+H]^+$ 417.1040, found 417.1119.



A7

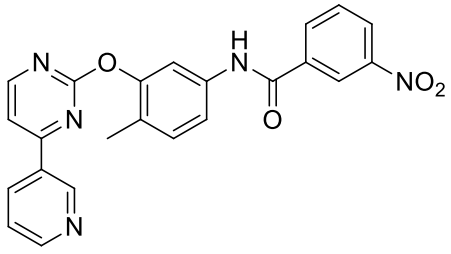
3-chloro-N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g of **8**, 0.17 g of 3-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.38 g of **A7** was obtained in the yield of 91%. HPLC R_t = 12.5 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.80 (s, 1H), 8.66 (d, J = 4.5 Hz, 1H), 8.55 (d, J = 5.1 Hz, 1H), 8.32 (d, J = 7.9 Hz, 2H), 7.78 (s, 1H), 7.67 (d, J = 7.9 Hz, 2H), 7.44 – 7.31 (m, 4H), 7.28 – 7.30 (m, 1H), 7.20 (d, J = 8.2 Hz, 1H), 2.14 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 164.7, 164.4, 160.6, 152.0, 151.4, 148.6, 136.8, 136.7, 134.9, 134.8, 131.8, 131.4, 130.0, 127.4,

126.9, 125.2, 123.8, 117.6, 114.2, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{17}N_4O_2Cl+H]+$ 417.1040, found 417.1119.



A8

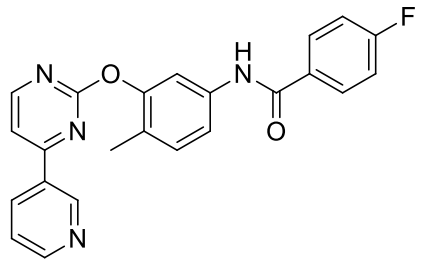
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)-4-nitrobenzamide: A round bottom flask was charged with 0.28 g of **8**, 0.18 g of 4-nitrobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.32 g of **A8** was obtained in the yield of 75%. HPLC R_t = 9.8 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.22 (d, J = 1.7 Hz, 1H), 8.72 (dd, J = 4.8 Hz, J = 1.5 Hz, 1H), 8.33 (dt, J = 8.0 Hz, J = 1.7 Hz, 1H), 8.30 (d, J = 8.6 Hz, 2H), 8.14 (s, 1H), 8.01 (d, J = 8.7 Hz, 2H), 7.67 (s, 1H), 7.49 (d, J = 5.2 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.30 (d, J = 8.3 Hz, 1H), 2.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 164.6, 163.8, 160.6, 151.8, 151.4, 149.6, 148.5, 140.4, 136.4, 134.9, 131.7, 131.5, 128.4, 127.5, 123.9, 117.7, 114.4, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{17}N_5O_4+H]+$ 427.1281, found 427.1407.



A9

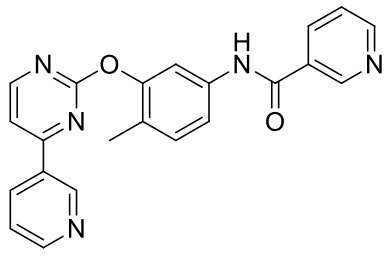
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)-3-nitrobenzamide: A round bottom flask was charged with 0.28 g of **8**, 0.18 g of 3-nitrobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.33 g of **A9** was obtained in the yield of 77%. HPLC R_t = 8.1 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.27 (s, 1H), 9.16 (d, J = 1.5 Hz, 1H), 8.67 – 8.66 (m, 2H), 8.57 (d, J = 5.2Hz, 1H), 8.32 – 8.20 (m, 3H), 7.65 (d, J = 1.3 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.46 – 7.37 (m, 3H), 7.20 (d, J = 8.3 Hz, 1H), 2.13 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 164.6, 163.6, 160.6, 151.9, 151.4, 148.5, 148.0, 136.6, 136.4, 134.9, 133.6, 131.7, 131.4, 129.9, 127.2,

126.2, 123.9, 122.0, 117.9, 114.5, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{17}N_5O_4+H]+$ 427.1281, found 427.1405.



A10

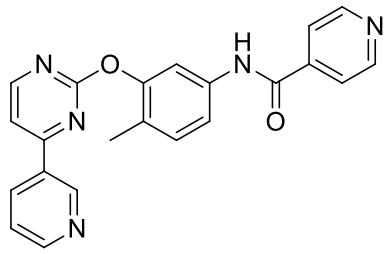
4-fluoro-N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g of **8**, 0.15 g of 4-fluorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.38 g of **A10** was obtained in the yield of 95%. HPLC R_t = 11.9 min, purity: 98%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.60 (d, J = 3.9 Hz, 1H), 8.48 (d, J = 5.0 Hz, 1H), 8.38 (s, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.75 (dd, J = 7.8, 5.5 Hz, 2H), 7.56 (s, 1H), 7.33 (dd, J = 14.9, 6.5 Hz, 3H), 7.14 (d, J = 8.2 Hz, 1H), 6.96 (t, J = 8.4 Hz, 2H), 2.08 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 165.3, 164.6, 160.6, 151.8, 151.4, 148.5, 137.0, 134.9, 131.8, 131.4, 129.6, 129.5, 126.7, 123.8, 117.6, 115.8, 115.5, 114.2, 111.6, 15.9 ppm; HRMS (ESI) calcd for $[C_{23}H_{17}N_4O_2F+H]+$ 401.1336, found 401.1414.



A11

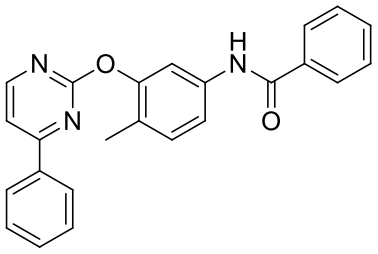
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)nicotinamide: A round bottom flask was charged with 0.28 g of **8**, 0.13 g of nicotinic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 30:1(v:v) as eluent. 0.34 g of **A11** was obtained in the yield of 89%. HPLC R_t = 7.6 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.76 (s, 1H), 8.69 (s, 1H), 8.59 (d, J = 5.1 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 7.68 – 7.65 (m, 3H), 7.47 – 7.40 (m, 3H), 7.26 (d, J = 8.4 Hz, 1H), 2.18 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 164.7, 163.9, 160.6, 152.0, 151.4, 150.5, 148.6, 142.1, 136.5, 134.8, 131.7, 131.5, 127.4, 123.8, 121.0, 117.7, 114.4, 111.7, 16.0 ppm; HRMS (ESI)

calcd for $[C_{22}H_{17}N_5O_2+H]+$ 384.1382, found 384.1463.



A12

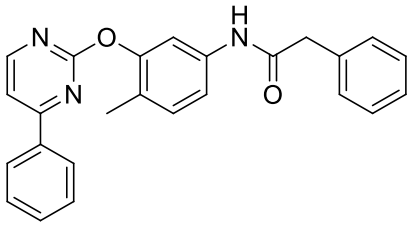
N-(4-methyl-3-((4-(pyridin-3-yl)pyrimidin-2-yl)oxy)phenyl)isonicotinamide: A round bottom flask was charged with 0.28 g of **8**, 0.13 g of isonicotinic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 30:1(v:v) as eluent. 0.31 g of **A12** was obtained in the yield of 82%. HPLC R_t = 8.3 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) 9.20 (s, 1H), 9.08 (d, J = 1.4 Hz, 1H), 8.96 (s, 1H), 8.66 – 8.50 (m, 2H), 8.47 (d, J = 5.2 Hz, 1H), 8.27 – 8.16 (m, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 1.5 Hz, 1H), 7.41 – 7.26 (m, 3H), 7.22 (dd, J = 7.5, 4.6 Hz, 1H), 7.12 (d, J = 8.3 Hz, 1H), 2.06 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 164.6, 164.1, 160.6, 152.0, 151.8, 151.3, 148.4, 148.0, 136.9, 135.6, 134.9, 131.7, 131.4, 130.9, 127.0, 123.9, 123.6, 117.9, 114.4, 111.7, 15.9 ppm; HRMS (ESI) calcd for $[C_{22}H_{17}N_5O_2+H]+$ 384.1382, found 384.1459.



B1

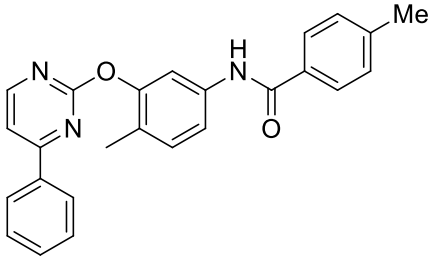
N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.13 g benzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.33 g of **B1** was obtained in the yield of 86%. HPLC R_t = 15.1 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) 8.85 (s, 1H), 8.37 (d, J = 5.2 Hz, 1H), 7.96 (d, J = 6.3 Hz, 2H), 7.74 (d, J = 7.3 Hz, 2H), 7.61 (s, 1H), 7.51 (d, J = 6.9 Hz, 1H), 7.41 – 7.30 (m, 5H), 7.24 (t, J = 7.6 Hz, 2H), 7.13 (d, J = 8.3 Hz, 1H), 2.09 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 166.3, 165.2, 159.8, 151.4, 137.4, 135.8, 134.8, 131.6, 131.4, 131.3, 128.9, 128.5, 127.4, 127.2, 126.5, 117.8, 114.3, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{19}N_3O_2+H]+$

382.1477, found 382.1554.



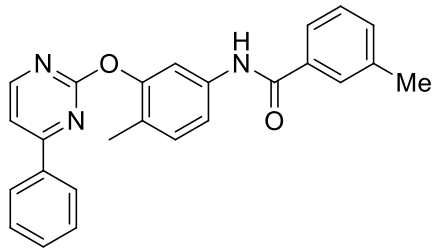
B2

N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)-2-phenylacetamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.15 g 2-phenylacetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.37 g of **B2** was obtained in the yield of 94%. HPLC R_t = 16.9 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, J = 5.1 Hz, 1H), 7.97 (d, J = 6.5 Hz, 2H), 7.41 (d, J = 6.5 Hz, 4H), 7.34 (d, J = 5.1 Hz, 1H), 7.29 – 7.21 (m, 6H), 7.11 (d, J = 8.1 Hz, 1H), 3.61 (s, 2H), 2.09 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 167.2, 165.3, 160.0, 151.500, 136.708, 136.0, 134.5, 131.4, 131.2, 129.5, 129.1, 128.9, 127.6, 127.4, 126.6, 117.0, 113.6, 111.6, 44.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{25}H_{21}N_3O_2+H]^+$ 396.1634, found 396.1711.



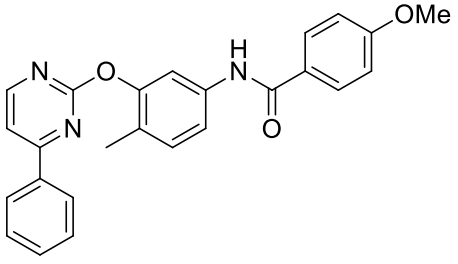
B3

4-methyl-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.13 g of 4-methylbenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.36 g of **B3** was obtained in the yield of 91%. HPLC R_t = 14.6 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, J = 5.2 Hz, 1H), 8.22 (s, 1H), 8.03 – 8.00 (m, 2H), 7.62 – 7.56 (m, 3H), 7.51 – 7.38 (m, 5H), 7.27 – 7.20 (m, 3H), 2.33 (s, 3H), 2.15 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 166.0, 165.3, 159.9, 151.5, 138.5, 137.2, 135.9, 134.9, 134.0, 132.5, 131.4, 131.3, 130.6, 128.9, 128.3, 127.4, 127.2, 126.6, 124.1, 117.5, 114.0, 111.6, 21.3, 16.0 ppm; HRMS (ESI) calcd for $[C_{25}H_{21}N_3O_2+H]^+$ 396.1634, found 396.1714.



B4

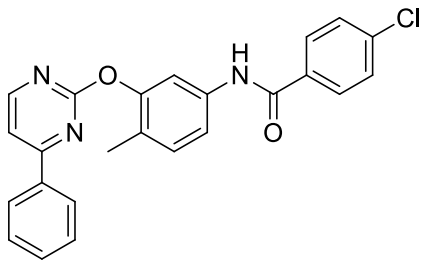
3-methyl-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.13 g of 4-methylbenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.32 g of **B4** was obtained in the yield of 81%. HPLC R_t = 15.8 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, J = 5.1 Hz, 1H), 7.97 – 7.94 (m, 3H), 7.64 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 1.6 Hz, 1H), 7.41 (s, 1H), 7.40 – 7.32 (m, 5H), 7.18– 7.12 (m, 3H), 2.29 (s, 3H), 2.09 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.3, 160.0, 142.3, 151.6, 142.3, 137.1, 136.0, 131.4, 128.9, 127.0, 117.4, 113.9, 111.6, 21.3, 16.0 ppm; HRMS (ESI) calcd for $[C_{25}H_{21}N_3O_2+H]+$ 396.1634, found 396.1713.



B5

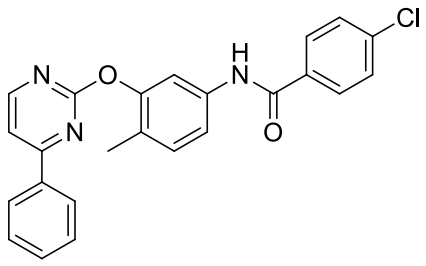
4-methoxy-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.16 g of 4-methoxybenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.35 g of **B5** was obtained in the yield of 86%. HPLC R_t = 14.1 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 5.2 Hz, 1H), 8.37 (s, 1H), 8.00 (d, J = 7.7Hz, 2H), 7.76 (d, J = 8.7Hz, 2H), 7.55 (s, 1H), 7.49 – 7.34 (m, 5H), 7.17 (d, J = 8.2 Hz, 1H), 6.81 (d, J = 8.7 Hz, 3H), 3.75 (s, 3H), 2.13 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 165.5, 165.3, 159.9, 151.5, 137.4, 135.9, 131.4, 131.3, 129.0, 128.9, 127.3, 127.0, 126.3, 117.6, 114.1, 113.8, 111.6, 55.4, 16.0 ppm; HRMS (ESI) calcd for $[C_{25}H_{21}N_3O_3+H]+$ 412.1583, found

412.1662.



B6

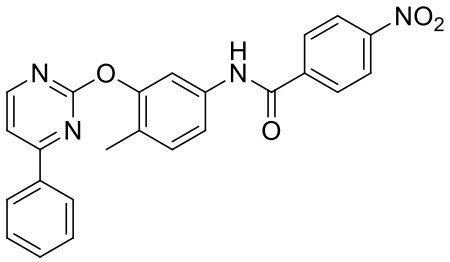
4-chloro-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.16 g of 4-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.37 g of **B6** was obtained in the yield of 89%. HPLC R_t = 11.7 min, purity: 97%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.04 (dd, J = 7.3, 1.5Hz, 2H), 7.88 (s, 1H), 7.77 (d, J = 8.5 Hz, 2H), 7.53 – 7.41 (m, 8H), 7.29 – 7.26 (m, 1H), 2.19 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.2, 164.6, 159.9, 151.6, 138.0, 136.8, 135.9, 133.3, 131.4, 128.9, 128.5, 127.3, 127.0, 117.5, 114.1, 111.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{18}N_3O_2Cl+H]^+$ 416.1088, found 416.1665.



B7

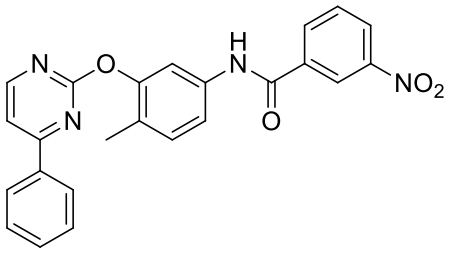
3-chloro-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.16 g of 3-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 150:1(v:v) as eluent. 0.35 g of **B7** was obtained in the yield of 84%. HPLC R_t = 13.6 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.39 (d, J = 5.2 Hz, 1H), 7.96 (d, J = 6.6 Hz, 2H), 7.71 (s, 1H), 7.61 – 7.48 (m, 3H), 7.43 – 7.34 (m, 5H), 7.18 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 2.08 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.1, 164.9, 159.8, 151.4, 137.0, 136.6, 135.8, 134.5, 131.5, 131.3, 129.8, 127.5, 127.3, 126.8, 125.4, 117.9, 114.4, 111.8, 16.0 ppm;

HRMS (ESI) calcd for $[C_{24}H_{18}N_3O_2Cl+H]+$ 416.1088, found 416.1165.



B8

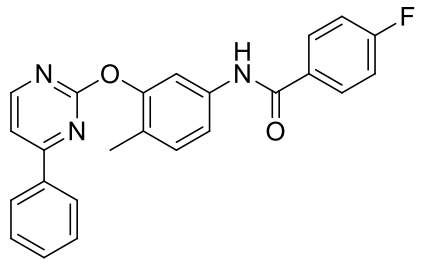
N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)-4-nitrobenzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.16 g of 4-nitrobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.33 g of **B8** was obtained in the yield of 77%. HPLC R_t = 11.8 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, J = 5.1 Hz, 1H), 8.33 (d, J = 8.7 Hz, 2H), 8.14 – 7.93 (m, 4H), 7.84 (s, 1H), 7.56 (s, 1H), 7.50 – 7.44 (m, 4H), 7.32 (d, J = 8.2 Hz, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 165.1, 163.9, 159.9, 151.5, 149.5, 140.4, 136.4, 135.7, 131.5, 129.0, 128.4, 127.3, 123.8, 117.8, 114.3, 111.8, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{18}N_4O_4+H]+$ 427.1328, found 427.1403.



B9

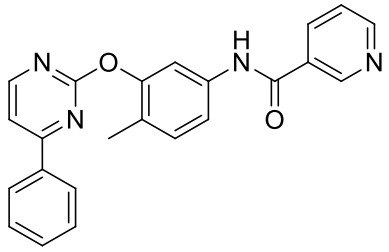
N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)-3-nitrobenzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.16 g of 3-nitrobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.31 g of **B9** was obtained in the yield of 73%. HPLC R_t = 12.6 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (t, J = 1.7 Hz, 1H), 8.58 (s, 1H), 8.49 (d, J = 5.2 Hz, 1H), 8.35 – 8.24 (m, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.99 (dd, J = 7.9, 1.6 Hz, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.45 – 7.35 (m, 4H), 7.24 (dd, J = 9.7, 5.3 Hz, 1H), 2.14 (s, 3H). ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 165.1, 163.5, 159.8, 151.4, 148.0, 136.5, 135.7, 133.5, 131.5, 129.9,

128.9, 127.3, 126.2, 122.0, 117.8, 114.4, 111.8, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{18}N_4O_4+H]+$ 427.1328, found 427.1407.



B10

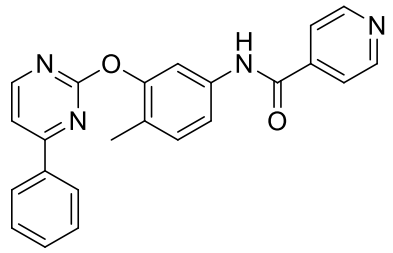
4-fluoro-N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.15 g of 4-fluorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.32 g of **B10** was obtained in the yield of 80%. HPLC R_t = 10.6 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, J = 5.2 Hz, 1H), 8.04 (dd, J = 7.5, 1.7 Hz, 2H), 7.91 (s, 1H), 7.84 (dd, J = 8.7, 5.3 Hz, 2H), 7.58 – 7.37 (m, 6H), 7.27 (d, J = 6.3 Hz, 1H), 7.12 (t, J = 8.6 Hz, 2H), 2.19 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 166.5, 160.0, 151.6, 136.8, 136.0, 131.4, 129.4, 129.3, 128.9, 127.3, 127.0, 117.4, 115.9, 115.6, 114.1, 111.6, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{18}N_3O_2F+H]+$ 400.1383, found 400.1463.



B11

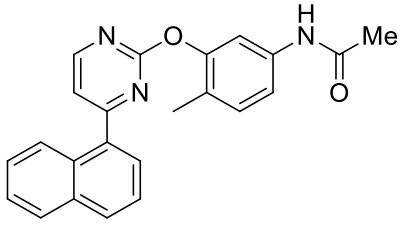
N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)nicotinamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.13 g of nicotinic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.34 g of **B11** was obtained in the yield of 89%. HPLC R_t = 10.9 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.55 (d, J = 4.3 Hz, 2H), 8.43 (d, J = 5.1 Hz, 1H), 7.98 (d, J = 6.9 Hz, 2H), 7.61 – 7.50 (m, 4H), 7.46 – 7.36 (m, 4H), 7.19 (d, J = 8.2 Hz, 1H), 2.13 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.1, 164.2, 159.9, 151.5, 150.2, 142.2, 136.7, 135.7, 131.5,

131.4, 128.9, 127.3, 121.3, 117.9, 114.4, 111.8, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{18}N_4O_2+H]+$ 383.1430, found 383.1506.



B12

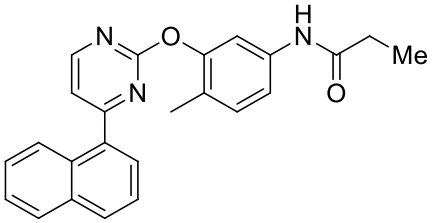
N-(4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)phenyl)isonicotinamide: A round bottom flask was charged with 0.28 g **8 (4-methyl-3-((4-phenylpyrimidin-2-yl)oxy)aniline)**, 0.13 g of isonicotinic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.34 g of **B12** was obtained in the yield of 89%. HPLC R_t = 11.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (d, J = 1.5 Hz, 1H), 8.91 (s, 1H), 8.63 (dd, J = 4.7, 1.3 Hz, 1H), 8.45 (d, J = 5.2 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.61 – 7.50 (m, 4H), 7.51 (s, 2H), 7.48 – 7.38 (m, 4H), 7.30 – 7.28 (m, 1H), 7.21 (d, J = 8.8 Hz, 1H), 2.14 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 165.1, 164.0, 159.8, 152.2, 151.5, 148.0, 136.8, 135.8, 135.5, 131.4, 130.8, 128.9, 127.3, 123.6, 117.8, 114.3, 111.8, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{18}N_4O_2+H]+$ 383.1430, found 383.1507.



C1

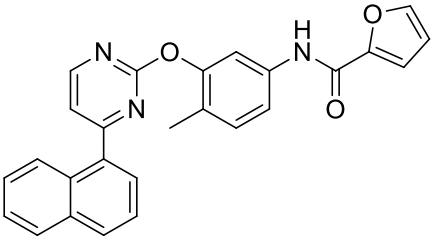
N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)acetamide: A round bottom flask was charged with 0.32 g **8 (4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.07 g of acetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.37 g of **C1** was obtained in the yield of 96%. HPLC R_t = 20.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, J = 5.1 Hz, 1H), 8.22 – 8.08 (m, 1H), 7.90 – 7.71 (m, 3H), 7.60 (d, J = 6.6 Hz, 1H), 7.50 – 7.34 (m, 4H), 7.23 (d, J = 5.1 Hz, 1H), 7.13 – 7.05 (m, 2H), 2.10 (s, 3H), 1.92 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 168.4, 165.1, 159.4, 151.4, 137.3, 135.0, 133.9,

131.3, 130.8, 130.4, 128.6, 128.3, 127.1, 126.3, 126.0, 125.2, 125.0, 117.0, 116.8, 113.6, 24.4, 16.0 ppm; HRMS (ESI) calcd for $[C_{23}H_{19}N_3O_2+H]+$ 370.1477, found 370.1556.



C2

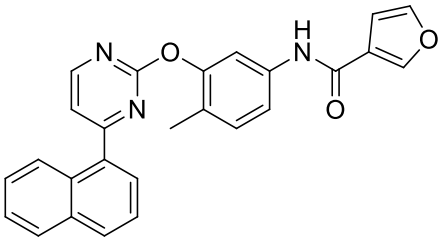
N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)propionamide: A round bottom flask was charged with 0.32 g **8** **(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.08 g of acetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.36 g of **C2** was obtained in the yield of 94%. HPLC R_t = 19.1 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, J = 5.0 Hz, 1H), 8.23 – 8.10 (m, 1H), 7.91 – 7.69 (m, 3H), 7.59 (d, J = 7.0 Hz, 1H), 7.52 – 7.33 (m, 4H), 7.20 (t, J = 7.1 Hz, 1H), 7.12 (d, J = 7.9 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 2.21 – 2.12 (m, 2H), 2.10 (s, 3H), 1.04 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 169.8, 165.1, 159.4, 151.4, 137.4, 135.0, 133.9, 131.2, 130.8, 130.4, 128.6, 128.3, 127.1, 126.3, 125.8, 125.2, 125.1, 116.9, 116.8, 113.6, 30.4, 16.0, 9.6 ppm; HRMS (ESI) calcd for $[C_{24}H_{21}N_3O_2+H]+$ 384.1634, found 384.1712.



C3

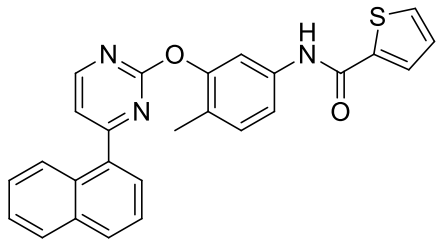
N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)furan-2-carboxamide: A round bottom flask was charged with 0.32 g **8** **(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.12 g of furan-2-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.35 g of **C3** was obtained in the yield of 83%. HPLC R_t = 18.3 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, J = 5.1 Hz, 1H), 8.32 – 8.22 (m, 1H), 8.13 (s, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.89 (dd, J = 6.4, 3.0 Hz, 1H), 7.77 – 7.67 (m, 2H), 7.60 – 7.43 (m,

4H), 7.42 – 7.29 (m, 2H), 7.23 (dd, J = 11.5, 5.5 Hz, 2H), 6.52 (dd, J = 3.4, 1.7 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 165.1, 159.6, 155.9, 151.7, 147.8, 144.2, 136.4, 135.0, 133.9, 131.4, 130.7, 130.4, 128.5, 128.3, 127.1, 126.7, 126.2, 125.2, 125.1, 117.0, 116.8, 115.3, 113.8, 112.6, 16.0 ppm; HRMS (ESI) calcd for $[C_{26}H_{19}N_3O_3+H]+$ 422.1426, found 422.1504.



C4

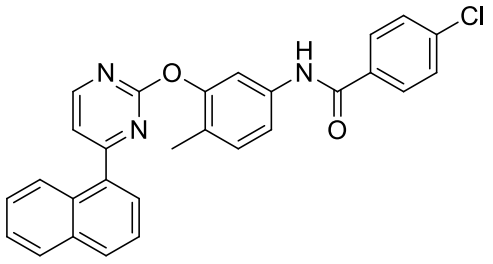
N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)furan-3-carboxamide: A round bottom flask was charged with 0.32 g **8 (4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.12 g of furan-3-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.38 g of **C4** was obtained in the yield of 90%. HPLC R_t = 20.3 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, J = 5.1 Hz, 1H), 8.29 – 8.18 (m, 1H), 7.97 (s, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.88 (dd, J = 6.1, 3.2 Hz, 1H), 7.78 (s, 1H), 7.69 (d, J = 7.1 Hz, 1H), 7.61 (s, 1H), 7.56 – 7.43 (m, 3H), 7.40 (s, 1H), 7.33 (dd, J = 11.0, 3.4 Hz, 2H), 7.27 – 7.16 (m, 1H), 6.68 (s, 1H), 2.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 165.1, 160.7, 159.5, 151.6, 145.1, 143.9, 136.7, 135.0, 133.9, 131.4, 130.8, 130.4, 128.6, 128.3, 127.1, 126.7, 126.25, 125.2, 125.1, 123.0, 117.4, 116.8, 114.1, 108.4, 16.0 ppm; HRMS (ESI) calcd for $[C_{26}H_{19}N_3O_3+H]+$ 422.1426, found 422.1506.



C5

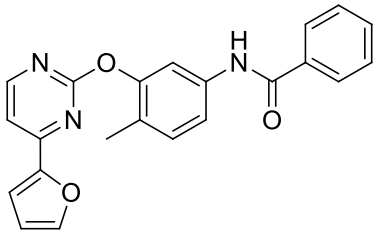
N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)thiophene-2-carboxamide: A round bottom flask was charged with 0.32 g **8 (4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.14 g of thiophene-2-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash

chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.38 g of **C5** was obtained in the yield of 90%. HPLC R_t = 19.7 min, purity: 98%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, J = 5.1 Hz, 1H), 8.32 – 8.23 (m, 1H), 7.99 – 7.85 (m, 3H), 7.78 – 7.64 (m, 3H), 7.59 – 7.42 (m, 4H), 7.35 (dd, J = 7.3, 3.9 Hz, 3H), 7.25 (d, J = 7.8 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 159.5, 136.8, 135.1, 133.9, 131.4, 130.7, 130.4, 128.6, 128.5, 128.3, 127.1, 126.9, 126.2, 126.1, 125.2, 125.1, 117.2, 116.8, 114.0, 16.0 ppm; HRMS (ESI) calcd for $[C_{26}H_{19}N_3O_2S+H]+$ 438.1198, found 438.1276.



C6

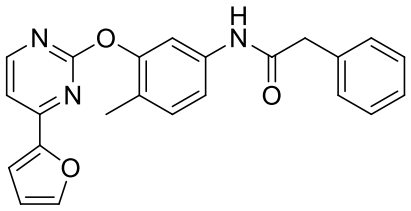
4-chloro-N-(4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)phenyl)benzamide: A round bottom flask was charged with 0.32 g **8 (4-methyl-3-((4-(naphthalen-1-yl)pyrimidin-2-yl)oxy)aniline)**, 0.14 g of 4-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 200:1(v:v) as eluent. 0.40 g of **C6** was obtained in the yield of 86%. HPLC R_t = 9.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 – 8.44 (m, 2H), 8.21 – 8.12 (m, 1H), 7.90 – 7.76 (m, 2H), 7.67 – 7.55 (m, 4H), 7.43 (dd, J = 9.0, 5.6 Hz, 3H), 7.39 – 7.31 (m, 1H), 7.27 – 7.10 (m, 4H), 2.18 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 165.1, 164.9, 159.5, 151.5, 137.8, 137.0, 134.8, 133.8, 133.1, 131.4, 130.8, 130.3, 128.7, 128.6, 128.2, 127.1, 126.7, 126.2, 125.1, 125.0, 117.7, 116.9, 114.3, 16.0 ppm; HRMS (ESI) calcd for $[C_{28}H_{20}N_3O_2Cl+H]+$ 466.1244, found 466.1313.



D1

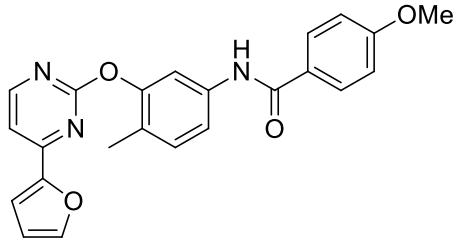
N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)benzamide: A round bottom flask was charged with 0.26 g **8 3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.13 g of benzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced

pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.31 g of **D1** was obtained in the yield of 83%. HPLC R_t = 15.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, J = 5.2 Hz, 1H), 7.99 (s, 1H), 7.82 (d, J = 7.5 Hz, 2H), 7.60 (s, 1H), 7.56 – 7.37 (m, 5H), 7.31 (t, J = 4.6 Hz, 2H), 7.25 (d, J = 8.8 Hz, 1H), 6.63 – 6.49 (m, 1H), 2.17 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 164.9, 159.7, 158.1, 151.3, 151.1, 145.5, 137.2, 134.8, 131.6, 131.2, 128.4, 127.8, 126.5, 117.7, 114.2, 113.5, 112.7, 109.7, 15.9 ppm; HRMS (ESI) calcd for $[C_{22}H_{17}N_3O_3+H]^+$ 372.1270, found 372.1344.



D2

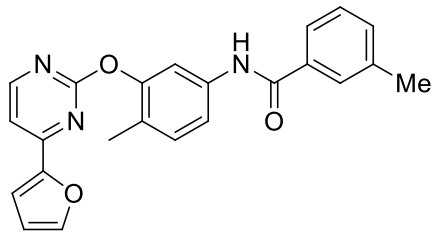
N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-2-phenylacetamide: A round bottom flask was charged with 0.26 g **8** **3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.14 g of 2-phenylacetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.36 g of **D2** was obtained in the yield of 93%. HPLC R_t = 16.5 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, J = 5.2 Hz, 1H), 7.63 (s, 1H), 7.58 (dd, J = 1.5, 0.6 Hz, 1H), 7.39 – 7.19 (m, 10H), 7.14 (d, J = 8.2 Hz, 1H), 6.54 (dd, J = 3.5, 1.7 Hz, 1H), 3.64 (s, 2H), 2.12 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 164.9, 159.8, 158.2, 151.3, 151.2, 145.5, 137.9, 136.8, 134.5, 131.2, 129.5, 129.4, 129.1, 128.6, 127.5, 127.1, 126.6, 117.2, 113.6, 113.6, 112.7, 109.7, 44.6, 15.9 ppm; HRMS (ESI) calcd for $[C_{23}H_{19}N_3O_3+H]^+$ 386.1426, found 386.1501.



D3

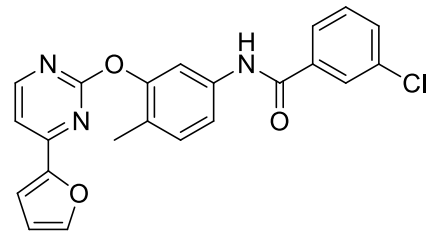
N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-4-methoxybenzamide: A round bottom flask was charged with 0.26 g **8** **3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.16 g of 4-methoxybenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced

pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.37 g of **D3** was obtained in the yield of 92%. HPLC R_t = 16.9 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 5.2 Hz, 1H), 8.12 – 7.98 (m, 1H), 7.87 – 7.70 (m, 2H), 7.58 (dd, J = 1.6, 0.6 Hz, 1H), 7.50 (d, J = 2.1 Hz, 1H), 7.46 (dd, J = 8.1, 2.2 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.21 (d, J = 8.2 Hz, 1H), 6.92 – 6.85 (m, 2H), 6.55 (dd, J = 3.5, 1.8 Hz, 1H), 3.82 (s, 3H), 2.15 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 165.0, 162.4, 159.9, 158.2, 151.43, 151.2, 145.4, 137.2, 131.3, 128.9, 127.1, 126.4, 117.5, 113.9, 113.8, 113.5, 112.7, 109.7, 29.7, 16.0 ppm; HRMS (ESI) calcd for [$C_{23}H_{19}N_3O_4$+H]+ 402.1376, found 402.1451.



D4

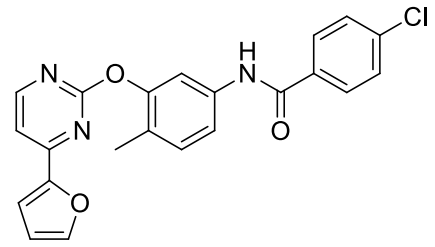
N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-3-methylbenzamide: A round bottom flask was charged with 0.26 g **8** **3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.14 g of 3-methylbenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.36 g of **D4** was obtained in the yield of 93%. HPLC R_t = 15.2 min, purity: 96%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.37 (d, J = 5.2 Hz, 1H), 7.62 – 7.44 (m, 5H), 7.32 – 7.08 (m, 5H), 6.49 (dd, J = 3.5, 1.7 Hz, 1H), 2.25 (s, 3H), 2.08 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 164.9, 159.8, 158.2, 151.3, 151.1, 145.5, 138.3, 138.1, 137.3, 134.8, 133.9, 132.4, 131.3, 130.5, 128.4, 128.2, 127.9, 127.2, 126.4, 124.2, 117.7, 114.2, 113.6, 112.7, 109.7, 21.3, 15.9 ppm; HRMS (ESI) calcd for [$C_{23}H_{19}N_3O_3$+H]+ 386.1426, found 386.1499.



D5

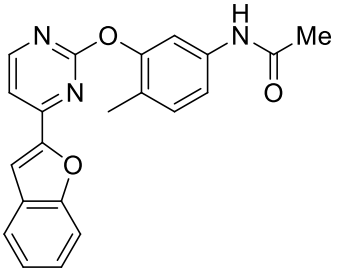
3-chloro-N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)benzamide: A round bottom flask was charged with 0.26 g **8** **3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.14 g of 3-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with

DCM:MeOH = 100:1(v:v) as eluent. 0.38 g of **D5** was obtained in the yield of 94%. HPLC R_t = 14.7 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.38 (d, J = 5.2 Hz, 1H), 7.74 (t, J = 1.7 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.50 – 7.44 (m, 2H), 7.37 (ddd, J = 7.9, 1.9, 1.0 Hz, 1H), 7.31 – 7.20 (m, 3H), 7.20 – 7.08 (m, 1H), 6.52 (dd, J = 3.5, 1.7 Hz, 1H), 2.08 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 164.7, 163.5, 159.7, 158.2, 156.7, 151.3, 151.1, 148.0, 145.5, 140.7, 136.9, 136.7, 134.6, 133.8, 131.6, 131.3, 129.8, 127.5, 126.8, 125.9, 125.3, 123.8, 117.8, 117.2, 114.2, 114.0, 113.6, 112.7, 110.0, 109.8, 101.2, 15.9 ppm; HRMS (ESI) calcd for $[C_{22}H_{16}N_3O_3Cl+H]+$ 406.0880, found 406.0954.



D6

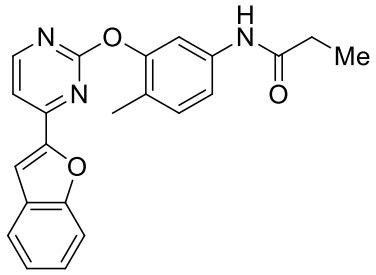
4-chloro-N-(3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)benzamide: A round bottom flask was charged with 0.26 g **8** **3-((4-(furan-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.14 g of 4-chlorobenzoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.32 g of **D6** was obtained in the yield of 81%. HPLC R_t = 15.3 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.37 (d, J = 5.1 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.56 (s, 1H), 7.46 (d, J = 7.1 Hz, 2H), 7.37 – 7.19 (m, 4H), 7.15 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 1.6 Hz, 1H), 2.10 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 164.9, 159.7, 158.2, 151.3, 151.1, 145.5, 137.8, 137.0, 133.2, 131.3, 128.7, 128.7, 126.8, 117.8, 114.3, 113.6, 112.7, 109.8, 15.9 ppm; HRMS (ESI) calcd for $[C_{22}H_{16}N_3O_3Cl+H]+$ 406.0880, found 406.0951.



E1

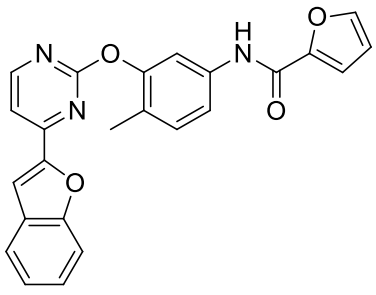
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)acetamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.07 g of acetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were

combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.33 g of **E1** was obtained in the yield of 92%. HPLC R_t = 13.3 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (d, J = 5.1 Hz, 1H), 7.88 (s, 1H), 7.70 – 7.58 (m, 2H), 7.53 (dd, J = 9.5, 6.8 Hz, 2H), 7.46 – 7.23 (m, 5H), 7.19 (d, J = 8.2 Hz, 1H), 2.15 (s, 3H), 2.07 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 165.1, 160.3, 158.6, 155.8, 152.3, 151.3, 137.2, 131.3, 128.1, 126.8, 126.2, 123.7, 122.5, 117.2, 113.6, 111.8, 110.8, 109.4, 24.4, 15.9 ppm; HRMS (ESI) calcd for $[C_{21}H_{17}N_3O_3+H]+$ 360.1270, found 360.1362.



E2

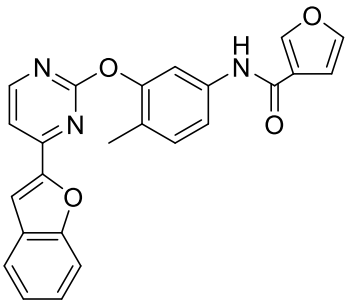
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)propionamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.08 g of propionic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.32 g of **E2** was obtained in the yield of 86%. HPLC R_t = 12.5 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 5.1 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.52 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 5.1 Hz, 1H), 7.37 – 7.22 (m, 3H), 7.18 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 8.2 Hz, 1H), 2.23 (q, J = 7.5 Hz, 2H), 2.07 (s, 3H), 1.09 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 160.3, 158.5, 155.8, 152.4, 151.4, 137.2, 131.3, 128.1, 126.7, 126.07, 123.7, 122.5, 117.1, 115.0, 113.6, 111.8, 110.8, 109.4, 30.6, 15.9, 9.6 ppm; HRMS (ESI) calcd for $[C_{22}H_{19}N_3O_3+H]+$ 374.1426, found 374.1497.



E3

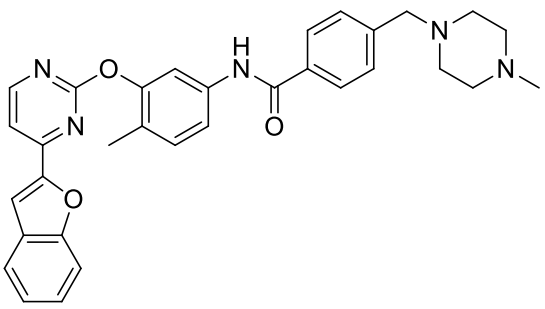
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)furan-2-carboxamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.12 g of

furan-2-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.36 g of **E4** was obtained in the yield of 87%. HPLC R_t = 12.8 min, purity: 96%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, J = 5.1 Hz, 1H), 8.08 (s, 1H), 7.61 – 7.52 (m, 2H), 7.52 – 7.35 (m, 5H), 7.35 – 7.25 (m, 1H), 7.18 (dd, J = 9.0, 5.7 Hz, 2H), 7.11 (d, J = 3.3 Hz, 1H), 6.42 (dd, J = 3.4, 1.7 Hz, 1H), 2.11 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 160.5, 158.5, 156.0, 155.8, 152.5, 151.6, 147.8, 144.2, 136.4, 131.4, 128.2, 126.7, 126.7, 123.6, 122.5, 117.2, 115.2, 113.8, 112.6, 111.8, 110.7, 109.3, 16.0 ppm; HRMS (ESI) calcd for $[C_{24}H_{17}N_3O_4+H]^+$ 412.1219, found 412.1291.



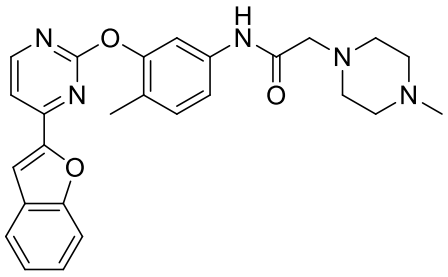
E4

N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)furan-3-carboxamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.12 g of furan-3-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 100:1(v:v) as eluent. 0.33 g of **E5** was obtained in the yield of 80%. HPLC R_t = 12.0 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, J = 5.1 Hz, 1H), 8.08 (s, 1H), 7.90 (s, 1H), 7.57 – 7.46 (m, 2H), 7.46 – 7.33 (m, 4H), 7.33 – 7.24 (m, 2H), 7.16 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 7.9 Hz, 1H), 6.63 (d, J = 0.9 Hz, 1H), 2.05 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 160.9, 160.4, 158.5, 155.8, 152.3, 151.4, 145.2, 143.8, 136.8, 131.4, 128.1, 126.8, 126.6, 123.7, 123.0, 122.5, 117.8, 114.2, 111.8, 110.8, 109.4, 108.5, 15.9 ppm; HRMS (ESI) calcd for $[C_{24}H_{17}N_3O_4+H]^+$ 412.1219, found 412.1289.



E5

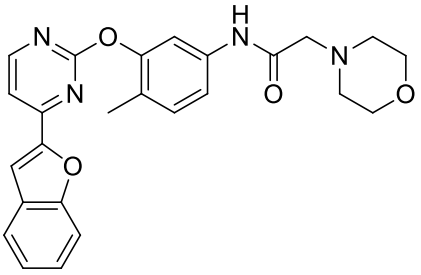
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-4-((4-methylpiperazin-1-yl)methyl)benzamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.50 g of 3-(4-methylpiperazin-1-yl)-2-oxopropanoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 10:1(v:v) as eluent. 0.25 g of **G2** was obtained in the yield of 47%. HPLC R_t = 6.8 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, J = 5.1 Hz, 1H), 7.87 (s, 1H), 7.79 (d, J = 8.1 Hz, 2H), 7.72 – 7.60 (m, 2H), 7.55 (dd, J = 6.3, 4.6 Hz, 3H), 7.51 – 7.33 (m, 4H), 7.33 – 7.21 (m, 3H), 3.55 (s, 2H), 2.46 (s, 8H), 2.29 (s, 3H), 2.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 165.0, 160.5, 158.5, 155.8, 152.4, 151.5, 136.5, 131.4, 128.1, 126.8, 126.7, 125.6, 124.4, 123.7, 122.5, 118.7, 116.9, 113.4, 111.8, 110.8, 110.4, 109.3, 61.5, 54.3, 51.8, 44.7, 16.0 ppm; HRMS (ESI) calcd for $[C_{32}H_{31}N_5O_3+H]^+$ 534.2427, found 534.2520.



E6

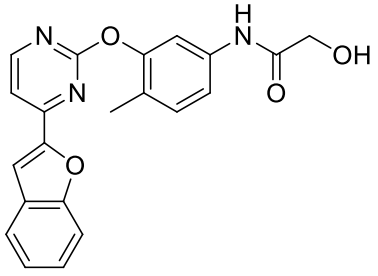
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-2-(4-methylpiperazin-1-yl)acetamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.30 g of 3-(4-methylpiperazin-1-yl)-2-oxopropanoic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 10:1(v:v) as eluent. 0.29 g of **G2** was obtained in the yield of 63%. HPLC R_t = 7.9 min, purity: 97%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.57 (d, J = 5.1 Hz, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.63 (d, J = 0.8 Hz, 1H), 7.59 – 7.54 (m, 1H), 7.53 (d, J = 5.1 Hz, 1H), 7.48 (d, J

= 2.0 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.32 – 7.21 (m, 2H), 3.11 (s, 2H), 2.64 (s, 4H), 2.48 (s, 4H), 2.29 (s, 3H), 2.18 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 164.1, 159.5, 157.5, 154.8, 151.5, 150.5, 141.7, 136.0, 132.7, 130.4, 128.3, 127.2, 126.0, 125.7, 122.6, 121.5, 116.4, 112.9, 110.8, 109.7, 108.3, 61.5, 54.1, 52.1, 45.0, 15.0 ppm; HRMS (ESI) calcd for $[C_{26}H_{27}N_5O_3+H]+$ 458.2114, found 458.1998.



E7

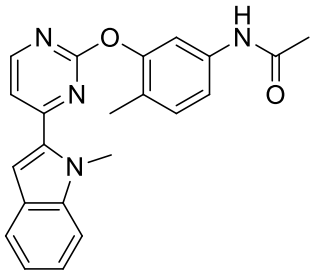
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-2-morpholinoacetamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.30 g of 2-morpholinoacetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 10:1(v:v) as eluent. 0.23 g of **G3** was obtained in the yield of 51%. HPLC R_t = 8.1 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.49 (d, J = 5.1 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.52 – 7.38 (m, 3H), 7.32 (dd, J = 7.9, 6.7 Hz, 2H), 7.26 – 7.13 (m, 2H), 3.72 – 3.59 (m, 4H), 3.03 (s, 2H), 2.57 – 2.44 (m, 4H), 2.10 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 165.1, 160.5, 158.5, 155.8, 152.4, 151.5, 136.5, 131.4, 128.1, 126.7, 126.6, 123.7, 122.4, 116.8, 113.2, 111.5, 110.7, 109.3, 67.0, 62.4, 53.8, 16.0 ppm; HRMS (ESI) calcd for $[C_{25}H_{24}N_4O_4+H]+$ 445.1798, found 445.1875.



E8

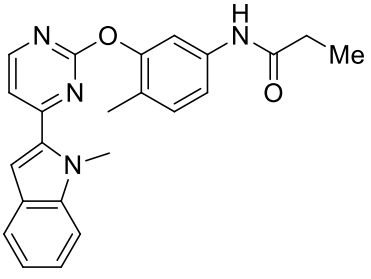
N-(3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylphenyl)-2-hydroxyacetamide: A round bottom flask was charged with 0.32 g **8** **3-((4-(benzofuran-2-yl)pyrimidin-2-yl)oxy)-4-methylaniline**, 0.30 g of 2-hydroxyacetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 10:1(v:v) as eluent. 0.12 g of **G4**

was obtained in the yield of 31%. HPLC R_t = 5.9 min, purity: 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.72 (d, J = 5.1 Hz, 1H), 7.81 (d, J = 9.1 Hz, 2H), 7.76 – 7.67 (m, 2H), 7.63 (s, 1H), 7.50 (dd, J = 15.7, 8.3 Hz, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.26 (d, J = 8.3 Hz, 1H), 5.65 (t, J = 5.9 Hz, 1H), 3.98 (d, J = 5.9 Hz, 2H), 3.33 (s, 8H), 2.07 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 165.0, 161.7, 157.9, 155.6, 152.4, 151.4, 138.1, 131.3, 128.1, 127.5, 125.1, 124.3, 123.2, 117.1, 113.5, 112.2, 111.6, 109.9, 62.3, 15.9 ppm; HRMS (ESI) calcd for $[C_{21}H_{17}N_3O_4+H]+$ 376.1219, found 376.1298.



F1

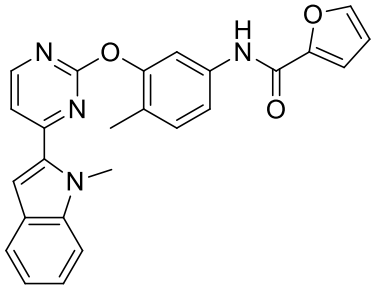
N-(4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)phenyl)acetamide: A round bottom flask was charged with 0.33 g **8** **4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)aniline**, 0.07 g of acetic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.31 g of **F1** was obtained in the yield of 84%. HPLC R_t = 11.7 min, purity: 99%; ^{1}H NMR (300 MHz, DMSO-*d6*) δ 8.52 (d, J = 5.2 Hz, 1H), 8.40 (s, 1H), 7.86-7.97 (m, 1H), 7.70-7.47 (m, 4H), 7.31 (d, J = 1.8 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1H), 3.89 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-*d6*) δ 168.7, 165.3, 164.6, 159.1, 151.9, 138.9, 138.0, 134.0, 131.3, 126.0, 125.1, 122.8, 122.7, 121.4, 116.2, 113.4, 112.1, 110.8, 110.7, 33.6, 24.4, 16.0 ppm; HRMS (ESI) calcd for $[C_{22}H_{20}N_4O_2+H]+$ 373.1586, found 373.1660.



F2

N-(4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)phenyl)propionamide: A round bottom flask was charged with 0.33 g **8** **4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)aniline**, 0.08 g of propionic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic

layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.33 g of **F1** was obtained in the yield of 85%. HPLC R_t = 12.1 min, purity: 99%; ^{1}H NMR (300 MHz, DMSO-*d6*) δ 9.91 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H), 8.38 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.59 – 7.39 (m, 4H), 7.28 (d, J = 8.3 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 6.96 (t, J = 7.3 Hz, 1H), 3.85 (s, 3H), 3.33 (s, 5H), 2.29 (q, J = 7.5 Hz, 2H), 2.06 (s, 3H), 1.06 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-*d6*) δ 171.9, 164.8, 164.1, 158.6, 151.5, 138.5, 137.6, 133.5, 130.8, 125.5, 124.5, 122.3, 122.2, 120.9, 115.7, 112.9, 110.4, 110.3, 33.1, 29.5, 15.5, 9.6 ppm; HRMS (ESI) calcd for $[C_{23}H_{22}N_4O_2+H]+$ 387.1743, found 387.1822.



F3

N-(4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)phenyl)furan-2-carboxamide: A round bottom flask was charged with 0.33 g **8** **4-methyl-3-((4-(1-methyl-1H-indol-2-yl)pyrimidin-2-yl)oxy)aniline**, 0.12 g of furan-2-carboxylic acid and 10 mL DCM. 0.15 g HOBt and 0.21 g of EDCI were added to the solution at room temperature. After stirring for 2 hours, 20 mL distilled water was added and the mixture was extracted with 20 mL DCM for two times. The organic layers were combined and washed with water and brine. The solvent was removed under reduced pressure and the residue was purified through flash chromatography on silica gel with DCM:MeOH = 50:1(v:v) as eluent. 0.37 g of **F4** was obtained in the yield of 97%. HPLC R_t = 11.8 min, purity: 99%; ^{1}H NMR (300 MHz, DMSO-*d6*) δ 10.33 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H), 8.38 (s, 1H), 8.00 – 7.91 (m, 2H), 7.88 (d, J = 8.0 Hz, 1H), 7.79 – 7.67 (m, 2H), 7.61 – 7.44 (m, 5H), 7.36 (d, J = 8.2 Hz, 1H), 7.19 (dd, J = 11.3, 4.0 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 3.85 (s, 3H), 2.12 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-*d6*) δ 164.8, 164.1, 158.6, 156.1, 151.4, 147.4, 145.6, 137.7, 137.6, 133.5, 130.8, 125.6, 125.5, 122.3, 122.2, 121.0, 117.0, 114.6, 114.1, 112.1, 111.6, 110.4, 110.3, 33.0, 15.5 ppm; HRMS (ESI) calcd for $[C_{25}H_{20}N_4O_3+H]+$ 425.1535, found 425.1609.

Cell culture

Liver cancer cell lines of Hep3B, MHCC97-L, QGY-7703, SMMC-7721 and SNU368 were obtained from HD Biosciences (China) Co., Ltd. Hep3B cells were cultured in DMEM medium and all the other cell lines in RPMI 1640 medium. All media contained 10% fetal bovine serum (FBS) (Bioind, US origin) and all cells were incubated in a humidified atmosphere of 5 % CO_2 at 37 °C. All the cell lines were

authenticated by using short tandem repeat (STR) matching analysis. No mycoplasma contamination was detected.

CellTiter-Glo luminescent cell viability assay

For experiments hepatocellular carcinoma cells were seeded at 4000 cells per well in 96-well plates. After overnight incubation, solution of compounds in DMSO at various concentrations were added to the cells and further incubated for 120 h. Cell viability was measured with the CellTiter-Glo Luminescent Cell Viability Assay (Promega) according to the manufacturer's instructions. Luminescence was measured using an EnVision Multilabel Plate Reader (Perkin-Elmer). The cytotoxicity of the compounds was expressed as the percentage of luminescence relative to that of untreated cells. The concentration of compound producing 50% of cell proliferation (IC_{50}) was calculated by nonlinear regression analysis of the response-concentration (log) curve, using the Graph-Pad Prism program package (Graph Pad Software; San Diego, CA). Results are expressed as the means of two dependent experiments performed in triplicate.

Supplementary Table S1 PDGFR kinase inhibition of 2-phenyloxypyrimidine derivatives

Compound ID	Inhibition effect (%)[a]		IC_{50} (μM)[b]		Selectivity index[c]
	PDGFRα	PDGFRβ	PDGFRα	PDGFRβ	
A1	39.11	21.40	N.D.[d]	N.D.	N.D.
A2	65.72	40.73	N.D.	N.D.	N.D.
A3	45.45	45.50	N.D.	N.D.	N.D.
A4	66.71	43.74	N.D.	N.D.	N.D.
A5	45.20	33.70	N.D.	N.D.	N.D.
A6	47.73	35.96	N.D.	N.D.	N.D.
A7	62.93	40.23	N.D.	N.D.	N.D.
A8	55.65	43.24	N.D.	N.D.	N.D.
A9	23.63	23.41	N.D.	N.D.	N.D.
A10	40.63	30.94	N.D.	N.D.	N.D.
A11	42.91	6.84	N.D.	N.D.	N.D.
A12	43.17	31.94	N.D.	N.D.	N.D.
B1	2.32	12.87	N.D.	N.D.	N.D.
B2	21.09	17.63	N.D.	N.D.	N.D.
B3	23.12	26.17	N.D.	N.D.	N.D.
B4	35.04	24.42	N.D.	N.D.	N.D.
B5	1.81	19.39	N.D.	N.D.	N.D.
B6	12.21	18.64	N.D.	N.D.	N.D.
B7	31.49	16.63	N.D.	N.D.	N.D.
B8	26.17	37.71	N.D.	N.D.	N.D.
B9	21.34	19.14	N.D.	N.D.	N.D.
B10	19.57	15.63	N.D.	N.D.	N.D.
B11	32.00	5.08	N.D.	N.D.	N.D.
B12	25.66	20.65	N.D.	N.D.	N.D.
C1	33.27	1.32	N.D.	N.D.	N.D.
C2	33.78	2.07	N.D.	N.D.	N.D.
C3	46.46	11.61	N.D.	N.D.	N.D.
C4	13.73	2.83	N.D.	N.D.	N.D.
C5	16.27	5.08	N.D.	N.D.	N.D.
C6	24.14	-0.94	N.D.	N.D.	N.D.
D1	13.74	28.93	N.D.	N.D.	N.D.
D2	36.82	46.75	N.D.	N.D.	N.D.
D3	22.61	37.72	N.D.	N.D.	N.D.
D4	45.70	46.00	N.D.	N.D.	N.D.
D5	51.79	43.49	N.D.	N.D.	N.D.
D6	33.02	37.47	N.D.	N.D.	N.D.
E1	1.56	1.82	N.D.	N.D.	N.D.
E2	19.06	10.10	N.D.	N.D.	N.D.
E3	-2.00	3.83	N.D.	N.D.	N.D.

E4	27.18	7.35	N.D.	N.D.	N.D.
E5	**86.12**	**66.41**	**0.40**	**0.93**	**2.32**
E6	-1.24	-0.44	N.D.	N.D.	N.D.
E7	18.56	19.39	N.D.	N.D.	N.D.
E8	26.16	14.62	N.D.	N.D.	N.D.
F1	6.37	2.32	N.D.	N.D.	N.D.
F2	12.21	-4.46	N.D.	N.D.	N.D.
F3	24.14	25.67	N.D.	N.D.	N.D.

[a] Inhibition effect (%): kinase inhibition activities of compounds at 1 μM.

[b] IC_{50}: 50% inhibitory concentration (averages of two separate experiments).

[c] Selectivity index=IC_{50} (PDGFRβ)/ IC_{50} (PDGFRα).

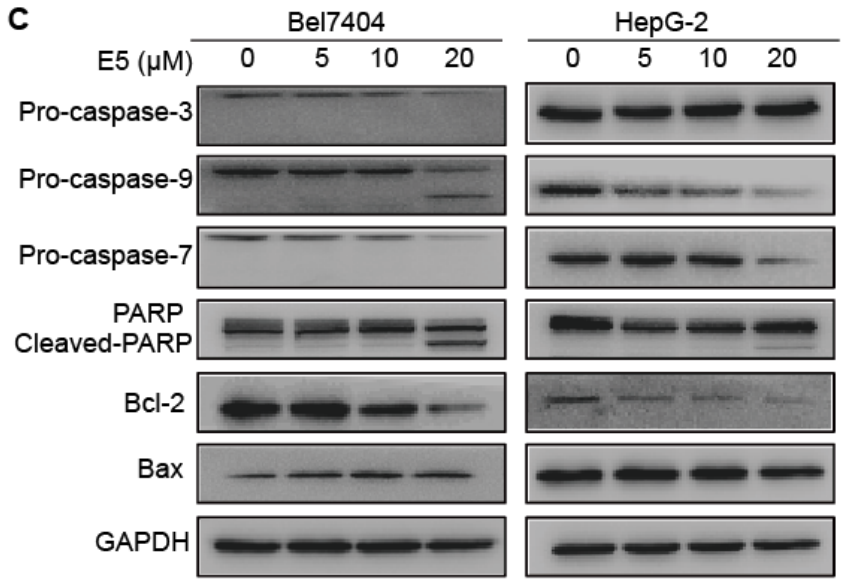
[d] N.D. = not determined.

Supplementary Table S2 Anti-proliferative activity of 2-phenyloxypyrimidine derivatives on HCC cell lines determined by CellTiter-Glo luminescent cell viability assay (IC_{50}, μM)

Compound ID	BEL7404	Hep3B	MHCC97-L	QGY-7703	SMMC-7721	SNU368
A1	10.8	15.8	15.1	24.5	13.6	85.7
A2	39.3	39.5	>200	59.8	84.3	112.2
A3	32.8	21.2	22.3	47.0	25.1	51.4
A4	12.2	17.5	24.5	39.8	17.5	54.0
A5	15.6	23.3	31.3	40.5	23.5	49.5
A6	9.5	10.7	16.2	21.9	12.3	24.0
A7	32.8	18.9	51.5	57.8	27.2	45.9
A8	20.1	14.3	34.6	24.6	10.1	25.7
A9	23.8	28.4	53.2	48.4	26.8	51.5
A10	28.2	20.1	35.7	43.4	21.1	38.7
A11	74.2	105.4	89.3	252.0	79.7	94.6
A12	133.7	130.3	281.3	170.4	112.6	286.6
B1	10.5	2.7	4.9	5.8	2.7	17.7
B2	14.4	13.0	16.9	20.6	11.7	24.8
B3	3.7	4.6	6.1	7.3	6.0	12.8
B4	9.5	6.4	7.0	10.2	6.2	12.9
B5	7.9	9.2	9.8	14.9	8.4	15.8
B6	13.4	7.9	10.5	15.4	9.7	15.0
B7	18.3	15.5	>200	25.8	17.0	14.0
B8	9.9	9.0	14.0	14.4	7.5	12.0
B9	12.9	83.2	>200	19.2	13.8	16.8
B10	8.1	5.8	6.3	10.9	3.9	12.6
B11	21.6	44.2	53.5	81.1	20.2	18.0
B12	13.4	17.7	44.0	27.6	8.8	18.0
C1	36.2	32.0	108.6	91.6	21.0	43.0
C2	48.2	36.3	110.7	119.5	29.5	55.9
C3	39.7	33.5	91.0	70.7	27.2	37.9
C4	8.8	22.9	96.4	14.9	12.0	15.8
C5	20.8	17.0	28.0	35.2	16.8	28.4
C6	6.7	19.7	>200	19.2	14.3	17.2
D1	48.7	11.4	1.6	2.5	1.5	37.3
D2	32.8	28.3	26.4	42.2	21.6	43.8
D3	17.6	9.7	8.5	15.7	7.9	22.2
D4	4.5	6.0	3.4	7.5	3.7	23.2
D5	12.4	11.2	14.7	22.5	12.4	24.0
D6	10.9	7.3	24.6	25.8	8.2	12.7
E1	10.1	86.8	5.7	0.3	0.3	8.5
E2	8.2	74.6	5.5	0.4	0.2	13.2

E3	1.2	125.0	9.6	0.7	0.7	1.3
E4	5.2	15.8	0.0	0.0	0.4	11.4
E5	**0.8**	**2.6**	**10.0**	**15.1**	**1.0**	**8.9**
E6	38.1	11.7	16.7	29.5	27.7	31.6
E7	5.9	9.0	59.1	10.3	4.6	14.7
E8	2.8	3.8	13.6	3.3	2.5	6.3
F1	37.1	31.0	48.4	195.4	34.5	29.3
F2	19.0	33.8	31.8	51.9	27.9	29.1
F3	15.6	41.8	>200	97.7	18.4	26.5

Supplementary Figure S1 Original gel images for Manuscript Fig. 5C



Bel7404

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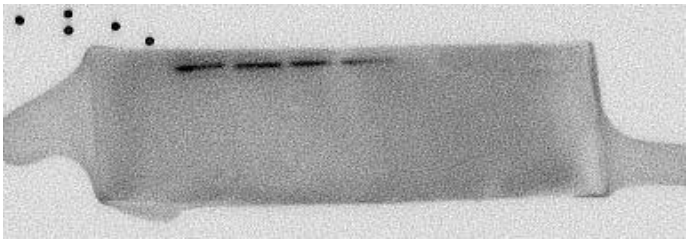

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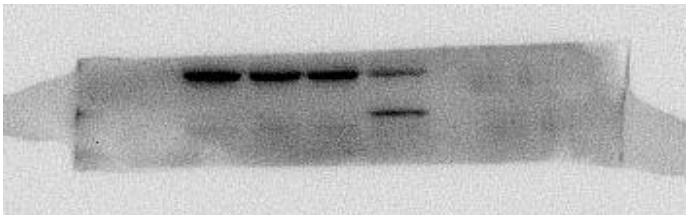

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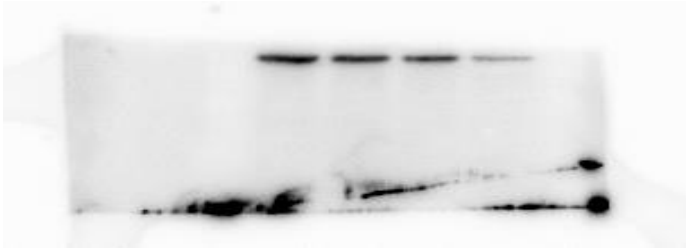

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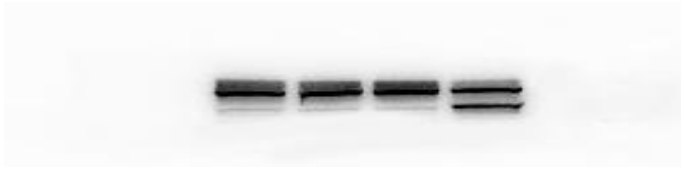

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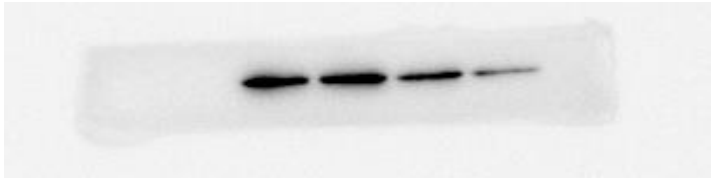

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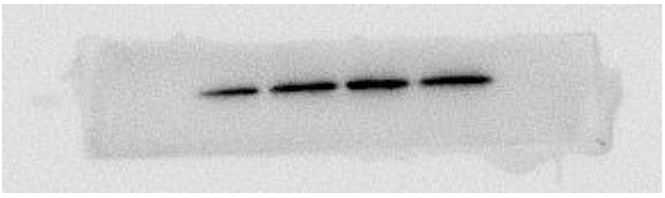

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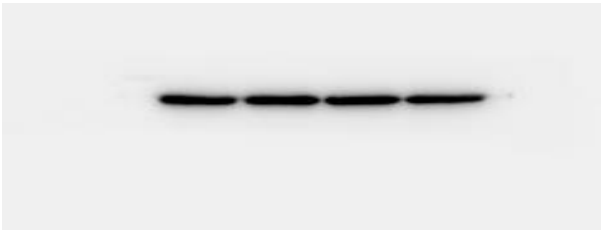

HepG-2

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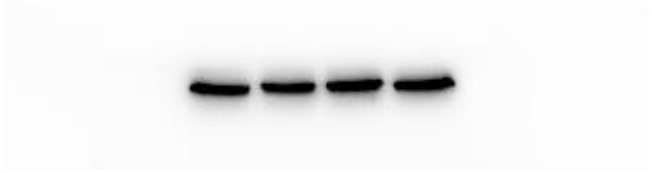

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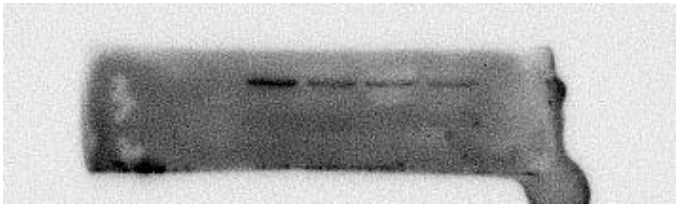

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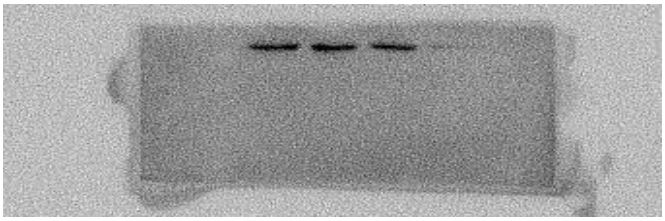

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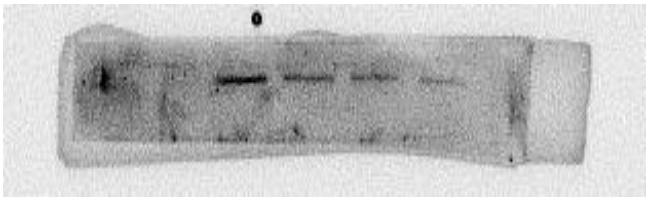

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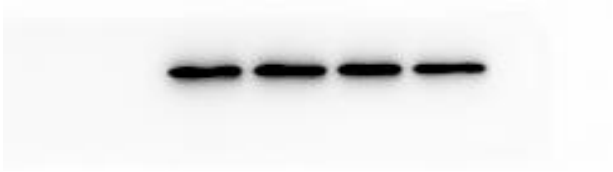

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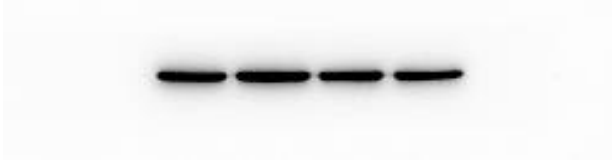
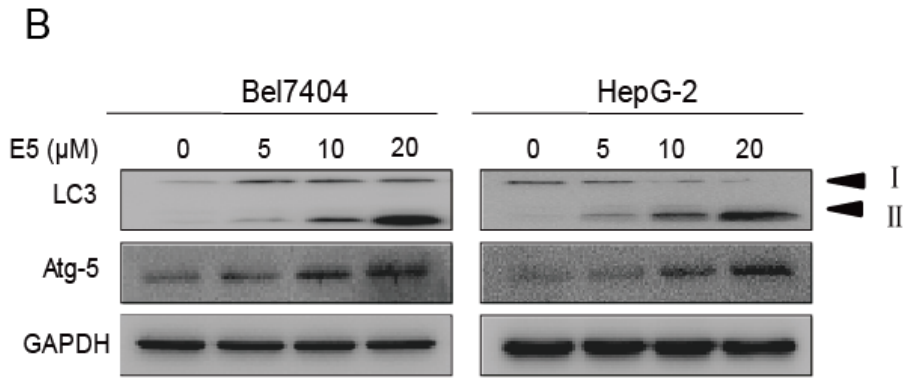


Supplementary Figure S2 Original gel images for Manuscript Fig. 6B



Bel7404

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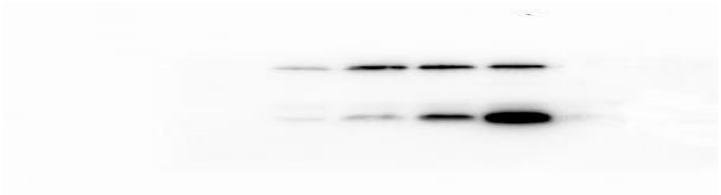

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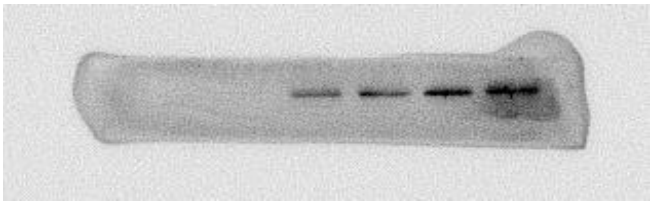

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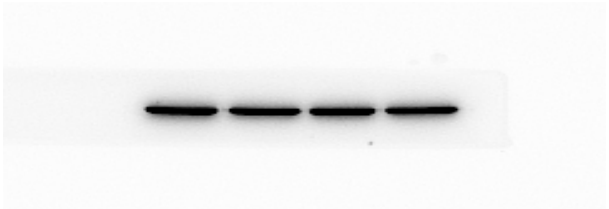

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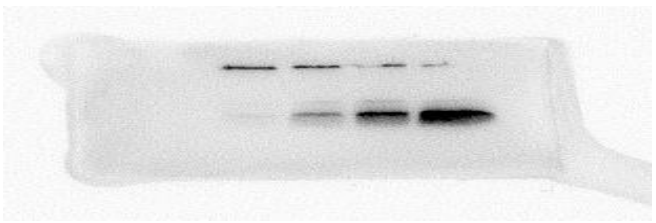

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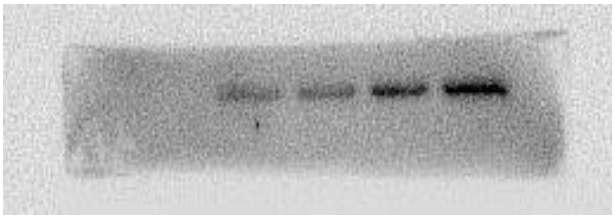

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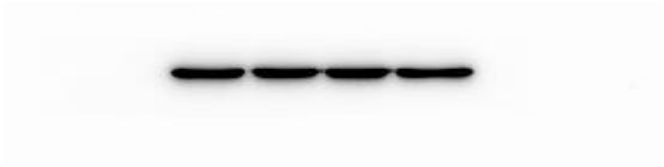
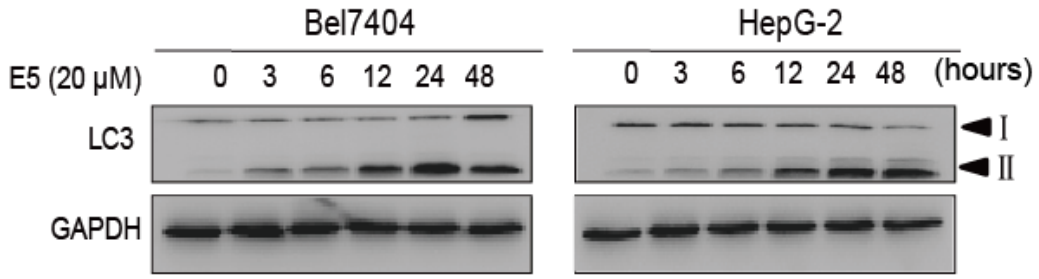


Supplementary Figure S3 Original gel images for Manuscript Fig. 6C

C



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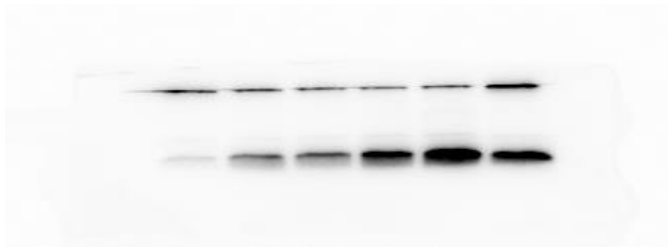

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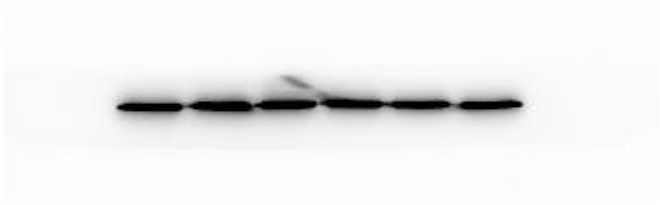

HepG-2

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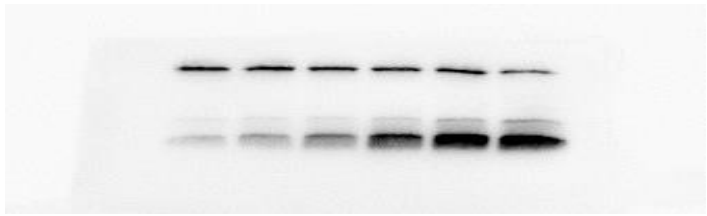

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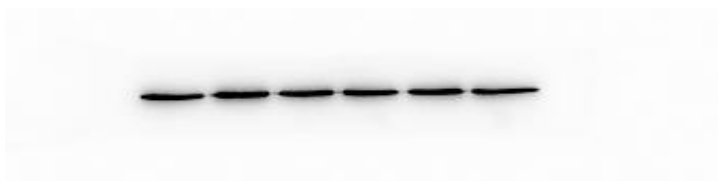
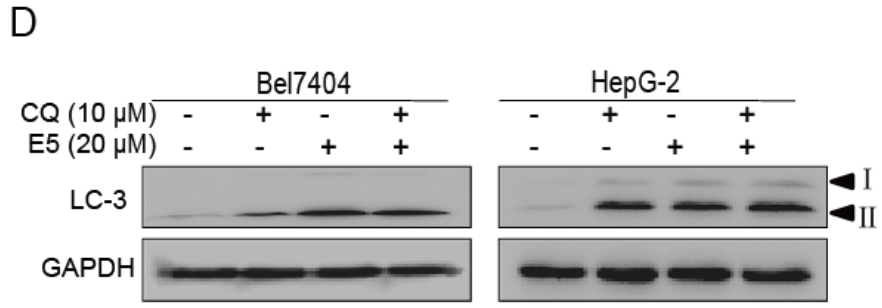


Supplementary Figure S4 Original gel images for Manuscript Fig. 6D



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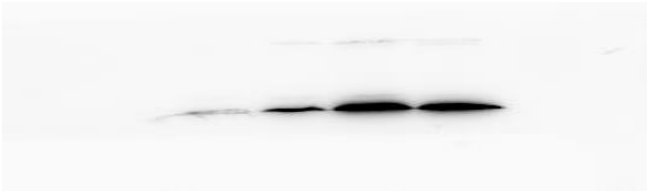

GAPDH:

HepG-2

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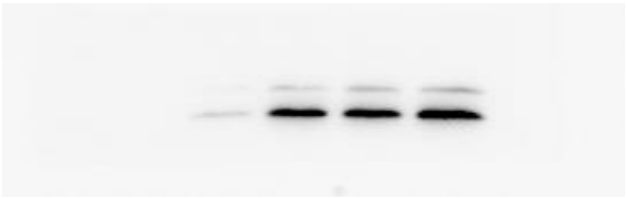

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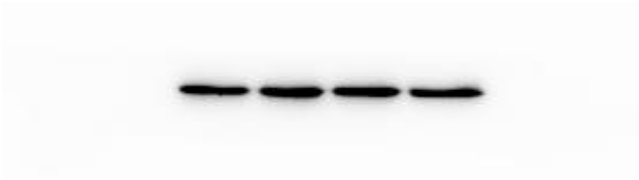
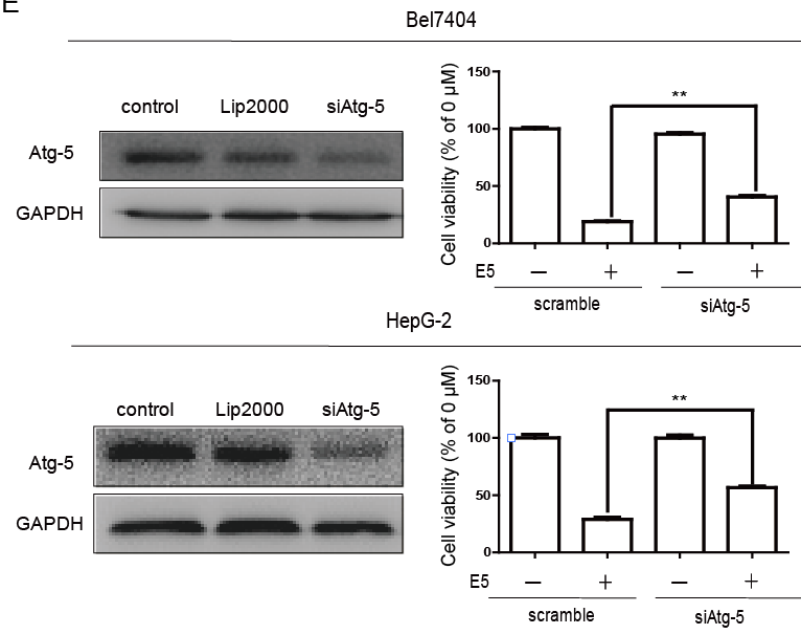


Supplementary Figure S5 Original gel images for Manuscript Fig. 6E

E



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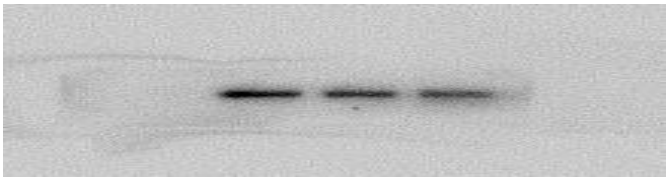

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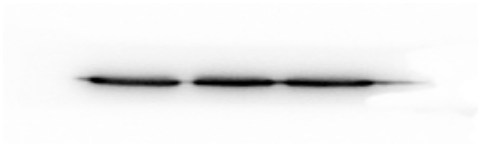

HepG-2

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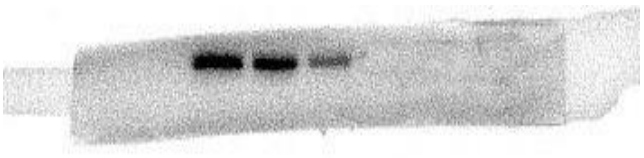
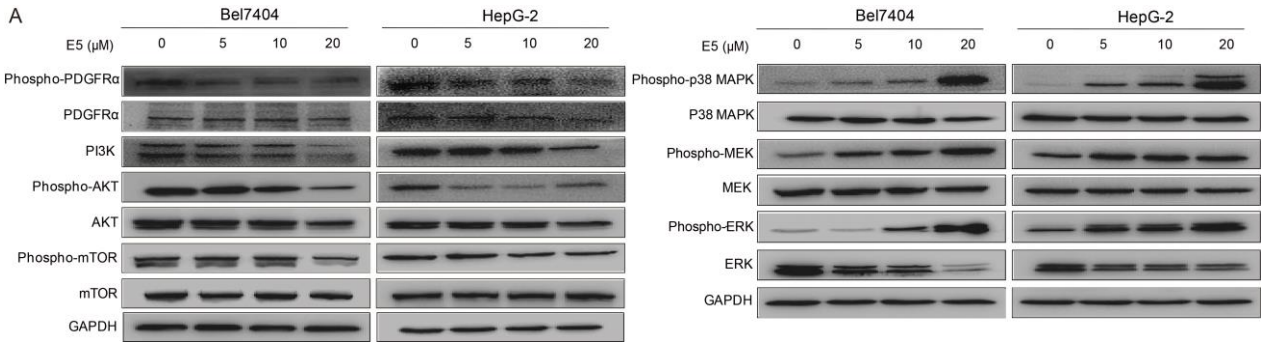


GAPDH:

Supplementary Figure S6 Original gel images for Manuscript Fig. 7A



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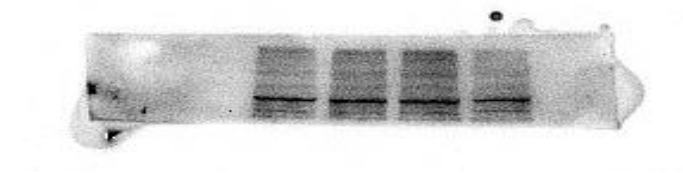
Phospho-PDGFRα:

PDGFRα:



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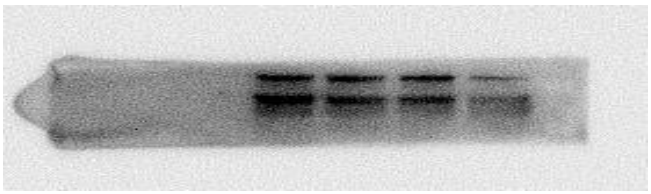

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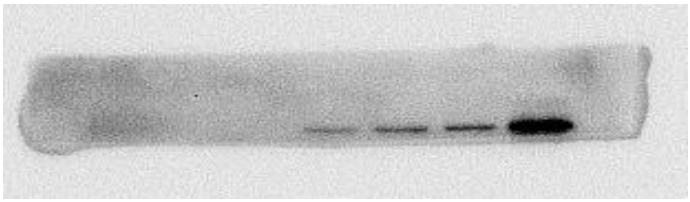
AKT:

Phospho-mTOR:

mTOR:

Phospho-p38 MAPK:



p38 MAPK:

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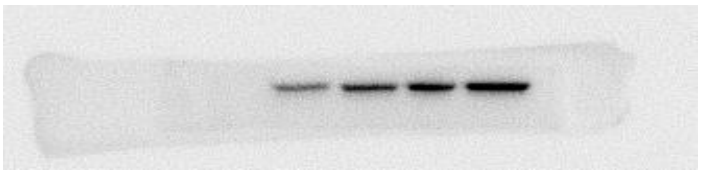

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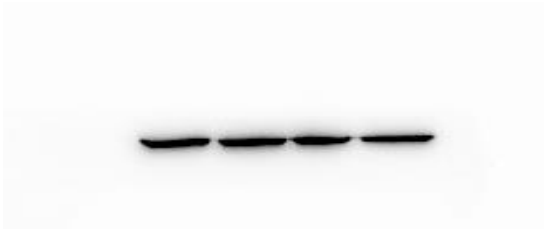
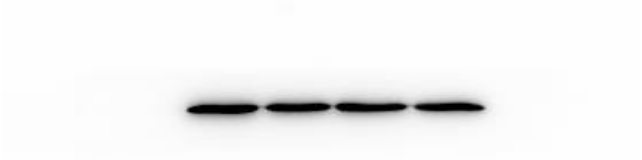


Phospho-ERK:

ERK:

GAPDH:



HepG-2

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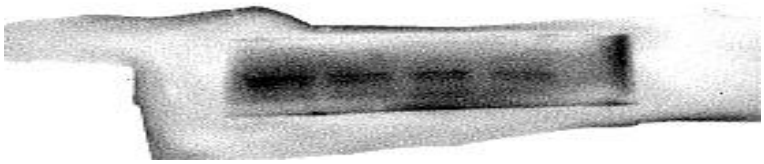

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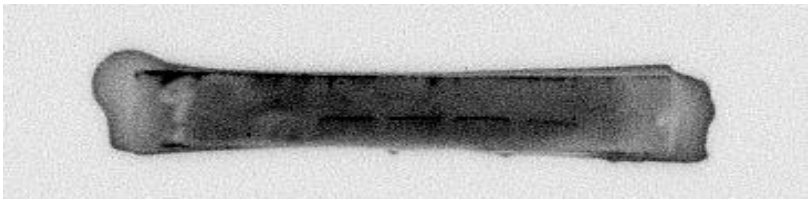

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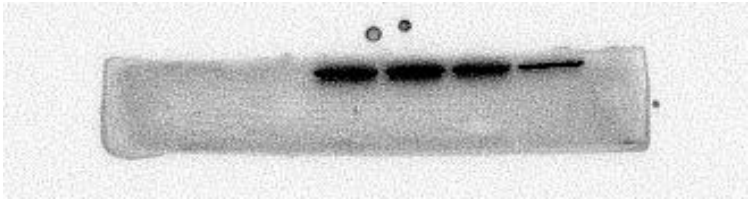
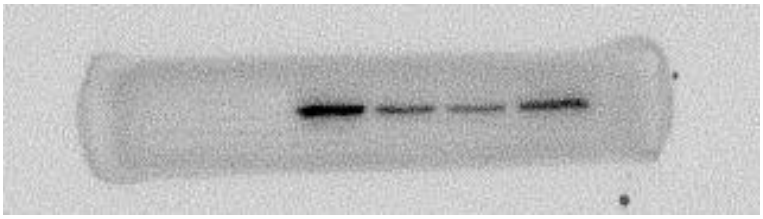


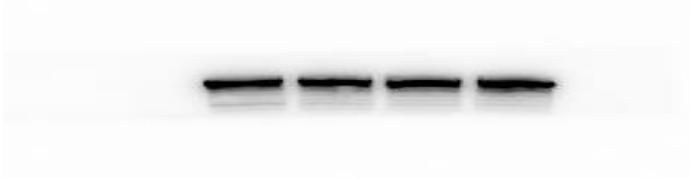
Phospho-AKT:



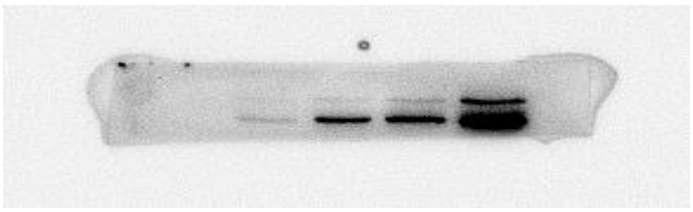
AKT:

Phospho-mTOR:

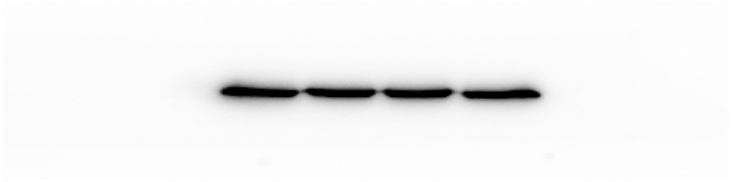
mTOR:



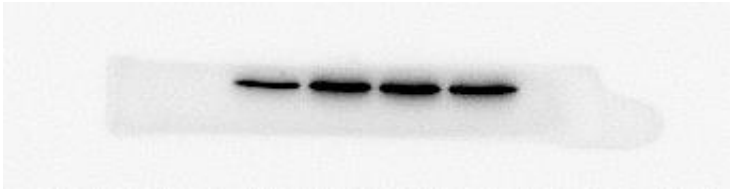
Phospho-p38 MAPK:



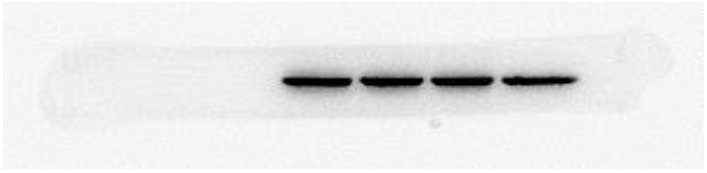
p38 MAPK:



Phospho-MEK:



MEK:



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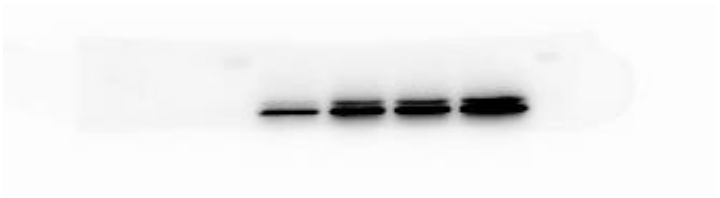
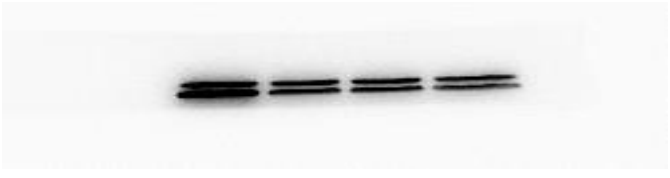
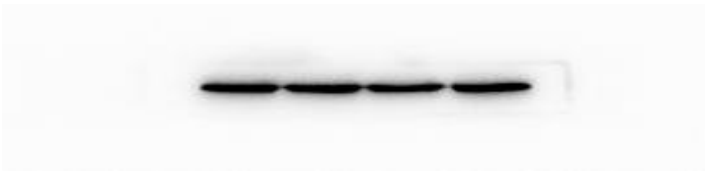


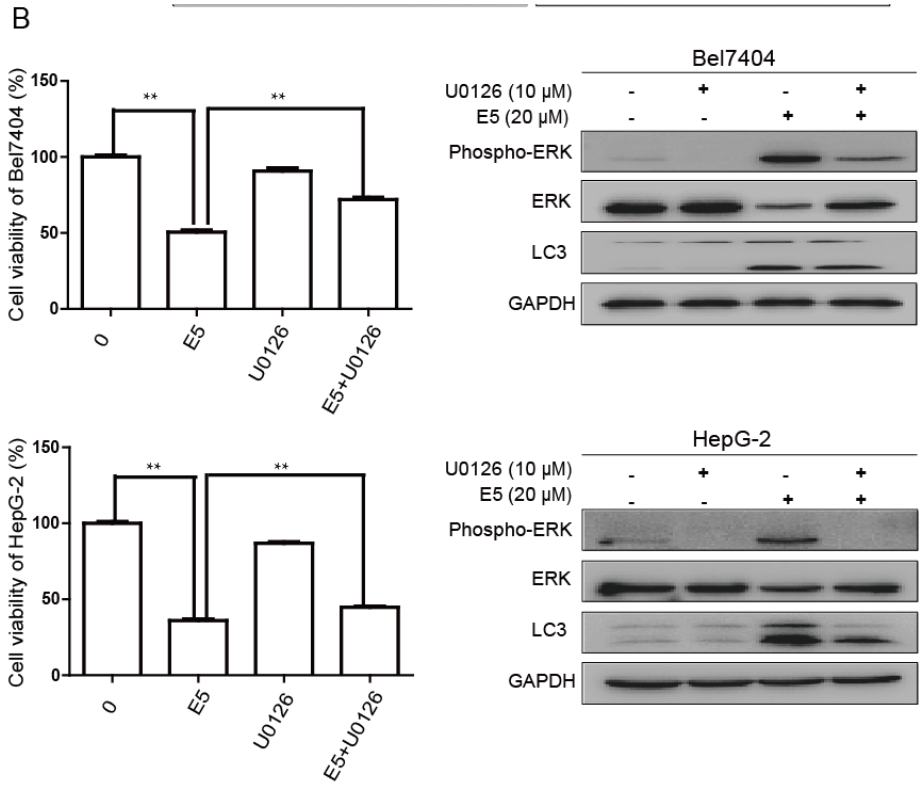
ERK:



GAPDH:

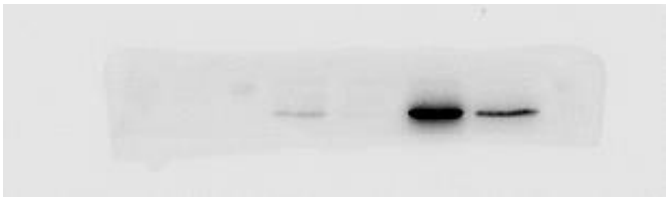


Supplementary Figure S7 Original gel images for Manuscript Fig. 7B



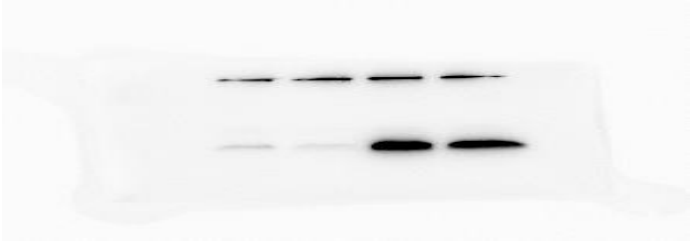
Bel7404

Phospho-ERK:



ERK:

LC3:

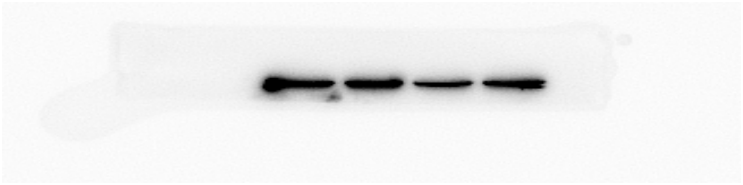


GAPDH:

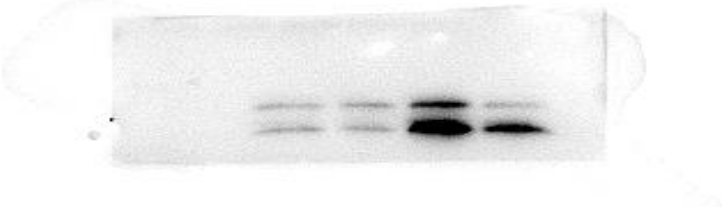
HepG-2

Phospho-ERK:

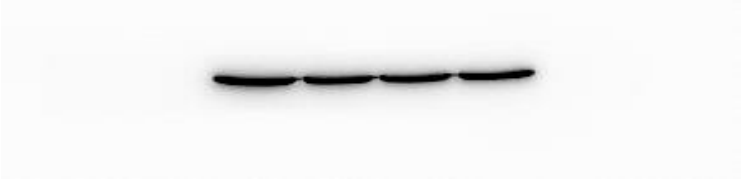
ERK:



LC3 :



GAPDH:



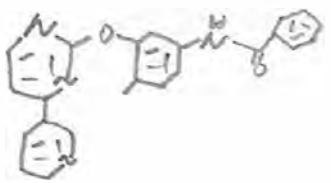
A1

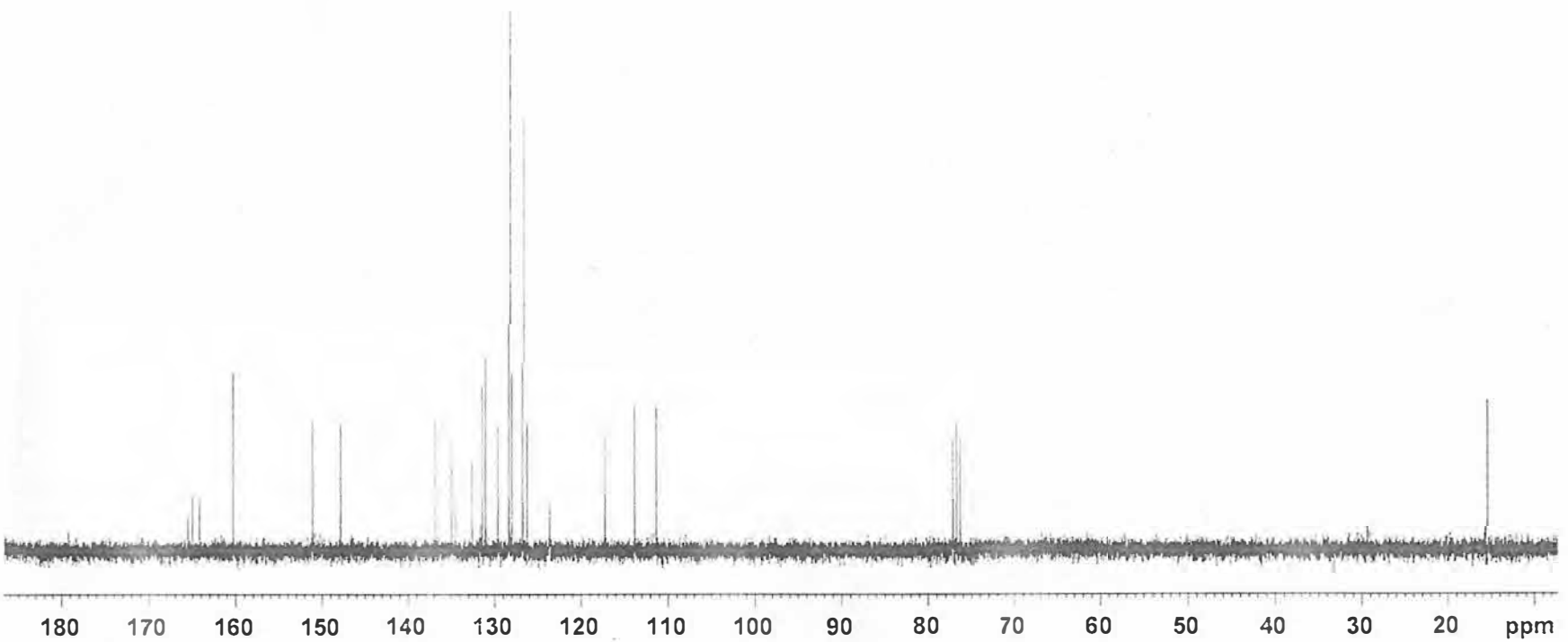
SP1308303-2-C C13-NMR CDCL3 303K AV-300

165.354
164.837
163.994
160.116
150.960
150.906
147.664
136.627
134.755
134.351
132.409
131.250
130.861
129.425
128.151
127.813
126.588
126.074
123.477
117.060
113.635
111.159

77.002
76.577
76.152

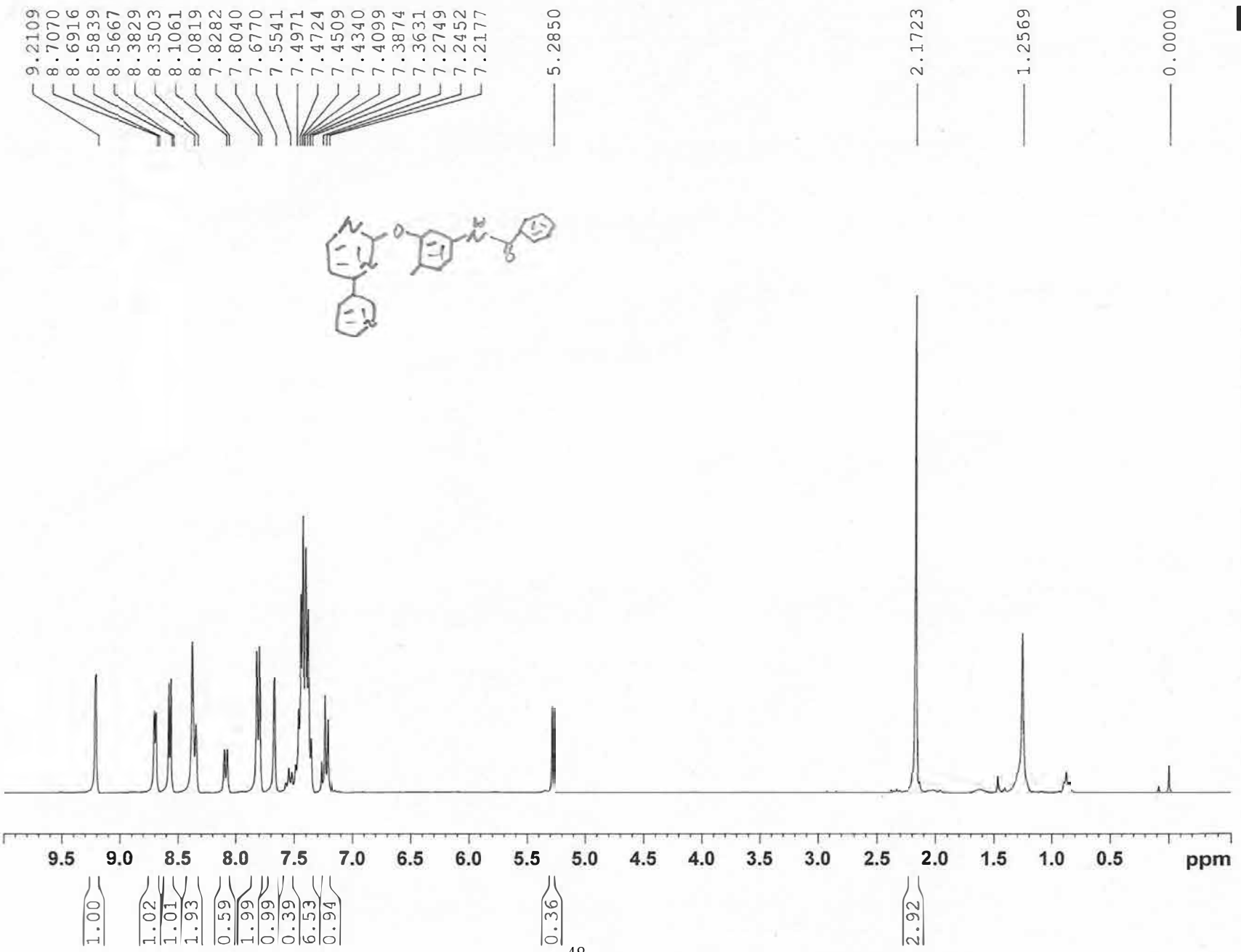
15.458



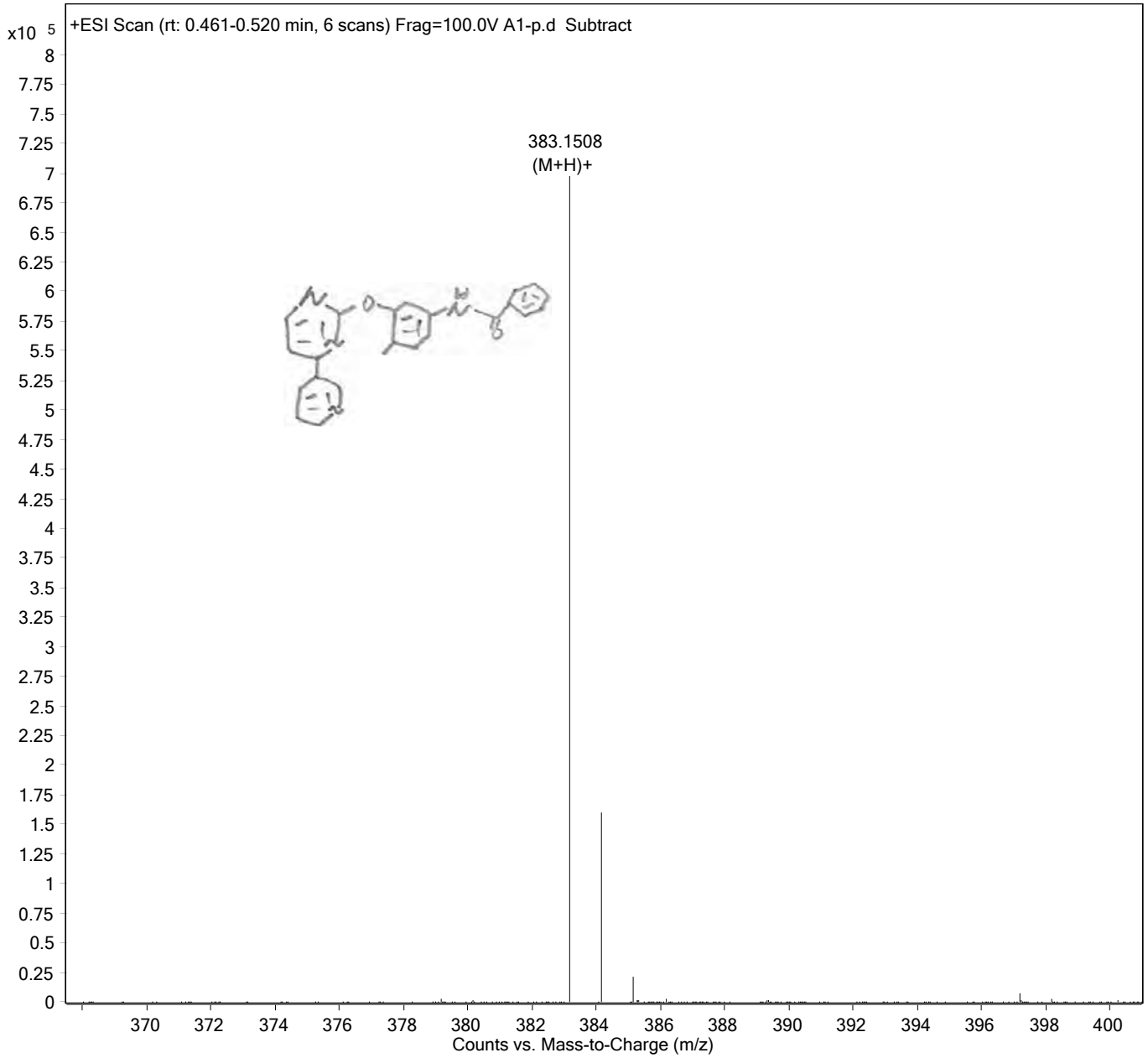


A1

SP121031-2 1H-NMR CDCl3 303K AV-300

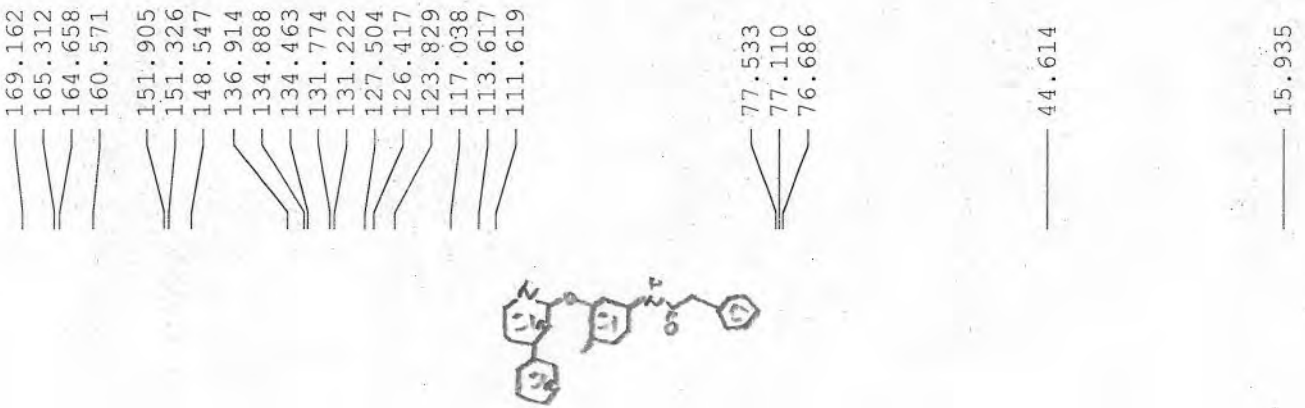


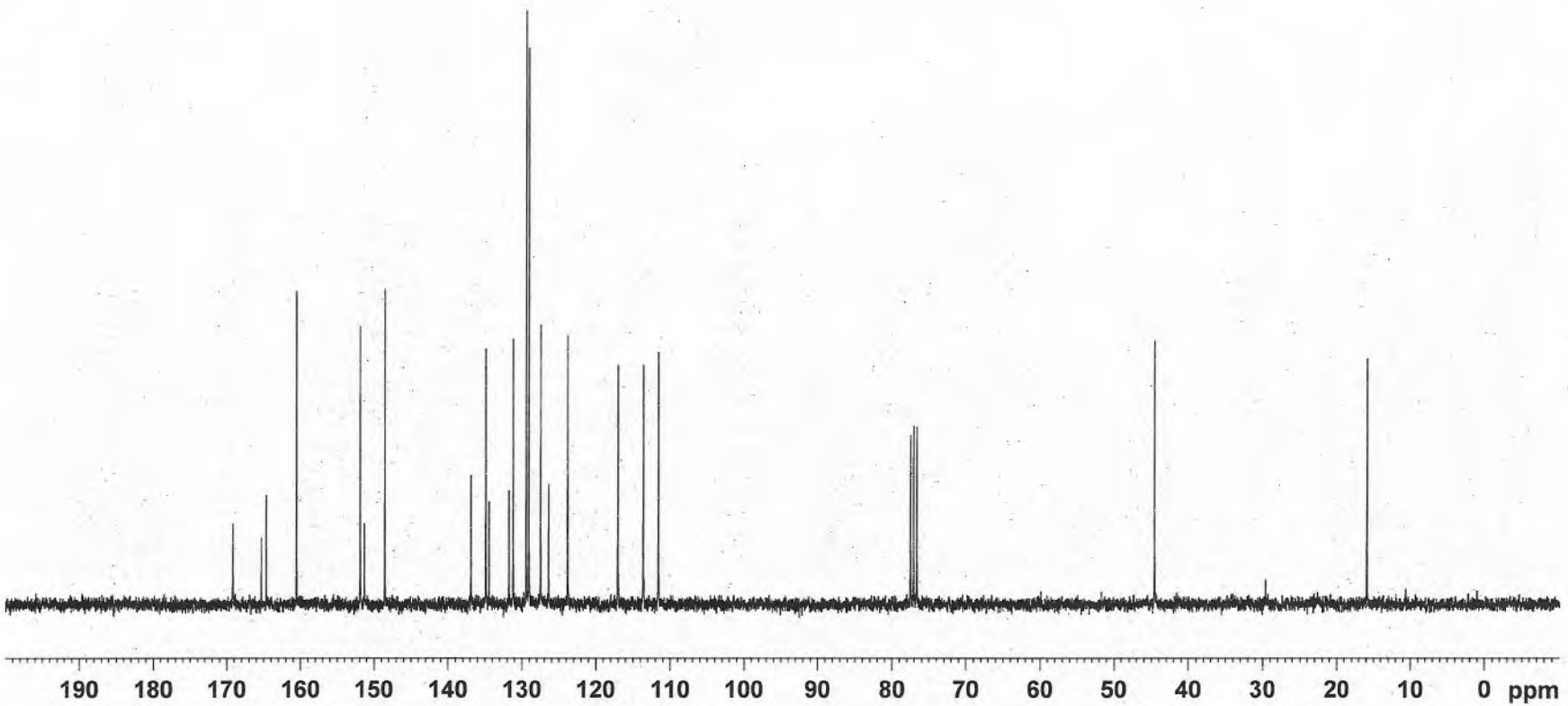
Sample Name		**Position**	p2d6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.2	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 2:50:16 PM



A2

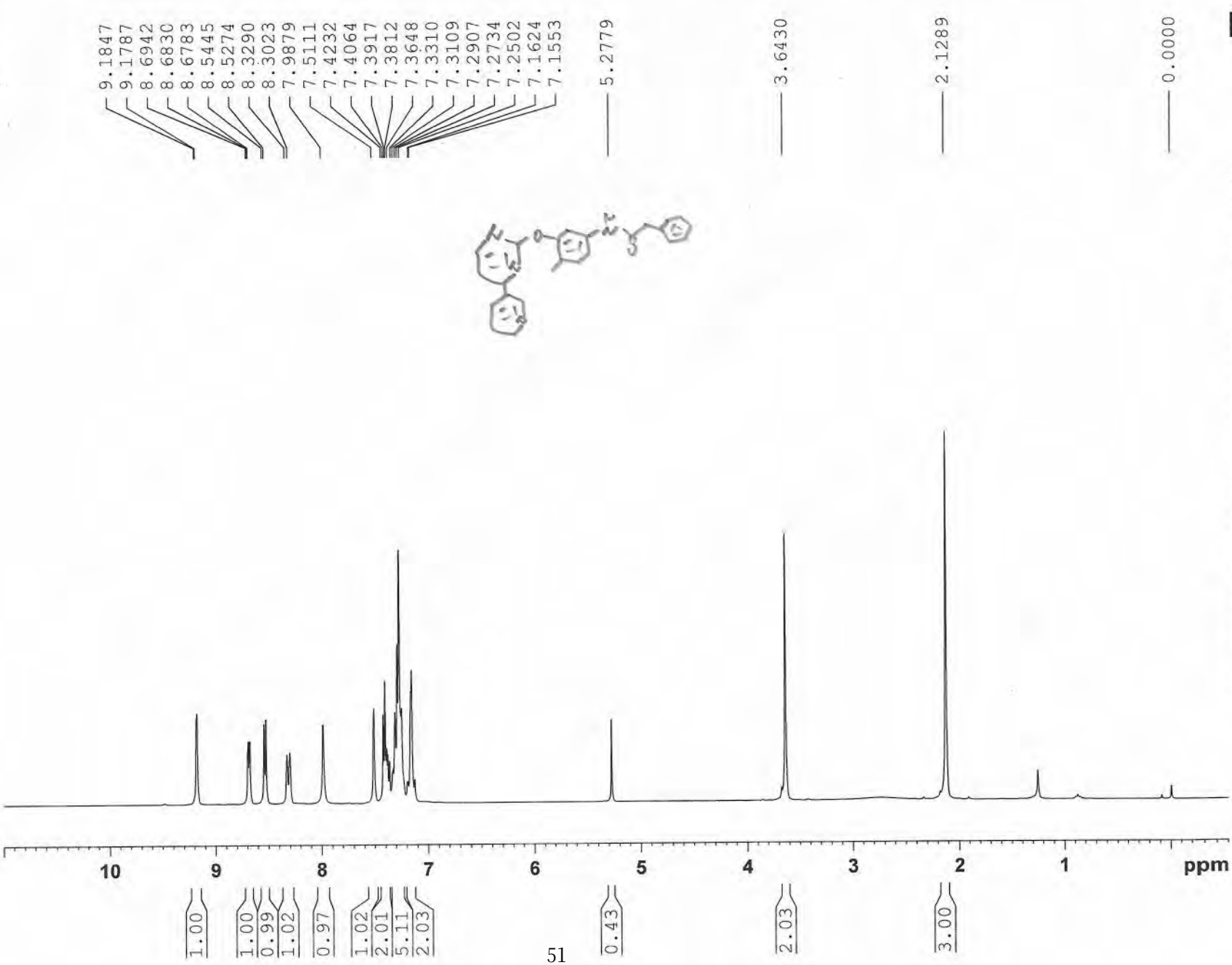
SP121126 CDCl3 303K C13-NMR AV300



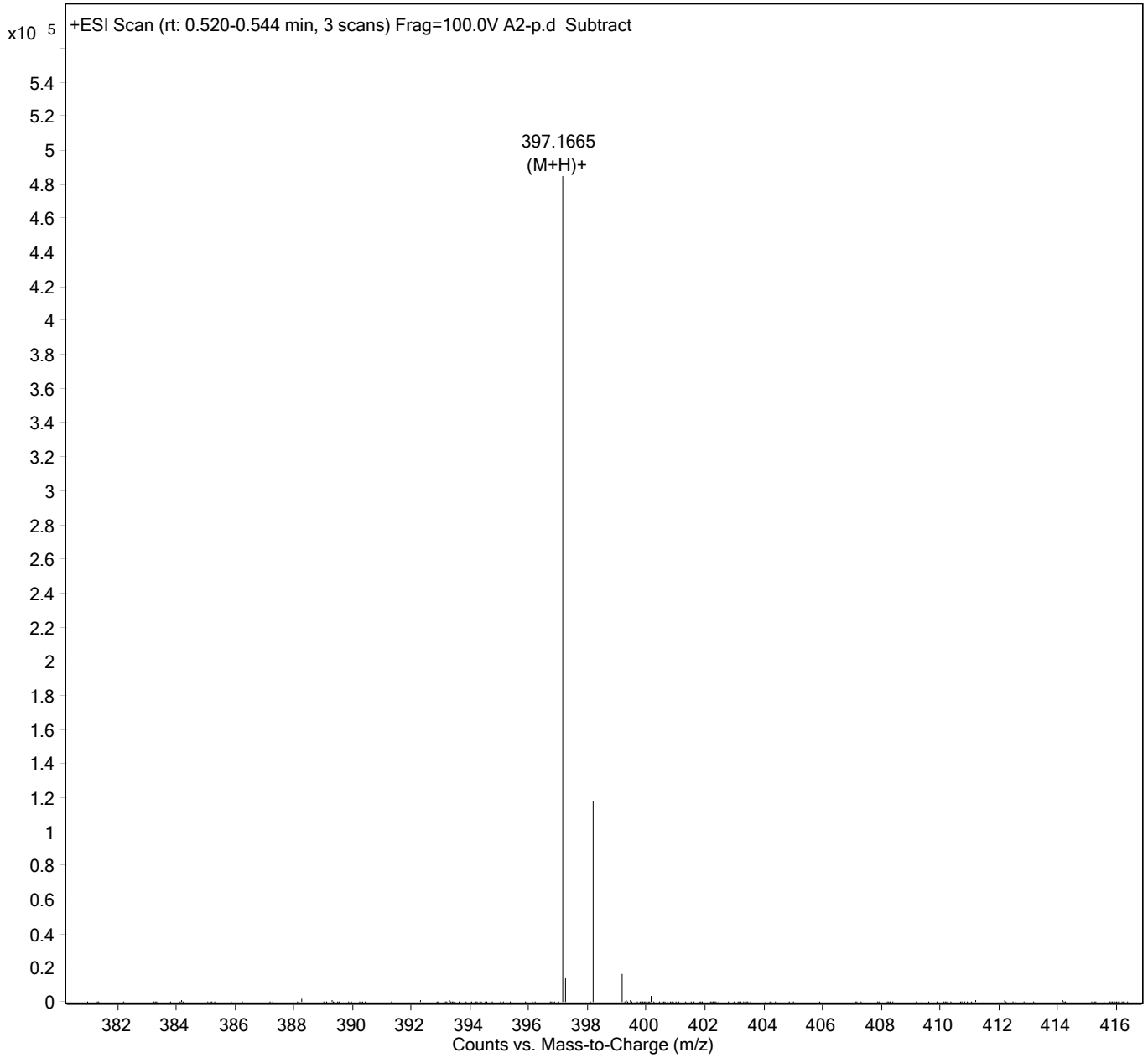


A2

SP121109-3 1H-NMR CDCl3 303K AV-300

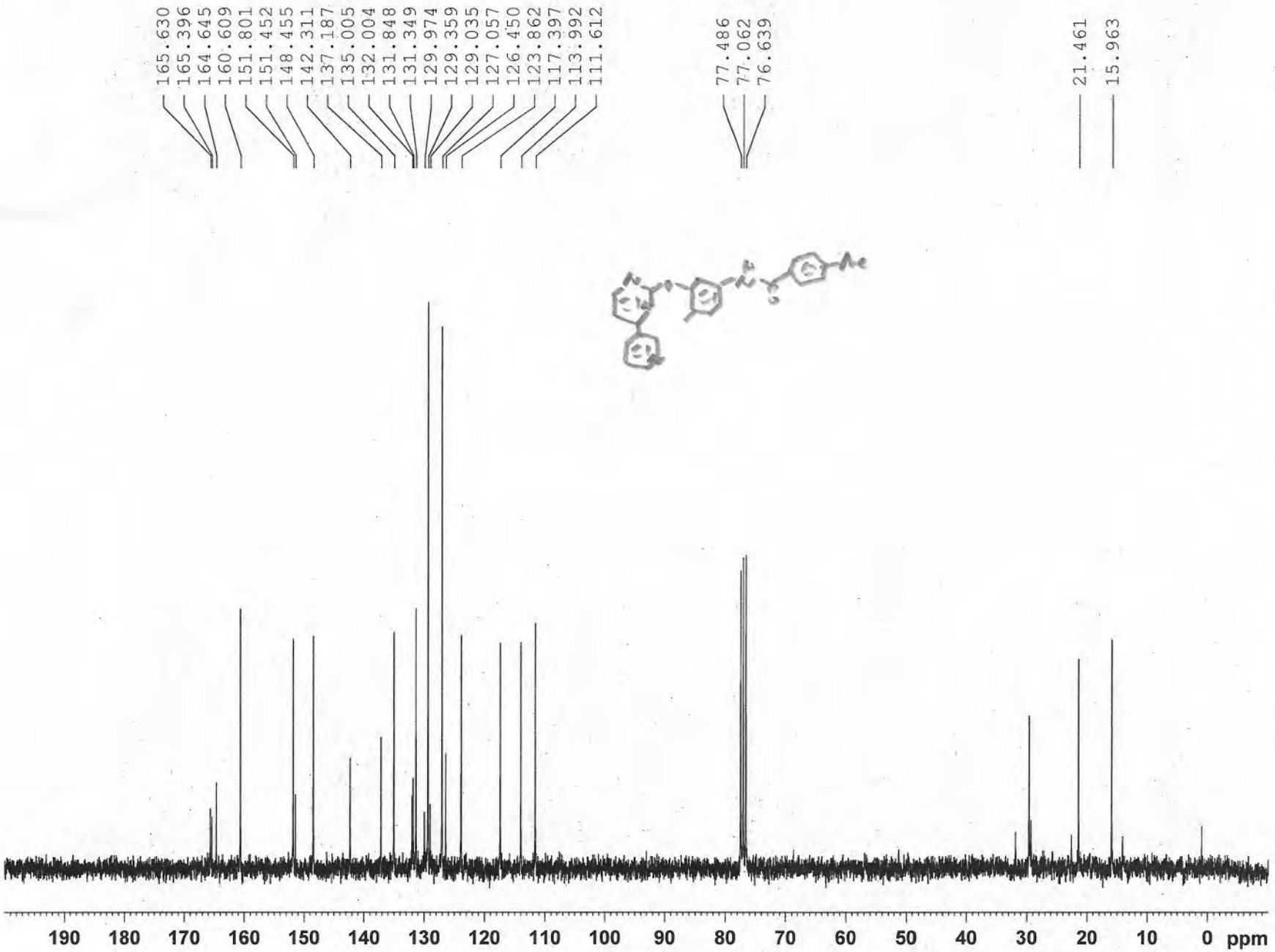


Sample Name		**Position**	p2d7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.2	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 2:52:45 PM



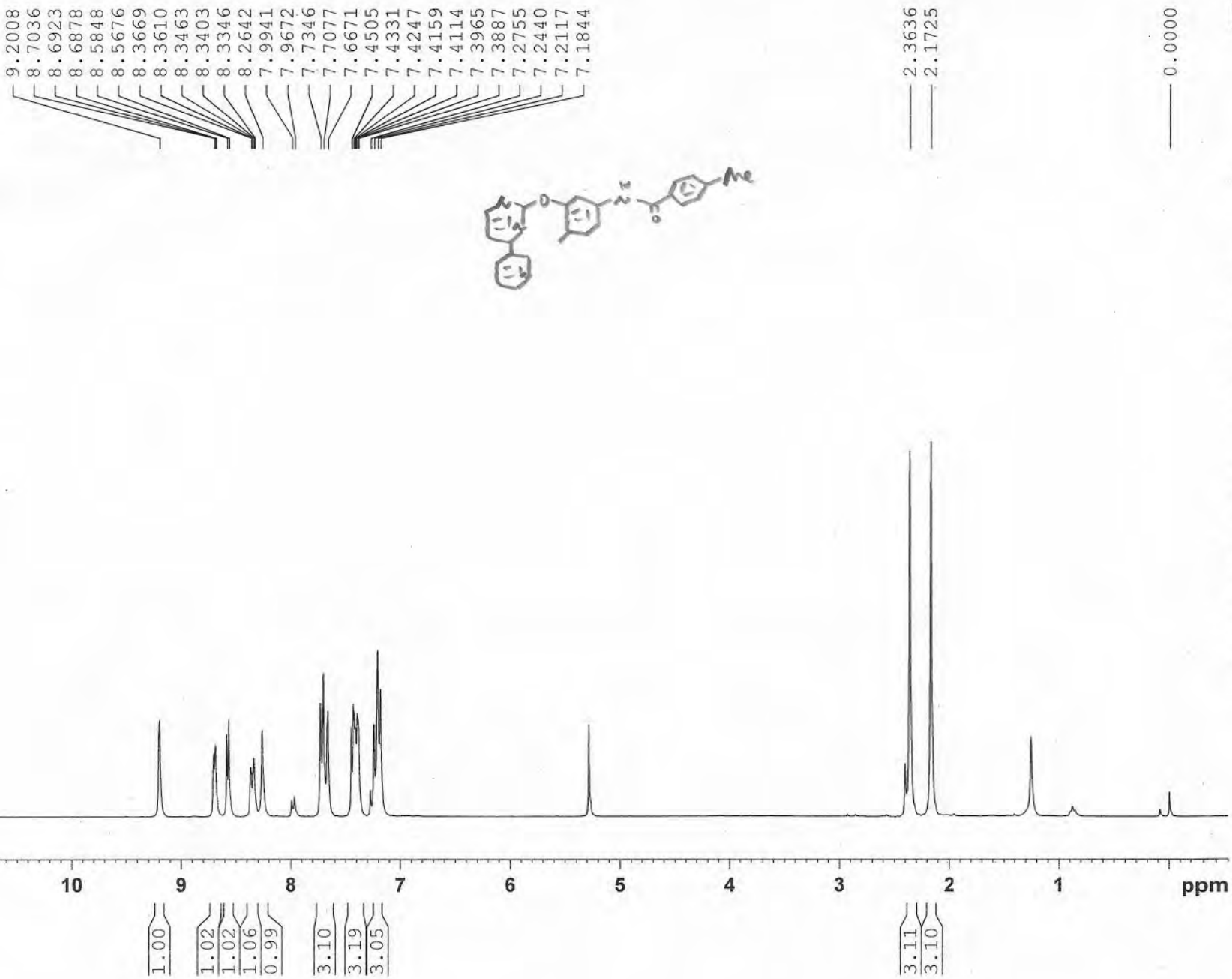
A 3

SP121128-2 CDCl3 303K C13-NMR AV300

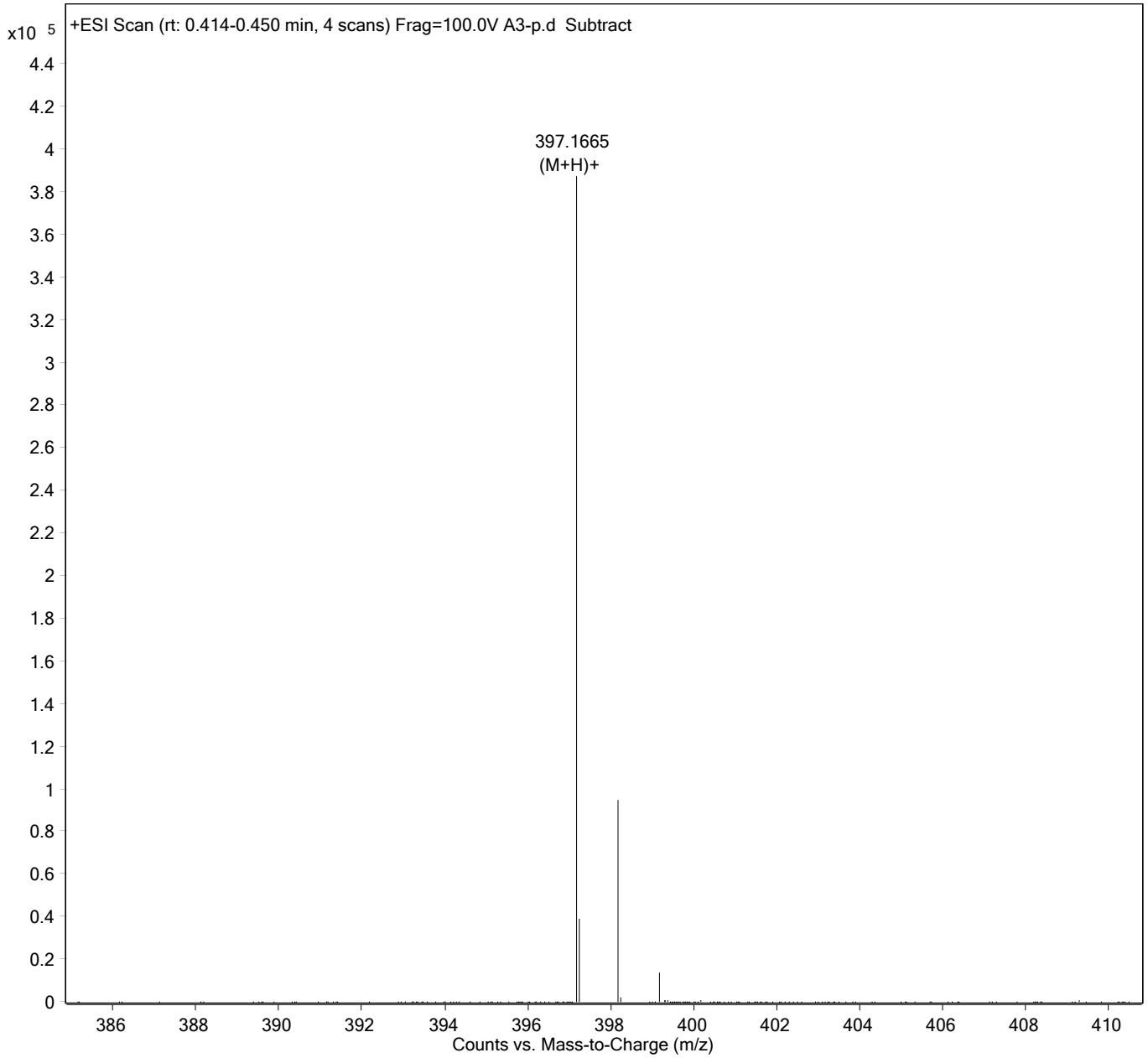


A3

SP121107-1 1H-NMR CDCl3 303K AV-300



Sample Name		**Position**	p2d8	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 2:54:56 PM



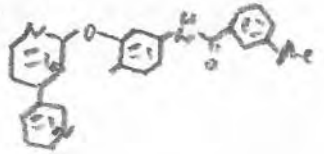
A 4

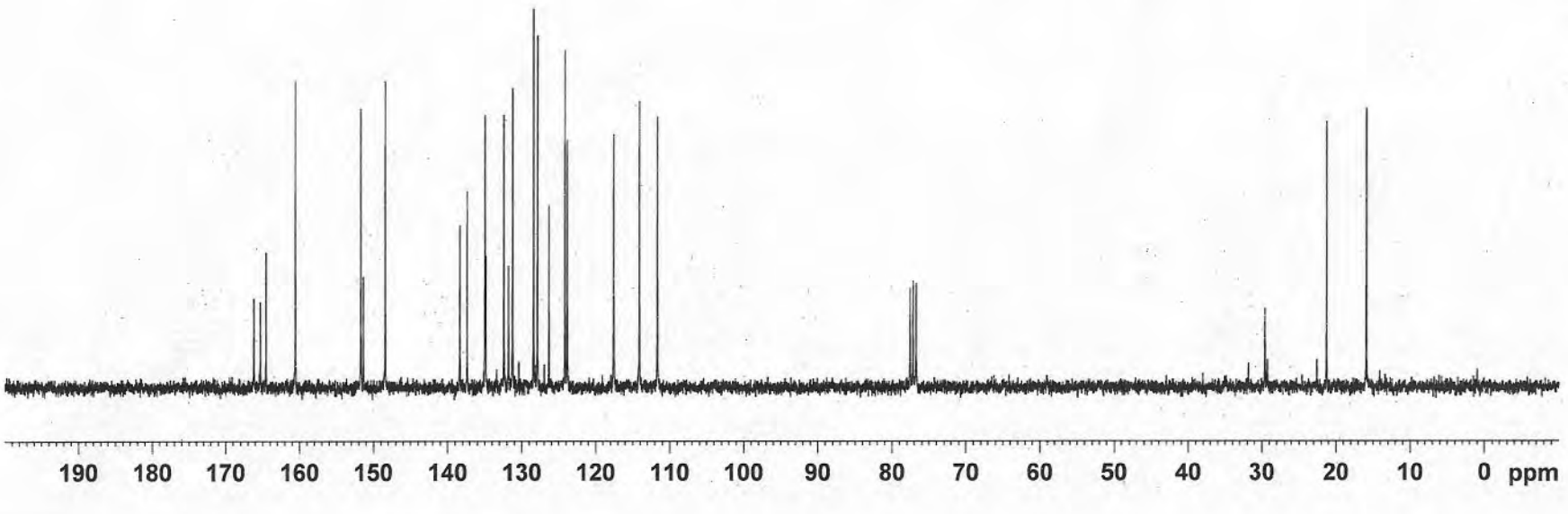
SP121212-1 CDCl3 303K C13-NMR AV300

166.198
165.319
164.541
160.557
151.725
151.358
148.395
138.380
137.370
134.968
134.857
132.398
131.780
131.270
128.411
127.881
126.324
124.152
123.852
117.564
114.093
111.637

77.610
77.187
76.760

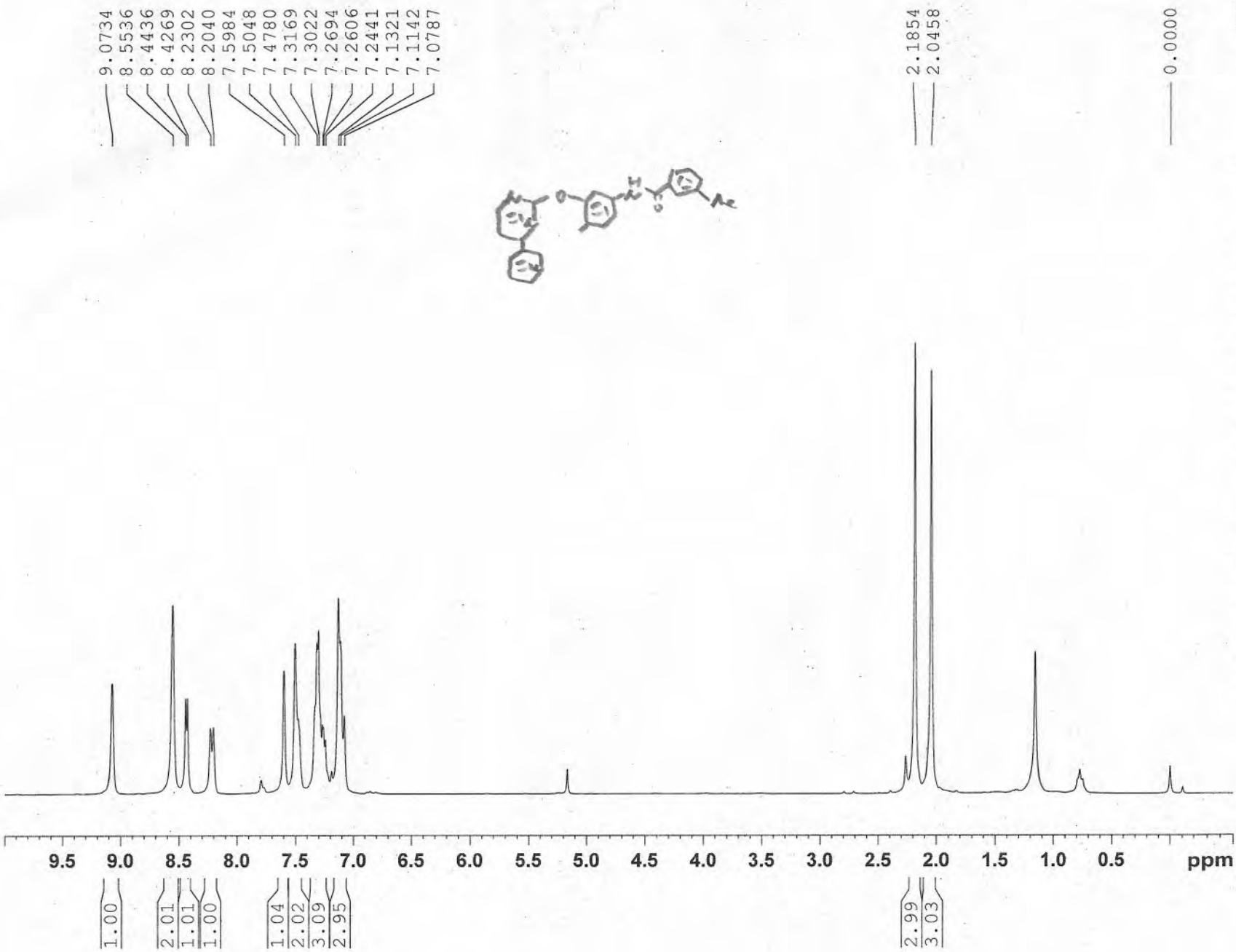
21.273
15.944



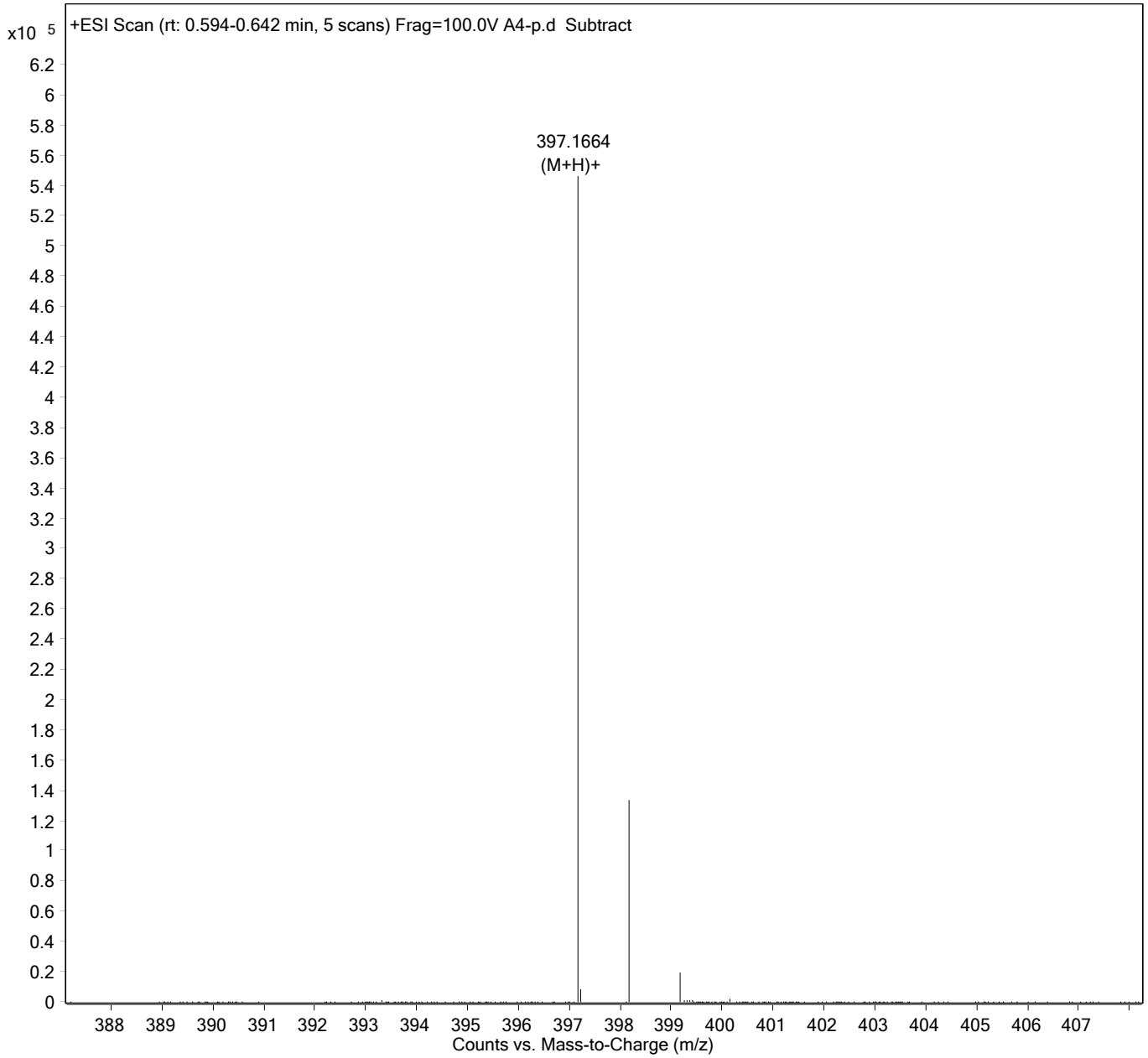


A4

SP121212-1 1H-NMR CDCl3 303K AV-300



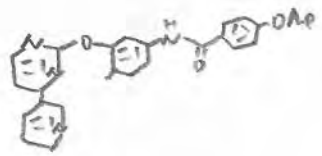
Sample Name		**Position**	p2d9	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A4-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 2:57:46 PM

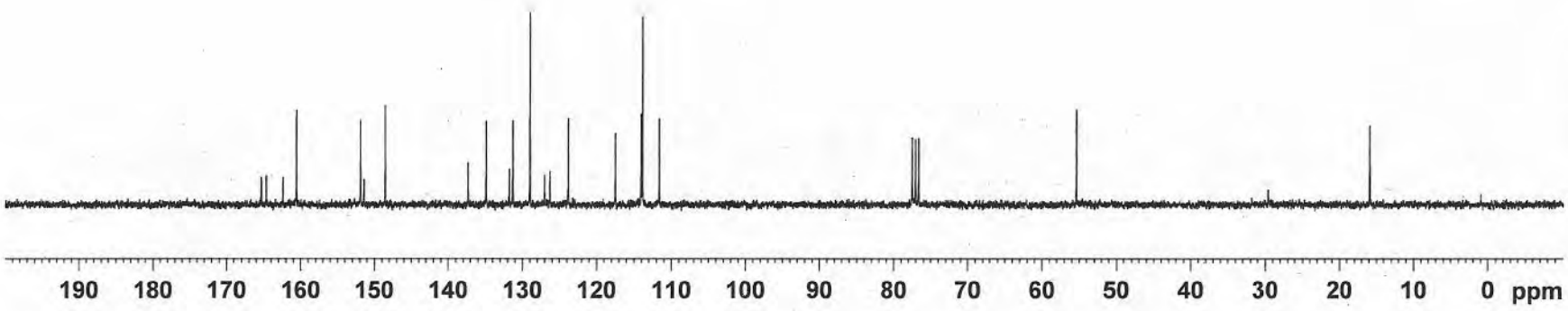


A5

SP121119 CDCl3 303K C13-NMR AV300

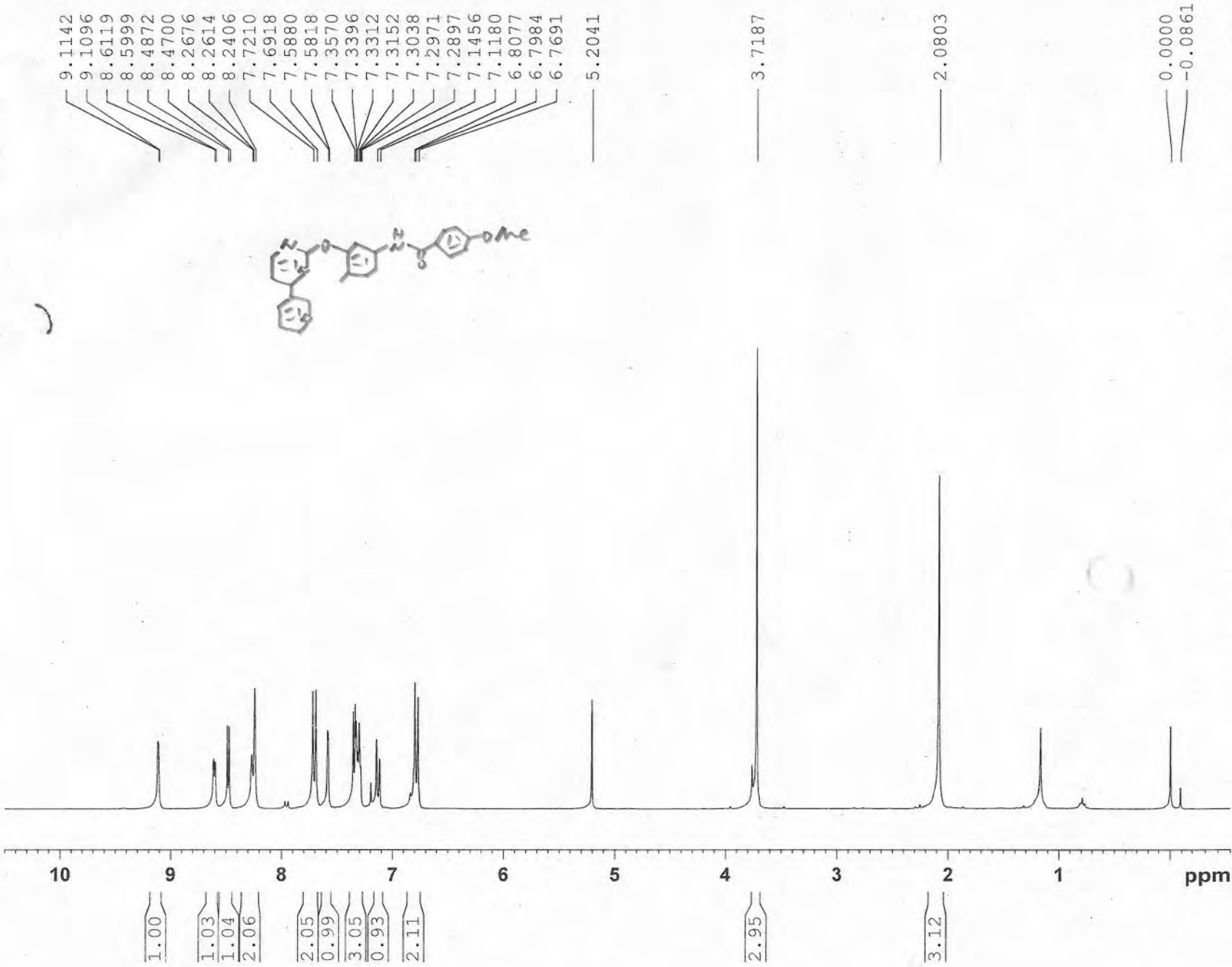
165.369
164.670
162.391
160.570
151.899
151.400
148.541
137.337
134.899
131.774
131.309
128.981
127.023
126.300
123.820
117.478
114.038
113.845
111.616
77.512
77.089
76.665
55.417
15.953



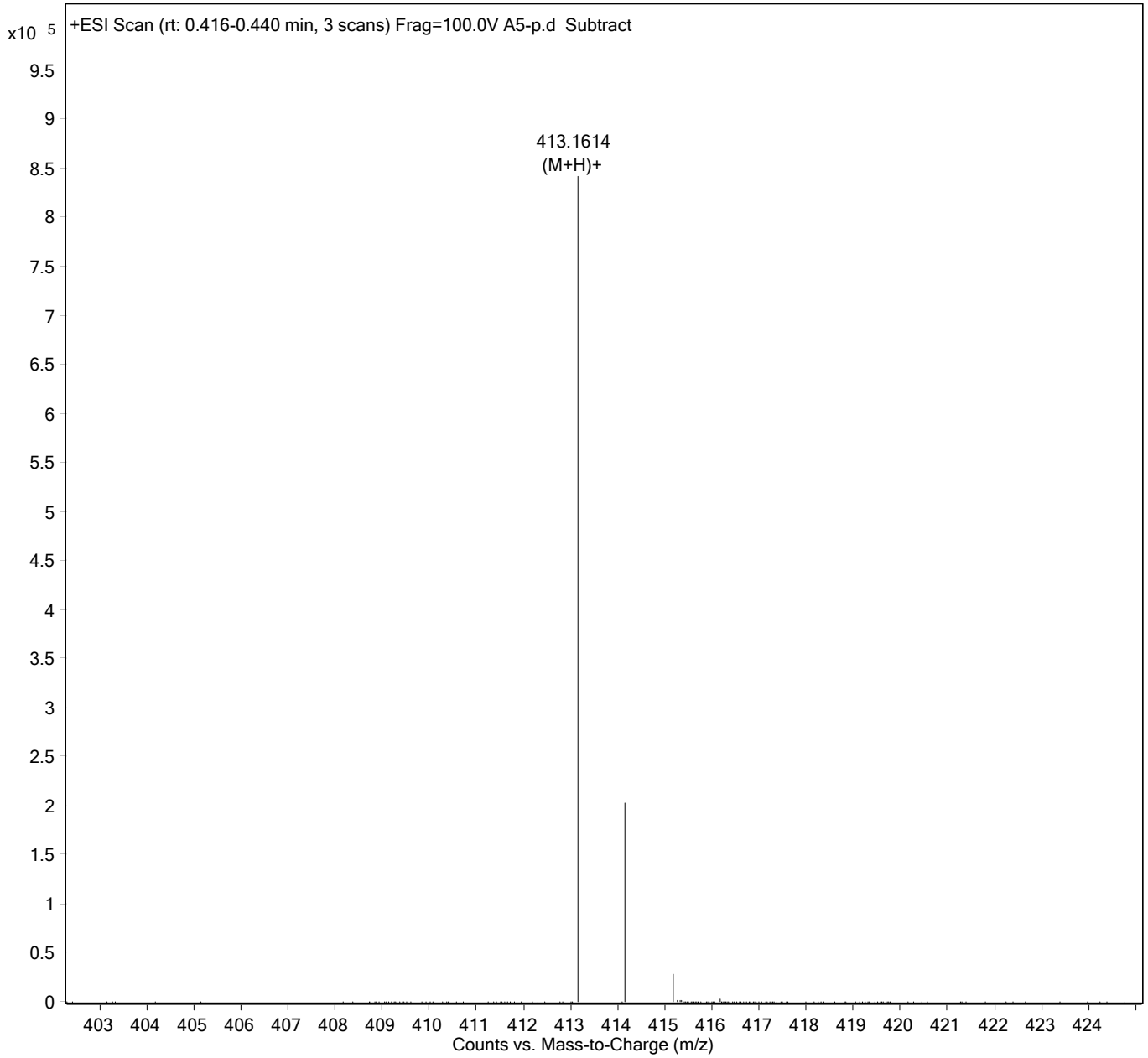


At.

SP121105-2 1H-NMR CDCl3 303K AV-300



Sample Name		**Position**	p2E1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A5-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:00:14 PM



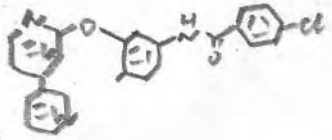
A6.

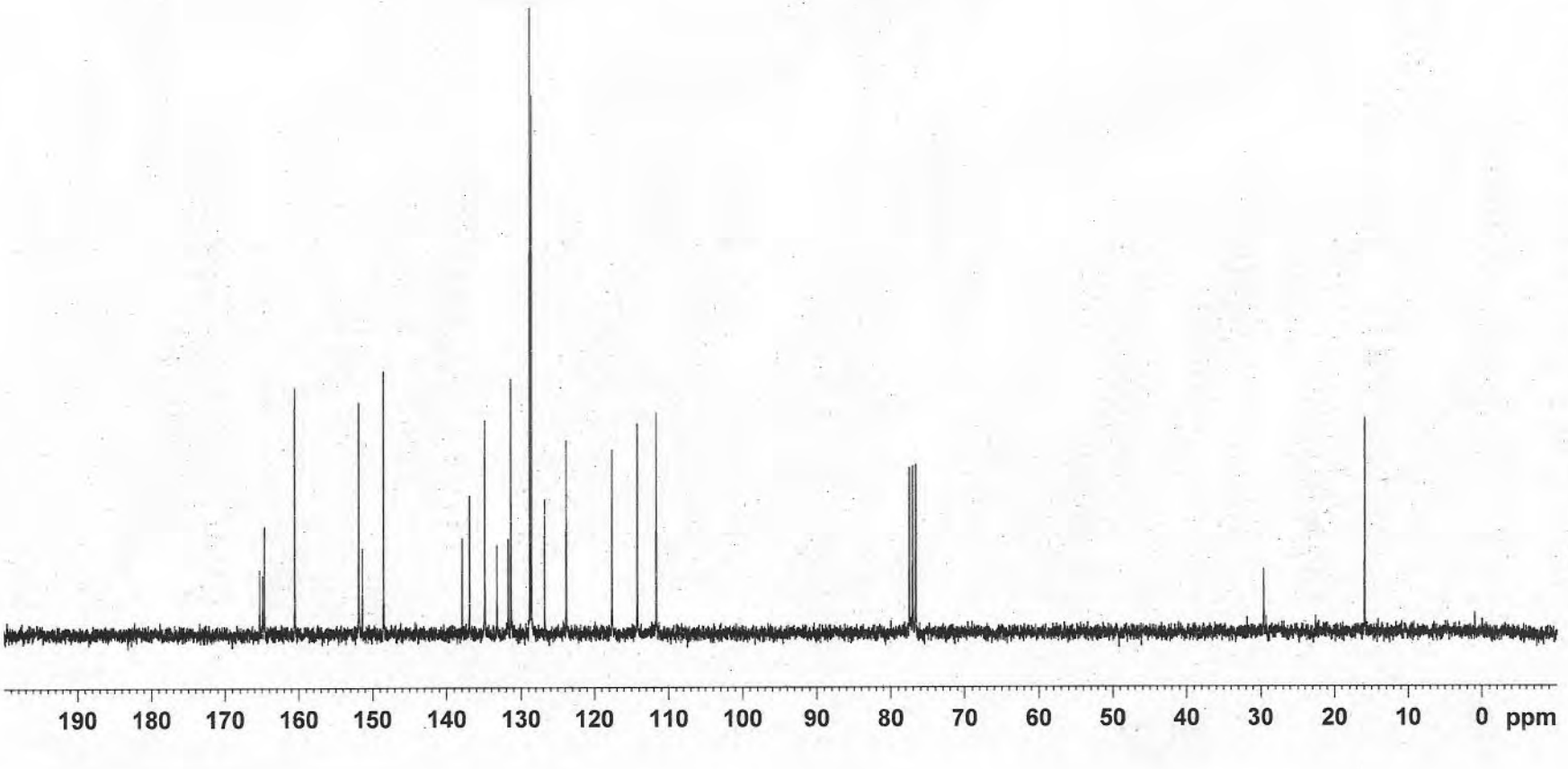
SP121205-1 CDCl3 303K C13-NMR AV300

165.303
164.903
164.657
160.566
151.890
151.389
148.524
137.947
136.952
134.880
133.221
131.727
131.388
128.833
128.604
126.805
123.836
117.641
114.222
111.672

77.516
77.093
76.670

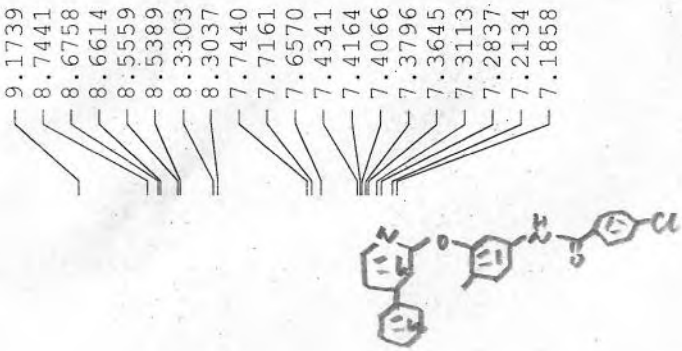
15.981

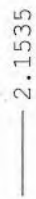


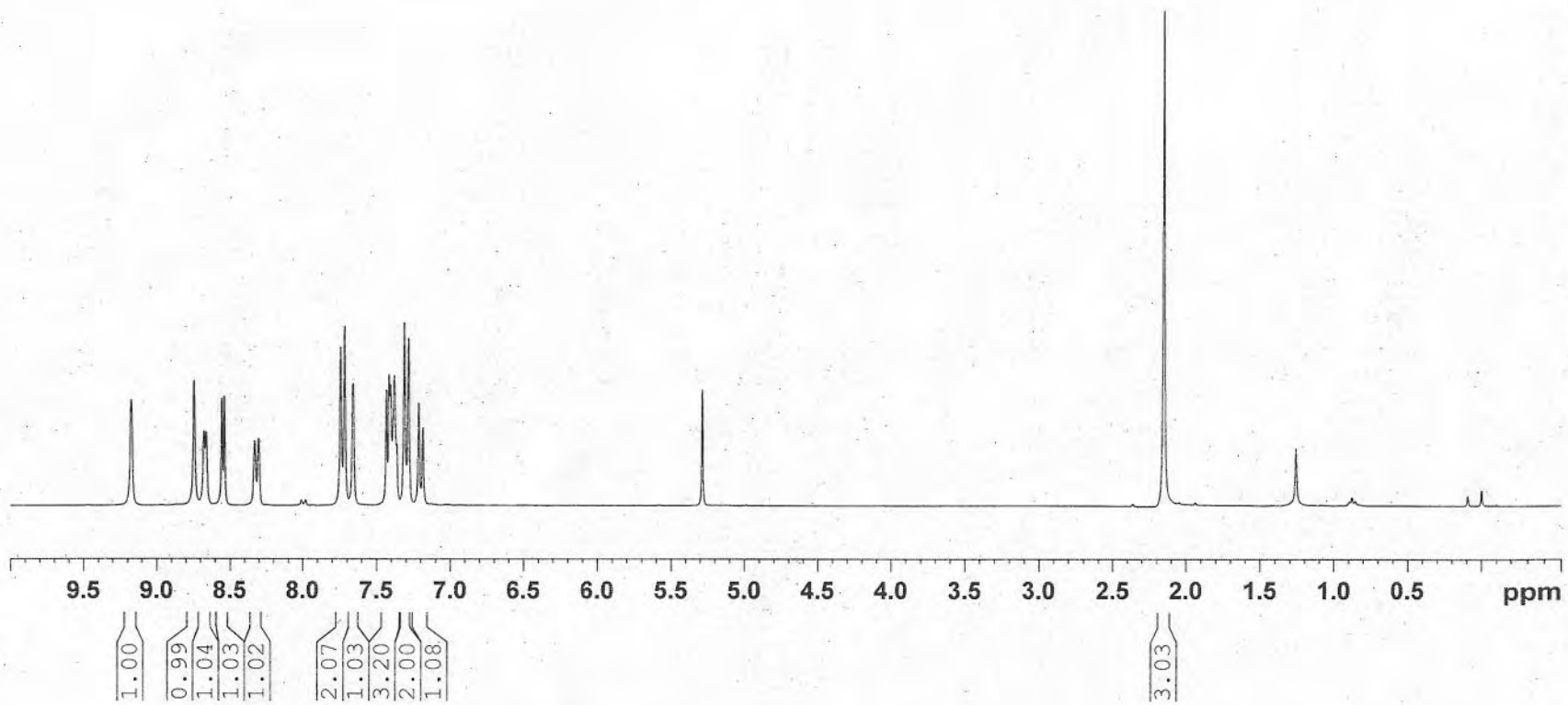


A6

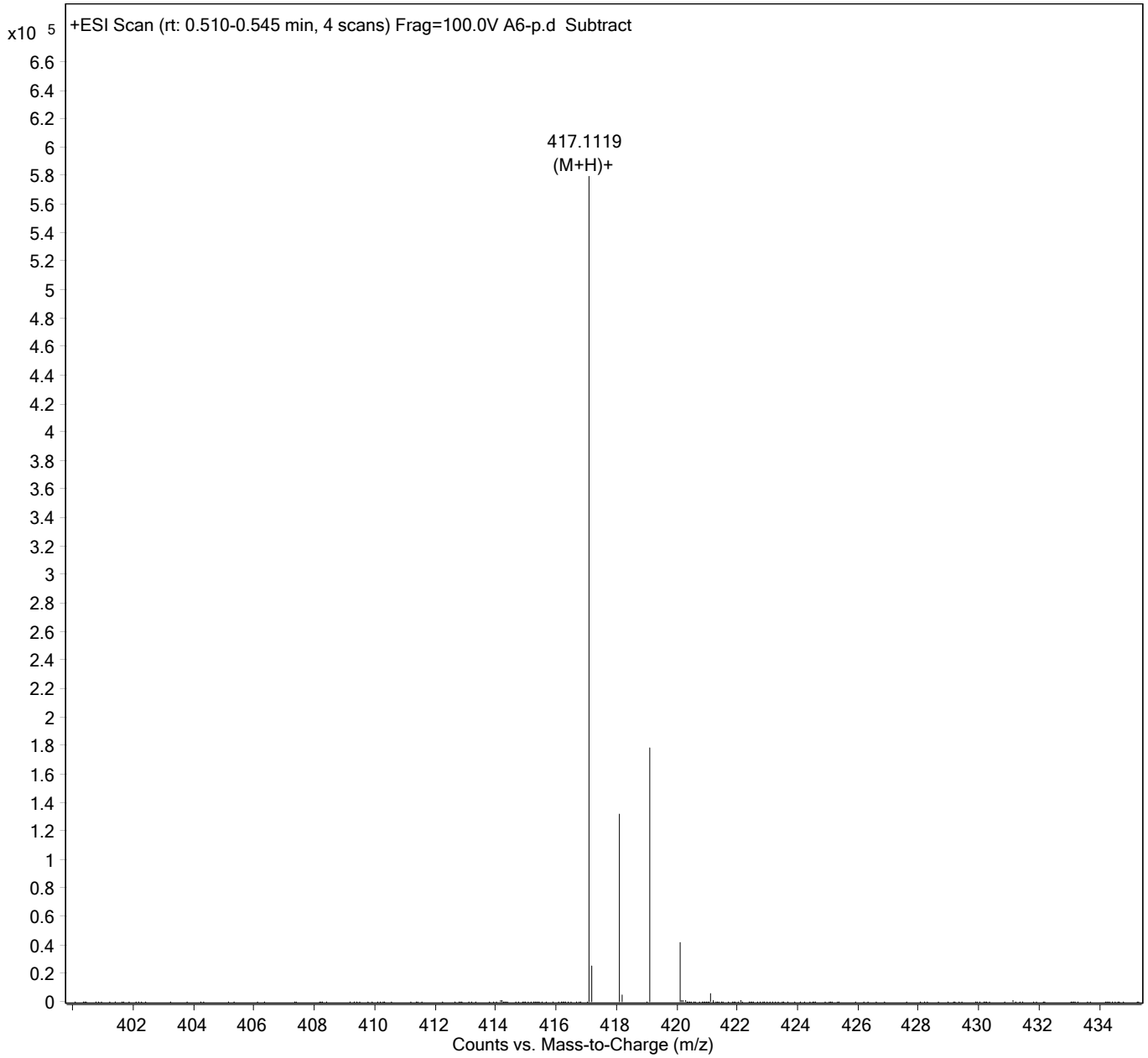
SP121114-3 1HNMR CDCl3 303K AV-300







Sample Name		**Position**	p2E2	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A6-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:02:19 PM



A7

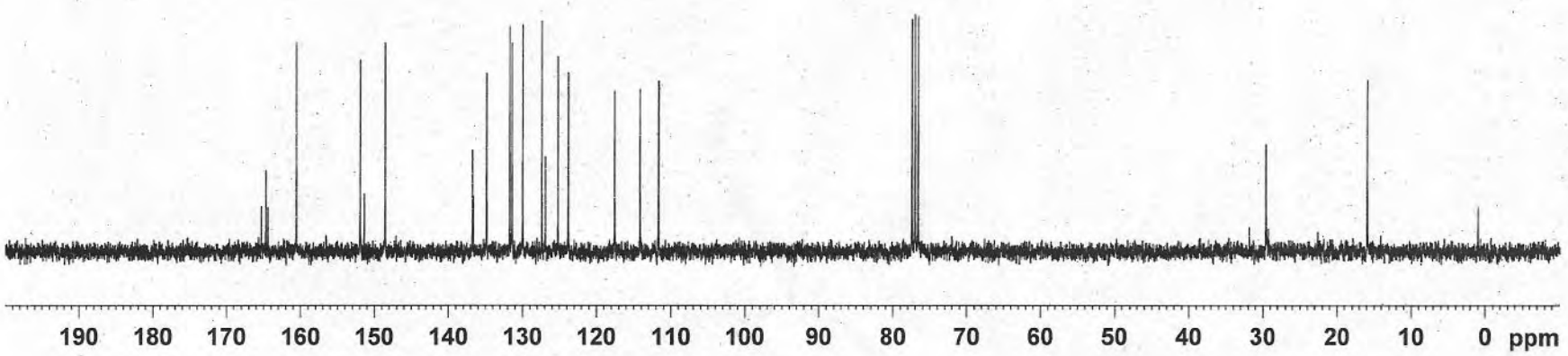
SP121202-1 CDCl3 303K C13-NMR AV300

165.327
164.710
164.437
160.588
151.962
151.422
148.571
136.793
136.679
134.864
134.807
131.753
131.430
129.998
127.422
126.945
125.221
123.824
117.560
114.170
111.667

77.483
77.060
76.636

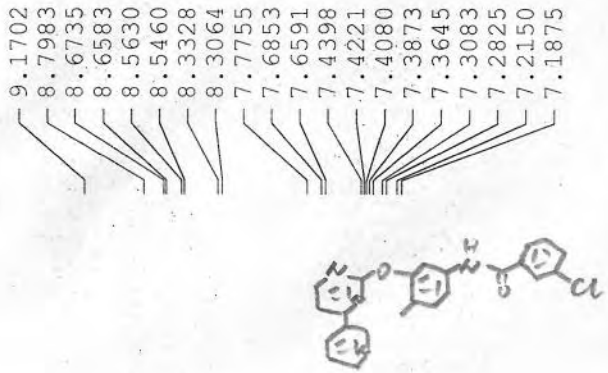
29.696

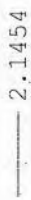
15.991

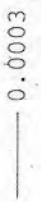


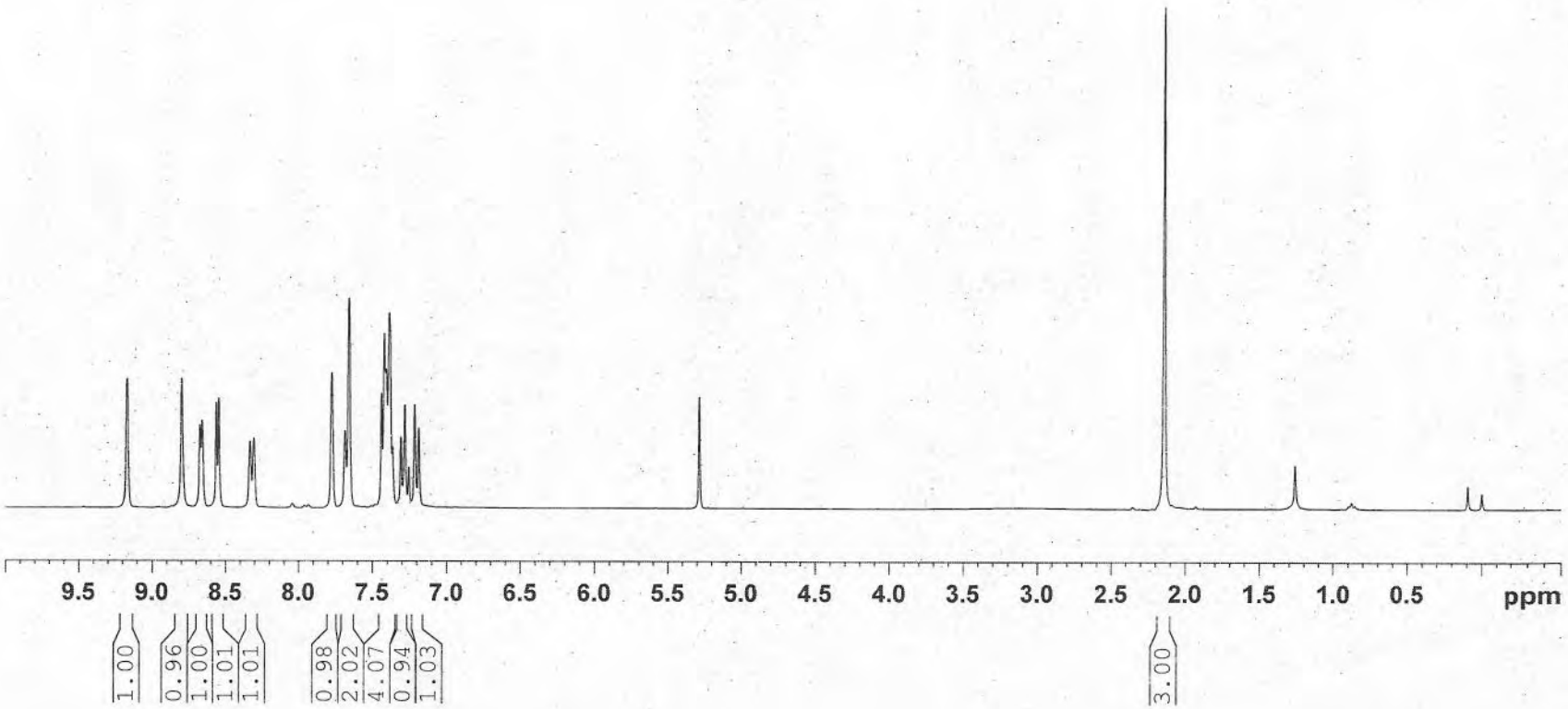
A7

SP121114-2 1HNMR CDCl3 303K AV-300



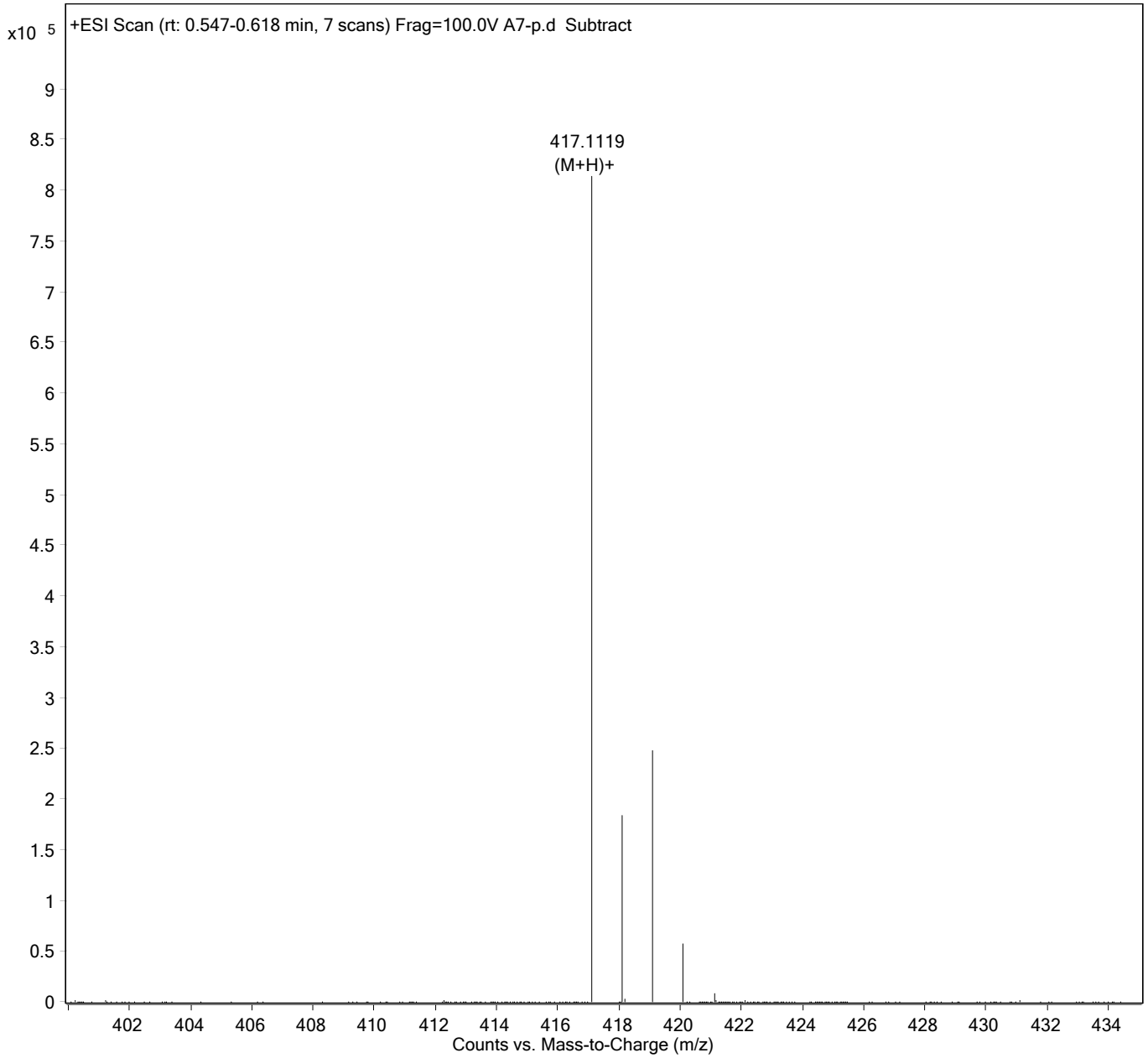






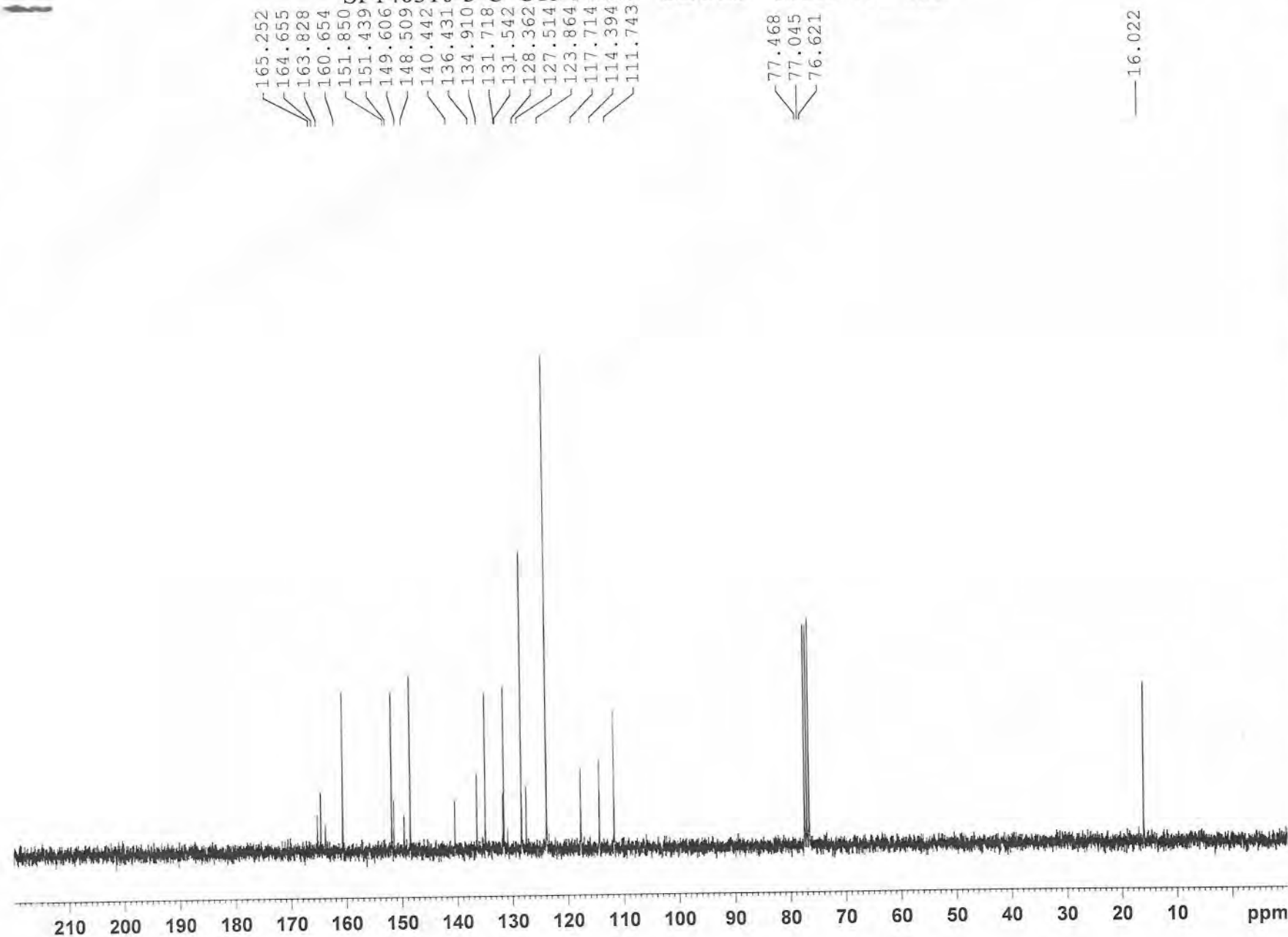
99

Sample Name		**Position**	p2E3	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A7-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:04:19 PM



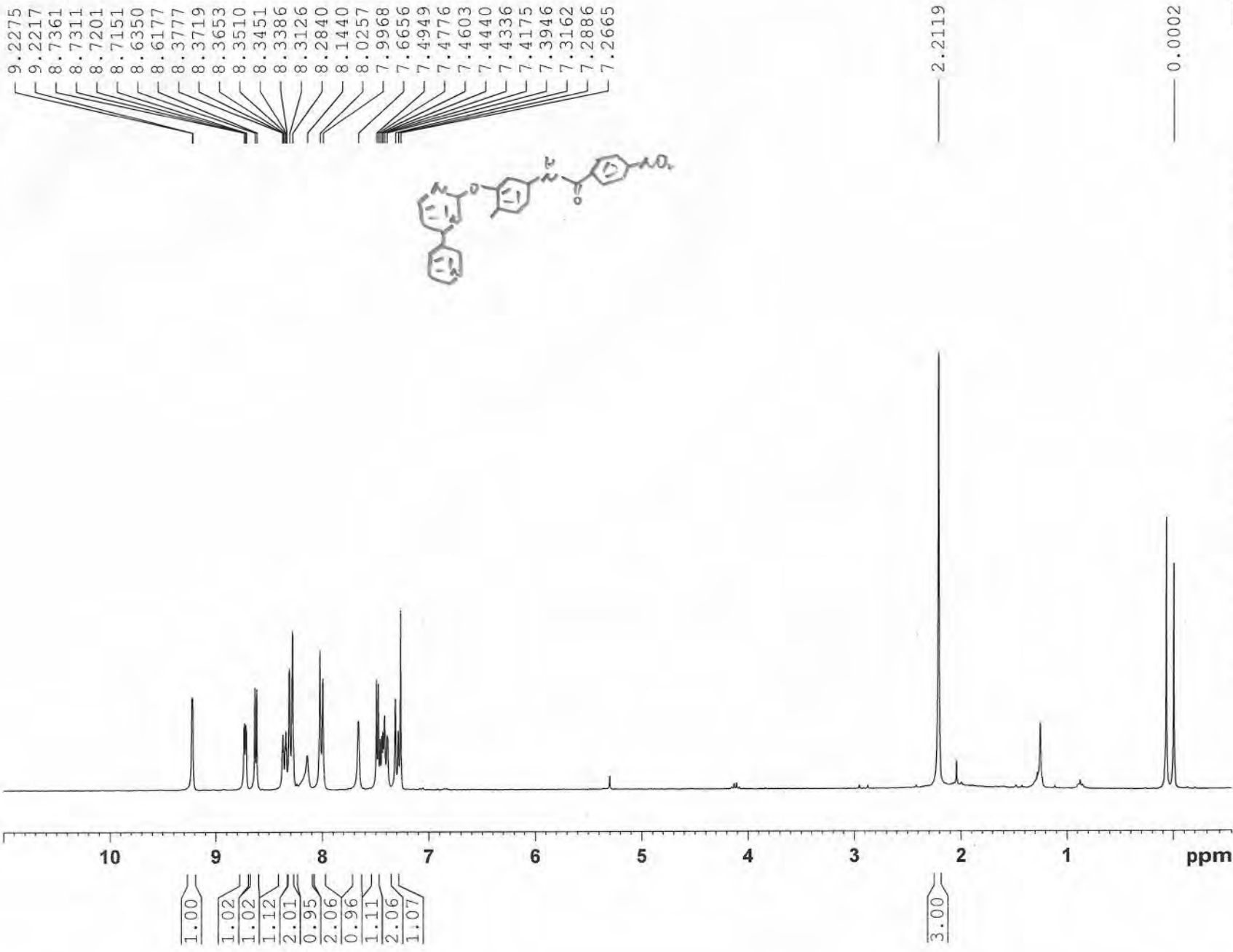
A 8

SP140310-3-C C13-NMR CDCL3 303K AV-300

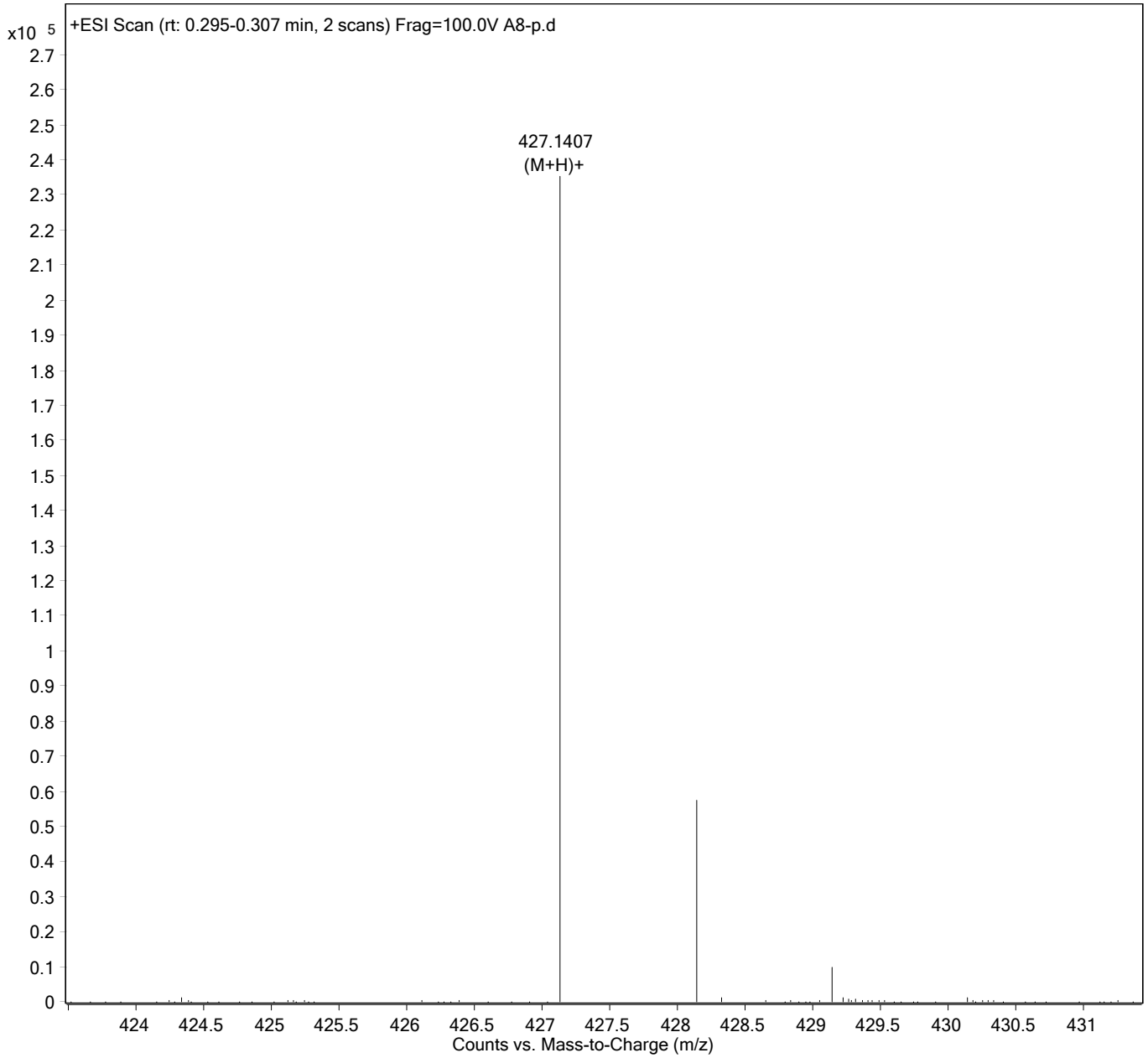


A8

SP121109-1 1H-NMR CDCl3 303K AV-300



Sample Name		**Position**	p2E4	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A8-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:07:26 PM

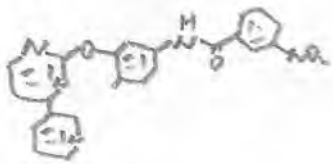


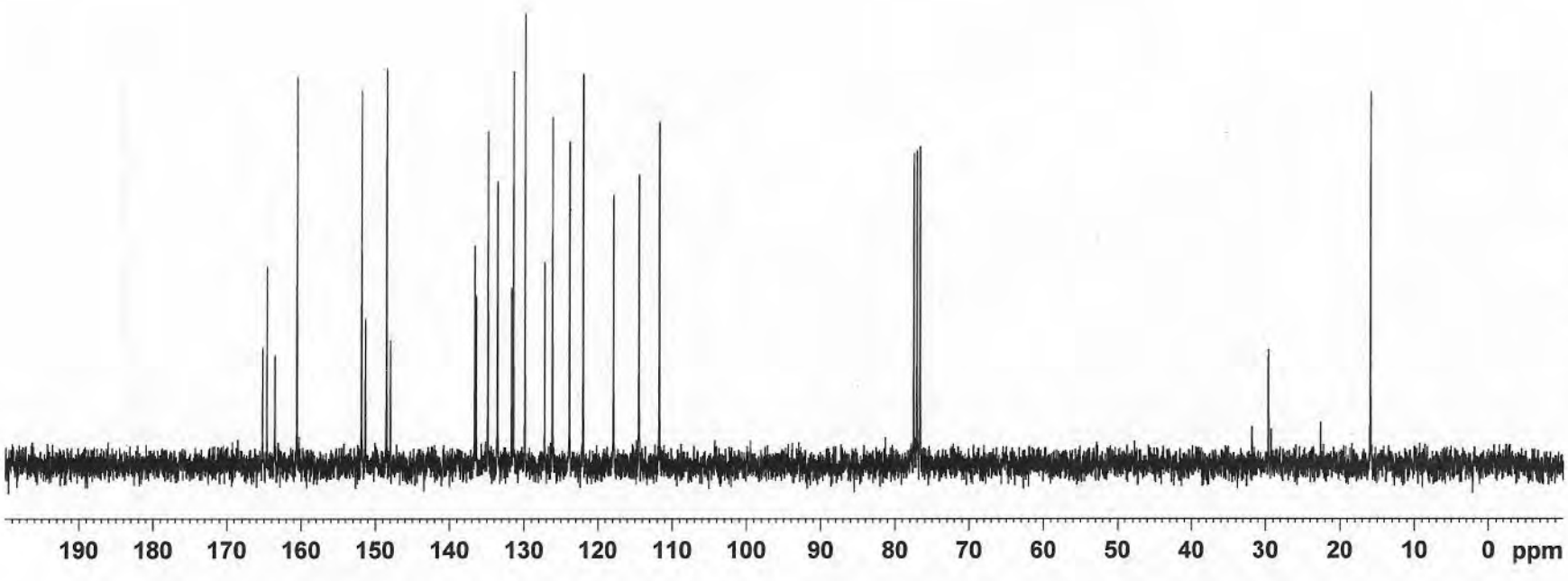
A9

SP121121-1 CDCl3 303K C13-NMR AV300

165.233
164.648
163.572
160.590
151.891
151.352
148.516
147.999
136.653
136.445
134.870
133.614
131.702
131.439
129.884
127.236
126.176
123.867
122.022
117.887
114.466
111.738

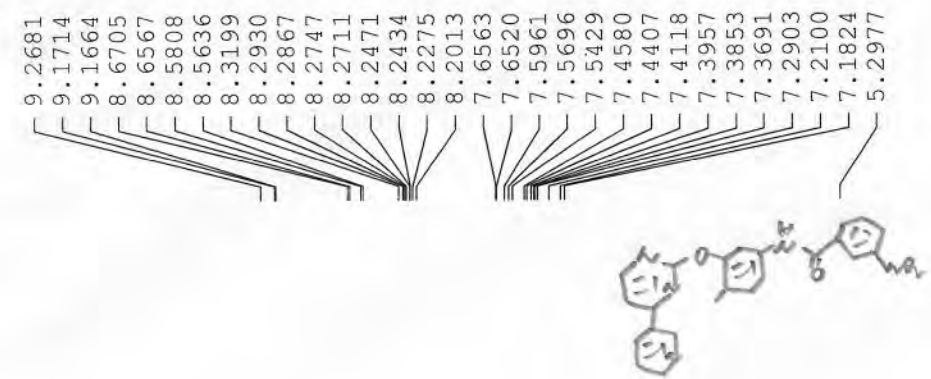
15.959

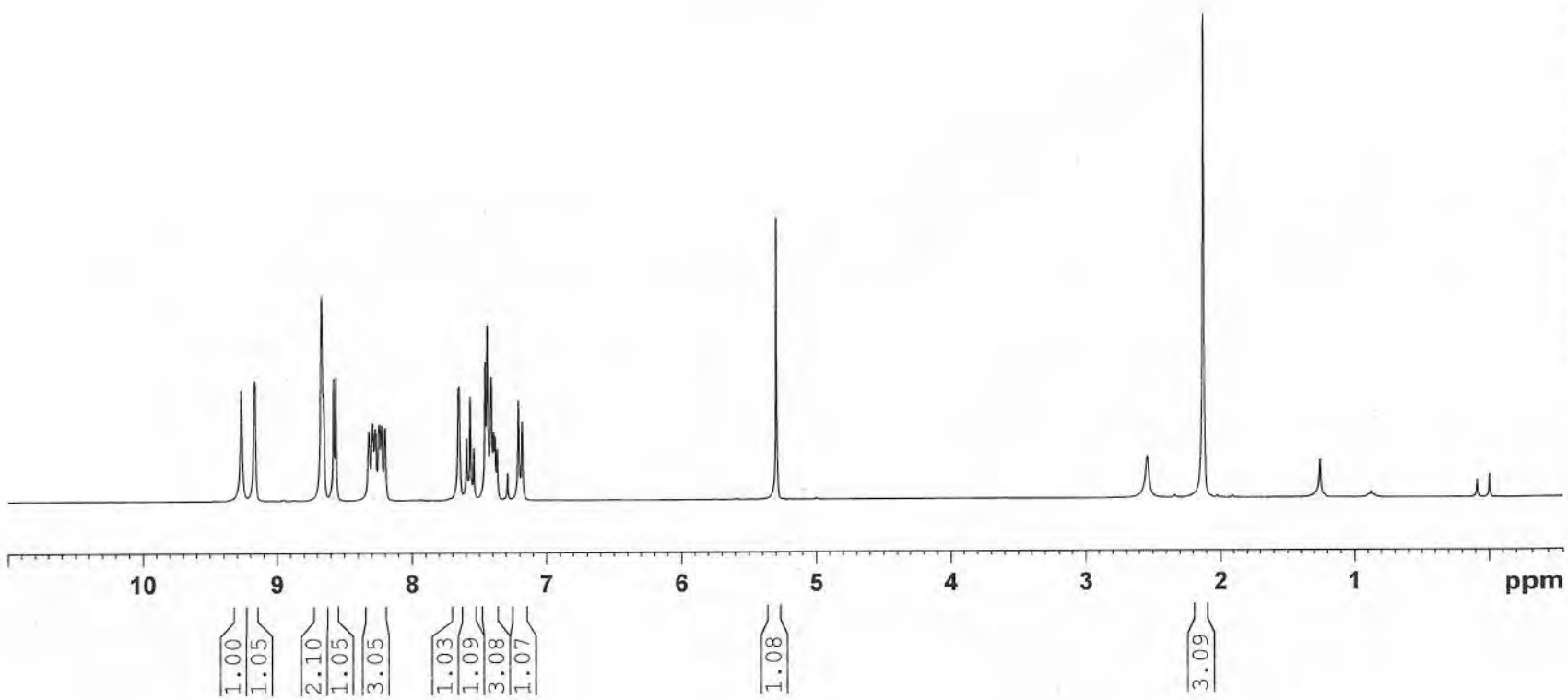




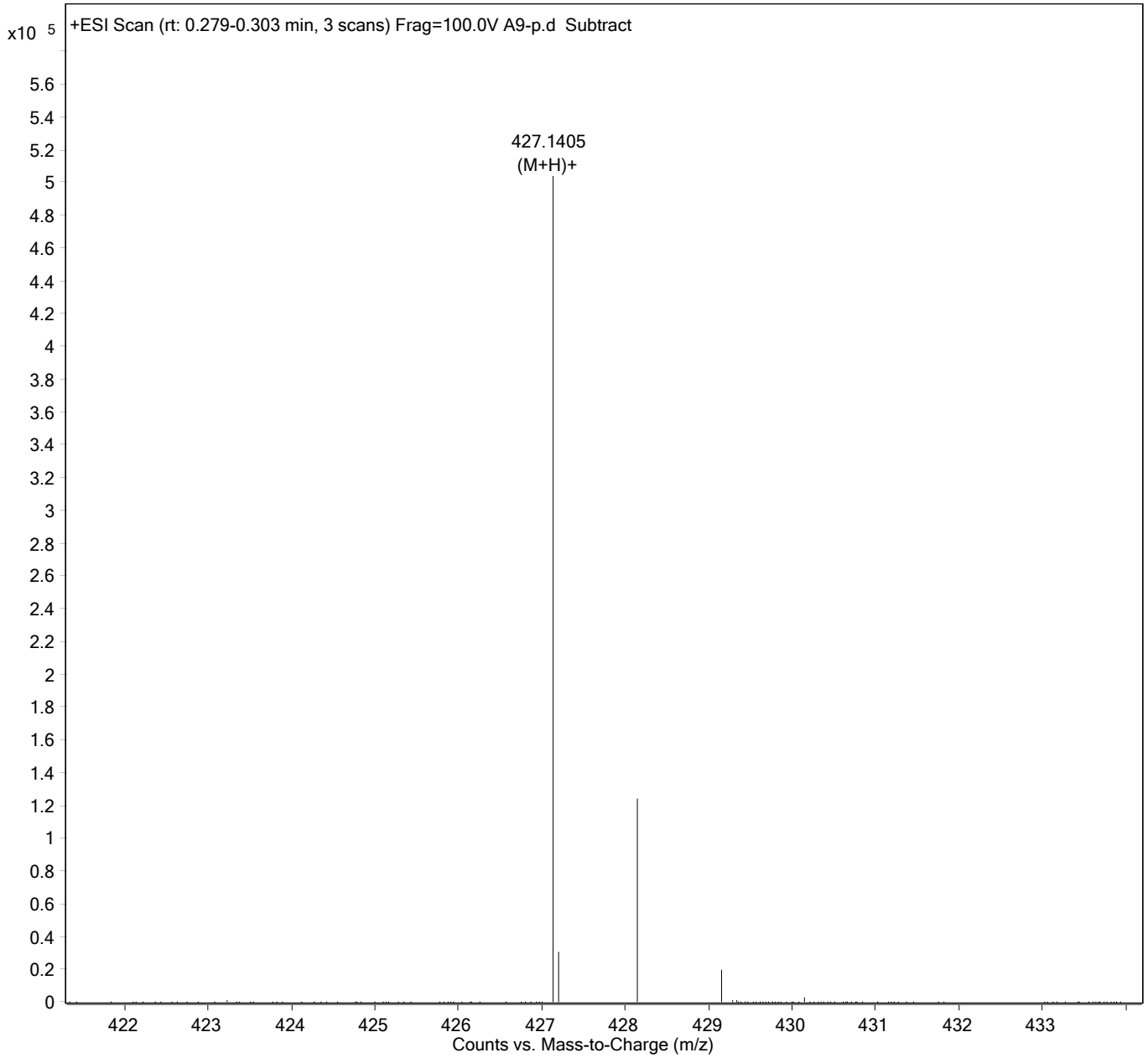
A 9

SP121109-2 1H-NMR CDCl3 303K AV-300



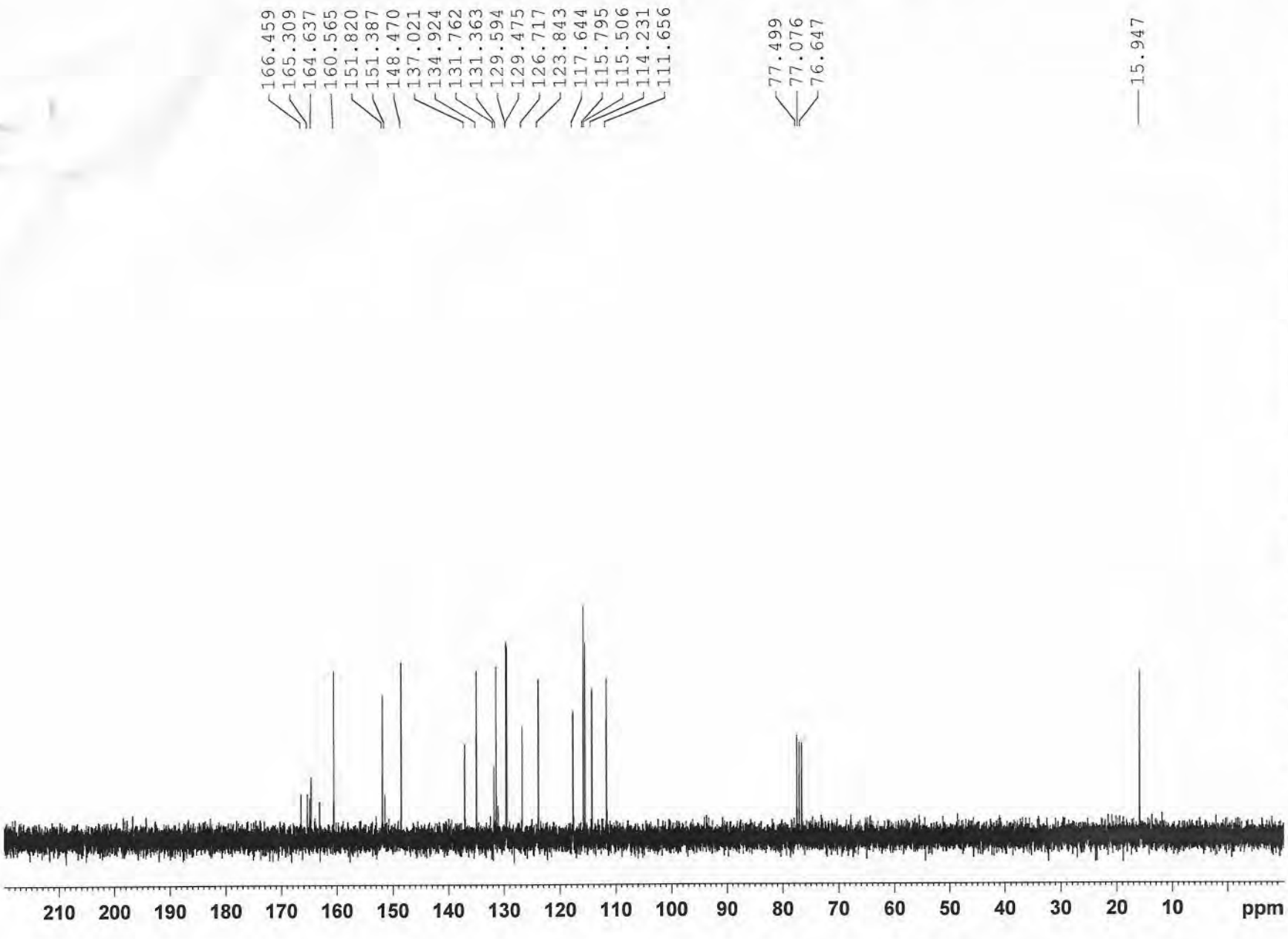


Sample Name		**Position**	p2E5	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A9-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:09:32 PM



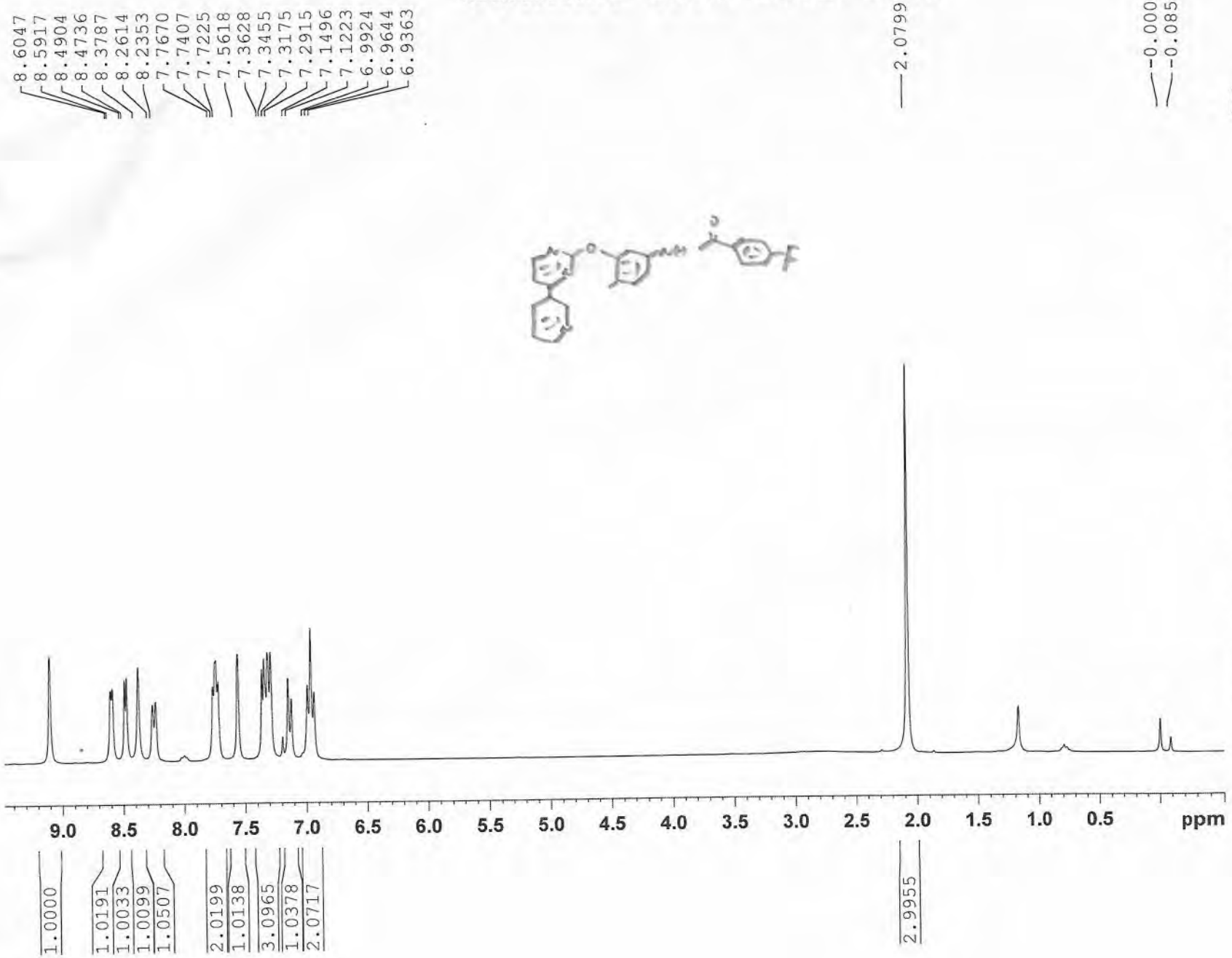
A 10

SP20131108-2-C C13-NMR CDCL3 303K AV-300

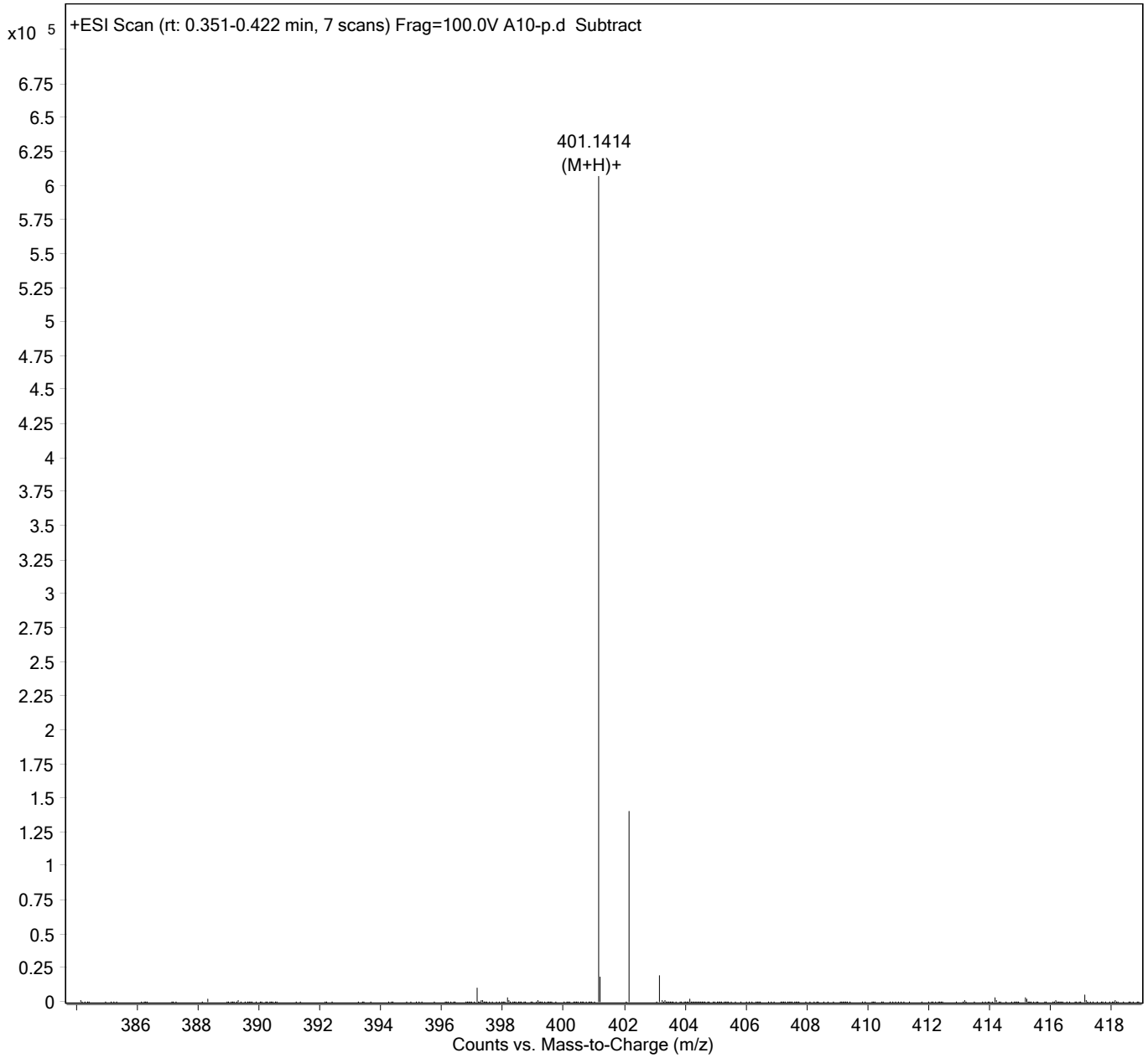


A 10

SP20131108-2 CDCL3 1HNMR AV300



Sample Name		**Position**	p2E6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A10-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:16:43 PM



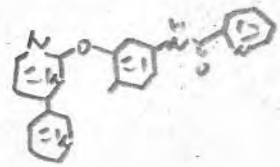
A11

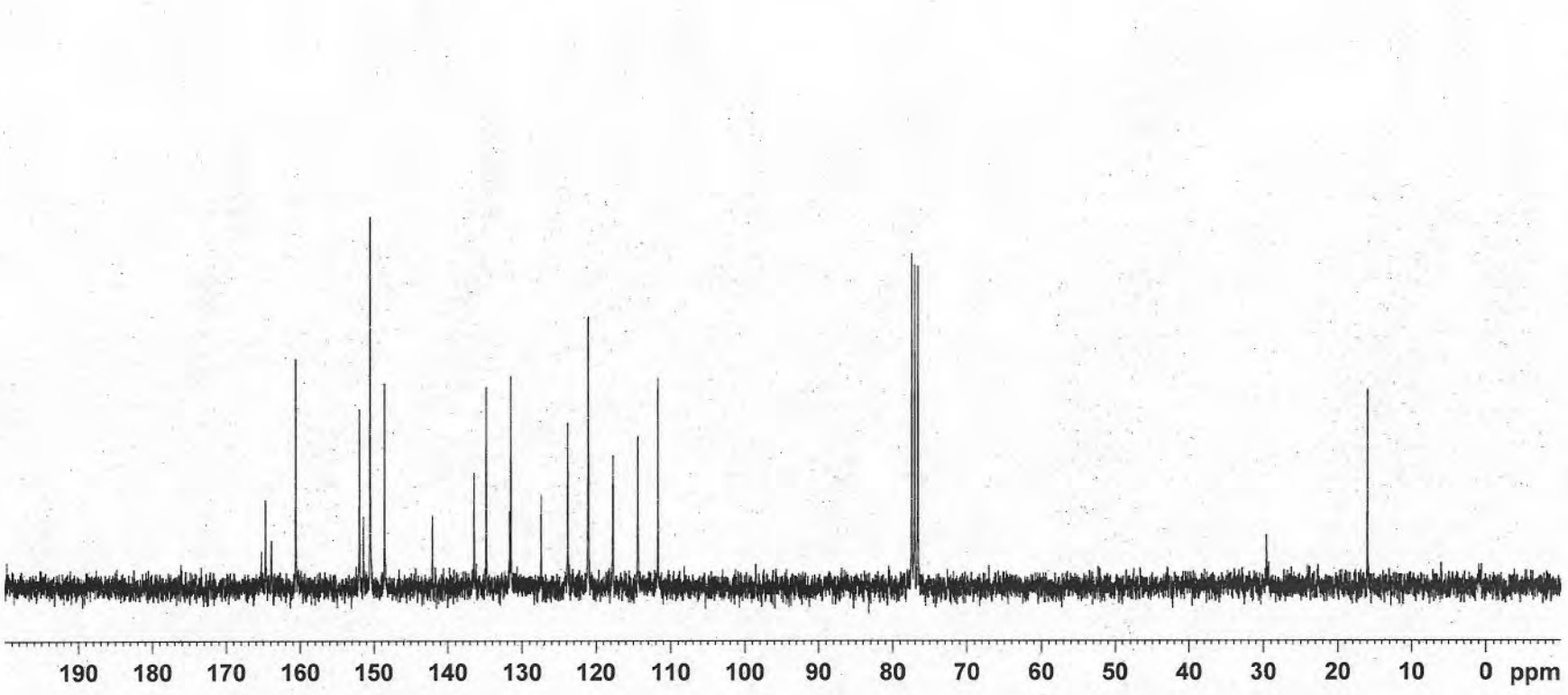
SP121205-2 CDCl3 303K C13-NMR AV300

165.267
164.714
163.896
160.617
151.964
151.435
150.518
148.575
142.092
136.467
134.833
131.691
131.512
127.423
123.836
121.050
117.715
114.374
111.726

77.484
77.060
76.636

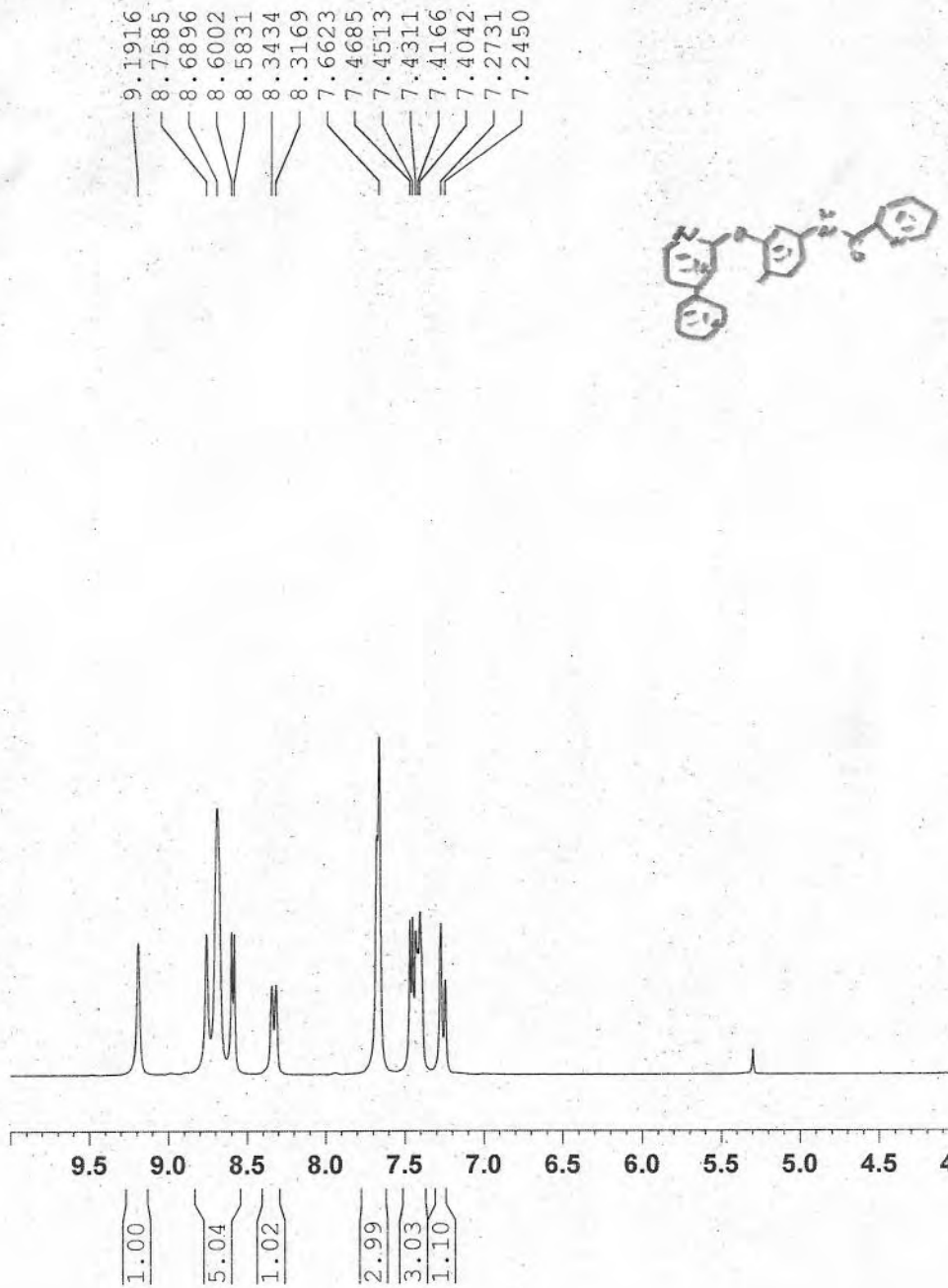
16.015



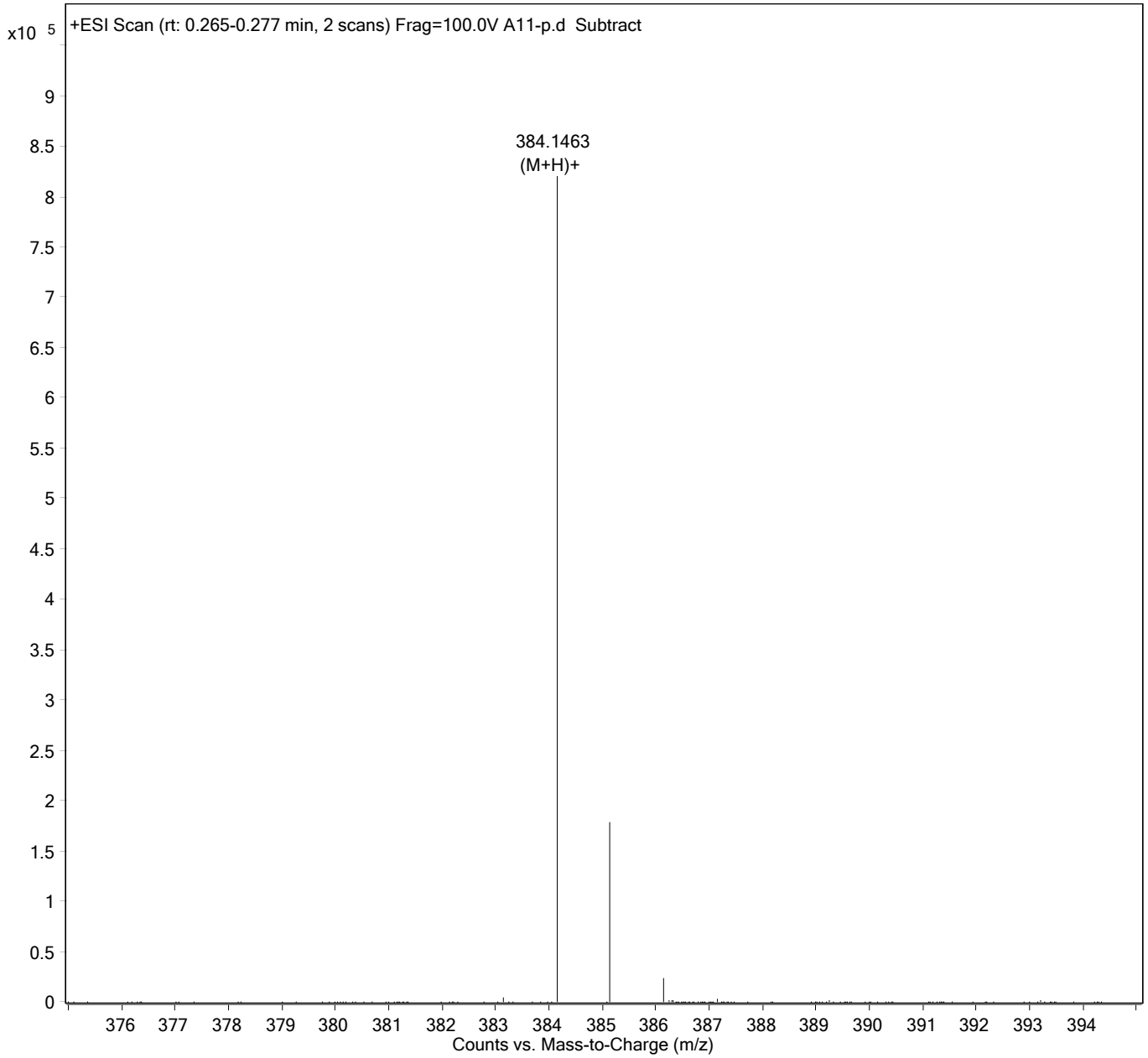


A11

SP121205-2 1H-NMR CDCl3 303K AV-300



Sample Name		**Position**	p2E7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A11-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:19:42 PM



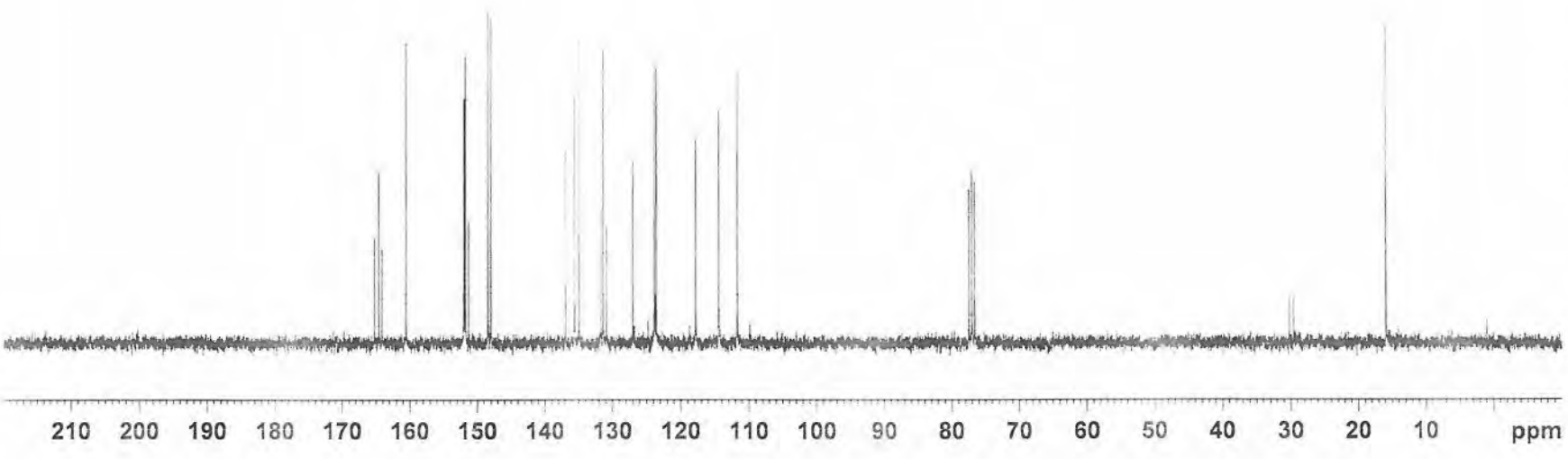
A12

SP130830-3-C C13-NMR CDCL3 303K AV-300

165.242
164.595
164.130
160.548
152.010
151.792
151.332
148.443
148.016
136.914
135.605
134.907
131.723
131.379
130.884
126.987
123.851
123.582
117.869
114.445
111.698

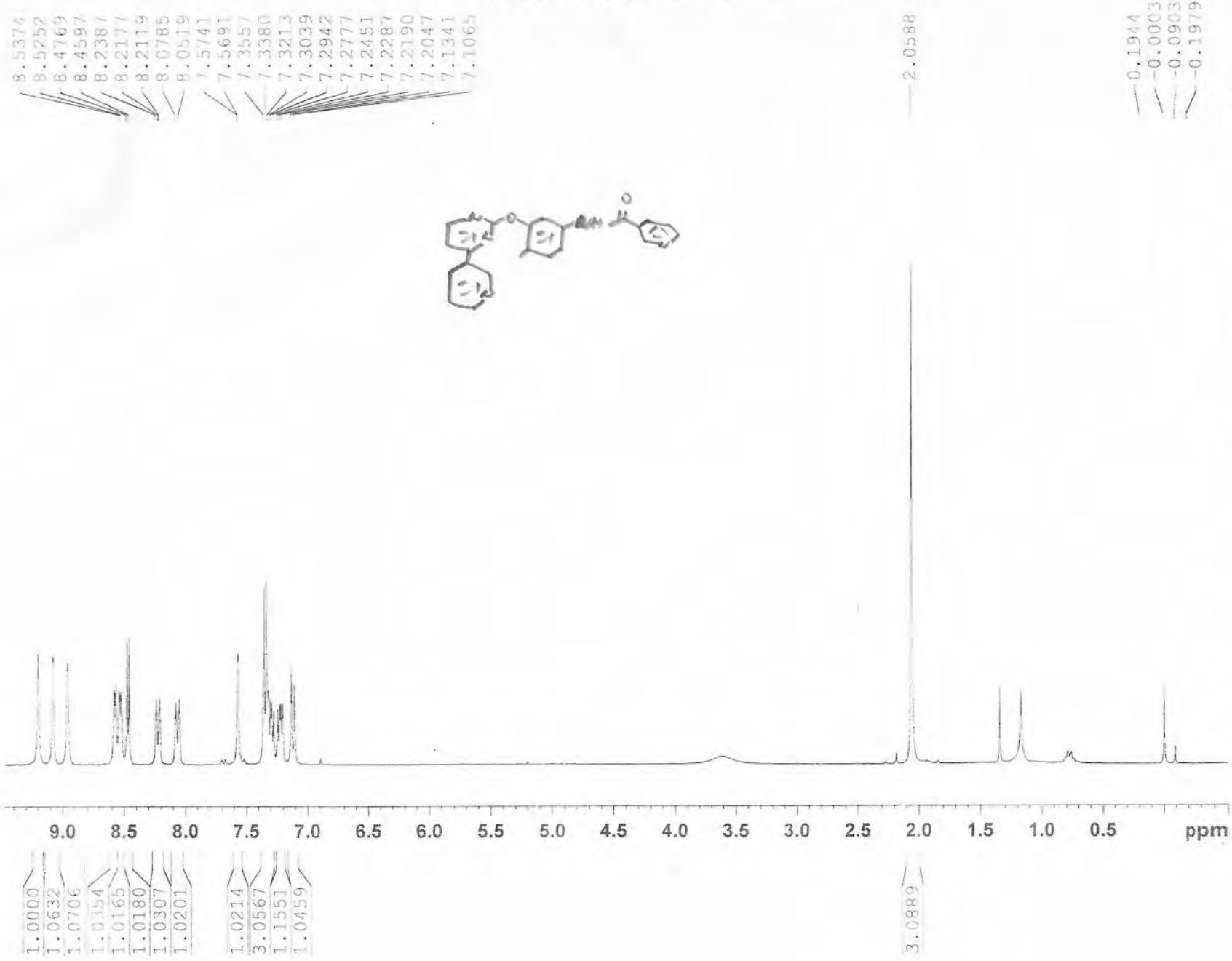
77.526
77.100
76.676

15.940



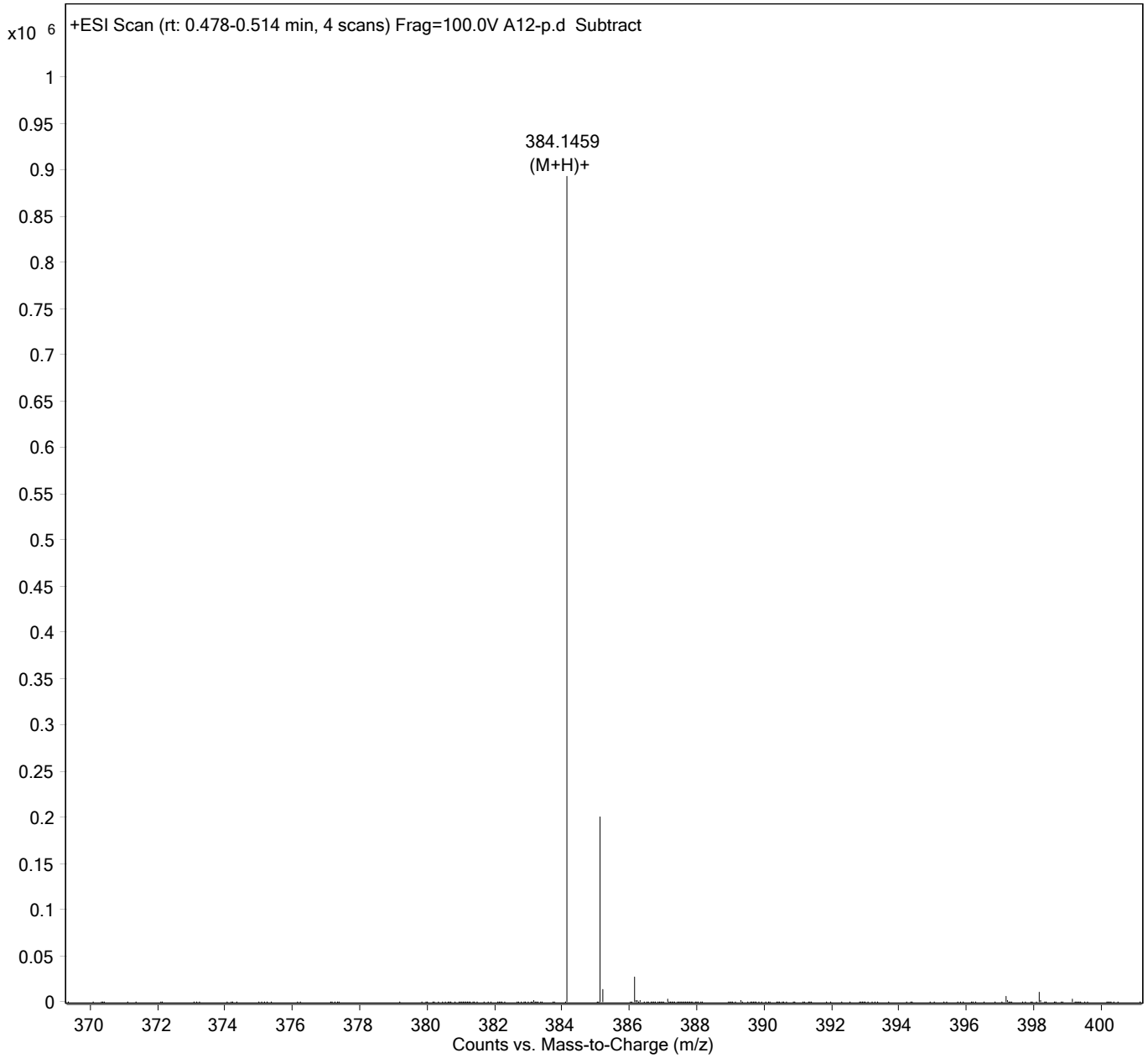
A12

SP20130830-3 CDCL3 1HNMR AV300



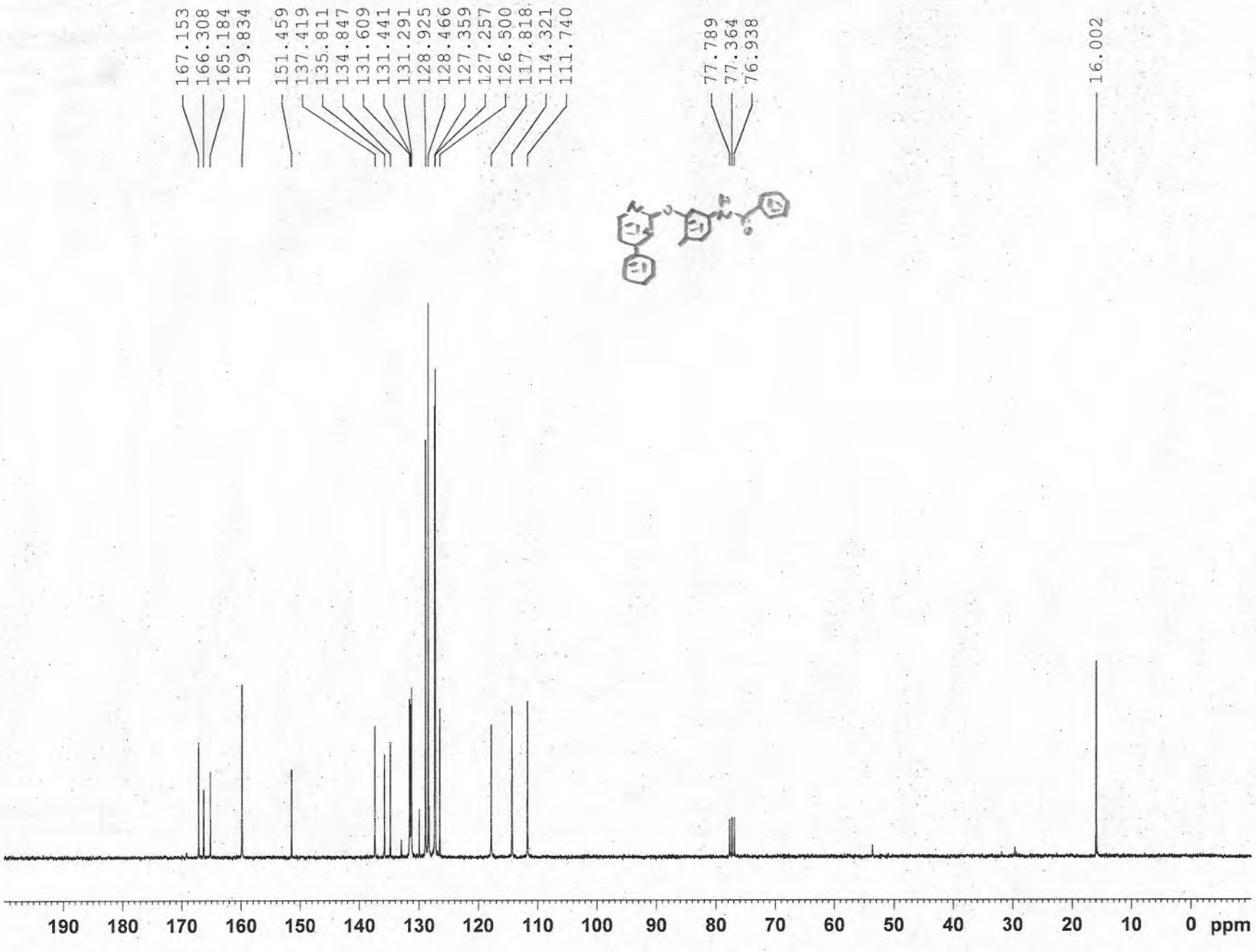
81

Sample Name		**Position**	p2E8	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	A12-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:24:41 PM



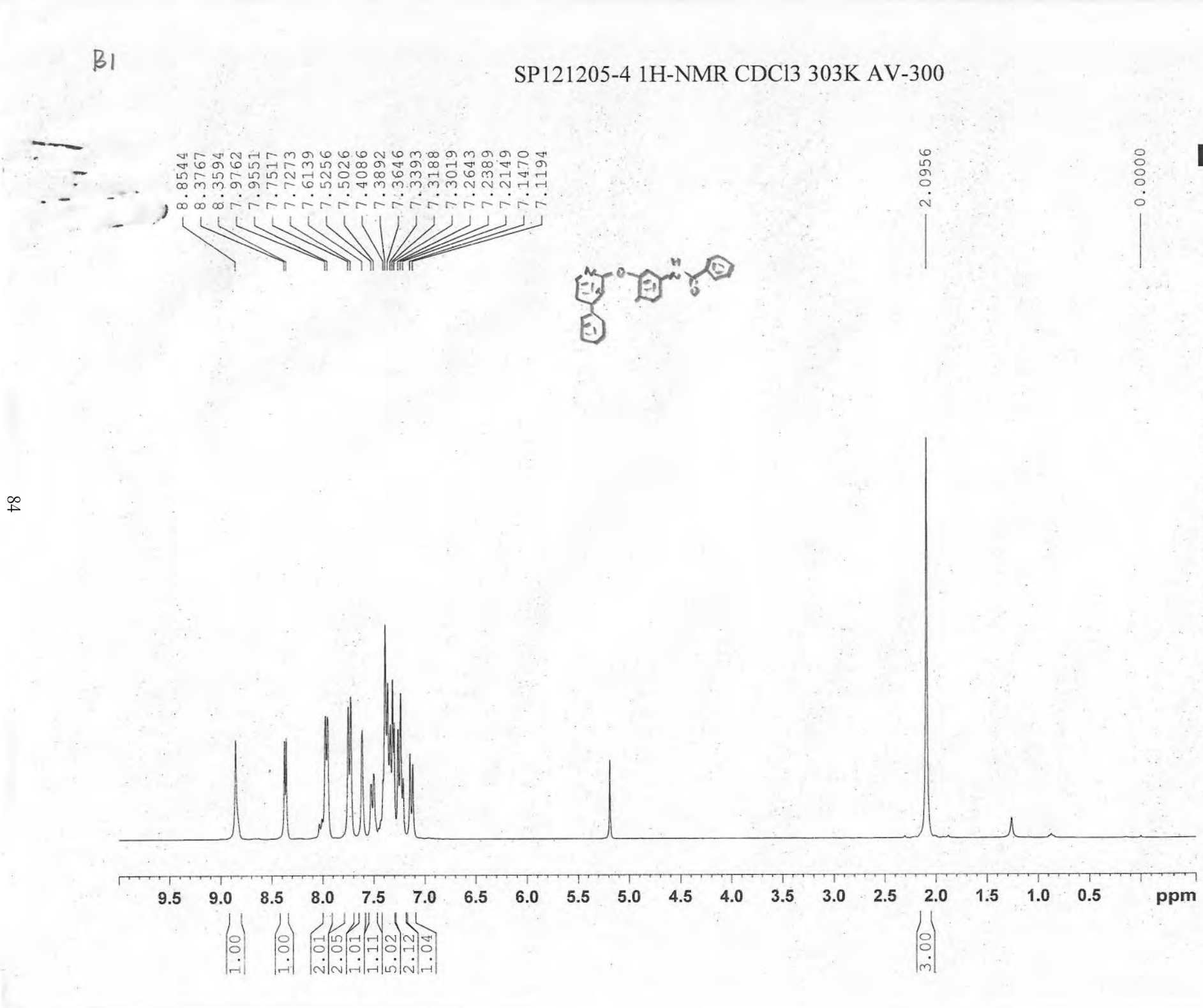
B1

SP121205-4 CDCl3 303K C13-NMR AV300

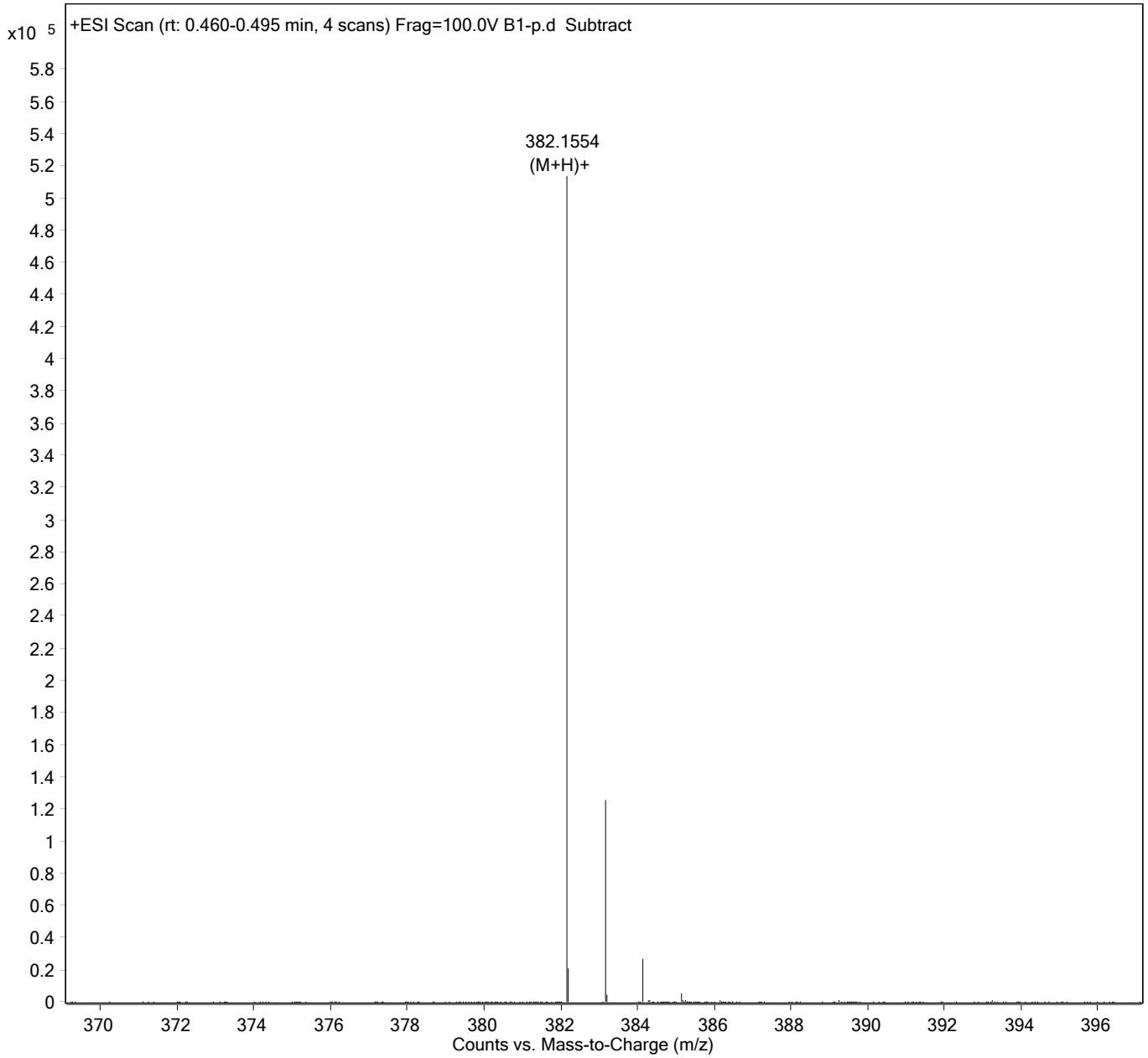


B1

SP121205-4 1H-NMR CDCl3 303K AV-300



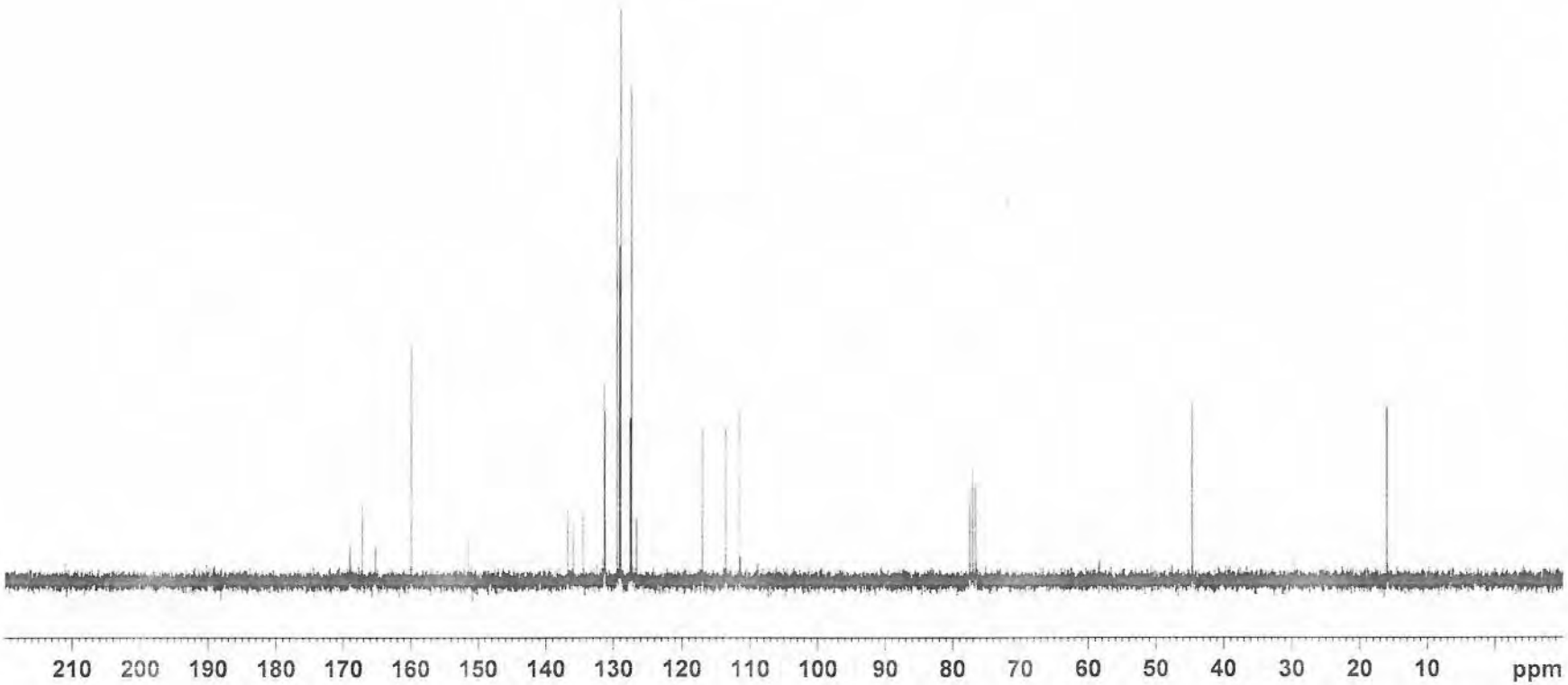
Sample Name		**Position**	p2E9	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:27:08 PM



B2

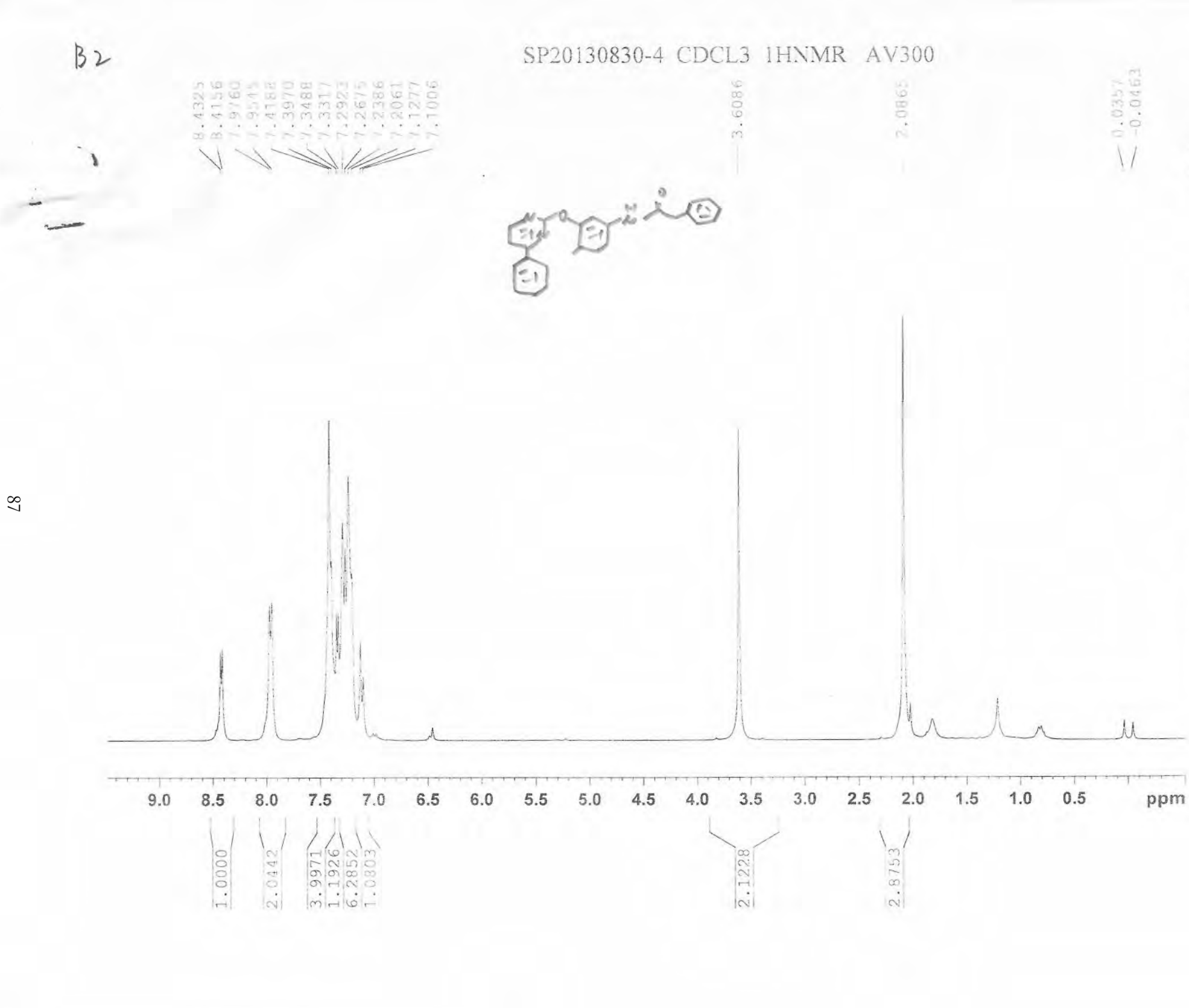
SP130830-4-C C13-NMR CDCL3 303K AV-300

169.024
167.187
165.251
159.942
151.497
136.780
135.951
134.457
131.374
131.238
129.474
129.116
128.921
127.542
127.345
126.621
117.025
113.620
111.611
111.387
77.504
77.079
76.656
44.680
15.953

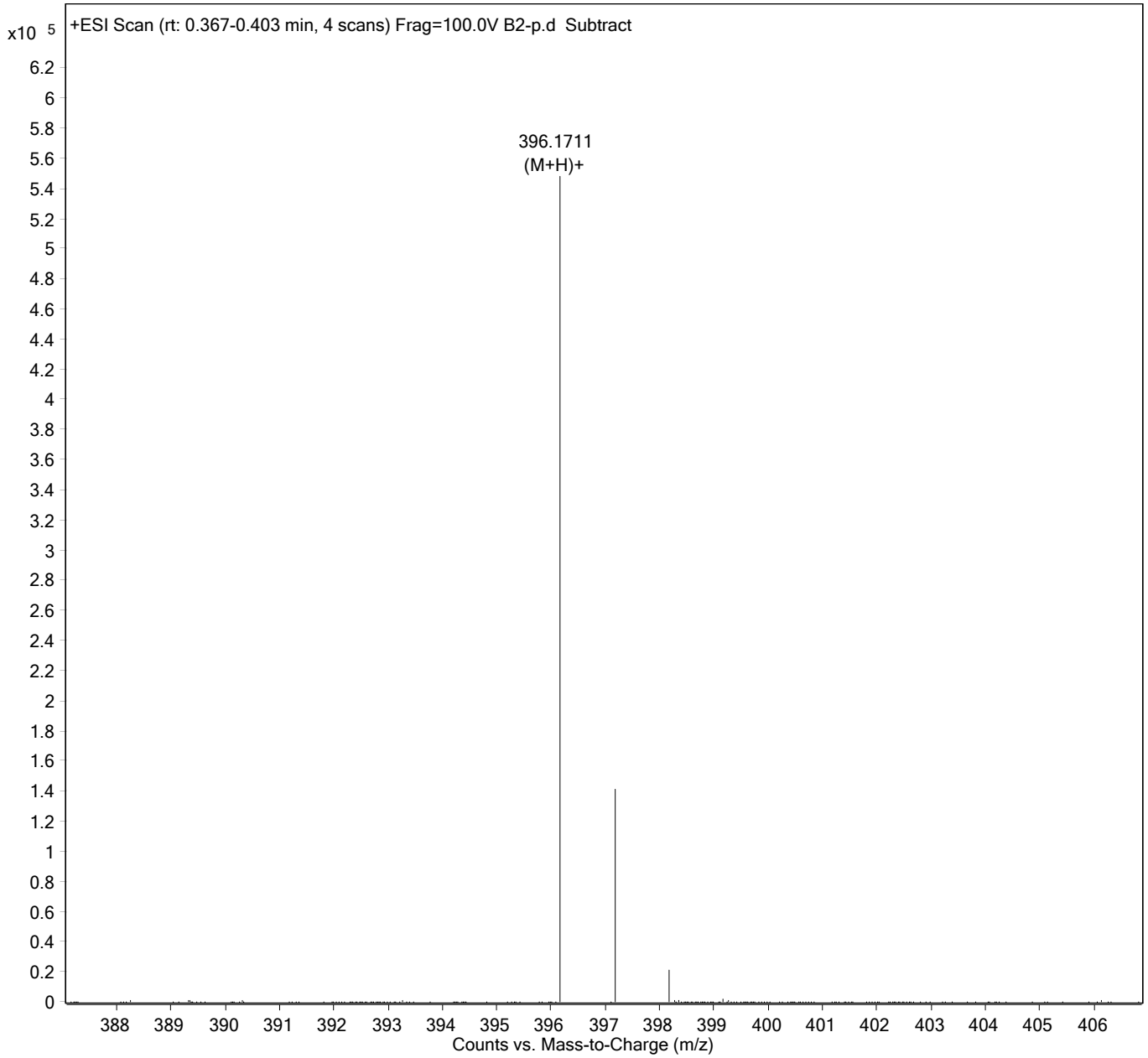


B2

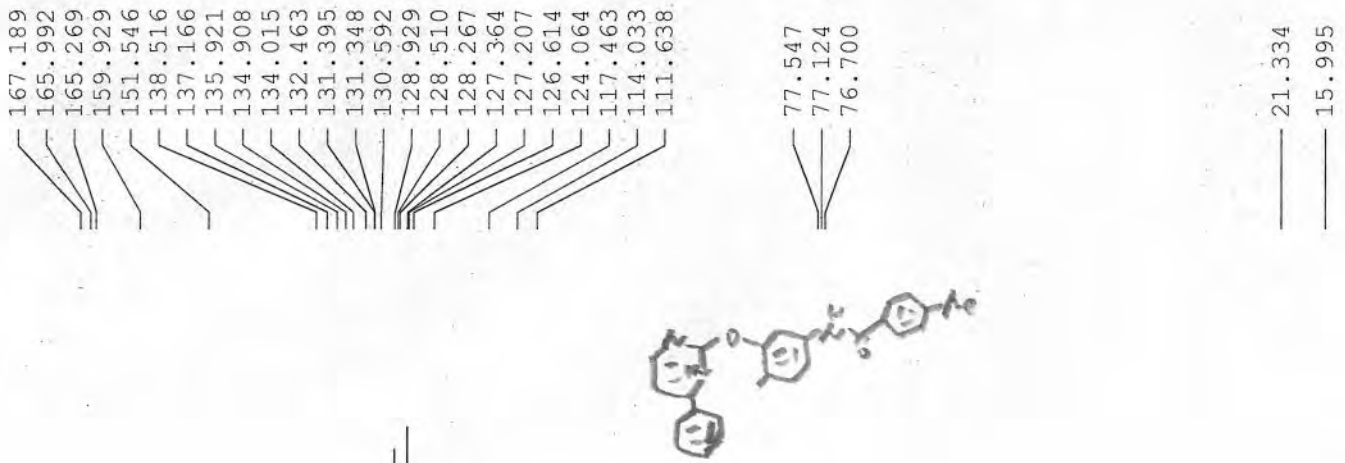
SP20130830-4 CDCL3 1HNMR AV300

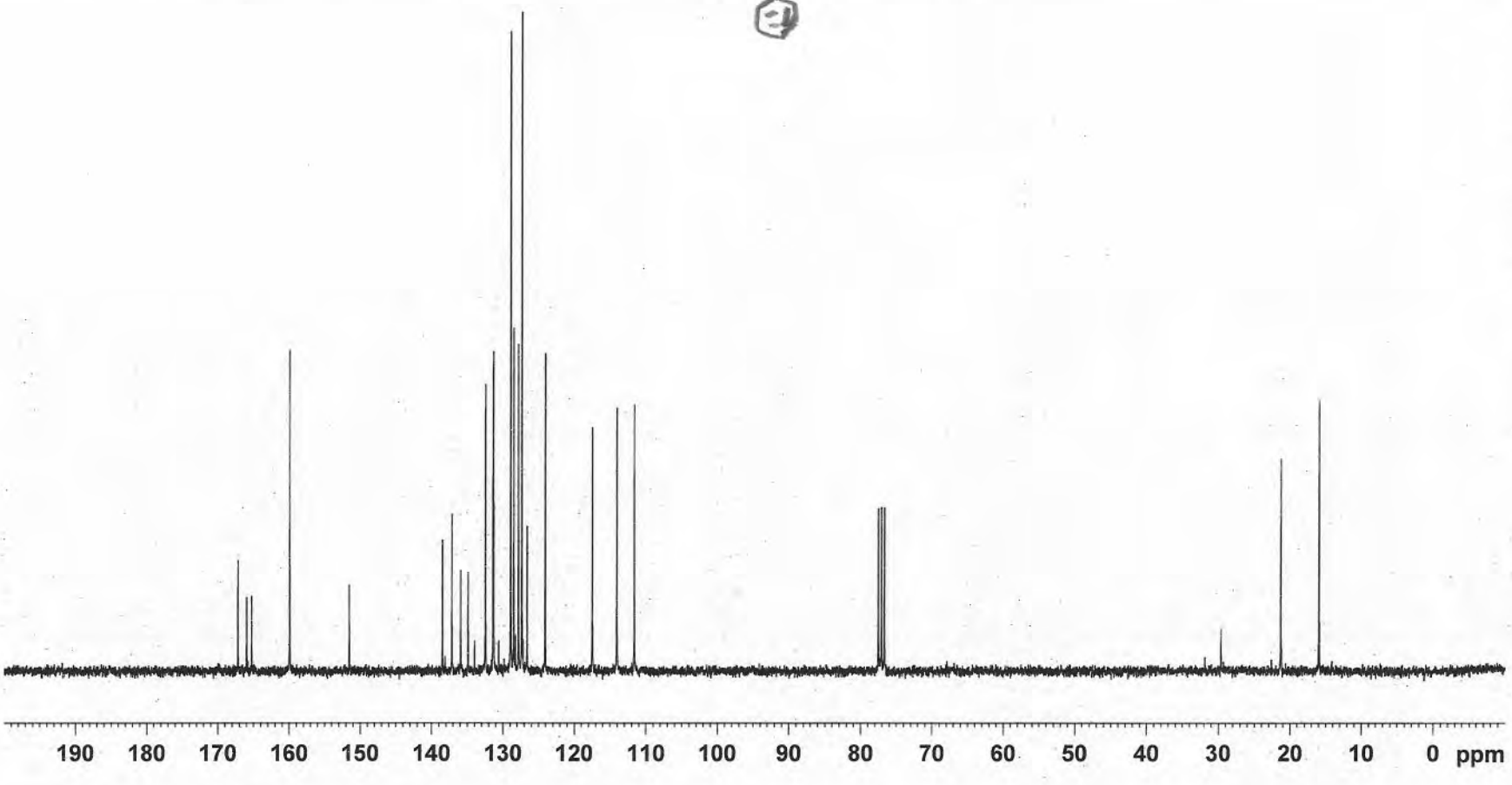


Sample Name		**Position**	p2F1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:29:48 PM



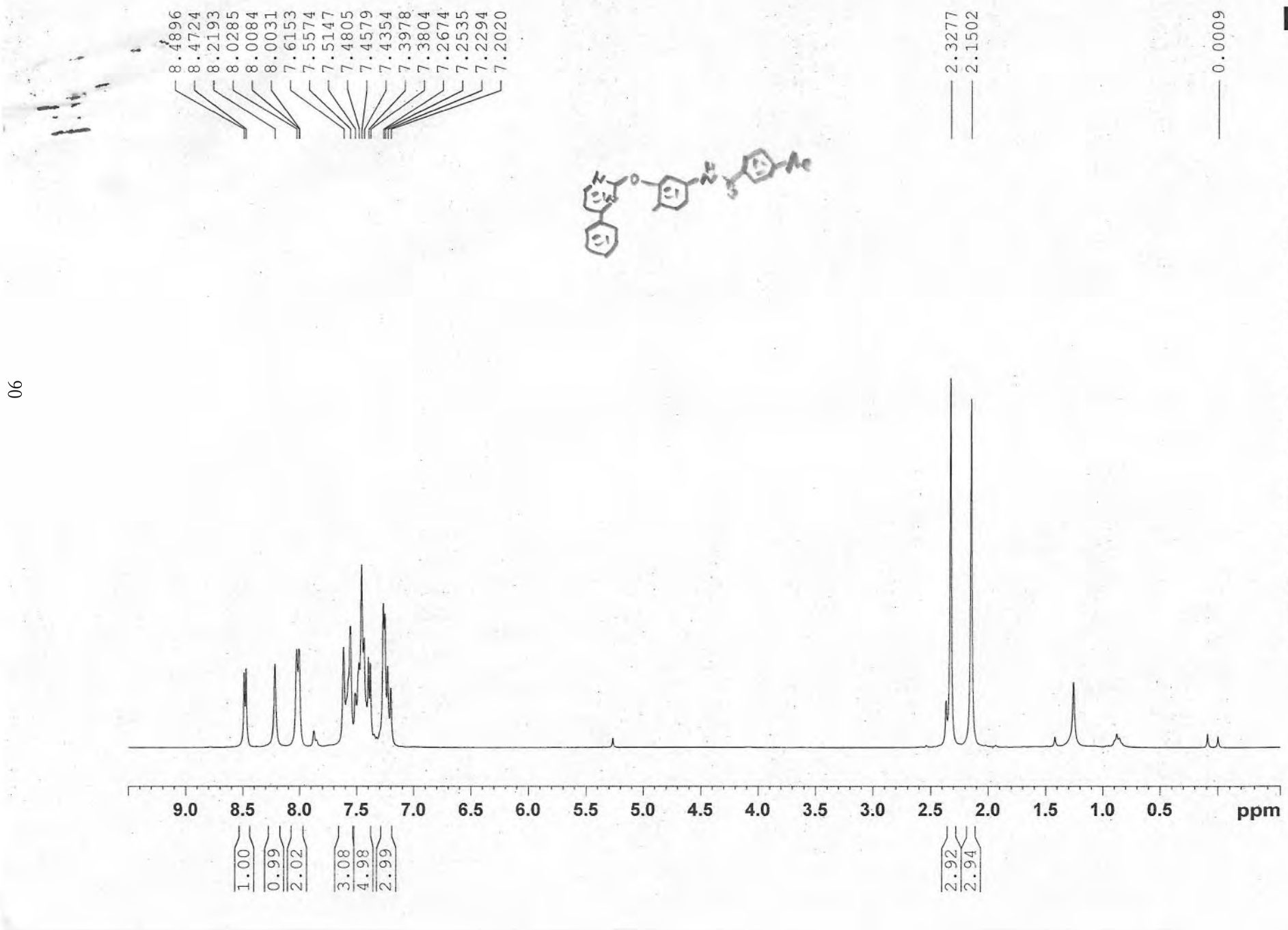
SP121128-3 CDCl3 303K C13-NMR AV300



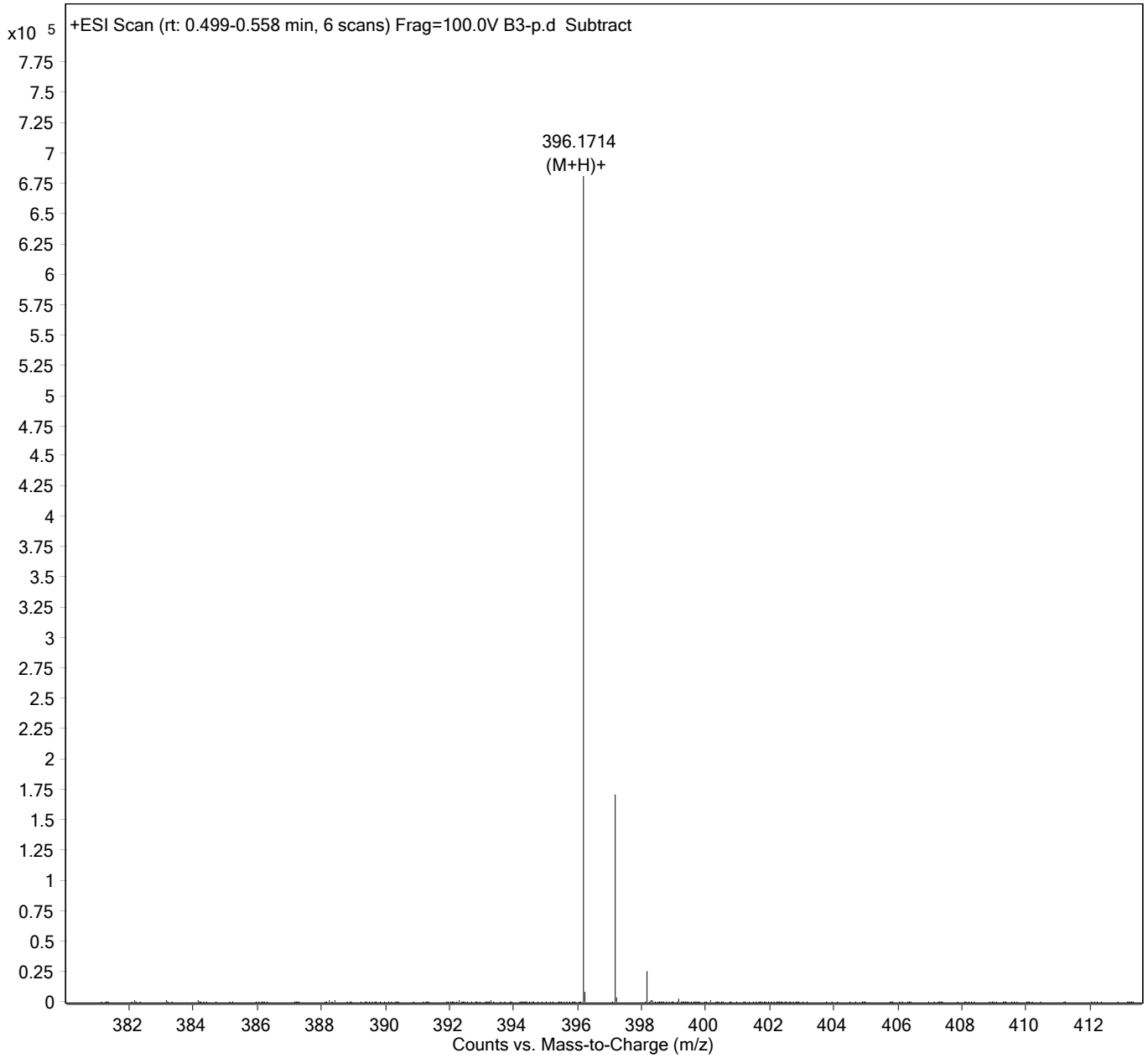


B 3

SP121128-3 1HNMR CDCl3 303K AV-300



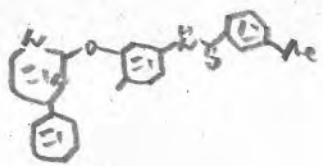
Sample Name		**Position**	p2F2	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:32:10 PM

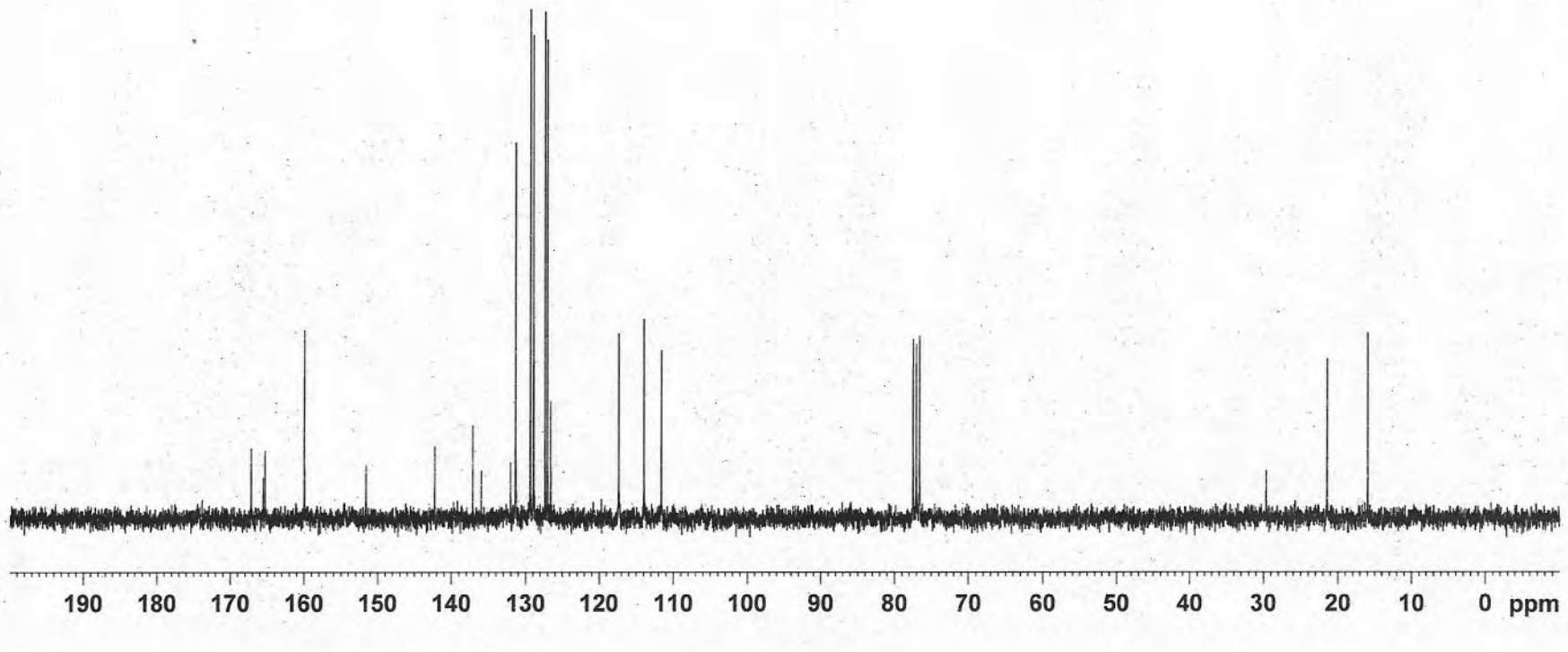


B4

SP121202-2 CDCl3 303K C13-NMR AV300

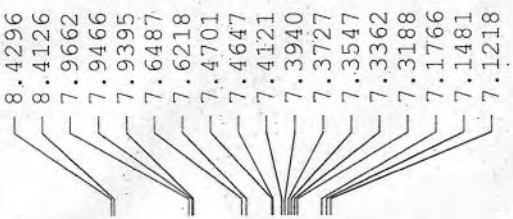
167.192
165.316
159.977
151.585
142.274
137.135
135.964
131.374
128.936
127.054
117.351
113.941
111.630
77.501
77.076
76.653
21.483
16.015

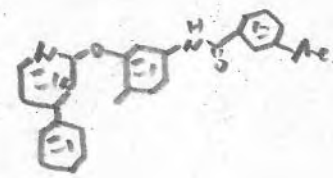


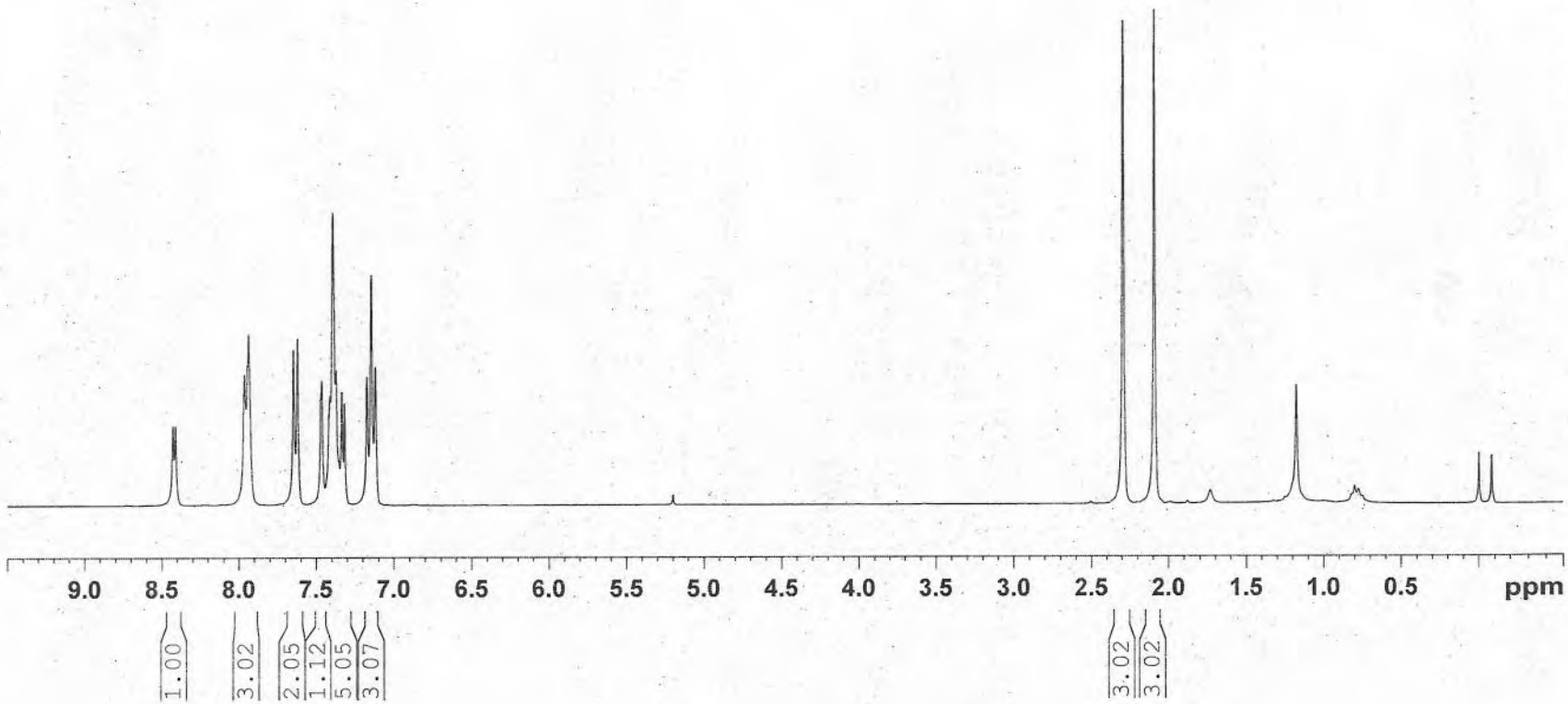


B4

SP121202-2 1HNMR CDCL3 303K AV-300

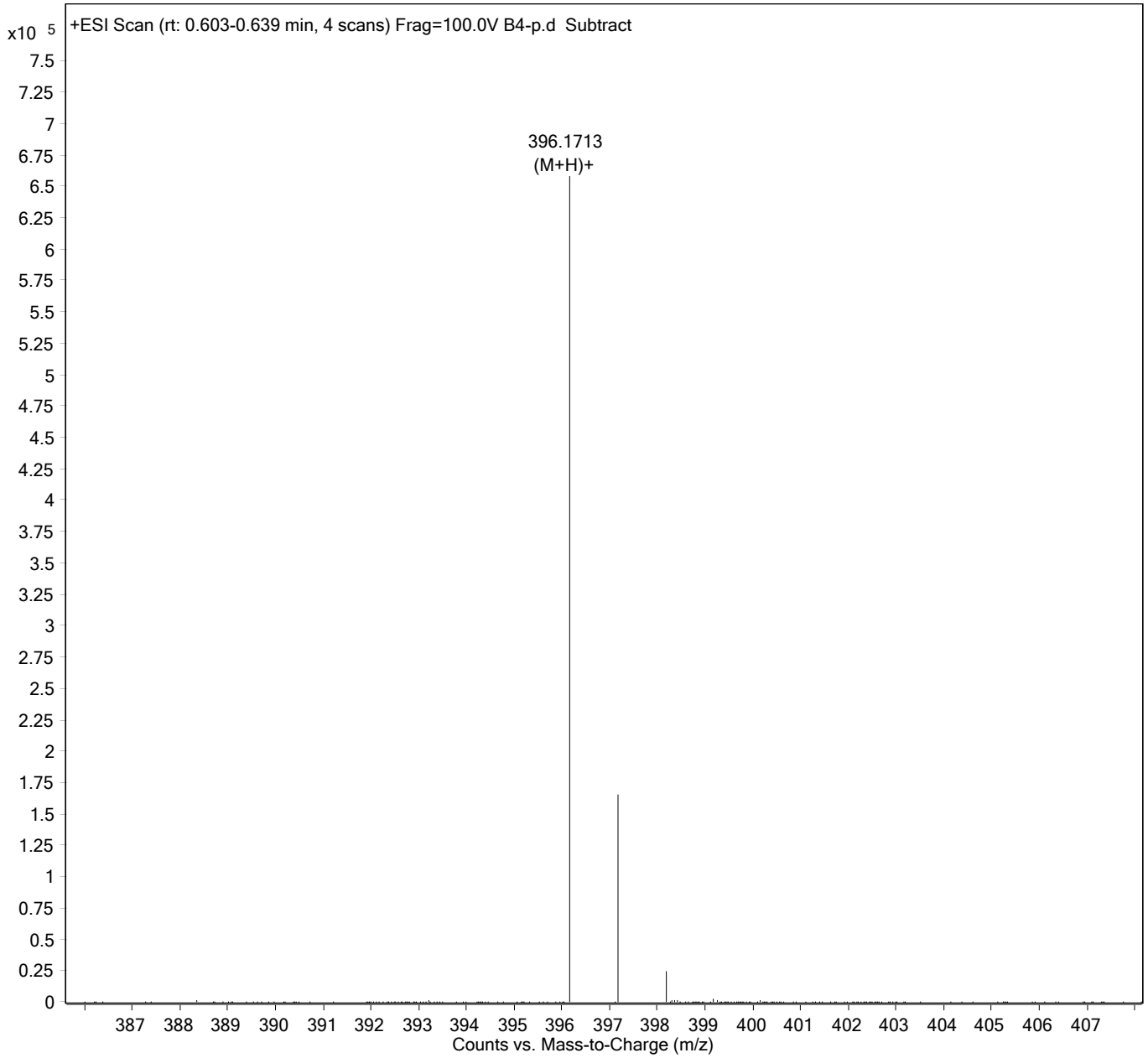






93

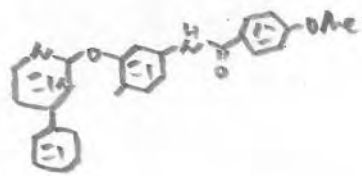
Sample Name		**Position**	p2F3	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B4-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:34:31 PM

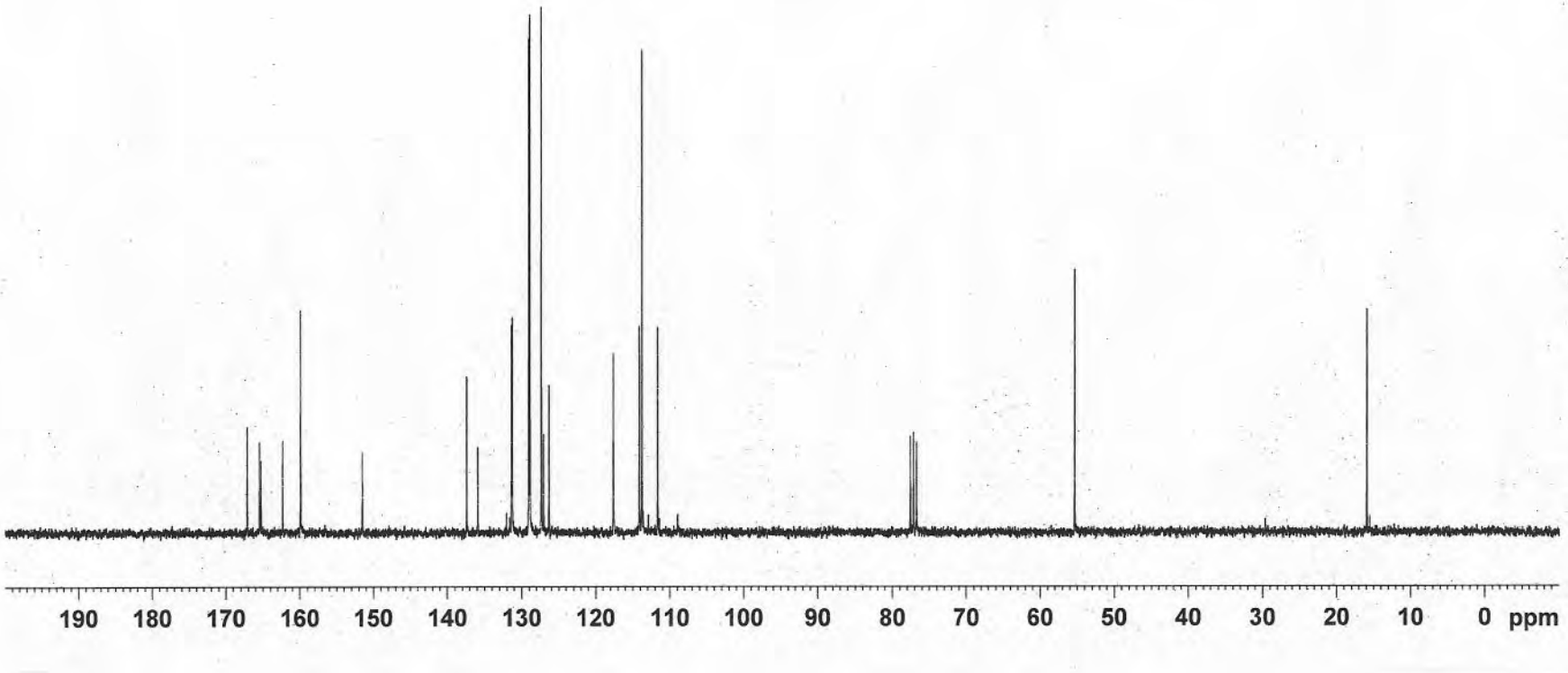


B5

SP121212-2 CDCl3 303K C13-NMR AV300

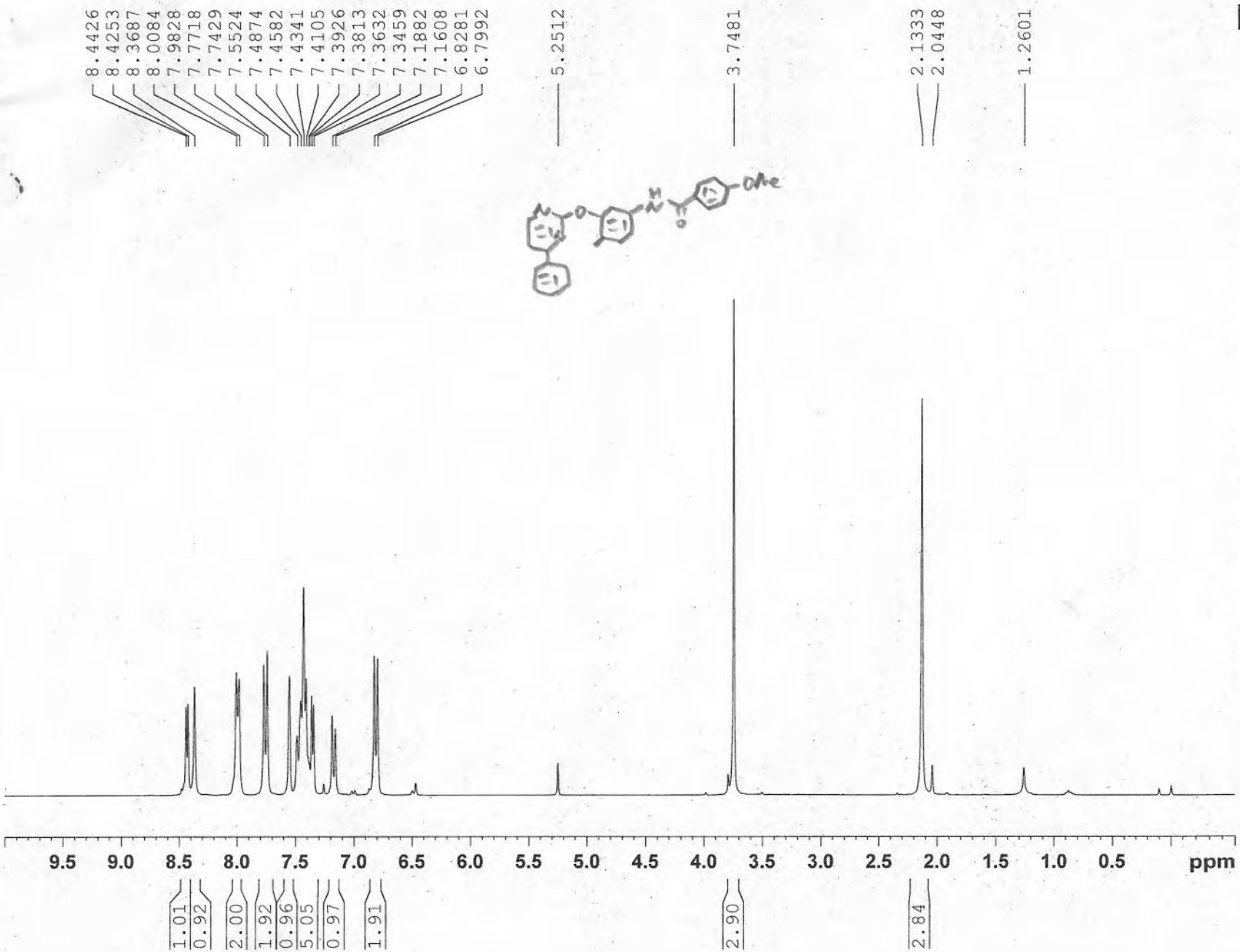
167.147
165.468
165.262
159.892
151.500
137.418
135.895
131.384
131.275
129.056
128.914
127.347
127.042
126.324
117.597
114.118
113.760
111.655
77.606
77.180
76.756
55.374
15.978



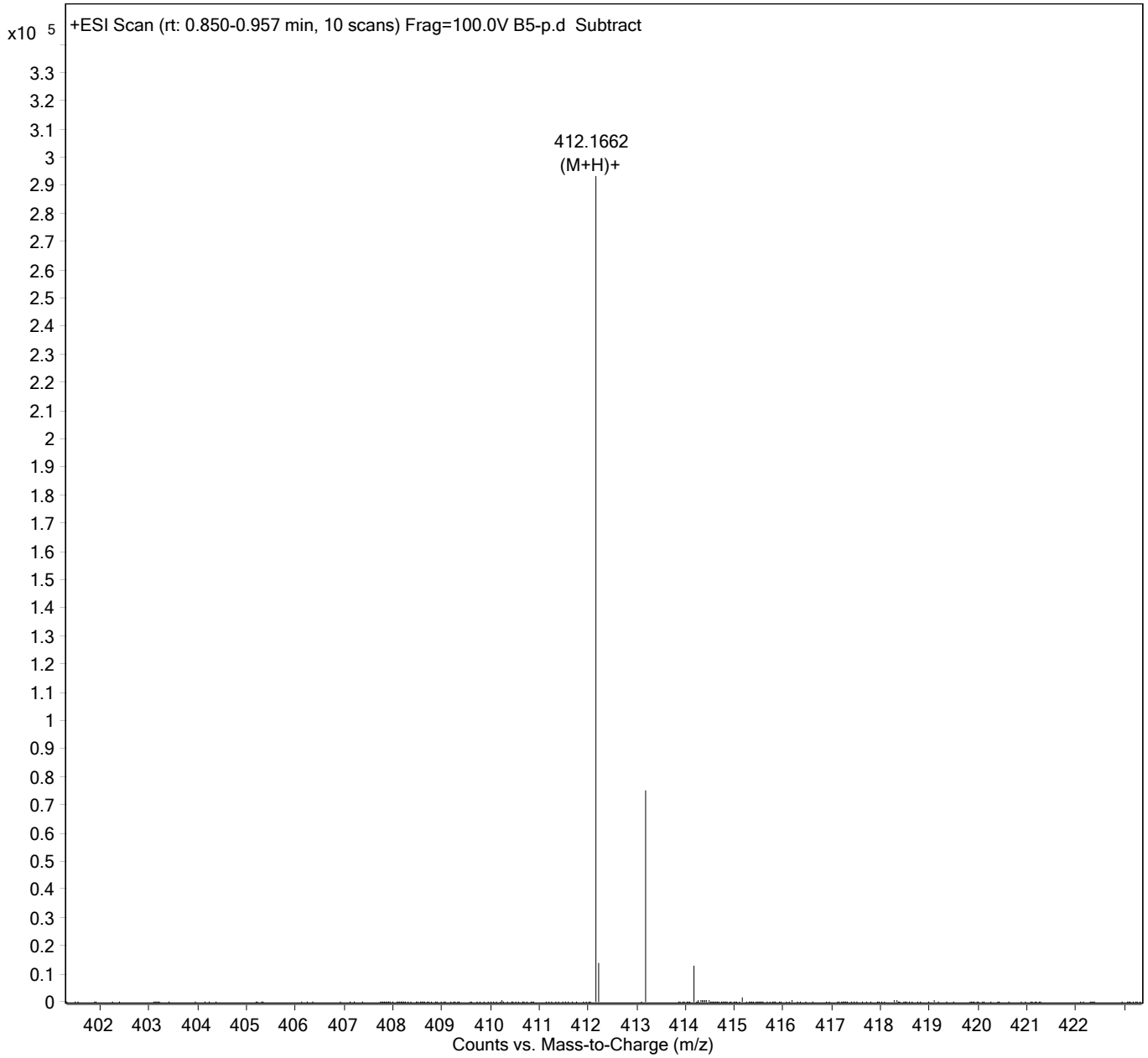


B5.

SP121212-2 1H-NMR CDCl3 303K AV-300



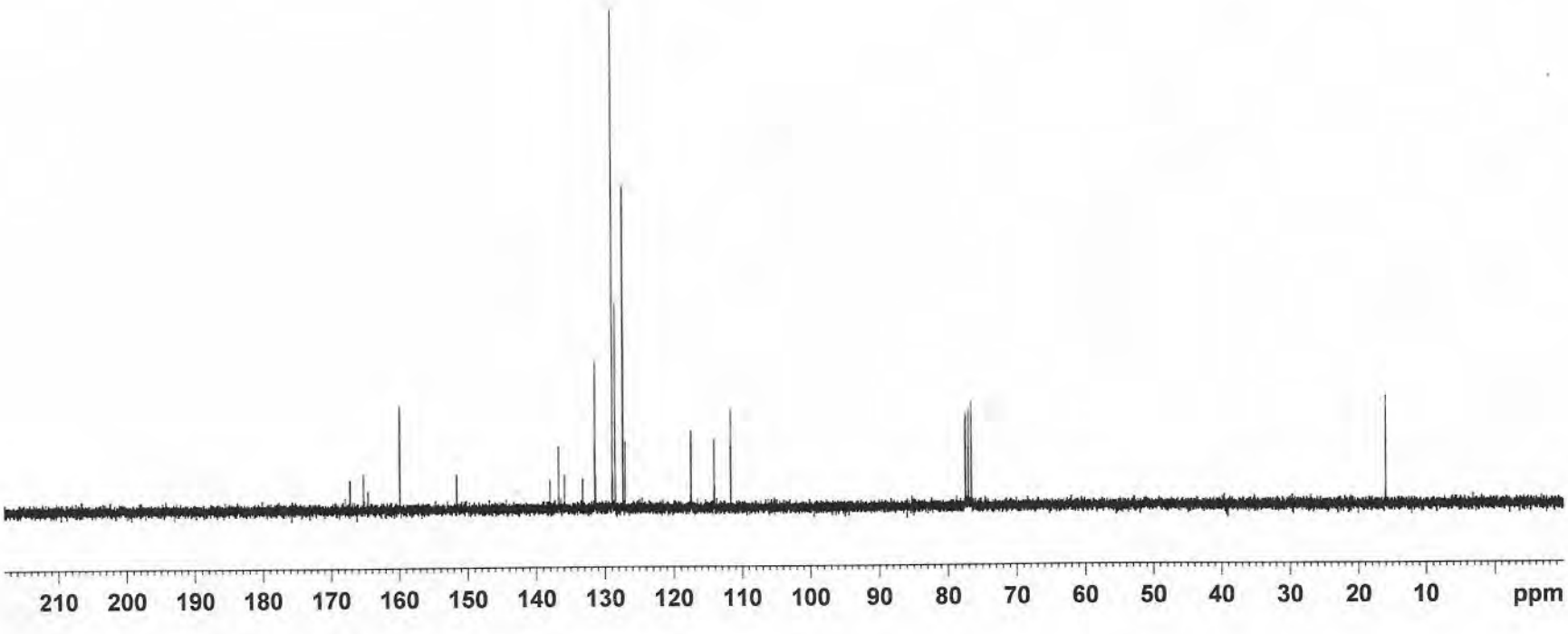
Sample Name		**Position**	p2F4	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B5-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:36:31 PM



SP140506-1-C C13-NMR CDCL3 303K AV-300

167.240
165.250
164.611
159.926
151.602
138.021
136.755
135.909
133.271
131.431
128.930
128.507
127.349
127.040
117.476
114.107
111.672
77.460
77.037
76.612
16.002

B6



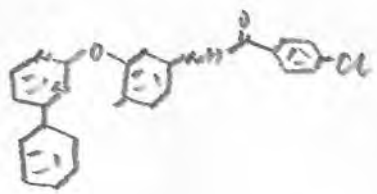
B6

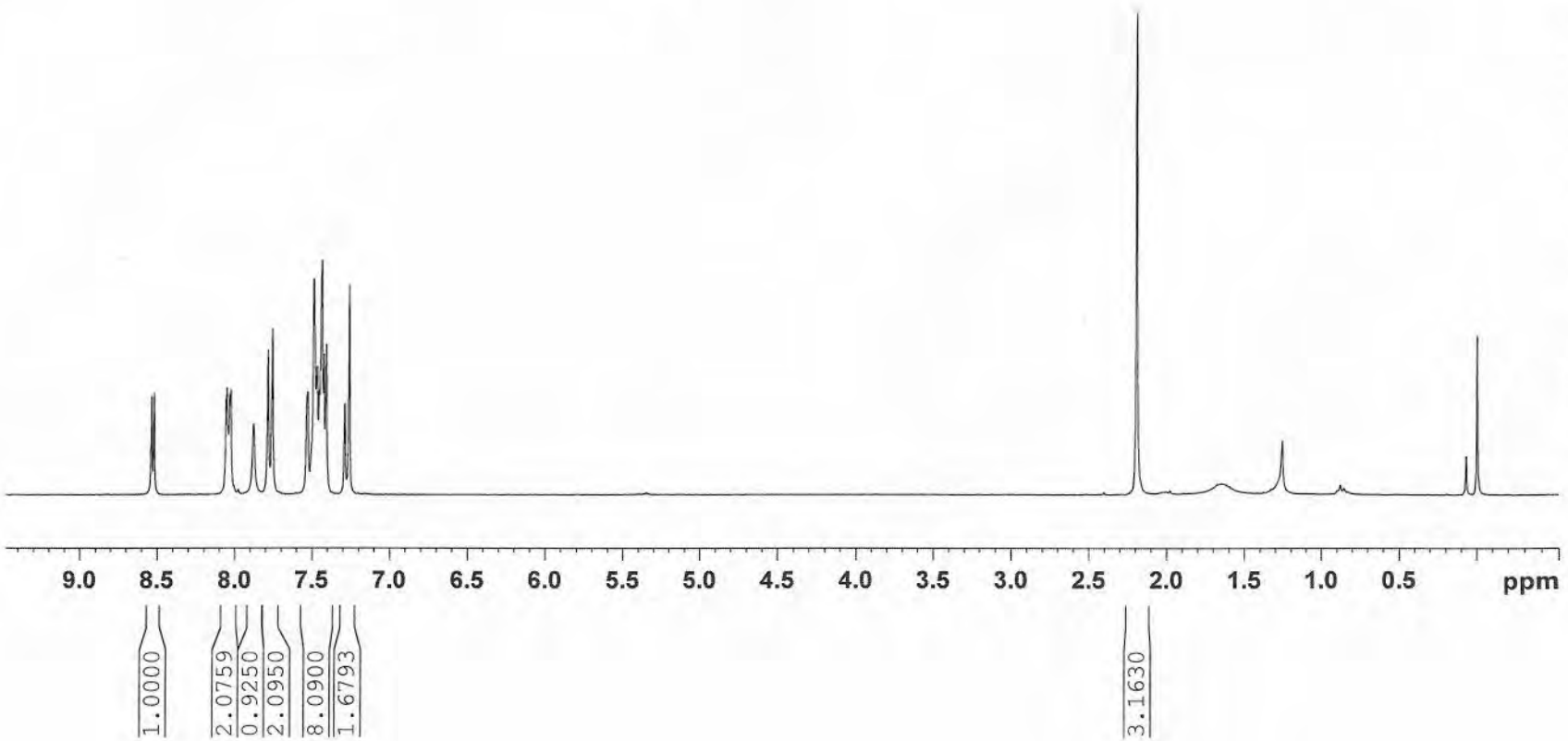
SP20131108-4 CDCL3 1HNMR AV300

8.5394
8.5220
8.0584
8.0535
8.0342
8.0272
7.8795
7.7867
7.7584
7.5296
7.4900
7.4671
7.4548
7.4404
7.4373
7.4238
7.4085
7.2895
7.2603

2.1945

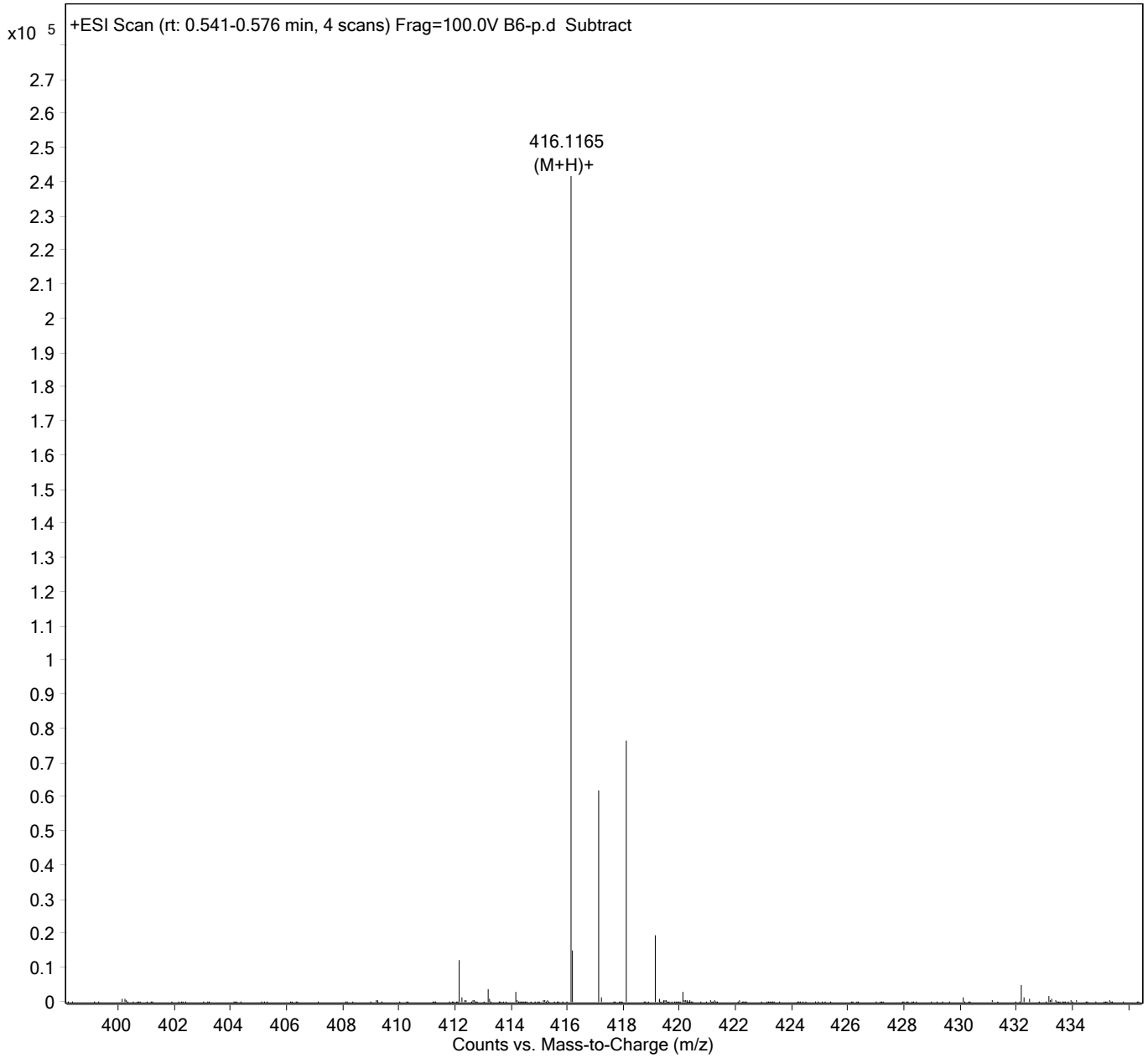
0.0718
-0.0003





99

Sample Name		**Position**	p2F5	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B6-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:39:16 PM



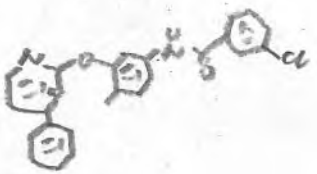
B7

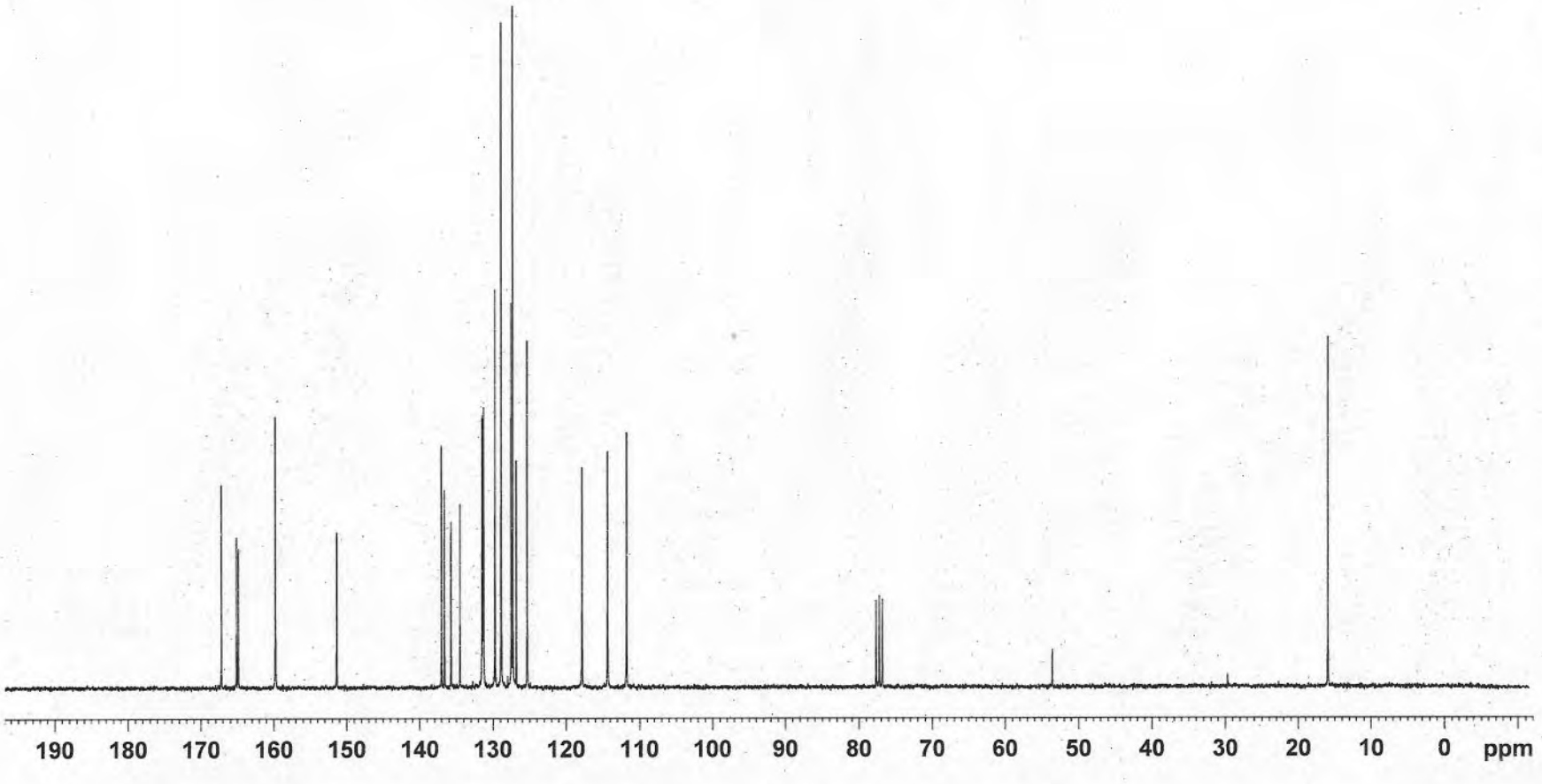
SP121205-3 CDCl3 303K C13-NMR AV300

167.191
165.149
164.899
159.817
151.414
137.052
136.653
135.762
134.512
131.525
131.460
131.334
129.784
128.922
127.540
127.331
126.849
125.380
117.867
114.374
111.780

77.707
77.282
76.858

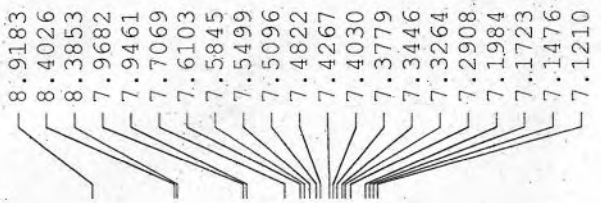
15.982

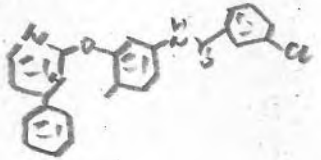




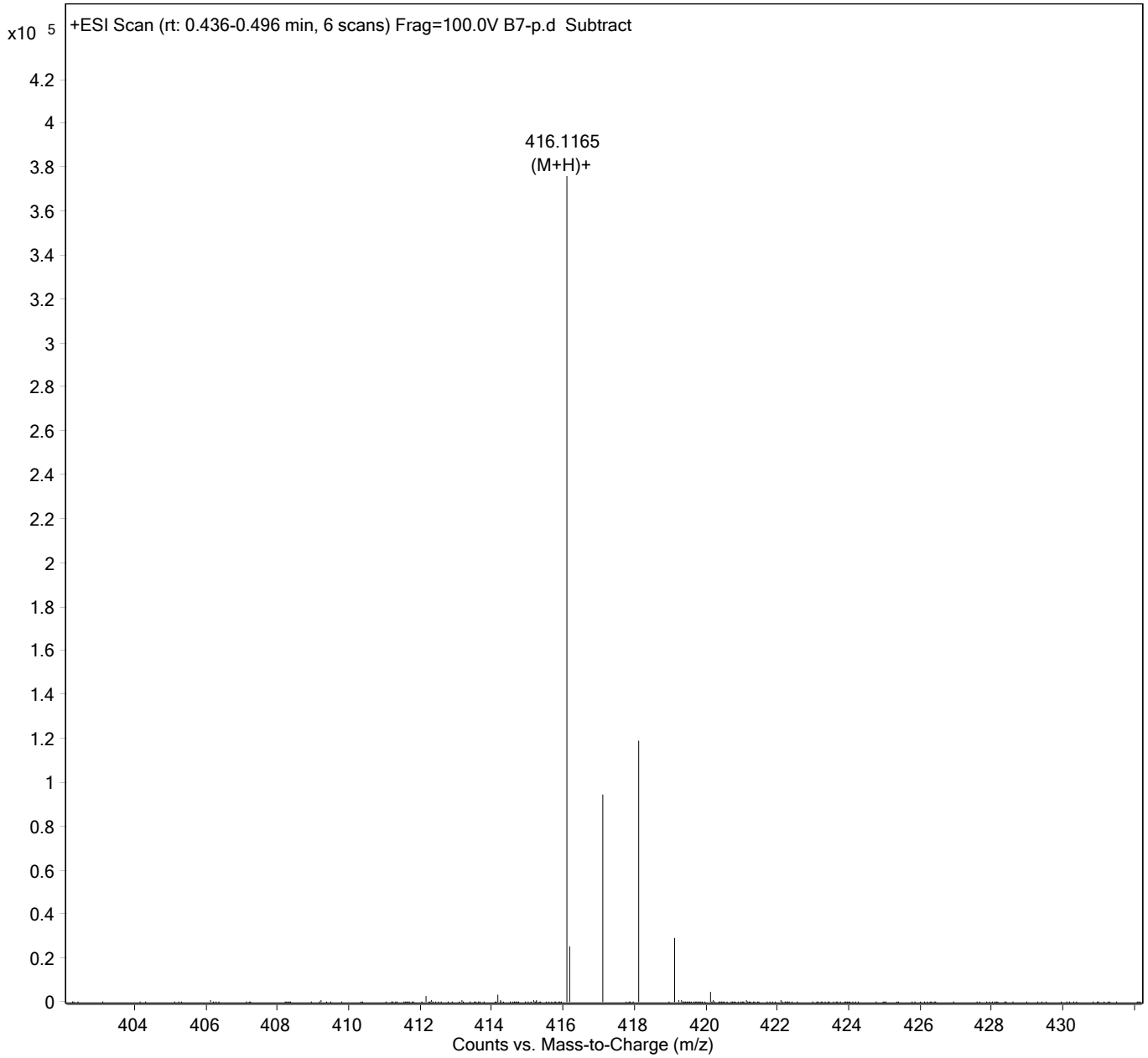
B7

SP121205-3 1H-NMR CDCl3 303K AV-300





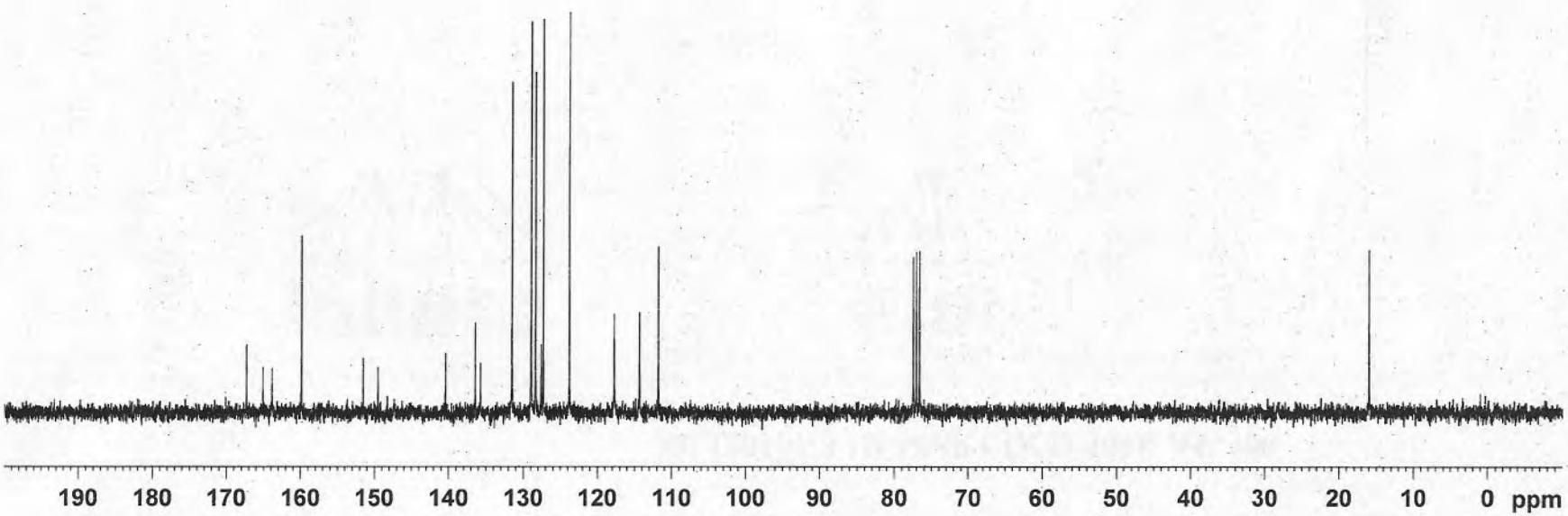
Sample Name		**Position**	p2F6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B7-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:41:26 PM



B8

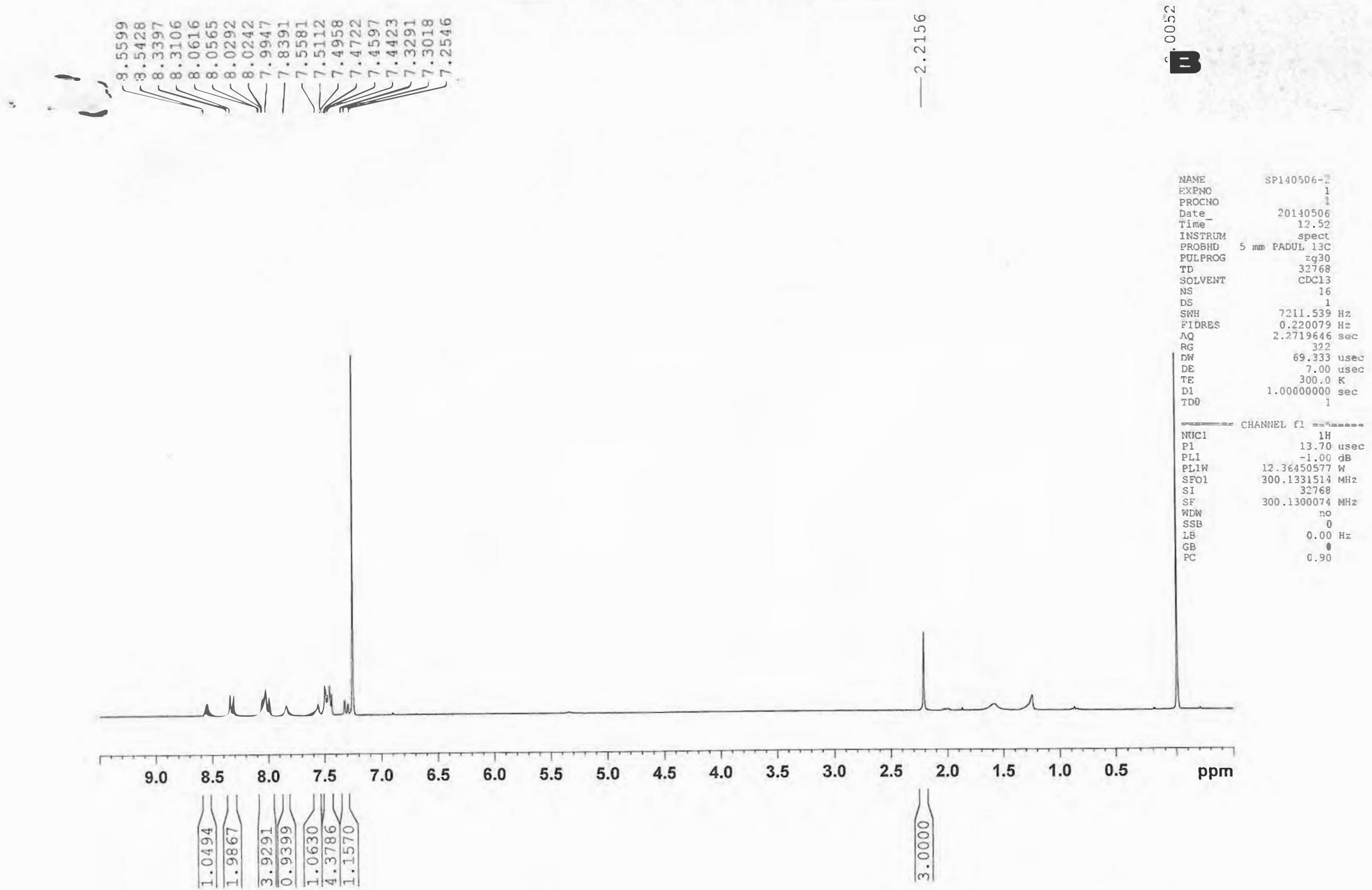
SP121202-3 CDCl3 303K C13-NMR AV300

167.313
165.107
163.865
159.878
151.526
149.547
140.414
136.441
135.722
131.539
128.965
128.382
127.324
123.802
117.756
114.343
111.816
77.485
77.062
76.639
16.031

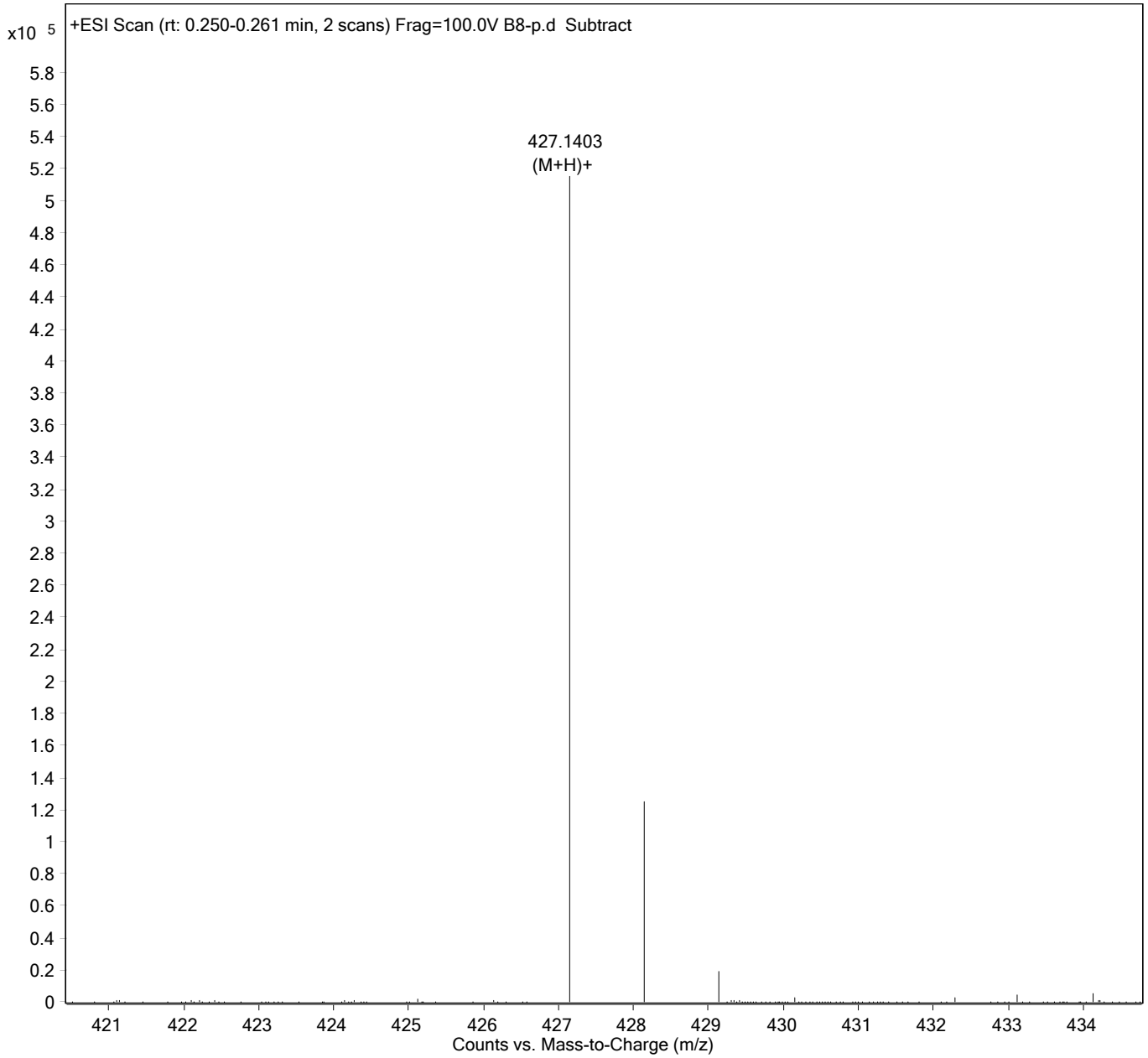


B8

SP140506-2 CDCL3 1HNMR AV300

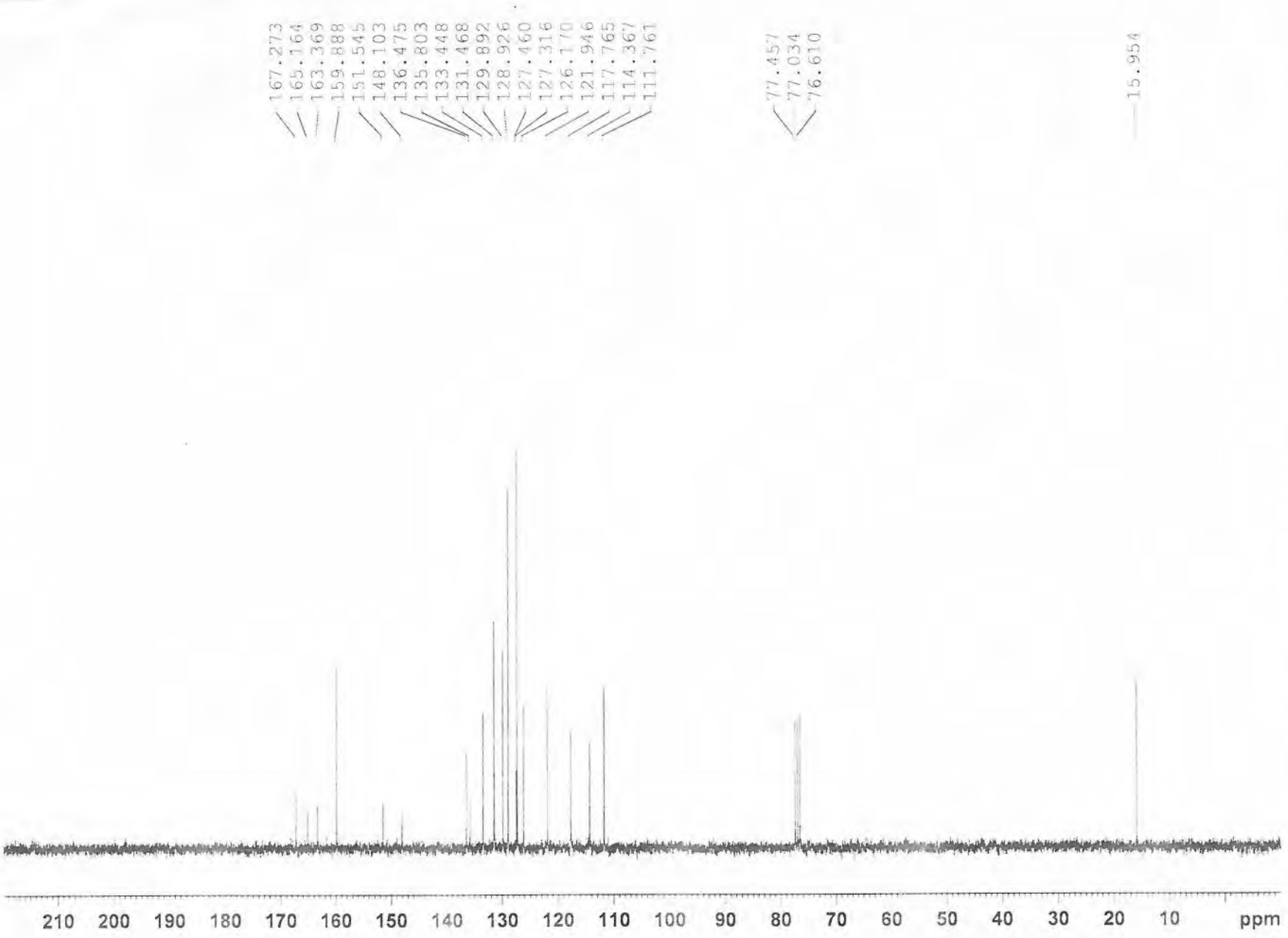


Sample Name		**Position**	p2F7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B8-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:43:49 PM



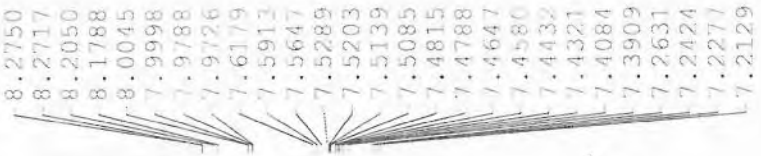
B9

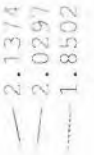
SP130828-C C13-NMR CDCL3 303K AV-300

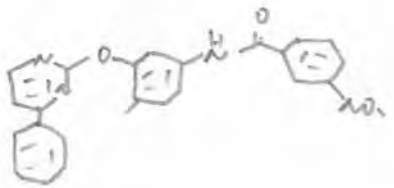


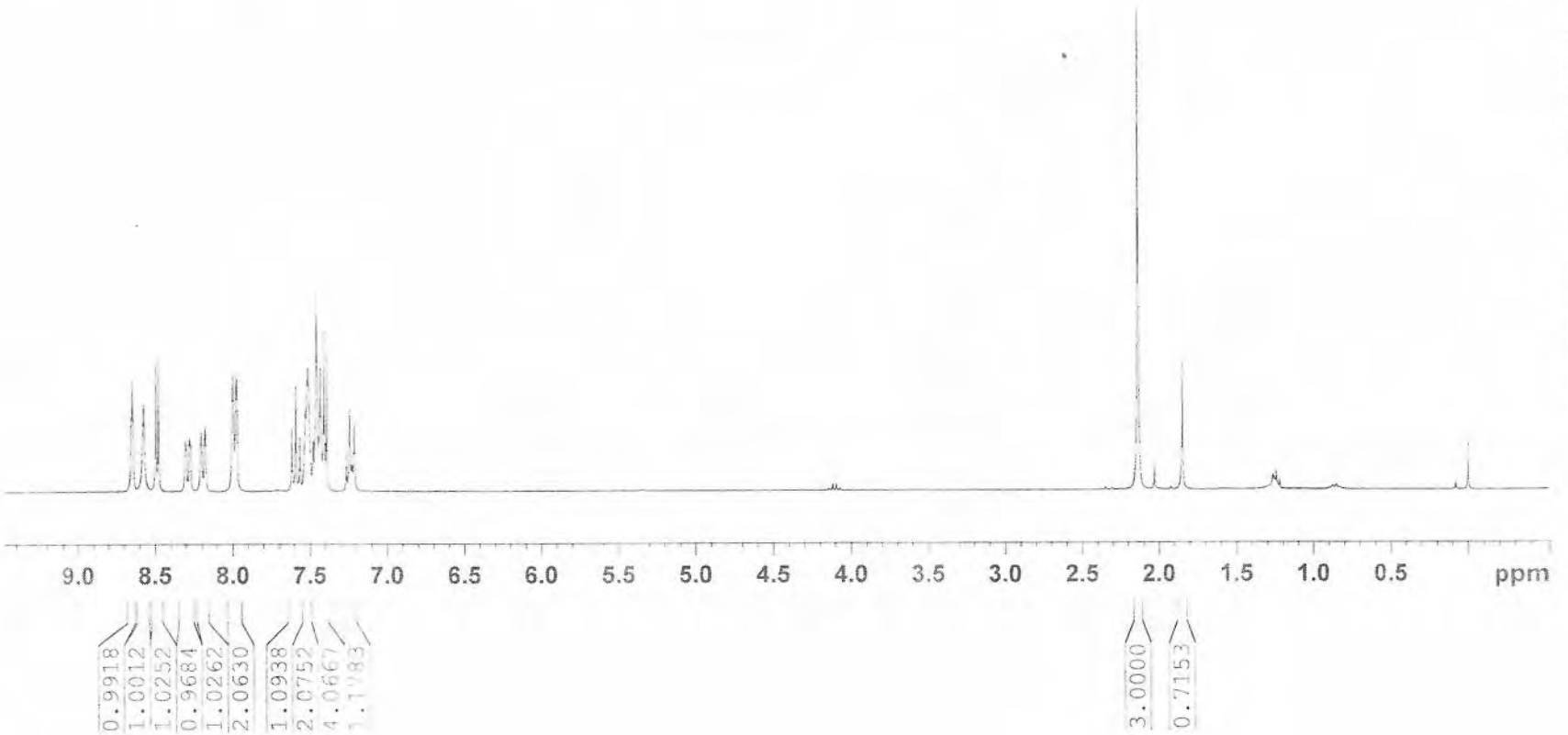
B9

SP20130828 CDCL3 1HNMR AV300

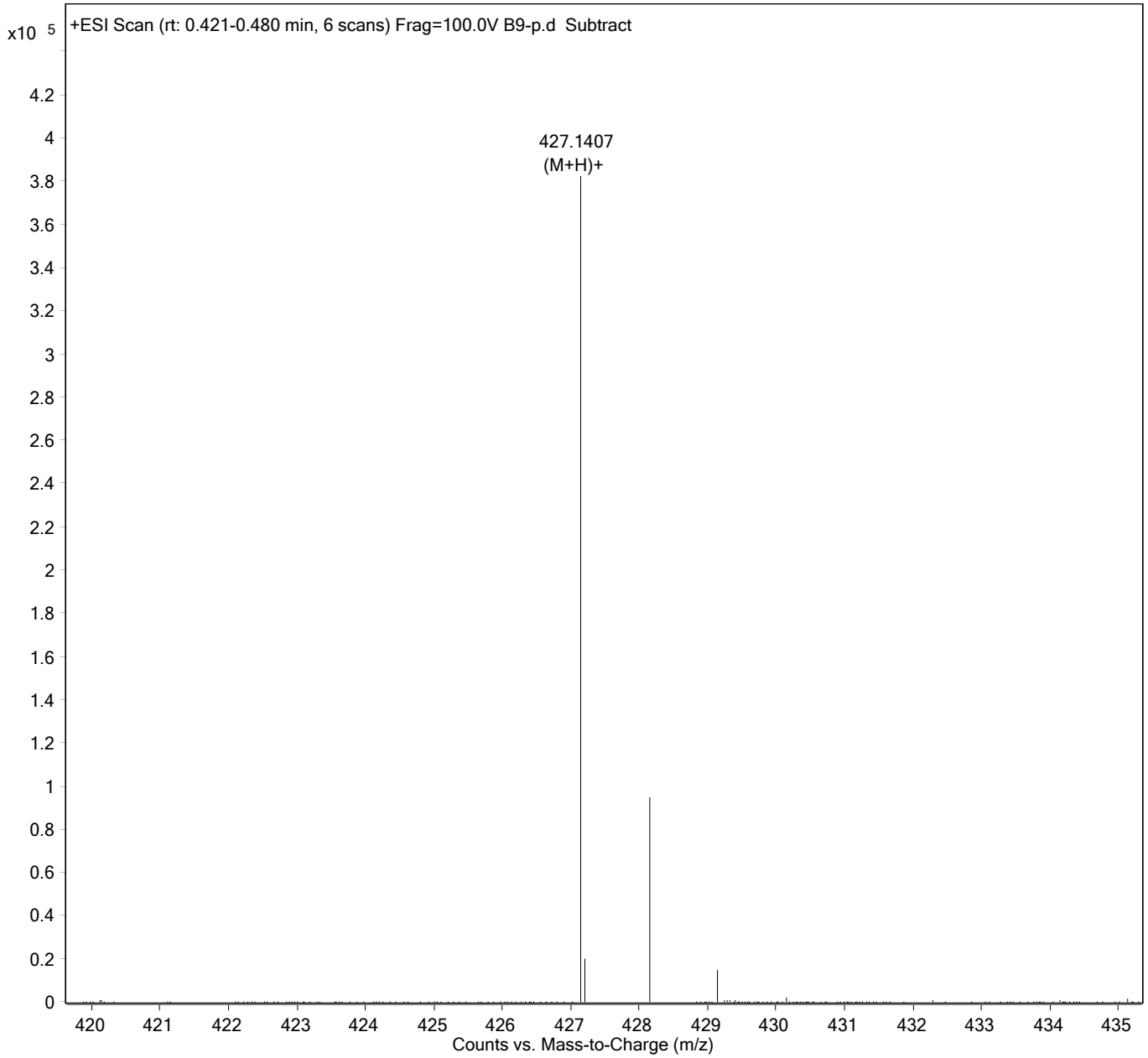






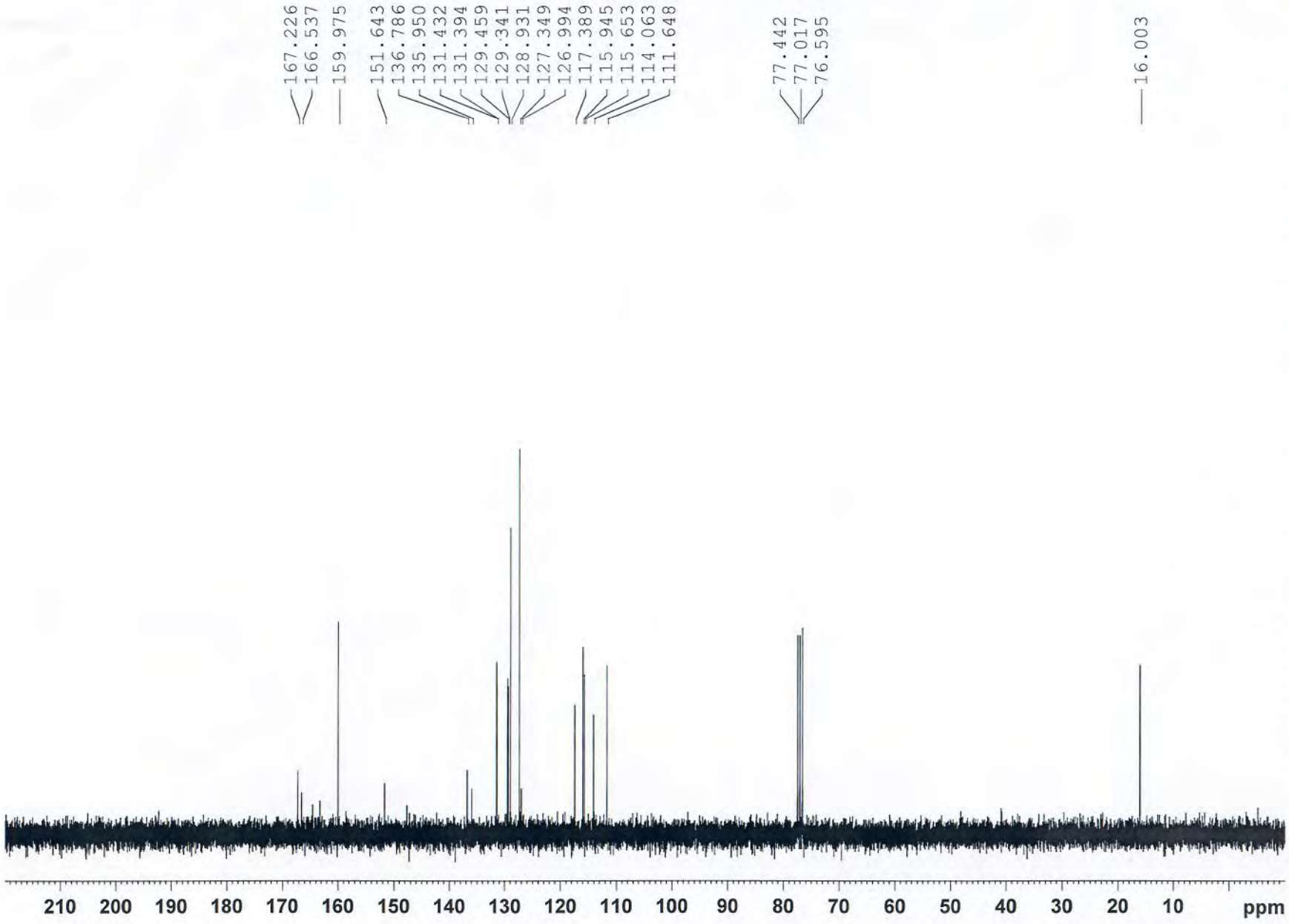


Sample Name		**Position**	p2F8	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B9-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:45:31 PM



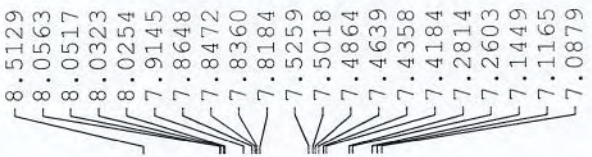
B10

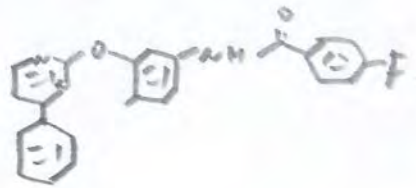
SP20131108-3-C C13-NMR CDCL3 303K AV-300

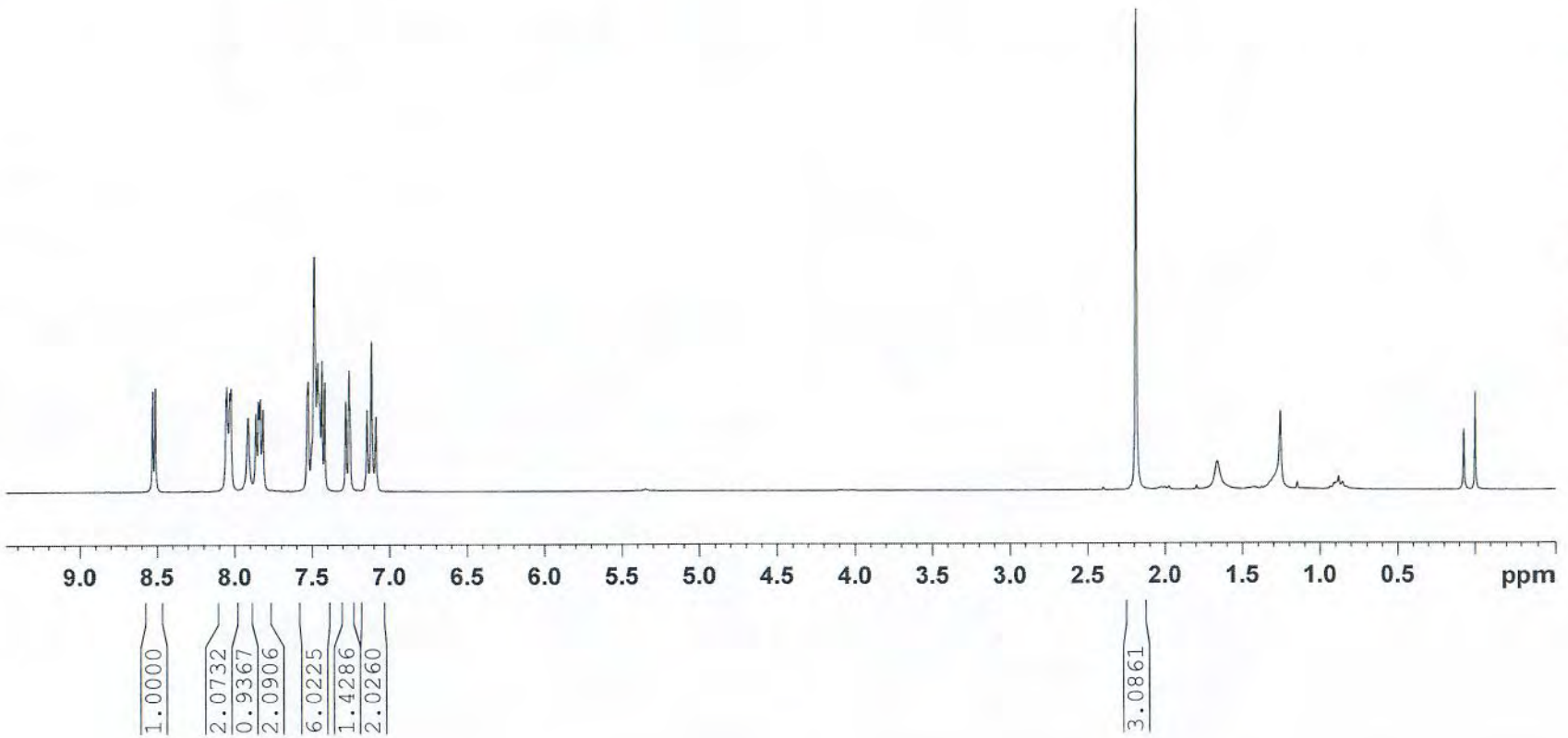


B10

SP20131108-3 CDCL3 1HNMR AV300

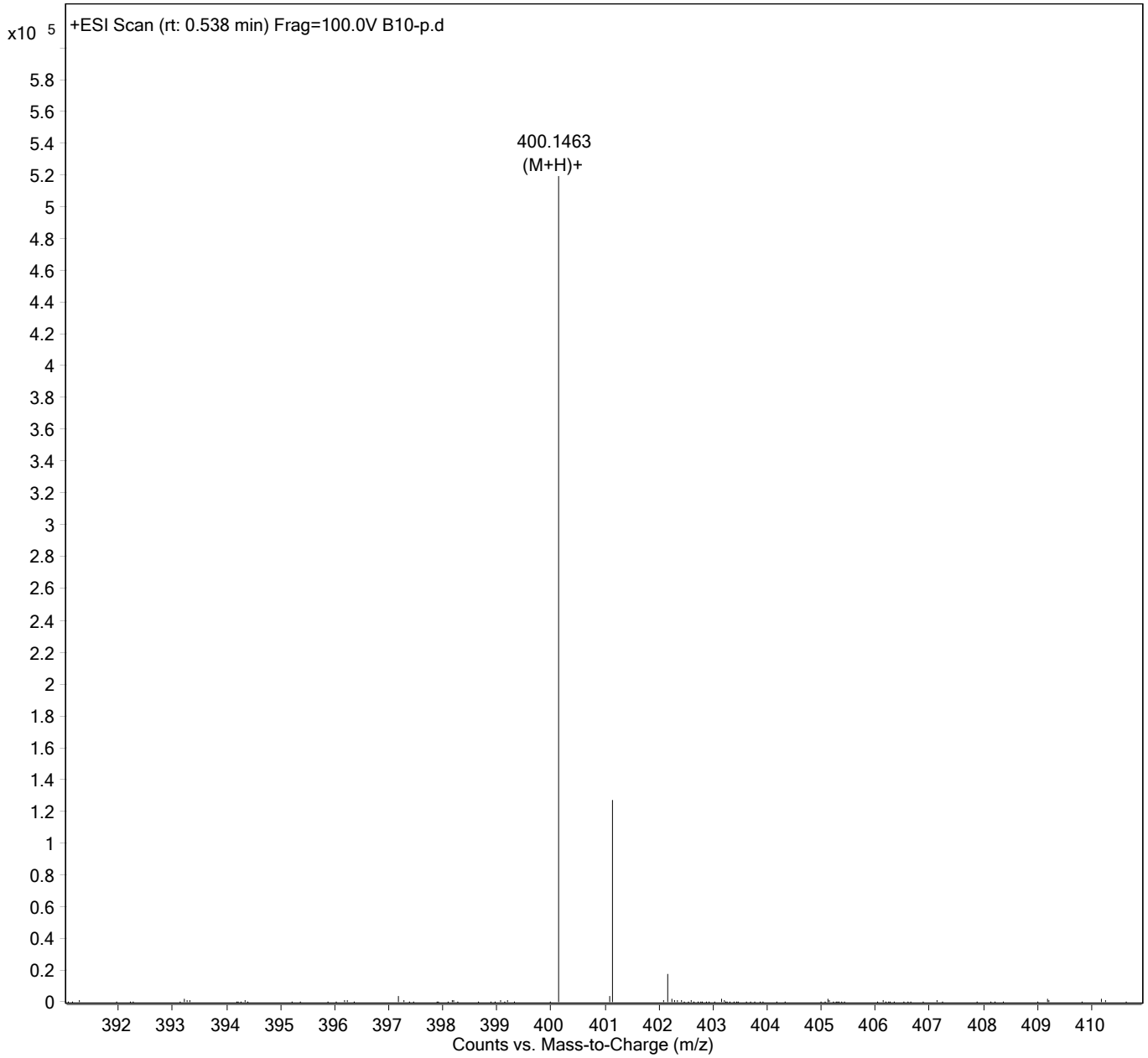






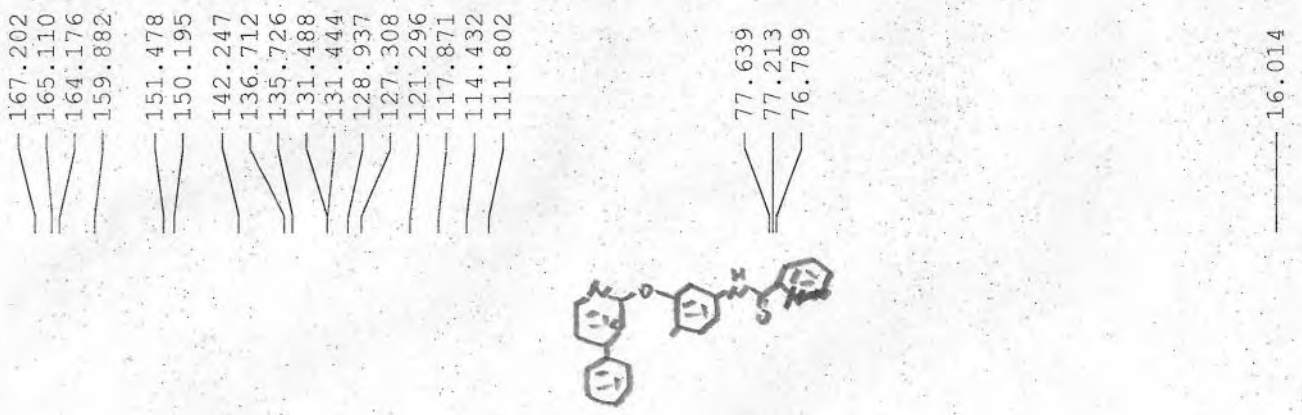
111

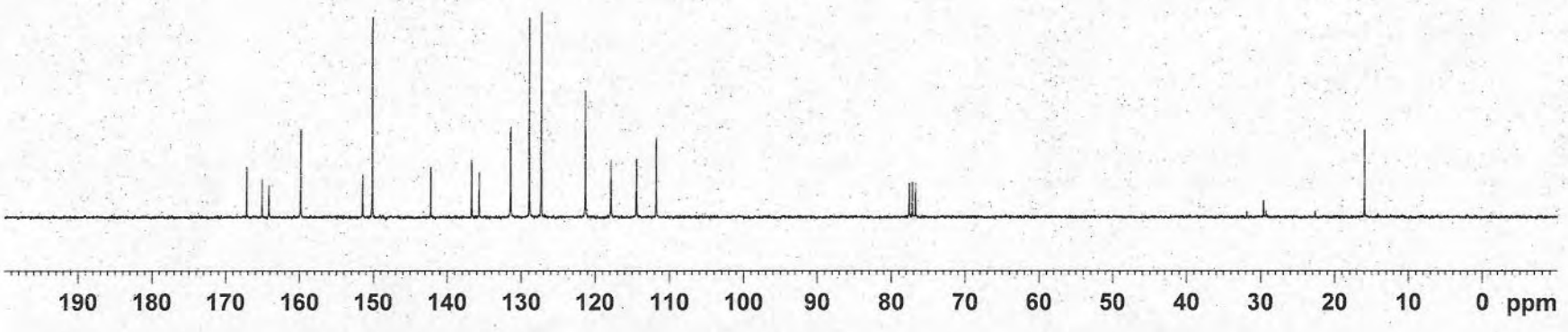
Sample Name		**Position**	p2F9	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B10-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:53:13 PM



B11

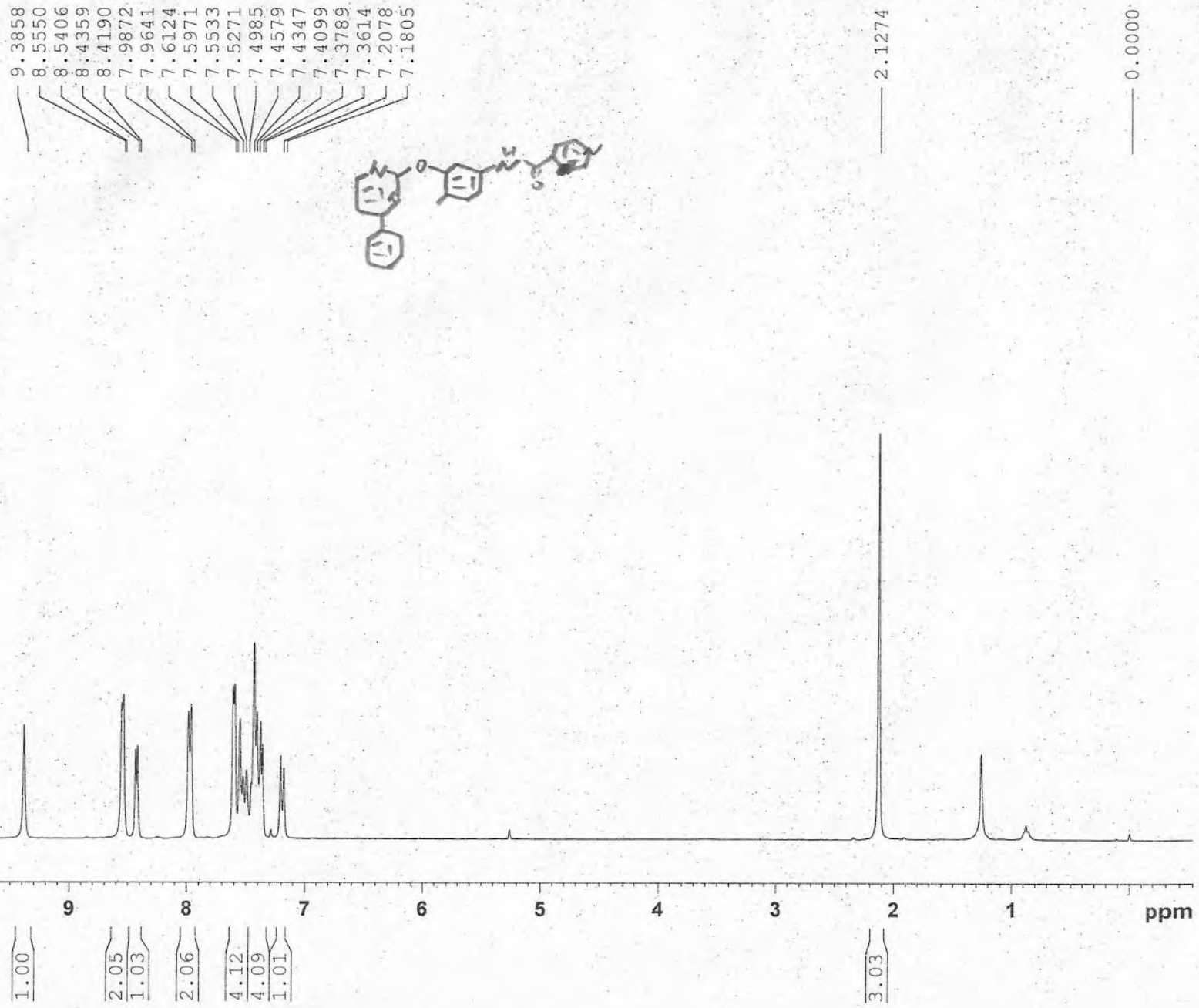
SP121210-1 CDCl3 303K C13-NMR AV300



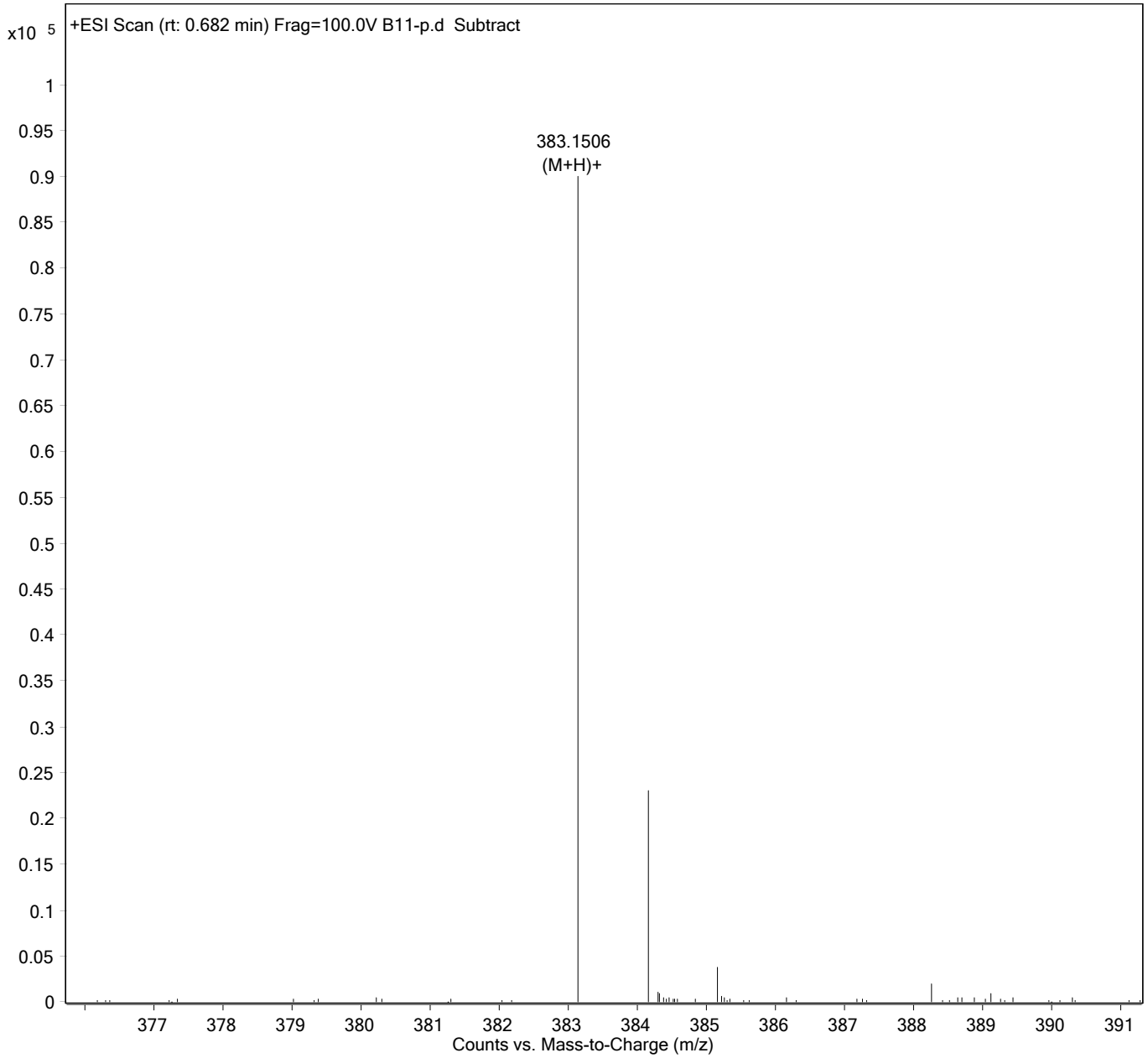


B11

SP121210-1 1H-NMR CDCl3 303K AV-300



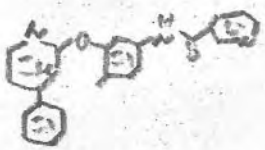
Sample Name		**Position**	p1A1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B11-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:50:54 PM

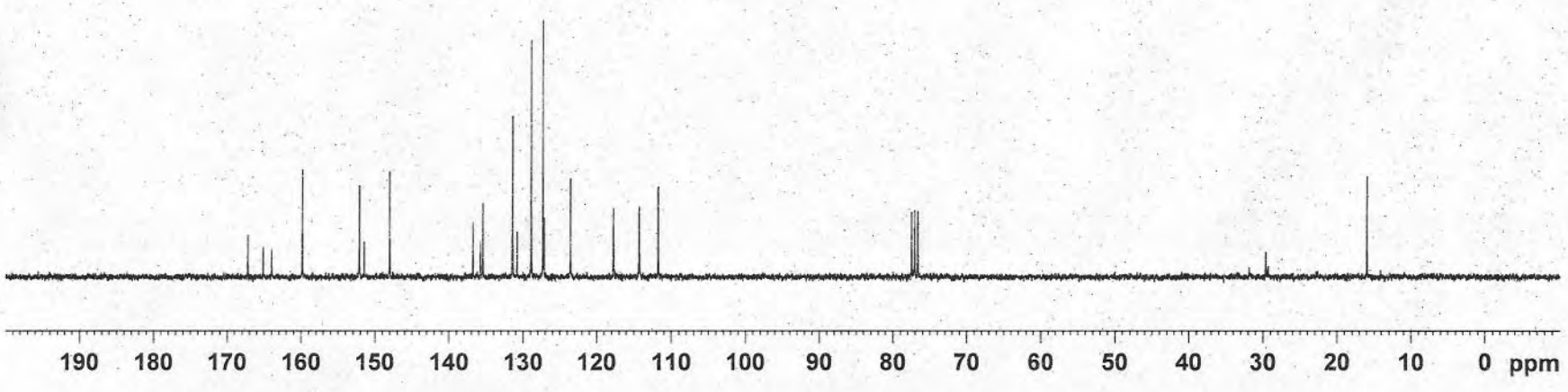


B12

SP121210-2 CDCl3 303K C13-NMR AV300

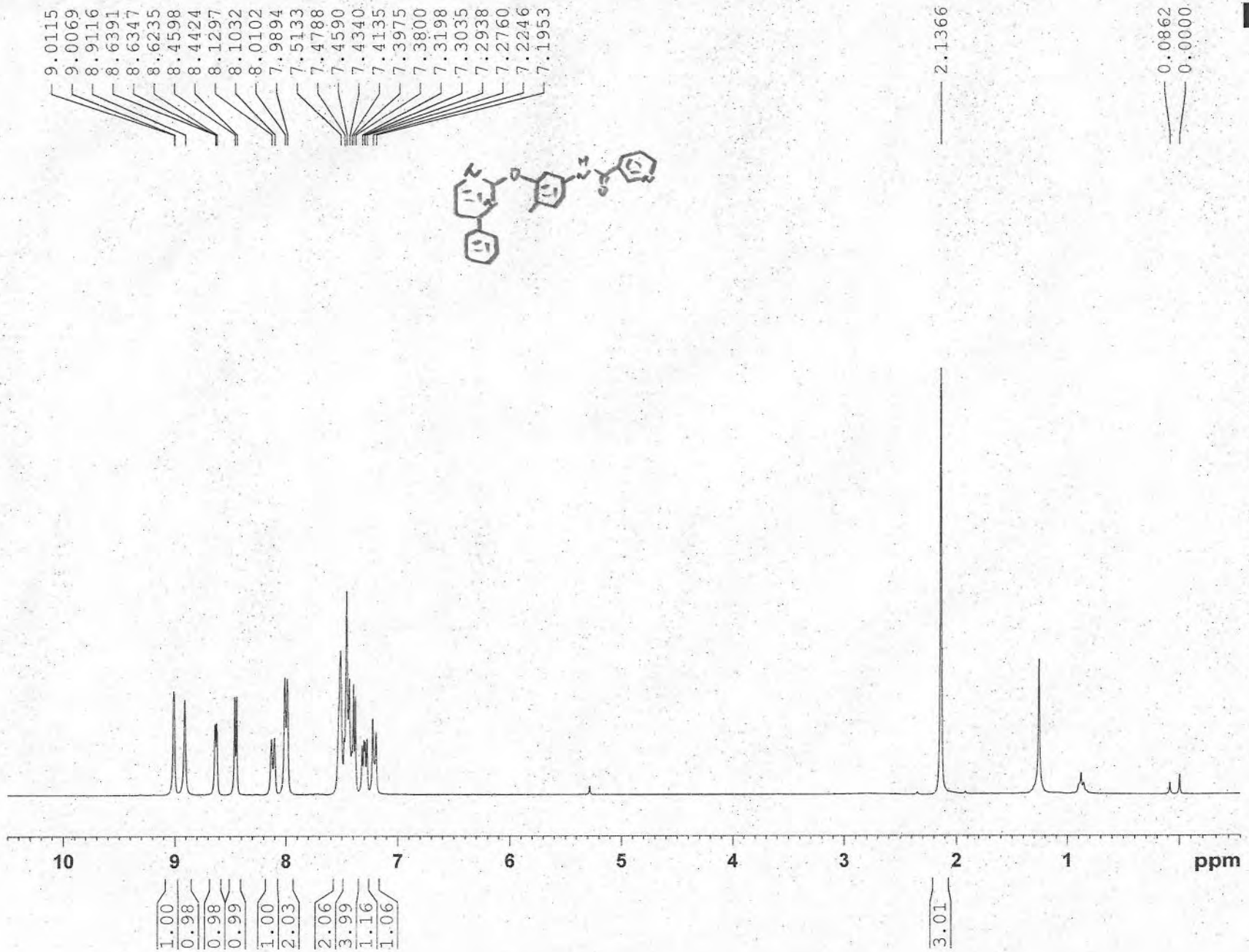
167.258
165.173
164.022
159.847
152.163
151.490
148.041
136.807
135.807
135.460
131.451
130.840
128.938
127.336
123.575
117.756
114.297
111.764
77.530
77.106
76.681
15.991



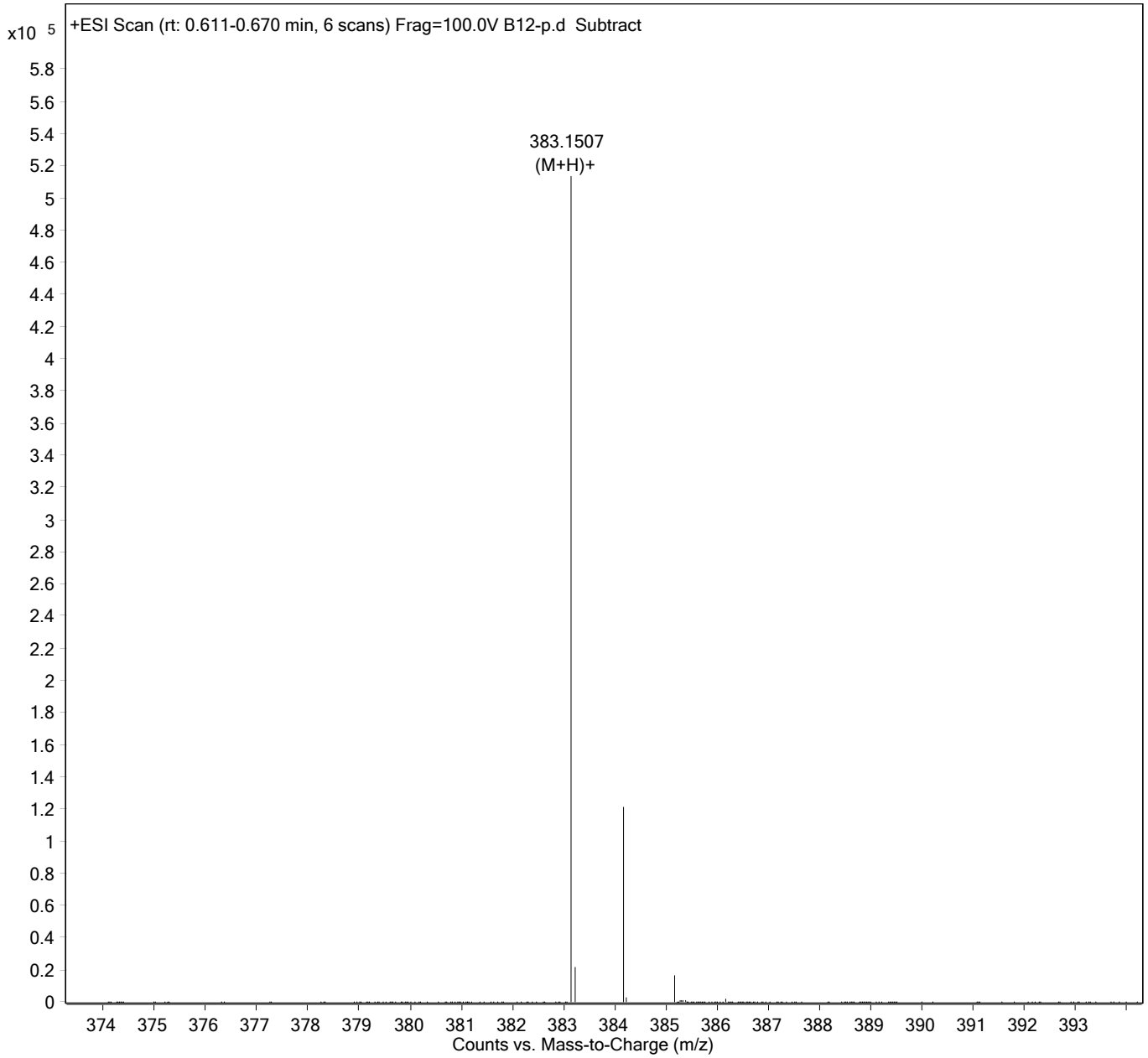


B12

SP121210-2 1H-NMR CDCl3 303K AV-300

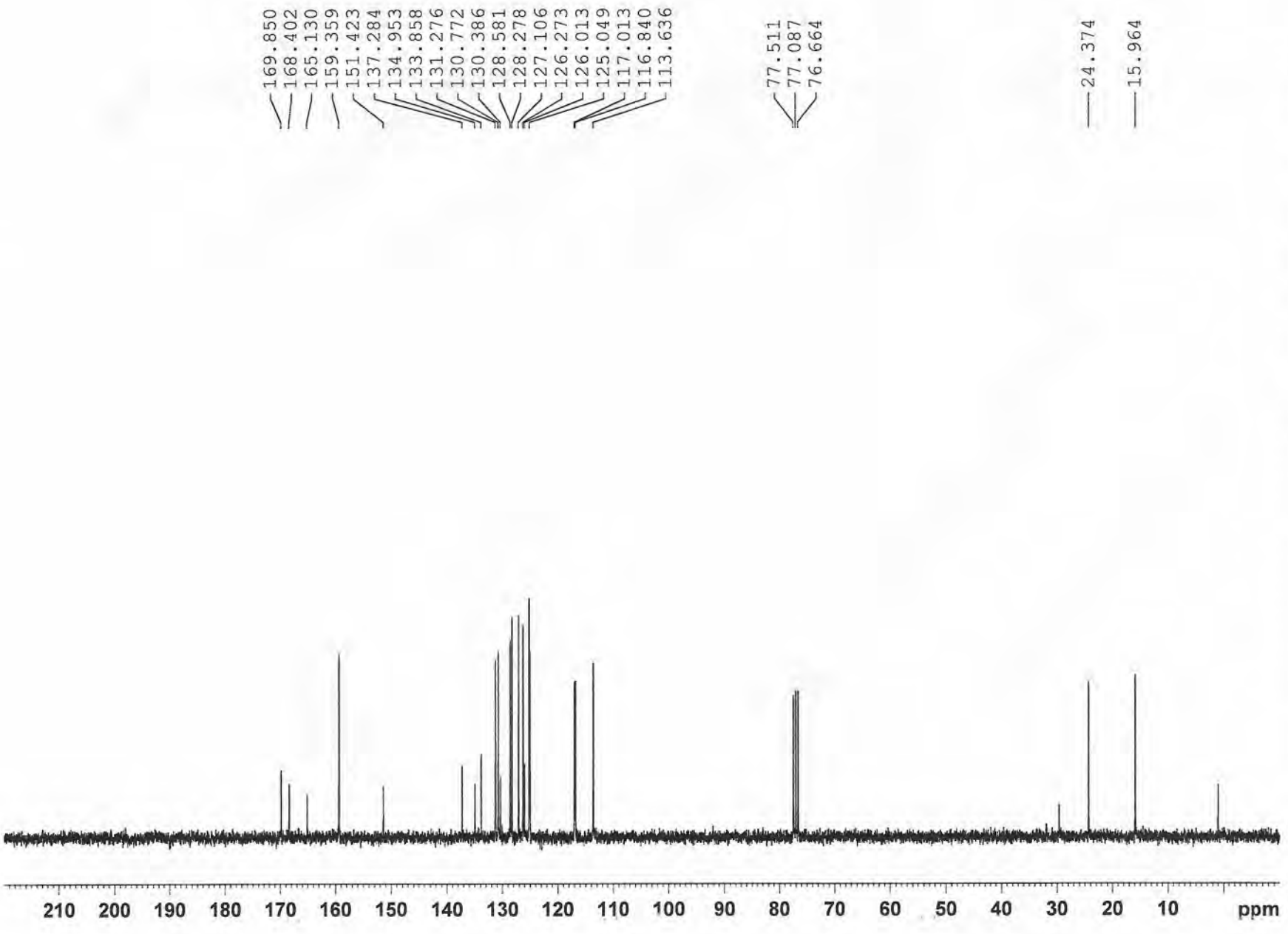


Sample Name		**Position**	p1A2	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	B12-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:55:07 PM



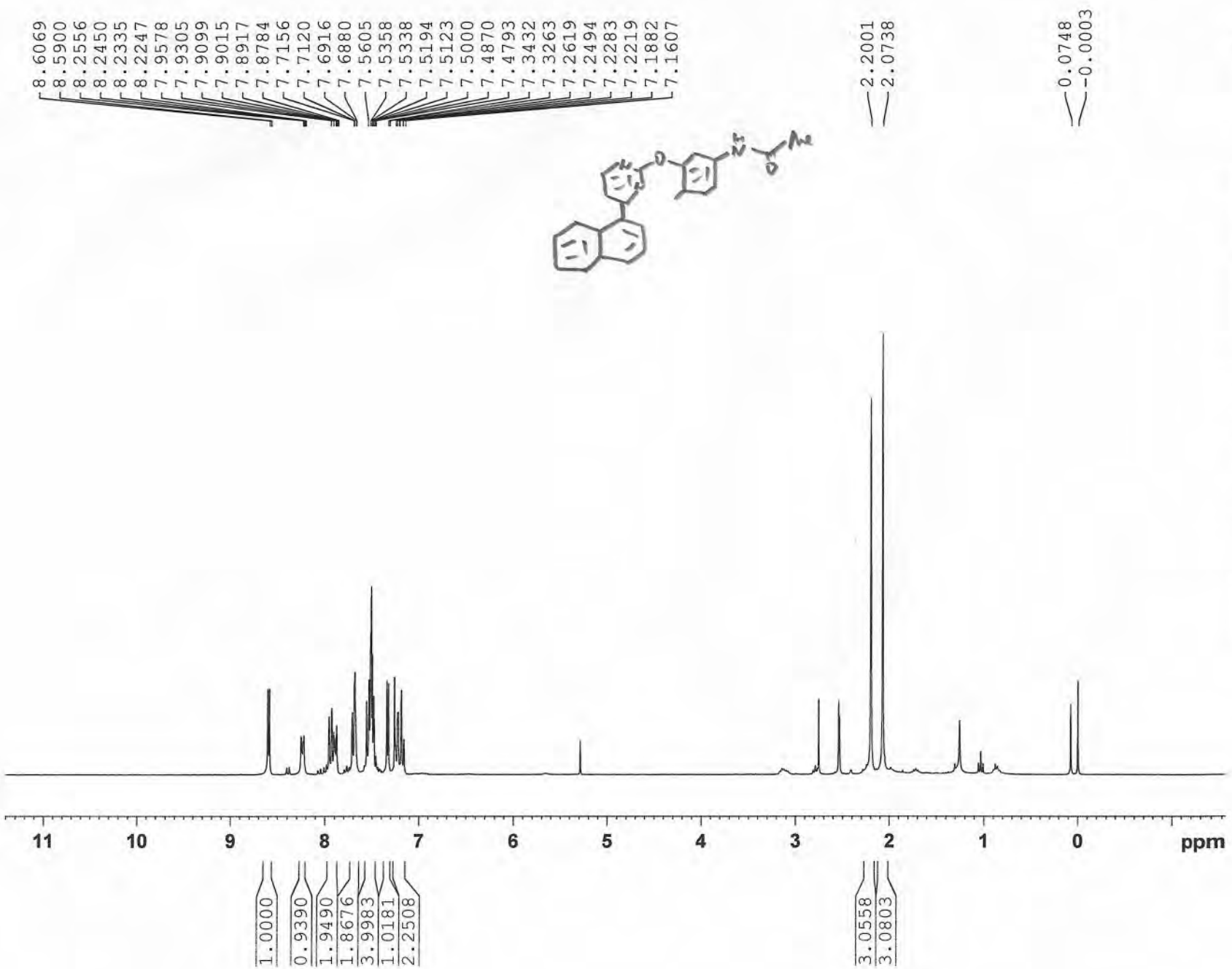
C1

SP130325-2-C C13-NMR CDCL3 303K AV-300

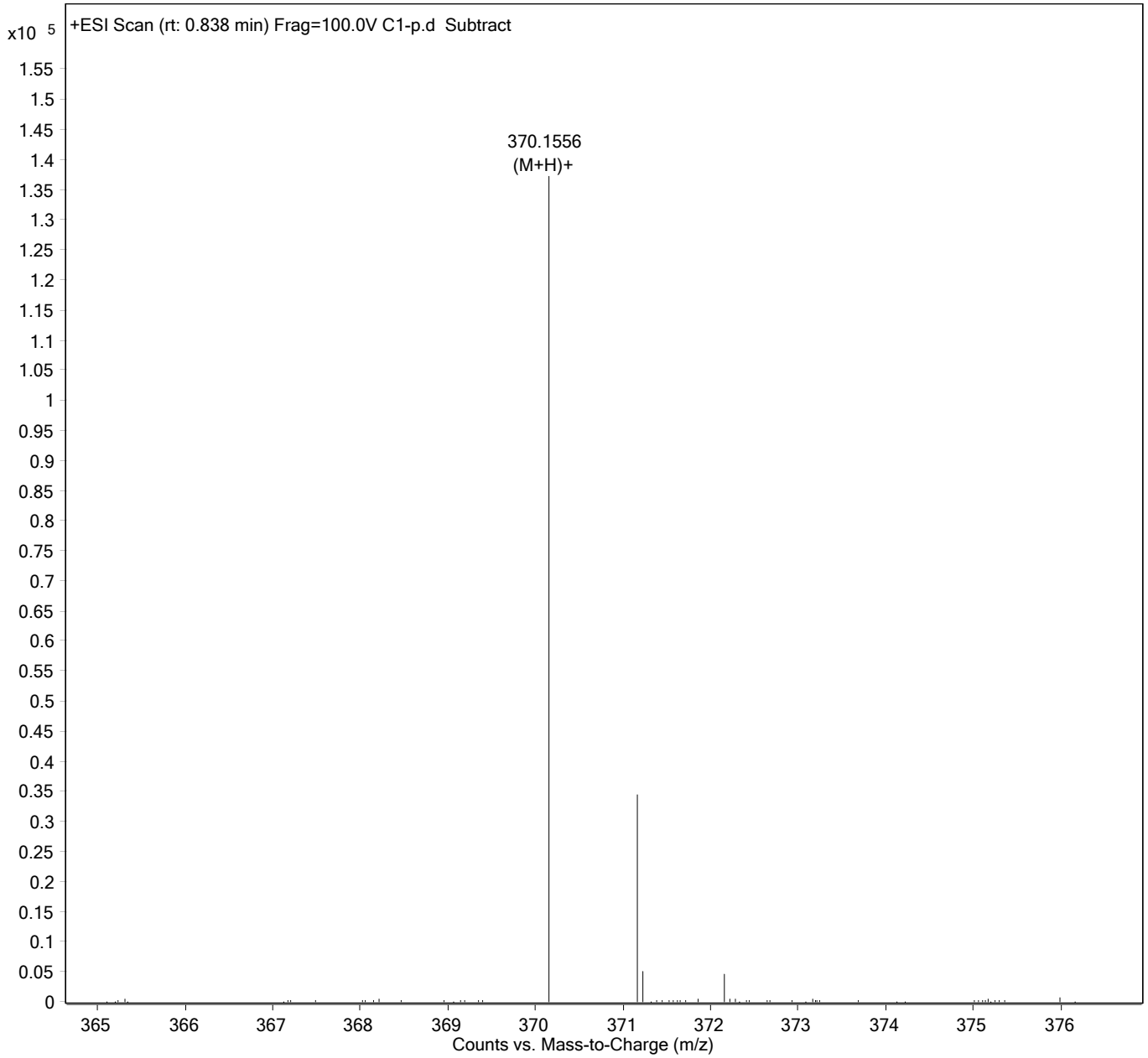


C I

SP2013-03-22-2 CDCL3 1HNMR AV300

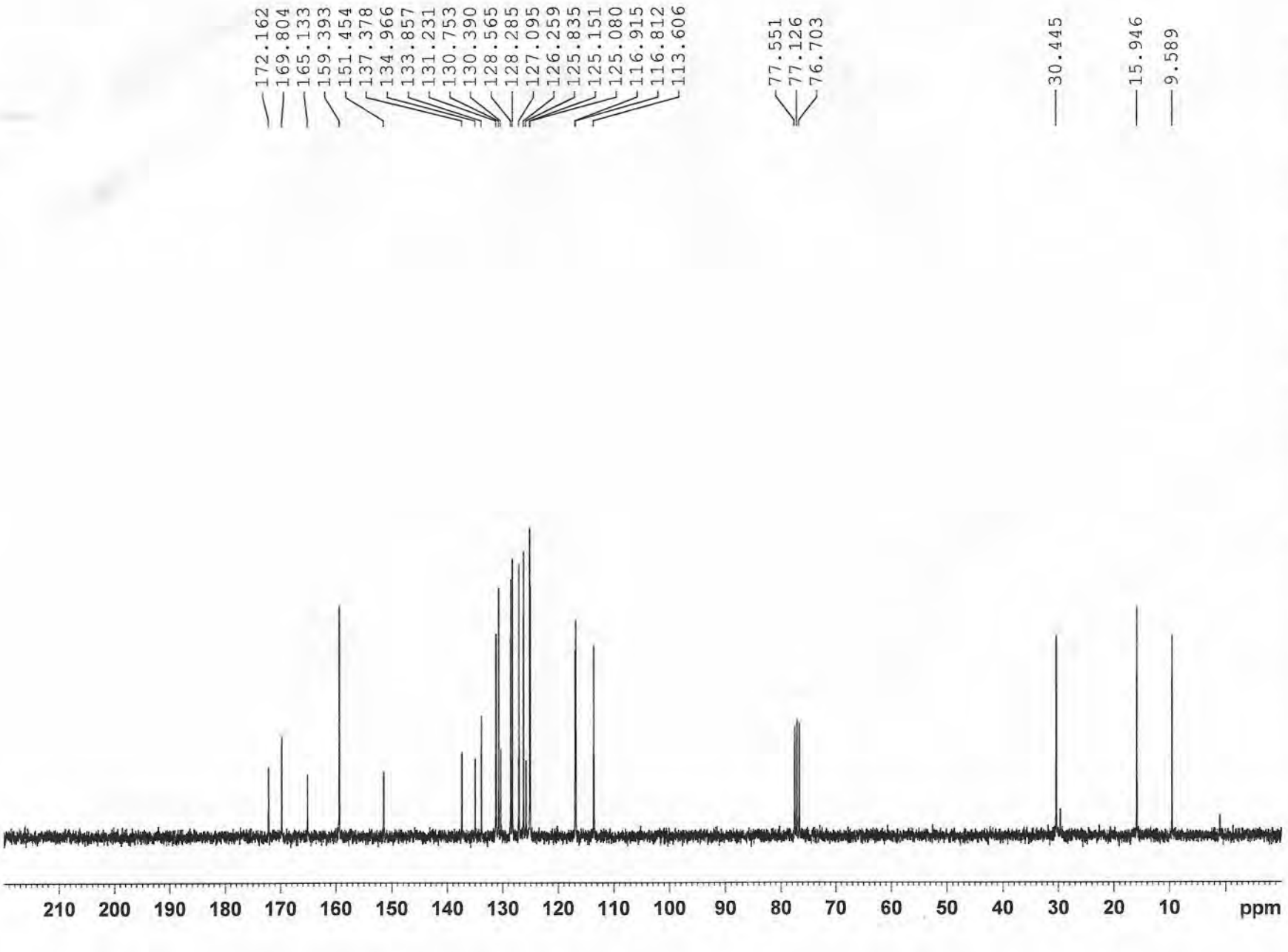


Sample Name		**Position**	p1A3	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:57:44 PM



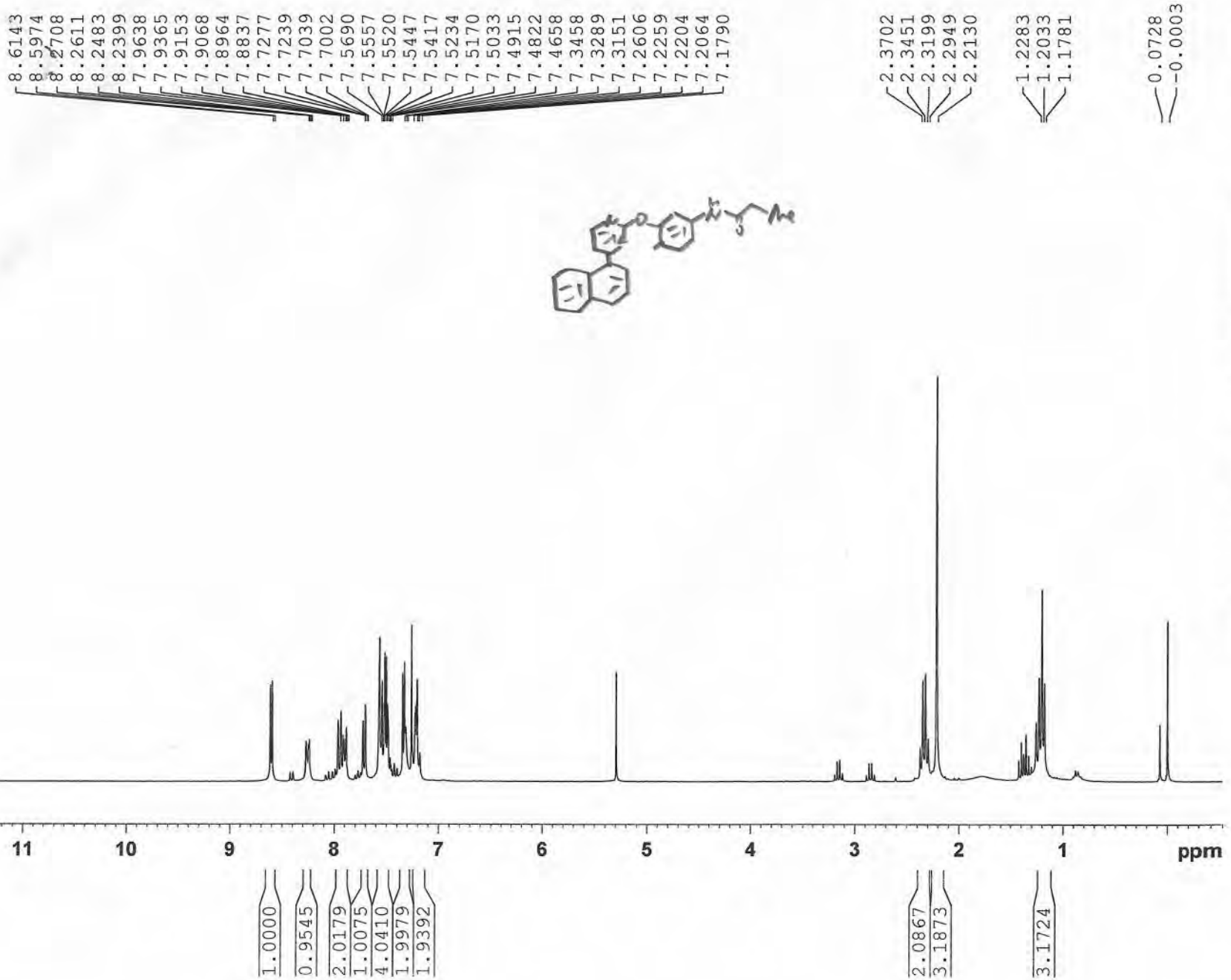
C2

SP130325-3-C C13-NMR CDCL3 303K AV-300

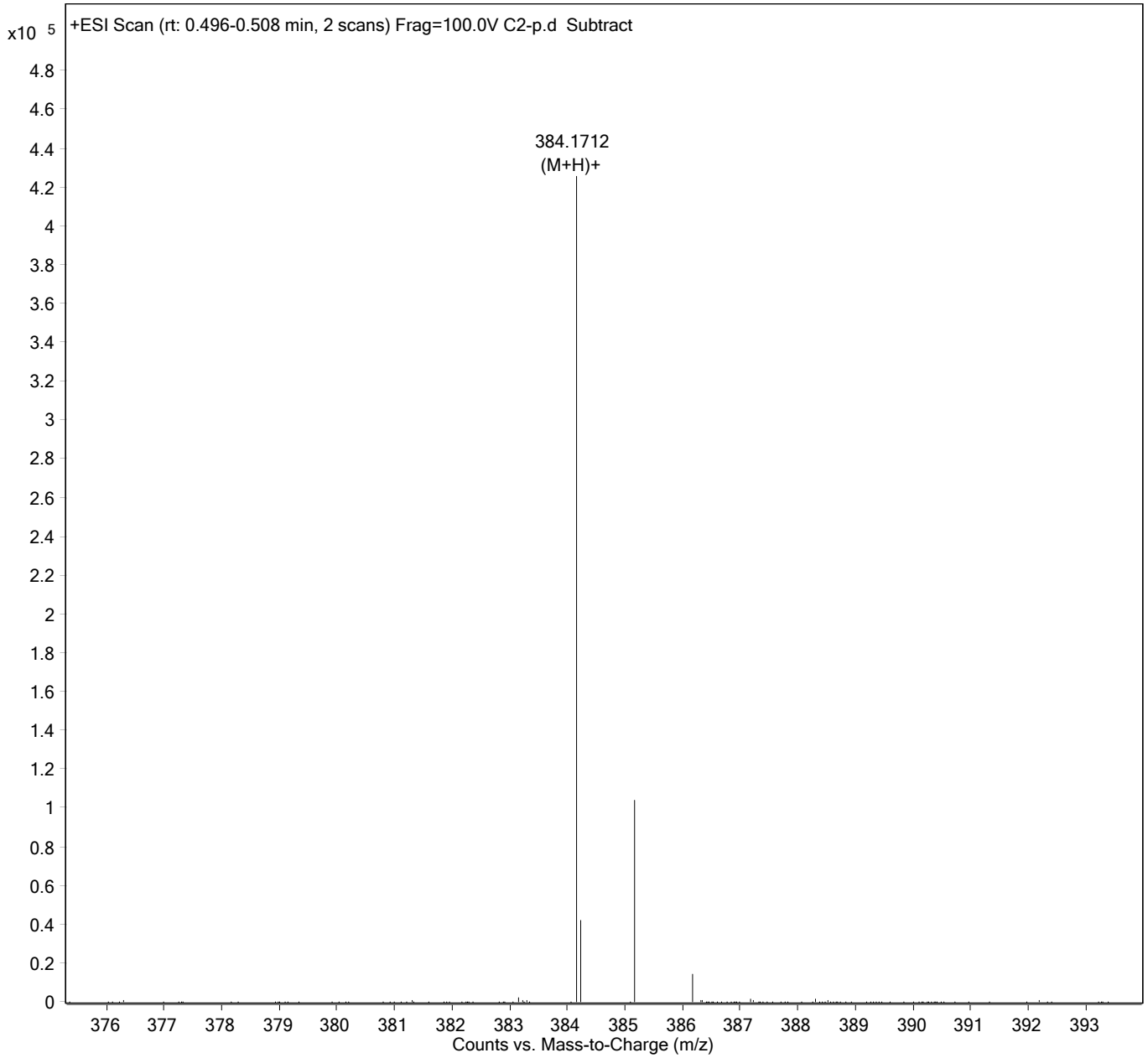


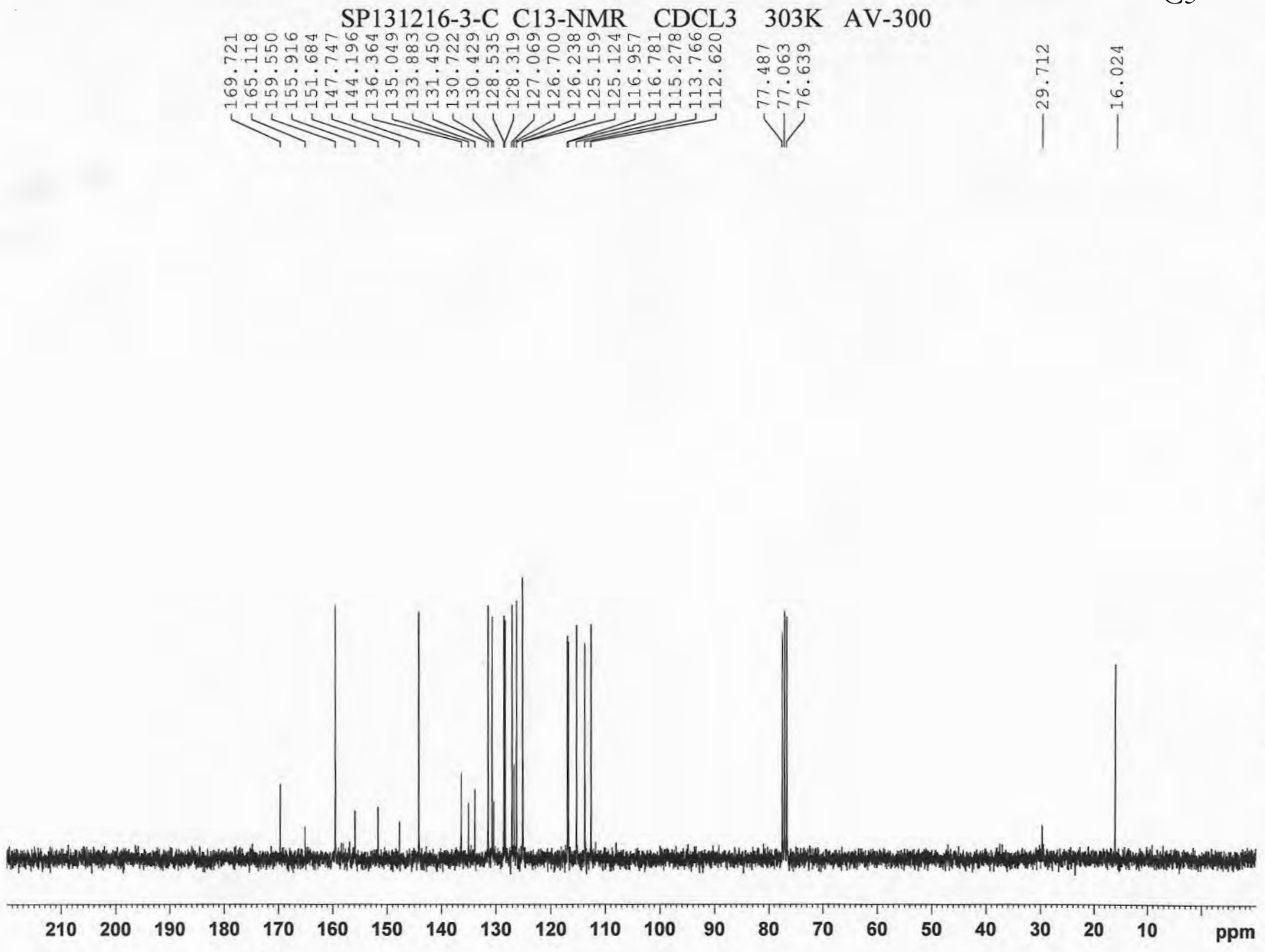
C 2

SP2013-03-22-3 CDCL3 1HNMR AV300

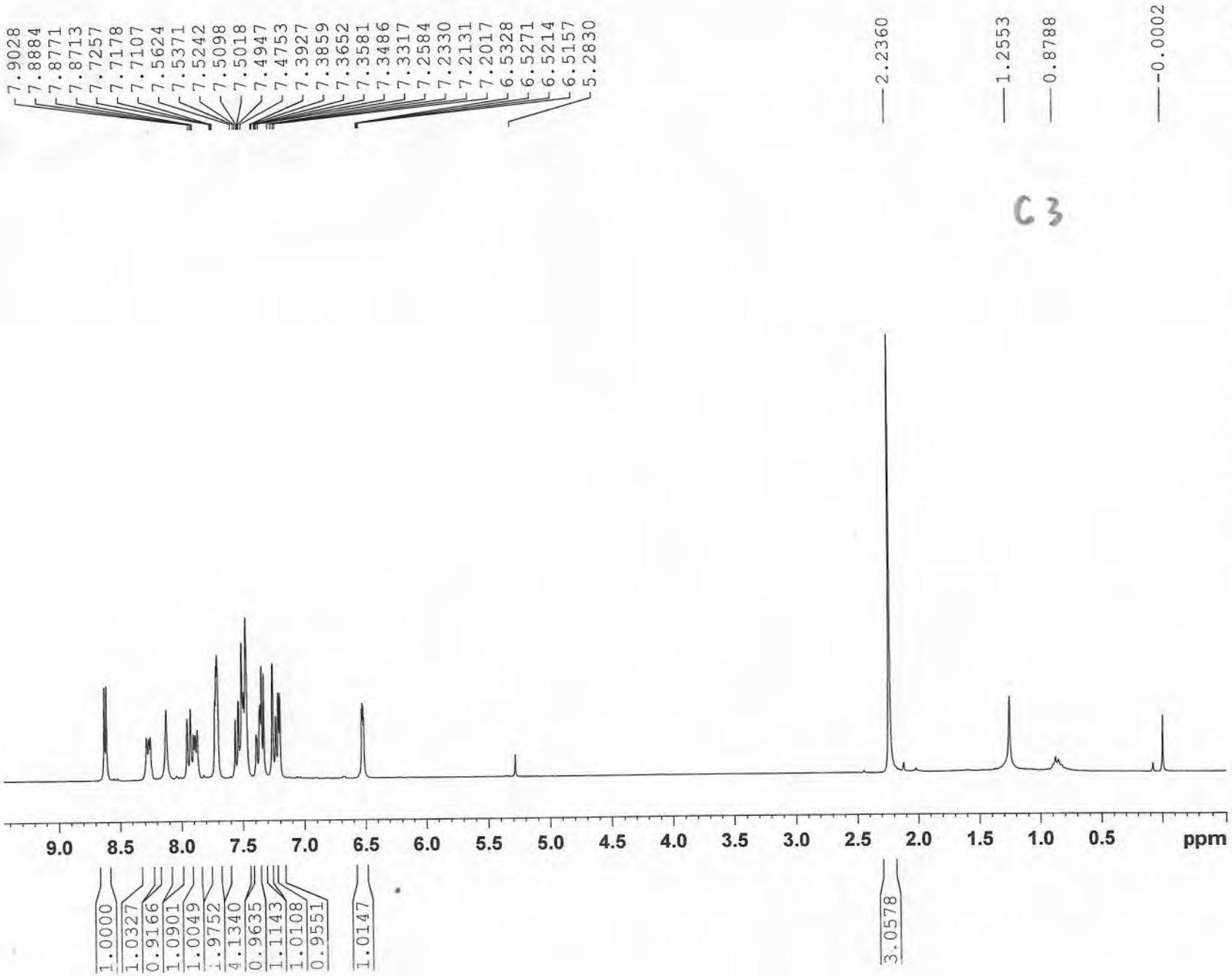


Sample Name		**Position**	p1A4	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 3:59:34 PM

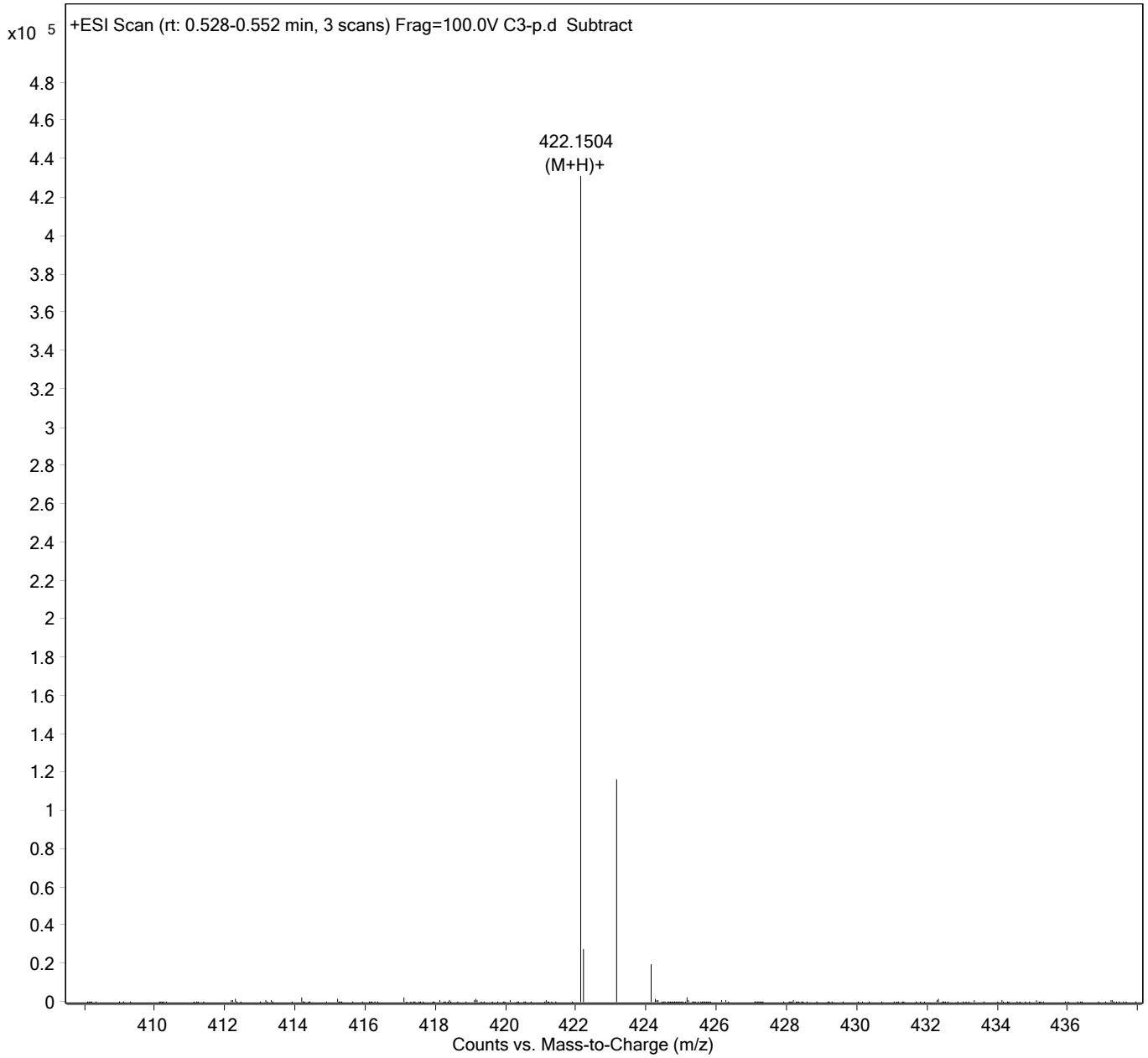



SP131216-3-C C13-NMR CDCL3 303K AV-300
169.721
165.118
159.550
155.916
151.684
147.747
144.196
136.364
135.049
133.883
131.450
130.722
130.429
128.535
128.319
127.069
126.700
126.238
125.159
125.124
116.957
116.781
115.278
113.766
112.620
77.487
77.063
76.639
29.712
16.024
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

SP131216-3 CDCL3 1HNMR AV300



Sample Name		**Position**	p1A5	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:01:18 PM



C4

SP131216-4-C C13-NMR CDCL3 303K AV-300

169.750
165.094
160.667
159.502
151.582
145.141
143.928
136.685
134.968
133.867
131.411
130.746
130.396
128.548
128.298
127.068
126.669
126.243
125.142
125.075
122.956
117.388
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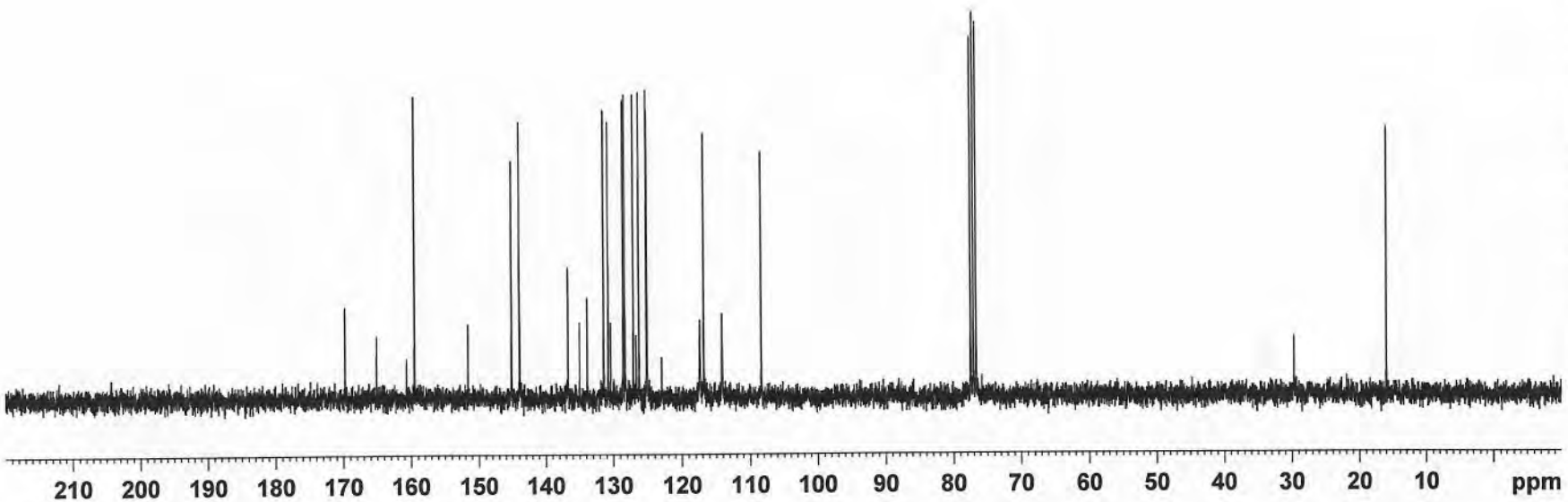
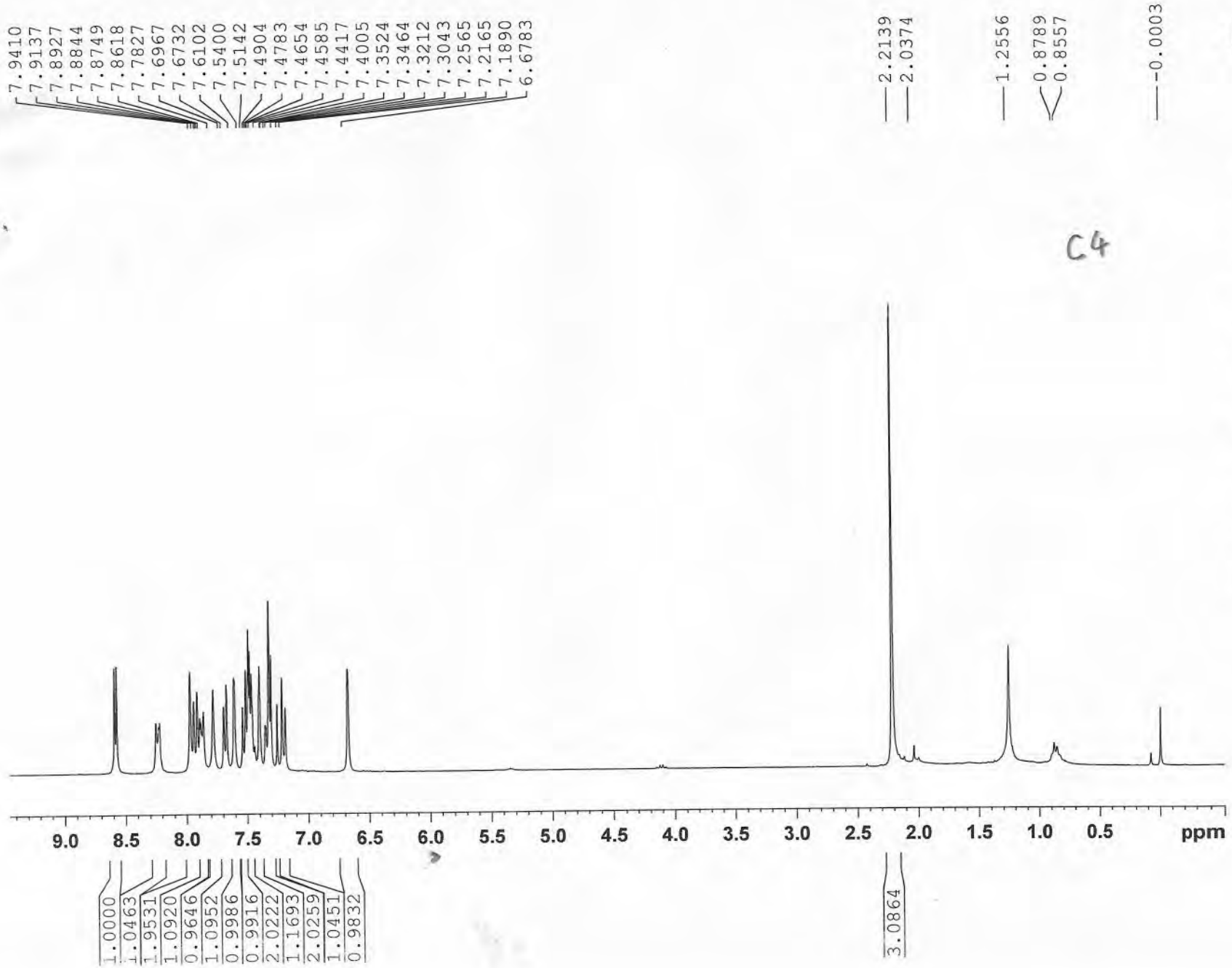
77.477
77.053
76.629
29.705
15.987

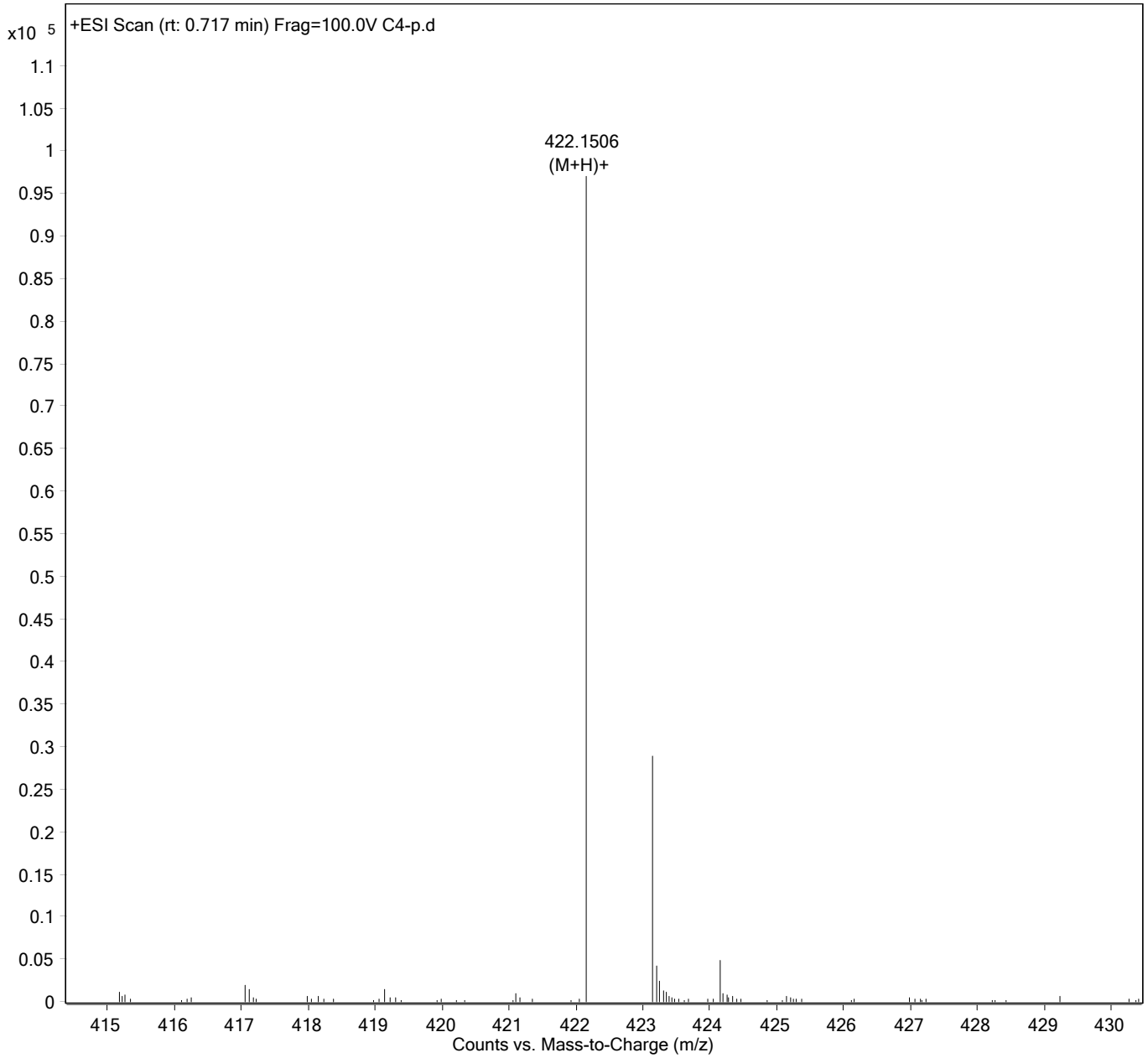


c4

SP131216-4 CDCL3 1HNMR AV300

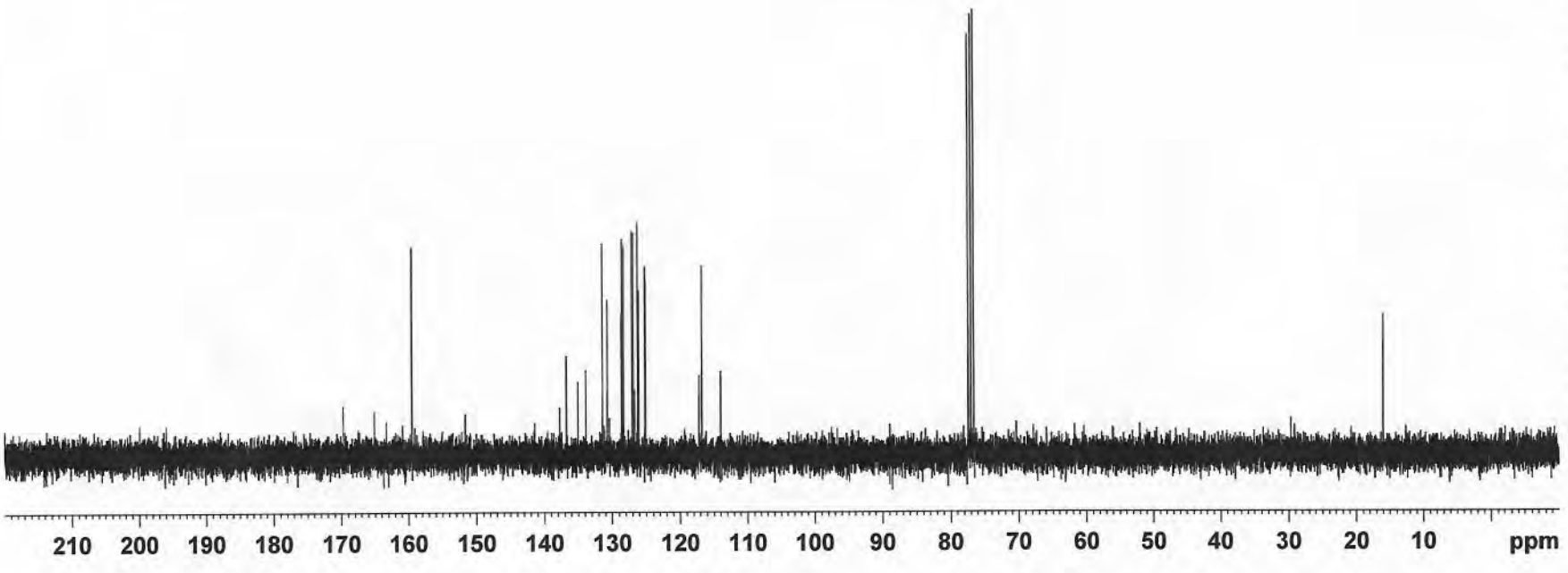


Sample Name		**Position**	p1A6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C4-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:03:38 PM



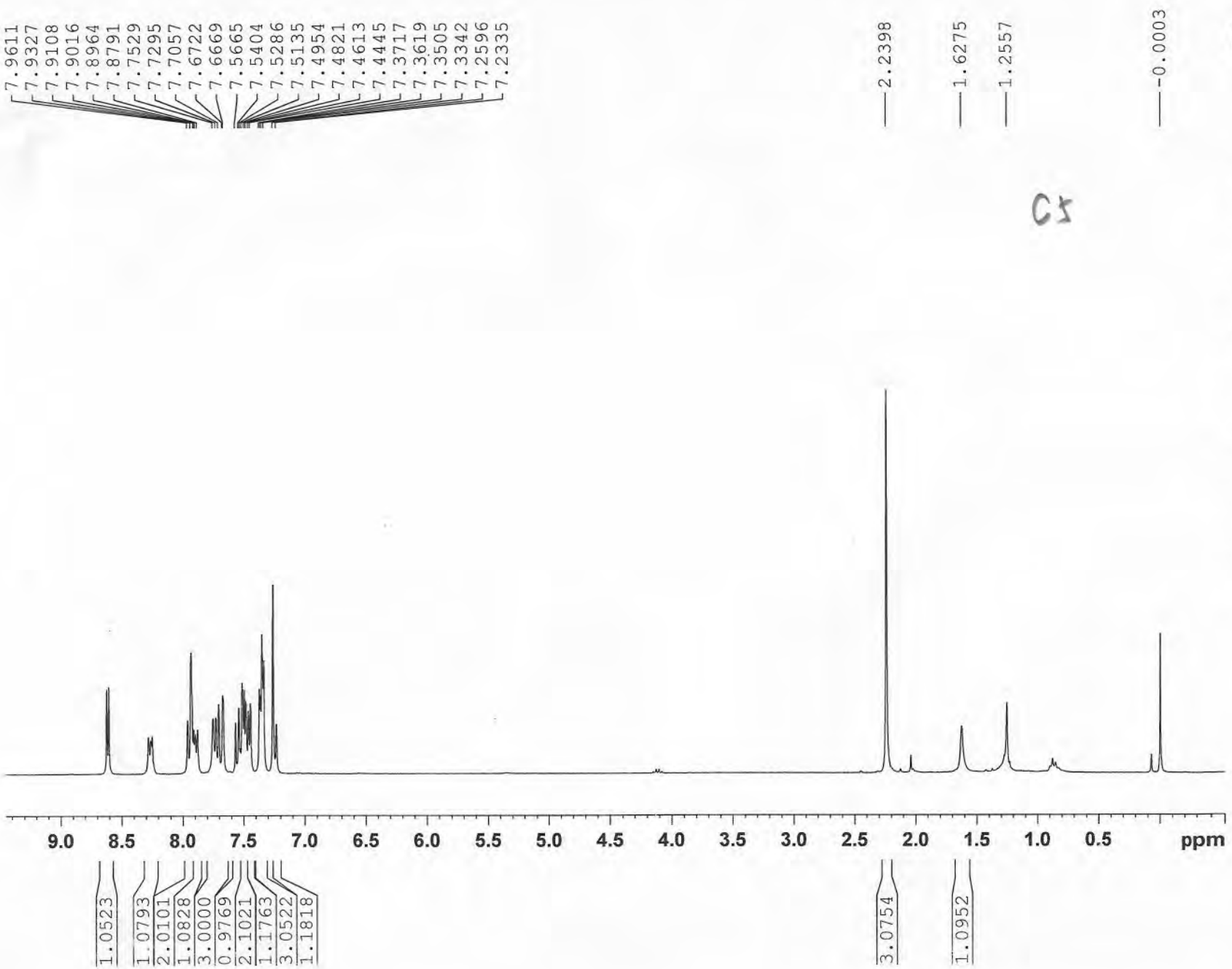
SP131216-5-C C13-NMR CDCL3 303K AV-300

169.727
165.133
160.930
159.535
151.676
137.750
136.763
135.055
133.889
131.425
130.718
130.432
128.631
128.541
128.305
127.064
126.859
126.685
126.235
126.071
125.156
125.119
117.198
116.781
114.016
77.444
77.021
76.597
16.014

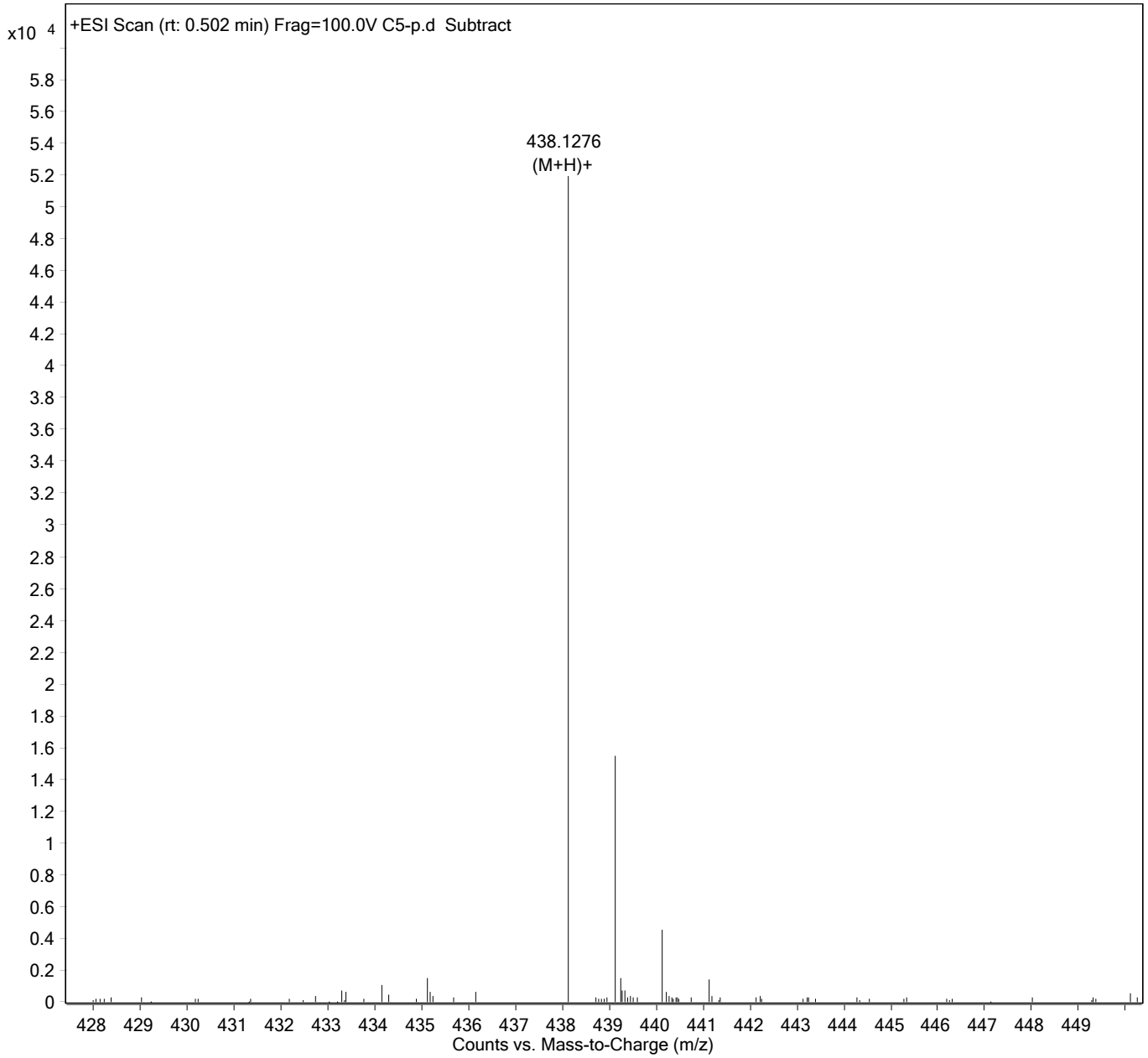


C5

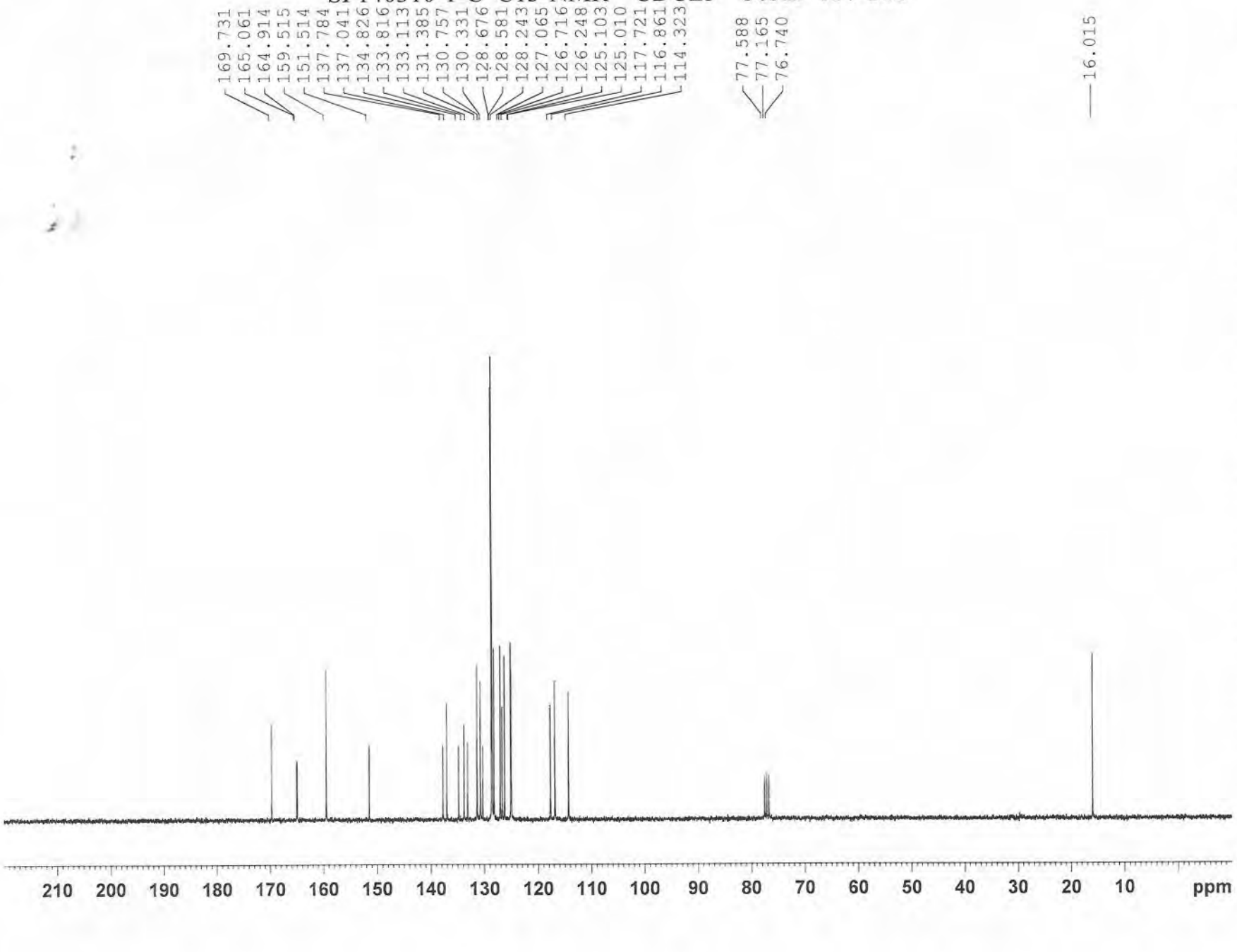
SP131216-5 CDCL3 1HNMR AV300



Sample Name		**Position**	p1A7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C5-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:05:27 PM

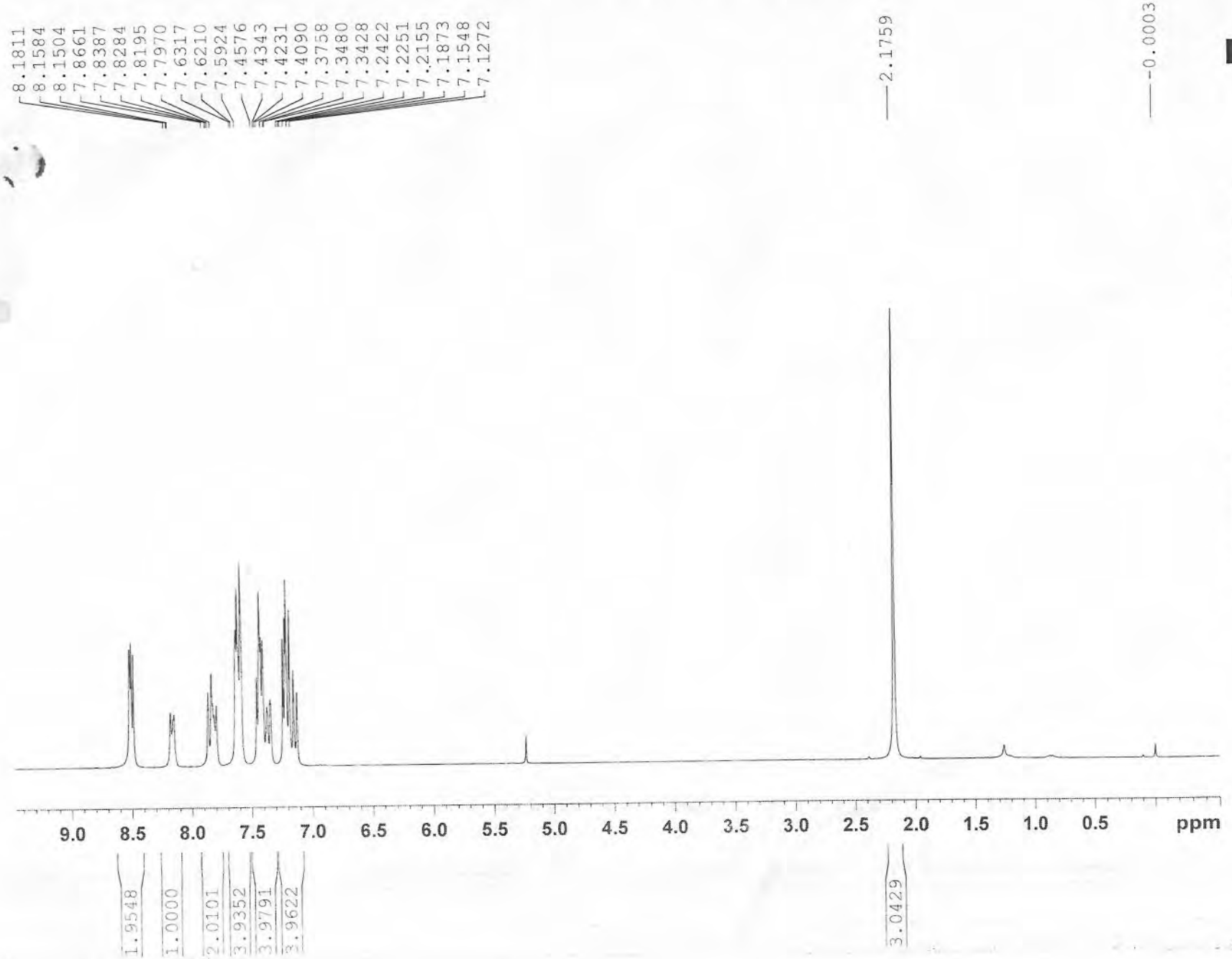


SP140310-1-C C13-NMR CDCL3 303K AV-300

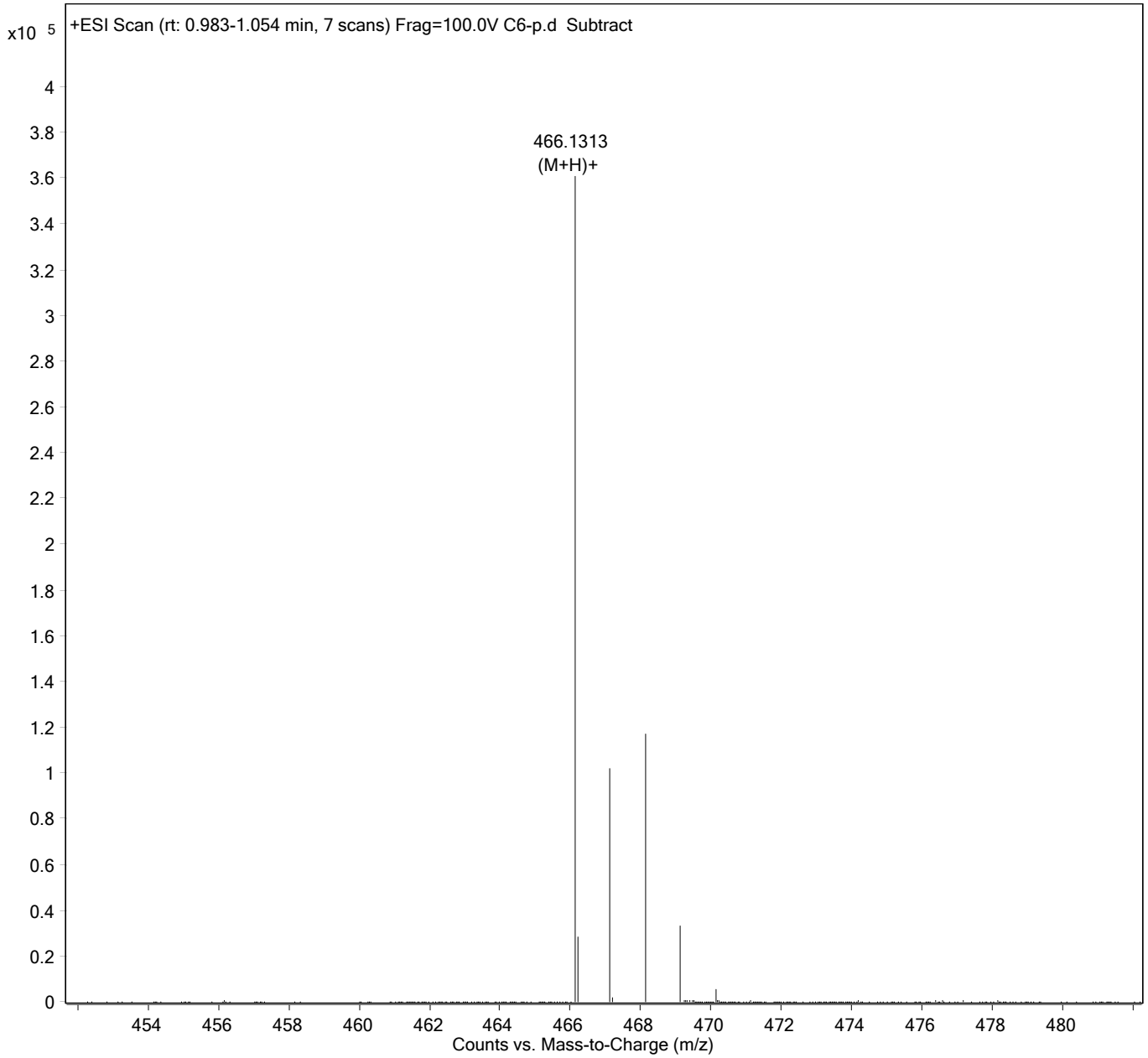


C6

SP140310-1 CDCL3 1HNMR AV300

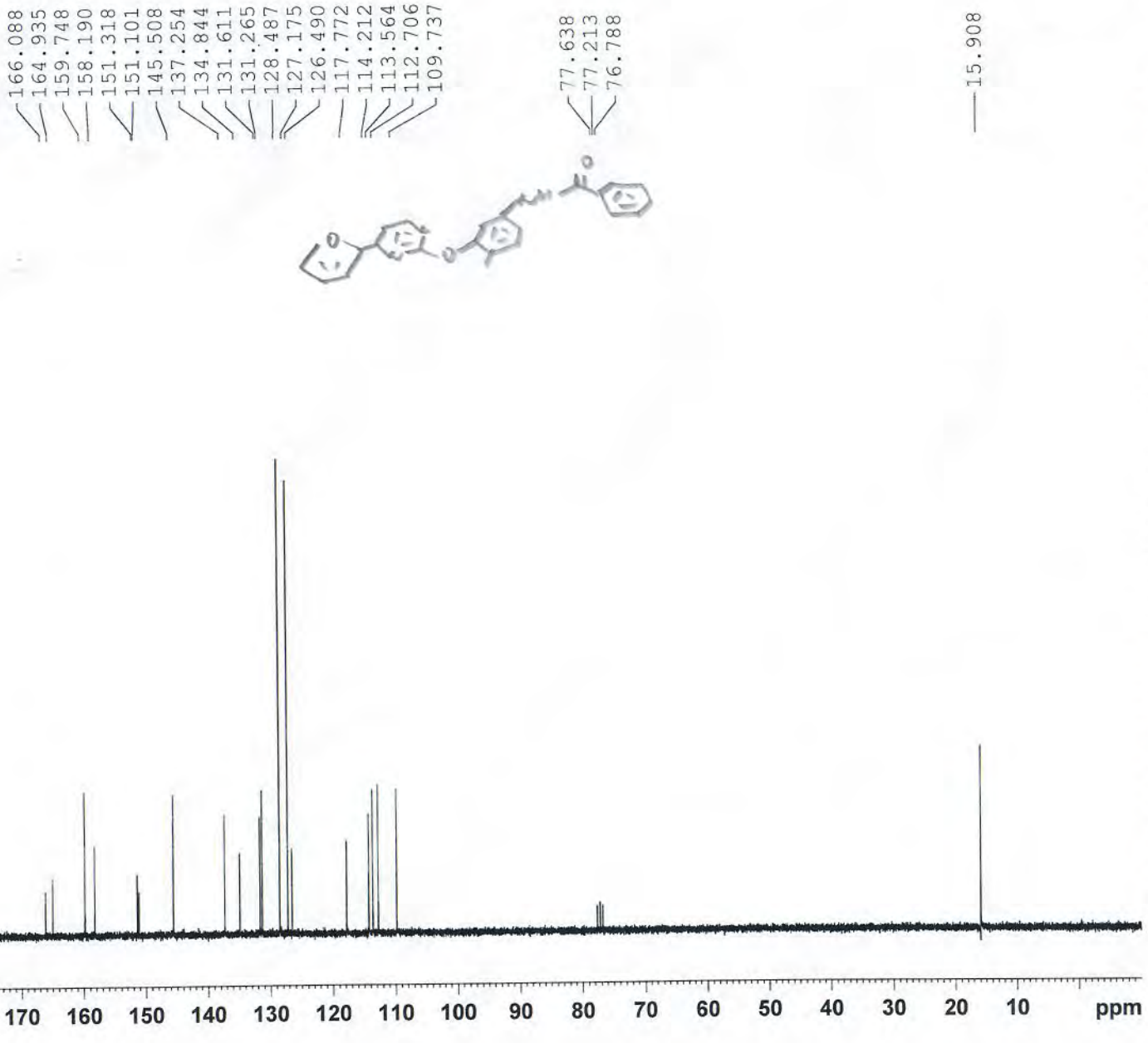


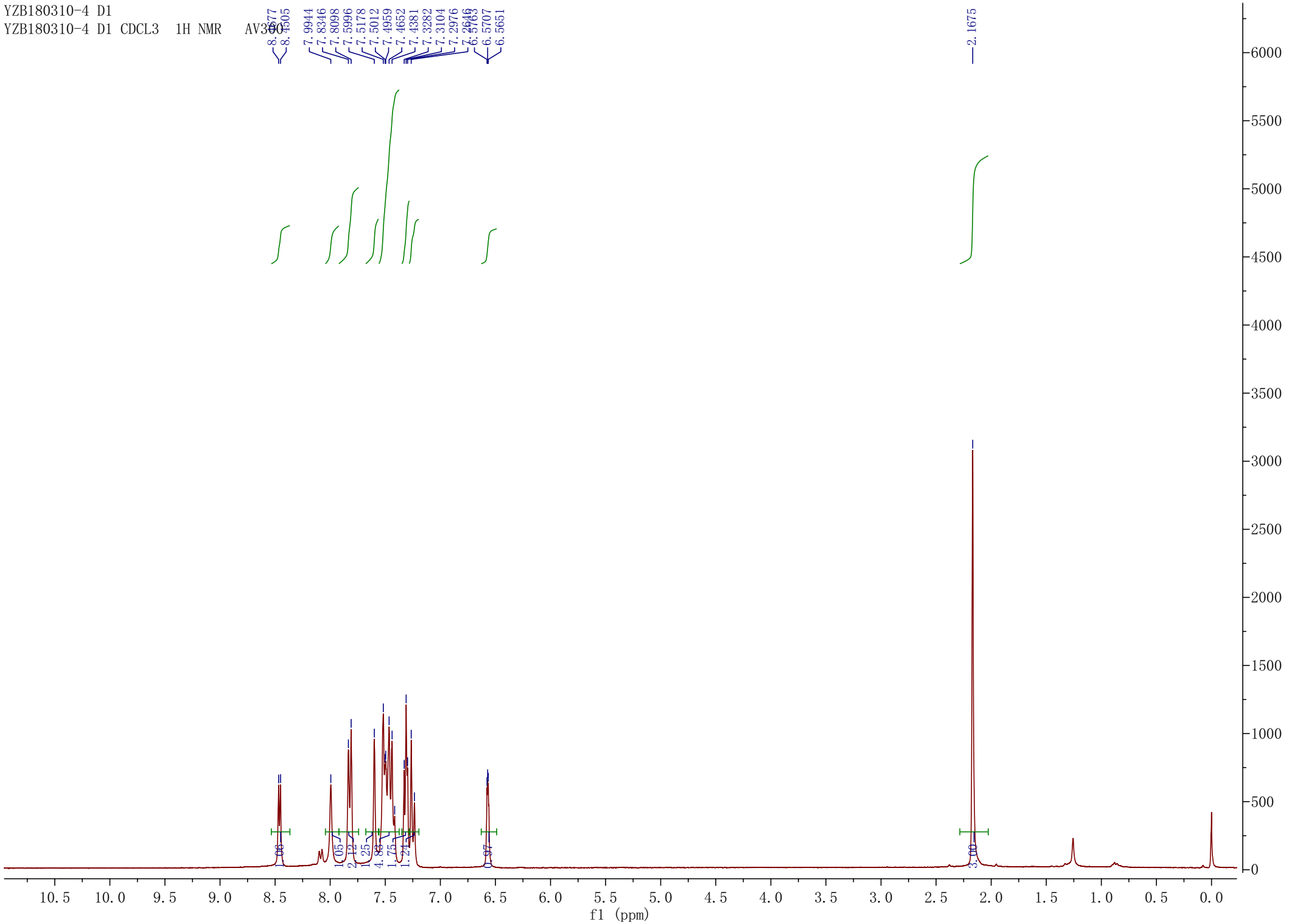
Sample Name		**Position**	p1A8	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	C6-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:11:03 PM



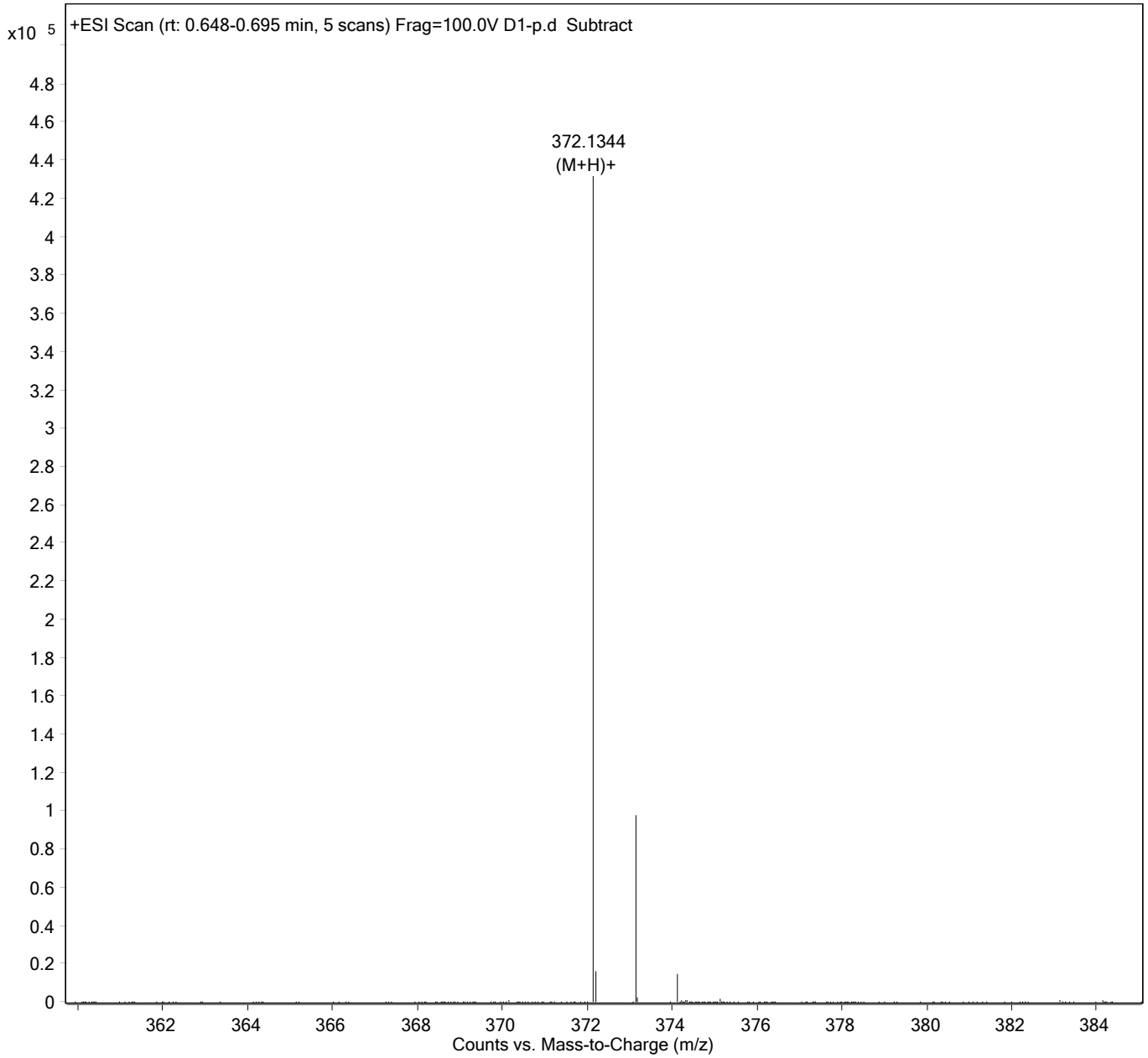
D1

SP131028-2-C C13-NMR CDCL3 303K AV-300



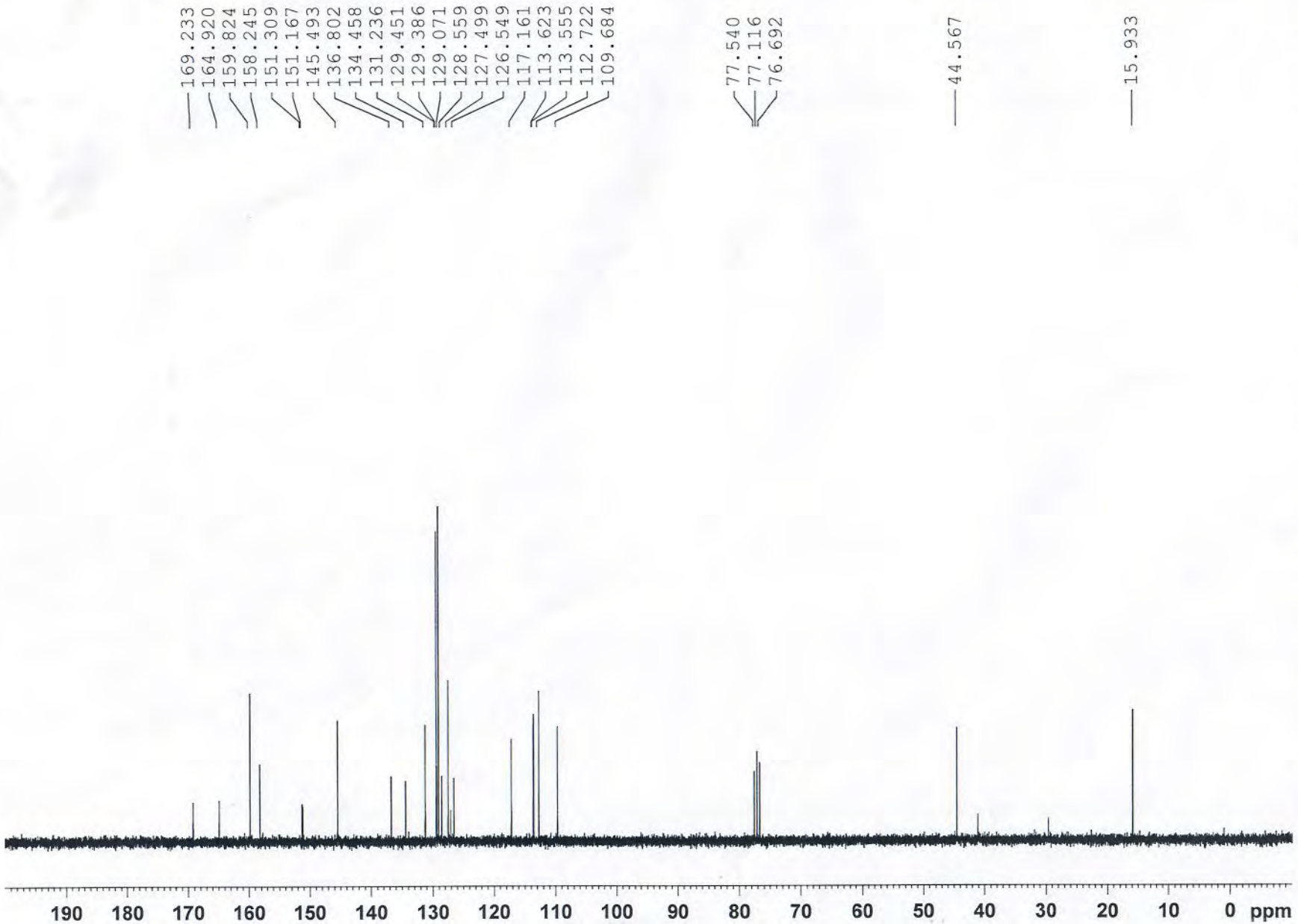

YZB180310-4 D1
YZB180310-4 D1 CDCL3 1H NMR AV300
8.4677
8.4505
7.9944
7.8346
7.8098
7.5996
7.5178
7.5012
7.4959
7.4652
7.4381
7.3282
7.3104
7.2976
6.5707
6.5651
2.1675
1.08
1.05
2.12
1.25
4.83
1.75
1.21
0.97
3.00
f1 (ppm)

Sample Name		**Position**	p1A9	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:13:43 PM



D2

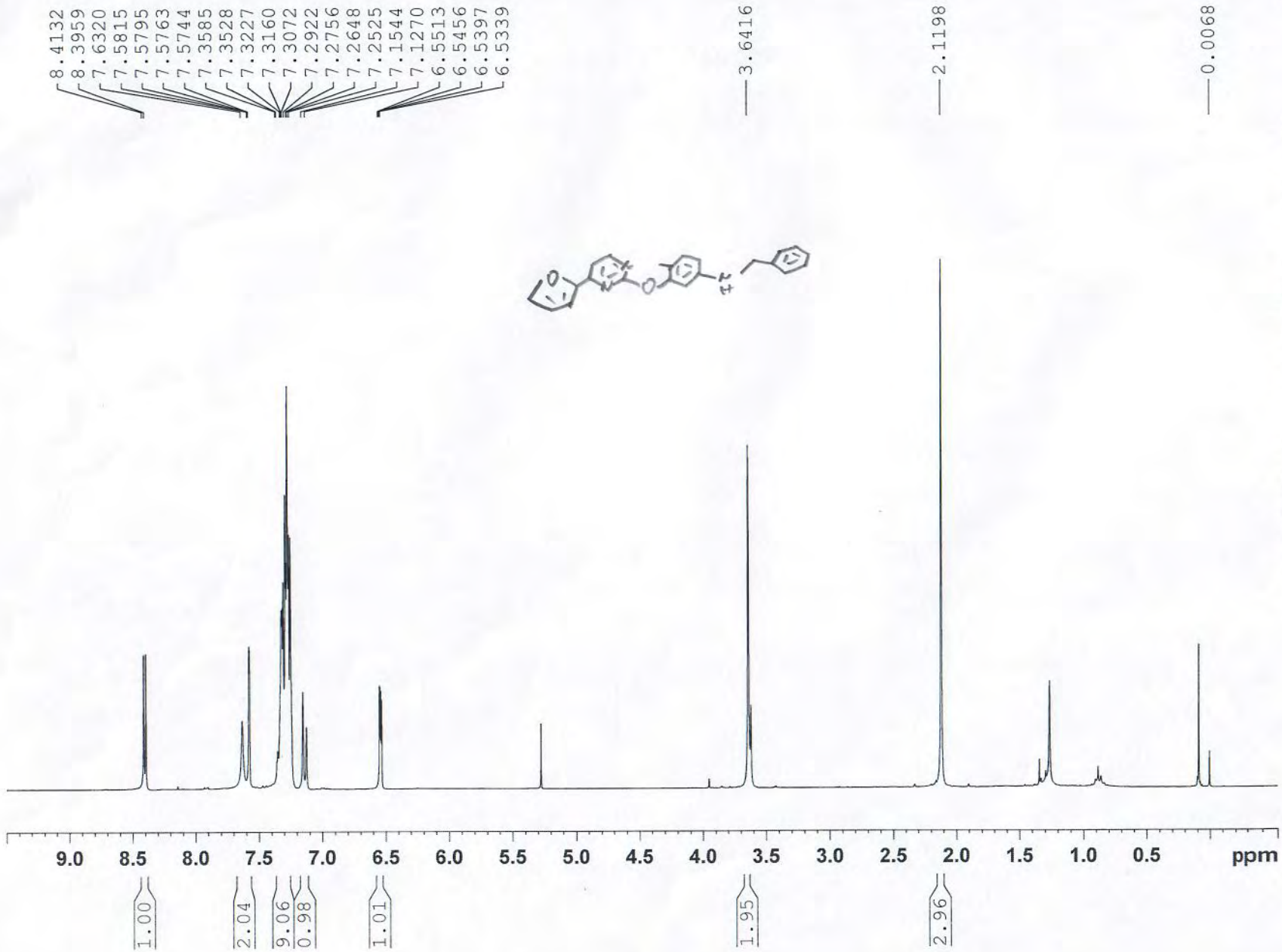
SP130116-2-C C13-NMR CDCL3 303K AV-300



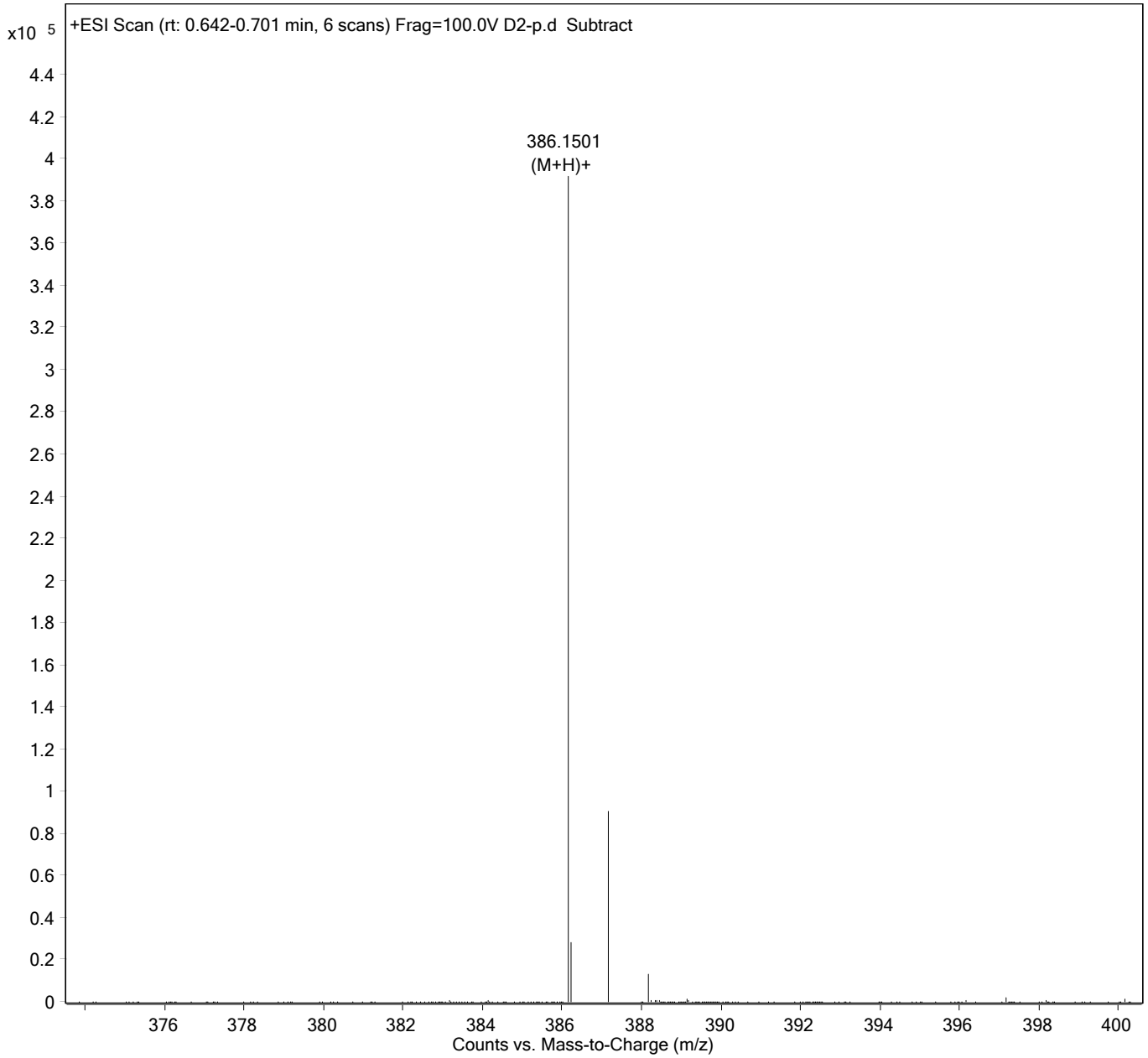
140

D2

SP130116-2 CDCL3 1HNMR AV300

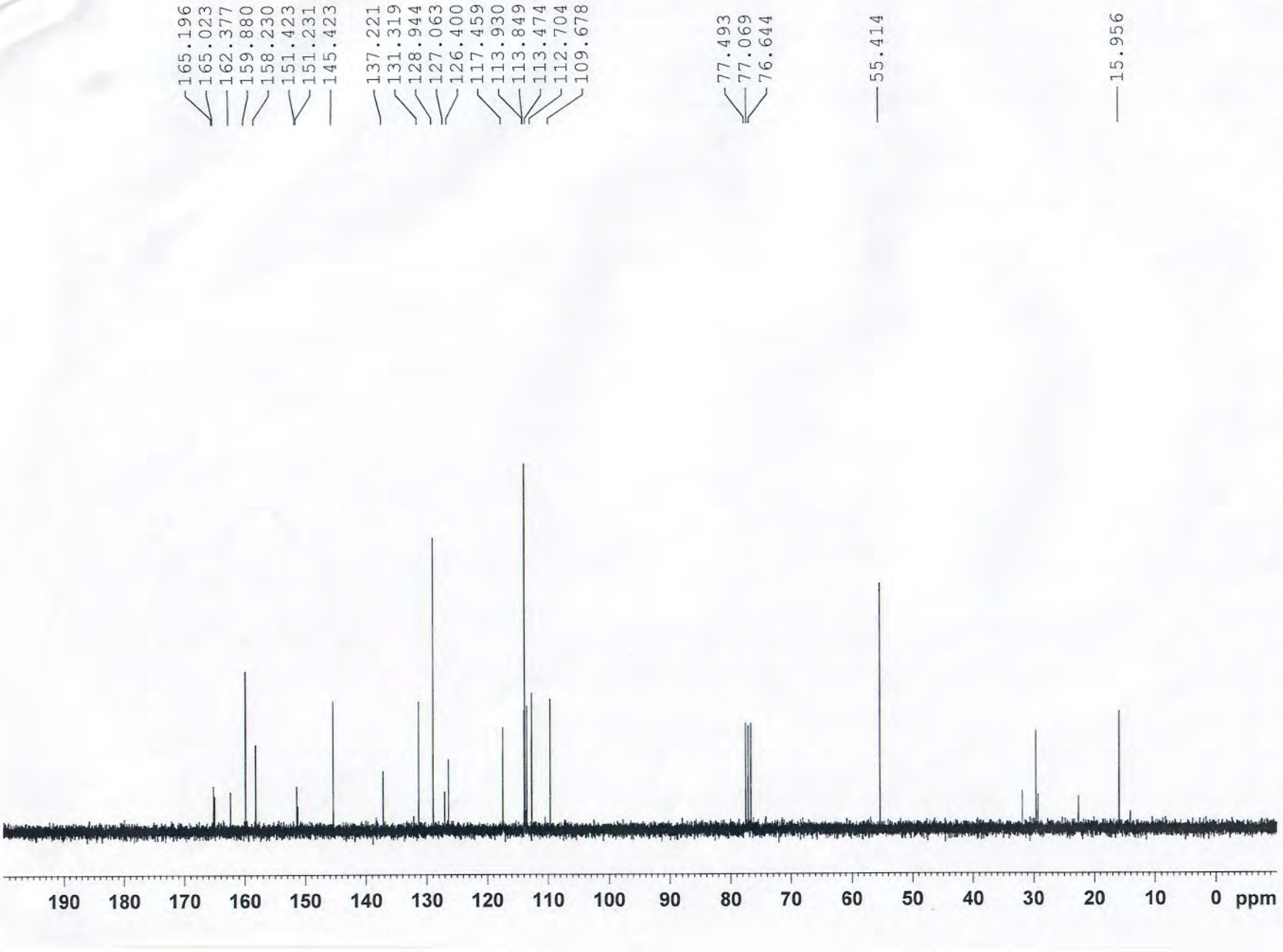


Sample Name		**Position**	p1B1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:16:05 PM



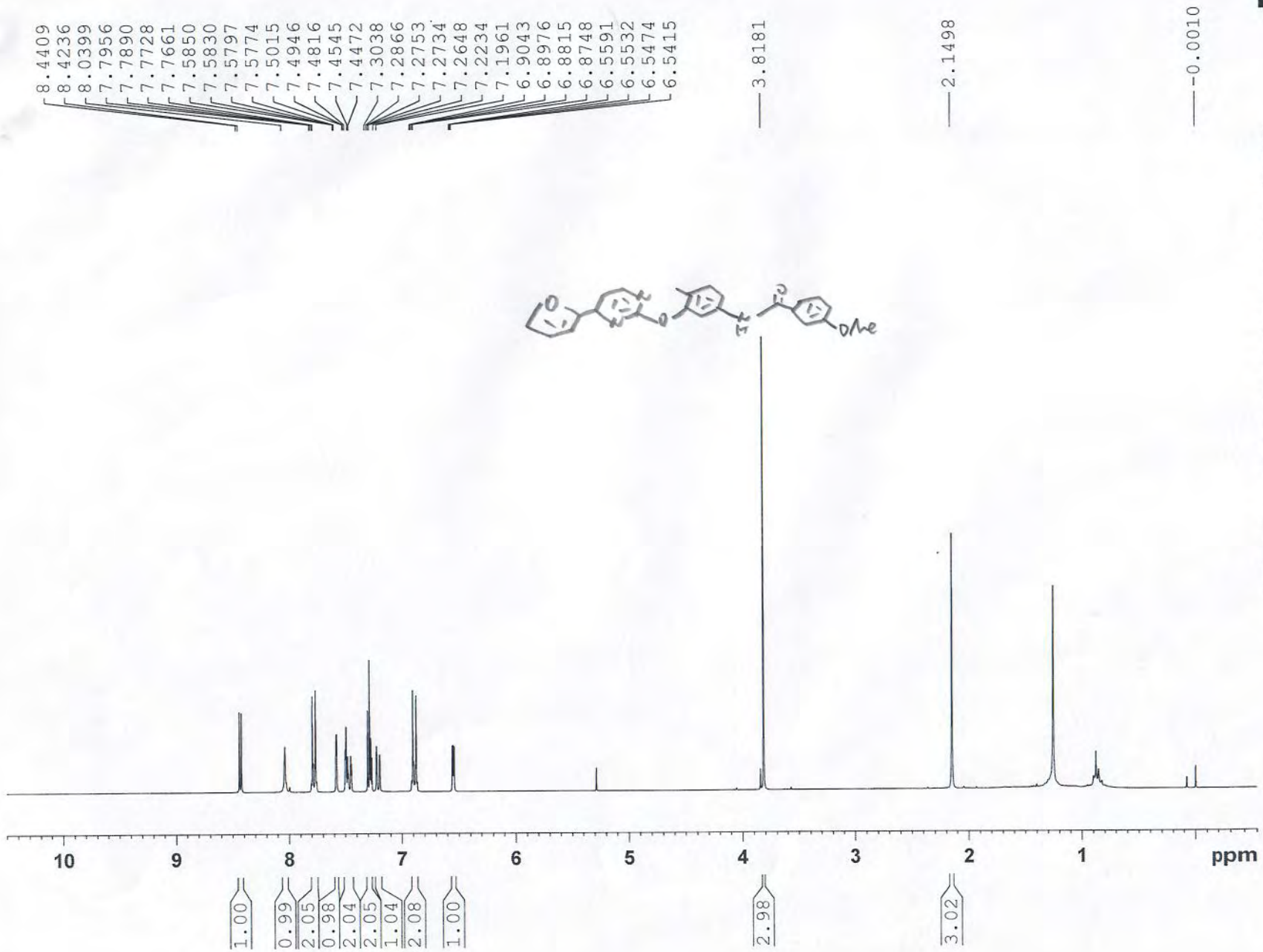
D3

SP130116-4-C C13-NMR CDCL3 303K AV-300

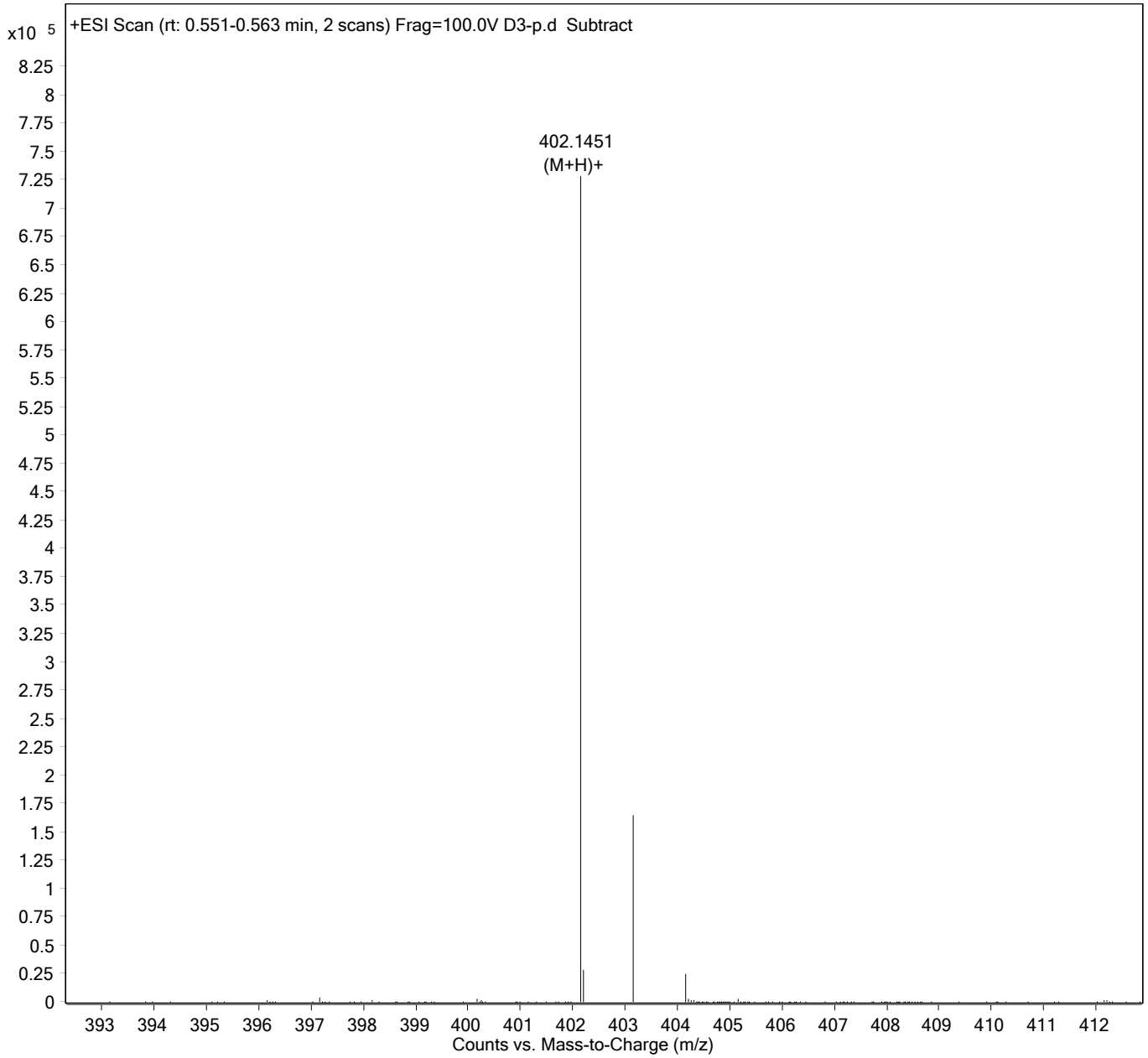


D3

SP130116-4 CDCL3 1HNMR AV300

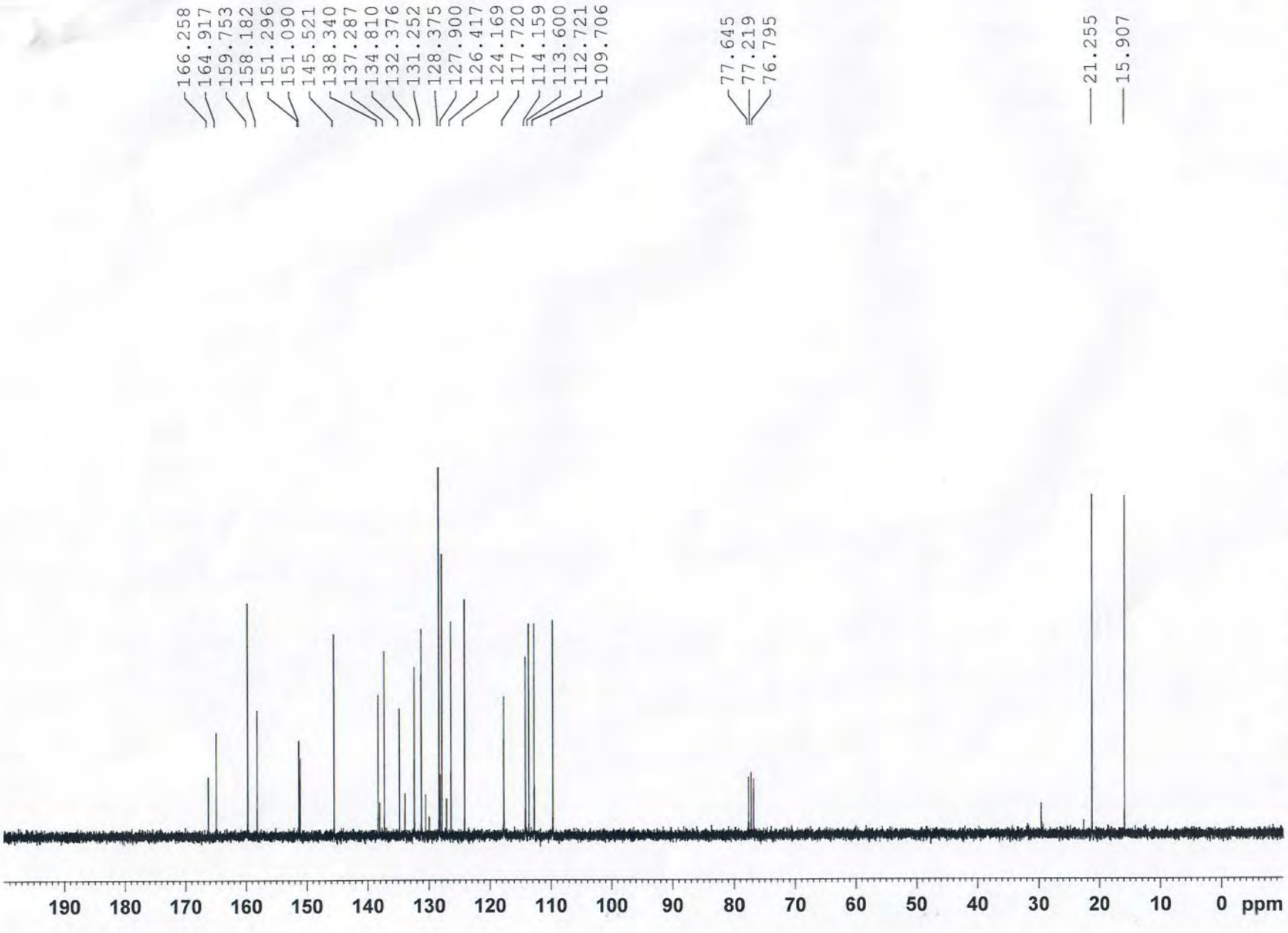


Sample Name		**Position**	p1B2	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:18:57 PM



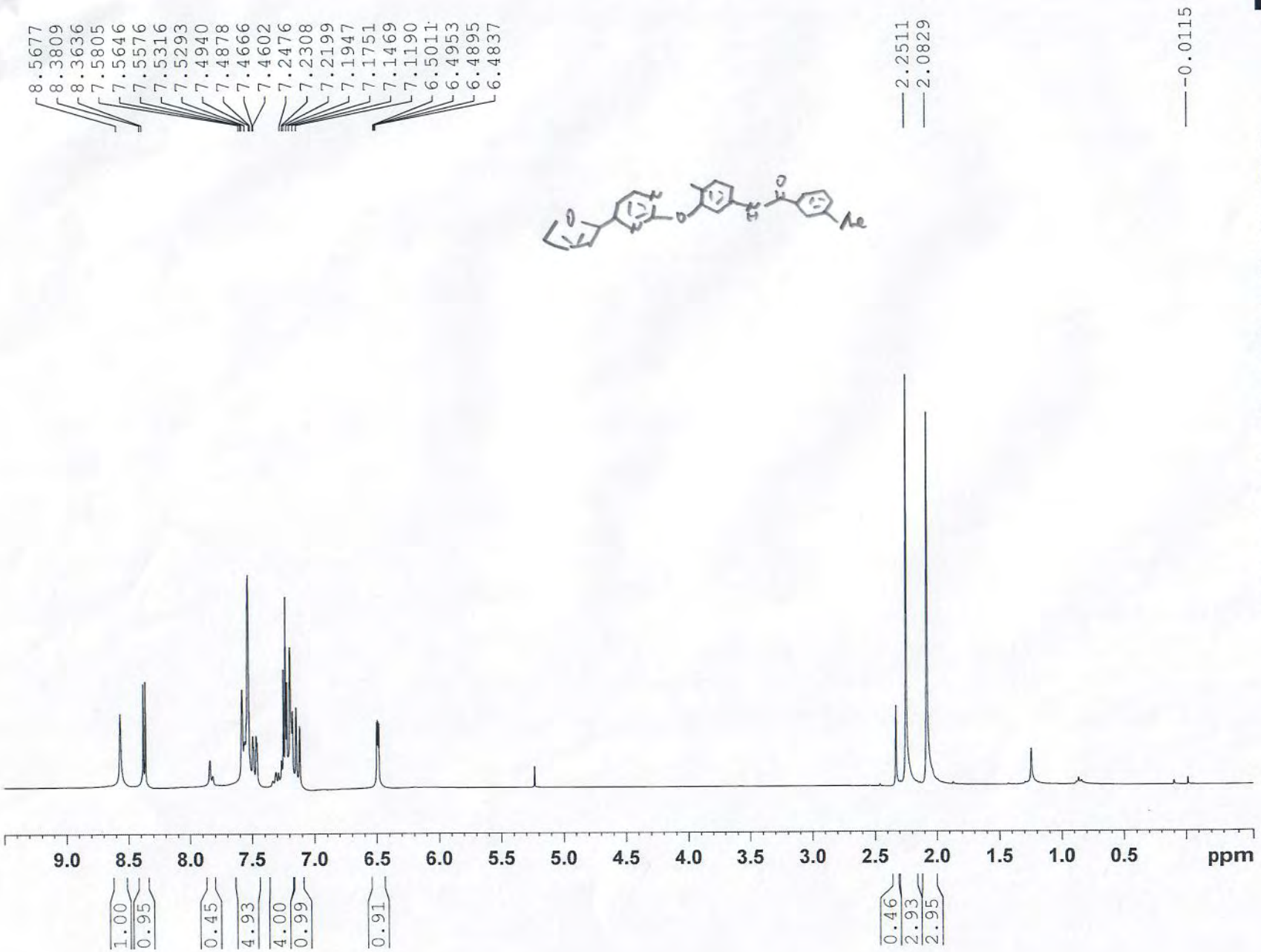
D4

SP130116-3-C C13-NMR CDCL3 303K AV-300

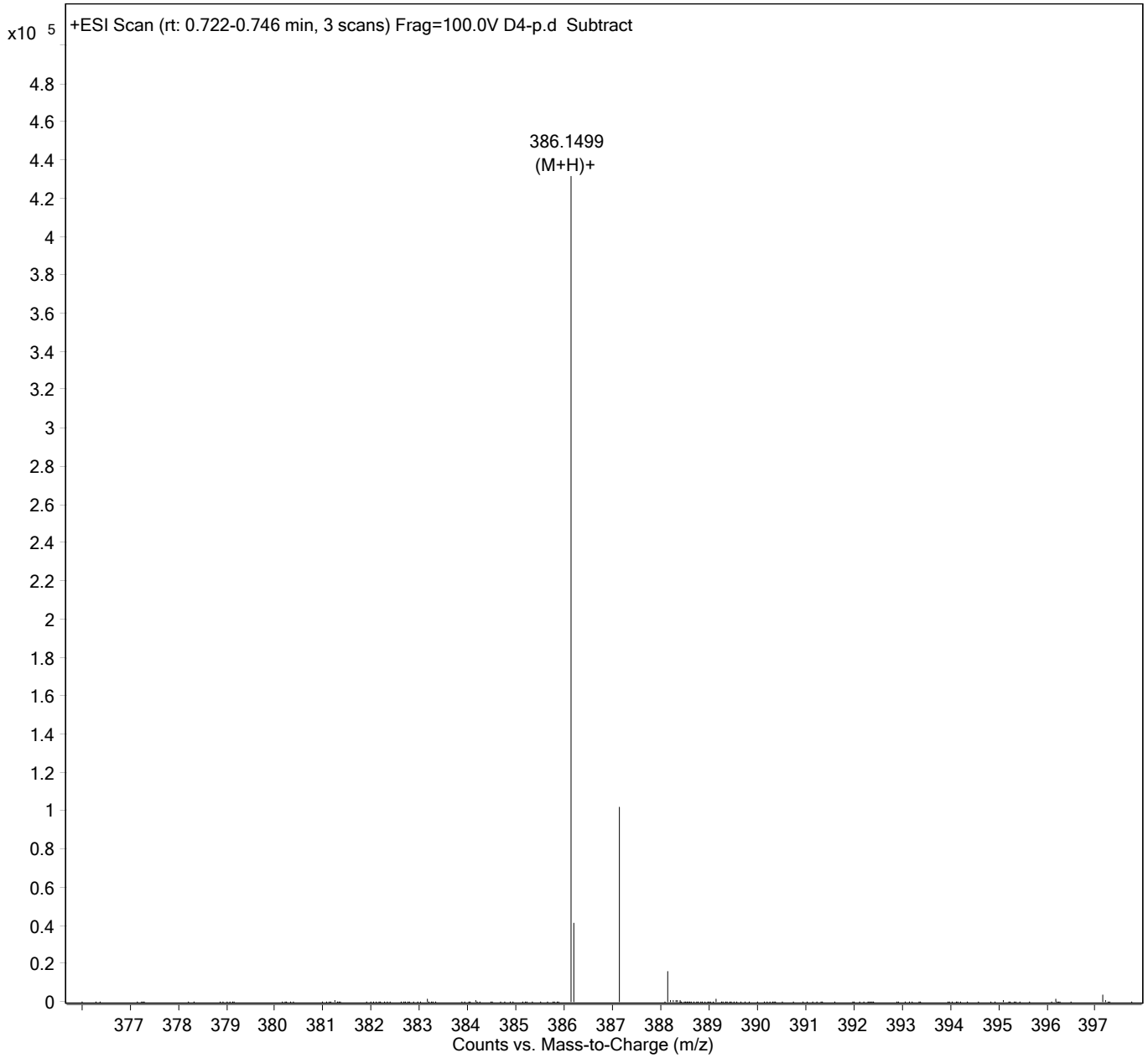


D4

SP130116-3 CDCL3 1HNMR AV300

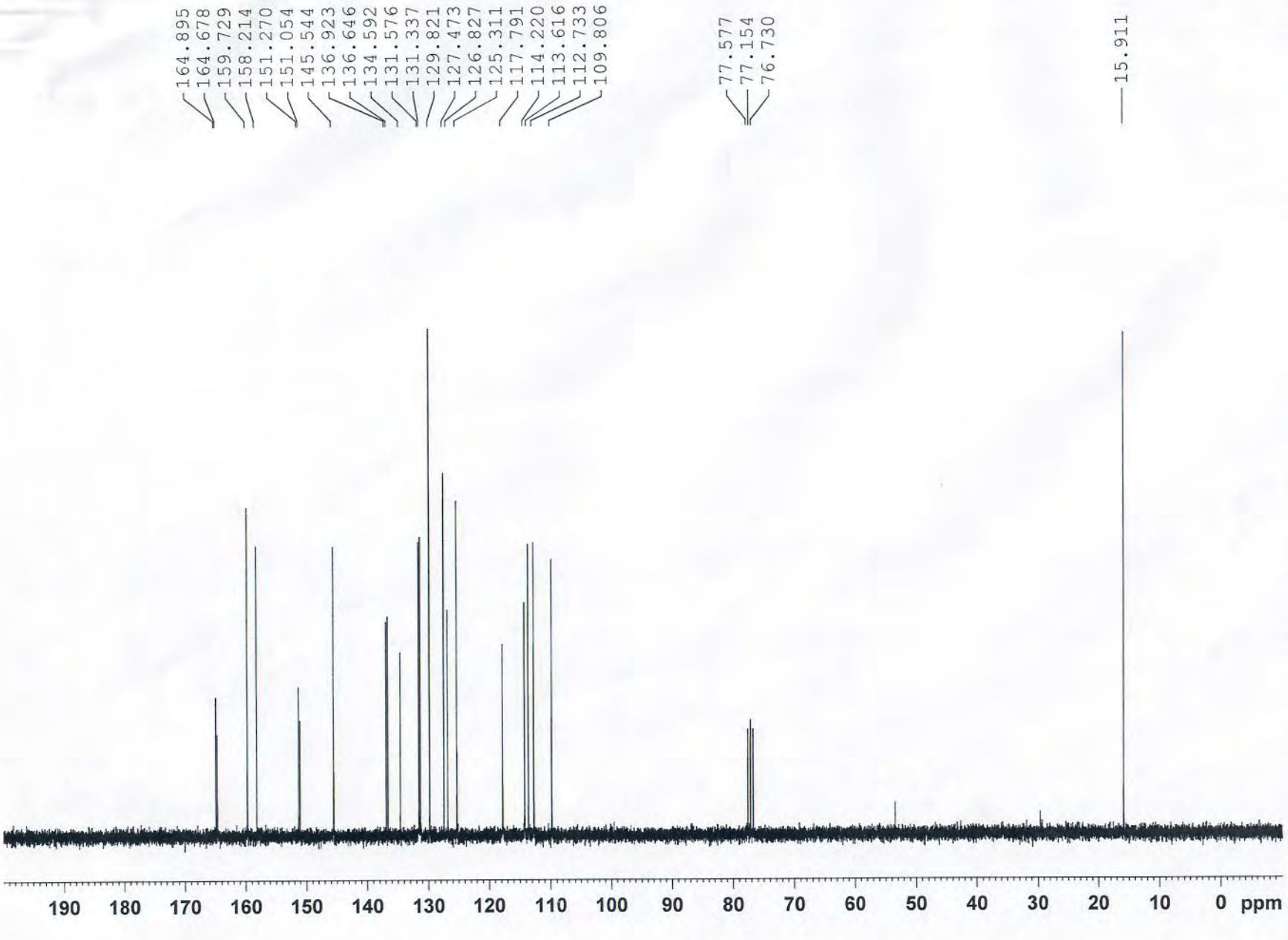


Sample Name		**Position**	p1B3	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D4-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:21:07 PM



D5

SP130116-5-C C13-NMR CDCL3 303K AV-300



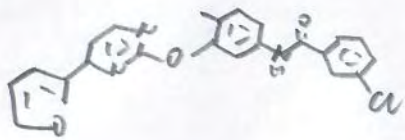
D5

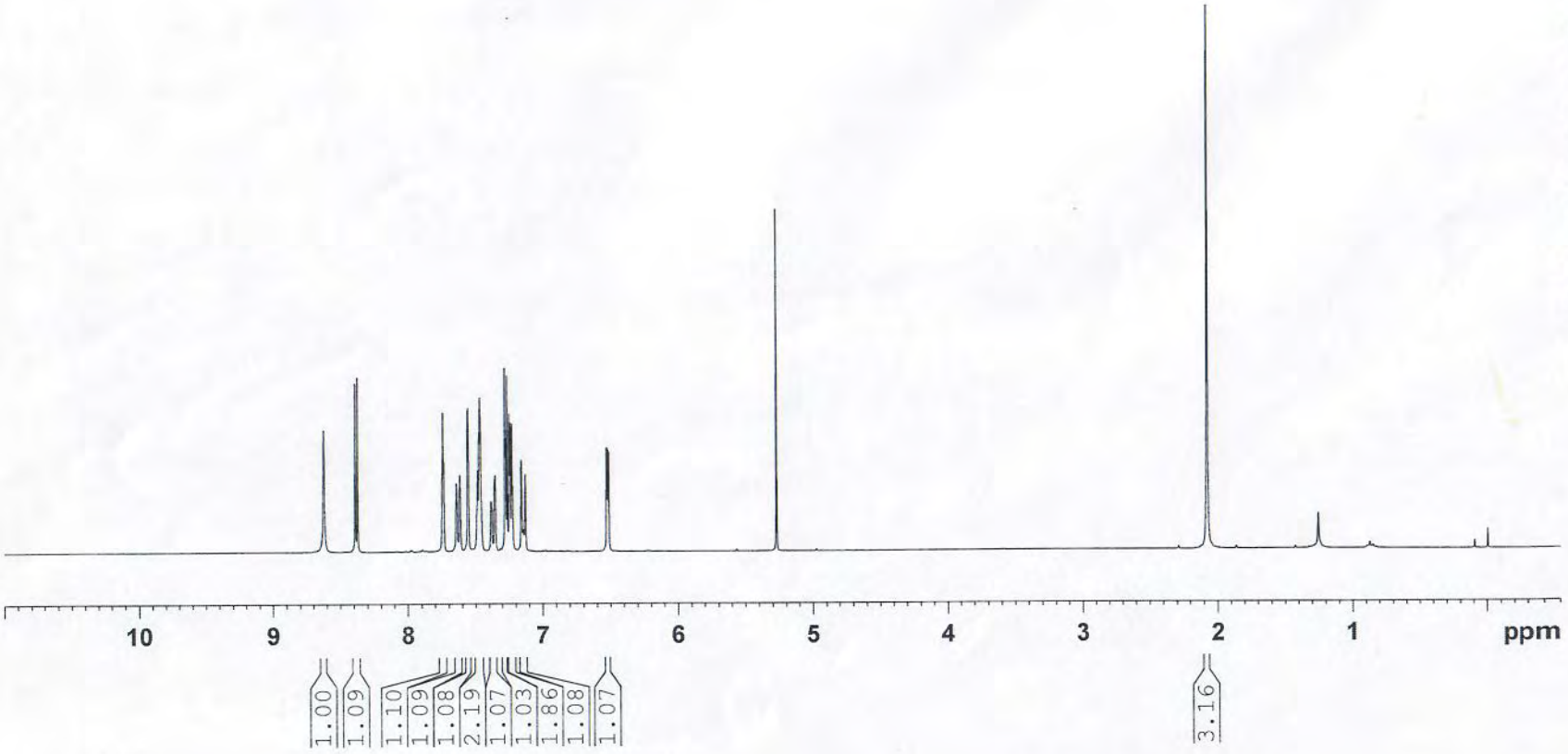
SP130116-5 CDCL3 1HNMR AV300

8.6230
8.3903
8.3729
7.7488
7.7431
7.7373
7.6440
7.6179
7.5588
7.5555
7.5536
7.4849
7.4745
7.4676
7.3882
7.3851
7.3819
7.3785
7.3617
7.3584
7.3553
7.3520
7.2812
7.2753
7.2639
7.2486
7.2419
7.2403
7.2301
7.2285
7.2228
7.1582
7.1283
6.5305
6.5247
6.5188
6.5130

2.0803

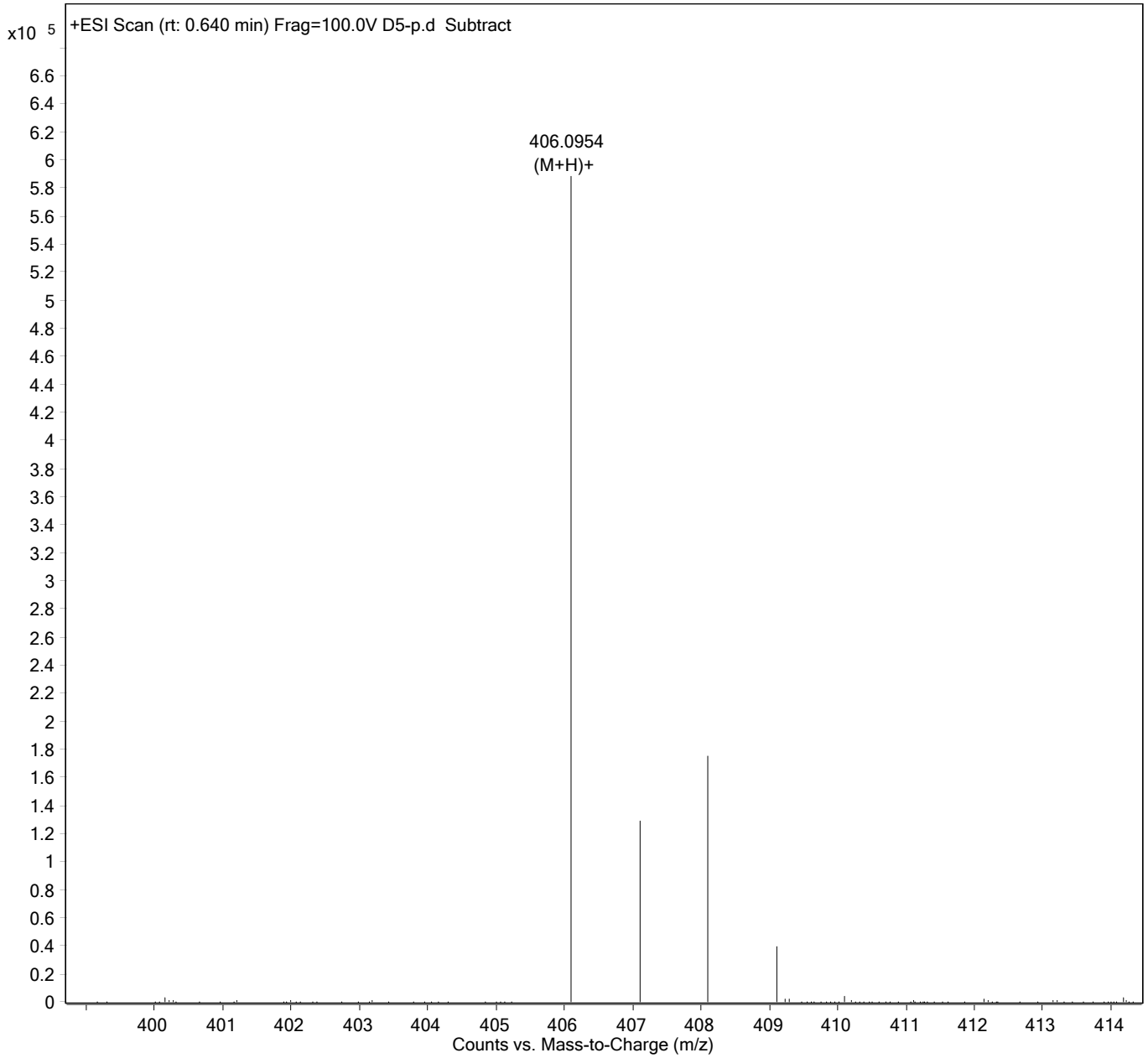
-0.0014





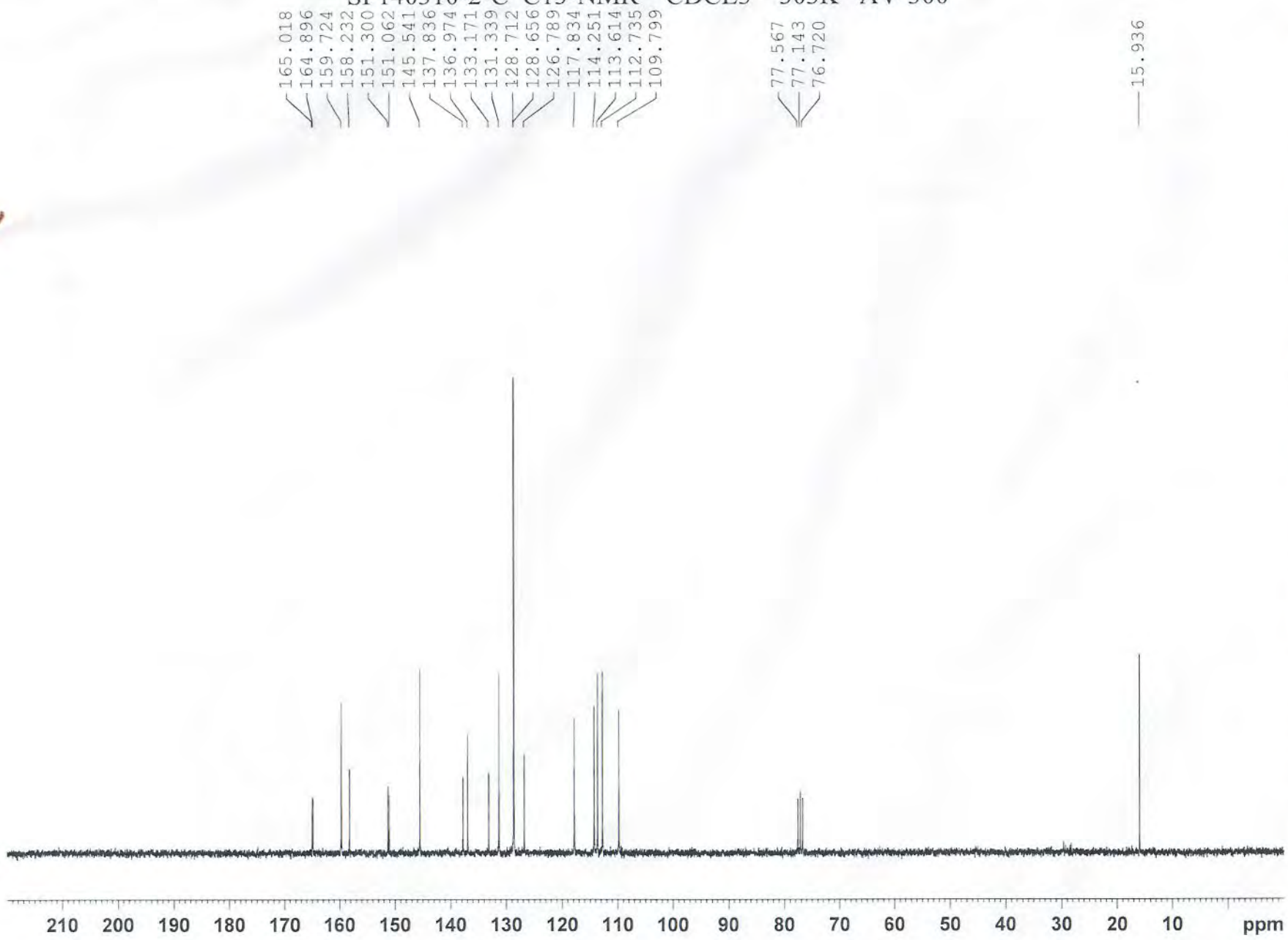
150

Sample Name		**Position**	p1B4	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D5-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:23:06 PM



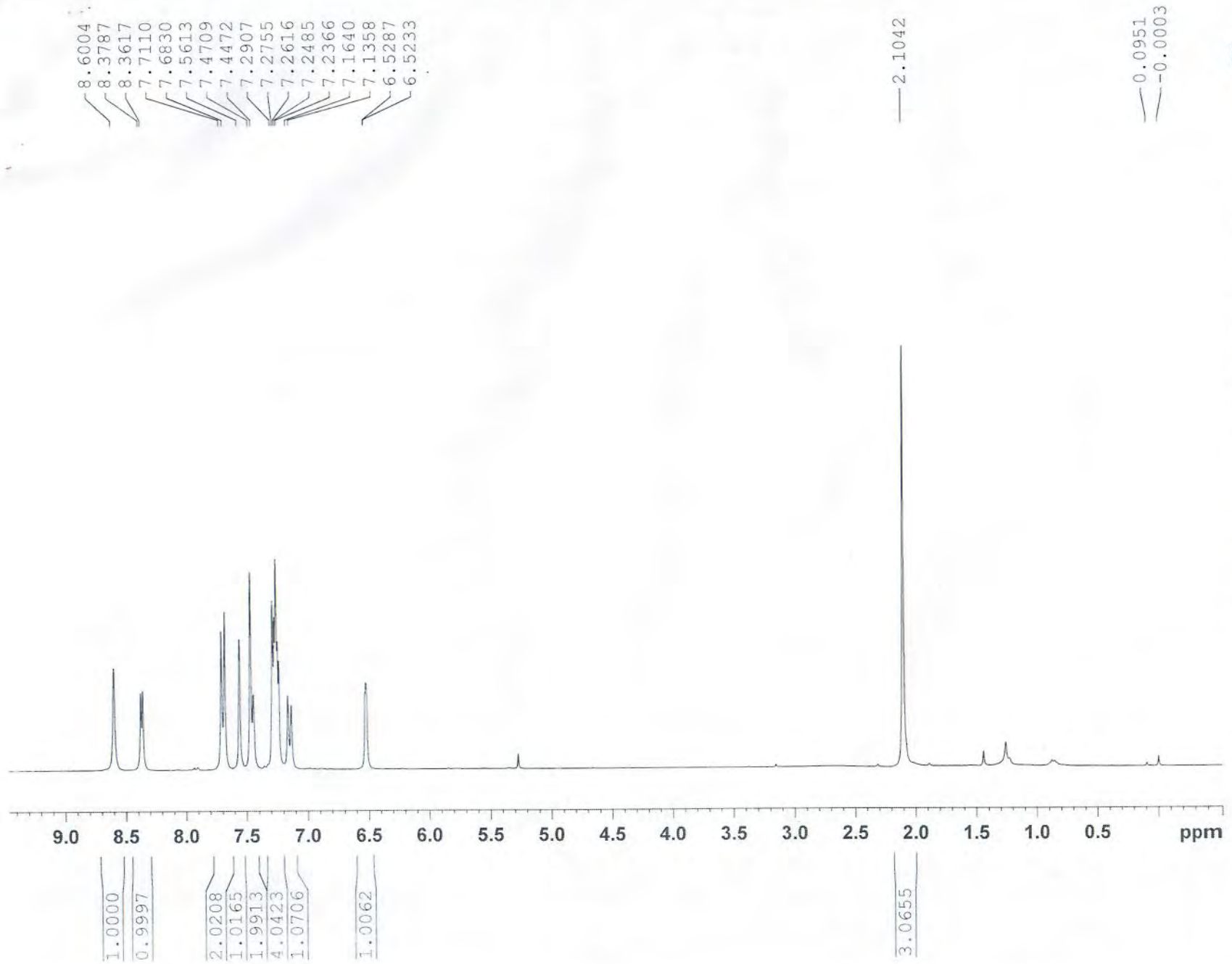
06

SP140310-2-C C13-NMR CDCL3 303K AV-300

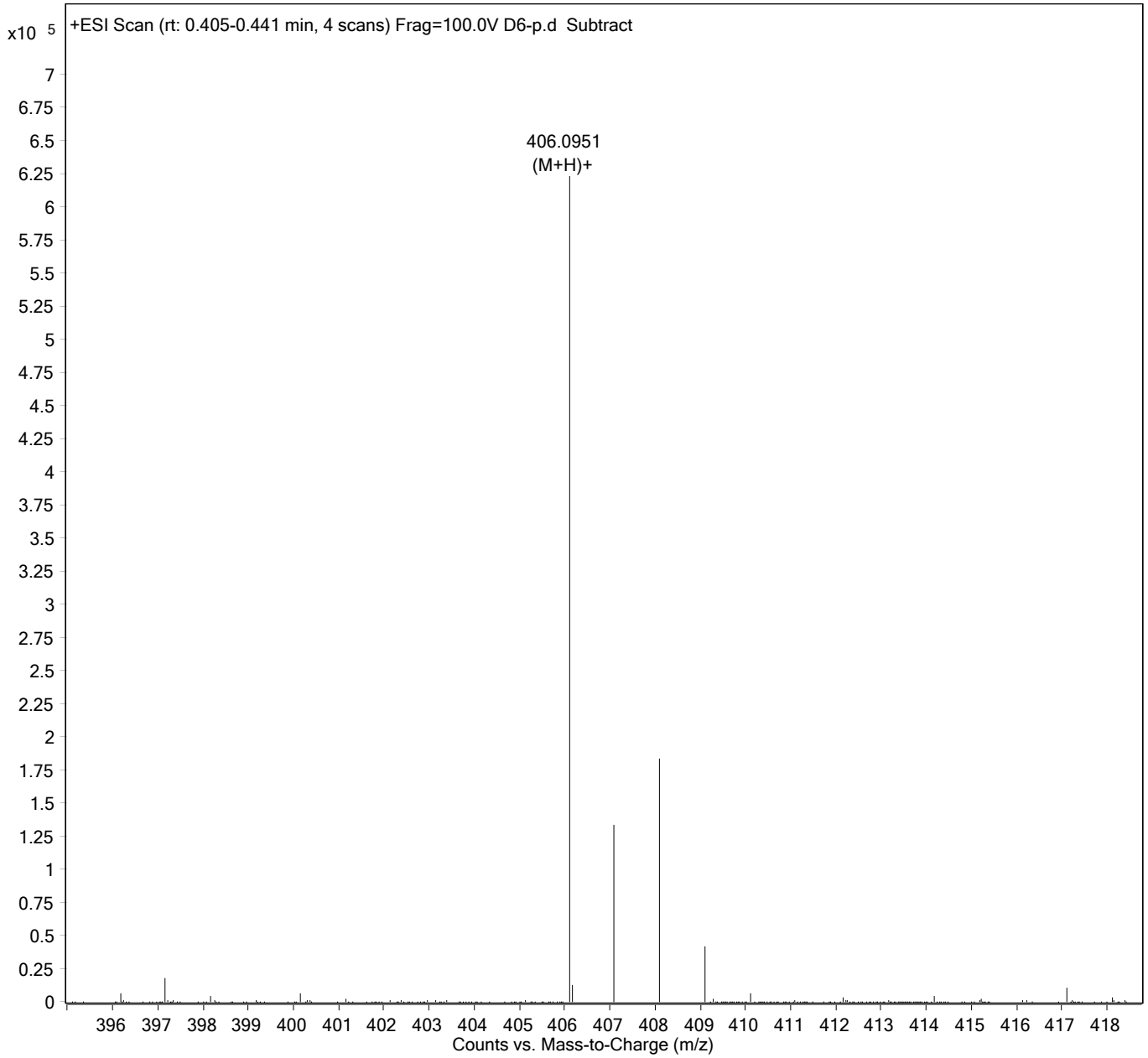


D6.

SP140310-2 CDCL3 1HNMR AV300

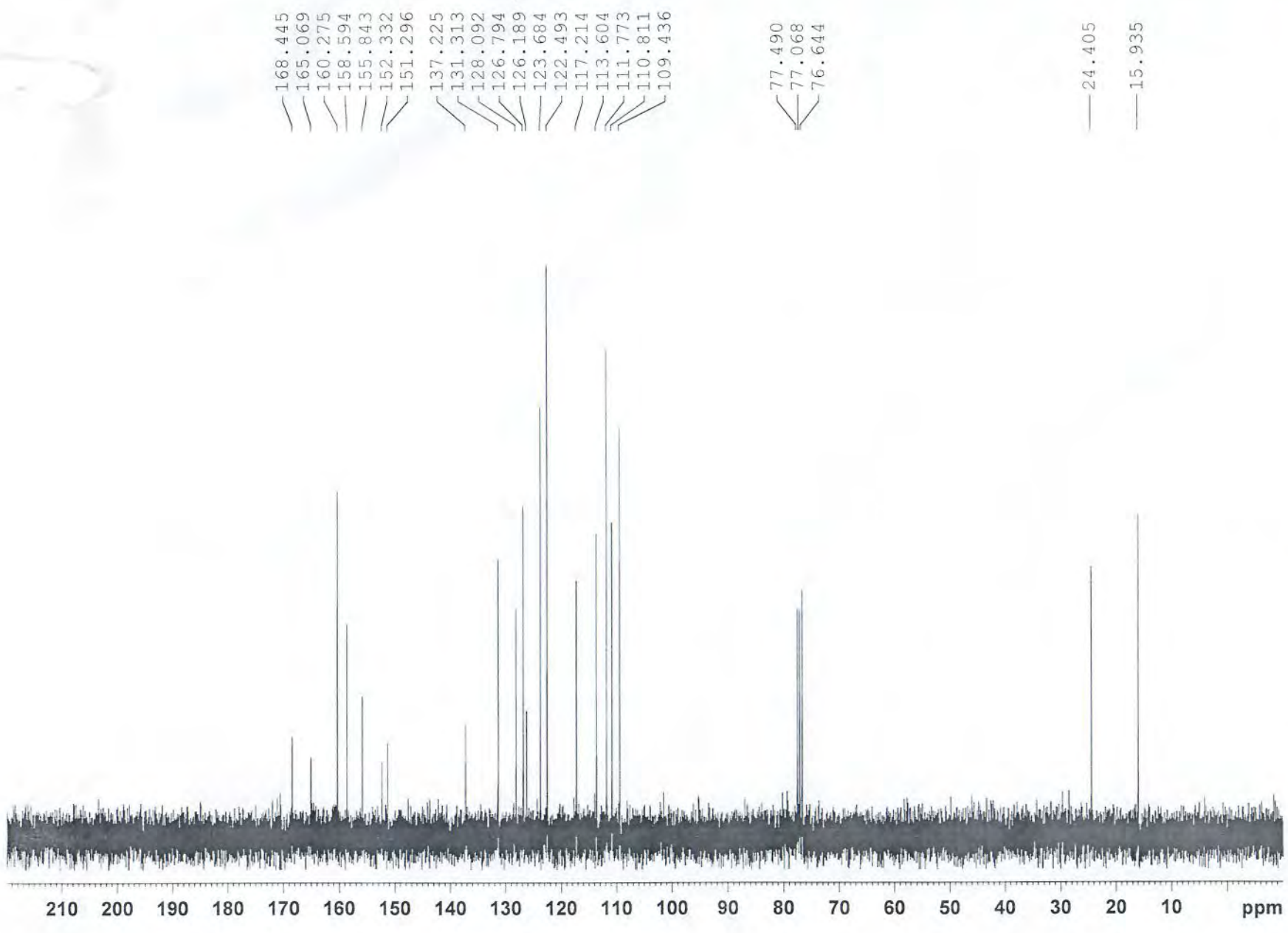


Sample Name		**Position**	p1B5	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	D6-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:25:23 PM



E1

SP130609-2-C C13-NMR CDCL3 303K AV-300



E1

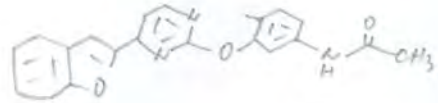
SP20130609-2 CDCL3 1HNMR AV300

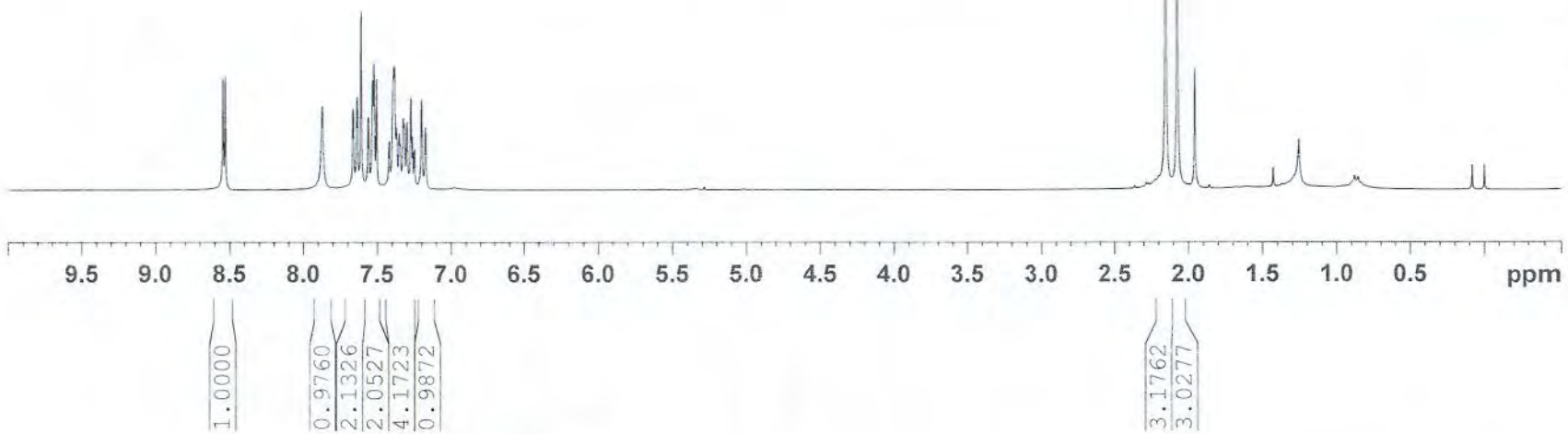
8.8305
8.5471
8.5300
8.2248
7.8748
7.8062
7.6639
7.6382
7.6104
7.5601
7.5319
7.5229
7.5056
7.4185
7.3888
7.3815
7.3706
7.3508
7.3233
7.3172
7.2987
7.2742
7.2634
7.2491
7.2007
7.1733
6.9791
5.3478
5.2851
5.0193

3.6248

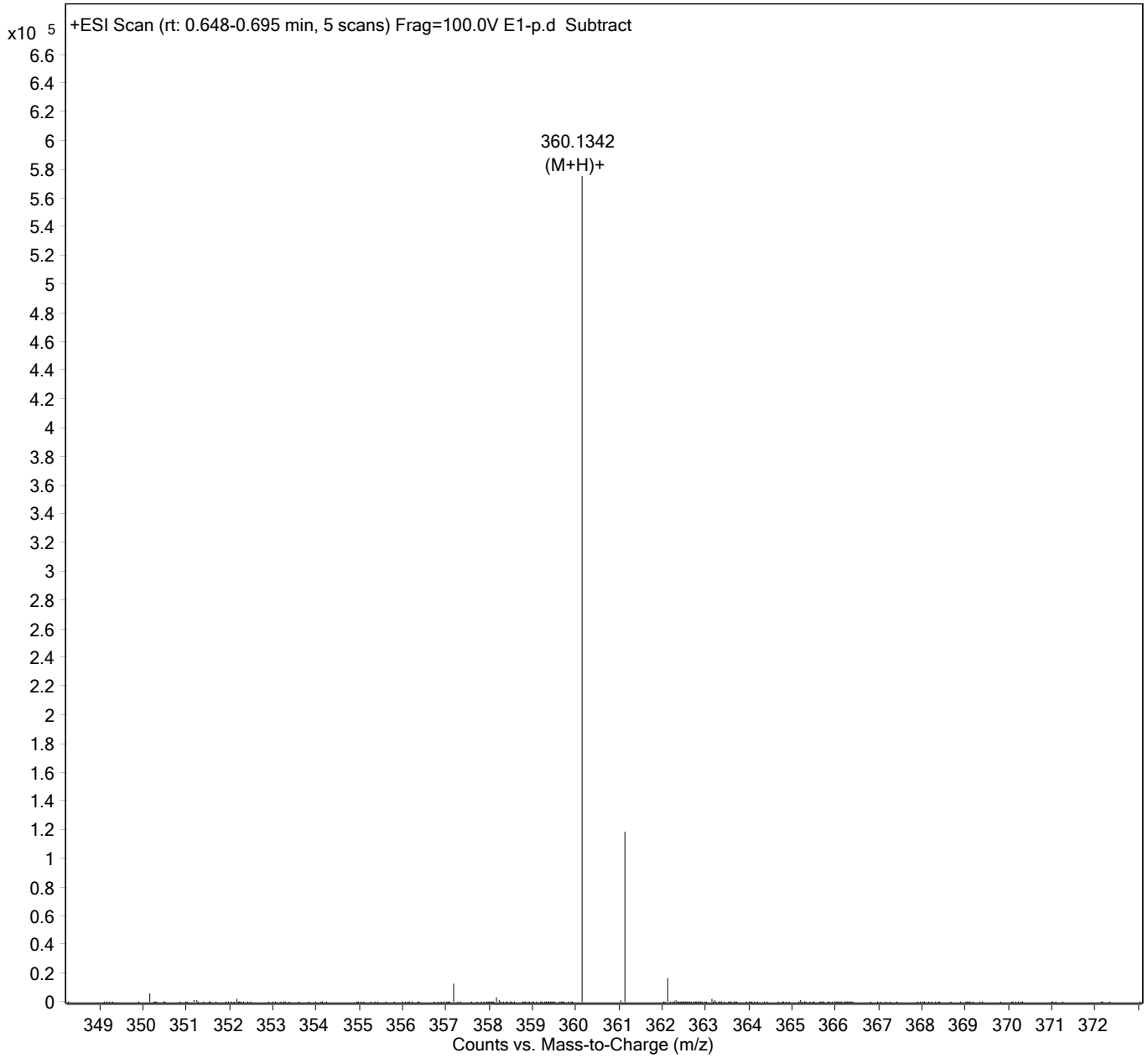
2.3640
2.2853
2.2709
2.1531
2.0735
1.9558
1.8582
1.6824
1.5912
1.4297
1.3665
1.2558
0.8782
0.8557

0.0812
-0.0004



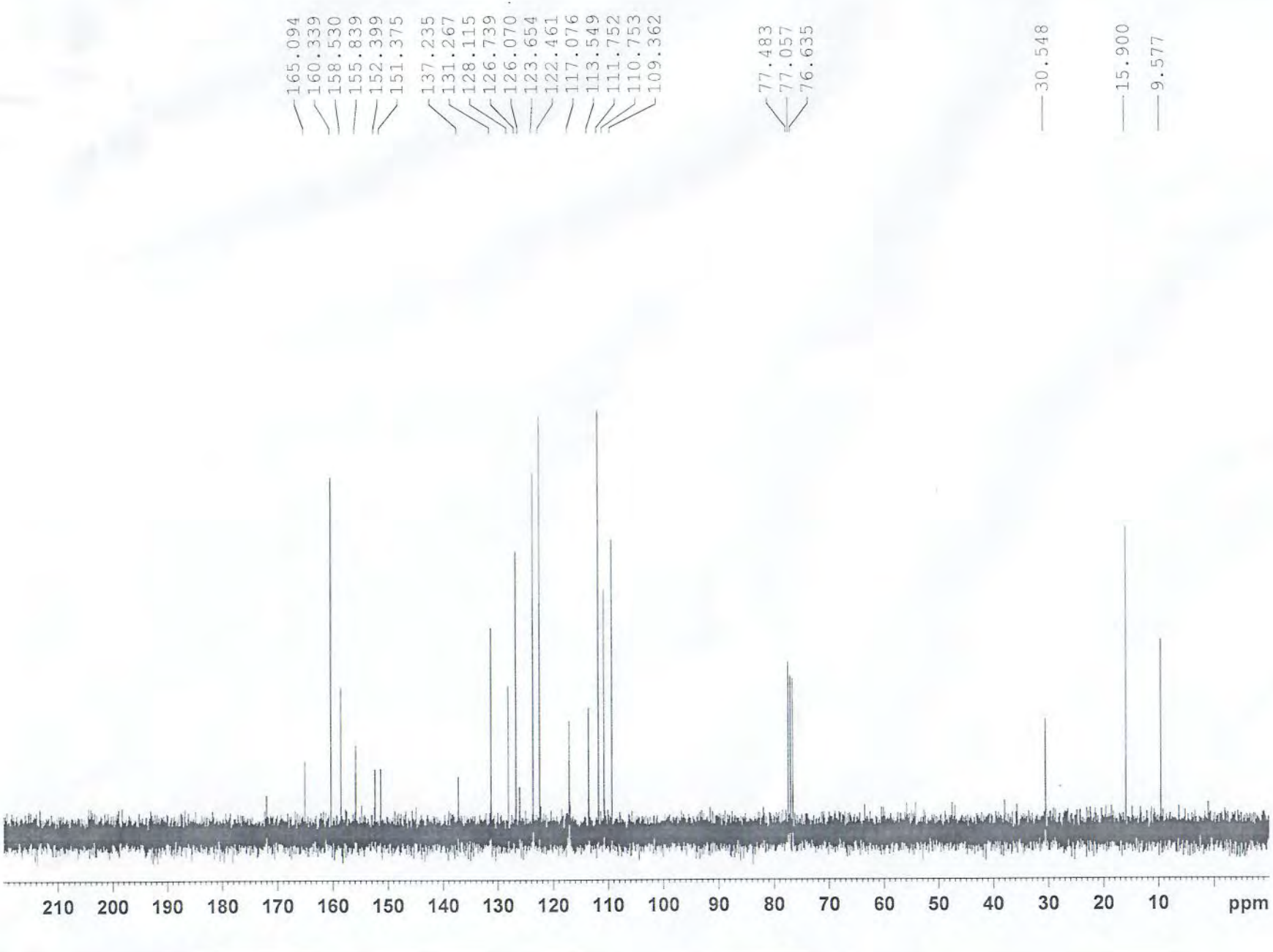


Sample Name		**Position**	p1B6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:27:24 PM



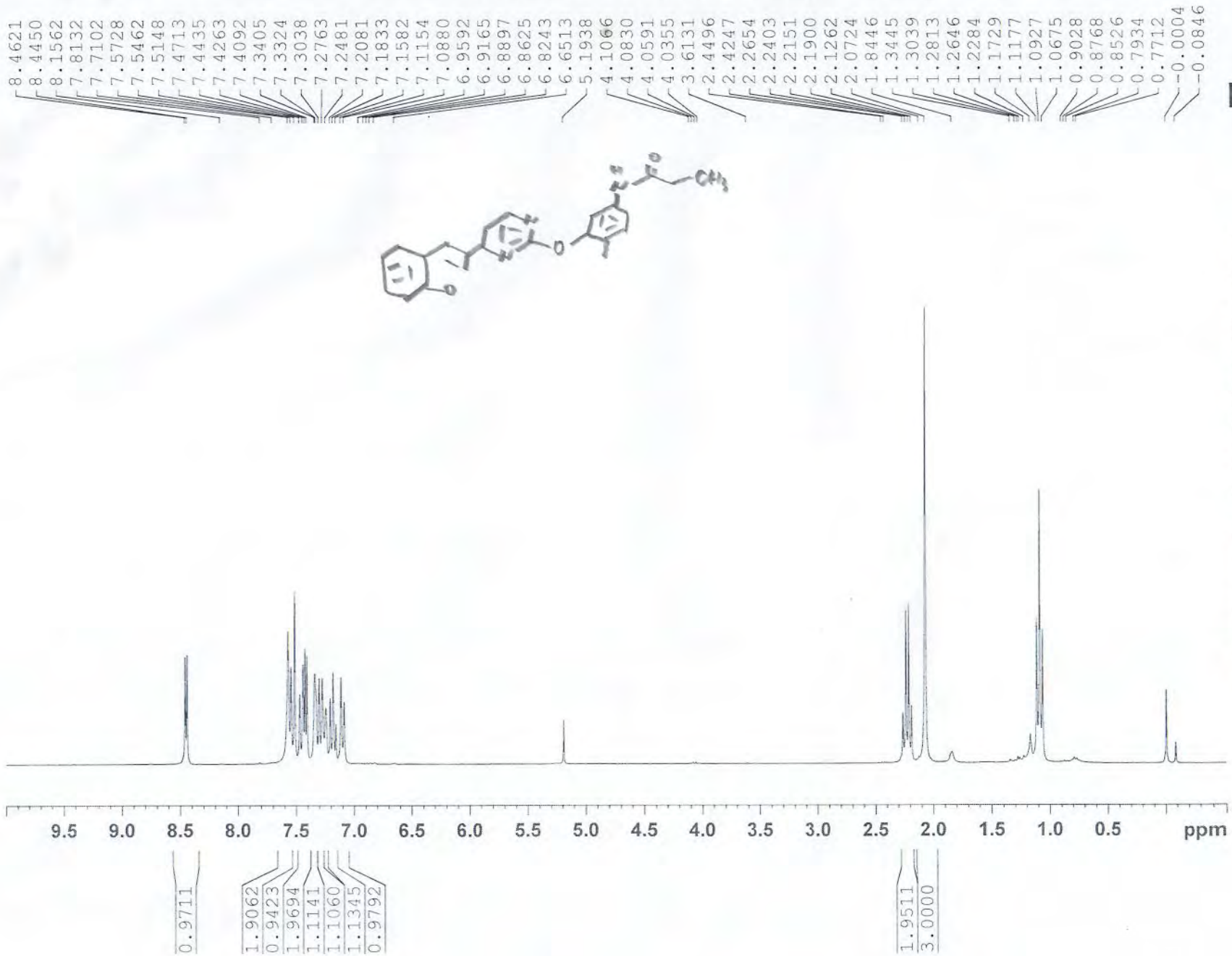
E2

SP130619-1-C C13-NMR CDCL3 303K AV-300

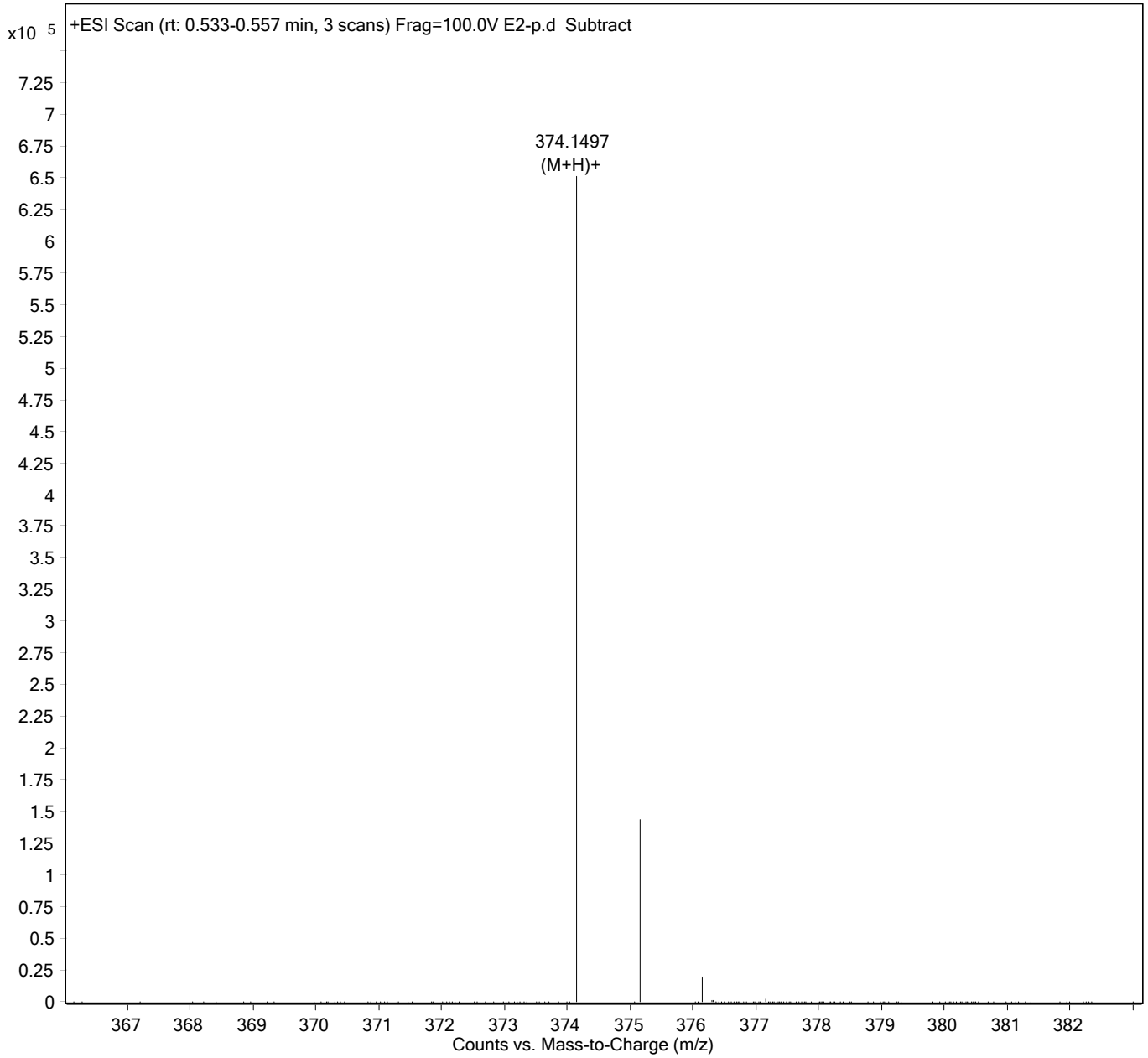


E2

SP20130619-1 CDCL3 1HNMR AV300

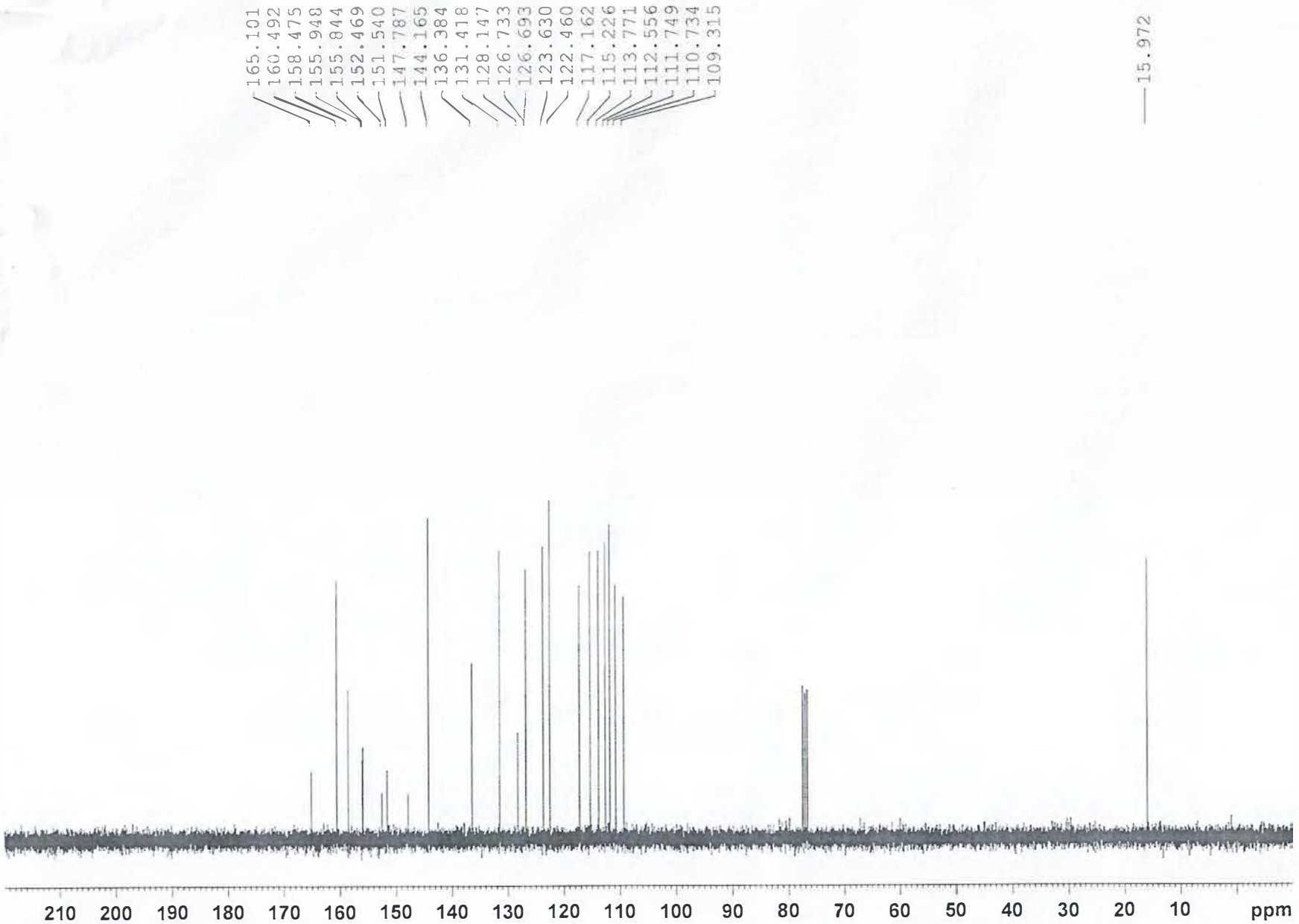


Sample Name		**Position**	p1B7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:29:34 PM



E3

SP130621-2-C C13-NMR CDCL3 303K AV-300



E3

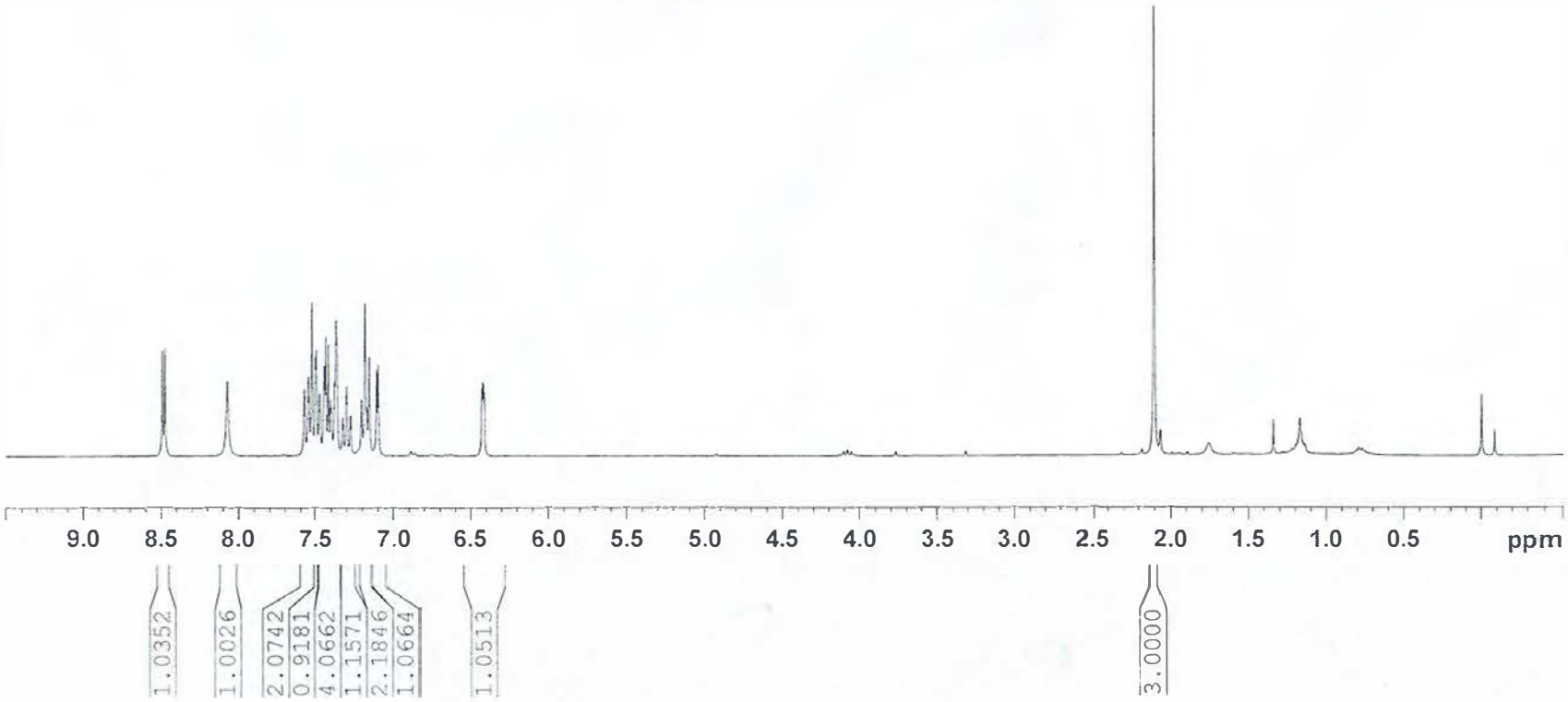
SP20130621-2 CDCL3 1HNMR AV300

7.5768
7.5511
7.5286
7.5050
7.4984
7.4790
7.4506
7.4403
7.4232
7.4082
7.4013
7.3803
7.3719
7.3314
7.3282
7.3042
7.2800
7.2767
7.2085
7.1856
7.1745
7.1593
7.1117
7.1006
6.4314
6.4258
6.4200
6.4143

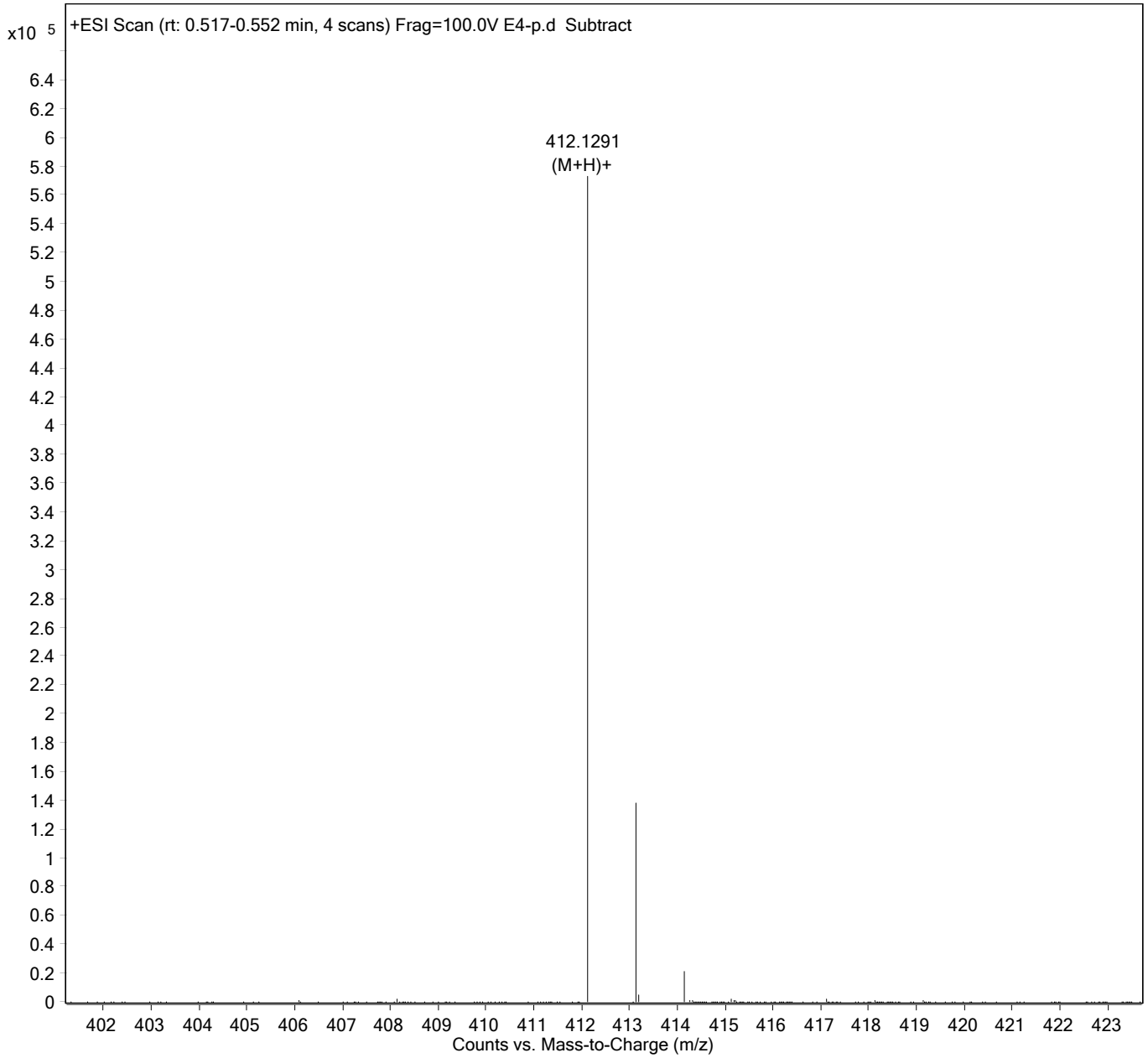
2.1088
2.0659

1.3441
1.1726

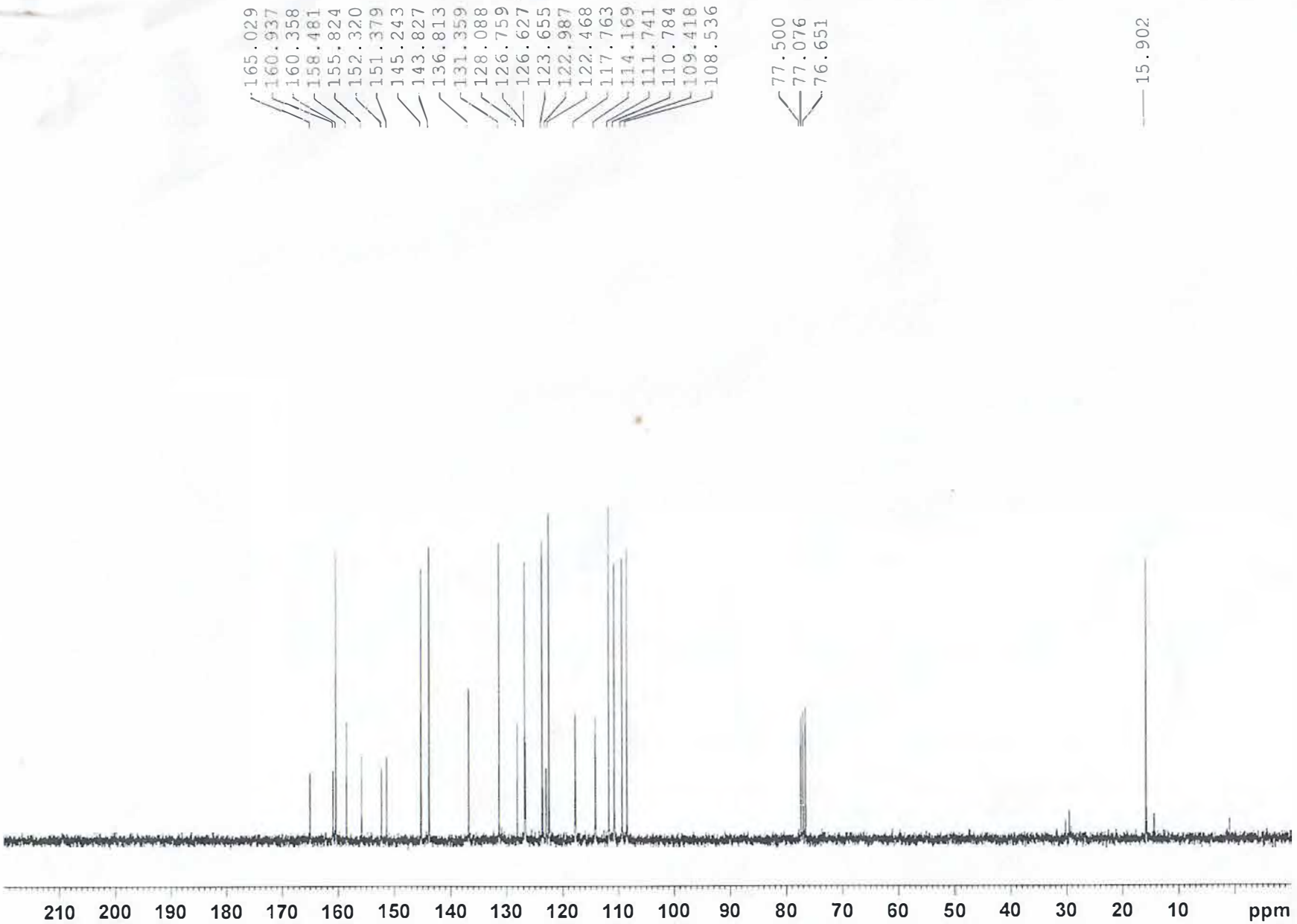
-0.0004
-0.0852



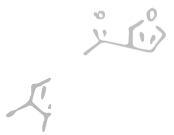
Sample Name		**Position**	p1B9	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:33:55 PM

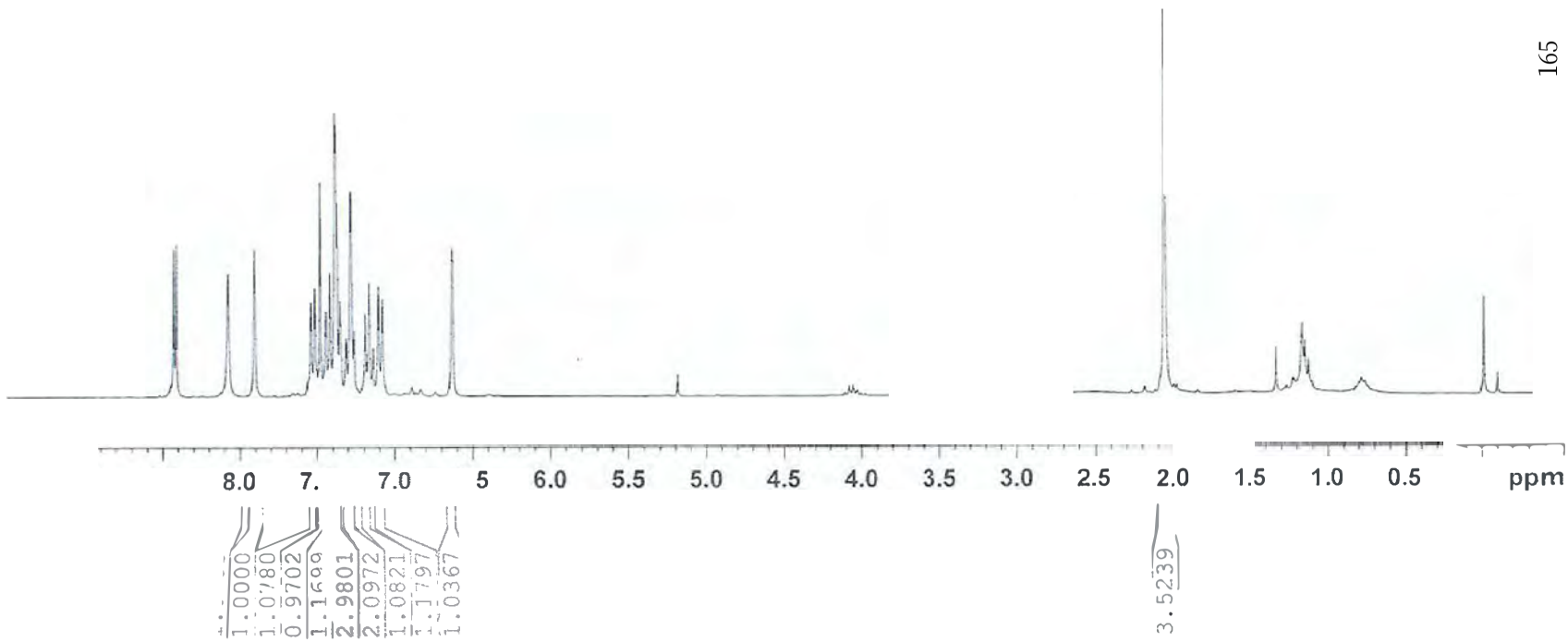


SP130624-C C13-NMR cdcl3 303K AV-300



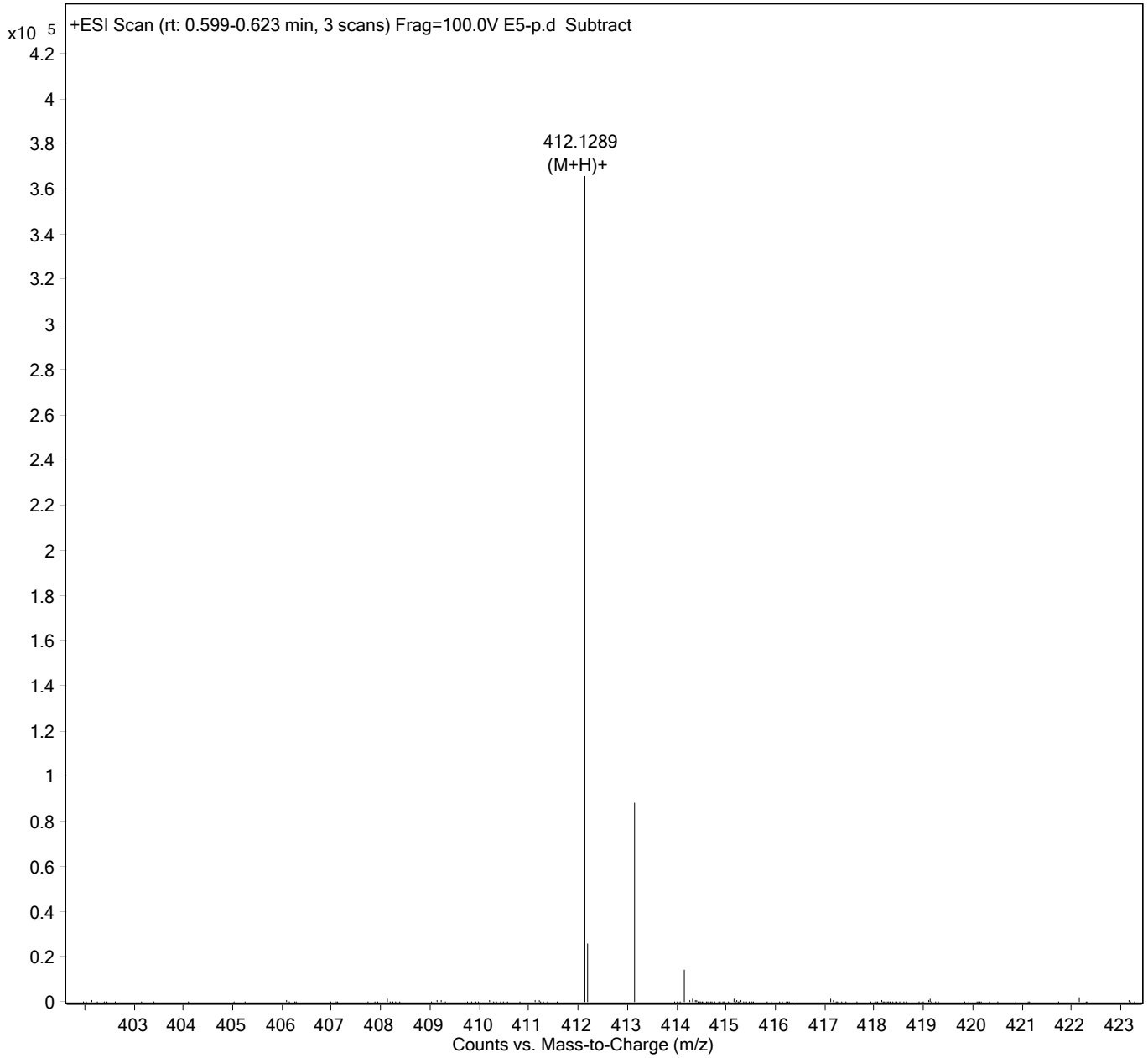
SP20130624 CDCL3 1HNMR AV300





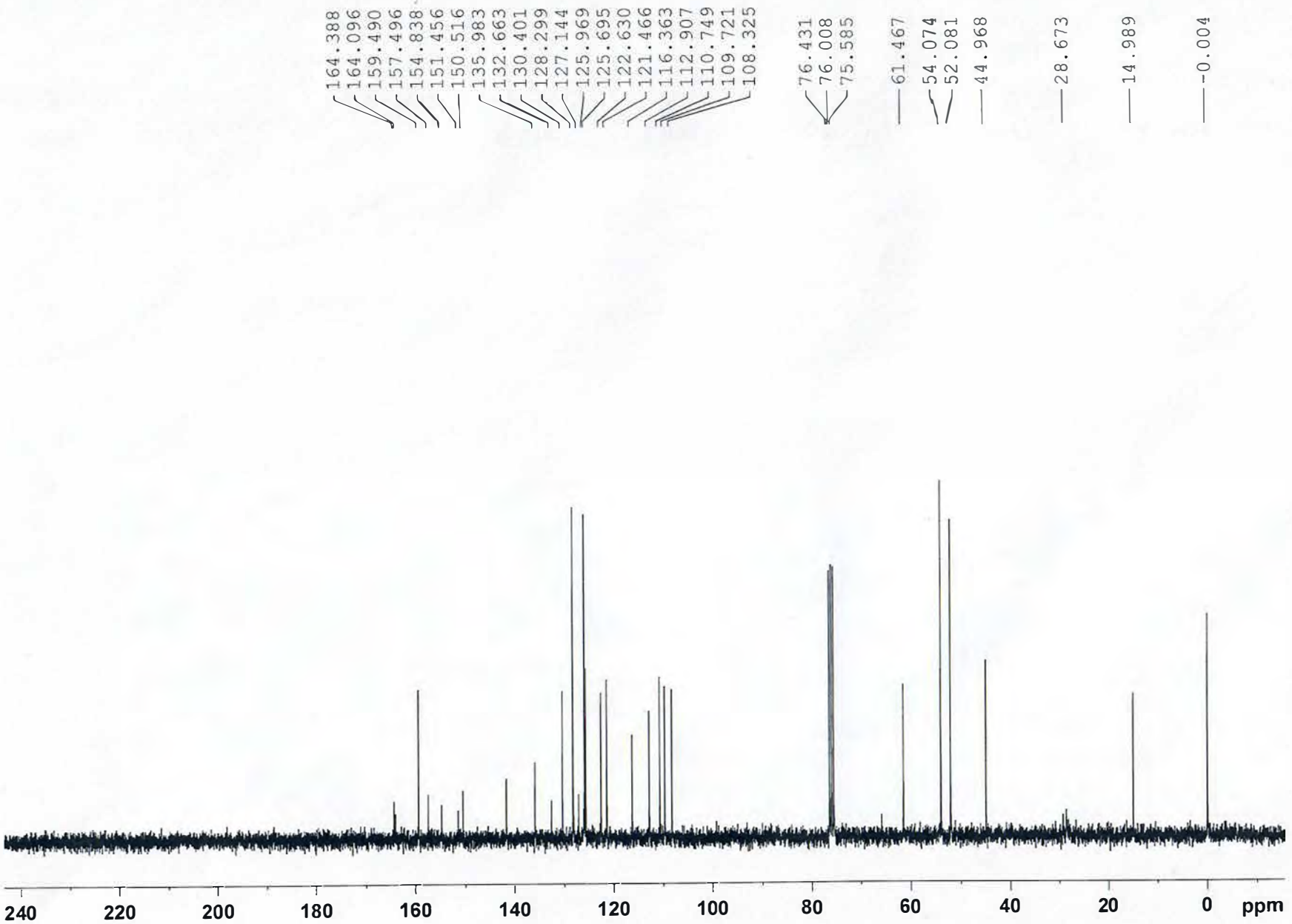
165

Sample Name		**Position**	P1C1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E4-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:36:07 PM



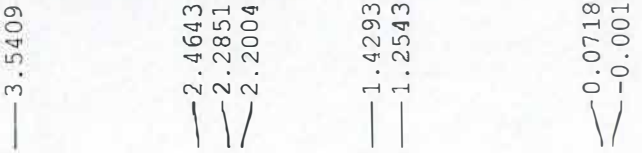
E5

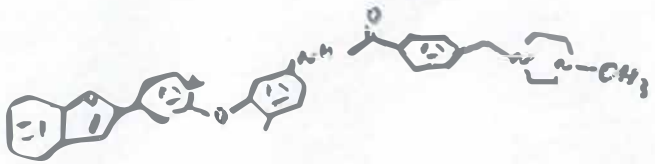
SP131021-C C13-NMR CDCL3 303K AV-300



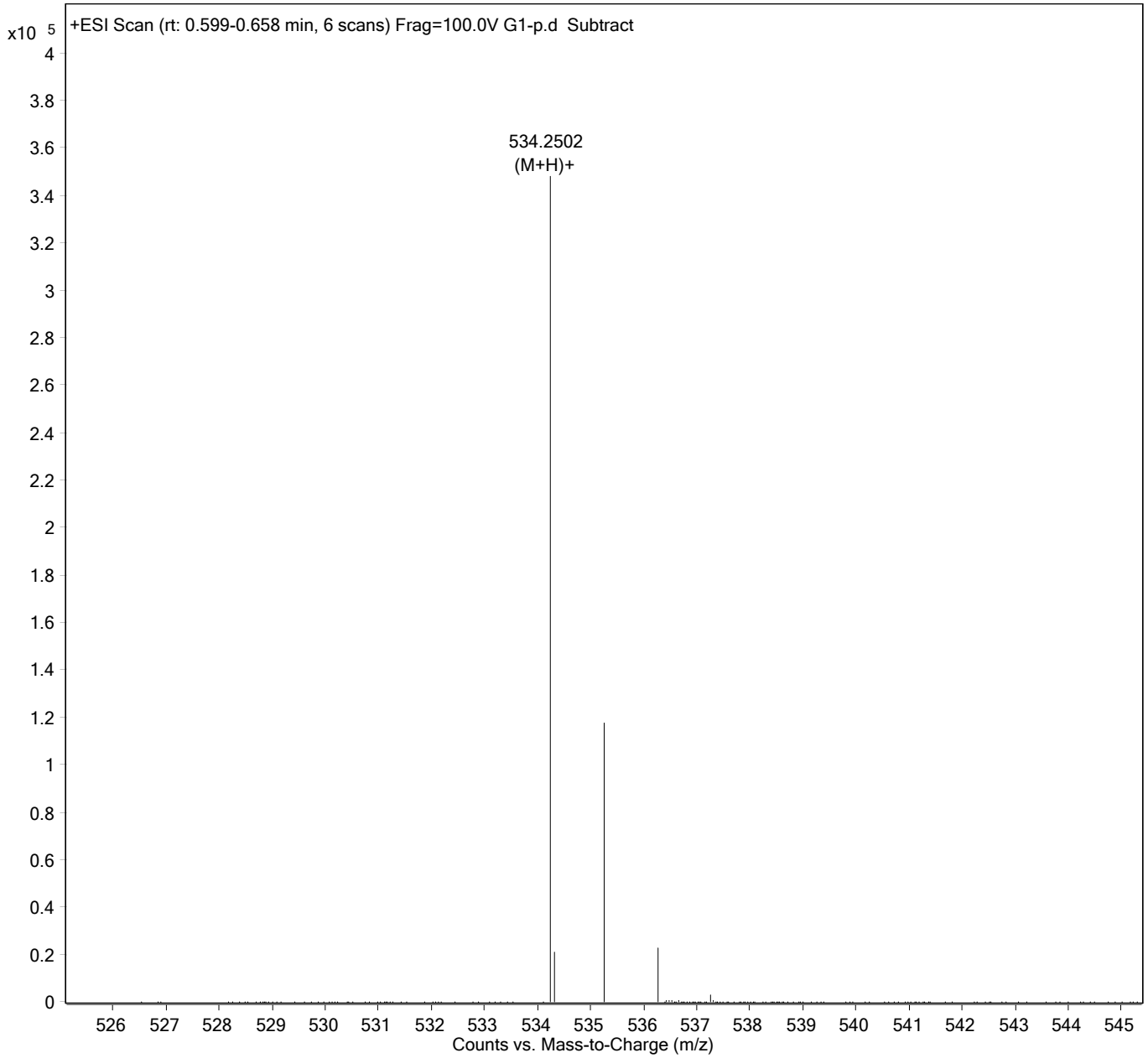
E5

SP20131021 CDCL3 1HNMR AV300

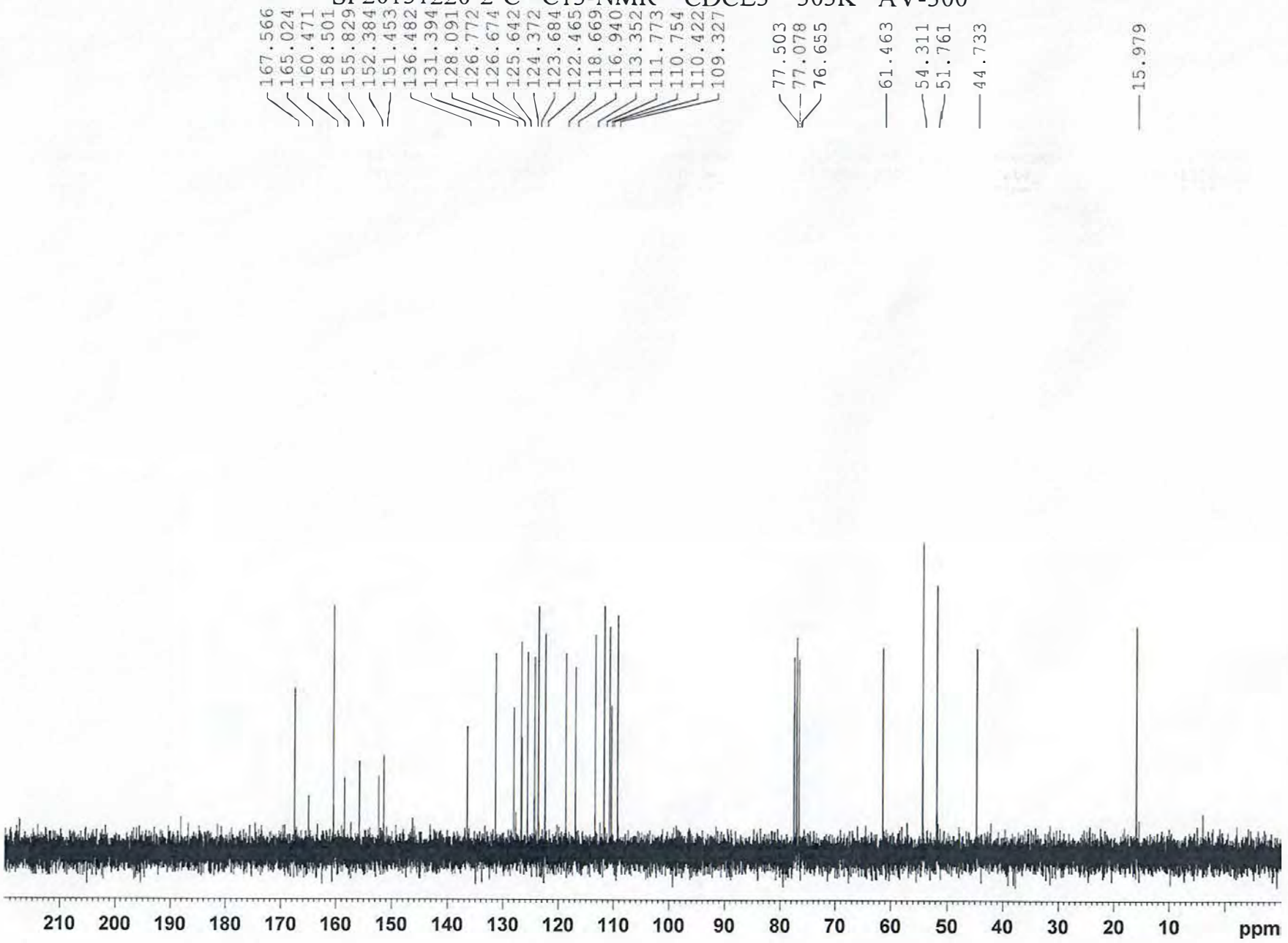




Sample Name		**Position**	P2a5	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E5-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/13/2018 1:50:42 PM

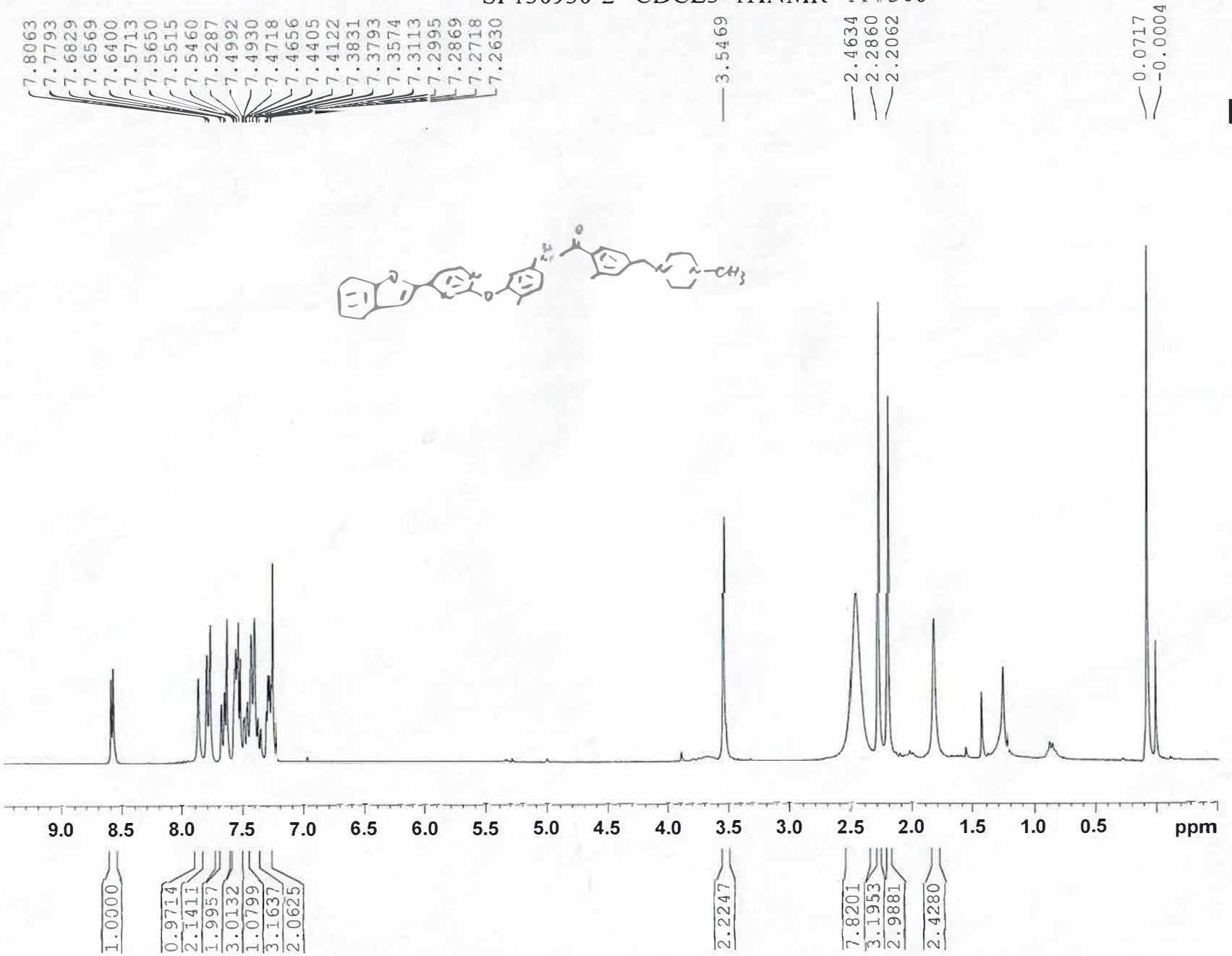


E6


SP20131220-2-C C13-NMR CDCL3 303K AV-300
167.566
165.024
160.471
158.501
155.829
152.384
151.453
136.482
131.394
128.091
126.772
126.674
125.642
124.372
123.684
122.465
118.669
116.940
113.352
111.773
110.754
110.422
109.327
77.503
77.078
76.655
61.463
54.311
51.761
44.733
15.979
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

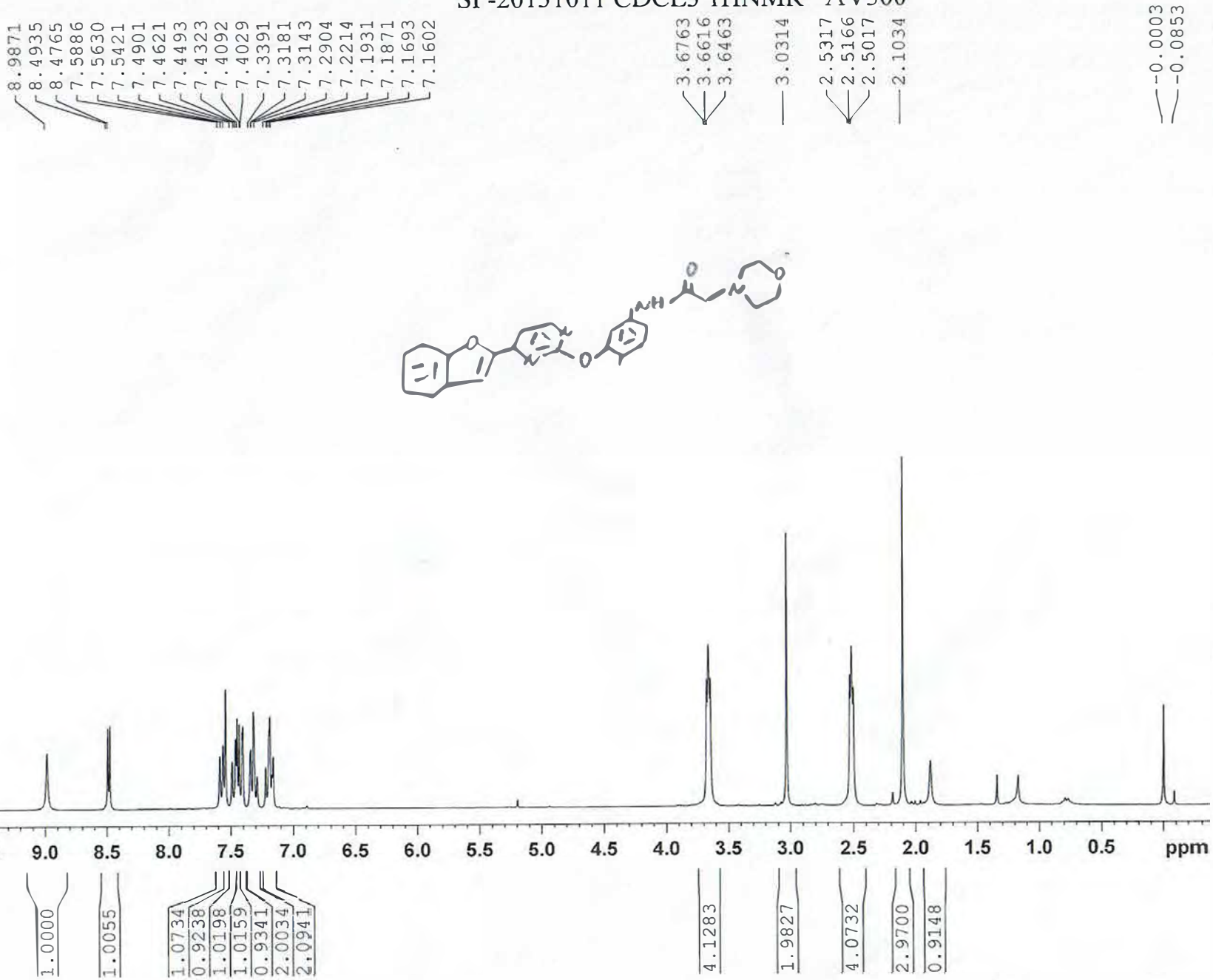
E6

SP130930-2 CDCL3 1HNMR AV300



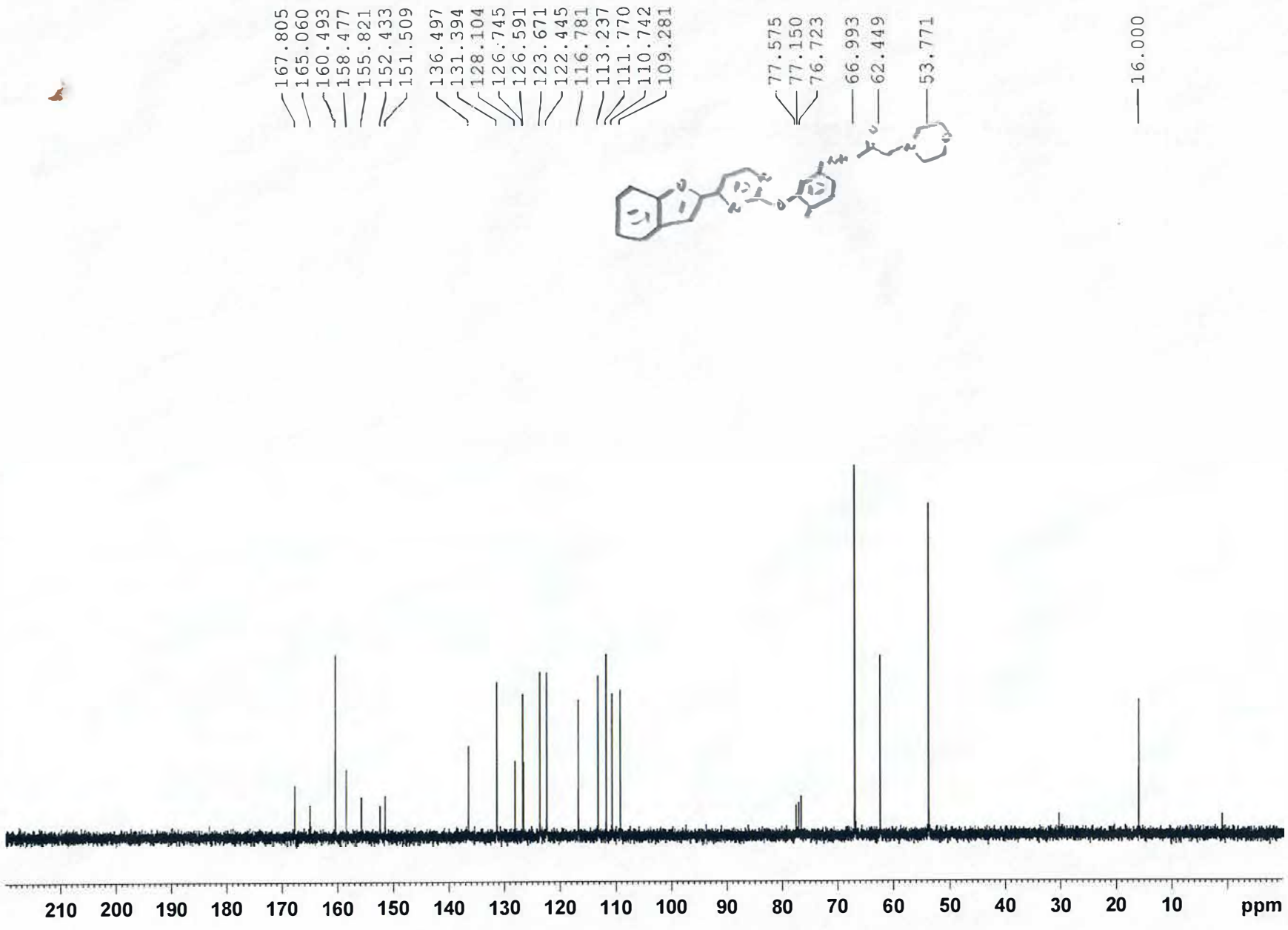
E7

SP-20131011 CDCL3 1HNMR AV300

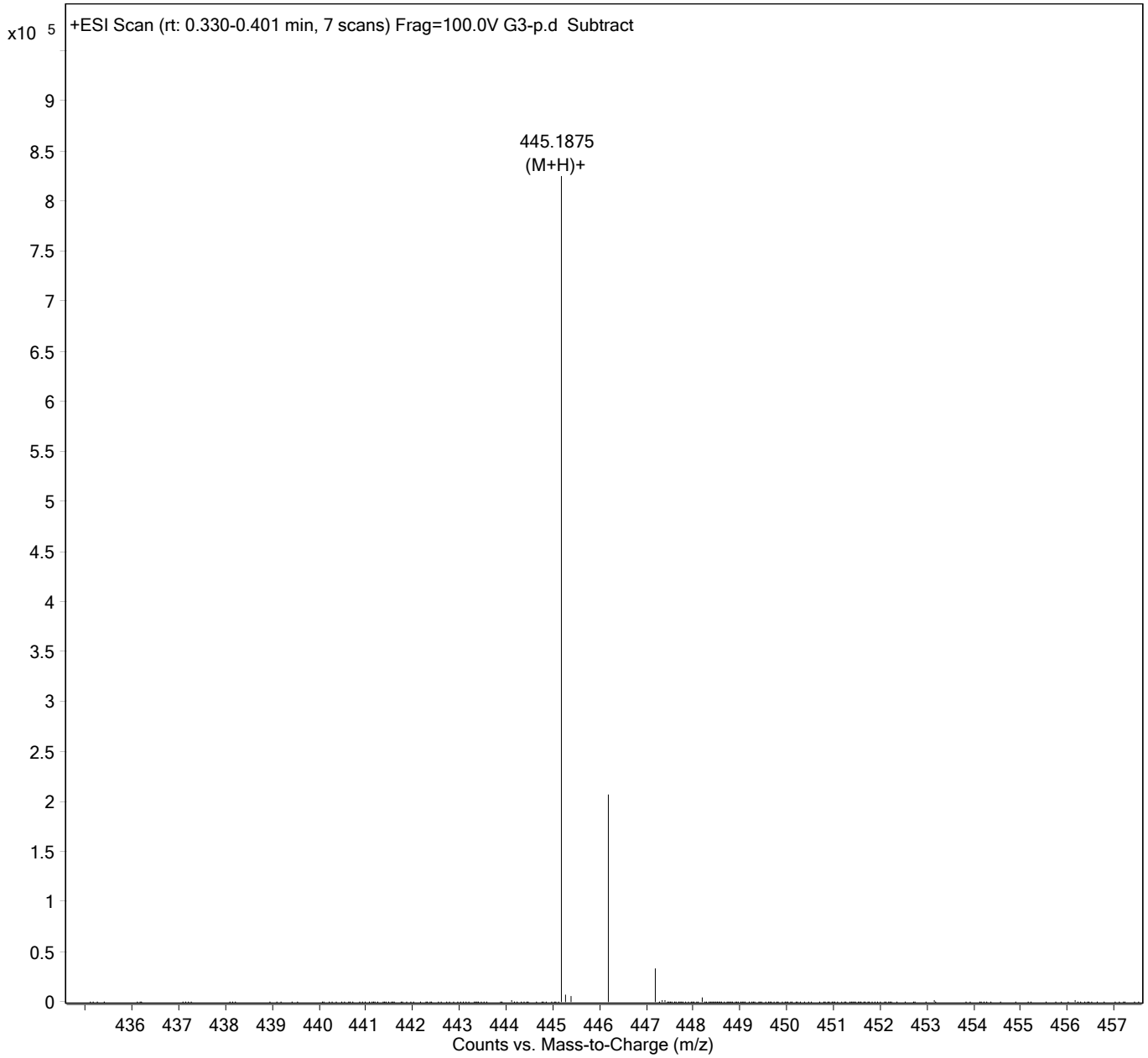


E7

SP20131018-C C13-NMR cdcl3 303K AV-300



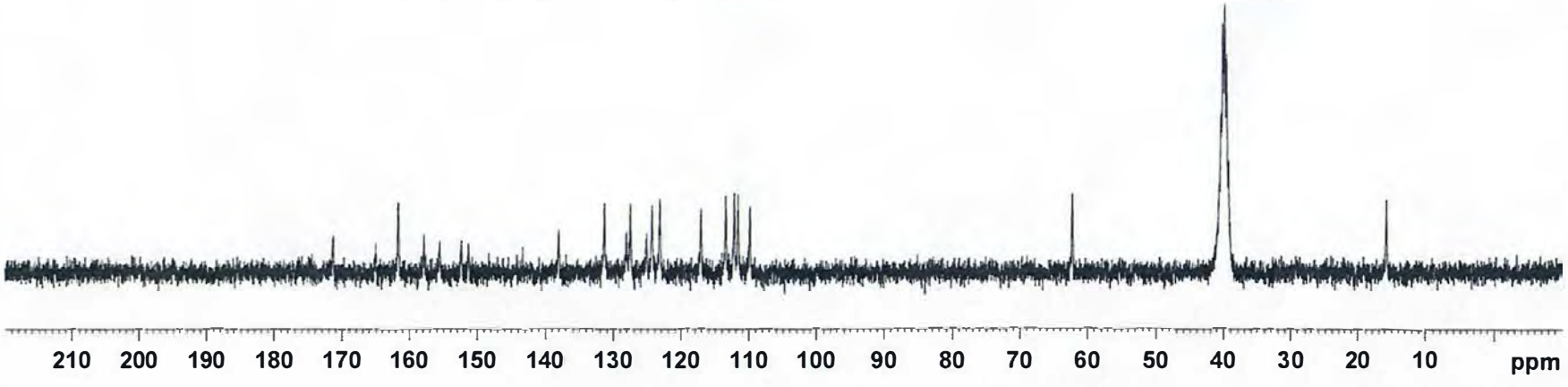
Sample Name		**Position**	P2a6	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E7-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/13/2018 1:53:04 PM



E8

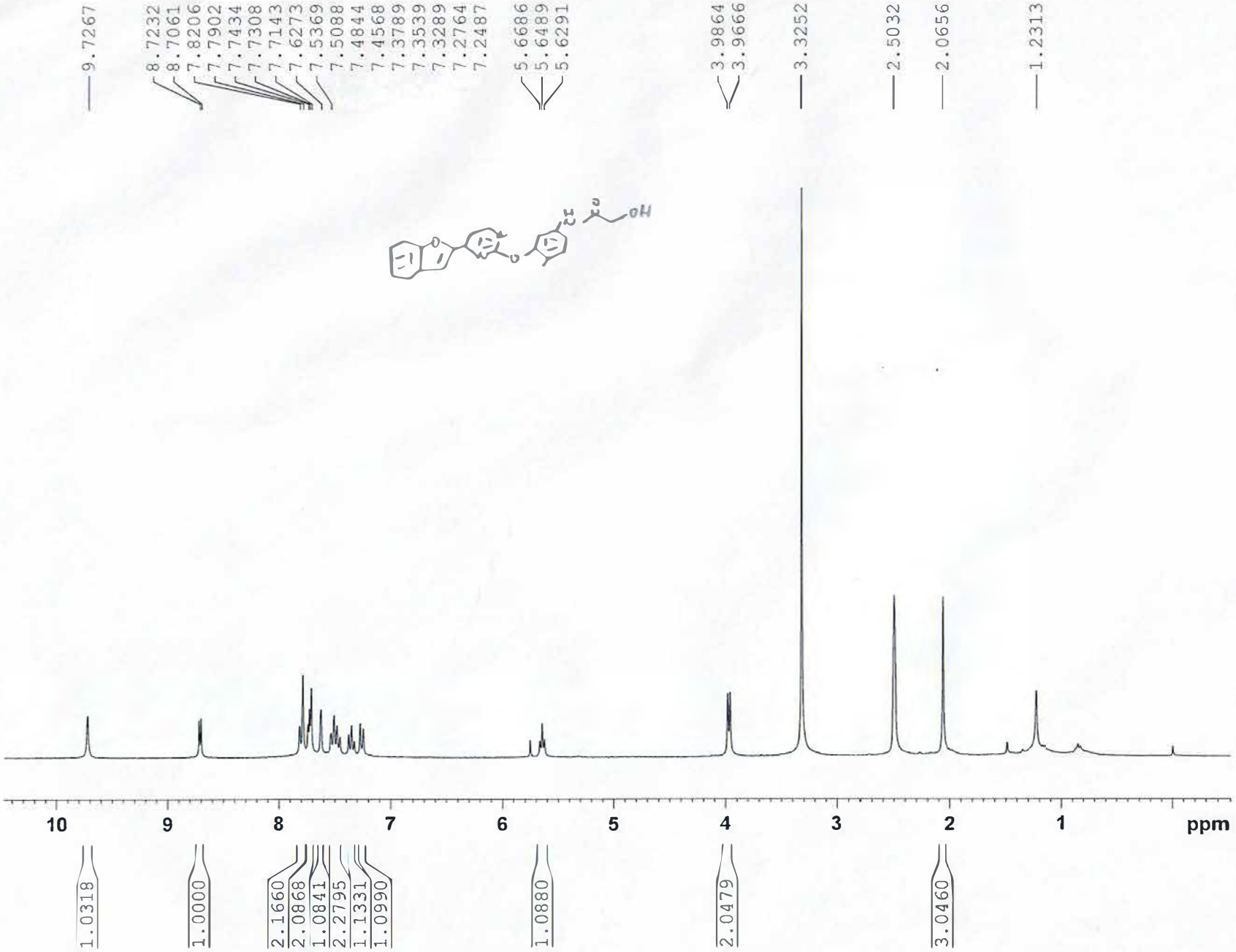
SP131223-1-C C13-NMR DMSO 303K AV-300

171.309
165.045
161.677
157.914
155.578
152.398
151.391
138.050
131.339
128.087
127.475
125.138
124.324
123.177
117.066
113.420
112.189
111.614
109.837
62.307
40.195
39.916
39.633
15.892

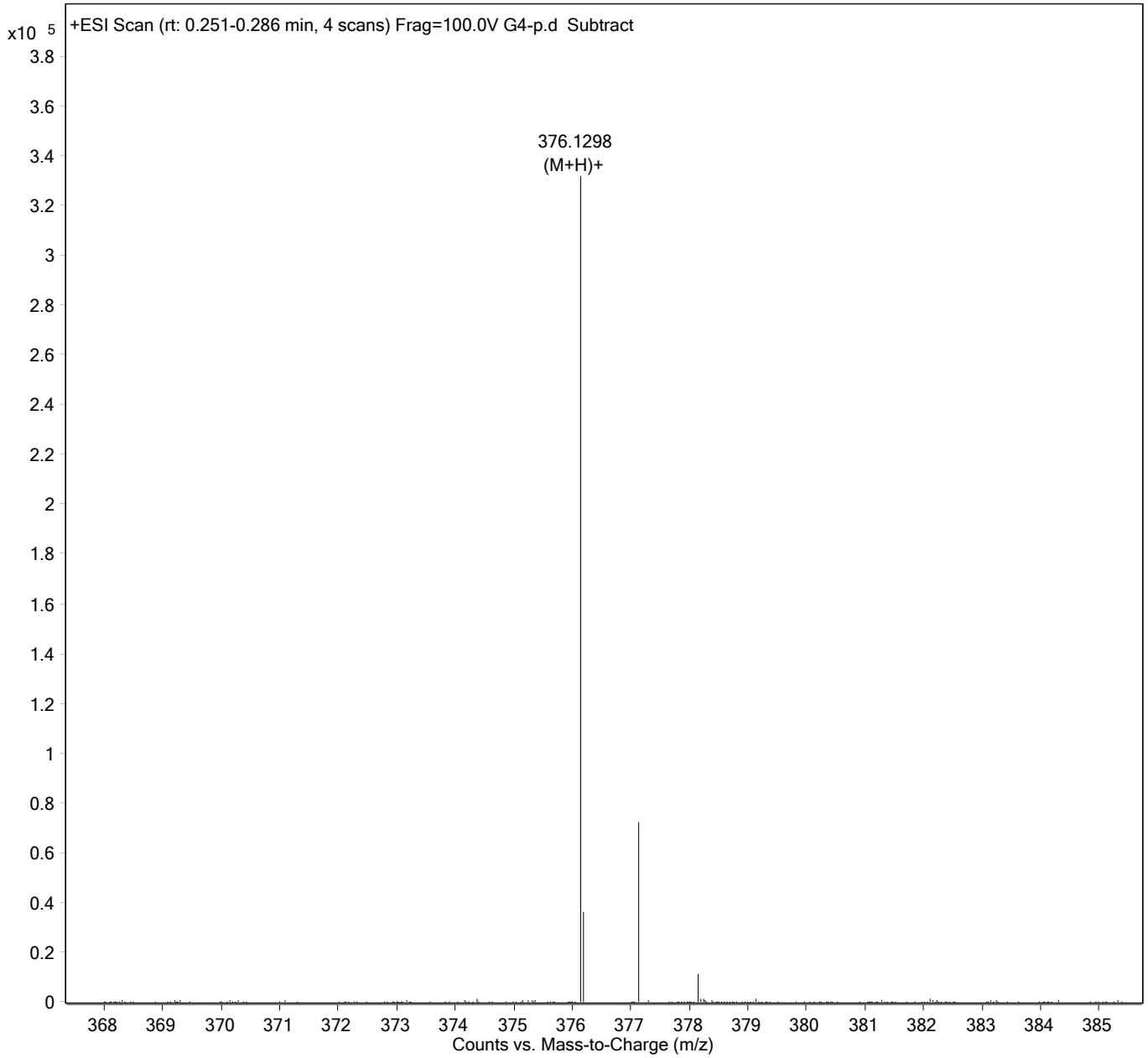


E8

SP130930-3 CDCL3 1HNMR AV300

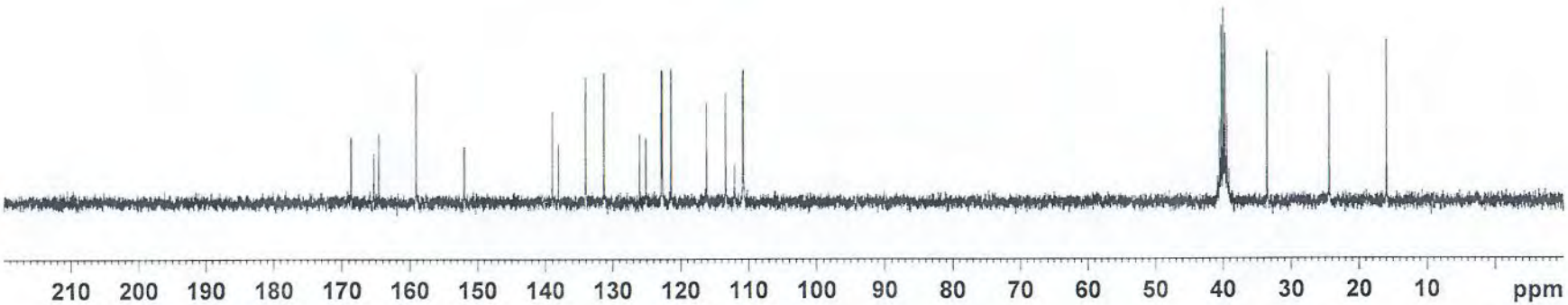


Sample Name		**Position**	P2a7	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	E8-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/13/2018 1:56:22 PM



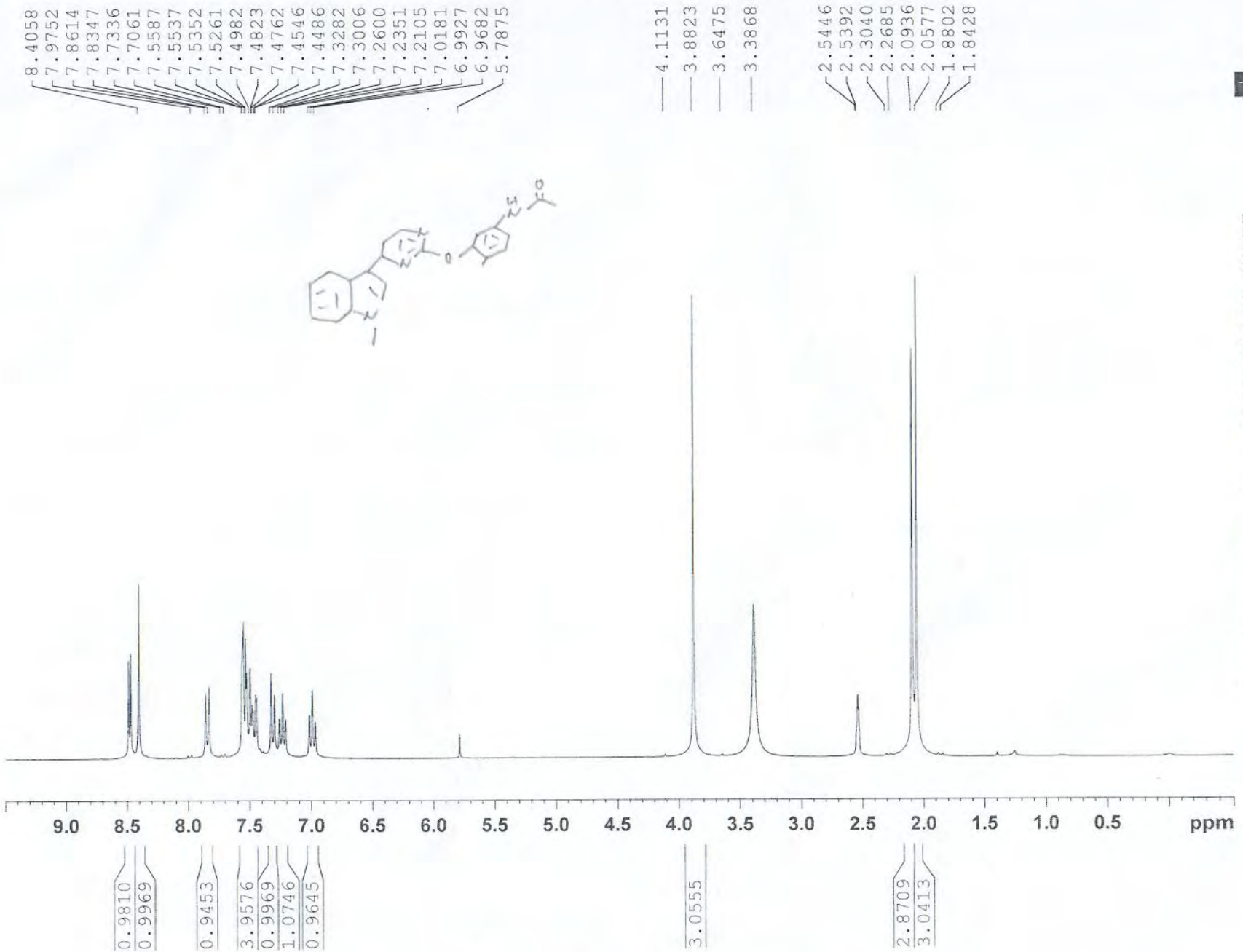
F1

SP1300701-C C13-NMR cdcl3 303K AV-300

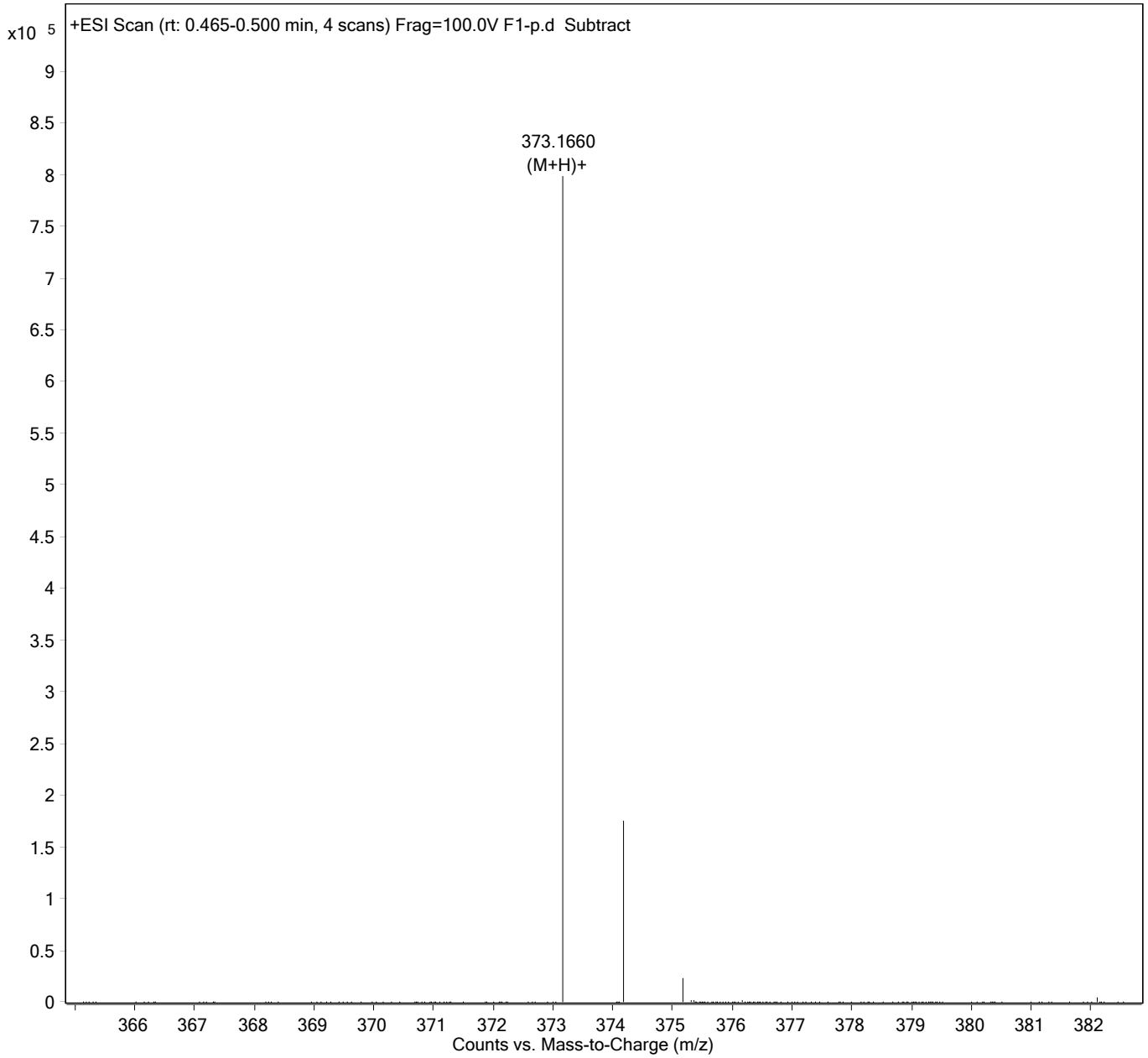


F1

SP-20130701 DMSO 1HNMR AV300

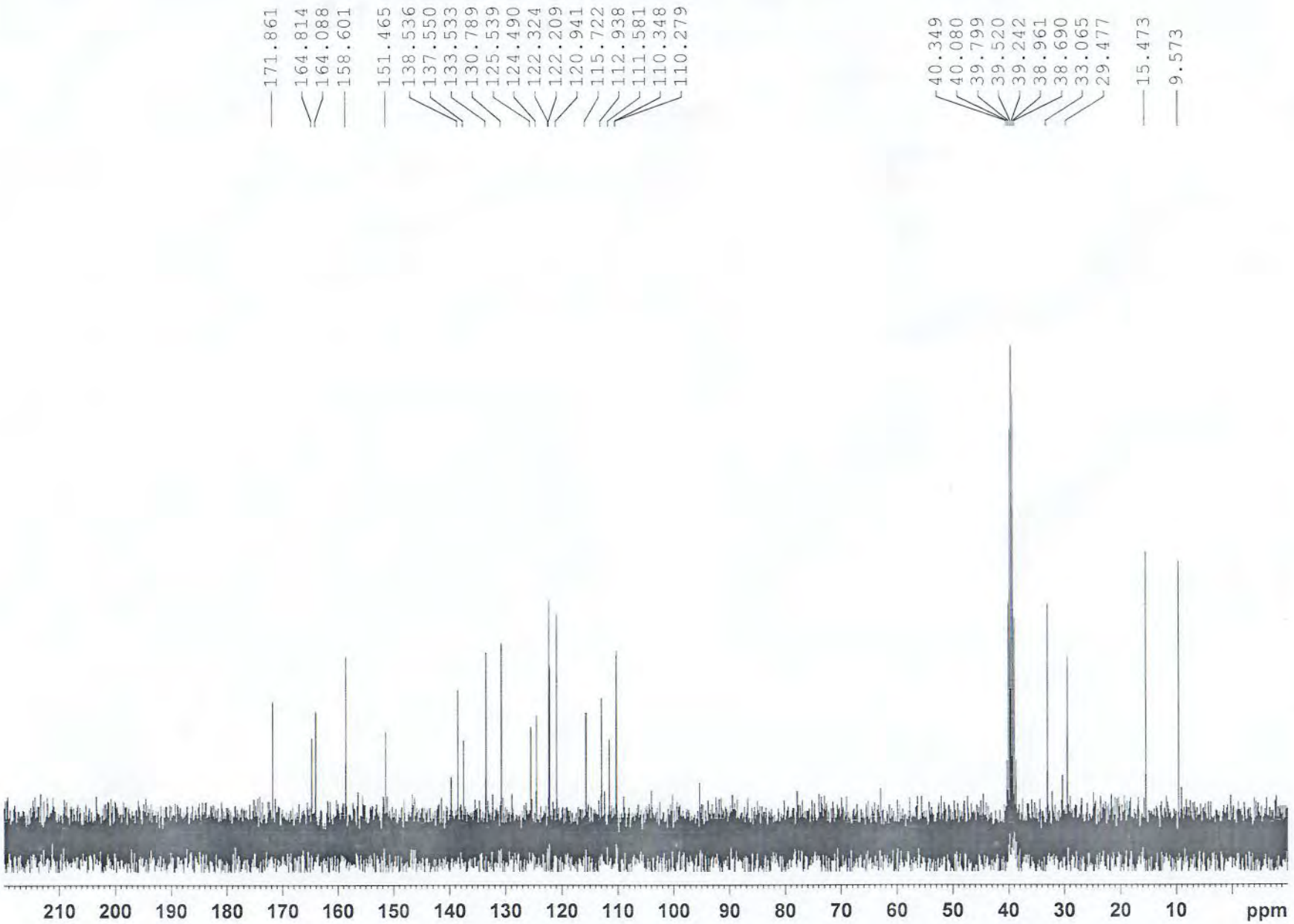


Sample Name		**Position**	P1C2	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	F1-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/12/2018 4:38:05 PM



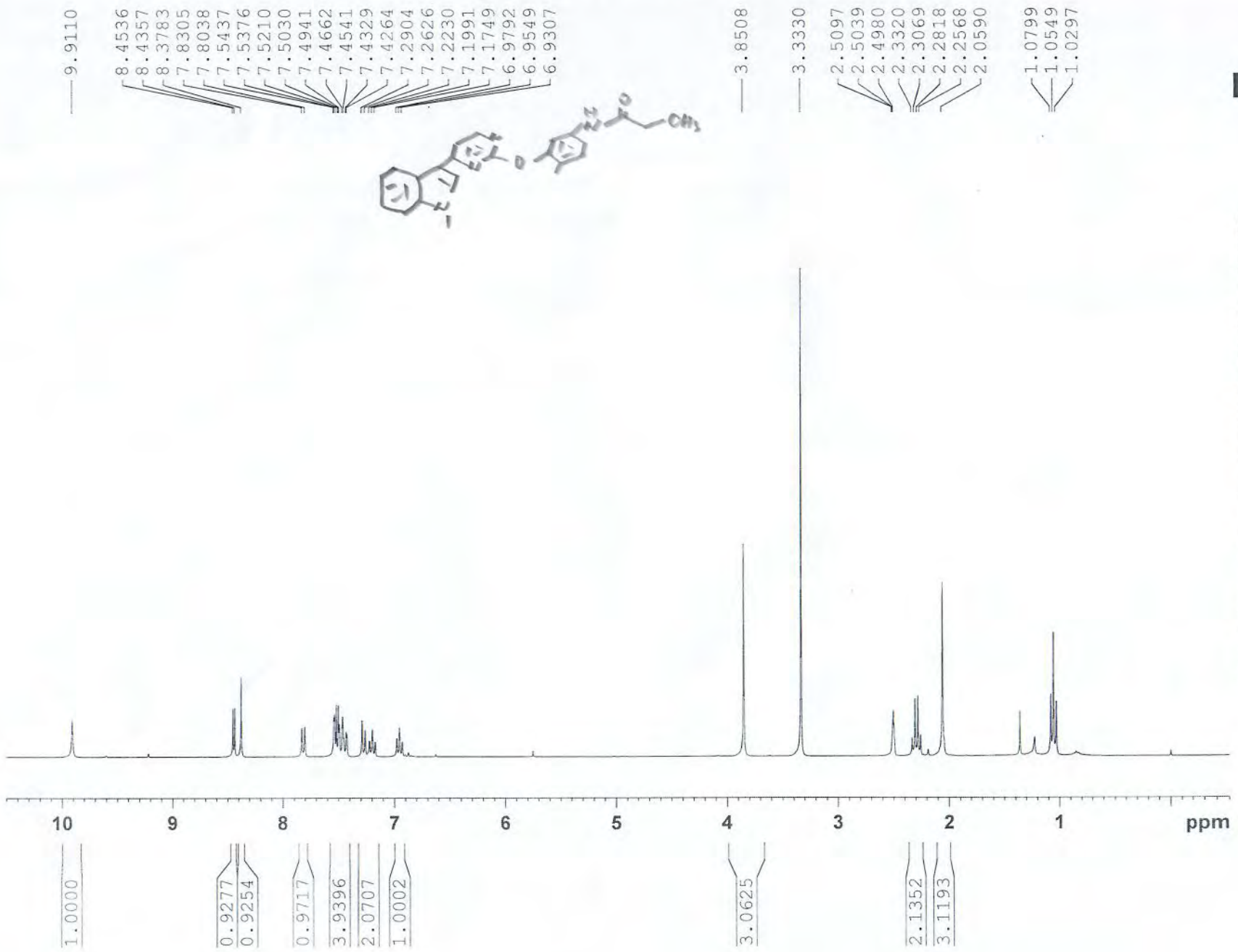
F2

SP130703-3-C C13-NMR DMSO 303K AV-300

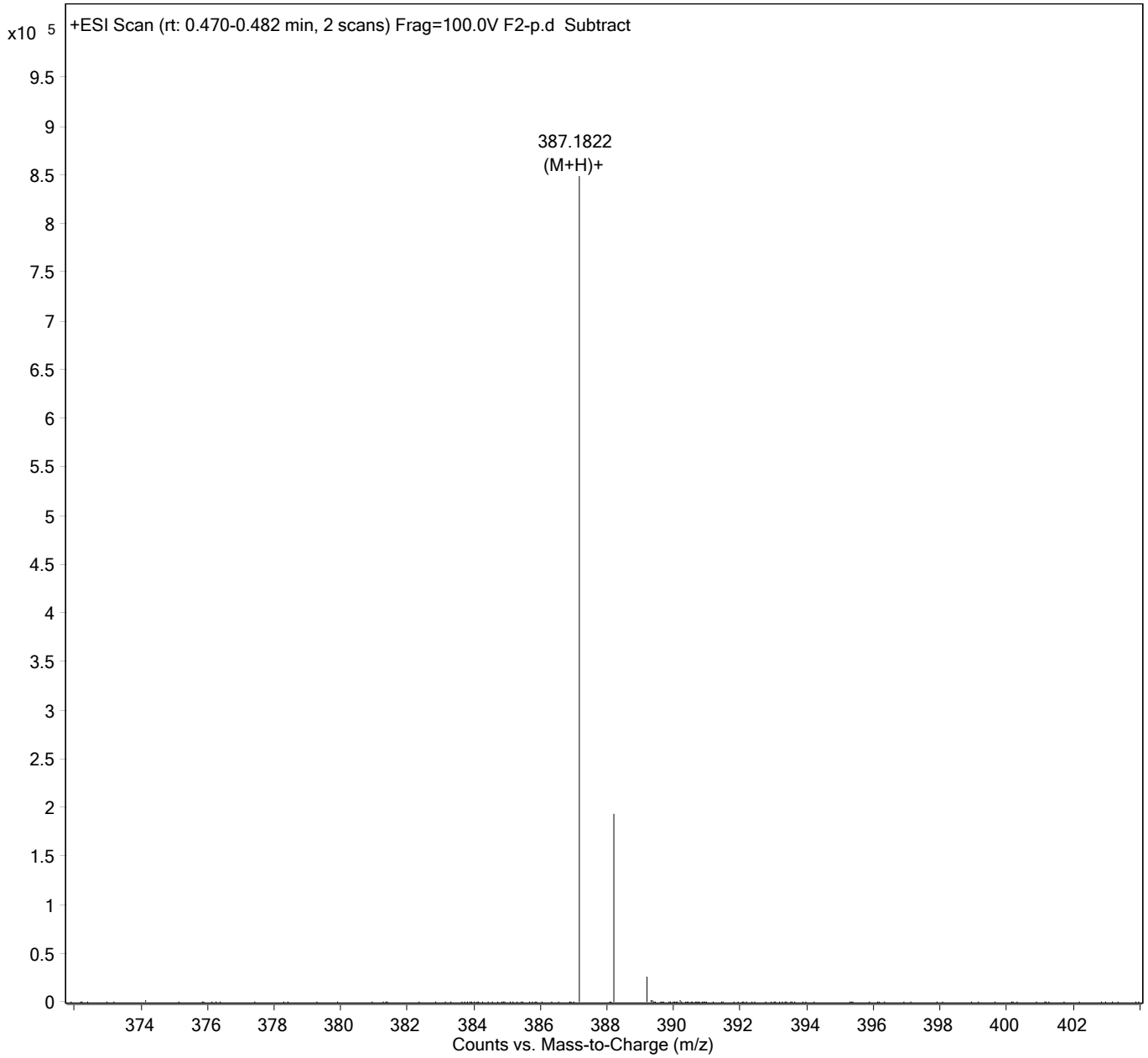


F2

SP20130703-3 DMSO 1HNMR AV300

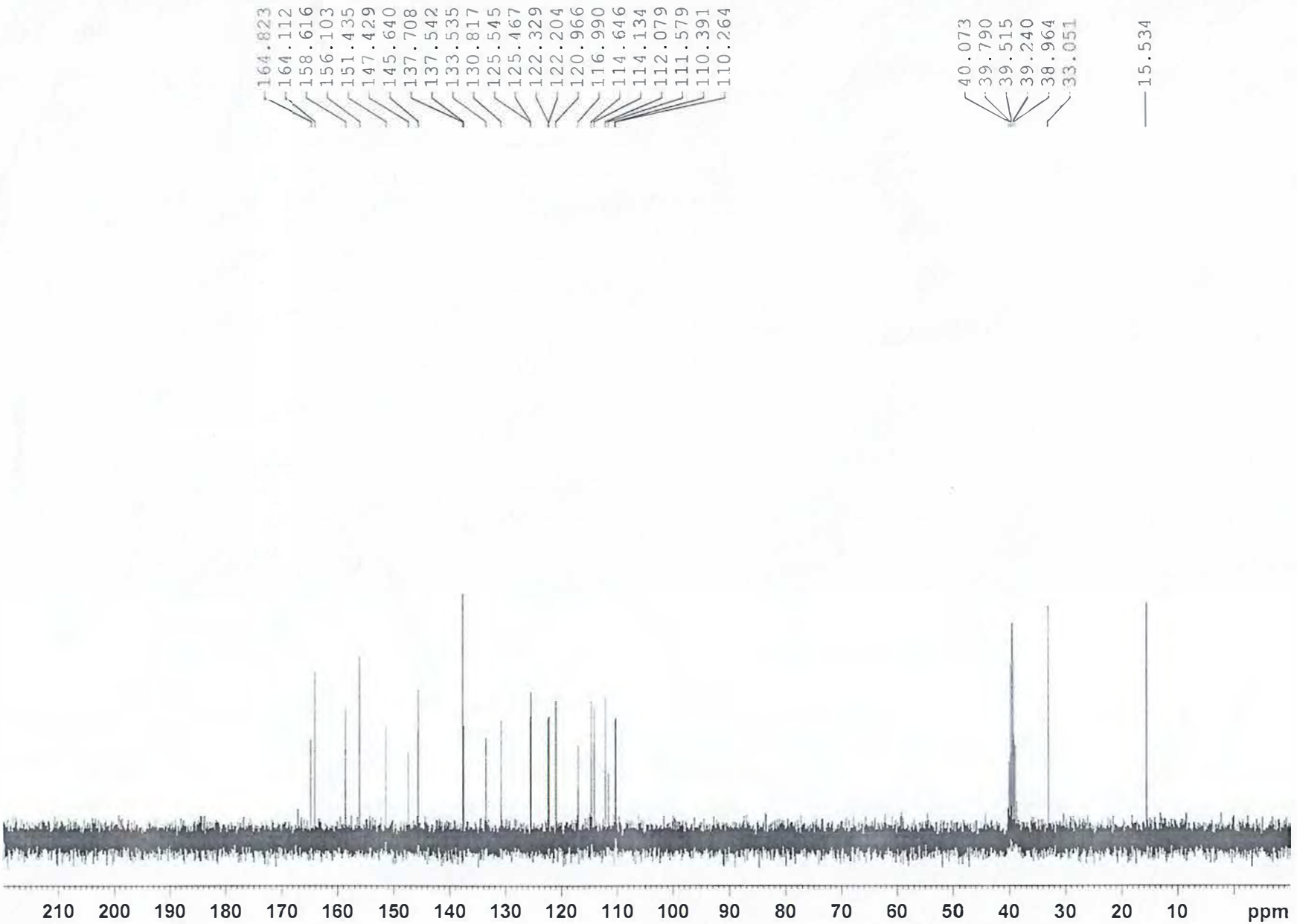


Sample Name		**Position**	P2a1	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	F2-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/13/2018 1:42:53 PM



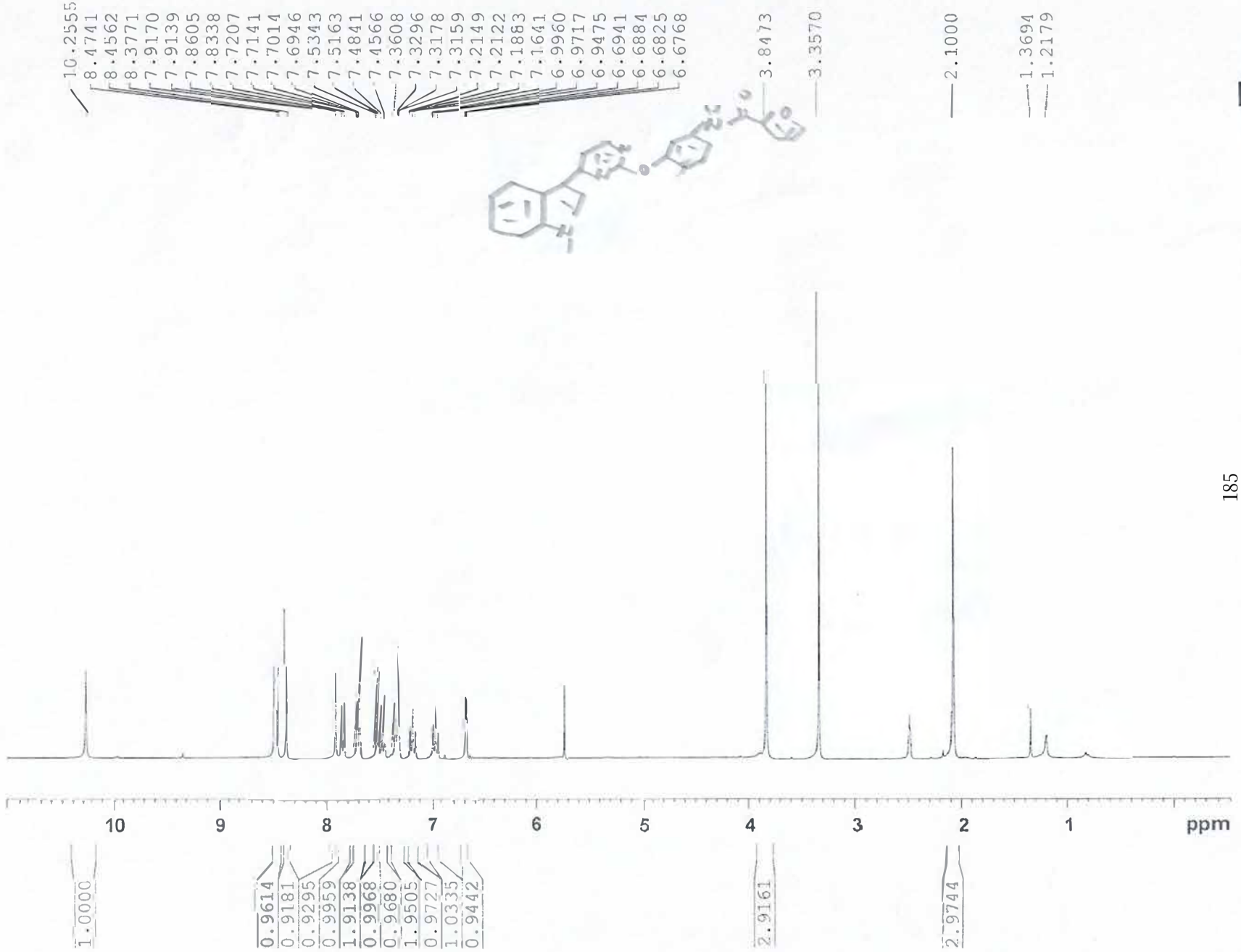
F3

SP130705-2-C C13-NMR DMSO 303K AV-300



SP20130705-2 DMSO 1HNMR AV300

F3



Sample Name		**Position**	P2a3	**Instrument Name**	Instrument 1
User Name	QTOF-PC\QTOF	**Inj Vol**	0.1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	F3-p.d
ACQ Method	20110418-MSonly-p.m	**Comment**		**Acquired Time**	3/13/2018 1:46:49 PM