One-pot Synthesis of 4(3H)-Quinazolinones from Azides, Alkynes, Anilines, and Carbon Monoxide

Yang Shen, Chao Han, Shuying Cai, Ping Lu and Yanguang Wang**

Department of Chemistry, Zhejiang University, Hangzhou 310027, China
E-mail: pinglu@zju.edu.cn (P. Lu); orgwyg@zju.edu.cn (Y. G. Wang)

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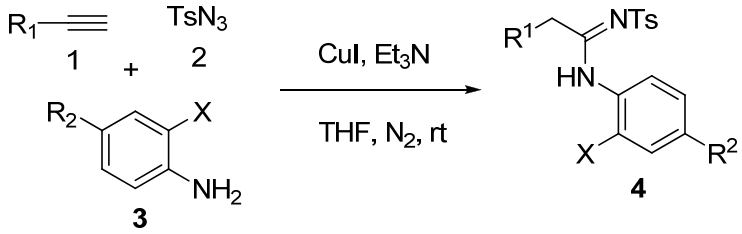
General Considerations

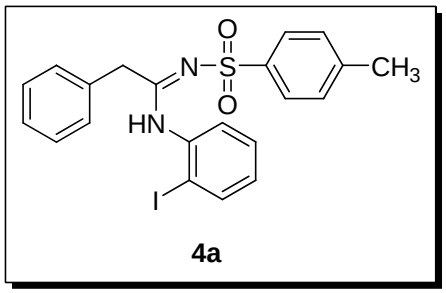
Infrared spectra were obtained on a FTIR spectrometer. ^{1}H NMR spectra were recorded on 400 MHz spectrometer unless noted otherwise and the chemical shifts were reported relative to internal standard TMS (0 ppm). The following abbreviations are used to describe peak patterns where appropriate: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants are reported in Hertz (Hz). ^{13}C NMR were recorded on 100 MHz unless noted otherwise and referenced to the internal solvent signals (central peak is 77.0 ppm for $CDCl_3$ or 40.0 ppm for DMSO-*d6*). MS and HRMS were obtained using EI ionization. Melting points were measured with micro melting point apparatus.

General Procedure for the synthesis of amidine 4



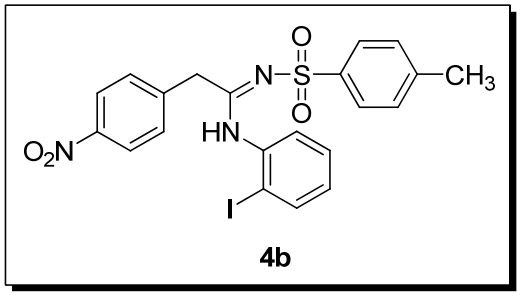
To a solution of alkyne **1** (1.2 mmol), azide **2** (1.2 mmol), 2-iodoaniline **3** (1.0 mmol), and CuI (0.1 mmol) in THF (5 mL) was slowly added TEA (1.2 mmol) via a syringe under nitrogen atmosphere over 3-5 min. The reaction mixture was stirred at room temperature for 12 h. The solution was diluted with ethyl acetate (20 mL), washed with water (10 mL) and then brine (10 mL), and dried over sodium sulfate. The solvent was removed in vacuum and the residue was subject to flash chromatography on silica gel (petroleum ether/ethyl acetate, 3:1 to 1:2) to afford pure **4**.

Characterization of 4



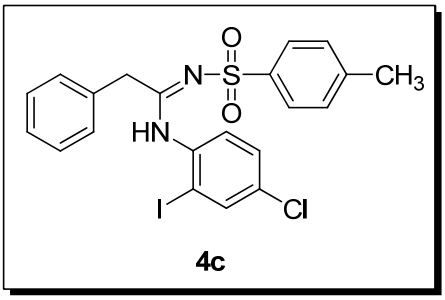
4a

Yellow solid, (446mg, 91%) m.p. 137~138^{o}C; IR 3431, 3232, 1590, 1563, 1524, 1280, 1143, 1096 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.09-7.40 (m, 7H), 7.29 (d, J=8.0Hz, 2H), 7.22-6.80 (m, 4H), 4.52 (s, 1.4H), 3.49 (s, 0.5H), 2.42 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1, 142.7, 140.1, 139.0, 137.4, 132.4, 131.1, 129.9, 129.4, 128.9, 128.7, 127.2, 126.5, 123.5, 90.9, 40.9, 21.6 ppm; MS (ESI) m/z 489 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{21}H_{19}N_2O_2SI$ ([M]$^{+}$): 490.0212; found: 490.0209.



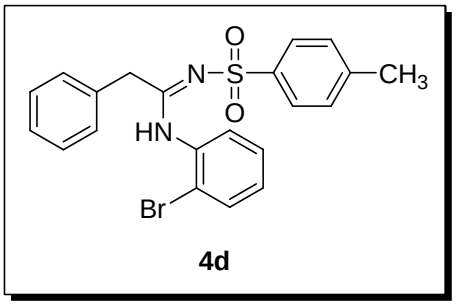
4b

Yellow solid, (470mg, 88%) m.p. 150~151^{o}C; IR 3414, 3265, 1530, 1349, 1286, 1146, 1087, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.91 (s, 0.6H), 8.28-7.66 (m, 6H), 7.39-6.85 (m, 6H), 4.63 (s, 0.6H), 3.58 (s, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.0, 162.0, 151.0, 147.2, 147.2, 143.6, 141.1, 140.0, 139.0, 138.5, 136.9, 131.6, 130.5, 129.5, 129.0, 127.6, 126.7, 124.6, 124.0, 123.5, 99.3, 40.5, 21.6 ppm; MS (ESI) m/z 534.7 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{21}H_{18}N_3O_4SI$ ([M]$^{+}$): 535.0063; found: 535.0073.



4c

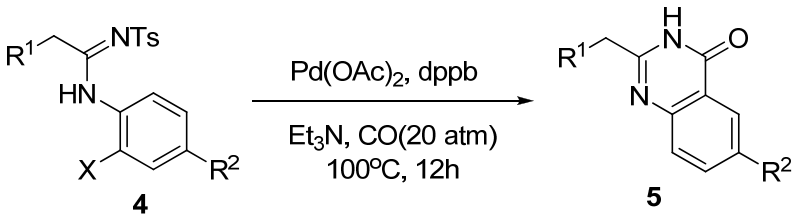
Pale purple solid, (455mg, 87%) m.p. 147~148^{o}C; IR 3435, 3311, 1600, 1566, 1520, 1283, 1150, 715, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.04-6.84 (m, 12H), 4.52 (s, 1.6H), 3.48 (s, 0.3H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1, 142.9, 139.9, 138.1, 136.2, 132.2, 131.2, 131.0, 129.9, 129.4, 128.9, 128.8, 126.5, 123.7, 90.7, 40.8, 21.6 ppm; MS (ESI) m/z 523.5 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{21}H_{18}N_2O_2SClI$ ([M]$^{+}$): 523.9822; found: 523.9826.



4d

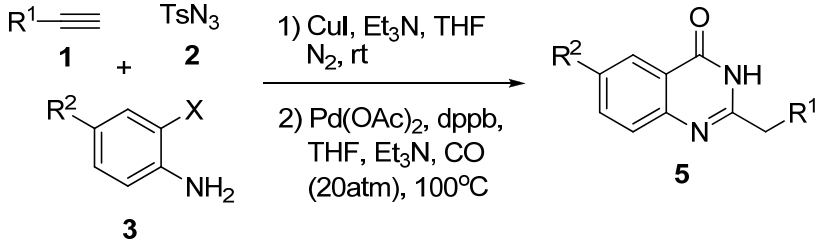
White solid, (398mg, 90%) m.p. 100~101^{o}C; IR 3446, 3324, 1601, 1572, 1536, 1438, 1280, 1143, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.22-6.82 (m, 13H), 4.53 (s, 1.6H), 3.52 (s, 0.3H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.9, 142.7, 140.1, 134.8, 132.4, 130.8, 129.8, 129.4, 128.7, 128.1, 126.5, 126.4, 123.2, 114.8, 40.9, 21.6 ppm; MS (ESI) m/z 445.1 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{21}H_{19}N_2O_2SBr$ ([M]$^{+}$): 442.0351; found: 442.0354.

General Procedure for the Synthesis of 5



A mixture of **4** (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), Et_3N (3.0 mmol) and tetrahydrofuran (10 mL) were sequentially added to a 25 mL beaker with a magnetic bar in it. Then put the beaker into a 50ml autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with 20 atm of CO, and then heated at 100°C for 12 h. The autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The reaction mixture was filtered and the filtrate was concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel with a mixture of hexane and ethyl acetate (2:1 to 1:1) as the eluent to afford the desired products **5**.

General Procedure for the One-pot Synthesis of 5



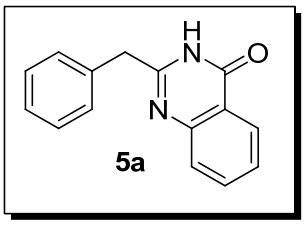
To a solution of alkyne **1** (1.2 mmol), azide **2** (1.2 mmol), 2-iodoaniline **3** (1.0 mmol), and CuI (0.1 mmol) in THF (10 mL) was slowly added TEA (1.2 mmol) via a syringe under nitrogen atmosphere over 3-5 min. The reaction mixture was stirred at room temperature for 12 h. The reactions mixture was added $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol) and Et_3N (1.8 mmol). Then put the flask into a 50ml autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with 20 atm of CO, and then heated at 100°C for 12 h. The autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The reaction mixture was filtered and the filtrate was concentrated by

rotary evaporation. The residue was purified by flash chromatography on silica gel with a mixture of hexane and ethyl acetate (4:1 to 1:1) as the eluent to afford the desired products **5**.

Gram Scale for the One-pot Synthesis of 5a

To a solution of phenyl acetylene **1a** (7.2 mmol, 0.734g), tosyl azide **2** (7.2 mmol, 1.418g), 2-iodoaniline **3a** (6.0 mmol, 1.314g), and CuI (0.6 mmol, 0.114g) in THF (50 mL) was slowly added TEA (7.2 mmol, 1.0ml) via a syringe under nitrogen atmosphere over 15 min. The reaction mixture was stirred at room temperature for 12 h. The reactions mixture was added $Pd(OAc)_2$ (0.3 mmol, 0.067g), dppb (0.6 mmol, 0.247g) and Et_3N (10.8 mmol, 1.5ml). Then put the flask into a 50ml autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with 20 atm of CO, and then heated at 100°C for 12 h. The autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The reaction mixture was filtered and the filtrate was concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel with a mixture of hexane and ethyl acetate (4:1 to 1:1) as the eluent to afford the desired products **5a** in 69% yield, 983mg.

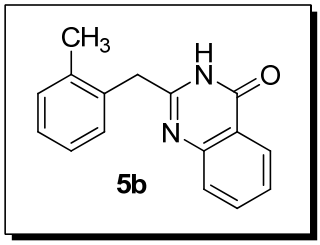
Characterization of 5



5a

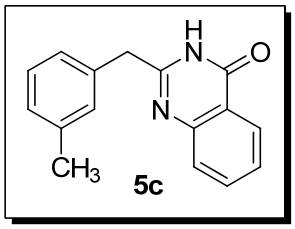
White solid, (174mg, 74%) m.p. 254~255^{o}C; IR 2917, 1679, 1615, 1466, 1158, 1000, 776, 716 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 8.11-8.10 (m, 1H), 7.79-7.34 (m, 8H), 3.97 (s, 2H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.3, 156.3, 149.4, 137.0, 134.9, 129.4, 129.0, 127.4, 127.3, 126.7, 126.2, 121.2, 41.3 ppm; HRMS (EI): m/z

calcd for $C_{15}H_{12}N_2O$ ($[M]^+$): 236.0950; found: 236.0951.



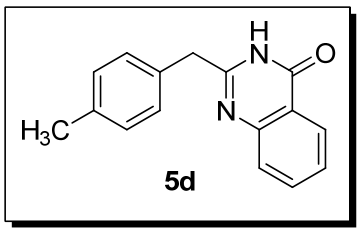
5b

Yellow solid, (145mg, 58%) m.p. 225~227^{o}C; IR 2895, 1682, 1622, 1466, 1338, 1191, 1000, 769 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.38 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.77-7.74 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.23-7.14 (m, 4H), 3.97 (s, 2H), 2.35 (s, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.9, 155.8, 148.8, 136.6, 135.1, 134.3, 130.0, 129.2, 126.9, 126.8, 126.1, 125.9, 125.7, 120.8, 38.3, 19.5 ppm; MS (ESI) m/z 249.2 ($[M-H]^-$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O$ ($[M]^+$): 250.1106; found: 250.1102.



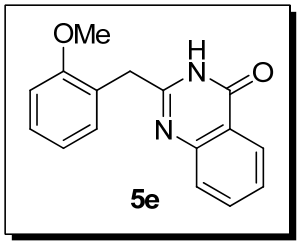
5c

Yellow solid, (190mg, 76%) m.p. 202~203^{o}C; IR 2921, 1673, 1612, 1469, 1328, 1178, 772, 691 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.38 (s, 1H), 8.10 (d, J =8.0Hz, 1H), 7.78 (t, J = 6.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 6.0 Hz, 1H), 7.23-7.19 (m, 3H), 7.07-7.05 (m, 1H), 3.92 (s, 2H), 2.28 (s, 1H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.3, 156.4, 149.4, 138.0, 136.9, 134.8, 129.9, 128.8, 127.9, 127.4, 126.6, 126.4, 126.1, 121.2, 41.2, 21.4 ppm; MS (ESI) m/z 250.9 ($[M+H]^+$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O$ ($[M]^+$): 250.1106; found: 250.1107.



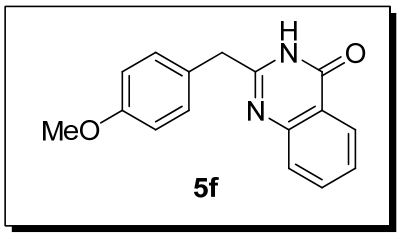
5d

White solid, (192mg, 77%) m.p. 231~233^{o}C; IR 2919, 1679, 1611, 1468, 1161, 1003, 885, 773 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.40 (s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 3.89 (s, 2H), 2.25 (s, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.9, 156.1, 148.9, 135.8, 134.3, 133.5, 129.0, 128.7, 126.9, 126.1, 125.7, 120.7, 40.4, 20.6 ppm; MS (ESI) m/z 249.9 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O$ ([M]$^{+}$): 250.1106; found: 250.1109.



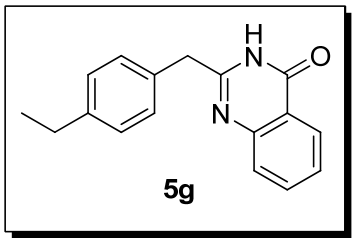
5e

Yellow solid, (178mg, 67%) m.p. 160~161^{o}C; IR 2968, 1654, 1608, 1470, 1331, 1153, 1006, 779 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.69 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.72-7.68 (m, 2H), 7.43-7.27 (m, 3H), 6.98-6.95 (m, 2H), 4.06 (s, 2H), 3.94 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.3, 157.0, 155.2, 149.2, 134.7, 131.6, 129.6, 127.4, 126.64, 126.57, 123.4, 121.8, 121.2, 111.4, 56.0, 37.6 ppm; MS (ESI) m/z 266.9 ([M+H]+); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O_2$ ([M]$^{+}$): 266.1055; found: 266.1055.



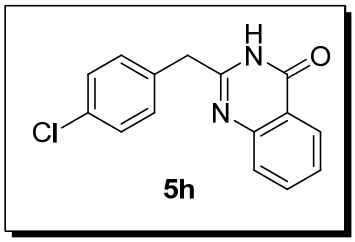
5f

Yellow solid, (234mg, 88%) m.p. 219~220^{o}C; IR 2917, 1681, 1611, 1511, 1252, 1033, 820, 771 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.40 (s, 1H), 8.12 (d, J = 7.5 Hz, 1H), 7.80-7.76 (m, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 3.90 (s, 2H), 3.73 (s, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.4, 158.7, 156.8, 149.5, 134.8, 130.4, 128.9, 127.4, 126.6, 126.2, 121.2, 114.4, 55.5, 40.5 ppm; MS (ESI) m/z 266.9 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O_2$ ([M]$^{+}$): 266.1055; found: 266.1057.



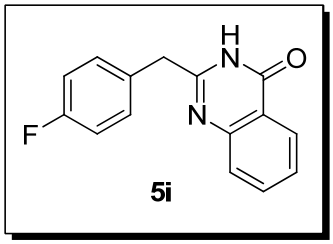
5g

Pale white solid, (216mg, 82%) m.p. 229~231^{o}C; IR 2964, 2921, 1676, 1161, 1469, 1332, 1002, 770 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.39 (s, 1H), 8.10 (d, J = 7.5 Hz, 1H), 7.77 (t, J = 7.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 3.91 (s, 2H), 2.56 (q, J = 7.5 Hz, 2H), 1.14 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.3, 156.6, 149.4, 142.7, 134.8, 134.2, 129.2, 128.3, 127.4, 126.6, 126.1, 121.2, 40.9, 28.2, 16.0 ppm; MS (ESI) m/z 264.9 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{17}H_{16}N_2O$ ([M]$^{+}$): 264.1263; found: 264.1258.



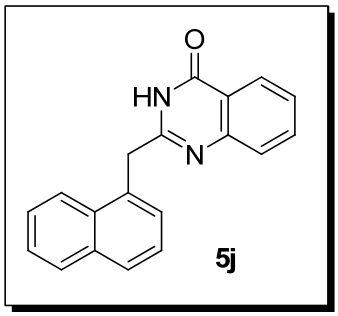
5h

Brown solid, (210mg, 77%) m.p. 242~244^{o}C; IR 2894, 1677, 1676, 1614, 1466, 1329, 1162, 1011, 773 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.44 (s, 1H), 8.08 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.42-7.38 (m, 4H), 3.95 (s, 2H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.8, 155.6, 148.8, 135.5, 134.4, 131.5, 130.8, 128.4, 126.9, 126.2, 125.7, 120.8, 40.0 ppm; MS (ESI) m/z 269.0 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{15}H_{11}N_2OCl$ ([M]$^{+}$): 270.0560; found: 270.0562.



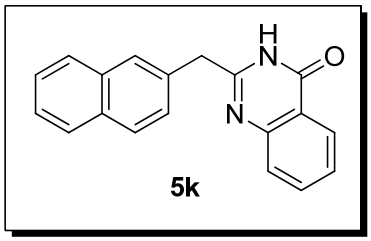
5i

Yellow solid, (160mg, 63%) m.p. 227~229^{o}C; IR 2915, 1676, 1612, 1505, 1465, 1223, 1158, 770 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.42 (s, 1H), 8.08 (d, J = 7.5 Hz, 1H), 7.77 (t, J = 7.5 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.48-7.42 (m, 3H), 7.16 (t, J = 9.0 Hz, 2H), 3.94 (s, 2H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.8, 161.2 (d, J = 241.2 Hz), 155.8, 156.8, 148.8, 134.4, 132.6 (d, J = 3.25 Hz), 130.8 (d, J = 8.13 Hz), 126.9, 126.2, 125.7, 120.7, 115.3, 115.1, 39.9 ppm; MS (ESI) m/z 254.9 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{15}H_{11}N_2OF$ ([M]$^{+}$): 254.0855; found: 254.0857.



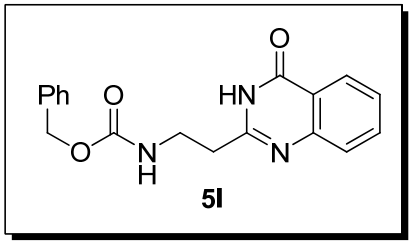
5j

Yellow solid, (205mg, 72%) m.p. 242~243^{o}C; IR 3037, 1677, 1612, 1468, 1321, 1157, 1000, 769 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.50 (s, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 7.5 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.56-7.54 (m, 1H), 7.52-7.50 (m, 3H), 7.48-7.46 (m, 2H), 4.46 (s, 2H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.8, 155.8, 148.7, 134.3, 133.4, 132.7, 131.7, 128.5, 127.4, 127.3, 126.9, 126.2, 125.8, 125.7, 125.6, 124.1, 120.8, 38.1 ppm; MS (ESI) m/z 287.1 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O$ ([M]$^{+}$): 286.1106; found: 286.1103.



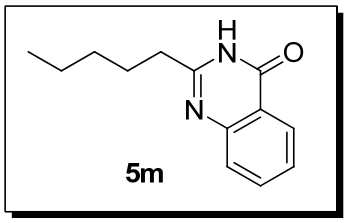
5k

Brown solid, (203mg, 71%) m.p. 234~235^{o}C; IR 2917, 1678, 1611, 1468, 1321, 1000, 882, 769 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.50 (s, 1H), 8.25 (d, J = 8.5 Hz, 1H), 8.13-8.11 (m, 1H), 7.95 (d, J = 7.5 Hz, 1H), 7.75-7.72 (m, 1H), 7.58-7.46 (m, 6H), 4.47 (s, 2H), ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.3, 156.3, 149.2, 134.8, 133.9, 133.2, 132.2, 129.0, 127.9, 127.8, 127.4, 126.7, 126.24, 126.18, 126.1, 124.6, 121.3, 38.6 ppm; MS (ESI) m/z 284.9 ([M-H]$^{-}$); HRMS (EI): m/z calcd for $C_{19}H_{14}N_2O$ ([M]$^{+}$): 286.1106; found: 286.1110.



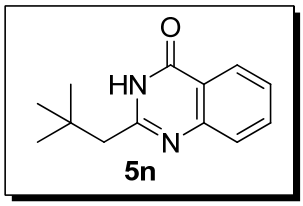
5l

Light yellow solid, (229mg, 71%) m.p. 177~178^{o}C; IR 2916, 1675, 1613, 1543, 1260, 986, 774, 693 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.20 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 7.0 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.40-7.28 (m, 6H), 5.00 (s, 2H), 3.49 (q, J = 6.5 Hz, 2H), 2.78 (t, J = 7.0 Hz, 2H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.7, 156.1, 155.3, 148.8, 137.1, 134.2, 128.3, 127.7, 127.6, 126.9, 126.0, 125.6, 121.0, 85.2, 38.0, 34.9 ppm; MS (ESI) m/z 324.2 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{18}H_{17}N_3O_3$ ([M]$^{+}$): 323.1270; found: 323.1268.



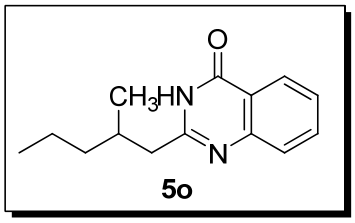
5m

Yellow solid, (123mg, 57%) m.p. 153~154^{o}C; IR 2924, 1672, 1612, 1468, 1149, 1003, 891, 765 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.18 (s, 1H), 8.09-8.07 (m, 1H), 7.78-7.73 (m, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 2.60-2.51 (m, 2H), 1.73-1.70 (m, 2H), 1.31-1.28 (m, 4H), 0.86 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.8, 157.5, 148.9, 134.2, 126.8, 125.8, 125.6, 120.8, 34.5, 30.7, 26.5, 21.8, 13.8 ppm; MS (ESI) m/z 217.0 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{13}H_{16}N_2O$ ([M]$^{+}$): 216.1263; found: 216.1266.



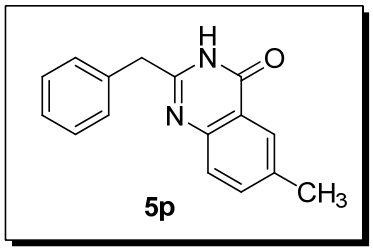
5n

Yellow solid, (136mg, 63%) m.p. 197~198^{o}C; IR 2968, 1654, 1608, 1470, 1331, 1006, 779, 692 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 8.12 (d, J = 7.5 Hz, 1H), 7.79 (t, J = 6.5 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 3.43 (s, 1H), 2.54 (s, 1H), 1.03 (s, 9H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.2, 156.0, 149.3, 134.7, 127.4, 126.4, 121.1, 47.7, 32.4, 29.9 ppm; MS (ESI) m/z 216.9 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{13}H_{16}N_2O$ ([M]$^{+}$): 216.1263; found: 216.1261.



5o

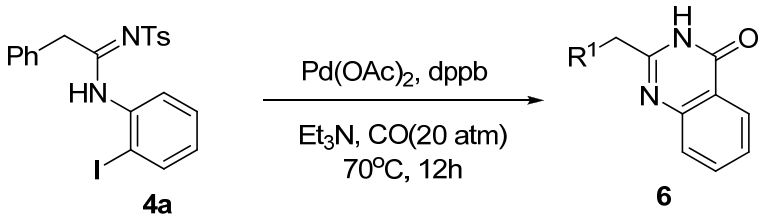
Yellow solid, (151mg, 66%) m.p. 131~133^{o}C; IR 2957, 1670, 1610, 1469, 1337, 1002, 898, 768 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.17 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.79-7.76 (m, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 2.63-2.59 (m, 1H), 2.42-2.37 (m, 1H), 2.10-2.08 (m, 1H), 1.35-1.18 (m, 4H), 0.90-0.84 (m, 6H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 162.3, 157.3, 149.4, 134.7, 127.3, 126.3, 126.1, 121.2, 42.4, 38.9, 31.7, 19.9, 19.6, 14.5 ppm; HRMS (EI): m/z calcd for $C_{14}H_{18}N_2O$ ([M]$^{+}$): 230.1419; found: 230.1417.



5p

Light yellow solid, (197mg, 79%) m.p. 237~239^{o}C; IR 2923, 1666, 1617, 1489, 1315, 1014, 841, 731 cm^{-1}; ^{1}H NMR (d_6-DMSO, 500 MHz): δ 12.33 (s, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.59-7.50 (m, 2H), 7.39-7.24 (m, 5H), 3.93 (s, 2H), 2.41 (s, 3H) ppm; ^{13}C NMR (d_6-DMSO, 125 MHz): δ 161.8, 155.0, 146.9, 133.6, 135.8, 135.6, 128.8, 128.4, 126.8, 126.7, 125.0, 120.5, 40.7, 20.7 ppm; MS (ESI) m/z 250.9 ([M+H]$^{+}$); HRMS (EI): m/z calcd for $C_{16}H_{14}N_2O$ ([M]$^{+}$): 250.1106; found: 250.1104.

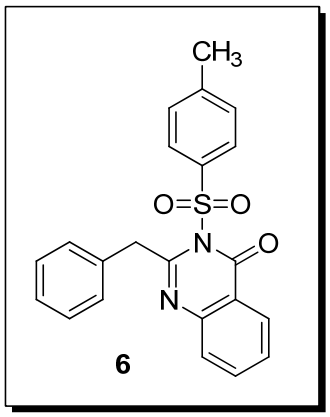
General Procedure for the Synthesis of 6



A mixture of **4** (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), Et_3N (3.0 mmol) and tetrahydrofuran (10 mL) were sequentially added to a 25 mL beaker with a magnetic bar in it. Then put the beaker into a 50ml autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with 20 atm of CO, and then heated at 70°C for 12 h. The autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The reaction mixture was filtered and the filtrate was concentrated by rotary evaporation. The

residue was purified by flash chromatography on silica gel with a mixture of hexane and ethyl acetate (2:1 to 1:1) as the eluent to afford the desired products **6**.

Characterization of 6



Yellow solid, (323mg, 83%) m.p. 111~113^{o}C; IR 3572, 3451, 1715, 1652, 1587, 1366, 1173, 771 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.09-8.07 (m, 1H), 7.76-7.73 (m, 1H), 7.66-7.64 (m, 1H), 7.47 (d, J=9.0 Hz, 2H), 7.44-7.41 (m, 1H), 7.33-7.30 (m, 5H), 7.15 (d, J=8.5 Hz, 2H), 4.76 (s, 2H), 2.36 (s, 3H) ppm; ^{13}C NMR $CDCl_3$, 125 MHz): δ 161.7, 152.4, 145.6, 145.1, 136.7, 136.1, 135.6, 129.3, 129.2, 128.7, 127.8, 127.5, 127.1, 127.0, 121.5, 43.7, 21.7 ppm; MS (ESI) m/z 412.9 ([M+Na]$^{+}$); HRMS (EI): m/z calcd for $C_{22}H_{18}N_2O_3S$ ([M]$^{+}$):390.1038; found: 390.1039.

Copies of NMR Spectra of 4, 5 and 6

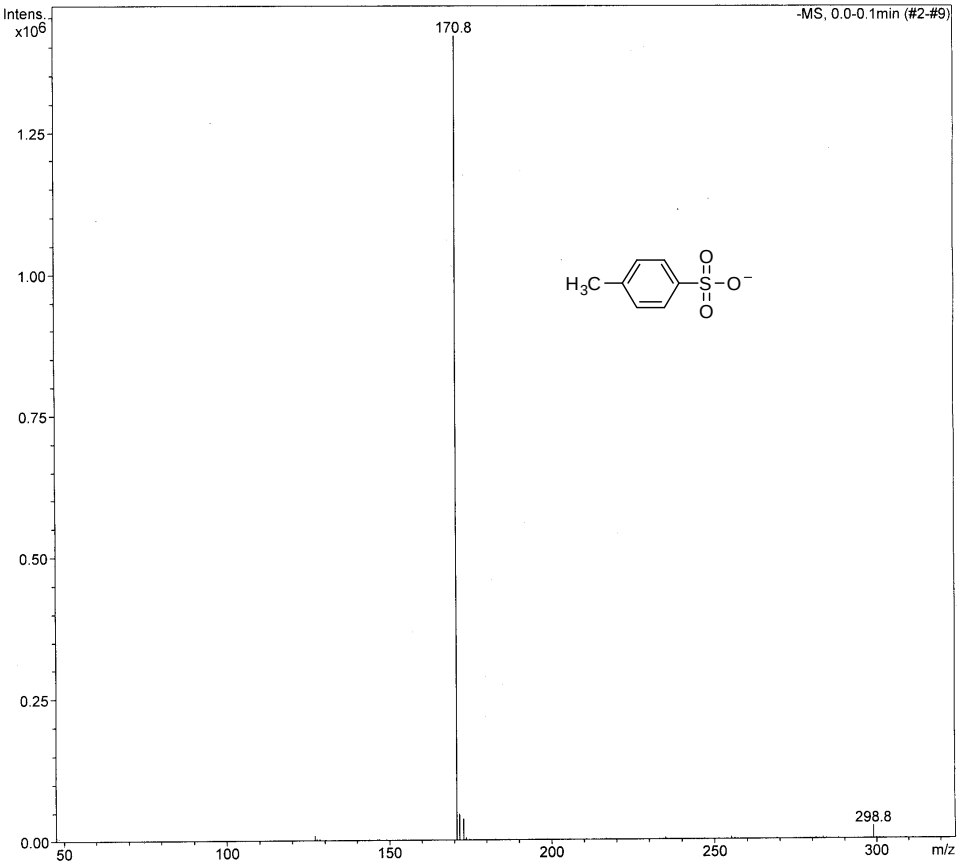
Display Report

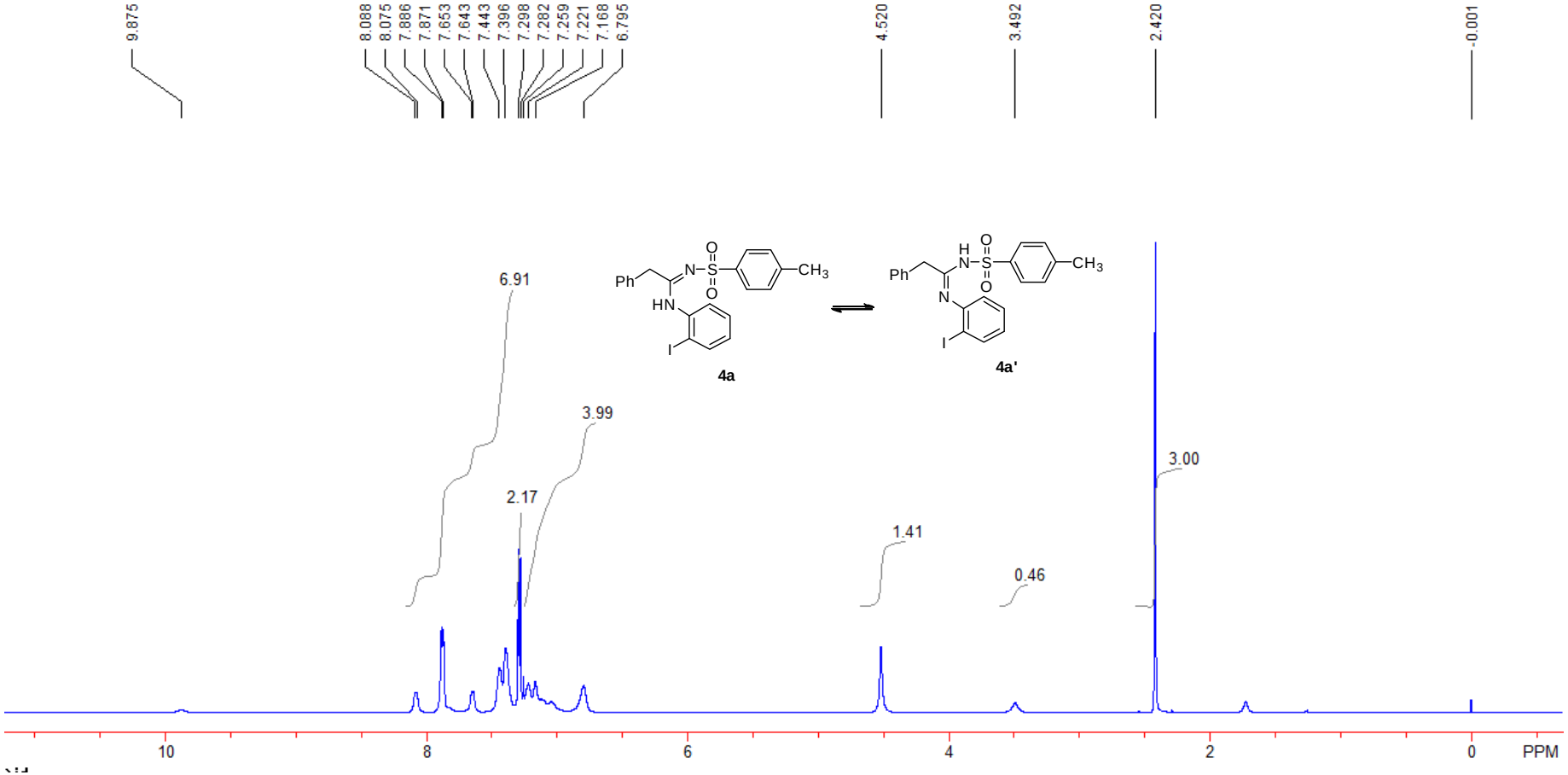
Analysis Info

Analysis Name	12040622.d	Acquisition Date	04/06/12 20:39:50
Method	Copy of E3Kp Default.ms	Operator	Administrator
Sample Name	455-170	Instrument	esquire3000plus
Comment			

Acquisition Parameter

Ion Source Type	ESI	Ion Polarity	Negative	Alternating Ion Polarity	off
Mass Range Mode	Std/Normal	Scan Begin	50 m/z	Scan End	1000 m/z
Capillary Exit	-106.0 Volt	Skim 1	-40.0 Volt	Trap Drive	35.6
Accumulation Time	10415 µs	Averages	5 Spectra	Auto MS/MS	off

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7.221
7.168
6.795
4.520
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2.420
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6
4
2
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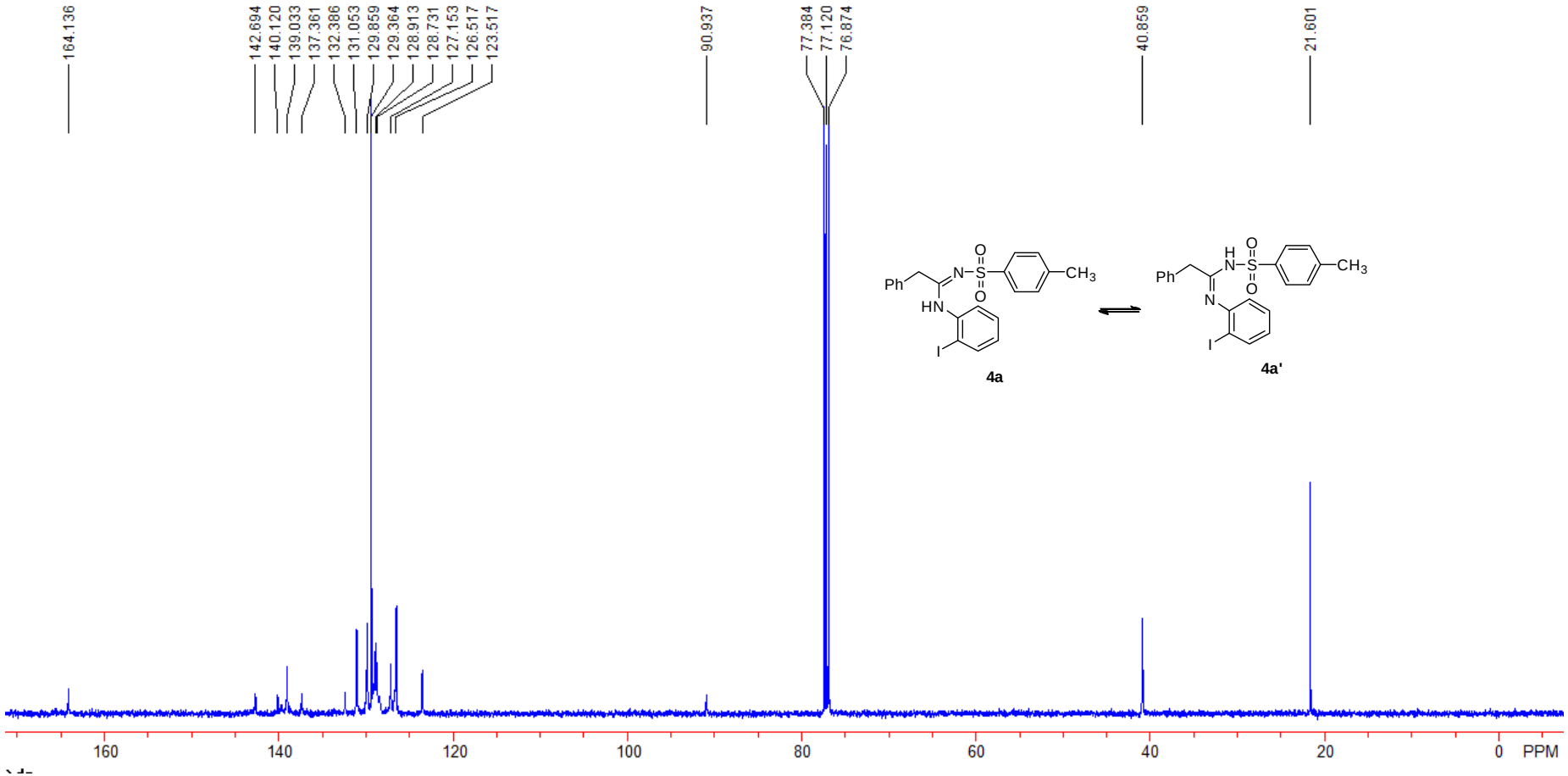
PPM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123.517
90.937
77.384
77.120
76.874
40.859
21.601
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O
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I
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4a'
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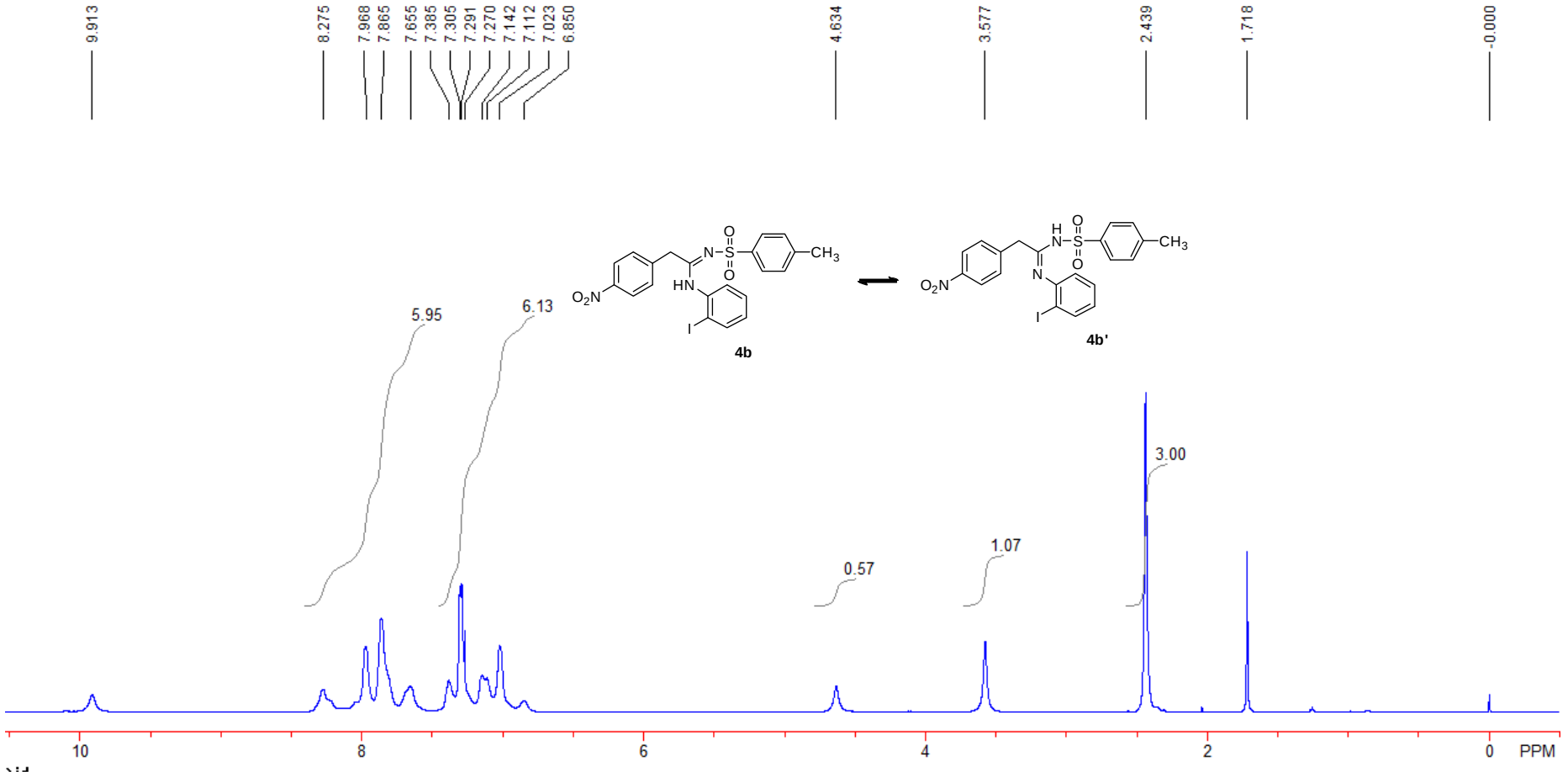
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4.634
3.577
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1.718
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10
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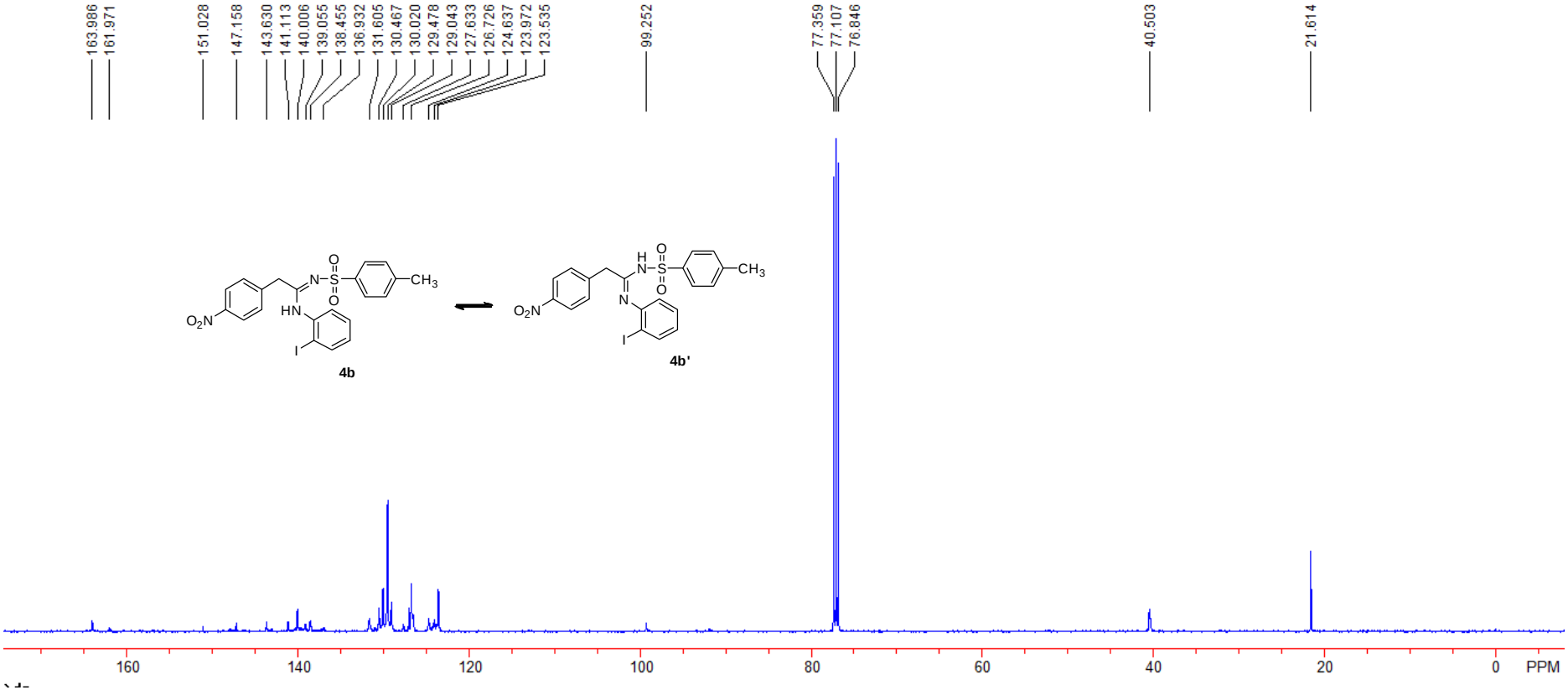
PPM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130.020
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129.043
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124.637
123.972
123.535
99.252
77.359
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40.503
21.614
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4b'
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120
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60
40
20
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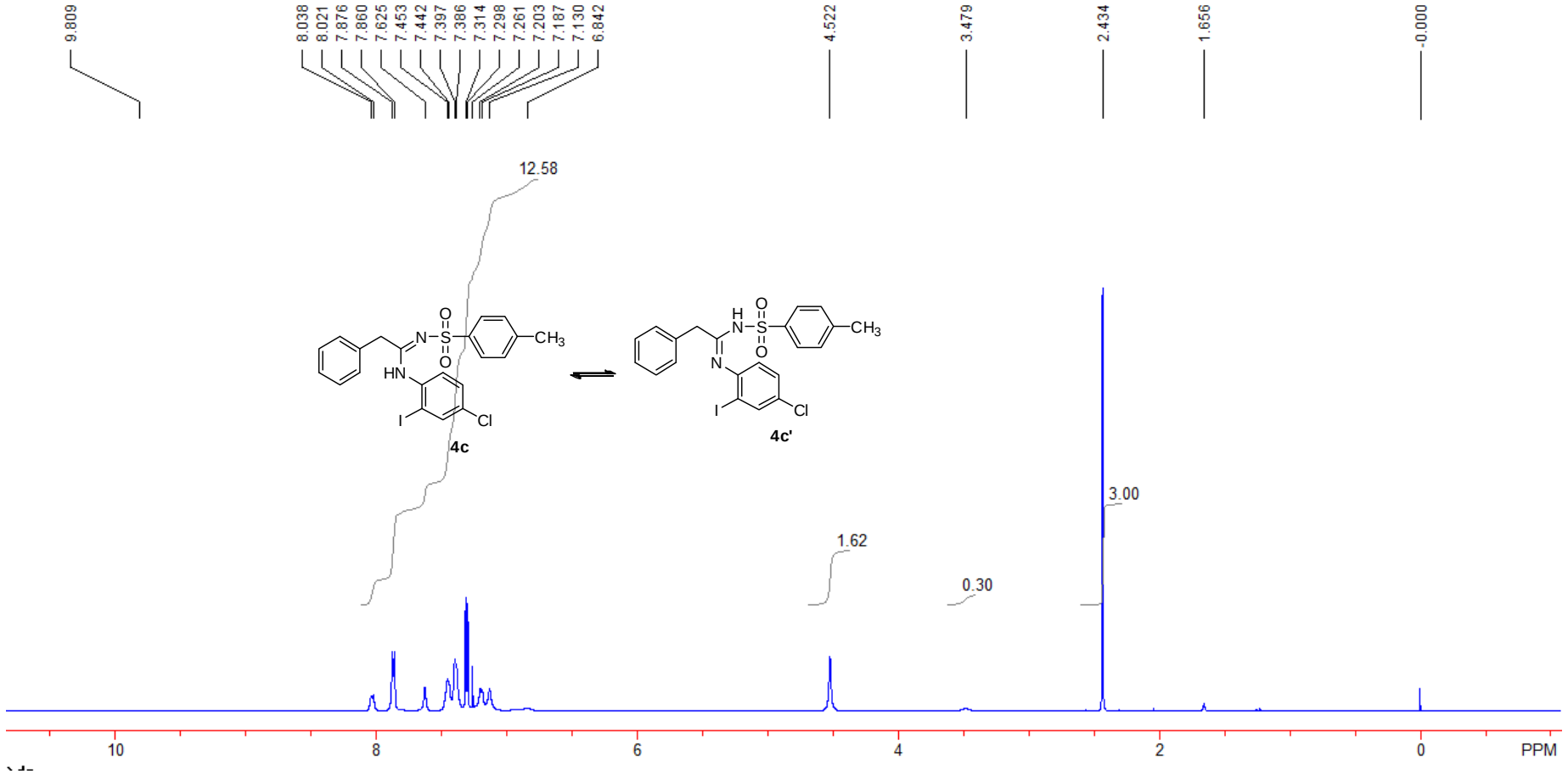
PPM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4
2
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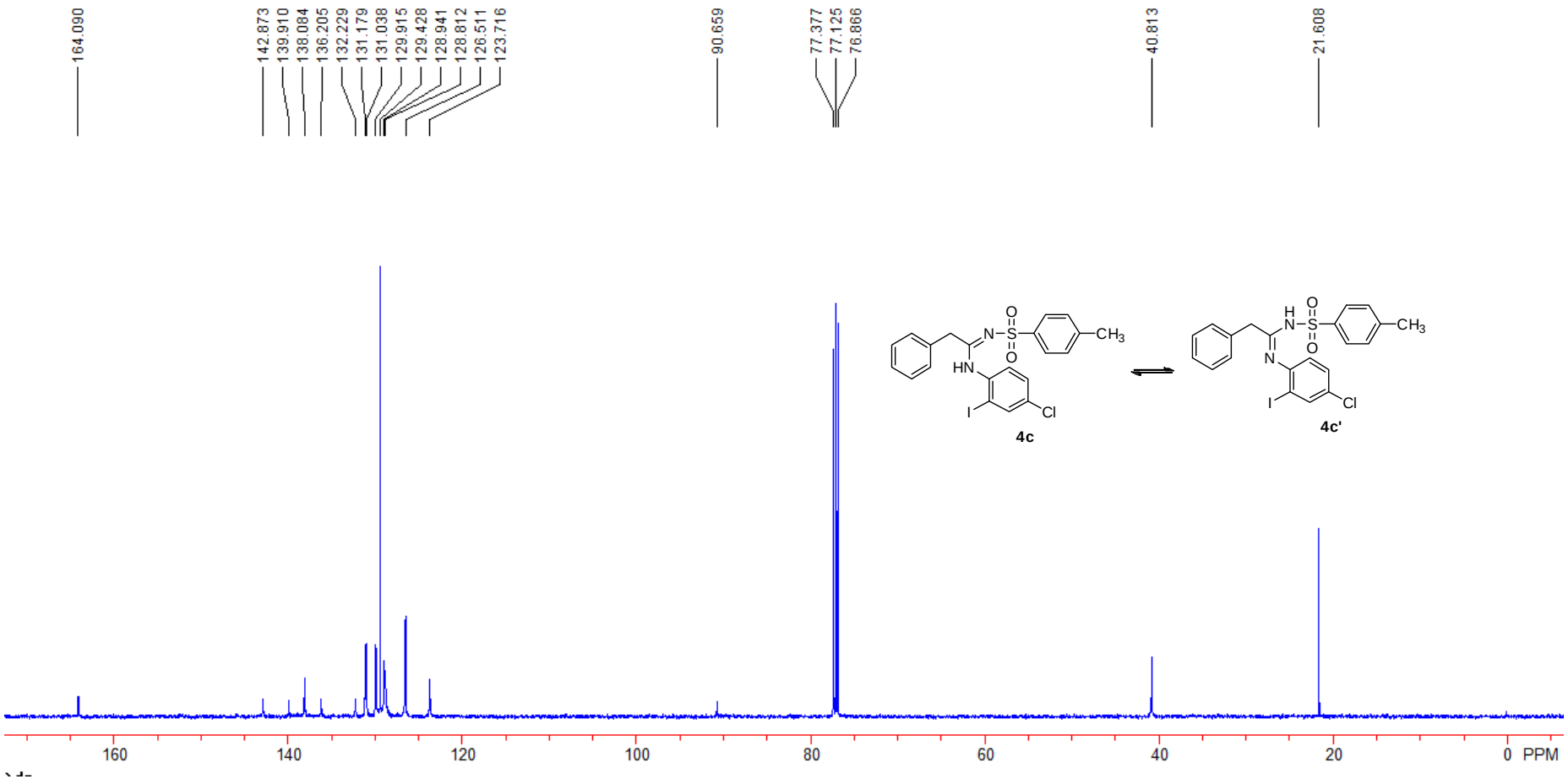
PPM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126.511
123.716
90.659
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80
60
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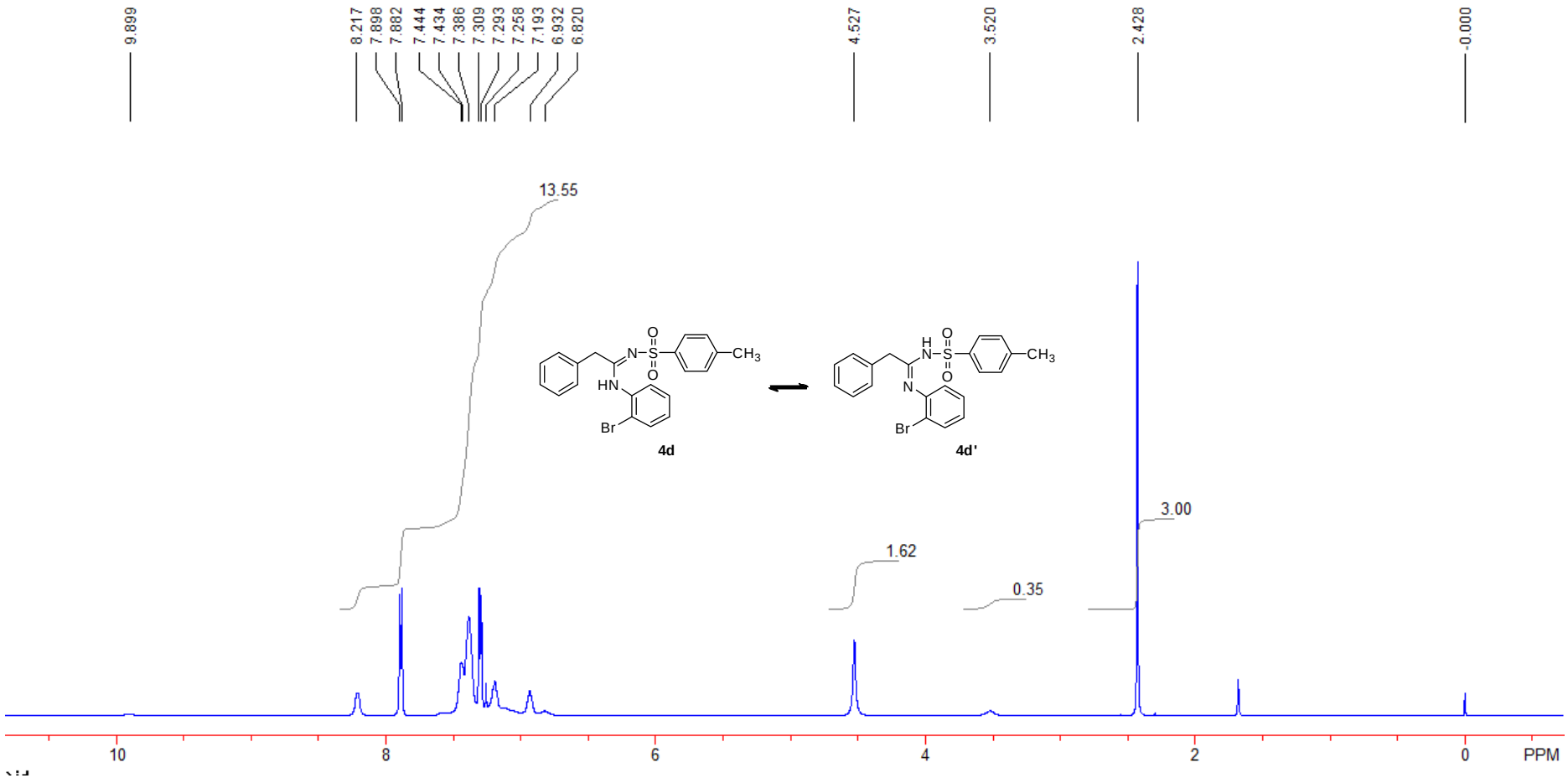
4c

4c'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3.00
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4
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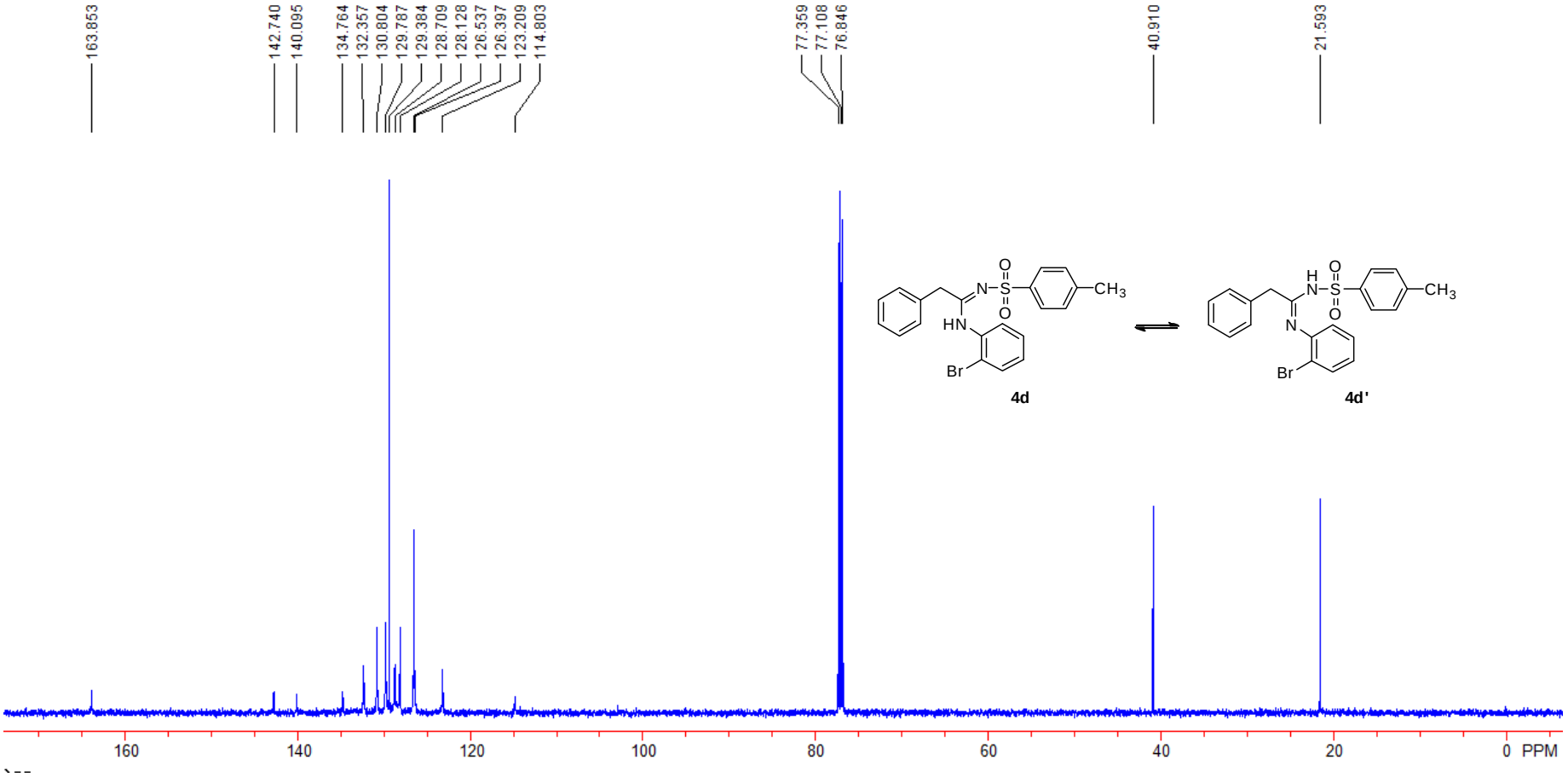
PPM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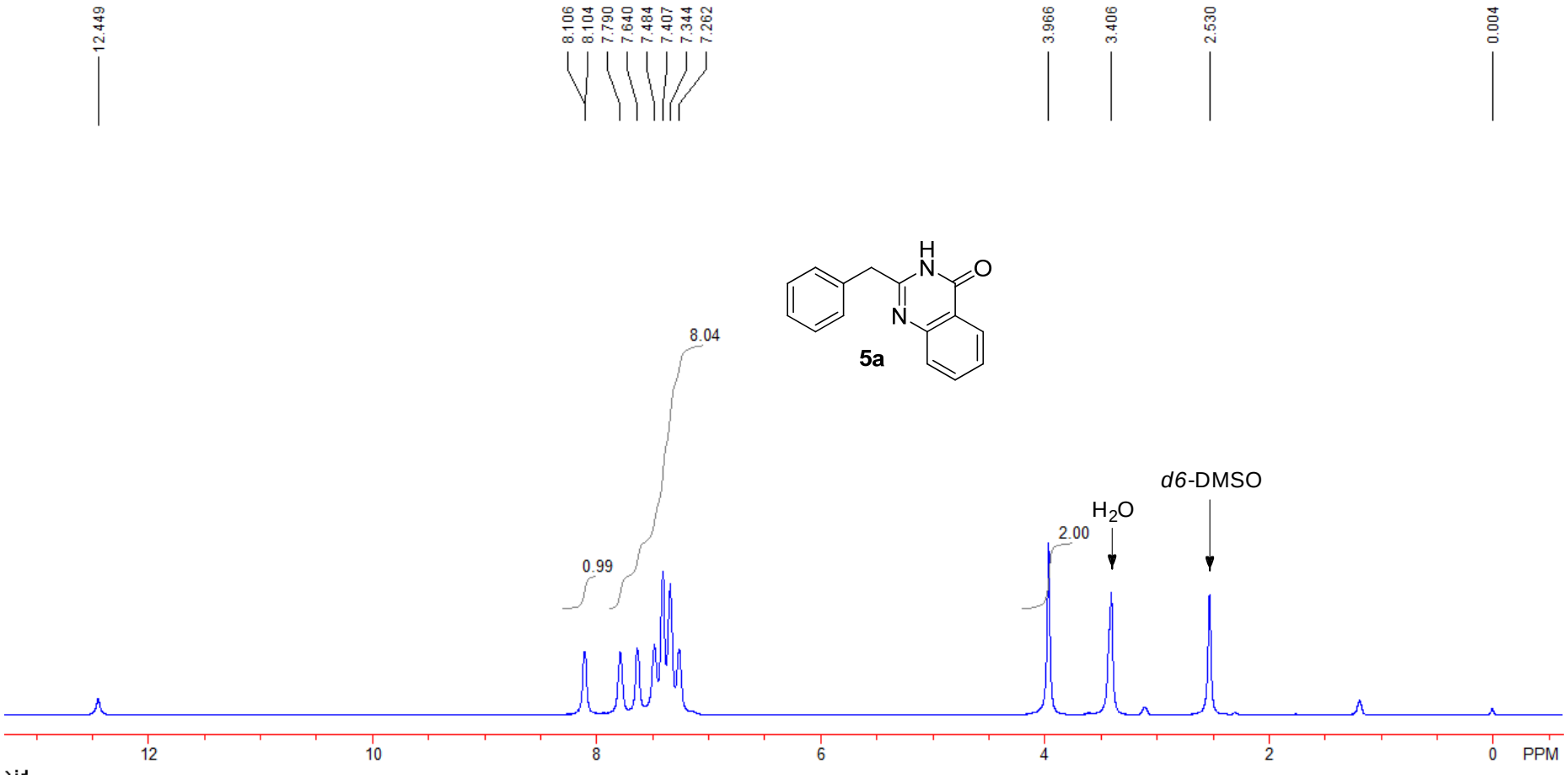
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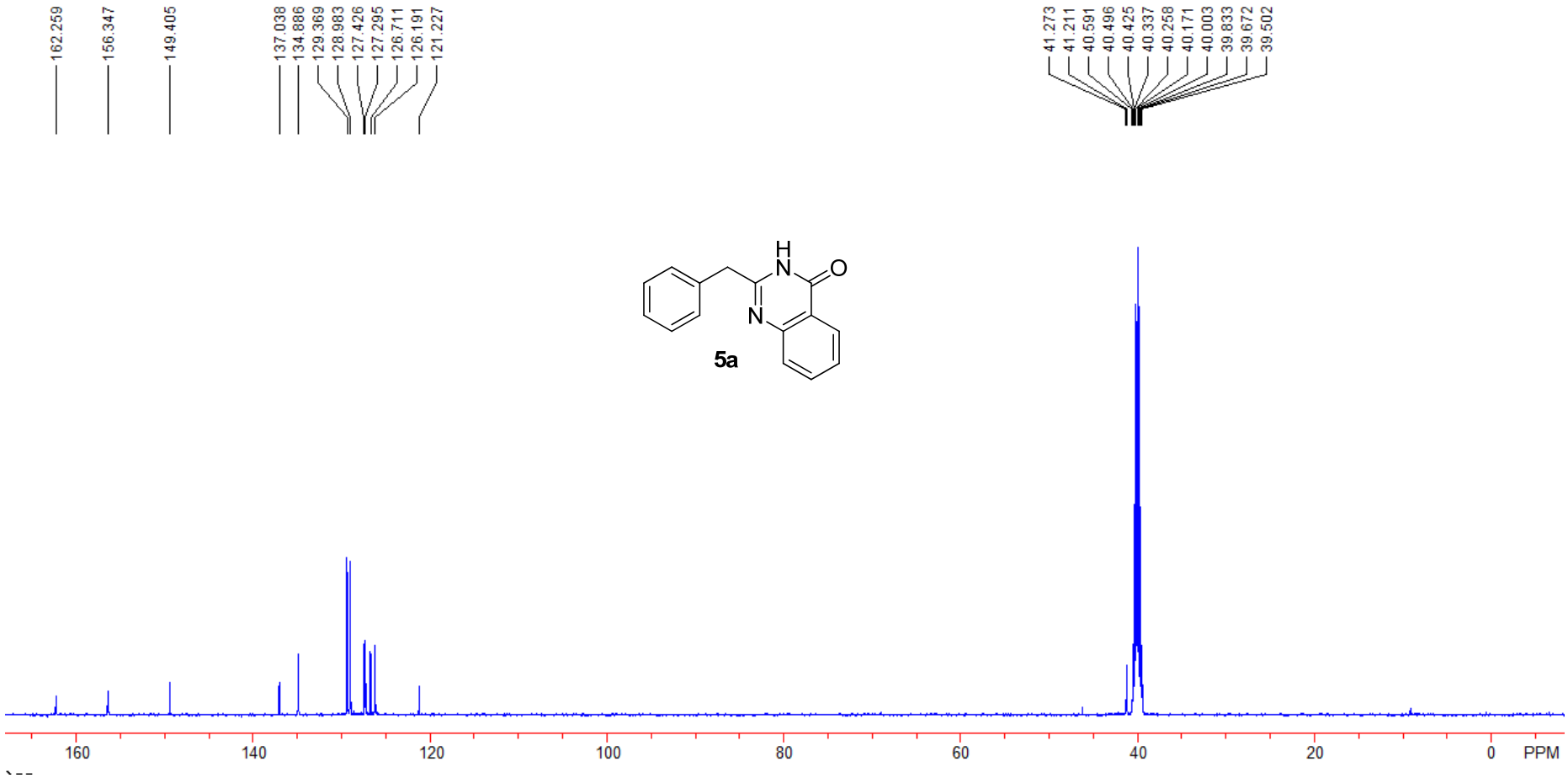
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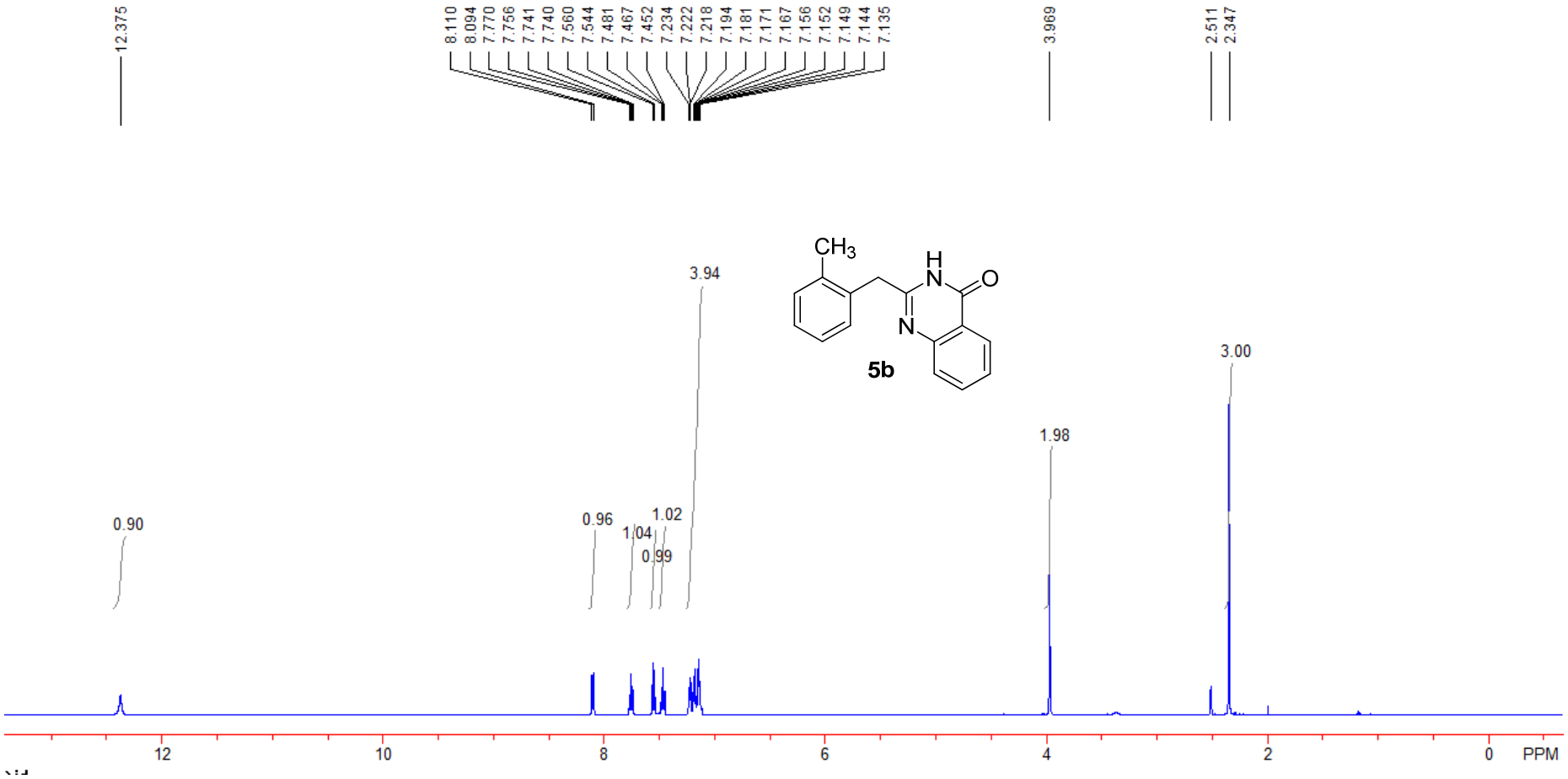
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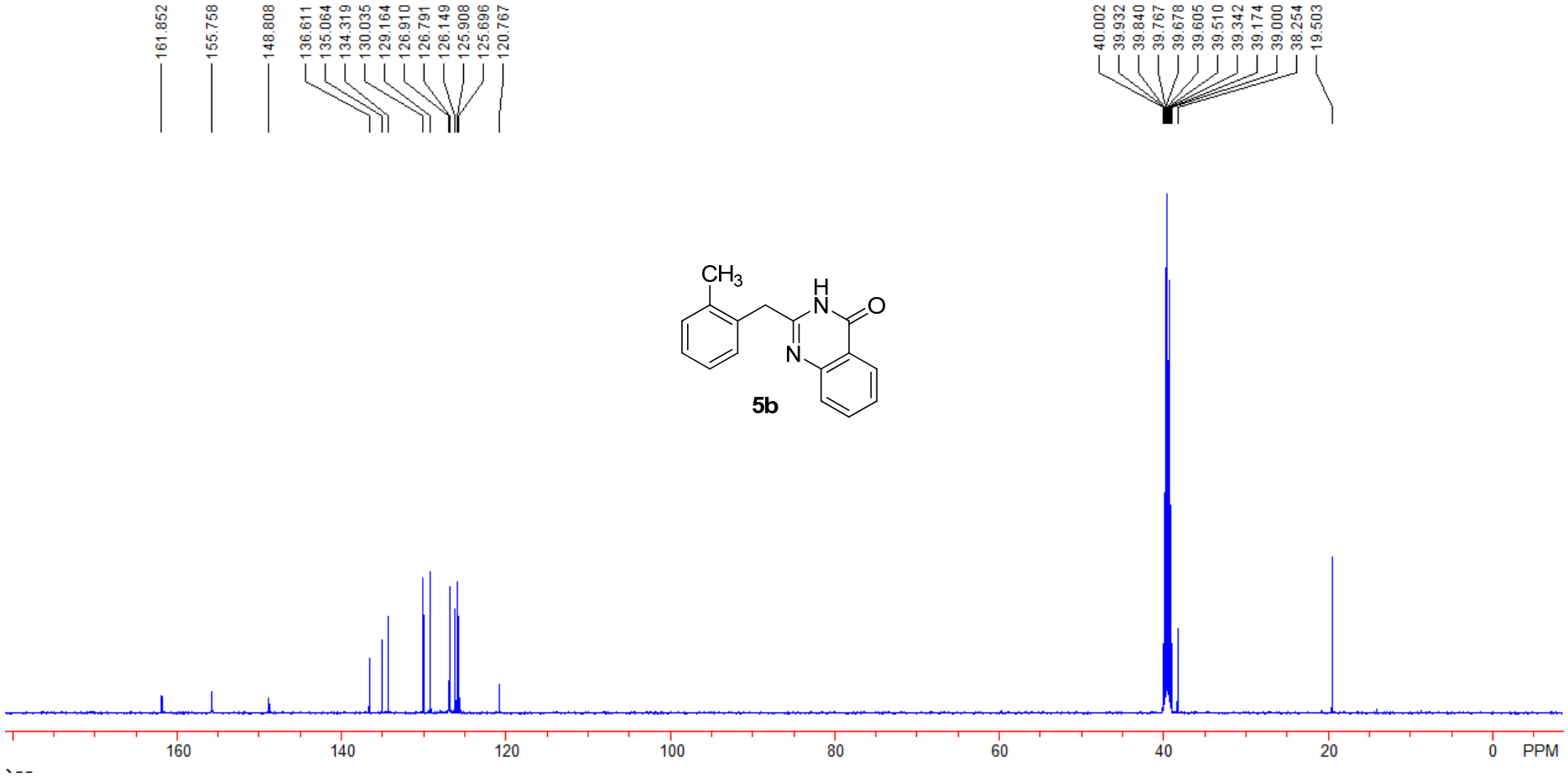
PPM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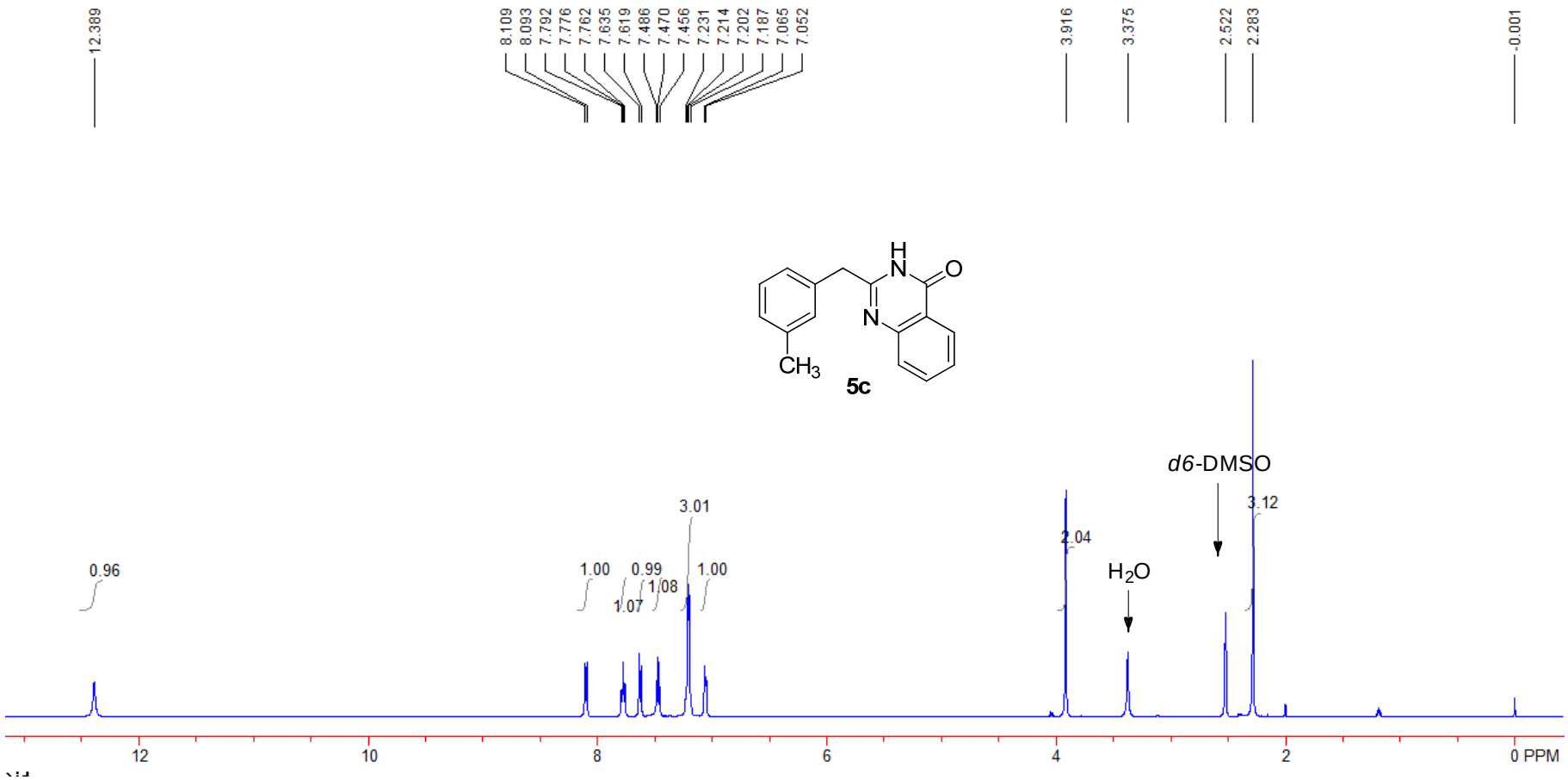
PPM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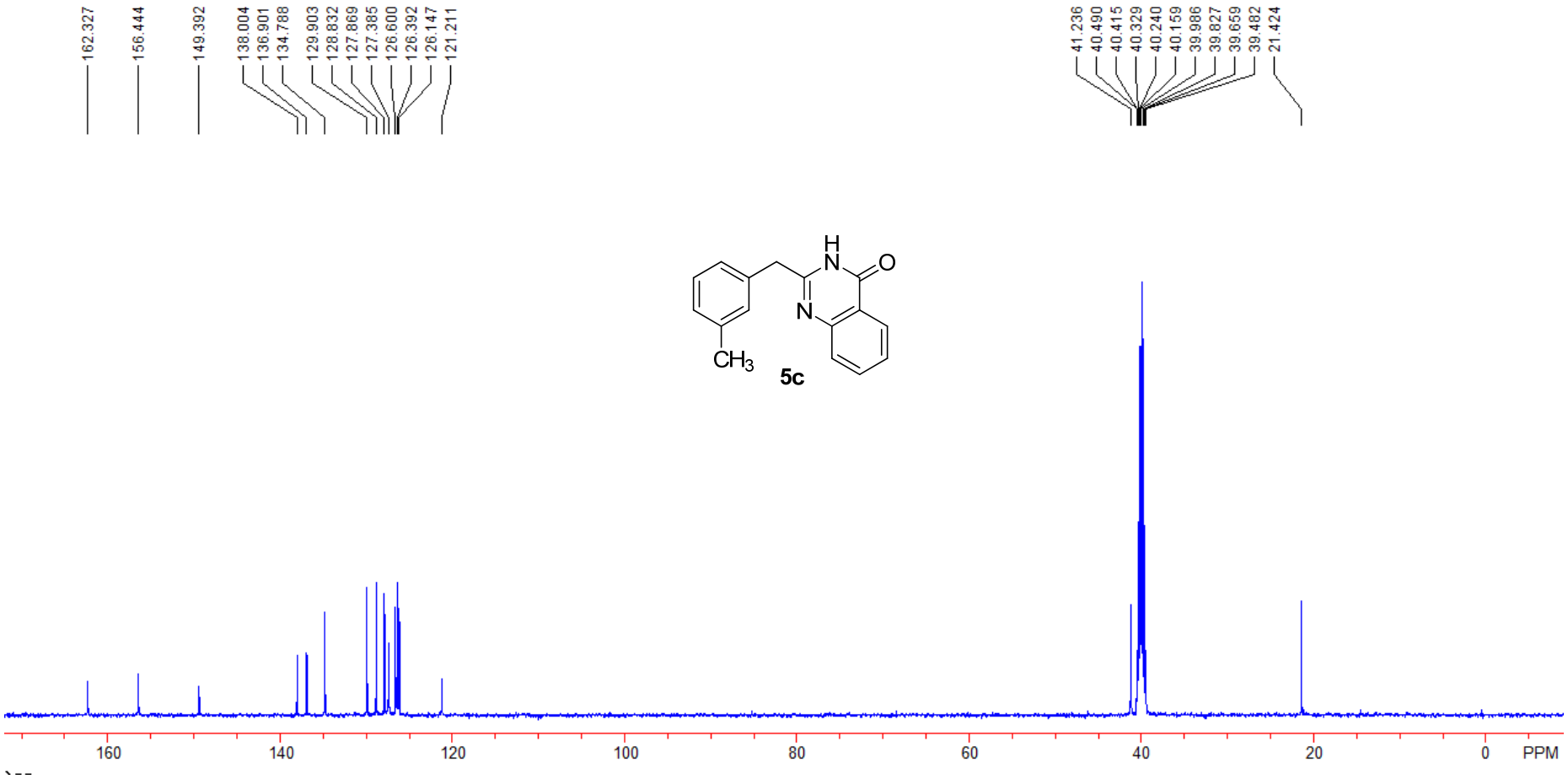
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39.659
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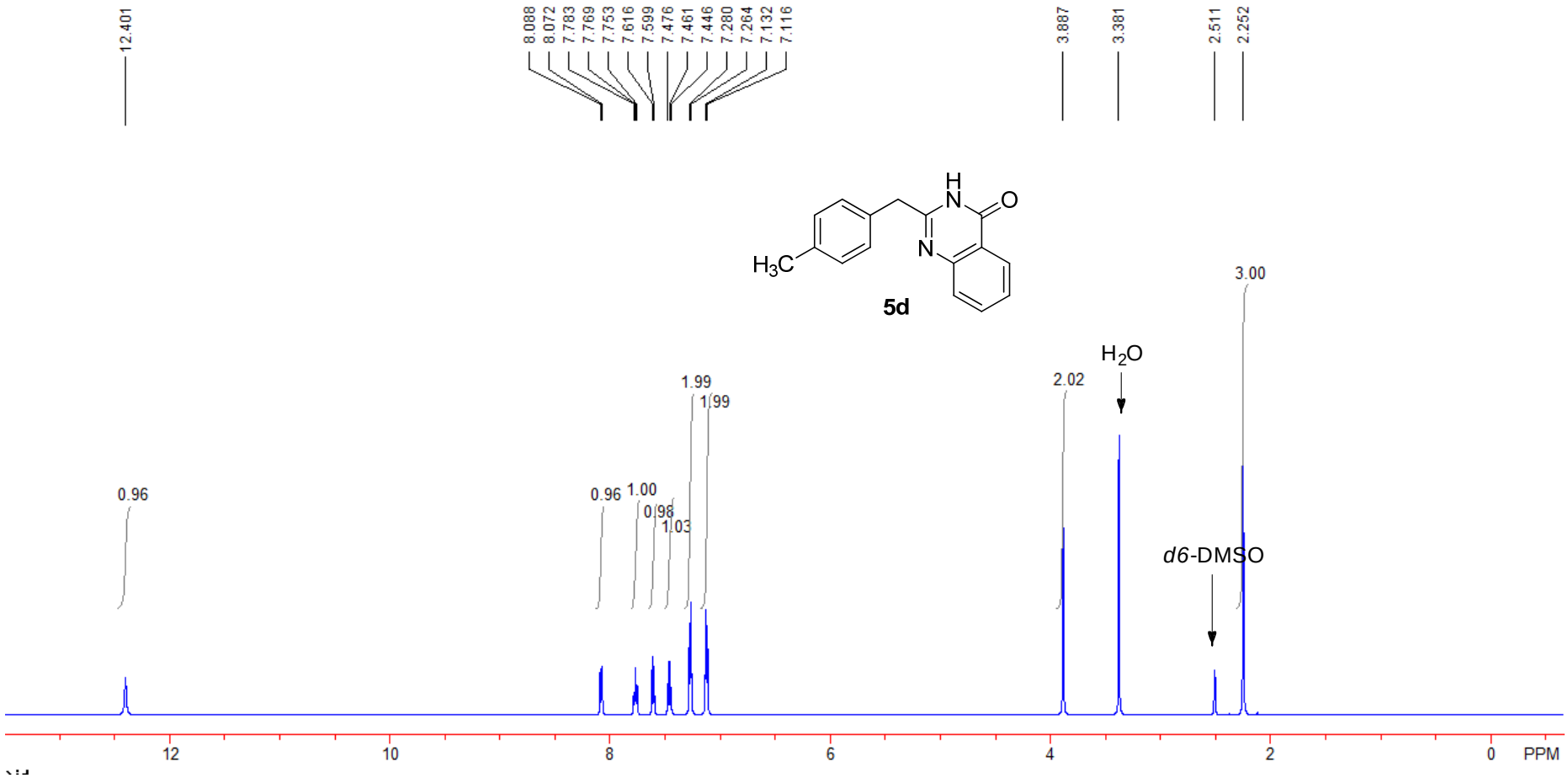
PPM

5c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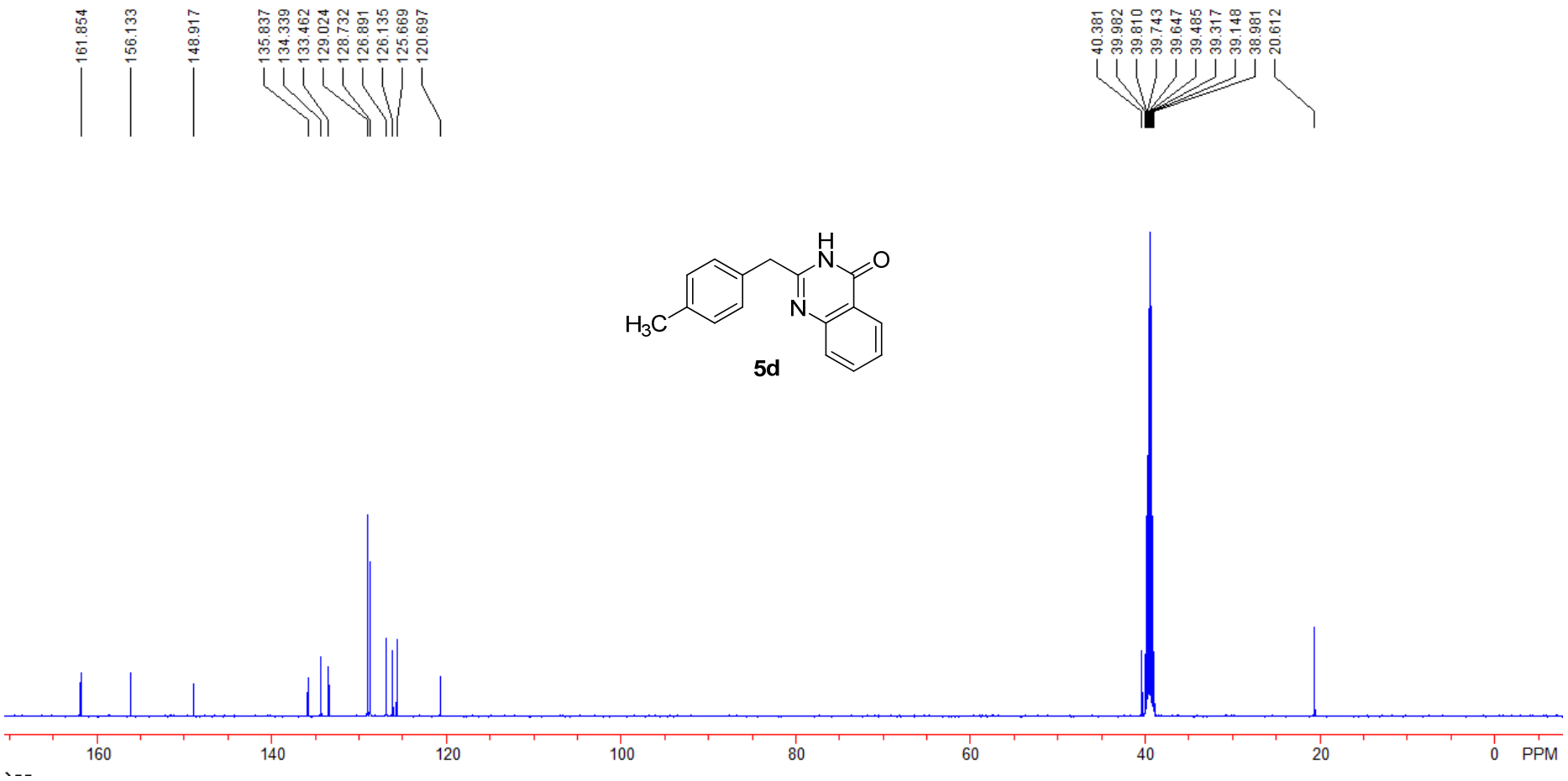
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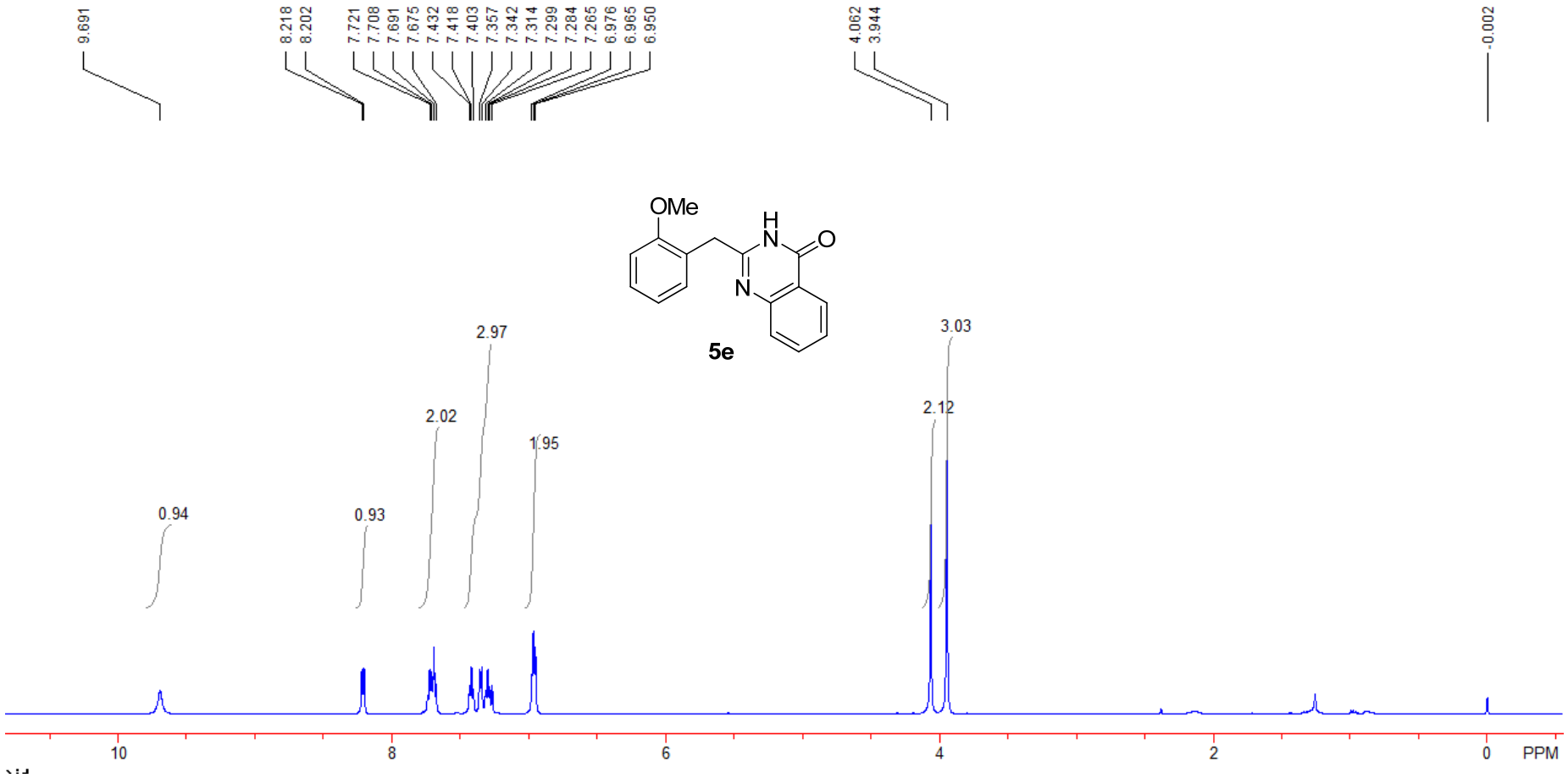
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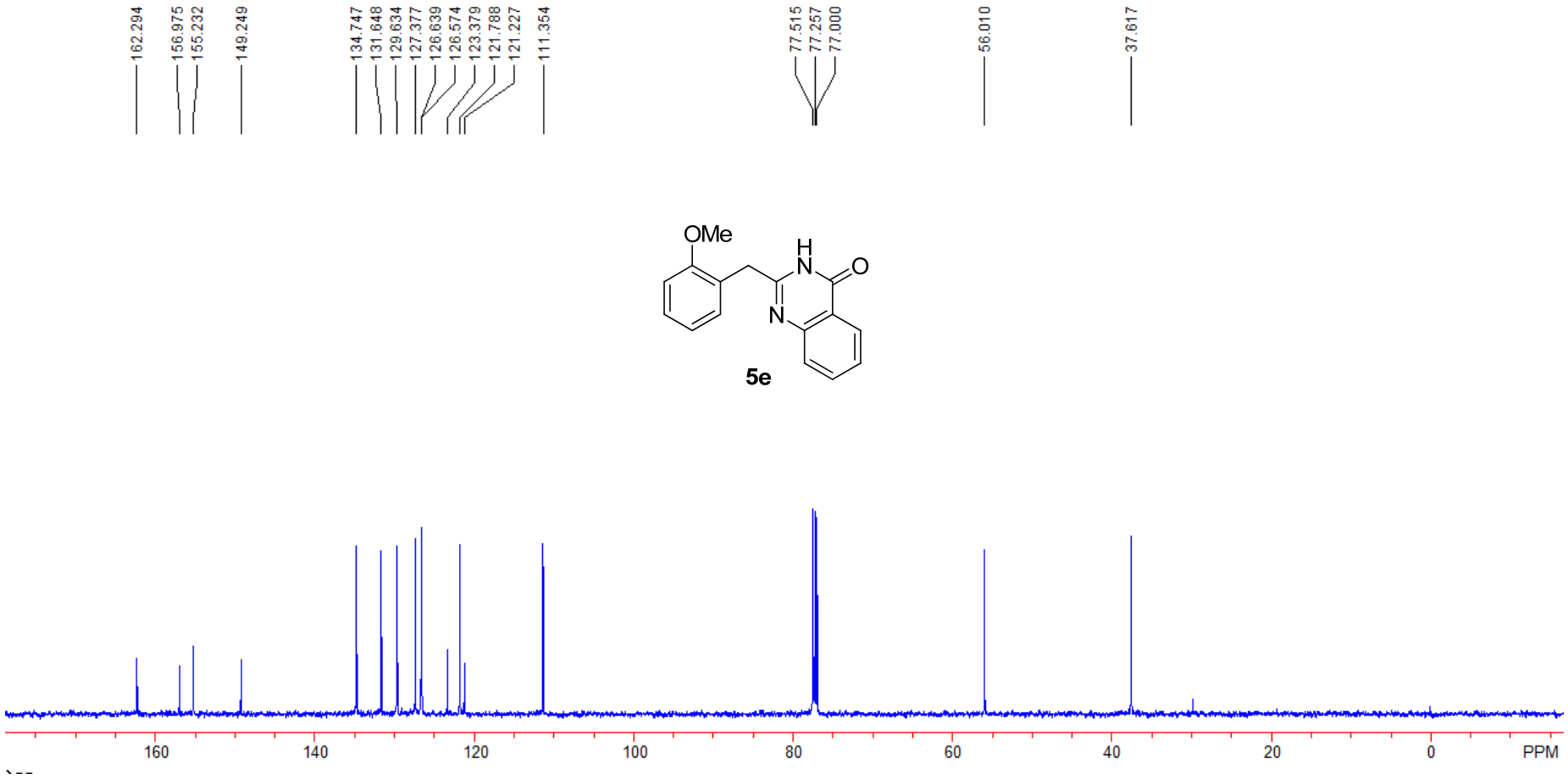
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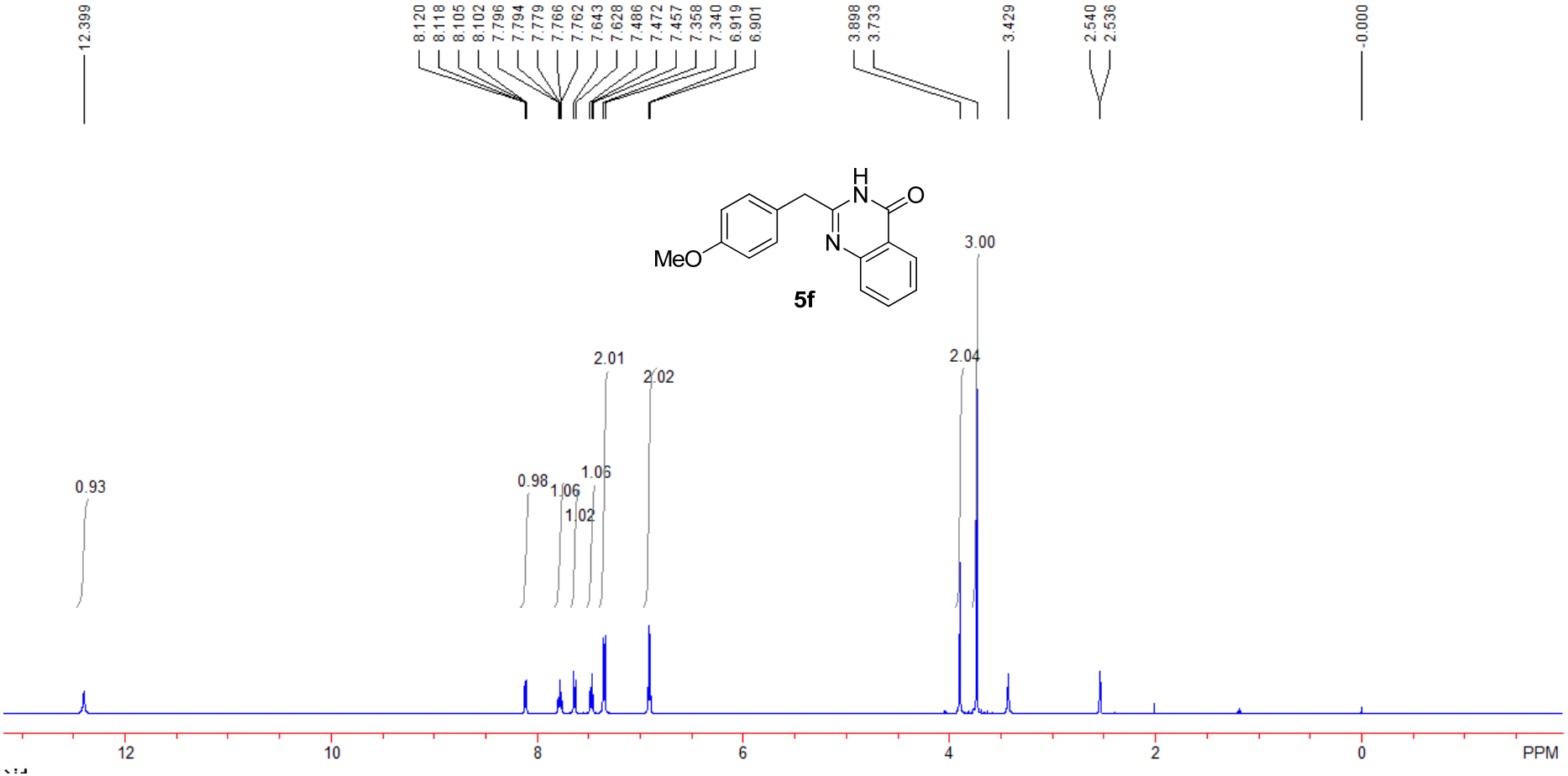
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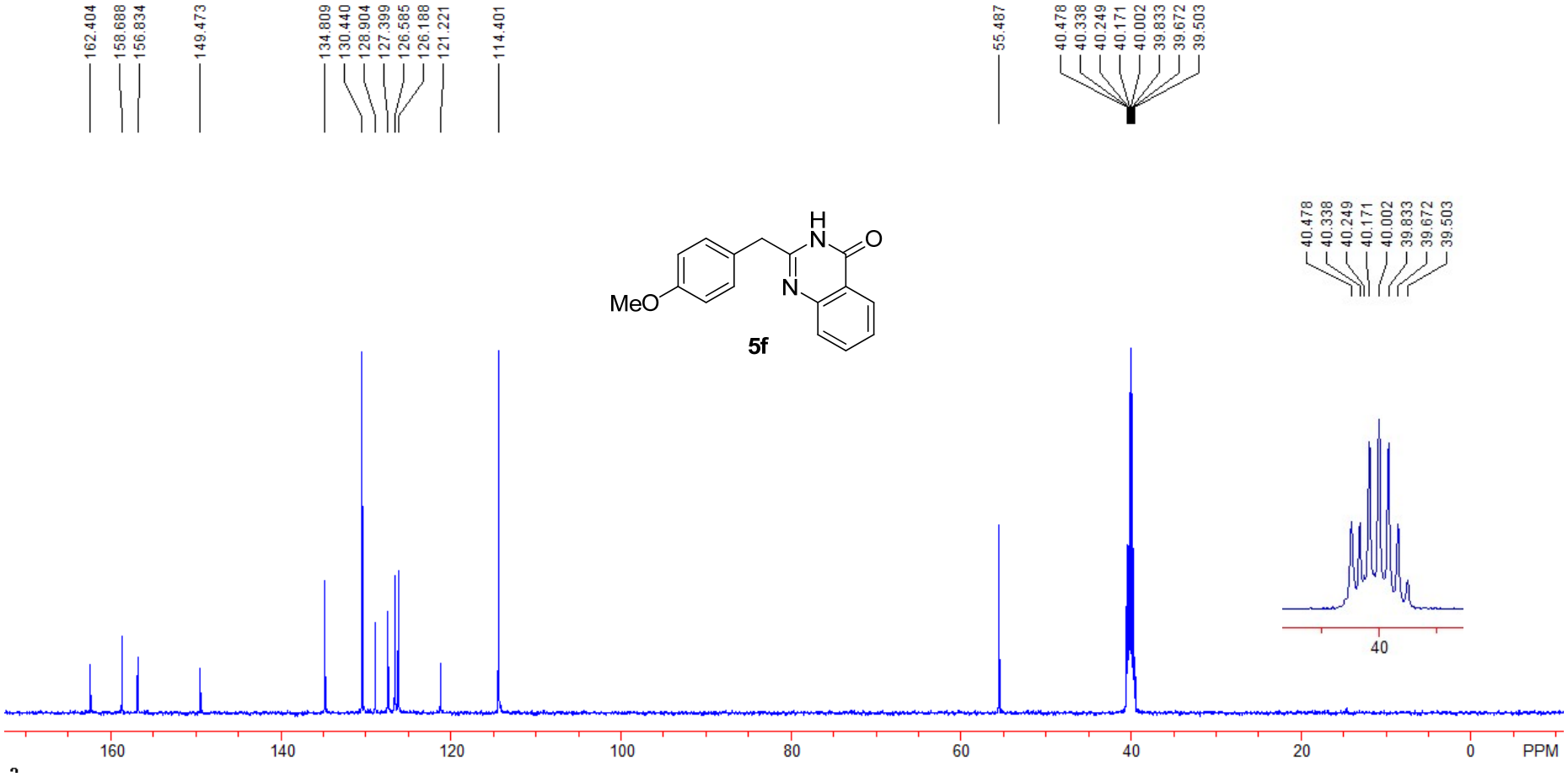
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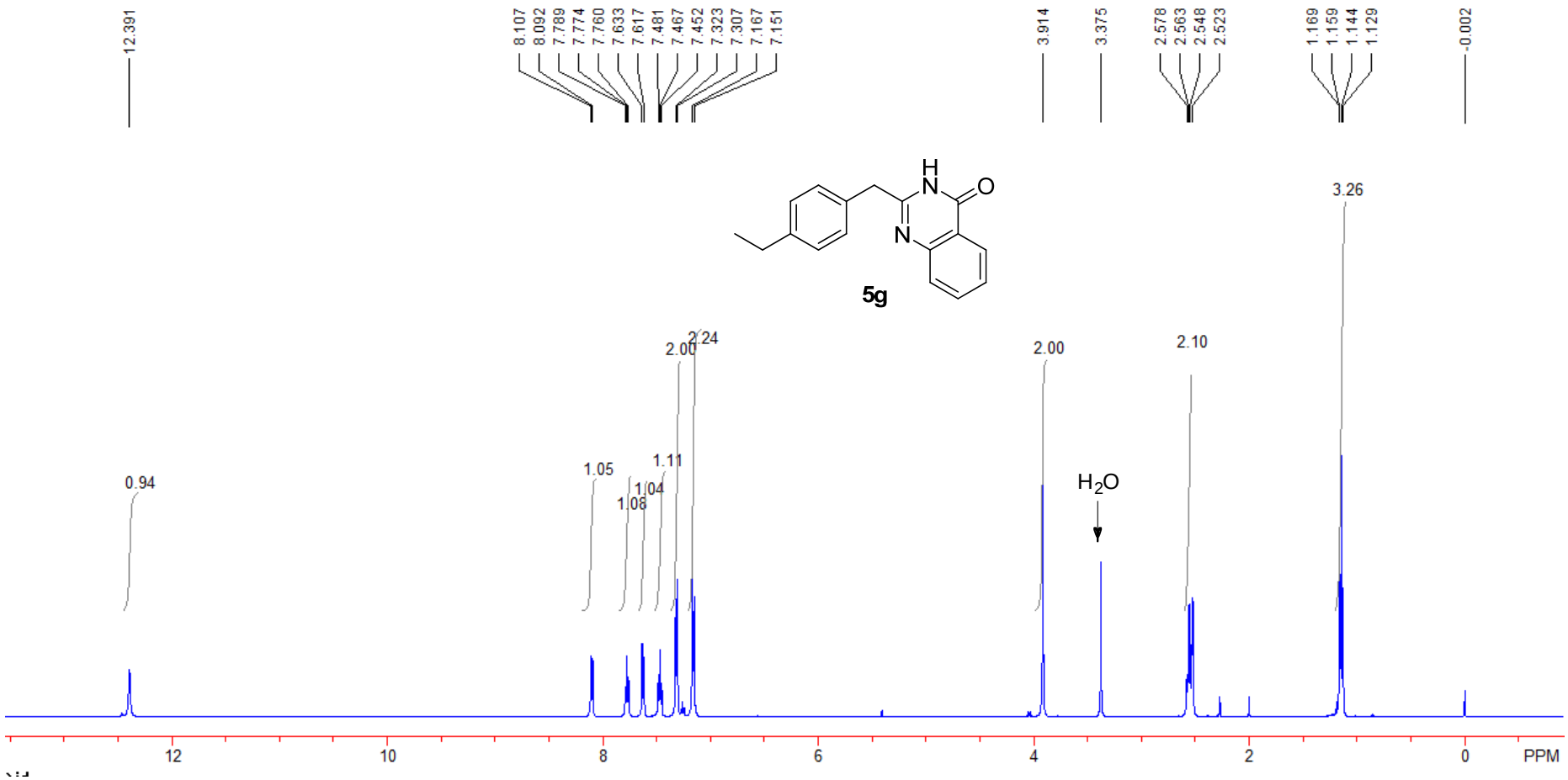
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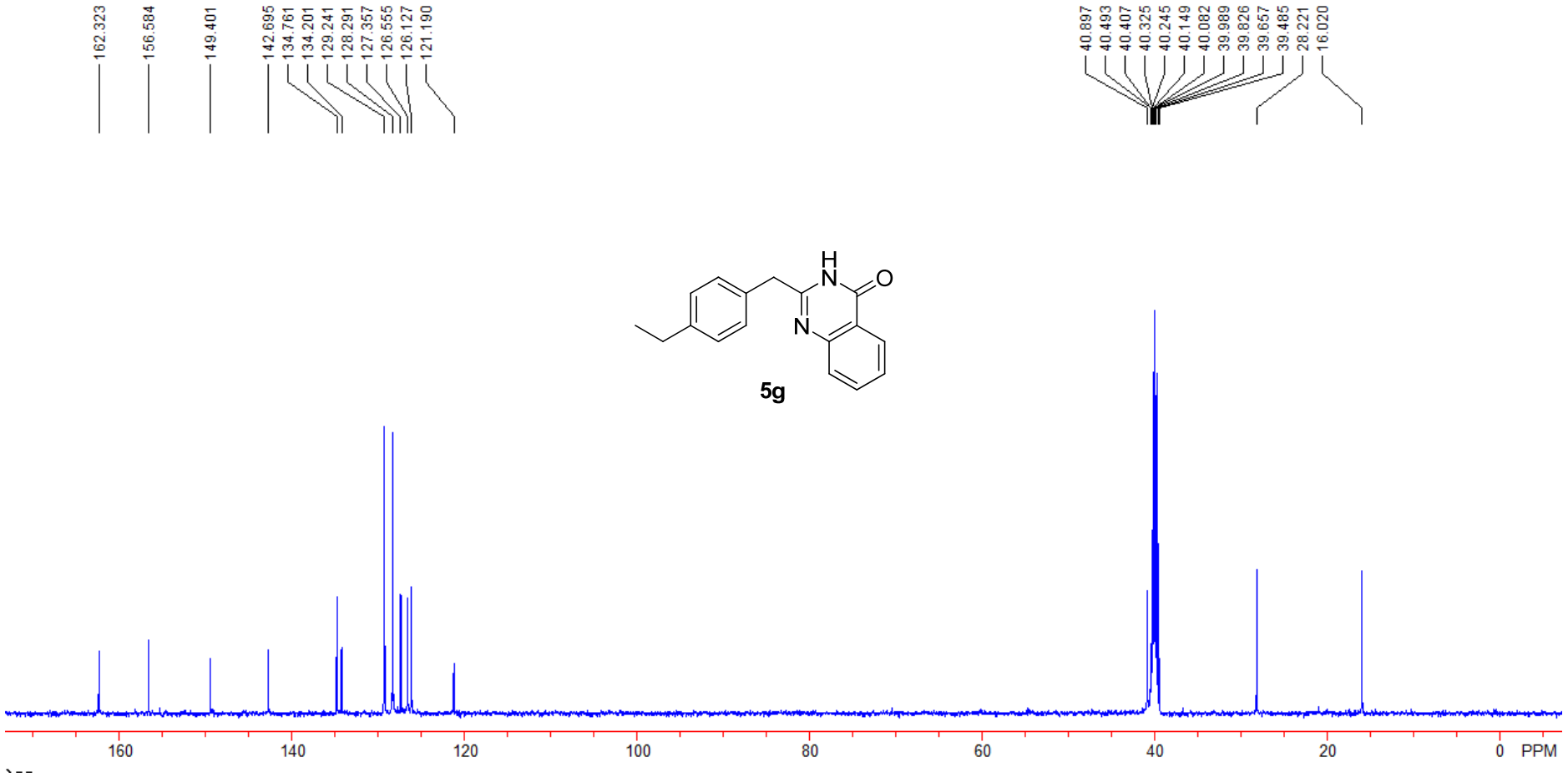
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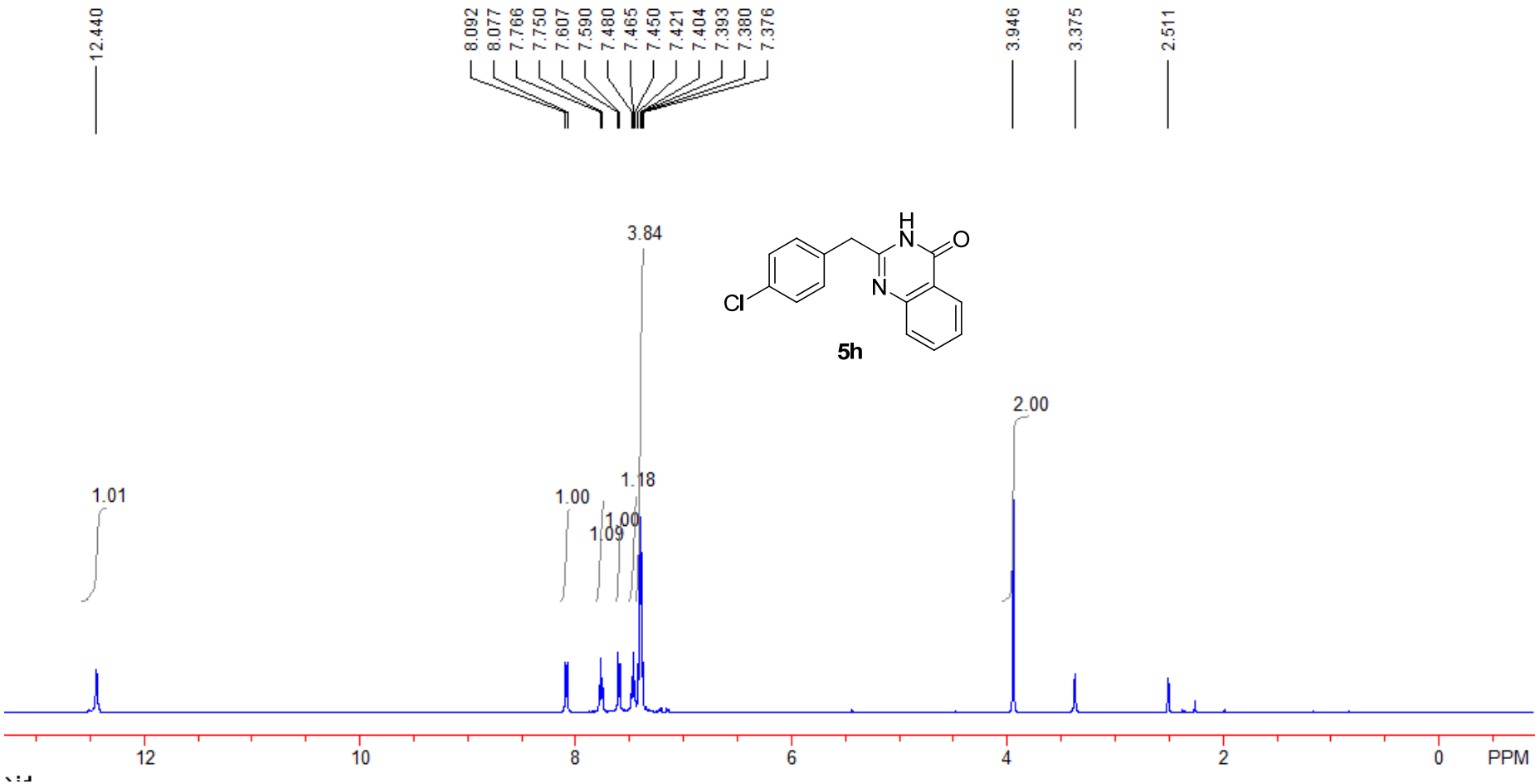
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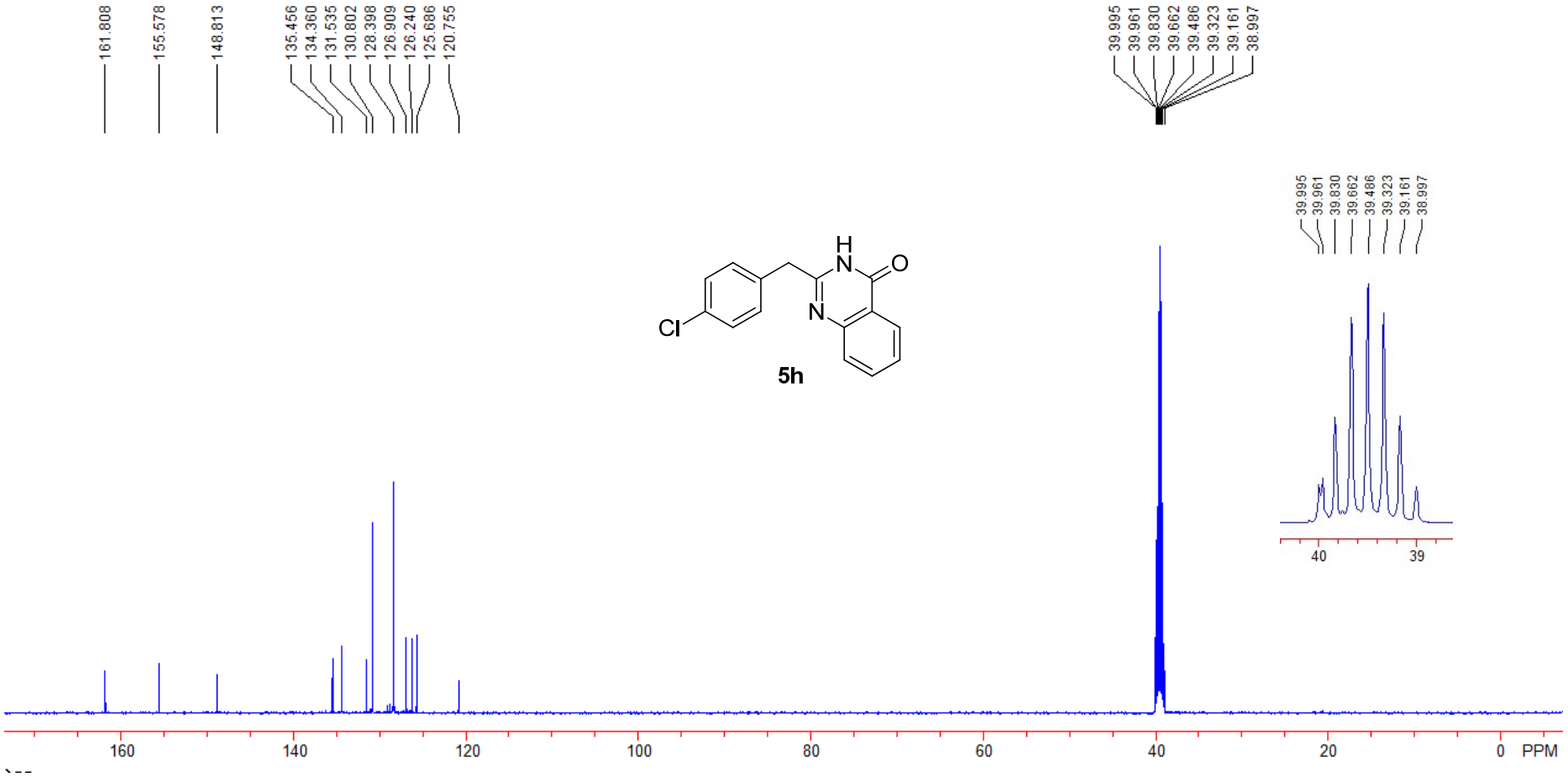
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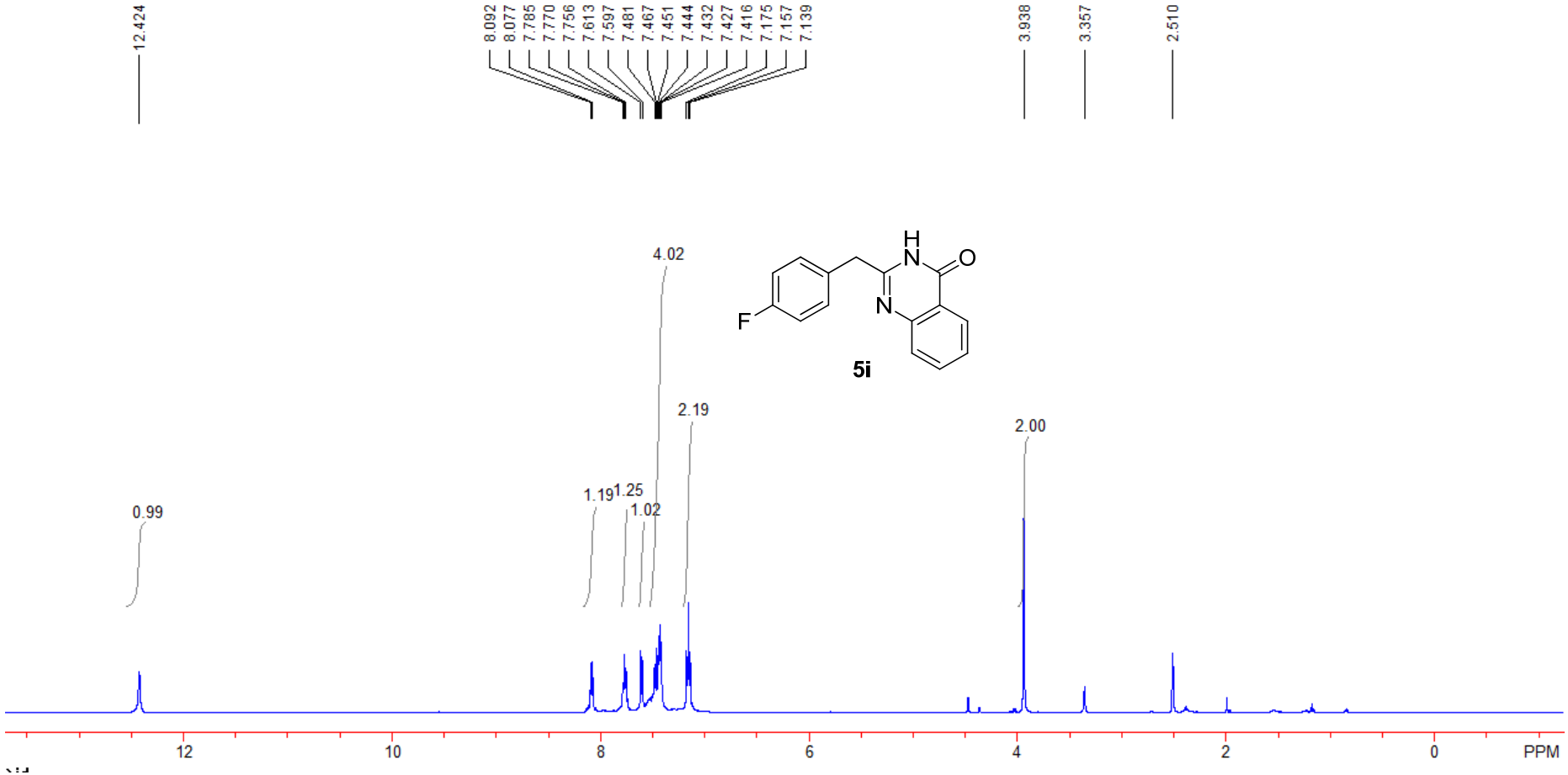
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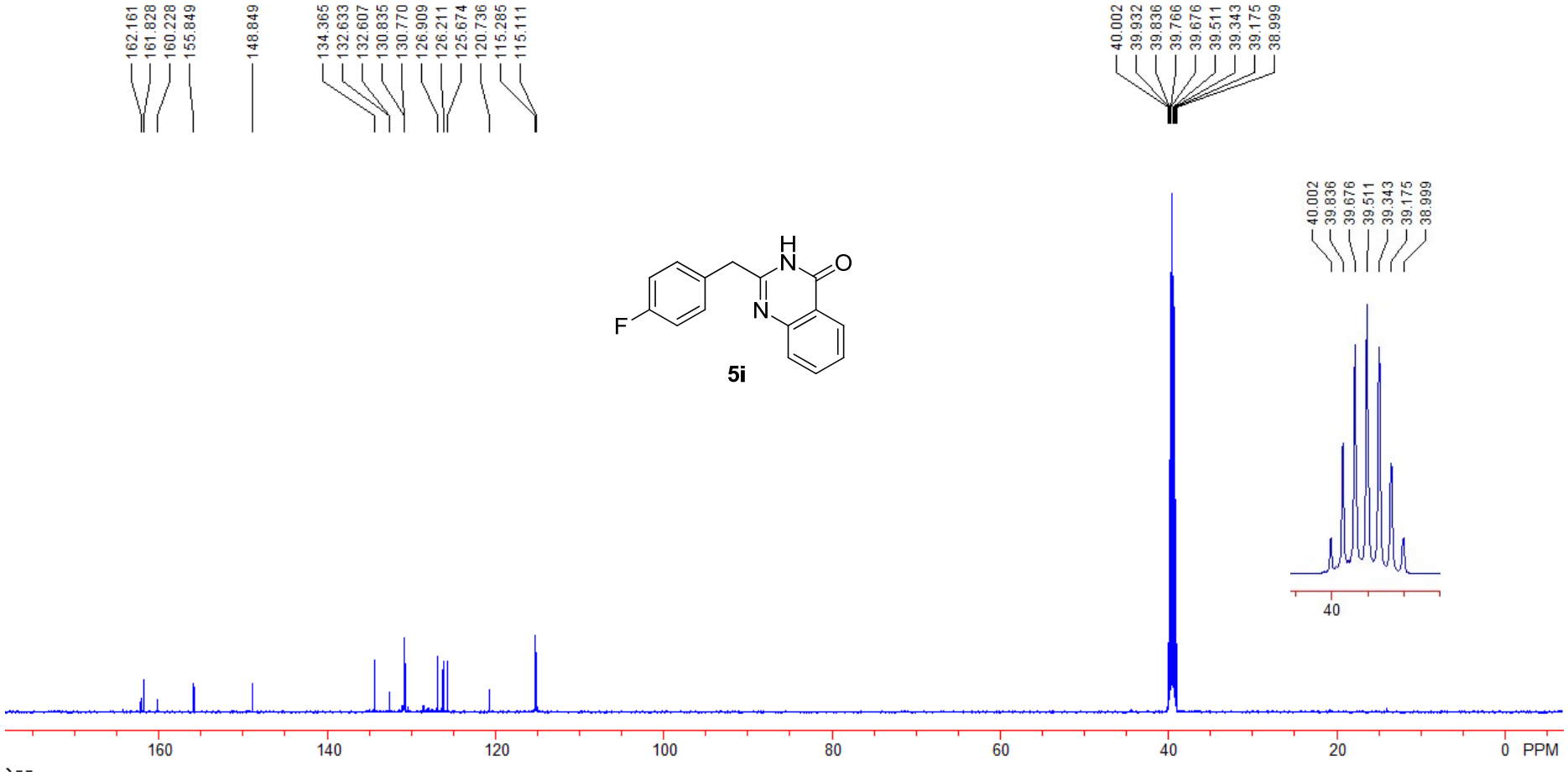
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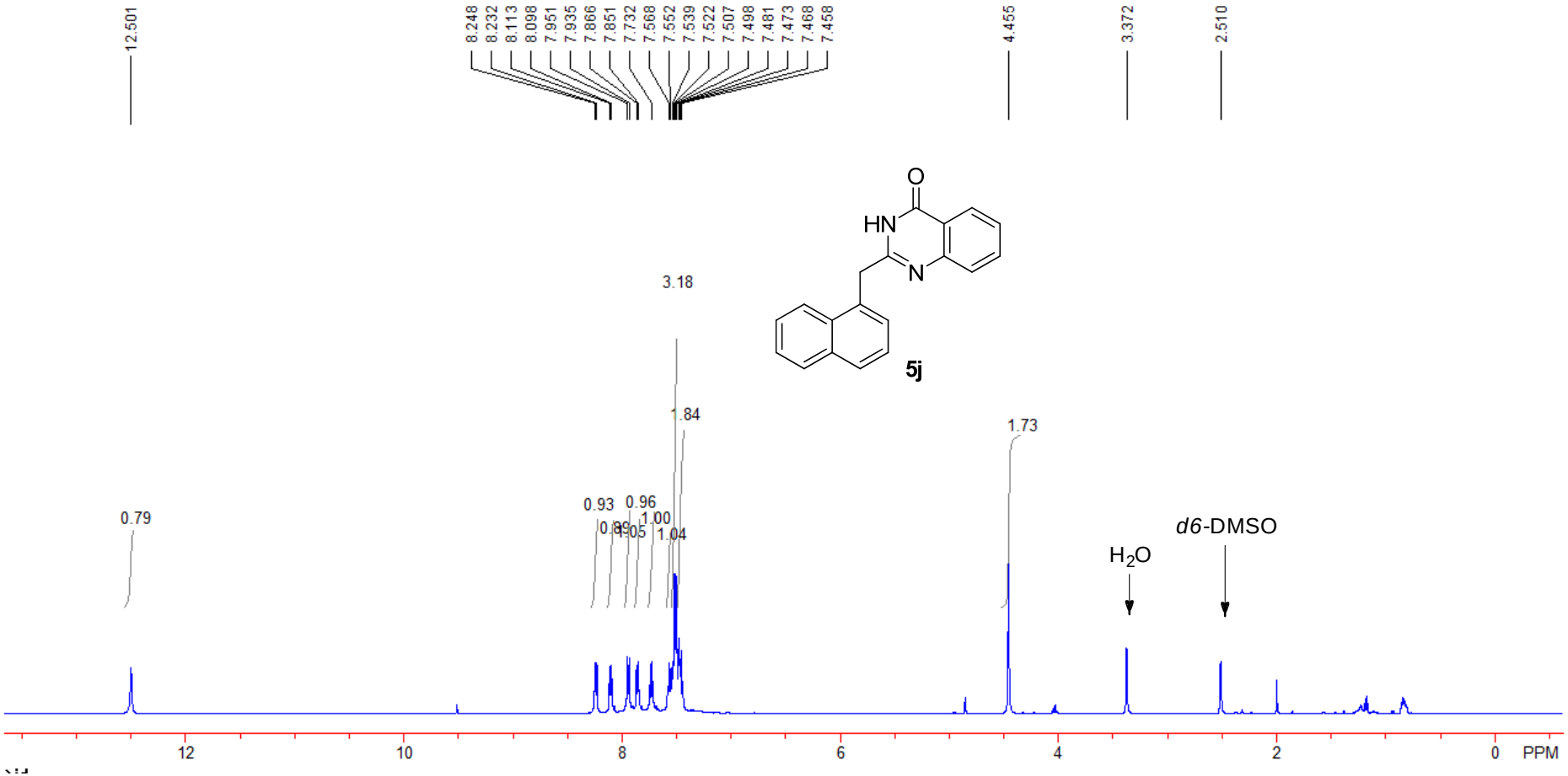
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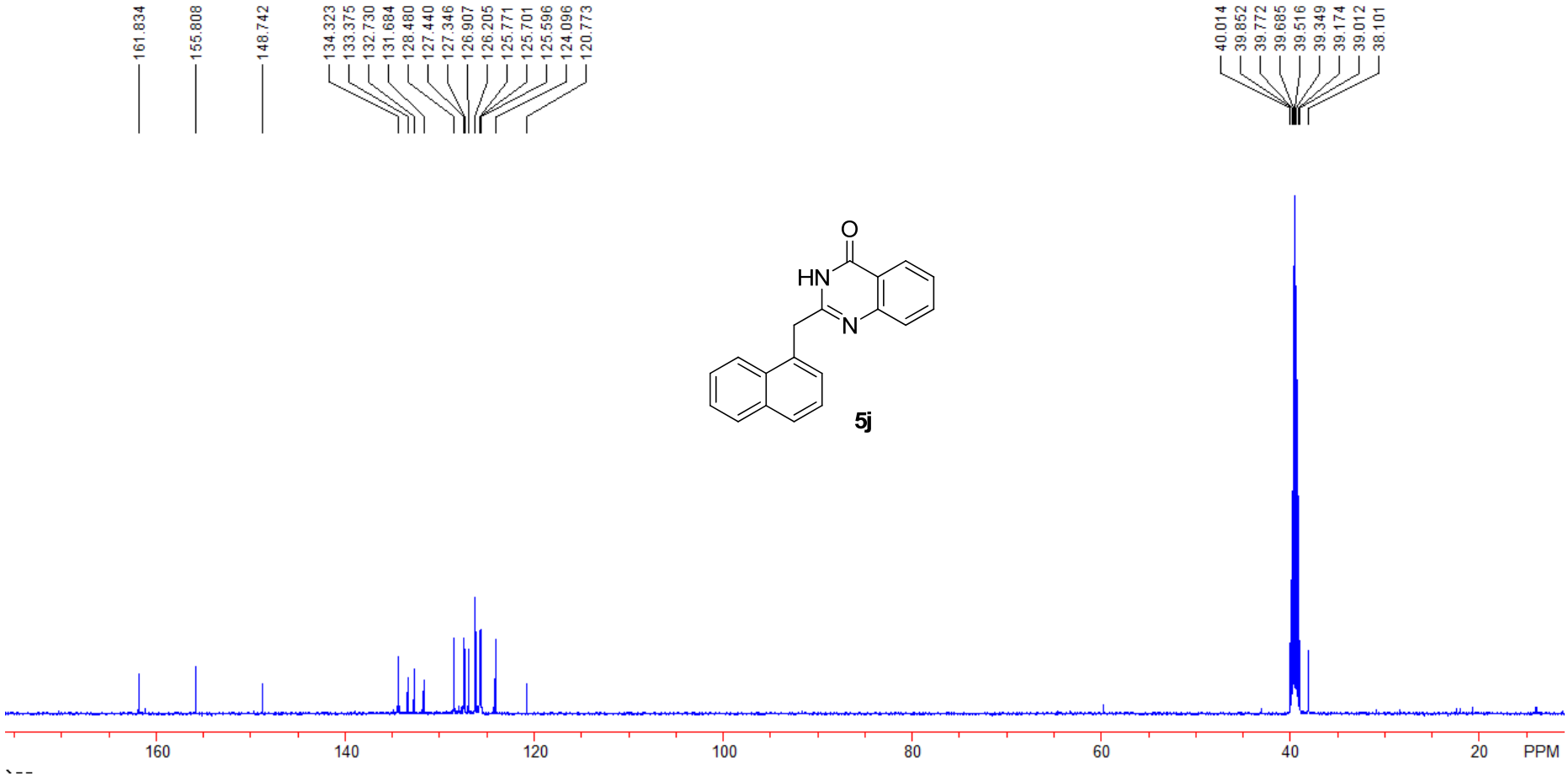
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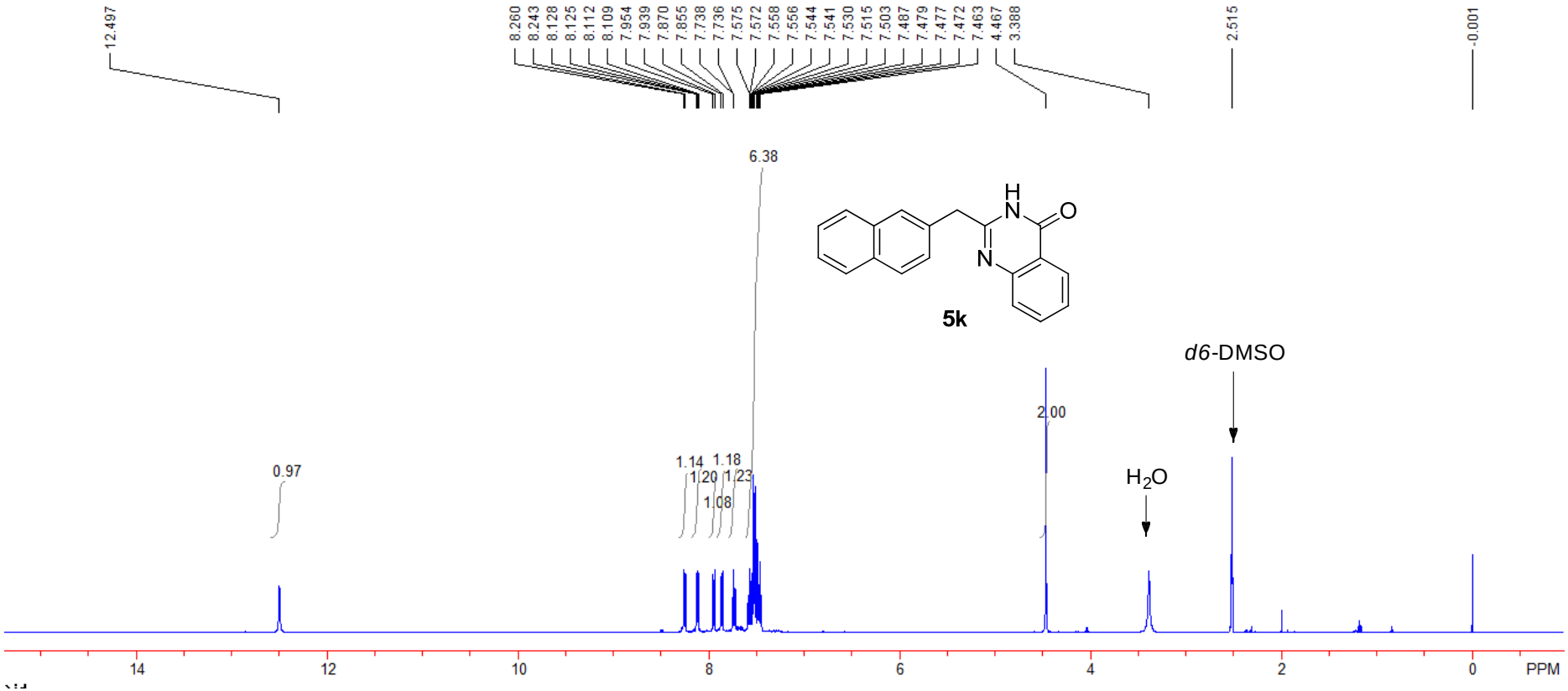
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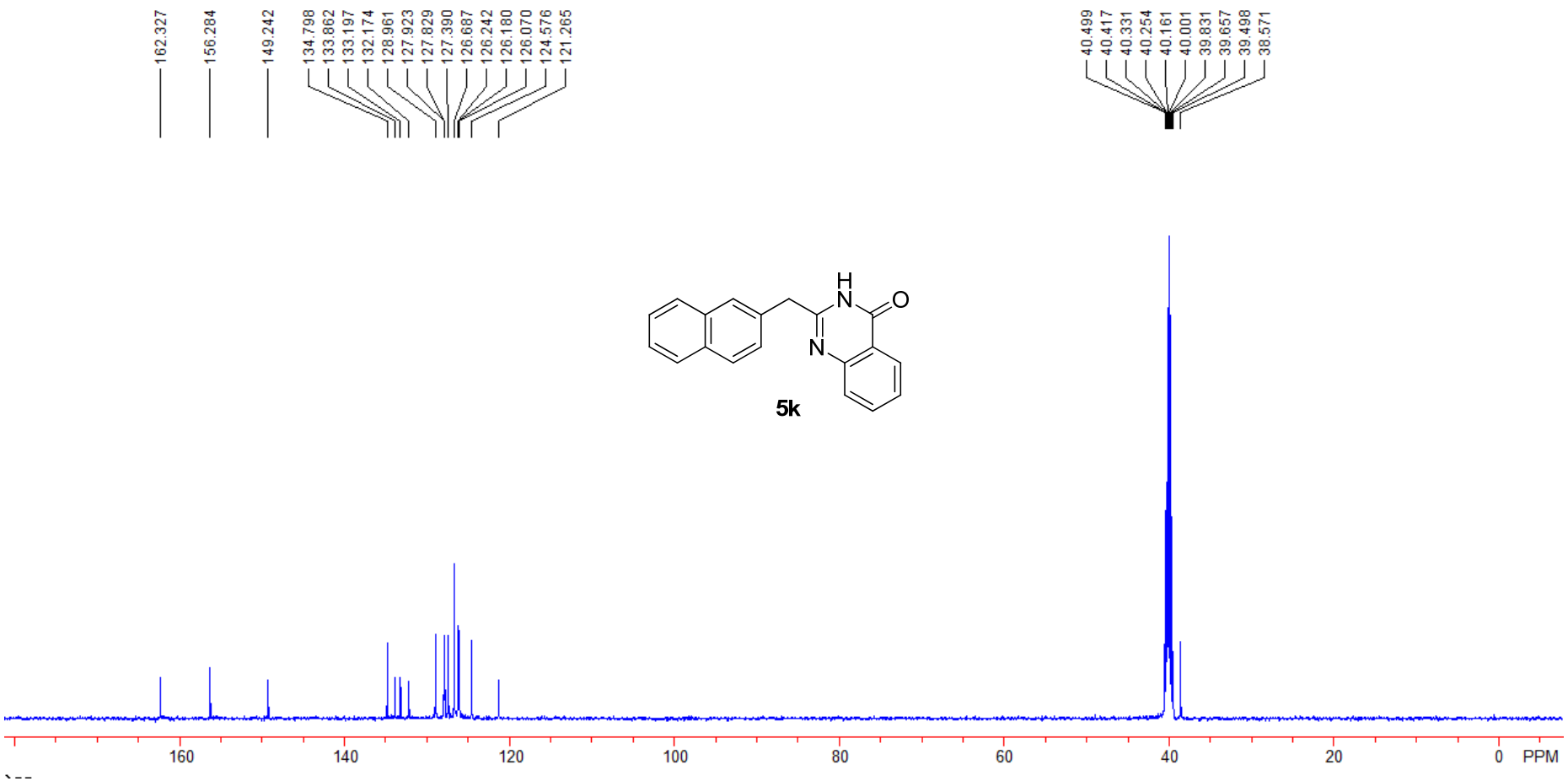
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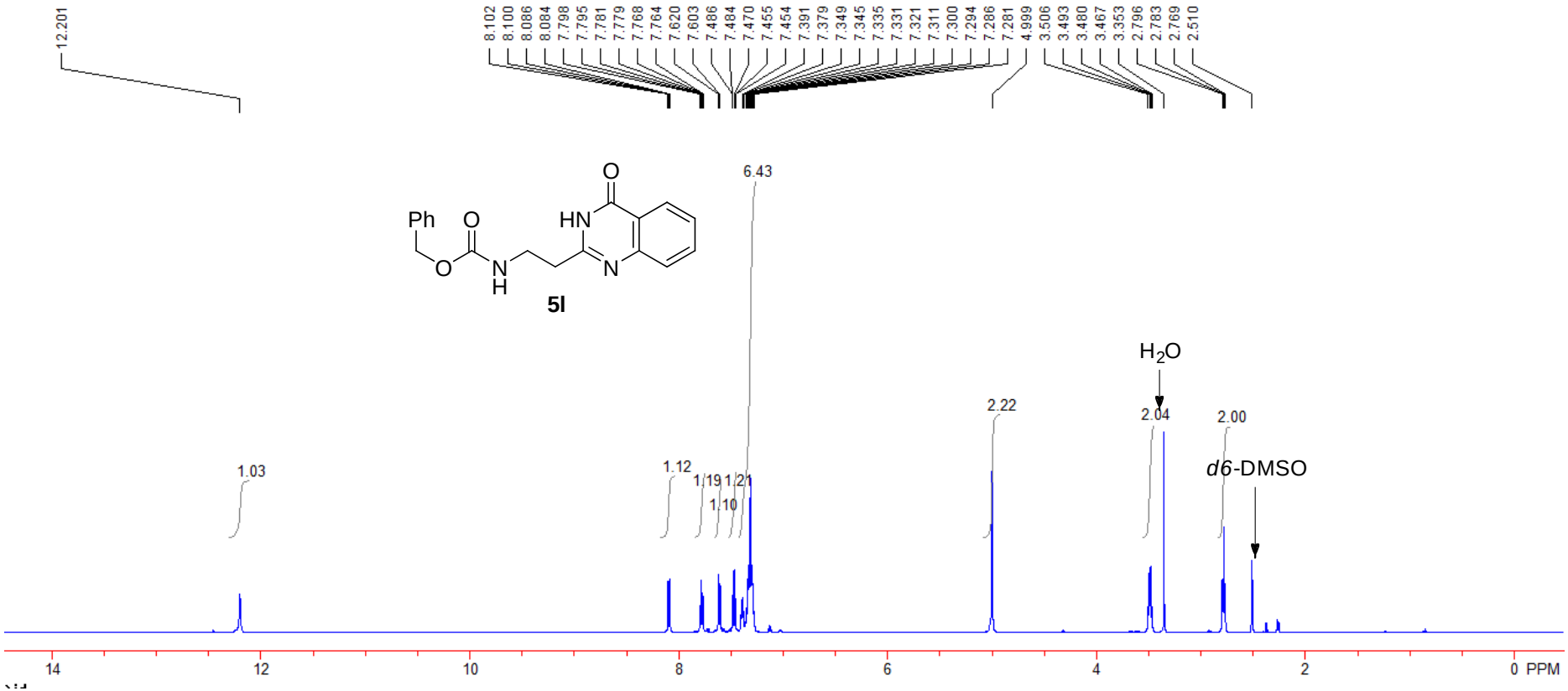
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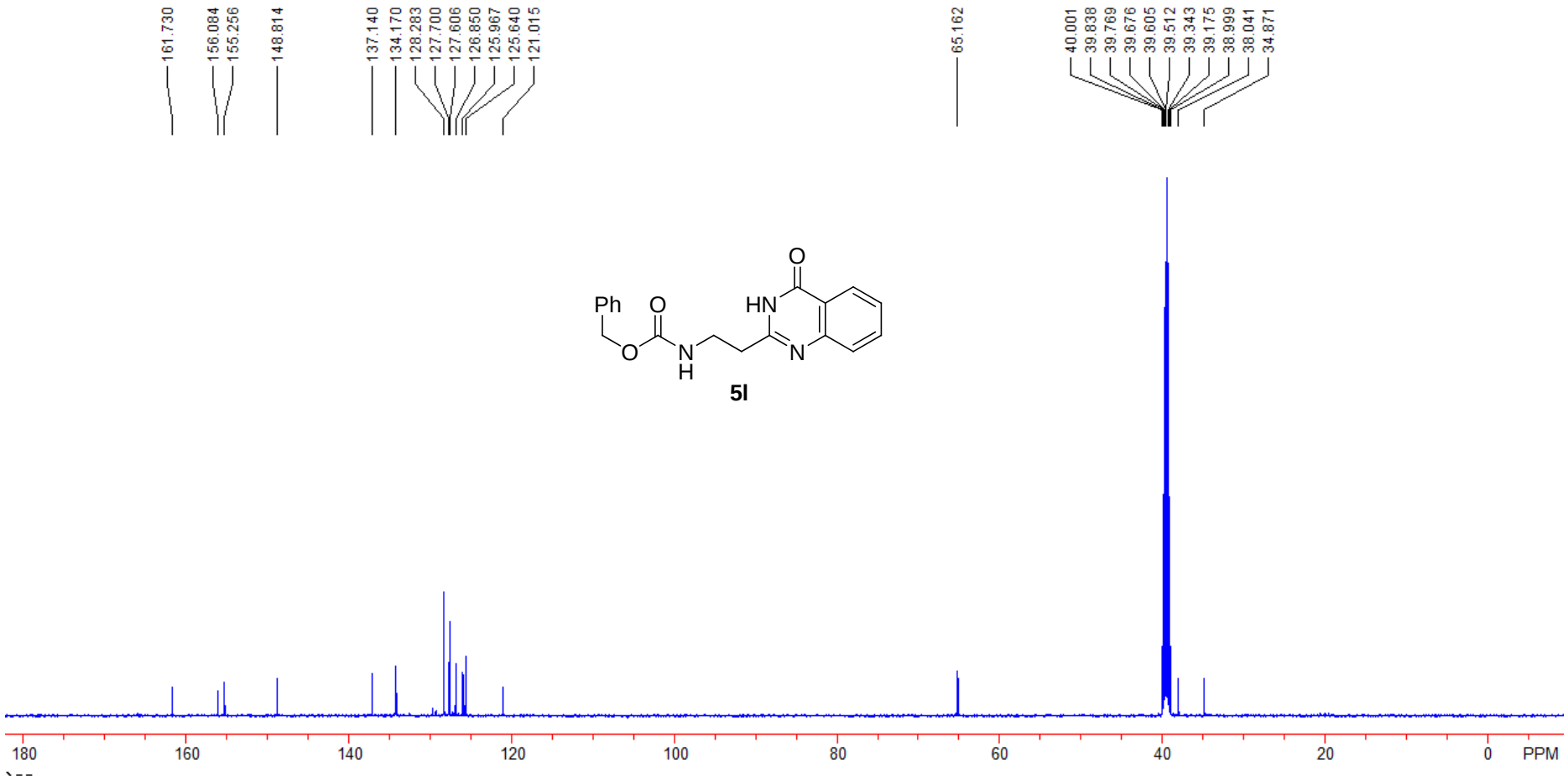
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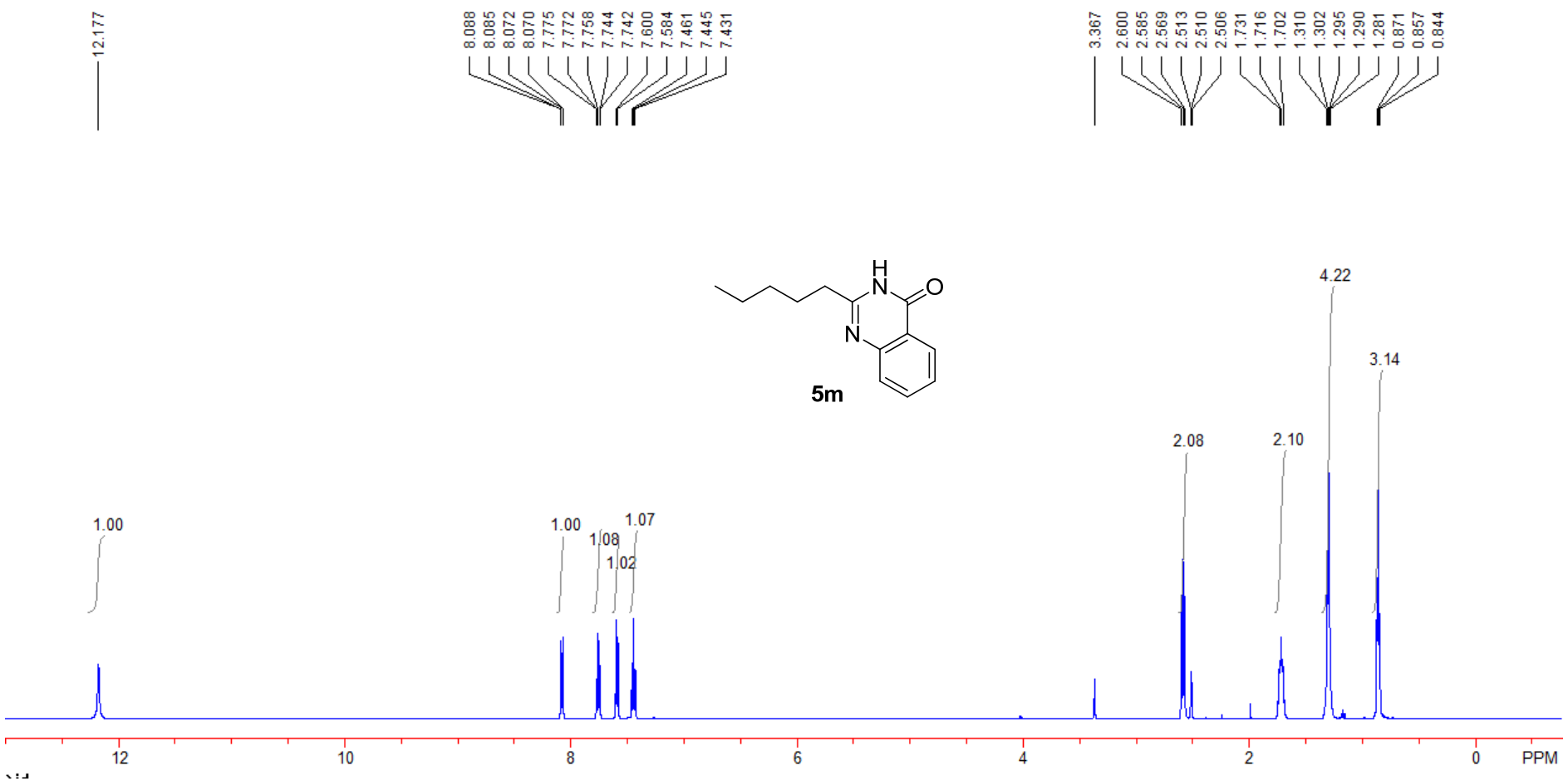
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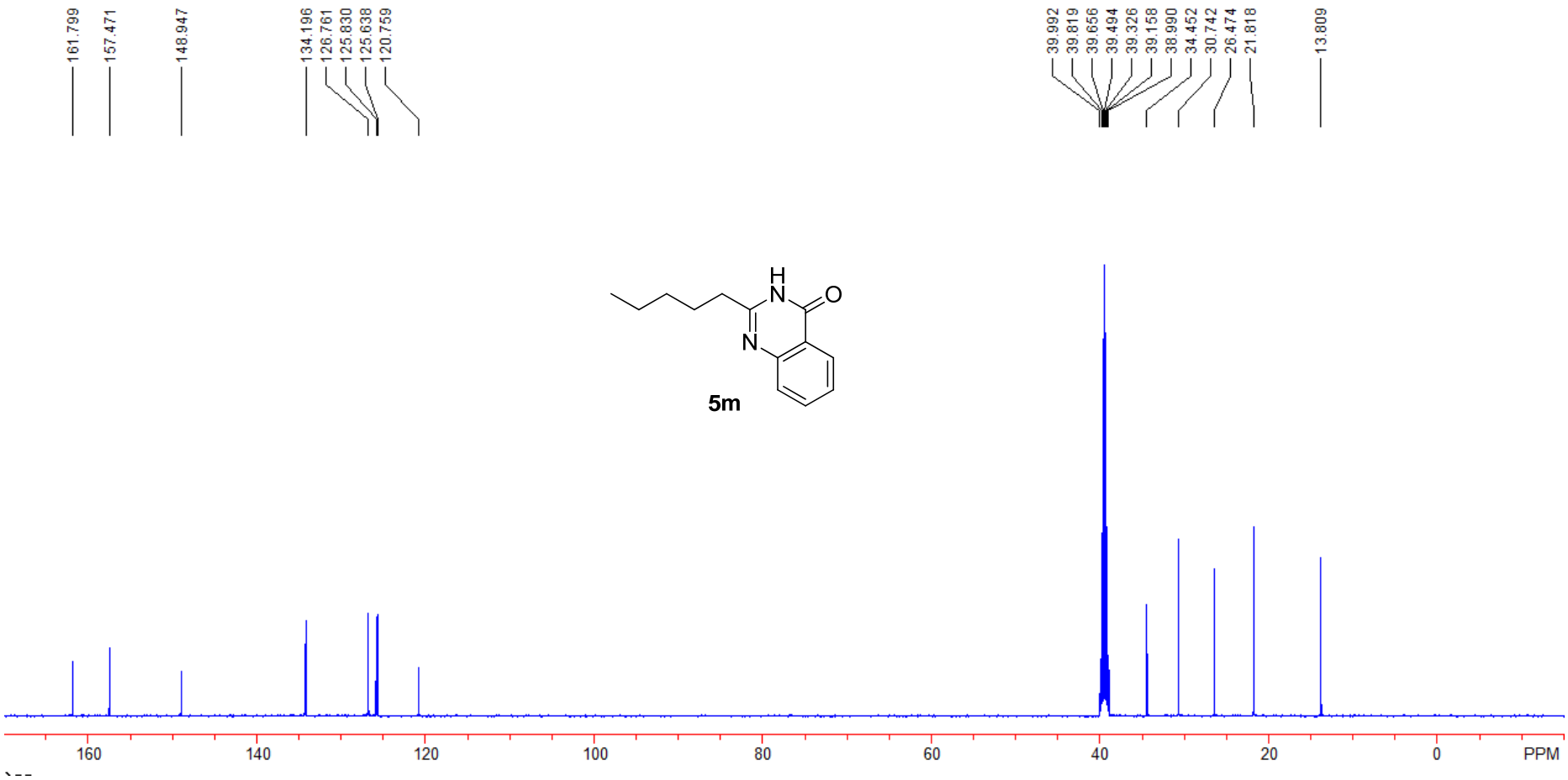
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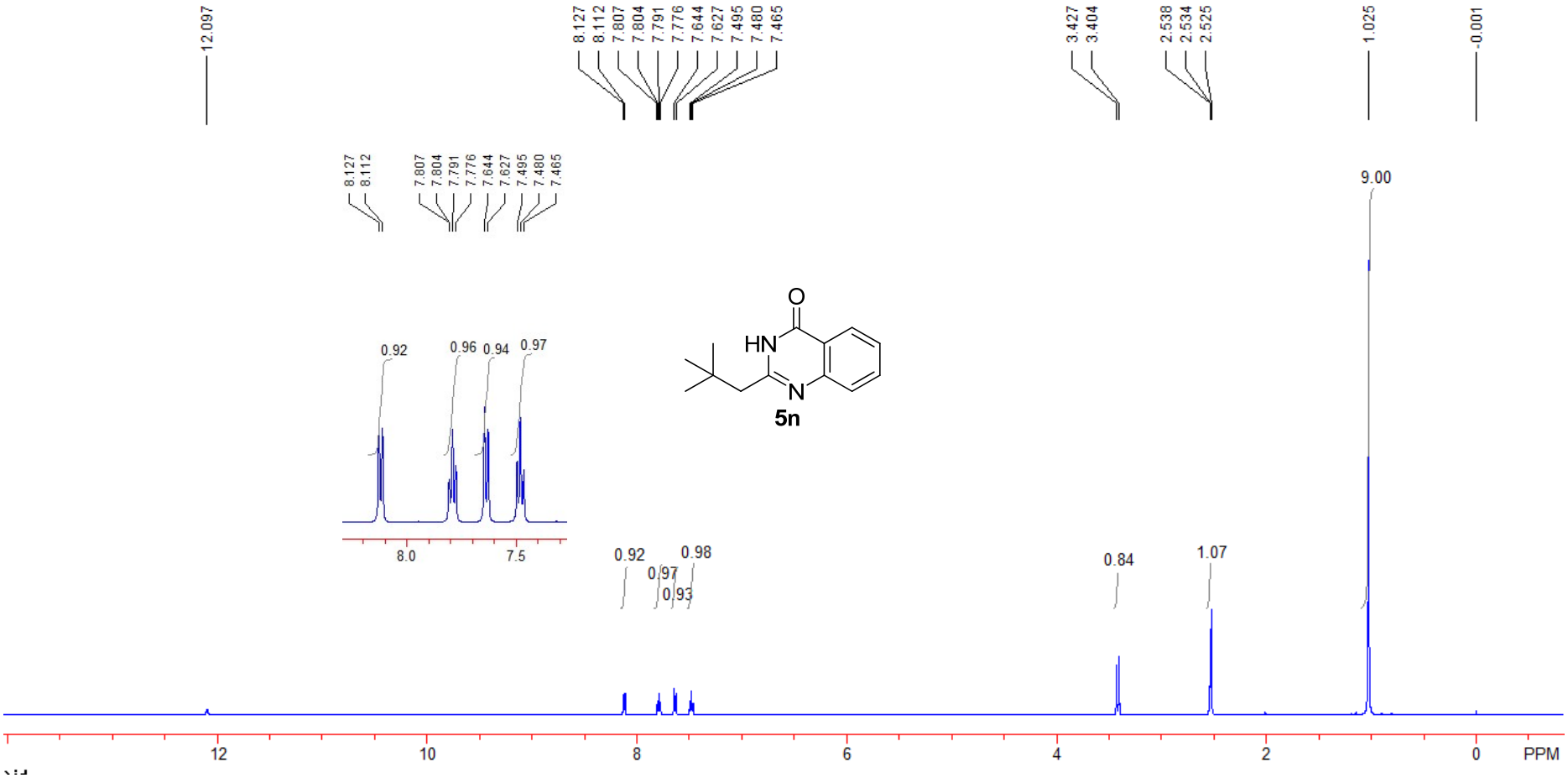
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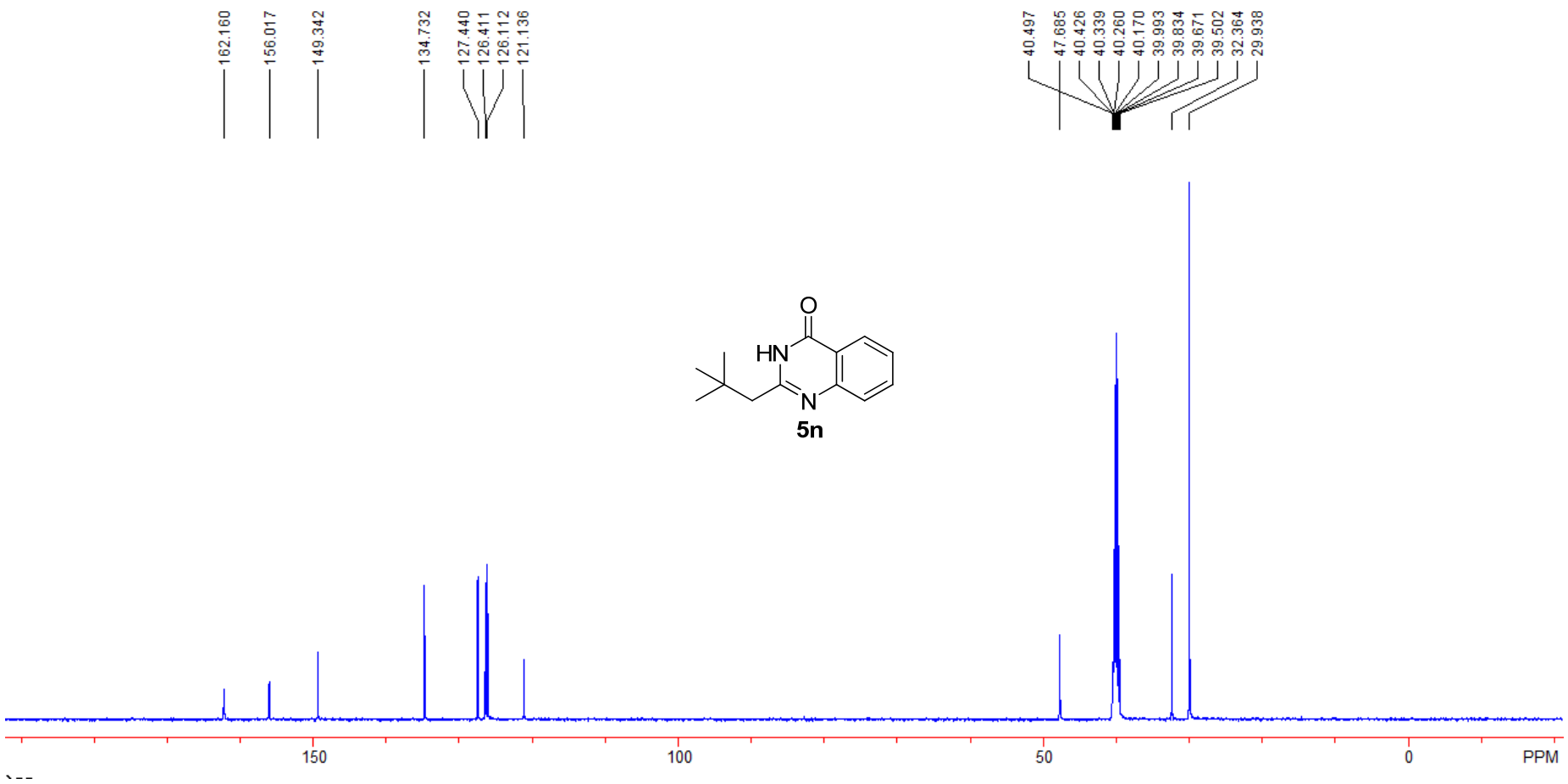
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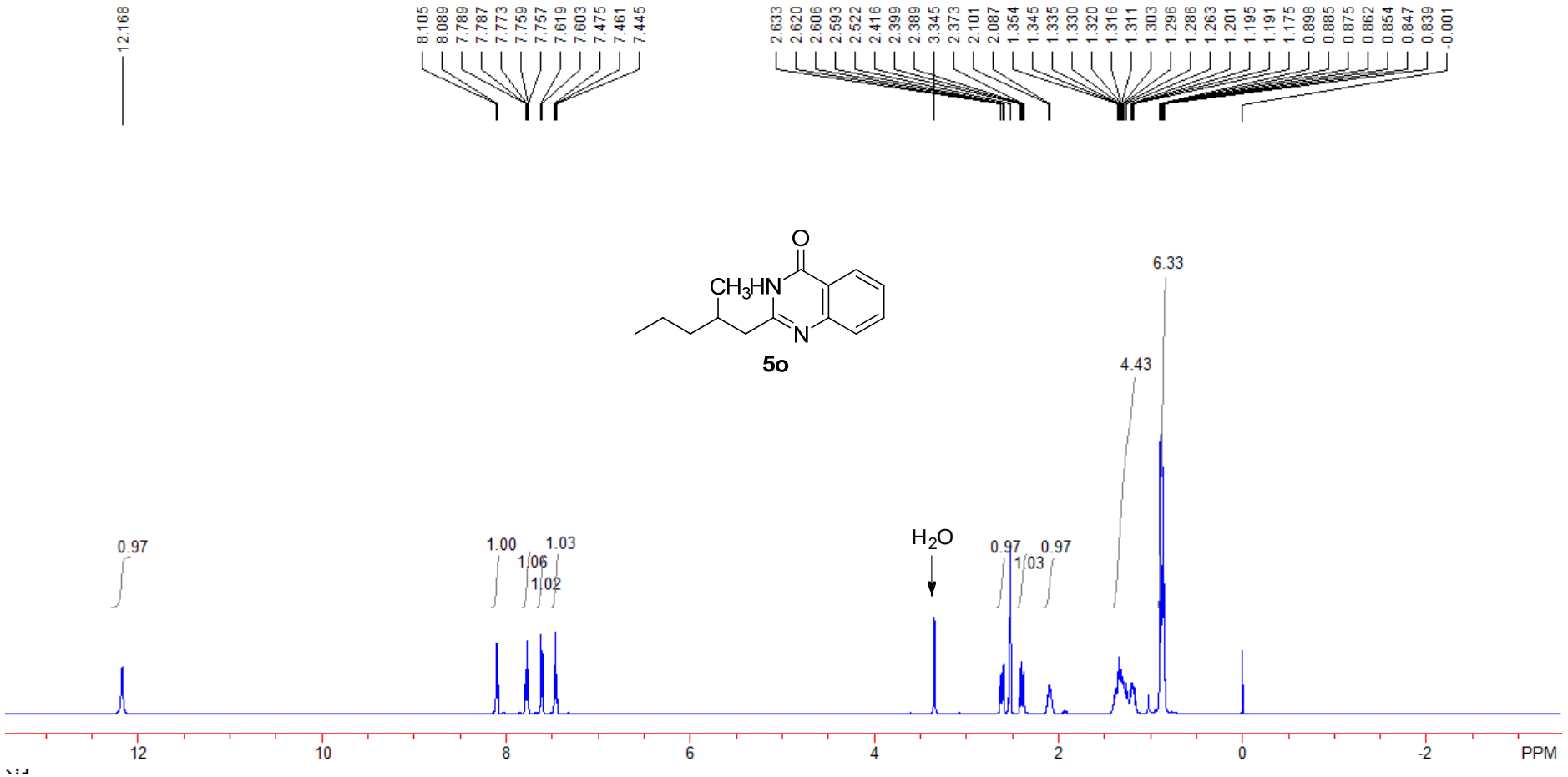
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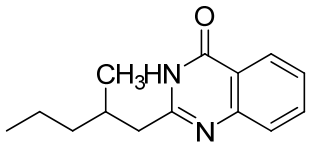
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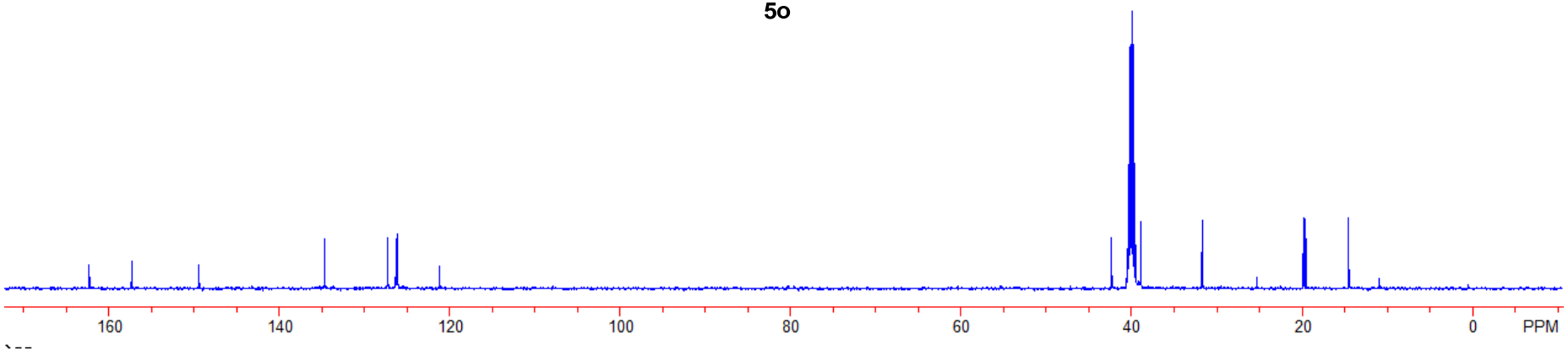
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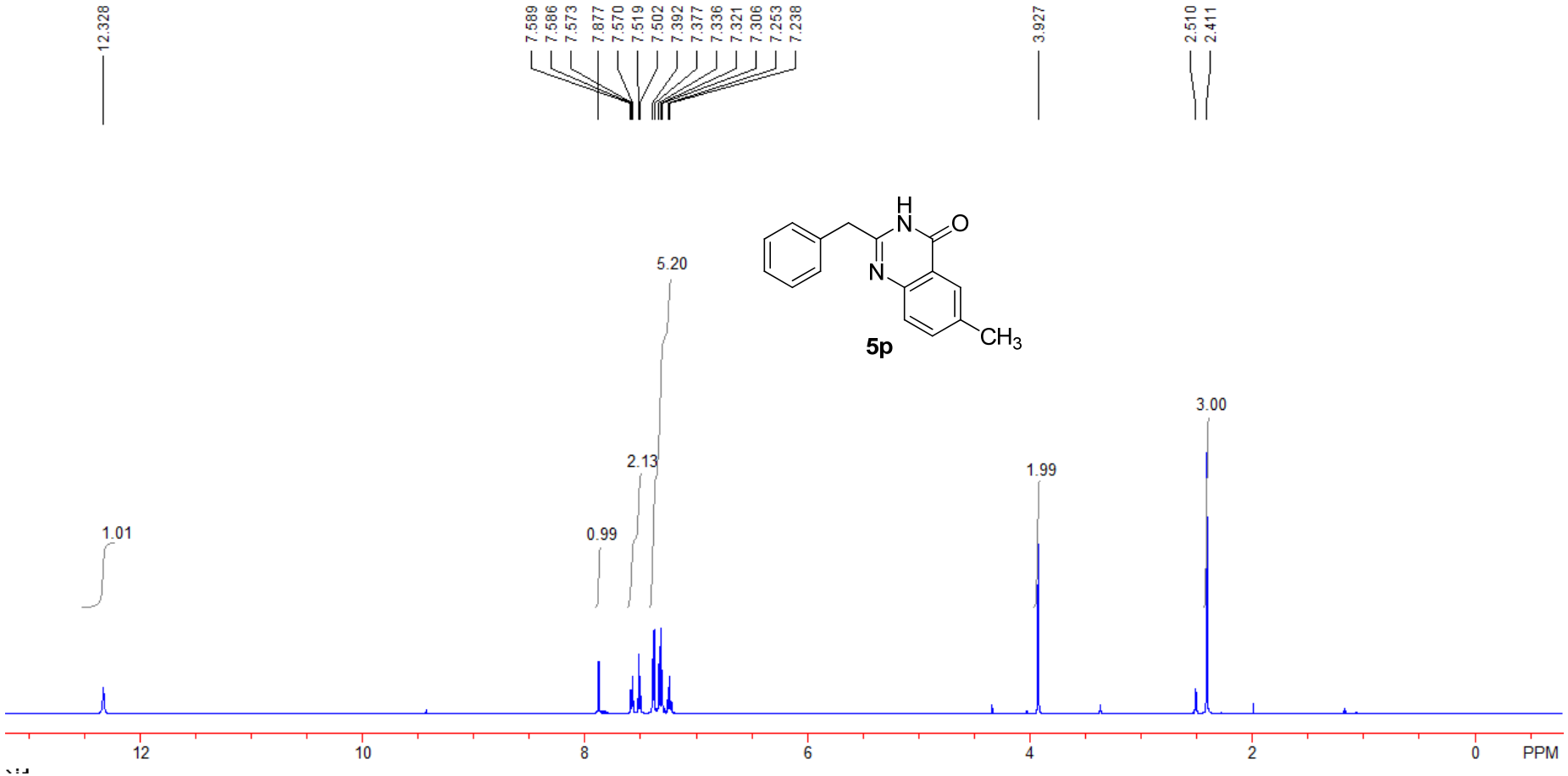
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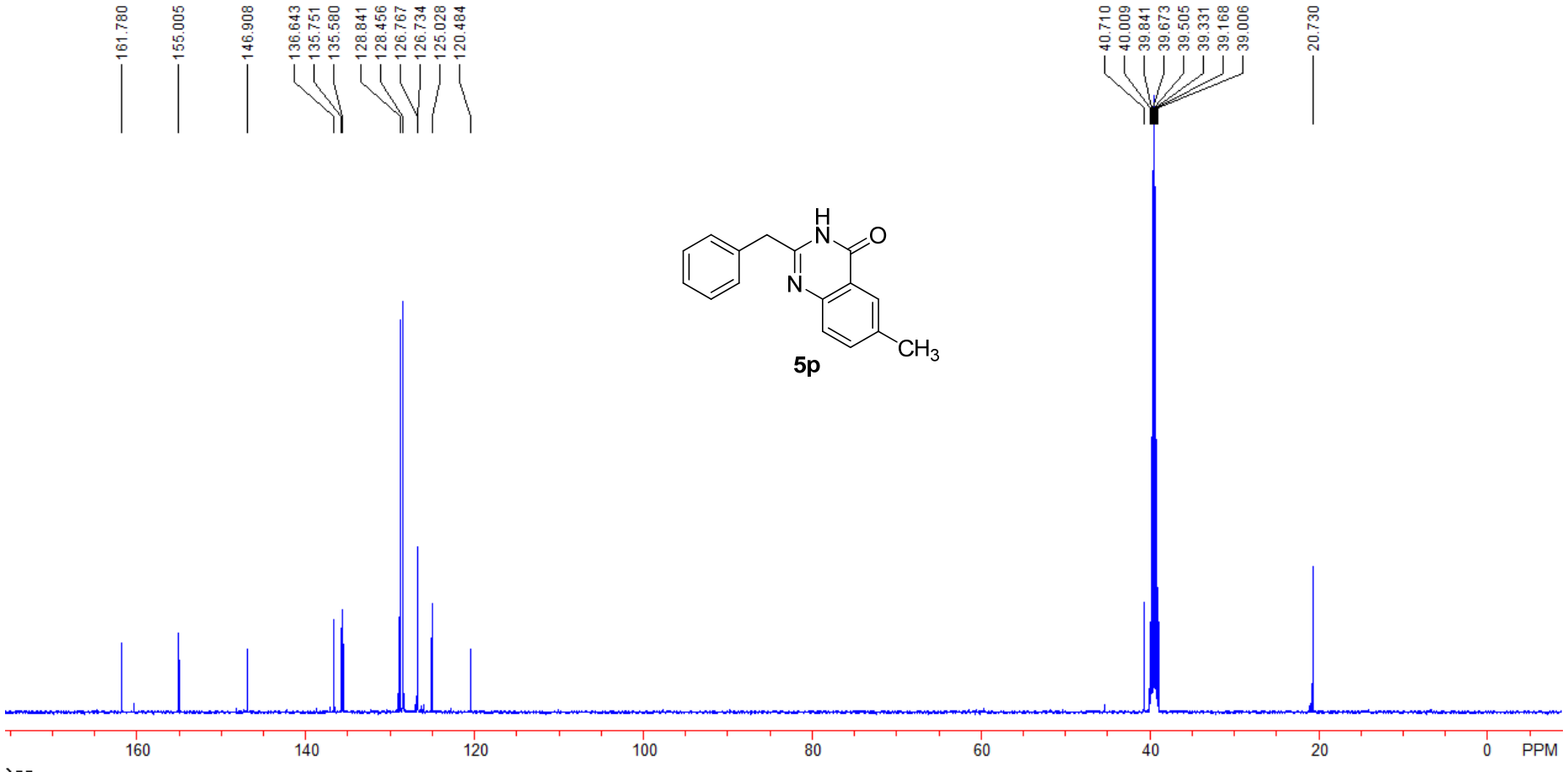
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128.456
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40.009
39.841
39.673
39.505
39.331
39.168
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N
O
N
CH3
160
140
120
100
80
60
40
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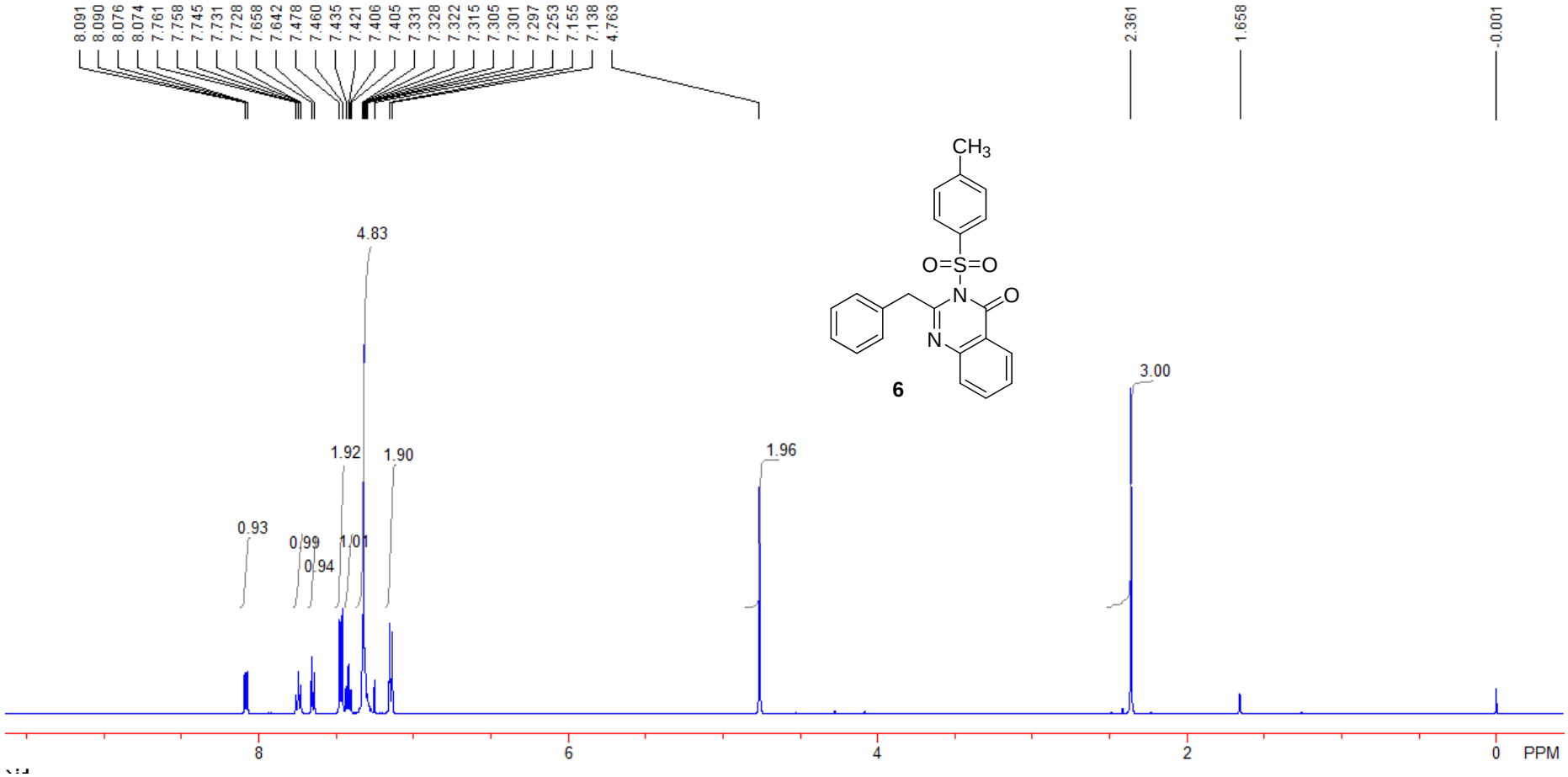
0
PPM

5p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7.406
7.405
7.331
7.328
7.322
7.315
7.305
7.301
7.297
7.253
7.155
7.138
4.763
2.361
1.658
-0.001
CH3
O=S=O
N
O
N
6
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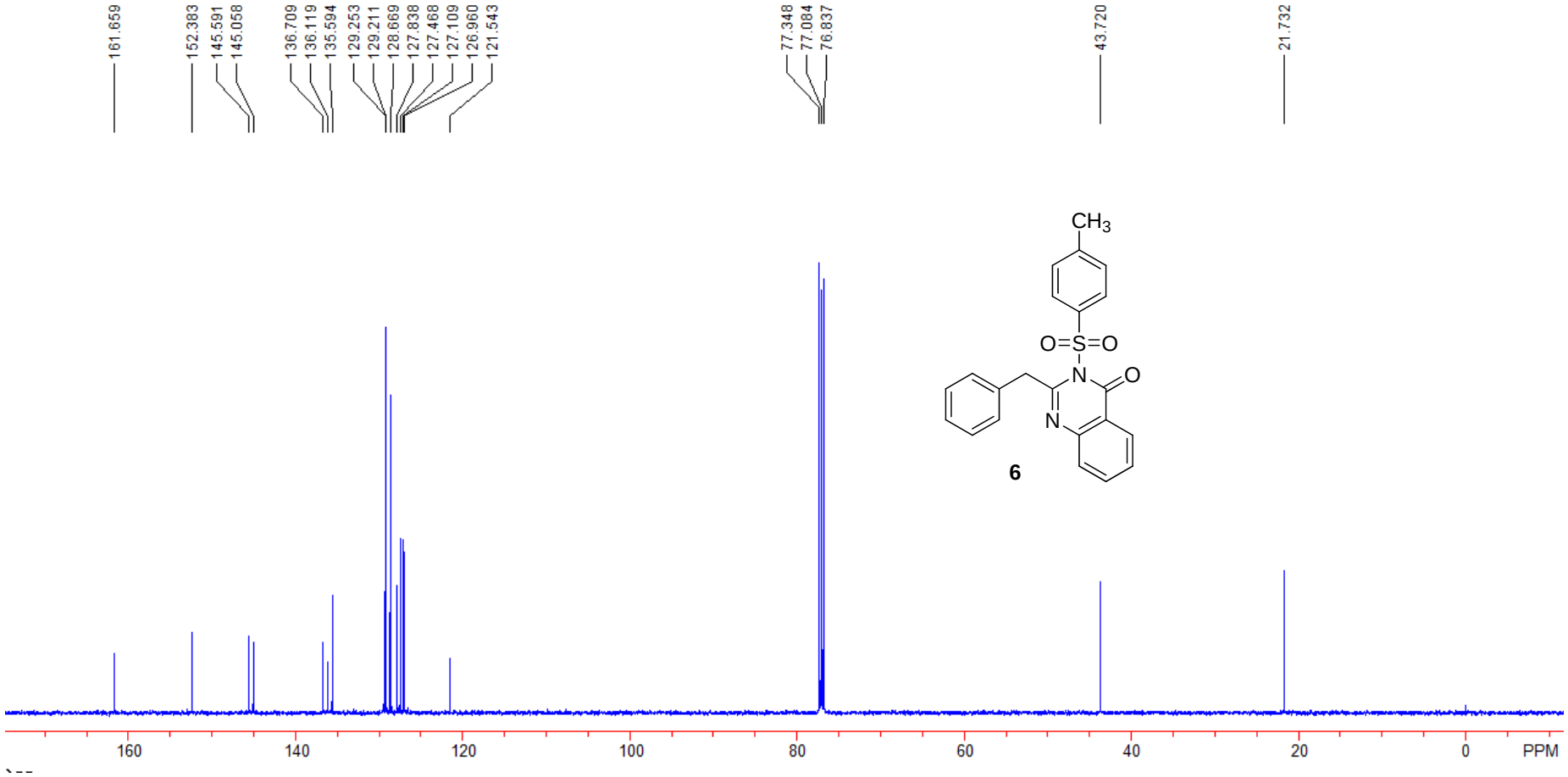
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126.960
121.543
77.348
77.084
76.837
43.720
21.732
CH3
O=S=O
N
O
N
160
140
120
100
80
60
40
20
0
PPM

6