Supporting Information

Iridium-Catalyzed Selective Hydrogenation of 3-Hydroxypyridinium Salts: A Facile Synthesis of Piperidin-3-ones

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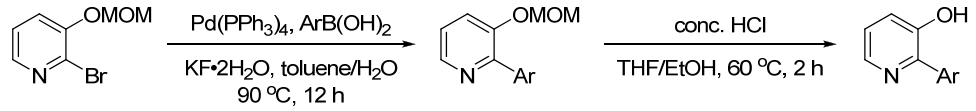
1. General:

Commercially available reagents were used without further purification. Solvents were treated prior to use according to the standard methods. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at room temperature in DMSO-d6 or $CDCl_3$ on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC or NMR analysis.

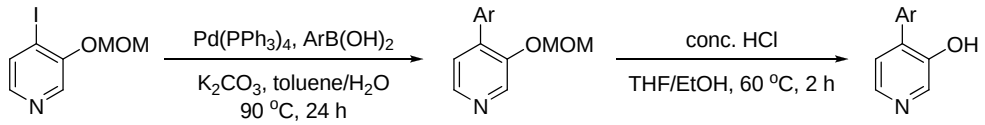
2. General Procedure for the Synthesis of Pyridin-3-ols

2-Aryl substituted pyridin-3-ols were synthesized from 2-bromo-3-(methoxymethoxy) –pyridine with the corresponding aryl boronic acids *via* $Pd(PPh_3)_4$-catalyzed Suzuki coupling.[1] 2-Methylpyridin-3-ol **1o**, pyridin-3-ol **1q** and 4-methylpyridin-3-ol **1w** were commecially available. 2-Butylpyridin-3-ol **1p** was synthesized following the literature reported method.[2] 4-Aryl substituted pyridin-3-ols were synthesized from 4-iodo-3-(methoxymethoxy)pyridine in a similar way as the 2-aryl substituted ones.



Under nitrogen atmosphere, a suspension of 2-bromo-3-(methoxymethoxy)pyridine (654 mg, 3.0 mmol), aryl boronic acid (4.5 mmol), $Pd(PPh_3)_4$ (35 mg, 0.03 mmol) in toluene (12.0 mL) and water (12.0 mL) was heated to 90 ^{o}C for 10 min, at which point it was allowed to cool to room temperature. Then potassium fluoride dihydrate (565 mg, 6.0 mmol) was added in one portion. The resulted mixture was stirred and heated at 90 ^{o}C overnight. The reaction mixture was cooled down and phases were separated. The aqueous phase was extracted extracted with ethyl acetate (10 mL×2). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in *vacuo*. Column chromatography of the residue on silica gel using petroleum ether/ethyl acetate (10:1) as the eluent gave the desired coupling product.

The coupling product was dissolved in THF (6.0 mL) and EtOH (6.0 mL), an excess conc. HCl (aq.) was added. The resulted mixture was heated at 60 ^{o}C for two hours. Then it was cooled down, poured into saturated solution of $NaHCO_3$. The resulted mixture was extracted with ethyl acetate (20 ml×2). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in *vacuo*. Column chromatography of the residue on silica gel using petroleum ether/THF (3:1) as the eluent gave desired product.



4-Aryl substituted pyridin-3-ols were synthesized in a similar way, except K_2CO_3 was used as the base. A longer reaction time was also needed for the full consumption of starting material. 4-iodo-3-(methoxymethoxy)pyridine was synthesized according to the known literature method.[3]

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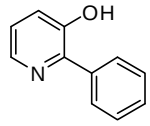
(1) Gomez-Galeno, J. E.; Hecker, S. J.; Dang, Q.; Grot, M. P. WO 2010019828, **2010**.

(2) O'Malley, M. M.; Damkaci, F.; Kelly, T. R. *Org. Lett.* **2006**, *8*, 2651;

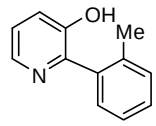
(3) Hoveyda, H.; Fraser, G. L.; Benakli, K.; Beauchemin, S.; Brassard, M.; Drutz, D.; Marsault, E.; Ouellet, L.; Peterson, M. L.; Wang, Z. US 20080194672, **2008**.

2-Phenylpyridin-3-ol (1a): 467 mg, 91% yield, known compound,[4] white solid, mp 211-212 °C.

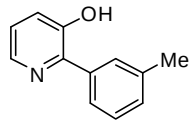


^{1}H NMR (400 MHz, DMSO-d6) δ 10.13 (s, 1H), 8.16 (d, *J* = 3.4 Hz, 1H), 8.02 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.20 (dd, *J* = 8.1, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.0, 144.9, 140.7, 138.5, 129.3, 128.2, 124.0, 123.8.

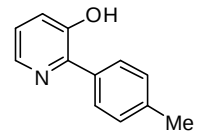
2-*o*-Tolylpyridin-3-ol (1b): 380 mg, 68% yield, white solid, mp 206-207 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 9.84 (s, 1H), 8.12 (dd, *J* = 4.5, 1.3 Hz, 1H), 7.40-7.15 (m, 6H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.5, 148.1, 140.2, 138.9, 136.5, 130.2, 130.0, 128.0, 125.6, 123.8, 123.0, 20.0. HRMS Calculated for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, found 186.0914. IR (KBr): 2924, 1573, 1375, 1303, 1183, 799, 751, 630 cm^{-1}.



2-*m*-Tolylpyridin-3-ol (1c): 520 mg, 94% yield, white solid, mp 172-173 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.06 (s, 1H), 8.15 (dd, *J* = 4.4, 1.2 Hz, 1H), 7.89-7.76 (m, 2H), 7.40-7.25 (m, 2H), 7.25-7.10 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.0, 145.1, 140.6, 138.5, 137.1, 129.9, 128.8, 128.0, 126.5, 124.0, 123.7, 21.7. HRMS Calculated for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, found 186.0914. IR (KBr): 2922, 1573, 1360, 1284, 1117, 803, 755, 697 cm^{-1}.

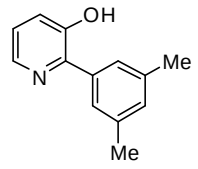


2-*p*-Tolylpyridin-3-ol (1d): 516 mg, 93% yield, known compound,[5] white solid, mp 204-205 °C.

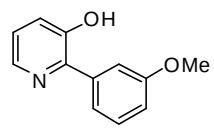


^{1}H NMR (400 MHz, DMSO-d6) δ 10.13 (s, 1H), 8.19-8.10 (m, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.40-7.30 (m, 1H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.18 (dd, *J* = 8.1, 4.5 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.0, 144.8, 140.4, 137.6, 135.5, 129.2, 128.8, 124.1, 123.5, 21.3.

2-(3,5-Dimethylphenyl)pyridin-3-ol (1e): 389 mg, 65% yield, white solid, mp 183-184 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 9.99 (s, 1H), 8.20-8.07 (m, 1H), 7.61 (s, 2H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.16 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.98 (s, 1H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.9, 145.3, 140.5, 138.5, 136.9, 129.6, 127.2, 123.9, 123.5, 21.6. HRMS Calculated for $C_{13}H_{14}NO$ $[M+H]^+$ 200.1070, found 200.1073. IR (KBr): 2919, 1575, 1461, 1291, 1118, 854, 766, 653 cm^{-1}.



2-(3-Methoxyphenyl)pyridin-3-ol (1f): 552 mg, 91% yield, known compound,[6] white solid, mp 181-182 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.16 (s, 1H), 8.17 (d, *J* = 4.4 Hz, 1H), 7.70-7.57 (m, 2H), 7.41-7.27 (m, 2H), 7.20 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.94 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 159.3, 152.1, 144.5, 140.6, 139.8, 129.2, 124.1, 123.9, 121.8, 114.8, 113.8, 55.5.

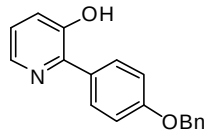


(4) Jida, M.; Ollivier, J. *Eur. J. Org. Chem.* **2008**, 4041.

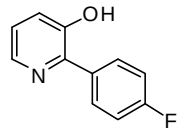
(5) Misawa, N.; Shindo, K.; Takahashi, H.; Suenaga, H.; Iguchi, K.; Okazaki, H.; Harayama, S.; Furukawa, K. *Tetrahedron* **2002**, *58*, 9605.

(6) Leditschke, H. *Chem. Ber.* **1953**, *86*, 123.

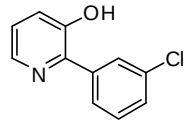
2-(4-(Benzyloxy)phenyl)pyridin-3-ol (1g): 490 mg, 74% yield, white solid, mp 208-209 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.38 (s, 1H), 8.15 (d, *J* = 4.4 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 2H), 7.58-7.28 (m, 6H), 7.20 (dd, *J* = 7.7, 4.7 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 5.17 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d6) δ 158.8, 152.0, 144.2, 139.7, 137.5, 130.7, 130.3, 128.9, 128.3, 128.1, 124.7, 123.4, 114.6, 69.7. HRMS Calculated for $C_{18}H_{16}NO_2$ $[M+H]^+$ 278.1176, found 278.1177. IR (KBr): 2982, 1458, 1286, 1251, 1178, 838, 767, 735 cm^{-1}.



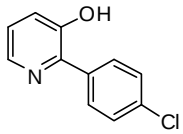
2-(4-Fluorophenyl)pyridin-3-ol (1h): 503 mg, 89% yield, known compound,[7] white solid, mp 228-229 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.23 (s, 1H), 8.22-8.05 (m, 3H), 7.40-7.32 (m, 1H), 7.30-7.15 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 162.3 (d, J_{C-F} = 243.4 Hz), 151.9, 143.8, 140.7, 134.9 (d, J_{C-F} = 3.0 Hz), 131.3 (d, J_{C-F} = 8.1 Hz), 124.1, 123.8, 115.0 (d, J_{C-F} = 21.0 Hz); ^{19}F NMR (376 MHz, DMSO-d6) δ -114.30.



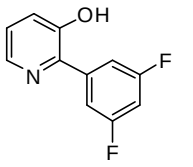
2-(3-Chlorophenyl)pyridin-3-ol (1i): 566 mg, 92% yield, white solid, mp 225-226 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.41 (s, 1H), 8.18 (d, *J* = 3.8 Hz, 1H), 8.14-7.98 (m, 2H), 7.54-7.32 (m, 3H), 7.31-7.18 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.4, 142.6, 140.5, 140.1, 133.1, 130.2, 128.8, 128.2, 127.9, 124.8, 124.6. HRMS Calculated for $C_{11}H_9ClNO$ $[M+H]^+$ 206.0367, found 206.0369. IR (KBr): 2923, 1578, 1359, 1302, 1182, 787, 752, 633 cm^{-1}.



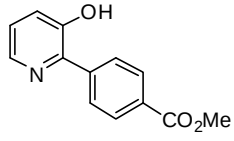
2-(4-Chlorophenyl)pyridin-3-ol (1j): 526 mg, 85% yield, known compound,[8] white solid, mp 231-232 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.36 (s, 1H), 8.22-8.15 (m, 1H), 8.12-8.05 (m, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.43-7.36 (m, 1H), 7.24 (dd, *J* = 8.2, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.2, 143.2, 140.6, 137.1, 133.0, 131.0, 128.3, 124.5, 124.3.



2-(3,5-Difluorophenyl)pyridin-3-ol (1k): 570 mg, 92% yield, white solid, mp 217-218 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.58 (s, 1H), 8.18 (d, *J* = 3.6 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.26 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.23-7.12 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 162.5 (dd, J_{C-F} = 242.4, 13.4 Hz), 152.6, 141.9 (t, J_{C-F} = 9.8 Hz), 141.3 (t, J_{C-F} = 3.1 Hz), 140.8, 125.1, 124.8, 111.9 (dd, J_{C-F} = 19.1, 7.0 Hz), 103.5 (t, J_{C-F} = 25.8 Hz); ^{19}F NMR (376 MHz, DMSO-d6) δ -110.34. HRMS Calculated for $C_{11}H_8F_2NO$ $[M+H]^+$ 208.0568, found 208.0570. IR (KBr): 3624, 2959, 1601, 1296, 1118, 864, 801, 683 cm^{-1}.



Methyl 4-(3-hydroxypyridin-2-yl)benzoate (1l): 375 mg, 82% yield, known compound,[9] white solid, mp 221-222 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.41 (s, 1H), 8.32-8.14 (m, 3H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.47-7.34 (m, 1H), 7.27 (dd, *J* = 8.2, 4.4 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 166.7, 152.6, 143.3, 143.0, 141.0, 129.4, 129.2, 129.0, 124.7, 124.5, 52.5.



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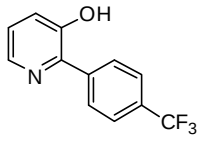
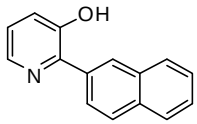
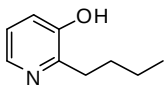
(9) Obrecht, D.; Ermert, P.; Oumouch, S.; Piettre, A.; Gosalbes, J.-F.; Thommen, M. WO 2013139697, **2013**;

2-(4-(Trifluoromethyl)phenyl)pyridin-3-ol (1m): 675 mg, 94% yield, white solid, mp 214-215 

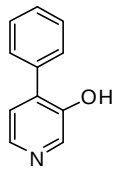
°C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.43 (s, 1H), 8.29 (d, *J* = 8.2 Hz, 2H), 8.24-8.17 (m, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.46-7.36 (m, 1H), 7.29 (dd, *J* = 8.2, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.6, 143.0, 142.4 (d, $J_{C\text{-}F}$ = 0.9 Hz), 140.9, 129.9, 128.5 (q, $J_{C\text{-}F}$ = 31.5 Hz), 125.0 (q, $J_{C\text{-}F}$ = 3.4 Hz), 124.7, 124.5, 123.5; ^{19}F NMR (376 MHz, DMSO-d6) δ -61.04. HRMS Calculated for $C_{12}H_9F_3NO$ $[M+H]^+$ 240.0631, found 240.0632. IR (KBr): 2606, 1573, 1461, 1331, 1106, 843, 735, 650 cm^{-1}.

2-(Naphthalen-2-yl)pyridin-3-ol (1n): 619 mg, 93% yield, white solid, mp 170-171 °C. ^{1}H NMR 

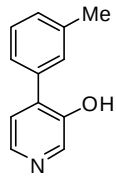
(400 MHz, DMSO-d6) δ 10.30 (s, 1H), 8.72-8.55 (m, 1H), 8.32-8.17 (m, 2H), 8.07-7.85 (m, 3H), 7.60-7.47 (m, 2H), 7.42 (dd, *J* = 7.7, 4.4 Hz, 1H), 7.25 (dd, *J* = 8.0, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 152.7, 144.3, 140.1, 135.2, 133.2, 133.1, 129.0, 128.7, 127.9, 127.5, 127.3, 126.9, 126.6, 125.0, 124.2. HRMS Calculated for $C_{15}H_{12}NO$ $[M+H]^+$ 222.0913, found 222.0913. IR (KBr): 3055, 1578, 1457, 1297, 1113, 861, 801, 775 cm^{-1}.

2-Butylpyridin-3-ol (1p): 153 mg, 34% yield, white solid, mp 123-124 °C. ^{1}H NMR (400 MHz, 

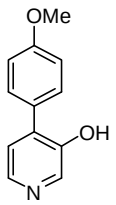
DMSO-d6) δ 9.65 (s, 1H), 7.92 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.00 (dd, *J* = 8.1, 4.6 Hz, 1H), 2.70 (t, *J* = 7.7 Hz, 2H), 1.69-1.54 (m, 2H), 1.38-1.25 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.5, 150.2, 139.7, 122.2, 121.5, 31.8, 30.3, 22.5, 14.3. HRMS Calculated for $C_9H_{14}NO$ $[M+H]^+$ 152.1070, found 152.1071. IR (KBr): 2959, 1577, 1460, 1291, 1195, 797, 733, 618 cm^{-1}.

4-Phenylpyridin-3-ol (1r): 383 mg, 75% yield, known compound,[10] light yellow solid, mp 

159-160 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.04 (s, 1H), 8.30 (s, 1H), 8.11 (d, *J* = 4.7 Hz, 1H), 7.66 (d, *J* = 7.3 Hz, 2H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.42-7.35 (m, 1H), 7.30 (d, *J* = 4.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.2, 141.4, 139.1, 136.3, 134.3, 129.3, 128.7, 128.4, 124.4.

4-*m*-Tolylpyridin-3-ol (1s): 395 mg, 71% yield, white solid, mp 160-161 °C. ^{1}H NMR (400 MHz, 

DMSO-d6) δ 9.93 (s, 1H), 8.29 (s, 1H), 8.10 (d, *J* = 4.7 Hz, 1H), 7.33-7.19 (m, 3H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.10-7.03 (m, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.4, 140.9, 138.4, 136.8, 136.3, 135.8, 130.1, 129.8, 128.3, 126.0, 125.6, 20.0. HRMS Calculated for $C_{12}H_{12}NO$ $[M+H]^+$ 186.0913, found 186.0914. IR (KBr): 3051, 1421, 1295, 1222, 1066, 834, 750, 631 cm^{-1}.

4-(4-Methoxyphenyl)pyridin-3-ol (1t): 365 mg, 60% yield, white solid, mp 149-150 °C. ^{1}H 

NMR (400 MHz, DMSO-d6) δ 9.96 (s, 1H), 8.25 (s, 1H), 8.07 (d, *J* = 4.9 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 4.9 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 159.6, 151.1, 141.3, 139.0, 134.0, 130.6, 128.4, 124.0, 114.2, 55.6. HRMS Calculated for $C_{12}H_{12}NO_2$ $[M+H]^+$ 202.0863, found 202.0862. IR (KBr): 2957, 1609, 1440, 1291, 1251, 1074, 823, 799 cm^{-1}.

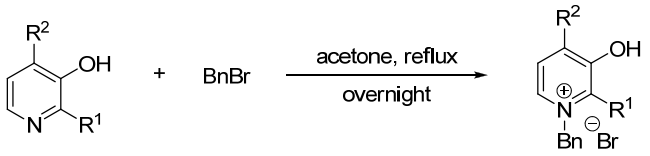
(10) Yoshida, K.; Kawagoe, F.; Hayashi, K.; Horiuchi, S.; Imamoto, T.; Yanagisawa, A. *Org. Lett.* **2009**, *11*, 515.

4-(3-Chlorophenyl)pyridin-3-ol (1u): 494 mg, 80% yield, white solid, mp 172-173 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.20 (s, 1H), 8.31 (s, 1H), 8.12 (d, *J* = 4.9 Hz, 1H), 7.72 (s, 1H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.55-7.41 (m, 2H), 7.34 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ 151.1, 141.4, 139.3, 138.3, 133.4, 132.6, 130.6, 129.1, 128.3, 128.0, 124.3. HRMS Calculated for $C_{11}H_9ClNO$ $[M+H]^+$ 206.0367, found 206.0366. IR (KBr): 2594, 1566, 1451, 1306, 1073, 817, 780, 687 cm^{-1}.

4-(4-Bromophenyl)pyridin-3-ol (1v): 458 mg, 61% yield, white solid, mp 189-190 °C. ^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 8.27 (s, 1H), 8.09 (d, *J* = 4.9 Hz, 1H), 7.69-7.54 (m, 4H), 7.30 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 151.2, 141.6, 139.3, 135.6, 133.1, 131.9, 131.6, 124.3, 122.1. HRMS Calculated for $C_{11}H_9BrNO$ $[M+H]^+$ 249.9862, found 249.9864. IR (KBr): 2958, 1434, 1391, 1312, 1290, 1070, 808, 745 cm^{-1}.

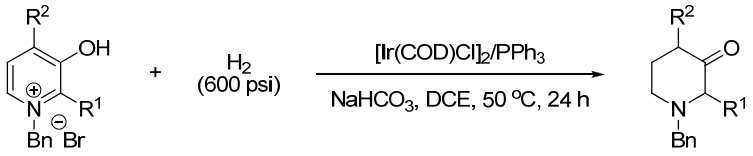
Methyl 4-(3-hydroxypyridin-4-yl)benzoate (1w): 407 mg, 59% yield, white solid, mp 216-217 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 10.24 (s, 1H), 8.33 (s, 1H), 8.14 (d, *J* = 4.9 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 4.9 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 166.5, 151.2, 141.4, 141.1, 139.4, 133.0, 129.7, 129.5, 129.4, 124.3, 52.6. HRMS Calculated for $C_{13}H_{12}NO_3$ $[M+H]^+$ 230.0812, found 230.0812. IR (KBr): 2953, 1722, 1435, 1288, 1114, 824, 776, 746 cm^{-1}.

3. General Procedure for the Hydrogenation of Pyridin-3-ols



1 **2**

A mixture of 2-substituted or 4-substituted pyridin-3-ol (2.0 mmol), benzyl bromide (0.36 mL, 3.0 mmol) and acetone (3.0 mL) was refluxed overnight. The resulting precipitate was collected and rinsed with cold acetone and ethyl acetate. The obtained 3-hydroxypyridinium salt was used for the subsequent hydrogenation without further purification. If the desired 3-hydroxypyridinium salt didn't precipitate, the reaction mixture was concentrated in *vacuo* and purified by column chromatography on silica gel using CH_2Cl_2/MeOH (20:1) as the eluent to give the desired product **2** (white solid, 31-88% yield).

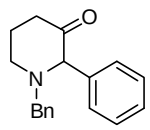


2 **3**

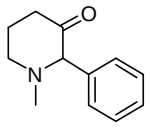
A mixture of $[Ir(COD)Cl]_2$ (0.7 mg, 0.001 mmol) and PPh_3 (1.2 mg, 0.0044 mmol) was stirred in 1,2-dichloroethane (1.0 mL) at room temperature for 10 min in a glove box, then the mixture was transferred to a vial which charged with the 3-hydroxypyridinium salt **2** (0.2 mmol) and $NaHCO_3$ (16.8 mg, 0.2 mmol). The total solution was made to 3.0 mL. Then the vial was taken to an autoclave, which was charged with 600 psi of H_2. The hydrogenation was performed at 50 °C for 20 h. After careful release of the hydrogen gas, the reaction mixture was filtrated and

concentrated in *vacuo*. Flash chromatography on silica gel using petroleum ether/ethyl acetate as the eluent gave the piperidin-3-one product.

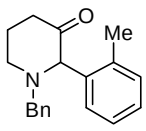
1-Benzyl-2-phenylpiperidin-3-one (3a): 49 mg, 93% yield, known compound,[4] white solid, mp 129-130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.19 (m, 10H), 3.93 (s, 1H), 3.78 (d, *J* = 13.6 Hz, 1H), 3.21 (d, *J* = 13.6 Hz, 1H), 3.12 (dt, *J* = 12.1, 4.5 Hz, 1H), 2.69 (dt, *J* = 14.8, 6.1 Hz, 1H), 2.50-2.32 (m, 2H), 2.11-1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 138.5, 137.6, 128.7, 128.6, 128.6, 128.3, 127.9, 127.1, 77.8, 59.3, 49.0, 38.1, 23.4.



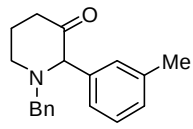
1-Methyl-2-phenylpiperidin-3-one (3a'): 32 mg, 84% yield, known compound,[11] yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.20 (m, 5H), 3.58 (s, 1H), 3.14 (dt, *J* = 11.7, 3.5 Hz, 1H), 2.70-2.50 (m, 2H), 2.43-2.31 (m, 1H), 2.23-2.08 (m, 4H), 2.07-1.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 137.3, 129.0, 128.4, 127.9, 79.9, 54.1, 44.6, 38.2, 23.5.



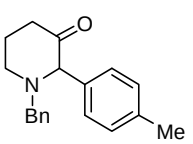
1-Benzyl-2-*o*-tolylpiperidin-3-one (3b): 54 mg, 96% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.43 (m, 1H), 7.32-7.11 (m, 8H), 4.05 (s, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.18-3.08 (m, 1H), 3.04 (d, *J* = 13.5 Hz, 1H), 2.71 (ddd, *J* = 8.3, 7.2, 4.3 Hz, 1H), 2.47-2.27 (m, 5H), 2.13-1.97 (m, 1H), 1.97-1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 138.6, 137.5, 136.2, 130.9, 129.5, 128.7, 128.3, 127.7, 127.0, 126.0, 76.2, 59.7, 50.4, 38.7, 23.1, 20.2. HRMS Calculated for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1696, found 280.1709. IR (film): 2953, 1720, 1494, 1285, 1134, 968, 755, 699 cm^{-1}.



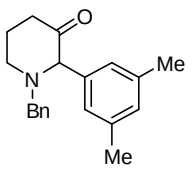
1-Benzyl-2-*m*-tolylpiperidin-3-one (3c): 52 mg, 93% yield, white solid, mp 86-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.17 (m, 8H), 7.14-7.06 (m, 1H), 3.88 (s, 1H), 3.78 (d, *J* = 13.6 Hz, 1H), 3.19 (d, *J* = 13.6 Hz, 1H), 3.11 (dt, *J* = 12.2, 4.6 Hz, 1H), 2.68 (dt, *J* = 14.9, 6.1 Hz, 1H), 2.46-2.30 (m, 5H), 2.09-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2, 138.6, 138.2, 137.5, 129.4, 128.7, 128.7, 128.5, 128.3, 127.1, 125.7, 77.8, 59.3, 49.0, 38.1, 23.4, 21.5. HRMS Calculated for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1696, found 280.1704. IR (KBr): 2952, 1720, 1453, 1151, 973, 777, 740, 701 cm^{-1}.



1-Benzyl-2-*p*-tolylpiperidin-3-one (3d): 51 mg, 91% yield, white solid, mp 107-108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.13 (m, 9H), 3.88 (s, 1H), 3.78 (d, *J* = 13.6 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 3.10 (dt, *J* = 12.1, 4.5 Hz, 1H), 2.68 (dt, *J* = 14.9, 6.0 Hz, 1H), 2.46-2.29 (m, 5H), 2.07-1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 138.6, 137.6, 134.5, 129.4, 128.6, 128.6, 128.3, 127.1, 77.6, 59.3, 49.2, 38.2, 23.4, 21.2. HRMS Calculated for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1696, found 280.1709. IR (KBr): 2950, 1722, 1512, 1452, 1131, 809, 742, 699 cm^{-1}.



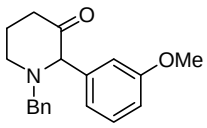
1-Benzyl-2-(3,5-dimethylphenyl)piperidin-3-one (3e): 50 mg, 85% yield, yellow solid, mp 74-75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.18 (m, 5H), 7.04 (s, 2H), 6.92 (s, 1H), 3.84 (s, 1H), 3.79 (d, *J* = 13.6 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 3.11 (dt, *J* = 12.0, 4.6 Hz, 1H), 2.77-2.62 (m, 1H), 2.47-2.25 (m, 8H), 2.11-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.3, 138.7, 138.0, 137.4, 129.7, 128.7,



(11) Cervinka, D.; Jursik, T., *Stud. Org. Chem.* **1988,** *35*, 233.

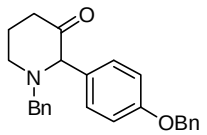
128.3, 127.0, 126.5, 77.8, 59.3, 49.0, 38.0, 23.3, 21.4. HRMS Calculated for $C_{20}H_{24}NO$ $[M+H]^+$ 294.1852, found 294.1869. IR (KBr): 2949, 1722, 1607, 1452, 1152, 845, 740, 700 cm^{-1}.

1-Benzyl-2-(3-methoxyphenyl)piperidin-3-one (3f): 52 mg, 88% yield, colorless oil. ^1H NMR



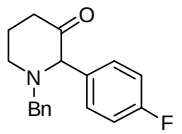
(400 MHz, $CDCl_3$) δ 7.34-7.17 (m, 6H), 7.07-6.97 (m, 2H), 6.89-6.79 (m, 1H), 3.90 (s, 1H), 3.85-3.75 (m, 4H), 3.21 (d, J = 13.6 Hz, 1H), 3.11 (dt, J = 12.2, 4.6 Hz, 1H), 2.68 (dt, J = 14.8, 6.1 Hz, 1H), 2.47-2.30 (m, 2H), 2.09-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9, 159.9, 139.2, 138.5, 129.6, 128.6, 128.3, 127.1, 121.1, 114.2, 113.4, 77.6, 59.3, 55.2, 49.0, 38.1, 23.4. HRMS Calculated for $C_{19}H_{22}NO_2$ $[M+H]^+$ 296.1645, found 296.1654. IR (film): 2952, 1721, 1599, 1453, 1261, 1045, 742, 700 cm^{-1}.

1-Benzyl-2-(4-(benzyloxy)phenyl)piperidin-3-one (3g): 65 mg, 88% yield, white solid, mp



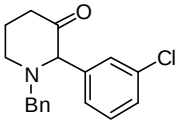
115-116 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.17 (m, 12H), 7.00-6.94 (m, 2H), 5.03 (s, 2H), 3.85 (s, 1H), 3.78 (d, J = 13.6 Hz, 1H), 3.16 (d, J = 13.6 Hz, 1H), 3.09 (dt, J = 12.0, 4.4 Hz, 1H), 2.66 (dt, J = 14.8, 5.9 Hz, 1H), 2.48-2.28 (m, 2H), 2.06-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2, 158.6, 138.6, 137.1, 129.9, 129.9, 128.7, 128.6, 128.3, 128.0, 127.6, 127.1, 115.0, 77.3, 70.1, 59.3, 49.3, 38.2, 23.4. HRMS Calculated for $C_{25}H_{26}NO_2$ $[M+H]^+$ 372.1958, found 372.1970. IR (KBr): 2947, 1721, 1509, 1243, 1027, 826, 739, 698 cm^{-1}.

1-Benzyl-2-(4-fluorophenyl)piperidin-3-one (3h): 49 mg, 86% yield, yellow solid, mp 94-95 °C.



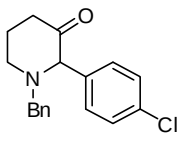
^1H NMR (400 MHz, $CDCl_3$) δ 7.44-7.35 (m, 2H), 7.33-7.20 (m, 5H), 7.12-6.99 (m, 2H), 3.89 (s, 1H), 3.75 (d, J = 13.6 Hz, 1H), 3.18 (d, J = 13.6 Hz, 1H), 3.11 (dt, J = 12.1, 4.2 Hz, 1H), 2.66 (dt, J = 15.0, 5.5 Hz, 1H), 2.49-2.31 (m, 2H), 2.10-1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 162.5 (d, J_{C-F} = 244.7 Hz), 138.3, 133.3 (d, J_{C-F} = 3.2 Hz), 130.3 (d, J_{C-F} = 7.9 Hz), 128.6, 128.3, 127.2, 115.5 (d, J_{C-F} = 21.3 Hz), 77.1, 59.4, 49.4, 38.3, 23.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.53. HRMS Calculated for $C_{18}H_{19}NO$ $[M+H]^+$ 284.1445, found 284.1451. IR (KBr): 2953, 1722, 1508, 1184, 1155, 828, 743, 699 cm^{-1}.

1-Benzyl-2-(3-chlorophenyl)piperidin-3-one (3i): 54 mg, 90% yield, colorless oil. ^1H NMR (400



MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.37-7.18 (m, 8H), 3.89 (s, 1H), 3.76 (d, J = 13.6 Hz, 1H), 3.21 (d, J = 13.6 Hz, 1H), 3.11 (dt, J = 12.1, 4.4 Hz, 1H), 2.66 (dt, J = 15.0, 5.7 Hz, 1H), 2.50-2.32 (m, 2H), 2.09-1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.1, 139.8, 138.1, 134.6, 129.8, 128.8, 128.6, 128.4, 128.1, 127.3, 127.0, 77.2, 59.5, 49.2, 38.2, 23.3. HRMS Calculated for $C_{18}H_{19}ClNO$ $[M+H]^+$ 300.1150, found 300.1151. IR (film): 2953, 1721, 1574, 1472, 1132, 780, 740, 698 cm^{-1}.

1-Benzyl-2-(4-chlorophenyl)piperidin-3-one (3j): 50 mg, 83% yield, colorless oil. ^1H NMR



(400 MHz, $CDCl_3$) δ 7.40-7.19 (m, 9H), 3.89 (s, 1H), 3.74 (d, J = 13.6 Hz, 1H), 3.19 (d, J = 13.6 Hz, 1H), 3.11 (dt, J = 12.1, 4.3 Hz, 1H), 2.65 (dt, J = 15.0, 5.6 Hz, 1H), 2.49-2.31 (m, 2H), 2.10-1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 138.1, 136.2, 133.7, 130.1, 128.8, 128.6, 128.4, 127.2, 77.1, 59.4, 49.4, 38.3, 23.4. HRMS Calculated for $C_{18}H_{19}ClNO$ $[M+H]^+$ 300.1150, found 300.1151. IR (film): 2953, 1721, 1489, 1089, 1015, 818, 741, 699 cm^{-1}.

1-Benzyl-2-(3,5-difluorophenyl)piperidin-3-one (3k): 57 mg, 95% yield, white solid, mp 98-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.18 (m, 5H), 7.01-6.93 (m, 2H), 6.79-6.68 (m, 1H), 3.90 (s, 1H), 3.76 (d, J = 13.6 Hz, 1H), 3.25 (d, J = 13.6 Hz, 1H), 3.12 (dt, J = 12.2, 4.3 Hz, 1H), 2.64 (dt, J = 15.1, 5.7 Hz, 1H), 2.52-2.30 (m, 2H), 2.08-1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 163.2 (dd, J_{C-F} = 247.1, 12.6 Hz), 141.8 (t, J_{C-F} = 8.9 Hz), 137.7, 128.6, 128.4, 127.4, 111.5 (dd, J_{C-F} = 25.5, 11.7 Hz), 103.4 (t, J_{C-F} = 25.3 Hz), 76.8, 59.5, 49.1, 38.2, 23.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.58. HRMS Calculated for $C_{18}H_{18}F_2NO$ $[M+H]^+$ 302.1351, found 302.1358. IR (KBr): 2955, 1723, 1598, 1454, 1117, 851, 742, 699 cm^{-1}.

Methyl 4-(1-benzyl-3-oxopiperidin-2-yl)benzoate (3l): 61 mg, 94% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.36-7.18 (m, 5H), 3.98 (s, 1H), 3.90 (s, 3H), 3.72 (d, J = 13.6 Hz, 1H), 3.21 (d, J = 13.6 Hz, 1H), 3.13 (dt, J = 12.1, 4.3 Hz, 1H), 2.65 (dt, J = 15.0, 5.6 Hz, 1H), 2.52-2.34 (m, 2H), 2.09-1.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 166.9, 143.0, 138.0, 129.9, 129.8, 128.8, 128.6, 128.4, 127.3, 77.5, 59.5, 52.1, 49.3, 38.4, 23.4. HRMS Calculated for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found 324.1598. IR (film): 2951, 1722, 1435, 1279, 1113, 765, 738, 703 cm^{-1}.

1-Benzyl-2-(4-(trifluoromethyl)phenyl)piperidin-3-one (3m): 62 mg, 93% yield, white solid, mp 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 7.37-7.20 (m, 6H), 3.99 (s, 1H), 3.72 (d, J = 13.6 Hz, 1H), 3.22 (d, J = 13.6 Hz, 1H), 3.14 (dt, J = 12.0, 4.2 Hz, 1H), 2.66 (dt, J = 15.1, 5.5 Hz, 1H), 2.55-2.35 (m, 2H), 2.13-1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 141.9 (d, J_{C-F} = 1.2 Hz), 137.9, 130.1 (q, J_{C-F} = 24.2 Hz), 129.2, 128.6, 128.4, 127.3, 125.5 (q, J_{C-F} = 2.8 Hz), 122.8, 77.3, 59.6, 49.4, 38.4, 23.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48. HRMS Calculated for $C_{19}H_{19}F_3NO$ $[M+H]^+$ 334.1413, found 334.1418. IR (KBr): 2955, 1723, 1326, 1125, 1067, 828, 747, 699 cm^{-1}.

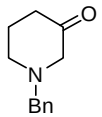
1-Benzyl-2-(naphthalen-2-yl)piperidin-3-one (3n): 53 mg, 84% yield, white solid, mp 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.76 (m, 4H), 7.64-7.56 (m, 1H), 7.50-7.40 (m, 2H), 7.33-7.17 (m, 5H), 4.08 (d, J = 9.0 Hz, 1H), 3.80 (d, J = 13.6 Hz, 1H), 3.21 (d, J = 13.6 Hz, 1H), 3.15 (dt, J = 12.1, 4.4 Hz, 1H), 2.71 (dt, J = 14.9, 5.8 Hz, 1H), 2.52-2.34 (m, 2H), 2.12-1.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9, 138.4, 135.2, 133.4, 133.3, 128.7, 128.4, 128.3, 128.3, 128.0, 127.8, 127.1, 126.2, 126.1, 126.0, 78.0, 59.5, 49.3, 38.4, 23.5. HRMS Calculated for $C_{22}H_{22}NO$ $[M+H]^+$ 316.1696, found 316.1704. IR (KBr): 2952, 1720, 1452, 1283, 1131, 819, 742, 699 cm^{-1}.

1-Benzyl-2-methylpiperidin-3-one (3o): 38 mg, 93% yield, known compound,[4] colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.18 (m, 5H), 3.85 (d, J = 13.5 Hz, 1H), 3.48 (d, J = 13.5 Hz, 1H), 3.17 (q, J = 6.7 Hz, 1H), 2.98-2.83 (m, 1H), 2.57-2.43 (m, 2H), 2.40-2.27 (m, 1H), 1.99-1.82 (m, 2H), 1.28 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.0, 138.6, 128.7, 128.3, 127.1, 66.2, 57.8, 47.5, 37.7, 24.1, 12.2.

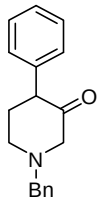
1-Benzyl-2-butylpiperidin-3-one (3p): 42 mg, 86% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.20 (m, 5H), 3.78 (d, J = 13.5 Hz, 1H), 3.62 (d, J = 13.5 Hz, 1H), 3.13-2.96 (m, 2H), 2.66-2.47 (m, 2H), 2.35 (dt, J = 15.0, 5.8 Hz, 1H),

2.11-1.89 (m, 2H), 1.90-1.61 (m, 2H), 1.38-1.18 (m, 4H), 0.97-0.79 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.0, 139.0, 128.8, 128.5, 127.3, 70.9, 57.5, 46.0, 38.0, 28.1, 26.9, 24.3, 22.9, 14.1. HRMS Calculated for $C_{16}H_{24}NO$ $[M+H]^+$ 246.1852, found 246.1859. IR (film): 2928, 1715, 1482, 1434, 1092, 743, 696, 521 cm^{-1}.

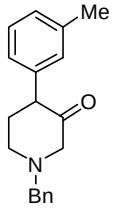
1-Benzylpiperidin-3-one (3q): 37 mg, 97% yield, known compound,[12] yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.15 (m, 5H), 3.58 (s, 2H), 3.00 (s, 2H), 2.64 (t, *J* = 5.5 Hz, 2H), 2.35 (t, *J* = 6.9 Hz, 2H), 2.03-1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 137.3, 129.0, 128.4, 127.3, 64.6, 62.6, 51.6, 38.7, 24.0.



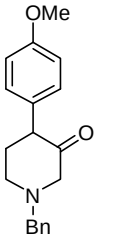
1-Benzyl-4-phenylpiperidin-3-one (3r): 45 mg, 85% yield, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.07 (m, 10H), 3.69-3.59 (m, 2H), 3.58-3.48 (m, 1H), 3.36 (d, *J* = 14.1 Hz, 1H), 3.12-3.00 (m, 1H), 2.95 (d, *J* = 14.1 Hz, 1H), 2.67-2.54 (m, 1H), 2.30-2.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 138.1, 137.1, 129.1, 128.7, 128.5, 128.4, 127.5, 127.1, 64.5, 62.6, 55.0, 52.0, 32.5. HRMS Calculated for $C_{18}H_{20}NO$ $[M+H]^+$ 266.1539, found 266.1541. IR (film): 2928, 1721, 1496, 1453, 1266, 1097, 739, 699 cm^{-1}.



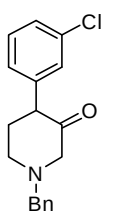
1-Benzyl-4-m-tolylpiperidin-3-one (3s): 49 mg, 88% yield, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.19 (m, 6H), 7.11-6.92 (m, 3H), 3.69-3.58 (m, 2H), 3.50 (dd, *J* = 11.2, 7.6 Hz, 1H), 3.36 (dd, *J* = 14.1, 1.6 Hz, 1H), 3.10-3.00 (m, 1H), 2.94 (d, *J* = 14.1 Hz, 1H), 2.59 (ddd, *J* = 11.6, 9.7, 4.6 Hz, 1H), 2.33 (s, 3H), 2.28-2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 138.0, 138.0, 137.1, 129.5, 129.2, 128.4, 128.4, 128.0, 127.5, 125.8, 64.5, 62.5, 55.1, 52.0, 32.4, 21.5. HRMS Calculated for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1696, found 280.1696. IR (film): 2923, 1721, 1494, 1454, 1267, 786, 738, 700 cm^{-1}.



1-Benzyl-4-(4-methoxyphenyl)piperidin-3-one (3t): 50 mg, 85% yield, white solid, mp 119-120 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.22 (m, 5H), 7.11-7.02 (m, 2H), 6.91-6.83 (m, 2H), 3.78 (s, 3H), 3.68-3.58 (m, 2H), 3.53-3.44 (m, 1H), 3.35 (dd, *J* = 14.0, 1.6 Hz, 1H), 3.04 (dtd, *J* = 11.4, 3.8, 1.5 Hz, 1H), 2.93 (d, *J* = 14.0 Hz, 1H), 2.64-2.52 (m, 1H), 2.28-2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 158.7, 137.2, 130.1, 129.7, 129.1, 128.4, 127.4, 114.0, 64.6, 62.6, 55.3, 54.3, 52.1, 32.6. HRMS Calculated for $C_{19}H_{22}NO_2$ $[M+H]^+$ 296.1645, found 296.1651. IR (KBr): 2937, 1721, 1514, 1248, 1035, 831, 741, 701 cm^{-1}.



1-Benzyl-4-(3-chlorophenyl)piperidin-3-one (3u): 53 mg, 88% yield, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.20 (m, 7H), 7.15 (s, 1H), 7.03 (dt, *J* = 6.7, 1.9 Hz, 1H), 3.69-3.59 (m, 2H), 3.56-3.46 (m, 1H), 3.36 (dd, *J* = 14.1, 1.6 Hz, 1H), 3.06 (dtd, *J* = 11.6, 3.9, 1.7 Hz, 1H), 2.94 (d, *J* = 14.1 Hz, 1H), 2.58 (ddd, *J* = 11.7, 8.1, 6.1 Hz, 1H), 2.28-2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 140.0, 137.0, 134.3, 129.7, 129.1, 129.0, 128.5, 127.5, 127.3, 127.1, 64.4, 62.5, 54.7, 51.9, 32.4. HRMS Calculated for $C_{18}H_{19}ClNO$ $[M+H]^+$ 300.1150, found 300.1154. IR (film): 2927, 1722, 1596, 1433, 1097, 785, 740, 698 cm^{-1}.



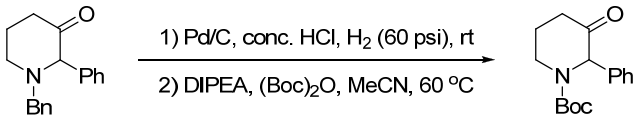
(12) Hirsch, J. A.; Jarmas, A. A. *J. Org. Chem.* **1978**, *43*, 4106.

1-Benzyl-4-(3-bromophenyl)piperidin-3-one (3v): 59 mg, 86% yield, white solid, mp 106-107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.43 (m, 2H), 7.39-7.24 (m, 5H), 7.04 (d, *J* = 8.4 Hz, 2H), 3.71-3.60 (m, 2H), 3.52 (dd, *J* = 11.0, 8.0 Hz, 1H), 3.39 (dd, *J* = 14.0, 1.5 Hz, 1H), 3.13-3.04 (m, 1H), 2.95 (d, *J* = 14.0 Hz, 1H), 2.65-2.53 (m, 1H), 2.27-2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.1, 137.2, 137.2, 131.8, 130.7, 129.3, 128.6, 127.7, 121.3, 64.7, 62.7, 54.7, 52.1, 32.7. HRMS Calculated for $C_{18}H_{19}BrNO$ $[M+H]^+$ 344.0645, found 344.0648. IR (KBr): 2946, 1722, 1490, 1099, 1011, 815, 742, 700 cm^{-1}.

Methyl 4-(1-benzyl-3-oxopiperidin-4-yl)benzoate (3w): 54 mg, 83% yield, white solid, mp 125-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.40-7.19 (m, 7H), 3.90 (s, 3H), 3.71-3.56 (m, 3H), 3.38 (dd, *J* = 14.1, 1.5 Hz, 1H), 3.12-3.03 (m, 1H), 2.96 (d, *J* = 14.1 Hz, 1H), 2.67-2.53 (m, 1H), 2.30-2.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 166.9, 143.3, 137.0, 129.8, 129.1, 129.0, 128.9, 128.5, 127.5, 64.5, 62.5, 55.0, 52.0, 51.9, 32.4. HRMS Calculated for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found 324.1599. IR (KBr): 2949, 1721, 1436, 1281, 1107, 772, 742, 700 cm^{-1}.

1-Benzyl-4-methylpiperidin-3-one (3x): 35 mg, 84% yield, known compound,[13] colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H), 3.63-3.50 (m, 2H), 3.23 (dd, *J* = 13.8, 1.6 Hz, 1H), 2.97-2.88 (m, 1H), 2.79 (d, *J* = 13.8 Hz, 1H), 2.45 (td, *J* = 11.4, 3.1 Hz, 1H), 2.40-2.28 (m, 1H), 2.04 (ddt, *J* = 13.2, 6.6, 3.3 Hz, 1H), 1.70-1.57 (m, 1H), 1.08 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 137.4, 129.0, 128.4, 127.3, 64.1, 62.6, 51.9, 42.9, 32.9, 14.2.

4. General Procedure for the Removal of Benzyl Group



3a **5a**

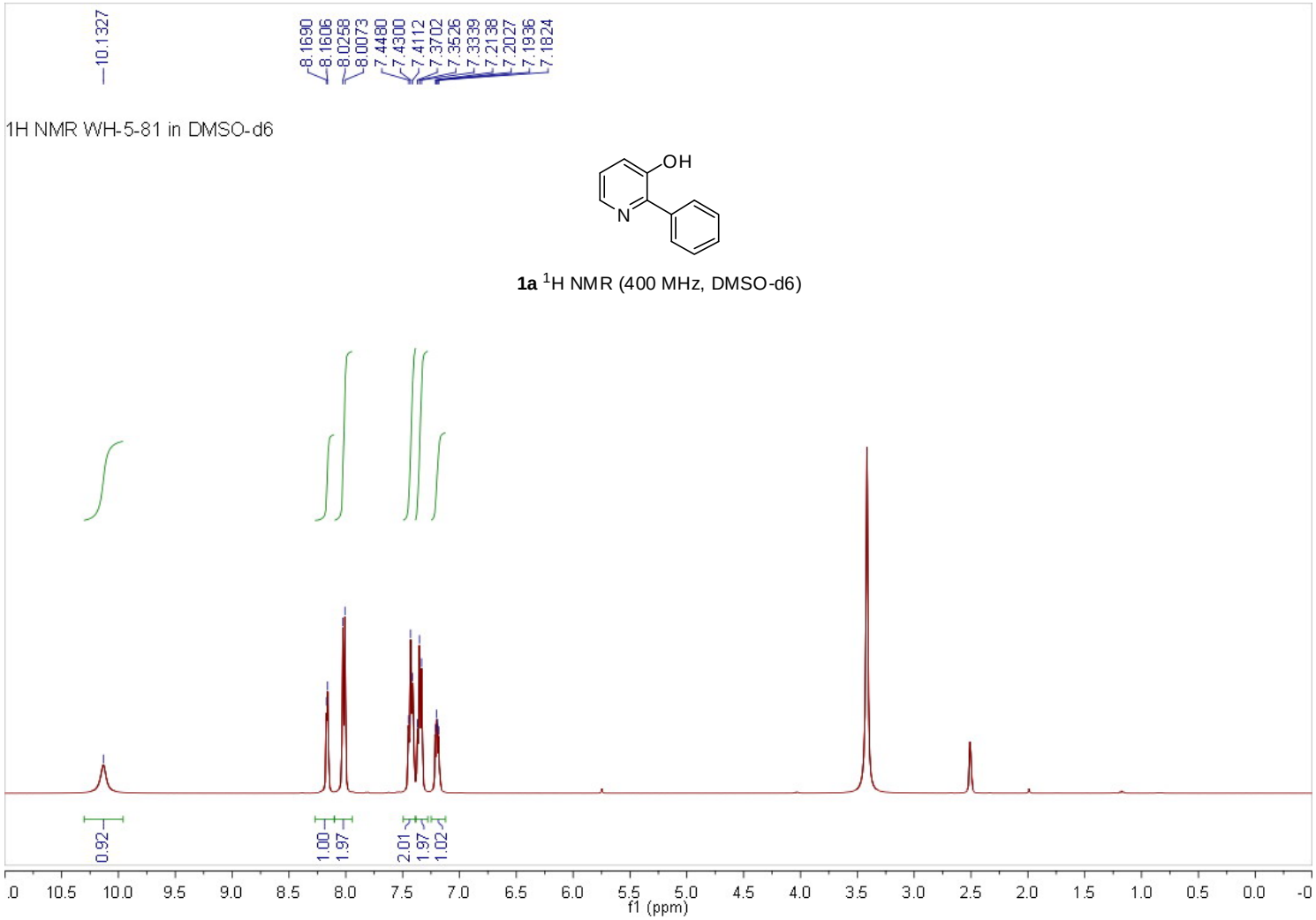
5% Pd/C (21 mg) was added to the solution of **3a** (53 mg, 0.2 mmol), conc. HCl (20.0 μL, 0.2 mmol, 10 M) in MeOH (3.0 mL), the resulted mixture was taken to an autoclave and stired under H_2 (60 psi) at room temperature for 12 h. After careful release of the hydrogen gas, the reaction mixture was filtrated through a small pad of celite and concentrated in *vacuo*. The crude product was dissolved in MeCN (3.0 mL) and then treated with DIPEA (100 μL, 0.6 mmol) and $(Boc)_2O$ (87 mg, 0.4 mmol). The reaction mixture was stirred for 5 h at 60 °C and then concentrated in *vacuo* to colorless oil. The oil was purified by Flash chromatography on silica gel using petroleum ether/ethyl acetate (10/1) as the eluent to yield **5a** (46 mg, 84% yield).

***tert*-Butyl 3-oxo-2-phenylpiperidine-1-carboxylate (5a):** 46 mg, 84% yield, known compound,[14] colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.07 (m, 5H), 5.65 (s, 1H), 4.08 (s, 1H), 3.43-3.19 (m, 1H), 2.57-2.34 (m, 2H), 2.07-1.79 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 155.0, 135.6, 128.9, 127.6, 125.4, 80.7, 66.4, 40.0, 37.3, 28.3, 22.9.

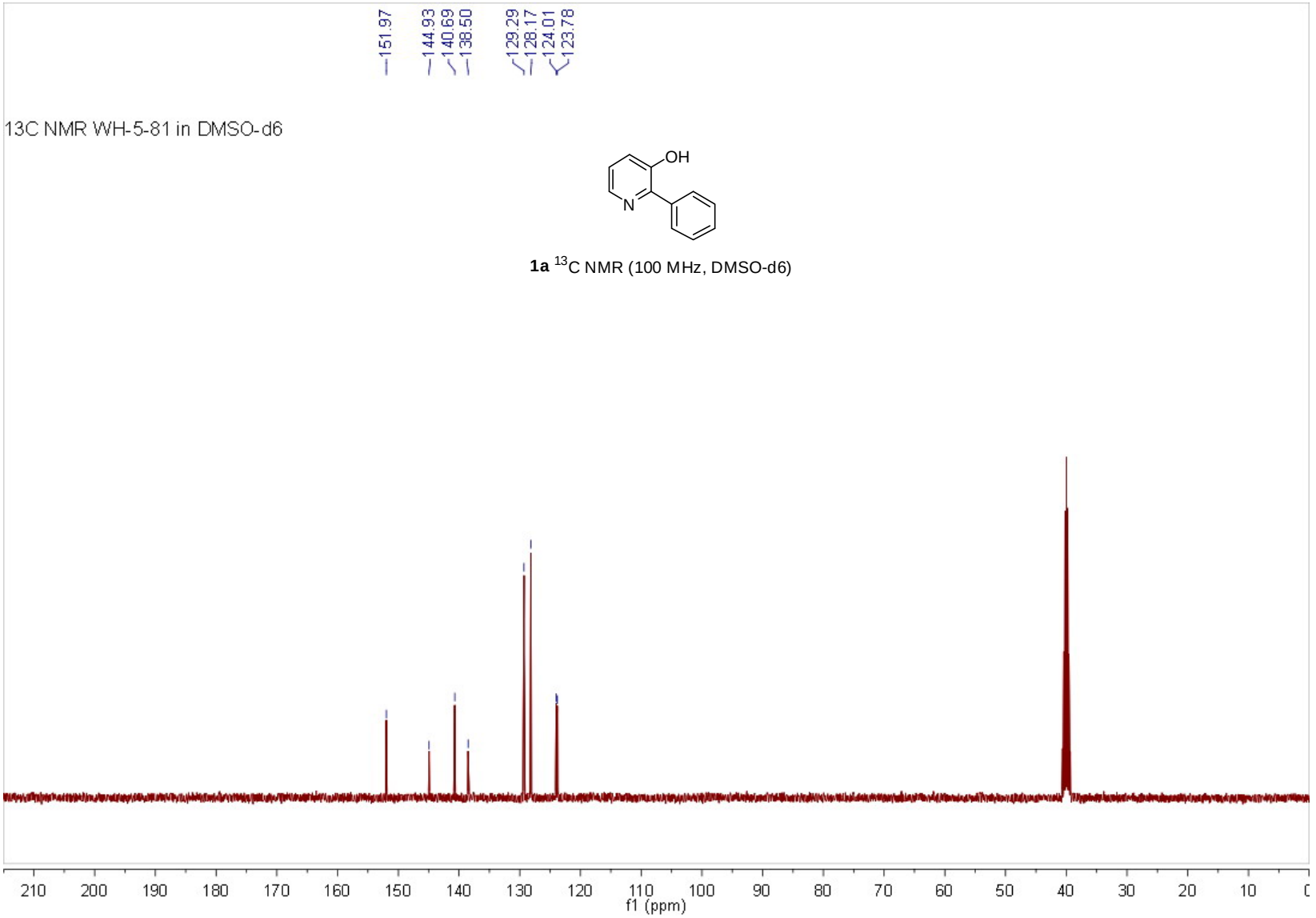
(13) Iorio, M. A.; Ciuffa, P.; Damia, G.; *Tetrahedron* **1970**, *26*, 5519.

(14) Pansare, S. V.; Paul, E. K. *Org. Biomol. Chem.* **2012**, *10*, 2119.

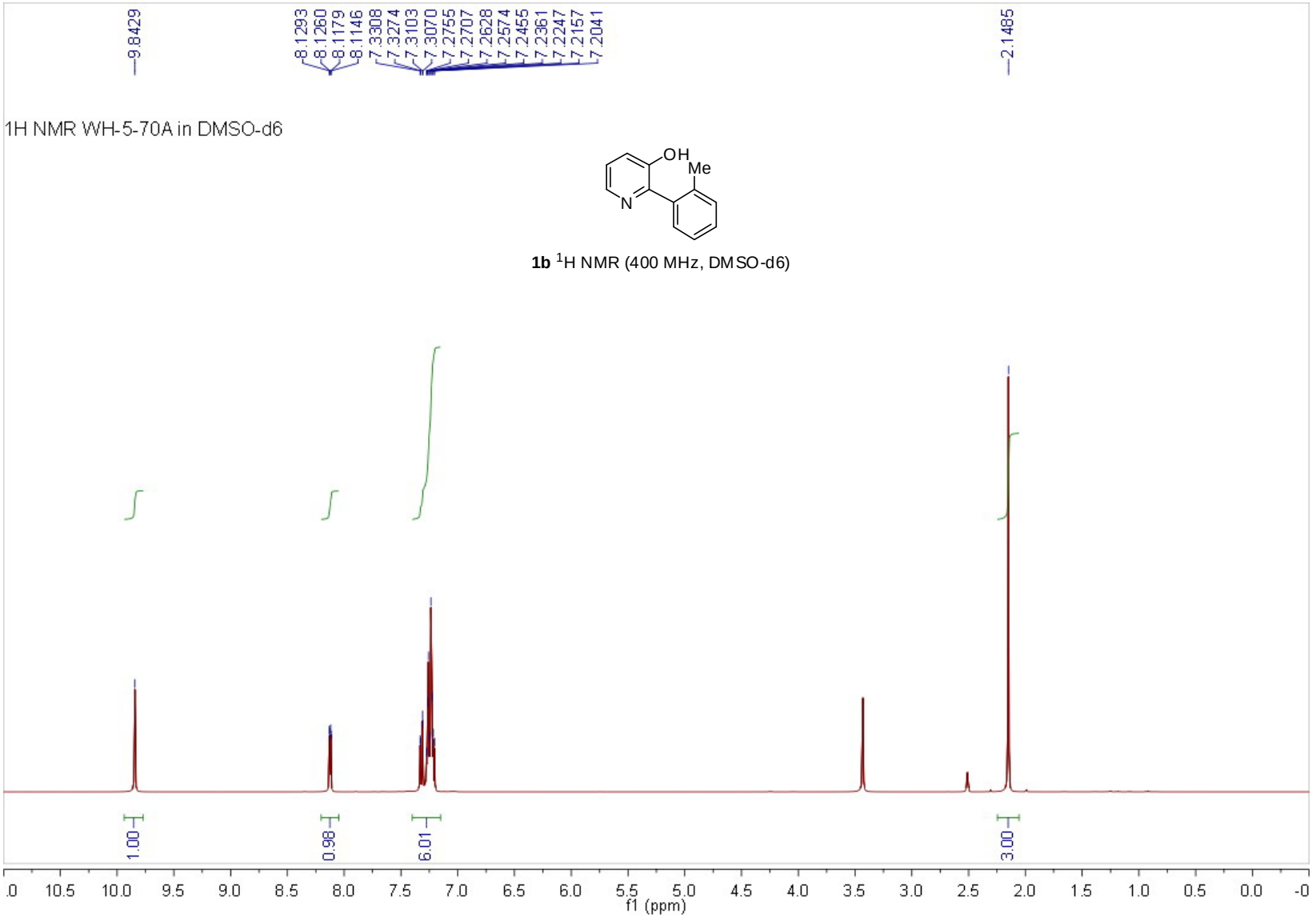
5. Copy of NMR for the Substrates and Products



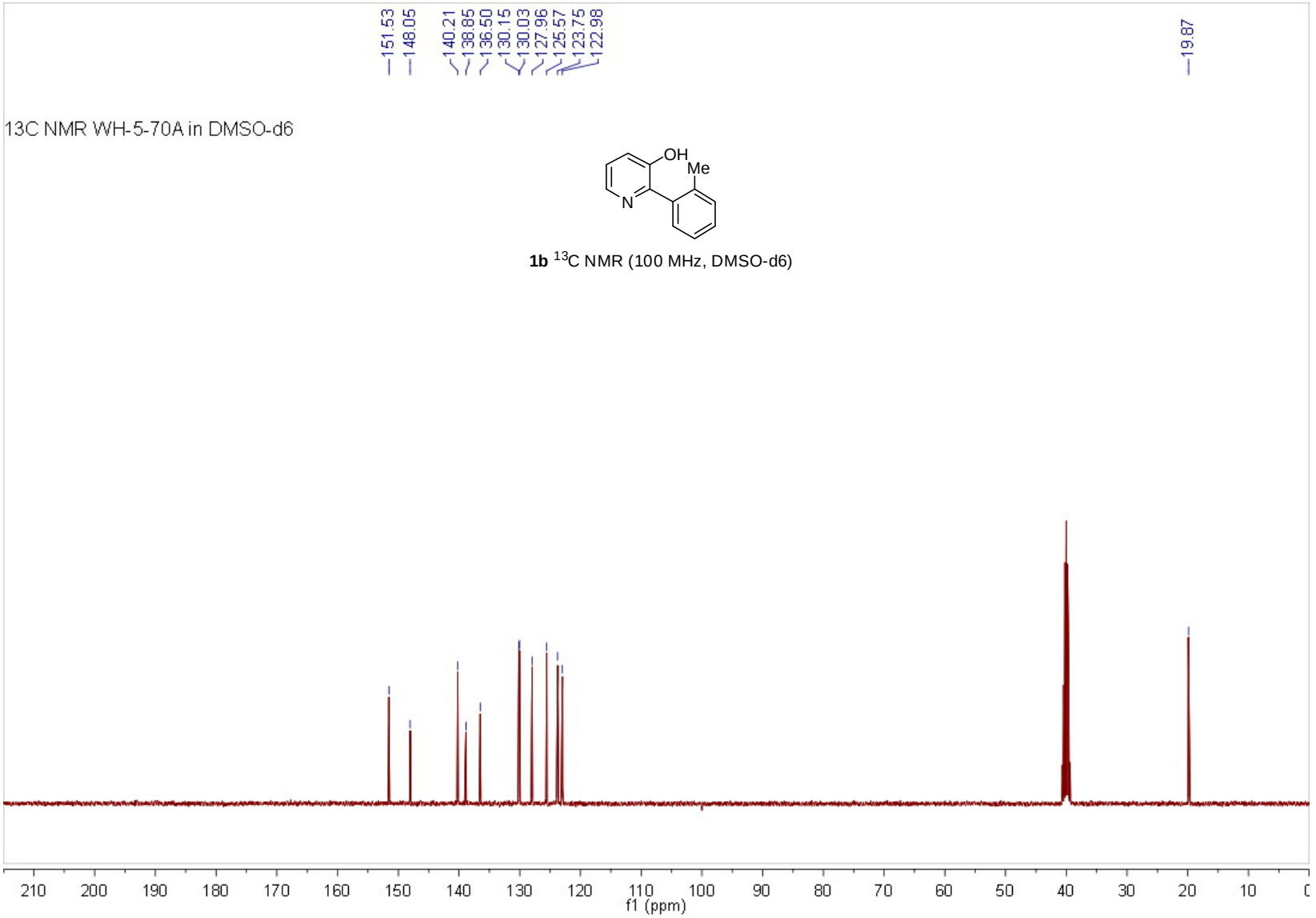
1a ^{1}H NMR (400 MHz, DMSO-d6)



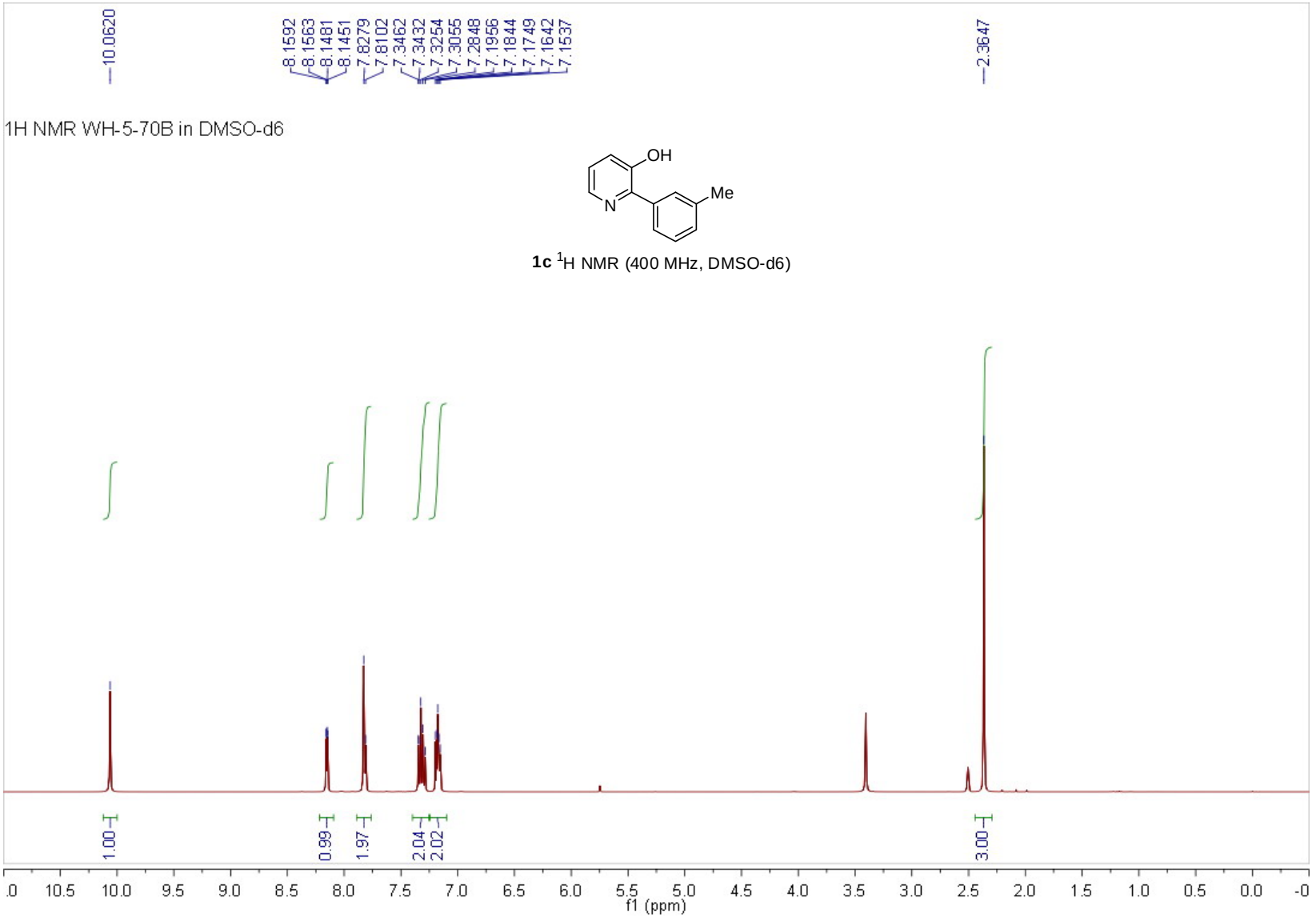
1a ^{13}C NMR (100 MHz, DMSO-d6)



1b ^{1}H NMR (400 MHz, DMSO-d6)



1b ^{13}C NMR (100 MHz, DMSO-d6)



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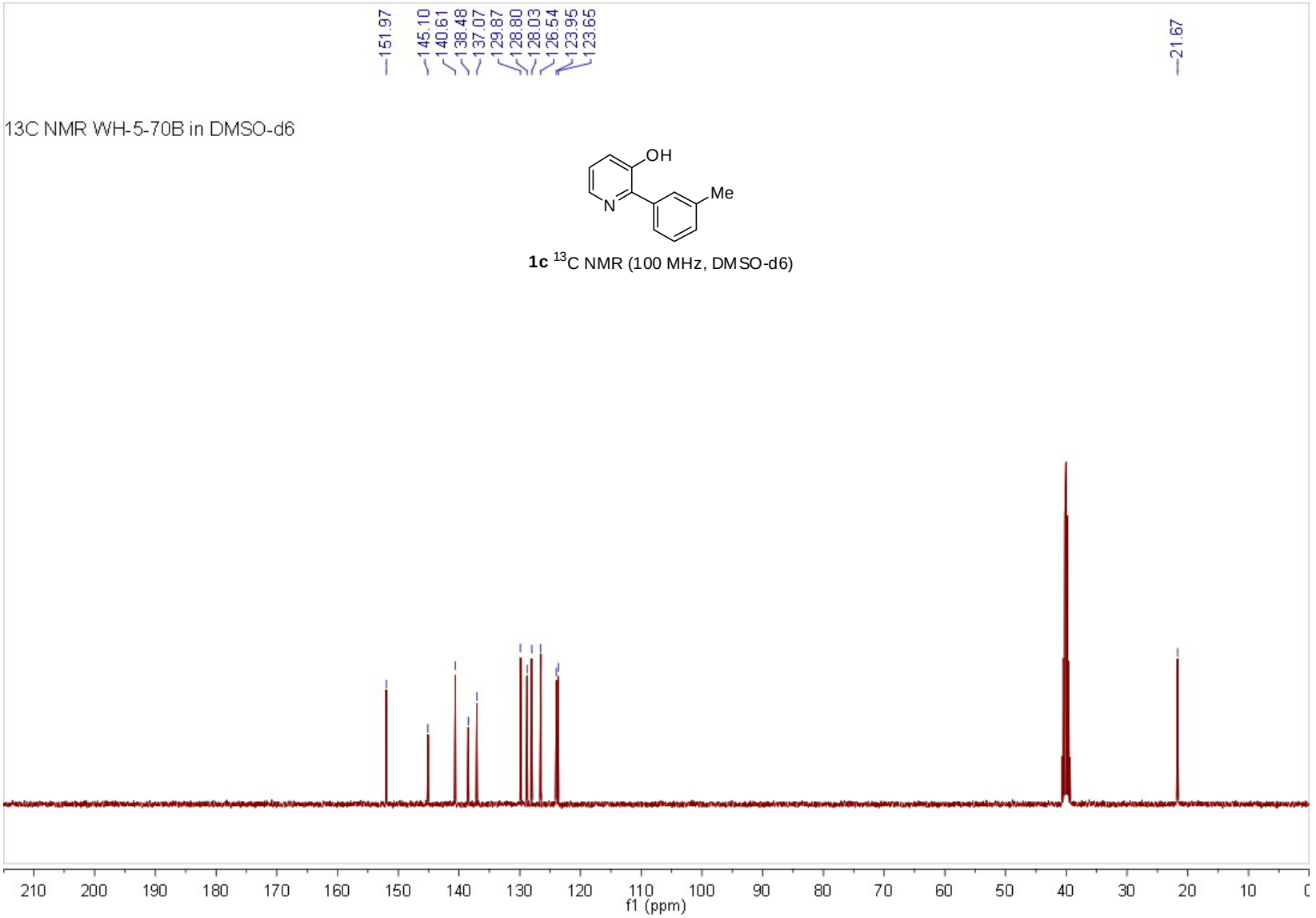

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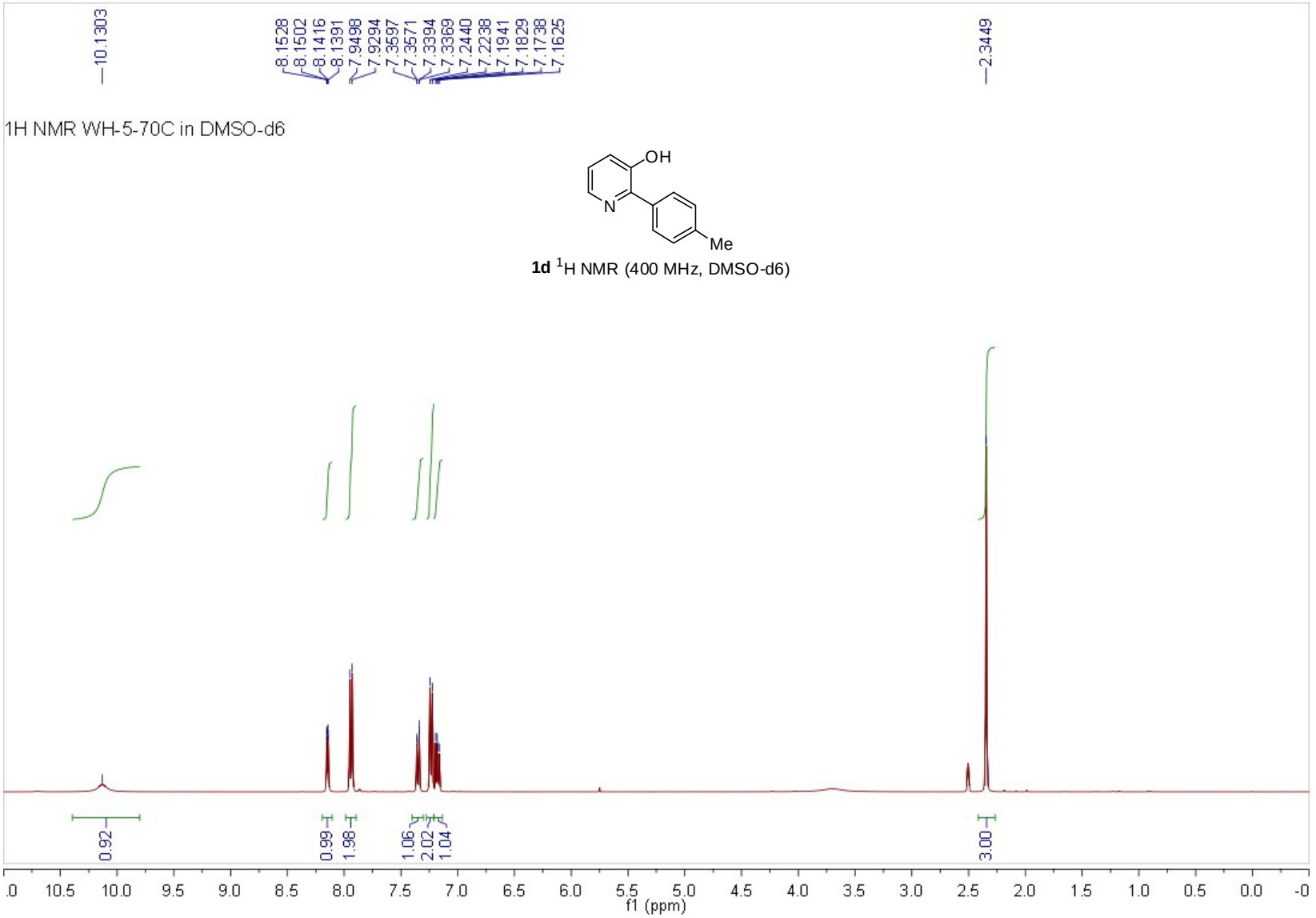

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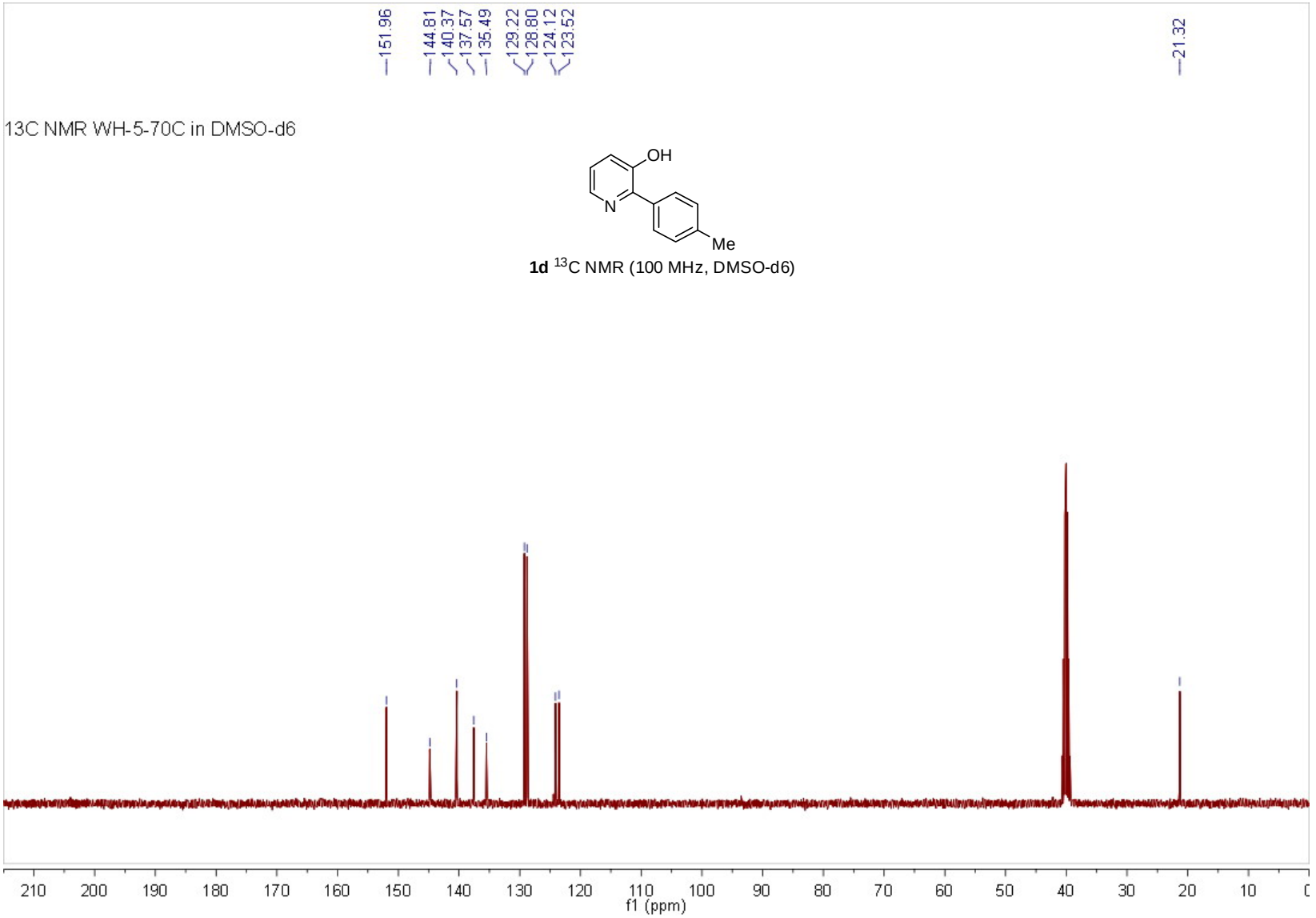
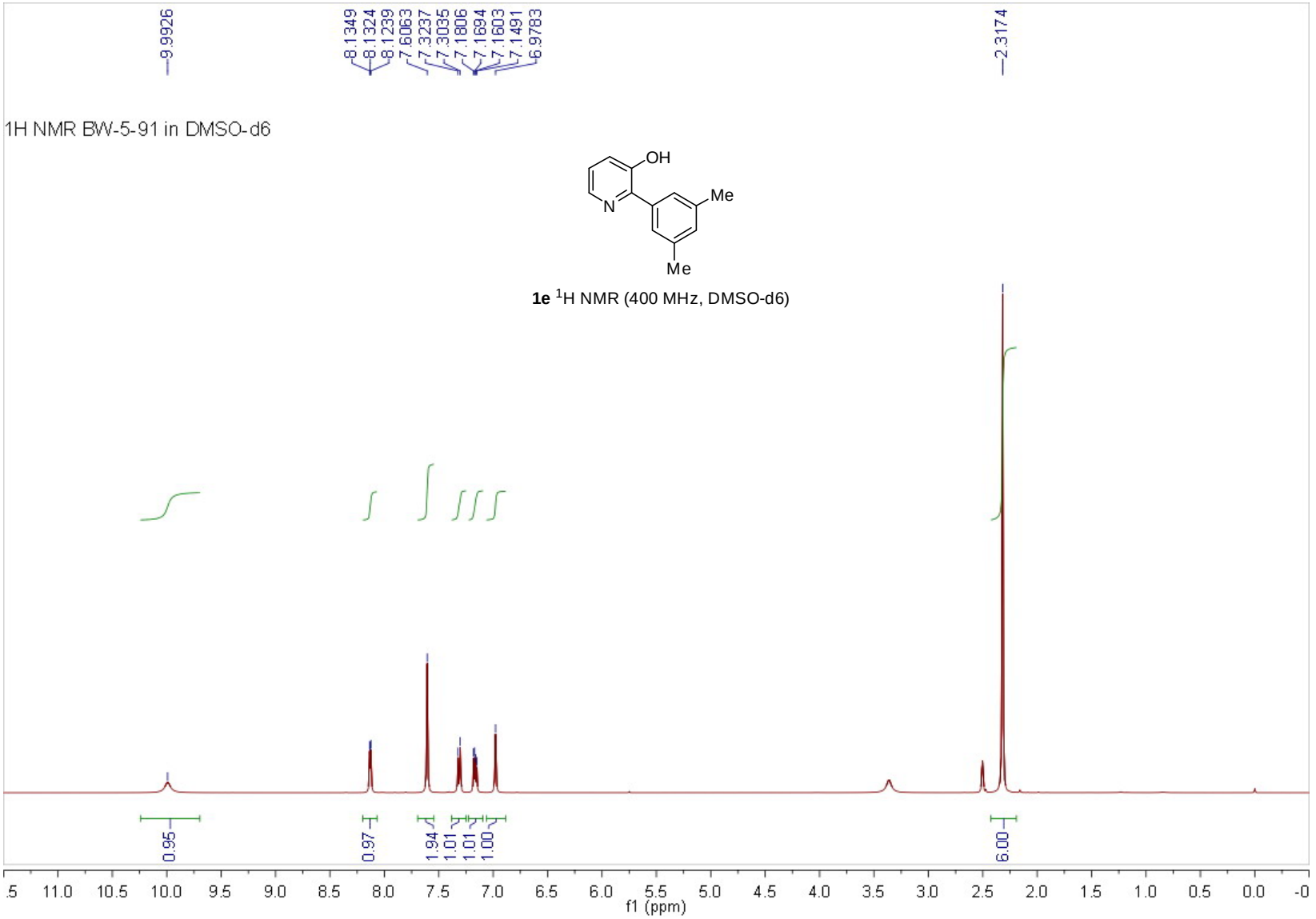
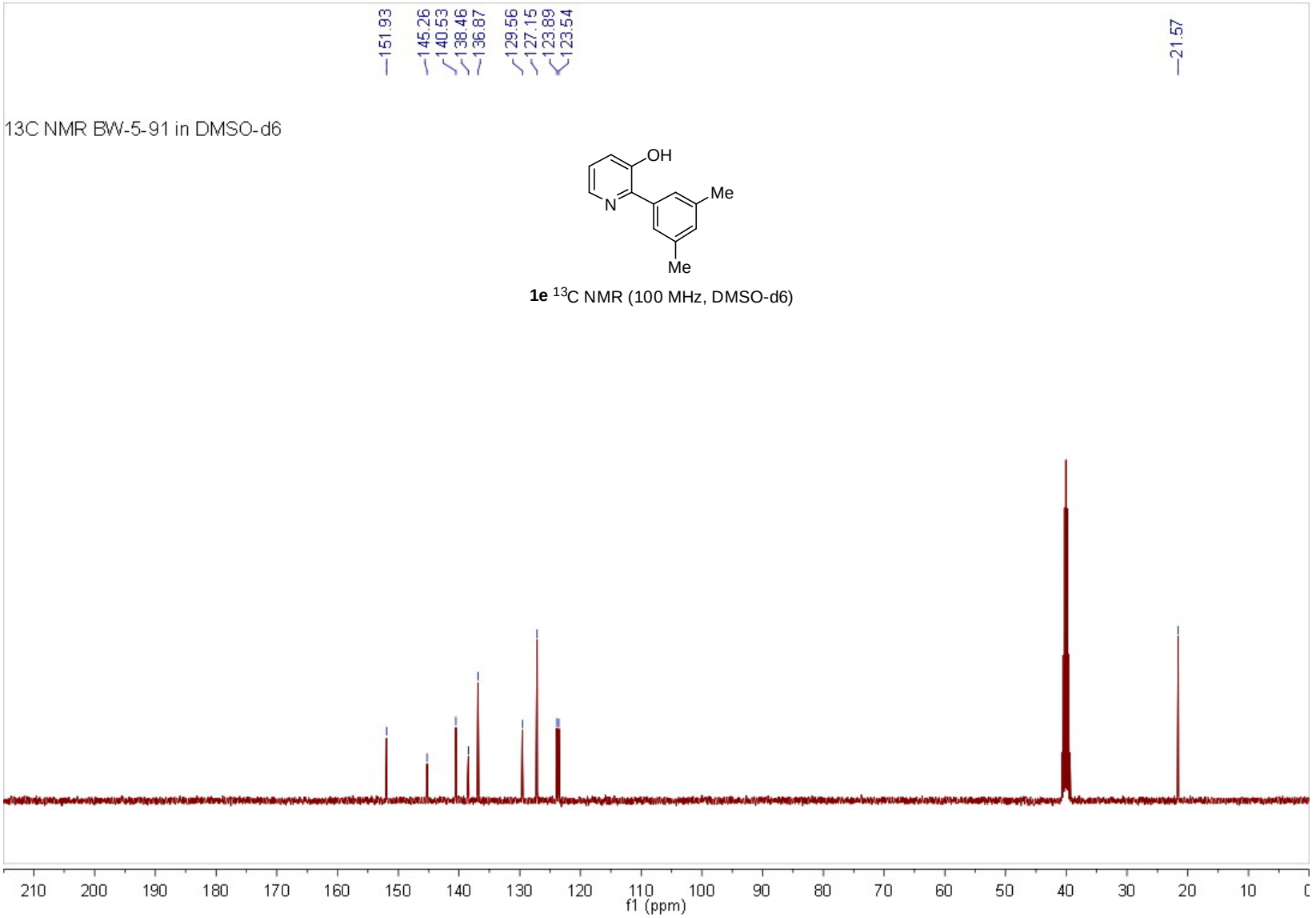


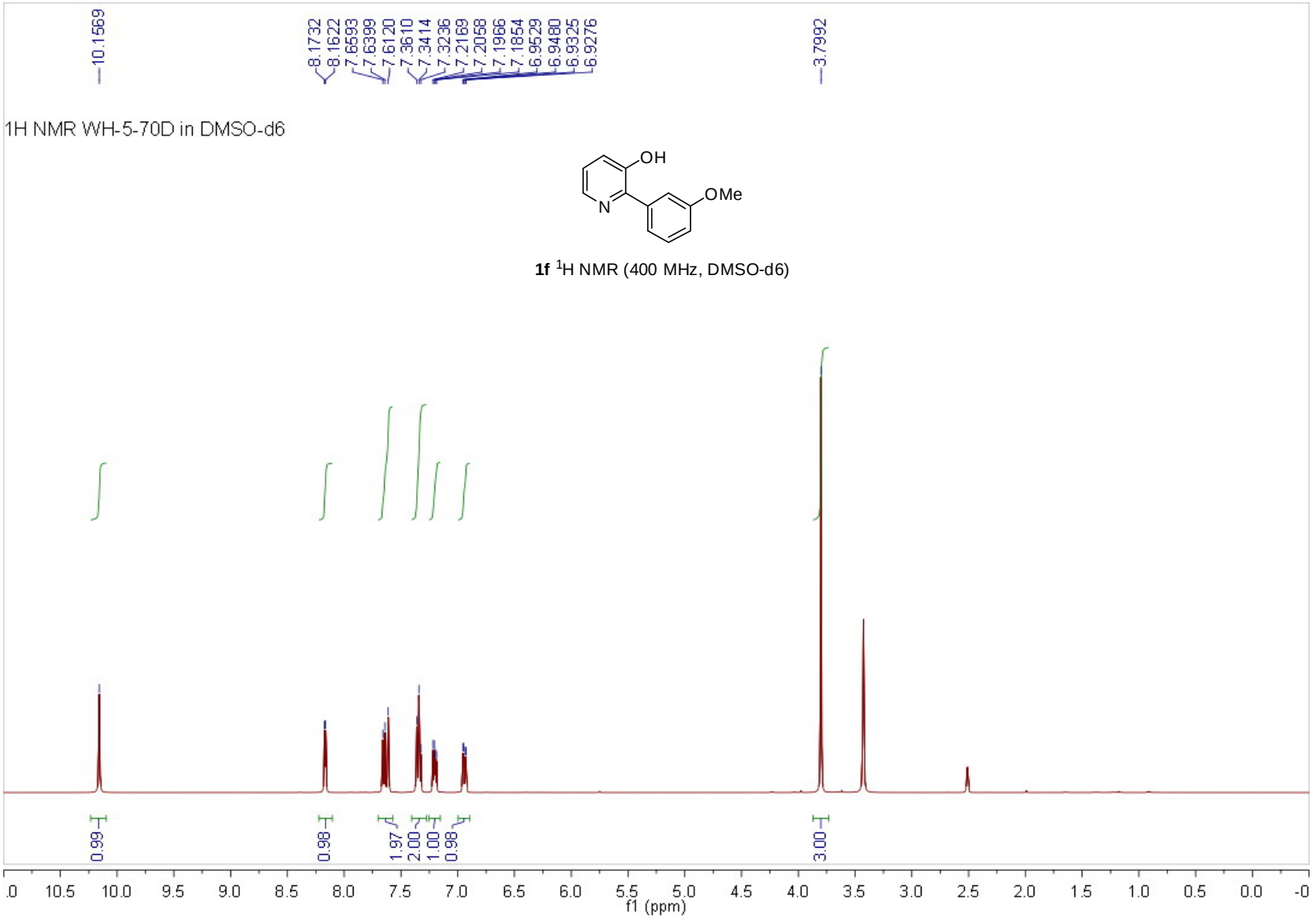
1d ^{13}C NMR (100 MHz, DMSO-d6)



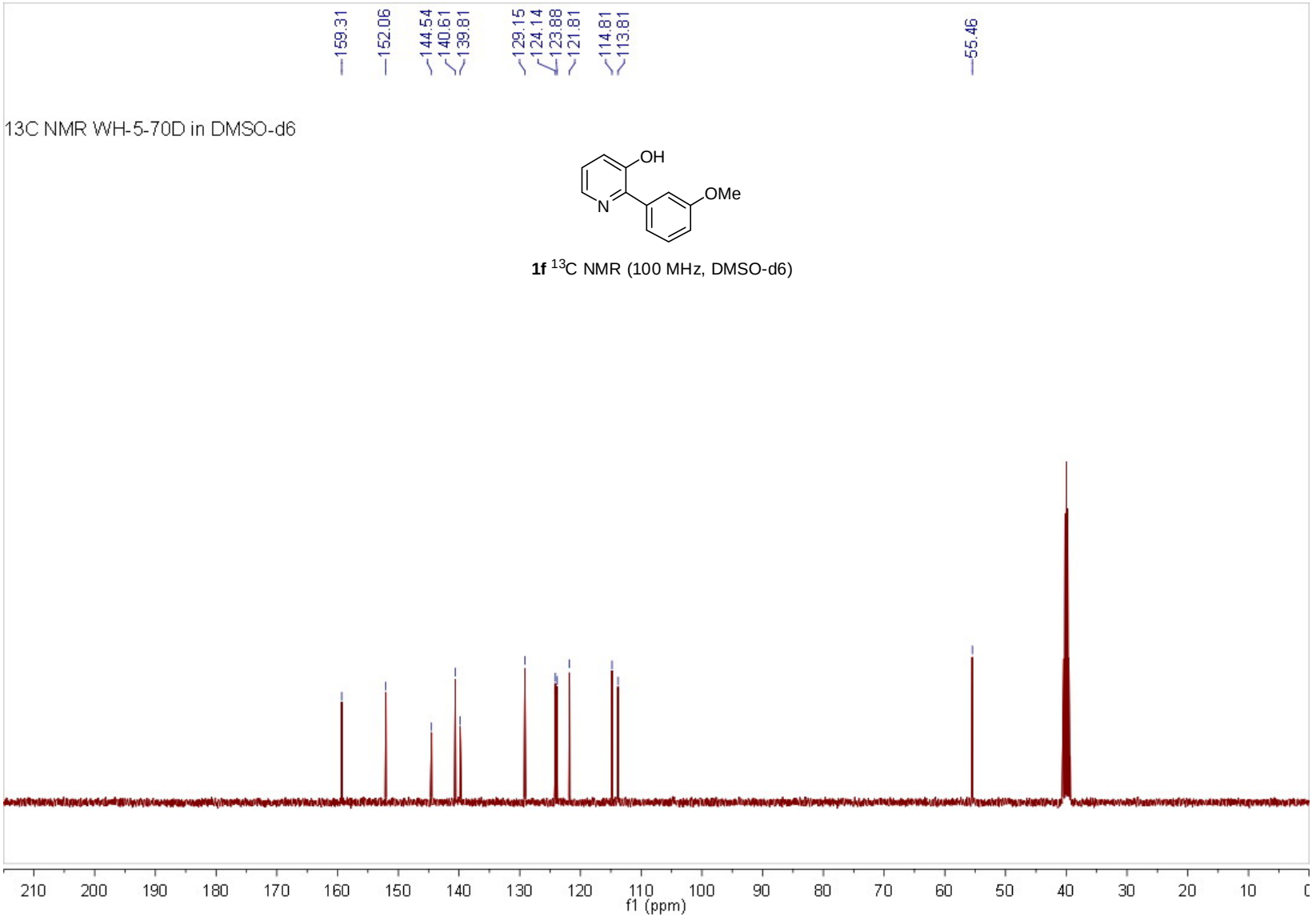
1e ^{1}H NMR (400 MHz, DMSO-d6)



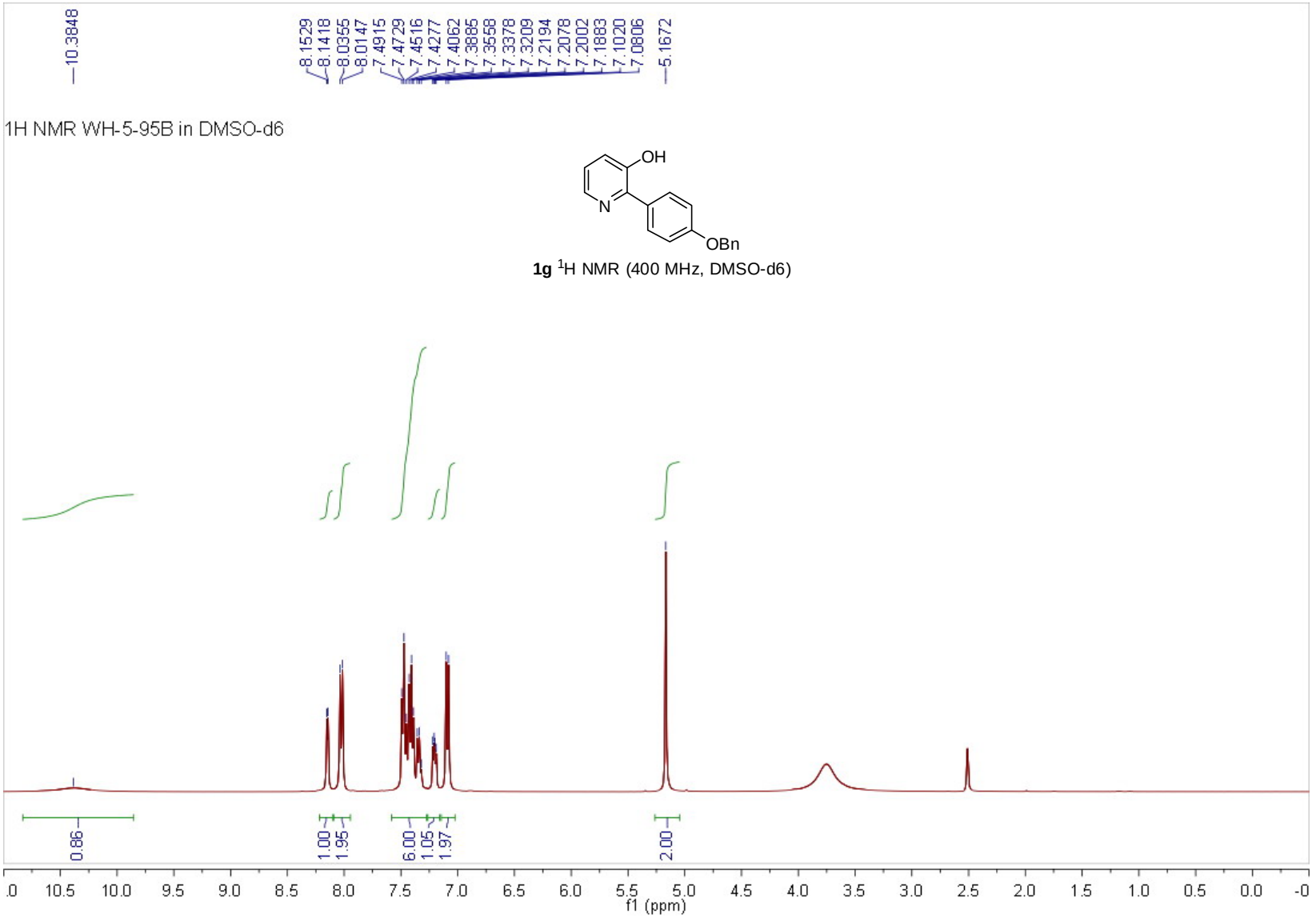
1e ^{13}C NMR (100 MHz, DMSO-d6)



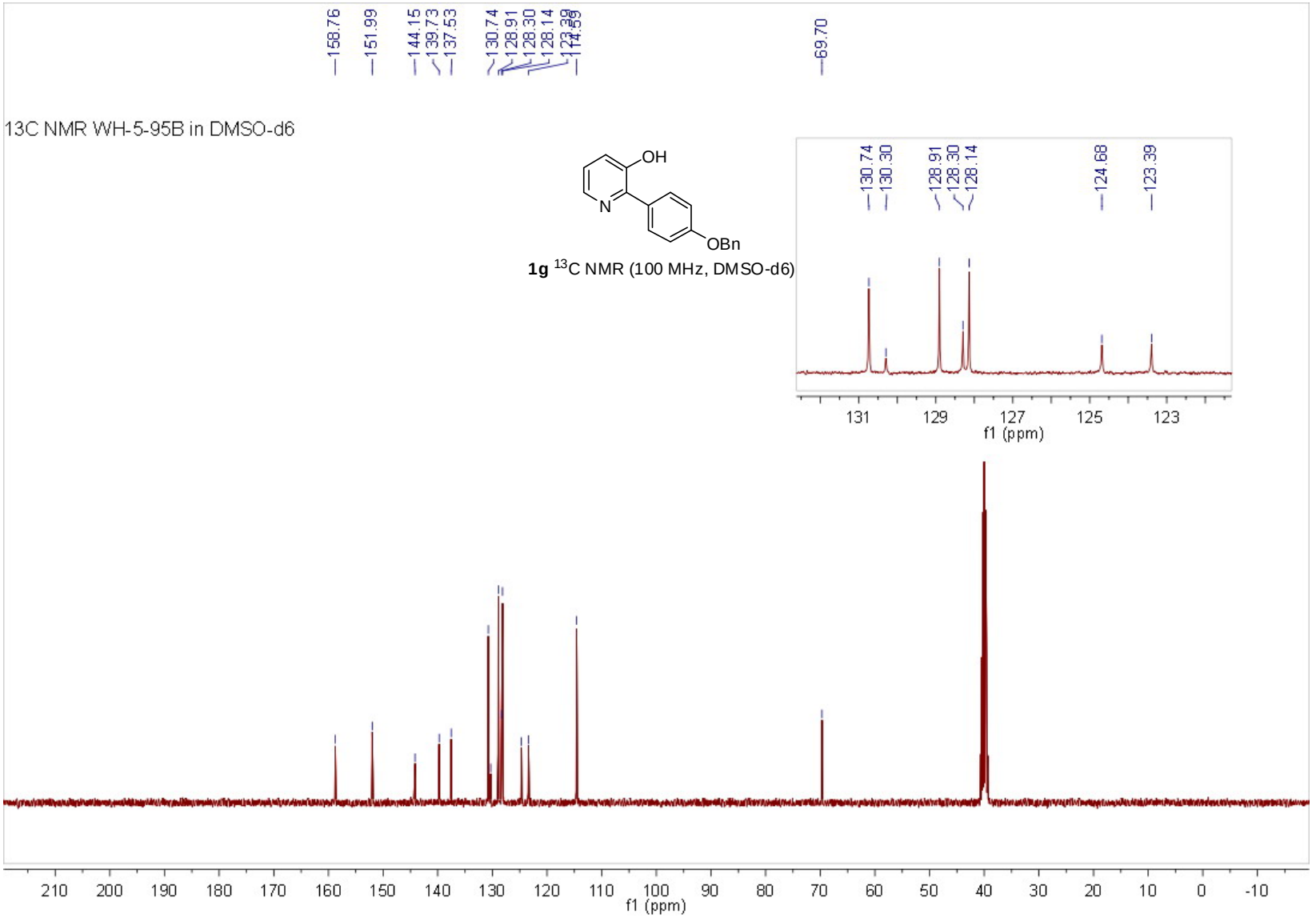
1f ^{1}H NMR (400 MHz, DMSO-d6)

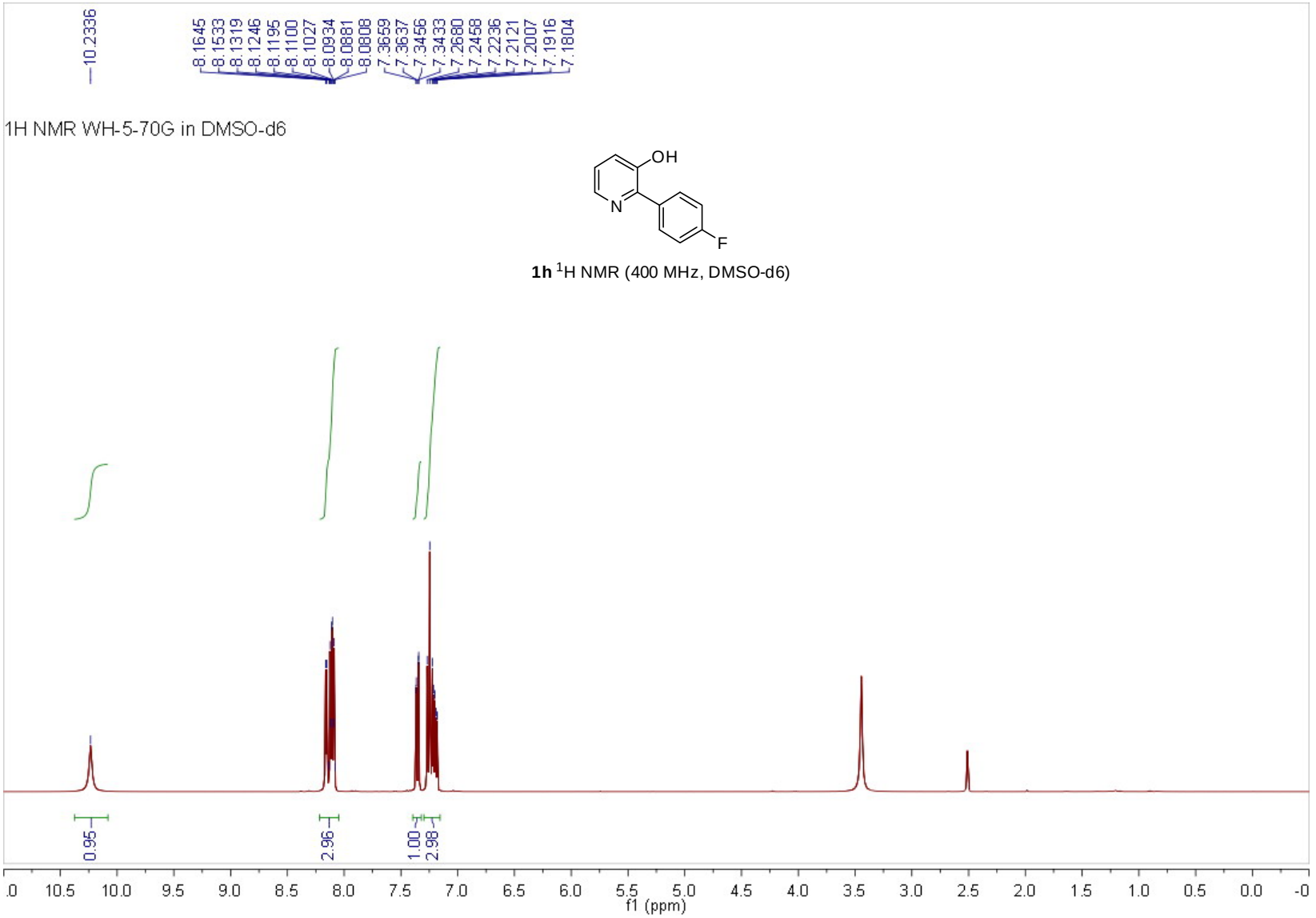


1f ^{13}C NMR (100 MHz, DMSO-d6)

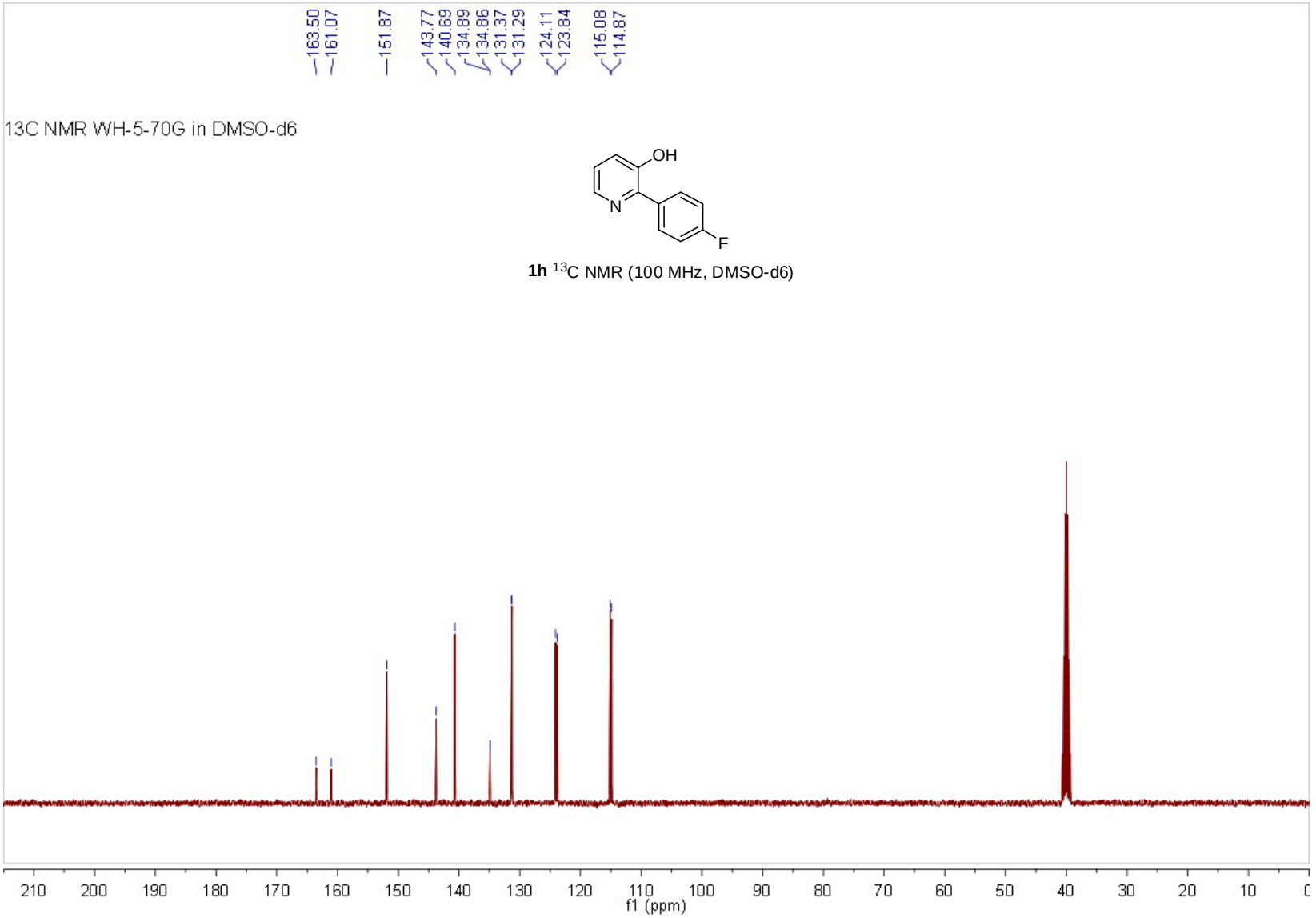


1g ^{1}H NMR (400 MHz, DMSO-d6)

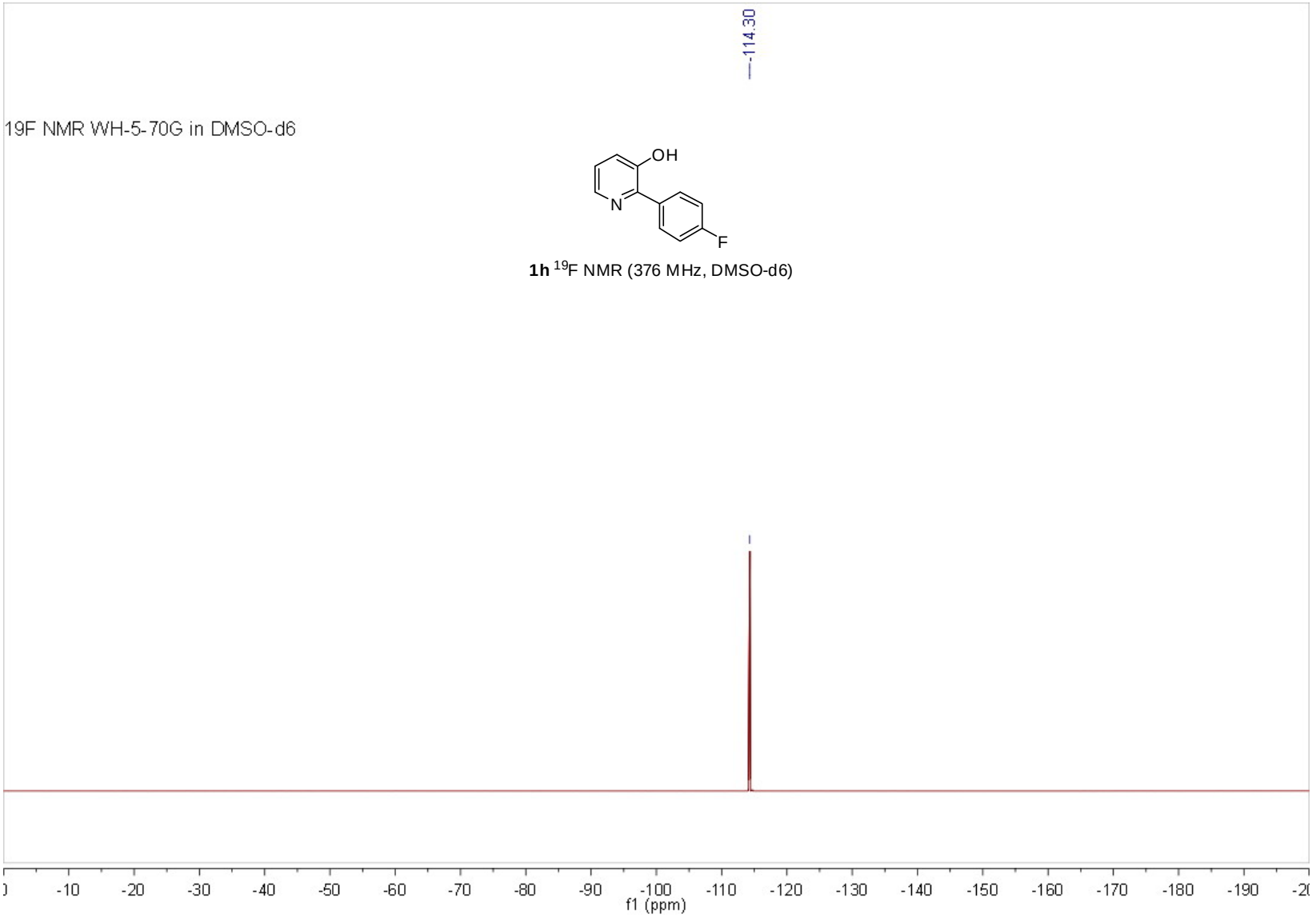

158.76
151.99
144.15
139.73
137.53
130.74
128.91
128.30
128.14
69.70
13C NMR WH-5-95B in DMSO-d6
OH
N
OBn
1g 13C NMR (100 MHz, DMSO-d6)
130.74
130.30
128.91
128.30
128.14
124.68
123.39
131
129
127
125
123
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



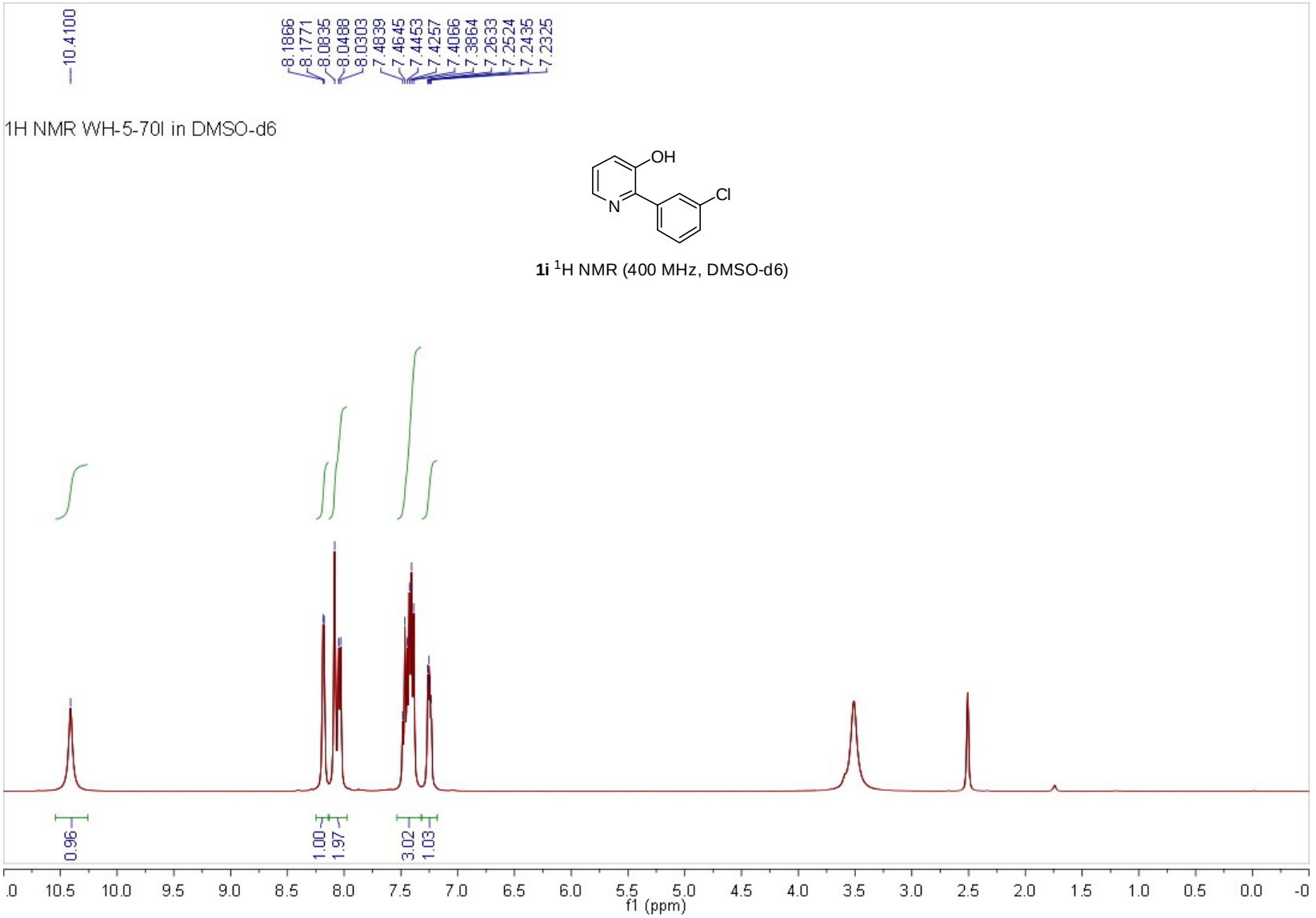
1h ^{1}H NMR (400 MHz, DMSO-d6)



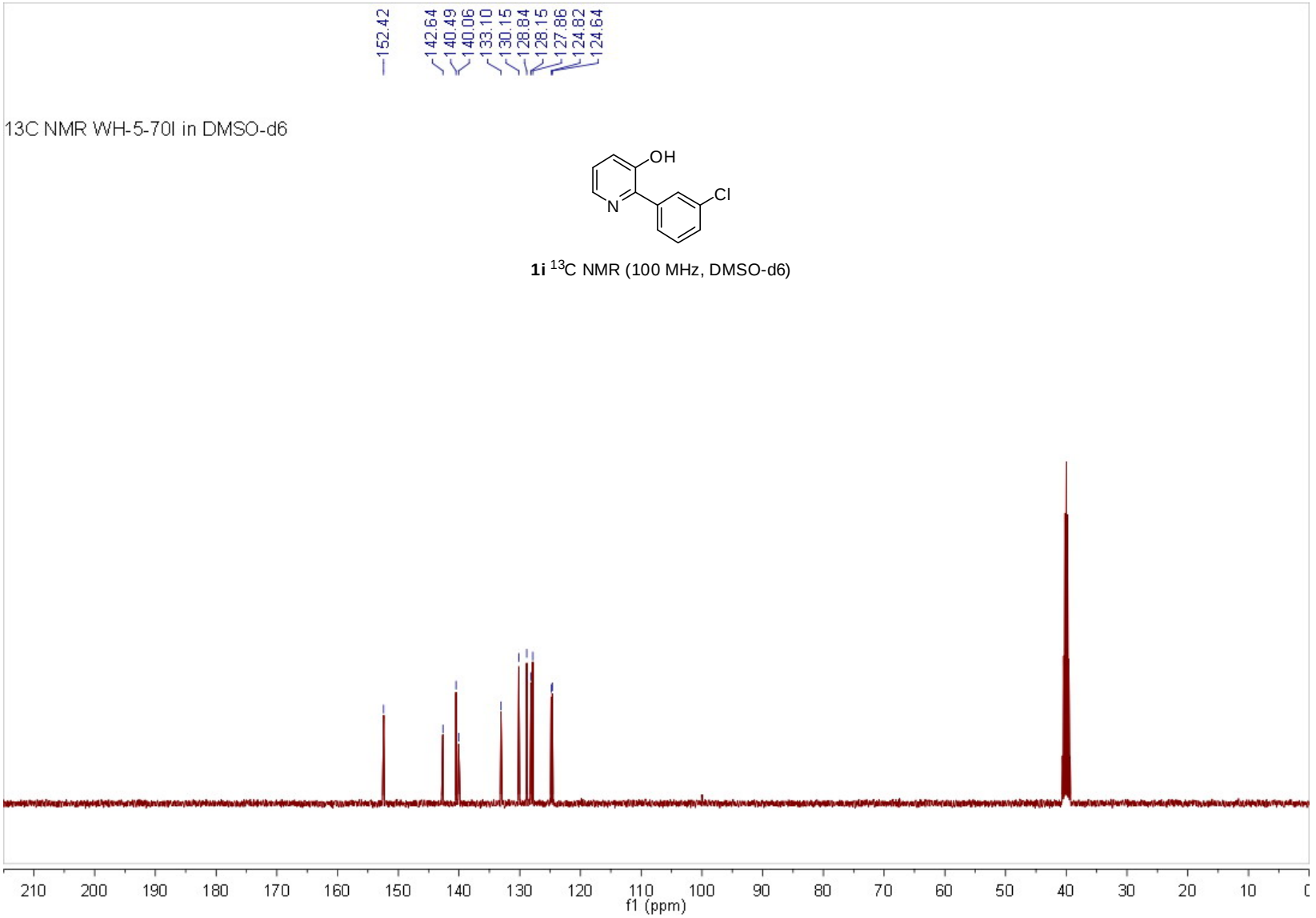
1h ^{13}C NMR (100 MHz, DMSO-d6)



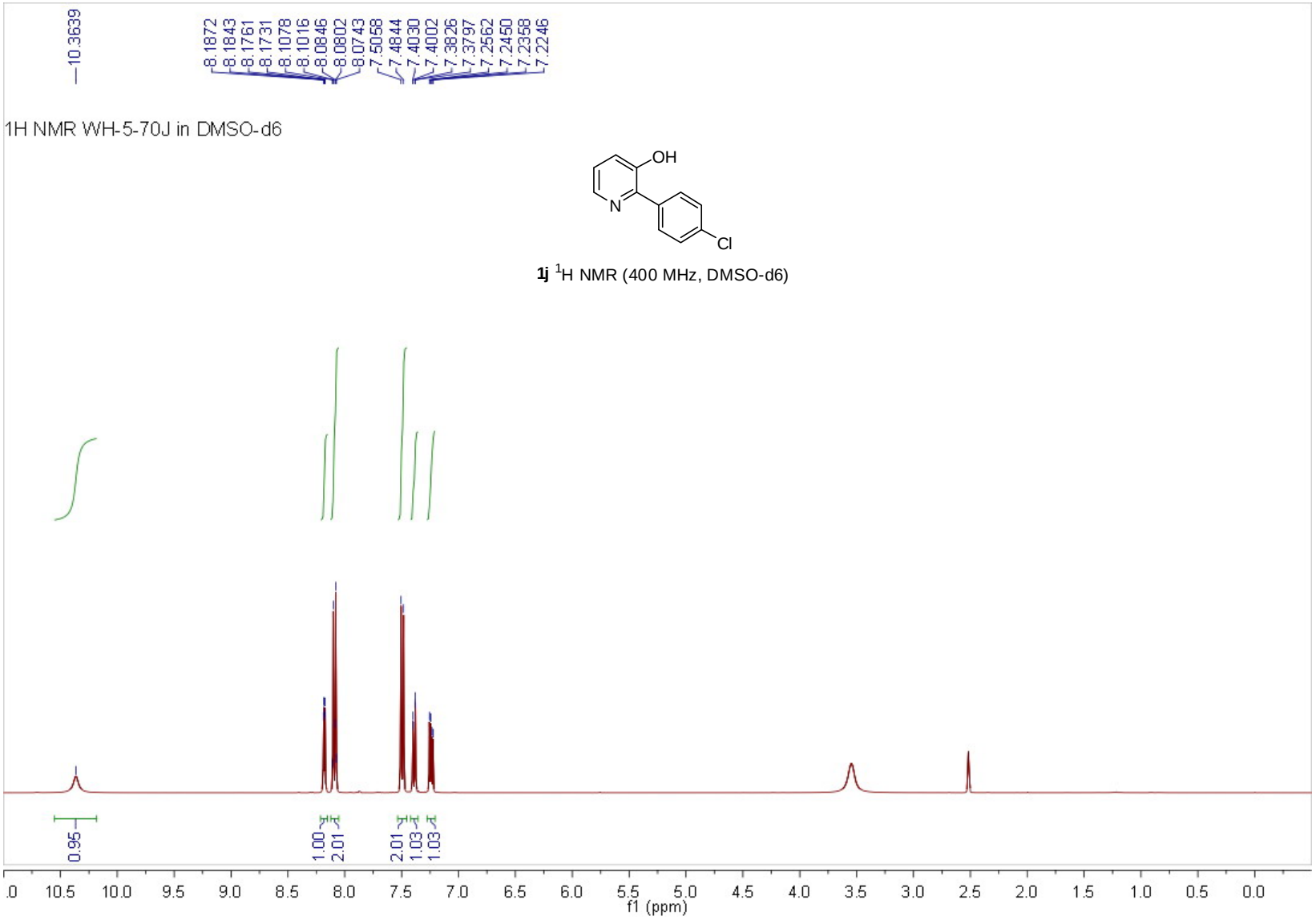
1h ^{19}F NMR (376 MHz, DMSO-d6)



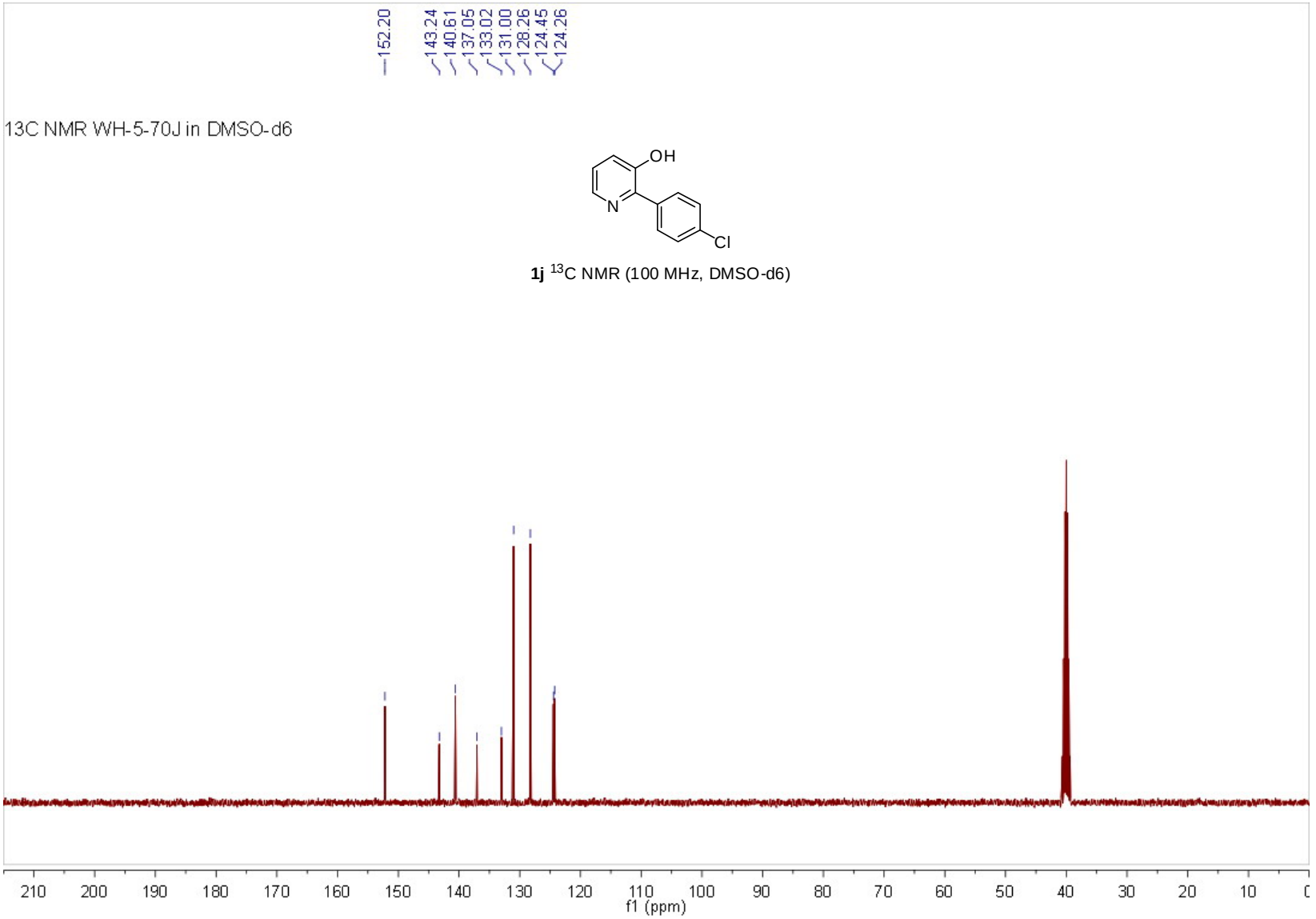
1i ^{1}H NMR (400 MHz, DMSO-d6)



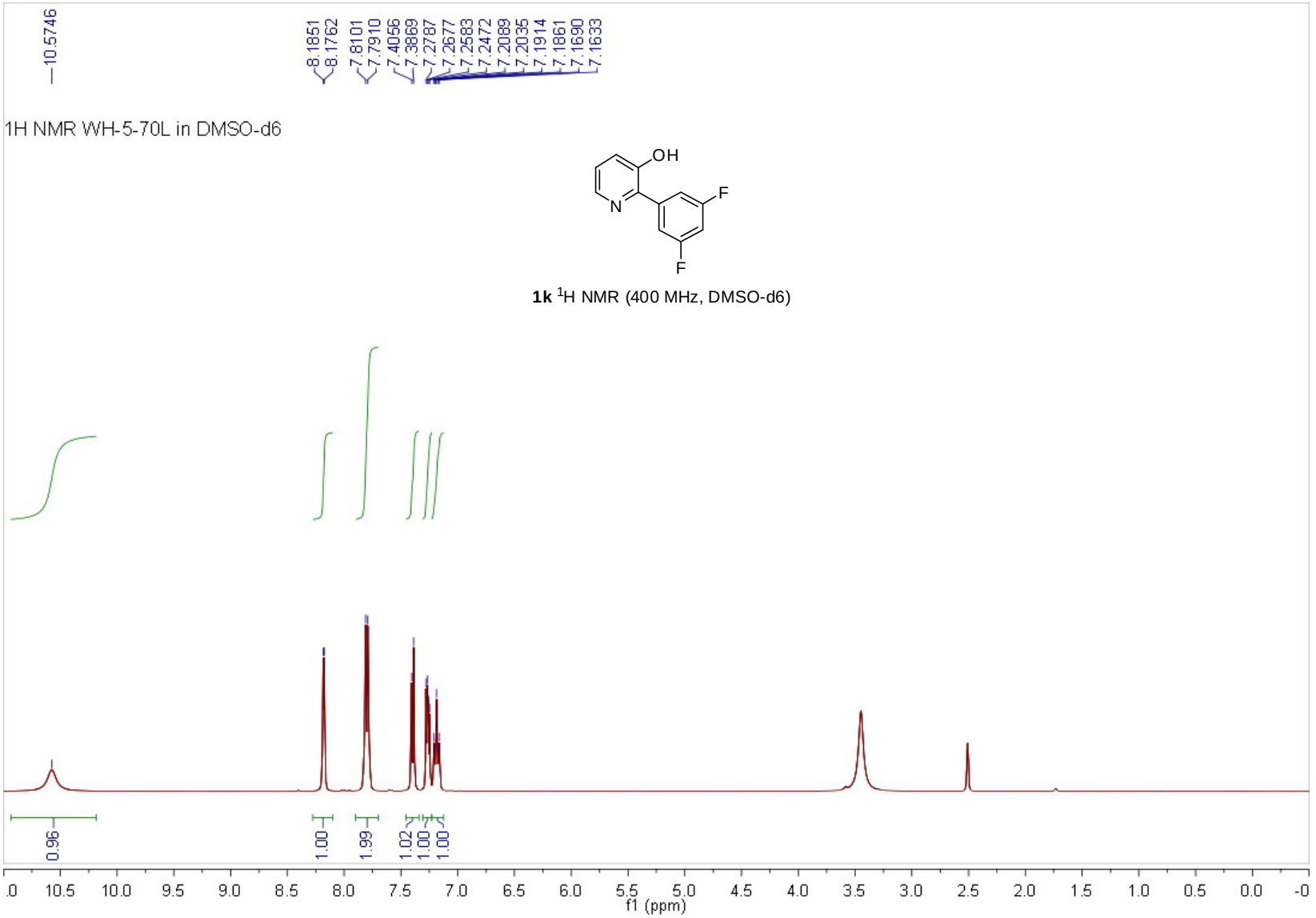
1i ^{13}C NMR (100 MHz, DMSO-d6)



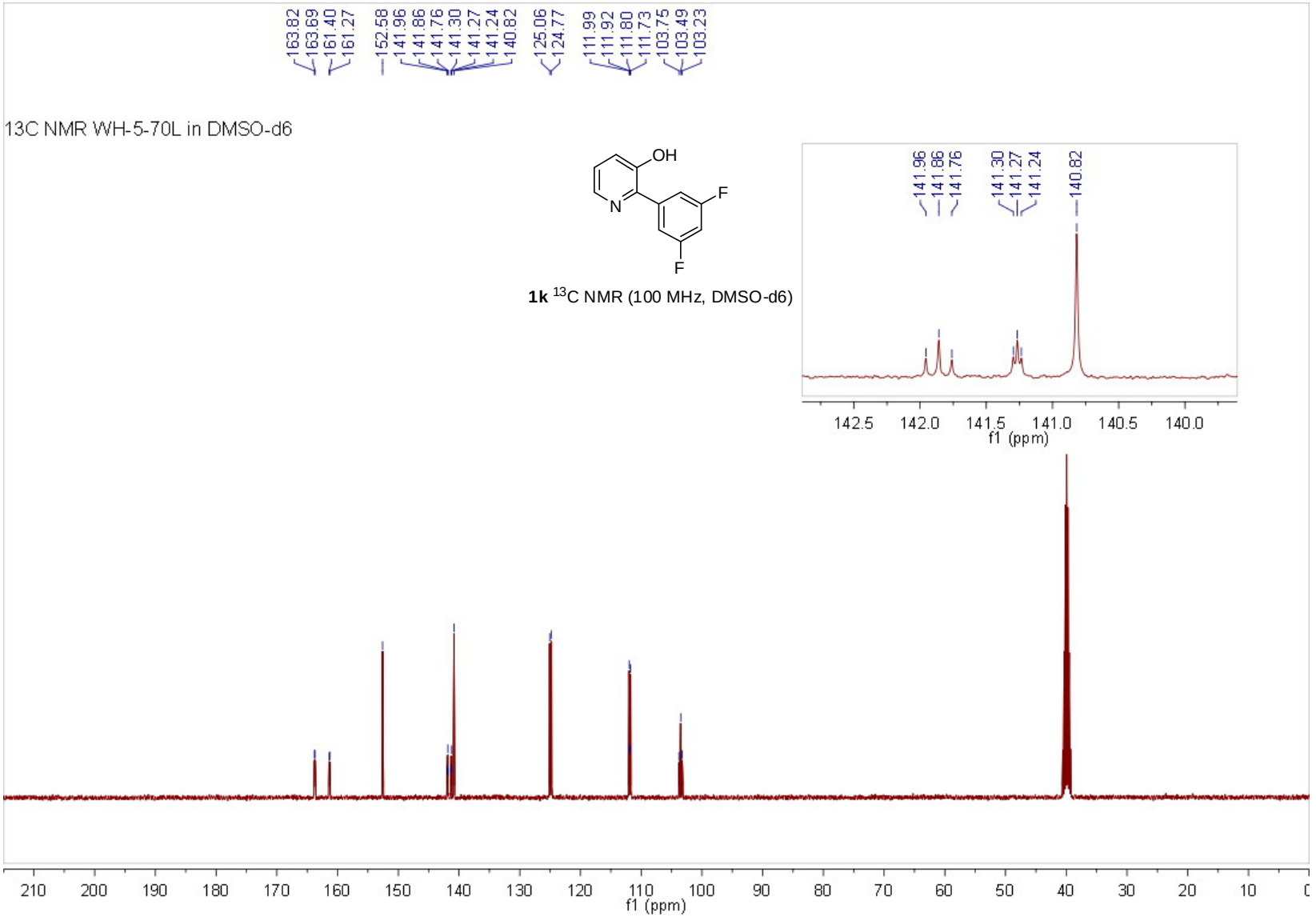
1j ^{1}H NMR (400 MHz, DMSO-d6)



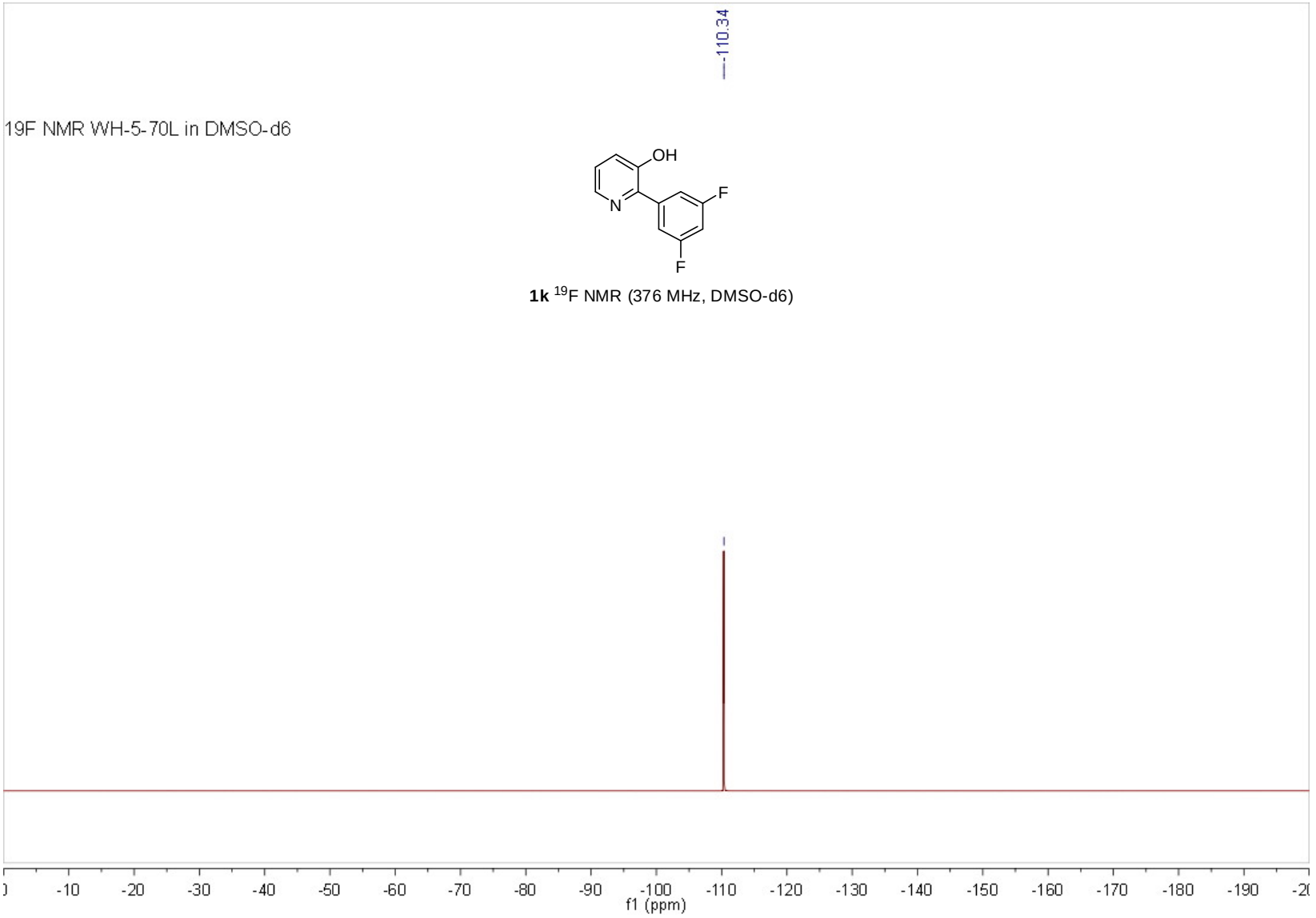
1j ^{13}C NMR (100 MHz, DMSO-d6)



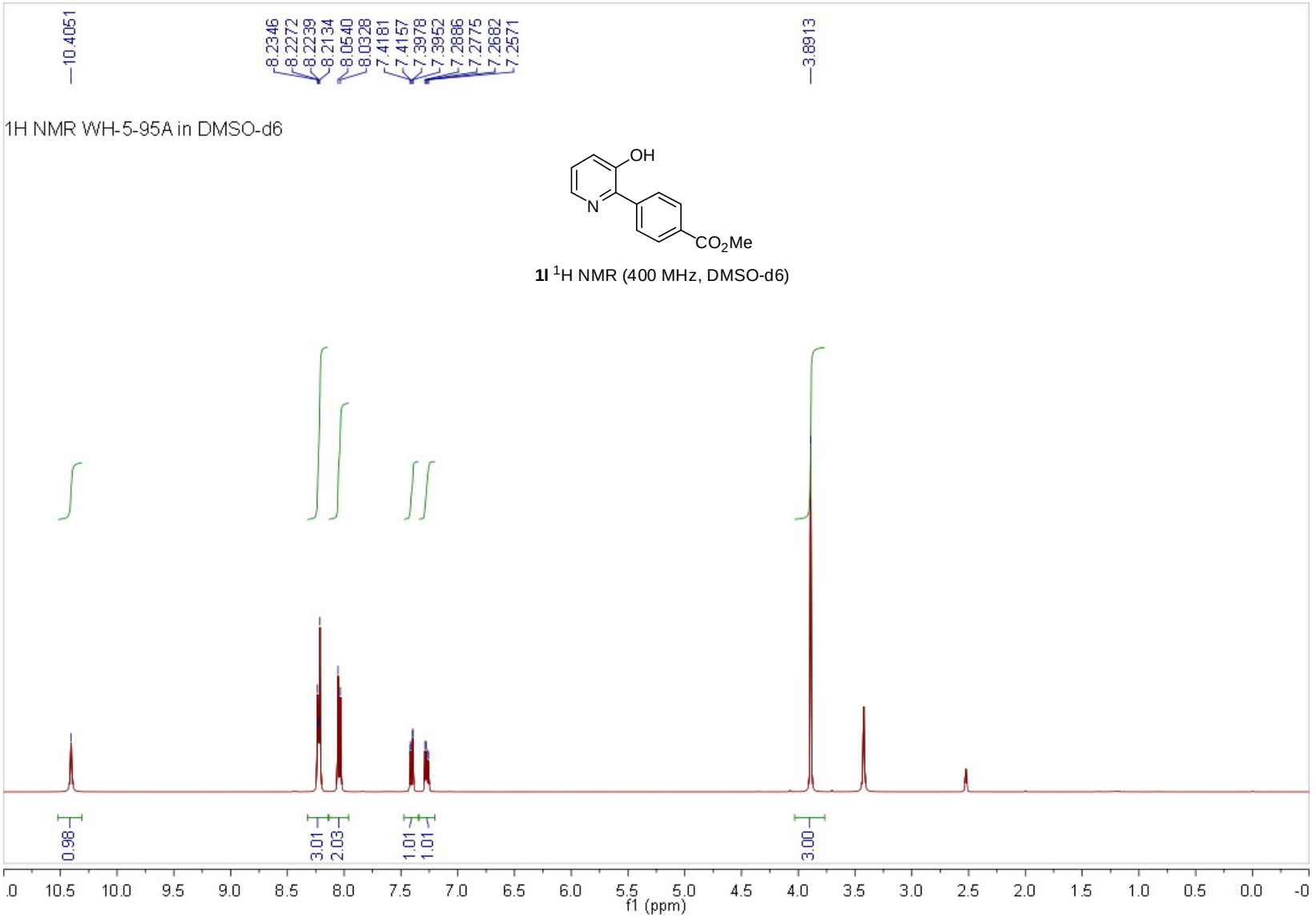
1k ^{1}H NMR (400 MHz, DMSO-d6)



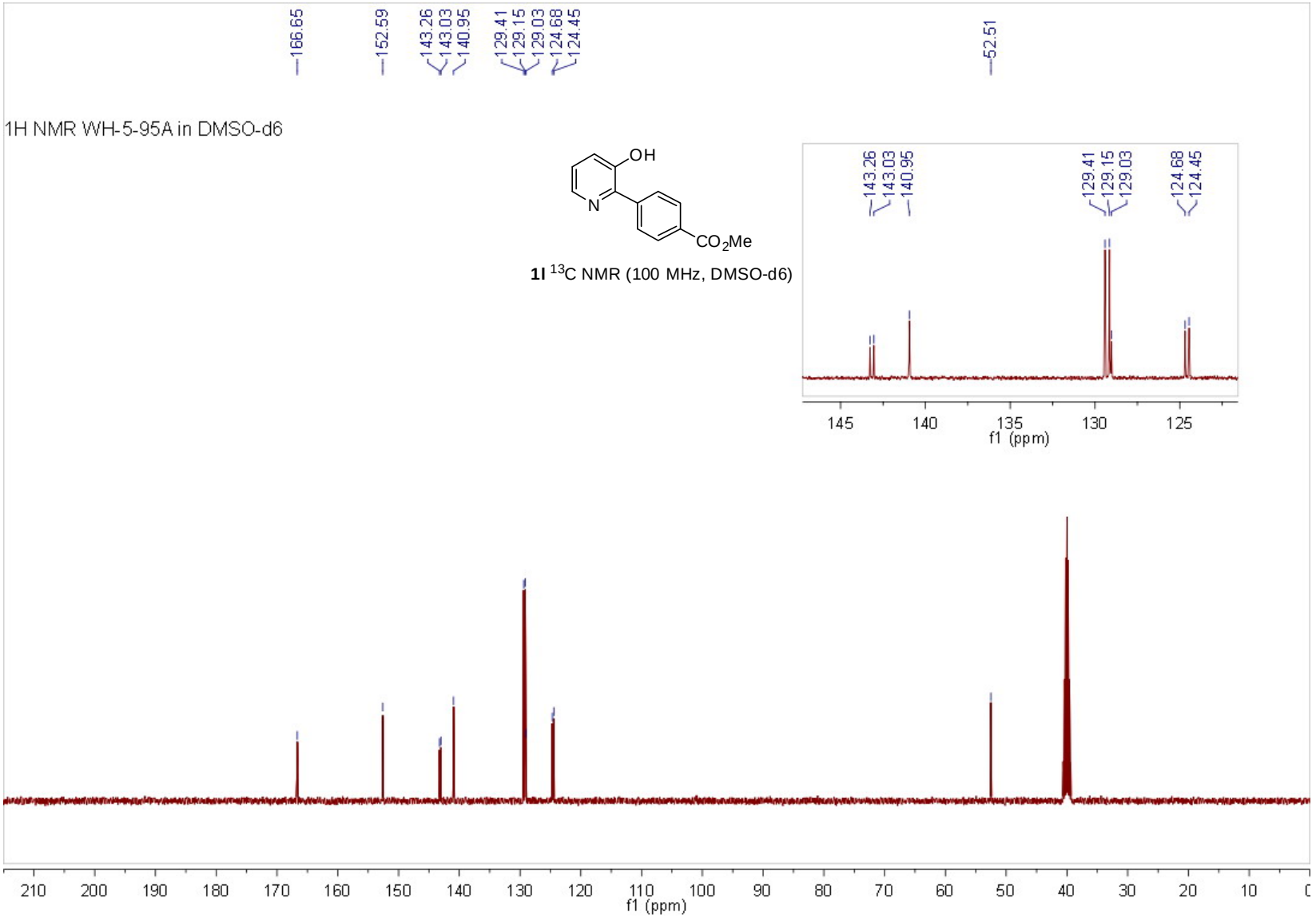
1k ^{13}C NMR (100 MHz, DMSO-d6)



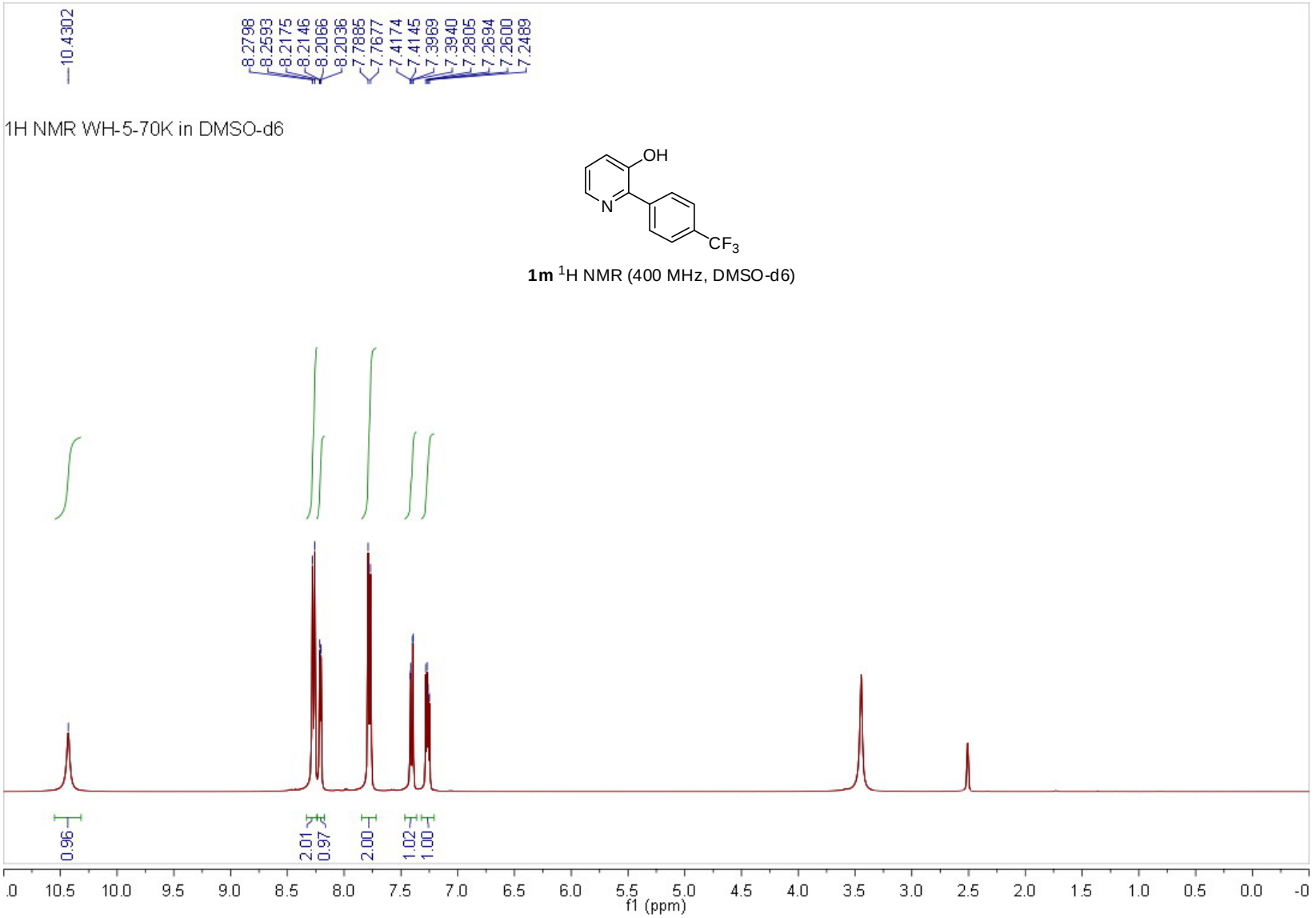
1k ^{19}F NMR (376 MHz, DMSO-d6)



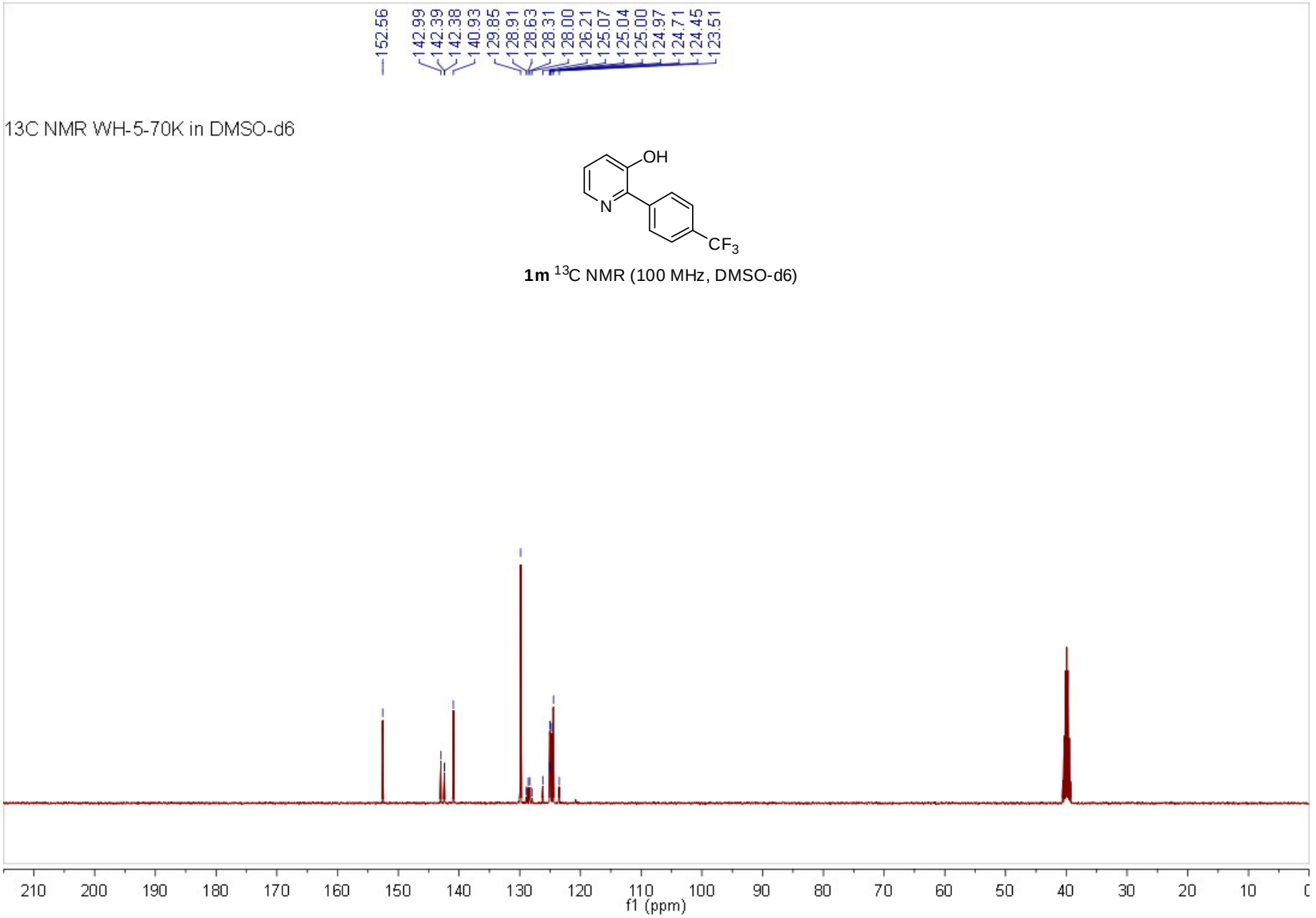
1l ^{1}H NMR (400 MHz, DMSO-d6)



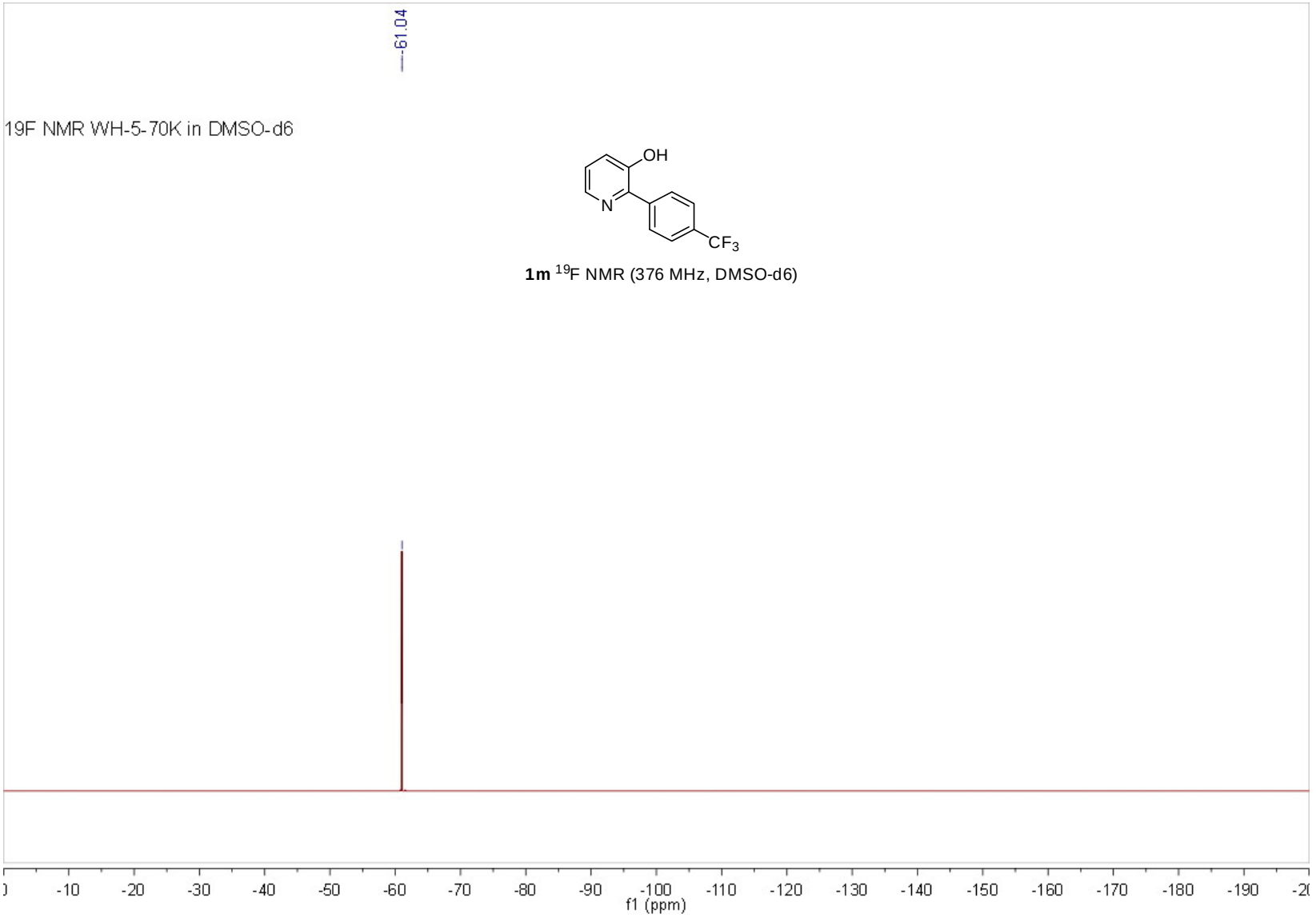
1l ^{13}C NMR (100 MHz, DMSO-d6)



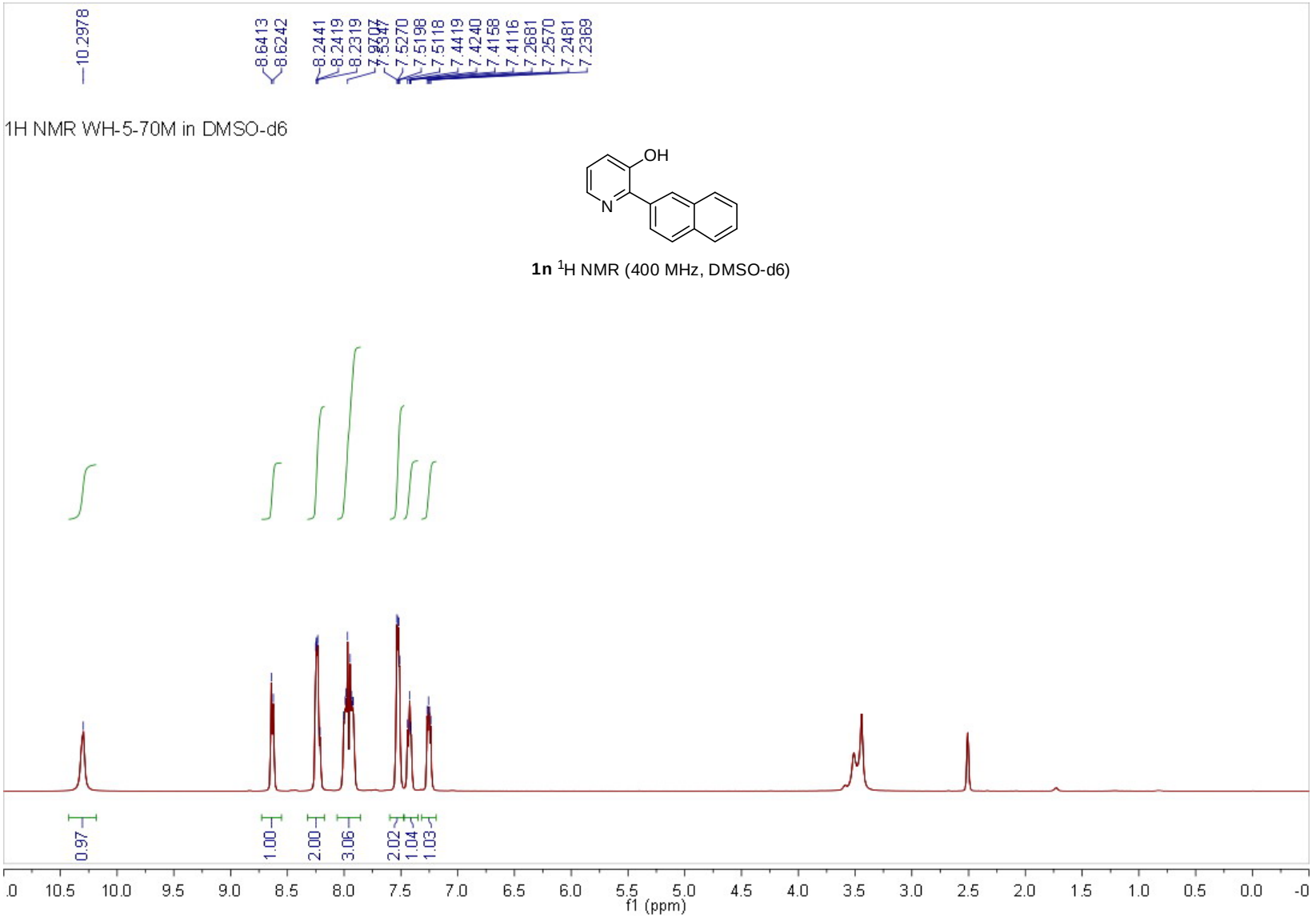
1m ^{1}H NMR (400 MHz, DMSO-d6)



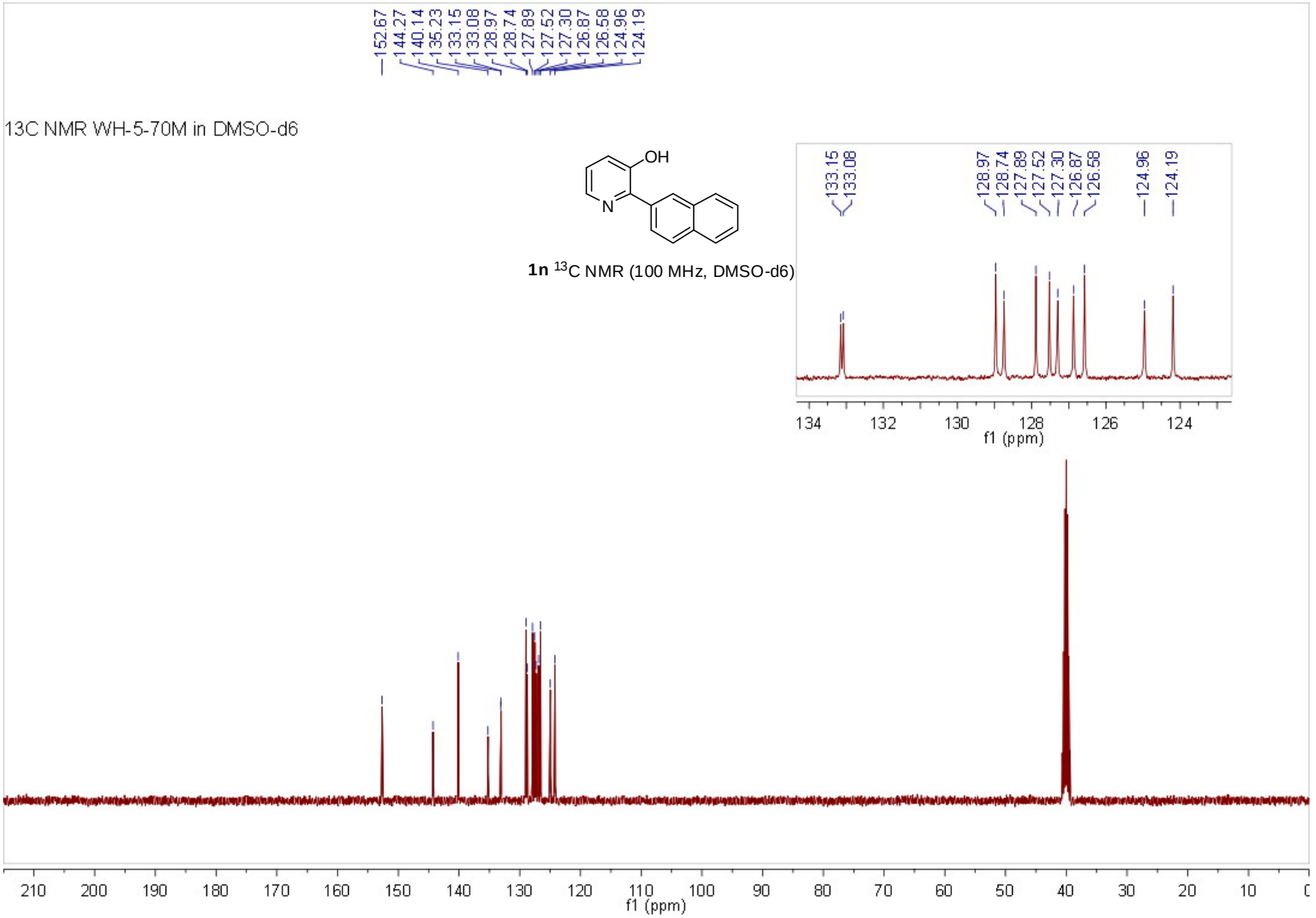
1m ^{13}C NMR (100 MHz, DMSO-d6)

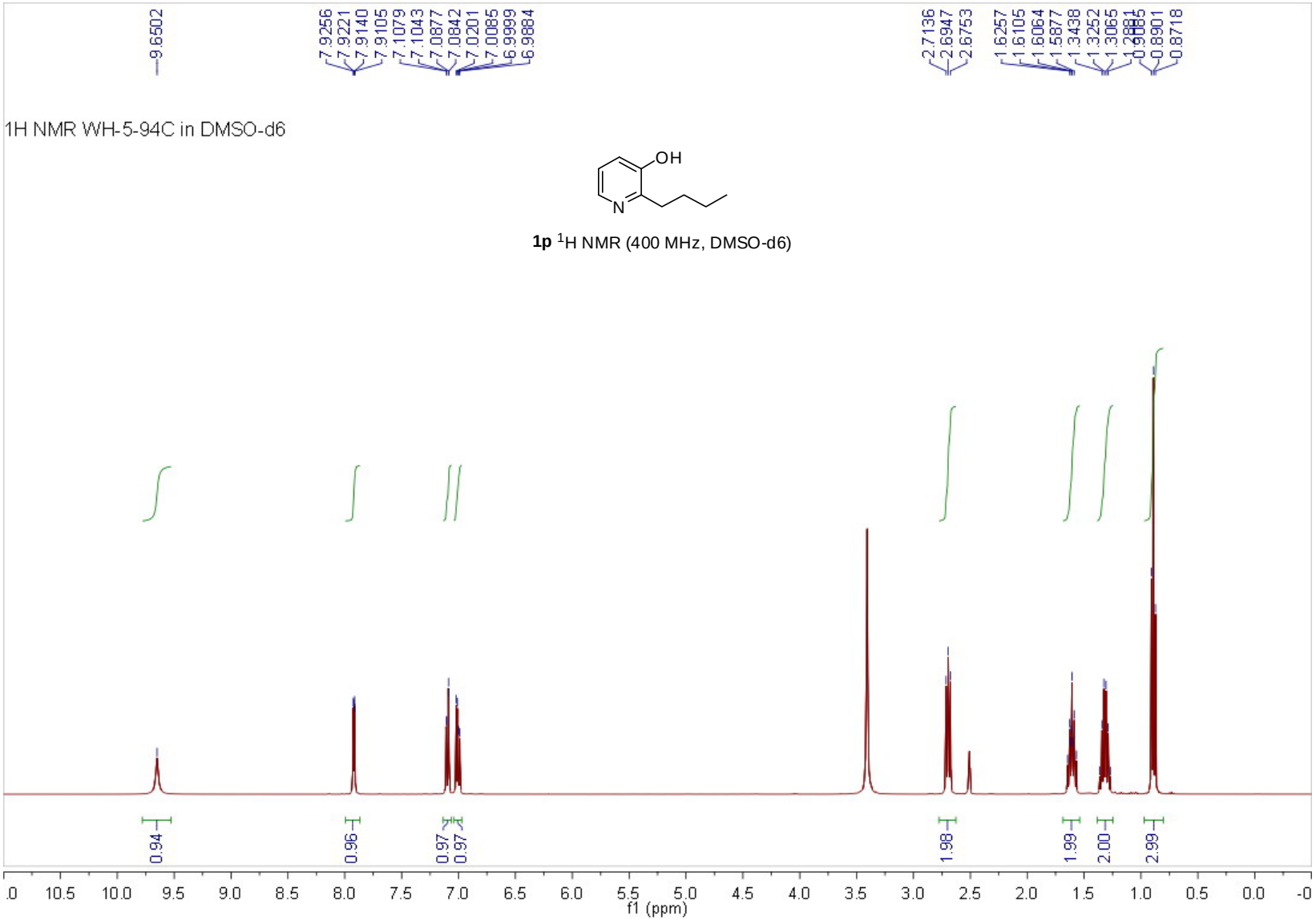


1m ^{19}F NMR (376 MHz, DMSO-d6)

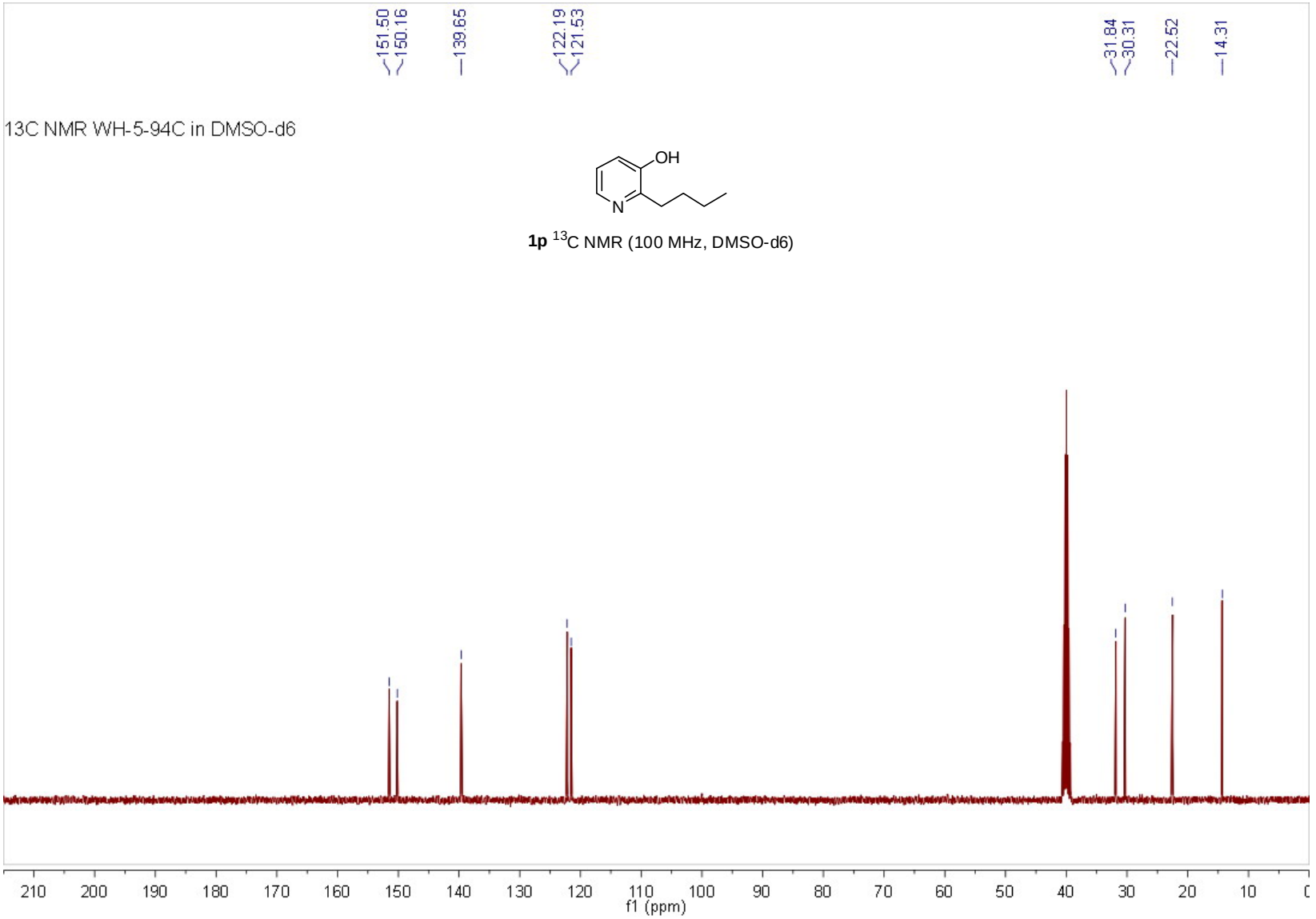


1n ^{1}H NMR (400 MHz, DMSO-d6)

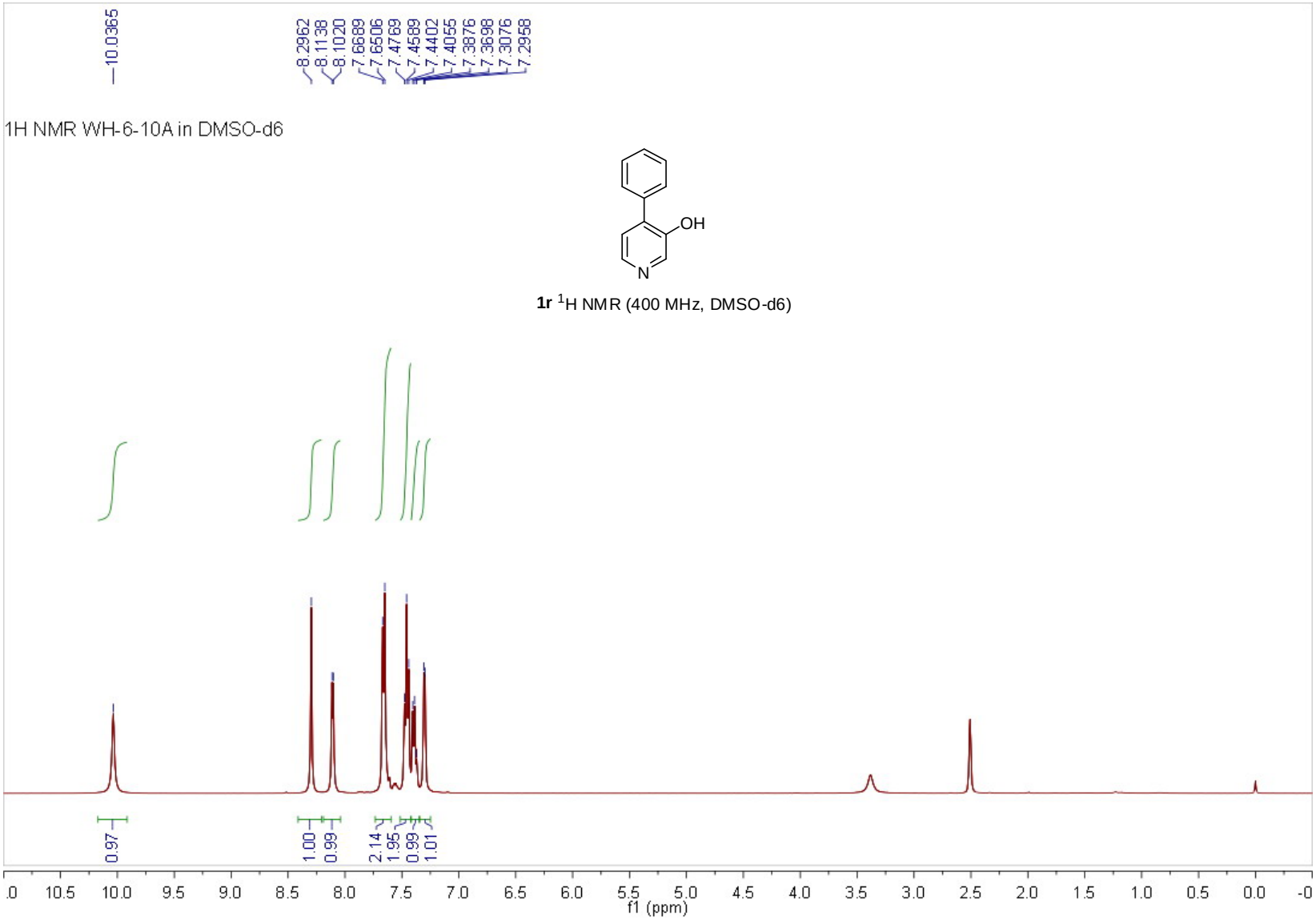

152.67
144.27
140.14
135.23
133.15
133.08
128.97
128.74
127.89
127.52
127.30
126.87
126.58
124.96
124.19
13C NMR WH-5-70M in DMSO-d6
OH
N
1n 13C NMR (100 MHz, DMSO-d6)
133.15
133.08
128.97
128.74
127.89
127.52
127.30
126.87
126.58
124.96
124.19
134
132
130
128
126
124
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



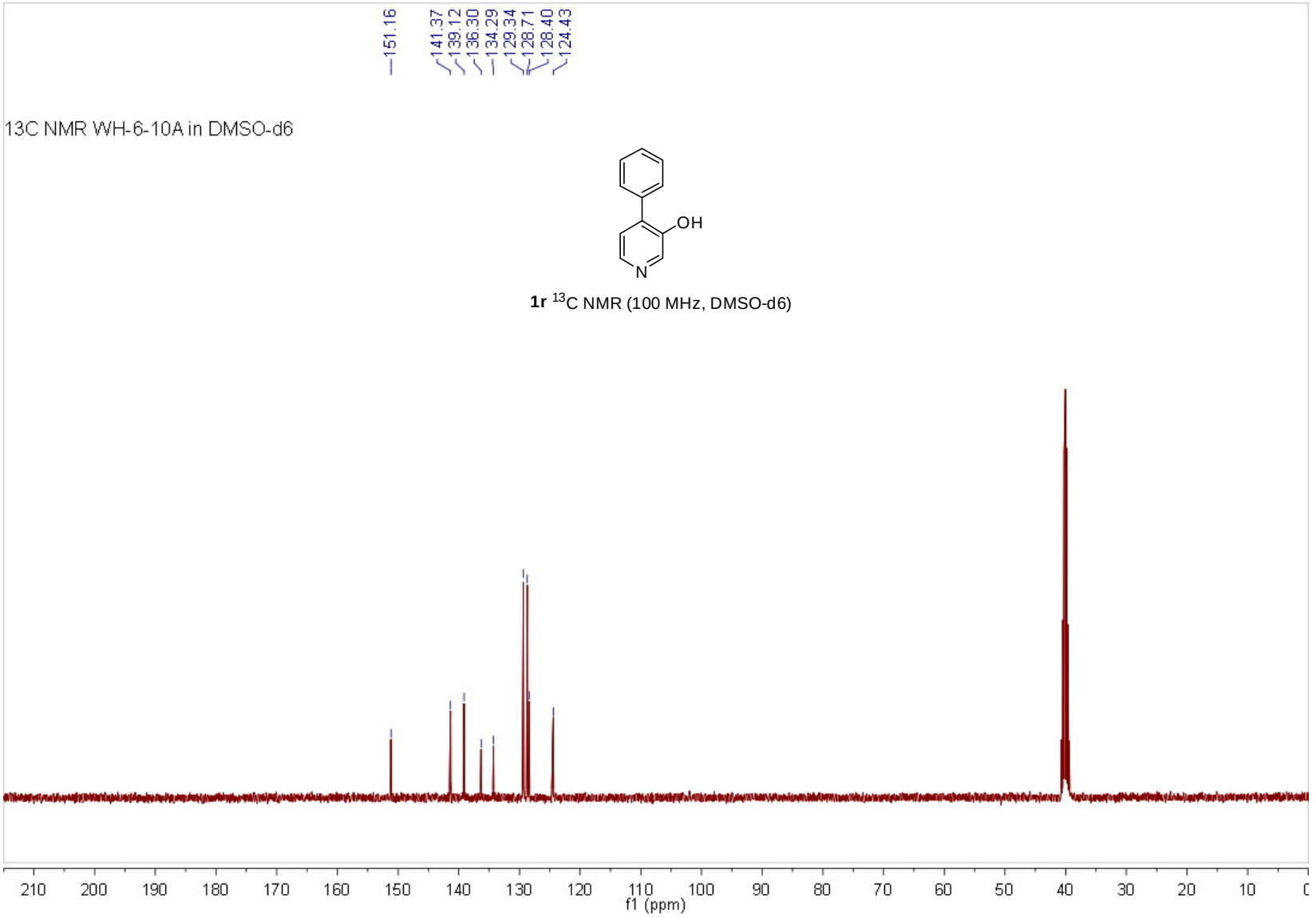
1p ^{1}H NMR (400 MHz, DMSO-d6)



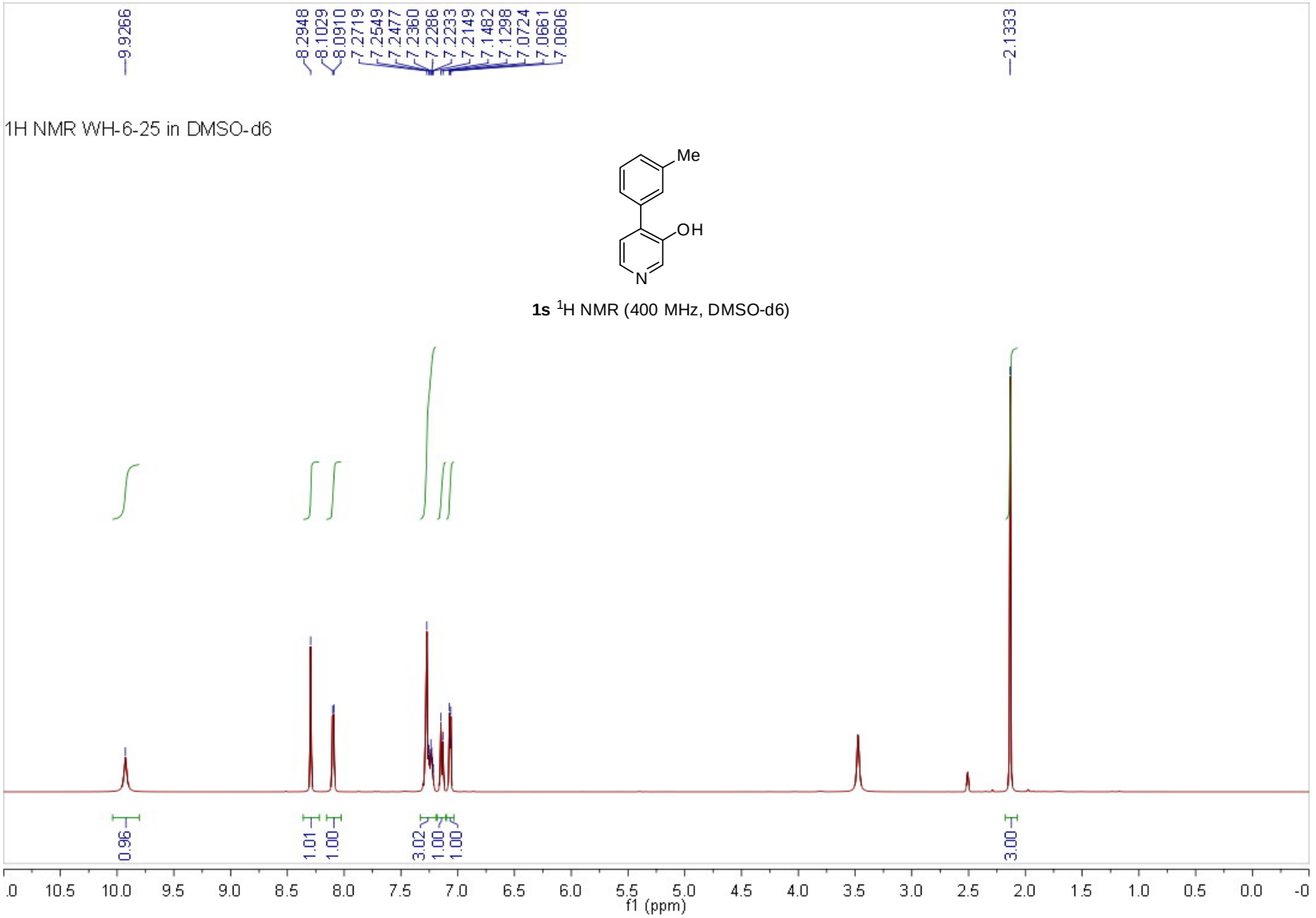
1p ^{13}C NMR (100 MHz, DMSO-d6)



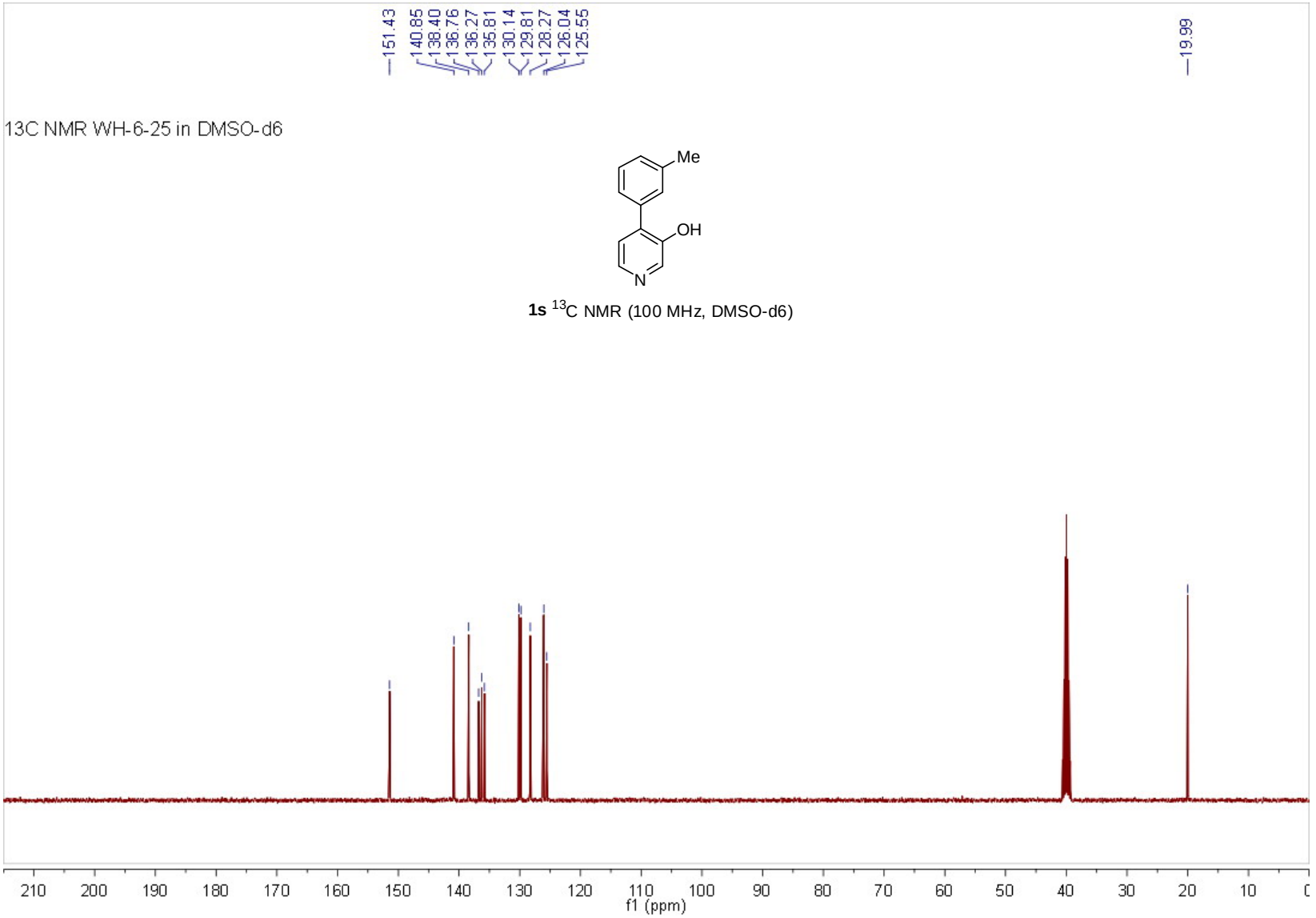
1r ^{1}H NMR (400 MHz, DMSO-d6)



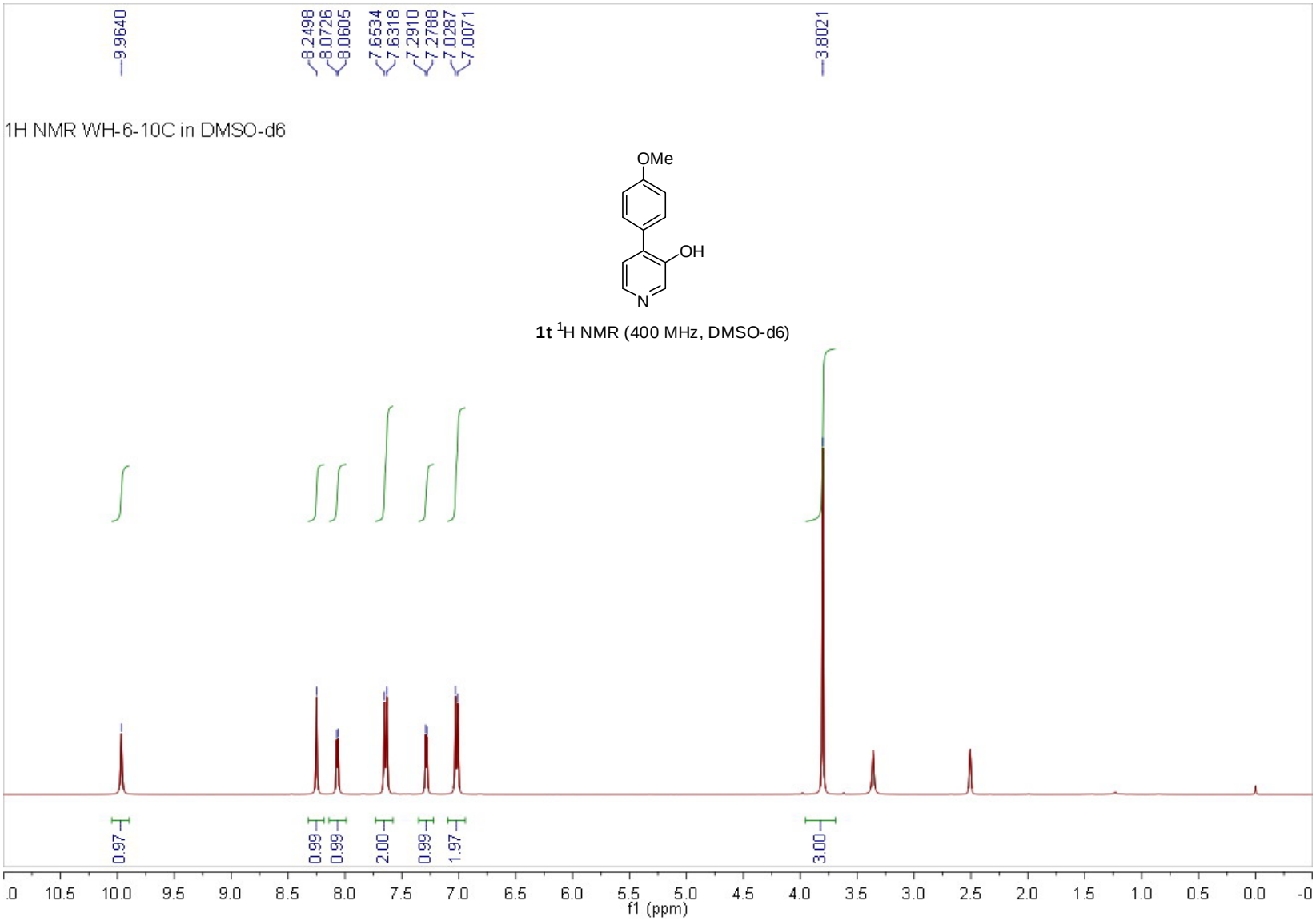
1r ^{13}C NMR (100 MHz, DMSO-d6)



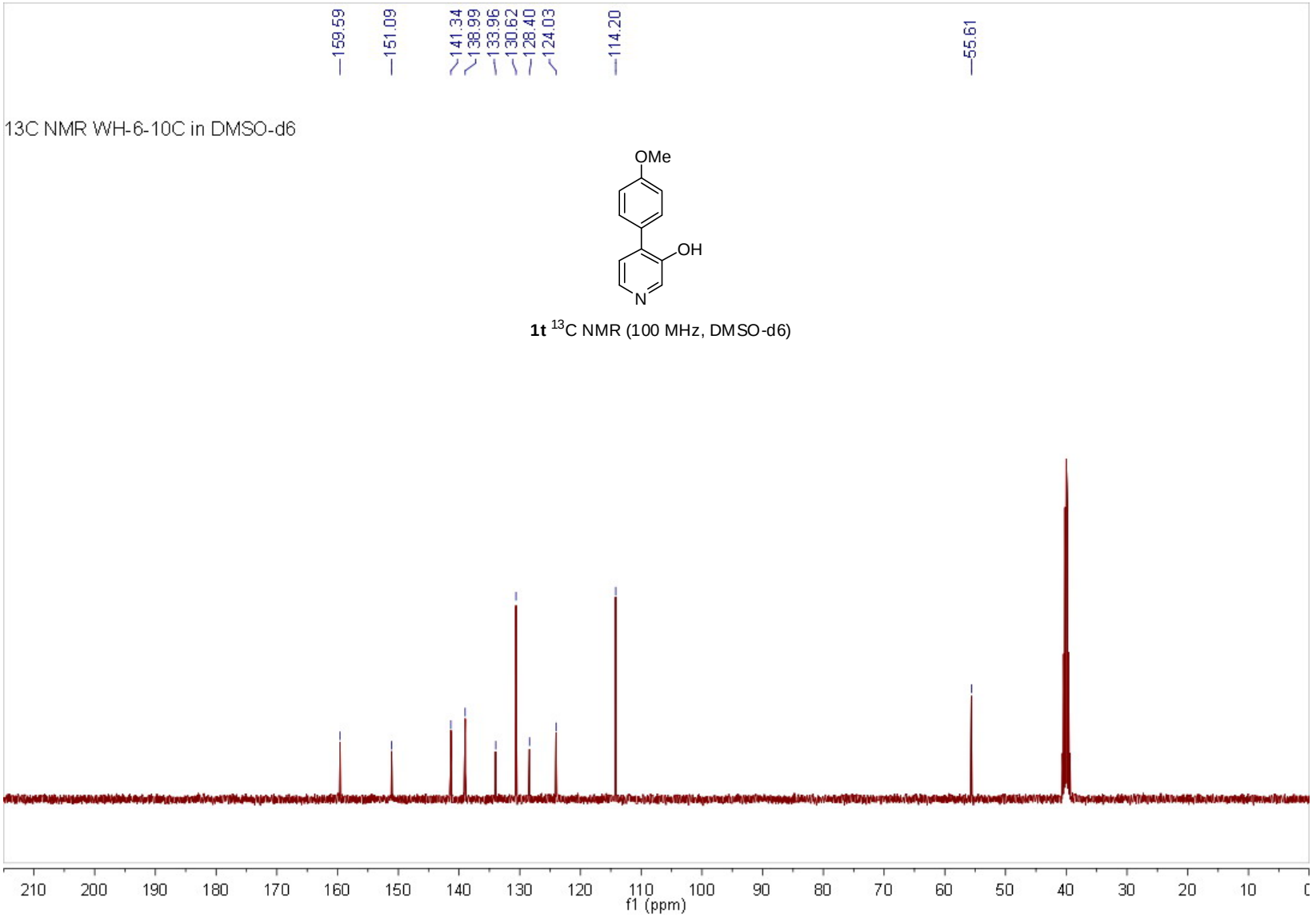
1s ^{1}H NMR (400 MHz, DMSO-d6)



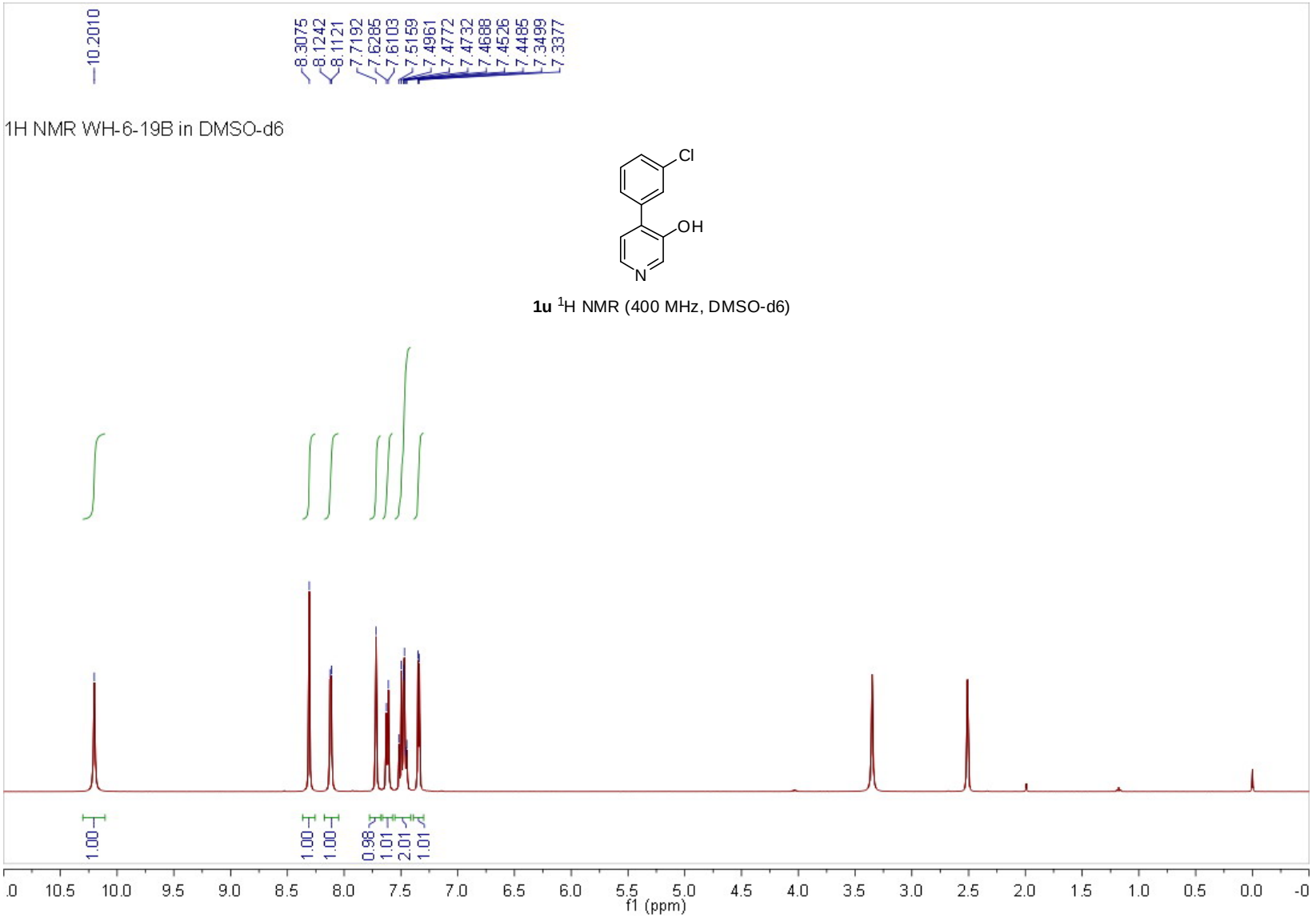
1s ^{13}C NMR (100 MHz, DMSO-d6)



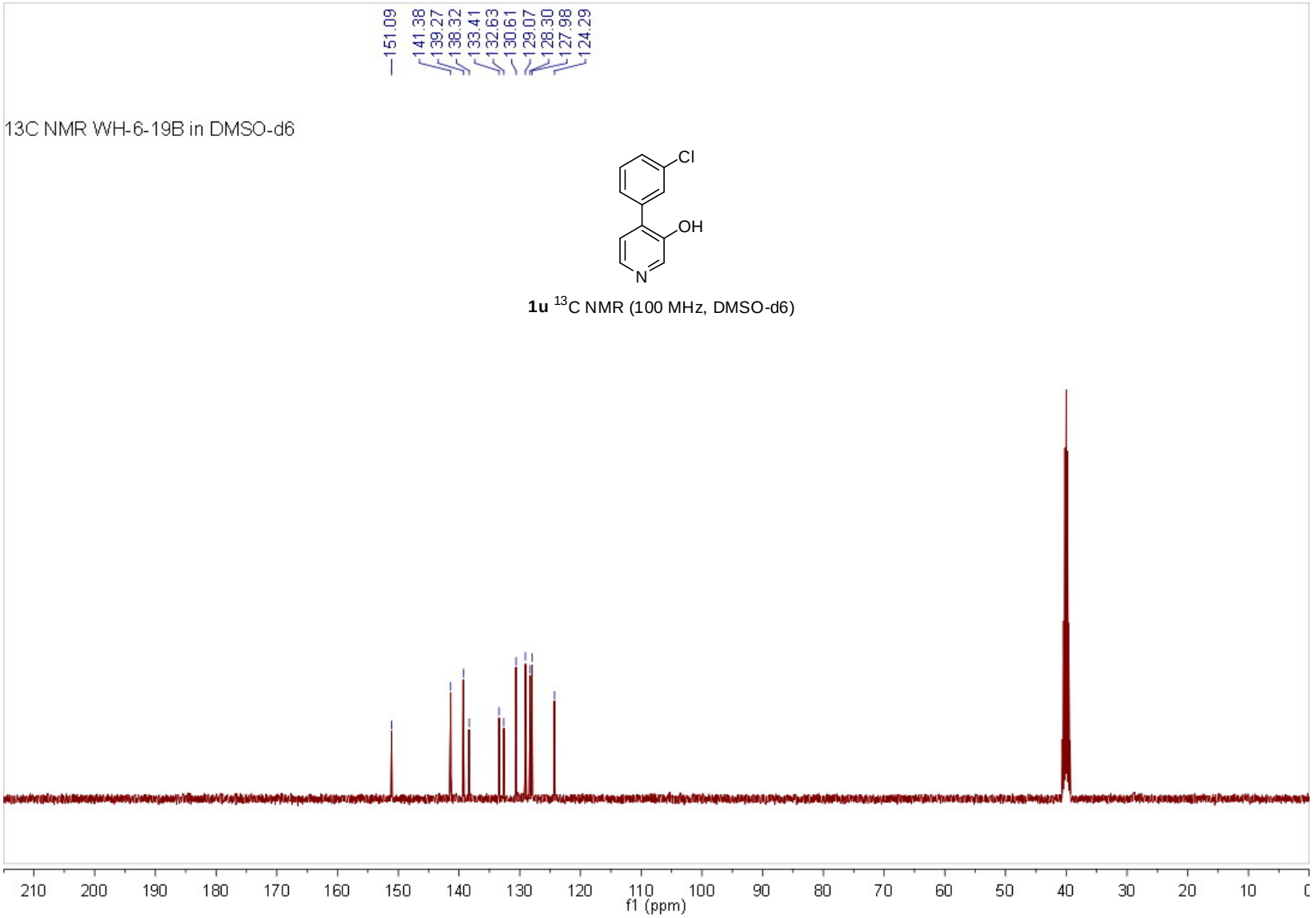
1t ^{1}H NMR (400 MHz, DMSO-d6)



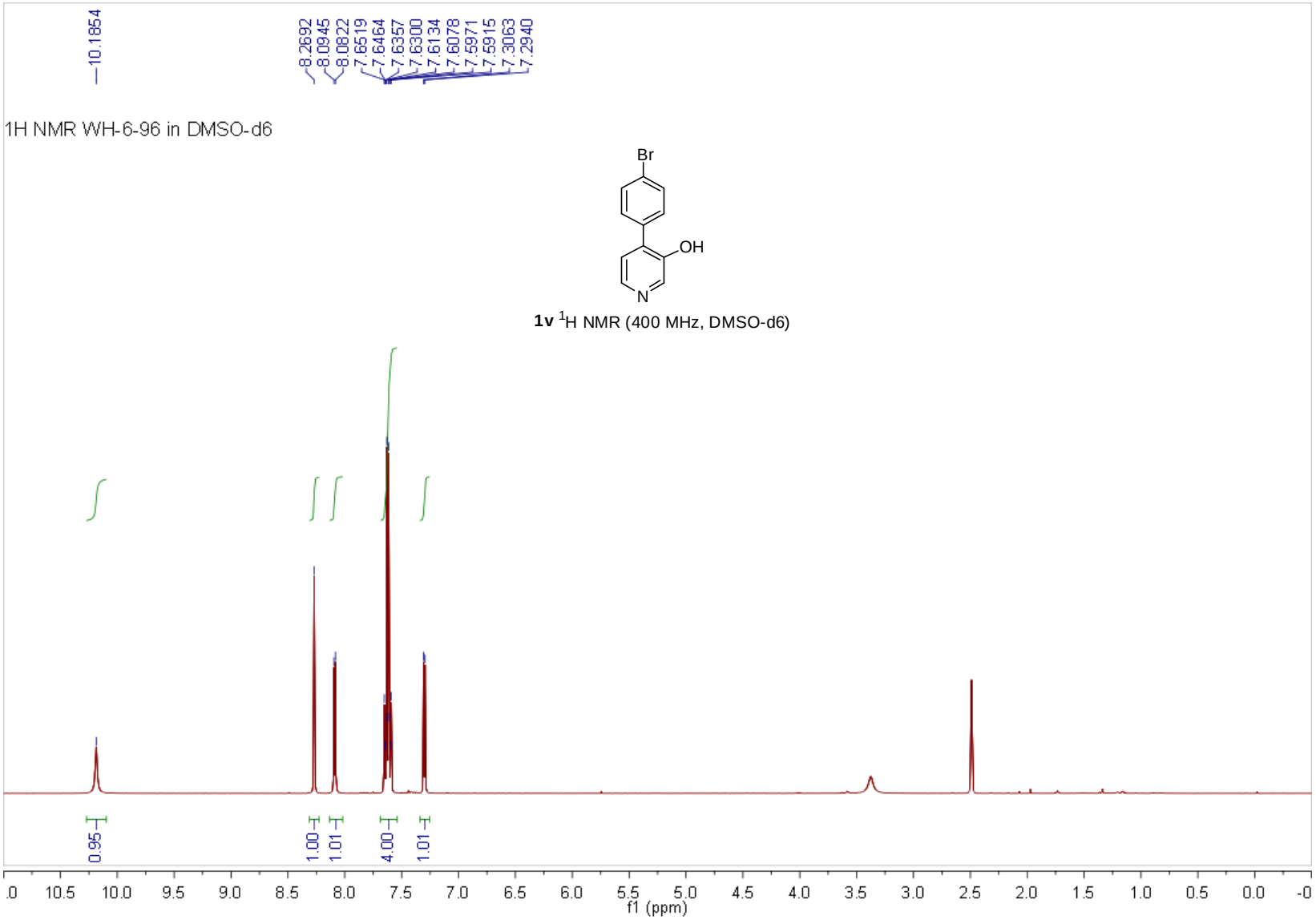
1t ^{13}C NMR (100 MHz, DMSO-d6)



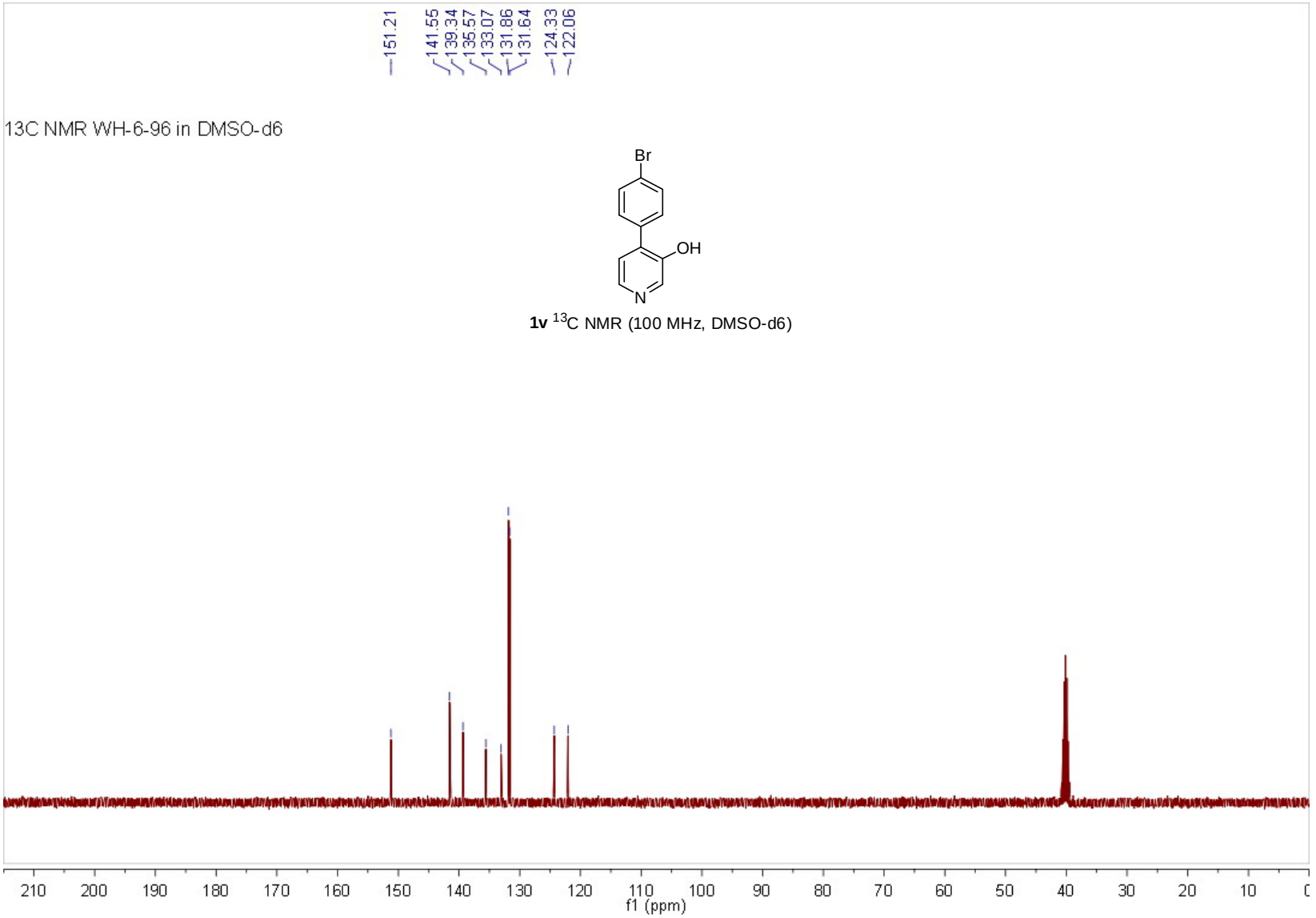
1u ^{1}H NMR (400 MHz, DMSO-d6)



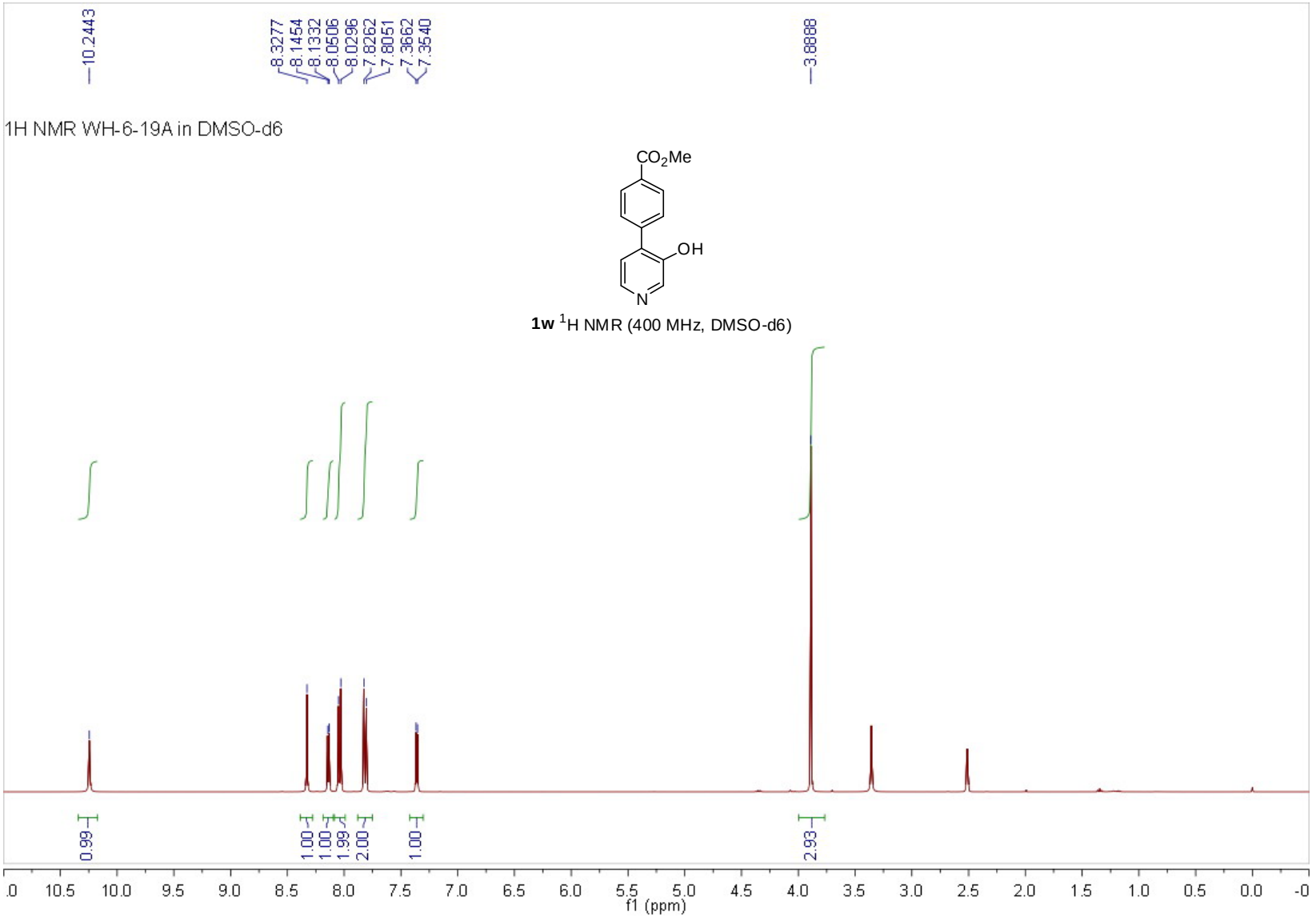
1u ^{13}C NMR (100 MHz, DMSO-d6)



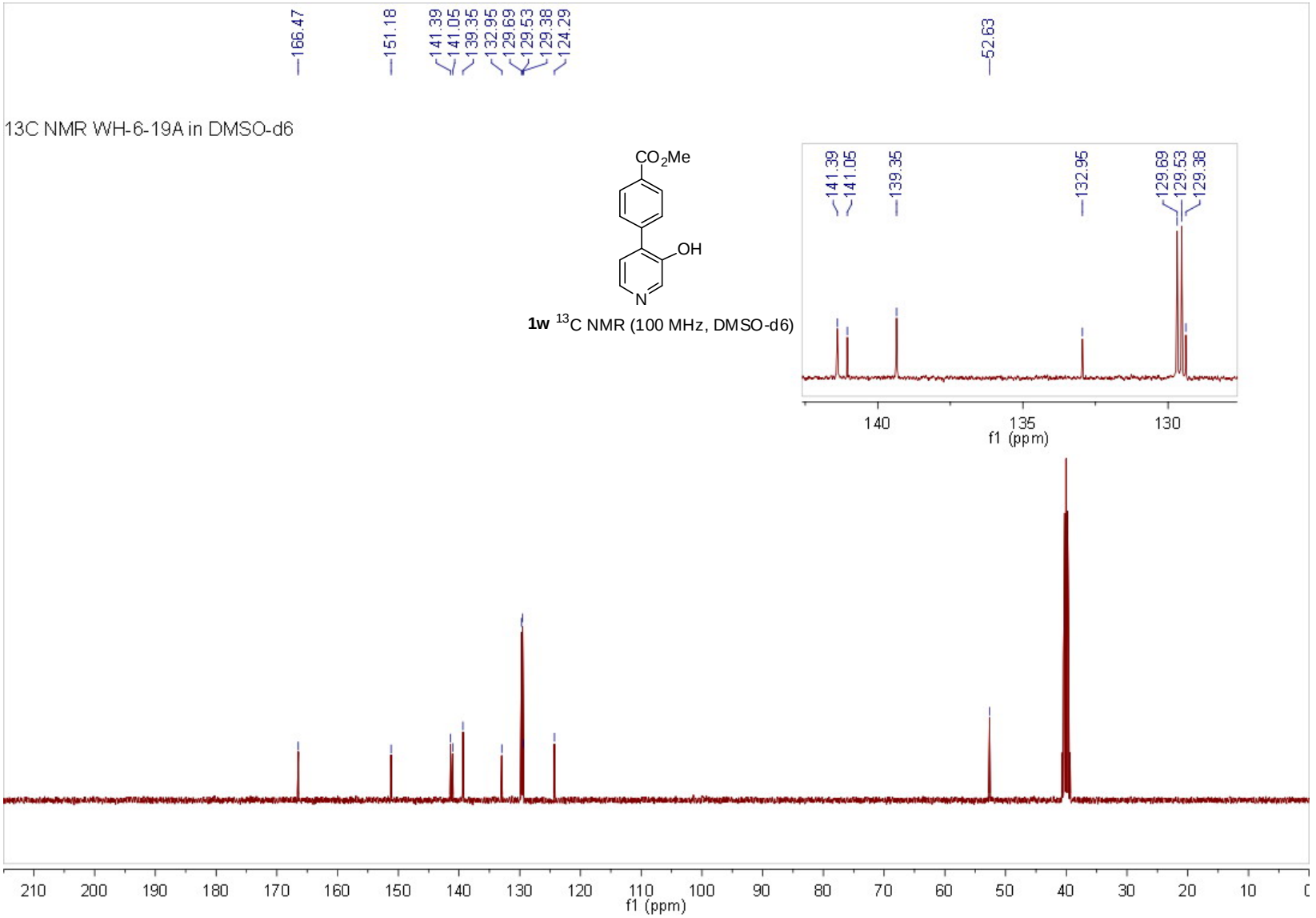
1v ^{1}H NMR (400 MHz, DMSO-d6)

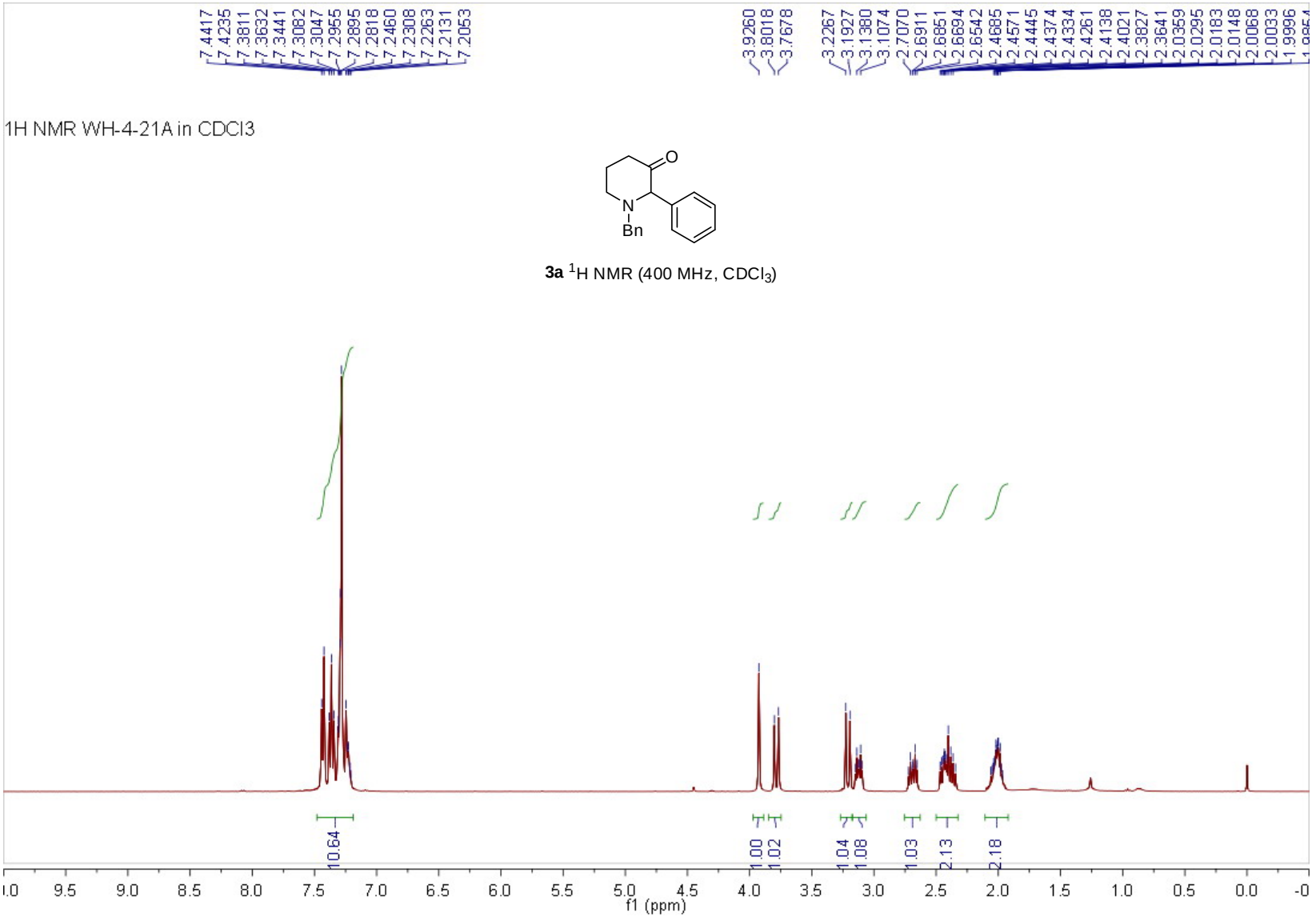


1v ^{13}C NMR (100 MHz, DMSO-d6)

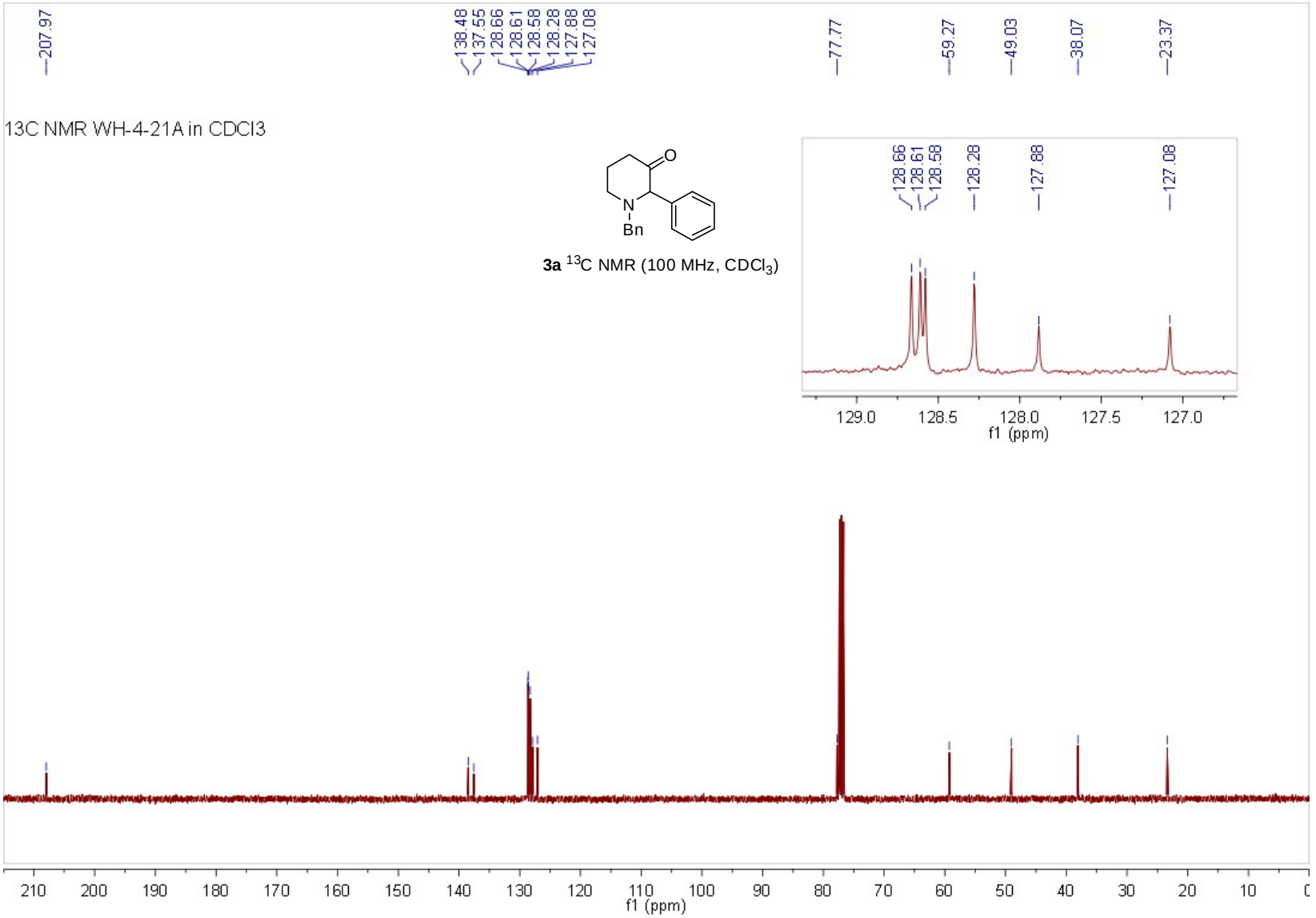


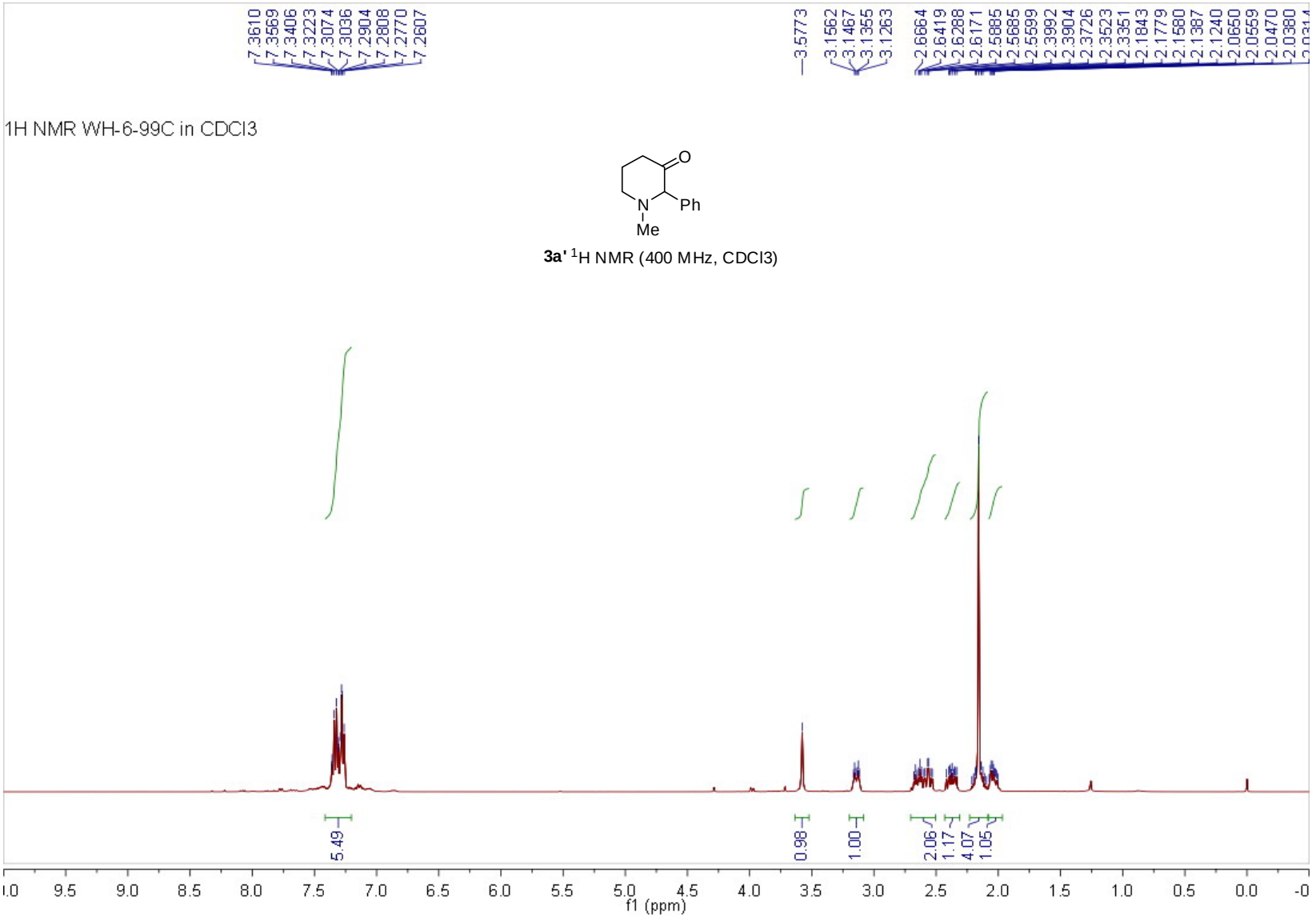
1w ^{1}H NMR (400 MHz, DMSO-d6)


166.47
151.18
141.39
141.05
139.35
132.95
129.69
129.53
129.38
124.29
52.63
13C NMR WH-6-19A in DMSO-d6
CO2Me
OH
N
1w 13C NMR (100 MHz, DMSO-d6)
141.39
141.05
139.35
132.95
129.69
129.53
129.38
140
135
130
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

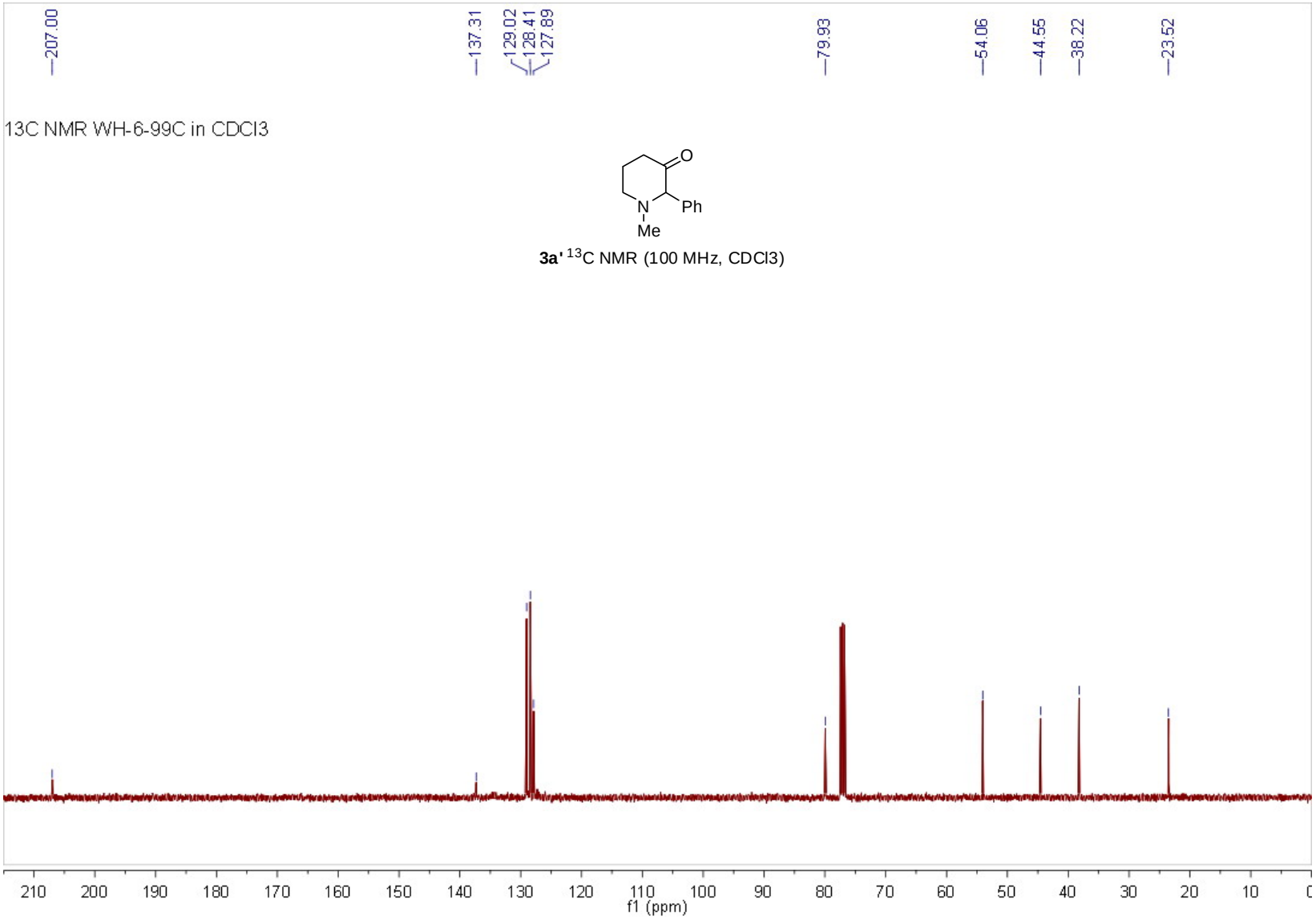


3a ^{1}H NMR (400 MHz, $CDCl_3$)

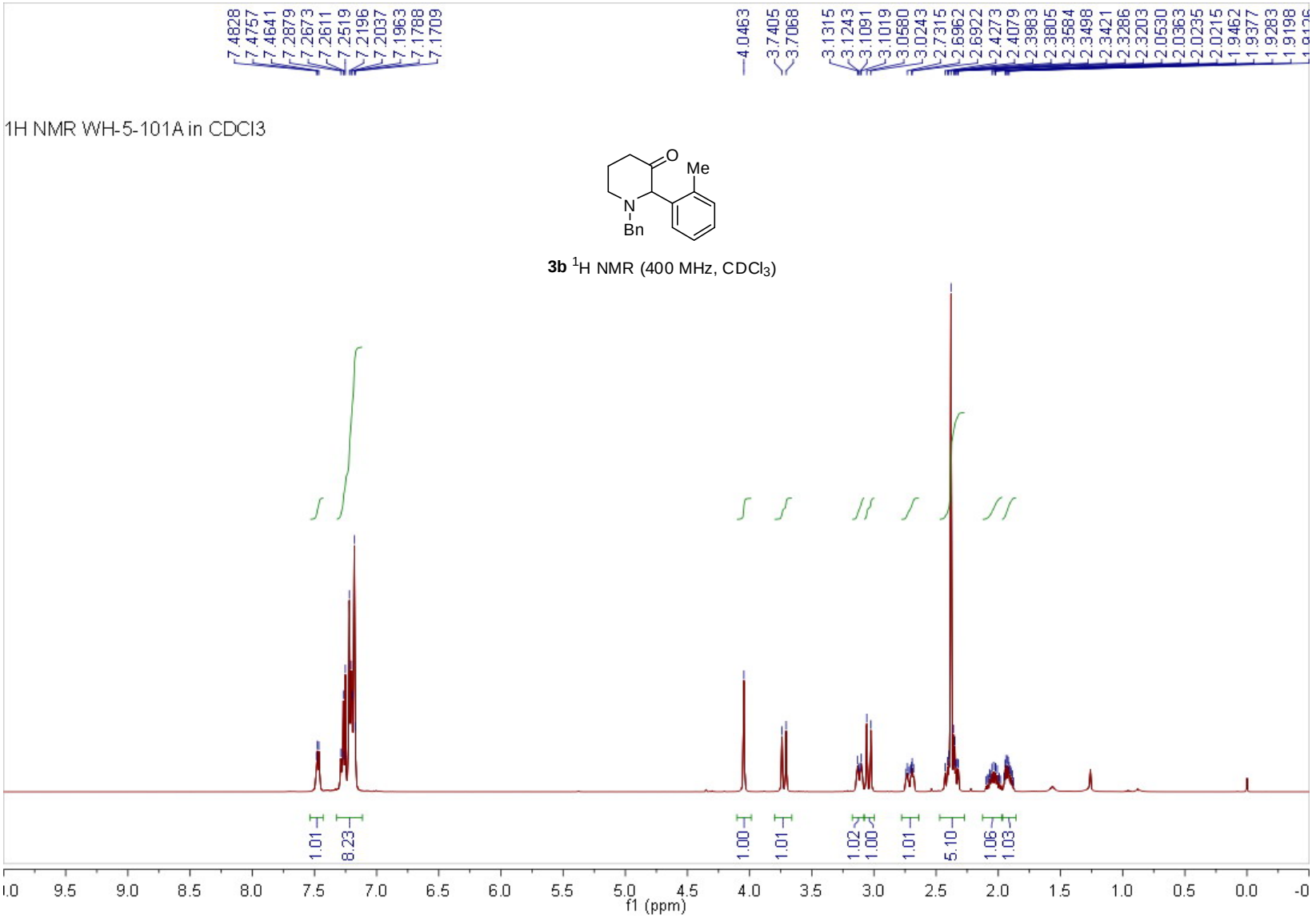

207.97
138.48
137.55
128.66
128.61
128.58
128.28
127.88
127.08
77.77
59.27
49.03
38.07
23.37
13C NMR WH-4-21A in CDCl3
O
N
Bn
3a 13C NMR (100 MHz, CDCl3)
128.66
128.61
128.58
128.28
127.88
127.08
129.0
128.5
128.0
127.5
127.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



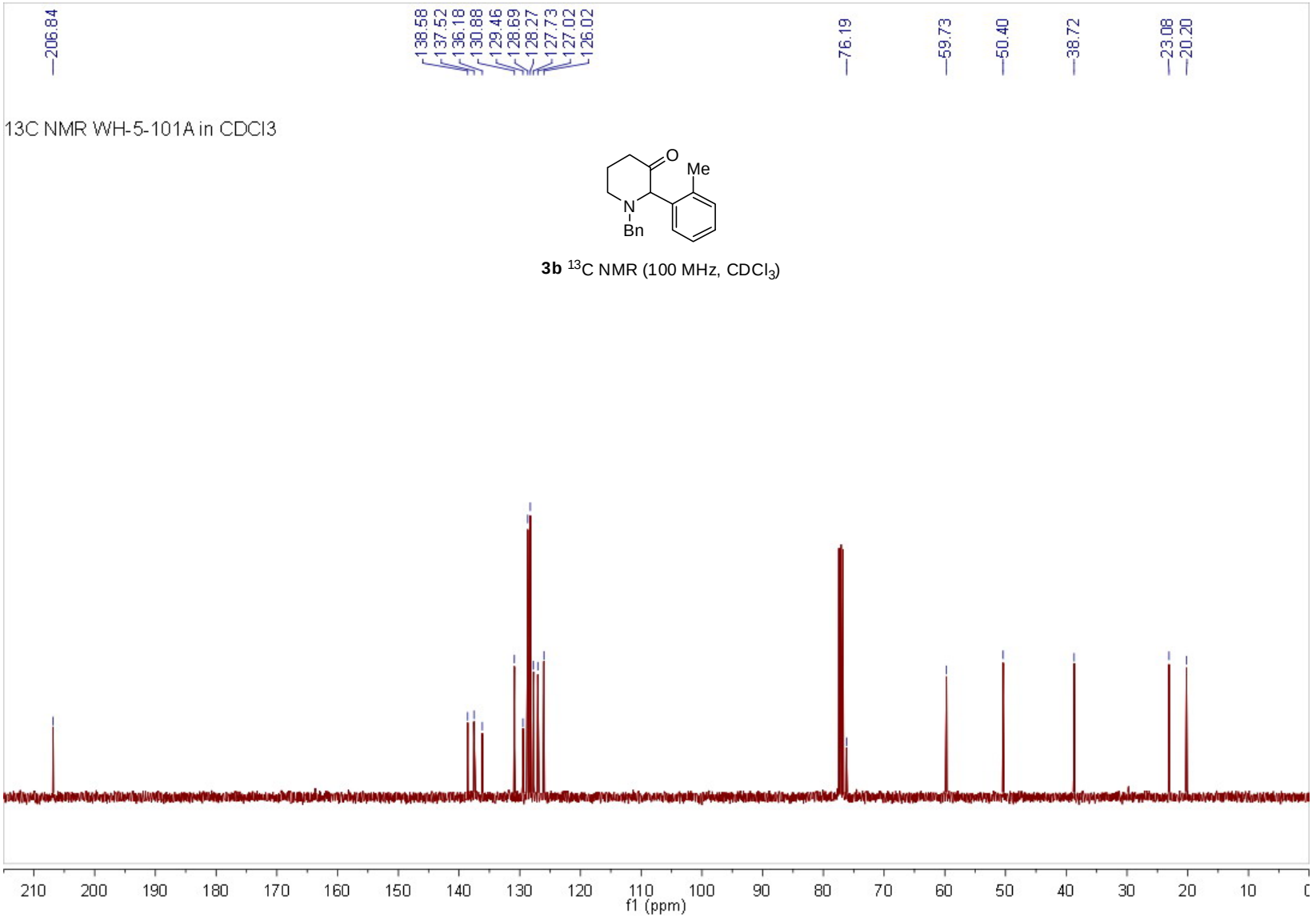
3a' ^{1}H NMR (400 MHz, CDCl3)



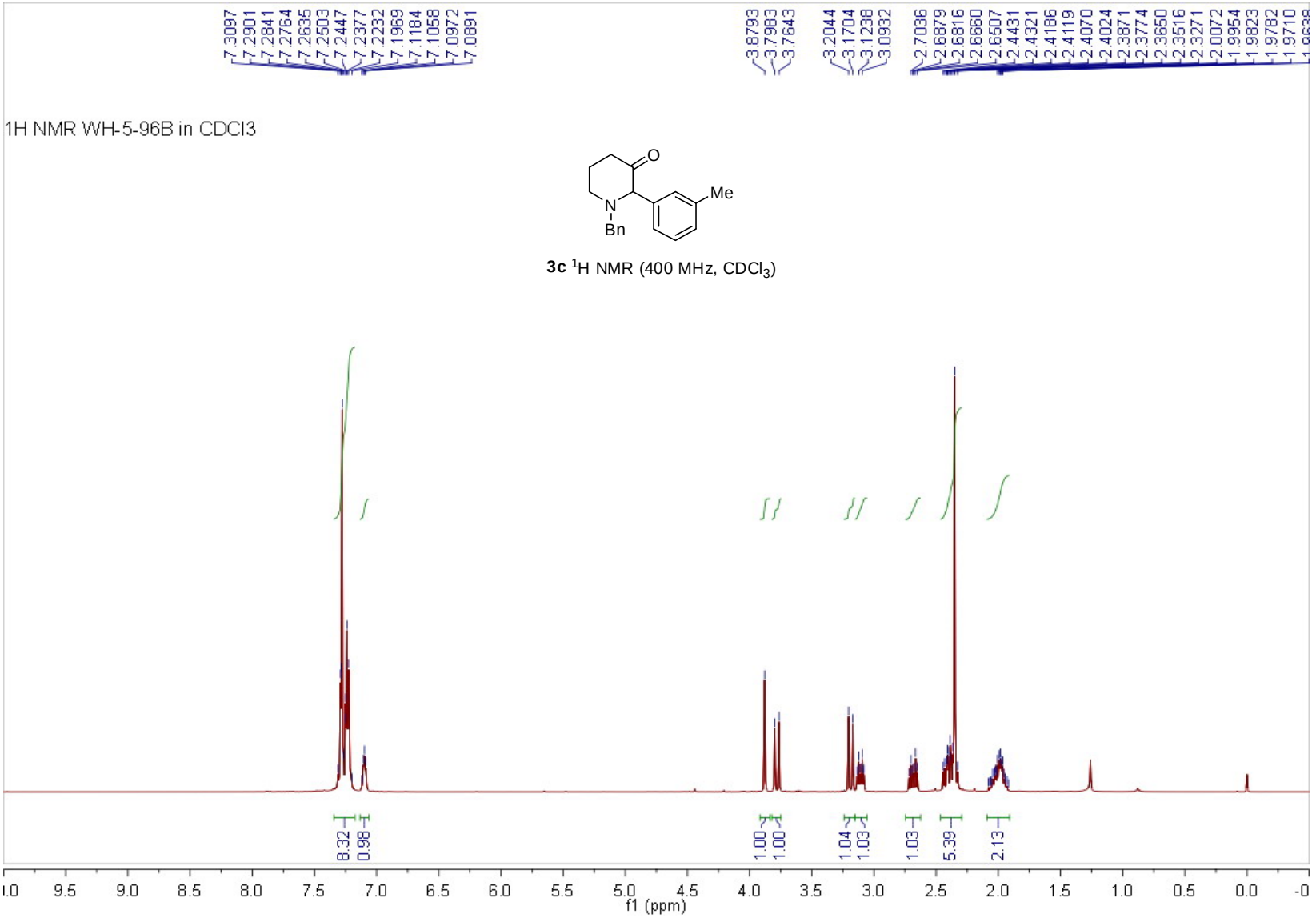
3a' ^{13}C NMR (100 MHz, CDCl3)



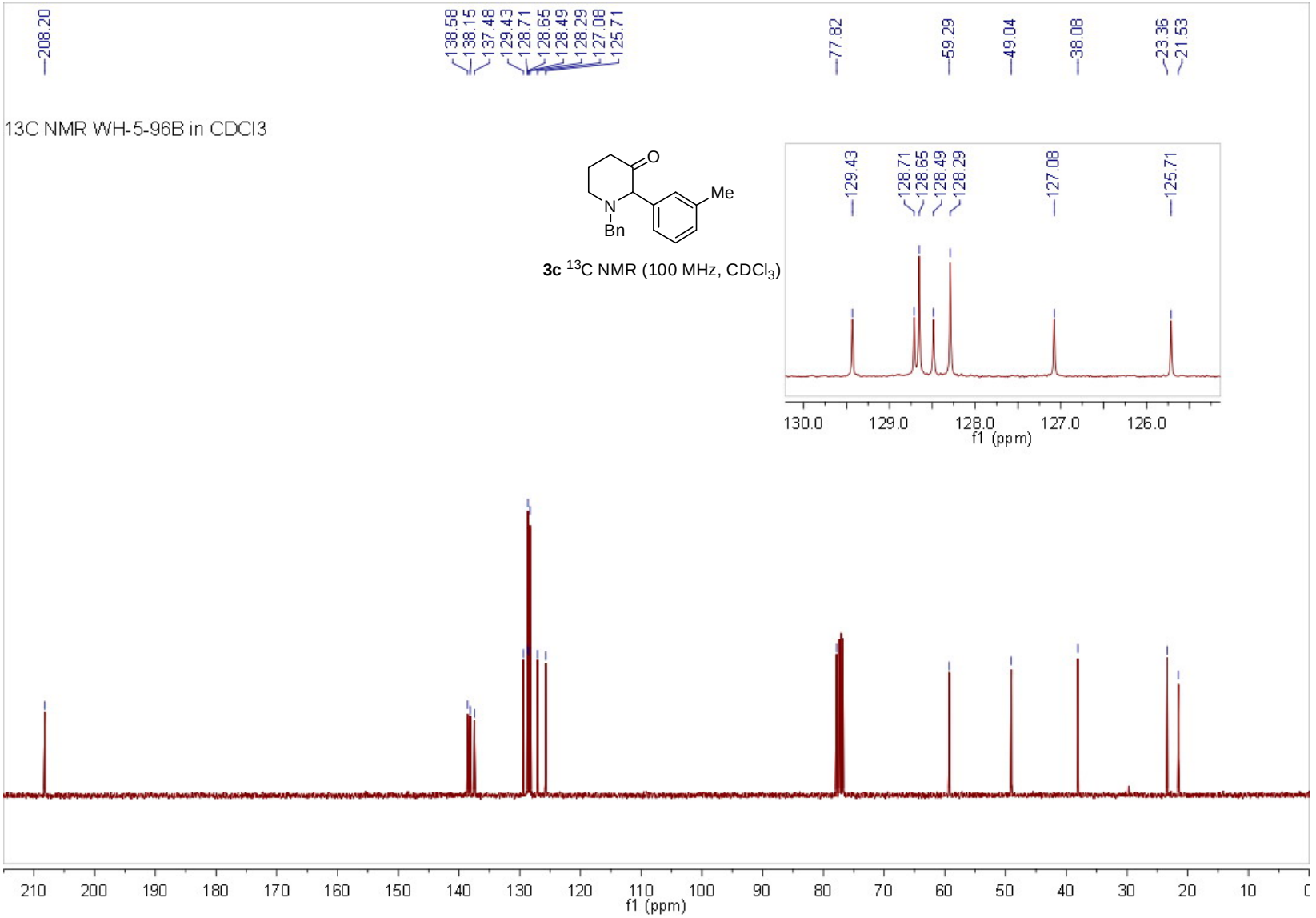
3b ^{1}H NMR (400 MHz, $CDCl_3$)



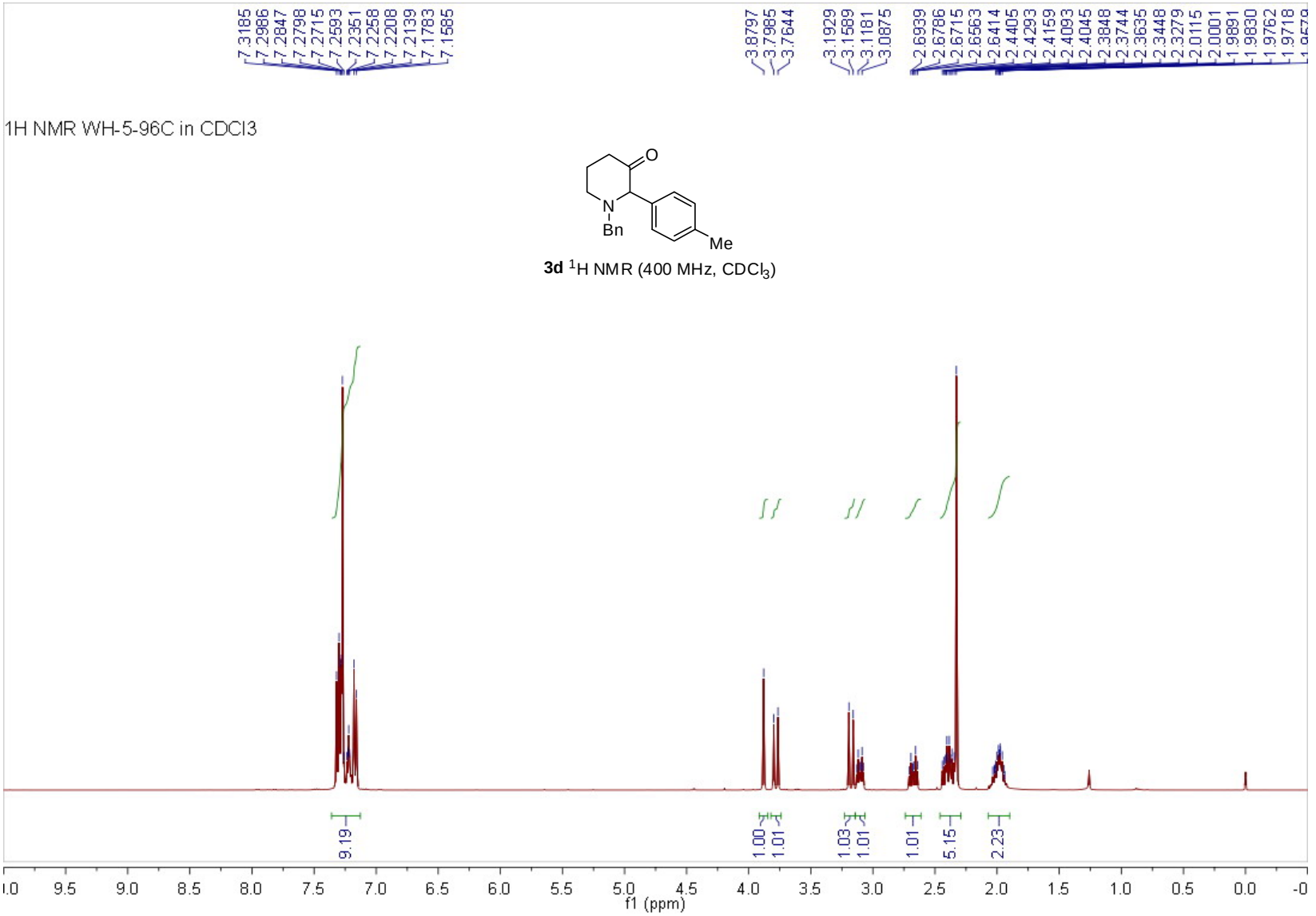
3b ^{13}C NMR (100 MHz, $CDCl_3$)



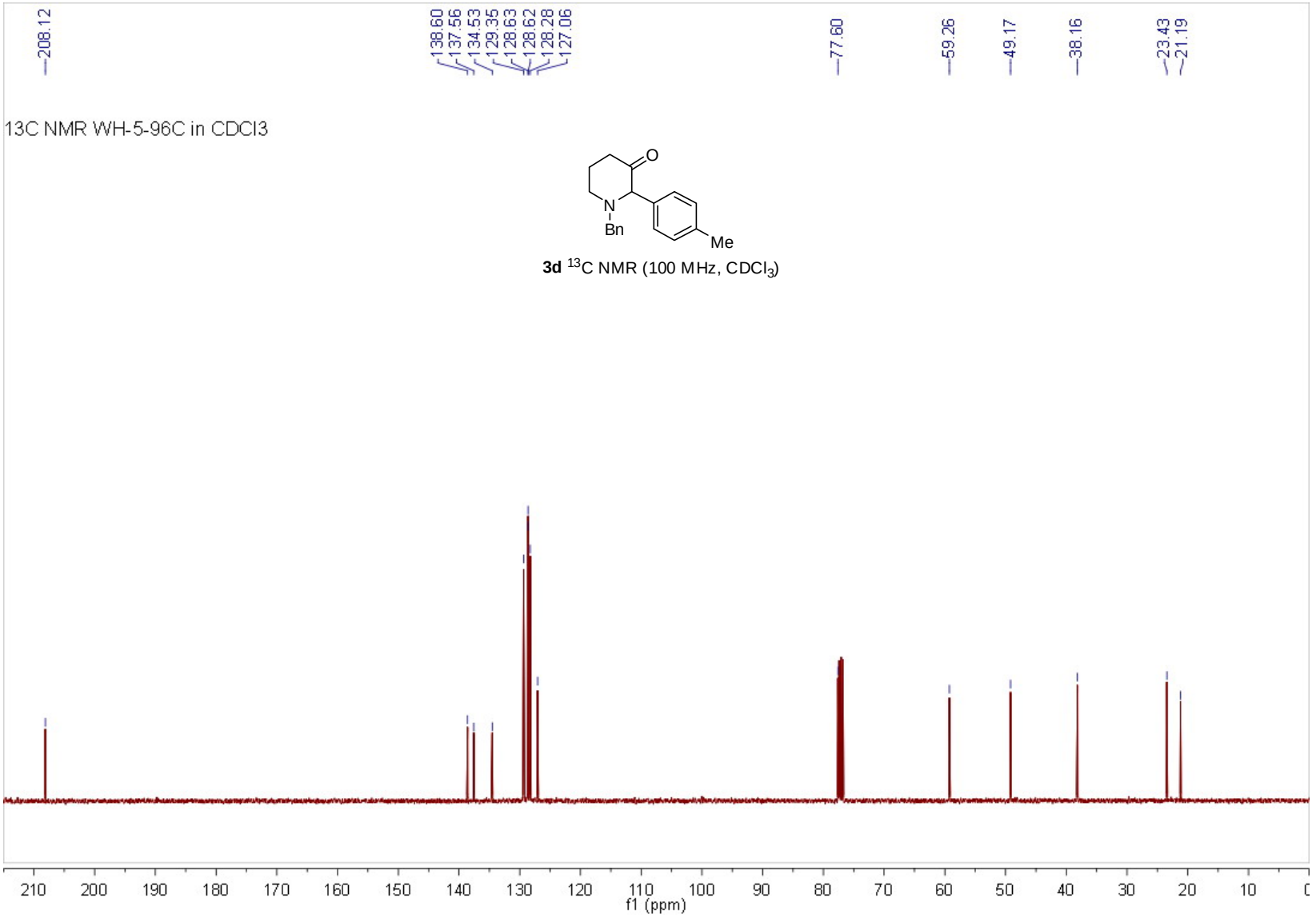
3c ^{1}H NMR (400 MHz, $CDCl_3$)



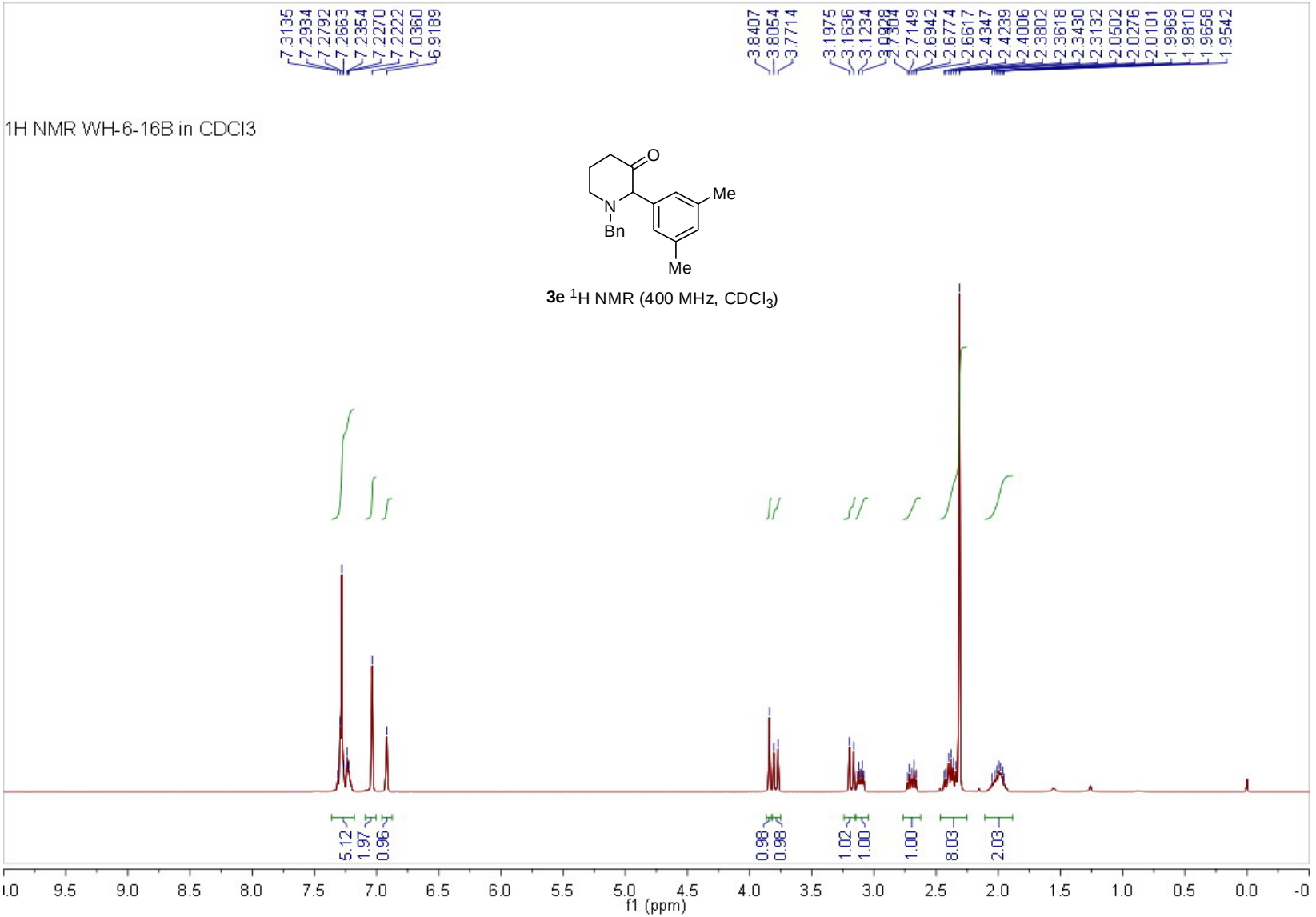
3c ^{13}C NMR (100 MHz, $CDCl_3$)



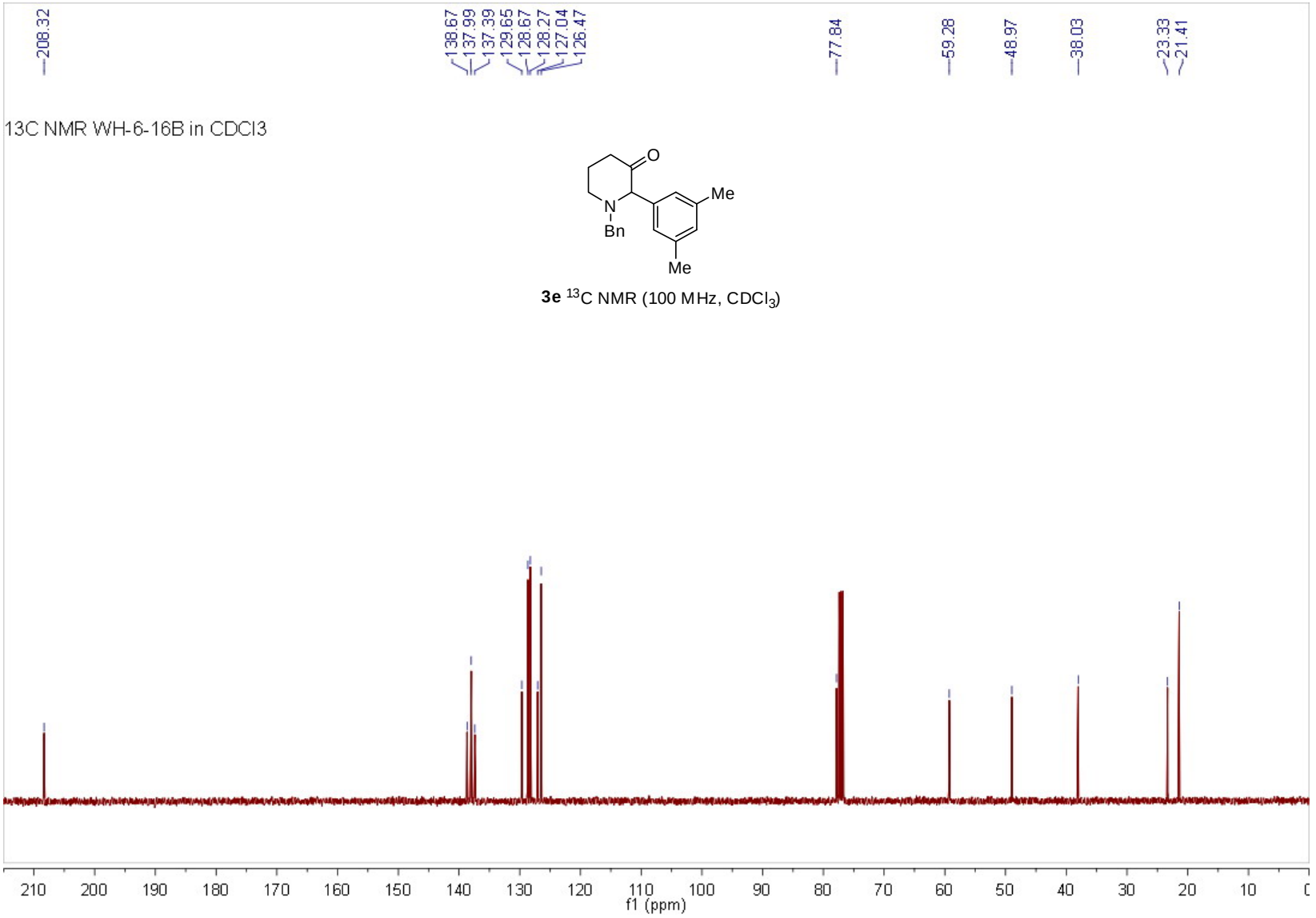
3d ^{1}H NMR (400 MHz, $CDCl_3$)



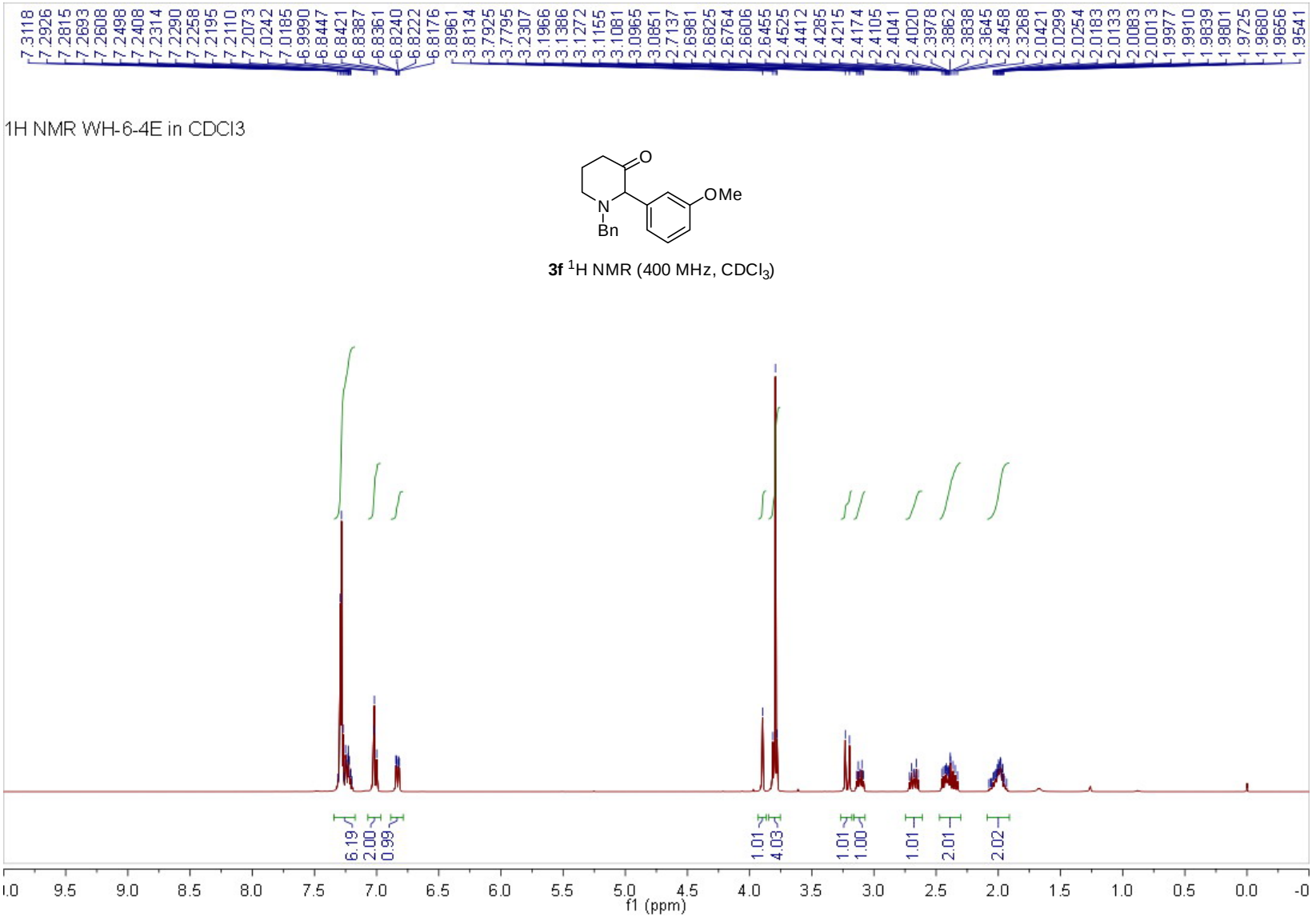
3d ^{13}C NMR (100 MHz, $CDCl_3$)



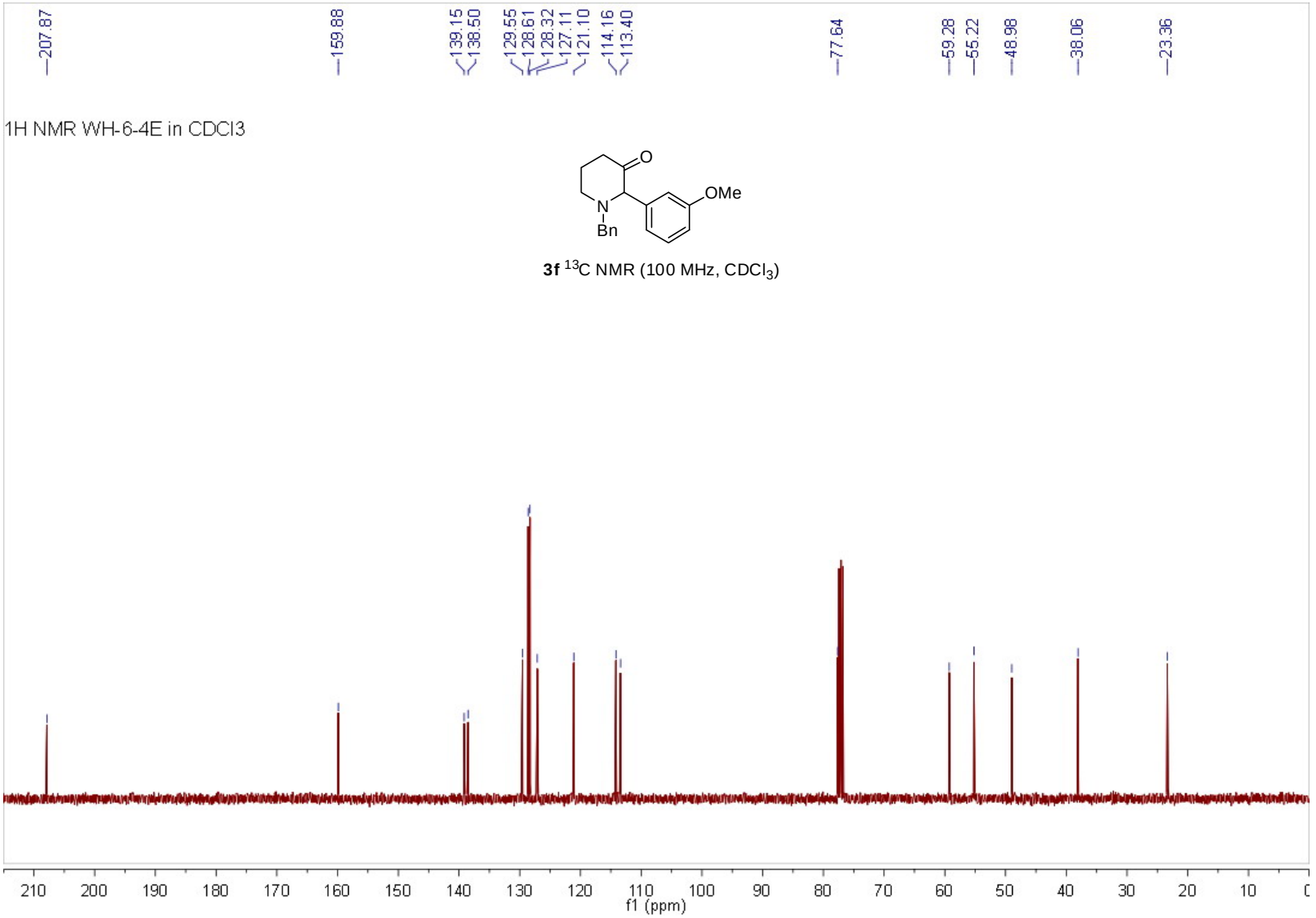
3e ^{1}H NMR (400 MHz, $CDCl_3$)



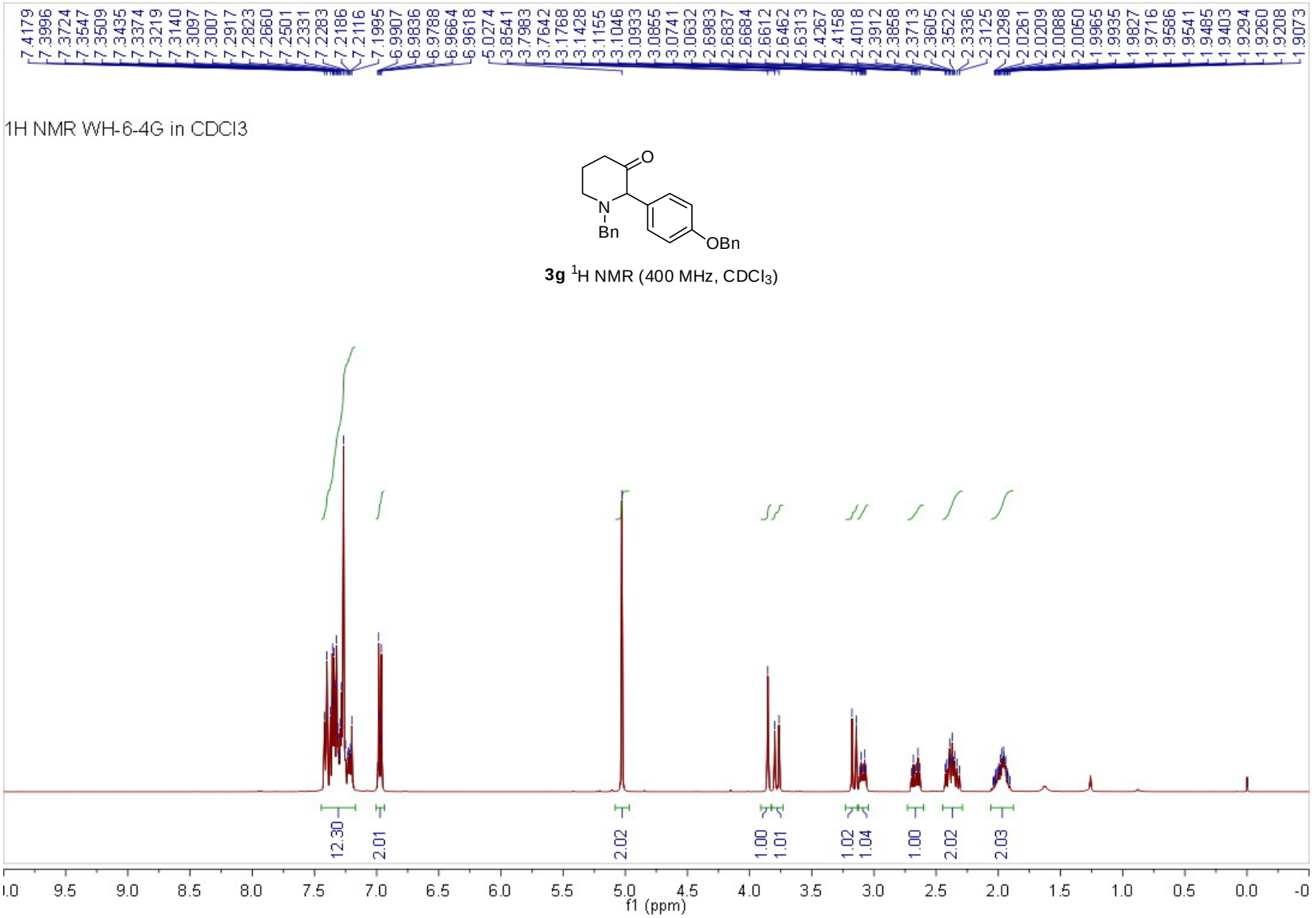
3e ^{13}C NMR (100 MHz, $CDCl_3$)



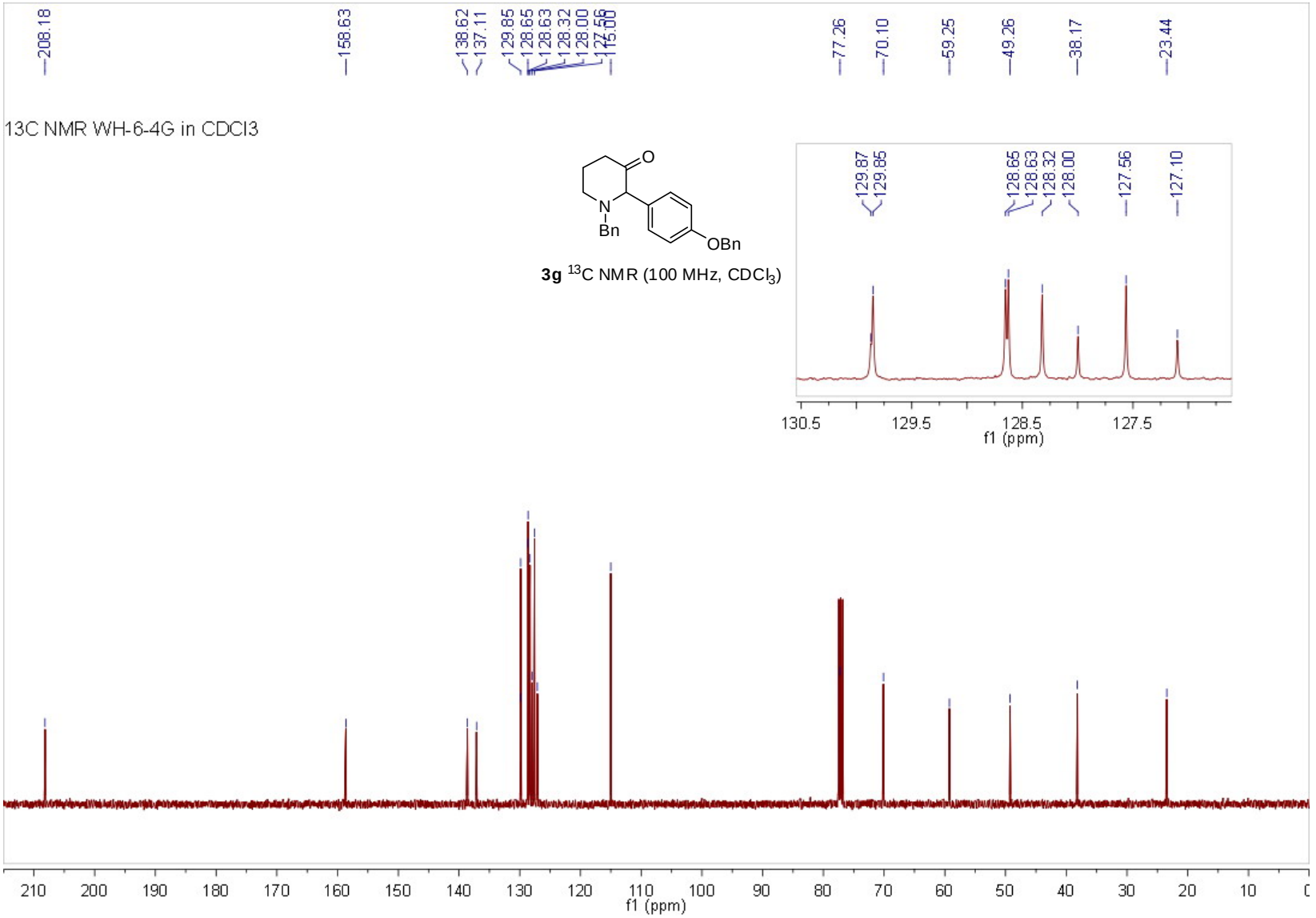
3f ^{1}H NMR (400 MHz, $CDCl_3$)



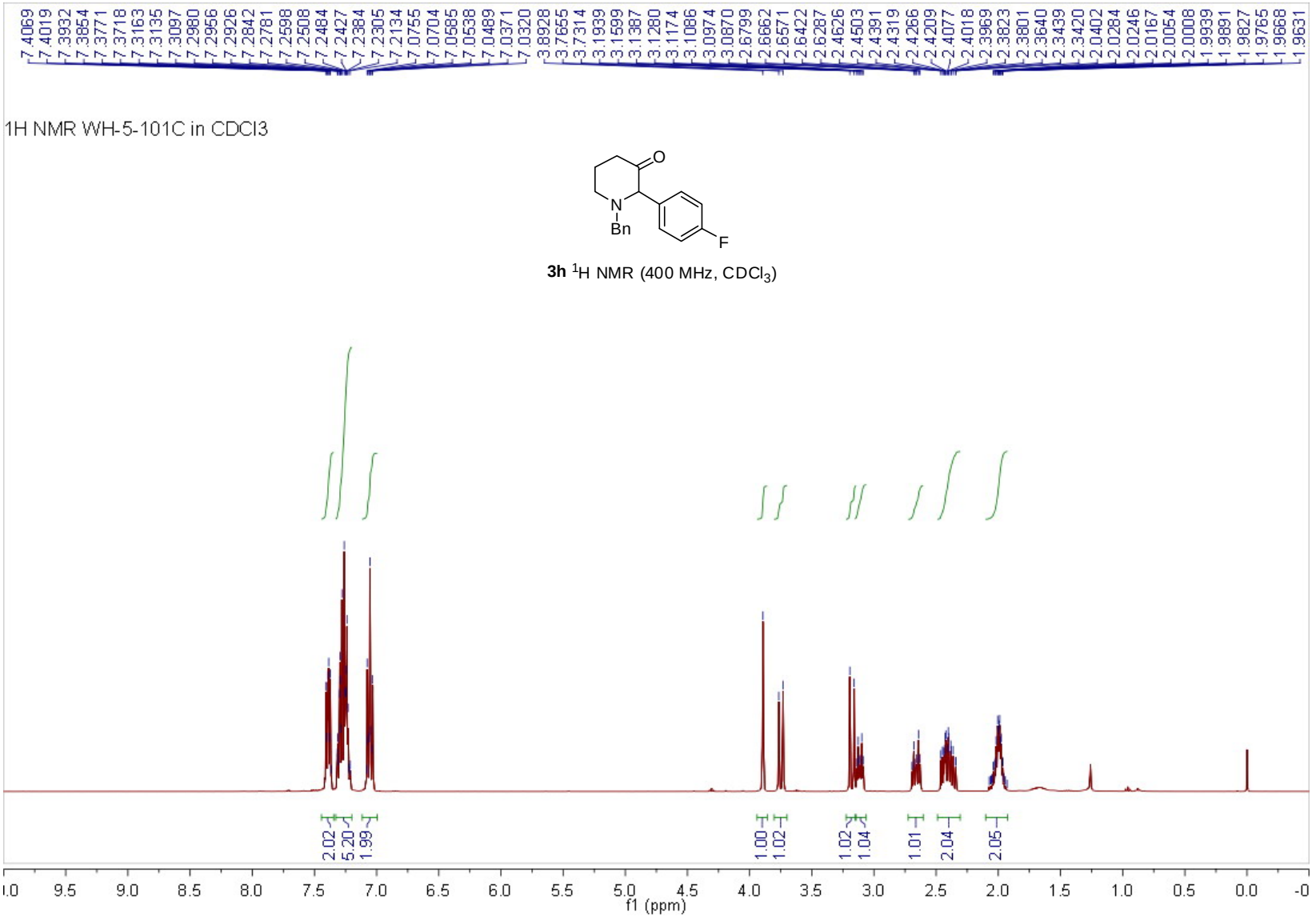
3f ^{13}C NMR (100 MHz, $CDCl_3$)



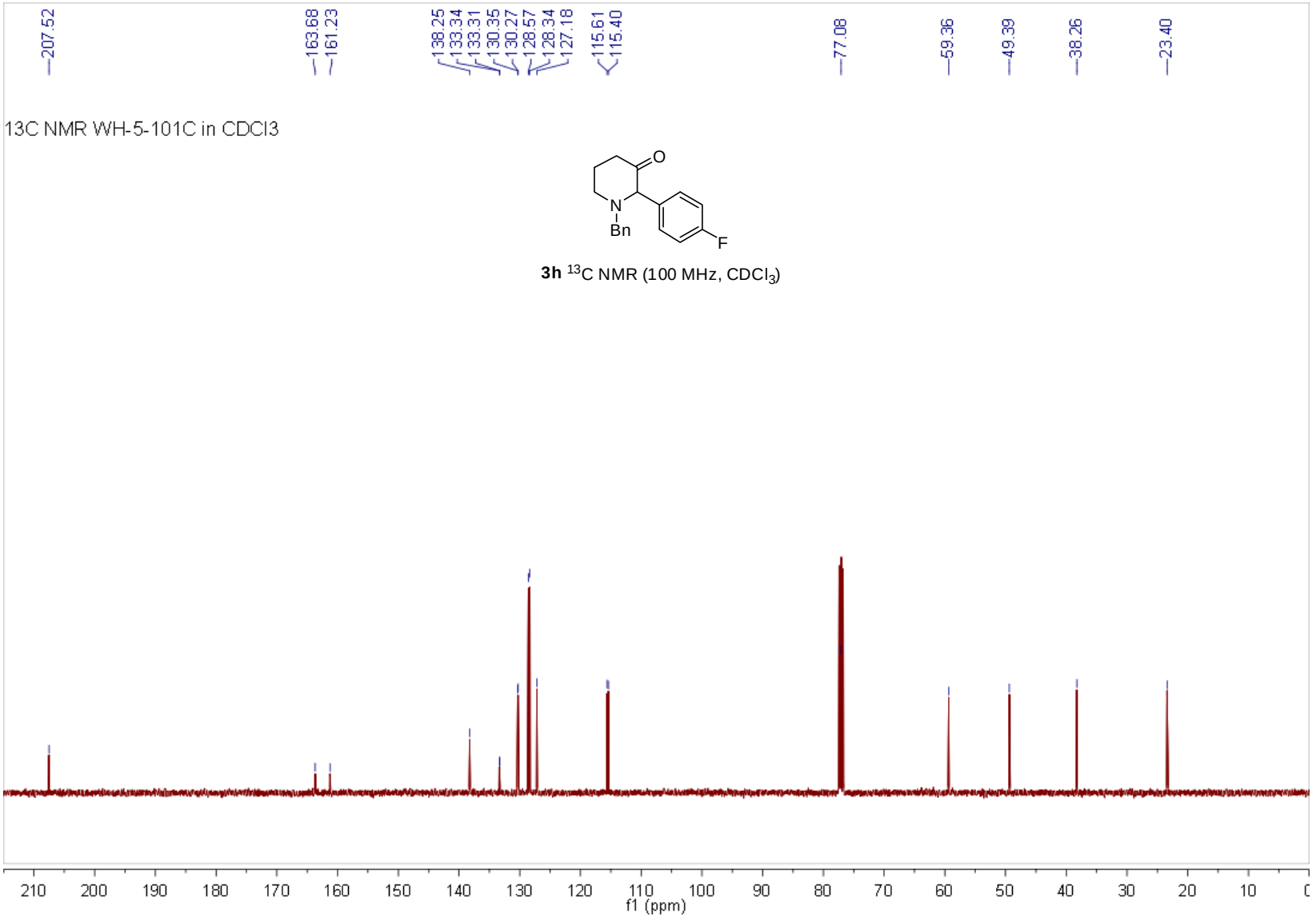
3g ^{1}H NMR (400 MHz, $CDCl_3$)



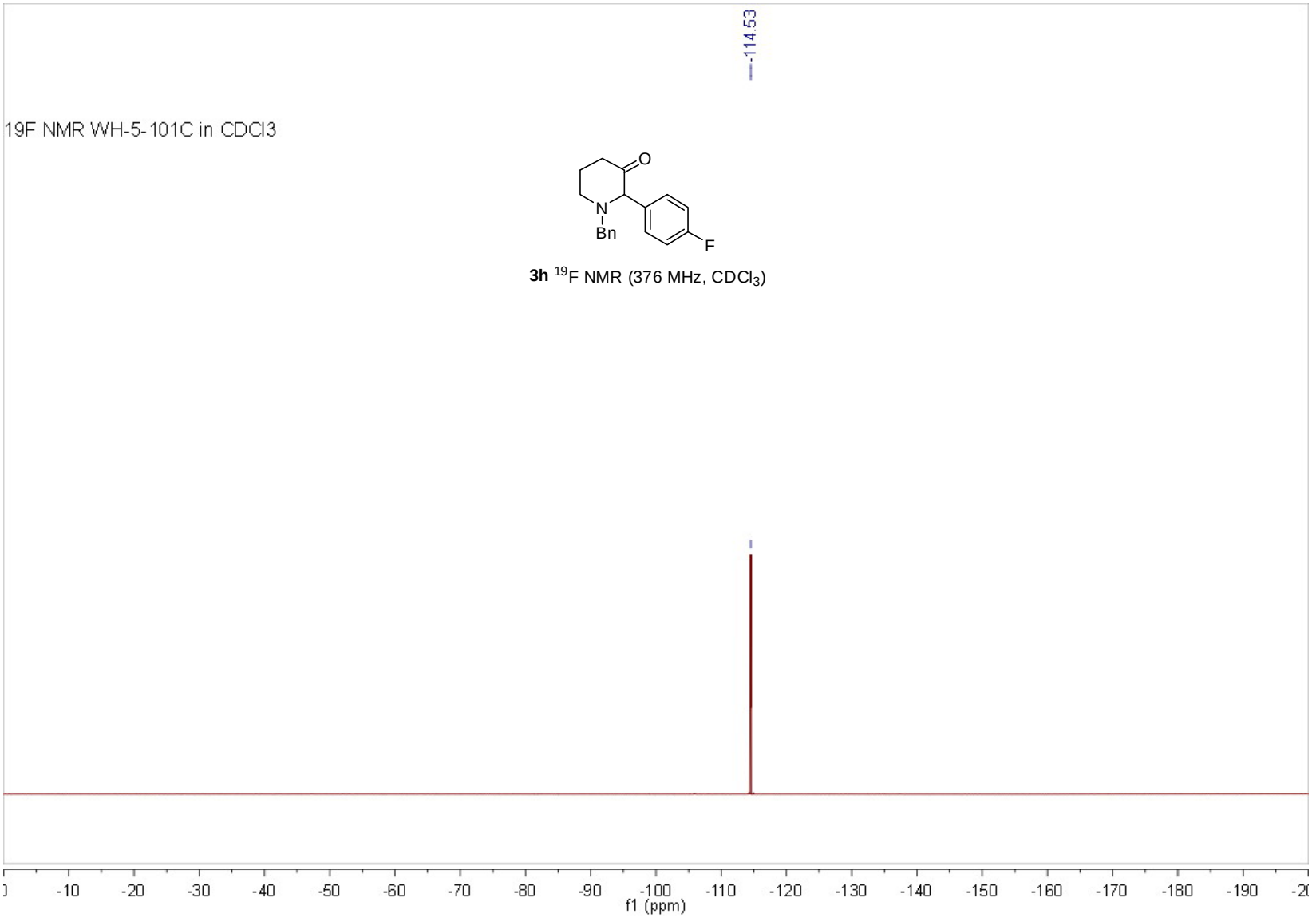
3g ^{13}C NMR (100 MHz, $CDCl_3$)



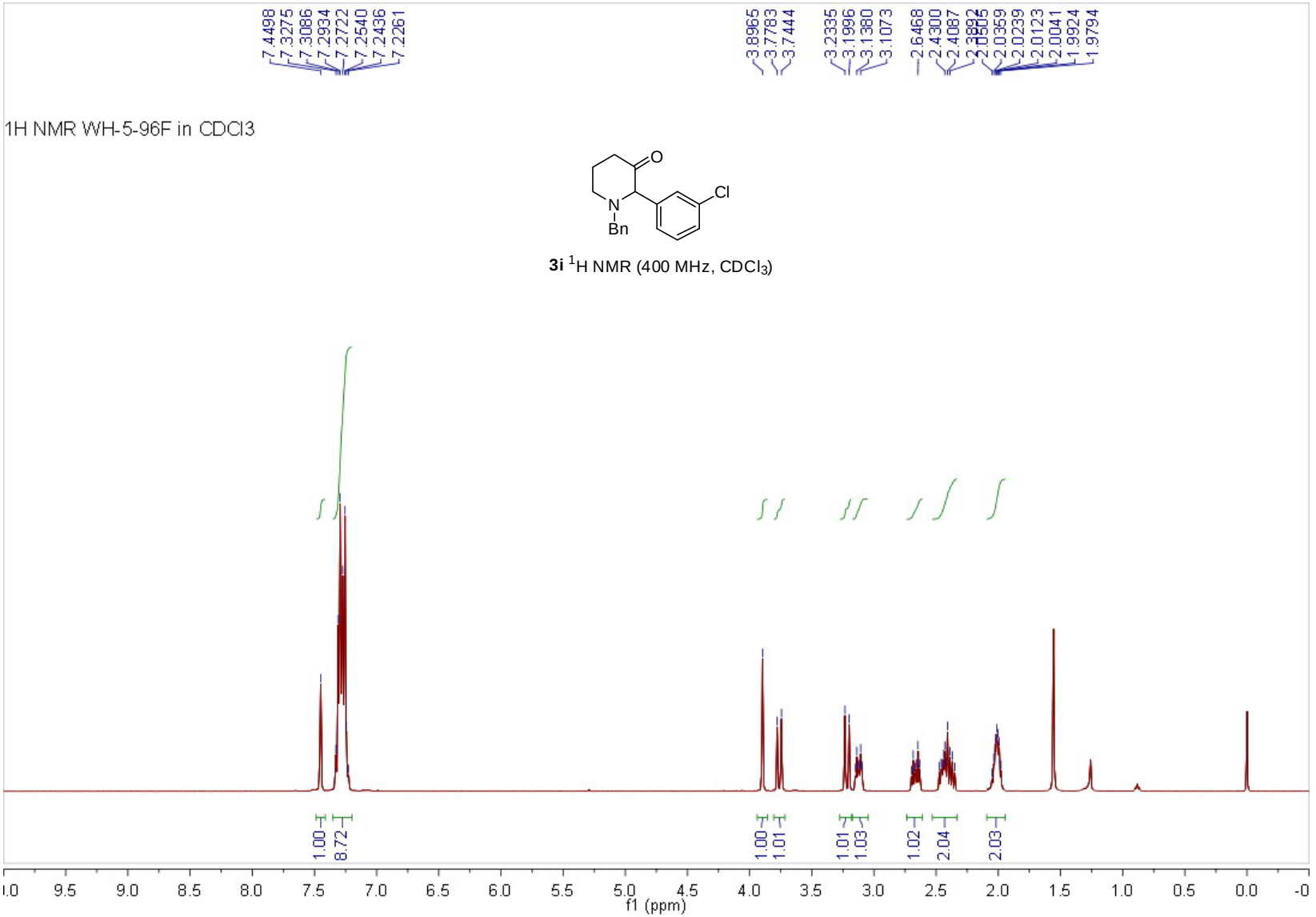
3h ^{1}H NMR (400 MHz, $CDCl_3$)



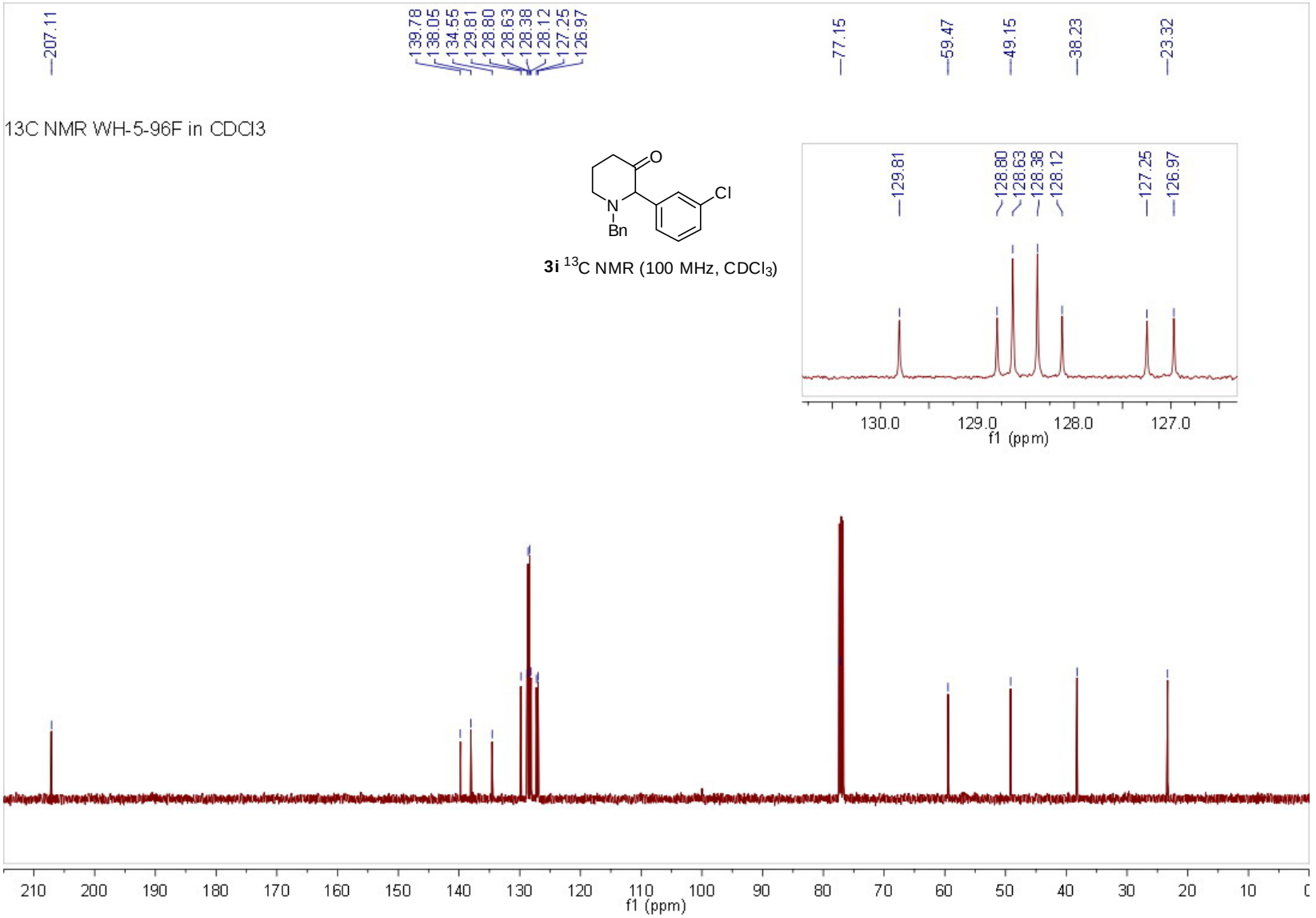
3h ^{13}C NMR (100 MHz, $CDCl_3$)



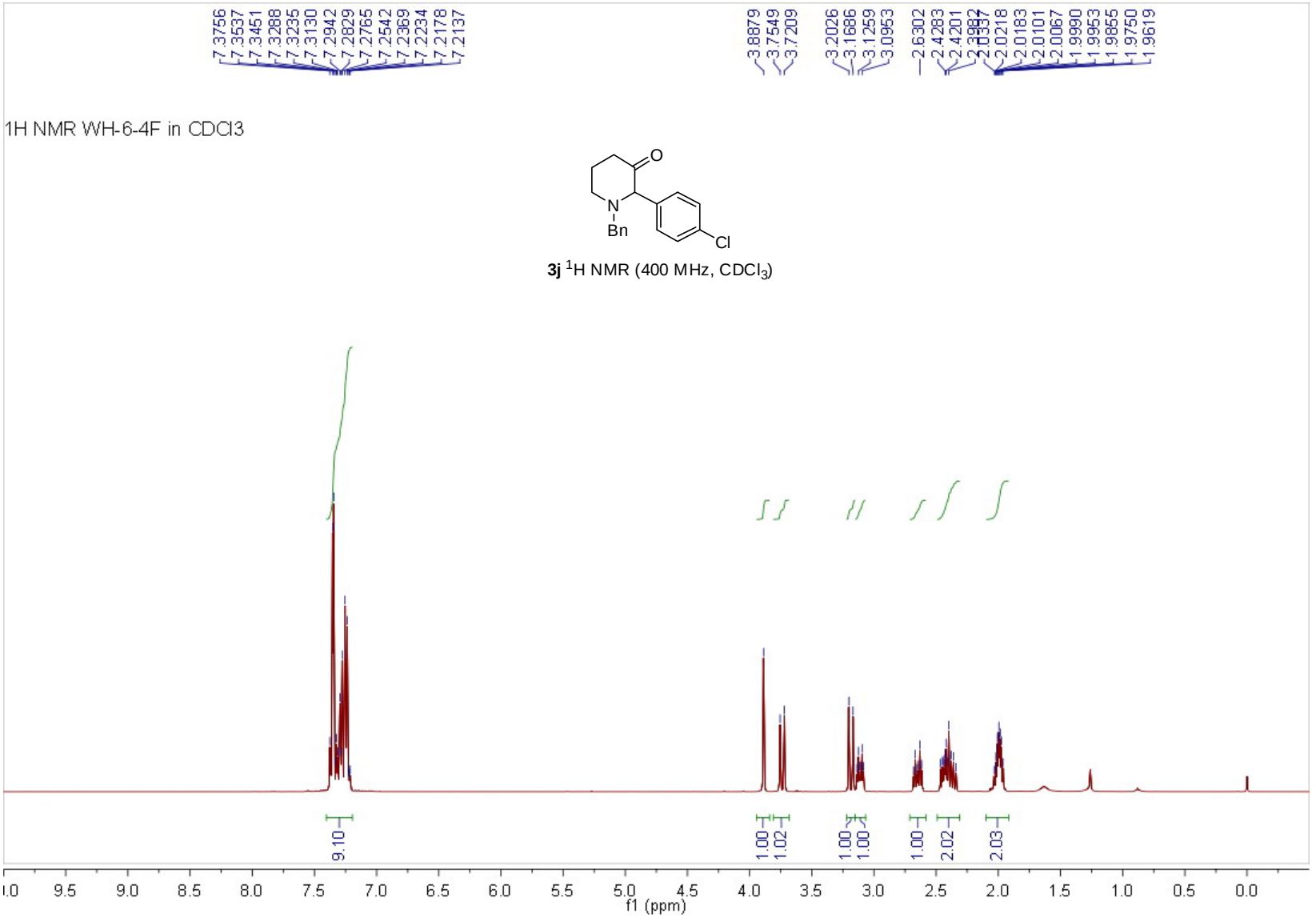
3h ^{19}F NMR (376 MHz, $CDCl_3$)



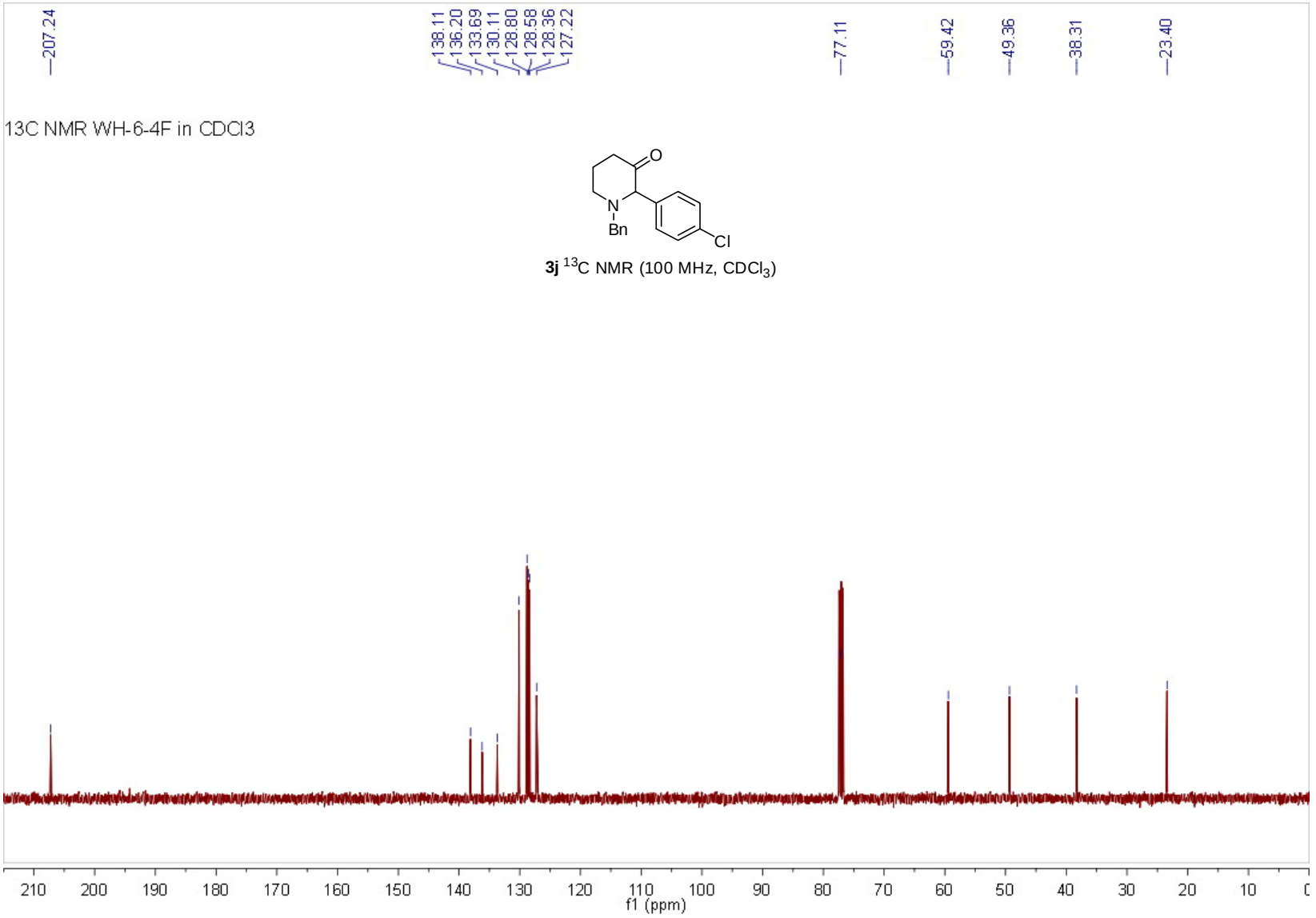
3i ^{1}H NMR (400 MHz, $CDCl_3$)



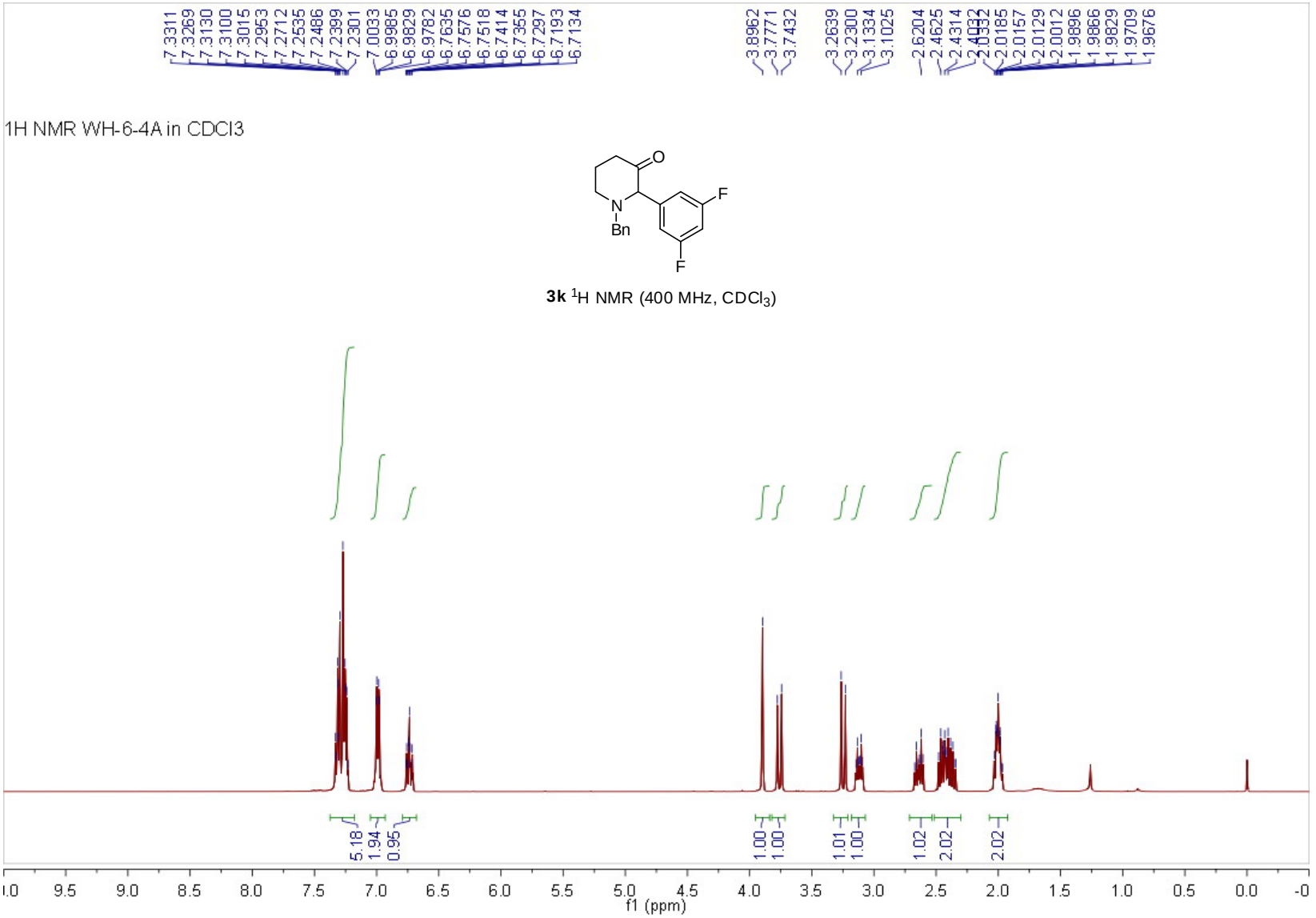
3i ^{13}C NMR (100 MHz, $CDCl_3$)



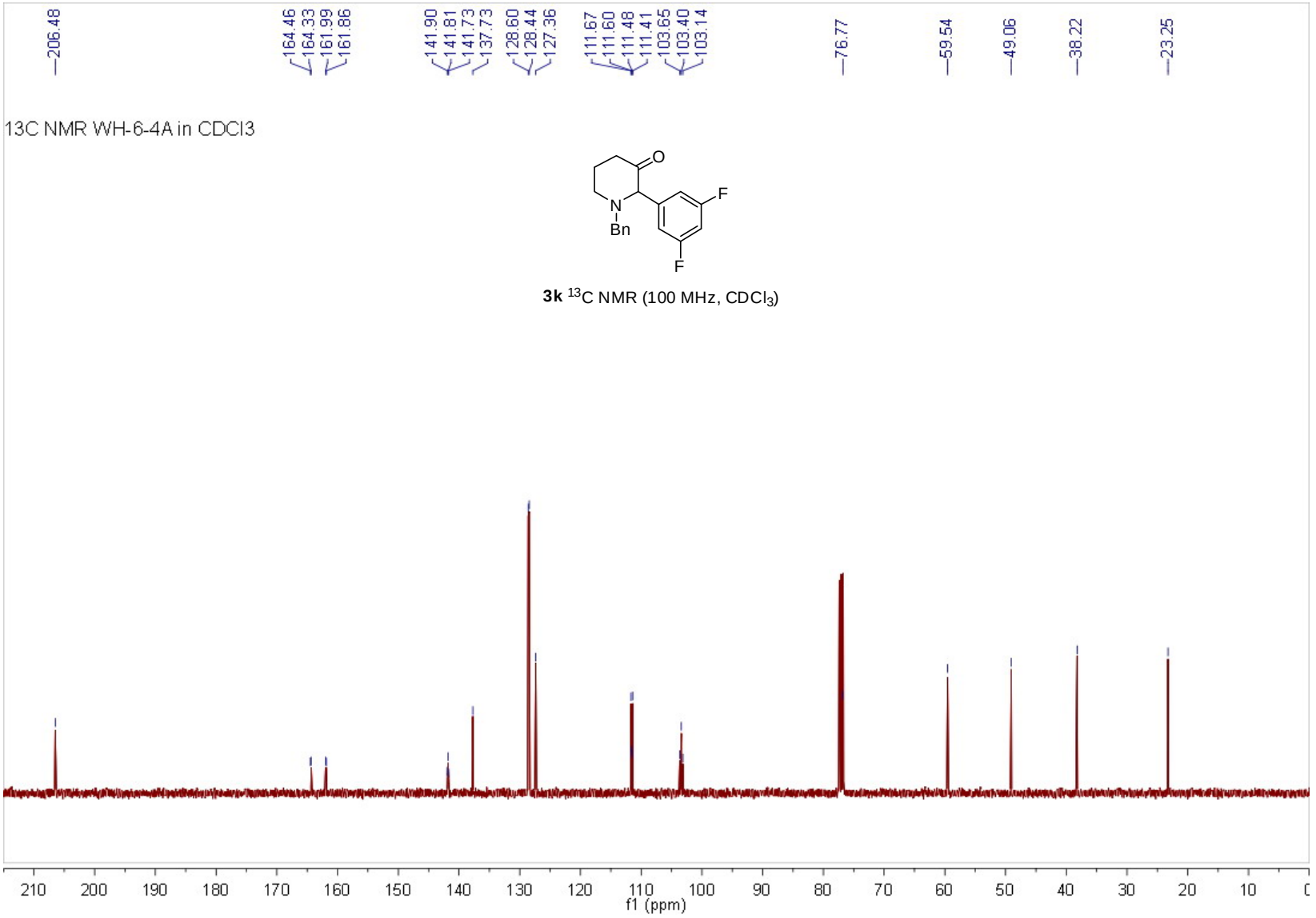
3j ^{1}H NMR (400 MHz, $CDCl_3$)



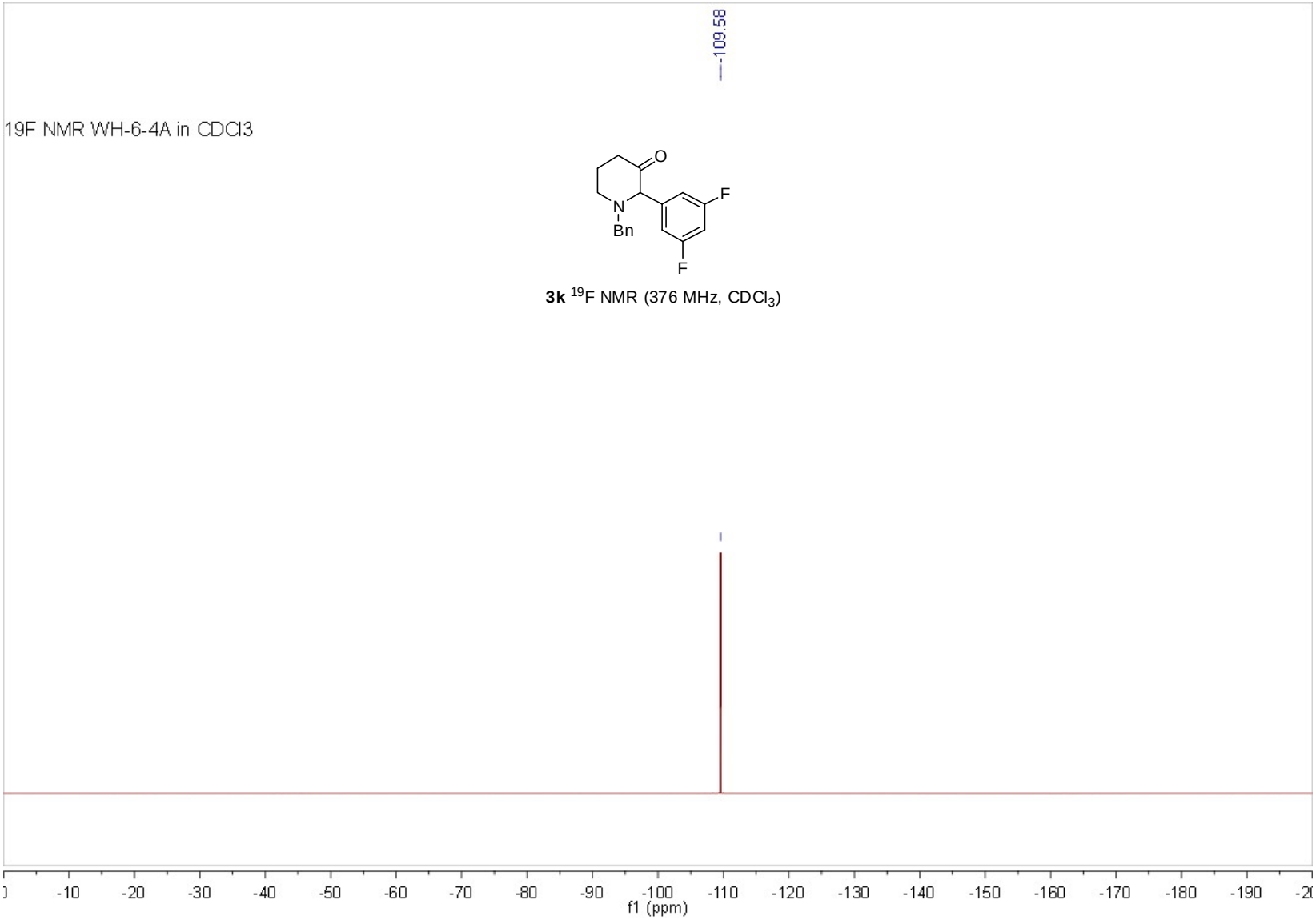
3j ^{13}C NMR (100 MHz, $CDCl_3$)



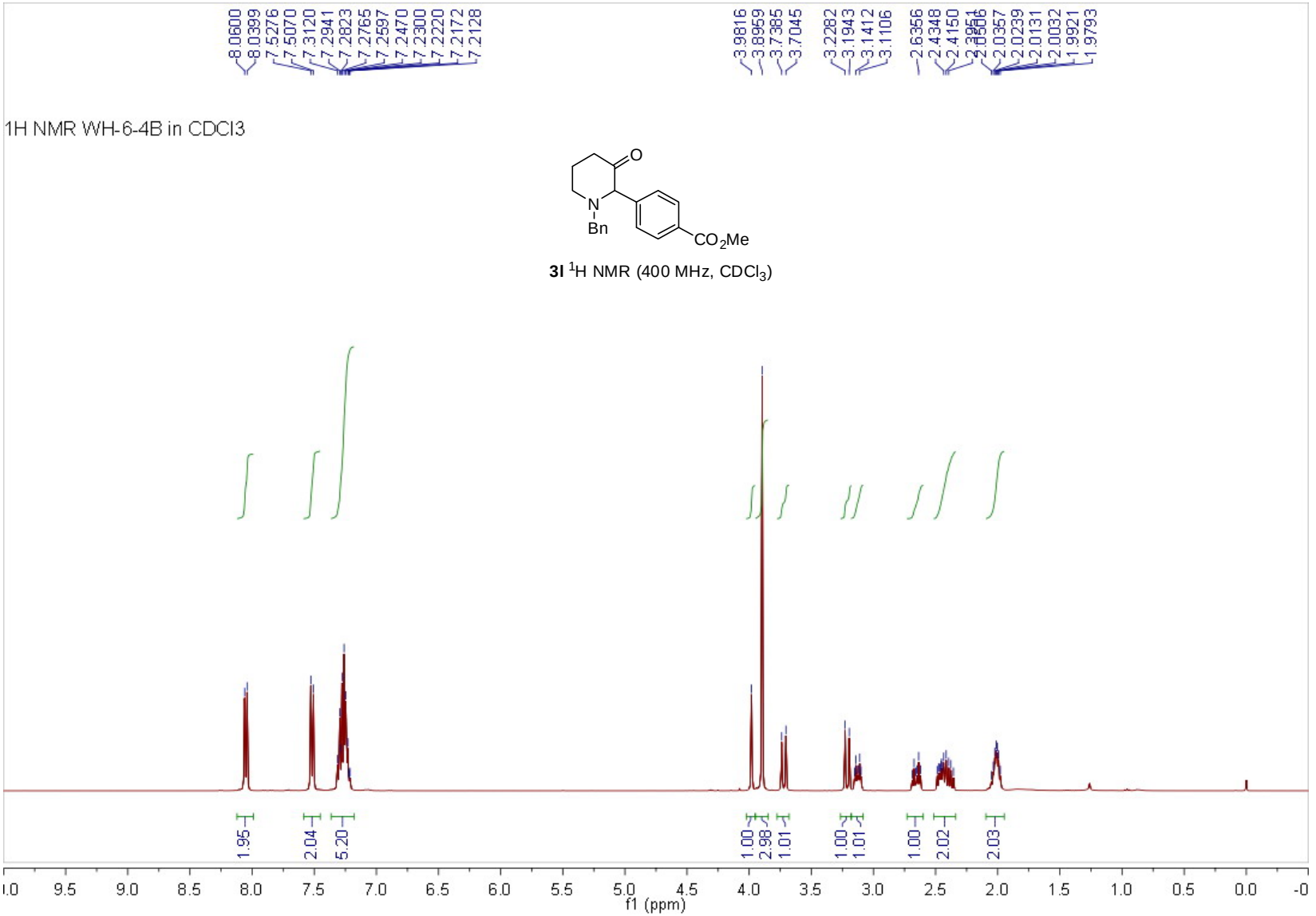
3k ^{1}H NMR (400 MHz, $CDCl_3$)



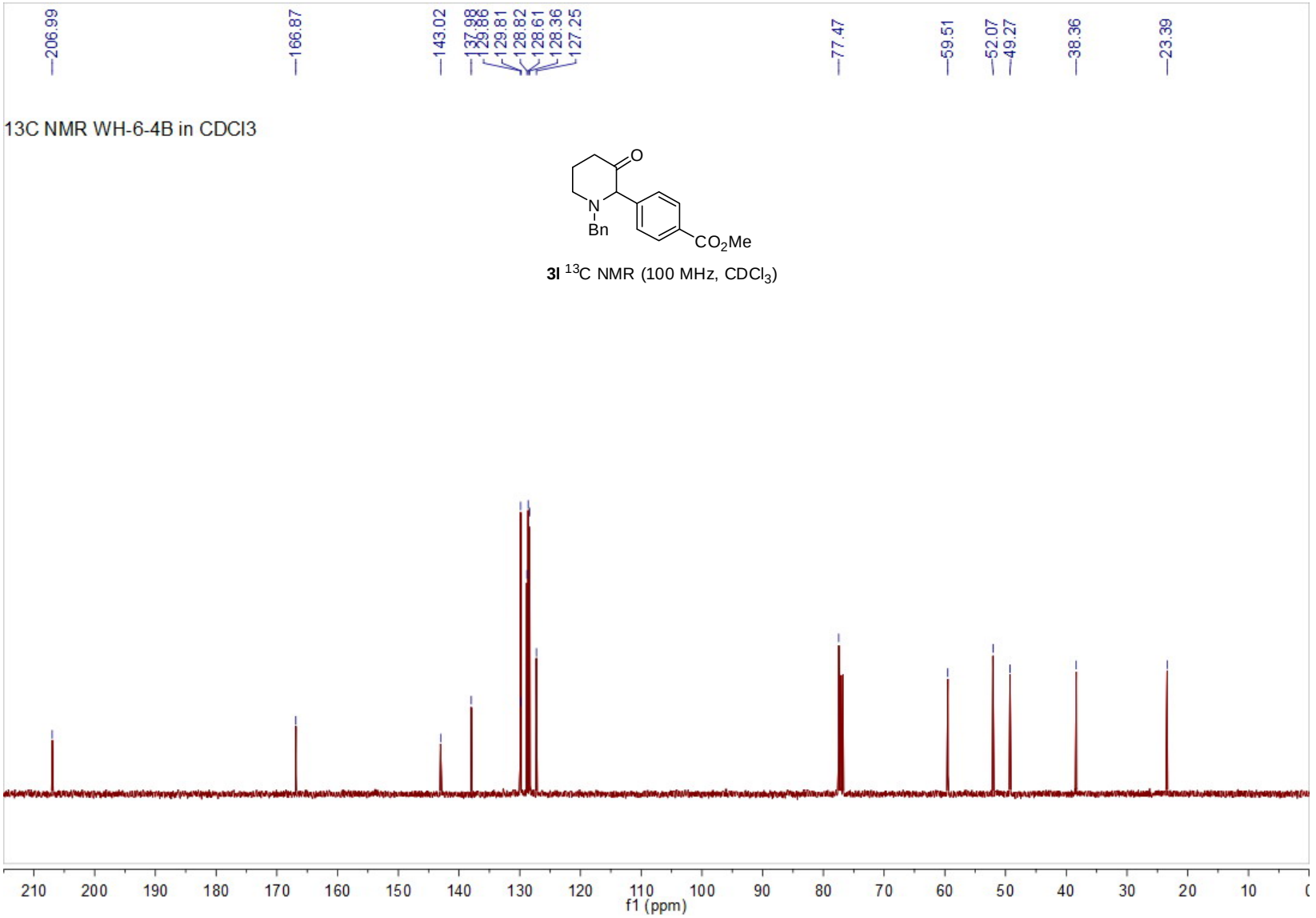
3k ^{13}C NMR (100 MHz, $CDCl_3$)



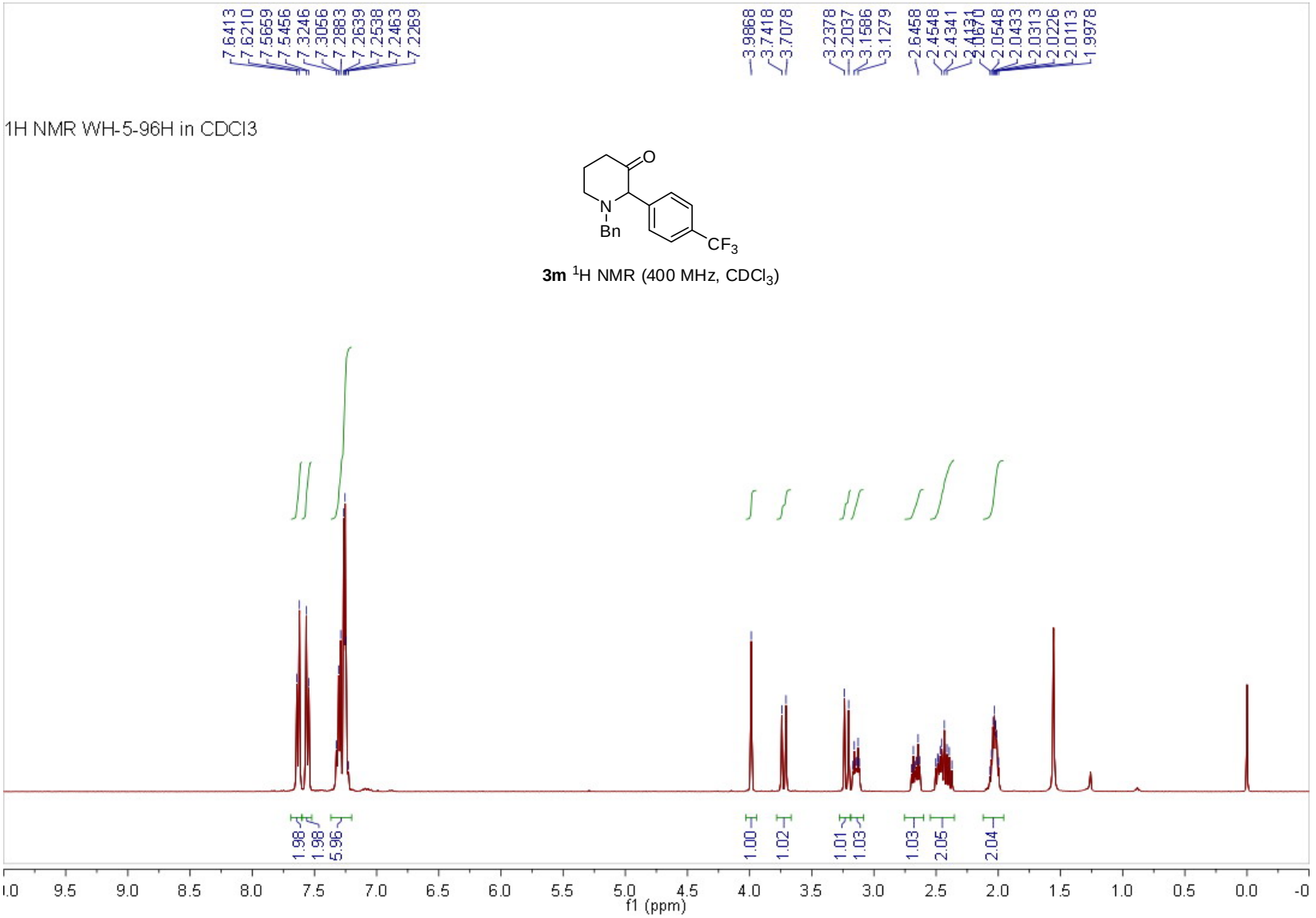
3k ^{19}F NMR (376 MHz, $CDCl_3$)



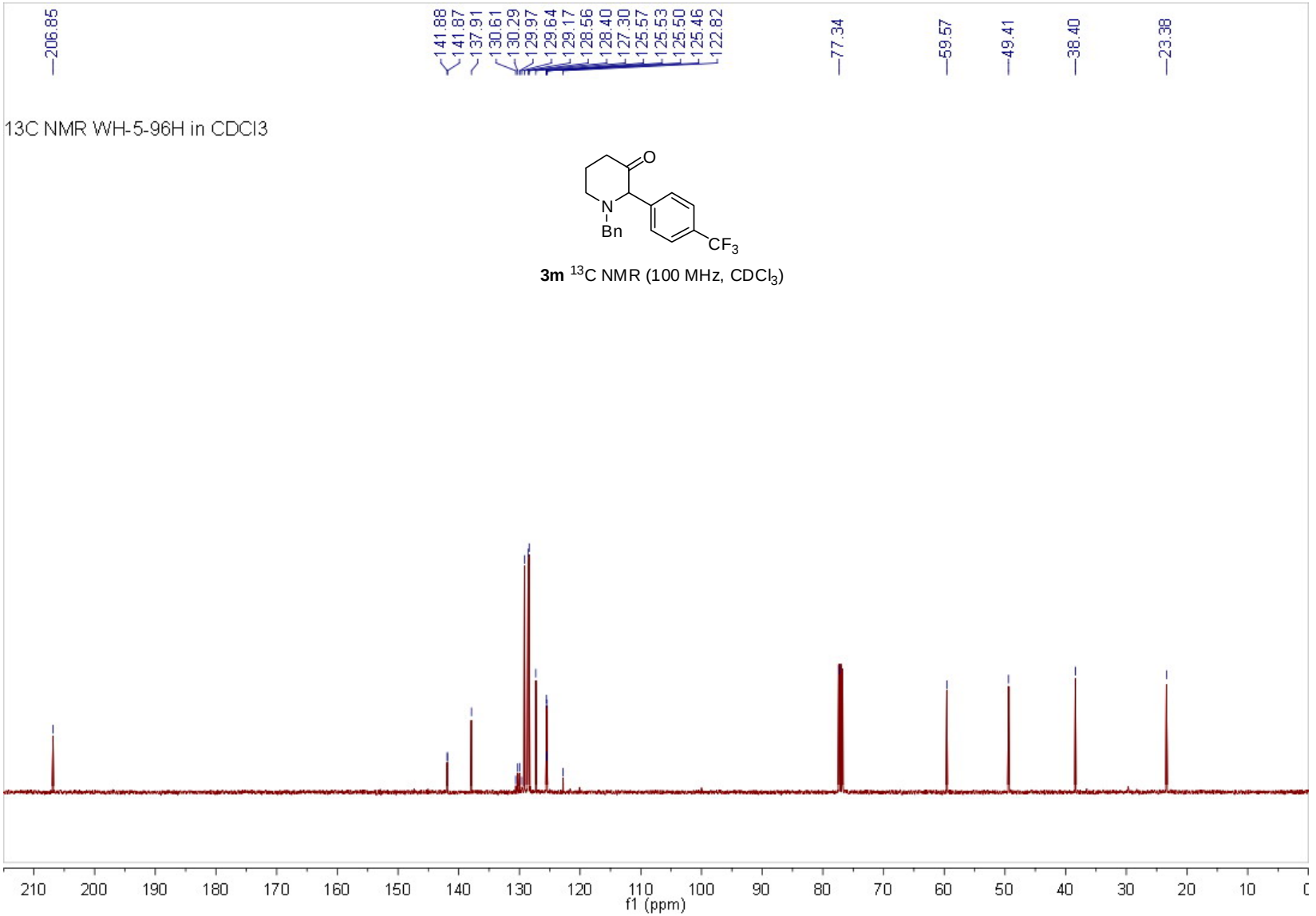
3l ^{1}H NMR (400 MHz, $CDCl_3$)



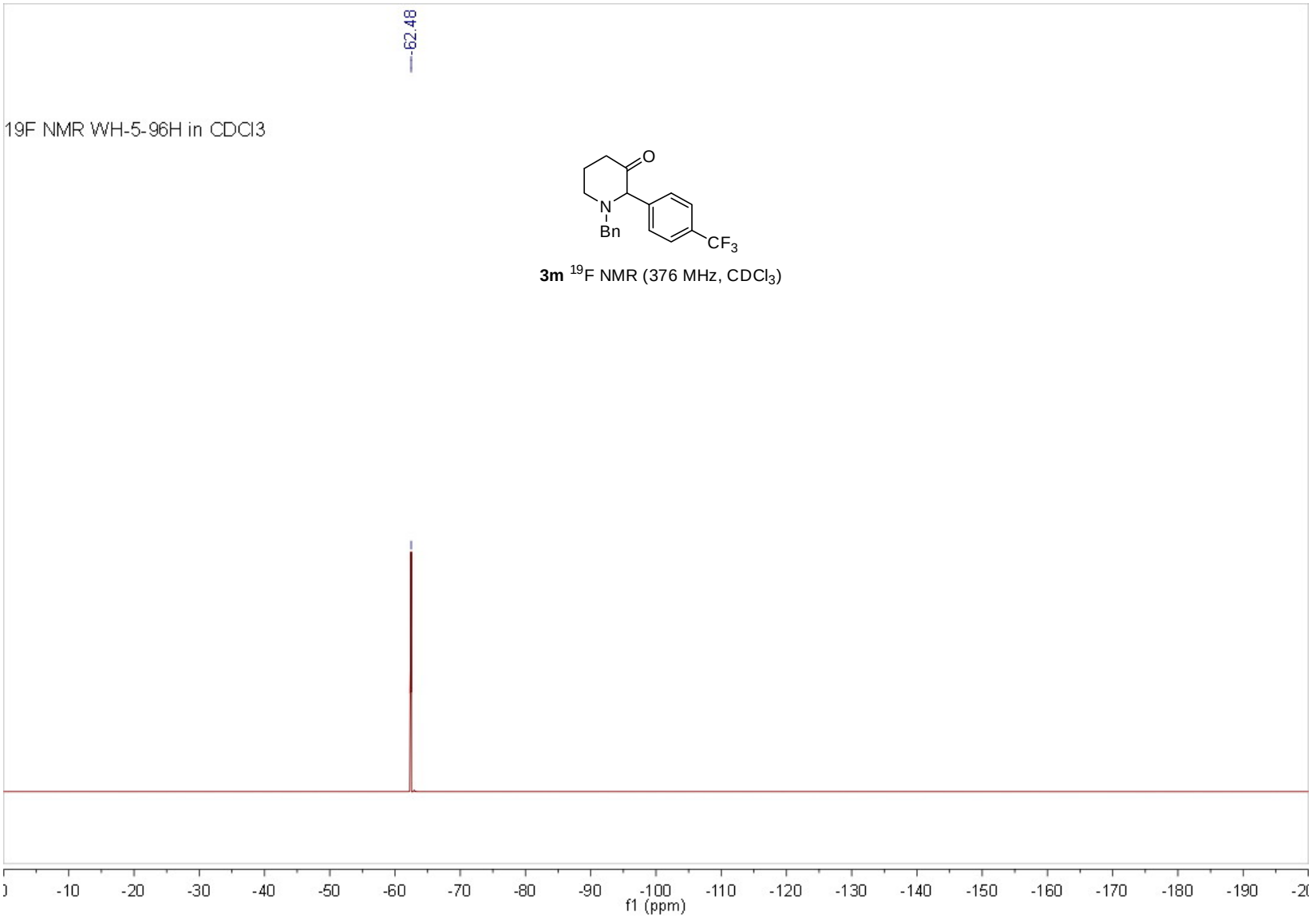
3l ^{13}C NMR (100 MHz, $CDCl_3$)



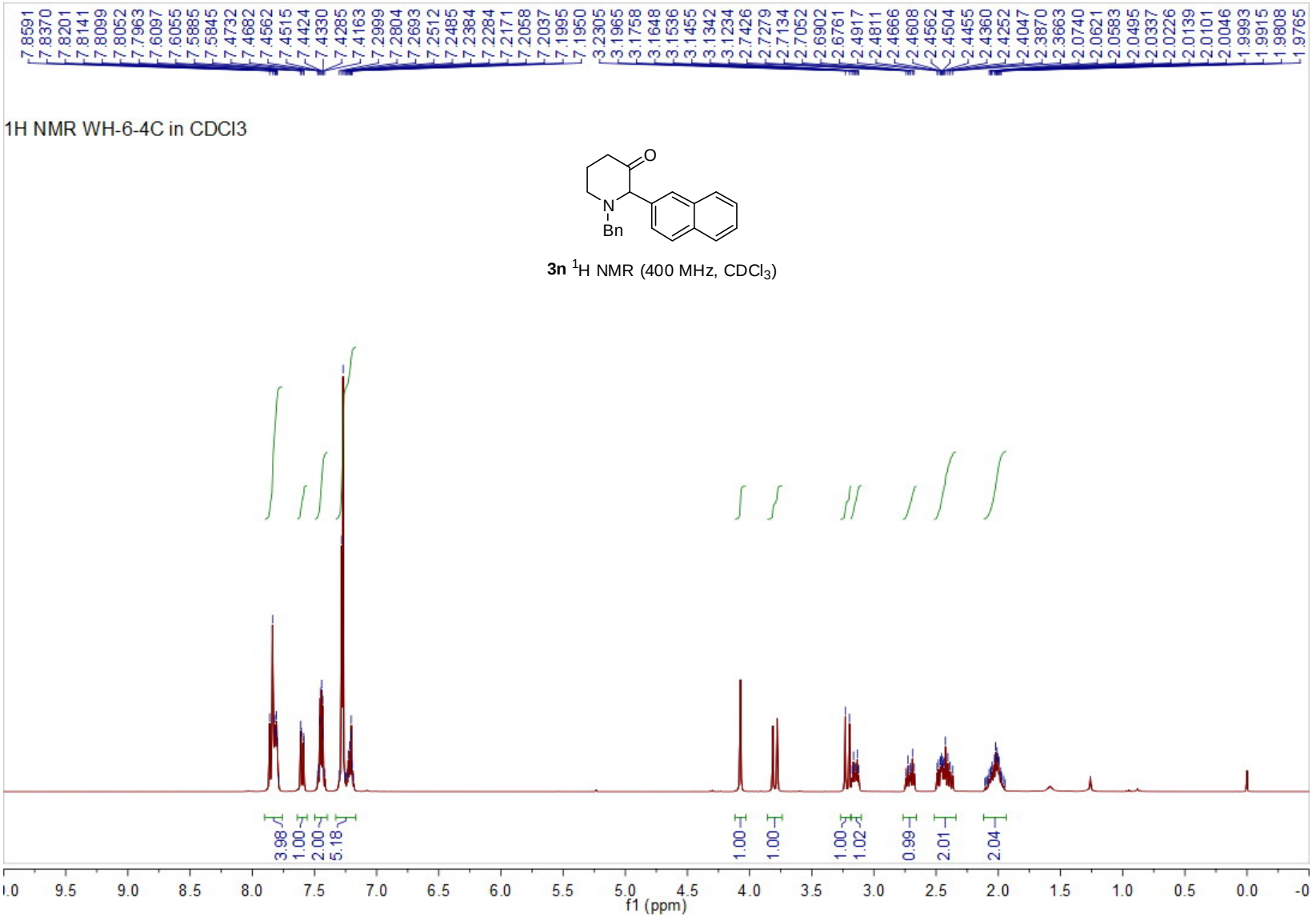
3m ^{1}H NMR (400 MHz, $CDCl_3$)



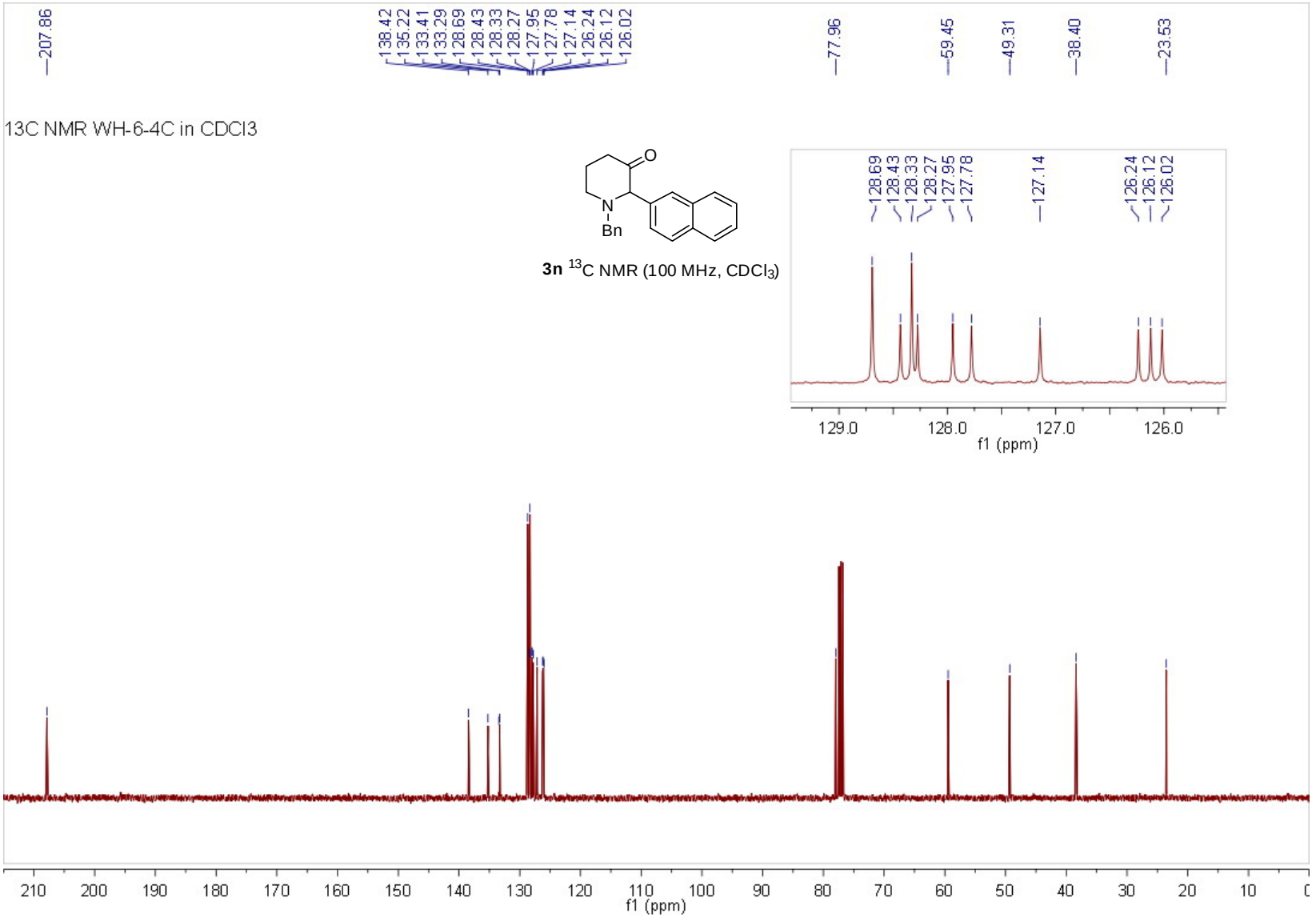
3m ^{13}C NMR (100 MHz, $CDCl_3$)

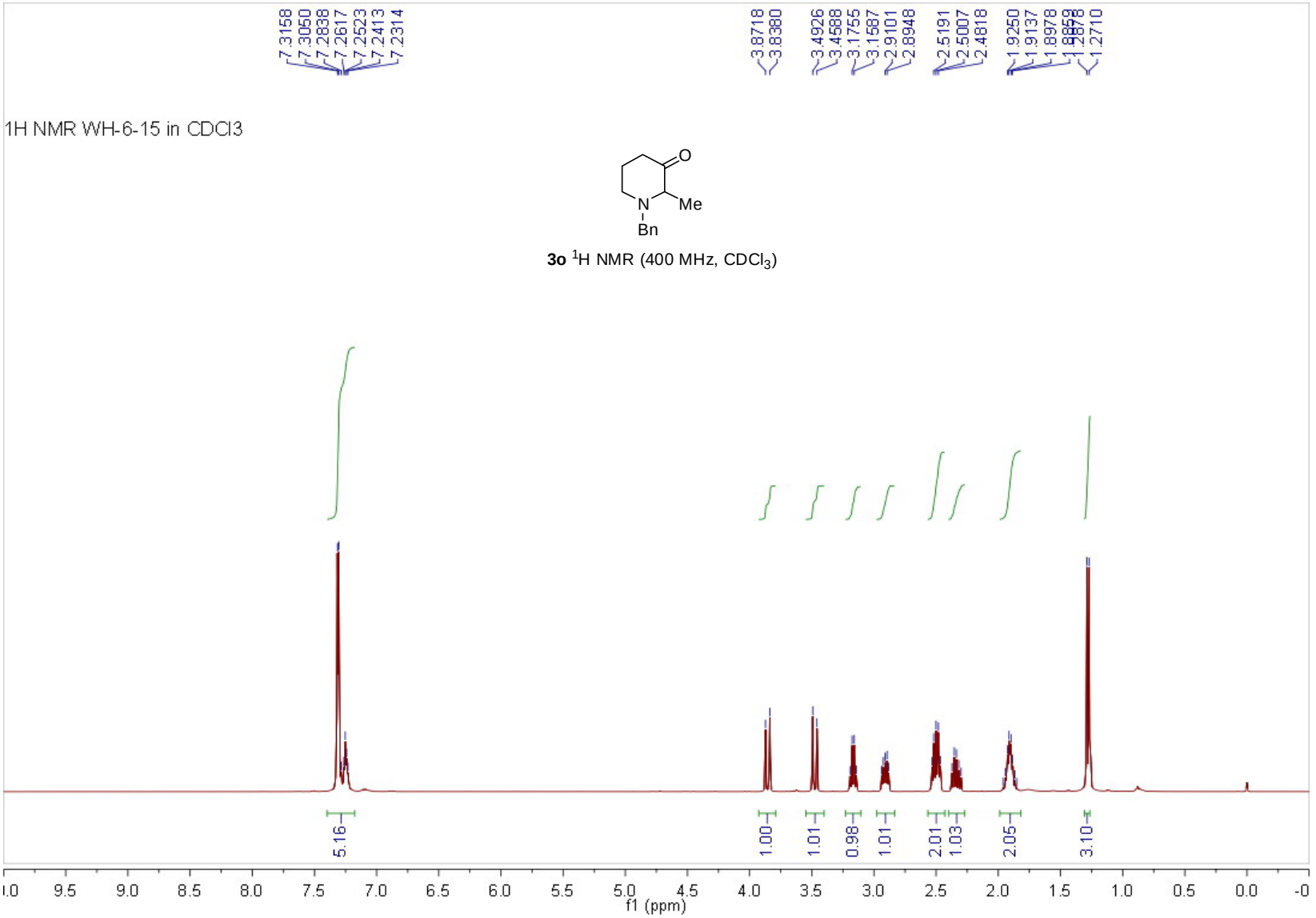


3m ^{19}F NMR (376 MHz, $CDCl_3$)

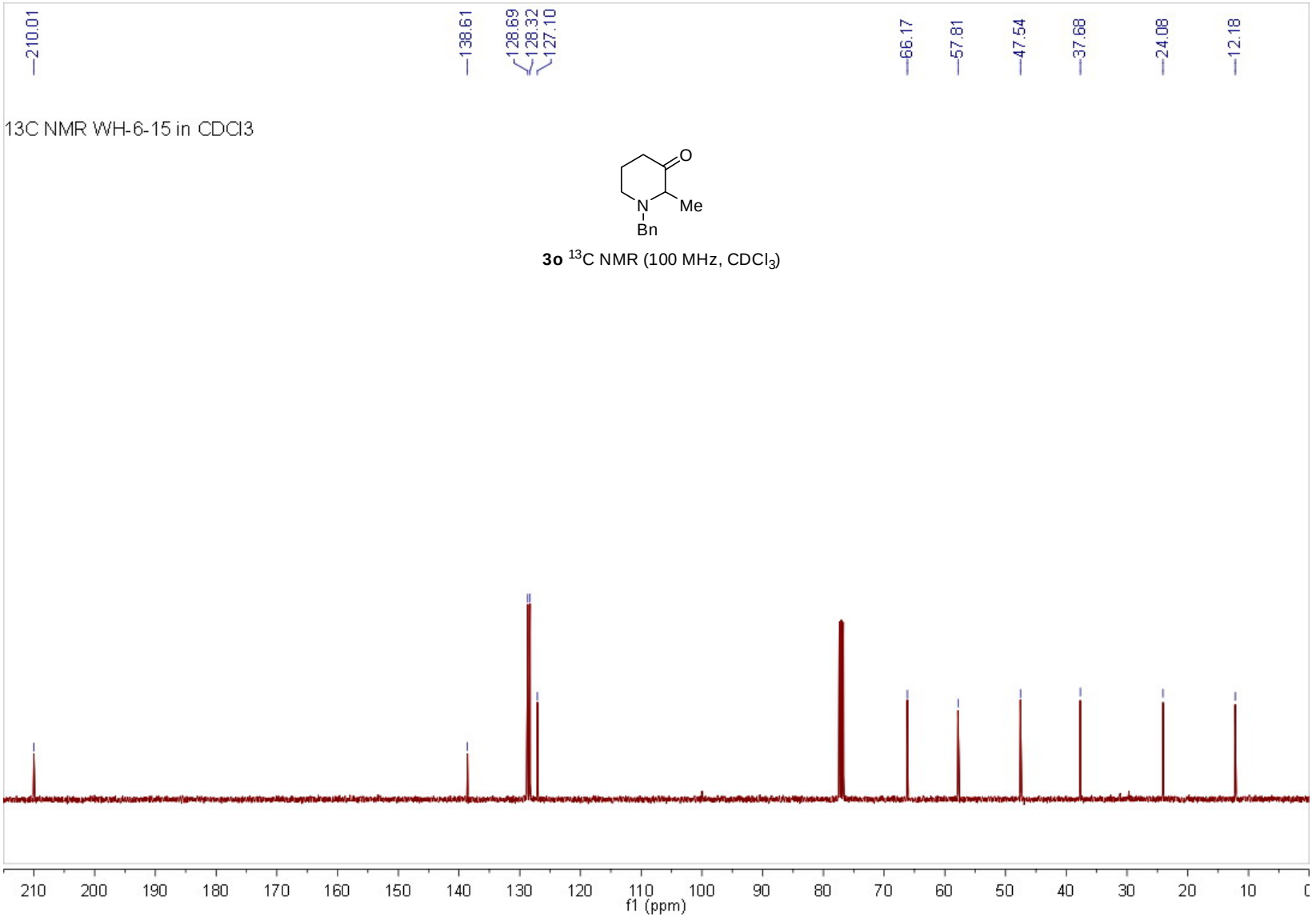


3n ^{1}H NMR (400 MHz, $CDCl_3$)

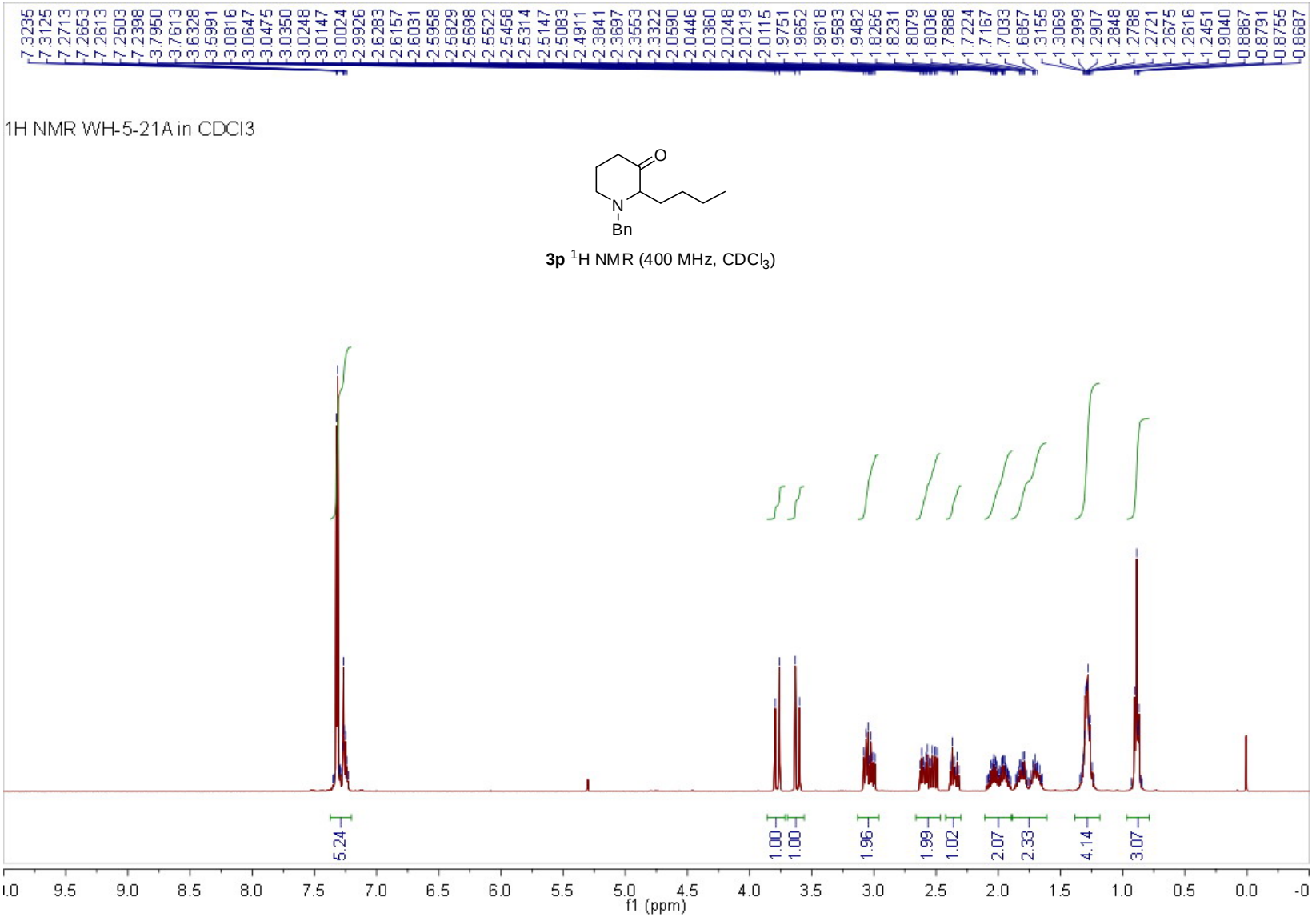

207.86
138.42
135.22
133.41
133.29
128.69
128.43
128.33
128.27
127.95
127.78
127.14
126.24
126.12
126.02
77.96
59.45
49.31
38.40
23.53
13C NMR WH-6-4C in CDCl3
O
N
Bn
3n 13C NMR (100 MHz, CDCl3)
128.69
128.43
128.33
128.27
127.95
127.78
127.14
126.24
126.12
126.02
129.0
128.0
127.0
126.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



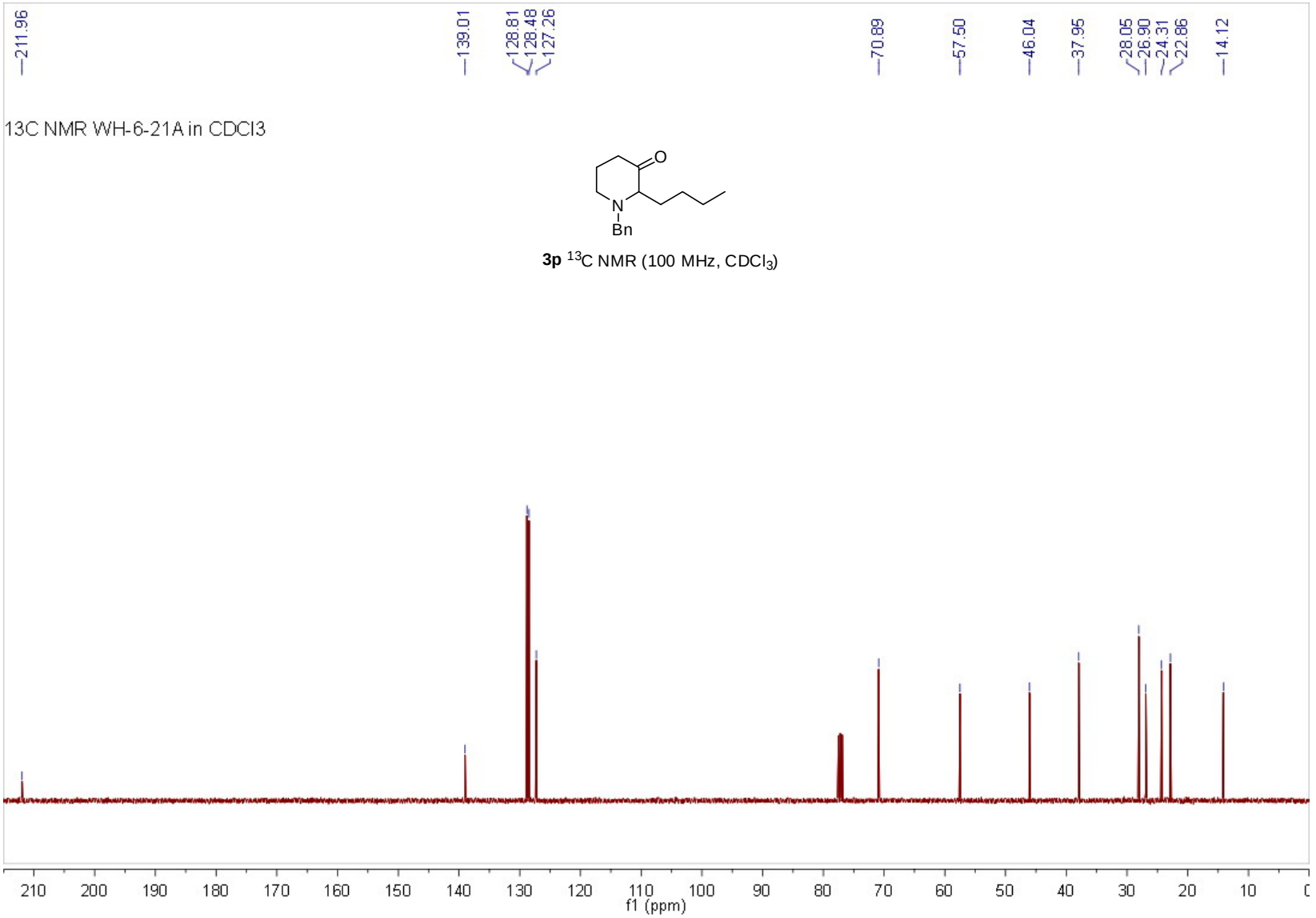
3o ^{1}H NMR (400 MHz, $CDCl_3$)



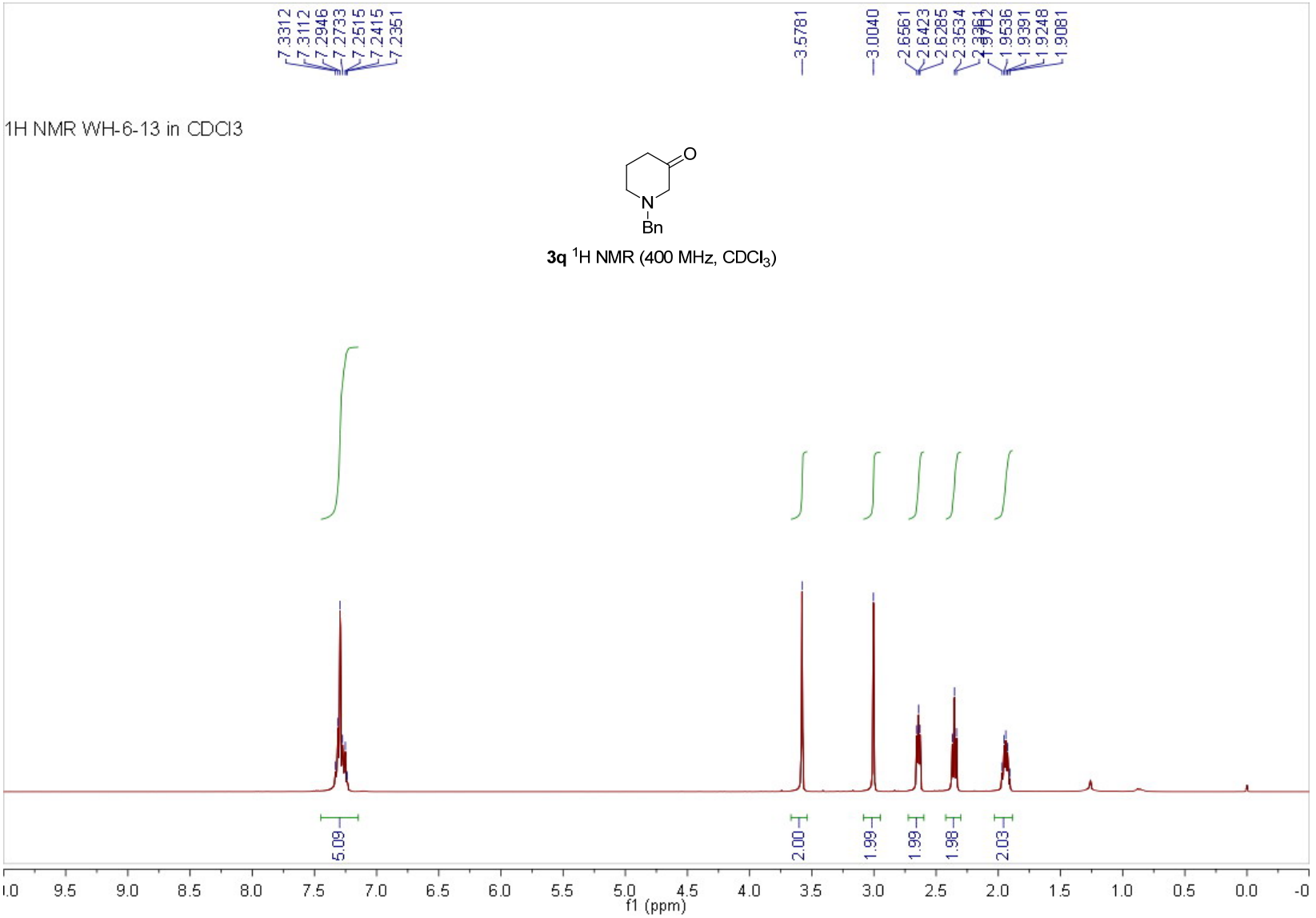
3o ^{13}C NMR (100 MHz, $CDCl_3$)



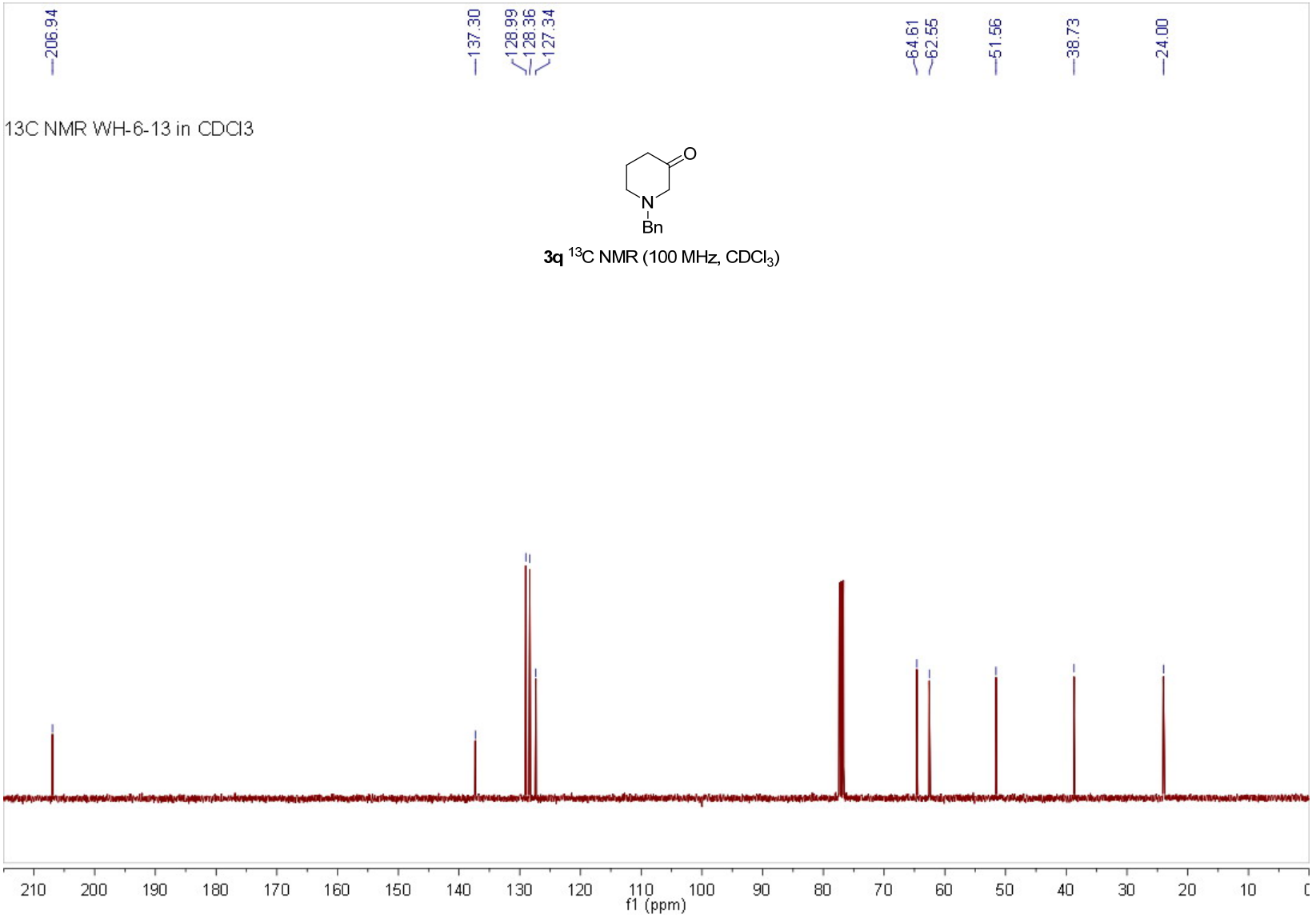
3p ^{1}H NMR (400 MHz, $CDCl_3$)



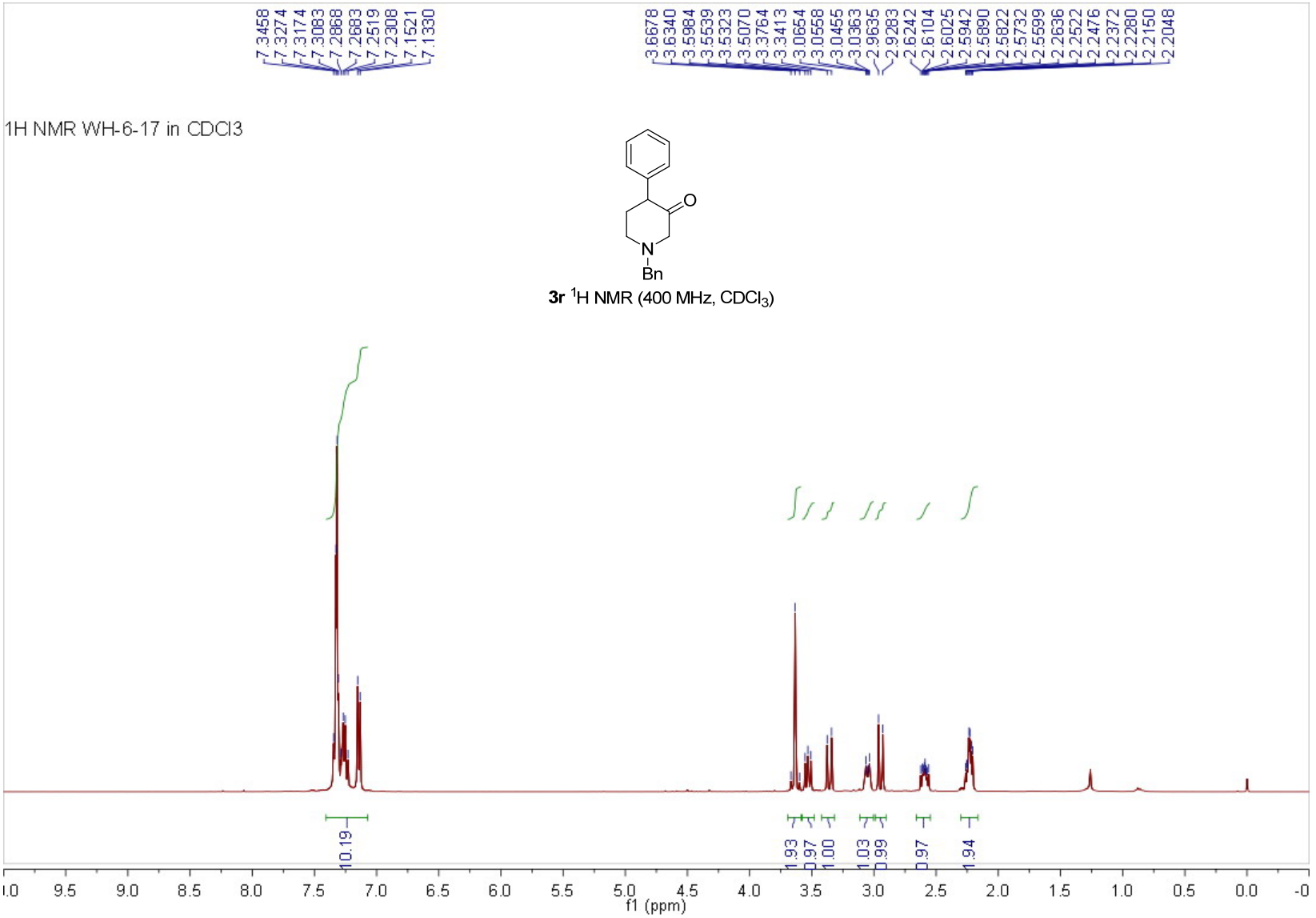
3p ^{13}C NMR (100 MHz, $CDCl_3$)



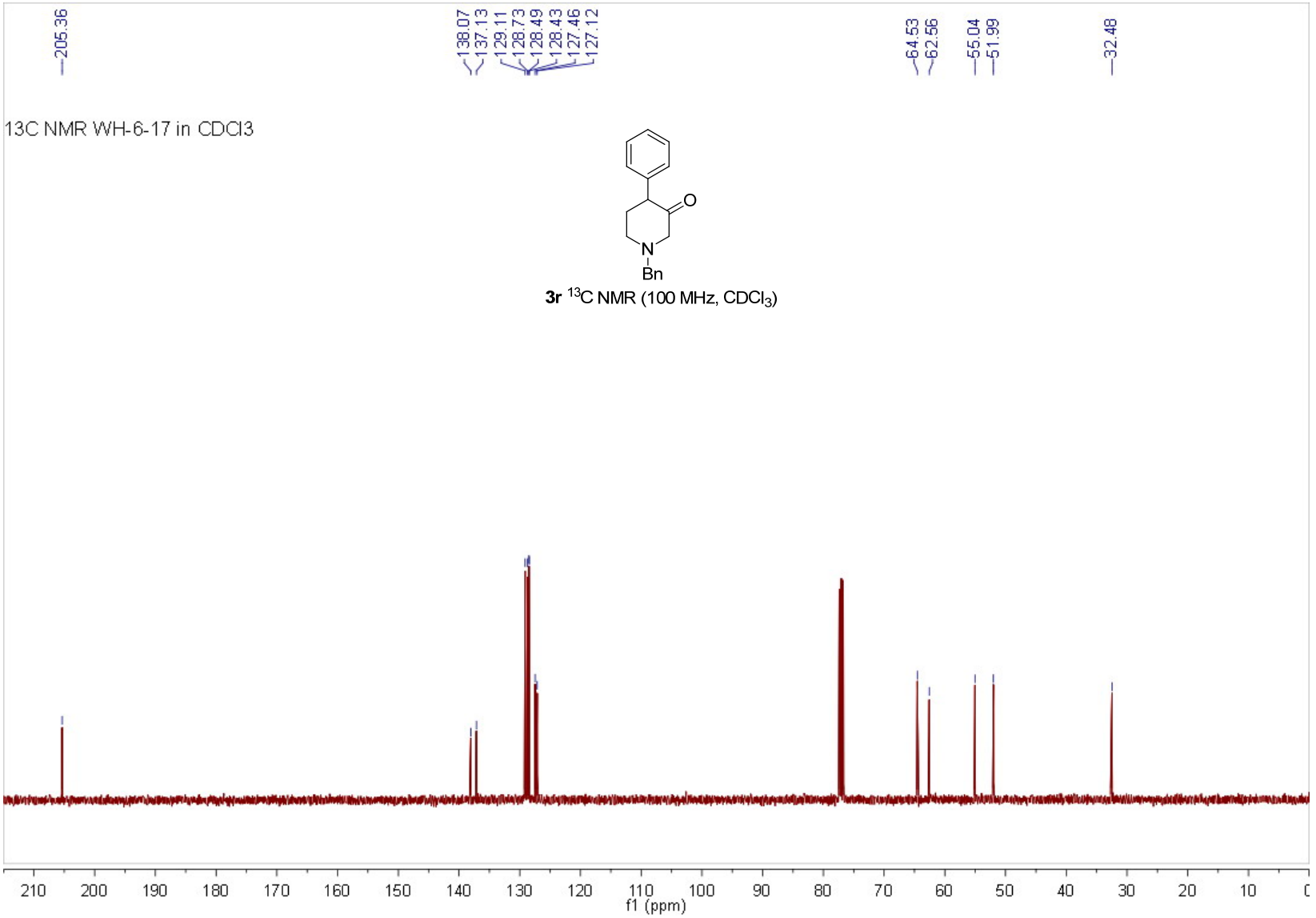
3q ^{1}H NMR (400 MHz, $CDCl_3$)



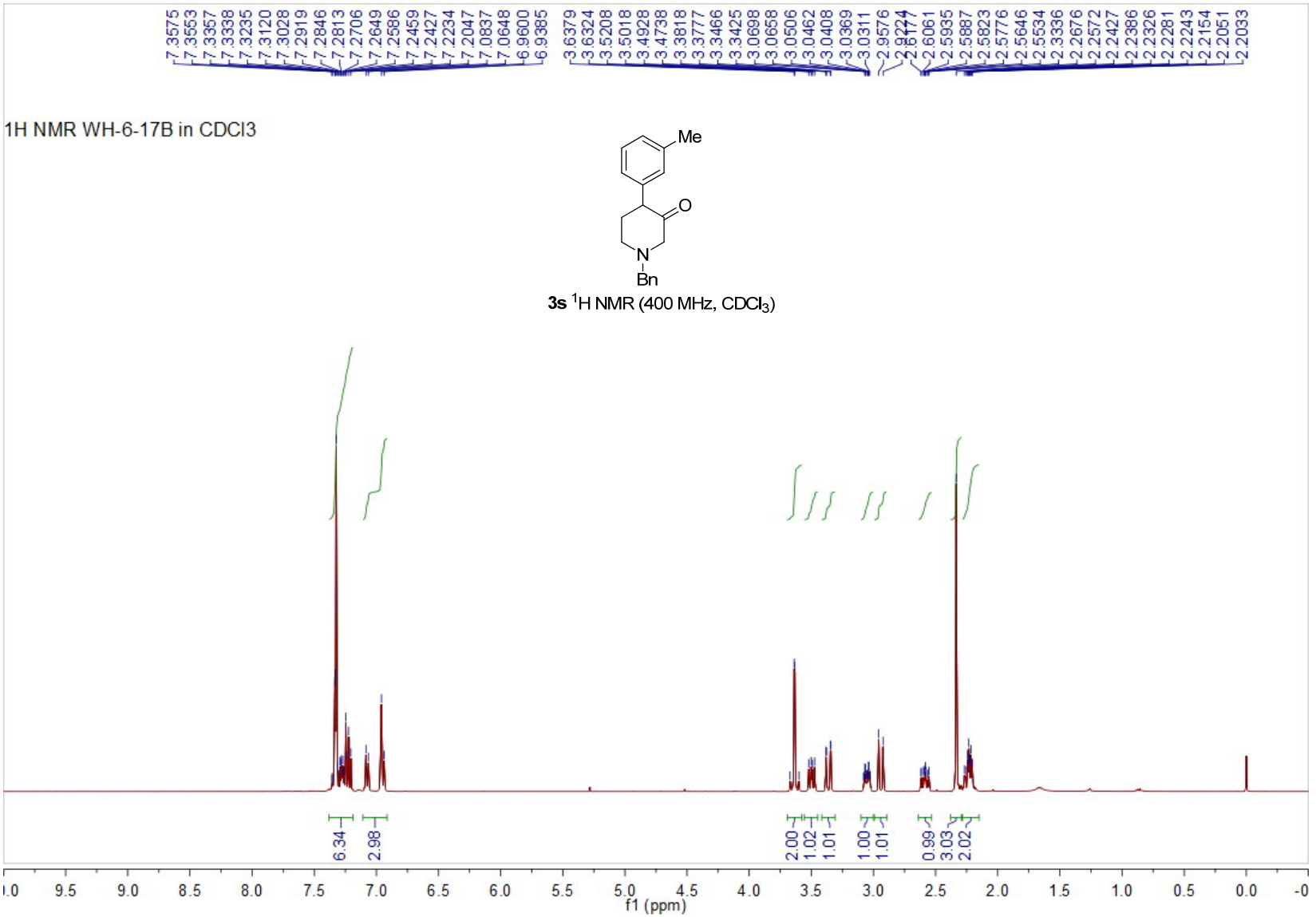
3q ^{13}C NMR (100 MHz, $CDCl_3$)



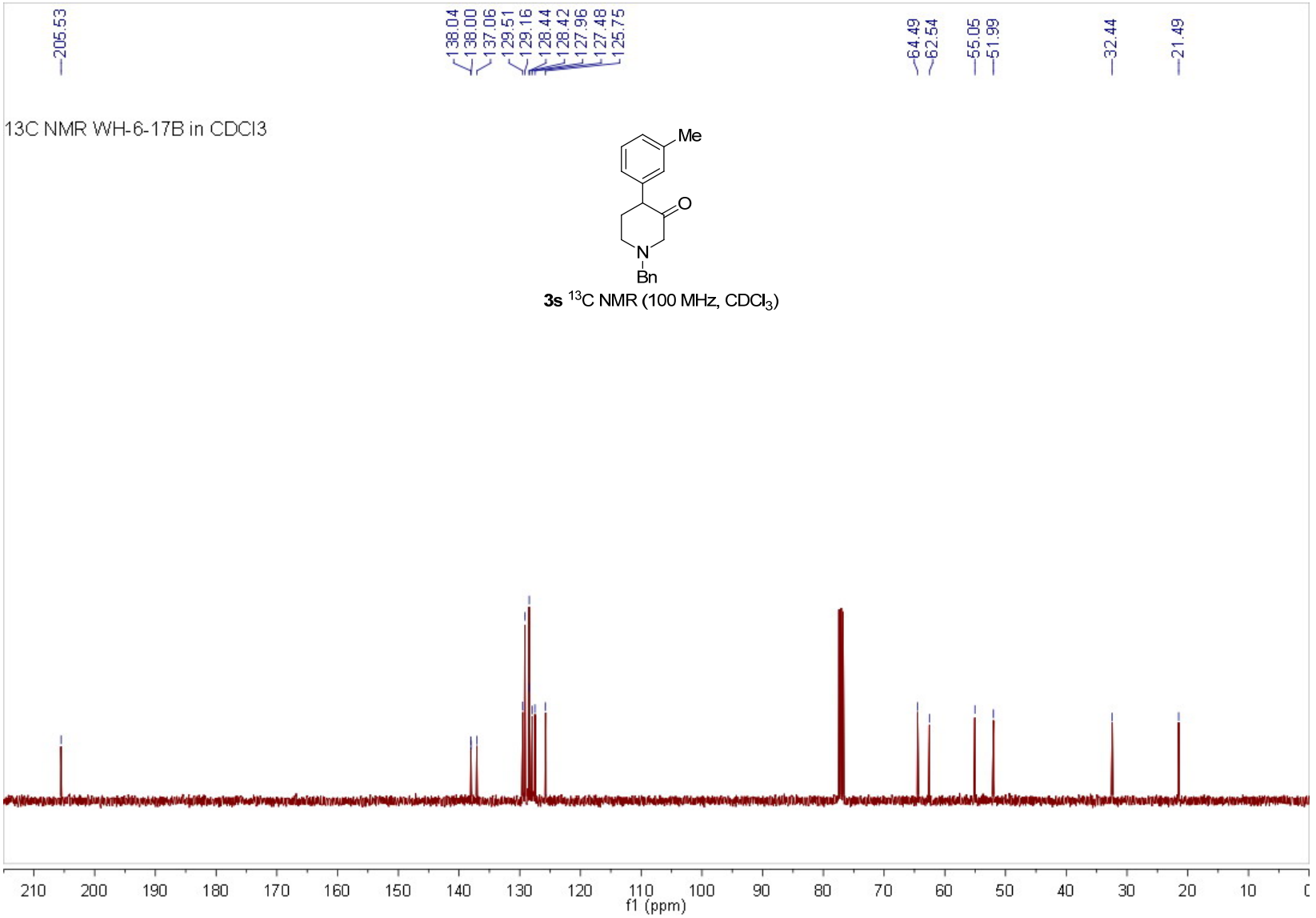
3r ^{1}H NMR (400 MHz, $CDCl_3$)



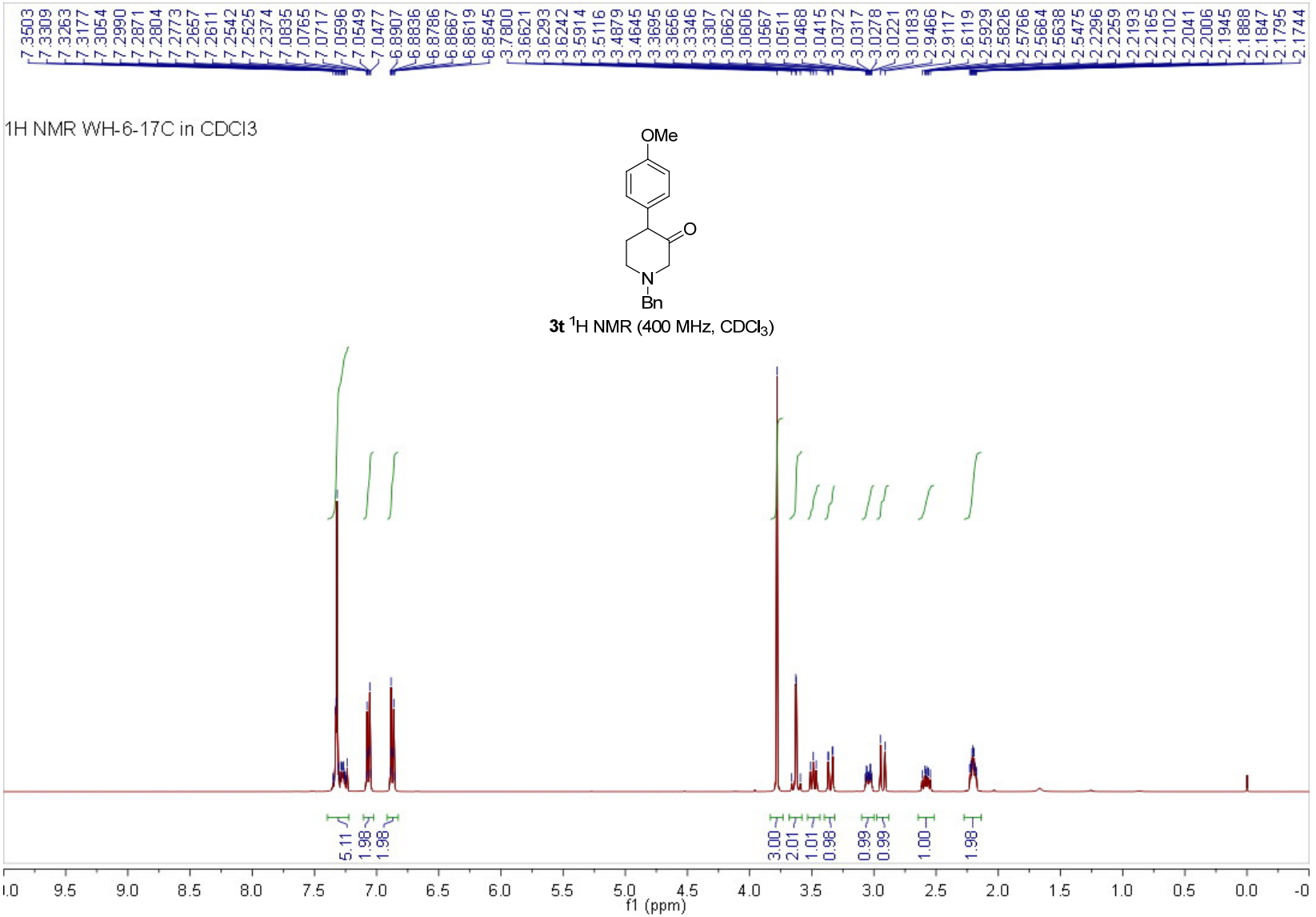
3r ^{13}C NMR (100 MHz, $CDCl_3$)



3s ^{1}H NMR (400 MHz, $CDCl_3$)



3s ^{13}C NMR (100 MHz, $CDCl_3$)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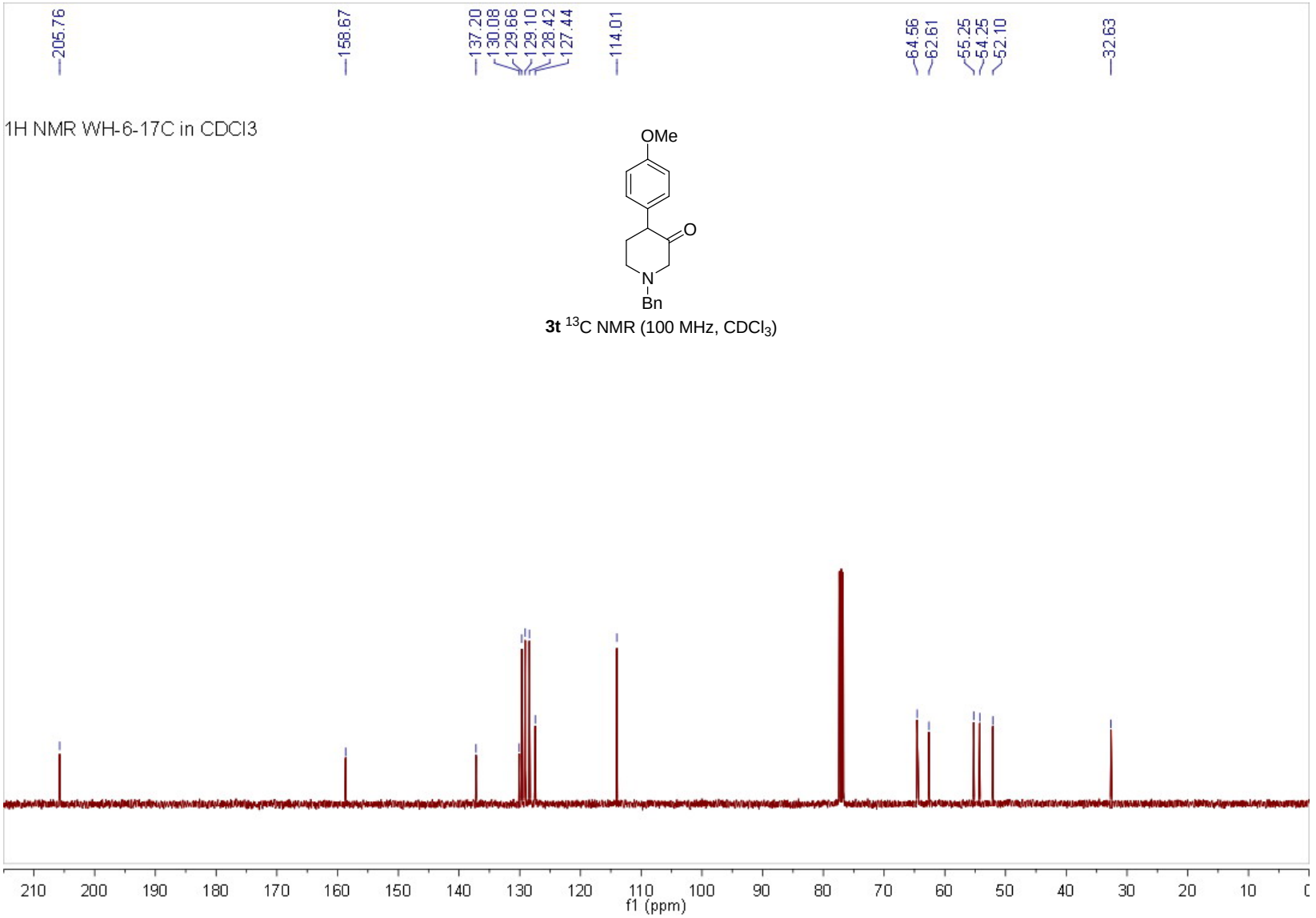
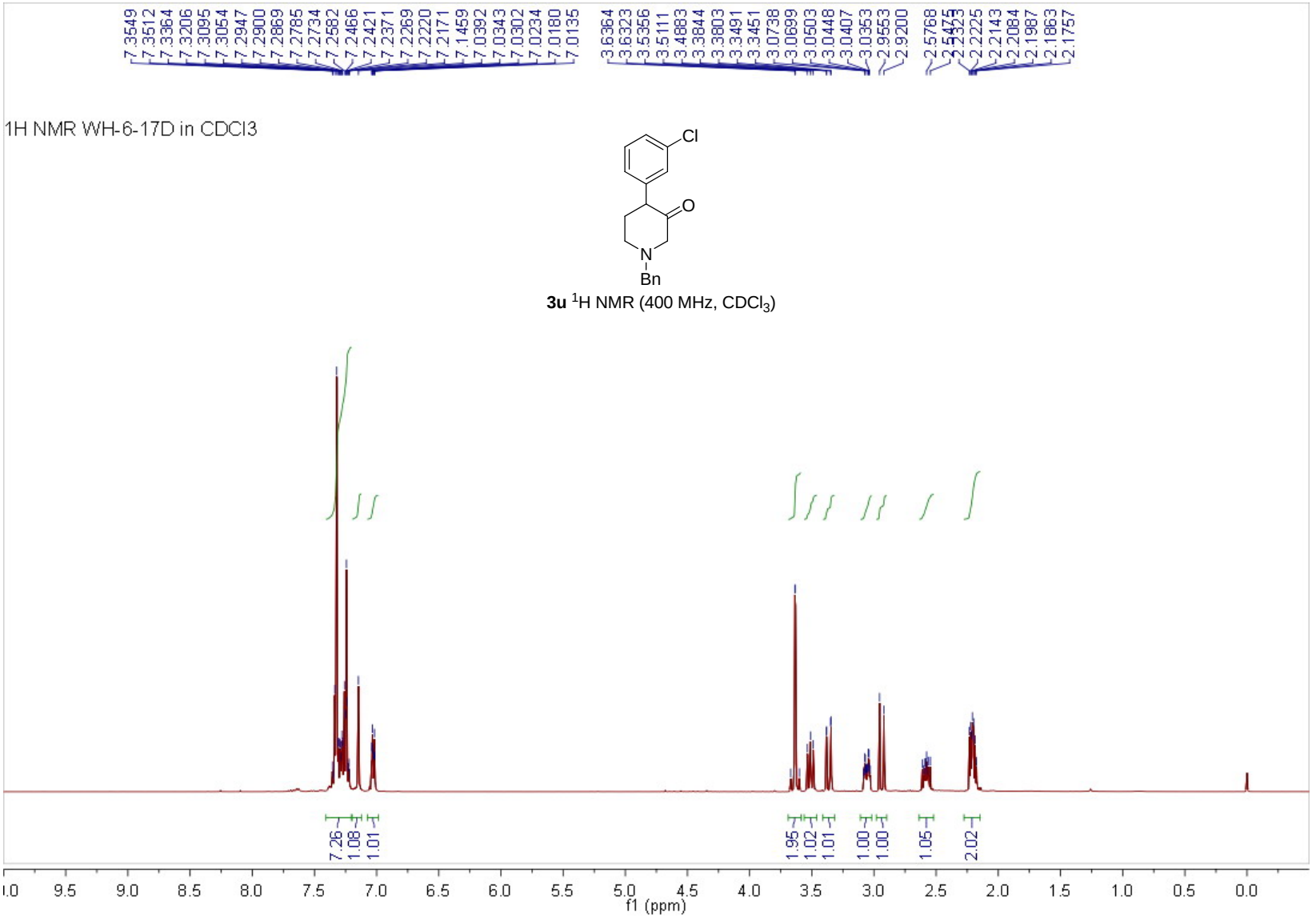
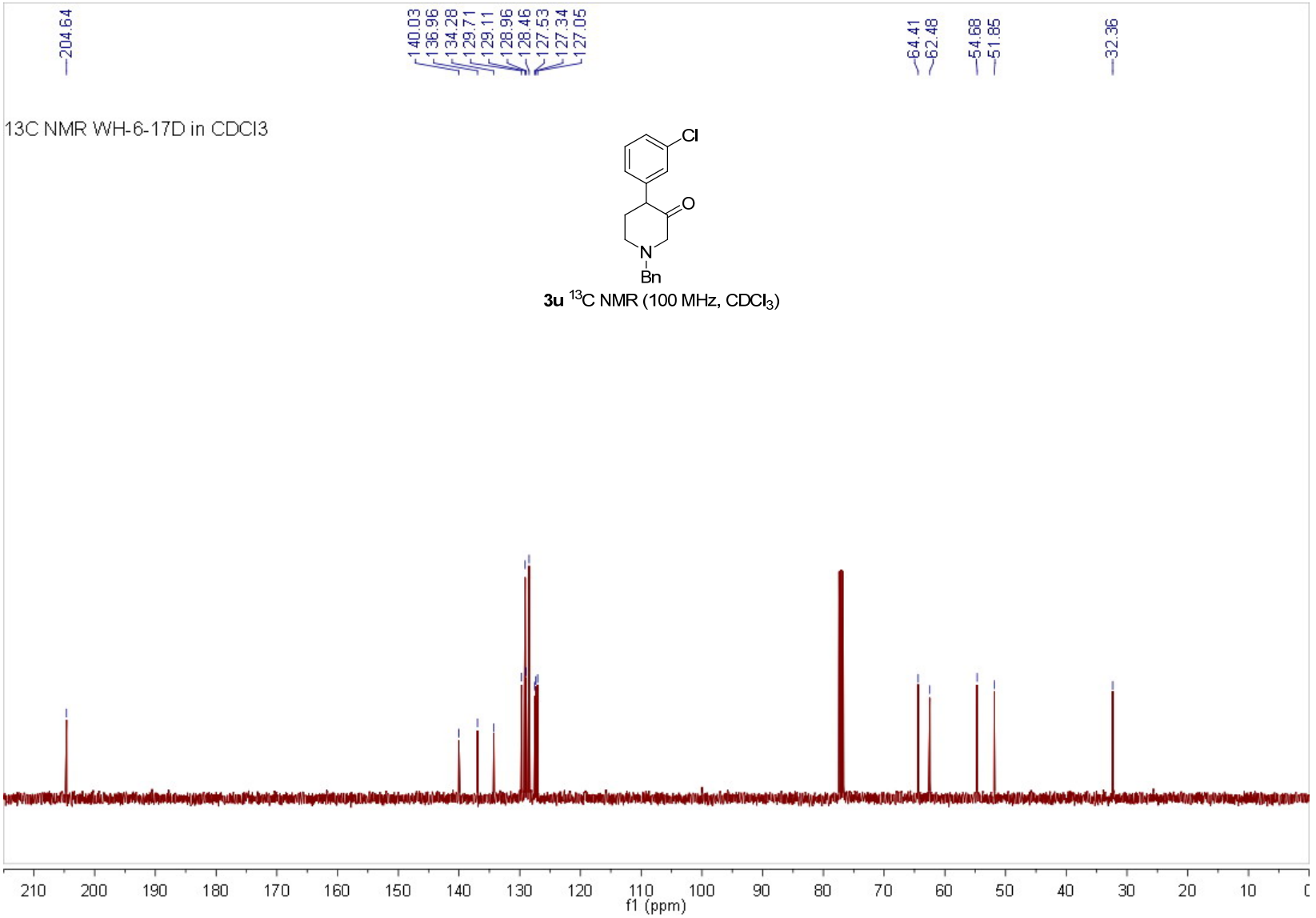
7.3309
7.3263
7.3177
7.3054
7.2990
7.2871
7.2804
7.2773
7.2657
7.2611
7.2542
7.2525
7.2374
7.0835
7.0765
7.0717
7.0596
7.0549
7.0477
6.8907
6.8836
6.8786
6.8667
6.8619
6.8545
3.7800
3.6621
3.6293
3.6242
3.5914
3.5116
3.4879
3.4645
3.3695
3.3656
3.3346
3.3307
3.0662
3.0606
3.0567
3.0511
3.0468
3.0415
3.0372
3.0317
3.0278
3.0221
3.0183
2.9466
2.9117
2.6119
2.5929
2.5826
2.5766
2.5664
2.5638
2.5475
2.2296
2.2259
2.2193
2.2165
2.2102
2.2041
2.2006
2.1945
2.1888
2.1847
2.1795
2.1744
1H NMR WH-6-17C in CDCl3
OMe
O
N
Bn
3t 1H NMR (400 MHz, CDCl3)
5.11
1.98
1.98
3.00
2.01
1.01
0.98
0.99
0.99
1.00
1.98
f1 (ppm)



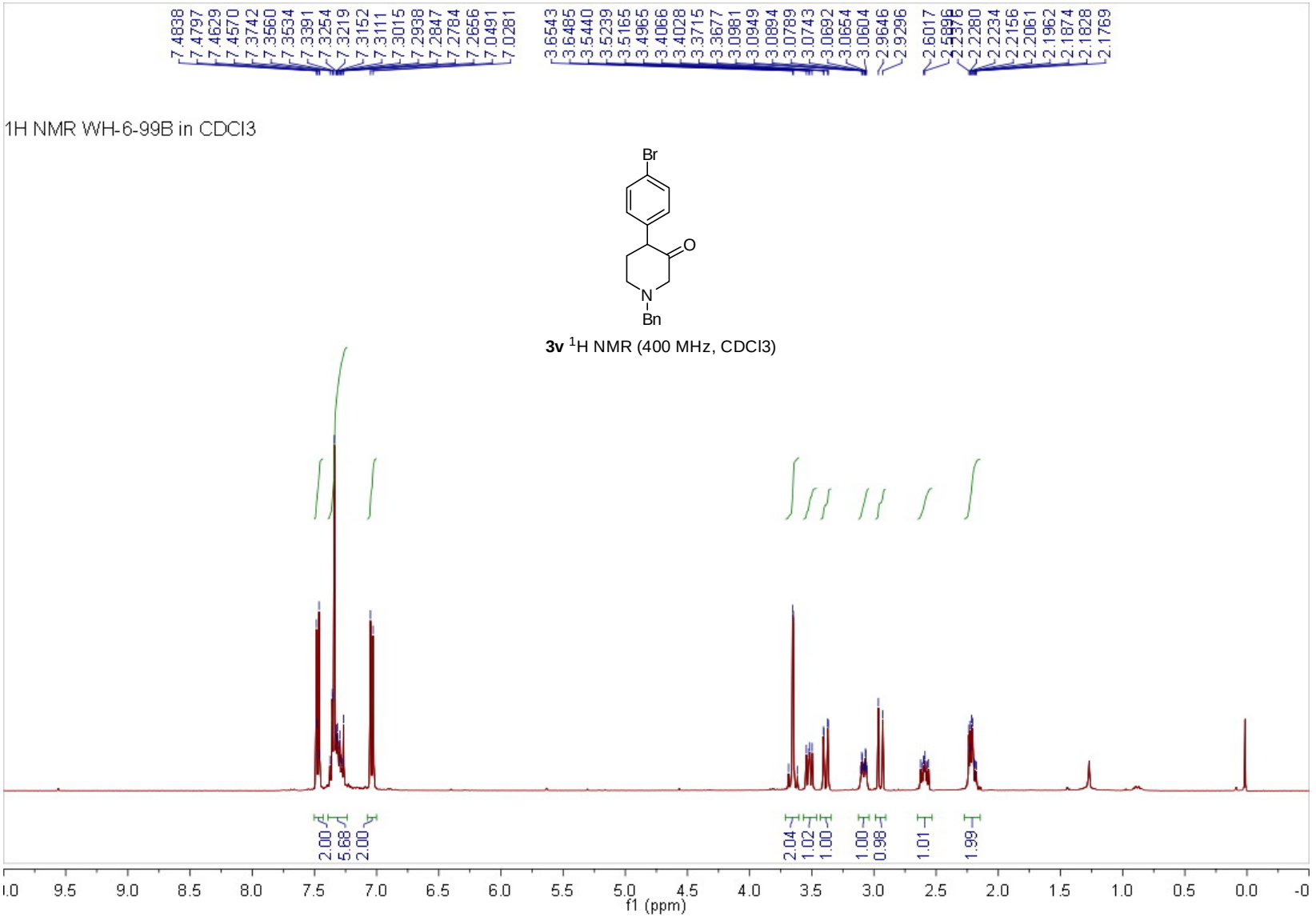
3t ^{13}C NMR (100 MHz, $CDCl_3$)



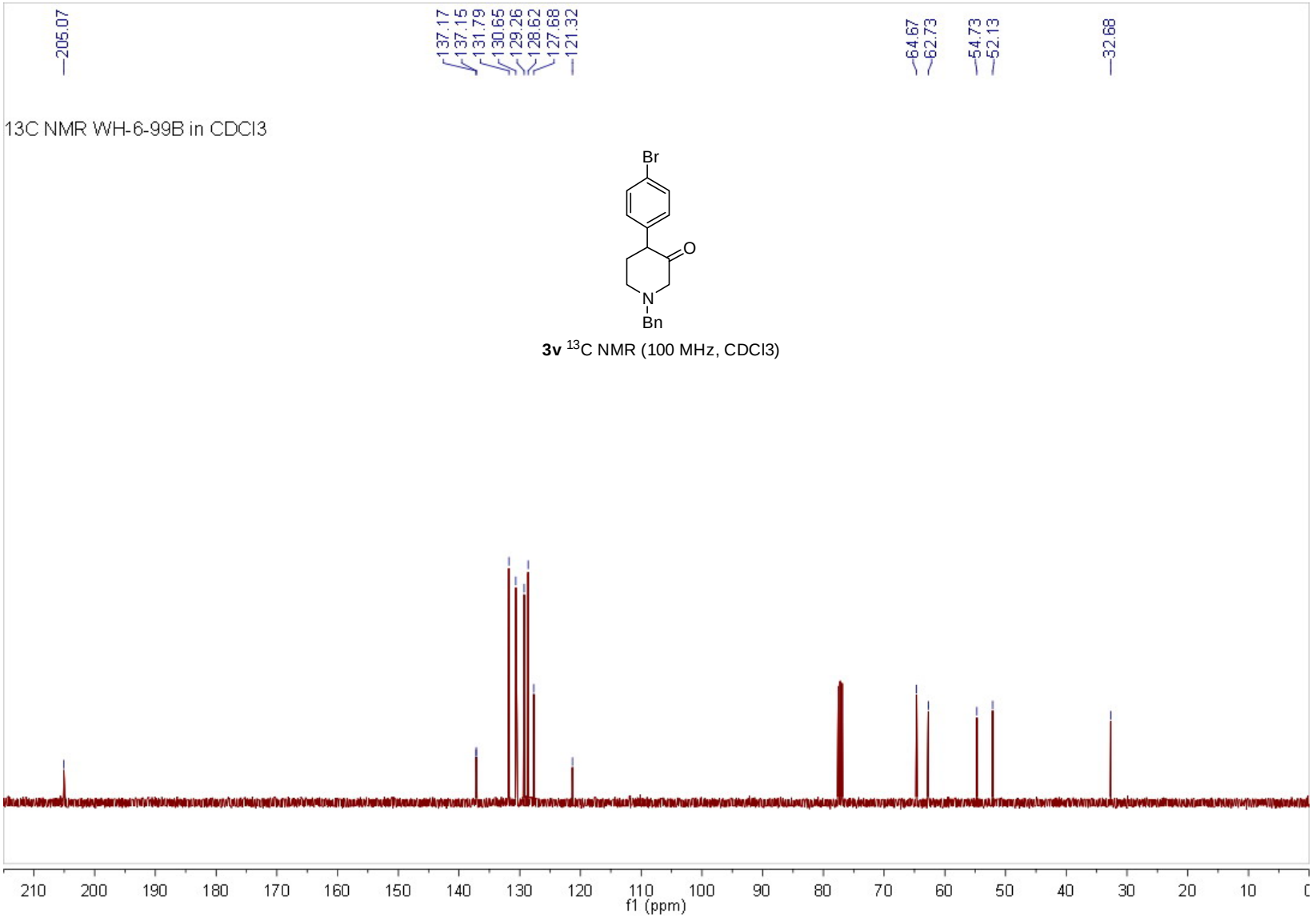
3u ^{1}H NMR (400 MHz, $CDCl_3$)



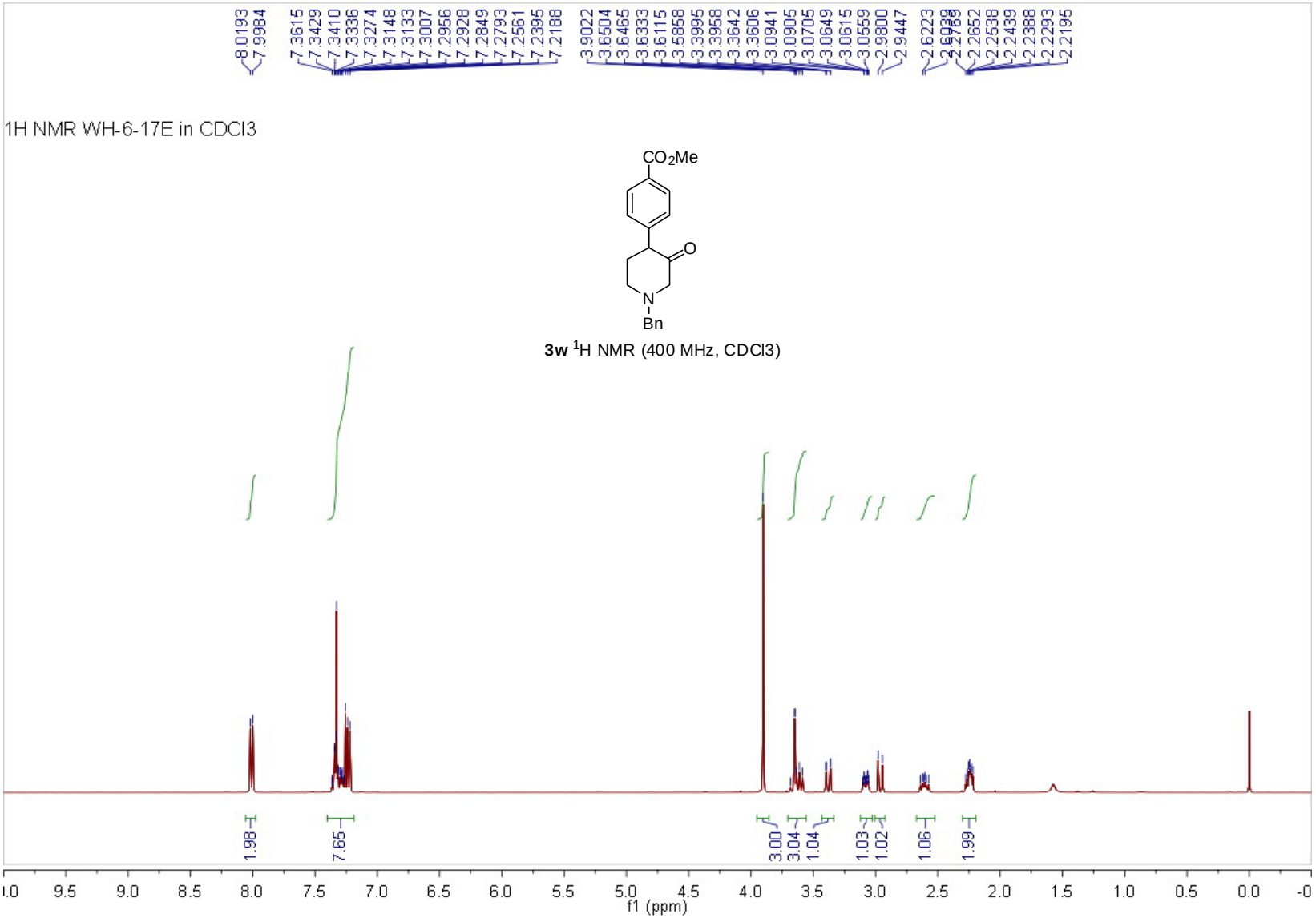
3u ^{13}C NMR (100 MHz, $CDCl_3$)



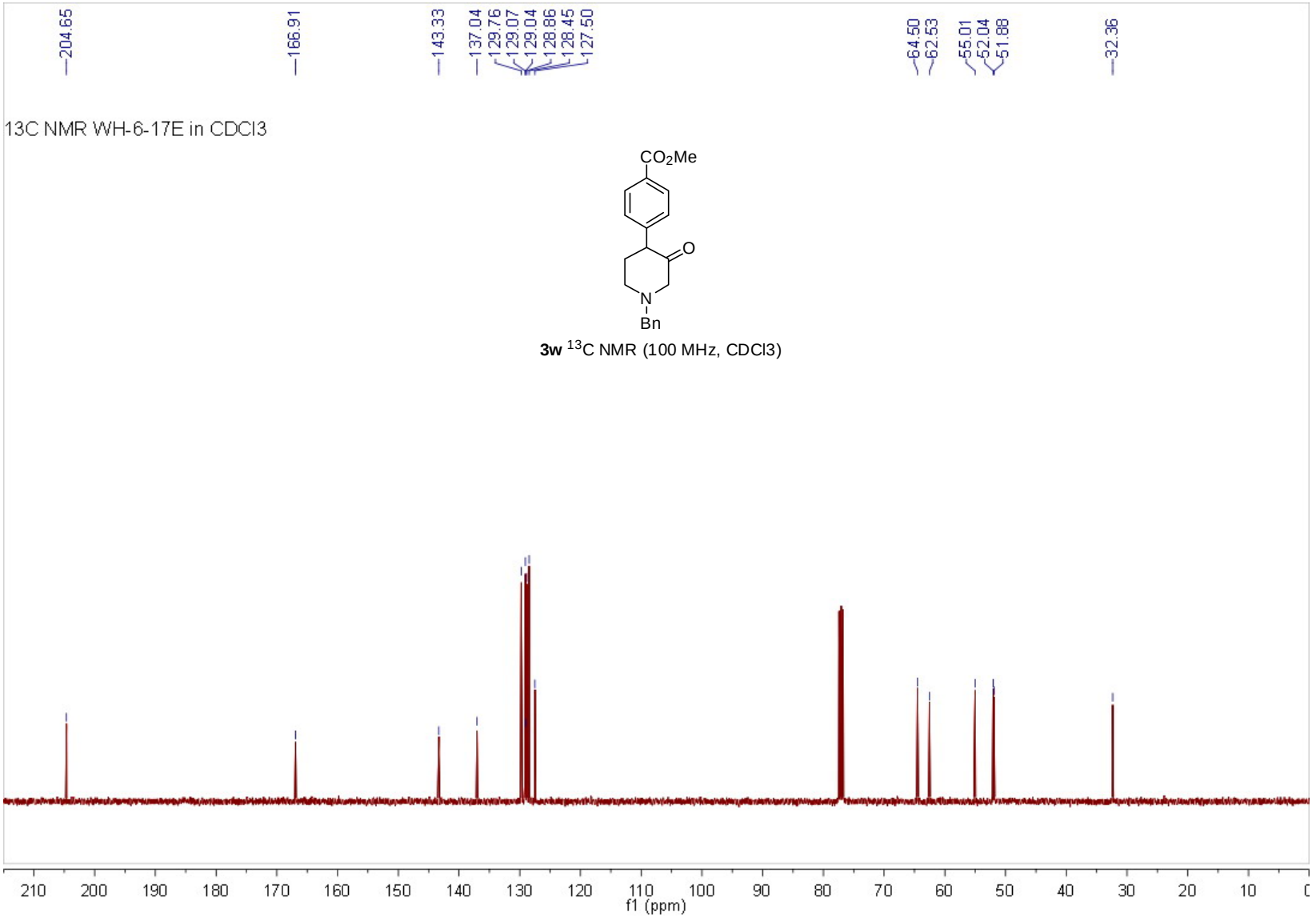
3v ^{1}H NMR (400 MHz, CDCl3)



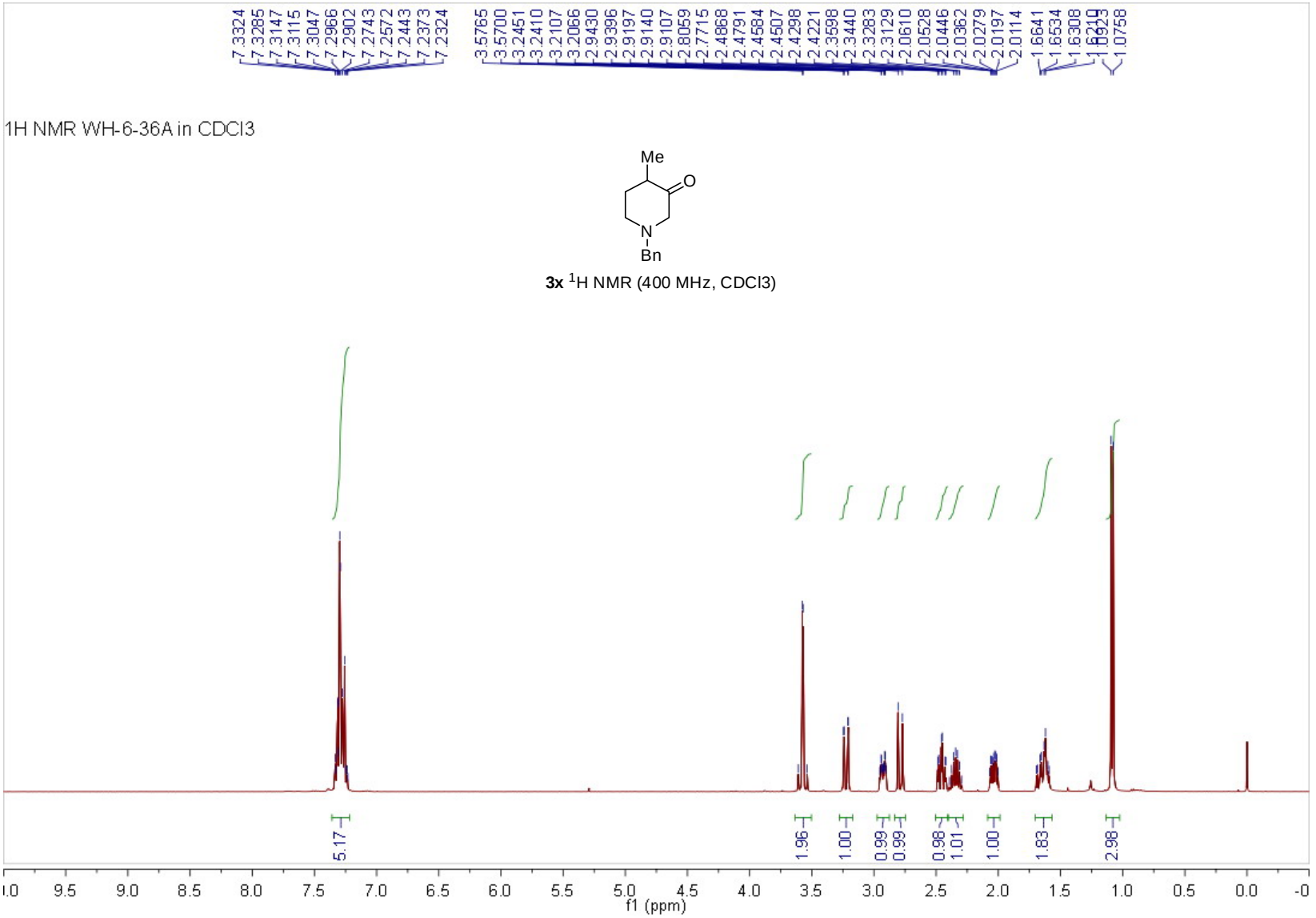
3v ^{13}C NMR (100 MHz, CDCl3)



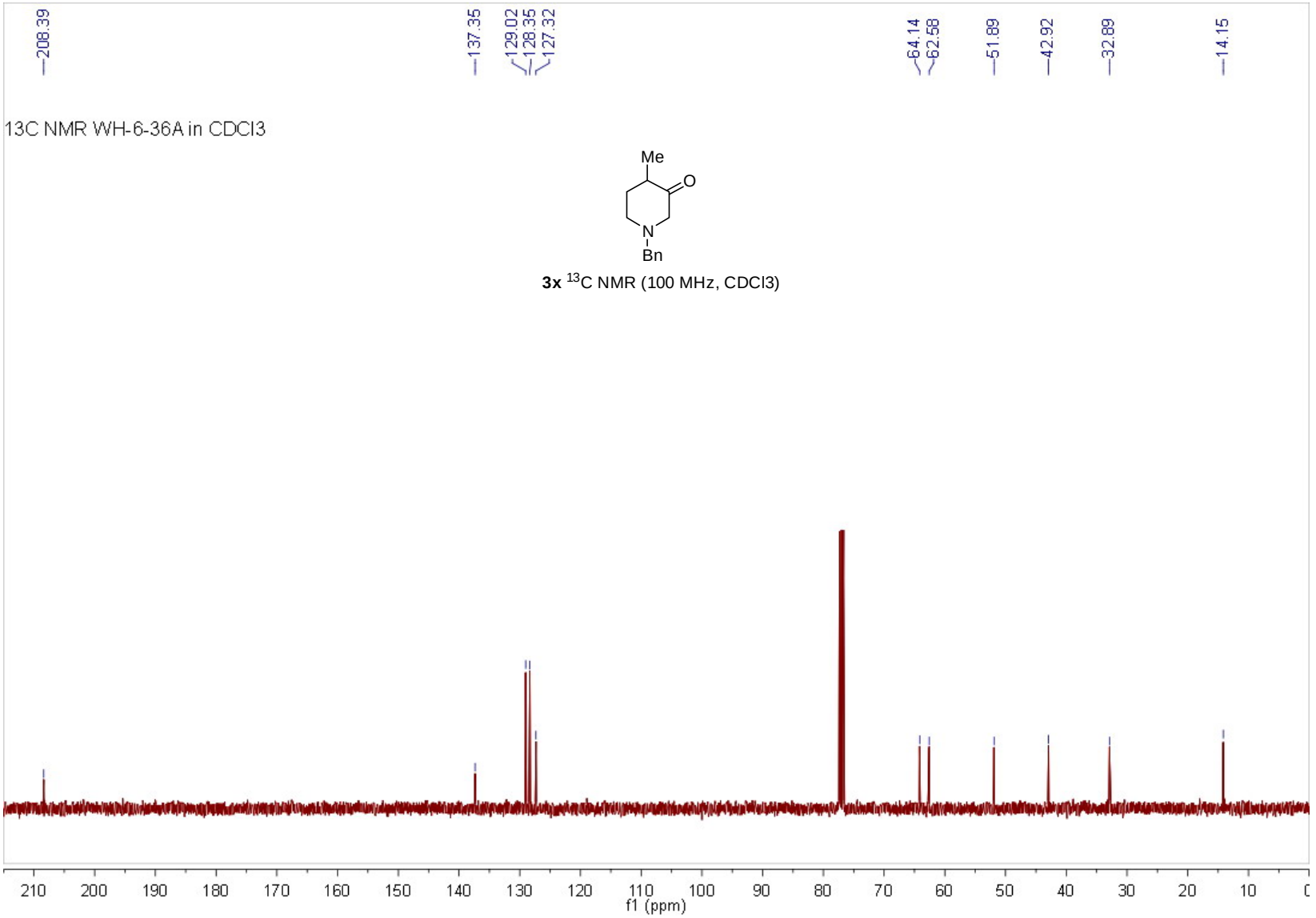
3w ^{1}H NMR (400 MHz, CDCl3)



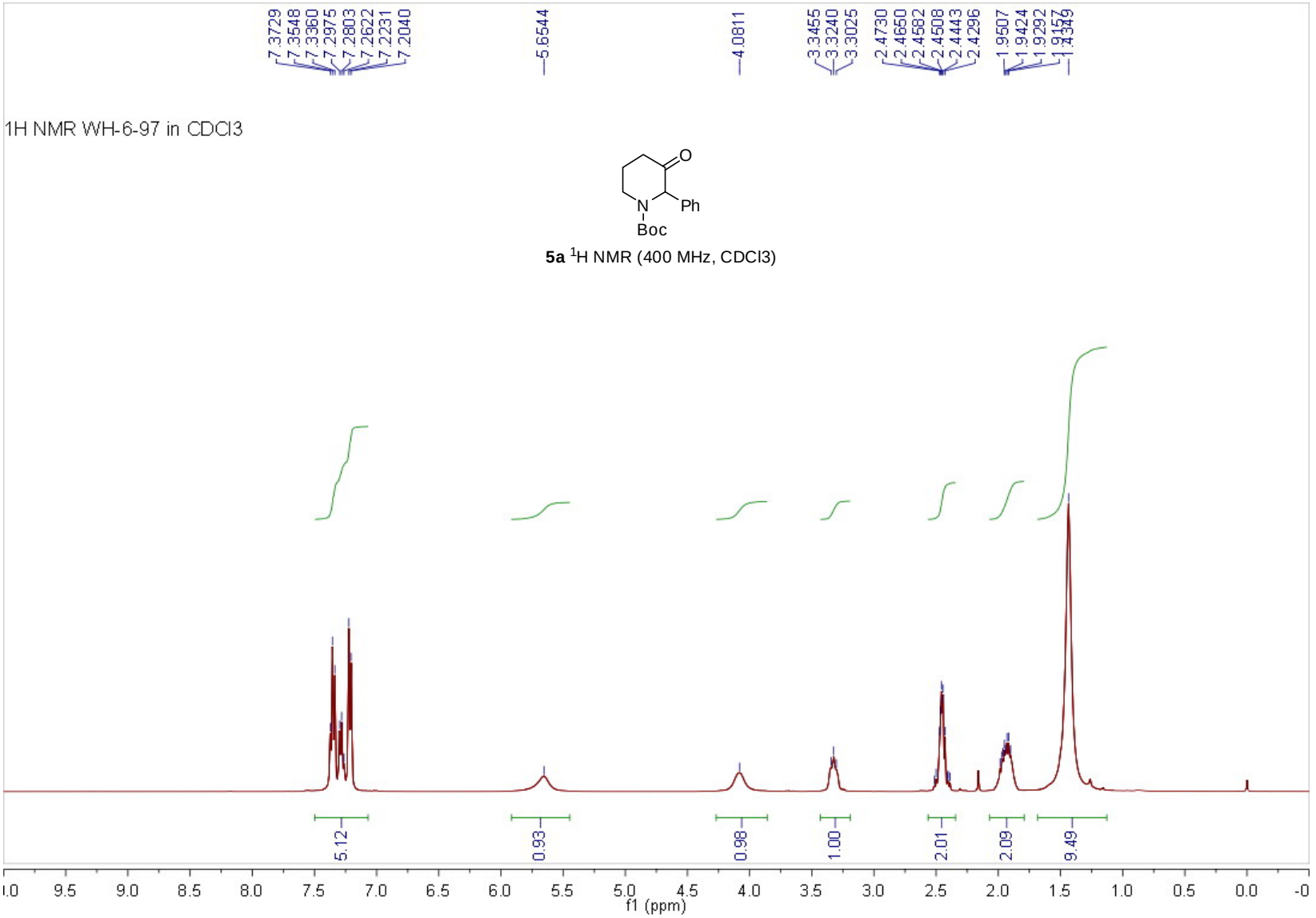
3w ^{13}C NMR (100 MHz, CDCl3)



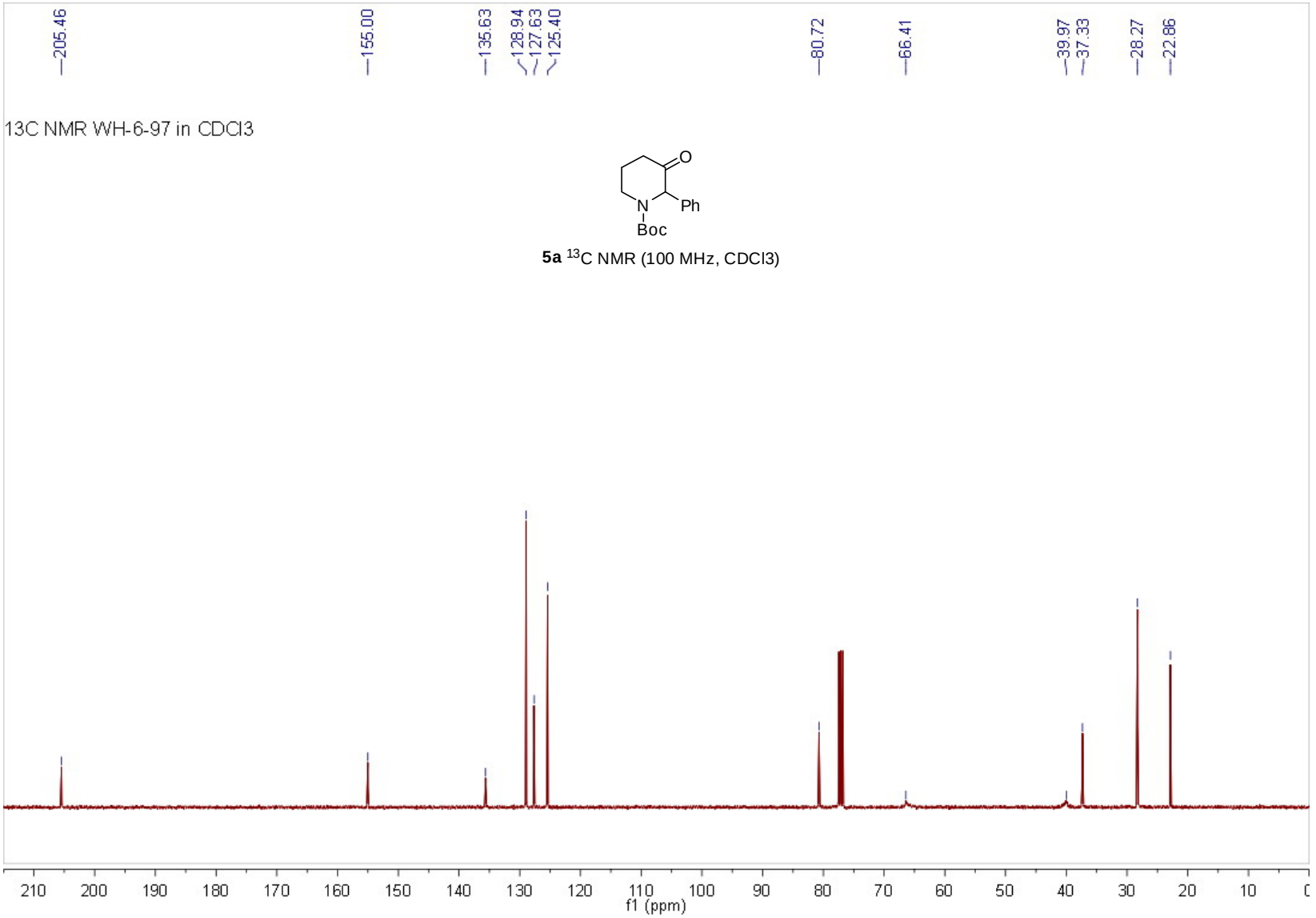
3x ^{1}H NMR (400 MHz, CDCl3)



3x ^{13}C NMR (100 MHz, CDCl3)



5a ^{1}H NMR (400 MHz, CDCl3)



5a ^{13}C NMR (100 MHz, CDCl3)