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Supporting Information

C3-Functionalization of indoles with α-heteroaryl-substituted methyl alcohols

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Table of Contents

1. General information

Unless stated otherwise, all reactions were performed under an atmosphere of N_2 that was passed through a cartridge (10 x 2 cm) of Drierite®. Prior to use, Et_2O and THF were freshly distilled over sodium/benzophenone ketyl radical anion, and CH_2Cl_2 was freshly distilled over CaH_2. DMSO, DMF, MeCN were freshly distilled over CaH_2 and stored over 3 Å molecular sieves. For water-sensitive reactions, glassware and stir bars were dried in an oven at 140 °C for at least 16 h prior to use. Reactions were monitored by ^{1}H-NMR and TLC analysis (pre-coated silica gel 60 F254). TLC spots were visualized by UV light (254 nm and 395 nm), $KMnO_4$ stain, or a DNP stain. All NMR spectra were recorded on Bruker Avance 300 MHz, Bruker Avance 400 MHz, or Bruker Avance 500 MHz instruments. High resolution mass spectra were obtained on a Micromass UK Limited, Q-TOF Ultima API or a Thermo Scientific Exactive Orbitrap LC-MS. Chemical shifts were reported in parts per million (ppm) with the residual solvent peak ($CDCl_3$: 7.26 ppm for ^{1}H, 77.16 ppm for ^{13}C; DMSO: 2.50 ppm for ^{1}H, 39.52 ppm for ^{13}C; D_2O: 4.79 ppm for ^{1}H) as the internal standard. Chemical shifts were tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, brs = broad singlet, m = multiplet), coupling constant(s), and integration. IR spectra were obtained using neat samples on a PerkinElmer 100 IR-ATR spectrometer. Temperature was monitored with a Chemglass Life Sciences high temperature (-10–260 °C) or a low temperature (-100–50 °C) thermometer. Melting points were obtained using a Mel-Temp instrument and are uncorrected. Listed reaction concentrations refer to the indole component. The products were mostly air- and temperature-sensitive, making rigorous drying conditions difficult and leading, in some cases, to small residual solvent contamination.

2. Comparison of oxone® and air oxidation conditions

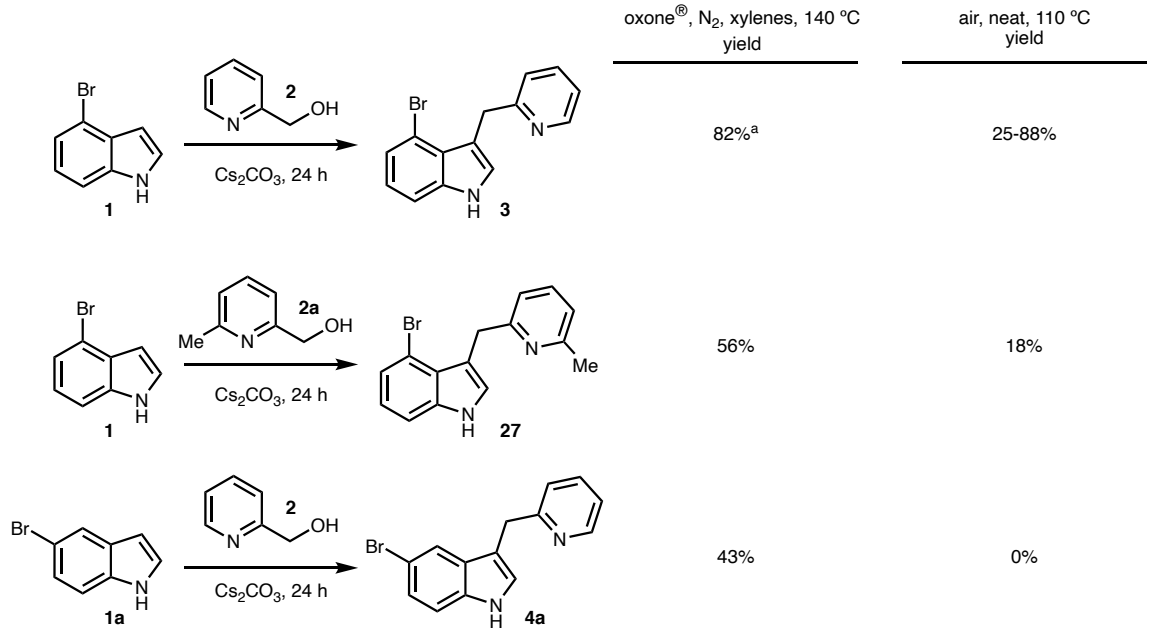


Figure S1 Substrates were assessed in parallel under conditions utilizing oxone® versus air as the oxidant. Standard reaction conditions: 1 mmol scale, 3 equiv of **2**/**2a**, 1.1 equiv of Cs_2CO_3, and either: 0.1 equiv of oxone®, nitrogen atmosphere, concentration 2 M in xylenes, 140 °C, 24 h reaction time, or: air atmosphere, neat, 110 °C, 24 h reaction time. Yields are based on ^{1}H NMR analysis ($CDCl_3$) in the presence of an internal standard (1,3,5-trimethoxybenzene). [a]^{1}H NMR analysis used DMSO-d_6 as solvent.

3. Effects of indole substituent position on reaction rate and bis-indole formation

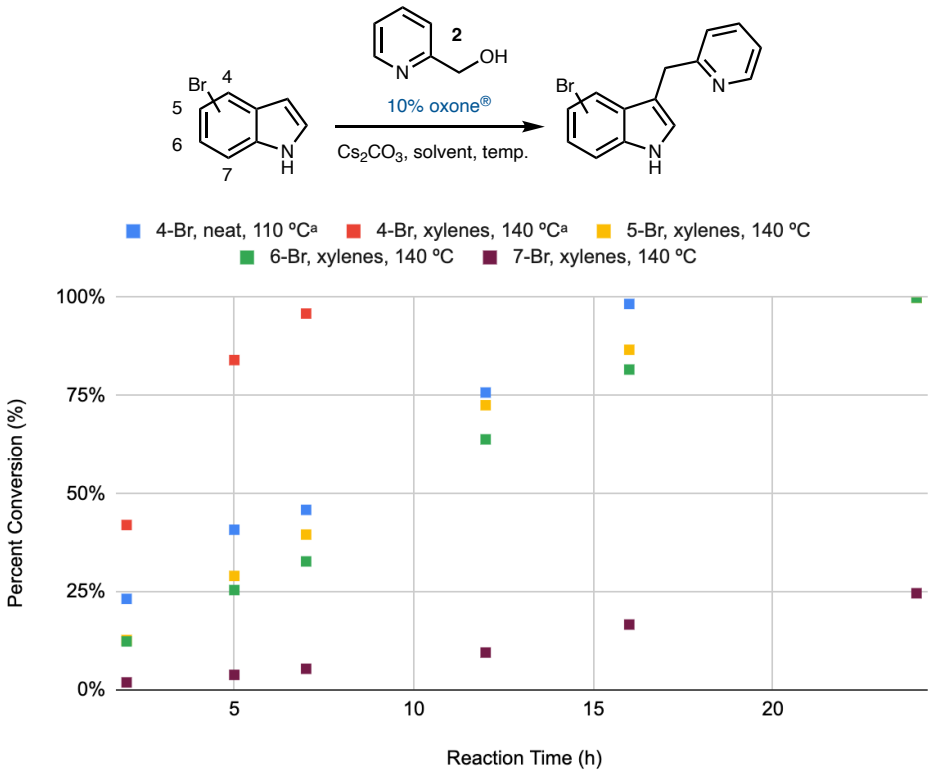


Figure S2 Effects of indole substituent position on reaction rate. Standard reaction conditions: 1 mmol scale, 3 equiv of **2**, 1.1 equiv of Cs_2CO_3, 0.1 equiv of oxone® and either: neat, 110 °C, or: 2 M in xylenes, 140 °C. Percent conversion measured by ^{1}H NMR analysis ($CDCl_3$). [a]Analysis by ^{1}H NMR analysis using DMSO-d_6 as solvent.

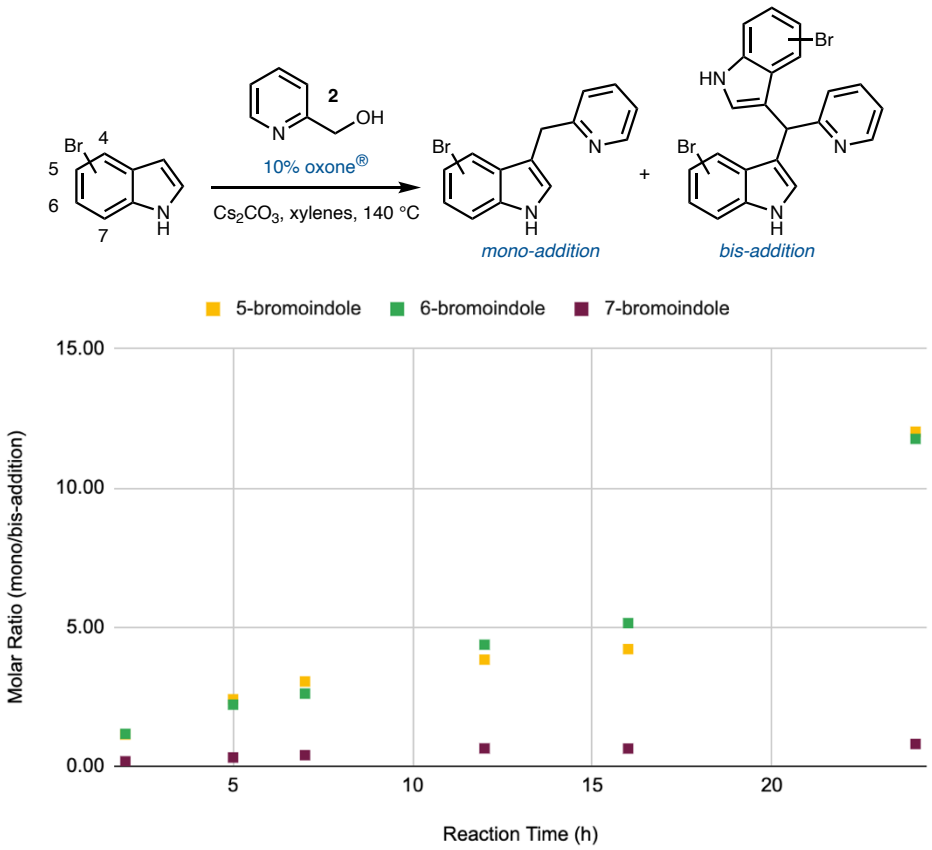


Figure S3 Changes in molar ratio of mono/bis-addition products during the first 24 h reaction time. Standard reaction conditions: 1 mmol scale, 3 equiv of **2**, 1.1 equiv of Cs_2CO_3, 0.1 equiv of oxone®, concentration 2 M in xylenes, 140 °C. Molar ratio determined by ^1H NMR analysis ($CDCl_3$).

4. DFT calculations of α-pyridyl methyl alcohol tautomers

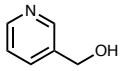
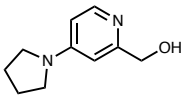
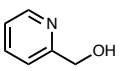
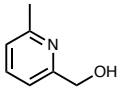
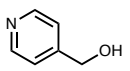
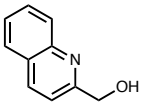
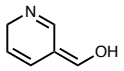
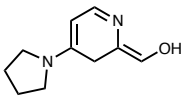
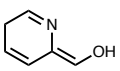
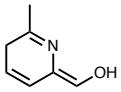
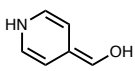
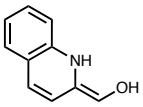
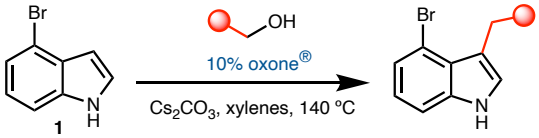
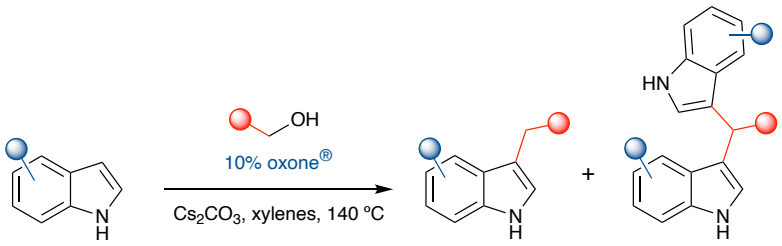
substrate						
lowest energy tautomer						
relative DFT energy difference (kcal/mol) vs yield	+1.64 14%[a]	+1.12 < 5%[b]	0 67%	–0.51 60%	–2.59 81%	–7.54 51%

Table S1 Lowest energy tautomers of pyridyl methyl alcohols and corresponding reference reaction yields. Relative energy gap differences between substrates and lowest energy tautomers were calculated as a function of 2-pyridinemethanol and its corresponding tautomer. Density Functional Theory (DFT) calculations were performed with a ωB97X-D functional and 6-311+G** basis set using Spartan v8.02 GUI. Standard reaction conditions: 1 mmol scale, 3 equiv of alcohol, 1.1 equiv of Cs_2CO_3, 0.1 equiv of oxone®, concentration 2 M in xylenes, 140 °C, 24 h. [a]Heated for 144 h. [b]Reaction performed using the following conditions: 1 mmol scale, 3 equiv of alcohol, 1.1 equiv of Cs_2CO_3, air, neat, 110 °C, 24 h.

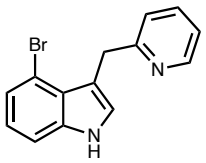
Reference Reaction:



5. Synthesis and characterization of C3-substituted indoles

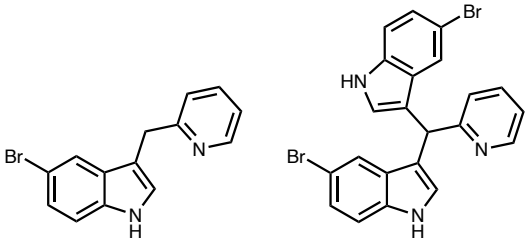


General Procedure: A mixture of indole (1 equiv), pyridyl alcohol (3.0 equiv), Cs_2CO_3 (1.1 equiv), and oxone® (0.10 equiv) in xylenes (2 M) in a sealed vessel was stirred at 140 °C under an atmosphere of N_2 until starting material was completely consumed by TLC analysis. The reaction mixture was cooled to room temperature, and H_2O (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (35% EtOAc/CH_2Cl_2) to afford product and bis-addition product.



3

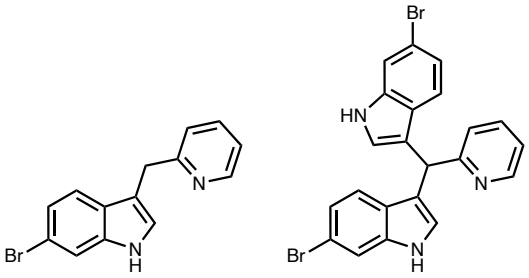
4-Bromo-3-(pyridin-2-ylmethyl)-1*H*-indole (**3**). Synthesized according to the general procedure utilizing 4-bromoindole (1.00 mL, 7.83 mmol) and 24 h reaction time; volumes of solvents used for extraction were scaled by 10 to give **3** (1.50 g, 5.22 mmol, 67%) as a tan solid: M.p. 185–186 °C; IR (ATR) ν_{max} 3112, 3021, 2917, 1725, 1596, 1559, 1543, 1473, 1434, 1424, 1409, 1331, 1249, 1174, 1042, 1002, 912, 843, 743, 717 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 11.30 (brs, 1 H), 8.48 (ddd, *J* = 4.8, 1.7, 0.8 Hz, 1 H), 7.63 (td, *J* = 7.7, 1.9 Hz, 1 H), 7.40 (dd, *J* = 8.0, 0.5 Hz, 1 H), 7.21 (d, *J* = 2.0 Hz, 1 H), 7.18—7.15 (m, 1 H), 7.13 (dd, *J* = 7.8, 0.8 Hz, 1 H), 7.02 (d, *J* = 7.8 Hz, 1 H), 6.97 (t, *J* = 7.8 Hz, 1 H), 4.44 (s, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.7, 148.7, 137.8, 136.3, 126.5, 124.8, 122.7, 122.3, 122.1, 120.9, 112.9, 112.1, 111.3, 34.3; HRMS (ESI+) *m/z* calcd for $C_{14}H_{12}N_2Br$ ($[M+H]^+$) 287.0178, found 287.0175.



4a **4b**

5-Bromo-3-(pyridin-2-ylmethyl)-1*H*-indole (**4a**) and **3,3'-(pyridin-2-ylmethylene)bis(5-bromo-1*H*-indole)** (**4b**). Synthesized according to the general procedure utilizing 5-bromoindole (0.200 g, 1.02 mmol) and 24 h reaction time to give **4a** (0.190 g, 0.663 mmol, 65%) and **4b** (0.0154 g, 0.0320 mmol, 6%) as tan solids. **4a**: M.p. 154.3 °C (dec.); IR (ATR) ν_{max} 3153, 2892, 1593, 1569, 1472, 1455, 1436, 1351, 1337, 1314, 1291, 1249, 1233, 1115, 1091, 1051, 1043, 1000, 879, 861, 792, 765, 776, 757, 719, 664 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.2 Hz, 1 H), 8.12 (brs, 1 H), 7.65 (s, 1 H), 7.57 (td, *J* = 7.7, 1.7 Hz, 1 H), 7.28–7.23 (m, 2 H), 7.20–7.10 (m, 2 H), 7.08 (d, *J* = 2.1 Hz, 1 H), 4.25 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 149.5, 136.7, 135.2, 129.4, 125.1, 124.0, 122.8, 121.9, 121.4, 113.9, 112.9, 112.7, 34.5; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{12}N_2Br$ ($[M+H]^+$) 287.0178, found 287.0187.

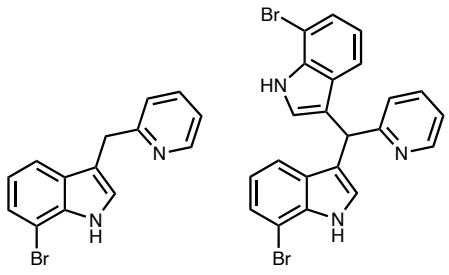
4b: M.p. 123.8 °C (dec.); IR (ATR) ν_{max} 3420, 3131, 2891, 1592, 1569, 1455, 1432, 1318, 1278, 1213, 1150, 1137, 1093, 1049, 1000, 883, 793, 768, 751, 686, 655 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.0 Hz, 1 H), 8.36 (brs, 2 H), 7.64 (td, *J* = 7.7, 1.7 Hz, 1 H), 7.46 (d, *J* = 1.4 Hz, 2 H), 7.28 (d, *J* = 7.7 Hz, 1 H), 7.22–7.11 (m, 5 H), 6.65 (d, *J* = 1.7 Hz, 2 H), 5.89 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 149.5, 137.1, 135.5, 128.7, 125.0, 124.9, 123.1, 122.2, 122.0, 117.5, 112.82, 112.77, 42.8; HRMS (ESI$^-$) *m/z* calcd for $C_{22}H_{14}N_3Br_2$ ([M–H]$^-$) 477.9549, found 477.9565.



5a **5b**

6-Bromo-3-(pyridin-2-ylmethyl)-1*H*-indole (**5a**) and **3,3'-(pyridin-2-ylmethylene)bis(6-bromo-1*H*-indole)** (**5b**). Synthesized according to the general procedure utilizing 6-bromoindole (0.200 g, 1.00 mmol) and 24 h reaction time to give **5a** (0.205 g, 0.714 mmol, 71%) and **5b** (0.0230 g, 0.0478 mmol, 10%) as tan solids. **5a**: M.p. 152.5 °C (dec.); IR (ATR) ν_{max} 3010, 2880, 1594, 1567, 1473, 1455, 1435, 1411, 1346, 1324, 1251, 1233, 1136, 1118, 1091, 1067, 1048, 1004, 925, 893, 830, 807, 761, 750, 742, 719 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.1 Hz, 1 H), 8.14 (brs, 1 H), 7.55 (td, *J* = 7.7, 1.8 Hz, 1 H) 7.49 (d, *J* = 1.7 Hz, 1 H) 7.36 (d, *J* = 8.4 Hz, 1 H), 7.18–7.09 (m, 3 H), 7.05–7.04 (m, 1 H), 4.27 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 149.4, 137.4, 136.7, 126.5, 123.3, 122.92, 122.85, 121.37, 120.6, 115.86, 114.4, 114.2, 34.6; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{12}N_2Br$ ([M+H]$^+$) 287.0178, found 287.0192.

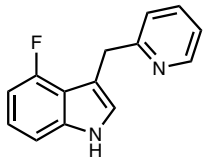
5b: M.p. 128.0 °C (dec.); IR (ATR) ν_{max} 3424, 3134, 2929, 2879, 1615, 1592, 1570, 1539, 1470, 1453, 1433, 1398, 1332, 1219, 1134, 1096, 1050, 1040, 1000, 893, 848, 802, 771, 753, 686, 657 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.8, 0.8 Hz, 1 H), 8.24 (brs, 2 H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.44 (d, *J* = 1.4 Hz, 2 H), 7.27 (d, *J* = 8.3 Hz, 1 H), 7.20–7.15 (m, 3 H), 7.08 (dd, *J* = 8.4, 1.6 Hz, 2 H), 6.65 (d, *J* = 1.6 Hz, 2 H), 5.95 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 149.5, 137.6, 137.0, 125.9, 124.2, 123.1, 122.8, 121.9, 121.0, 118.1, 115.7, 114.2, 42.9; HRMS (ESI$^-$) *m/z* calcd for $C_{22}H_{14}N_3Br_2$ ([M–H]$^-$) 477.9549, found 477.9564.



6a **6b**

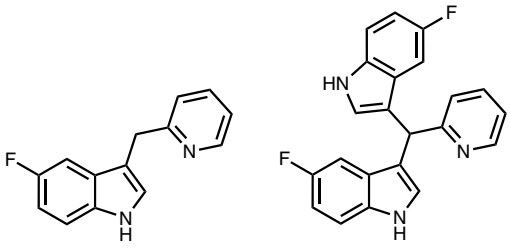
7-Bromo-3-(pyridin-2-ylmethyl)-1*H*-indole (**6a**) and **3,3'-(pyridin-2-ylmethylene)bis(7-bromo-1*H*-indole)** (**6b**). Synthesized according to the general procedure utilizing 7-bromoindole (0.200 g, 1.01 mmol) and 96 h reaction time to give **6a** (0.175 g, 0.609 mmol, 60%) and **6b** (0.0139 g, 0.0289 mmol, 6%) as tan solids. **6a**: M.p. 131.0–132.2 °C; IR (ATR) ν_{max} 3090, 2907, 2841, 1646, 1568, 1594, 1495, 1481, 1432, 1356, 1338, 1309, 1285, 1249, 1194, 1149, 1118, 1092, 1059, 1048, 1003, 880, 887, 847, 790, 831, 772, 748, 727, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.1, 0.8 Hz, 1 H), 8.22 (brs, 1 H), 7.55 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.46 (d, *J* = 7.9 Hz, 1 H), 7.33 (d, *J* = 7.3 Hz, 1 H) 7.16–7.09 (m, 3 H), 6.95 (t, *J* = 7.8 Hz, 1 H), 4.29 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 149.4, 136.6, 135.3, 128.8 124.6, 123.3, 122.8, 121.4, 120.8, 118.7, 115.5, 104.9, 34.8; HRMS (ESI$^+$) calcd *m/z* for $C_{14}H_{12}N_2Br$ ([M+H]$^+$) 287.0178, found 287.0170.

6b: M.p. 111.4 °C (dec.); IR (ATR) ν_{max} 3676, 3419, 2971, 2901, 1591, 1568, 1488, 1470, 1432, 14051335, 1242, 1192, 1140, 1066, 1046, 880, 792, 777, 752, 732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 4.9, 0.8 Hz, 1 H), 8.21 (brs, 2 H), 7.60 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.33–7.26 (m, 5 H), 7.15 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1 H), 6.89 (t, *J* = 7.8 Hz, 2 H), 6.84 (d, *J* = 1.7 Hz, 2 H), 6.00 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 149.7, 136.8, 135.45, 128.2, 124.6, 124.1, 122.9, 121.8, 120.8, 119.4, 119.1, 104.9, 43.5; HRMS (ESI$^+$) *m/z* calcd for $C_{22}H_{16}N_3Br_2$ ([M+H]$^+$) 479.9706, found 479.9683.



7

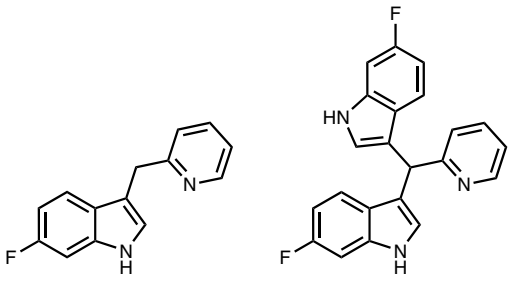
4-Fluoro-3-(pyridin-2-ylmethyl)-1*H*-indole (**7**). Synthesized according to the general procedure utilizing 4-fluoroindole (0.168 g, 1.22 mmol) and 36 h reaction time to give **7** (0.248 g, 1.09 mmol, 90%) as a tan solid: M.p. 178.3 °C (dec.); IR (ATR) ν_{max} 3117, 3071, 2927, 2877, 1881, 1634, 1595, 1581, 1510, 1456, 1437, 1411, 1350, 1228, 1032, 1002, 831, 780, 754, 733, 723, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 4.8, 0.8 Hz, 1 H) 8.20 (brs, 1 H), 7.57 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.24 (d, *J* = 7.9 Hz, 1 H), 7.13–7.04 (m, 3 H), 6.99 (d, *J* = 1.7 Hz, 1 H), 6.72 (ddd, *J* = 11.0, 7.6, 0.8 Hz, 1 H), 4.39 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 158.7, 156.2, 149.3, 139.3 (d, $J_{C,F}$ = 11.3 Hz), 136.6, 123.0 (d, $J_{C,F}$ = 3.2 Hz), 122.7 (d, $J_{C,F}$ = 7.9 Hz), 122.1 (d, $J_{C,F}$ = 117.2 Hz), 116.4 (d, $J_{C,F}$ = 20.9 Hz), 112.8 (d, $J_{C,F}$ = 2.4 Hz), 107.4 (d, $J_{C,F}$ = 3.6 Hz), 104.8 (d, $J_{C,F}$ = 19.2 Hz), 34.4; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{12}N_2F$ ([M+H]$^+$) 227.0979, found 227.0984.



8a **8b**

5-Fluoro-3-(pyridine-2-ylmethyl)-1*H*-indole (**8a**) and **3,3'-(pyridin-2-ylmethylene)bis(5-fluoro-1*H*-indole)** (**8b**). Synthesized according to the general procedure utilizing 5-fluoroindole (0.150 g, 1.09 mmol) and 9 h reaction time to give **8a** (0.191 g, 0.845 mmol, 78%) and **8b** (0.0215 g, 0.0598 mmol, 11%) as tan solids. **8a**: M.p. 151.8 °C (dec.); IR (ATR) ν_{max} 3134, 2893, 1569, 1595, 1489, 1466, 1438, 1410, 1340, 1304, 1246, 1234, 1193, 1167, 1050, 1002, 936, 925, 918, 852, 836, 792, 757, 709 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.8, 0.5 Hz, 1 H) 8.24 (brs, 1 H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.24 (dd, *J* = 8.8, 4.4 Hz, 1 H), 7.17–7.10 (m, 4 H), 6.91 (td, *J* = 9.1, 2.5 Hz, 1 H), 4.25 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 159.1, 156.7, 149.4, 136.7, 133.1, 128.0 (d, $J_{C,F}$ = 9.8 Hz), 124.5, 122.1 (d, $J_{C,F}$ = 148.9 Hz), 114.3 (d, $J_{C,F}$ = 4.5 Hz), 111.8 (d, $J_{C,F}$ = 9.7 Hz) 110.6 (d, $J_{C,F}$ = 26.2 Hz), 104.3 (d, $J_{C,F}$ = 23.2 Hz), 34.7; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{12}N_2F$ ([M+H]$^+$) 227.0979, found 227.0973.

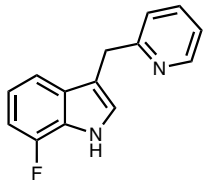
8b: M.p. 102.2 °C (dec.); IR (ATR) ν_{max} 3462, 3136, 2919, 2335, 1628, 1584, 1484, 1453, 1435, 1349, 1161, 1092, 937, 845, 793, 750, 718, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 4.8, 0.9 Hz, 1 H) 8.09 (brs, 2 H), 7.61 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.29 (d, *J* = 7.9 Hz, 1 H), 7.25 (d, *J* = 5.5 Hz, 1 H), 7.22 (d, *J* = 4.4 Hz, 1 H), 7.16 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1 H), 7.00 (dd, *J* = 9.7, 2.4 Hz, 2 H), 6.89 (td, *J* = 9.1, 2.5 Hz, 2 H), 6.82 (d, *J* = 2.2 Hz, 2 H), 5.90 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 159.3, 156.2, 149.7, 136.8, 133.3, 127.4 (d, $J_{C,F}$ = 9.8 Hz), 125.3, 122.4 (d, $J_{C,F}$ = 90.5 Hz), 118.2 (d, $J_{C,F}$ = 4.7 Hz), 111.9 (d, $J_{C,F}$ = 9.7 Hz), 110.6 (d, $J_{C,F}$ = 26.3 Hz), 104.8 (d, $J_{C,F}$ = 23.5 Hz), 43.2; HRMS (ESI$^+$) *m/z* calcd for $C_{22}H_{16}N_3F_2$ ([M+H]$^+$) 360.1307, found 360.1288.



9a **9b**

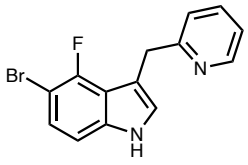
6-Fluoro-3-(pyridin-2-ylmethyl)-1*H*-indole (**9a**) and **3,3'-(pyridin-2-ylmethylene)bis(6-fluoro-1*H*-indole)** (**9b**). Synthesized according to the general procedure utilizing 6-fluoroindole (0.150 g, 1.09 mmol) and 36 h reaction time to give **9a** (0.246 g, 0.682 mmol, 63%) and **9b** (0.0275 g, 0.0765 mmol, 14%) as tan solids. **9a**: M.p. 134.5–135.7 °C; IR (ATR) ν_{max} 3151, 3092, 2993, 2913, 2837, 1835, 1625, 1596, 1569, 1559, 1477, 1457, 1435, 1344, 1307, 1227, 1141, 1099, 1051, 1002, 950, 833, 793, 801, 775, 757, 748, 727, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.8, 0.8 Hz, 1 H) 8.20 (brs, 1 H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.40 (dd, *J* = 8.7, 5.3 Hz, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 7.11 (dd, *J* = 7.4, 5.3 Hz, 1 H), 7.03–7.00 (m, 2 H), 6.83 (tdd, *J* = 8.8, 2.3, 0.9 Hz, 1 H), 4.28 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 161.2, 159.1, 149.4, 136.8, 136.6 (d, $J_{C,F}$ = 12.4 Hz), 124.3, 123.1 (d, $J_{C,F}$ = 3.6 Hz), 122.2 (d, $J_{C,F}$ = 153.1 Hz), 120.2 (d, $J_{C,F}$ = 10.2 Hz), 114.3, 108.5 (d, $J_{C,F}$ = 24.2 Hz), 97.6 (d, $J_{C,F}$ = 26.0 Hz), 34.7; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{12}N_2F$ ($[M+H]^+$) 227.0979, found 227.0984.

9b: M.p. 103.2 °C (dec.); IR (ATR) ν_{max} 3416, 3154, 1626, 1591, 1497, 1455, 1434, 1343, 1306, 1252, 1213, 1139, 1118, 1091, 1001, 951, 834, 765, 800, 750, 714, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 4.9, 0.9 Hz, 1 H) 8.00 (brs, 2 H), 7.60 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.29–7.26 (m, 3 H), 7.15 (ddd, *J* = 7.4, 4.8, 0.9 Hz, 1 H), 7.02 (dd, *J* = 9.6, 2.3 Hz, 2 H), 6.79–6.74 (m, 4 H), 5.98 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 158.9 (d, $J_{C,F}$ = 13.7 Hz), 149.6, 136.75, 136.71 (d, $J_{C,F}$ = 12.7 Hz), 123.747 (d, $J_{C,F}$ = 7.9 Hz), 123.754, 122.3 (d, $J_{C,F}$ = 122.9 Hz), 120.6 (d, $J_{C,F}$ = 9.9 Hz), 118.4, 108.3 (d, $J_{C,F}$ = 24.2 Hz), 97.5 (d, $J_{C,F}$ = 26.1 Hz), 43.2; HRMS (ESI^+) *m/z* calcd for $C_{22}H_{16}N_3F_2$ ($[M+H]^+$) 360.1307, found 360.1317.



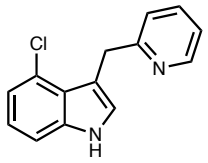
10

7-Fluoro-3-(pyridin-2-ylmethyl)-1*H*-indole (**10**). Synthesized according to the general procedure utilizing 7-fluoroindole (0.150 g, 1.08 mmol) and 120 h reaction time to give **10** (0.158 g, 0.698 mmol, 65%) as a tan solid: M.p. 131.2–132.6 °C; IR (ATR) ν_{max} 3078, 3022, 2848, 1719, 1632, 1595, 1578, 1569, 1504, 1481, 1462, 1434, 1353, 1287, 1228, 1219, 1148, 1089, 1049, 964, 828, 774, 749, 722, 708, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.5 Hz, 1 H), 8.30 (brs, 1 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.27 (d, *J* = 8.5 Hz, 1 H), 7.16–7.11 (m, 3 H), 7.00–6.95 (m, 1 H), 6.91–6.86 (m, 1 H), 4.29 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 150.9, 149.4, 148.5, 136.7, 131.3 (d, $J_{C,F}$ = 5.1 Hz), 124.9 (d, $J_{C,F}$ = 13.4 Hz), 123.1 (d, $J_{C,F}$ = 56.1 Hz), 121.3, 119.8 (d, $J_{C,F}$ = 6.1 Hz), 115.1 (d, $J_{C,F}$ = 3.5 Hz), 115.0 (d, $J_{C,F}$ = 2.2 Hz), 107.1 (d, $J_{C,F}$ = 15.9 Hz), 34.7; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{12}N_2F$ ($[M+H]^+$) 227.0979, found 227.0978.



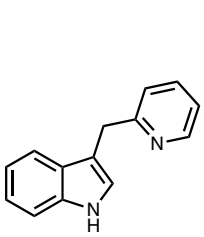
11

5-Bromo-4-fluoro-3-(pyridin-2-ylmethyl)-1*H*-indole (**11**). A mixture of 5-bromo-4-fluoroindole (0.200 g, 0.916 mmol), 2-pyridinemethanol (0.270 mL, 2.75 mmol), Cs_2CO_3 (0.328 g, 1.00 mmol), and oxone® (0.0563 g, 0.0916 mmol) in xylenes (0.46 mL) in a sealed vessel was stirred at 110 °C under an atmosphere of N_2 for 96 h. The reaction mixture was cooled to room temperature, and H_2O (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (3% MeOH/CH_2Cl_2) to afford **11** (0.122 g, 0.400 mmol, 44%) as a brown solid: M.p. 168.0 °C (dec.); IR (ATR) ν_{max} 3098, 3045, 2894, 2926, 2305, 1981, 1628, 1595, 1570, 1494, 1455, 1477, 1435, 1346, 1257, 1196, 1145, 1124, 1044, 1003, 850, 787, 748, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.3 Hz, 1 H), 8.34 (brs, 1 H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.29–7.26 (m, 1 H), 7.22 (dd, *J* = 8.6, 6.5 Hz, 1 H), 7.14 (dd, *J* = 7.2, 5.5 Hz, 1 H), 7.04–6.98 (m, 2 H), 4.37 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 153.2, 150.7, 148.9, 138.3 (d, $J_{C,F}$ = 11.5 Hz), 136.5, 125.1 (d, $J_{C,F}$ = 135.4 Hz), 122.1, 121.2, 116.5 (d, $J_{C,F}$ = 19.7 Hz), 110.5 (d, $J_{C,F}$ = 3.4 Hz), 109.6 (d, $J_{C,F}$ = 3.6 Hz), 95.6 (d, $J_{C,F}$ = 19.1 Hz), 34.4; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{11}N_2BrF$ ([M+H]$^+$) 305.0084, found 305.0085.

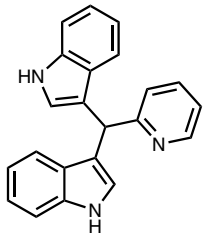


12

4-Chloro-3-(pyridin-2-ylmethyl)-1*H*-indole (**12**). Synthesized following the general procedure utilizing 4-chloroindole (0.160 g, 1.03 mmol) and 24 h reaction time; **12** (0.244 g, 1.00 mmol, 97%), light-tan solid: M.p. 181.4 °C (decomp); IR (ATR) ν_{max} 3081, 3008, 2917, 2859, 1893, 1685, 1597, 1567, 1547, 1474, 1449, 1435, 1409, 1333, 1300, 1275, 1243, 1177, 1092, 1072, 1044, 1003, 934, 922, 805, 781, 750, 734, 718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.8, 0.75 Hz, 1 H), 8.32 (brs, 1 H), 7.56 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.24 (dd, *J* = 6.5, 2.6 Hz, 1 H), 7.16–7.03 (m, 4 H), 6.98 (d, *J* = 2.4 Hz, 1 H), 4.57 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 149.2, 138.1, 136.6, 126.6, 124.7, 124.4, 123.1, 122.8, 121.1, 120.7, 114.1, 110.1, 35.3; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{12}N_2Cl$ ([M+H]$^+$) 243.0684, found 243.0678.



13a



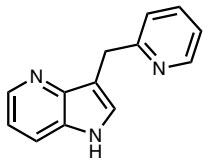
13b

3-(Pyridin-2-ylmethyl)-1*H*-indole (**13a**) and **3,3'-(pyridin-2-ylmethylene)bis(1*H*-indole)** (**13b**). Synthesized according to the general procedure utilizing indole (0.120 g, 1.01 mmol) and 24 h reaction time to give **13a** (0.169 g, 0.811 mmol, 80%) and **13b** (0.0123 g, 0.0380 mmol, 8%) as yellow solids. **13a**: ^1H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.9, 0.8 Hz, 1 H), 8.23 (brs, 1 H), 7.56–7.51 (m, 2 H), 7.35 (d, *J* = 8.1 Hz, 1 H), 7.21–7.16 (m, 2 H), 7.12–7.05 (m, 3 H), 4.32 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 149.2, 136.5, 127.6, 122.9, 122.8, 122.2, 121.2, 119.5, 119.3, 114.0, 111.3, 34.7; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{13}N_2$ ([M+H]$^+$) 209.1073, found 209.1067. Spectral data were consistent with previously reported properties.[1]

13b: ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.2 Hz, 1 H), 8.01 (brs, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.40 (d, *J* = 7.9 Hz, 2 H), 7.36–7.32 (m, 3 H), 7.18–7.12 (m ,3 H), 7.00 (t, *J* = 7.4 Hz, 2 H), 6.79 (s, 2 H), 6.07 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 136.8, 136.7, 127.2, 123.6, 123.1, 122.1, 121.5, 120.0, 119.4, 118.5, 111.2, 43.4. Spectral data were consistent with previously reported properties.[2]

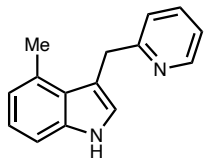
3-(Pyridin-2-ylmethyl)-1*H*-indole (**13a**). Preparation from 2-aminophenylethyl alcohol: A mixture of 2-aminophenylethyl alcohol (0.200 mL, 1.52 mmol), 2-pyridinemethanol (0.450 mL, 4.57 mmol), Cs_2CO_3 (0.546 g, 1.68 mmol) and oxone® (0.0937 g, 0.152

mmol) in xylenes (0.76 mL) in a sealed vessel was stirred at 140 °C under an atmosphere of N_2 for 264 h. The reaction mixture was cooled to room temperature, and H_2O (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (35% EtOAc/CH_2Cl_2) to afford **13a** (0.0434 g, 0.208 mmol, 14%) as a brown solid.



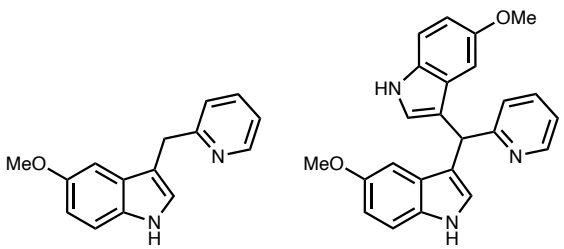
14

3-(Pyridin-2-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridine (**14**). A mixture of 4-azaindole (0.120 g, 1.02 mmol), 2-pyridinemethanol (0.300 mL, 3.04 mmol), Cs_2CO_3 (0.364 g, 1.12 mmol) and oxone® (0.0625 g, 0.102 mmol) in xylenes (0.5 mL) in a sealed vessel was stirred under an atmosphere of N_2 at 140 °C for 120 h. The reaction mixture was cooled to room temperature, and H_2O/MeOH (1:1, 20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL), and the combined organic layers were dried ($MgSO_4$), filtered through a celite plug, and concentrated. The crude residue was purified by reverse-phase chromatography on C18-SiO_2 (30 g, 10% MeCN/H_2O to 100% MeCN). Fractions containing the desired product were combined and extracted with CH_2Cl_2/MeOH (9:1, 3 x 30 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to afford **14** (0.186 g, 0.889 mmol, 88%) as a yellow-tan solid: M.p. 157.9 °C (dec.); IR (ATR) ν_{max} 3045, 2891, 2851, 2818, 1714, 1590, 1568, 1505, 1473, 1439, 1410, 1368, 1301, 1292, 1218, 1109, 1098, 1086, 894, 810, 783, 772, 761, 750, 717, 648, 624 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 11.11 (brs, 1 H), 8.46 (dd, *J* = 4.8, 0.9 Hz, 1 H), 8.29 (dd, *J* = 4.6, 1.4 Hz, 1 H), 7.72 (dd, *J* = 8.1, 1.4 Hz, 1 H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.45 (d, *J* = 2.6 Hz, 1 H), 7.28 (d, *J* = 7.8 Hz, 1 H), 7.16 (ddd, *J* = 7.3, 4.9, 0.8 Hz, 1 H), 7.08 (dd, *J* = 8.2, 4.6 Hz, 1 H), 4.24, (s, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.2, 148.7, 144.8, 141.8, 136.3, 128.6, 127.2, 122.6, 121.0, 118.3, 116.2, 112.7, 32.5; HRMS (ESI^+) *m/z* calcd for $C_{13}H_{12}N_3$ ($[M+H]^+$) 210.1031, found 210.1025.



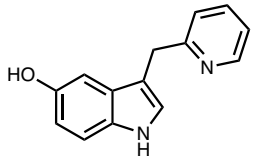
15

4-Methyl-3-(pyridin-2-ylmethyl)-1*H*-indole (**15**). Synthesized according to the general procedure utilizing 4-methylindole (0.130 mL, 1.01 mmol) and 14 h reaction time to give **15** (0.214 g, 0.963 mmol, 95%) as a light-tan solid: M.p. 159.1 °C (dec.); IR (ATR) ν_{max} 3148, 3112, 2997, 2938, 1680, 1594, 1568, 1472, 1436, 1412, 1345, 1299, 1245, 1153, 1065, 841, 752, 740, 721, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.8, 0.7 Hz, 1 H), 8.15 (brs, 1 H), 7.52 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.21 (d, *J* = 8.1 Hz, 1 H), 7.12–7.02 (m, 3H), 6.97 (d, *J* = 2.3 Hz, 1 H), 6.81 (d, *J* = 7.1 Hz, 1 H), 4.48 (s, 2 H), 2.48 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 149.2, 137.2, 136.6, 131.2, 126.2, 123.6, 122.8, 122.4, 121.2, 121.1, 114.2, 109.2, 36.3, 20.2; HRMS (ESI^+) *m/z* calcd for $C_{15}H_{15}N_2$ ($[M+H]^+$) 223.1230, found 223.1240.



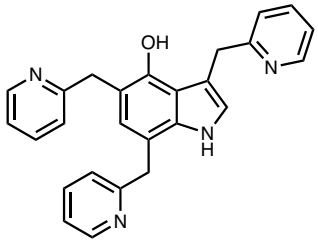
16a **16b**

5-Methoxy-3-(pyridin-2-ylmethyl)-1*H*-indole (**16a**) and **3,3'-(pyridin-2-ylmethylene)bis(5-methoxy-1*H*-indole)** (**16b**). Synthesized according to the general procedure utilizing 5-methoxyindole (0.150 g, 1.02 mmol) and 24 h reaction time to give **16a** (0.197 g, 0.826 mmol, 81%) and **16b** (0.0159 g, 0.0415 mmol, 8%) as tan solids. **16b**: M.p. 109.6–110.7 °C; IR (ATR) $\nu_{\max}$ 3036, 2998, 2878, 2824, 1625, 1595, 1583, 1569, 1488, 1474, 1436, 1411, 1303, 1256, 1236, 1217, 1172, 1109, 1029, 1003, 914, 829, 795, 759, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.2 Hz, 1 H), 8.00 (brs, 1 H), 7.54 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.25 (d, *J* = 9.3 Hz, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 7.10 (dd, *J* = 5.3, 1.6 Hz, 1 H), 7.06 (d, *J* = 2.0 Hz, 1 H), 6.95 (d, *J* = 2.3 Hz, 1 H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1 H), 4.28 (s, 2 H), 3.79 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 154.2, 149.2, 136.6, 131.7, 128.0, 123.6, 122.9, 121.2, 113.8, 112.4, 111.9, 101.2, 56.0, 34.7; HRMS (ESI^+) *m/z* calcd for $C_{15}H_{15}ON_2$ ($[M+H]^+$) 239.1179, found 239.1184.
16b: M.p. 91.3 °C (dec.); IR (ATR) $\nu_{\max}$ 3401, 2931, 1624, 1587, 1483, 1435, 1292, 1210, 1171, 1093, 1042, 926, 830, 795, 753, 715, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.0 Hz, 1 H), 8.03 (brs, 2 H), 7.58 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.30 (d, *J* = 7.8 Hz, 1 H), 7.22–7.19 (m, 2 H), 7.13 (dd, *J* = 6.6, 5.1 Hz, 1 H), 6.83–6.80 (m, 4 H), 6.72 (d, *J* = 2.0 Hz, 2 H), 5.96 (s, 1 H), 3.69 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 153.9, 149.4, 136.7, 132.0, 127.6, 124.5, 123.1, 121.5, 118.0, 112.2, 111.9, 101.8, 56.0, 43.3; HRMS (ESI^+) *m/z* calcd for $C_{24}H_{22}O_2N_3$ ($[M+H]^+$) 384.1707, found 384.1713.



17

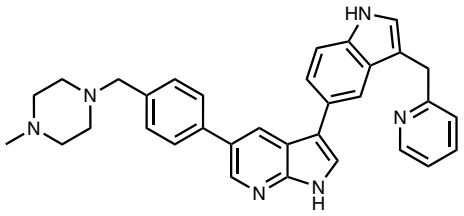
3-(Pyridin-2-ylmethyl)-1*H*-indol-5-ol (**17**). A mixture of 5-hydroxyindole (0.150 g, 1.10 mmol), 2-pyridinemethanol (0.326 mL, 3.31 mmol), Cs_2CO_3 (0.755 g, 2.32 mmol) and oxone® (0.0679 g, 0.110 mmol) in xylenes (0.55 mL) was stirred in a sealed vessel under an atmosphere of N_2 at 140 °C for 36 h. The reaction mixture was cooled to room temperature, and H_2O/MeOH (1:1, 20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was dissolved in 5% MeOH/CH_2Cl_2 (3 mL) and loaded onto a SiO_2 column. The column was washed with CH_2Cl_2 (20 mL) and then the mixture was eluted with 100% EtOAc to afford **17** (0.188 g, 0.838 mmol, 76%) as a light-brown solid: M.p. 63.5 °C (dec.); IR (ATR) $\nu_{\max}$ 3285, 3050, 2854, 2607, 1837, 1595, 1583, 1570, 1469, 1436, 1403, 1310, 1197, 1092, 1051, 1009, 937, 831, 794, 784, 774, 749, 696, 667 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 10.55 (brs, 1 H), 8.53 (brs, 1 H), 8.47 (ddd, *J* = 4.7, 1.7, 1.1 Hz, 1 H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.18–7.15 (m, 2 H), 7.12–7.10 (m, 2 H), 6.72 (d, *J* = 2.3 Hz, 1 H), 6.56 (dd, *J* = 8.6, 2.3 Hz, 1 H), 4.07 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 150.2, 148.7, 136.3, 130.9, 127.7, 123.9, 122.4, 121.0, 111.7, 111.34, 111.28, 102.6, 34.2; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{13}ON_2$ ($[M+H]^+$) 225.1022, found 225.1021.



18

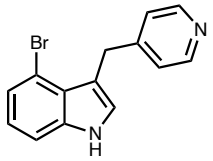
3,5,7-Tris(pyridin-2-ylmethyl)-1*H*-indol-4-ol (**18**). A mixture of 4-hydroxyindole (0.150 g, 1.12 mmol), 2-pyridinemethanol (0.329 mL, 3.35 mmol), Cs_2CO_3 (0.763 g, 2.34 mmol) and oxone® (0.0686 g, 0.112 mmol) in xylenes (0.56 mL) in a sealed vessel was stirred at 140 °C under an atmosphere of N_2 for 24 h. The reaction mixture was cooled to room temperature, and H_2O/MeOH (1:1, 20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (3% MeOH/CH_2Cl_2) to afford **18**

(0.248 g, 0.610 mmol, 55%) as a reddish-brown solid: M.p. 70.6 °C (dec.); IR (ATR) ν_{max} 3007, 2901, 2573, 1591, 1568, 1494, 1473, 1433, 1354, 1317, 1256, 1223, 1148, 1092, 1050, 1012, 995, 935, 748, 706, 658 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.81 (brs, 1 H), 10.66 (brs, 1 H), 8.45–8.43 (m, 3 H), 7.81 (td, *J* = 7.6, 1.6 Hz, 1 H), 7.65 (td, *J* = 7.7, 1.7 Hz, 1 H), 7.60 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.45 (d, *J* = 7.8 Hz, 1 H), 7.27 (dd, *J* = 6.7, 5.2 Hz, 1 H), 7.22 (d, *J* = 7.8 Hz, 1 H), 7.18–7.12 (m, 3 H), 7.06 (d, *J* = 2.1 Hz, 1 H), 6.71 (s, 1 H), 4.26 (s, 2 H), 4.13 (s, 2 H), 4.09 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 161.4, 160.6, 148.8, 148.3, 147.7, 147.1, 138.5, 136.6, 136.54, 136.51, 125.0, 123.3, 122.6, 122.5, 122.3, 121.7, 121.1, 121.0, 117.8, 115.3, 114.2, 111.7, 39.0, 38.5, 34.3; HRMS (ESI$^+$) *m/z* calcd for $C_{26}H_{23}ON_4$ ([M+H]$^+$) 407.1866, found 407.1861.



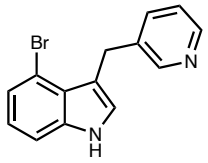
19

5-(4-((4-Methylpiperazin-1-yl)methyl)phenyl)-3-(3-(pyridin-2-ylmethyl)-1*H*-indol-5-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (**19**). A mixture of URMC-099 (0.100 g, 0.237 mmol), 2-pyridinemethanol (0.0701 mL, 0.712 mmol), Cs_2CO_3 (0.162 g, 0.498 mmol) and oxone® (0.0146 g, 0.0237 mmol) in xylenes (0.24 mL) in a sealed vessel was stirred at 140 °C under an atmosphere of N_2 for 24 h. The reaction mixture was cooled to room temperature and MeOH (5 mL) was added. The suspension was sonicated in a warm water bath at 50 °C for 30 min. The supernatant was pipetted into a round-bottom flask containing 1.0 g of celite. The residual grey solid in the reaction vessel was extracted with MeOH (3 x 5 mL) and the combined organic extracts were added to the MeOH/celite suspension. Separately, a short silica plug was washed with MeOH (100 mL). The celite suspension was concentrated in vacuo and the celite was added on top of the washed silica plug. The plug was washed with MeOH (100 mL), and the yellow filtrate was discarded. The plug was then washed with additional MeOH (500 mL), and the colorless filtrate was collected, concentrated, and dried in vacuo to afford **19** (0.106 g, 0.206 mmol, 87%) as a light-tan solid: M.p. 138.2 °C (dec.); IR (ATR) ν_{max} 3400, 3126, 3021, 2928, 2801, 1592, 1568, 1472, 1456, 1435, 1418, 1370, 1349, 1292, 1250, 1161, 1139, 1103, 1050, 1008, 912, 885, 802, 777, 748 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 11.81 (brs, 1 H), 10.90 (brs, 1 H), 8.52 (d, *J* = 2.0 Hz, 1 H), 8.33 (bd, *J* = 3.9 Hz, 1 H), 8.25 (d, *J* = 2.0 Hz, 1 H), 7.79 (s, 1 H), 7.71 (s, 1 H), 7.64 (d, *J* = 8.1 Hz, 2 H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1 H), 7.44–7.41 (m, 4 H), 7.30 (d, *J* = 7.9 Hz, 1 H), 7.27 (s, 1 H), 7.03 (dd, *J* = 6.6, 4.8 Hz, 1 H), 4.22 (s, 2 H), 3.52 (s, 2 H), 2.47–2.21 (m, 8 H), 2.15 (s, 3 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.4, 148.6, 148.5, 141.7, 137.9, 137.0, 136.3, 135.2, 129.5, 128.4, 127.6, 126.9, 125.2, 125.1, 123.8, 123.3, 122.6, 121.0, 120.8, 117.7, 116.6, 116.4, 112.6, 111.9, 61.7, 54.8, 52.6, 45.7, 34.3; HRMS (ESI$^+$) *m/z* calcd for $C_{33}H_{33}N_6$ ([M+H]$^+$) 513.2761, found 513.2761.



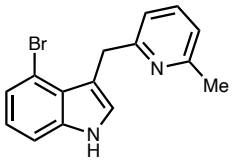
25

4-Bromo-3-(pyridin-4-ylmethyl)-1*H*-indole (**25**)**.** Synthesized according to the general procedure utilizing 4-bromoindole (0.150 mL, 1.17 mmol), 4-pyridinemethanol (0.388 g, 3.52 mmol), a 24 h reaction time, and 3% MeOH/CH_2Cl_2 as eluent for purification by chromatography on SiO_2 gave **25** (0.273 g, 0.951 mmol, 81%) as a tan solid: M.p. 184–186 °C; IR (ATR) ν_{max} 3072, 3021, 2919, 2857, 1684, 1604, 1558, 1542, 1495, 1417, 1331, 1260, 1121, 1088, 1064, 1040, 1005, 806, 774, 747, 730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 4.5, 1.5 Hz, 2 H), 8.38 (brs, 1 H), 7.33 (dd, *J* = 8.5, 1.0 Hz, 1 H), 7.27 (dd, *J* = 0.5 Hz, 1 H), 7.16 (d, *J* = 6.0 Hz, 2 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 6.93 (d, *J* = 2.0 Hz, 1 H), 4.42 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6. 149.6. 138.0. 125.5. 125.0. 124.4. 124.2. 123.3. 114.3. 114.0. 110.9. 31.9; HRMS (ESI$^+$) *m/z* calcd for $C_{33}H_{33}N_6$ ([M+H]$^+$) 287.0184, found 287.0157.



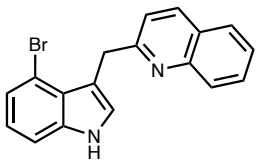
26

4-Bromo-3-(pyridin-3-ylmethyl)-1*H*-indole (**26**)**.** Synthesized according to the general procedure utilizing 4-bromoindole (0.150 mL, 1.17 mmol), 3-pyridinemethanol (0.343 mL, 3.52 mmol), a 144 h reaction time, and 3% MeOH/CH_2Cl_2 as eluent for purification by chromatography on SiO_2 gave **26** (0.0472 g, 0.164 mmol, 14%) as a tan solid: M.p. 171.3–173.0 °C; IR (ATR) ν_{max} 3056, 2850, 2342, 2102, 1578, 1561, 1478, 1427, 1419, 1337, 1306, 1290, 1198, 1163, 1100, 1071, 1043, 1030, 916, 801, 773, 750, 728, 709, 657, 635 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.32 (brs, 1 H), 8.45 (d, *J* = 1.6 Hz, 1 H), 8.37 (dd, *J* = 4.7, 1.4 Hz, 1 H), 7.53 (dt, *J* = 7.8, 1.7 Hz, 1 H), 7.39 (dd, *J* = 8.1, 0.7 Hz, 1 H), 7.27 (dd, *J* = 7.5, 4.5 Hz, 1 H), 7.22 (d, *J* = 2.4 Hz, 1 H), 7.14 (dd, *J* = 7.5, 0.7 Hz, 1 H), 6.98 (t, *J* = 7.8 Hz, 1 H), 4.32 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 147.4, 137.9, 137.3, 136.5, 125.4, 124.8, 124.2, 123.4, 123.3, 115.5, 114.4, 110.8, 29.9; HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{12}N_2Br$ ([M+H]$^+$) 287.0184, found 287.0179.



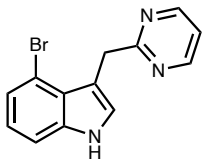
27

4-Bromo-3-((6-methylpyridin-2-yl)methyl)-1*H*-indole (**27**). Synthesized according to the general procedure utilizing 4-bromoindole (0.150 mL, 1.17 mmol), 6-methyl-2-pyridinemethanol (0.442 g, 3.52 mmol), a 24 h reaction time, and 20% EtOAc/CH_2Cl_2 as eluent for purification by chromatography on SiO_2 gave **27** (0.212 g, 0.704 mmol, 60%) as a tan solid: M.p. 165–167 °C; IR (ATR) ν_{max} 3121, 2916, 1675, 1597, 1577, 1459, 1408, 1334, 1290, 1251, 1195, 1170, 1155, 1113, 1096, 1069, 1044, 993, 915 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (brs, 1 H), 7.44 (t, *J* = 8.0 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.50 (overlap with $CDCl_3$ residual solvent peak, 1 H), 7.01 (t, *J* = 8.0 Hz, 1 H), 6.97 (d, *J* = 7.5 Hz, 1 H), 6.95 (d, *J* = 2.5 Hz, 1 H), 6.86 (d, *J* = 7.5 Hz, 1 H), 4.58 (s, 2 H), 2.58 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 157.7, 137.8, 136.8, 125.9, 125.0, 124.1, 123.0, 120.6, 120.1, 114.8, 114.6, 110.6, 35.3, 24.7; HRMS (ESI$^+$) *m/z* calcd for $C_{15}H_{14}N_2Br$ ([M+H]$^+$) 301.0335, found 301.0327.



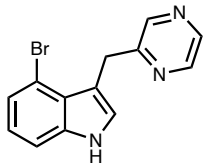
28

2-((4-Bromo-1*H*-indol-3-yl)methyl)quinoline (**28**). Synthesized according to the general procedure utilizing 4-bromoindole (0.150 mL, 1.17 mmol), 2-quinolinylmethanol (0.561 g, 3.52 mmol), a 24 h reaction time, and 15% EtOAc/CH_2Cl_2 as eluent for purification by chromatography on SiO_2 gave **28** (0.203 g, 0.602 mmol, 51%) as an orange-tan solid: M.p. 185–187 °C; IR (ATR) ν_{max} 3149, 1617, 1598, 1561, 1505, 1423, 1411, 1334, 1249, 1217, 1200, 1173, 1141, 1114, 1075, 1044, 955, 909 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (brs, 1 H), 8.09 (d, *J* = 8.5 Hz, 1 H), 8.03 (d, *J* = 8.5 Hz, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.70 (td, *J* = 7.0, 1.0 Hz, 1 H), 7.50 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.32 (t, *J* = 8.0 Hz, 1 H), 7.28 (dd, *J* = 7.5, 0.5 Hz, 1 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 6.95 (d, *J* = 2.0 Hz, 1 H), 4.82 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 147.8, 137.9, 136.7, 129.6, 128.8, 127.7, 127.0, 126.0, 125.7, 125.3, 124.2, 123.1, 121.9, 114.5, 114.3, 110.8, 35.9; HRMS (ESI$^+$) *m/z* calcd for $C_{18}H_{14}N_2Br$ ([M+H]$^+$) 337.0328, found 337.0335.



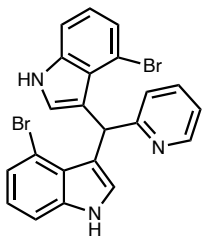
29

4-Bromo-3-(pyrimidin-2-ylmethyl)-1*H*-indole (**29**)**.** A mixture of 4-bromoindole (0.150 mL, 1.17 mmol), 2-pyrimidinemethanol (0.396 g, 3.52 mmol), Cs_2CO_3 (0.421 g, 1.29 mmol) and oxone® (0.0721 g, 0.117 mmol) in xylenes (0.59 mL) in a sealed vessel was stirred at 140 °C under an atmosphere of N_2 for 96 h. The reaction mixture was cooled to room temperature, and additional xylenes (0.50 mL) was added. After another 48 h at 140 °C, the solution was cooled to room temperature and H_2O/MeOH (1:1, 20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (4 x 30 mL), and the combined organic layers were dried ($MgSO_4$), filtered through a celite plug, and concentrated. The crude residue was purified by reverse-phase chromatography on C18 SiO_2 (30 g, 10% MeCN/H_2O to 100% MeCN). Fractions containing the desired product were combined and extracted with CH_2Cl_2/MeOH (9:1, 3 x 30 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to afford **29** (0.177 g, 0.614 mmol, 52%) as a brown solid: M.p. 196.8 °C (dec.); IR (ATR) ν_{max} 3156, 2914, 2329, 1573, 1559, 1487, 1422, 1403, 1329, 1226, 1200, 1171, 1140, 1118, 1073, 1042, 912, 815, 802, 762, 726, 638 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.24 (brs, 1 H), 8.69 (d, *J* = 4.9 Hz, 2 H), 7.38 (d, *J* = 7.2 Hz, 1 H), 7.30 (t, *J* = 4.8 Hz, 1 H), 7.20 (d, *J* = 2.1 Hz, 1 H), 7.10 (d, *J* = 7.5 Hz, 1 H), 6.95 (t, *J* = 7.8 Hz, 1 H), 4.58 (s, 2 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 157.1, 137.7, 126.4, 125.2, 122.5, 122.0, 118.8, 113.0, 111.3, 111.2, 35.8; HRMS (ESI^+) *m/z* calcd for $C_{13}H_{11}N_3Br$ ($[M+H]^+$) 288.0136, found 288.0130.



30

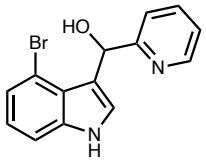
4-Bromo-3-(pyrazin-2-ylmethyl)-1*H*-indole (**30**)**.** A mixture of 4-bromoindole (0.150 mL, 1.17 mmol), pyrazin-2-ylmethanol (0.315 mL, 3.52 mmol), Cs_2CO_3 (0.421 g, 1.29 mmol) and oxone® (0.0721 g, 0.117 mmol) in xylenes (0.59 mL) was stirred at 140 °C in a sealed vessel under an atmosphere of N_2 for 24 h. The reaction mixture was cooled to room temperature and H_2O (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered through a celite plug, and concentrated. The crude residue was purified by reverse-phase chromatography on C18 SiO2 (30 g, 10% MeCN/H_2O to 100% MeCN). Fractions containing the desired product were combined and diluted with brine (10 mL). The aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 3 x 30 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to afford **30** (0.298 g, 1.03 mmol, 88%) as an orange-brown solid: M.p. 148.0–149.3 °C; IR (ATR) ν_{max} 3191, 3039, 2903, 1615, 1548, 1531, 1489, 1477, 1439, 1403, 1333, 1300, 1283, 1250, 1205, 1176, 1133, 1111, 1074, 1057, 1043, 1025, 944, 913, 831, 802, 773, 757, 739, 731, 666 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 11.37 (brs, 1 H), 8.55 (dd, *J* = 2.5 1.6 Hz, 1 H), 8.44 (d, *J* = 2.5 Hz, 1 H), 8.38 (d, *J* = 1.3 Hz, 1 H), 7.41 (dd, *J* = 8.1, 0.7 Hz, 1 H), 7.28 (d, *J* = 2.5 Hz, 1 H), 7.14 (dd, *J* = 7.5, 0.7 Hz, 1 H), 6.98 (t, *J* = 7.8 Hz, 1 H), 4.50 (s, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 157.1, 144.2, 143.8, 142.0, 137.8, 126.8, 124.7, 122.7, 122.3, 112.7, 111.4, 110.9, 31.8; HRMS (ESI^+) *m/z* calcd for $C_{13}H_{11}N_3Br$ ($[M+H]^+$) 288.0131, found 288.0124.



32

3,3'-(Pyridin-2-ylmethylene)bis(4-bromo-1*H*-indole) (**32**). A mixture of 4-bromoindole (0.100 mL, 0.783 mmol), 2-pyridinemethanol (0.227 mL, 2.35 mmol) and Cs_2CO_3 (0.281 g, 0.861 mmol) was stirred at 110 °C in a sealed vessel under an atmosphere of O_2 for 24 h. The reaction mixture was cooled to room temperature, and H_2O (10 mL) and CH_2Cl_2/MeOH (9:1, 20 mL) were added. The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), filtered, and concentrated. The crude residue was triturated with CH_2Cl_2 and filtered off. The filtrate was concentrated, and the residue was purified by chromatography on SiO_2 (35% EtOAc/CH_2Cl_2). The triturated solid was combined with the purified filtrate and dried in vacuo to afford **32** (0.131 g, 0.260 mmol, 70%) as a light-tan solid: M.p. >250 °C; IR (ATR) ν_{max} 3433, 3116, 1593, 1570, 1472, 1432, 1416, 1333, 1283, 1181, 1141, 1093, 1034, 1004 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 11.17 (d, *J* = 1.8 Hz, 2 H), 8.49 (d, *J* = 4.5 Hz, 1 H), 7.66 (td, *J* = 6.0, 1.5 Hz, 1 H), 7.39 (d, *J* = 7.5 Hz, 2 H), 7.21–7.17 (m, 2 H), 7.09 (d, *J* = 6.9 Hz, 2 H), 7.03 (d, *J* = 7.8 Hz, 1 H), 6.96 (t, *J* = 7.8 Hz, 2 H), 6.54 (d, *J* = 2.1 Hz, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.7, 148.9, 138.1, 136.2, 126.7, 124.0, 122.8, 122.7, 122.0, 121.0, 118.6, 113.1, 111.3; HRMS (ESI^+) *m/z* calcd for $C_{22}H_{16}N_3Br_2$ ($[M+H]^+$) 479.9706, found 479.9710.

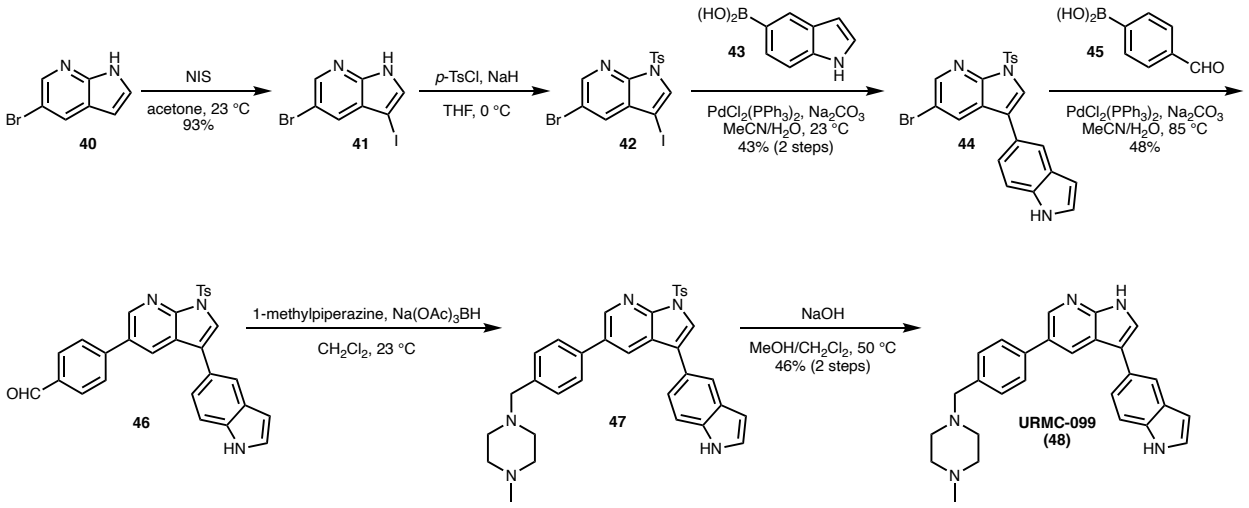
6. Synthesis and characterization of putative intermediate 33



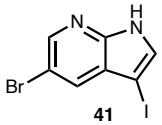
33

(4-Bromo-1*H*-indol-3-yl)(pyridin-2-yl)methanol (**33**). To a solution of 4-bromoindole (0.128 mL, 1.00 mmol) and tetramethylguanidine (0.00775 g, 0.0667 mmol) in H_2O (1.7 mL) was added 2-pyridinemethanol (0.0320 mL, 0.333 mmol). The solution was stirred at room temperature for 24 h before it was diluted with EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were treated with Et_3N (0.5 mL), dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (60% EtOAc/CH_2Cl_2) to afford **40** (0.0510 g, 0.168 mmol, 50%) as a tan solid: M.p. 132–134 °C; IR (ATR) ν_{max} 3159, 1592, 1571, 1425, 1339, 1184, 1145, 1096, 1066, 1044, 1017, 996 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.5 Hz, 1 H), 8.49 (brs, 1 H), 7.64 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.32 (d, *J* = 7.5 Hz, 1 H), 7.30 (d, *J* = 8.0 Hz, 1 H), 7.22 (dd, *J* = 7.8, 5.8 Hz, 1 H), 7.02 (app t, *J* = 8.0 Hz, 1 H), 6.93 (d, *J* = 2.5 Hz, 1 H), 6.77 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 148.0, 137.8, 136.9, 125.2, 124.8, 123.2, 122.4, 122.0, 119.7, 113.8, 110.9, 67.8; HRMS (ESI^+) *m/z* calcd for $C_{14}H_{12}O_2N_2Br$ ($[M+H]^+$) 303.0128; found 303.0119.

7. Synthesis and characterization of URMC-099

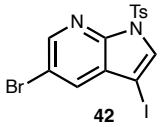


Scheme S1 Synthesis of URMC-099 (**48**) according to a literature protocol.[3]



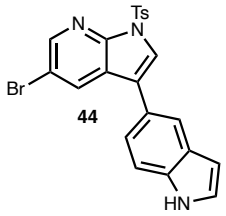
41

5-Bromo-3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine (**41**). To a solution of 5-bromo-7-azaindole (5.00 g, 24.9 mmol) in acetone (124 mL) at room temperature was added *N*-iodosuccinimide (6.15 g, 27.4 mmol). The solution was stirred at room temperature for 1.5 h before being cooled to 0 °C. The resulting precipitate was filtered off and collected. The filtrate was concentrated in vacuo and redissolved in acetone (50 mL). The solution was cooled to 0 °C and the resulting precipitate was filtered off and collected. The combined crops of precipitate were dried in vacuo to afford **41** (7.47 g, 23.1 mmol, 93%) as a pink solid: ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.35 (brs, 1 H), 8.31 (d, J = 2.5 Hz, 1 H), 7.86 (d, J = 2.0 Hz, 1 H), 7.80 (d, J = 2.5 Hz, 1 H). Spectral data were consistent with previously reported properties.[3]



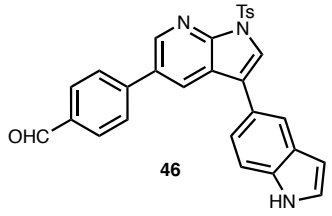
42

5-Bromo-3-iodo-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine (**42**). To a stirred suspension of NaH (1.39 g, 34.7 mmol, 60% in mineral oil) in THF (116 mL) at 0 °C was added portionwise **41** (7.47 g, 23.1 mmol). After 20 min, *p*-TsCl (4.95, 25.4 mmol) was added portionwise. The solution was stirred at 0 °C for 2 h and then quenched with saturated aqueous NH_4Cl (100 mL). The solution was extracted with CH_2Cl_2 (3 x 100 mL), and the combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated to afford **42** (11.0, 23.1 mmol) as a pinkish-white solid. The material was used for the next step without additional purification.



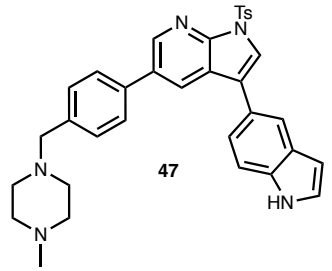
44

5-Bromo-3-(1*H*-indol-5-yl)-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine (**44**). To a mixture of **42** (11.0 g, 23.1 mmol), indole-5-boronic acid (**43**, 4.17 g, 25.4 mmol), and MeCN (115 mL) at room temperature was added aqueous Na_2CO_3 (1 M, 58 mL) followed by bis(triphenylphosphine)palladium(II) chloride (1.62 g, 2.31 mmol). The reaction mixture was stirred under an atmosphere of N_2 at room temperature for 6 h, treated with EtOAc (200 mL) and quenched with H_2O (100 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 x 200 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (CH_2Cl_2) to afford **44** (4.61 g, 9.89 mmol, 43% over two steps) as a light-brown foam which was gently crushed into a fine powder with a spatula: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.0 Hz, 1 H), 8.26 (d, *J* = 2.0 Hz, 2 H), 8.08 (d, *J* = 8.4 Hz, 2 H), 7.85 (s, 1 H), 7.81 (brs, 1 H), 7.51 (d, *J* = 8.4 Hz, 1 H), 7.36 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.30–7.28 (m, 3 H), 6.63 (brs, 1 H), 2.39 (s, 3 H). Spectral data were consistent with previously reported properties.[3]



46

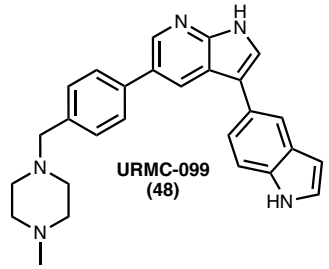
4-(3-(1*H*-Indol-5-yl)-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridin-5-yl)benzaldehyde (**46**). To a mixture of **44** (2.50 g, 5.36 mmol) and 4-formylphenylboronic acid (**45**, 0.964 g, 6.43 mmol) in MeCN (27 mL) was added aqueous Na_2CO_3 (1 M, 13 mL) at room temperature followed by bis(triphenylphosphine)palladium(II) chloride (0.376 g, 0.536 mmol). The reaction mixture was stirred in a sealed vessel under an atmosphere of N_2 at 85 °C for 4 h, cooled to room temperature, and treated with saturated aqueous NH_4Cl (50 mL). The solution was extracted with CH_2Cl_2 (3 x 50 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (5% EtOAc/CH_2Cl_2) to afford **46** (1.27 g, 2.58 mmol, 48%) as a yellow-tan solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.07 (s, 1 H), 8.73 (d, *J* = 2.1 Hz, 1 H), 8.34 (d, *J* = 2.2 Hz, 1 H), 8.30 (d, *J* = 2.0 Hz, 1 H), 8.16 (d, *J* = 8.4 Hz, 2 H), 7.98 (d, *J* = 8.3 Hz, 2 H), 7.91 (s, 1 H), 7.88 (brs, 1 H), 7.75 (d, *J* = 8.2 Hz, 2 H), 7.53 (d, *J* = 8.4 Hz, 1 H), 7.43 (dd, *J* = 8.4, 1.6 Hz, 1 H), 7.33–7.29 (m, 3 H), 6.64–6.63 (m, 1 H), 2.39 (s, 3 H). Spectral data were consistent with previously reported properties.[3]



47

3-(1*H*-Indol-5-yl)-5-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine (**47**). To a solution of **46** (1.27 g, 2.58 mmol) in CH_2Cl_2 (26 mL) at room temperature was added 1-methylpiperazine (1.16 mL, 10.3 mmol). After 15 min, sodium

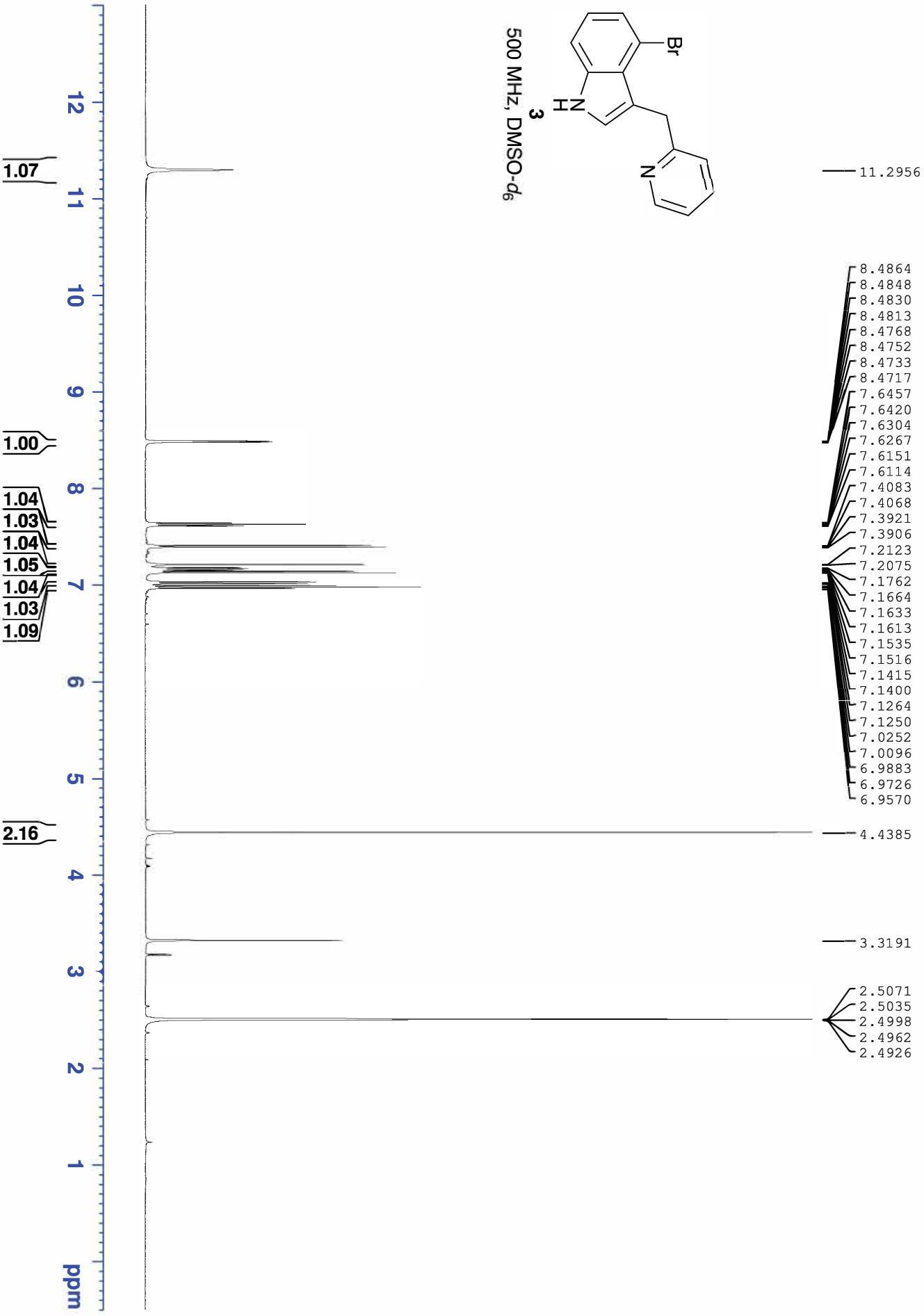
triacetoxyborohydride (0.847 g, 3.87 mmol) was added portionwise. The solution was stirred at room temperature for 1 h before brine (20 mL) was added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2/MeOH (9:1, 2 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated to afford **47** (1.49 g, 2.58 mmol) as a brown solid. The material was used for the next step without additional purification.



3-(1*H*-Indol-5-yl)-5-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine (**URMC-099, 48**). To a solution of **47** (1.49 g, 2.58 mmol) in MeOH/CH_2Cl_2 (3:1, 9 mL) at room temperature was added NaOH (0.310 g, 7.75 mmol). The solution was stirred in a sealed vessel at 50 °C for 2 h, cooled to room temperature and treated with H_2O (15 mL. The aqueous layer was extracted with CH_2Cl_2 (3 x 15 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (100% MeOH) to afford **48** (0.497 g, 1.18 mmol, 46% over two steps) as a colorless solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.82 (brs, 1 H), 11.07 (brs, 1 H), 8.54 (d, *J* = 1.9 Hz, 1 H), 8.41 (d, *J* = 2.0 Hz, 1 H), 7.90, (s, 1 H), 7.76 (s, 1 H), 7.69 (d, *J* = 8.0 Hz, 2 H), 7.48 (s, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.36–7.34 (m, 1 H), 6.49 (brs, 1 H), 3.50 (s, 2 H), 2.45–2.26 (m, 8 H), 2.15 (s, 3 H). Spectral data were consistent with previously reported properties.[3]

8. References

1. R. Cano, M. Yus and D. J. Ramon, *Tetrahedron Lett.*, 2013, **54**, 3394-3397.
2. S. Rinkam, W. Senapak, S. Watchasit, R. Saeeng and U. Sirion, *Synlett.*, 2022, **33**, 1383–1390.
3. V. S. Goodfellow, C. J. Loweth, S. B. Ravula, T. Wiemann, T. Nguyen, Y. Xu, D. E. Todd, D. Sheppard, S. Pollack, O. Polesskaya, D. F. Marker, S. Dewhurst and H. Gelbard, *J. Med. Chem.*, 2013, **56**, 8032–8048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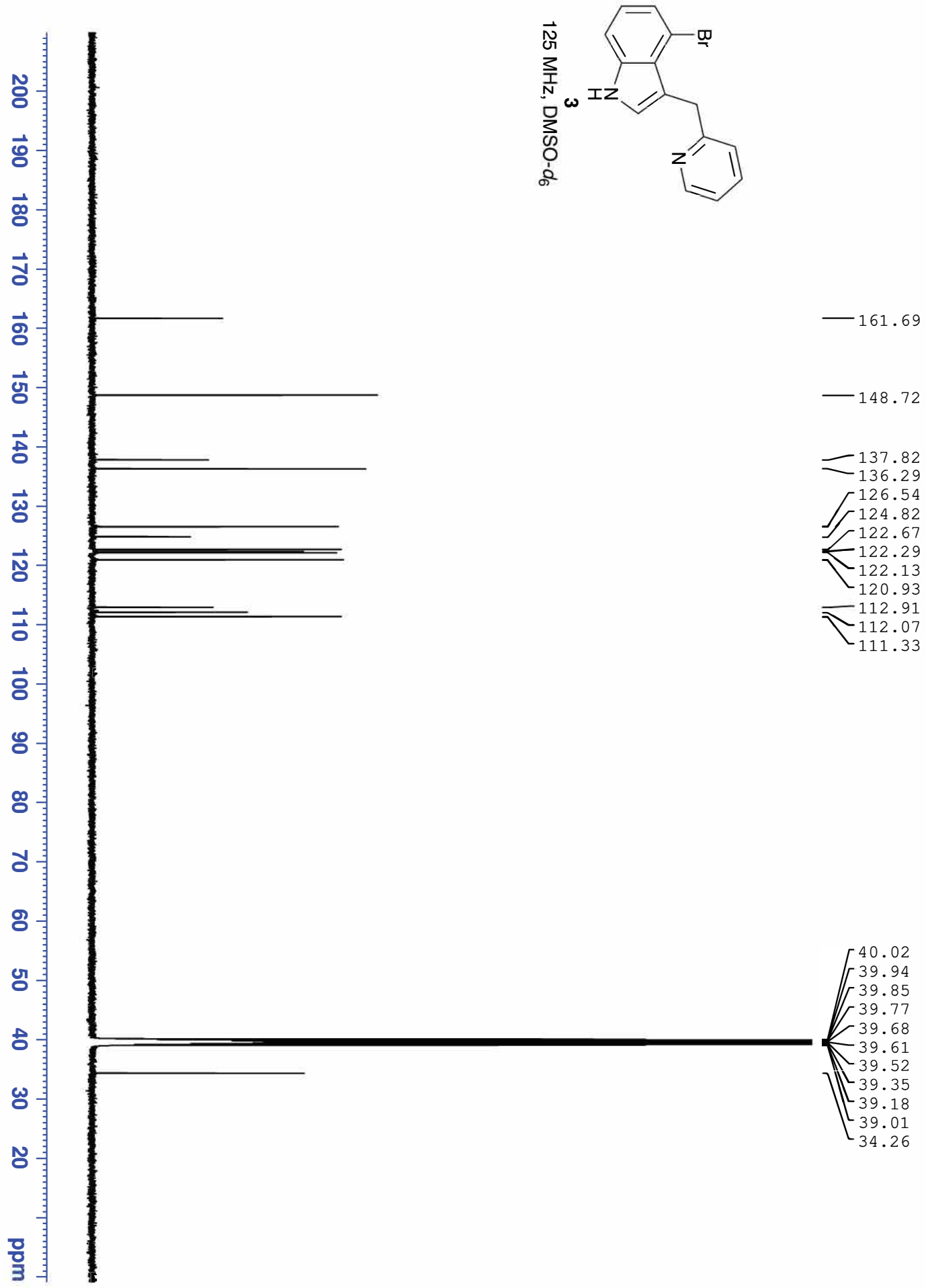
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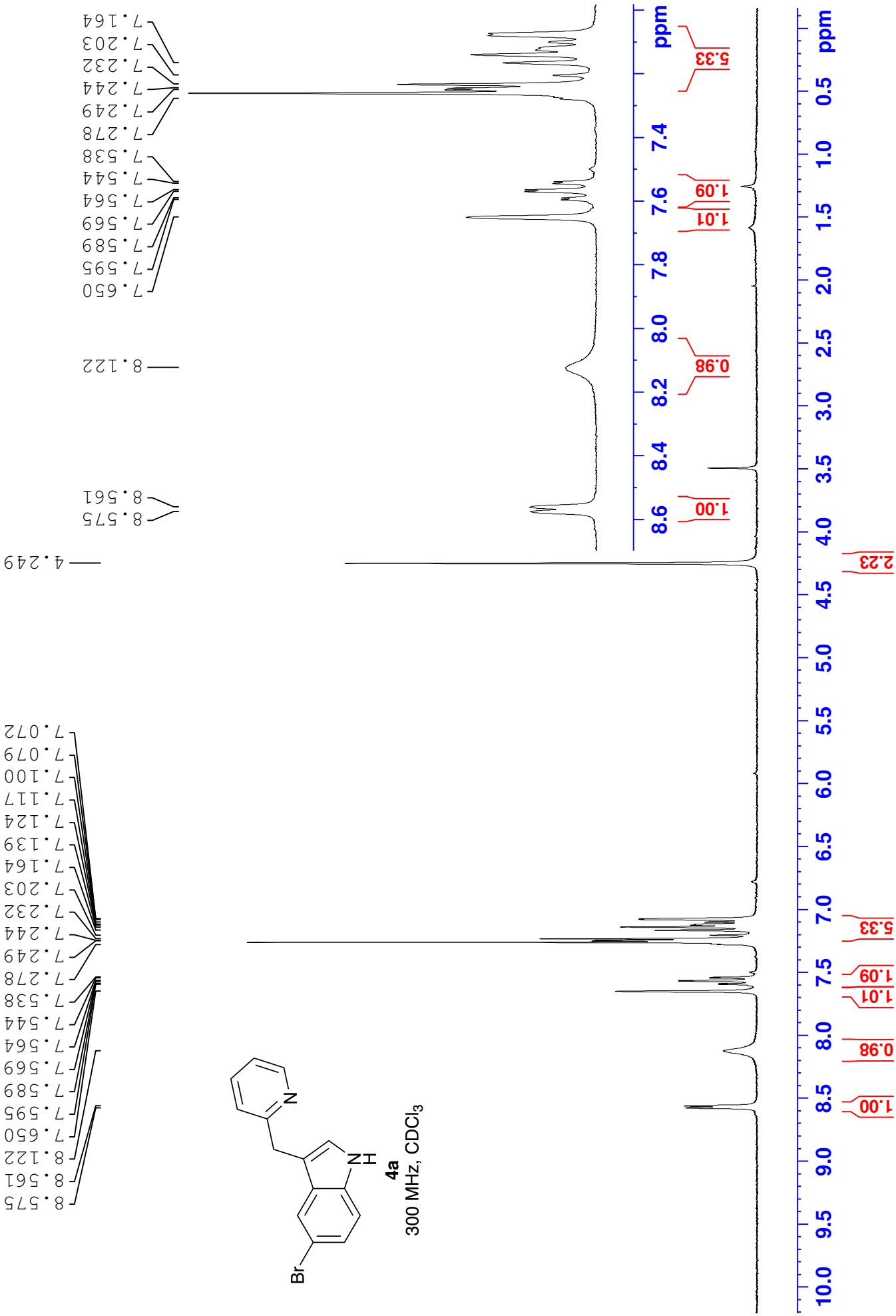
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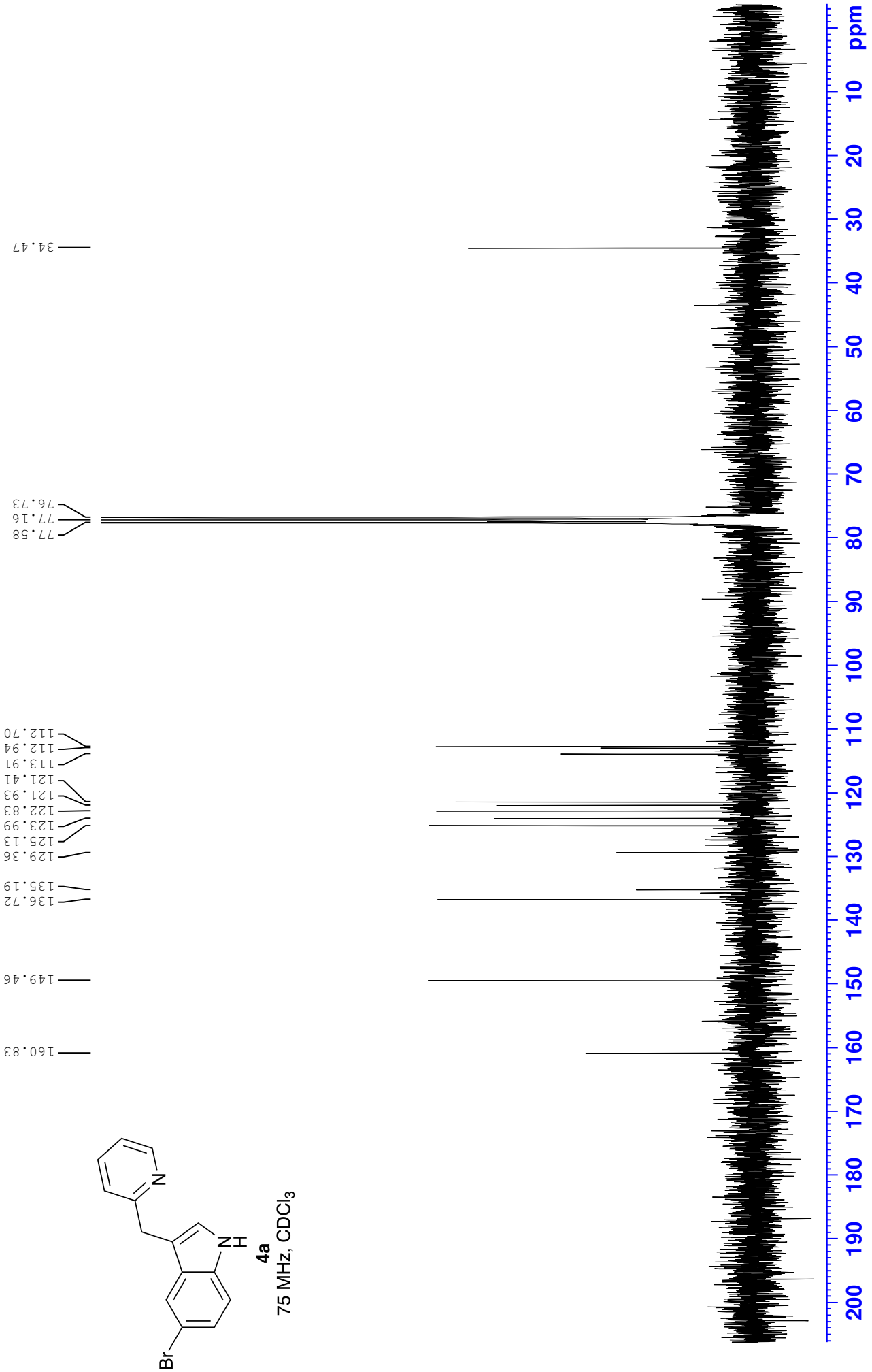
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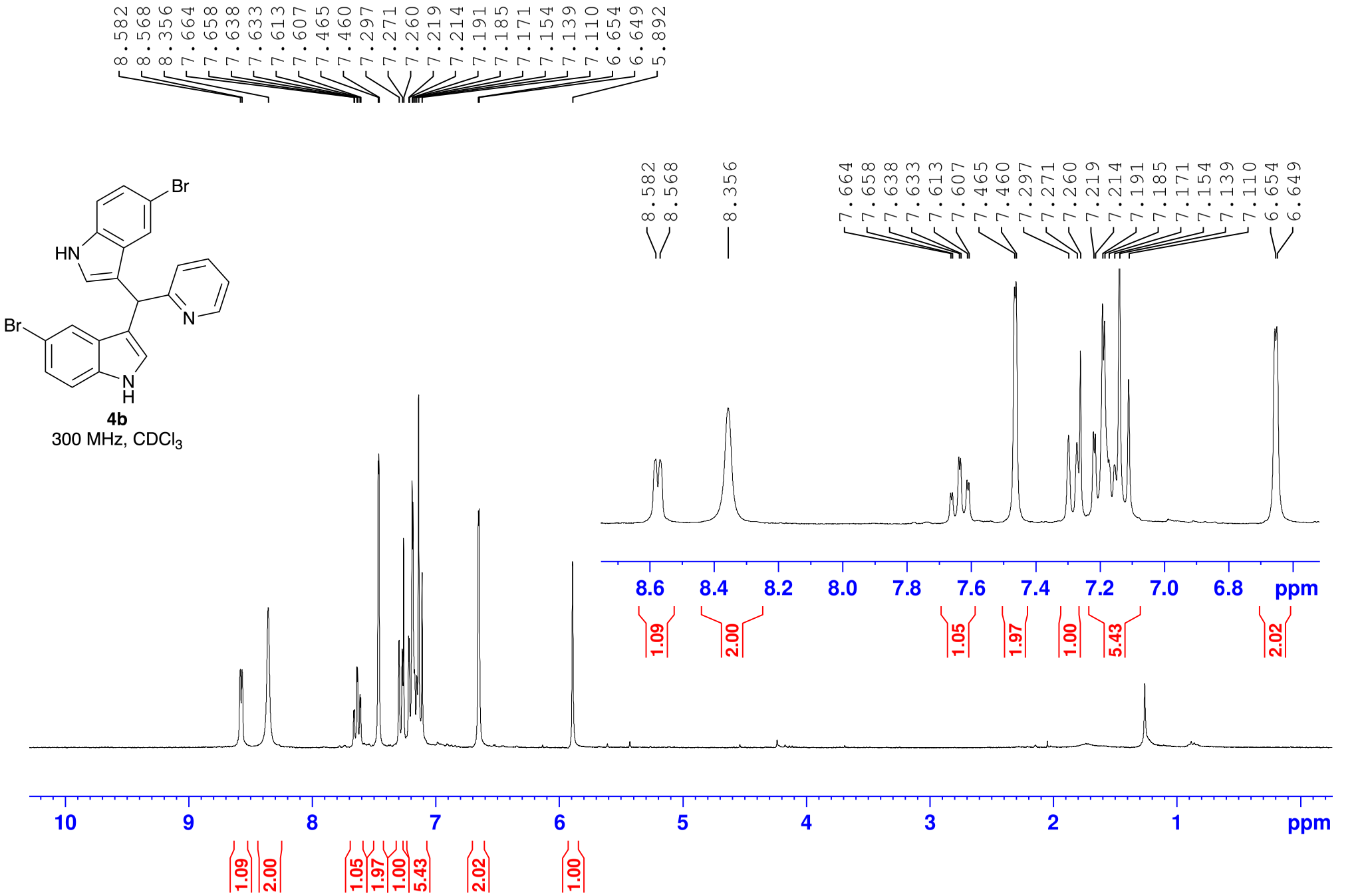
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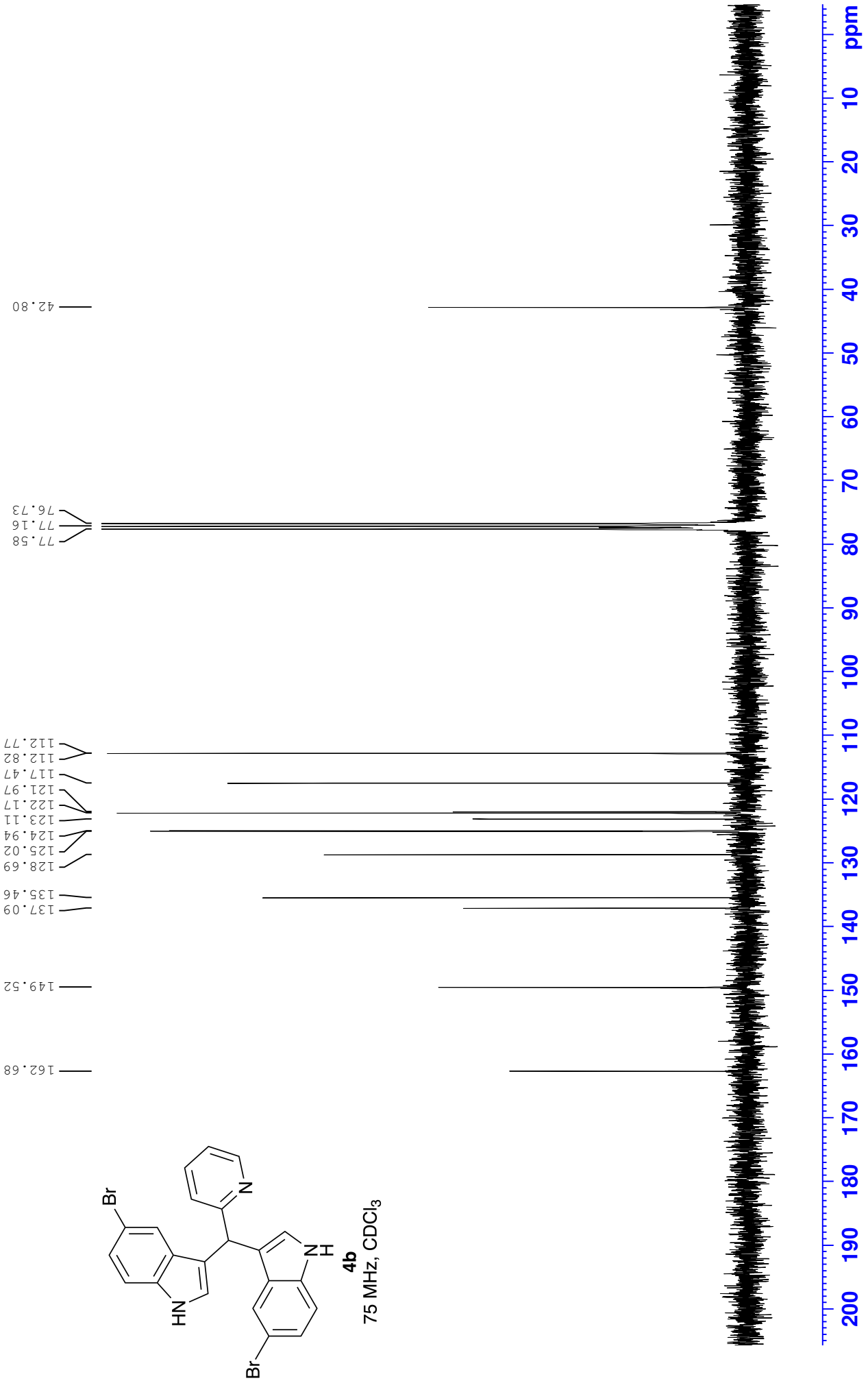
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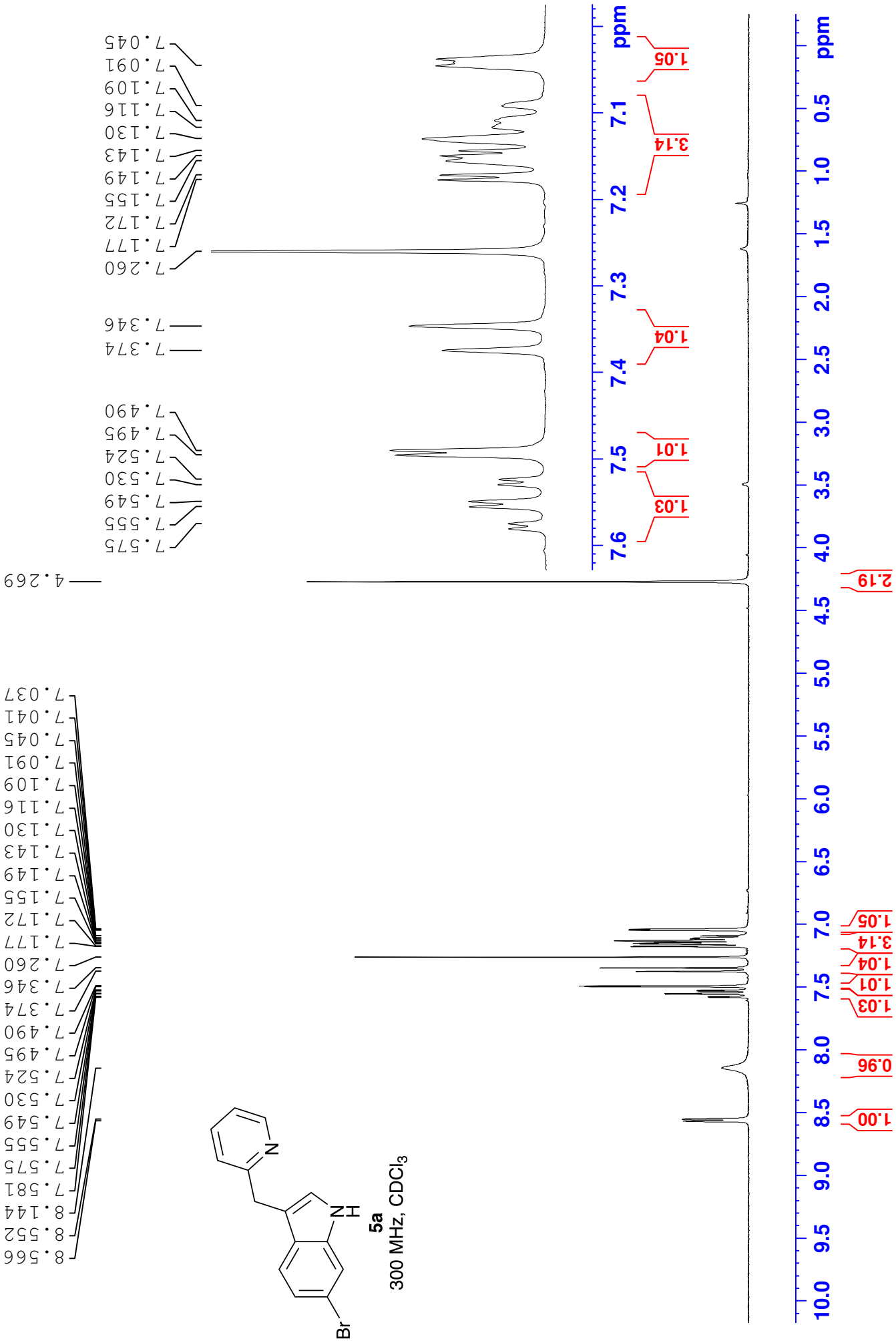
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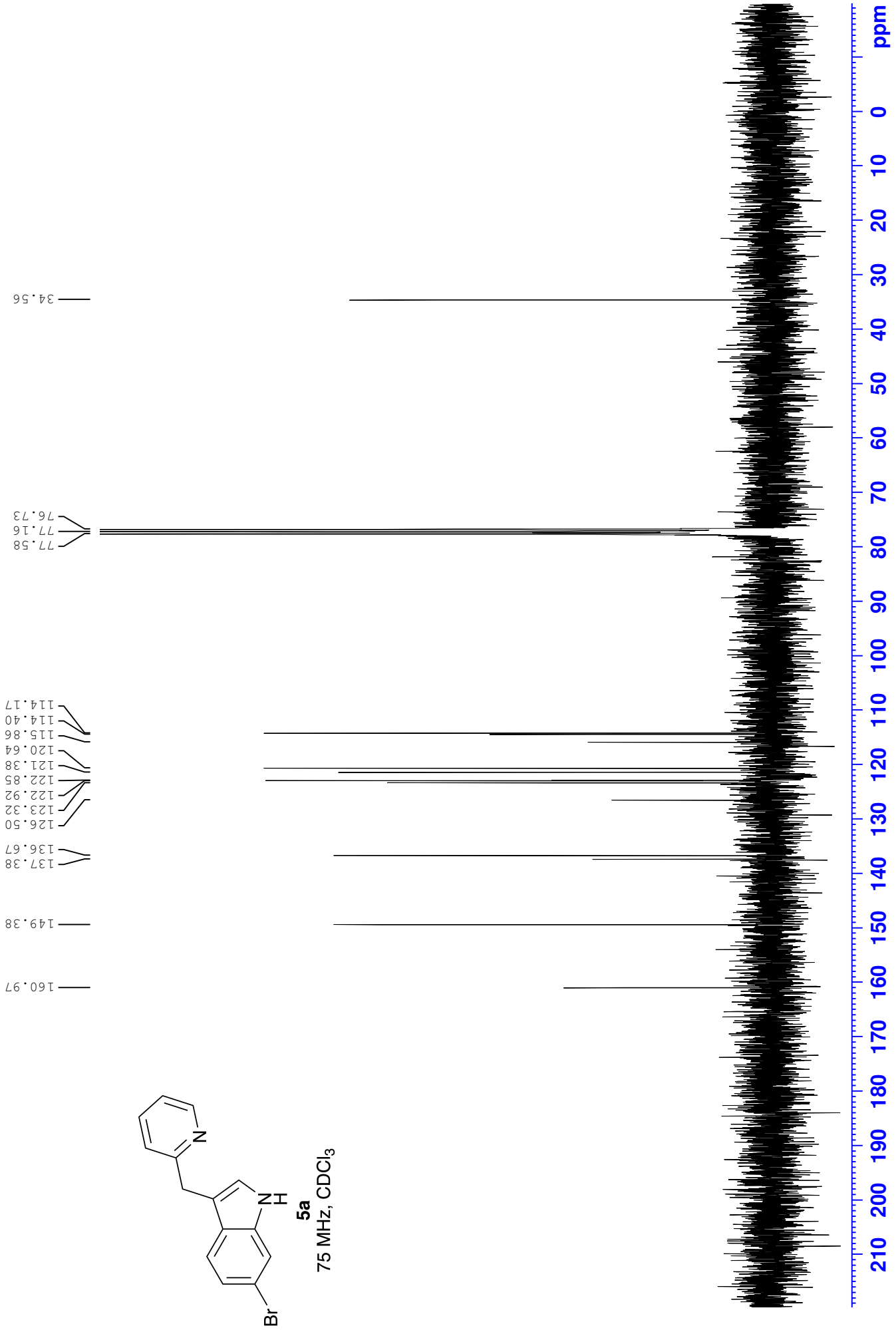
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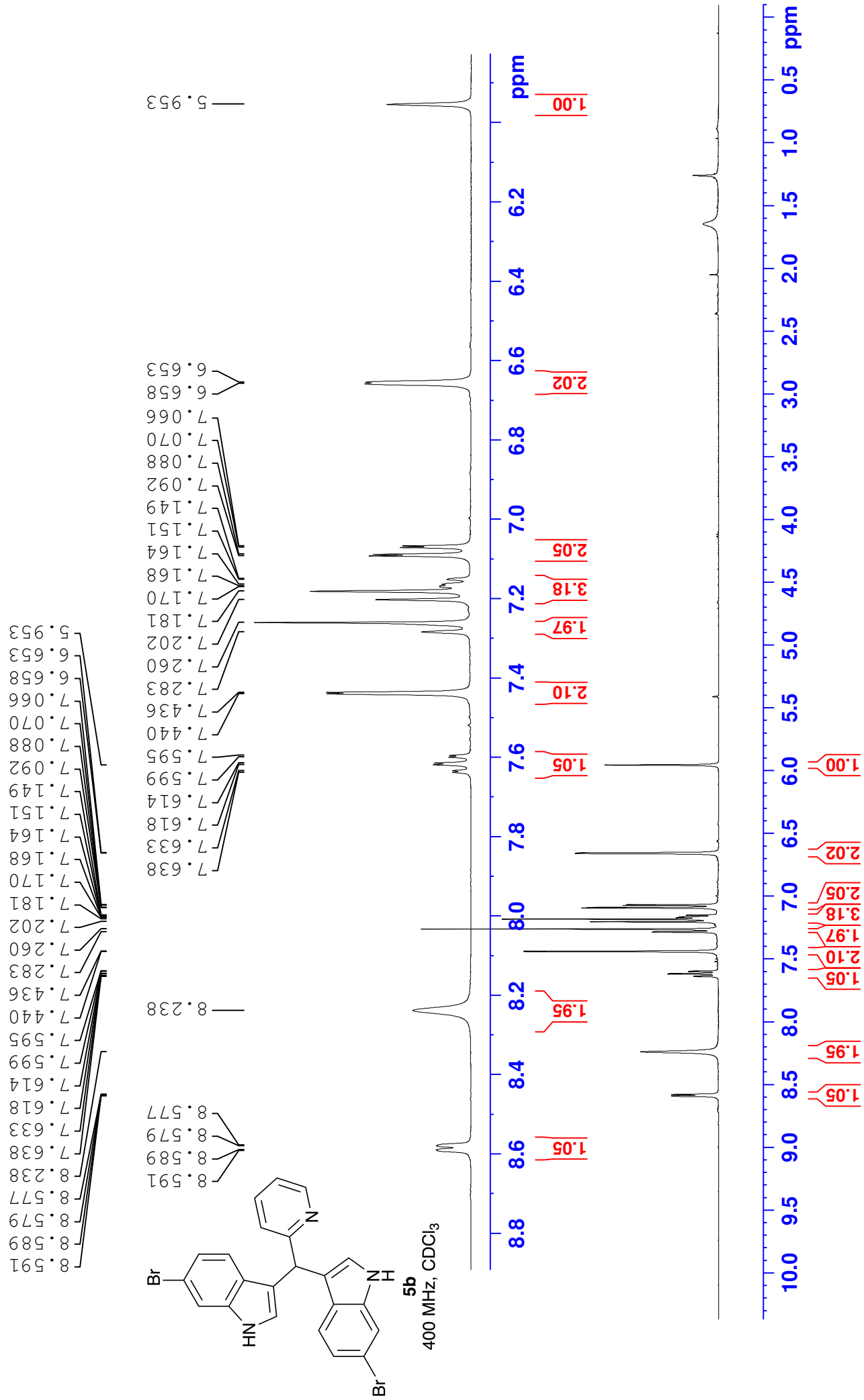
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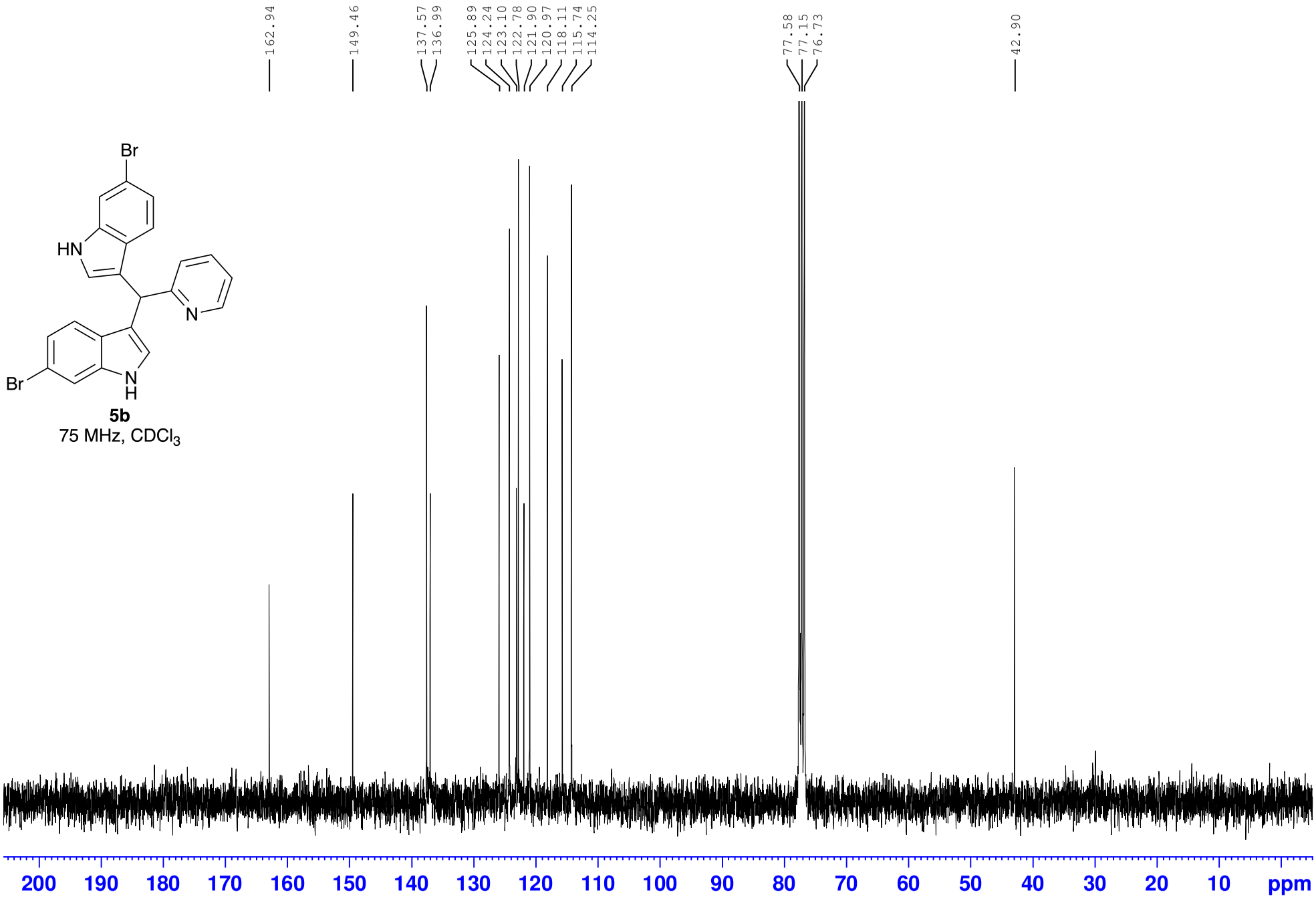
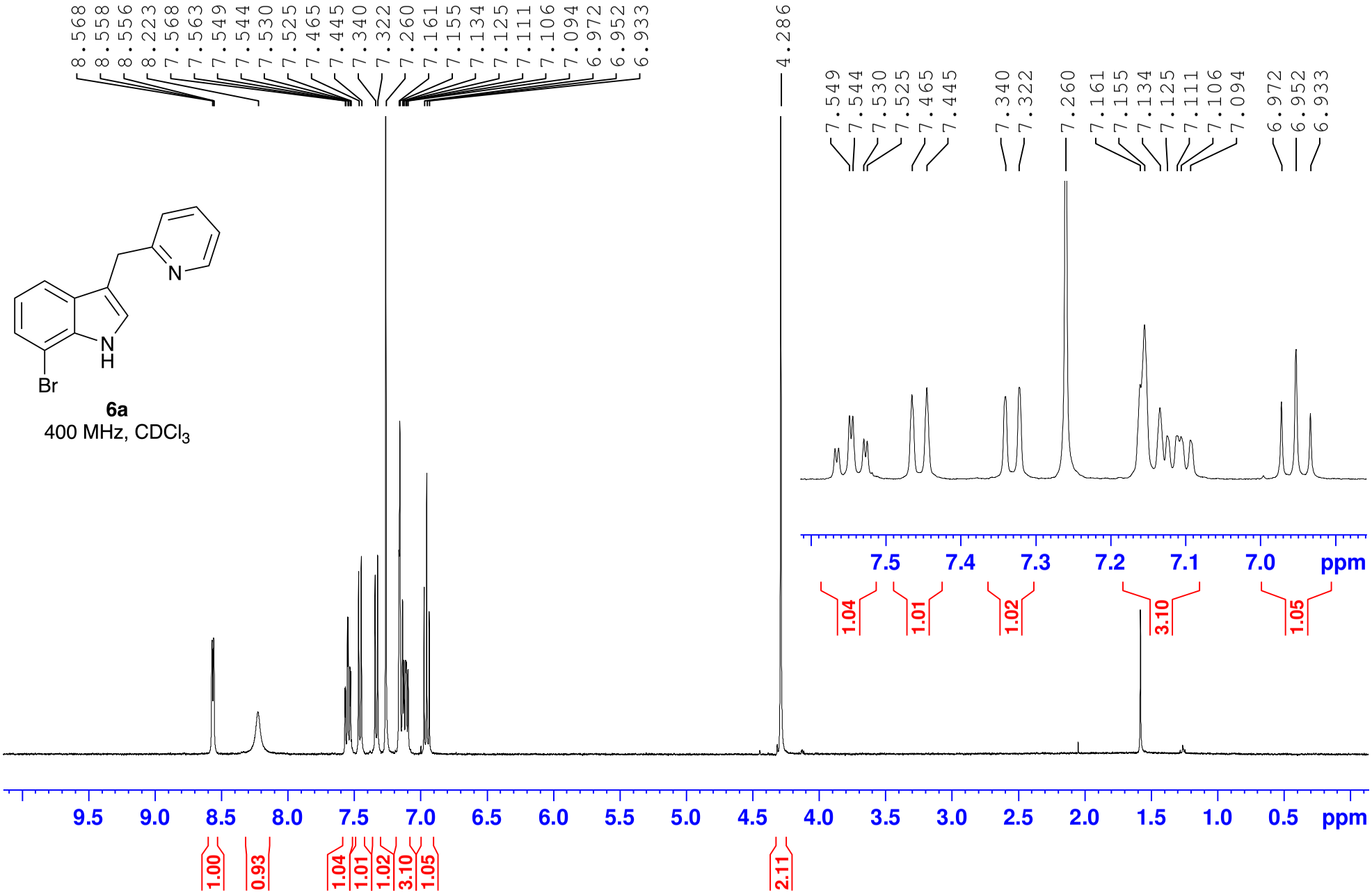
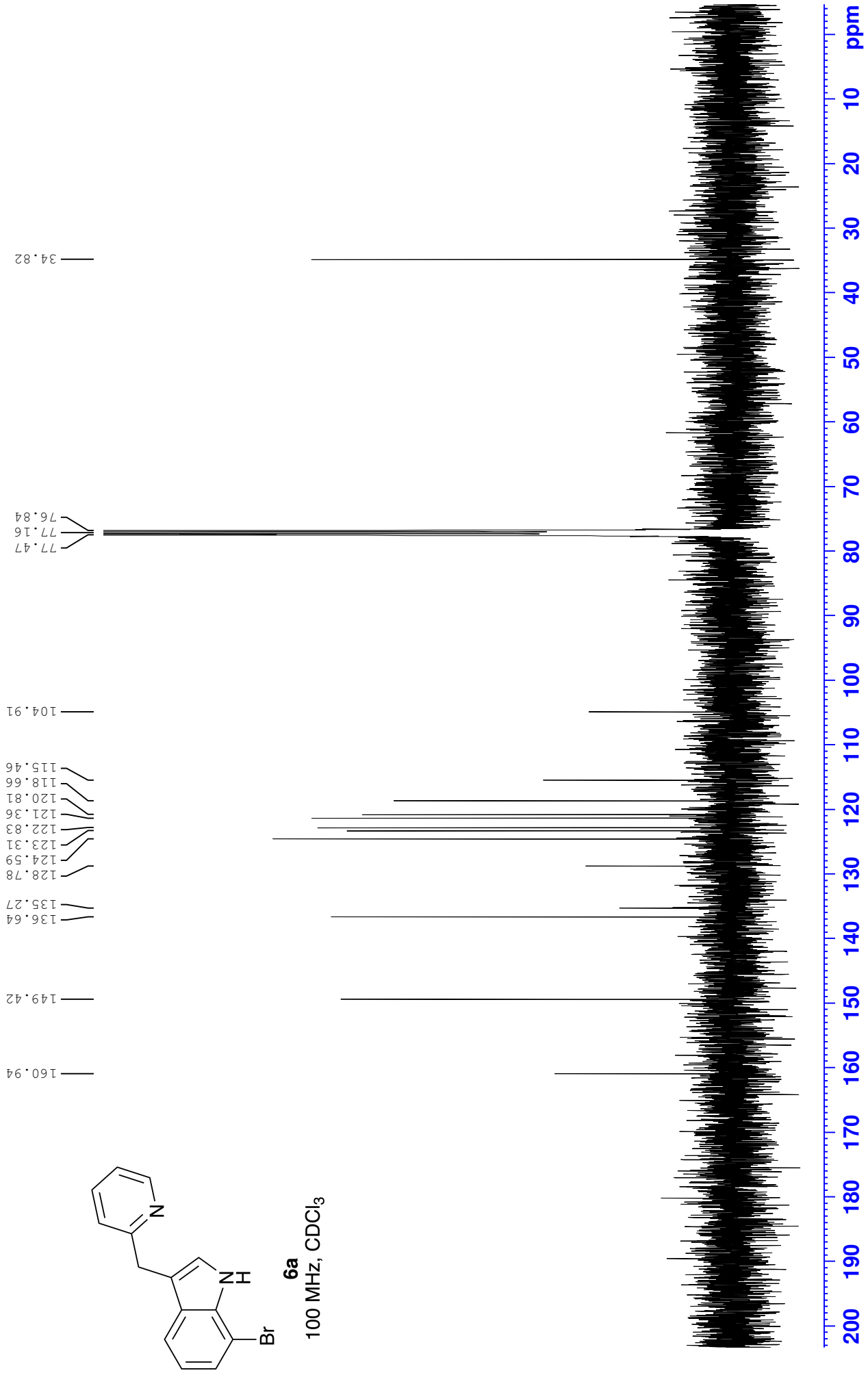
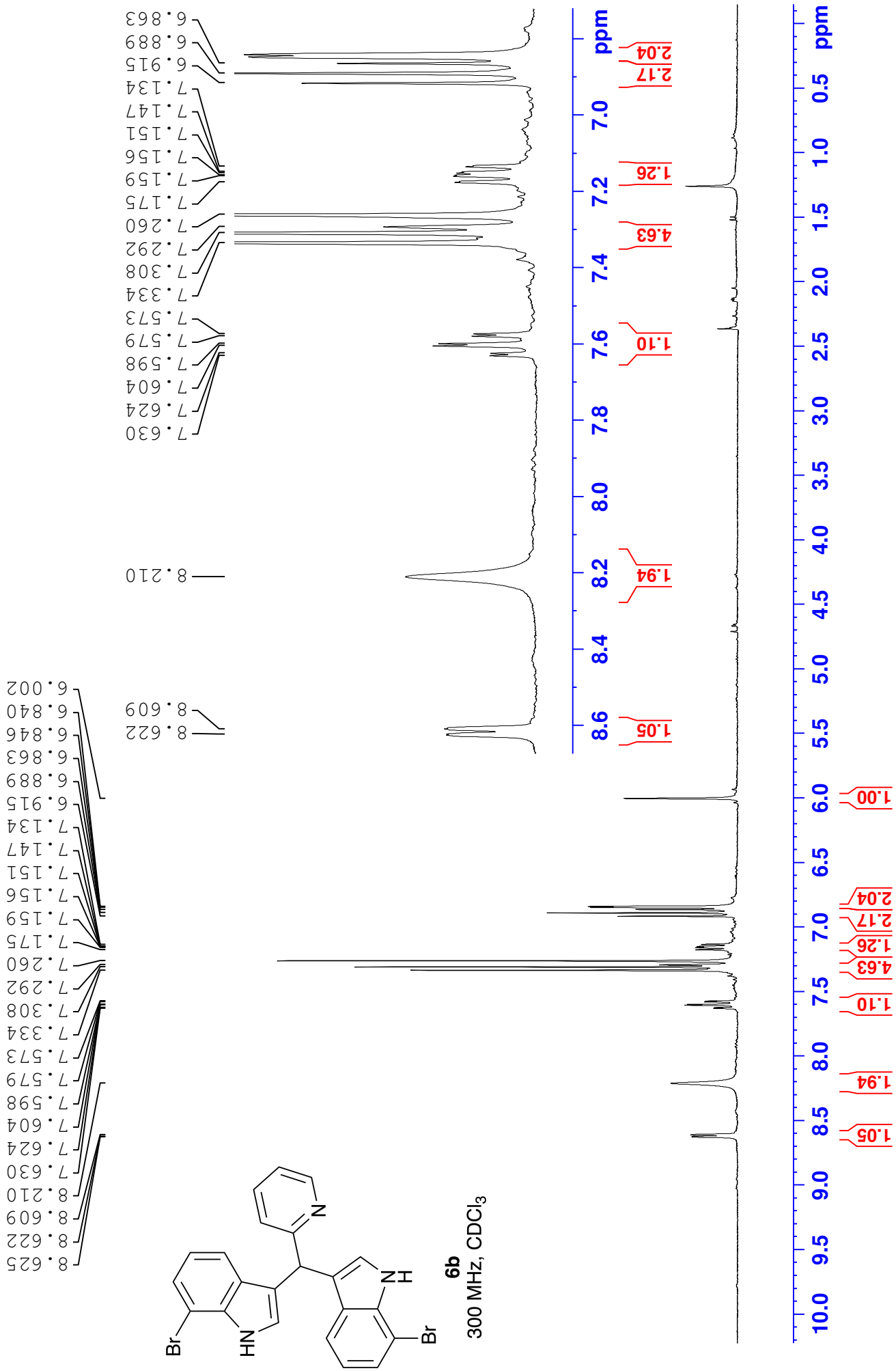
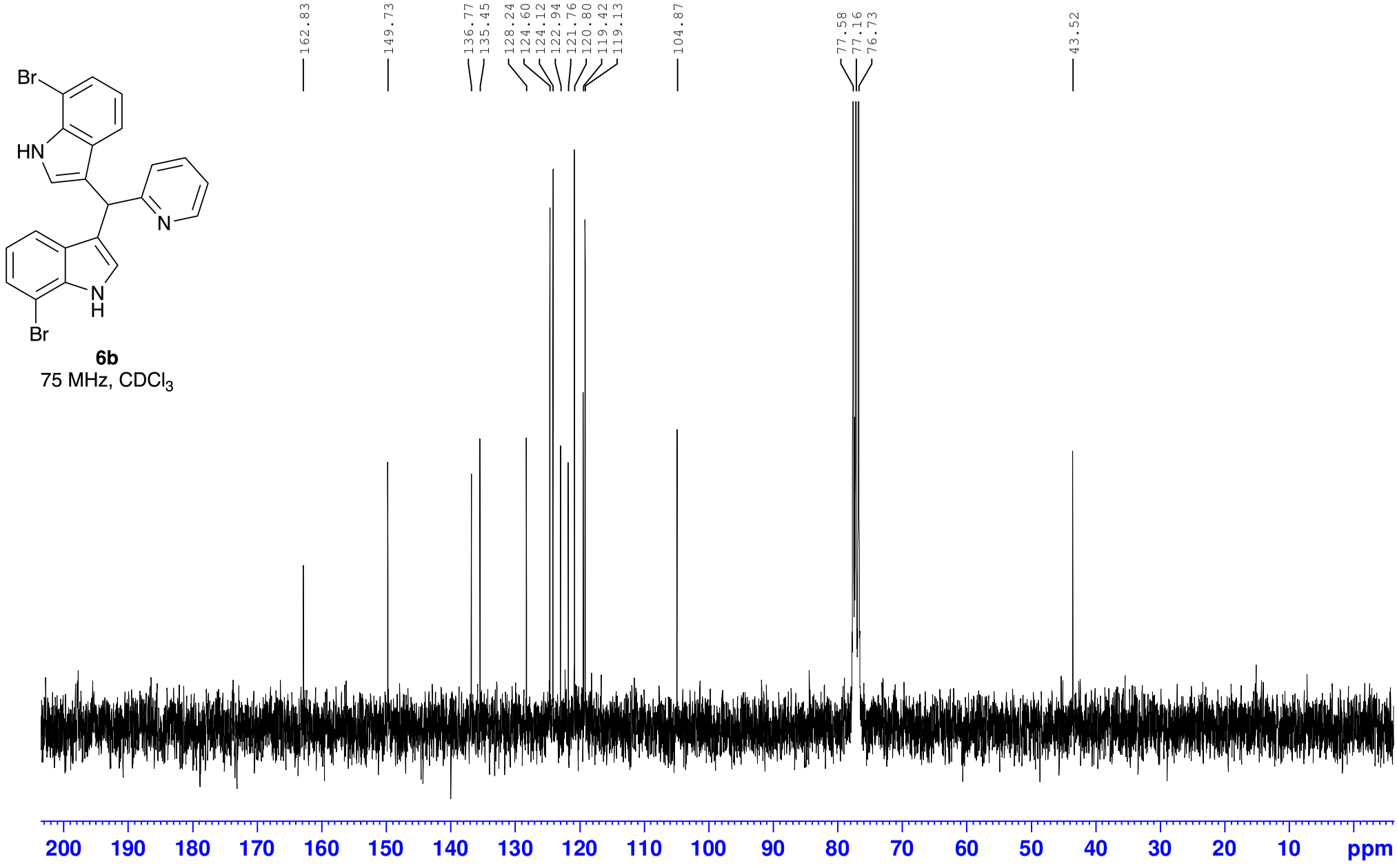
6.653
5.953

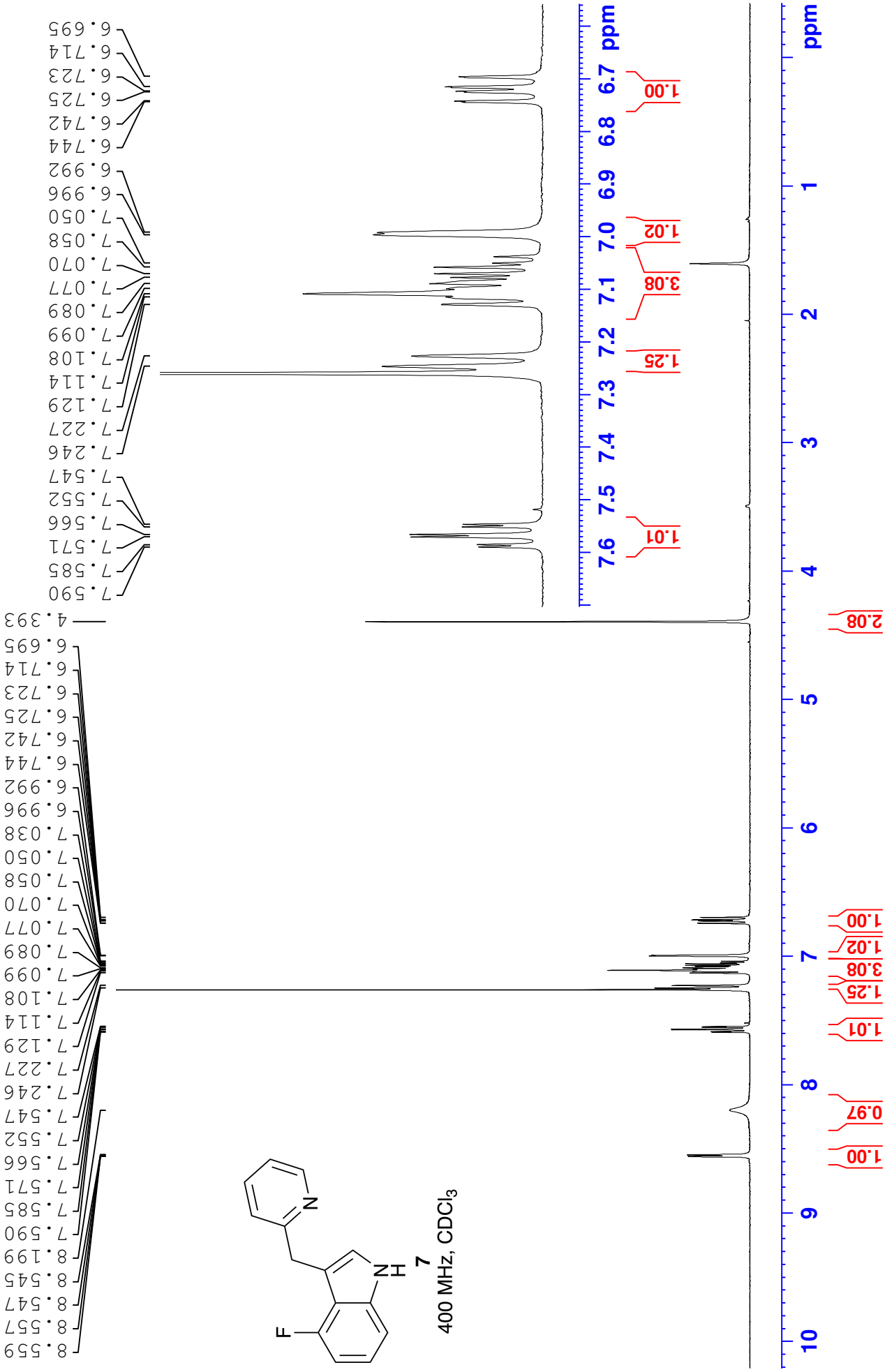

162.94
149.46
137.57
136.99
125.89
124.24
123.10
122.78
121.90
120.97
118.11
115.74
114.25
77.58
77.15
76.73
42.90
Br
HN
N
Br
N
H
5b
75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

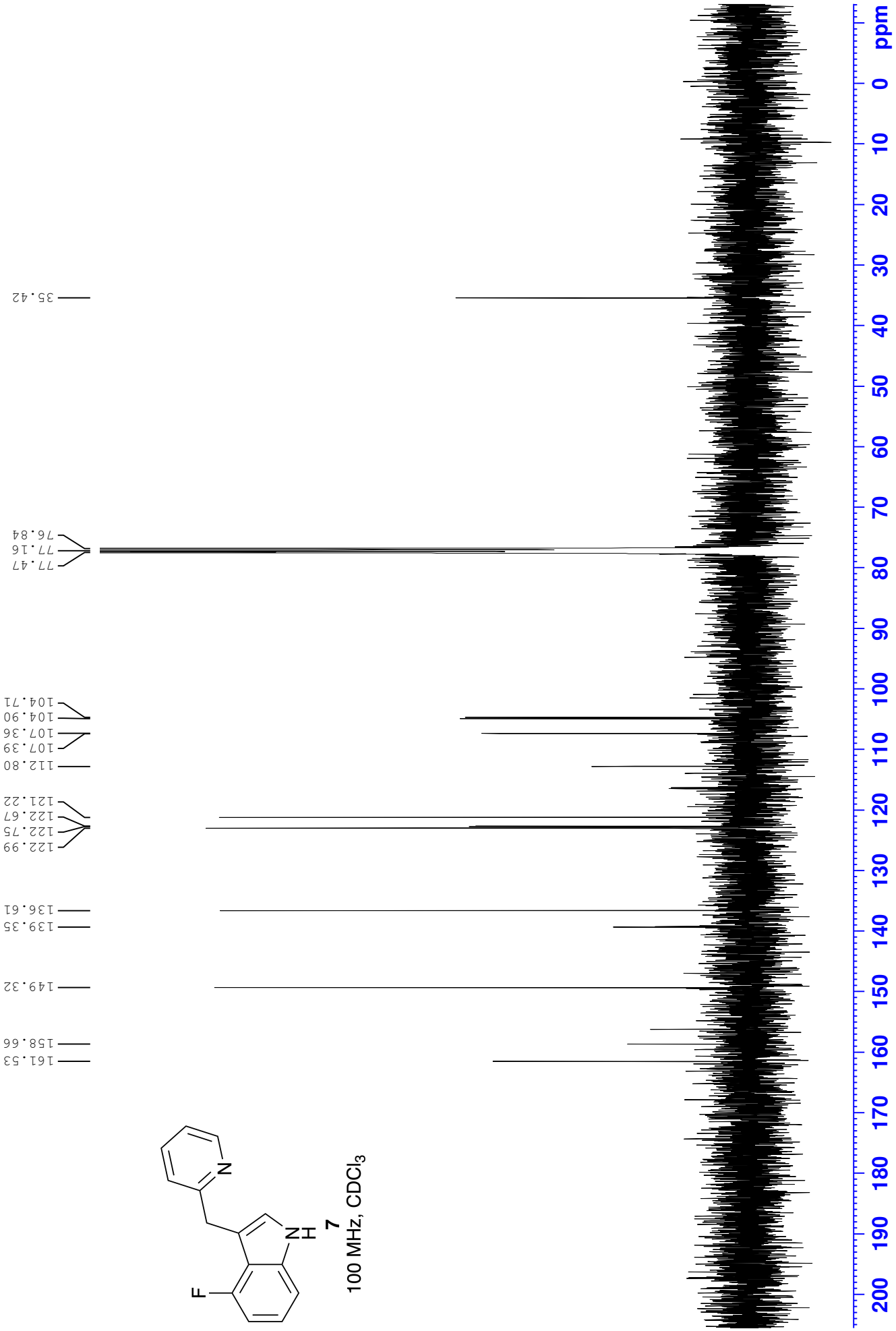

8.568
8.558
8.556
8.223
7.568
7.563
7.549
7.544
7.530
7.525
7.465
7.445
7.340
7.322
7.260
7.161
7.155
7.134
7.125
7.111
7.106
7.094
6.972
6.952
6.933
4.286
N
N
H
Br
6a
400 MHz, CDCl3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
0.93
1.04
1.01
1.02
3.10
1.05
2.11
7.5 7.4 7.3 7.2 7.1 7.0 ppm
1.04
1.01
1.02
3.10
1.05

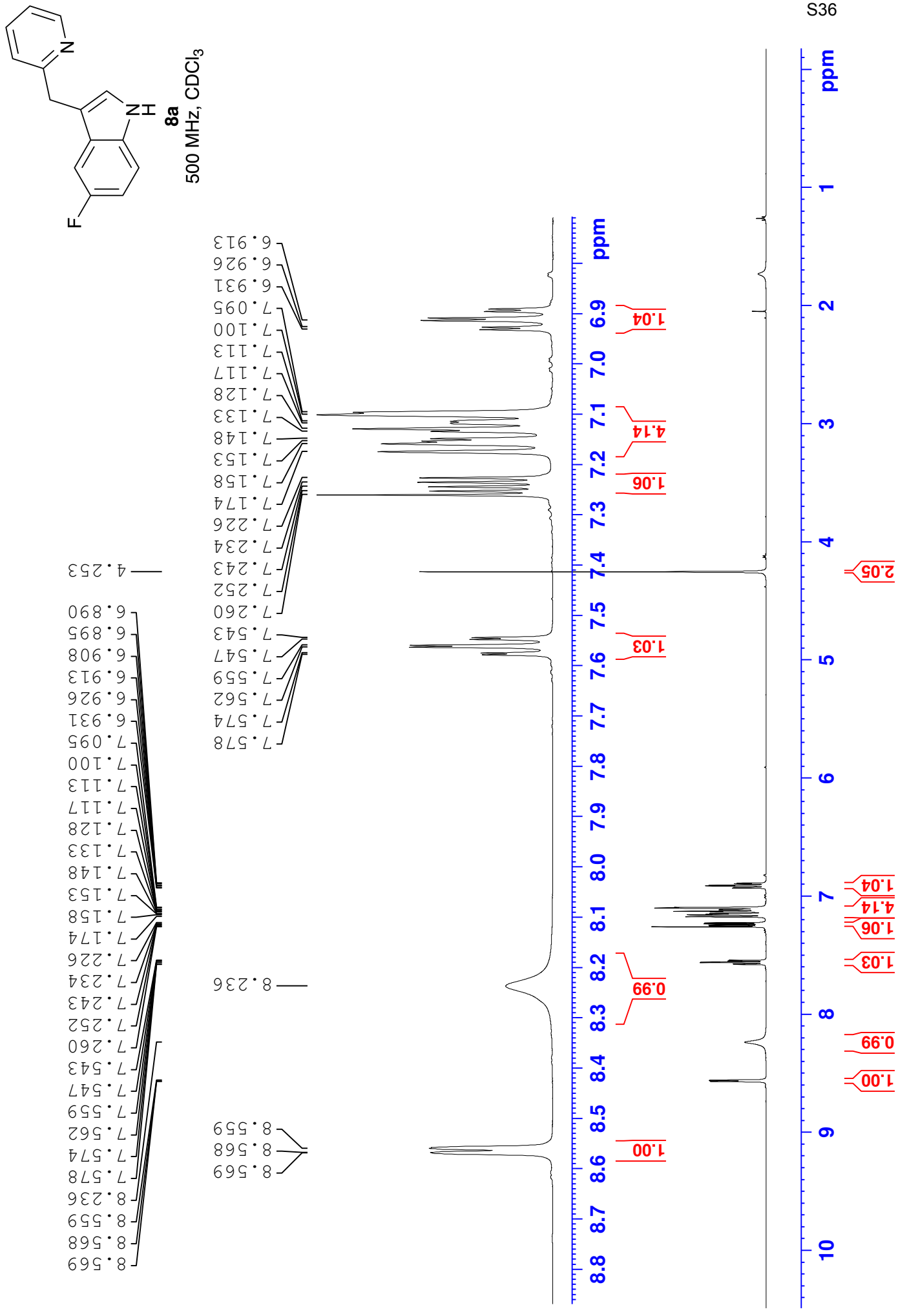

34.82
76.84
77.16
77.47
104.91
115.46
118.66
120.81
121.36
122.83
123.31
124.59
128.78
135.27
136.64
149.42
160.94
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
6a
100 MHz, CDCl3
N
H
Br

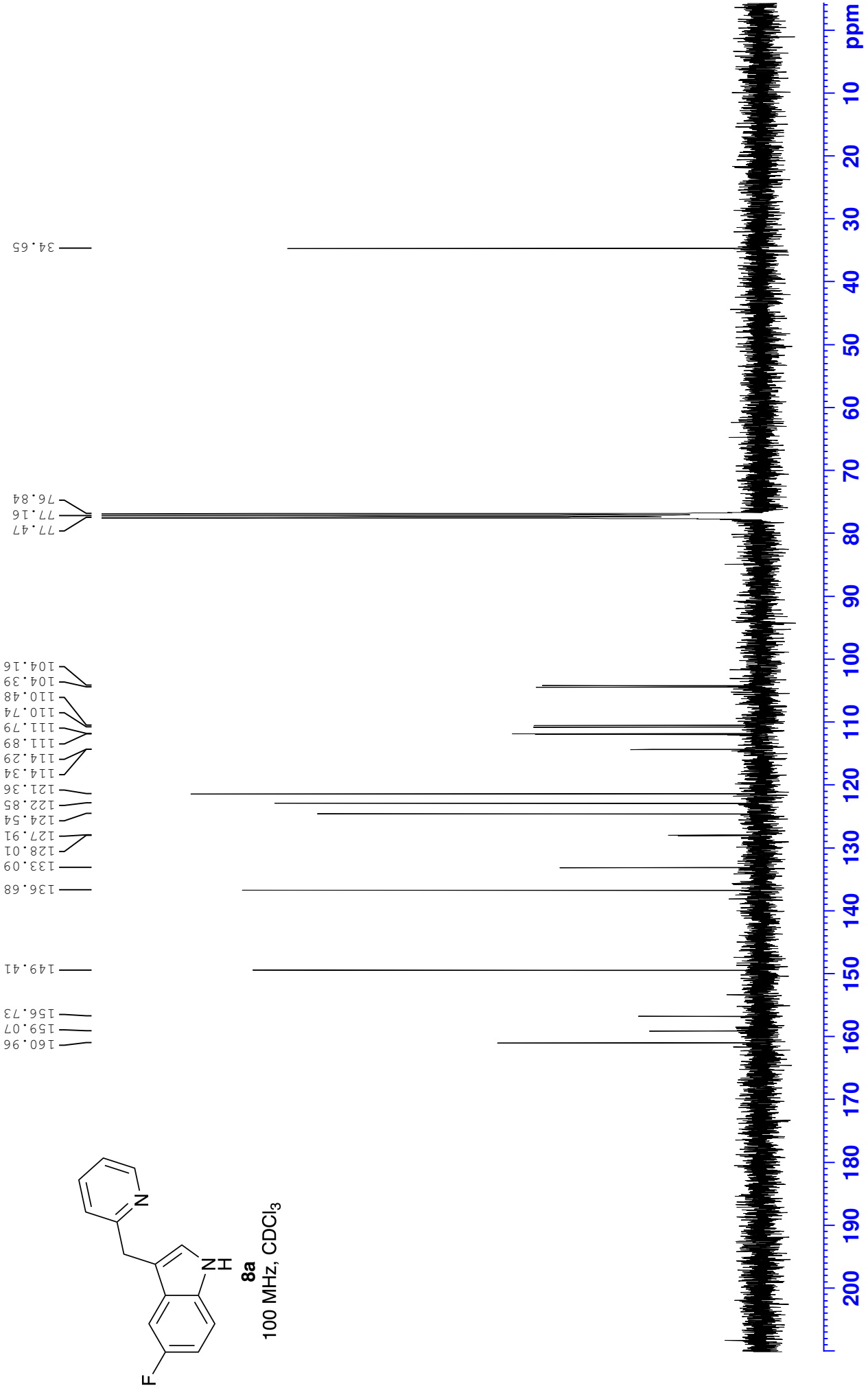

6b
300 MHz, CDCl3
Br
HN
N
H
N
Br
ppm
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.05
1.94
1.10
4.63
1.26
2.17
2.04
1.00
8.625
8.622
8.609
8.210
7.630
7.624
7.604
7.598
7.579
7.573
7.334
7.308
7.292
7.260
7.175
7.159
7.156
7.151
7.147
7.134
6.915
6.889
6.863
6.846
6.840
6.002

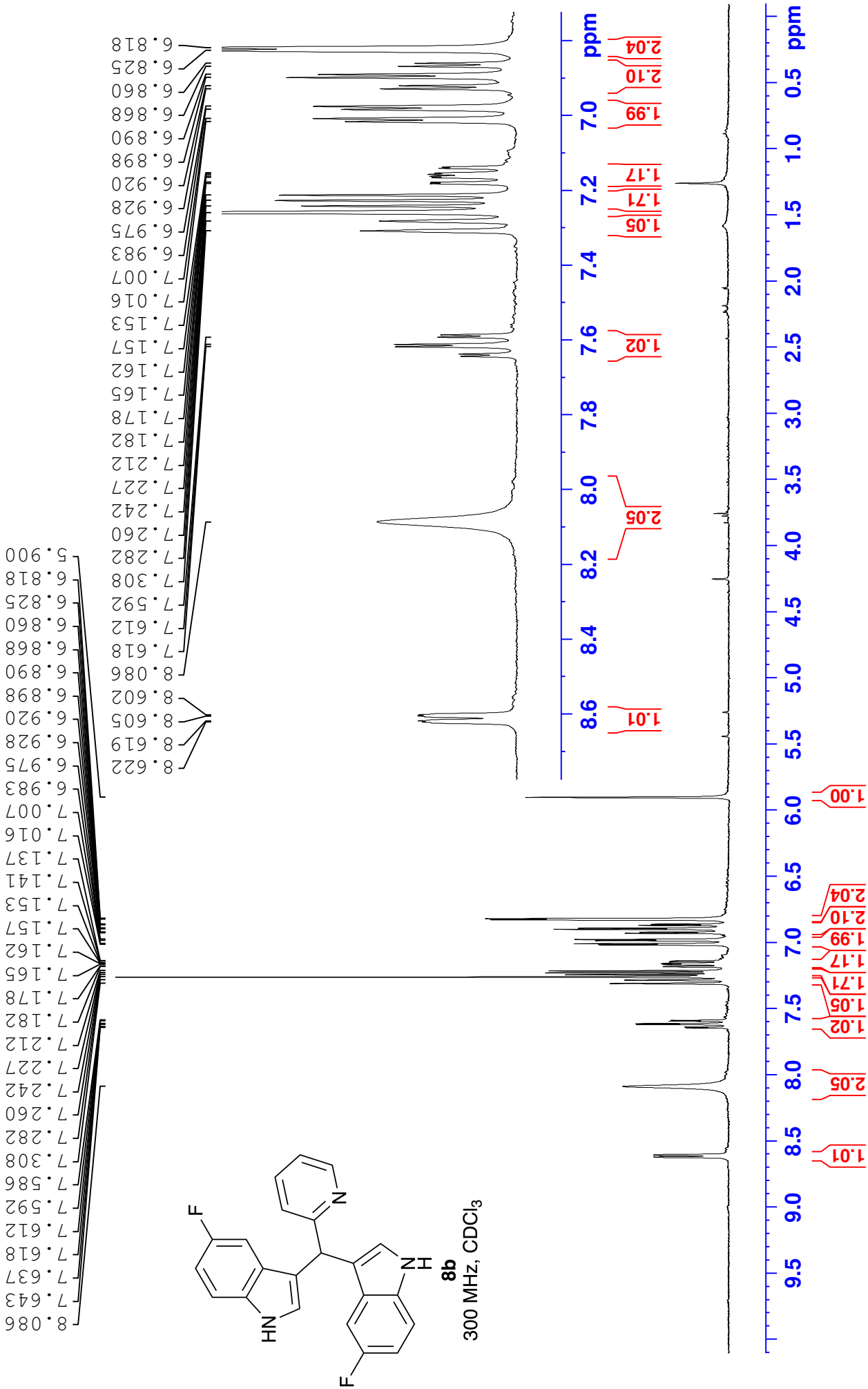

162.83
149.73
136.77
135.45
128.24
124.60
124.12
122.94
121.76
120.80
119.42
119.13
104.87
77.58
77.16
76.73
43.52
Br
HN
N
N
H
Br
6b
75 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

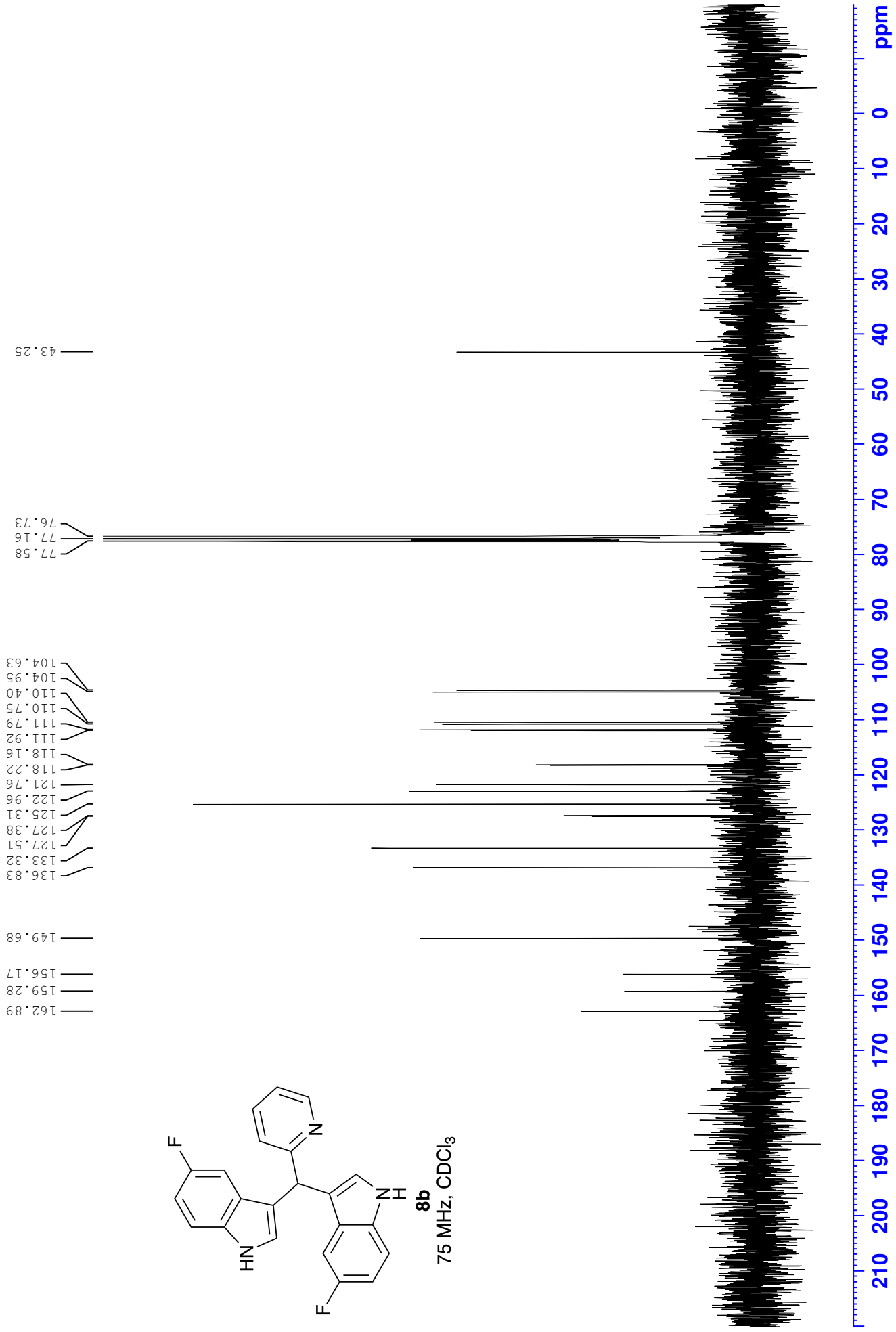

8.559
8.557
8.547
8.545
8.199
7.590
7.585
7.571
7.566
7.552
7.547
7.246
7.227
7.129
7.114
7.108
7.099
7.089
7.077
7.070
7.058
7.050
7.038
6.996
6.992
6.744
6.742
6.725
6.723
6.714
6.695
4.393
7.590
7.585
7.571
7.566
7.552
7.547
7.246
7.227
7.129
7.114
7.108
7.099
7.089
7.077
7.070
7.058
7.050
6.996
6.992
6.744
6.742
6.725
6.723
6.714
6.695
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
ppm
1.01
1.25
3.08
1.02
1.00
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.97
1.00
1.01
1.25
3.08
1.02
1.00
2.08
N
H
N
F
7
400 MHz, CDCl3

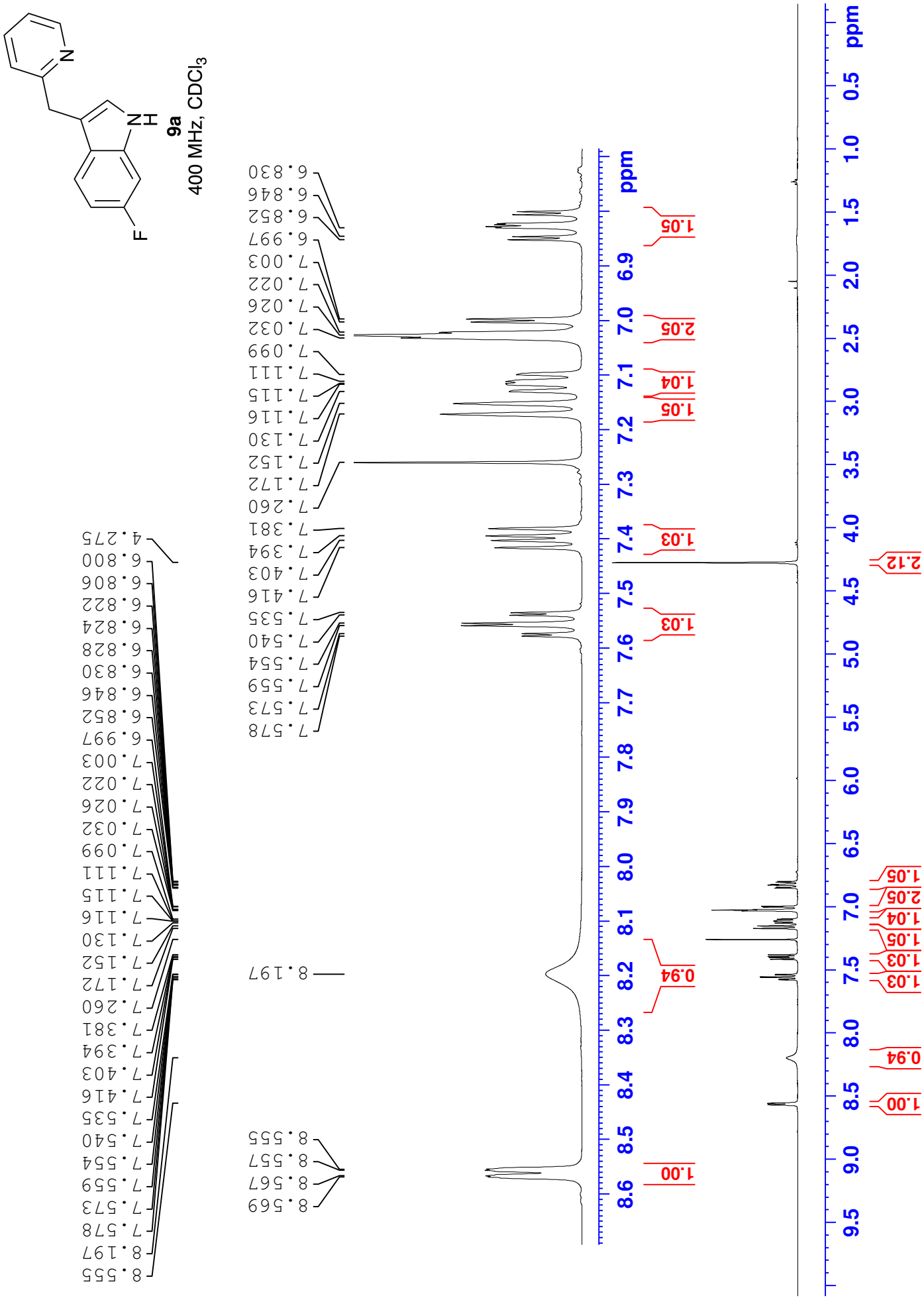

35.42
76.84
77.16
77.47
104.71
104.90
107.36
107.39
112.80
121.22
122.67
122.75
122.99
136.61
139.35
149.32
158.66
161.53
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
F
7
100 MHz, CDCl3

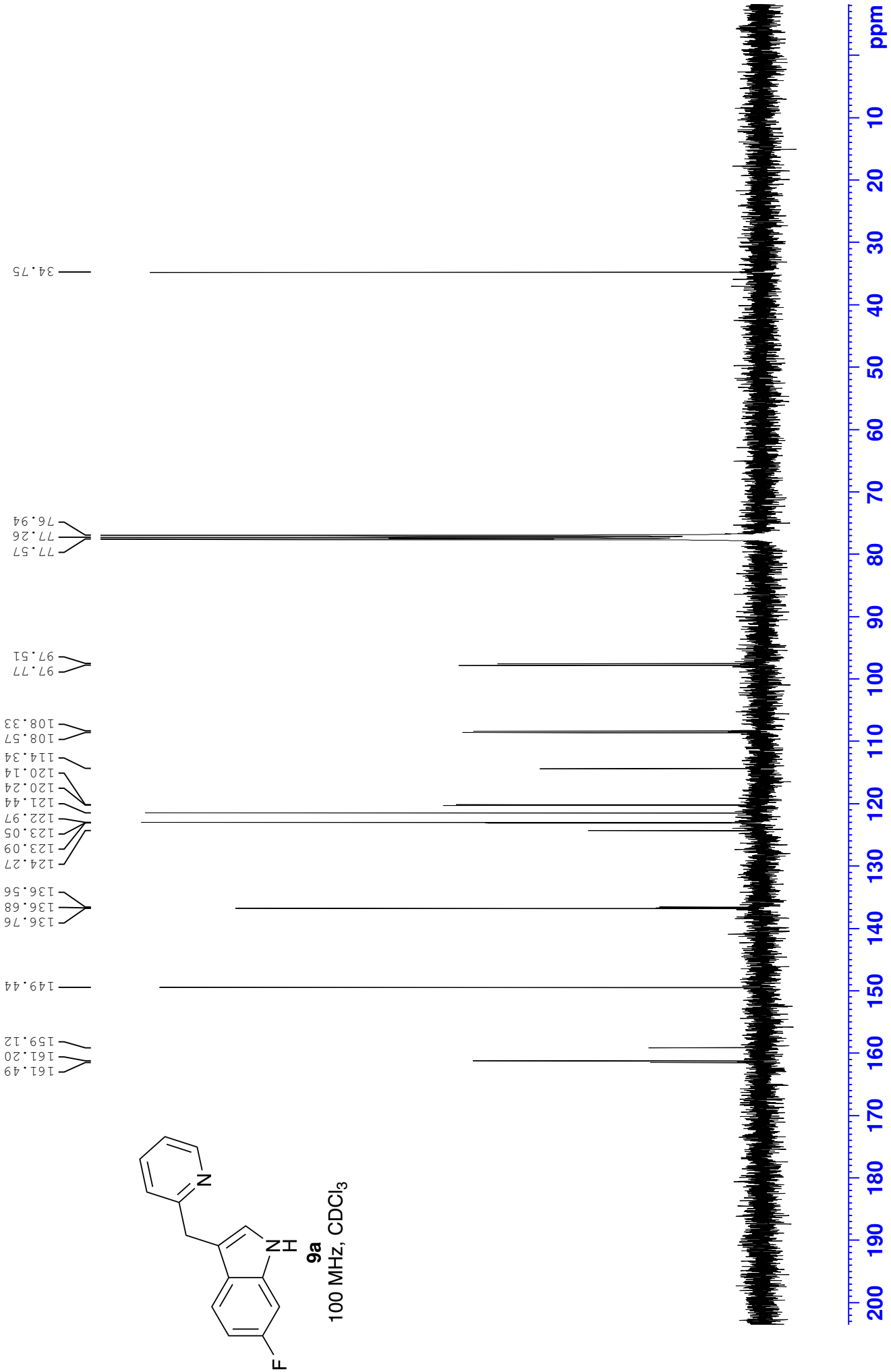

8a
500 MHz, CDCl3
N
H
F
ppm
1.04
4.14
1.06
1.03
0.99
1.00
2.05
8.569
8.568
8.559
8.236
7.578
7.574
7.562
7.559
7.547
7.543
7.260
7.252
7.243
7.234
7.226
7.174
7.158
7.153
7.148
7.133
7.128
7.117
7.113
7.100
7.095
6.931
6.926
6.913
6.908
6.895
6.890
4.253

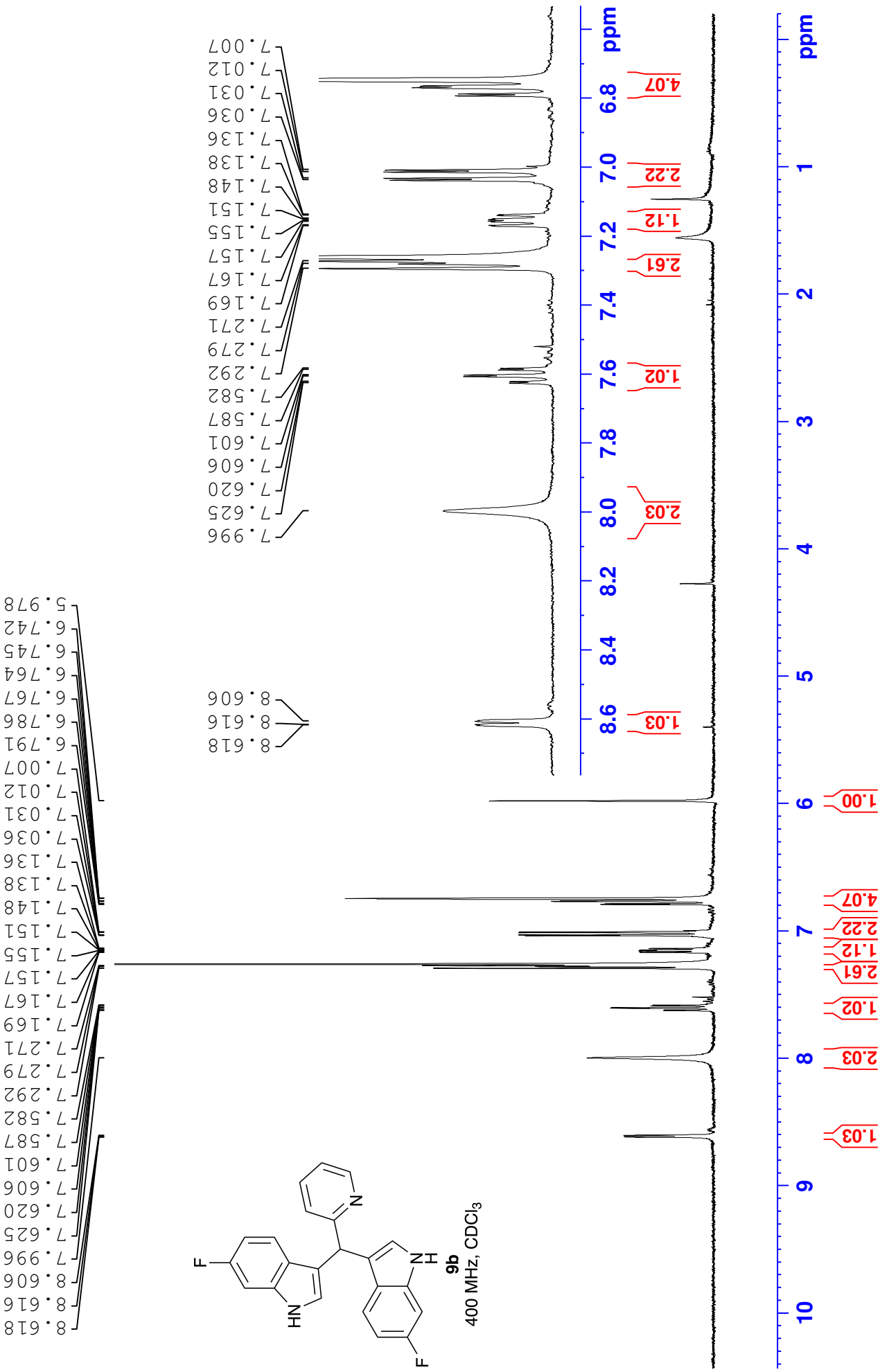

ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
34.65
76.84
77.16
77.47
104.16
104.39
110.48
110.74
111.79
111.89
114.29
114.34
121.36
122.85
124.54
127.91
128.01
133.09
136.68
149.41
156.73
159.07
160.96
N
H
F
8a
100 MHz, CDCl3

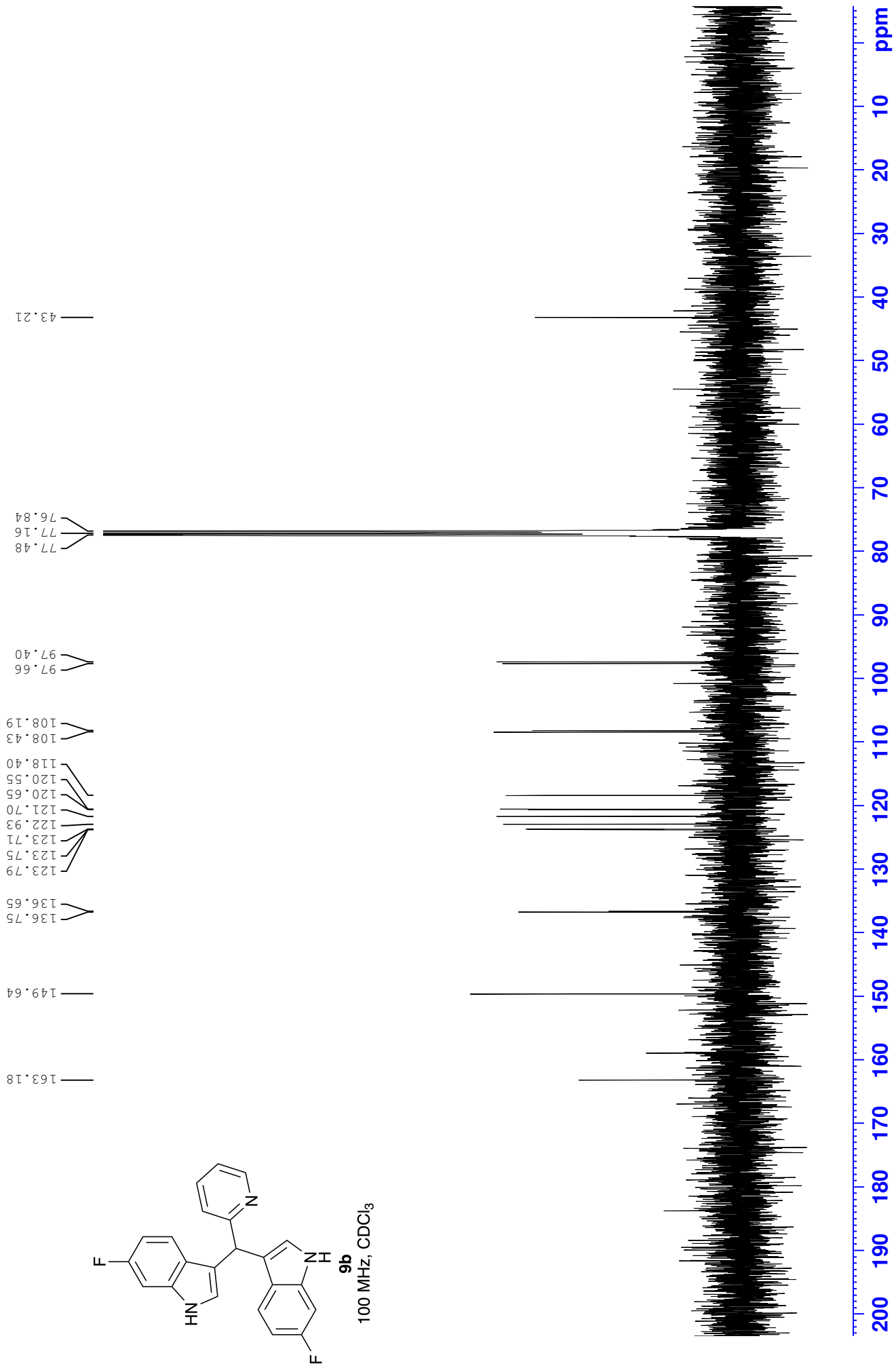

8b
300 MHz, CDCl3

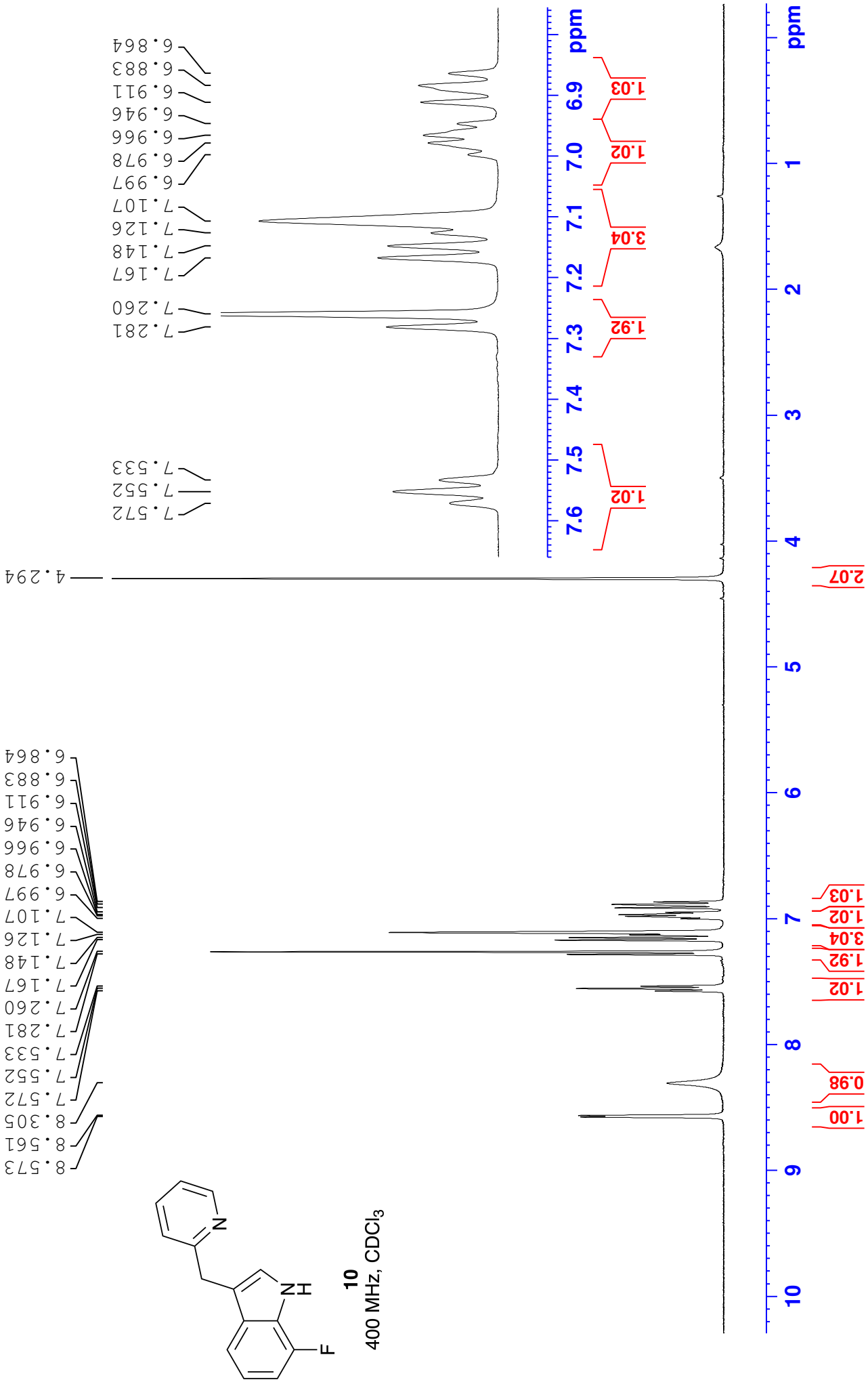

ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
43.25
76.73
77.16
77.58
104.63
104.95
110.40
110.75
111.79
111.92
118.16
118.22
121.76
122.96
125.31
127.38
127.51
133.32
136.83
149.68
156.17
159.28
162.89
F
HN
N
NH
F
8b
75 MHz, CDCl3

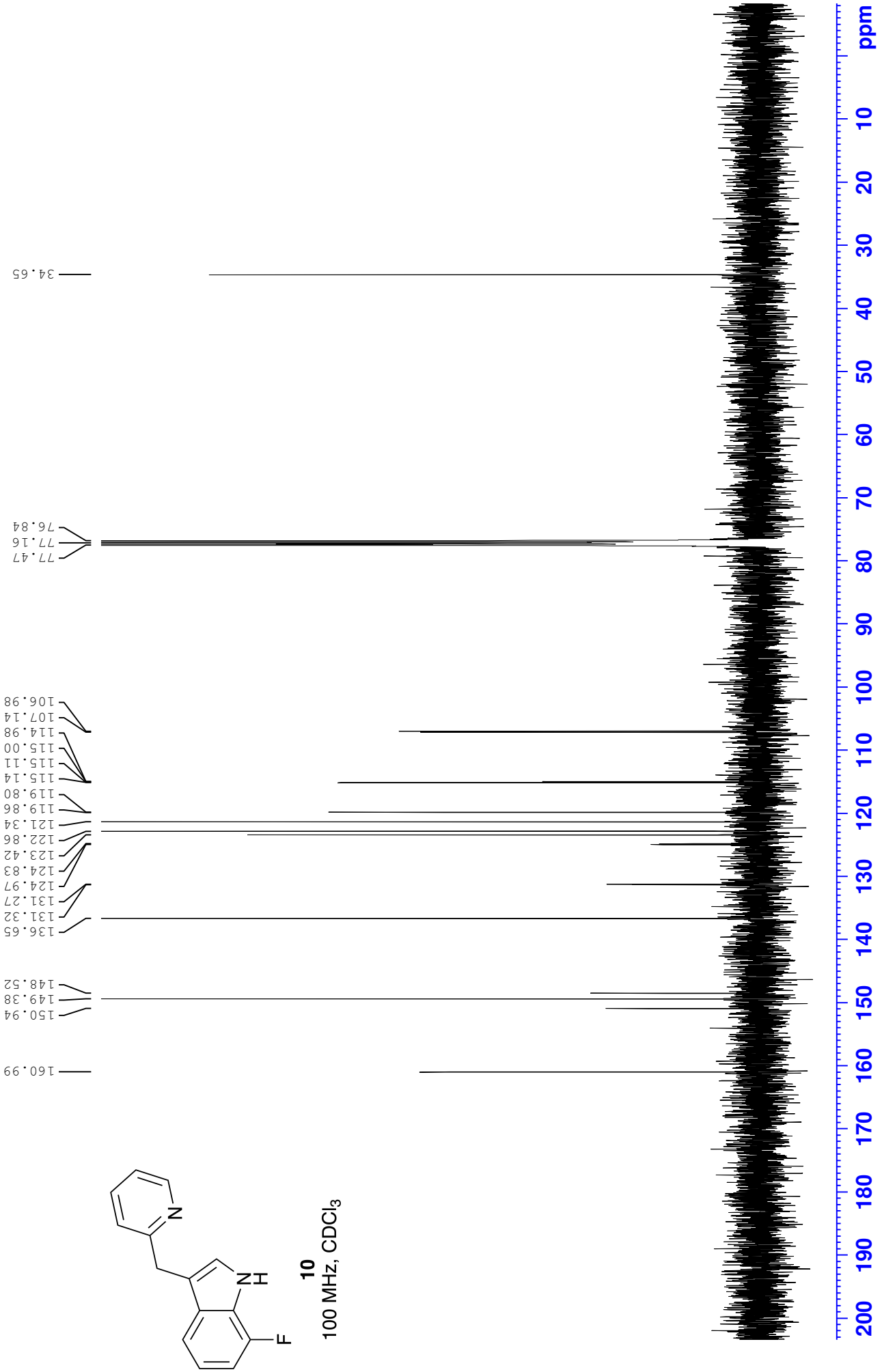

9a
400 MHz, CDCl3
ppm
1.00
0.94
1.03
1.03
1.05
1.04
1.05
2.05
1.05
2.12

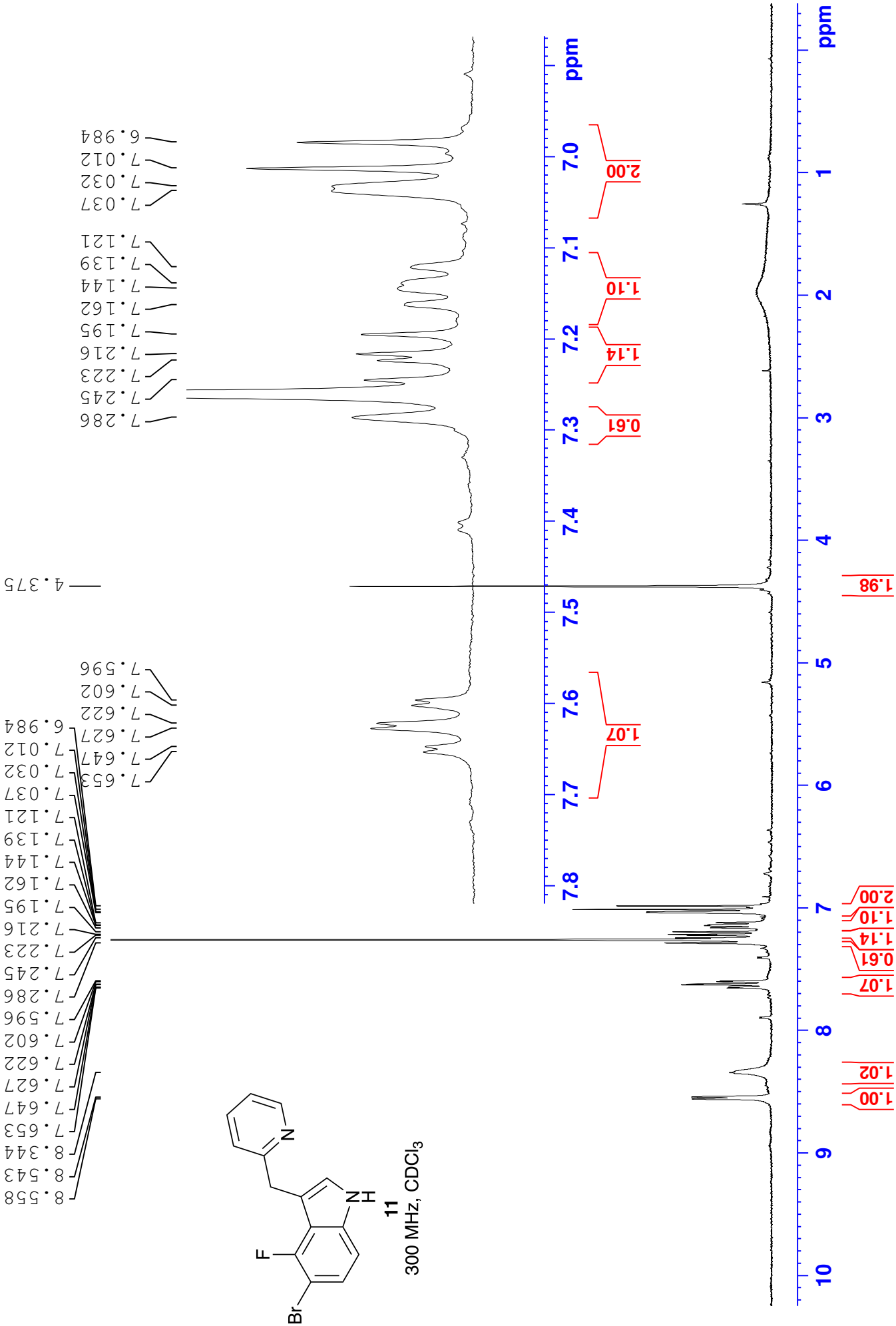

34.75
76.94
77.26
77.57
97.51
97.77
108.33
108.57
114.34
120.14
120.24
121.44
122.97
123.05
123.09
124.27
136.56
136.68
136.76
149.44
159.12
161.20
161.49
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
F
9a
100 MHz, CDCl3

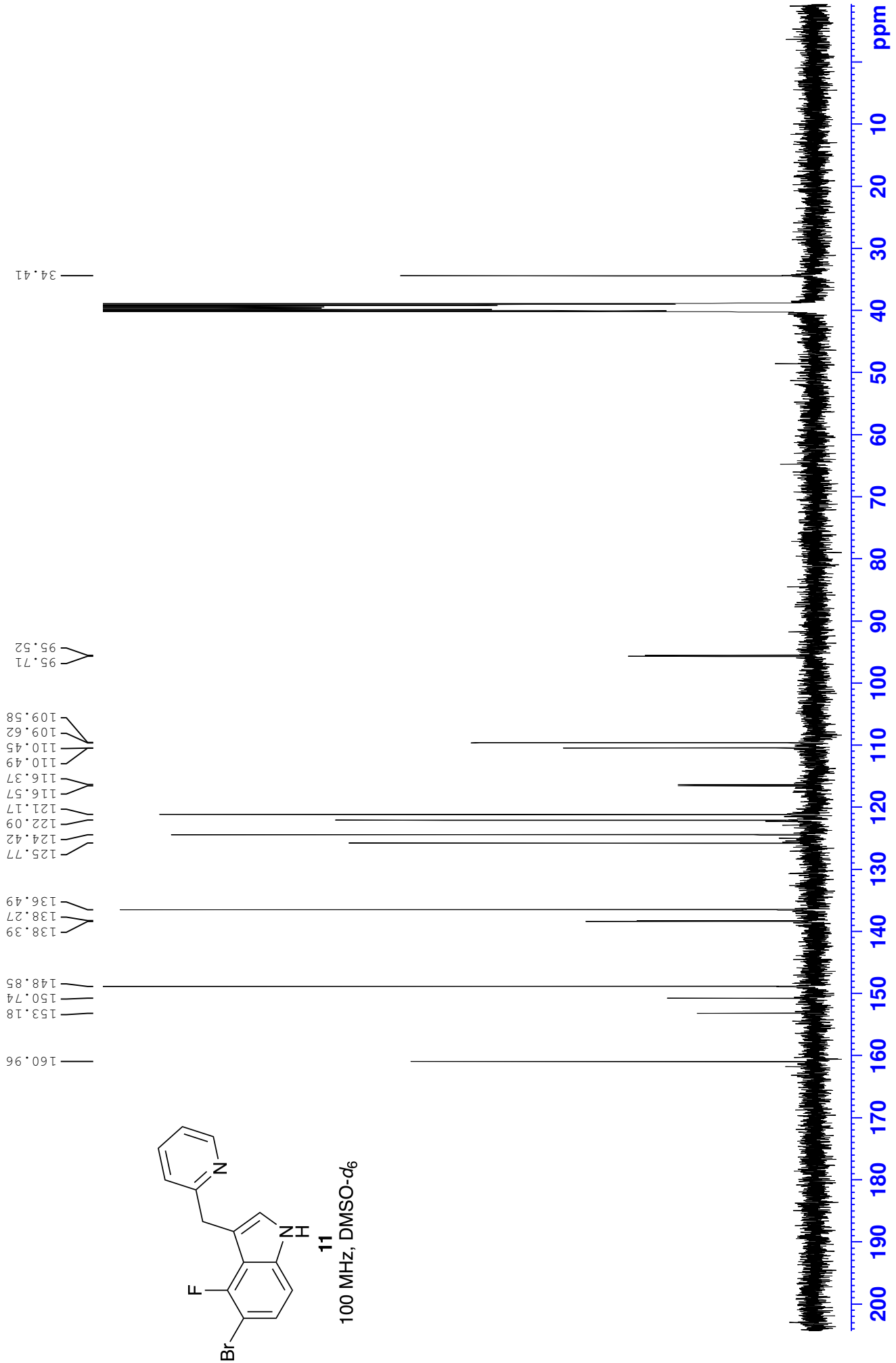

9b
400 MHz, CDCl3
ppm
1.03
2.03
1.02
2.61
1.12
2.22
4.07
1.00

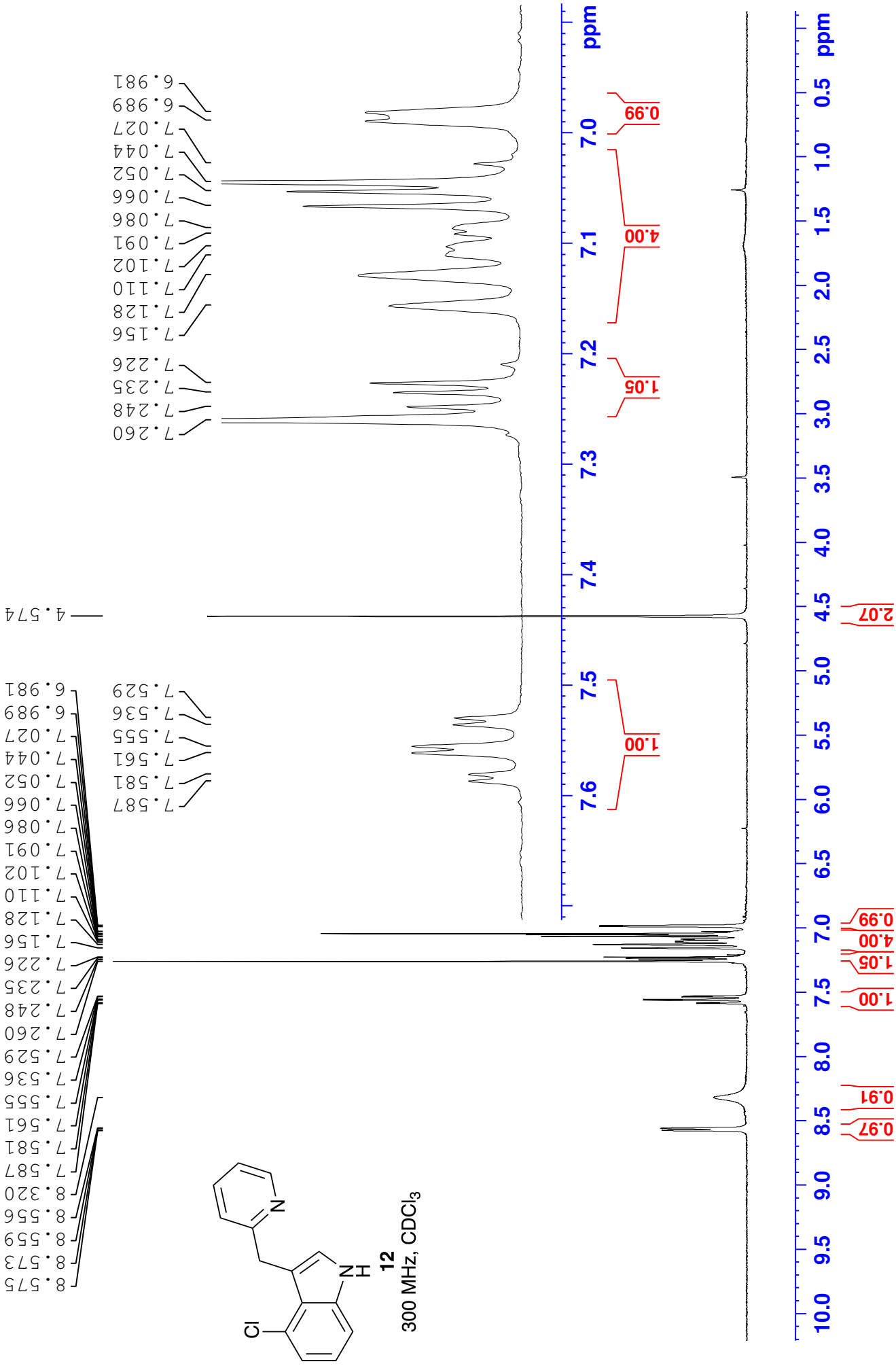

43.21
76.84
77.16
77.48
97.40
97.66
108.19
108.43
118.40
120.55
120.65
121.70
122.93
123.71
123.75
123.79
136.65
136.75
149.64
163.18
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
F
HN
N
NH
F
9b
100 MHz, CDCl3

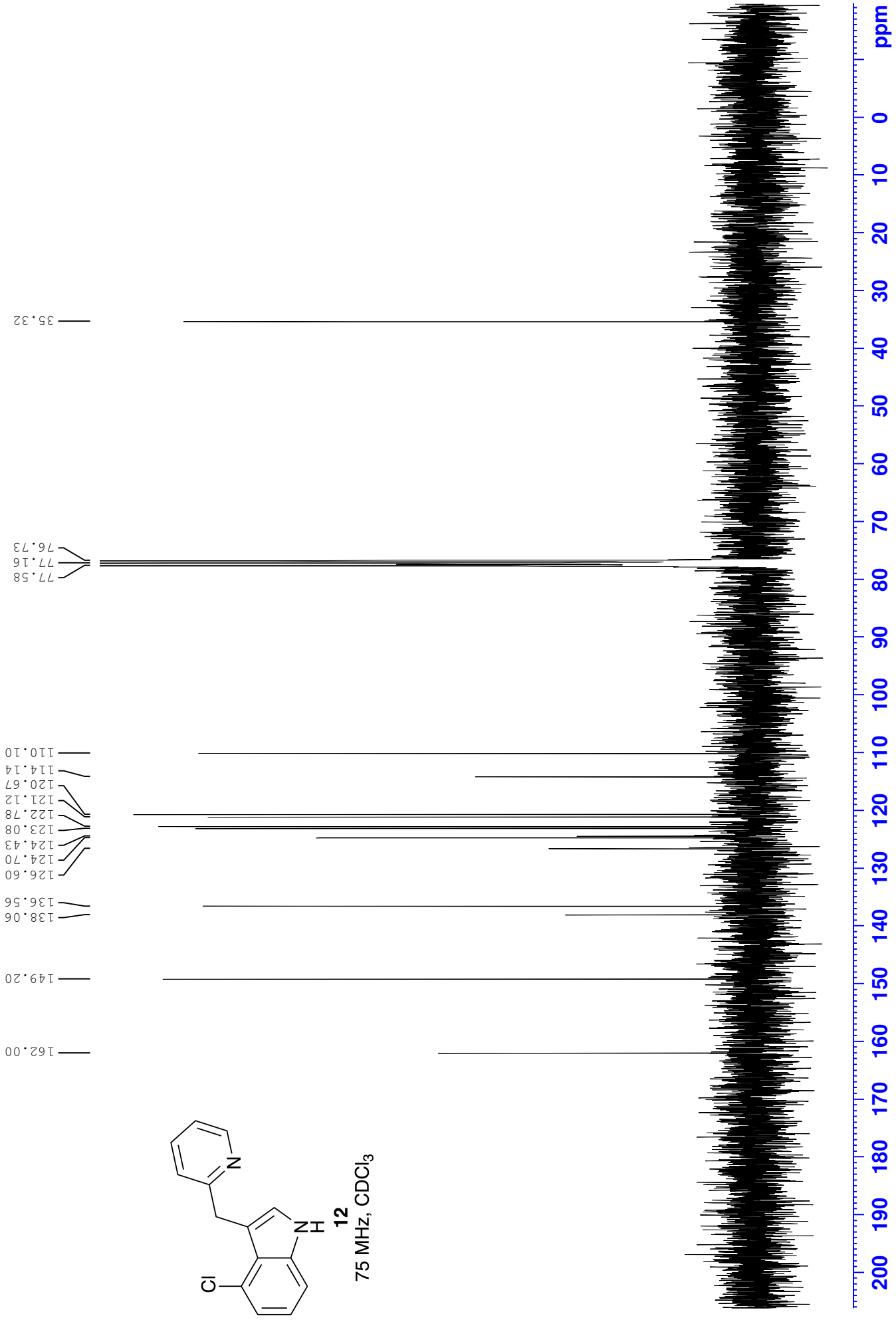

10
400 MHz, CDCl3
N
NH
F
8.573
8.561
8.305
7.572
7.552
7.533
7.281
7.260
7.167
7.148
7.126
7.107
6.997
6.978
6.966
6.946
6.911
6.883
6.864
4.294
7.572
7.552
7.533
7.281
7.260
7.167
7.148
7.126
7.107
6.997
6.978
6.966
6.946
6.911
6.883
6.864
ppm
1.03
1.02
3.04
1.92
1.02
2.07
1.03
1.02
3.04
1.92
1.02
0.98
1.00

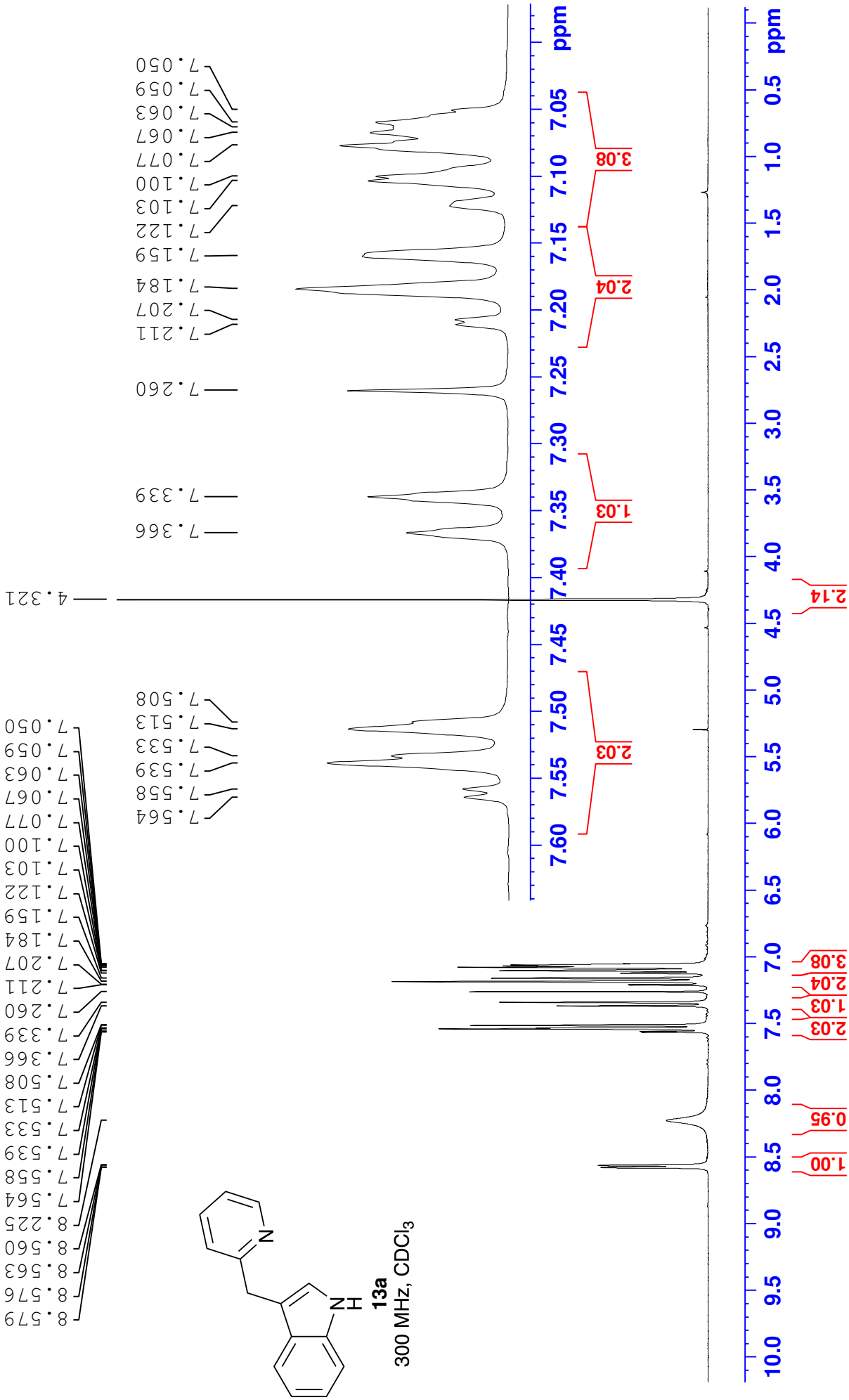

34.65
76.84
77.16
77.47
106.98
107.14
114.98
115.00
115.11
115.14
119.80
119.86
121.34
122.86
123.42
124.83
124.97
131.27
131.32
136.65
148.52
149.38
150.94
160.99
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
10
100 MHz, CDCl3
N
H
N
F

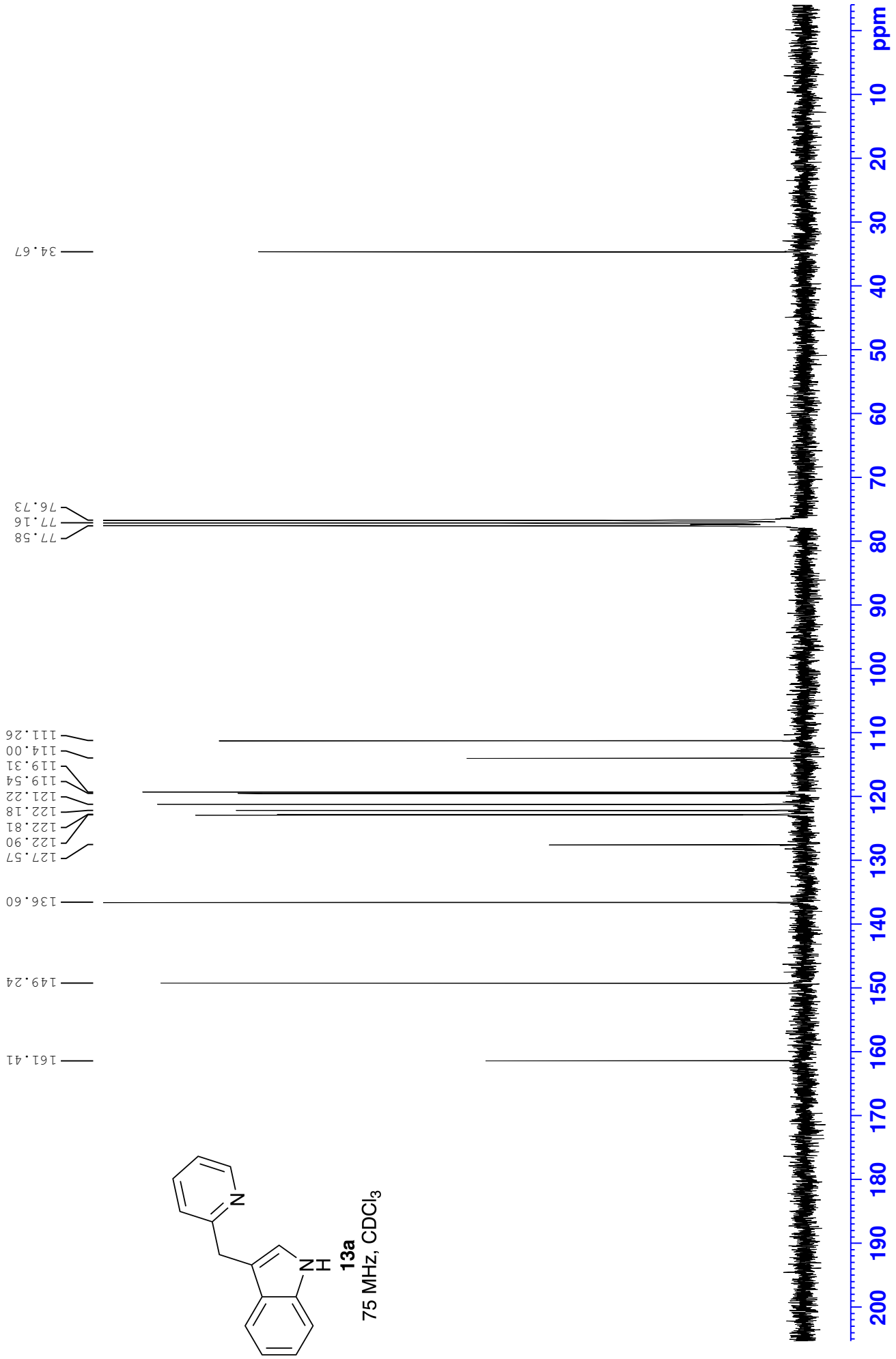

11
300 MHz, CDCl3
F
Br
N
H
ppm
1.00
1.02
1.07
0.61
1.14
1.10
2.00
1.98
4.375
8.558
8.543
8.344
7.653
7.647
7.627
7.622
7.602
7.596
7.286
7.245
7.223
7.216
7.195
7.162
7.144
7.139
7.121
7.037
7.032
7.012
6.984

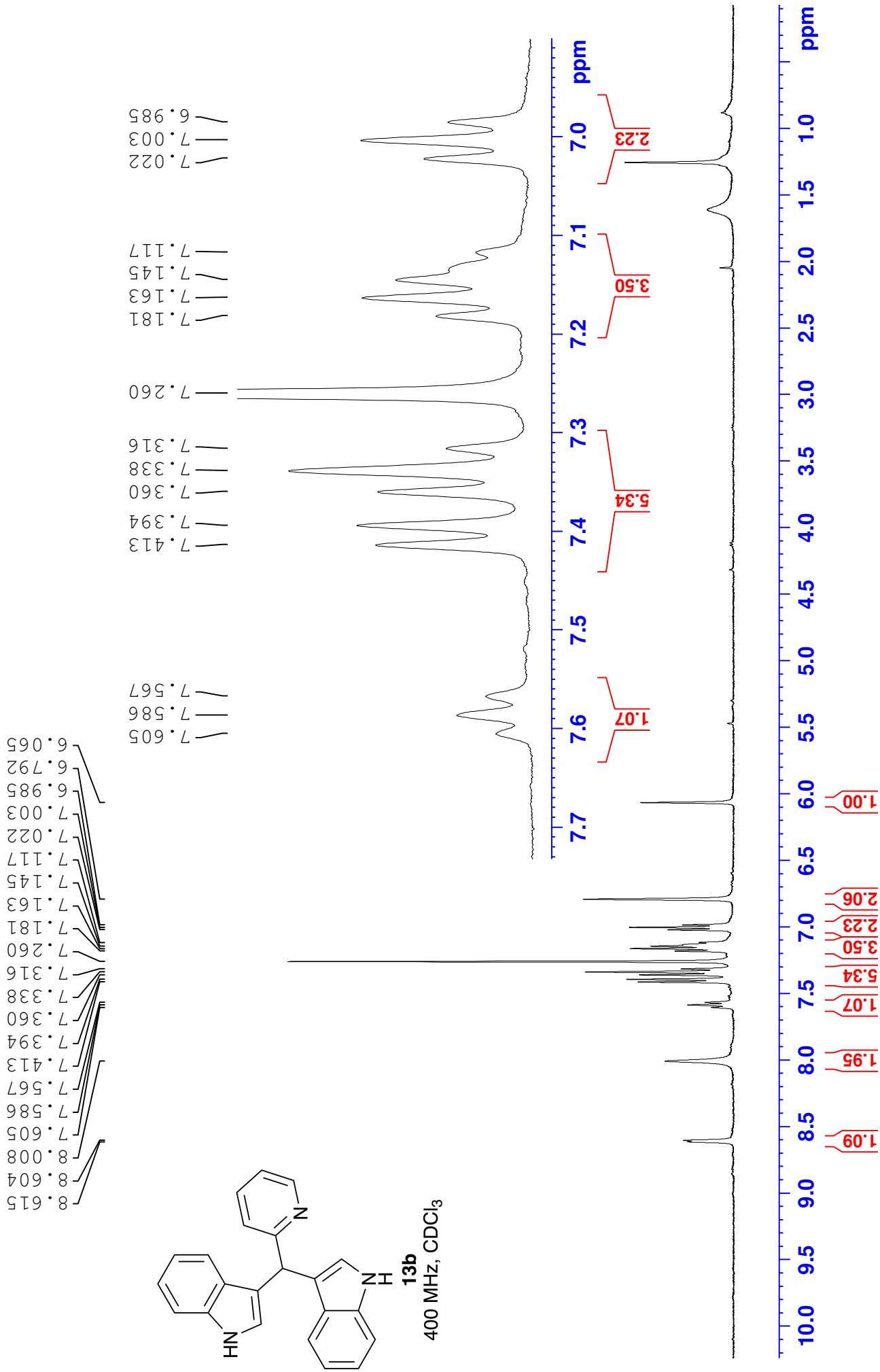

34.41
95.71
95.52
109.58
109.62
110.45
110.49
116.37
116.57
121.17
122.09
124.42
125.77
136.49
138.27
138.39
148.85
150.74
153.18
160.96
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
F
Br
11
100 MHz, DMSO-d_6

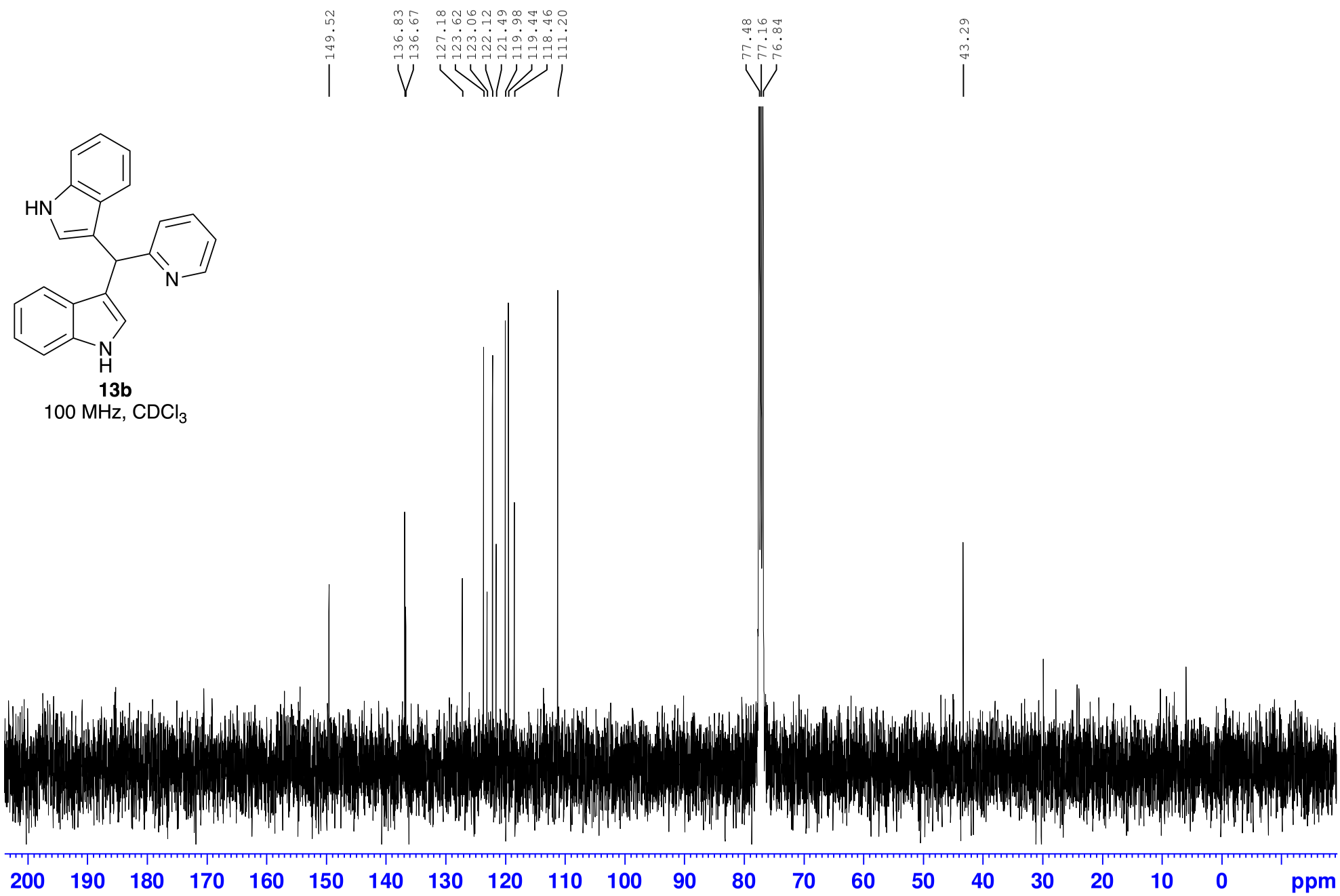

12
300 MHz, CDCl3
Cl
N
H
N
8.575
8.573
8.559
8.556
8.320
7.587
7.581
7.561
7.555
7.536
7.529
7.260
7.248
7.235
7.226
7.156
7.128
7.110
7.102
7.091
7.086
7.066
7.052
7.044
7.027
6.989
6.981
4.574
7.587
7.581
7.561
7.555
7.536
7.529
7.260
7.248
7.235
7.226
7.156
7.128
7.110
7.102
7.091
7.086
7.066
7.052
7.044
7.027
6.989
6.981
ppm
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
7.6
7.5
7.4
7.3
7.2
7.1
7.0
1.00
1.05
4.00
0.99
2.07
0.97
0.91
1.00
1.05
4.00
0.99

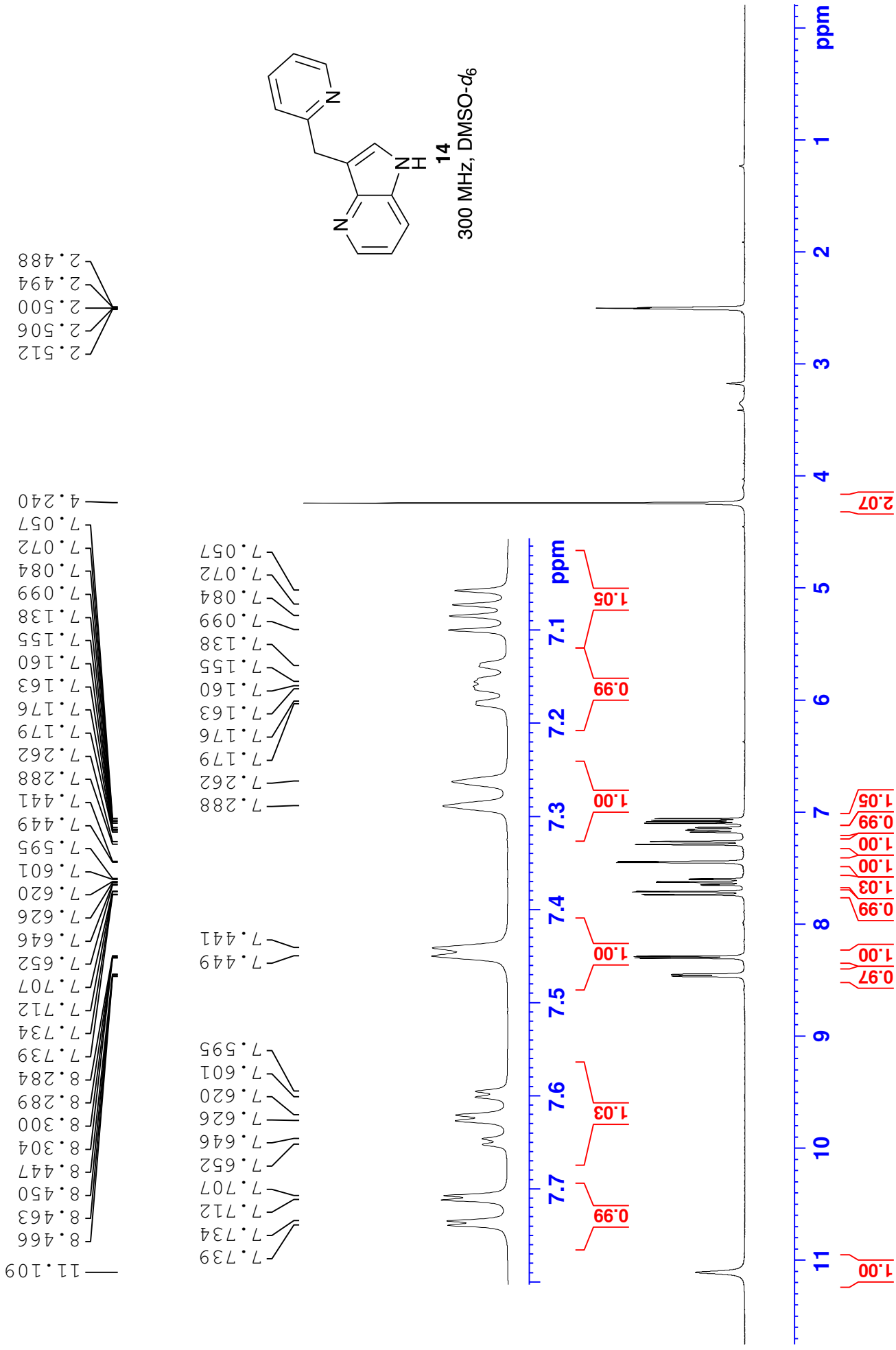

35.32
76.73
77.16
77.58
110.10
114.14
120.67
121.12
122.78
123.08
124.43
124.70
126.60
136.56
138.06
149.20
162.00
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
Cl
N
H
N
12
75 MHz, CDCl3

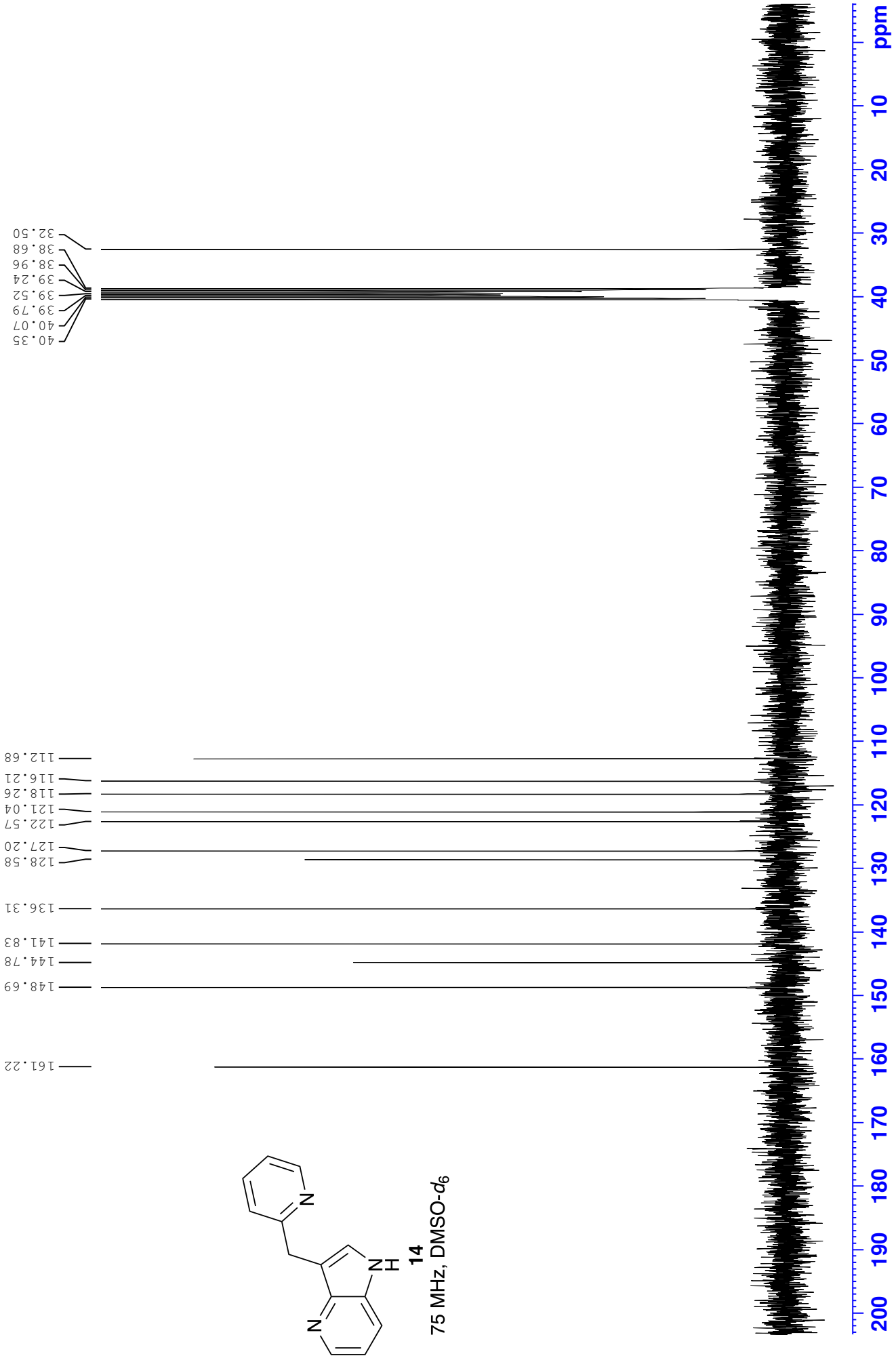

13a
300 MHz, CDCl3
ppm
2.14
0.95
1.00
2.03
1.03
2.04
3.08
2.03
1.03
2.04
3.08
4.321
8.579
8.576
8.563
8.560
8.225
7.564
7.558
7.539
7.533
7.513
7.508
7.366
7.339
7.260
7.211
7.207
7.184
7.159
7.122
7.103
7.100
7.077
7.067
7.063
7.059
7.050

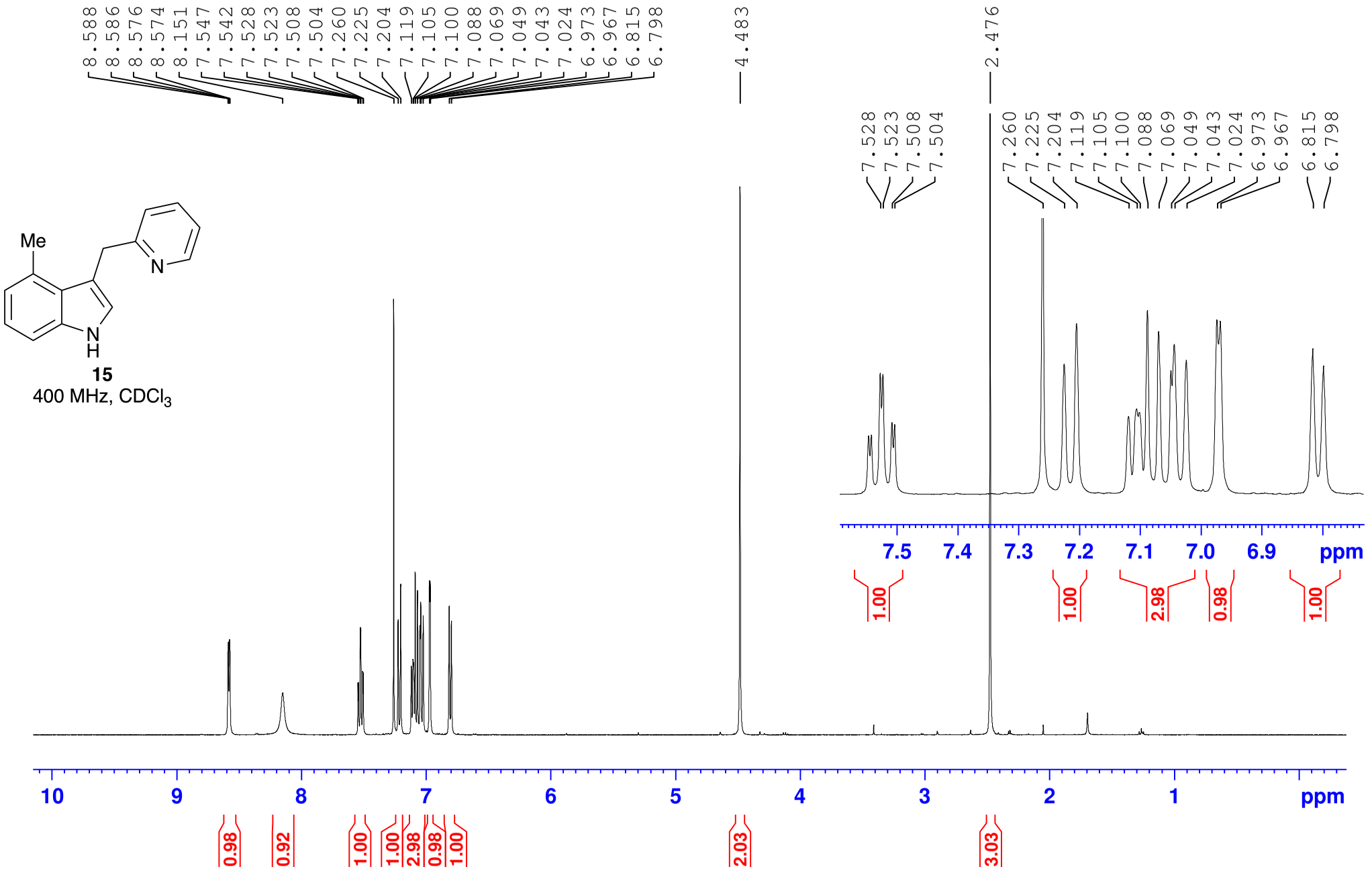

34.67
76.73
77.16
77.58
111.26
114.00
119.31
119.54
121.22
122.18
122.81
122.90
127.57
136.60
149.24
161.41
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
N
H
N
13a
75 MHz, CDCl3

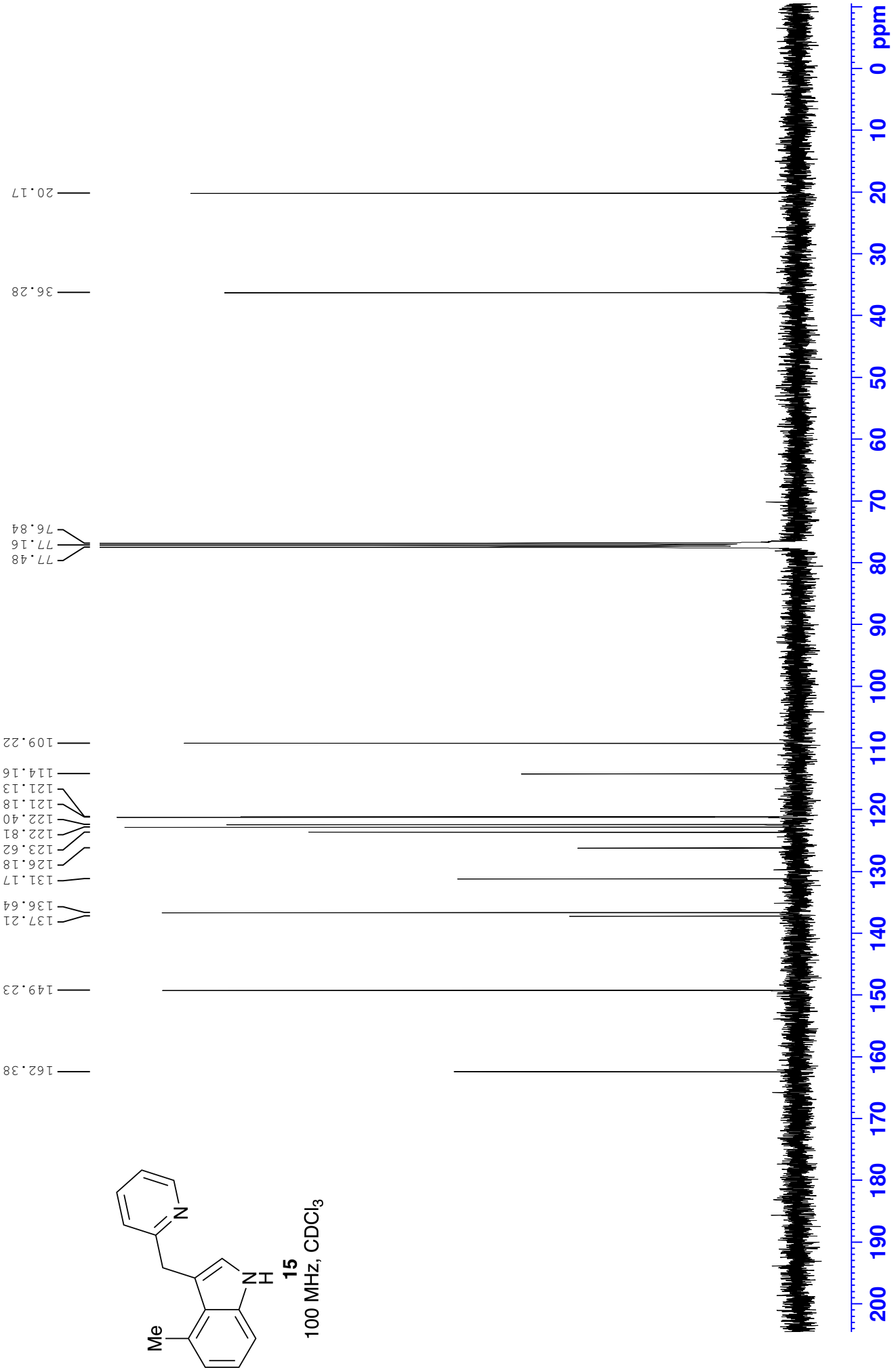

13b
400 MHz, CDCl3
NH
N
H
N
ppm
1.00
2.06
2.23
3.50
5.34
1.07
1.95
1.09
2.23
3.50
5.34
1.07
8.615
8.604
8.008
7.605
7.586
7.567
7.413
7.394
7.360
7.338
7.316
7.260
7.181
7.163
7.145
7.117
7.022
7.003
6.985
6.792
6.065
7.605
7.586
7.567
7.413
7.394
7.360
7.338
7.316
7.260
7.181
7.163
7.145
7.117
7.022
7.003
6.985

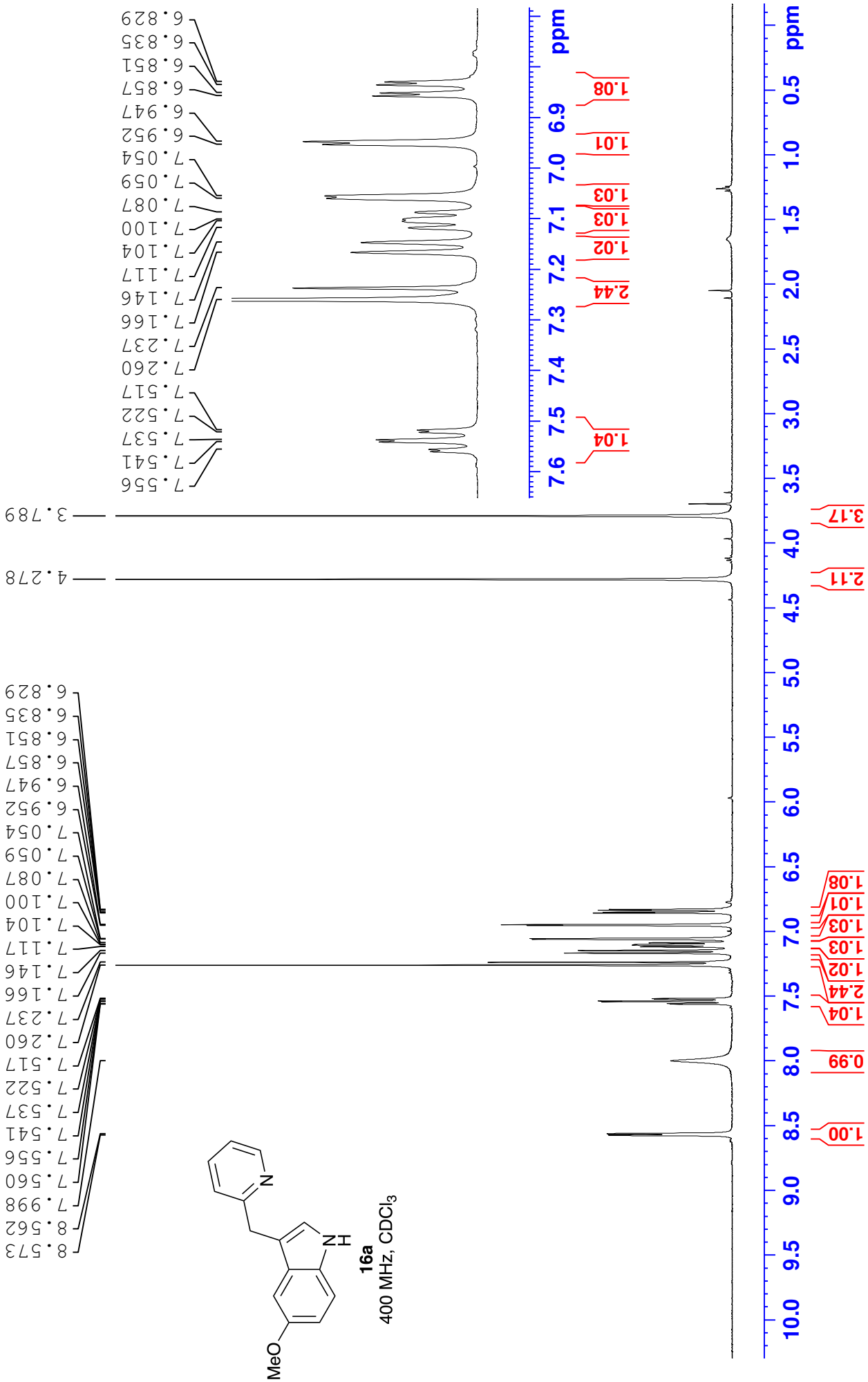

149.52
136.83
136.67
127.18
123.62
123.06
122.12
121.49
119.98
119.44
118.46
111.20
77.48
77.16
76.84
43.29
HN
N
N
H
13b
100 MHz, CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

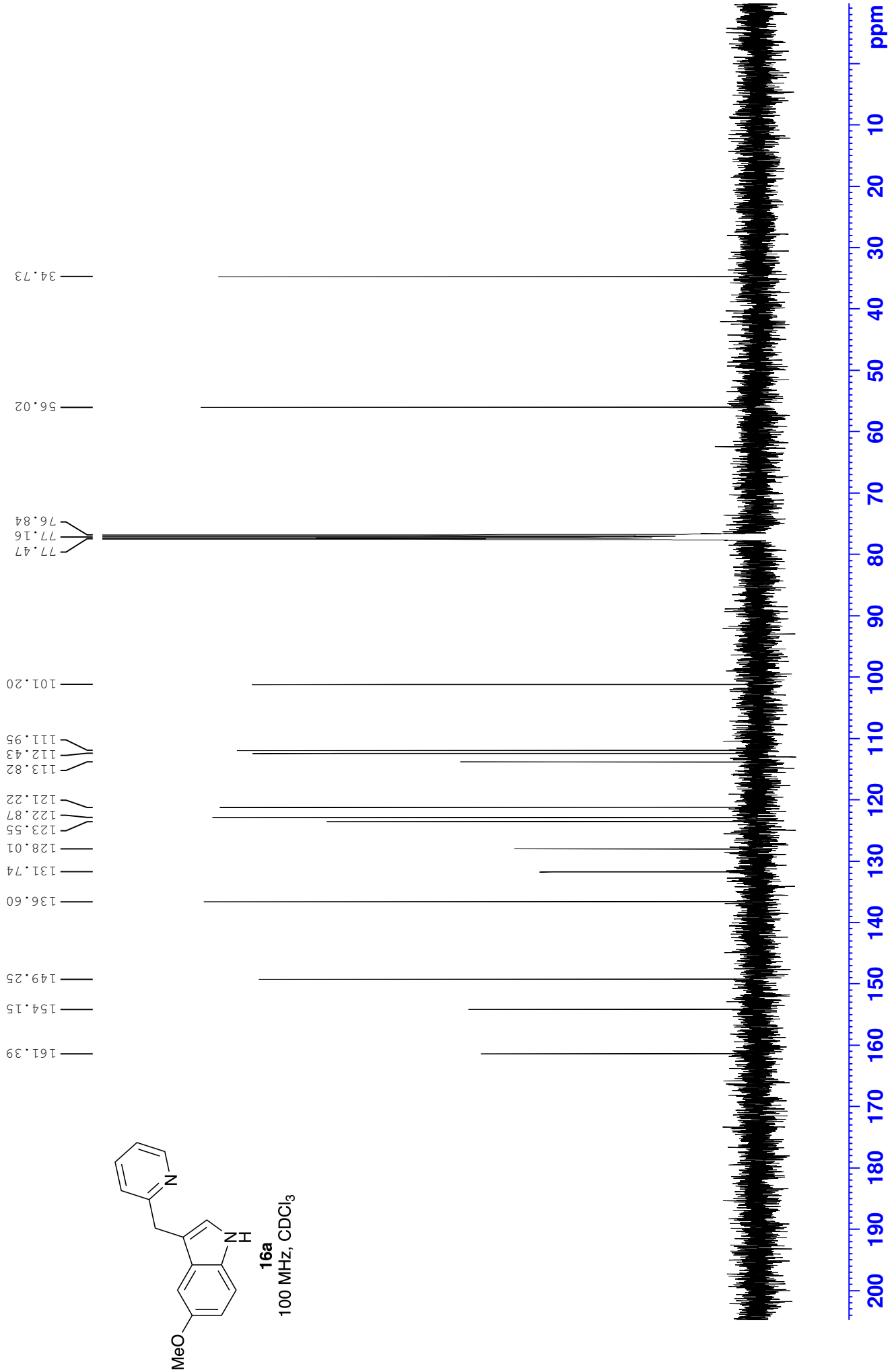

14
300 MHz, DMSO-d_6
ppm
11.109
8.466
8.463
8.450
8.447
8.304
8.300
8.289
8.284
7.739
7.734
7.712
7.707
7.652
7.646
7.626
7.620
7.601
7.595
7.449
7.441
7.288
7.262
7.179
7.176
7.163
7.160
7.155
7.138
7.099
7.084
7.072
7.057
4.240
2.512
2.506
2.500
2.494
2.488
2.07
1.00
0.97
1.00
0.99
1.03
1.00
1.00
0.99
1.05
1.05
0.99
1.03
1.00
1.00
0.99
1.05

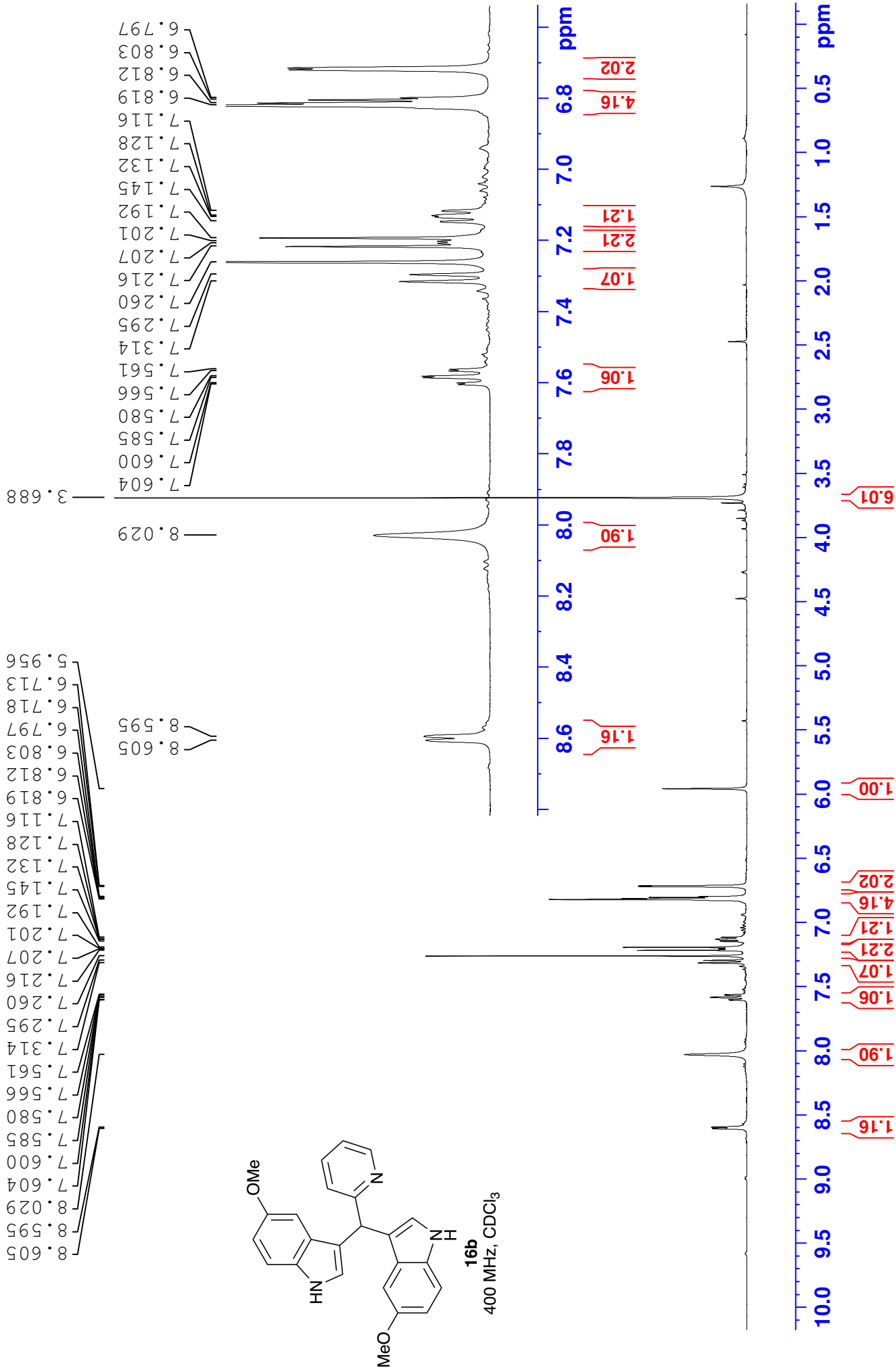

32.50
38.68
38.96
39.24
39.52
39.79
40.07
40.35
112.68
116.21
118.26
121.04
122.57
127.20
128.58
136.31
141.83
144.78
148.69
161.22
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
N
N
14
75 MHz, DMSO-d_6

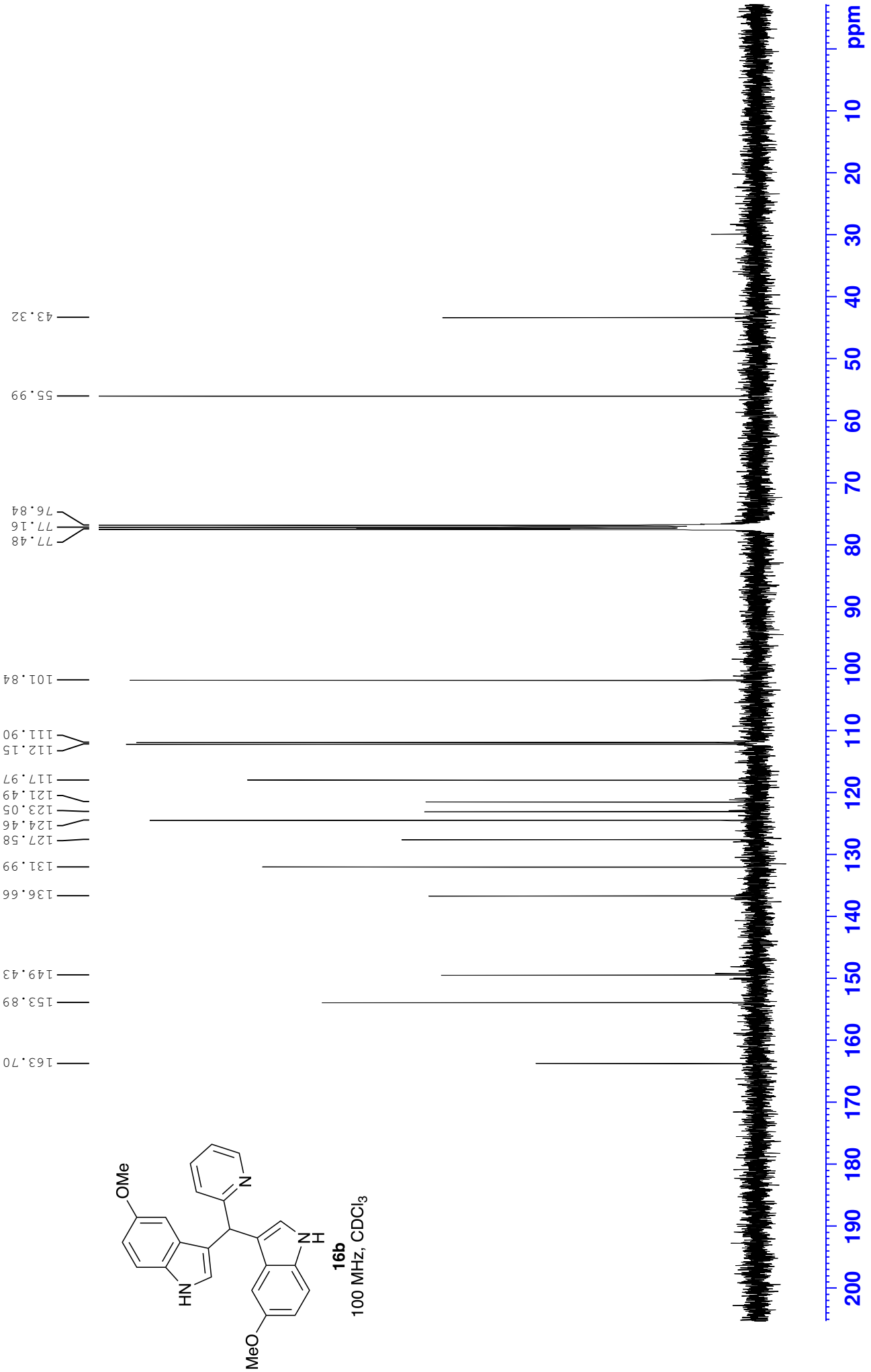

8.588
8.586
8.576
8.574
8.151
7.547
7.542
7.528
7.523
7.508
7.504
7.260
7.225
7.204
7.119
7.105
7.100
7.088
7.069
7.049
7.043
7.024
6.973
6.967
6.815
6.798
4.483
2.476
Me
N
N
H
15
400 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
ppm
0.98
0.92
1.00
1.00
2.98
0.98
1.00
2.03
3.03
7.5
7.4
7.3
7.2
7.1
7.0
6.9
ppm
1.00
1.00
2.98
0.98
1.00

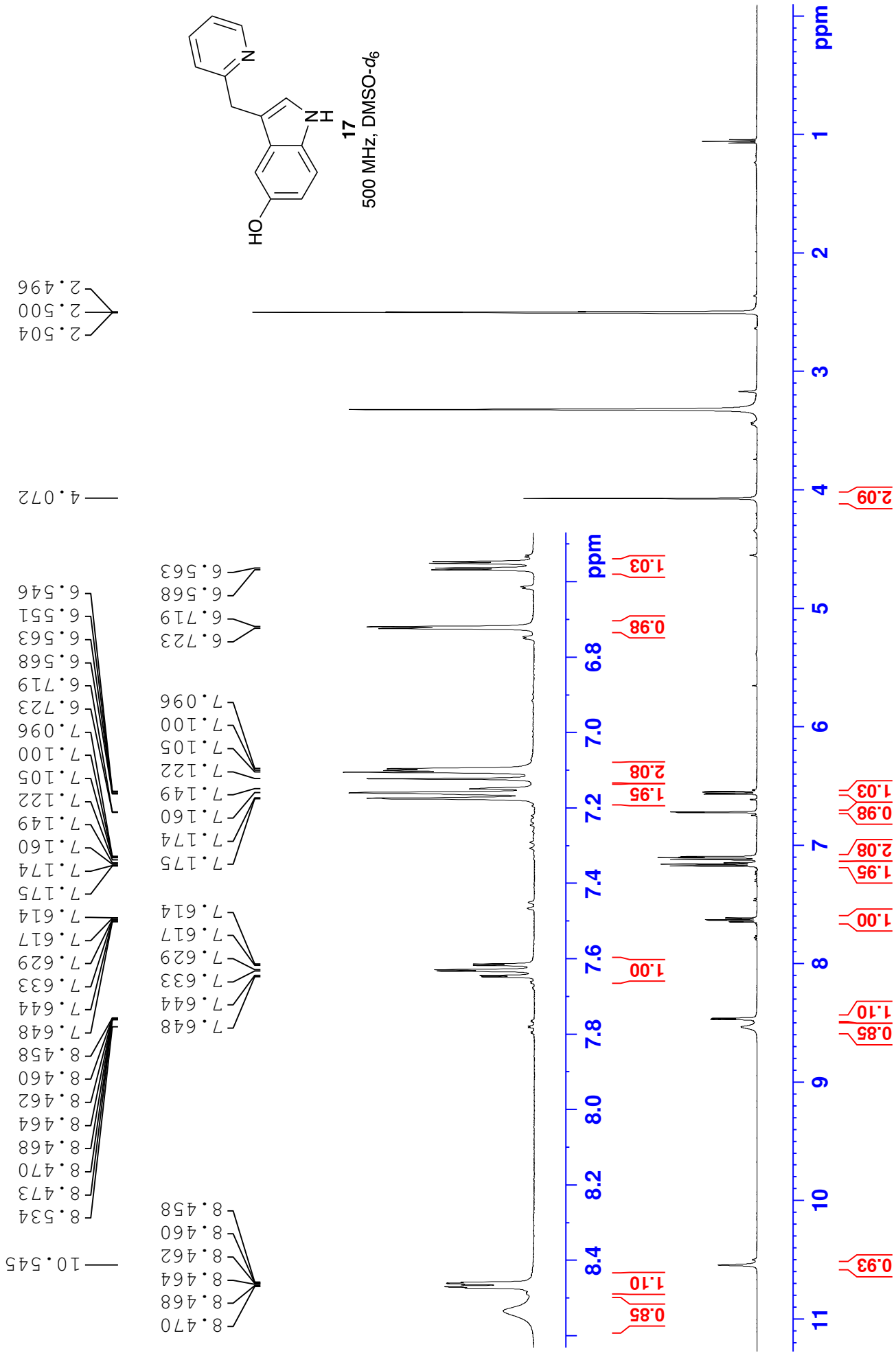

20.17
36.28
76.84
77.16
77.48
109.22
114.16
121.13
121.18
122.40
122.81
123.62
126.18
131.17
136.64
137.21
149.23
162.38
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm
N
H
Me
15
100 MHz, CDCl3

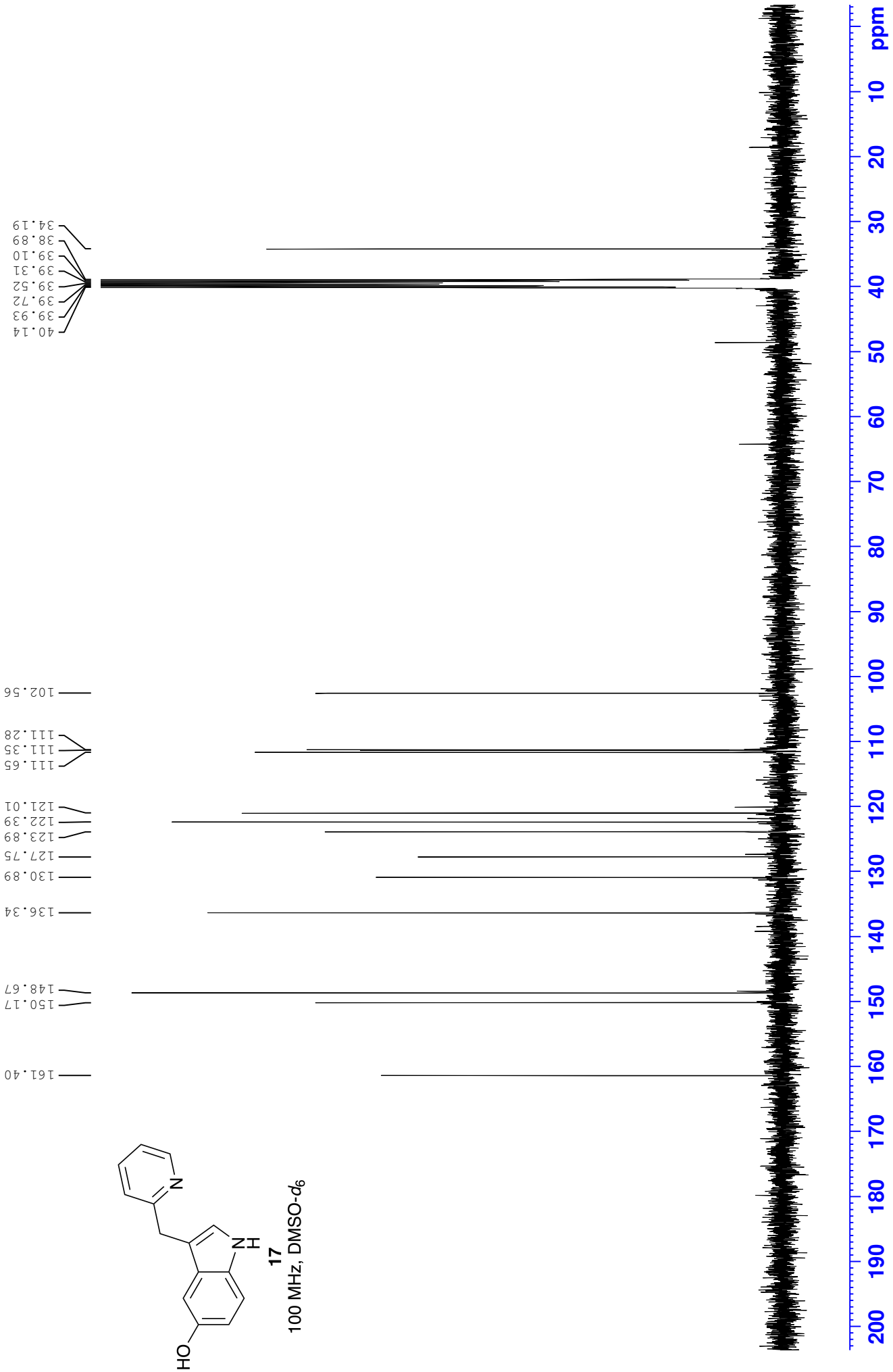

16a
400 MHz, CDCl3
MeO
N
H
ppm
3.17
2.11
1.00
0.99
1.04
2.44
1.02
1.03
1.03
1.03
1.01
1.08
8.573
8.562
7.998
7.560
7.556
7.541
7.537
7.522
7.517
7.260
7.237
7.166
7.146
7.117
7.104
7.100
7.087
7.059
7.054
6.952
6.947
6.857
6.851
6.835
6.829
4.278
3.789

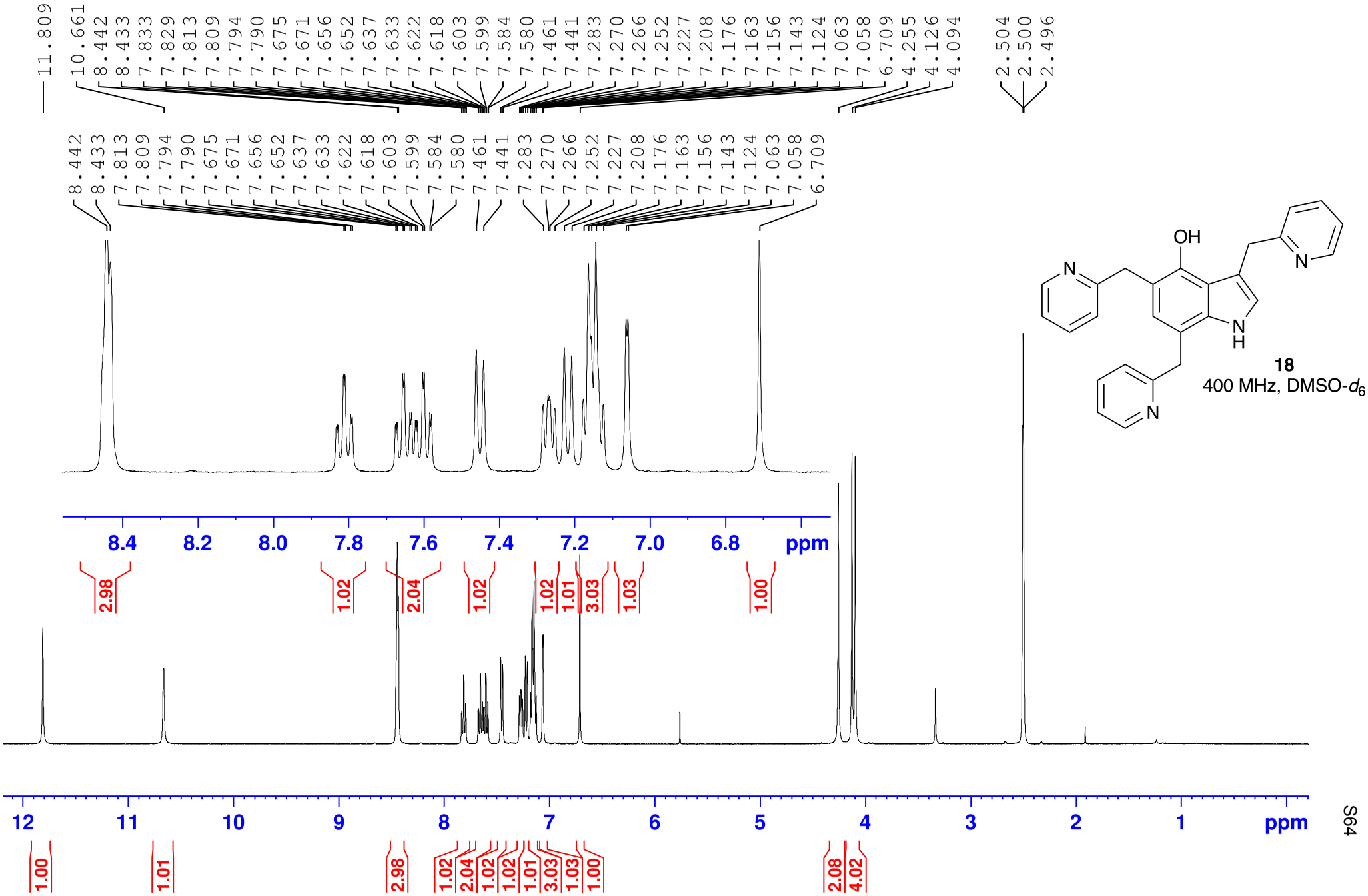

34.73
56.02
76.84
77.16
77.47
101.20
111.95
112.43
113.82
121.22
122.87
123.55
128.01
131.74
136.60
149.25
154.15
161.39
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
MeO
16a
100 MHz, CDCl3

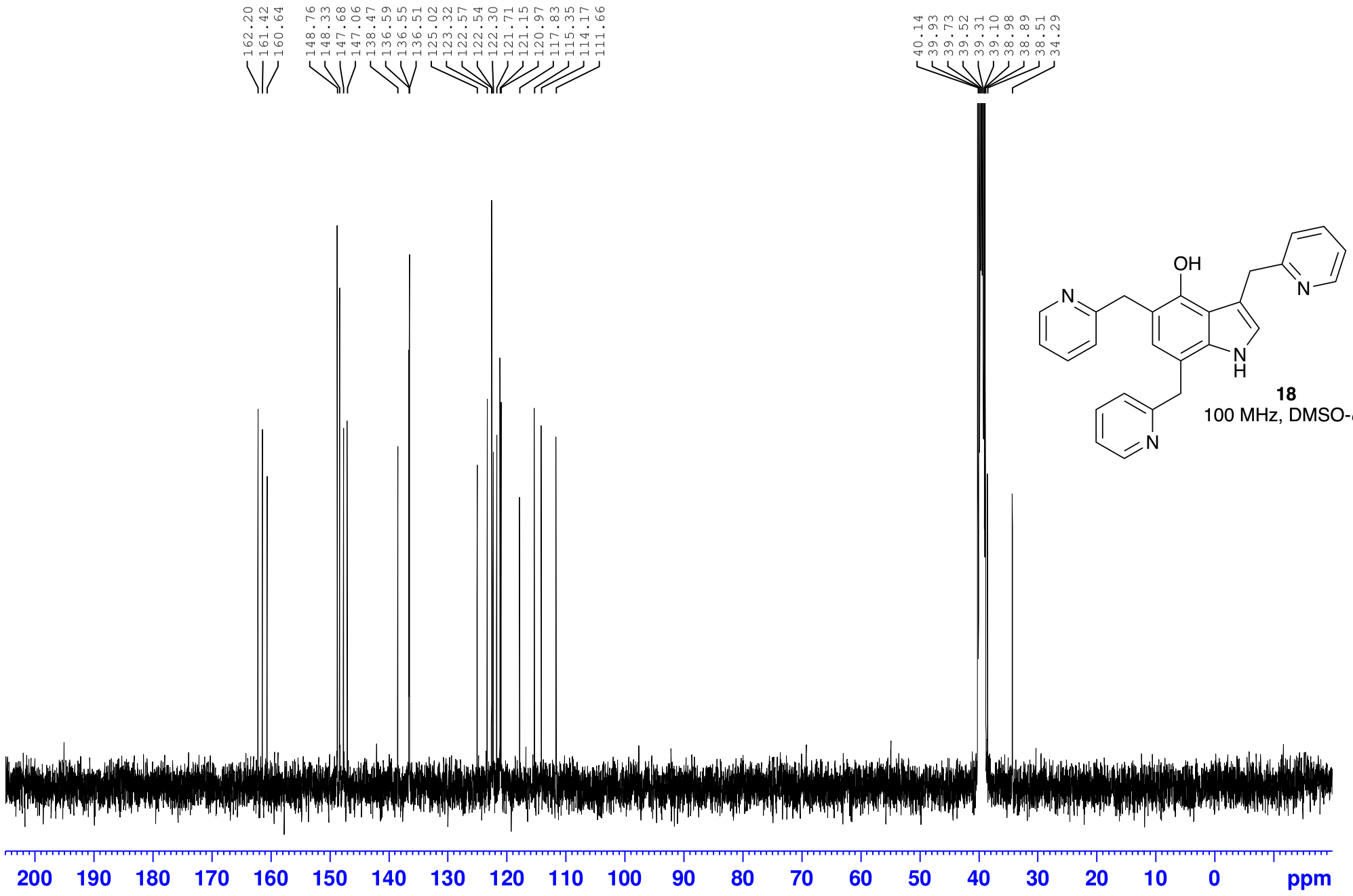

16b
400 MHz, CDCl3
OMe
MeO
NH
N
H
N
ppm

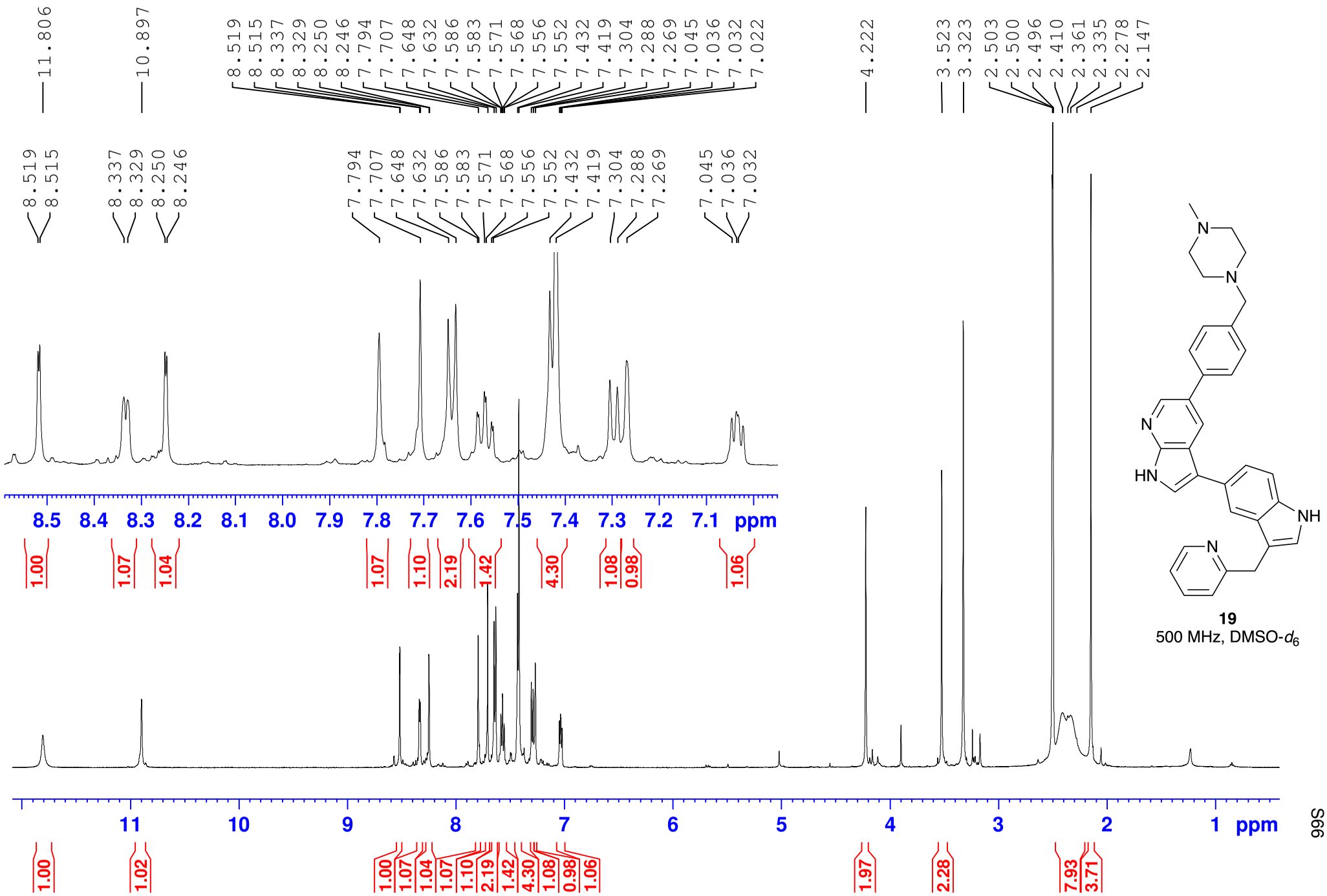

43.32
55.99
76.84
77.16
77.48
101.84
111.90
112.15
117.97
121.49
123.05
124.46
127.58
131.99
136.66
149.43
153.89
163.70
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
OMe
MeO
HN
N
H
N
16b
100 MHz, CDCl3


17
500 MHz, DMSO-d_6
HO
N
H
N
ppm
0.93
1.10
0.85
1.00
2.08
1.95
0.98
1.03
2.09
10.545
8.534
8.473
8.470
8.468
8.464
8.462
8.460
8.458
7.648
7.644
7.633
7.629
7.617
7.614
7.175
7.174
7.160
7.149
7.122
7.105
7.100
7.096
6.723
6.719
6.568
6.563
6.551
6.546
4.072
2.504
2.500
2.496

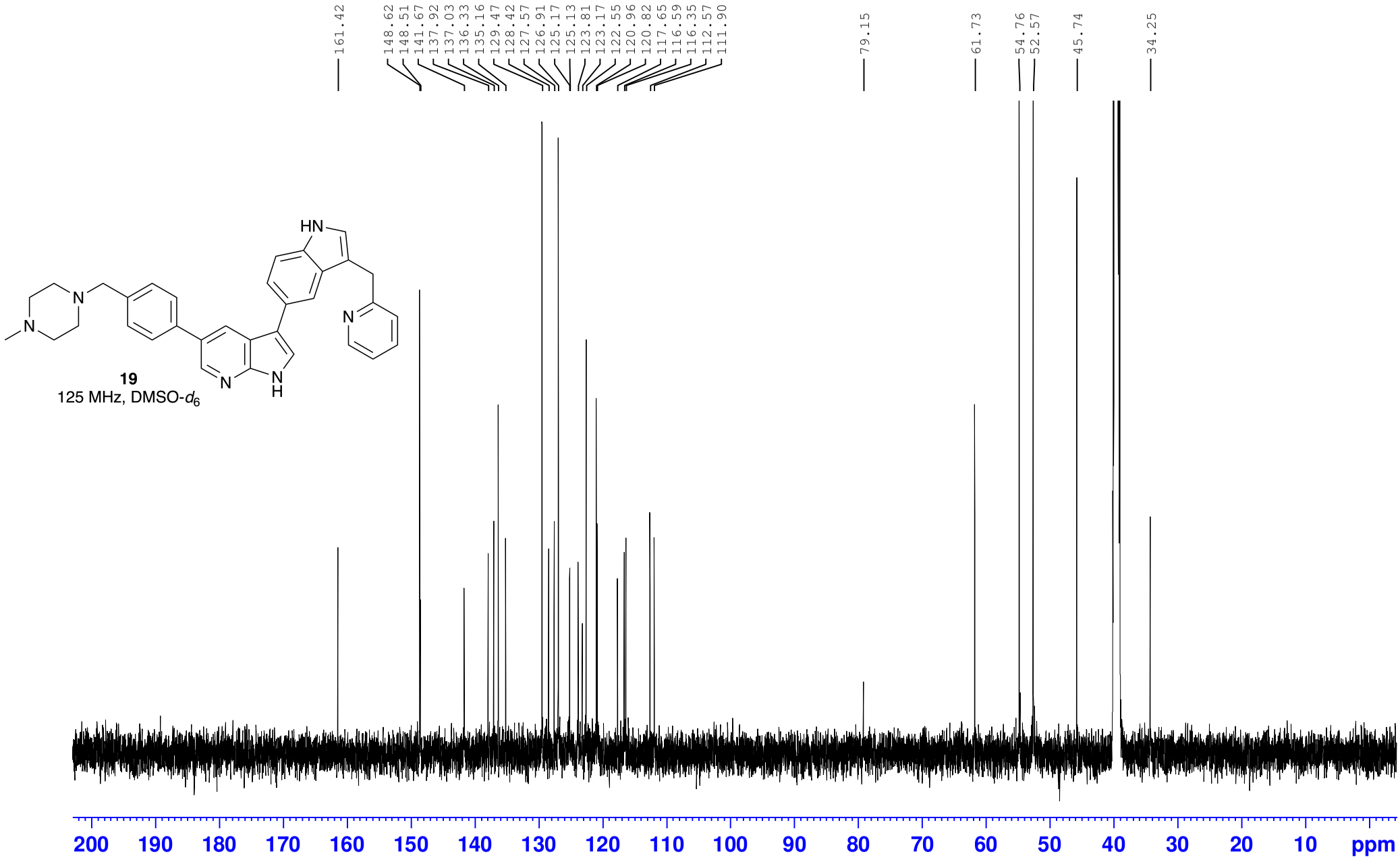

34.19
38.89
39.10
39.31
39.52
39.72
39.93
40.14
102.56
111.28
111.35
111.65
121.01
122.39
123.89
127.75
130.89
136.34
148.67
150.17
161.40
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
HO
N
H
N
17
100 MHz, DMSO-d_6

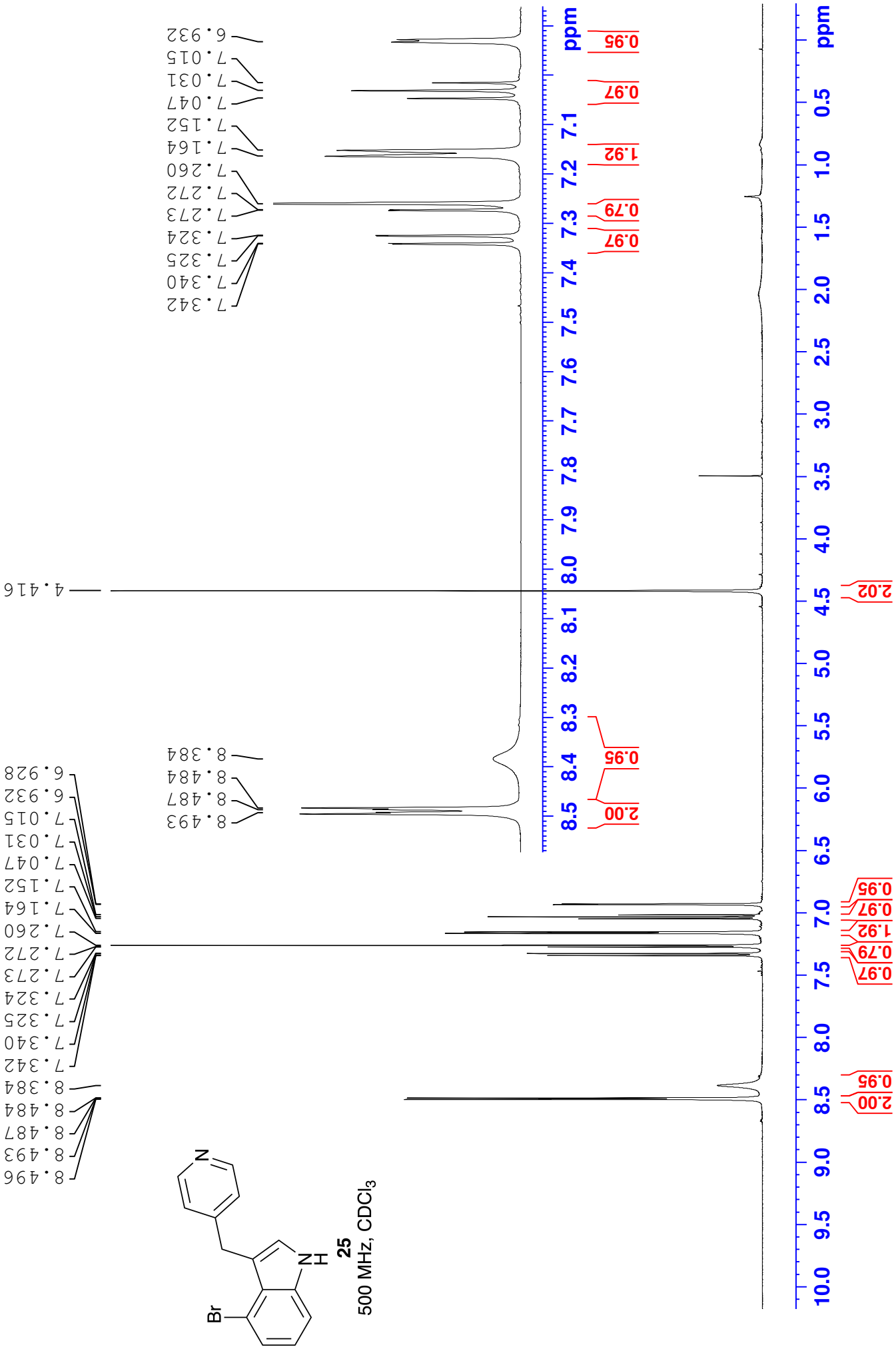

11.809
10.661
8.442
8.433
8.833
7.829
7.813
7.809
7.794
7.790
7.675
7.671
7.656
7.652
7.637
7.633
7.622
7.618
7.603
7.599
7.584
7.580
7.461
7.441
7.283
7.270
7.266
7.252
7.227
7.208
7.176
7.163
7.156
7.143
7.124
7.063
7.058
6.709
4.255
4.126
4.094
2.504
2.500
2.496
OH
N
N
N
H
N
18
400 MHz, DMSO-d_6
ppm
2.98
1.02
2.04
1.02
1.02
1.01
3.03
1.03
1.00
1.00
1.01
2.98
1.02
2.04
1.02
1.02
1.01
3.03
1.03
1.00
2.08
4.02

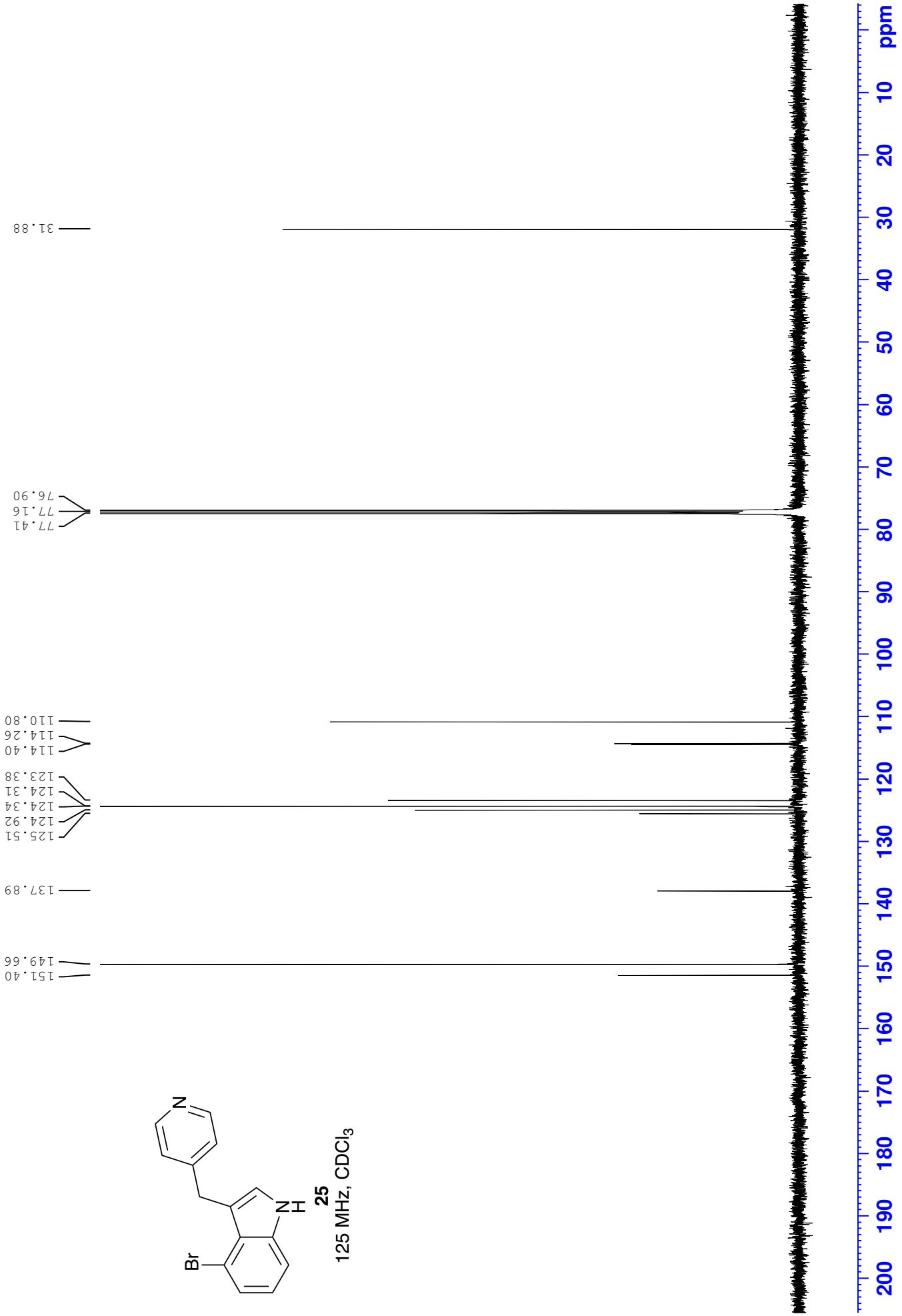

162.20
161.42
160.64
148.76
148.33
147.68
147.06
138.47
136.59
136.55
136.51
125.02
123.32
122.57
122.54
122.30
121.71
121.15
120.97
117.83
115.35
114.17
111.66
40.14
39.93
39.73
39.52
39.31
39.10
38.98
38.89
38.51
34.29
OH
N
N
N
H
N
18
100 MHz, DMSO-d_6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

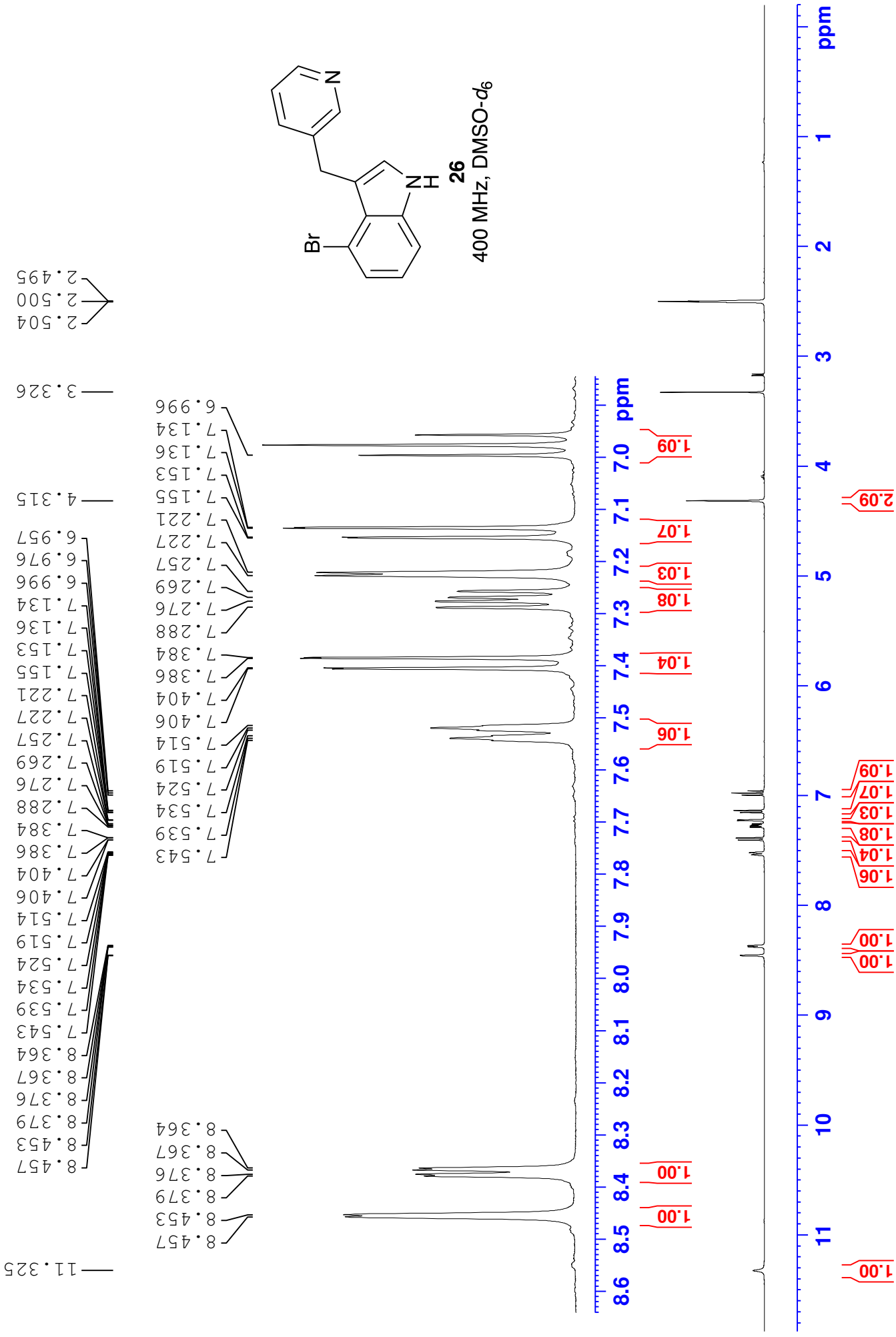


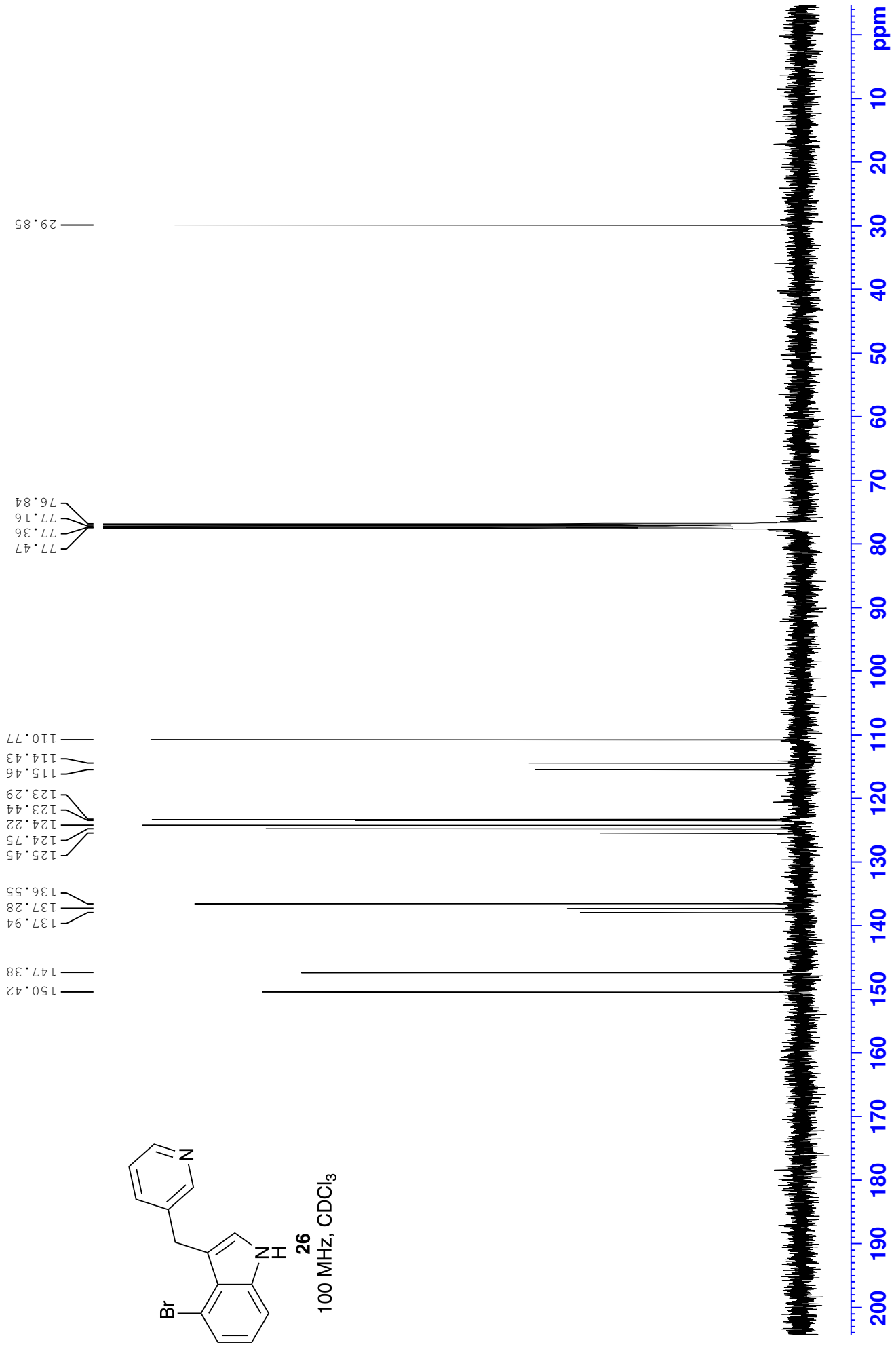
19
500 MHz, DMSO-d_6

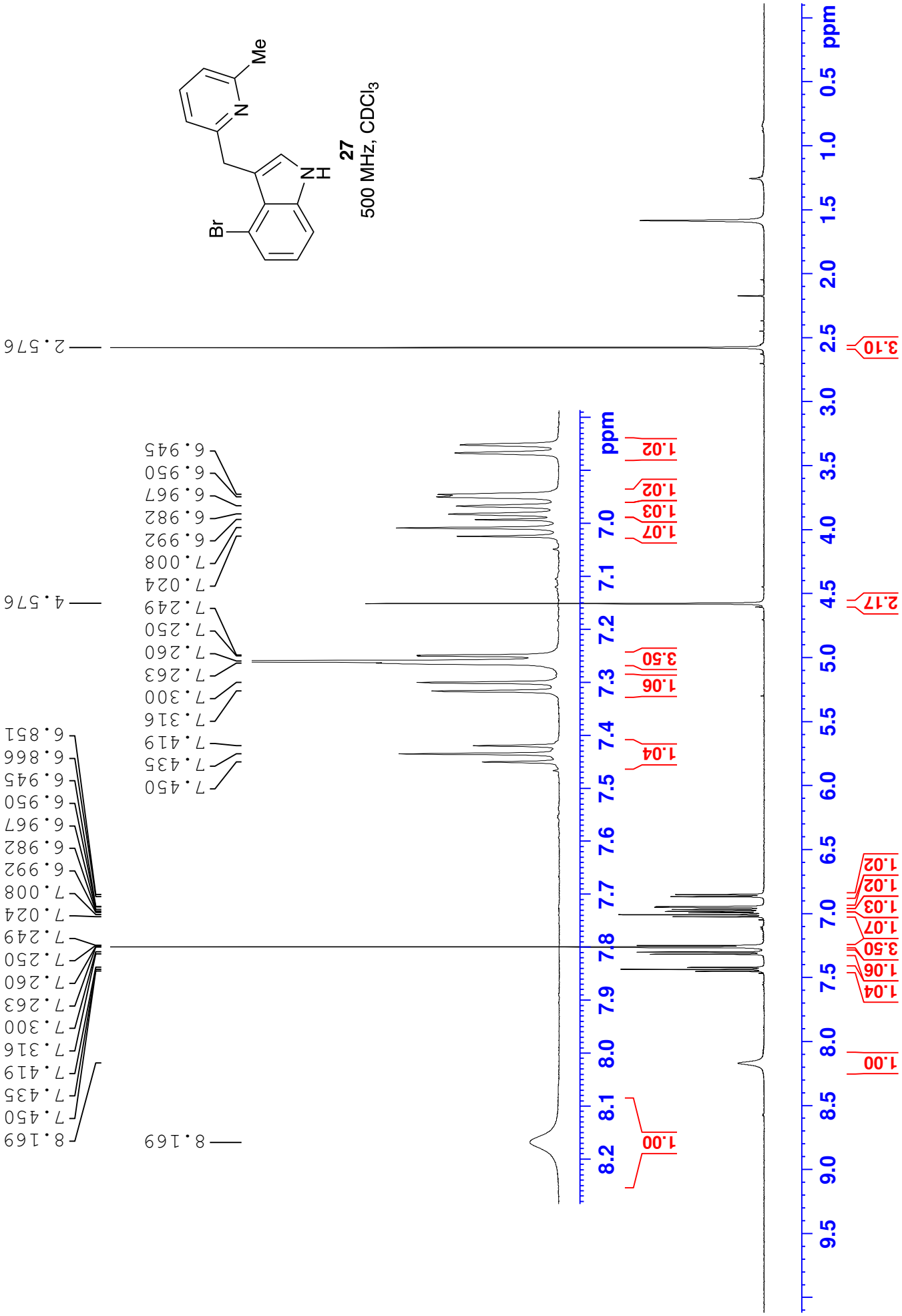

161.42
148.62
148.51
141.67
137.92
137.03
136.33
135.16
129.47
128.42
127.57
126.91
125.17
125.13
123.81
123.17
122.55
120.96
120.82
117.65
116.59
116.35
112.57
111.90
79.15
61.73
54.76
52.57
45.74
34.25
HN
N
N
N
N
H
19
125 MHz, DMSO-d_6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

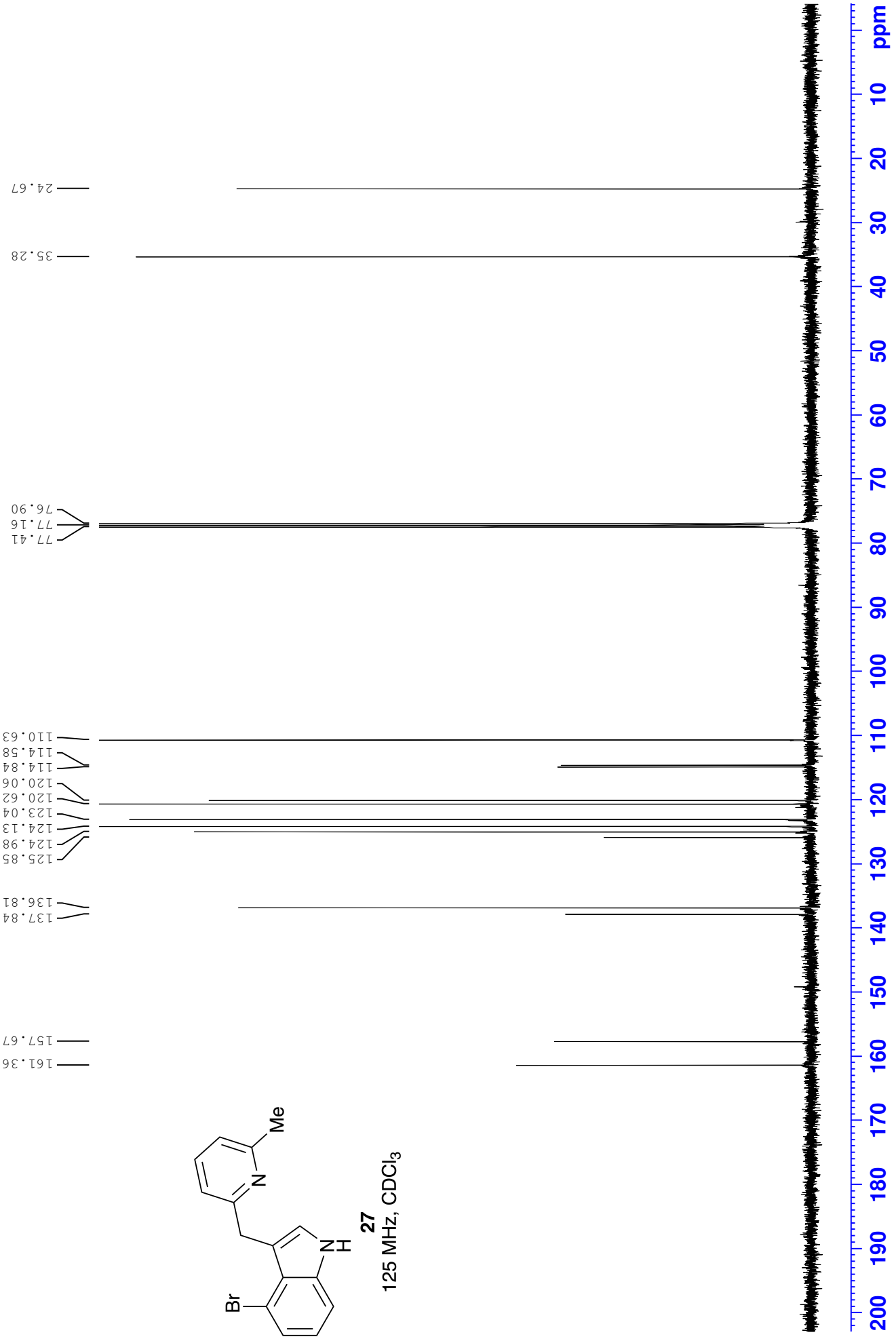

25
500 MHz, CDCl3
Br
N
H
N
8.496
8.493
8.487
8.484
8.384
7.342
7.340
7.325
7.324
7.273
7.272
7.260
7.164
7.152
7.047
7.031
7.015
6.932
6.928
4.416
8.493
8.487
8.484
8.384
7.342
7.340
7.325
7.324
7.273
7.272
7.260
7.164
7.152
7.047
7.031
7.015
6.932
ppm
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
2.00
0.95
0.97
0.79
1.92
0.97
0.95
2.02
2.00
0.95
0.97
0.79
1.92
0.97
0.95

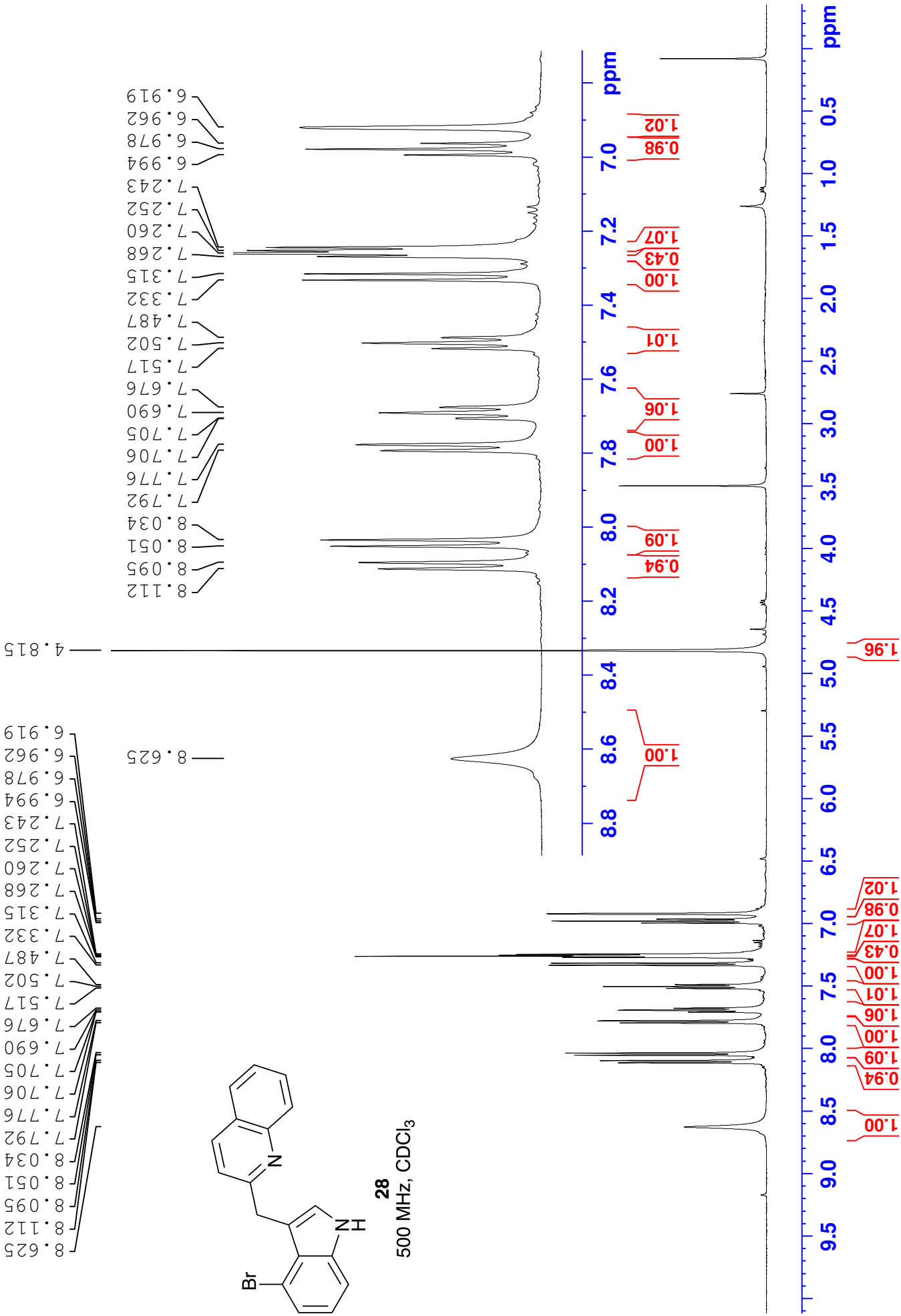

31.88
76.90
77.16
77.41
110.80
114.26
114.40
123.38
124.31
124.34
124.92
125.51
137.89
149.66
151.40
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
Br
25
125 MHz, CDCl3

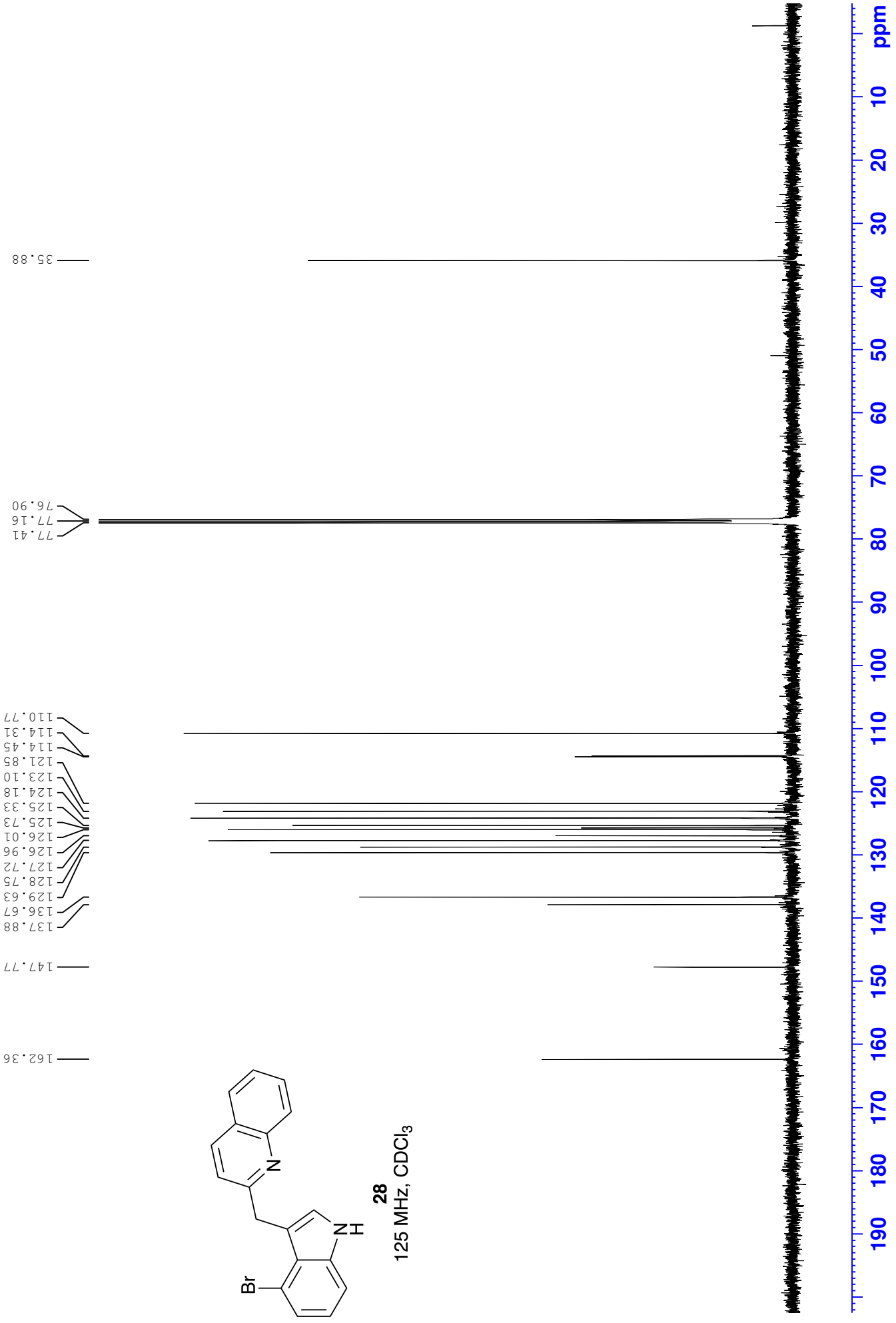

26
400 MHz, DMSO-d_6
Br
N
H
N
ppm
1.09
1.07
1.03
1.08
1.04
1.06
2.09
1.00
1.00
1.00
11.325
8.457
8.453
8.379
8.376
8.367
8.364
7.543
7.539
7.534
7.524
7.519
7.514
7.406
7.404
7.386
7.384
7.288
7.276
7.269
7.257
7.227
7.221
7.155
7.153
7.136
7.134
6.996
4.315
3.326
2.504
2.500
2.495

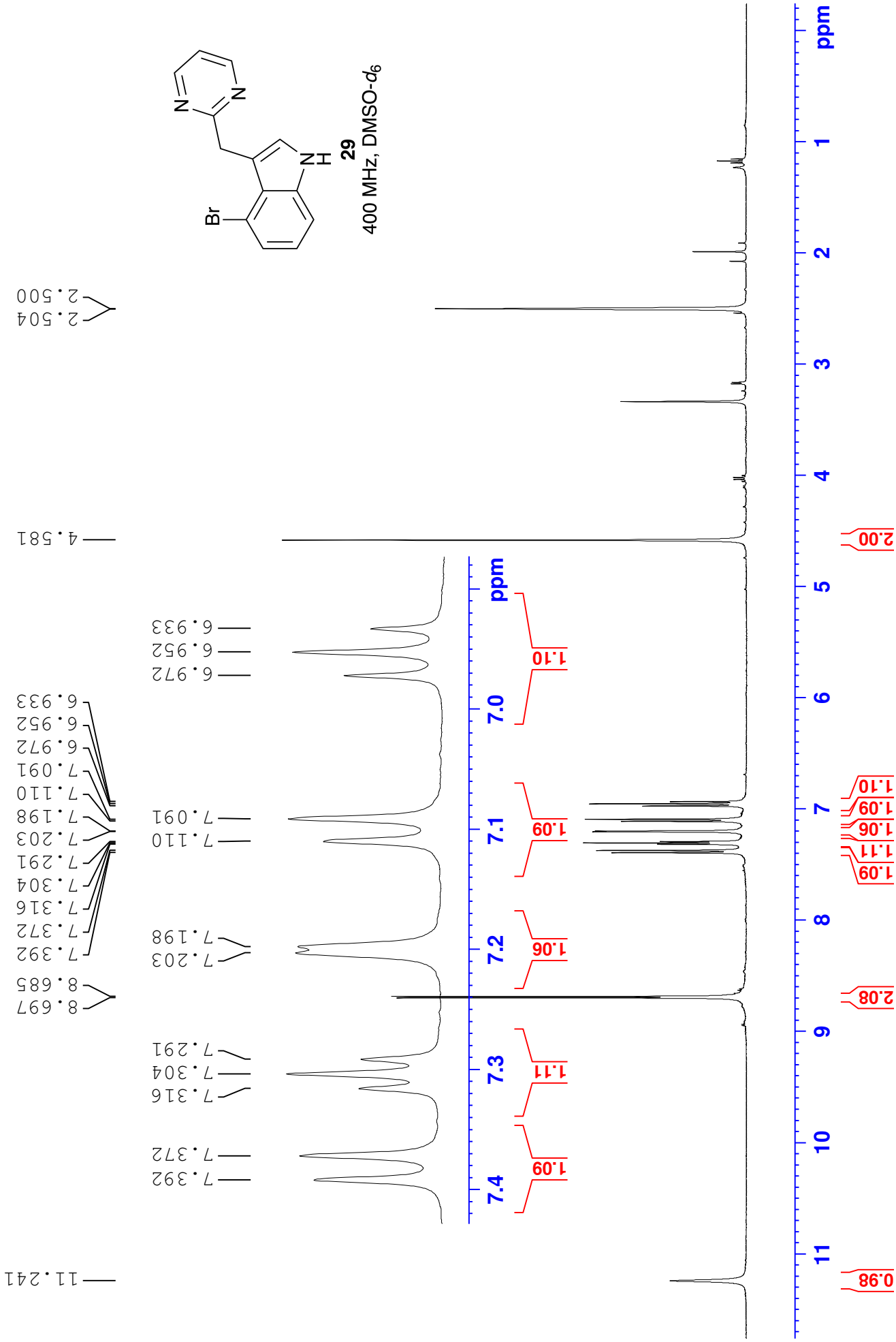

29.85
76.84
77.16
77.36
77.47
110.77
114.43
115.46
123.29
123.44
124.22
124.75
125.45
136.55
137.28
137.94
147.38
150.42
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
N
H
N
Br
26
100 MHz, CDCl3

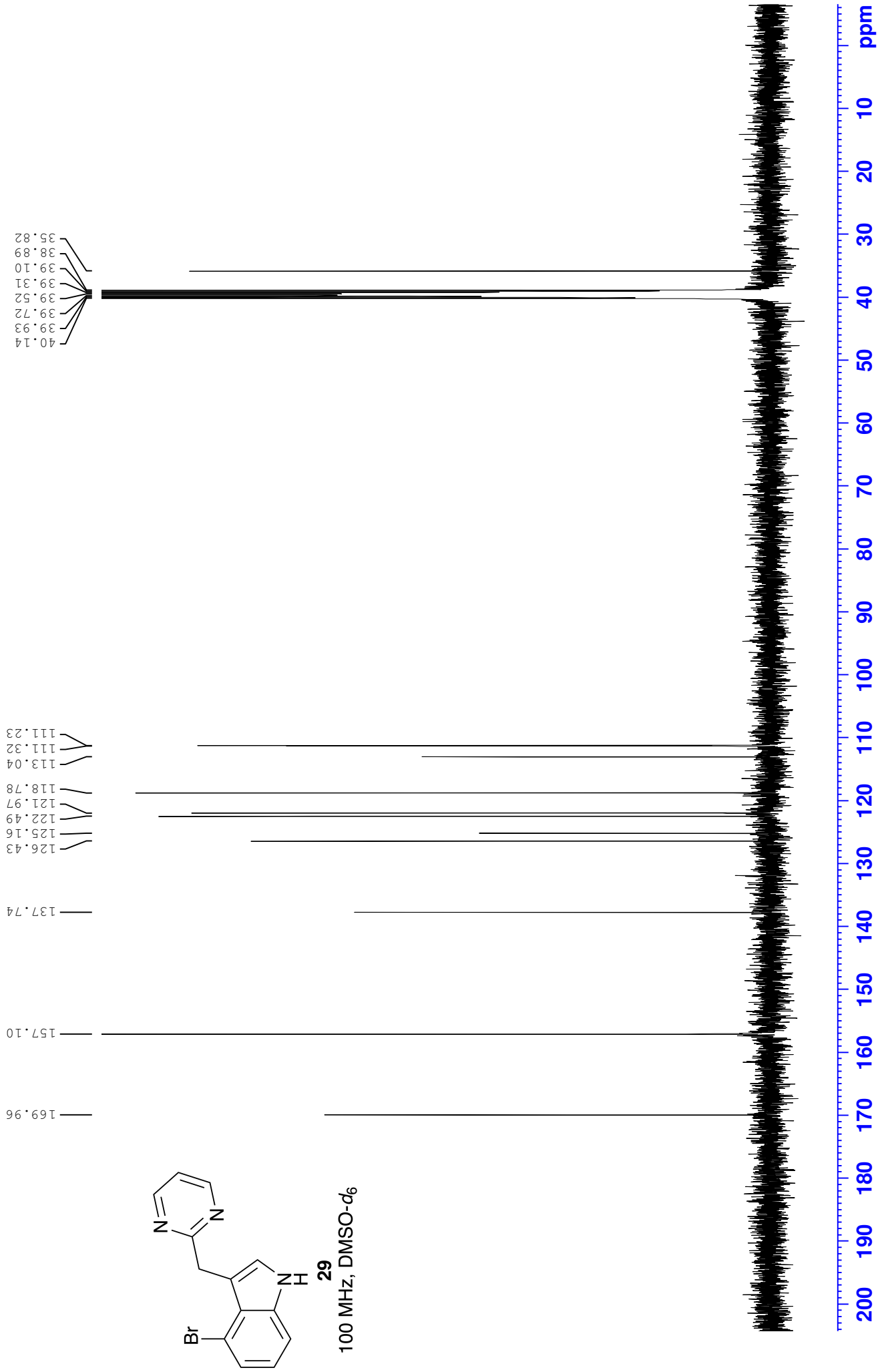

Me
N
N
H
Br
27
500 MHz, CDCl3
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
3.10
2.17
1.00
1.04
1.06
3.50
1.07
1.03
1.02
1.02
1.00
1.02
1.03
1.07
3.50
1.06
1.04
2.576
4.576
8.169
7.450
7.435
7.419
7.316
7.300
7.263
7.260
7.250
7.249
7.024
7.008
6.992
6.982
6.967
6.950
6.945
6.851

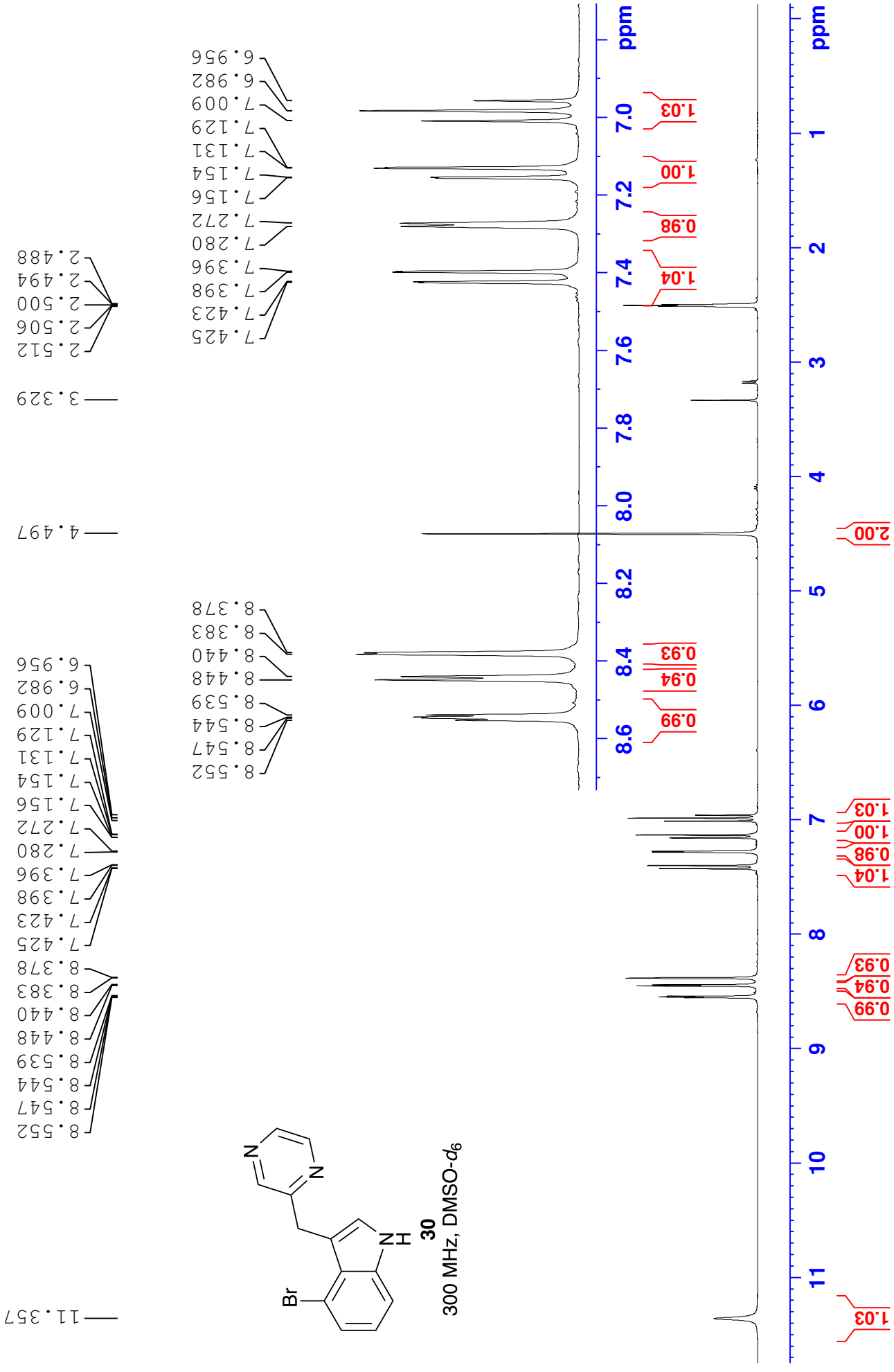

24.67
35.28
76.90
77.16
77.41
110.63
114.58
114.84
120.06
120.62
123.04
124.13
124.98
125.85
136.81
137.84
157.67
161.36
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
Me
N
H
N
Br
27
125 MHz, CDCl3

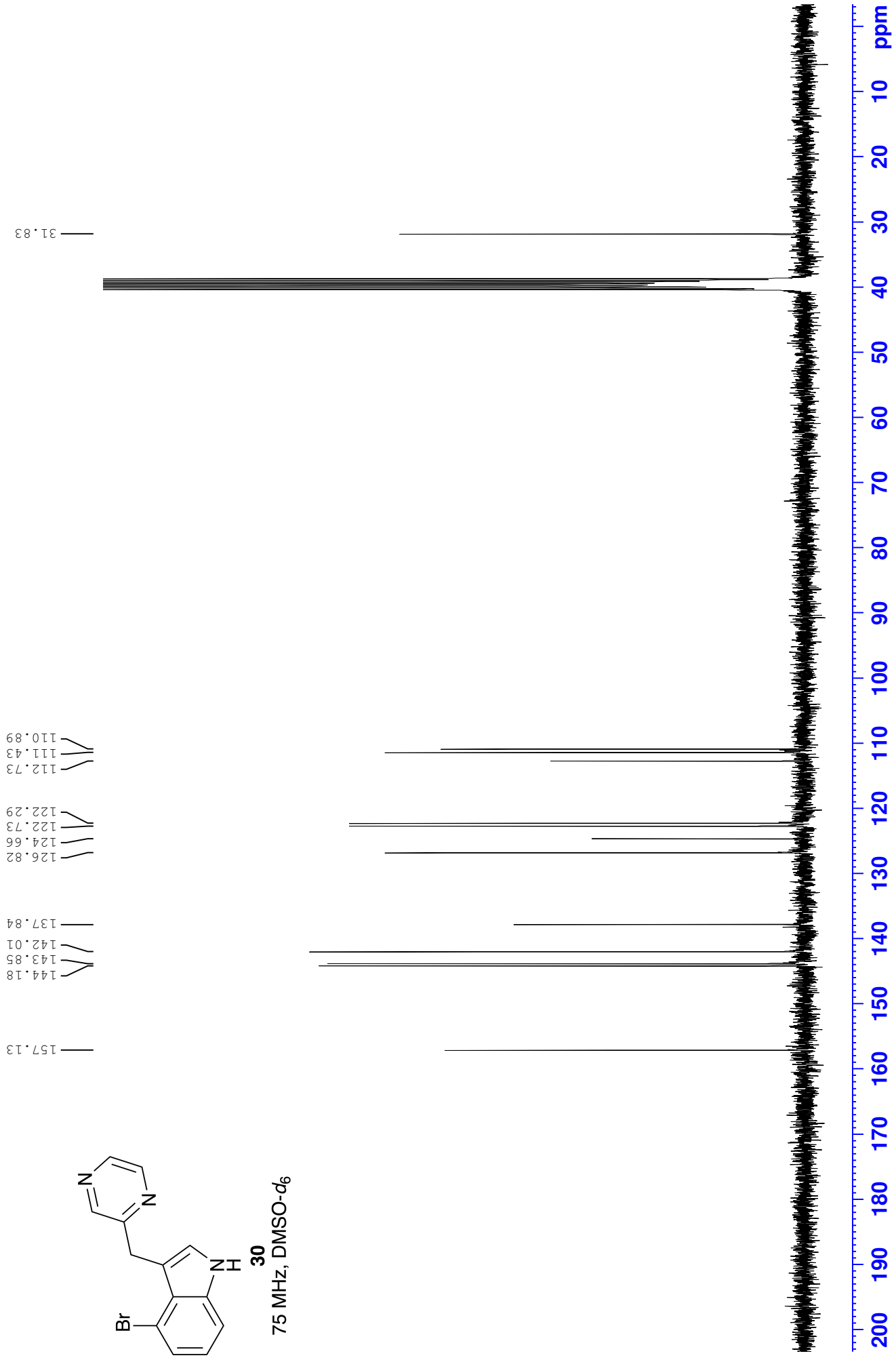

28
500 MHz, CDCl3
Br
N
H
ppm
8.625
8.112
8.095
8.051
8.034
7.792
7.776
7.706
7.705
7.690
7.676
7.517
7.502
7.487
7.332
7.315
7.268
7.260
7.252
7.243
6.994
6.978
6.962
6.919
4.815
1.00
0.94
1.09
1.00
1.06
1.01
1.00
0.43
1.07
0.98
1.02
1.96


35.88
76.90
77.16
77.41
110.77
114.31
114.45
121.85
123.10
124.18
125.33
125.73
126.01
126.96
127.72
128.75
129.63
136.67
137.88
147.77
162.36
Br
N
H
28
125 MHz, CDCl3
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190


29
400 MHz, DMSO-d_6
Br
N
N
H
ppm
11.241
8.697
8.685
7.392
7.372
7.316
7.304
7.291
7.203
7.198
7.110
7.091
6.972
6.952
6.933
4.581
2.504
2.500
0.98
2.08
2.00
1.10
1.09
1.06
1.11
1.09
1.10
1.09
1.06
1.09
1.09

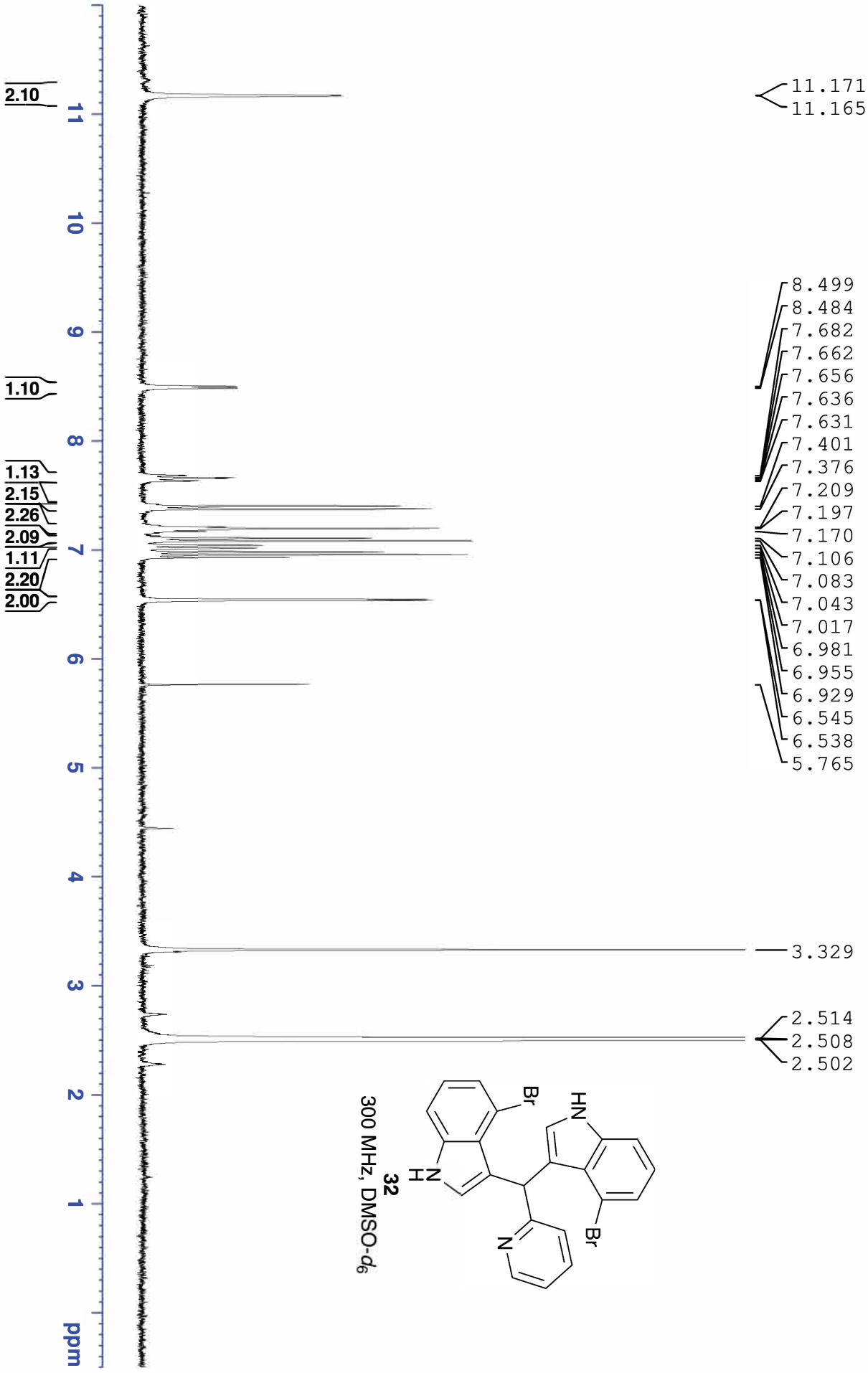

35.82
38.89
39.10
39.31
39.52
39.72
39.93
40.14
111.23
111.32
113.04
118.78
121.97
122.49
125.16
126.43
137.74
157.10
169.96
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
Br
N
N
H
29
100 MHz, DMSO-d_6

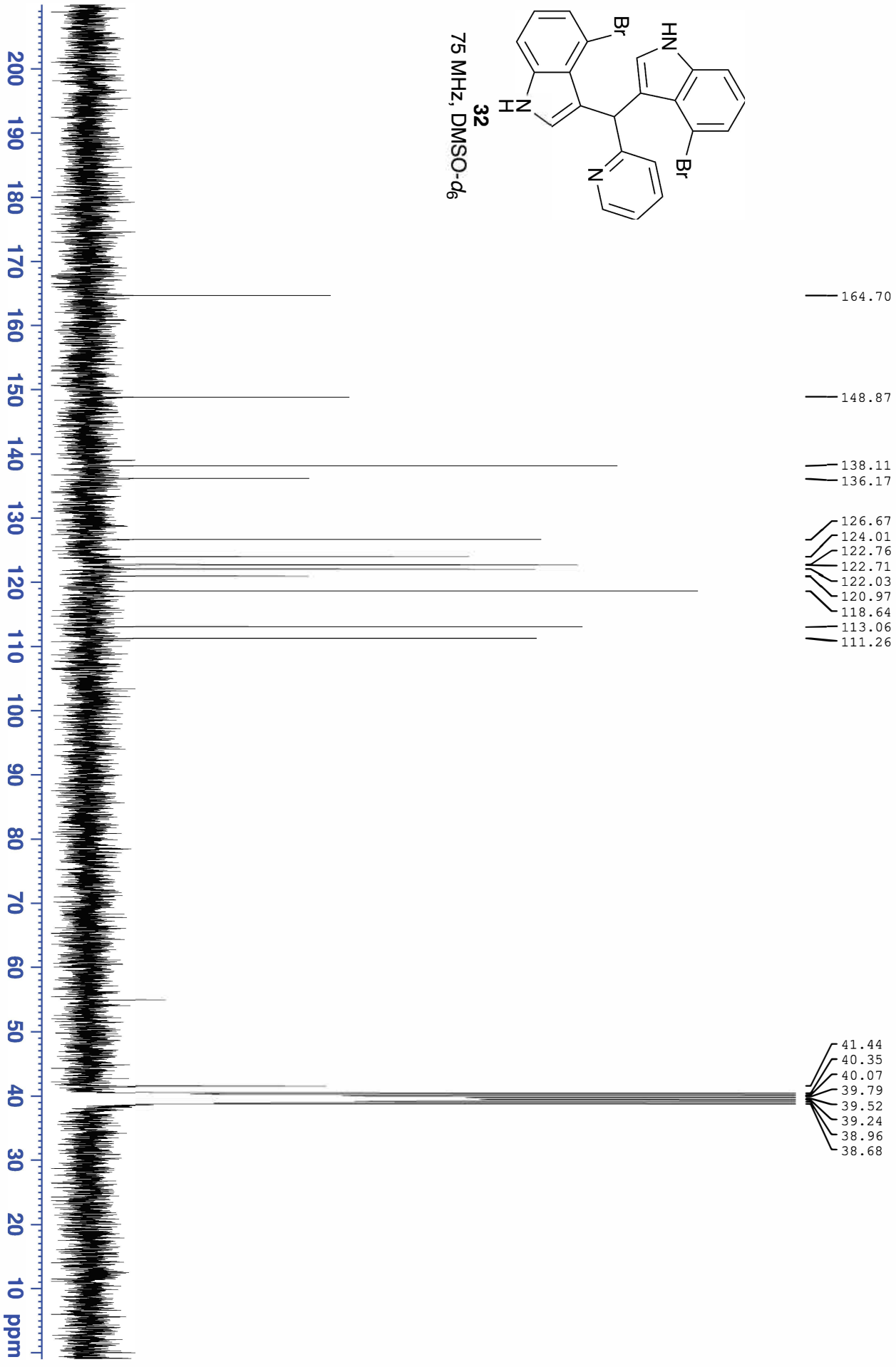

11.357
8.552
8.547
8.544
8.539
8.448
8.440
8.383
8.378
7.425
7.423
7.398
7.396
7.280
7.272
7.156
7.154
7.131
7.129
7.009
6.982
6.956
4.497
3.329
2.512
2.506
2.500
2.494
2.488
8.552
8.547
8.544
8.539
8.448
8.440
8.383
8.378
7.425
7.423
7.398
7.396
7.280
7.272
7.156
7.154
7.131
7.129
7.009
6.982
6.956
N
N
H
Br
30
300 MHz, DMSO-d6
ppm
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
0.99
0.94
0.93
1.04
0.98
1.00
1.03
2.00
ppm
11
10
9
8
7
6
5
4
3
2
1
0.99
0.94
0.93
1.04
0.98
1.00
1.03
2.00
1.03

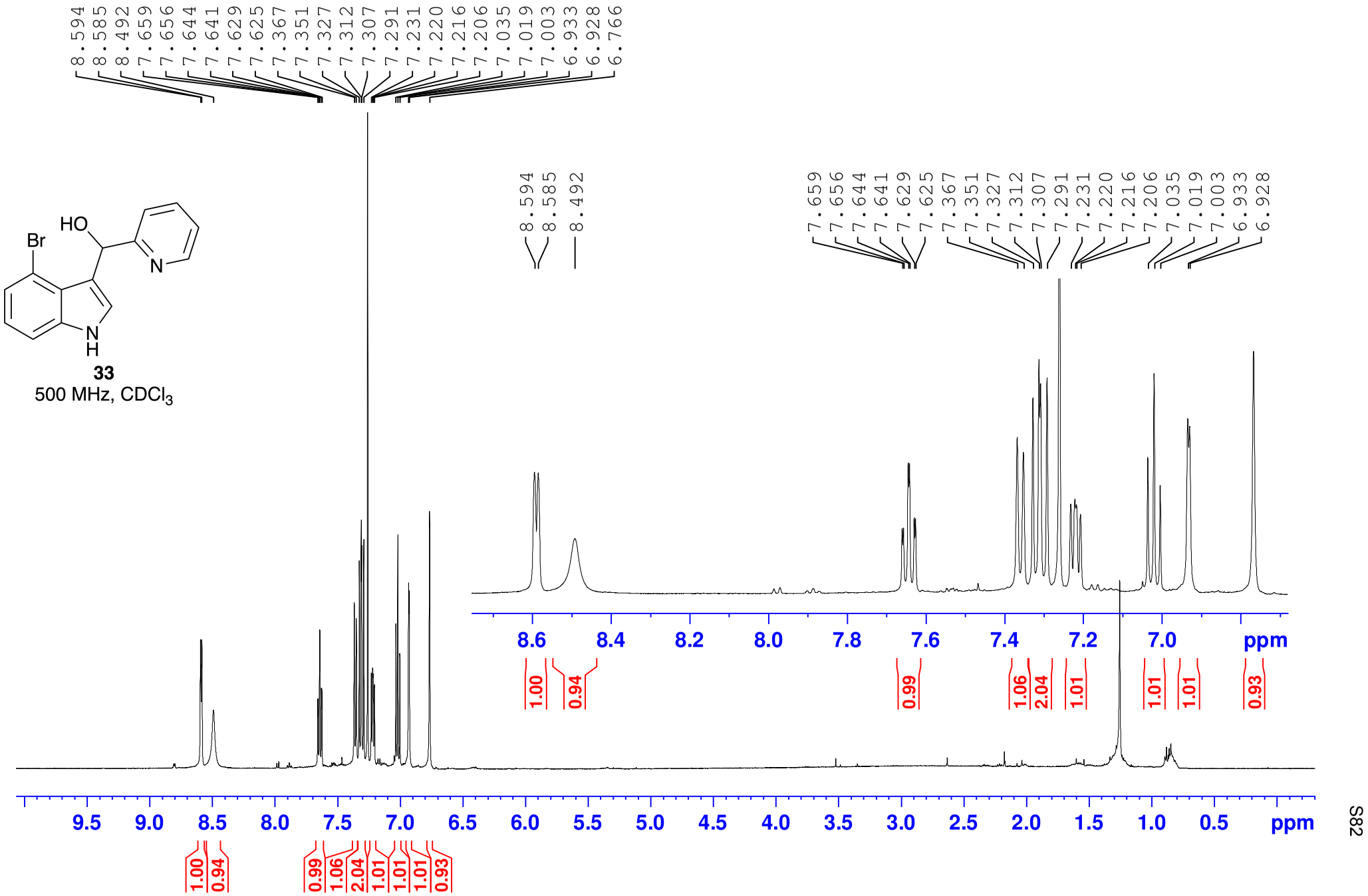


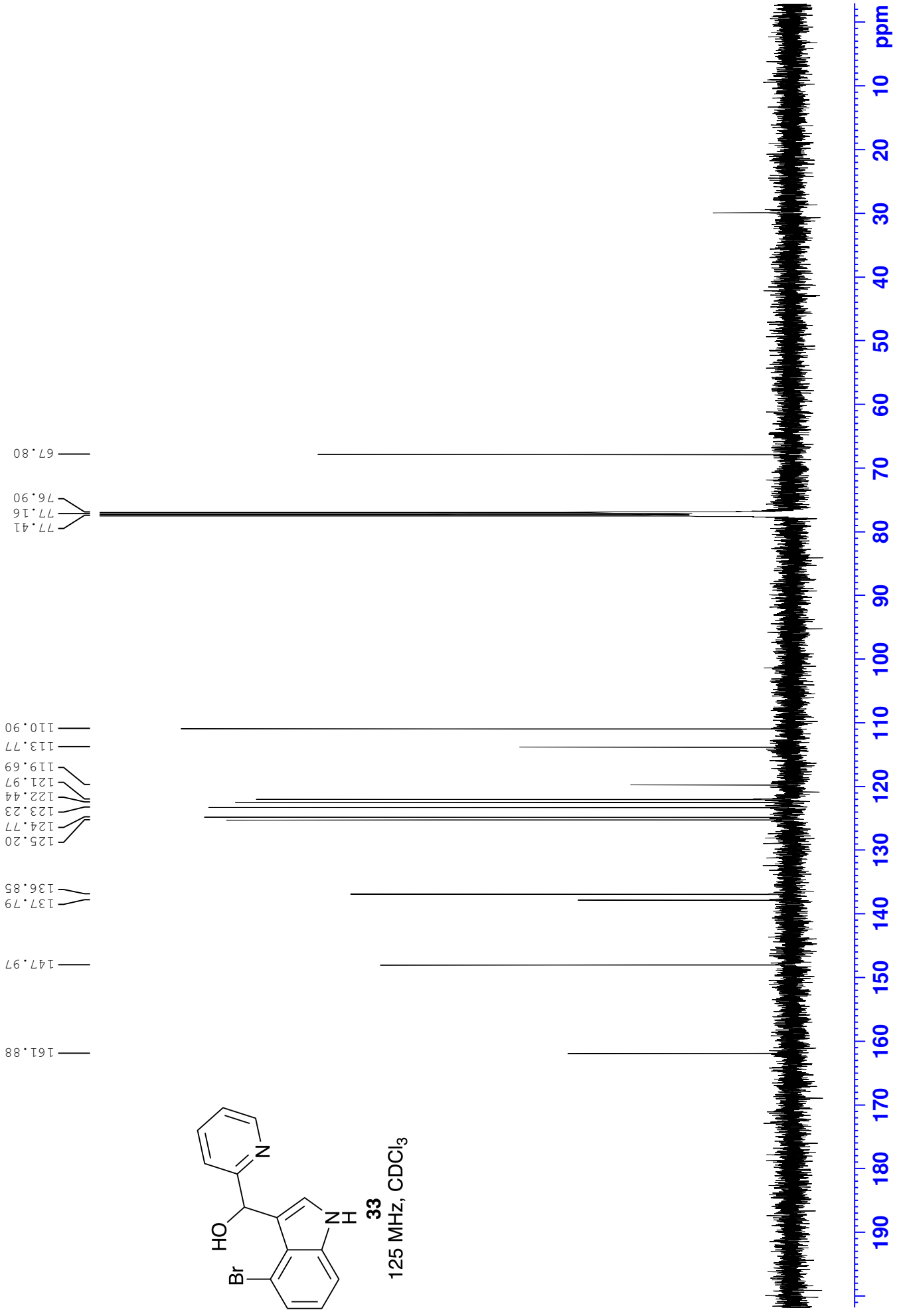
30

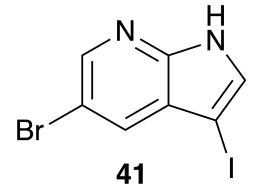
75 MHz, DMSO-d_6


11.171
11.165
8.499
8.484
7.682
7.662
7.656
7.636
7.631
7.401
7.376
7.209
7.197
7.170
7.106
7.083
7.043
7.017
6.981
6.955
6.929
6.545
6.538
5.765
3.329
2.514
2.508
2.502
2.10
1.10
1.13
2.15
2.26
2.09
1.11
2.20
2.00
11
10
9
8
7
6
5
4
3
2
1
ppm
Br
HN
N
H
N
Br
32
300 MHz, DMSO-d_6


32
75 MHz, DMSO-d_6
Br
HN
N
H
N
Br
164.70
148.87
138.11
136.17
126.67
124.01
122.76
122.71
122.03
120.97
118.64
113.06
111.26
41.44
40.35
40.07
39.79
39.52
39.24
38.96
38.68
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

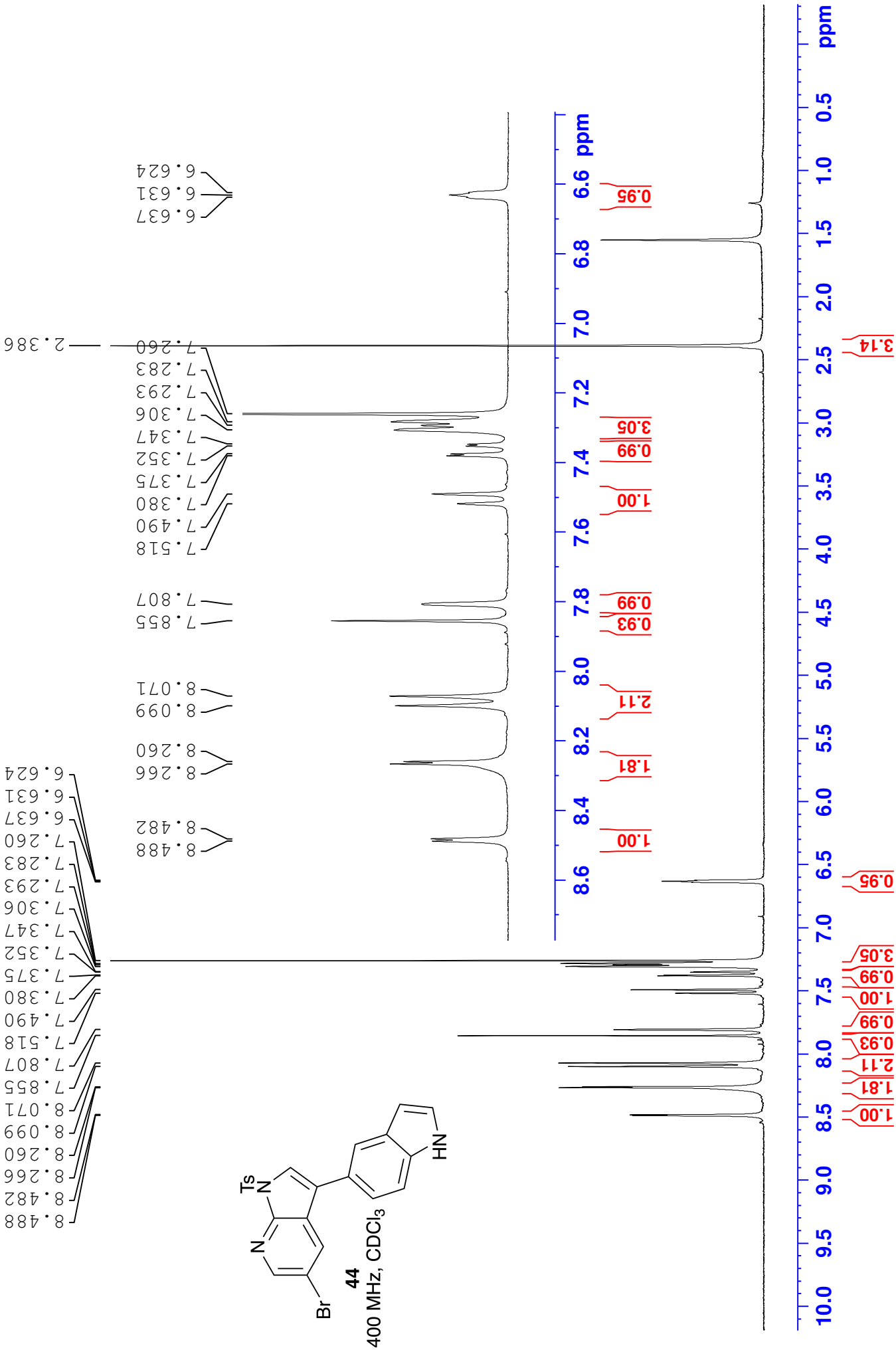

8.594
8.585
8.492
7.659
7.656
7.644
7.641
7.629
7.625
7.367
7.351
7.327
7.312
7.307
7.291
7.231
7.220
7.216
7.206
7.035
7.019
7.003
6.933
6.928
6.766
HO
Br
N
N
H
33
500 MHz, CDCl3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00 0.94 0.99 1.06 2.04 1.01 1.01 1.01 0.93
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 ppm
1.00 0.94 0.99 1.06 2.04 1.01 1.01 1.01 0.93

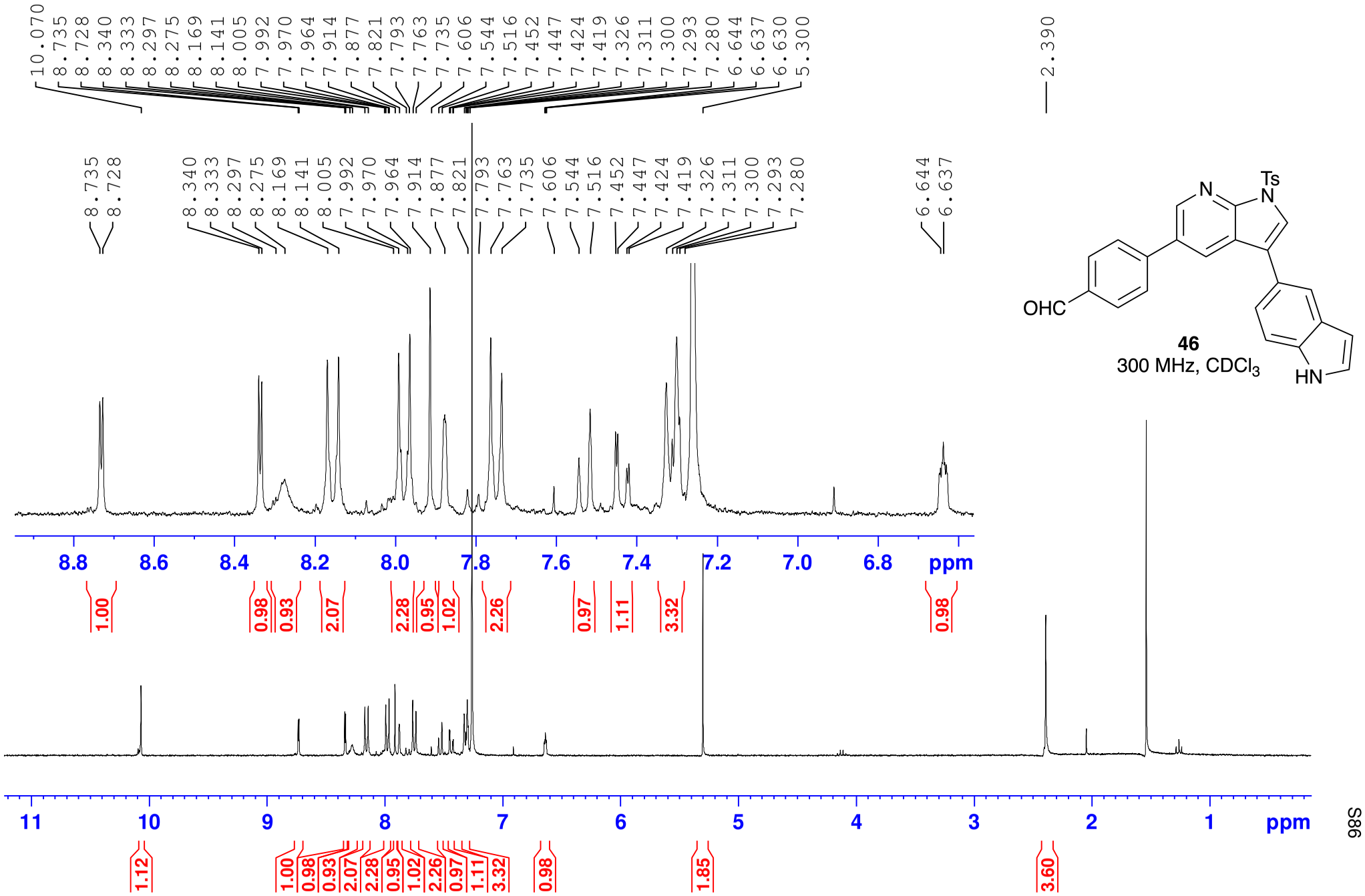

67.80
76.90
77.16
77.41
110.90
113.77
119.69
121.97
122.44
123.23
124.77
125.20
136.85
137.79
147.97
161.88
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
HO
Br
N
H
N
33
125 MHz, CDCl3

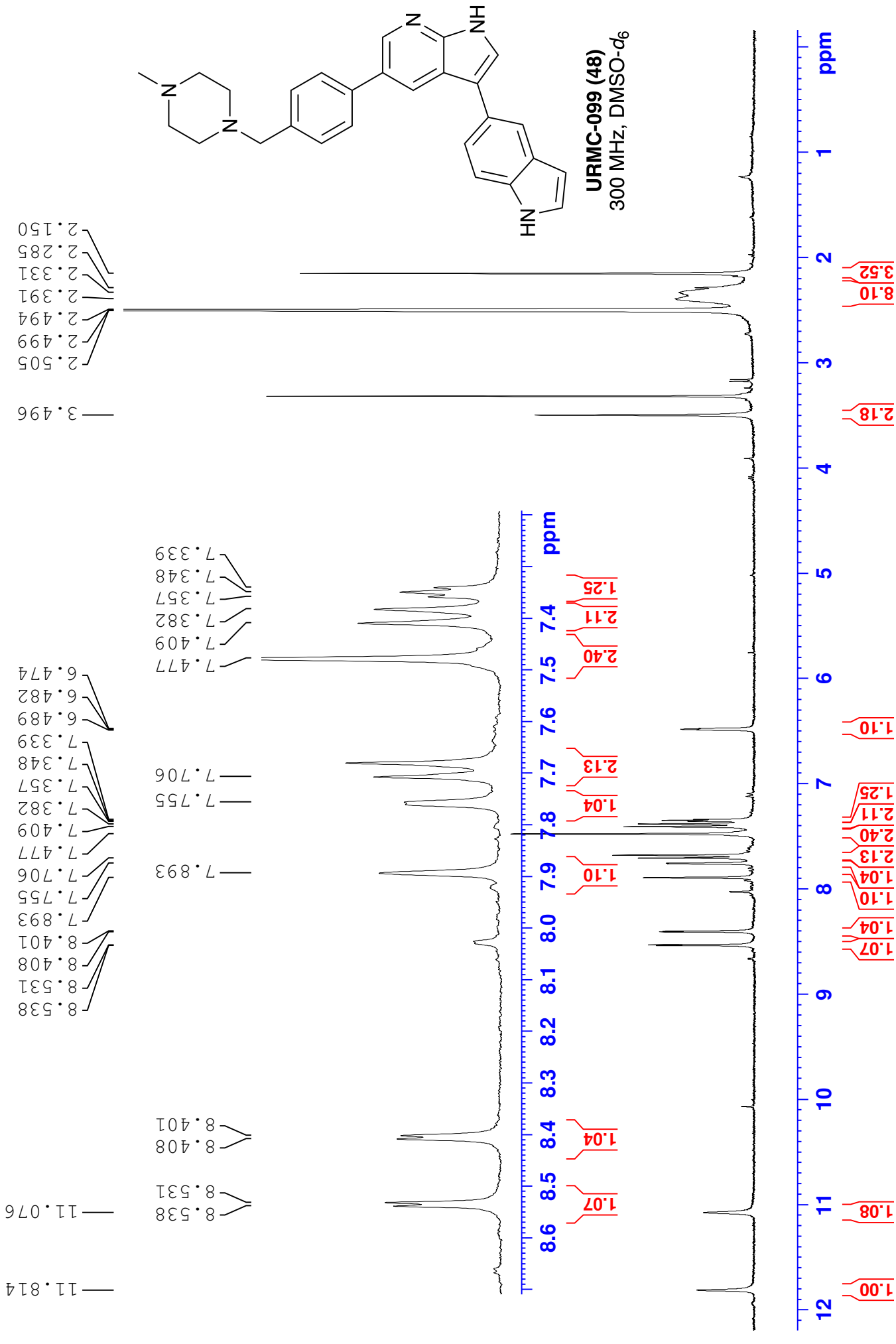


41

500 MHz, DMSO-d_6


44
400 MHz, CDCl3
Ts
N
N
Br
NH
8.488
8.482
8.266
8.260
8.099
8.071
7.855
7.807
7.518
7.490
7.380
7.375
7.352
7.347
7.306
7.293
7.283
7.260
6.637
6.631
6.624
2.386
ppm
1.00
1.81
2.11
0.93
0.99
1.00
0.99
3.05
0.95
3.14


10.070
8.735
8.728
8.340
8.333
8.297
8.275
8.169
8.141
8.005
7.992
7.970
7.964
7.914
7.877
7.821
7.793
7.763
7.735
7.606
7.544
7.516
7.452
7.447
7.424
7.419
7.326
7.311
7.300
7.293
7.280
6.644
6.637
6.630
5.300
2.390
Ts
N
N
OHC
HN
46
300 MHz, CDCl3
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
ppm
1.00
0.98
0.93
2.07
2.28
0.95
1.02
2.26
0.97
1.11
3.32
0.98
11
10
9
8
7
6
5
4
3
2
1
ppm
1.12
1.00
0.98
0.93
2.07
2.28
0.95
1.02
2.26
0.97
1.11
3.32
0.98
1.85
3.60


URMC-099 (48)
300 MHz, DMSO-d_6
ppm
11.814
11.076
8.538
8.531
8.408
8.401
7.893
7.755
7.706
7.477
7.409
7.382
7.357
7.348
7.339
6.489
6.482
6.474
3.496
2.505
2.499
2.494
2.391
2.331
2.285
2.150