Copper-Catalyzed Cascade Azidation-Cyclization of Tryptophols and Tryptamines

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Supporting Information

Table of Content:

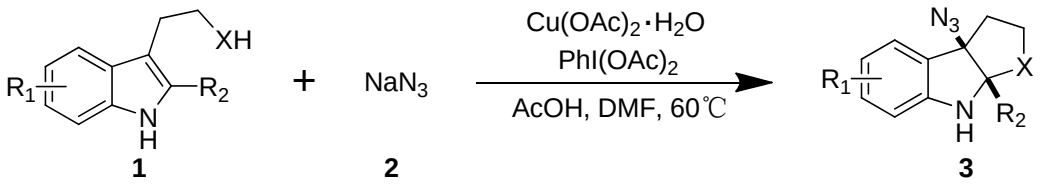
I. General remarks

Most of all reactions were carried out with the reaction system open to air. All reagents and metal catalysts were obtained from commercial sources without further purification. All solvents were purified and dried according to standard methods prior to use.

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Varian instrument (300 MHz, 75 MHz and 282 MHz) spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C NMR and ^{19}F NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI ionization sources. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated.

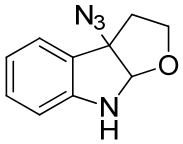
II. General Procedure for the reaction

1a-1j were prepared by the reported procedure.[1] **1k-1q** were prepared by the reported procedure.[2] **1r** were prepared by the reported procedure.[3]



In an ordinary vial, amixture of NaN_3 (0.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.08 mmol), $PhI(OAc)_2$ (0.2 mmol), AcOH (0.24 mmol) and DMF (2 mL) were stirred at room temperature for 30 min, and then 1 (0.2 mmol) was added, and the mixture was stirred at 60℃ for 10 h. After cooling to room temperature, the mixture was quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt) to afford the product **3**.

III. Characterization of products



3a-azido-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3a)

93% yield;

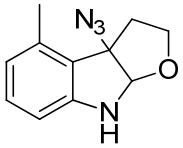
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.6 Hz, 1H), 7.23 – 7.17 (m, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.53 (d, *J* = 2.3 Hz, 1H), 4.72 (s, 1H), 4.09 – 4.03 (m, 1H), 3.72 – 3.64 (m, 1H), 2.43 – 2.32 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.70, 130.70, 125.88, 124.30, 119.68, 109.70, 98.06, 78.01, 67.44, 39.48;

IR: ν_{max} = 3349, 2925, 2100, 1610, 1234, 1118, 1042, 747 cm^{-1};

HRMS (ESI) m/z calcd for $C_{10}H_{11}N_4O$ $[M+H]^+$: 203.0927, found 203.0929.



3a-azido-4-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3b)

93% yield;

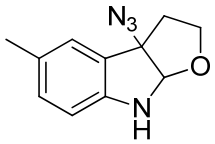
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (t, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 7.9 Hz, 1H), 5.65 (d, *J* = 2.8 Hz, 1H), 4.69 (s, 1H), 4.06 – 3.99 (m, 1H), 3.73 (td, *J* = 9.4, 5.6 Hz, 1H), 2.43 – 2.36 (m, 4H), 2.33– 2.23 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.82, 135.50, 130.63, 123.57, 121.55, 107.21, 98.85, 78.75, 66.75, 38.20, 17.80;

IR: ν_{max} = 3375, 2924, 2372, 2098, 1595, 1459, 1119, 778 cm^{-1};

HRMS (ESI) m/z calcd for $C_{11}H_{13}N_4O$ $[M+H]^+$: 217.1084, found 217.1089.



3a-azido-5-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3c)

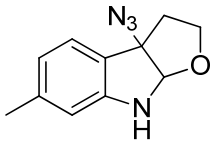
85% yield;

colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (s, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 5.53 (d, *J* = 2.6 Hz, 1H), 4.58 (s, 1H), 4.09 – 4.02 (m, 1H), 3.68 (td, *J* = 9.3, 6.4 Hz, 1H), 2.41 – 2.35 (m, 2H), 2.30 (s, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.43, 131.27, 129.26, 126.15, 124.68, 109.79, 98.41, 78.11, 67.43, 39.39, 20.86;

IR: ν_{max} = 3357, 2947, 2872, 2100, 1619, 1497, 1257, 1044, 954, 812 cm^{-1}; HRMS (ESI) m/z calcd for $C_{11}H_{13}N_4O$ $[M+H]^+$: 217.1084, found 217.1087.



3a-azido-6-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3d)

98% yield;

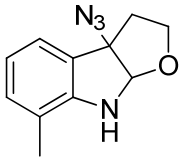
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.49 (s, 1H), 5.51 (d, *J* = 2.3 Hz, 1H), 4.67 (s, 1H), 4.07 – 4.01 (m, 1H), 3.67 (td, *J* = 9.2, 6.3 Hz, 1H), 2.39 – 2.33 (m, 2H), 2.29 (s, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.01, 141.03, 123.98, 123.00, 120.57, 110.42, 98.33, 77.90, 67.49, 39.50, 21.71;

IR: ν_{max} = 3356, 2924, 2101, 1619, 1463, 1313, 1249, 1044, 802 cm^{-1};

HRMS (ESI) m/z calcd for $C_{11}H_{13}N_4O$ $[M+H]^+$: 217.1084, found 217.1088.



3a-azido-7-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3e)

70% yield;

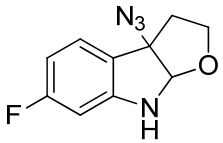
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 5.56 (d, *J* = 2.7 Hz, 1H), 4.55 (s, 1H), 4.09 – 4.03 (m, 1H), 3.72 – 3.64 (m, 1H), 2.42 – 2.37 (m, 2H), 2.17 (s, 3H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.34, 131.45, 125.28, 121.64, 119.92, 119.30, 98.05, 78.46, 67.46, 39.53, 16.65;

IR: ν_{max} = 3375, 2924, 2373, 1591, 1460, 1119, 782 cm^{-1};

HRMS (ESI) m/z calcd for $C_{11}H_{13}N_4O$ $[M+H]^+$: 217.1084, found 217.1089.



3a-azido-6-fluoro-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3f)

89% yield;

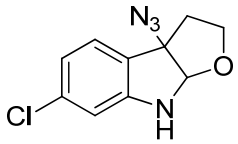
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 8.3, 5.5 Hz, 1H), 6.56 – 6.49 (m, 1H), 6.36 (dd, *J* = 9.6, 2.3 Hz, 1H), 5.56 (d, *J* = 2.1 Hz, 1H), 4.81 (s, 1H), 4.11 – 4.04 (m, 1H), 3.72 – 3.64 (m, 1H), 2.42 – 2.30 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.95 (*J* = 244.5 Hz), 151.27 (*J* = 12.75 Hz), 125.36 (*J* = 11.25 Hz), 121.41 (*J* = 2.25 Hz), 106.23 (*J* = 23.25 Hz), 98.51, 97.17 (*J* = 26.25 Hz), 77.35, 67.58, 39.55; ^{19}F NMR (282 MHz, $CDCl_3$) δ -110.66;

IR: ν_{max} = 3353, 2927, 2368, 2102, 1620, 1464, 1259, 1147, 1043, 952, 838 cm^{-1};

HRMS (ESI) m/z calcd for $C_{10}H_{10}FN_4O$ $[M+H]^+$: 221.0833, found 221.0836.



3a-azido-6-chloro-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3g)

94% yield;

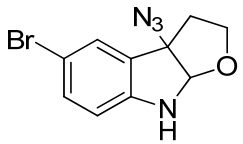
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.0 Hz, 1H), 6.81 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.65 (d, *J* = 1.8 Hz, 1H), 5.55 (s, 1H), 4.80 (s, 1H), 4.10 – 4.04 (m, 1H), 3.71 – 3.63 (m, 1H), 2.42 – 2.29 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.71, 136.47, 125.15, 124.37, 119.58, 109.67, 98.24, 67.51, 39.48;

IR: ν_{max} = 3363, 2951, 2878, 2102, 1608, 1485, 1311, 1245, 1042, 910 cm^{-1};

HRMS (ESI) m/z calcd for $C_{10}H_{10}ClN_4O$ $[M+H]^+$: 237.0538, found 237.0541.



3a-azido-5-bromo-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3h)

42% yield;

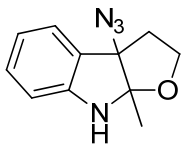
colorless gummy liquid;

^{1}H NMR (300 MHz, CDCl3) δ 7.37 (d, *J* = 2.0 Hz, 1H), 7.29 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.56 (d, *J* = 2.3 Hz, 1H), 4.73 (s, 1H), 4.11 – 4.05 (m, 1H), 3.72 – 3.64 (m, 1H), 2.42 – 2.34 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.63, 133.46, 128.15, 127.30, 111.03, 98.21, 77.70, 67.44, 39.36;

IR: ν_{max} = 3359, 2929, 2100, 1605, 1479, 1261, 1042, 812, 748 cm^{-1};

HRMS (ESI) m/z calcd for $C_{10}H_{10}BrN_4O$ $[M+H]^+$: 281.0032, found 281.0034.



3a-azido-8a-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3i)

41% yield;

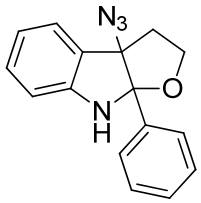
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.4 Hz, 1H), 7.18 (td, *J* = 7.7, 1.0 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 7.9 Hz, 1H), 4.46 (s, 1H), 3.99 – 3.93 (m, 1H), 3.61 – 3.53 (m, 1H), 2.40 – 2.33 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.96, 130.56, 126.02, 124.48, 119.44, 109.39, 103.03, 77.97, 65.60, 39.64, 22.33;

IR: ν_{max} = 3347, 2925, 2374, 2100, 1610, 1467, 1261, 1111, 746 cm^{-1};

HRMS (ESI) m/z calcd for $C_{11}H_{13}N_4O$ $[M+H]^+$: 217.1084, found 217.1090.



3a-azido-8a-phenyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (3j)

80% yield;

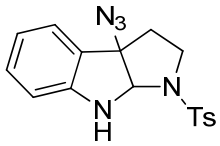
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.45 – 7.38 (m, 3H), 7.27 – 7.22 (m, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 4.79 (s, 1H), 4.30 – 4.24 (m, 1H), 3.83 – 3.75 (m, 1H), 2.42 (td, *J* = 5.2, 1.7 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.63, 139.10, 130.72, 128.87, 128.22, 127.15, 125.03, 124.71, 119.61, 109.14, 105.26, 79.97, 66.90, 39.02;

IR: ν_{max} = 3369, 2924, 2374, 2101, 1603, 1247, 1118, 746 cm^{-1};

HRMS (ESI) m/z calcd for $C_{16}H_{15}N_4O$ $[M+H]^+$: 279.1240, found 279.1247.



3a-azido-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3k)

78% yield;

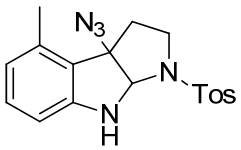
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.19 (m, 2H), 6.85 (td, *J* = 7.5, 0.7 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 5.21 (d, *J* = 1.0 Hz, 1H), 5.03 (s, 1H), 3.48 – 3.40 (m, 1H), 3.22 (td, *J* = 10.2, 6.1 Hz, 1H), 2.44 (s, 3H), 2.34 (dq, *J* = 12.6, 3.0 Hz, 1H), 2.10 – 2.00 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.47, 144.08, 135.12, 131.19, 130.00, 127.23, 124.58, 123.67, 119.86, 110.78, 83.05, 47.30, 35.89, 21.60;

IR: ν_{max} = 3387, 2925, 2373, 2102, 1611, 1470, 1246, 1160, 818, 749 cm^{-1};

HRMS (ESI) m/z calcd for $C_{17}H_{18}N_5O_2S$ $[M+H]^+$: 356.1176, found 356.1182.



3a-azido-4-methyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3l)

88% yield;

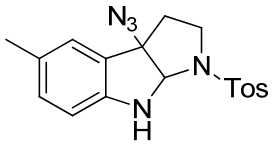
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.9 Hz, 1H), 5.27 (s, 1H), 4.98 (s, 1H), 3.33 – 3.28 (m, 2H), 2.45 (s, 3H), 2.39 (dd, *J* = 12.4, 6.3 Hz, 1H), 2.32 (s, 3H), 2.10 – 2.00 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.54, 144.14, 135.15, 134.57, 131.02, 129.96, 127.49, 122.45, 121.77, 108.07, 83.71, 78.86, 46.97, 35.59, 21.61, 17.90;

IR: ν_{max} = 3385, 2925, 2374, 2100, 1599, 1464, 1343, 1240, 1161, 779 cm^{-1};

HRMS (ESI) m/z calcd for $C_{18}H_{20}N_5O_2S$ $[M+H]^+$: 370.1332, found 370.1338.



3a-azido-5-methyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3m)

81% yield;

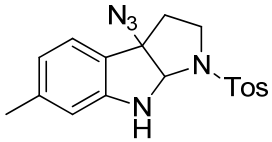
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 1H), 7.00 (s, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 4.87 (s, 1H), 3.48 – 3.40 (m, 1H), 3.22 (td, *J* = 10.2, 6.1 Hz, 1H), 2.45 (s, 3H), 2.36 – 2.31 (m, 1H), 2.29 (s, 3H), 2.08 – 1.98 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.21, 144.01, 135.19, 131.78, 129.96, 129.42, 127.24, 124.78, 124.01, 110.76, 83.34, 77.53, 47.30, 35.76, 21.59, 20.86;

IR: v_{max} = 3387, 2924, 2103, 1619, 1496, 1342, 1245, 1161, 1094, 1046, 815 cm^{-1};

HRMS (ESI) m/z calcd for $C_{18}H_{20}N_5O_2S$ $[M+H]^+$: 370.1332, found 370.1338.



3a-azido-6-methyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3n)

95% yield;

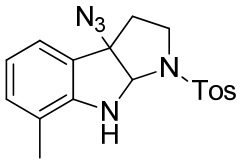
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.55 (s, 1H), 5.19 (s, 1H), 4.95 (s, 1H), 3.47-3.40 (m, 1H), 3.21 (td, *J* = 10.3, 6.1 Hz, 1H), 2.44 (s, 3H), 2.34 – 2.27 (m, 4H), 2.07 – 1.96 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.78, 144.02, 141.59, 135.22, 129.98, 127.22, 123.36, 121.73, 120.78, 111.46, 83.31, 77.37, 47.33, 35.88, 21.73, 21.58;

IR: v_{max} = 3387, 2925, 2373, 2104, 1619, 1461, 1243, 1160, 809 cm^{-1};

HRMS (ESI) m/z calcd for $C_{18}H_{20}N_5O_2S$ $[M+H]^+$: 370.1332, found 370.1341.



3a-azido-7-methyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3o)

47% yield;

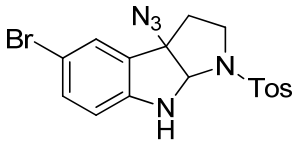
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.80 (t, *J* = 7.5 Hz, 1H), 5.26 (s, 1H), 4.78 (s, 1H), 3.50 – 3.42 (m, 1H), 3.21 (td, *J* = 10.1, 6.1 Hz, 1H), 2.45 (s, 3H), 2.33 (dq, *J* = 12.3, 3.0 Hz, 1H), 2.16 (s, 3H), 2.12 –2.02 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.10, 144.04, 135.30, 131.93, 129.95, 127.25, 124.03, 121.00, 120.30, 120.05, 82.97, 77.98, 47.32, 36.10, 21.59, 16.60;

IR: ν_{max} = 3379, 2924, 2103, 1602, 1466, 1342, 1244, 1160, 1093, 1053, 813, 749 cm^{-1};

HRMS (ESI) m/z calcd for $C_{18}H_{20}N_5O_2S$ $[M+H]^+$: 370.1332, found 370.1339.



3a-azido-5-bromo-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3p)

51% yield;

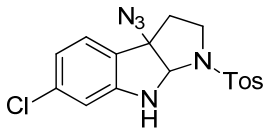
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.30 (m, 4H), 6.62 (d, *J* = 8.3 Hz, 1H), 5.22 (s, 1H), 5.05 (s, 1H), 3.47 – 3.39 (m, 1H), 3.24 (td, *J* = 10.1, 6.1 Hz, 1H), 2.46 (s, 3H), 2.30 (dq, *J* = 12.6, 3.0 Hz, 1H), 2.09 – 1.99 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.39, 144.26, 134.90, 133.96, 130.05, 127.22, 126.91, 126.69, 112.16, 111.29, 83.22, 77.10, 47.17, 35.82, 21.61;

IR: ν_{max} = 3383, 2925, 2100, 1601, 1477, 1339, 1246, 1160, 1044, 812, 753 cm^{-1};

HRMS (ESI) m/z calcd for $C_{17}H_{17}BrN_5O_2S$ $[M+H]^+$: 434.0281, found 434.0289.



3a-azido-6-chloro-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (3q)

79% yield;

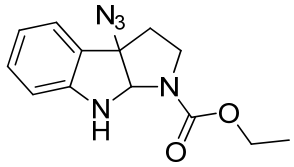
colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.81 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.70 (d, *J* = 1.6 Hz, 1H), 5.23 (s, 1H), 5.13 (s, 1H), 3.47 – 3.40 (m, 1H), 3.22 (td, *J* = 10.1, 6.1 Hz, 1H), 2.45 (s, 3H), 2.30 (dq, *J* = 12.9, 3.0 Hz, 1H), 2.10 – 2.00 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 150.48, 144.25, 136.97, 134.99, 130.05, 127.21, 124.55, 123.21, 119.84, 110.83, 83.26, 76.88, 47.22, 35.95, 21.60;

IR: ν_{max} = 3385, 2925, 2103, 1607, 1485, 1449, 1340, 1243, 1160, 1044, 812 cm^{-1};

HRMS (ESI) m/z calcd for $C_{17}H_{17}ClN_5O_2S$ $[M+H]^+$: 390.0786, found 390.0783.



ethyl 3a-azido-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)- carboxylate (3r)

93% yield;

colorless gummy liquid;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (m, 2H), 6.86 (m, 1H), 6.71 (s, 0.53H), 6.68 (s, 0.44H), 5.34 (s, 0.6H), 5.31 (s, 0.4H), 5.25 (s, 0.56H), 4.82 (s, 0.39H), 4.26 – 4.08 (m, 2H), 3.84 – 3.78 (m, 0.43H), 3.74 – 3.67 (m, 0.61H), 3.18 – 3.09 (m, 1H), 2.47 – 2.30 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 1.3H), 1.25 (t, *J* = 7.1 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.02, (154.12), 149.82, (149.49), 130.99, 124.89, 123.80, (123.86), 119.43, (119.74), 110.49, (110.32), 80.69, (80.25), 76.21, (77.30), 61.42, (61.68), 45.49, (45.73), 35.12, (35.00), 14.64, (14.83);

IR: ν_{max} = 3355, 2926, 2374, 2101, 1689, 1611, 1423, 1199, 1116, 746 cm^{-1};

HRMS (ESI) m/z calcd for $C_{13}H_{16}N_5O_2$ $[M+H]^+$: 274.1299, found 274.1304.

ethyl 3a-amino-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (4)[4]

Triethylamine (315 μL, 2.34 mmol, 6.23 equiv) was added via syringe to a solution of azide **3r** (98 mg, 0.359 mmol, 1 equiv) and dithiothreitol (328 mg, 2.13 mmol, 5.93 equiv) in methanol (4 mL) at room temperature. After 10 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with aqueous saturated sodium bicarbonate solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous sodium sulfate, and filtered. The volatiles were removed under reduced pressure and the residue was purified by flash column chromatography (DCM/MeOH) on silica gel to give amine **4** as a colorless liquid.

96% yield;

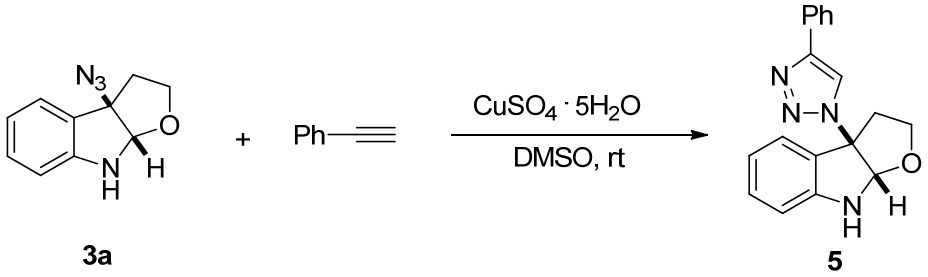
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (s, 0.48H), 7.23 (s, 0.51H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.84 – 6.78 (m, 1H), 6.65 (s, 0.54H), 6.62 (s, 0.45H), 5.15 (s, 0.55H), 5.08 (s, 0.61H), 5.06 (s, 0.41H), 4.71 (s, 0.38H), 4.25 – 4.05 (m, 2H), 3.80 – 3.64 (m, 1H), 3.17 – 3.07 (m, 1H), 2.41 – 2.32 (m, 1H), 2.27 – 2.16 (m, 1H), 2.09 (s, 2H), 1.33 (t, *J* = 7.1 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 155.32, (154.48), 149.03, (148.69), 129.46, (131.51), 123.12, 119.22, (119.47), 109.95, (109.77), 83.27, (82.92), 77.38, 69.36, (70.44), 61.19, (61.40), 45.49, (45.76), 37.58, (37.47), 14.67, (14.88);

IR: ν_{max} = 3352, 2977, 2927, 2369, 1687, 1611, 1483, 1468, 1425, 1381, 1350, 1327, 1200, 1112, 1047, 895, 746 cm^{-1};

HRMS (ESI) m/z calcd for $C_{13}H_{17}N_3O_2$ $[M+H]^+$: 248.1394, found 248.1402.

3a-(4-phenyl-1H-1,2,3-triazol-1-yl)-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (5)



3a **5**

The reaction of 3a-azido-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole **3a** (40.5 mg, 0.2 mmol), ethynylbenzene **4** (26 mg, 0.25 mmol), CuSO4·5H2O (5.0mg, 0.02 mmol) and Cu powder (56 mg, 0.8 mmol) were placed in a flame-dried Schlenk tube under air, followed by the addition of DMSO (1.0 mL).The reaction was conducted at rt for 3 h in dark place. After that, 2.5 mL water was added and the reaction was extracted by ethyl acetate. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 4: 1) to afford the product **5** as colorless solid.

85% yield;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.75 (m, 2H), 7.56 (s, 1H), 7.41 – 7.36 (m, 2H), 7.31 (dt, *J* = 5.1, 2.1 Hz, 1H), 7.28 – 7.27 (m, 1H), 7.25 – 7.24 (m, 1H), 6.88 (td, *J* = 7.5, 0.8 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 5.76 (s, 1H), 4.85 (s, 1H), 4.35 – 4.29 (m, 1H), 3.92 – 3.84 (m, 1H), 3.67 – 3.57 (m, 1H), 2.76 – 2.70 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.89, 147.85, 131.23, 130.34, 128.79, 128.22, 126.07, 125.70, 124.86, 120.16, 119.05, 110.16, 98.39, 78.48, 67.82, 38.94;

IR: ν_{max} = 3346, 2925, 2395, 1763, 1610, 1379, 1156, 1041, 825, 757 cm^{-1};

HRMS (ESI) m/z calcd for $C_{18}H_{16}N_4O$ $[M+H]^+$: 305.1397, found 305.1398.

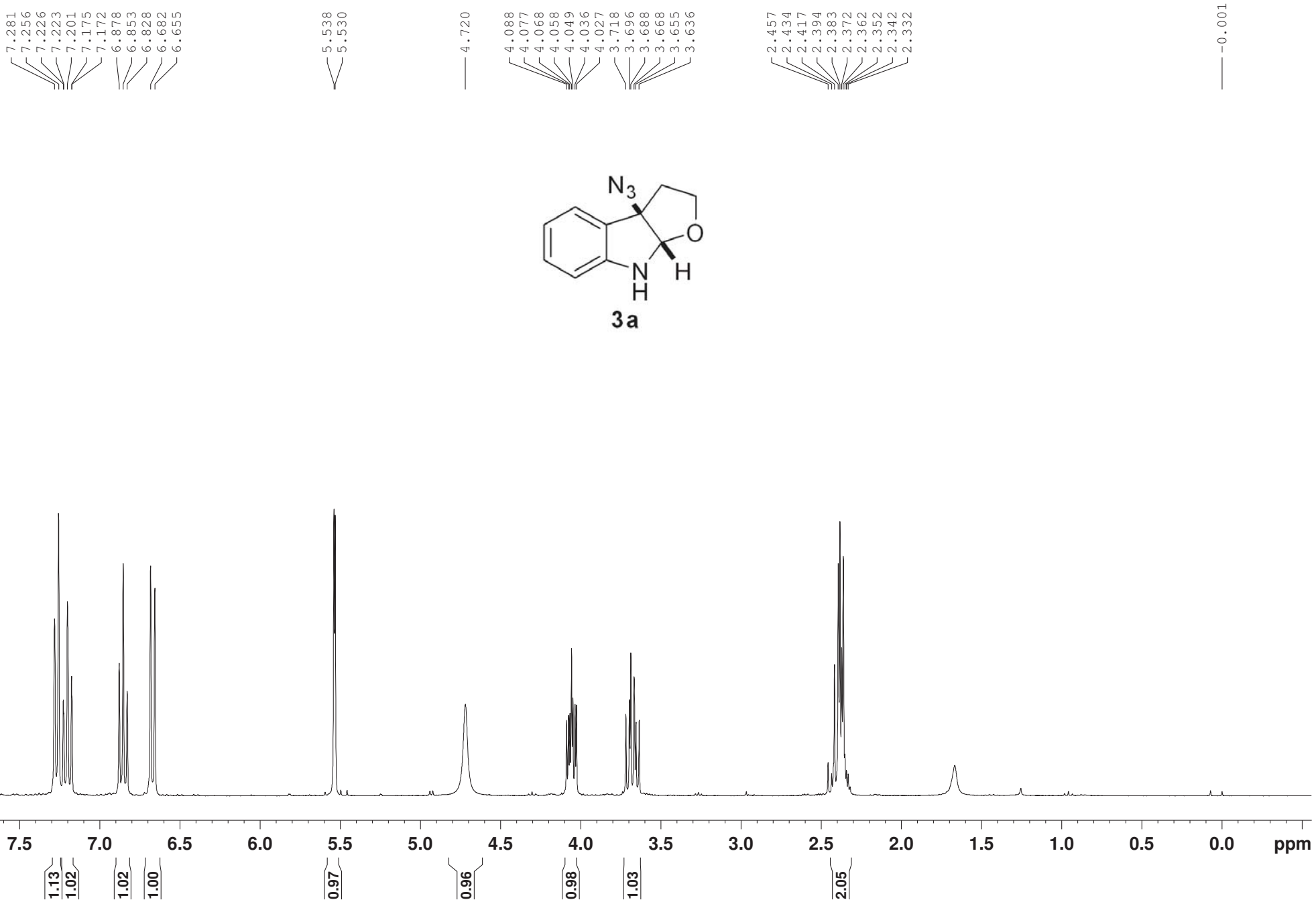
Ⅳ. References:

(1) Liu, C.; Zhang W.; Dai L.-X.; You S.-L. *Org. Lett.* 2012, *14*, 4525.

(2) (a) Hara, T.; Durell, S. R.; Myers, M. C.; Appella, D. H. *J. Am. Chem. Soc.* 2006, 128, 1995. (b) Guo, X. K.; Yang, Q.; Xu, J.; Zhang, L.; Chu, H. X.; Yu, P.; Zhu, Y. Y.; Wei, J. L.; Chen, W. L.; Zhang, Y. Z.; Zhang, X. J.; Sun, H. P.; Tang, Y. Q.; You, Q. D. *Bioorg. Med. Chem.* 2013, 21, 6466.

(3) Jenkins, P. R.; Wilson, J.; Emmerson, D.; Garcia, M. D.; Smith, M. R.; Gray, S. J.; Britton, R. G.; Mahale, S.; Chaudhuri, B. *Bioorg. Med. Chem.* 2008,16, 7728.

(4) Movassaghi, M.; Ahmad, O. K.; Lathrop S. P. *J. Am. Chem. Soc.* 2011, 133, 13002.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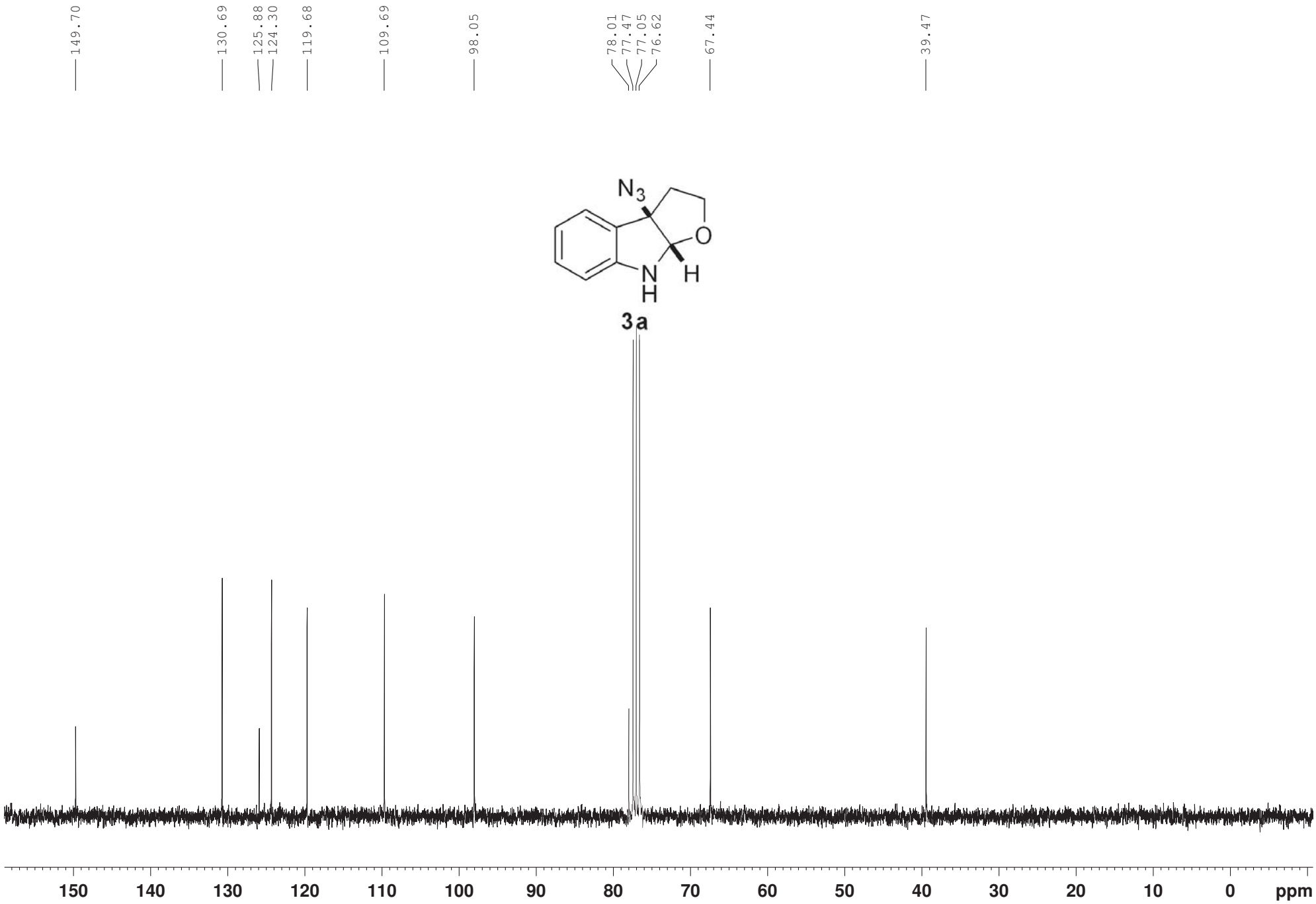
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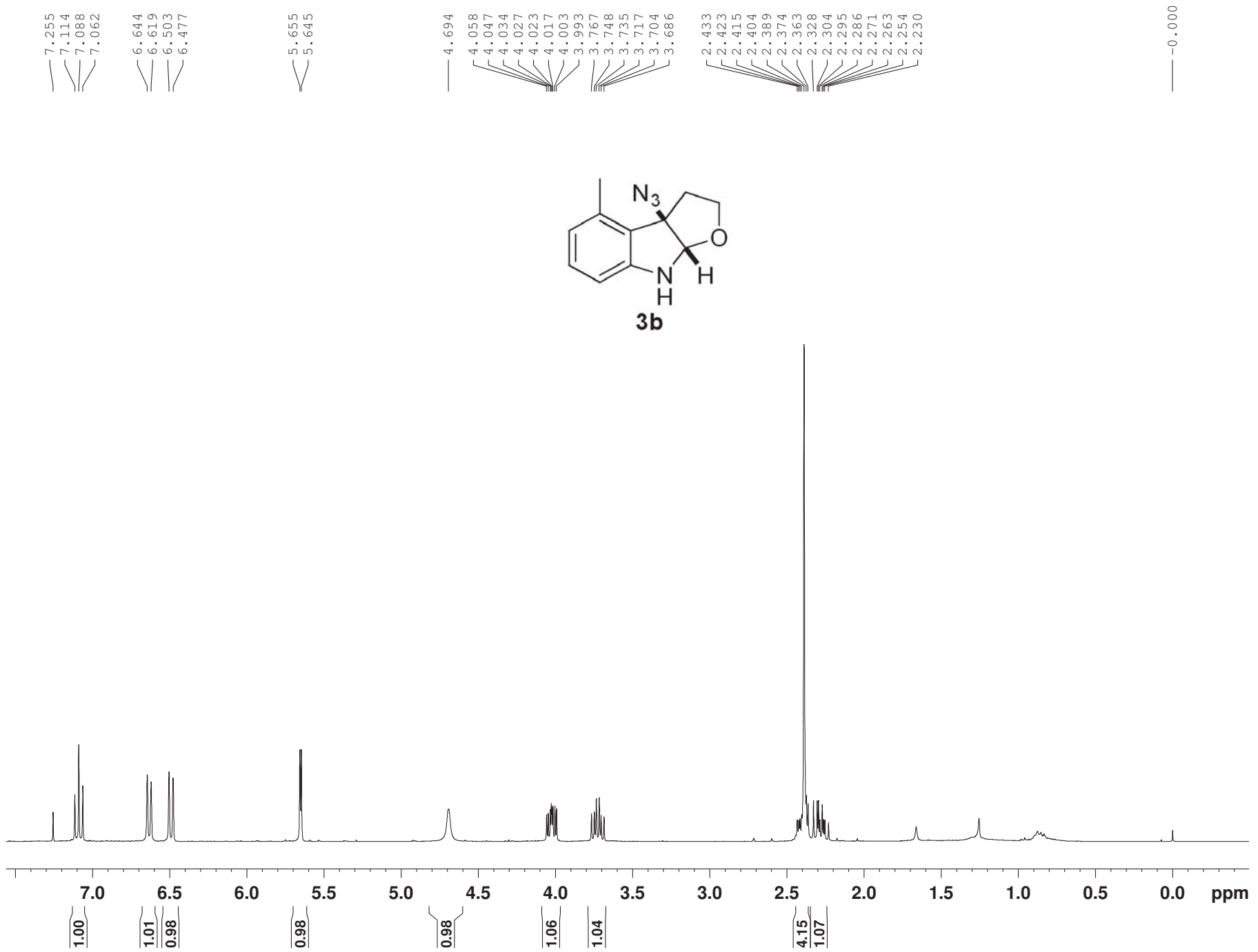
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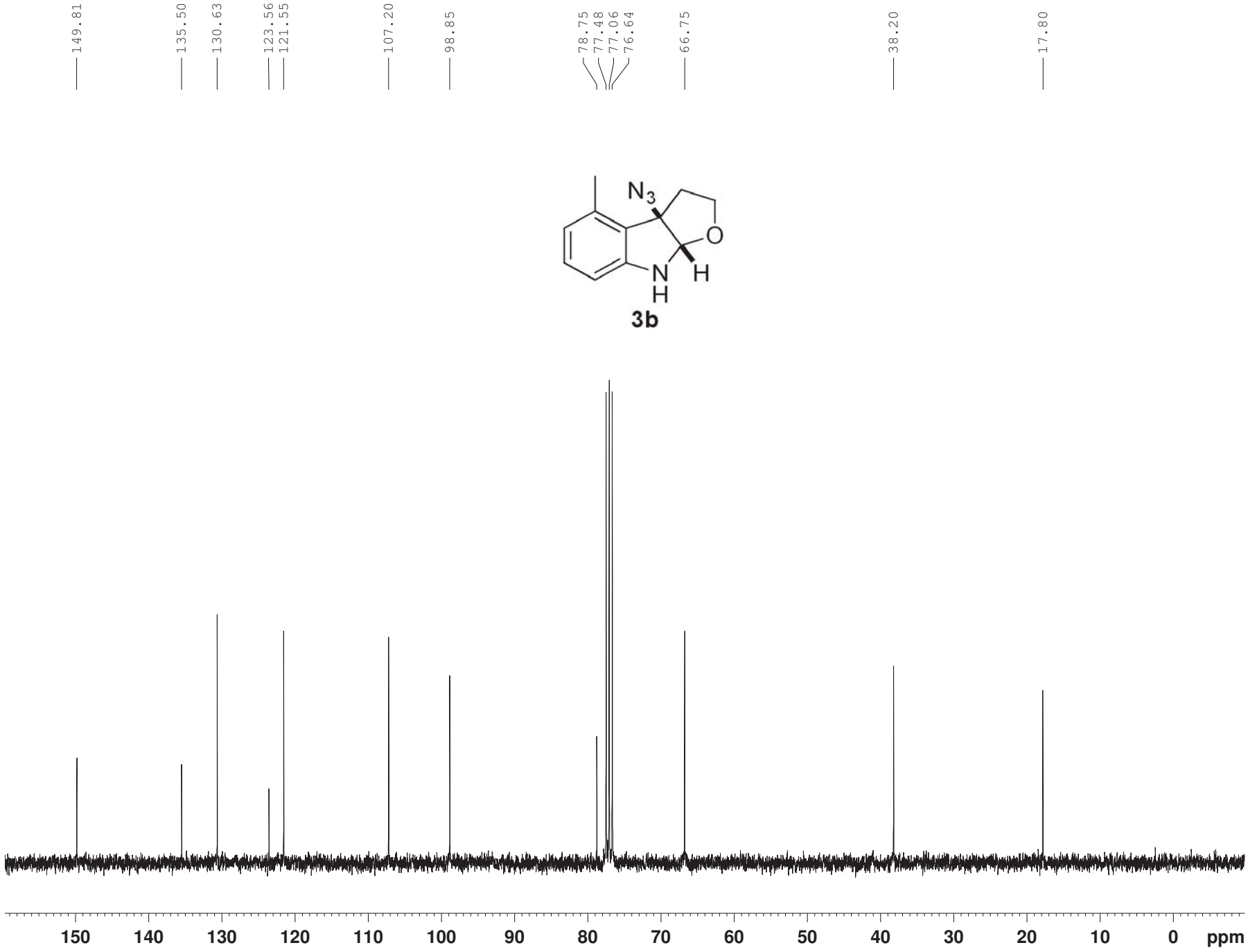
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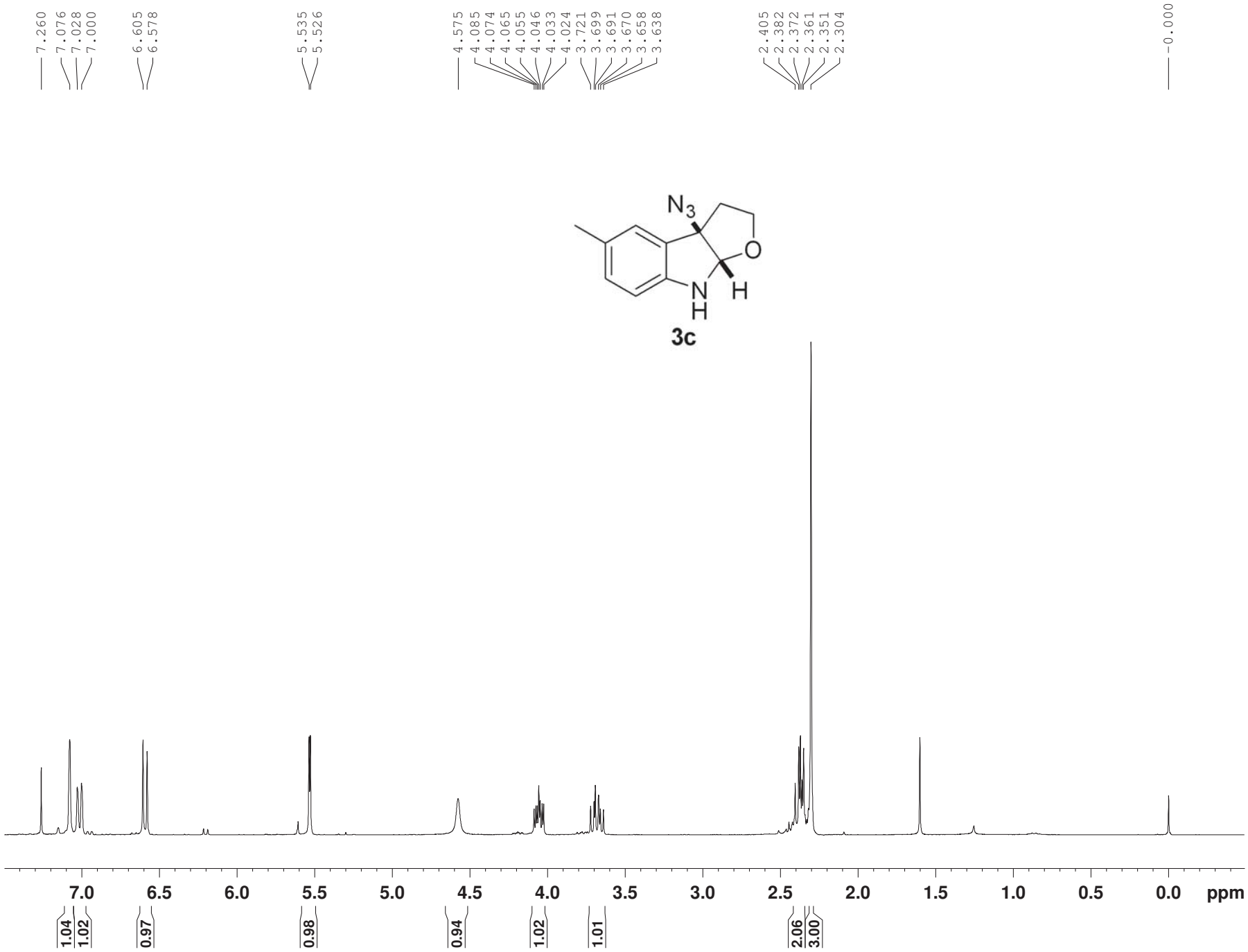
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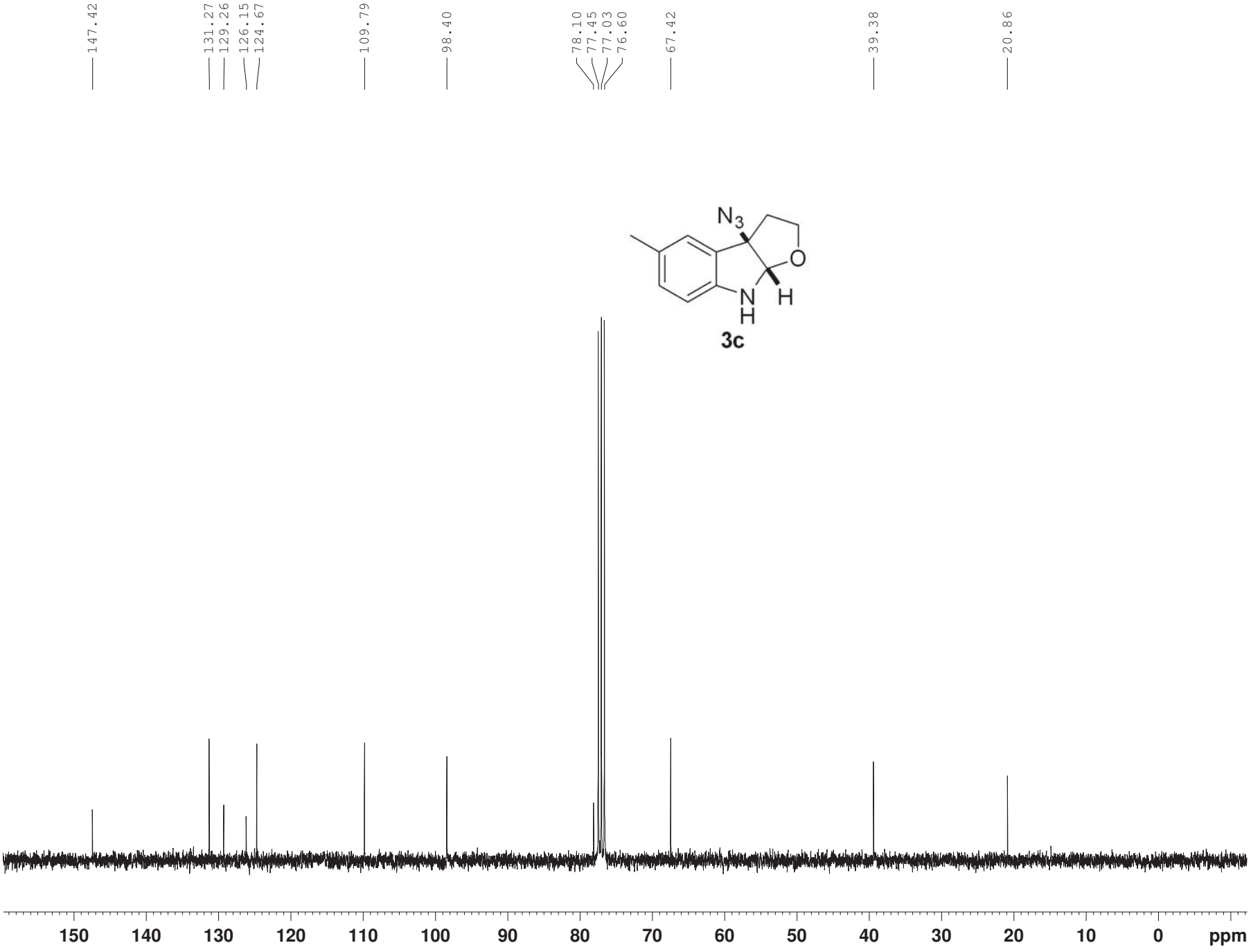
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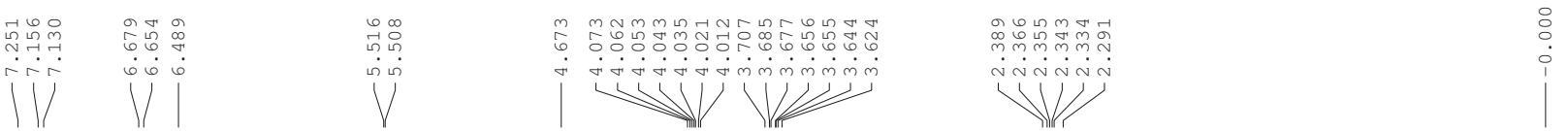
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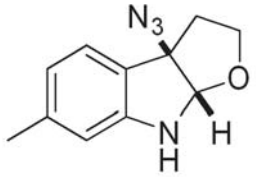
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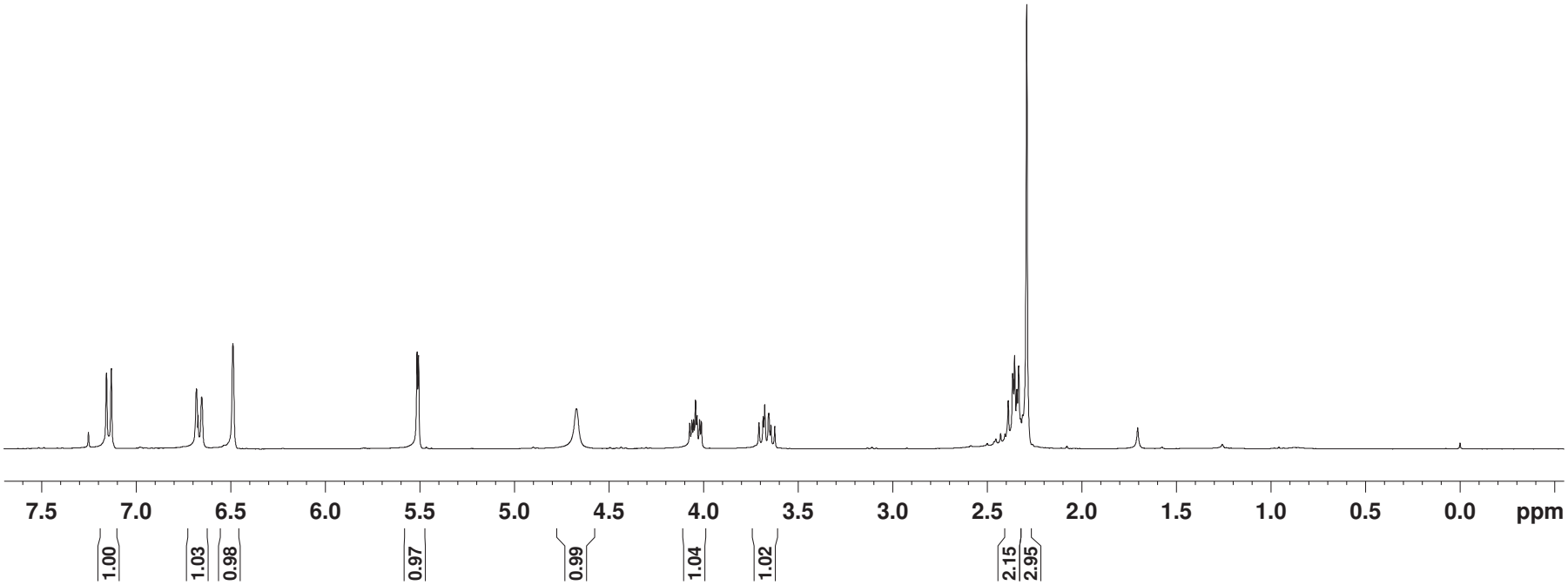
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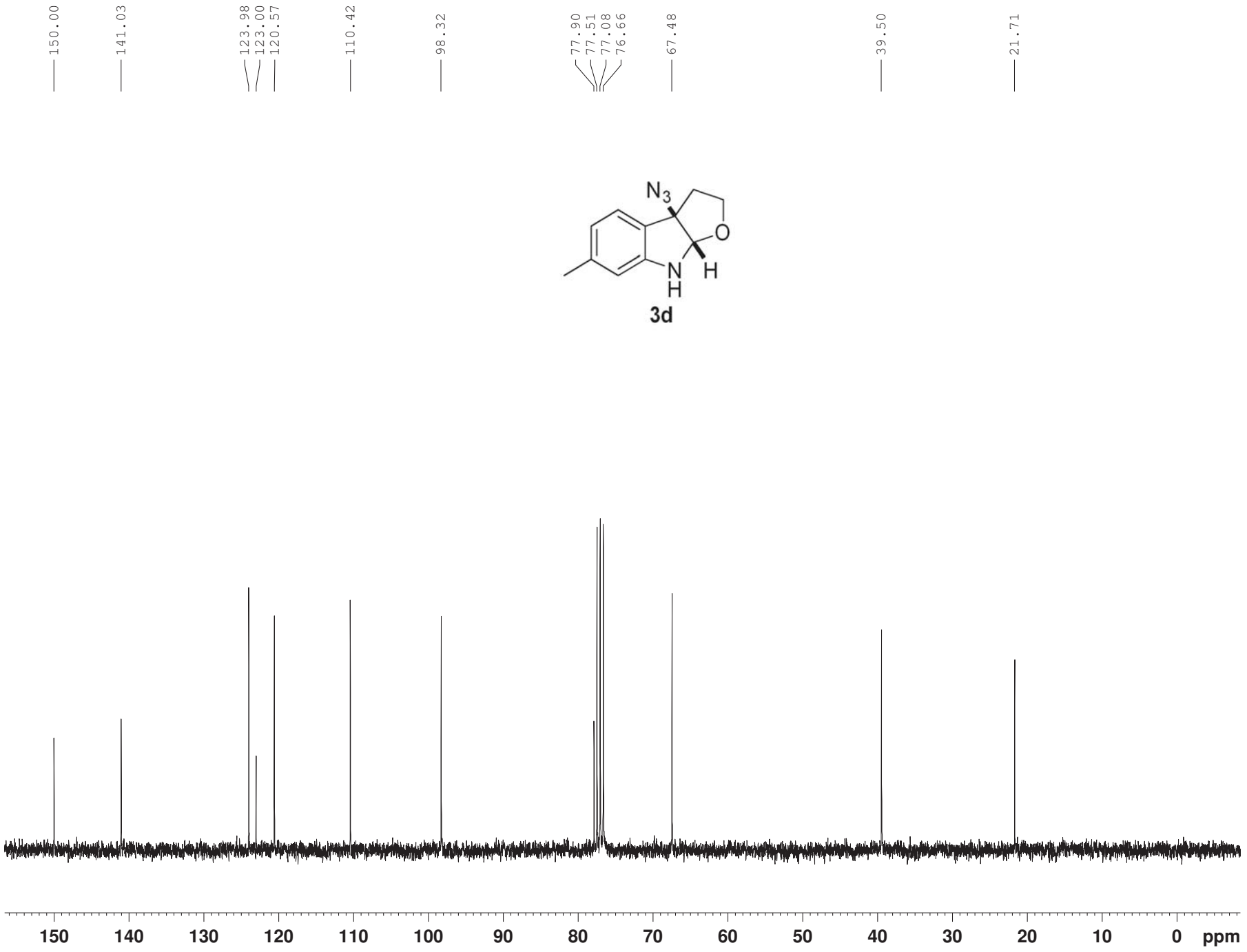
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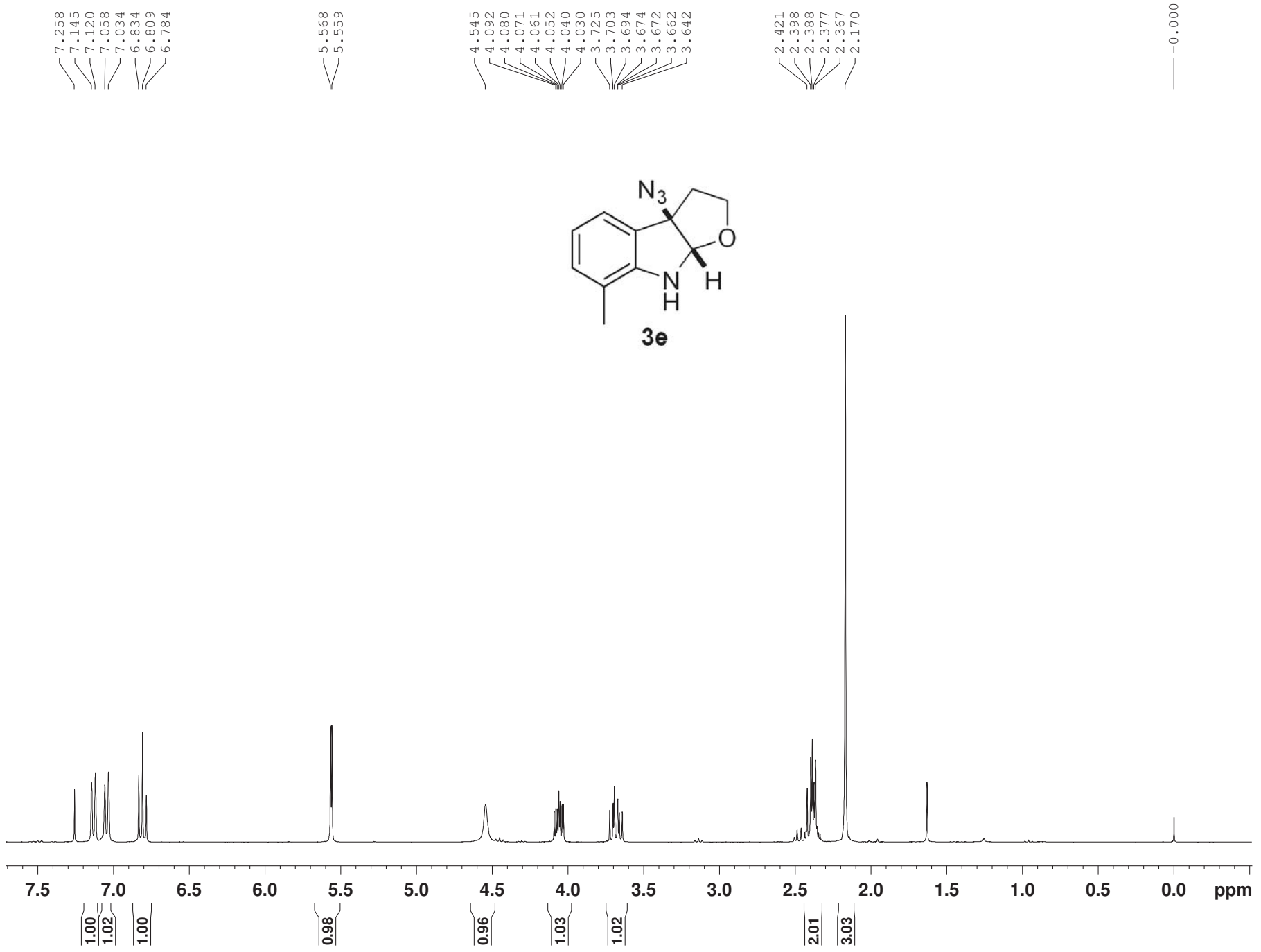
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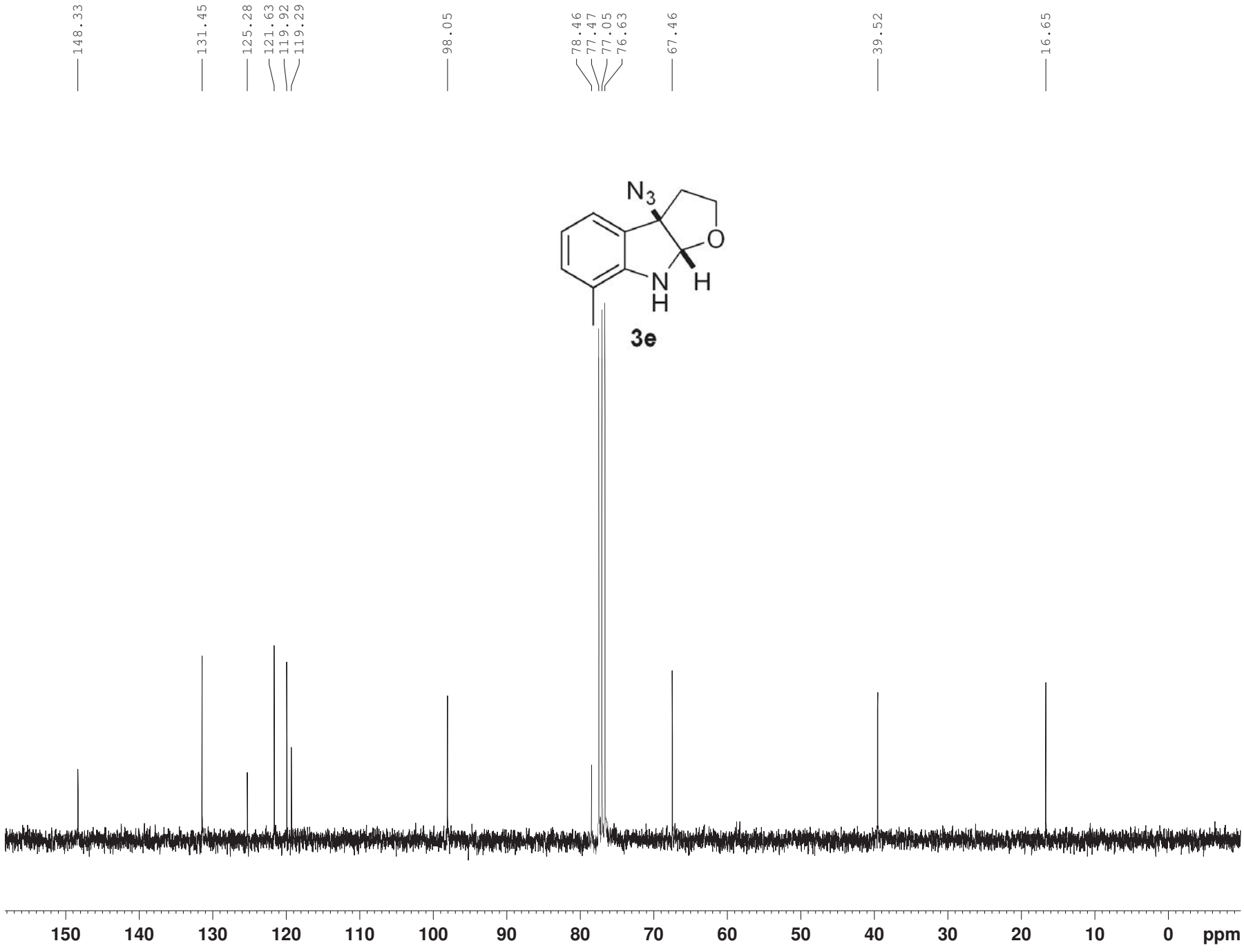
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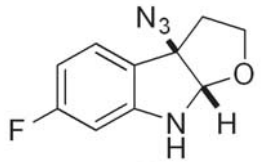
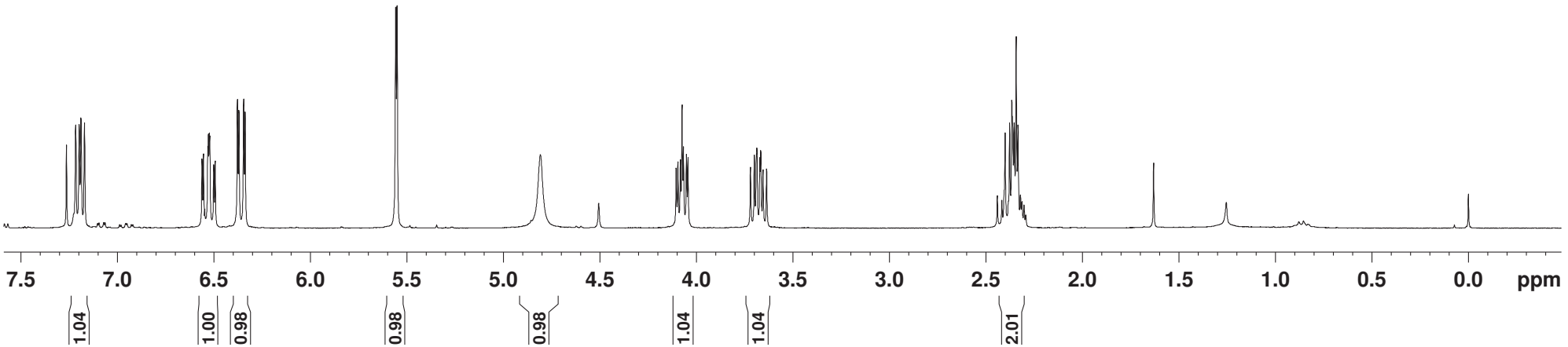
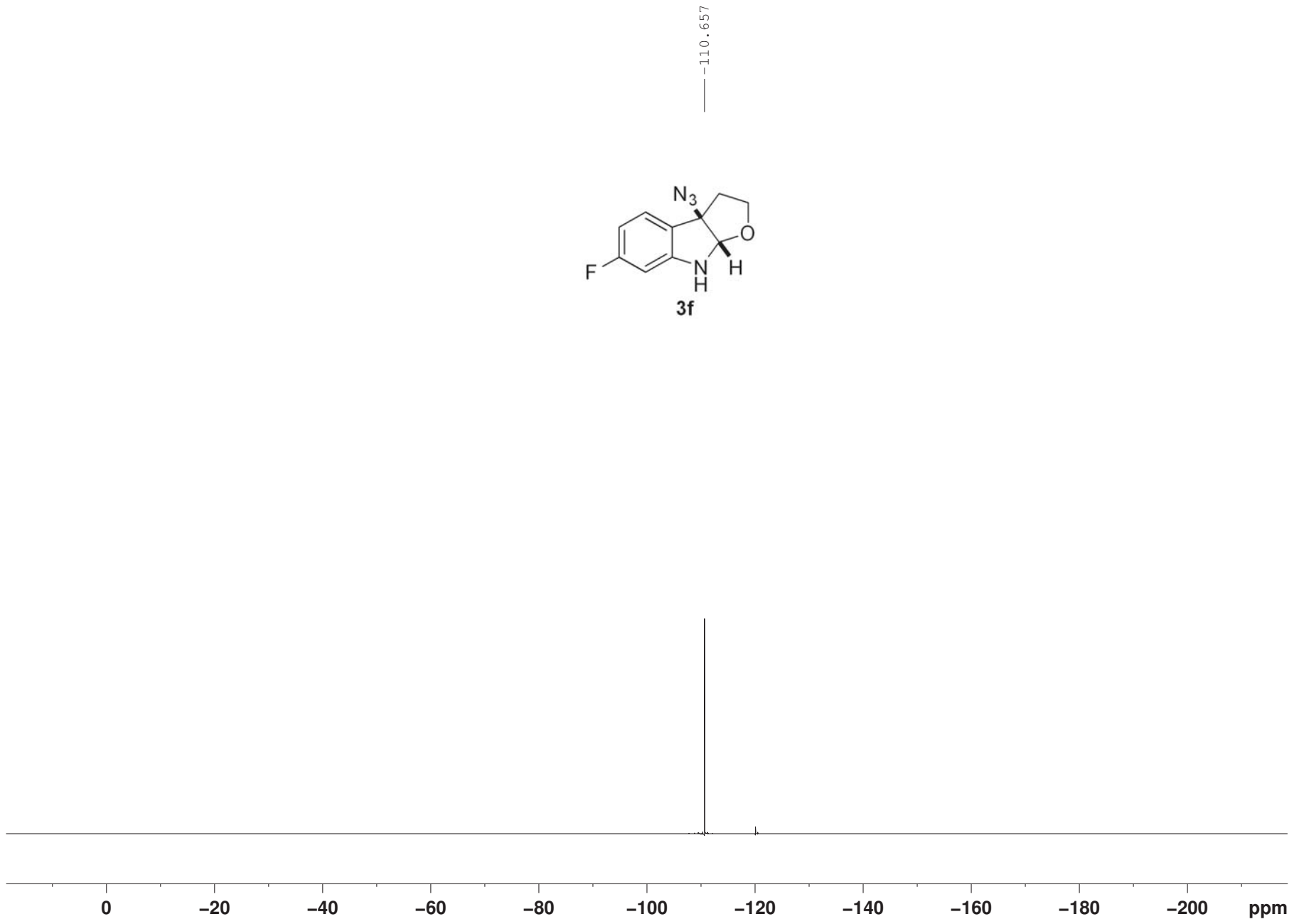


3f

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F
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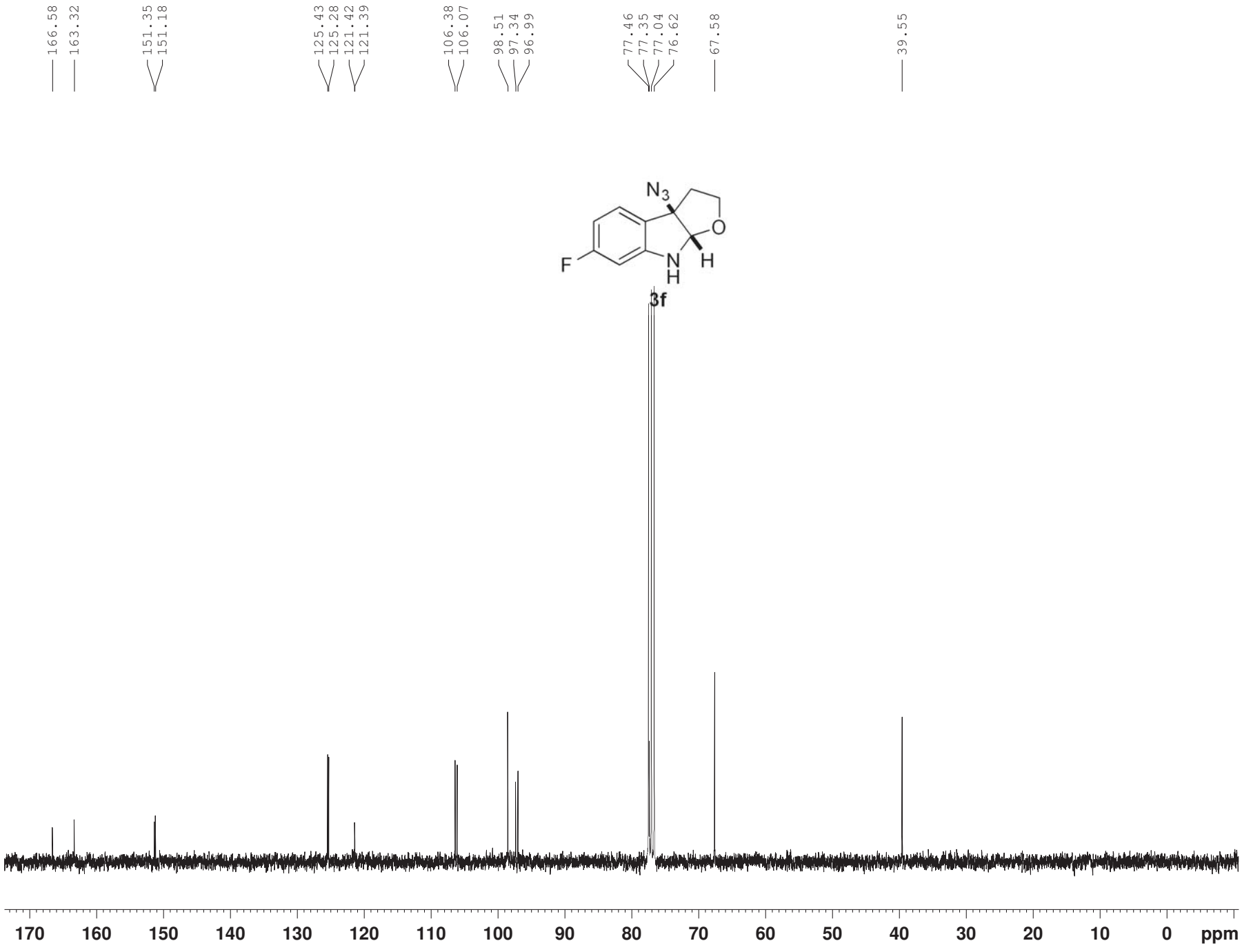
−160
−180
−200
ppm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121.39
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97.34
96.99
77.46
77.35
77.04
76.62
67.58
39.55
N3
O
F
N
H
H
3f
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140
130
120
110
100
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80
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60
50
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30
20
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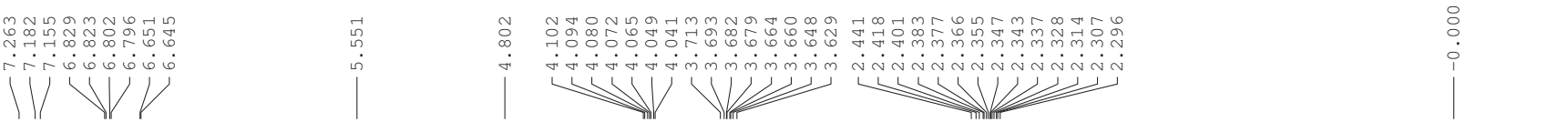
0
ppm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5.551
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4.094
4.080
4.072
4.065
4.049
4.041
3.713
3.693
3.682
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3.664
3.660
3.648
3.629
2.441
2.418
2.401
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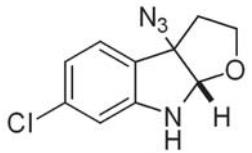
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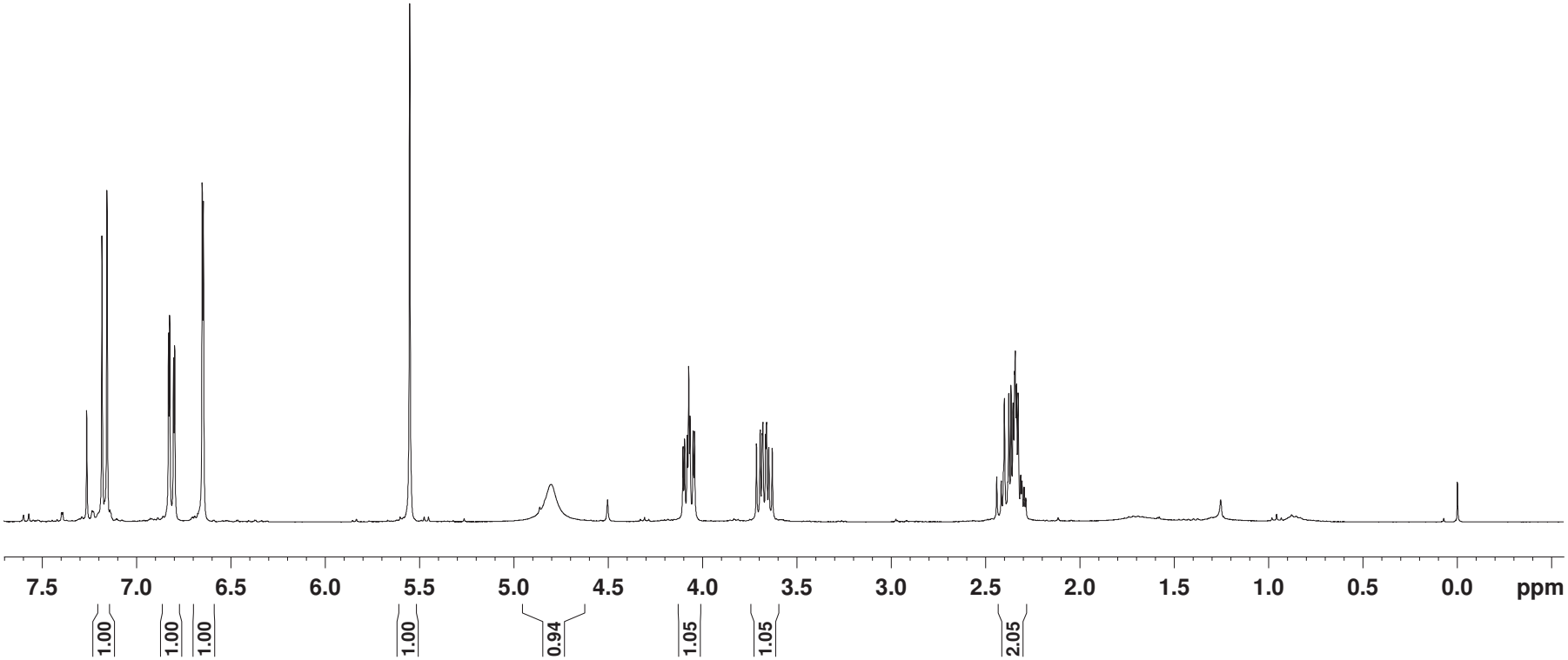
O
Cl
N
H
H

3g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4.0
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3.0
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2.0
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0.0
ppm
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1.00
1.00
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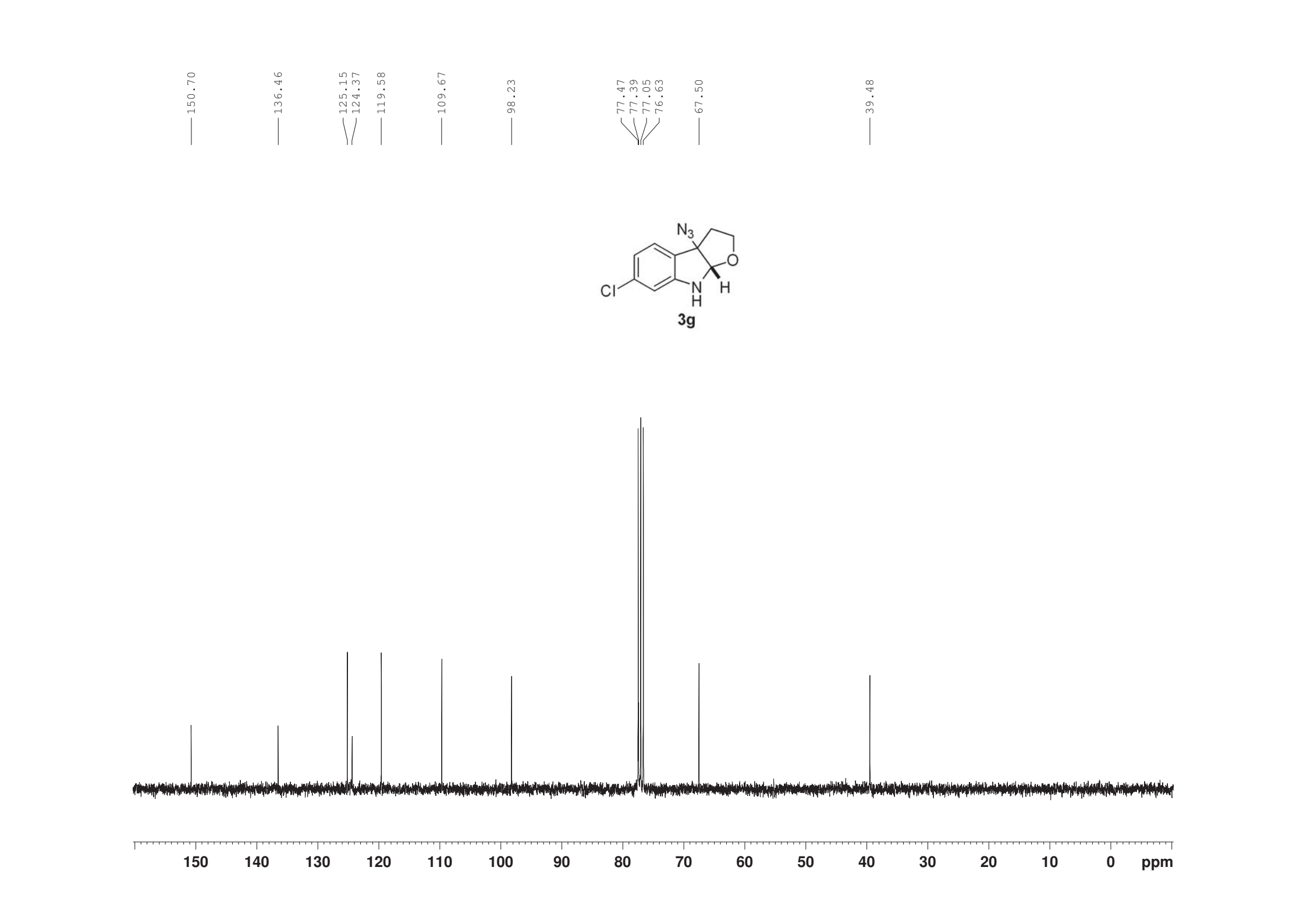
1.05
2.05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136.46
125.15
124.37
119.58
109.67
98.23
77.47
77.39
77.05
76.63
67.50
39.48
N3
O
Cl
N
H
H
3g
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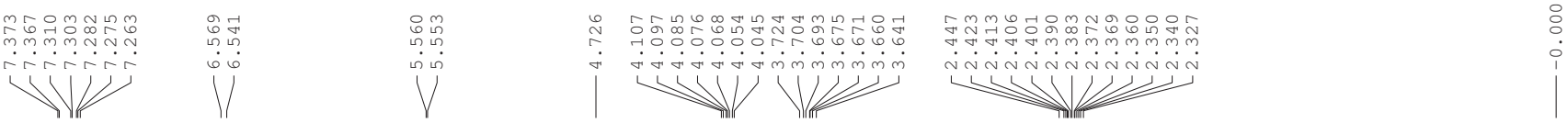
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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5.553
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4.107
4.097
4.085
4.076
4.068
4.054
4.045
3.724
3.704
3.693
3.675
3.671
3.660
3.641
2.447
2.423
2.413
2.406
2.401
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2.372
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2.340
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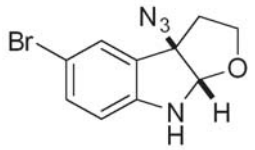
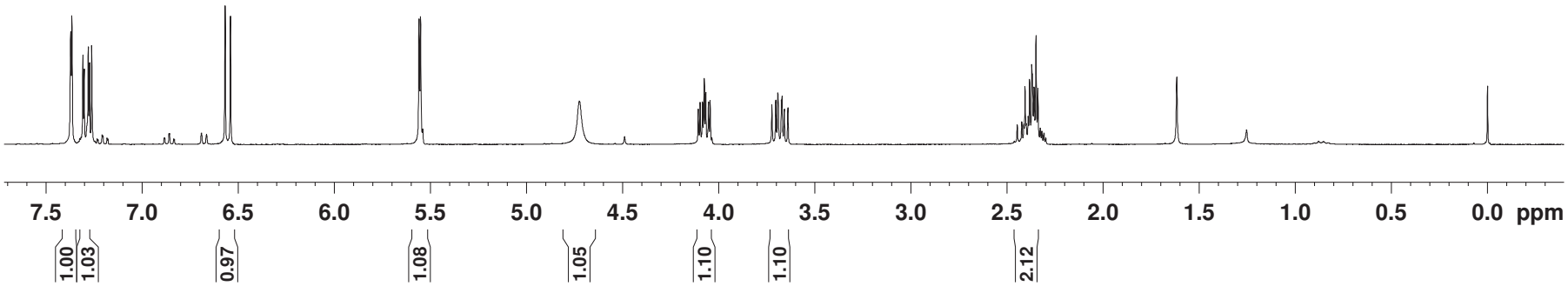

Br
N3
O
N
H
H

3h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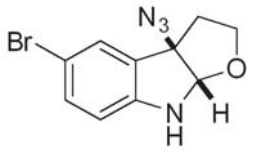
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
1.00
1.03
0.97
1.08
1.05
1.10
1.10
2.12

148.62
133.45
128.14
127.30
111.02
98.20
77.70
77.46
77.04
76.62
67.44
39.36



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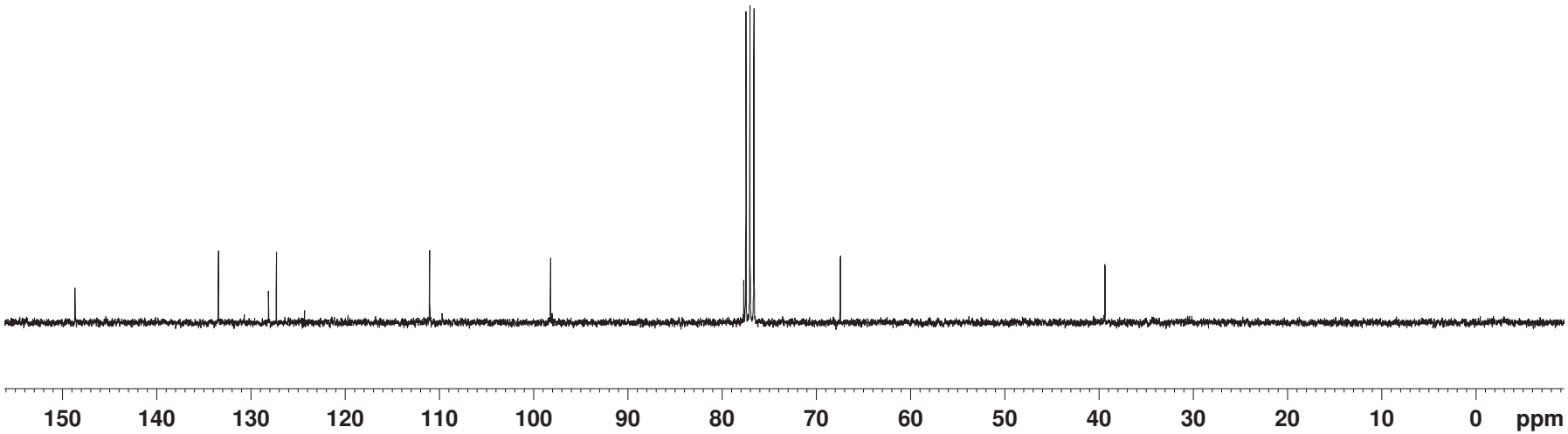

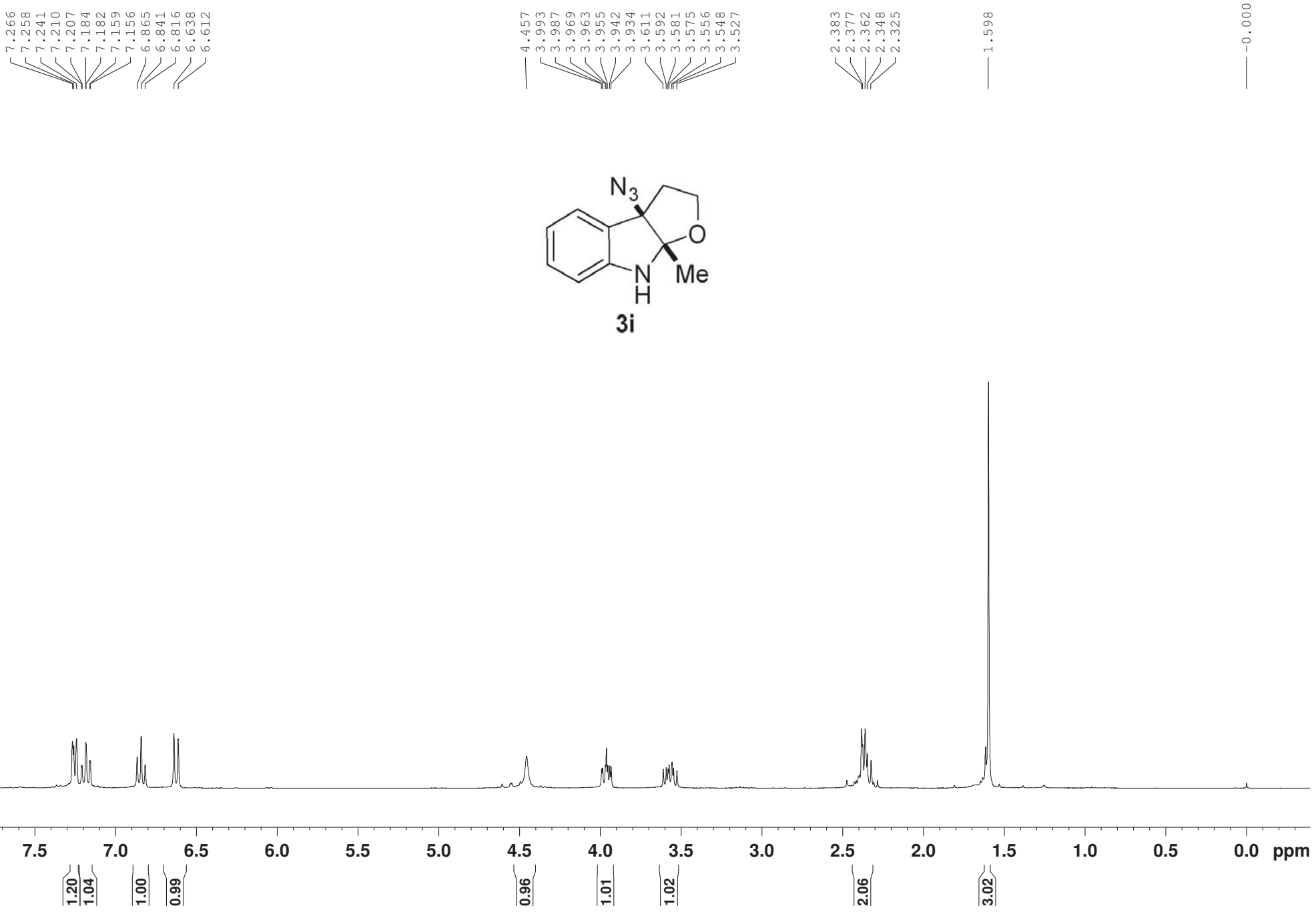
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6.841
6.816
6.638
6.612
4.457
3.993
3.987
3.969
3.963
3.955
3.942
3.934
3.611
3.592
3.581
3.575
3.556
3.548
3.527
2.383
2.377
2.362
2.348
2.325
1.598
0.000
N3
O
N
H
Me
3i
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.20
1.04
1.00
0.99
0.96
1.01
1.02
2.06
3.02

148.95
130.56
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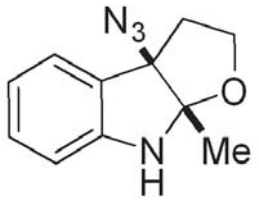
124.47
119.44
109.39
103.03
77.97
77.46
77.03
76.61
65.59
39.63
22.32



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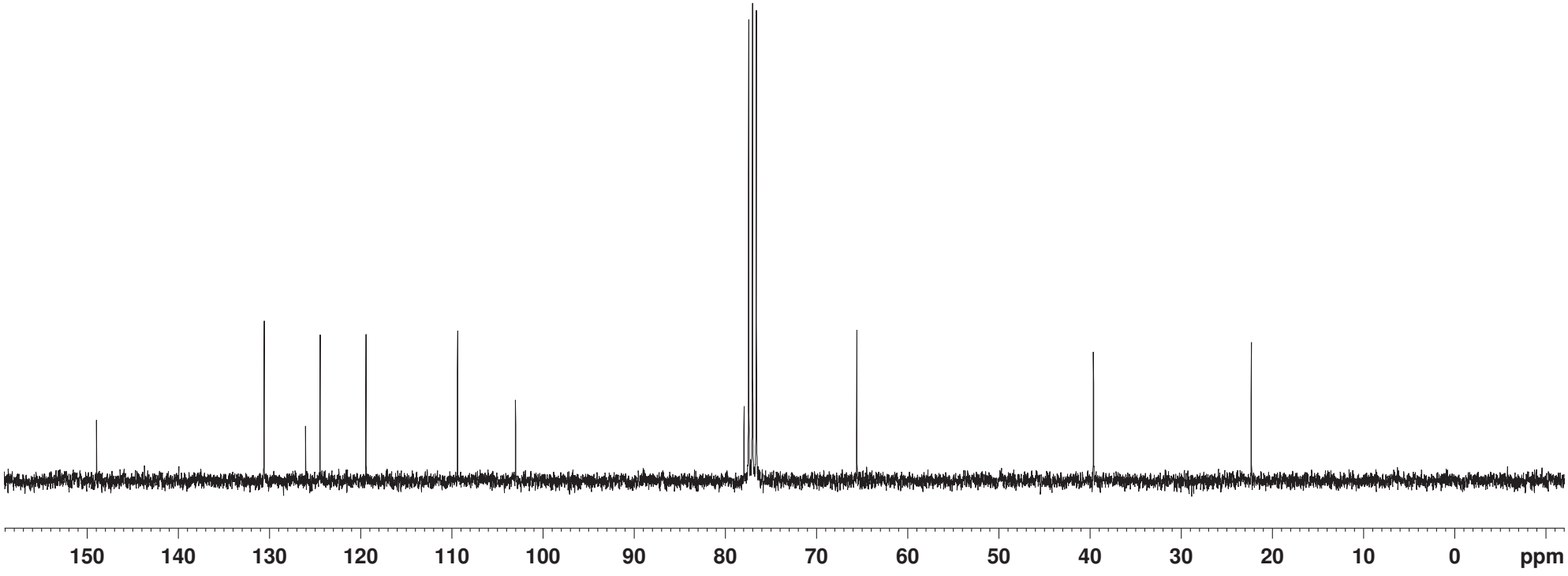

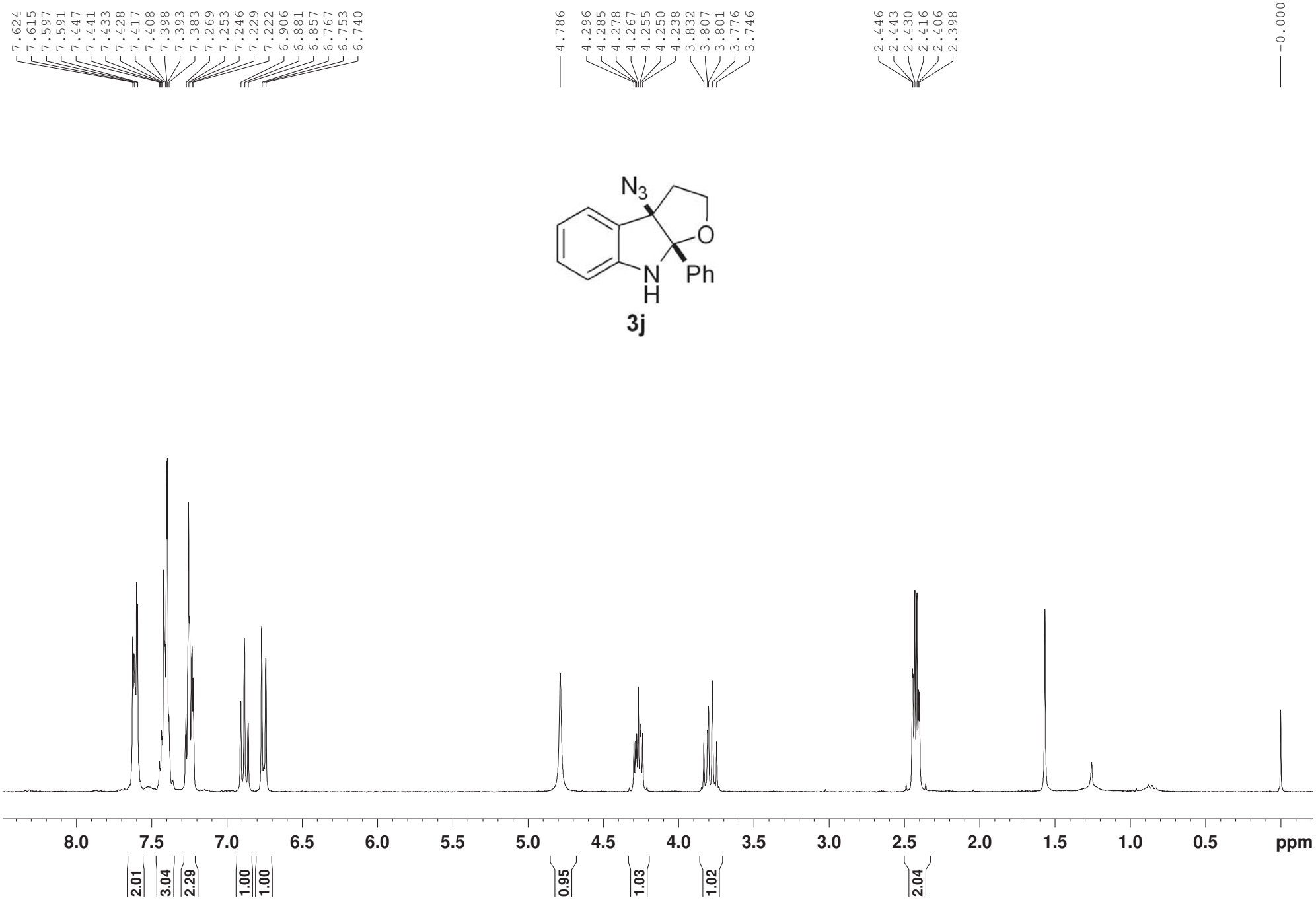
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7.398
7.393
7.383
7.269
7.253
7.246
7.229
7.222
6.906
6.881
6.857
6.767
6.753
6.740
4.786
4.296
4.285
4.278
4.267
4.255
4.250
4.238
3.832
3.807
3.801
3.776
3.746
2.446
2.443
2.430
2.416
2.406
2.398
-0.000
N3
O
N
H
Ph
3j
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.01
3.04
2.29
1.00
1.00
0.95
1.03
1.02
2.04

149.63
139.10
130.71
128.87
128.22
127.15
125.03
124.71
119.61
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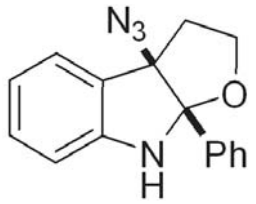
105.26
79.97
77.51
77.09
76.67
66.90
39.02



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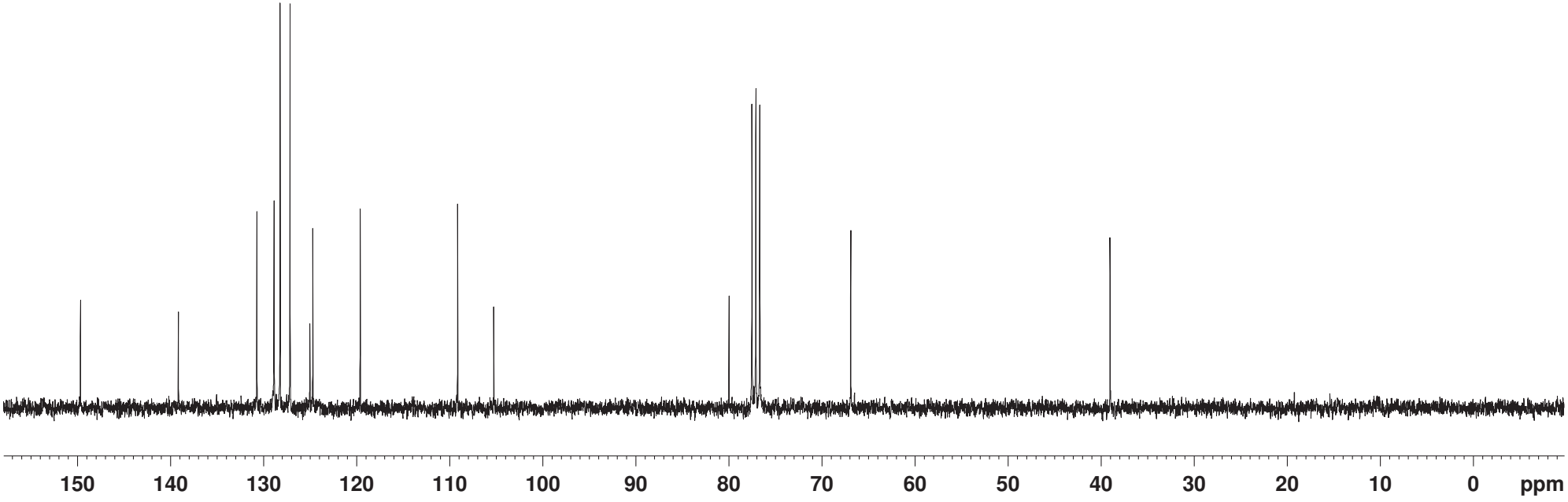

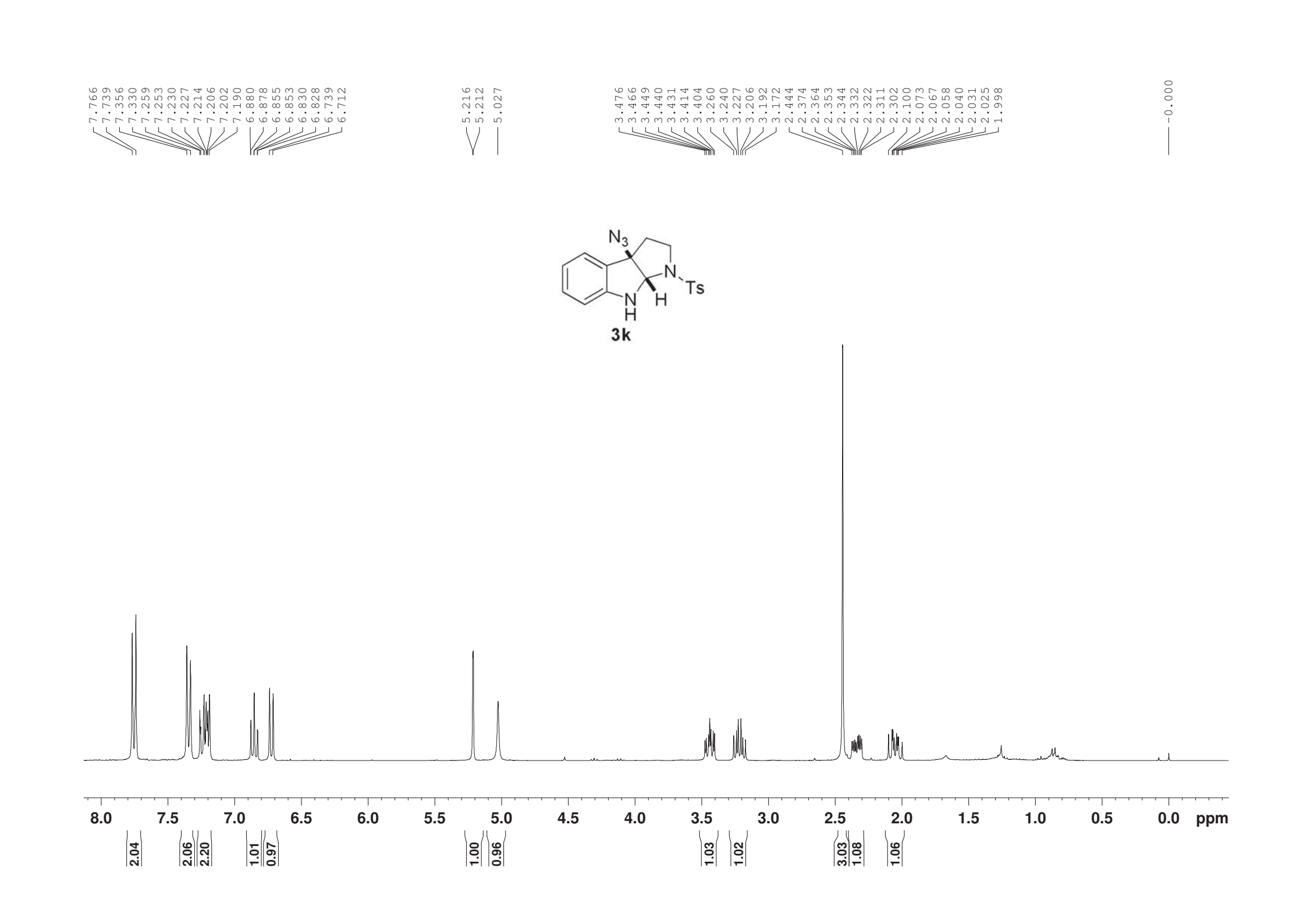
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7.206
7.202
7.190
6.880
6.878
6.855
6.853
6.830
6.828
6.739
6.712
5.216
5.212
5.027
3.476
3.466
3.449
3.440
3.431
3.414
3.404
3.260
3.240
3.227
3.206
3.192
3.172
2.444
2.374
2.364
2.353
2.344
2.332
2.322
2.311
2.302
2.100
2.073
2.067
2.058
2.040
2.031
2.025
1.998
0.000
N3
N
Ts
H
N
H
3k
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.04
2.06
2.20
1.01
0.97
1.00
0.96
1.03
1.02
3.03
1.08
1.06

149.46
144.08
135.12
131.18
129.99
127.23
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77.06
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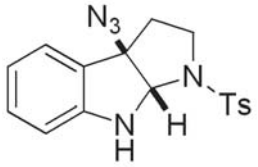
35.88
21.60



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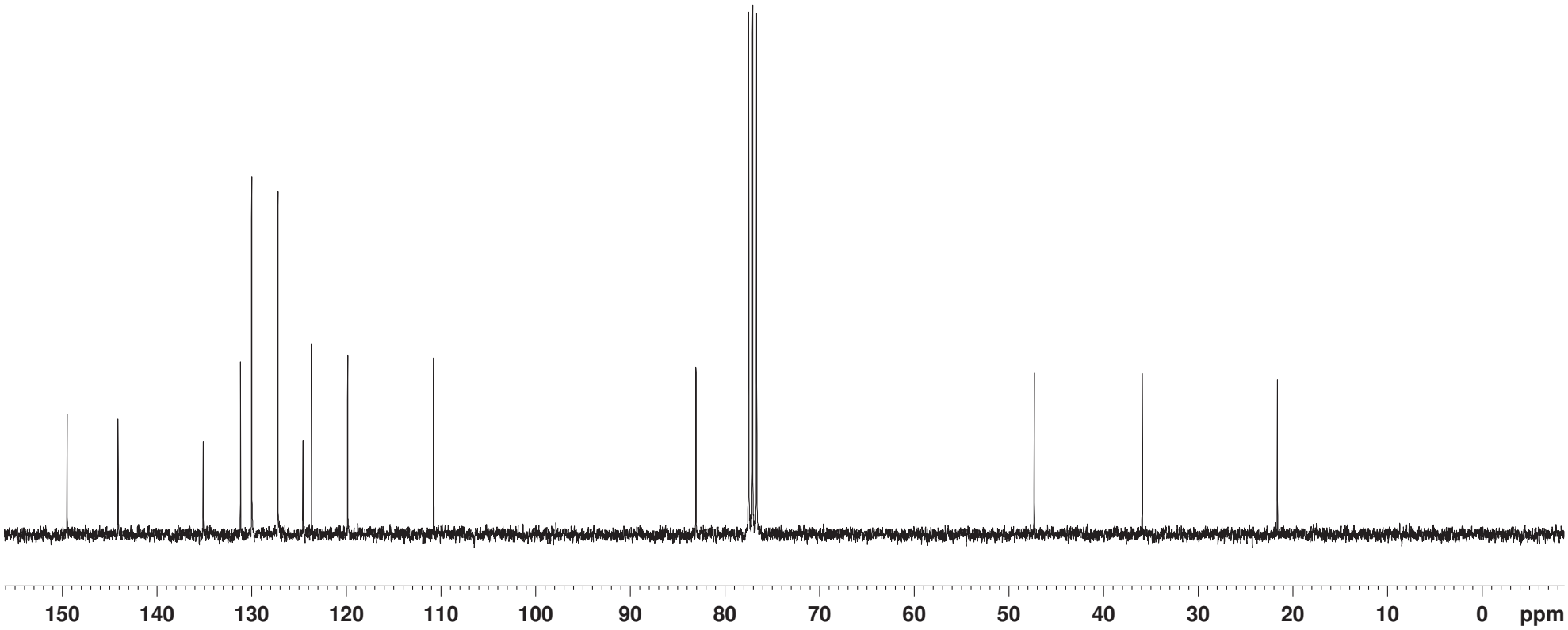

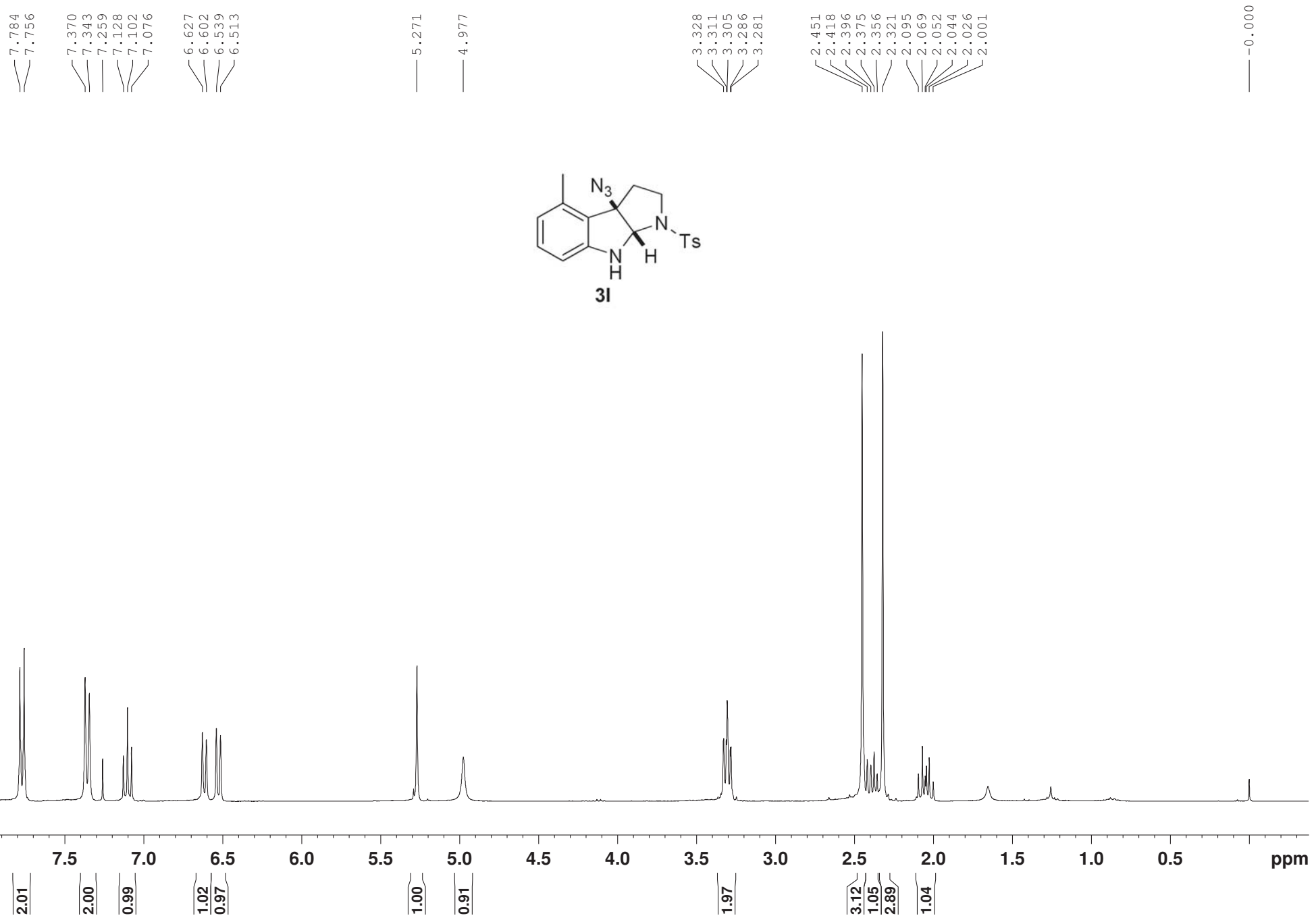
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6.602
6.539
6.513
5.271
4.977
3.328
3.311
3.305
3.286
3.281
2.451
2.418
2.396
2.375
2.356
2.321
2.095
2.069
2.052
2.044
2.026
2.001
0.000
N3
N
Ts
H
N
H
3l
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.00
0.99
1.02
0.97
1.00
0.91
1.97
3.12
1.05
2.89
1.04

149.54
144.14
135.15
134.56
131.01
129.95
127.48
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77.05
76.63
46.97
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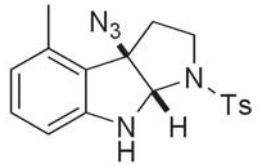
21.60
17.89



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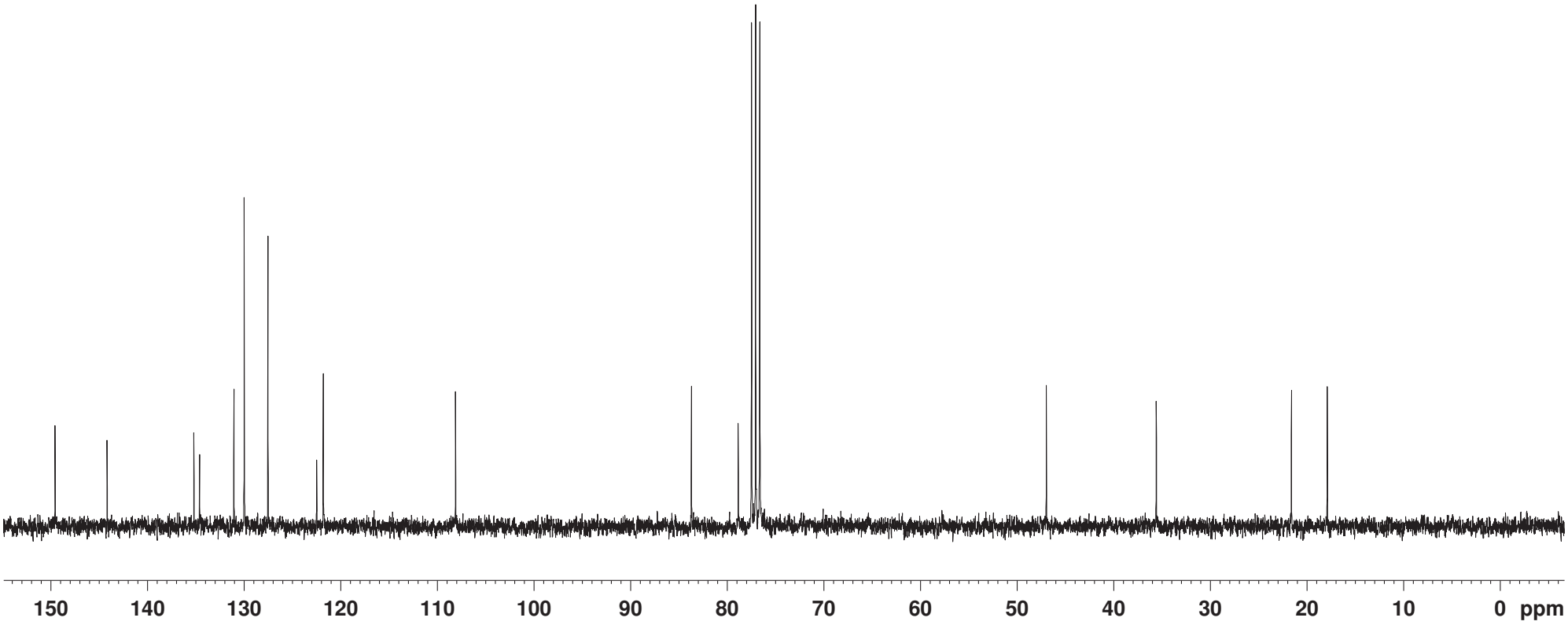

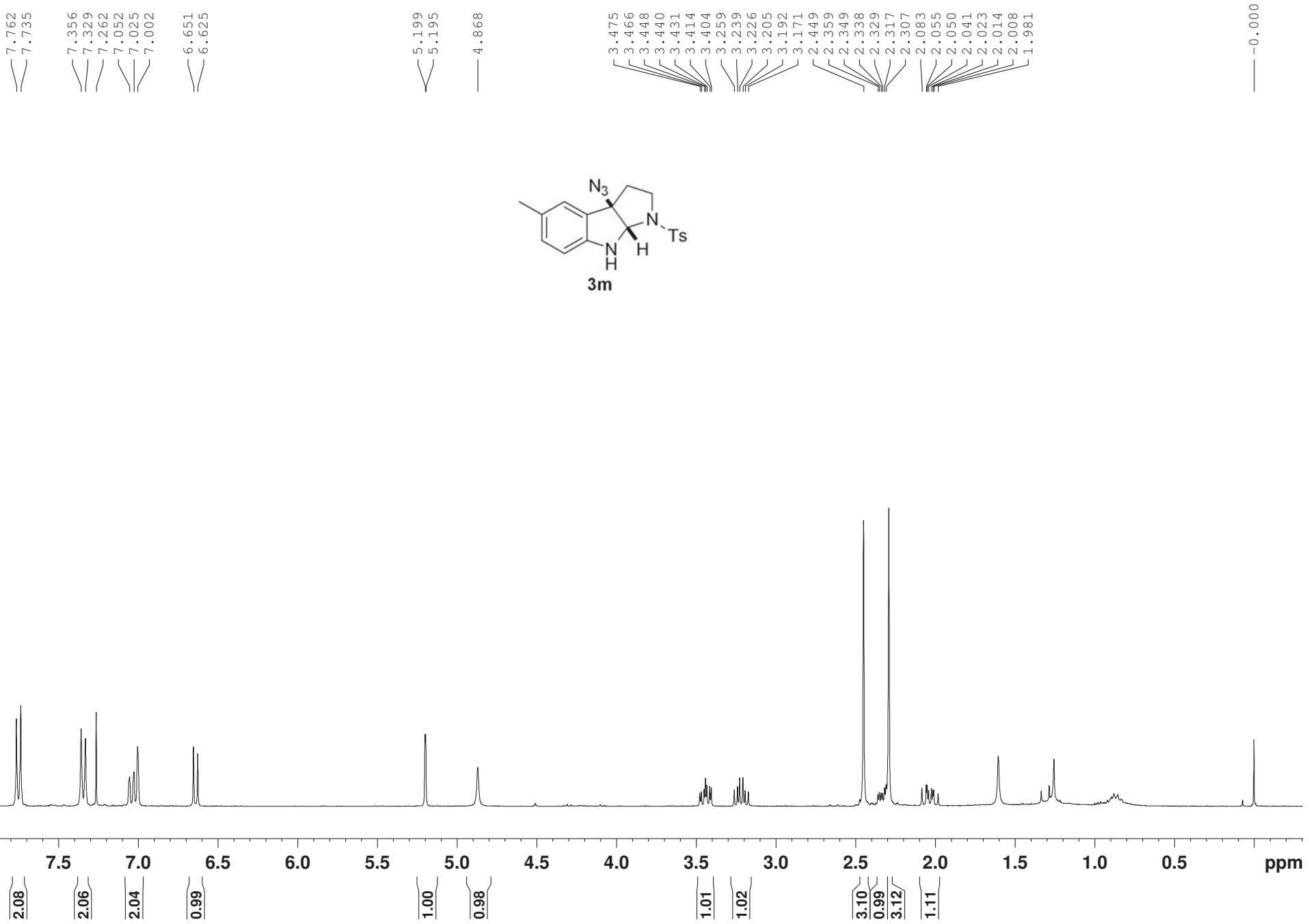
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3.475
3.466
3.448
3.440
3.431
3.414
3.404
3.259
3.239
3.226
3.205
3.192
3.171
2.449
2.359
2.349
2.338
2.329
2.317
2.307
2.083
2.055
2.050
2.041
2.023
2.014
2.008
1.981
0.000
N3
N
Ts
H
N
H
3m
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7.5
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
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1.02
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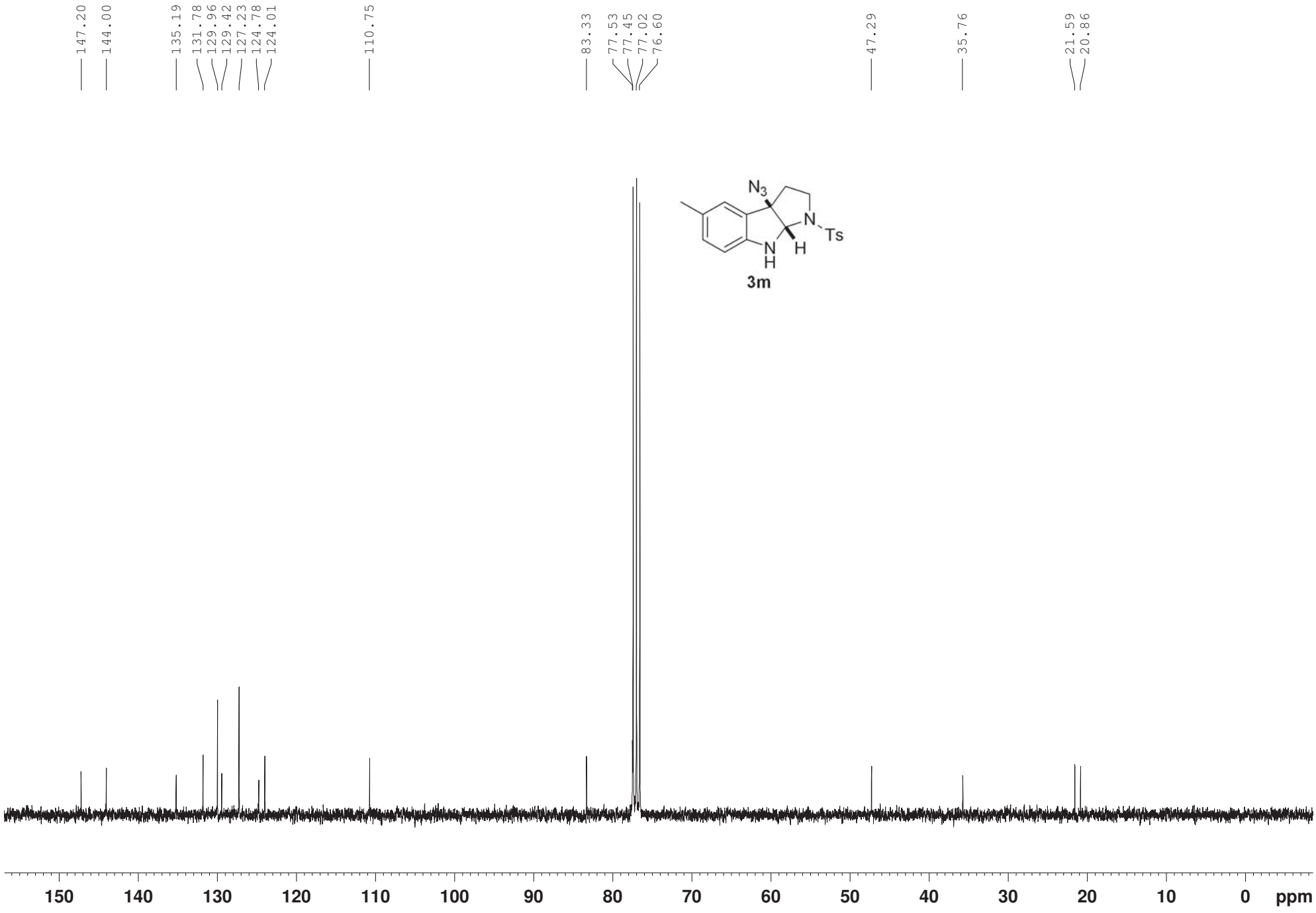
1.11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77.53
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77.02
76.60
47.29
35.76
21.59
20.86
N3
N
Ts
N
H
H
3m
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140
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60
50
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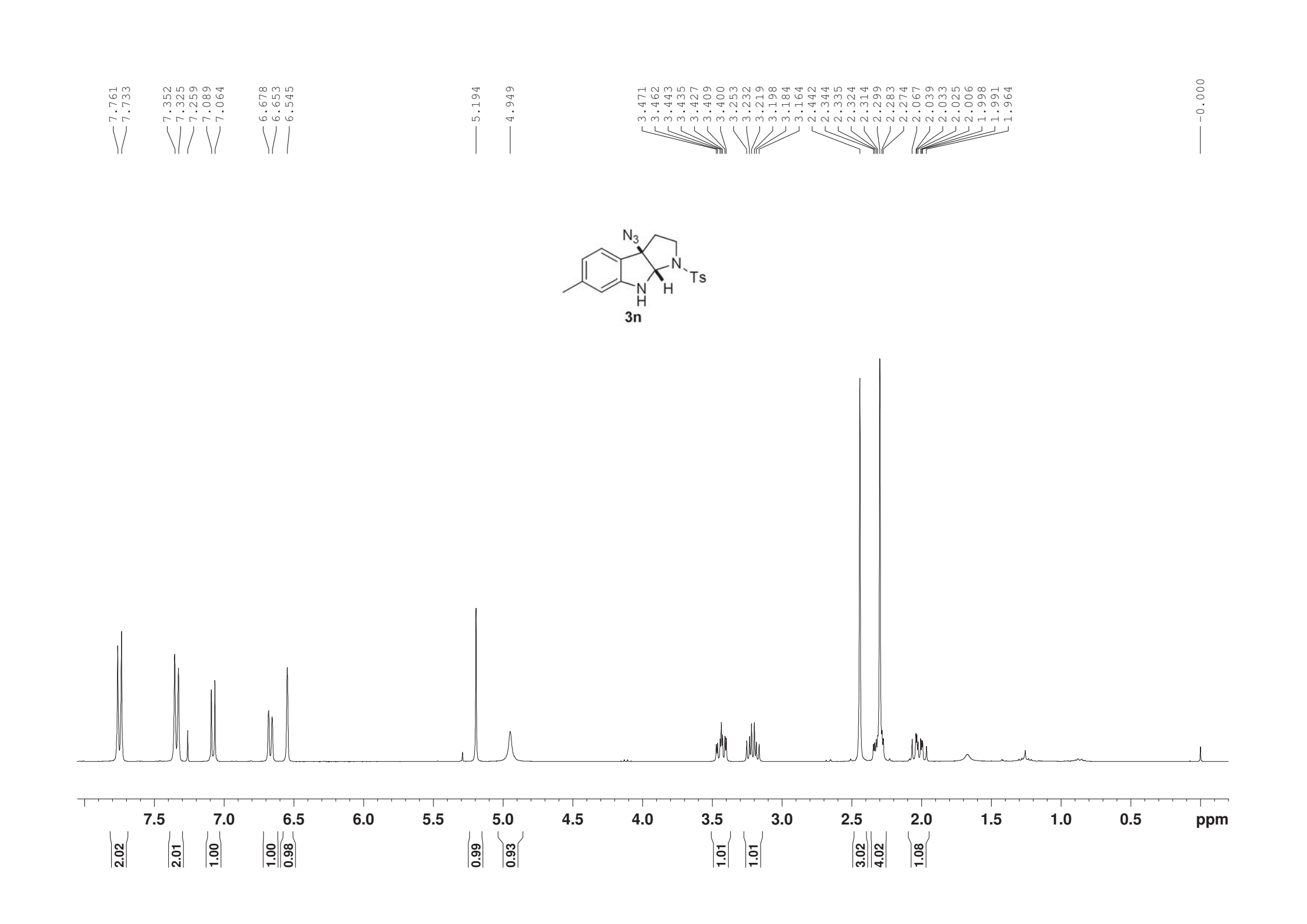
20
10
0
ppm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5.194
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3.435
3.427
3.409
3.400
3.253
3.232
3.219
3.198
3.184
3.164
2.442
2.344
2.335
2.324
2.314
2.299
2.283
2.274
2.067
2.039
2.033
2.025
2.006
1.998
1.991
1.964
0.000
N3
N
Ts
H
N
H
3n
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
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1.00
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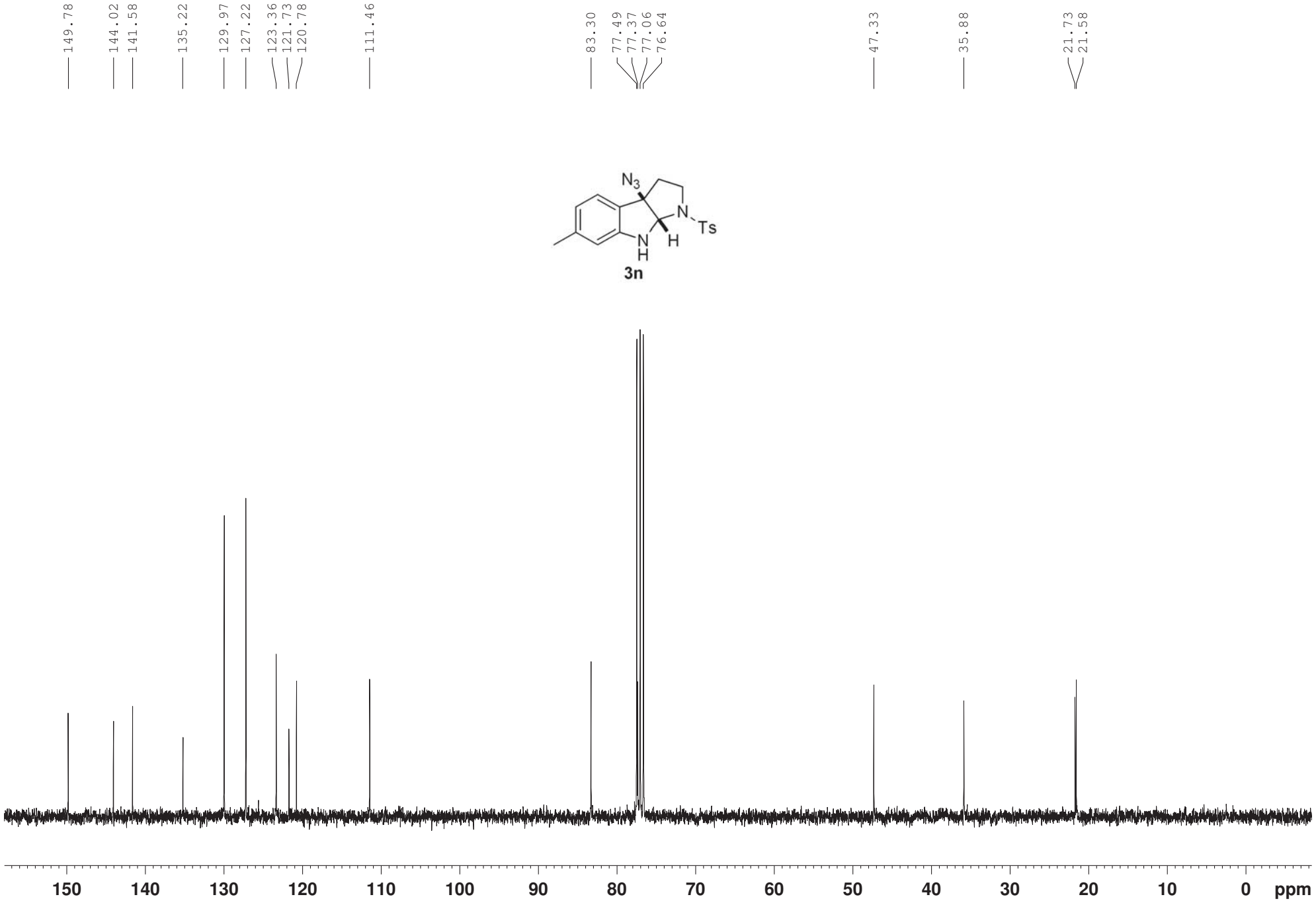
0.99
0.93
1.01
1.01
3.02
4.02
1.08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127.22
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121.73
120.78
111.46
83.30
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77.37
77.06
76.64
47.33
35.88
21.73
21.58
N3
N
Ts
N
H
H
3n
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140
130
120
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100
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80
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60
50
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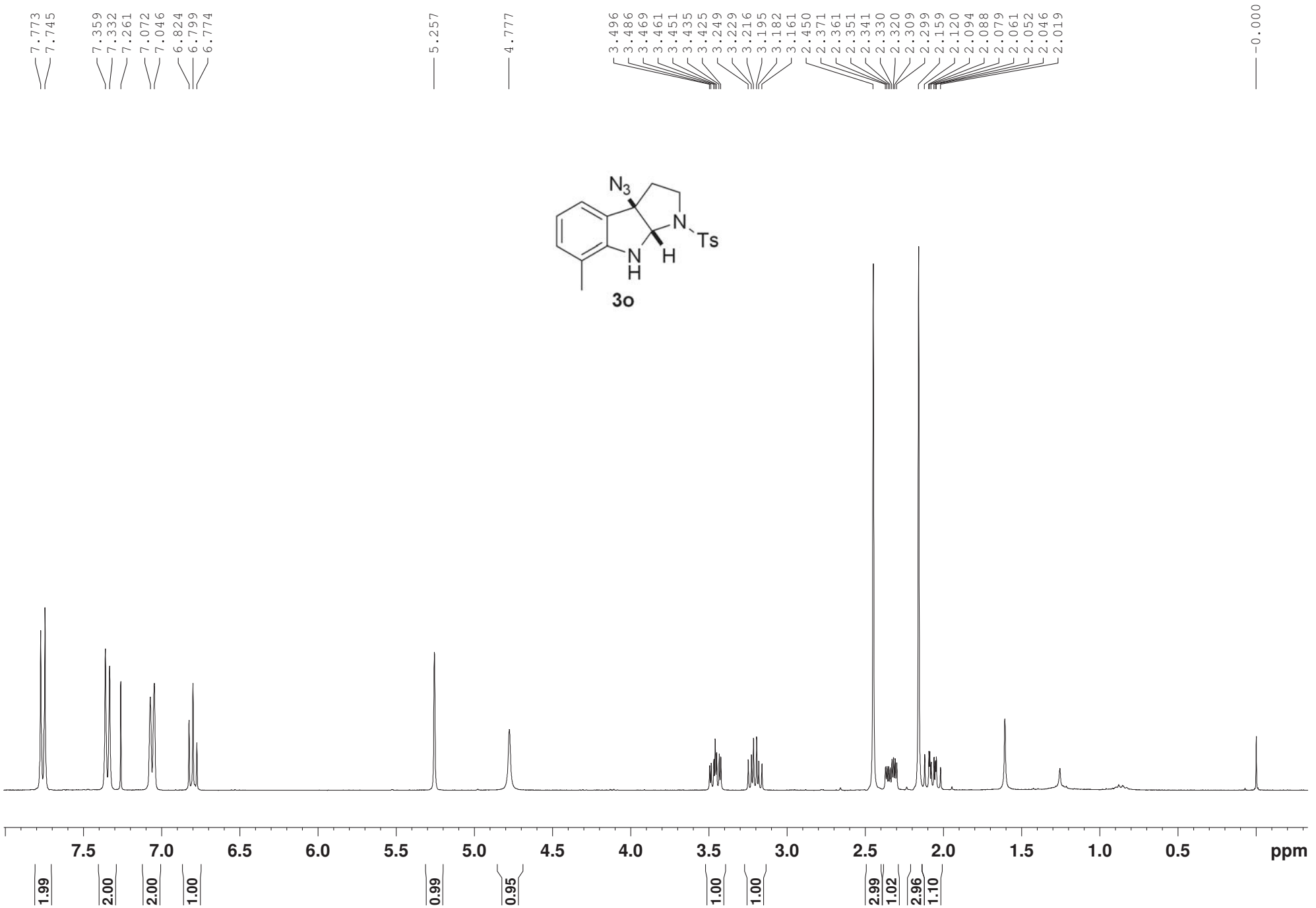
20
10
0
ppm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3.496
3.486
3.469
3.461
3.451
3.435
3.425
3.249
3.229
3.216
3.195
3.182
3.161
2.450
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2.361
2.351
2.341
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2.320
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2.079
2.061
2.052
2.046
2.019
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N3
N
Ts
H
N
H
3o
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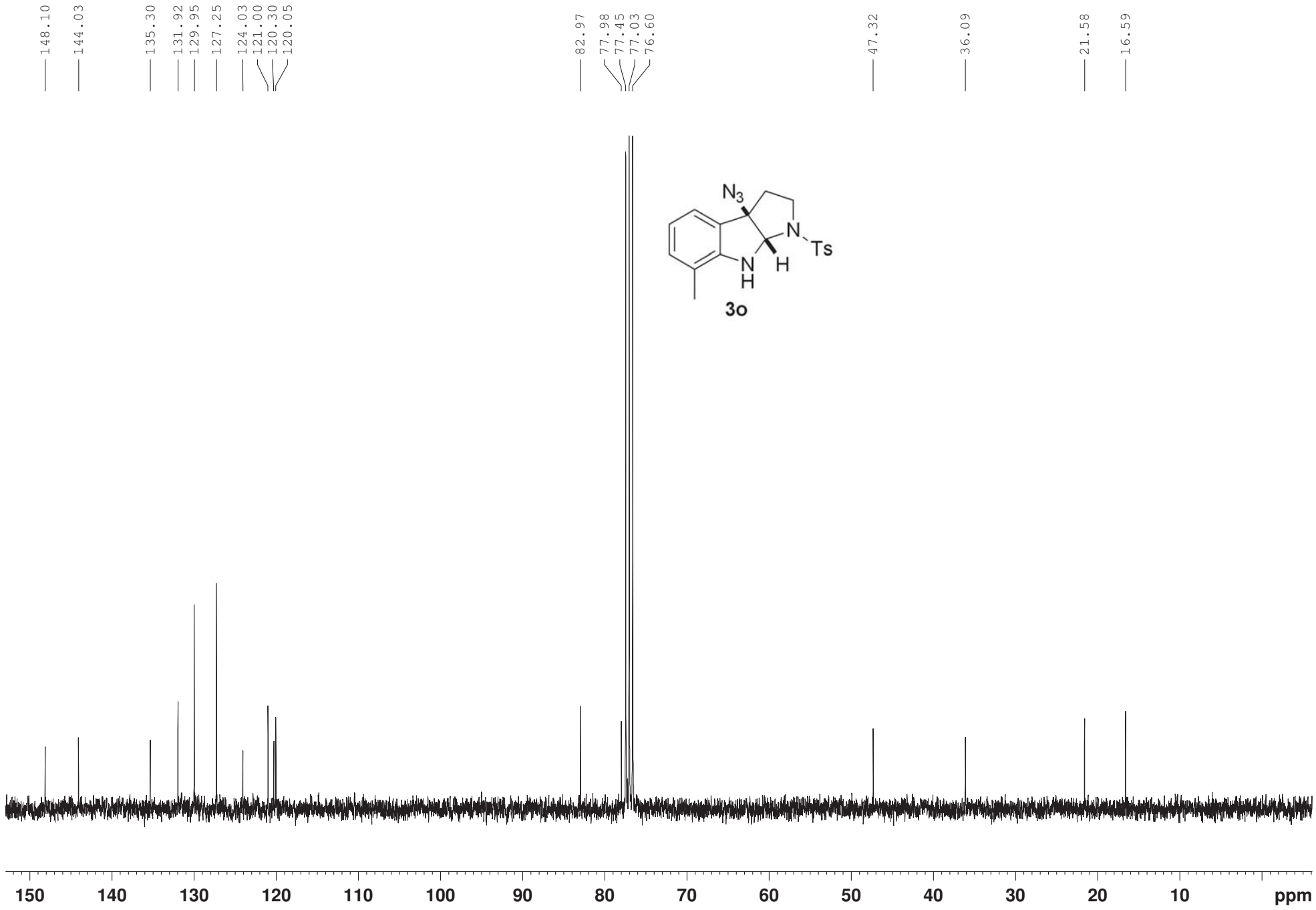
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76.60
47.32
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21.58
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N3
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Ts
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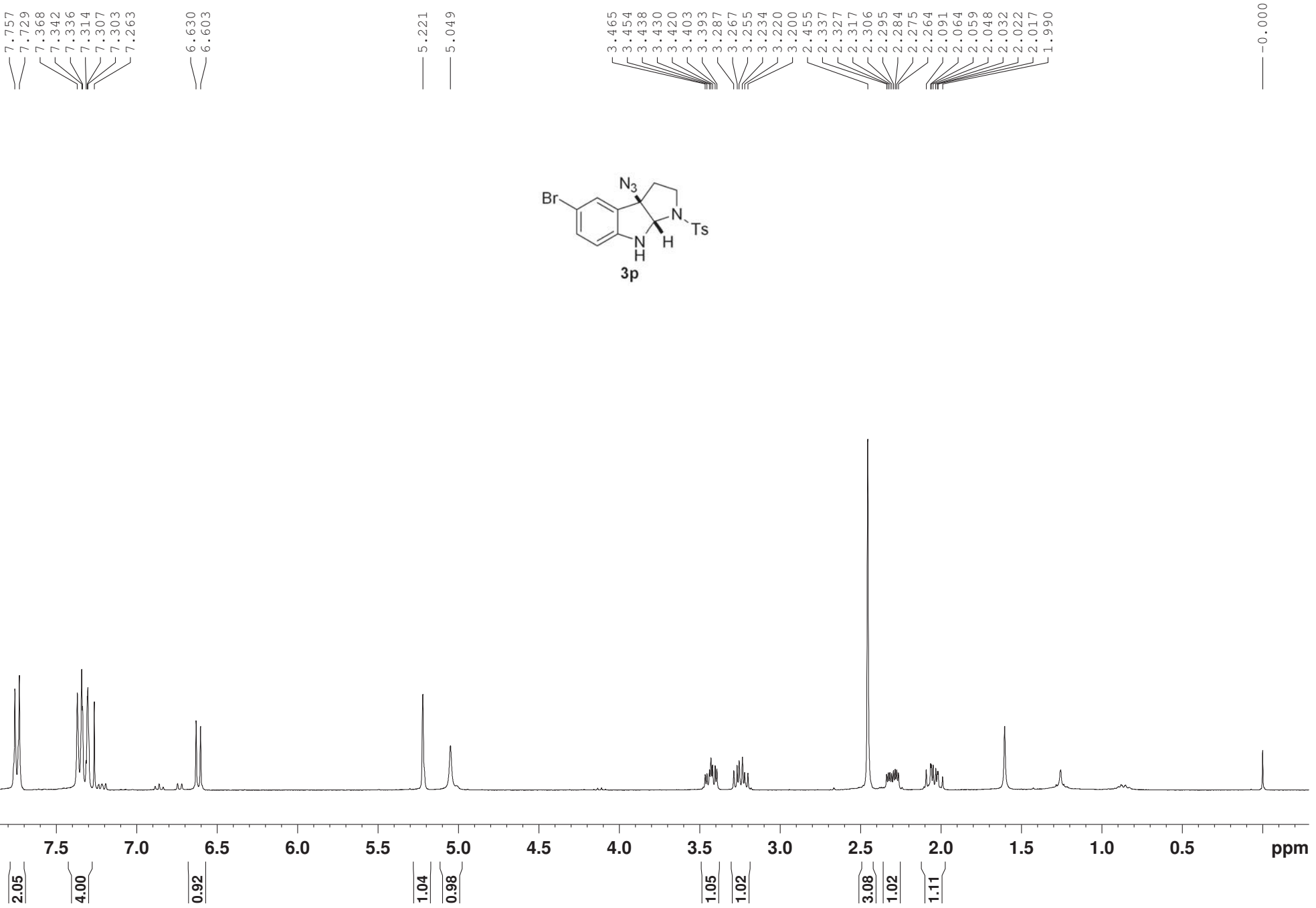
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3.200
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2.327
2.317
2.306
2.295
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2.275
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Ts
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N
H
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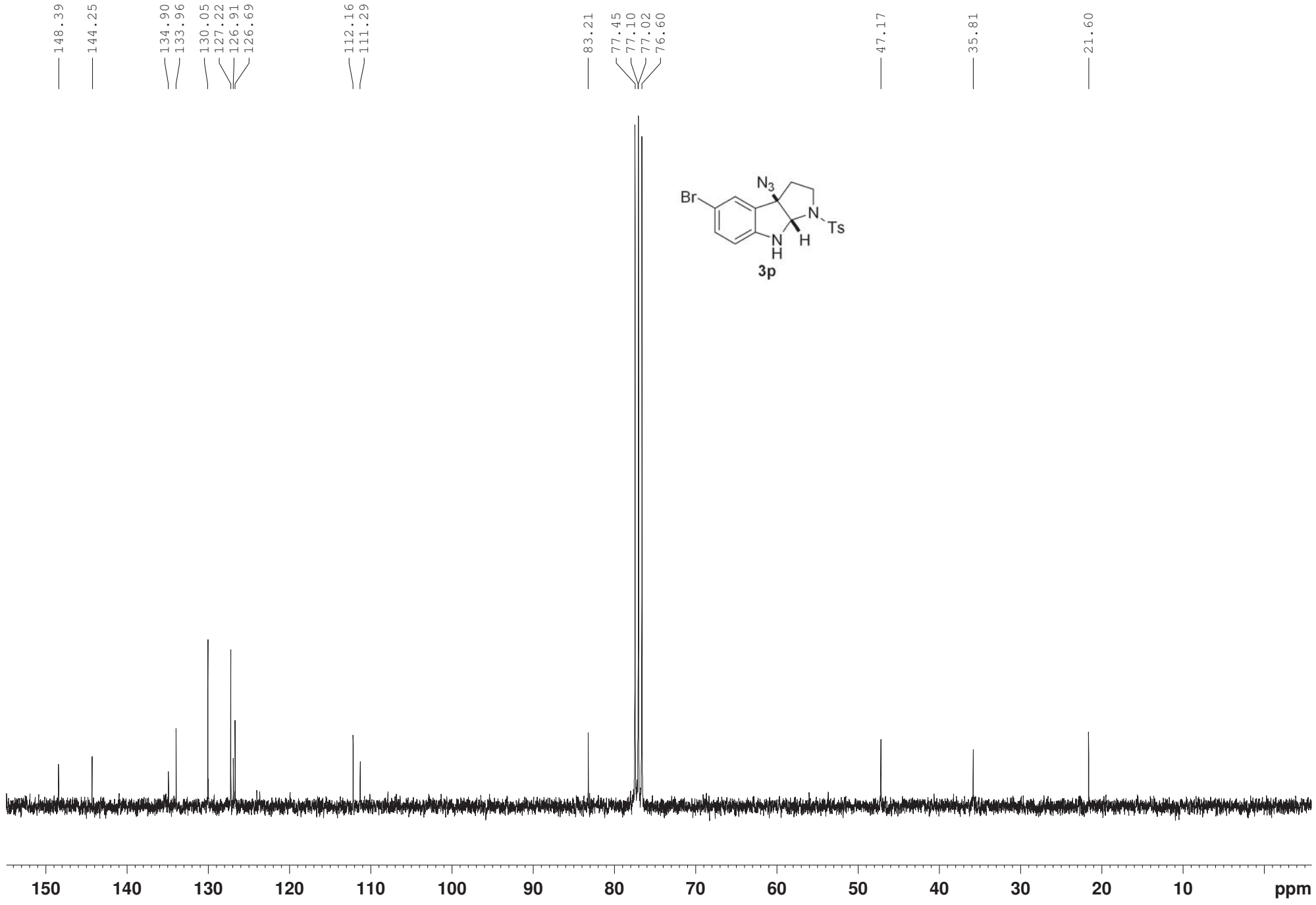
1.11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77.02
76.60
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35.81
21.60
Br
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N
Ts
N
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120
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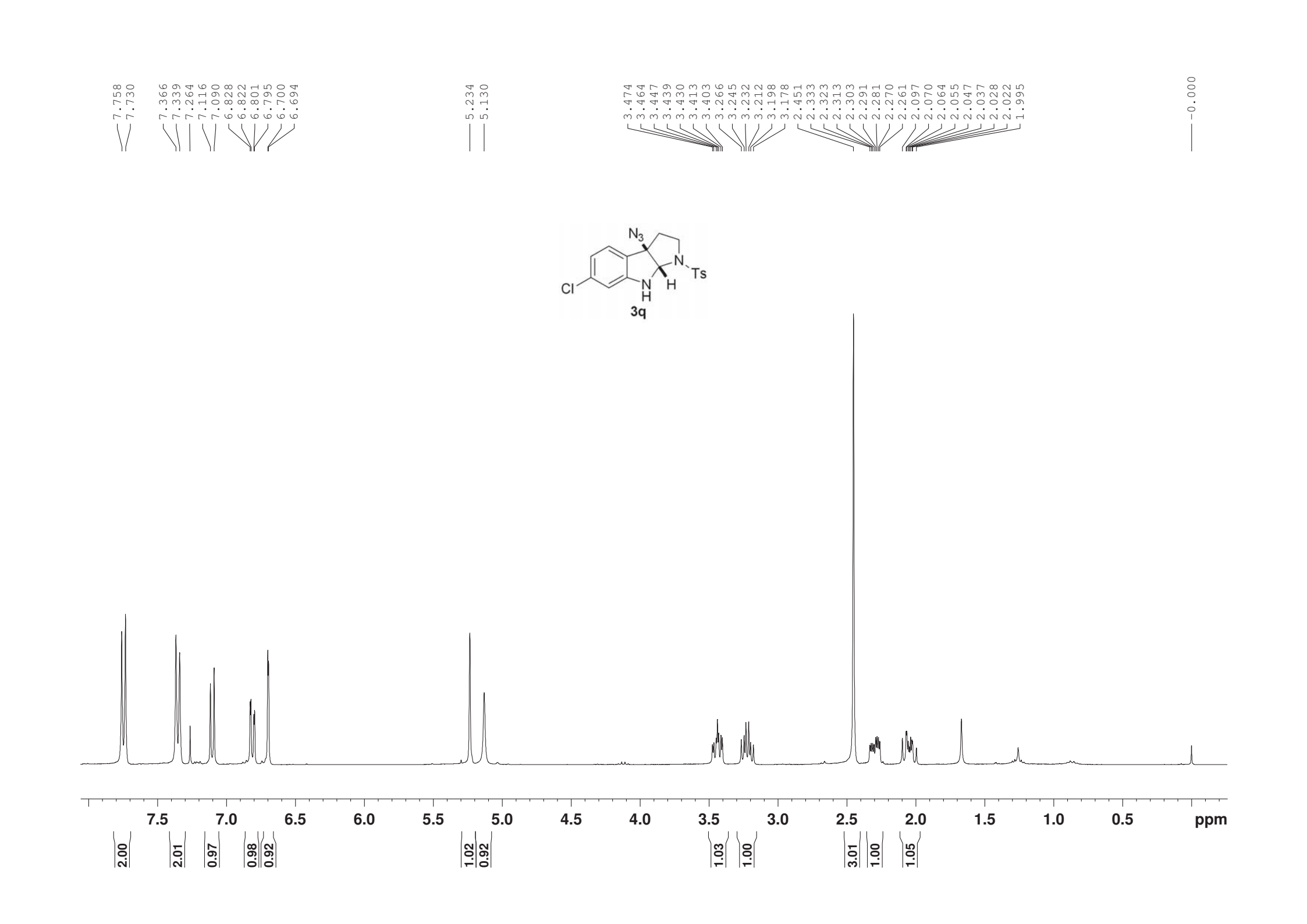
ppm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3.403
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3.245
3.232
3.212
3.198
3.178
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2.333
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2.070
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Cl
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H
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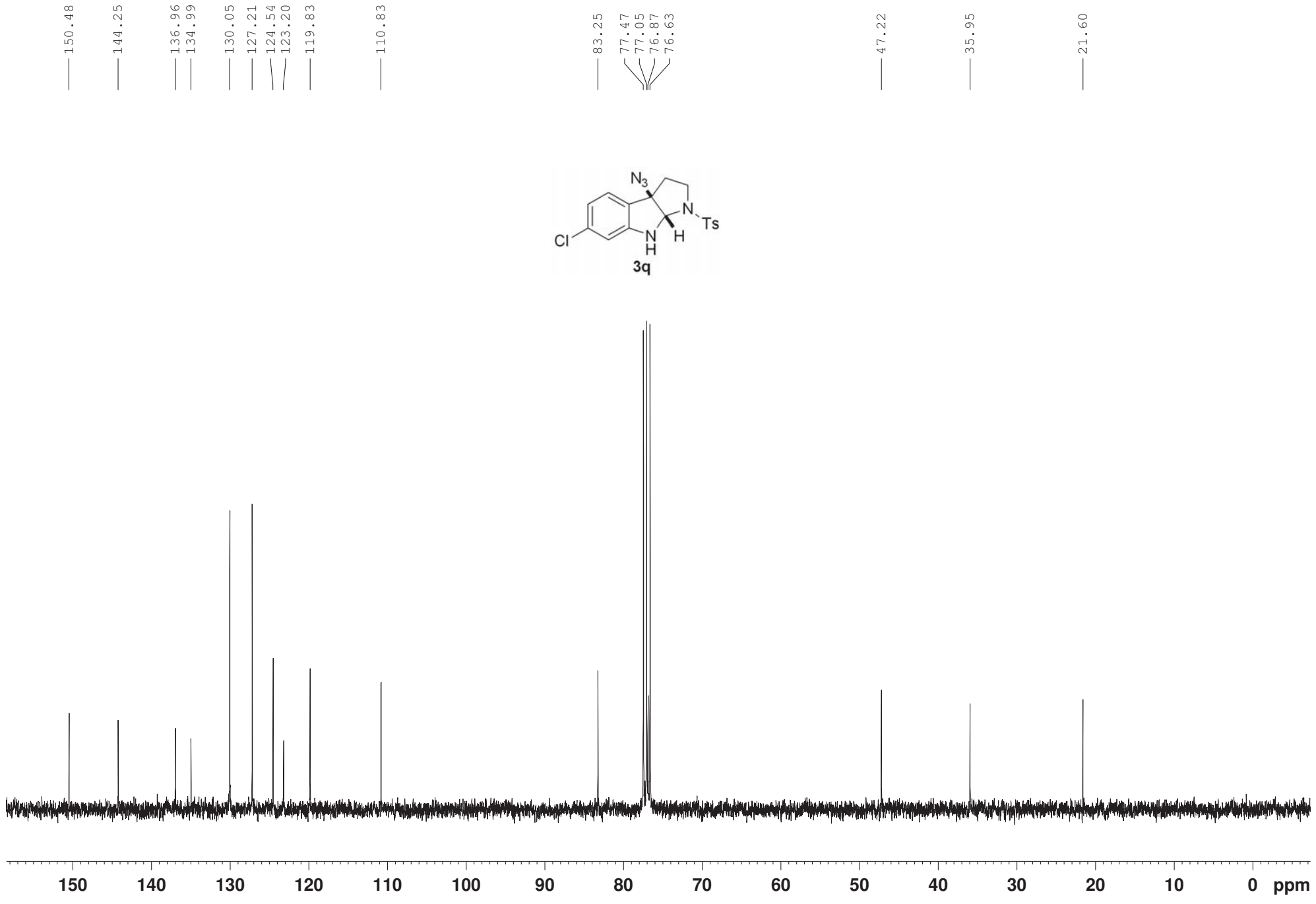
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35.95
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H
Cl
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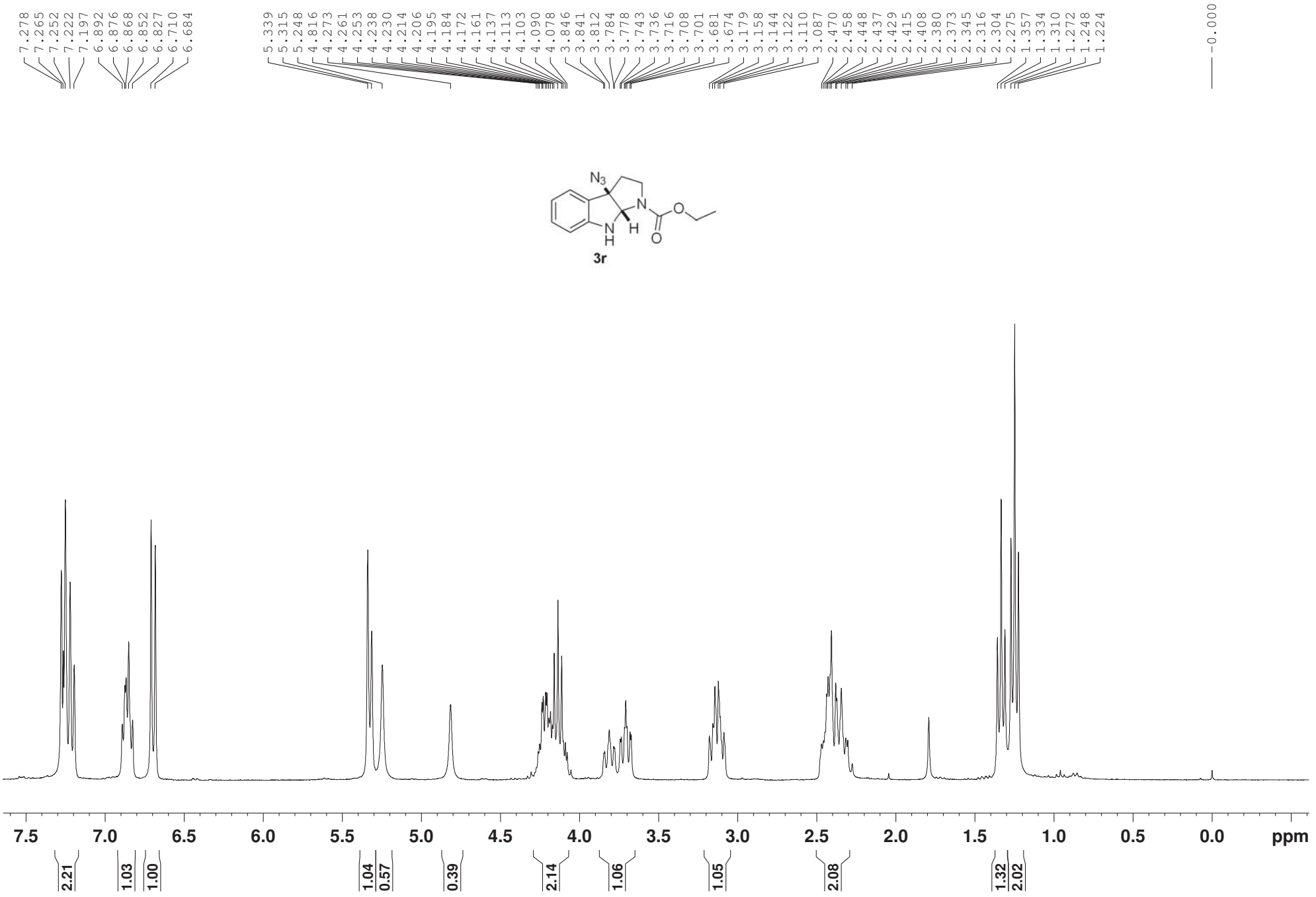
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5.248
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4.273
4.261
4.253
4.238
4.230
4.214
4.206
4.195
4.184
4.172
4.161
4.137
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4.078
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3.841
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3.708
3.701
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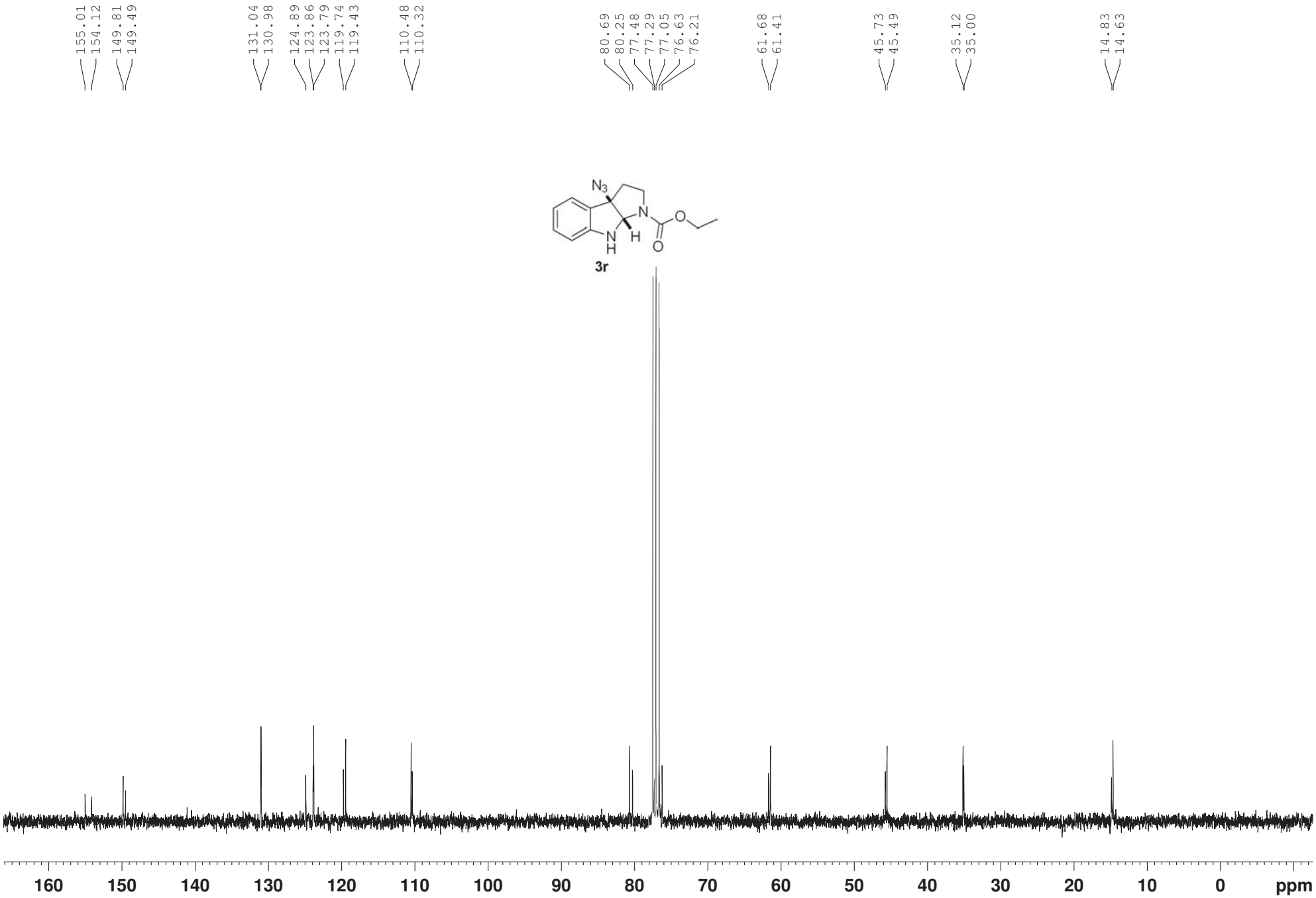
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H
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H
O
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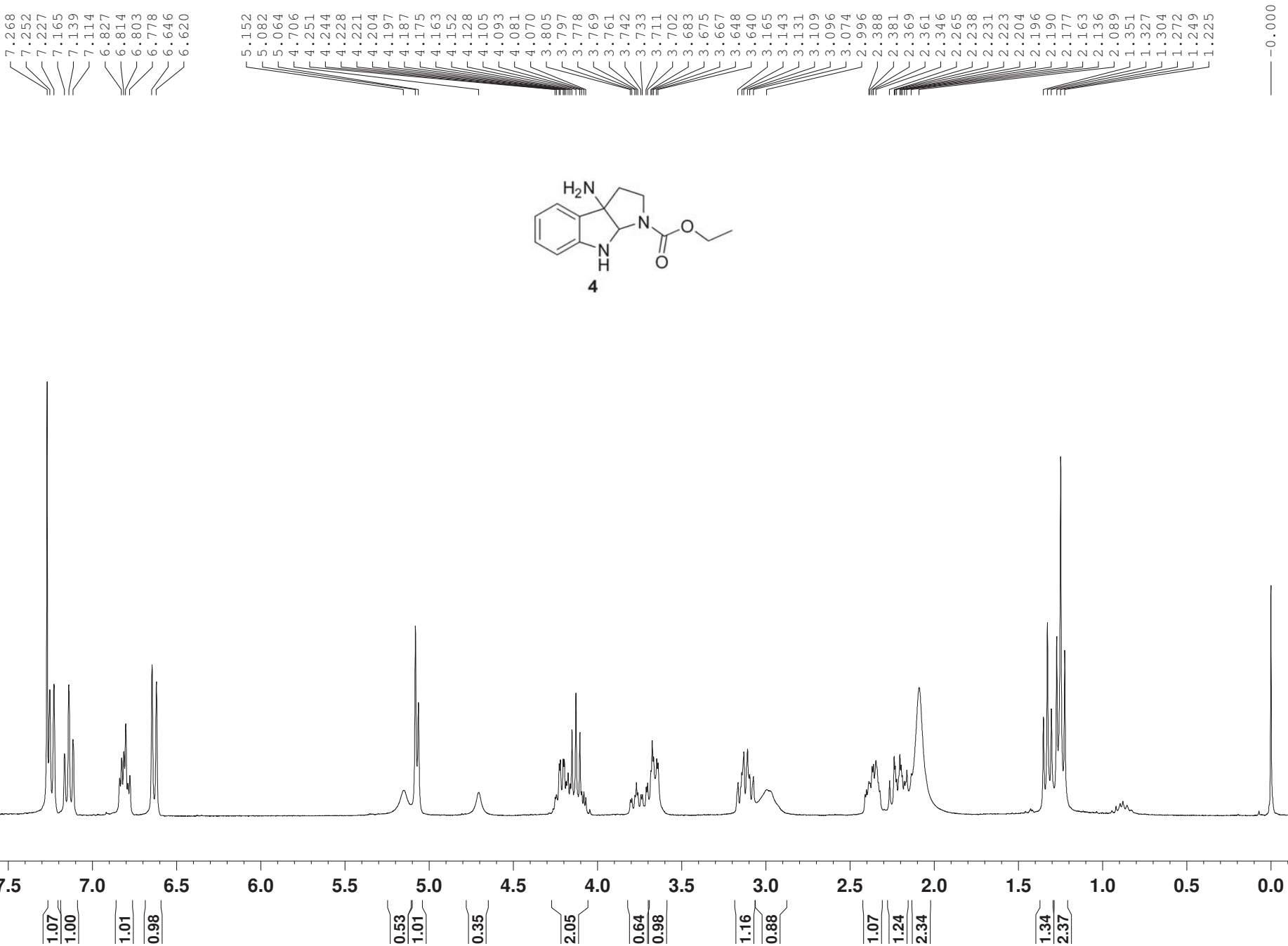
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5.064
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4.228
4.221
4.204
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37.47
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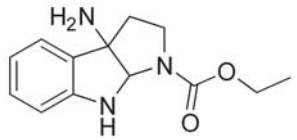

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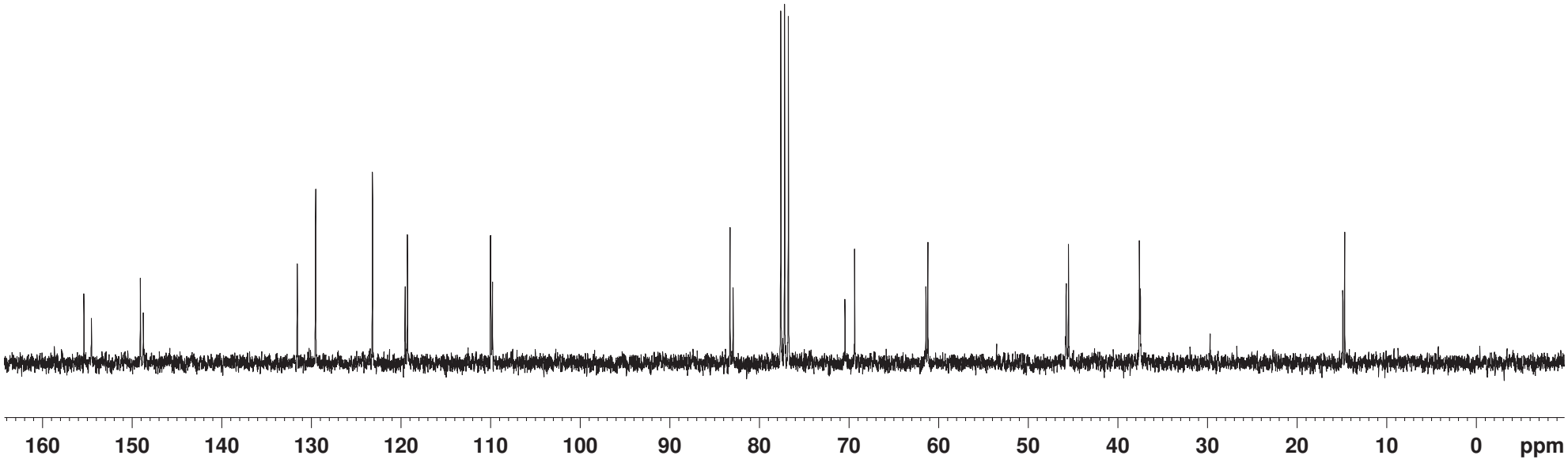

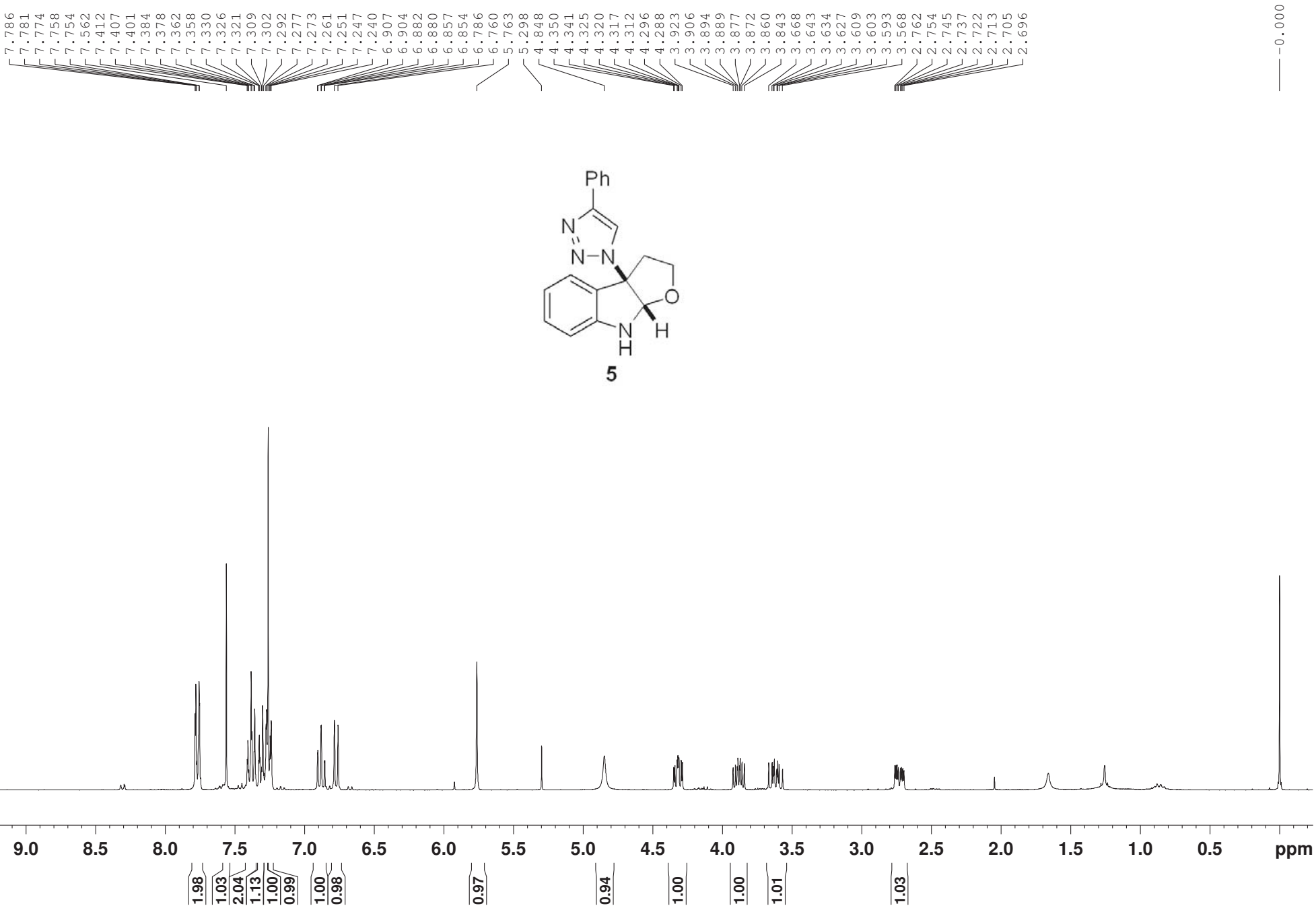
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7.240
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6.904
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1.00
1.01
1.03

Z4

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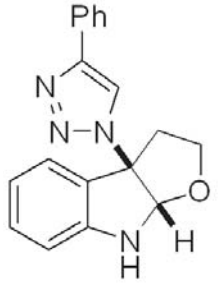

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