Supporting Information

Cu-Catalyzed Amidation of Halogenated Imidazoles

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Table of Contents

1. General Details

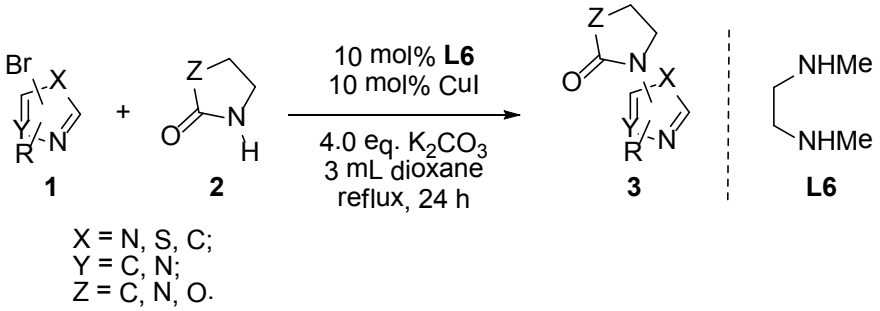
All reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen, and the workup was carried out in air, unless otherwise noted. 1,4-Dioxane, toluene and *N*,*N*-dimethylformamide (DMF) were dried and distilled from calcium hydride. Tetrahydrofuran (THF) were dried and distilled from metal sodium and benzophenone. The amides were used after distillation. Other reagents were used without further purification. The purity of CuI is 99.5%. The purity of CuBr is 98%. The purity of CuCl is 98%. The purity of Cu_2O is 99%. The purity of $CuBr_2$ is 99%. The purity of $Cu(OAc)_2$ is 98.5%.

Column chromatographic purification of products was carried out using silica gel 60 (100~200 mesh). The NMR spectra were recorded on a Varian MERCURY plus-400 (400 MHz, ^1H; 100 MHz, ^{13}C) spectrometer with chemical shifts reported in ppm relative to the residual deuterated solvent and the internal standard tetramethylsilane. Mass spectrometry analysis was carried out using an electrospray spectrometer Waters Micromass Q-TOF Premier Mass Spectrometer. Melting points were measured with SGW X-4 micro melting point apparatus. CSP-HPLC was performed using Shimadzu LC-20 system on Daicel Chiralpak® columns. Optical rotations were measured on a Rudolph Research Analytical Autopol VI automatic polarimeter using a 50 mm path-length cell at 589 nm.

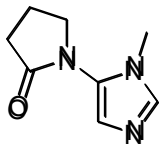
2. Cu-Catalyzed Amidation

General Procedure for Amidation

To CuI (0.05 mmol, 10 mol%) and K_2CO_3 (2.0 mmol) under nitrogen was added dioxane (3 mL) followed by *N*,*N'*-dimethyl ethylenediamine **L6** (0.05 mmol, 10 mol%), **1** (0.5 mmol) and **2** (0.6 mmol). The reaction mixture was stirred at reflux for 24 h, cooled to rt, diluted with CH_2Cl_2 (10 mL), filtered, washed with CH_2Cl_2 (10 mL), and concentrated under reduced pressure. The crude residue was purified by flash chromatography to give the product **3**.

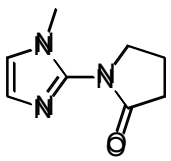


The Data of Characterization



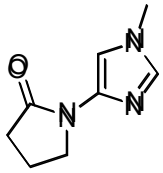
1-(1-Methyl-1*H*-imidazol-5-yl)pyrrolidin-2-one (3a).

92% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (s, 1H), 6.89 (s, 1H), 3.72 (t, *J* = 7.0 Hz, 2H), 3.52 (s, 3H), 2.56 (t, *J* = 8.2 Hz, 2H), 2.27~2.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2, 136.9, 128.6, 123.2, 51.7, 31.7, 31.1, 19.4; FT-IR (KBr pellet): 3697, 3182, 3114, 2919, 2902, 1681, 1562, 1513, 1501, 1460, 1435, 1420, 1384, 1359, 1311, 1268, 1236, 1175, 1099, 1002, 829, 747, 624, 562 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{12}N_3O$ $(M+H)^+$ 166.0980, found 166.0972.



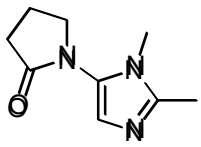
1-(1-Methyl-1*H*-imidazol-2-yl)pyrrolidin-2-one (3b).

43% yield, a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (s, 1H), 6.82 (s, 1H), 3.96 (t, *J* = 7.0 Hz, 2H), 3.58 (s, 3H), 2.57 (t, *J* = 8.2 Hz, 2H), 2.29~2.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5, 140.3, 126.4, 120.2, 49.5, 33.6, 31.3, 19.3; FT-IR (KBr pellet): 3710, 3114, 2956, 2922, 2853, 1704, 1531, 1506, 1468, 1412, 1391, 1284, 1269, 1234, 1146, 1019, 839, 755, 547 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{12}N_3O$ $(M+H)^+$ 166.0980, found 166.0967.



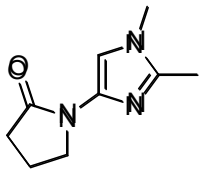
1-(1-Methyl-1*H*-imidazol-4-yl)pyrrolidin-2-one (3c).

97% yield, a yellow solid. Mp > 250 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.27 (s, 1H), 4.00 (t, *J* = 7.2 Hz, 2H), 3.69 (s, 3H), 2.57 (t, *J* = 8.0 Hz, 2H), 2.22~2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 138.9, 133.5, 108.5, 46.8, 34.0, 32.3, 18.6; FT-IR (KBr pellet): 3421, 3114, 2959, 2922, 2896, 2148, 1858, 1694, 1579, 1508, 1460, 1405, 1298, 1257, 1108, 907, 833, 672, 544 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{12}N_3O$ $(M+H)^+$ 166.0980, found 166.0969.



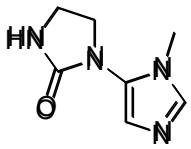
1-(1,2-Dimethyl-1*H*-imidazol-5-yl)pyrrolidin-2-one (3d).

85% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 3.70 (t, *J* = 7.0 Hz, 2H), 3.37 (s, 3H), 2.56 (t, *J* = 8.2 Hz, 2H), 2.36 (s, 3H), 2.27~2.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 139.1, 122.9, 116.2, 46.9, 26.1, 25.5, 14.4, 9.1; FT-IR (KBr pellet): 3422, 2956, 2483, 2418, 2329, 2126, 1692, 1586, 1508, 1488, 1460, 1437, 1405, 1300, 1257, 1142, 997, 975, 911, 834, 720, 674, 567, 540 cm^{-1}; HRMS (ESI): calcd. for $C_9H_{14}N_3O$ $(M+H)^+$ 180.1137, found 180.1122.



1-(1,2-Dimethyl-1*H*-imidazol-4-yl)pyrrolidin-2-one (3e).

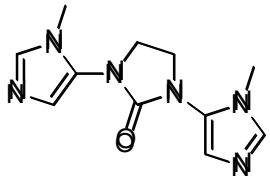
89% yield, a yellow solid. Mp = 132~133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (s, 1H), 4.03 (t, *J* = 6.8 Hz, 2H), 3.58 (s, 3H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.43 (s, 3H), 2.21~2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 140.9, 136.4, 108.6, 47.0, 33.2, 32.2, 18.6, 12.8; FT-IR (KBr pellet) 3443, 2926, 2377, 1688, 1563, 1489, 1462, 1432, 1420, 1405, 1385, 1326, 1268, 1115, 1052, 997, 788, 646, 570 cm^{-1}; HRMS (ESI): calcd. for $C_9H_{14}N_3O$ $(M+H)^+$ 180.1137, found 180.1131.



1-(1-Methyl-1*H*-imidazol-5-yl)imidazolidin-2-one (3f).

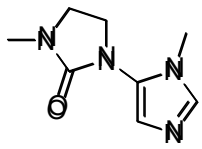
25% yield, a light yellow solid. Mp = 140~141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (s, 1H), 6.92 (s, 1H), 5.80 (s, 1H), 3.80 (t, *J* = 7.8 Hz, 2H), 3.60 (t, *J* = 8.0 Hz, 2H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 136.5, 129.1, 122.9, 48.9, 38.8, 31.3; FT-IR (KBr pellet): 3360, 3114,

2923, 2853, 1701, 1584, 1509, 1487, 1429, 1296, 1262, 1139, 1109, 1064, 918, 820, 735, 673, 658, 567 cm^{-1}; HRMS (ESI): calcd. for $C_7H_{11}N_4O$ $(M+H)^+$ 167.0933, found 167.0923.



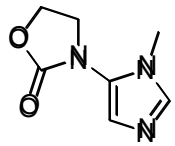
1,3-Bis(1-methyl-1*H*-imidazol-5-yl)imidazolidin-2-one (3f').

37% yield, a yellow solid. Mp = 204~205 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (s, 2H), 6.98 (s, 2H), 3.91 (s, 4H), 3.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 136.7, 128.8, 122.7, 46.4, 31.5; FT-IR (KBr pellet): 3406, 2923, 2853, 1707, 1578, 1505, 1476, 1422, 1290, 1249, 1103, 907, 803, 737, 665 cm^{-1}; HRMS (ESI): calcd. for $C_{11}H_{15}N_6O$ $(M+H)^+$ 247.1307, found 247.1298.



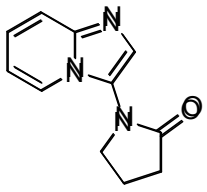
1-Methyl-3-(1-methyl-1*H*-imidazol-5-yl)imidazolidin-2-one (3g).

70% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (s, 1H), 6.89 (s, 1H), 3.70 (t, J = 7.8 Hz, 2H), 3.57 (s, 3H), 3.51 (t, J = 7.8 Hz, 2H), 2.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 136.2, 130.0, 122.2, 46.0, 45.2, 31.5, 31.3; FT-IR (KBr pellet): 3427, 3115, 2923, 2888, 2161, 1698, 1584, 1503, 1442, 1407, 1288, 1242, 1109, 1023, 935, 904, 820, 744, 661, 530 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{13}N_4O$ $(M+H)^+$ 181.1089, found 181.1079.



3-(1-Methyl-1*H*-imidazol-5-yl)oxazolidin-2-one (3h).

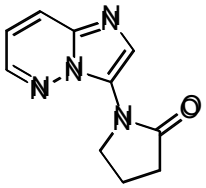
82% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (s, 1H), 6.99 (s, 1H), 4.55 (t, J = 7.8 Hz, 2H), 3.95 (t, J = 8.0 Hz, 2H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 137.2, 127.5, 123.9, 63.3, 48.9, 31.6; FT-IR (KBr pellet): 3369, 3115, 2958, 2922, 2853, 2119, 1751, 1658, 1633, 1585, 1508, 1479, 1296, 1238, 1217, 1128, 1109, 1034, 993, 957, 914, 826, 763, 745, 698, 671, 657, 570 cm^{-1}; HRMS(ESI): calcd for $C_7H_{10}N_3O_2$ $(M+H)^+$ 168.0773, found 168.0771.



1-(Imidazo[1,2-*a*]pyridin-3-yl)pyrrolidin-2-one (3i).

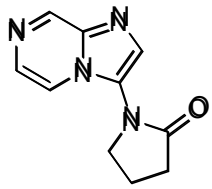
96% yield, a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 6.8 Hz, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.52 (s, 1H), 7.22~7.18 (m, 1H), 6.85~6.82 (m, 1H), 3.83 (t, J = 7.0 Hz, 2H), 2.65 (t, J =

8.0 Hz, 2H), 2.35~2.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5, 143.9, 127.7, 124.8, 123.5, 121.0, 118.4, 112.6, 50.9, 30.9, 19.4; FT-IR (KBr pellet): 3401, 3105, 2924, 2894, 1699, 1634, 1566, 1500, 1458, 1397, 1356, 1308, 1268, 1245, 1145, 1128, 1019, 1008, 894, 834, 758, 741, 662, 534, 501 cm^{-1}; HRMS (ESI): calcd. for $C_{11}H_{12}N_3O$ $(M+H)^+$ 202.0980, found 202.0966.



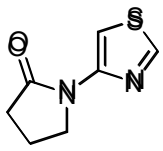
1-(Imidazo[1,2-*b*]pyridazin-3-yl)pyrrolidin-2-one (3j).

85% yield, a yellow solid. Mp = 110~111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (dd, *J* = 4.2, 1.4 Hz, 1H), 7.95 (dd, *J* = 9.2, 1.2 Hz, 1H), 7.82 (s, 1H), 7.07 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.98 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 8.2 Hz, 2H), 2.37~2.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 138.5, 132.7, 124.8, 121.6, 119.4, 112.2, 44.5, 26.1, 14.5; FT-IR (KBr pellet): 3424, 2961, 2922, 2118, 1700, 1562, 1525, 1482, 1459, 1402, 1350, 1297, 1257, 1218, 1140, 1122, 1021, 835, 797, 760, 739, 715, 667, 601, 537 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{11}N_4O$ $(M+H)^+$ 203.0933, found 203.0926.



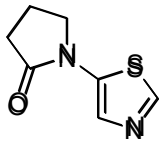
1-(Imidazo[1,2-*a*]pyrazin-3-yl)pyrrolidin-2-one (3k).

41% yield, a brown solid. Mp = 139~140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.08 (s, 1H), 7.91 (d, *J* = 4.8 Hz, 1H), 7.83 (d, *J* = 3.6 Hz, 1H), 7.66 (s, 1H), 3.91 (t, *J* = 7.0 Hz, 2H), 2.68 (t, *J* = 8.2 Hz, 2H), 2.41~2.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 144.3, 138.9, 129.5, 128.9, 122.8, 117.4, 50.6, 30.9, 19.6; FT-IR (KBr pellet): 3414, 3098, 3061, 2988, 2948, 1709, 1694, 1618, 1543, 1491, 1457, 1384, 1373, 1345, 1315, 1265, 1243, 1199, 1171, 1141, 1068, 1019, 899, 819, 790, 715, 670, 609, 554, 500 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{11}N_4O$ $(M+H)^+$ 203.0933, found 203.0923.



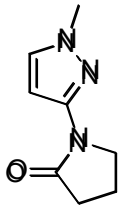
1-(Thiazol-4-yl)pyrrolidin-2-one (3l).

96% yield, a yellow solid. Mp = 68~69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 2.4 Hz, 1H), 7.89 (d, *J* = 2.4 Hz, 1H), 4.15 (t, *J* = 7.2 Hz, 2H), 2.63 (t, *J* = 8.2 Hz, 2H), 2.24~2.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 149.9, 149.4, 102.1, 48.4, 32.4, 18.5; FT-IR (KBr pellet): 3430, 2924, 1678, 1513, 1488, 1460, 1433, 1411, 1385, 1314, 1284, 1231, 1197, 1078, 977, 889, 878, 832, 734, 707, 636, 556, 496 cm^{-1}; HRMS (ESI): calcd. for $C_7H_9N_2OS$ $(M+H)^+$ 169.0436, found 169.0426.



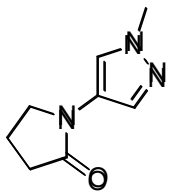
1-(Thiazol-5-yl)pyrrolidin-2-one (3m).

28% yield, a light yellow solid. Mp = 123~124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 7.47 (s, 1H), 3.92 (t, *J* = 7.2 Hz, 2H), 2.65 (t, *J* = 8.2 Hz, 2H), 2.34~2.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.5, 172.6, 146.9, 127.7, 48.7, 30.9, 18.2; FT-IR (KBr pellet): 3433, 3099, 3077, 2988, 2965, 2926, 2905, 1686, 1522, 1485, 1459, 1441, 1422, 1317, 1298, 1262, 1237, 1174, 1111, 1097, 1088, 1027, 939, 900, 869, 837, 779, 610, 539 cm^{-1}; HRMS (ESI): calcd. for $C_7H_9N_2OS$ $(M+H)^+$ 169.0436, found 169.0433.



1-(1-Methyl-1*H*-pyrazol-3-yl)pyrrolidin-2-one (3n).

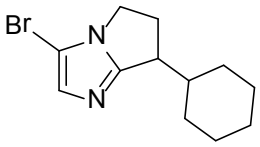
75% yield, a white solid. Mp = 111~112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.42 (s, 1H), 3.89 (s, 3H), 3.74 (t, *J* = 7.0 Hz, 2H), 2.55 (t, *J* = 8.2 Hz, 2H), 2.25~2.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 148.2, 131.2, 96.7, 47.2, 39.1, 32.3, 18.5; FT-IR (KBr pellet): 3433, 3334, 3169, 3146, 2993, 2945, 2902, 1675, 1585, 1493, 1446, 1420, 1393, 1279, 1193, 1108, 1068, 988, 900, 835, 815, 657, 627, 567 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{12}N_3O$ $(M+H)^+$ 166.0980, found 166.0978.



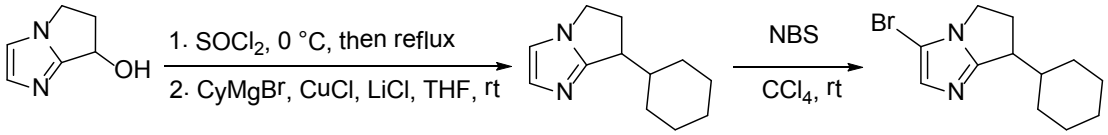
1-(1-Methyl-1*H*-pyrazol-4-yl)pyrrolidin-2-one (3o).

76% yield, a light yellow solid. Mp = 103~104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.44 (s, 1H), 3.89 (s, 3H), 3.74 (t, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 8.2 Hz, 2H), 2.25~2.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 124.3, 119.0, 116.8, 43.2, 34.8, 26.7, 13.7; FT-IR (KBr pellet): 3440, 3118, 2946, 1698, 1533, 1498, 1411, 1357, 1300, 1272, 1242, 1131, 1072, 1052, 1031, 1012, 870, 762, 694, 560 cm^{-1}; HRMS (ESI): calcd. for $C_8H_{12}N_3O$ $(M+H)^+$ 166.0980, found 166.0975.

3. Synthesis of (+)-Cy-PDPI



3-Bromo-7-cyclohexyl-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole (1p)



OH-DPI **Cy-DPI** **1p**

In a dry two-necked flask, **OH-DPI**[1] (2.0 g, 16 mmol) was treated with $SOCl_2$ (16.0 mL, 221 mmol, 13.8 eq.) dropwise at 0 °C, then the solution was heated under reflux conditions until it turned black. $SOCl_2$ was removed under reduced pressure and a suspension of CuCl (99 mg, 1.0 mmol, 6 mol%) and LiCl (85 mg, 2.0 mmol, 12 mol%) in THF (25 mL) was added. In another dry two-necked flask, a solution of CyMgBr in THF (40 mL) was freshly produced using CyBr (7.9 mL, 64 mmol, 4.0 eq.) and Mg (1.7 g, 71 mmol, 4.4 eq.). The resulting solution of CyMgBr in THF was added to the first flask, and then heated under reflux conditions for 12 h at room temperature. The reaction mixture was quenched by addition of water in ice bath. The resulting suspension was filtered and THF was removed under reduced pressure. The remaining residue was extracted with EtOAc (150 mL × 3), dried over Na_2SO_4, and evaporated in vacuo. The crude product was purified by flash chromatography on neutral Al_2O_3 (EtOAc/MeOH = 10/1, Rf = 0.32) to give 679 mg of **Cy-DPI**.

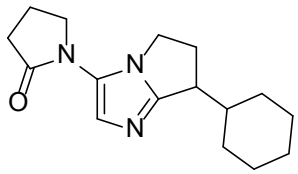
7-Cyclohexyl-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole (Cy-DPI).

22% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J = 0.8 Hz, 1H), 6.82 (d, J = 1.2 Hz, 1H), 3.98~3.80 (m, 2H), 2.96~2.86 (m, 1H), 2.70~2.58 (m, 1H), 2.40~2.28 (m, 1H), 2.14~2.02 (m, 1H), 1.80~1.46 (m, 5H), 1.34~0.98 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 132.6, 113.8, 43.8, 41.4, 41.3, 30.6, 30.4, 29.9, 26.3, 26.2, 26.1; HRMS (EI): calcd. for $C_{12}H_{18}N_2$ [M^+] 190.1470, found 190.1471.

To a solution of **Cy-DPI** (202 mg, 1.06 mmol) in CCl_4 (40 mL) was added NBS (189 mg, 1.06 mmol, 1.0 eq.) at room temperature and the mixture stirred for approximately 2 h. The reaction mixture was washed by 2 M NaOH twice and brine, dried over Na_2SO_4 and solvent evaporated under reduced pressure. The crude product was purified by flash chromatography on neutral Al_2O_3 (PE/EtOAc = 4/1, Rf = 0.28) to give 182 mg of **1p**.

3-Bromo-7-cyclohexyl-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole (1p).

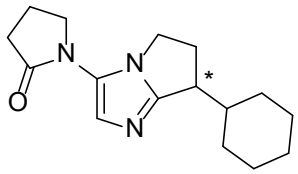
64% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (s, 1H), 3.89~3.67 (m, 2H), 3.07~2.94 (m, 1H), 2.71~260 (m, 1H), 2.41~2.30 (m, 1H), 2.08~2.00 (m, 1H), 1.79~1.55 (m, 5H), 1.32~0.98 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 131.2, 97.4, 43.9, 43.0, 41.2, 30.4, 30.0, 29.9, 26.3, 26.2, 26.1; HRMS (EI): calcd. for $C_{12}H_{17}BrN_2$ [M^+] 268.0575, found 268.0576.



(±)-1-(7-Cyclohexyl-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazol-3-yl)pyrrolidin-2-one (3p).

To CuI (0.05 mmol, 10 mol%) and K_2CO_3 (2.0 mmol, 4.0 eq.) under argon was added dioxane (3 mL) followed by *N,N'*-dimethyl ethylenediamine **L6** (0.05 mmol, 10 mol%), **1p** (0.5 mmol) and pyrrolidin-2-one (0.6 mmol). The reaction mixture was stirred at reflux for 24 h, cooled to rt, diluted with CH_2Cl_2 (10 mL), filtered, washed with CH_2Cl_2 (10 mL), and concentrated under reduced pressure. The crude residue was purified by flash chromatography.

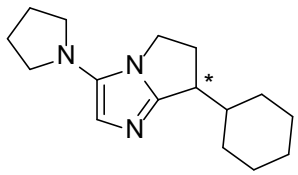
80% yield, a white solid. Mp = 76~78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (s, 1H), 4.01~3.85 (m, 2H), 3.71 (t, *J* = 3.2 Hz, 2H), 2.92~2.83 (m, 1H), 2.64~2.53 (m, 1H), 2.50 (t, *J* = 8.0 Hz, 2H), 2.35~2.23 (m, 1H), 2.23~2.13 (m, 2H), 2.13~2.07 (m, 1H), 1.78~1.69 (m, 2H), 1.69~1.57 (m, 3H), 1.31~0.98 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 154.0, 125.3, 123.0, 50.3, 45.0, 42.0, 41.3, 31.0, 30.6, 30.2, 26.4, 26.3, 26.2, 18.8; HPLC: Daicel CHIRALCEL OD-H, 25 cm × 4.6 μm, 0.5 mL/min, *i*-Propanol/Hexane = 70/30, Rt = 20.4 min, 25.6 min; HRMS (ESI): calcd. for $C_{16}H_{23}N_3O$ [M^+] 273.1841, found 273.1840.



(+)-1-(7-Cyclohexyl-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazol-3-yl)pyrrolidin-2-one ((+)-3p)

3p were separated using CSP-HPLC (Daicel CHIRALCEL OD, 15 cm × 0.46 cm, ethanol/hexanes = 10/90, 1 mL/min, 220 nm), Rt = 7.6 min for (+)-**3p**, 9.7 min for (-)-**3p**.

For (+)-**3p**: 48% yield, ee > 99%, a white solid. Mp = 89~91°C; $[\alpha]_D^{25}$ = 89 (MeOH, *c* 0.074).



(+)-7-Cyclohexyl-3-(pyrrolidin-1-yl)-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazole ((+)-Cy-PDPI)

In a dry two-necked flask, a solution of (+)-**3p** (54 mg, 0.20 mmol) in THF (5 mL) was added into a suspension of LAH (23 mg, 0.61 mmol, 3.0 eq.) in THF (1 mL), and the reaction mixture was heated at reflux for 4 h. After it was cooled to room temperature a few drops of Na_2SO_4 saturated solution was added to quench the reaction, then the reaction mixture was filtered and the residue was washed with MeOH. Solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on neutral Al_2O_3 (Pure PE followed Pure EtOAc, Rf = 0.35 in EtOAc/MeOH = 15/1) to give 34 mg of (+)-**Cy-PDPI**.

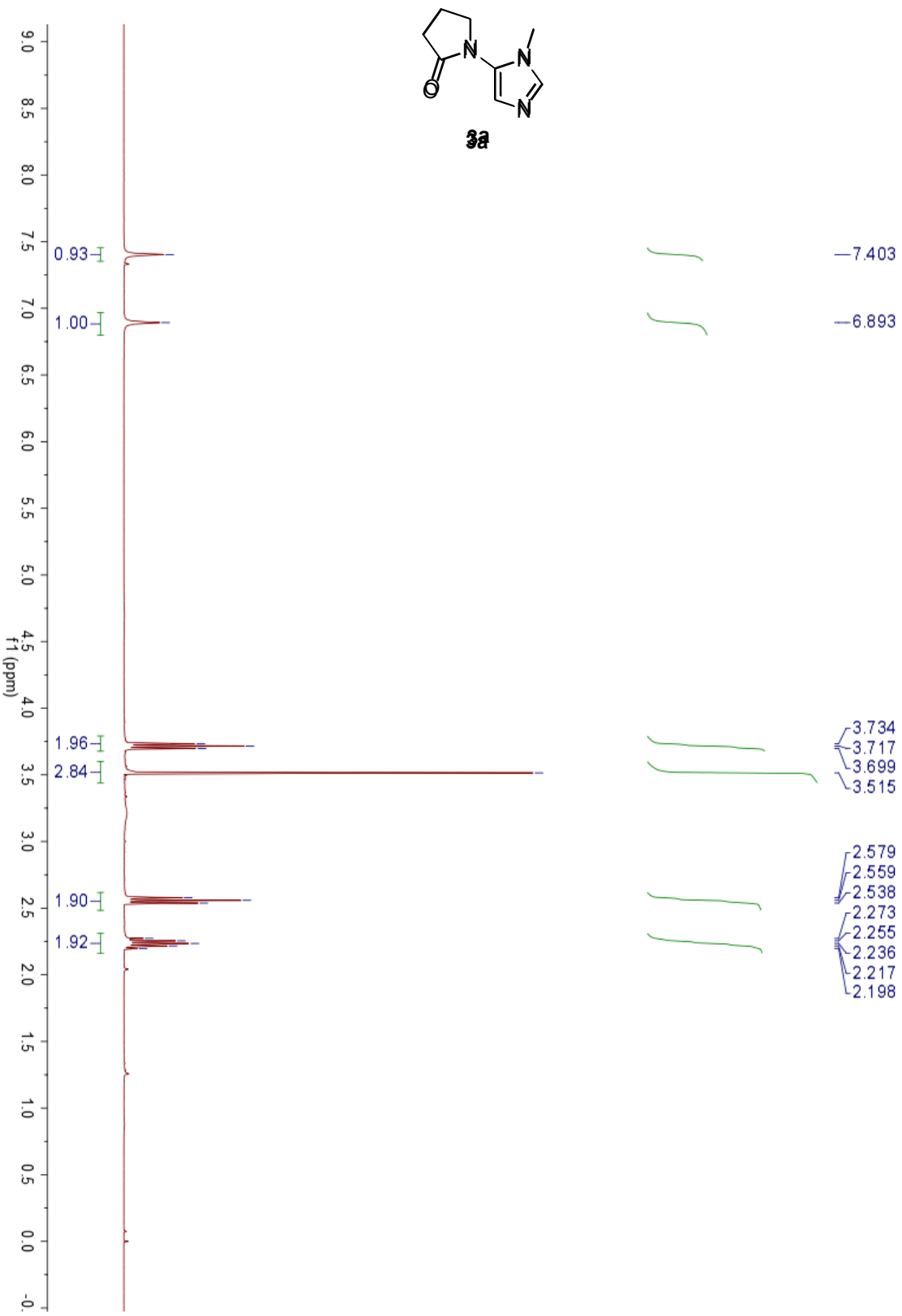
66% yield, a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.22 (s, 1H), 3.91~3.74 (m, 2H), 3.13~2.98 (m, 4H), 2.86~2.77 (m, 1H), 2.62~2.51 (m, 1H), 2.33~2.21 (m, 1H), 2.14~2.04 (m, 1H),

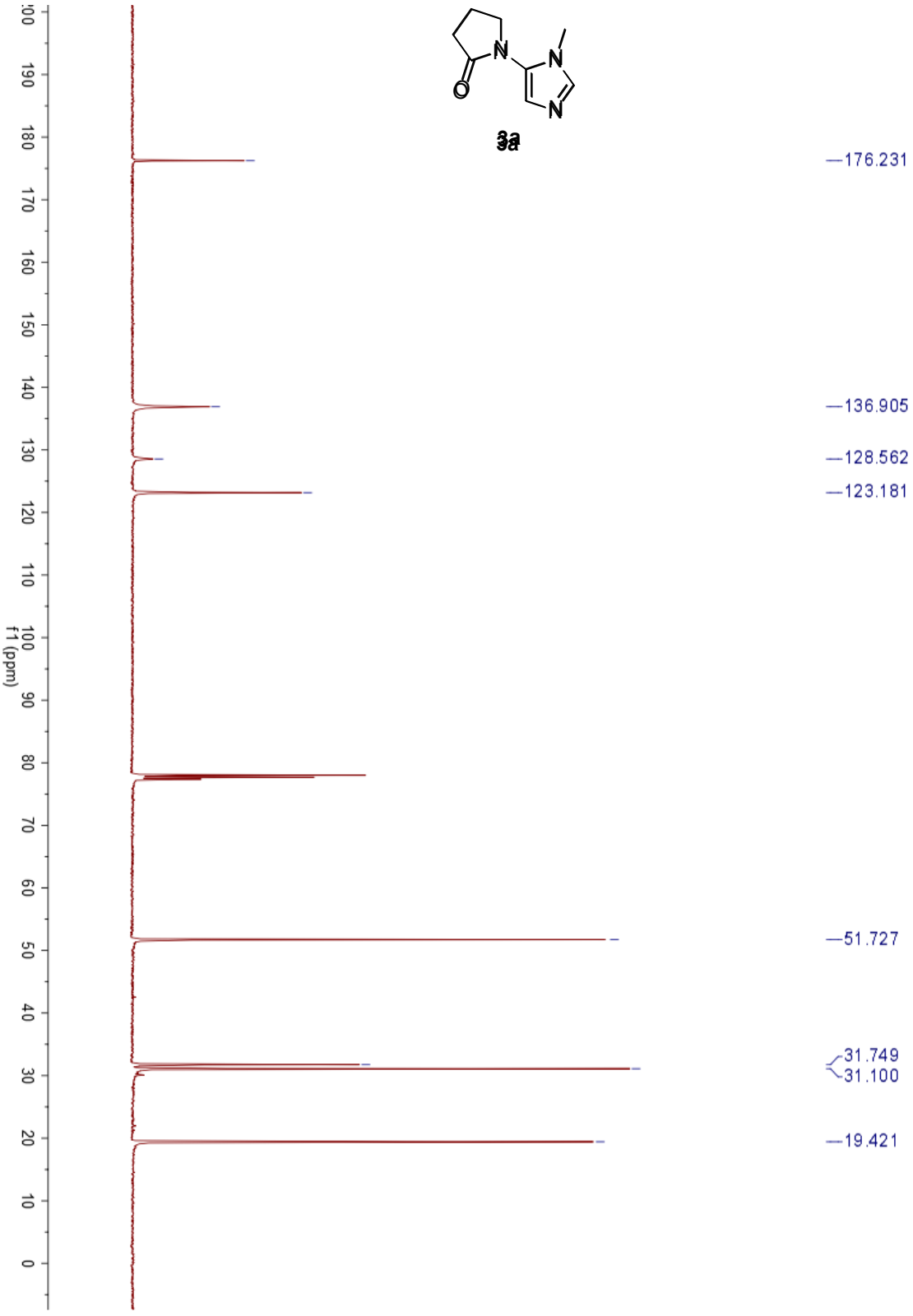
1.96~1.85 (m, 4H), 1.77~1.54 (m, 5H), 1.30~0.97 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 138.9, 112.9, 50.9, 43.5, 41.51, 41.47, 30.9, 30.6, 30.1, 26.4, 26.34, 26.27, 24.5; $[\alpha]_D^{37}$ = 62 (MeOH, *c* 0.129); HRMS (EI): calcd. for $C_{16}H_{25}N_3$ [M^+] 259.2048, found 259.2050.

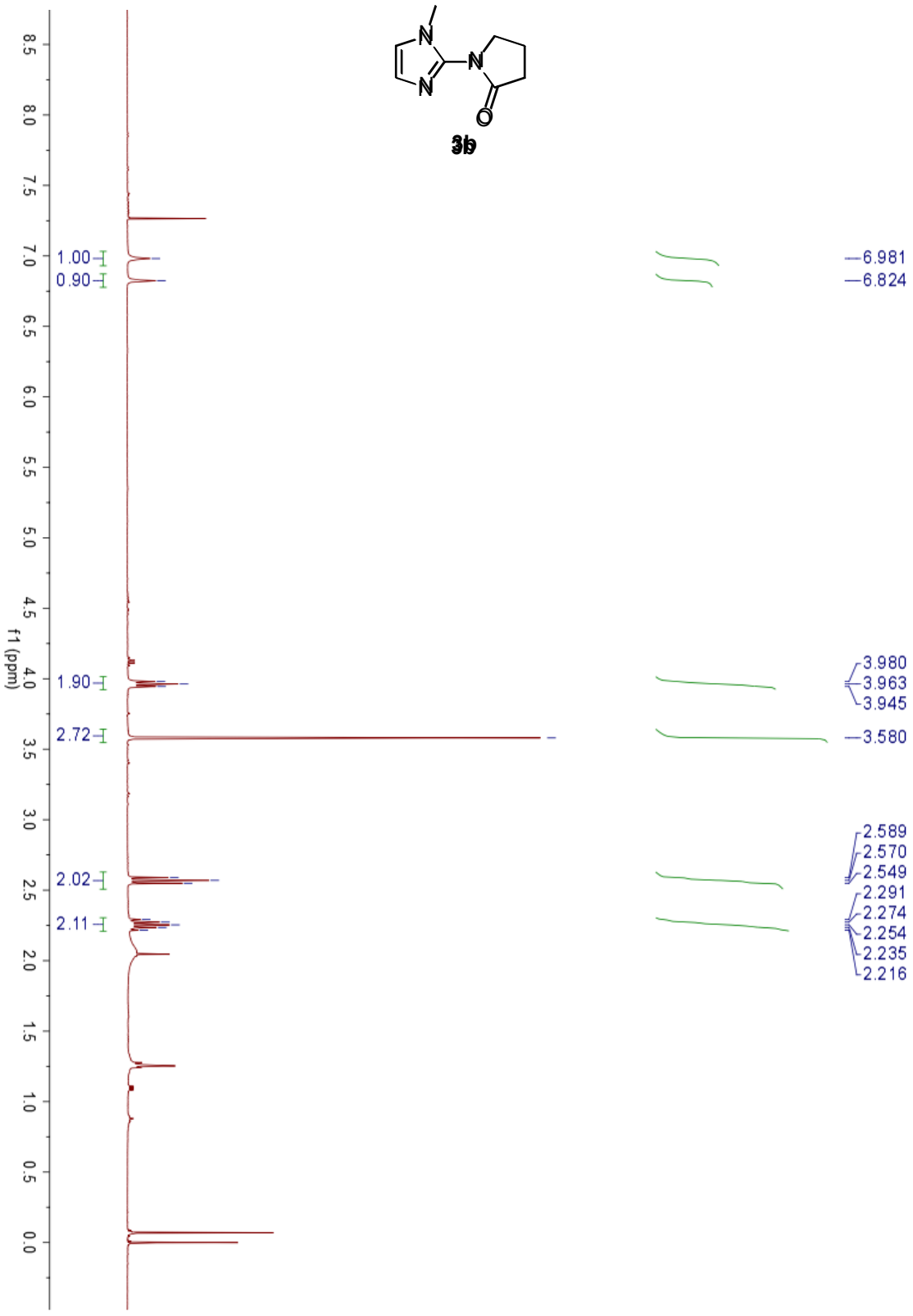
4. Reference

[1] Z. Zhang, F. Xie, J. Jia, W. Zhang, *J. Am. Chem. Soc.* 2010, **132**, 15939.

5. NMR Spectra



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1.90
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2.02
2.11
6.981
6.824
3.980
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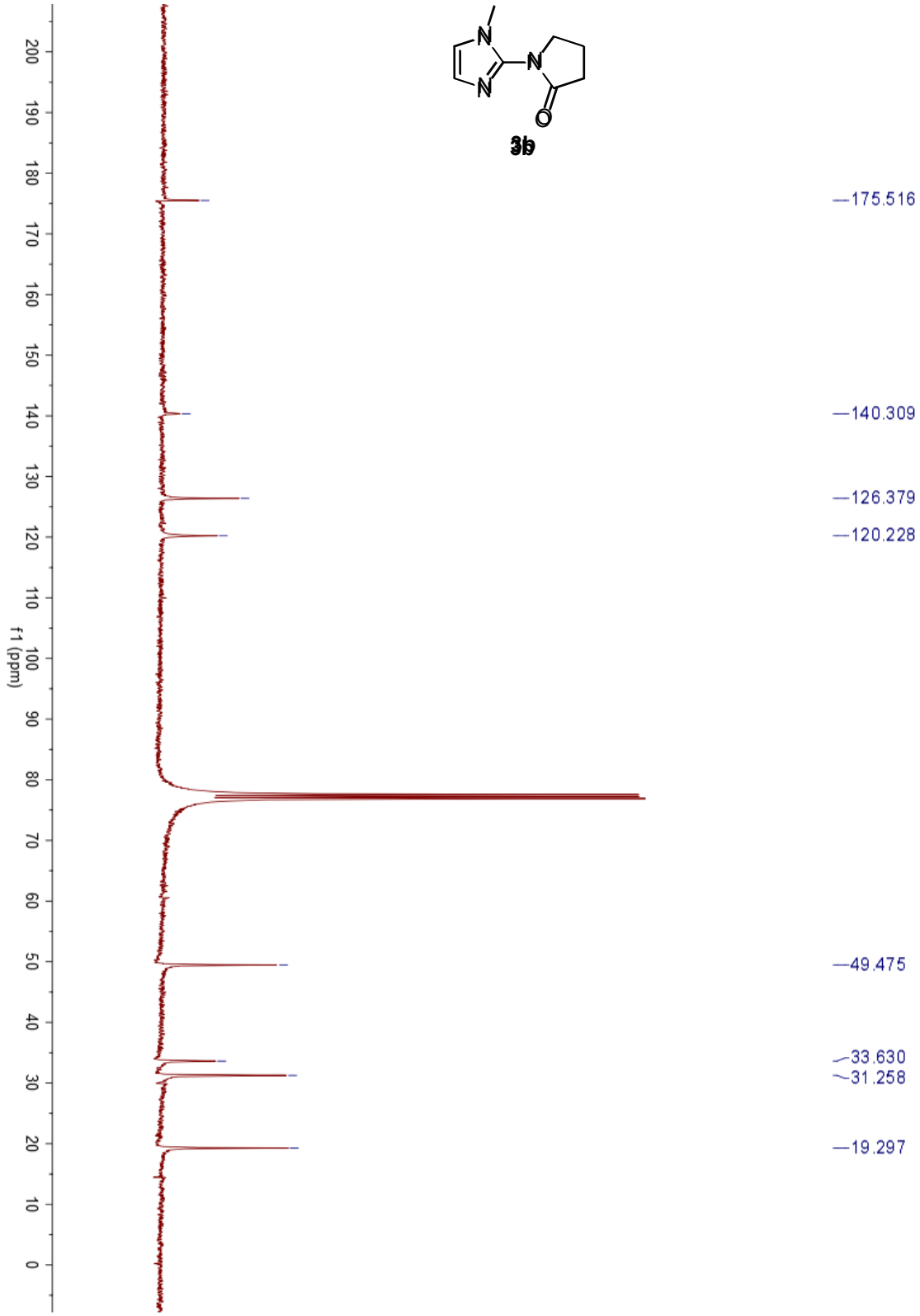
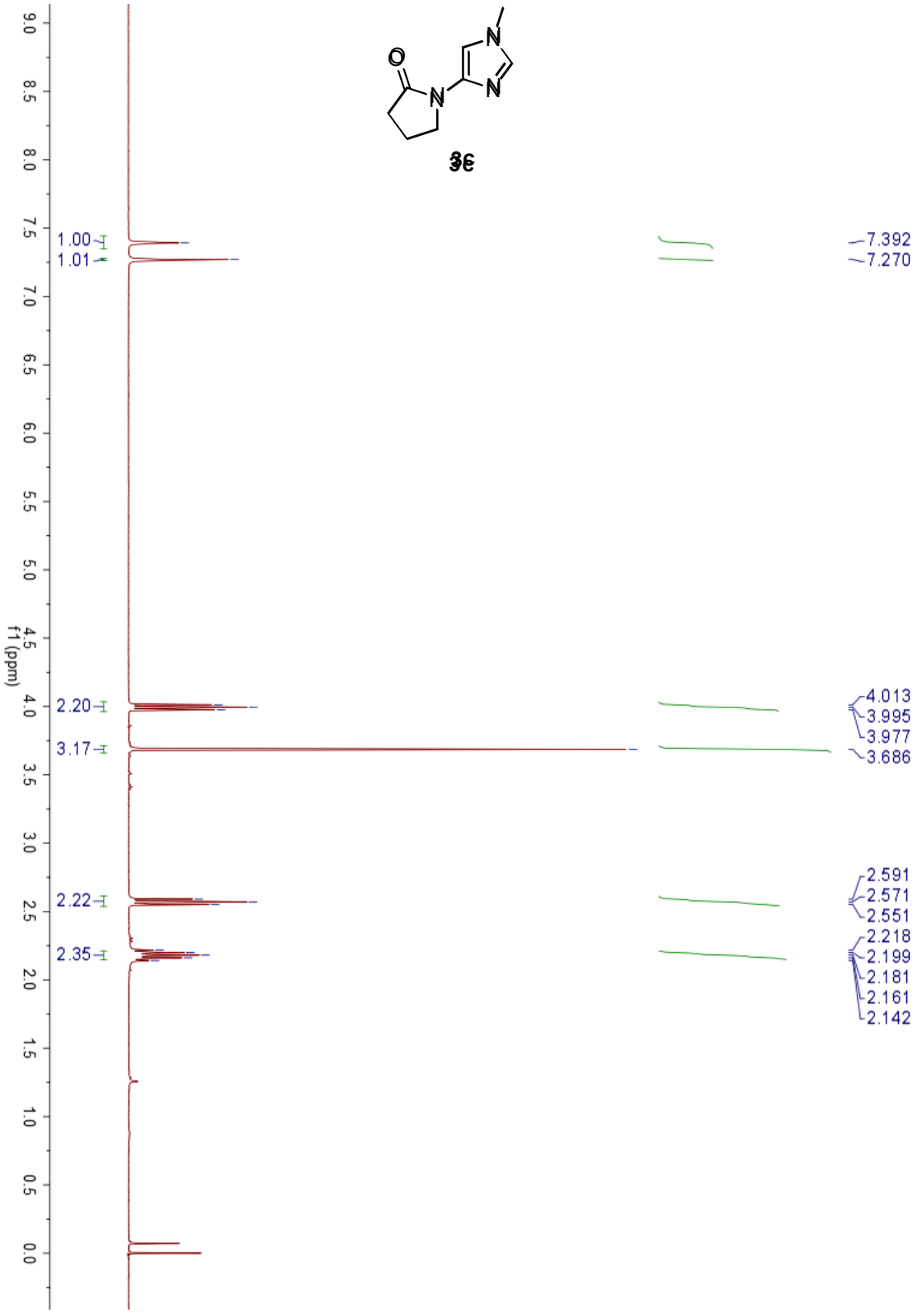
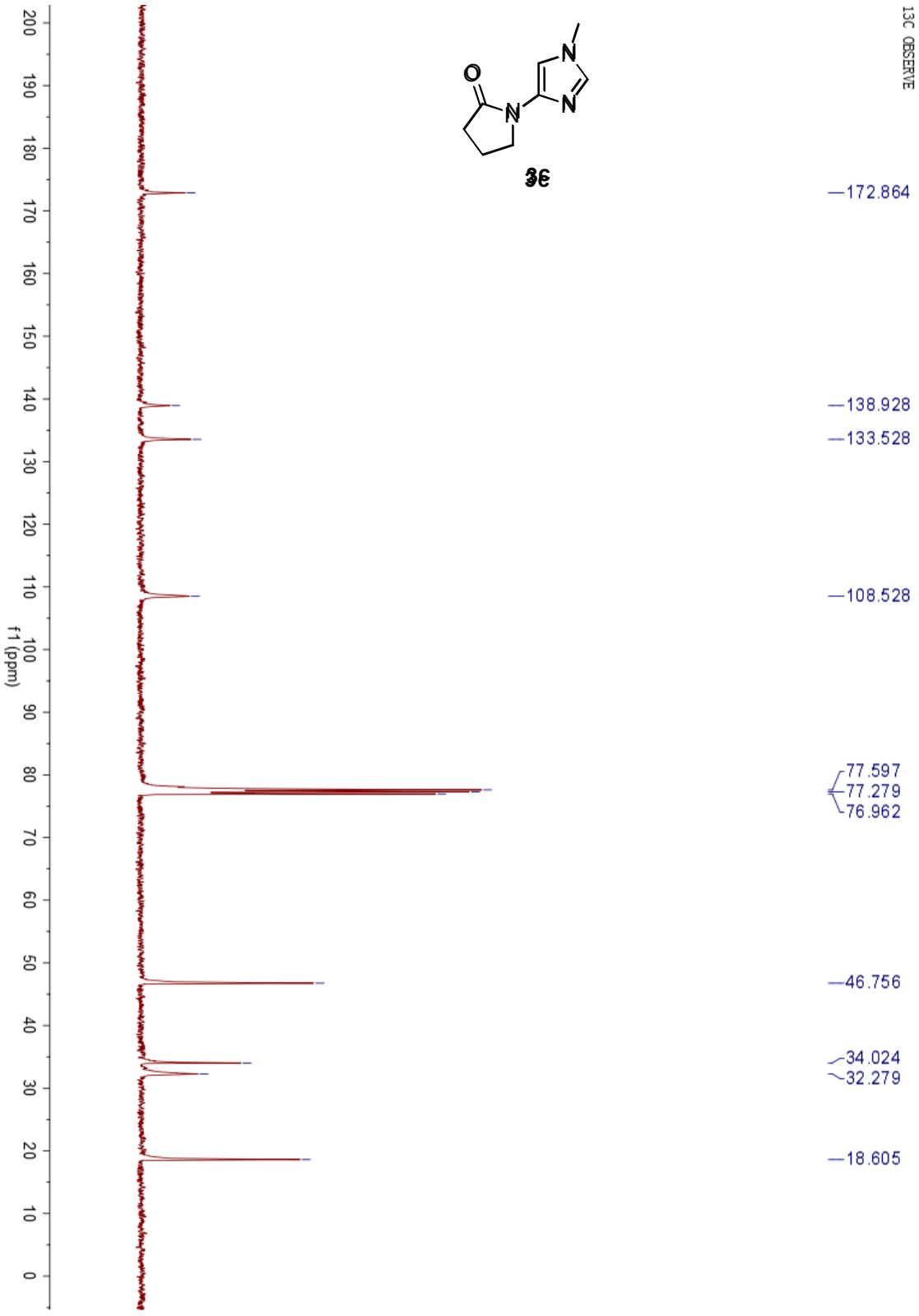
2.549
2.291
2.274
2.254
2.235
2.216





3e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200
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180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O
N
N
N
3e
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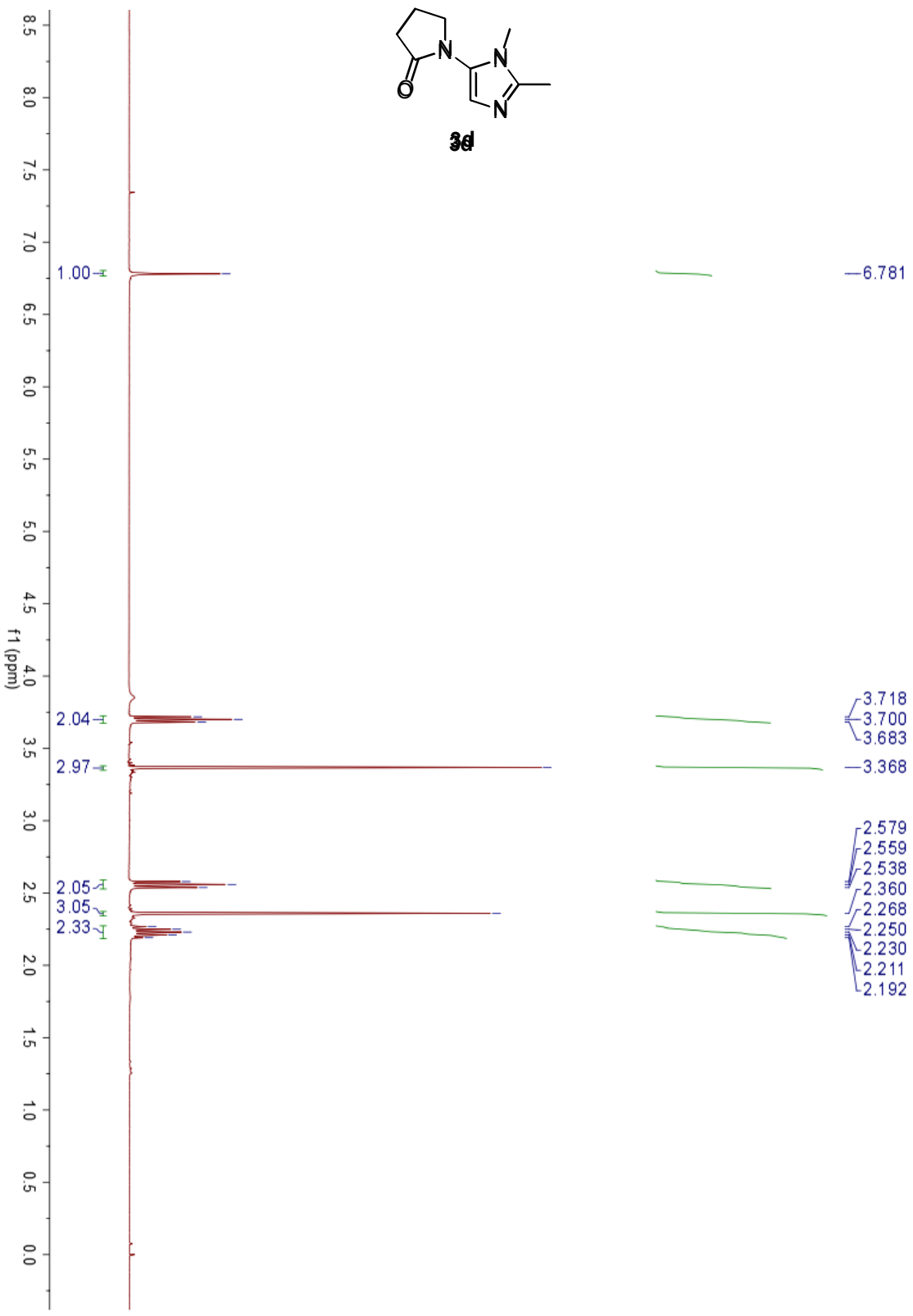
133.528
108.528
77.597
77.279
76.962
46.756
34.024
32.279
18.605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2.05
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2.33
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3.718
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2.360
2.268
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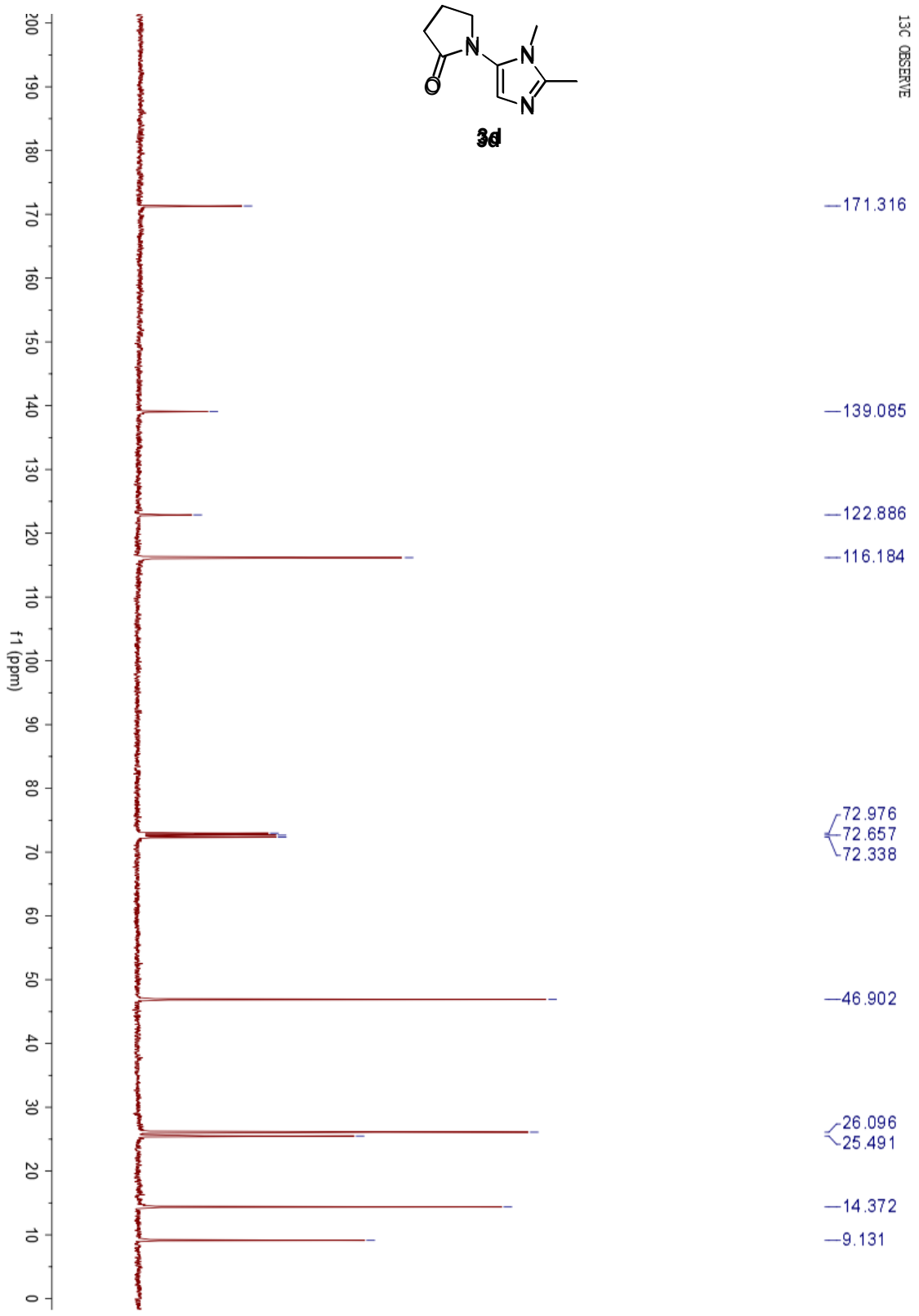
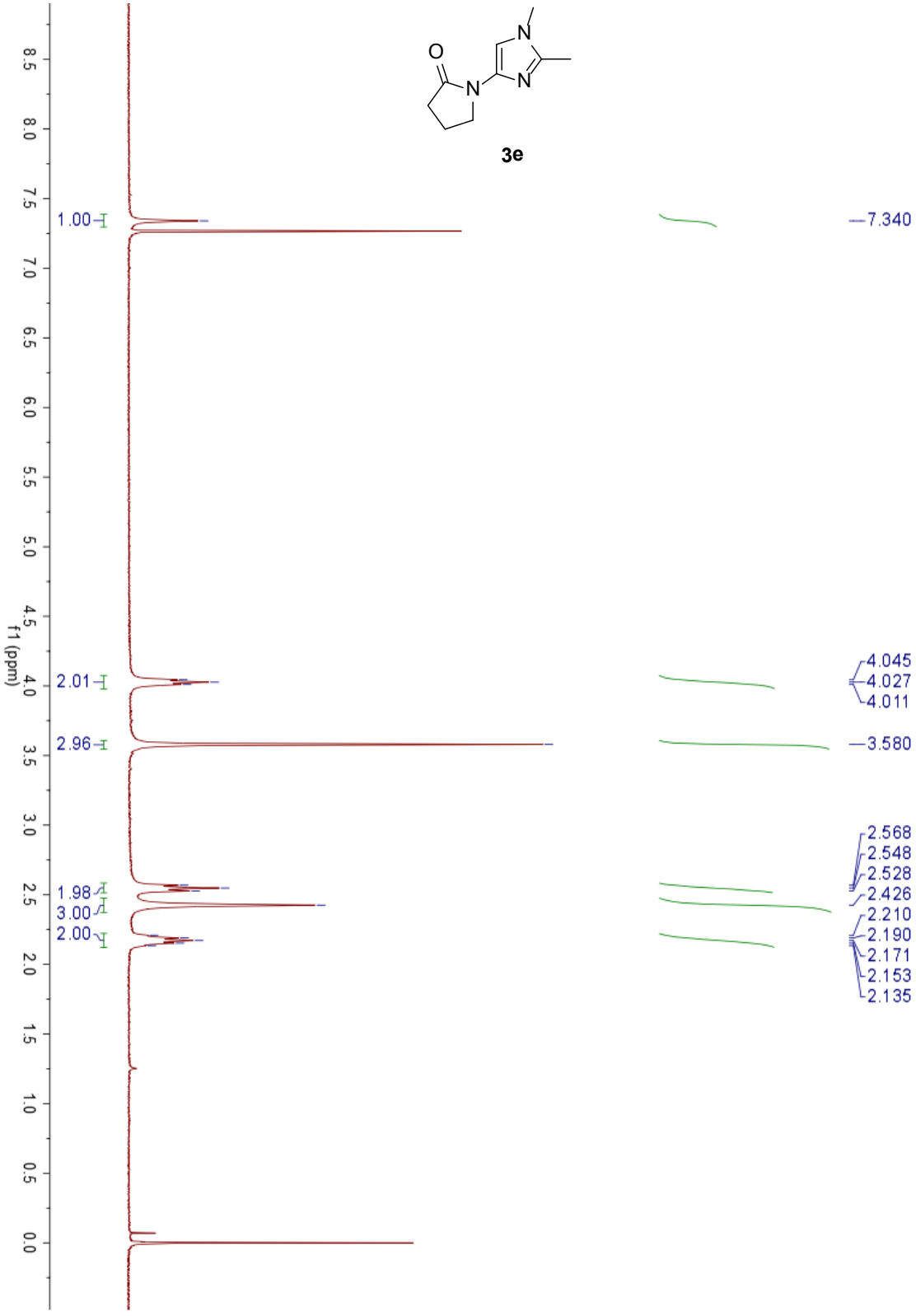
2.230
2.211
2.192


13C OBSERVE
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
171.316
139.085
122.886
116.184
72.976
72.657
72.338
46.902
26.096
25.491
14.372
9.131
O
N
N
N

3d


O
N
N
N
3e
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2.01
2.96
1.98
3.00
2.00
7.340
4.045
4.027
4.011
3.580
2.568
2.548
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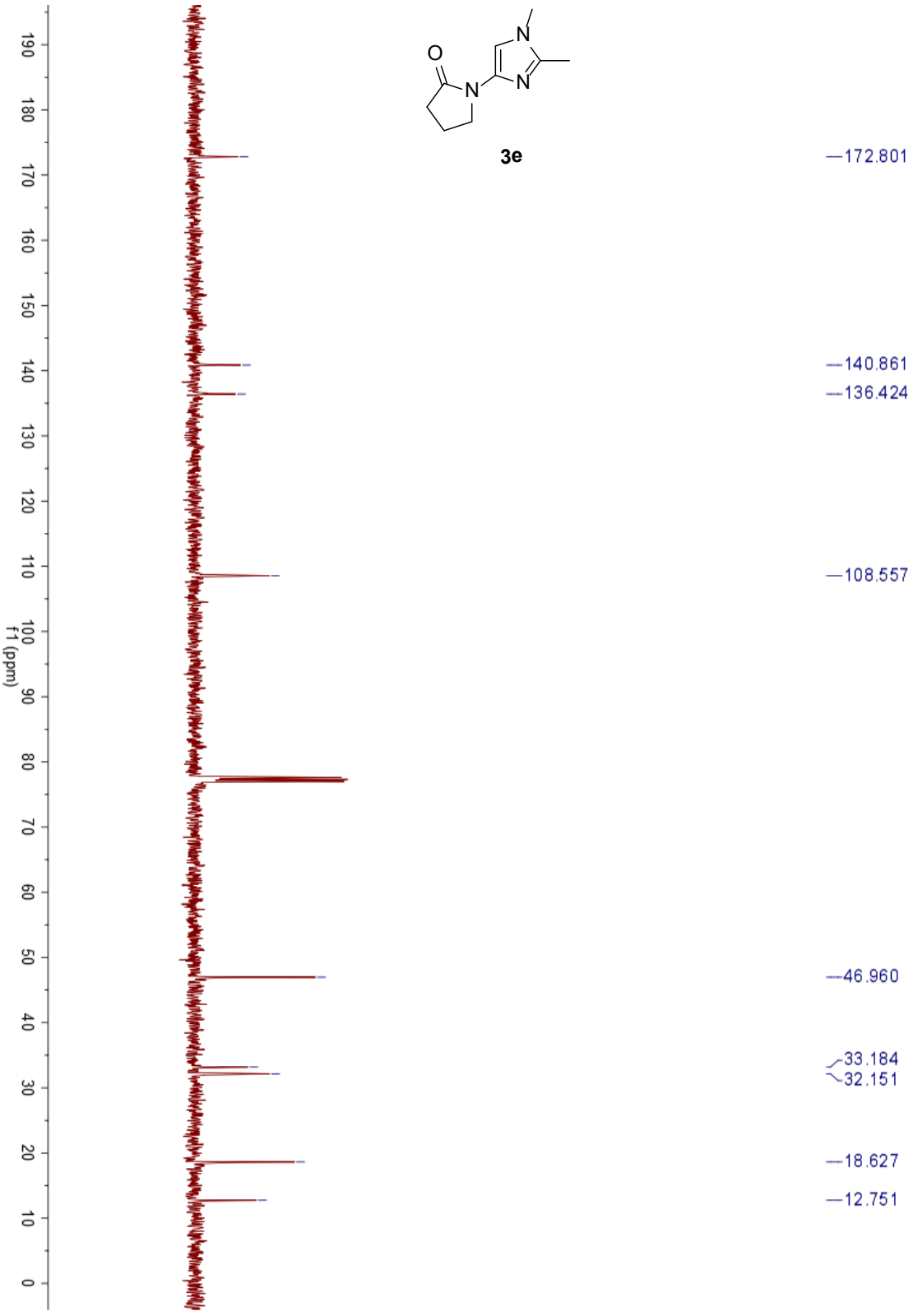
2.426
2.210
2.190
2.171
2.153
2.135
f1 (ppm)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N
N
N
3e
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46.960
33.184
32.151
18.627
12.751
f1 (ppm)
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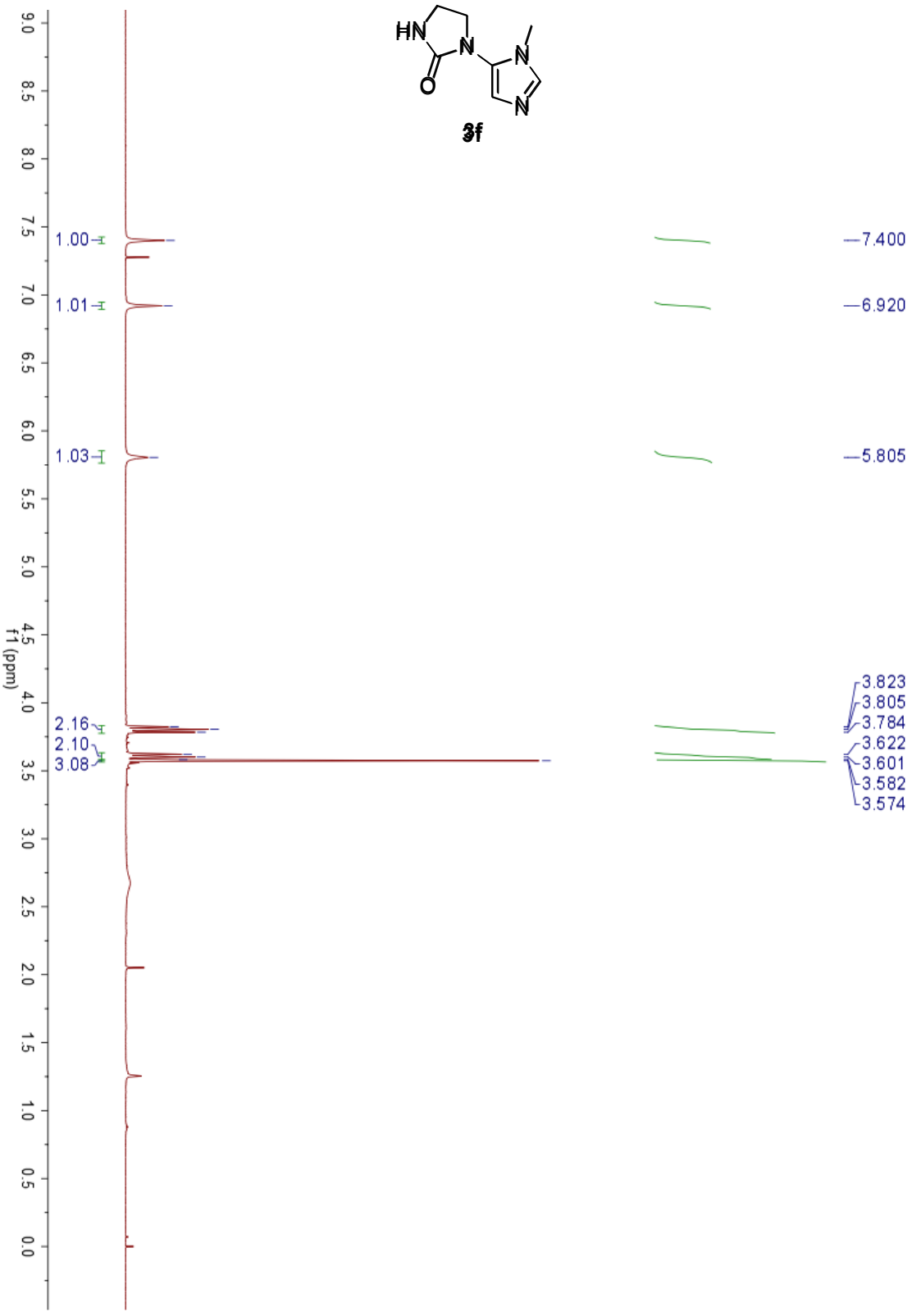
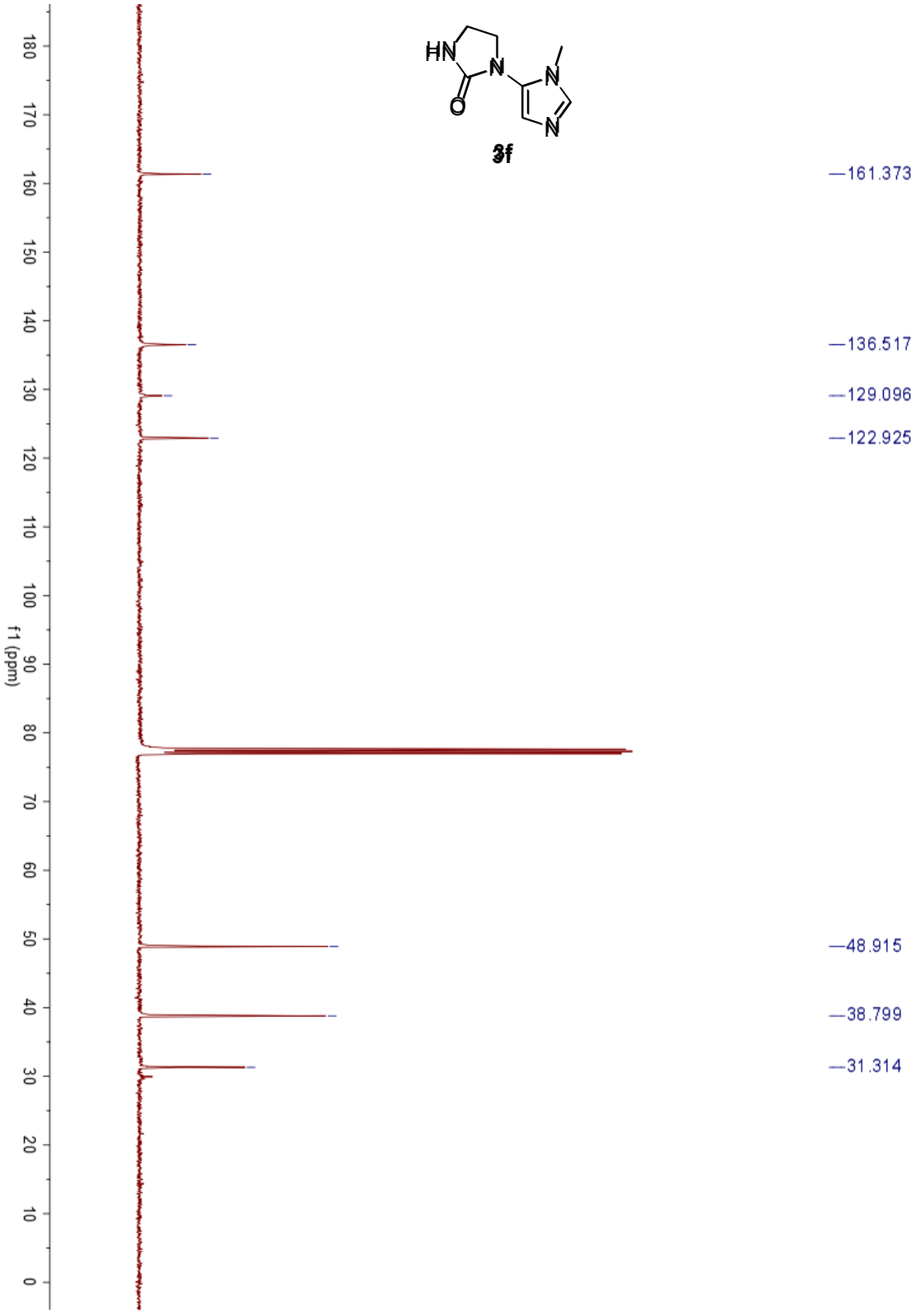
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


HN
N
N
N
O
3f
1.00
1.01
1.03
2.16
2.10
3.08
7.400
6.920
5.805
3.823
3.805
3.784
3.622
3.601
3.582
3.574
f1 (ppm)


HN
N
N
N
O
3f
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—136.517
—129.096
—122.925
—48.915
—38.799
—31.314
f1 (ppm)
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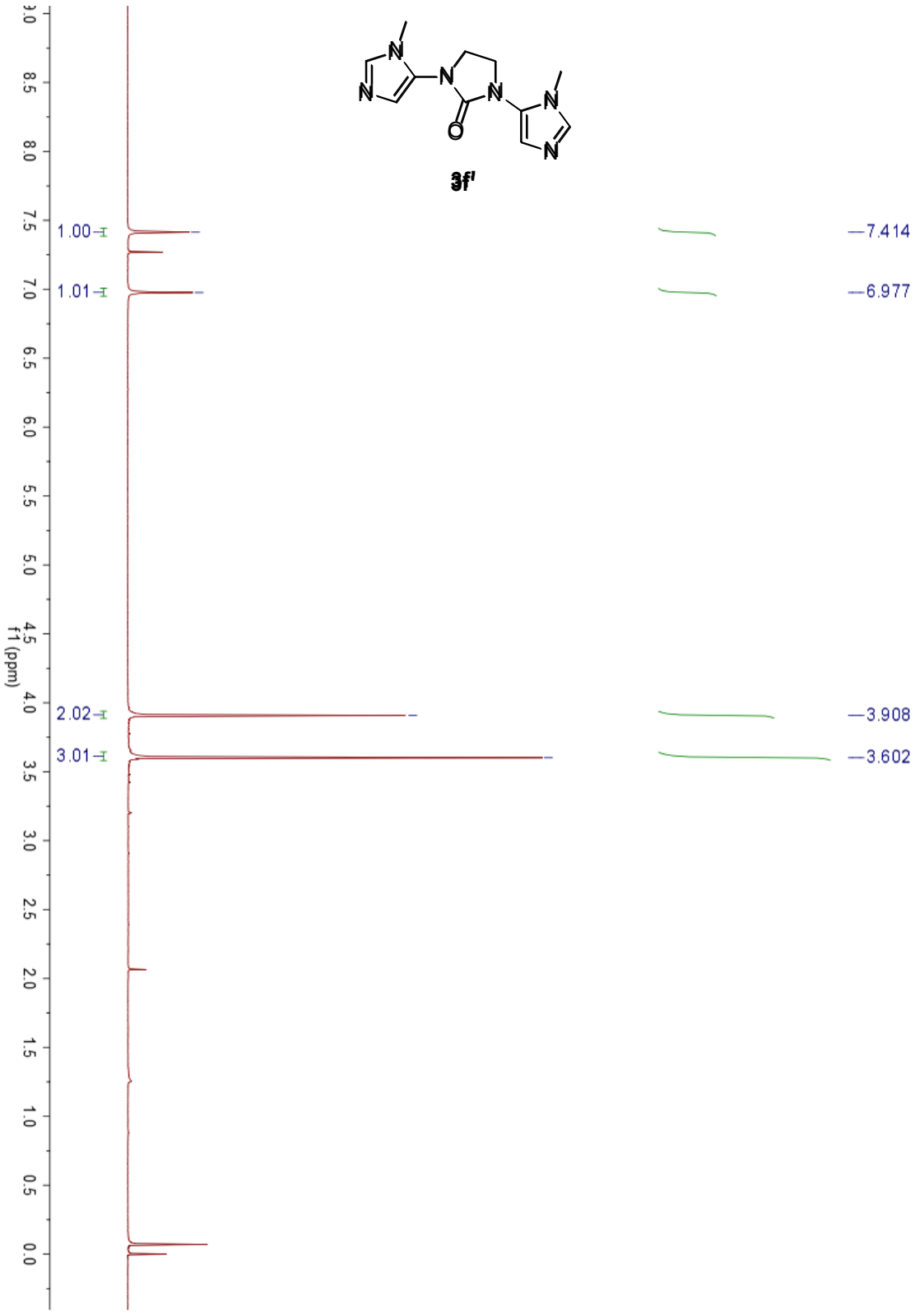
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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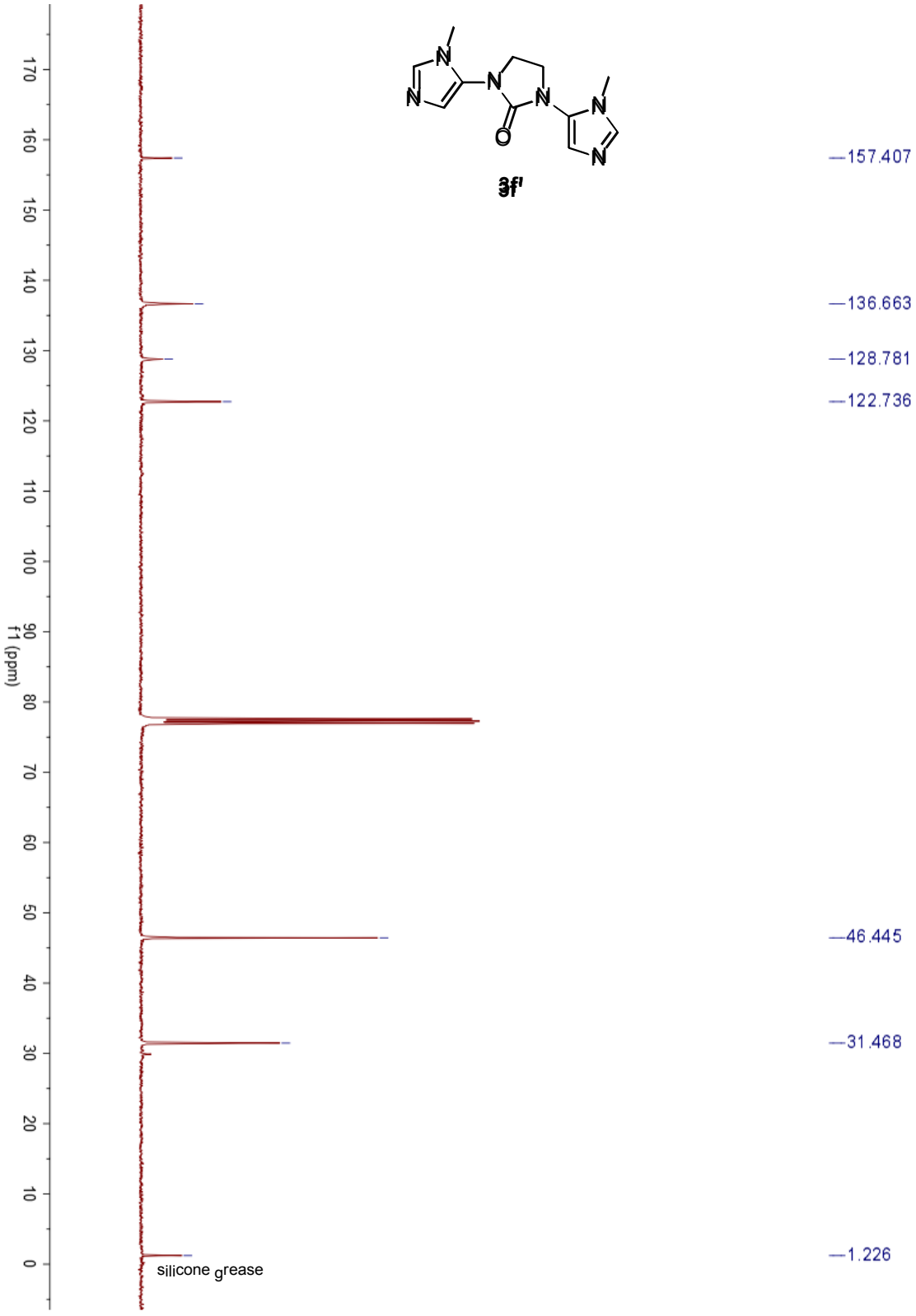
3.01
7.414
6.977
3.908
3.602
f1 (ppm)


3f'
3f
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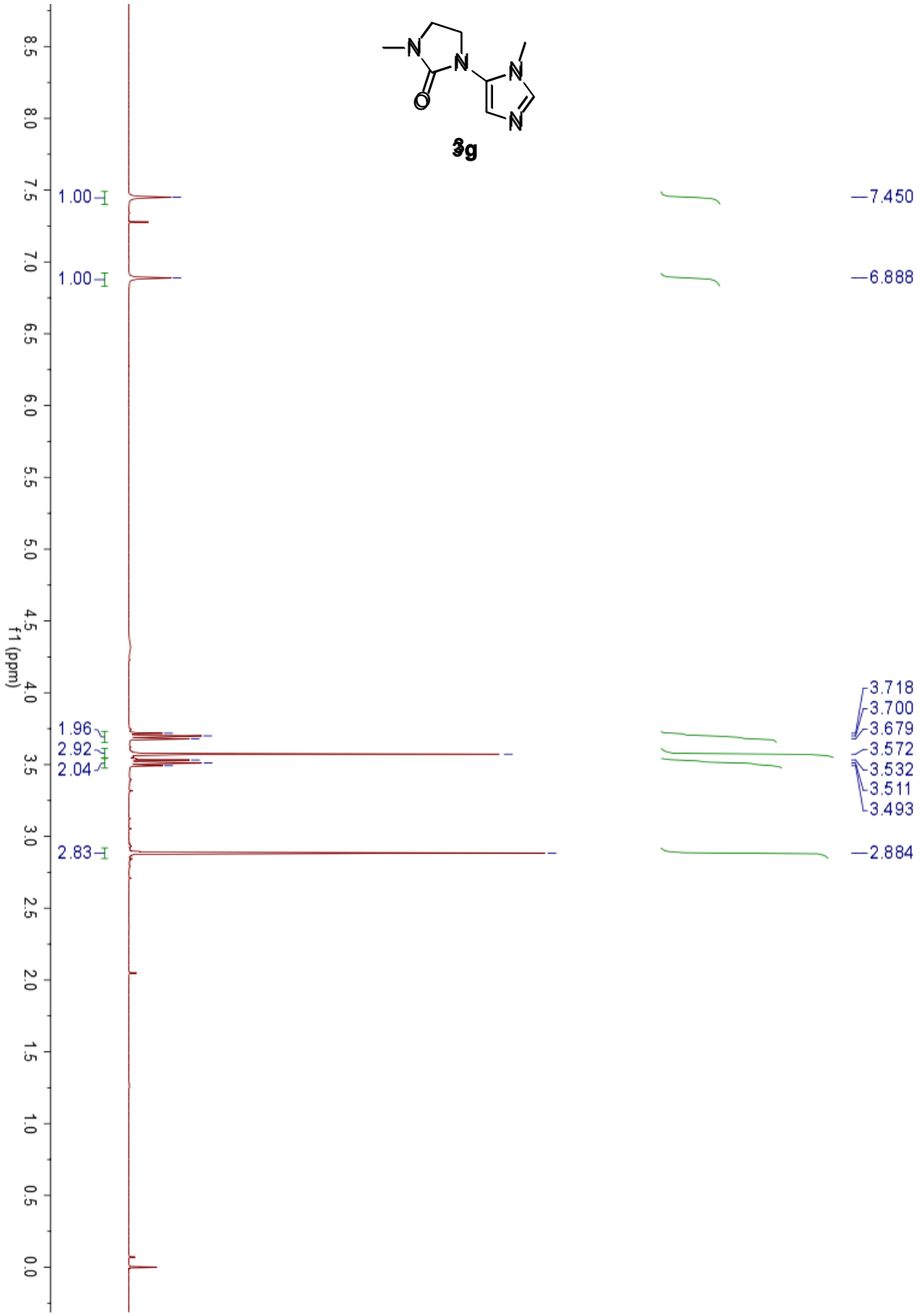
1.226
silicone grease
f1 (ppm)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2.04
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3.700
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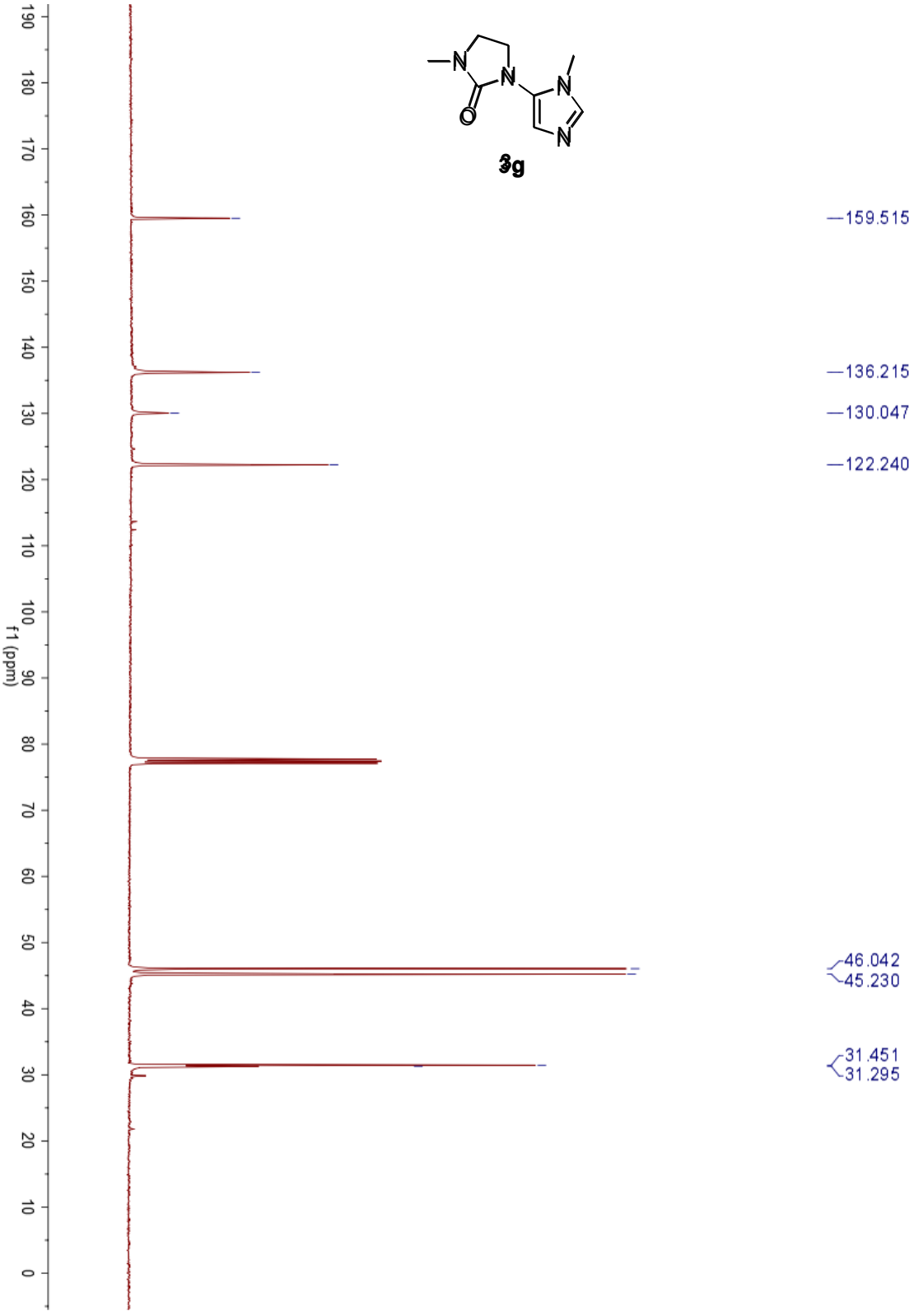
3.532
3.511
3.493
2.884
f1 (ppm)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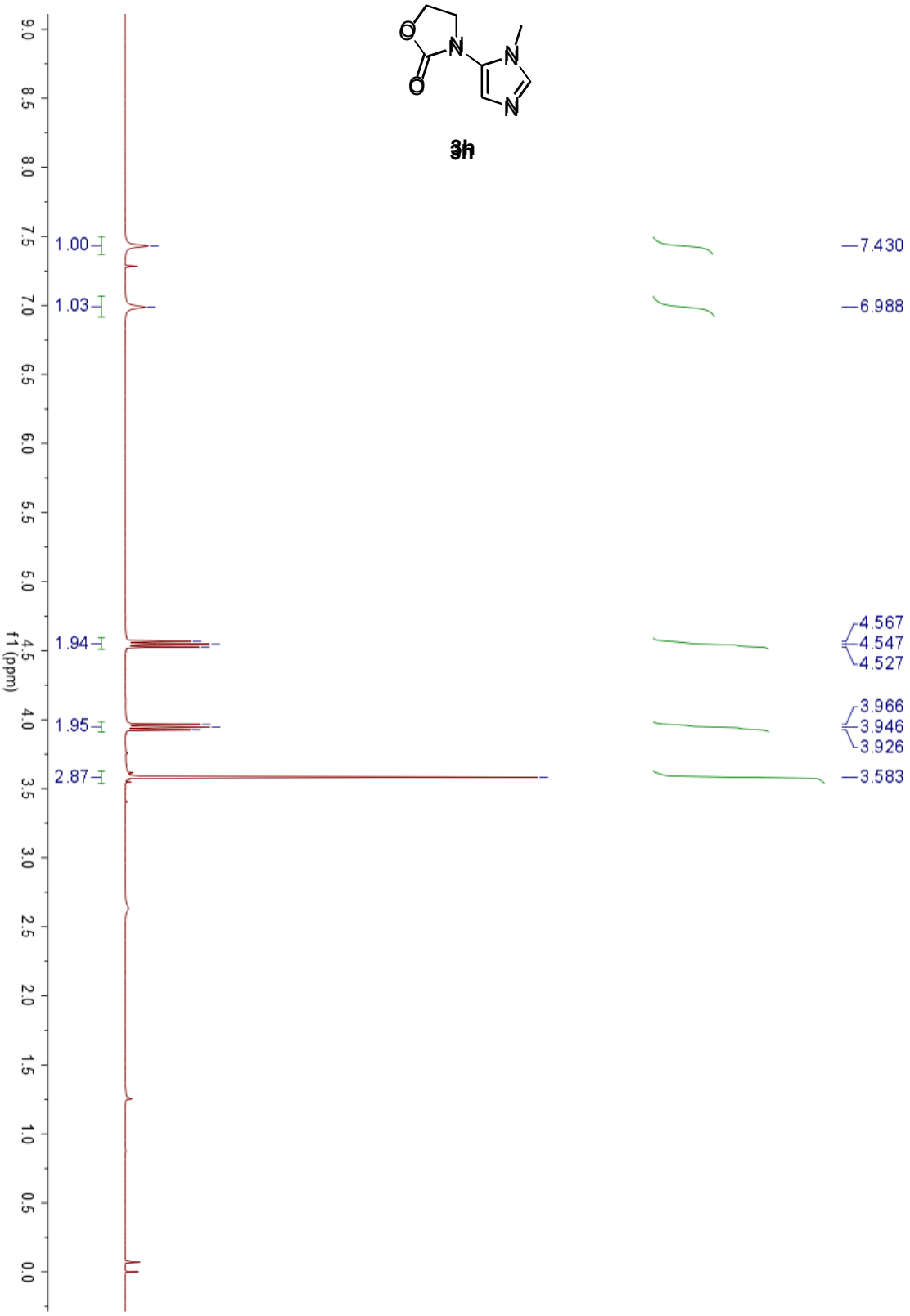
f1 (ppm)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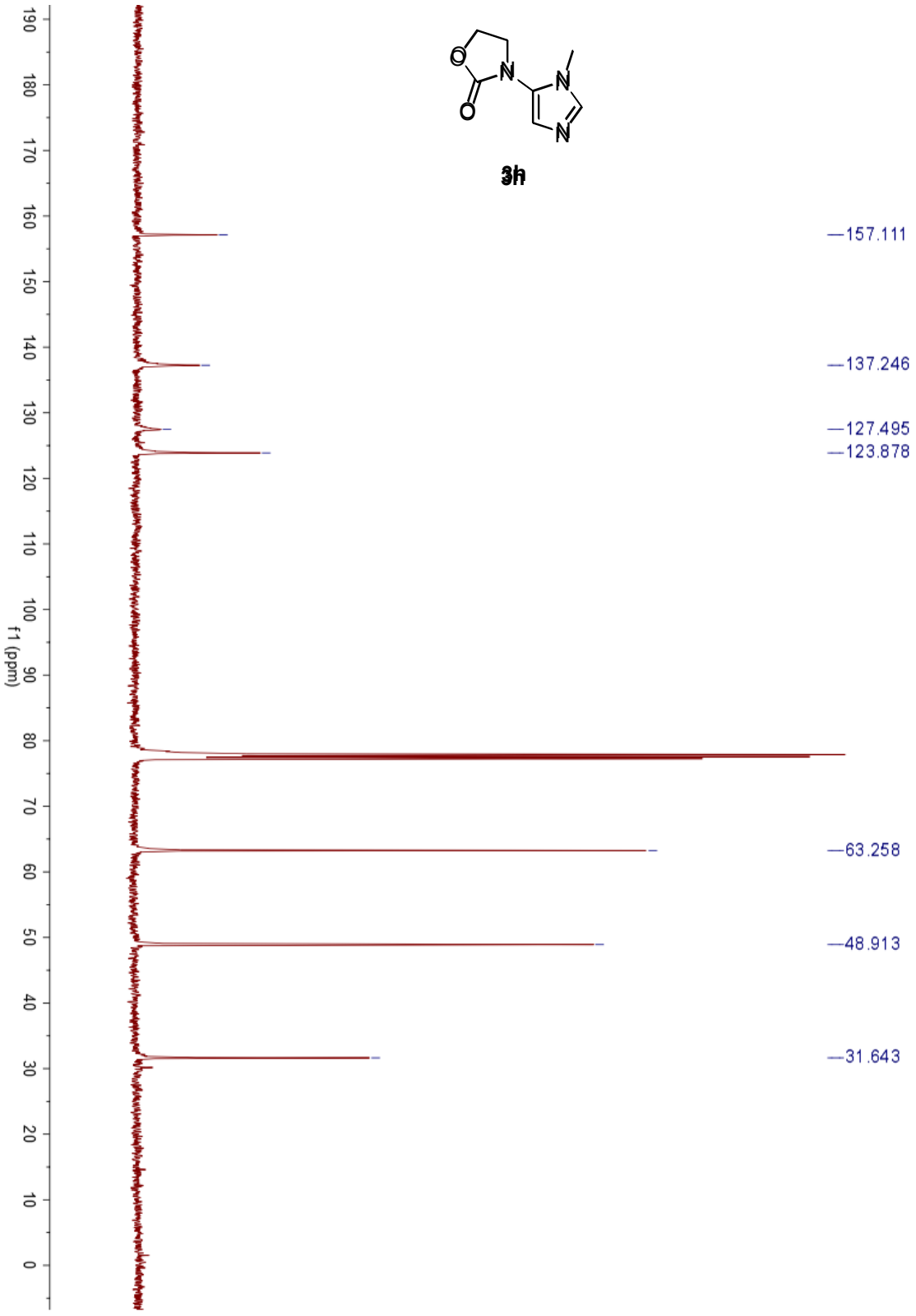
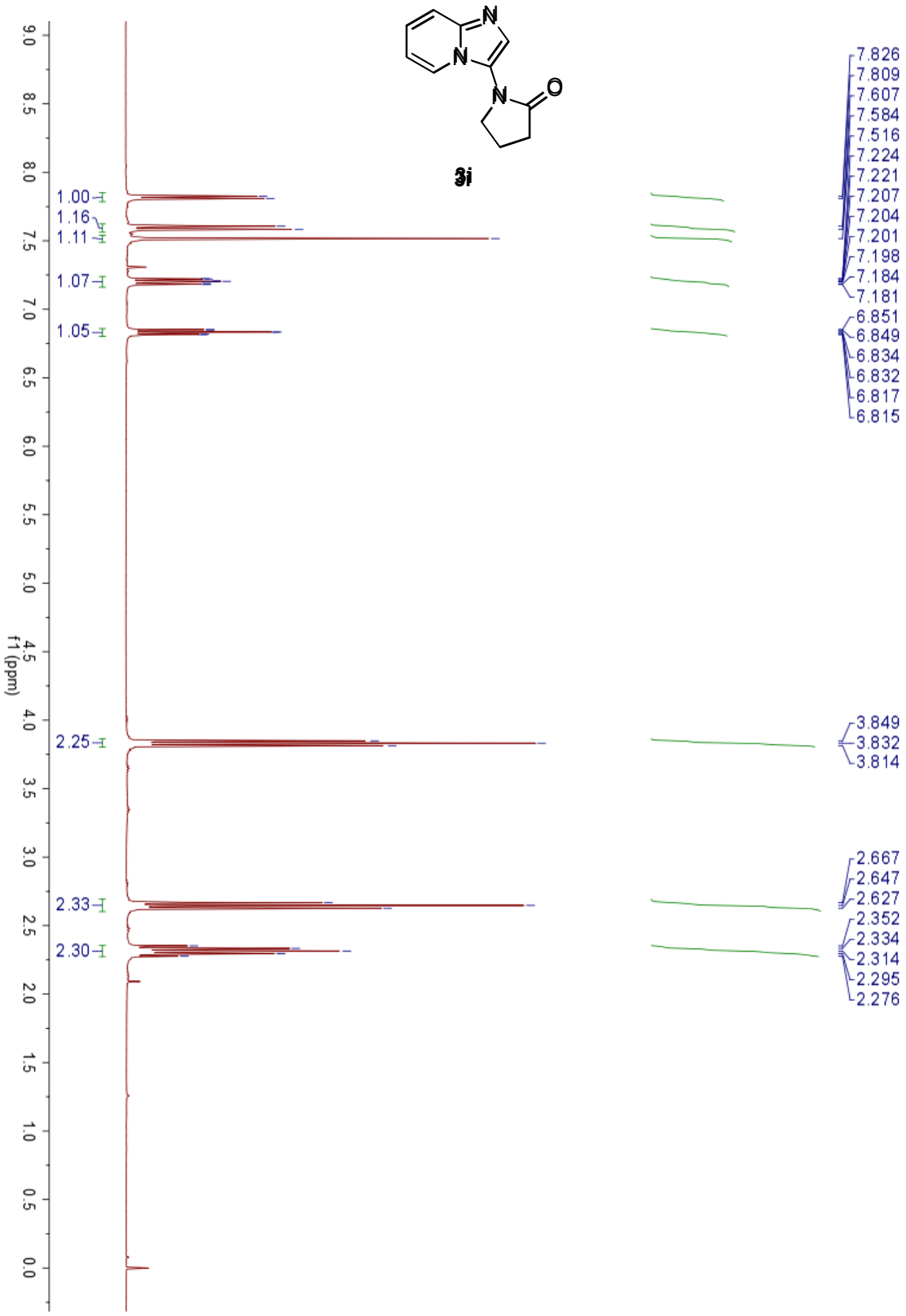
3.946
3.926
3.583
f1 (ppm)

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1.05
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2.30
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7.584
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7.224
7.221
7.207
7.204
7.201
7.198
7.184
7.181
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6.849
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2.352
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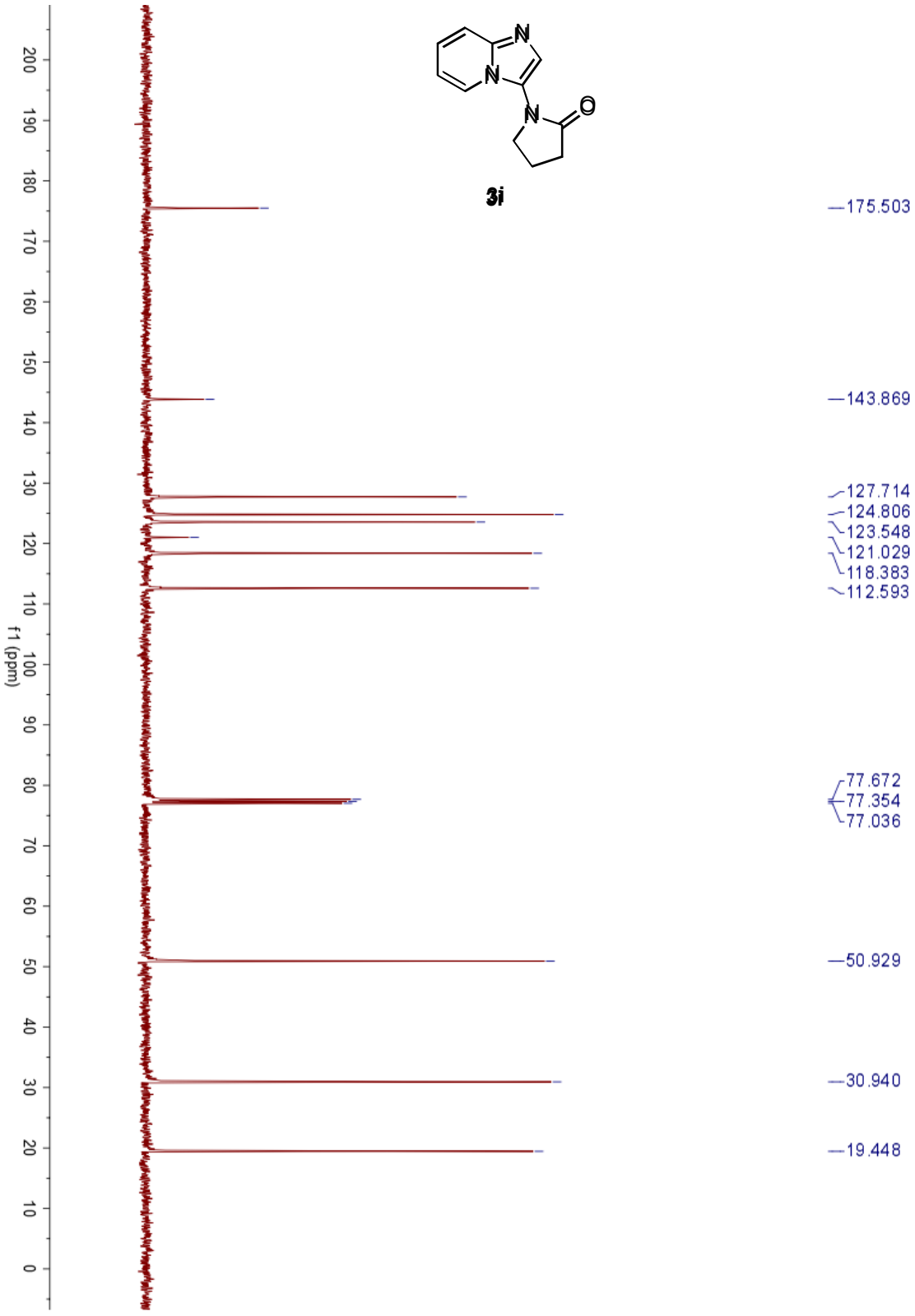
2.314
2.295
2.276


3i
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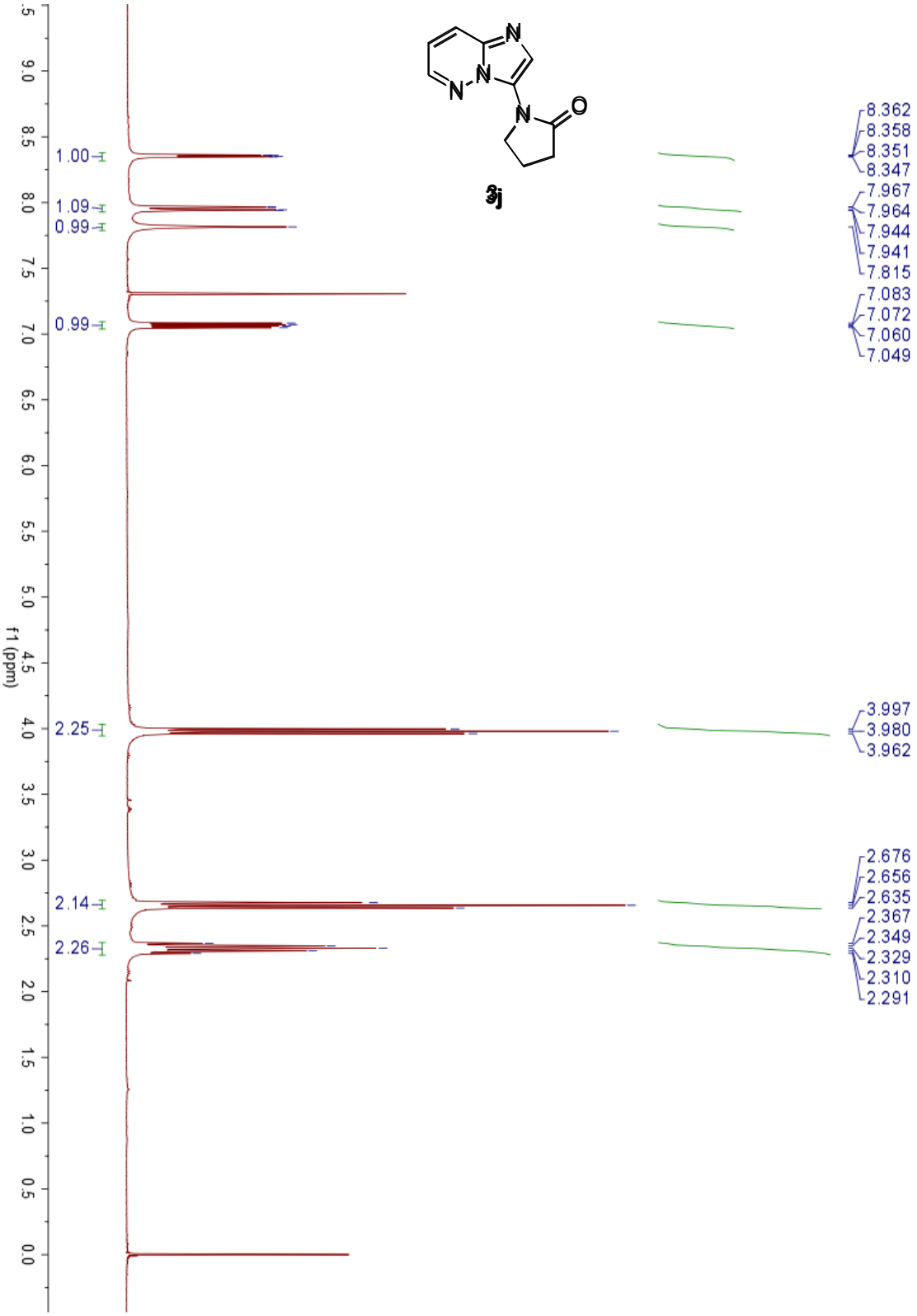
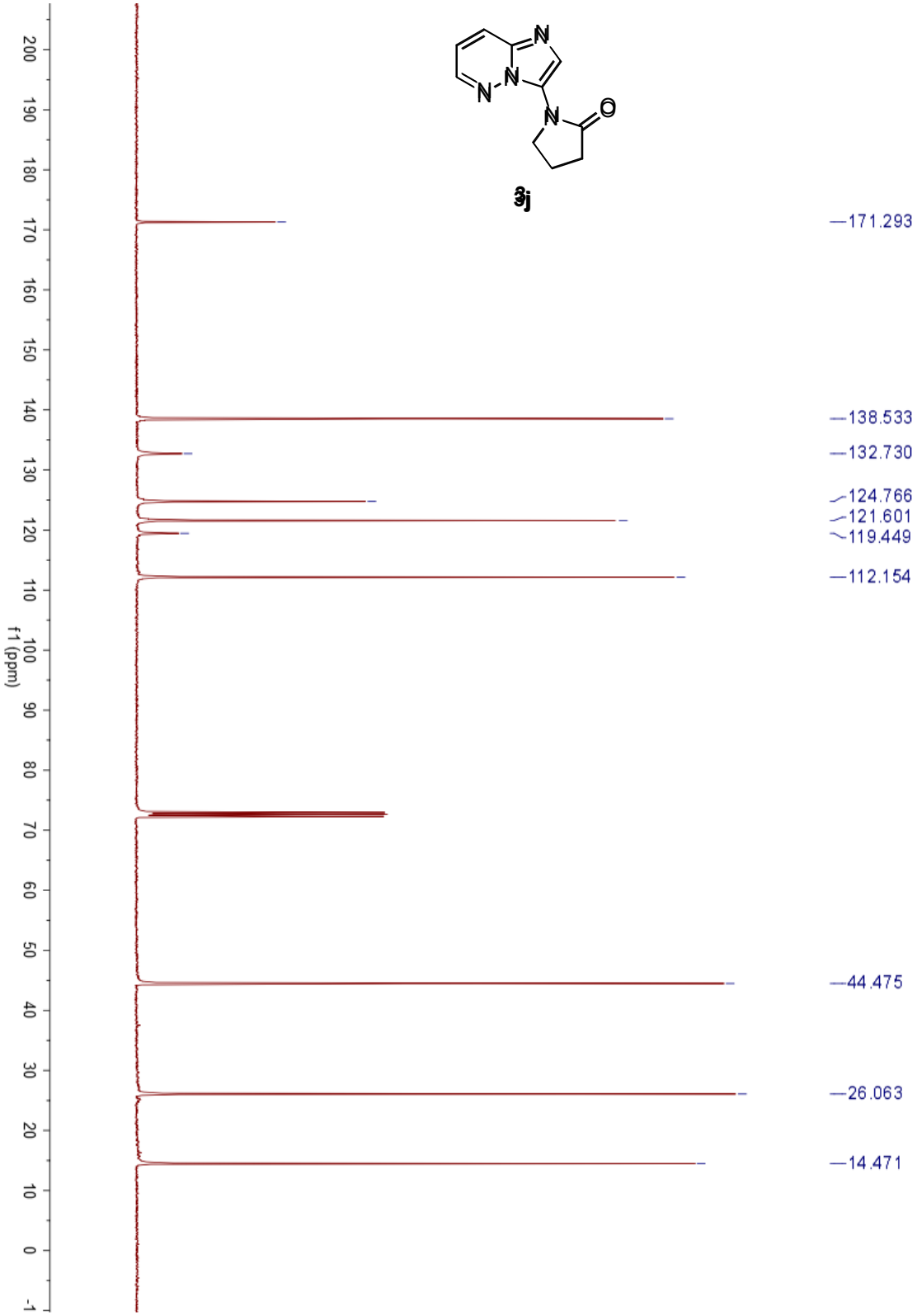
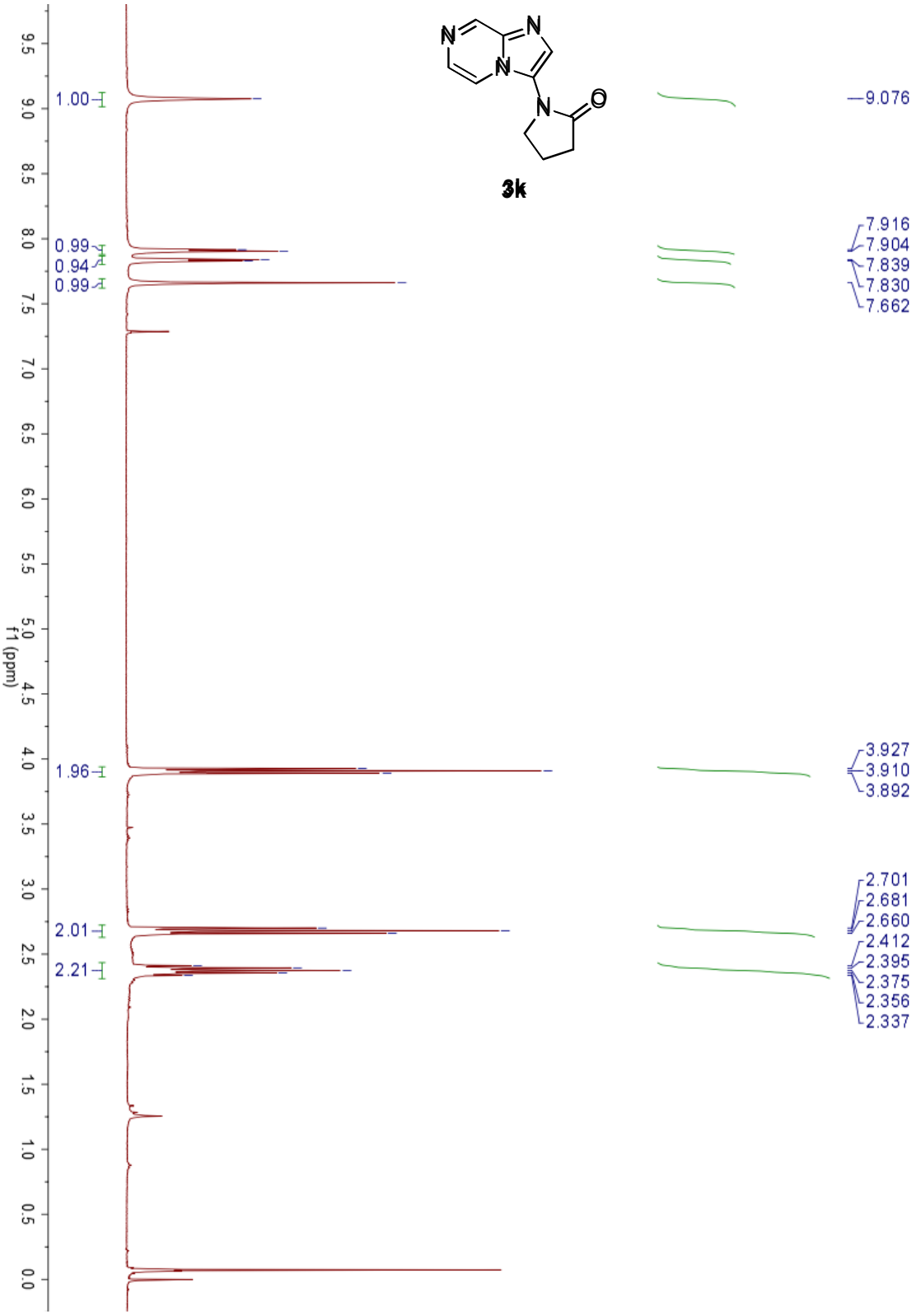
19.448
f1 (ppm)



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0.94
0.99
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7.916
7.904
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7.662
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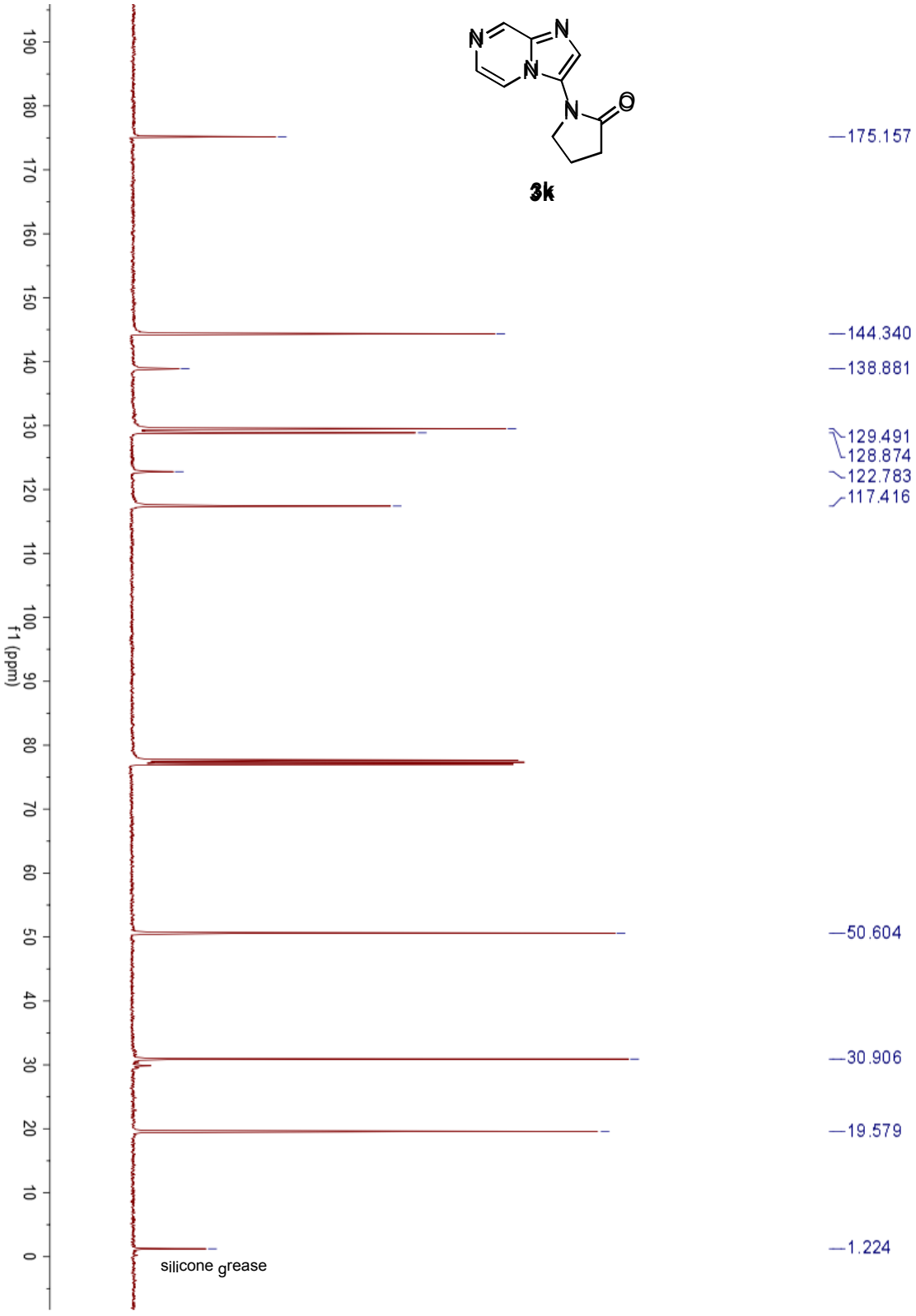
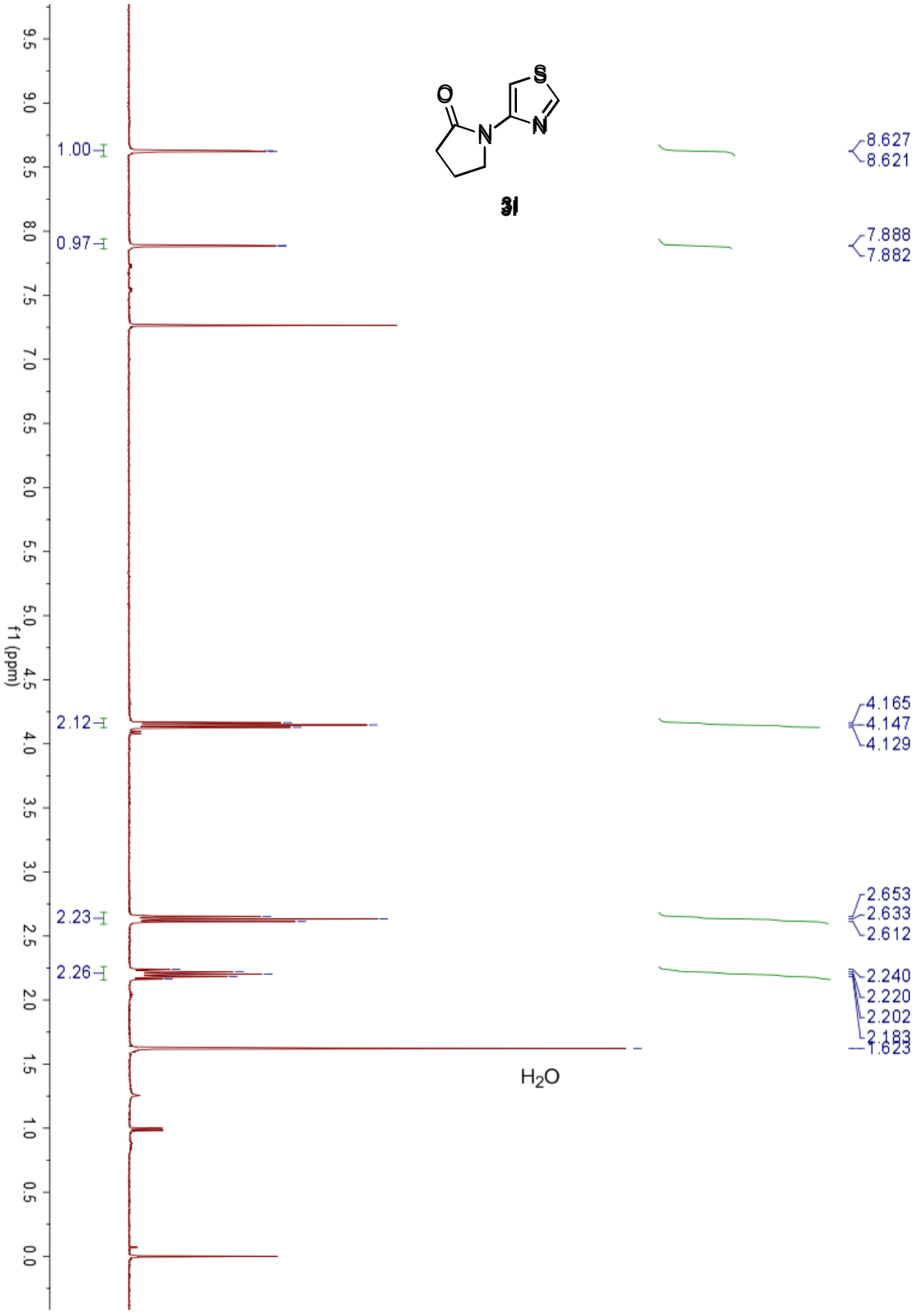
2.337
f1 (ppm)




O
N
S
N
3l
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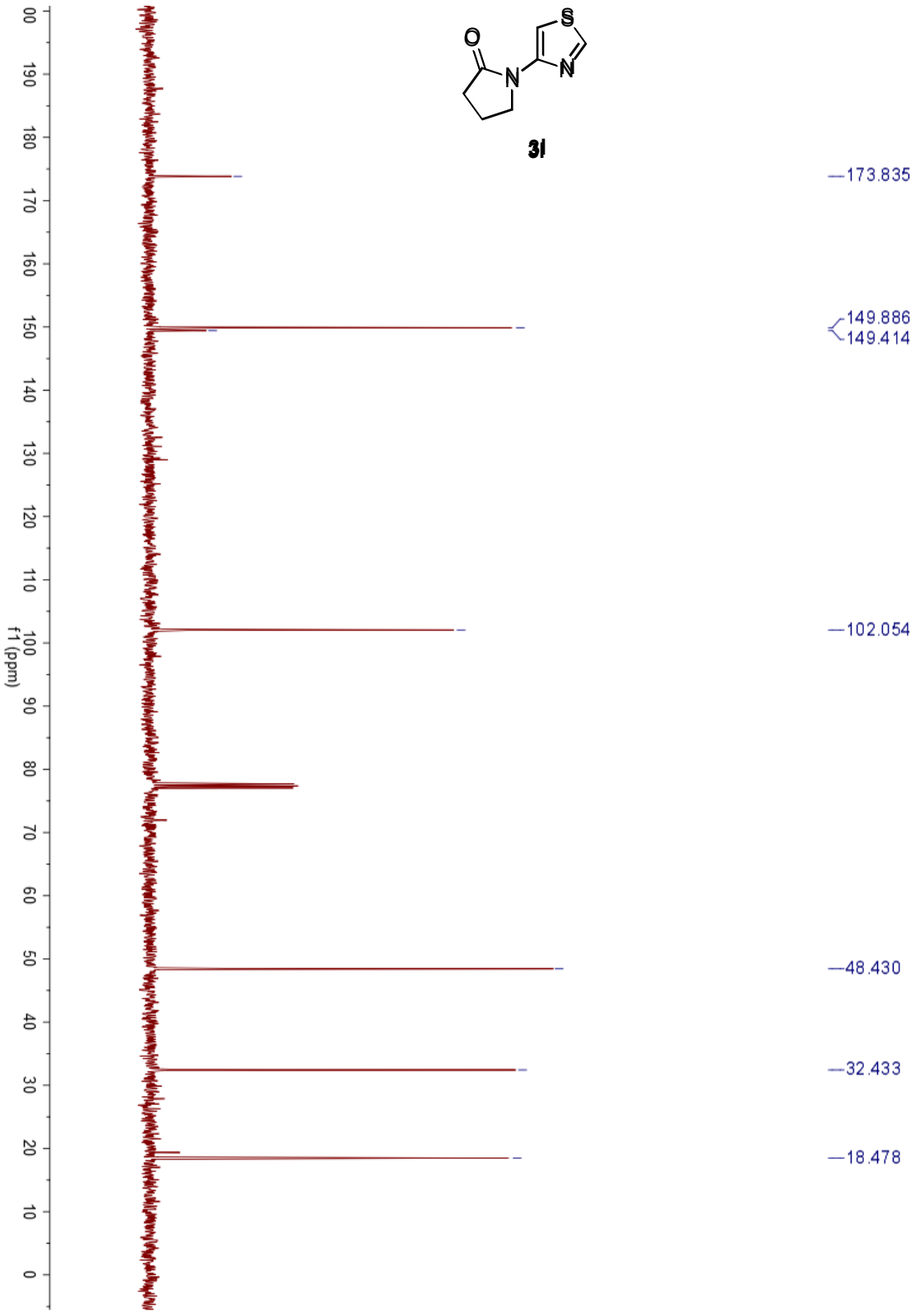
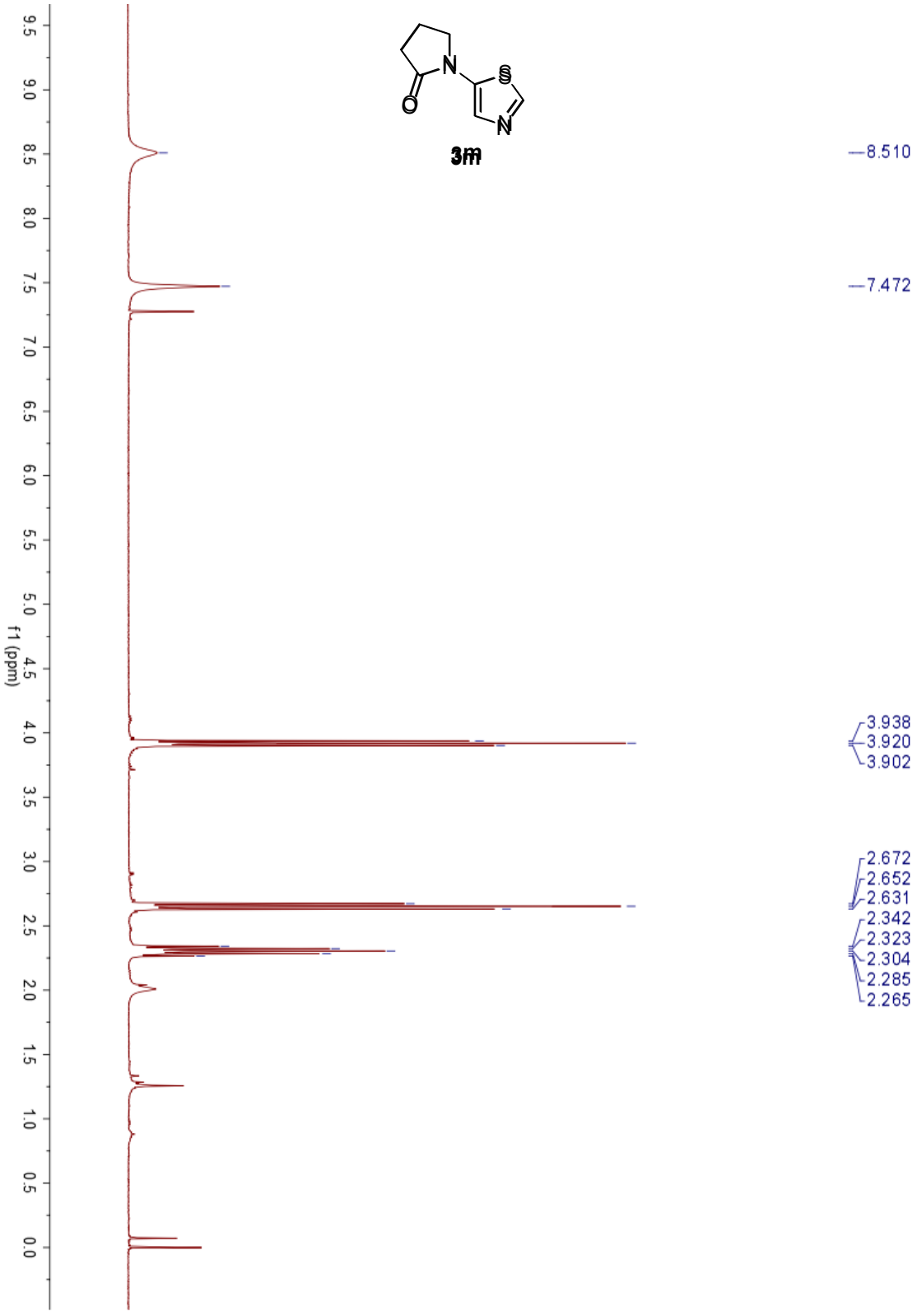
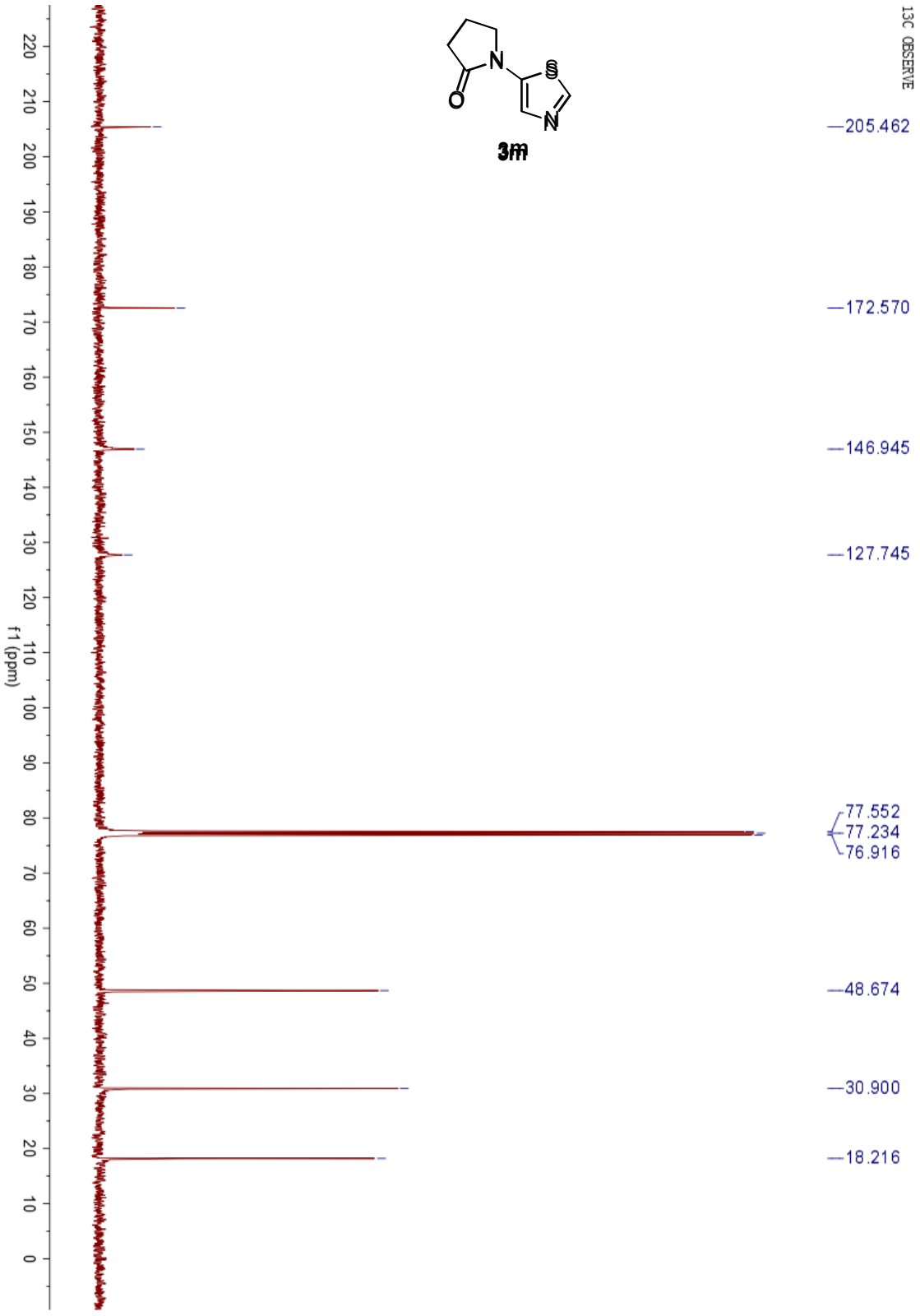
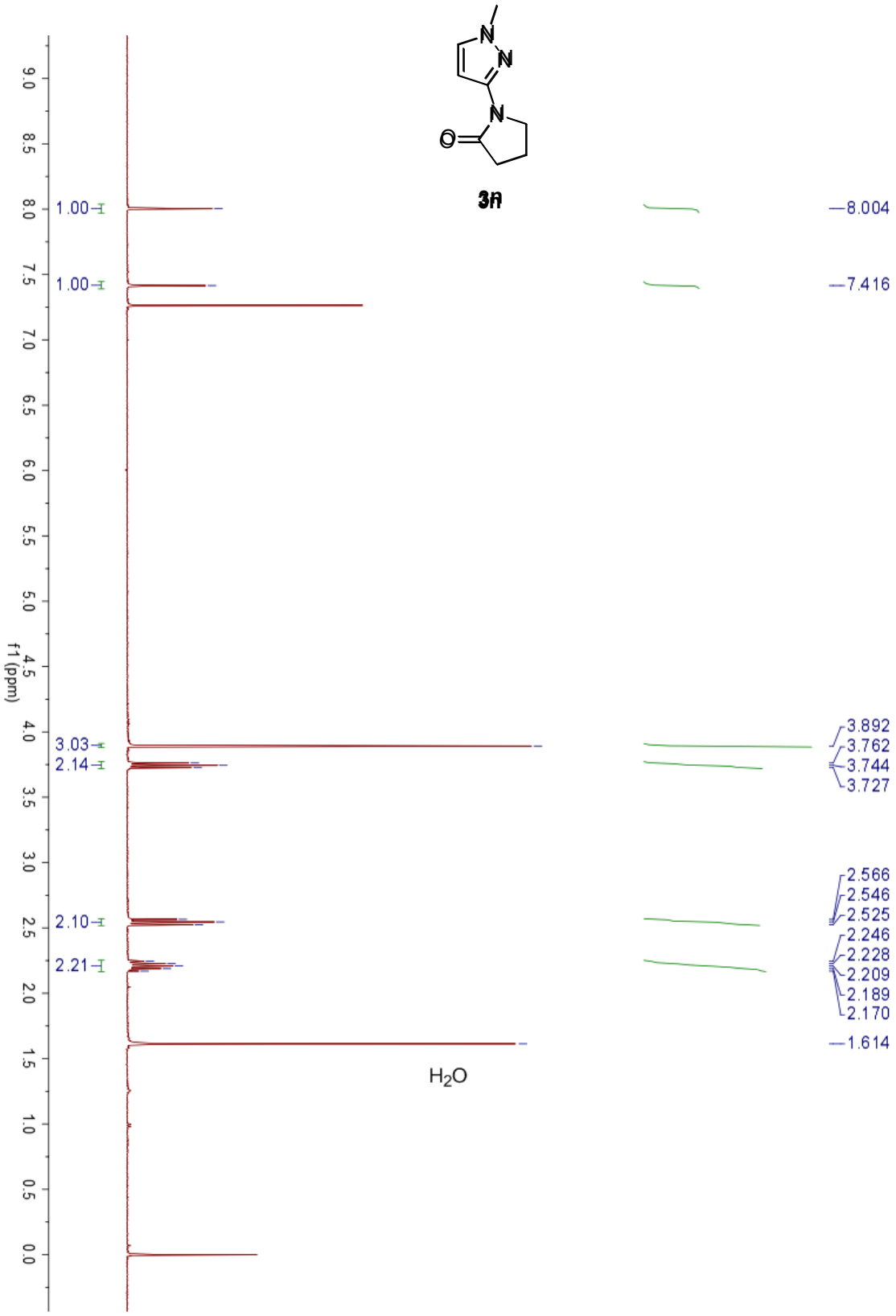
0.97
2.12
2.23
2.26
f1 (ppm)
8.627
8.621
7.888
7.882
4.165
4.147
4.129
2.653
2.633
2.612
2.240
2.220
2.202
2.183
1.623
H2O

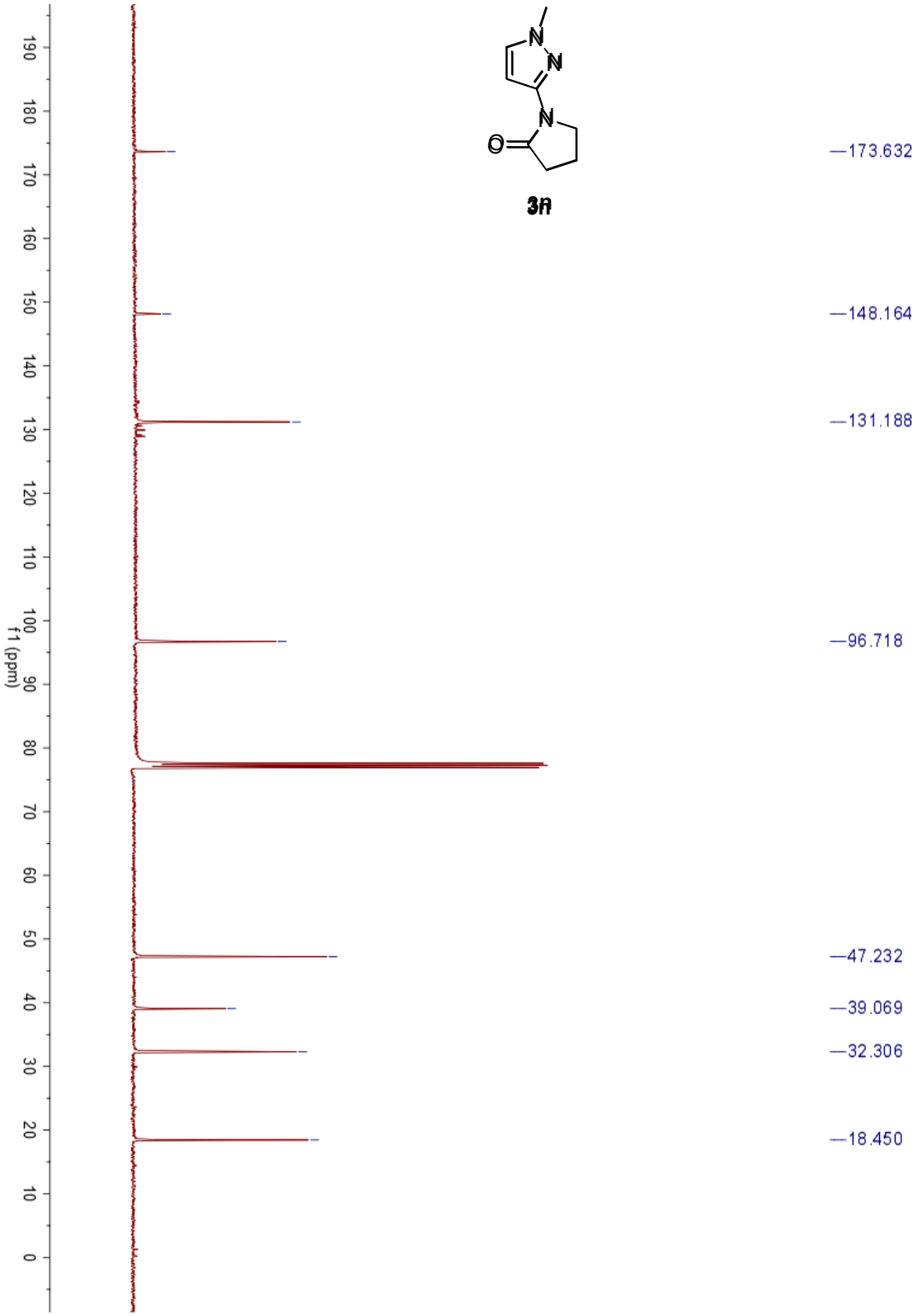



3m
8.510
7.472
3.938
3.920
3.902
2.672
2.652
2.631
2.342
2.323
2.304
2.285
2.265
f1 (ppm)

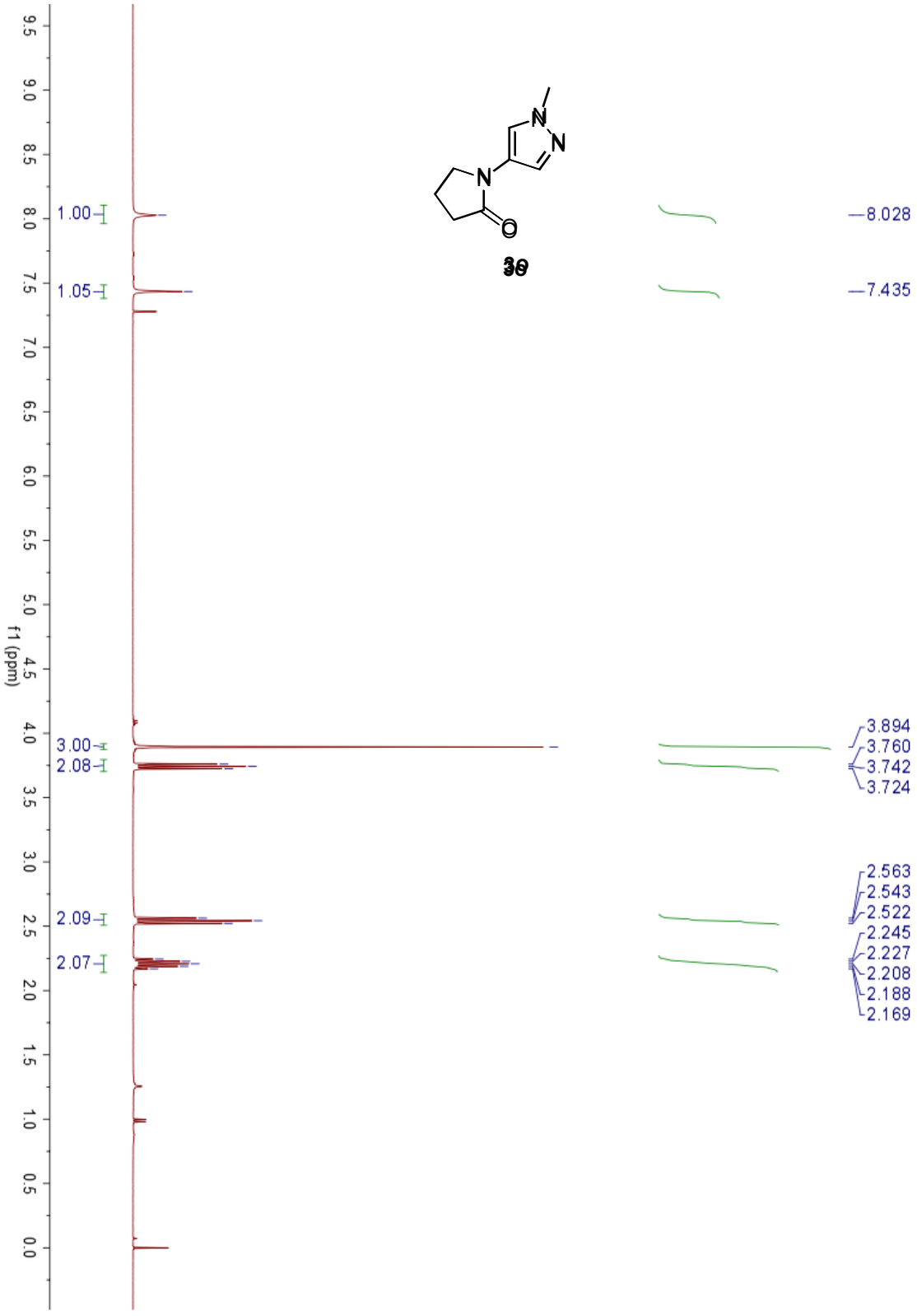

13C OBSERVE
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
205.462
172.570
146.945
127.745
77.552
77.234
76.916
48.674
30.900
18.216
O
N
S
N

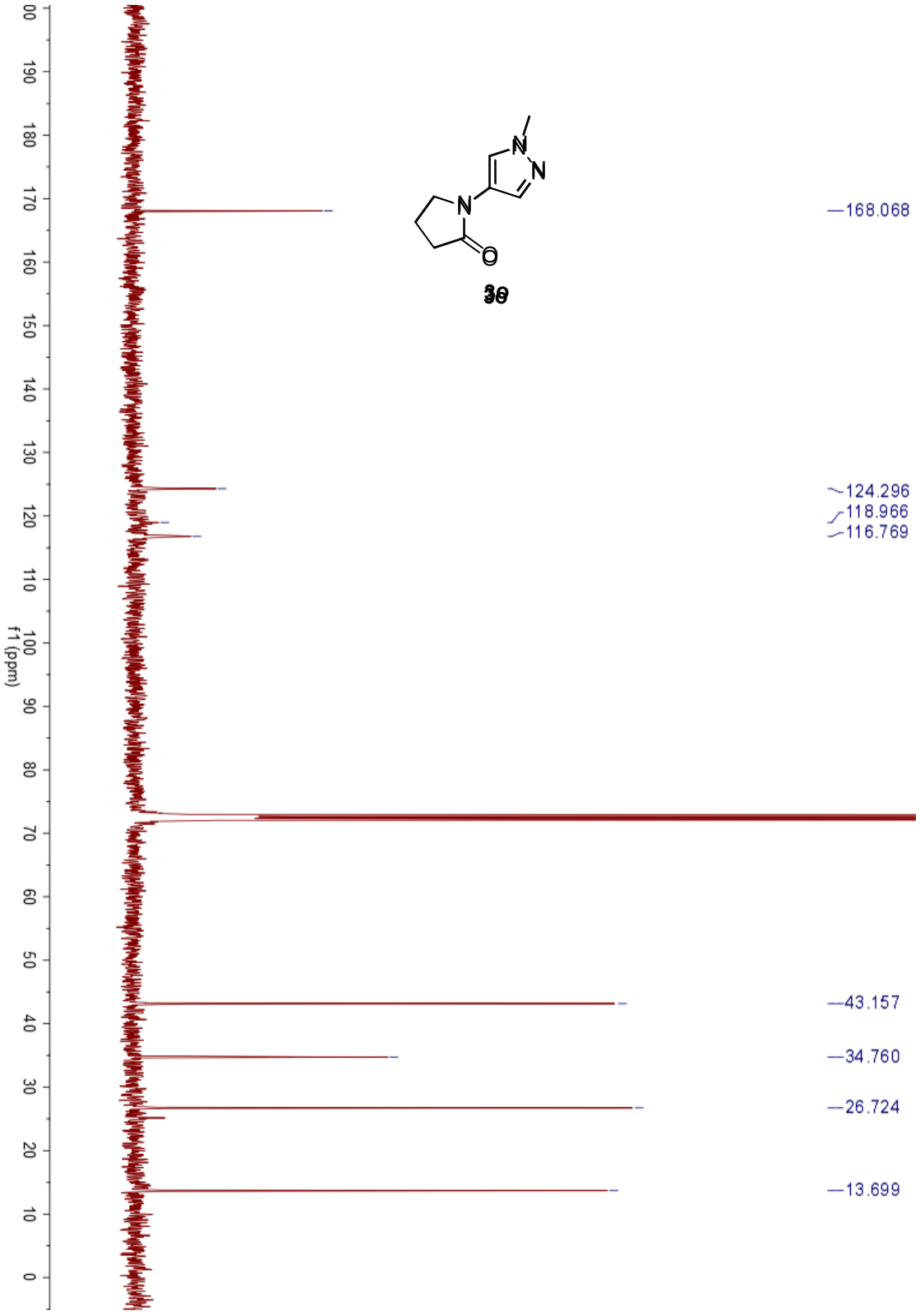
3m

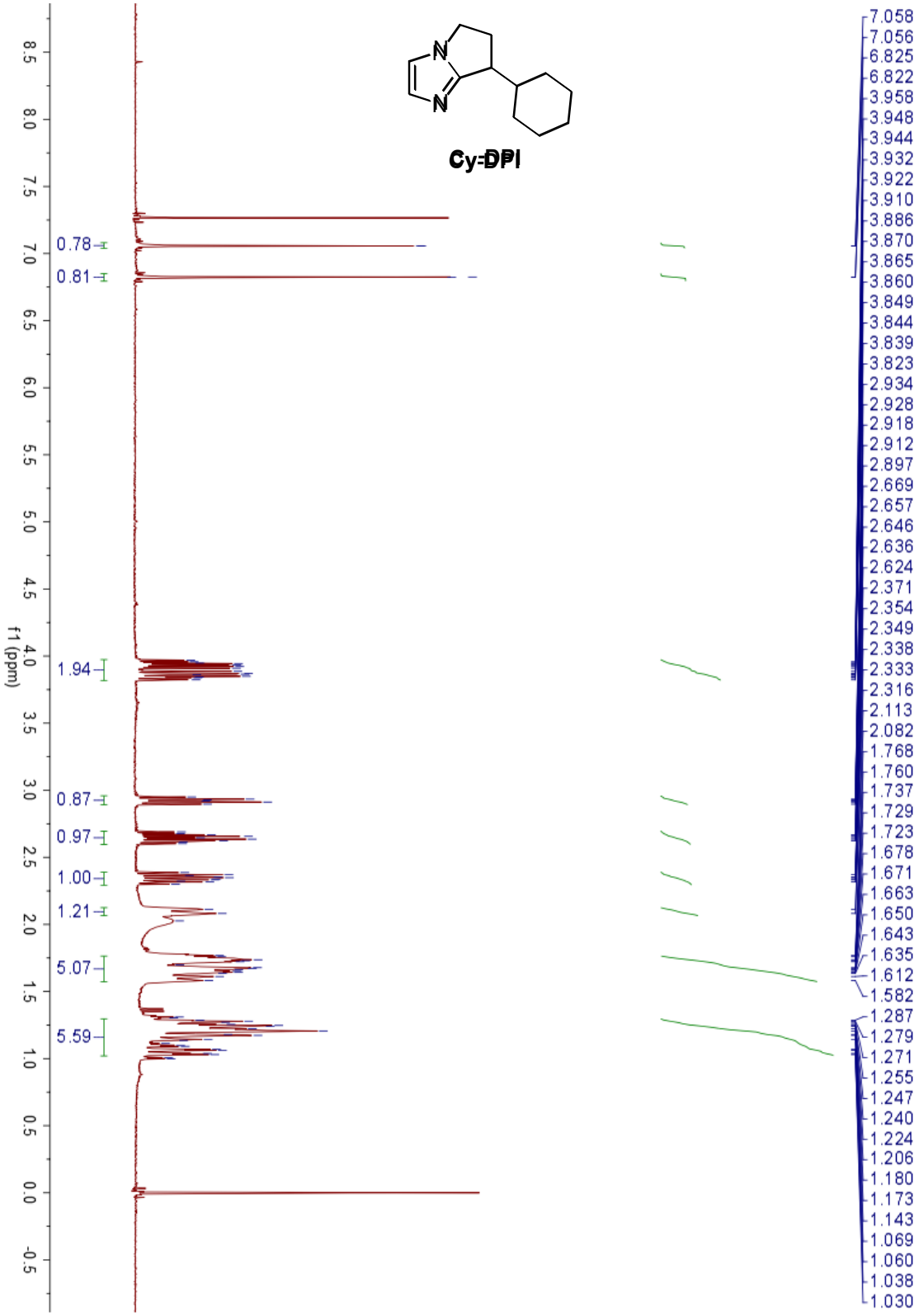

3n
1.00
1.00
3.03
2.14
2.10
2.21
8.004
7.416
3.892
3.762
3.744
3.727
2.566
2.546
2.525
2.246
2.228
2.209
2.189
2.170
1.614
H2O
f1 (ppm)

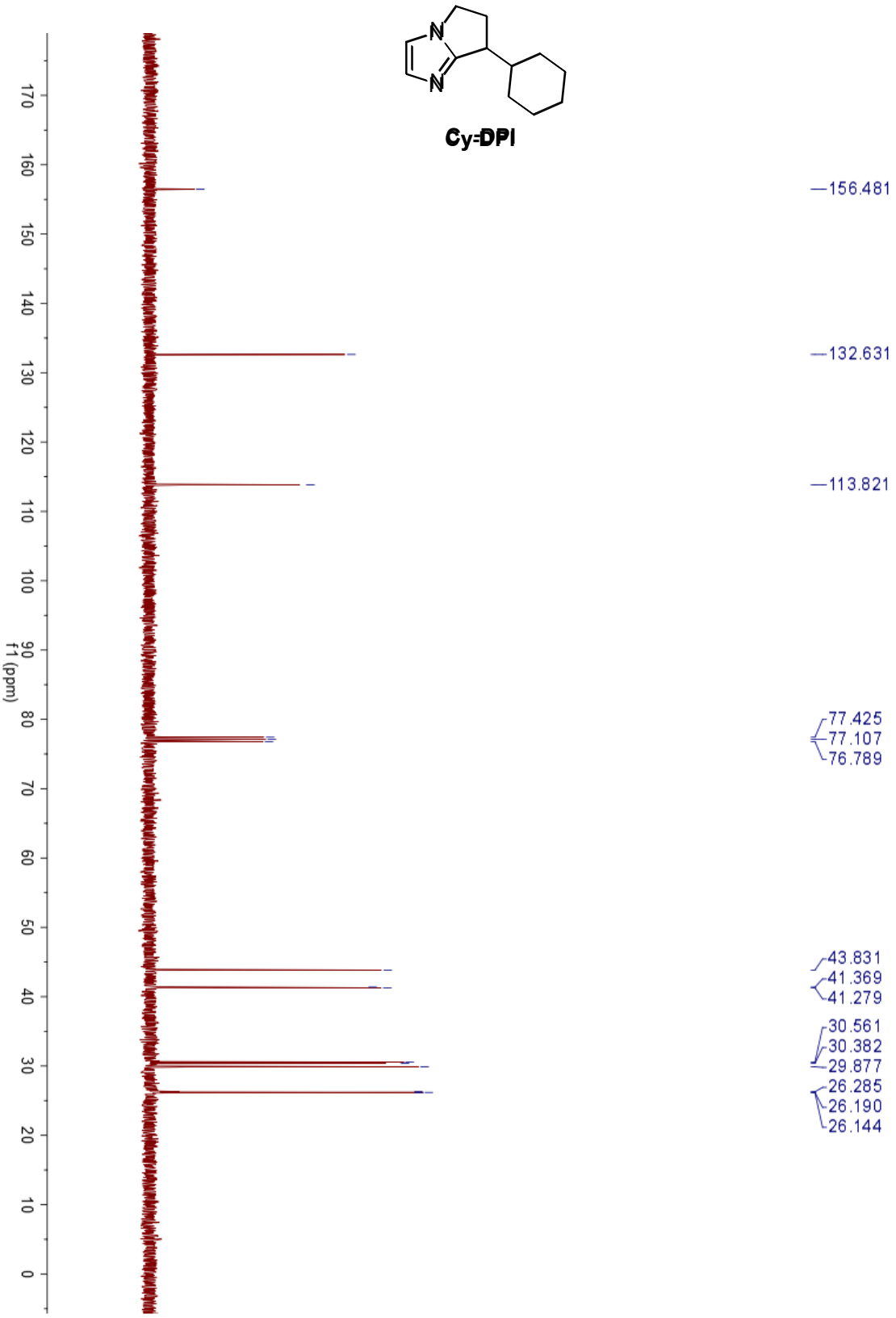


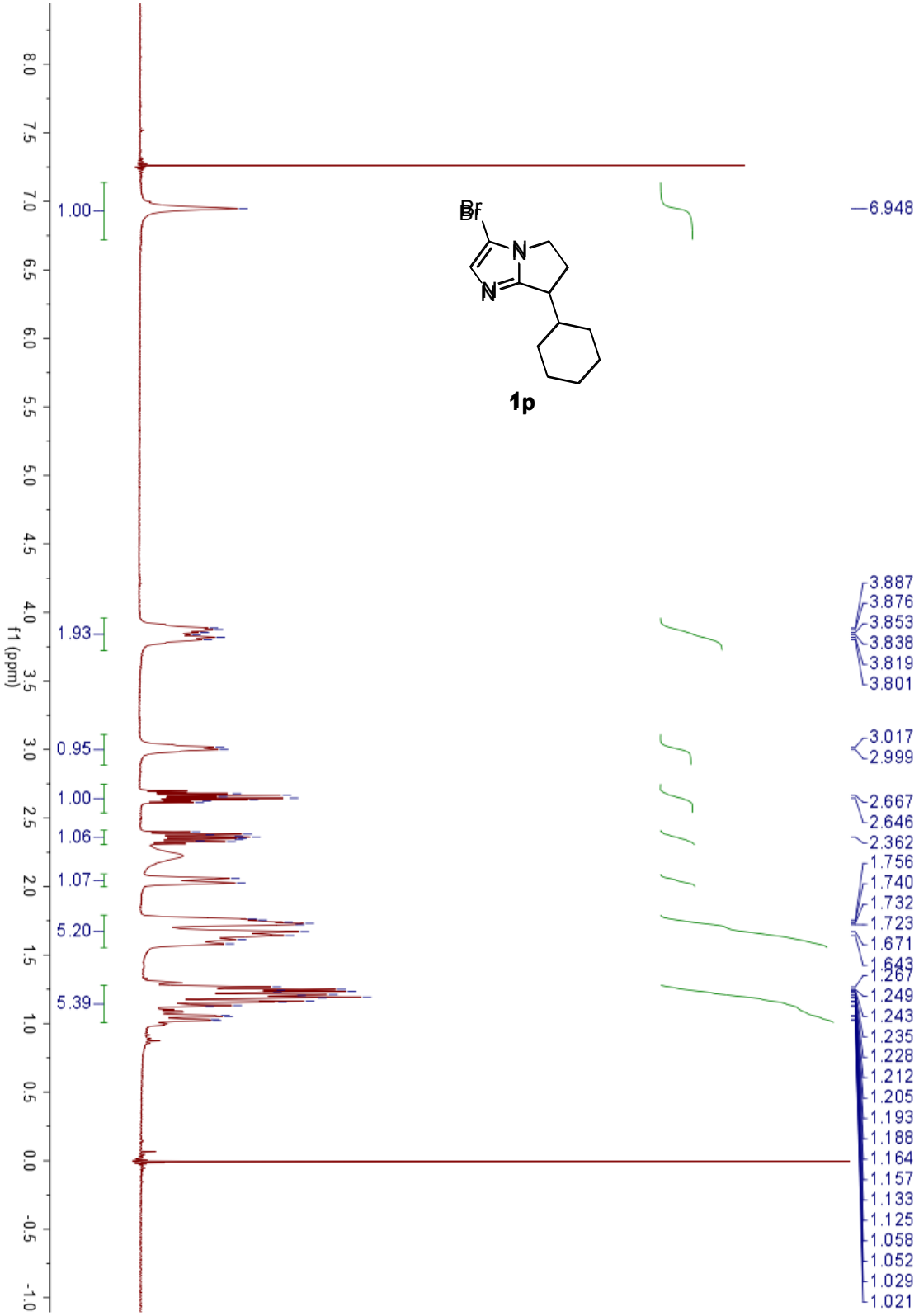
3n

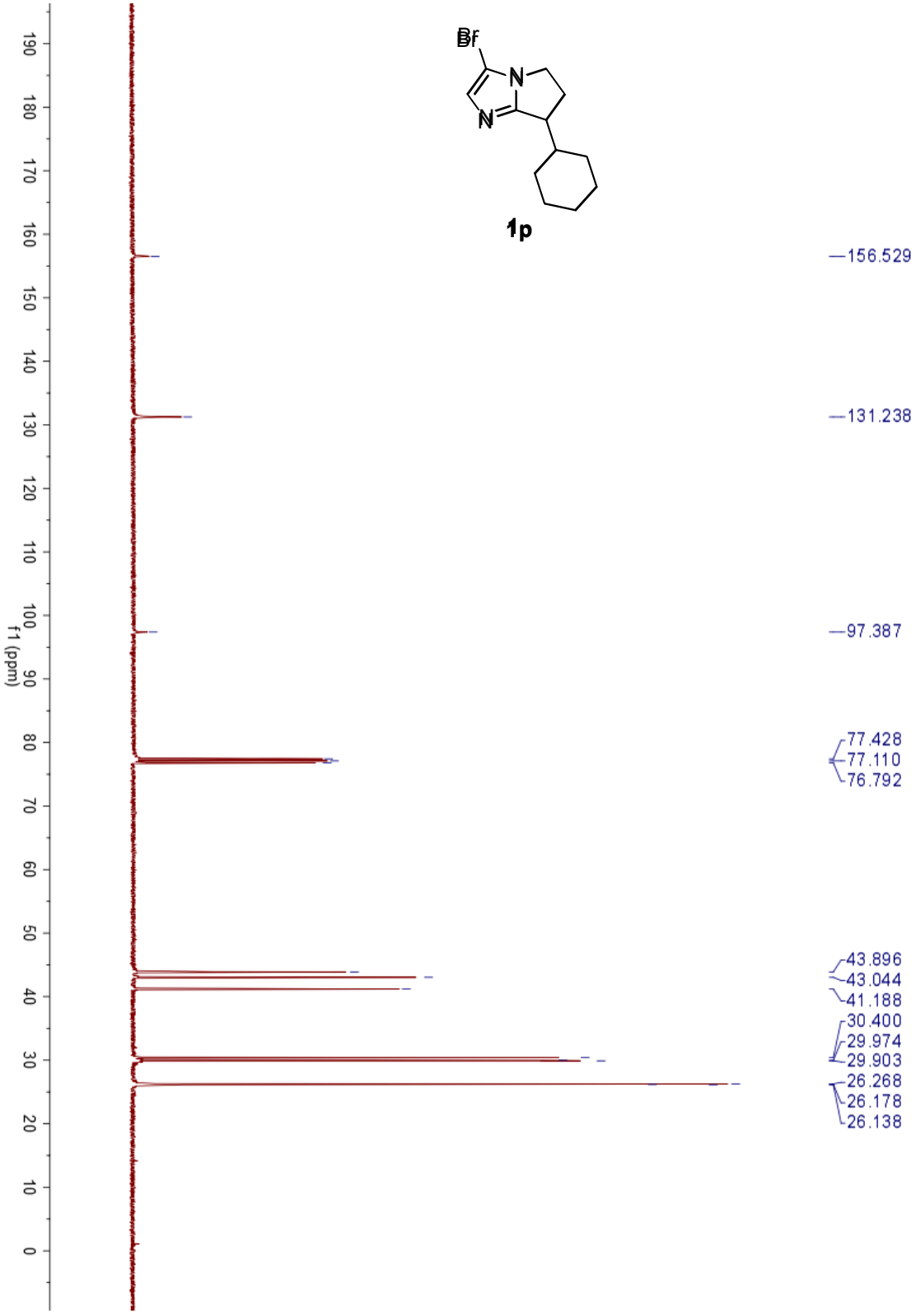

f1 (ppm)
1.00
1.05
3.00
2.08
2.09
2.07
8.028
7.435
3.894
3.760
3.742
3.724
2.563
2.543
2.522
2.245
2.227
2.208
2.188
2.169

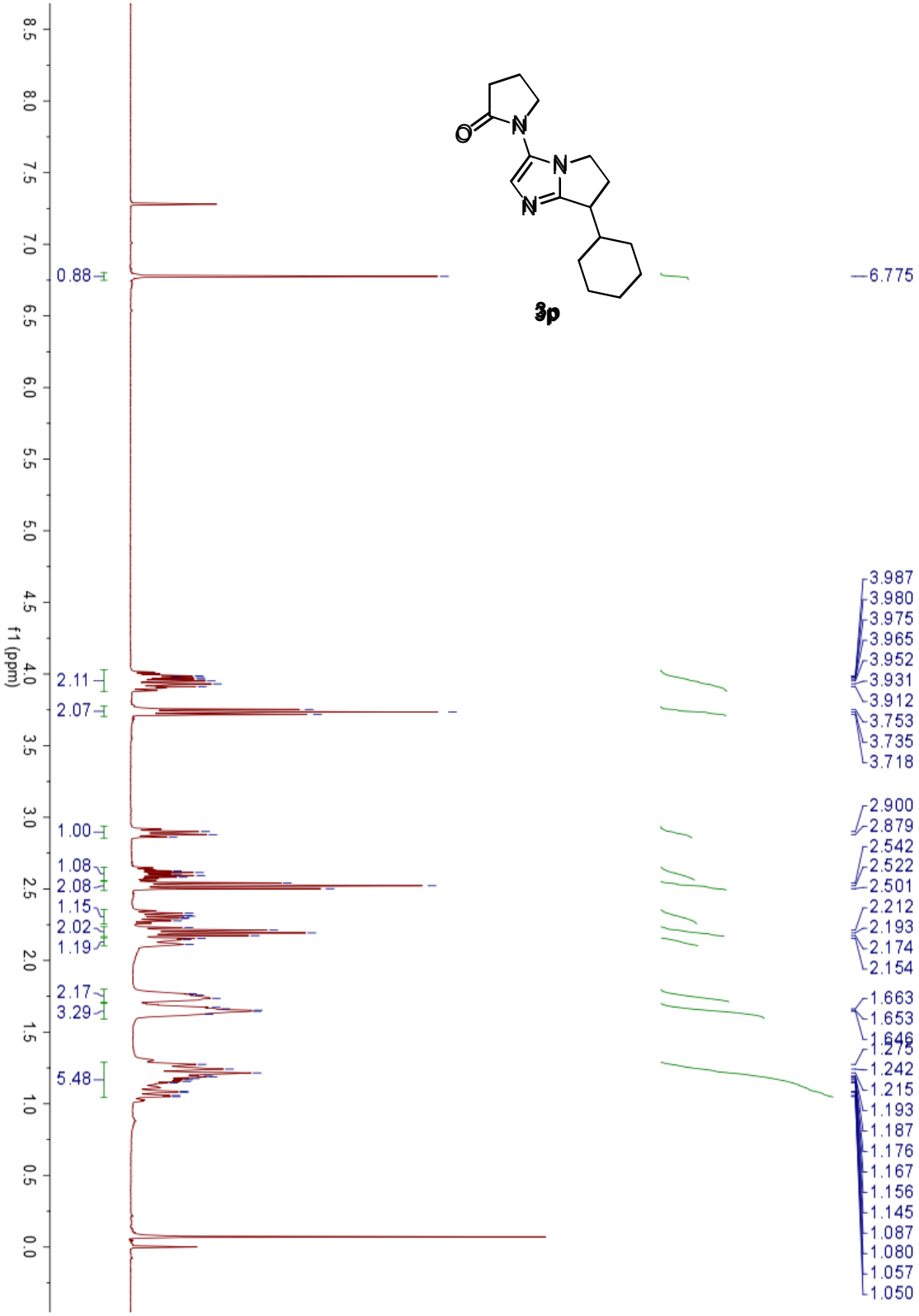

f1 (ppm)
168.068
124.296
118.966
116.769
43.157
34.760
26.724
13.699

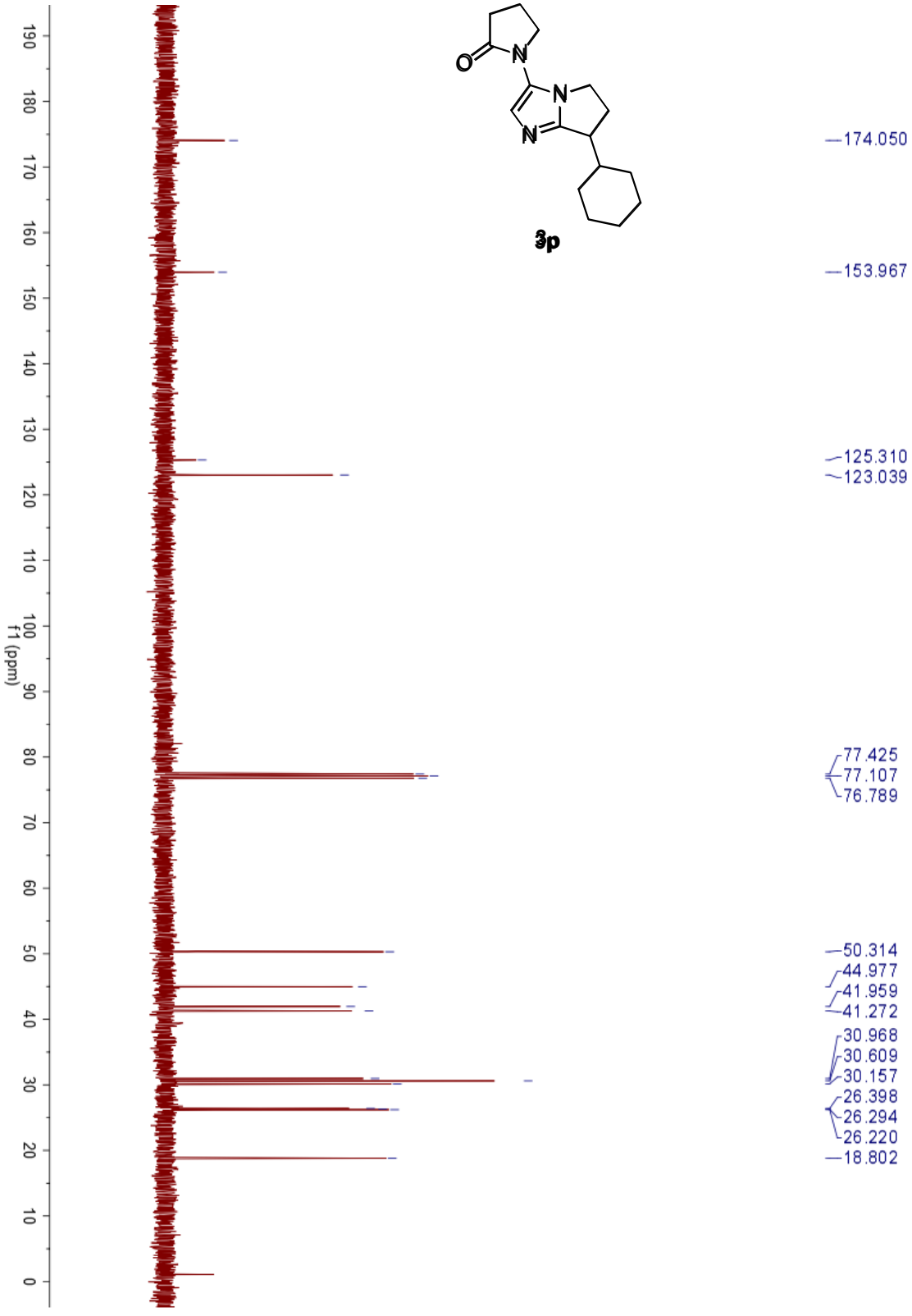





Br
N
N
1p
f1 (ppm)
1.00
1.93
0.95
1.00
1.06
1.07
5.20
5.39
6.948
3.887
3.876
3.853
3.838
3.819
3.801
3.017
2.999
2.667
2.646
2.362
1.756
1.740
1.732
1.723
1.671
1.643
1.267
1.249
1.243
1.235
1.228
1.212
1.205
1.193
1.188
1.164
1.157
1.133
1.125
1.058
1.052
1.029
1.021


Br
N
N
1p
156.529
131.238
97.387
77.428
77.110
76.792
43.896
43.044
41.188
30.400
29.974
29.903
26.268
26.178
26.138
f1 (ppm)


3p
f1 (ppm)
0.88
2.11
2.07
1.00
1.08
2.08
1.15
2.02
1.19
2.17
3.29
5.48
6.775
3.987
3.980
3.975
3.965
3.952
3.931
3.912
3.753
3.735
3.718
2.900
2.879
2.542
2.522
2.501
2.212
2.193
2.174
2.154
1.663
1.653
1.242
1.215
1.193
1.187
1.176
1.167
1.156
1.145
1.087
1.080
1.057
1.050


O
N
N
N
3p
174.050
153.967
125.310
123.039
77.425
77.107
76.789
50.314
44.977
41.959
41.272
30.968
30.609
30.157
26.398
26.294
26.220
18.802
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0