One-pot, telescoped syntheses of *N*-aryl-5-aminopyrazoles from anilines in environmentally benign conditions

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SUPPORTING INFORMATION

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General Information

Commercially available starting materials, reagents, and solvents were used as supplied. MPC was performed on Merck LiChroprep Si 60 Lobar columns. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC400 spectrometer as solutions in $CDCl_3$ or DMSO-d6. Chemical shifts were recorded in ppm (d) downfield of tetramethylsilane. The spin multiplicities are indicated by the symbols s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dt (doublet of triplet) tt (triplet of triplet) and bs (broad). IR spectra were recorded on a JASCO FT/IR-410,420 spectrometer using KBr pellets. Melting points were determined by the capillary method on a Büchi 535 electrothermal apparatus and are uncorrected.

1-(2-Chlorophenyl)-3-methyl-1*H*-pyrazol-5-amine (3a)

Light petroleum-EtOAc (1:1). Yield: 70 %. Mp 99-102 °C (from light petroleum/EtOAc) (lit.[1] 102-103 °C). IR (KBr): ν_{max}/cm^{-1} 3427, 3297, 2356, 1627, 1558, 1507, 1388, 1256, 1026, 762. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59-7.57 (m, 1H), 7.54-7.52 (m, 1H), 7.46-7.43 (m, 2H), 5.53 (s, 1H), 3.66 (bs, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.88, 146.50, 135.81, 132.01, 130.23, 130.16, 127.79, 90.00, 13.91. Found: C, 58.0; H, 4.9, Cl, 17.2, N, 20.2. Calc. for $C_{10}H_{10}ClN_3$: C, 57.84; H, 4.85; Cl, 17.07, N, 20.24.

1-(3-Chlorophenyl)-3-methyl-1*H*-pyrazol-5-amine (3b)

Light petroleum-EtOAc (1:1). Yield: 65 %. Mp 135-138 °C (from light petroleum/EtOAc) (lit.[2] 138-140 °C). IR (KBr): ν_{max}/cm^{-1} 3351, 3186, 2919, 2345, 1633, 1599, 1585, 1558, 1501, 1430, 1393, 1306, 1097, 1013, 884, 825, 780, 754, 734. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (t, 1H, J = 1.94 Hz), 7.50 (ddd, 1H, J = 1.07, 1.96 and 8.00 Hz), 7.40 (t, 1H, J = 8.00), 7.30 (ddd, 1H, J = 1.07, 1.96 and 8.00), 5.48 (s, 1H), 3.80 (bs, 2H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.89, 145.35, 139.78, 134.98, 130.27, 126.81, 123.61, 121.23, 91.34, 13.80. Found: C, 58.1; H, 4.9; Cl, 17.2; N, 20.3. Calc. for $C_{10}H_{10}ClN_3$: C, 57.84; H, 4.85; Cl, 17.07, N, 20.24.

1-(4-Chlorophenyl)-3-methyl-1*H*-pyrazol-5-amine (3c)

Light petroleum-EtOAc (4:6). Yield: 68 %. Mp 109-110 °C (from light petroleum/EtOAc) (lit.[3] 109-111 °C). IR (KBr): ν_{max}/cm^{-1} 3368, 3245, 2264, 1905, 1563, 1505, 1302, 1173, 1091, 1014, 837. ^{1}H NMR

(400 MHz, $CDCl_3$) δ = 8.34 (d, 2H, J = 9.20 Hz), 7.91 (d, 2H, J = 9.20 Hz), 5.49 (s, 1H), 3.90 (bs, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.70, 145.26, 137.22, 132, 43, 129.42, 124.73, 91.20, 13.81. Found: C, 58.1; H, 4.9; Cl, 17.2; N, 20.2. Calc. for $C_{10}H_{10}ClN_3$: C, 57.84; H, 4.85; Cl, 17.07, N, 20.24.

1-(2-Bromophenyl)-3-methyl-1*H*-pyrazol-5-amine (3d)

Light petroleum-EtOAc (6:4). Yield: 67 %. IR (KBr): ν_{max}/cm^{-1} 3438, 3296, 3173, 2925, 2335, 1627, 1554, 1500, 1385, 1305, 1254, 1071, 1028, 952, 800, 763. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.77-7.76 (d, 1H, J = 8.01 Hz), 7.53-7.50 (m, 2H), 7.40-7.32 (m, 1H), 5.53 (s, 1H), 3.66 (bs, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.78, 146.26, 137.46, 133.44, 130.56, 130.44, 128.48, 122.29, 90.02, 13.98. Found: C, 47.8; H, 4.1; Br, 33.0; N, 16.7. Calc. for $C_{10}H_{10}BrN_3$: C, 47.64; H, 4.00; Br, 31.69, N, 16.67.

3-Methyl-1-(2-nitrophenyl)-1*H*-pyrazol-5-amine (3e)

Light petroleum-EtOAc (4:6). Yield: 50 %. Mp 116-118 °C (from light petroleum/EtOAc) (lit.[4] 117-118 °C). IR (KBr): ν_{max}/cm^{-1} 3299, 3217, 2354, 1630, 1585, 1565, 1528, 1387, 1355, 1299, 1151, 1025, 1007, 955, 853, 780, 747. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.98 (dd, 1H, J = 1.2 and 8.00 Hz), 7.72 (dt, 1H, J = 1.6 and 8.0 Hz), 7.63 (dd, 1H, J = 1.2 and 8.0 Hz), 7.57 (dt, 1H, J = 1.6 and 8.0 Hz), 5.50 (s, 1H), 3.70 (bs, 2H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.93, 146.50, 145.91, 133.37, 131.56, 129.12, 128.91, 125.07, 91.69, 13.82. Found: C, 55.1; H, 4.7; N, 25.4. Calc. for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.62; N, 25.68, O, 14.66.

3-Methyl-1-(4-nitrophenyl)-1*H*-pyrazol-5-amine (3f)

Light petroleum-EtOAc (4:6). Yield: 48 %. Mp 160-164 °C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 3402, 3307, 2433, 1599, 1514, 1340, 1176, 1113. 1035, 1012, 854, 770, 751. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.56 (d, 2H, J = 8.70 Hz), 7.46 (d, 2H, 8.70 Hz), 5.58 (s, 1H), 3.75 (bs, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.27, 145.84, 144.97, 144.32, 124.98, 122.05, 93.26, 13.89. Found: C, 55.1; H, 4.7; N, 25.5 . Calc. for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.62; N, 25.68, O, 14.66.

2-(5-Amino-3-methyl-1*H*-pyrazol-1-yl)benzoic acid (3g)

Light petroleum-EtOAc (4:6). Yield: 65 %. Mp 245-248 °C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 2900, 1682, 1608, 1580, 1191, 1389, 1340, 1235, 1160, 1120, 860, 754. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.10 (s, 1H), 8.16-8.14 (dd, 1H, J = 1.4 and 7.9 Hz), 8.05-8.03 (dd, 1H, 0.4 and 7.74 Hz), 7.89 (td, 1H, J = 7.34 and 1.48 Hz), 7.48 (td, 1H, 8.25 and 1.03 Hz), 5.8 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 158.87, 151.64, 139.39, 137.79, 135.45, 128.57, 125.11, 116.13, 114.49, 88.89, 14.38. Found: C, 61.1; H, 5.0; N, 19.2. Calc. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34; O,14.73.

3-(5-Amino-3-methyl-1*H*-pyrazol-1-yl)benzoic acid hydrochloride (3h)

Yield: 45 %. Mp 270-274 °C (from MeOH/H_2O). IR (KBr): ν_{max}/cm^{-1} 3294, 2806, 1689, 1635, 1579, 1494, 1464, 1251, 1122, 1013, 900, 854, 795, 757. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.12-8.10 (dd, 2H, J = 1.75 and 3.49 Hz), 7.91-7.89 (d, 1H, J = 8.59 Hz), 7.79-7.75 (t, 1H, J = 8.1 Hz), 5.77 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 166.70, 151.25, 148.72, 134.74, 133.03, 130.86, 130.40, 130, 126.43, 91.96, 12.28. Found: C, 52.2; H, 4.8; Cl, 13.8; N, 17.0. Calc. for $C_{11}H_{12}ClN_3O_2$: C, 52.08; H, 4.77; Cl, 13.98; N, 16.56; O,12.61.

4-(5-Amino-3-methyl-1*H*-pyrazol-1-yl)benzoic acid hydrochloride (3i)

Yield: 65 %. Mp 232-233 °C (from MeOH/H_2O) (lit.[5] 232 °C). IR (KBr): ν_{max}/cm^{-1} 3308, 2714, 1696, 1629, 1574, 1513, 1457, 1419, 1388, 1236, 1189, 1119, 1011, 862, 782, 766. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.11-8.09 (d, 2H, J = 8.47 Hz), 7.75-7.73 (d, 2H, J = 8.52 Hz), 6.40-4.20 (bs, 2H), 5.65 (s, 1H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 166.90, 150.90, 149.25, 138.47, 131.29 (x2), 131.11, 124.91 (x2), 91.96, 12.28. Found: C, 53.0; H, 4.9; Cl, 14.0; N, 16.1. Calc. for $C_{11}H_{12}ClN_3O_2$: C, 52.08; H, 4.77; Cl, 13.98; N, 16.56; O,12.61.

2-(5-Amino-3-methyl-1*H*-pyrazol-1-yl)benzenesulfonamide (3j)

Light petroleum-EtOAc (1:1). Yield: 61 %. Mp 181-183°C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 3460, 3366, 3225, 2357, 1634, 1558, 1516, 1347, 1162, 1301, 1127, 1086, 1011, 769. ^{1}H NMR (400 MHz, MeOH-d_4) δ = 8.20-8.18 (d, 1H, J = 7.8 Hz), 7.83-7.79 (t, 1H, J = 7.8 Hz), 7.73-7.69

(t, 1H, J = 7.8 Hz), 7.55-7.53 (d, 1H, J = 7.8 Hz), 5.51 (s, 1H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ = 152.05, 151.03, 141.79, 136.68, 134.57, 131.45, 130.63, 129.91, 90.93, 13.74. Found: C, 47.5; H, 4.8 ; N, 22.2; S, 12.5. Calc. for $C_{10}H_{12}N_4O_2S$: C, 47.61; H, 4.79; N, 22.21, O, 12.68, S, 12.71.

3-Methyl-1-phenyl-1*H*-pyrazol-5-amine (3k)

Light petroleum-EtOAc (1:1). Yield: 36 %. Mp 110-113 °C (from light petroleum/EtOAc) (lit.[6] 110-111.5°C). IR (KBr): ν_{max}/cm^{-1} 3445 3144, 2358, 1622, 1594, 1553, 1510, 1436, 1391, 1367, 1315, 1141, 1072, 1023, 1010, 914, 798, 761. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 (dd, 2H, J = 1.3 and 7.5 Hz), 7.50 (t, 2H, J = 7.5 Hz), 7.37 (tt, 1H, J = 1.3 and 7.5 Hz), 5.49 (s, 1H), 3.75 (bs, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.32, 145.24, 138.58, 129.33, 126.98, 123.75, 90.65, 13.83. Found: C, 69.5; H, 6.55; N, 24.2. Calc. for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26.

[4-(5-Amino-3-methyl-pyrazol-1-yl)-phenyl]-acetic acid hydrochloride (3o)

Yield: 65 %. Mp 258-260 °C (from H_2O). IR (KBr): ν_{max}/cm^{-1} 3469, 3321, 3194, 2326, 1714, 1631, 1574, 1516, 1403, 1288, 1227, 1204, 1182, 1113, 1017, 915, 859, 828, 790. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 7.55-7.49 (m, 4H), 5.68 (s, 1H), 3.71 (s, 2H), 2.26 (s, 3H). Found: C, 53.9; H, 5.4; Cl, 13.2; N, 15.6. Calc. for $C_{12}H_{14}ClN_3O_2$: C, 53.84; H, 5.27; Cl, 13.24; N, 15.70; O, 11.95.

1-(2-Methoxyphenyl)-3-methyl-1*H*-pyrazol-5-amine (3q)

Light petroleum-EtOAc (1:1). Yield: 20 %. IR (KBr): ν_{max}/cm^{-1} 3316, 3199, 2838, 2356, 1598, 1559, 1515, 1464, 1389, 1280 1021, 1241, 1123, 756. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.50 (dd, 1H, J = 1.7 and 7.7 Hz), 7.49 (dt, 1H, J = 1.7 and 7.7 Hz), 7.12-7.07 (m, 2H), 5.50 (s, 1H), 3.91 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.39, 149.71, 146.88, 129.47, 129.01, 127.58, 121.58, 112.31, 90.40, 56.22, 13.98. Found: C, 66.1; H, 6.6; N, 21.2. Calc. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.68, O, 7.87.

3-Methyl-1-[3-(methylsulfonyl)phenyl]-1*H*-pyrazol-5-amine (3r)

Light petroleum-EtOAc (1:1). Yield: 25 %. Mp 164-167 °C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 3398, 3163, 2284, 1563, 1296, 1148, 964, 896, 741. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (s,

1H), 7.96 (d, 1H, J = 7.6 Hz), 7.88 (d, 1H, J = 7.6 Hz), 7.71 (t, 1H, J = 7.6 Hz), 5.54 (s, 1H), 3.90 (bs, 2H), 3.12 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.49, 145.61, 141.74, 139.88, 130.43, 127.88, 124.87, 121.69, 92.28, 44.28, 13.80. Found: C, 53.0; H, 5.3; N, 12.5, S, 12.9. Calc. for $C_{11}H_{13}N_3O_2S$: C, 52.57; H, 5.21; N, 16.72, O, 12.73, S, 12.76.

3-Methyl-1-(2-methyl-6-nitrophenyl)-1*H*-pyrazol-5-amine (3s)

Light petroleum-EtOAc (4:6). Yield: 45 %. Mp 107-108 °C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 3426, 3326, 2287, 1626, 1570, 1532, 1362, 1303, 1145, 1007, 920, 813, 801, 751. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 (d, 1H, J = 7.8 Hz), 7.61 (d, 1H, 7.8 Hz), 7.52, (t, 1H, J = 7.8 Hz), 5.51 (s, 1H), 3.66 (bs, 2H), 2.23 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.84, 148.50, 147.51, 141.09, 134.94, 130.16, 129.57, 122.13, 90.39, 17.32, 13.96. Found: C, 56.75; H, 5.1; N, 24.1. Calc. for $C_{11}H_{12}N_4O_2$: C, 56.89; H, 5.21; N, 24.12, O, 13.78.

1**-(2-Methoxy-4-nitrophenyl)-3-methyl-1*H*-pyrazol-5-amine (3t)**

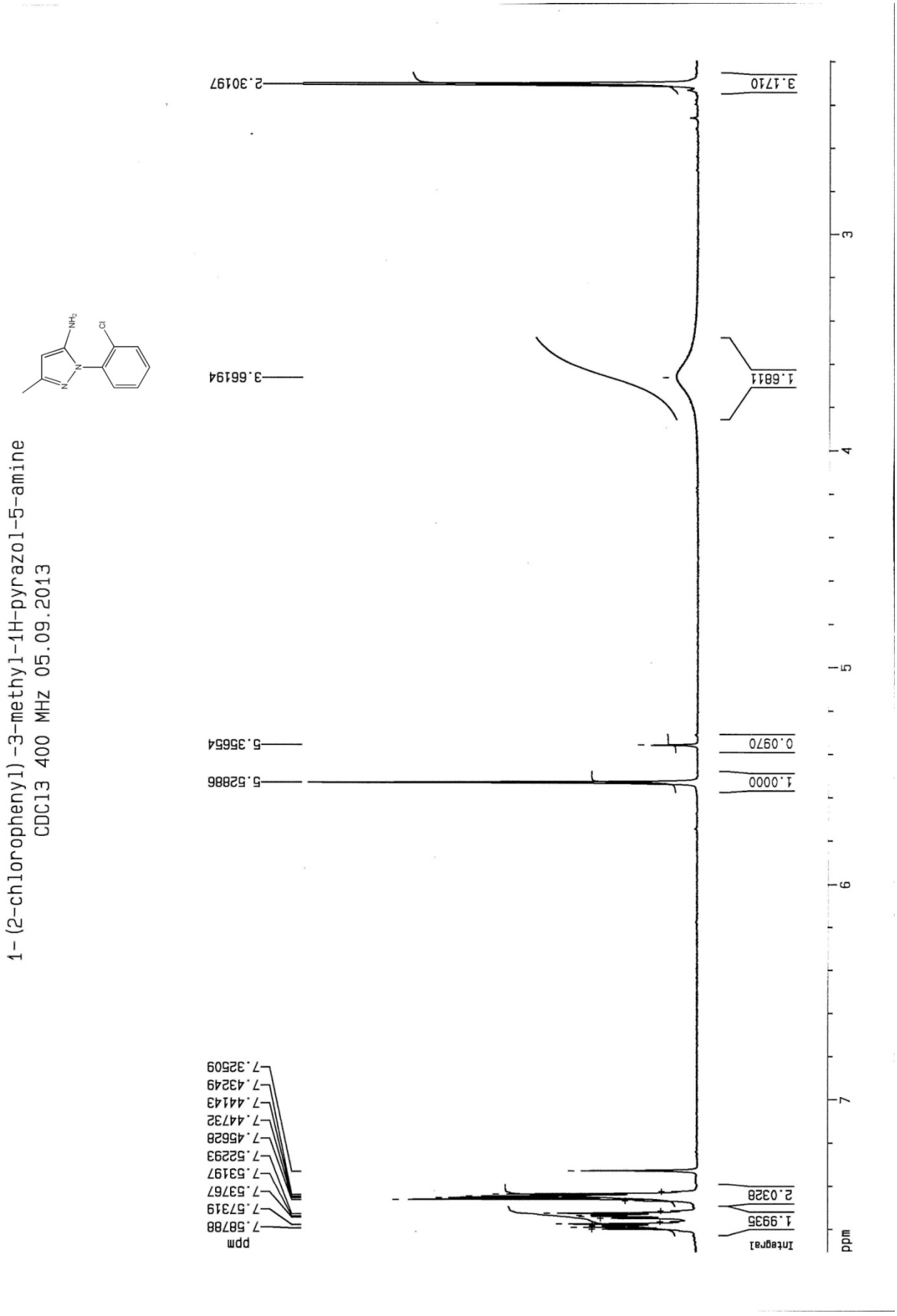
Light petroleum-EtOAc (1:1). Yield: 42 %. Mp 121-123 °C (from light petroleum/EtOAc). IR (KBr): ν_{max}/cm^{-1} 3628, 3432, 3330, 2349, 1631, 1563, 1515, 1341, 1251, 1028, 1101, 875, 821, 740. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (dd, 1H, J = 2.4 and 8.6 Hz), 7.97 (d, 1H, J = 2.4 Hz), 7.69 (d, 1H, J = 8.6 Hz), 5.53 (s, 1H), 4.05 (s, 3H), 3.90 (bs, 2H), 2.28 (s, 3H). ^{1}H NMR (100 MHz, $CDCl_3$) δ = 152.60, 151.55, 147.54, 147.42, 133.90, 129.05, 116.92, 107.71, 91.66, 56.98, 13.95. Found: C, 53.1; H, 4.8; N, 22.3. Calc. for $C_{11}H_{12}N_4O_3$: C, 53.22; H, 4.87; N, 22.57, O, 19.34.

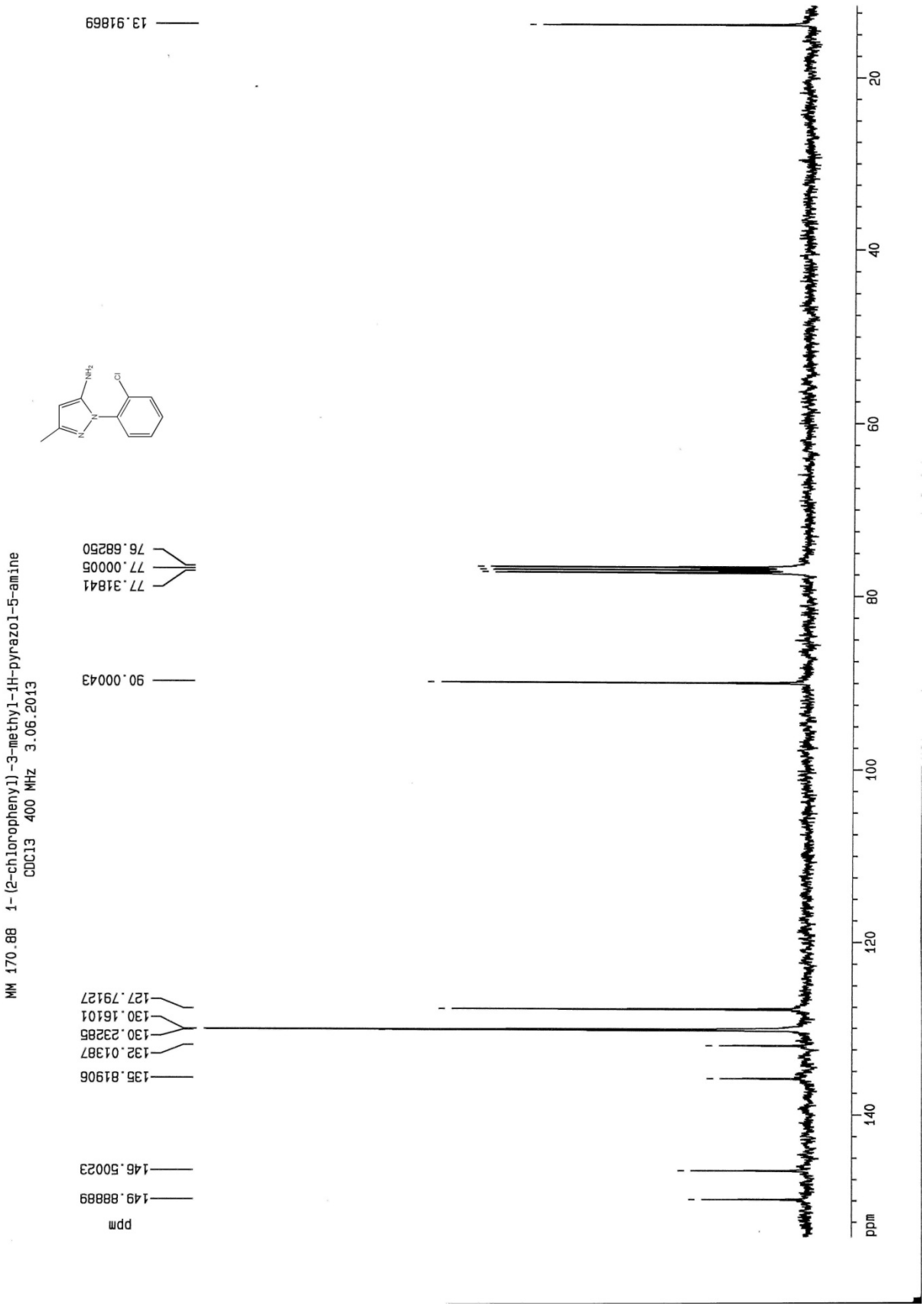
1-(2-Chlorophenyl)-1*H*-pyrazol-5-amine (12)

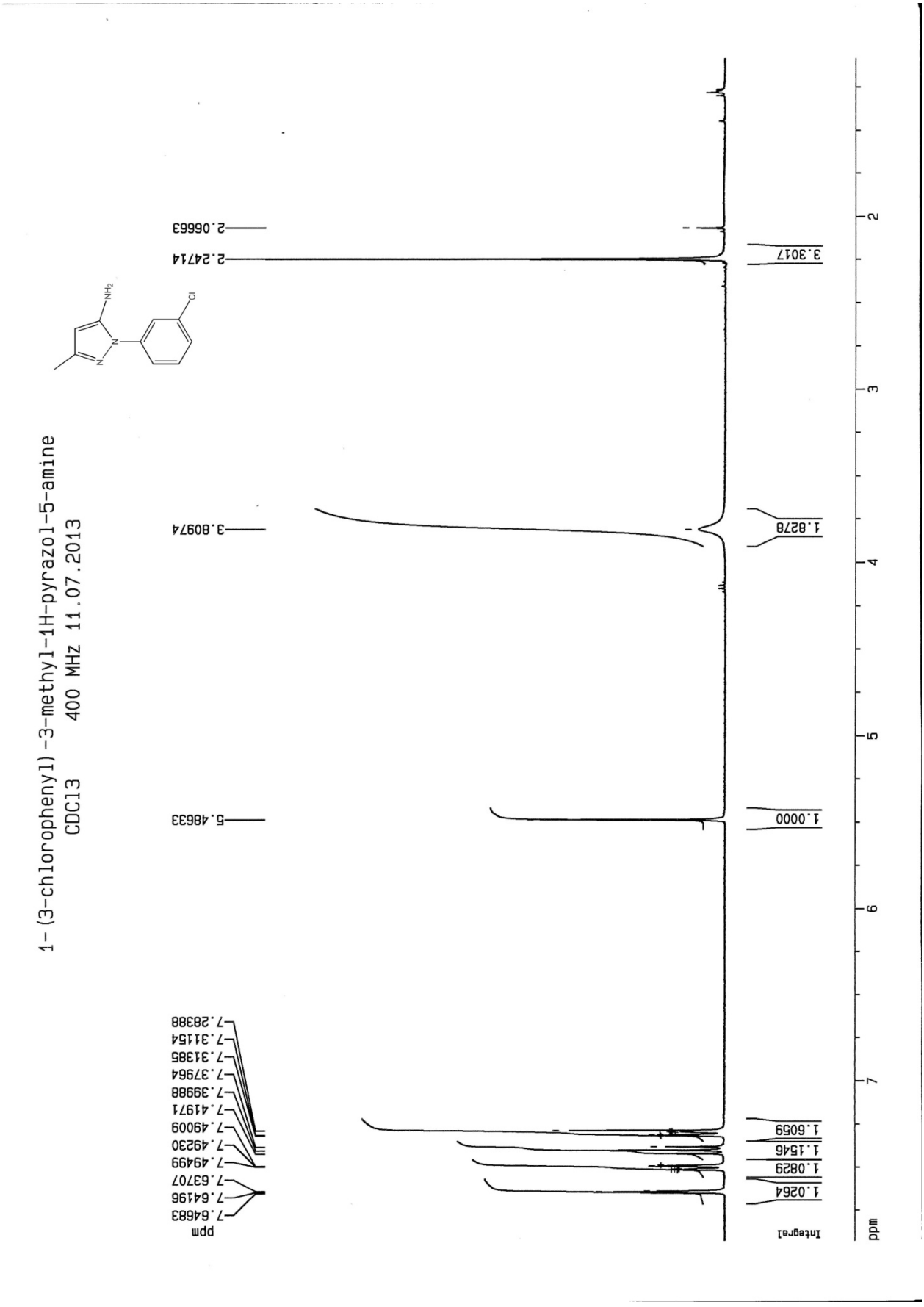
Light petroleum-EtOAc (7:3). IR (KBr): ν_{max}/cm^{-1} 3316, 3193, 2280, 1622, 1558, 1512, 1480, 1444, 1407, 1346, 1215, 1035, 920, 762. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62-7.46 (m, 5H), 5.71-5.70 (d, 1H, J = 1.7 Hz), 3.77- 3.20 (bs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.93, 140.85, 135.72, 132.2, 130.52, 130.46, 130.1, 127.93, 90.16. Found: C, 56.0; H, 4.25; Cl, 18.2; N, 21.2. Calc. for $C_9H_8ClN_3$: C, 55.83; H, 4.16; Cl, 18.31; N, 21.70.

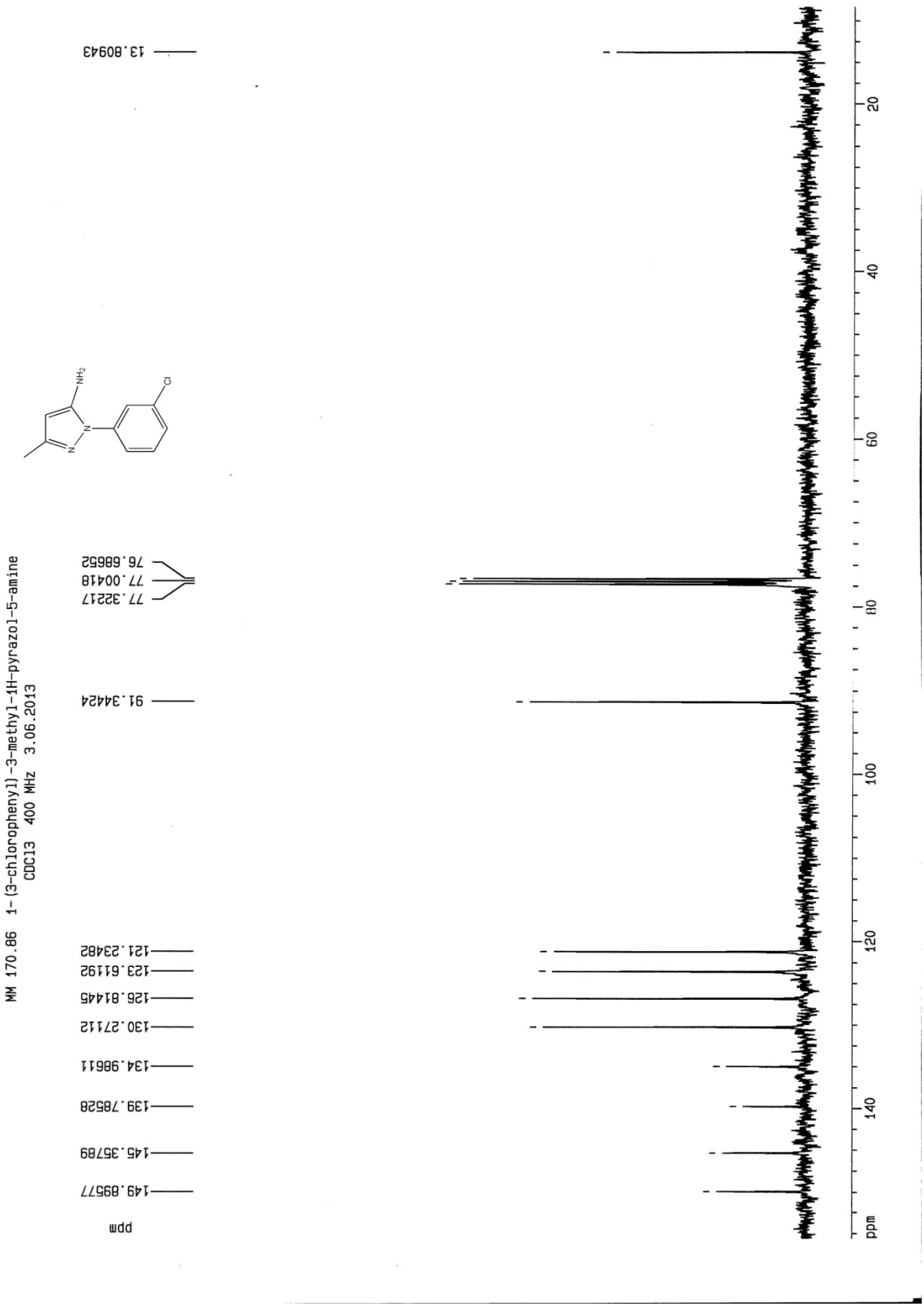
1-(2-Chlorophenyl)-3-phenyl-1*H*-pyrazol-5-amine (13)

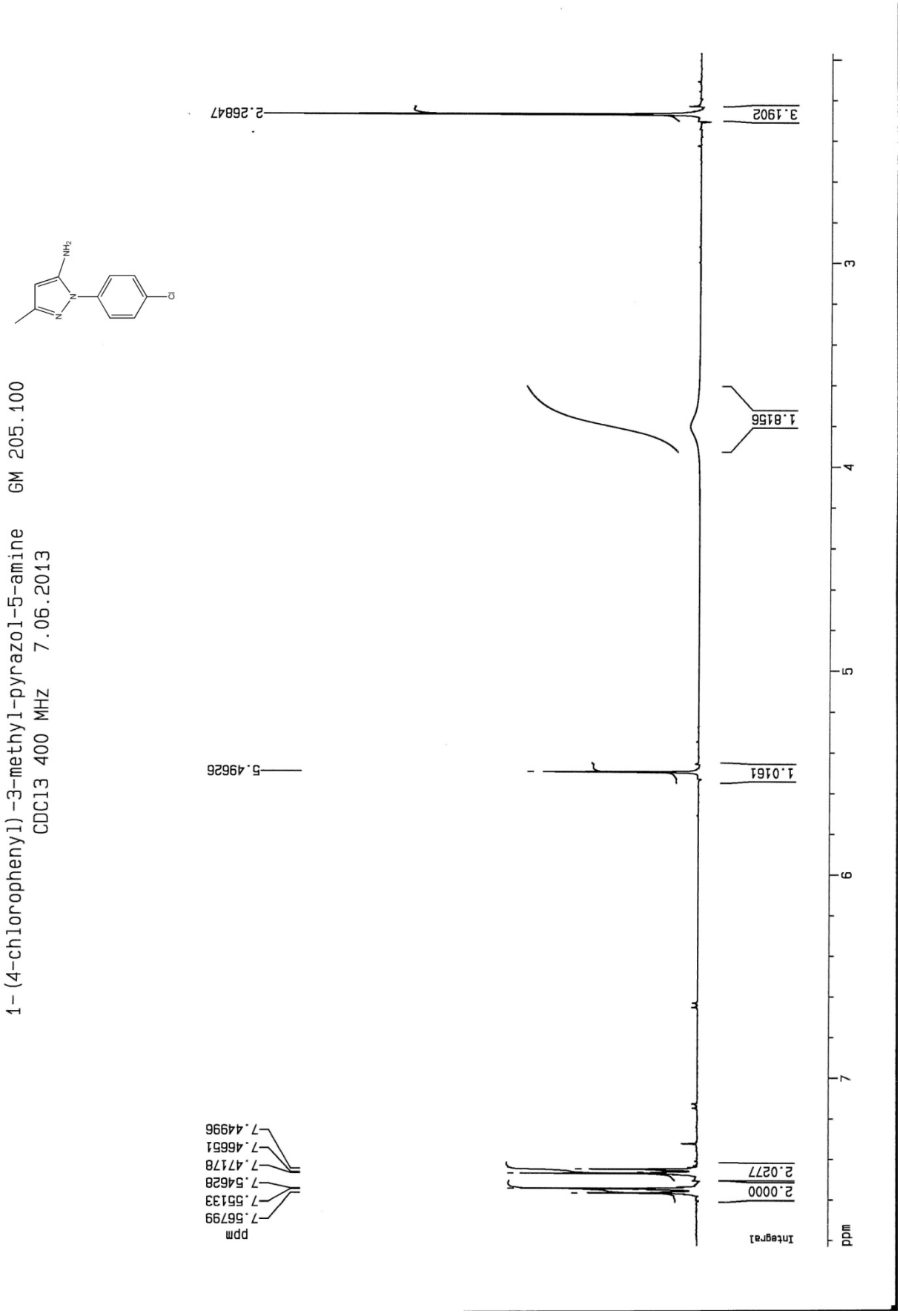
Light petroleum-EtOAc (6:4). Mp 102-104 °C (from light petroleum/EtOAc) (lit.[7] 107-109 °C). IR (KBr): ν_{max}/cm^{-1} 3309, 3167, 2310, 1559, 1503, 1374, 1253, 1082, 1033, 953, 757. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.89-7.87 (m, 2H), 7.64-7.62 (m, 2H), 7.49-7.32 (m, 5H), 6.05 (s, 1H), 4.1-3.45 (bs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.13, 135.74, 146.99, 133.22, 132.22, 130.58, 130.48, 130.37, 128.46 (x2), 128.03, 127.92, 125.70 (x2), 87.63. Found: C, 66.9; H, 4.5; Cl, 13.2; N, 15.4. Calc. for $C_{15}H_{12}ClN_3$: C, 66.79; H, 4.48; Cl, 13.14; N, 15.58.

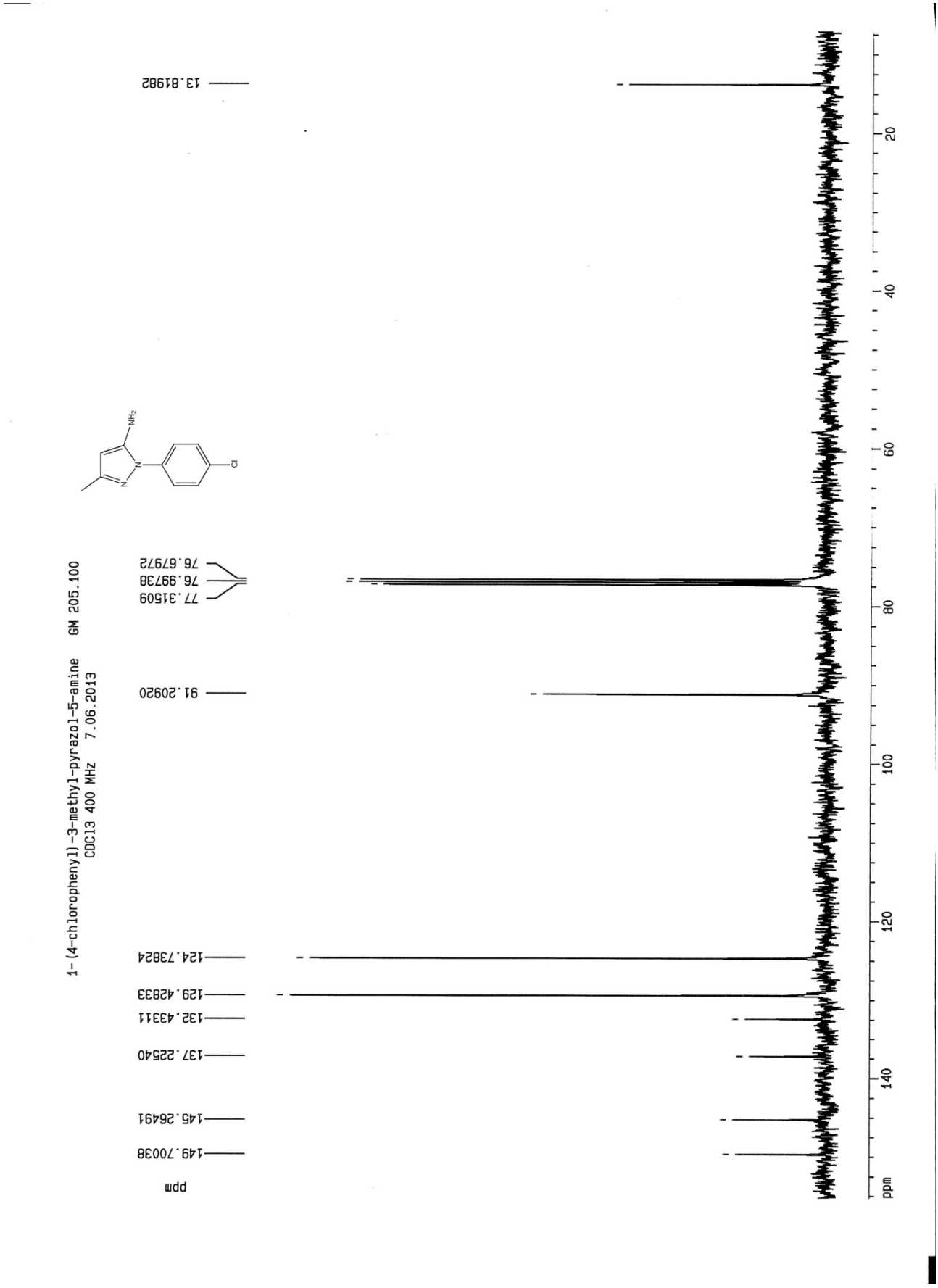


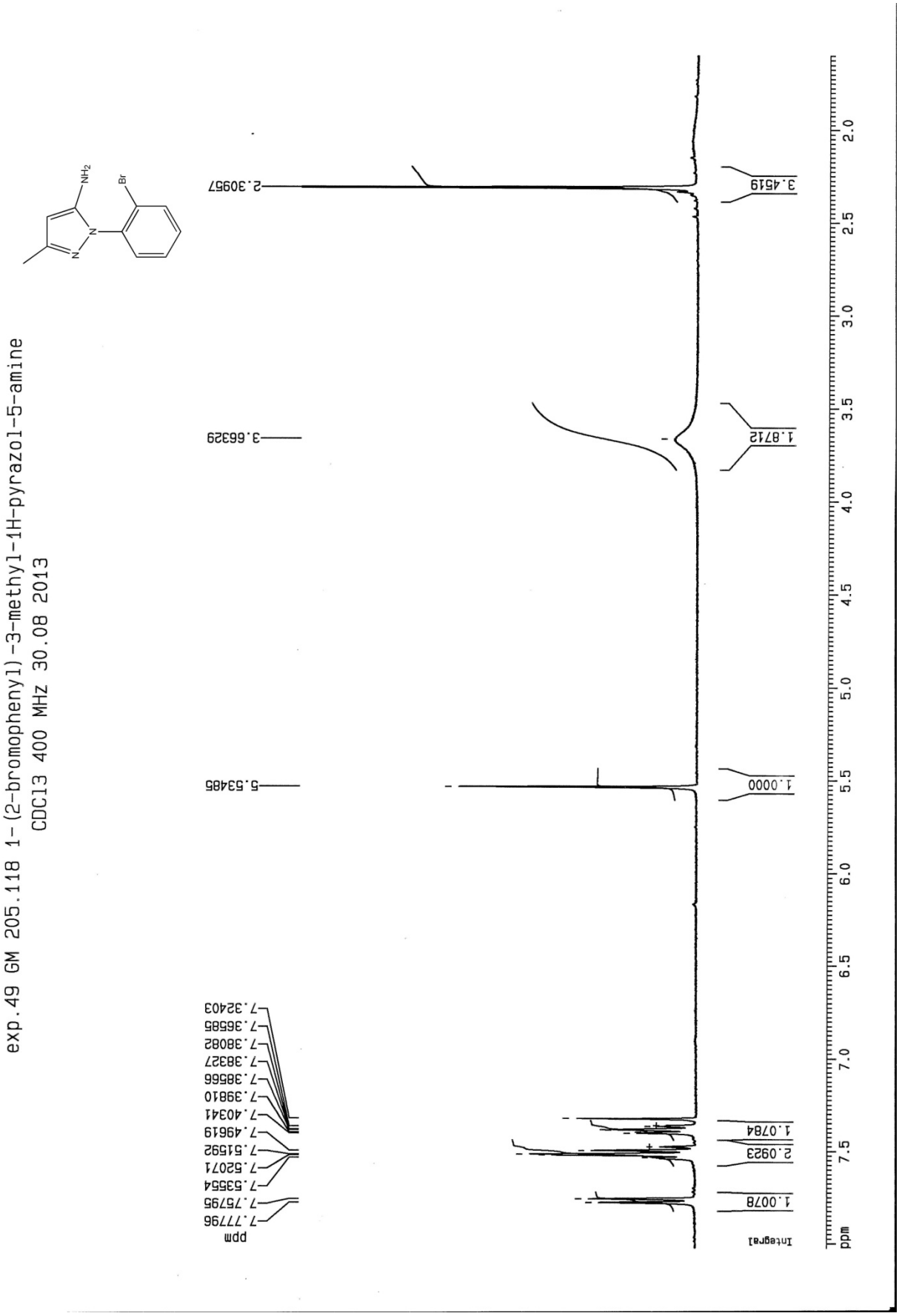


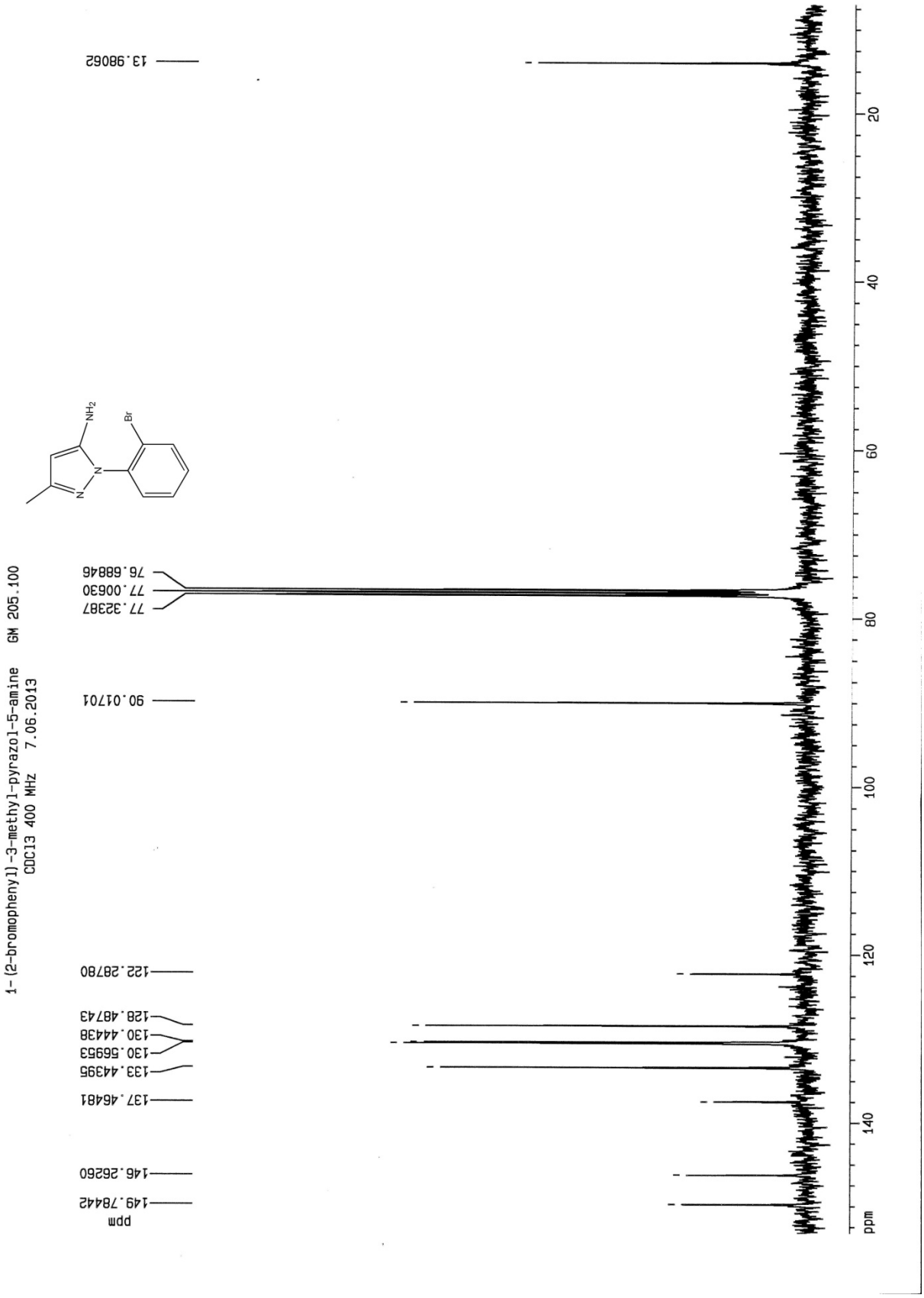


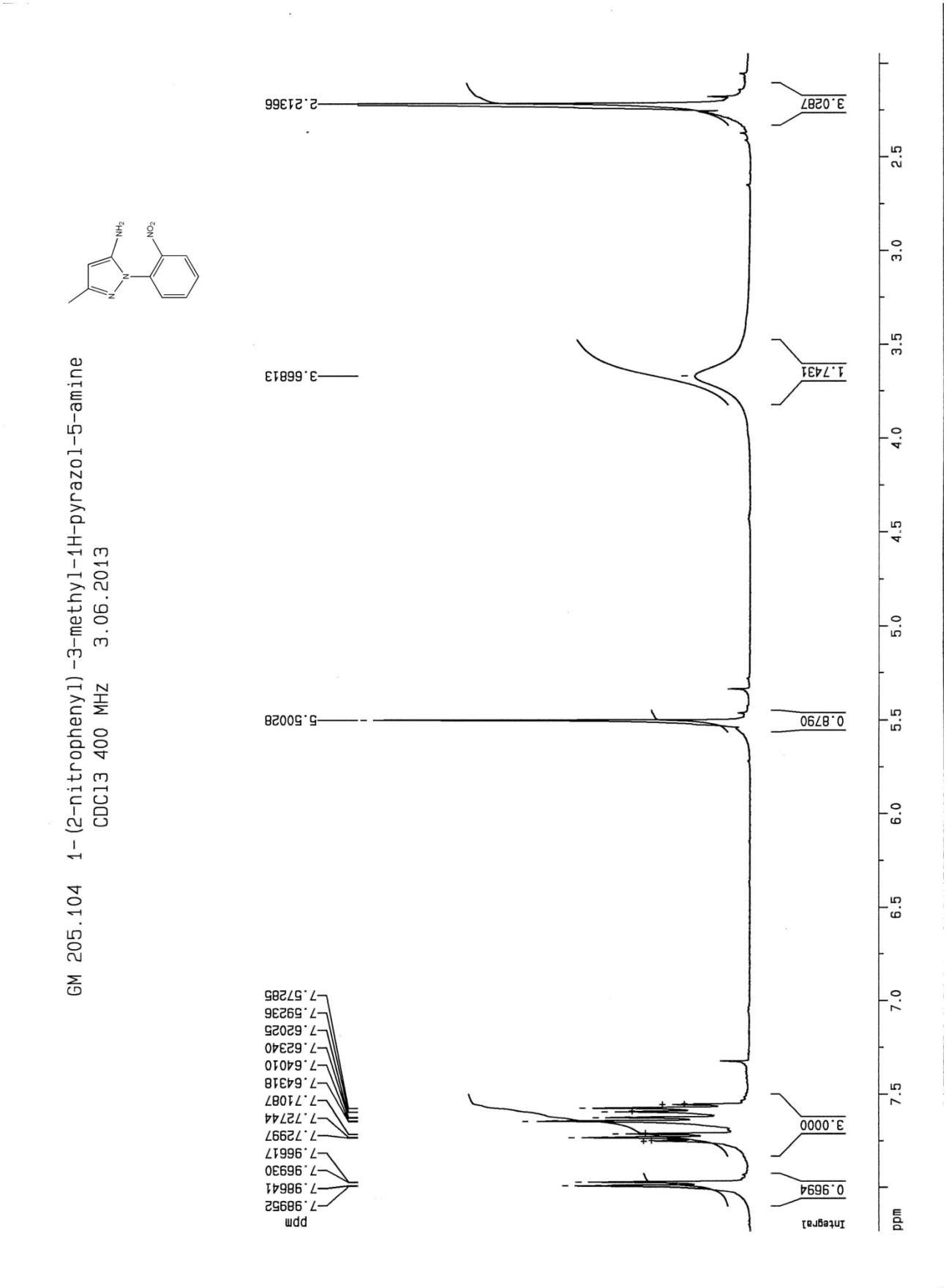








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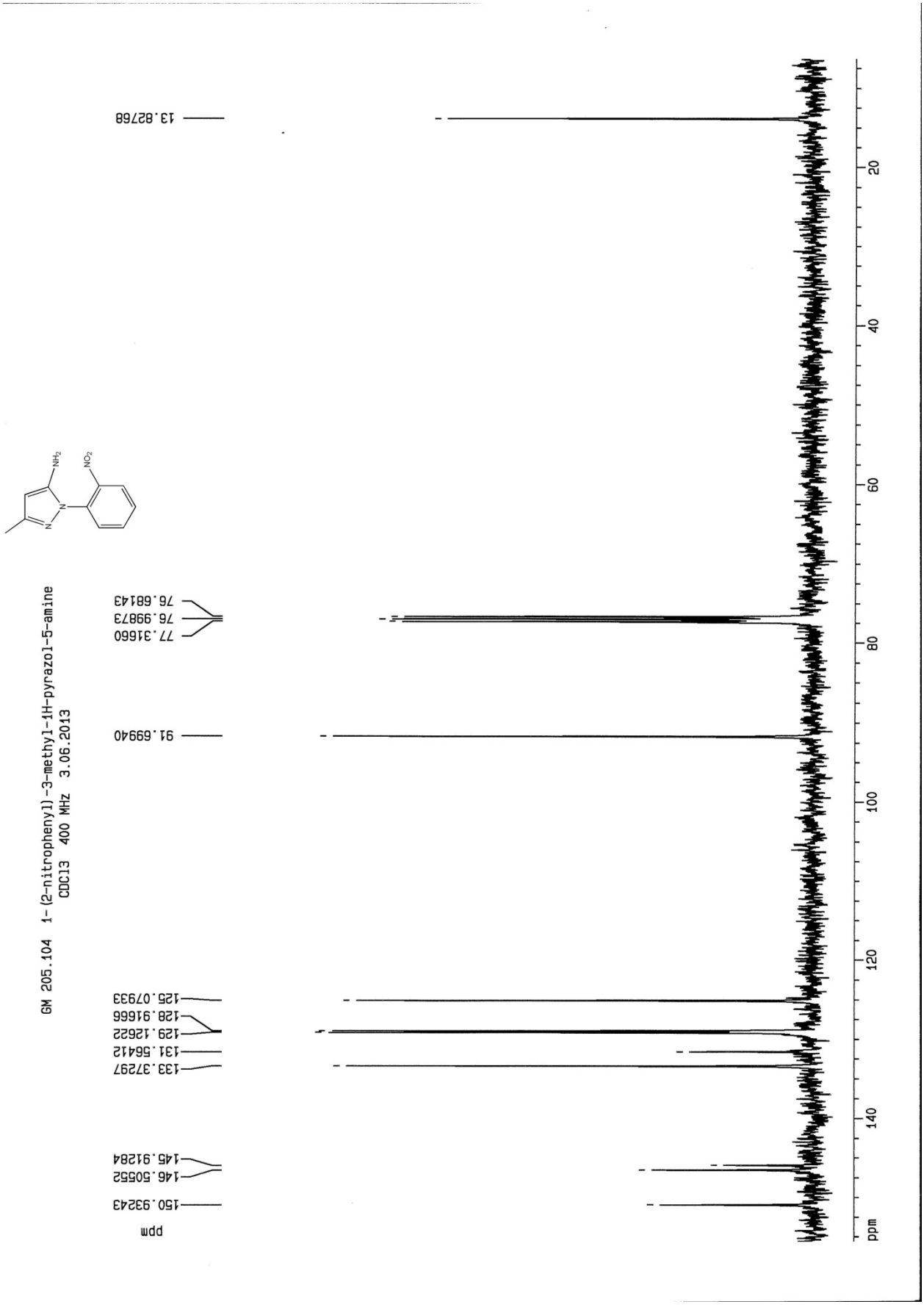

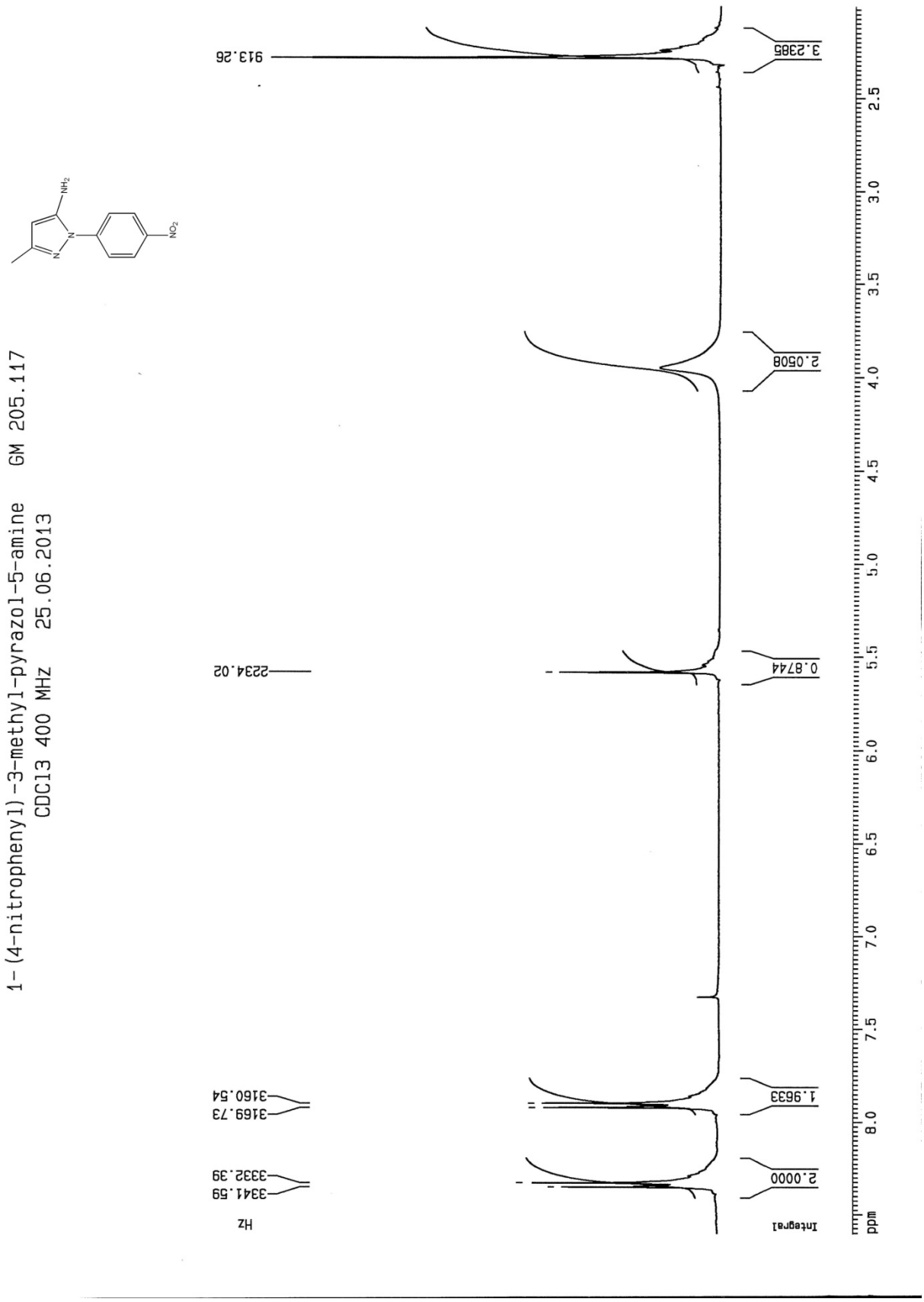

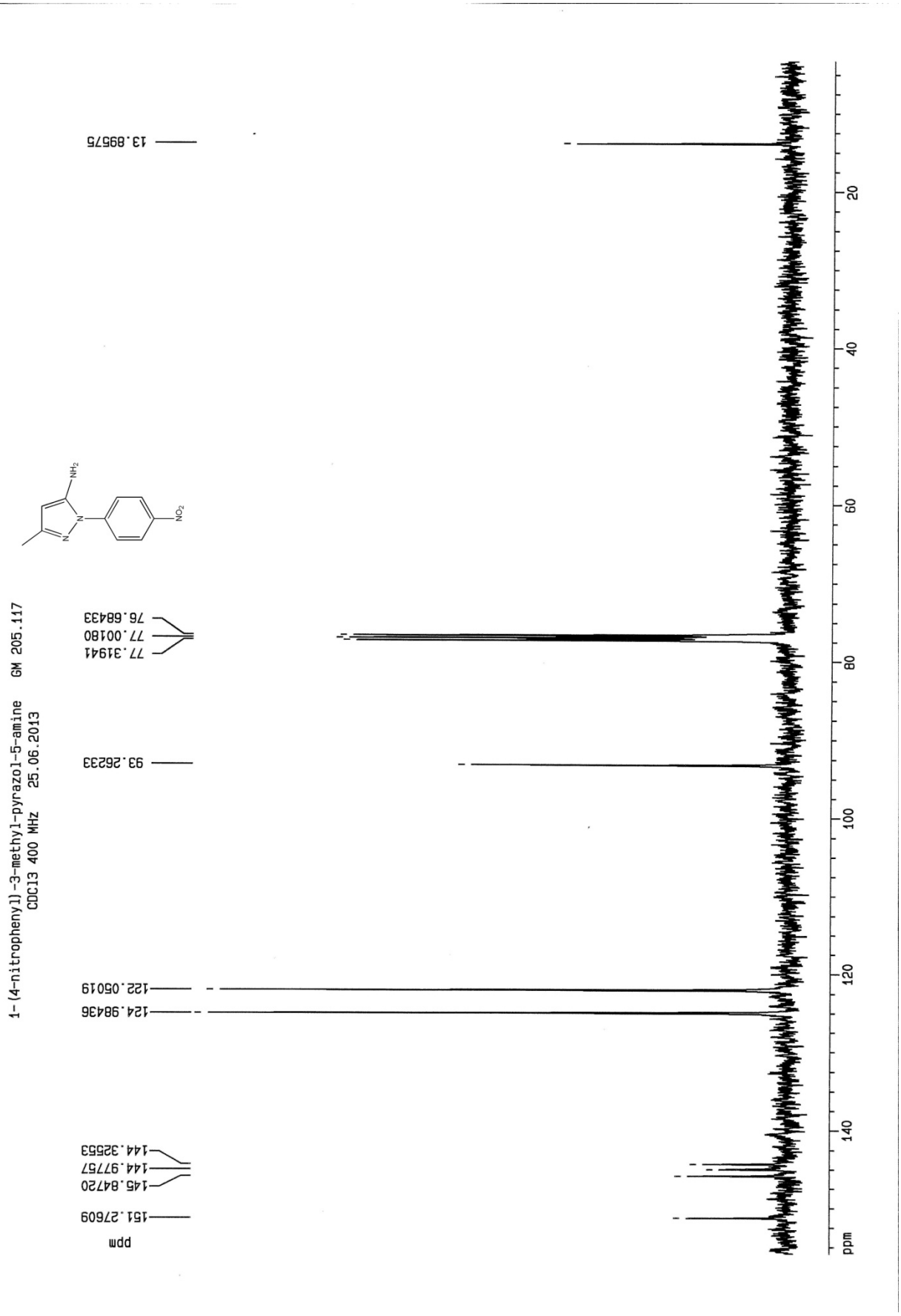

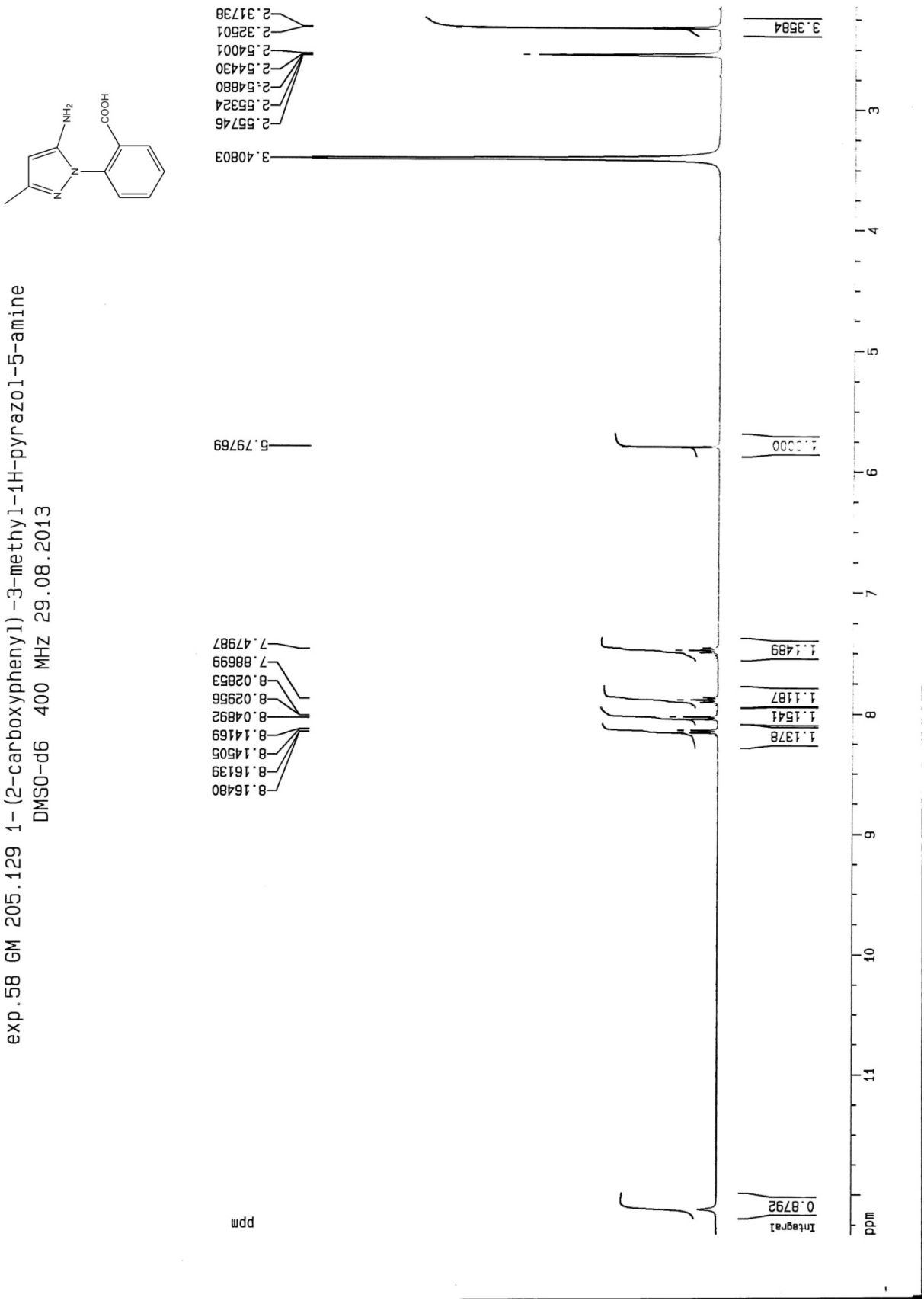

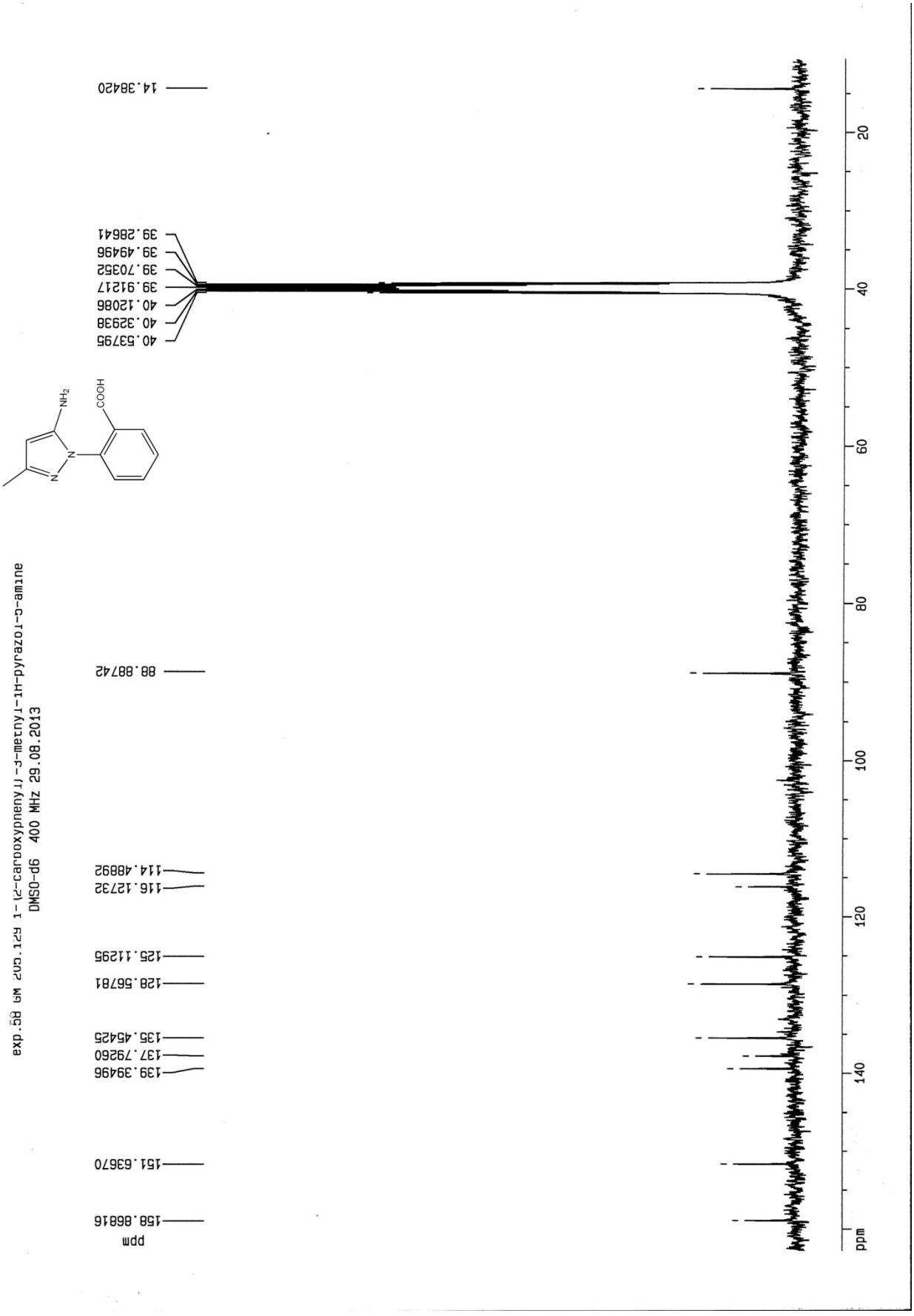

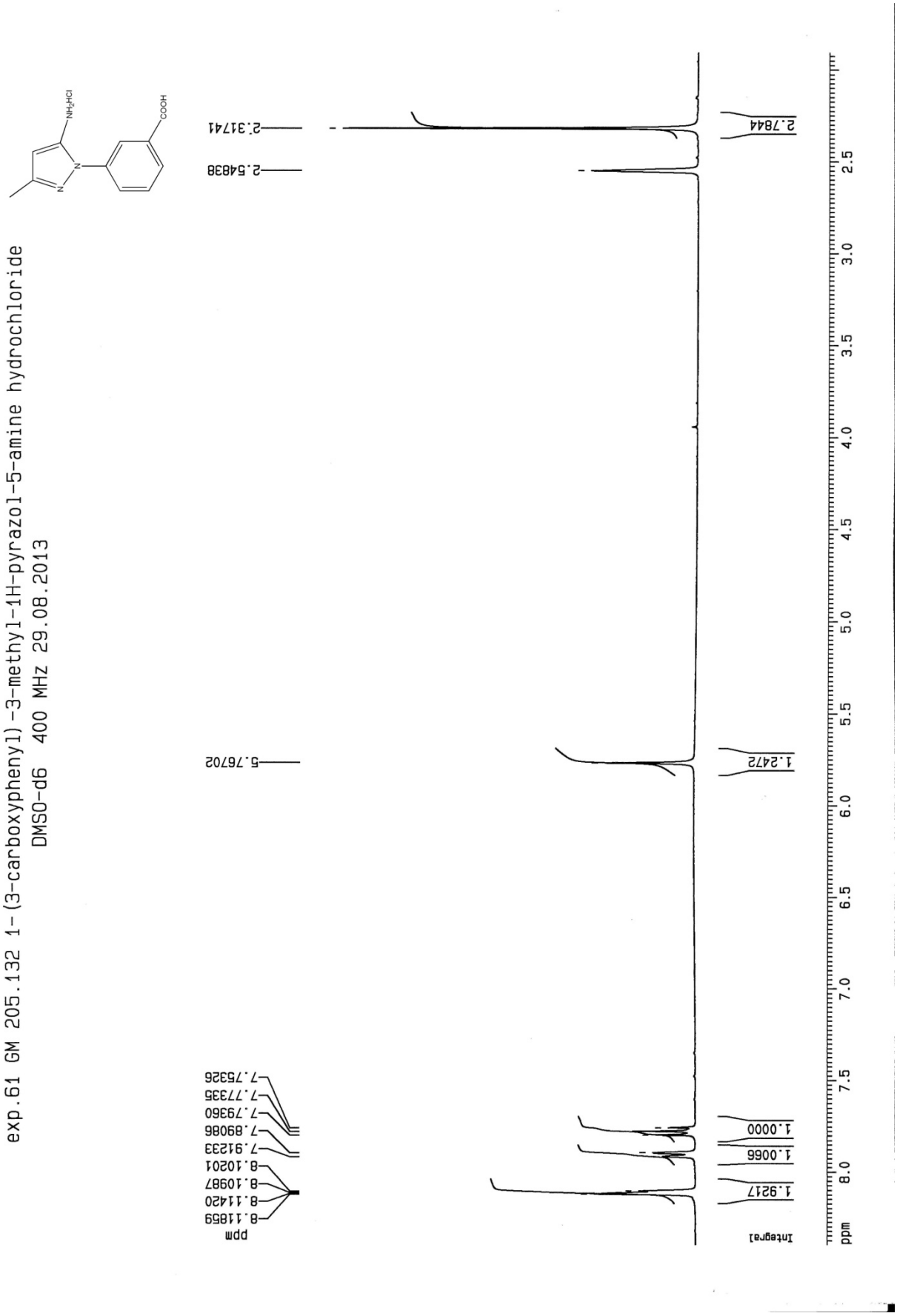

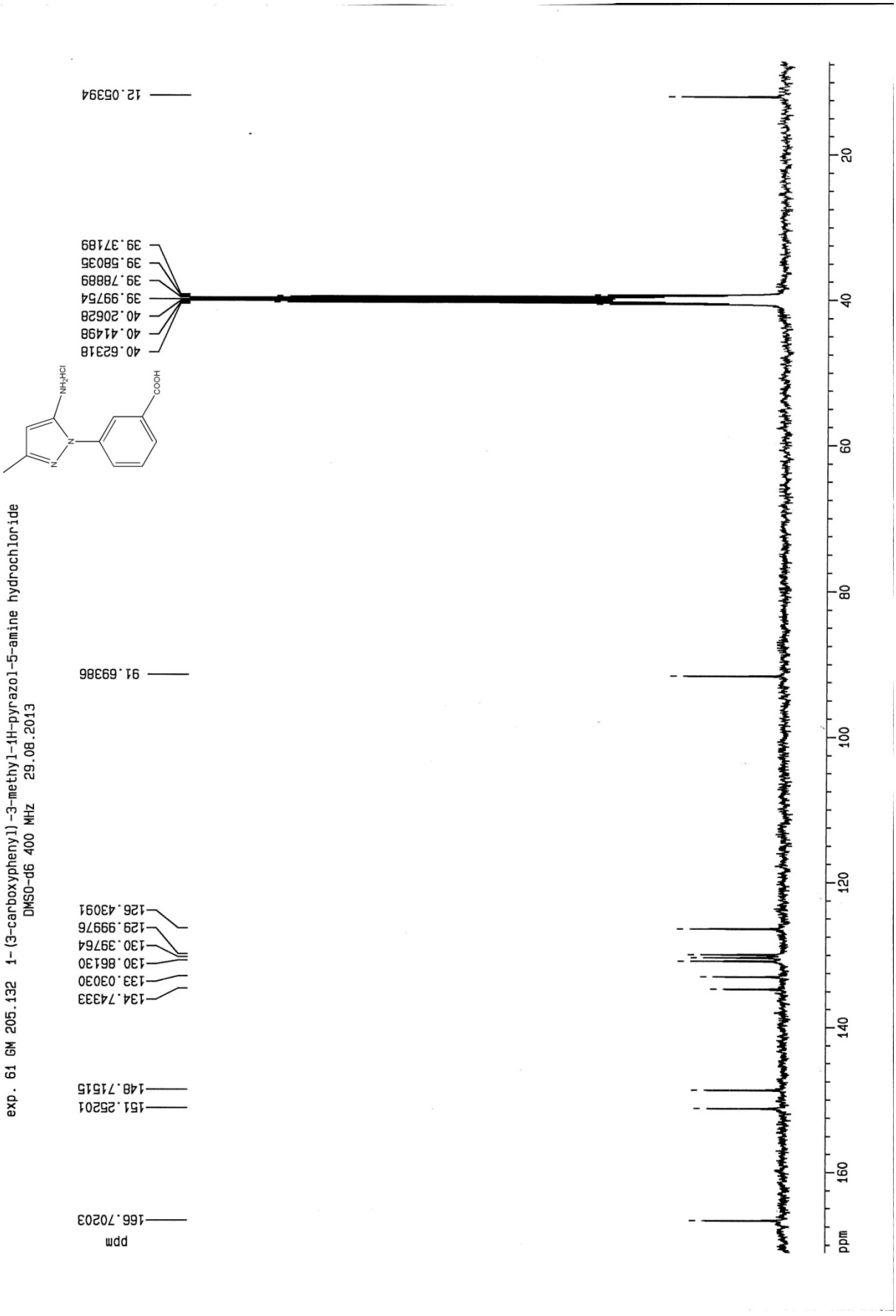

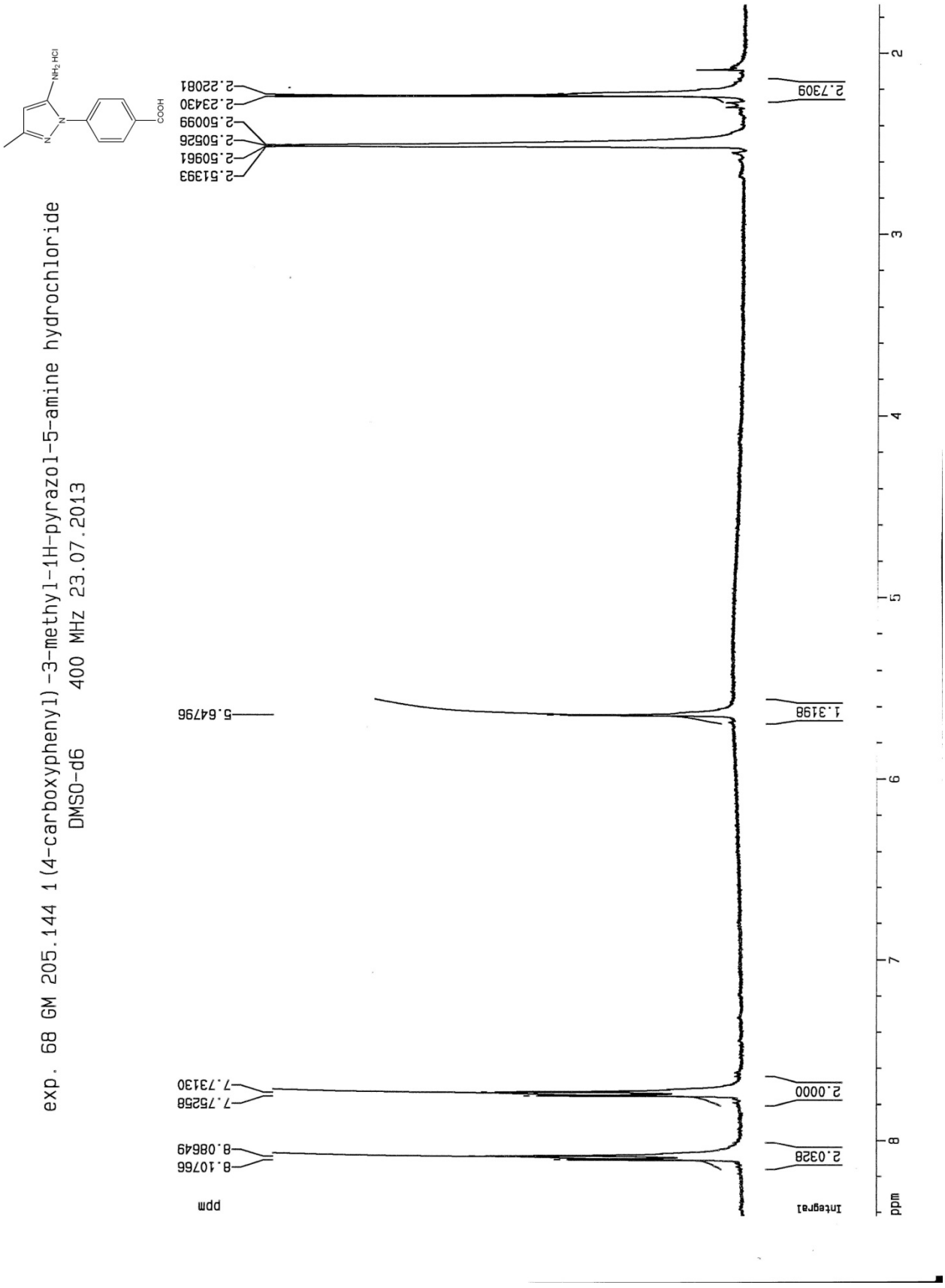

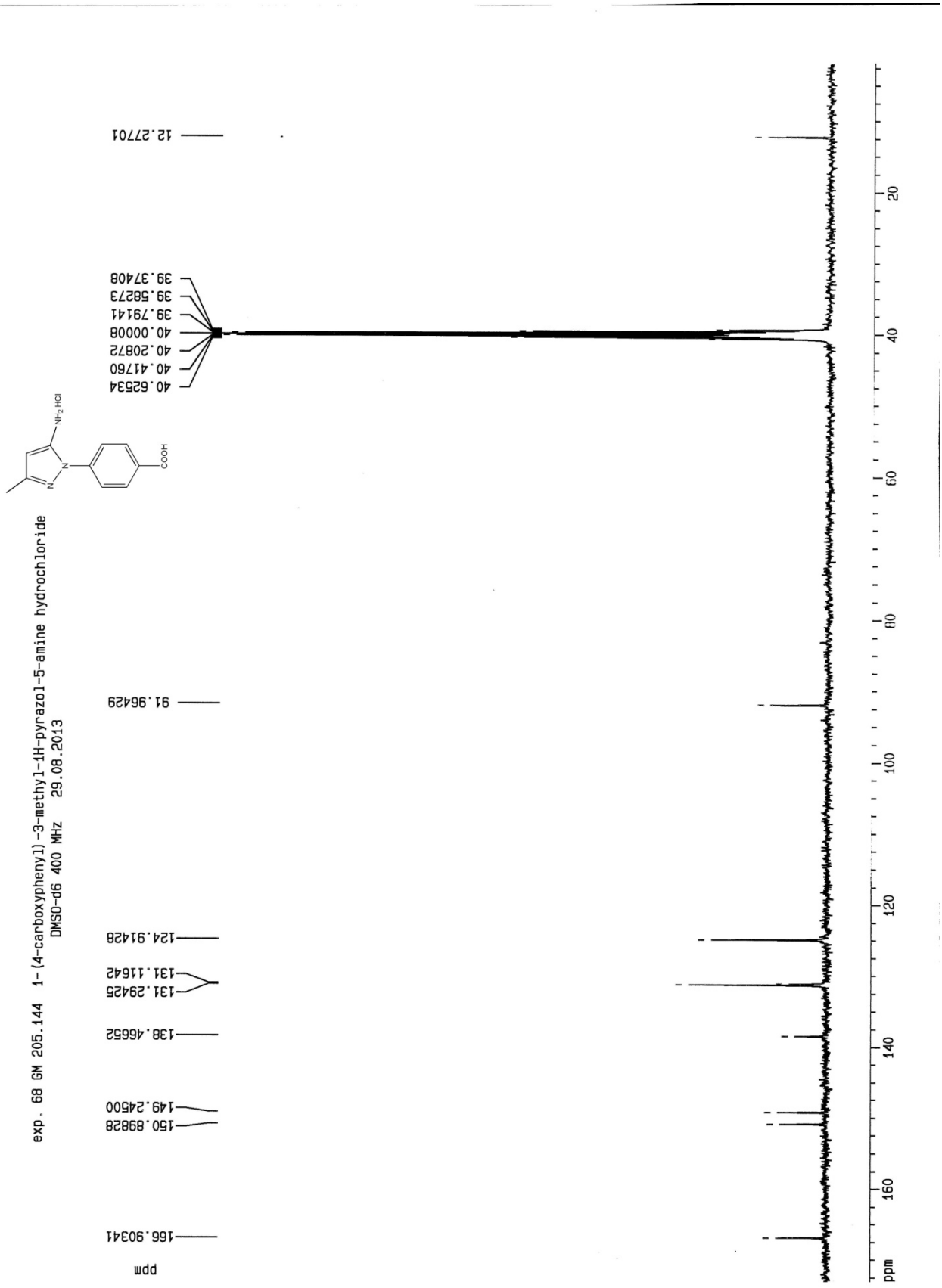
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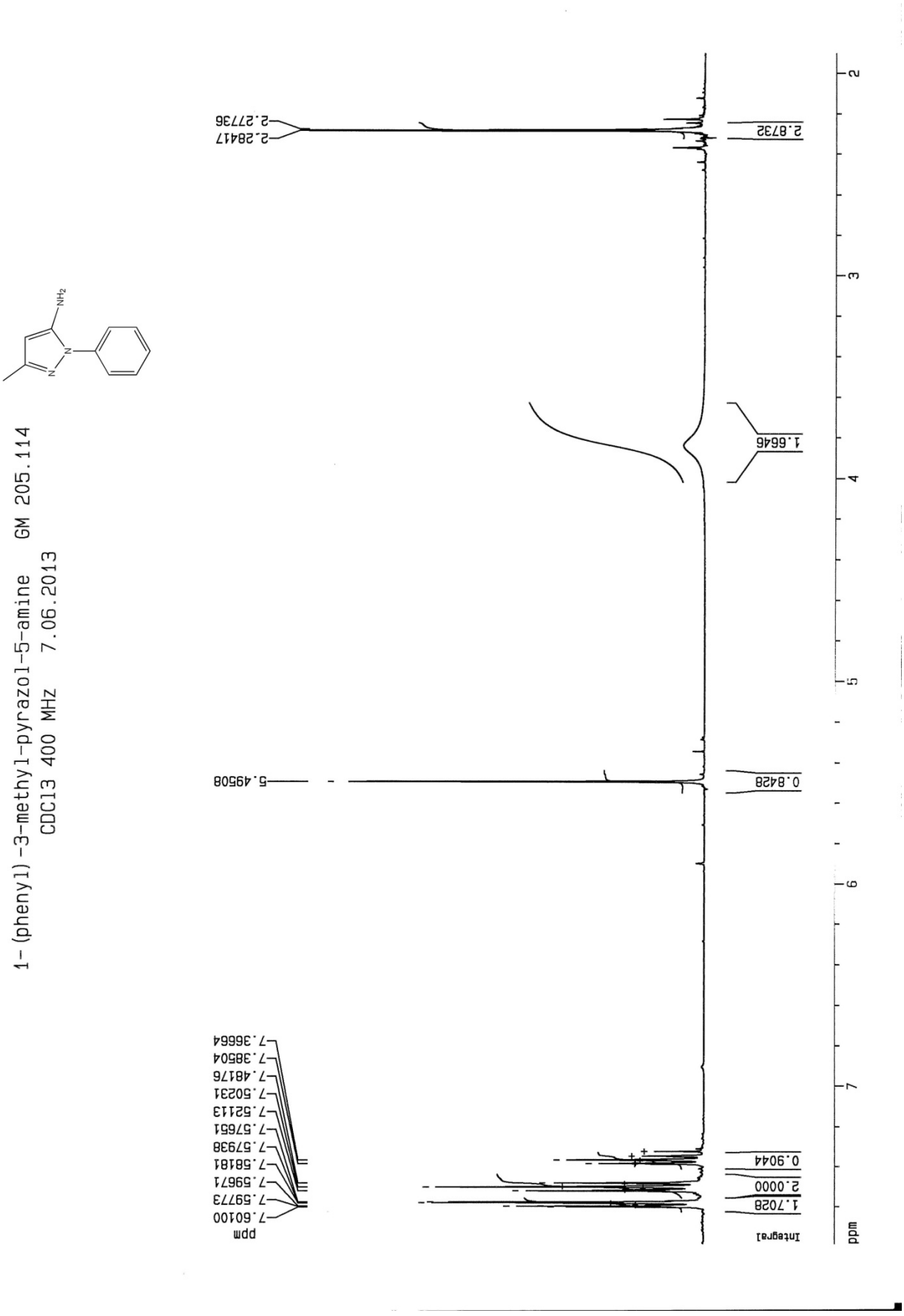

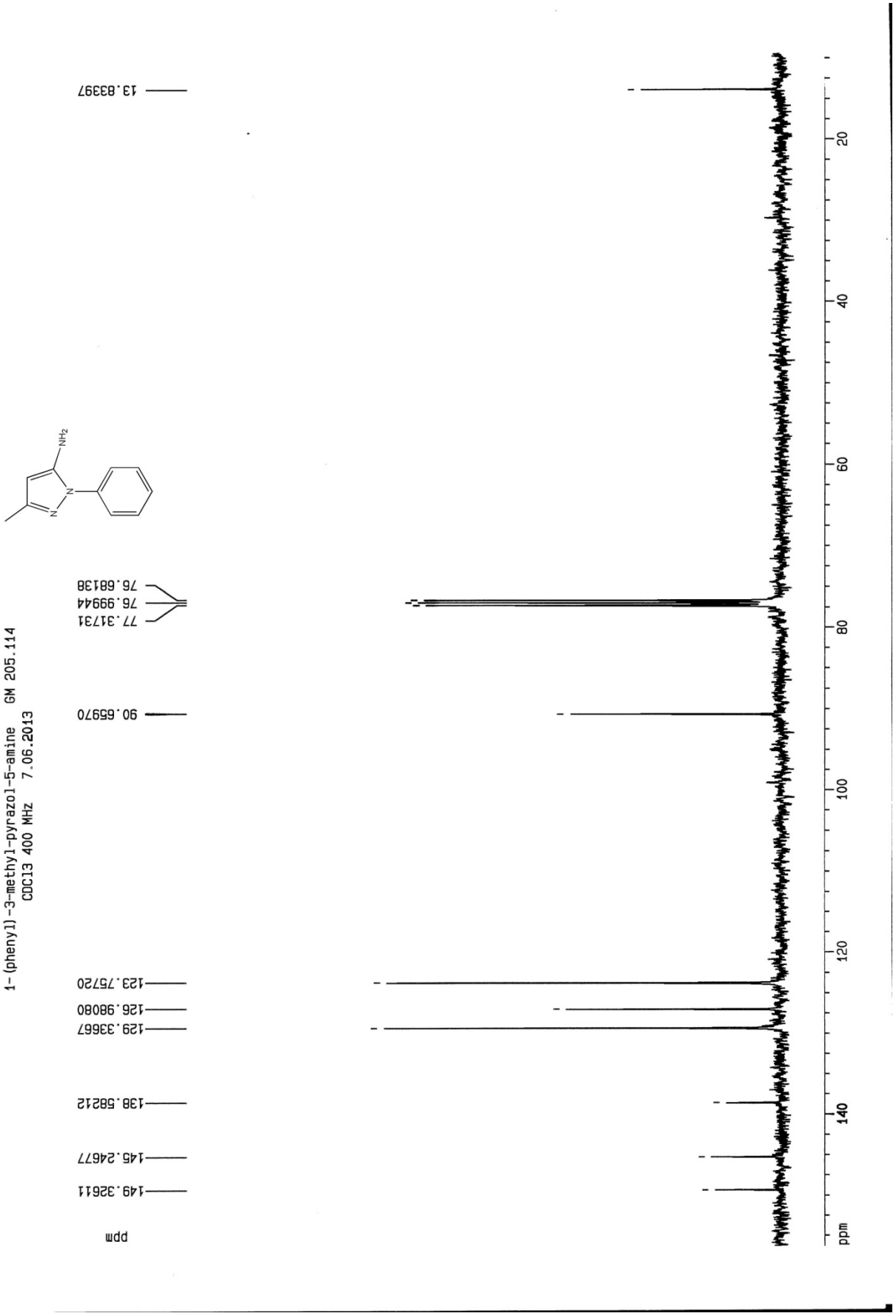

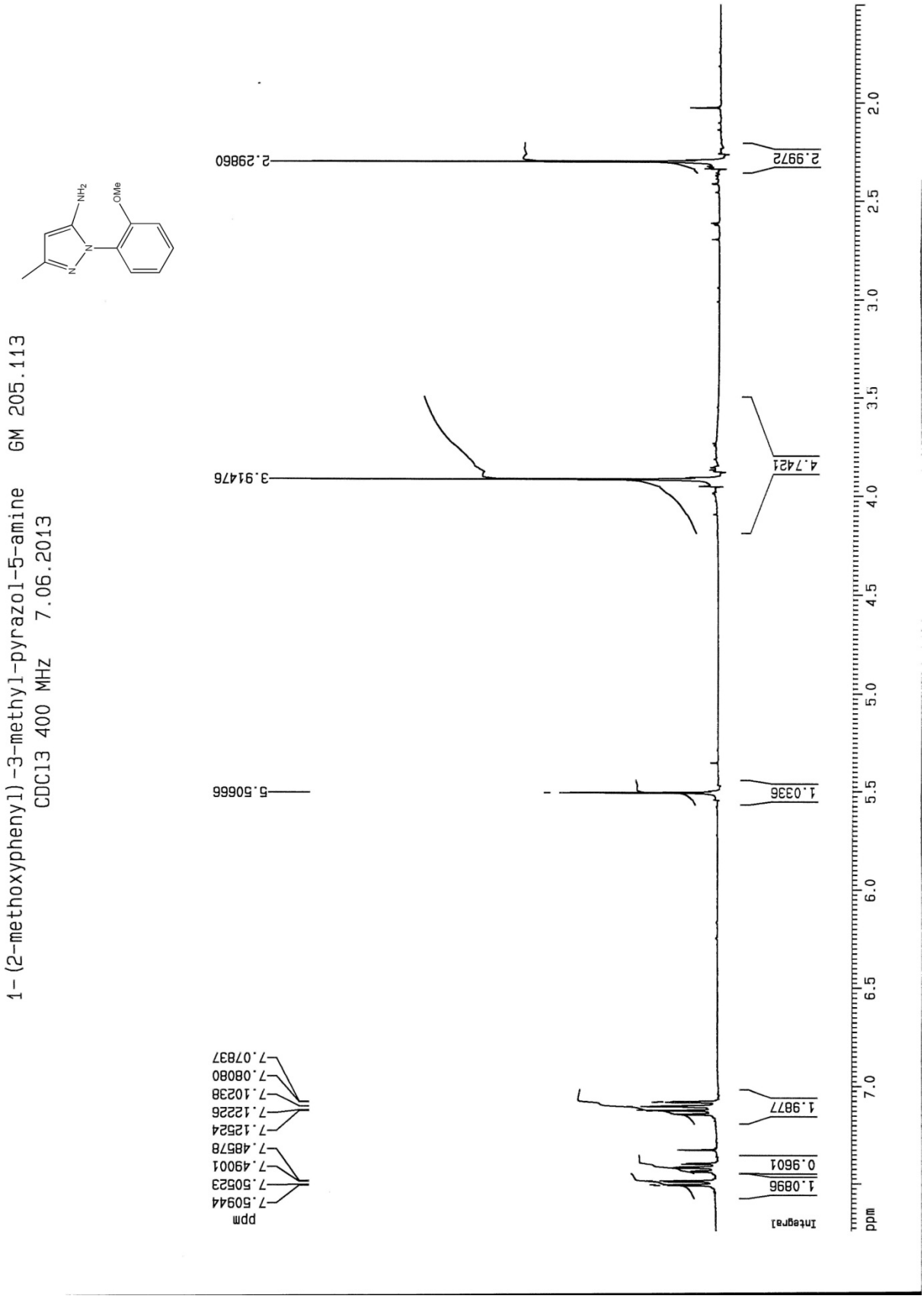

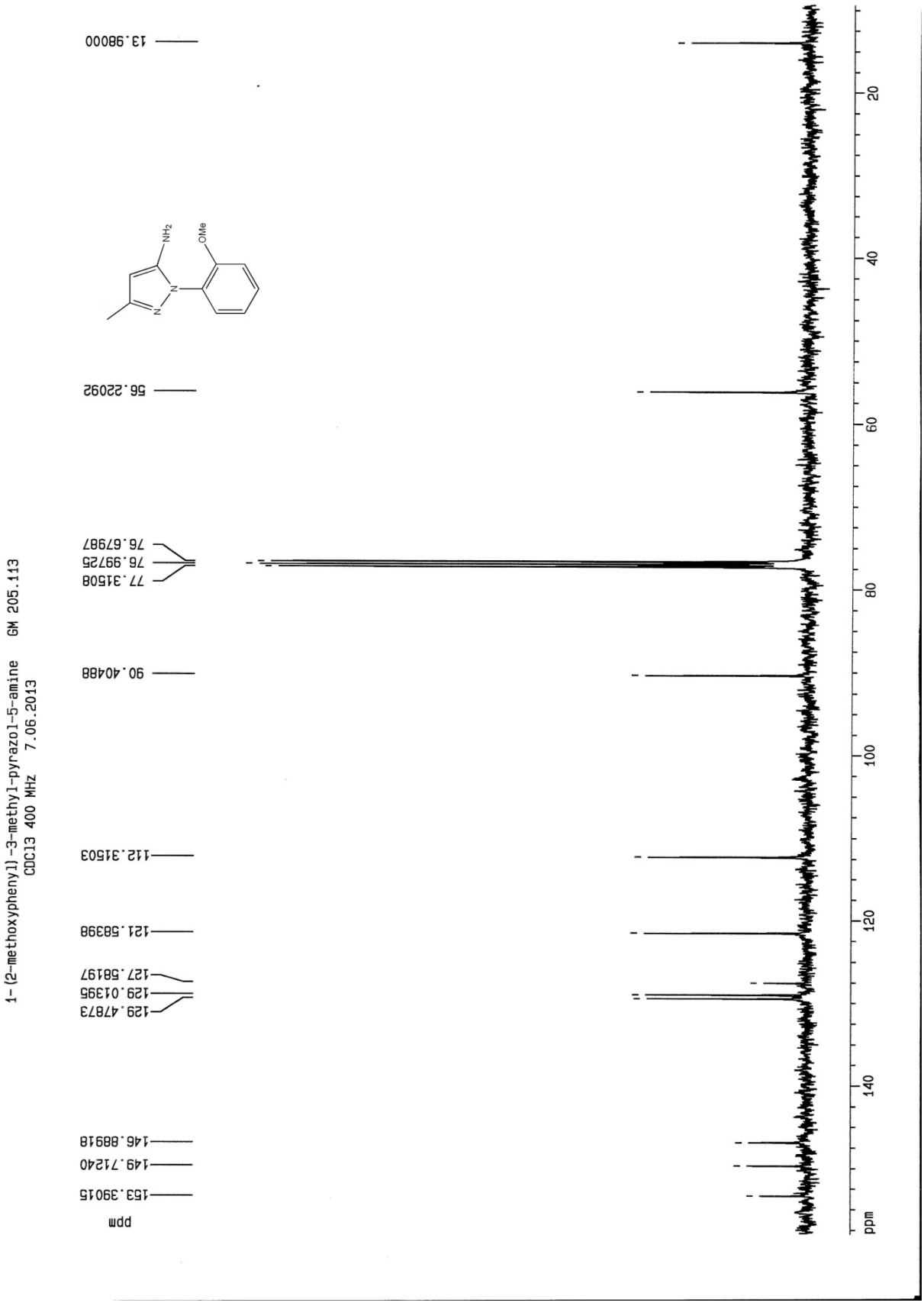

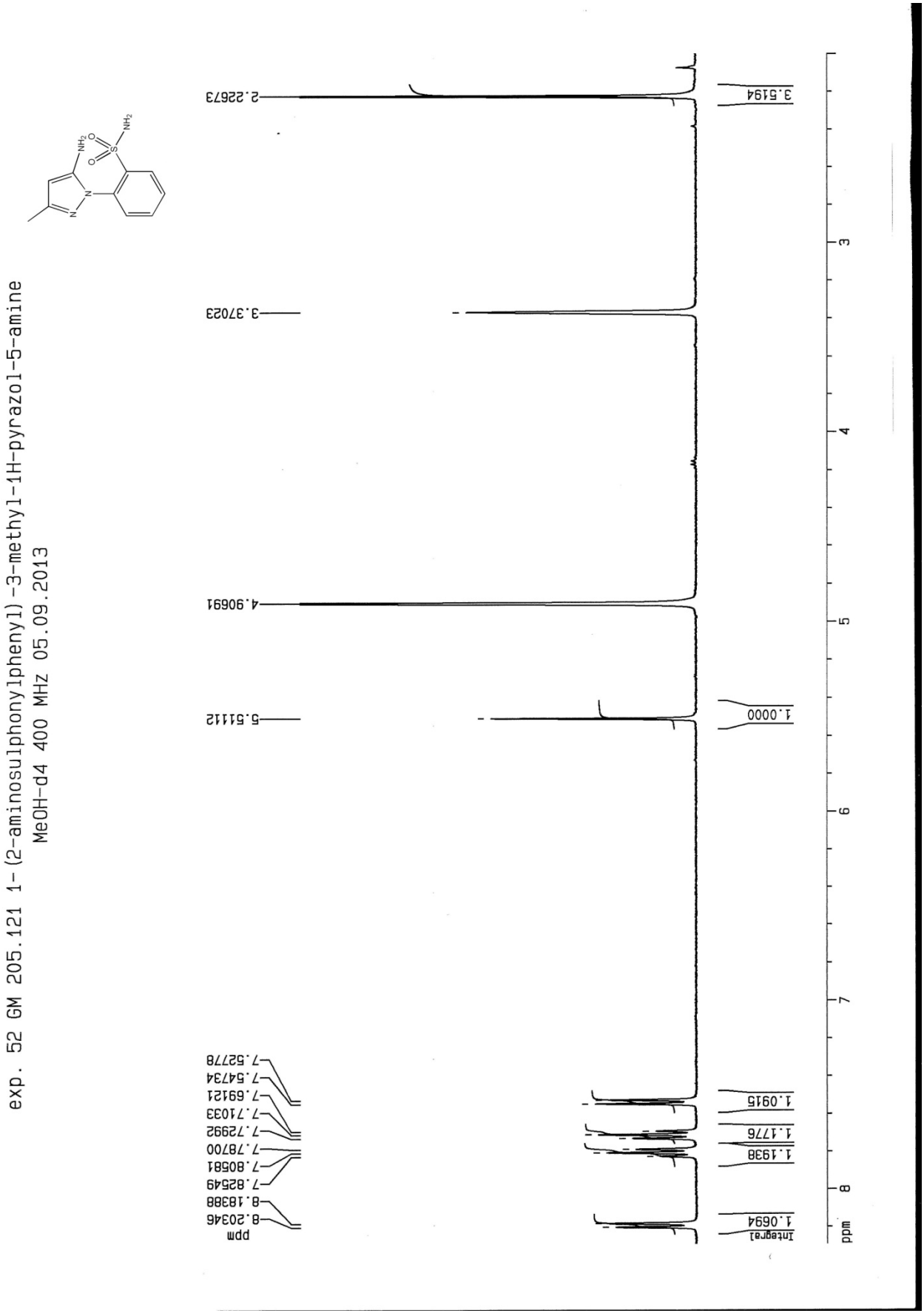

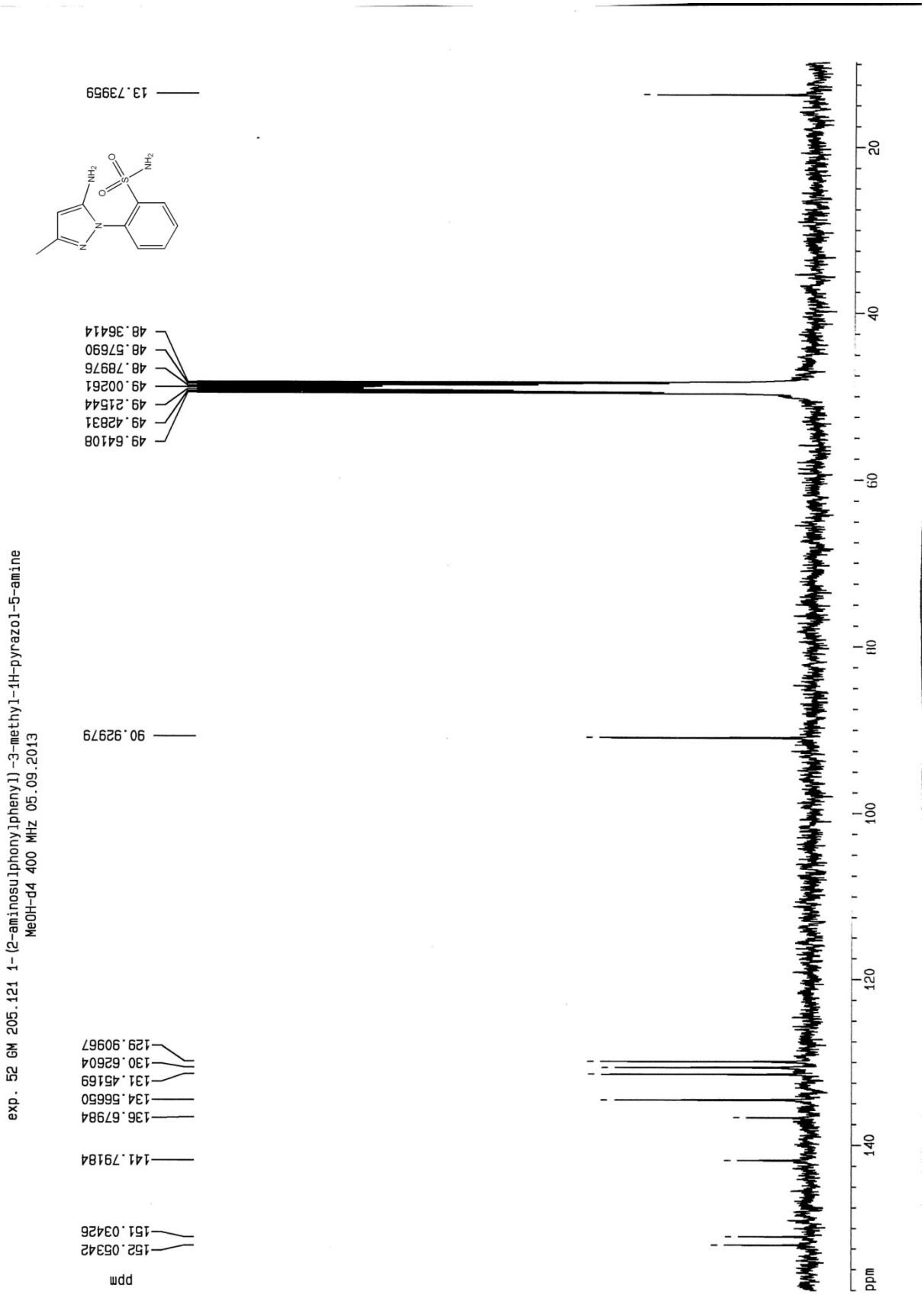

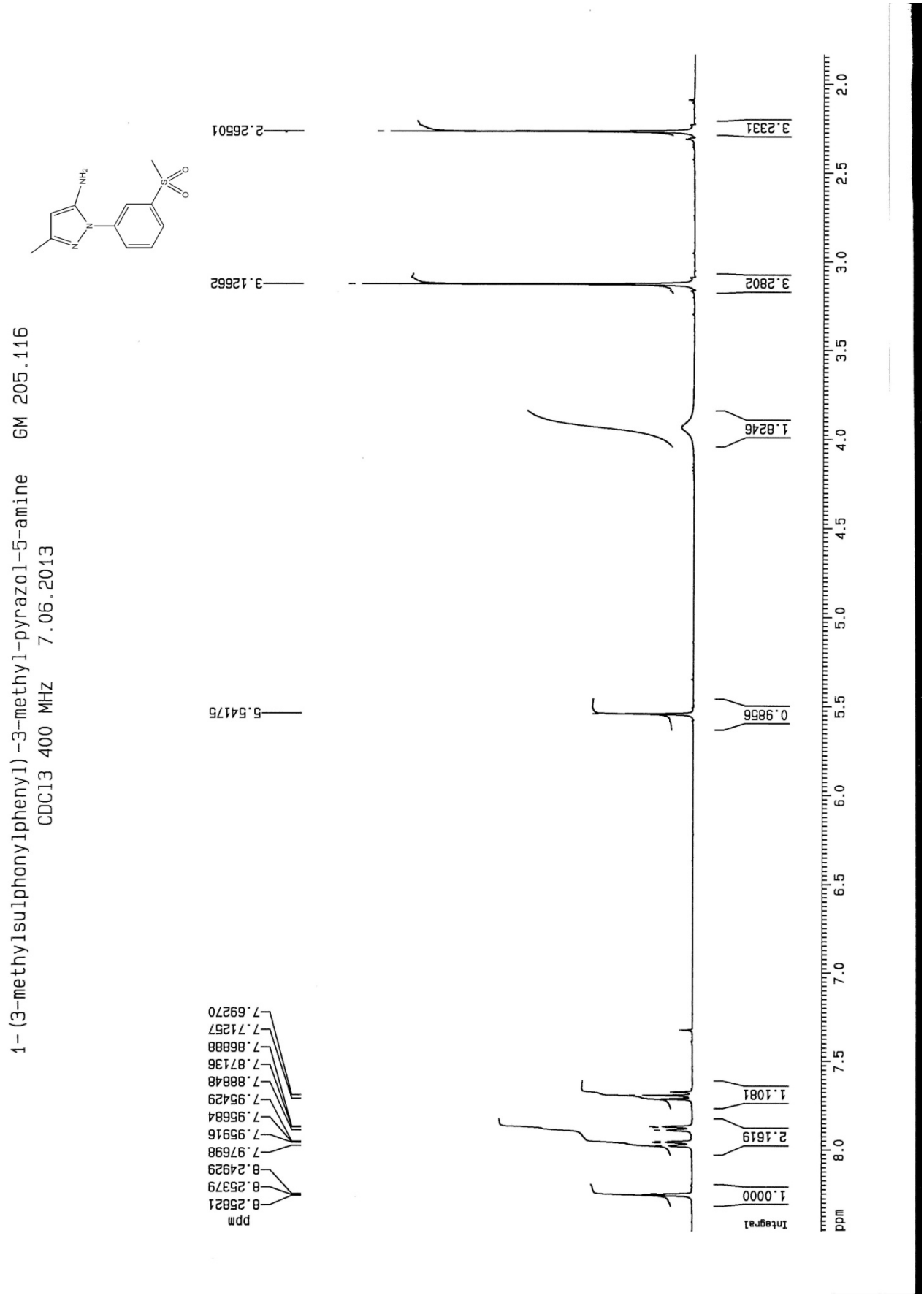

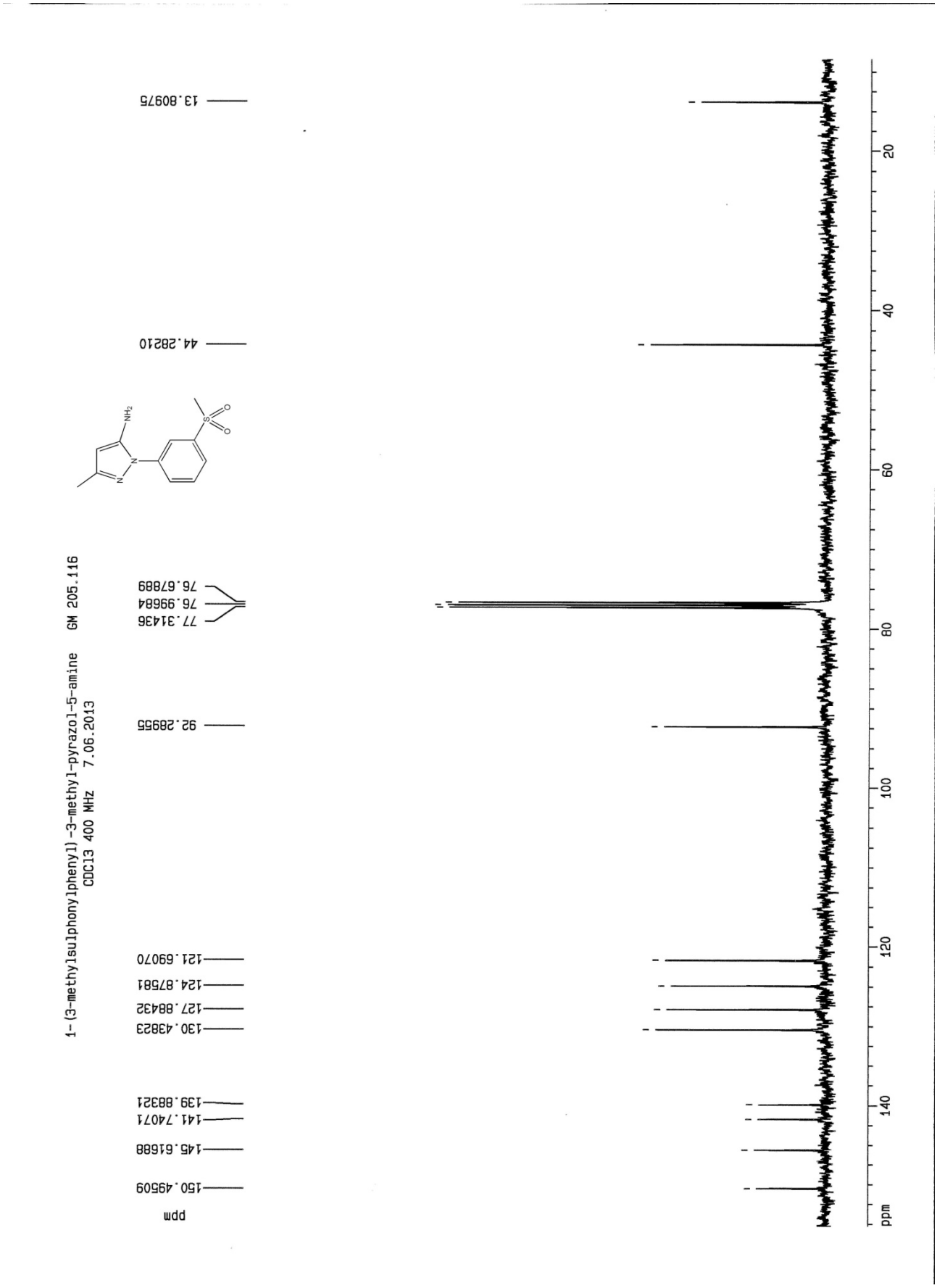

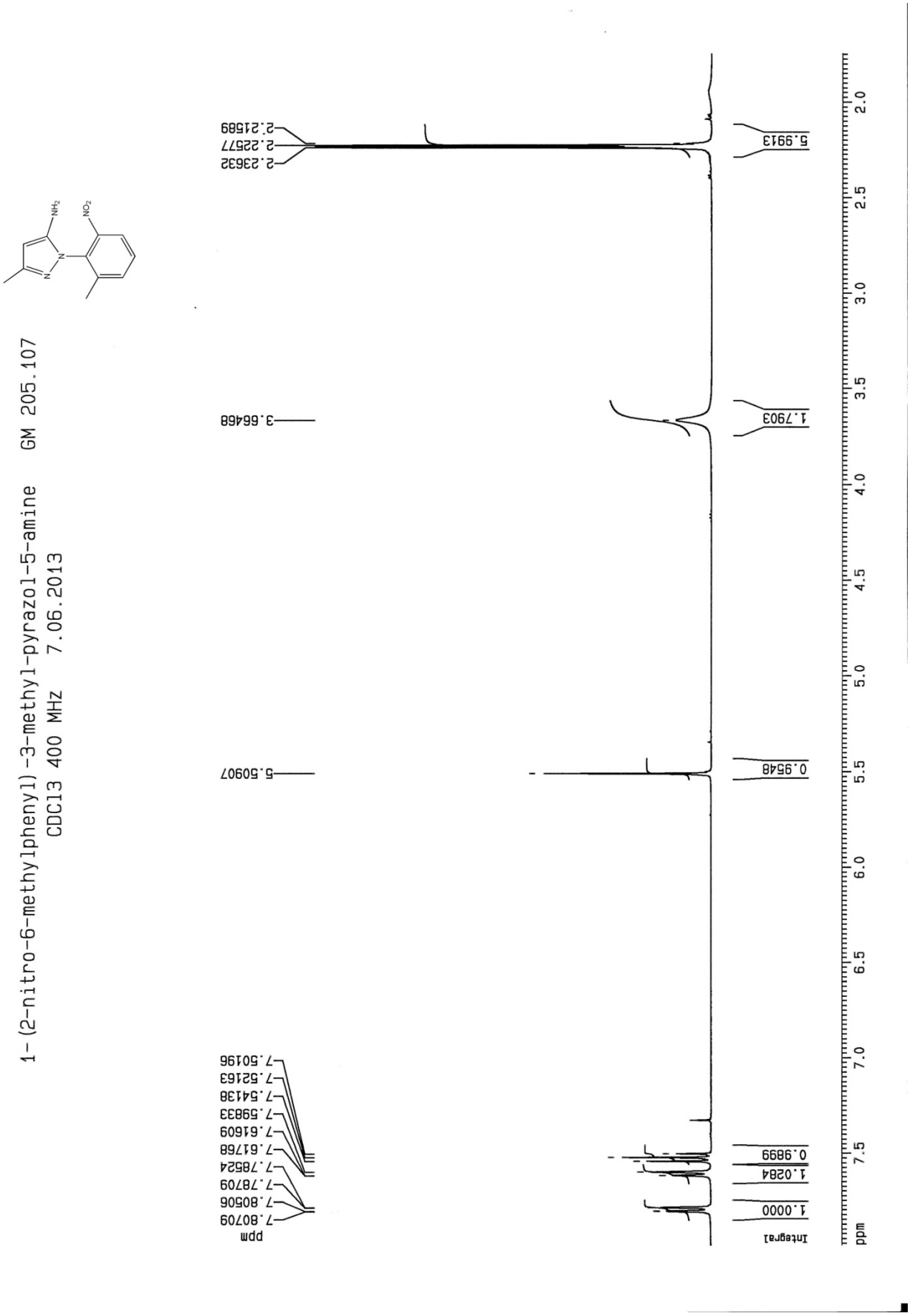

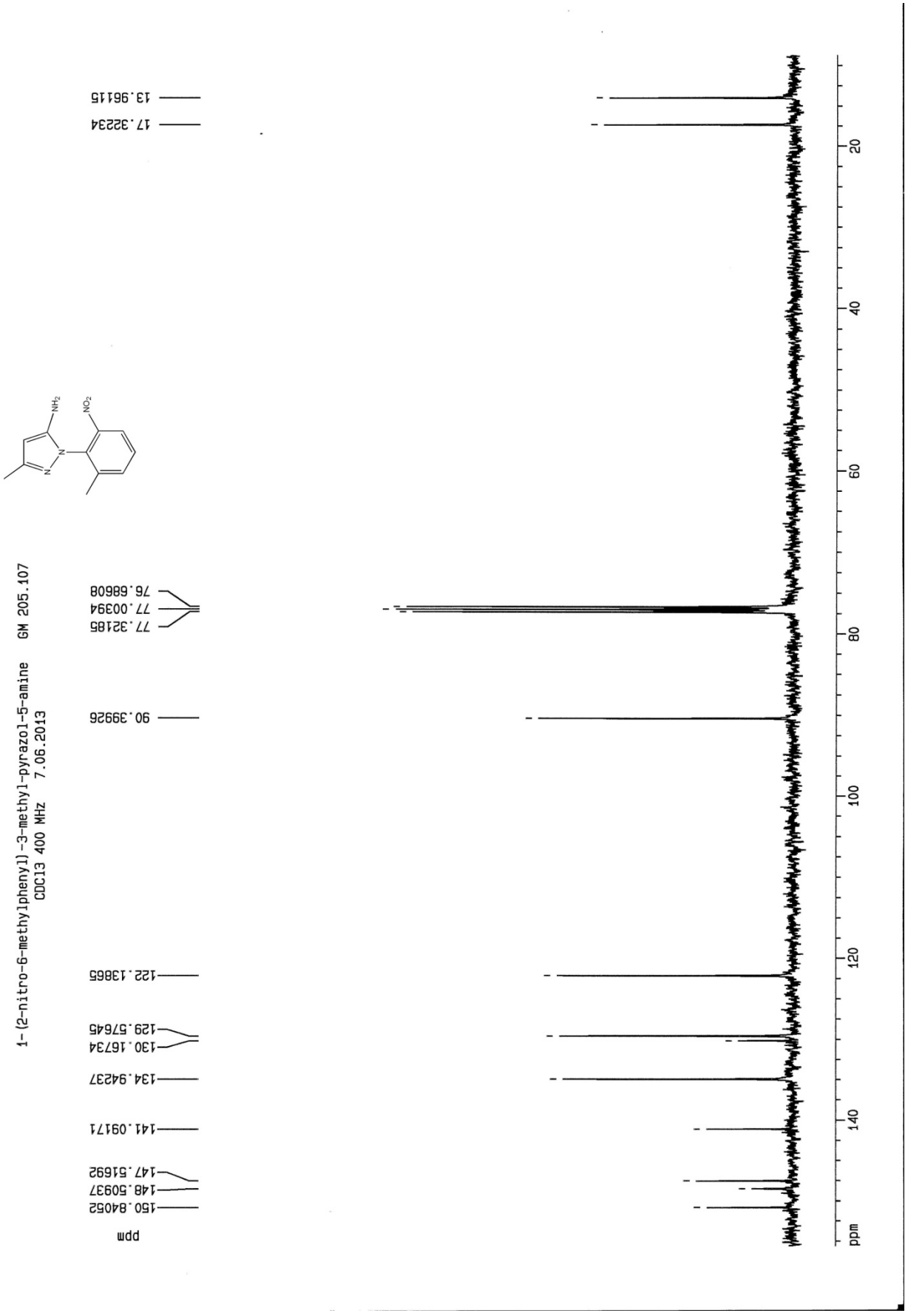

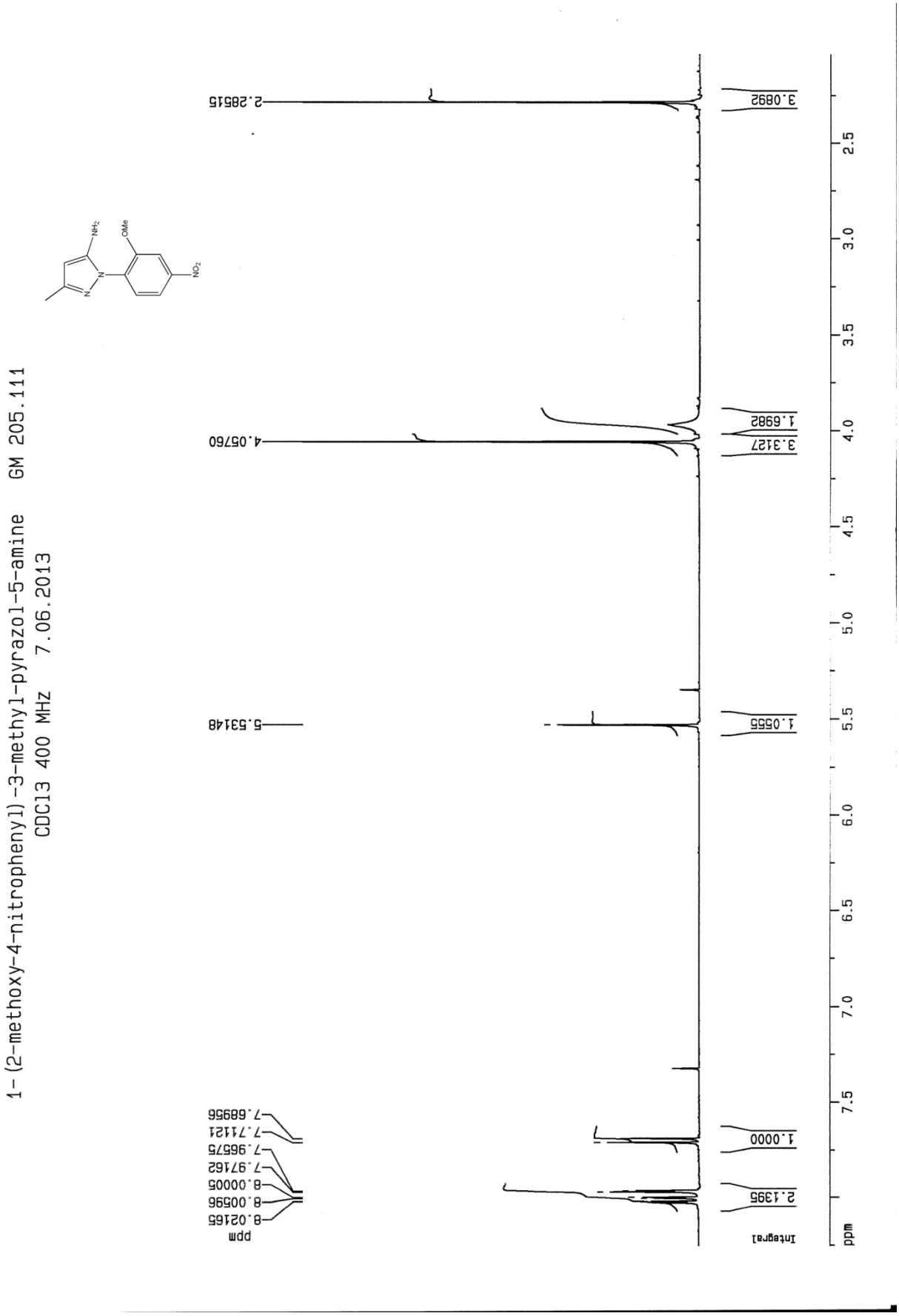

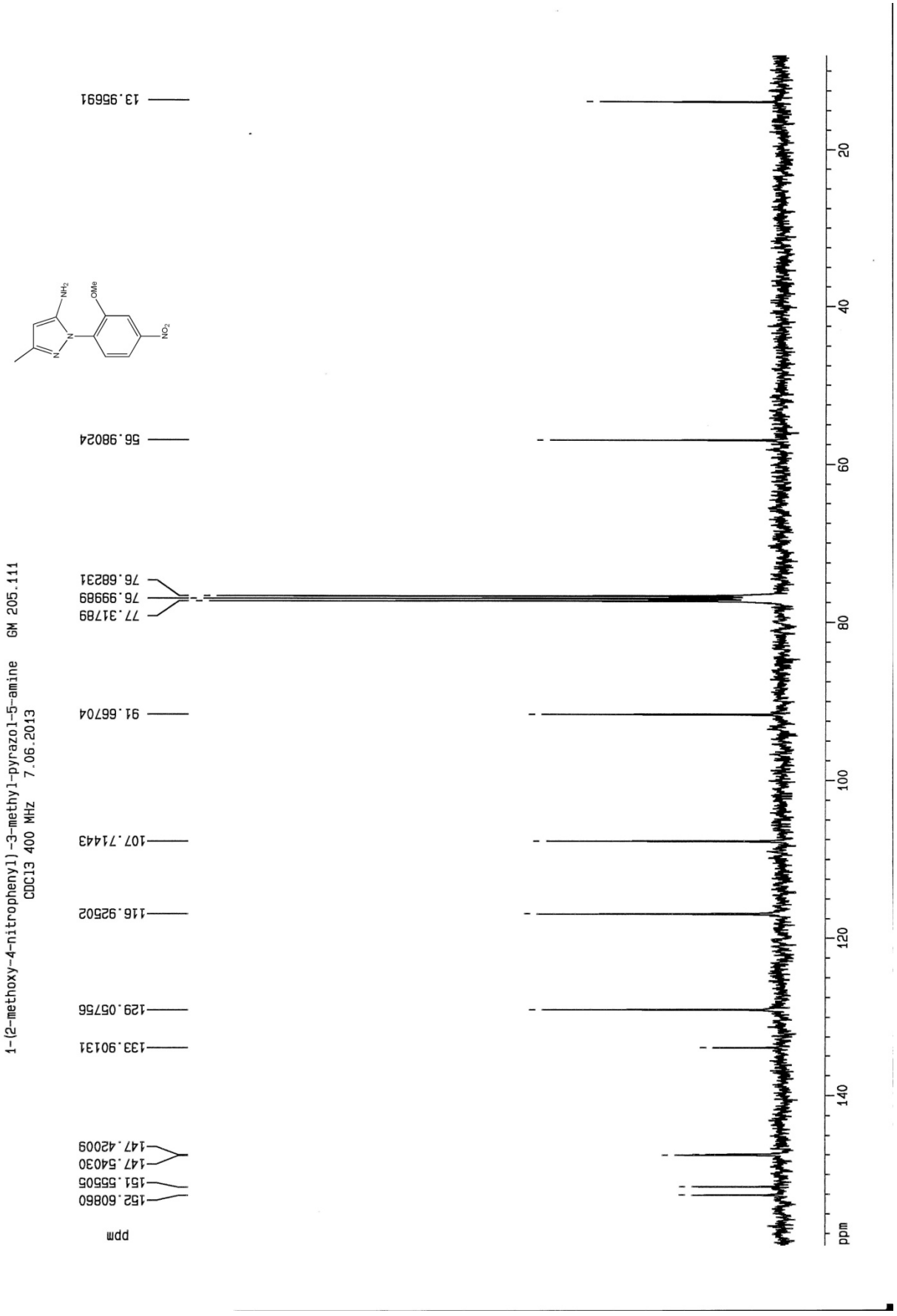

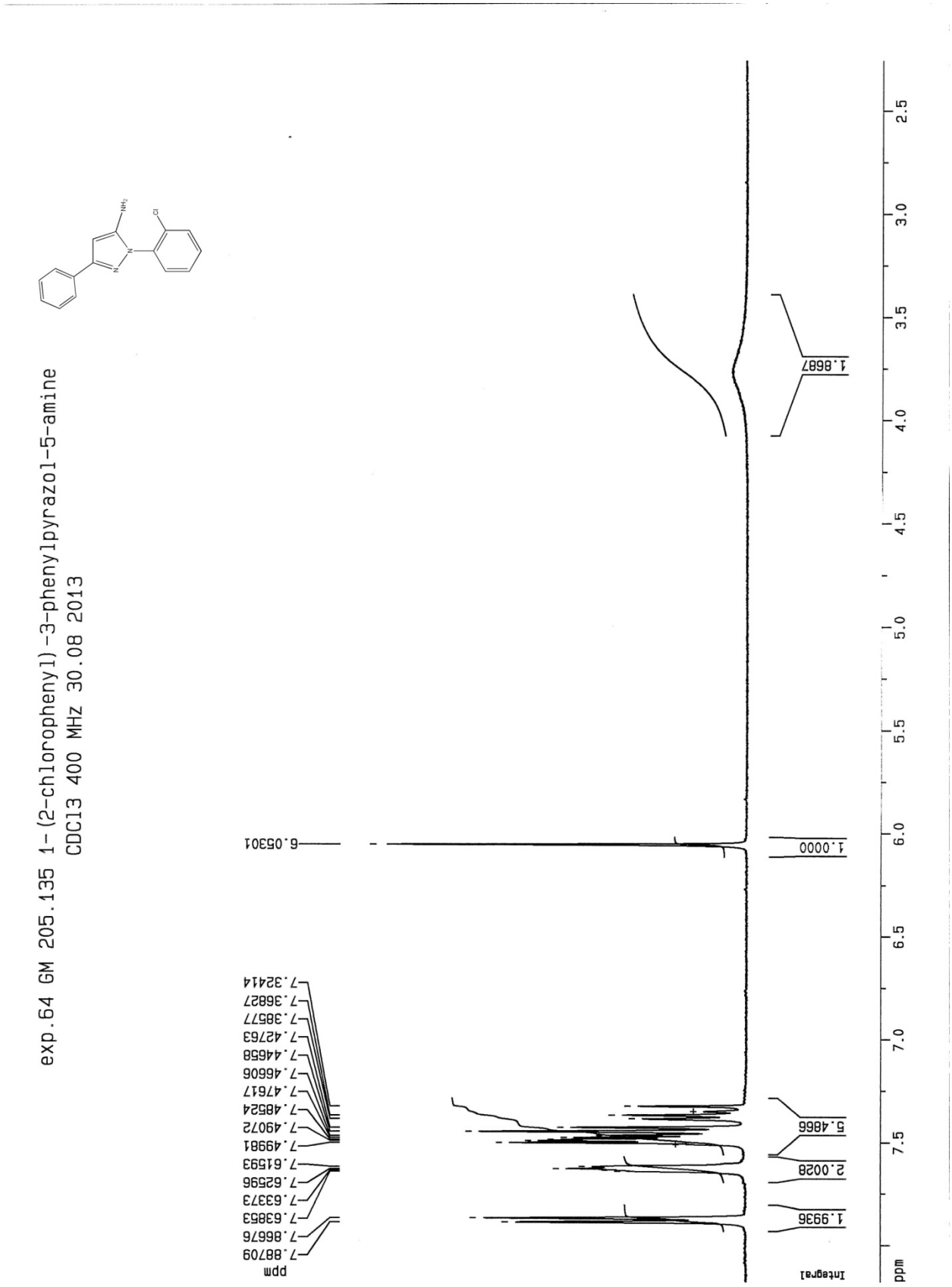

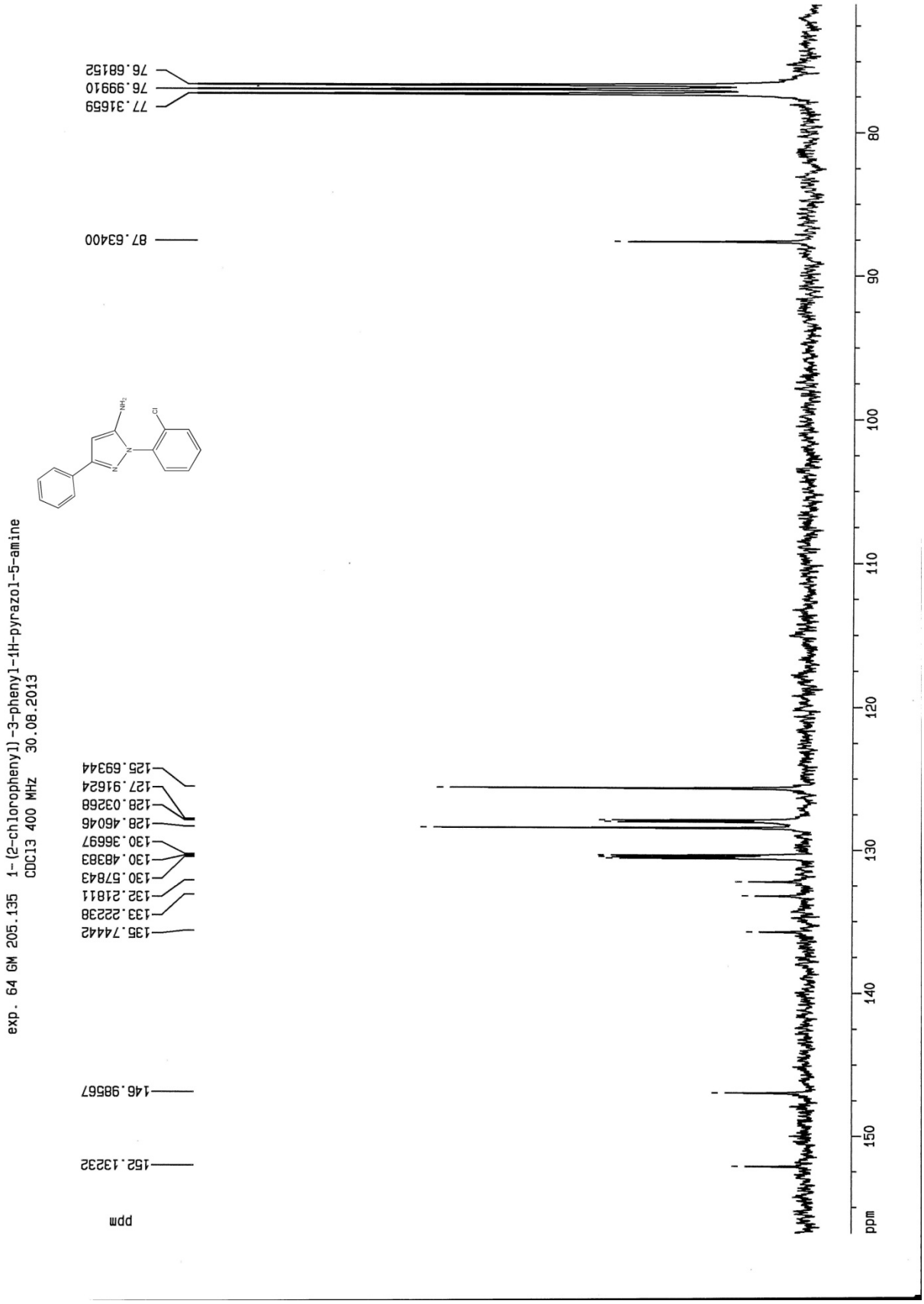

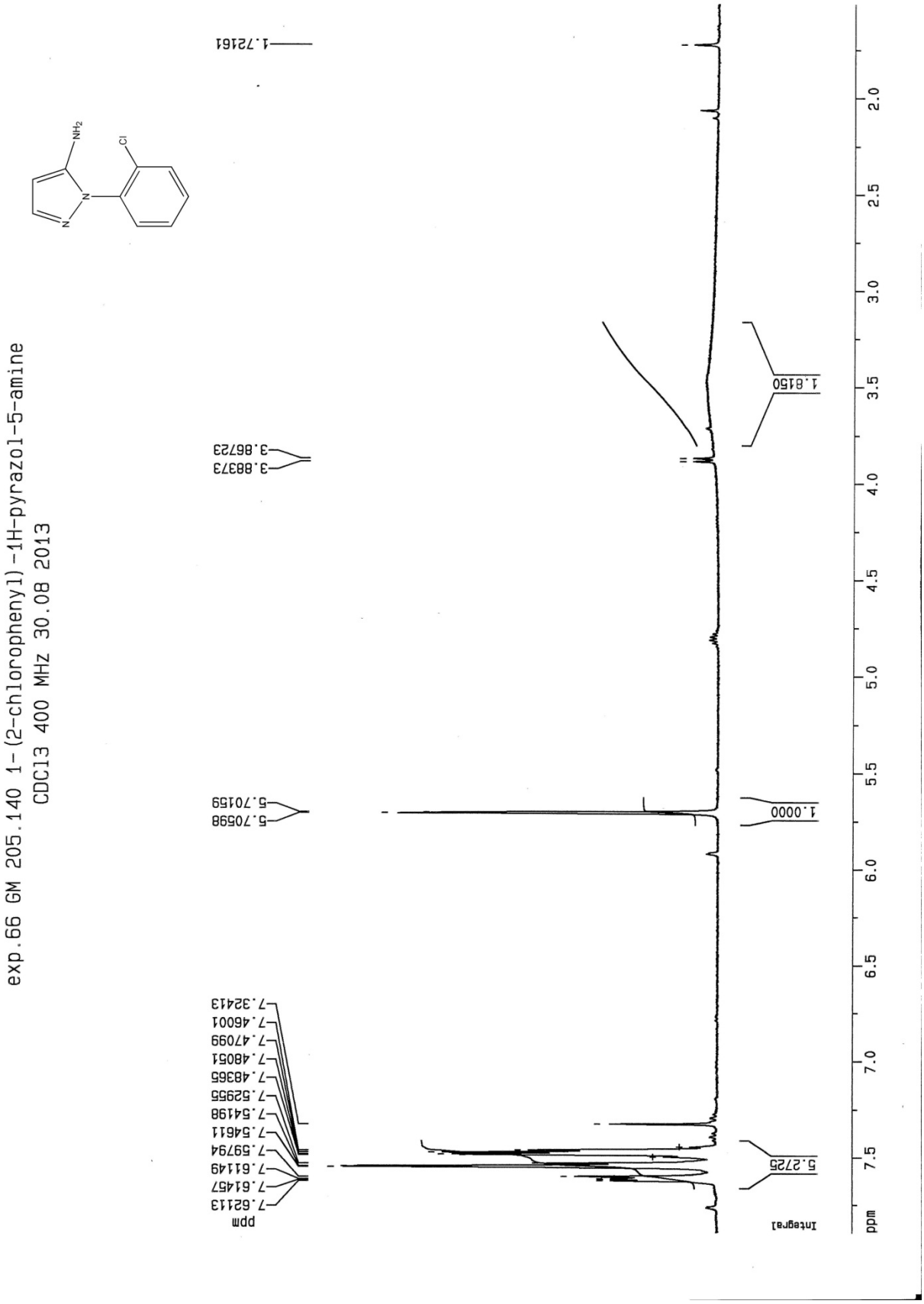

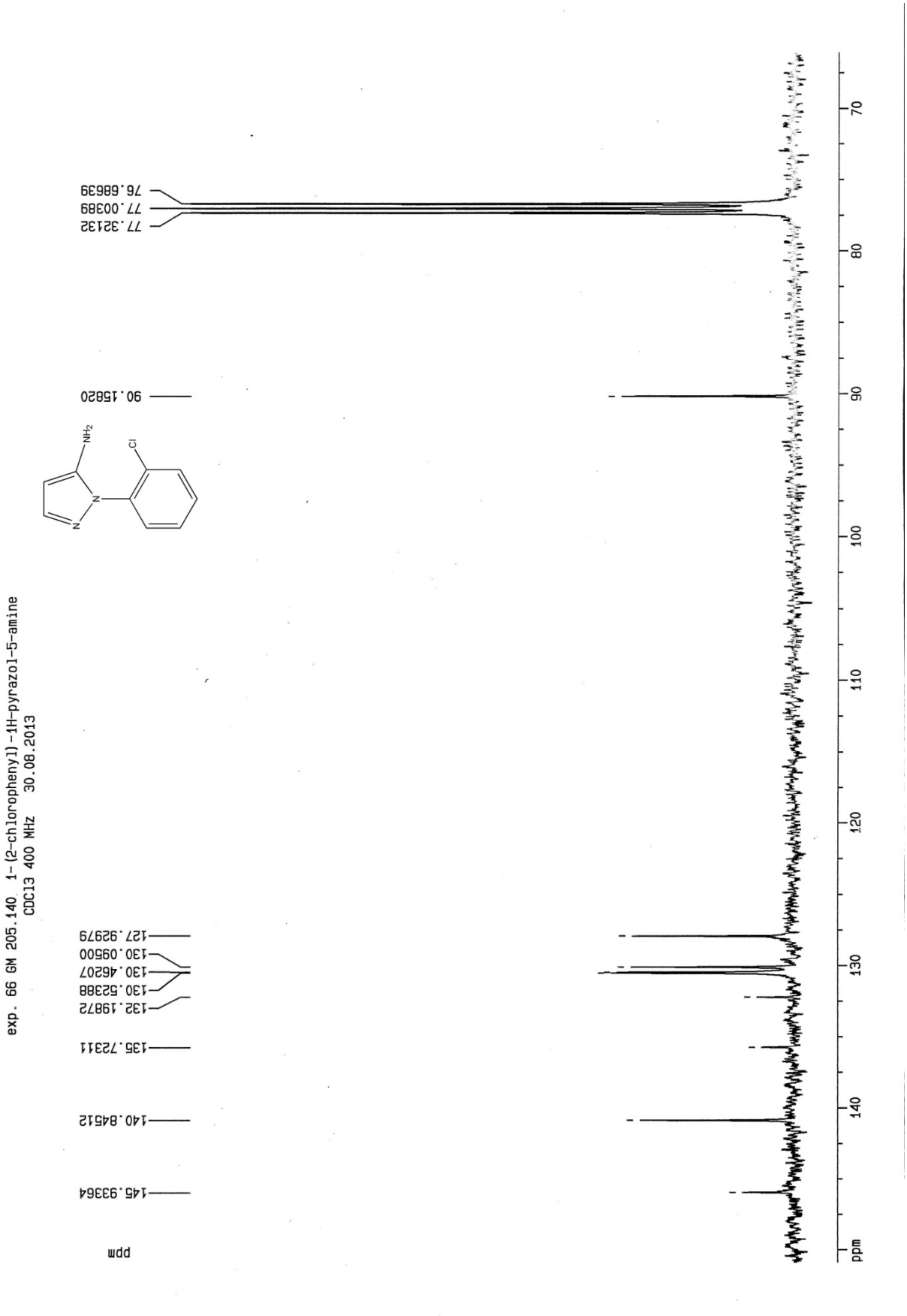

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