Supporting Information

2-Guanidinoquinazolines as new inhibitors of the STAT3 pathway

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Contents:

General: All reactions were performed under an argon atmosphere and all glassware was flame dried prior to use. Reactions carried out at -78 °C employed a dry ice/acetone bath. THF was distilled over sodium/benzophenone ketyl. Et_3N was distilled from CaH_2 and CH_2Cl_2 and toluene were purified using an alumina column filtration system. Reactions were monitored by TLC analysis (EM Science pre-coated silica gel 60 F_{254} plates, 250 mM layer thickness) and visualization was accomplished with a 254 nM UV light or staining with a PMA solution (5 g of phosphomolybdic acid in 100 mL of 95% EtOH), *p*-anisaldehyde solution (2.5 mL of *p*-anisaldehyde, 2 mL of AcOH, and 3.5 mL of conc. H_2SO_4 in 100 mL of 95% EtOH), CAM solution (5 g of cerium sulfate, 25 g of ammonium molybdate, 50 mL of conc. H_2SO_4 and 450 mL of H_2O) or a $KMnO_4$ solution (1.5 g of $KMnO_4$ and 1.5 g of K_2CO_3 in 100 mL of a 0.1% NaOH solution). Purifications by chromatography were performed using SiO_2 (SiliaFlash® F60, Silicycle) or using an ISCO-Companion flash chromatography system. $^1H/^{13}C$ NMR spectra were recorded on either a Bruker Avance 300/75 MHz, Bruker Avance 400/100 MHz or Bruker Avance 500/125 MHz instruments. Chemical shifts were reported in parts per million with the residual solvent

peak used as the internal standard ($^{1}H/^{13}C$: $CDCl_3$, 7.27, 77.0 ppm; DMSO, 2.50, 40.5 ppm). Chemical shifts were tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, dt = doublet of triplet, m = multiplet, br = broad, app = apparent), coupling constants, and integration. All 1D NMR spectra were processed using Bruker Topspin NMR. IR spectra were obtained on an Identity IR-ATR spectrometer. Microwave reactions were performed using a Biotage Initiator in glass microwave vials (cap sealed) with continuous magnetic stirring and an external surface temperature sensor. Mass spectra were obtained on a Micromass Autospec double focusing instrument or LCMS-high resolution and LC/MS analyses were completed on a Thermo Scientific Exactive spectrometer with purities determined using an Agilent Technologies 385-ELSD using MeCN/H_2O with 0.1% formic acid. Melting points (uncorrected) were determined using a Mel-Temp instrument with a fiber-optic temperature probe. The kinase activities for **11a** were performed by EMD Millipore. The CAL33 and 686LN cell lines were kind gifts from Jean Louis Fischel, Centre Antoine Lacassagne, Nice, France and Georgia Chen, Emory University, Atlanta, Georgia, respectively. The FADU AND OSC19 lines were obtained from American Type Culture Collection (ATCC), Manassas, Virginia.

Compounds **13**, **14, 11b-c**, **19a**, **19e-h**, **19j**, **19o-r** were prepared according to literature procedures and **11a**, **11d**, **19b-d**, **19i**, **19k-n**, **19s-t** were purchased from commercial sources.

X-ray coordinates for **11b** (CCDC 1020633) have been deposited in Cambridge Crystallographic Data Center.

General procedure for the synthesis of series 17.[1]

4-Methyl-N-phenylquinazolin-2-amine (**17a**). A mixture of **16** (20 mg, 0.11 mmol), aniline (0.012 mL, 0.13 mmol) and K_2CO_3 (23 mg, 0.17 mmol) in CH_3CN (0.90 mL) was placed in sealed vial. The mixture was heated using microwave irradiation at 160 °C for 1 h. The reaction mixture was filtered and concentrated and the residue was purified by chromatography on SiO_2 (benzene/ether, 4:1) to afford **17a** (17 mg, 65%) as a yellow solid: Mp 76-77 °C; IR (neat) 3392, 3260, 3055, 1569, 1521, 1491, 1441, 1428, 1387, 746, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, J = 8.4 Hz, 1 H), 7.84 (d, J = 8.0 Hz, 2 H), 7.76-7.69 (m, 2 H), 7.39-7.30 (m, 4 H), 7.06 (t, J = 7.2 Hz, 1 H), 2.83 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 155.9, 151.0, 139.8, 133.9, 128.9, 126.8, 125.2, 123.5, 122.3, 120.3, 118.9, 21.6; HRMS (ESI) *m/z* calcd for $C_{15}H_{14}N_3$ $[M+H]^+$ 236.1188, found 236.1186; ELS purity 99.2%.

N-Benzyl-4-methylquinazolin-2-amine (**17b**). According to general procedure, and purified by chromatography on SiO_2 (benzene/ether, 9:1) to afford **17b** (32 mg, 76%) as a yellow solid: Mp 98 °C; IR (neat) 3305, 3059, 3025, 2924, 1577, 1564, 1534, 1495, 1316, 1322, 1261, 1238, 1075, 1102, 755, 746 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, J = 8.2 Hz, 1 H), 7.56-7.49 (m, 2 H),

7.30 (d, *J* = 7.4 Hz, 2 H), 7.22 (t, *J* = 7.2 Hz, 2 H), 7.16 (d, *J* = 7.0 Hz, 1 H), 7.11 (t, *J* = 7.6 Hz, 1 H), 5.51 (br s, 1 H), 4.67 (d, *J* = 5.8 Hz, 2 H), 2.65 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6, 158.8, 151.8, 139.4, 133.7, 128.5, 127.7, 127.2, 126.2, 125.3, 122.3, 119.8, 45.6, 21.6; HRMS (EI) *m/z* calcd for $C_{16}H_{16}N_3$ $[M+H]^+$ 250.1344, found 250.1364; ELS purity 100%.

N-(2-(1H-Indol-3-yl)ethyl)-4-methylquinazolin-2-amine (**17c**). According to general procedure, and purified by chromatography on SiO_2 (hexanes/EtOAc, 1:1) to afford **17c** (17 mg, 50%) as a white solid: Mp 170-171 °C; IR (neat) 3425, 3407, 3205, 3195, 2919, 1580, 1566, 1526, 1512, 1457, 1303, 1236, 747, 728 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.34 (br s, 1 H), 7.84 (d, *J* = 8.2 Hz, 1 H), 7.72 (d, *J* = 7.8 Hz, 1 H), 7.64-7.63 (m, 2 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.26-7.12 (m, 3 H), 7.04 (br s, 1 H), 5.41 (br s, 1 H), 3.90 (dt, *J* = 6.2, 6.6 Hz, 2 H), 3.14 (t, *J* = 6.8 Hz, 2 H), 2.74 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.6, 158.7, 151.6, 136.5, 133.8, 129.1, 128.3, 127.5, 125.8, 125.4, 122.2, 122.0, 119.6, 119.3, 119.0, 113.3, 111.2, 41.6, 25.4, 21.6; HRMS (EI) *m/z* calcd for $C_{19}H_{19}N_4$ $[M+H]^+$ 303.1610, found 303.1586; ELS purity 100%.

4-Methyl-N-(2-morpholinoethyl)quinazolin-2-amine (**17d**). According to general procedure, and purified by chromatography on SiO_2 (EtOAc/MeOH, 19:1) to afford **17d** (9 mg, 29%) as a colorless oil: IR (neat) 2952, 2937, 2932, 2851, 1582, 1562, 1534, 1499, 1113, 757, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400

MHz) δ 7.84 (d, *J* = 8.2 Hz, 1 H), 7.65-7.61 (m, 1 H), 7.57 (d, *J* = 8.3 Hz, 1 H), 7.20 (t, *J* = 7.4 Hz, 1 H), 5.74 (br s, 1 H), 3.73 (t, *J* = 4.3 Hz, 4 H), 3.63 (dt, *J* = 5.6, 11 Hz, 2 H), 2.76 (s, 3 H), 2.64 (t, *J* = 5.9 Hz, 2 H), 2.52 (br s, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5, 158.7, 151.8, 133.7, 126.0, 125.3, 122.2, 119.6, 66.9, 57.3, 53.4, 37.7, 21.6; HRMS (EI) *m/z* calcd for $C_{15}H_{21}N_4O$ $[M+H]^+$ 273.1715, found 273.1710; ELS purity 90.8%.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-methylquinazolin-2-amine (**17e**). According to general procedure, and purified by chromatography on SiO_2 (hexanes/EtOAc, 7:3) to afford **17e** (13 mg, 38%) as a green oil: IR (neat) 3409, 3275, 3269, 2915, 2894, 1578, 1562, 1486, 1439, 1243, 1232, 755, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (d, *J* = 8.2 Hz, 1 H), 7.67-7.59 (m, 2 H), 7.22 (t, *J* = 7.3 Hz, 1 H), 6.91 (br s, 1 H), 6.86 (d, *J* = 7.9 Hz, 1 H), 6.75 (d, *J* = 7.8 Hz, 1 H), 5.92 (s, 2 H), 5.53 (br s, 1 H), 4.66 (d, *J* = 5.6 Hz, 2 H), 2.76 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.7, 158.6, 151.6, 147.8, 146.7, 133.7, 133.3, 126.1, 125.3, 122.4, 120.9, 119.8, 108.4, 108.2, 100.9, 45.4, 21.6; HRMS (EI) *m/z* calcd for $C_{17}H_{16}N_3O_2$ $[M+H]^+$ 294.1243, found 294.1216; ELS purity 97.9%.

4-Methyl-N-((5-methylfuran-2-yl)methyl)quinazolin-2-amine (**17f**). According to general procedure, and purified by chromatography on SiO_2 (hexanes/CH_2Cl_2/ether, 5:4:1 to afford **17f** (27 mg, 56%) as a white solid:

Mp 83 °C; IR (neat) 3267, 3087, 3075, 2937, 1581, 1547, 1323, 779, 751, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, *J* = 8.2 Hz, 1 H), 7.66-7.60 (m, 2 H), 7.21 (t, *J* = 7.0 Hz, 1 H), 6.15 (s, 1 H), 5.87 (s, 1 H), 5.54 (br s, 1 H), 4.69 (d, *J* = 5.5 Hz, 2 H), 2.75 (s, 3 H), 2.25 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.6, 158.4, 151.7, 151.6, 150.6, 133.6, 126.2, 125.3, 122.4, 119.8, 107.8, 106.1, 38.8, 21.6, 13.5; HRMS (EI) *m/z* calcd for $C_{15}H_{16}N_3O$ $[M+H]^+$ 254.1293, found 254.1318; ELS purity 99.7%.

4-Methyl-N-(naphthalen-1-ylmethyl)quinazolin-2-amine (**17g**). According to general procedure, and purified by chromatography on SiO_2 (toluene/ether, 9:1 to afford **17g** (21 mg, 73%) as a yellow solid: Mp 137-138 °C; IR (neat) 2964, 2932, 2835, 1925, 1666, 1588, 1577, 1508, 1461, 1441, 1420, 1238, 1139, 1090, 1036 cm^{-1}; ^{1}H NMR ($CDCl_3$ with 0.5% TMS, 500 MHz) δ 8.15-8.13 (m 1 H), 7.87-7.83 (m, 2 H), 7.79 (d, *J* = 8.3 Hz, 1 H), 7.65-7.64 (m, 2 H), 7.56 (d, *J* = 7.0 Hz, 1 H), 7.51-7.46 (m, 2 H), 7.41 (dd, *J* = 7.3, 8.1 Hz, 1 H), 7.24-7.20 (m, 1 H), 5.54 (s, 1 H), 5.20 (d, *J* = 5.5 Hz, 2 H), 2.72 (s, 3 H); ^{13}C NMR ($CDCl_3$ with 0.5% TMS, 125 MHz) δ 169.6, 158.6, 151.9, 134.6, 133.9, 133.7, 131.6, 128.7, 128.2, 126.3, 126.2, 125.8, 125.4, 125.3, 123.8, 122.3, 119.9, 43.7, 21.6; HRMS (EI) *m/z* calcd for $C_{20}H_{18}N_3$ $[M+H]^+$ 300.1501, found 300.1499; ELS purity 100%.

N-Cyclohexyl-4-methylquinazolin-2-amine (**17h**). According to general procedure, and purified by chromatography on SiO_2 (hexanes/EtOAc, 7:3 to afford **17h** (22 mg, 53%) as a colorless oil: IR (neat) 3286, 3273, 2923, 2848, 1580, 1562, 1499, 1486, 1433, 753, 731 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, *J* = 8.2 Hz, 1 H), 7.63-7.59 (m, 1 H), 7.55 (d, *J* = 9.6 Hz, 1 H), 7.16 (t, *J* = 7.4 Hz, 1 H), 5.15 (app d, *J* = 6.7 Hz, 1 H), 4.04-3.97 (m, 1 H), 2.73 (s, 3 H), 2.11-2.08 (m, 2 H), 1.77-1.74 (m, 2 H), 1.66-1.63 (m, 1 H), 1.50-1.41 (m, 2 H), 1.29-1.22 (m, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.4, 158.2, 151.9, 133.5, 126.0, 125.3, 121.9, 119.5, 49.4, 33.3, 25.8, 24.9, 21.6; HRMS (ESI) *m/z* calcd for $C_{15}H_{20}N_3$ $[M+H]^+$ 242.1652, found 242.1645; ELS purity 98.0%.

4-Methyl-N-(pyridin-2-yl)quinazolin-2-amine (**17i**). According to general procedure and heated for 2 h at 160 °C under microwave irradiation and purified by chromatography on SiO_2 (hexanes/EtOAc, 4:1 to afford **17i** (2 mg, 5%) as a white solid and recovered **16** (9 mg, 30%): ^1H NMR ($CDCl_3$, 400 MHz) δ 8.81 (d, *J* = 8.4 Hz, 1 H), 8.30 (d, *J* = 4.0 Hz, 1 H), 7.96 (d, *J* = 8.0 Hz, 1 H), 7.82-7.74 (m, 3 H), 7.39 (app t, *J* = 7.2 Hz, 1 H), 6.97 (app t, *J* = 6.0 Hz, 1 H), 2.87 (s, 3 H); HRMS (ESI) *m/z* calcd for $C_{14}H_{13}N_4$ $[M+H]^+$ 237.1135, found 237.1128; ELS purity 95.9%.

General procedure for the synthesis of series 19.

2-(8-Methyl-[1,3]dioxolo[4,5-g]quinazolin-6-ylamino)-5,6-dimethylpyrimidin-4(1H)-one (**19p**). A solution of 1-(8-methyl-[1,3]dioxolo[4,5-g]quinazolin-6-yl)guanidine (0.20 g, 0.82 mmol) in minimal hot DMSO was treated with ethyl 2-methylacetoacetate (0.14 mL, 0.98 mmol) and $NaHCO_3$ (0.082 g, 0.98 mmol). The reaction mixture was heated at 100 °C for 48 h. The solution was cooled and the product was collected by filtration, washed with acetone and H_2O and dried to afford **19p** (0.14 g, 54%) as a tan solid: Mp > 250 °C; IR (neat) 3359, 1644, 1605, 1560, 1461, 1431, 1234, 1215, 1234, 768 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 7.46 (s, 1 H), 7.04 (s, 1 H), 6.20 (s, 2 H), 2.67 (s, 3 H), 2.11 (s, 3 H), 1.85 (s, 3 H); HRMS (ESI) *m/z* calcd for $C_{16}H_{16}N_5O_3$ $[M+H]^+$ 326.1248, found 326.1244; ELS purity 100%.

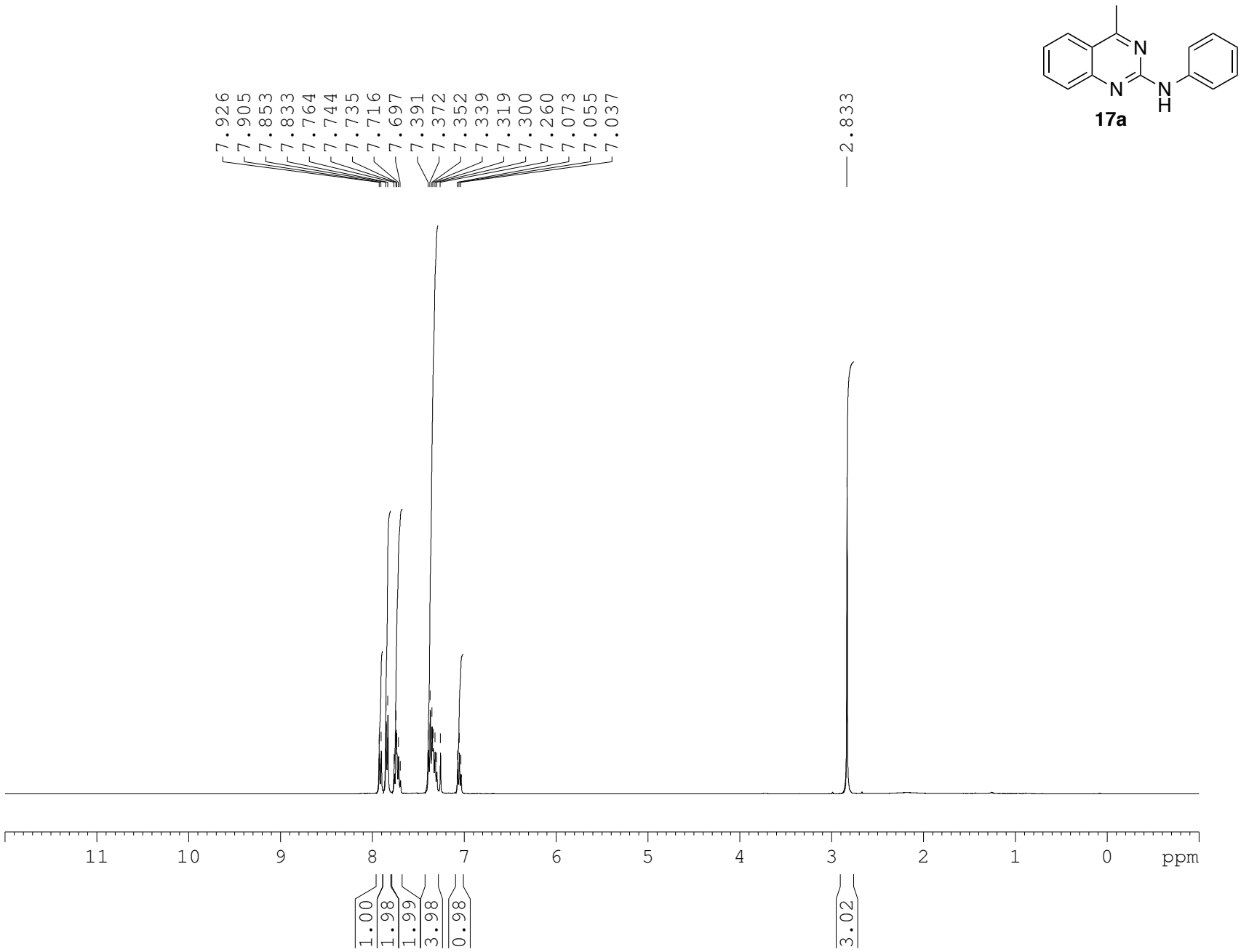
2-(8-Methyl-[1,3]dioxolo[4,5-g]quinazolin-6-ylamino)-6-phenylpyrimidin-4(1H)-one (**19q**). According to general procedure using ethyl 3-oxo-3-phenylpropanoate to give **19q** (0.15 g, 49%) as a red solid: Mp (dec) 266 °C; IR (neat) 3411, 3066, 3059, 3055, 3049, 1664, 1610, 1547, 1486, 1426, 1371, 1223, 1215, 809, 680 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 8.05-8.04 (m, 2 H), 7.52 (s, 1 H), 7.47 (s, 3 H), 7.10 (s, 1 H), 6.41 (s, 1 H), 6.23 (s, 2 H), 2.76 (s, 3 H); ^{13}C NMR (DMSO-d_6, 125 MHz, 100 °C) δ 167.2, 162.5, 161.5, 154.0, 152.3, 148.3, 146.3, 136.7, 129.5, 127.9, 126.4, 116.2, 102.1, 100.9,

100.4, 21.2; HRMS (ESI) *m/z* calcd for $C_{20}H_{16}N_5O_3$ $[M+H]^+$ 374.1248, found 374.1239; ELS purity 100%.

2-(8-Methyl-[1,3]dioxolo[4,5-g]quinazolin-6-ylamino)-5-benzyl-6-methylpyrimidin-4(1H)-one (**19r**). According to general procedure using ethyl 2-benzylacetoacetate to give **19r** (0.061 g, 37%) as a brown solid: Mp 238 °C; IR (neat) 3353, 3062, 3025, 2919, 1622, 1610, 1551, 1491, 1452, 1431, 1390, 1232, 1215, 1033 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 13.30 (br s, 1 H), 11.01 (br s, 1 H), 7.55 (s, 1 H), 7.27-7.21 (m, 4 H), 7.17-7.10 (m, 2 H), 6.25 (s, 2 H), 3.76 (s, 2 H), 2.74 (s, 3 H), 2.16 (s, 3 H); ^{13}C NMR (DMSO-d_6, 100 MHz, 100 °C) δ 167.2, 154.0, 153.6, 148.8, 148.1, 146.3, 140.1, 127.5, 127.4, 125.0, 116.2, 114.4, 102.0, 100.8, 29.8, 20.9, 20.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{20}N_5O_3$ $[M+H]^+$ 402.1561, found 402.1549; ELS purity 100%.

References

1. Henriksen, S.T.; Sørensen, U.S. *Tetrahedron Lett*. **2006**, *47*, 8251-8254.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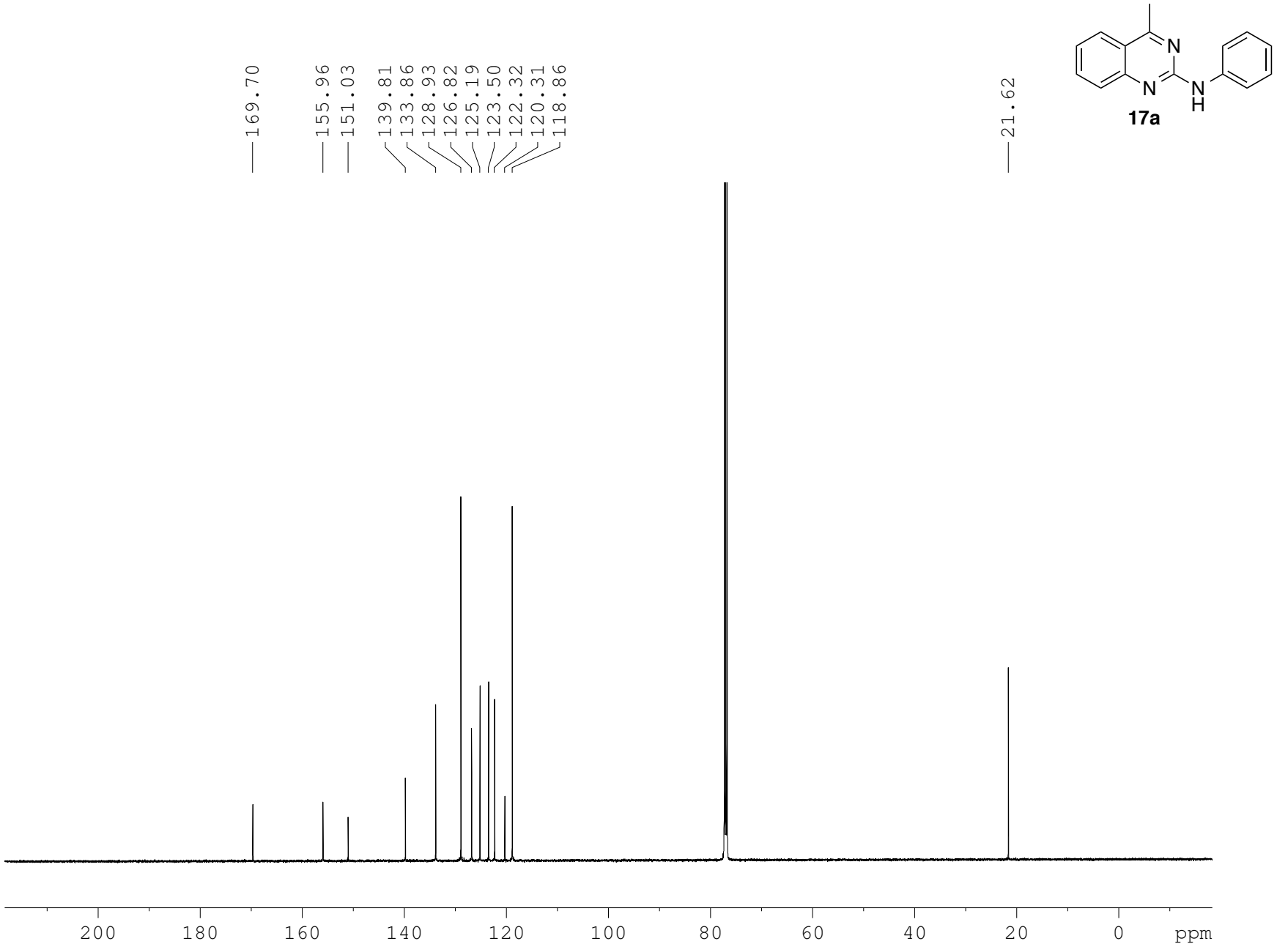
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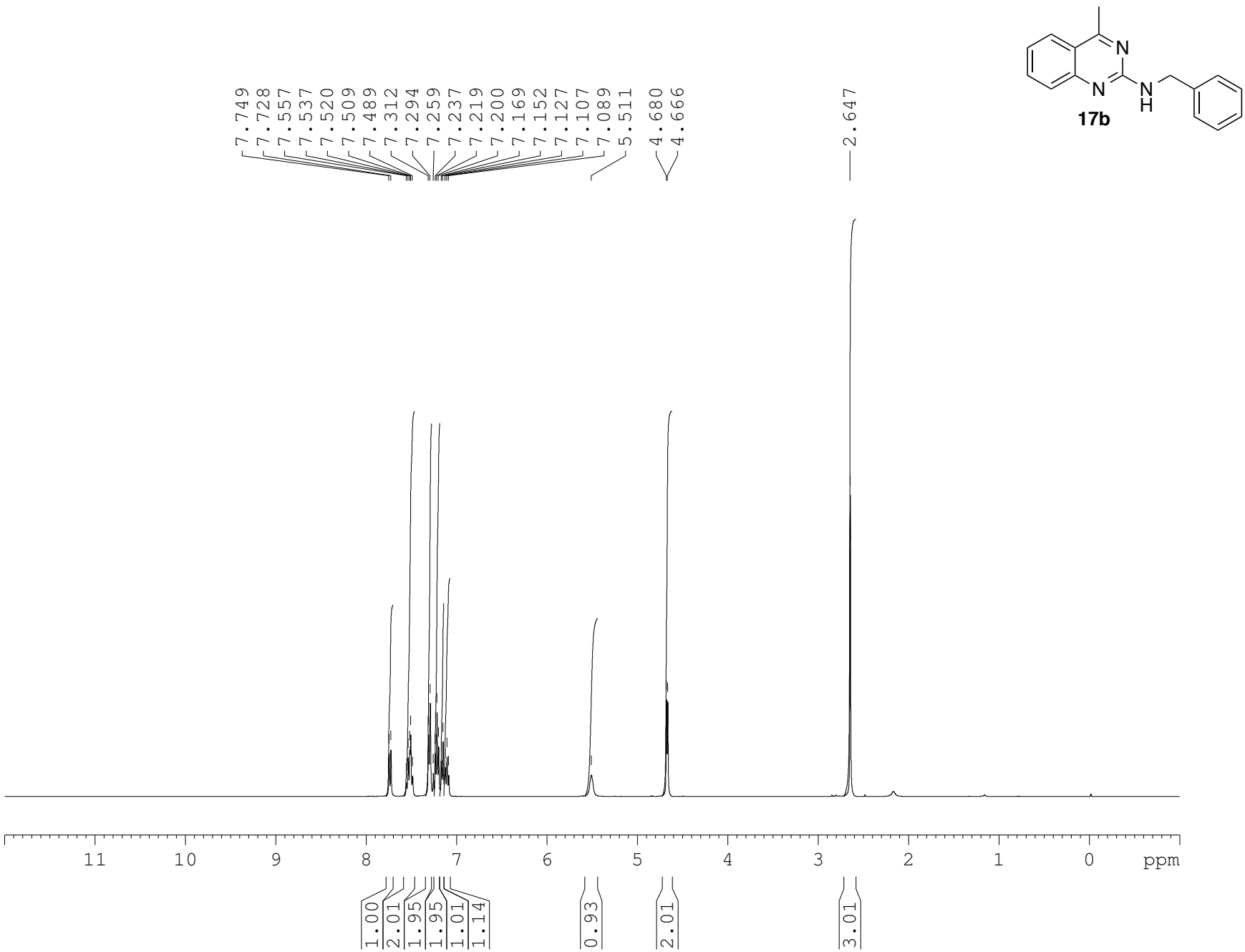
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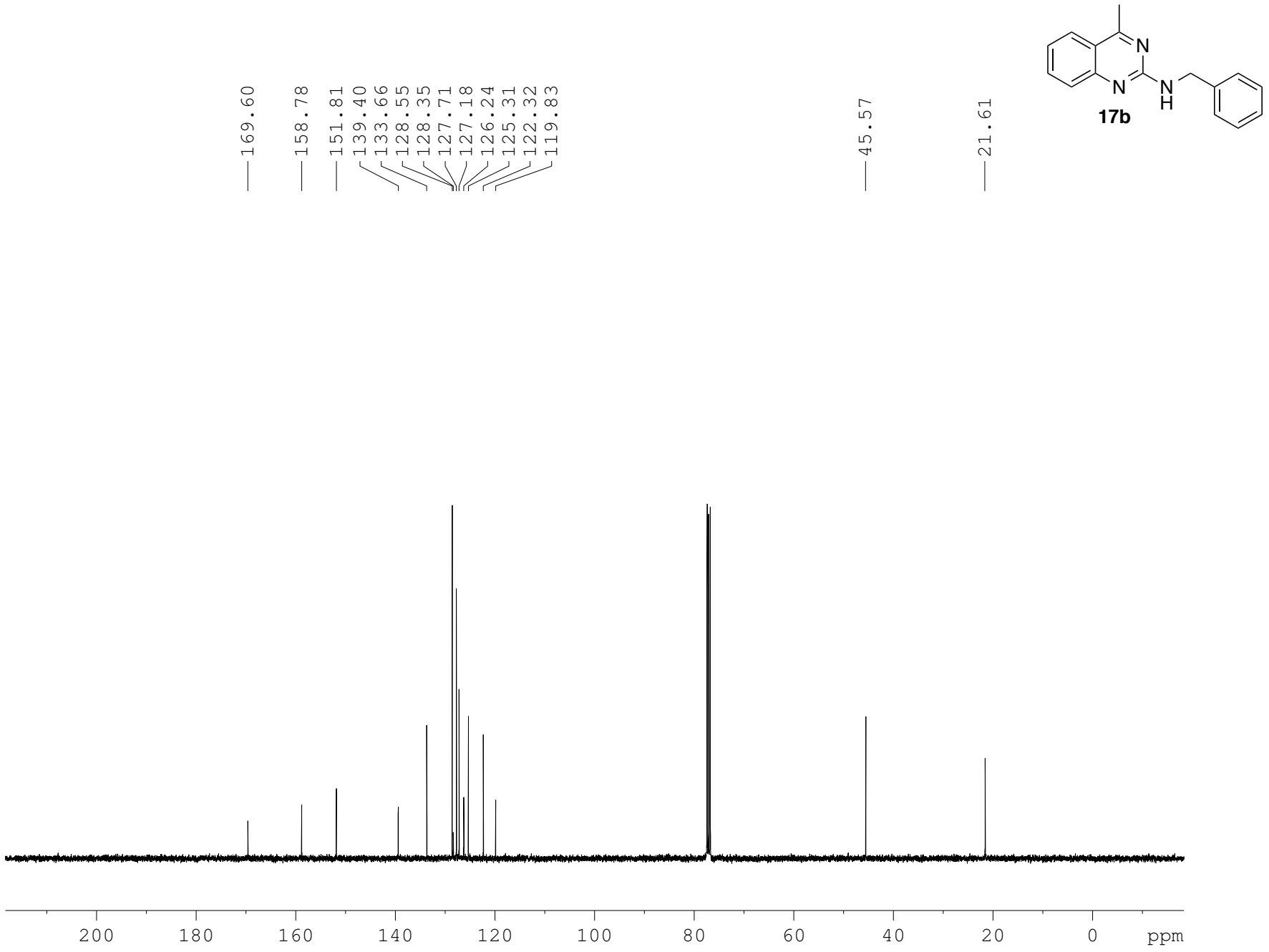
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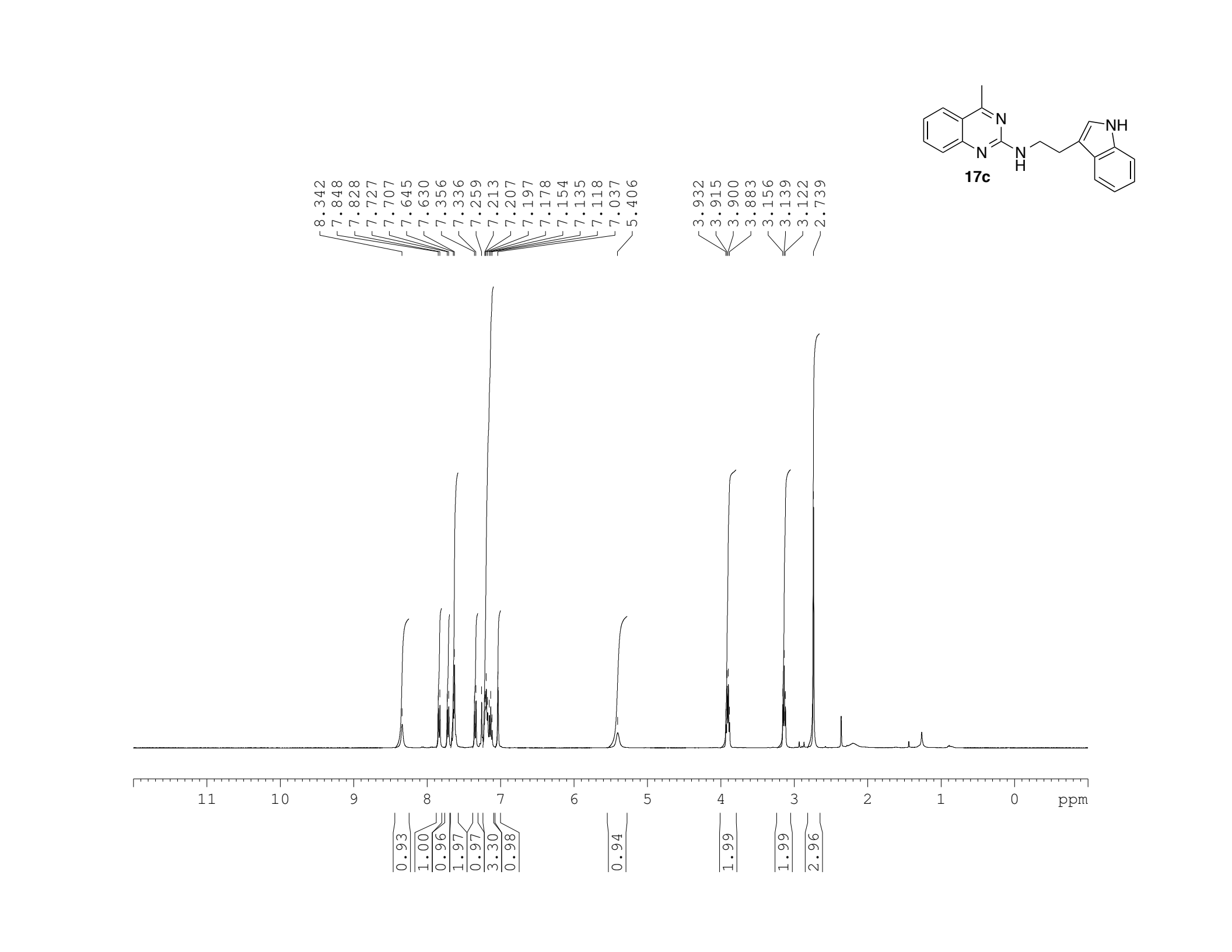
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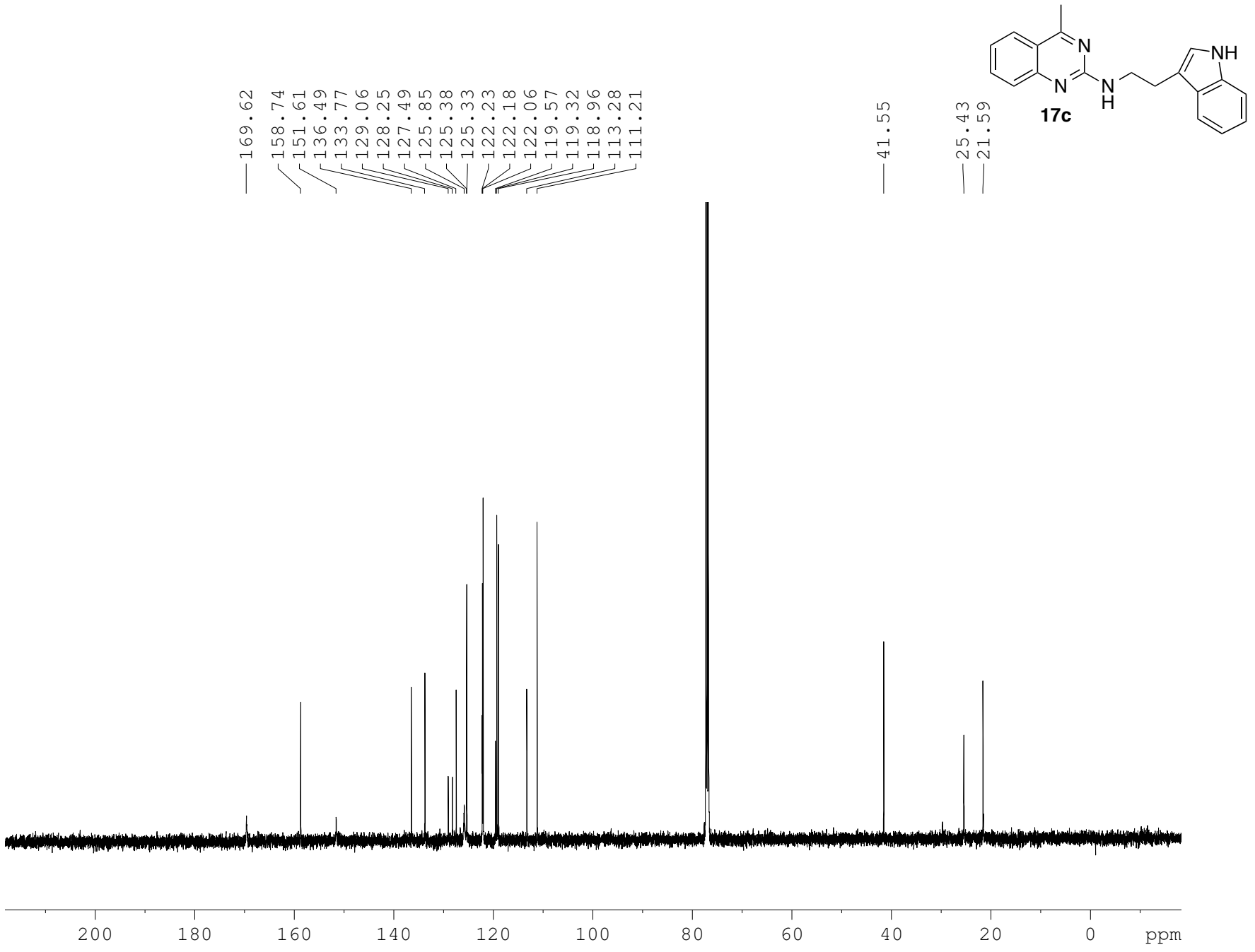
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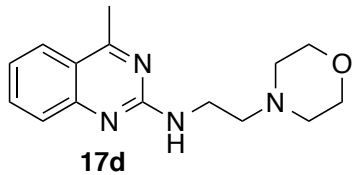

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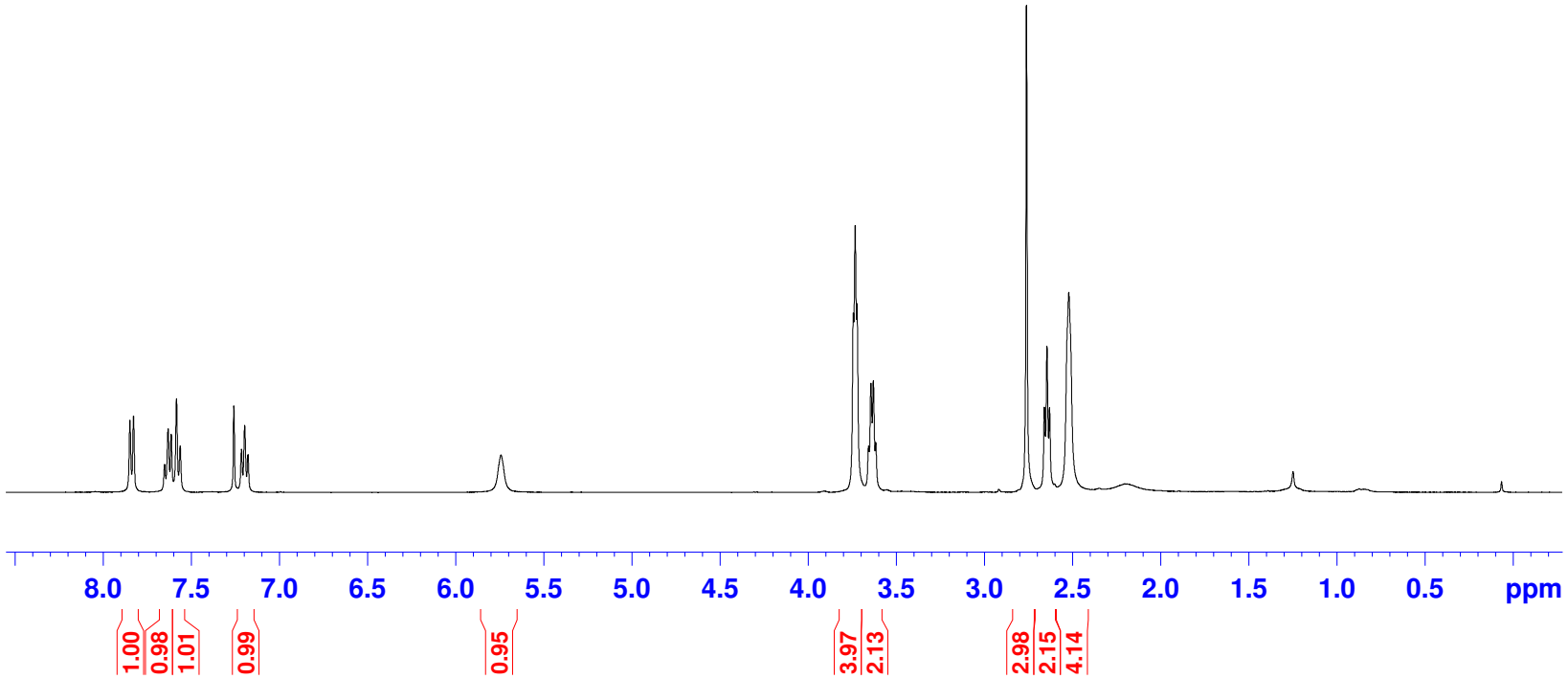

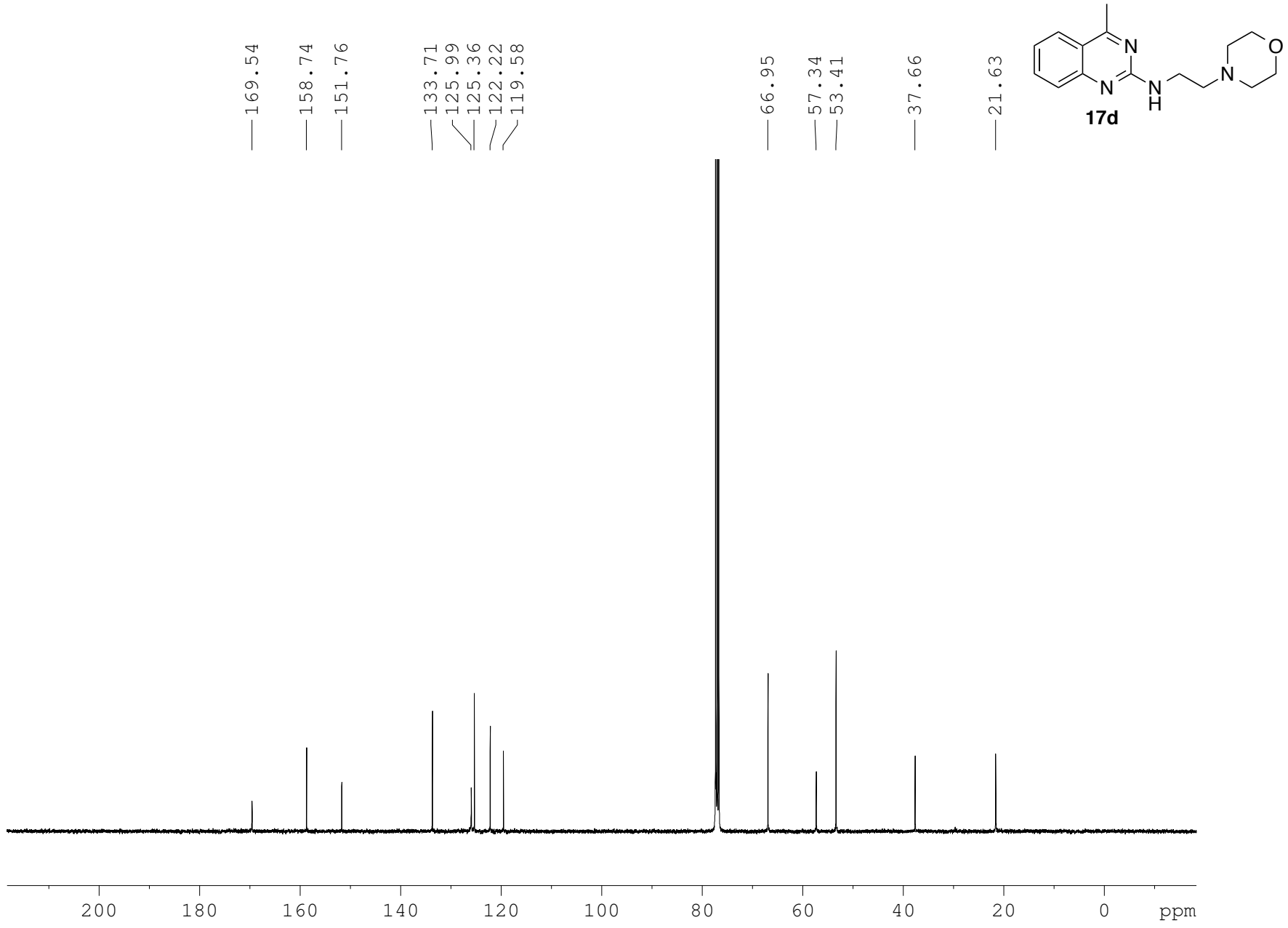
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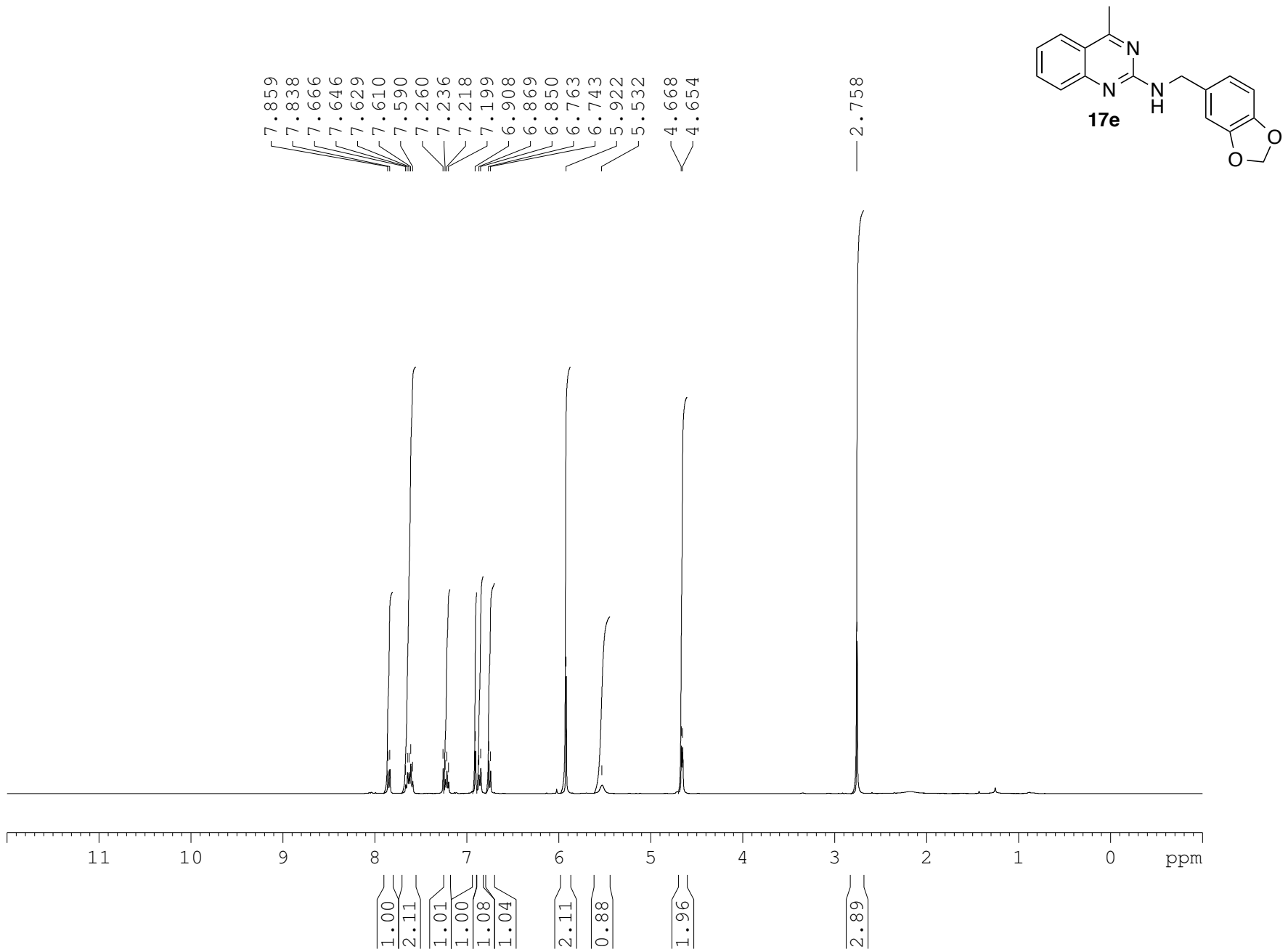
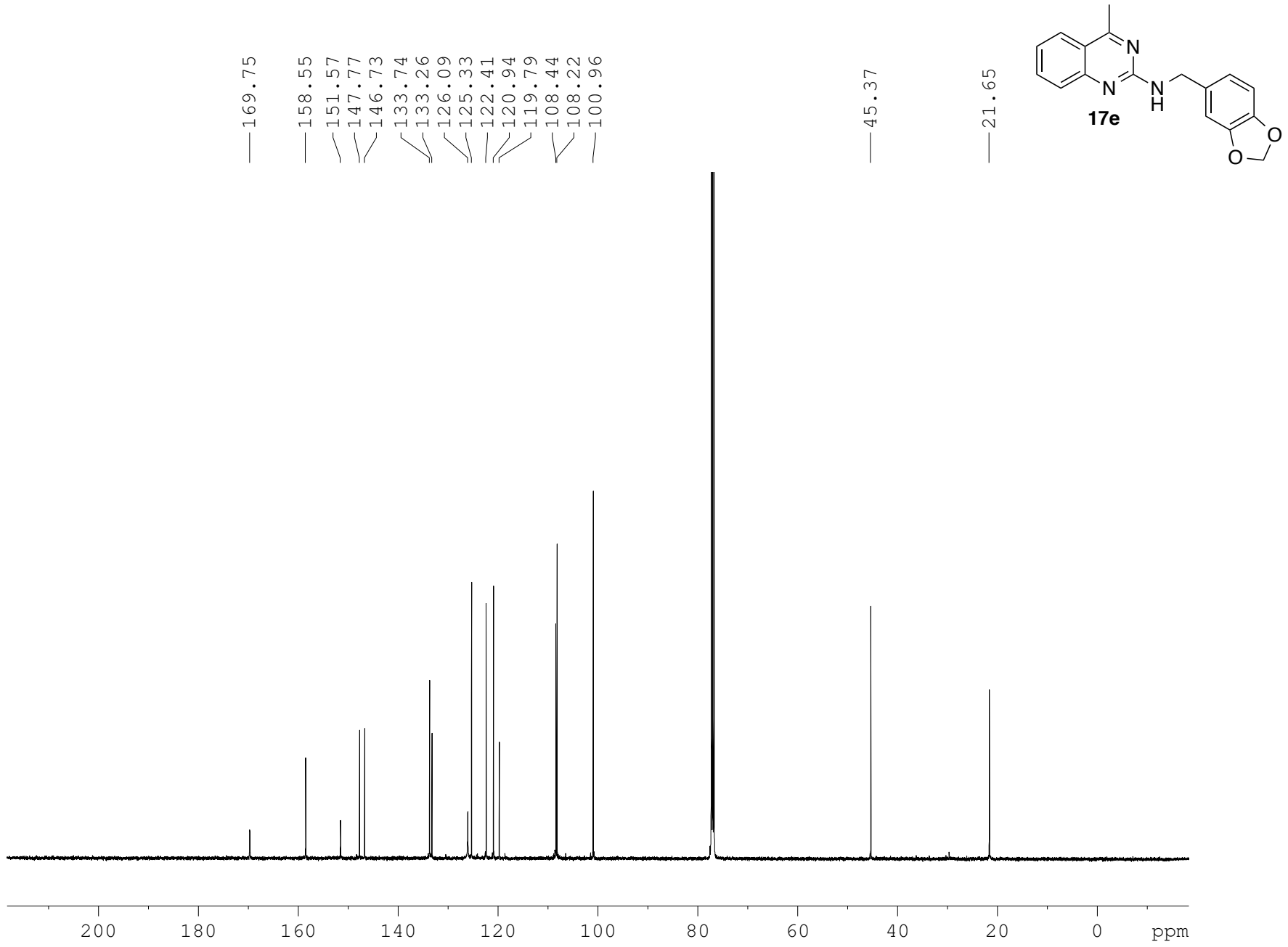
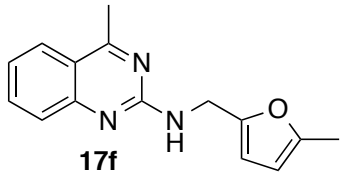

7.859
7.838
7.666
7.646
7.629
7.610
7.590
7.260
7.236
7.218
7.199
6.908
6.869
6.850
6.763
6.743
5.922
5.532
4.668
4.654
2.758
N
N
N
H
O
O
17e
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.11
1.01
1.00
1.08
1.04
2.11
0.88
1.96
2.89

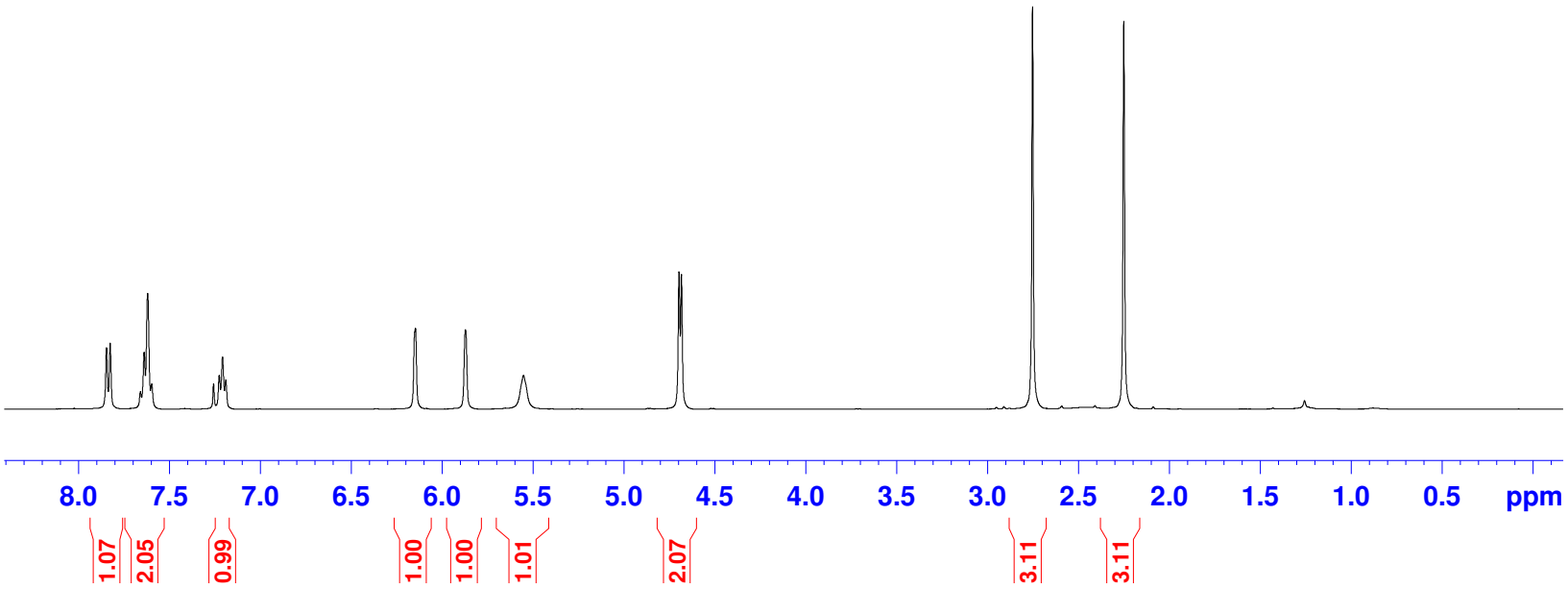

169.75
158.55
151.57
147.77
146.73
133.74
133.26
126.09
125.33
122.41
120.94
119.79
108.44
108.22
100.96
45.37
21.65
N
N
H
O
O
17e
200
180
160
140
120
100
80
60
40
20
0
ppm

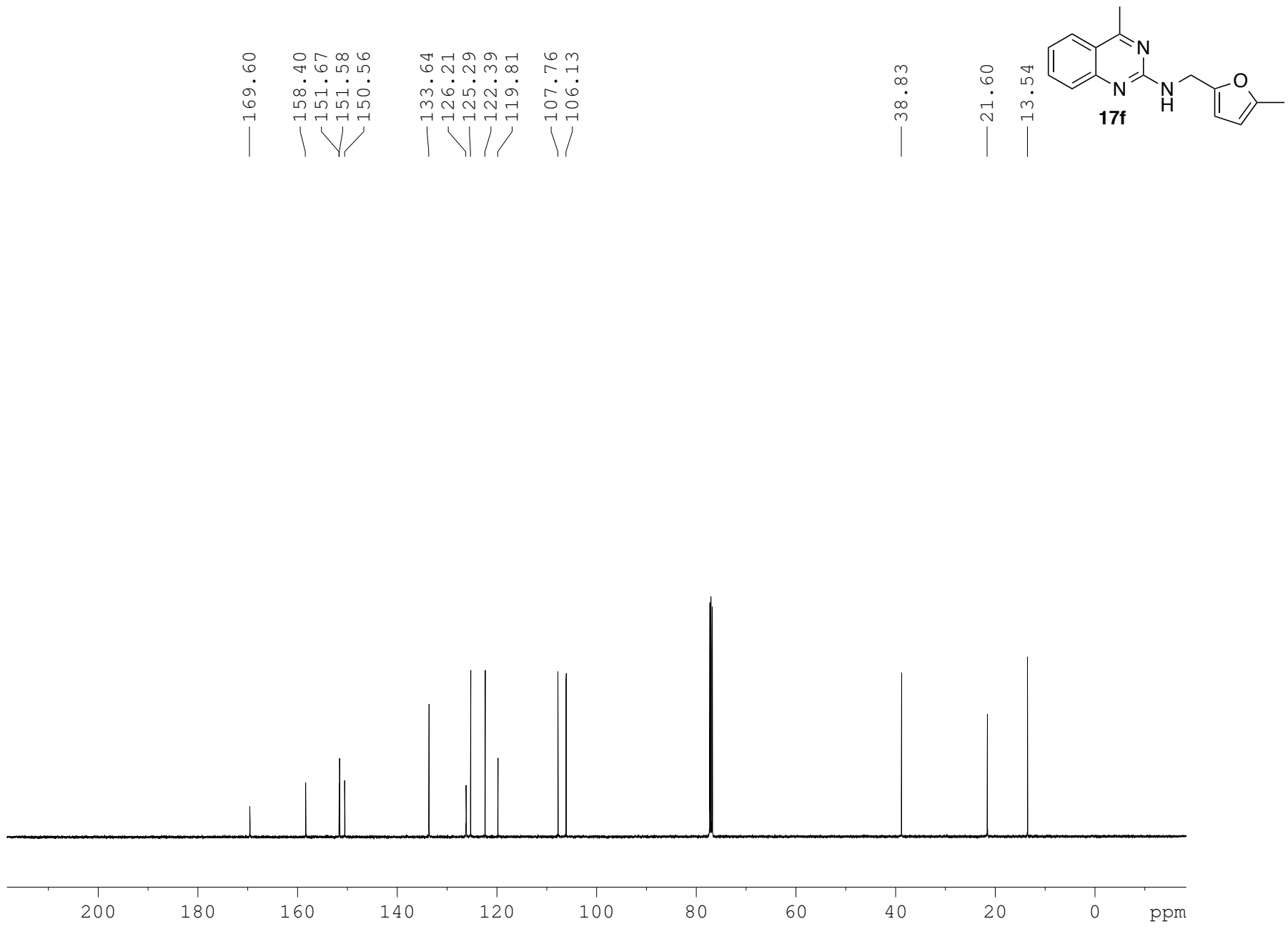
NB-00310.084-9 a 14, 1H, CDCl3, 400 MHz

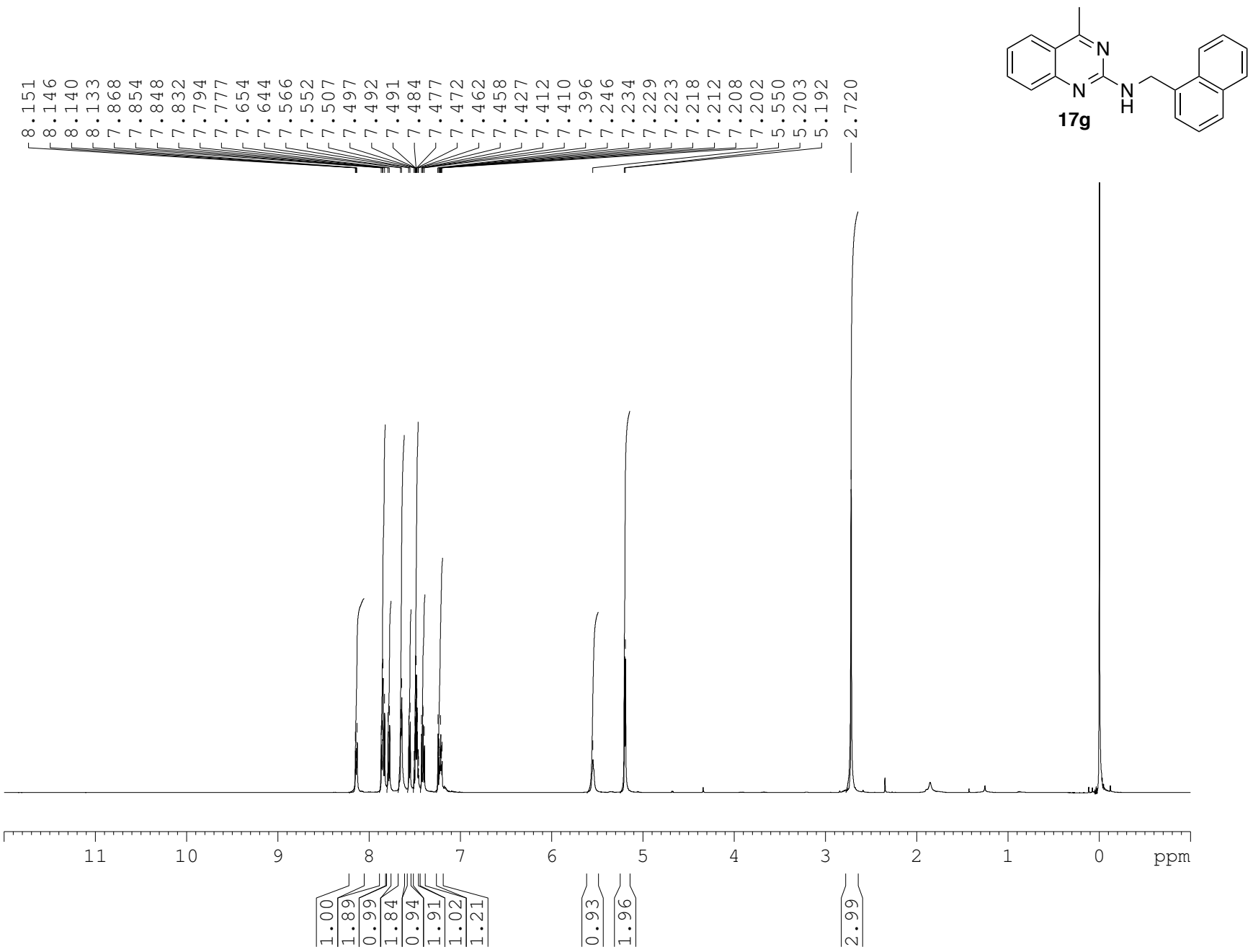
7.848
7.827
7.661
7.641
7.622
7.599
7.259
7.227
7.210
7.191
6.148
5.873
5.554
4.699
4.685
2.754
2.252



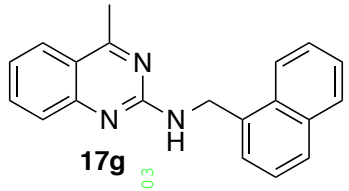
17f




169.60
158.40
151.67
151.58
150.56
133.64
126.21
125.29
122.39
119.81
107.76
106.13
38.83
21.60
13.54
N
N
N
H
O
17f
200
180
160
140
120
100
80
60
40
20
0
ppm

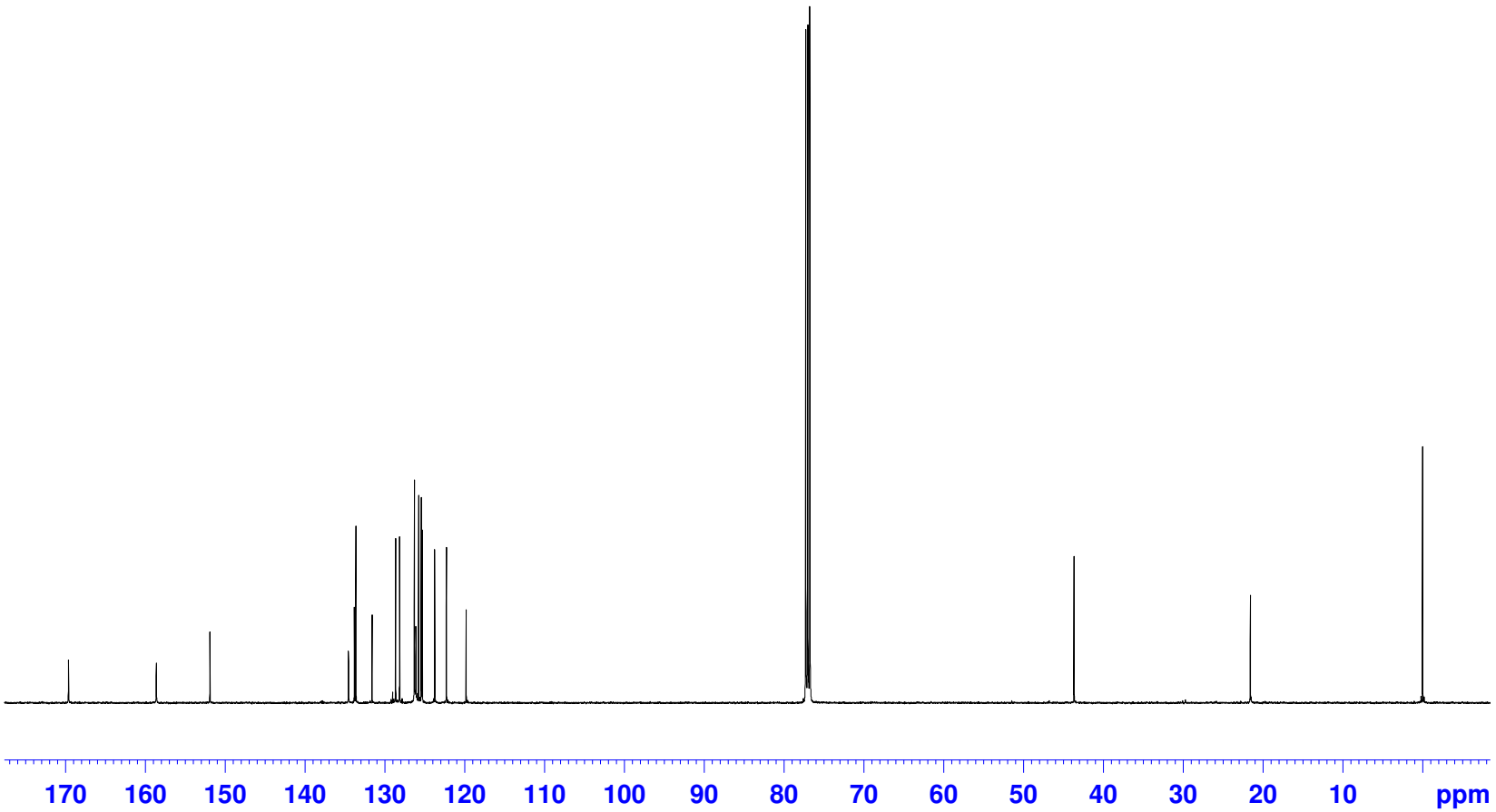

8.151
8.146
8.140
8.133
7.868
7.854
7.848
7.832
7.794
7.777
7.654
7.644
7.566
7.552
7.507
7.497
7.492
7.491
7.484
7.477
7.472
7.462
7.458
7.427
7.412
7.410
7.396
7.246
7.234
7.229
7.223
7.218
7.212
7.208
7.202
5.550
5.203
5.192
2.720
N
N
N
H
17g
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.89
0.99
1.84
0.94
1.91
1.02
1.21
0.93
1.96
2.99

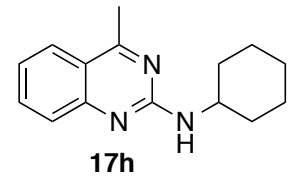
NB-00310.085 -7 a 10, 13C, CDCl3-TMS, 500 MHz



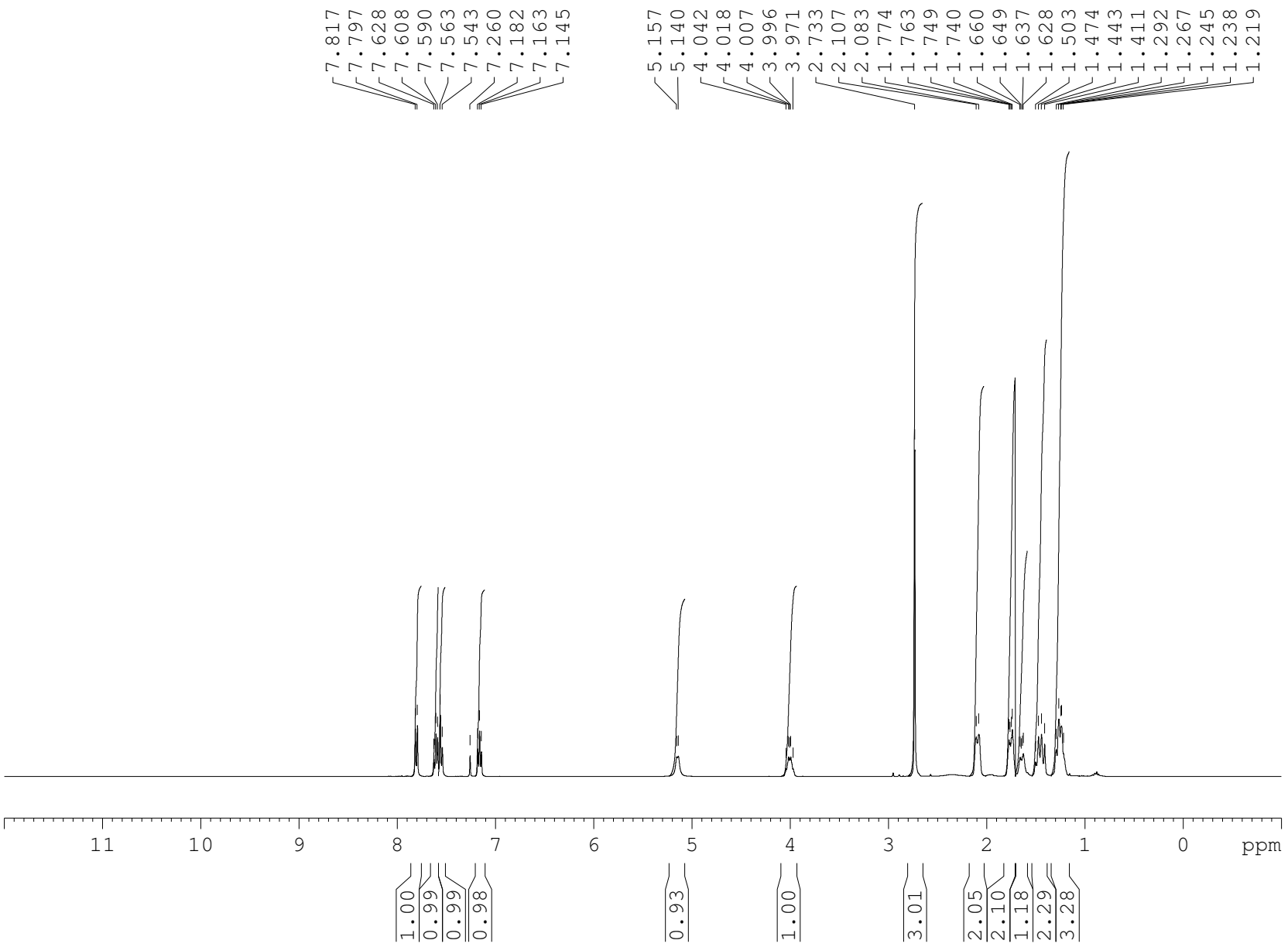
17g

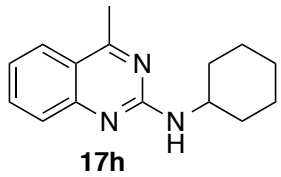
169.62
158.61
151.90
134.59
133.86
133.67
131.64
128.69
128.19
126.34
126.14
125.81
125.48
125.35
123.79
122.33
119.85
43.70
21.60
0.03




N
N
N
H

17h

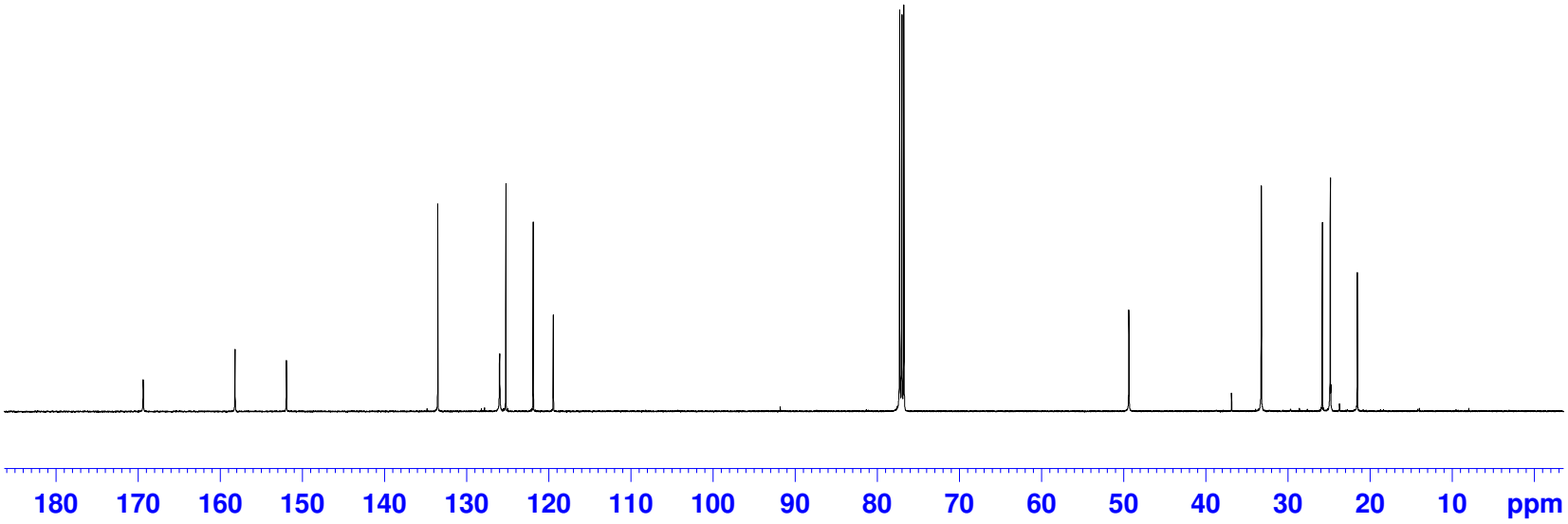

7.817
7.797
7.628
7.608
7.590
7.563
7.543
7.260
7.182
7.163
7.145
5.157
5.140
4.042
4.018
4.007
3.996
3.971
2.733
2.107
2.083
1.774
1.763
1.749
1.740
1.660
1.649
1.637
1.628
1.503
1.474
1.443
1.411
1.292
1.267
1.245
1.238
1.219
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
0.99
0.98
0.93
1.00
3.01
2.05
2.10
1.18
2.29
3.28

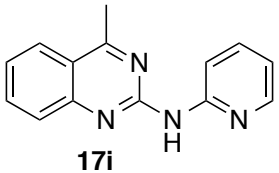


17h

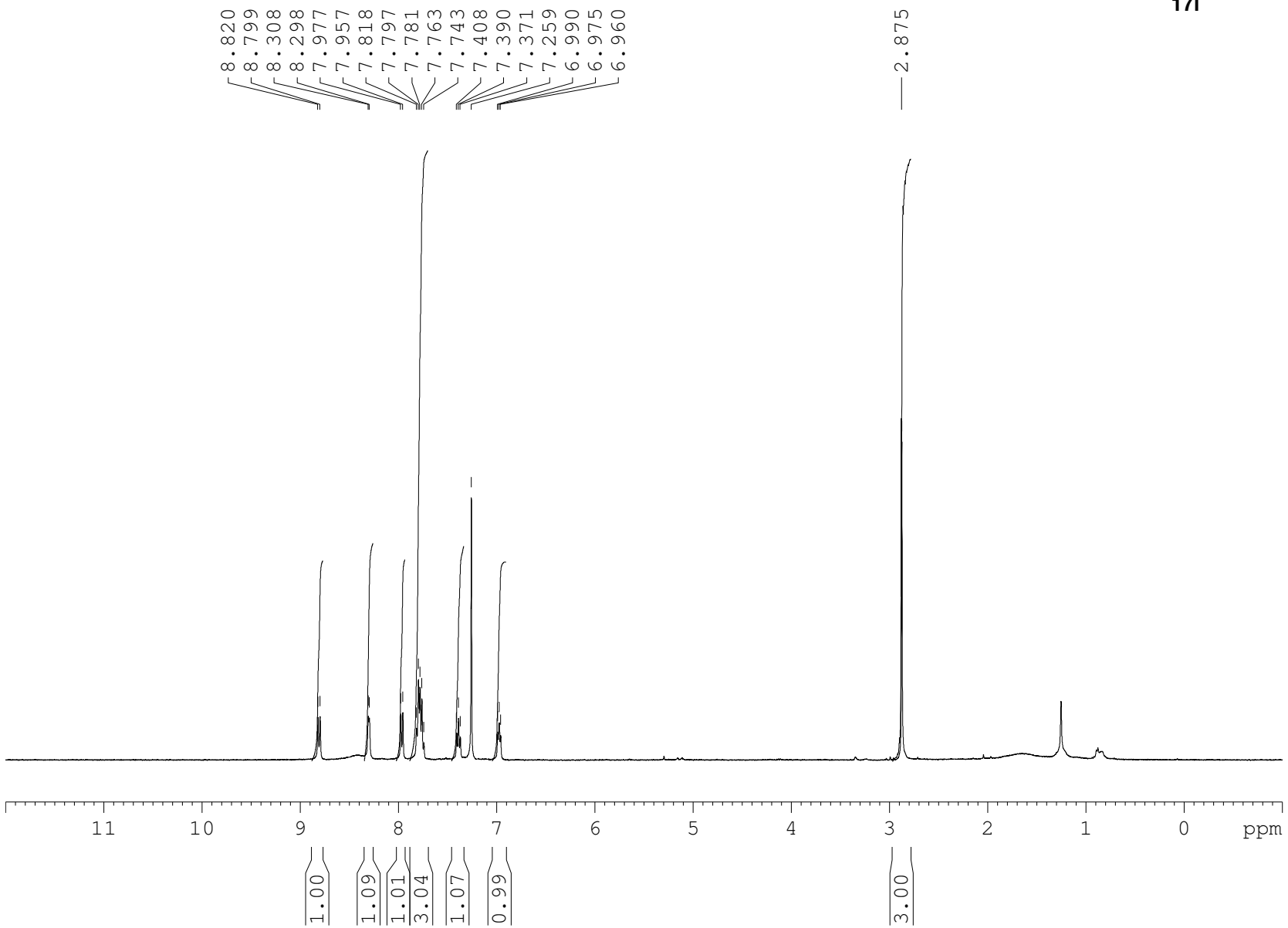
NB-00358.087 - 11 a 15, 13C, CDCl3, 500 MHz

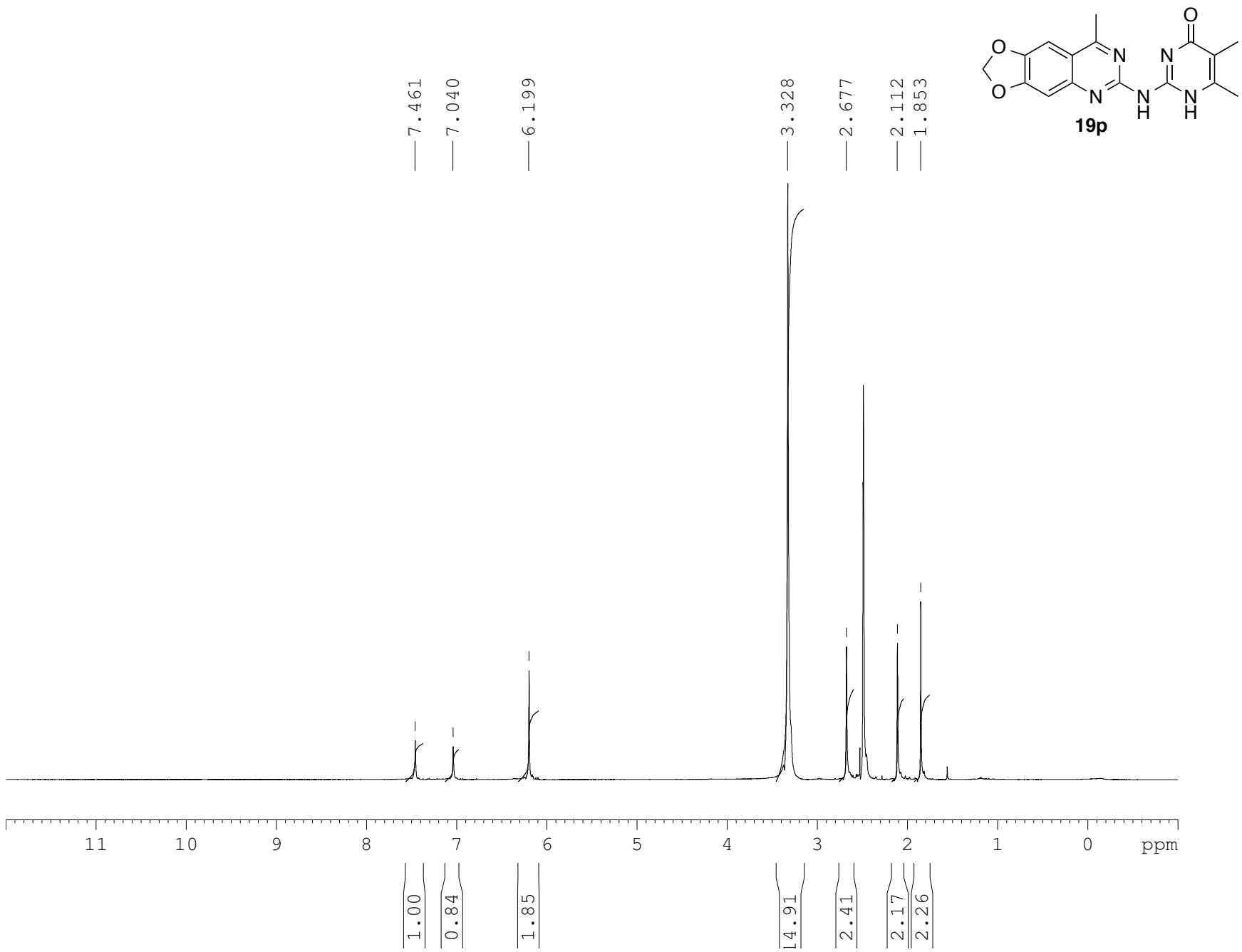
169.37
158.18
151.93
133.55
126.01
125.26
121.92
119.48
49.38
33.26
25.83
24.86
21.57

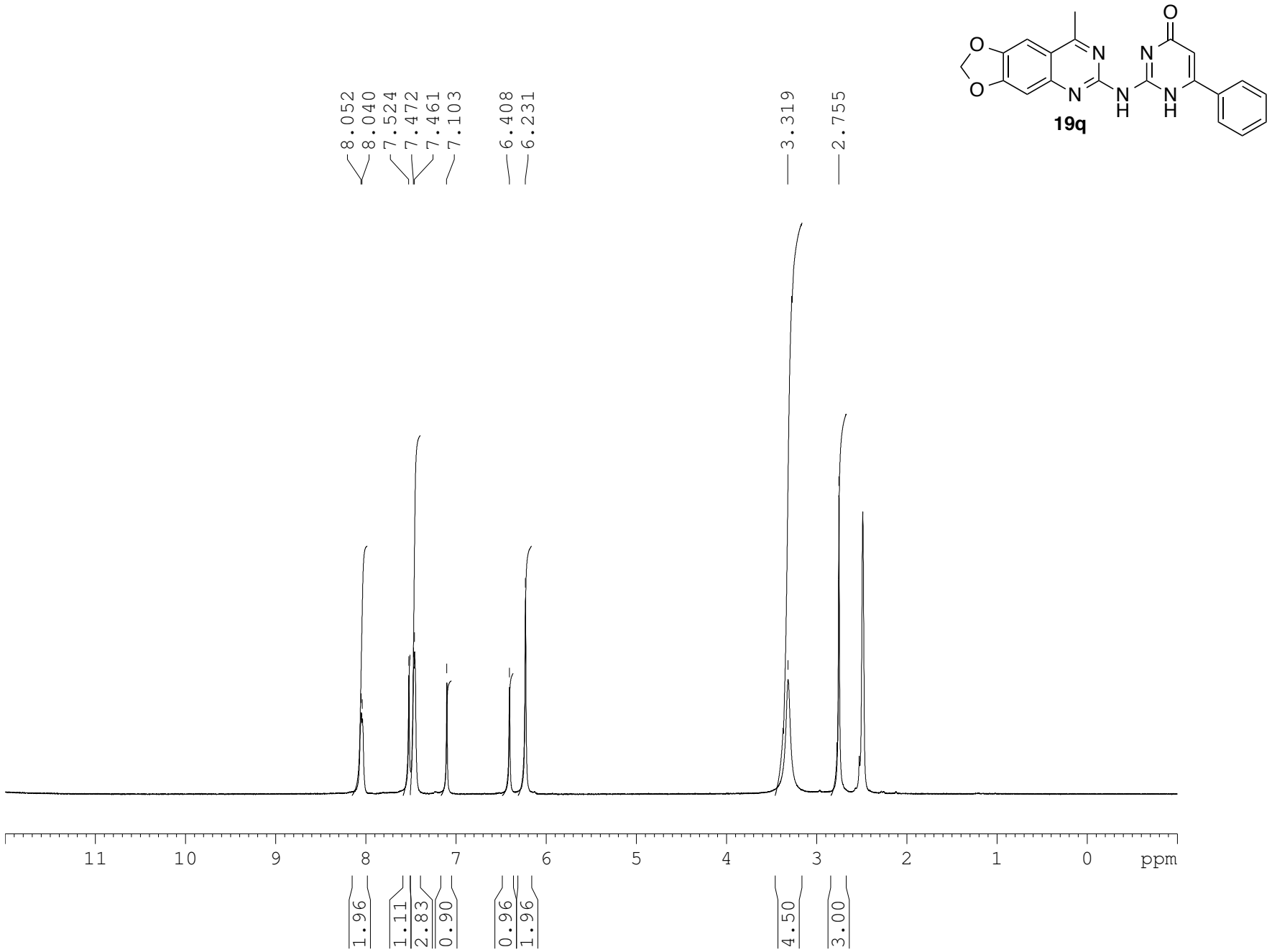



N
N
N
H
N

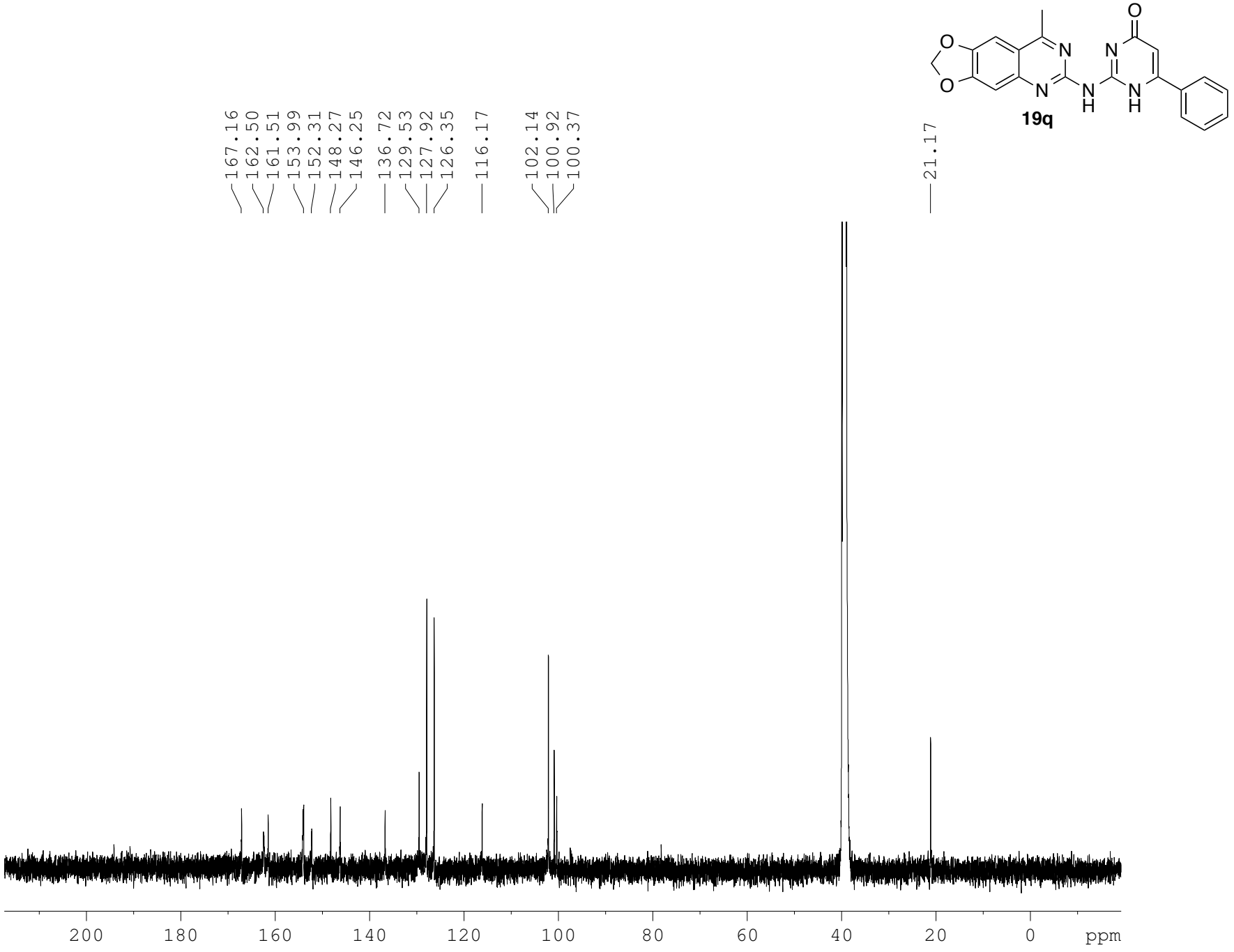
17i

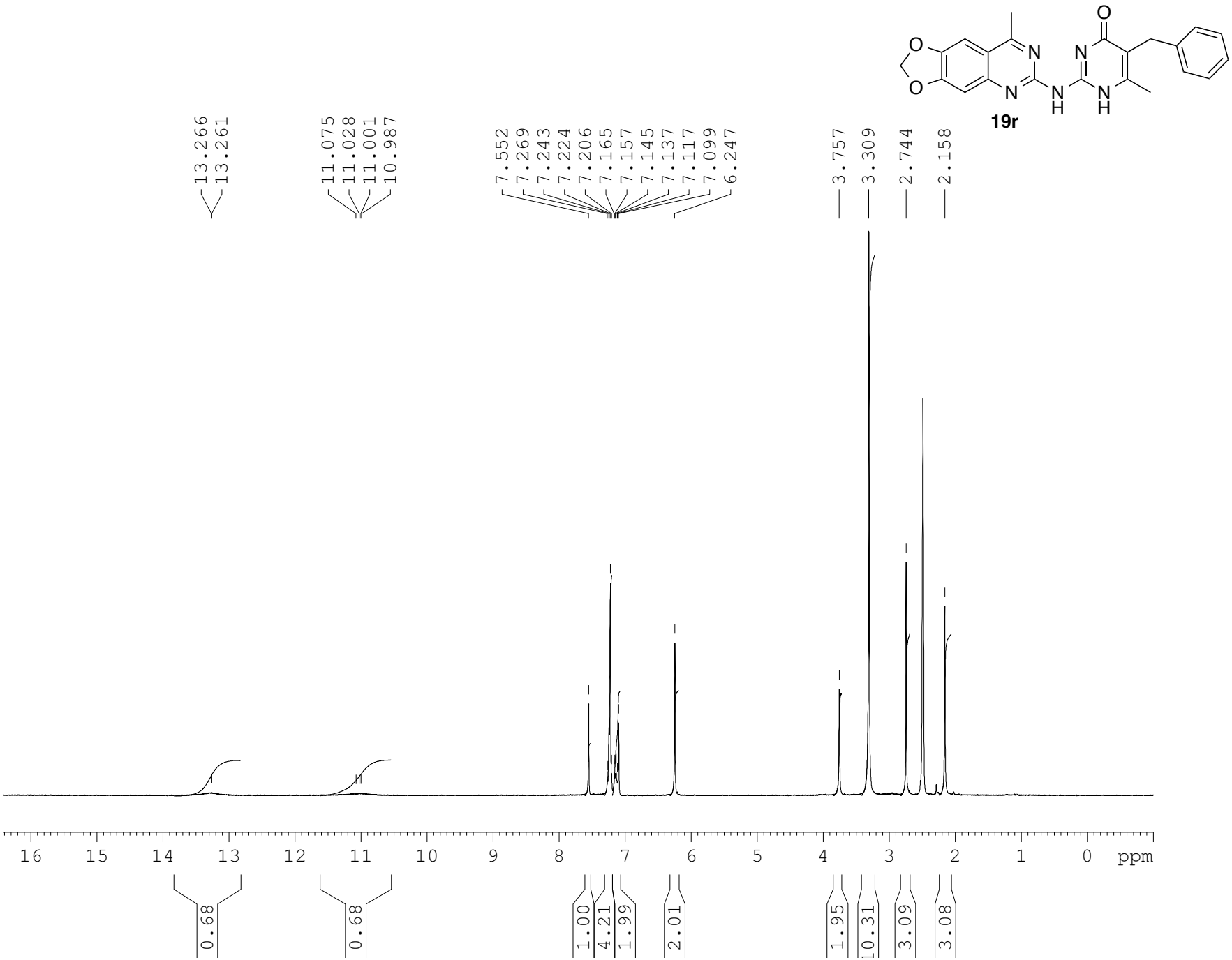

8.820
8.799
8.308
8.298
7.977
7.957
7.818
7.797
7.781
7.763
7.743
7.408
7.390
7.371
7.259
6.990
6.975
6.960
2.875
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.09
1.01
3.04
1.07
0.99
3.00

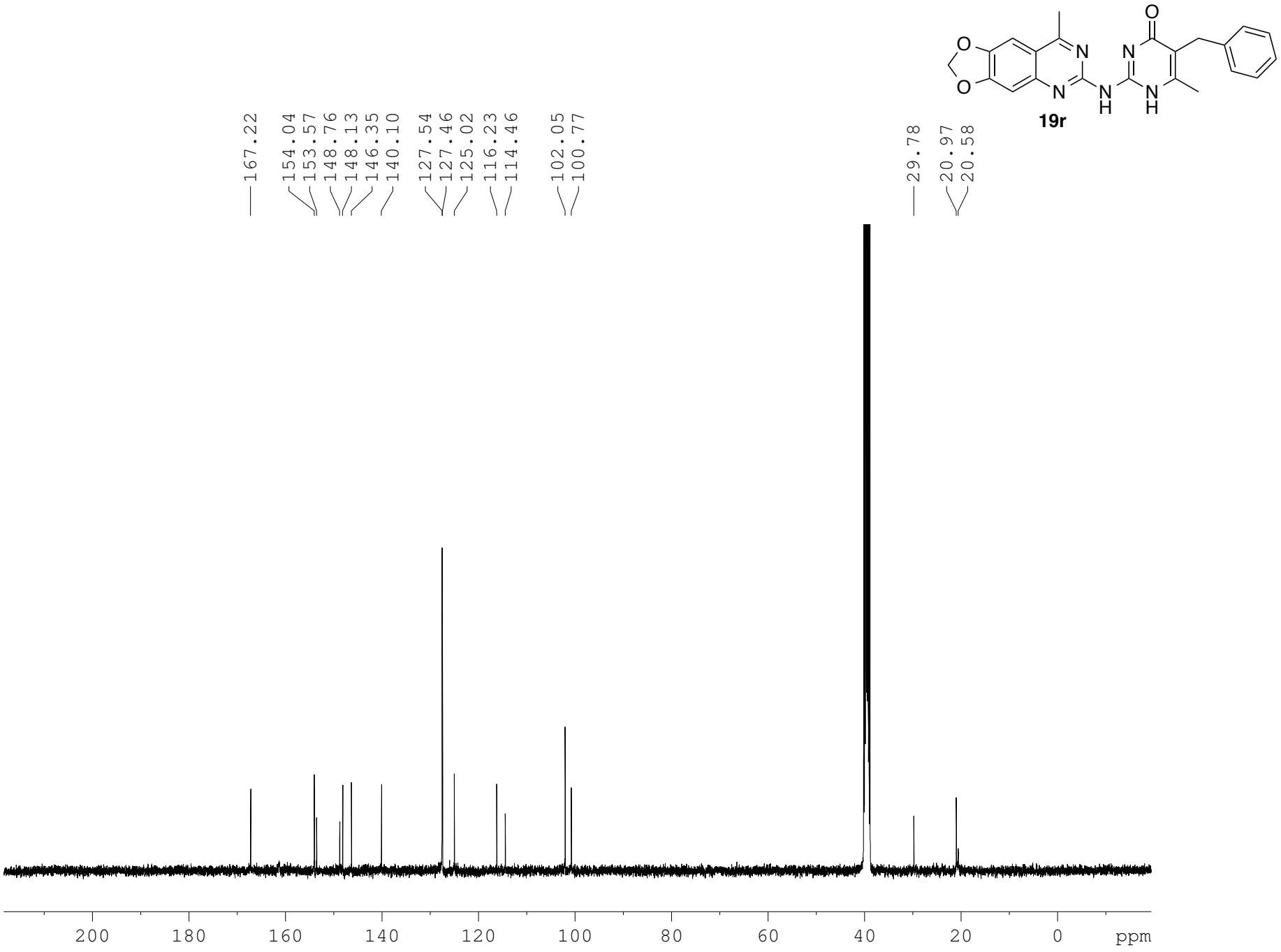

7.461
7.040
6.199
3.328
2.677
2.112
1.853
19p
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.84
1.85
14.91
2.41
2.17
2.26


8.052
8.040
7.524
7.472
7.461
7.103
6.408
6.231
3.319
2.755
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.96
1.11
2.83
0.90
0.96
1.96
4.50
3.00

19q


167.16
162.50
161.51
153.99
152.31
148.27
146.25
136.72
129.53
127.92
126.35
116.17
102.14
100.92
100.37
21.17
19q
200
180
160
140
120
100
80
60
40
20
0
ppm


19r
13.266
13.261
11.075
11.028
11.001
10.987
7.552
7.269
7.243
7.224
7.206
7.165
7.157
7.145
7.137
7.117
7.099
6.247
3.757
3.309
2.744
2.158
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.68
0.68
1.00
4.21
1.99
2.01
1.95
10.31
3.09
3.08


167.22
154.04
153.57
148.76
148.13
146.35
140.10
127.54
127.46
125.02
116.23
114.46
102.05
100.77
29.78
20.97
20.58
200
180
160
140
120
100
80
60
40
20
0
ppm

19r