Synthesis of carbonyl 2-amino-pyrimidines via tandem regioselective heterocyclization of 1,3-diynes with guanidine and selective oxidation

Liang Zhang, Mingzhu Zhao, and Xiaoming Zhao*

Shanghai Key Lab of Chemical Assessment and Sustainability, Department of Chemistry, Tongji University, 1239 Siping Road, 200092 Shanghai, P.R. China
E-mail: xmzhao08@mail.tongji.edu.cn

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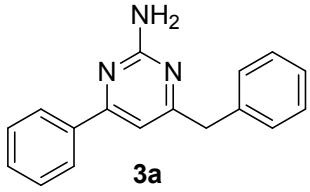
General: All manipulations were carried out under the air atmosphere using standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. All solvents were purified and dried according to standard methods prior to use, unless stated otherwise.
All reagents were obtained from commercial sources, most of them buy from Adamas-beta and used without further purification. ^{1}H NMR spectra were obtained at 400 MHz and recorded relative to tetramethylsilane signal (0 ppm) or residual protio-solvent. ^{13}C NMR spectra were obtained at 100 MHz and chemical shifts were recorded relative to the solvent resonance ($CDCl_3$, 77.0 ppm). ^{19}F NMR spectra were obtained at 376 MHz. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm).

General procedure for the synthesis of 4a–l
1,3-Diynes **1** (0.2 mmol), guanidine hydrochloride **2** (22.9 mg, 0.24 mmol), Cs_2CO_3 (130.2 mg, 0.4 mmol), were dissolved in DMSO (2 mL) in a sealed tube, then the reaction mixture was stirred at 120 °C for 12 h. The mixture was diluted with NaCl solution and AcOEt (3 × 20 mL), dried with Na_2SO_4. After concentration of the filtrate to dryness, purification of the residue by silica gel column chromatography (Petroleum ether/AcOEt = 90/10), the desired product **4a–l** was obtained. The 1,3-diynes was prepared according to known procedures. [1]

Compound characterization

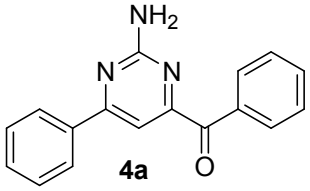
4-Benzyl-6-phenylpyrimidin-2-amine (3a)



3a

White solid, mp 140–141 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.87 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.41 – 7.33 (m, 3H), 7.31 – 7.17 (m, 5H), 6.77 (s, 1H), 5.89 (s, 2H), 3.92 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.9, 165. 9, 163.7, 138.1, 137.6, 130.4, 129.3, 128.8, 128.7, 127.2, 126.8, 106. 9, 44.2. IR (KBr): ν_{max} (cm^{-1}) = 3479, 3319, 3173, 2360, 1572, 1361. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}N_3Na$: 284.1158; Found: 284.1155.

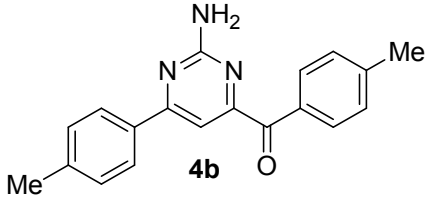
(2-Amino-6-phenylpyrimidin-4-yl)(phenyl)methanone (4a)



4a

White solid, mp 122–124 °C, 99% yield (53.9 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 – 7.95 (m, 4H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 6.1 Hz, 6H), 5.82 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.5, 167.3, 163.6, 163.0, 136.8, 135.3, 133.7, 131.1, 130.8, 128. 9, 128.5, 127.3, 106.5. IR (KBr): ν_{max} (cm^{-1}) = 3482, 3319, 3197, 1673, 1566, 1364, 1218. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{13}N_3NaO$: 298.0951; Found: 298.0945.

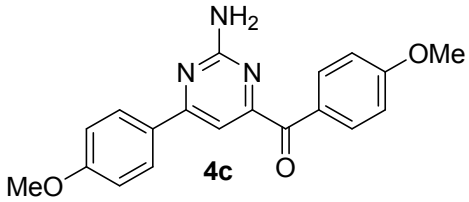
(2-Amino-6-(p-tolyl)pyrimidin-4-yl)(p-tolyl)methanone (4b)



4b

White solid, mp 162–164 °C, 99% yield (60.1 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (dd, *J* = 9.8, 8.3 Hz, 4H), 7.42 (s, 1H), 7.29 – 7.22 (m, 4H), 5.65 (s, 2H), 2.40 (d, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.2, 167.1, 163. 9, 162.9, 144.7, 141. 5, 134.1, 132.7, 130.9, 129.6, 129.2, 127.2, 106.2, 21.8, 21.5. IR (KBr): ν_{max} (cm^{-1}) = 3491, 3319, 3194, 1667, 1566, 1363. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{19}H_{18}N_3O$: 304.1444; Found: 304.1437.

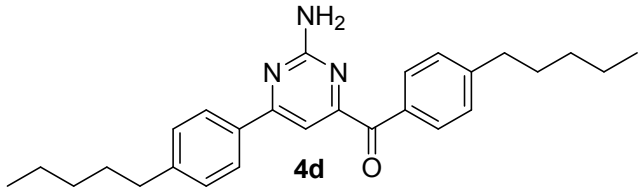
(2-Amino-6-(4-methoxyphenyl)pyrimidin-4-yl)(4-methoxyphenyl)methanone (4c)



4c

White solid, mp 173−174 °C, 90% yield (60.3 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (t, *J* = 8.1 Hz, 4H), 7.40 (s, 1H), 6.99 (dd, *J* = 12.7, 8.4 Hz, 4H), 5.86 (s, 2H), 3.88 (d, *J* = 4.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 191. 5, 165.6, 164.5, 164.3, 162.5, 161.8, 133.4, 129.1, 128.1, 127.8, 114.4, 113.8, 105.8, 55.6, 55.5. IR (KBr): ν_{max} (cm^{-1}) = 3378, 3304, 3199, 1659, 1593, 1361, 1254. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{19}H_{17}N_3NaO_3$: 358.1162; Found: 358.1163.

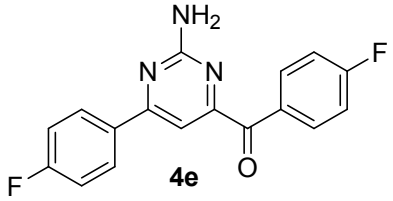
(2-Amino-6-(4-pentylphenyl)pyrimidin-4-yl)(4-pentylphenyl)methanone (4d)



4d

White solid, mp 128−129 °C, 98% yield (81.1 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (dd, *J* = 11.6, 8.2 Hz, 4H), 7.42 (s, 1H), 7.27 (d, *J* = 7.2 Hz, 4H), 5.72 (d, *J* = 5.7 Hz, 2H), 2.65 (dd, *J* = 13.5, 7.1 Hz, 4H), 1.69 – 1.57 (m, 4H), 1.36 – 1.28 (m, 8H), 0.88 (td, *J* = 6.8, 2.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.2, 167.2, 163.9, 162.9, 149.6, 146.4, 134.3, 132.9, 131.0, 128.9, 128.5, 127.2, 106.2, 36.1, 35.8, 31.5, 30.9, 30.8, 22. 6, 22.5, 14.1, 14.0. IR (KBr): ν_{max} (cm^{-1}) = 3491, 3315, 3194, 2926, 1679, 1541, 1364, 1230. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{27}H_{33}N_3NaO$: 438.2516; Found: 438.2515.

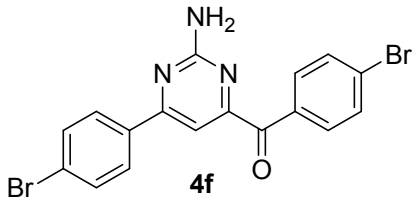
(2-Amino-6-(4-fluorophenyl)pyrimidin-4-yl)(4-fluorophenyl)methanone (4e)



4e

White solid, mp 141−142 °C, 90% yield (55.9 mg).
^{1}H NMR (400 MHz, DMSO) δ = 7.92 – 7.87 (m, 4H), 7.33 (t, *J* = 8.9 Hz, 5H), 7.09 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ = 163.2, 160.8, 152.2, 127.2(d, *J* = 3.0 Hz), 126.0(d, *J* = 8.2 Hz), 116.3(d, *J* = 21.3 Hz), 108.5. ^{19}F NMR (377 MHz, DMSO) δ = -114.00. IR (KBr): ν_{max} (cm^{-1}) = 3535, 3343, 3171, 1650, 1557, 1233, 768. HRMS (ESI): *m/z* [M + Na]+ calcd for $C_{17}H_{11}F_2N_3NaO$: 334.0762; Found: 334.0762.

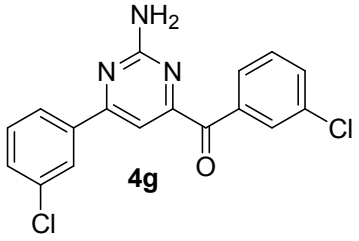
(2-Amino-6-(4-bromophenyl)pyrimidin-4-yl)(4-bromophenyl)methanone (4f)



4f

White solid, mp 210–211 °C, 91% yield (78.2 mg).
^{1}H NMR (400 MHz, DMSO) δ = 8.11 (d, *J* = 8.6 Hz, 2H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.76 (dd, *J* = 19.8, 8.5 Hz, 4H), 7.51 (s, 1H), 7.16 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ = 192.9, 165.1, 164.1, 163.7, 136.1, 134.5, 132.8, 132.3, 132.1, 129.5, 129. 5, 128.5, 125.2, 104.1. IR (KBr): ν_{max} (cm^{-1}) = 3476, 3313, 3185, 1670, 1619, 1360, 1247, 756. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{11}Br_2N_3NaO$: 453.9161; Found: 453.9154.

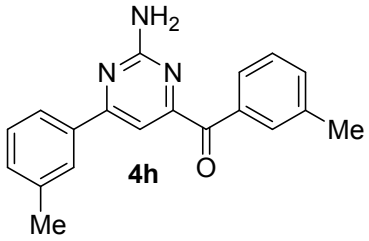
(2-Amino-6-(3-chlorophenyl)pyrimidin-4-yl)(3-chlorophenyl)methanone (4g)



4g

White solid, mp 157–158 °C, 97% yield (67.0 mg).
^{1}H NMR (400 MHz, DMSO) δ = 8.25 (s, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 8.02 – 7.91 (m, 2H), 7.83 – 7.76 (m, 1H), 7.59 (dt, *J* = 13.3, 7.9 Hz, 4H), 7.24 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ = 192.5, 164.7, 163.9, 163.6, 139.1, 137.4, 134.3, 133.9, 133.8, 131.2, 131.1, 130.2, 129.6, 127.1, 126.1, 104.5. IR (KBr): ν_{max} (cm^{-1}) = 3459, 3313, 3181, 1640, 1536, 1352, 1212. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{11}Cl_2N_3NaO$: 366.0171; Found: 366.0171.

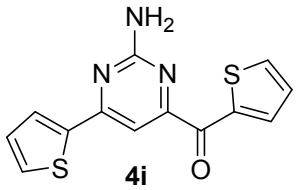
(2-Amino-6-(m-tolyl)pyrimidin-4-yl)(m-tolyl)methanone (4h)



4h

White solid, mp 139–140 °C, 99% yield (60.1 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (ddd, *J* = 17.8, 7.5, 3.9 Hz, 4H), 7.44 (d, *J* = 7.1 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.31 (d, *J* = 7.5 Hz, 1H), 5.70 (s, 2H), 2.42 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.8, 167.5, 163.8, 163.0, 138.6, 138.3, 136.8, 135.3, 134.5, 131.8, 131.0, 128.8, 128.3, 128.2, 127.9, 124.4, 106.6, 21.5, 21.4. IR (KBr): ν_{max} (cm^{-1}) = 3488, 3316, 3196, 1670, 1569, 1358, 1271. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{17}N_3NaO$: 326.1264; Found: 326.1264.

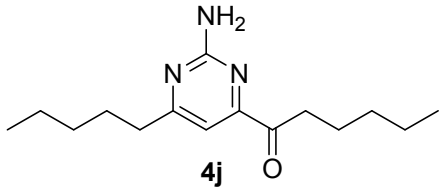
(2-Amino-6-(thiophen-2-yl)pyrimidin-4-yl)(thiophen-2-yl)methanone (4i)



4i

White solid, mp 134–135 °C, 91% yield (52.2 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (dd, *J* = 2.9, 1.1 Hz, 1H), 8.11 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.82 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.68 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.50 (s, 1H), 7.40 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.34 (dd, *J* = 5.1, 2.9 Hz, 1H), 5.47 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 185.7, 163.4, 162.9, 162.8, 140.1, 139.3, 137.4, 128.9, 127.2, 126.8, 126.2, 125.7, 106.4. IR (KBr): ν_{max} (cm^{-1}) = 3488, 3351, 3197, 1656, 1572, 1423, 1230. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{10}N_3OS_2$: 288.0260; Found: 288.0260.

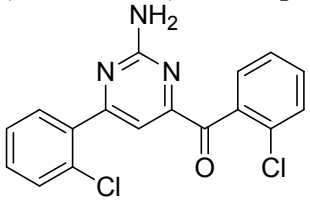
1-(2-Amino-6-pentylpyrimidin-4-yl)hexan-1-one (4j)



4j

Colorless oil, 90% yield (47.3 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.36 (s, 1H), 5.10 (s, 2H), 2.60 – 2.43 (m, 4H), 1.76 – 1.56 (m, 4H), 1.31 (ddd, *J* = 9.5, 7.2, 3.6 Hz, 8H), 0.98 – 0.83 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.9, 162.8, 109.4, 37.8, 37.8, 37.5, 31.7, 31.6, 31.6, 31.0, 29.4, 29.1, 28.9, 28.9, 28.6, 22.6, 22.5, 22.5, 22.5, 14.1, 14.1, 14.0, 13.9. IR (KBr): ν_{max} (cm^{-1}) = 3500, 3310, 3169, 1629, 1578, 1453, 1381. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{26}N_3O$: 264.2070; Found:264.2093.

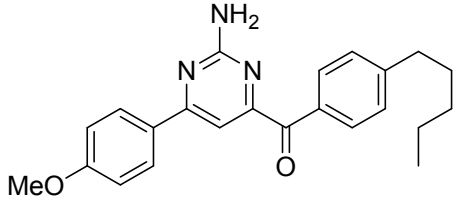
(2-Amino-6-(2-chlorophenyl)pyrimidin-4-yl)(2-chlorophenyl)methanone (4k)



4k

Yellow solid, mp 165–166 °C, 85% yield (58.3 mg).
^{1}H NMR (400 MHz, DMSO) δ = 7.62 (ddd, *J* = 14.7, 6.0, 2.8 Hz, 5H), 7.51 (dt, *J* = 8.7, 2.4 Hz, 3H), 7.28 (s, 1H), 7.20 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ = 195.3, 167.2, 164.3, 161.4, 137.6, 137.4, 132.9, 131.6, 131.5, 131.4, 131.2, 130.9, 130.6, 130.5, 130.33, 127.9, 127.6, 108.0. IR (KBr): ν_{max} (cm^{-1}) = 3319, 3203, 3062, 1694, 1539, 1358, 1215. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{11}Cl_2N_3NaO$: 366.0171; Found: 366.0156.

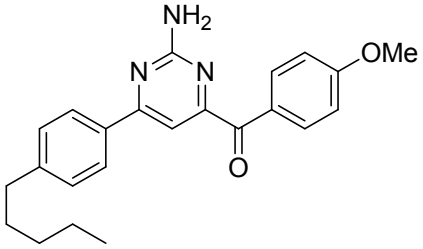
(2-Amino-6-(4-methoxyphenyl)pyrimidin-4-yl)(4-pentylphenyl)methanone (4l)



4l

White solid, mp 162−163 °C, 43% yield (31.4 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (dd, *J* = 16.1, 8.6 Hz, 4H), 7.41 (s, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 5.51 (s, 2H), 3.86 (s, 3H), 2.74 – 2.60 (m, 2H), 1.71 – 1.58 (m, 2H), 1.39 – 1.27 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.3, 166.6, 163.8, 162.8, 162.1, 149.7, 132.9, 131.0, 129.3, 128.9, 128.5, 114.2, 105.8, 55.4, 36.2, 31.5, 30.8, 22.5, 14.0. IR (KBr): ν_{max} (cm^{-1}) = 3485, 3316, 3197, 1664, 1608, 1361, 1254, 1171. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{23}H_{25}N_3NaO_2$: 398.1839; Found: 398.1810.

(2-Amino-6-(4-pentylphenyl)pyrimidin-4-yl)(4-methoxyphenyl)methanone (4l')



4l'

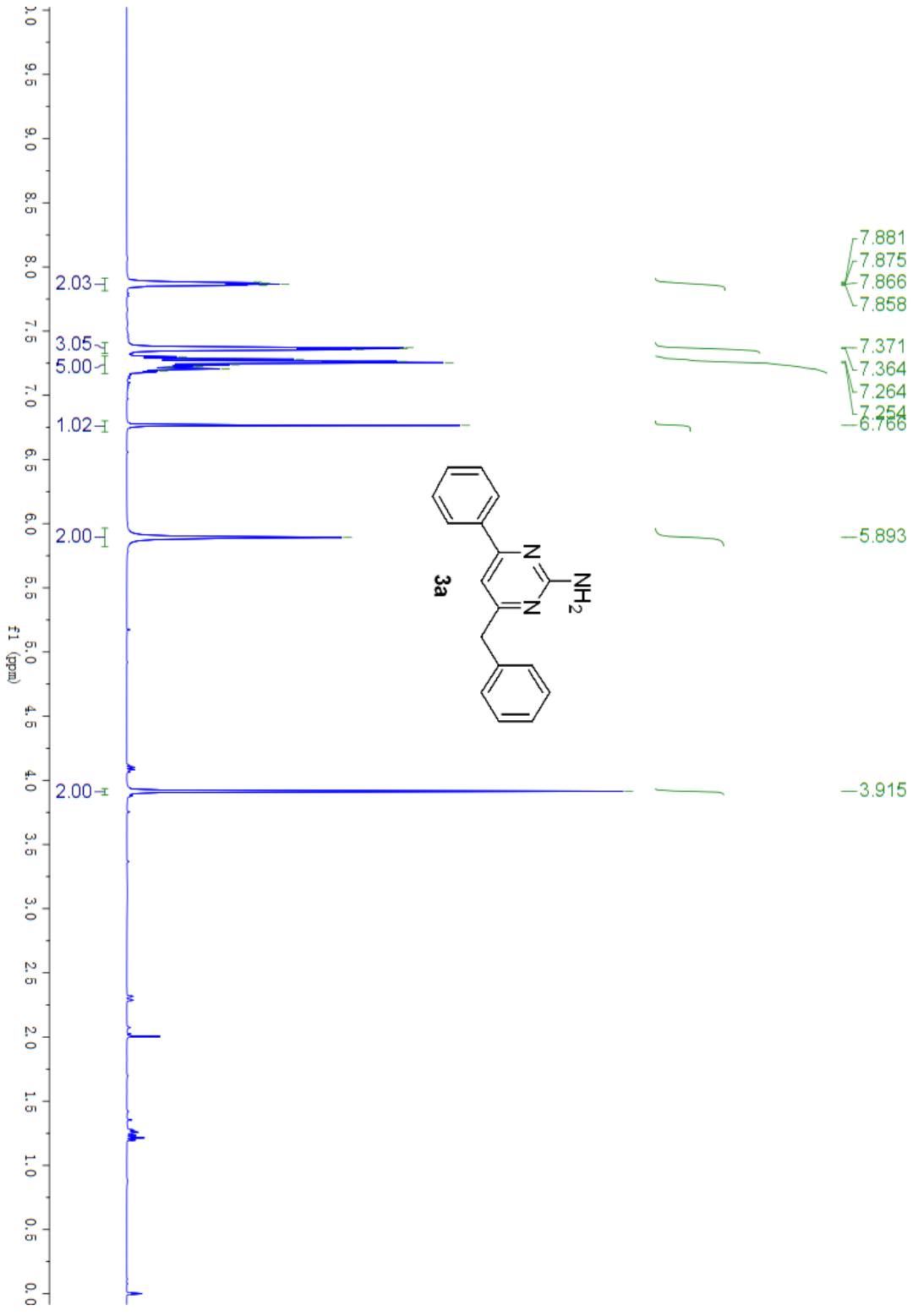
White solid, mp 118−120 °C, 51% yield (37.2 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 (dd, *J* = 50.4, 8.4 Hz, 4H), 7.47 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.60 (s, 2H), 3.91 (s, 3H), 2.70 (t, *J* = 7.7 Hz, 2H), 1.80 – 1.61 (m, 2H), 1.37 (d, *J* = 3.4 Hz, 4H), 0.94 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 192.0, 167.2, 164.3, 164.1, 162.8, 146.5, 134.3, 133.4, 129.0, 128.1, 127.2, 113.8, 106.3, 55.6, 35.8, 31.5, 31.0, 22.6, 14.1. IR (KBr): ν_{max} (cm^{-1}) = 3491, 3310, 3194, 1653, 1596, 1536, 1254, 1158. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{23}H_{25}N_3NaO_2$: 398.1839; Found: 398.1812.

Controlled experiments for the synthesis of 3 ab

1,3-Diynes **1** (0.2 mmol), guanidine hydrochloride **2** (191.1 mg, 2.0 mmol), Cs_2CO_3 (130.2 mg, 0.4 mmol), were dissolved in DMSO-d_6 (2 mL) and H_2O (50 μl) in a sealed tube, then the reaction was stirred at 120 °C for 12 h. The mixture was diluted with NaCl solution and AcOEt (3 × 20 mL), dried with Na_2SO_4. After concentration of the filtrate to dryness, purification of the residue by silica gel column chromatography (Petroleum ether/AcOEt = 90/10) gave **3 ab** (46.9 mg), 89% yield (53.9 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, *J* = 6.4, 2.7 Hz, 2H), 7.44–7.34 (m, 3H), 7.33–7.11 (m, 5H), 6.79 (s, 0.52H), 5.82 (s, 2H), 3.91 (s, 0.2H).

References:

1 For selective review, see: (a) P. Siemsen, R. C. Livingston and F. Diederich, *Angew. Chem., Int. Ed.* 2000, **39**, 2632; for selective methods for the synthesis of 1,3-diynes, see: (a) F. Sondheimer, Y. Amiel and R. Wolovsky, *J. Am. Chem. Soc.* 1957, **79**, 4247; (b) A. S. Hay, *J. Org. Chem.* 1960, **25**, 1275; (c) A. S. Hay, *J. Org. Chem.* 1962, **27**, 3320; (d) A. L. K. S. Shun and R. R. Tykwinski, *Angew. Chem., Int. Ed.* 2006, **45**, 1034; (e) G. Cahiez, A. Moyeux, J. Buendia and C. Duplais, *J. Am. Chem. Soc.* 2007, **129**, 13788; (f) K. Kamata, S. Yamaguchi, M. Kotani, K. Yamaguchi and N. Mizuno, *Angew. Chem., Int. Ed.* 2008, **47**, 2407; (g) W. Shi,; Y. D. Luo, X. C. Luo, L. Chao,; H. Zhang, J. Wang and A. W. Lei, *J. Am. Chem. Soc.* 2008, **130**, 14713; (h) W. Yin, C. He, M. Chen, H. Zhang and A. Lei, *Org. Lett.* 2009, **11**, 709; (i) Y. Weng, B. Cheng, C. He and A. Lei, *Angew. Chem. ,Int. Ed.* 2012, **51**, 9547; (j) G. Zhang, H. Yi, G. Zhang, Y. Deng, R. Bai, H. Zhang, J. T. Miller, A. J. Kropf, E. E. Bunel and A. Lei, *J. Am. Chem. Soc.* 2014, **136**, 924.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7.858
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7.264
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5.893
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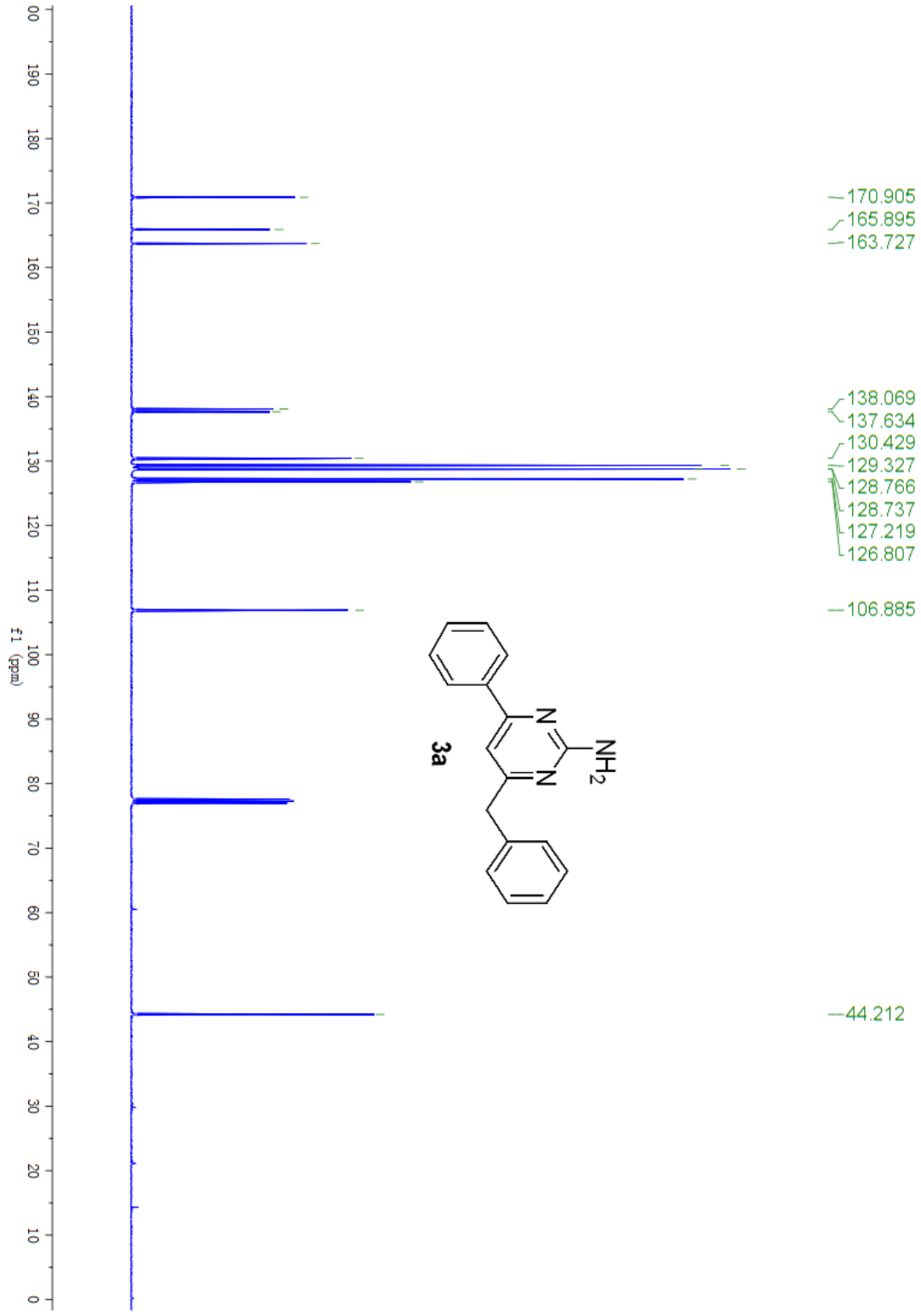
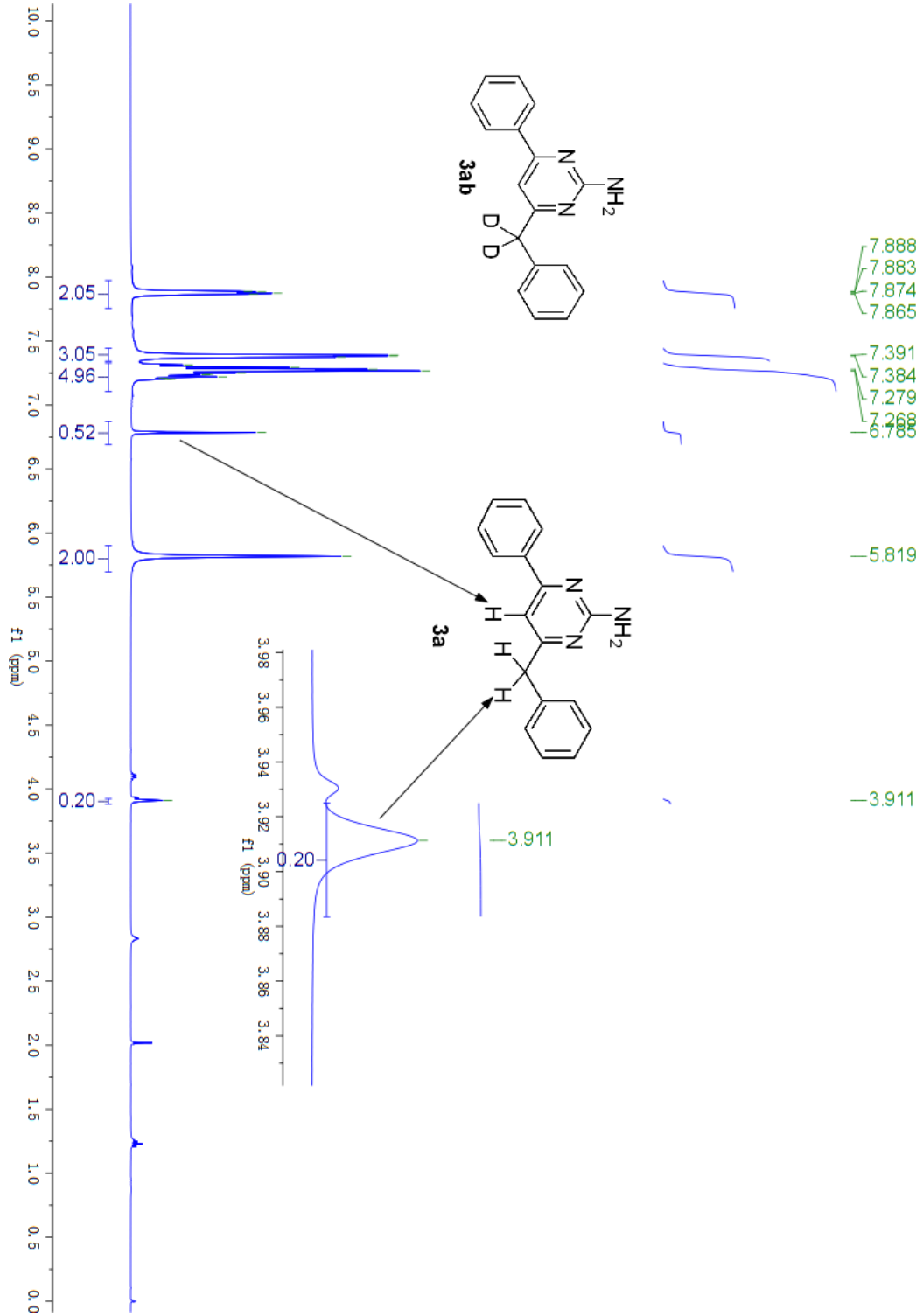
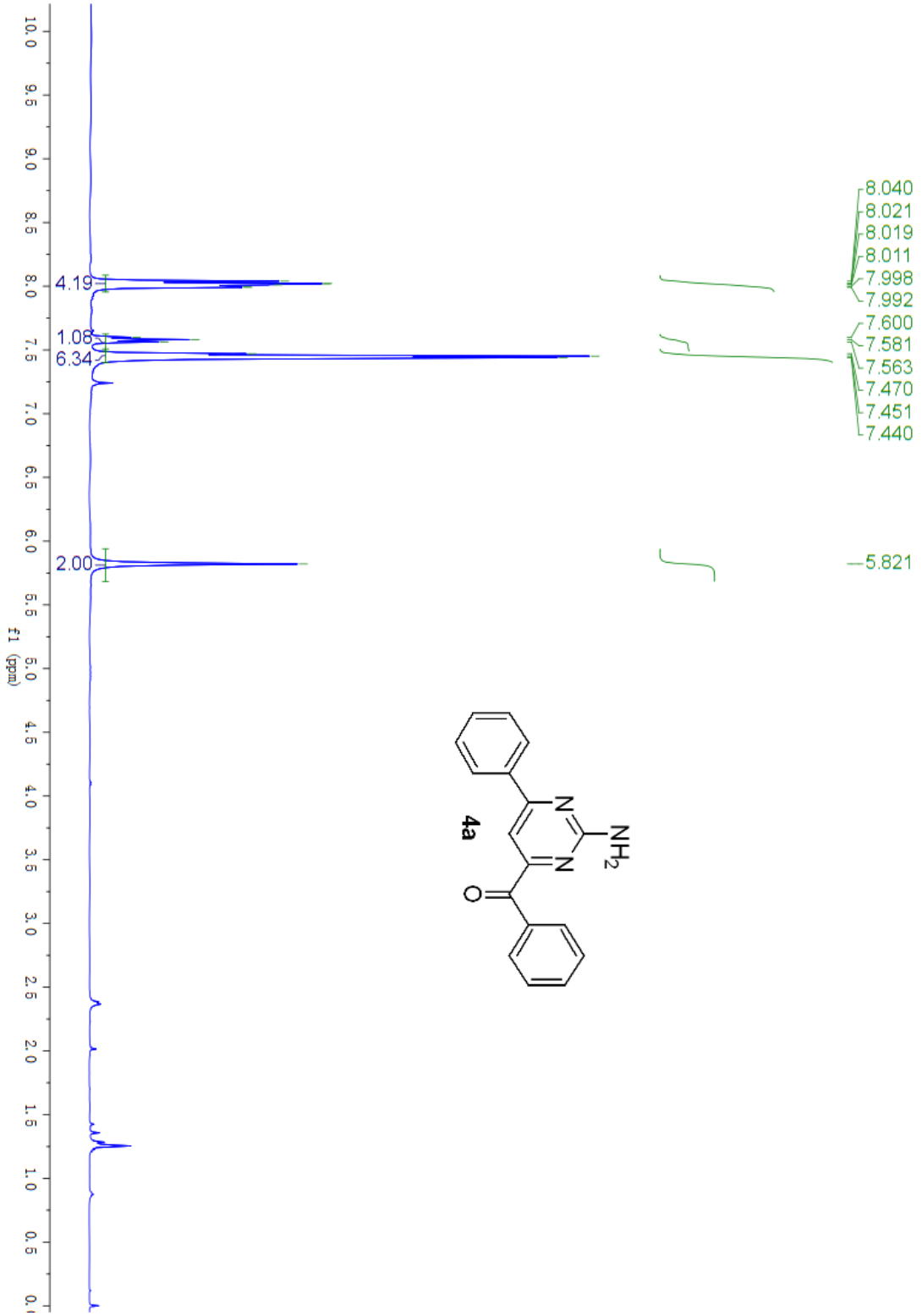
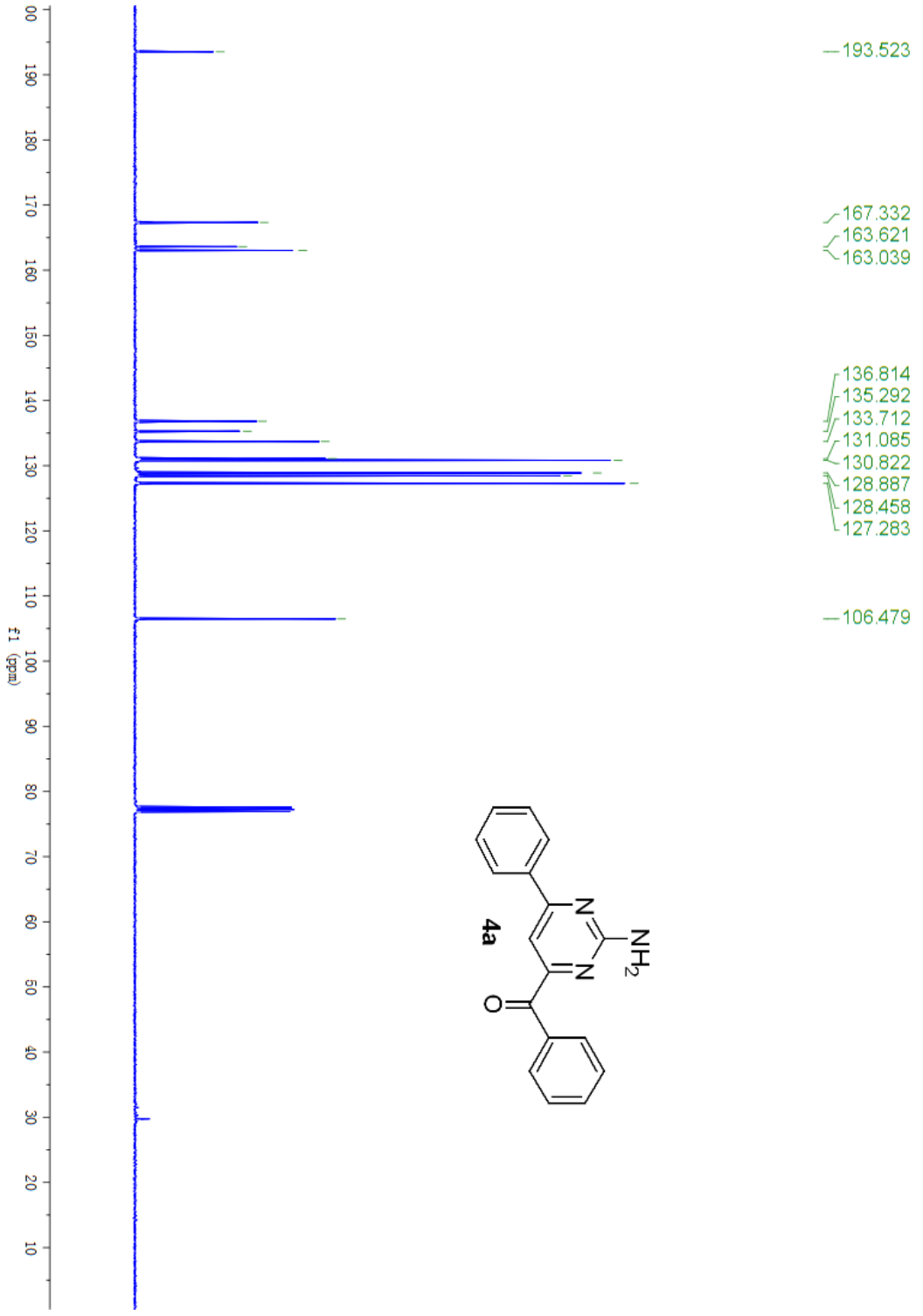
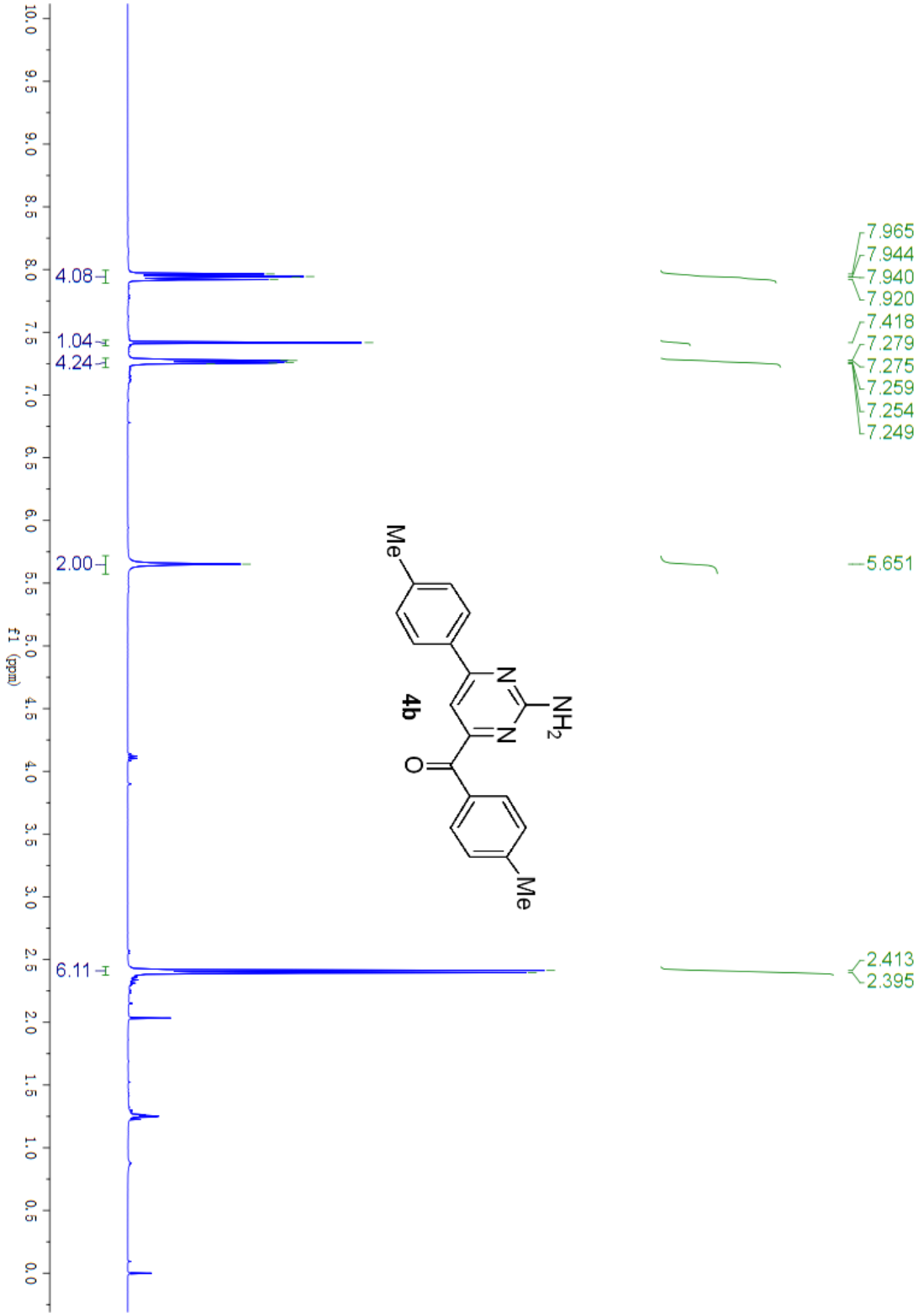
5.00
1.02
2.00
2.00
3a
NH2
N
N
f1 (ppm)

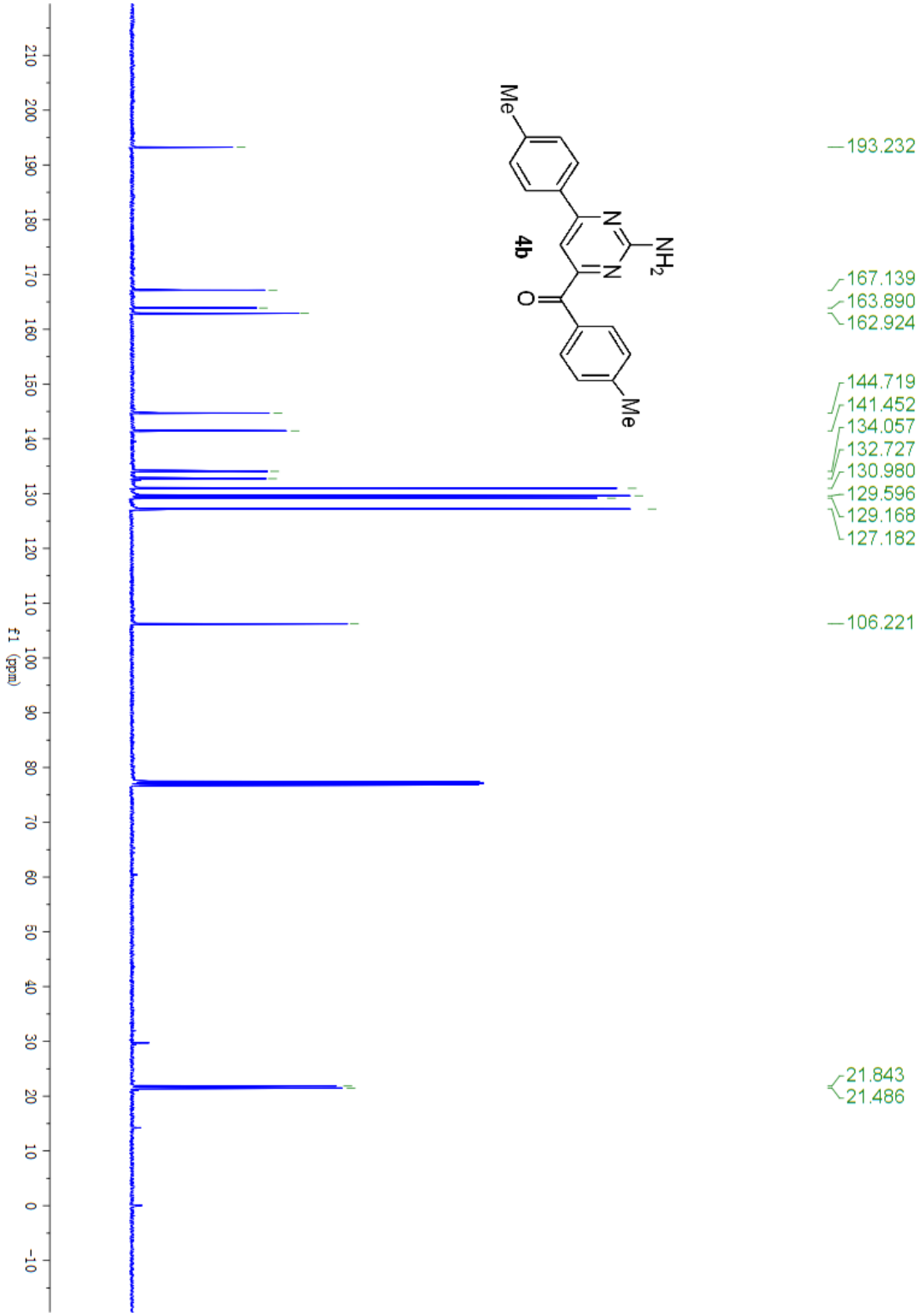

170.905
165.895
163.727
138.069
137.634
130.429
129.327
128.766
128.737
127.219
126.807
106.885
44.212
f1 (ppm)
3a
NH2
N
N

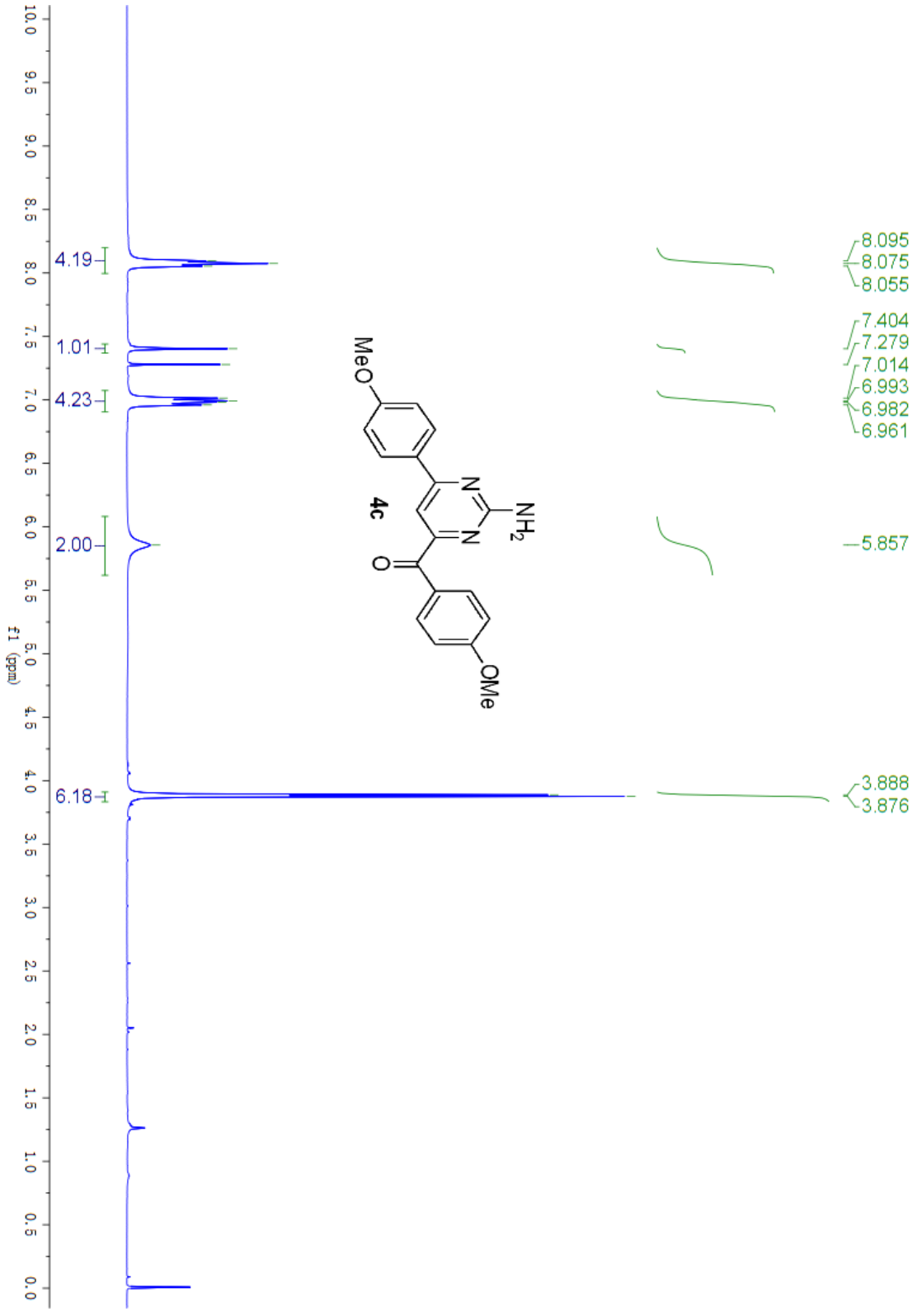

3ab
3a
2.05
3.05
4.96
0.52
2.00
0.20
7.888
7.883
7.874
7.865
7.391
7.384
7.279
7.268
6.785
5.819
3.911
f1 (ppm)

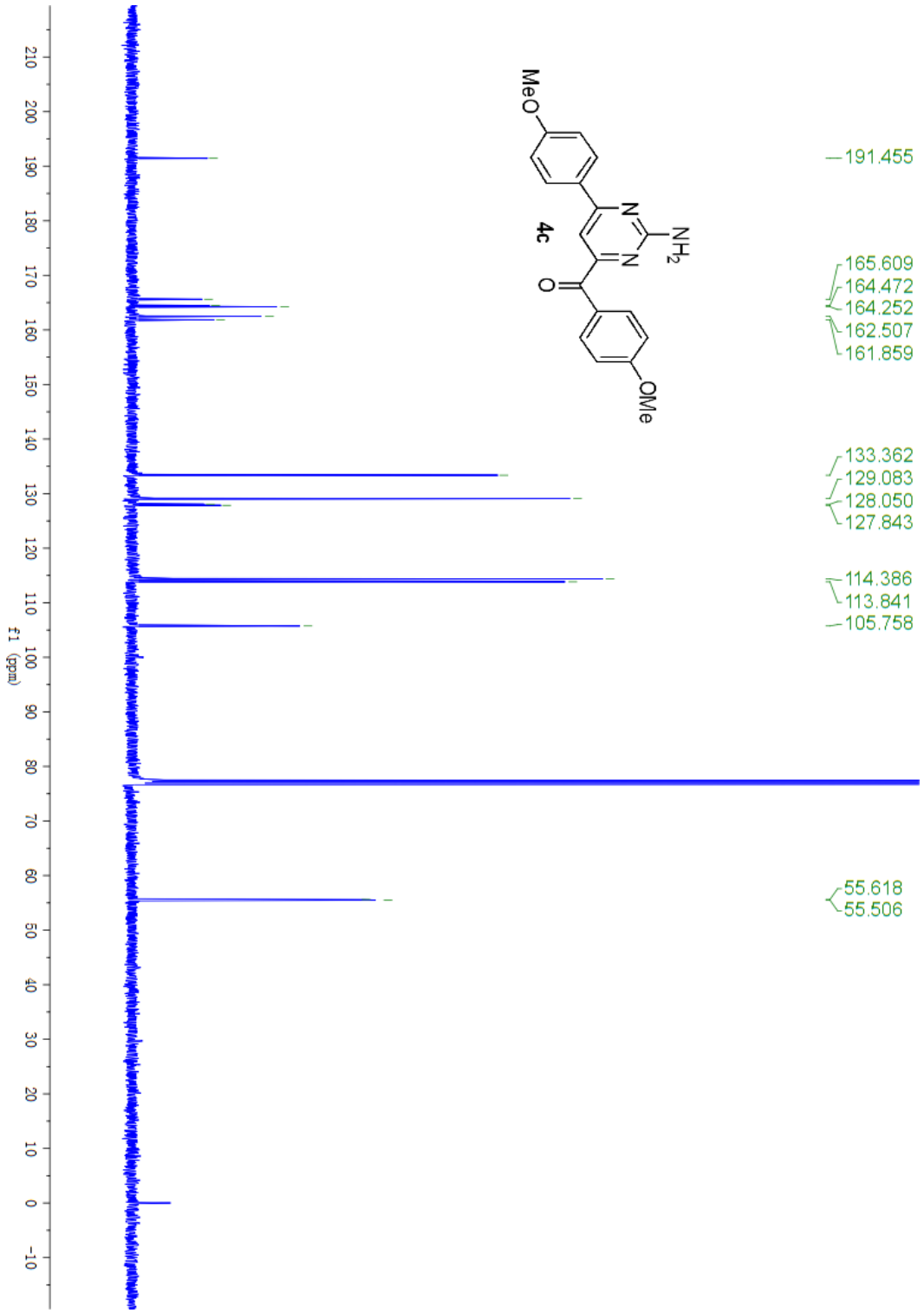

8.040
8.021
8.019
8.011
7.998
7.992
7.600
7.581
7.563
7.470
7.451
7.440
5.821
4.19
1.08
6.34
2.00
f1 (ppm)
4a
O
N
N
NH2

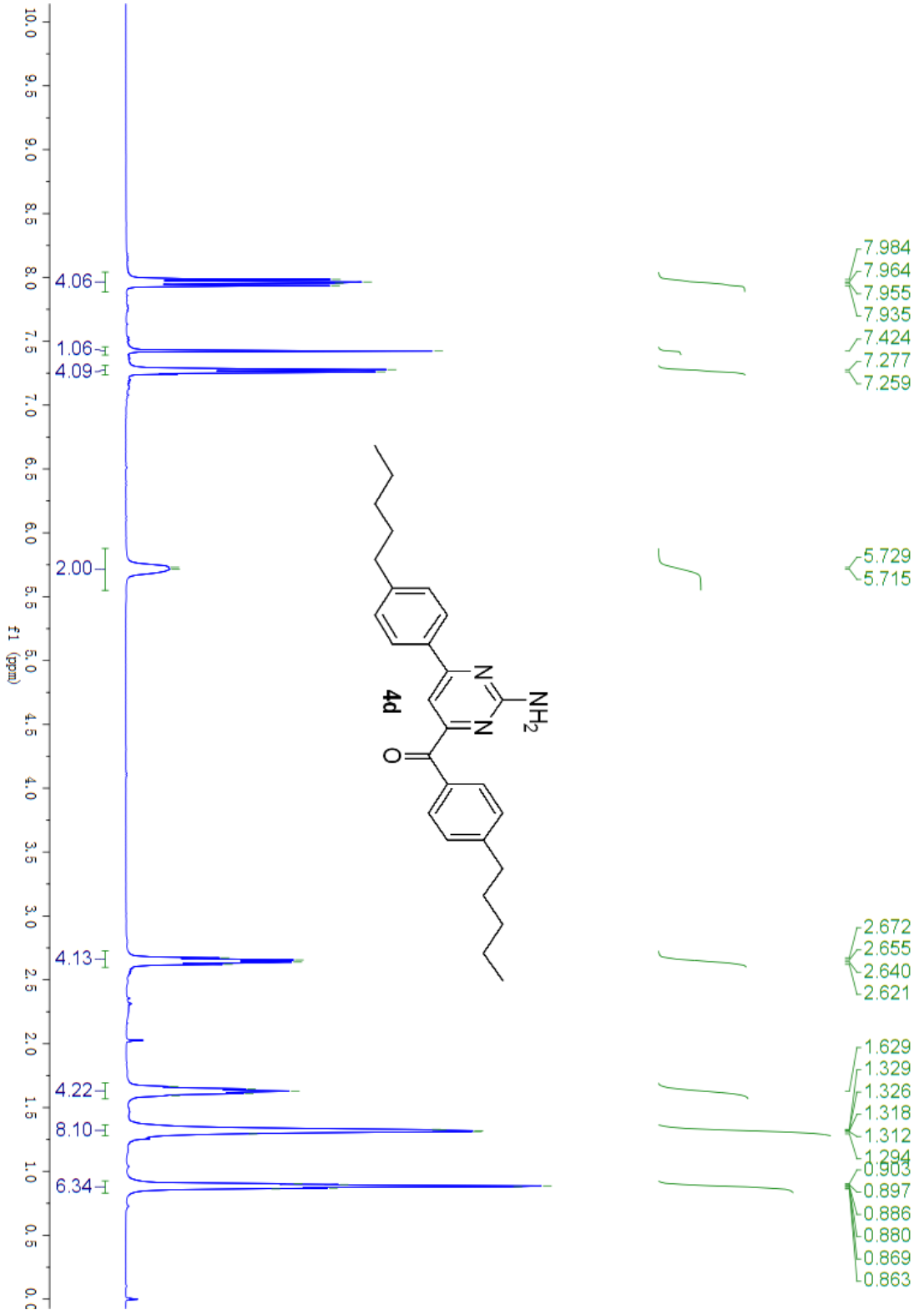

193.523
167.332
163.621
163.039
136.814
135.292
133.712
131.085
130.822
128.887
128.458
127.283
106.479
f1 (ppm)
4a
N
N
NH2
O

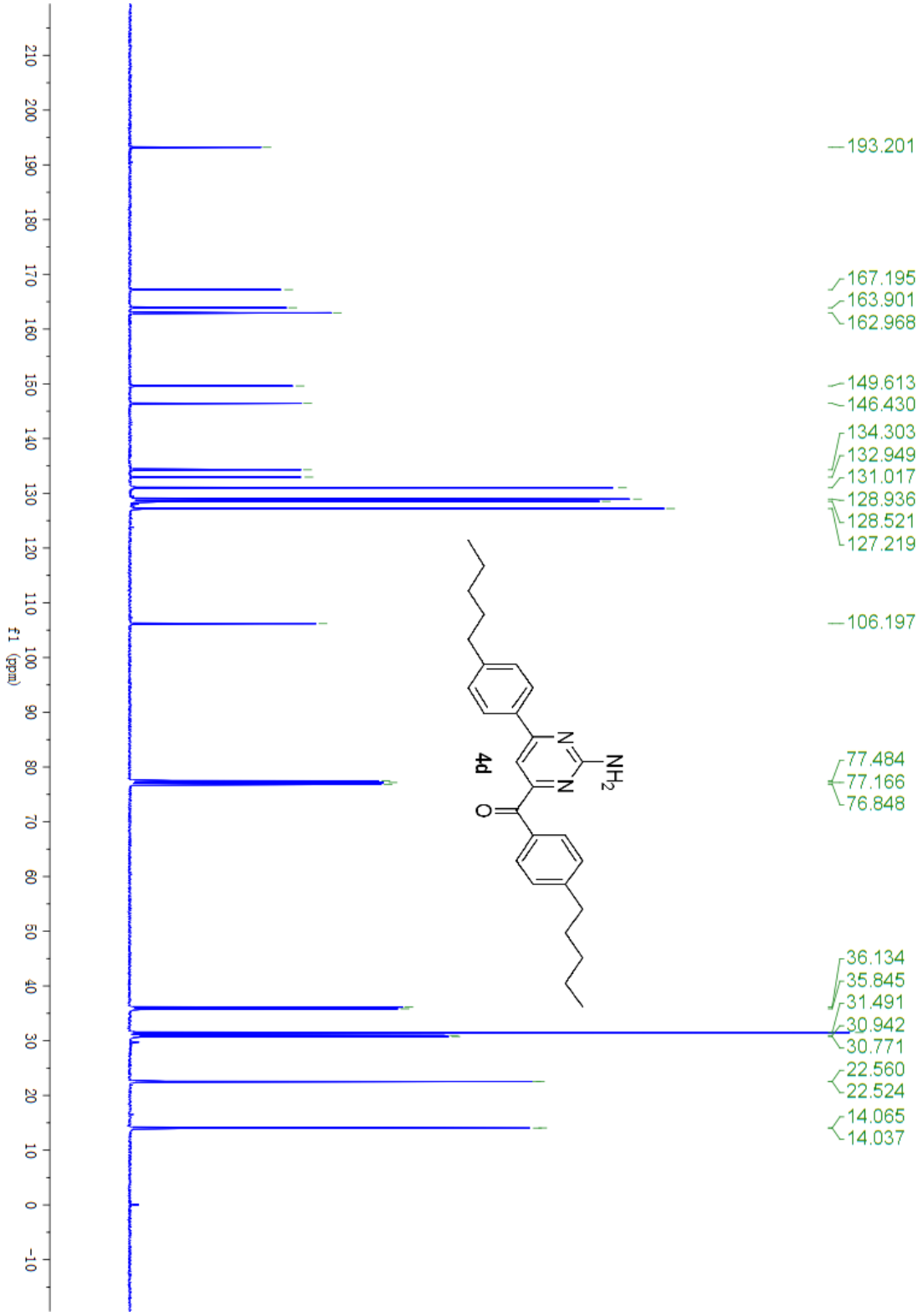

4.08
1.04
4.24
2.00
6.11
f1 (ppm)
7.965
7.944
7.940
7.920
7.418
7.279
7.275
7.259
7.254
7.249
5.651
2.413
2.395
Me
N
N
NH2
O
Me
4b

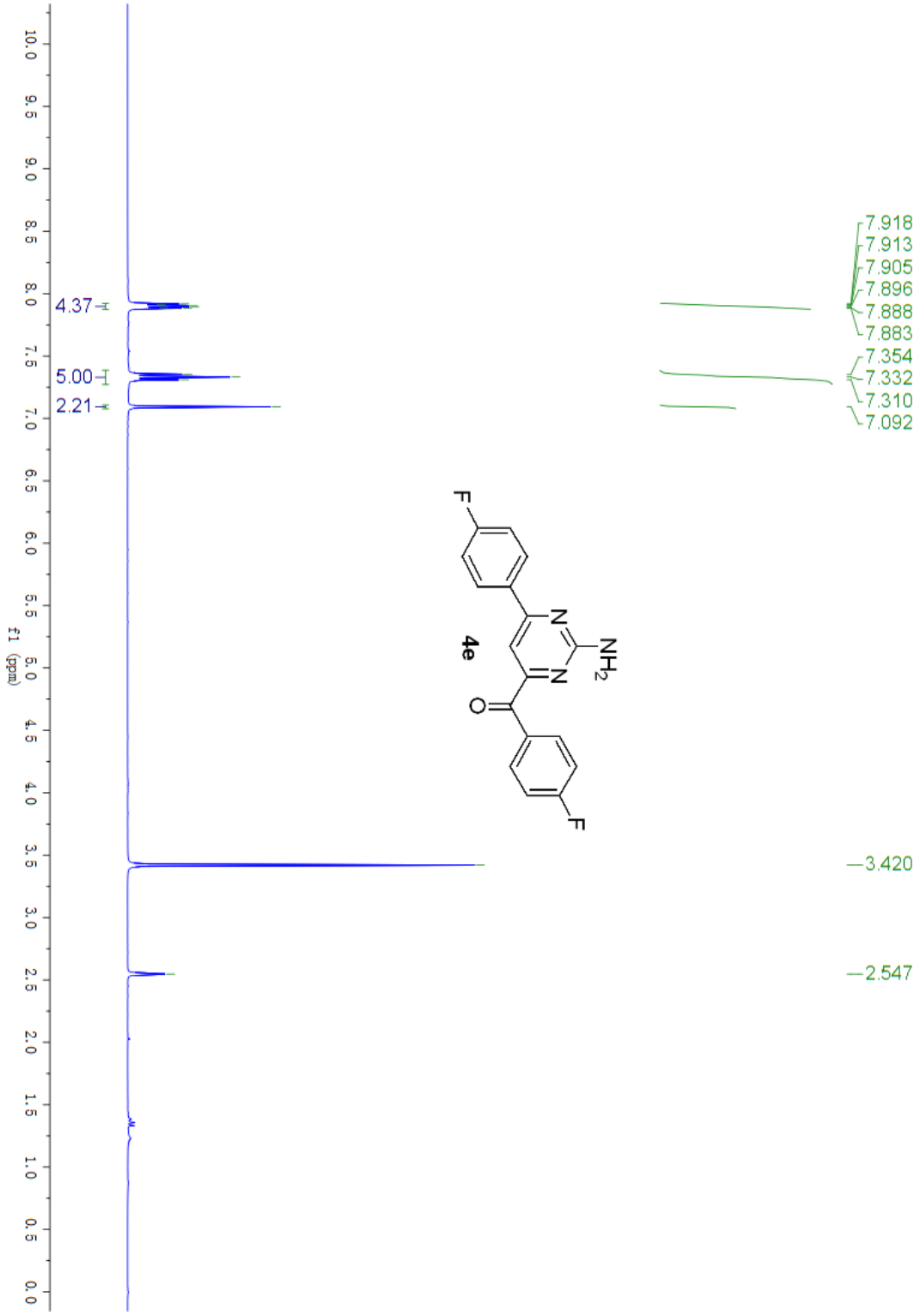

Me
N
N
NH2
4b
O
Me
193.232
167.139
163.890
162.924
144.719
141.452
134.057
132.727
130.980
129.596
129.168
127.182
106.221
21.843
21.486
f1 (ppm)

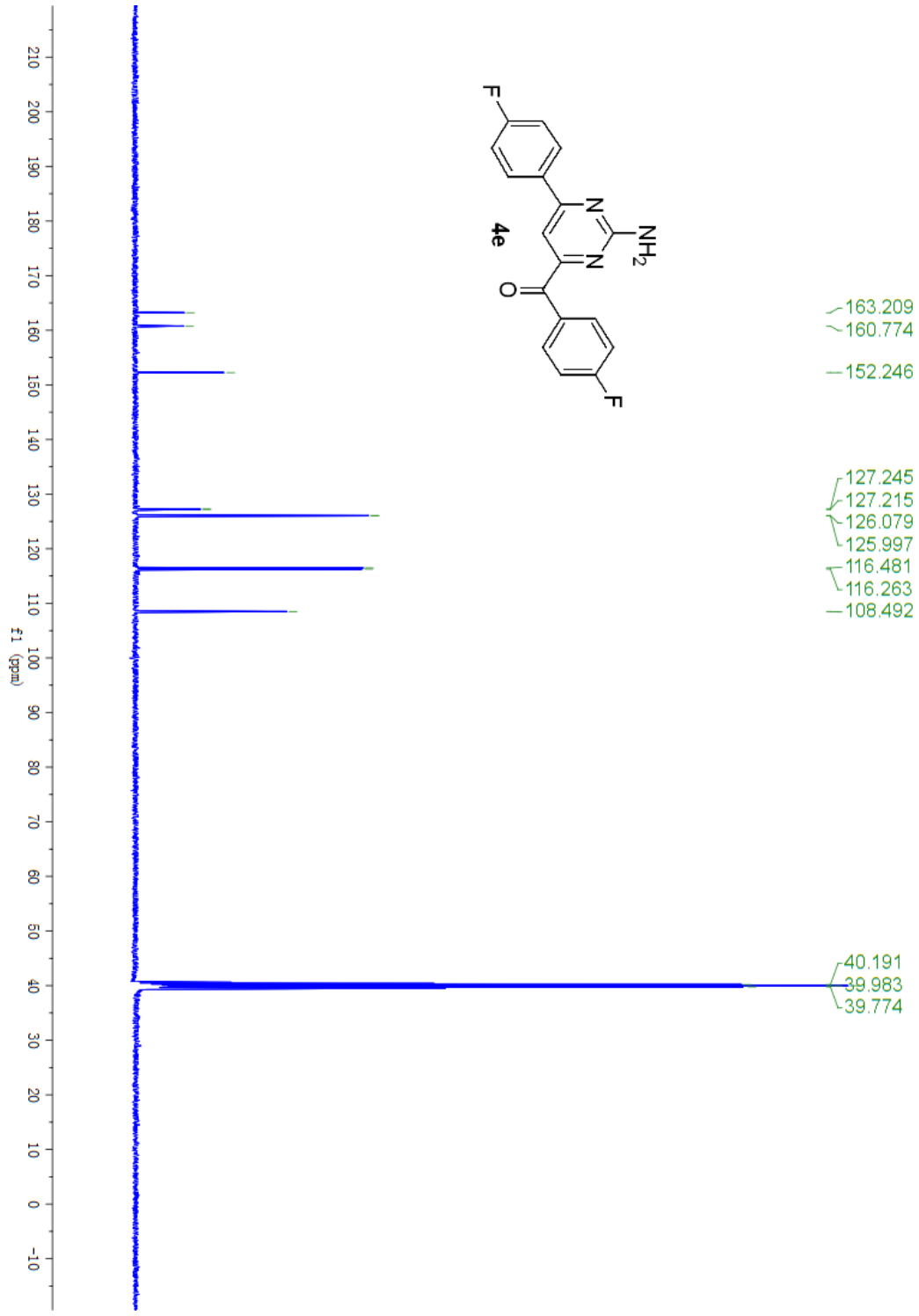

8.095
8.075
8.055
7.404
7.279
7.014
6.993
6.982
6.961
5.857
3.888
3.876
4.19
1.01
4.23
2.00
6.18
MeO
NH2
N
N
O
OMe
4c
f1 (ppm)

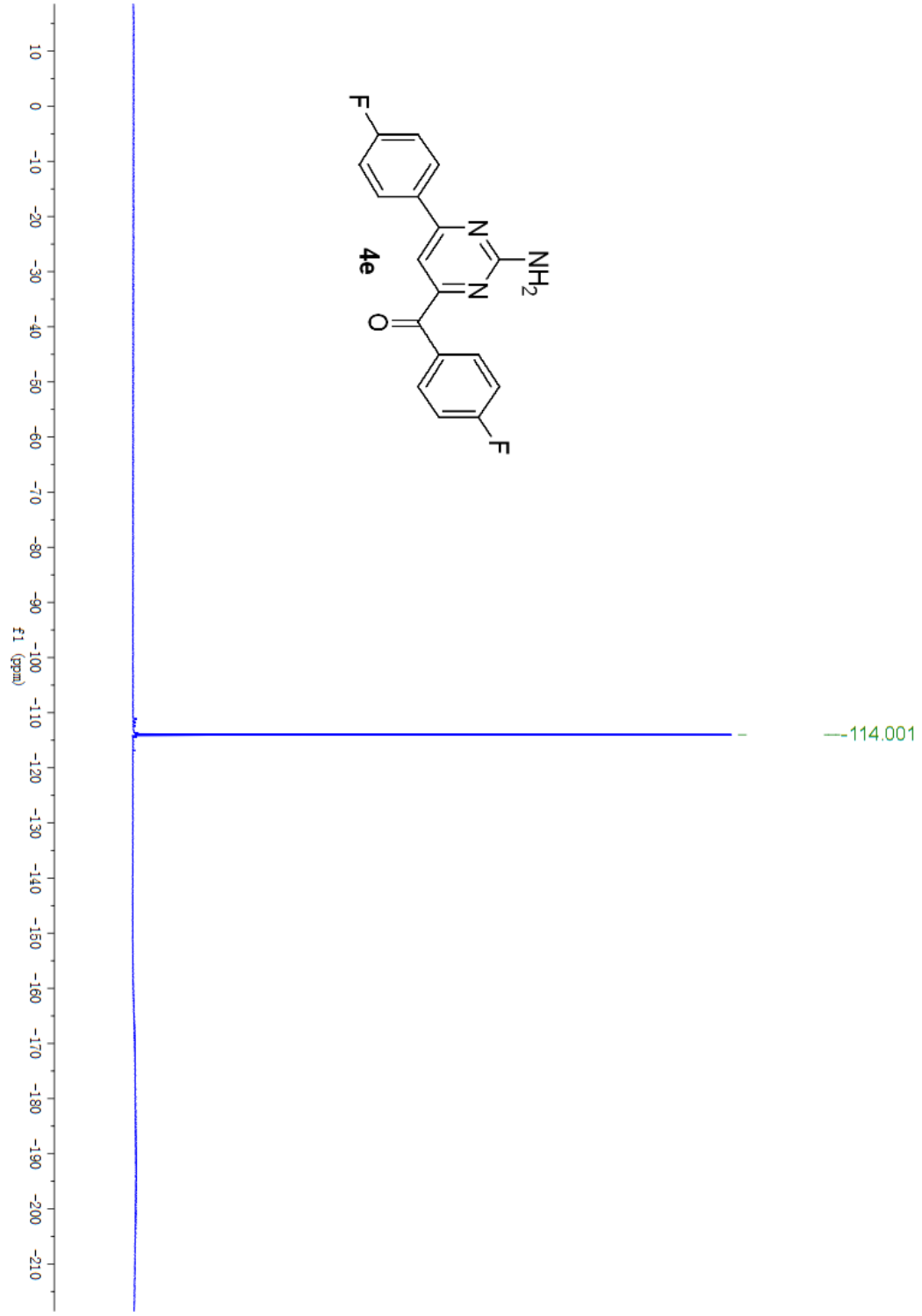

MeO
4c
O
NH2
OMe
191.455
165.609
164.472
164.252
162.507
161.859
133.362
129.083
128.050
127.843
114.386
113.841
105.758
55.618
55.506
f1 (ppm)

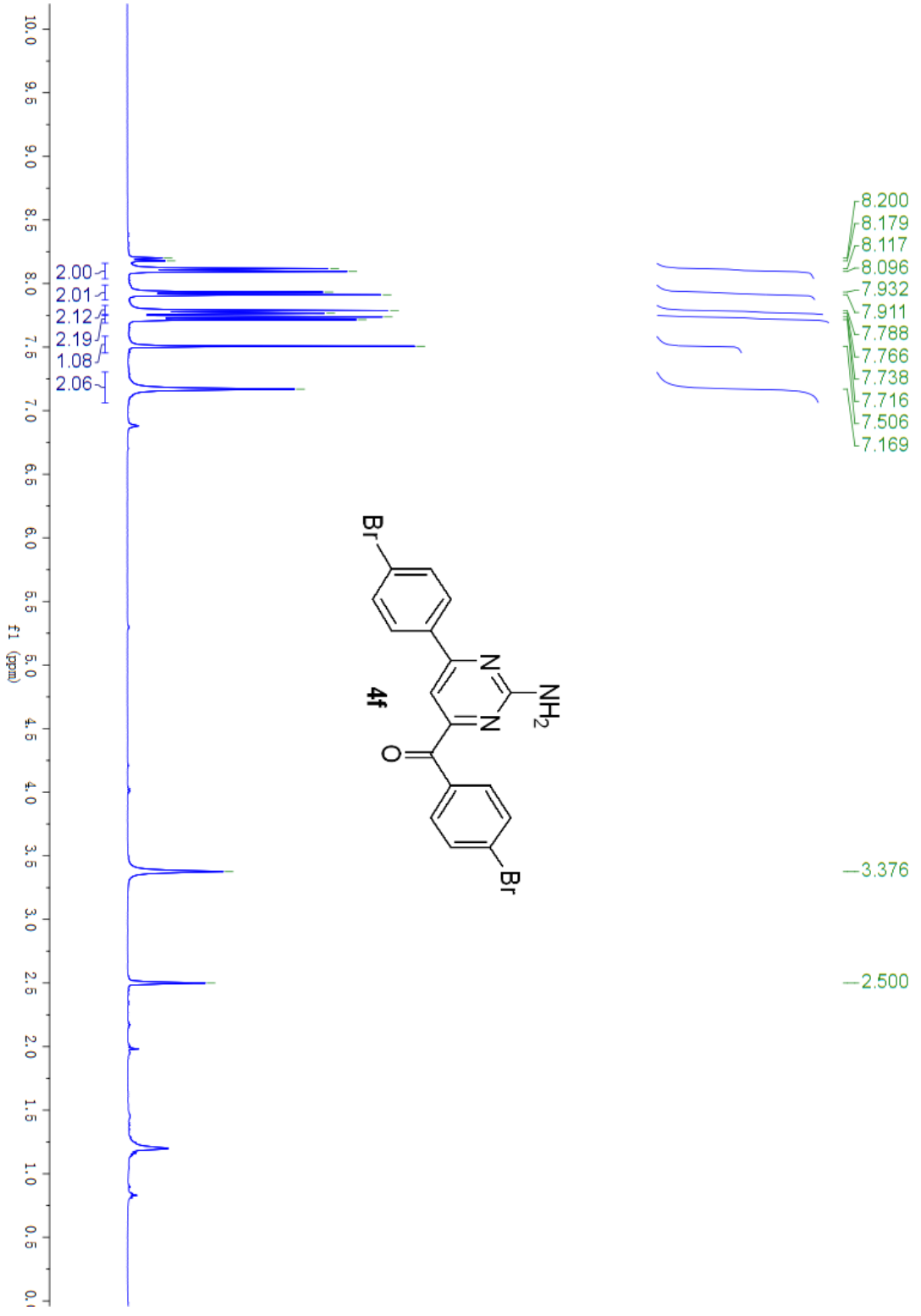

4.06
1.06
4.09
2.00
4.13
4.22
8.10
6.34
7.984
7.964
7.955
7.935
7.424
7.277
7.259
5.729
5.715
2.672
2.655
2.640
2.621
1.629
1.329
1.326
1.318
1.312
1.294
0.903
0.897
0.886
0.880
0.869
0.863
4d
NH2
O
f1 (ppm)

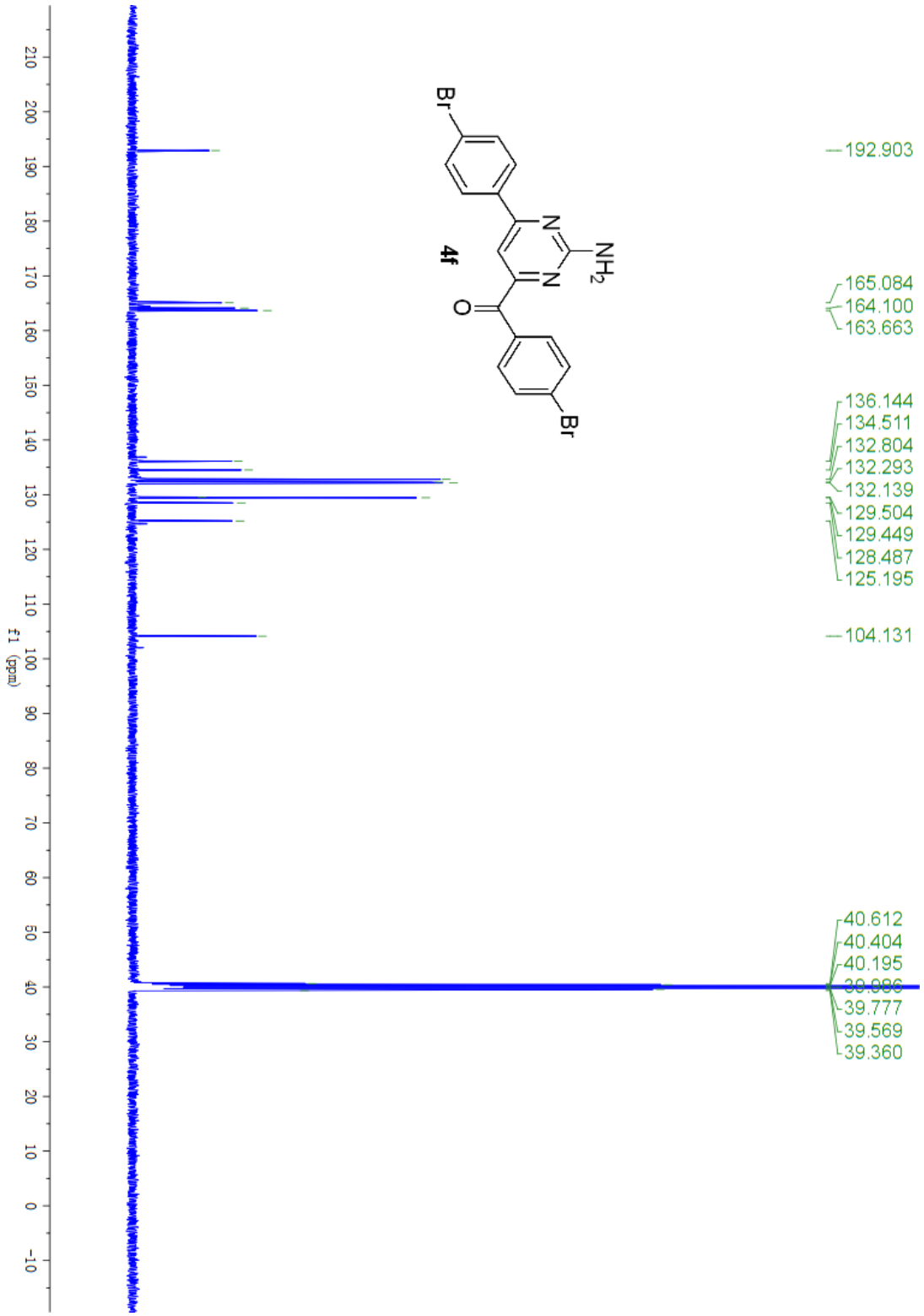

193.201
167.195
163.901
162.968
149.613
146.430
134.303
132.949
131.017
128.936
128.521
127.219
106.197
77.484
77.166
76.848
36.134
35.845
31.491
30.942
30.771
22.560
22.524
14.065
14.037
4d
NH2
O
f1 (ppm)

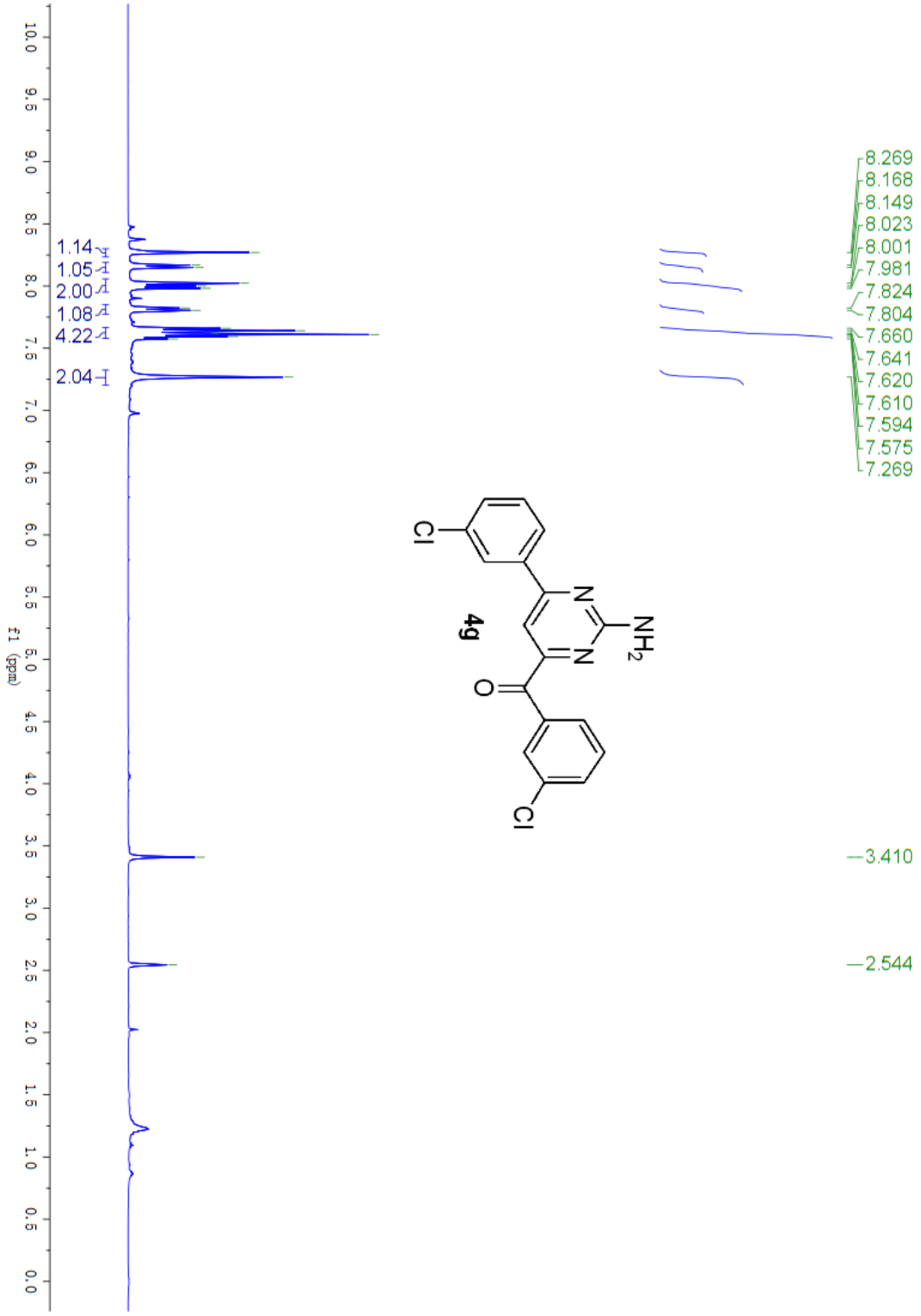

7.918
7.913
7.905
7.896
7.888
7.883
7.354
7.332
7.310
7.092
4.37
5.00
2.21
3.420
2.547
f1 (ppm)
4e
F
N
NH2
O
F

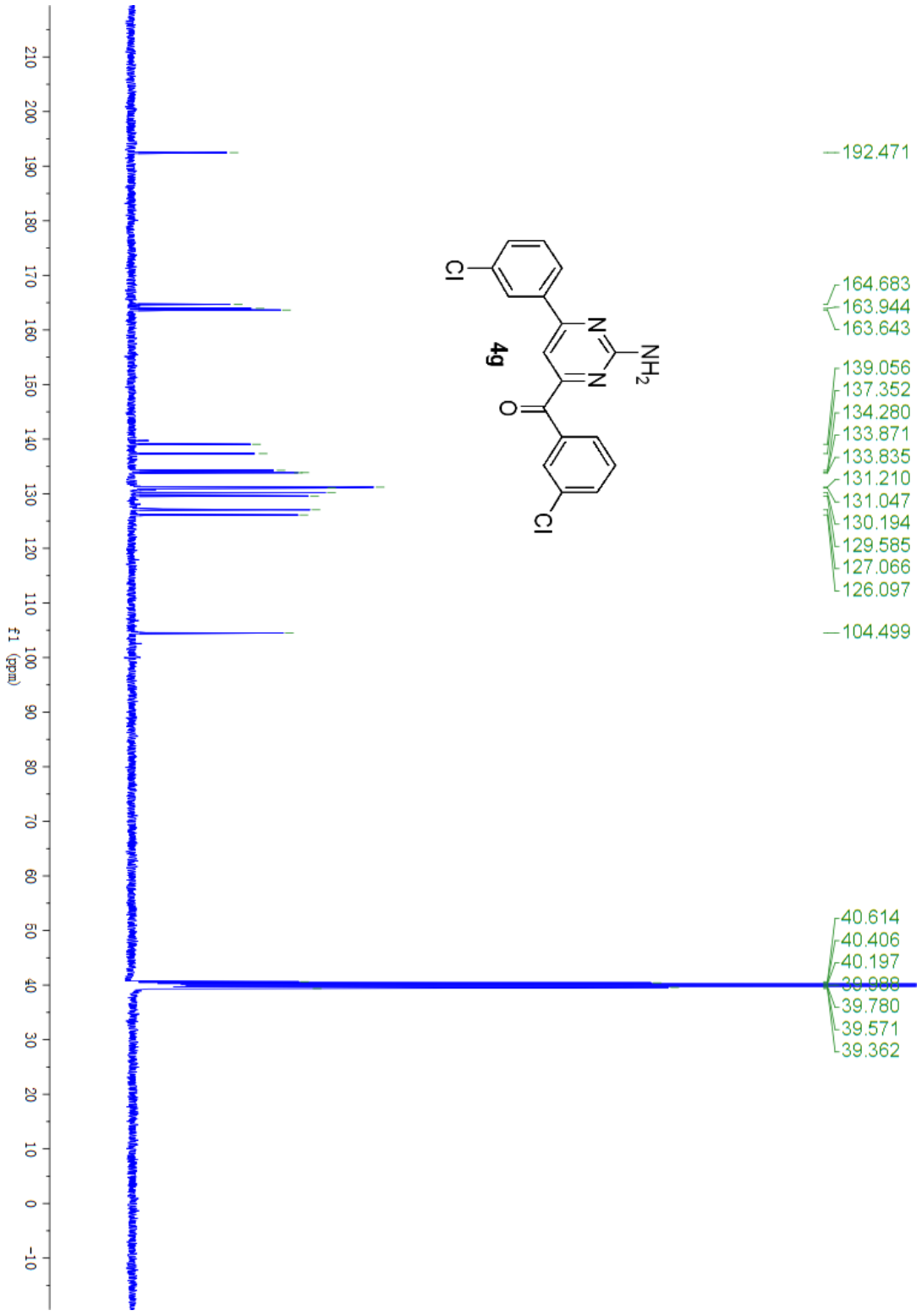

F
N
NH2
N
4e
O
F
163.209
160.774
152.246
127.245
127.215
126.079
125.997
116.481
116.263
108.492
40.191
39.983
39.774
f1 (ppm)

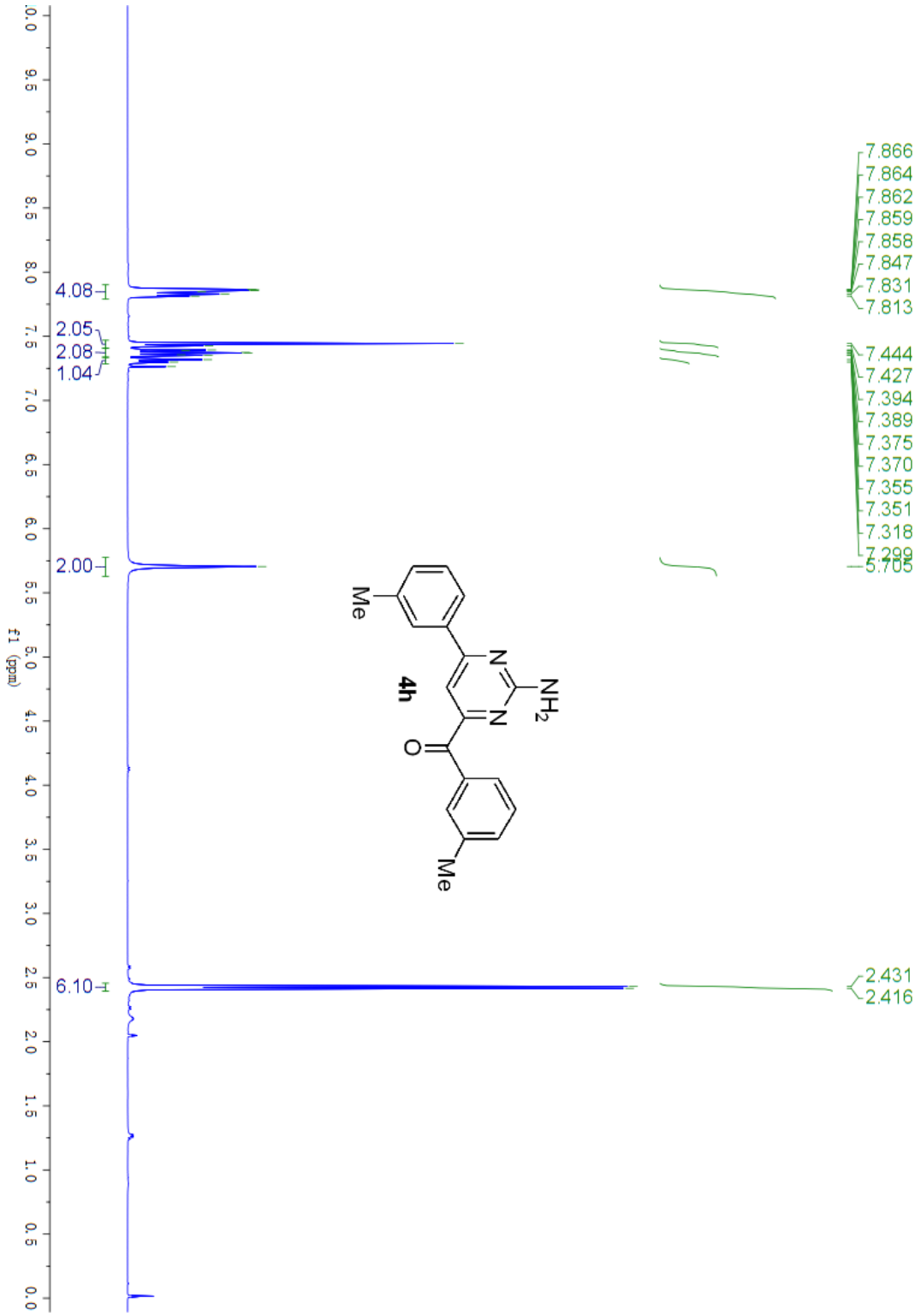

F
N
N
NH2
O
F
4e
-114.001
f1 (ppm)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

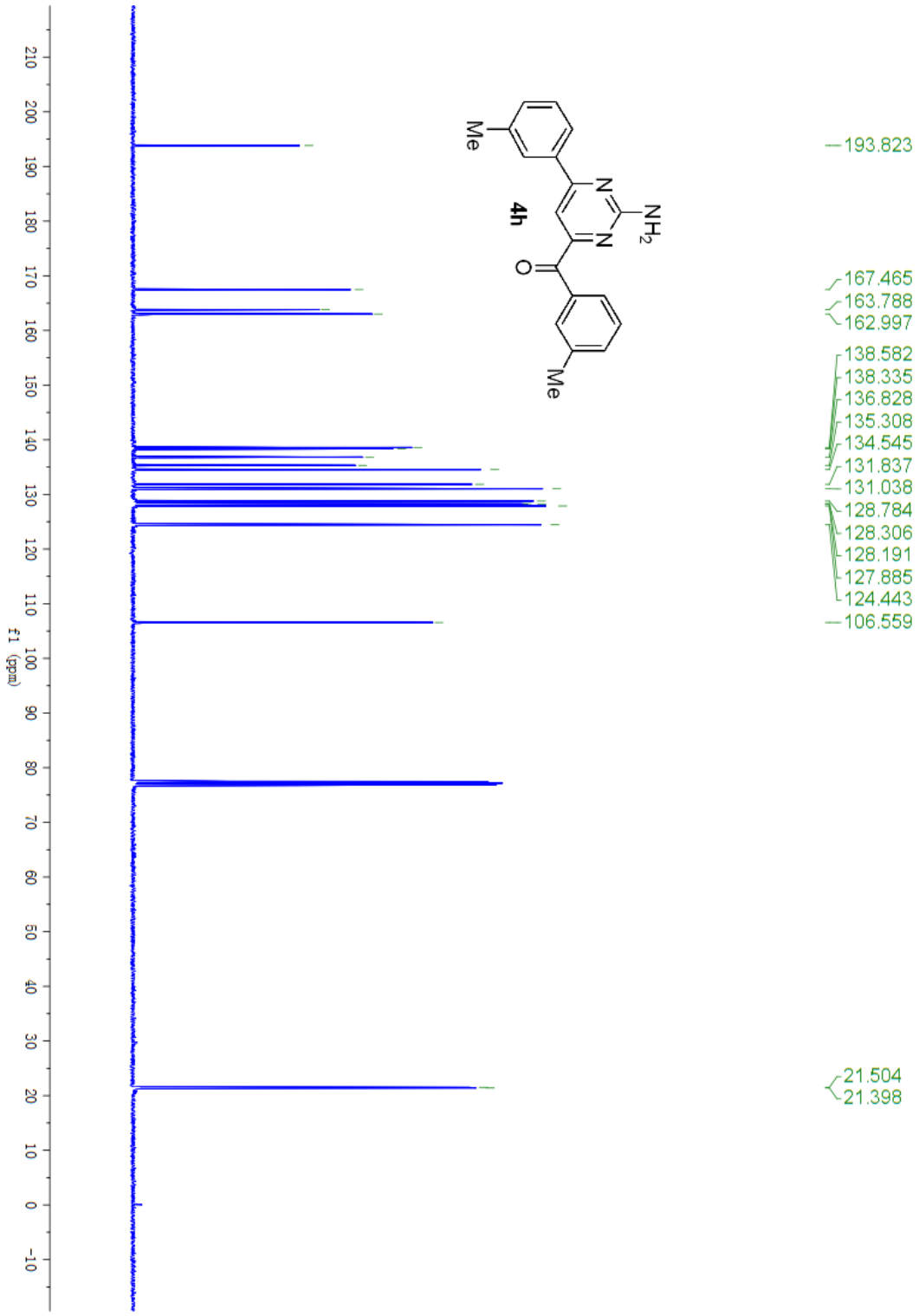

8.200
8.179
8.117
8.096
7.932
7.911
7.788
7.766
7.738
7.716
7.506
7.169
3.376
2.500
2.00
2.01
2.12
2.19
1.08
2.06
f1 (ppm)
Br
N
N
NH2
O
Br
4f

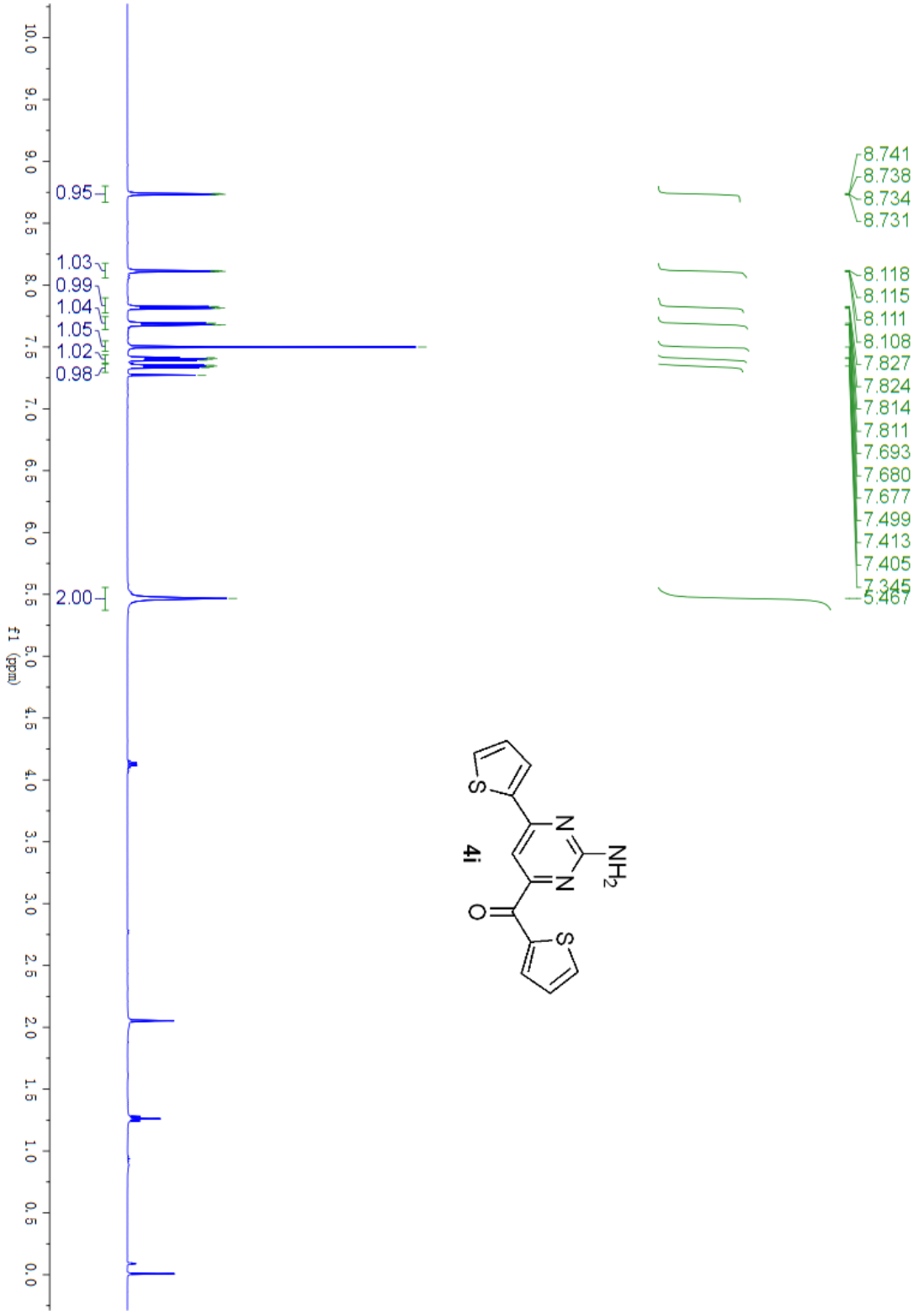

Br
N
NH2
N
4f
O
Br
192.903
165.084
164.100
163.663
136.144
134.511
132.804
132.293
132.139
129.504
129.449
128.487
125.195
104.131
40.612
40.404
40.195
39.777
39.569
39.360
f1 (ppm)

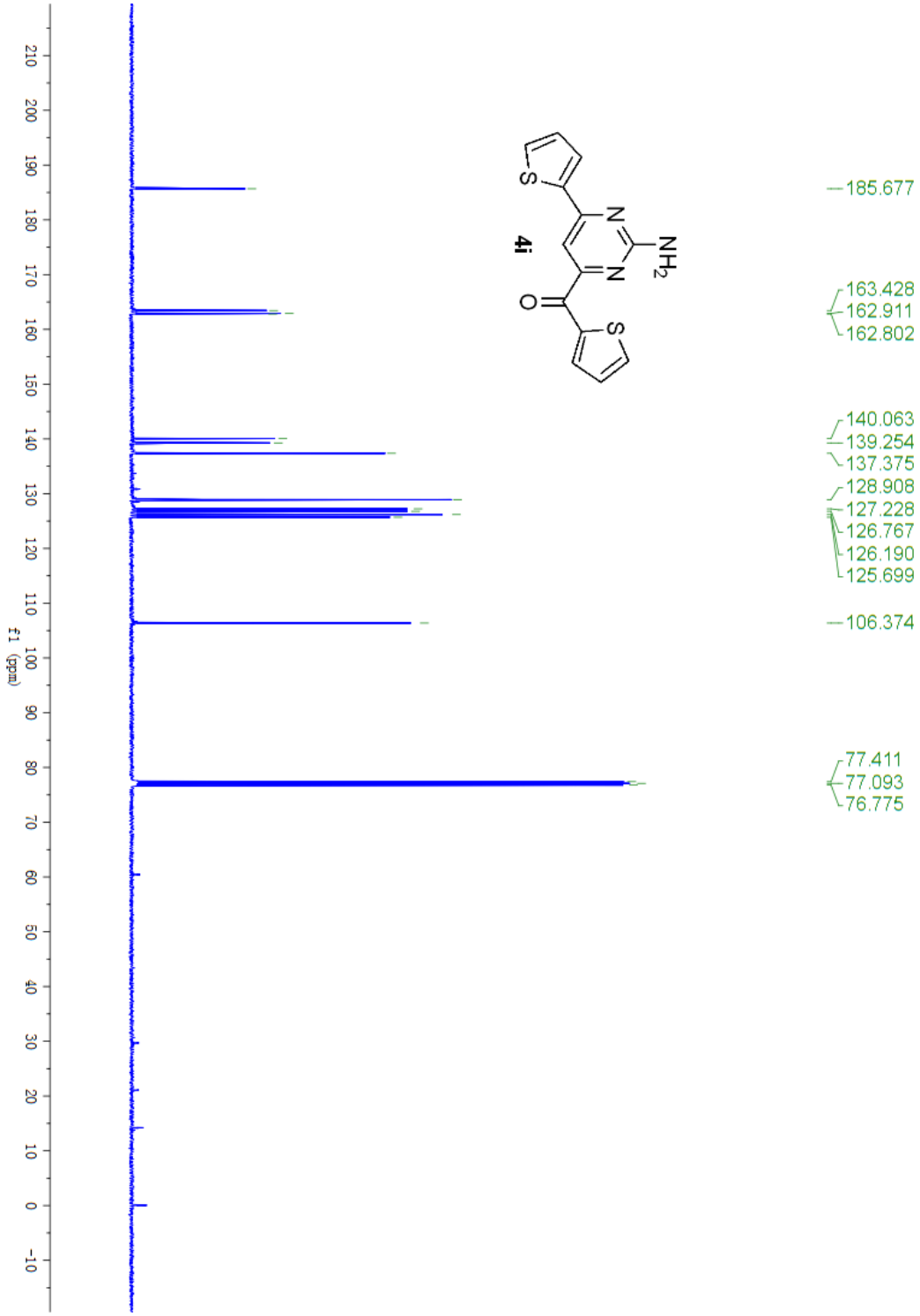

8.269
8.168
8.149
8.023
8.001
7.981
7.824
7.804
7.660
7.641
7.620
7.610
7.594
7.575
7.269
1.14
1.05
2.00
1.08
4.22
2.04
3.410
2.544
4g
Cl
N
N
NH2
O
Cl
f1 (ppm)

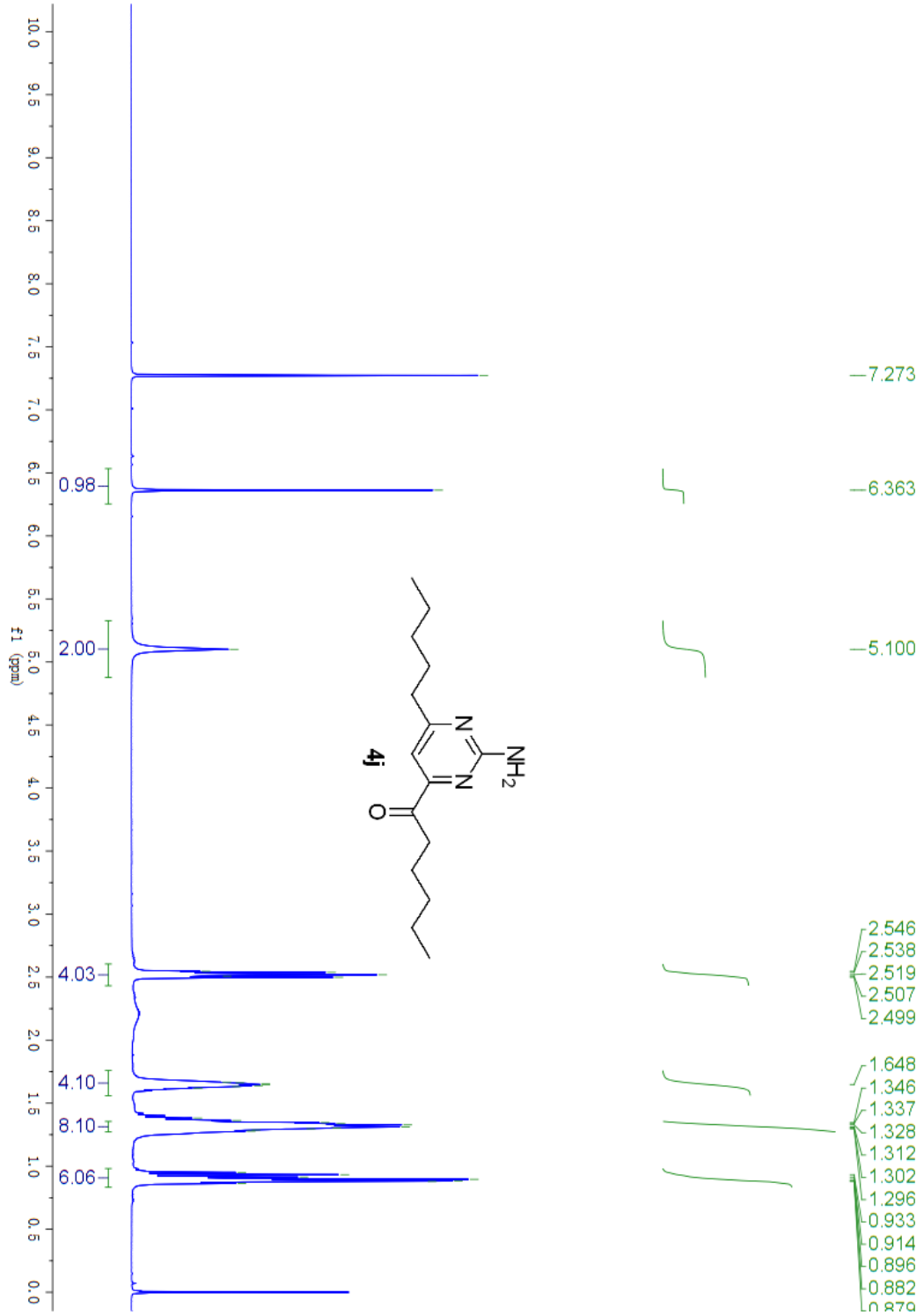

192.471
164.683
163.944
163.643
139.056
137.352
134.280
133.871
133.835
131.210
131.047
130.194
129.585
127.066
126.097
104.499
40.614
40.406
40.197
39.988
39.780
39.571
39.362
Cl
N
N
NH2
4g
O
Cl
f1 (ppm)

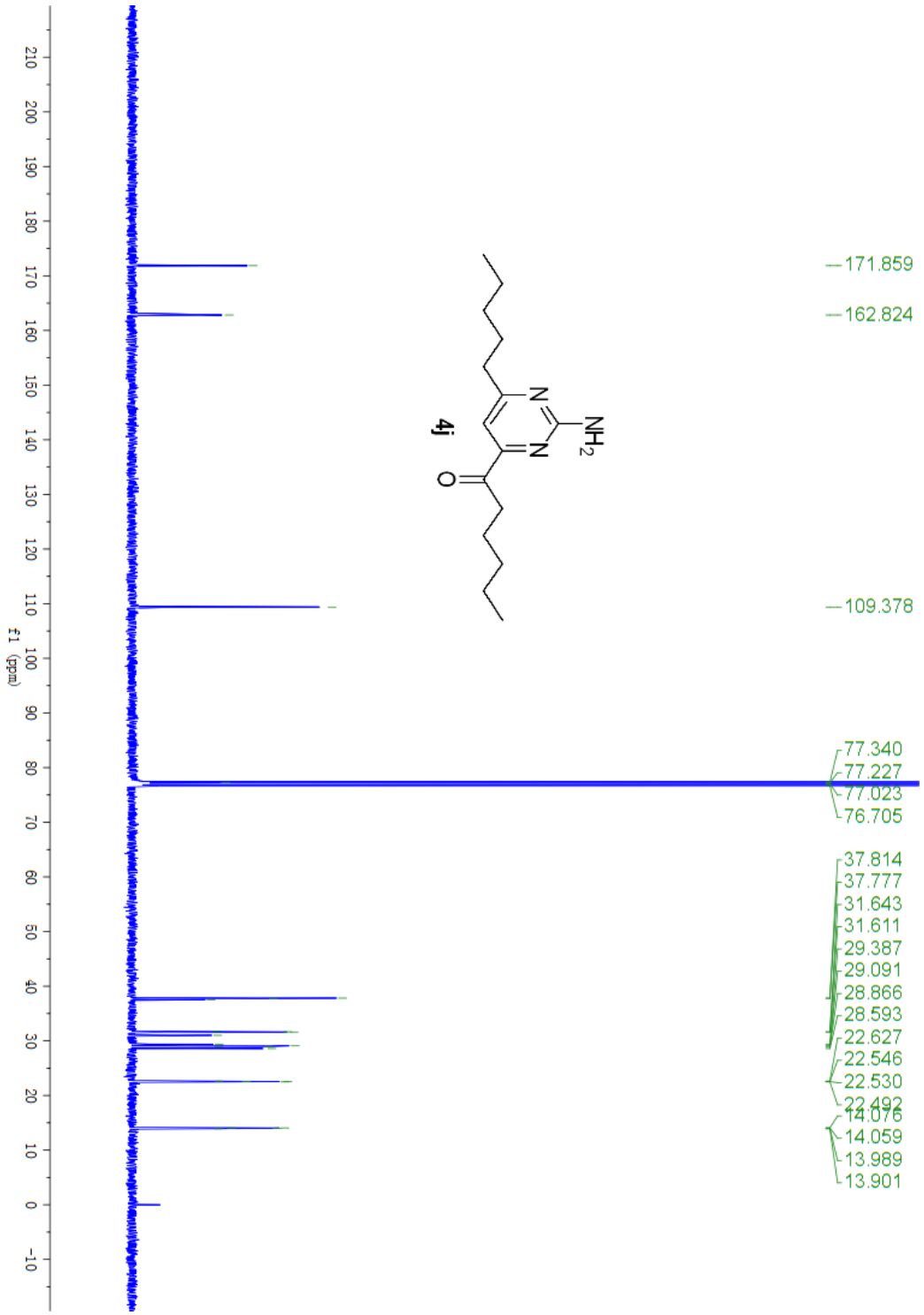

7.866
7.864
7.862
7.859
7.858
7.847
7.831
7.813
7.444
7.427
7.394
7.389
7.375
7.370
7.355
7.351
7.318
7.299
5.705
2.431
2.416
4.08
2.05
2.08
1.04
2.00
6.10
f1 (ppm)
Me
N
NH2
N
O
Me
4h

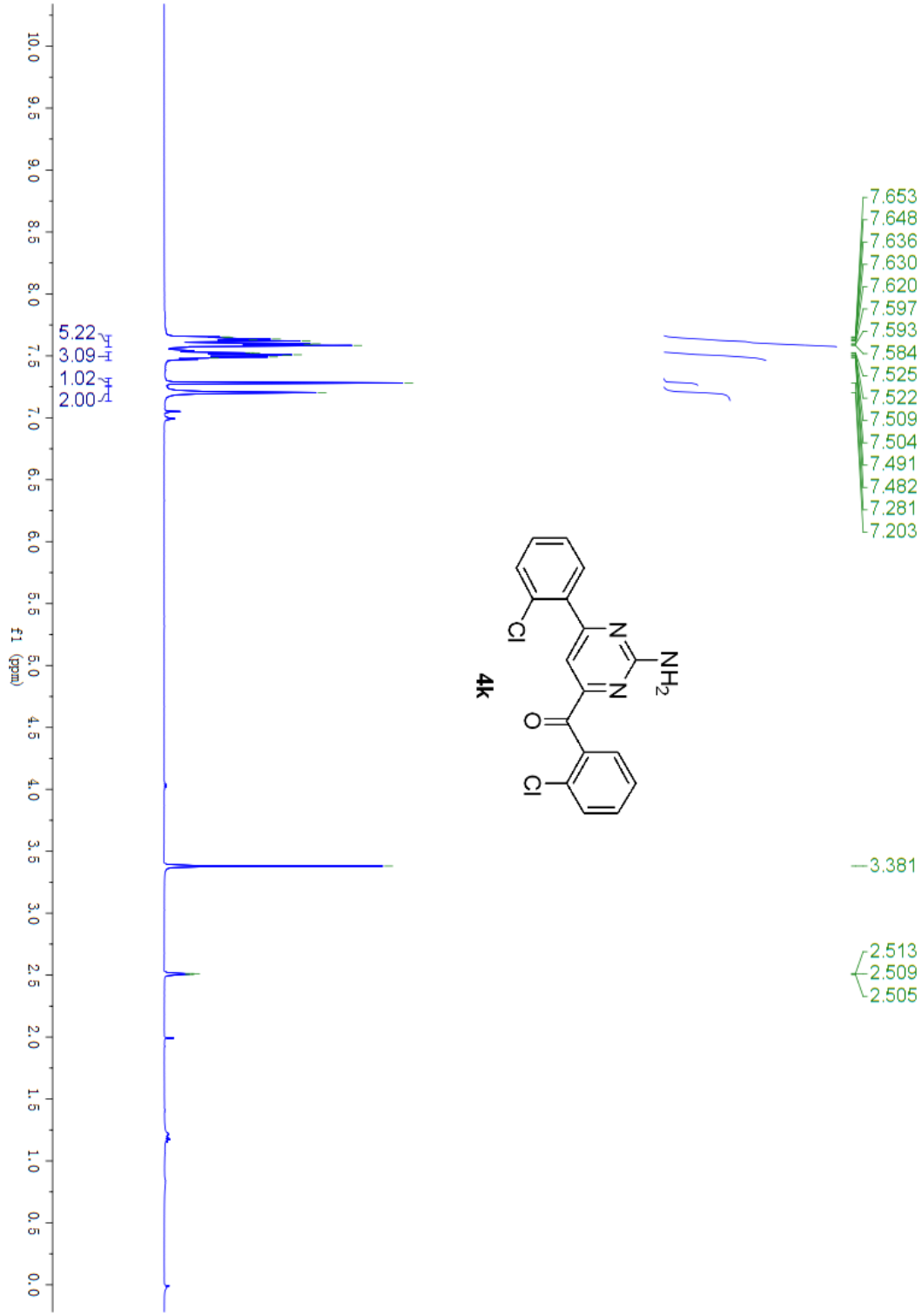

Me
4h
NH2
O
Me
193.823
167.465
163.788
162.997
138.582
138.335
136.828
135.308
134.545
131.837
131.038
128.784
128.306
128.191
127.885
124.443
106.559
21.504
21.398
f1 (ppm)

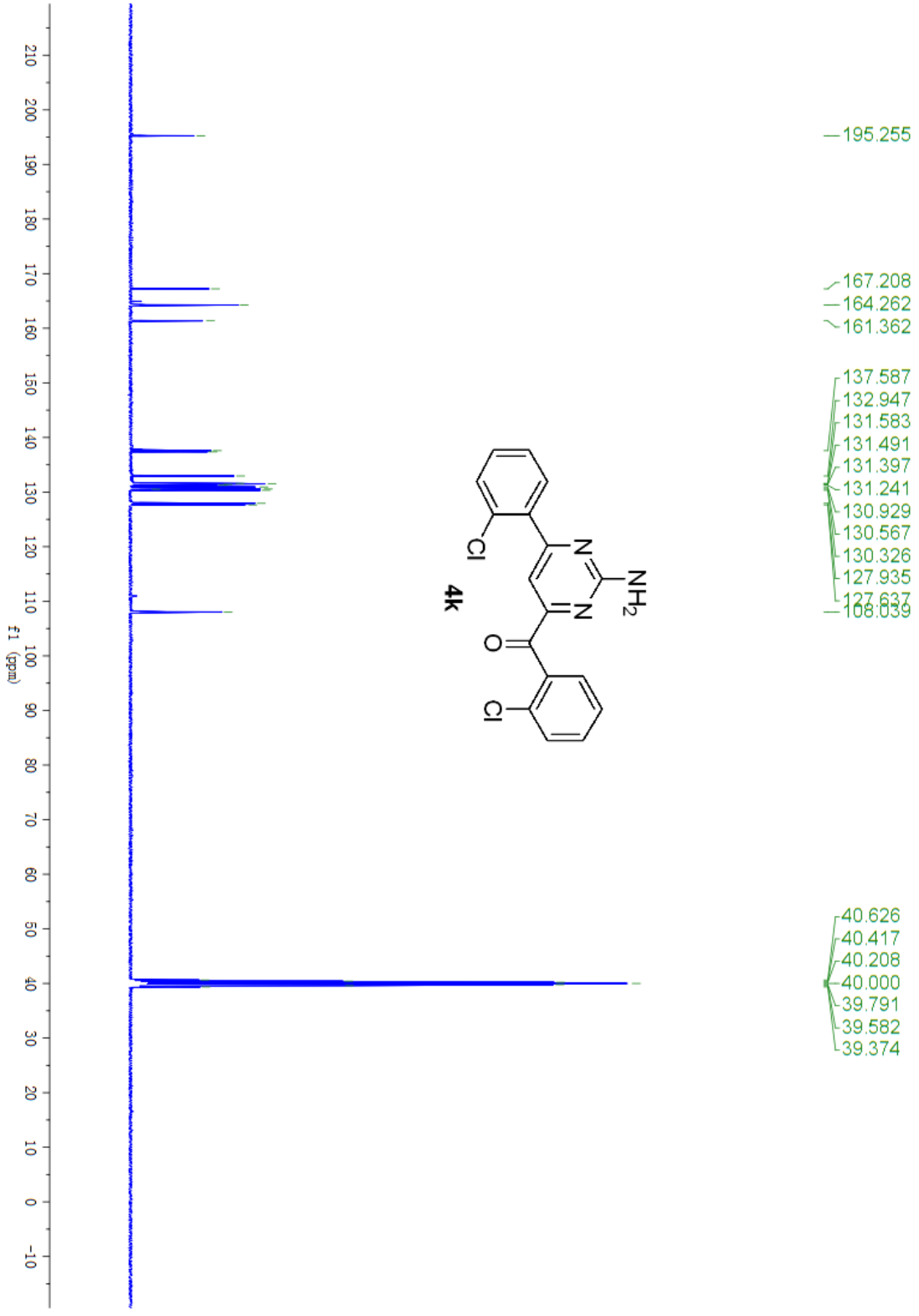

8.741
8.738
8.734
8.731
8.118
8.115
8.111
8.108
7.827
7.824
7.814
7.811
7.693
7.680
7.677
7.499
7.413
7.405
7.345
5.467
0.95
1.03
0.99
1.04
1.05
1.02
0.98
2.00
f1 (ppm)
4i
NH2
N
N
S
S
O

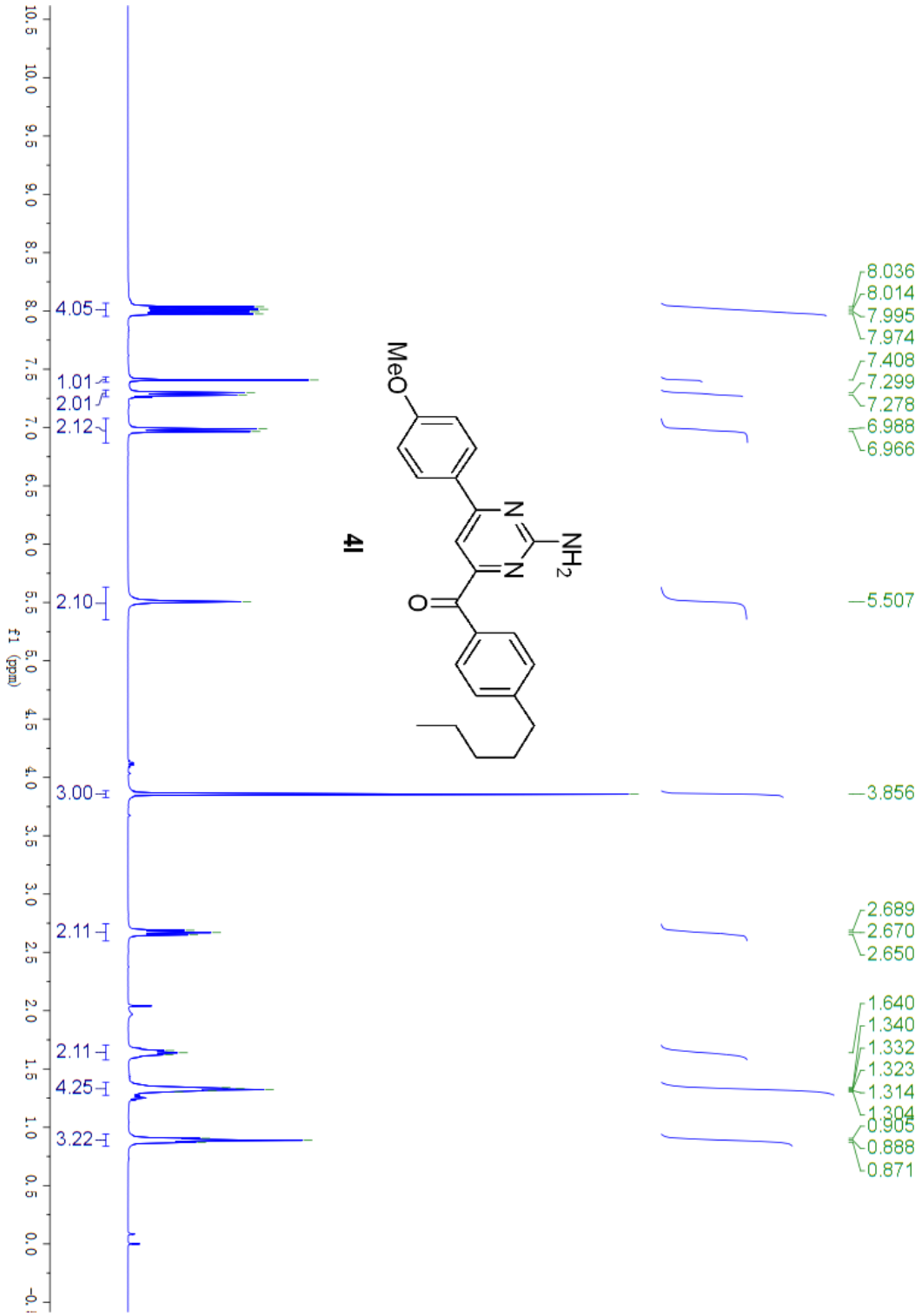

4i
185.677
163.428
162.911
162.802
140.063
139.254
137.375
128.908
127.228
126.767
126.190
125.699
106.374
77.411
77.093
76.775
f1 (ppm)

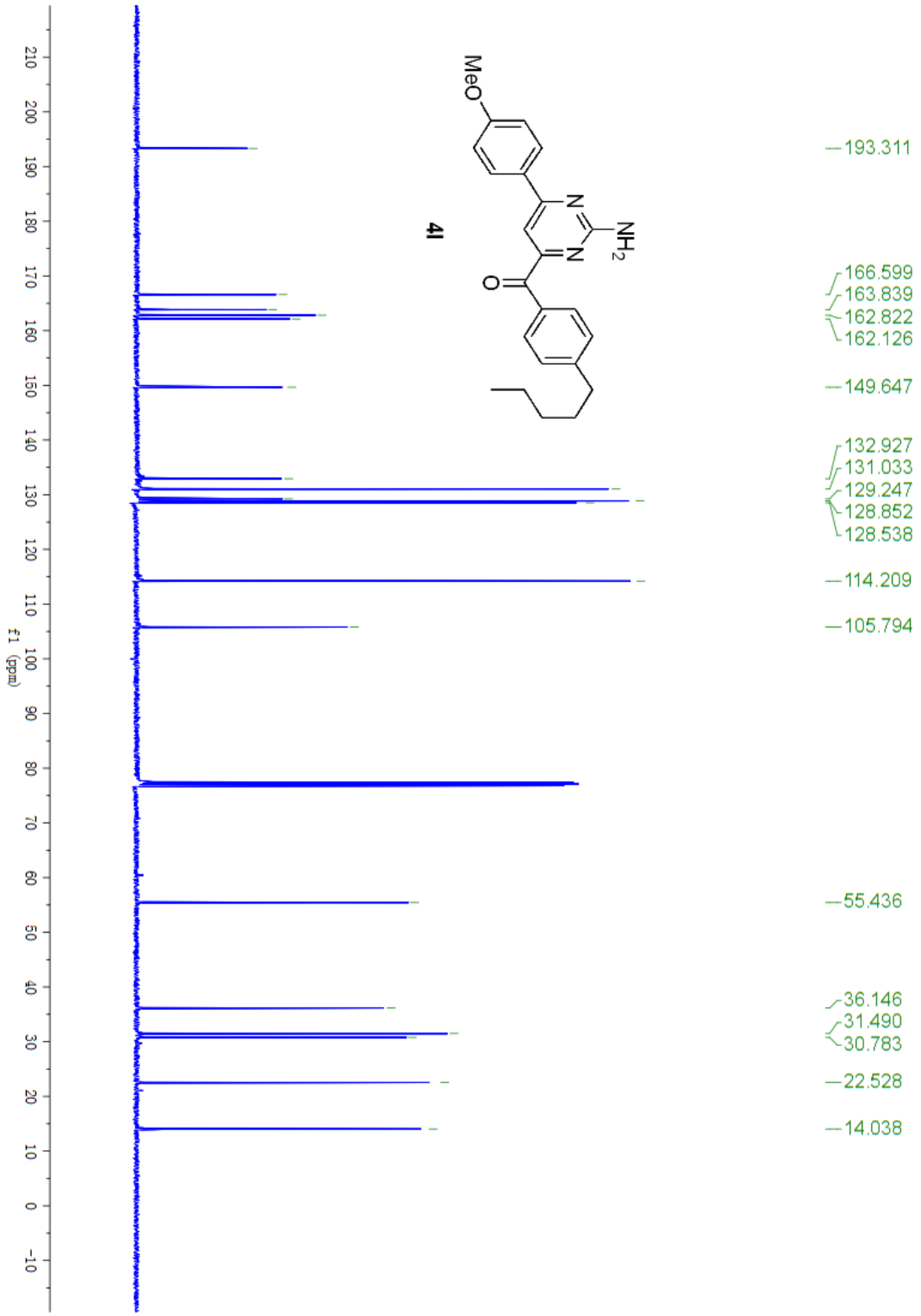

f1 (ppm)
0.98
2.00
4.03
4.10
8.10
6.06
4j
NH2
7.273
6.363
5.100
2.546
2.538
2.519
2.507
2.499
1.648
1.346
1.337
1.328
1.312
1.302
1.296
0.933
0.914
0.896
0.882

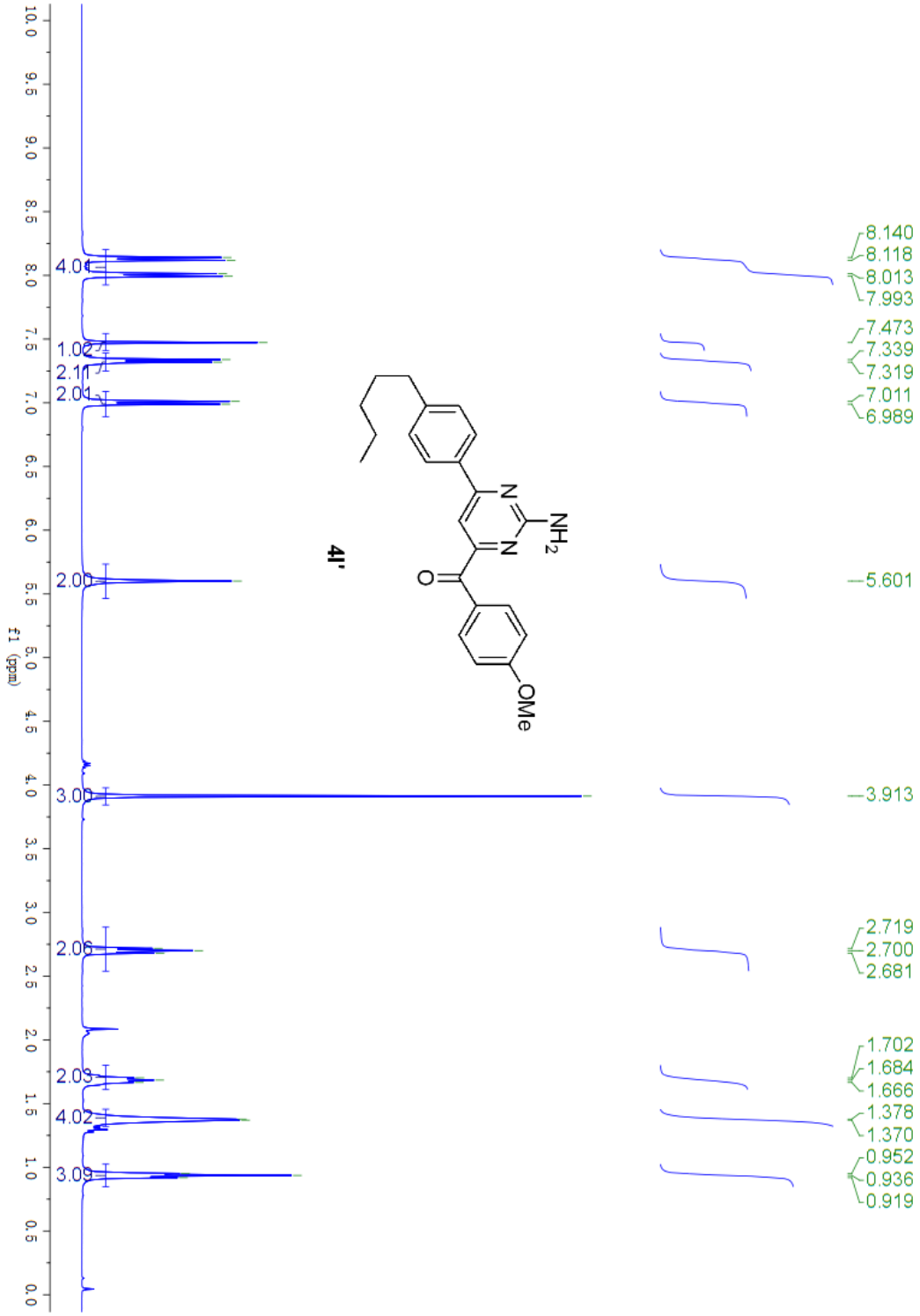

4j
O
NH2
N
N
171.859
162.824
109.378
77.340
77.227
77.023
76.705
37.814
37.777
31.643
31.611
29.387
29.091
28.866
28.593
22.627
22.546
22.530
22.492
14.076
14.059
13.989
13.901
f1 (ppm)

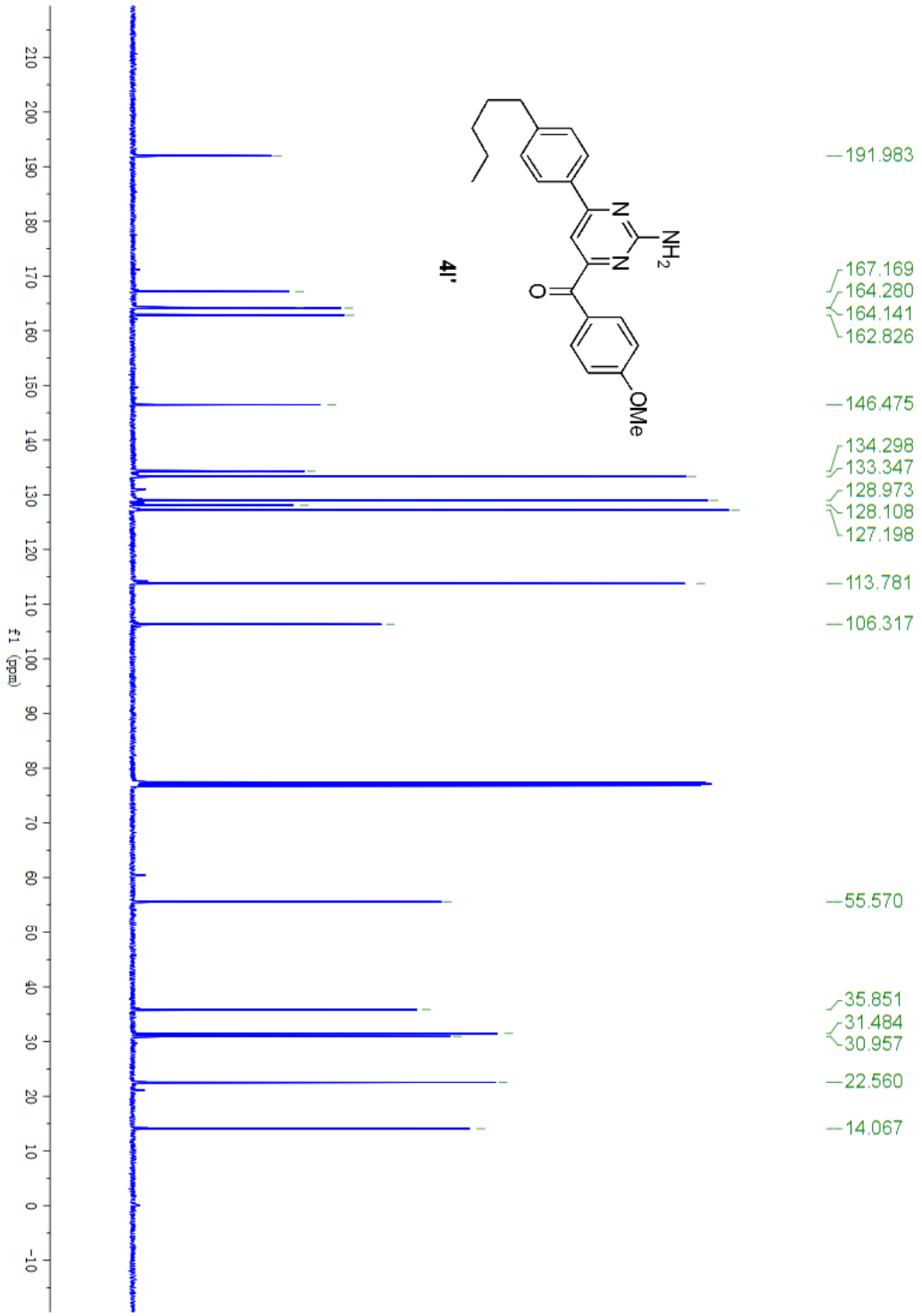

7.653
7.648
7.636
7.630
7.620
7.597
7.593
7.584
7.525
7.522
7.509
7.504
7.491
7.482
7.281
7.203
3.381
2.513
2.509
2.505
5.22
3.09
1.02
2.00
f1 (ppm)
4k
Cl
N
NH2
O
Cl


195.255
167.208
164.262
161.362
137.587
132.947
131.583
131.491
131.397
131.241
130.929
130.567
130.326
127.935
127.637
108.039
40.626
40.417
40.208
40.000
39.791
39.582
39.374
Cl
N
NH2
N
O
Cl
4k
f1 (ppm)


4l
MeO
NH2
O
f1 (ppm)
4.05
1.01
2.01
2.12
2.10
3.00
2.11
2.11
4.25
3.22
8.036
8.014
7.995
7.974
7.408
7.299
7.278
6.988
6.966
5.507
3.856
2.689
2.670
2.650
1.640
1.340
1.332
1.323
1.314
1.304
0.905
0.888
0.871


MeO
N
N
NH2
O
4l
193.311
166.599
163.839
162.822
162.126
149.647
132.927
131.033
129.247
128.852
128.538
114.209
105.794
55.436
36.146
31.490
30.783
22.528
14.038
f1 (ppm)


4.00
1.06
2.11
2.04
2.00
3.00
2.06
2.03
4.02
3.09
8.140
8.118
8.013
7.993
7.473
7.339
7.319
7.011
6.989
5.601
3.913
2.719
2.700
2.681
1.702
1.684
1.666
1.378
1.370
0.952
0.936
0.919
4i.
NH2
N
N
O
OMe
f1 (ppm)


4l'
NH2
N
N
O
OMe
191.983
167.169
164.280
164.141
162.826
146.475
134.298
133.347
128.973
128.108
127.198
113.781
106.317
55.570
35.851
31.484
30.957
22.560
14.067
f1 (ppm)