

## SUPPORTING INFORMATION

### **A Green Synthesis of N-heterocyclic Pyrimido [4,5-b] Quinolines and Pyrido [2,3-d] Pyrimidines Via Mechanochemical Approach**

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## Experimental section:

### A. General information:

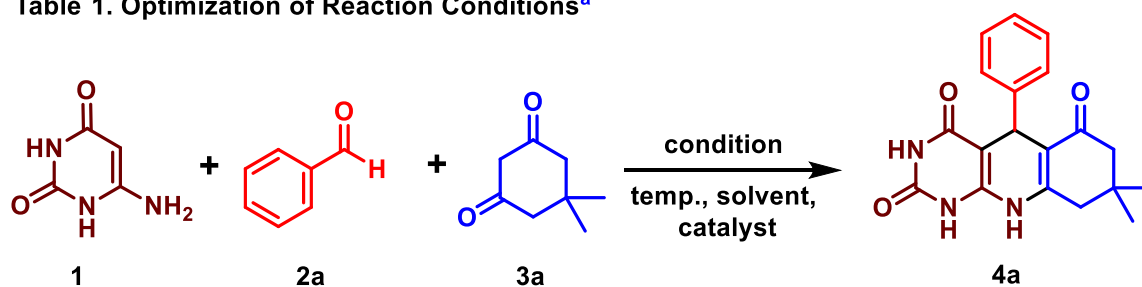
All the starting chemicals were bought from Sigma-Aldrich and E. Merck chemical co, and directly used as a reactant without purification. A planetary Ball-milling apparatus Retsch PM100 was employed using 10 balls (stainless steel, size 10 mm). The reaction was performed in a 50 mL grinding jar. The progress of the reaction was monitored using ethyl acetate: hexane as an eluent by thin-layer chromatography for visualization using UV light. The compound was determined by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra recorded through Bruker 500 MHz spectrometer in  $\text{DMSO-}d_6$  and the chemical shift was indicated in  $\delta$  ppm, using TMS as the internal reference. Perkin-Elmer FT-IR spectrometer was used to record Infra-Red (IR) spectra. Perkin Elmer Micro analyzer was used for Elemental analysis (C, H, and N).

### B. General Procedure for the Synthesis of Compounds 4 and 5.

A reaction chamber was set up using a 50 mL grinding beaker and milling balls (10×10 mm). A mixture of aromatic aldehydes, 6-amino uracil, and 1, 3-diketo compounds were milled for 30-35 minutes at 650 rpm at room temperature for each reaction. The obtained solid product was filtered off through a Büchner funnel following the reaction's completion (monitored by thin-layer chromatography) and thoroughly washed with a solution of ethanol and hexane (1:4).

## Optimization of reaction condition

Table 1. Optimization of Reaction Conditions<sup>a</sup>



entry	catalyst (mol%)	solvent	condition	temperature (°C)	time (h)	yield <sup>b</sup> (%)
1	Sulfamic acid (10 mol%)	H <sub>2</sub> O	stirring	rt	5	58
2	p-TSA (10 mol%)	H <sub>2</sub> O	stirring	rt	6	31
3	L-proline (10 mol%)	H <sub>2</sub> O	stirring	rt	12	21
4	CF <sub>3</sub> COOH	H <sub>2</sub> O	stirring	rt	12	18
5	DBU (10 mol%)	H <sub>2</sub> O	stirring	rt	12	25
6	Sulfamic acid (10 mol%)	ethanol	stirring	rt	6	55
7	Sulfamic acid (10 mol%)	MeCN	stirring	rt	12	none
8	Sulfamic acid (10 mol%)	DCM	stirring	rt	12	none
9	Sulfamic acid (10 mol%)	THF	stirring	rt	12	none
10	Sulfamic acid (10 mol%)	H <sub>2</sub> O	stirring	reflux	4	65
11	Sulfamic acid (10 mol%)	EtOH	stirring	reflux	5	61
12	Sulfamic acid (10 mol%)	Neat	stirring	120	8	52
13	no catalyst	Neat	grinding <sup>c</sup>	rt	1	71
14	no catalyst	Neat	ball milling <sup>d</sup>	rt	2	82
15	no catalyst	Neat	ball milling <sup>e</sup>	rt	1.5	88
16	no catalyst	Neat	ball milling <sup>f</sup>	rt	1	92
17	no catalyst	Neat	ball milling <sup>g</sup>	rt	0.5	95
18	no catalyst	Neat	ball milling <sup>h</sup>	rt	0.5	88

<sup>a</sup>Experimental condition : 6 amino uracil **1a** (1 mmol), benzaldehyde **2a** (1 mmol) and dimedone **3a** (1 mmol) were subjected to ball milling for 30 min. <sup>b</sup>Isolated yields. <sup>c</sup>grinding for 1 h <sup>d</sup>planetary ball-milling apparatus Shivam Instruments Pvt. Ltd., India PM100 was employed using 10 balls (stainless steel, size 10 mm), 400 rpm, 2 h. <sup>e</sup>ball milling at 600 rpm, 90 min. <sup>f</sup>ball milling at 800 rpm, 60min. <sup>g</sup>ball milling at 1000 rpm, 30 min. <sup>h</sup>The reaction was carried out on the 10 mmol scale.

**Table 2. Effect of number of milling balls on the yield of the product 4a.**

Entry	Number of milling balls	Yield (%)
1	2	0
2	4	trace
3	6	24
4	8	38
5	10	95
6	12	95
7	14	95

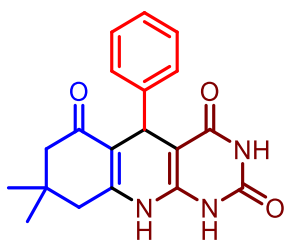
**Table 3. Effect of Milling Ball material and ball mass on the product 4a**

milling ball	ball material	ball mass (g) <sup>a</sup>
BR	brass	59
CU	copper	59
SS1	stainless steel	59
SS2	stainless steel	107
SS3	stainless steel	92

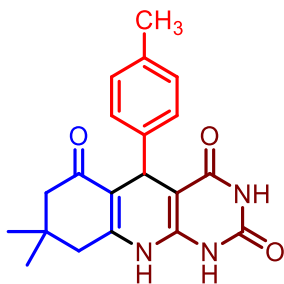
<sup>a</sup>All balls have the same diameter (10 mm) and are empty. They are filled with different solids (sand) to change their mass

## **Spectroscopic Data for Products**

**8,8-dimethyl-5-phenyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4a)** : White solid (95%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3401, 3251, 3191, 2931, 1651. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.73 (s, 1H), 10.22 (s, 1H), 8.79 (s, 1H), 7.19 (d, *J* = 4.3 Hz, 4H), 7.12 – 7.05 (m, 1H), 4.75 (s, 1H), 2.46 (d, *J* = 12.2 Hz, 2H), 2.21 (d, *J* = 16.1 Hz, 1H), 2.02 (d, *J* = 16.1 Hz, 1H), 1.03 (s, 3H), 0.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.71, 165.12, 163.12, 150.30, 149.88, 146.62, 128.19, 128.01, 126.37, 111.57, 89.70, 50.61, 33.47, 32.60, 29.42, 26.92. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub> 338.1504; found: 338.1514.

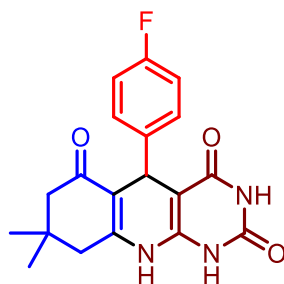


**8,8-dimethyl-5-(p-tolyl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4b)** : Off-white solid (94%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3402, 3252, 3192, 2932, 1653. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.73 (s, 1H), 10.22 (s, 1H), 8.79 (s, 1H), 7.95 (d, 2H), 7.53 (d, 2H), 2.47 (d, *J* = 12.2 Hz, 2H), 2.22 (d, *J* = 16.1 Hz, 1H), 2.03 (d, *J* = 16.1 Hz, 1H), 1.04 (s, 3H), 0.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.66, 170.82, 166.14, 163.12, 149.60, 133.67, 130.41, 129.52, 129.17, 115.33, 90.28, 61.15, 44.37, 32.56, 29.45, 26.92, 20.99, 14.67. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> calculated for C<sub>20</sub>H<sub>23</sub>N<sub>3</sub>O<sub>3</sub> 352.1661; found: 352.1664.

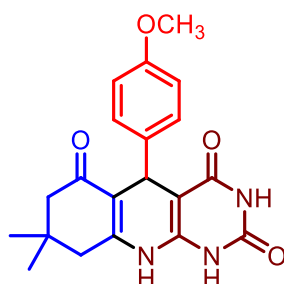


**5-(4-fluorophenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4c)** : Brown solid (96%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3402, 3252, 3192, 2932, 1652. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.75 (s, 1H), 10.24 (s, 1H), 8.79 (s, 1H), 7.22 – 7.17 (m, 2H), 7.01 (t, *J* = 8.9 Hz, 2H), 4.74 (s, 1H), 2.48 – 2.39 (m, 2H), 2.09 (s, 2H), 1.06 (s, 6H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.81, 163.13, 161.92, 159.97, 150.24, 149.73,

144.22, 129.75, 129.68, 114.89, 114.72, 111.60, 89.93, 56.49, 50.47, 32.95, 32.59, 29.29, 26.93. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{19}H_{19}FN_3O_3$  356.1410; found: 356.1418.

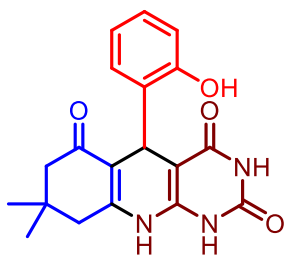


**5-(4-methoxyphenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4d)** : Yellow solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3403, 3253, 3193, 2933, 1653.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.71 (s, 1H), 10.18 (s, 1H), 8.71 (s, 1H), 7.09 (d,  $J = 8.6$  Hz, 2H), 6.74 (d,  $J = 11.6$  Hz, 2H), 4.69 (s, 1H), 3.34 (s, 3H), 2.44 (d,  $J = 14.3$  Hz, 2H), 2.13 (dd,  $J = 68.4, 22.8$  Hz, 2H), 1.02 (s, 3H), 0.89 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  194.79, 163.24, 157.86, 150.29, 149.30, 144.01, 139.25, 129.14, 113.56, 111.92, 90.36, 56.20, 55.37, 50.63, 32.59, 32.55, 29.53, 26.96. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{20}H_{22}N_3O_4$  368.1610; found: 368.1618.

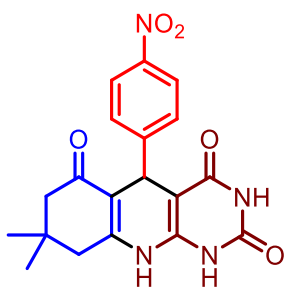


**5-(2-hydroxyphenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4e)** : Light Brown solid (92%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3404, 3254, 3194, 2934, 1654.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.71 (s, 1H), 10.18 (s, 1H), 9.80 (s, 1H), 8.71 (s, 1H), 7.17 (t,  $J = 5.8$  Hz, 1H), 7.10 – 7.04 (m, 2H), 6.96 (d,  $J = 8.1$  Hz, 1H), 4.67 (s, 1H), 2.43 (s, 2H), 2.12 (s,  $J = 91.2$  Hz, 2H), 1.03 (s, 3H), 0.90 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  194.79, 164.38, 163.17, 157.86, 150.29, 149.34, 144.10, 139.15, 137.95, 128.92, 113.64, 112.01, 89.98, 56.04, 50.81, 35.98, 32.64, 29.35, 26.96. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{19}H_{20}N_3O_4$  354.1453; found: 354.1450.

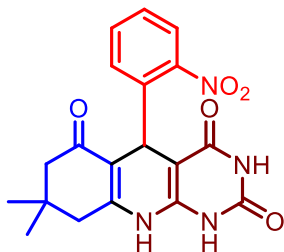




**8,8-dimethyl-5-(4-nitrophenyl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4f)** : Off -white solid (96%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3405, 3255, 3195, 2936, 1655. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.60 (s, 2H), 10.41 (s, 1H), 8.09 (d, *J* = 8.9 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.86 (s, 1H), 2.45 (d, 2H), 2.12 (d, 2H), 1.02 (s, 3H), 0.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.69, 165.04, 160.01, 154.86, 150.18, 149.32, 145.75, 128.41, 123.35, 110.50, 85.37, 50.54, 33.45, 32.67, 29.12, 27.10. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>19</sub>H<sub>19</sub>N<sub>4</sub>O<sub>5</sub> 383.1355; found: 383.1348.

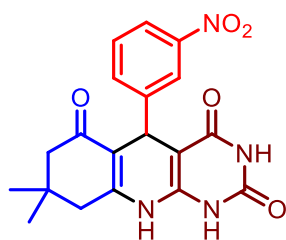


**8,8-dimethyl-5-(2-nitrophenyl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4g)** : Reddish brown solid (93%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3406, 3256, 3196, 2936, 1656. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.68 (s, 1H), 10.38 (s, 1H), 8.88 (s, 1H), 7.74 (d, *J* = 7.3 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.34 – 7.30 (m, 1H), 4.96 (s, 1H), 2.16 (s, 2H), 1.98 (s, 2H), 1.02 (s, 3H), 0.88 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.70, 163.80, 162.96, 150.04, 148.91, 141.81, 133.04, 131.06, 127.21, 124.07, 111.00, 89.41, 50.82, 32.56, 32.23, 29.09, 27.11, 19.05. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>19</sub>H<sub>19</sub>N<sub>4</sub>O<sub>5</sub> 383.1355; found: 383.1360.

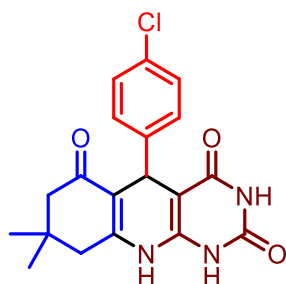


**8,8-dimethyl-5-(3-nitrophenyl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4h)** : Light orange solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3408, 3257, 3198, 2939, 1658. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.75 (s, 1H), 10.24 (s, 1H), 8.79 (s, 1H), 8.01 (d, *J* = 7.3 Hz, 1H), 7.85 (s, 1H), 7.57 – 7.54 (m, 2H), 4.49 (s, 1H), 2.46 (s, 2H), 2.09 (s, 2H), 1.06 (s, 6H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 196.34, 165.81, 160.13, 154.77, 150.26,

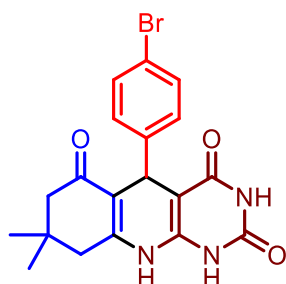
148.29, 142.81, 134.28, 129.62, 121.62, 120.76, 110.50, 85.63, 56.48, 45.44, 32.76, 28.43, 24.33, 21.65. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{19}H_{19}N_4O_5$  383.1355; found: 383.1350.



**5-(4-chlorophenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4i)** : White solid (92%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3409, 3259, 3199, 2939, 1659.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.30 (s, 1H), 10.14 (s, 1H), 8.79 (s, 1H), 7.20 (s, 1H), 7.10 (d, 2H), 6.90 (s, 1H), 4.32 (s, 1H), 2.13 (s, 2H), 1.93 (s, 1H), 1.80 (s, 1H), 1.03 (s, 3H), 0.89 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  195.38, 169.09, 167.91, 163.33, 159.68, 143.63, 138.66, 132.04, 124.85, 112.98, 76.18, 56.50, 32.19, 32.10, 27.58, 13.70. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{19}H_{19}ClN_3O_3$  372.1114; found: 372.1118.

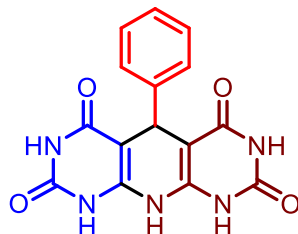


**5-(4-bromophenyl)-8,8-dimethyl-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,7H)-trione (4j)** : White solid (92%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3400, 3250, 3190, 2930, 1650.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.75 (s, 1H), 10.24 (s, 1H), 8.79 (s, 1H), 7.85 (d,  $J = 8.2$  Hz, 2H), 7.38 (d,  $J = 8.2$  Hz, 2H), 4.74 (s, 1H), 2.45 (d, 2H), 2.09 (d, 2H), 1.03 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  194.01, 169.09, 167.98, 162.95, 159.78, 143.55, 132.36, 127.15, 122.54, 110.20, 78.72, 59.06, 51.12, 32.19, 31.73, 18.96, 13.71. HRMS (ESI)  $m/z$ :  $[M+H]^+$  + calculated for  $C_{19}H_{19}BrN_3O_3$  416.0609; found: 416.0613.

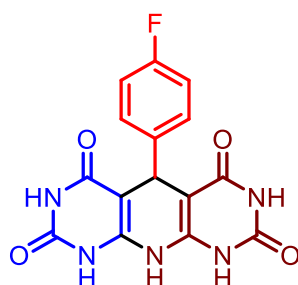


**5-phenyl-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4l)** : Reddish brown solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3410, 3210, 3110, 2910, 1610.

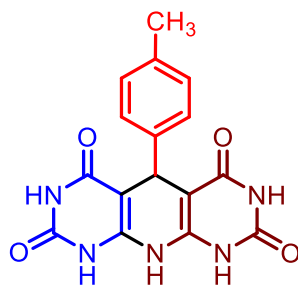
$^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.508 (s, 2H), 10.308 (s, 2H), 7.22 (m,  $J = 9.0$  Hz, 2H), 7.07 (m,  $J = 9.0$  Hz, 3H), 6.64 (s, 1H), 5.31 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  154.72, 150.32, 145.28, 139.81, 128.10, 126.99, 125.36, 89.69, 32.97. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{12}\text{N}_5\text{O}_4$  326.0889; found: 326.0888.



**5-(4-fluorophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4m)** : Light orange solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3420, 3220, 3120, 2920, 1620.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.53 (s, 2H), 10.32 (s, 2H), 7.07 (d,  $J = 9.0$  Hz, 2H), 7.02 (d,  $J = 9.0$  Hz, 2H), 6.66 (s, 1H), 5.27 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  161.76, 159.09, 150.20, 141.41, 128.83, 128.80, 114.55, 86.14, 32.20. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{FN}_5\text{O}_4$  344.0795; found: 326.0889.

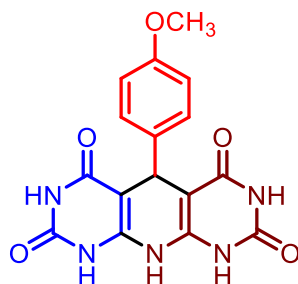


**5-(p-tolyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4n)** : White solid (94%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3421, 3221, 3121, 2921, 1621.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.49 (s, 2H), 10.28 (s, 2H), 7.01 (d,  $J = 8.0$  Hz, 2H), 6.94 (d,  $J = 8.0$  Hz, 2H), 6.65 (s, 1H), 5.26 (s, 1H), 2.23 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  165.53, 161.49, 150.23, 130.21, 130.07, 128.72, 126.92, 86.99, 32.53, 20.96. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{16}\text{H}_{14}\text{N}_5\text{O}_4$  340.1045; found: 340.1050.

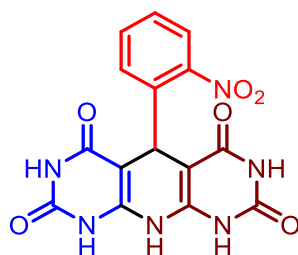


**5-(4-methoxyphenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4o)** : Orange solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ):

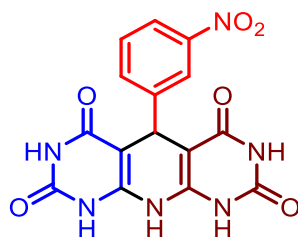
3431, 3231, 3131, 2931, 1631.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.48 (s, 2H), 10.28 (s, 2H), 8.26 (s, 1H), 7.07 (d,  $J = 9.0$  Hz, 2H), 6.77 (d,  $J = 8.8$  Hz, 2H), 5.25 (s, 1H), 3.87 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  164.39, 162.66, 155.04, 150.72, 138.27, 125.64, 114.43, 79.41, 56.17, 31.90. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{16}\text{H}_{14}\text{N}_5\text{O}_5$  356.0994; found: 356.0999.



**5-(2-nitrophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4p)** : Yellow solid (92%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3411, 3221, 3131, 2941, 1650.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  11.52 (s, 2H), 11.30 (s, 2H), 9.02 (s, 1H), 8.15 (d,  $J = 14.7$  Hz, 1H), 7.45 – 7.34 (m, 2H), 7.14 (ddd,  $J = 8.2, 6.9, 1.1$  Hz, 1H), 4.17 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  162.72, 162.21, 151.12, 150.71, 139.51, 133.57, 130.32, 127.16, 125.66, 79.99, 31.13. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{N}_6\text{O}_6$  371.0740; found: 371.0743.

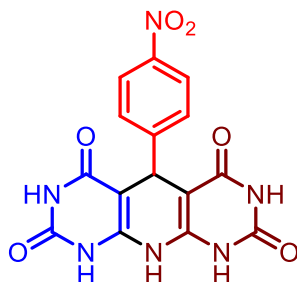


**5-(3-nitrophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4q)** : Brown solid (93%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3410, 3220, 3130, 2940, 1650.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.63 (s, 2H), 10.44 (s, 2H), 8.01 (d,  $J = 7.8$  Hz, 1H), 7.85 (s, 1H), 7.58 – 7.52 (m, 2H), 6.76 (s, 1H), 5.40 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  162.84, 161.79, 150.17, 147.96, 143.16, 133.66, 129.64, 121.56, 120.71, 79.99, 30.86. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{N}_6\text{O}_6$  371.0740; found: 371.0746.



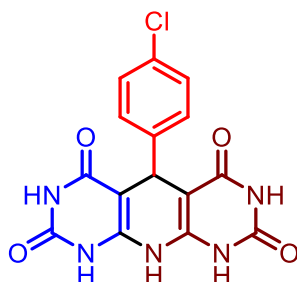
**5-(4-nitrophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4r)** : White solid (97%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3450, 3240, 3130, 2920, 1610.

$^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  11.18 (s, 2H), 10.91 (s, 2H), 8.12 (d,  $J$  = 8.9 Hz, 2H), 7.45 (d,  $J$  = 8.0 Hz, 8H), 6.73 (s, 1H), 5.37 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  169.068, 167.167, 150.110, 149.382, 145.836, 128.567, 123.683, 80.477, 31.412. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{N}_6\text{O}_6$  371.0740; found: 371.0738.



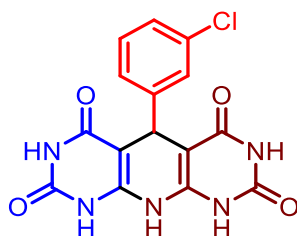
**5-(4-chlorophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-**

**2,4,6,8(1H,3H,7H,9H)-tetraone (4s)** : White solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3400, 3201, 3102, 2903, 1604.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.54 (s, 2H), 10.34 (s, 2H), 7.25 (d,  $J$  = 8.6 Hz, 2H), 7.08 (d,  $J$  = 8.5 Hz, 2H), 6.67 (s, 1H), 5.28 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  163.11, 161.21, 150.21, 139.13, 129.93, 129.02, 127.99, 86.15, 32.19. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{ClN}_5\text{O}_4$  360.0499; found: 360.0503.



**5-(3-chlorophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-**

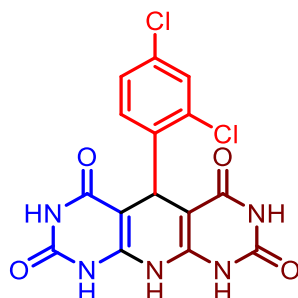
**2,4,6,8(1H,3H,7H,9H)-tetraone (4t)** : White solid (93%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3409, 3210, 3111, 2912, 1613.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  10.56 (s, 2H), 10.36 (s, 2H), 7.25 (t,  $J$  = 8.1 Hz, 1H), 7.17 (d,  $J$  = 9.7 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.69 (s, 1H), 5.29 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$  151.525, 148.795, 135.187, 133.186, 130.171, 127.232, 126.400, 125.298, 91.384, 31.414. HRMS (ESI)  $m/z$ :  $[\text{M}+\text{H}]^+$  + calculated for  $\text{C}_{15}\text{H}_{11}\text{ClN}_5\text{O}_4$  360.0499; found: 360.0501.



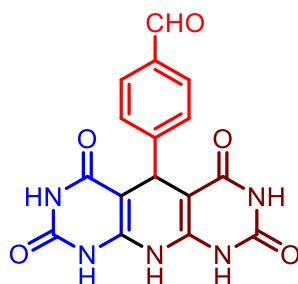
**5-(2,4-dichlorophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-**

**2,4,6,8(1H,3H,7H,9H)-tetraone (4u)** : Off-white solid (95%), mp  $>300^\circ\text{C}$ . IR (KBr,  $\text{cm}^{-1}$ ): 3415, 3216, 3117, 2918, 1619.  $^1\text{H}$  NMR (500 MHz, DMSO)  $\delta$  11.05 (s, 2H), 10.90 (s, 2H), 7.49 (s, 1H), 7.39 – 7.30 (m, 2H), 6.56 (s, 1H), 5.25 (s, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO)  $\delta$

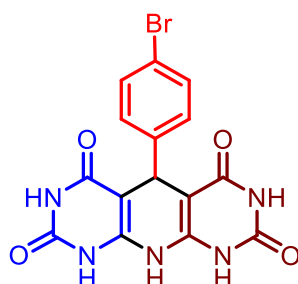
155.55, 153.71, 142.59, 136.91, 133.67, 131.54, 129.02, 126.37, 81.05, 30.84. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>15</sub>H<sub>10</sub>Cl<sub>2</sub>N<sub>5</sub>O<sub>4</sub> 394.0109; found: 394.0114.



**4-(2,4,6,8-tetraoxo-1,2,3,4,5,6,7,8,9,10-decahydropyrido[2,3-d:6,5-d']dipyrimidin-5-yl)benzaldehyde (4v)** : Brown solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3420, 3221, 3122, 2923, 1624. <sup>1</sup>H NMR (500 MHz, DMSO) δ 11.05 (s, 2H), 10.87 (s, 1H), 10.80 (s, 1H), 9.98 (s, 1H), 8.98 (s, 1H), 6.96 (d, *J* = 24.6 Hz, 2H), 6.66 (d, *J* = 34.4 Hz, 2H), 5.22 (s, 1H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 192.30, 166.10, 160.94, 155.82, 150.74, 133.16, 129.35, 126.64, 82.39, 30.85. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>16</sub>H<sub>12</sub>N<sub>5</sub>O<sub>5</sub> 354.0838; found: 354.0833.

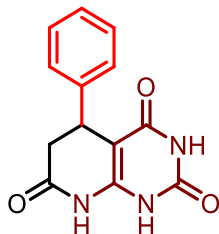


**5-(4-bromophenyl)-5,10-dihydropyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8(1H,3H,7H,9H)-tetraone (4w)** : White solid (94%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3437, 3238, 3139, 2940, 1641. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.54 (s, 2H), 10.34 (s, 2H), 7.42 (s, 1H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 5.26 (s, 1H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 150.28, 139.83, 132.90, 131.65, 130.89, 129.48, 118.14, 90.94, 32.69. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>15</sub>H<sub>11</sub>BrN<sub>5</sub>O<sub>4</sub> 402.9916; found: 402.9911.

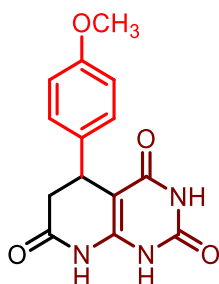


**5-phenyl-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5a)** : White solid (95%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3260, 3160, 1710, 1480, 750. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.49 (s, 2H), 10.29 (s, 1H), 7.39 (t, *J* = 4.3 Hz, 1H), 7.02 – 6.94 (m, 4H), 4.14 (s,

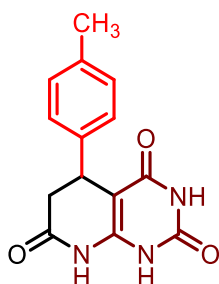
1H, diastereotopic CH), 2.24 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 169.84, 159.85, 150.20, 146.14, 136.71, 134.02, 130.21, 126.93, 86.44, 36.51, 32.48. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>O<sub>3</sub> 258.0878; found: 258.0872.



**5-(4-methoxyphenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5b) :** White solid (95%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3264, 3164, 1714, 1484, 754. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.48 (s, 1H), 10.28 (s, 1H), 9.88 (s, 1H), 7.07 (d, *J* = 13.7 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.50 (s, 1H, diastereotopic CH), 3.68 (s, 3H), 2.07 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 169.35, 166.09, 160.15, 149.88, 145.27, 135.29, 127.79, 113.42, 85.08, 55.13, 35.94, 31.91. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>14</sub>H<sub>14</sub>N<sub>3</sub>O<sub>4</sub> 288.0984; found: 288.0989.

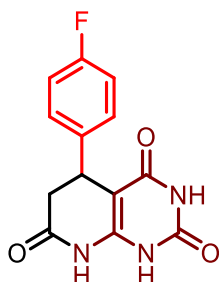


**5-(p-tolyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5c) :** Brown solid (94%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3265, 3165, 1715, 1485, 755. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.49 (s, 2H), 10.29 (s, 1H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 4.12 (s, 1H, diastereotopic CH), 2.41 (s, 2H, CH<sub>2</sub>), 2.24 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 169.84, 164.18, 150.24, 145.56, 136.77, 133.99, 130.21, 130.07, 86.16, 36.51, 32.50, 20.93. HRMS (ESI) m/z: [M+H]<sup>+</sup> + calculated for C<sub>14</sub>H<sub>14</sub>N<sub>3</sub>O<sub>3</sub> 272.1035; found: 272.1035.

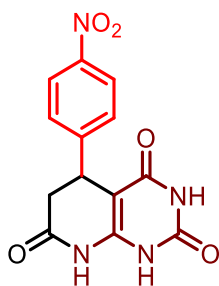


**5-(4-fluorophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5d) :** White solid (96%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3266, 3166, 1716, 1486, 757. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.60 (s, 2H), 10.40 (s, 1H), 8.09 (d, *J* = 8.7 Hz, 2H), 7.36 (d, *J* = 8.8 Hz, 2H),

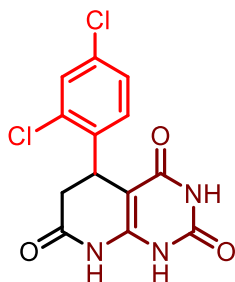
4.53 (s, 1H, diastereotopic CH), 2.11 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 165.85, 161.62, 159.65, 150.25, 135.87, 128.80, 114.74, 114.58, 86.71, 36.79, 32.76. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>F 276.0784; found: 276.0788.



**5-(4-nitrophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5e) :** White solid (97%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3268, 3168, 1718, 1488, 758. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.51 (s, 2H), 10.31 (s, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 4.64 (s, 1H, diastereotopic CH), 2.09 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 166.66, 161.21, 150.17, 149.33, 147.47, 145.75, 128.42, 123.35, 85.93, 37.09, 33.56. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>11</sub>N<sub>4</sub>O<sub>5</sub> 303.0729; found: 303.0725.



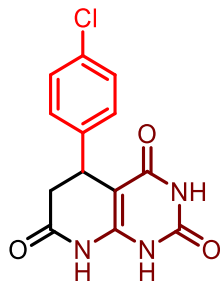
**5-(2,4-dichlorophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5f) :** White solid (95%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3269, 3169, 1719, 1487. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.42 (s, 3H), 7.42 (s, 1H), 7.30 (dd, *J* = 21.0, 7.8 Hz, 2H), 4.14 (s, 1H, diastereotopic CH) 1.97 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 167.45, 154.40, 150.22, 138.36, 133.66 131.57, 131.07, 130.89, 129.13, 128.78, 126.94, 89.41, 36.96, 32.12. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>10</sub>N<sub>3</sub>O<sub>3</sub>Cl<sub>2</sub> 326.0099; found: 326.0094.



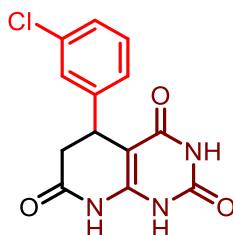
**5-(4-chlorophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5g) :** White solid (95%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3253, 3151, 1741, 1451, 751. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.55 (s, 2H), 10.35 (s, 1H), 7.25 (d, *J* = 8.6 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H),



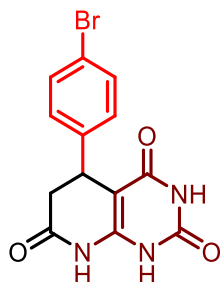
4.05 (s, 1H, diastereotopic CH), 2.05 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 166.94, 150.20, 139.16, 131.62, 129.92, 129.23, 129.01, 127.99, 89.24, 37.07, 32.58. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>Cl 292.0488; found: 292.0484.



**5-(3-chlorophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5h)** : White solid (93%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3276, 3178, 1713, 1485, 755. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.58 (s, 2H), 10.38 (s, 1H), 7.25 (t, *J* = 8.6 Hz, 1H), 7.16 (s, 1H), 7.05 (m, 2H), 4.37 (s, 1H, diastereotopic CH), 2.21 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 165.82, 154.76, 150.27, 142.97, 133.05, 129.95, 128.29, 126.81, 125.87, 125.47, 86.16, 37.07, 32.76. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>Cl 292.0488; found: 292.0492.

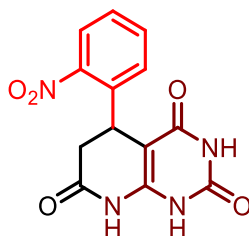


**5-(4-bromophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5i)** : Off-white solid (94%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3275, 3170, 1720, 1489, 752. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.56 (s, 2H), 10.35 (s, 1H), 7.85 (d, *J* = 2.9 Hz, 2H, CH<sub>2</sub>), 7.38 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 1H, diastereotopic CH), 2.21 (s, 2H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 171.15, 150.19, 139.62, 135.59, 132.80, 131.73, 130.89, 118.37, 89.69, 35.94, 32.76. HRMS (ESI) m/z: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>Br 335.9983; found: 335.9988.



**5-(2-nitrophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5j)** : Brown solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3166, 3169, 1715, 1491, 761. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.41 (s, 3H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* =

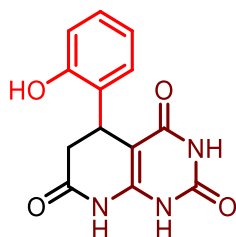
7.6 Hz, 1H), 7.31 (d,  $J = 7.9$  Hz, 1H), 4.00 (s, 1H, diastereotopic CH) 2.13 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO)  $\delta$  171.47, 162.35, 149.87, 134.69, 134.22, 131.96, 130.31, 127.07, 124.79, 123.99, 89.41, 37.08, 29.79. HRMS (ESI)  $m/z$ : [M+H]<sup>+</sup> + calculated for C<sub>13</sub>H<sub>11</sub>N<sub>4</sub>O<sub>5</sub> 303.0729; found: 303.0734.



**5-(3-nitrophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5k) :** Yellow solid (94%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3286, 3169, 1721, 1489, 759. <sup>1</sup>H NMR (500 MHz, DMSO)  $\delta$  10.64 (s, 1H), 10.46 (s, 2H), 8.01 (d,  $J = 6.9$  Hz, 1H), 7.85 (s, 1H), 7.54 (dt,  $J = 15.7, 7.9$  Hz, 2H), 3.98 (s, 1H, diastereotopic CH), 2.1 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO)  $\delta$  170.91, 162.35, 150.15, 148.18, 146.12, 142.87, 134.29, 129.64, 121.69, 120.78, 85.37, 33.02, 31.20. HRMS (ESI)  $m/z$ : [M+H]<sup>+</sup> + calculated for C<sub>13</sub>H<sub>11</sub>N<sub>4</sub>O<sub>5</sub> 303.0729; found: 303.0728.

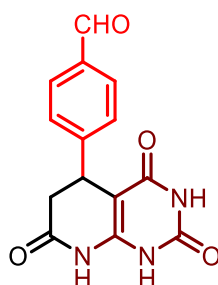


**5-(2-hydroxyphenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5l) :** Light Brown solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3388, 3182, 1722, 1376. <sup>1</sup>H NMR (500 MHz, DMSO)  $\delta$  11.68 (s, 1H), 10.87 (s, 1H), 9.96 (s, 2H), 7.17 (t,  $J = 5.8$  Hz, 1H), 7.10 – 7.04 (m, 2H), 6.96 (d,  $J = 8.1$  Hz, 1H), 6.45 (s, 2H), 4.01 (s, 1H, diastereotopic CH), 2.21 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO)  $\delta$  163.93, 163.03, 155.11, 150.65, 150.12, 129.18, 127.79, 125.24, 125.03, 115.58, 90.25, 37.18, 27.15. HRMS (ESI)  $m/z$ : [M+H]<sup>+</sup> + calculated for C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>O<sub>4</sub> 274.0827; found: 274.0831.



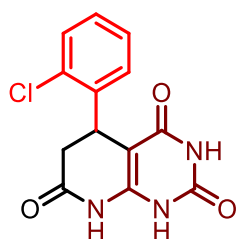
**4-(2,4,7-trioxo-1,2,3,4,5,6,7,8-octahydropyrido[2,3-d]pyrimidin-5-yl)benzaldehyde (5m) :**

Off -white solid (96%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3374, 3166, 1749, 785, 677. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.59 (s, 2H), 10.40 (s, 1H), 9.94 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 3.87 (s, 1H, diastereotopic CH), 2.09 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 193.06, 169.58, 150.24, 148.11, 140.25, 134.23, 130.46, 129.63, 127.83, 86.12, 37.57, 33.55. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>14</sub>H<sub>12</sub>N<sub>3</sub>O<sub>4</sub> 286.0827; found: 286.0823.



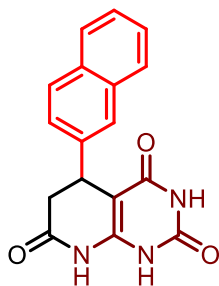
**5-(2-chlorophenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5n) :**

Reddish brown solid (94d%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3315, 3159, 1721. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.39 (s, 3H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 3.90 (s, 1H, diastereotopic CH), 2.05 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 167.66, 154.31, 150.10, 148.25, 138.99, 136.31, 132.88, 131.24, 129.77, 126.87, 86.14, 37.09, 31.89. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>Cl 292.0488; found: 292.0491.

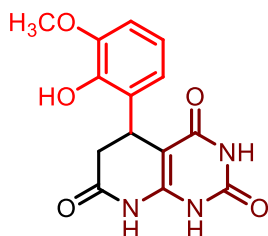


**5-(naphthalen-2-yl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5o) :**

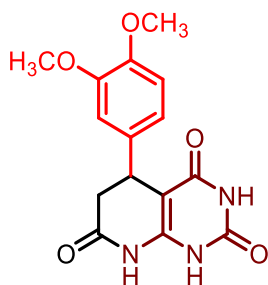
Light orange solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3380, 3170, 1712. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.56 (s, 1H), 10.38 (s, 2H), 7.82 (d, *J* = 9.3 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 1H), 7.54 (s, 1H), 7.41 (dd, *J* = 10.2, 6.5 Hz, 2H), 7.28 (d, *J* = 10.2 Hz, 1H), 4.00 (s, 1H, diastereotopic CH), 2.21 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 168.89, 161.06, 150.29, 147.66, 137.90, 136.38, 135.06, 133.57, 130.10, 129.47, 128.48, 125.34, 124.31, 127.78, 86.73, 37.07, 32.76. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>17</sub>H<sub>14</sub>N<sub>3</sub>O<sub>3</sub> 308.1035; found: 308.1039.



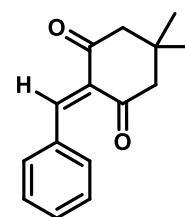
**5-(2-hydroxy-3-methoxyphenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5p)** : White solid (91%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3350, 3150, 1637. <sup>1</sup>H NMR (500 MHz, DMSO) δ 11.69 (s, 1H), 10.83 (s, 1H), 9.93 (s, 1H), 6.99 (t, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.64 (d, *J* = 7.5 Hz, 1H), 6.42 (s, 1H), 4.76 (s, 1H, diastereotopic CH), 3.78 (s, 3H), 2.07 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 169.85, 164.19, 149.61, 146.91, 142.71, 139.52, 128.03, 120.34, 110.66, 86.73, 56.49, 35.17, 28.93. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>14</sub>H<sub>14</sub>N<sub>3</sub>O<sub>5</sub> 304.0933; found: 304.0930.



**5-(3,4-dimethoxyphenyl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5q)** : White solid (92%), mp >300°C. IR (KBr, cm<sup>-1</sup>): 3321, 3155, 1705. <sup>1</sup>H NMR (500 MHz, DMSO) δ 11.32 (s, 1H), 11.20 (s, 1H), 8.42 (d, *J* = 1.8 Hz, 1H), 8.26 (s, 1H), 7.91 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.12 (d, *J* = 8.6 Hz, 1H), 4.23 (s, 1H, diastereotopic CH), 3.89 (s, 3H), 3.81 (s, 3H), 2.40 (s, 2H, CH<sub>2</sub>). <sup>13</sup>C NMR (126 MHz, DMSO) δ 164.47, 162.85, 155.91, 154.10, 150.67, 148.26, 132.17, 125.75, 117.25, 115.75, 111.56, 56.33, 55.88, 37.59, 29.56. HRMS (ESI) *m/z*: [M+H]<sup>+</sup> + calculated for C<sub>15</sub>H<sub>16</sub>N<sub>3</sub>O<sub>5</sub> 318.1089; found: 318.1086.



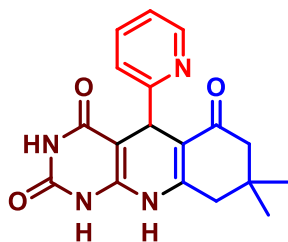
**2-benzylidene-5,5-dimethylcyclohexane-1,3-dione (Intermediate A)** : white solid, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.88 (s, 1H), 7.30 (t, 2H), 7.23 (t, 2H), 7.11 (t, 1H), 2.48 (m, 2H), 2.29-2.15 (m, 2H), 1.12 (s, 3H), 1.01 (s, 3H), <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 27.33, 29.26, 32.19, 40.87, 50.74, 123.66, 126.35, 128.03, 128.37, 139.25, 144.08, 190.37, 192.08.



Intermediate A

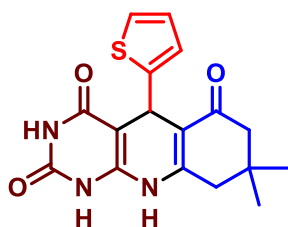
**8,8-dimethyl-5-(pyridin-2-yl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-**

**2,4,6(1H,3H,7H)-trione (4x):** Lime yellow solid (91%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.66 (s, 1H), 10.25 (s, 1H), 8.77 (s, 1H), 8.34 (d, *J* = 3.9 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.05 (m, 1H), 4.88 (s, 1H), 2.48 (d, *J* = 17.7 Hz, 1H), 2.36 (d, *J* = 17.5 Hz, 1H), 2.20 (d, *J* = 16.1 Hz, 1H), 1.97 (d, *J* = 16.0 Hz, 1H), 1.02 (s, 3H), 0.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.81, 163.83, 163.27, 150.25, 149.16, 144.50, 135.78, 123.64, 121.78, 110.80, 89.11, 50.60, 36.25, 32.75, 29.57, 26.63.



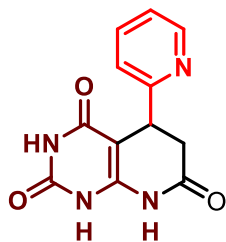
**8,8-dimethyl-5-(thiophen-2-yl)-5,8,9,10-tetrahydropyrimido[4,5-b]quinoline-**

**2,4,6(1H,3H,7H)-trione (4y):** Dark green solid (89%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.82 (s, 1H), 10.30 (s, 1H), 8.95 (s, 1H), 7.24 (d, *J* = 5.0 Hz, 1H), 7.18 (d, *J* = 4.9 Hz, 1H), 6.74 (d, *J* = 3.2 Hz, 1H), 5.08 (s, 1H), 2.48 (d, *J* = 17.7 Hz, 1H), 2.36 (d, *J* = 17.5 Hz, 1H), 2.20 (d, *J* = 16.1 Hz, 1H), 1.97 (d, *J* = 16.0 Hz, 1H), 1.02 (s, 3H), 0.89 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 194.70, 163.91, 163.16, 150.93, 149.96, 148.52, 127.03, 123.96, 123.61, 111.43, 89.64, 50.55, 32.55, 32.28, 29.52, 29.22, 26.92.

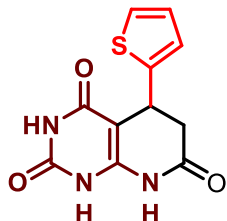


**5-(pyridin-2-yl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5r):**

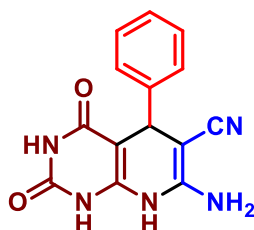
Yellow solid (90%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.42 (s, 1H), 10.0 (s, 1H), 8.81 (s, 1H), 8.30 (d, *J* = 23.9 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 4.02 (s, 1H), 2.07 (s, 2H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 163.34, 161.52, 152.64, 150.78, 150.16, 140.70, 137.18, 131.10, 125.84, 92.10, 36.52, 31.41.



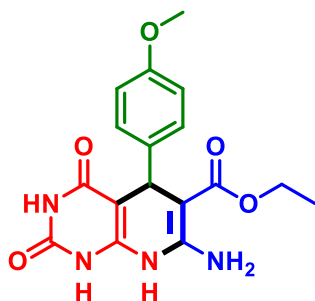
**5-(thiophen-2-yl)-5,8-dihydropyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione (5s):** ash grey solid (91%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.53 (s, 2H), 10.31 (s, 1H), 7.22 (d, *J* = 5.1 Hz, 1H), 6.85 – 6.82 (m, 1H), 6.61 (d, *J* = 3.3 Hz, 1H), 4.05 (s, 1H), 2.66 (s, 2H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 165.55, 154.41, 150.14, 146.08, 126.58, 123.82, 123.62, 87.33, 35.45, 30.45.



**7-amino-2,4-dioxo-5-phenyl-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carbonitrile (6a):** White solid (95%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.51 (s, 2H), 9.0 (s, 1H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.09 (dd, *J* = 11.0, 7.7 Hz, 3H), 6.74 (s, 2H), 4.69 (s, 1H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 161.26, 160.45, 159.41, 150.23, 139.91, 128.11, 126.99, 125.37, 116.05, 88.73, 56.67, 32.89.



**Ethyl 7-amino-5-(4-methoxyphenyl)-2,4-dioxo-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carboxylate (6b):** Pale yellow solid (93%), mp >300°C. <sup>1</sup>H NMR (500 MHz, DMSO) δ 10.49 (s, 1H), 10.29 (s, 1H), 9.0 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.60 (s, 2H), 5.26 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 164.75, 164.09, 162.83, 157.28, 154.97, 150.21, 133.96, 127.98, 115.47, 86.74, 74.60, 62.51, 55.36, 32.15, 14.51.



## <sup>1</sup>H NMR <sup>13</sup>C NMR Spectra

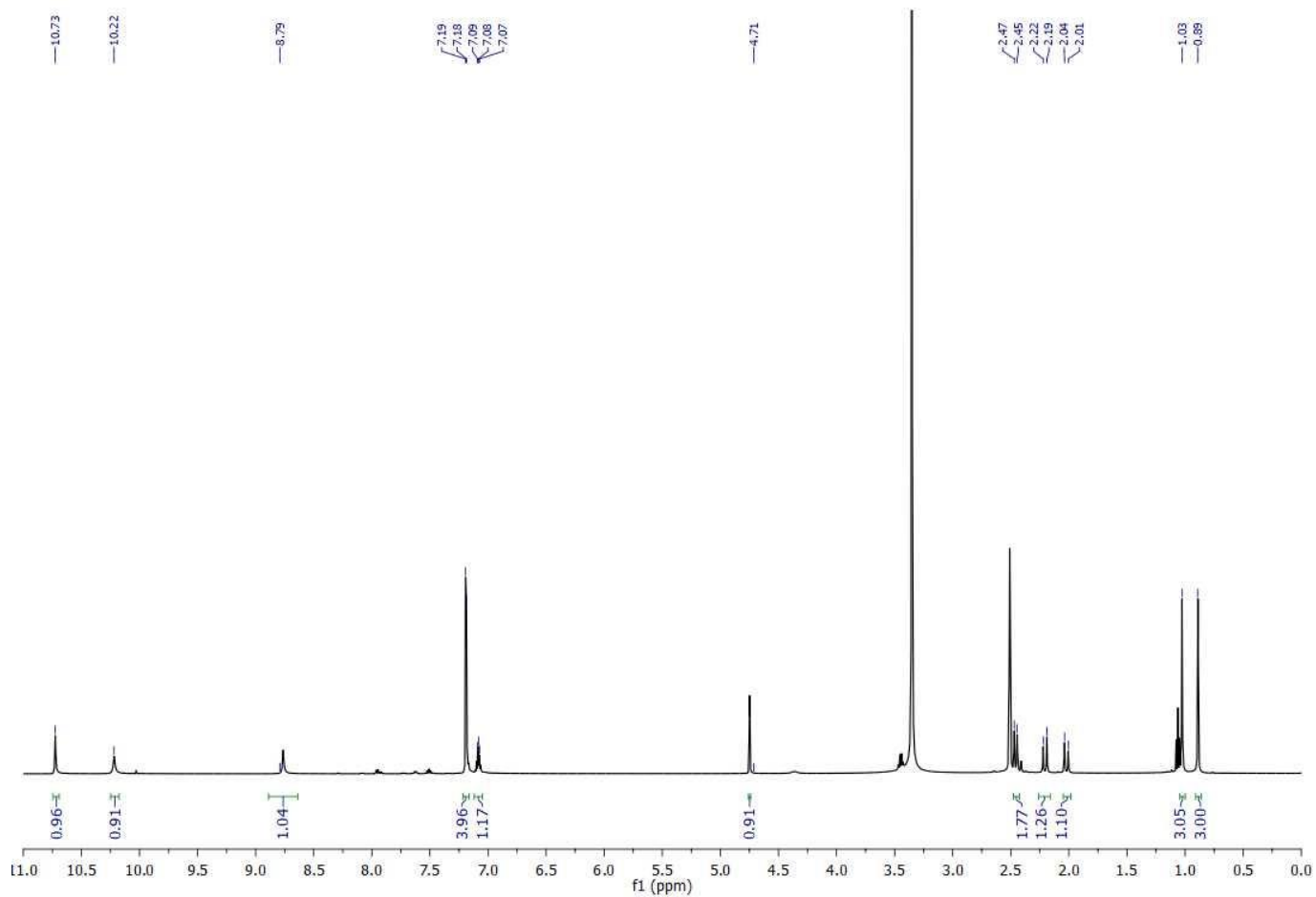


Figure S1. <sup>1</sup>H NMR spectrum of compound 4a

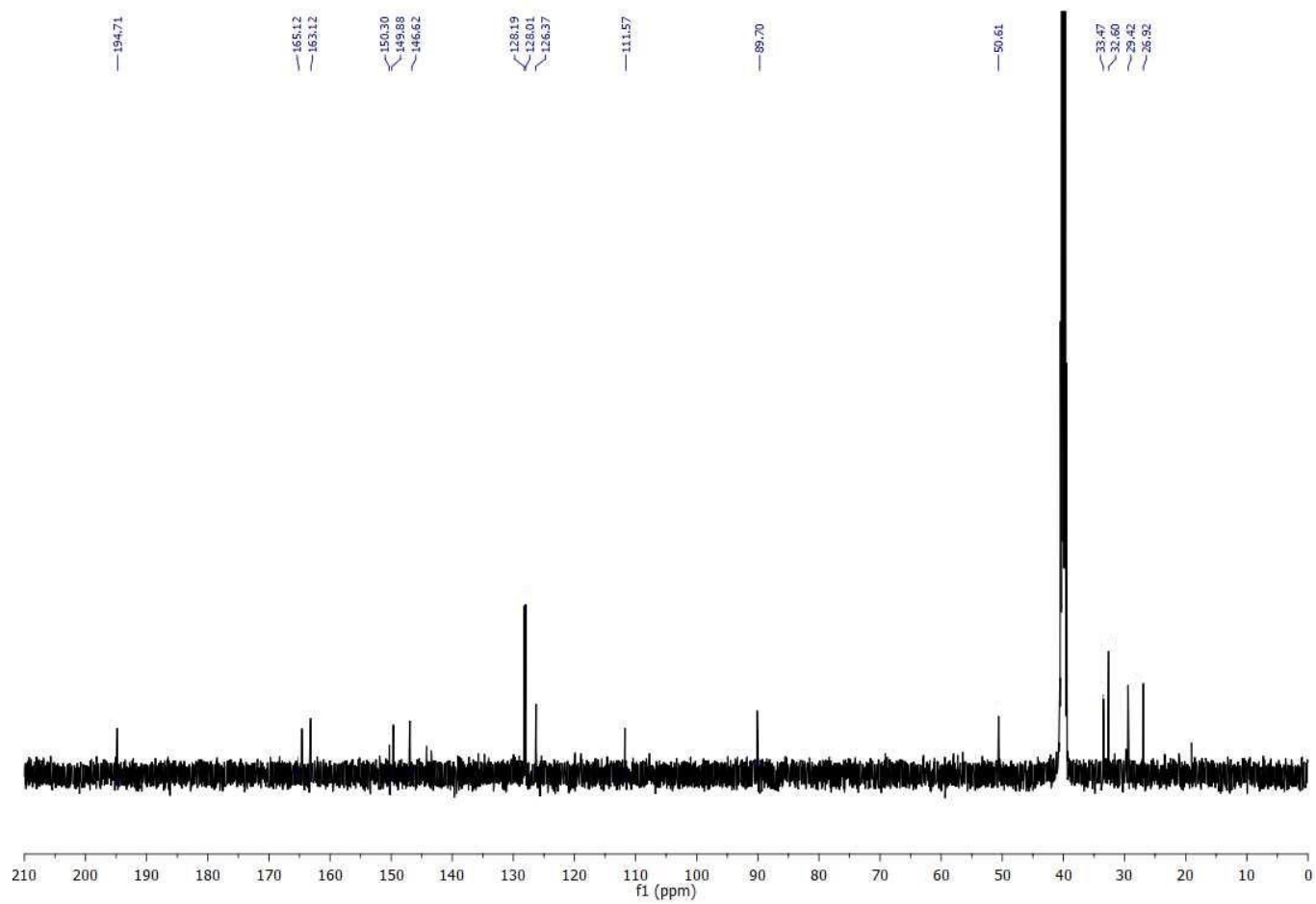


Figure S2.  $^{13}\text{C}$  NMR spectrum of compound 4a



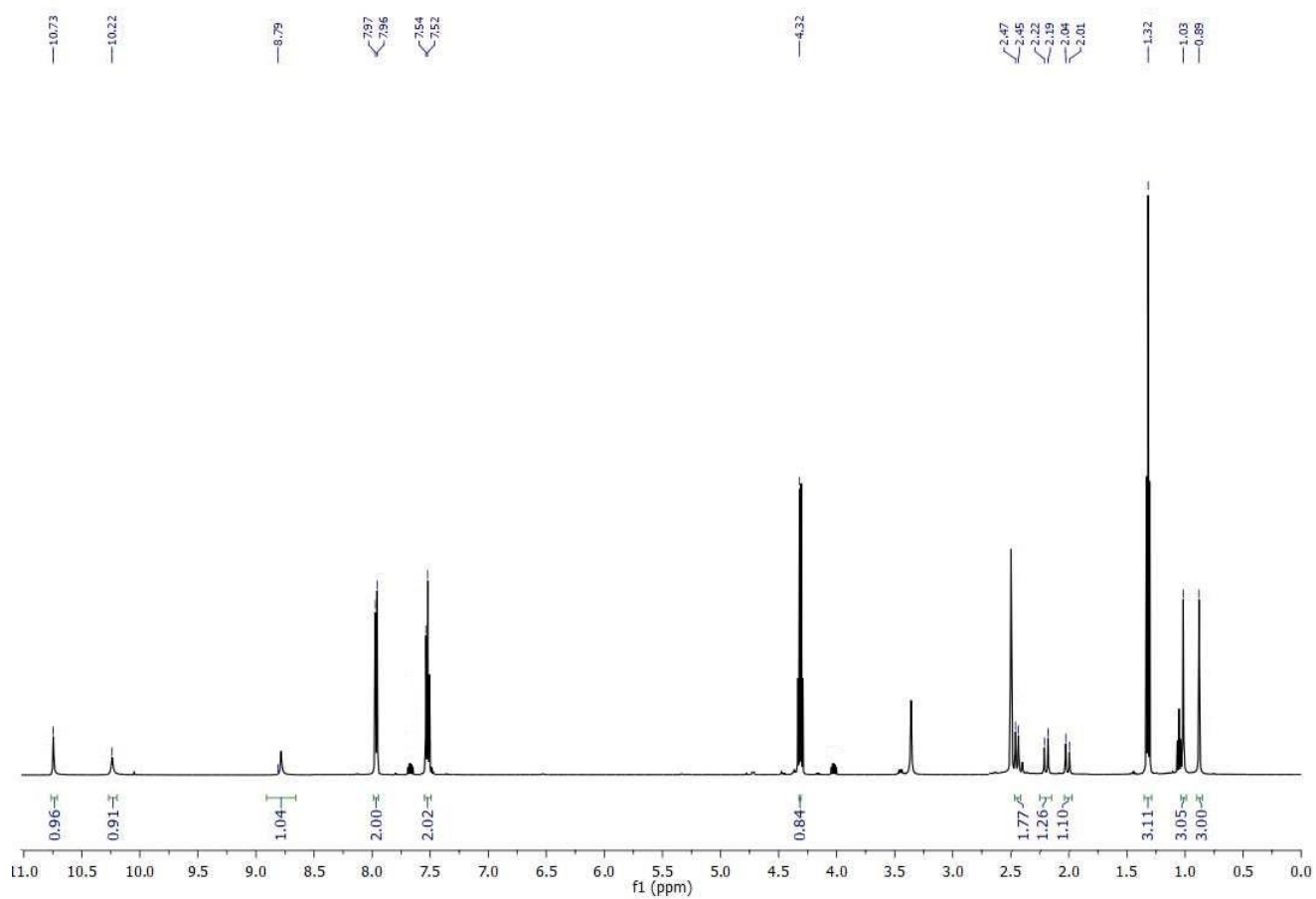


Figure S3. <sup>1</sup>H NMR spectrum of compound 4b

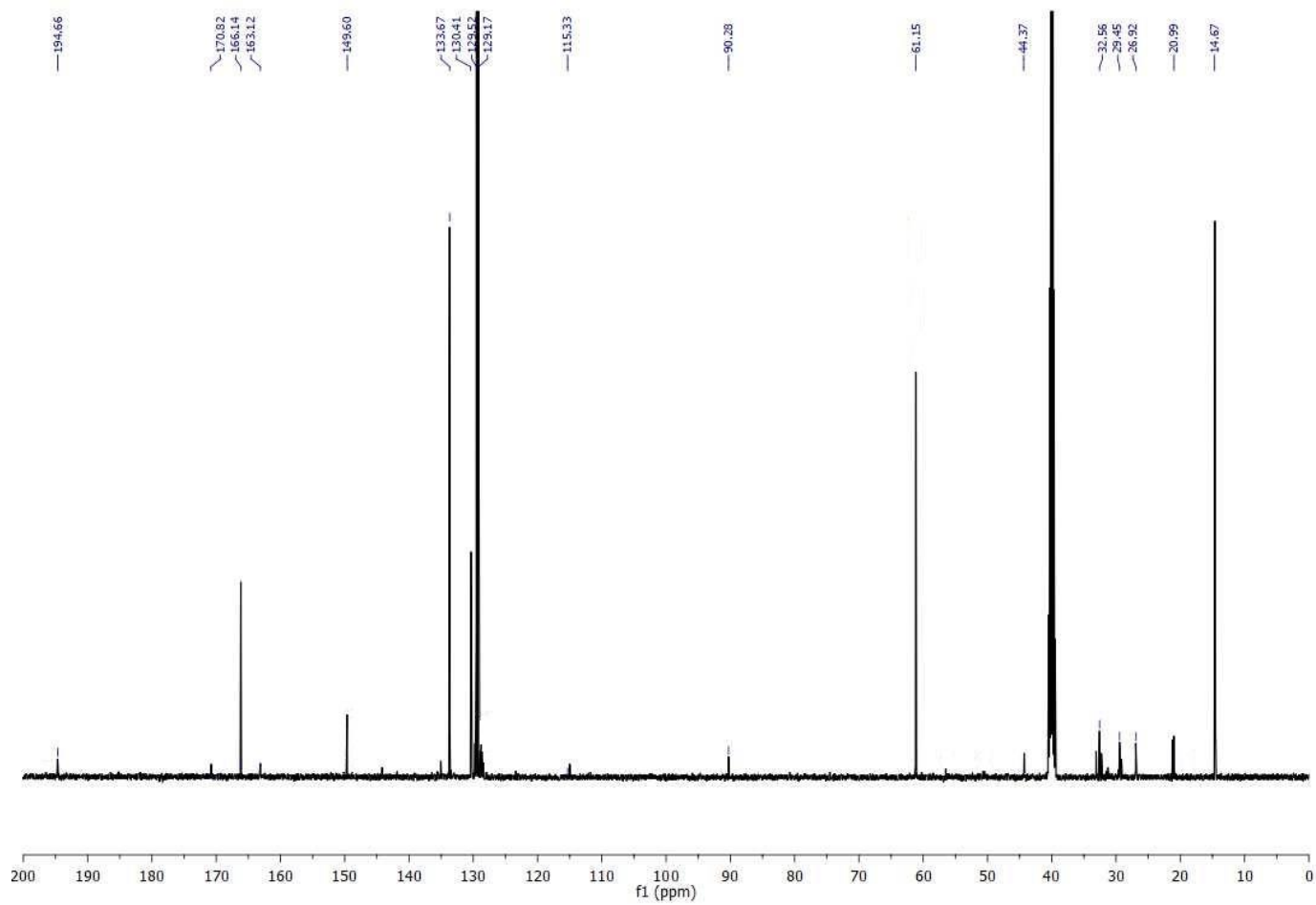


Figure S4.  $^{13}\text{C}$  NMR spectrum of compound 4b

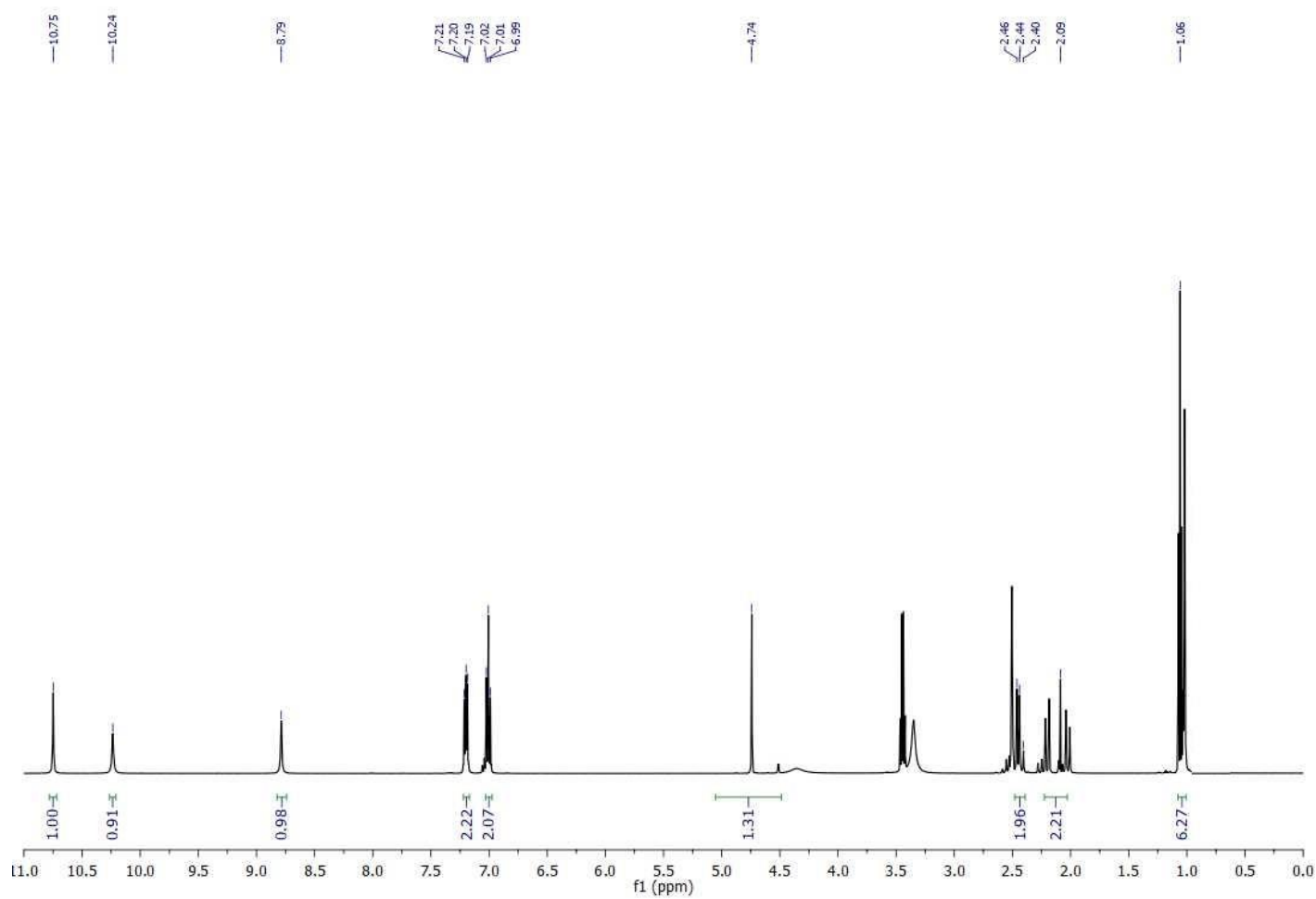


Figure S5. <sup>1</sup>H NMR spectrum of compound 4c

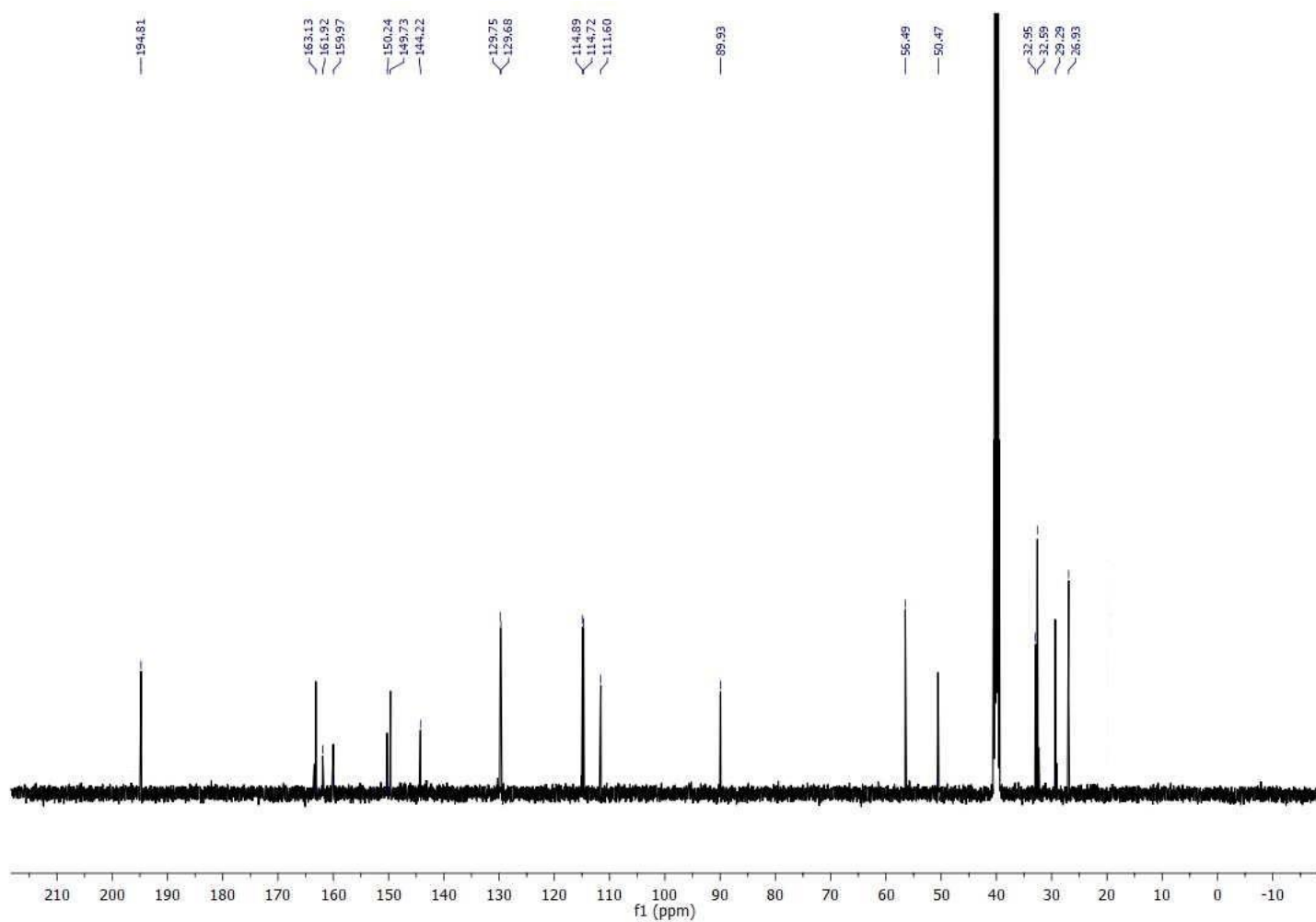


Figure S6.  $^{13}\text{C}$  NMR spectrum of compound 4c

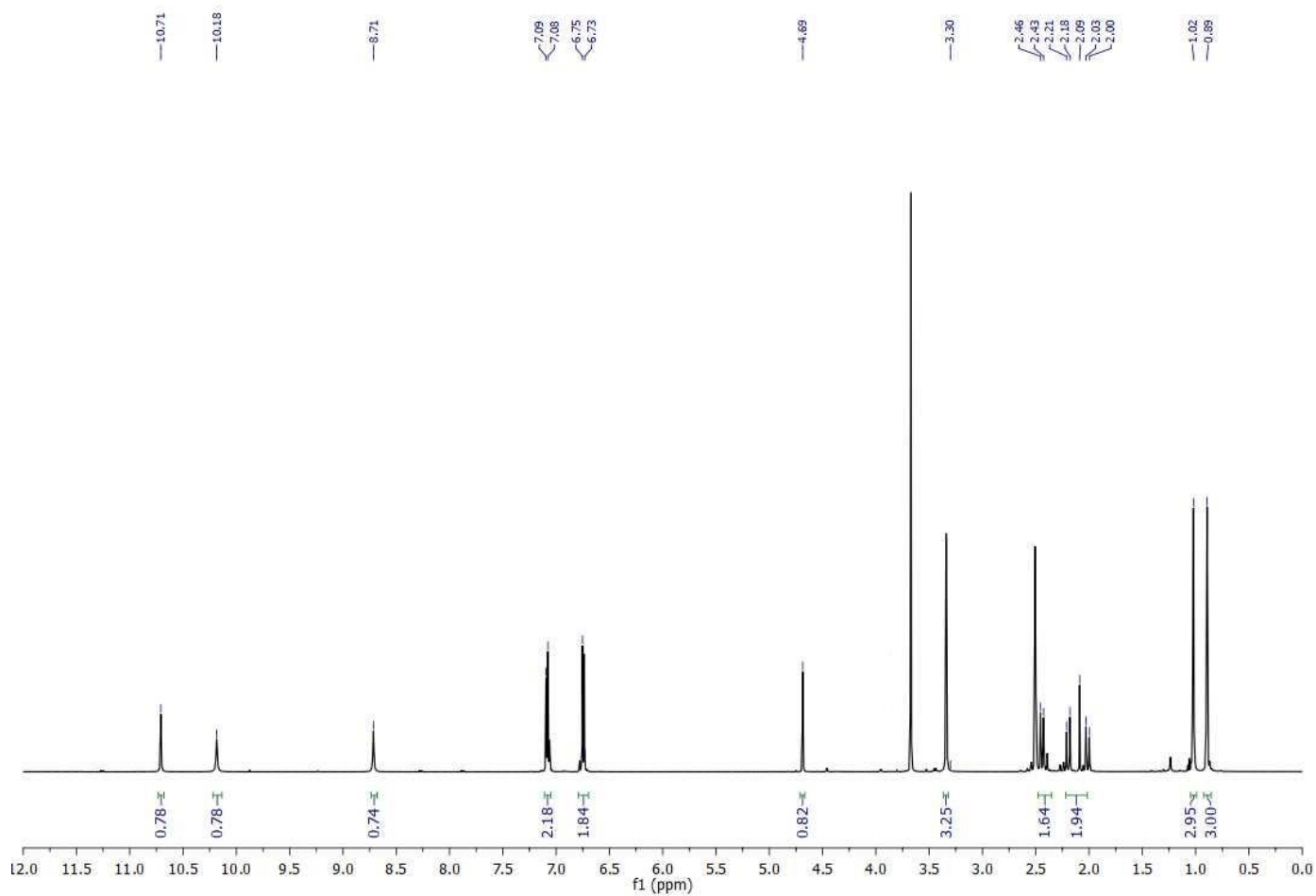


Figure S7. <sup>1</sup>H NMR spectrum of compound 4d

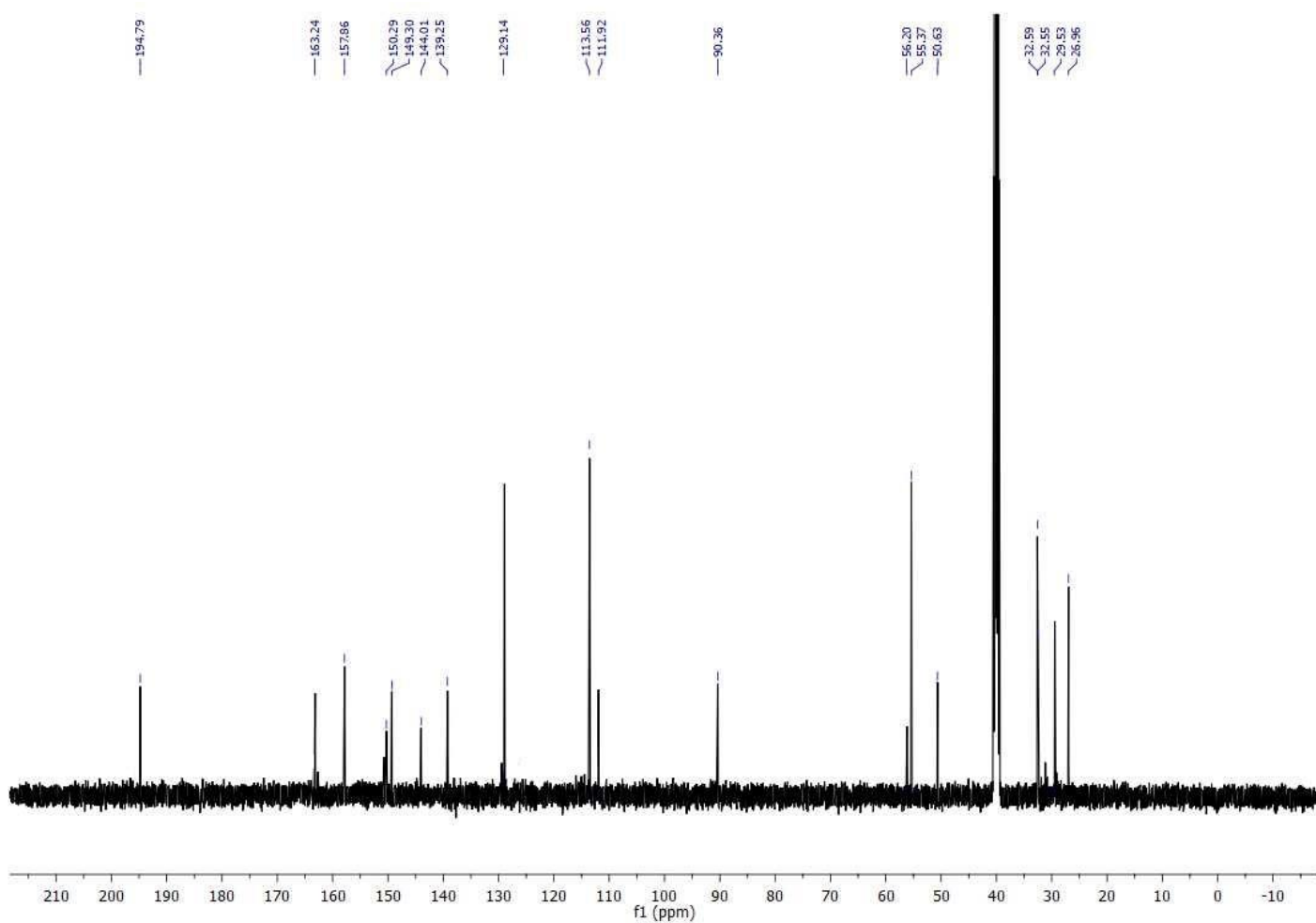


Figure S8.  $^{13}\text{C}$  NMR spectrum of compound 4d

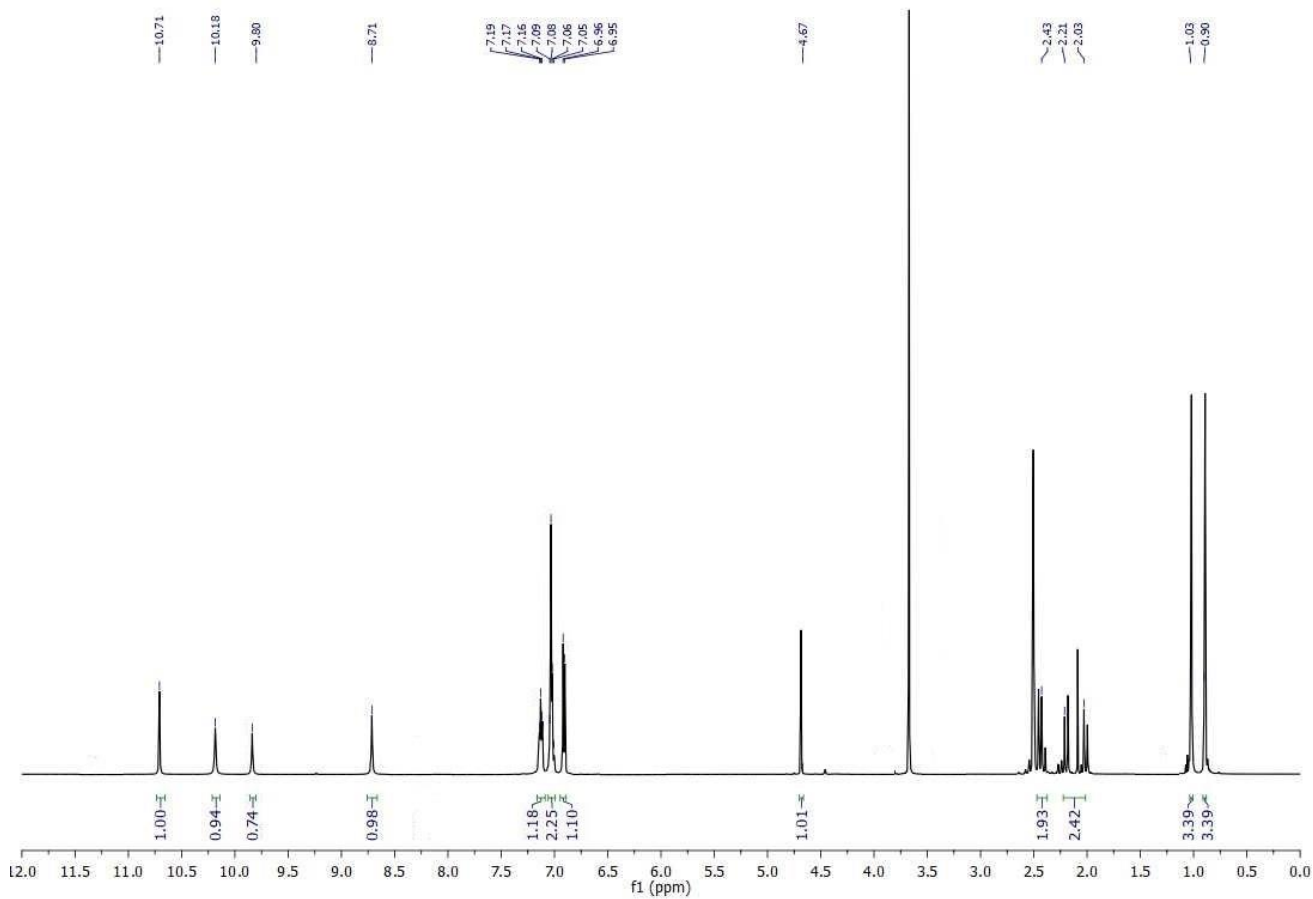


Figure S9.  $^1\text{H}$  NMR spectrum of compound 4e

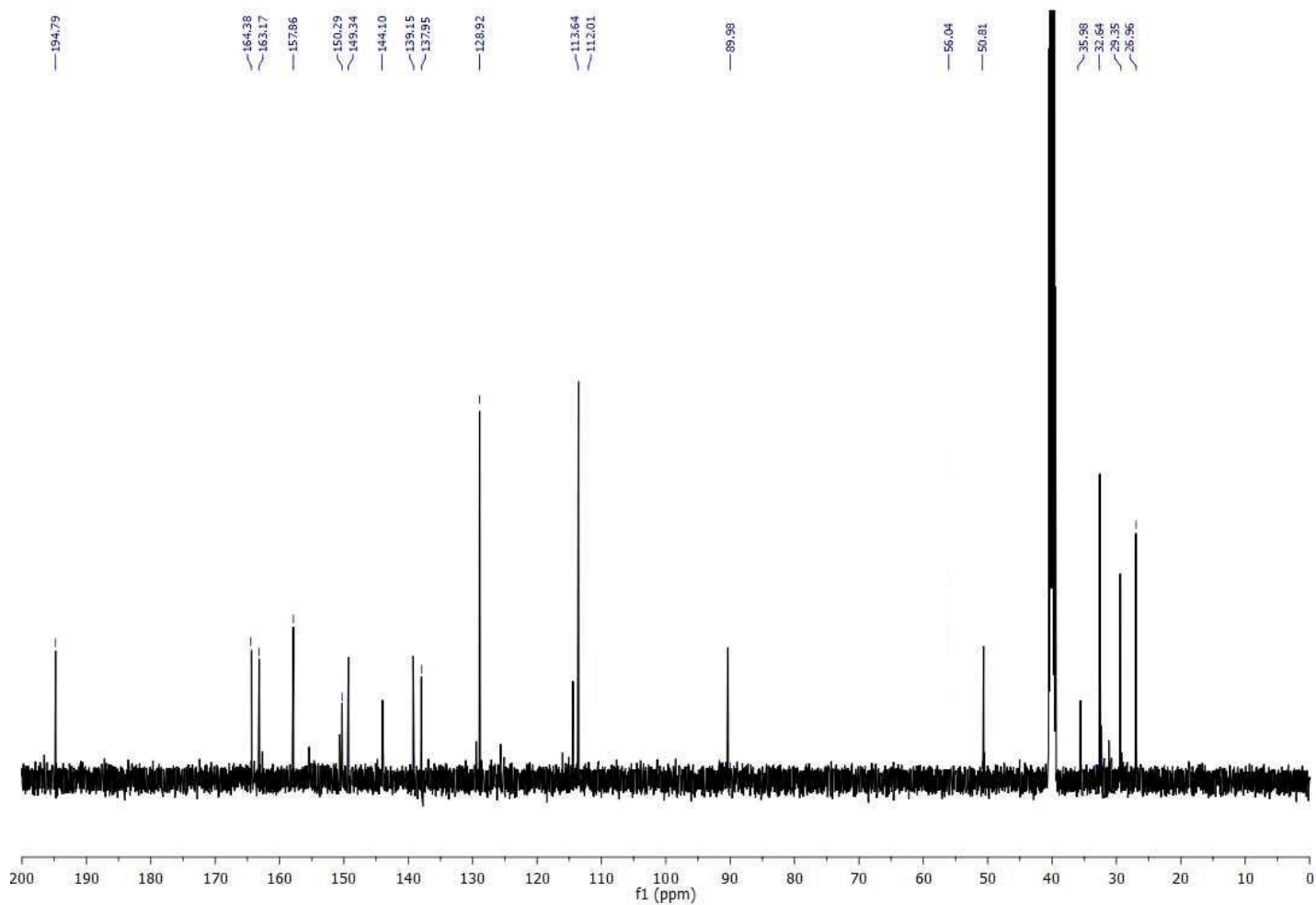


Figure S10.  $^{13}\text{C}$  NMR spectrum of compound 4e



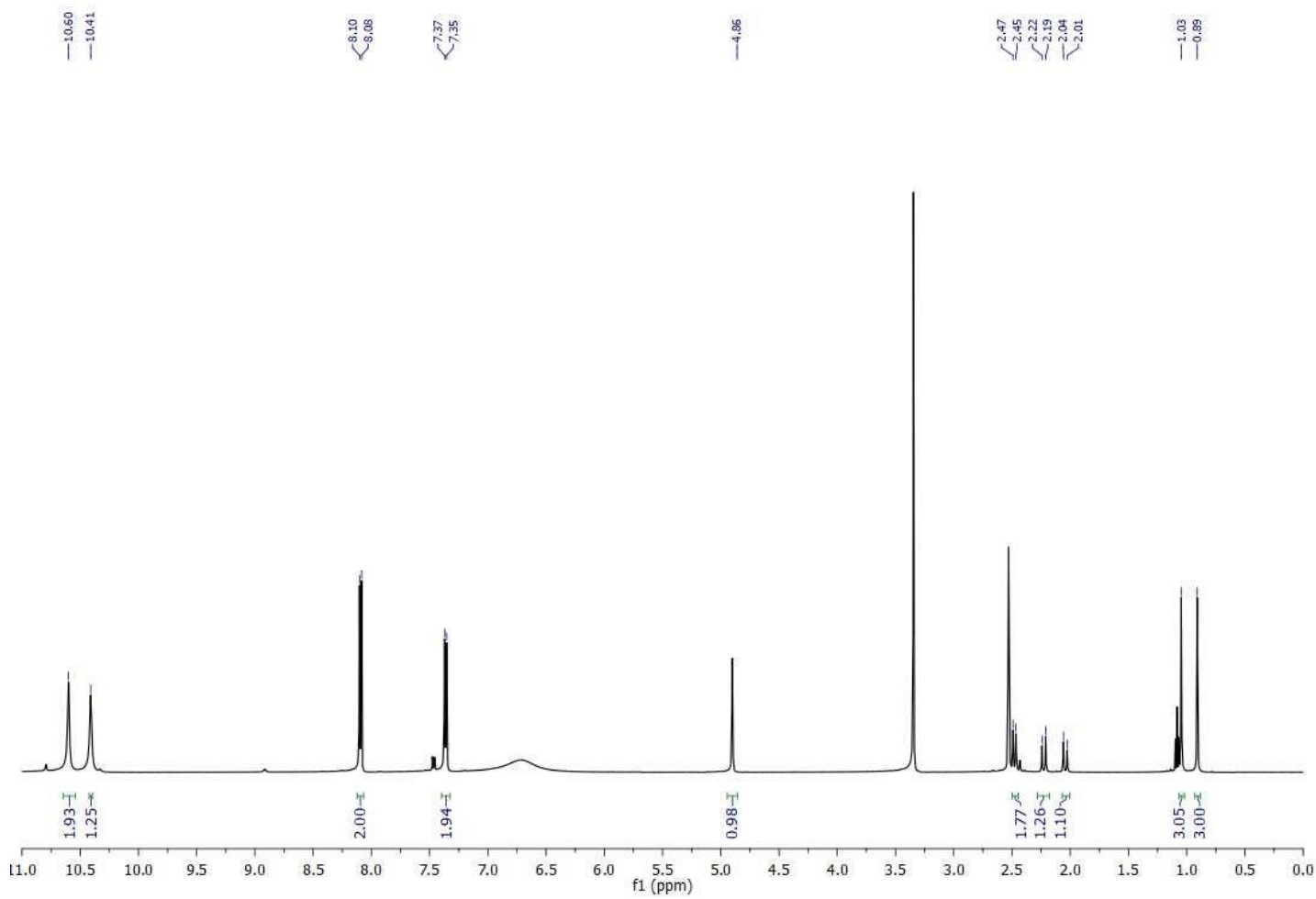


Figure S11. <sup>1</sup>H NMR spectrum of compound 4f

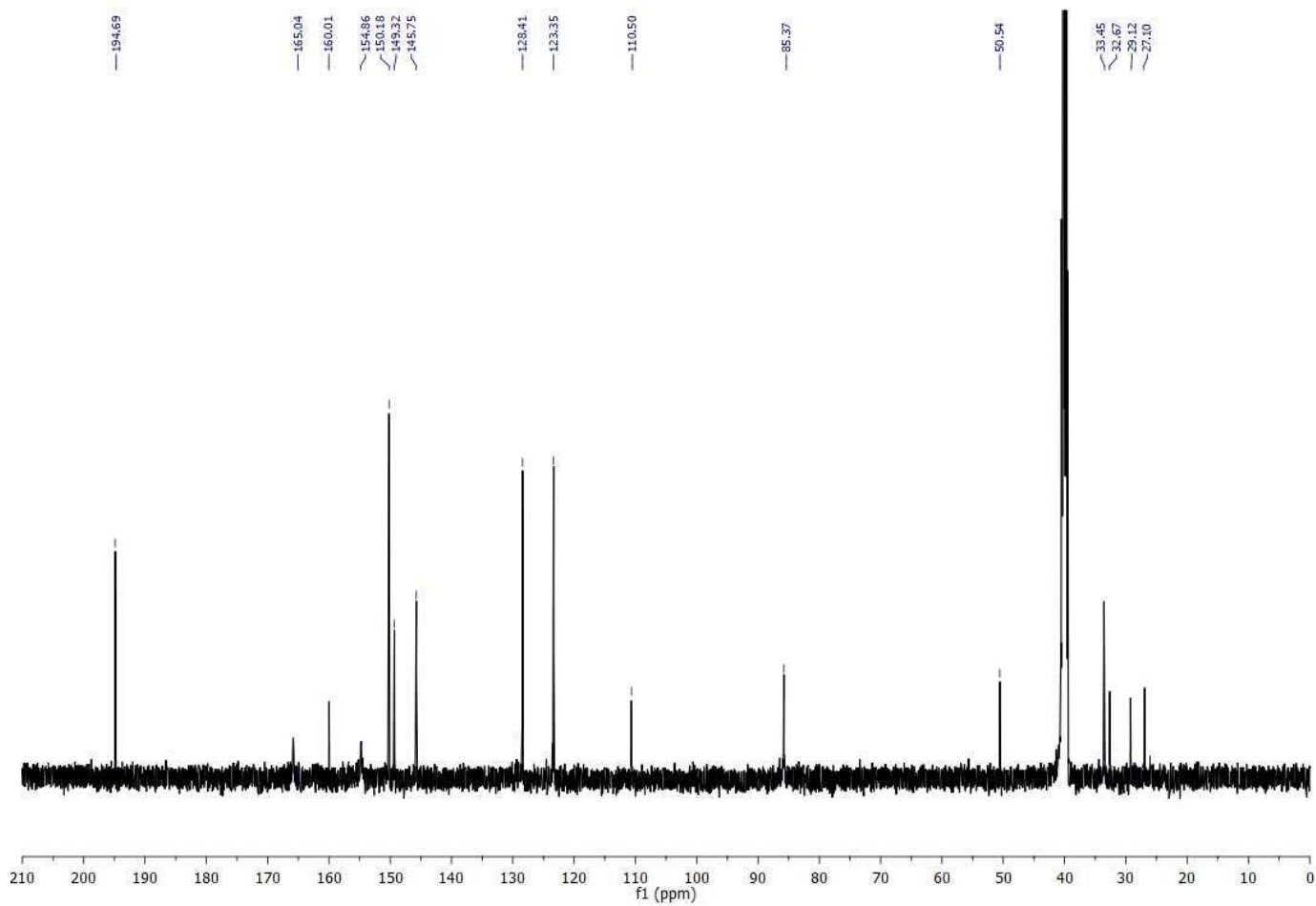


Figure S12.  $^{13}\text{C}$  NMR spectrum of compound 4f

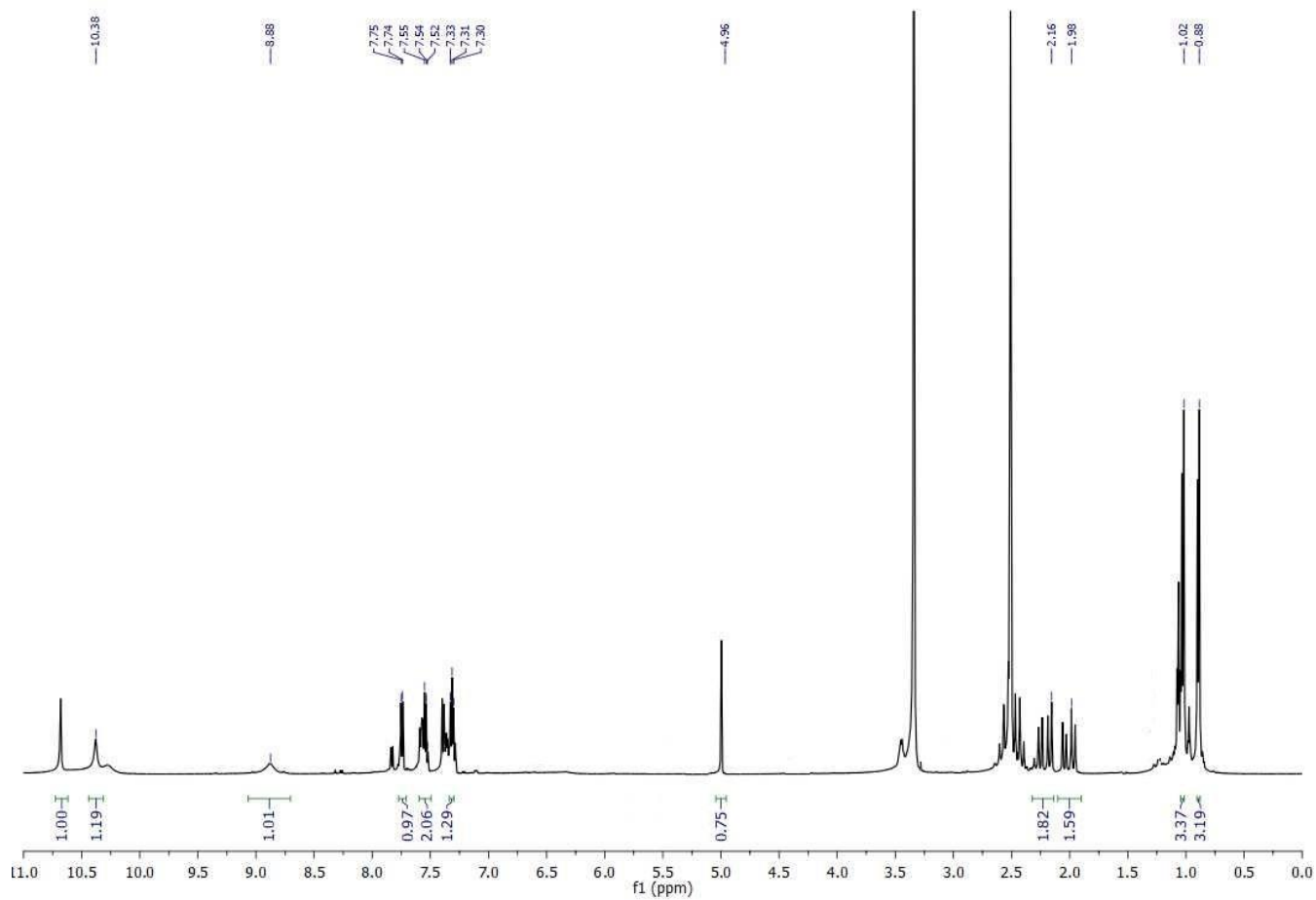


Figure S13. <sup>1</sup>H NMR spectrum of compound 4g

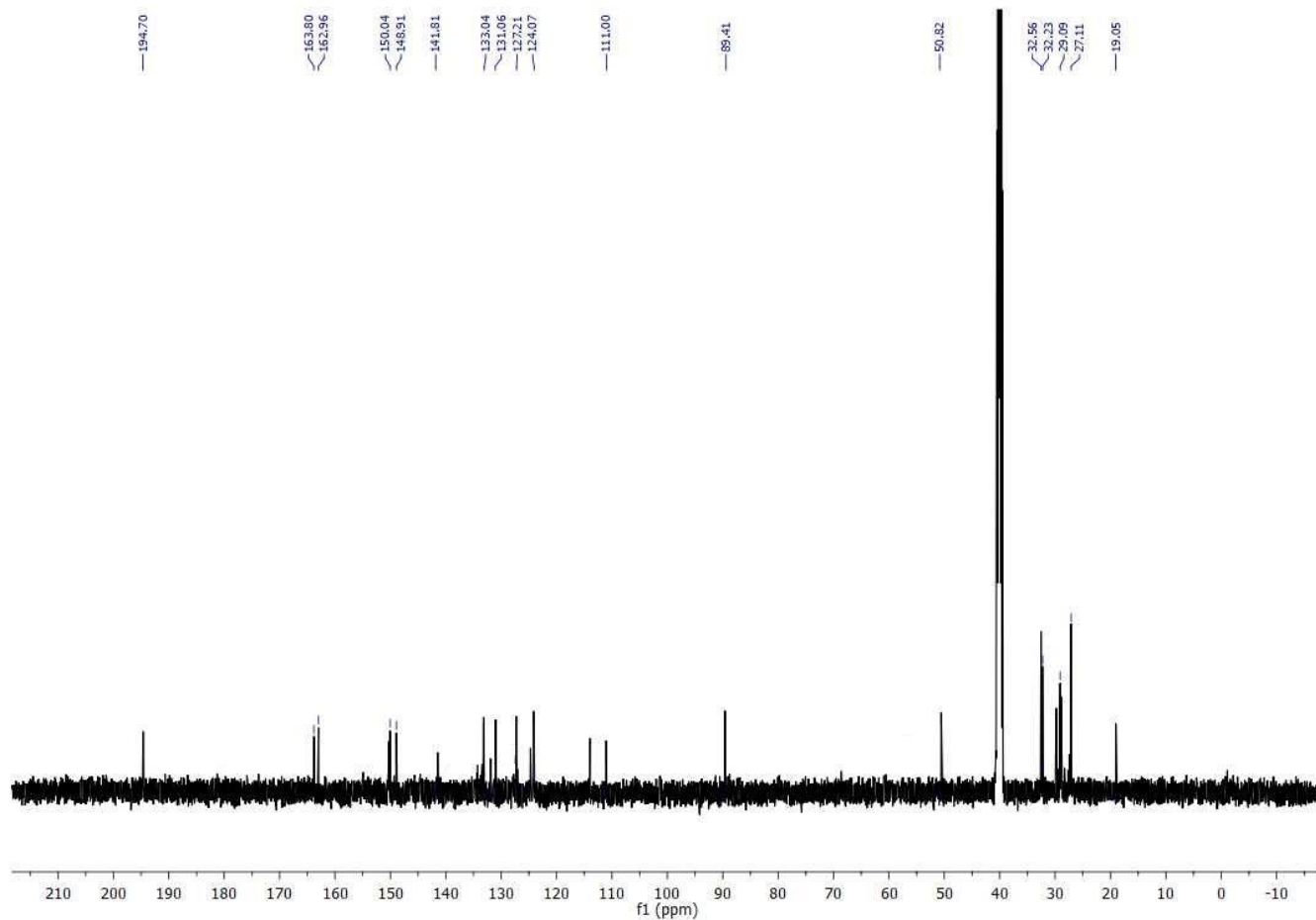


Figure S14.  $^{13}\text{C}$  NMR spectrum of compound 4g

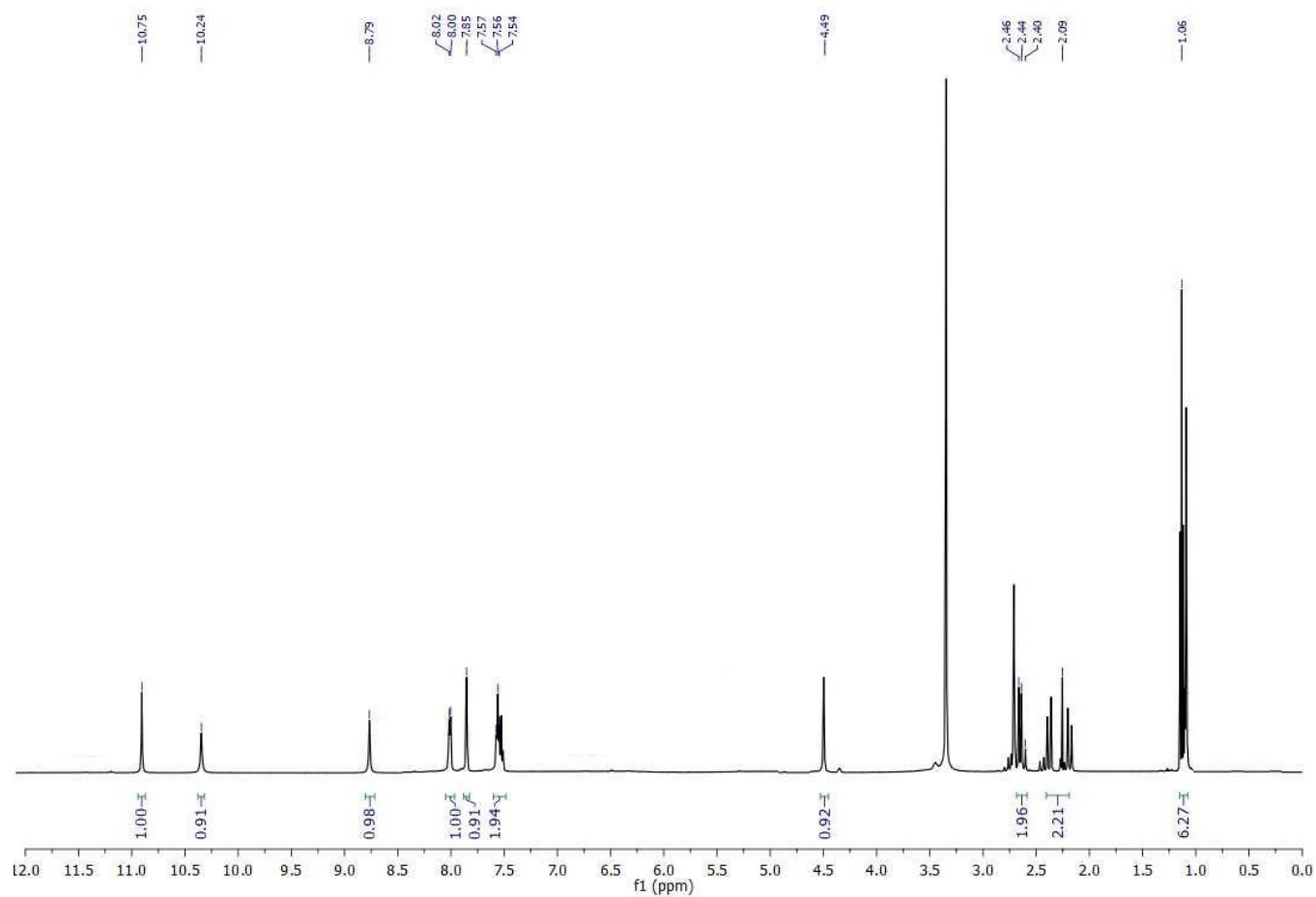


Figure S15. <sup>1</sup>H NMR spectrum of compound 4h

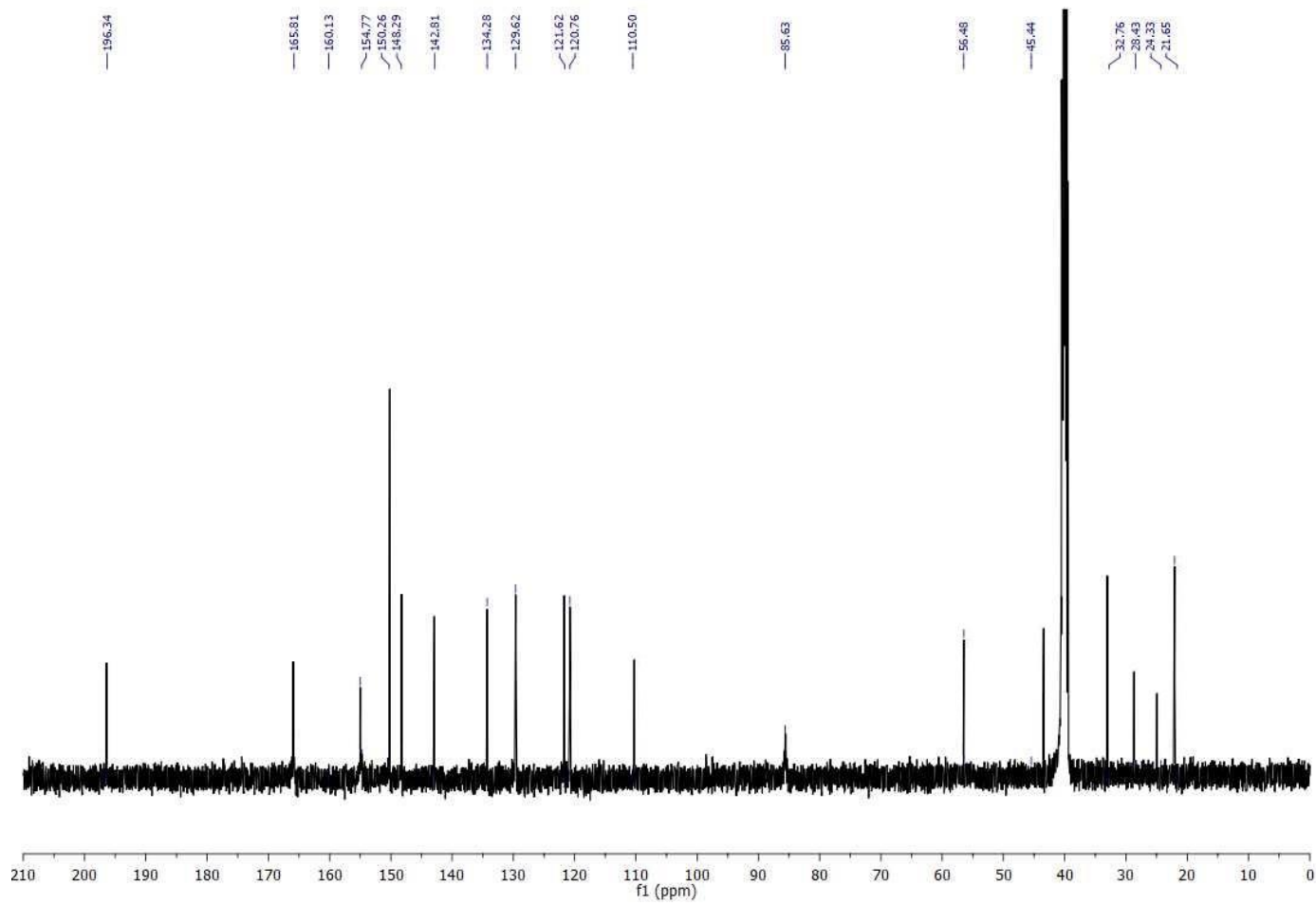


Figure S16.  $^{13}\text{C}$  NMR spectrum of compound 4h

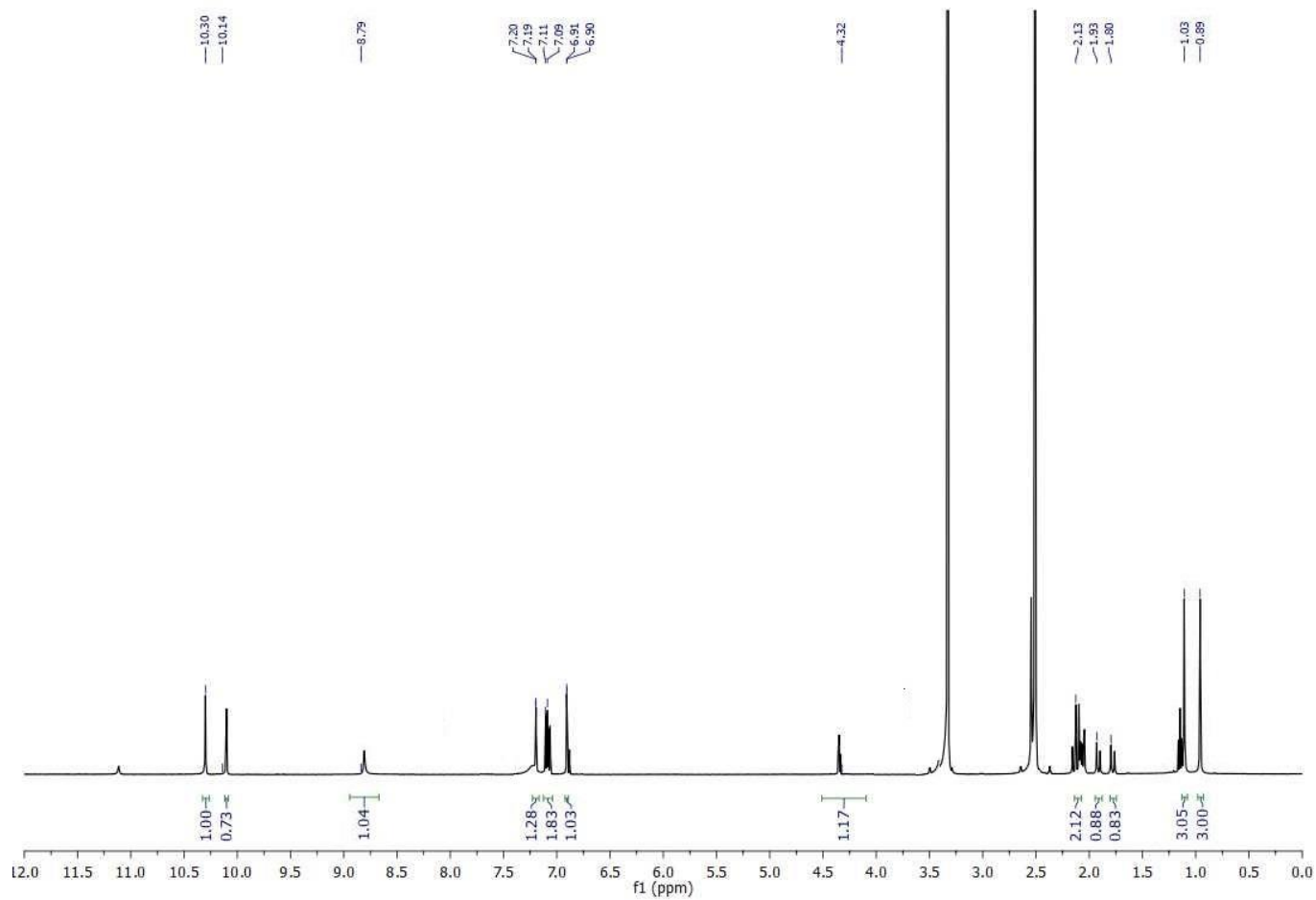


Figure S17. <sup>1</sup>H NMR spectrum of compound 4i

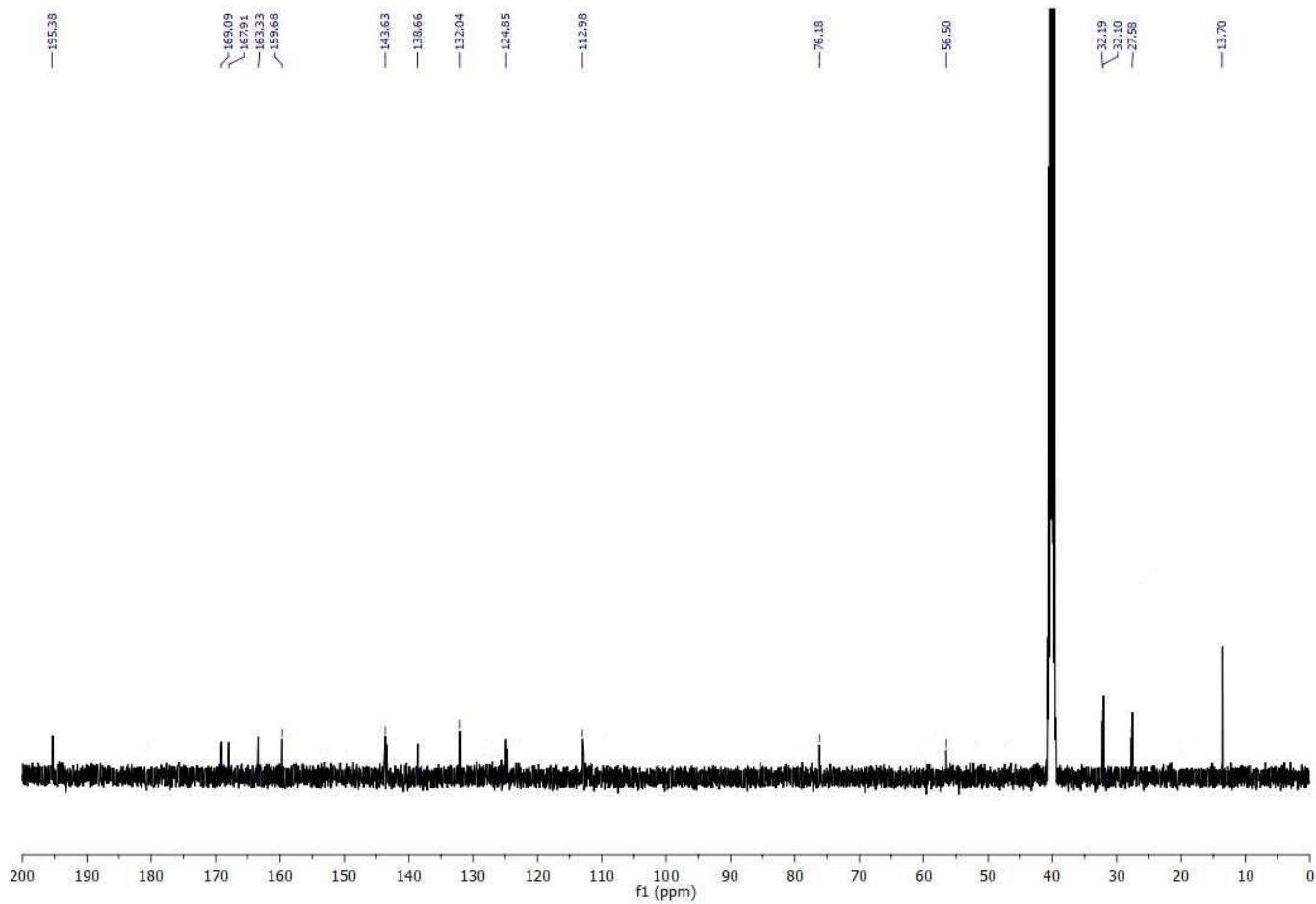


Figure S18.  $^{13}\text{C}$  NMR spectrum of compound 4i



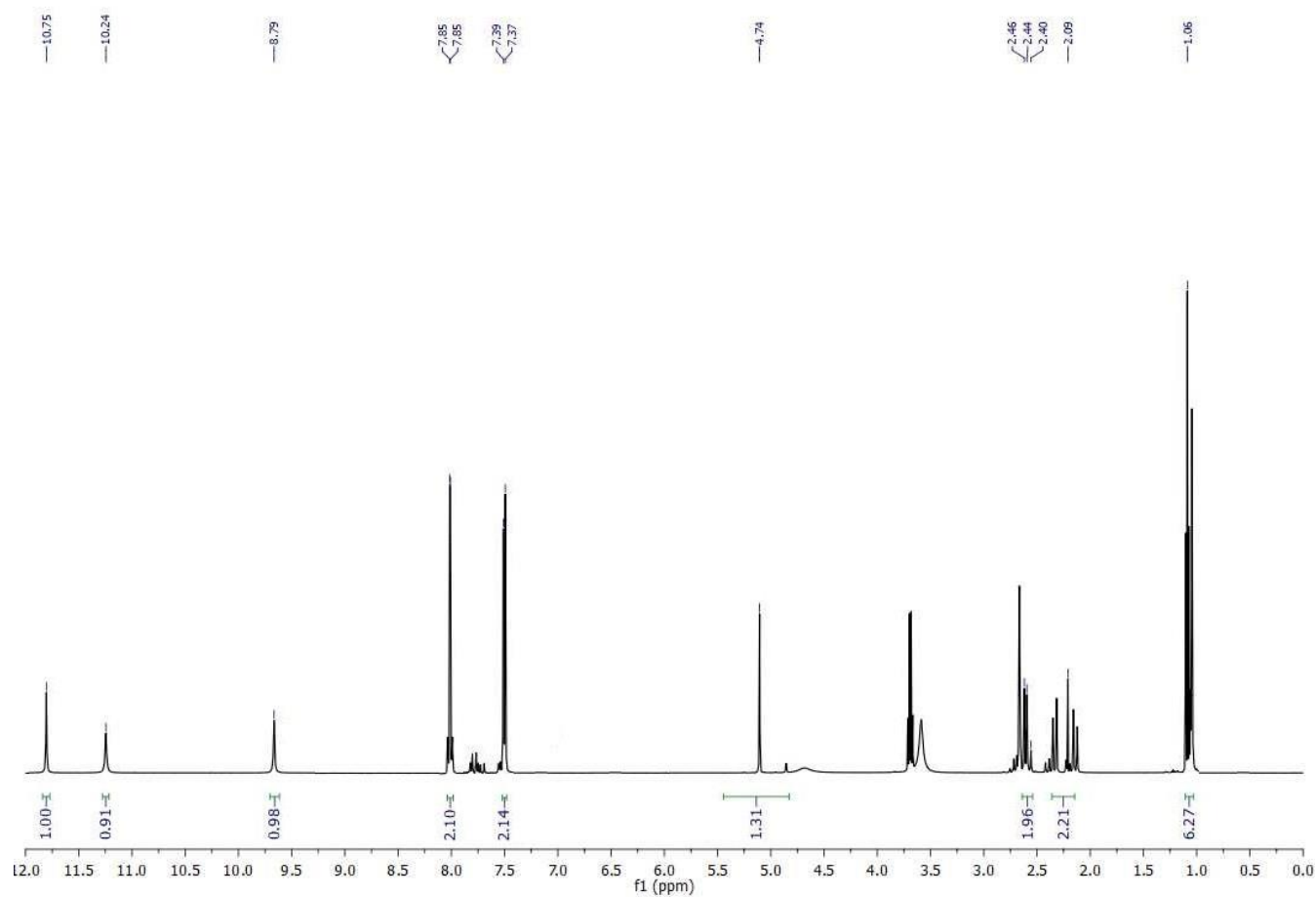


Figure S19. <sup>1</sup>H NMR spectrum of compound 4j

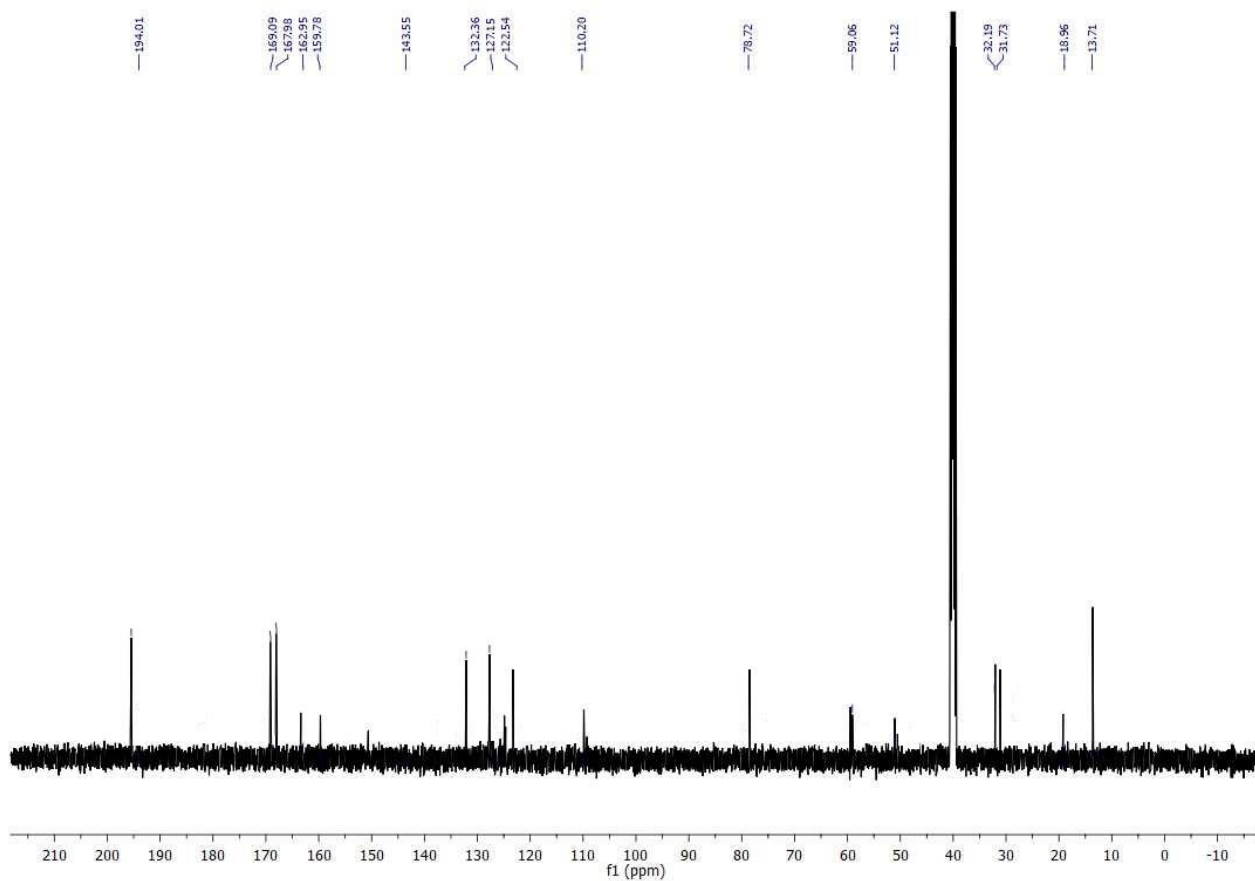


Figure S20.  $^{13}\text{C}$  NMR spectrum of compound 4j

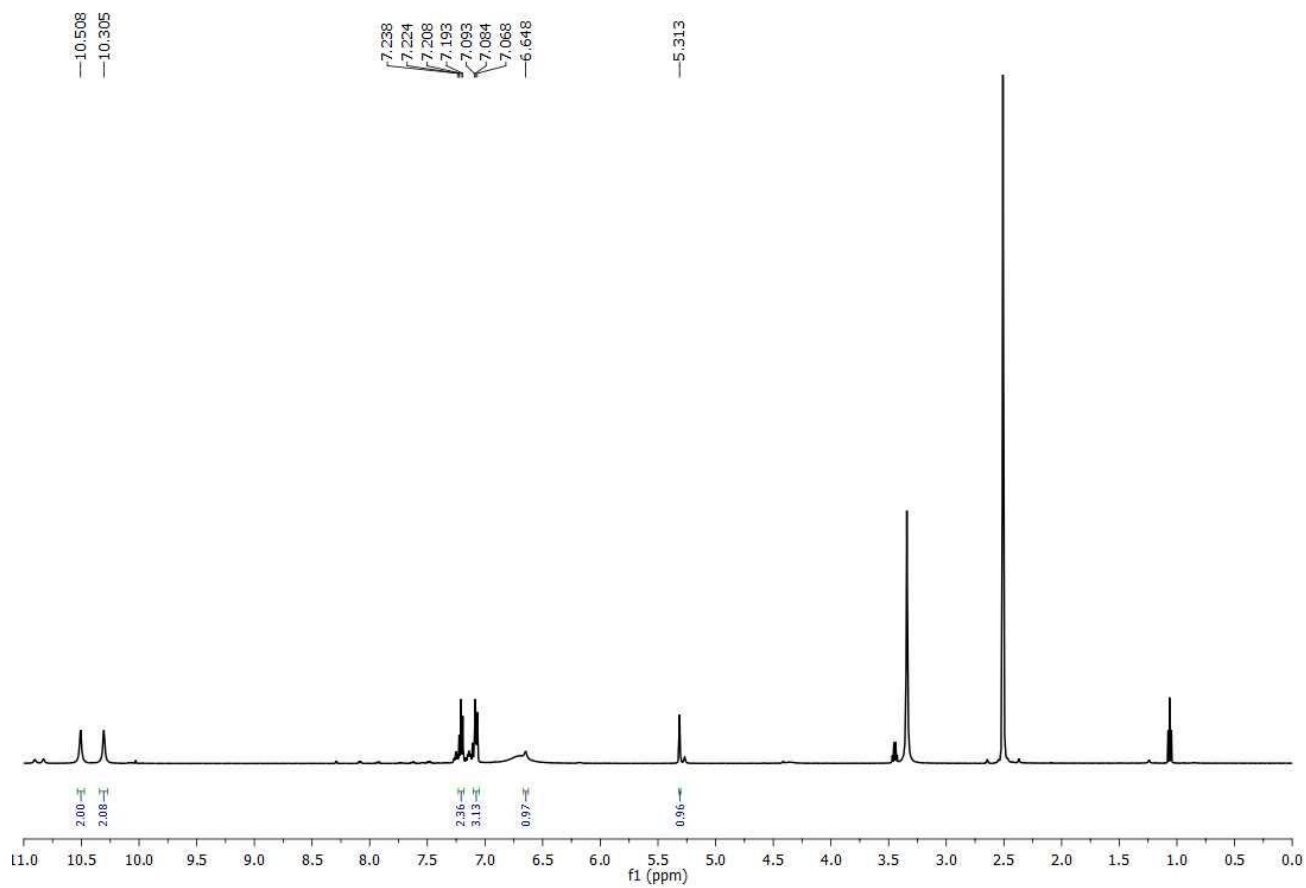


Figure S21. <sup>1</sup>H NMR spectrum of compound 41

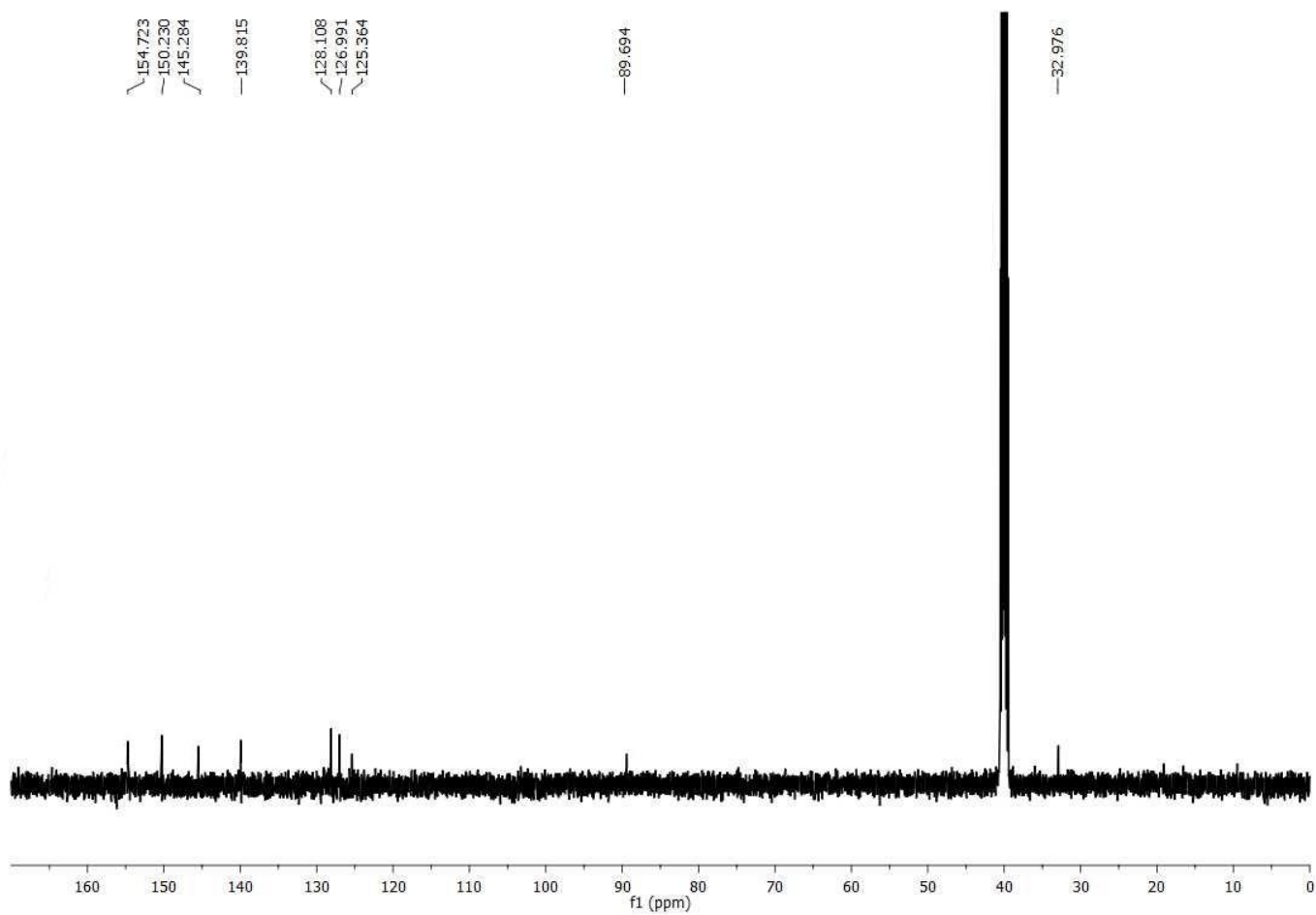


Figure S22.  $^{13}\text{C}$  NMR spectrum of compound 41

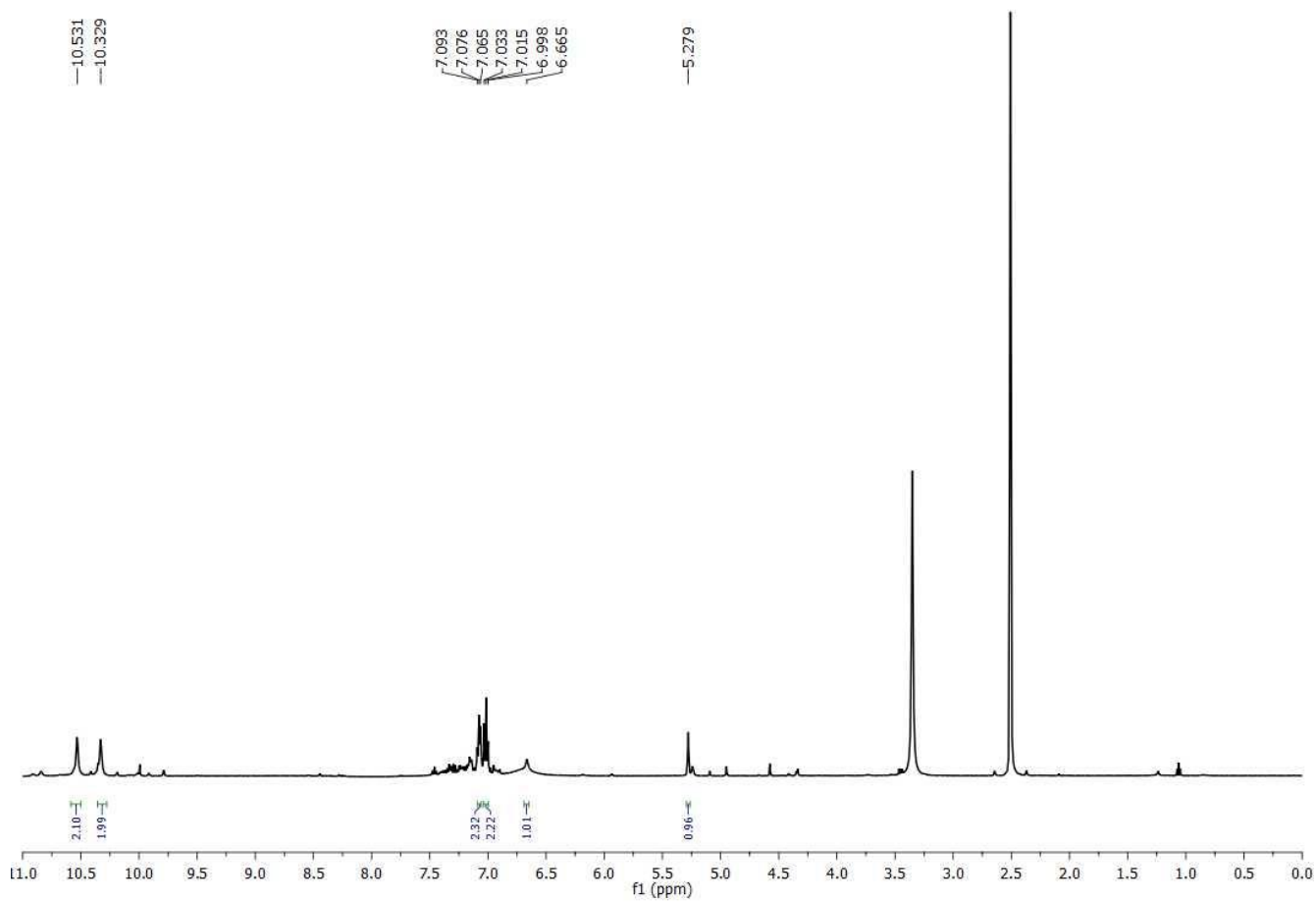


Figure S23. <sup>1</sup>H NMR spectrum of compound 4m

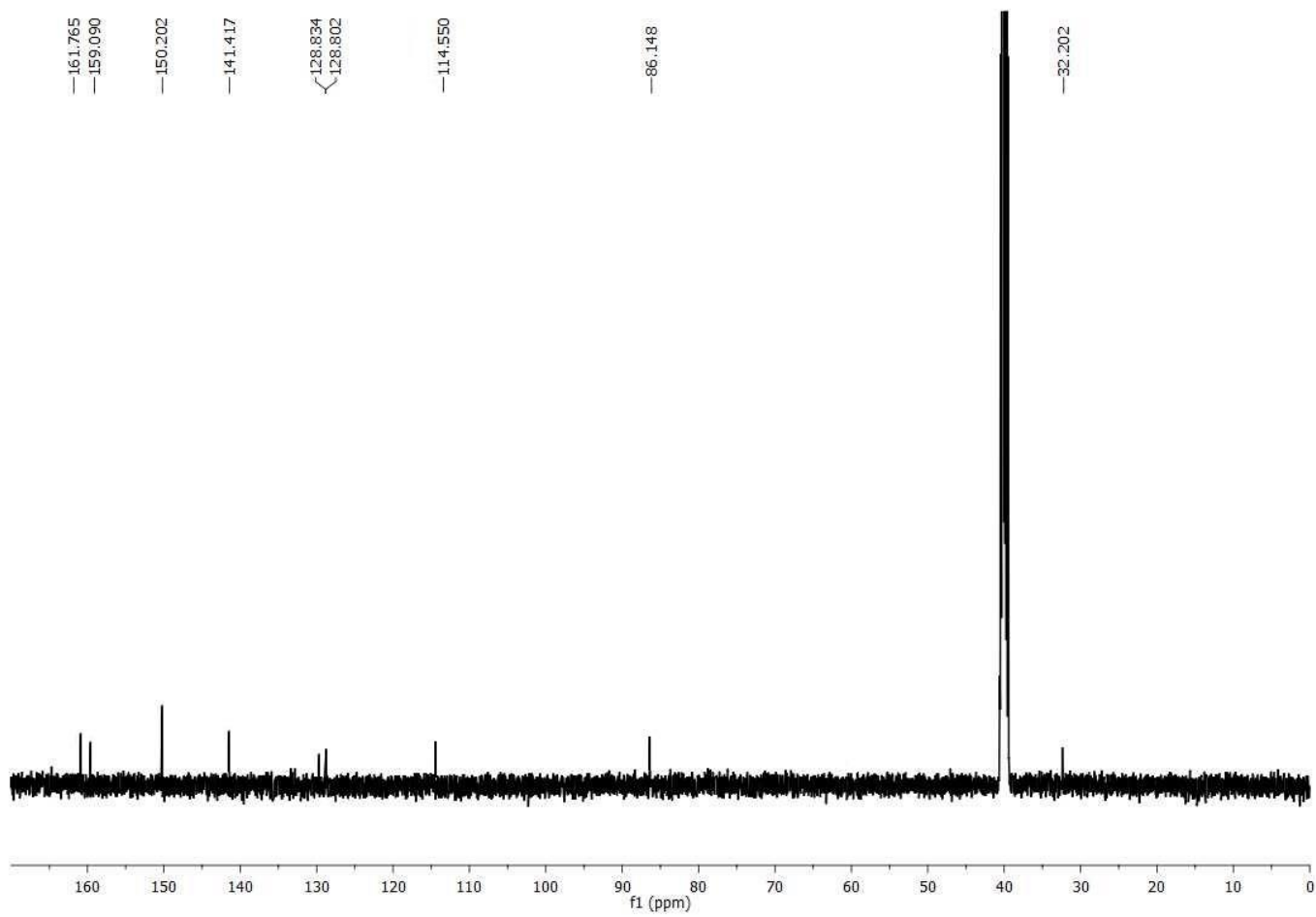


Figure S24.  $^{13}\text{C}$  NMR spectrum of compound 4m

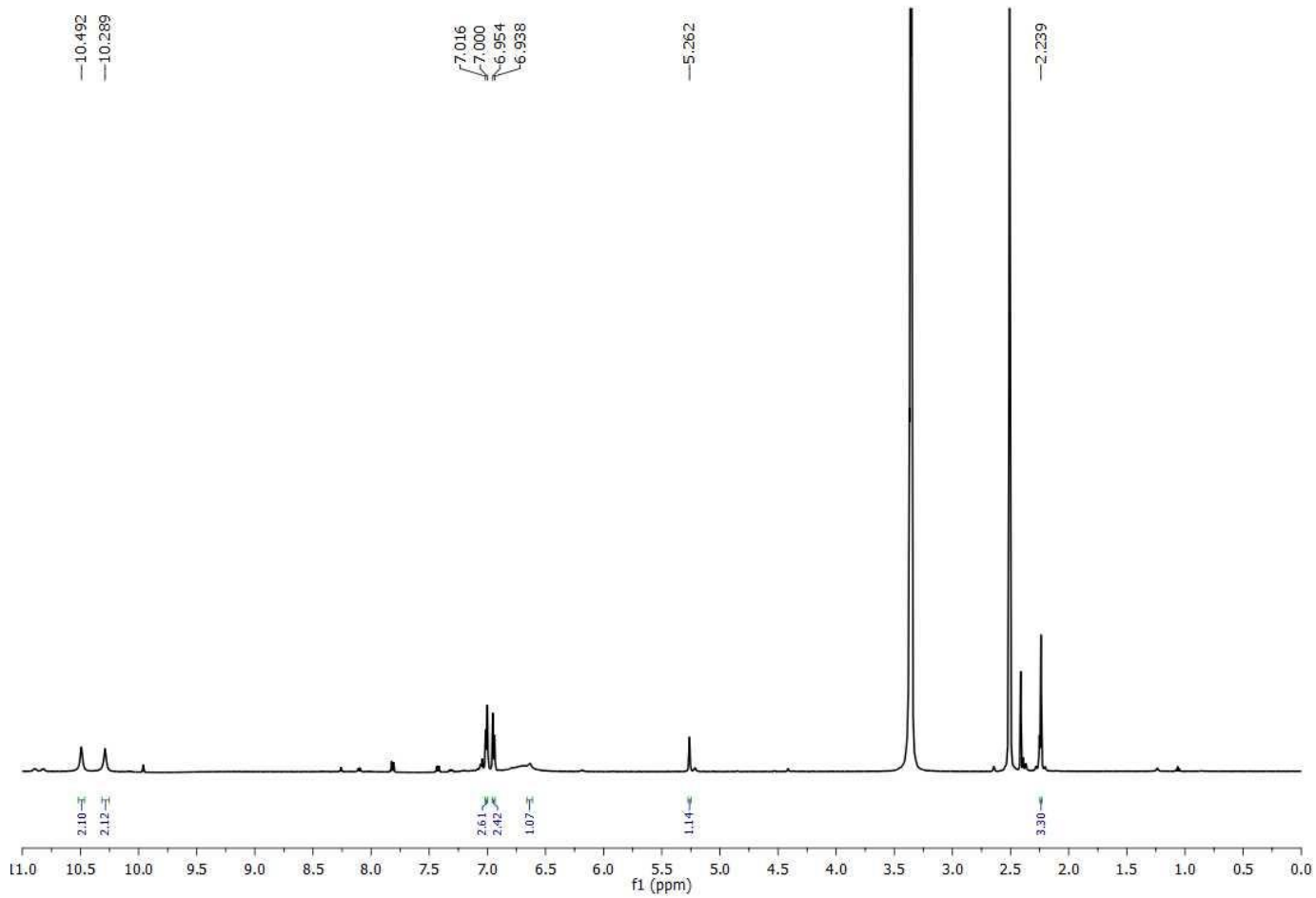


Figure S25. <sup>1</sup>H NMR spectrum of compound 4n

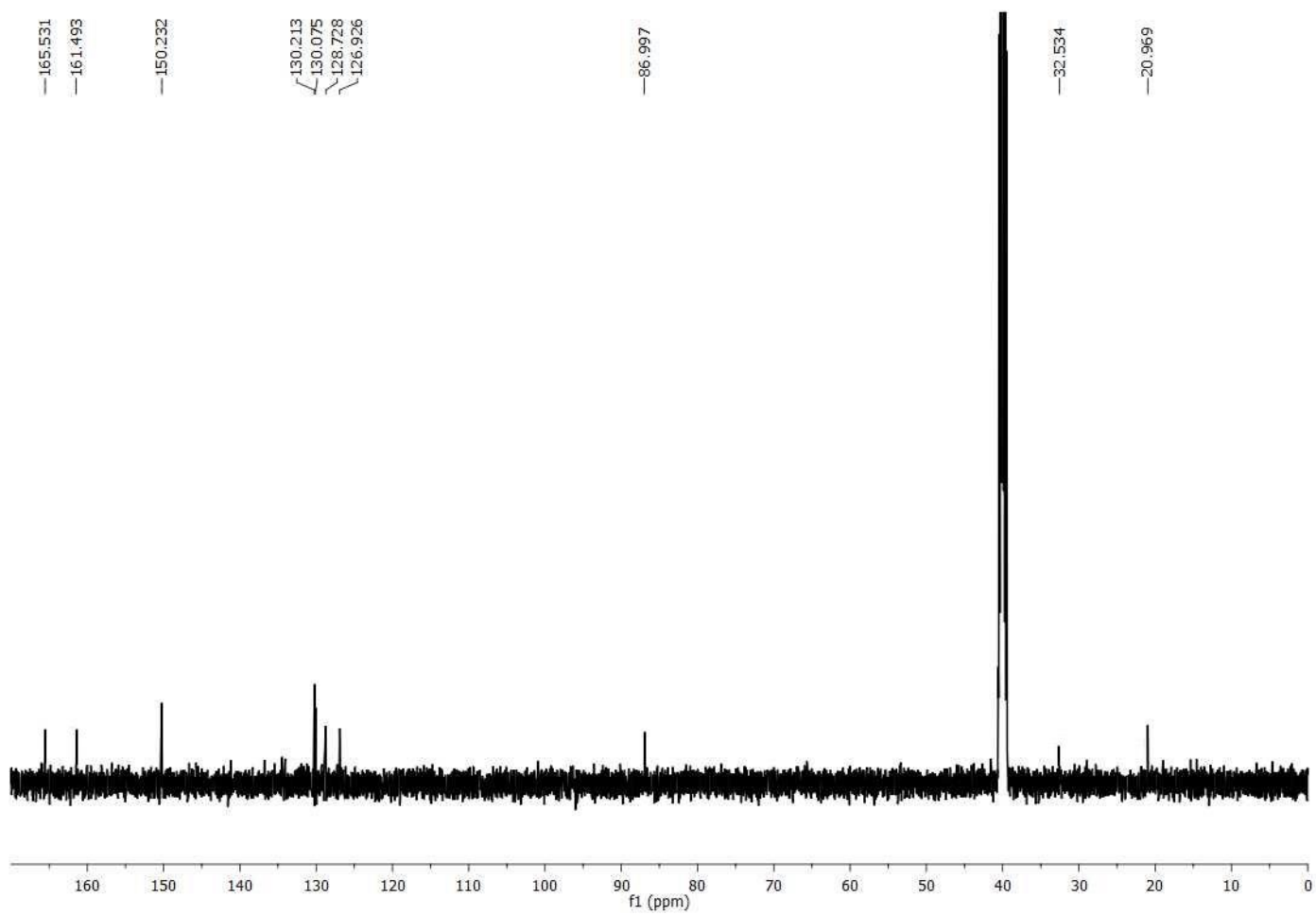


Figure S26.  $^{13}\text{C}$  NMR spectrum of compound 4n



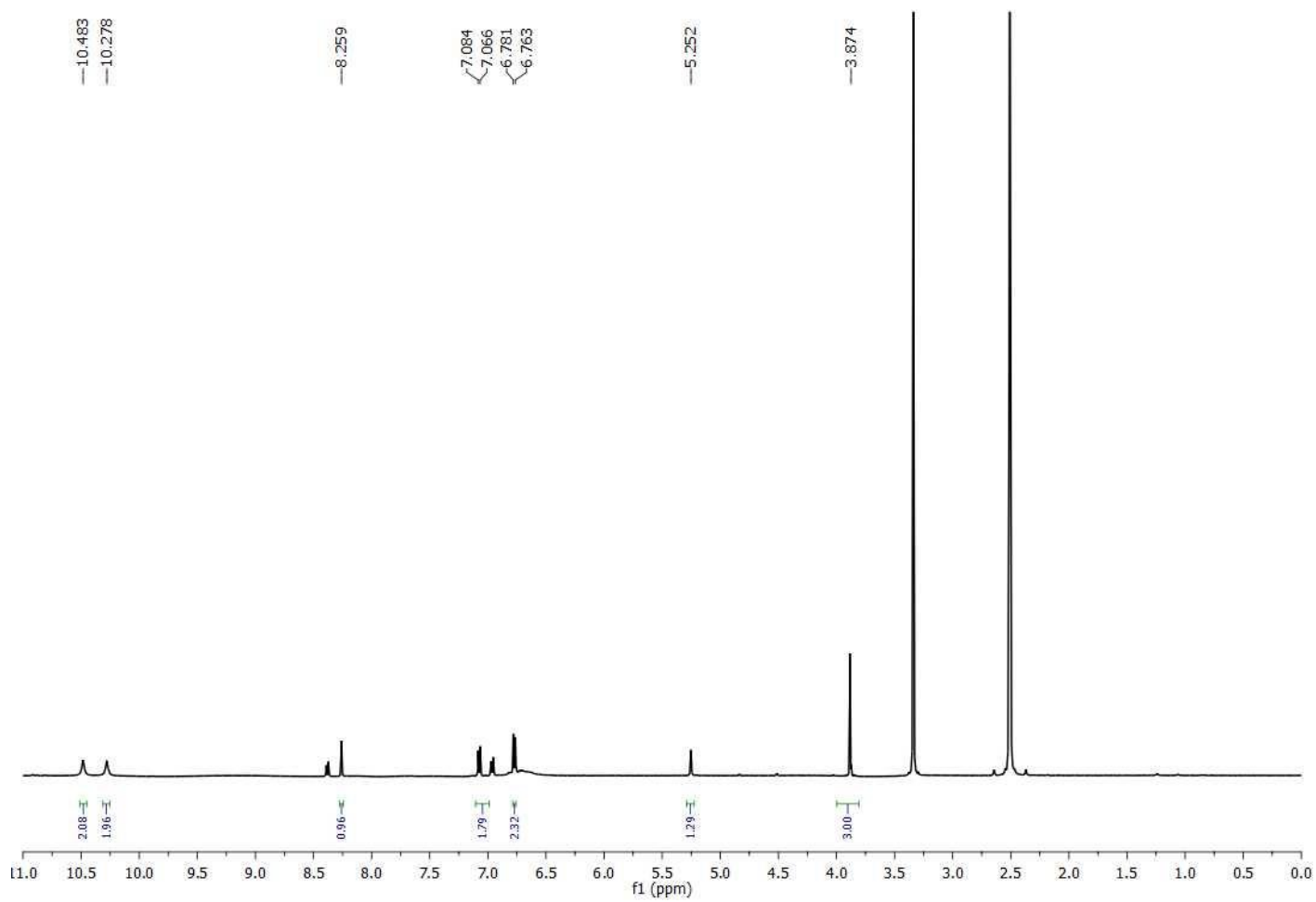


Figure S27. <sup>1</sup>H NMR spectrum of compound 4o

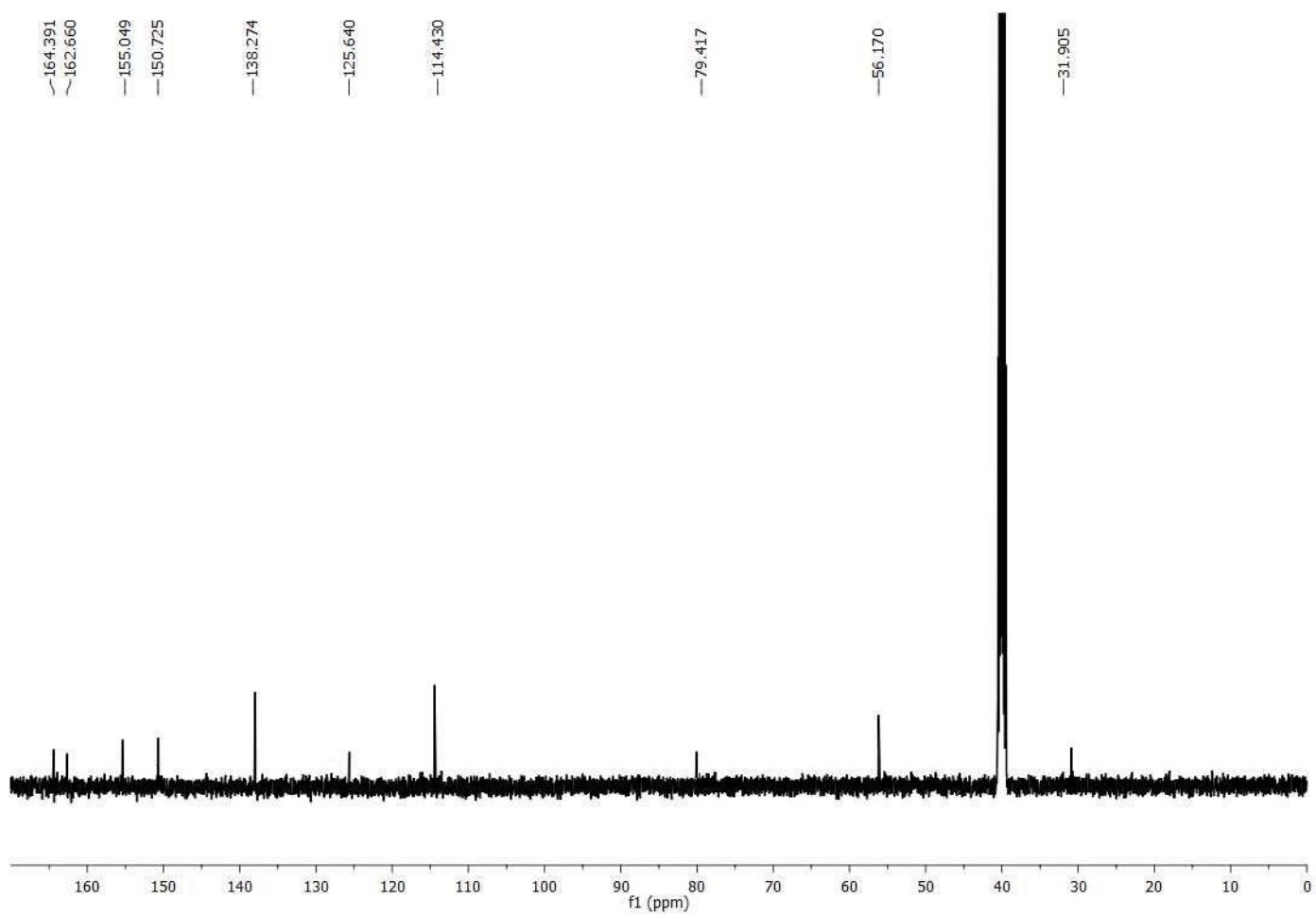


Figure S28.  $^{13}\text{C}$  NMR spectrum of compound 4o

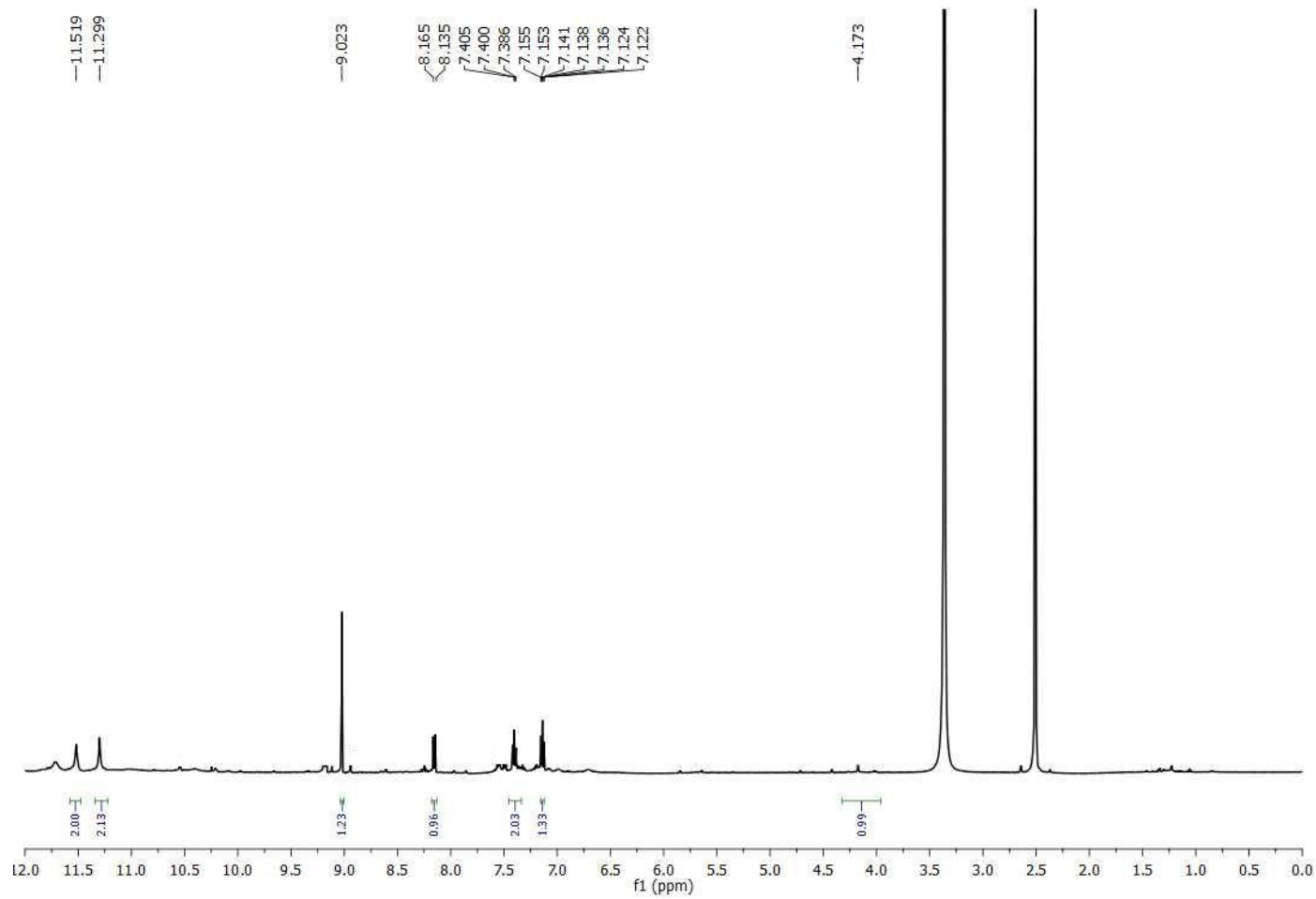


Figure S29. <sup>1</sup>H NMR spectrum of compound 4p

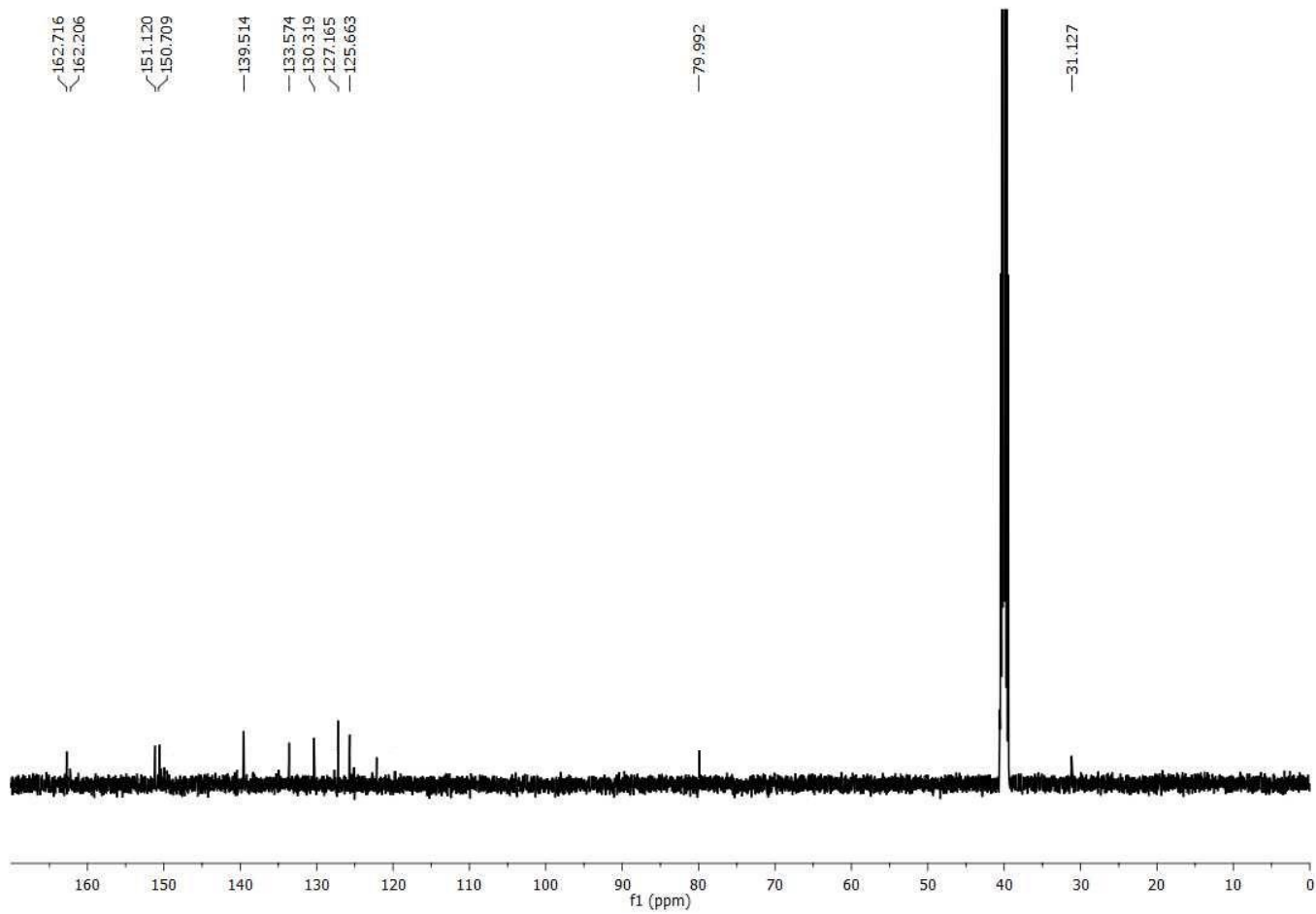


Figure S30.  $^{13}\text{C}$  NMR spectrum of compound 4p

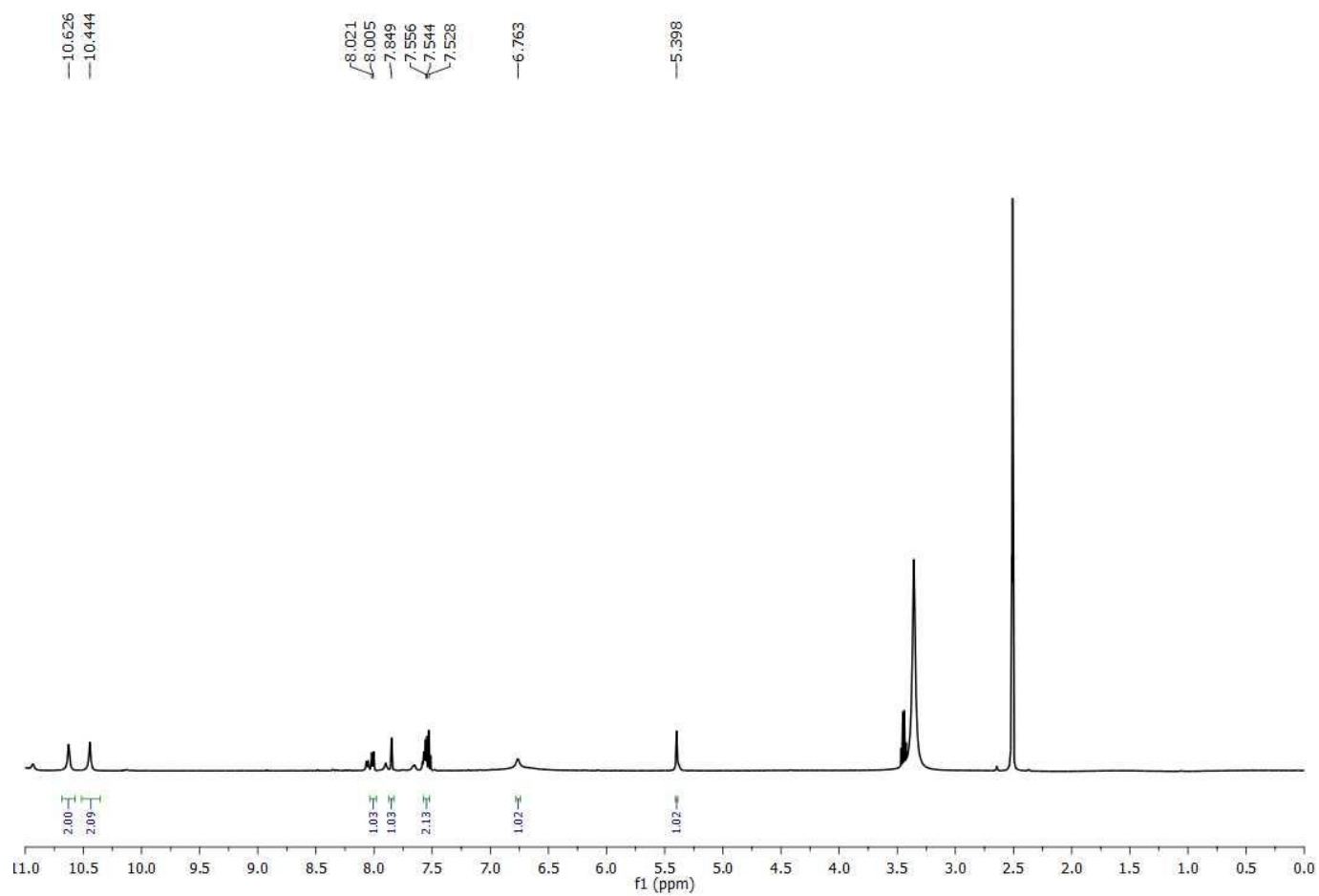


Figure S31.  $^1\text{H}$  NMR spectrum of compound 4q

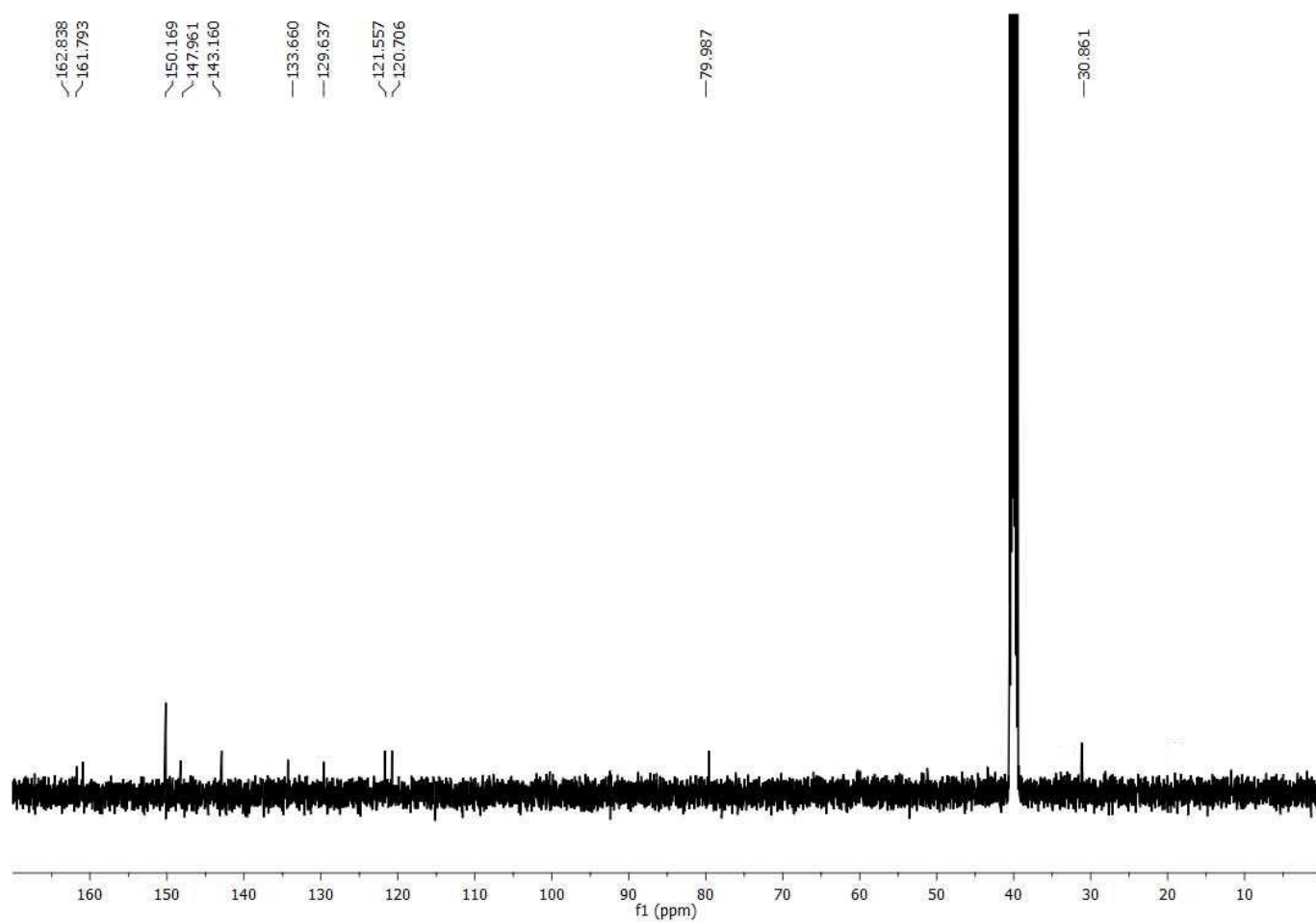


Figure S32.  $^{13}\text{C}$  NMR spectrum of compound 4q

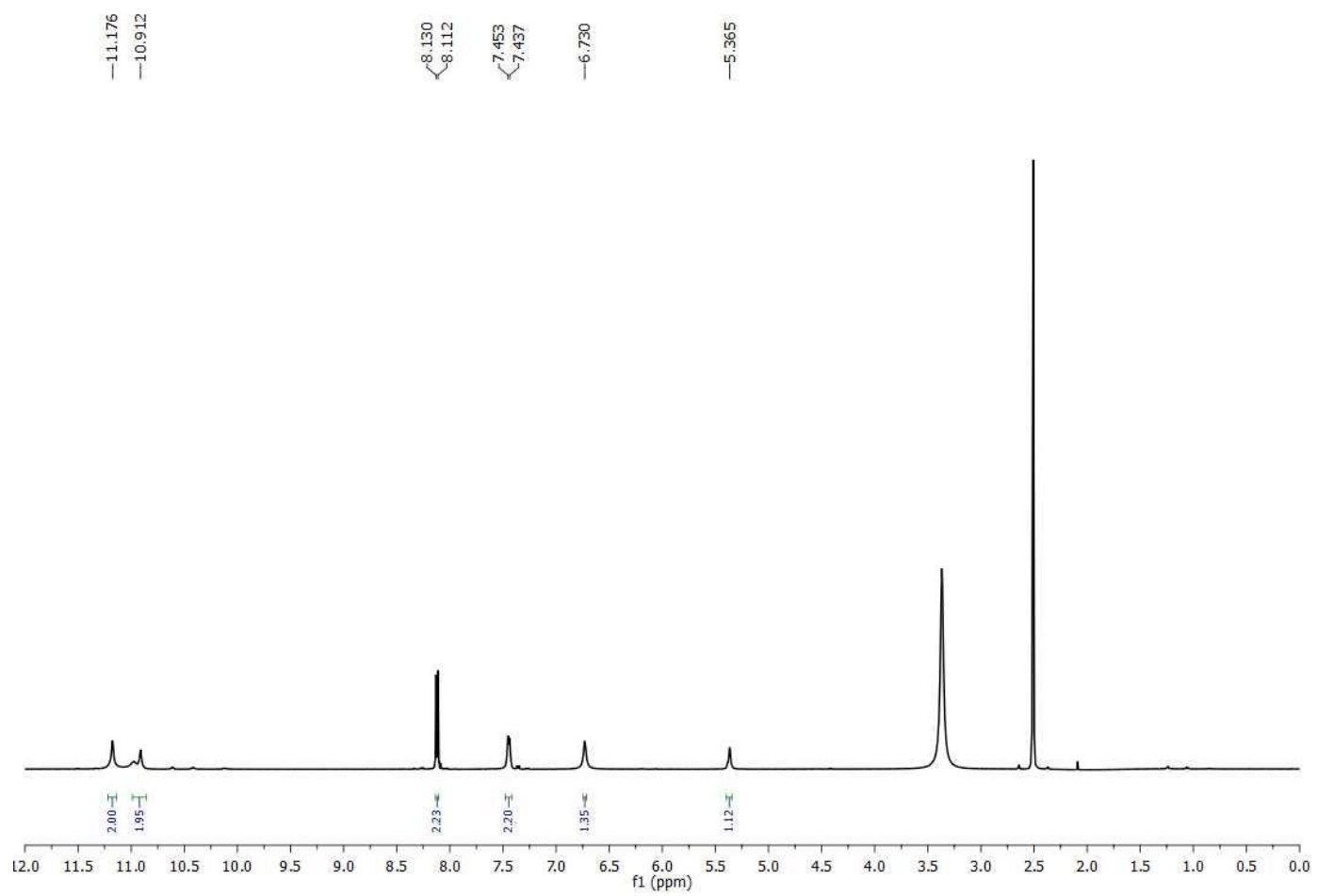


Figure S33. <sup>1</sup>H NMR spectrum of compound 4r

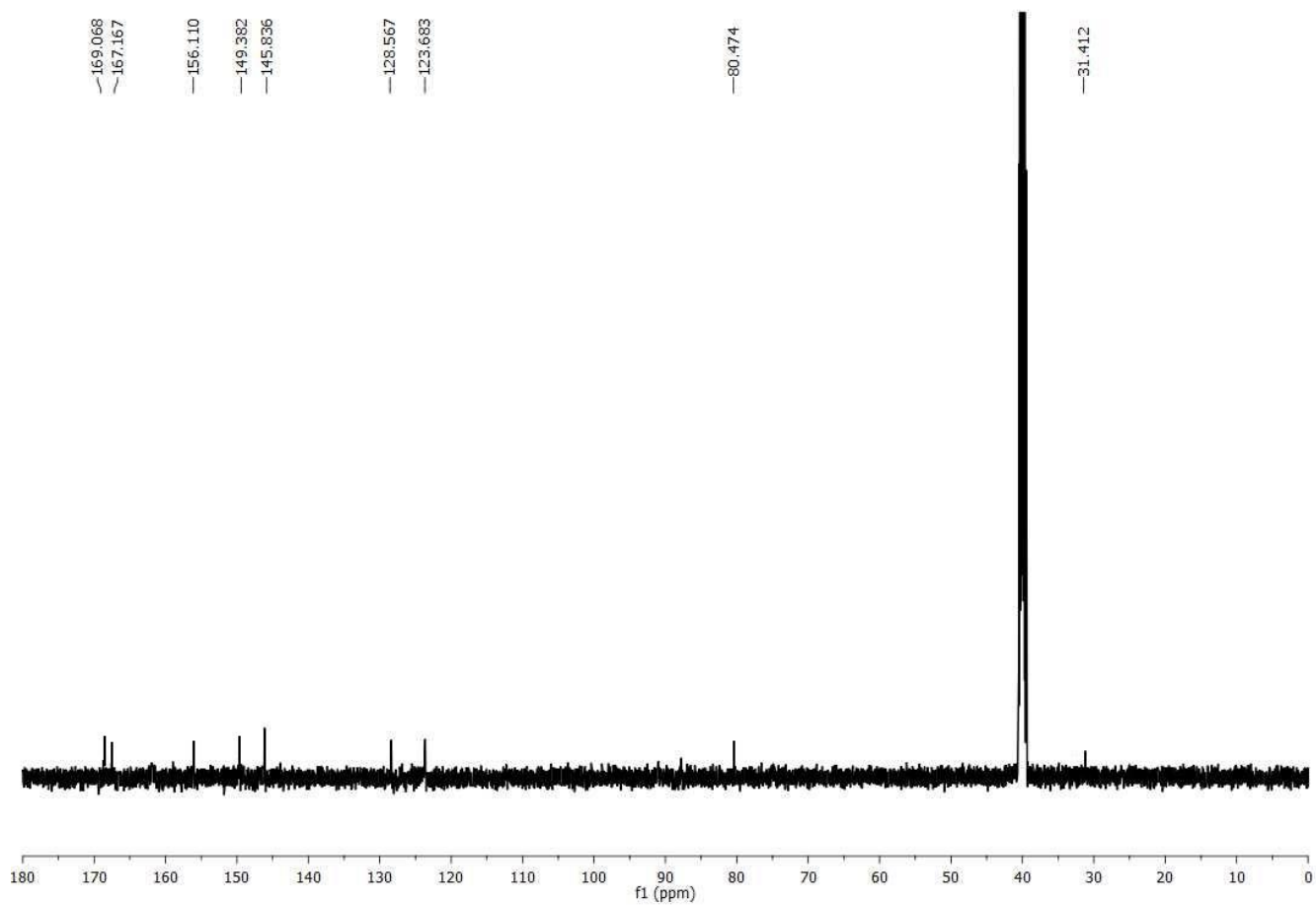


Figure S34.  $^{13}\text{C}$  NMR spectrum of compound 4r



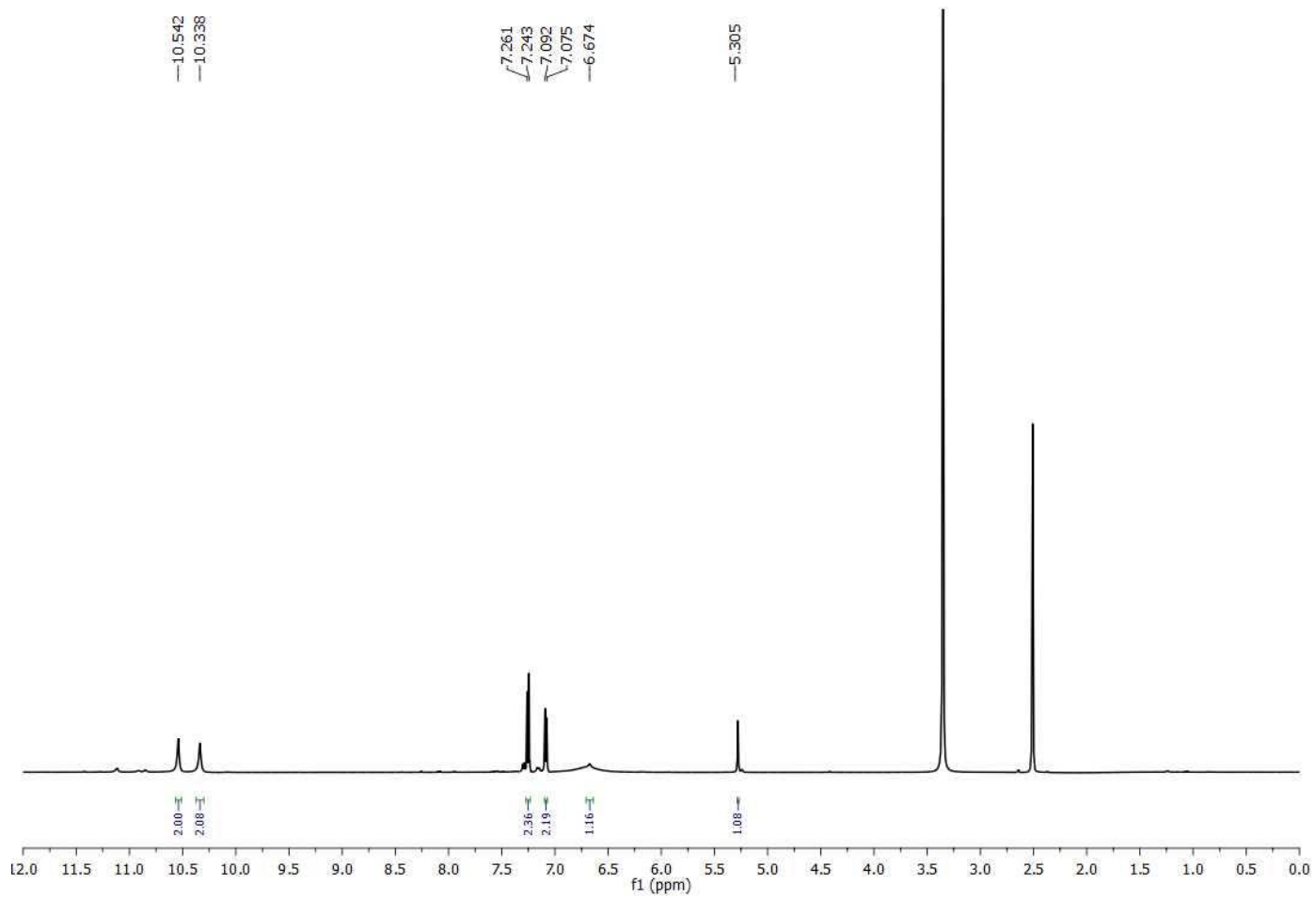


Figure S35. <sup>1</sup>H NMR spectrum of compound 4s

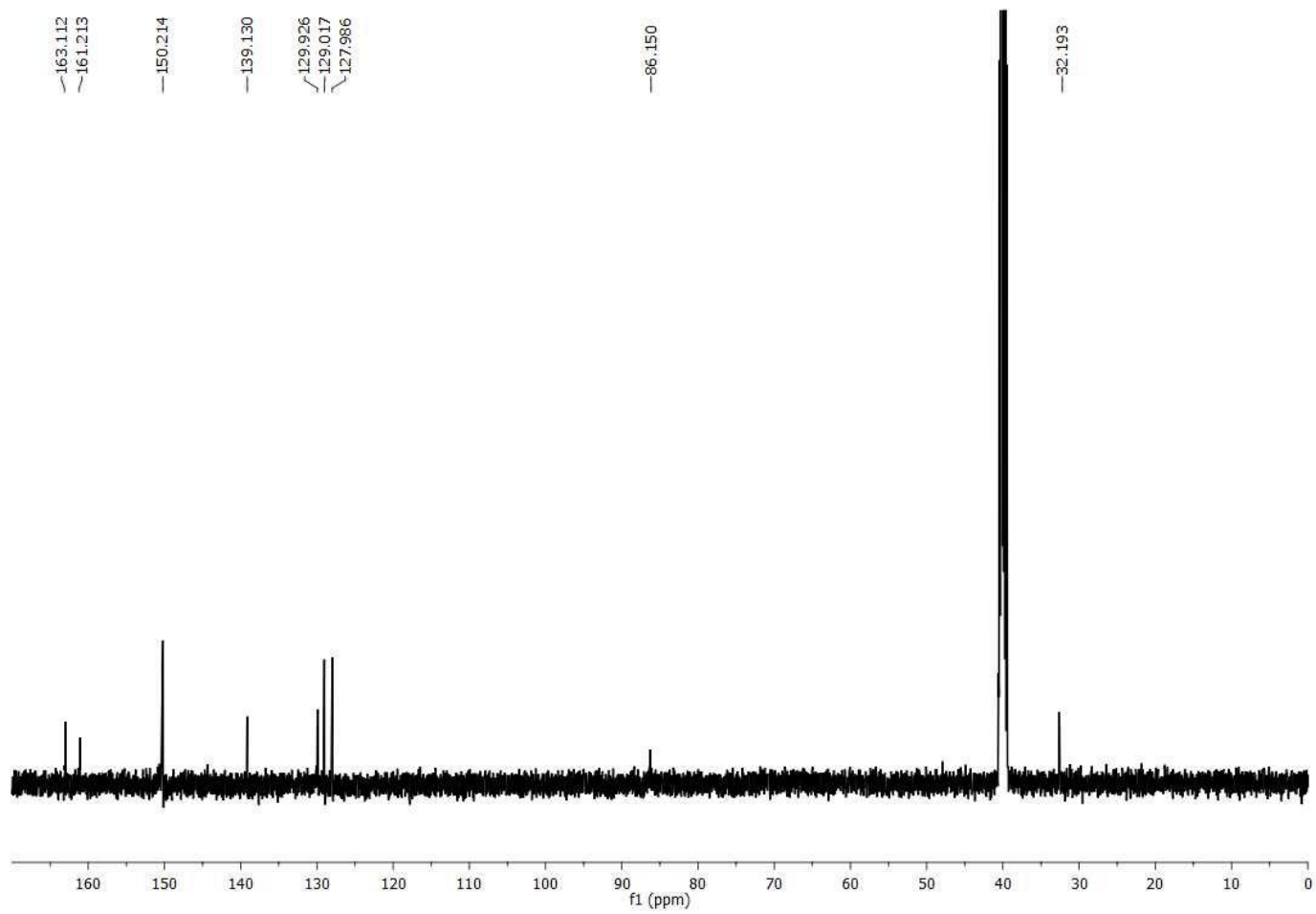


Figure S36.  $^{13}\text{C}$  NMR spectrum of compound 4s

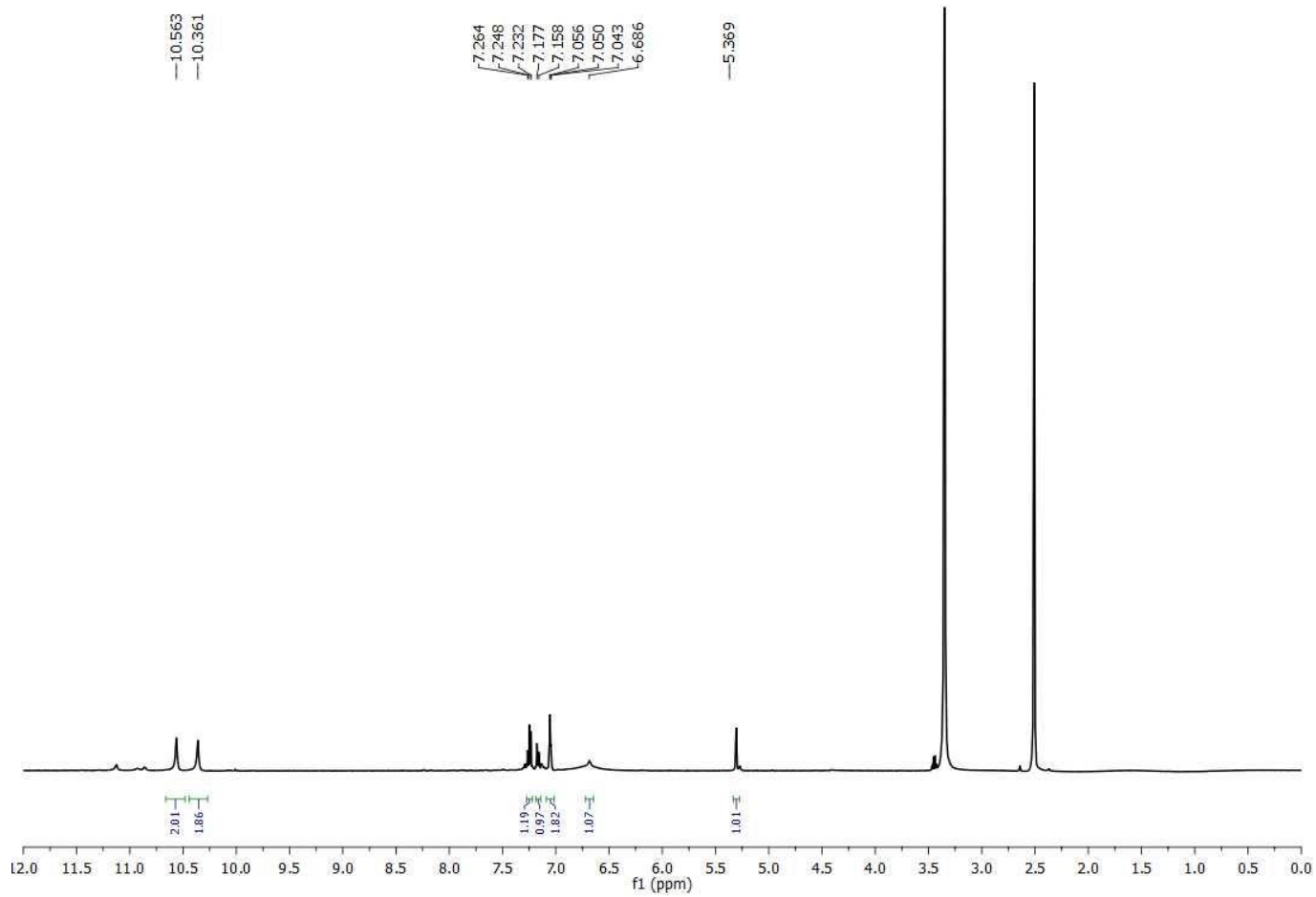


Figure S37. <sup>1</sup>H NMR spectrum of compound 4t

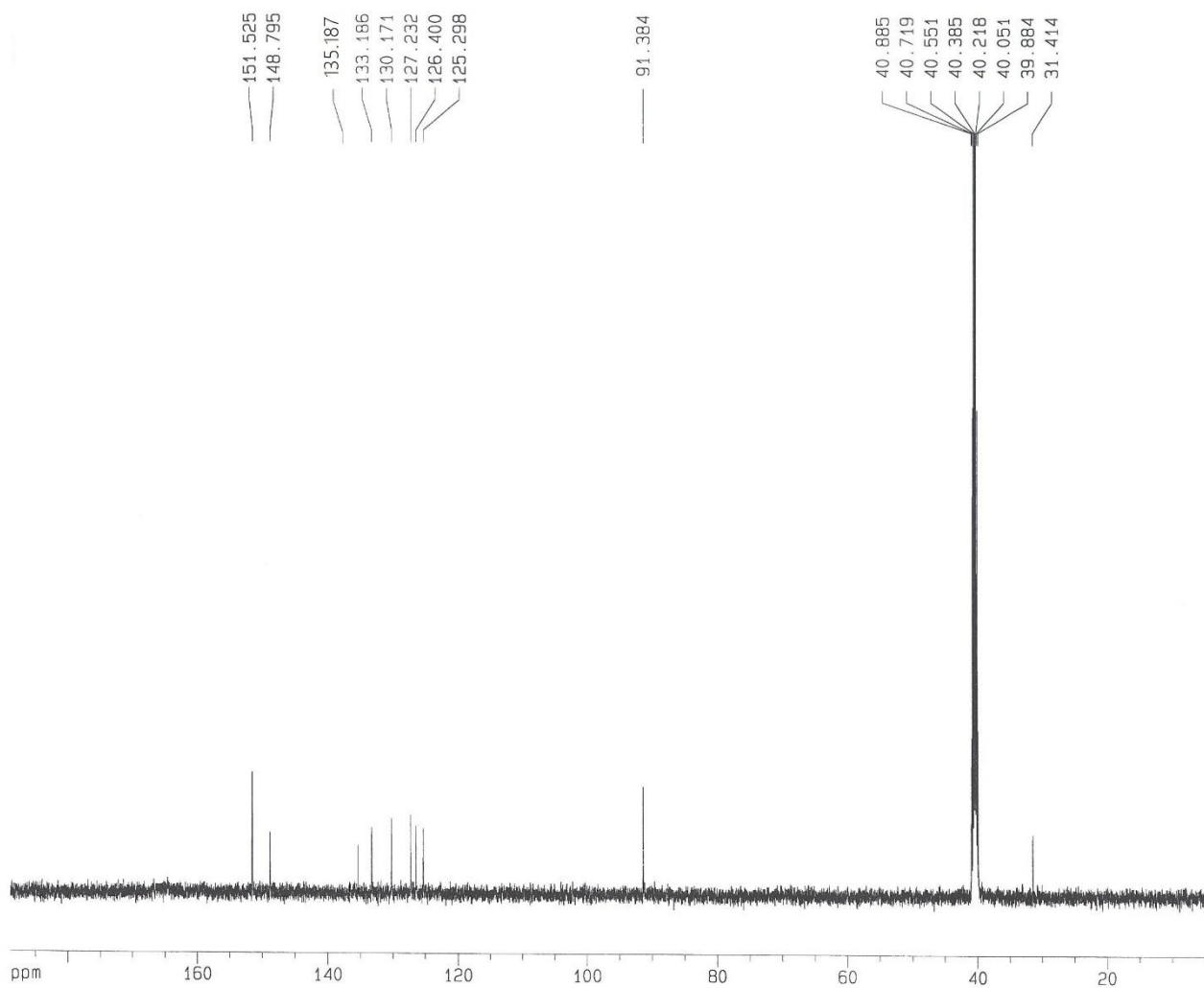


Figure S38.  $^{13}\text{C}$  NMR spectrum of compound 4t

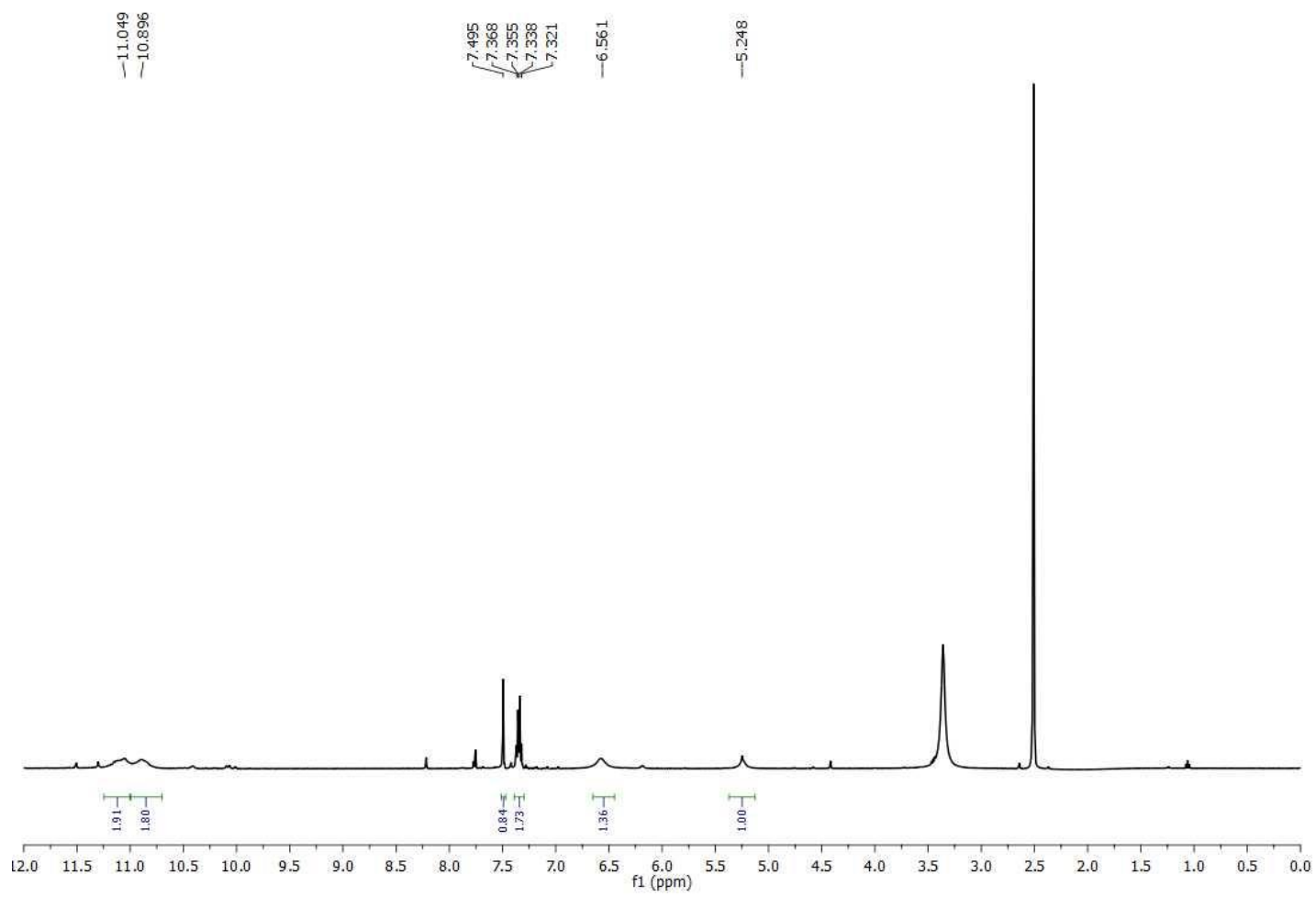


Figure S39. <sup>1</sup>H NMR spectrum of compound 4u

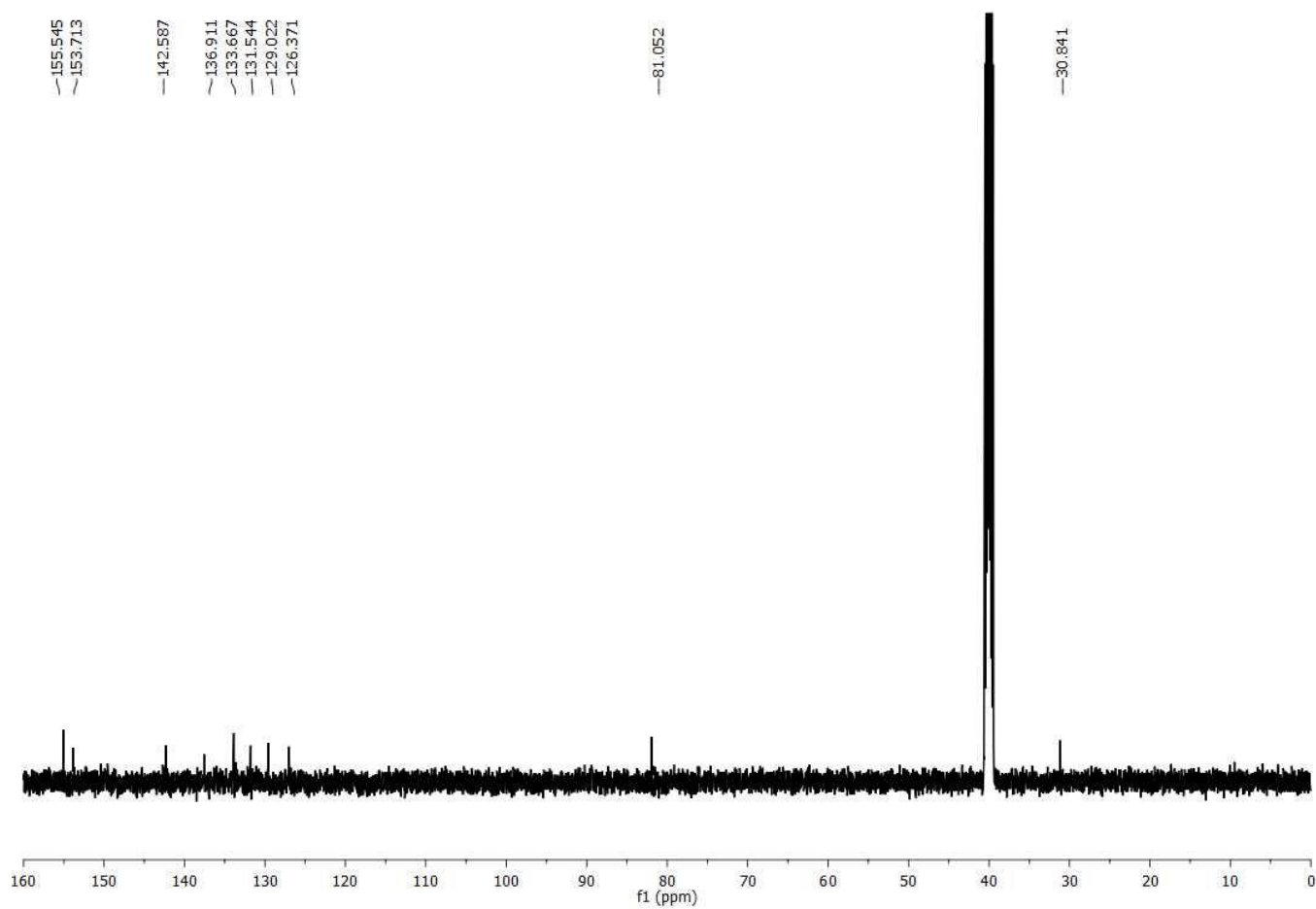


Figure S40.  $^{13}\text{C}$  NMR spectrum of compound 4u

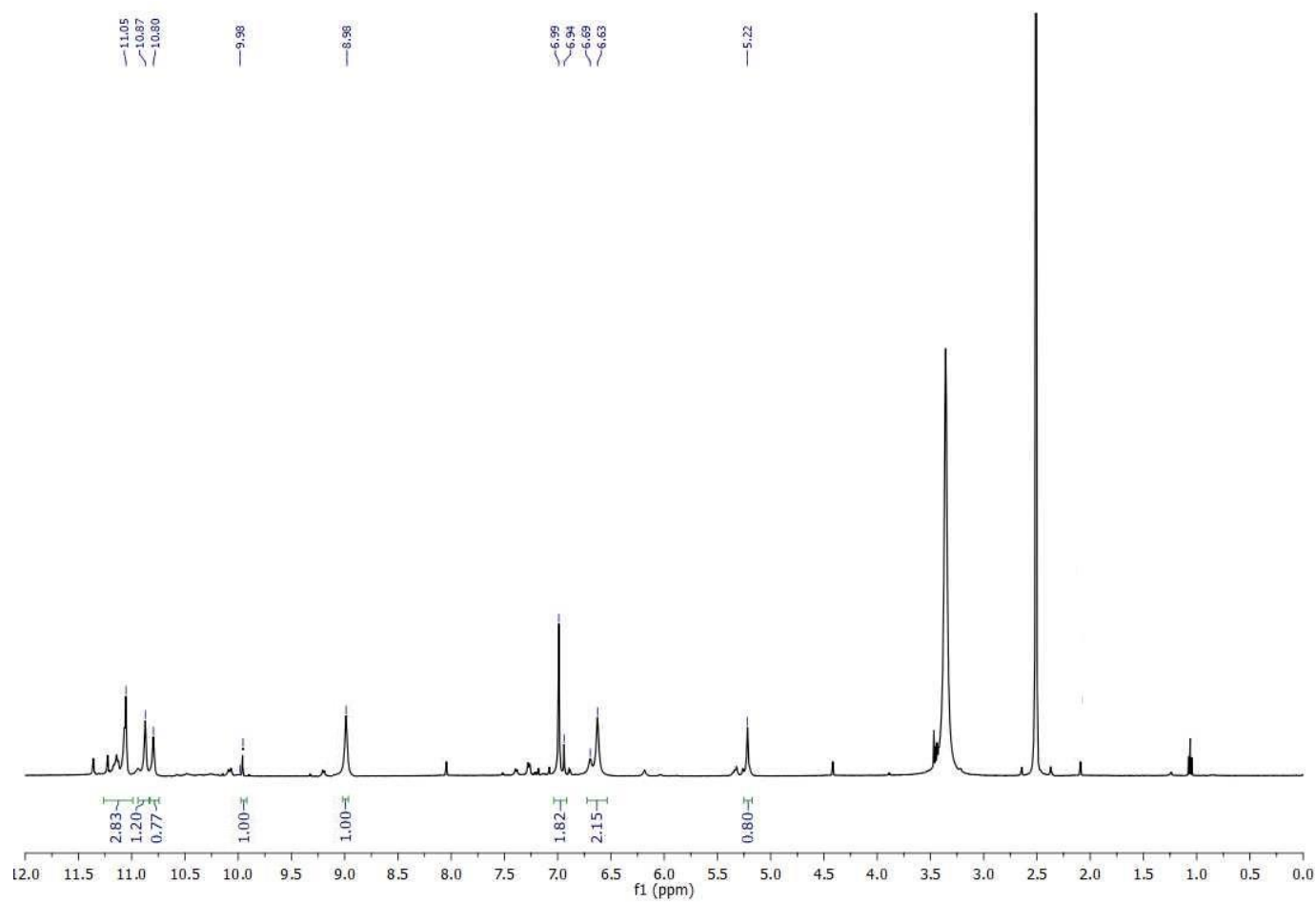


Figure S41. <sup>1</sup>H NMR spectrum of compound 4v

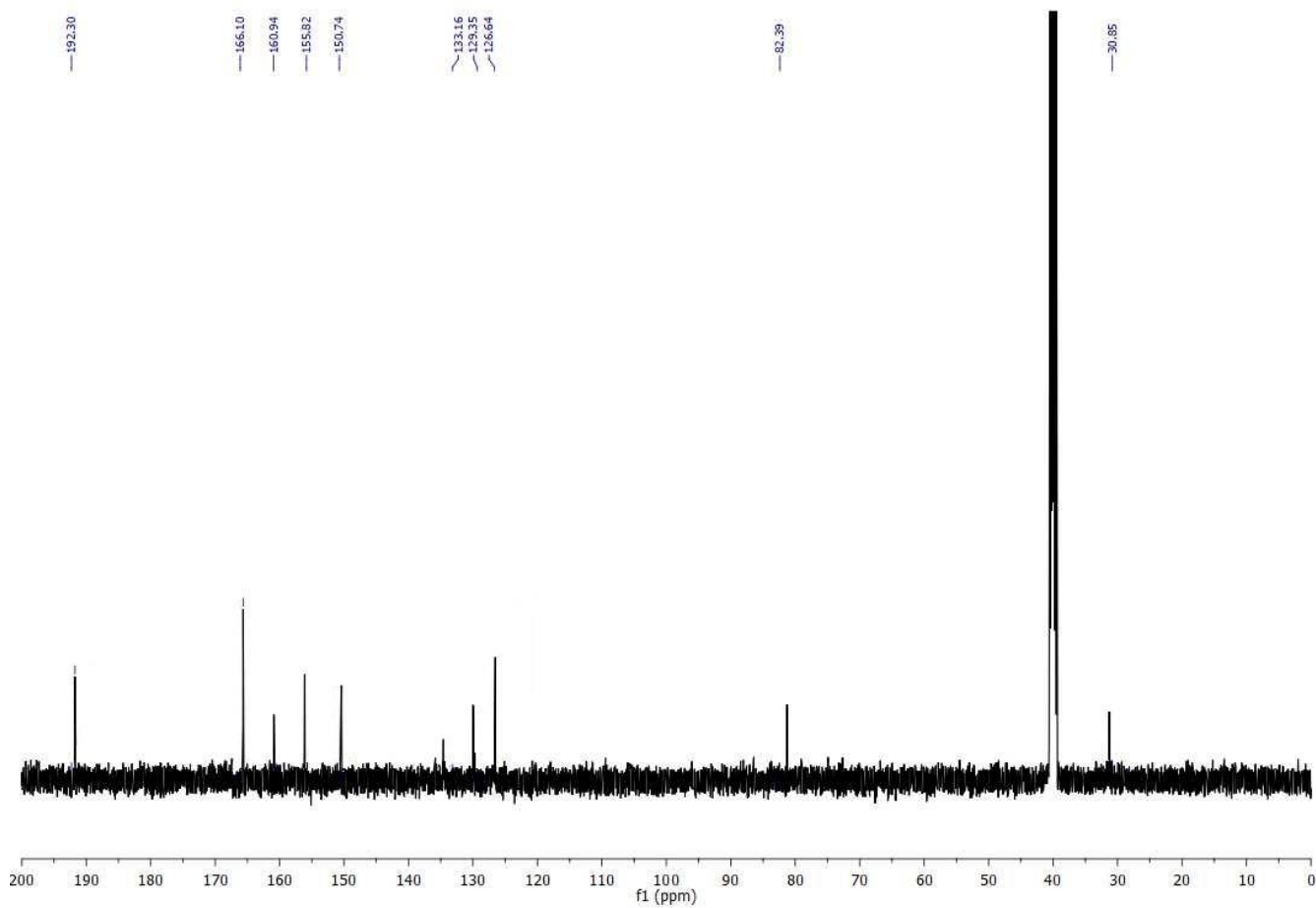


Figure S42.  $^{13}\text{C}$  NMR spectrum of compound 4v



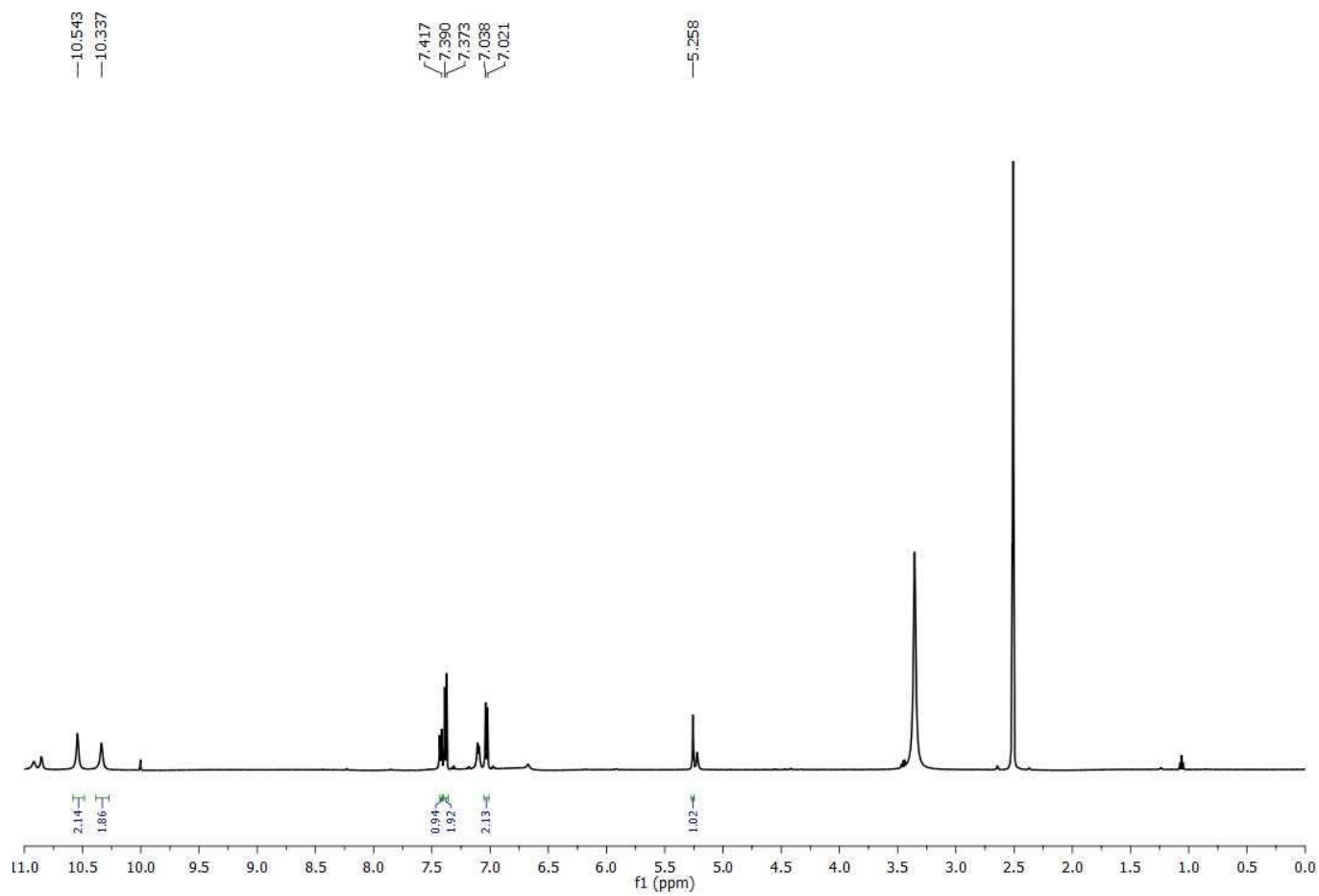


Figure S43. <sup>1</sup>H NMR spectrum of compound 4w

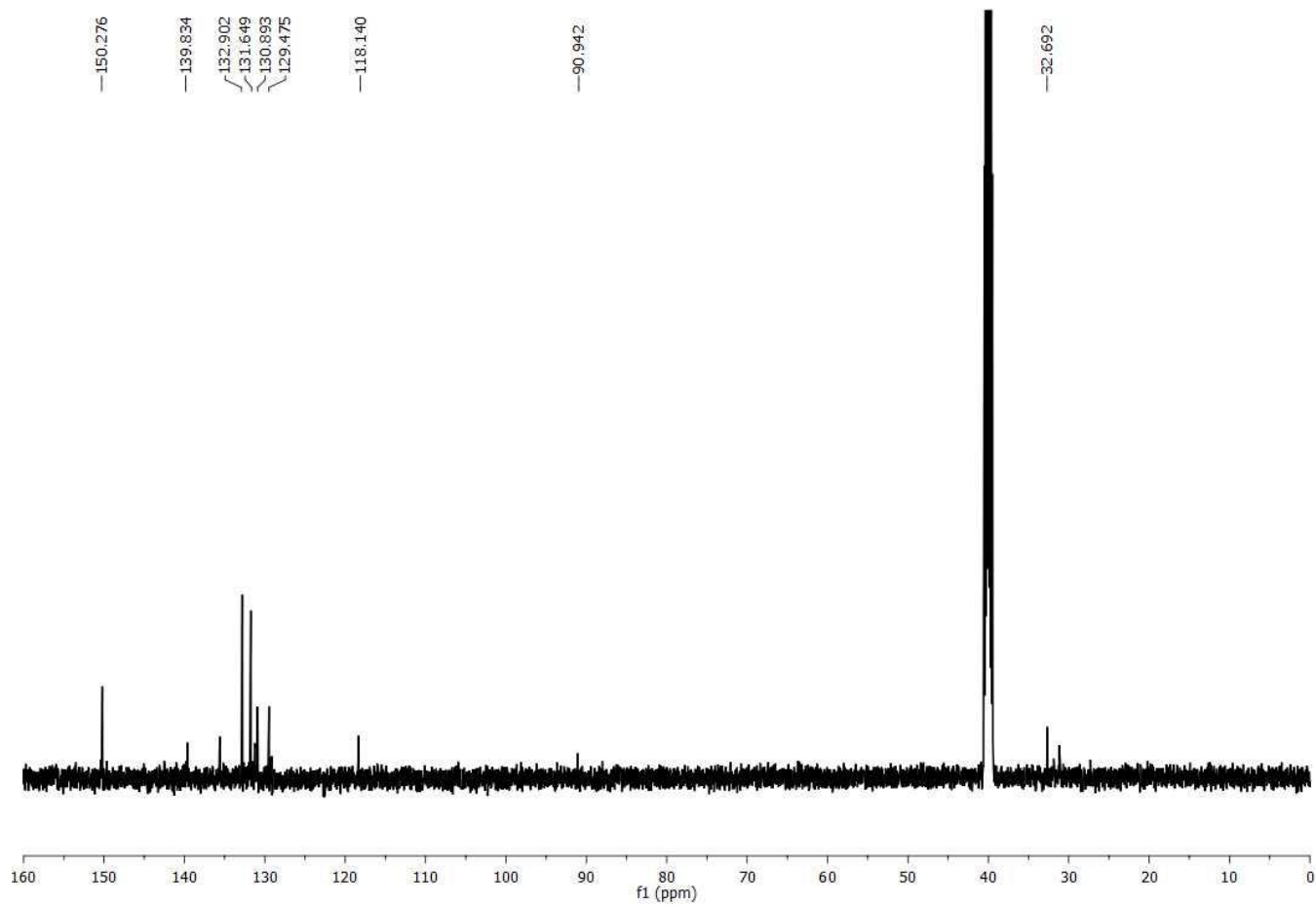


Figure S44.  $^{13}\text{C}$  NMR spectrum of compound 4w

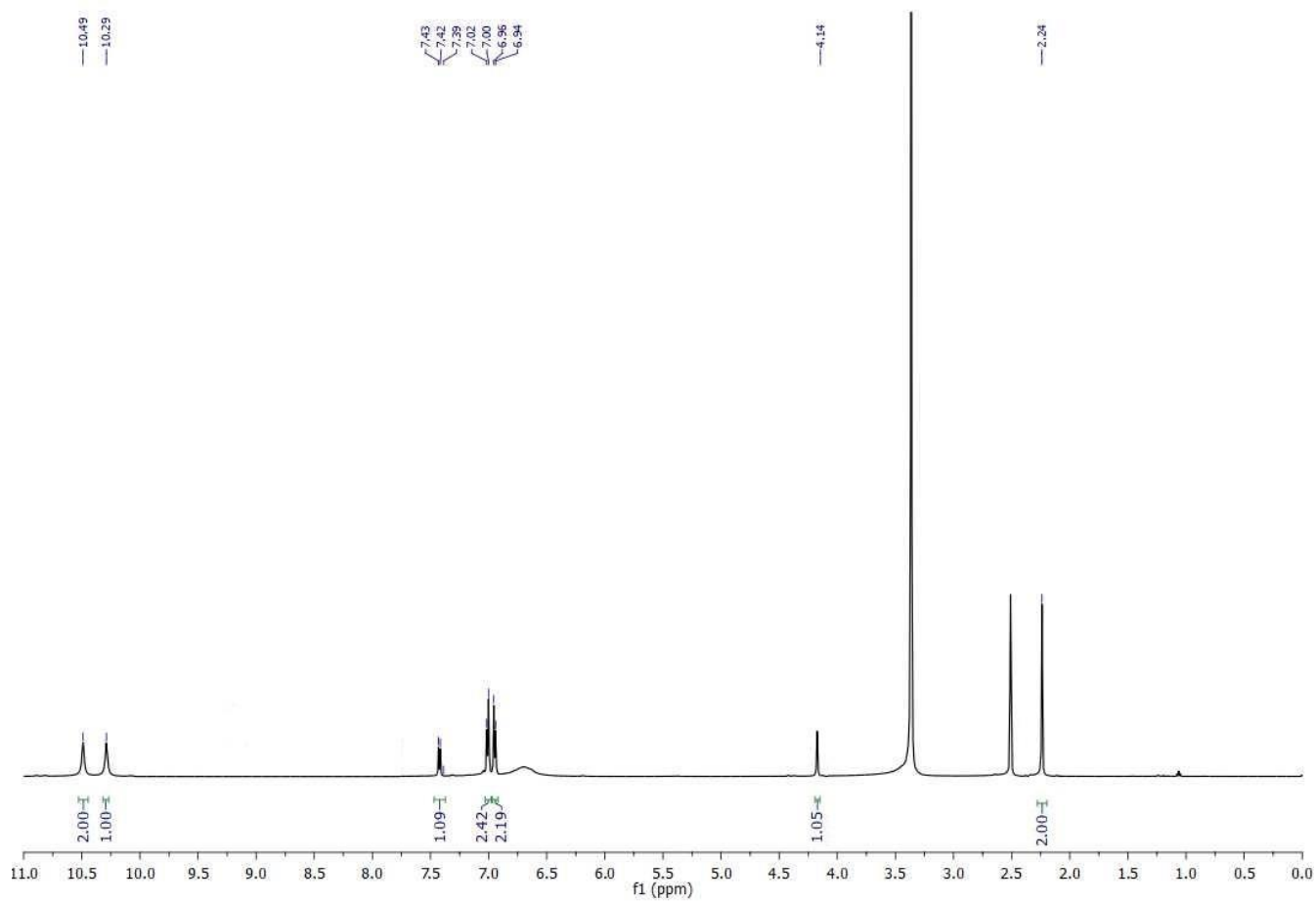


Figure S45. <sup>1</sup>H NMR spectrum of compound 5a

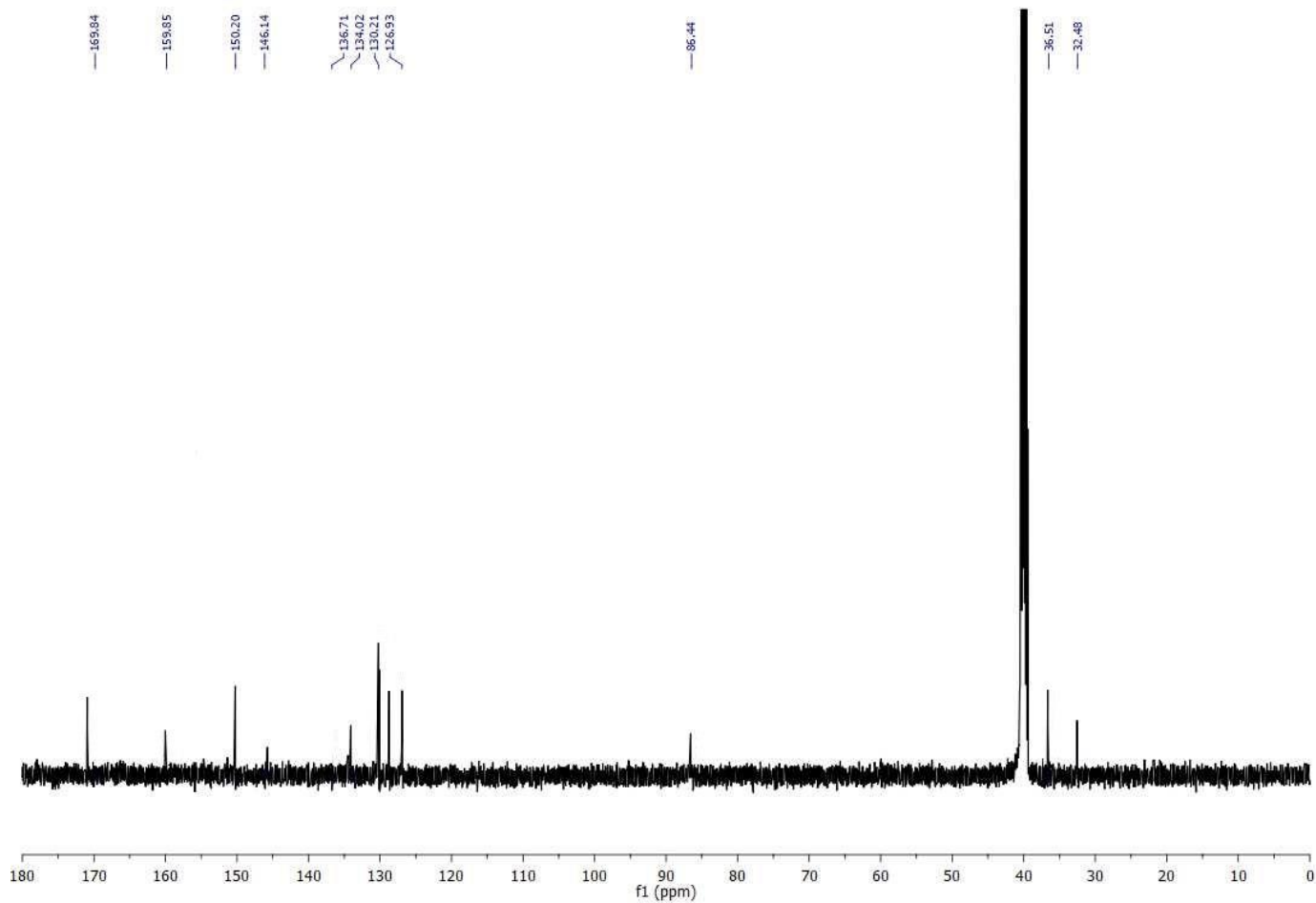


Figure S46.  $^{13}\text{C}$  NMR spectrum of compound 5a

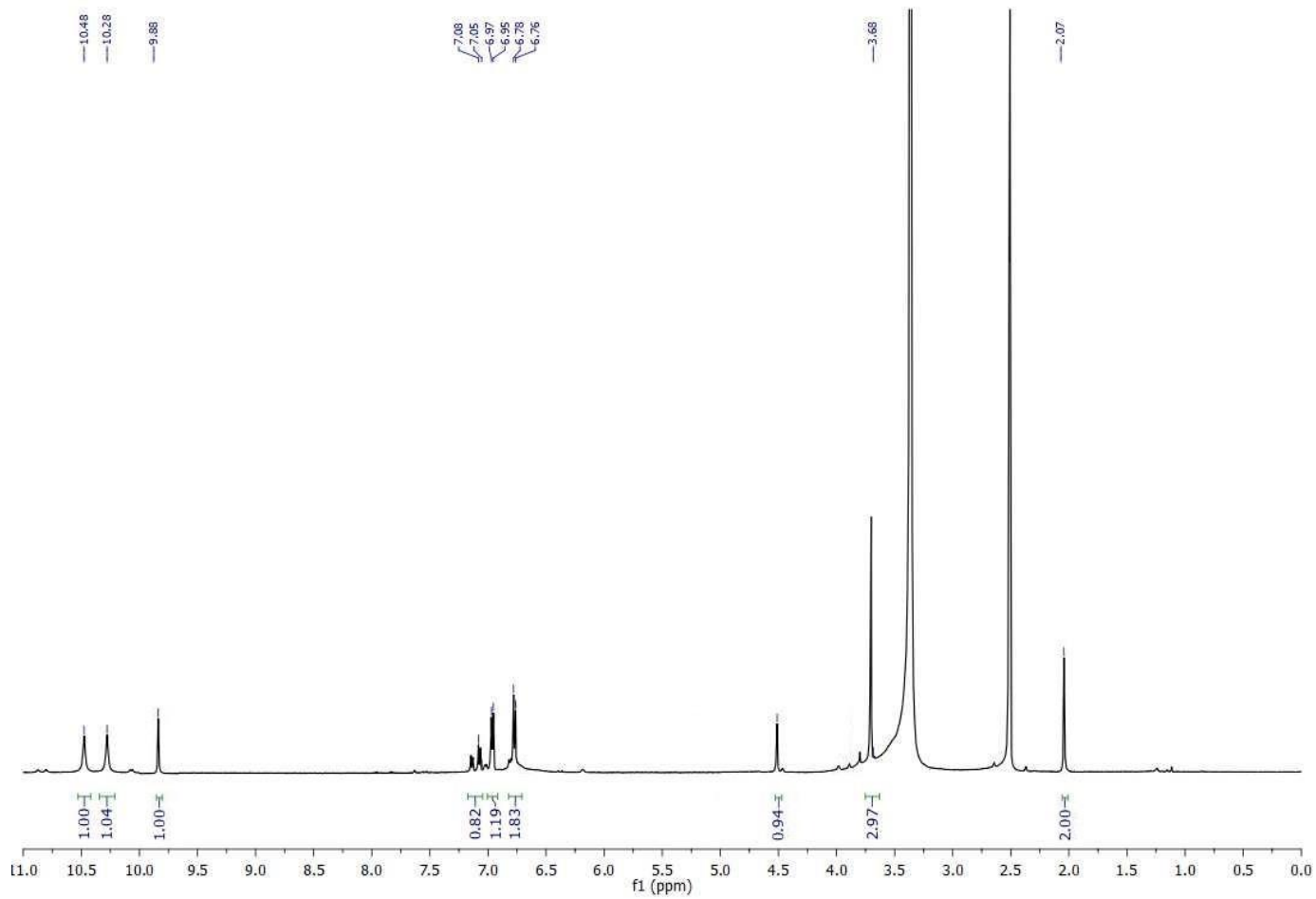


Figure S47. <sup>1</sup>H NMR spectrum of compound 5b

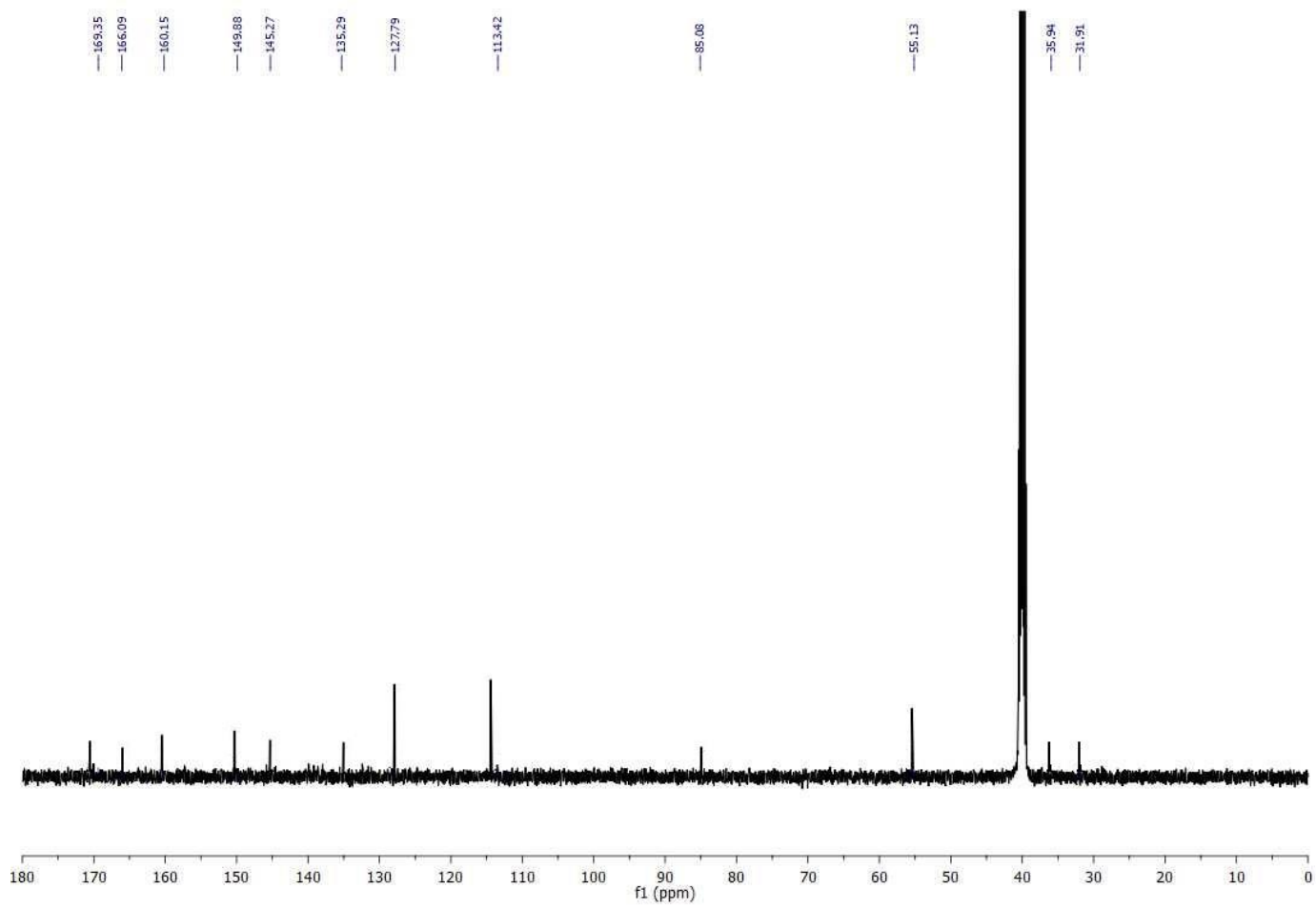


Figure S48.  $^{13}\text{C}$  NMR spectrum of compound 5b

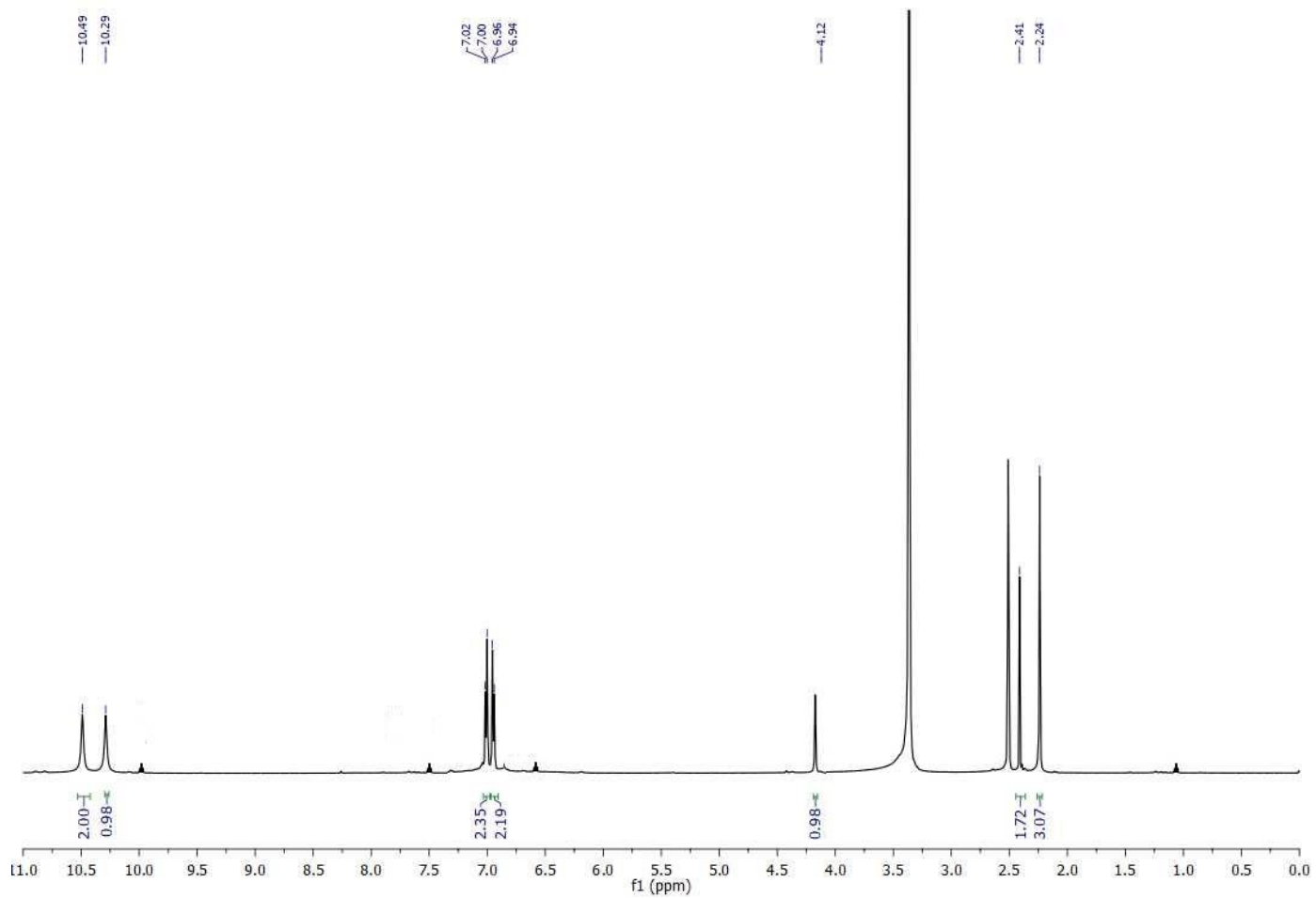


Figure S49. <sup>1</sup>H NMR spectrum of compound 5c

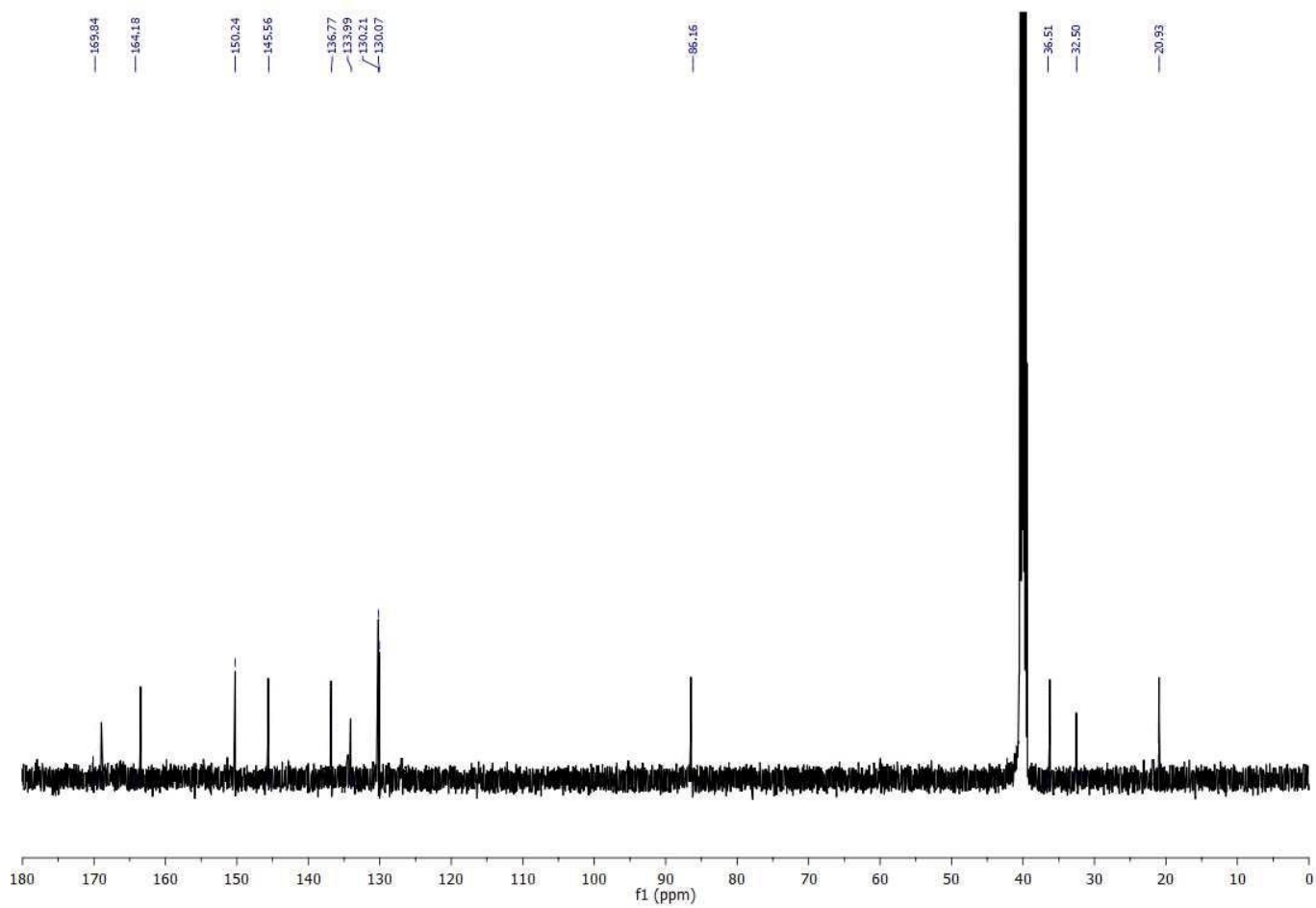


Figure S50.  $^{13}\text{C}$  NMR spectrum of compound 5c



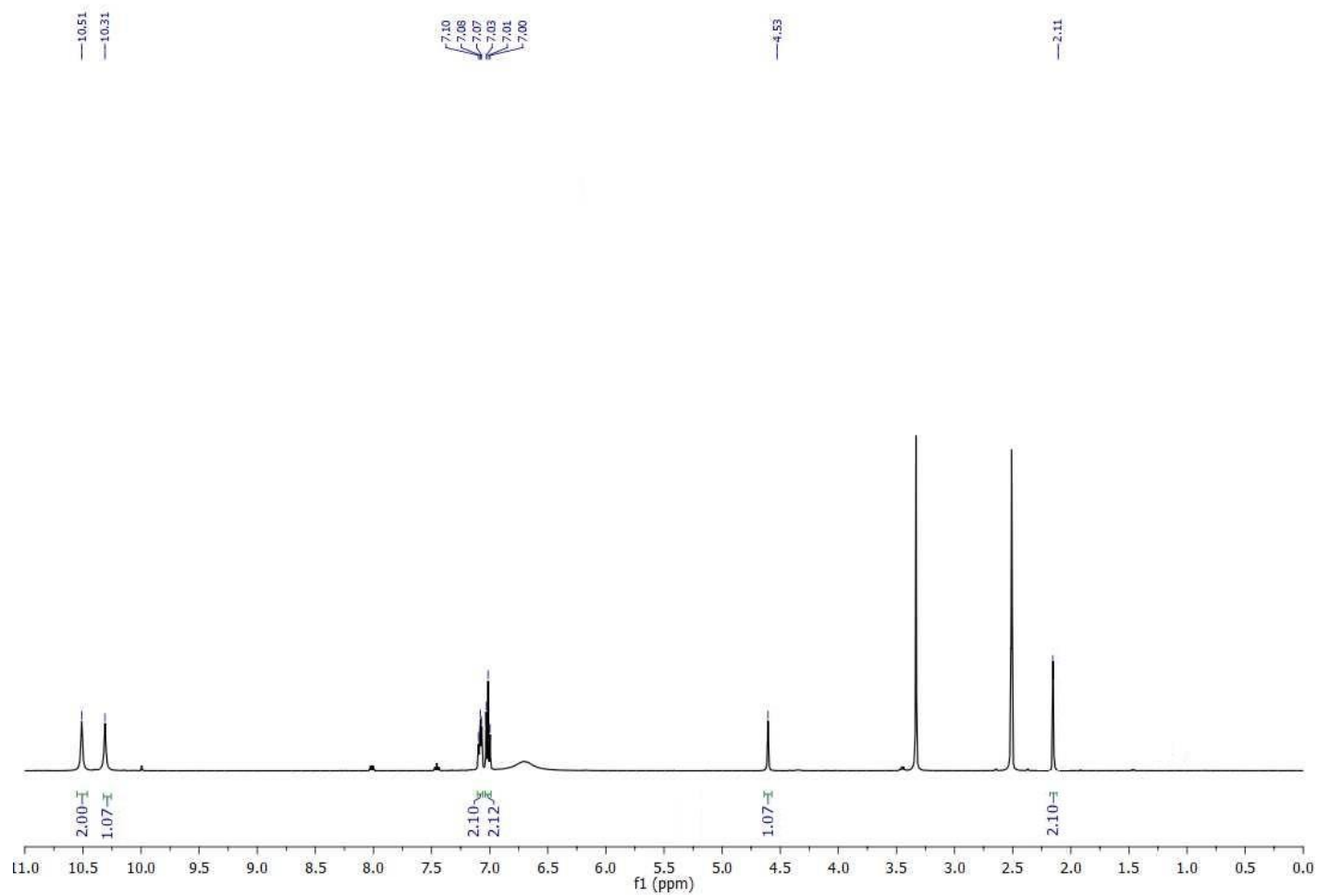


Figure S51. <sup>1</sup>H NMR spectrum of compound 5d

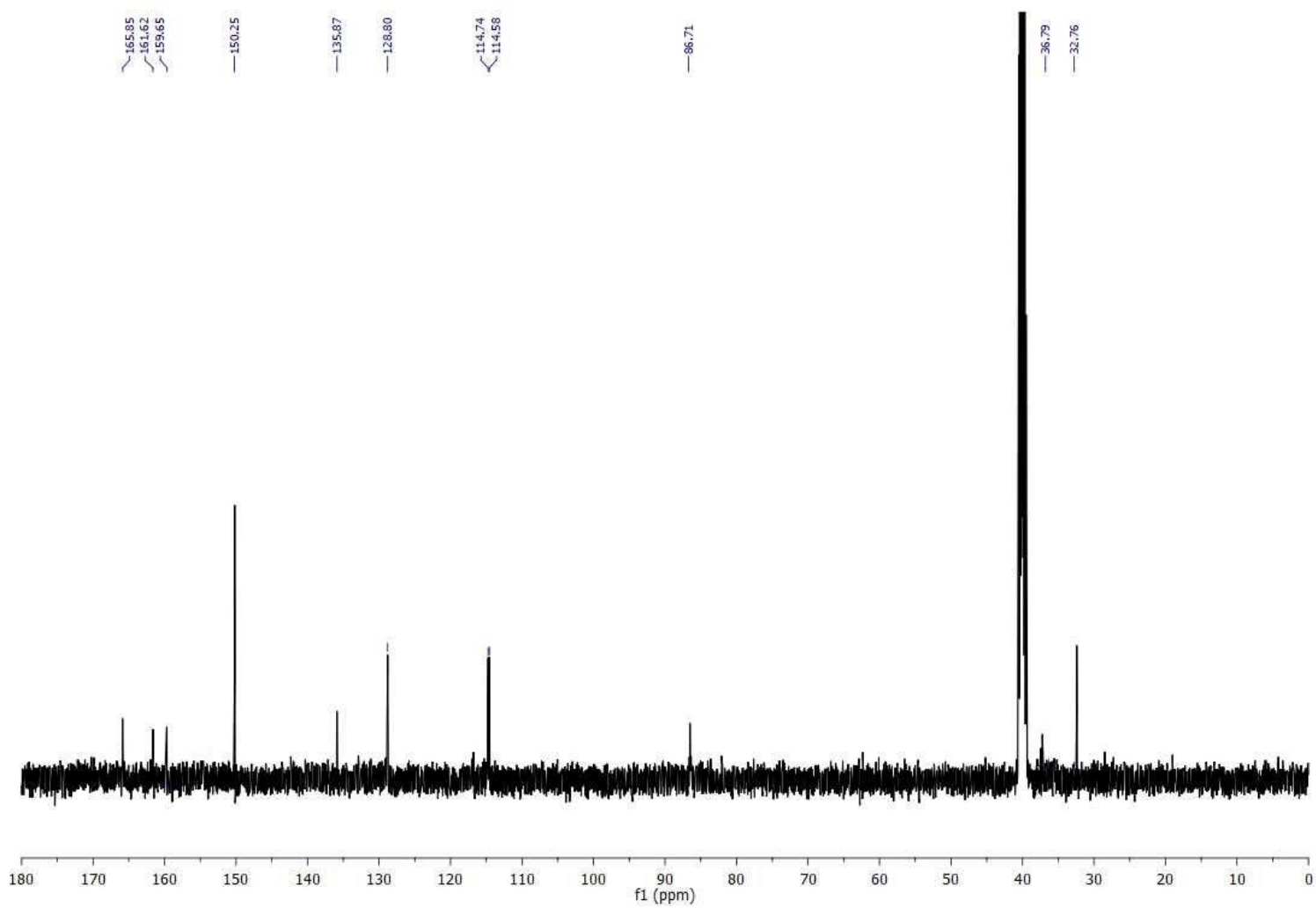


Figure S52.  $^{13}\text{C}$  NMR spectrum of compound 5d

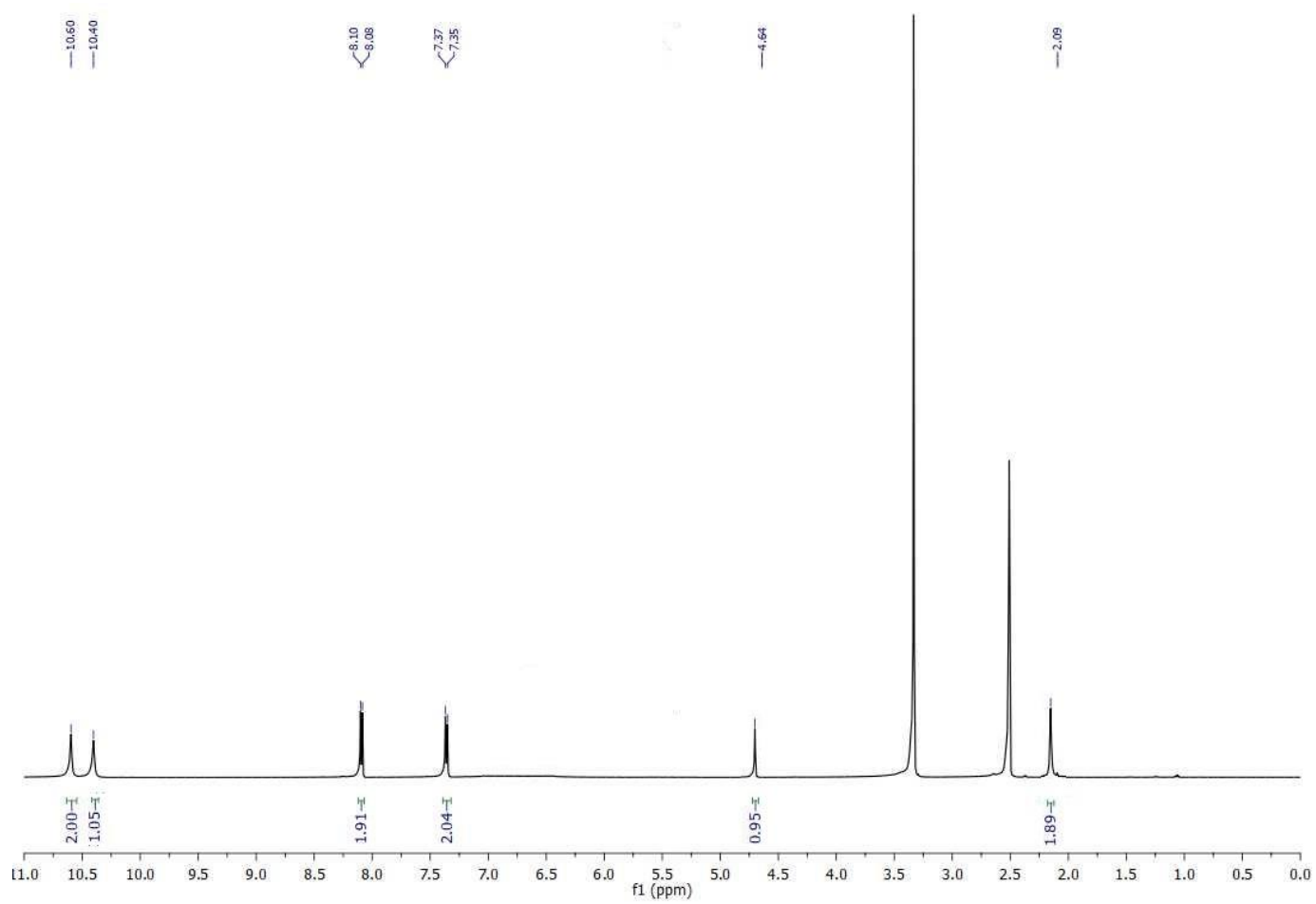


Figure S53. <sup>1</sup>H NMR spectrum of compound 5e

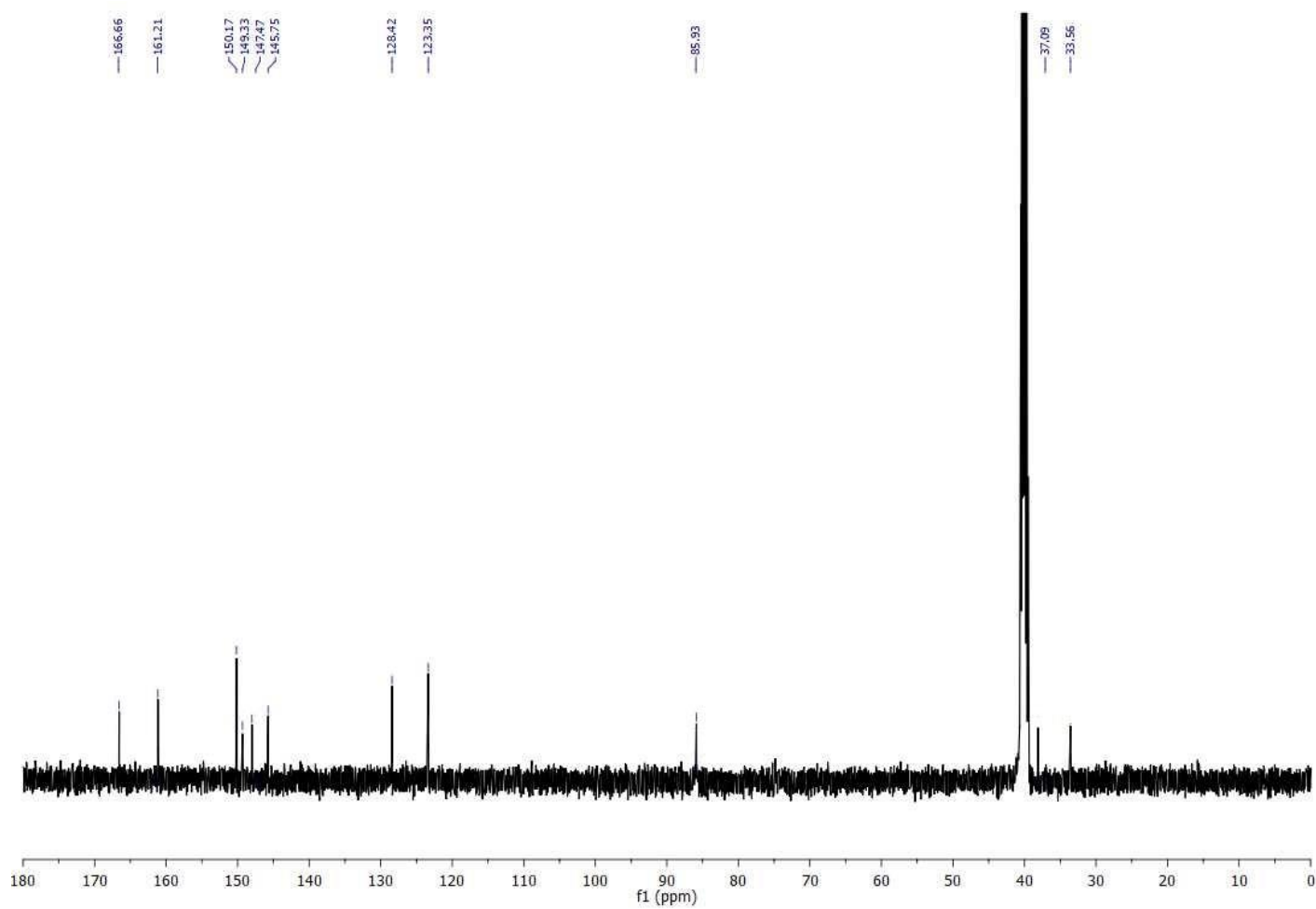


Figure S54.  $^{13}\text{C}$  NMR spectrum of compound 5e

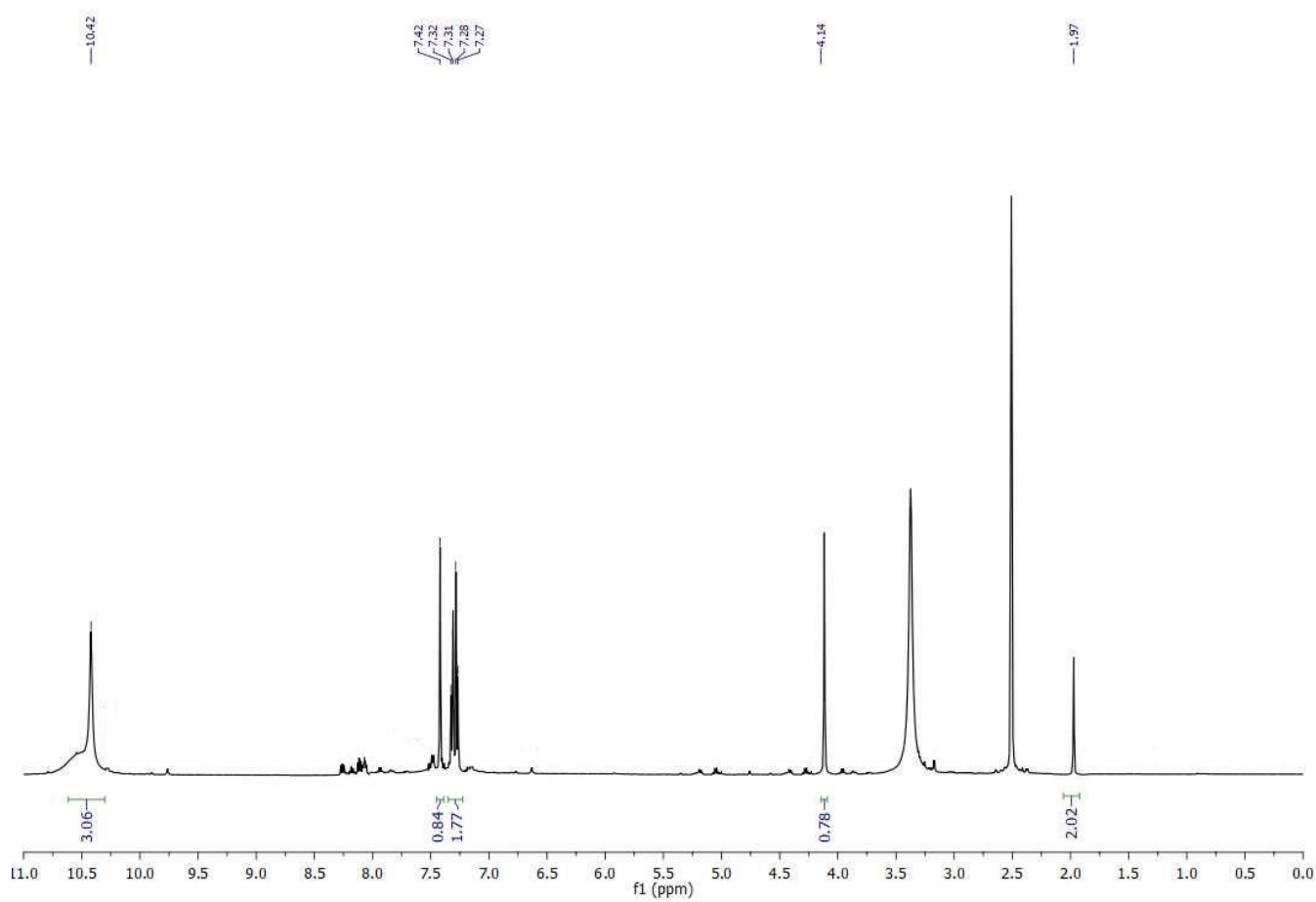


Figure S55. <sup>1</sup>H NMR spectrum of compound 5f

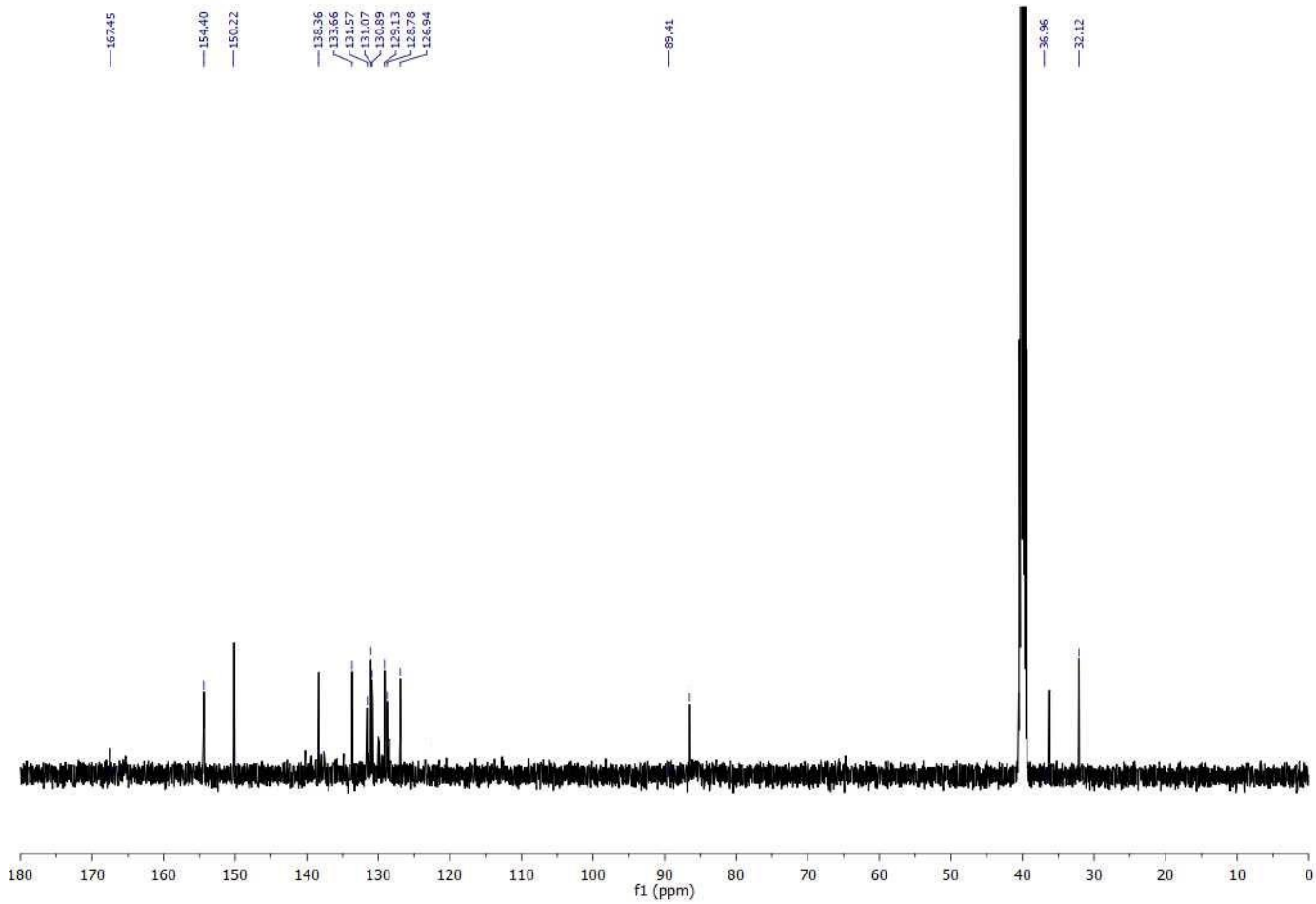


Figure S56.  $^{13}\text{C}$  NMR spectrum of compound 5f

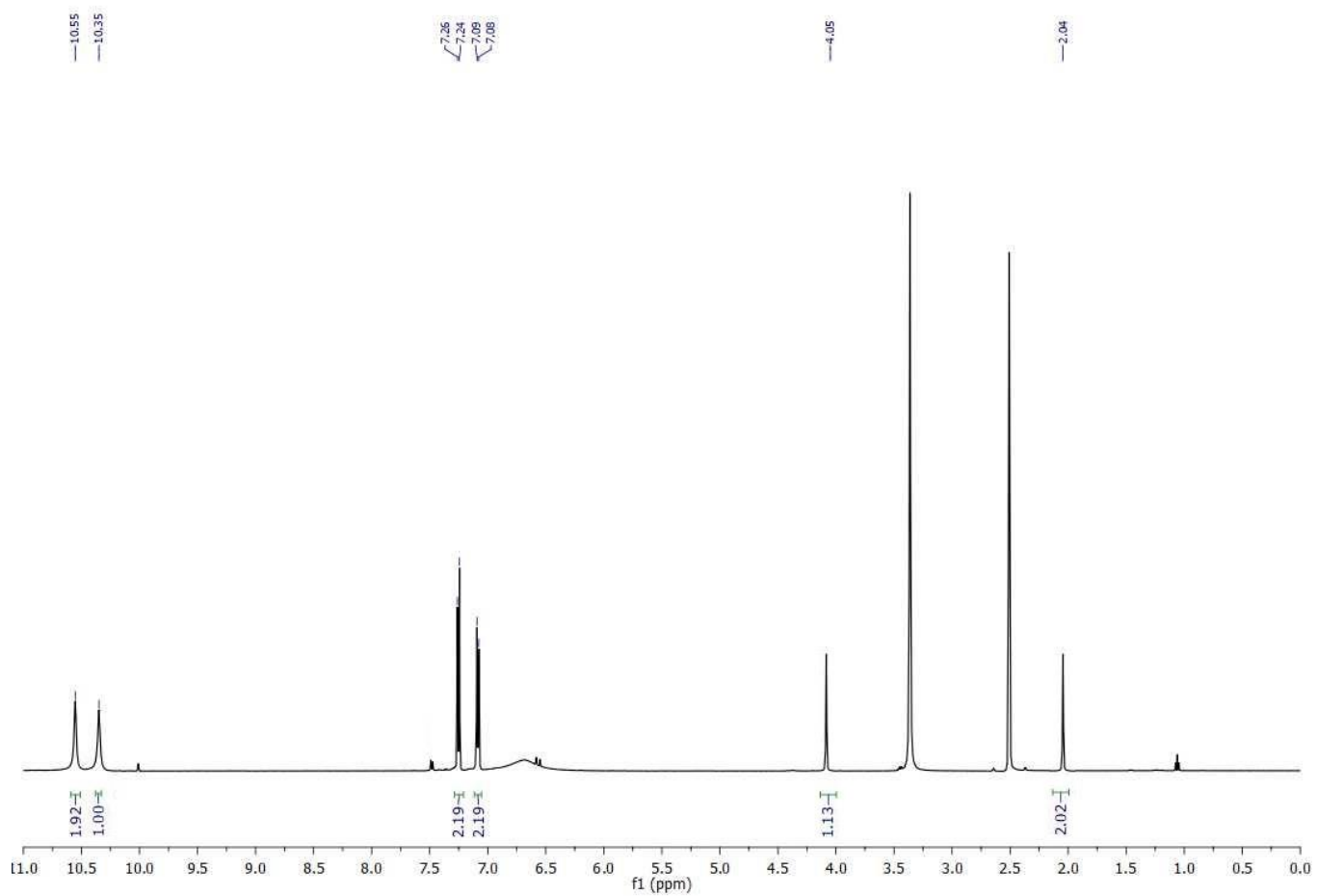


Figure S57. <sup>1</sup>H NMR spectrum of compound 5g

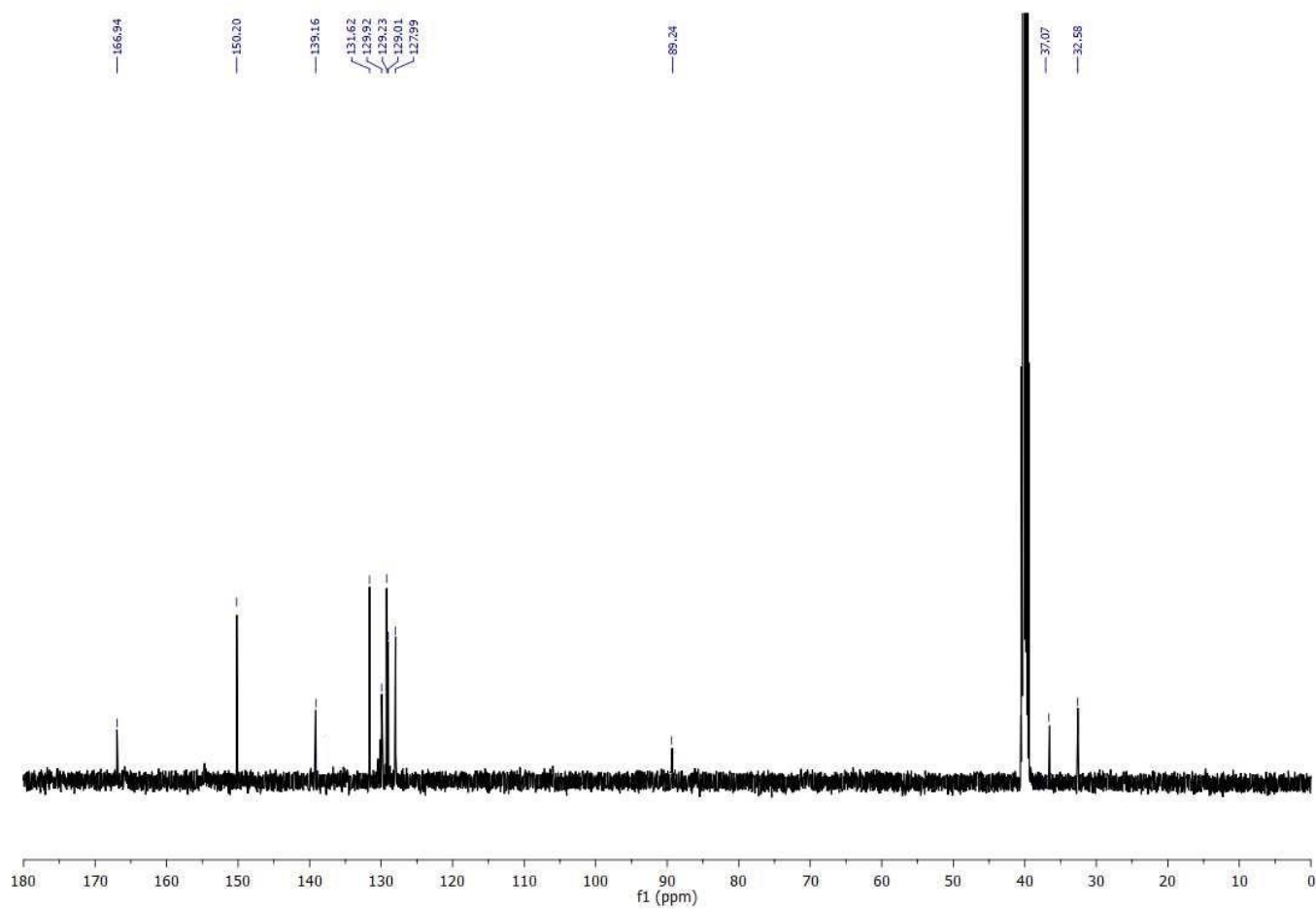


Figure S58.  $^{13}\text{C}$  NMR spectrum of compound 5g



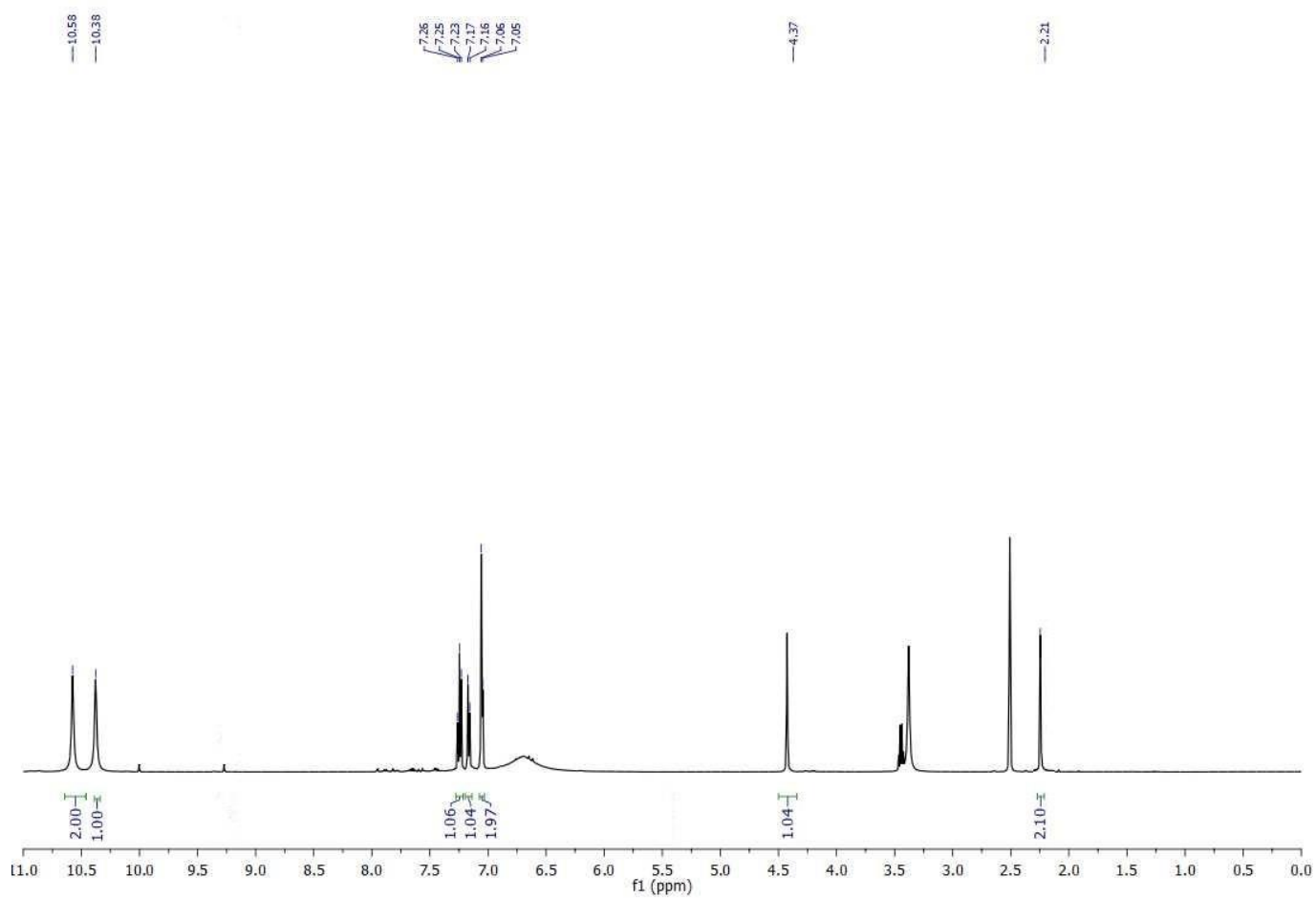


Figure S59.  $^1\text{H}$  NMR spectrum of compound 5h

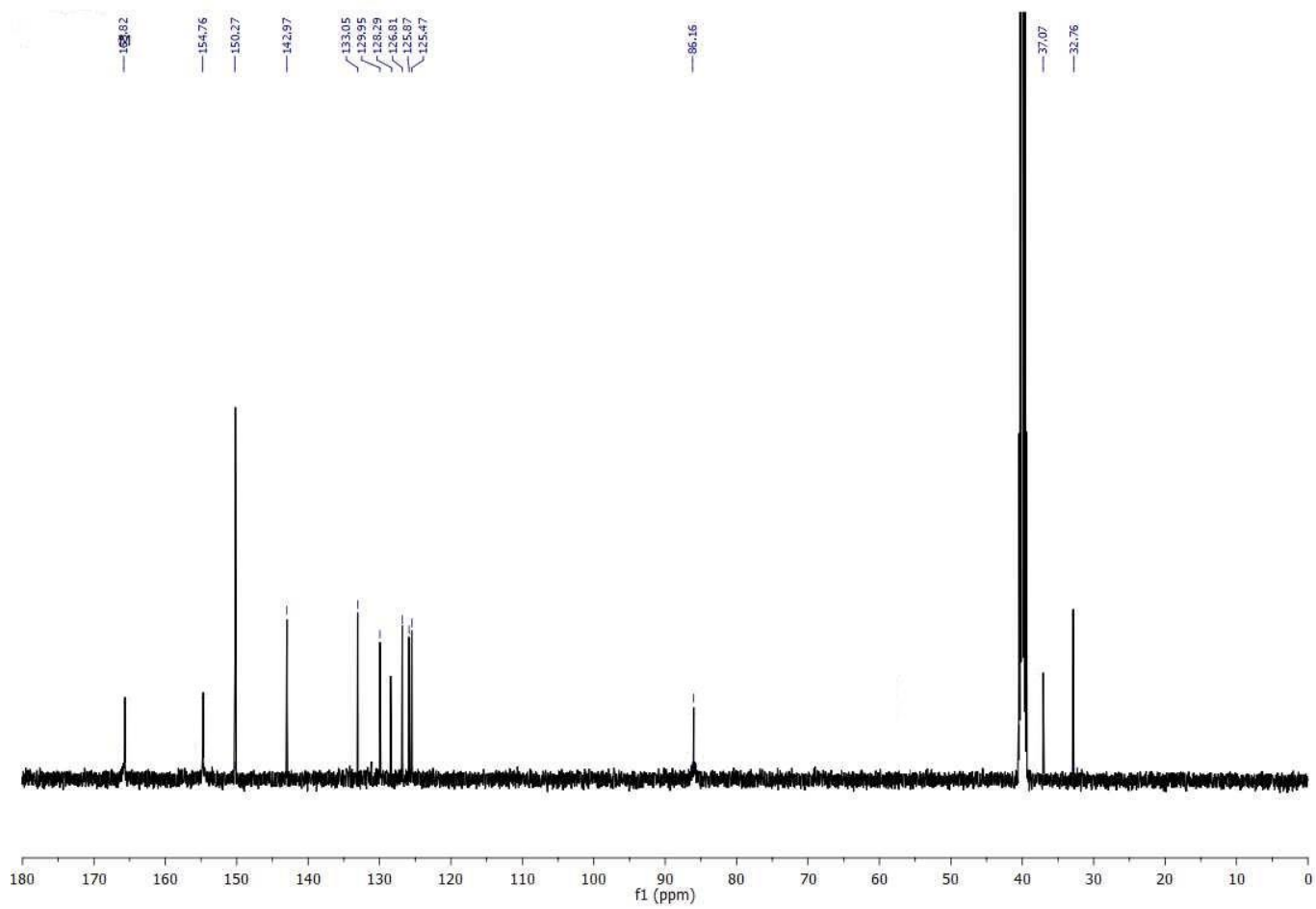


Figure S60.  $^{13}\text{C}$  NMR spectrum of compound 5h

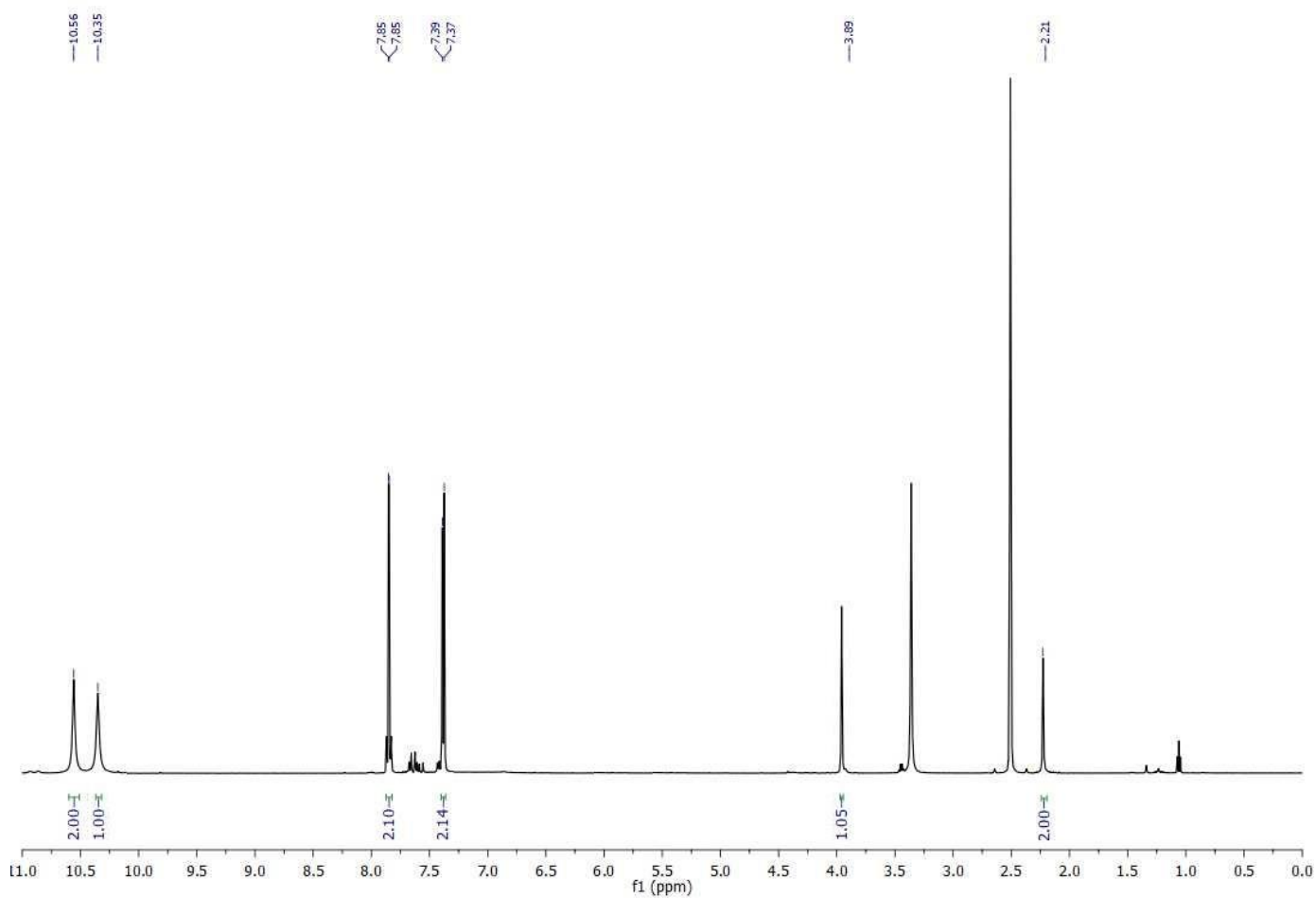


Figure S61. <sup>1</sup>H NMR spectrum of compound 5i

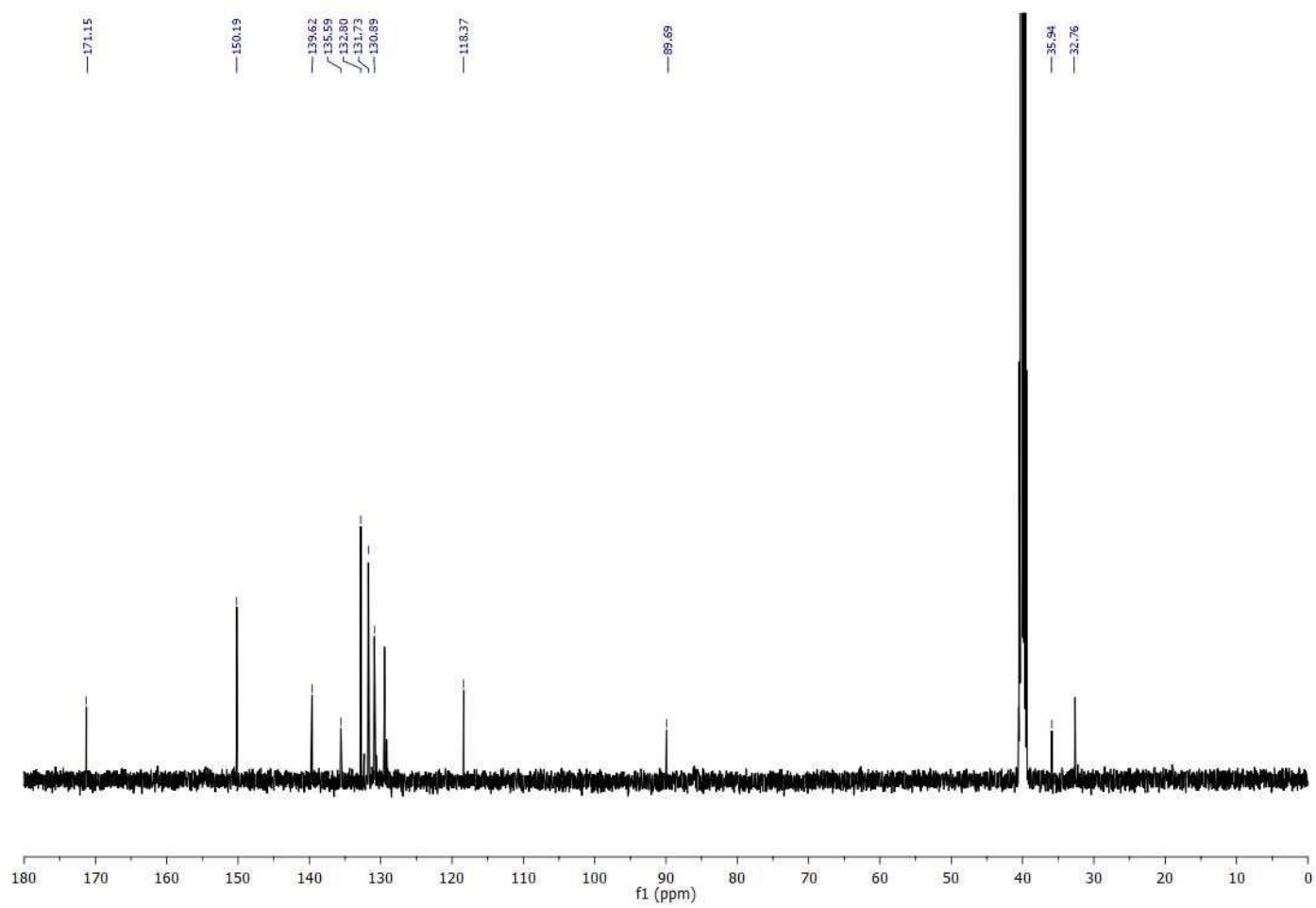


Figure S62.  $^{13}\text{C}$  NMR spectrum of compound 5i

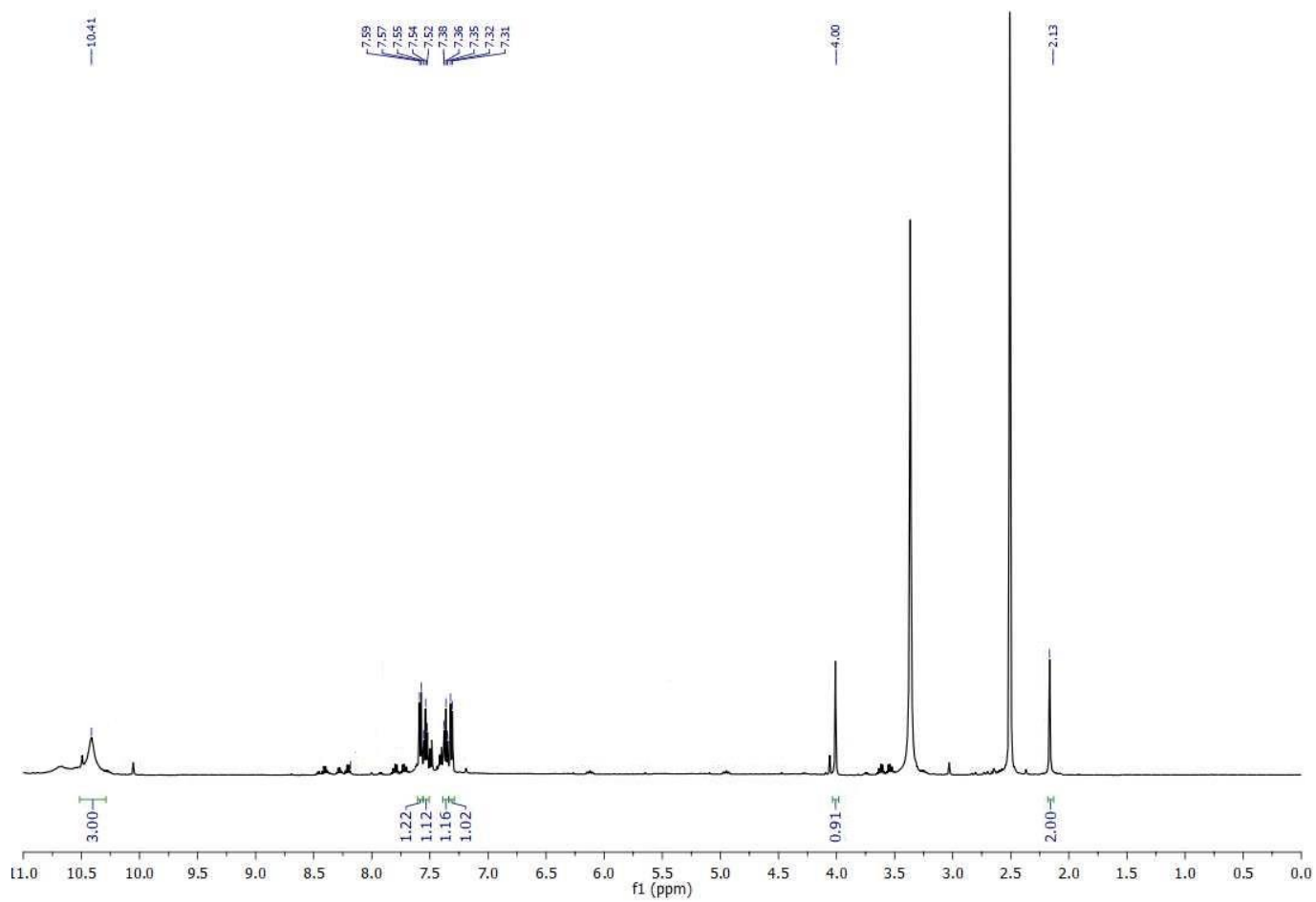


Figure S63.  $^1\text{H}$  NMR spectrum of compound 5j

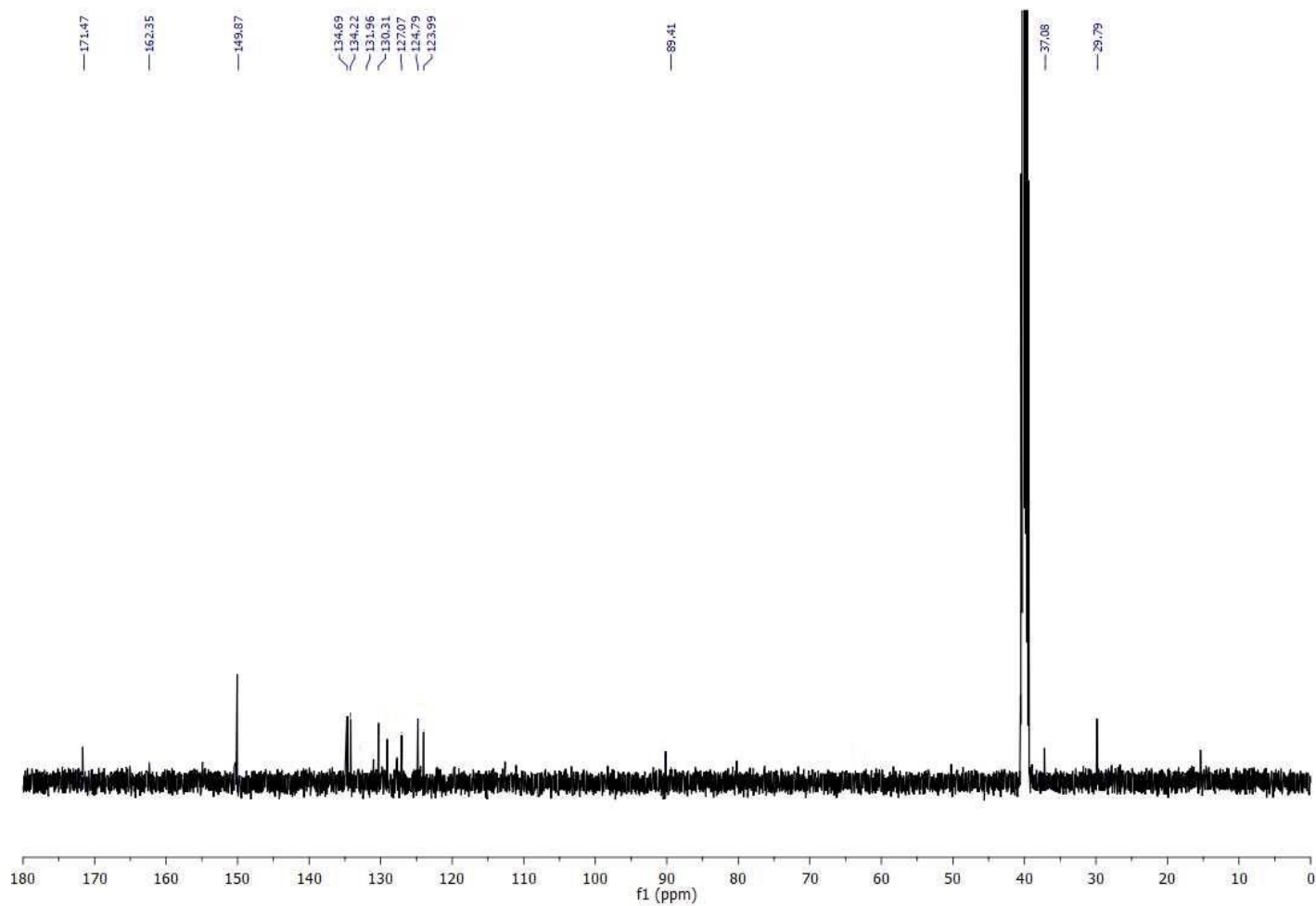


Figure S64.  $^{13}\text{C}$  NMR spectrum of compound 5j

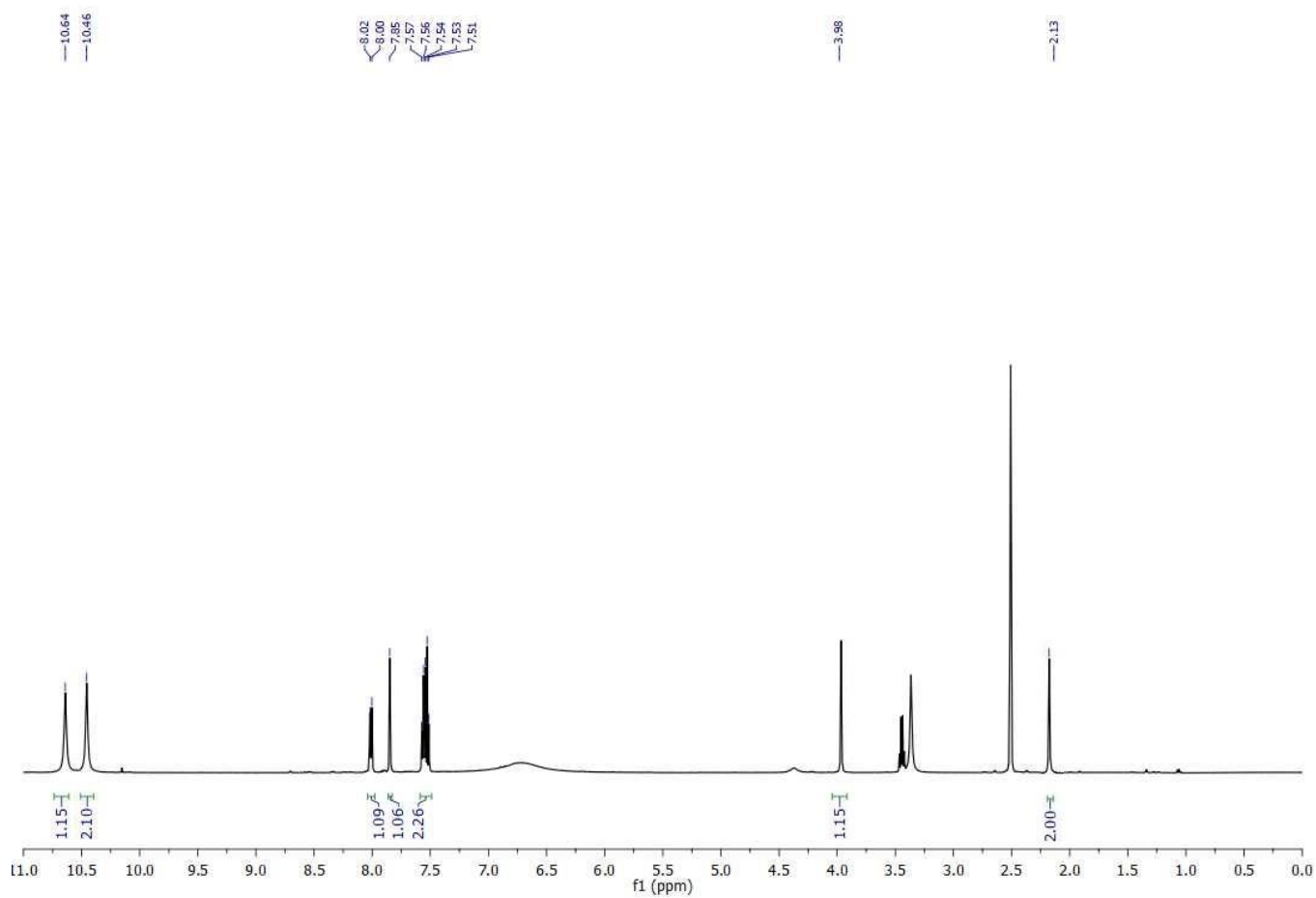


Figure S65.  $^1\text{H}$  NMR spectrum of compound 5k

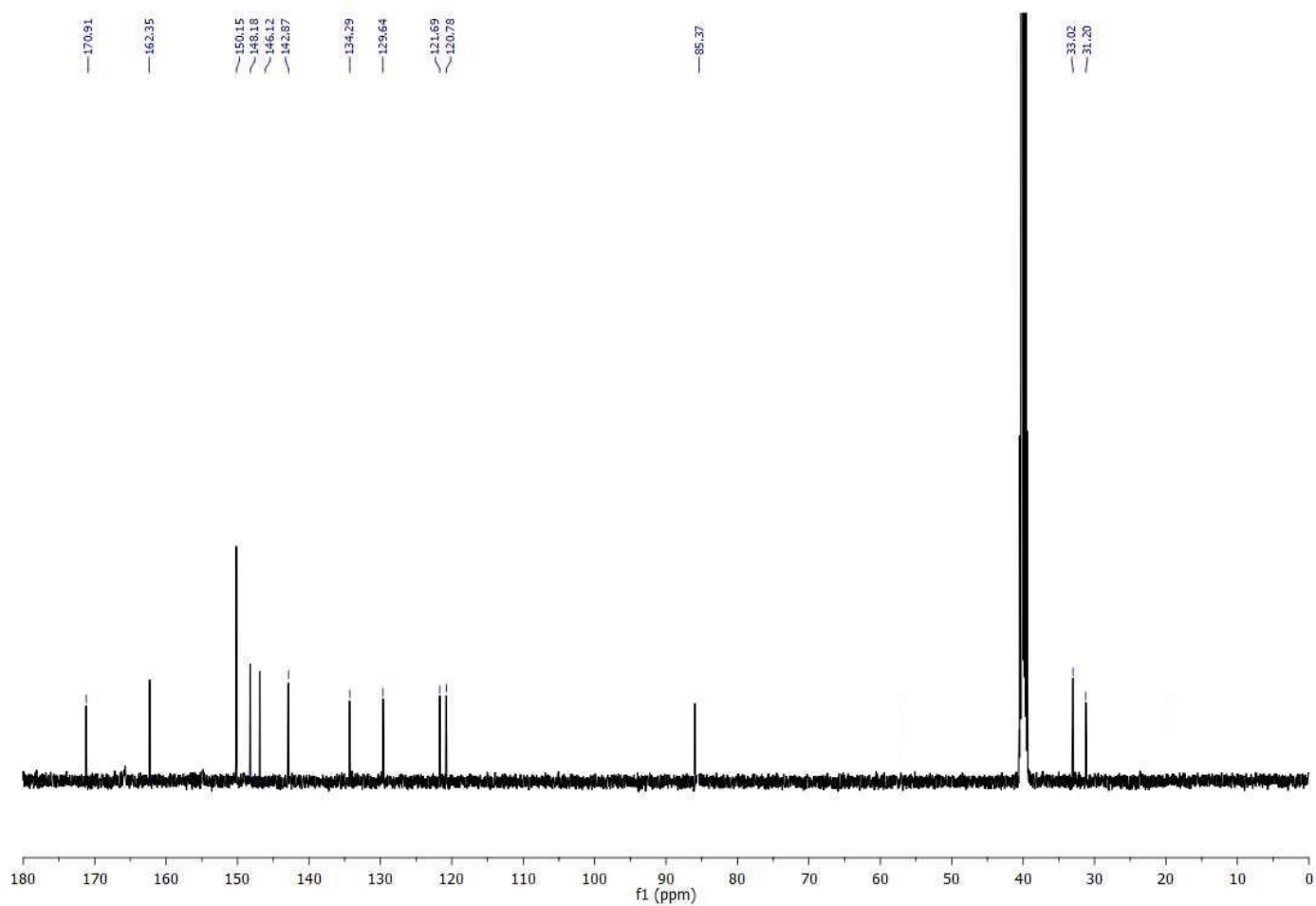


Figure S66.  $^{13}\text{C}$  NMR spectrum of compound 5k



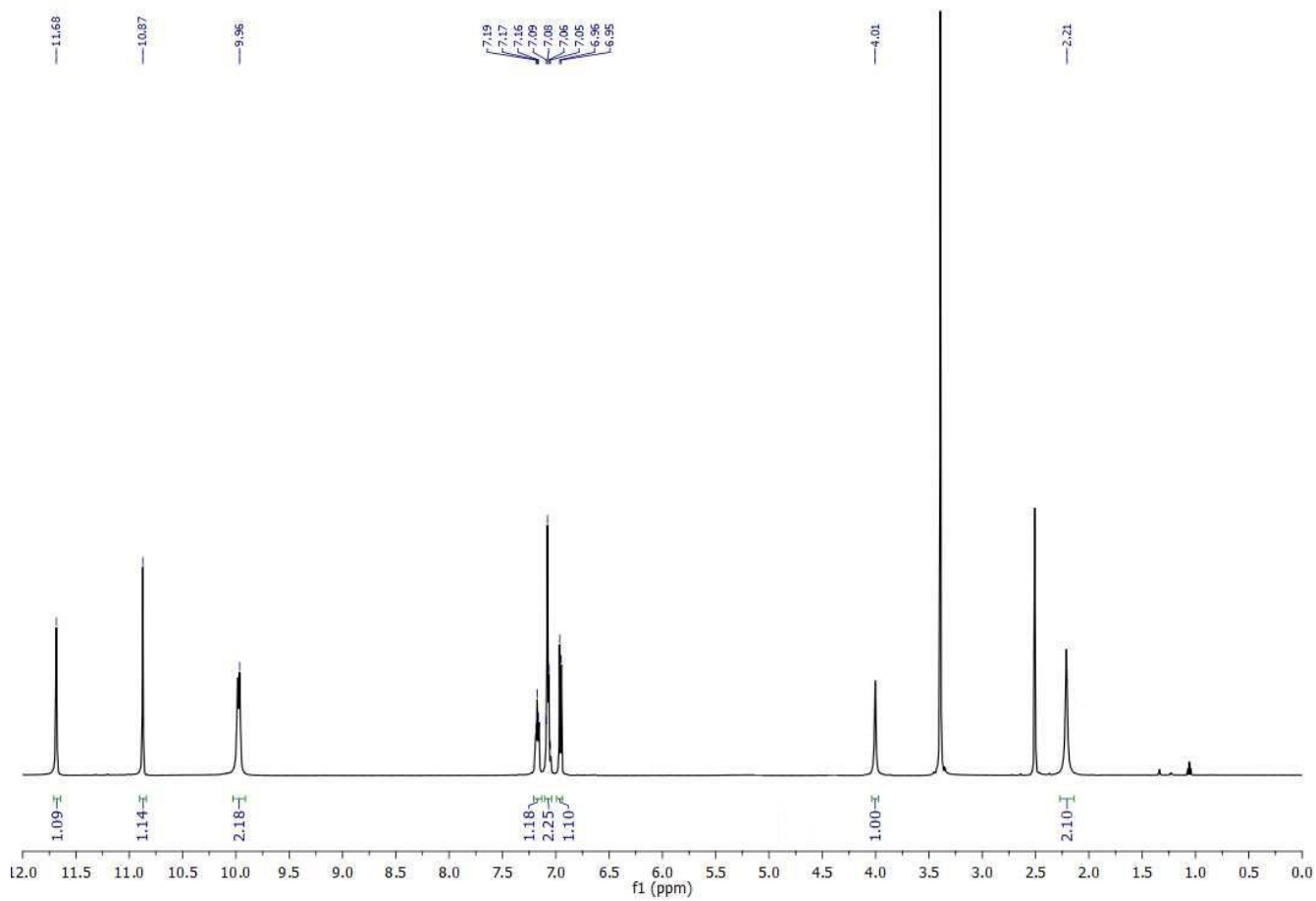


Figure S67.  $^1\text{H}$  NMR spectrum of compound 51

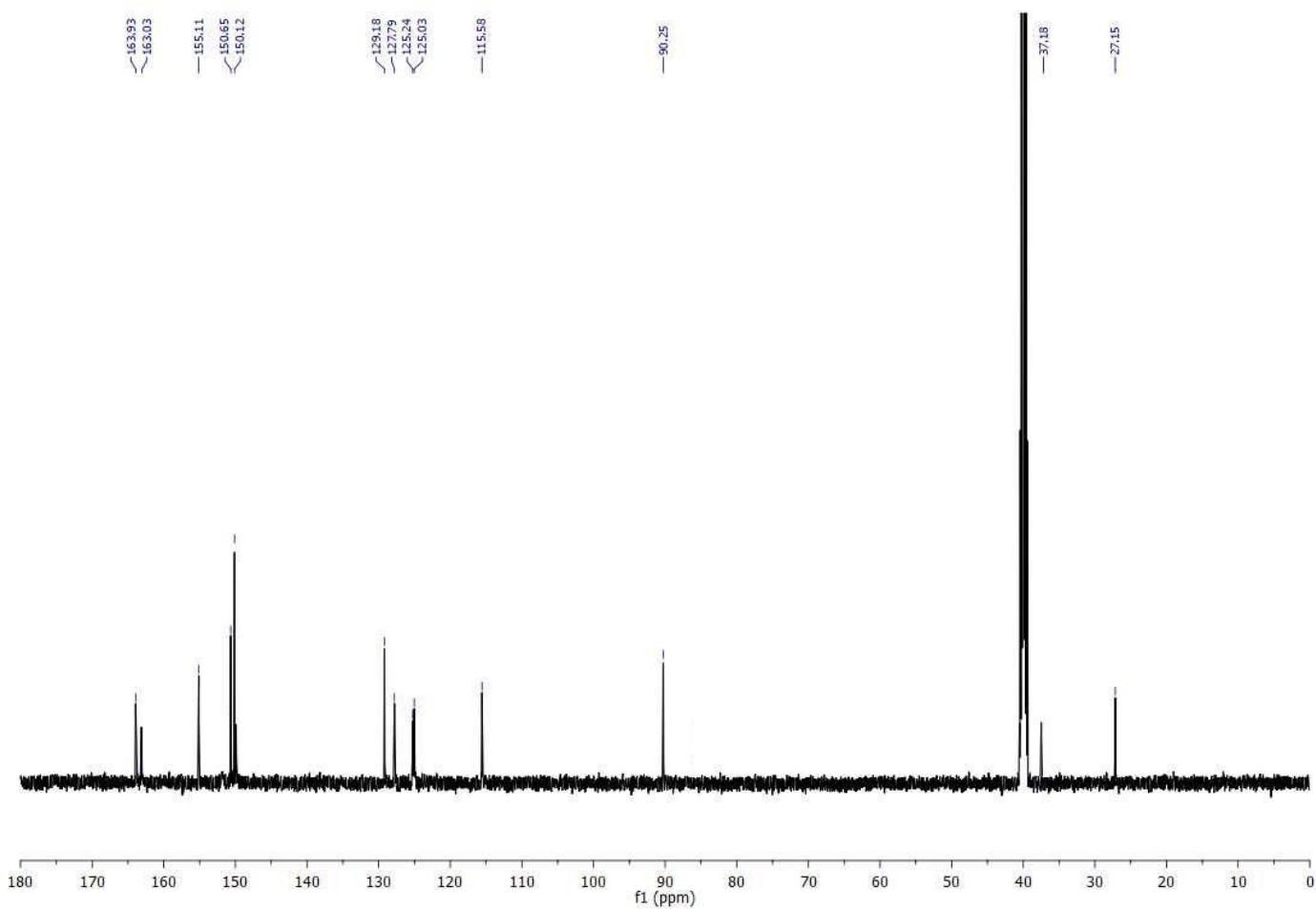


Figure S68.  $^{13}\text{C}$  NMR spectrum of compound 51

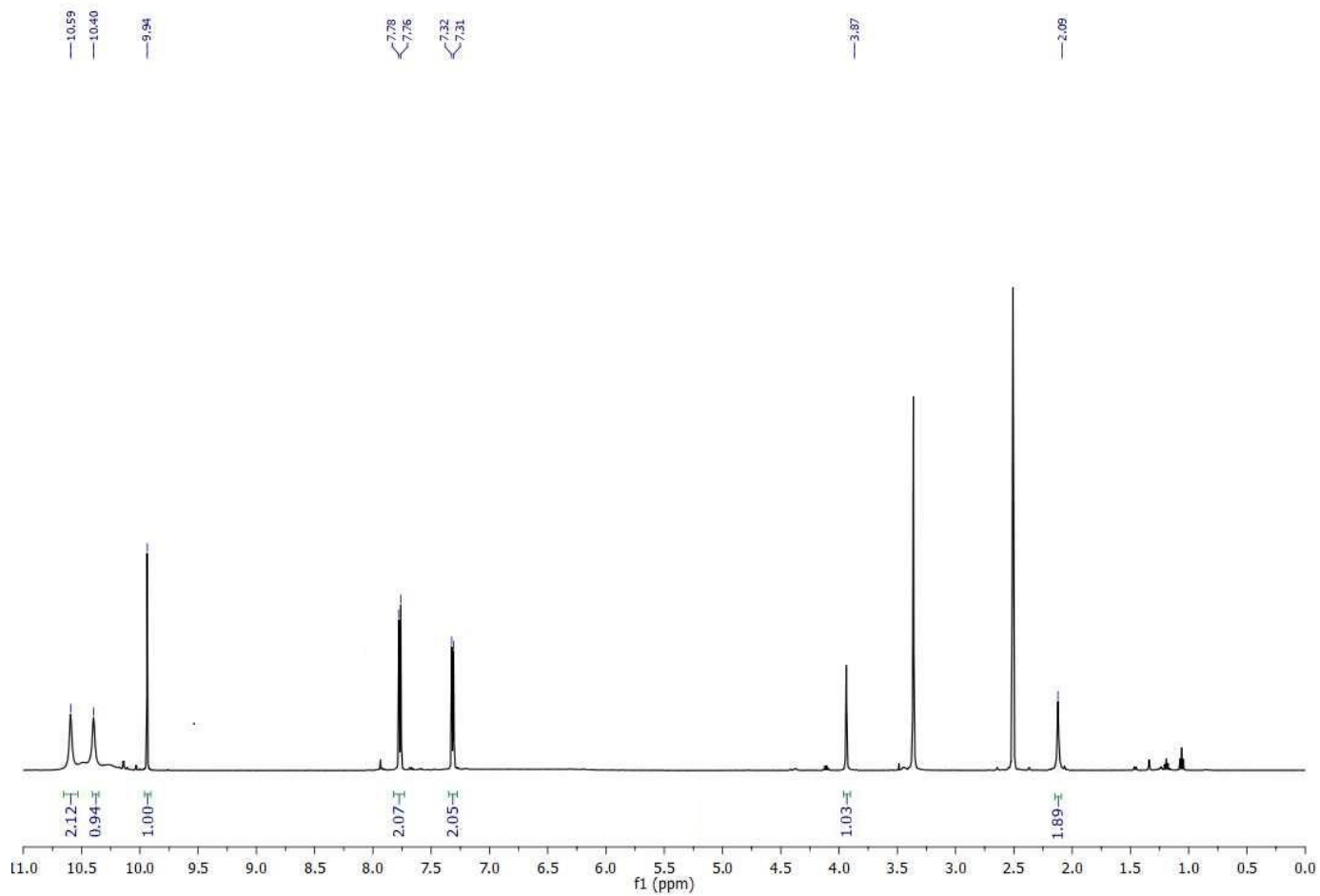


Figure S69.  $^1\text{H}$  NMR spectrum of compound 5m

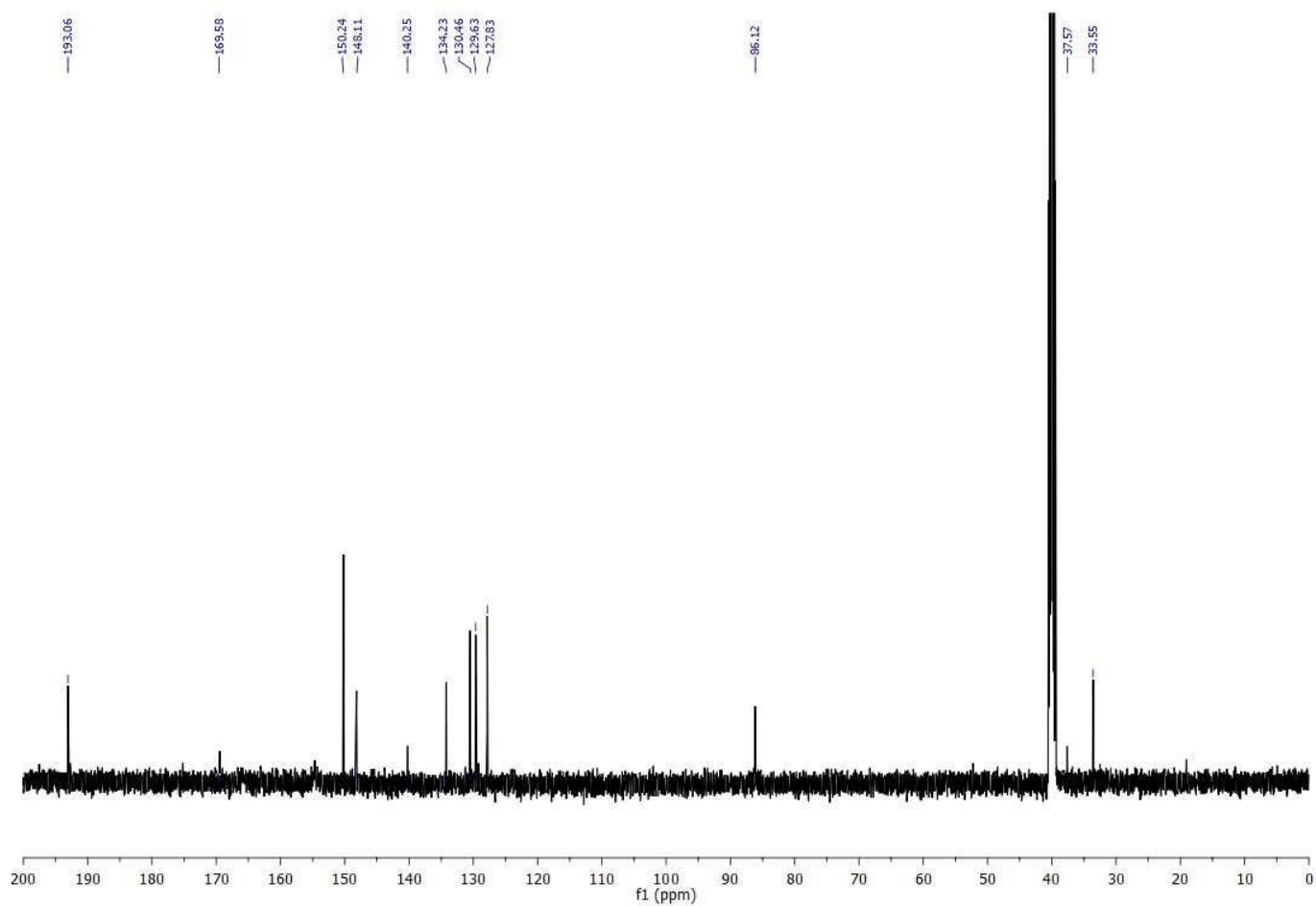


Figure S70.  $^{13}\text{C}$  NMR spectrum of compound 5m

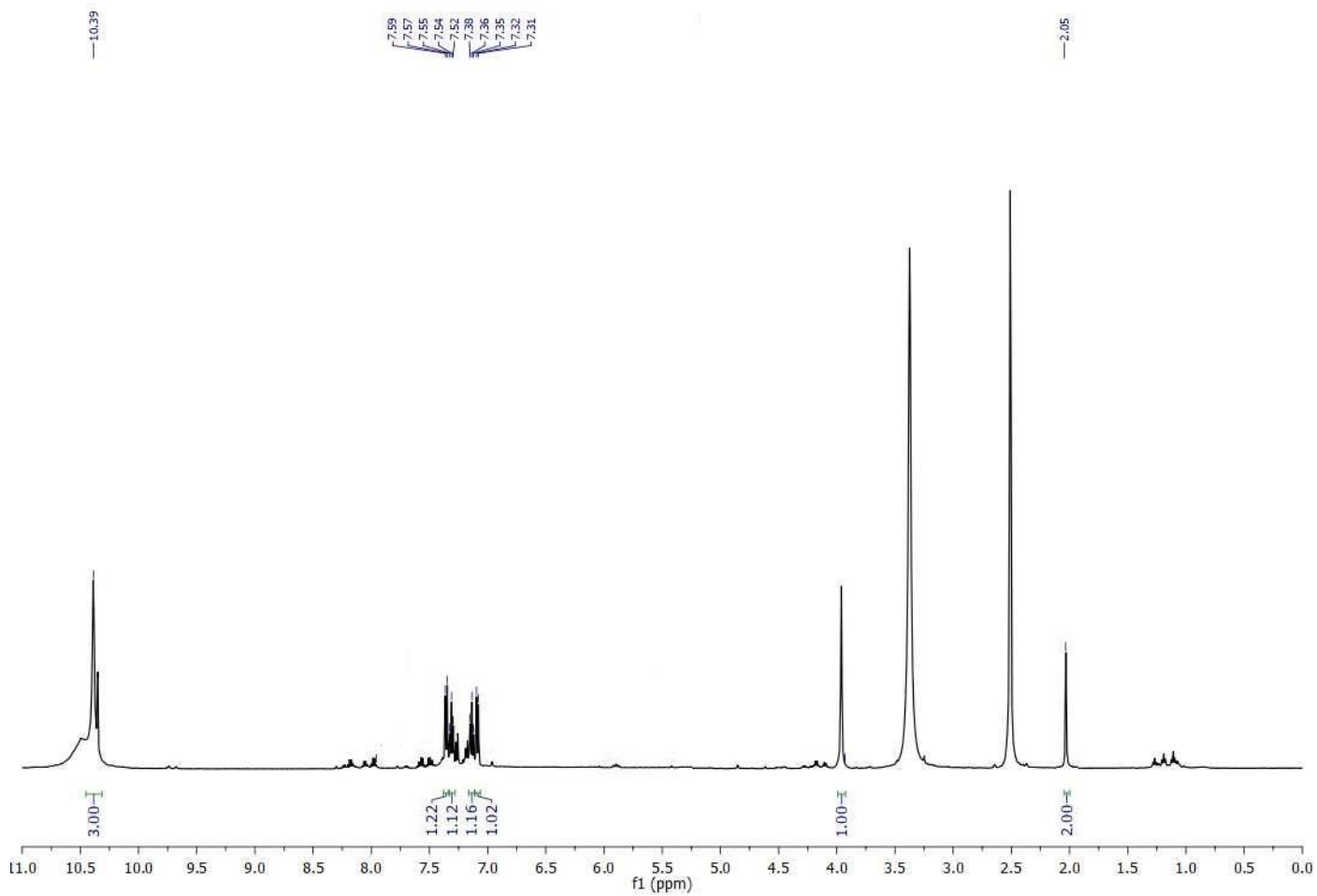


Figure S71. <sup>1</sup>H NMR spectrum of compound 5n

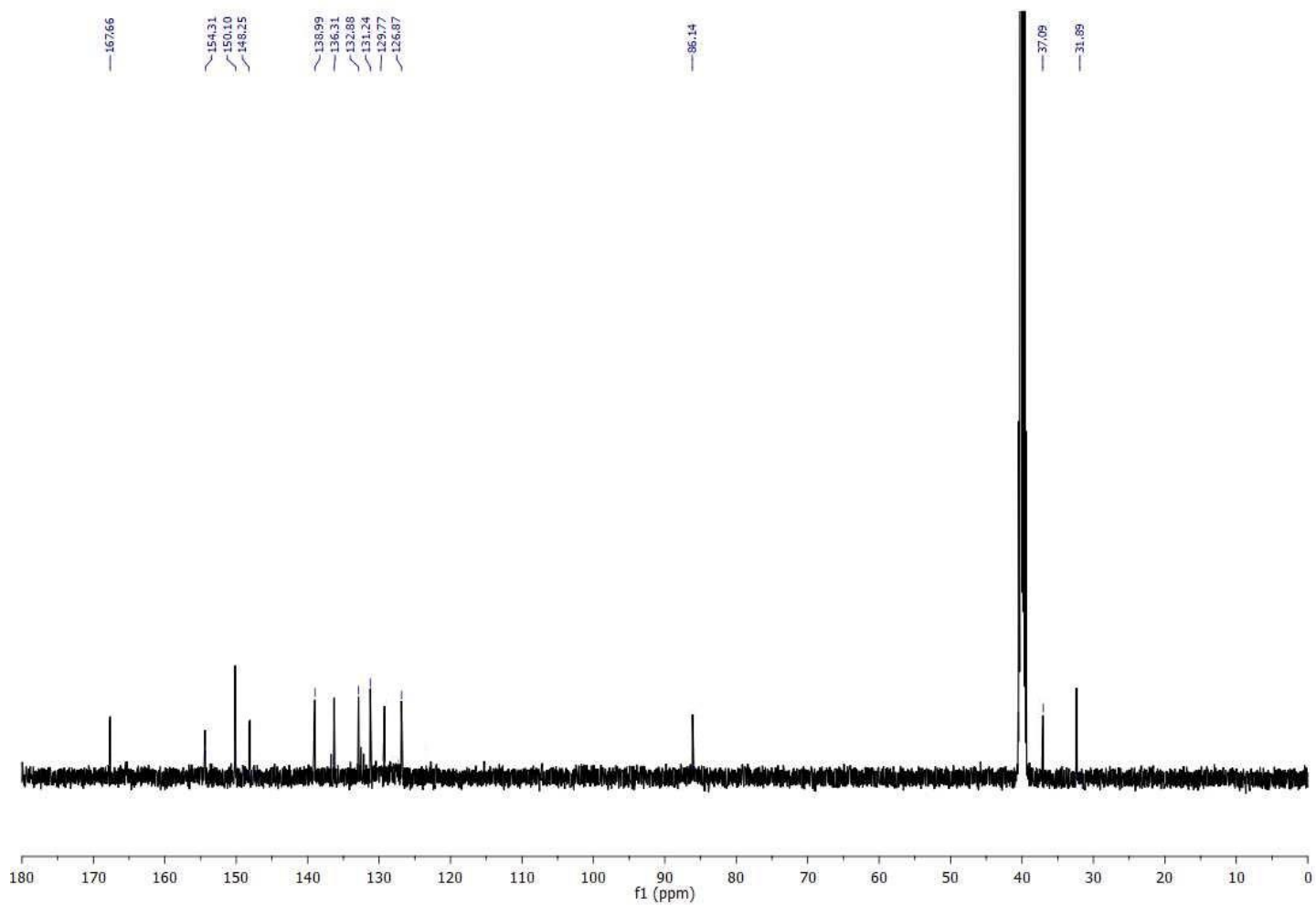


Figure S72.  $^{13}\text{C}$  NMR spectrum of compound 5n

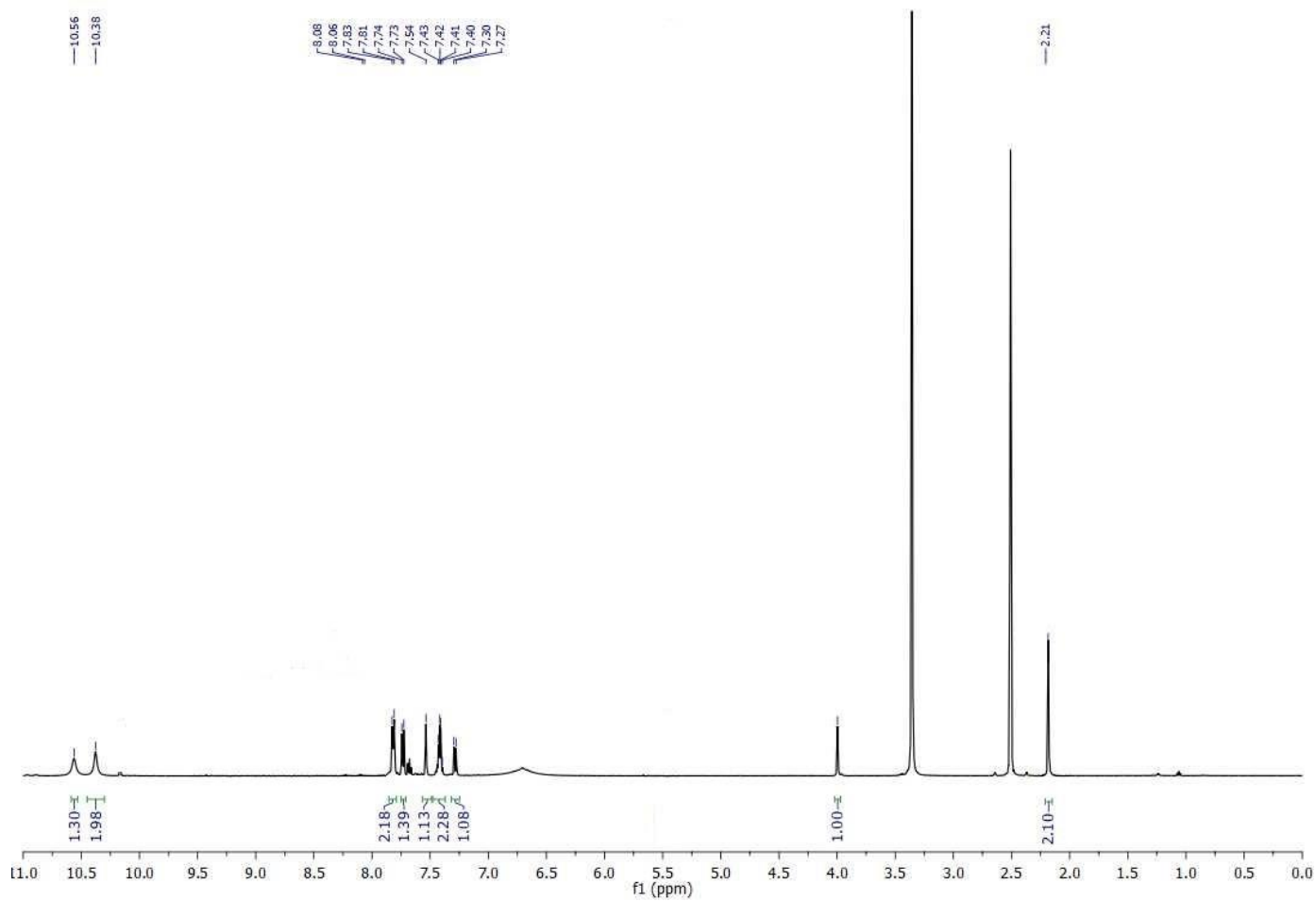


Figure S73.  $^1\text{H}$  NMR spectrum of compound 5o

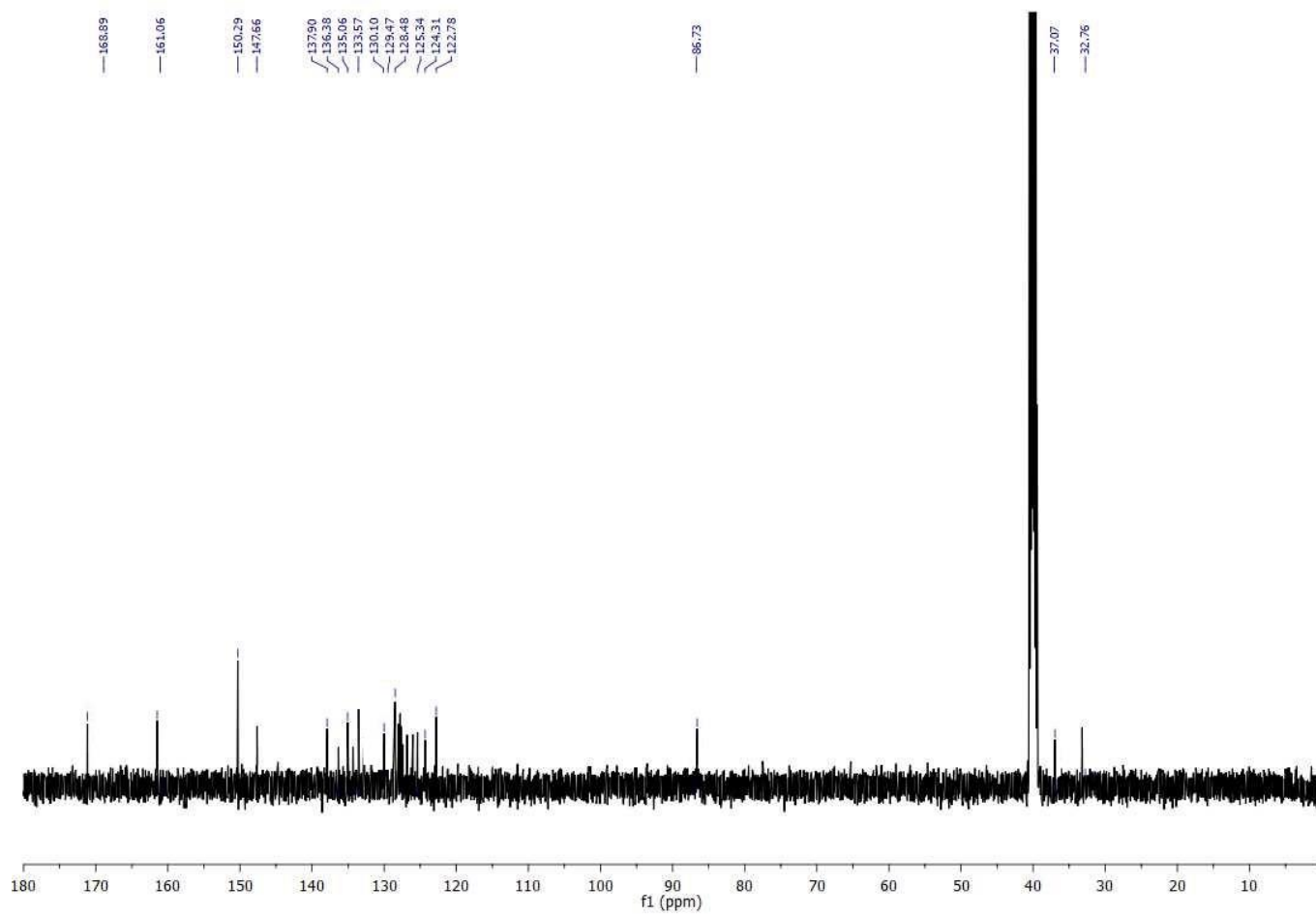


Figure S74.  $^{13}\text{C}$  NMR spectrum of compound 5o



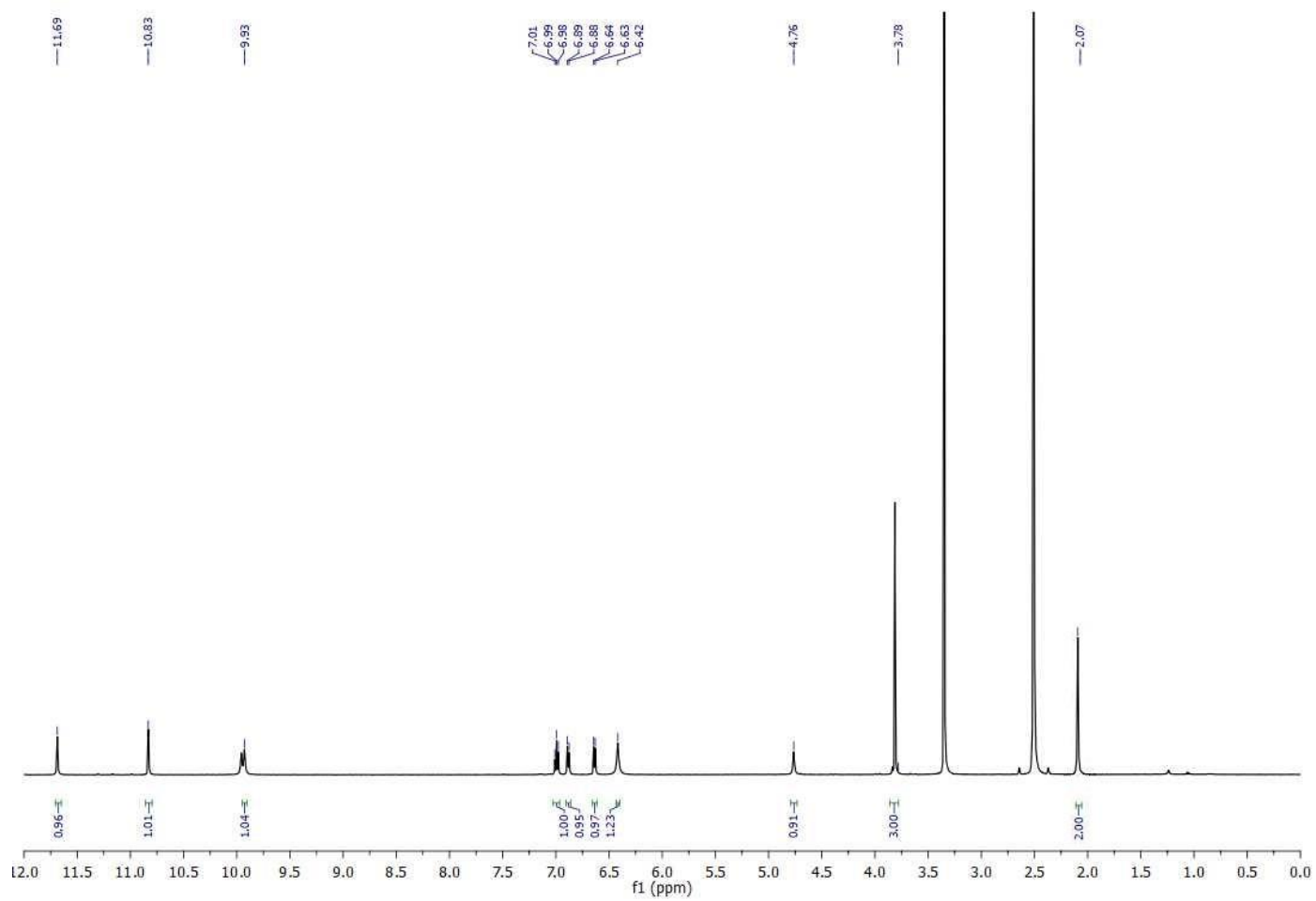


Figure S75.  $^1\text{H}$  NMR spectrum of compound 5p

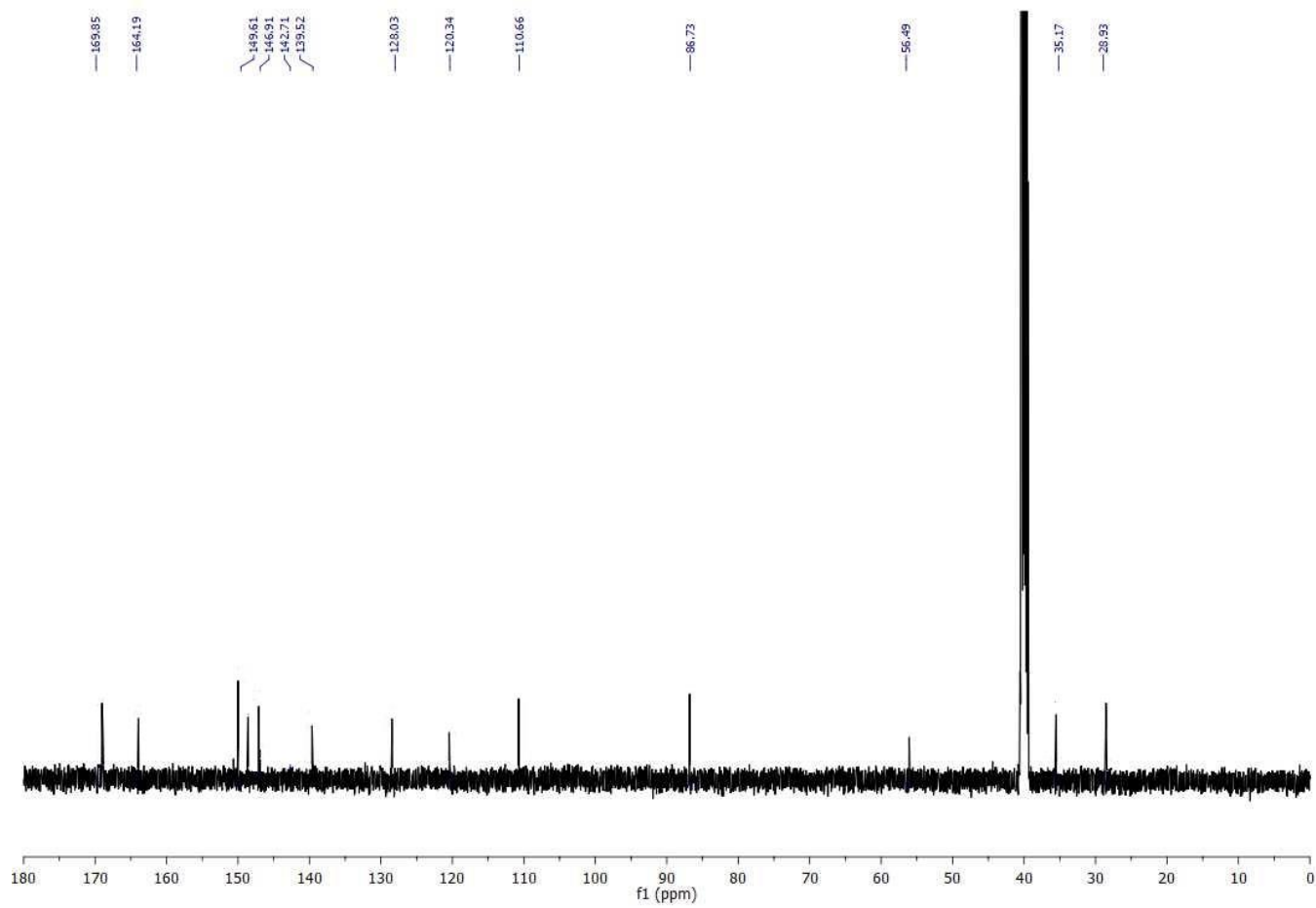


Figure S76.  $^{13}\text{C}$  NMR spectrum of compound 5p

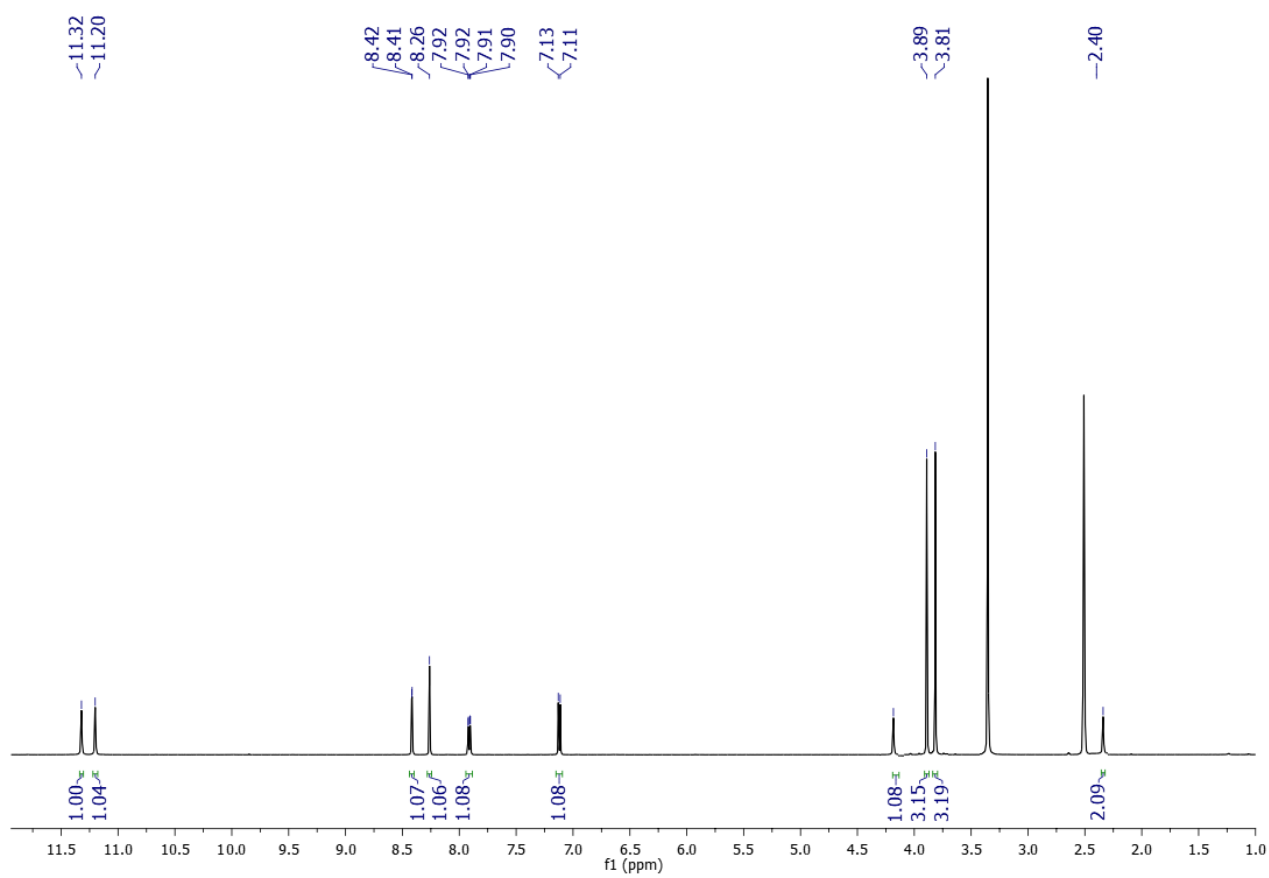


Figure S77.  $^1\text{H}$  NMR spectrum of compound 5q

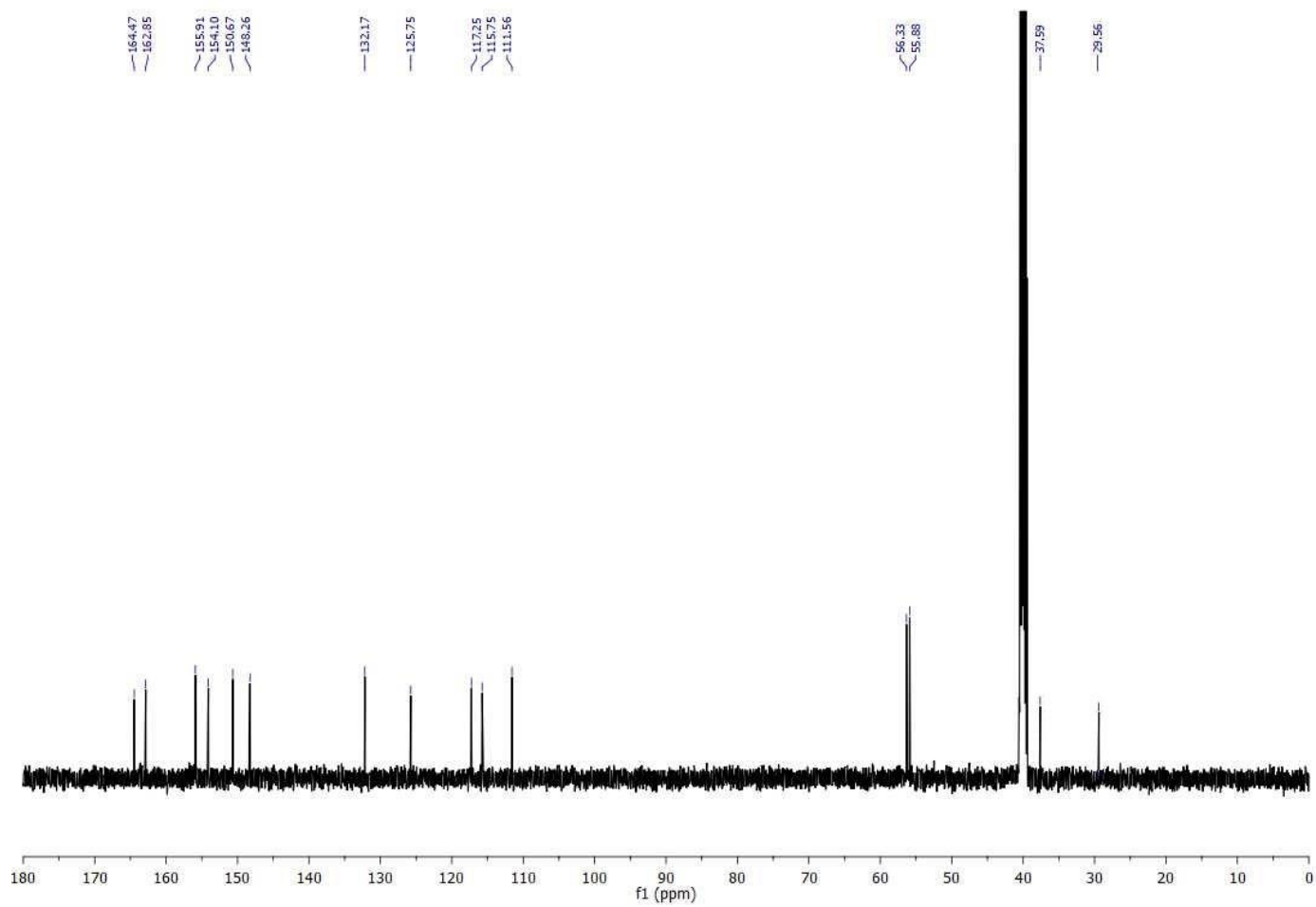


Figure S78.  $^{13}\text{C}$  NMR spectrum of compound 5q

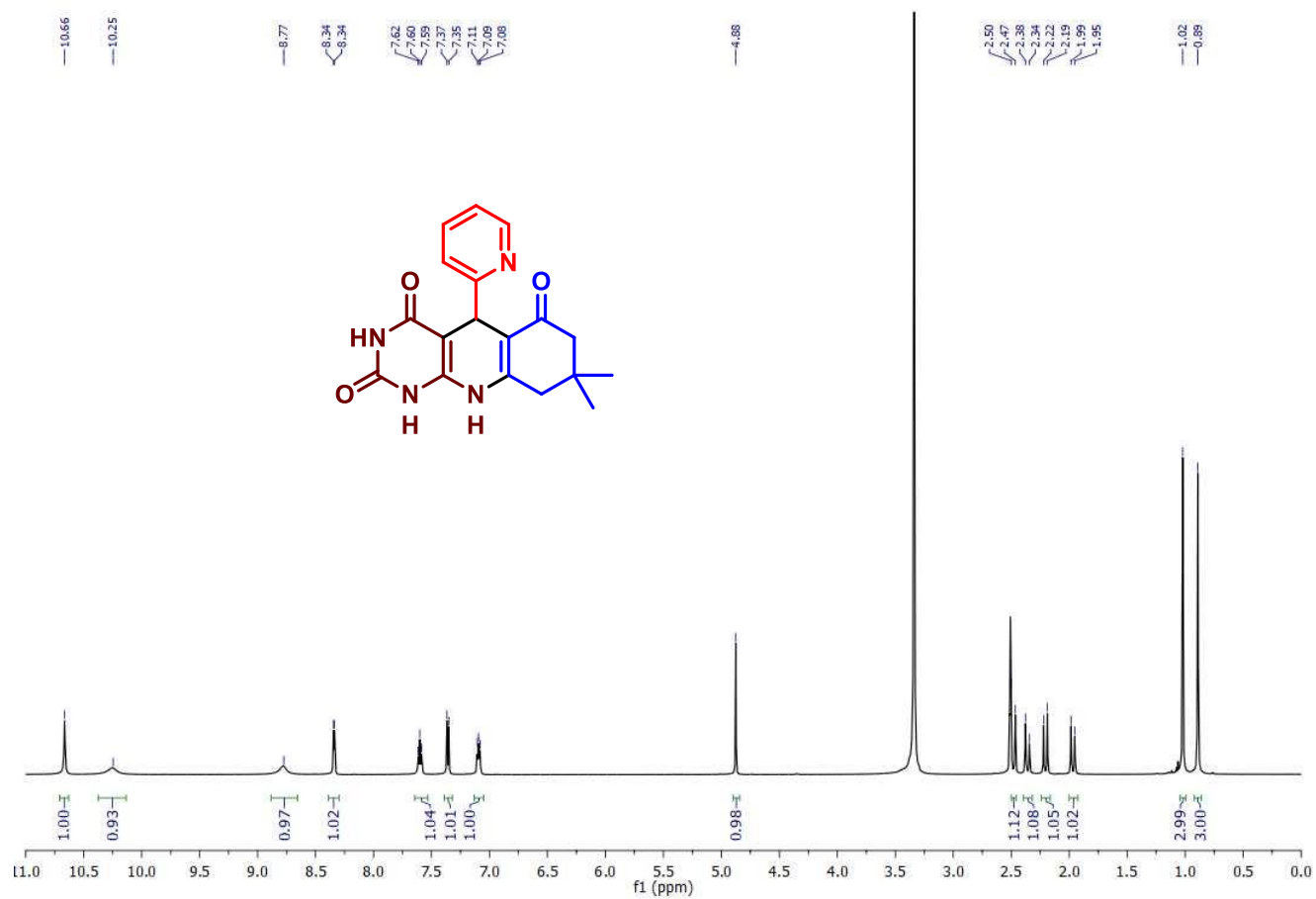


Figure S79.  $^1\text{H}$  NMR spectrum of compound 4x

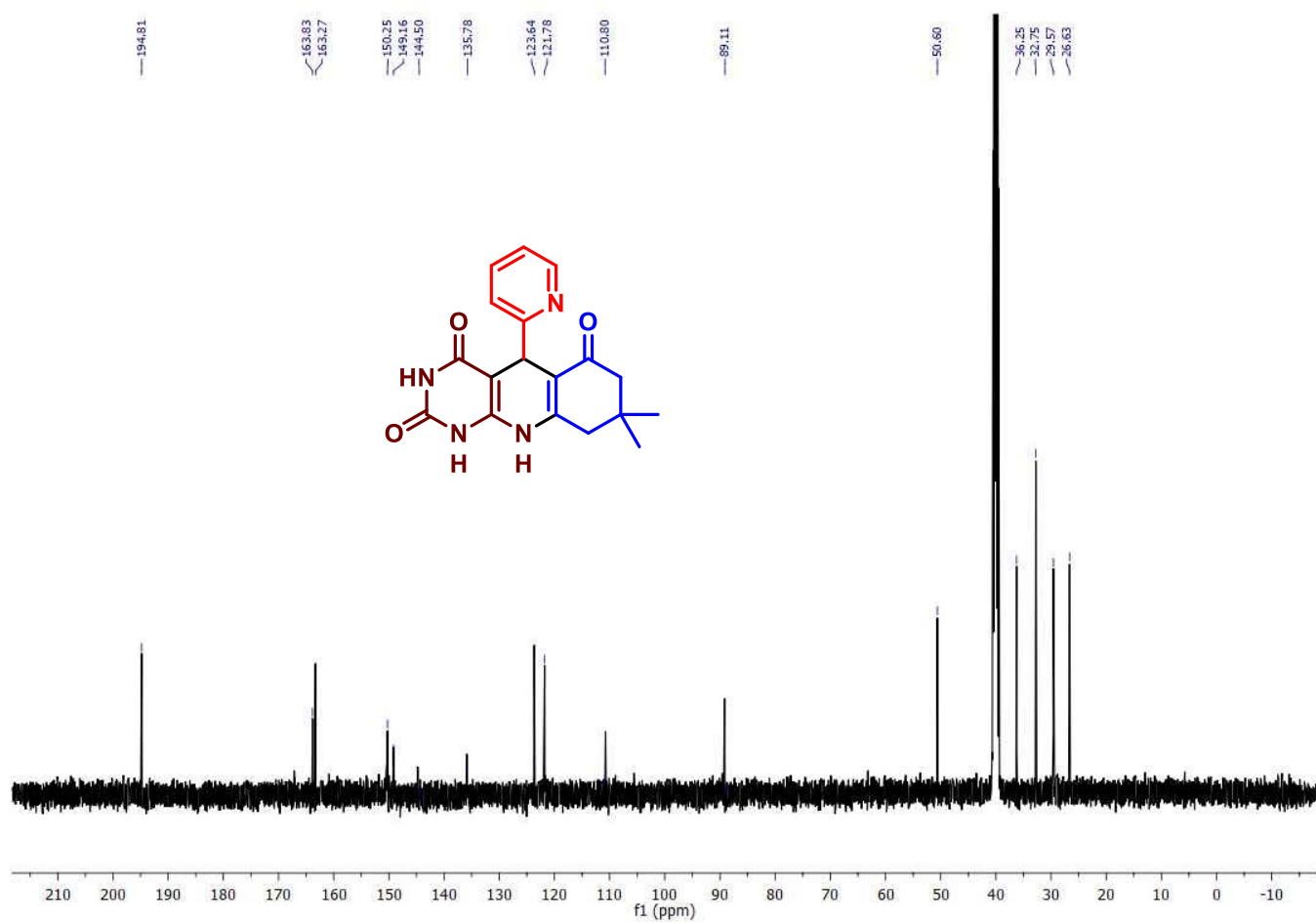


Figure S80. <sup>13</sup>C NMR spectrum of compound 4x

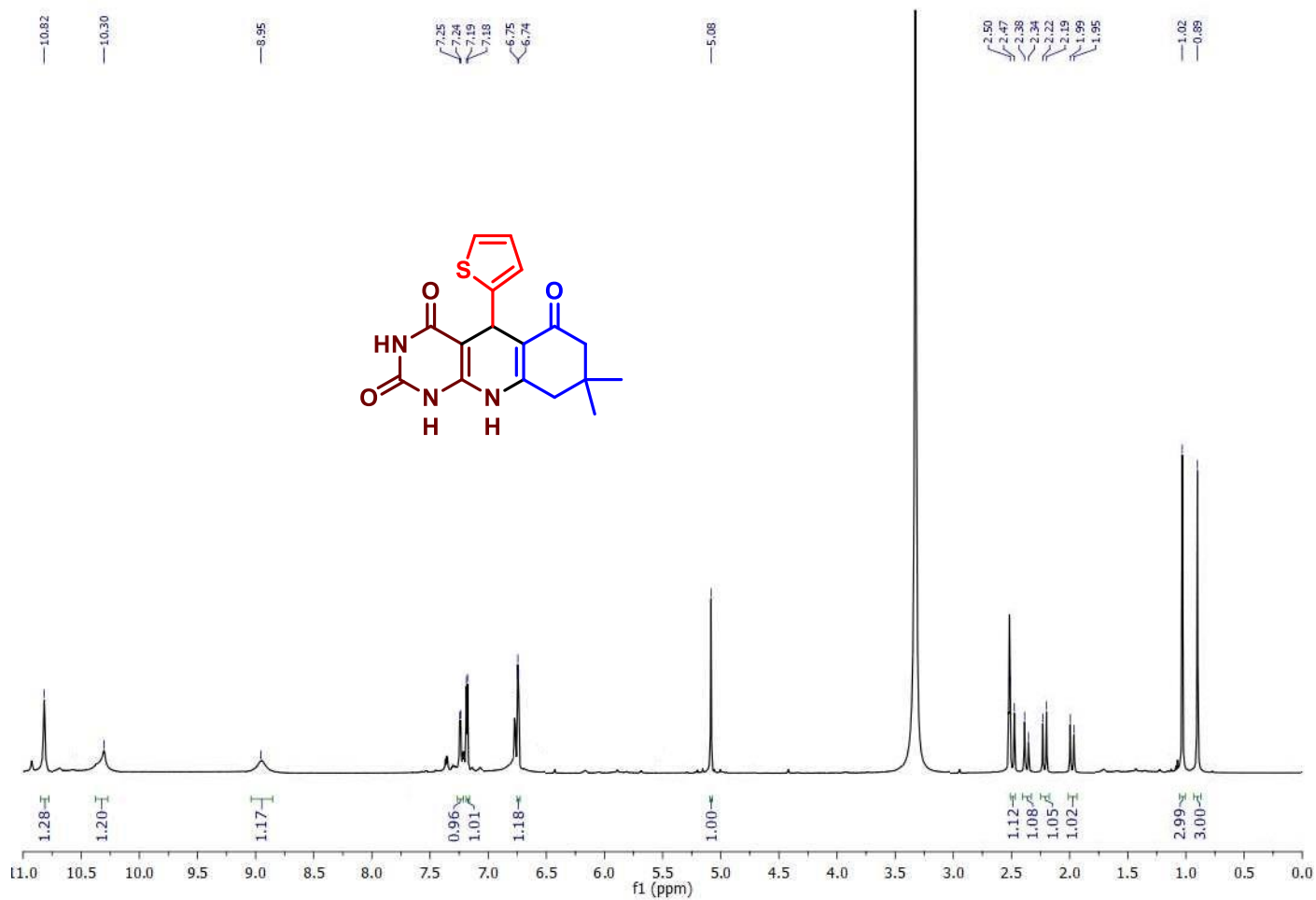


Figure S81.  $^1\text{H}$  NMR spectrum of compound 4y

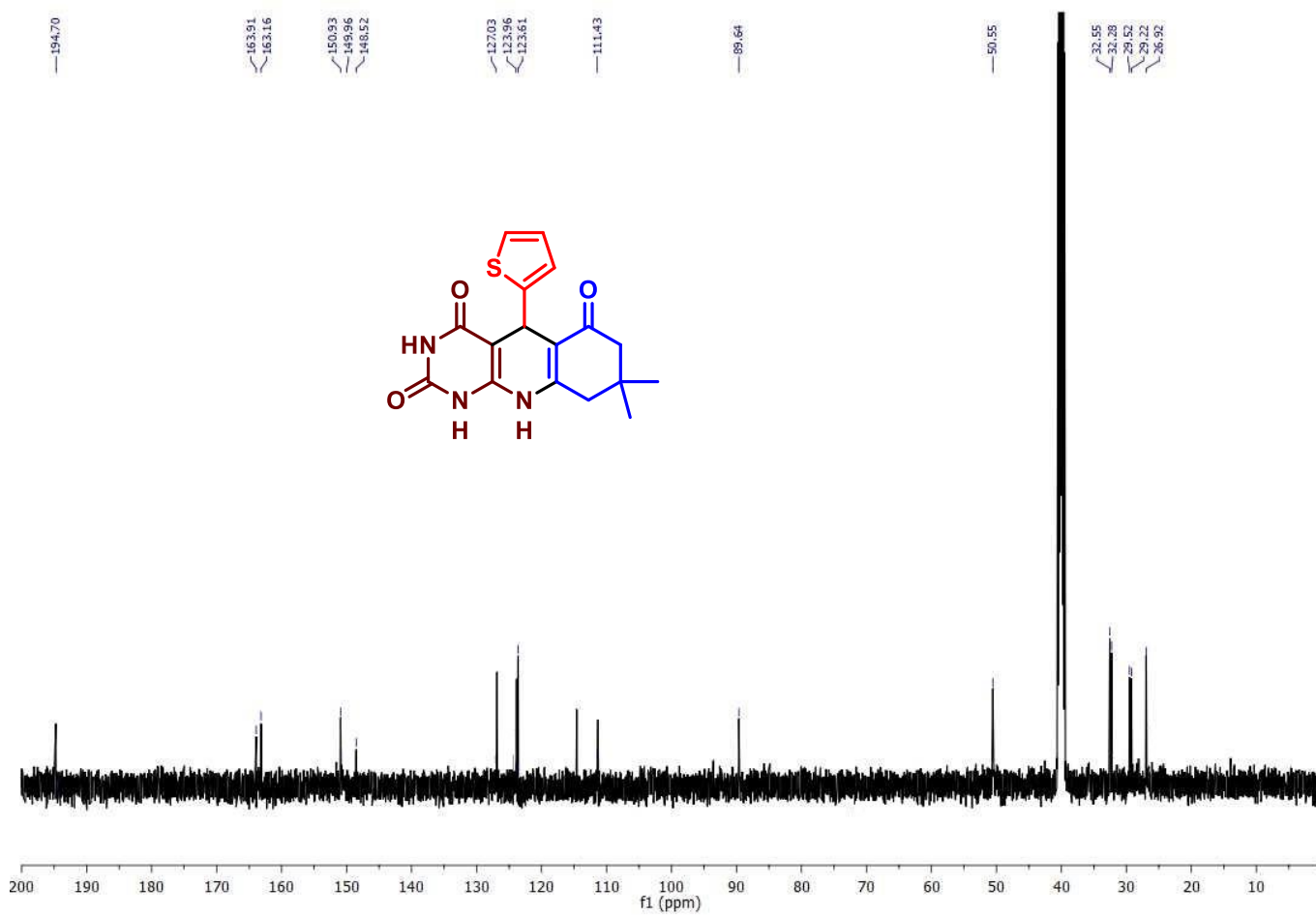


Figure S82. <sup>13</sup>C NMR spectrum of compound 4y



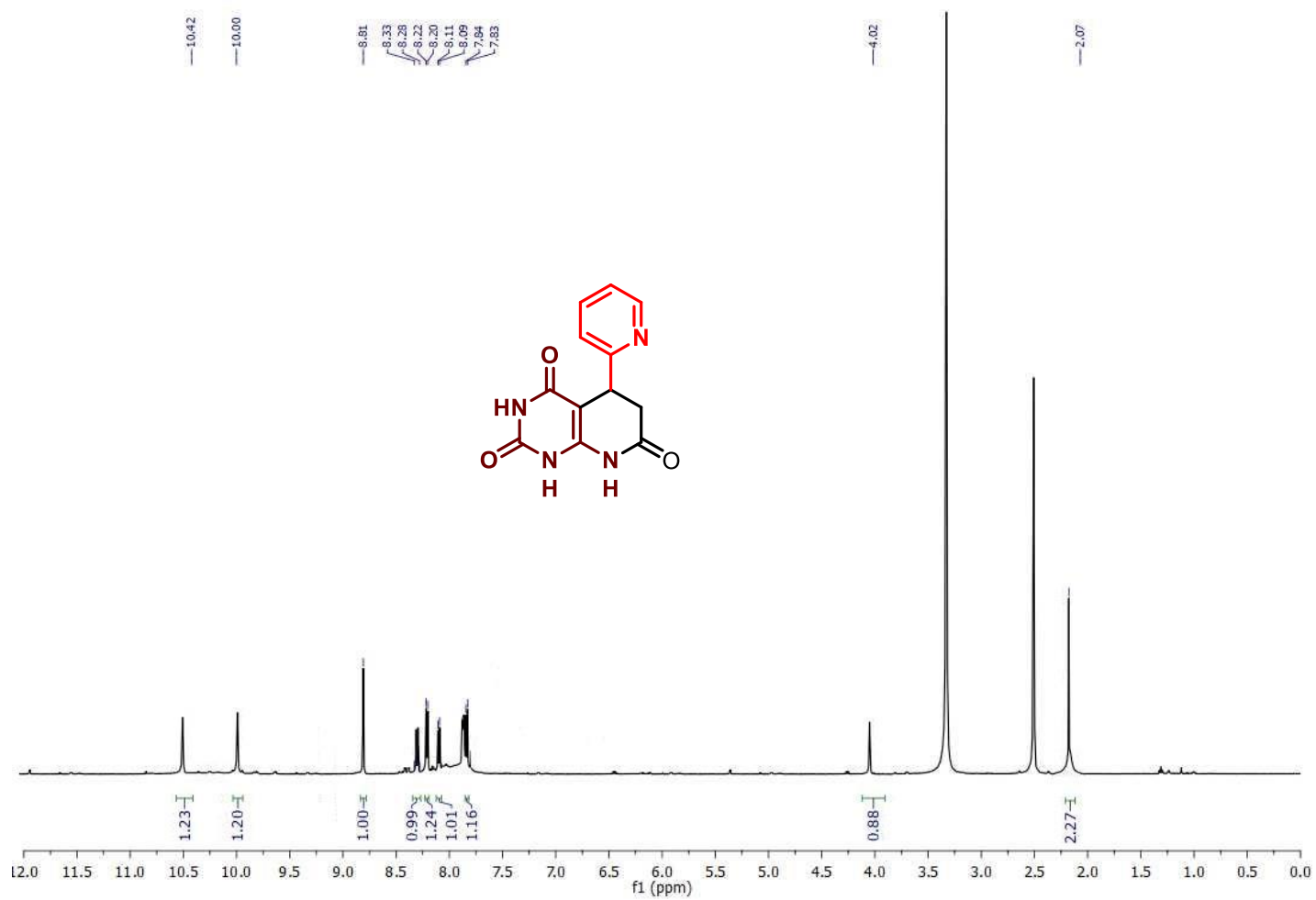


Figure S83. <sup>1</sup>H NMR spectrum of compound 5r

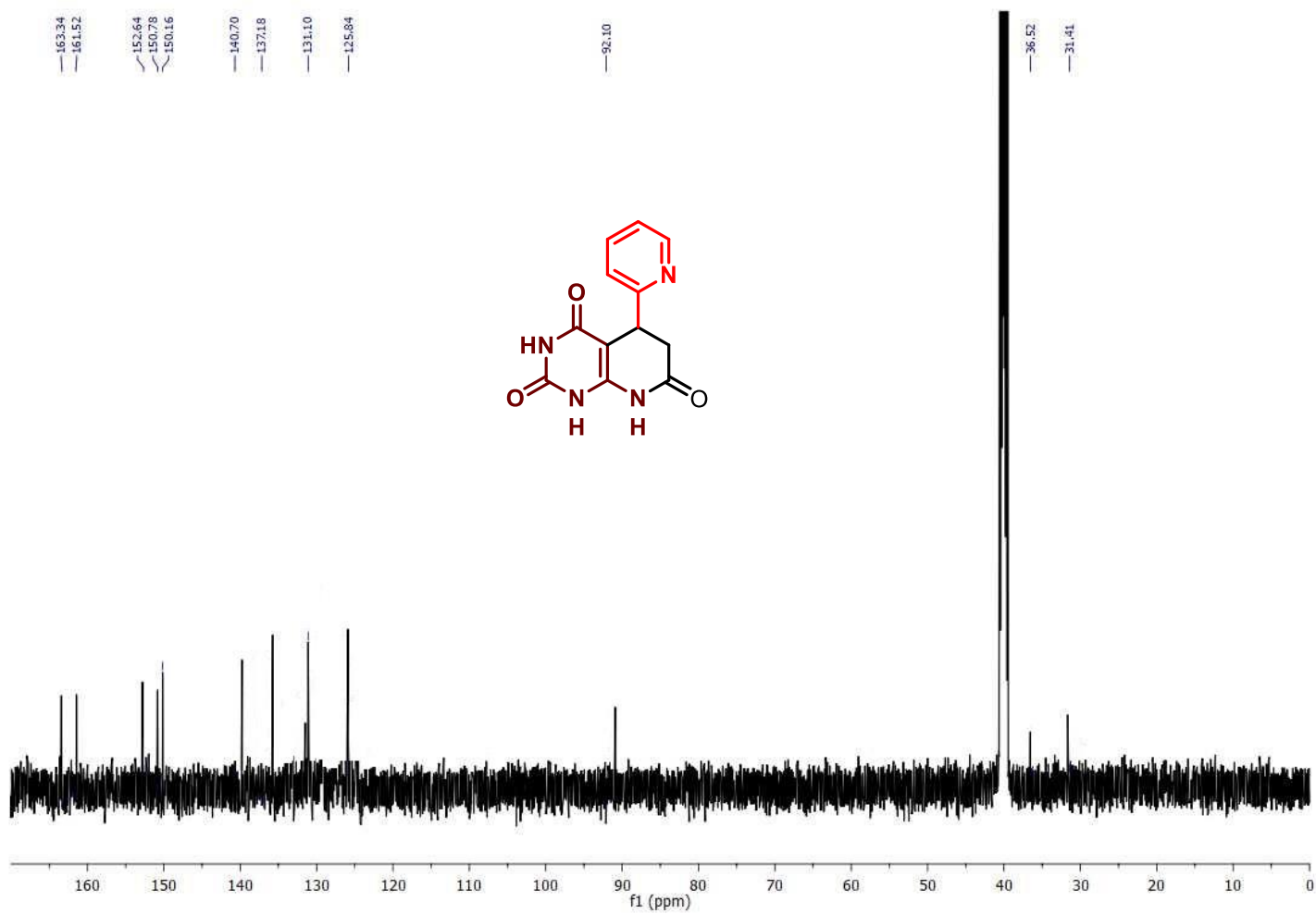


Figure S84. <sup>13</sup>C NMR spectrum of compound 5r

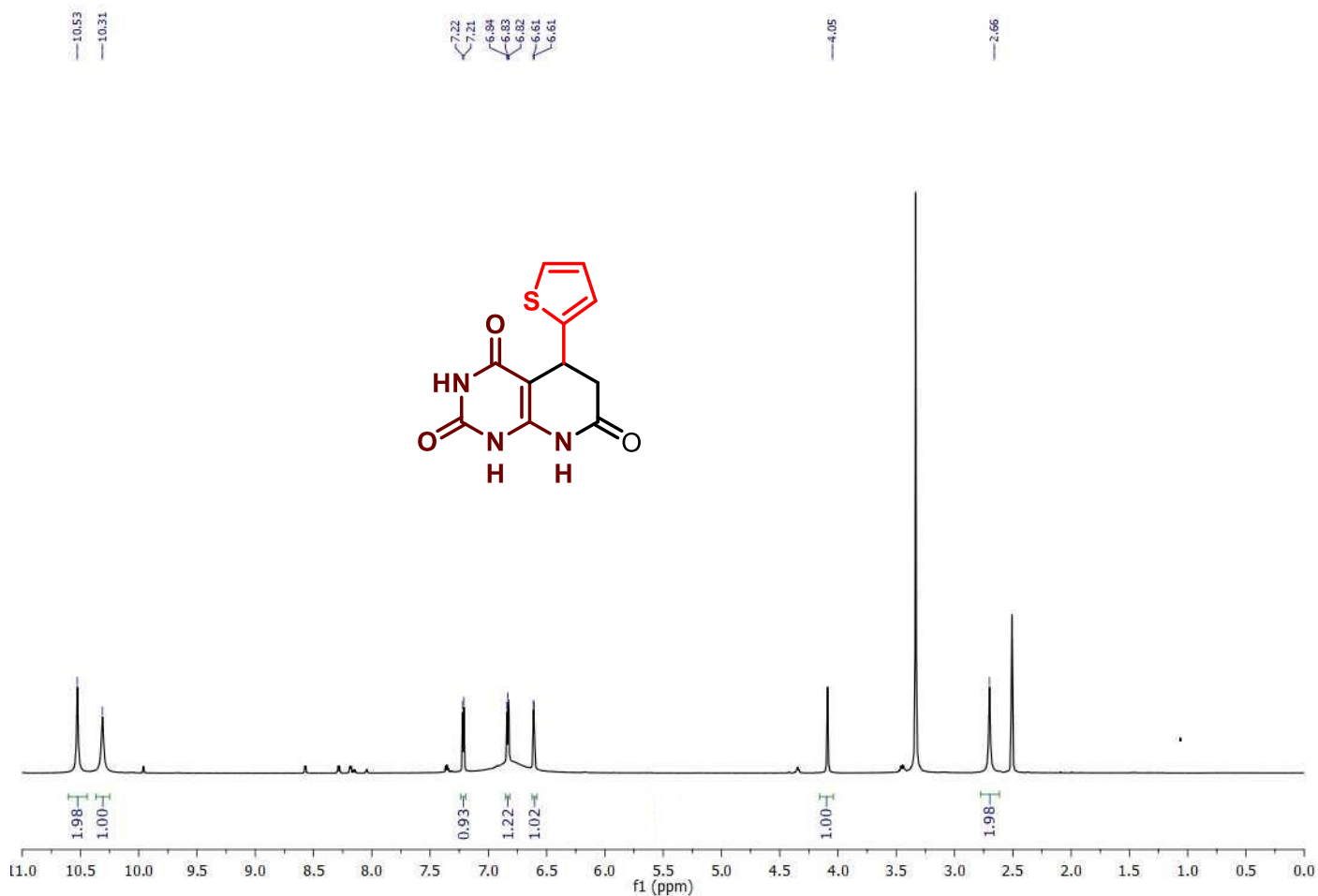


Figure S85. <sup>1</sup>H NMR spectrum of compound 5s

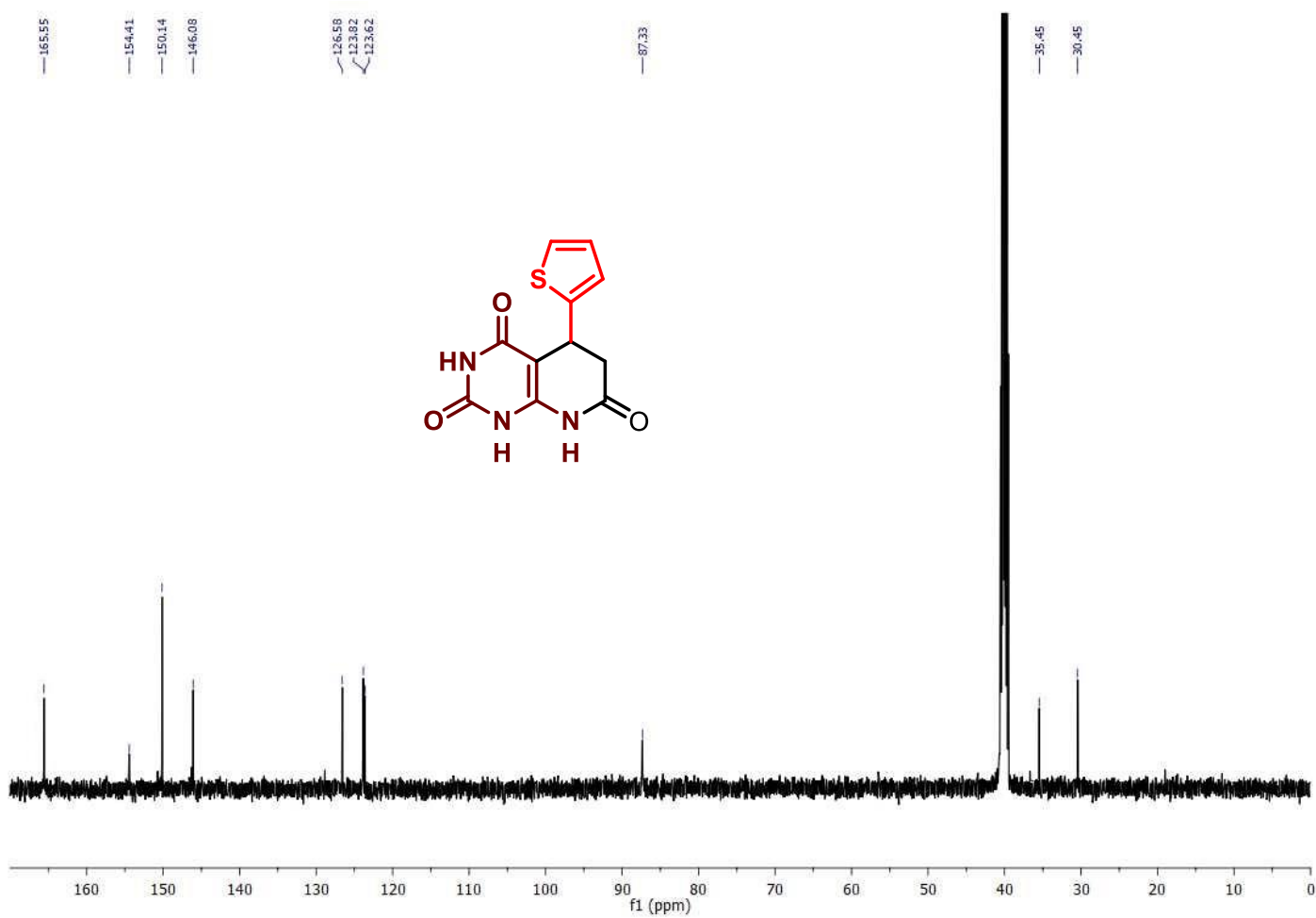


Figure S86.  $^{13}\text{C}$  NMR spectrum of compound 5s

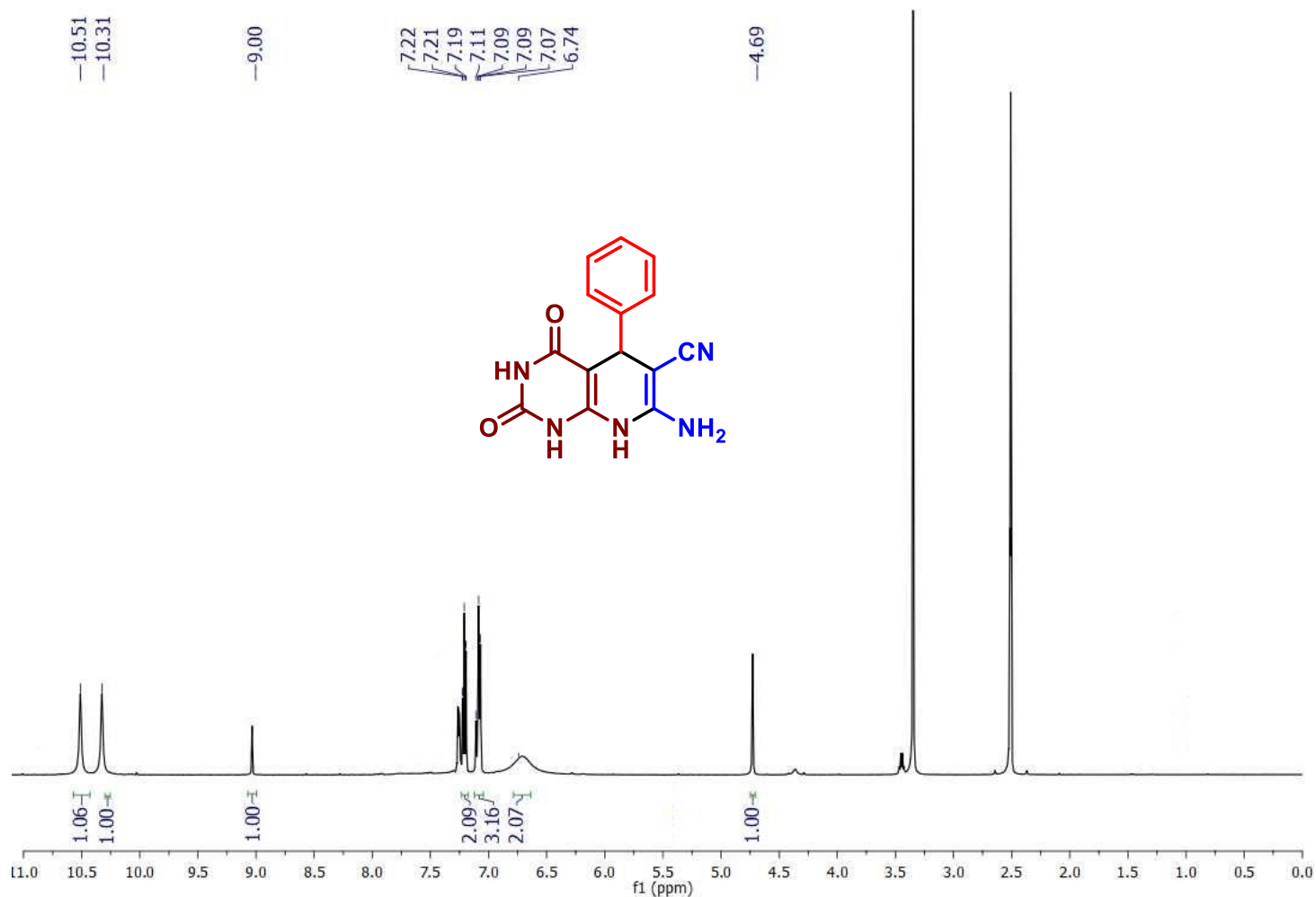


Figure S87. <sup>1</sup>H NMR spectrum of compound 7-amino-2,4-dioxo-5-phenyl-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carbonitrile

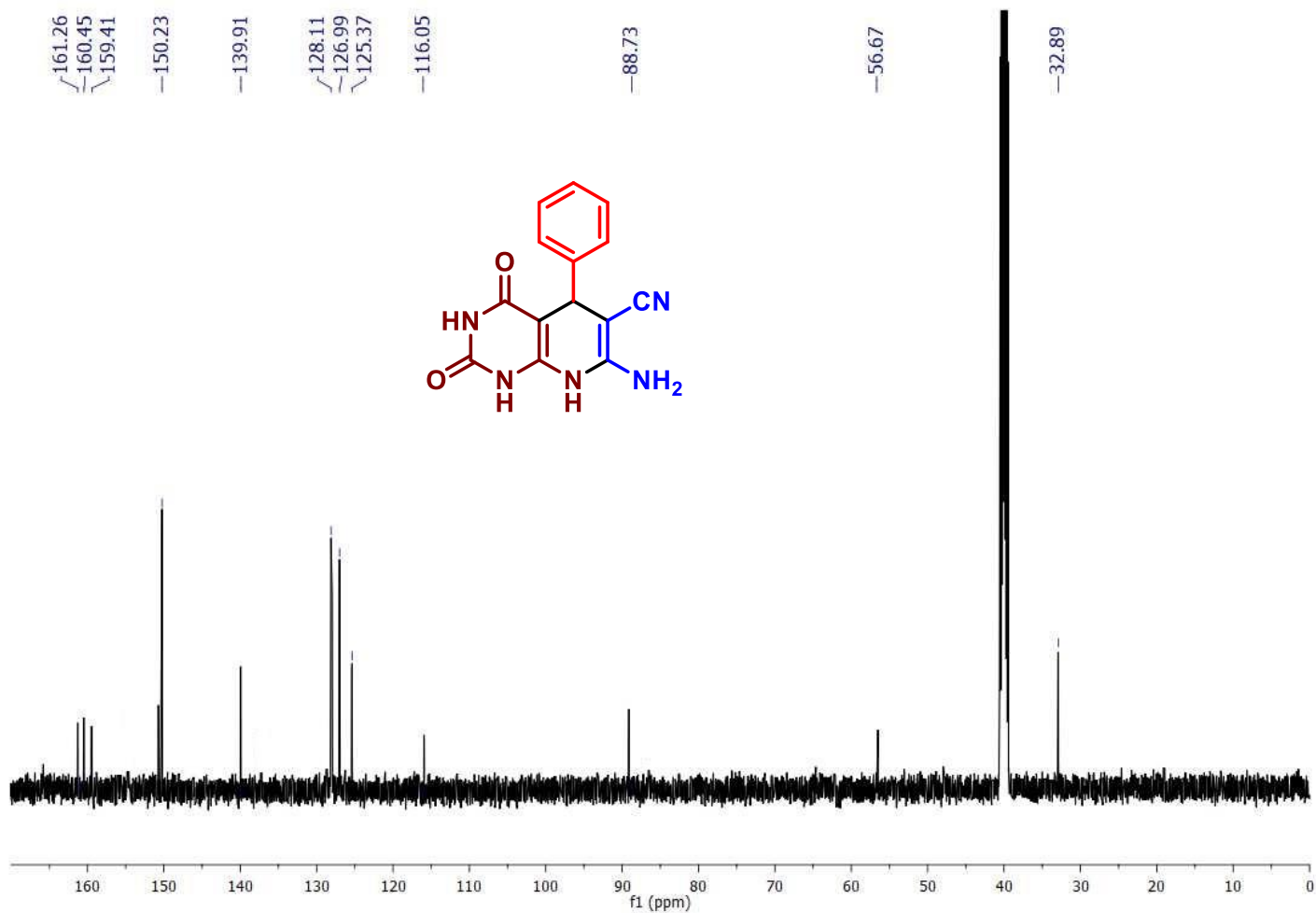


Figure S88.  $^{13}\text{C}$  NMR spectrum of compound 7-amino-2,4-dioxo-5-phenyl-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carbonitrile

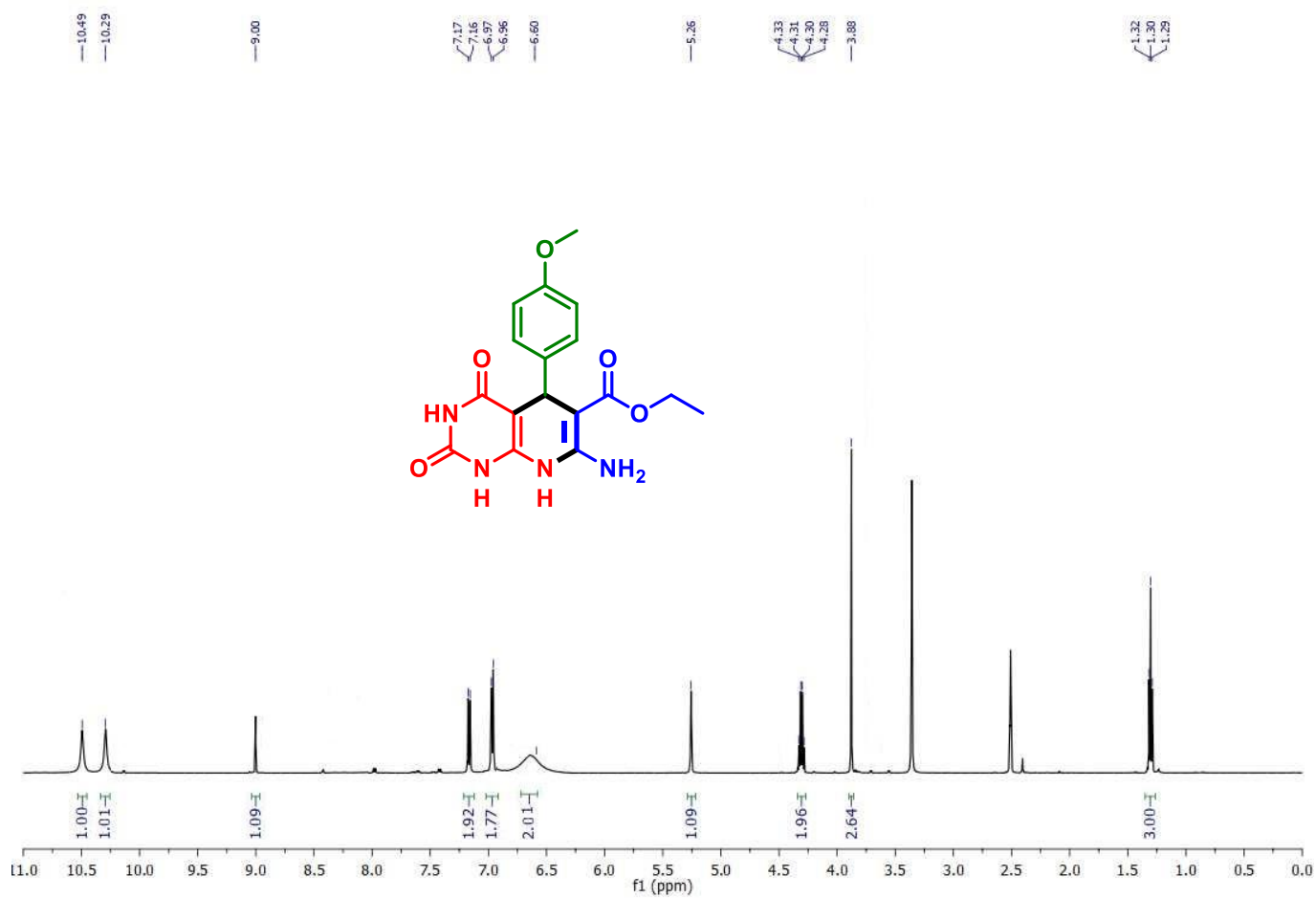


Figure S89. <sup>1</sup>H NMR spectrum of compound ethyl 7-amino-5-(4-methoxyphenyl)-2,4-dioxo-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carboxylate

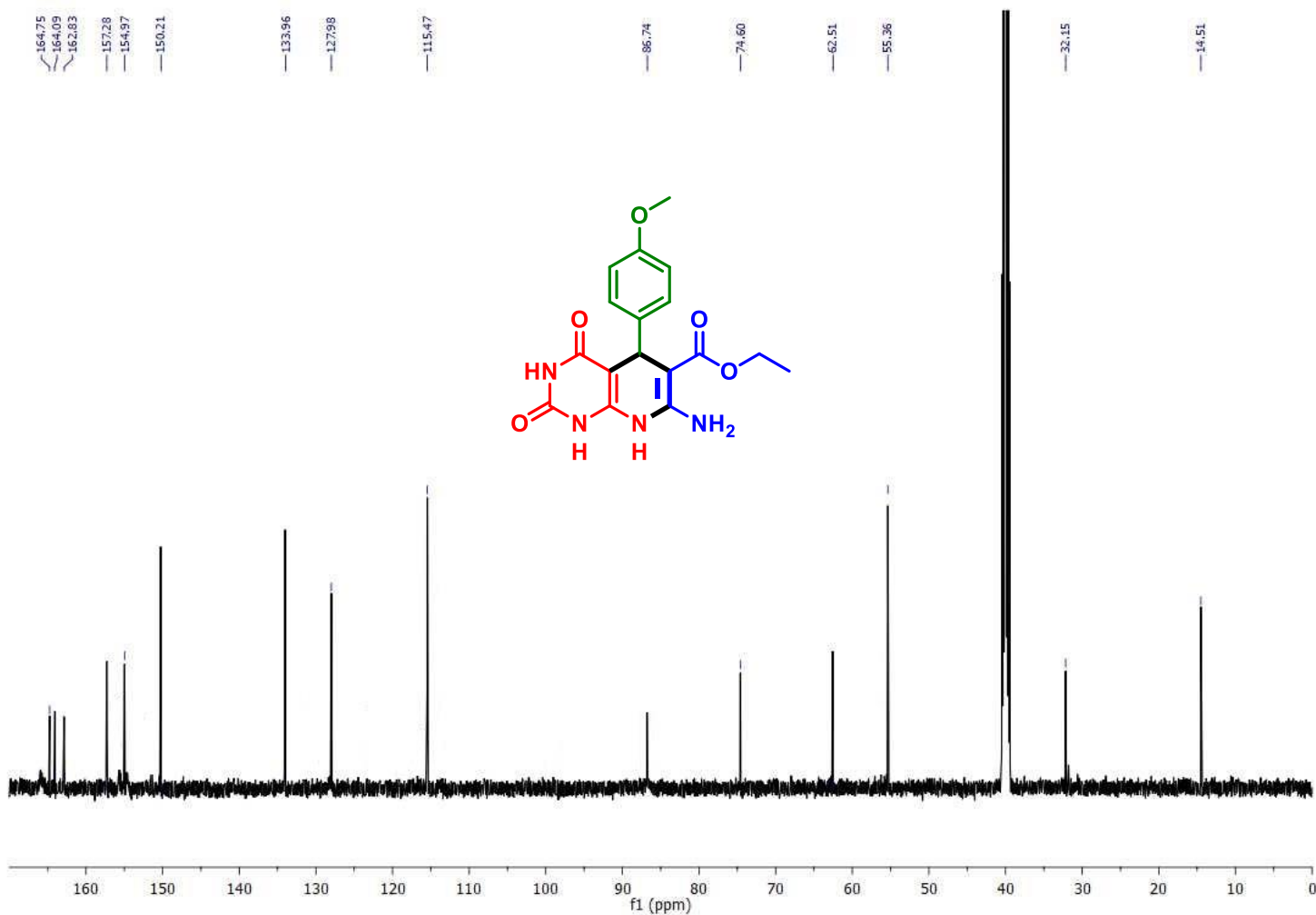


Figure S90.  $^{13}\text{C}$  NMR spectrum of compound ethyl 7-amino-5-(4-methoxyphenyl)-2,4-dioxo-1,2,3,4,5,8-hexahydropyrido[2,3-d]pyrimidine-6-carboxylate



# HRMS Spectra of product

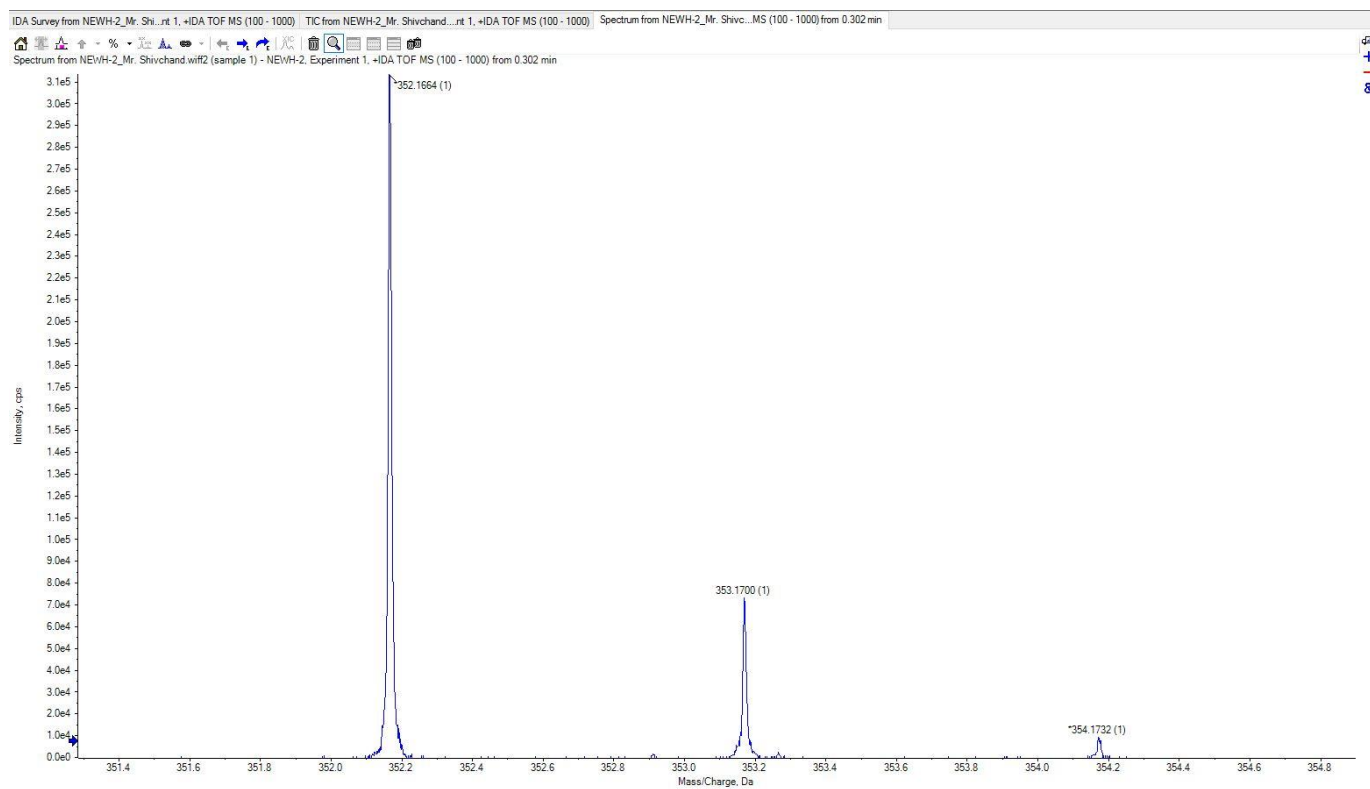


Figure S89. HRMS spectra of 4b



Figure S90. HRMS spectra of 4l

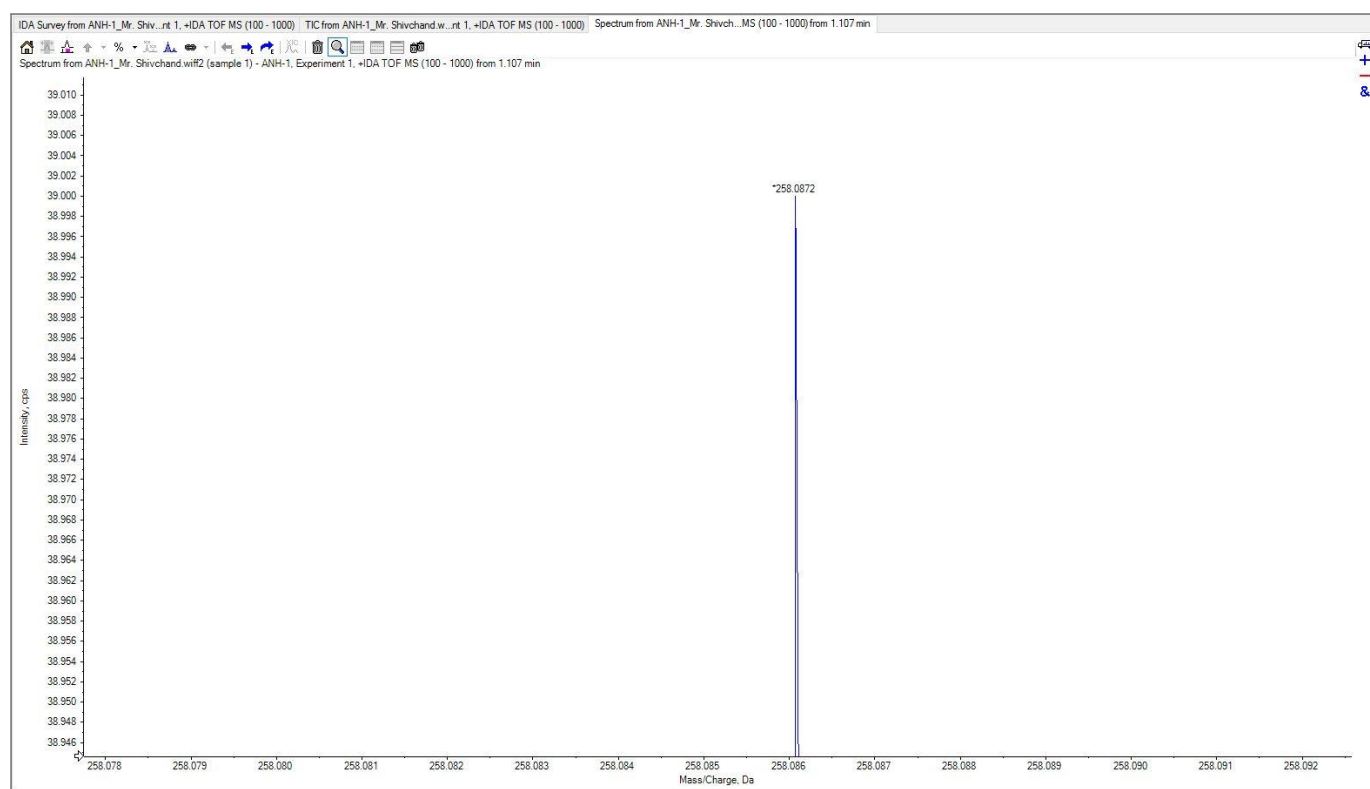


Figure S91. HRMS spectra of 5a

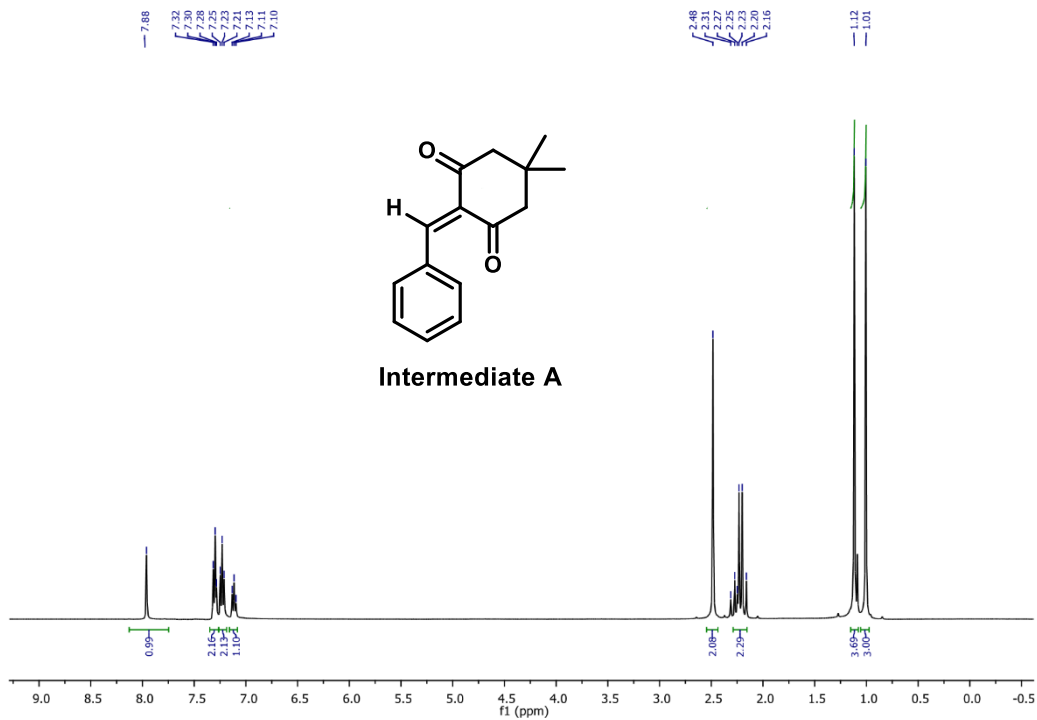


Figure S92. <sup>1</sup>H NMR spectra of Intermediate A

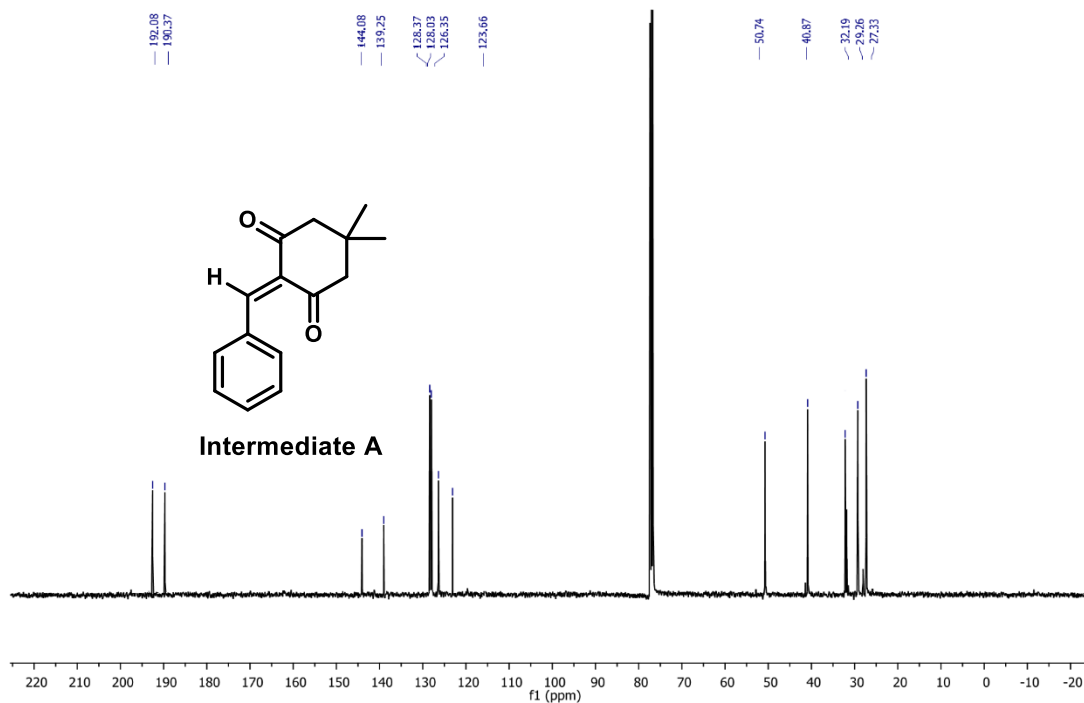


Figure S93. <sup>13</sup>C NMR spectra of Intermediate A

