

## **Synthesis and structural optimization of 2,7,9-trisubstituted purin-8-ones as FLT3-ITD inhibitors**

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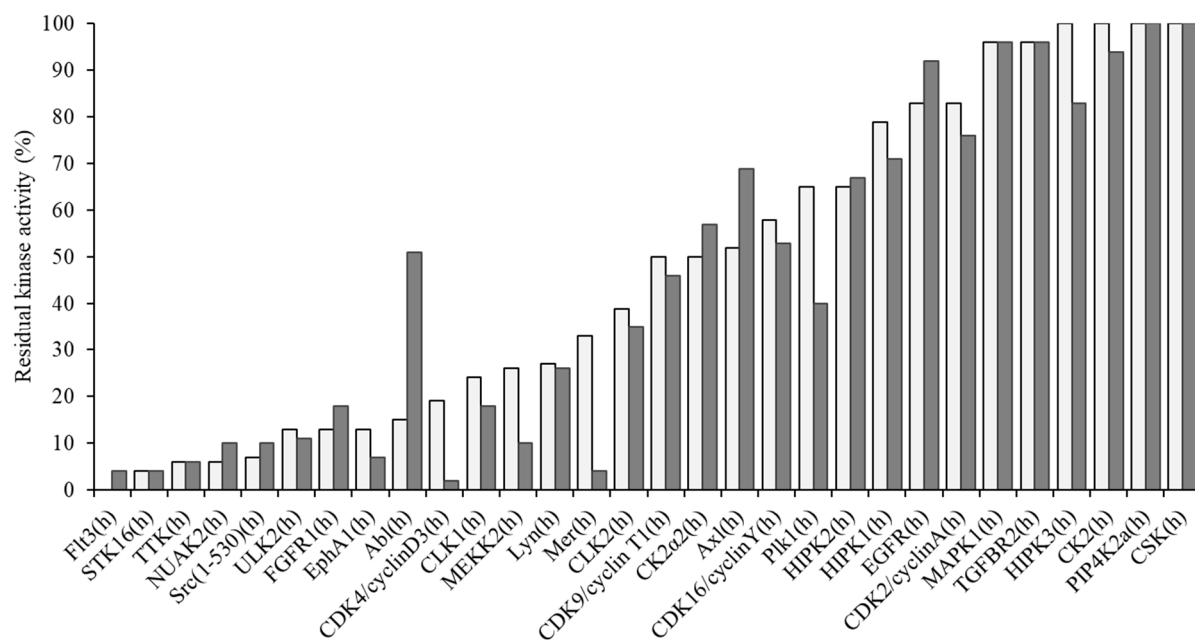
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References

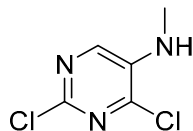
**Figure S1.** Kinase selectivity profiles of **14e** (white bars) and **14d** (grey bars) assayed at 1  $\mu$ M concentration.



## Procedures for the synthesis of intermediates 2-10

### Method i

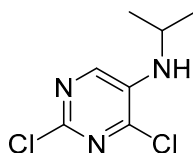
#### *2,4-dichloro-N-methylpyrimidin-5-amine 2* [1]



A solution of 2,4-dichloropyrimidine-5-amine **1** (5 g, 30.5 mmol) in MeOH (90 mL) was cooled to 0°C. Glacial acetic acid (10 mL, 183 mmol) was added, and then a solution of 37% aq. formaldehyde (2.7 mL, 36.6 mmol). A mixture was stirred for 1 hour, and then pulled out from an ice bath and an additional amount of acetic acid (20 mL) was added. After another 3 hours, NaBH<sub>3</sub>CN (4.6 g, 73.2 mmol) was added in two portions within two hours. After stirring a mixture for 20 hours at 5°C, a solvent was concentrated using RVO, diluted with water (100 mL), and cooled in an ice bath. Solid NaHCO<sub>3</sub> was added to neutralize acetic acid. Then, a water phase was extracted with DCM (2x 80 mL) and combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, and evaporated using RVO. The solid residue was diluted with MeOH (10 mL) and cooled in an ice bath and water (80 mL). After proper mixing, a solid was filtered off and washed with water to yield 4.4 g (81 %) of **2** as a white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.88 (s, 1H), 4.37 (s, 1H), 2.98 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 146.5, 146.0, 139.1, 138.7, 30.0. HRMS (ESI-TOF): calcd for C<sub>5</sub>H<sub>6</sub>Cl<sub>2</sub>N<sub>3</sub> [M+H]<sup>+</sup> 177.9933, found 177.9934.

### Method ii

#### *2,4-dichloro-N-isopropylpyrimidin-5-amine 3* [2]



A round bottom flask was charged with **1** (5 g, 30.5 mmol), 2,2-dimethoxypropane (61 mL, 50 mmol), and glacial acetic acid (7.3 mL, 134 mmol). A mixture was cooled in an ice bath. Then, a suspension of NaBH(OAc)<sub>3</sub> (26 g, 122 mmol) in DCM (61 mL) was added. After 2 hours, a reaction mixture was

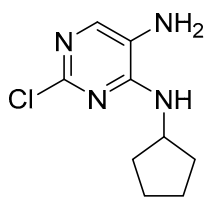
pulled out from the ice bath and mixed for 20 hours. The mixture was concentrated under reduced pressure; diluted with DCM (150 mL), washed with 10% K<sub>2</sub>CO<sub>3</sub> (100 mL), water (100 mL), and brine (100 mL), dried over MgSO<sub>4</sub>, and evaporated using RVO. The crude product was purified by chromatography (1:1 hexane/EtOAc) to yield 6.18 g, 98 % of **3** as a yellow oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (s, 1H), 4.09 (d, *J* = 6.3 Hz, 1H), 3.75 – 3.60 (m, 1H), 1.29 (d, *J* = 6.3 Hz, 6H). <sup>13</sup>C NMR (101 MHz CDCl<sub>3</sub>) δ 146.4, 145.6, 139.9, 137.2, 44.4, 22.6. HRMS (ESI-TOF): calcd for C<sub>7</sub>H<sub>10</sub>Cl<sub>2</sub>N<sub>3</sub> [M+H]<sup>+</sup> 206.0246, found 206.0246.

### Method iii

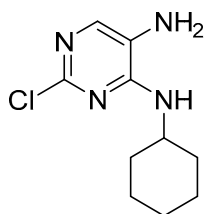
To a solution of **2** (R<sup>1</sup> = Me) or **3** (R<sup>1</sup> = *i*-Pr) (1.00 mmol) in butanol (10 mL), corresponding amine (1.00 mmol) and *N,N*-diisopropylethylamine (259 mg, 348 μL, 2.00 mmol) were added. The reaction mixture was heated at 85°C. After stirring for 48 hours, butanol was evaporated under reduced pressure and the residue was purified by column chromatography (usually in 1:1 hexane/EtOAc).

*2-chloro-N<sup>d</sup>-cyclopentylpyrimidine-4,5-diamine 4a* [3]



Yield 70 %, brown/pink solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.57 (s, 1H), 5.06 (d, *J* = 7.6 Hz, 1H), 4.40 (h, *J* = 7.0 Hz, 1H), 2.99 (s, 2H) 2.19 – 2.06 (m, 2H), 1.81 – 1.56 (m, 4H), 1.51 – 1.35 (m, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.2, 153.1, 142.1, 123.6, 52.7, 33.4 23.9. HRMS (ESI-TOF): calcd for C<sub>9</sub>H<sub>14</sub>ClN<sub>4</sub> [M+H]<sup>+</sup> 213.0902, found 213.0903.

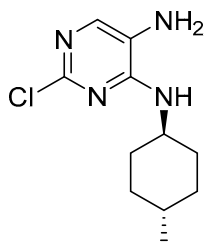
*2-chloro-N<sup>d</sup>-cyclohexylpyrimidine-4,5-diamine 4b* [4]



Yield 73 %, brown/pink solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.57 (s, 1H), 4.97 (d, *J* = 7.2 Hz, 1H), 4.08 – 3.90 (m, 1H), 2.97 (s, 2H), 2.12 – 1.96 (m, 2H), 1.74 (dt, *J* = 13.2, 3.6 Hz, 2H), 1.65 (dt, *J* = 12.9,

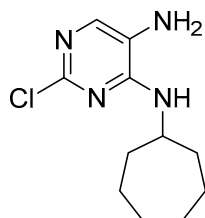
3.8 Hz, 1H), 1.43 (qt,  $J = 12.2, 3.4$  Hz, 2H), 1.20 (qd,  $J = 12.1, 3.5$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 153.2, 142.3, 123.4, 49.4, 33.2, 25.7, 24.9. HRMS (ESI-TOF): calcd for  $\text{C}_{10}\text{H}_{16}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  227.1058, found 227.1058.

*2-chloro- $N^d$ -(4-methylcyclohexyl)pyrimidine-4,5-diamine 4c*



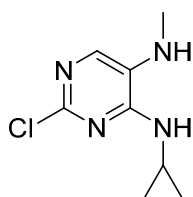
Yield 52 %, pale pink solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (s, 1H), 4.91 (d,  $J = 7.7$  Hz, 1H), 3.98 – 3.86 (m, 1H), 2.96 (s, 2H), 2.13 – 1.98 (m, 2H), 1.71 (d,  $J = 11.3$  Hz, 2H), 1.34 (tdd,  $J = 12.9, 6.1, 3.4$  Hz, 1H), 1.25 – 1.05 (m, 5H), 0.89 (d,  $J = 6.5$  Hz, 3H), 0.86 – 0.78 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 153.2, 142.2, 123.5, 49.7, 33.9, 33.3, 32.2, 22.3. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{18}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  241.1215, found 241.1216.

*2-chloro- $N^d$ -cycloheptylpyrimidine-4,5-diamine 4d*



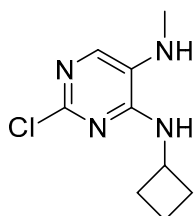
Yield 65 %, pale pink solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.35 (s, 1H), 6.54 (d,  $J = 7.5$  Hz, 1H), 4.92 (s, 2H), 4.07 – 3.97 (m, 1H), 2.00 – 1.83 (m, 2H), 1.74 – 1.31 (m, 10H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  152.4, 147.0, 135.5, 126.9, 50.9, 34.0, 28.0, 23.6. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{18}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  241.1215, found 241.1216.

*2-chloro- $N^d$ -cyclopropyl- $N^5$ -methylpyrimidine-4,5-diamine 5a*



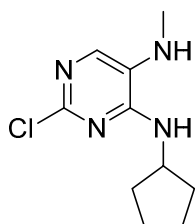
Yield 70 %, ochre solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (s, 1H), 5.36 (s, 1H), 3.01 (s, 1H), 2.94 – 2.86 (m, 1H), 2.80 (s, 3H), 0.94 – 0.76 (m, 2H), 0.64 – 0.47 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.3, 151.1, 135.6, 128.2, 31.1, 24.1, 7.3. HRMS (ESI-TOF): calcd for  $\text{C}_8\text{H}_{12}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  199.0745, found 199.0745.

*2-chloro- $N^4$ -cyclobutyl- $N^5$ -methylpyrimidine-4,5-diamine 5b*



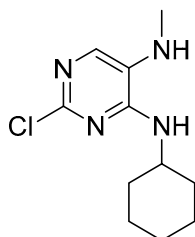
Yield 84 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (s, 1H), 5.25 (d,  $J$  = 6.9 Hz, 1H), 4.65 – 4.51 (m, 1H), 3.02 (s, 1H), 2.81 (s, 3H), 2.55 – 2.34 (m, 2H), 1.95 – 1.80 (m, 2H), 1.80 – 1.68 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ) 155.4, 151.2, 136.0, 127.8, 46.2, 31.5, 31.12 15.3. HRMS (ESI-TOF): calcd for  $\text{C}_9\text{H}_{14}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  213.0902, found 213.0903.

*2-chloro- $N^4$ -cyclopentyl- $N^5$ -methylpyrimidine-4,5-diamine 5c [5]*



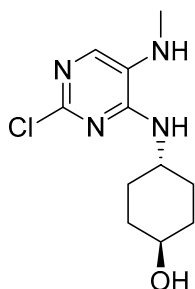
Yield 91 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 (s, 1H), 5.13 (d,  $J$  = 6.6 Hz, 1H), 4.41 (h,  $J$  = 7.0 Hz, 1H), 3.15 (s, 1H), 2.81 (s, 3H), 2.18 – 2.05 (m, 2H), 1.93 – 1.55 (m, 4H), 1.55 – 1.33 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 150.9, 135.0, 128.0, 52.8, 33.3, 31.0, 23.9. HRMS (ESI-TOF): calcd for  $\text{C}_{10}\text{H}_{16}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  227.1058, found 227.1058.

*2-chloro- $N^4$ -cyclohexyl- $N^5$ -methylpyrimidine-4,5-diamine 5d*



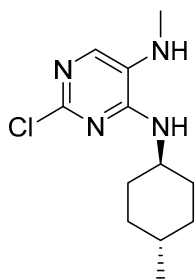
Yield 81 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (s, 1H), 4.84 (p,  $J = 8.4$  Hz, 1H), 3.42 (s, 3H), 2.33 – 2.14 (m, 2H), 2.10 – 1.89 (m, 4H), 1.83 – 1.48 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.7, 152.3, 151.2, 132.4, 122.3, 53.9, 29.5, 27.5, 24.9. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{18}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  241.1215, found 241.1214.

*4-((2-chloro-5-(methylamino)pyrimidin-4-yl)amino)cyclohexan-1-ol* **5e**



Yield 79 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.17 (s, 1H), 6.60 (d,  $J = 6.8$  Hz, 1H), 5.18 – 5.10 (br. s, 1H), 4.58 (t,  $J = 3.8$  Hz, 1H), 3.84 – 3.73 (br. s, 1H), 3.49 – 3.36 (br. s, 1H), 2.72 – 2.65 (m, 3H), 1.95 – 1.79 (m, 4H), 1.25 (t,  $J = 8.0$  Hz, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  152.8, 146.8, 130.8, 128.3, 68.3, 48.7, 34.0, 30.1, 29.4. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{18}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  257.1164, found 257.1162.

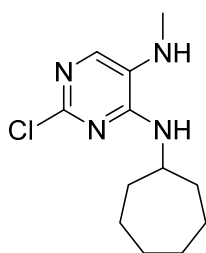
*2-chloro- $N^5$ -methyl- $N^4$ -(4-methylcyclohexyl)pyrimidine-4,5-diamine* **5f**



Yield 78 %, light brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (s, 1H), 4.81 (d,  $J = 7.6$  Hz, 1H), 4.00 – 3.88 (m, 1H), 2.81 (s, 3H), 2.17 – 1.99 (m, 2H), 1.78 – 1.68 (m, 2H), 1.22 – 1.07 (m, 4H), 0.91 (d,  $J = 6.4$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.9, 151.6, 136.2, 127.7, 49.7, 33.9, 33.3, 32.2, 31.2, 22.3. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{20}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  255.1371, found 255.1371.

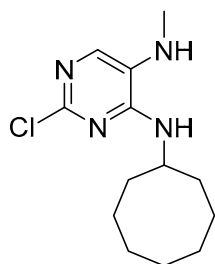


*2-chloro-N<sup>4</sup>-cycloheptyl-N<sup>5</sup>-methylpyrimidine-4,5-diamine 5g*



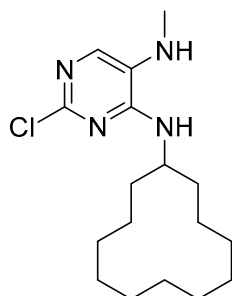
Yield 84 %, white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.43 (s, 1H), 4.97 (d, *J* = 7.5 Hz, 1H), 4.27 – 4.13 (m, 1H), 2.94 (s, 1H), 2.81 (s, 3H), 2.06 – 1.95 (m, 2H), 1.71 – 1.58 (m, 4H), 1.57 – 1.43 (m, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 155.5, 151.4, 135.9, 127.7, 51.5, 35.0, 31.1, 28.4, 24.0. HRMS (ESI-TOF): calcd for C<sub>12</sub>H<sub>20</sub>ClN<sub>4</sub> [M+H]<sup>+</sup> 255.1371, found 255.1375.

*2-chloro-N<sup>4</sup>-cyclooctyl-N<sup>5</sup>-methylpyrimidine-4,5-diamine 5h*



Yield 82 %, white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44 (s, 1H), 4.93 (d, *J* = 7.4 Hz, 1H), 4.28 – 4.17 (m, 1H), 2.81 (s, 3H), 1.98 – 1.80 (m, 2H), 1.79 – 1.35 (m, 12H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 155.6, 151.6, 136.1, 127.8, 50.6, 30.0, 31.2, 27.5, 25.6, 23.7. HRMS (ESI-TOF): calcd for C<sub>12</sub>H<sub>22</sub>ClN<sub>4</sub> [M+H]<sup>+</sup> 269.1528, found 269.1529.

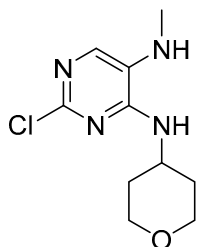
*2-chloro-N<sup>4</sup>-cyclododecyl-N<sup>5</sup>-methylpyrimidine-4,5-diamine 5i*



Yield 86 %, white solid. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.16 (s, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 5.12 (q, *J* = 4.8 Hz, 1H), 4.22 (h, *J* = 6.7 Hz, 1H), 2.70 (d, *J* = 4.9 Hz, 3H), 1.65 (dq, *J* = 13.3, 6.6, 6.1 Hz, 2H), 1.51 – 1.24 (m, 20H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 153.0, 146.8, 130.6, 128.1, 46.2, 29.6,

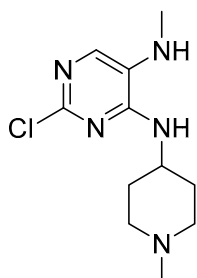
29.4, 23.4, 23.2, 23.1, 22.9, 21.3. HRMS (ESI-TOF): calcd for  $C_{17}H_{30}ClN_4$   $[M+H]^+$  325.2154, found 325.2152.

*2-chloro-N<sup>5</sup>-methyl-N<sup>4</sup>-(tetrahydro-2H-pyran-4-yl)pyrimidine-4,5-diamine 5j*



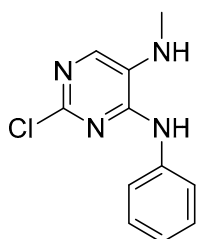
Yield 80 %, pale yellow solid.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.26 (s, 1H), 4.93 (d,  $J = 7.4$  Hz, 1H), 4.11 – 4.00 (m, 1H), 3.79 (ddd,  $J = 11.8, 3.9, 2.2$  Hz, 2H), 3.35 (td,  $J = 11.8, 2.5$  Hz, 2H), 1.84 (ddd,  $J = 12.6, 4.3, 2.1$  Hz, 2H), 1.32 (qd,  $J = 11.5, 4.5$  Hz, 2H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  155.4, 150.9, 135.7, 128.0, 66.9, 47.1, 33.2, 31.0. HRMS (ESI-TOF): calcd for  $C_{10}H_{16}ClN_4O$   $[M+H]^+$  243.1007, found 243.1008.

*2-chloro-N<sup>5</sup>-methyl-N<sup>4</sup>-(1-methylpiperidin-4-yl)pyrimidine-4,5-diamine 5k*



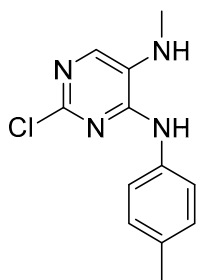
Yield 94 %, pale yellow solid.  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  7.19 (s, 1H), 6.93 (d,  $J = 7.2$  Hz, 1H), 5.41 (d,  $J = 4.5$  Hz, 1H), 4.01 – 3.86 (m, 1H), 3.09 – 3.00 (m, 2H), 2.69 (d,  $J = 4.9$  Hz, 3H), 2.41 (s, 3H), 2.01 – 1.88 (m, 2H), 1.65 (qd,  $J = 13.4, 12.6, 3.7$  Hz, 2H).  $^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  152.66, 146.43, 130.80, 128.47, 53.19, 46.04, 44.37, 29.93, 29.32. HRMS (ESI-TOF): calcd for  $C_{11}H_{19}ClN_5$   $[M+H]^+$  256.1323, found 256.1323.

*2-chloro-N<sup>5</sup>-methyl-N<sup>4</sup>-phenylpyrimidine-4,5-diamine 5l*



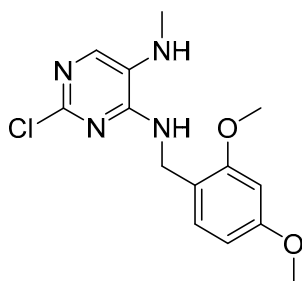
Yield 59 %, light brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.70 (s, 1H), 7.69 – 7.64 (m, 2H), 7.49 (s, 1H), 7.39 – 7.32 (m, 2H), 7.07 (tt,  $J = 7.2, 1.1$  Hz, 1H), 2.79 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  150.4, 145.6, 139.1, 133.6, 129.2, 128.7, 123.1, 120.7, 29.6. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{12}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  235.0745, found 235.0745.

*2-chloro- $N^5$ -methyl- $N^4$ -(*p*-tolyl)pyrimidine-4,5-diamine* **5m**



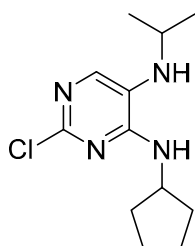
Yield 53 %, light brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.61 (s, 1H), 7.55 – 7.49 (m, 2H), 7.46 (s, 1H), 7.19 – 7.13 (m, 2H), 5.49 (d,  $J = 4.5$  Hz, 1H), 3.34 (s, 1H), 2.78 (d,  $J = 4.2$  Hz, 3H), 2.28 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  150.6, 145.7, 136.4, 133.3, 132.3, 129.1, 129.1, 121.0, 29.6, 20.5. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{14}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  249.0902, found 249.0902.

*2-chloro- $N^4$ -(2,4-dimethoxybenzyl)- $N^5$ -methylpyrimidine-4,5-diamine* **5n**



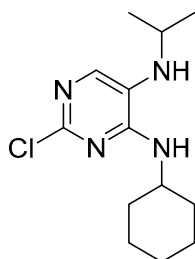
Yield 75 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 (s, 1H), 7.24 (s, 1H), 6.45 – 6.41 (m, 2H), 5.39 (d,  $J = 6.3$  Hz, 1H), 4.56 (d,  $J = 5.5$  Hz, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 2.77 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  160.8, 158.9, 156.0, 150.8, 135.1, 131.2, 128.2, 118.5, 104.1, 98.8, 55.5, 40.8, 30.9. HRMS (ESI-TOF): calcd for  $\text{C}_{14}\text{H}_{18}\text{ClN}_4\text{O}_2$   $[\text{M}+\text{H}]^+$  309.1113, found 309.1111.

*2-chloro-N<sup>4</sup>-cyclopentyl-N<sup>5</sup>-isopropylpyrimidine-4,5-diamine 6a*



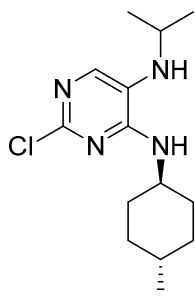
Yield 74 %, white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.49 (s, 1H), 5.21 (d, *J* = 6.8 Hz, 1H), 4.39 (h, *J* = 7.1 Hz, 1H), 3.39 (p, *J* = 6.2 Hz, 1H), 2.54 (s, 1H), 2.17 – 2.06 (m, 2H), 1.78 – 1.57 (m, 4H), 1.49 – 1.37 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.7, 152.4, 140.2, 125.4, 52.7, 45.6, 33.3, 23.9, 22.9. HRMS (ESI-TOF): calcd for C<sub>12</sub>H<sub>20</sub>ClN<sub>4</sub> [M+H]<sup>+</sup> 255.1371, found 255.1373.

*2-chloro-N<sup>4</sup>-cyclohexyl-N<sup>5</sup>-isopropylpyrimidine-4,5-diamine 6b*



Yield 73 %, pale yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.49 (s, 1H), 5.15 (d, *J* = 7.7 Hz, 1H), 4.04 – 3.93 (m, 1H), 3.39 (hept, *J* = 6.2 Hz, 1H), 2.50 (s, 1H), 2.11 – 1.93 (m, 2H), 1.73 (dt, *J* = 13.5, 3.6 Hz, 2H), 1.65 (dt, *J* = 11.4, 3.5 Hz, 1H), 1.50 – 1.36 (m, 2H), 1.26 – 1.19 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 157.4, 152.6, 140.7, 125.2, 77.5, 49.3, 45.8, 33.2, 25.8, 24.9, 22.9. HRMS (ESI-TOF): calcd for C<sub>13</sub>H<sub>22</sub>ClN<sub>4</sub> [M+H]<sup>+</sup> 269.1528, found 269.1529.

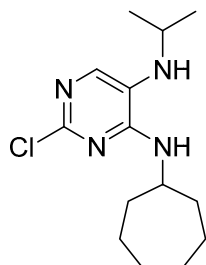
*2-chloro-N<sup>5</sup>-isopropyl-N<sup>4</sup>-(4-methylcyclohexyl)pyrimidine-4,5-diamine 6c*



Yield 60 %, pale yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.48 (s, 1H), 5.08 (d, *J* = 7.8 Hz, 1H), 3.93 (ddd, *J* = 11.5, 7.8, 3.8 Hz, 1H), 3.39 (hept, *J* = 6.2 Hz, 1H), 2.53 (s, 1H), 2.12 – 2.02 (m, 2H), 1.76 –

1.67 (m, 2H), 1.20 – 1.08 (m, 4H), 1.17 (d,  $J = 6.2$  Hz, 6H), 0.91 (d,  $J = 6.5$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.3, 152.4, 140.4, 125.3, 49.7, 45.6, 33.9, 33.2, 32.2, 22.9, 22.3. HRMS (ESI-TOF): calcd for  $\text{C}_{14}\text{H}_{24}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  283.1684, found 283.1682.

*2-chloro- $N^4$ -cycloheptyl- $N^5$ -isopropylpyrimidine-4,5-diamine 6d*

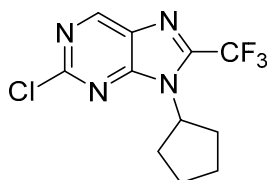


Yield 72 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48 (s, 1H), 5.24 (d,  $J = 7.7$  Hz, 1H), 4.23 – 4.10 (m, 1H), 3.38 (hept,  $J = 6.2$  Hz, 1H), 2.55 (s, 1H), 2.09 – 1.89 (m, 2H), 1.71 – 1.39 (m, 11H), 1.17 (d,  $J = 6.2$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.09, 152.55, 140.50, 125.28, 51.49, 45.74, 34.98, 28.36, 24.09, 22.93. HRMS (ESI-TOF): calcd for  $\text{C}_{14}\text{H}_{24}\text{ClN}_4$   $[\text{M}+\text{H}]^+$  283.1684, found 283.1685.

#### Method iv

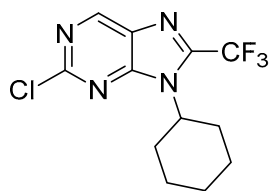
0.75 mmol of compound **4** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{cycloalkyl}$ ) was weight into a flask, toluene (1 mL) and trifluoroacetic anhydride (3 mL) were added and the mixture was heated under a condenser at  $70^\circ\text{C}$  for 16 hours. The crude mixture was diluted with dichloromethane (20 mL), washed with 10%  $\text{K}_2\text{CO}_3$  (30 mL), distilled water (30 mL), dried over  $\text{MgSO}_4$ , and evaporated.

*2-chloro-9-cyclopentyl-8-(trifluoromethyl)-9H-purine 7a*



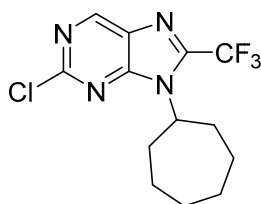
Yield 83 %, light brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.16 (s, 1H), 4.93 (p,  $J = 8.4$  Hz, 1H), 2.54 – 2.40 (m, 2H), 2.26 – 2.07 (m, 4H), 1.87 – 1.59 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.47, 153.66, 152.48, 144.39 (q,  $J = 39.6$  Hz), 131.56, 118.37 (q,  $J = 272.6$  Hz), 59.30, 31.33, 25.02. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{11}\text{ClF}_3\text{N}_4$   $[\text{M}+\text{H}]^+$  291.0619, found 291.0619.

*2-chloro-9-cyclohexyl-8-(trifluoromethyl)-9H-purine 7b*



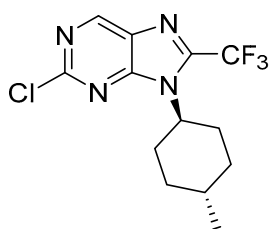
Yield 86 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.14 (s, 1H), 4.42 (tt,  $J = 12.1, 3.7$  Hz, 1H), 2.61 (qd,  $J = 12.2, 6.0$  Hz, 2H), 2.04 – 1.88 (m, 4H), 1.82 – 1.75 (m, 1H), 1.54 – 1.35 (m, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.42, 154.00, 152.50, 143.81 (q,  $J = 39.7$  Hz), 118.39 (q,  $J = 272.5$  Hz), 59.6, 30.9, 25.9, 24.8. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  267.1007, found 267.1008. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  305.0775, found 305.0778.

**2-chloro-9-cycloheptyl-8-(trifluoromethyl)-9H-purine 7c**



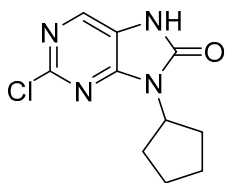
Yield 91 %, colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.14 (s, 1H), 4.59 (t,  $J = 10.8$  Hz, 1H), 2.83 – 2.60 (m, 2H), 2.15 – 1.89 (m, 4H), 1.82 – 1.66 (m, 4H), 1.66 – 1.48 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 153.8, 152.5, 143.4 (q,  $J = 39.6$  Hz), 131.4, 118.4 (q,  $J = 272.5$  Hz), 61.5, 33.7, 27.3, 25.3. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{15}\text{ClF}_3\text{N}_4$   $[\text{M}+\text{H}]^+$  319.0932, found 319.0930.

**2-chloro-9-(trans-4-methylcyclohexyl)-8-(trifluoromethyl)-9H-purine 7d**



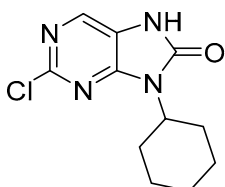
Yield 90%, colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.18 (s, 1H), 4.42 (tt,  $J = 12.3, 3.6$  Hz, 1H), 2.68 (qd,  $J = 12.4, 3.8$  Hz, 2H), 1.99 – 1.89 (m, 4H), 1.23 – 1.09 (m, 2H), 0.99 (d,  $J = 6.5$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.3, 154.0, 152.4, 144.08 (q,  $J = 39.9$  Hz), 131.3, 118.15 (qd,  $J = 272.6$  Hz), 59.6, 35.0, 31.4, 30.6, 22.1. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{15}\text{ClF}_3\text{N}_4$   $[\text{M}+\text{H}]^+$  319.0932, found 319.0927.

2-chloro-9-cyclopentyl-7,9-dihydro-8H-purin-8-one **8a** [3]



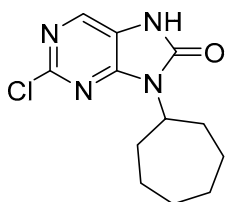
Yield 46 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  11.57 (s, 1H), 8.10 (s, 1H), 4.69 (p,  $J = 8.3$  Hz, 1H), 3.31 (s, 1H), 2.19 – 2.02 (m, 2H), 2.01 – 1.80 (m, 4H), 1.65 – 1.55 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  152.7, 151.6, 150.0, 133.8, 121.2, 52.3, 28.9, 24.5. HRMS (ESI-TOF): calcd for  $\text{C}_{10}\text{H}_{12}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  239.0694, found 239.0694.

2-chloro-9-cyclohexyl-7,9-dihydro-8H-purin-8-one **8b** [3]



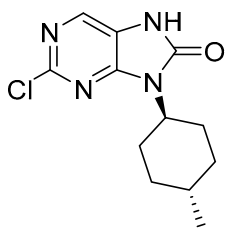
Yield 43 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  11.52 (s, 1H), 8.07 (s, 1H), 4.10 (tt,  $J = 12.3$ , 3.8 Hz, 1H), 2.13 (qd,  $J = 12.6$ , 3.3 Hz, 2H), 1.83 – 1.60 (m, 5H), 1.40 – 1.23 (m, 3H), 1.22 – 1.12 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  152.5, 151.6, 150.0, 133.9, 121.1, 52.0, 29.1, 25.2, 24.8. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{14}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  253.0851, found 253.0851.

2-chloro-9-cycloheptyl-7,9-dihydro-8H-purin-8-one **8c**



Yield 45 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  11.54 (s, 1H), 8.10 (s, 1H), 4.30 (tt,  $J = 10.8$ , 4.0 Hz, 1H), 2.29 – 2.15 (m, 2H), 1.90 – 1.72 (m, 4H), 1.70 – 1.39 (m, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  152.4, 151.4, 150.1, 133.8, 121.1, 53.9, 31.9, 27.2, 24.6. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  267.1007, found 267.1009.

2-chloro-9-(trans-4-methylcyclohexyl)-7,9-dihydro-8H-purin-8-one **8d**

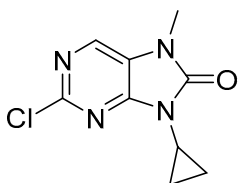


Yield 34%, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.57 (s, 1H), 8.11 (s, 1H), 4.12 (tt,  $J = 12.2$ , 3.7 Hz, 1H), 2.23 (qd,  $J = 12.5$ , 2.8 Hz, 2H), 1.84 – 1.66 (m, 4H), 1.16 – 1.01 (m, 2H), 0.91 (d,  $J = 6.5$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  152.5, 151.7, 150.0, 133.9, 121.1, 51.9, 33.7, 31.2, 28.8, 22.1. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  267.1007, found 267.1008.

#### Method v

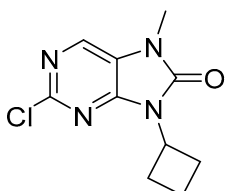
0.70 mmol of compound **4**, **5** or **6** was dissolved in anhydrous THF (10 mL) under an inert atmosphere of nitrogen and cooled to  $-10^\circ\text{C}$ . After slow addition of 15 wt %  $\text{COCl}_2$  in toluene (560  $\mu\text{L}$ , 0.85 mmol), 1M LiHMDS in hexane (1.4 mL, 1.40 mmol) was added portionwise. After 1 hour, the reaction mixture was cooled to ambient temperature and stirred for 20 minutes. The mixture was then evaporated under reduced pressure and purified by column chromatography (2:1 EtOAc/hexane) to yield **8-10**.

#### 2-chloro-9-cyclopropyl-7-methyl-7,9-dihydro-8H-purin-8-one **9a**



Yield 55 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (s, 1H), 3.42 (s, 3H), 3.03 – 2.97 (m, 1H), 1.18 – 1.12 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.3, 152.7, 152.1, 132.6, 122.2, 27.6, 23.2, 5.9. HRMS (ESI-TOF): calcd for  $\text{C}_9\text{H}_{10}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  225.0538, found 225.0537.

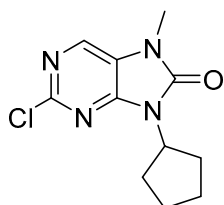
#### 2-chloro-9-cyclobutyl-7-methyl-7,9-dihydro-8H-purin-8-one **9b**





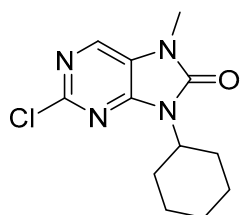
Yield 77 %, white solid.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.33 (s, 1H), 4.87 – 4.79 (m, 1H), 2.97 – 2.84 (m, 2H), 2.24 (dt,  $J = 13.4, 8.1, 2.5$  Hz, 2H), 1.91 – 1.82 (m, 1H), 1.79 (tdd,  $J = 10.5, 8.1, 2.4$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  152.8, 151.3, 150.8, 134.2, 123.2, 46.8, 27.9, 27.6, 15.2. HRMS (ESI-TOF): calcd for  $\text{C}_{10}\text{H}_{12}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  239.0695, found 239.0695.

*2-chloro-9-cyclopentyl-7-methyl-7,9-dihydro-8H-purin-8-one* **9c** [3]



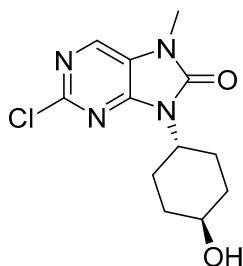
Yield 46 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (s, 1H), 4.84 (p,  $J = 8.4$  Hz, 1H), 3.42 (s, 3H), 2.30 – 2.11 (m, 2H), 2.08 – 1.89 (m, 4H), 1.74 – 1.53 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.7, 152.3, 151.2, 132.4, 122.3, 53.9, 29.5, 27.5, 24.9. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{14}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  253.0851, found 253.0852.

*2-chloro-9-cyclohexyl-7-methyl-7,9-dihydro-8H-purin-8-one* **9d** [3]



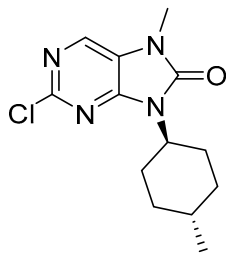
Yield 75 %, light yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (s, 1H), 4.33 (tt,  $J = 12.4, 3.9$  Hz, 1H), 3.41 (s, 3H), 2.31 (qd,  $J = 12.6, 3.7$  Hz, 2H), 1.91 – 1.82 (m, 2H), 1.81 – 1.73 (m, 2H), 1.50 – 1.29 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.7, 152.3, 151.2, 132.4, 122.3, 53.6, 29.7, 27.6, 25.8, 25.0. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  267.1007, found 267.1010.

*2-chloro-9-(trans-4-hydroxycyclohexyl)-7-methyl-7,9-dihydro-8H-purin-8-one* **9e** [3]



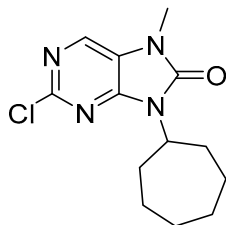
Yield 77 %, light yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.33 (s, 1H), 4.67 (s, 1H), 4.15 (tt,  $J$  = 12.3, 3.9 Hz, 1H), 3.47 (tq,  $J$  = 10.7, 3.8 Hz, 1H), 3.34 (s, 3H), 2.24 (qd,  $J$  = 13.4, 3.2 Hz, 2H), 1.97 – 1.88 (m, 2H), 1.77 – 1.66 (m, 2H), 1.36 – 1.23 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  152.0, 150.4, 150.2, 133.7, 122.7, 67.9, 51.9, 34.3, 27.4, 27.1.  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  267.1007, found 267.1010. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{16}\text{ClN}_4\text{O}_2$   $[\text{M}+\text{H}]^+$  283.0956, found 283.0954.

*2-chloro- $N^5$ -methyl- $N^4$ -(trans-4-methylcyclohexyl)pyrimidine-4,5-diamine 9f*



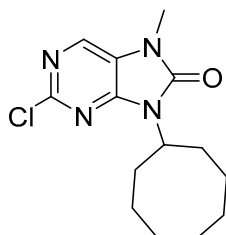
Yield 81 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (s, 1H), 4.32 (tt,  $J$  = 12.4, 4.0 Hz, 1H), 3.41 (s, 3H), 2.38 (qd,  $J$  = 12.7, 3.5 Hz, 2H), 1.89 – 1.70 (m, 4H), 1.12 (qd,  $J$  = 13.3, 3.3 Hz, 2H), 0.93 (d,  $J$  = 6.5 Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.7, 152.3, 151.2, 132.3, 122.3, 53.5, 34.3, 31.5, 29.4, 27.5, 22.3. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{18}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  281.1164, found 281.1163.

*2-chloro-9-cycloheptyl-7-methyl-7,9-dihydro-8H-purin-8-one 9g*



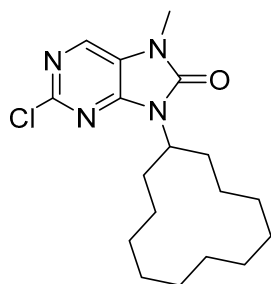
Yield 84 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (s, 1H), 4.49 (tt,  $J$  = 11.0, 3.8 Hz, 1H), 3.42 (s, 3H), 2.45 – 2.27 (m, 2H), 1.93 – 1.78 (m, 4H), 1.73 – 1.63 (m, 4H), 1.61 – 1.46 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.6, 152.4, 150.9, 132.3, 122.3, 55.7, 32.6, 27.6, 27.5, 25.2. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{18}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  281.1164, found 282.1161.

*2-chloro-9-cyclooctyl-7-methyl-7,9-dihydro-8H-purin-8-one 9h*



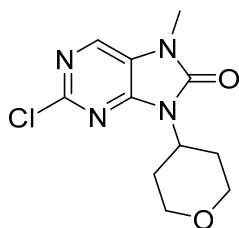
Yield 84 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (s, 1H), 4.59 (tt,  $J = 10.5, 3.3$  Hz, 1H), 3.44 (d,  $J = 14.6$  Hz, 3H), 2.48 – 2.37 (m, 2H), 1.90 – 1.74 (m, 4H), 1.68 – 1.53 (m, 8H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.6, 152.4, 150.9, 132.2, 122.2, 54.6, 31.4, 27.5, 26.5, 25.9, 24.9. HRMS (ESI-TOF): calcd for  $\text{C}_{14}\text{H}_{20}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  295.1320, found 295.1323.

*2-chloro-9-cyclododecyl-7-methyl-7,9-dihydro-8H-purin-8-one 9i*



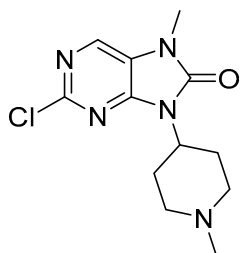
Yield 69 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (s, 1H), 4.65 (p,  $J = 6.9$  Hz, 1H), 3.43 (s, 3H), 2.31 – 2.13 (m, 2H), 1.93 – 1.76 (m, 2H), 1.65 – 1.48 (m, 3H), 1.39 (t,  $J = 11.0$  Hz, 15H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.2, 152.4, 151.4, 132.3, 122.3, 50.3, 28.2, 27.6, 24.3, 24.1, 22.7, 22.7, 22.7. HRMS (ESI-TOF): calcd for  $\text{C}_{18}\text{H}_{28}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  351.1946, found 351.1947.

*2-chloro-7-methyl-9-(tetrahydro-2H-pyran-4-yl)-7,9-dihydro-8H-purin-8-one 9j [3]*



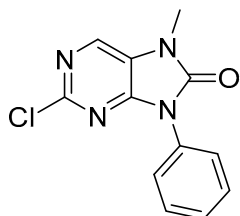
Yield 83 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (s, 1H), 4.58 (tt,  $J = 12.3, 4.2$  Hz, 1H), 4.15 – 4.08 (m, 2H), 3.52 (td,  $J = 12.6, 1.5$  Hz, 2H), 3.44 (s, 3H), 2.72 (qd,  $J = 12.5, 4.5$  Hz, 2H), 1.70 (dd,  $J = 13.1, 3.1$  Hz, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  152.5, 151.0, 132.7, 122.3, 67.4, 50.7, 29.8, 27.6. HRMS (ESI-TOF): calcd for  $\text{C}_{11}\text{H}_{14}\text{ClN}_4\text{O}_2$   $[\text{M}+\text{H}]^+$  269.0800, found 269.0801.

*2-chloro-7-methyl-9-(1-methylpiperidin-4-yl)-7,9-dihydro-8H-purin-8-one 9k*



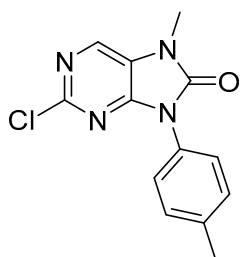
Yield 91 %, White solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.98 (s, 1H), 4.34 (tt,  $J = 12.3, 4.2$  Hz, 1H), 3.42 (s, 3H), 3.11 – 2.95 (m, 2H), 2.73 (qd,  $J = 12.6, 4.0$  Hz, 2H), 2.35 (s, 3H), 2.14 (td,  $J = 12.2, 2.2$  Hz, 2H), 1.84 – 1.60 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.71, 152.97, 150.70, 147.50, 133.15, 132.26, 120.38, 117.39, 116.95, 55.46, 51.48, 50.85, 46.37, 46.32, 28.95, 27.35. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{17}\text{ClN}_5\text{O}$   $[\text{M}+\text{H}]^+$  282.1116, found 282.1116.

*2-chloro-7-methyl-9-phenyl-7,9-dihydro-8H-purin-8-one* **9l** [3]



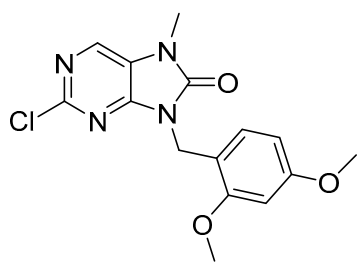
Yield 93 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.48 (s, 1H), 7.61 – 7.57 (m, 4H), 7.53 – 7.46 (m, 1H), 3.44 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  151.9, 150.6, 150.6, 134.4, 132.0, 129.2, 128.5, 126.4, 123.1, 27.7. HRMS (ESI-TOF): calcd for  $\text{C}_{12}\text{H}_{10}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  261.0538, found 261.0541.

*2-chloro-7-methyl-9-(p-tolyl)-7,9-dihydro-8H-purin-8-one* **9m**



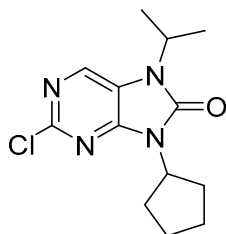
Yield 88 %, light yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.46 (s, 1H), 7.48 – 7.43 (m, 2H), 7.39 – 7.36 (m, 2H), 3.43 (s, 3H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  152.0, 150.7, 150.6, 138.2, 134.2, 129.6, 129.4, 126.3, 123.0, 39.7, 27.7, 20.8. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{12}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  275.0694, found 275.0692.

*2-chloro-9-(2,4-dimethoxybenzyl)-7-methyl-7,9-dihydro-8H-purin-8-one 9n*



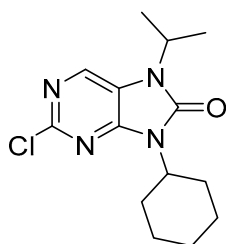
Yield 94 %, white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (s, 1H), 7.21 (d,  $J = 8.9$  Hz, 1H), 6.43 – 6.40 (m, 2H), 5.07 (s, 2H), 3.79 (s, 3H), 3.77 (s, 3H), 3.42 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.1, 158.6, 153.1, 152.7, 151.4, 132.4, 130.8, 122.5, 115.6, 104.2, 98.7, 55.5, 39.5, 27.6. HRMS (ESI-TOF): calcd for  $\text{C}_{15}\text{H}_{16}\text{ClN}_4\text{O}_3$   $[\text{M}+\text{H}]^+$  335.0905, found 335.0907.

*2-chloro-9-cyclopentyl-7-isopropyl-7,9-dihydro-8H-purin-8-one 10a*



Yield 92 %, yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.10 (s, 1H), 4.85 (q,  $J = 8.1$  Hz, 1H), 4.70 (q,  $J = 7.3$  Hz, 1H), 2.29 – 2.15 (m, 2H), 2.06 – 1.93 (m, 4H), 1.73 – 1.62 (m, 2H), 1.50 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  151.9, 151.9, 151.3, 133.4, 120.5, 53.8, 45.7, 29.5, 25.0, 20.7. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{18}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  281.1164, found 281.1164.

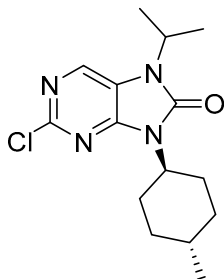
*2-chloro-9-cyclohexyl-7-isopropyl-7,9-dihydro-8H-purin-8-one 10b*



Yield 41 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (s, 1H), 4.71 (hept,  $J = 7.0$  Hz, 1H), 4.33 (tt,  $J = 12.4, 3.9$  Hz, 1H), 2.33 (qd,  $J = 12.4, 3.2$  Hz, 2H), 1.90 (dd,  $J = 9.6, 6.8$  Hz, 2H), 1.83 – 1.75 (m, 2H), 1.74 – 1.67 (m, 1H), 1.50 (s, 6H), 1.47 – 1.28 (m, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$

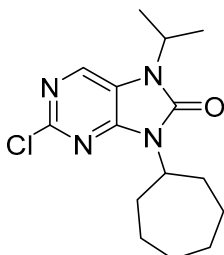
151.9, 151.9, 151.3, 133.3, 120.5, 53.6, 45.7, 29.7, 25.9, 25.1, 20.7. HRMS (ESI-TOF): calcd for  $C_{14}H_{20}ClN_4O$   $[M+H]^+$  295.1320, found 295.1321.

*2-chloro-7-isopropyl-9-(trans-4-methylcyclohexyl)-7,9-dihydro-8H-purin-8-one 10c*



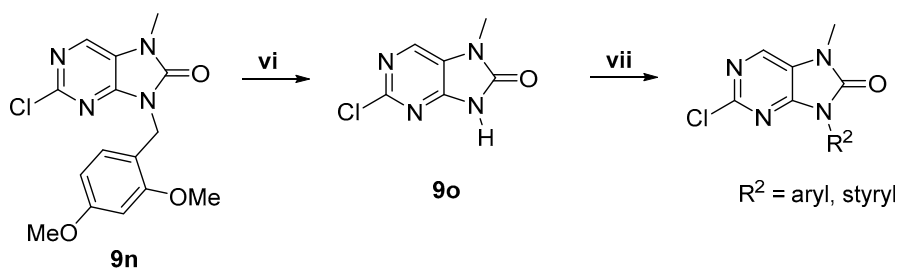
Yield 64 %, yellow oil.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.08 (s, 1H), 4.69 (hept,  $J = 7.0$  Hz, 1H), 4.30 (tt,  $J = 12.4, 4.0$  Hz, 1H), 2.38 (qd,  $J = 12.7, 3.5$  Hz, 2H), 1.89 – 1.79 (m, 2H), 1.79 – 1.69 (m, 2H), 1.48 (d,  $J = 7.0$  Hz, 6H), 1.10 (qd,  $J = 13.2, 3.3$  Hz, 2H), 0.92 (d,  $J = 6.5$  Hz, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  151.9, 151.4, 133.3, 120.5, 53.5, 45.7, 34.3, 31.5, 29.3, 22.3, 20.6. HRMS (ESI-TOF): calcd for  $C_{15}H_{22}ClN_4O$   $[M+H]^+$  309.1477, found 309.1476.

*2-chloro- $N^4$ -cycloheptyl- $N^5$ -isopropylpyrimidine-4,5-diamine 10d*



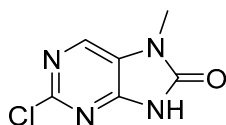
Yield 55 %, pale yellow solid.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.07 (s, 1H), 4.69 (hept,  $J = 7.0$  Hz, 1H), 4.47 (tt,  $J = 11.0, 3.8$  Hz, 1H), 2.42 – 2.19 (m, 2H), 1.94 – 1.72 (m, 4H), 1.69 – 1.60 (m, 4H), 1.59 – 1.50 (m, 2H), 1.47 (d,  $J = 7.0$  Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  152.0, 151.8, 151.0, 133.3, 120.5, 55.6, 45.7, 32.6, 27.6, 25.3, 20.7. HRMS (ESI-TOF): calcd for  $C_{15}H_{22}ClN_4O$   $[M+H]^+$  309.1477, found 309.1476.

**Scheme S2:** Synthesis of intermediates for Buchwald Hartwig amination prepared by Chan-Lam reaction.



#### Method vi

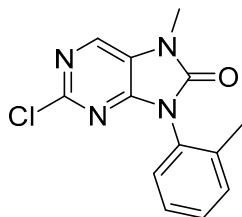
2-Chloro-9-(2,4-dimethoxybenzyl)-7-methyl-7,9-dihydro-8H-purin-8-one (200 mg, 0.59 mmol) was suspended in anisole (3.15 mL) and TFA (2.6 mL) was added. The reaction mixture was stirred at 90°C for 18 hours. TFA was evaporated by the flow of nitrogen and anisole was evaporated using RVO. A crude mixture was dissolved in MeOH, solid NaHCO<sub>3</sub> was added to neutralize the mixture and evaporated with silica gel. The product was purified by column chromatography (4:1 to 2:1 hexane/EtOAc). After evaporation and trituration with diethylether, the product was filtered-off to yield 2-chloro-7-methyl-7,9-dihydro-8H-purin-8-one 56 mg (52%) as a white solid. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  12.35 (s, 1H), 8.27 (s, 1H), 3.30 (s, 3H) ppm. <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  153.1, 151.5, 150.4, 133.3, 123.7, 26.9. HRMS (ESI-TOF): calcd for C<sub>6</sub>H<sub>6</sub>ClN<sub>4</sub>O [M+H]<sup>+</sup> 185.0225, found 185.0226. [6]



#### Method vii

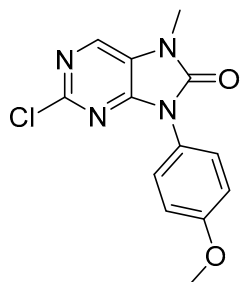
A 10 mL vial was charged with Cu<sub>2</sub>S (8 mg, 0.05 mmol), MeCN (0.6 mL), and *N,N,N',N'*-tetramethylethane-1,2-diamine (30  $\mu$ L, 0.20 mmol). After 1 h of stirring, 2-chloro-7-methyl-7,9-dihydro-8H-purin-8-one (18 mg, 0.10 mmol) and boronic acid (0.20 mmol) were added and the mixture was stirred at ambient temperature for 24 hours. A crude mixture was loaded on Celite, evaporated using RVO, and purified by column chromatography (2:1 hexane/EtOAc).

2-chloro-7-methyl-9-(*o*-tolyl)-7,9-dihydro-8*H*-purin-8-one **9p** [3]



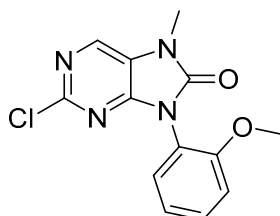
Yield 88 %, pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  7.48 – 7.45 (m, 2H), 7.41 – 7.36 (m, 2H), 3.46 (s, 3H), 2.11 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-}d_6$ )  $\delta$  189.4, 188.4, 188.3, 173.9, 172.0, 168.6, 168.4, 167.3, 166.5, 164.5, 160.9, 65.4, 54.9. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{11}\text{ClN}_4\text{O}$   $[\text{M}+\text{H}]^+$  275.0694, found 275.0694.

2-chloro-9-(4-methoxyphenyl)-7-methyl-7,9-dihydro-8*H*-purin-8-one **9q** [3]



White solid 57%.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.45 (s, 1H), 7.49 – 7.45 (m, 2H), 7.14 – 7.09 (m, 2H), 3.83 (s, 3H), 3.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  159.1, 152.1, 150.8, 150.6, 134.1, 128.0, 124.5, 123.0, 114.4, 55.5, 27.6. HRMS (ESI-TOF): calcd for  $\text{C}_{13}\text{H}_{11}\text{ClN}_4\text{O}_2$   $[\text{M}+\text{H}]^+$  291.0643, found 291.0640.

2-chloro-9-(2-methoxyphenyl)-7-methyl-7,9-dihydro-8*H*-purin-8-one **9r**

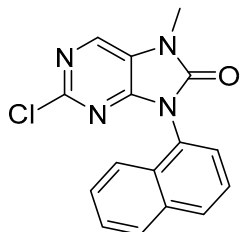


White foam 72%.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.45 (s, 1H), 7.55 (td,  $J$  = 8.5, 1.6 Hz, 1H), 7.43 (dd,  $J$  = 7.8, 1.6 Hz, 1H), 7.28 (dd,  $J$  = 7.8, 0.8 Hz, 1H), 7.13 (td,  $J$  = 7.8, 0.8 Hz, 1H), 3.75 (s, 3H), 3.45 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  = 155.3, 151.8, 151.0, 150.8, 134.3, 131.3, 130.0, 123.0,



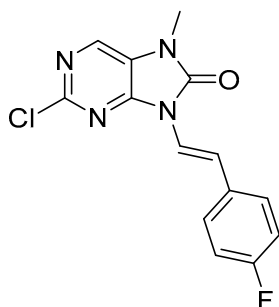
120.7, 119.9, 112.8, 55.9, 27.7. HRMS (ESI-TOF): calcd for C<sub>13</sub>H<sub>11</sub>ClN<sub>4</sub>O<sub>2</sub> [M+H]<sup>+</sup> 291.0643, found 291.0640.

2-chloro-7-methyl-9-(naphthalen-1-yl)-7,9-dihydro-8*H*-purin-8-one **9s**



Pale yellow solid 24%. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.54 (s, 1H), 8.19 (d, *J* = 4.7 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.73 - 7.62 (m, 4H), 7.55 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 3.51 (s, 3H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 152.3, 151.6, 150.7, 134.4, 133.9, 130.1, 129.7, 128.4, 128.2, 127.3, 127.3, 126.8, 125.7, 123.6, 122.7, 27.9. HRMS (ESI-TOF): calcd for C<sub>16</sub>H<sub>11</sub>ClN<sub>4</sub>O [M+H]<sup>+</sup> 311.0694, found 311.0692.

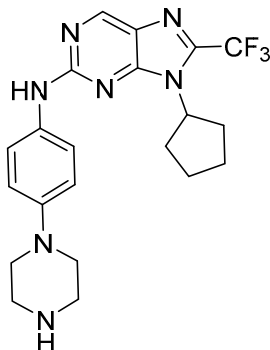
(*E*)-2-chloro-9-(4-fluorostyryl)-7-methyl-7,9-dihydro-8*H*-purin-8-one **9t**



White solid 53%. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.47 (s, 1H), 7.62 – 7.59 (m, 2H), 7.55 (d, *J* = 15.3 Hz, 1H), 7.37 (d, *J* = 15.3 Hz, 1H), 7.22 – 7.17 (m, 2H), 3.40 (s, 3H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 161.7 (d, *J* = 245 Hz), 150.9, 150.7, 148.9, 134.7, 131.4 (d, *J* = 3 Hz), 128.2 (d, *J* = 8 Hz), 122.9, 119.4, 118.3 (d, *J* = 2 Hz), 115.7 (d, *J* = 22 Hz), 27.6. HRMS (ESI-TOF): calcd for C<sub>14</sub>H<sub>10</sub>ClFN<sub>4</sub>O [M + H]<sup>+</sup> 305.0600, found 305.060

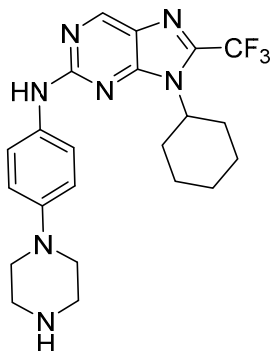
### Characterization of final compounds 12, 13, 14 and 15.

#### *9-Cyclopentyl-N-(4-(piperazin-1-yl)phenyl)-8-(trifluoromethyl)-9H-purin-2-amine (12a)*



Yield 21 %, yellow solid, m. p. 232-234 °C. HPLC purity: >99.9 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.59 (s, 2H), 8.95 (s, 1H), 7.73 – 7.57 (m, 2H), 7.16 – 7.00 (m, 2H), 4.80 (p,  $J$  = 8.6 Hz, 1H), 3.54 – 3.33 (m, 4H), 3.32 – 3.19 (m, 4H), 2.45 – 2.32 (m, 2H), 2.10 – 1.92 (m, 4H), 1.73 – 1.62 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  156.5, 152.5, 151.8, 143.5, 138.6 (q,  $J$  = 37.7 Hz), 134.3, 126.0, 120.5, 120.3, 118.7 (q,  $J$  = 272.5 Hz), 117.3, 57.5, 46.9, 42.0, 30.0, 24.4. HRMS (ESI):  $m/z$  calcd  $\text{C}_{21}\text{H}_{25}\text{F}_3\text{N}_7$  for  $[\text{M}+\text{H}]^+$  432.218, found  $[\text{M}+\text{H}]^+$  432.2117.

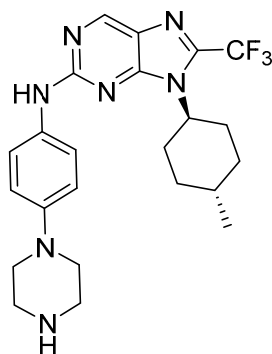
#### *9-Cyclohexyl-N-(4-(piperazin-1-yl)phenyl)-8-(trifluoromethyl)-9H-purin-2-amine (12b)*



Yield 43 %, yellow solid, m. p. 218-220 °C. HPLC purity: 98.2 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.71 (s, 1H), 8.93 (s, 1H), 7.71 – 7.60 (m, 2H), 6.94 – 6.82 (m, 2H), 4.22 (t,  $J$  = 12.3 Hz, 1H), 3.06 – 2.94 (m, 4H), 2.93 – 2.79 (m, 4H), 2.57 (qd,  $J$  = 11.8, 2.9, 2H), 1.93 – 1.80 (m, 4H), 1.77 – 1.70 (m, 1H), 1.44 – 1.32 (m, 2H), 1.32 – 1.23 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  156.6, 152.6, 152.5,

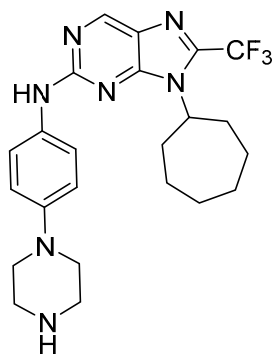
144.8, 137.6 (q,  $J = 38.3$  Hz), 133.8, 125.8, 120.0, 118.8 (q,  $J = 272.8$  Hz), 116.8, 57.2, 46.4, 42.5, 29.9, 25.2, 25.0. HRMS (ESI):  $m/z$  calcd  $C_{22}H_{27}F_3N_7$  for  $[M+H]^+$  446.2275, found  $[M+H]^+$  446.2273.

*9-(trans-4-Methylcyclohexyl)-N-(4-(piperazin-1-yl)phenyl)-8-(trifluoromethyl)-9H-purin-2-amine (12c)*



Yield 57 %, yellow solid, m. p. 228-230 °C. HPLC purity: 99.6 %.  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  9.82 (s, 1H), 9.37 (s, 2H), 8.99 (s, 1H), 7.82 – 7.66 (m, 2H), 7.04 – 6.92 (m, 2H), 4.24 (tt,  $J = 12.3, 3.2$  Hz, 1H), 3.53 (s, 3H), 3.38 – 3.30 (m, 4H), 3.28 – 3.15 (m, 4H), 2.64 (qd,  $J = 13.1, 3.6$  Hz, 2H), 1.94 – 1.79 (m, 4H), 1.62 – 1.45 (m, 1.2 1H), 1.15 (qd,  $J = 12.5, 12.3, 2.5$  Hz, 2H), 0.98 (d,  $J = 6.5$  Hz, 3H).  $^{13}C$  NMR (101 MHz,  $DMSO-d_6$ )  $\delta$  156.7, 152.6, 152.5, 145.0, 137.5 (q,  $J = 38.3$  Hz), 133.6, 125.8, 120.1, 118.8 (q,  $J = 271.6$  Hz), 116.8, 57.1, 46.4, 42.6, 33.6, 31.4, 29.6, 22.1. HRMS (ESI):  $m/z$  calcd  $C_{23}H_{29}F_3N_7$  for  $[M+H]^+$  460.2431, found  $[M+H]^+$  460.2429.

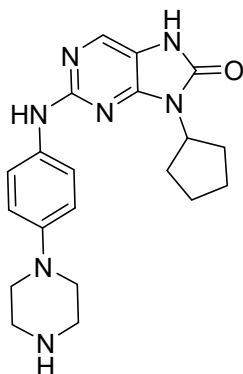
*9-Cycloheptyl-N-(4-(piperazin-1-yl)phenyl)-8-(trifluoromethyl)-9H-purin-2-amine (12d)*



Yield 34 %, yellow solid, m. p. 216-218 °C. HPLC purity: 98.30 %.  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  9.74 (s, 1H), 8.97 (s, 1H), 7.76 – 7.64 (m, 2H), 6.99 – 6.86 (m, 2H), 5.99 (br. s, 1H), 4.48 – 4.32 (m,

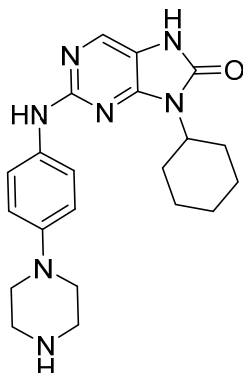
1H), 3.10 (s, 4H), 2.99 (s, 4H), 2.68 – 2.55 (m, 2H), 2.02 – 1.92 (m, 2H), 1.91 – 1.79 (m, 2H), 1.78 – 1.61 (m, 4H), 1.59 – 1.46 (m, 2H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 156.4, 152.6, 152.1, 142.4, 137.7 (q, *J* = 37.5 Hz), 135.6, 126.0, 120.2, 118.7 (q, *J* = 271.2 Hz), 118.1, 59.7, 47.6, 42.0, 32.7, 26.8, 24.2. HRMS (ESI): *m/z* calcd C<sub>23</sub>H<sub>29</sub>F<sub>3</sub>N<sub>7</sub> for [M+H]<sup>+</sup> 460.2431, found [M+H]<sup>+</sup> 460.2430.

*9-Cyclopentyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (13a)*



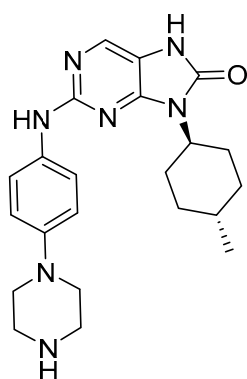
Yield 30 %, pale yellow solid, m. p. 200-202 °C. HPLC purity: 98.2 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 8.94 (s, 1H), 7.89 (s, 1H), 7.63 – 7.51 (m, 2H), 6.92 – 6.82 (m, 2H), 4.66 (p, *J* = 8.6 Hz, 1H), 3.12 – 2.99 (m, 4H), 2.97 – 2.84 (m, 4H), 2.29 – 2.11 (m, 2H), 2.00 – 1.80 (m, 4H), 1.70 – 1.54 (m, 2H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 155.5, 153.4, 151.1, 146.3, 134.3, 134.3, 120.0, 116.7, 114.9, 52.4, 49.8, 45.3, 29.2, 25.0. HRMS (ESI): *m/z* calcd C<sub>20</sub>H<sub>26</sub>N<sub>7</sub>O for [M+H]<sup>+</sup> 380.2193, found [M+H]<sup>+</sup> 380.2192.

*9-Cyclohexyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (13b)*



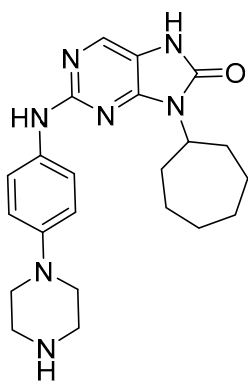
Yield 76 %, pale yellow solid, m. p. 210-212 °C. HPLC purity: 99.8 %.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.93 (s, 1H), 7.84 (s, 1H), 7.59 – 7.51 (m, 2H), 6.90 – 6.72 (m, 2H), 4.08 (tt,  $J$  = 12.1, 3.5 Hz, 1H), 3.06 – 2.94 (m, 4H), 2.92 – 2.91 (m, 4H), 2.27 (qd,  $J$  = 13.0, 3.2 Hz, 2H), 1.90 – 1.74 (m, 2H), 1.72 – 1.59 (m, 3H), 1.36 – 1.25 (m, 2H), 1.21 – 1.16 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  154.9, 152.7, 150.6, 145.8, 133.8, 133.8, 119.3, 116.2, 114.3, 51.2, 49.4, 44.9, 29.2, 25.4, 25.0. HRMS (ESI):  $m/z$  calcd  $\text{C}_{21}\text{H}_{28}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  394.2350, found  $[\text{M}+\text{H}]^+$  394.2349.

*9-(trans-4-Methylcyclohexyl)-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one*



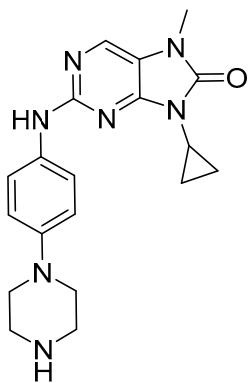
Yield 46 %, pale yellow solid, m. p. 274-276 °C. HPLC purity: >99.9 %.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.00 (s, 1H), 7.88 (s, 1H), 7.61 (d,  $J$  = 9.1 Hz, 2H), 6.88 (d,  $J$  = 9.1 Hz, 2H), 4.11 (tt,  $J$  = 12.5, 4.1 Hz, 1H), 3.25 – 3.15 (m, 4H), 3.09 (dd,  $J$  = 6.4, 3.5 Hz, 4H), 2.37 (qd,  $J$  = 12.9, 4.2 Hz, 1H), 1.80 (d,  $J$  = 13.1 Hz, 2H), 1.69 (dd,  $J$  = 12.3, 2.7 Hz, 2H), 1.53 – 1.39 (m, 1H), 1.06 (qd,  $J$  = 12.8, 2.5 Hz, 2H), 0.94 (d,  $J$  = 6.5 Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  154.8, 152.7, 150.7, 144.9, 134.4, 133.7, 119.3, 116.5, 114.4, 51.1, 47.6, 43.5, 34.0, 31.4, 28.9, 22.2. HRMS (ESI):  $m/z$  calcd  $\text{C}_{22}\text{H}_{30}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  408.2506, found  $[\text{M}+\text{H}]^+$  408.2504.

*9-Cycloheptyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (13d)*



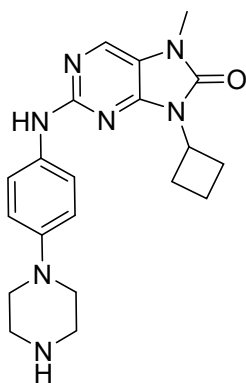
Yield 38 %, pale yellow solid, m. p. 230-232 °C. HPLC purity: 99.8 %.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  11.06 (s, 1H), 9.59 (s, 2H), 9.31 (s, 1H), 7.90 (s, 1H), 7.71 – 7.54 (m, 2H), 7.07 – 6.86 (m, 2H), 4.27 (ddt,  $J$  = 11.5, 7.9, 3.4 Hz, 1H), 3.41 – 3.25 (m, 4H), 3.23 – 3.05 (m, 4H), 2.31 (q,  $J$  = 10.9 Hz, 2H), 1.85 – 1.72 (m, 4H), 1.70 – 1.54 (m, 4H), 1.53 – 1.39 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  153.83, 152.56, 151.20, 144.95, 133.56, 119.99, 116.68, 114.56, 42.53, 31.96, 27.10, 24.50. HRMS (ESI):  $m/z$  calcd  $\text{C}_{22}\text{H}_{30}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  408.2506, found  $[\text{M}+\text{H}]^+$  408.2505.

*9-Cyclopropyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14b)*



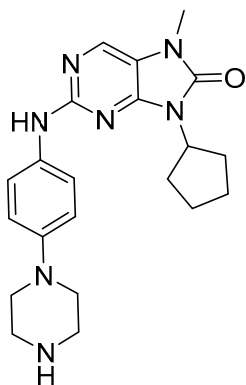
Yield 26 %, pale yellow solid, m. p. 156-158 °C. HPLC purity: 99.8 %.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.04 (s, 1H), 8.03 (s, 1H), 7.66 – 7.57 (m, 2H), 6.90 – 6.80 (m, 2H), 3.26 (s, 3H), 2.98 – 2.93 (m, 4H), 2.92 – 2.89 (m, 1H), 2.87 – 2.78 (m, 4H), 1.09 – 1.04 (m, 2H), 1.03 – 0.94 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  155.5, 152.9, 150.6, 146.3, 133.5, 133.1, 119.3, 116.0, 115.9, 50.5, 46.7, 27.0, 22.24, 5.4. HRMS (ESI):  $m/z$  calcd  $\text{C}_{19}\text{H}_{24}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  366.2037, found  $[\text{M}+\text{H}]^+$  366.2036.

*9-Cyclobutyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14c)*



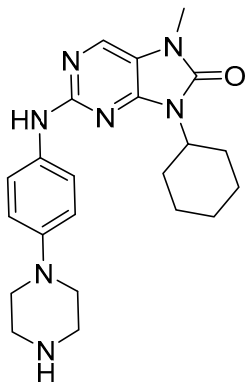
Yield 35 %, white solid, m. p. 112-114 °C. HPLC purity: >99.9 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.08 – 9.02 (m, 1H), 8.07 (s, 1H), 7.65 – 7.54 (m, 2H), 6.91 – 6.80 (m, 2H), 4.82 (p,  $J = 8.8$  Hz, 1H), 3.34 – 3.31 (m, 2H), 3.27 (s, 3H), 3.03 (pd,  $J = 9.9, 1.7$  Hz, 2H) 3.11 – 2.97 (m, 2H), 2.95 – 2.92 (m, 2H), 2.91 – 2.84 (m, 2H), 2.84 – 2.80 (m, 2H), 2.23 (qt,  $J = 8.3, 2.3$  Hz, 2H), 1.95 – 1.75 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  155.3, 152.1, 149.7, 146.4, 146.4, 133.7, 133.3, 119.4, 116.2, 115.9, 115.8, 50.4, 50.1, 45.7, 45.7, 44.4, 39.9, 27.1, 27.0, 14.6. HRMS (ESI):  $m/z$  calcd  $\text{C}_{20}\text{H}_{26}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  380.2193, found  $[\text{M}+\text{H}]^+$  380.1353.

*9-Cyclopentyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14d)*



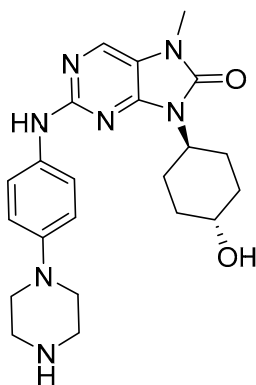
Yield 47 %, pale yellow solid, m. p. 110-112 °C. HPLC purity: 99.8 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.01 (s, 1H), 8.06 (s, 1H), 7.61 – 7.51 (m, 2H), 6.88 – 6.80 (m, 2H), 4.70 (p,  $J = 8.4$  Hz, 1H), 3.29 (s, 3H), 3.06 – 2.94 (m, 4H), 2.95 – 2.85 (m, 4H), 2.25 – 2.12 (m, 2H), 2.00 – 1.83 (m, 4), 1.69 – 1.53 (m, 2H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  155.2, 152.2, 149.4, 146.0, 133.4, 119.5, 116.1, 52.4, 49.7, 45.1, 28.8, 27.0, 24.4. HRMS (ESI):  $m/z$  calcd  $\text{C}_{21}\text{H}_{28}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  394.2350, found  $[\text{M}+\text{H}]^+$  394.2350.

*9-Cyclohexyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14e)*



Yield 56 %, pale yellow solid, m. p. 198-200 °C. HPLC purity: 98.1 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.00 (s, 1H), 8.02 (s, 1H), 7.58 – 7.51 (m, 2H), 6.83 – 6.77 (m, 2H), 4.12 (tt,  $J$  = 13.2, 3.7 Hz, 1H), 3.24 (s, 3H), 2.94 – 2.87 (m, 4H), 2.87 – 2.68 (m, 4H), 2.26 (qd,  $J$  = 12.9, 3.1 Hz, 2H), 1.87 – 1.76 (m, 2H), 1.72 – 1.61 (m, 3H), 1.40 – 1.10 (m, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  155.2, 152.0, 149.4, 146.4, 133.4, 133.4, 119.4, 115.9, 51.7, 50.5, 45.7, 29.3, 27.0, 25.4, 25.0. HRMS (ESI):  $m/z$  calcd  $\text{C}_{22}\text{H}_{30}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  408.2506, found  $[\text{M}+\text{H}]^+$  408.2503.

*9-(trans-4-Hydroxycyclohexyl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14f)*

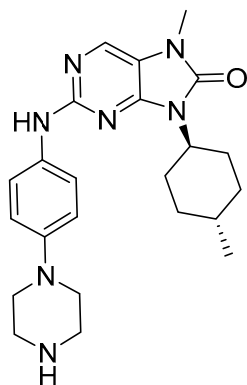


Yield 46 %, yellow solid, m. p. 272-274 °C. HPLC purity: 98.5 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.03 (s, 1H), 8.06 (s, 1H), 7.60 – 7.55 (m, 2H), 6.87 – 6.81 (m, 2H), 4.71 (s, 1H), 4.14 (tt,  $J$  = 12.3, 4.1 Hz, 1H), 3.58 – 3.47 (m, 1H), 3.28 (s, 3H) 2.97 – 2.83 (m, 4H), 2.86 – 2.80 (m, 4H), 2.38 (qd,  $J$  = 13.0, 3.1 Hz, 2H), 2.01 – 1.91 (m, 2H), 1.74 – 1.65 (m, 2H), 1.37 – 1.23 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,



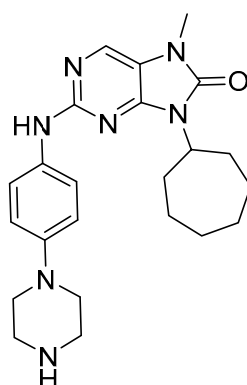
DMSO-*d*<sub>6</sub>)  $\delta$  155.2, 152.0, 149.4, 146.3, 133.5, 133.4, 119.4, 116.0, 68.2, 51.1, 50.4, 45.6, 34.6, 27.0, 27.0. HRMS (ESI):  $m/z$  calcd C<sub>22</sub>H<sub>30</sub>N<sub>7</sub>O<sub>2</sub> for [M+H]<sup>+</sup> 424.2455, found [M+H]<sup>+</sup> 424.2452.

*7-Methyl-9-(trans-4-methylcyclohexyl)-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14g)*



Yield 32 %, white solid, m. p. 114-116 °C. HPLC purity: 99.3 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  9.00 (s, 1H), 8.05 (s, 1H), 7.61 – 7.53 (m, 2H), 6.86 – 6.80 (m, 2H), 4.14 (tt,  $J$  = 12.2, 3.9 Hz, 1H), 3.28 (s, 3H), 2.97 – 2.91 (m, 4H), 2.85 – 2.79 (m, 4H), 2.36 (qd,  $J$  = 12.6, 3.2 Hz, 2H), 1.85 – 1.77 (m, 2H), 1.75 – 1.63 (m, 2H), 1.07 (qd, 12.3, 3.2 Hz, 2H), 0.94 (d,  $J$  = 6.5 Hz, 3H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  155.2, 152.1, 149.5, 146.4, 133.4, 119.4, 116.0, 115.9, 51.6, 50.5, 45.7, 33.9, 31.4, 28.9, 27.0, 22.2. HRMS (ESI):  $m/z$  calcd C<sub>23</sub>H<sub>32</sub>N<sub>7</sub>O for [M+H]<sup>+</sup> 422.2663, found [M+H]<sup>+</sup> 422.2661.

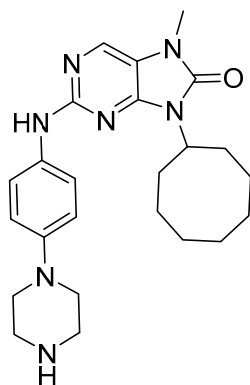
*9-Cycloheptyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14h)*



Yield 23 %, pale yellow solid, m. p. 256-258 °C. HPLC purity: 98.9 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.97 (s, 1H), 8.01 (s, 1H), 7.59 – 7.50 (m, 2H), 6.84 – 6.77 (m, 2H), 4.27 (tt,  $J$  = 11.0, 3.7 Hz,

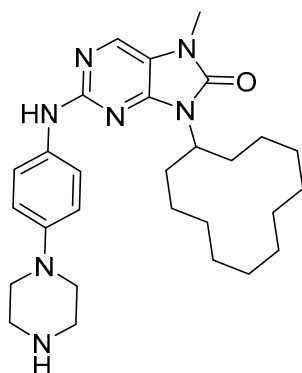
1H), 3.24 (s, 3H), 2.96 – 2.92 (m, 4H), 2.85 – 2.81 (m, 4H), 2.29 (qd,  $J = 10.8, 3.7$  Hz, 2H), 1.82 – 1.71 (m, 4H), 1.68 – 1.49 (m, 4H), 1.51 – 1.37 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  155.3, 151.9, 149.2, 146.1, 133.5, 133.4, 119.5, 116.0, 53.9, 50.0, 45.4, 32.1, 27.1, 27.0, 24.5. HRMS (ESI):  $m/z$  calcd  $\text{C}_{23}\text{H}_{32}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  422.2663, found  $[\text{M}+\text{H}]^+$  422.2188.

*9-Cyclooctyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14i)*



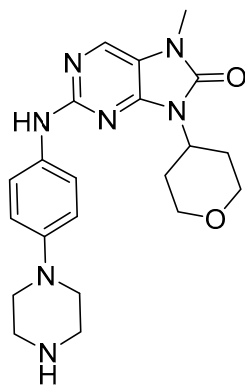
Yield 55 %, pale yellow solid, m. p. 122-124 °C. HPLC purity: 98.7 %.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.00 (s, 1H), 8.05 (s, 1H), 7.62 – 7.55 (m, 2H), 6.87 – 6.79 (m, 2H), 4.40 (tt,  $J = 10.5, 3.0$  Hz, 1H), 3.28 (s, 3H), 3.01 – 2.92 (m, 4H), 2.87 – 2.85 (m, 4H), 2.47 – 2.30 (m, 2H), 1.85 – 1.68 (m, 5H), 1.63 – 1.48 (m, 7H).  $^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  155.3, 151.9, 149.2, 146.2, 133.5, 133.4, 119.5, 115.9, 52.8, 50.2, 45.5, 30.7, 27.0, 26.2, 24.9, 24.3. HRMS (ESI):  $m/z$  calcd  $\text{C}_{24}\text{H}_{34}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  436.2819, found  $[\text{M}+\text{H}]^+$  436.2818.

*9-Cyclododecyl-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14j)*



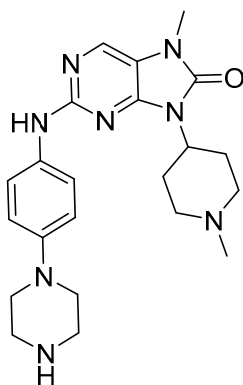
Yield 61 %, white solid, m. p. 114 °C. HPLC purity: >99.9 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.03 (s, 1H), 8.07 (s, 1H), 7.62 – 7.56 (m, 2H), 6.85 – 6.79 (m, 2H), 4.55 (p,  $J$  = 6.7 Hz, 1H), 3.29 (s, 3H), 3.00 – 2.89 (m, 4H), 2.89 – 2.77 (m, 4H), 2.16 – 2.09 (m, 2H), 1.85 – 1.78 (m, 2H), 1.63 – 1.49 (m, 3H), 1.43 – 1.31 (m, 15H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  155.4, 152.4, 149.7, 146.1, 133.7, 133.4, 119.2, 115.9, 115.7, 50.2, 47.7, 45.6, 27.5, 27.0, 23.8, 23.6, 22.1, 22.1, 22.0. HRMS (ESI):  $m/z$  calcd  $\text{C}_{28}\text{H}_{42}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  492.3445, found  $[\text{M}+\text{H}]^+$  492.3445.

*7-Methyl-2-((4-(piperazin-1-yl)phenyl)amino)-9-(tetrahydro-2H-pyran-4-yl)-7,9-dihydro-8H-purin-8-one (14k)*



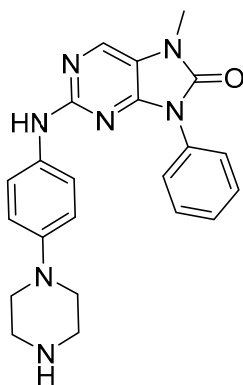
Yield 64 %, pale yellow solid, m. p. 124-126 °C. HPLC purity: >99.9 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ )  $\delta$  9.05 (s, 1H), 8.07 (s, 1H), 7.63 – 7.55 (m, 2H), 6.89 – 6.80 (m, 2H), 4.41 (tt,  $J$  = 12.1, 4.2 Hz, 1H), 3.99 (dd,  $J$  = 11.3, 4.2 Hz, 2H), 3.42 – 3.38 (m, 2H), 3.29 (s, 3H), 3.02 – 2.88 (m, 5H), 2.93 – 2.70 (m, 3H), 2.57 (qd, 11.6, 3.4 Hz, 2H), 1.66 (dd,  $J$  = 12.7, 2.9 Hz, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO-}d_6$ )  $\delta$  155.2, 152.0, 149.6, 146.3, 133.4, 119.4, 116.1, 116.0, 66.6, 50.4, 49.1, 45.6, 29.4, 27.1. HRMS (ESI):  $m/z$  calcd  $\text{C}_{21}\text{H}_{28}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  410.2299, found  $[\text{M}+\text{H}]^+$  410.2298.

*7-Methyl-9-(1-methylpiperidin-4-yl)-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14l)*



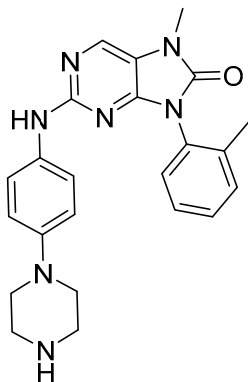
Yield 29 %, pale yellow solid, m. p. decomposition at 282 °C: HPLC purity: 98.7 %.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (s, 1H), 7.50 – 7.45 (m, 2H), 6.94 – 6.89 (m, 2H), 6.87 (s, 1H), 4.26 (tt,  $J = 12.3$ , 4.2 Hz, 1H), 3.35 (s, 3H), 3.10 – 3.06 (m, 4H), 3.05 – 3.02 (m, 4H), 2.98 (dt,  $J = 12.0$ , 1.5 Hz, 2H), 2.77 (qd,  $J = 12.5$ , 3.9 Hz, 2H), 2.33 (s, 3H), 2.09 (td,  $J = 12.2$ , 2.1 Hz, 2H), 1.79 – 1.66 (m, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 153.0, 150.7, 147.5, 133.2, 132.3, 120.4, 117.4, 117.0, 55.5, 51.5, 50.9, 46.4, 46.3, 29.0, 27.4. HRMS (ESI):  $m/z$  calcd  $\text{C}_{22}\text{H}_{31}\text{N}_8\text{O}$  for  $[\text{M}+\text{H}]^+$  423.2615, found  $[\text{M}+\text{H}]^+$  423.2605.

*7-Methyl-9-phenyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14m)*



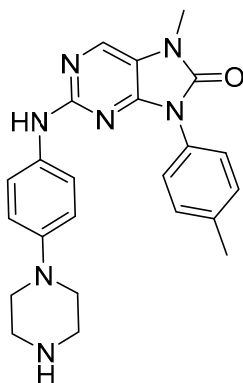
Yield 35 %, yellow solid, m. p. 120-122 °C. HPLC purity: 99.2 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  9.09 (s, 1H), 8.19 (s, 1H), 7.68 – 7.62 (m, 2H), 7.61 – 7.51 (m, 4H), 7.47 – 7.43 (m, 1H), 6.84 – 6.76 (m, 2H), 3.38 (s, 3H), 2.96 – 2.87 (m, 4H), 2.86 – 2.75 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  155.6, 151.7, 149.7, 146.4, 134.0, 133.3, 133.0, 128.9, 127.8, 126.4, 119.4, 116.3, 115.9, 50.5, 45.7, 27.3. HRMS (ESI):  $m/z$  calcd  $\text{C}_{22}\text{H}_{24}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  402.2037, found  $[\text{M}+\text{H}]^+$  402.2035.

7-Methyl-2-((4-(piperazin-1-yl)phenyl)amino)-9-(*o*-tolyl)-7,9-dihydro-8H-purin-8-one (**14n**)



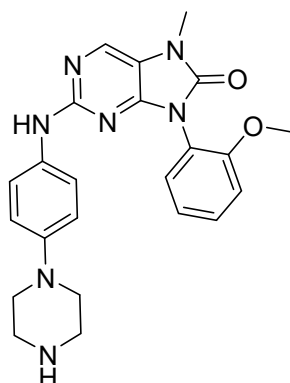
Yield 44 %, yellow solid, m. p. 152-154 °C. HPLC purity: 98.4 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  9.11 (s, 1H), 8.18 (s, 1H), 7.55 – 7.51 (m, 2H), 7.46 – 7.34 (m, 4H), 6.82 – 6.77 (m, 2H), 3.3 (s, 3H), 3.04 – 3.00 (m, 4H), 2.97 – 2.92 (m, 4H), 2.13 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  155.6, 151.7, 150.3, 145.7, 136.5, 133.8, 133.5, 131.8, 130.8, 129.3, 129.2, 126.8, 119.3, 116.7, 116.2, 49.0, 44.6, 27.3, 17.4. HRMS (ESI):  $m/z$  calcd  $\text{C}_{23}\text{H}_{27}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  416.2193, found  $[\text{M}+\text{H}]^+$  416.2190.

7-Methyl-2-((4-(piperazin-1-yl)phenyl)amino)-9-(*p*-tolyl)-7,9-dihydro-8H-purin-8-one (**14o**)



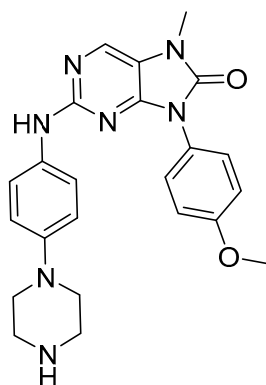
Yield 56 %, pale yellow solid, m. p. 126-128 °C. HPLC purity: 99.8 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  9.07 (s, 1H), 8.17 (s, 1H), 7.57 – 7.47 (m, 4H), 7.39 – 7.32 (m, 2H), 6.83 – 6.76 (m, 2H), 3.37 (s, 3H), 2.92 – 2.91 (m, 4H), 2.87 – 2.73 (m, 4H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  151.9, 151.9, 149.9, 146.4, 137.4, 133.8, 133.33, 130.4, 129.4, 126.3, 119.4, 116.3, 116.0, 50.5, 45.7, 27.3, 20.8. HRMS (ESI):  $m/z$  calcd  $\text{C}_{23}\text{H}_{26}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  416.2193, found  $[\text{M}+\text{H}]^+$  415.2190.

*9-(2-Methoxyphenyl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one*  
**(14p)**



Yield 28 %, pale yellow solid, m. p. 185-187 °C. HPLC purity: 99.3 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.14 (s, 1H), 8.15 (s, 1H), 7.58 - 7.54 (m, 2H), 7.51 (ddd, *J* = 8.2, 7.5, 1.5 Hz, 1H), 7.41 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.25 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.10 (td, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 3.38 (s, 3H), 3.20 - 3.15 (m, 4H), 3.13 - 3.09 (m, 4H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 155.6, 155.5, 151.9, 150.6, 144.8, 134.3, 133.3, 130.9, 130.4, 121.0, 120.6, 119.2, 116.7, 116.6, 112.6, 55.8, 47.2, 43.2, 27.3. HRMS (ESI): *m/z* calcd C<sub>23</sub>H<sub>25</sub>N<sub>7</sub>O<sub>2</sub> for 432.2142, found [M+H]<sup>+</sup> 432.2140.

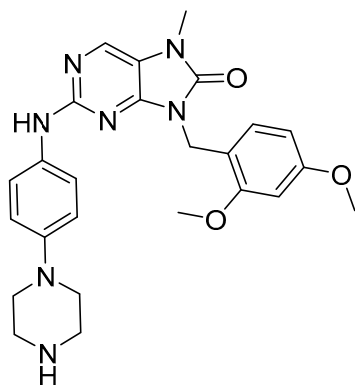
*9-(4-Methoxyphenyl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one* **(14q)**



Yield 21 %, pale yellow solid, m. p. 270-272°C. HPLC purity: 99.4 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.09 (s, 1H), 8.17 (s, 1H), 7.59 - 7.54 (m, 2H), 7.53 - 7.50 (m, 2H), 7.13 - 7.09 (m, 2H), 6.86 - 6.81 (m, 2H), 3.83 (s, 3H), 3.37 (s, 3H), 3.10 - 3.05 (m, 4H), 3.01 - 2.97 (m, 4H). <sup>13</sup>C NMR (100

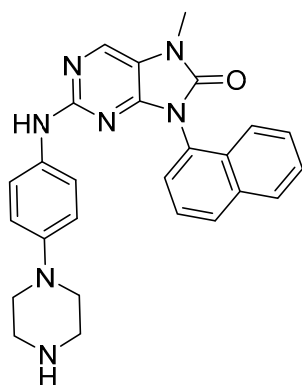
MHz, DMSO-*d*<sub>6</sub>)  $\delta$  158.7, 155.5, 152.0, 150.0, 145.4, 133.9, 133.7, 128.0, 125.5, 119.3, 116.4, 116.3, 114.2, 55.5, 48.5, 44.2, 27.3. HRMS (ESI): *m/z* calcd C<sub>23</sub>H<sub>25</sub>N<sub>7</sub>O<sub>2</sub> for [M+H]<sup>+</sup> 432.2142, found [M+H]<sup>+</sup> 432.2136.

*9-(2,4-Dimethoxybenzyl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14r)*



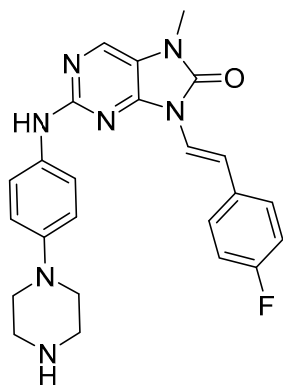
Yield 54 %, white solid, m. p. 102-104 °C. HPLC purity: 99.6 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  9.02 (s, 1H), 8.09 (s, 1H), 7.56 – 7.49 (m, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.82 – 6.77 (m, 2H), 6.58 (d, *J* = 2.4 Hz, 1H), 6.43 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.88 (s, 2H), 3.81 (s, 3H), 3.72 (s, 3H), 3.33 (s, 3H), 2.94 – 2.91 (m, 4H), 2.83 – 2.80 (m, 4H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  159.9, 157.4, 155.5, 152.7, 150.0, 146.3, 133.3, 133.3, 127.8, 119.3, 116.4, 116.0, 115.9, 104.5, 98.3, 55.5, 55.2, 45.7, 37.8, 27.2. HRMS (ESI): *m/z* calcd C<sub>25</sub>H<sub>30</sub>N<sub>7</sub>O<sub>3</sub> for [M+H]<sup>+</sup> 476.24059, found [M+H]<sup>+</sup> 476.2403.

*7-Methyl-9-(naphthalen-1-yl)-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14s)*



Yield 17 %, pale yellow solid, m. p. 178-180 °C. HPLC purity: 98.3 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.00 (s, 1H), 8.24 (s, 1H), 8.15 - 8.11 (m, 1H), 8.11 - 8.07 (m, 1H), 7.72 - 7.69 (m, 1H), 7.69 - 7.67 (m, 1H), 7.64 - 7.62 (m, 1H), 7.60 (s, 1H), 7.57 - 7.53 (m, 1H), 7.47 - 7.43 (m, 2H), 6.75 - 6.71 (m, 2H), 3.45 (s, 3H), 3.41 (br. s, 1H), 2.97 - 2.93 (m, 4H), 2.91 - 2.87 (m, 4H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 155.6, 152.3, 151.1, 145.8, 133.9, 133.6, 133.5, 130.1, 129.6, 129.3, 128.3, 127.5, 127.2, 126.7, 125.8, 122.8, 119.2, 116.9, 116.0, 49.5, 45.0, 27.5. HRMS (ESI): *m/z* calcd C<sub>26</sub>H<sub>25</sub>N<sub>7</sub>O for [M+H]<sup>+</sup> 452.2193, found [M+H]<sup>+</sup> 452.2190.

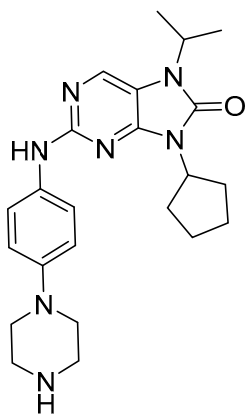
*(E)*-9-(4-Fluorostyryl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (**14t**)



Yield 23 %, pale yellow solid, m. p. 248-250 °C. HPLC purity: 96.2 %. <sup>1</sup>H (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.17 (s, 1H), 8.16 (s, 1H), 7.72 (d, *J* = 14.8 Hz, 1H), 7.53 – 7.48 (m, 4H), 7.37 (d, *J* = 14.8 Hz, 1H), 7.22 – 7.16 (m, 2H), 6.89 – 6.85 (m, 2H), 3.31 (s, 3H), 3.31 (br. s, 1H), 3.01 – 2.96 (m, 4H), 2.89 – 2.85 (m, 4H). <sup>13</sup>C (101 MHz, DMSO-*d*<sub>6</sub>) δ 161.4 (d, *J* = 240 Hz), 155.7, 150.6, 148.1, 146.4, 134.4, 132.8, 131.9 (d, *J* = 3 Hz), 127.4 (d, *J* = 8 Hz), 120.3, 118.8, 117.7, 116.0, 115.8, 115.5 (d, *J* = 22 Hz), 49.6, 45.1, 27.1. HRMS (ESI): *m/z* calcd C<sub>24</sub>H<sub>24</sub>FN<sub>7</sub>O for [M + H]<sup>+</sup> 446.2095, found [M + H]<sup>+</sup> 446.2099.

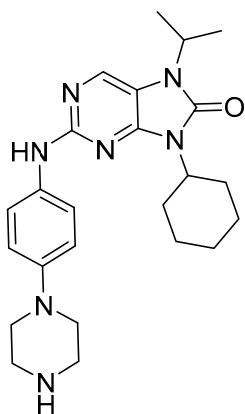
9-Cyclopentyl-7-isopropyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (**15a**)





Yield 20 %, white solid, m. p. 130-132 °C. HPLC purity: 98.6 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.99 (s, 1H), 8.24 (s, 1H), 7.58 – 7.51 (m, 2H), 6.87 – 6.81 (m, 2H), 4.70 (p,  $J$  = 8.5 Hz, 1H), 4.54 (hept,  $J$  = 7.1 Hz, 1H), 2.99 – 2.92 (m, 4H), 2.88 – 2.81 (m, 4H), 2.27 – 2.12 (m, 2H), 1.98 – 1.83 (m, 4H), 1.69 – 1.56 (m, 2H), 1.41 (d,  $J$  = 6.9 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  154.8, 151.2, 149.6, 146.3, 134.3, 133.3, 119.5, 115.9, 113.9, 52.2, 50.3, 45.6, 44.5, 28.7, 24.4, 20.1. HRMS (ESI):  $m/z$  calcd  $\text{C}_{23}\text{H}_{31}\text{N}_7\text{O}$  for  $[\text{M}+\text{H}]^+$  422.2663, found  $[\text{M}+\text{H}]^+$  422.2661.

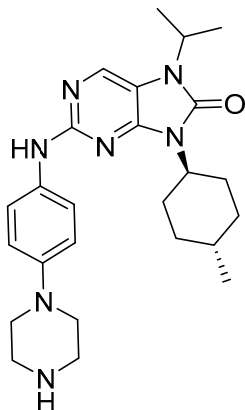
*9-Cyclohexyl-7-isopropyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (15b)*



Yield 27 %, white solid, m. p. 132-134 °C. HPLC purity: 98.4 %.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  9.02 (s, 1H), 8.23 (s, 1H), 7.62 – 7.55 (m, 2H), 6.88 – 6.81 (m, 2H), 4.54 (hept,  $J$  = 7.0 Hz, 1H), 4.16 (tt,  $J$  = 12.2, 3.8 Hz, 1H), 2.99 – 2.91 (m, 4H), 2.87 – 2.79 (m, 4H), 2.31 (qd,  $J$  = 12.5, 3.3 Hz, 2H), 1.90 – 1.80 (m, 2H), 1.76 – 1.66 (m, 3H), 1.40 (d,  $J$  = 6.9 Hz, 6H), 1.38 – 1.29 (m, 2H), 1.28 – 1.18 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{DMSO}-d_6$ )  $\delta$  154.8, 151.0, 149.6, 146.4, 134.3, 133.4, 119.4, 115.9,

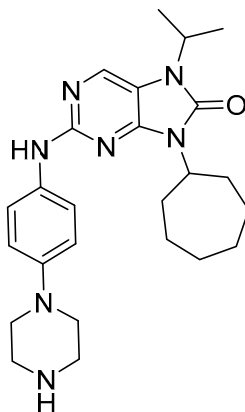
113.8, 51.7, 50.4, 45.7, 44.5, 29.2, 25.4, 25.0, 20.1. HRMS (ESI):  $m/z$  calcd  $C_{24}H_{33}N_7O$  for  $[M+H]^+$  436.2819, found  $[M+H]^+$  436.2817.

*7-Isopropyl-9-(4-methylcyclohexyl)-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (15c)*



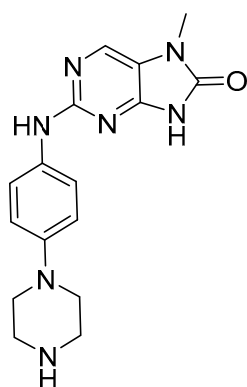
Yield 26 %, pale yellow solid, m. p. 264-266 °C. HPLC purity: 99.4 %.  $^1H$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  9.08 (s, 1H), 8.24 (s, 1H), 7.66 – 7.60 (m, 2H), 6.93 – 6.85 (m, 2H), 4.53 (hept,  $J$  = 6.9 Hz, 1H), 4.14 (tt,  $J$  = 12.3, 3.9 Hz, 1H), 3.25 – 3.20 (m, 4H), 3.17 – 3.12 (m, 4H), 2.36 (qd,  $J$  = 12.7, 3.3 Hz, 2H), 1.84 – 1.76 (m, 2H), 1.73 – 1.64 (m, 2H), 1.40 (d,  $J$  = 6.9 Hz, 6H), 1.06 (qd,  $J$  = 13.4, 3.0 Hz, 2H), 0.94 (d,  $J$  = 6.5 Hz, 3H).  $^{13}C$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  154.6, 151.1, 149.7, 144.7, 134.4, 134.2, 119.3, 116.6, 114.0, 51.6, 47.0, 44.5, 43.1, 34.0, 31.34 28.9, 22.2, 20.1. HRMS (ESI):  $m/z$  calcd  $C_{25}H_{35}N_7O$  for  $[M+H]^+$  450.2976, found  $[M+H]^+$  450.2975.

*9-Cycloheptyl-7-isopropyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (15d)*



Yield 68 %, pale yellow solid, m. p. 266-268 °C. HPLC purity: 98.6 %. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 9.05 (s, 1H), 8.23 (s, 1H), 7.66 – 7.59 (m, 2H), 6.93 – 6.84 (m, 2H), 4.53 (hept, *J* = 6.9 Hz, 1H), 4.31 (tt, 10.9, 3.4, 1H), 3.22 – 3.09 (m, 4H), 3.08 – 2.94 (m, 4H), 2.33 (q, *J* = 10.8 Hz, 2H), 1.85 – 1.72 (m, 4H), 1.71 – 1.54 (m, 4H), 1.52 – 1.43 (m, 2H), 1.40 (d, *J* = 6.9 Hz, 6H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 154.7, 151.0, 134.2, 134.1, 149.4, 145.2, 119.4, 116.4, 113.9, 53.9, 48.0, 44.5, 43.9, 32.0, 27.1, 24.5, 20.1. HRMS (ESI): *m/z* calcd C<sub>25</sub>H<sub>35</sub>N<sub>7</sub>O for [M+H]<sup>+</sup> 450.2976, found [M+H]<sup>+</sup> 450.2976.

*7-Methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (14a)*

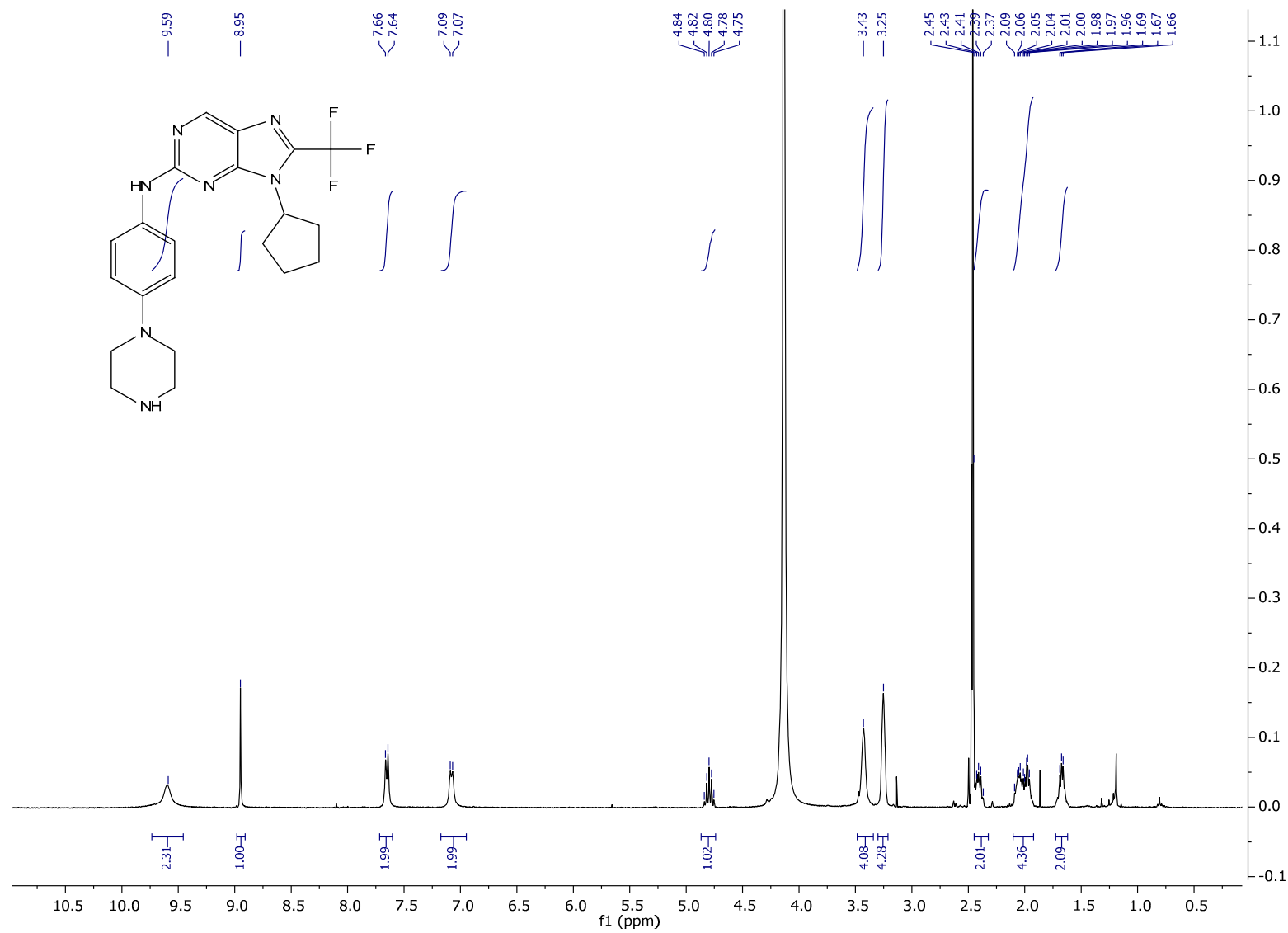


9-(2,4-Dimethoxybenzyl)-7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one (**14r**) (109 mg, 0.23 mmol) was dissolved in anisole (1.2 mL), then trifluoroacetic acid (1 mL) was added and a reaction mixture was heated in a round bottom flask with a condenser at 90°C for 5 days. TFA was evaporated by the flow of nitrogen and anisole was evaporated using RVO. Product was purified by column chromatography (5:1 DCM/MeOH). After evaporation, the product was diluted with H<sub>2</sub>O/MeOH (2 mL) and filtered off to yield 7-methyl-2-((4-(piperazin-1-yl)phenyl)amino)-7,9-dihydro-8H-purin-8-one 26 mg (35 %).

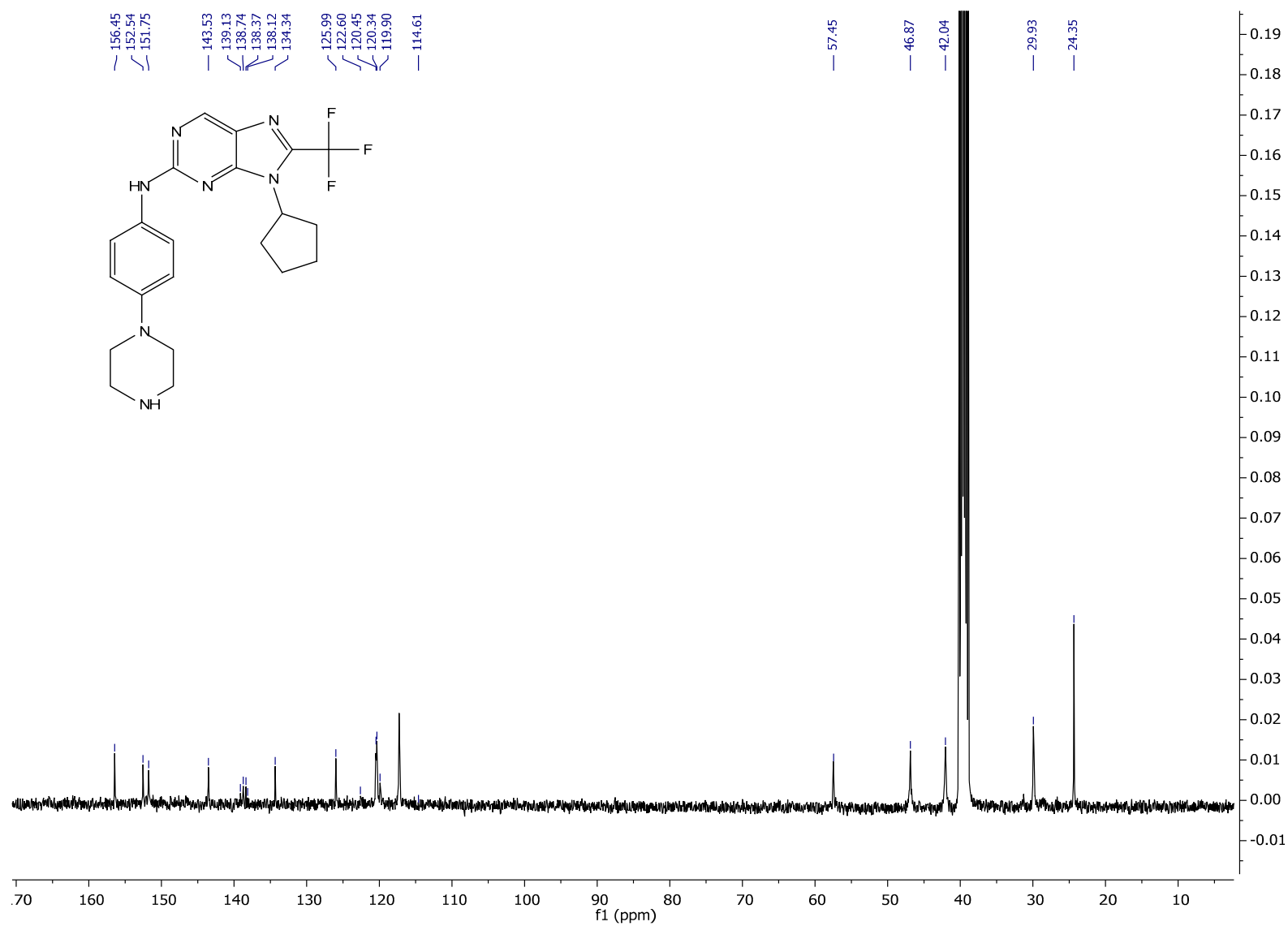
M. p. 232-234 °C. HPLC purity: >99.9 %. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 9.03 (s, 1H), 8.01 (s, 1H), 7.63 – 7.56 (m, 2H), 6.94 – 6.87 (m, 2H), 3.25 (s, 3H), 3.24 – 3.20 (m, 8H). <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 155.5, 153.2, 150.5, 144.4, 134.7, 132.8, 119.4, 117.5, 116.8, 46.7, 42.9, 26.6. HRMS (ESI): *m/z* calcd C<sub>16</sub>H<sub>20</sub>N<sub>7</sub>O for [M+H]<sup>+</sup> 326.1724, found [M+H]<sup>+</sup> 326.1724.



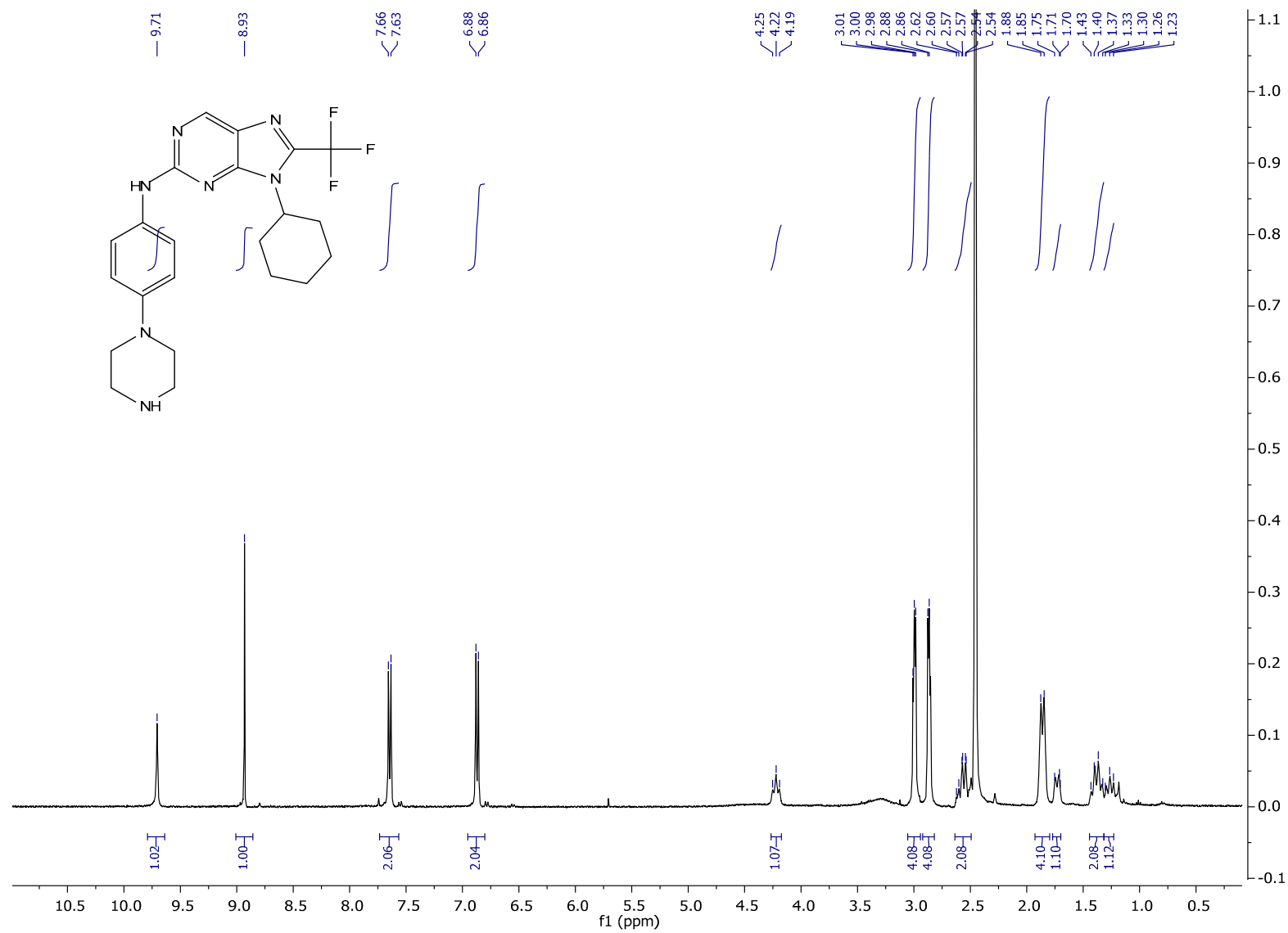
$^1\text{H}$  NMR spectrum of **12a**



$^{13}\text{C}$  NMR spectrum of **12a**



$^1\text{H}$  NMR spectrum of **12b**



Nc1ccc(N2C=NC3=C(N2)N(C3C(F)(F)F)C4CCCCC4)c5ccccc5N6CCCCN6

Chemical structure of the compound is shown above the spectrum. The structure is a complex molecule featuring a central pyrimidine ring system substituted with a piperidine ring, a phenyl ring, and a trifluoromethyl group.

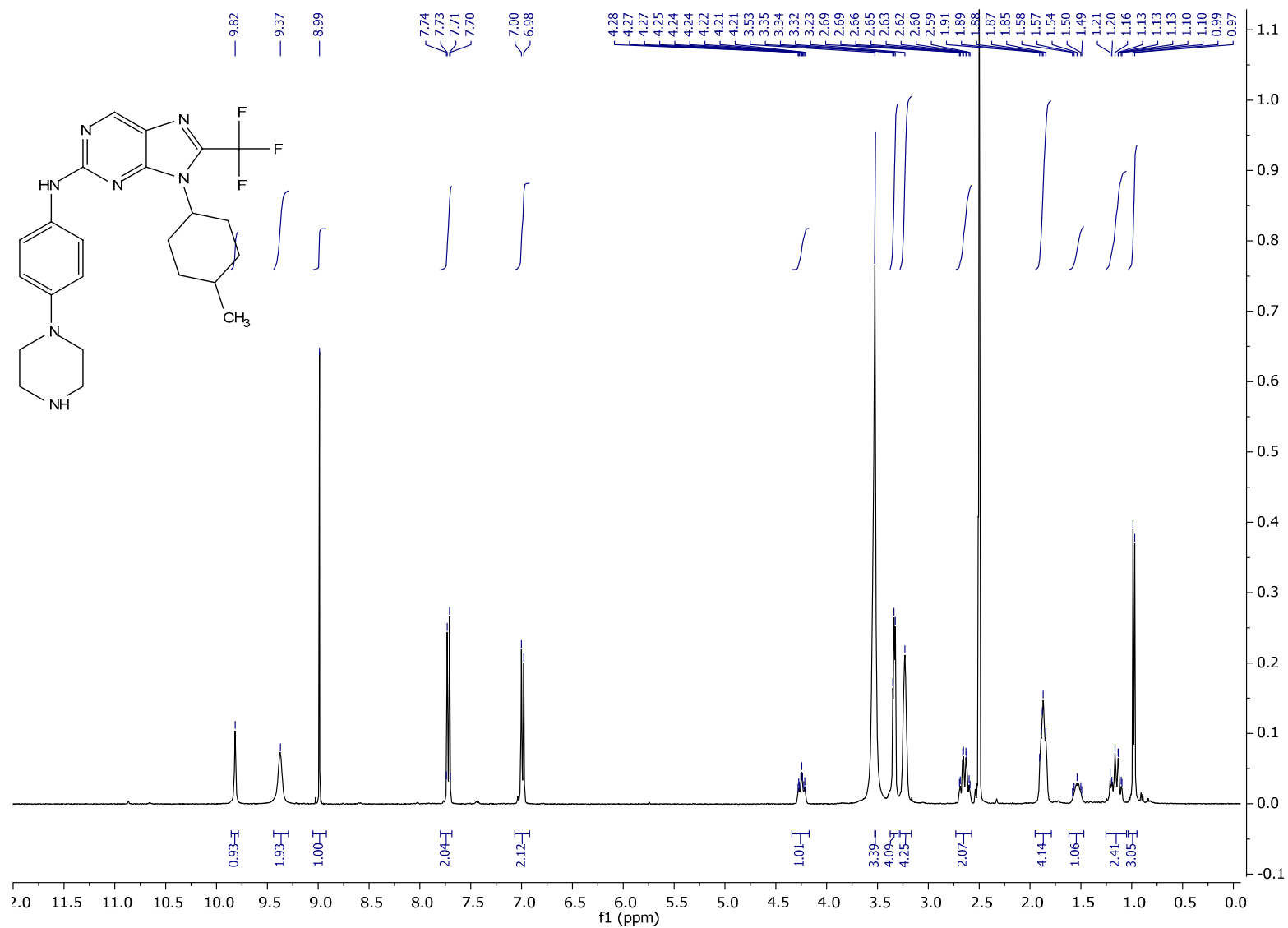
The <sup>13</sup>C NMR spectrum (f1 (ppm)) displays several peaks corresponding to the carbon atoms in the molecule. The peaks are labeled with their chemical shifts (ppm):

- 156.64
- 152.60
- 152.48
- 144.80
- 138.13
- 137.75
- 137.37
- 136.99
- 133.77
- 125.78
- 122.79
- 120.09
- 119.96
- 117.40
- 116.83
- 114.70
- 57.22
- 46.44
- 42.53
- 29.94
- 25.19
- 24.96

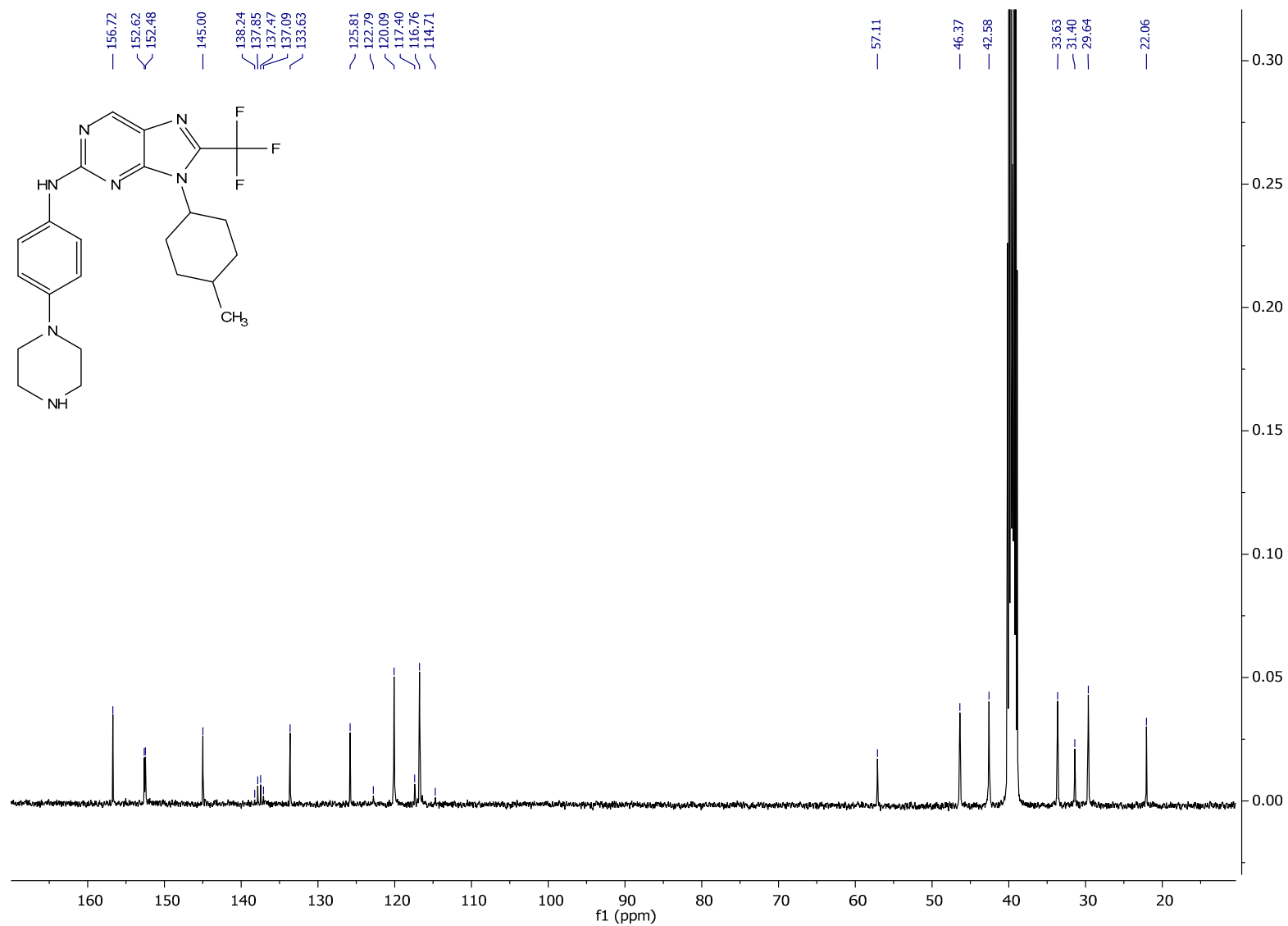
The spectrum shows a broad range of chemical shifts, from approximately 160 ppm down to 25 ppm, indicating a diverse range of carbon environments within the molecule.



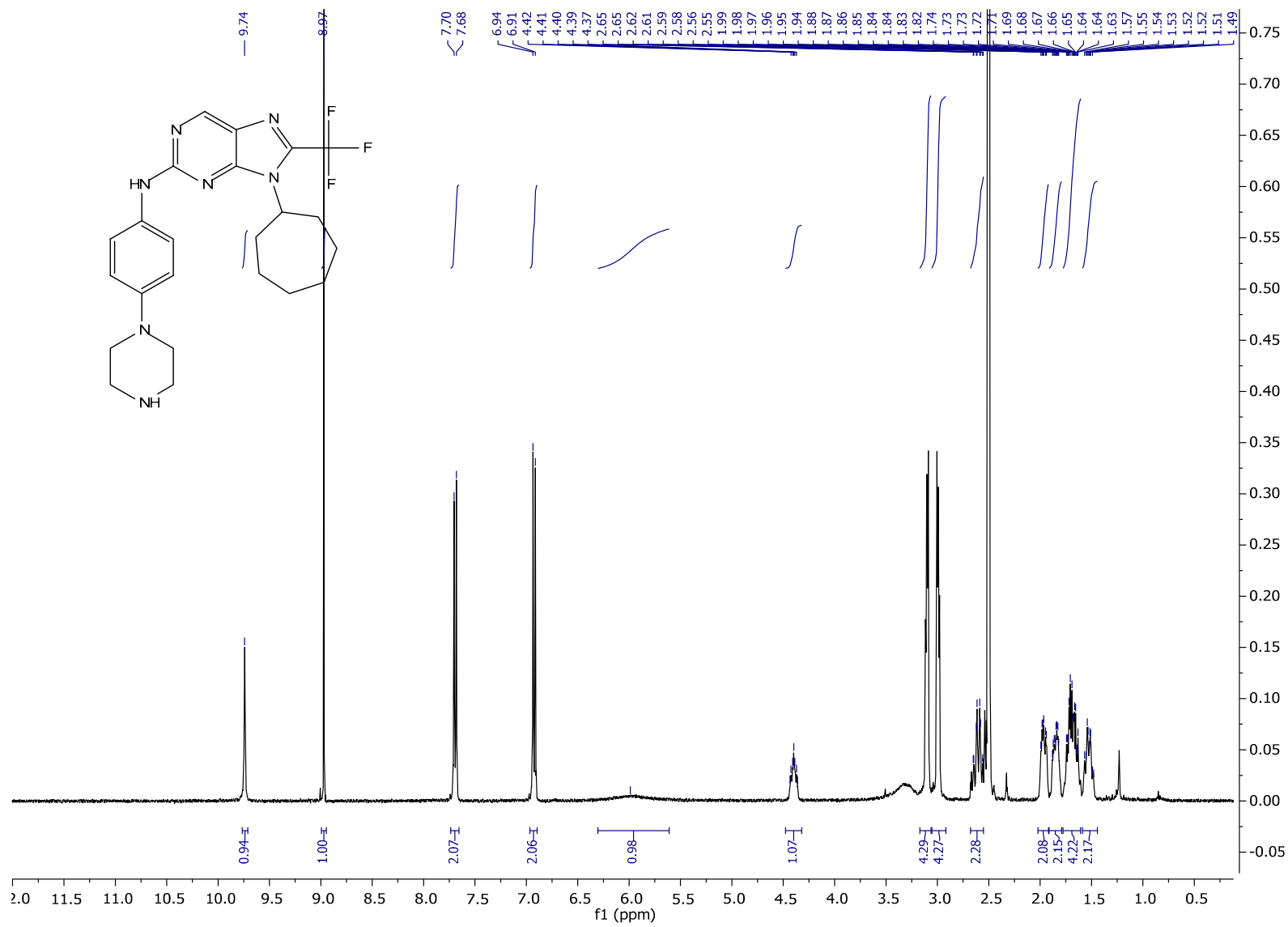
<sup>1</sup>H NMR spectrum of **12c**



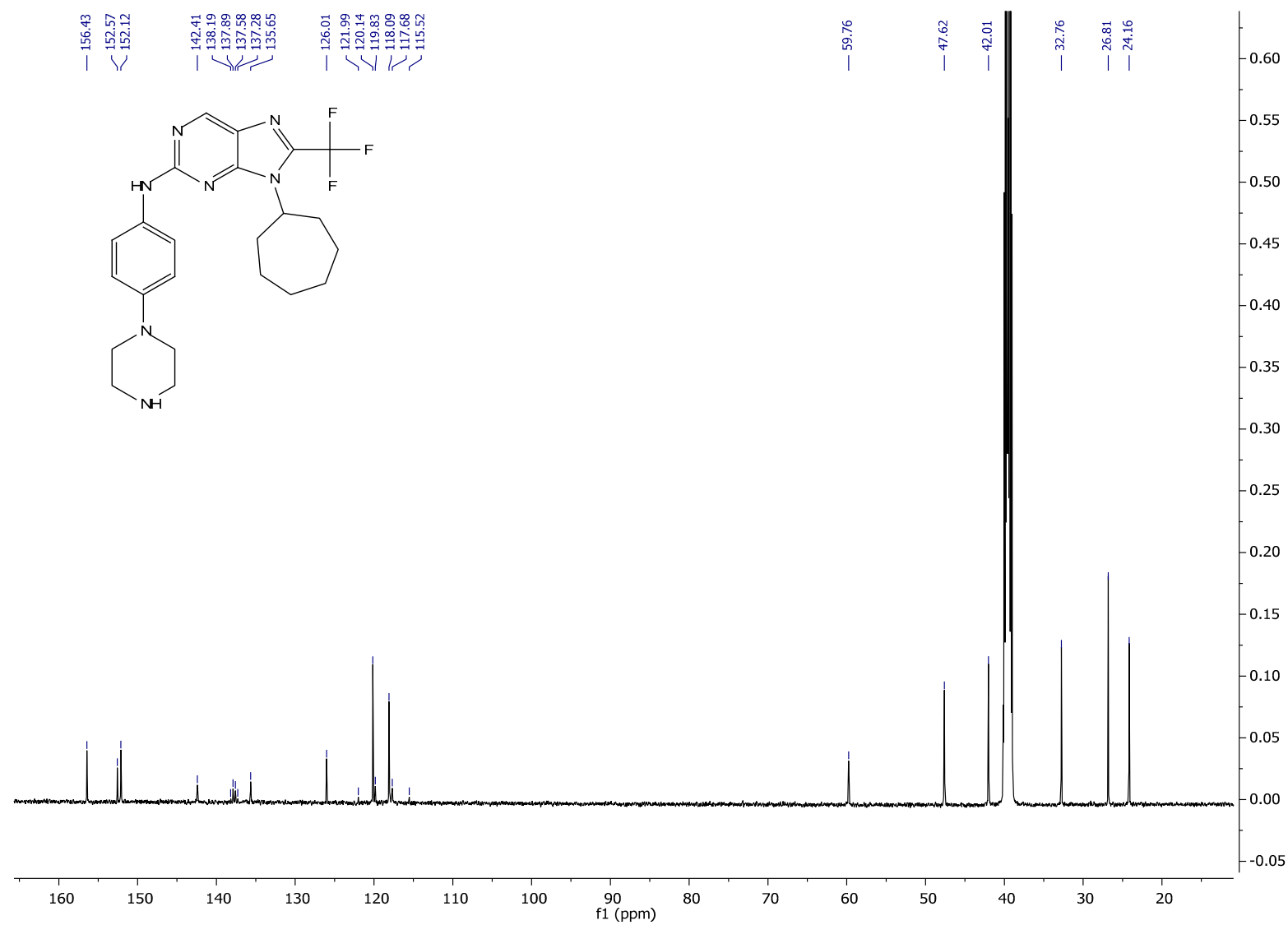
<sup>13</sup>C NMR spectrum of **12c**



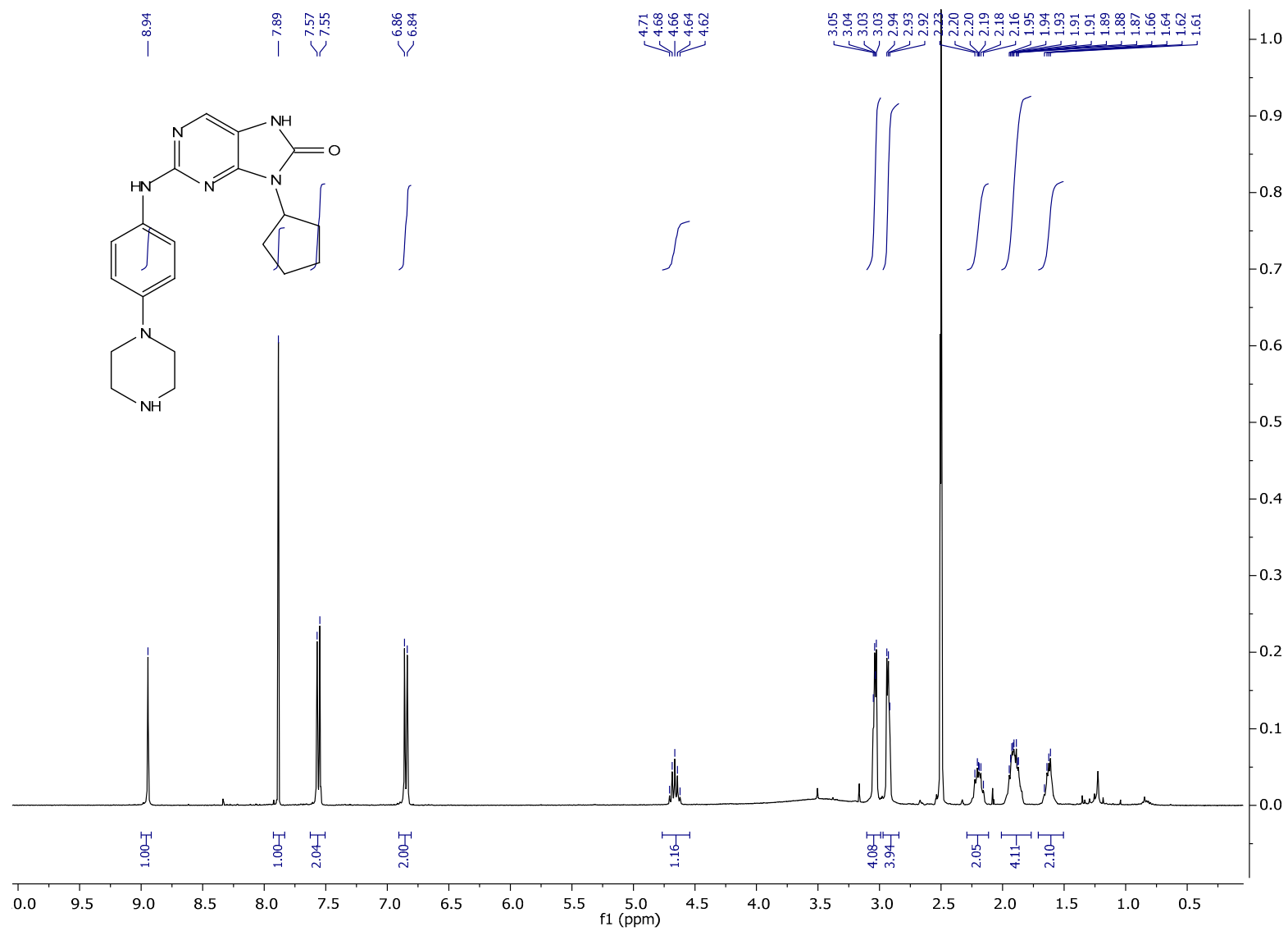
<sup>1</sup>H NMR spectrum of **12d**



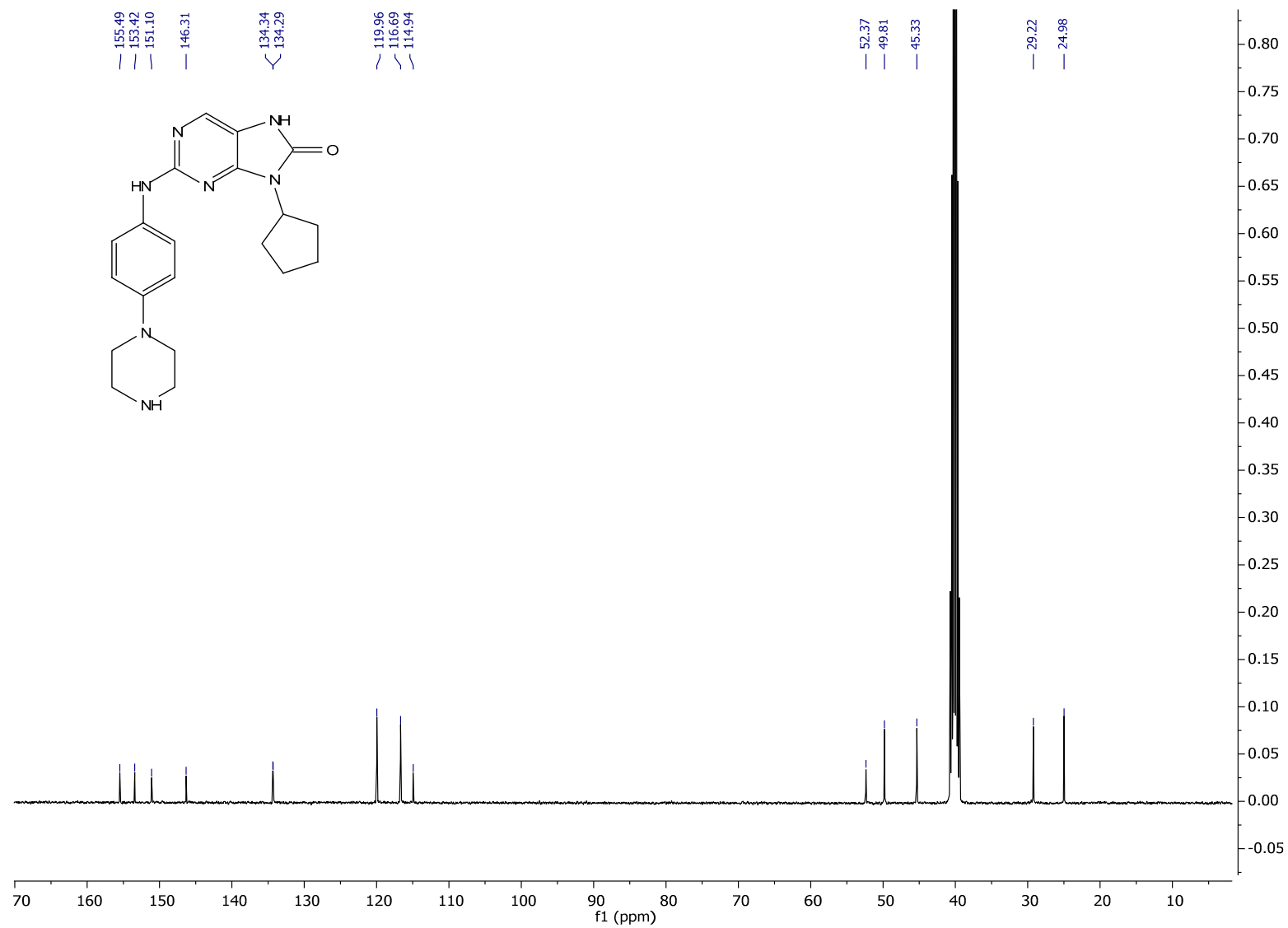
<sup>13</sup>C NMR spectrum of **12d**



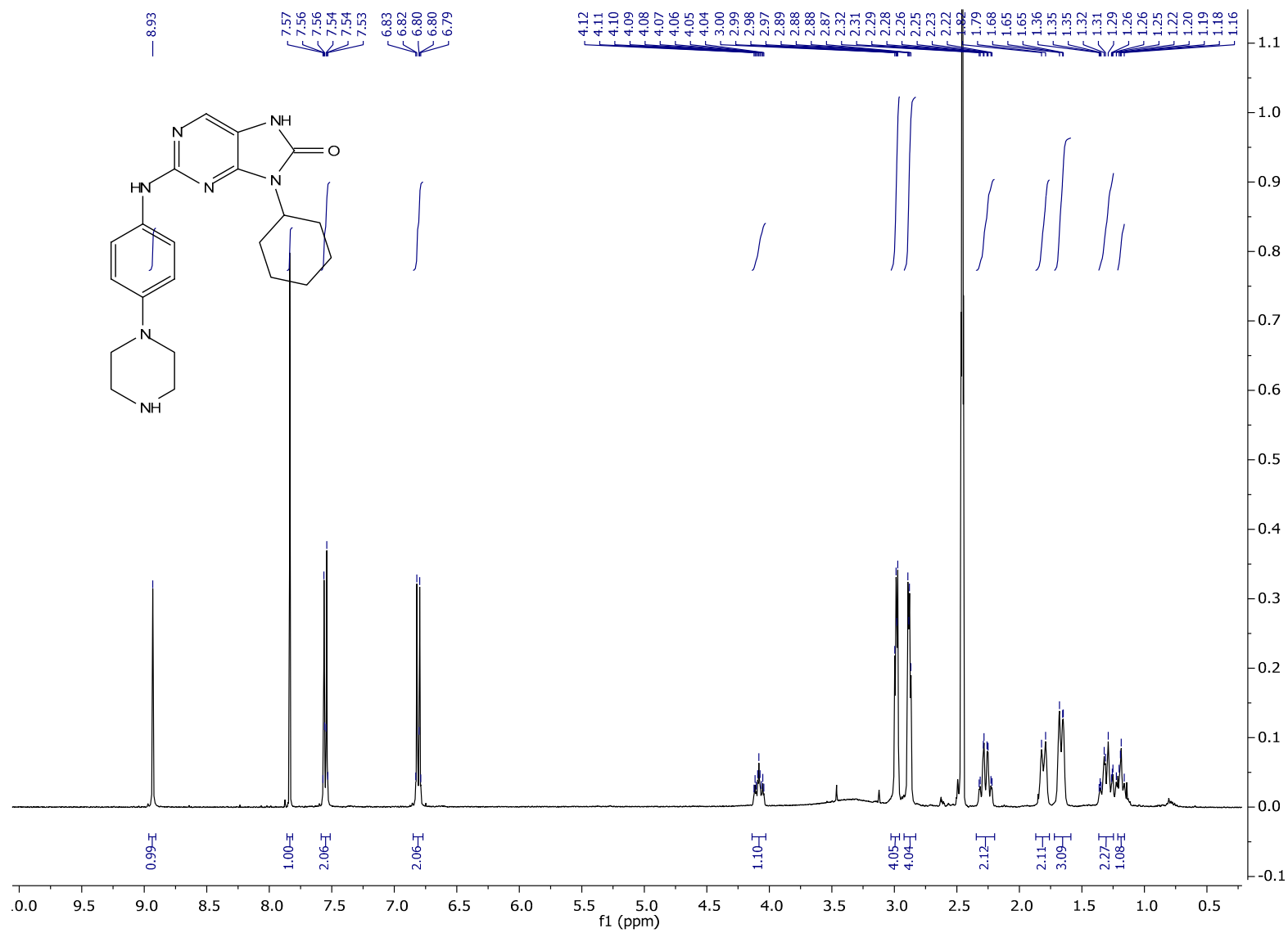
$^1\text{H}$  NMR spectrum of **13a**



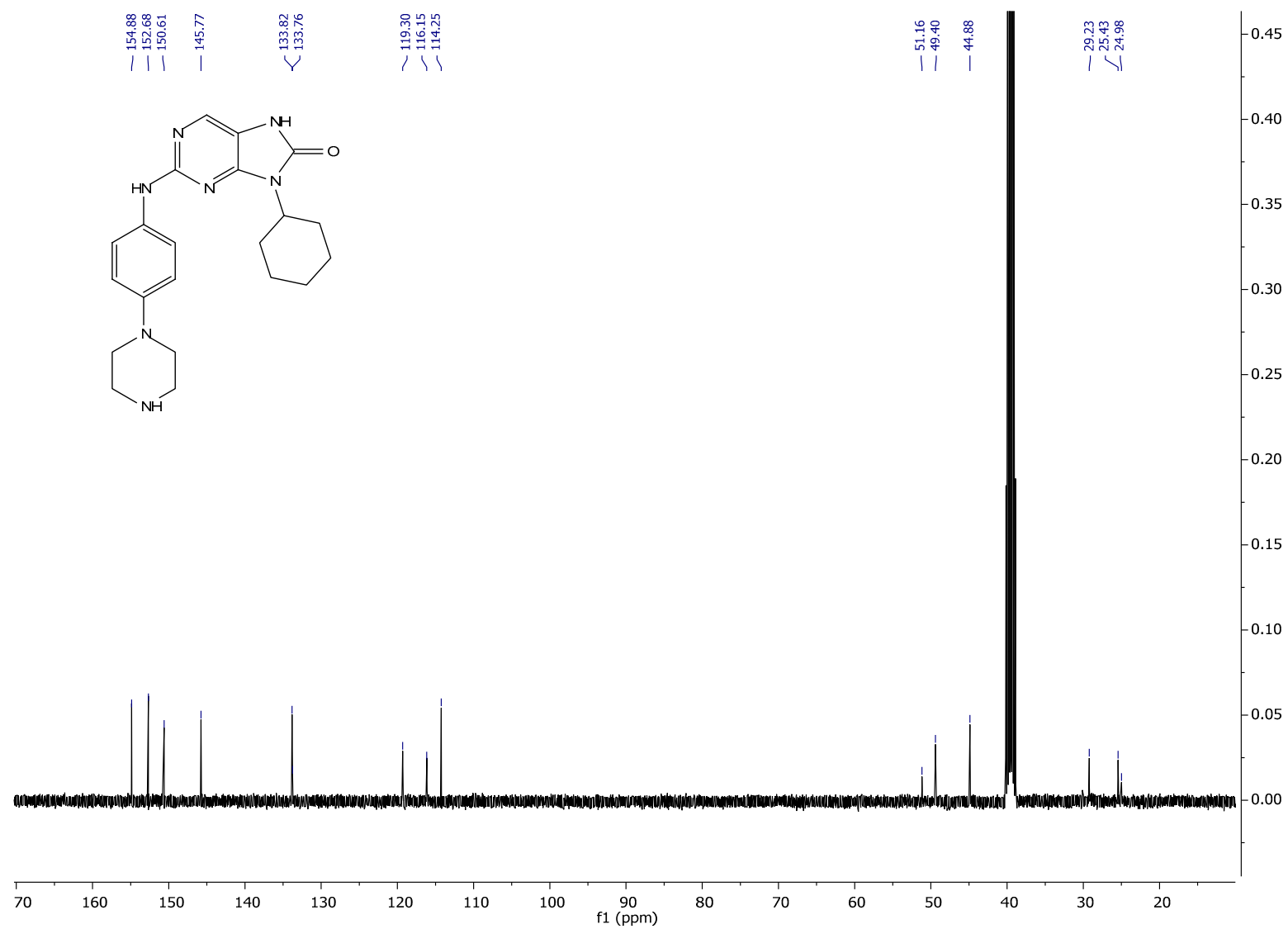
$^{13}\text{C}$  NMR spectrum of **13a**



$^1\text{H}$  NMR spectrum of **13b**

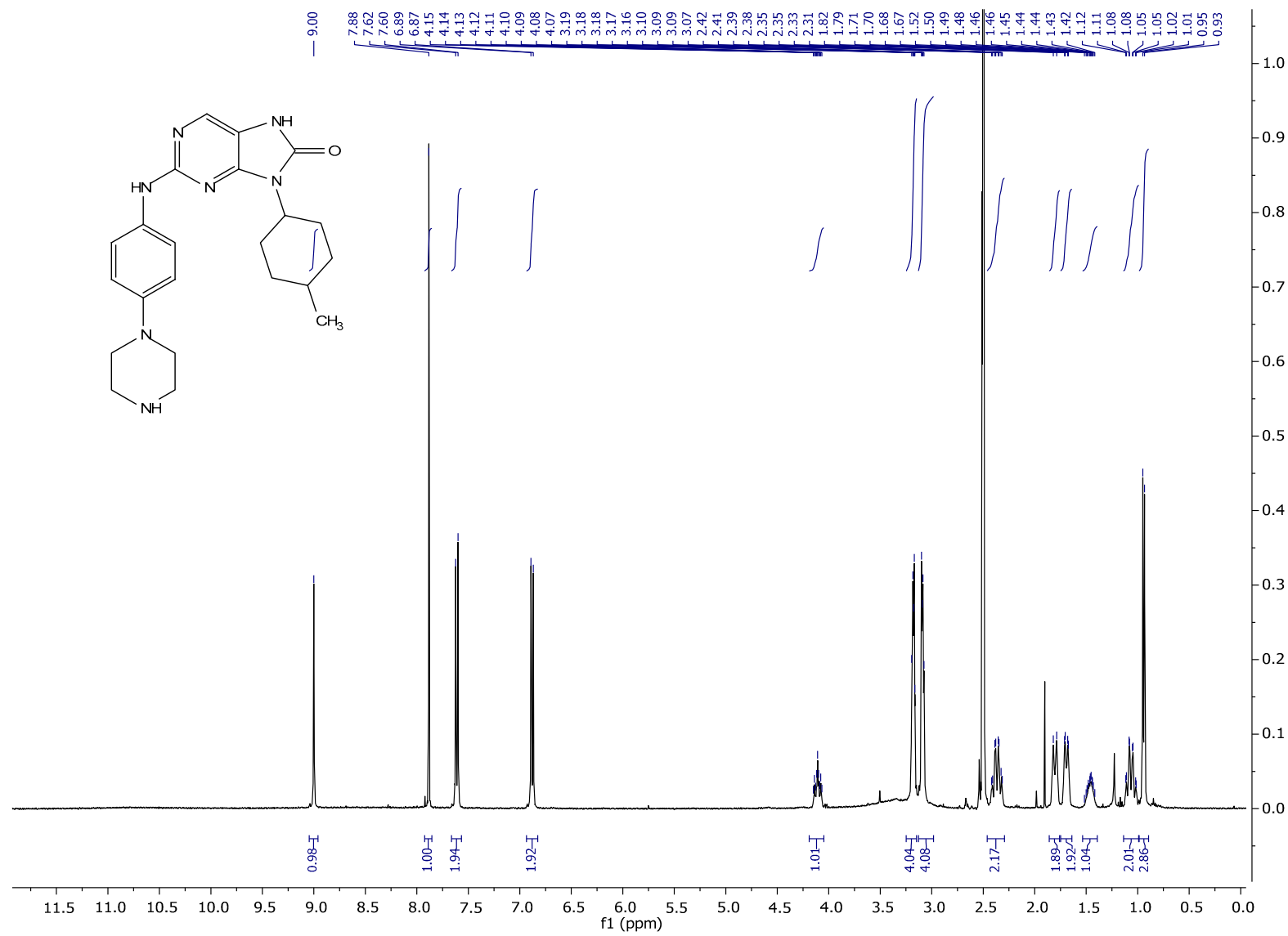


$^{13}\text{C}$  NMR spectrum of **13b**

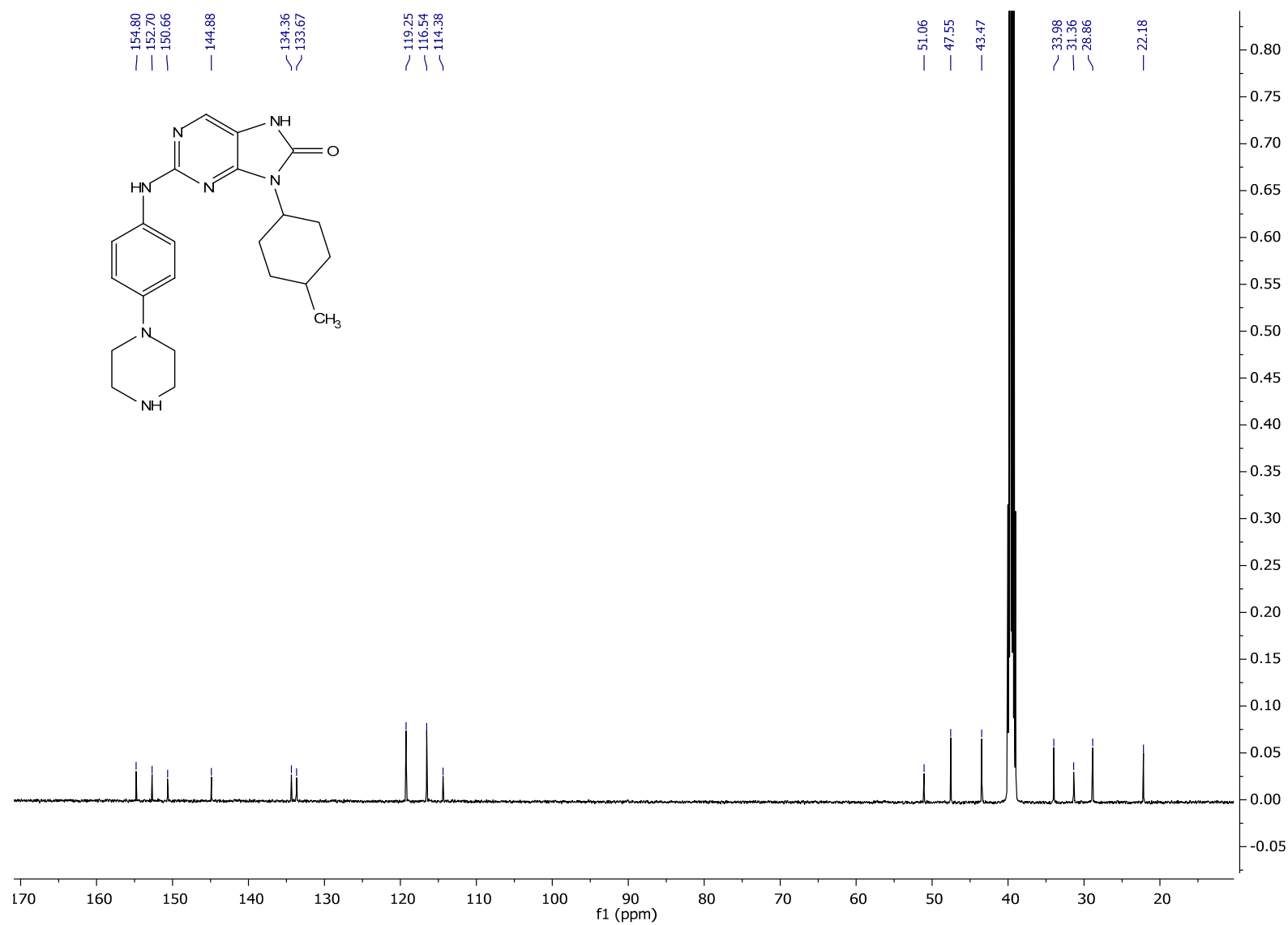




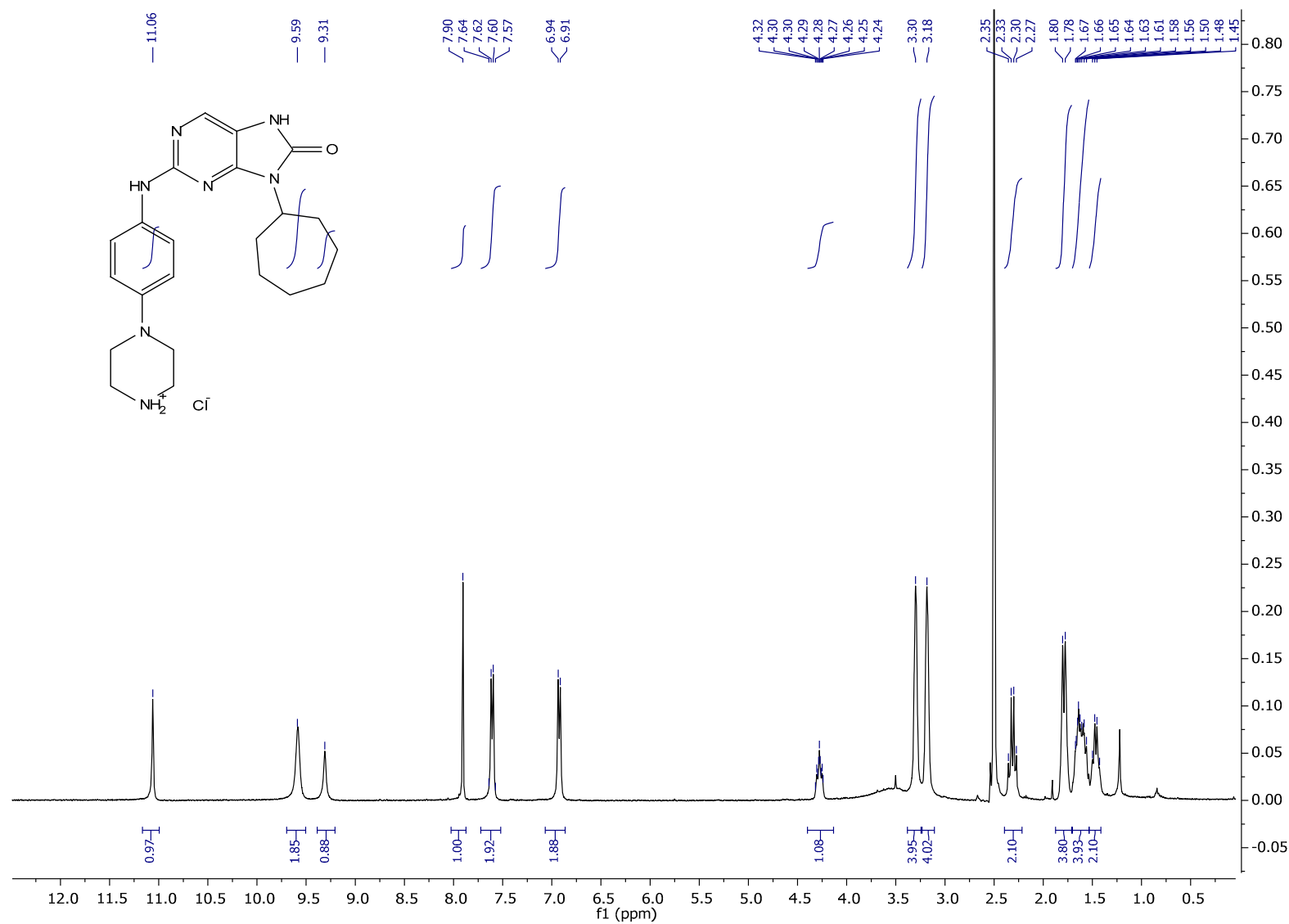
<sup>1</sup>H NMR spectrum of **13c**



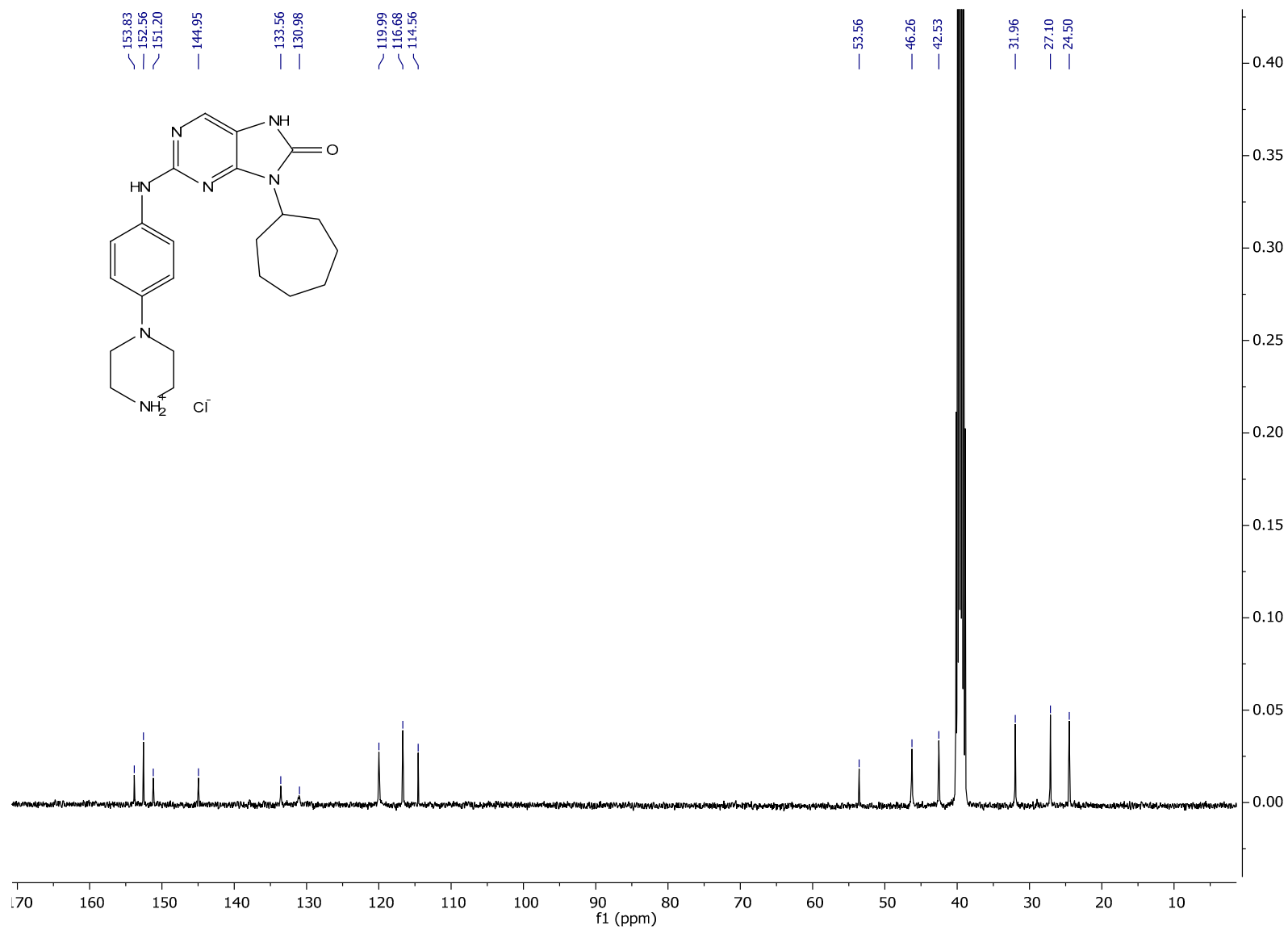
<sup>13</sup>C NMR spectrum of **13c**



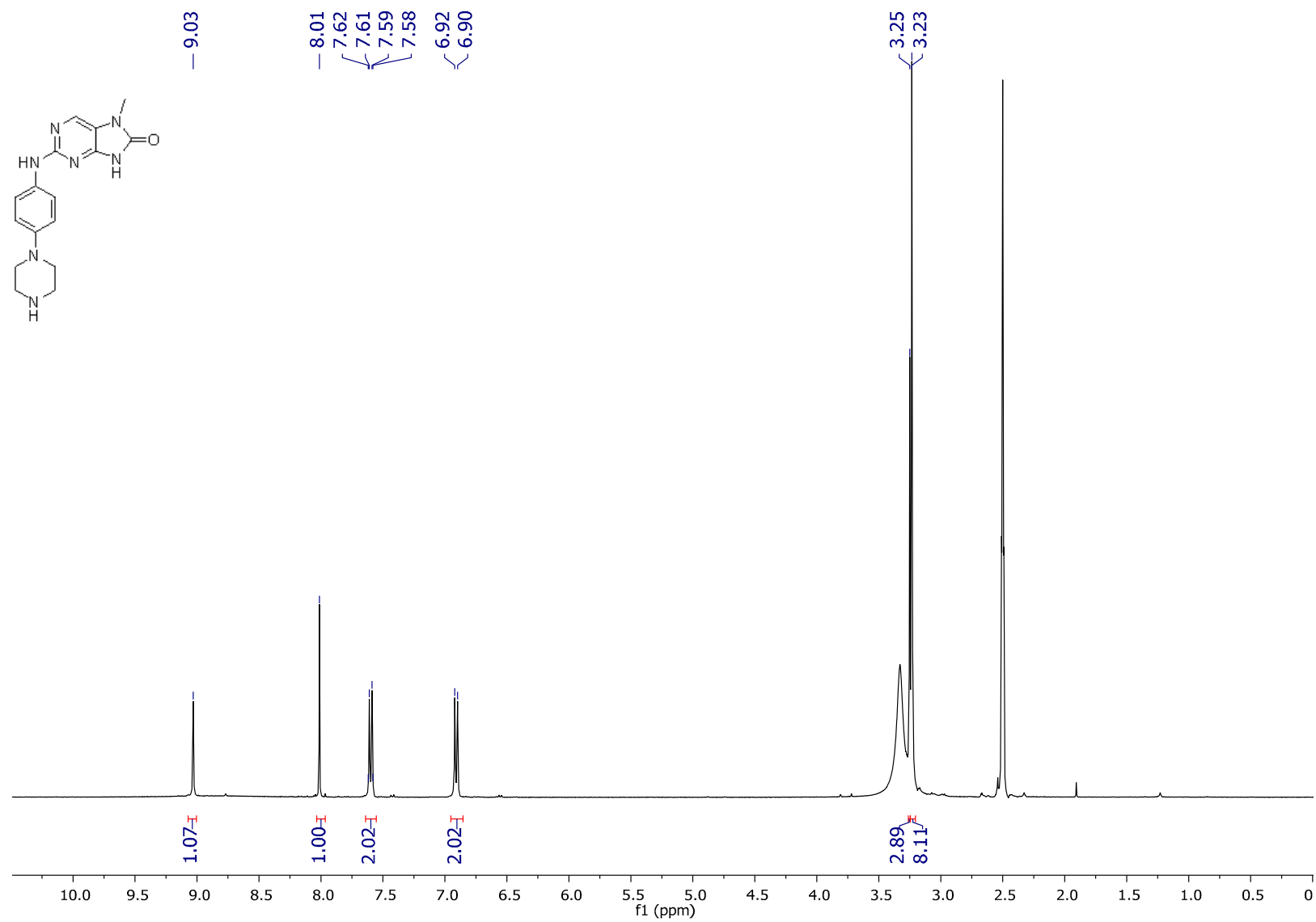
$^1\text{H}$  NMR spectrum of **13d**



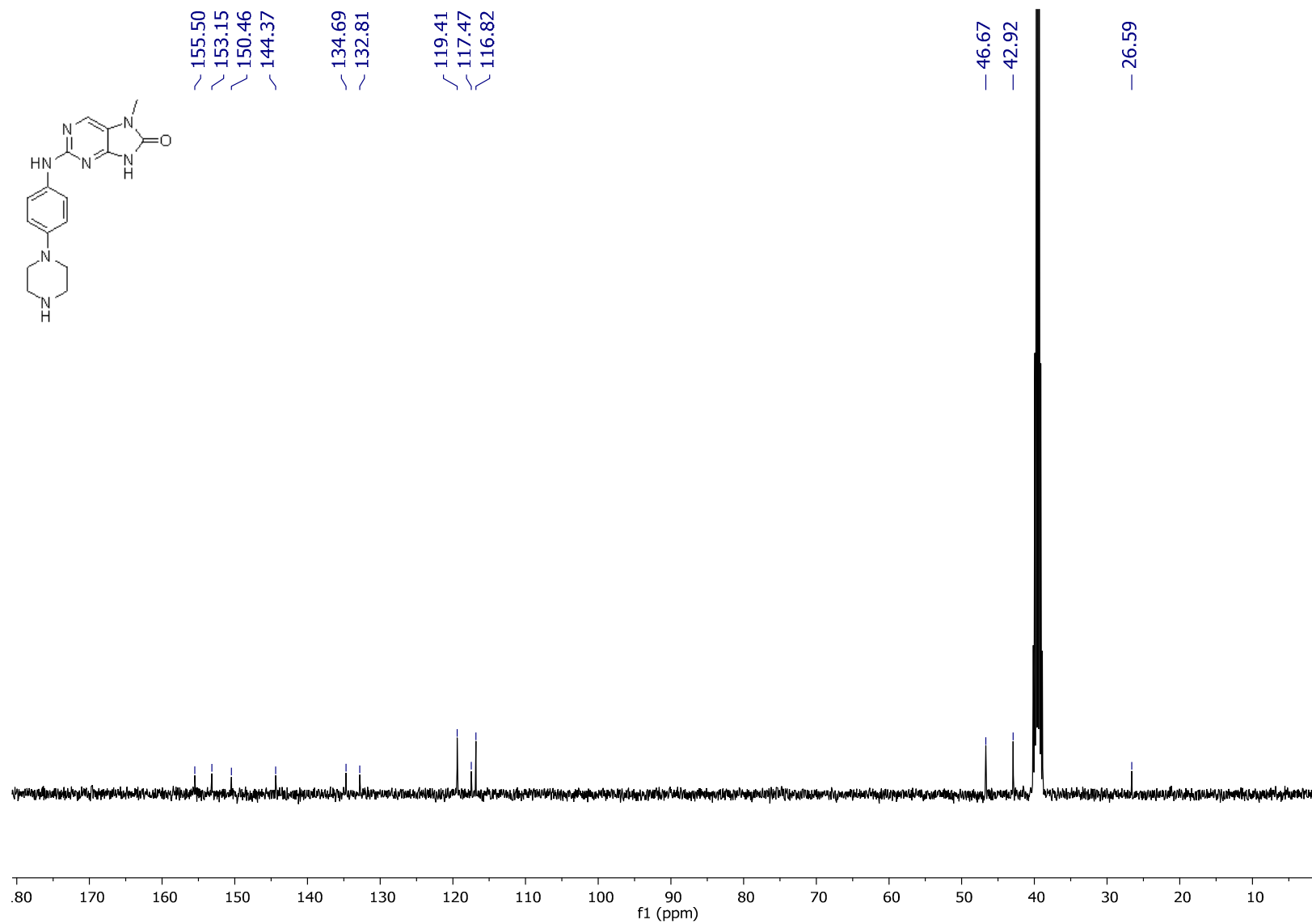
<sup>13</sup>C NMR spectrum of **13d**



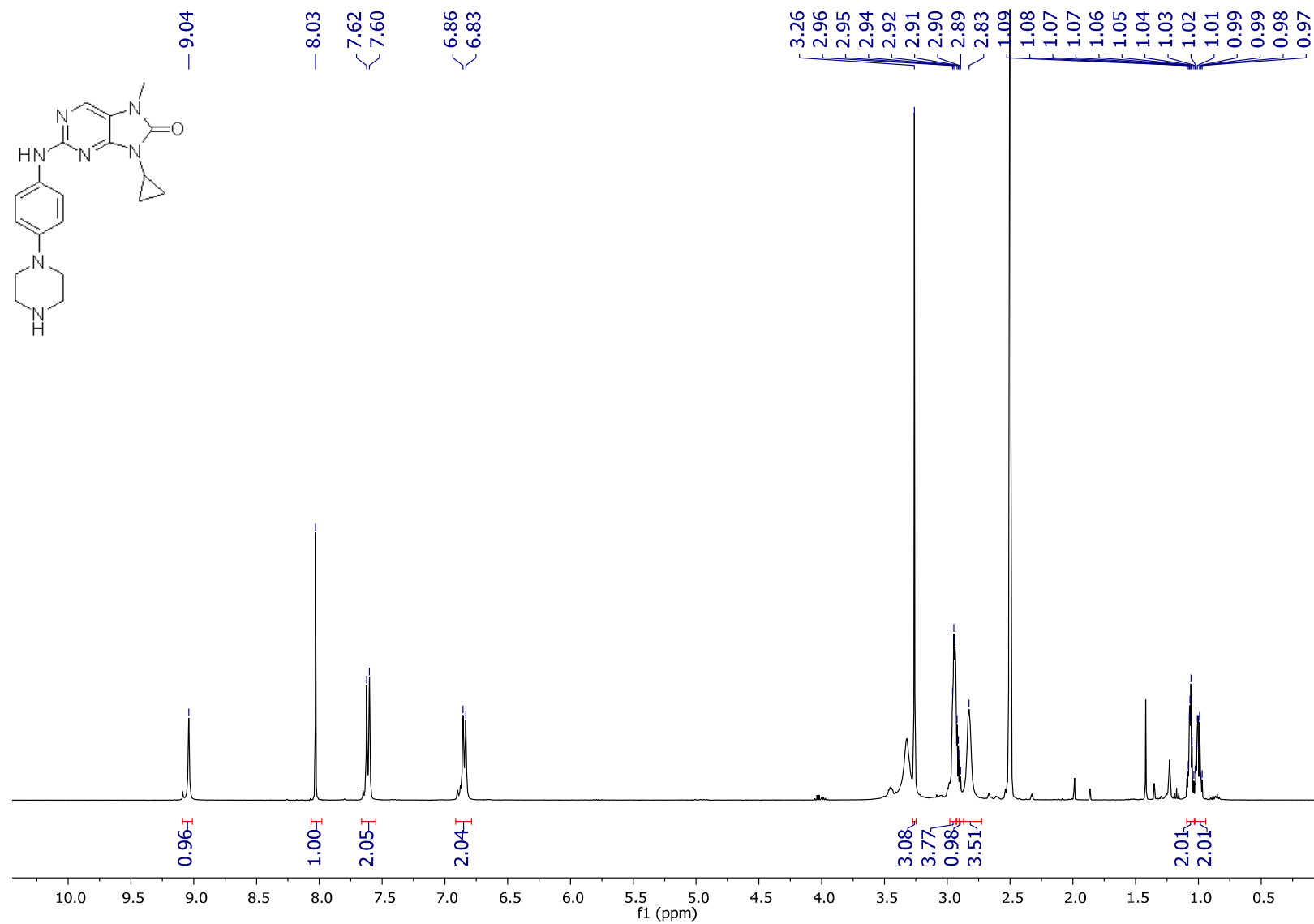
<sup>1</sup>H NMR spectrum of **14a**



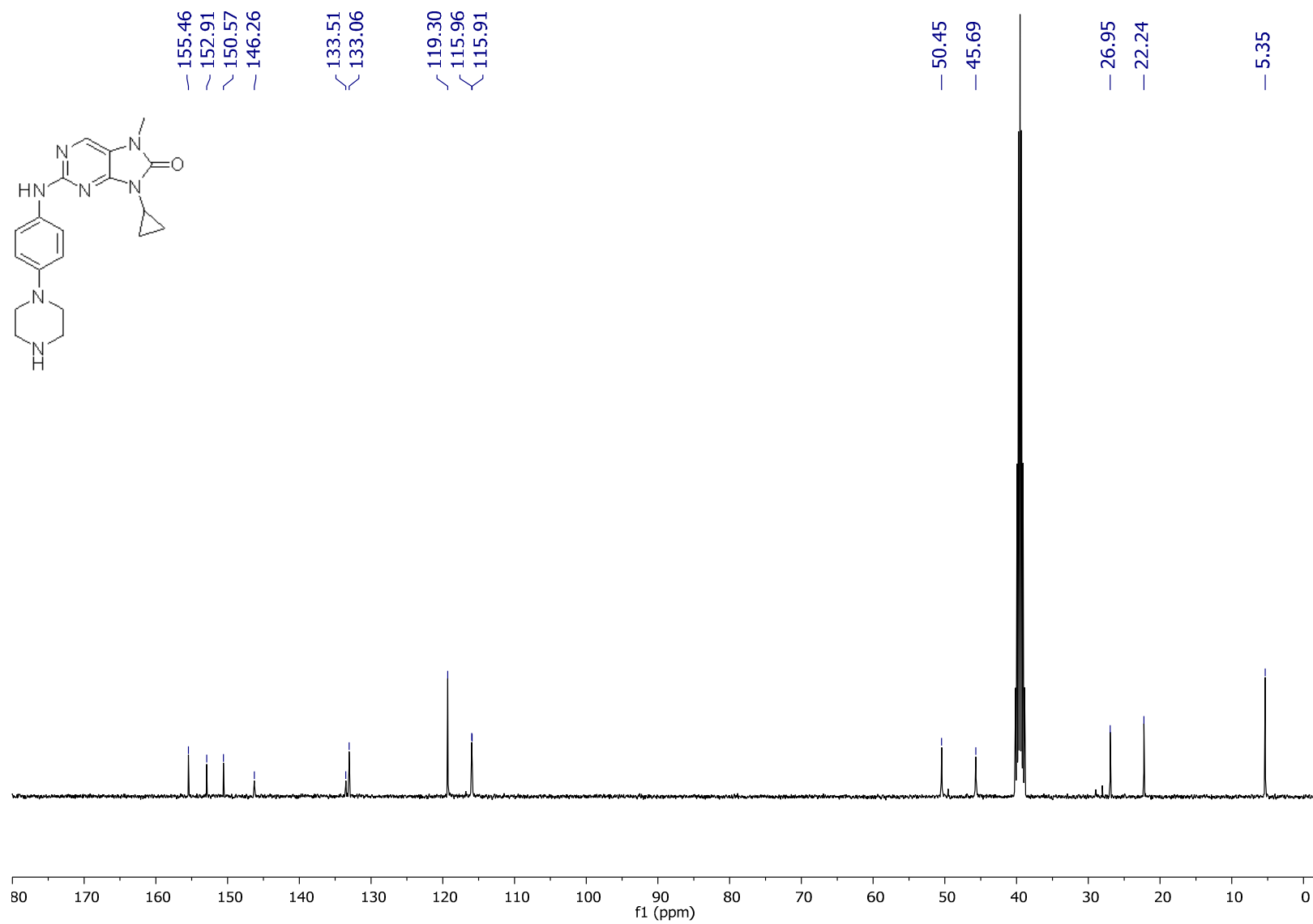
<sup>13</sup>C NMR spectrum of **14a**



<sup>1</sup>H NMR spectrum of **14b**

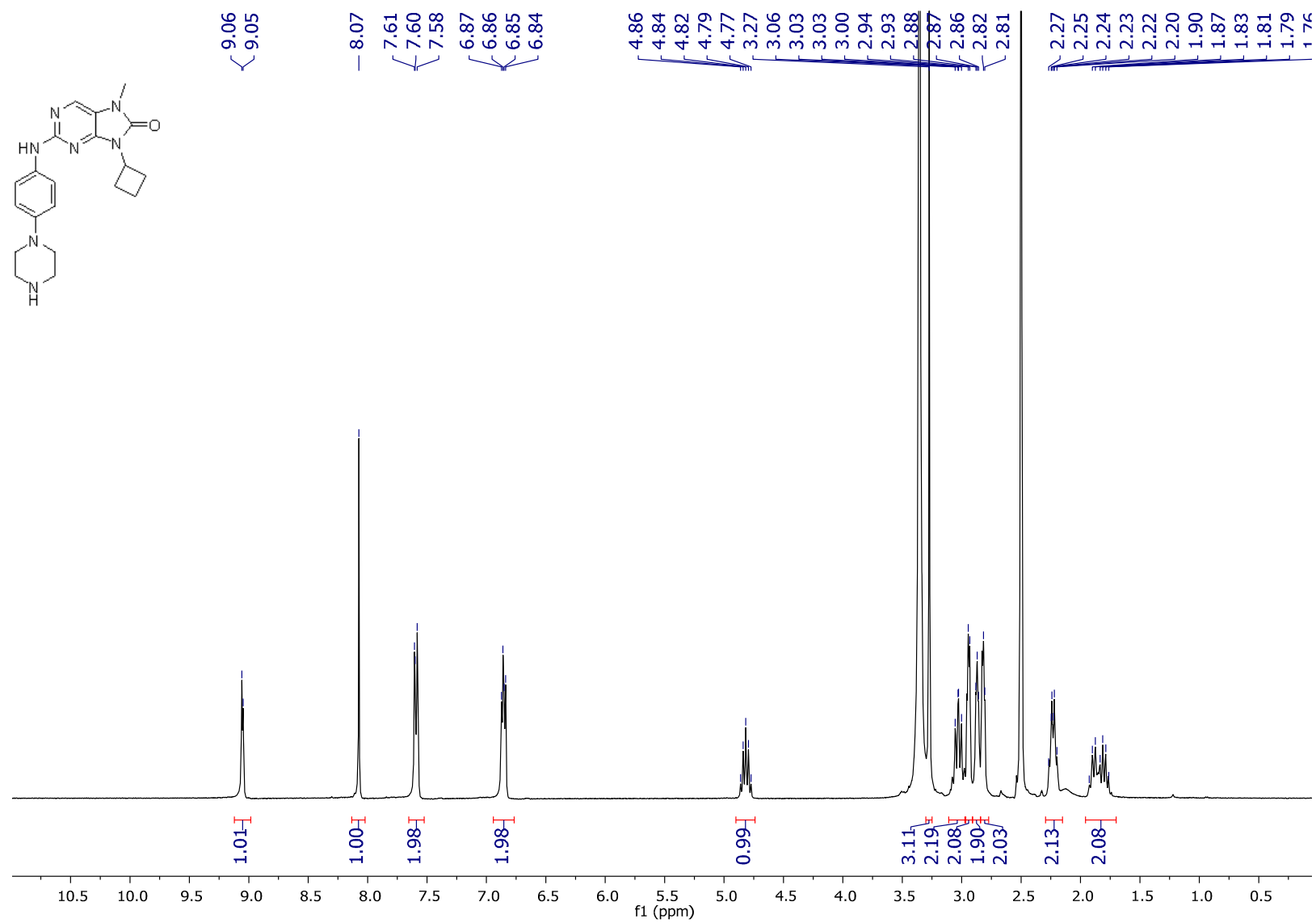


<sup>13</sup>C NMR spectrum of **14b**



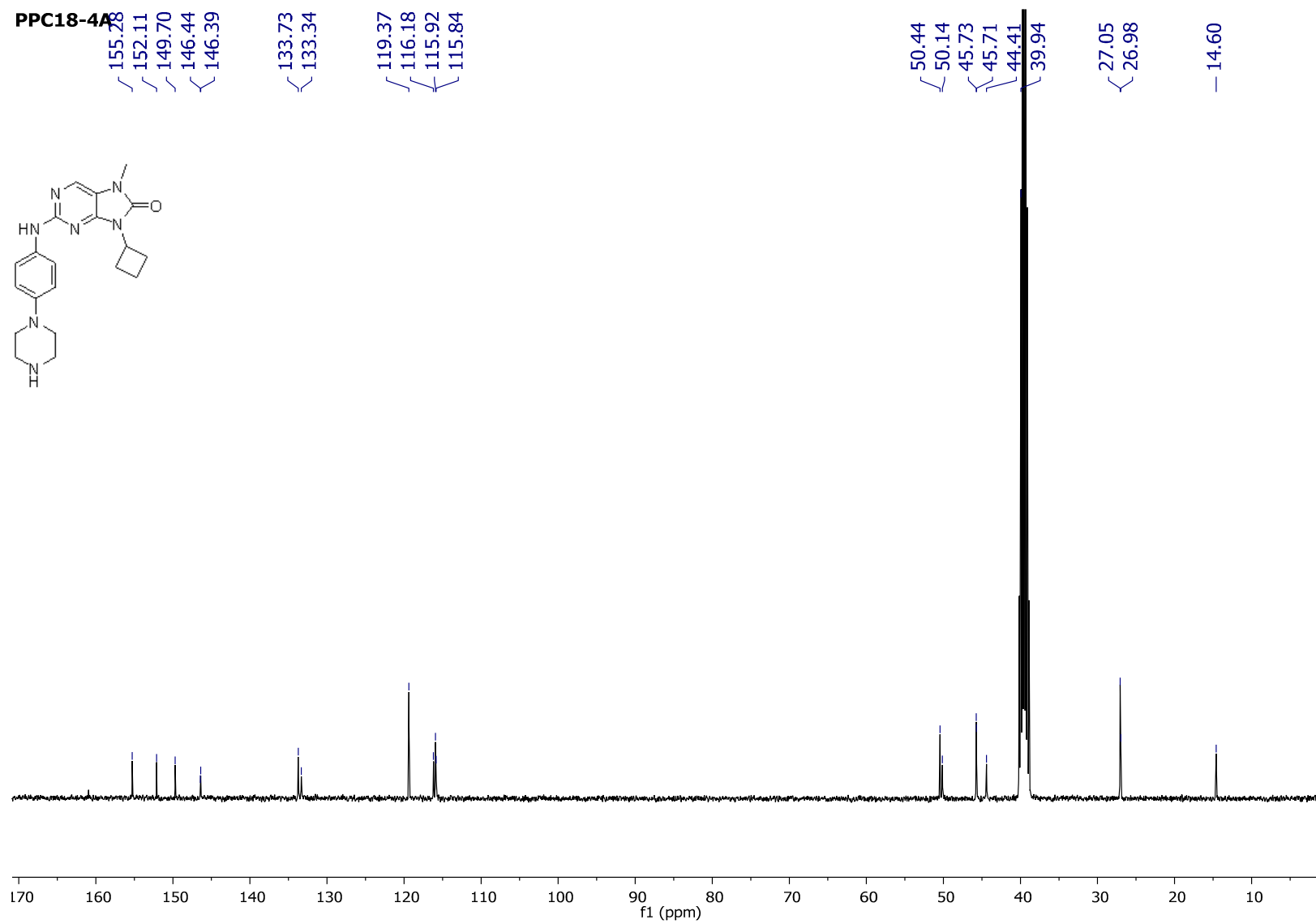


<sup>1</sup>H NMR spectrum of **14c**

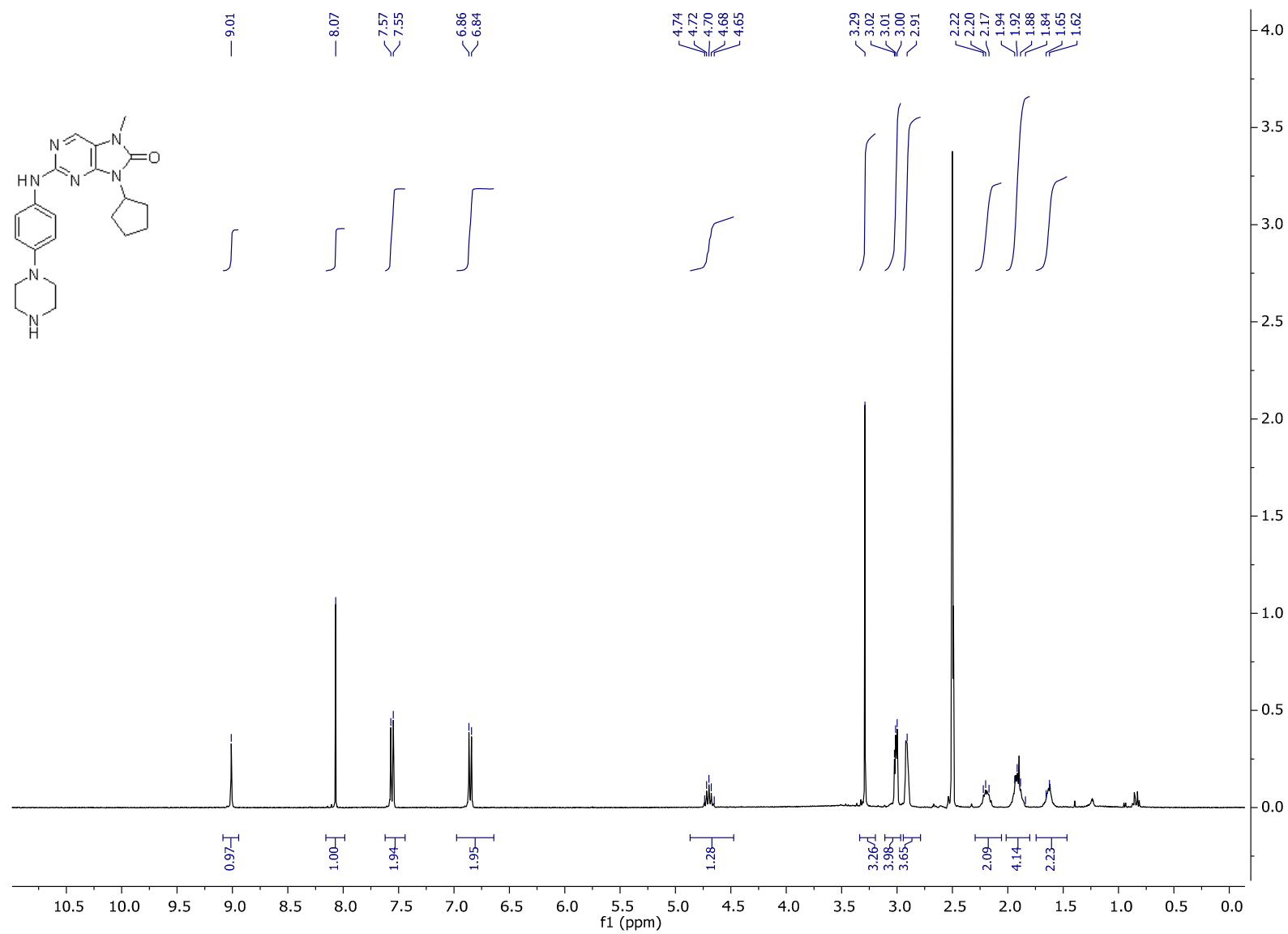


<sup>13</sup>C NMR spectrum of **14c**

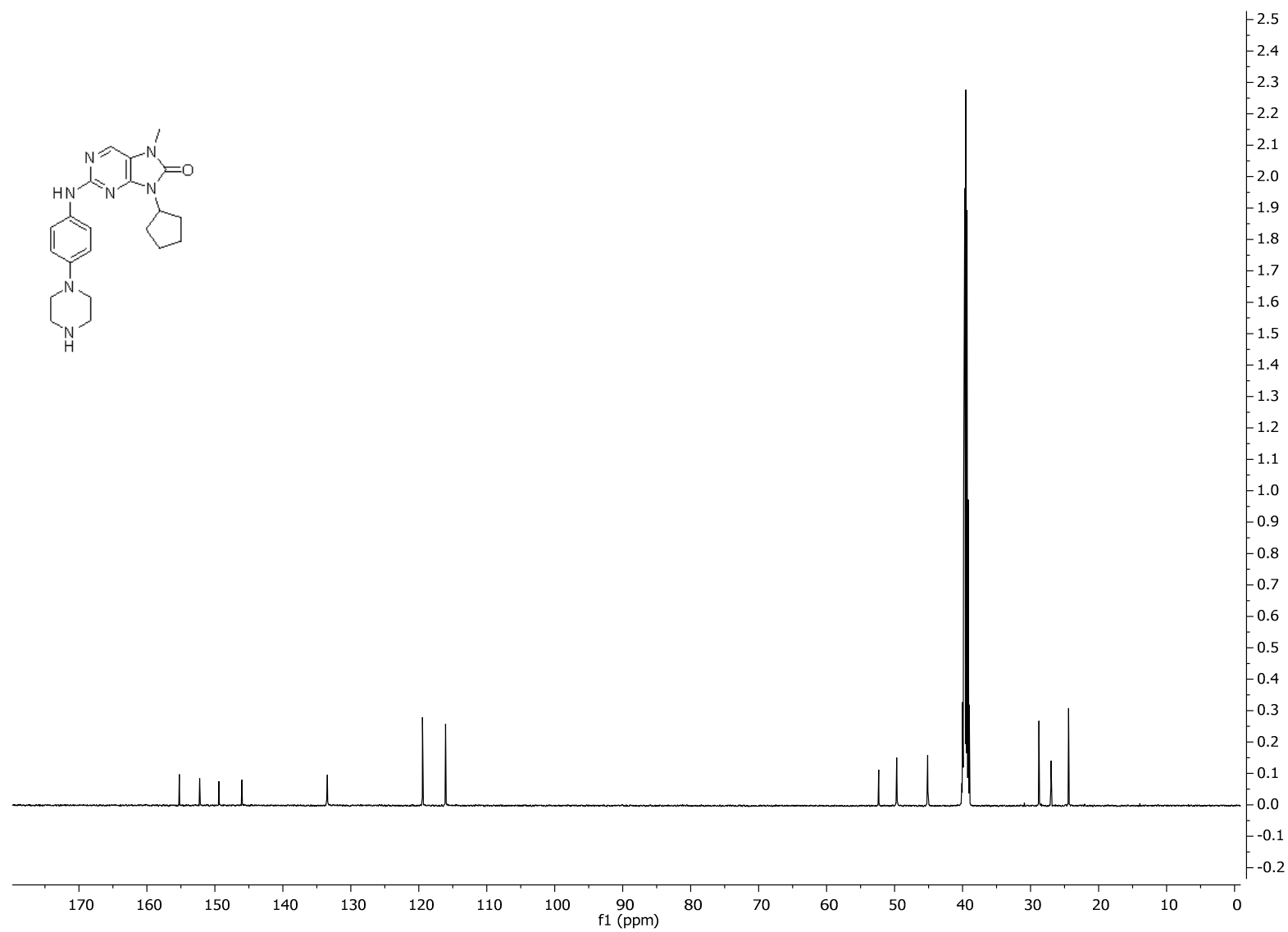
PPC18-4A



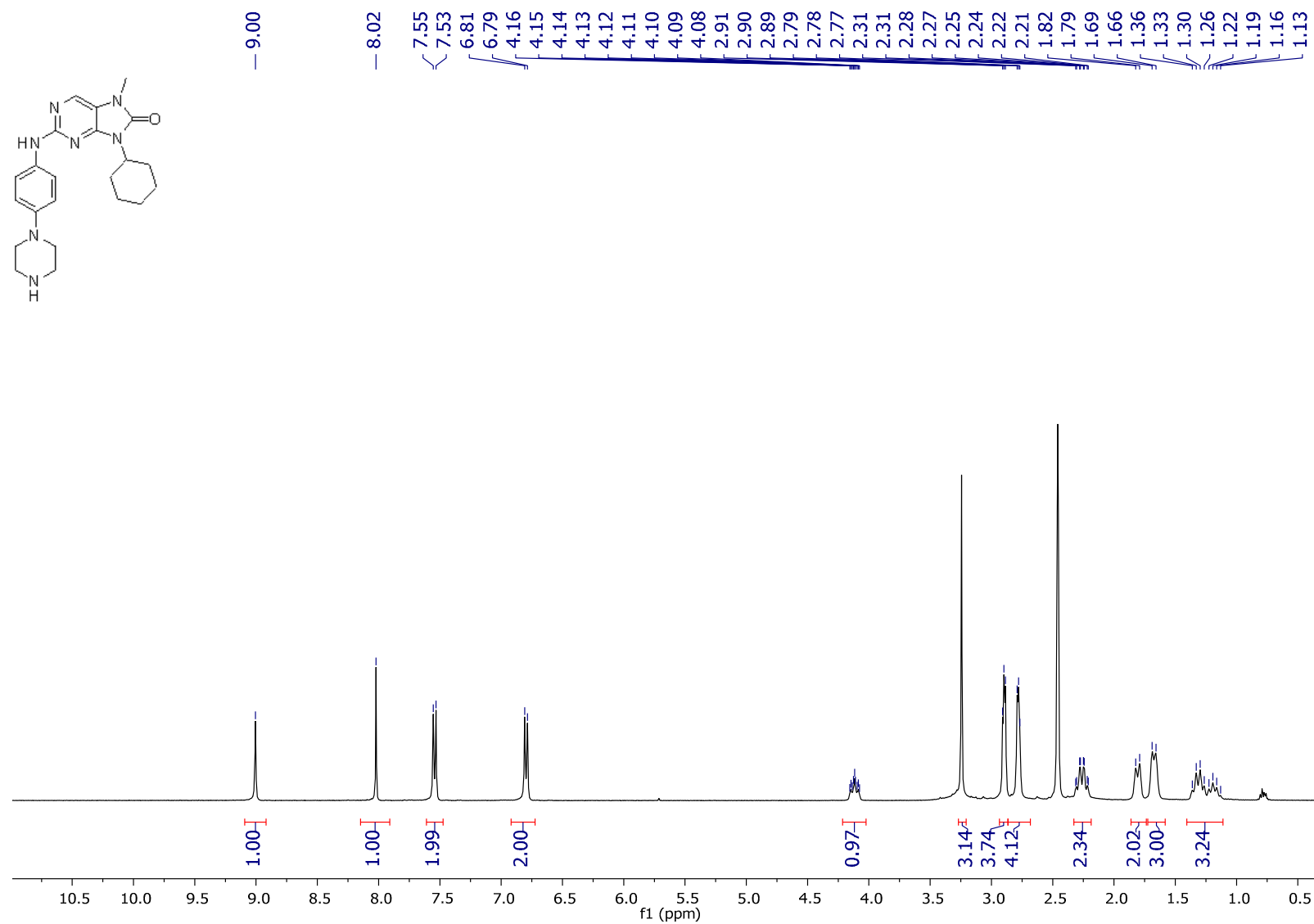
<sup>1</sup>H NMR spectrum of **14d**



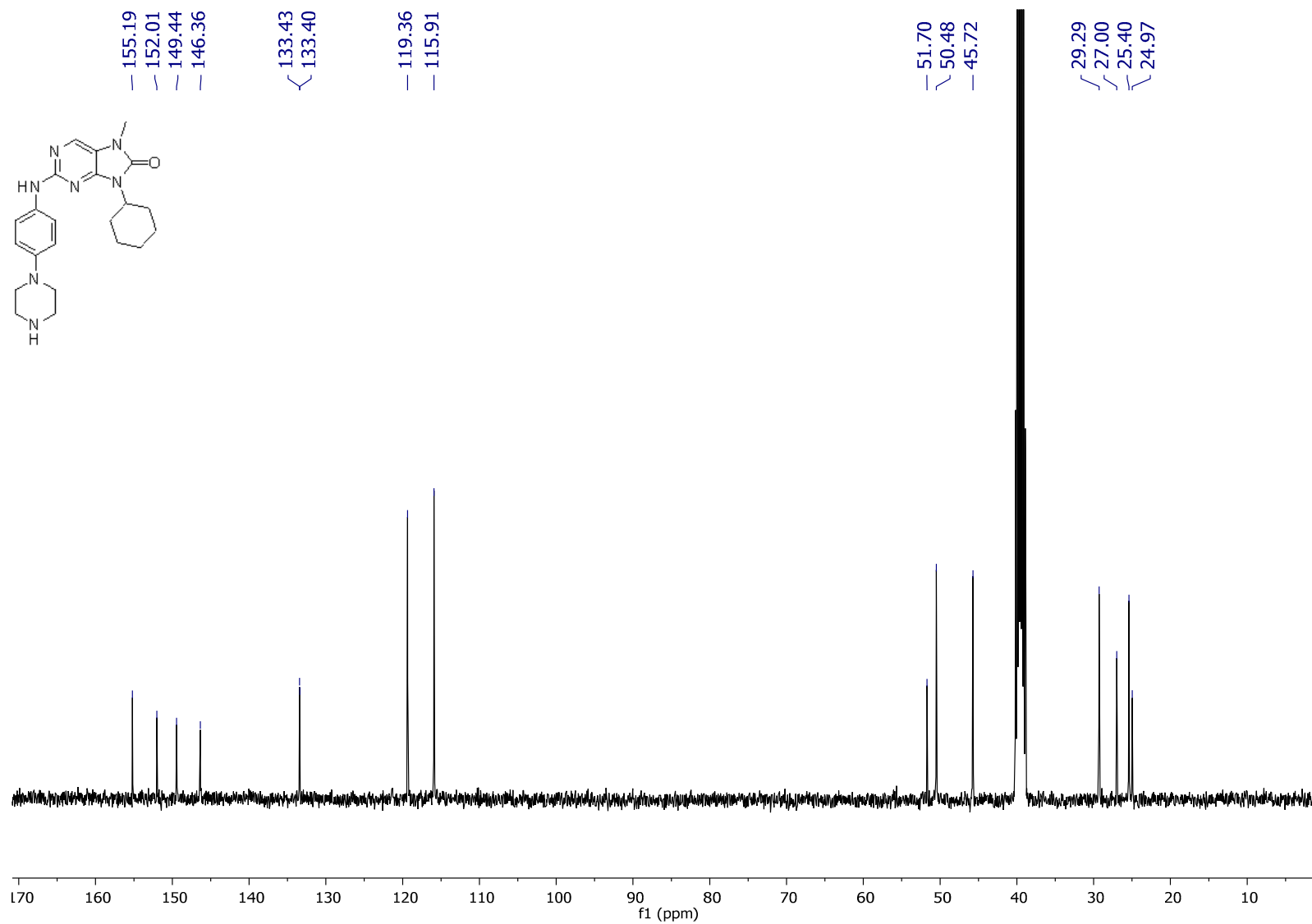
<sup>1</sup>H NMR spectrum of **14d**



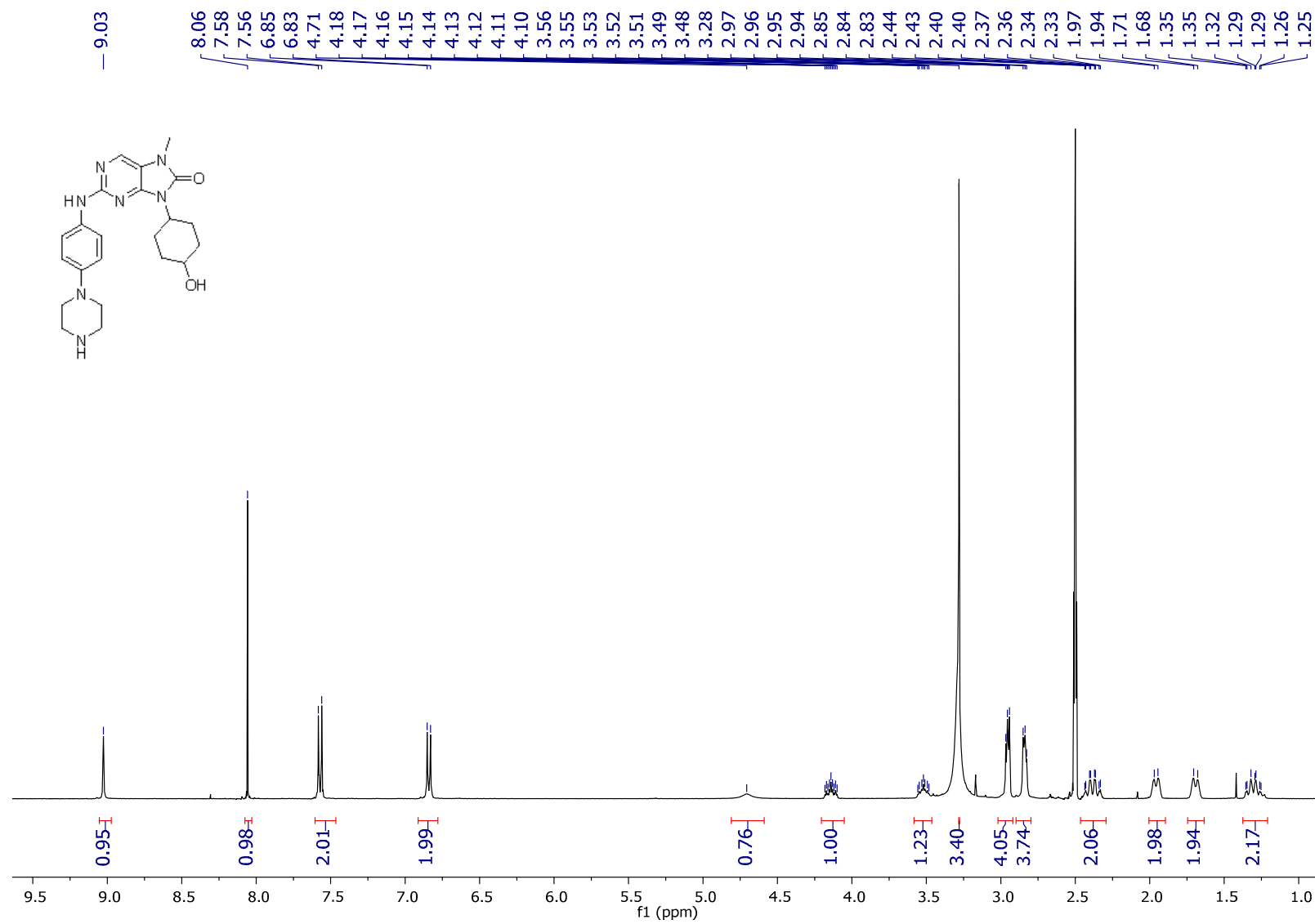
<sup>1</sup>H NMR spectrum of **14e**



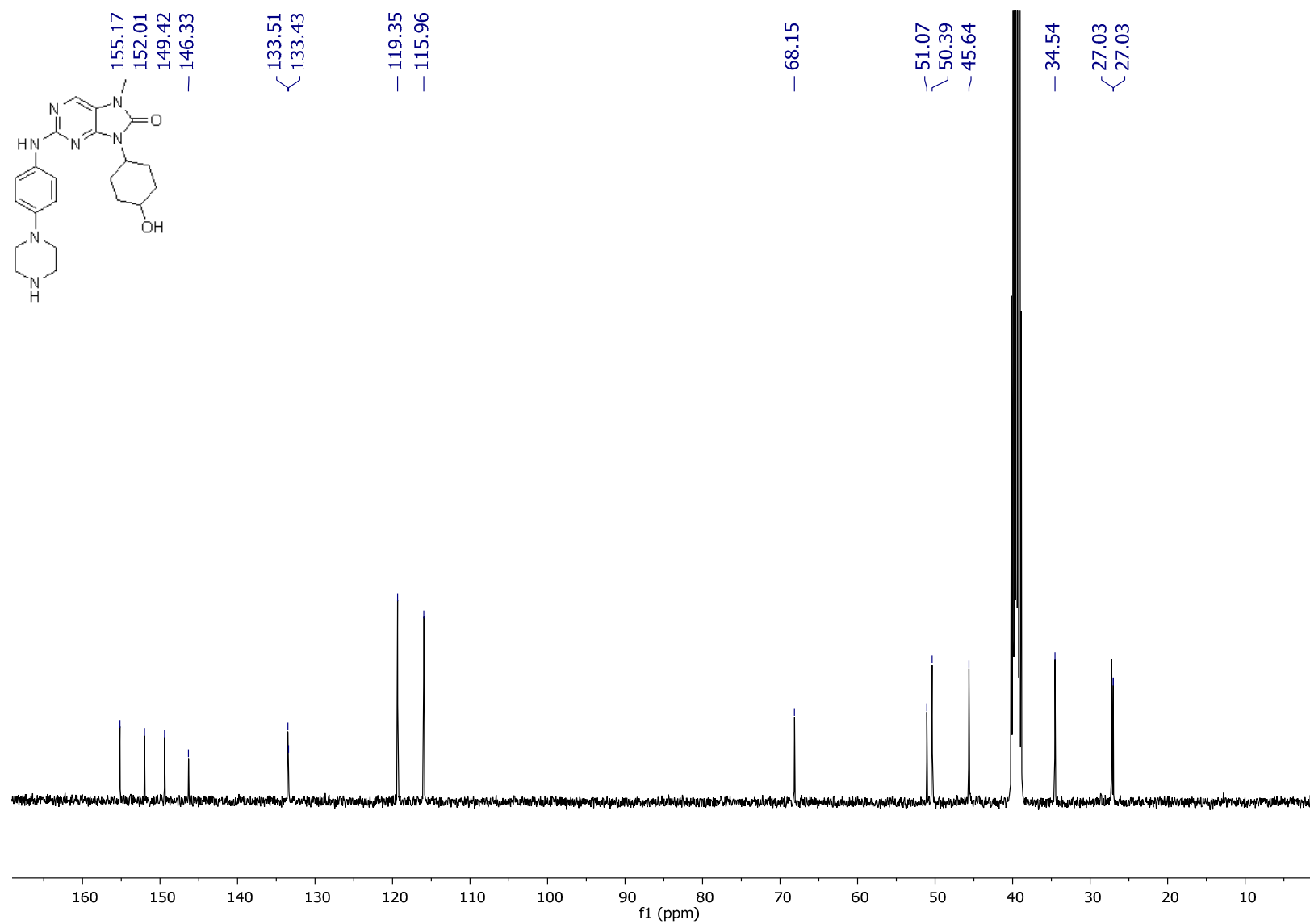
<sup>1</sup>H NMR spectrum of **14e**



<sup>1</sup>H NMR spectrum of **14f**

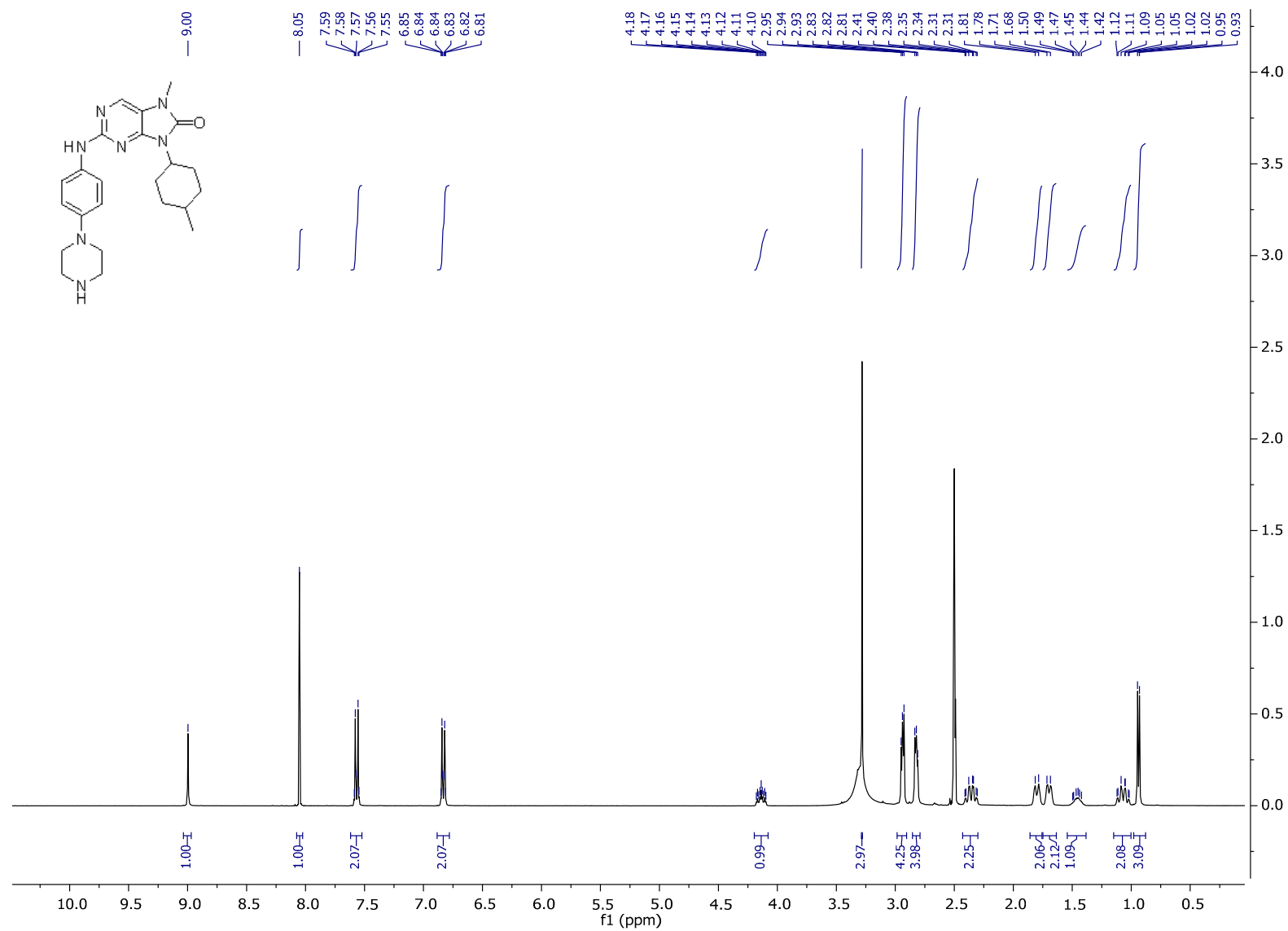


<sup>1</sup>H NMR spectrum of **14f**

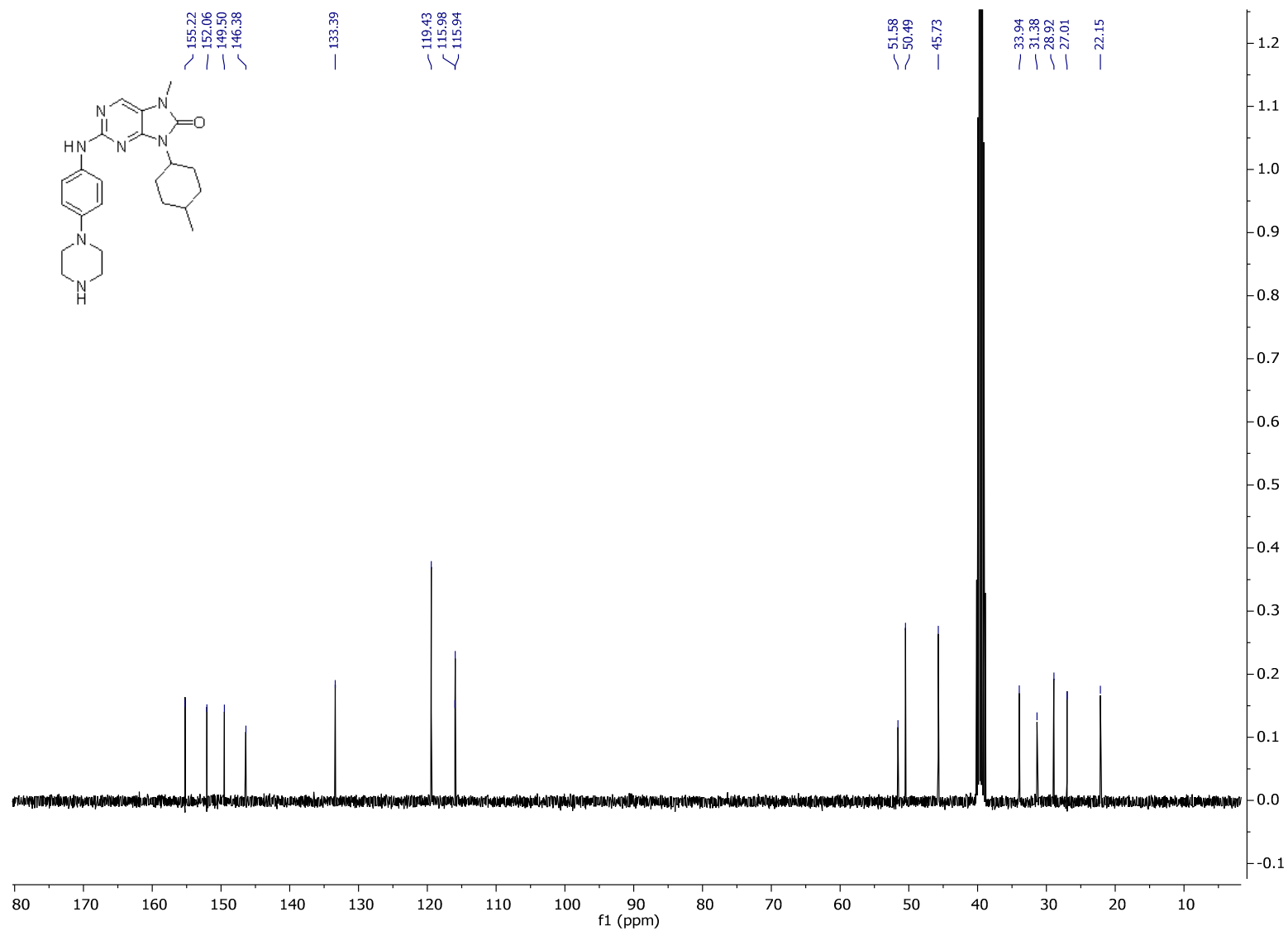




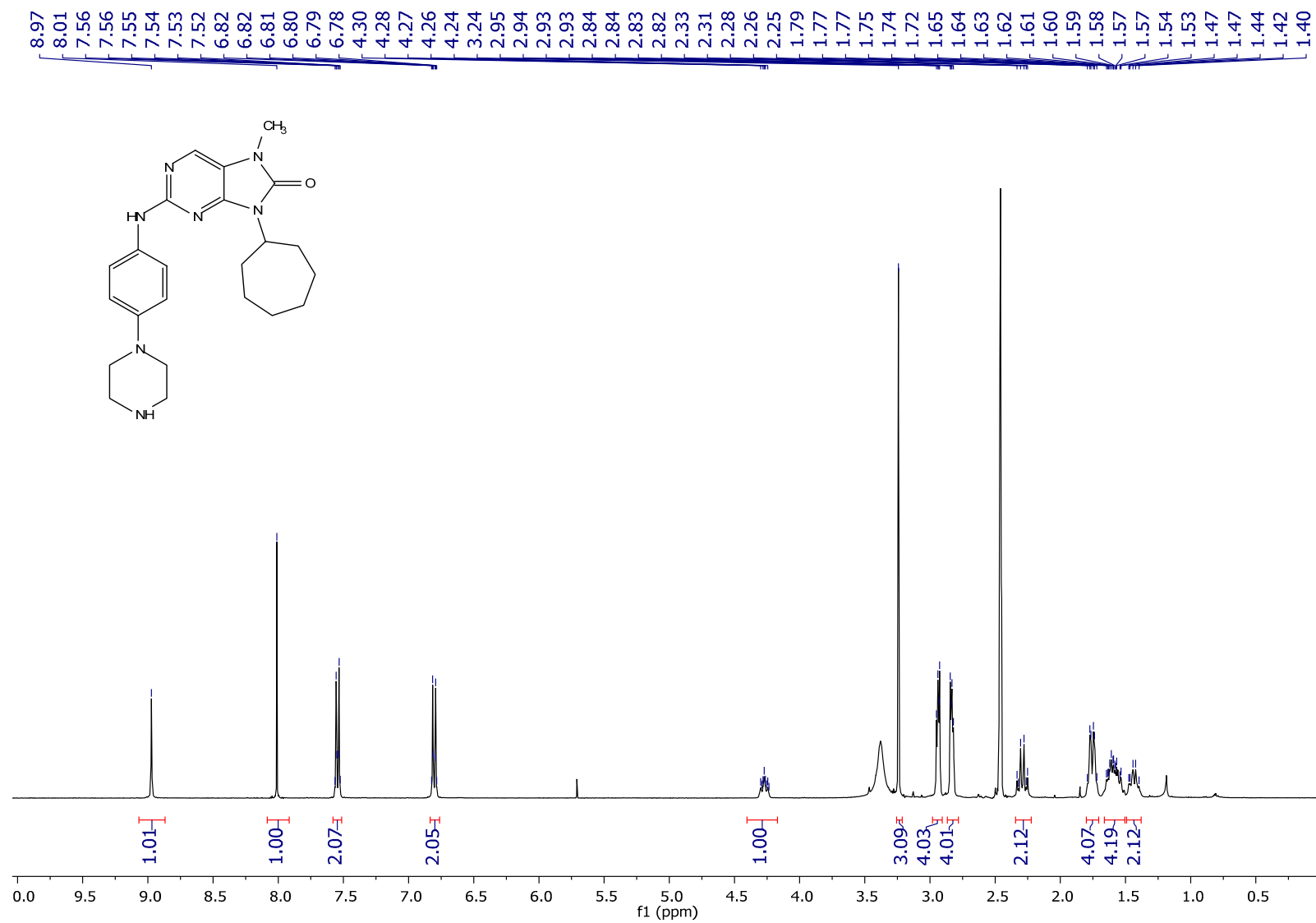
$^1\text{H}$  NMR spectrum of **14g**



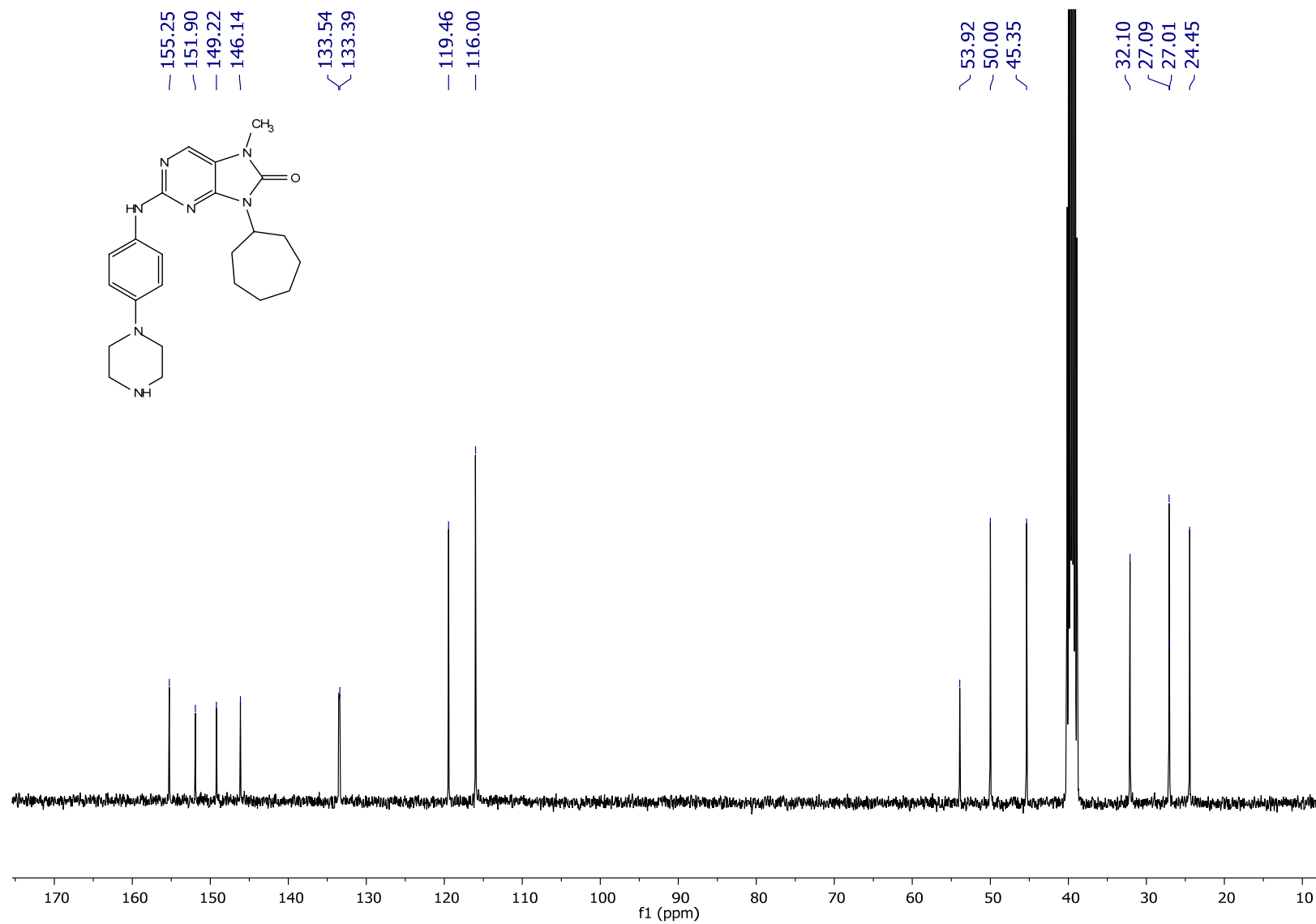
$^1\text{H}$  NMR spectrum of **14g**



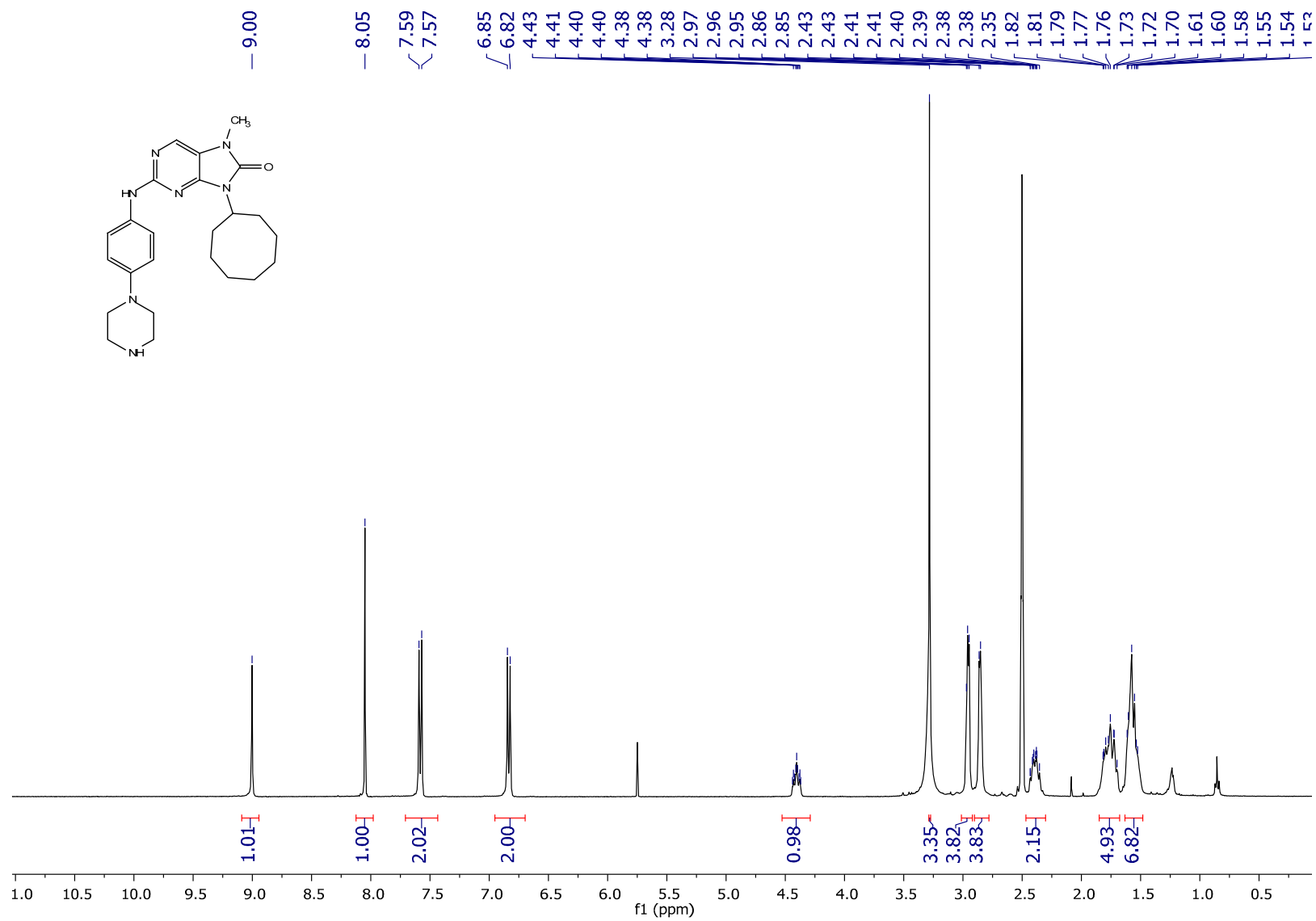
<sup>1</sup>H NMR spectrum of **14h**



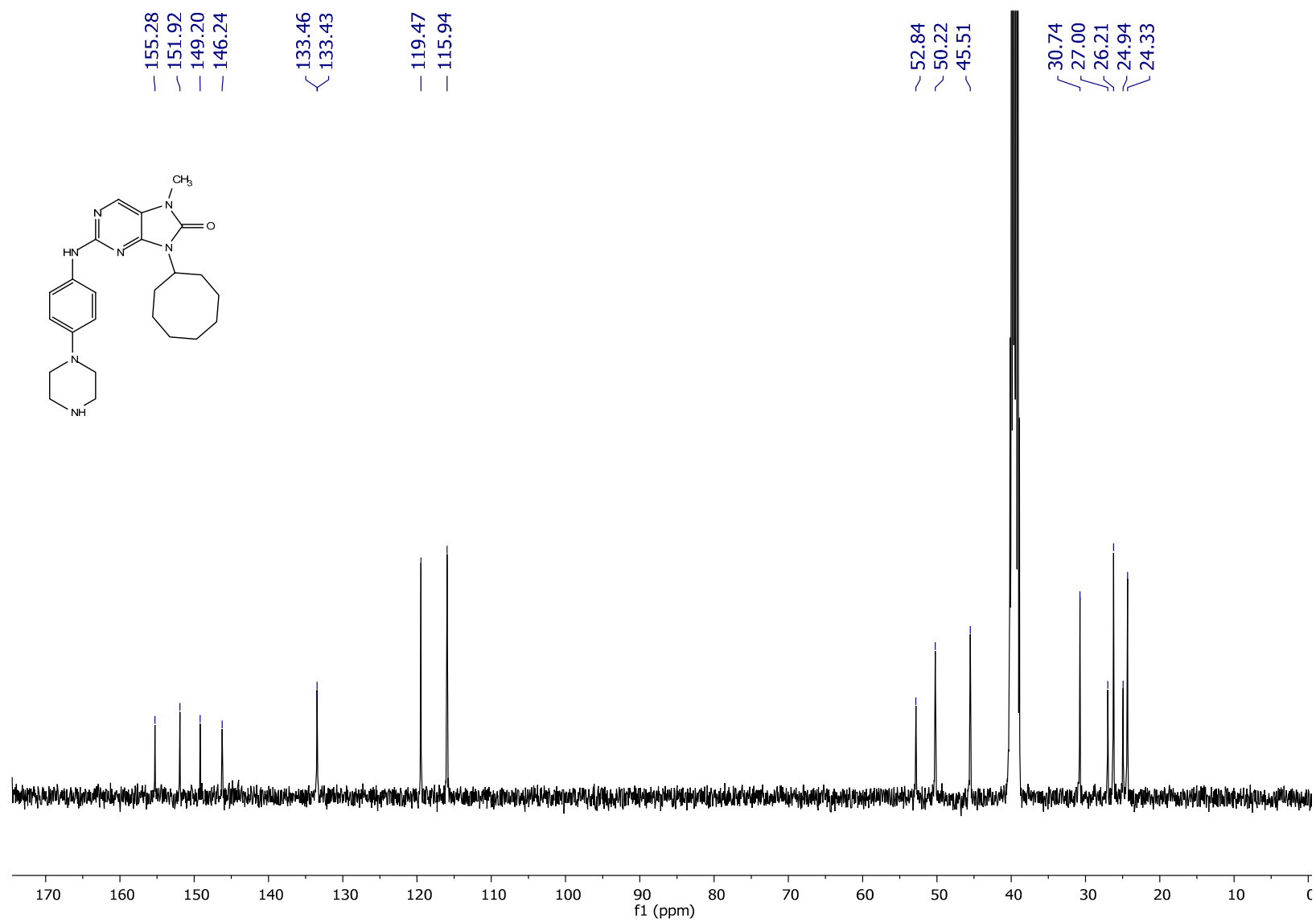
<sup>1</sup>H NMR spectrum of **14h**



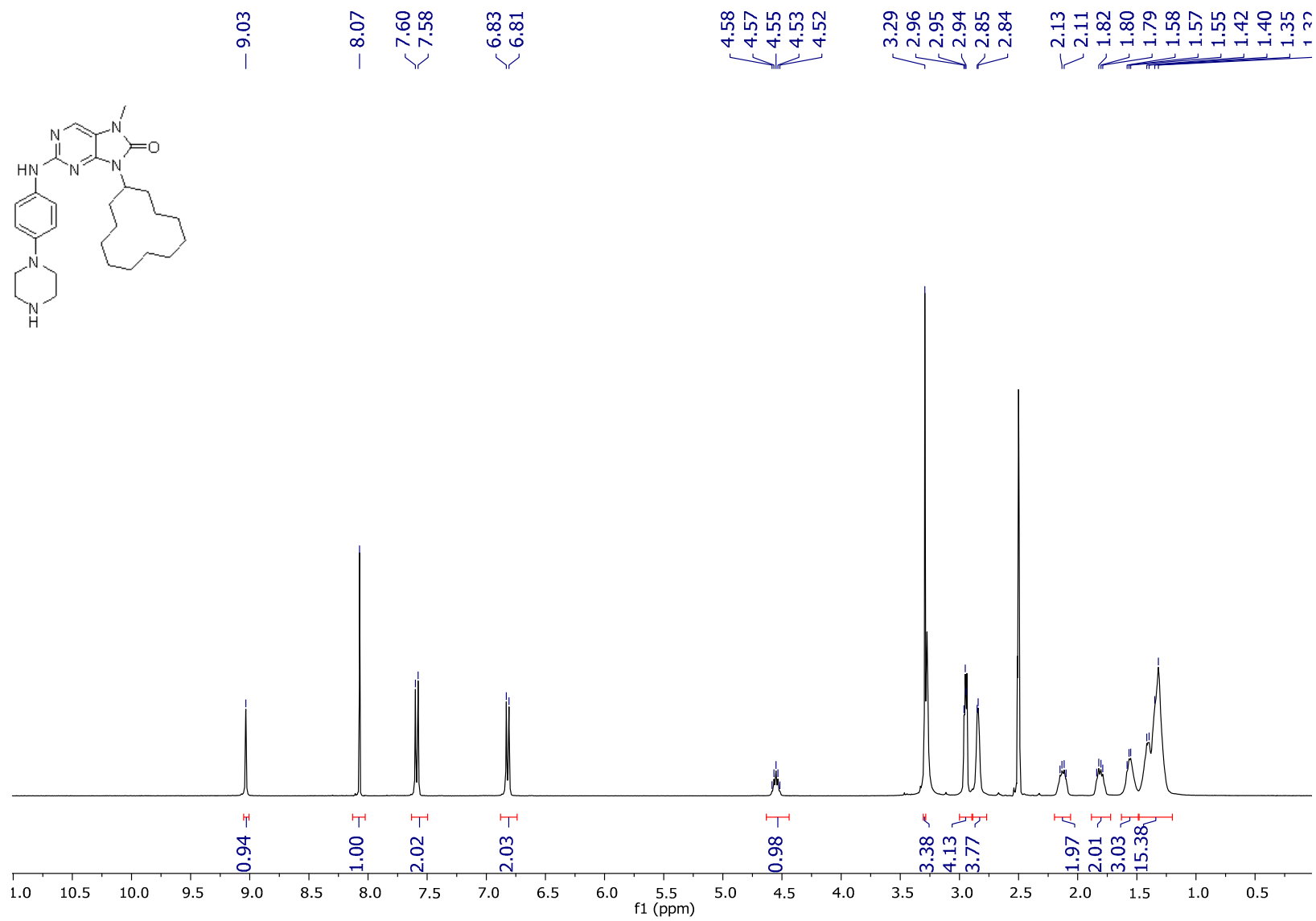
$^1\text{H}$  NMR spectrum of **14i**



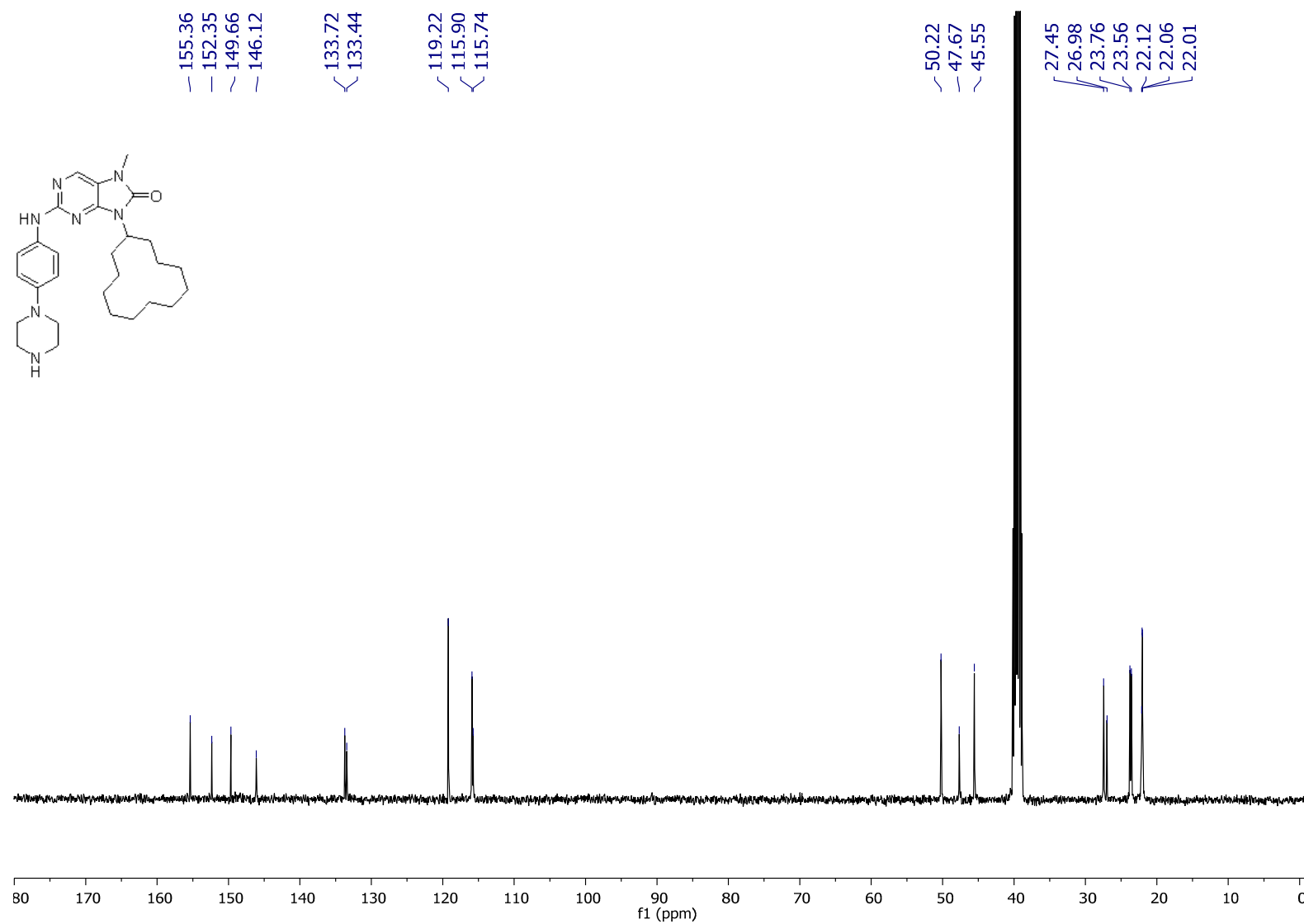
<sup>1</sup>H NMR spectrum of **14i**



<sup>1</sup>H NMR spectrum of **14j**

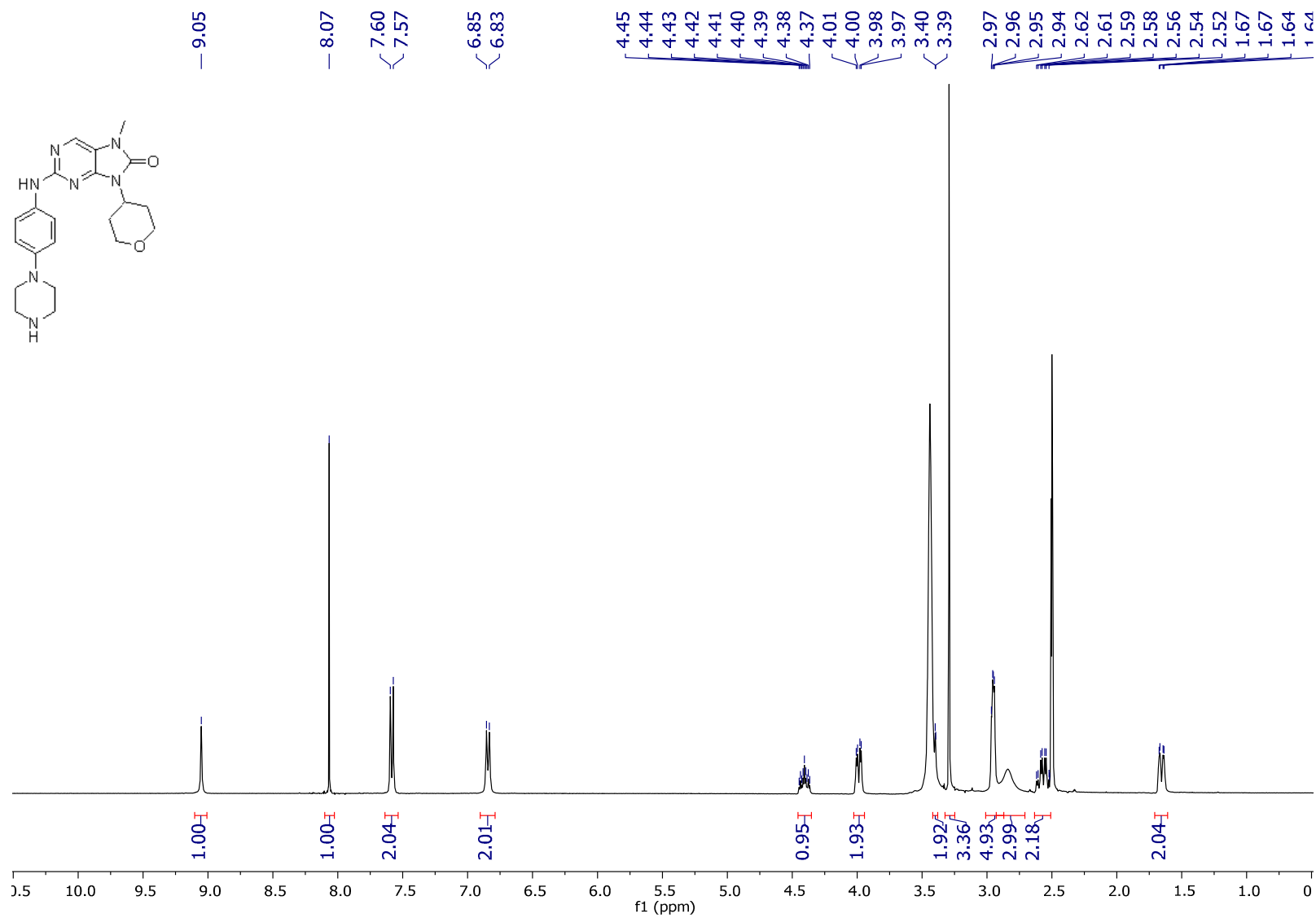


<sup>1</sup>H NMR spectrum of **14j**

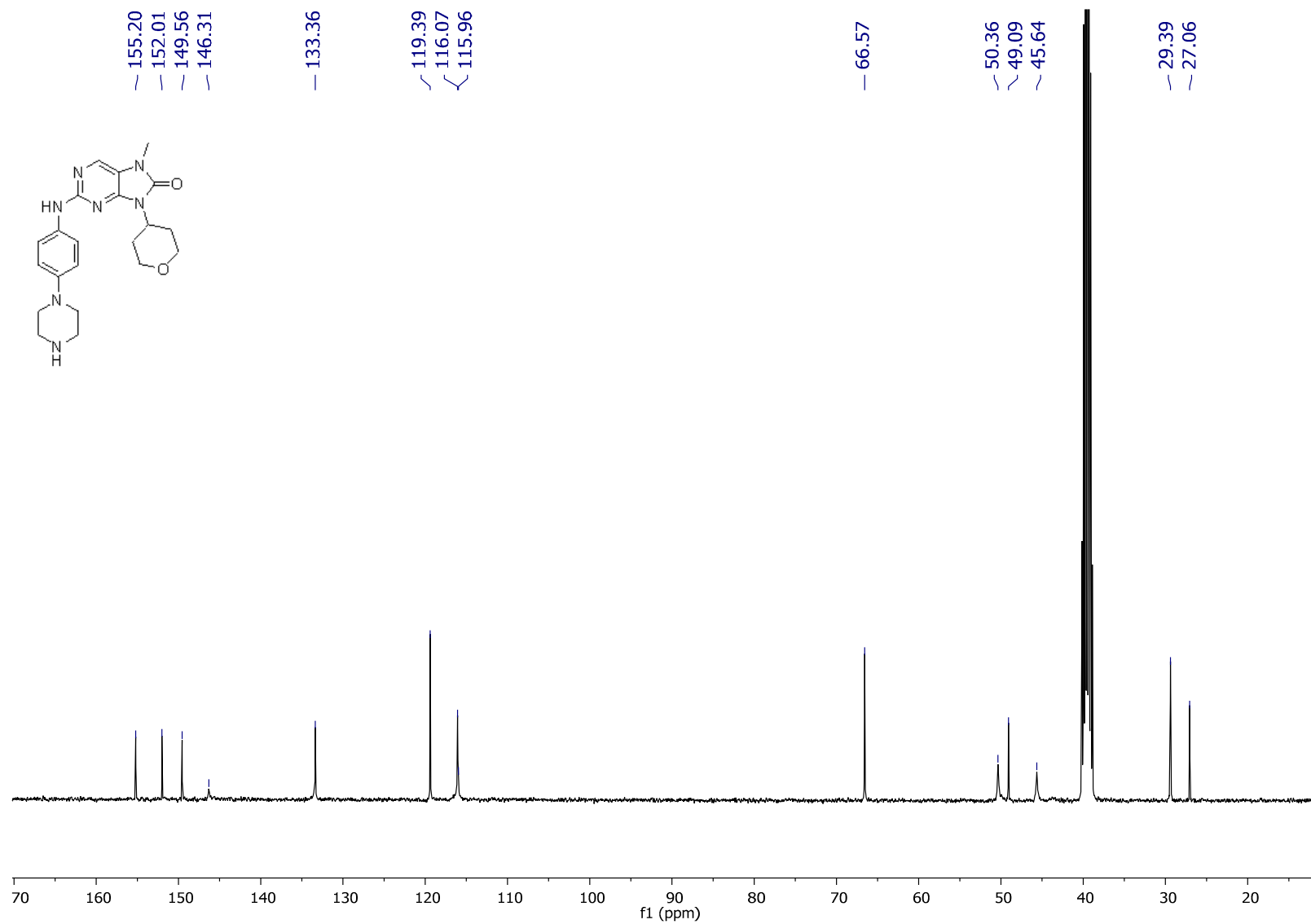




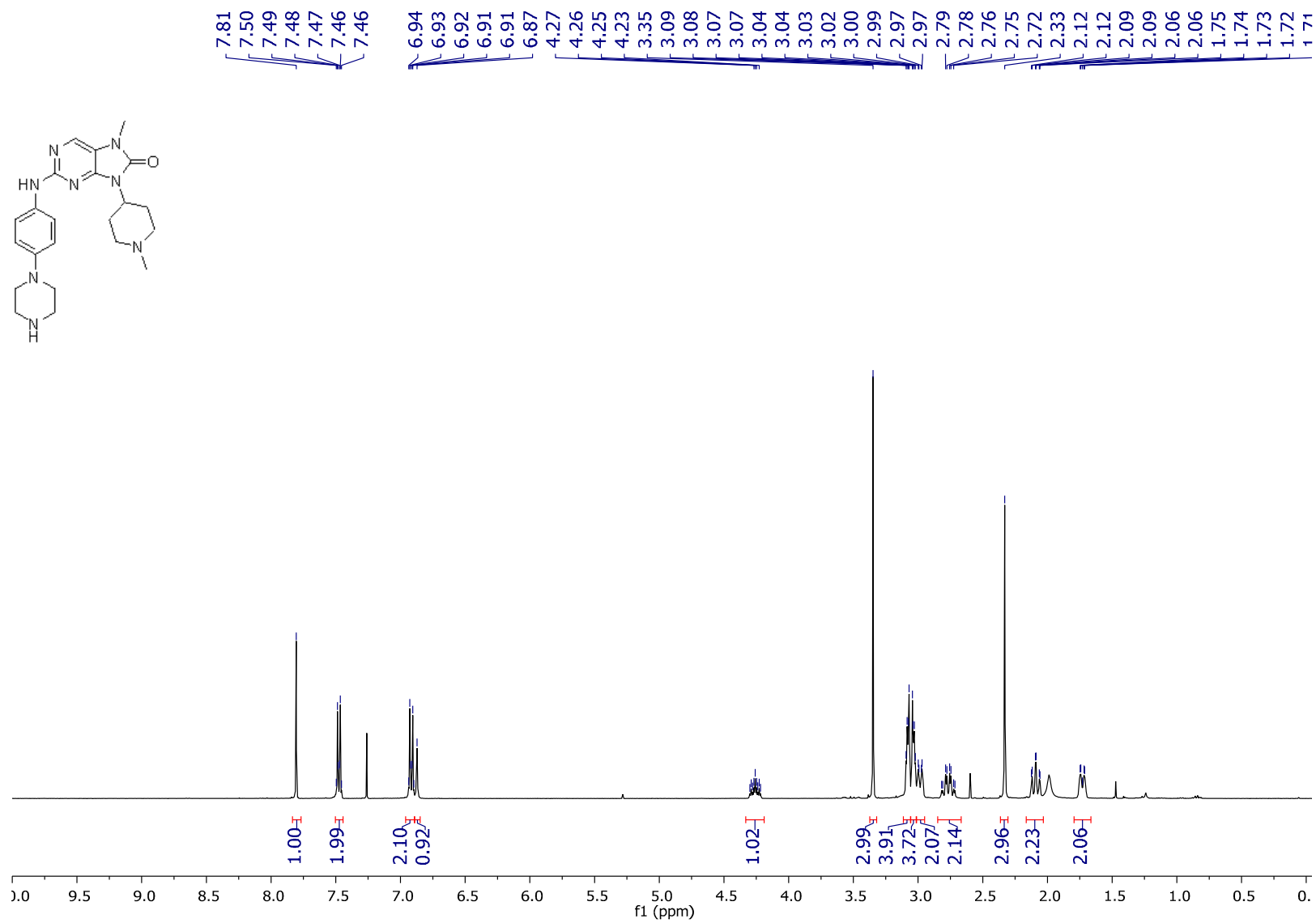
$^1\text{H}$  NMR spectrum of **14k**



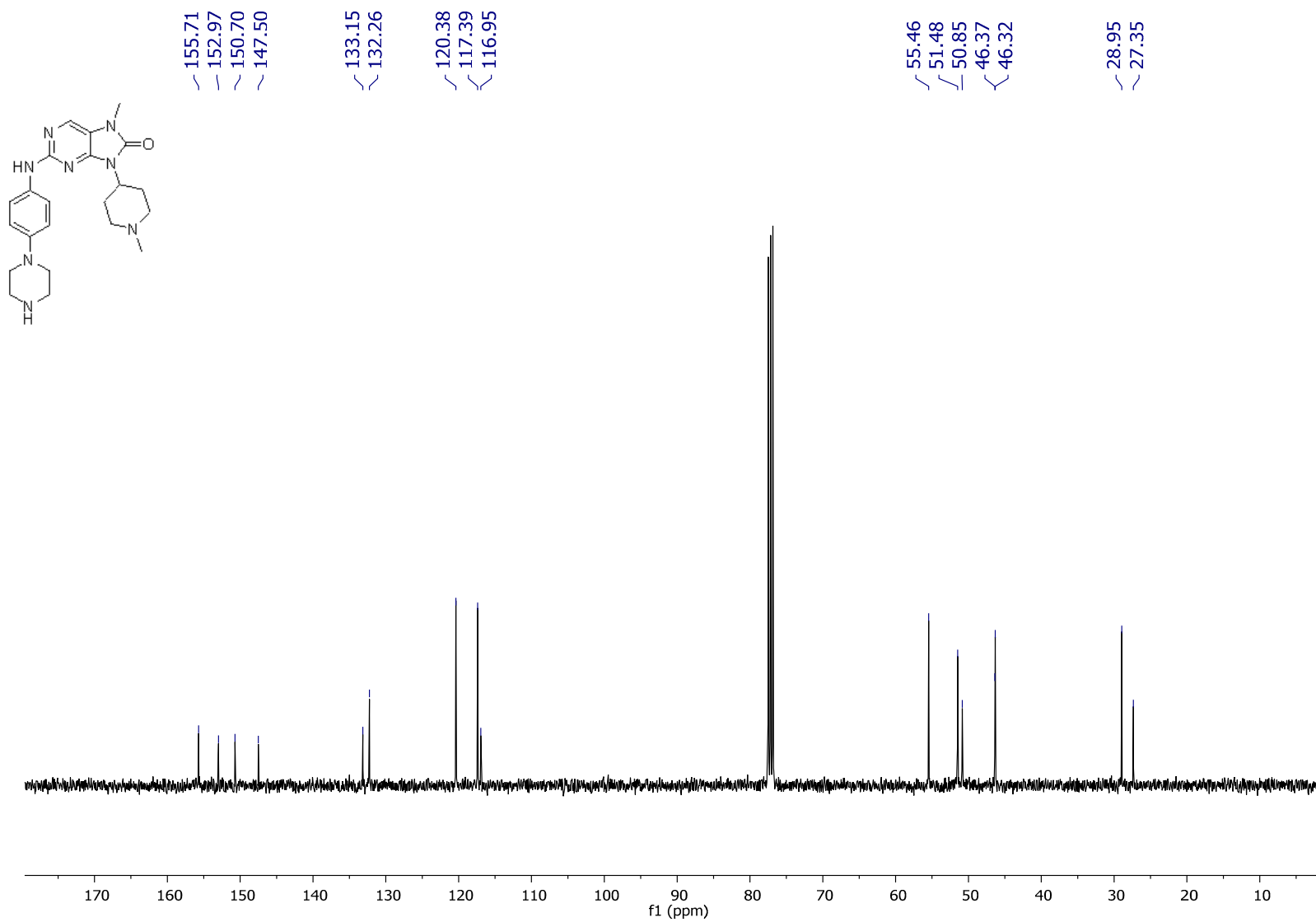
<sup>1</sup>H NMR spectrum of **14k**



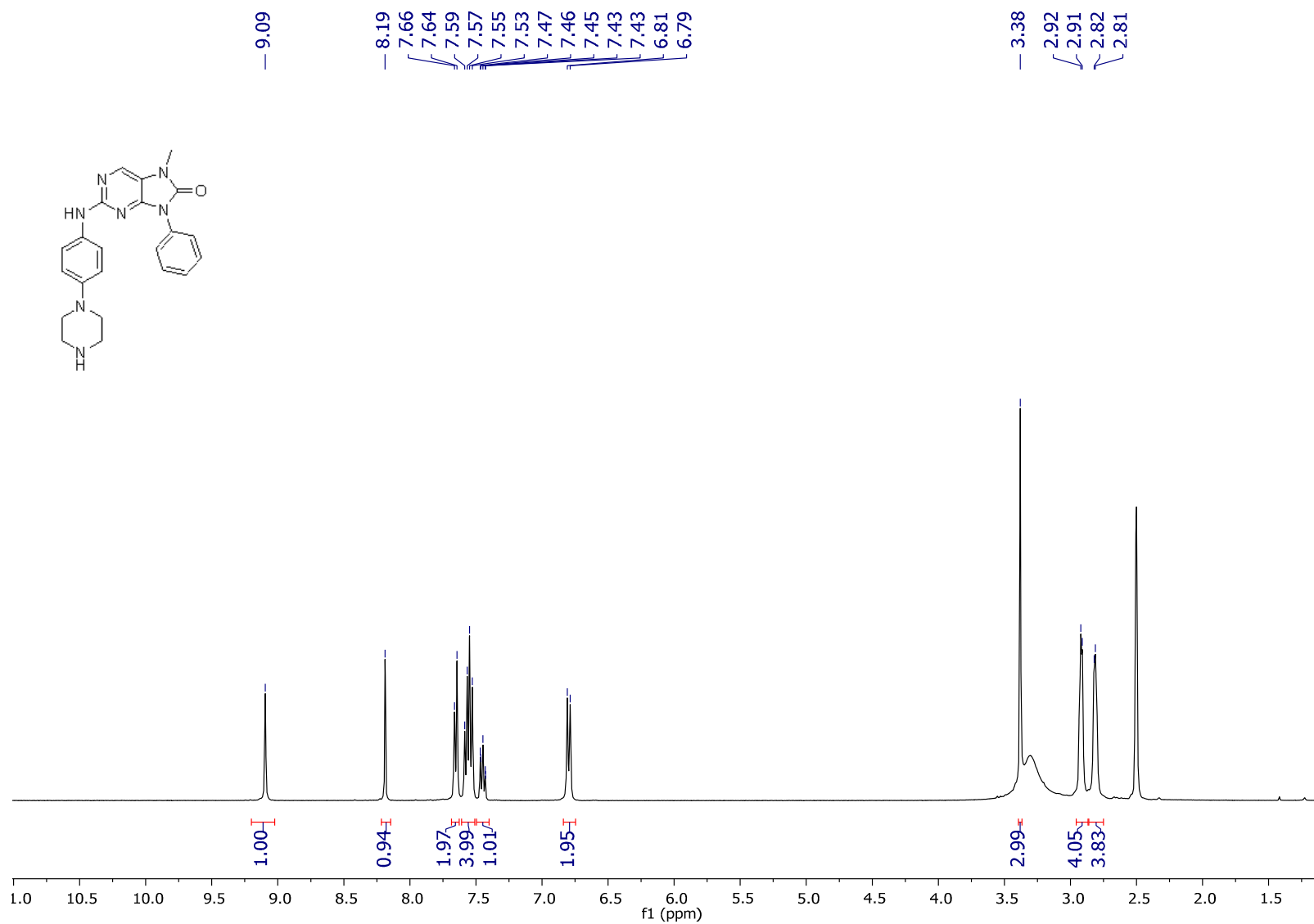
$^1\text{H}$  NMR spectrum of **14l**



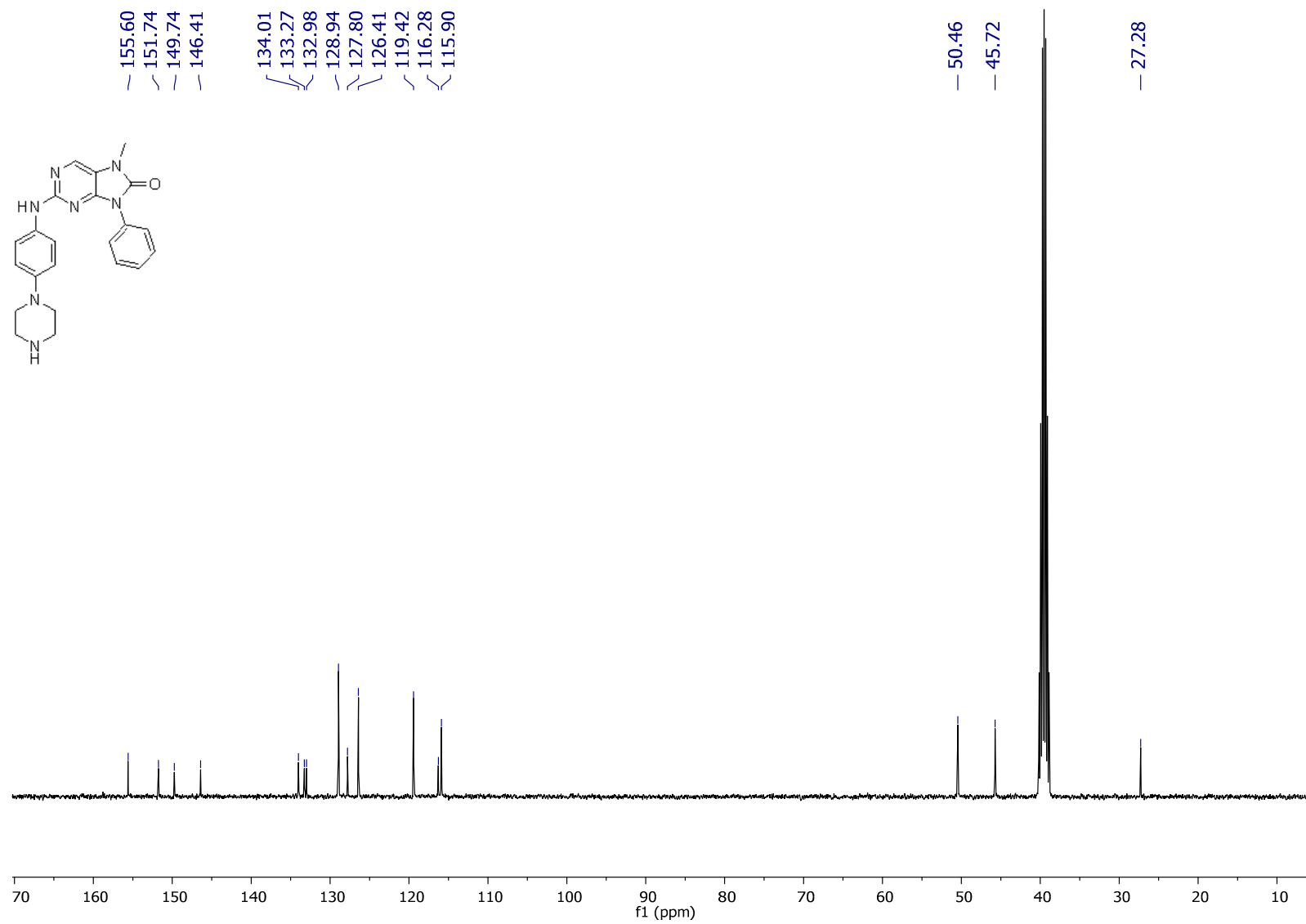
<sup>1</sup>H NMR spectrum of **14l**



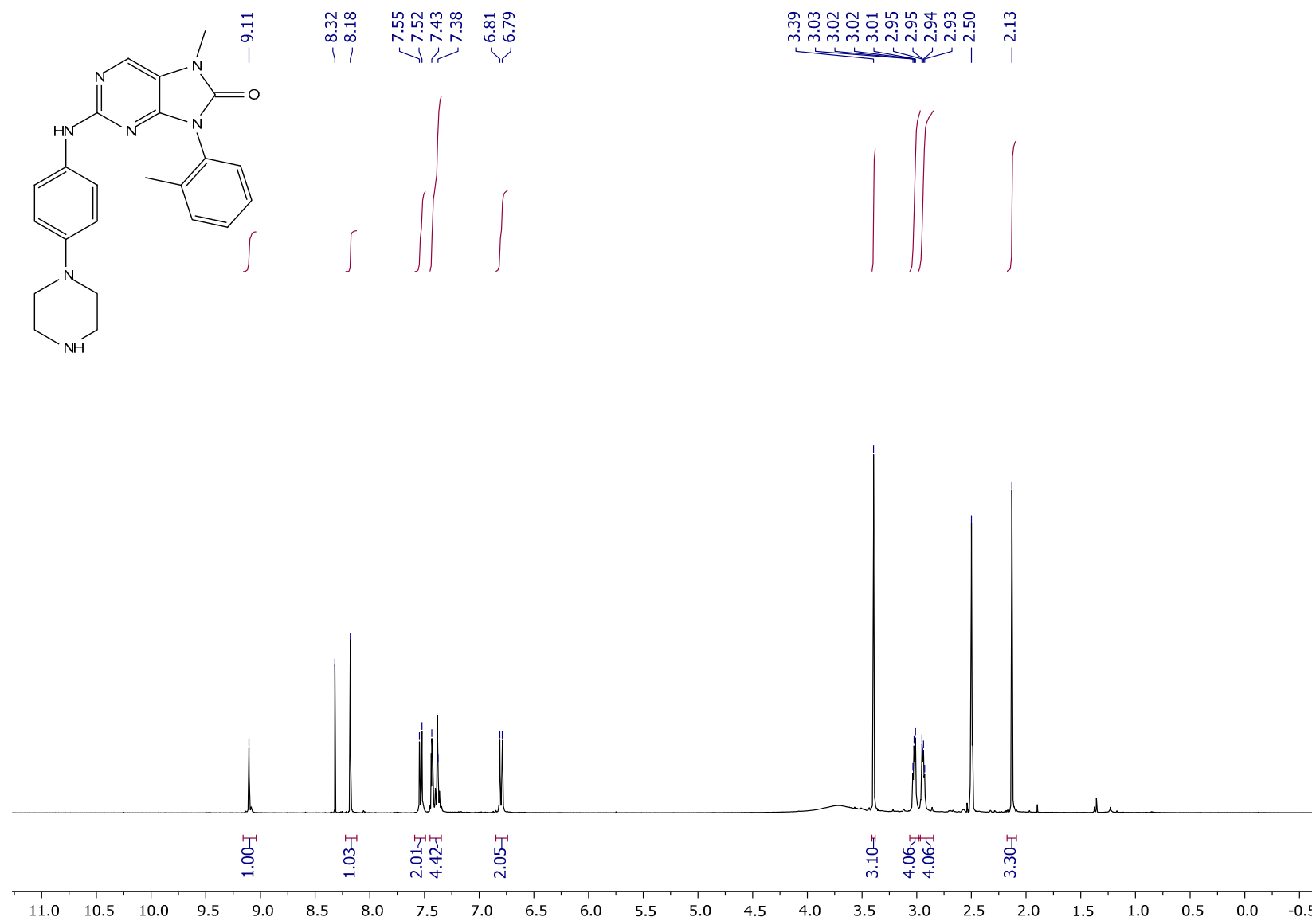
<sup>1</sup>H NMR spectrum of **14m**



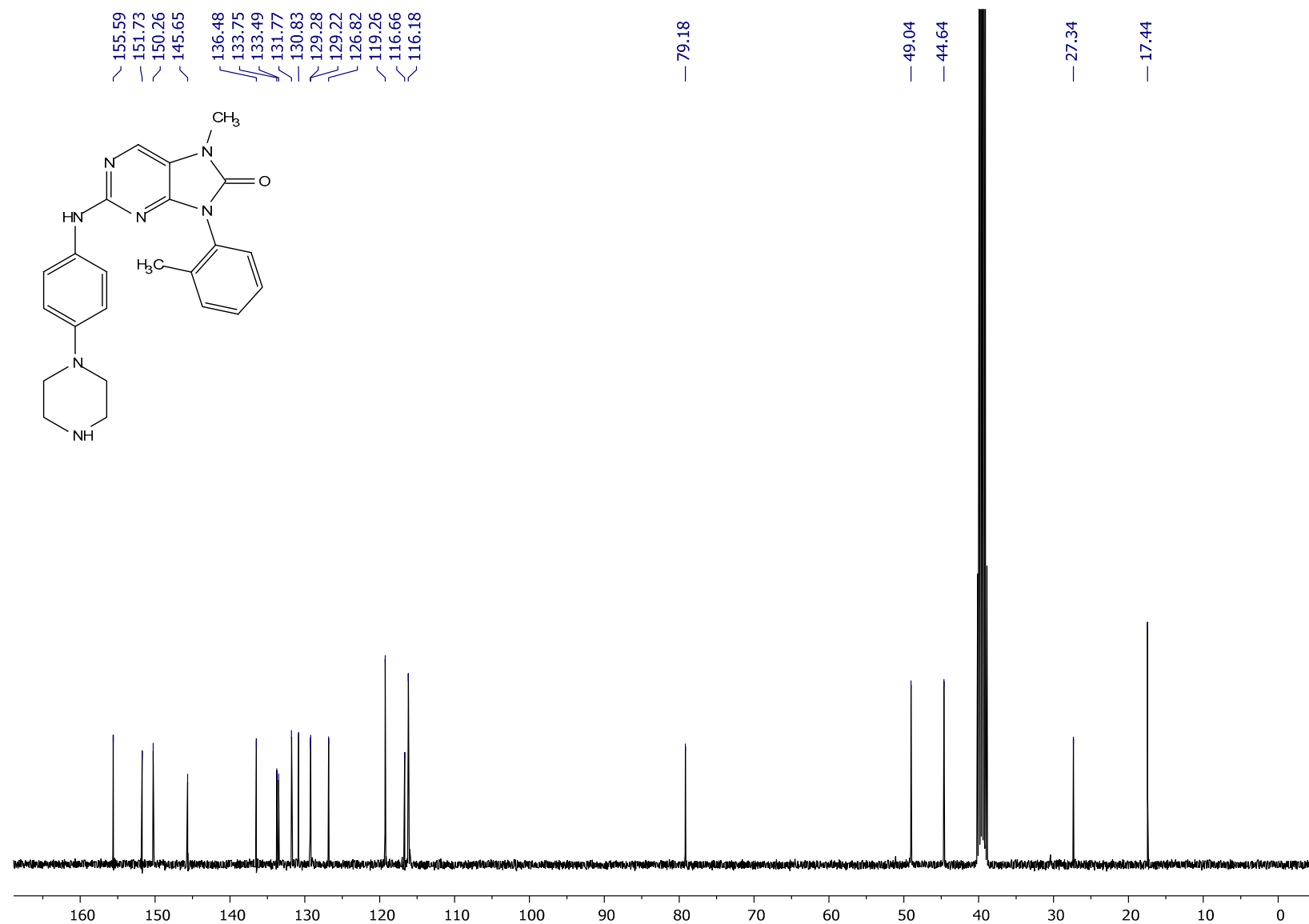
<sup>1</sup>H NMR spectrum of **14m**



$^1\text{H}$  NMR spectrum of **14n**

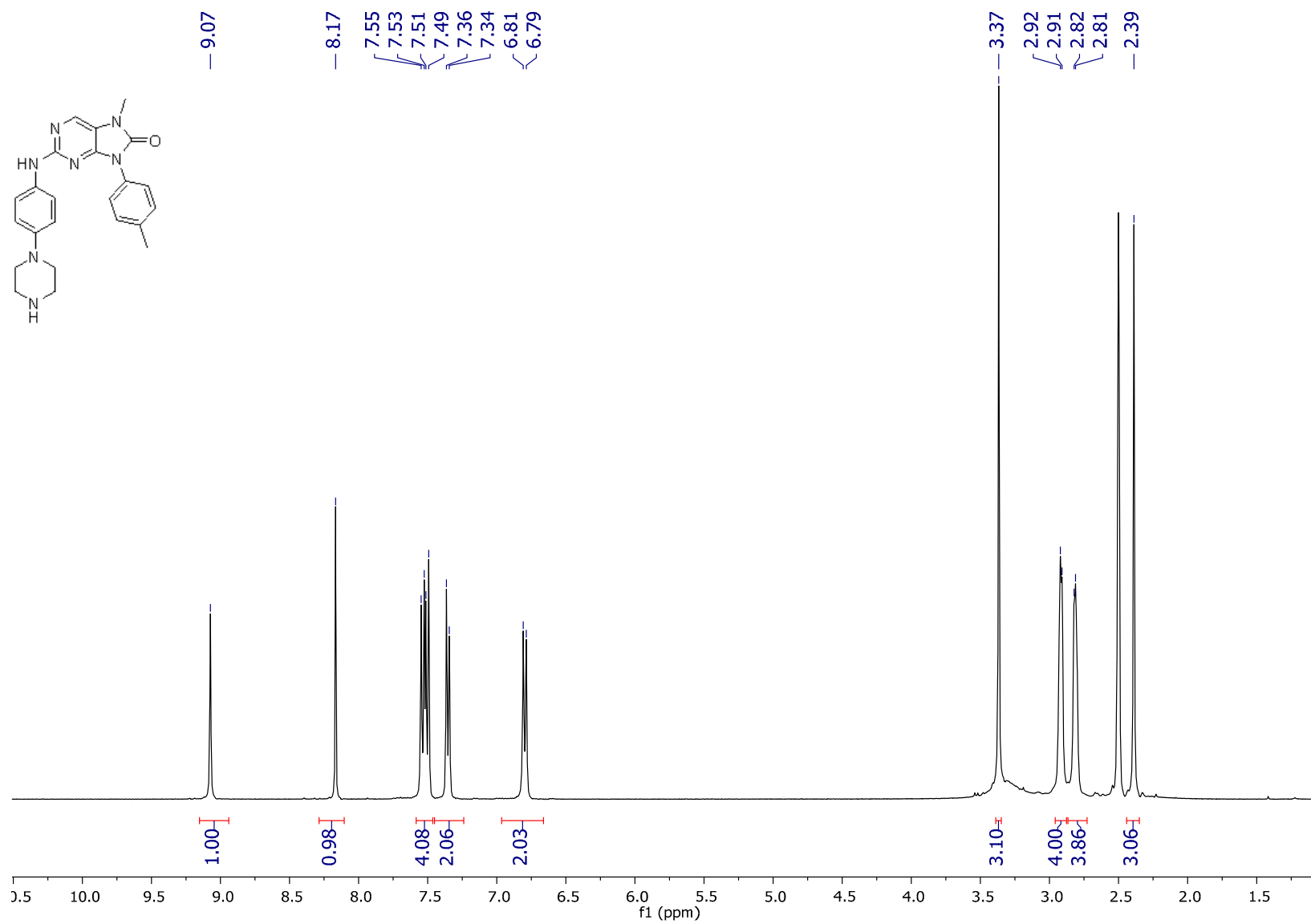


<sup>13</sup>C NMR spectrum of **14n**

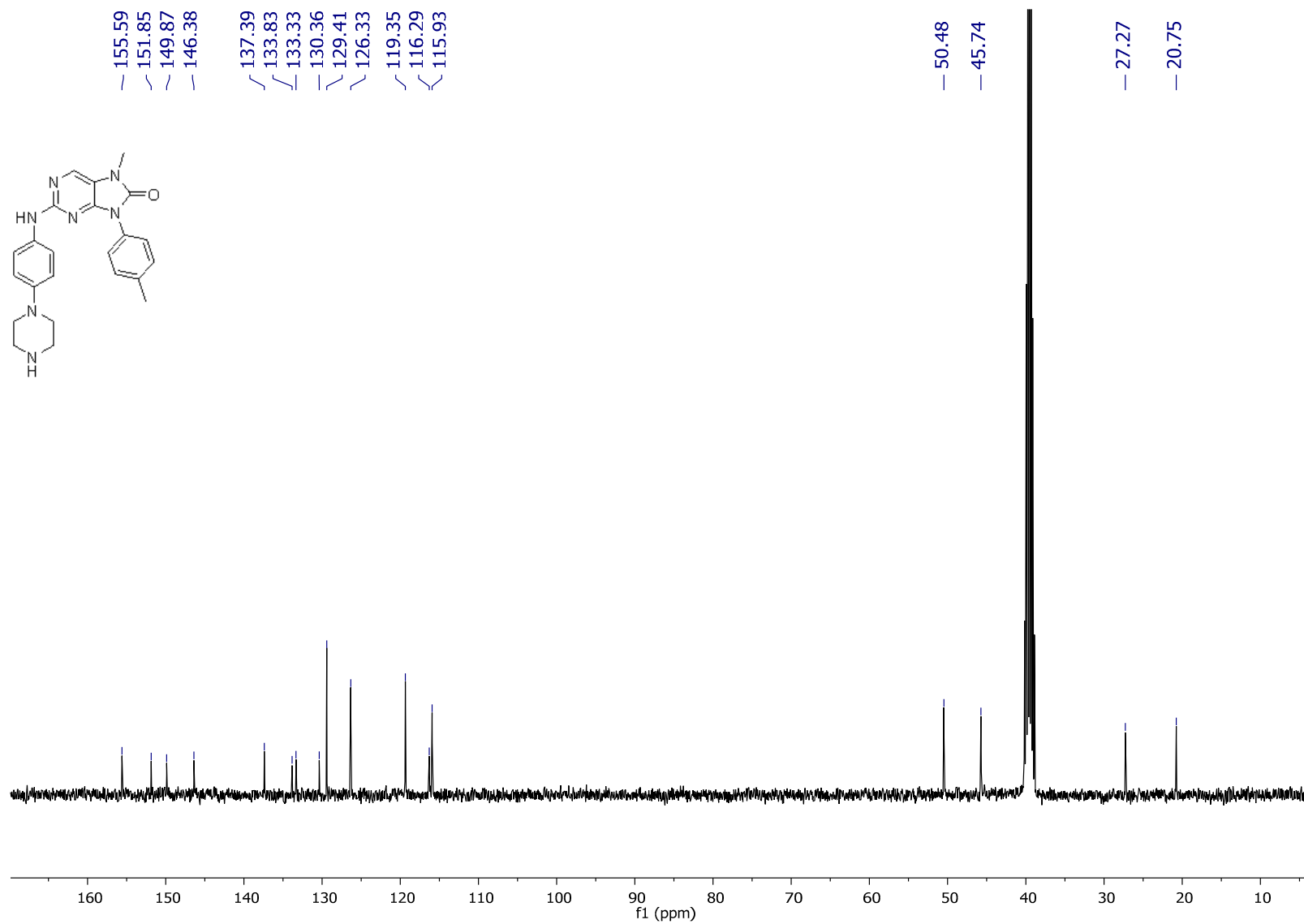




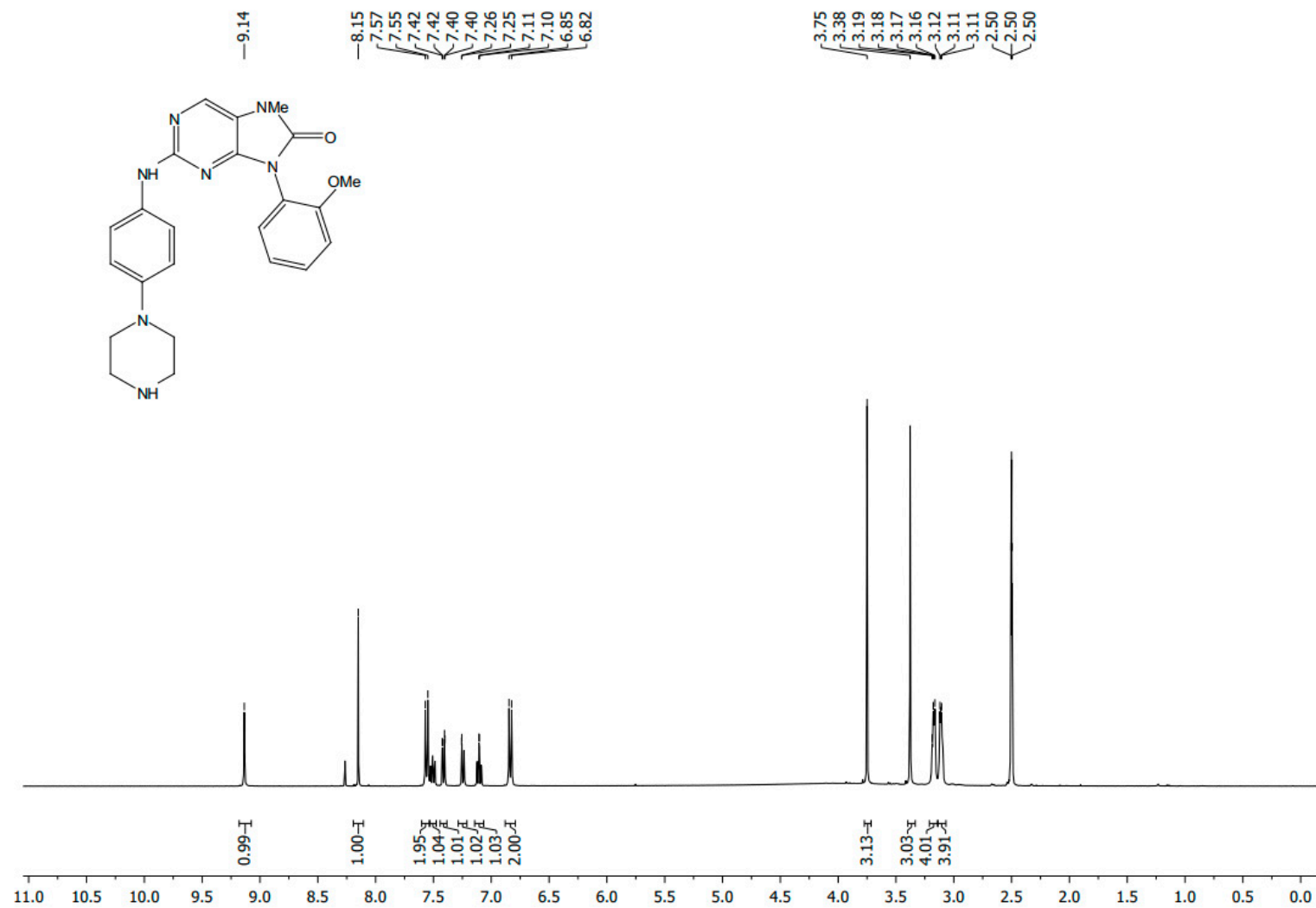
<sup>1</sup>H NMR spectrum of **14o**



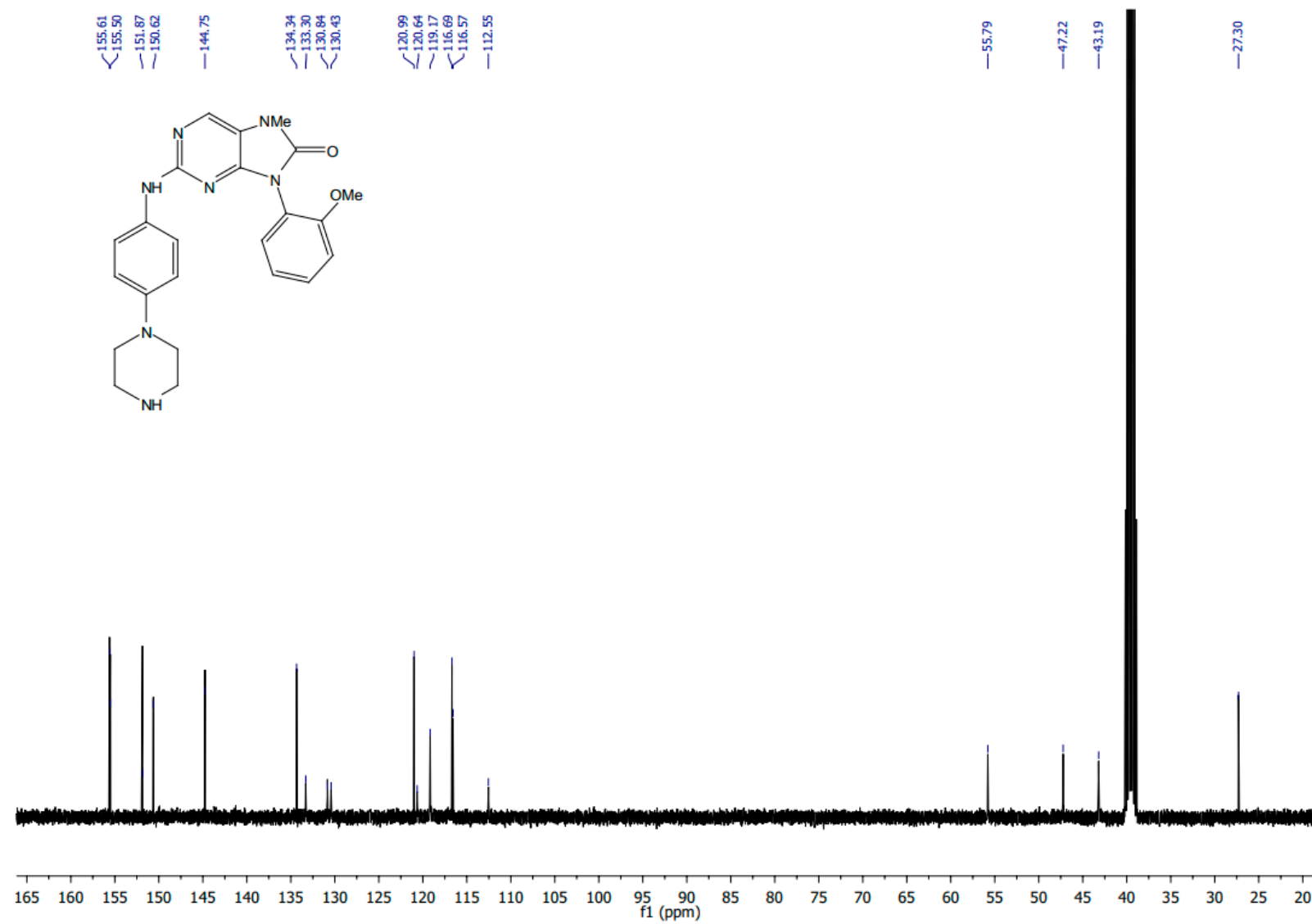
<sup>13</sup>C NMR spectrum of **14o**



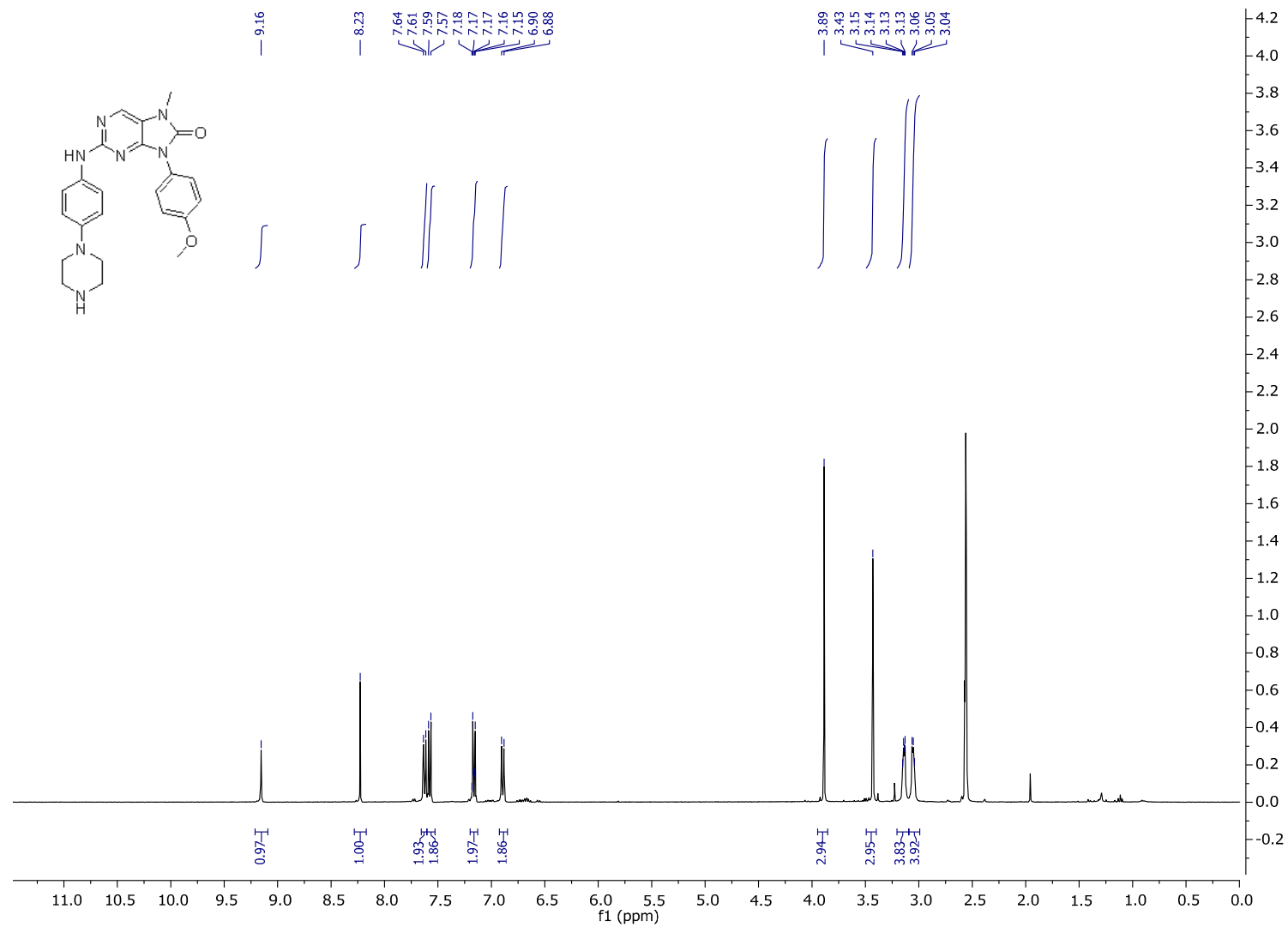
$^1\text{H}$  NMR spectrum of **14p**



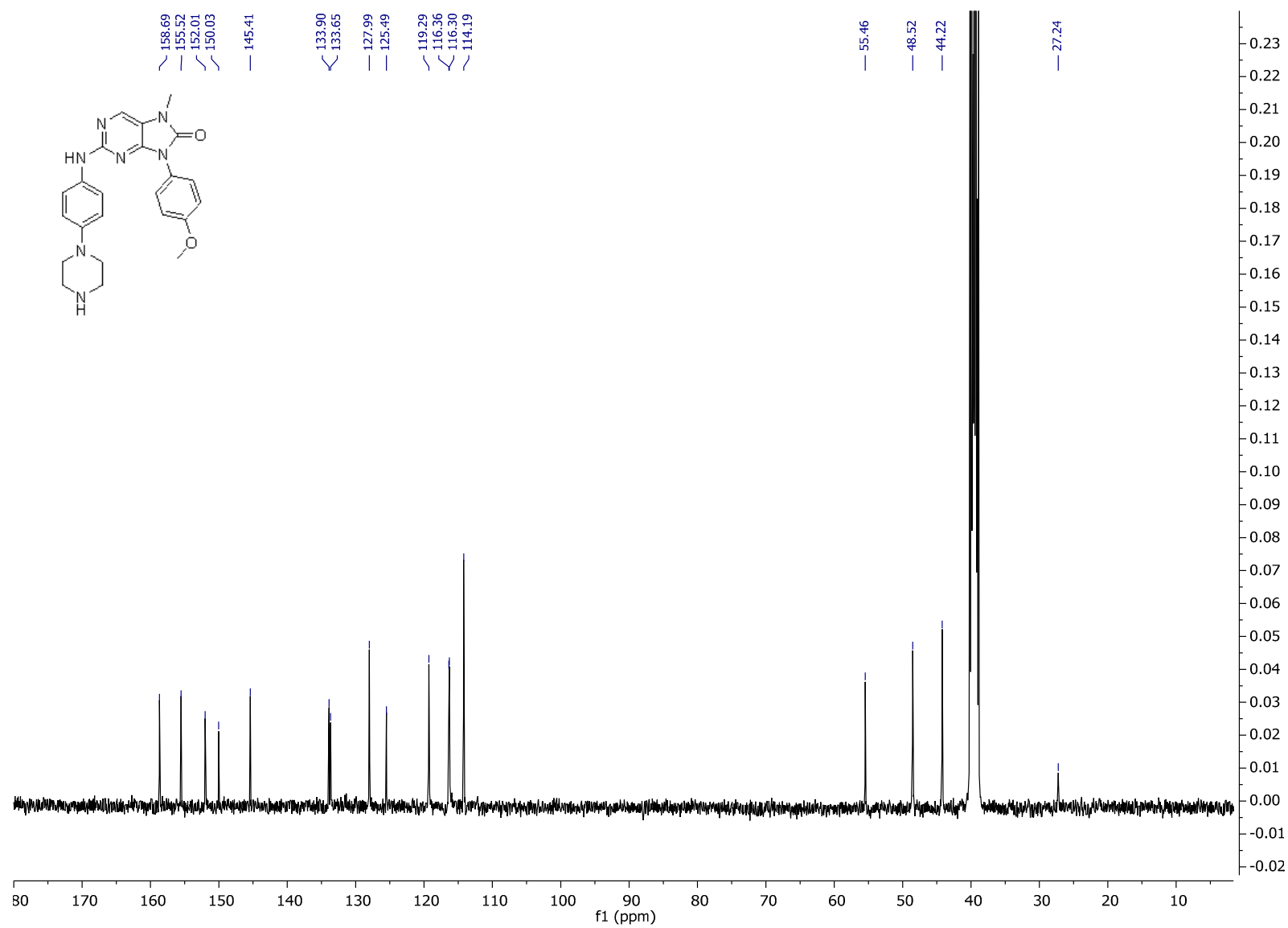
$^{13}\text{C}$  NMR spectrum of **14p**



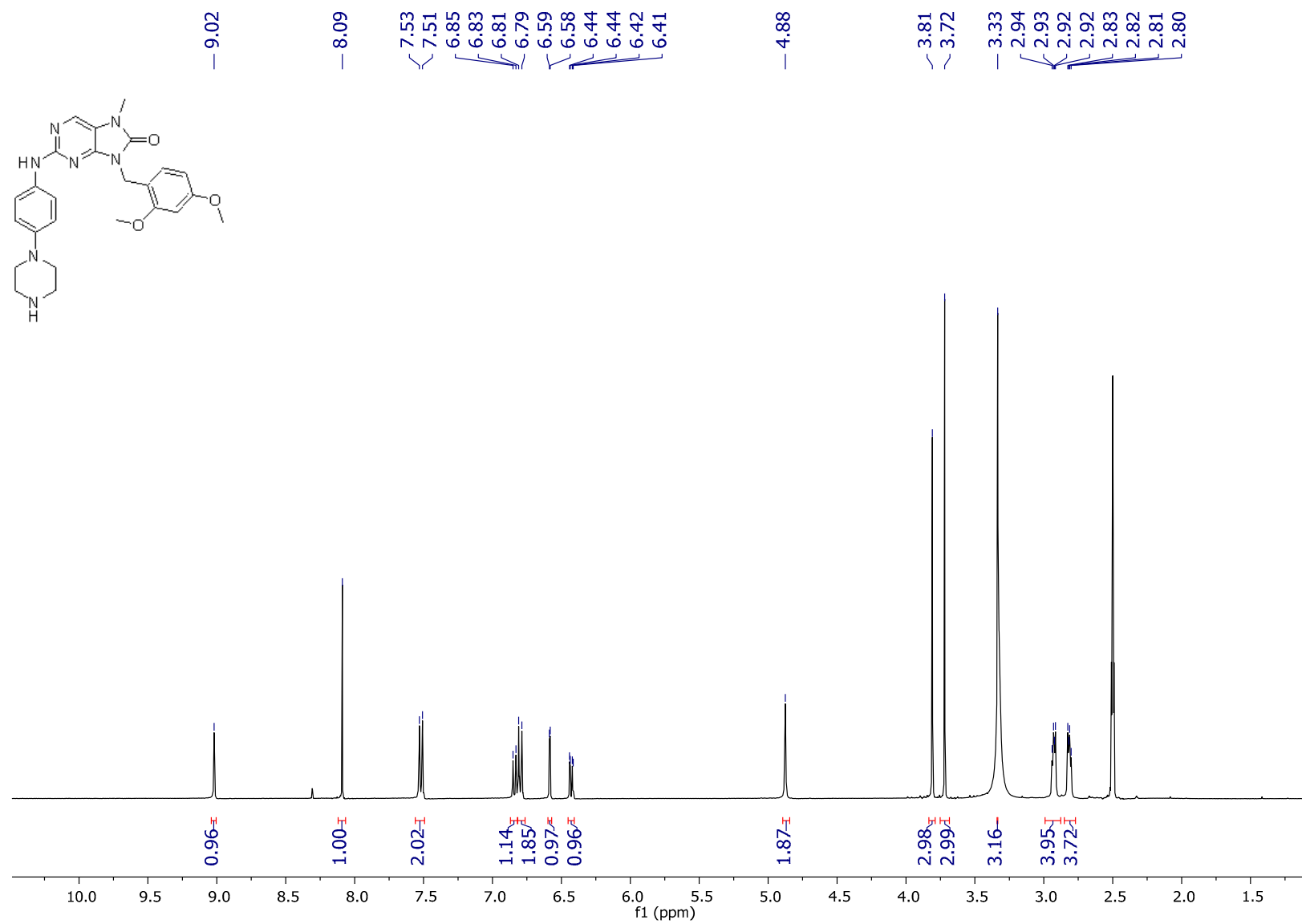
<sup>1</sup>H NMR spectrum of **14q**



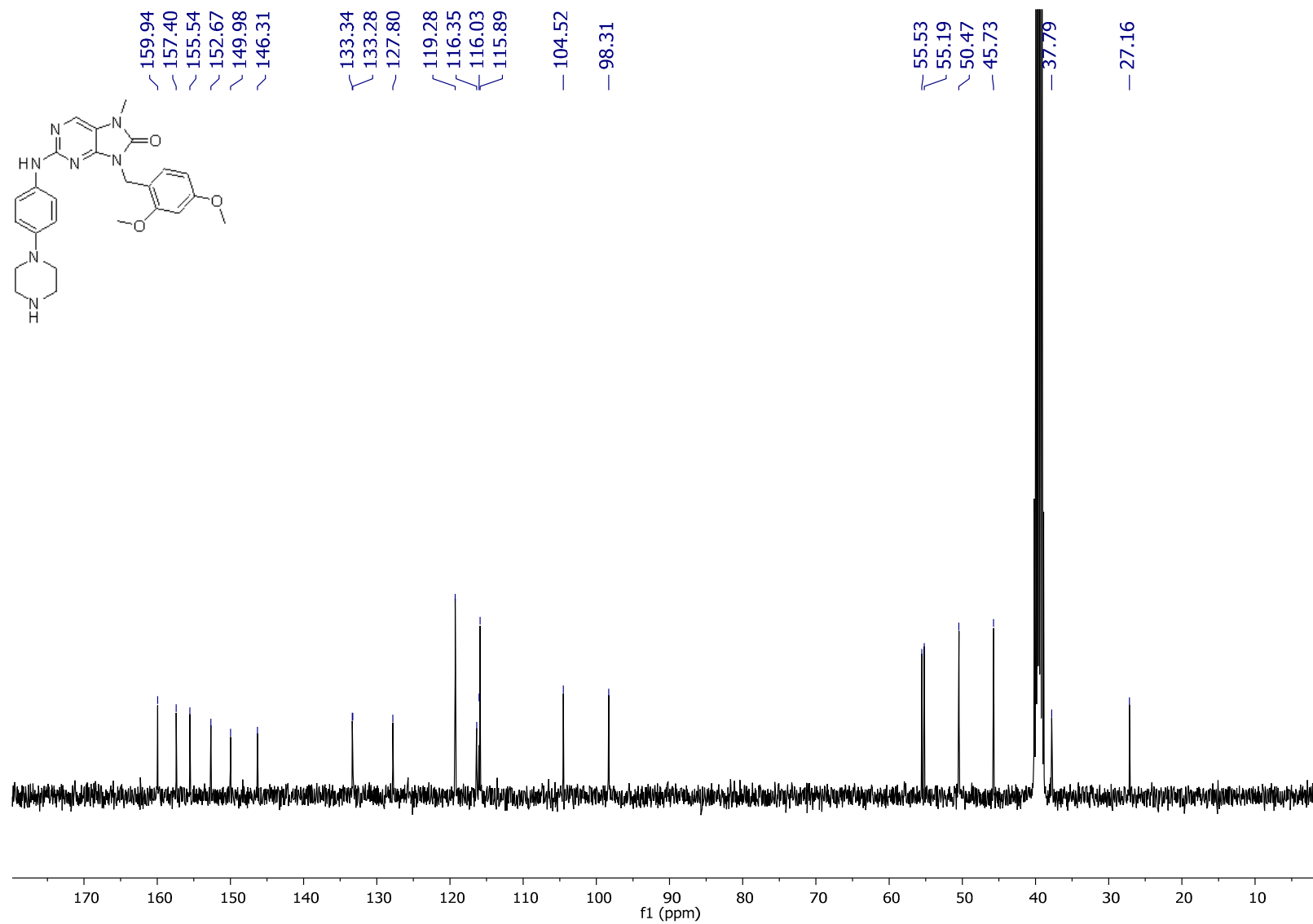
<sup>13</sup>C NMR spectrum of **14q**



<sup>1</sup>H NMR spectrum of **14r**

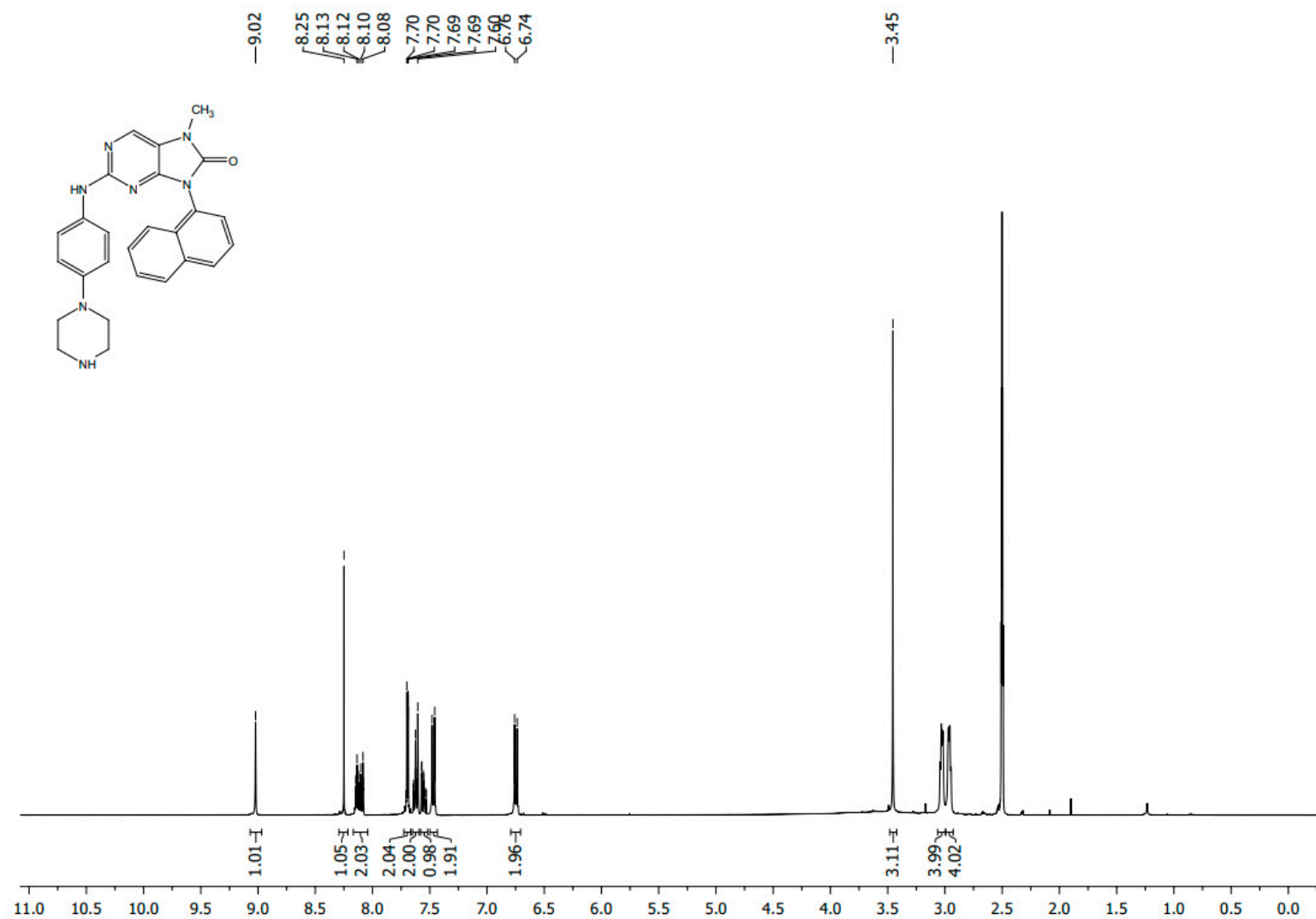


<sup>13</sup>C NMR spectrum of **14r**

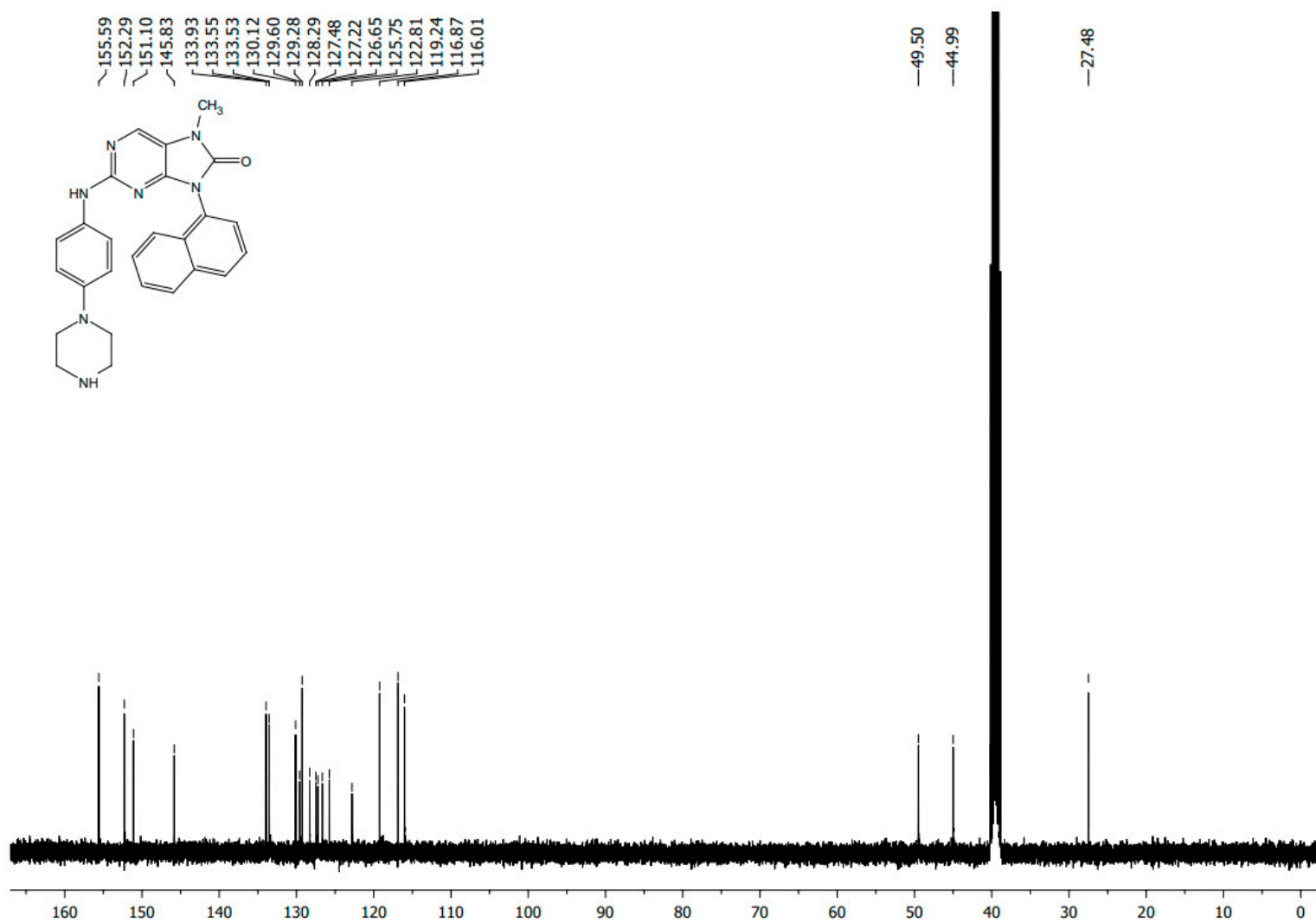




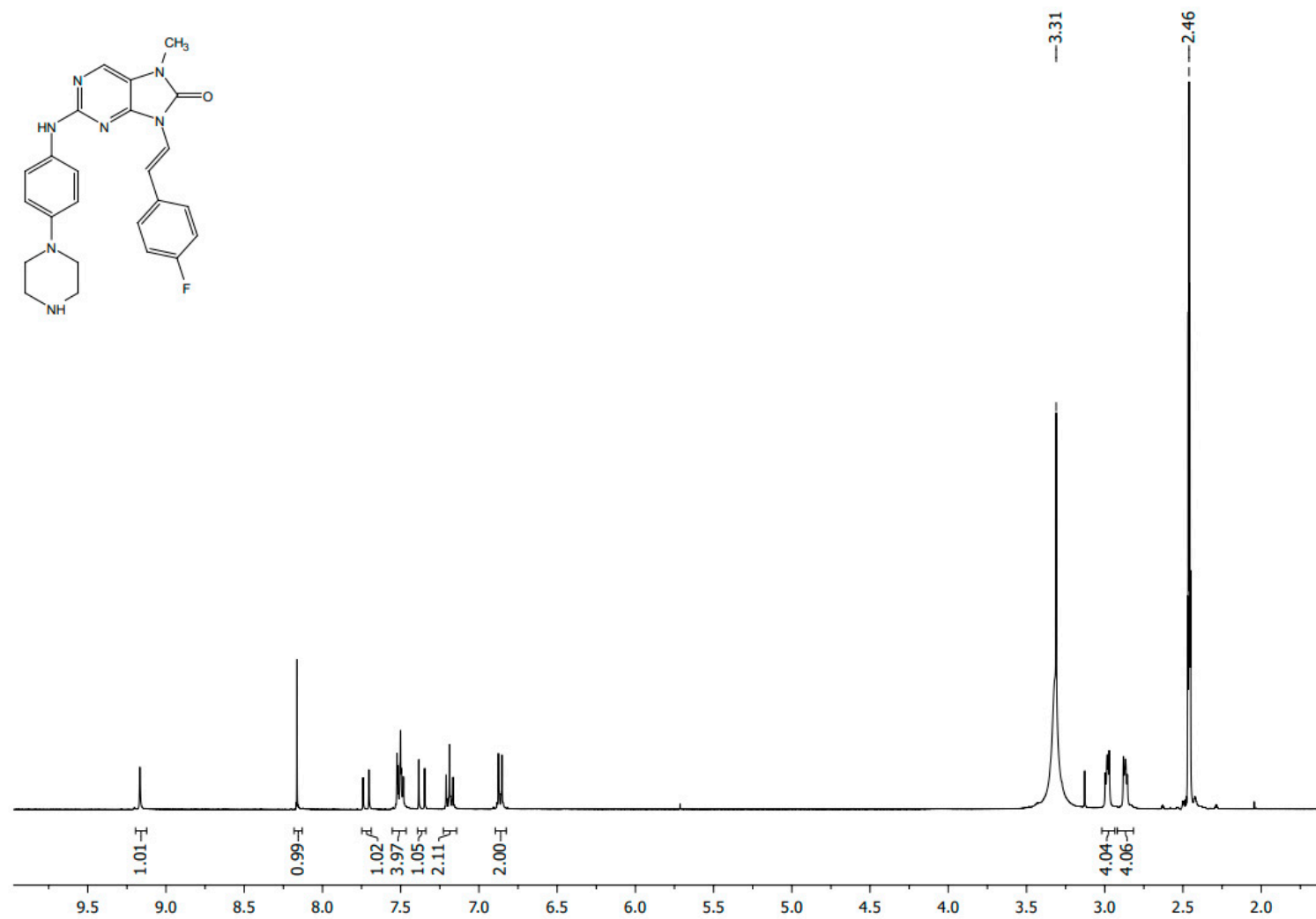
$^1\text{H}$  NMR spectrum of **14s**



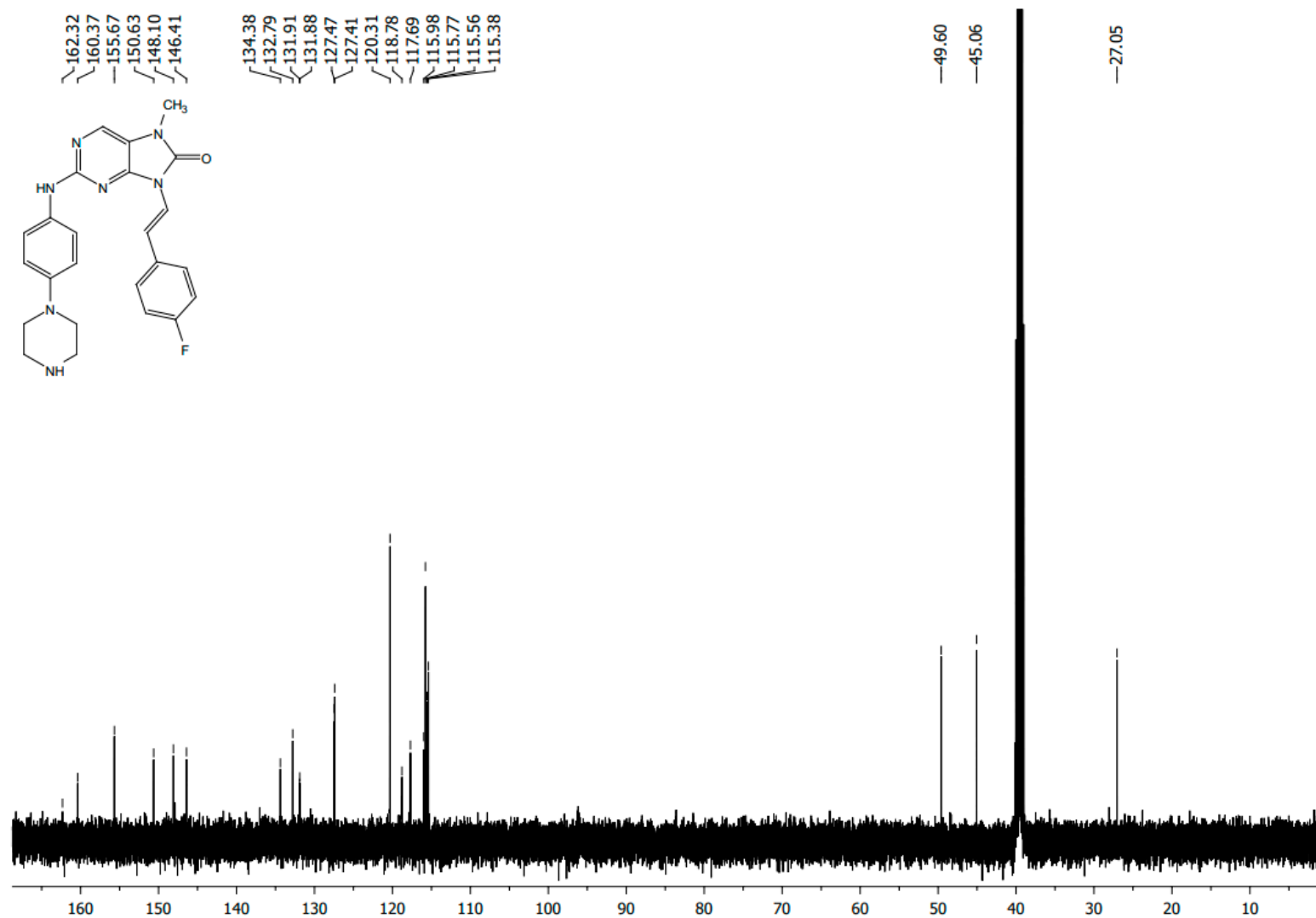
$^{13}\text{C}$  NMR spectrum of **14s**



$^1\text{H}$  NMR spectrum of **14t**



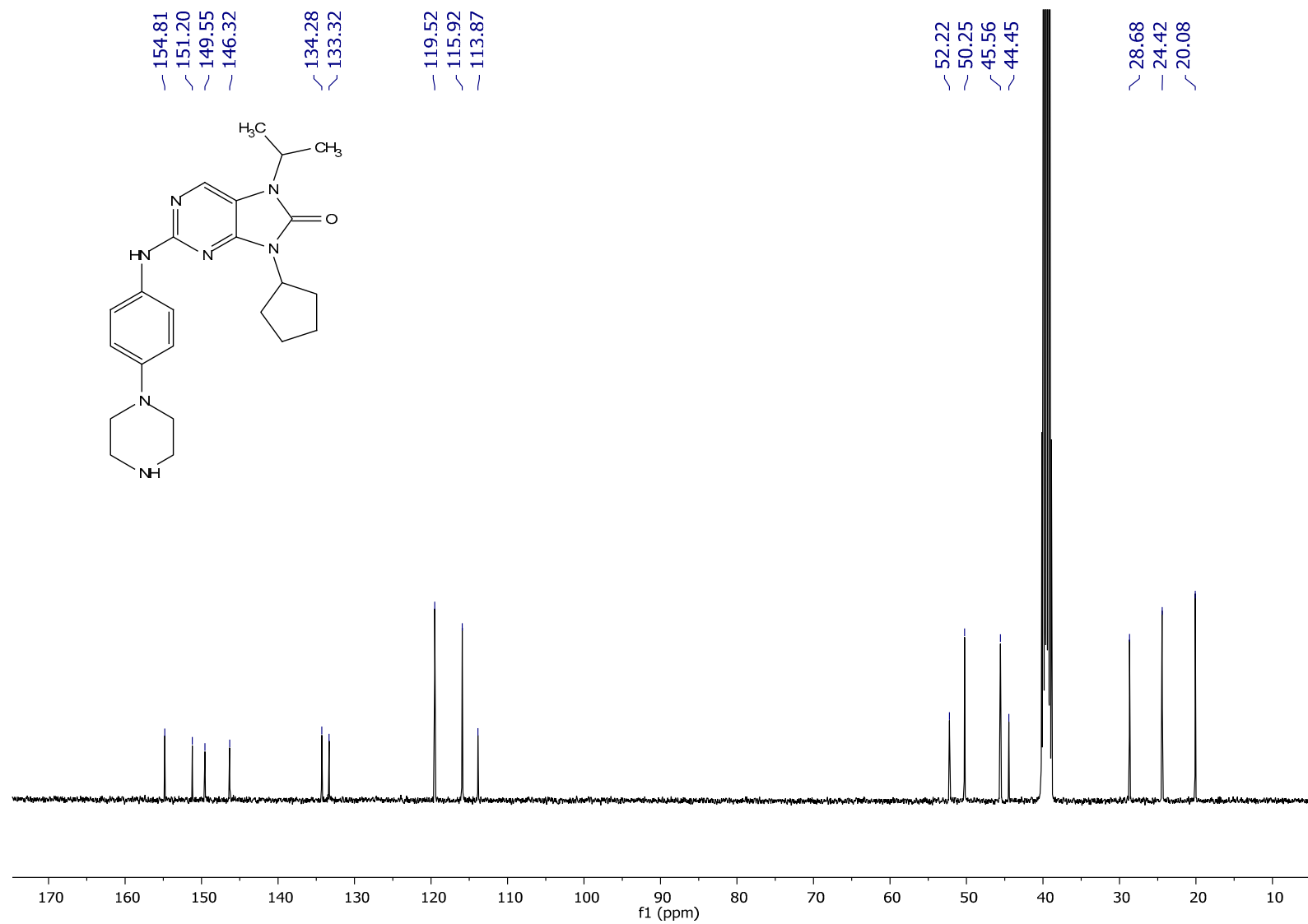
$^{13}\text{C}$  NMR spectrum of **14t**



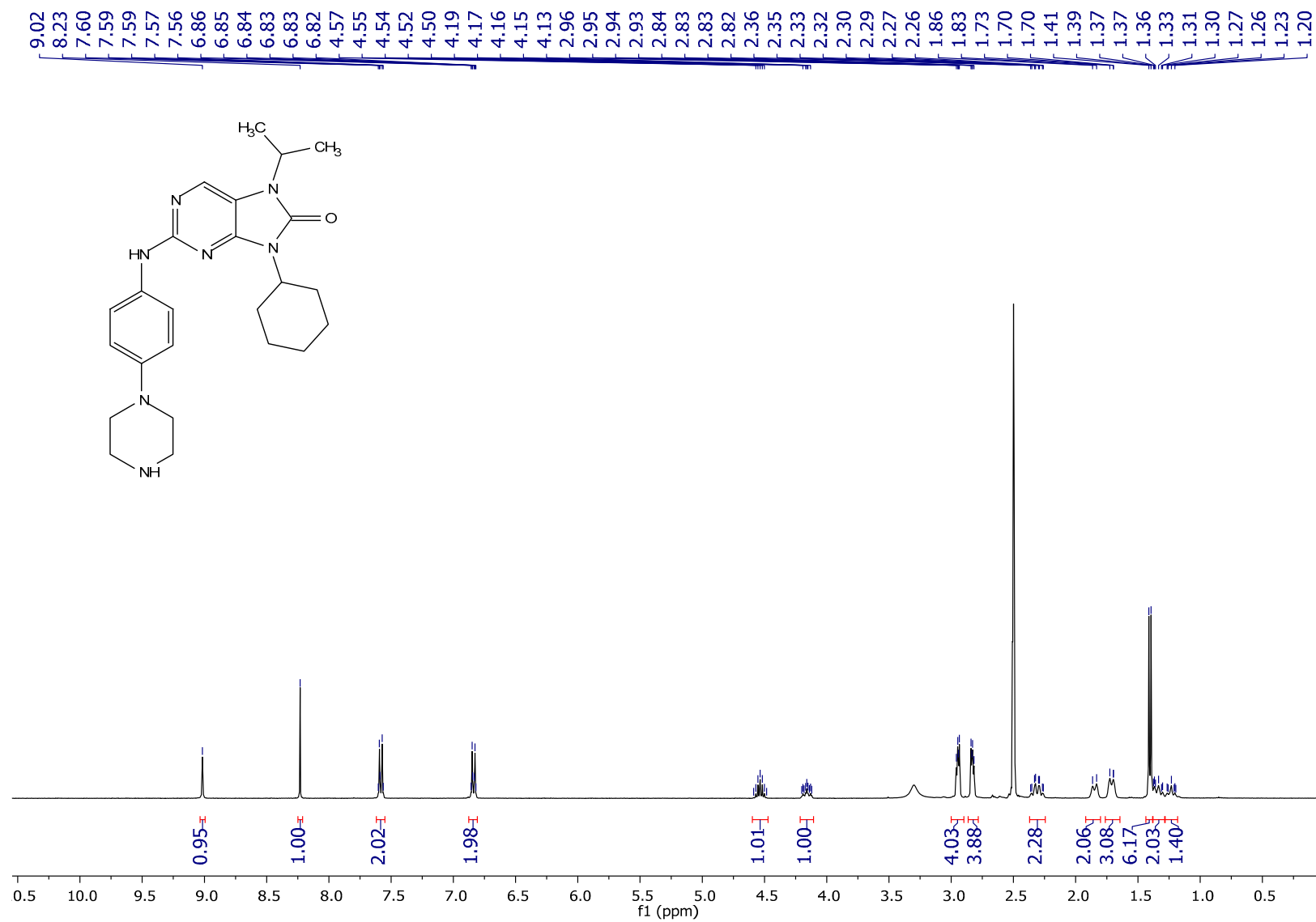
CC(C)N1C(=O)N(C2CCCC2)C3=NC=NC(=N3)NC4=CC=CC=C4N5CCNCC5

<sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of 1-(4-(4-morpholinyl)phenyl)-2-isopropyl-5-cyclopentyl-1H-imidazo[4,5-b]pyridine-3-carboxamide. The spectrum shows peaks from 0.5 to 8.5 ppm. Key peaks include aromatic protons at 8.24, 7.57, 7.56, 7.54, 7.53, 6.86, 6.85, 6.84, 6.83, 6.82, 4.72, 4.70, 4.68, 4.57, 4.56, 4.54, 4.52, 4.51, 2.97, 2.96, 2.95, 2.95, 2.86, 2.85, 2.84, 2.83, 2.50, 2.22, 2.21, 2.20, 2.19, 2.19, 2.18, 2.17, 2.15, 1.96, 1.94, 1.92, 1.91, 1.89, 1.89, 1.88, 1.86, 1.86, 1.85, 1.65, 1.64, 1.62, 1.61, 1.60, 1.42, and 1.40 ppm. Integration values are provided for several peaks: 0.97, 1.00, 2.02, 1.98, 1.04, 1.04, 3.98, 3.87, 2.07, 4.11, 2.10, and 6.09.

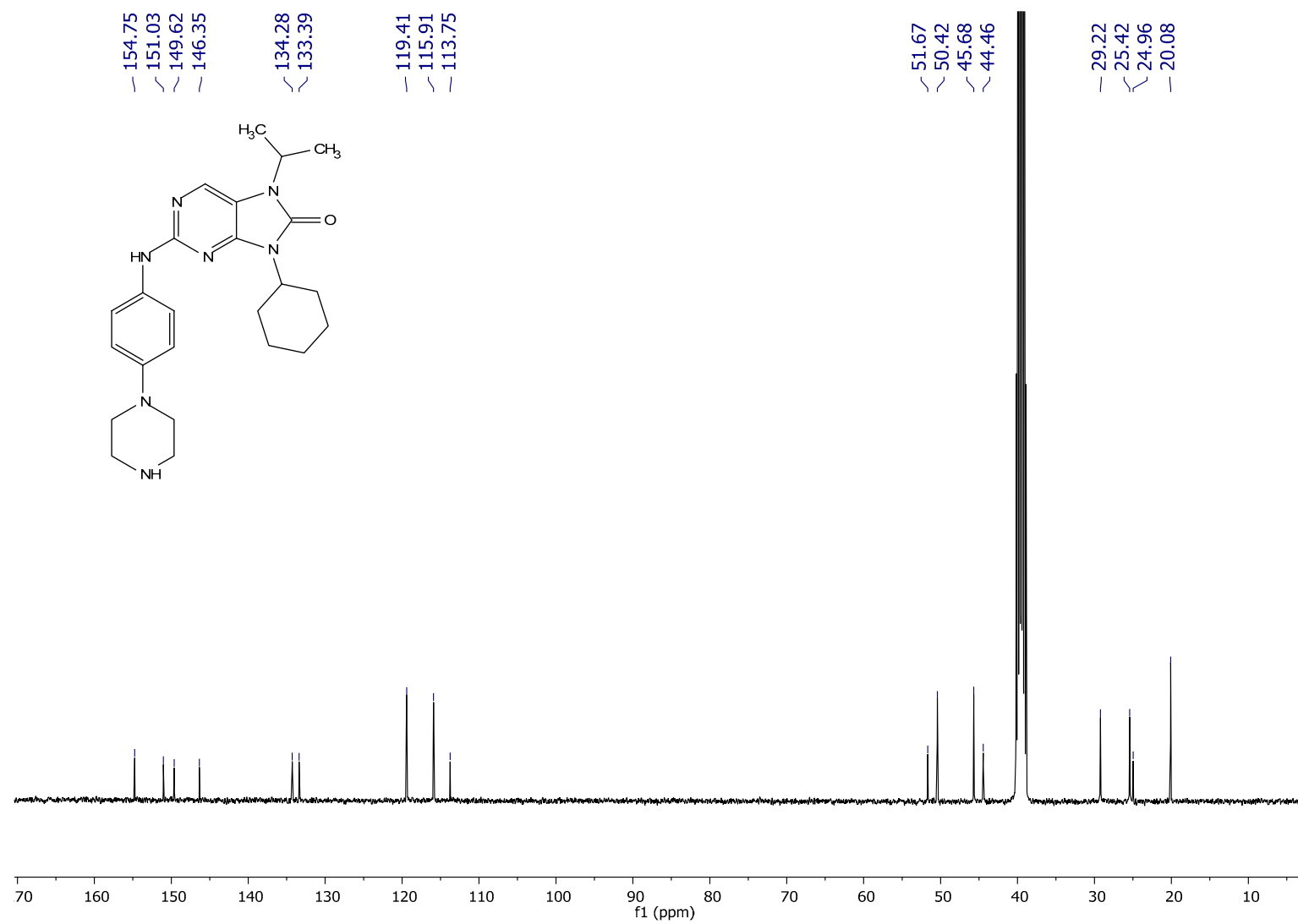
<sup>13</sup>C NMR spectrum of **15a**



<sup>1</sup>H NMR spectrum of **15b**

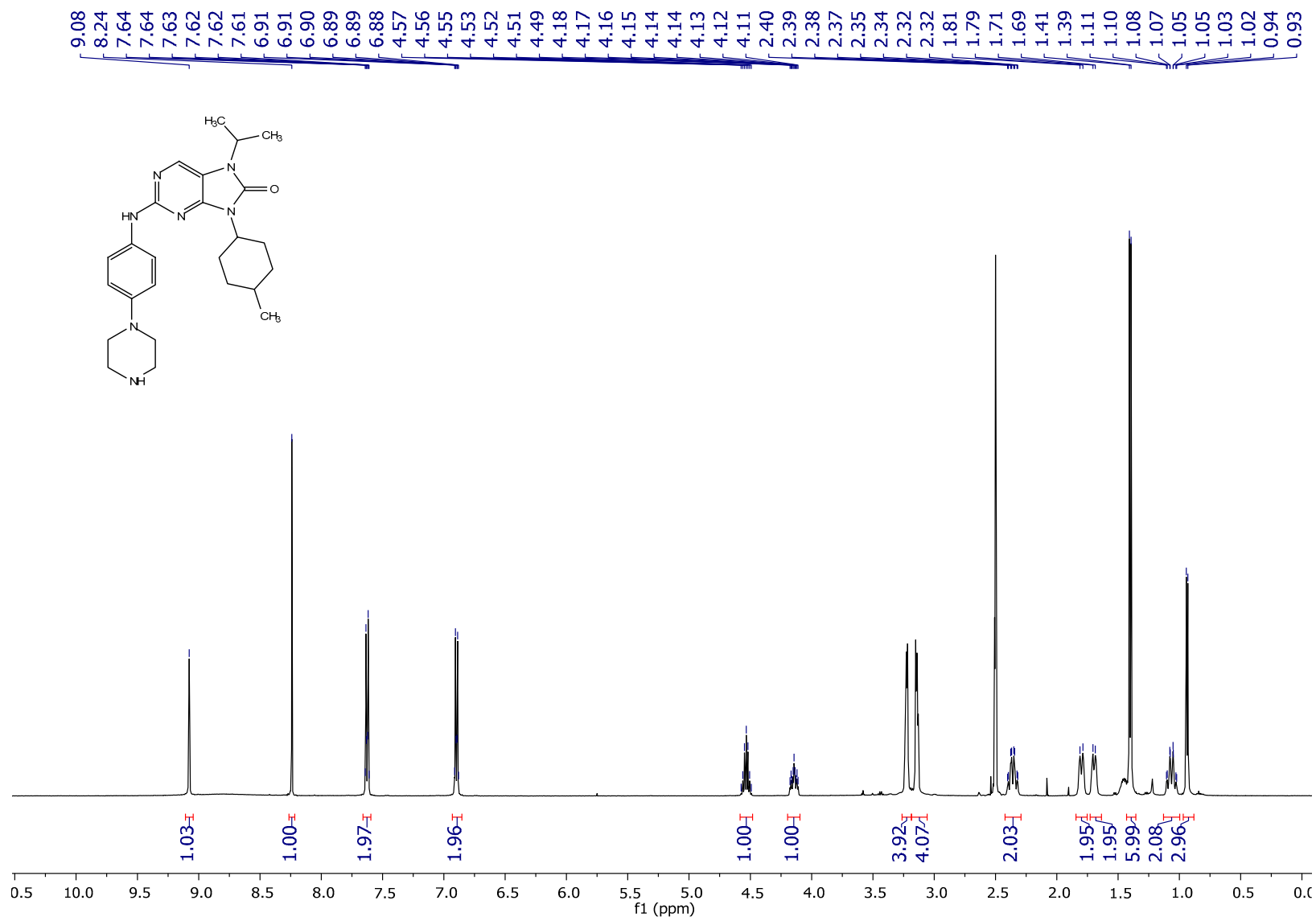


<sup>13</sup>C NMR spectrum of **15b**

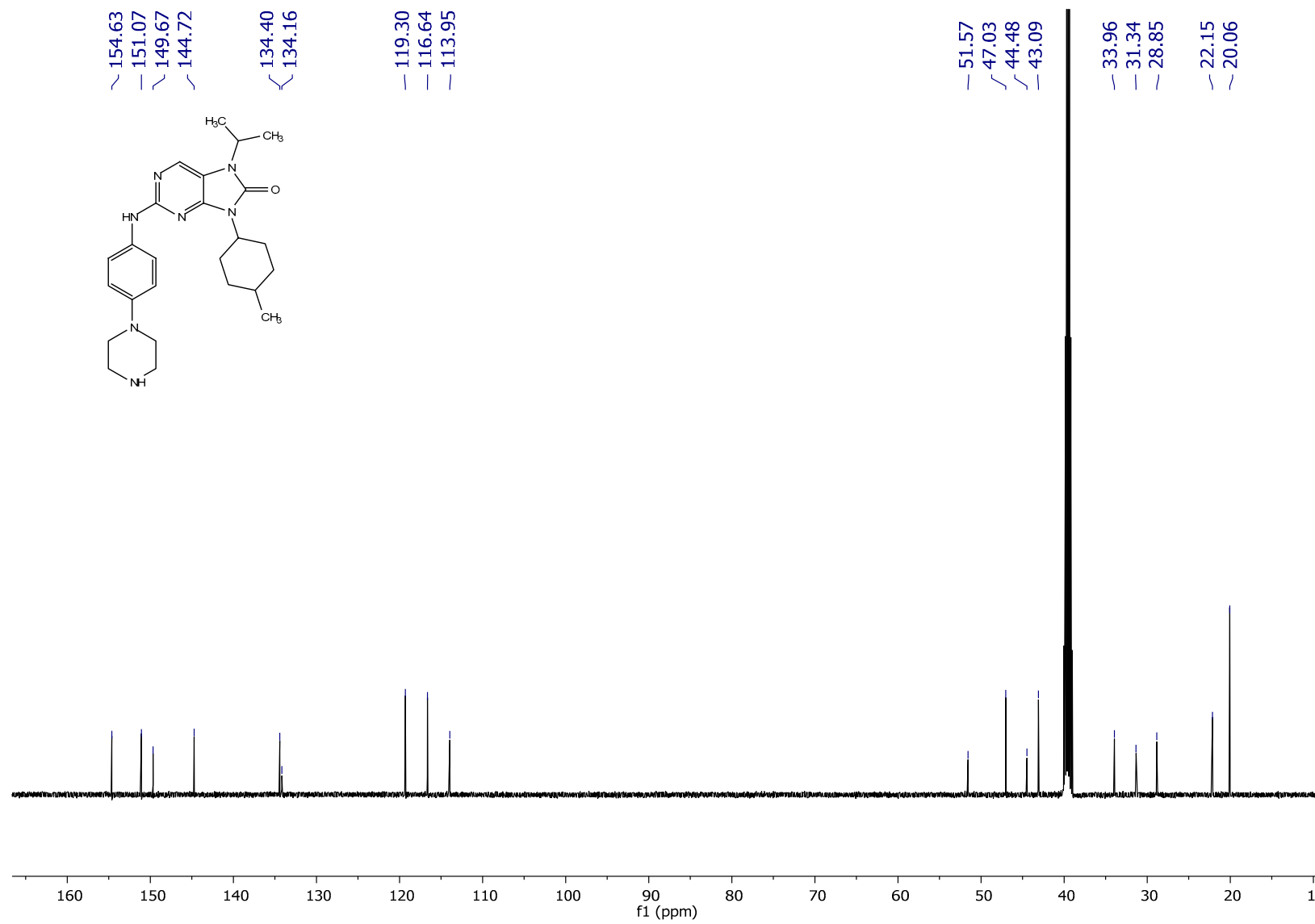




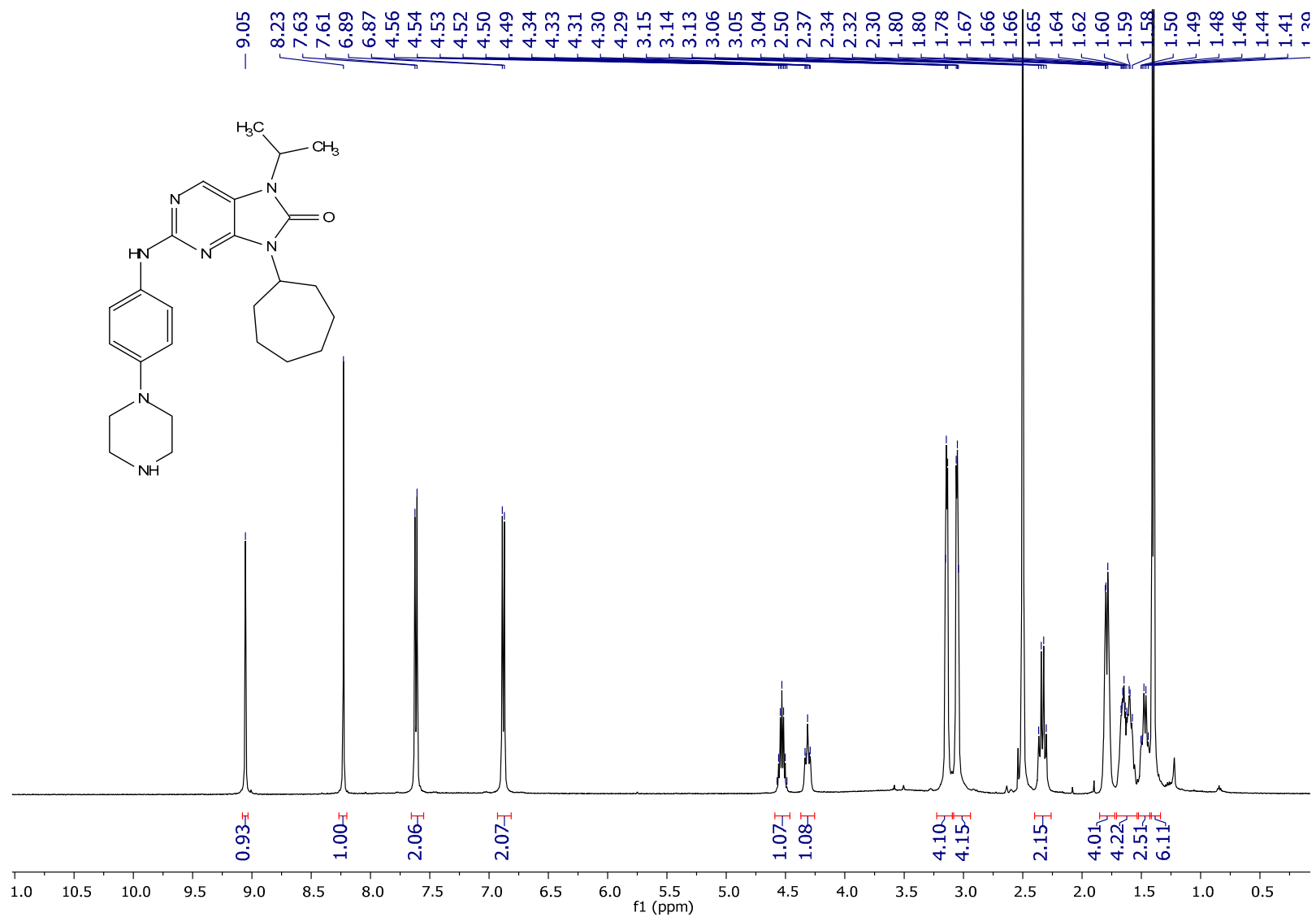
<sup>1</sup>H NMR spectrum of **15c**



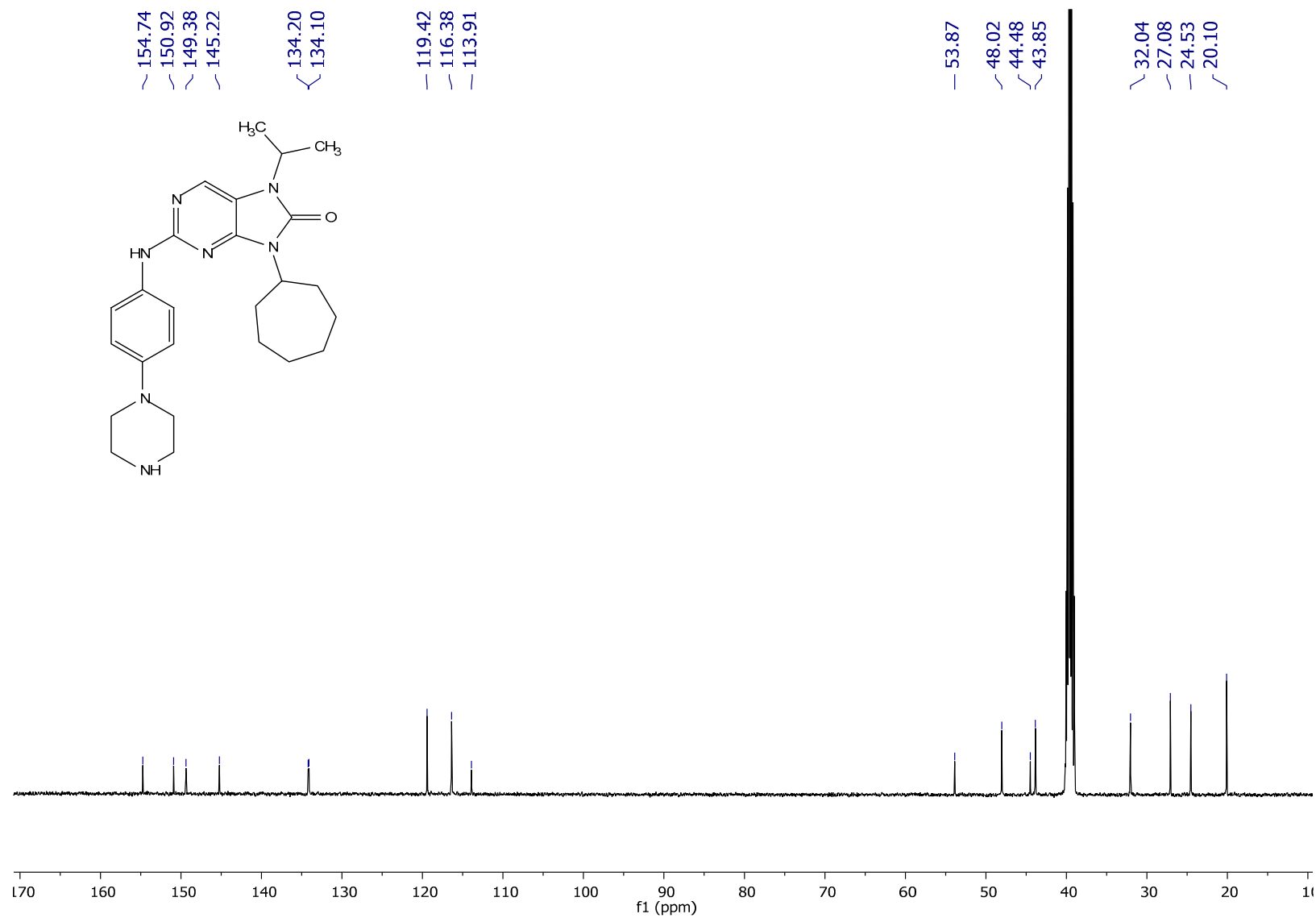
<sup>13</sup>C NMR spectrum of **15c**



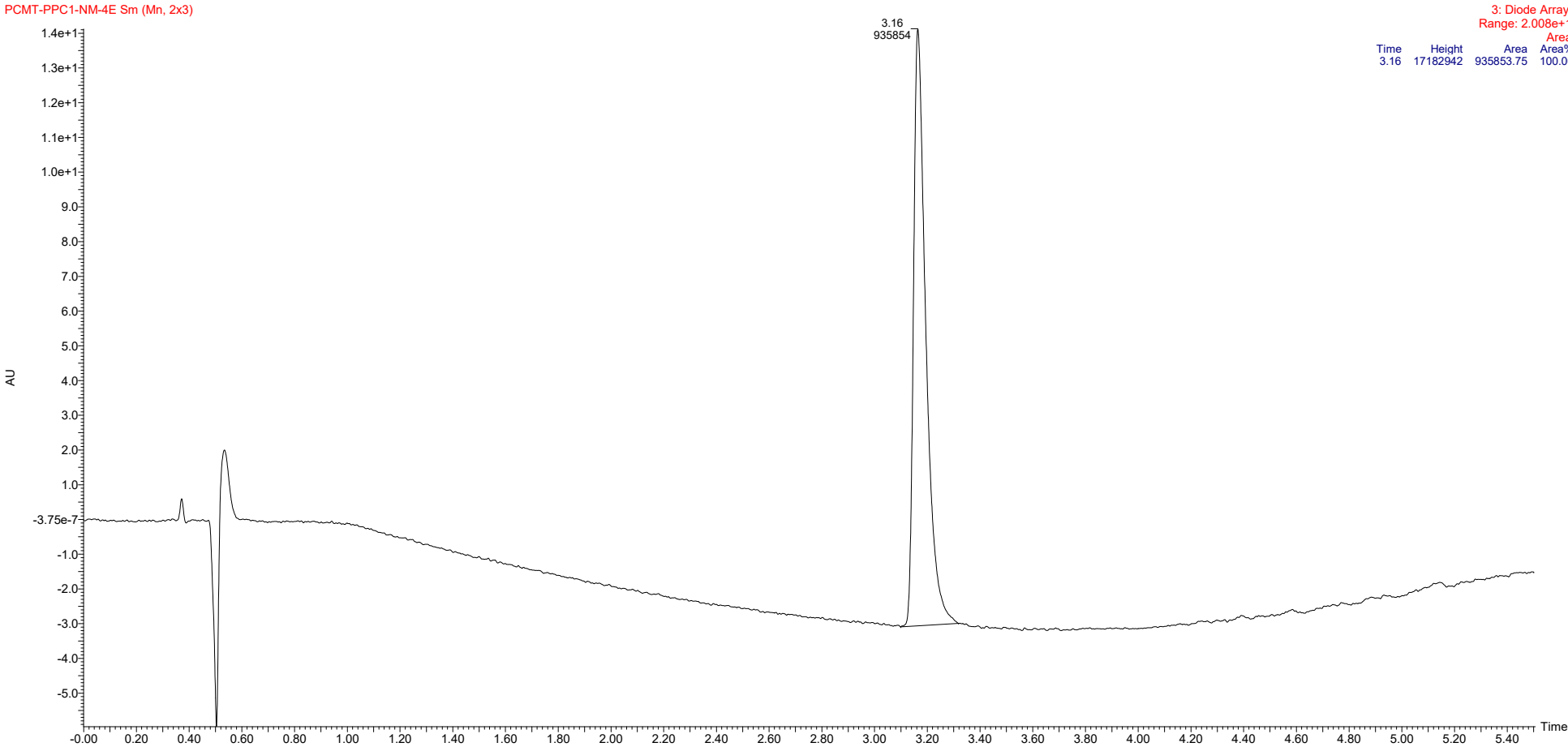
<sup>1</sup>H NMR spectrum of **15d**



<sup>13</sup>C NMR spectrum of **15d**

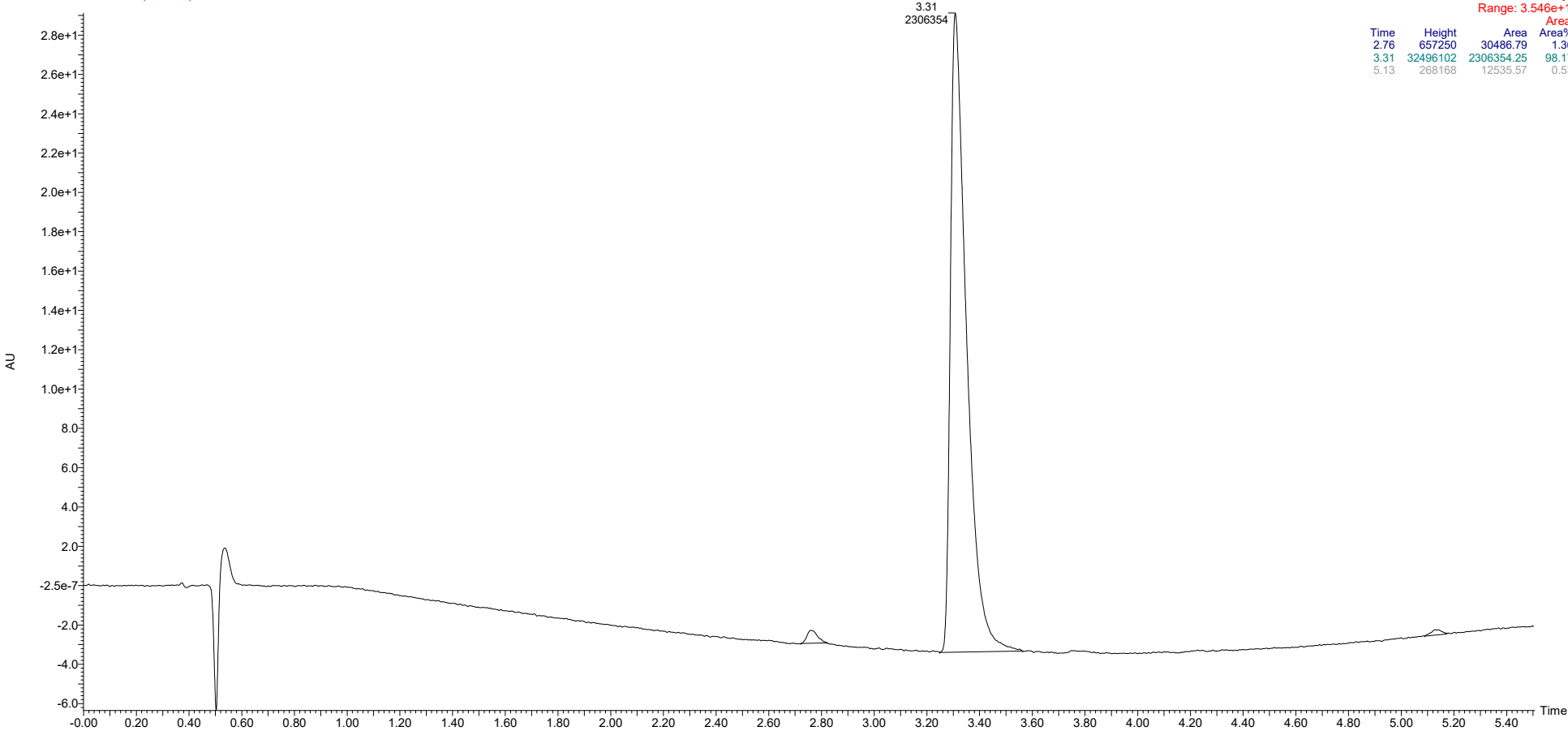


HPLC of compound **12a**

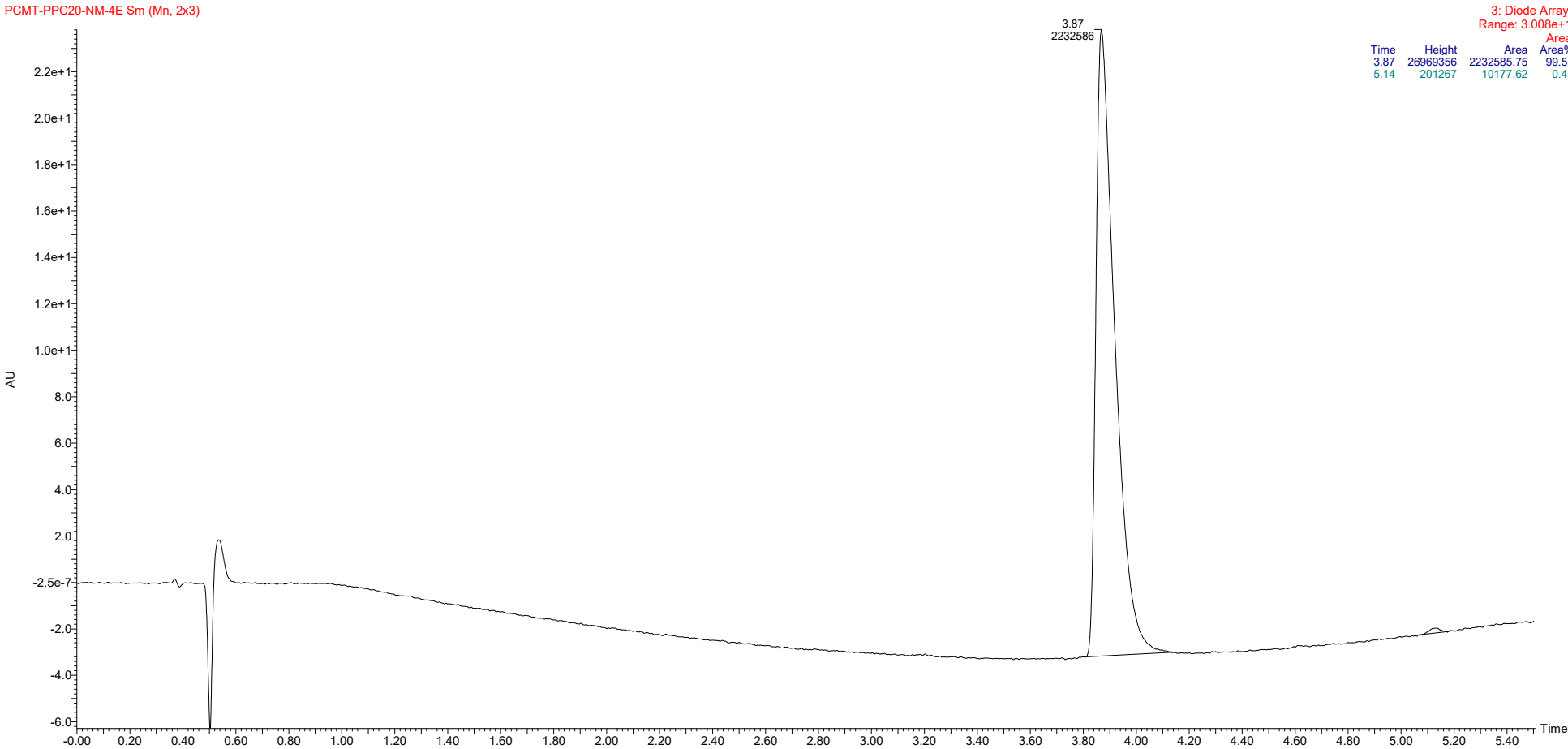


HPLC of compound 12b

PCMT-PPC2-NM-4E Sm (Mn, 2x3)

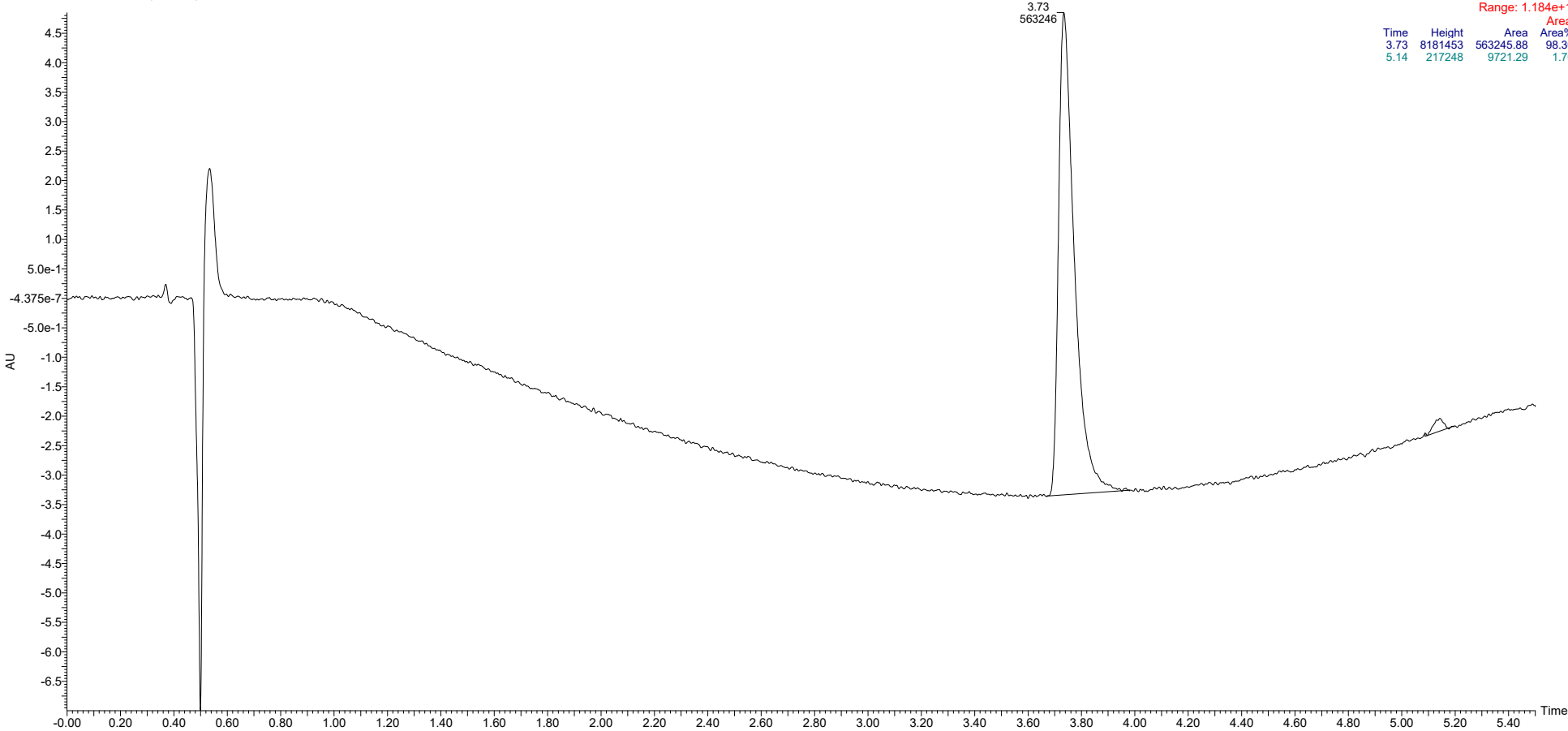


HPLC of compound 12c



HPLC of compound **12d**

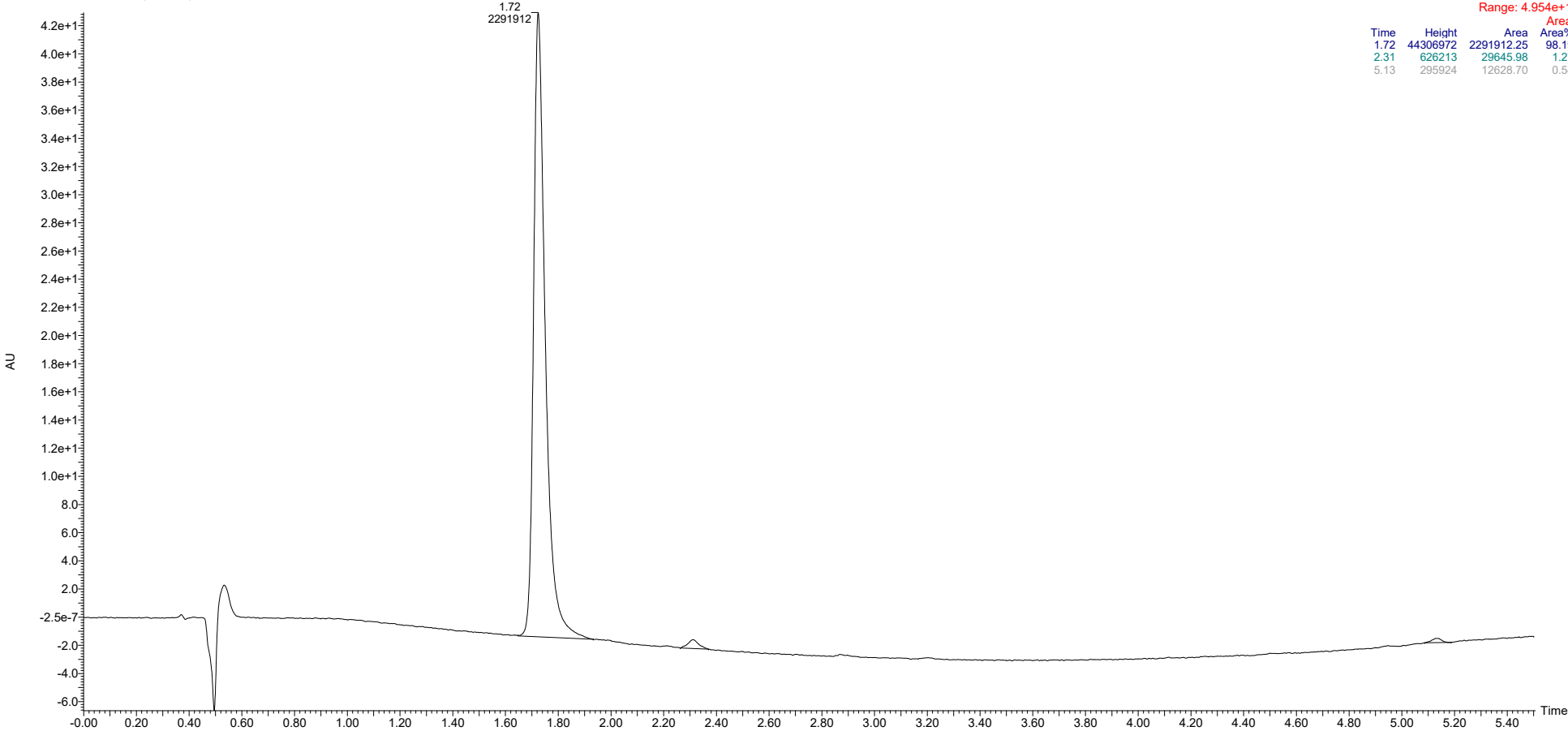
PCMT-PPC14-NM-4E Sm (Mn, 2x3)





HPLC of compound **13a**

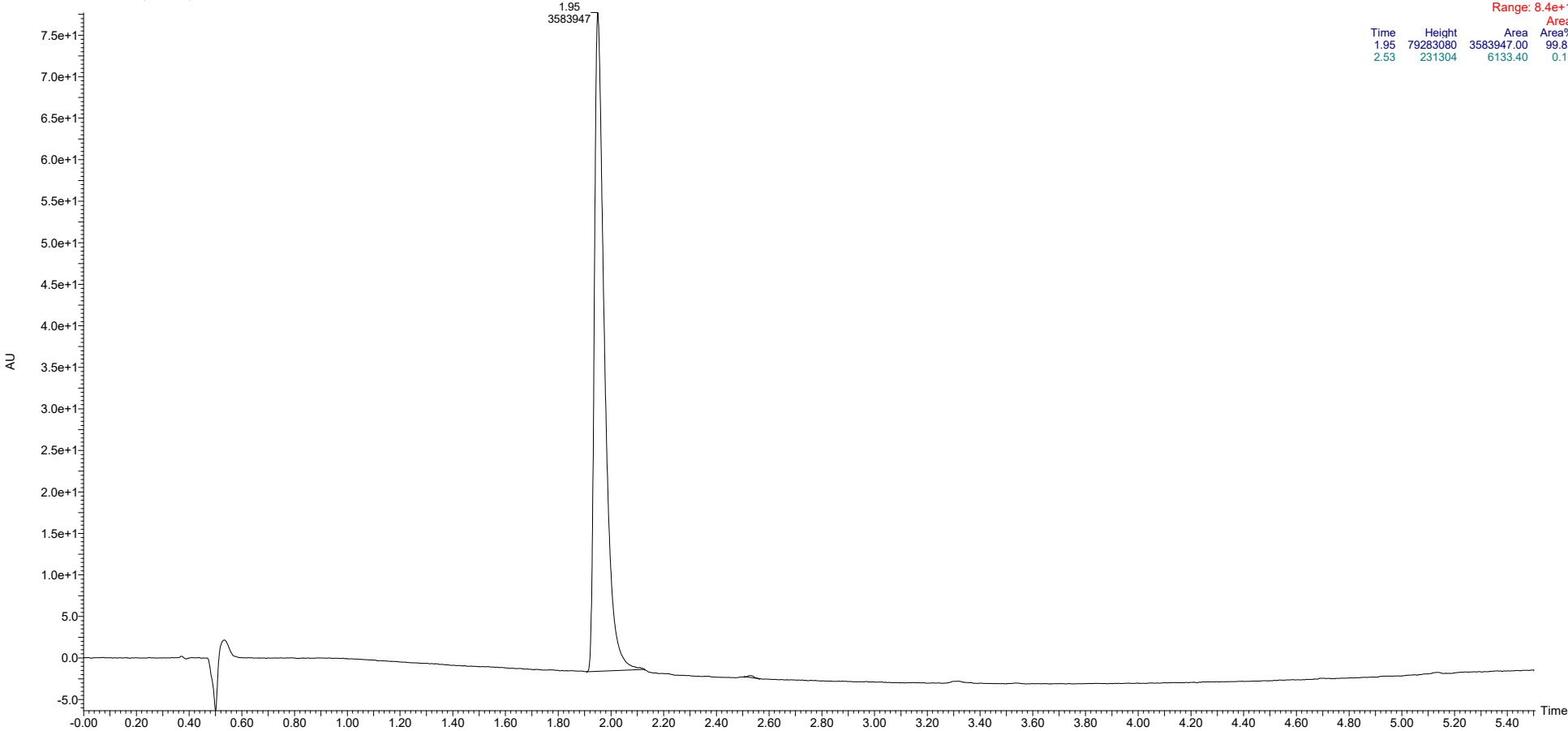
PCMT-PPC1-NM-4A Sm (Mn, 2x3)



3: Diode Array  
Range: 4.954e+1

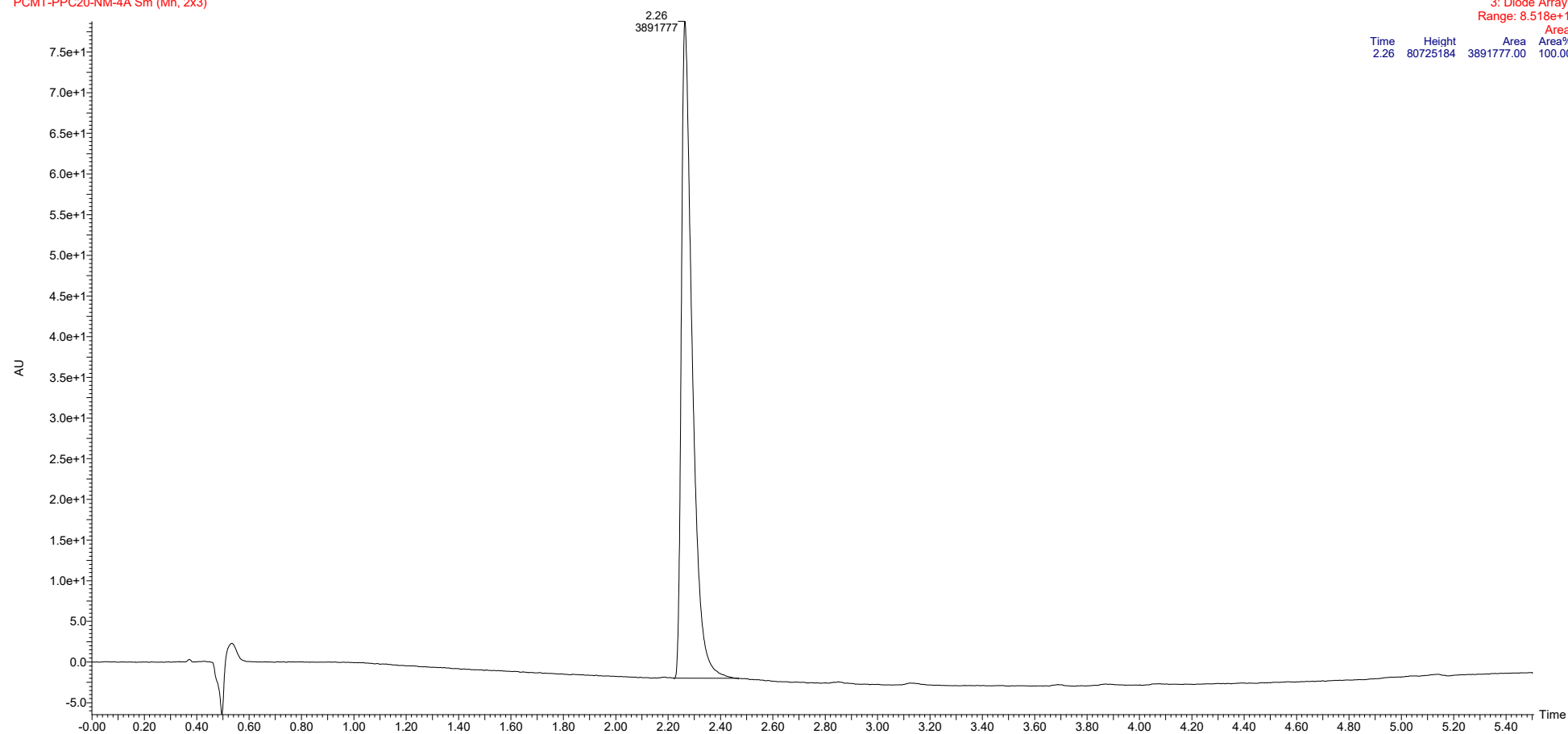
HPLC of compound **13b**

PCMT-PPC2-NM-4A Sm (Mn, 2x3)



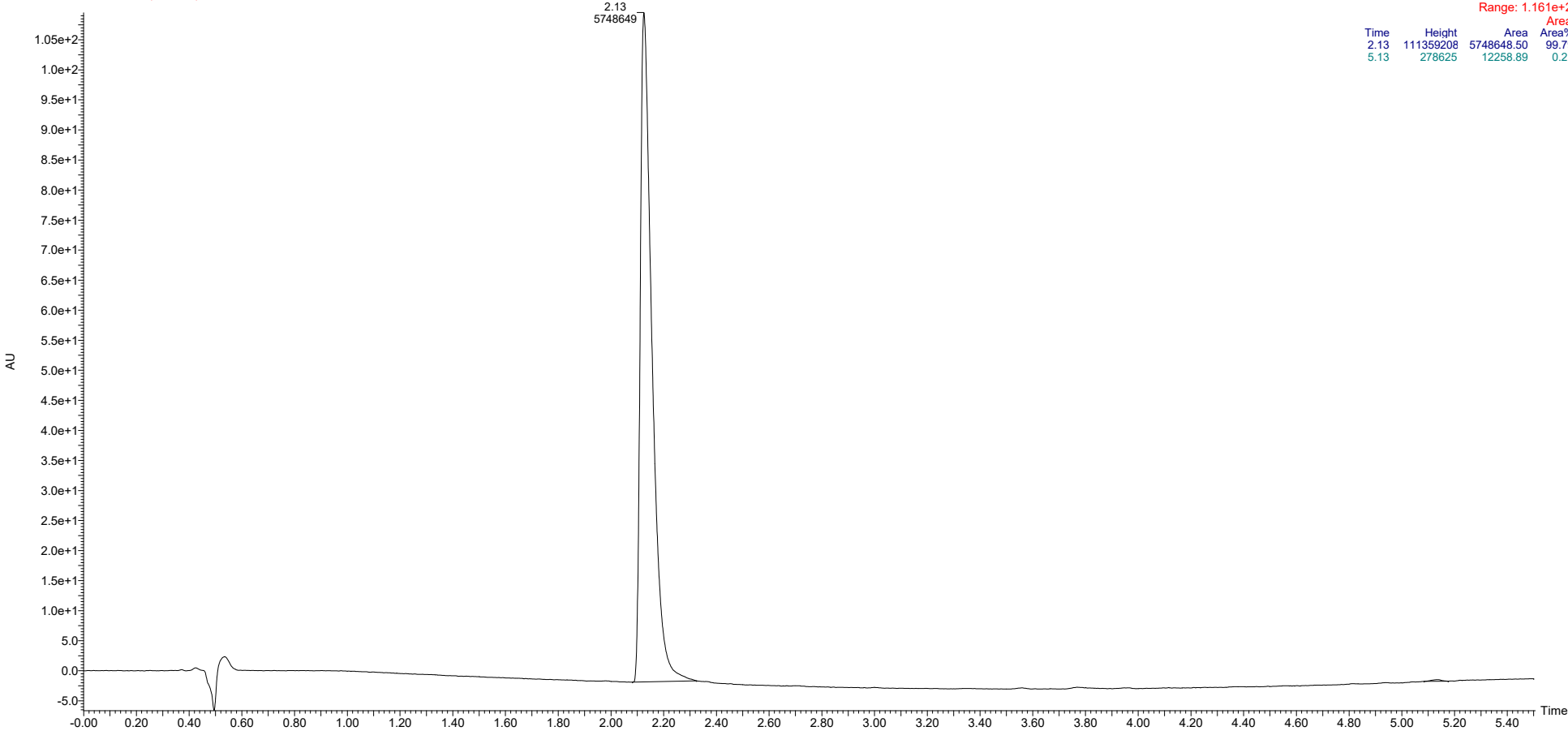
# HPLC of compound **13c**

PCMT-PPC20-NM-4A Sm (Mn, 2x3)



HPLC of compound **13d**

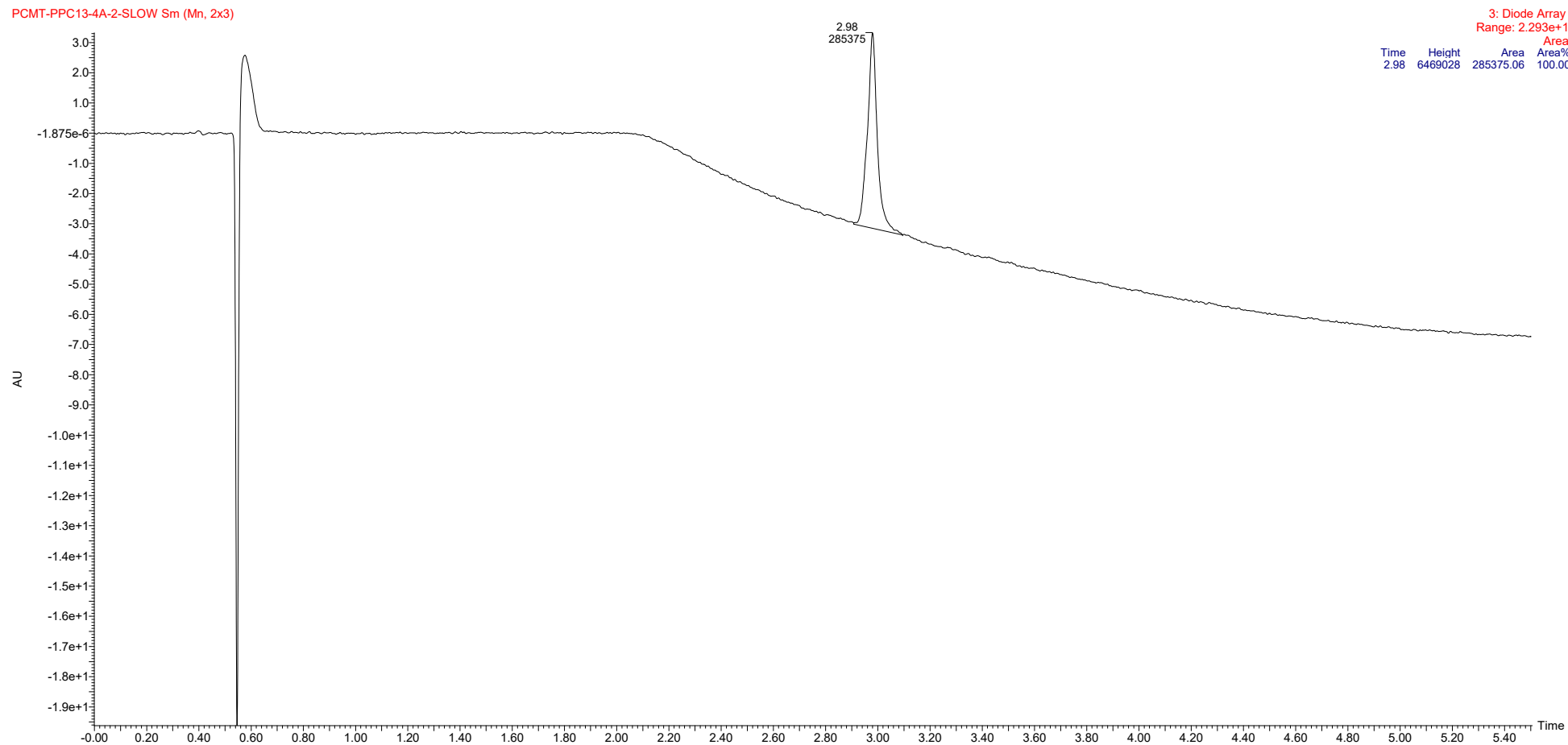
PCMT-PPC14-NM-4A Sm (Mn, 2x3)



3: Diode Array  
Range: 1.161e+2

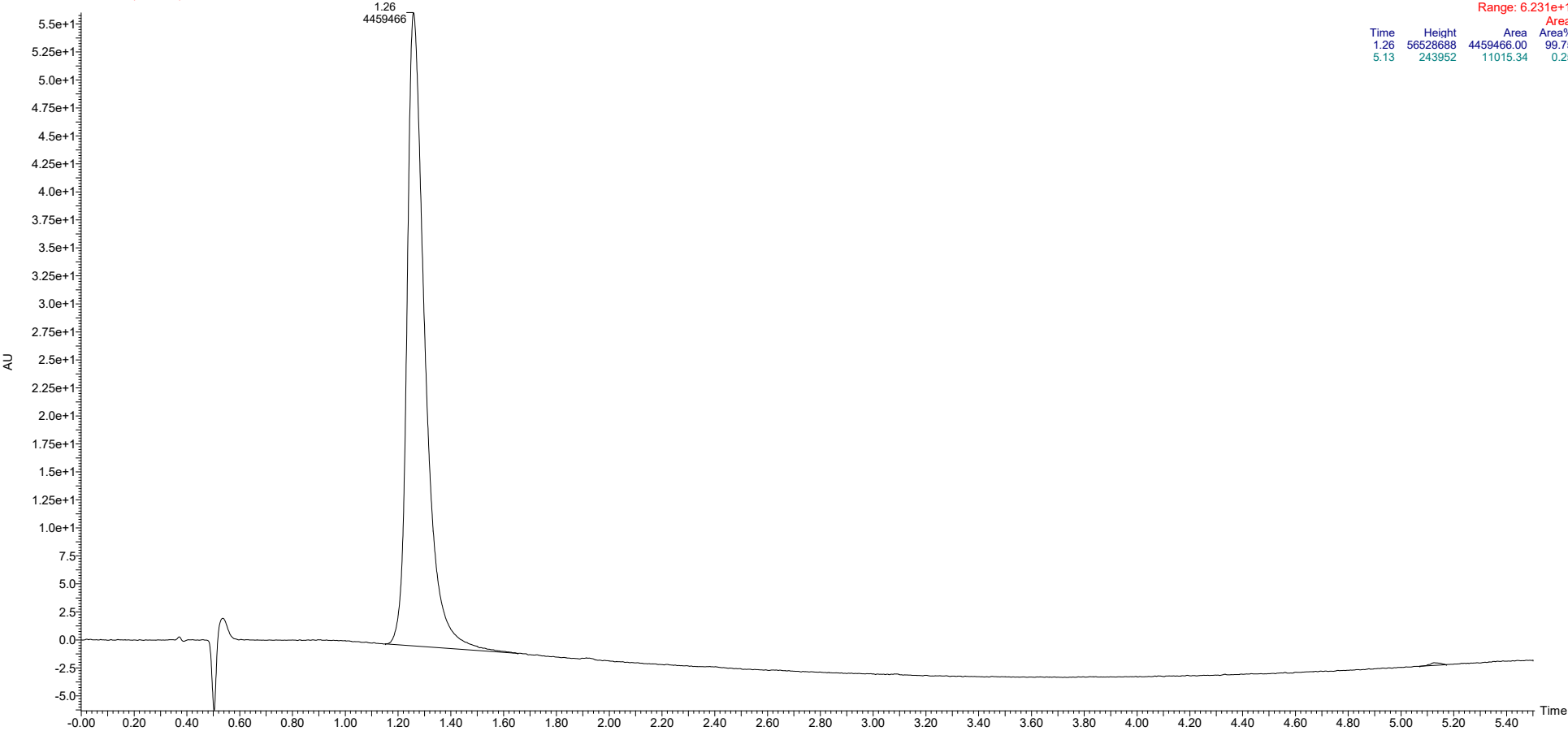
## HPLC of compound **14a**

PCMT-PPC13-4A-2-SLOW Sm (Mn, 2x3)



HPLC of compound 14b

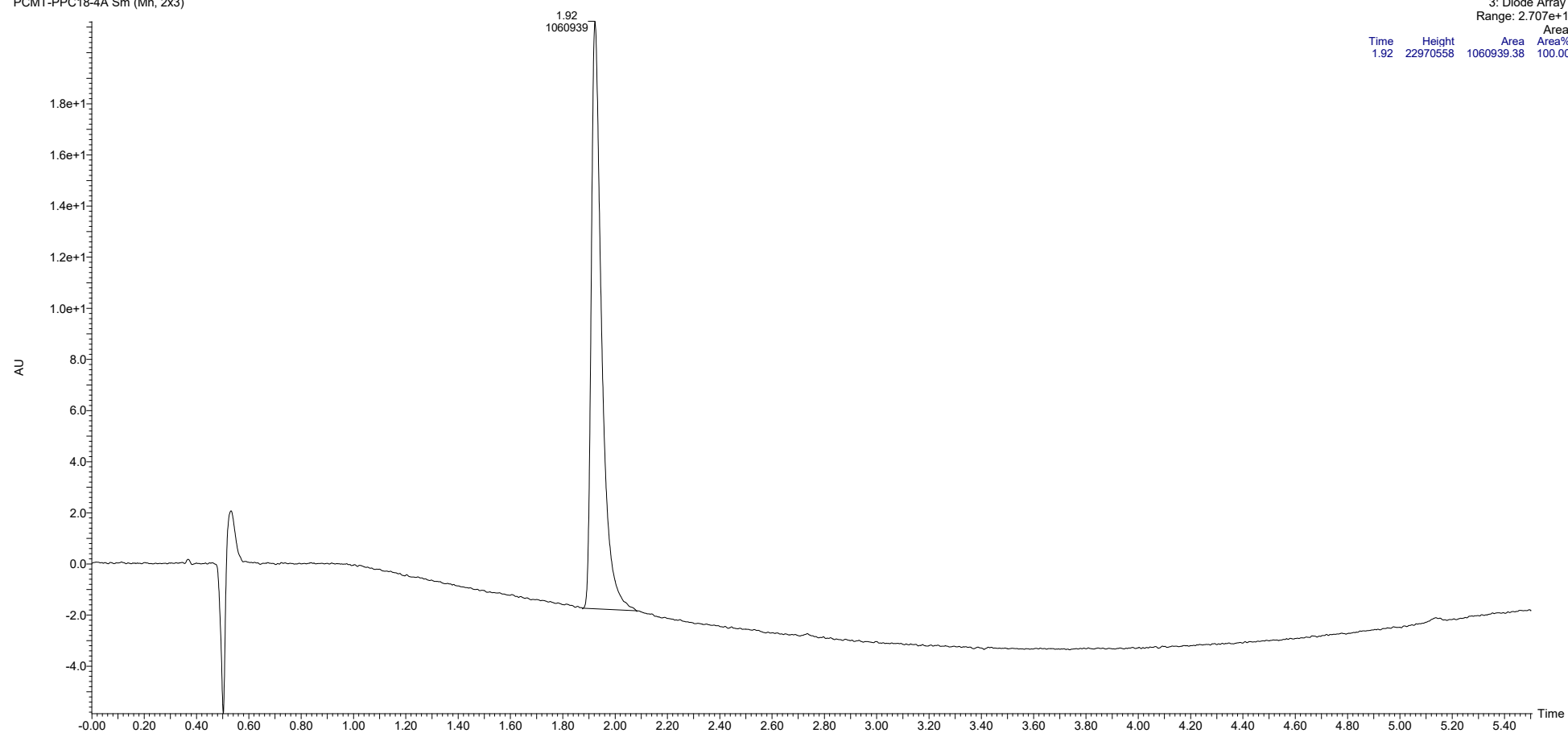
PCMT-PPC10-4AX Sm (Mn, 2x3)



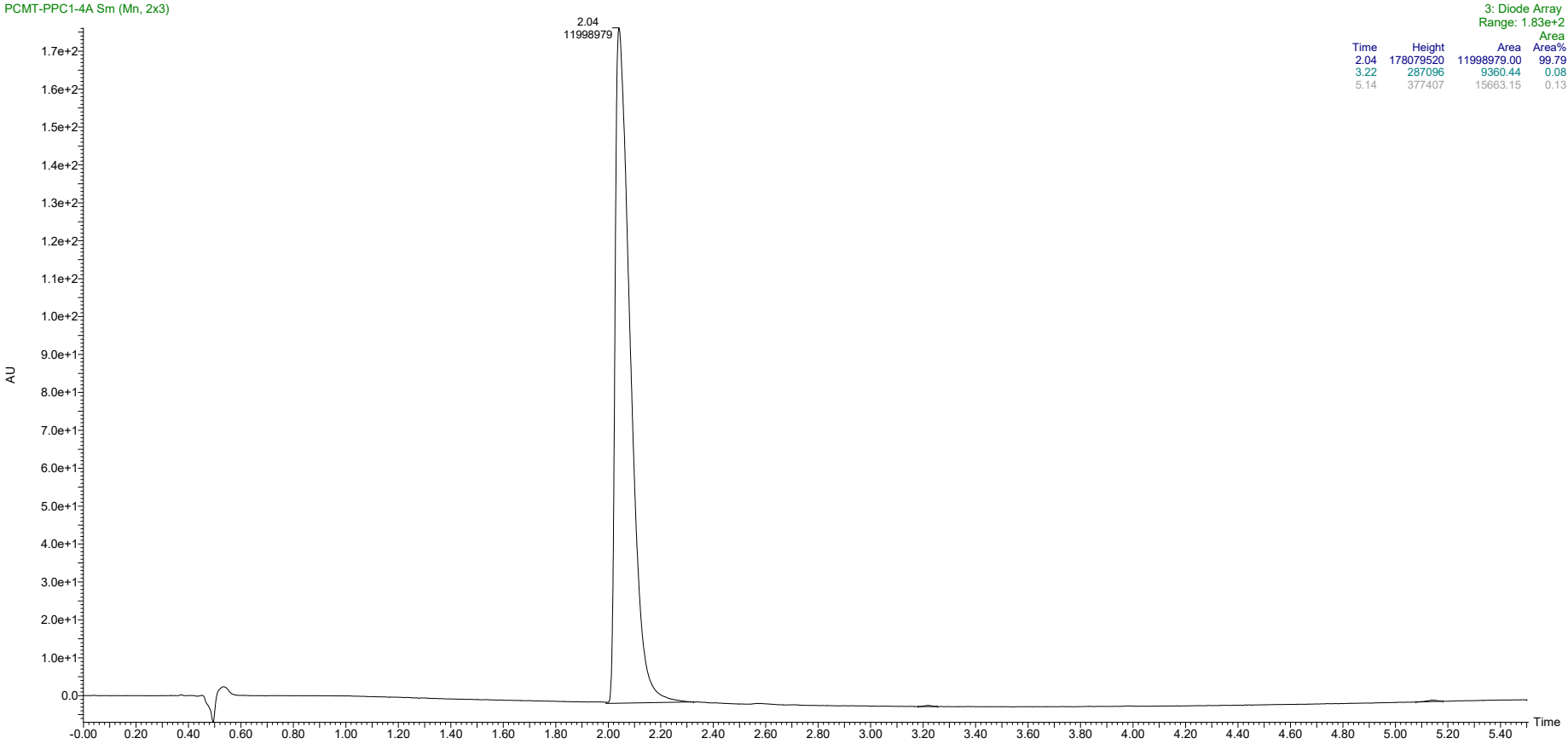
3: Diode Array  
Range: 6.231e+1

## HPLC of compound **14c**

PCMT-PPC18-4A Sm (Mn, 2x3)



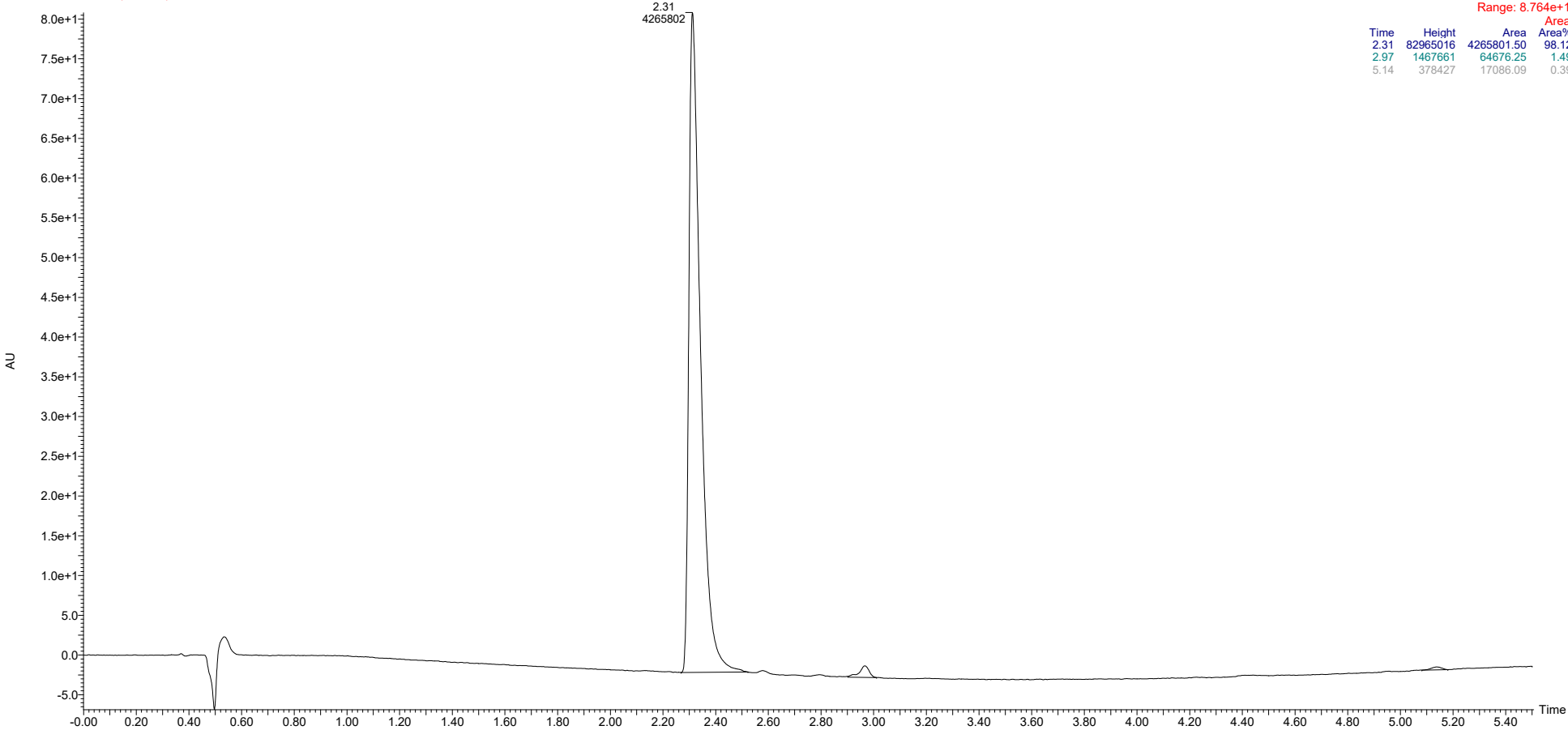
HPLC of compound **14d**





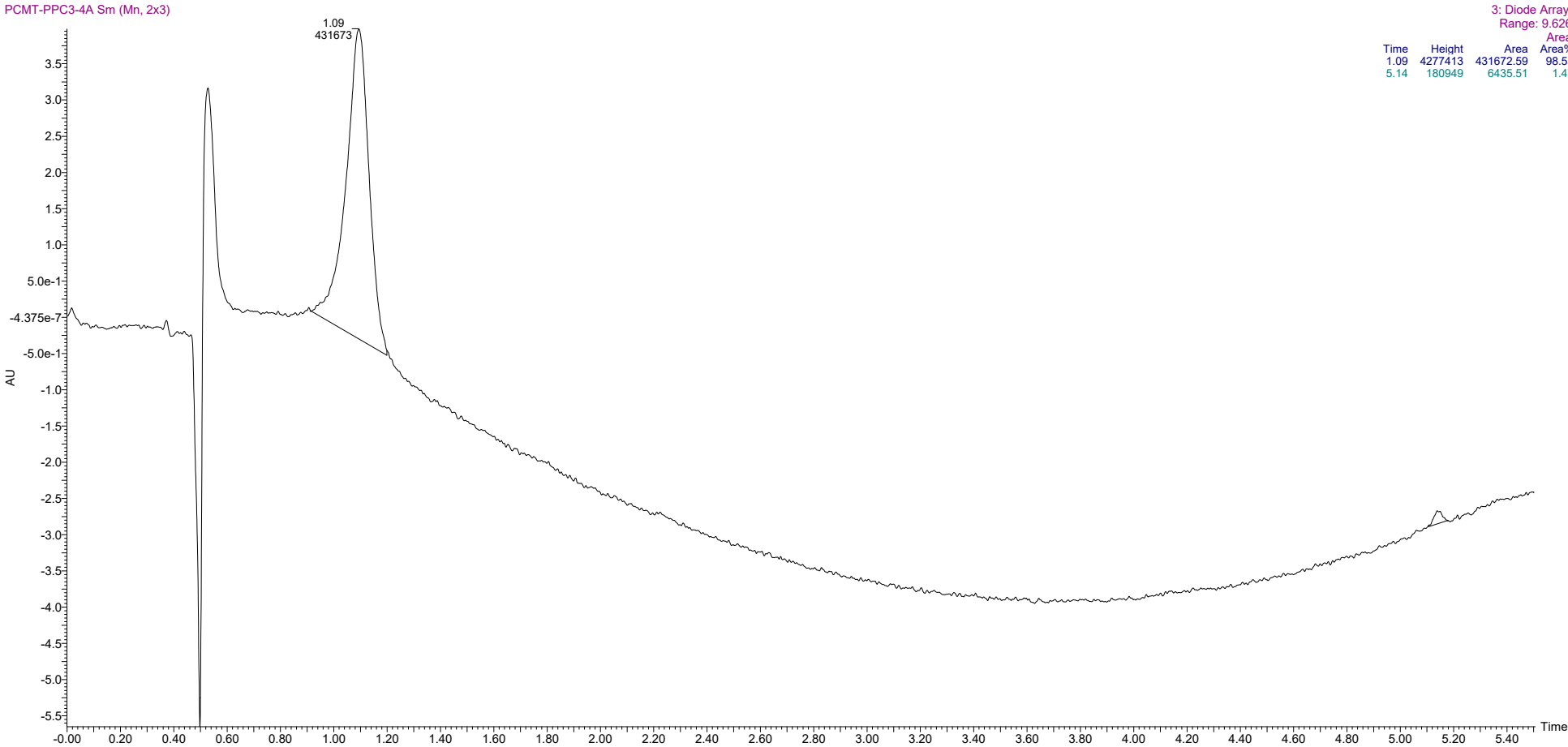
HPLC of compound **14e**

PCMT-PPC2-4A Sm (Mn, 2x3)

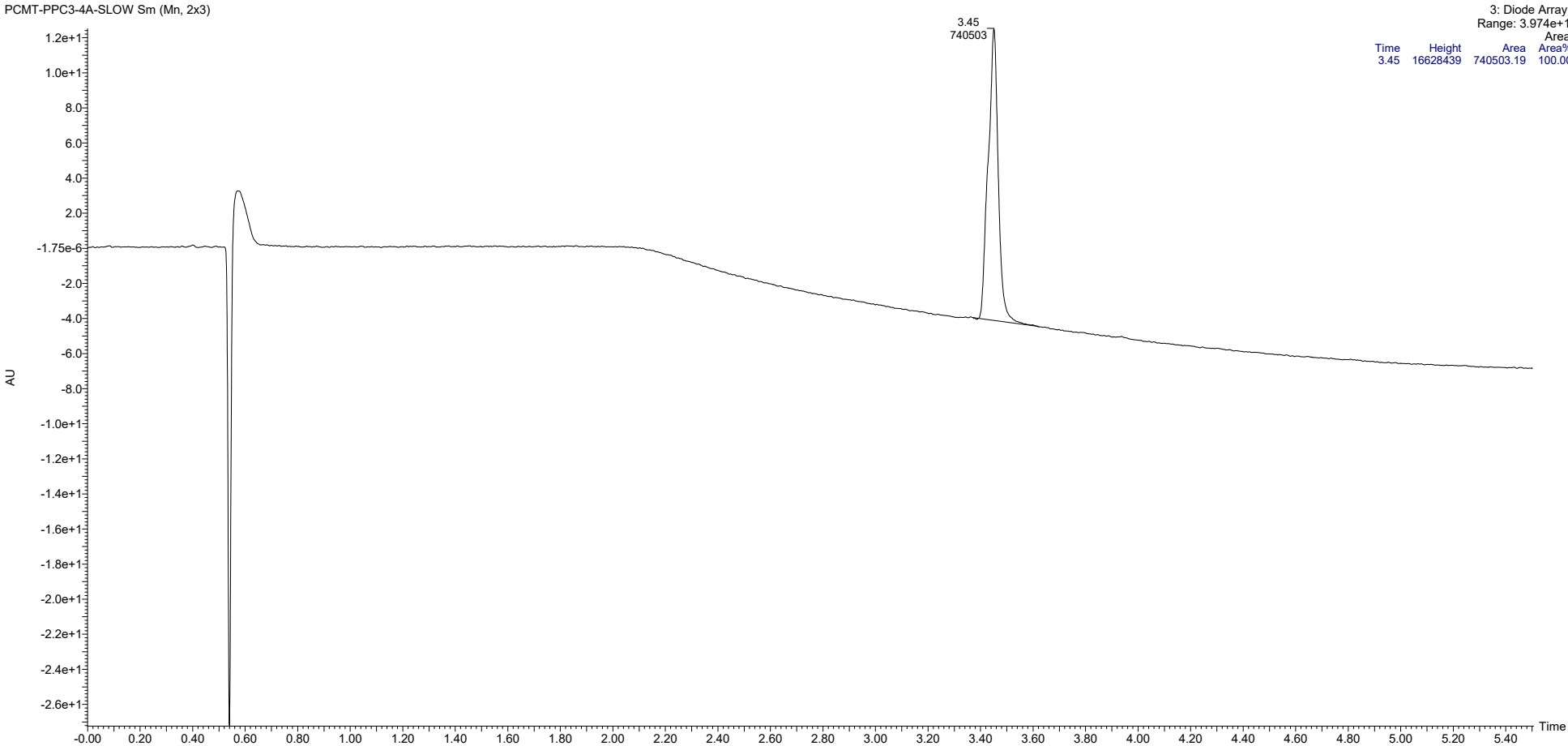


3: Diode Array  
Range: 8.764e+1

HPLC of compound 14f

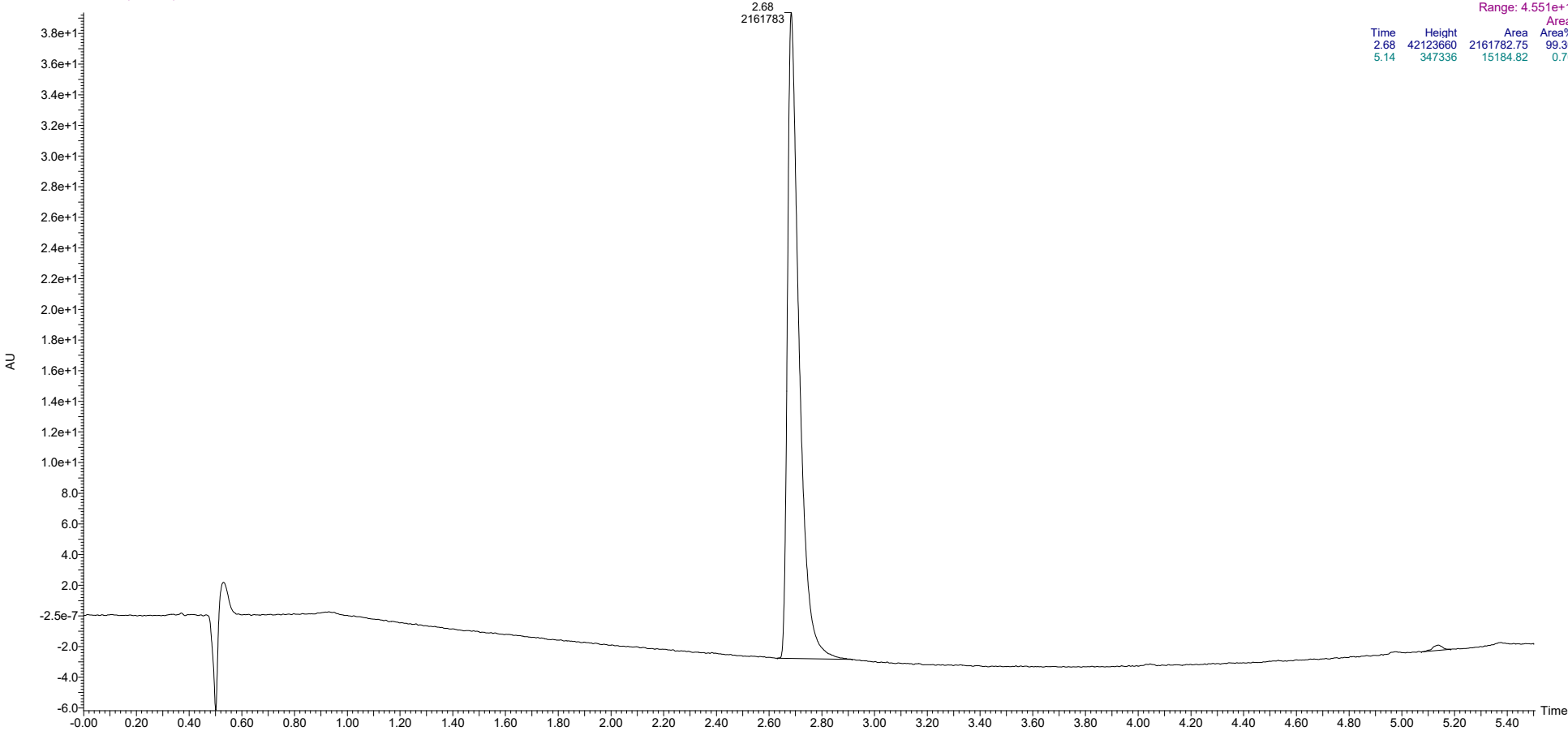


HPLC of compound 14f



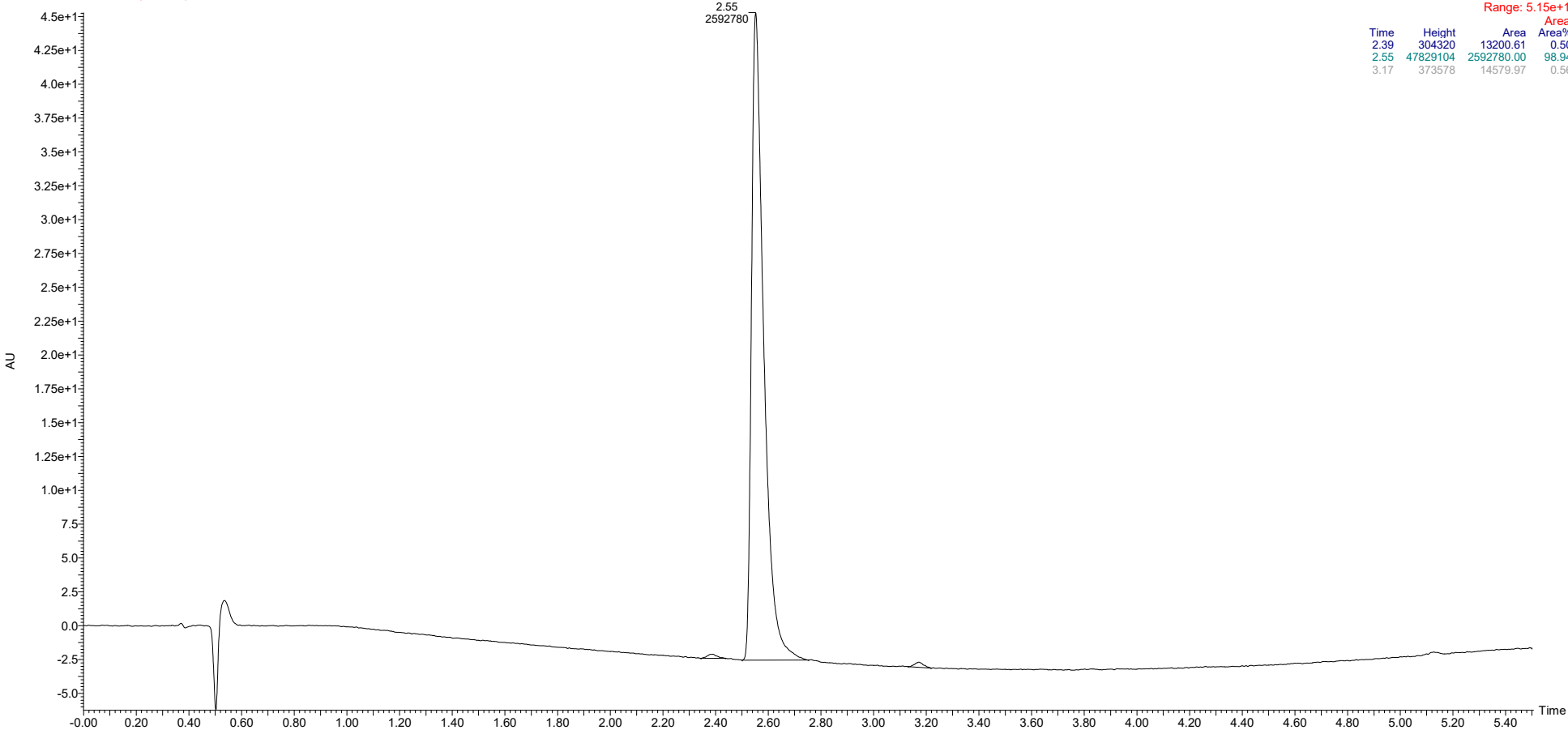
HPLC of compound **14g**

PCMT-PPC20-4A Sm (Mn, 2x3)



HPLC of compound **14h**

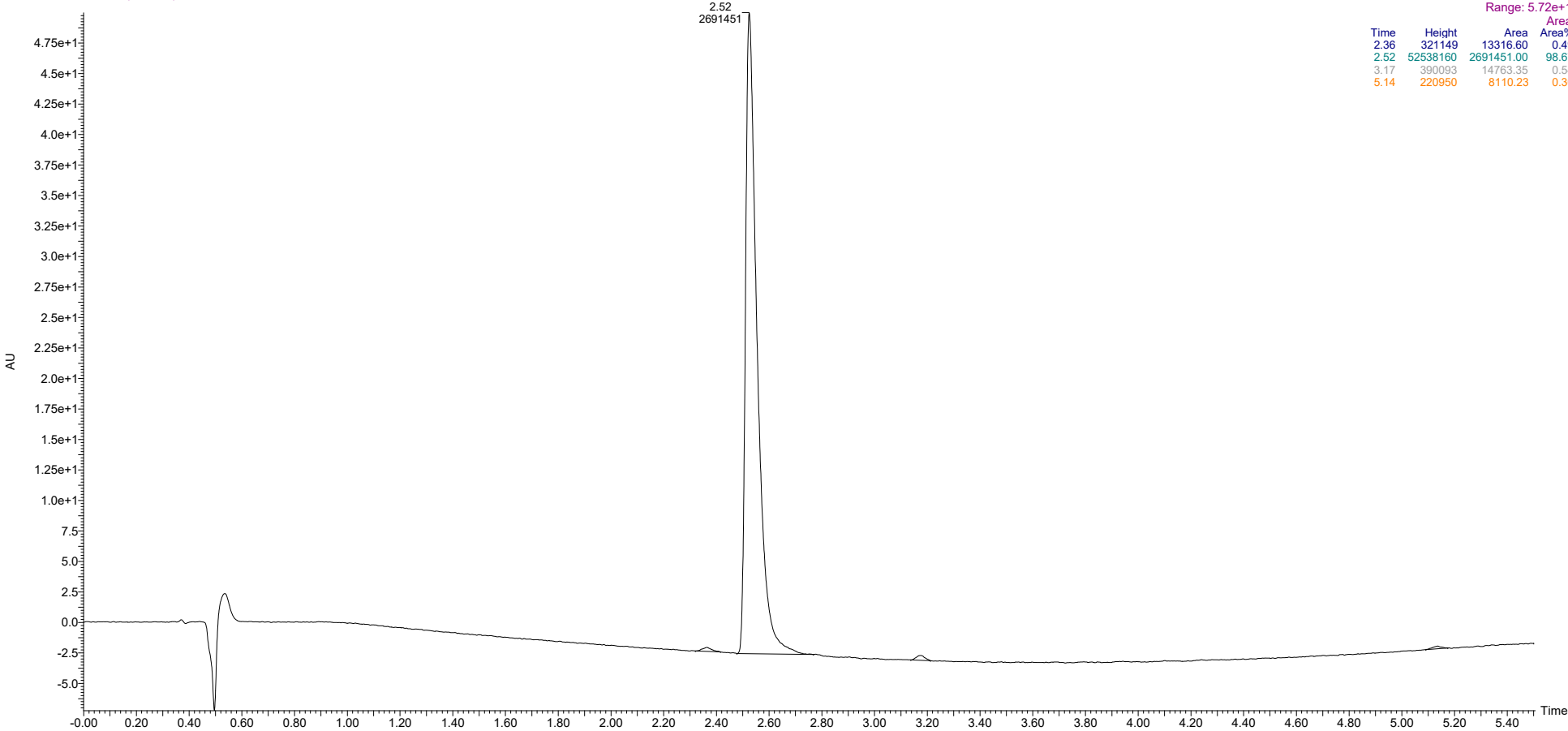
PCMT-PPC14-4A-X Sm (Mn, 2x3)



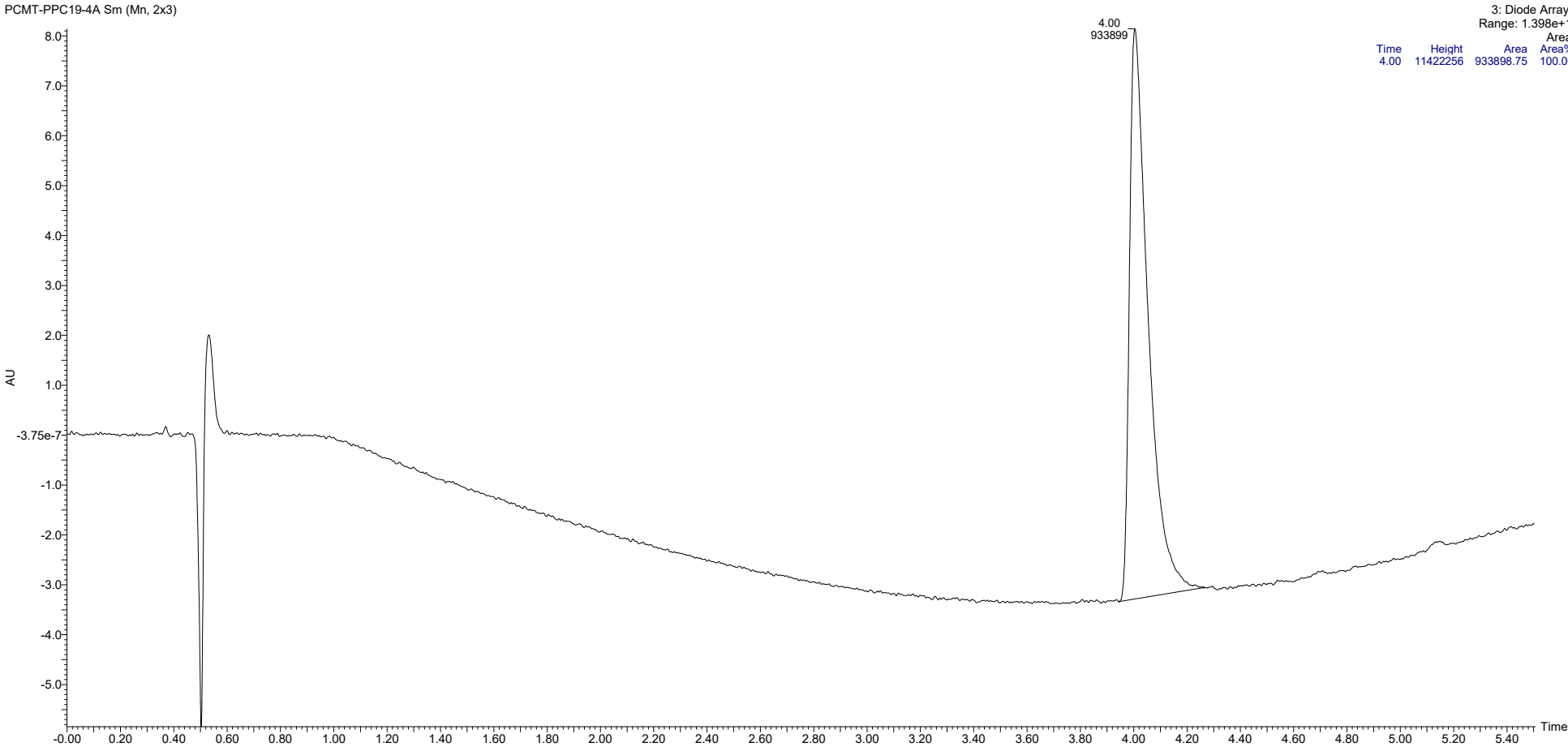
3: Diode Array  
Range: 5.15e+1

HPLC of compound 14i

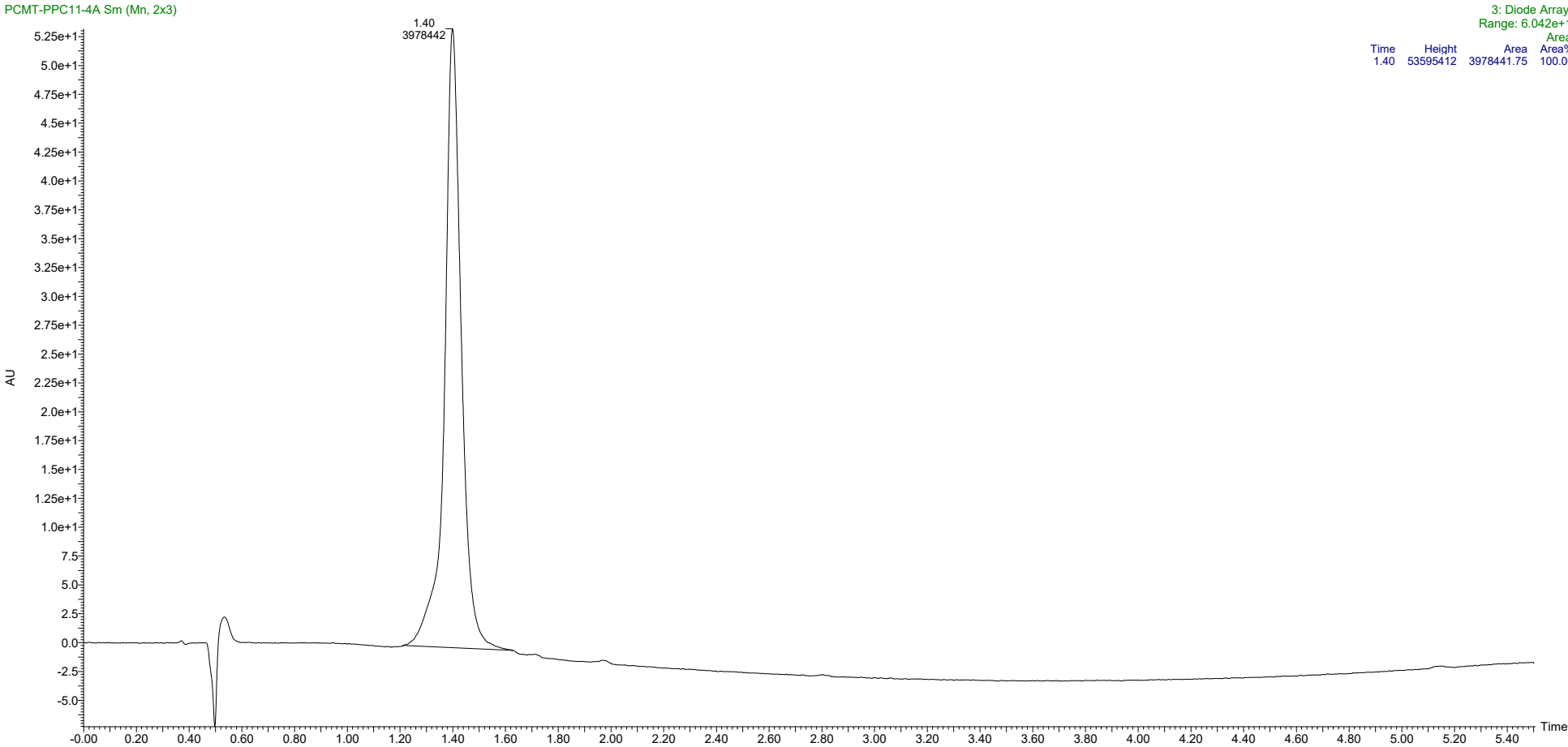
PCMT-PPC15-4A Sm (Mn, 2x3)



HPLC of compound 14j

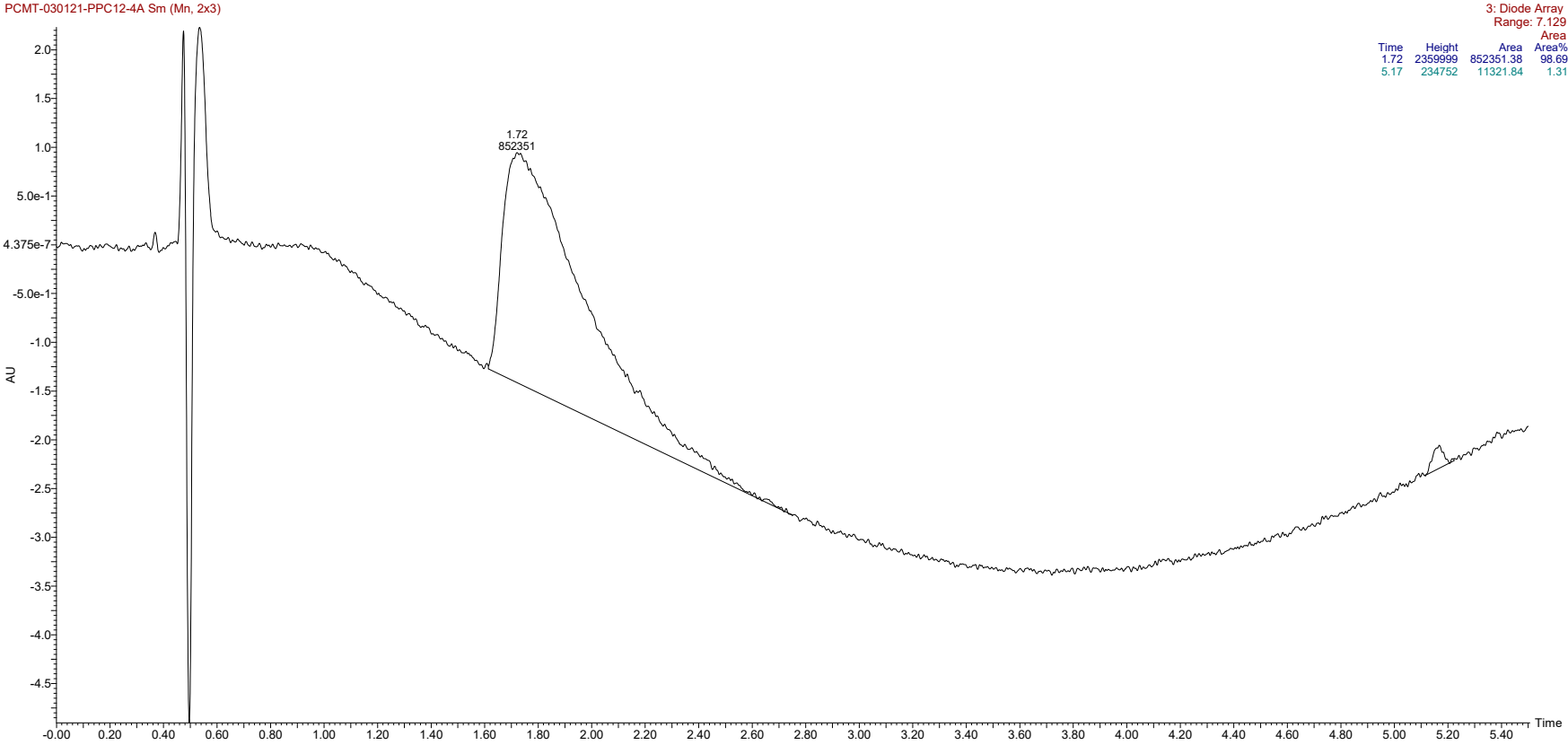


HPLC of compound **14k**

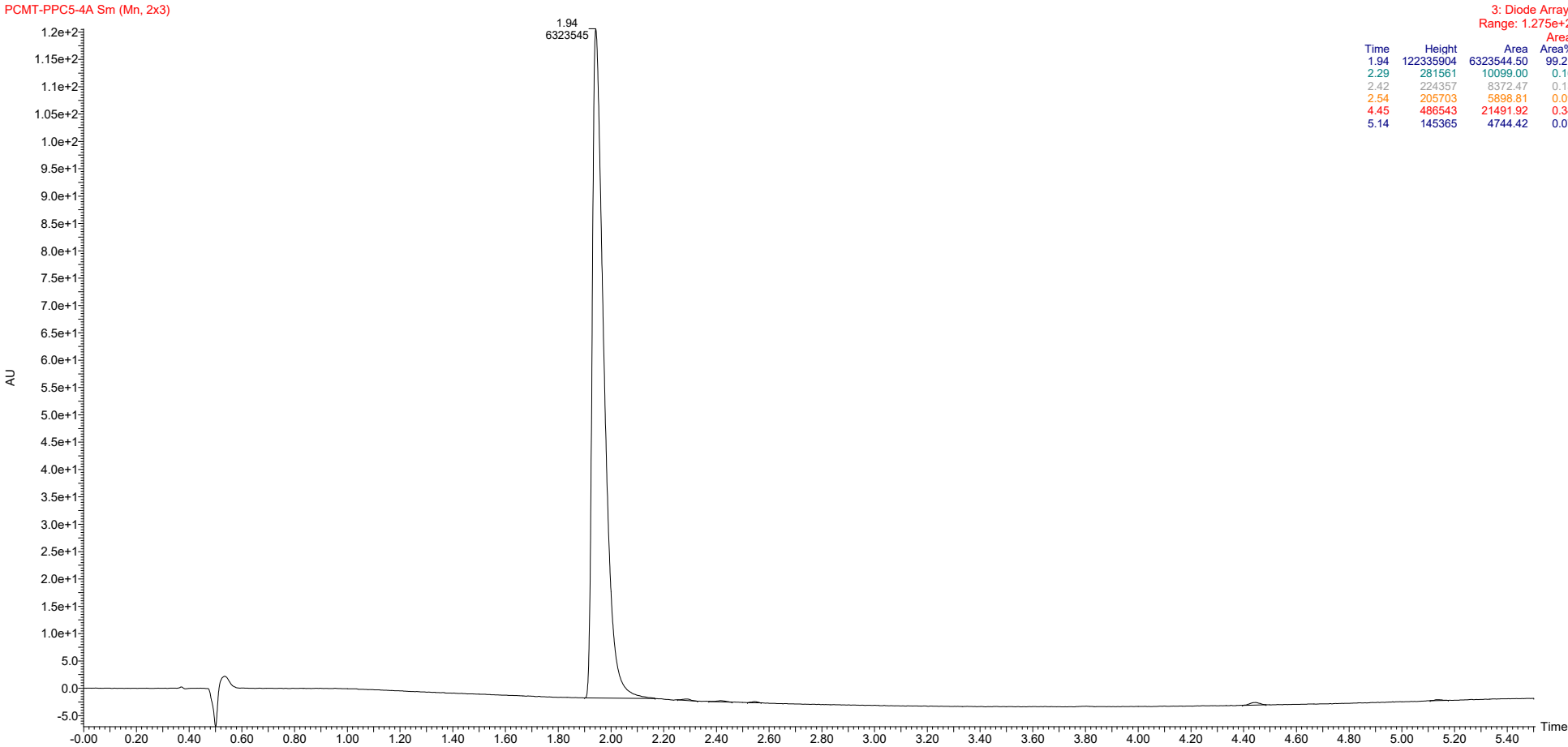




HPLC of compound 14I

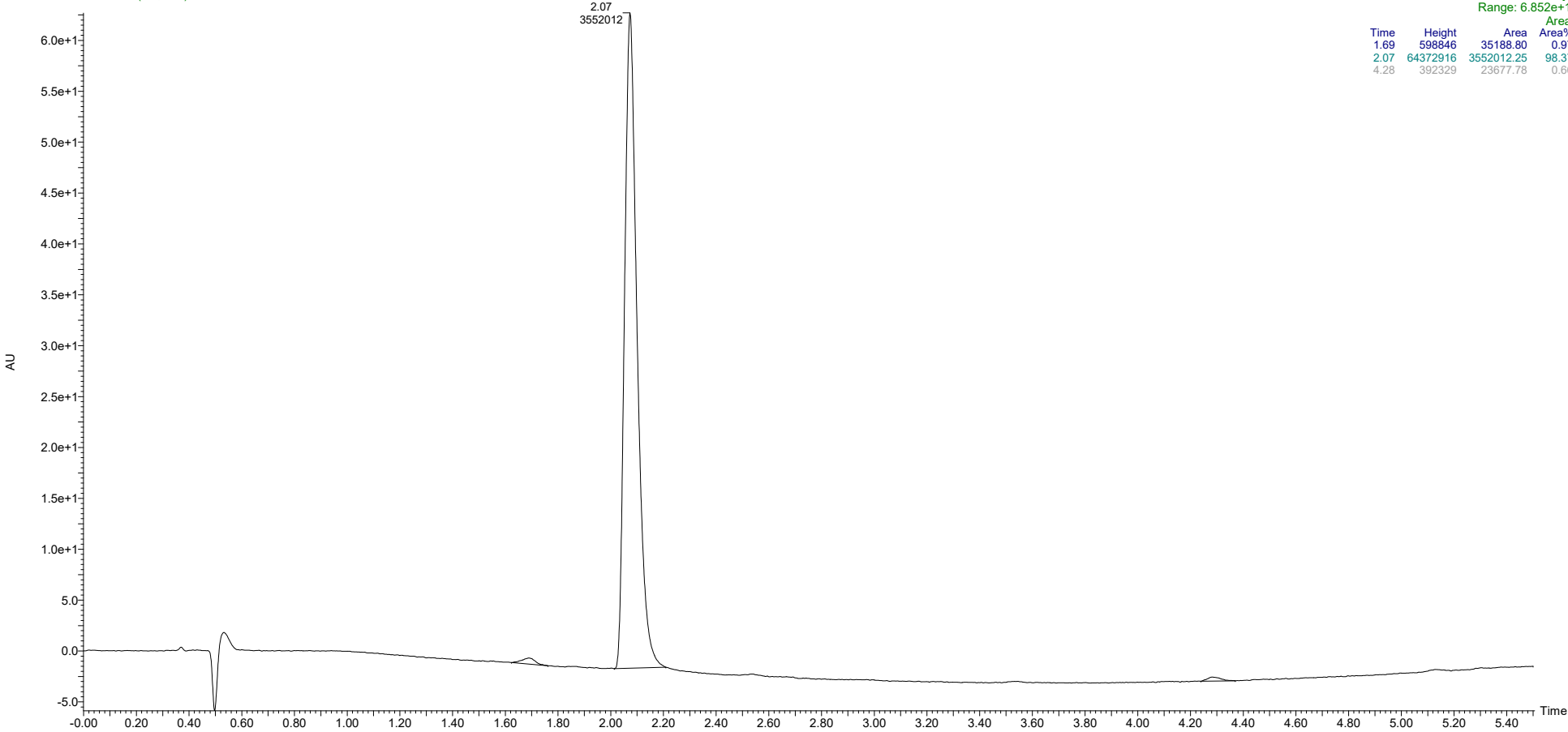


HPLC of compound **14m**

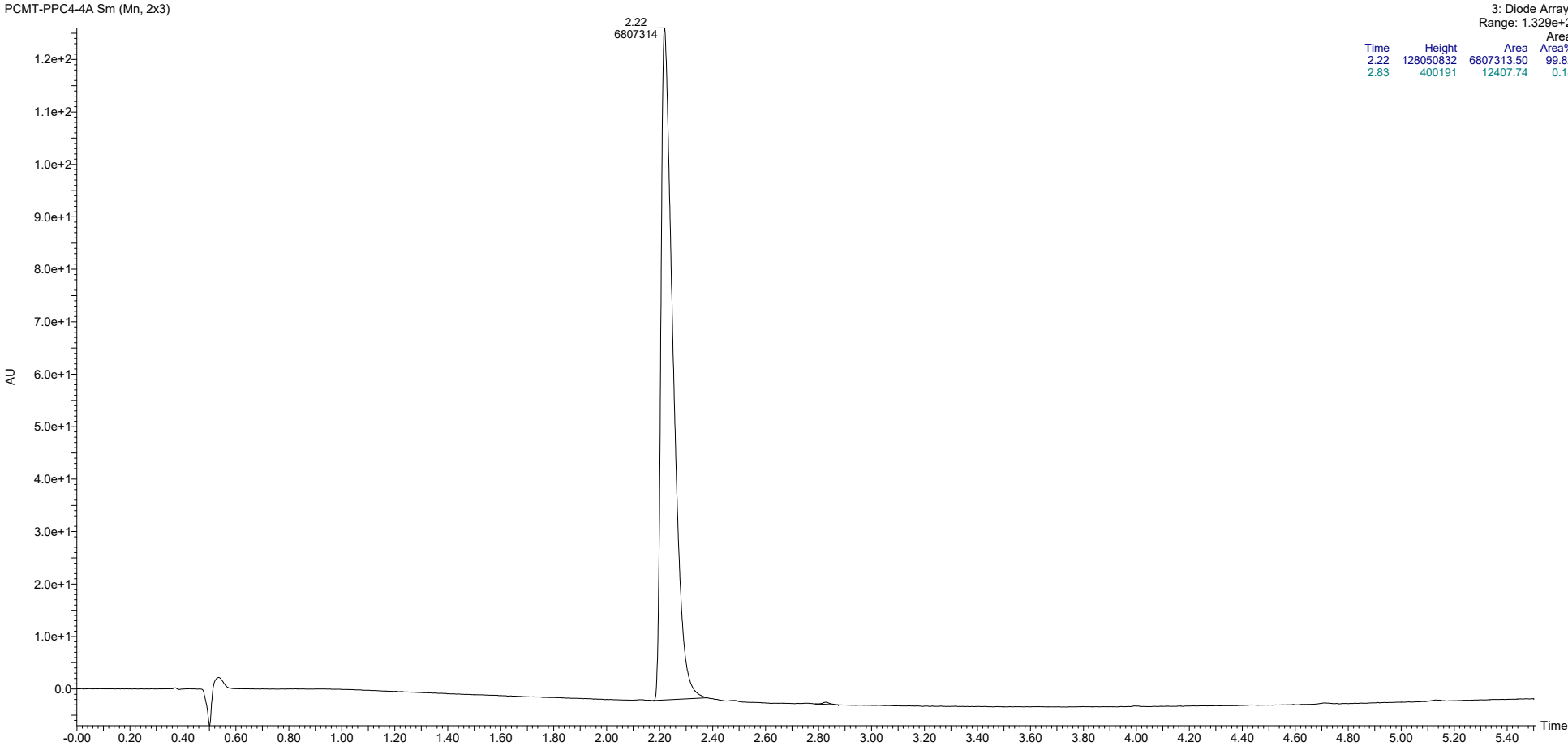


HPLC of compound 14n

PCTH-092119-01-X Sm (Mn, 2x3)

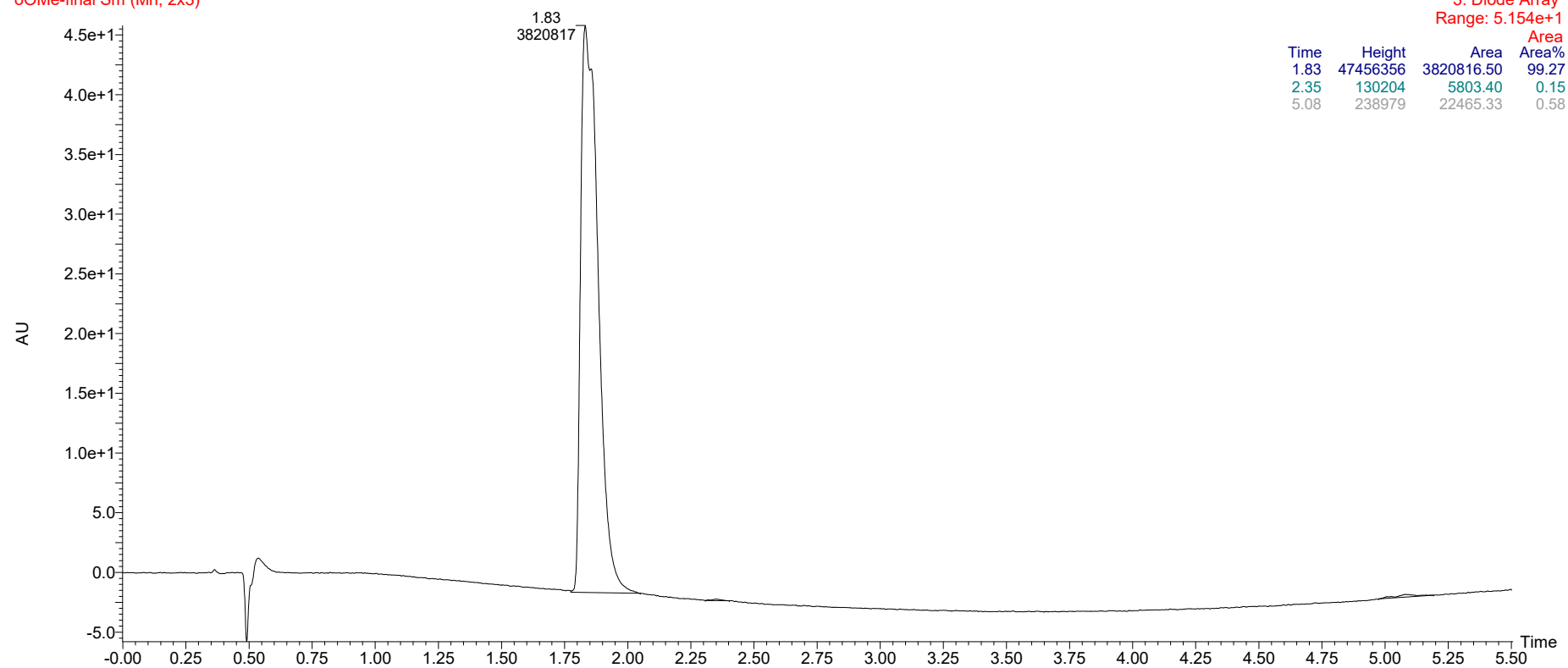


HPLC of compound **14o**

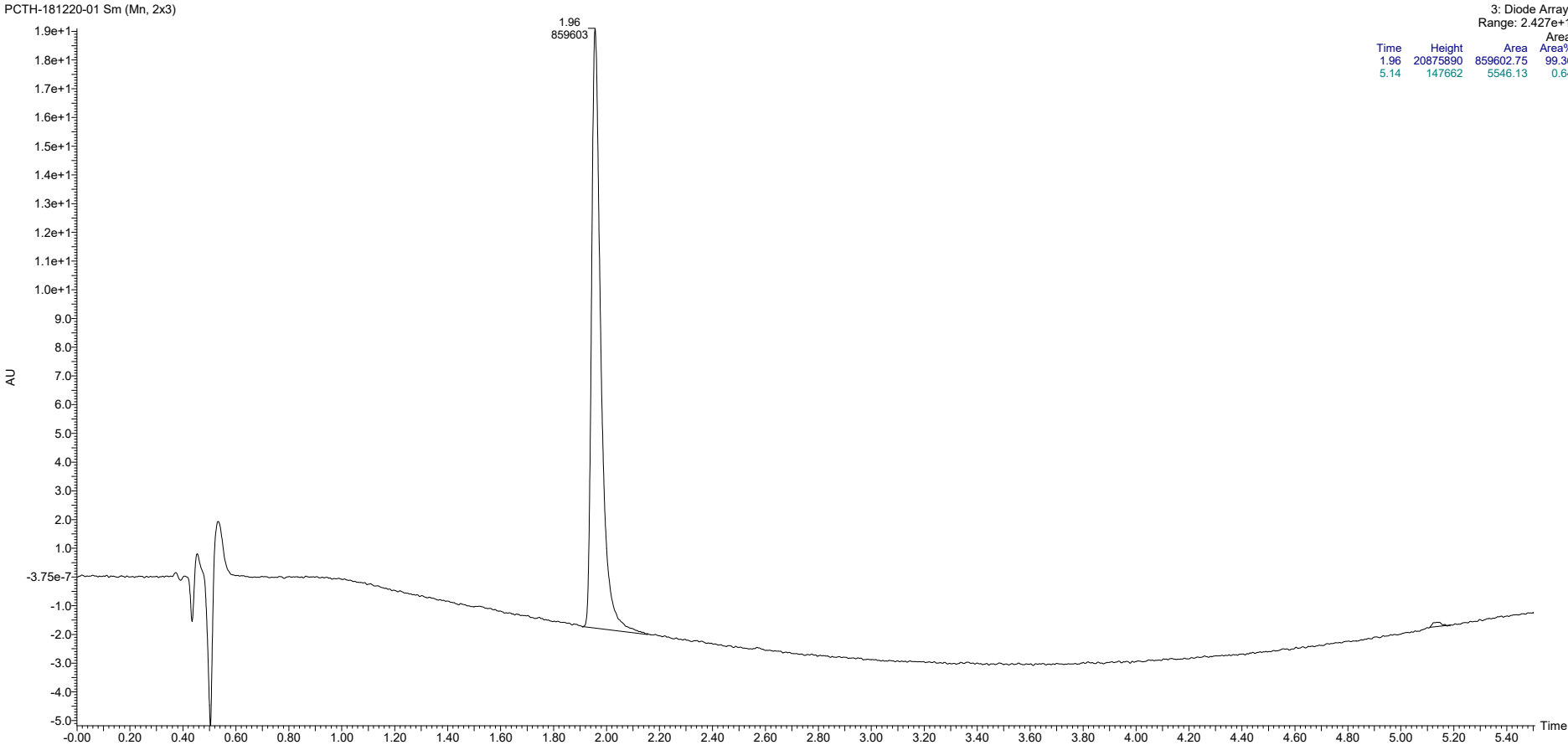


# HPLC of compound 14p

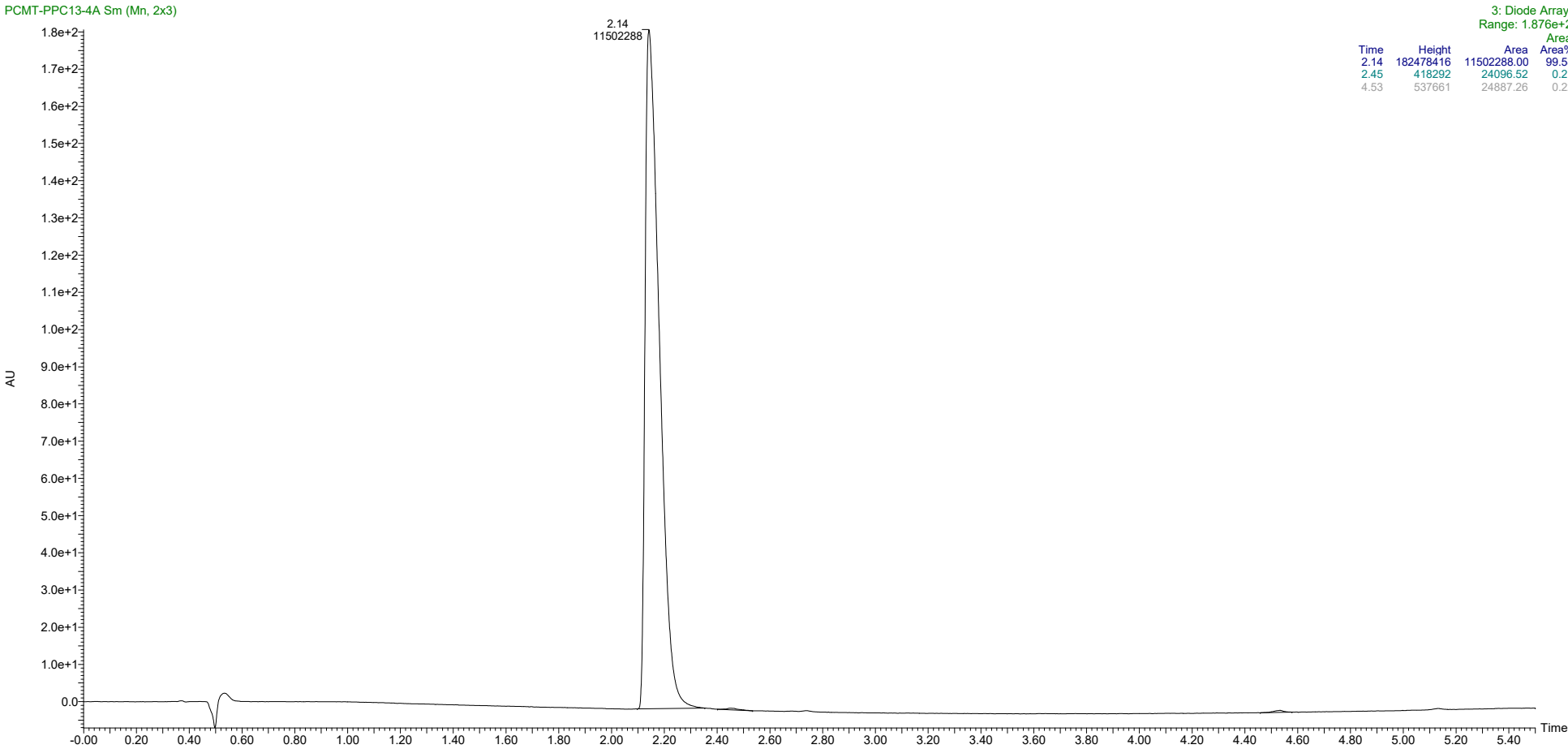
oOMe-final Sm (Mn, 2x3)



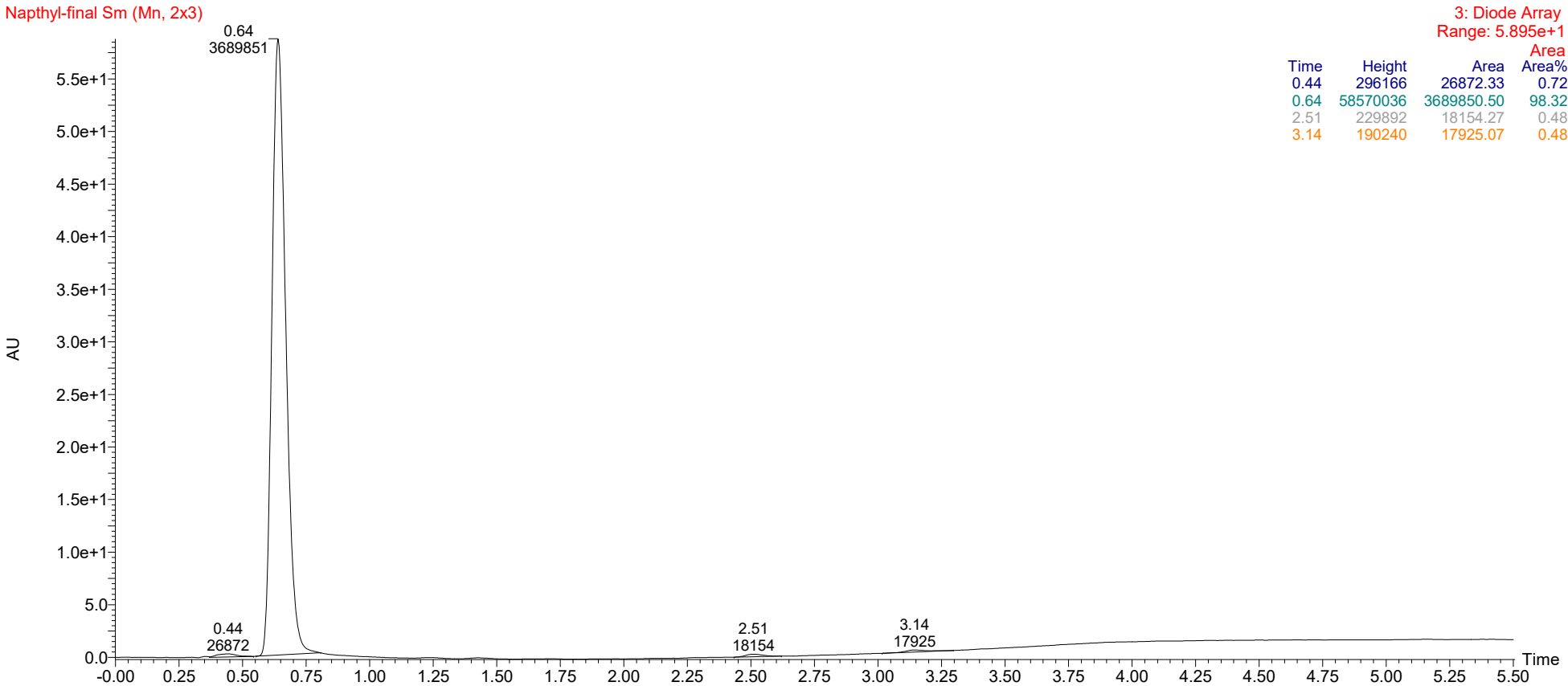
HPLC of compound 14q



HPLC of compound 14r



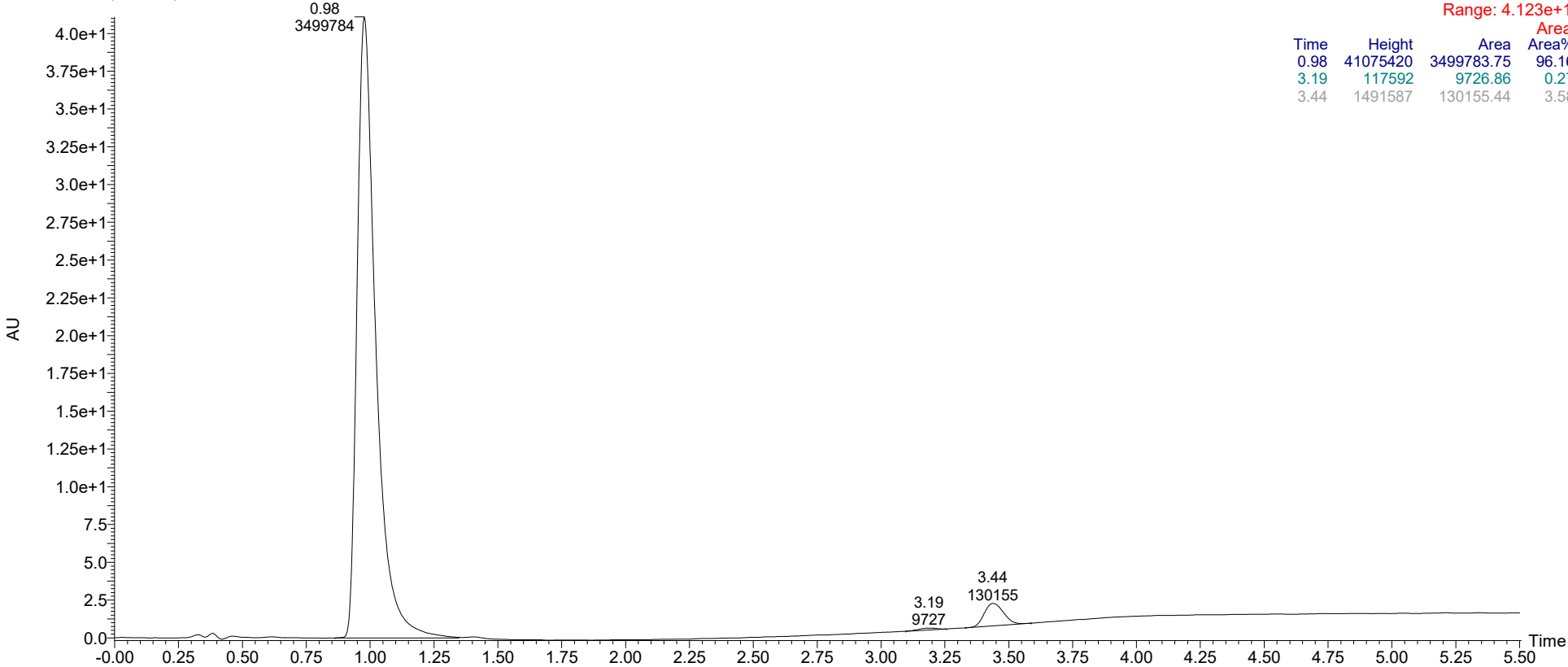
HPLC of compound 14s





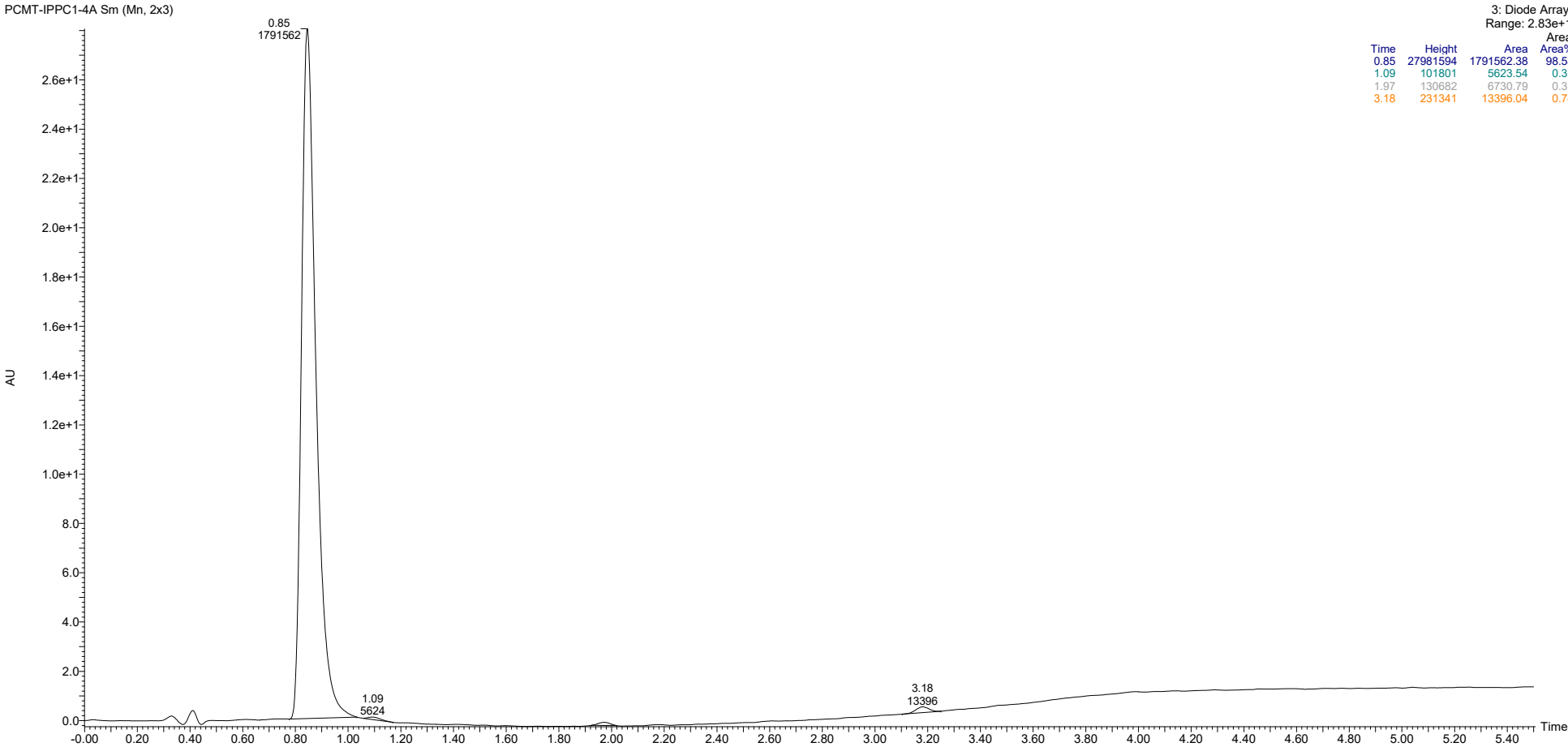
HPLC of compound 14t

FST-final Sm (Mn, 2x3)



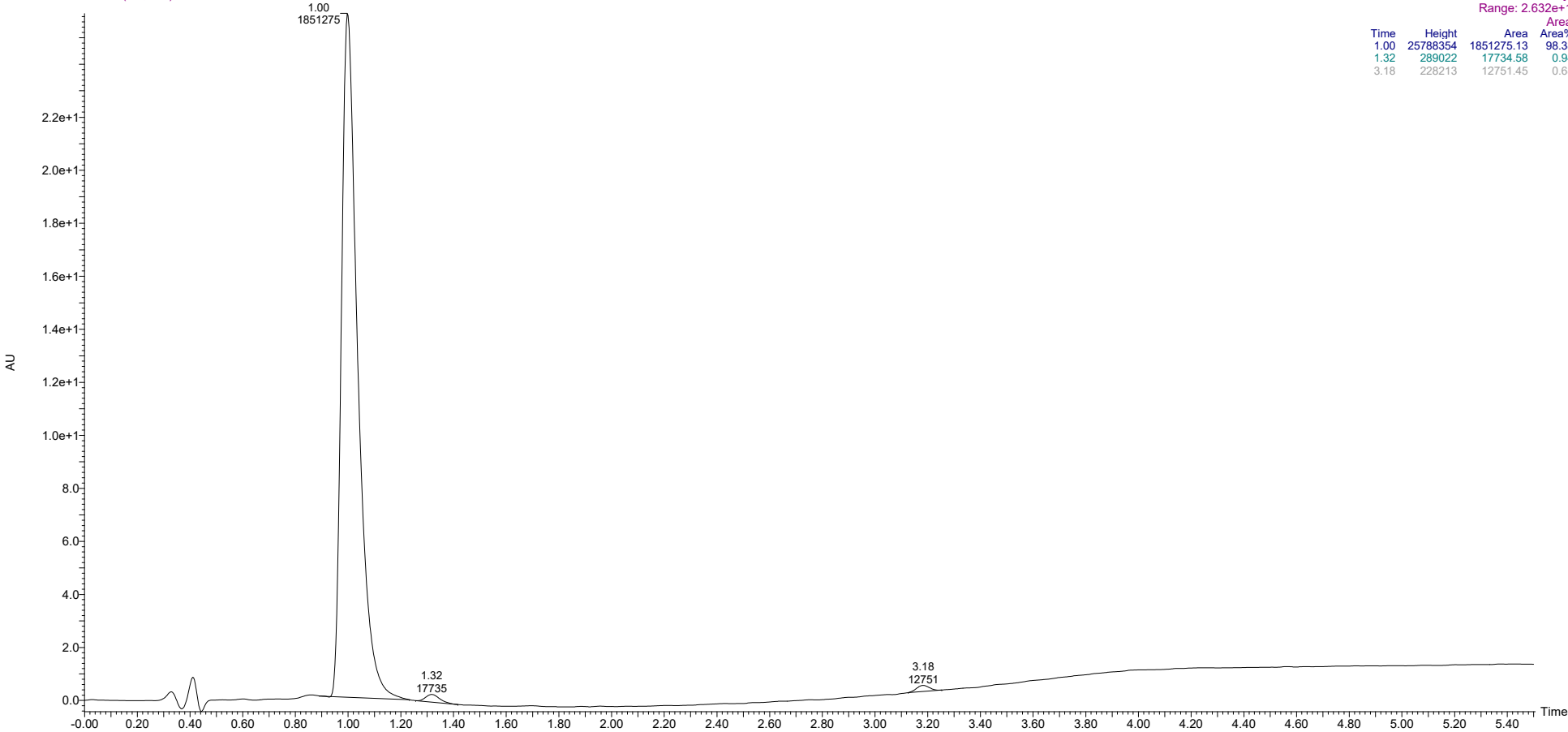
3: Diode Array  
Range: 4.123e+1

HPLC of compound **15a**



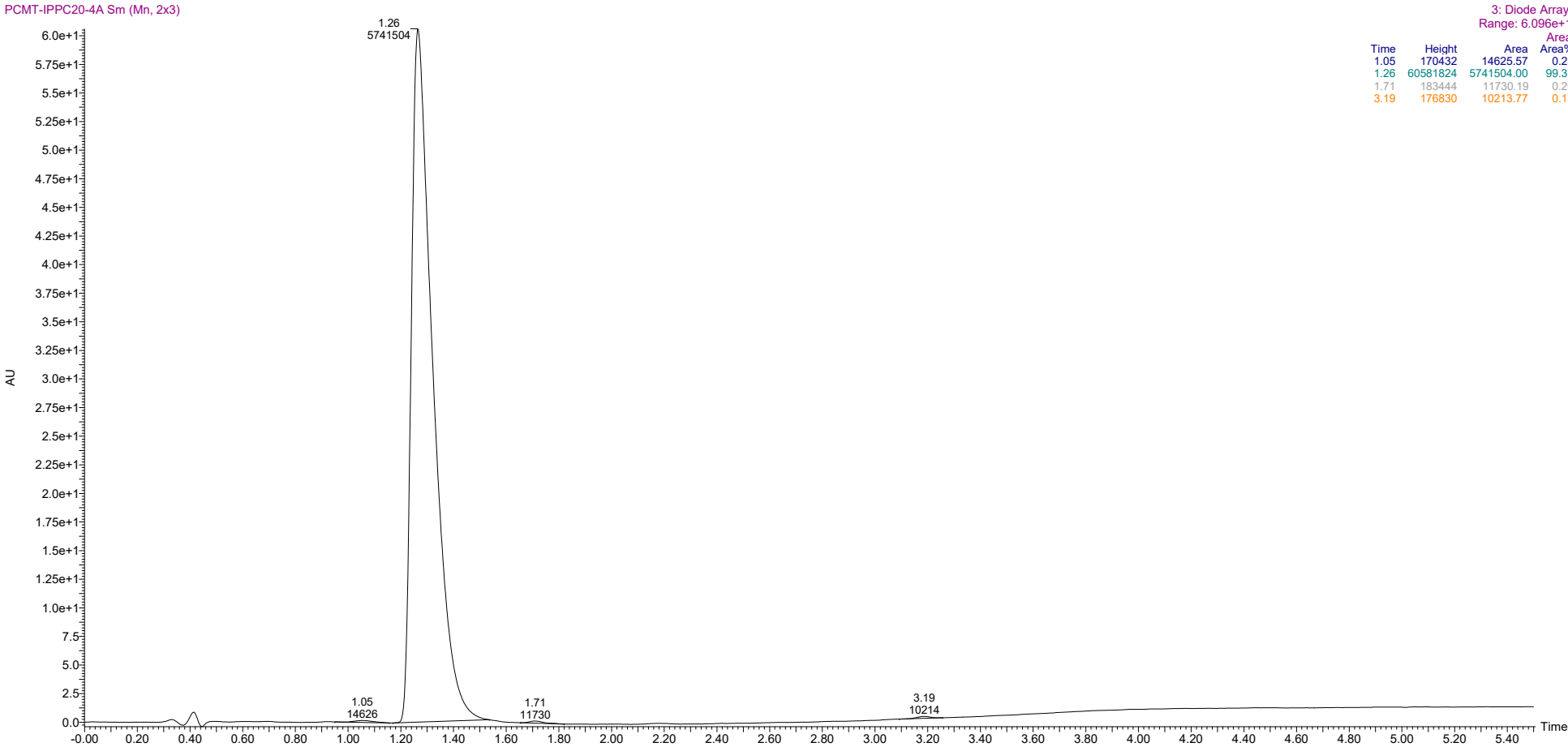
HPLC of compound **15b**

PCMT-IPPC2-4A Sm (Mn, 2x3)

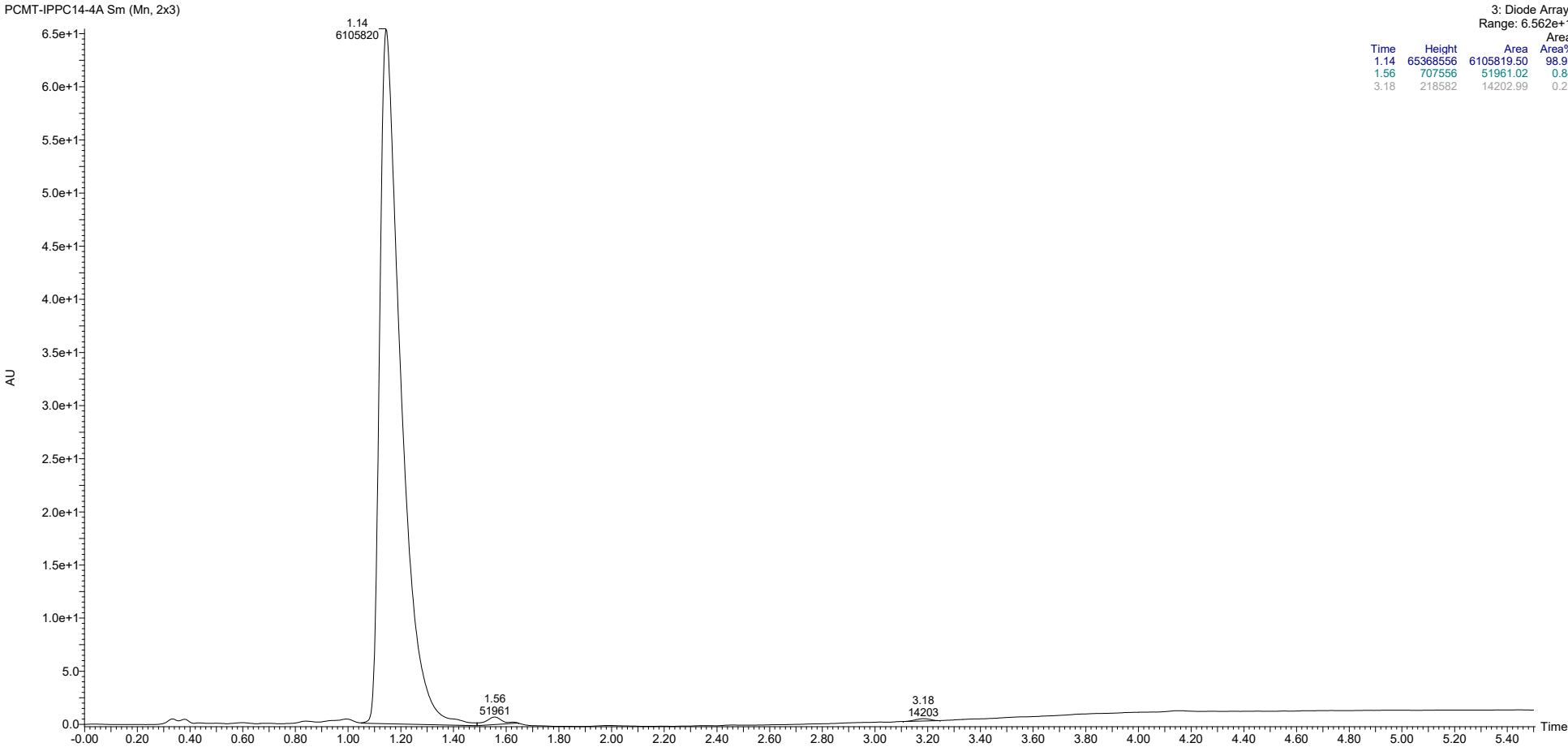


3: Diode Array  
Range: 2.632e+1

HPLC of compound 15c



HPLC of compound **15d**



## References

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