

# **6-(Ar)Alkylamino-Substituted Uracil Derivatives: Lipid Mimetics With Potent Activity at the Orphan G Protein-Coupled Receptor 84 (GPR84)**

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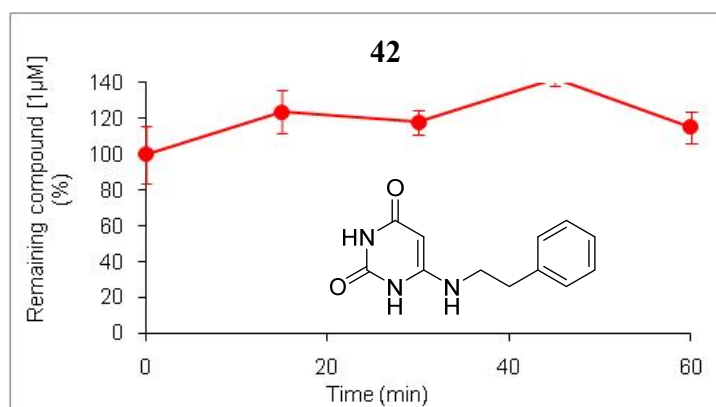
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**Figure S1.** Metabolic stability of compound **42** in human liver microsomes. The stability of the compound was tested at a concentration of 1  $\mu$ M in human liver microsomes (0.5 mg/ml, mixed gender, pooled).

**Table S1. Potency of GPR84 agonists at the human fatty acid receptor FFAR1**

Compound	<u>Agonist screening<sup>a</sup></u>	<u>Antagonist screening<sup>a</sup></u>
	EC <sub>50</sub> ± SEM (μM) (% effect ± SEM) <sup>b</sup>	IC <sub>50</sub> ± SEM (μM) (% inhibition ± SEM) <sup>b</sup>
<b>TUG-424</b>	<b>0.144 ± 0.048</b>	-
<b>4</b>	(-5 ± 3)	(-4 ± 5)
<b>13</b>	(3 ± 7)	(-19 ± 9)
<b>14</b>	(11 ± 11)	(1 ± 5)
<b>15</b>	(4 ± 3)	(-9 ± 5)
<b>16</b>	(-3 ± 4)	(5 ± 10)
<b>17</b>	(-6 ± 3)	(-16 ± 6)
<b>18</b>	(2 ± 2)	(-0 ± 4)
<b>19</b>	(3 ± 4)	(8 ± 9)
<b>20</b>	(5 ± 4)	(-0 ± 11)
<b>21</b>	(-2 ± 3)	(-1 ± 9)
<b>22</b>	(-5 ± 2)	(1 ± 2)
<b>23</b>	(5 ± 14)	(-8 ± 9)
<b>24</b>	(-6 ± 5)	(15 ± 16)
<b>25</b>	(3 ± 3)	(6 ± 10)
<b>26</b>	(2 ± 3)	(-11 ± 3)
<b>27</b>	(3 ± 2)	(2 ± 7)
<b>28</b>	(6 ± 2)	(12 ± 5)
<b>29</b>	(3 ± 3)	(1 ± 8)

<b>30</b>	$(-3 \pm 2)$	$(-10 \pm 3)$
<b>31</b>	$(4 \pm 3)$	$(8 \pm 4)$
<b>32</b>	$(-8 \pm 2)$	$(-3 \pm 5)$
<b>33</b>	$(3 \pm 7)$	$(-19 \pm 9)$
<b>34</b>	$(6 \pm 4)$	$(-2 \pm 5)$
<b>35</b>	$(5 \pm 11)$	$(2 \pm 6)$
<b>36</b>	$(2 \pm 7)$	$(9 \pm 25)$
<b>37</b>	$(7 \pm 3)$	$(1 \pm 9)$
<b>38</b>	$(5 \pm 1)$	$(-1 \pm 10)$
<b>39</b>	$(-6 \pm 4)$	$(-29 \pm 7)$
<b>40</b>	$(2 \pm 5)$	$(2 \pm 8)$
<b>41</b>	$(14 \pm 5)$	$(5 \pm 12)$
<b>42</b>	$(10 \pm 2)$	$(6 \pm 13)$
<b>43</b>	$(1 \pm 4)$	$(2 \pm 8)$
<b>44</b>	$(8 \pm 6)$	$(1 \pm 12)$
<b>45</b>	$(-2 \pm 1)$	$(5 \pm 10)$
<b>46</b>	$(25 \pm 14)$	$(-2 \pm 6)$
<b>47</b>	$(1 \pm 2)$	$(15 \pm 11)$
<b>48</b>	$(-2 \pm 4)$	$(6 \pm 13)$
<b>50</b>	$(-7 \pm 1)$	$(8 \pm 12)$
<b>51</b>	$(11 \pm 7)$	$(8 \pm 9)$
<b>53</b>	$(1 \pm 3)$	$(4 \pm 12)$
<b>54</b>	$(-1 \pm 5)$	$(9 \pm 7)$

<b>57</b>	(0 ± 7)	(21 ± 9)
<b>58</b>	(6 ± 8)	(-2 ± 6)
<b>60</b>	(15 ± 6)	(10 ± 9)
<b>61</b>	(19 ± 11)	(16 ± 10)
<b>62</b>	(23 ± 16)	(17 ± 9)
<b>63</b>	(14 ± 9)	(7 ± 6)
<b>64</b>	(8 ± 7)	(-24 ± 4)
<b>65</b>	(7 ± 8)	(4 ± 13)
<b>66</b>	(15 ± 2)	(8 ± 9)
<b>67</b>	(14 ± 5)	(9 ± 13)
<b>72</b>	(7 ± 13)	(14 ± 10)
<b>73</b>	(13 ± 17)	(7 ± 6)
<b>74</b>	(2 ± 5)	(-3 ± 11)
<b>75</b>	(-5 ± 4)	(2 ± 5)
<b>76</b>	(0 ± 3)	(3 ± 12)
<b>77</b>	(14 ± 8)	(0 ± 7)
<b>78</b>	(6 ± 2)	(2 ± 11)
<b>79</b>	(11 ± 1)	(10 ± 8)
<b>80</b>	(7 ± 2)	(-1 ± 6)

<sup>a</sup>Screening of compounds was performed at a concentration of 10  $\mu$ M at the human G<sub>q</sub> protein-coupled receptor FFAR1. The receptor was stably expressed in a 1321N1 astrocytoma cell line and intracellular calcium release was measured.

<sup>b</sup>Effects were normalized to the effects observed with 10  $\mu$ M (agonist screening) and 1  $\mu$ M (antagonist screening) of the standard agonist TUG-424.

Assays were essentially performed as previously described.<sup>1</sup> In brief, 50,000 cells were seeded per well into a black, clear-bottom 96-well plate. After incubating the cells for 1h in HBSS buffer containing 3  $\mu$ M of Fluo-4-AM and 0.06% Pluronic F-127, that solution was exchanged for HBSS. Test compounds were added by a FlexStation<sup>®</sup>3 plate reader.

**Table S2.** Potency of GPR84 agonists at the human fatty acid receptor FFAR4 (short form)

Compound	<u>Agonist screening</u> <sup>a</sup> EC <sub>50</sub> ± SEM (μM) (% effect ± SEM) <sup>b</sup>	<u>Antagonist screening</u> <sup>a</sup> IC <sub>50</sub> ± SEM (μM) (% inhibition ± SEM) <sup>b</sup>
<b>4</b>	(- 1 ± 0)	(22 ± 9)
<b>13</b>	(1 ± 0)	(13 ± 2)
<b>14</b>	(0 ± 0)	(21 ± 3)
<b>15</b>	(2 ± 1)	(20 ± 2)
<b>16</b>	(1 ± 0)	(23 ± 6)
<b>17</b>	(0 ± 0)	(24 ± 8)
<b>18</b>	(1 ± 0)	(18 ± 5)
<b>19</b>	(1 ± 0)	(17 ± 1)
<b>20</b>	(- 2 ± 2)	(11 ± 2)
<b>21</b>	(0 ± 0)	(18 ± 1)
<b>22</b>	(- 1 ± 0)	(26 ± 2)
<b>23</b>	(- 0 ± 0)	(32 ± 9)
<b>24</b>	(-1 ± 0)	(-13 ± 7)
<b>25</b>	(- 3 ± 2)	(21 ± 5)
<b>26</b>	(- 0 ± 0)	(25 ± 10)
<b>27</b>	(1 ± 0)	(13 ± 1)
<b>28</b>	(0 ± 0)	(11 ± 2)
<b>29</b>	(0 ± 0)	(16 ± 2)
<b>30</b>	(0 ± 0)	(23 ± 7)
<b>31</b>	(- 1 ± 0)	(20 ± 19)
<b>32</b>	(0 ± 0)	(17 ± 2)
<b>33</b>	(- 0 ± 1)	(15 ± 1)

<b>34</b>	$(-3 \pm 3)$	$(19 \pm 7)$
<b>35</b>	$(-1 \pm 1)$	$(25 \pm 9)$
<b>36</b>	$(1 \pm 0)$	$(30 \pm 3)$
<b>37</b>	$(1 \pm 0)$	$(16 \pm 13)$
<b>38</b>	$(1 \pm 0)$	$(22 \pm 2)$
<b>39</b>	$(-3 \pm 1)$	$(38 \pm 4)$
<b>40</b>	$(0 \pm 0)$	$(37 \pm 5)$
<b>41</b>	$(1 \pm 0)$	$(5 \pm 16)$
<b>42</b>	$(2 \pm 1)$	$(21 \pm 9)$
<b>43</b>	$(1 \pm 0)$	$(14 \pm 16)$
<b>44</b>	$(-3 \pm 2)$	$(21 \pm 3)$
<b>45</b>	$(1 \pm 1)$	$(15 \pm 6)$
<b>46</b>	$(2 \pm 1)$	$(11 \pm 3)$
<b>47</b>	$(0 \pm 0)$	$(10 \pm 4)$
<b>48</b>	$(0 \pm 1)$	$(17 \pm 3)$
<b>50</b>	$(0 \pm 0)$	$(14 \pm 5)$
<b>51</b>	$(-1 \pm 1)$	$(-8 \pm 12)$
<b>53</b>	$(0 \pm 0)$	$(11 \pm 5)$
<b>54</b>	$(1 \pm 1)$	$(7 \pm 5)$
<b>57</b>	$(1 \pm 1)$	$(15 \pm 4)$
<b>58</b>	$(0 \pm 0)$	$(9 \pm 2)$
<b>60</b>	$(1 \pm 0)$	$(-1 \pm 8)$
<b>61</b>	$(1 \pm 1)$	$(6 \pm 6)$
<b>62</b>	$(1 \pm 0)$	$(14 \pm 6)$
<b>63</b>	$(1 \pm 1)$	$(-19 \pm 8)$
<b>64</b>	$(-0 \pm 0)$	$(27 \pm 6)$



<b>65</b>	(- 2 ± 2)	(16 ± 6)
<b>66</b>	(0 ± 0)	(-12 ± 6)
<b>67</b>	(0 ± 1)	(-13 ± 7)
<b>72</b>	(0 ± 0)	(6 ± 4)
<b>73</b>	(0 ± 1)	(14 ± 3)
<b>74</b>	(0 ± 0)	(14 ± 5)
<b>75</b>	(0 ± 0)	(14 ± 1)
<b>76</b>	(1 ± 1)	(13 ± 3)
<b>77</b>	(0 ± 0)	(27 ± 5)
<b>78</b>	(0 ± 1)	(26 ± 4)
<b>79</b>	(1 ± 1)	(19 ± 8)
<b>80</b>	(1 ± 1)	(15 ± 12)

<sup>a</sup>Compounds were tested at a concentration of 10  $\mu$ M at the human FFAR4 receptor (short form). For  $\beta$ -arrestin assays the receptor was expressed in a CHO- $\beta$ -arrestin cell line (DiscoverX).<sup>2</sup>

<sup>b</sup>Effects were normalized to the effects observed with 30  $\mu$ M (agonist screening) or 4  $\mu$ M (antagonist screening) of the standard agonist TUG-891. N.D., not determined.

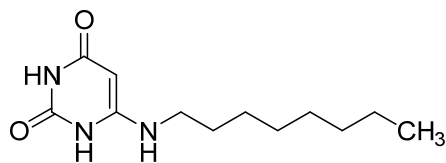
Assays were essentially performed as previously described.<sup>2</sup> In brief, 30,000 cells were seeded into each well of a white 96-well plate. Approximately 4 h before the assay the medium was exchanged for serum-free F12 medium. After addition of test compounds the cells were incubated for 90 min and then a detection reagent was added followed by another 60 min of incubation. The luminescence in each well was measured using an NXT plate reader.

**Table S3.** pEC<sub>50</sub> values of agonists in cAMP and  $\beta$ -arrestin assays

<b>Compound</b>	<b>pEC<sub>50</sub> cAMP assay</b>	<b>pEC<sub>50</sub> <math>\beta</math>-arrestin assay</b>
<b>5</b>	8.18	7.11
<b>4</b>	7.78	6.94
<b>19</b>	6.34	5.32
<b>20</b>	8.31	8.50
<b>21</b>	7.94	6.41
<b>22</b>	7.52	7.47
<b>23</b>	7.68	6.44
<b>28</b>	5.70	5.67
<b>37</b>	6.95	5.38
<b>38</b>	7.42	6.20
<b>42</b>	6.70	5.79
<b>44</b>	7.61	6.89
<b>45</b>	7.89	6.49
<b>46</b>	7.19	5.71
<b>47</b>	8.15	6.28
<b>48</b>	8.60	6.98
<b>49</b>	8.37	6.91
<b>50</b>	7.24	6.12
<b>51</b>	7.36	7.41
<b>52</b>	7.10	6.11
<b>53</b>	6.41	5.51
<b>54</b>	6.90	6.52
<b>55</b>	7.19	6.73
<b>57</b>	7.00	5.77
<b>61</b>	7.36	7.09
<b>63</b>	6.72	5.92
<b>64</b>	7.00	6.13
<b>65</b>	7.13	6.74
<b>67</b>	6.87	6.22
<b>68</b>	6.82	5.74
<b>74</b>	6.43	5.18
<b>77</b>	6.34	6.41
<b>78</b>	6.22	6.38

## Syntheses and analytical data of uracil derivatives

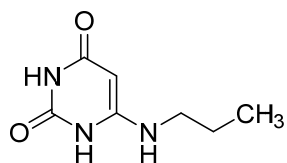
### 6-Octylamino-2,4(1*H*,3*H*)-pyrimidinedione (**4**)



Compound **4** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-aminooctane (50 mmol, 5 equiv.) and was isolated as a white solid (99.0% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)

δ 6.36 (s, 1H), 4.35 (s, 1H), 2.96 (td, *J* = 7.1, 5.1 Hz, 2H), 1.40 (dt, *J* = 62.4, 6.9 Hz, 2H), 1.31 – 1.18 (m, 11H), 0.90 – 0.70 (m, 3H); <sup>13</sup>C NMR (126 MHz, DMSO- *d*<sub>6</sub>) δ 164.44, 155.08, 151.83, 72.46, 32.51, 31.33, 28.75, 28.27, 26.42, 22.19, 14.06; LC-MS (*m/z*): positive mode 240 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 99.0%. Mp: 272-274 °C.

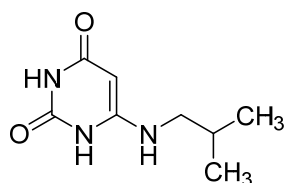
### 6-Propylamino-2,4(1*H*,3*H*)-pyrimidinedione (**14**)



Compound **14** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-aminopropane (50 mmol, 5 equiv.) and was isolated as a yellowish solid (94% yield). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 10.10 (s, 1H), 9.78 (s, 1H),

6.20 (s, 1H), 4.38 (d, *J* = 1.4 Hz, 1H), 2.95 (t, *J* = 7.0 Hz, 2H), 1.49-1.47 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 164.33, 154.20, 150.93, 72.60, 21.63, 11.34; LC-MS (*m/z*): positive mode 169 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 98%. Mp: 281-283°C.

### 6-Isobutylamino-2,4(1*H*,3*H*)-pyrimidinedione (**15**)

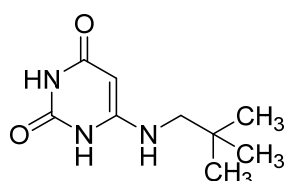


Compound **15** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-aminoisobutane (50 mmol, 5 equiv.) and was isolated as a white solid (98% yield). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ

10.61 – 9.88 (m, 1H), 9.72 (s, 1H), 6.28 – 5.80 (m, 1H), 4.40 (s, 1H), 2.82 (dd, *J* = 6.8, 5.6 Hz, 2H), 1.77 (hept, *J* = 6.7 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 164.34,

154.36, 150.93, 72.63, 48.80, 27.49, 20.04; LC-MS (m/z): positive mode 183  $[M+H]^+$ ; Purity by HPLC UV (254 nm)-ESI-MS: 98%. Mp: >300 °C.

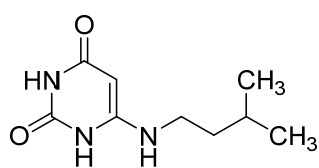
#### 6-Neopentylamino-2,4(1*H*,3*H*)-pyrimidinedione (**16**)



Compound **16** was synthesized using 6-chlorouracil (**11**, 10 mmol) and neopentylamine (50 mmol, 5 equiv.) and was isolated as a white solid (91% yield).  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  10.11 (s, 1H), 9.67 (s, 1H), 6.23 (s, 1H), 4.46 (s, 1H), 2.80 (d,  $J$  = 5.8 Hz, 2H), 0.89 (s, 9H);  $^{13}\text{C}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  164.41,

154.64, 150.79, 72.60, 52.66, 31.95, 27.11. LC-MS (m/z): positive mode 197  $[M+H]^+$ ; Purity by HPLC UV (254 nm)-ESI-MS: 98%. Mp: >300 °C.

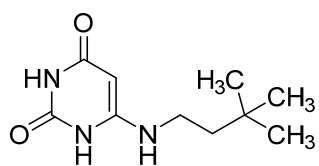
#### 6-Isopentylamino-2,4(1*H*,3*H*)-pyrimidinedione (**17**)



Compound **17** was synthesized using 6-chlorouracil (**11**, 10 mmol) and isopentylamine (50 mmol, 5 equiv.) and was isolated as a yellow solid (94% yield).  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.58 (m, 1H), 4.36 (s, 1H),

2.98 (q,  $J$  = 7.5, 5.3 Hz, 1H), 2.85 – 2.57 (m, 1H), 1.69 – 1.47 (m, 1H), 1.37 (m, 2H), 0.87 (dd,  $J$  = 9.9, 6.6 Hz, 6H);  $^{13}\text{C}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  164.42, 154.73, 151.35, 72.42, 38.03, 37.84, 25.34, 25.16, 22.44, 22.43, 22.40; LC-MS (m/z): positive mode 197  $[M+H]^+$ ; Purity by HPLC UV (254 nm)-ESI-MS: 98%. Mp: 157-159 °C.

#### 6-(3,3-Dimethylbutyl)amino-2,4(1*H*,3*H*)-pyrimidinedione (**18**)

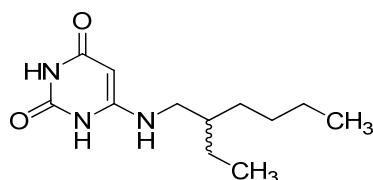


Compound **18** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 3,3-dimethylbutan-1-amine (50 mmol, 5 equiv.) and was isolated as a white solid (89% yield).  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.53 (s, 1H),

4.33 (s, 1H), 3.00 – 2.93 (m, 2H), 1.43 – 1.37 (m, 2H), 0.90 (s, 9H);  $^{13}\text{C}$  NMR (151 MHz, DMSO- $d_6$ )

$\delta$  164.52, 155.54, 152.42, 72.39, 41.84, 38.16, 29.32; LC-MS (m/z): positive mode 211  $[M+H]^+$ ; Purity by HPLC UV (254 nm)-ESI-MS: 98%. Mp:  $>300$  °C.

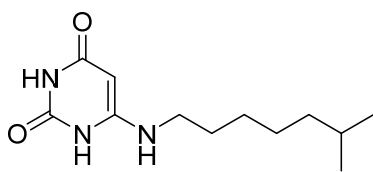
#### 6-(*R,S*)-(2-Ethylhexyl)amino-2,4(1*H*,3*H*)-pyrimidinedione (**24**)



Compound **24** was synthesized using 6-chlorouracil (**11**, 10 mmol) and (*R,S*)-1-amino-2-ethylhexane (50 mmol, 5 equiv.) and was isolated as a yellow solid (81% yield).  $^1\text{H}$  NMR (600 MHz, DMSO-

$d_6$ )  $\delta$  6.35 (s, 1H), 4.36 (s, 1H), 2.88 (t,  $J = 5.9$  Hz, 2H), 1.47 (m, 1H), 1.40 – 1.02 (m, 9H), 0.98 – 0.58 (m, 6H);  $^{13}\text{C}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  164.46, 155.20, 151.74, 72.43, 44.55, 30.48, 28.56, 28.38, 23.79, 22.63, 14.11, 14.05, 10.86, 10.76; LC-MS (m/z): positive mode 239  $[M+H]^+$ ; Purity by HPLC UV (254 nm)-ESI-MS: 97%. Mp: 140-142°C.

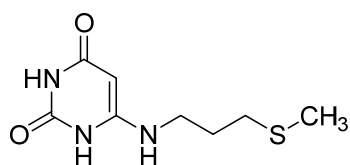
#### 6-(6-Methyl-1-heptylamino)-2,4(1*H*,3*H*)-pyrimidinedione (**25**)



Compound **25** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-amino-6-methylheptane (50 mmol, 5 equiv.) and was isolated as a brown solid (97% yield).  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$

(ppm) 6.39 (s, 1H, 6-NH), 4.38 (s, 1H, 5-H), 2.90 (t,  $J = 5.8$  Hz, 2H, NH-CH<sub>2</sub>), 1.49 (m, 1H, CH), 1.39 – 1.06 (m, 8H, 4 x CH<sub>2</sub>), 0.85 (m, 6H, 2 x CH<sub>3</sub>);  $^{13}\text{C}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  164.34, 150.83, 72.52, 44.46, 38.08, 30.45, 28.36, 23.75, 22.60, 14.03, 10.76; LC-MS (m/z): positive mode 239  $[M+H]^+$ ; Purity by HPLC-UV (254 nm)-ESI-MS: 98.7%. Mp: 166-168 °C

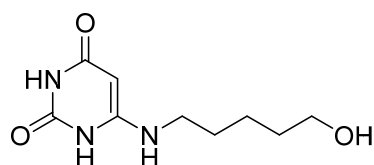
#### 6-(3-(Methylthio)propyl)amino-2,4(1*H*,3*H*)-pyrimidinedione (**26**)



Compound **26** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-amino-3-(methylthio)propane (50 mmol, 5 equiv.) and was isolated as a white solid (87% yield).  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.70 (s,

1H), 4.38 (s, 1H), 3.05 (q,  $J = 6.4$  Hz, 1H), 2.47 (d,  $J = 1.2$  Hz, 2H), 2.02 (s, 3H), 1.68 (m, 2H);  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  164.29, 154.14, 150.90, 72.57, 31.40, 29.08, 29.03, 28.79, 28.76, 28.24, 26.35, 22.19, 14.05; LC-MS (m/z): positive mode 215  $[\text{M}+\text{H}]^{1+}$ ; Purity by HPLC UV (254 nm)-ESI-MS: 99%. Mp: 190-192 °C.

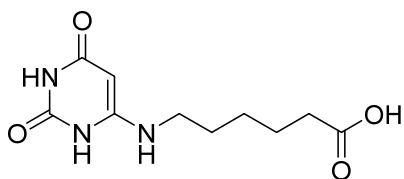
#### 6-(5-Hydroxypentyl)amino-2,4(1*H*,3*H*)-pyrimidinedione (27)



Compound **27** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 5-aminopentan-1-ol (50 mmol, 5 equiv.) and was isolated as a light yellow solid (83% yield).  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$

10.09 (s, 1H), 9.77 (s, 1H), 6.03 (t,  $J = 5.5$  Hz, 1H), 4.38 (d,  $J = 1.2$  Hz, 1H), 4.30 (t,  $J = 5.1$  Hz, 1H), 3.37 (m, 2H), 2.97 (m, 2H), 1.52 – 1.35 (m, 2H), 1.32 – 1.25 (m, 2H);  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  164.29, 154.14, 150.90, 72.57, 31.40, 29.08, 29.03, 28.79, 28.76, 26.35, 22.19, 14.05; LC-MS (m/z): positive mode 227  $[\text{M}+\text{H}]^{1+}$ ; Purity by HPLC UV (254 nm)-ESI-MS: 97.3%.

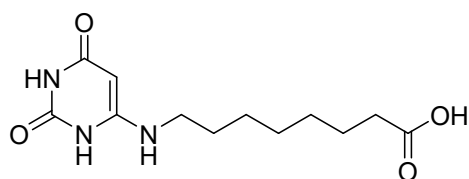
#### 6-((2,6-Dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)amino)hexanoic acid (29)



Compound **29** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 6-aminohexanoic acid (50 mmol, 5 equiv.) and was isolated as white solid (82% yield).  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  6.38

(s, 1H), 4.36 (s, 1H), 2.97 (dd,  $J = 6.5, 3.8$  Hz, 4H), 2.15 (dt,  $J = 18.2, 7.3$  Hz, 2H), 1.49 (m, 4H), 1.29 (m, 2H);  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  175.50, 165.08, 155.13, 151.76, 73.18, 34.87, 29.51, 26.79, 25.17; LC-MS (m/z): positive mode 241  $[\text{M}+\text{H}]^{1+}$ ; Purity by HPLC UV (254 nm)-ESI-MS: 96%. Mp: 235-237 °C.

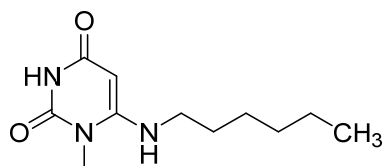
#### 8-((2,6-Dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)amino)octanoic acid (30)



The compound **30** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 8-aminooctanoic acid (50 mmol, 5 equiv.) and was isolated as a white solid (80% yield). <sup>1</sup>H NMR (500 MHz,

DMSO-*d*<sub>6</sub>) δ 10.06 (s, 3H), 6.24 (s, 1H), 4.37 (s, 1H), 2.97 (q, *J* = 6.5 Hz, 2H), 2.17 (t, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 10.0 Hz, 4H), 1.27 (s, 6H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 174.76, 164.33, 154.28, 150.96, 72.48, 47.17, 34.01, 32.15, 28.61, 28.53, 28.46, 28.35, 28.17, 26.23, 24.61; LC-MS (*m/z*): positive mode 269 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 98.4%. Mp: 221-223 °C.

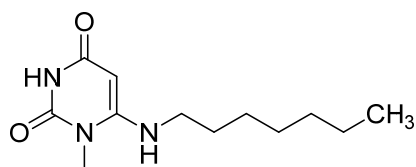
#### 6-Hexylamino-1-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**34**)



Compound **34** was synthesized using 6-chloro-1-methyluracil (**12b**, 10 mmol) and 1-aminohexane (50 mmol, 5 equiv.) and was isolated as white solid (95% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.82

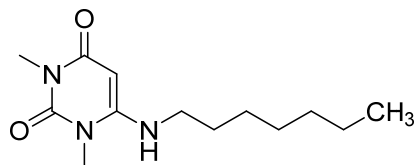
(s, 1H), 6.67 (s, 1H), 4.47 (s, 1H), 3.19 (s, 3H), 3.01 (q, *J* = 6.7 Hz, 2H), 1.71 – 1.40 (m, 2H), 1.28-1.26 (m, 2H), 0.86 (t, *J* = 6.7 Hz, 7H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 162.58, 154.78, 151.30, 73.62, 42.60, 30.85, 28.30, 27.07, 26.18, 25.62, 22.18, 14.03, 13.96; LC-MS (*m/z*): positive mode 225 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 98.4%. Mp: 146-148 °C.

#### 6-Heptylamino-1-methyl-2,4(1*H*,3*H*)-pyrimidinedione (**35**)



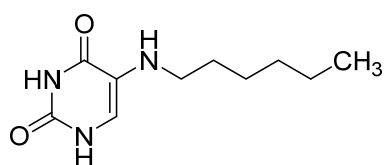
Compound **35** was synthesized using 6-chloro-1-methyluracil (**12b**, 10 mmol) and 1-aminoheptane (50 mmol, 5 equiv.) and was isolated as white solid (99% yield). <sup>1</sup>H NMR (500 MHz, DMSO-

*d*<sub>6</sub>) δ 10.35 (s, 1H), 6.63 (s, 1H), 4.47 (s, 1H), 3.19 (s, 3H), 3.08 – 2.84 (m, 2H), 1.53-1.53 (m, 2H), 1.28 (d, *J* = 8.2 Hz, 11H), 0.95 – 0.62 (m, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 162.59, 154.78, 151.30, 73.64, 42.61, 31.37, 28.27, 26.51, 22.21, 14.08. LC-MS (*m/z*): positive mode 253 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 100%. Mp: 211-213 °C.

**6-(Heptylamino)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (36)**

Compound **36** was synthesized using 6-chloro-1-methyluracil (**12c**, 10 mmol) and heptan-1-amine (50 mmol, 5 equiv.) and was isolated as white solid (91% yield). <sup>1</sup>H NMR (500 MHz, DMSO-

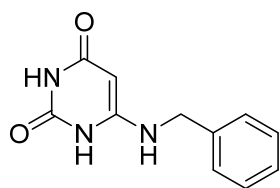
*d*<sub>6</sub>) δ 4.45 (s, 1H), 3.26 (s, 3H), 3.07 (s, 3H), 3.06 – 2.93 (m, 2H), 1.63 – 1.41 (m, 2H), 1.34 – 1.15 (m, 3H), 0.85 (td, *J* = 6.9, 2.6 Hz, 10H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 161.67, 153.29, 151.63, 73.30, 42.44, 31.34, 31.25, 29.39, 28.81, 28.73, 28.59, 28.58, 27.70, 27.14, 27.05, 26.47, 25.95, 22.18, 22.16, 14.03; LC-MS (*m/z*): positive mode 267 [*M*+*H*]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 100%. Mp: 171-173 °C.

**5-Hexylamino-2,4(1*H*,3*H*)-pyrimidinedione (39)**

Compound **39** was synthesized using 5-bromouracil (**13**, 10 mmol) and 1-aminohexane (50 mmol, 5 equiv.) and was isolated as a slightly yellow solid (87% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 6.26 (d,

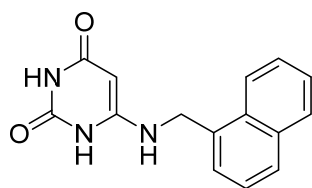
*J* = 4.7 Hz, 1H), 2.76 (q, *J* = 6.6 Hz, 2H), 1.49 (p, *J* = 6.9 Hz, 2H), 1.40 – 1.13 (m, 11H), 0.87 – 0.62 (m, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 14.06, 22.20, 26.81, 28.26, 28.92, 31.36, 43.58, 112.40, 124.12, 149.43, 161.49; LC-MS (*m/z*): positive mode 239 [*M*+*H*]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 98.5%.



**6-Benzylamino-2,4(1*H*,3*H*)-pyrimidinedione (40)**

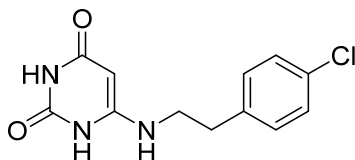
Compound **40** was synthesized using 6-chlorouracil (**11**, 10 mmol) and benzylamine (50 mmol, 5 equiv.) and was isolated as a white solid (82% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.14 (s, 1H), 9.98 (s, 1H), 7.35 (t,

*J* = 7.5 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.29 – 7.24 (m, 1H), 6.57 (t, *J* = 5.9 Hz, 1H), 4.38 (s, 1H), 4.25 (d, *J* = 5.7 Hz, 2H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 164.27, 154.12, 150.92, 138.06, 128.64, 127.35, 127.29, 73.59, 45.09; LC-MS (m/z): positive mode 218 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 100%. Mp: >300 °C.

**6-((Naphth-1-ylmethyl)amino)-2,4(1*H*,3*H*)-pyrimidinedione (41)**

Compound **41** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 1-naphthylmethylamine (50 mmol, 5 equiv.) and was isolated as white solid (92% yield). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 10.18 (s, 1H), 8.06 – 7.93

(m, 2H), 7.93 – 7.86 (m, 1H), 7.67 – 7.53 (m, 3H), 7.53 – 7.46 (m, 2H), 6.67 (t, *J* = 5.4 Hz, 1H), 4.71 (d, *J* = 5.4 Hz, 2H), 4.56 – 4.51 (m, 1H); <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 164.36, 154.15, 150.87, 133.55, 133.00, 130.91, 128.77, 128.19, 126.61, 126.13, 125.64, 123.57, 73.50, 43.33; LC-MS (m/z): positive mode 281 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 99.5%. Mp: >300 °C.

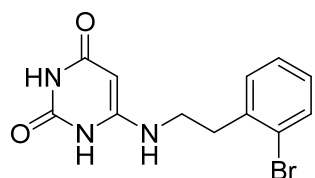
**6-(*p*-Chlorophenethyl)-2,4(1*H*,3*H*)-pyrimidinedione (47)**

Compound **47** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 2-(*p*-chlorophenyl)ethylamine (50 mmol, 5 equiv.) and was isolated as a pale yellow solid (84% yield). <sup>1</sup>H NMR (600 MHz,

DMSO-*d*<sub>6</sub>) δ 10.11 (s, 1H), 8.90 (s, 2H), 6.16 – 5.74 (m, 1H), 4.47 (s, 1H), 3.25 (d, *J* = 6.6 Hz, 2H), 2.78 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 33.53, 42.46, 72.90, 128.43, 128.58,

130.75, 130.80, 131.13, 137.92, 150.95, 154.07, 164.36; LC-MS (m/z): positive mode 265 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 98.5%. Mp: 289-291°C.

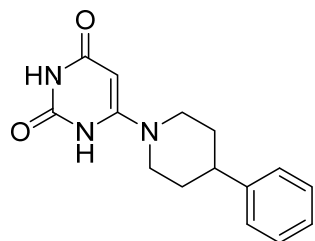
### 6-(*o*-Bromophenethyl)-2,4(1*H*,3*H*)-pyrimidinedione (**59**)



Compound **59** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 2-(*o*-bromophenyl)ethylamine (50 mmol, 5 equiv.) and was isolated as a light yellow solid (85% yield). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 7.50 –

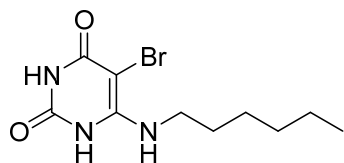
7.36 (m, 4H, Ar-H), 6.22 (s, 1H, NH), 4.50 (s, 1H, 5-H), 3.26 (d, *J* = 7.2 Hz, 2H, NH-CH<sub>2</sub>), 2.81 (t, *J* = 7.2 Hz, 2H, Ar-CH<sub>2</sub>); <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 164.30 (4-C), 153.01 (2-C), 150.92 (6-C), 143.81 (Ar-C), 131.94 (Ar-C), 130.13 (Ar-C), 129.75 (Ar-C), 128.37 (Ar-C), 128.02 (Ar-C), 72.82 (5-C), 41.36 (NHCH<sub>2</sub>), 32.71 (Ar-CH<sub>2</sub>); LC-MS (m/z): positive mode 309 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 96.5%. Mp: >300 °C.

### 6-(4-Phenylpiperidin-1-yl)-2,4(1*H*,3*H*)-pyrimidinedione (**66**)



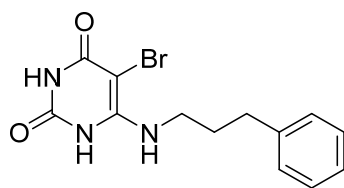
Compound **66** was synthesized using 6-chlorouracil (**11**, 10 mmol) and 4-phenylpiperidine (50 mmol, 5 equiv.) and was isolated as a white solid (78% yield). <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 7.32 – 7.25 (m, 2H), 7.26 – 7.21 (m, 2H), 7.21 – 7.14 (m, 1H), 4.92 – 4.28 (m, 1H), 3.86-3.85 (m,

2H), 2.89 (dd, *J* = 12.9, 2.4 Hz, 2H), 2.74-2.72(m, 1H), 1.78-1.76 (m, 2H), 1.61-1.59 (m, 2H); <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ 164.43, 155.50, 151.70, 145.56, 128.57, 126.83, 126.38, 77.70, 47.19, 41.39, 41.39, 32.19; LC-MS (m/z): positive mode 271 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 100%. Mp: 288-290°C.

**5-Bromo-6-(hexylamino)-2,4(1*H*,3*H*)-pyrimidinedione (72)**

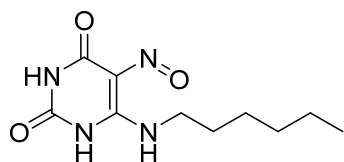
Compound **72** was synthesized using **20** (10 mmol) in pyridine (2 mL) and *N*-bromosuccinimide (NBS, 12 mmol) and was isolated as a yellow solid (93% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 3.21 (q, *J* = 6.9 Hz,

2H), 1.41 (t, *J* = 7.4 Hz, 2H), 1.24 (q, *J* = 7.7, 7.1 Hz, 6H), 0.85 (t, *J* = 6.6 Hz, 3H); <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 159.15, 150.20, 150.01, 147.10, 129.15, 97.76, 41.54, 30.97, 29.19, 25.68, 22.11, 13.99; LC-MS (*m/z*): positive mode 288 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 95.3%. Mp: 293-295 °C.

**5-Bromo-6-((3-phenylpropyl)amino)-2,4(1*H*,3*H*)-pyrimidinedione (75)**

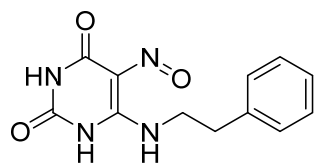
Compound **75** was synthesized from **43** (10 mmol) in pyridine (2 mL) and NBS (12 mmol) and was isolated as a yellow solid (93% yield). <sup>1</sup>H

NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.47 (t, *J* = 6.0 Hz, 1H), 7.27 (dd, *J* = 8.4, 6.8 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 2H), 3.27 – 3.14 (m, 2H), 2.60 – 2.52 (m, 2H), 1.92 – 1.46 (m, 2H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 159.17, 150.38, 150.04, 147.13, 141.50, 129.17, 128.46, 126.00, 97.87, 32.21, 31.13. LC-MS (*m/z*): positive mode 322 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 95.3%. Mp: 273-275 °C.

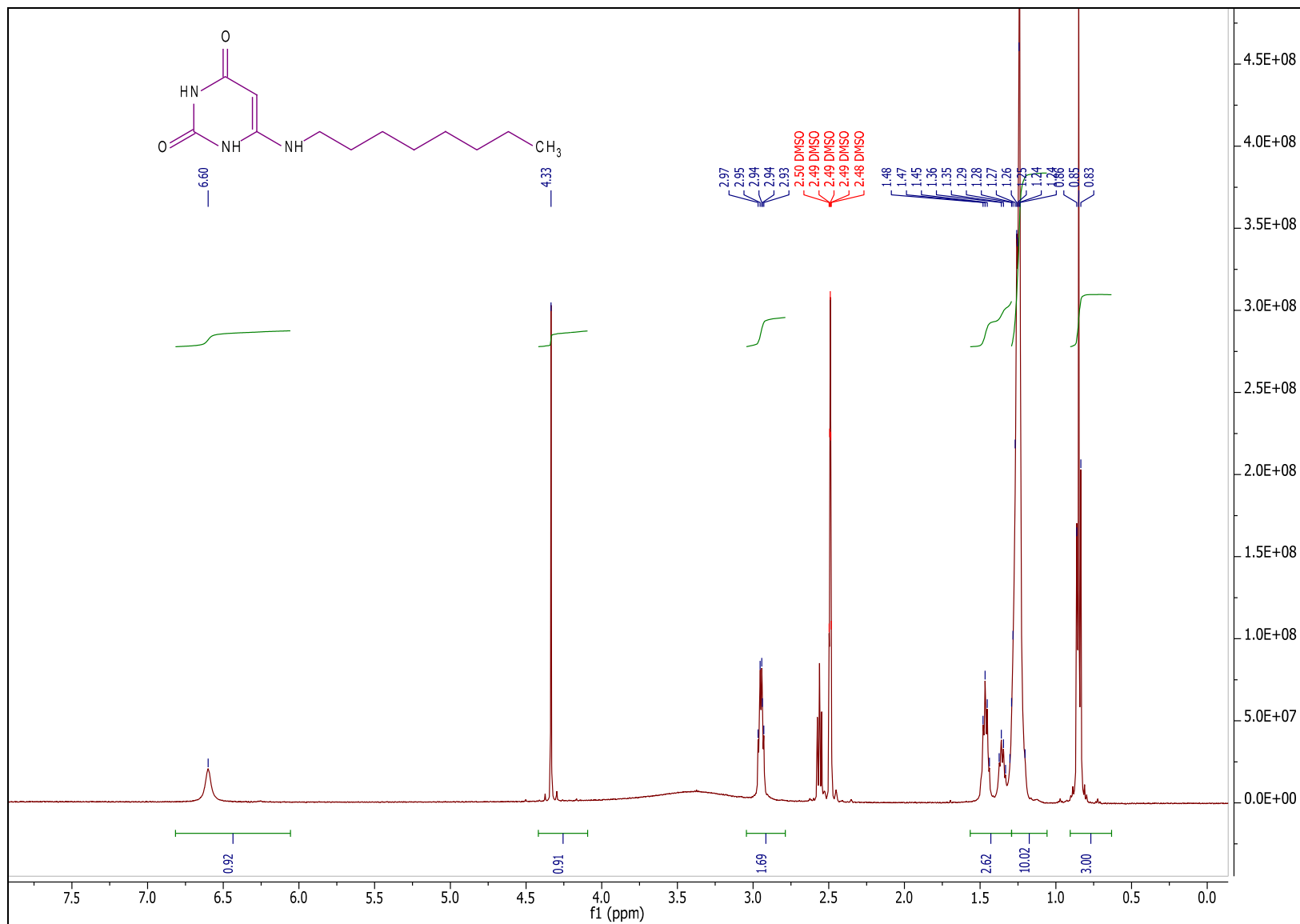
**6-(Hexylamino)-5-nitroso-2,4(1*H*,3*H*)-pyrimidinedione (76)**

Compound **76** was synthesized from **20** (10 mmol) and *N*-bromosuccinimide (10 mmol) in dry pyridine (2 mL) and was isolated as a pink solid (79% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 10.68 (s,

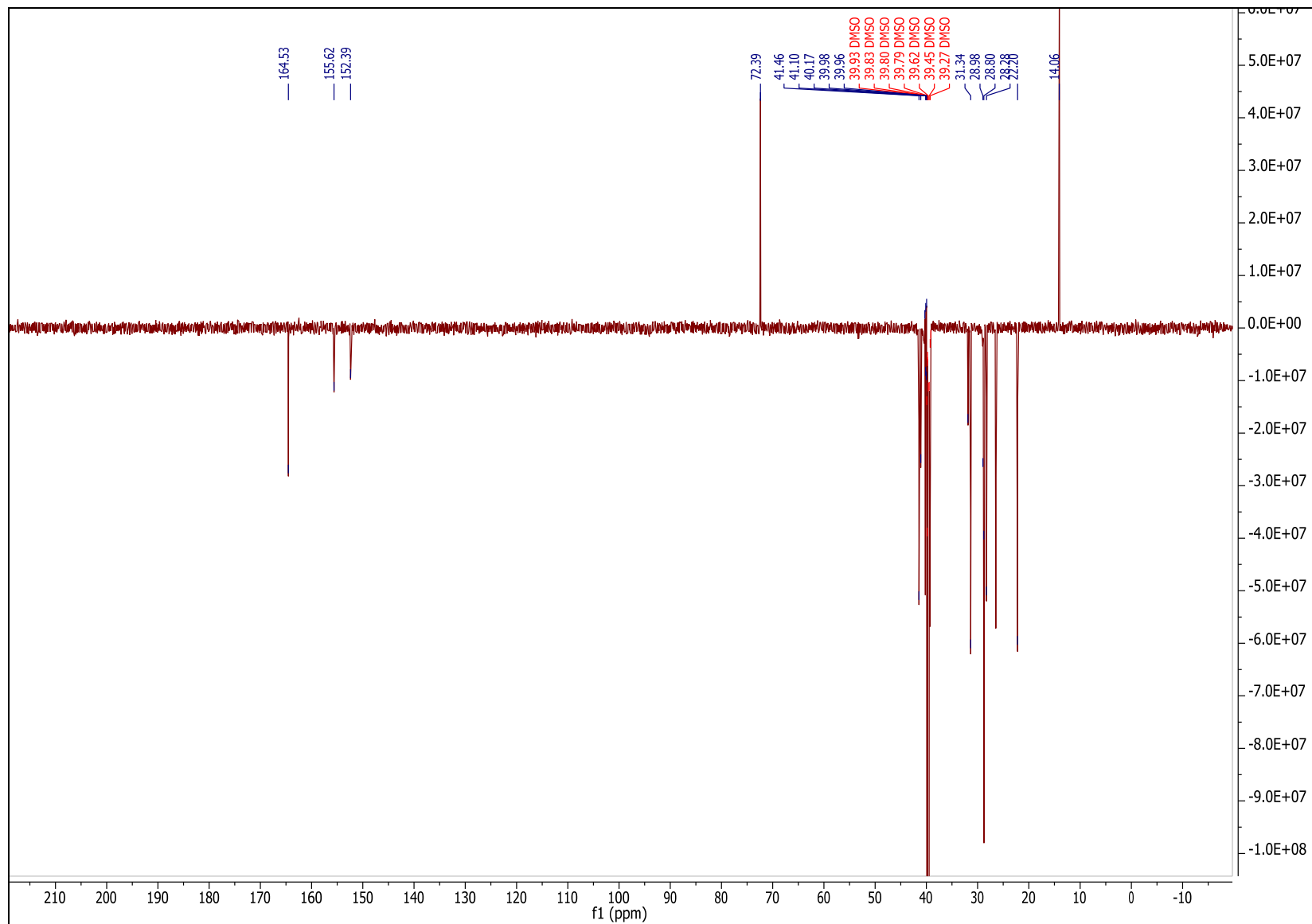
1H), 3.38 – 3.31 (m, 2H), 1.50 (p, *J* = 7.2 Hz, 2H), 1.28-1.26 (m, 6H), 0.99 – 0.72 (m, 3H); <sup>13</sup>C NMR (126 MHz, DMSO) δ 161.97, 152.24, 150.38, 149.59, 138.34, 30.91, 28.31, 26.03, 22.12, 14.00. LC-MS (*m/z*): positive mode 240 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: 97%. Mp: 157-159 °C.

**5-Nitroso-6-(2-phenylethyl)amino-2,4(1*H*,3*H*)-pyrimidinedione (79)**

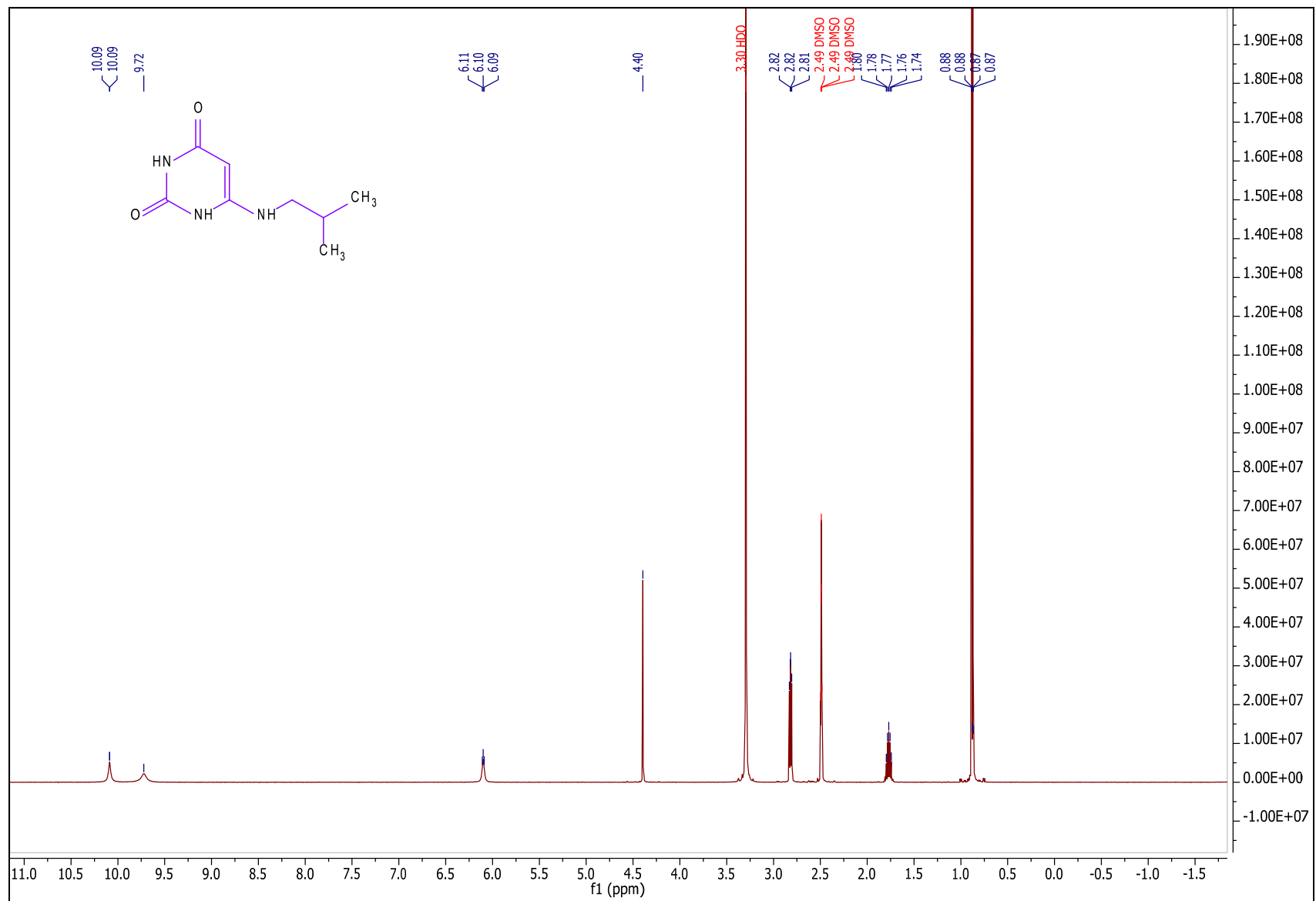
Compound **79** was synthesized from **42** (10 mmol) and *N*-bromosuccinimide (10 mmol) in dry pyridine (2 mL) and was isolated as a pink solid (67% yield). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.82 – 7.10 (m, 5H), 3.80 – 3.50 (m, 2H), 2.86 (t, *J* = 7.3 Hz, 2H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 34.13, 42.49, 126.67, 126.67, 128.53, 128.97, 138.18, 150.10, 160.76. LC-MS (*m/z*): positive mode 260 [M+H]<sup>1+</sup>; Purity by HPLC UV (254 nm)-ESI-MS: >99%. Mp: 219-221°C.



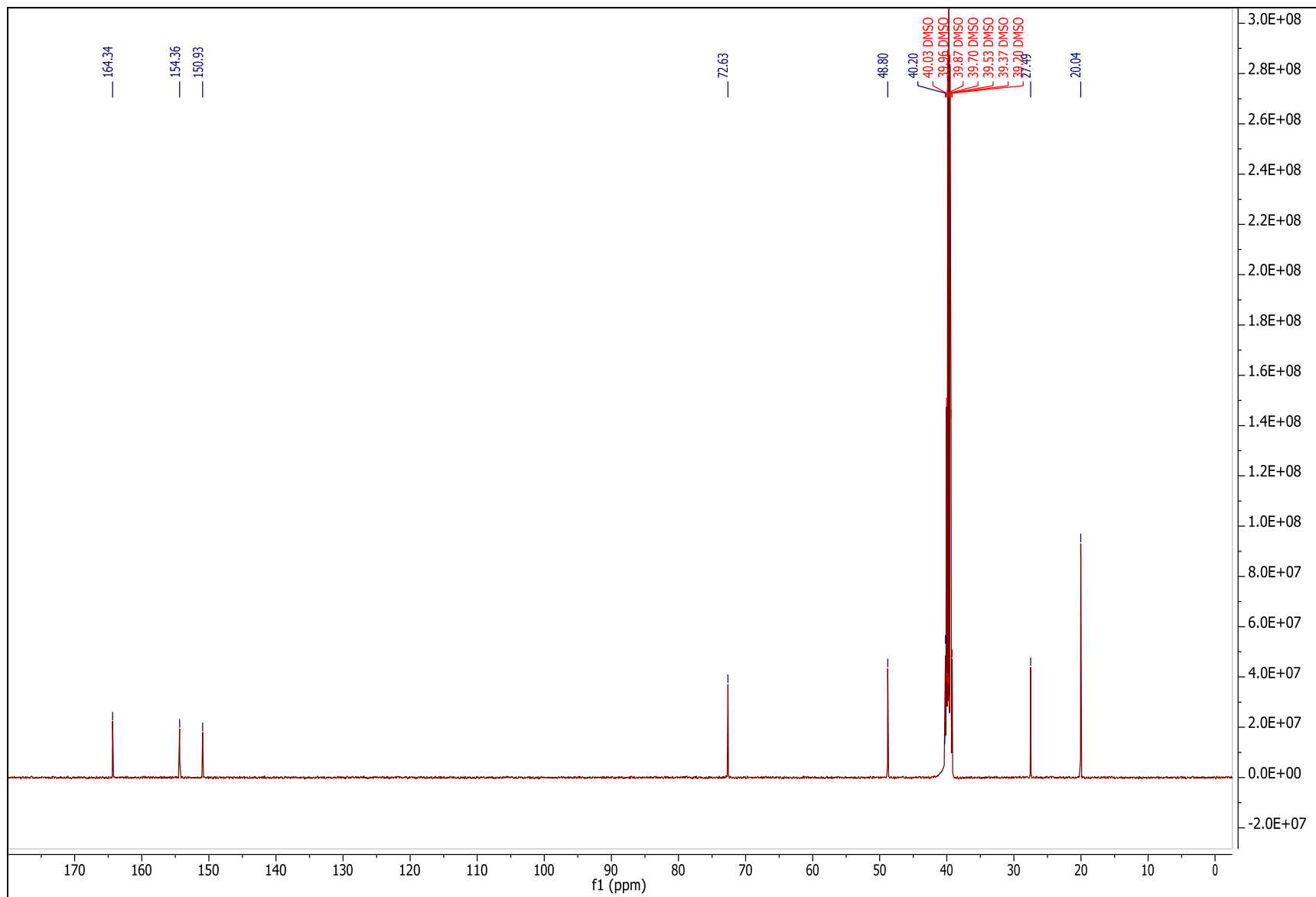
**Figure S1.** <sup>1</sup>H-NMR spectrum of **6** (500 MHz)



**Figure S2.**  $^{13}\text{C}_{\text{apt}}$ -NMR spectrum of **6** (126 MHz)

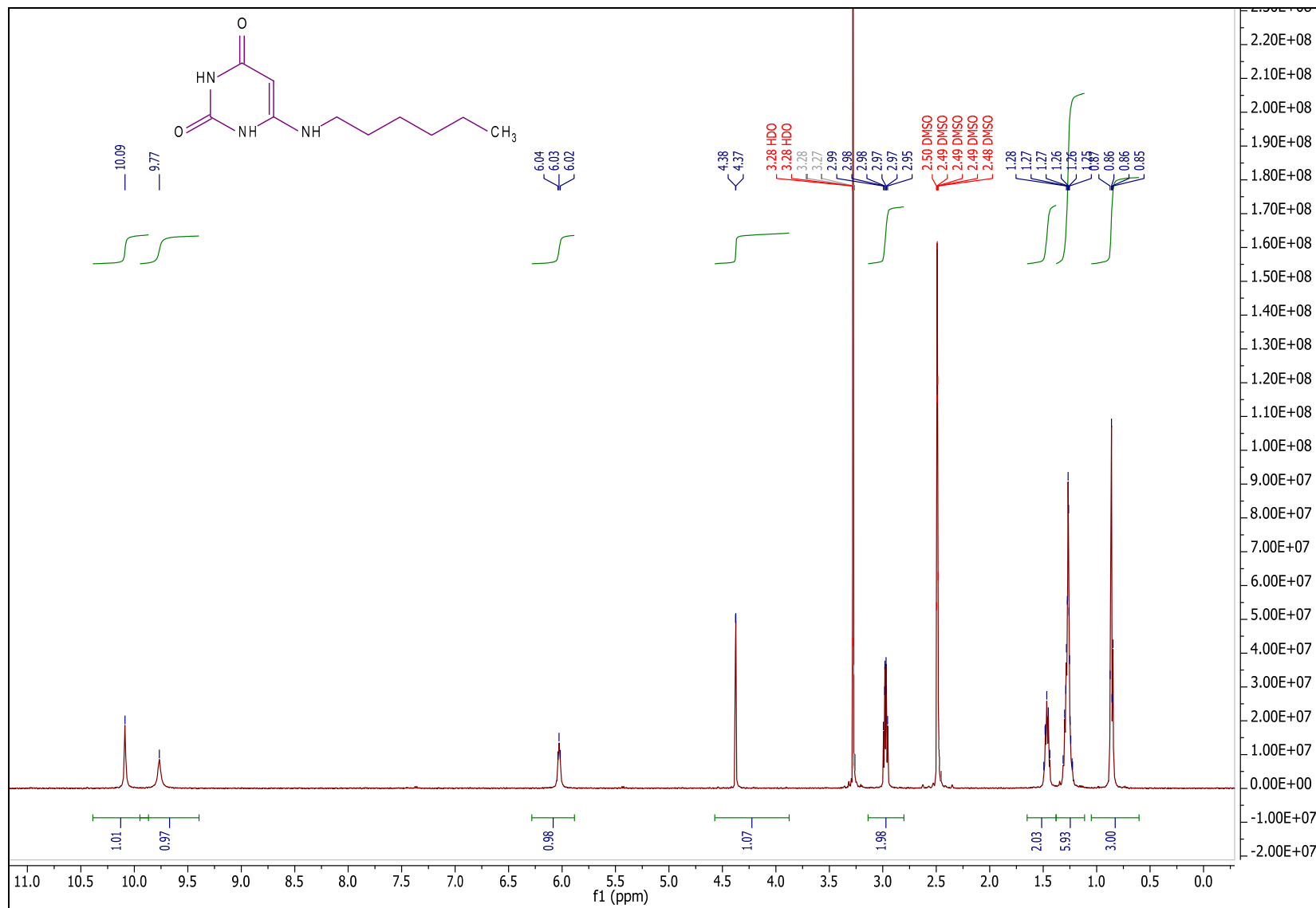


**Figure S3.** <sup>1</sup>H-NMR spectrum of **15** (500 MHz)

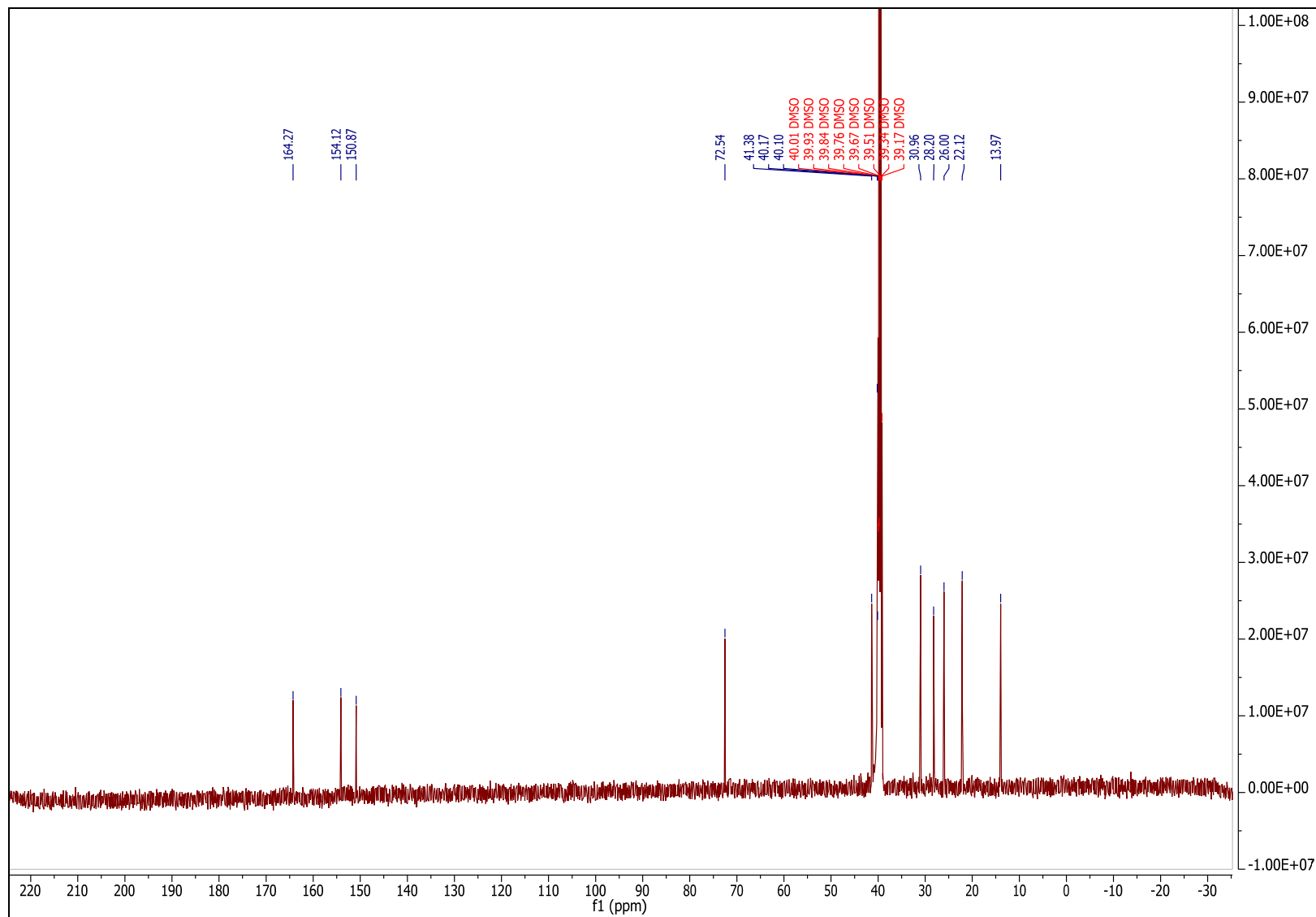


**Figure S4.** <sup>13</sup>C-NMR spectrum of **15** (126 MHz)





**Figure S5.**  $^1\text{H}$ -NMR spectrum of **20** (500 MHz)



**Figure S6.**  $^{13}\text{C}$ -NMR spectrum of **20** (126 MHz)

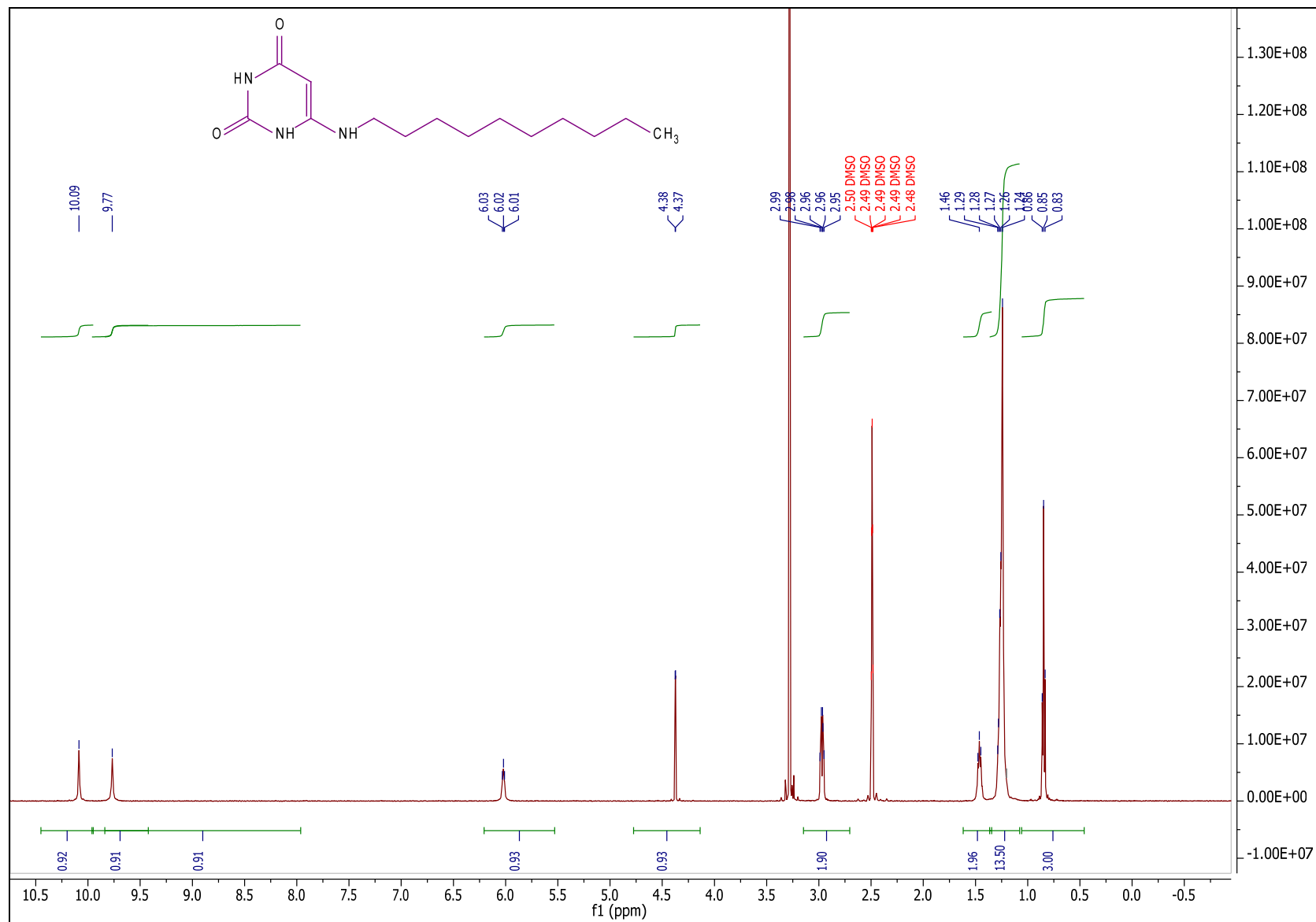


Figure S7.  $^1\text{H}$ -NMR spectrum of **23** (500 MHz)

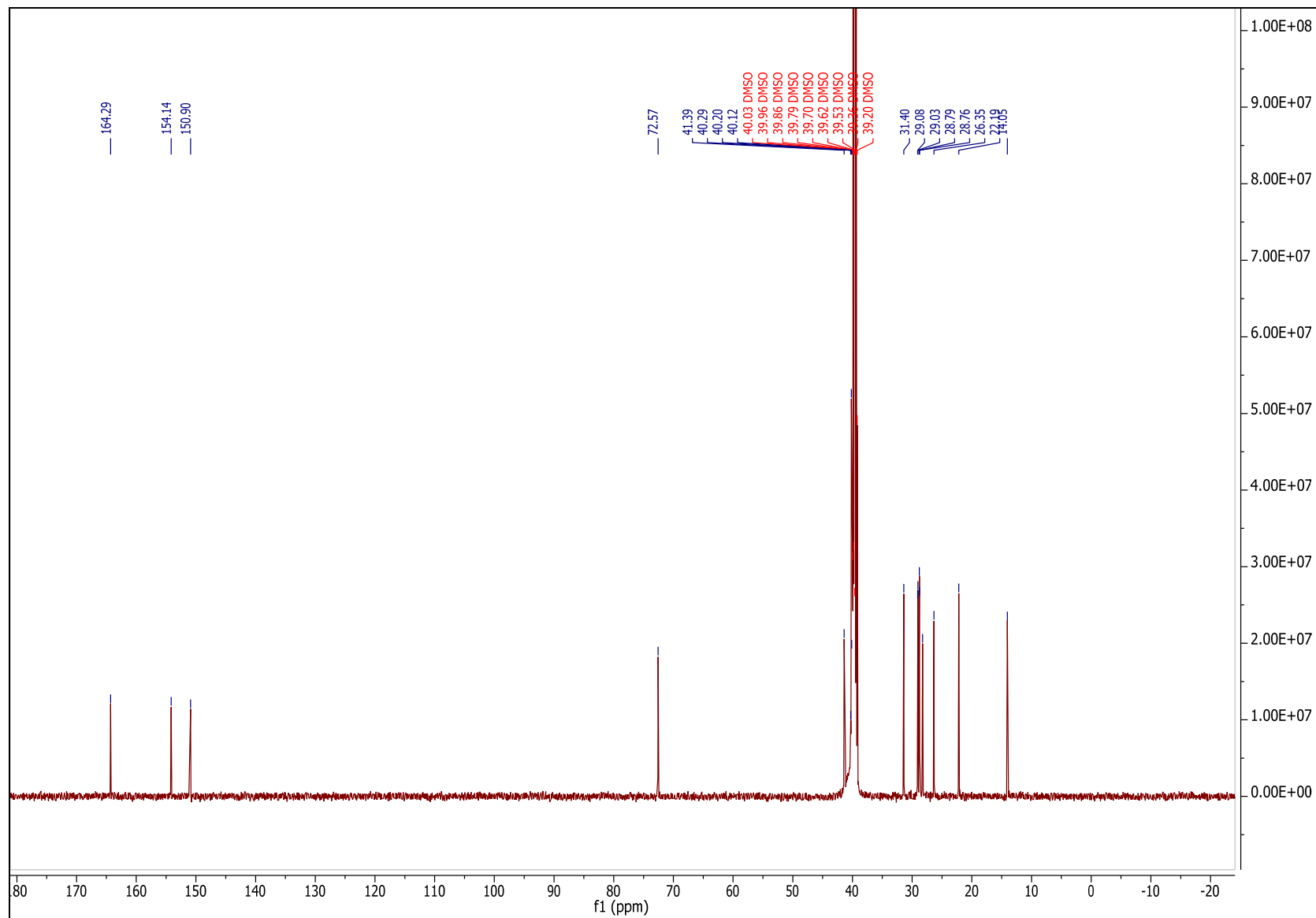
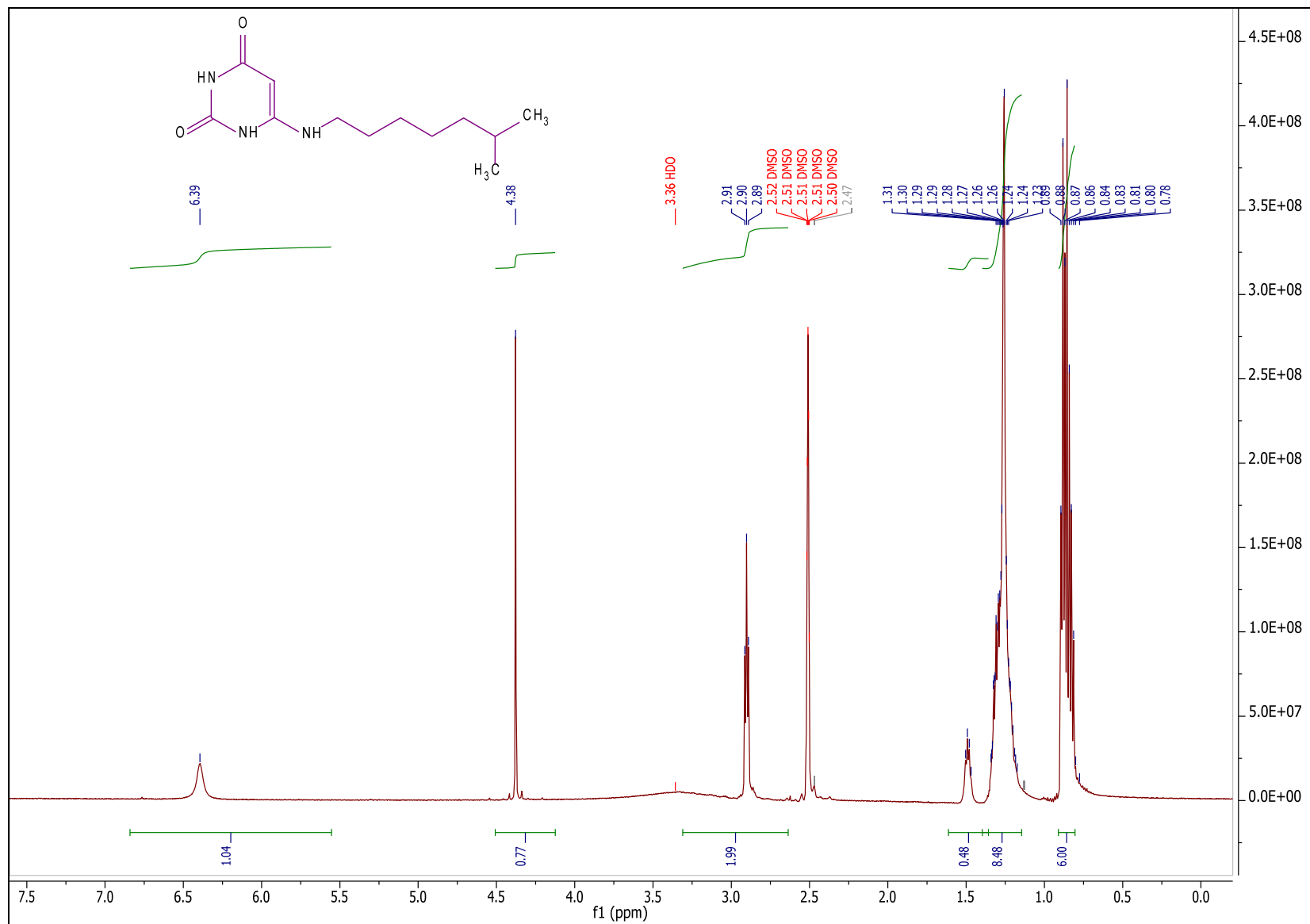
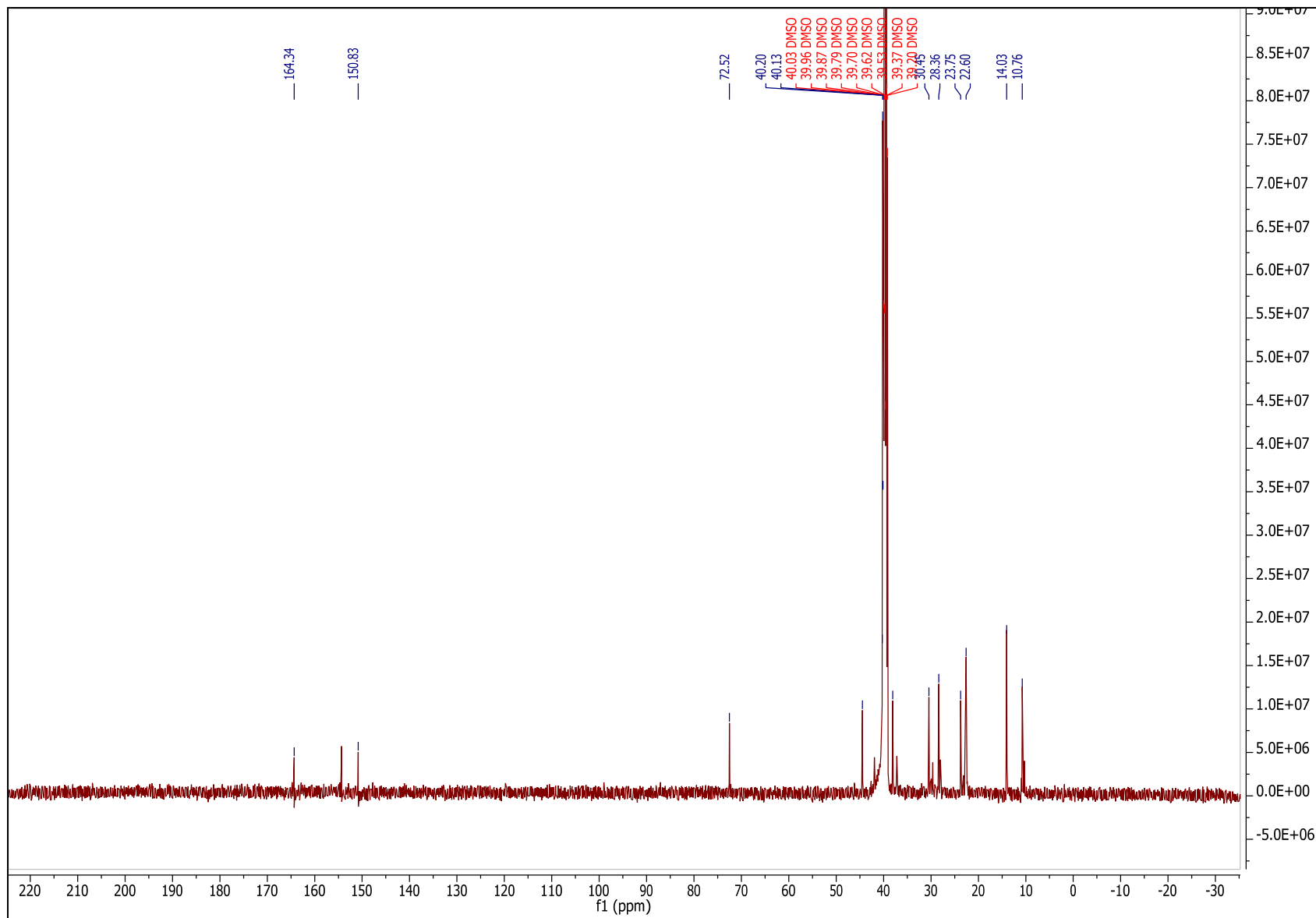


Figure S8. <sup>13</sup>C-NMR spectrum of **23** (126 MHz)



**Figure S9.** <sup>1</sup>H-NMR spectrum of **25** (500 MHz)



**Figure S10.**  $^{13}\text{C}$ -NMR spectrum of **25** (126 MHz)

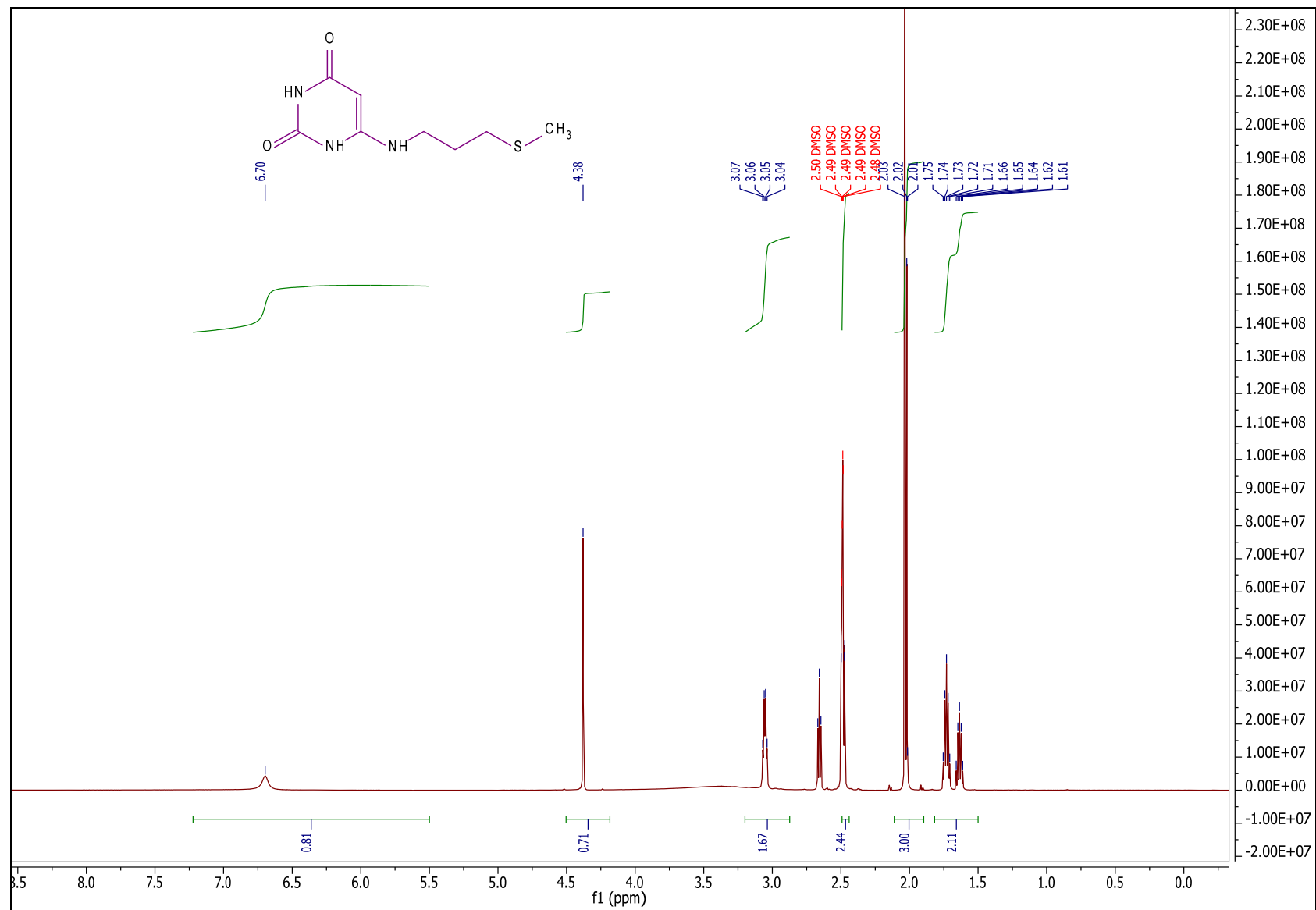


Figure S11. <sup>1</sup>H-NMR spectrum of **26** (600 MHz)

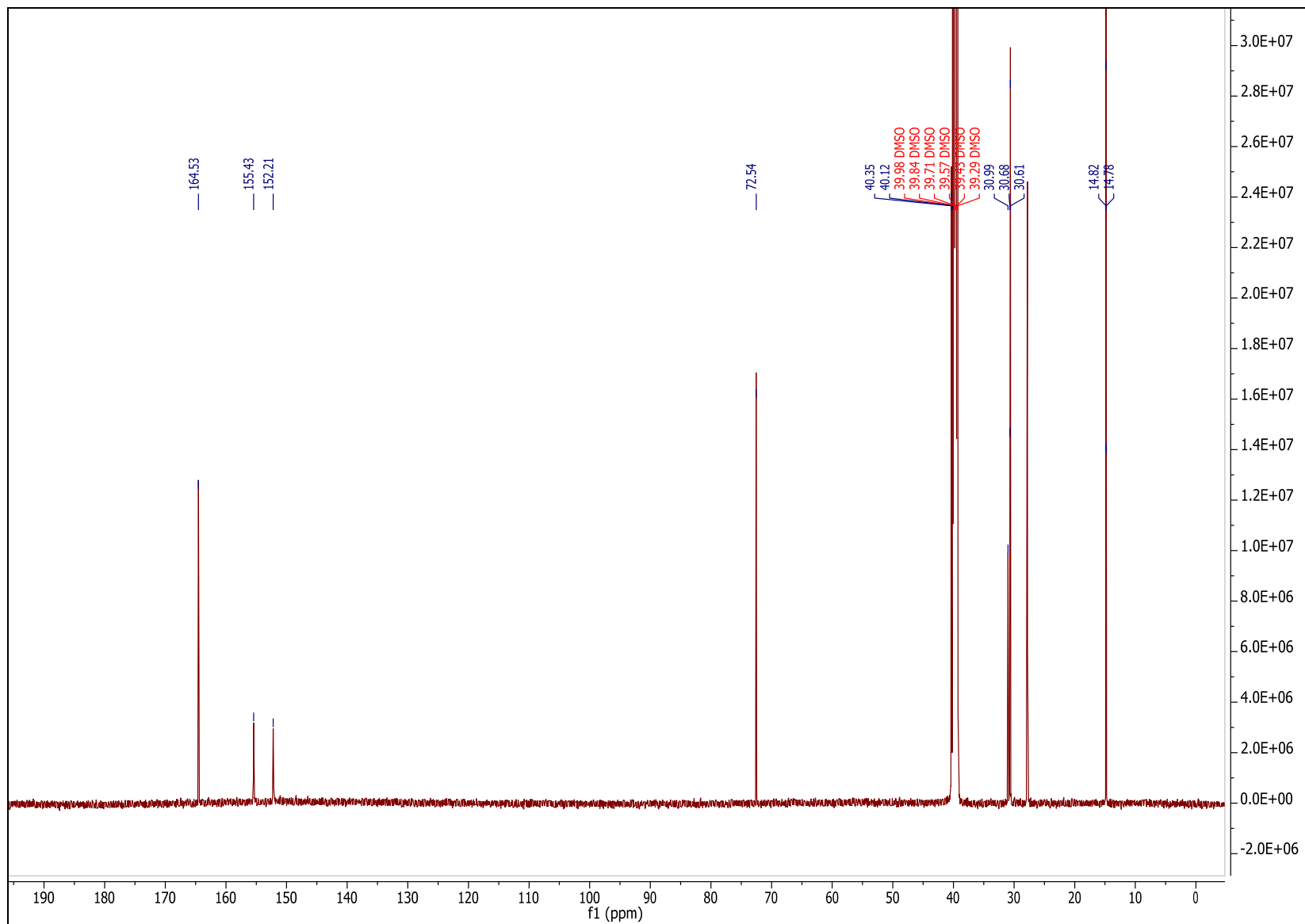
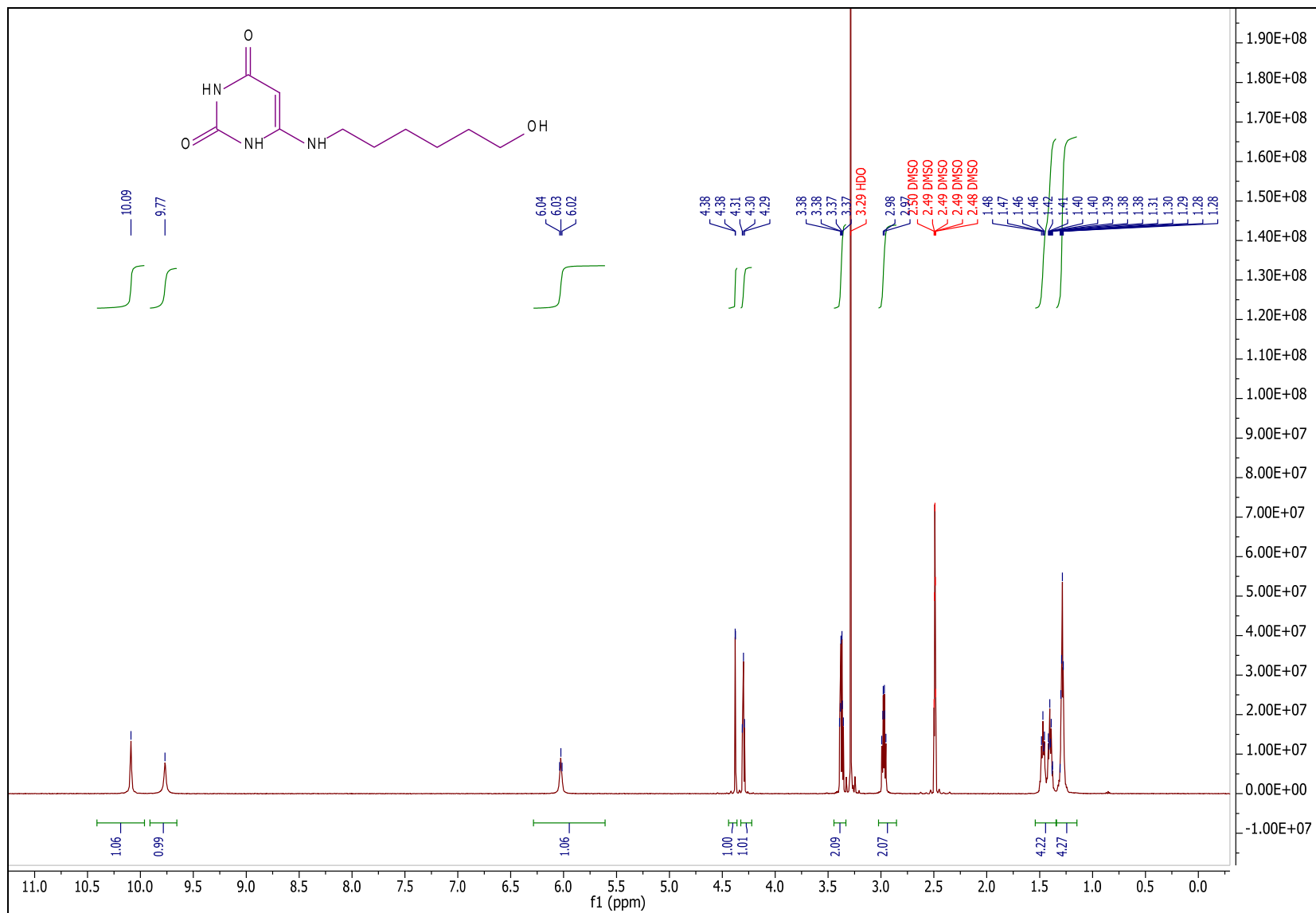
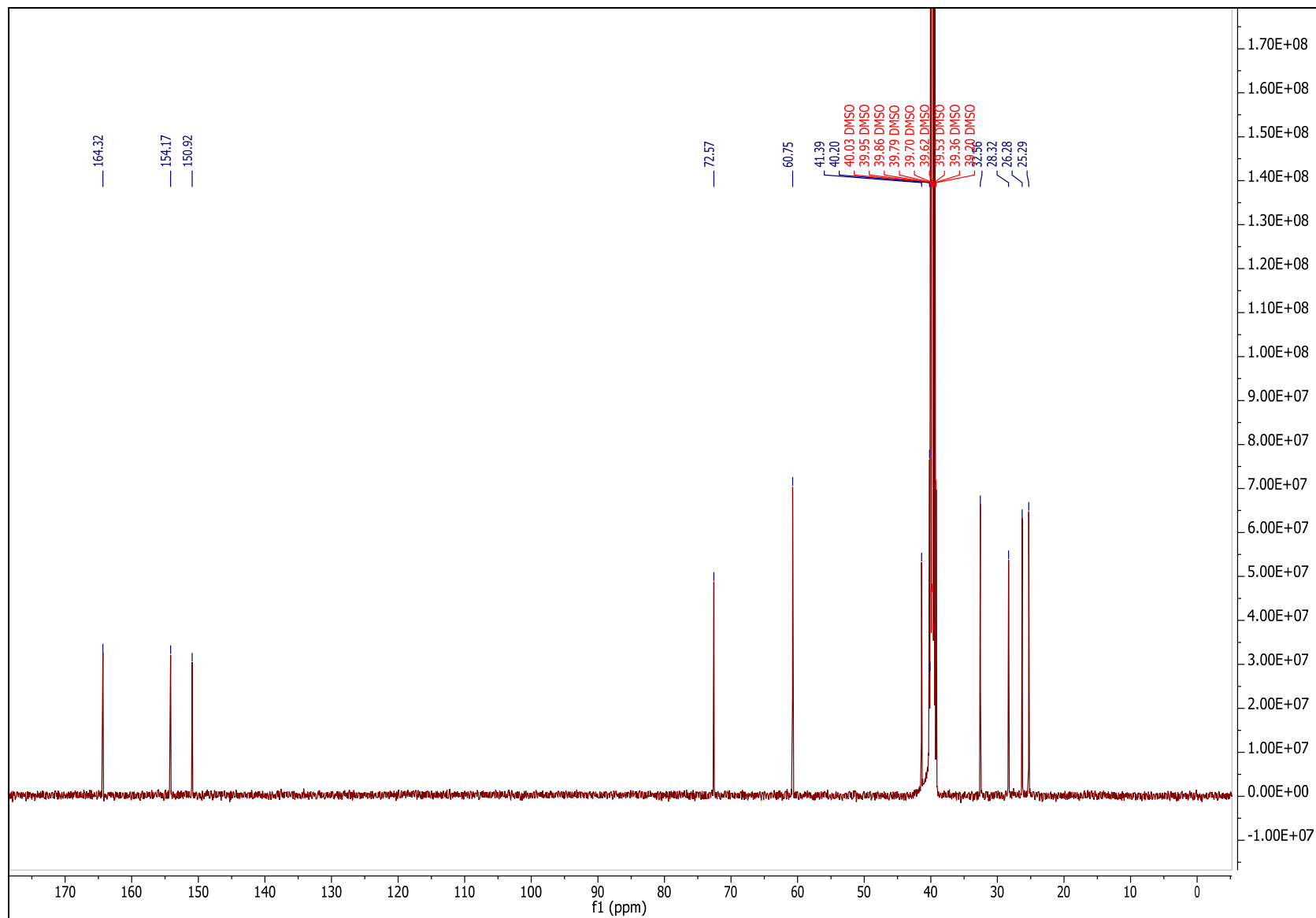


Figure S12.  $^{13}\text{C}$ -NMR spectrum of **26** (151 MHz)





**Figure S13.** <sup>1</sup>H-NMR spectrum of **27** (500 MHz)



**Figure S14.** <sup>13</sup>C-NMR spectrum of **27** (126 MHz)

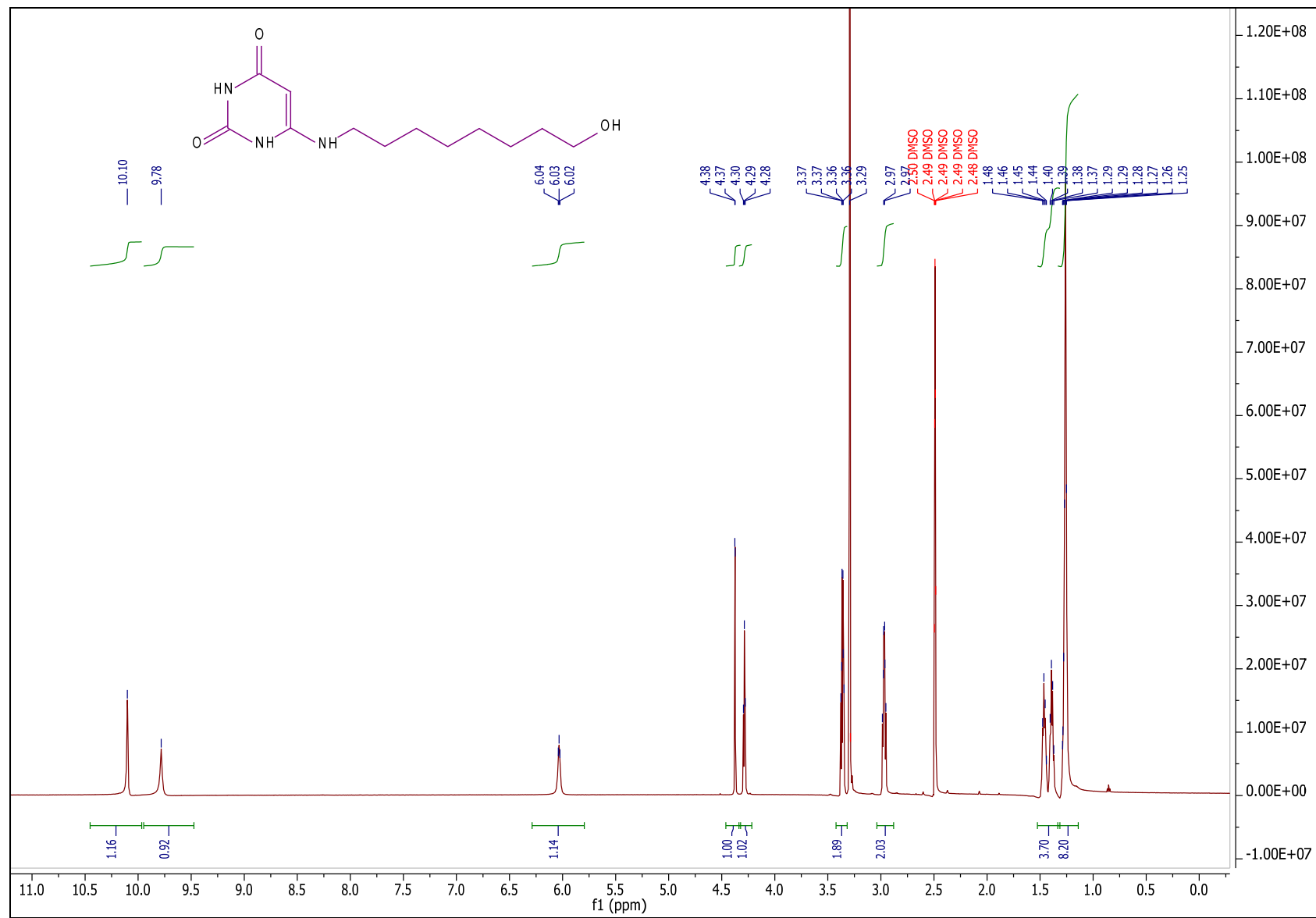


Figure S15. <sup>1</sup>H-NMR spectrum of **28** (600 MHz)

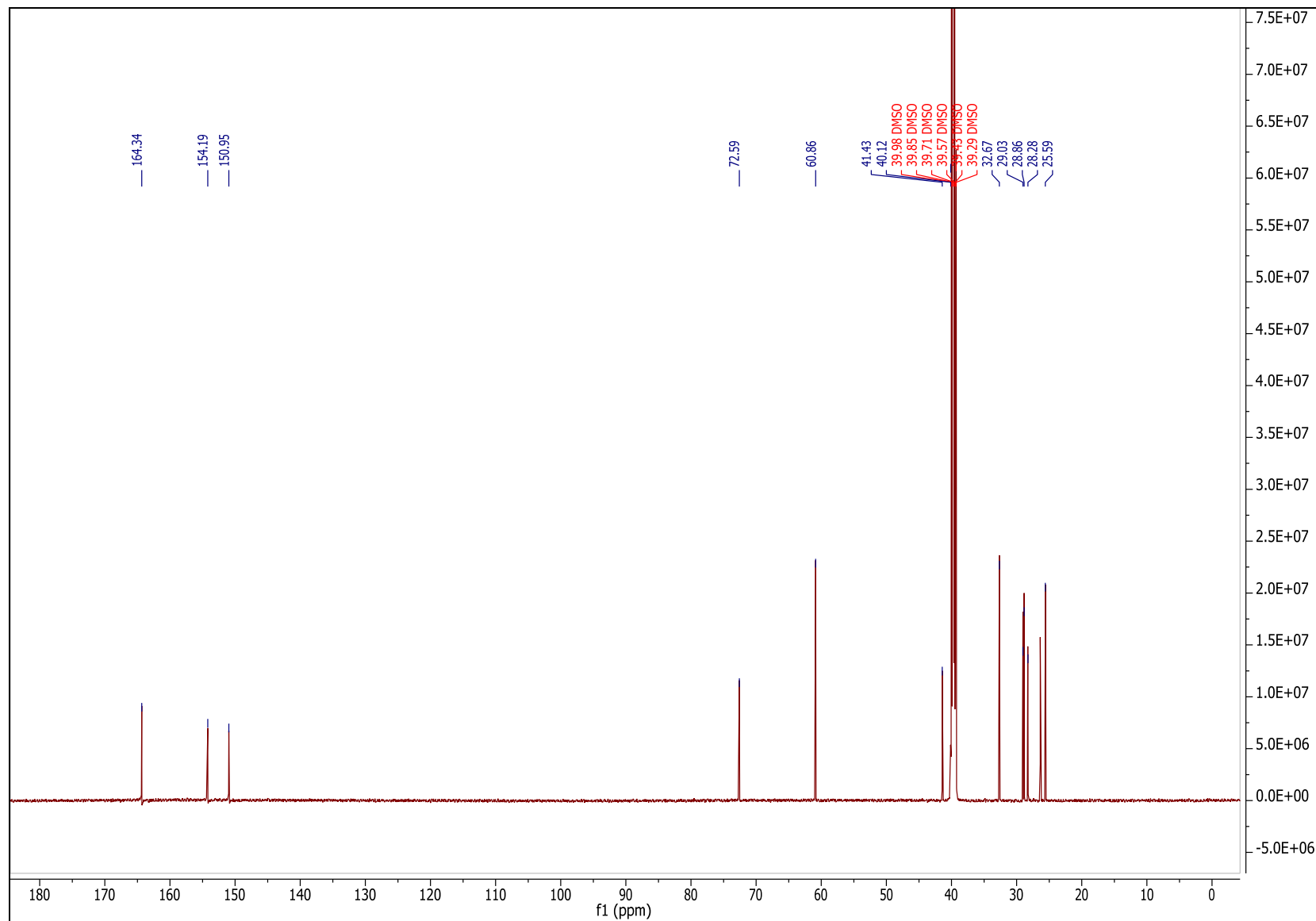


Figure S16.  $^{13}\text{C}$ -NMR spectrum of **28** (151 MHz)

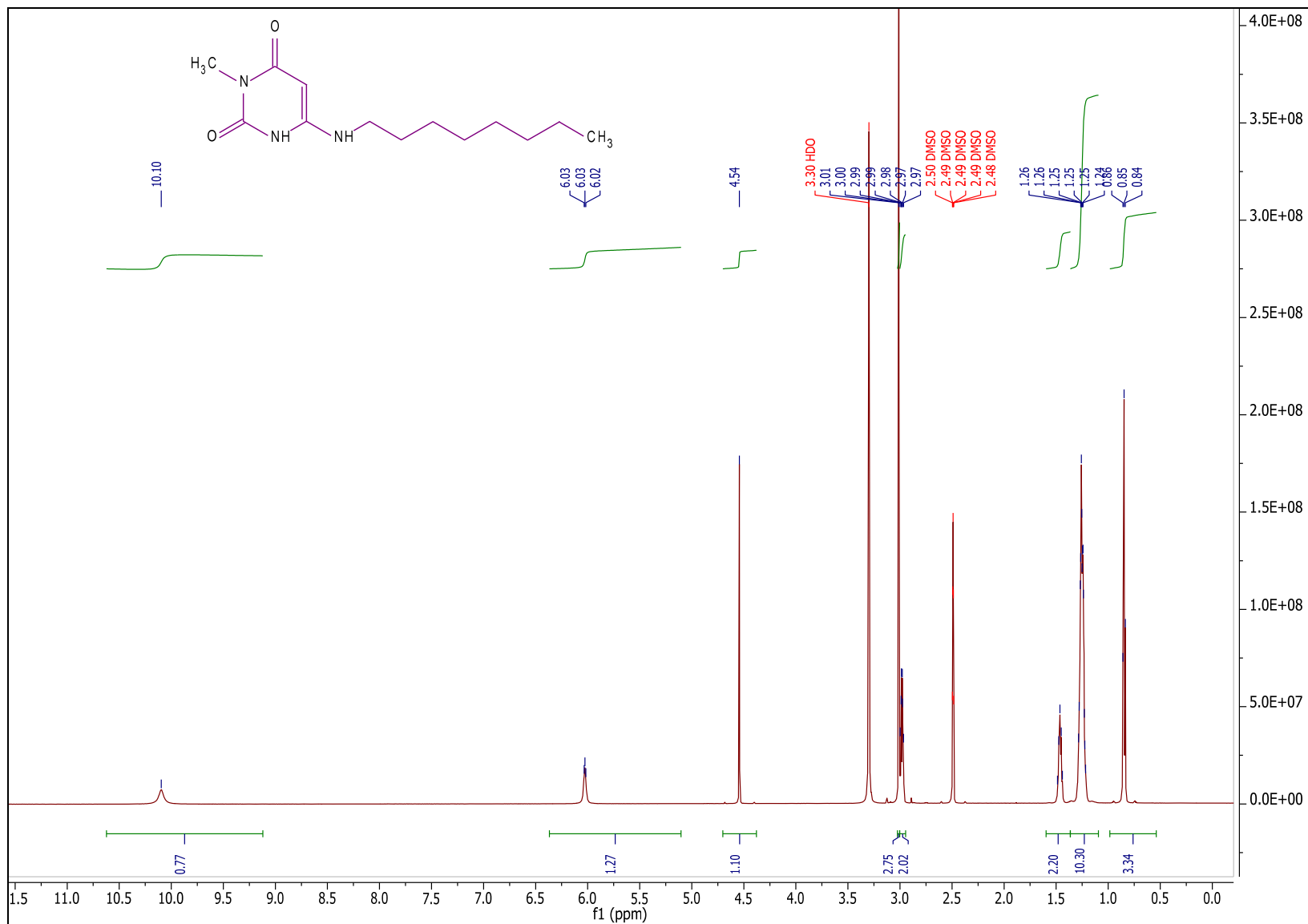
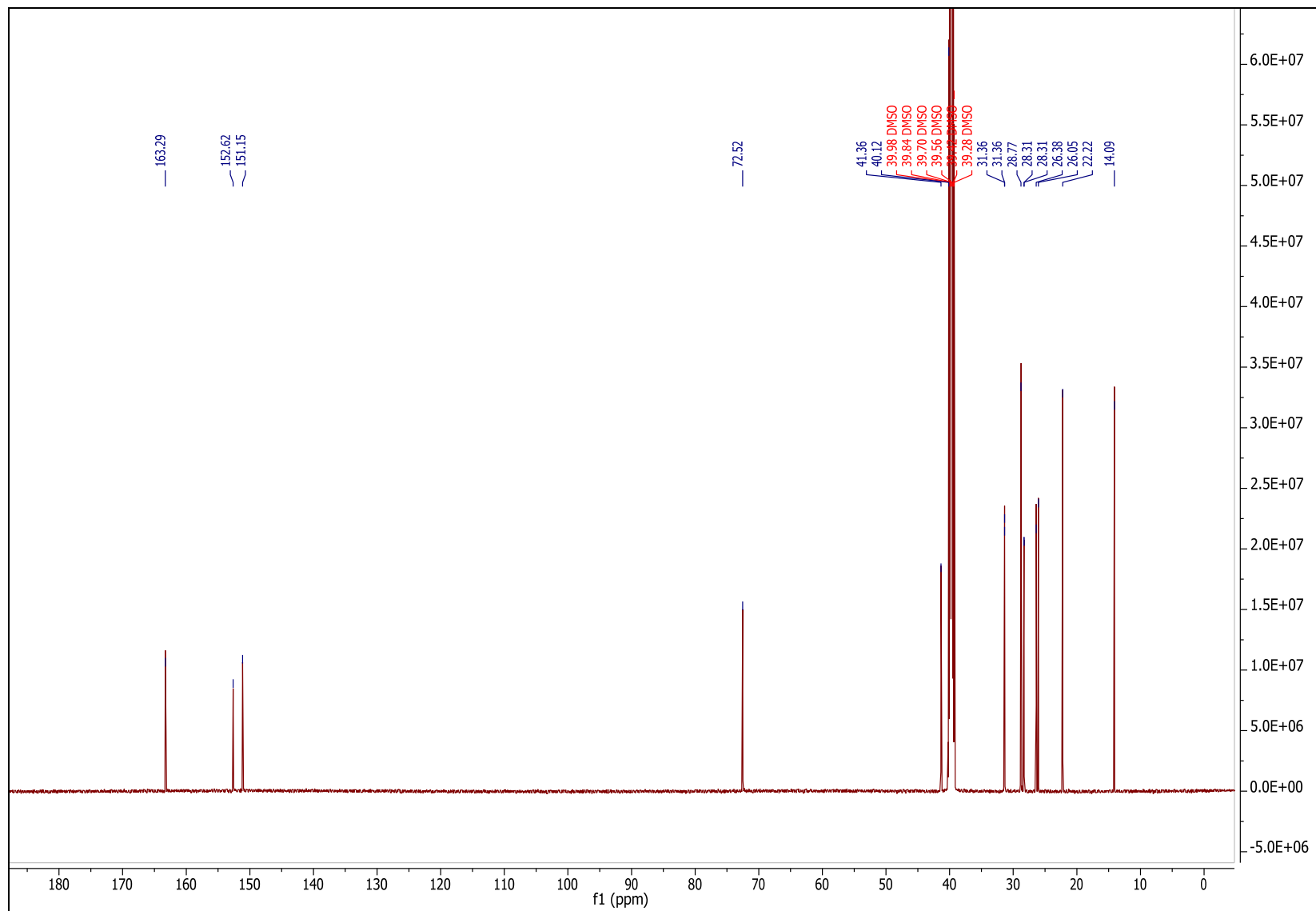


Figure S17. <sup>1</sup>H-NMR spectrum of **31** (600 MHz)



**Figure S18.** <sup>13</sup>C-NMR spectrum of **31** (151 MHz)

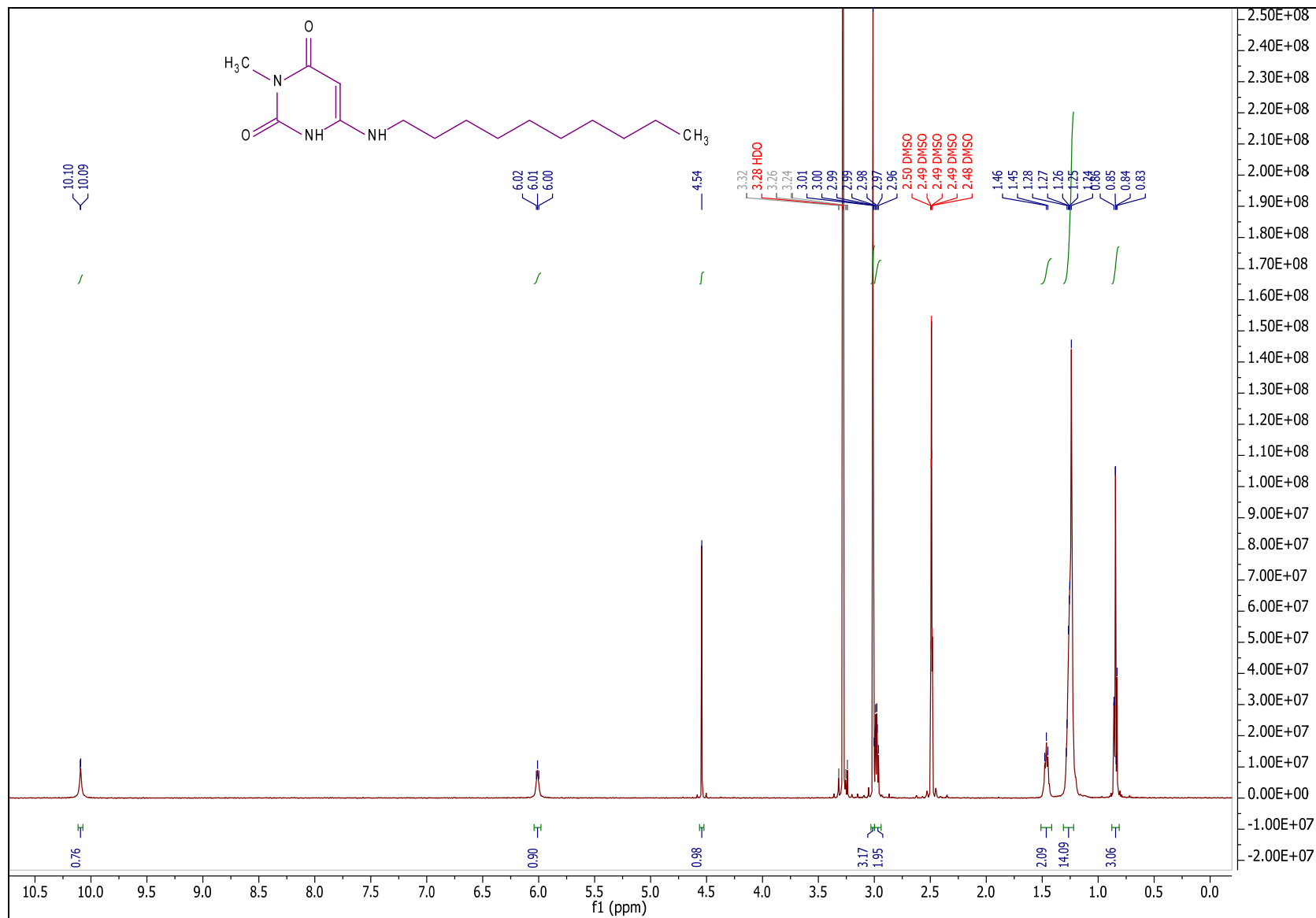


Figure S19. <sup>1</sup>H-NMR spectrum of **33** (500 MHz)

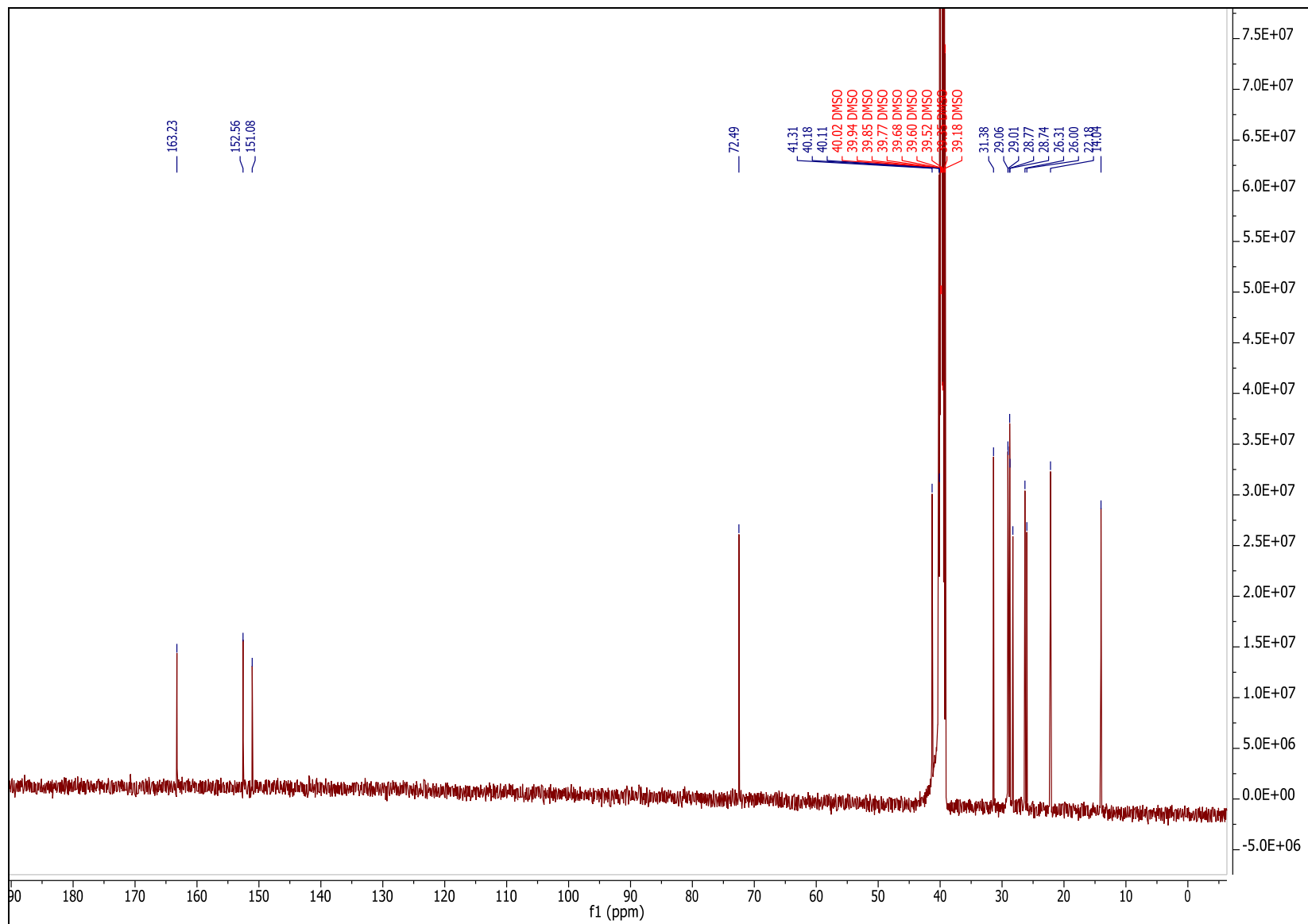
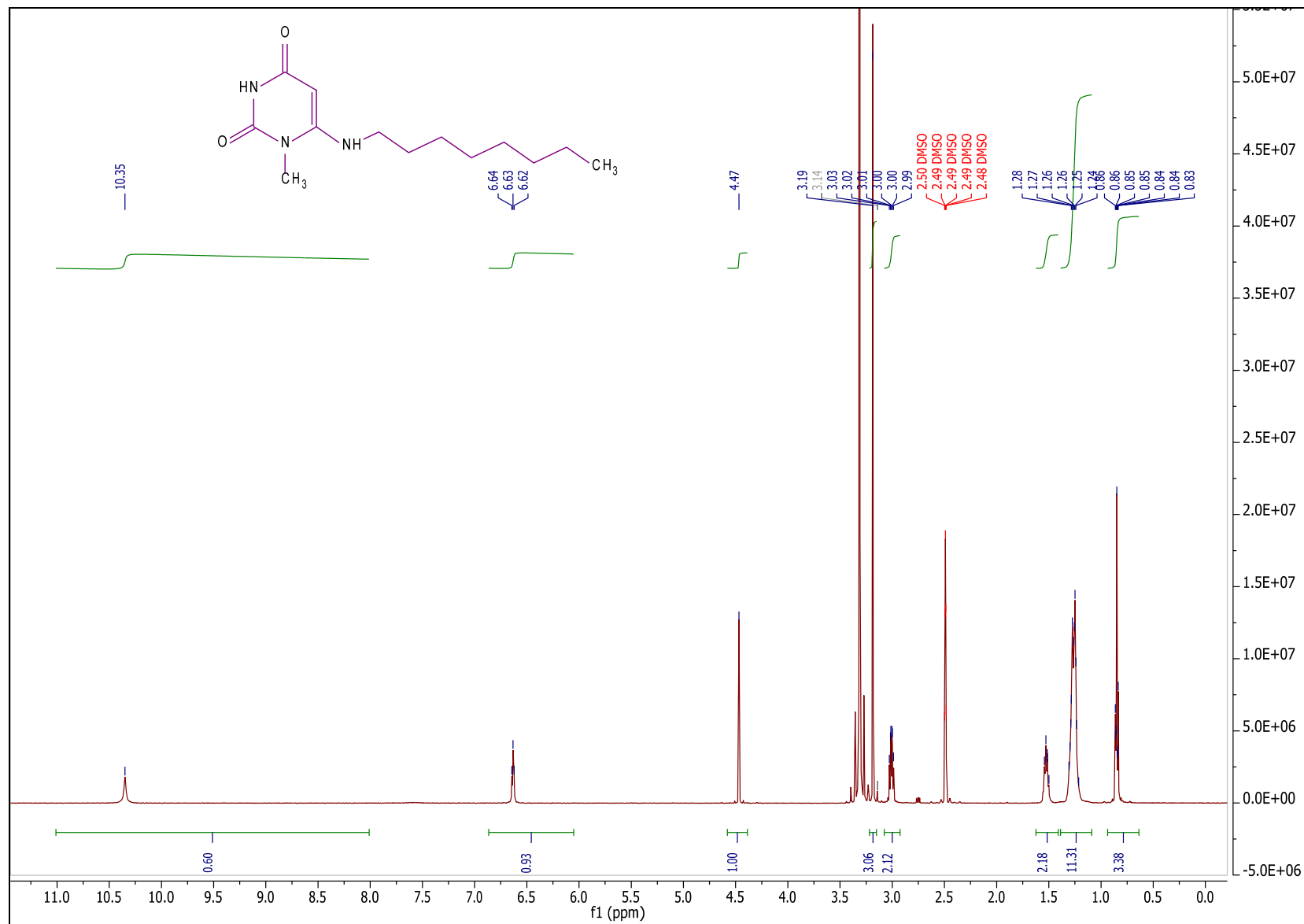
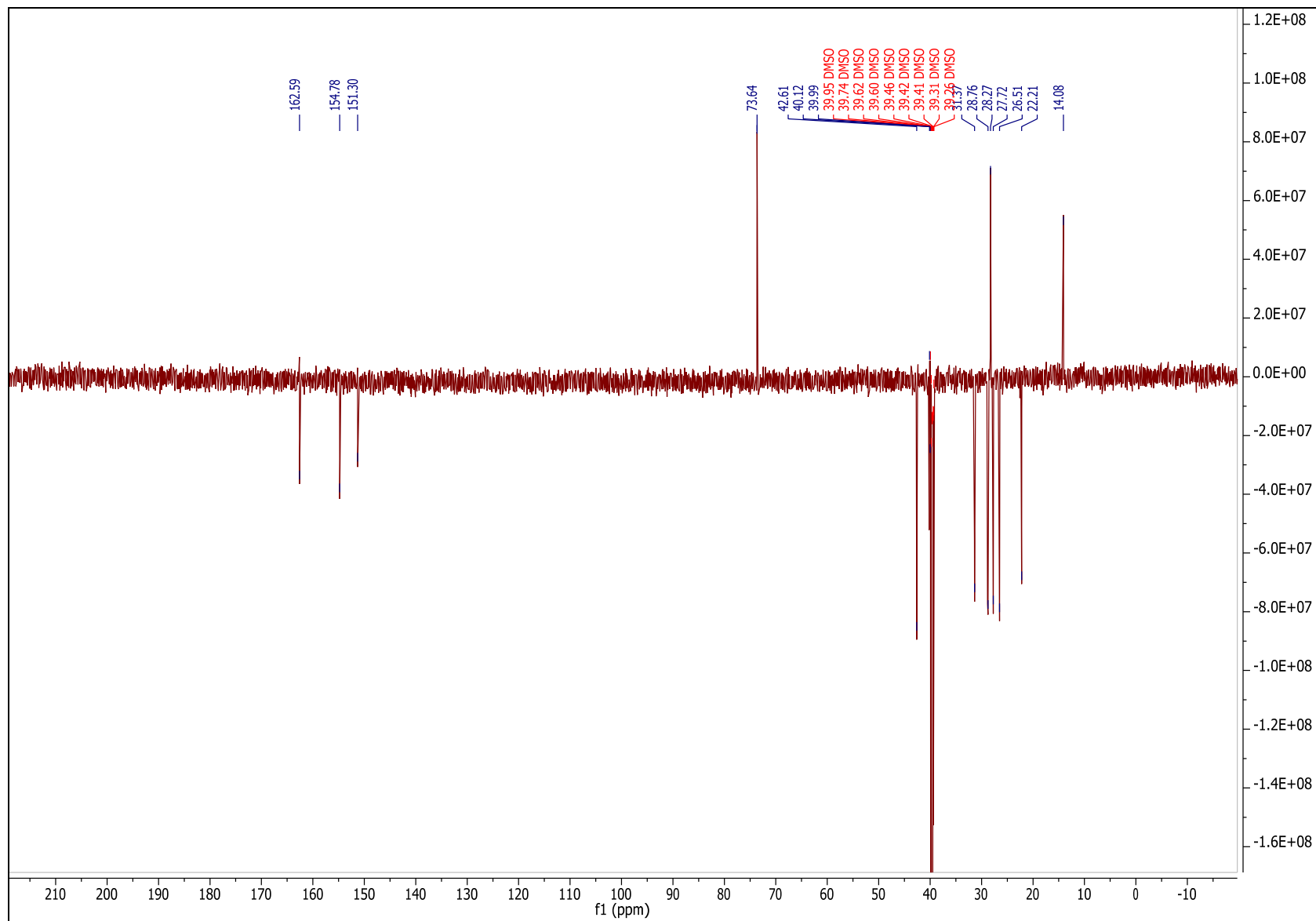


Figure S20. <sup>13</sup>C-NMR spectrum of **33** (126 MHz)





**Figure S21.** <sup>1</sup>H-NMR spectrum of **35** (500 MHz)



**Figure S22.**  $^{13}\text{C}_{\text{Capt}}$ -NMR spectrum of **35** (126 MHz)

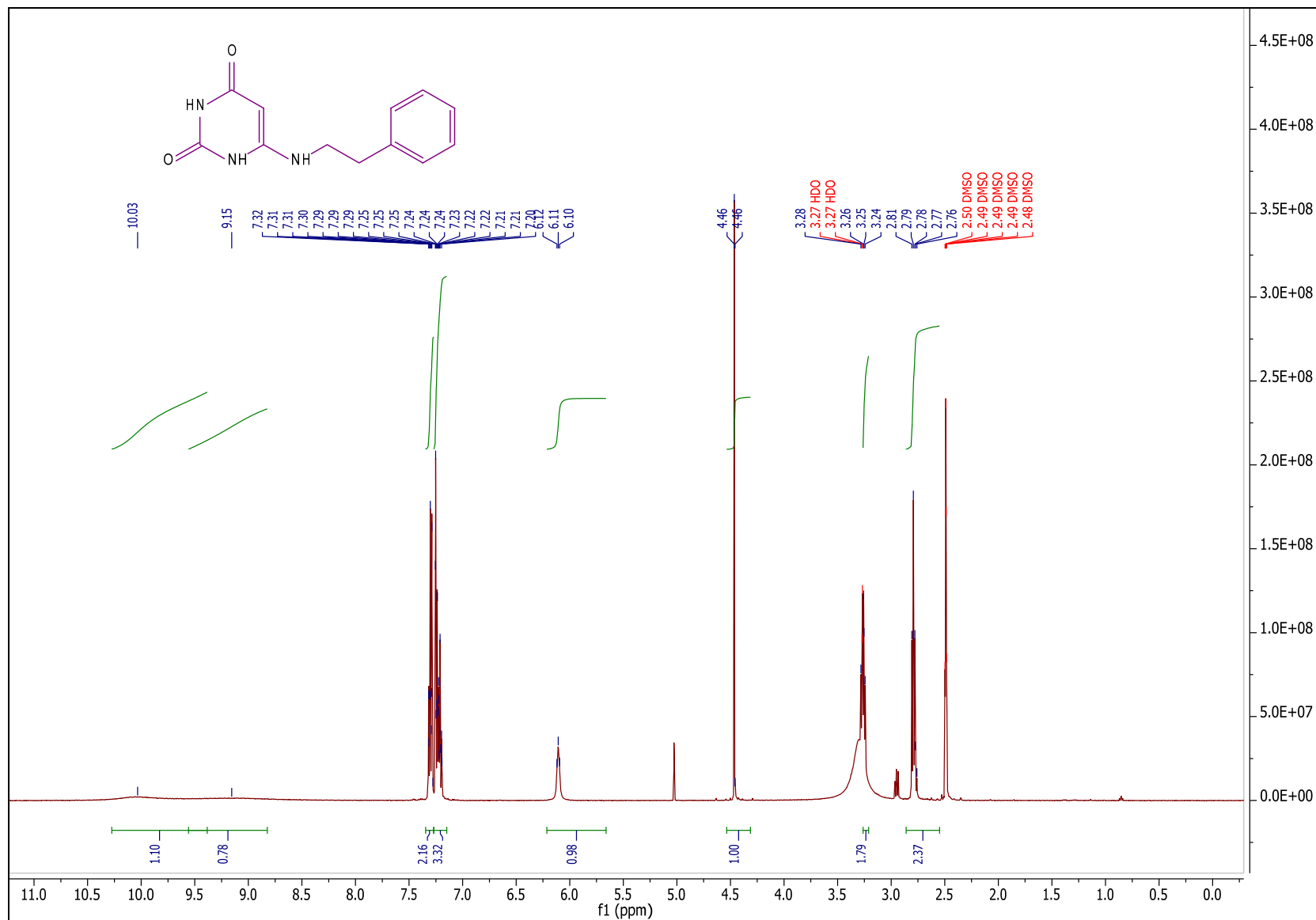


Figure S23. <sup>1</sup>H-NMR spectrum of **42** (500 MHz)

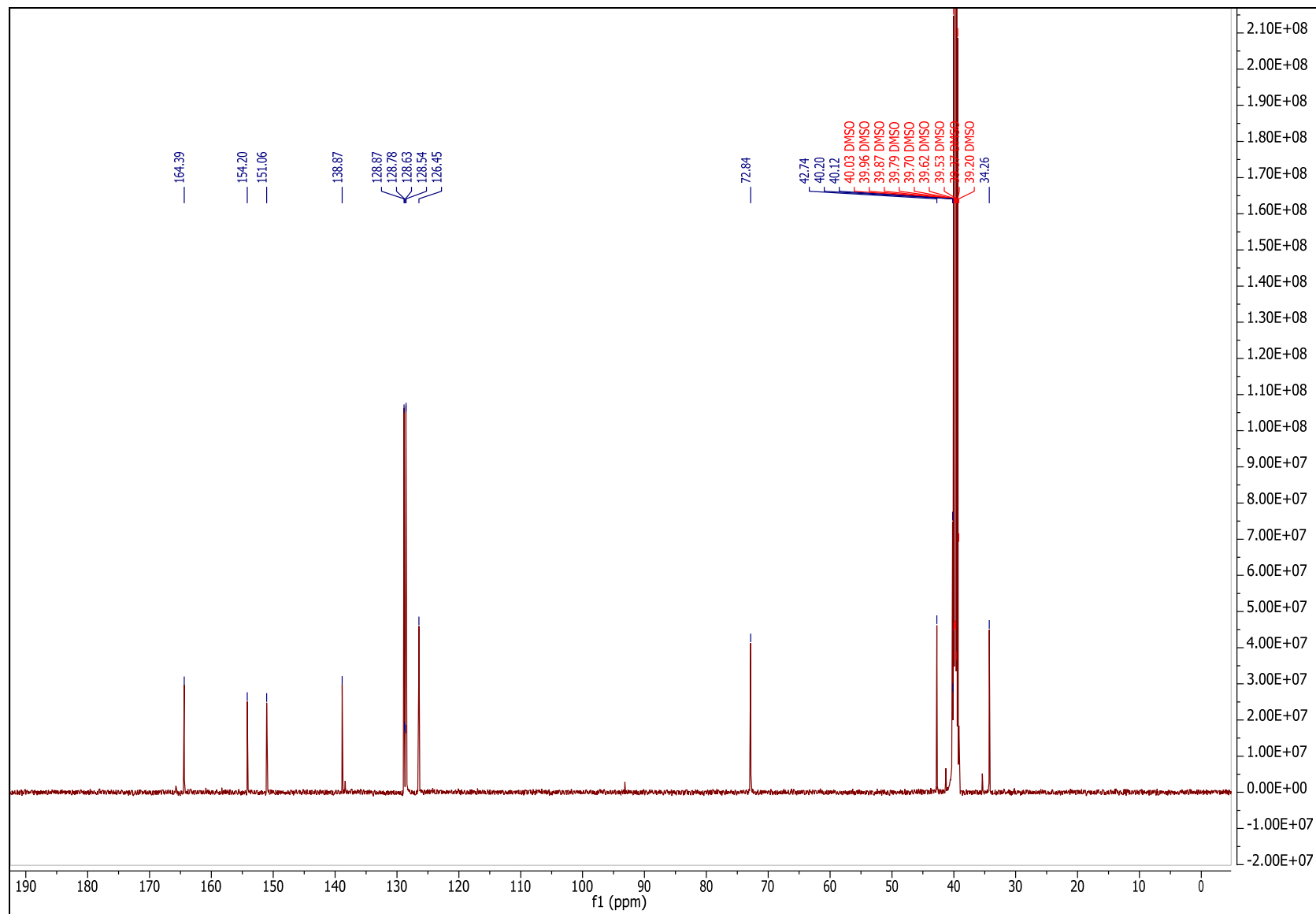


Figure S24. <sup>13</sup>C-NMR spectrum of **42** (126 MHz)

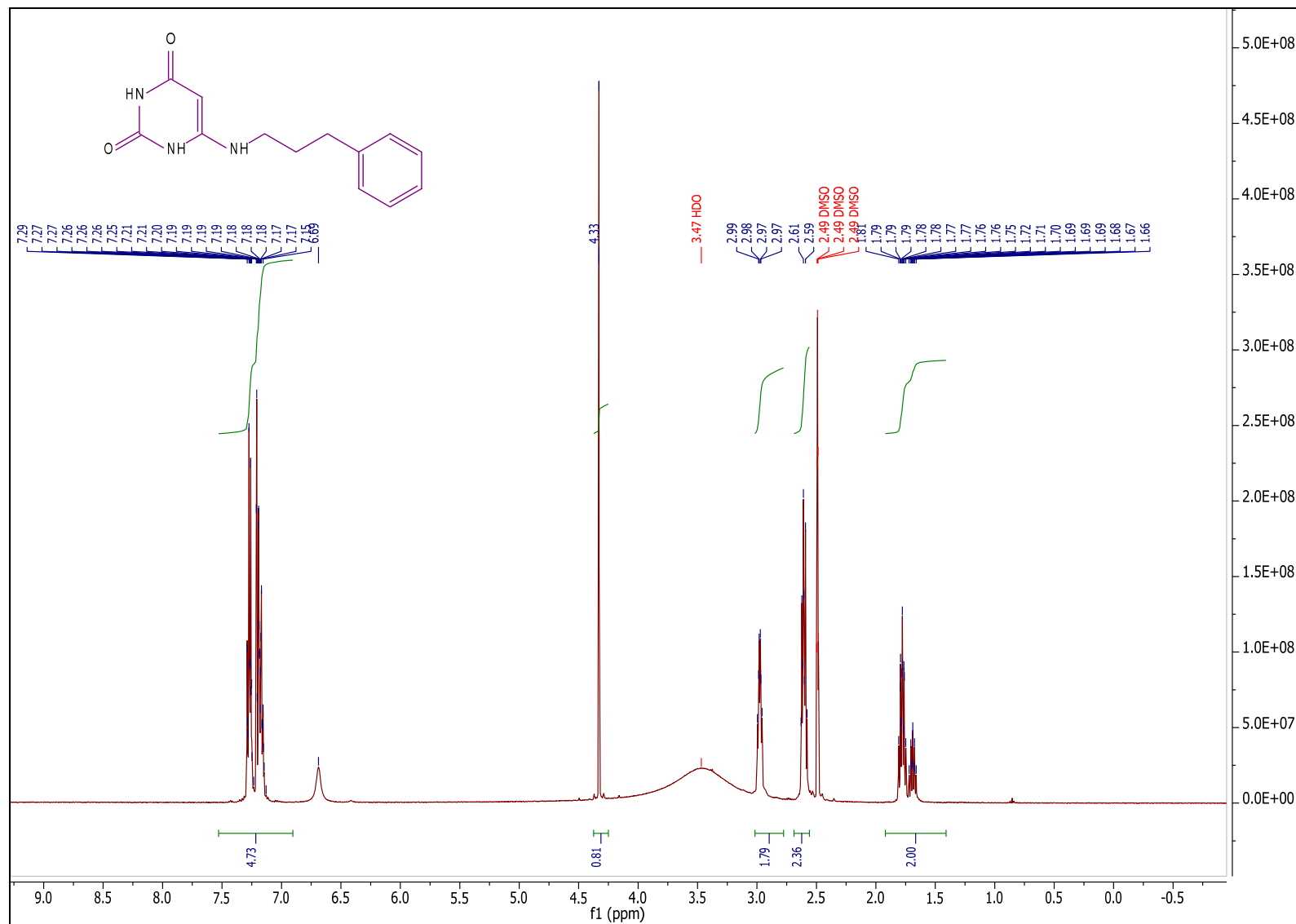


Figure S25.  $^1\text{H}$ -NMR spectrum of **43** (500 MHz)

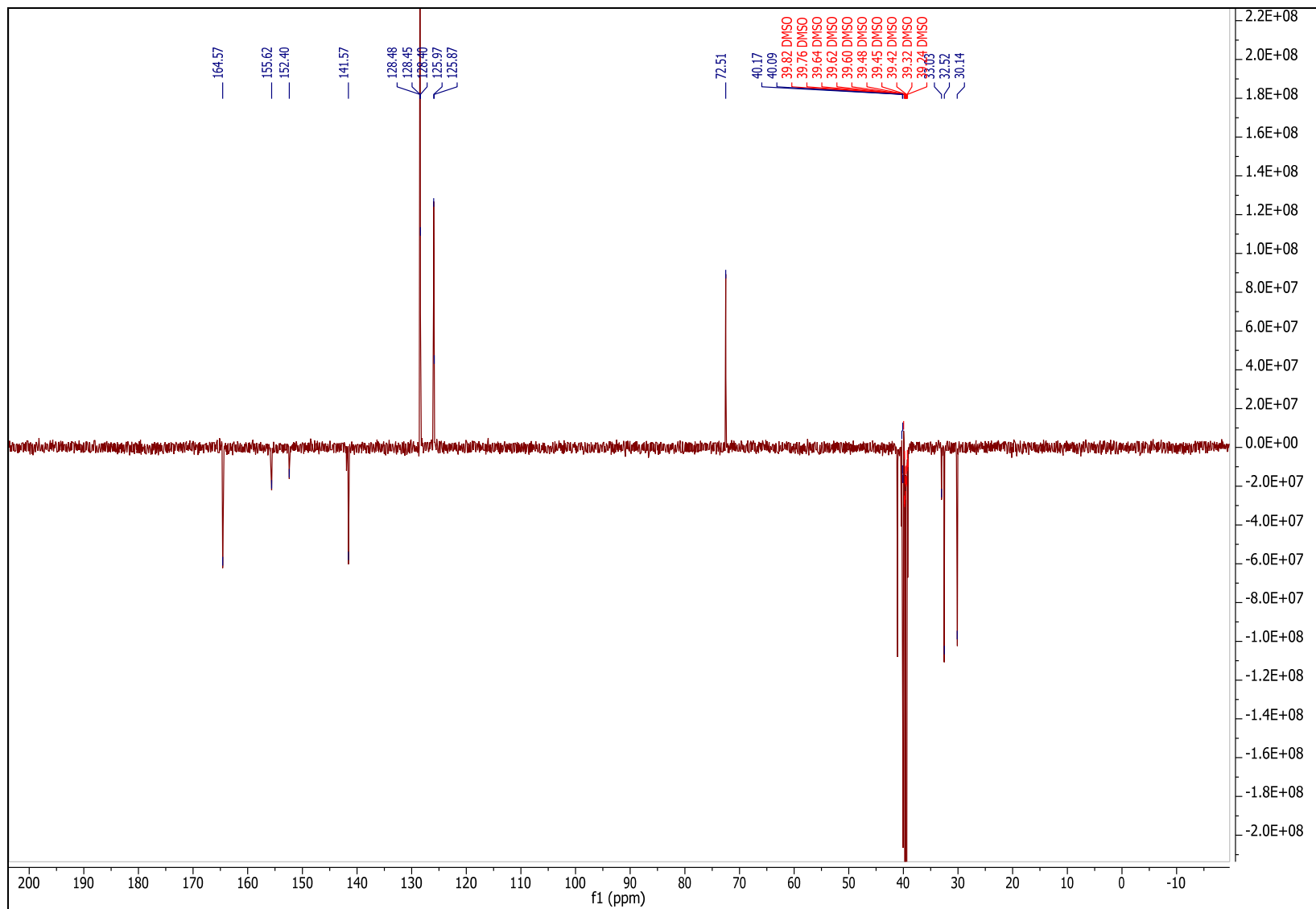


Figure S26. <sup>13</sup>C-NMR spectrum of **43** (126 MHz)

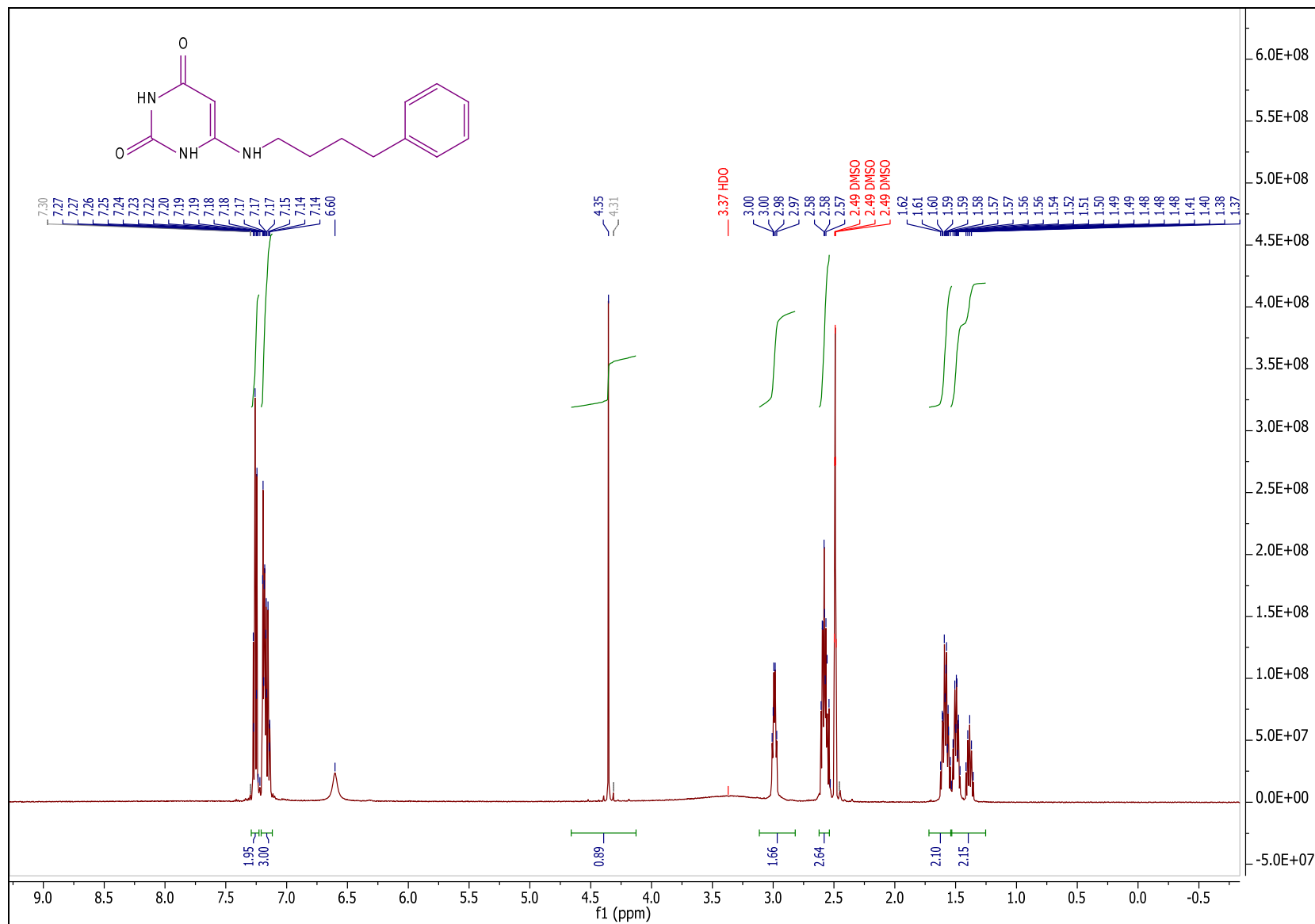


Figure S27. <sup>1</sup>H-NMR spectrum of **44** (500 MHz)

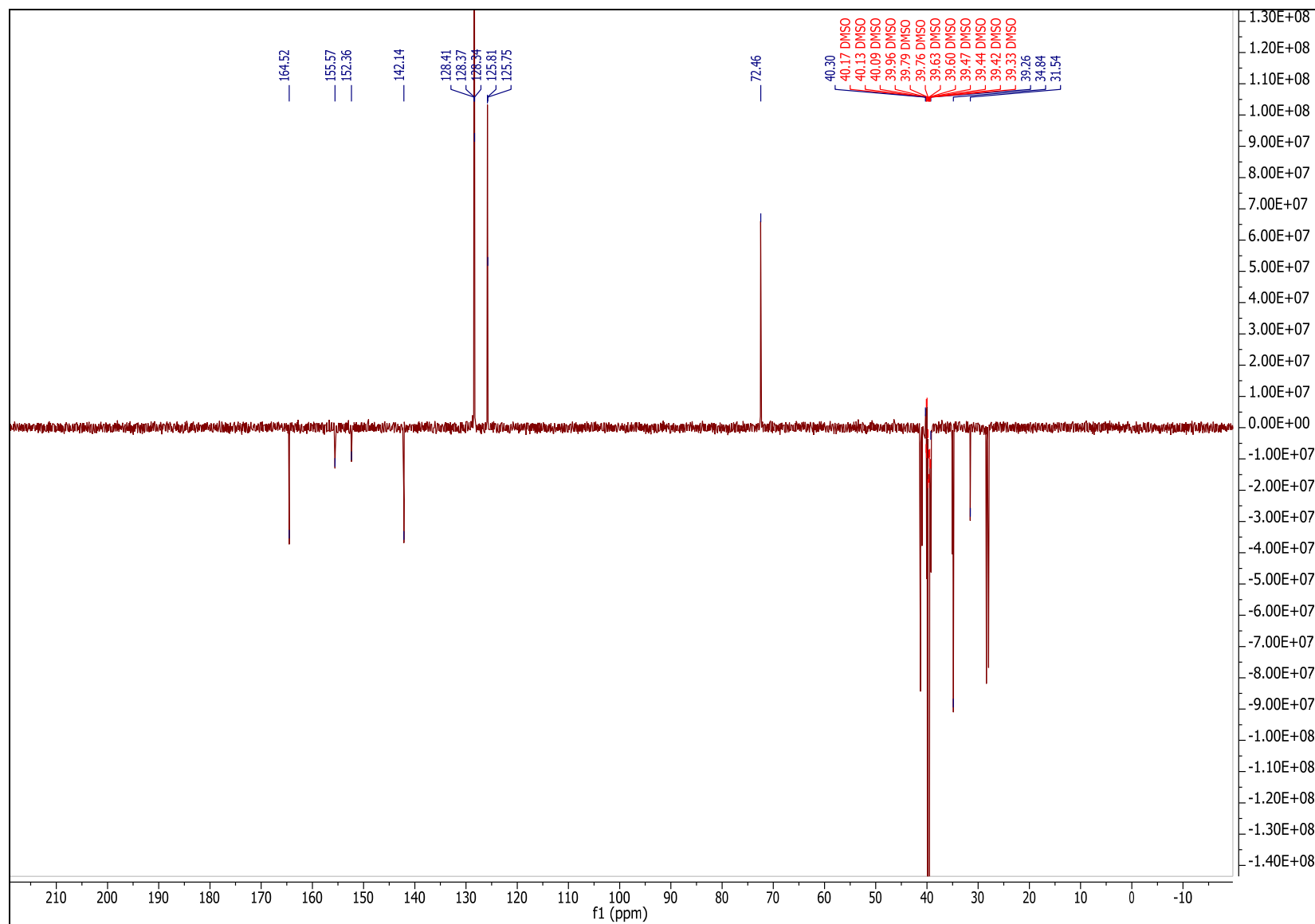


Figure S28.  $^{13}\text{C}_{\text{apt}}$ -NMR spectrum of **44** (126 MHz)



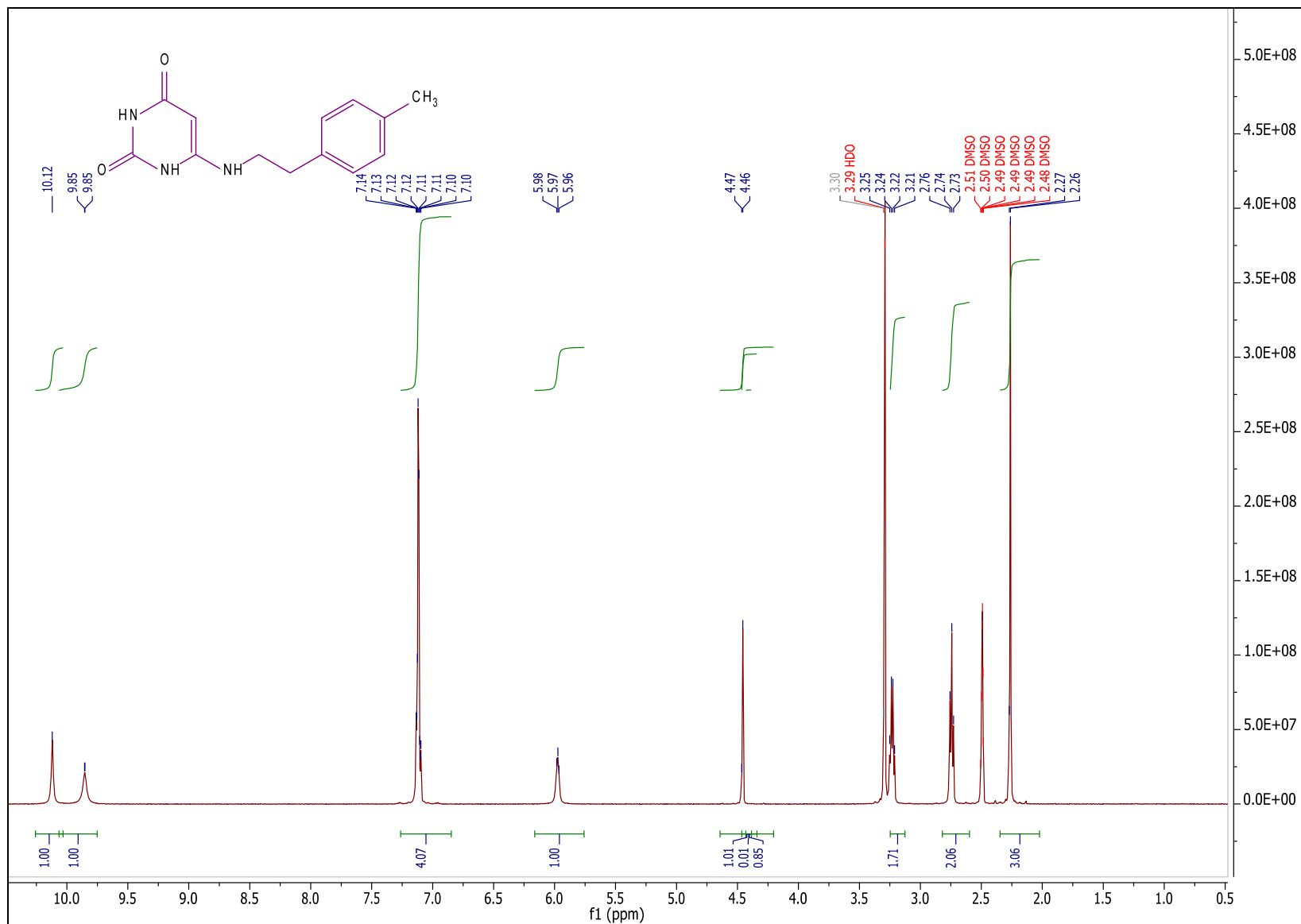


Figure S29.  $^1\text{H}$ -NMR spectrum of **45** (500 MHz)

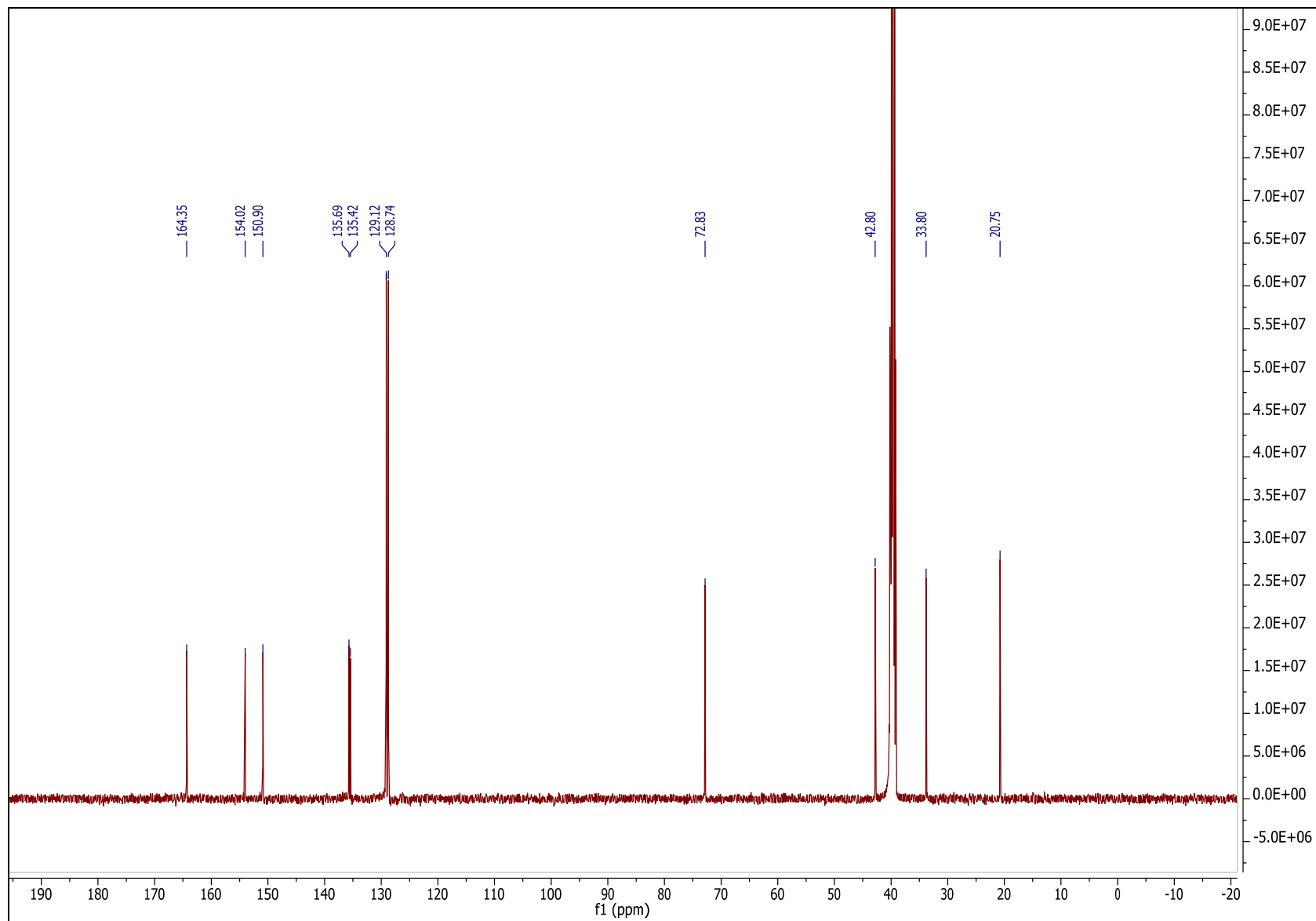


Figure S30.  $^{13}\text{C}$ -NMR spectrum of **45** (126 MHz)

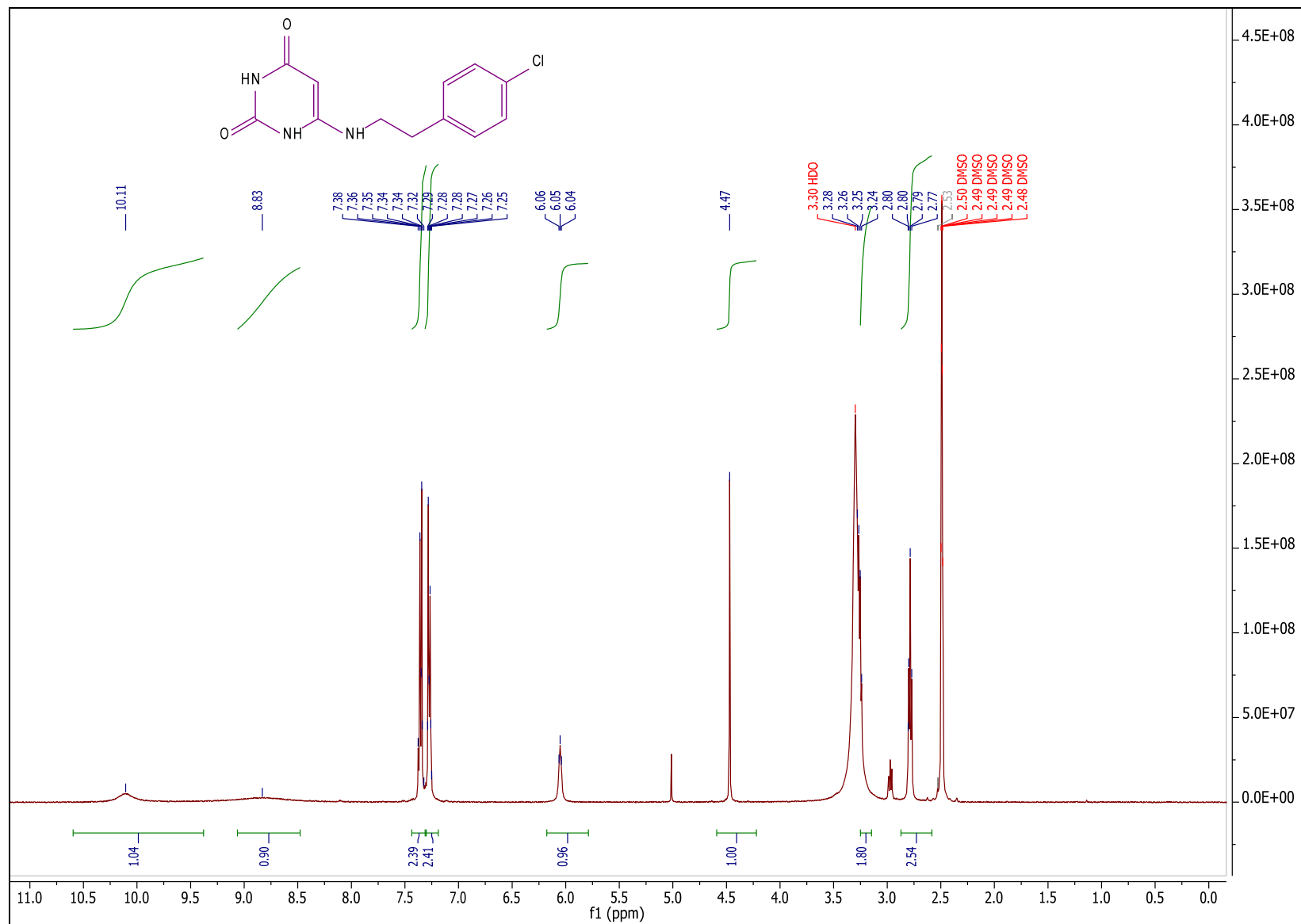
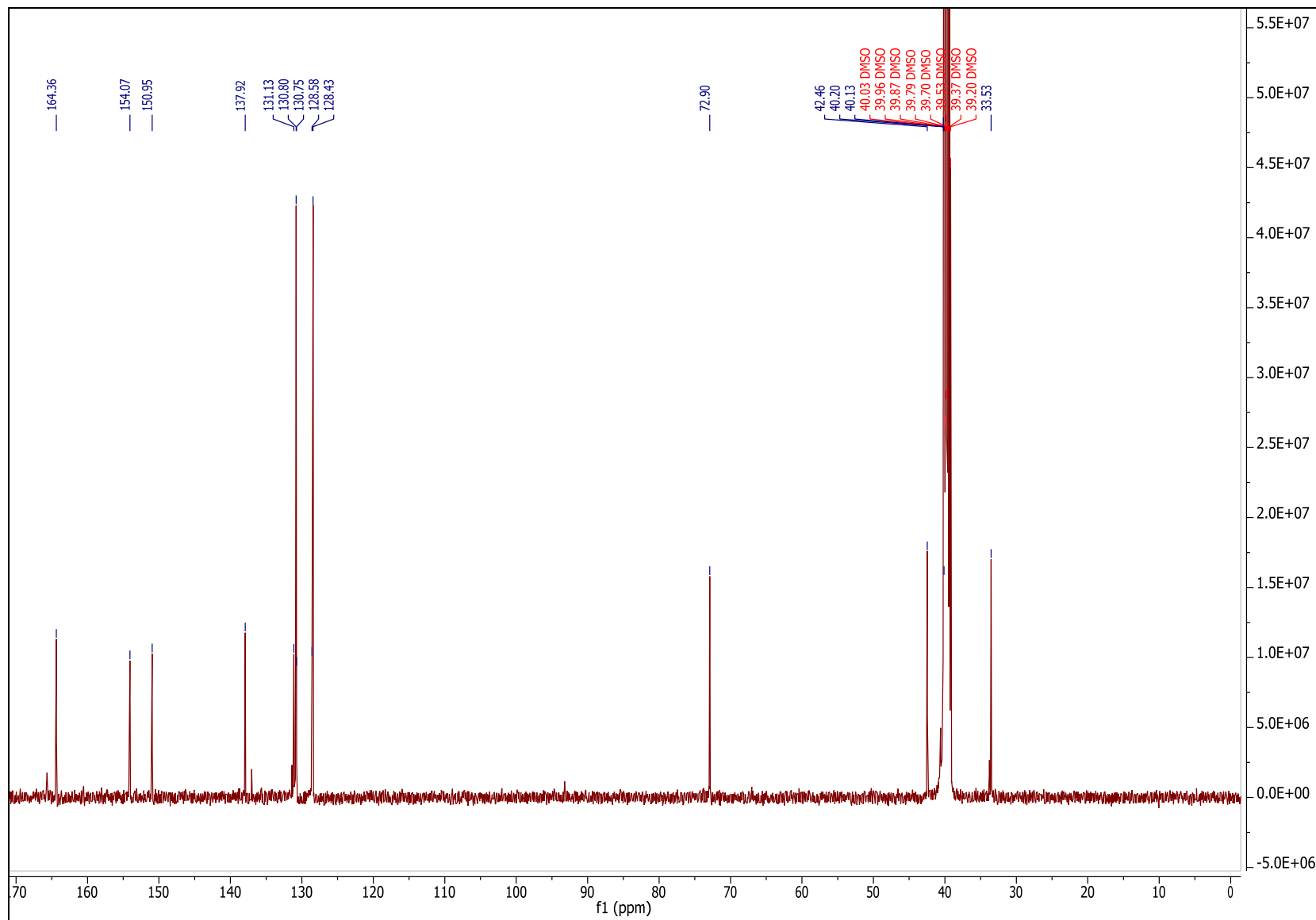
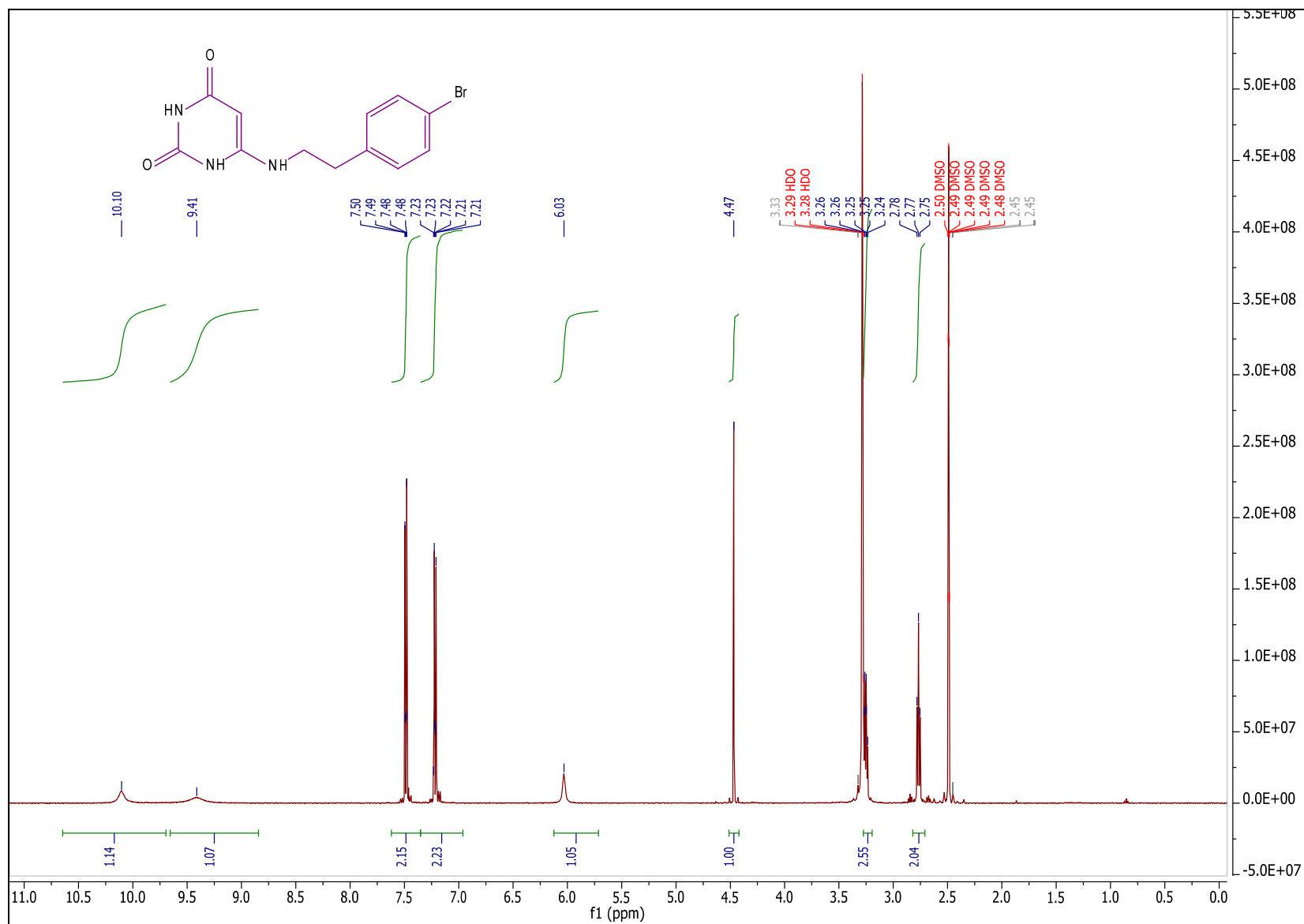


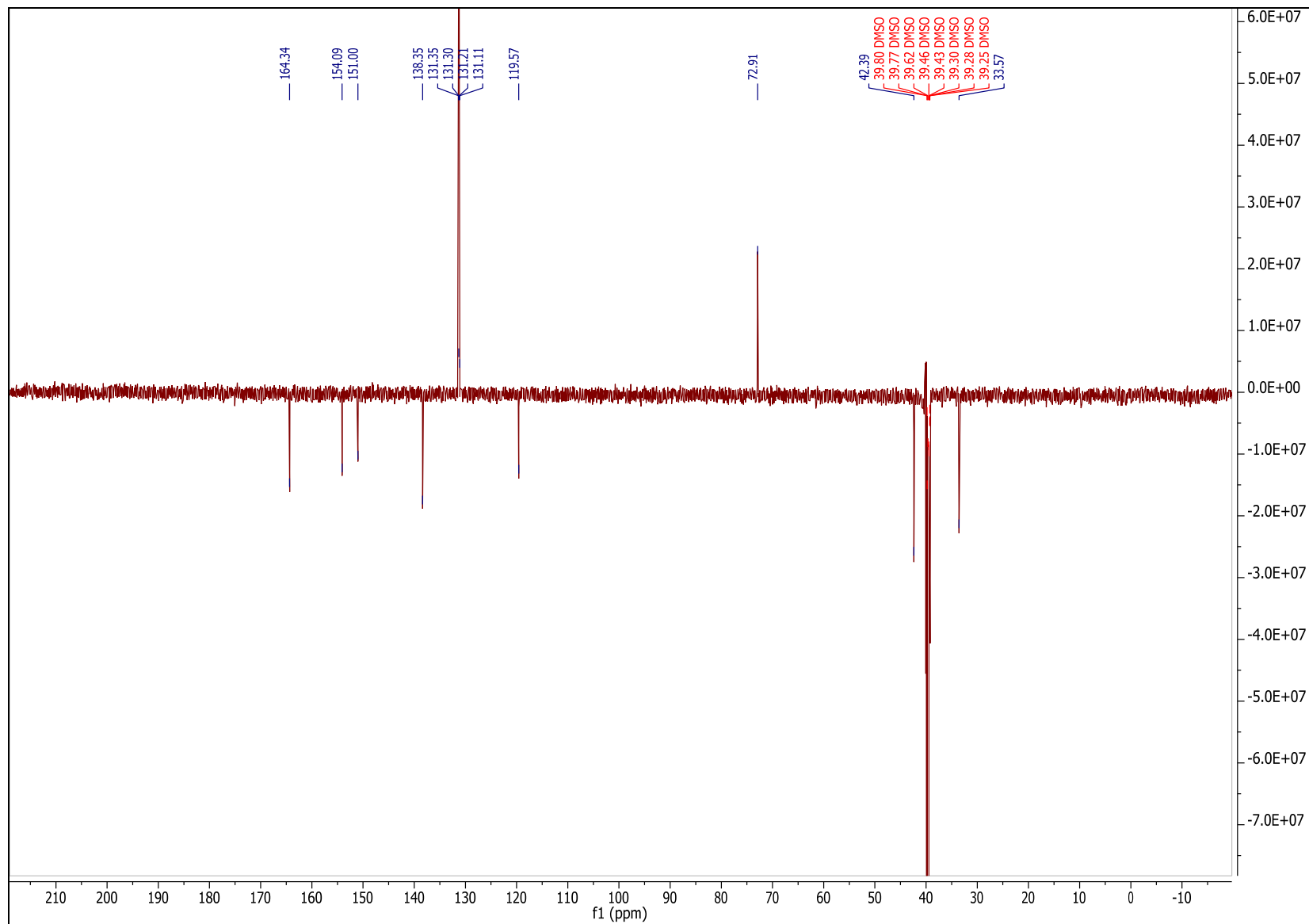
Figure S31. <sup>1</sup>H-NMR spectrum of **47** (500 MHz)



**Figure S32.** <sup>13</sup>C-NMR spectrum of **47** (126 MHz)



**Figure S33.** <sup>1</sup>H-NMR spectrum of **48** (500 MHz)



**Figure S34.**  $^{13}\text{C}_{\text{Capt}}$ -NMR spectrum of **48** (126 MHz)

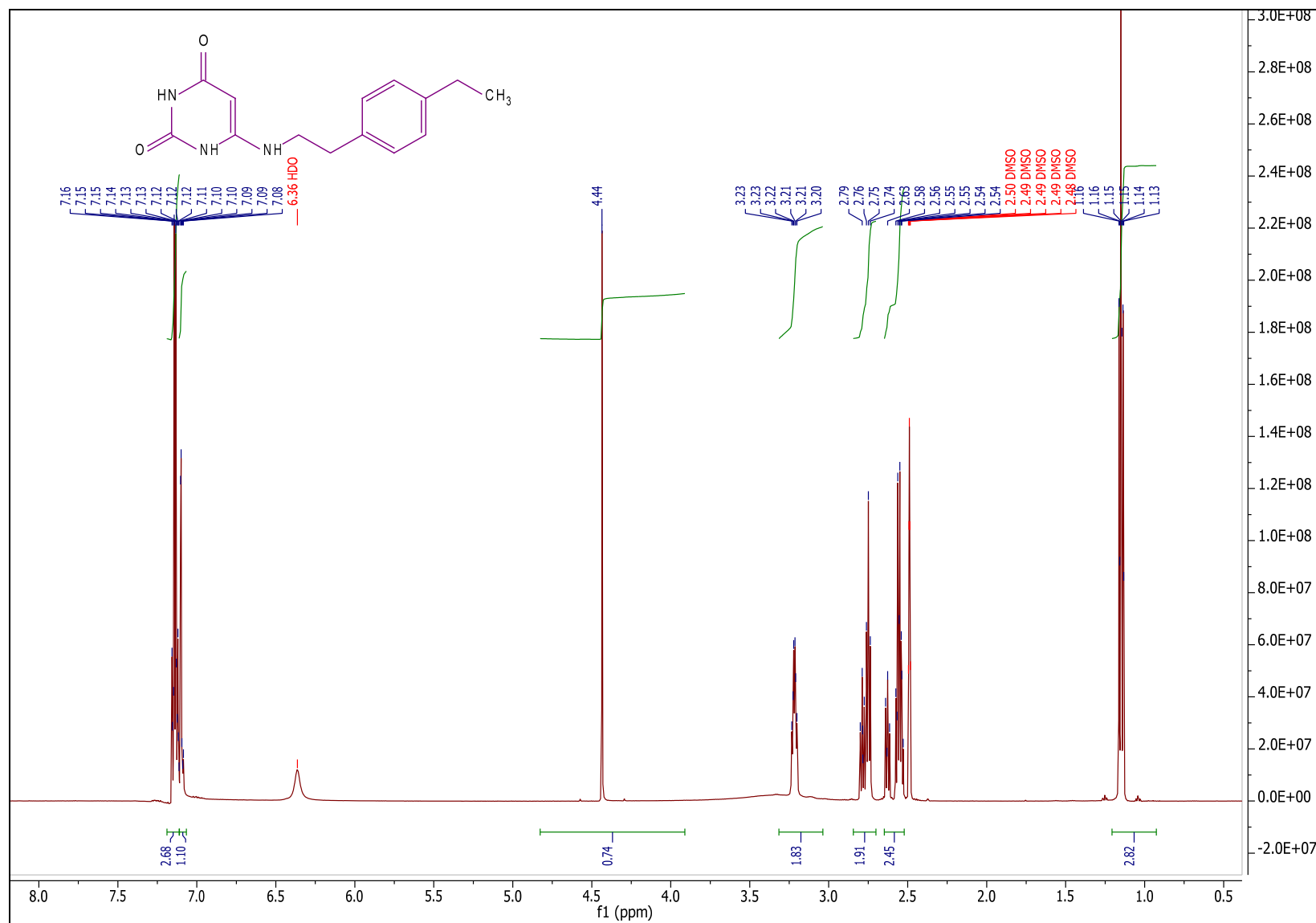


Figure S35. <sup>1</sup>H-NMR spectrum of **49** (600 MHz)

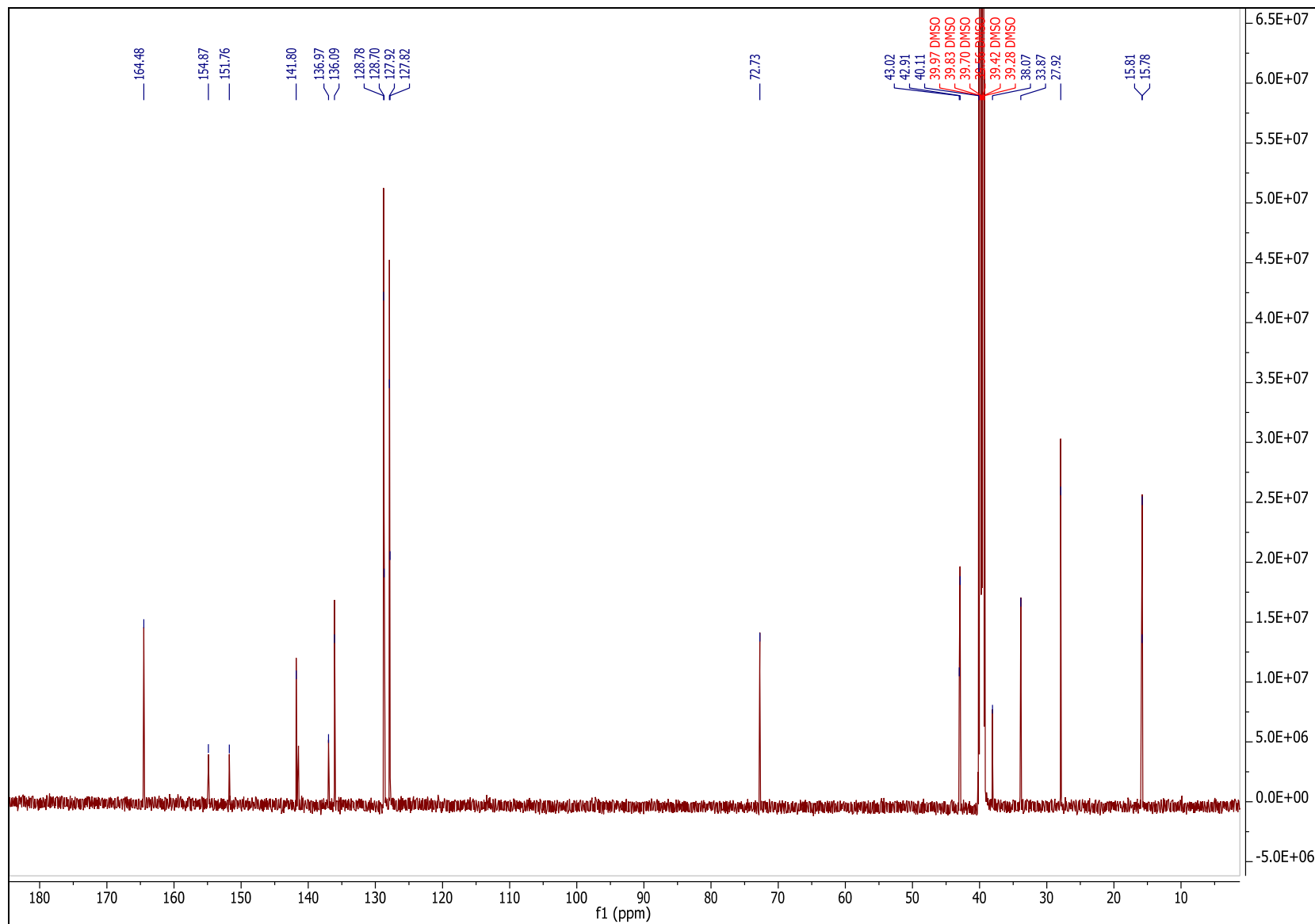


Figure S36. <sup>13</sup>C-NMR spectrum of **49** (151 MHz)



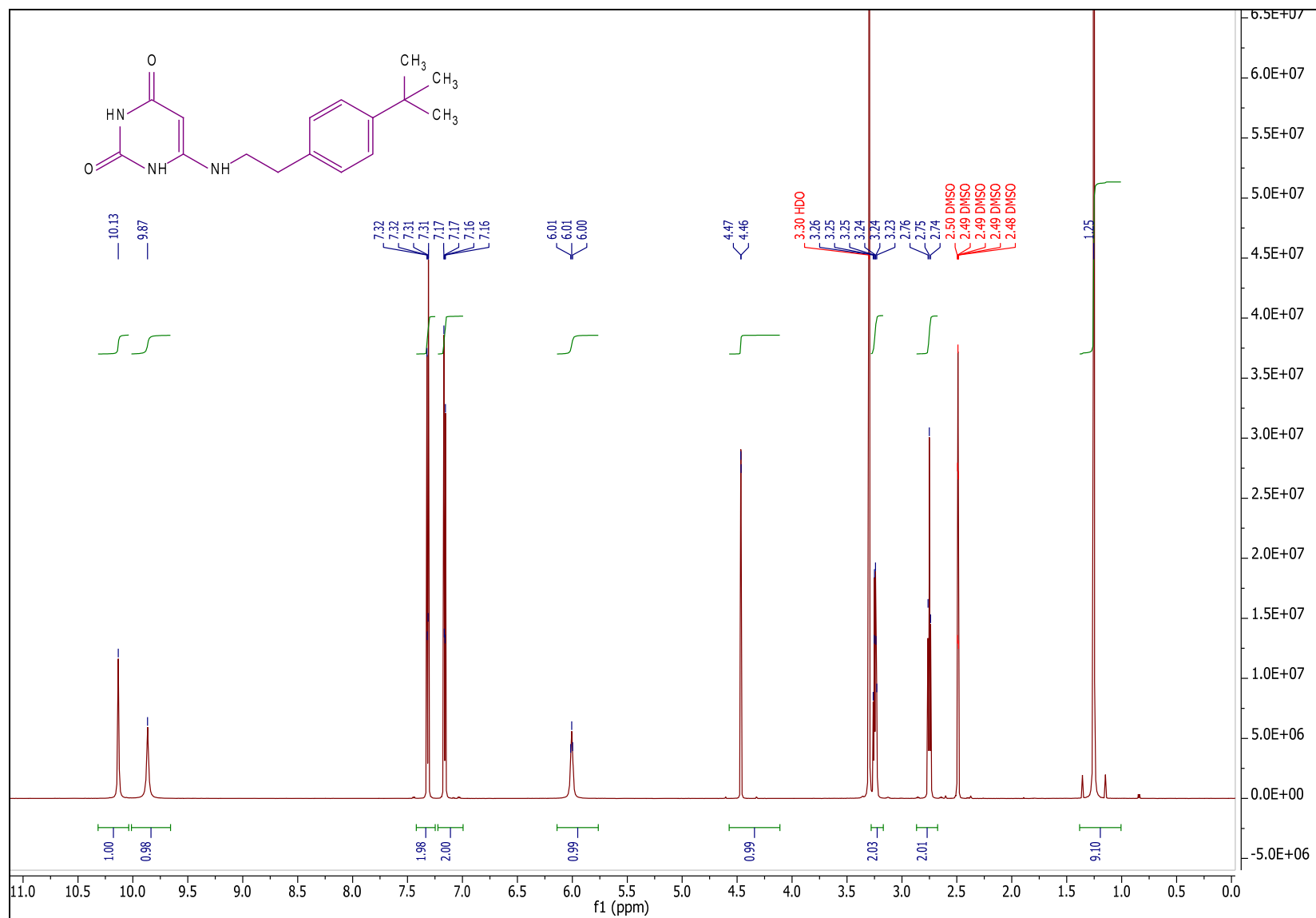


Figure S37. <sup>1</sup>H-NMR spectrum of **51** (600 MHz)

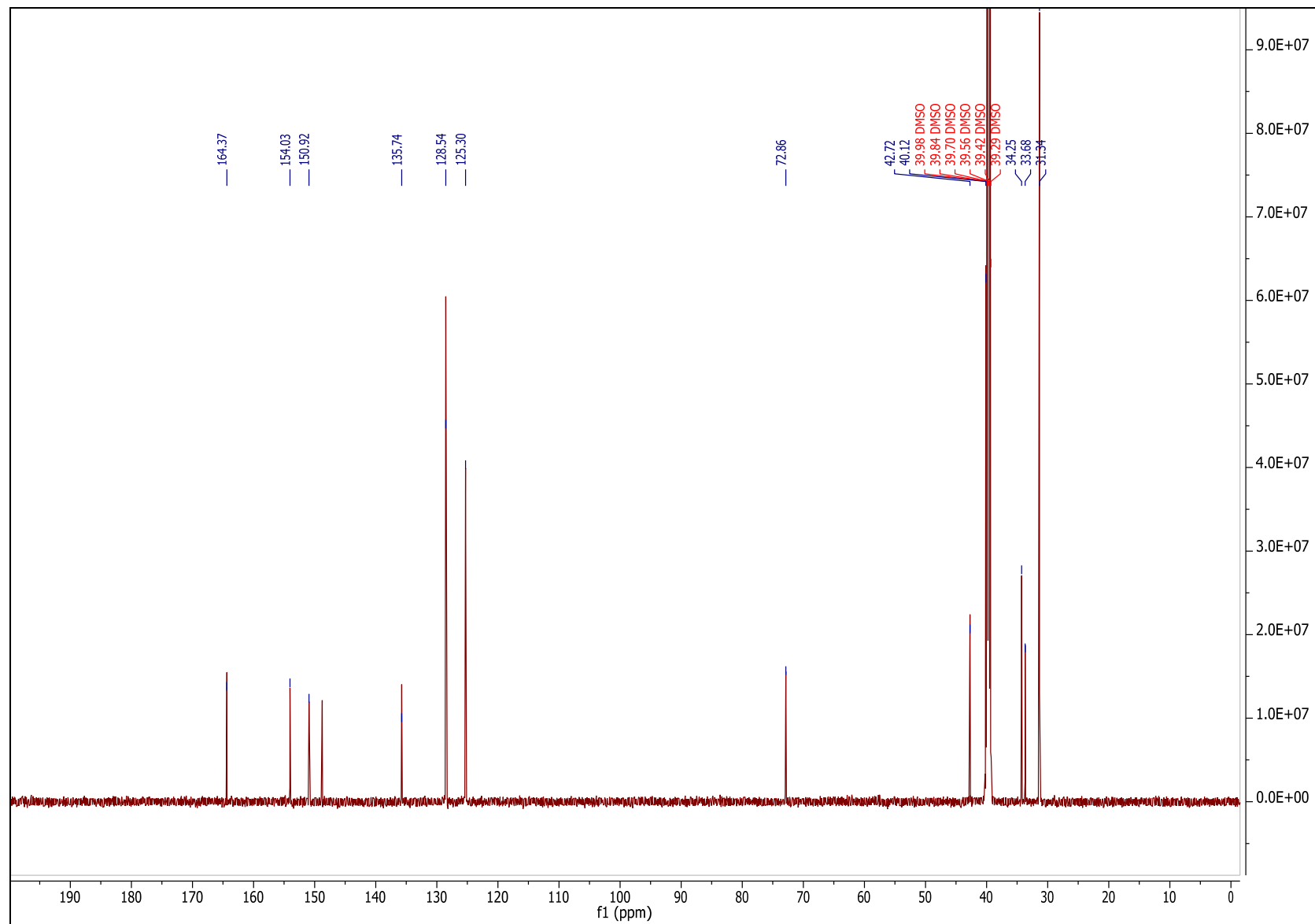
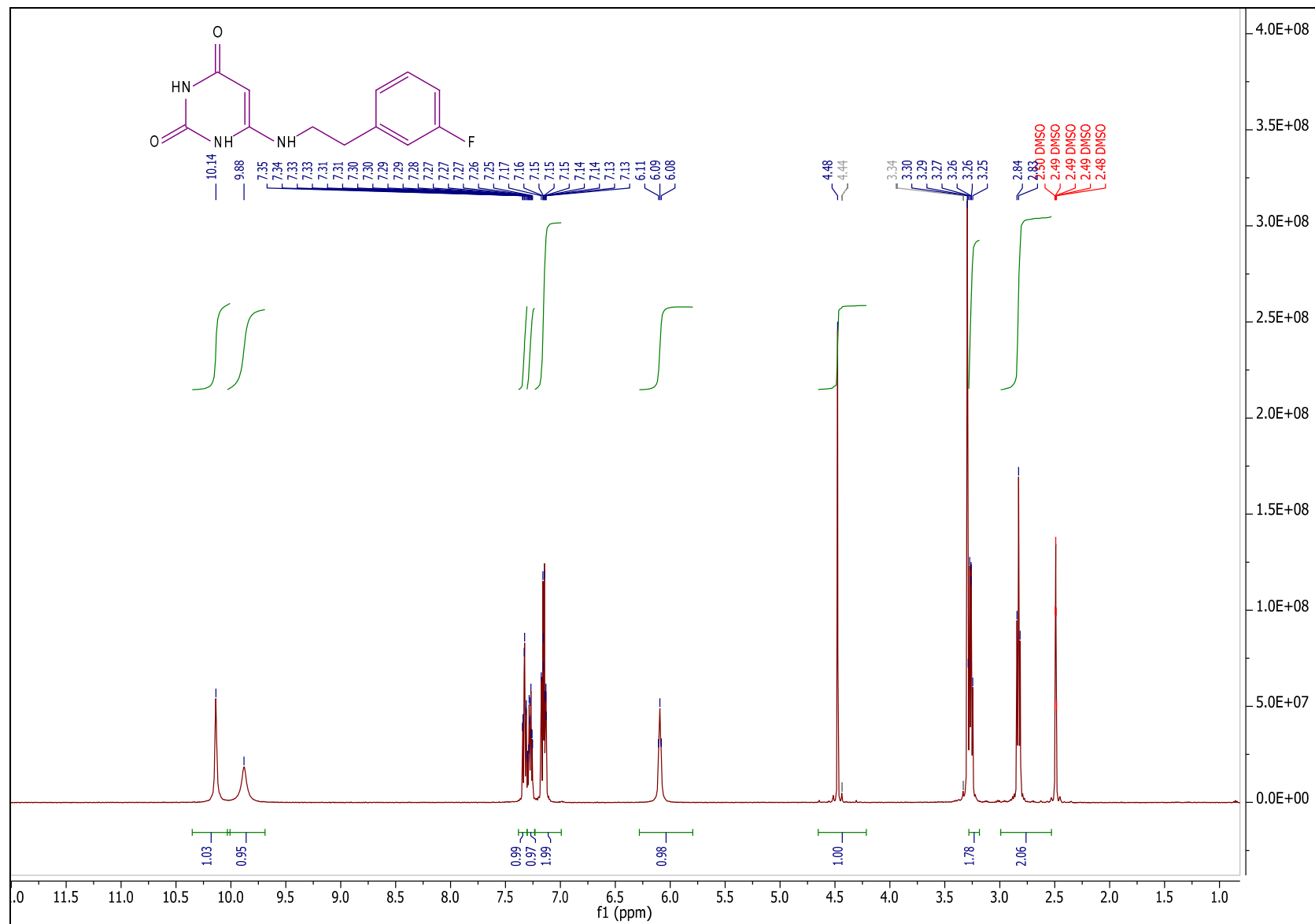


Figure S38.  $^{13}\text{C}$ -NMR spectrum of **51** (151 MHz)



**Figure S39.**  $^1\text{H}$ -NMR spectrum of **53** (500 MHz)

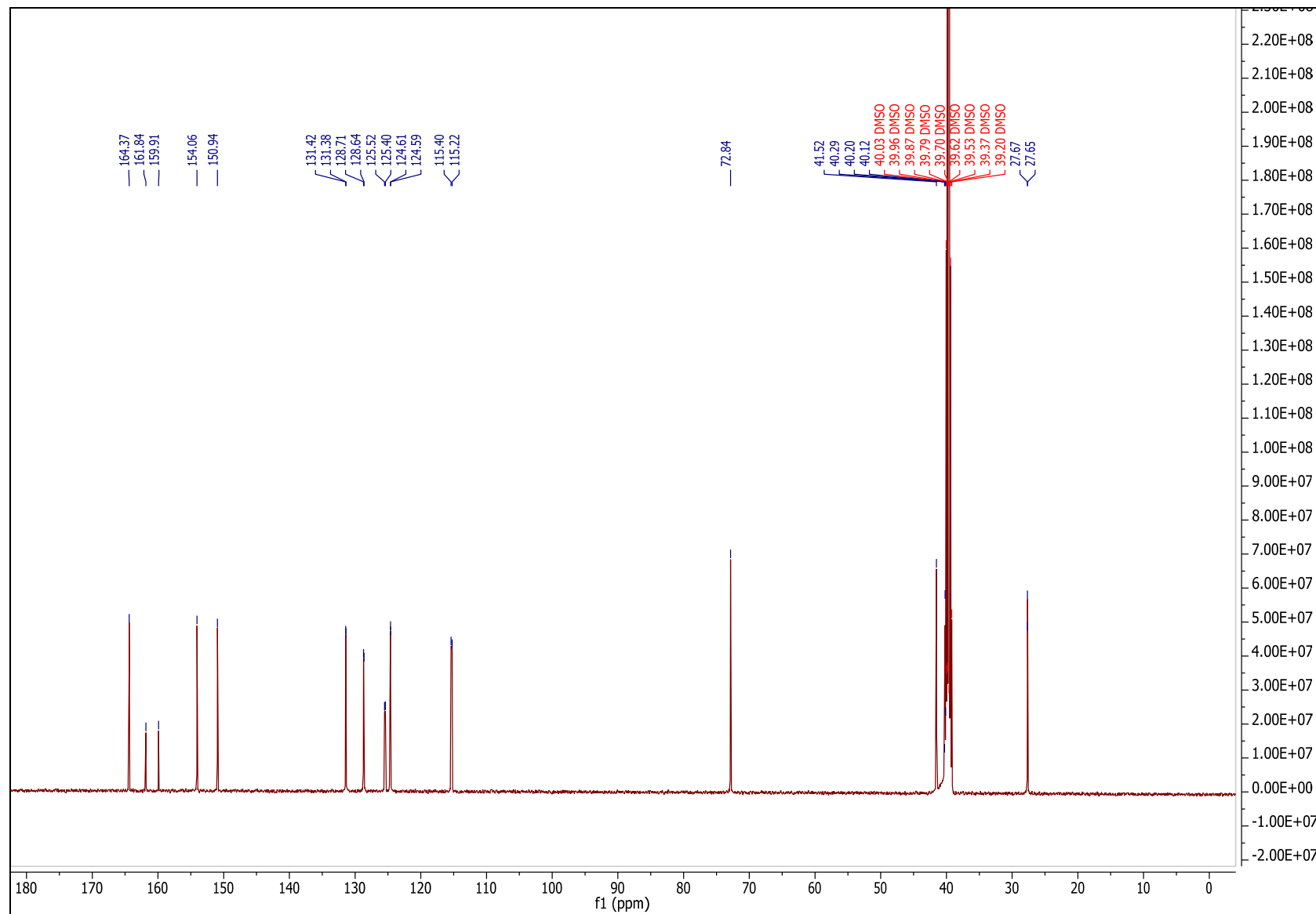


Figure S40. <sup>13</sup>C-NMR spectrum of **53** (126 MHz)

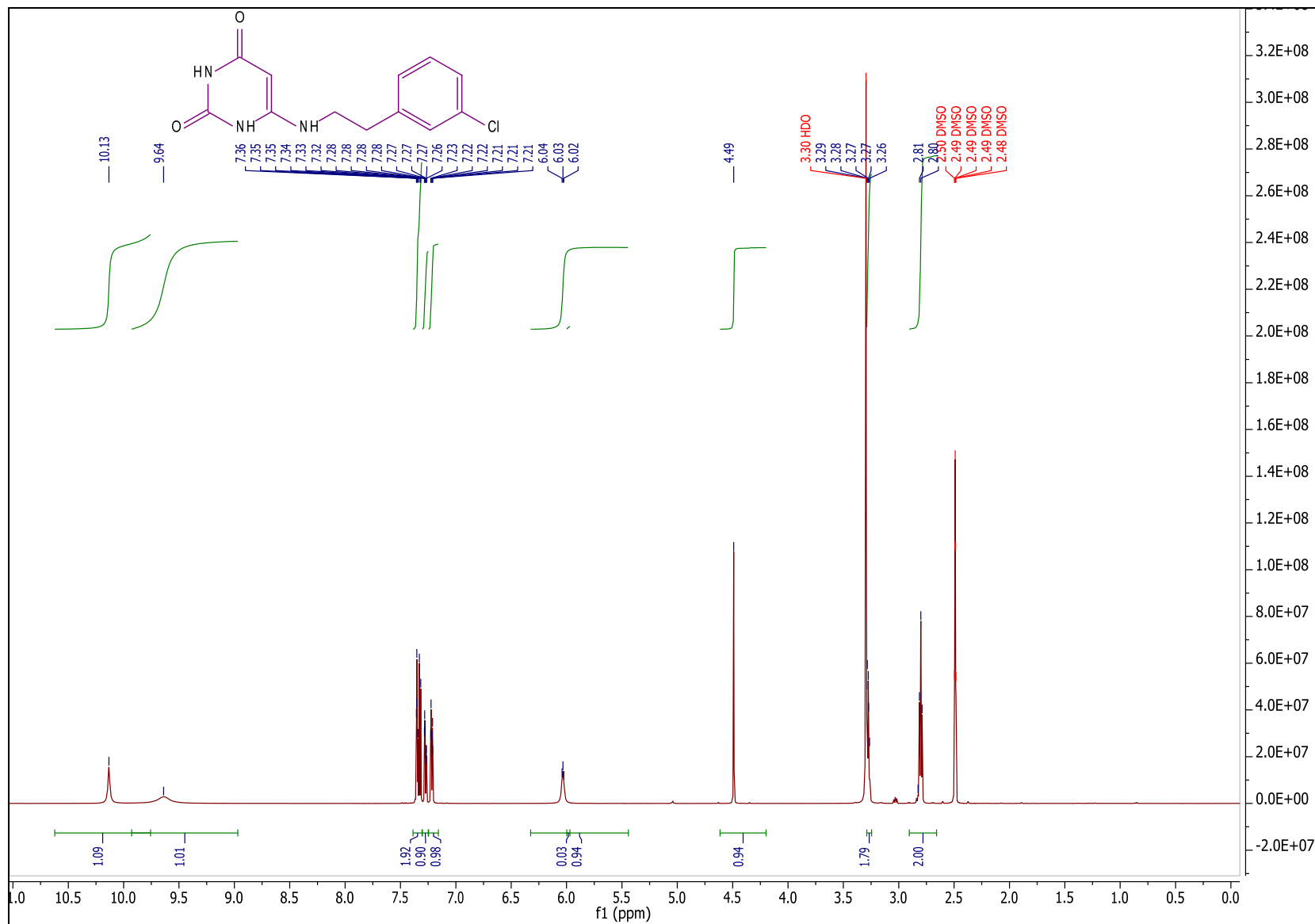


Figure S41. <sup>1</sup>H-NMR spectrum of **54** (600 MHz)

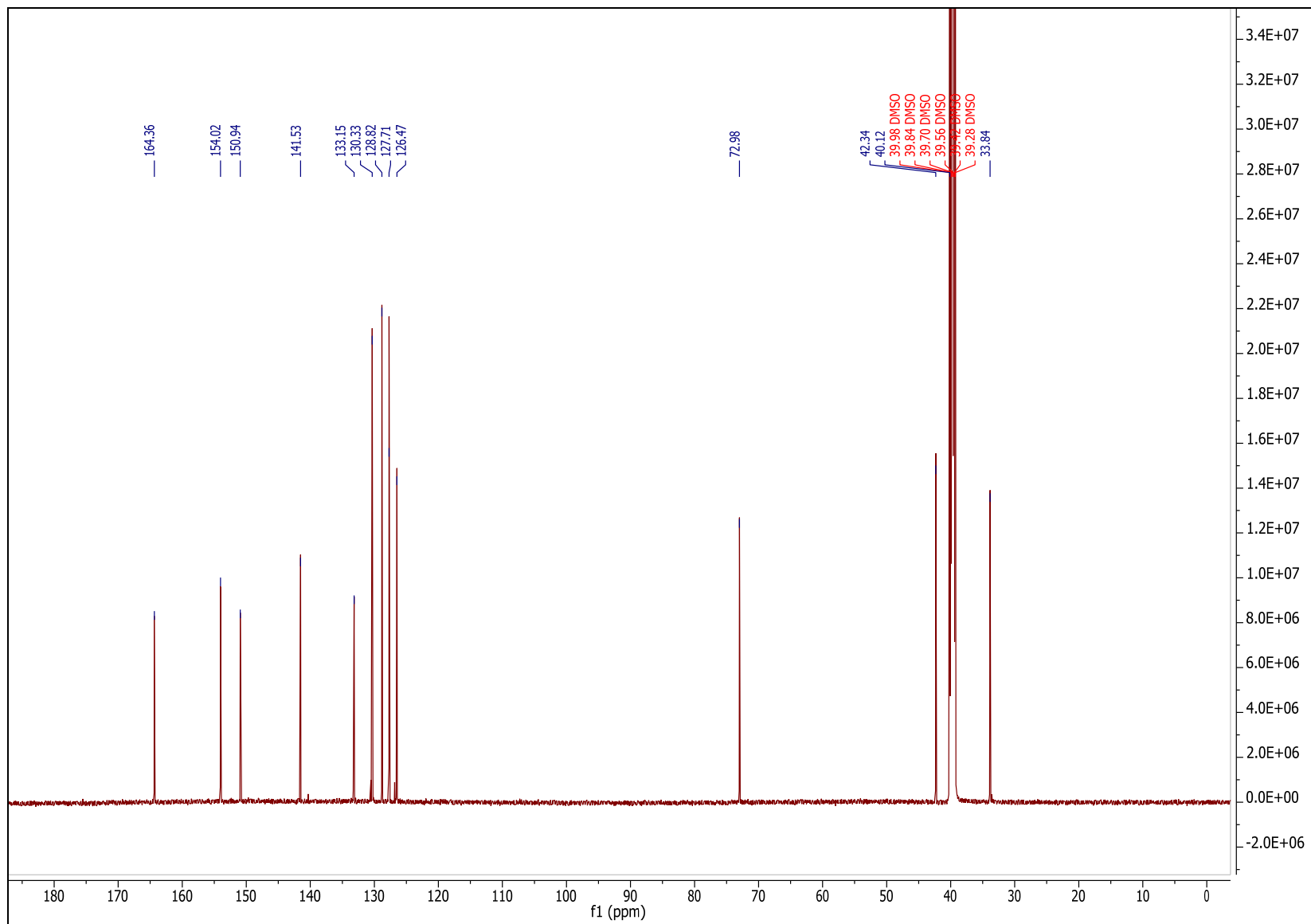


Figure S42. <sup>13</sup>C-NMR spectrum of **54** (151 MHz)

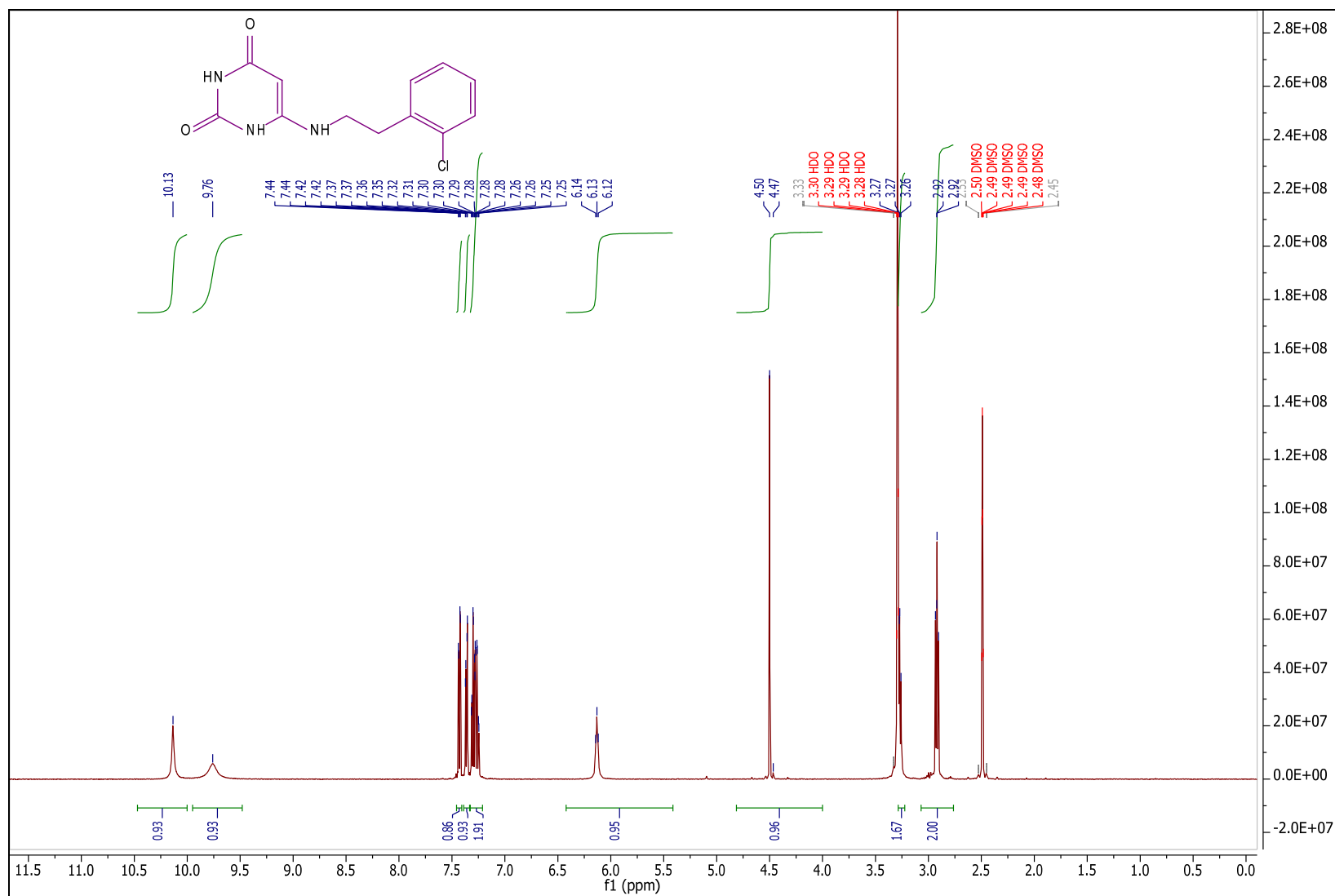


Figure S43. <sup>1</sup>H-NMR spectrum of **58** (500 MHz)

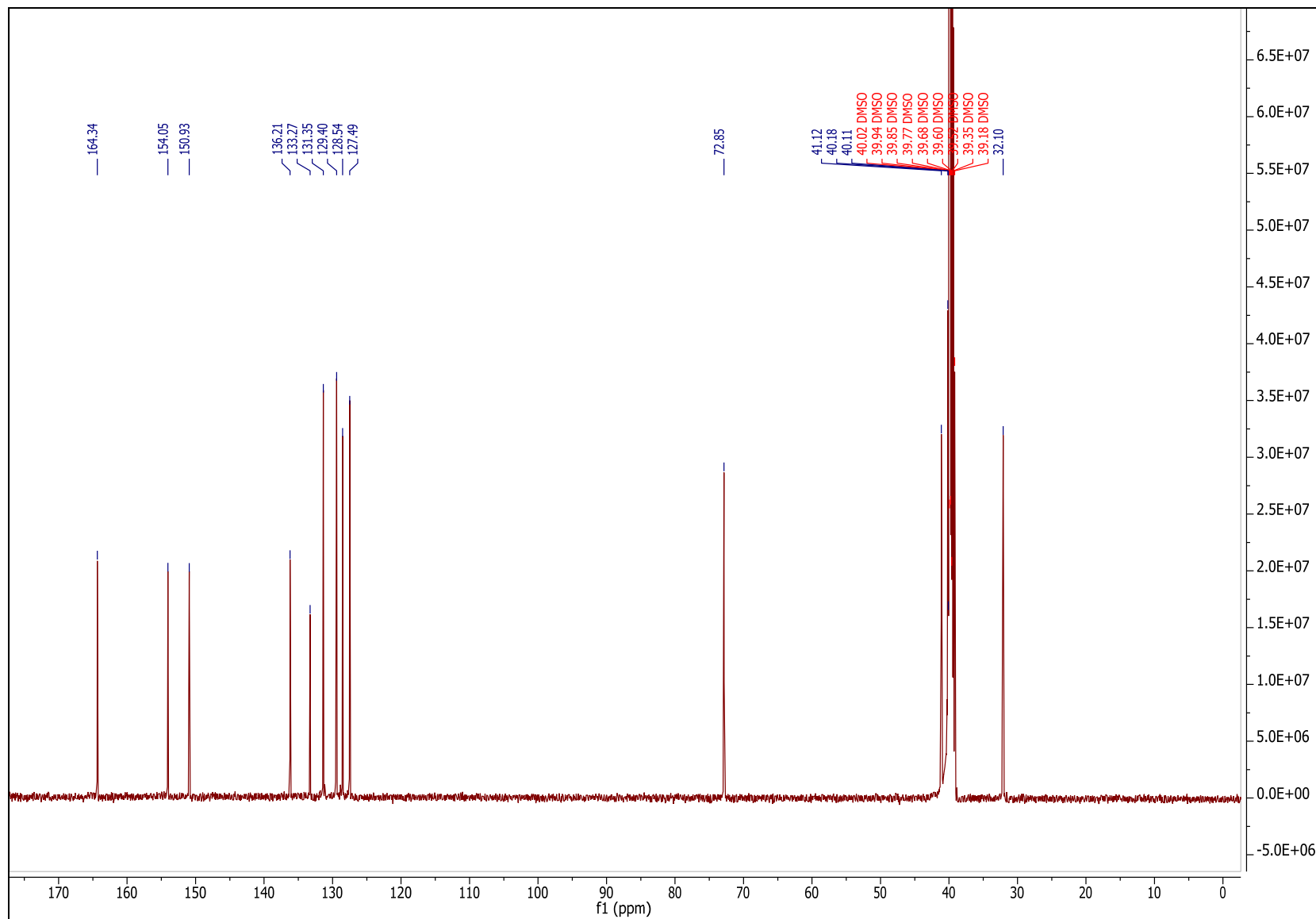


Figure S44. <sup>13</sup>C-NMR spectrum of **58** (126 MHz)



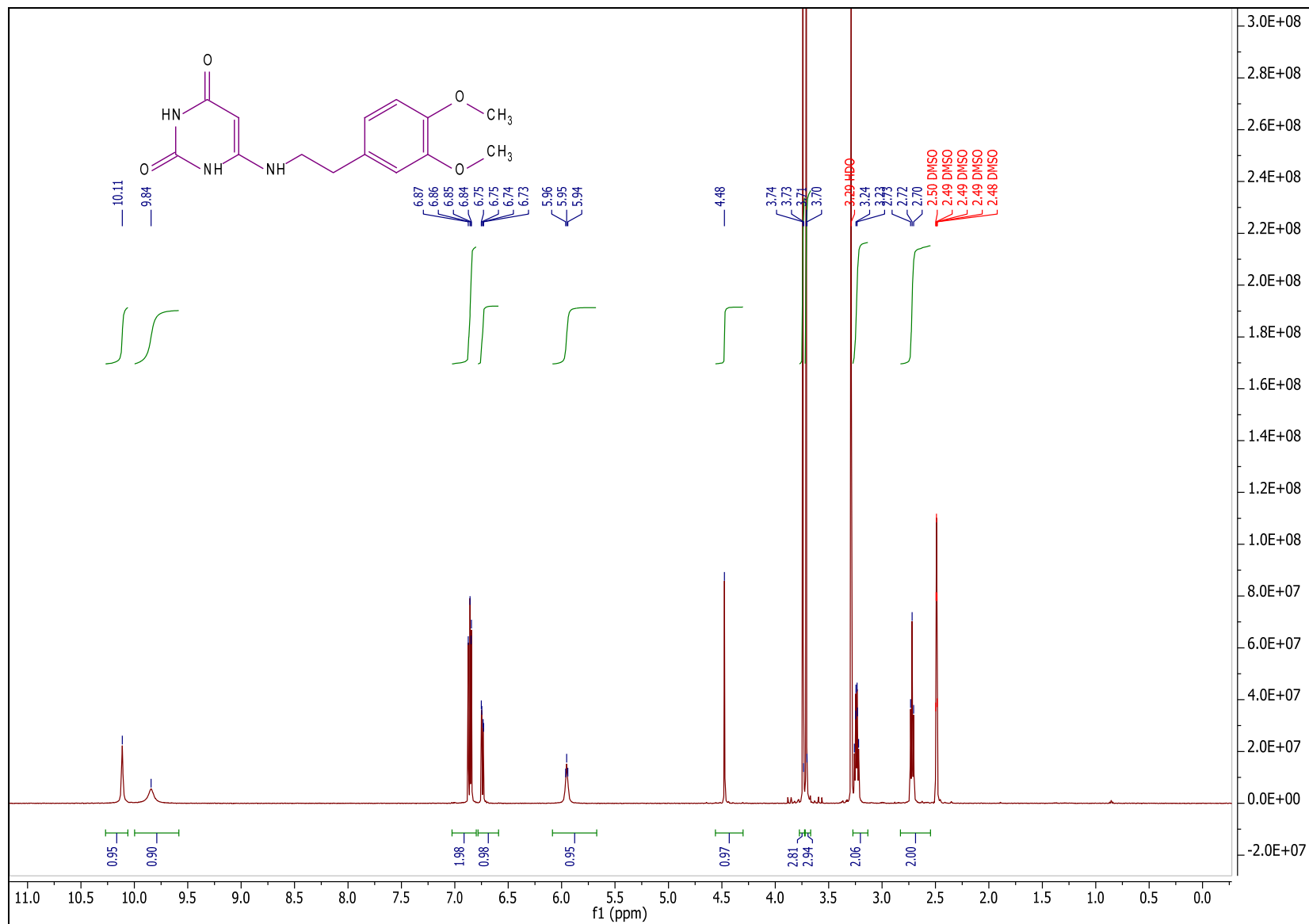
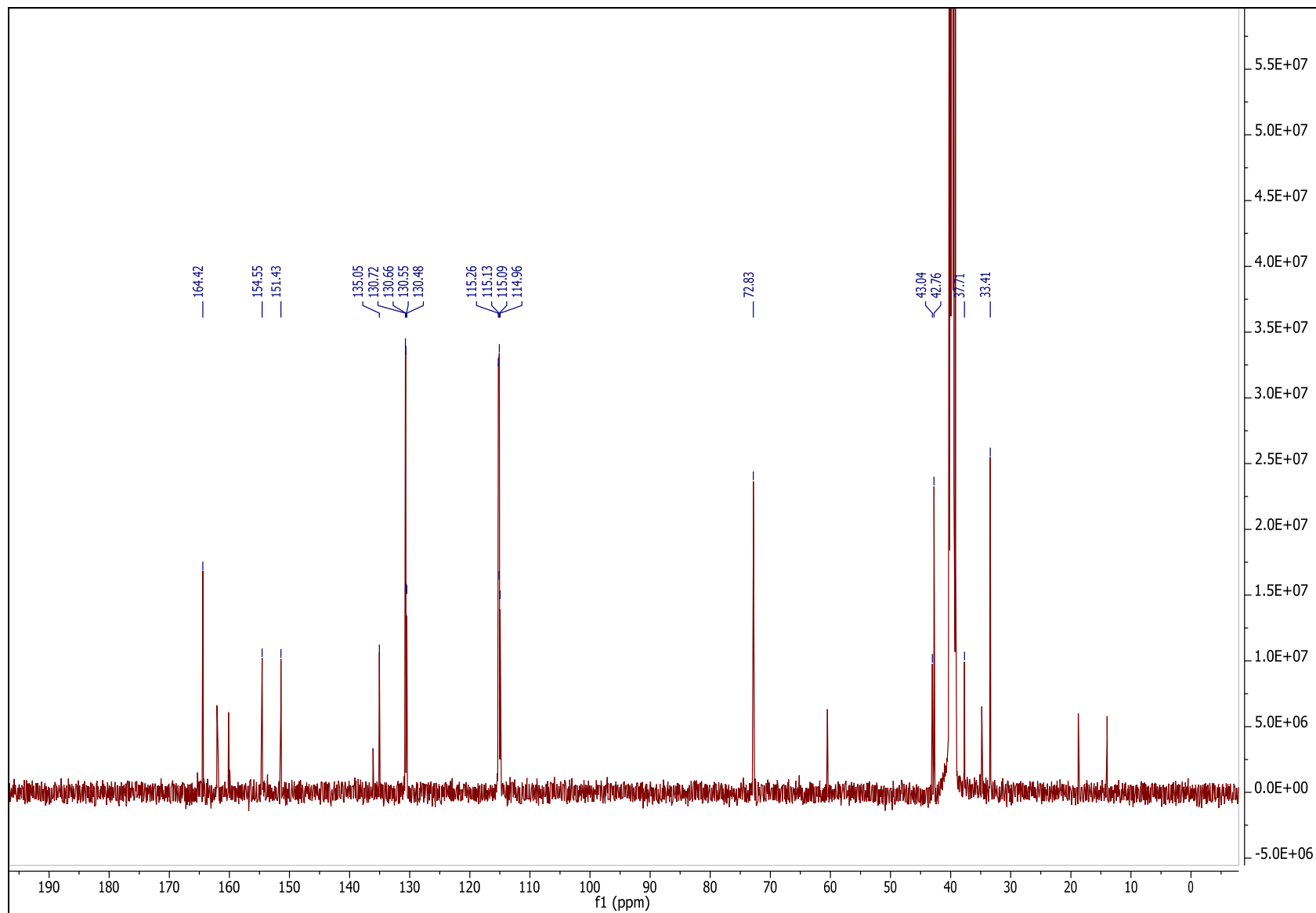


Figure S45. <sup>1</sup>H-NMR spectrum of **60** (500 MHz)



**Figure S46.**  $^{13}\text{C}$ -NMR spectrum of **60** (126 MHz)

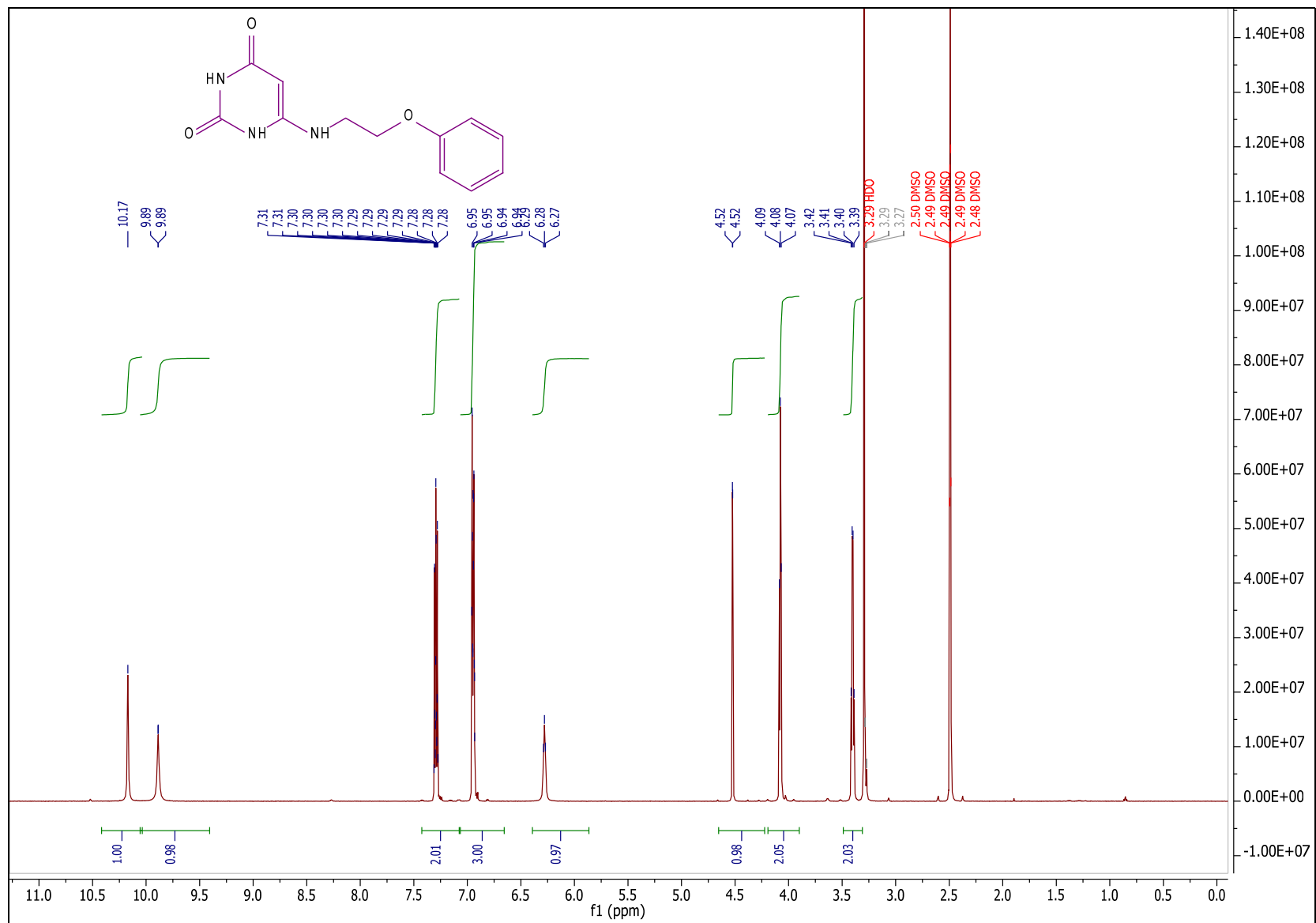


Figure S47. <sup>1</sup>H-NMR spectrum of **64** (600 MHz)

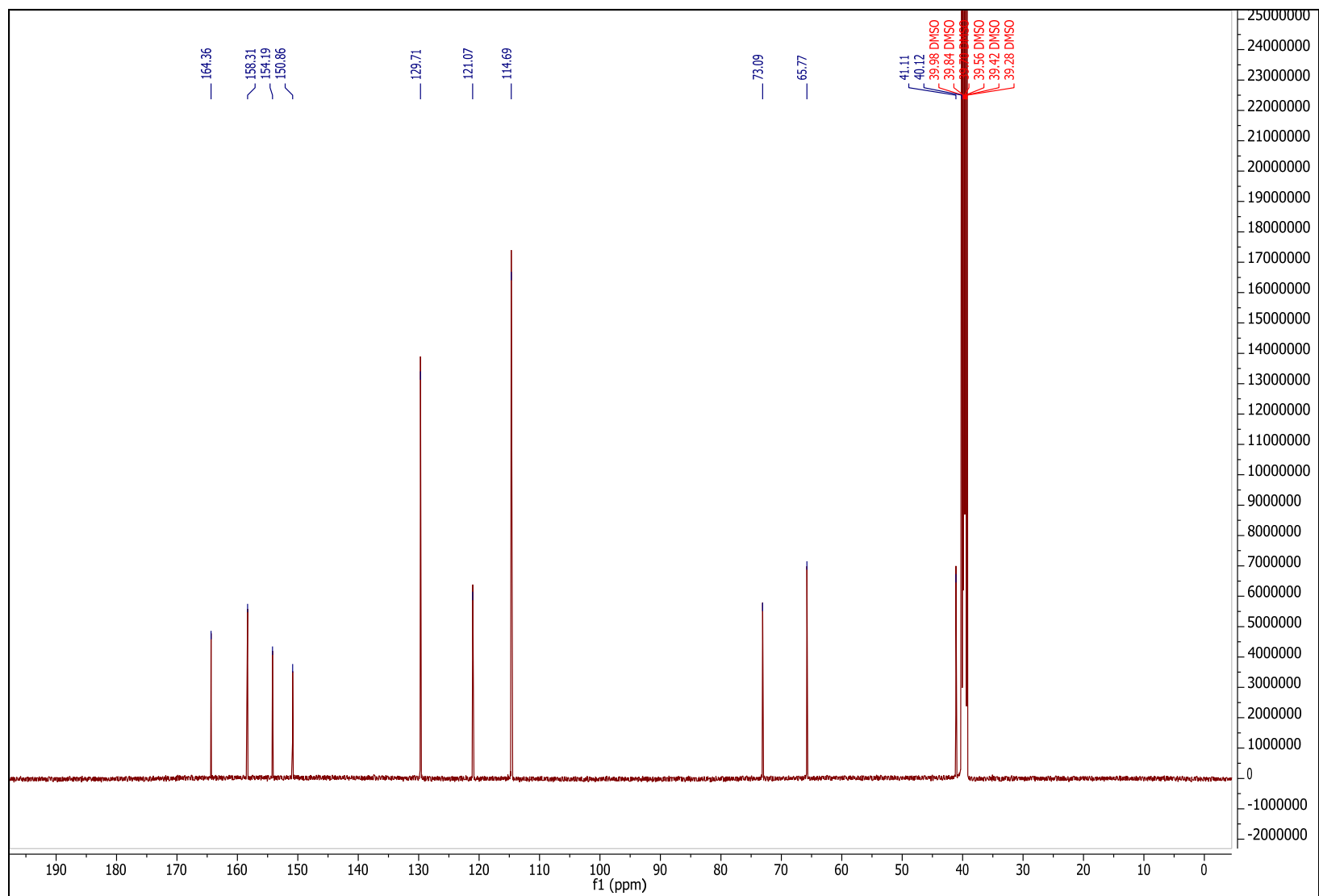


Figure S48. <sup>13</sup>C-NMR spectrum of **64** (151 MHz)

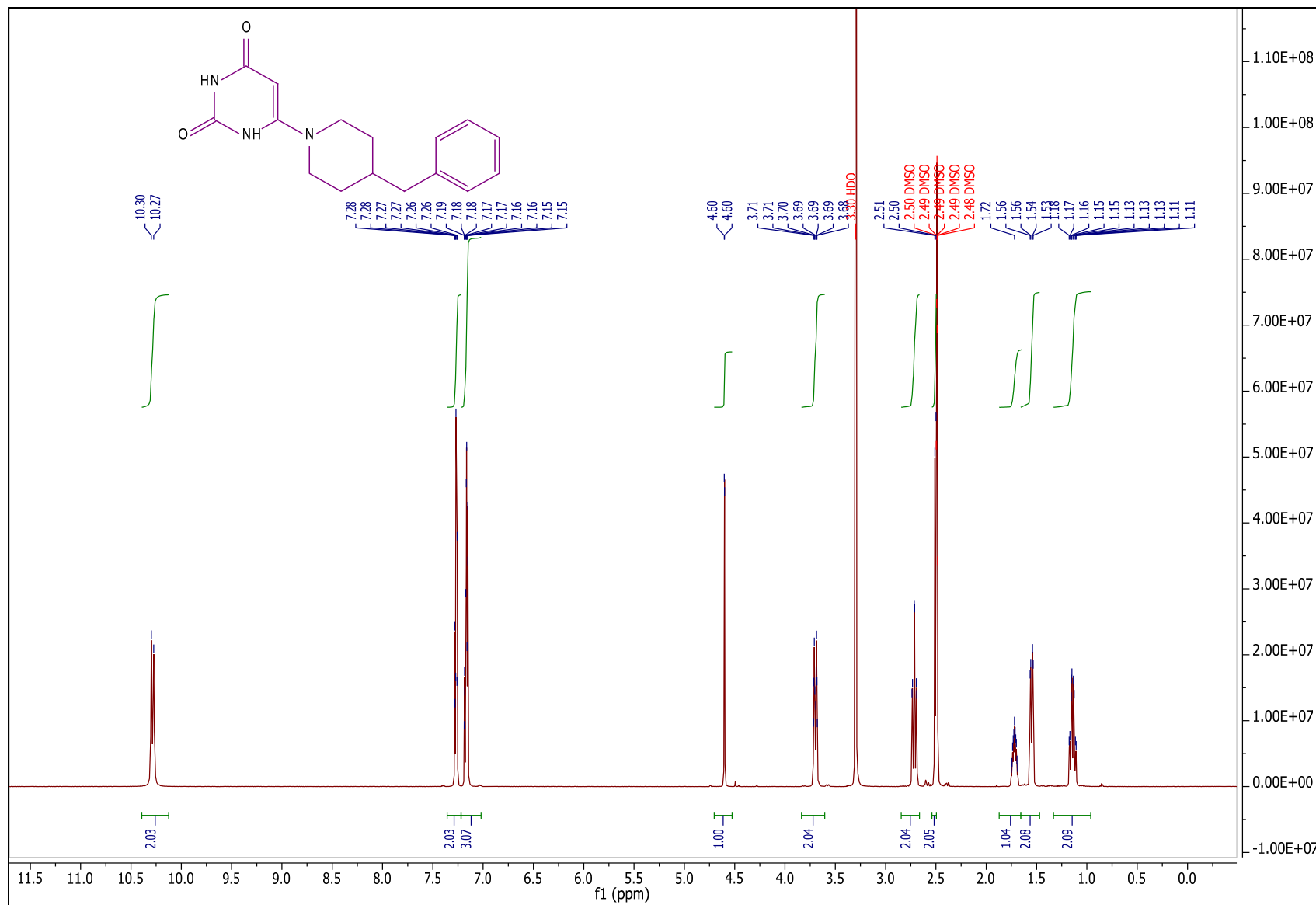


Figure S49.  $^1\text{H}$ -NMR spectrum of **67** (600 MHz)

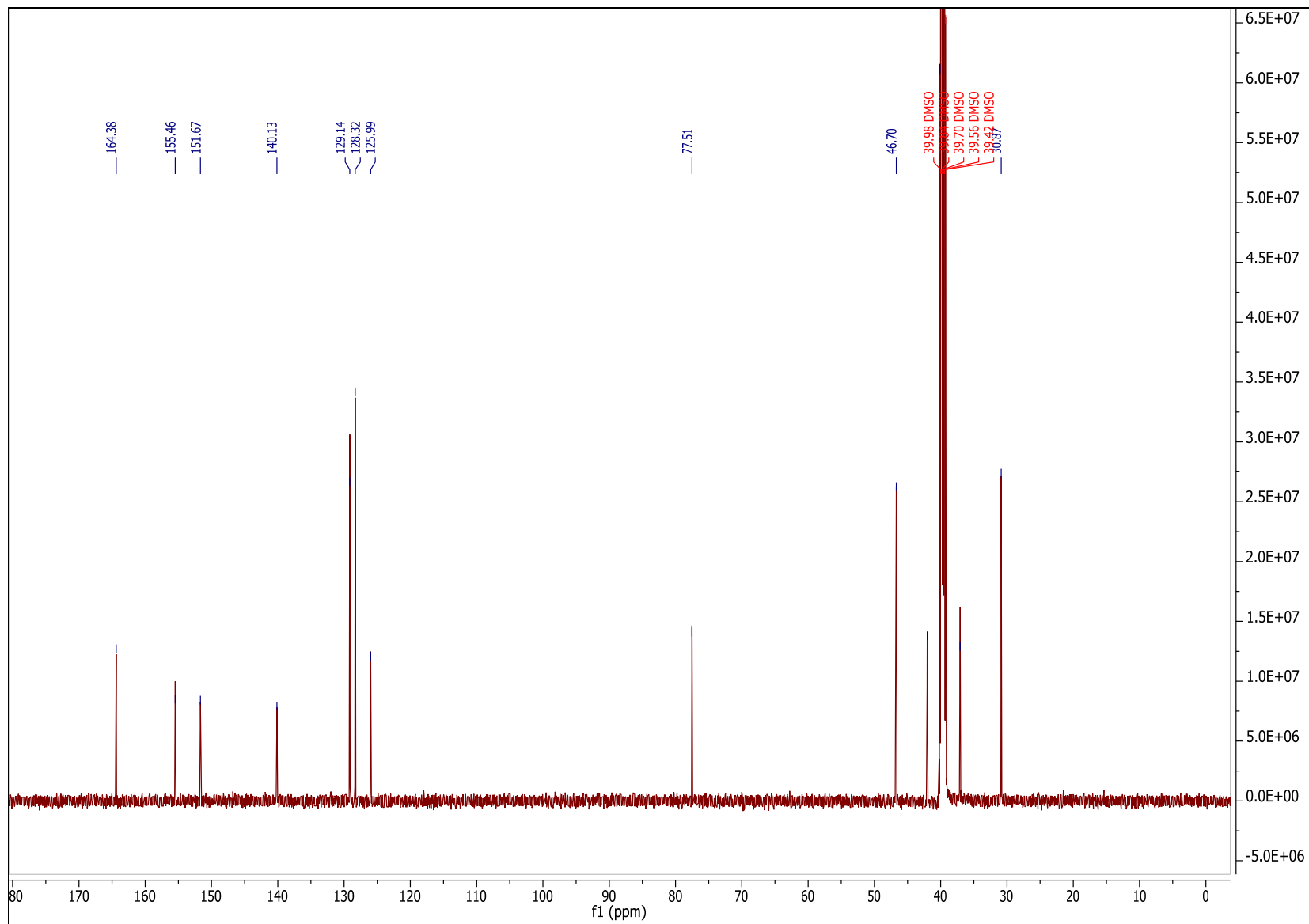


Figure S50. <sup>13</sup>C-NMR spectrum of **67** (151 MHz)

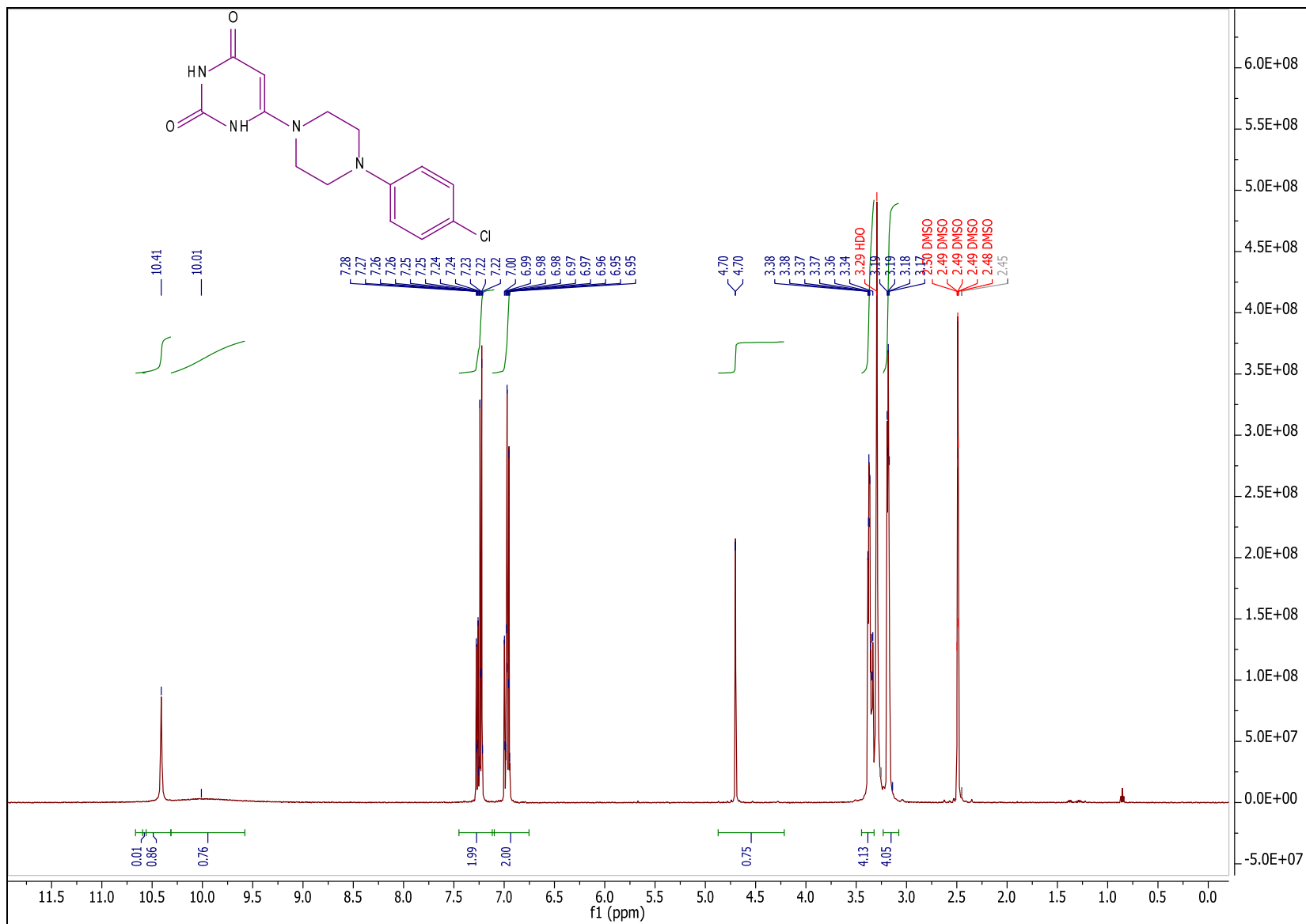


Figure S51.  $^1\text{H}$ -NMR spectrum of **68** (500 MHz)

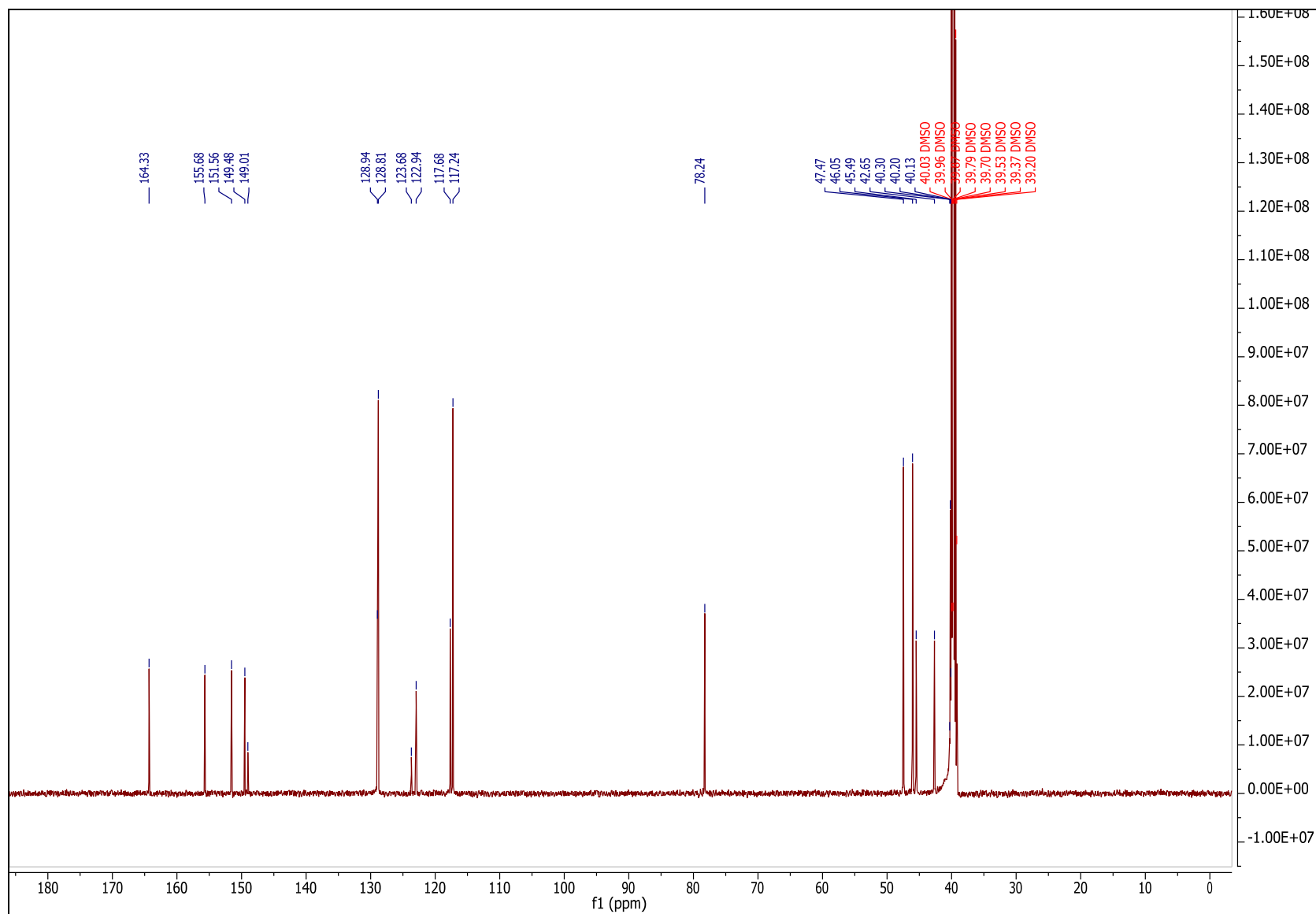
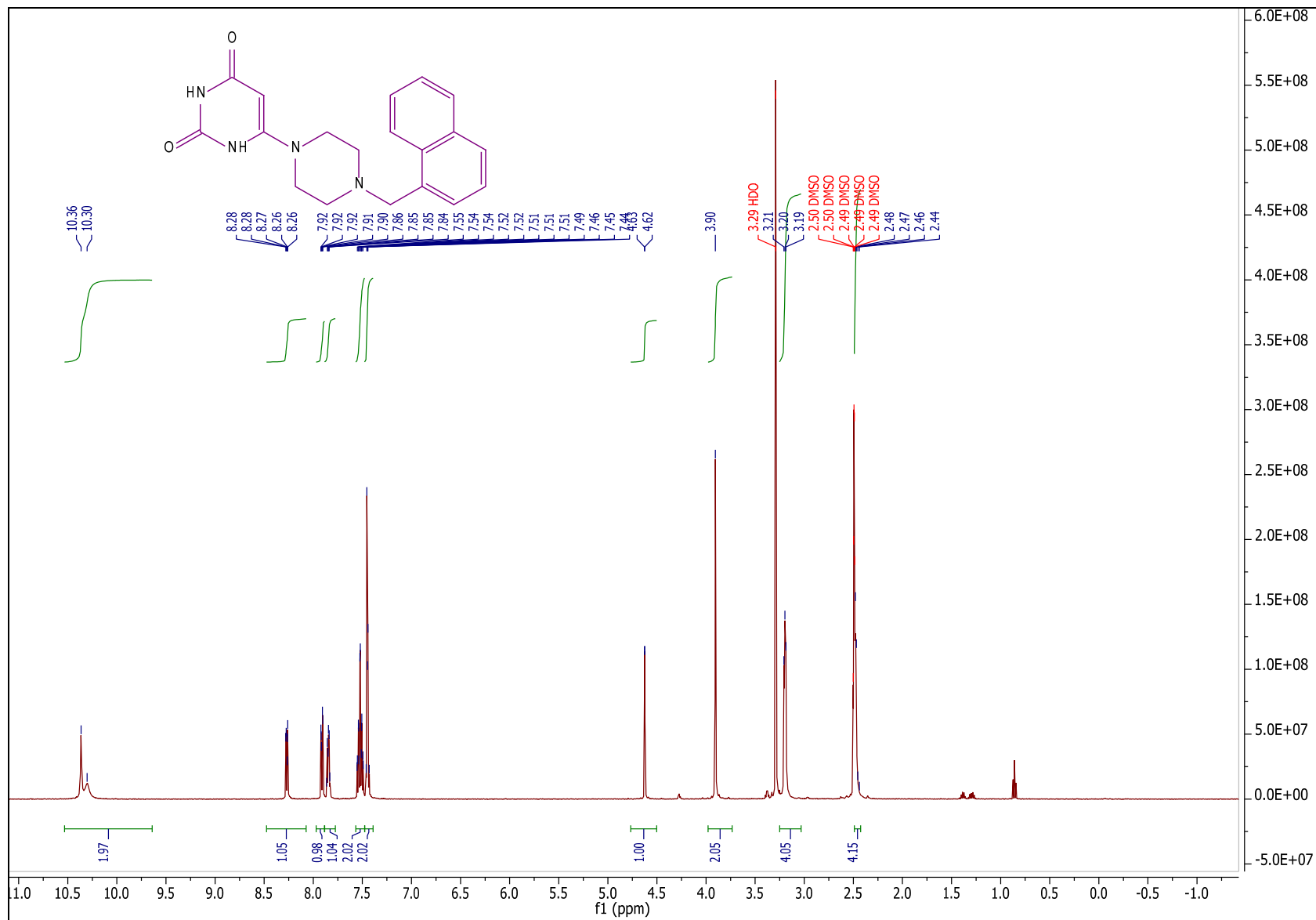


Figure S52. <sup>13</sup>C-NMR spectrum of **68** (121 MHz)





**Figure S53.**  $^1\text{H}$ -NMR spectrum of **71** (500 MHz)

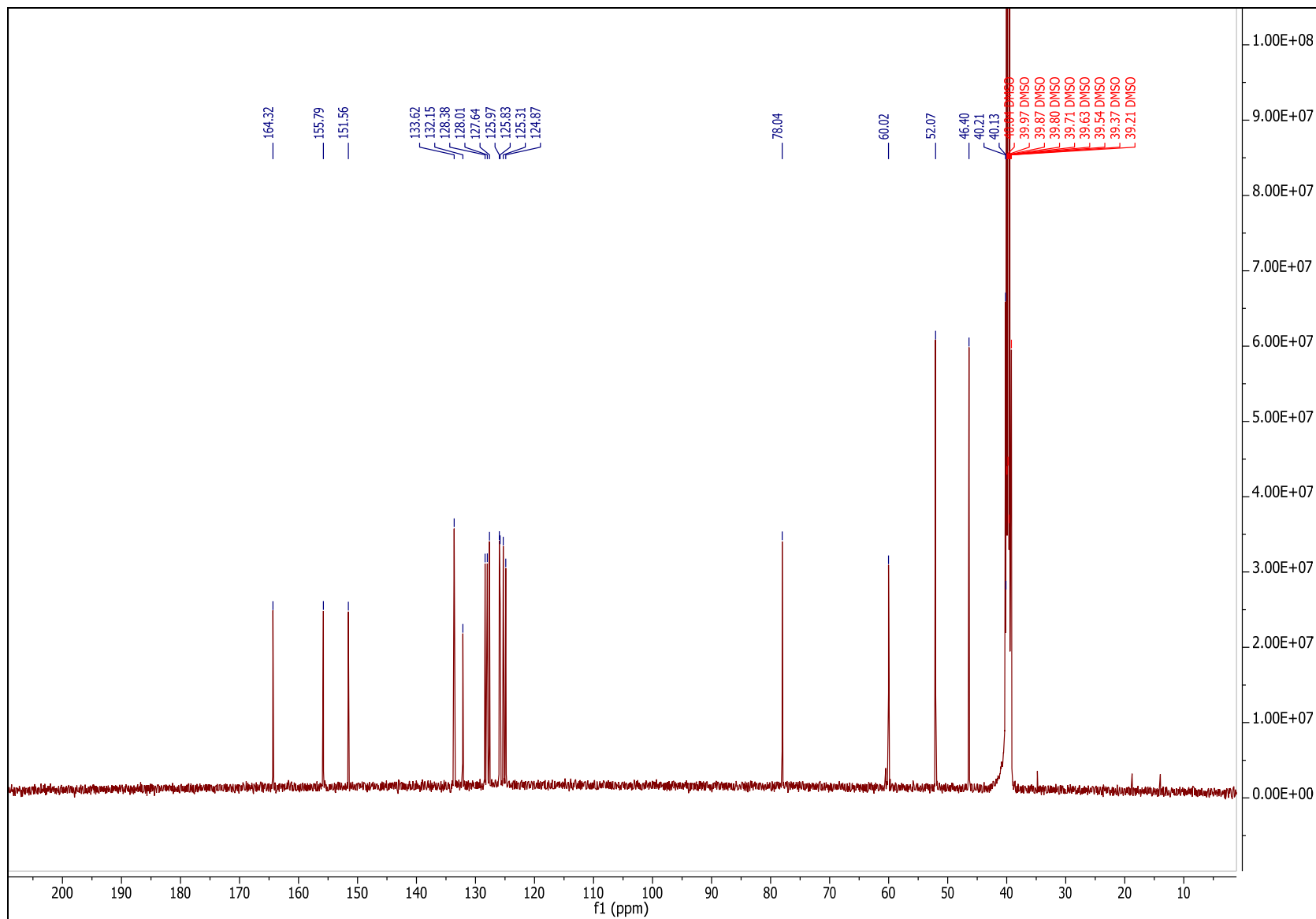


Figure S54. <sup>13</sup>C-NMR spectrum of **71** (126 MHz)

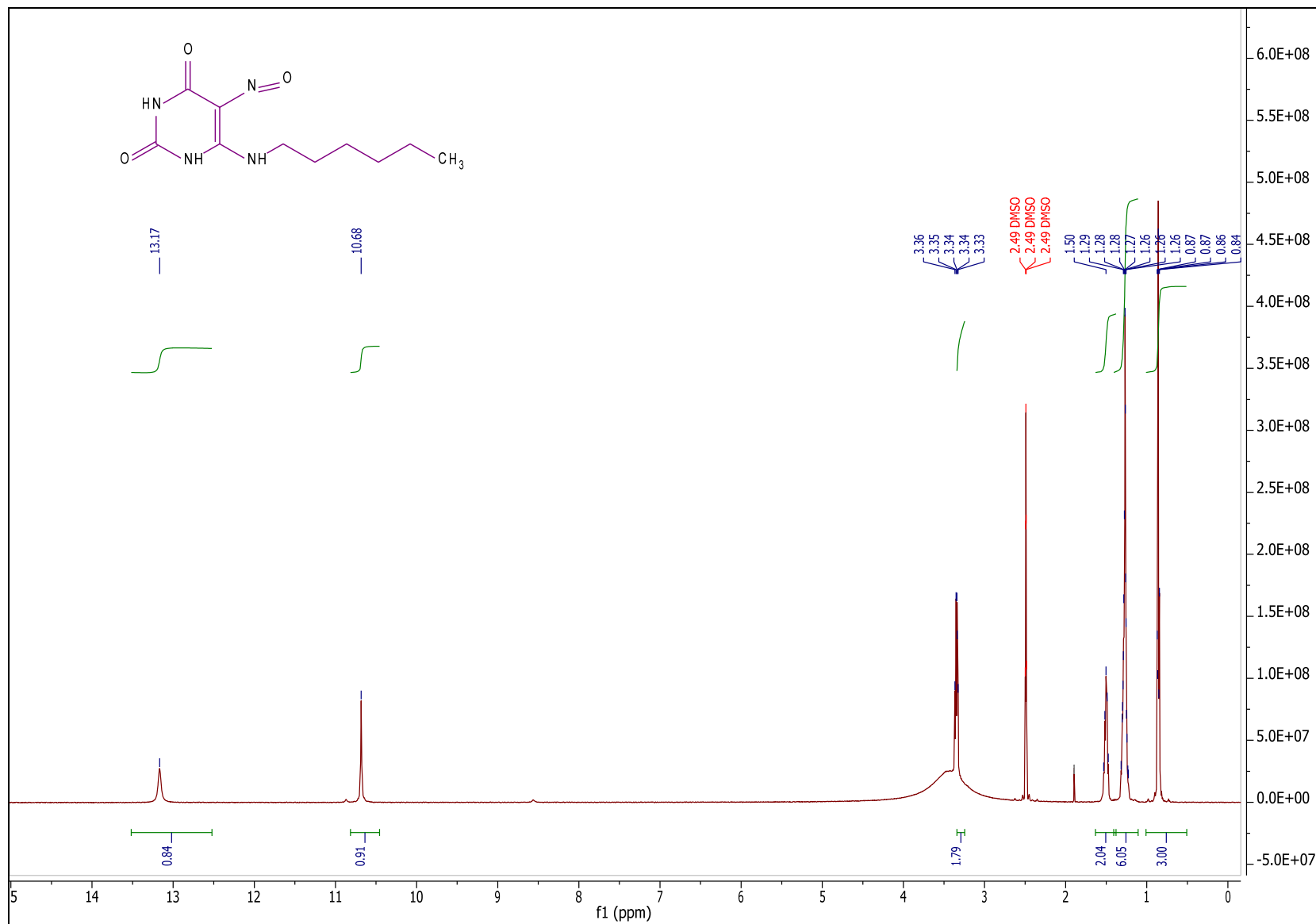
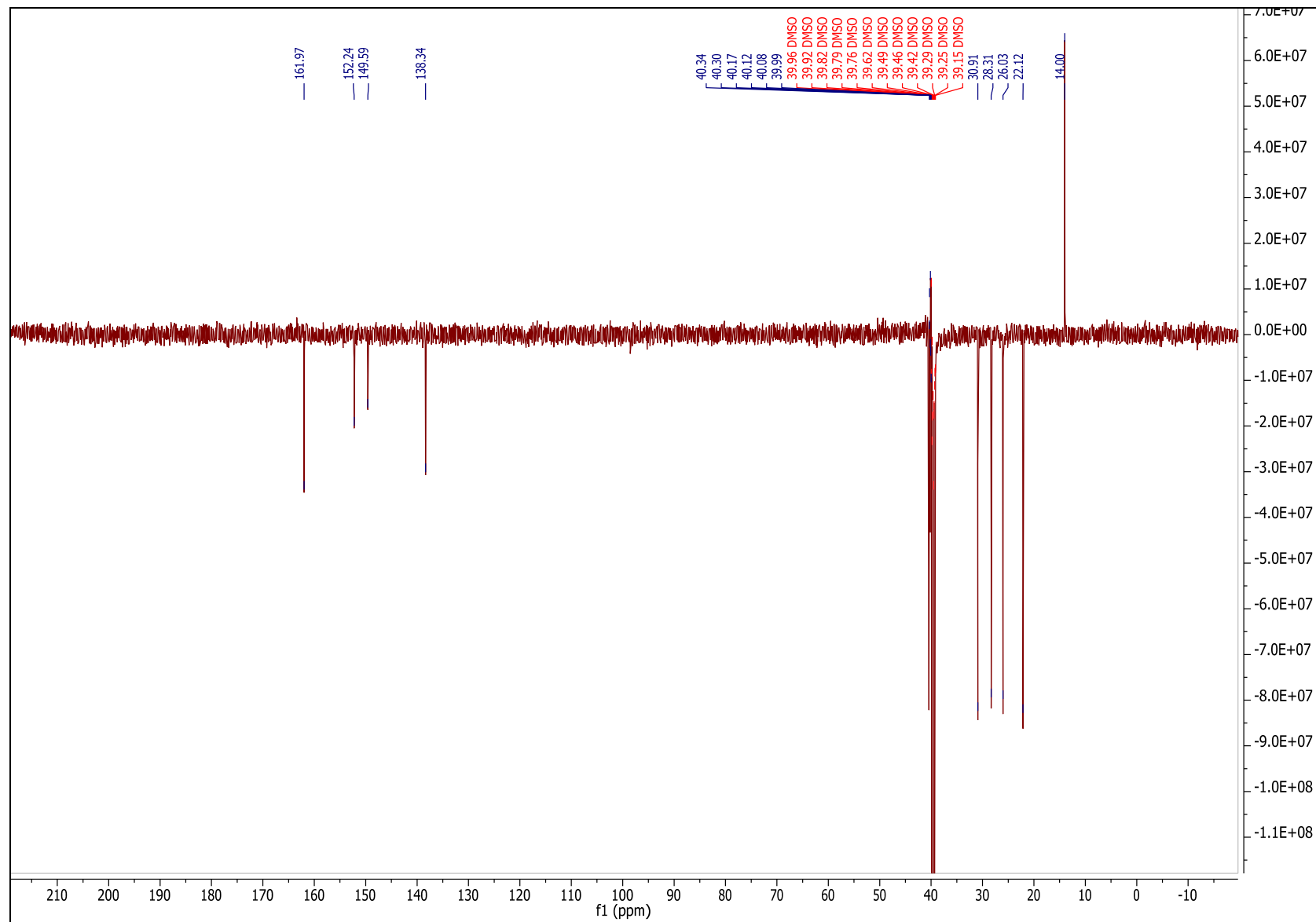


Figure S55.  $^1\text{H}$ -NMR spectrum of **76** (500 MHz)



**Figure S56.** <sup>13</sup>C<sub>capt</sub>-NMR spectrum of **76** (126 MHz)

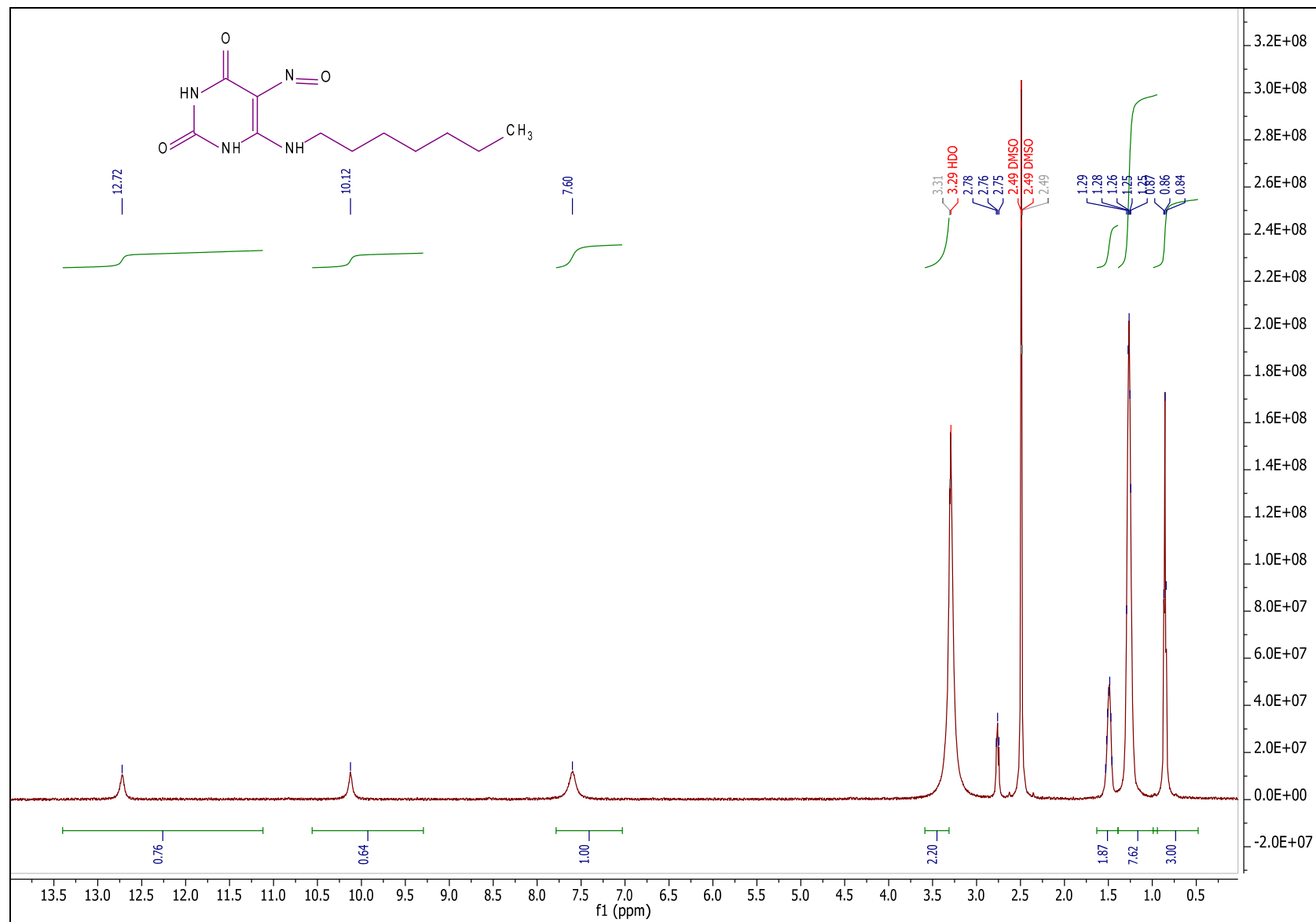
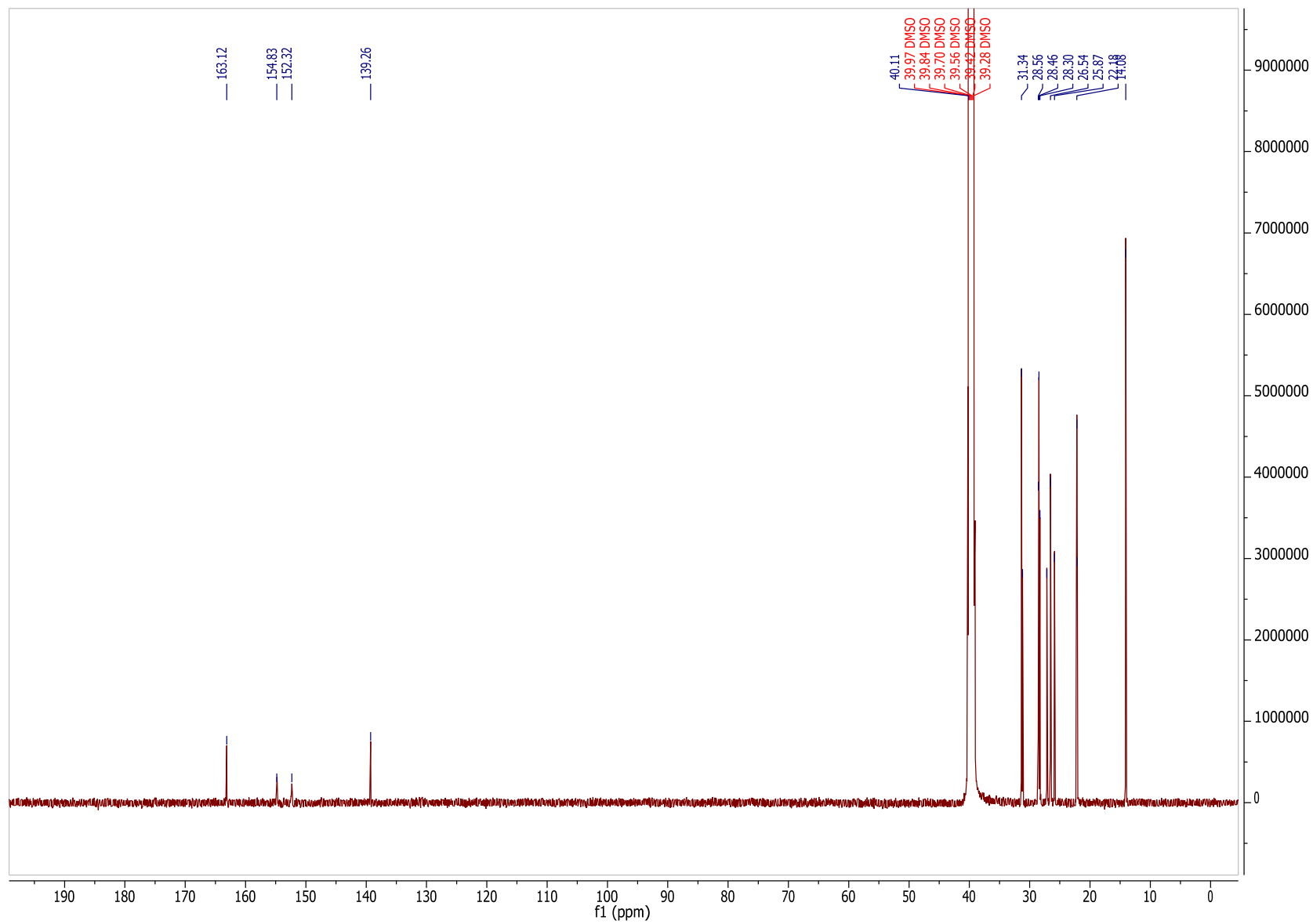


Figure S57. <sup>1</sup>H-NMR spectrum of 77 (500 MHz)



**Figure S58.** <sup>13</sup>C-NMR spectrum of **77** (126 MHz)

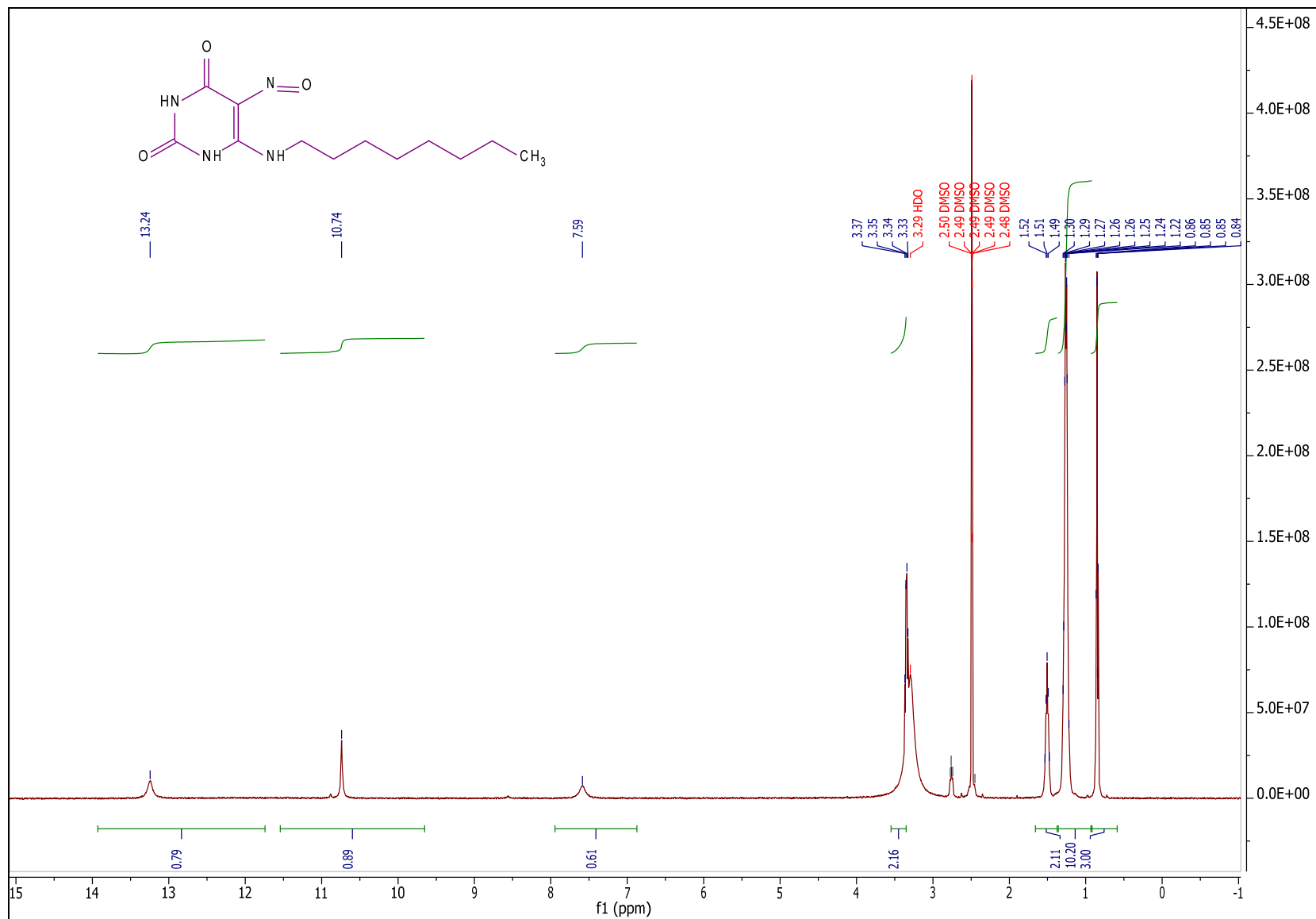
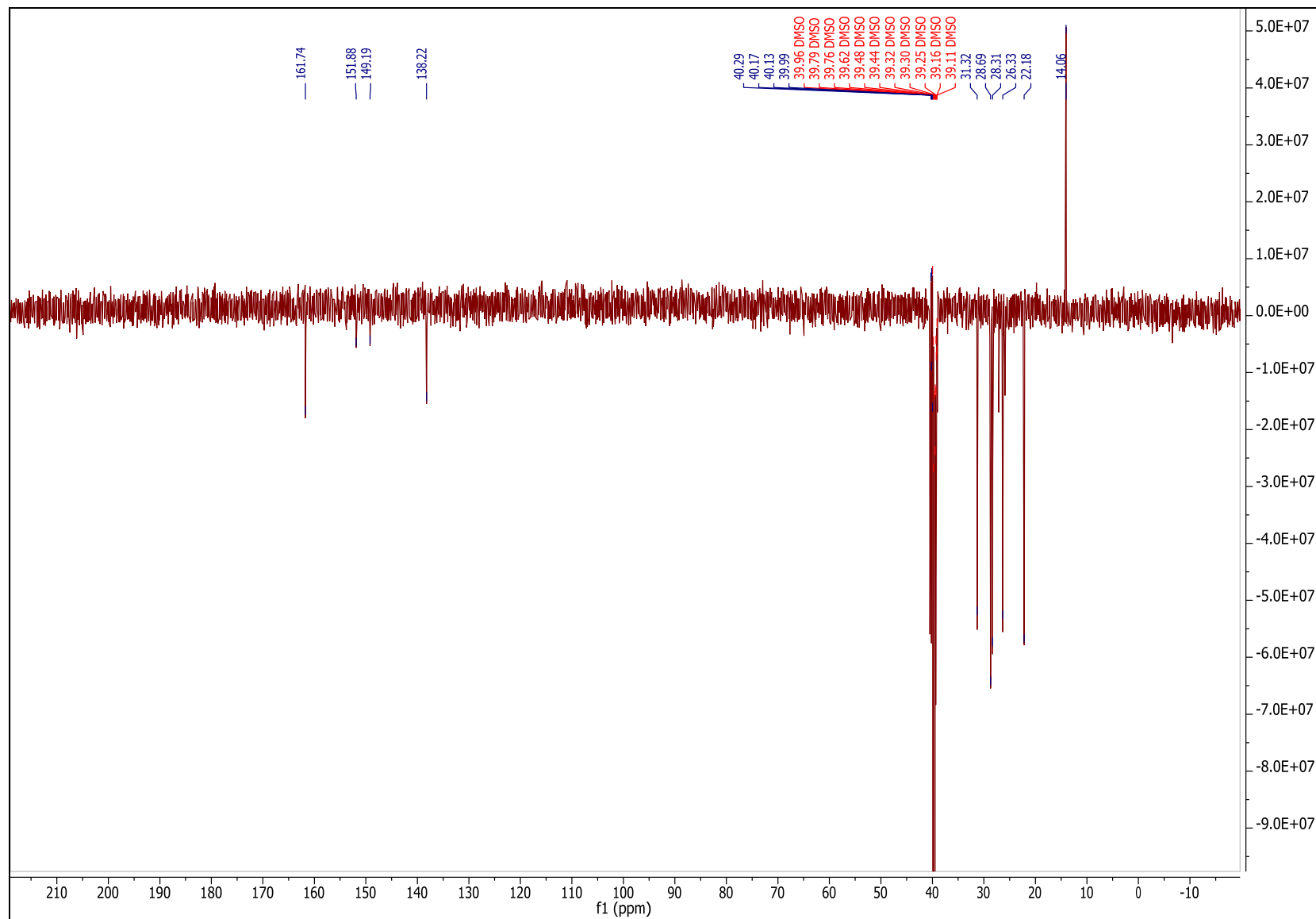


Figure S59. <sup>1</sup>H-NMR spectrum of **78** (126 MHz)



**Figure S60.** <sup>13</sup>C<sub>apt</sub>-NMR spectrum of **78** (126 MHz)



## References

1. Rafehi, M.; Burbiel, J. C.; Attah, I. Y.; Abdelrahman, A.; Müller, C. E. Synthesis, characterization, an in vitro evaluation of the selective P2Y<sub>2</sub> receptor antagonist AR-C118925. *Purinergic Signal.* **2016**, *13*, 89-103.
2. Funke, M.; Thimm, D; Schiedel, A. C.; Müller, C. E. 8-Benzamidochromen-4-one-2-carboxylic acids: potent and selective agonists for the orphan G protein-coupled receptor GPR35. *J. Med. Chem.* **2013**, *56*, 5182-5197.