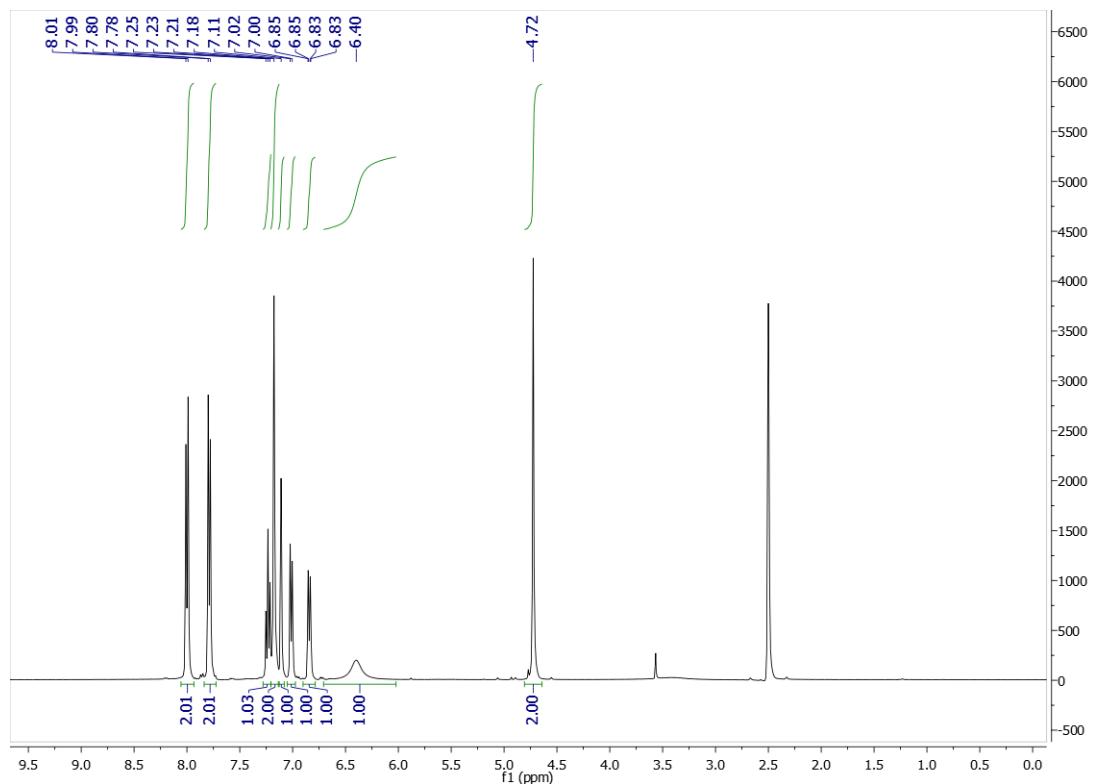


# Synthesis of Novel Benzenesulfonamide-Bearing Functionalized Imidazole Derivatives as Novel Candidates Targeting Multidrug-Resistant *Mycobacterium abscessus* complex

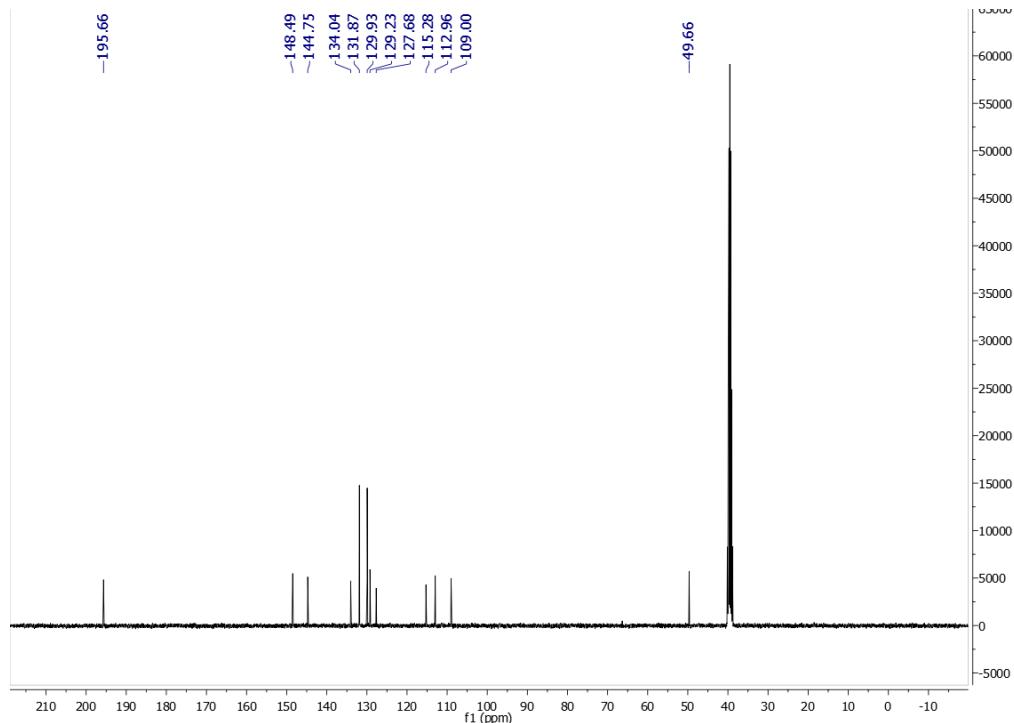
Benas Balandis<sup>1</sup>, Povilas Kavaliauskas<sup>1,2,3,4, 5\*</sup>, Birutė Grybaitė<sup>1</sup>, Vidmantas Petraitis<sup>2,4,5</sup>, Rūta Petraitiienė<sup>2,4</sup>, Ethan Naing<sup>2</sup>, Andrew Garcia<sup>2</sup>, Ramunė Grigalevičiūtė<sup>5</sup>, and Vytautas Mickevičius<sup>1</sup>

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- \* Correspondence: pok4001@med.cornell.edu

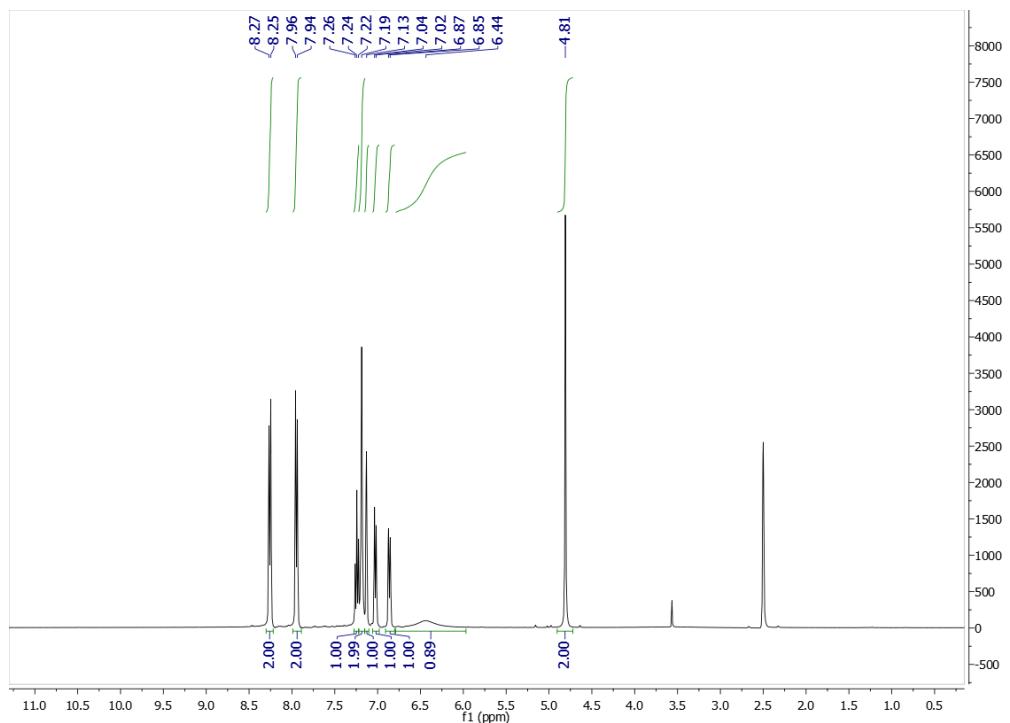
## NMR data



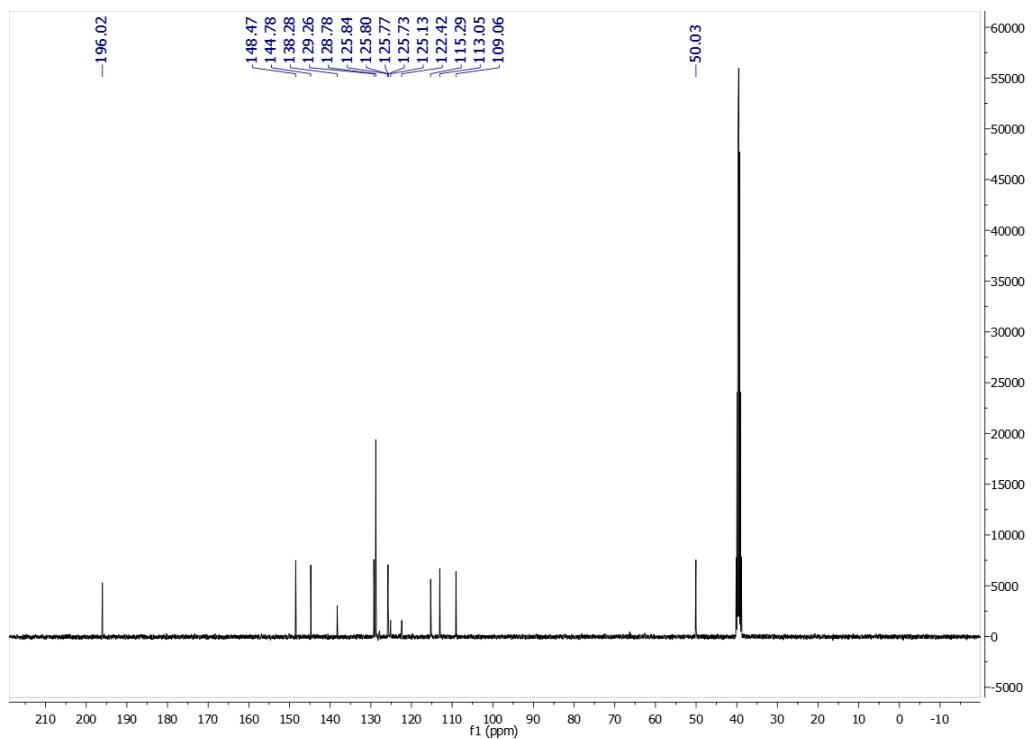
**Figure S1.** <sup>1</sup>H NMR of compound 3 at 400 MHz (DMSO- $d_6$ )



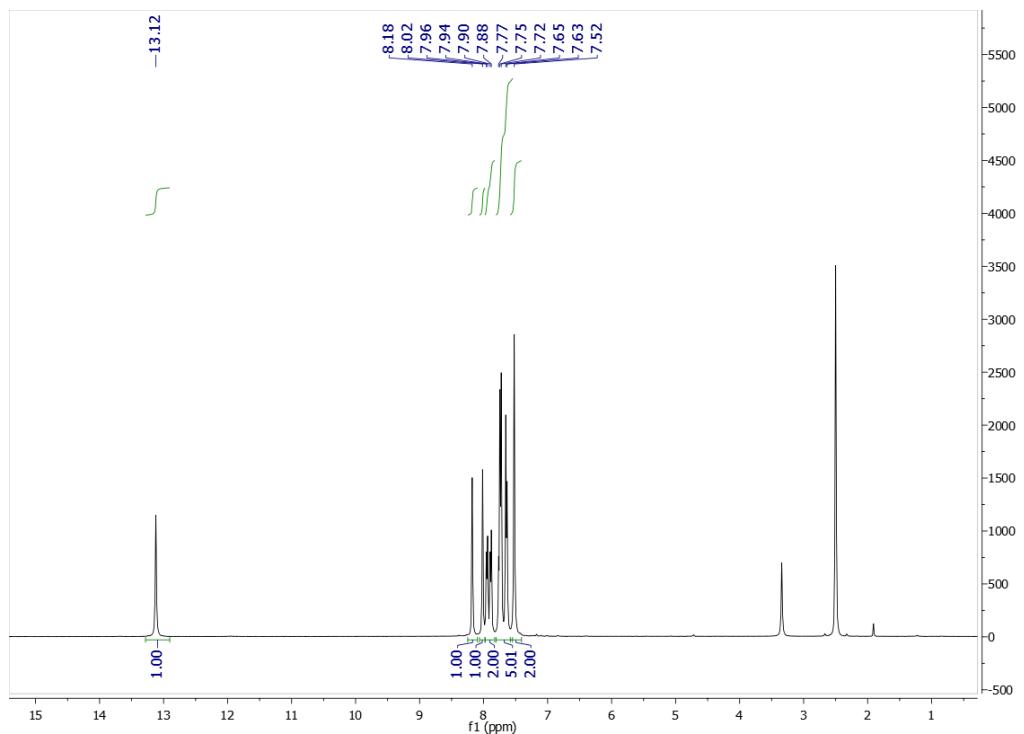
**Figure S2.** <sup>13</sup>C NMR spectrum of compound 3 at 101 MHz (DMSO- $d_6$ )



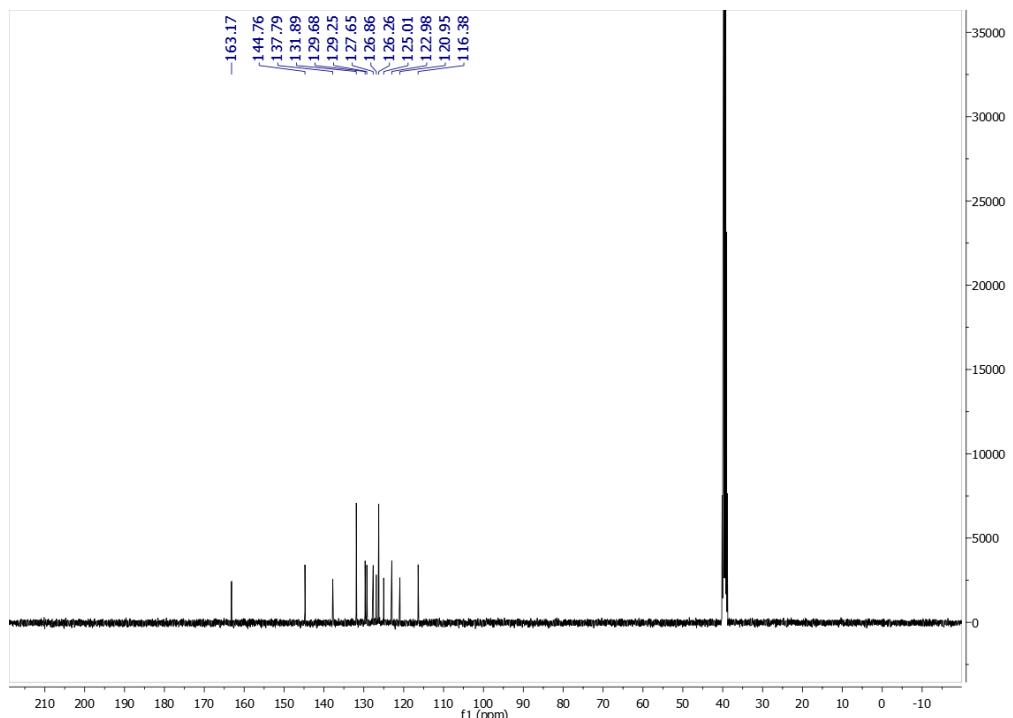
**Figure S3.**  $^1\text{H}$  NMR of compound **6** at 400 MHz (DMSO-*d*<sub>6</sub>)



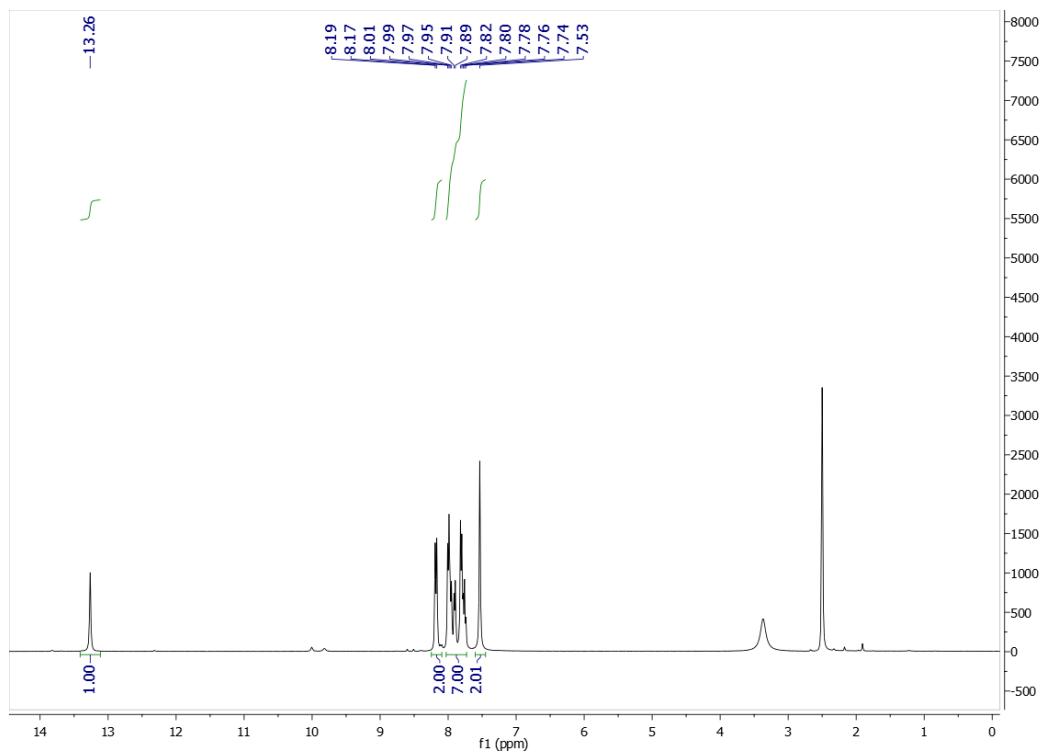
**Figure S4.**  $^{13}\text{C}$  NMR spectrum of compound **6** at 101 MHz (DMSO- $d_6$ )



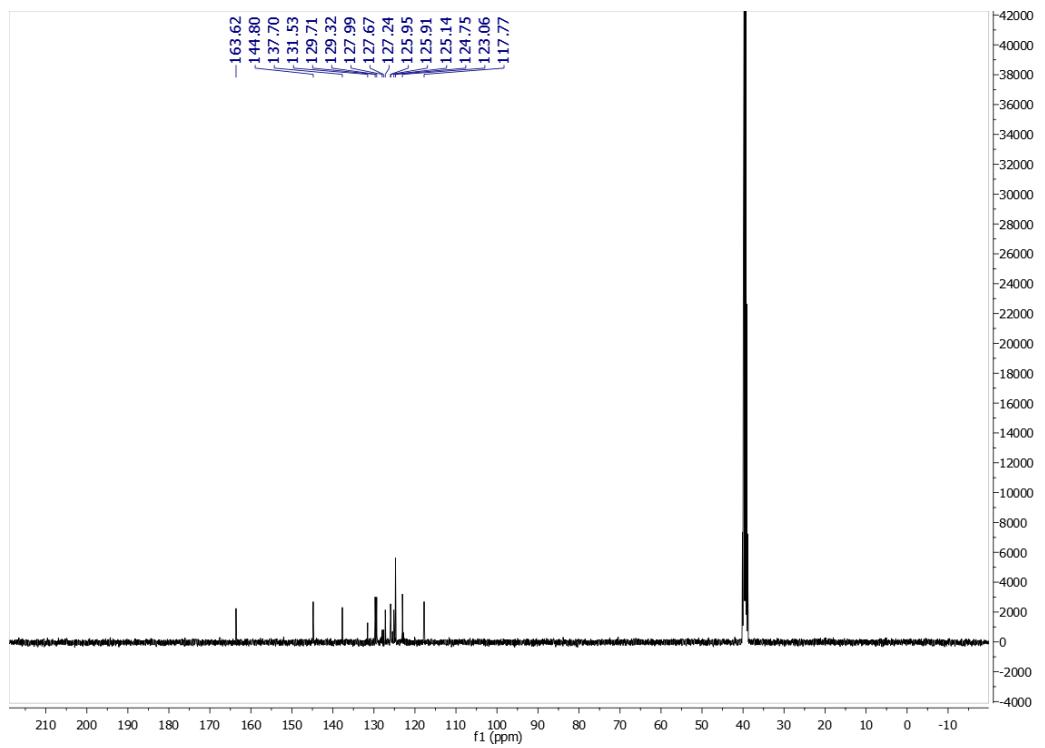
**Figure S5.** <sup>1</sup>H NMR of compound **10** at 400 MHz (DMSO-*d*<sub>6</sub>)



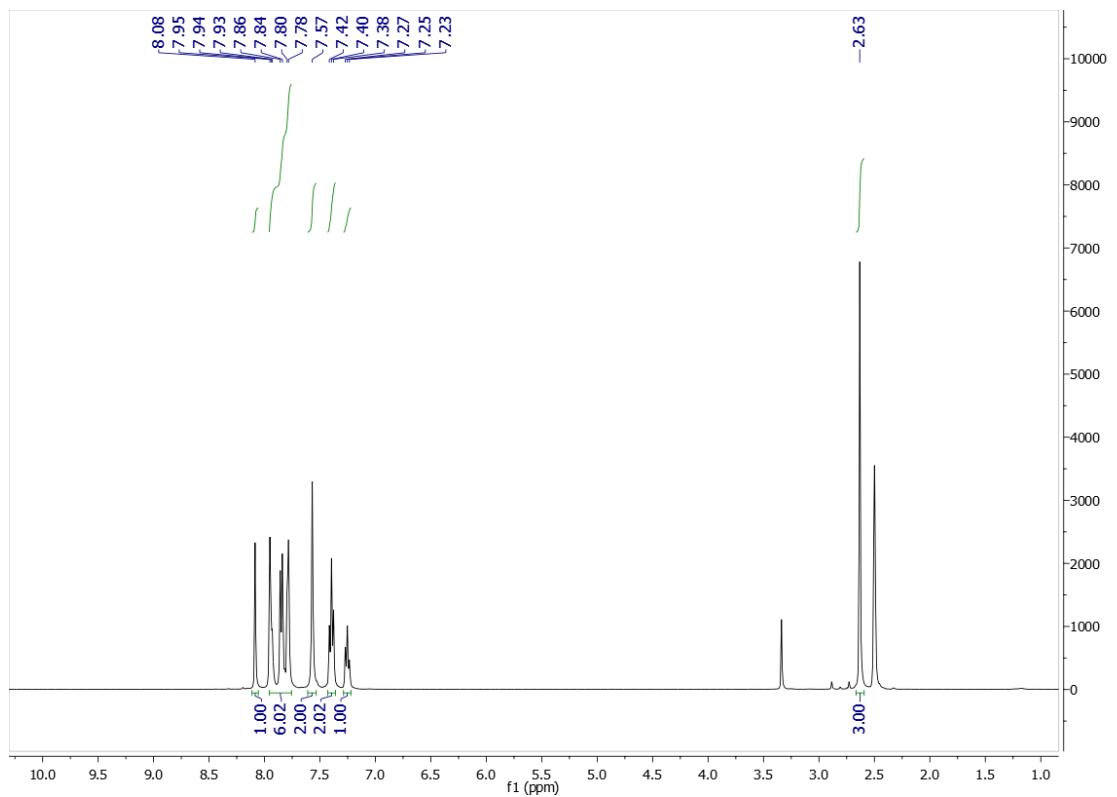
**Figure S6.** <sup>13</sup>C NMR spectrum of compound **10** at 101 MHz (DMSO-*d*<sub>6</sub>)



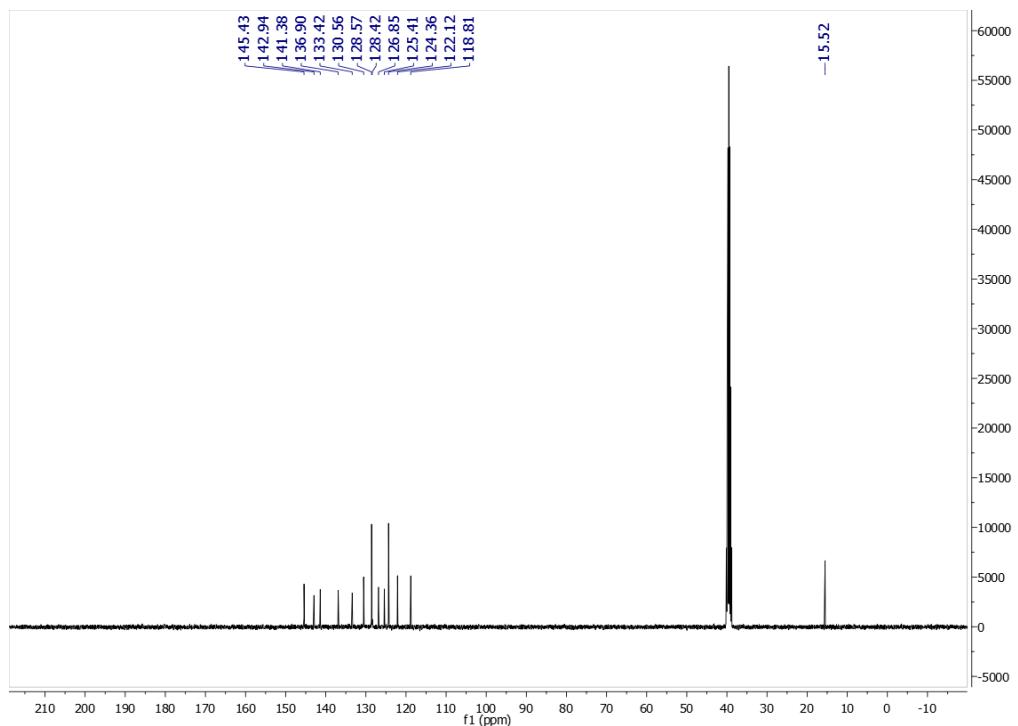
**Figure S7.**  $^1\text{H}$  NMR of compound **13** at 400 MHz (DMSO- $d_6$ )



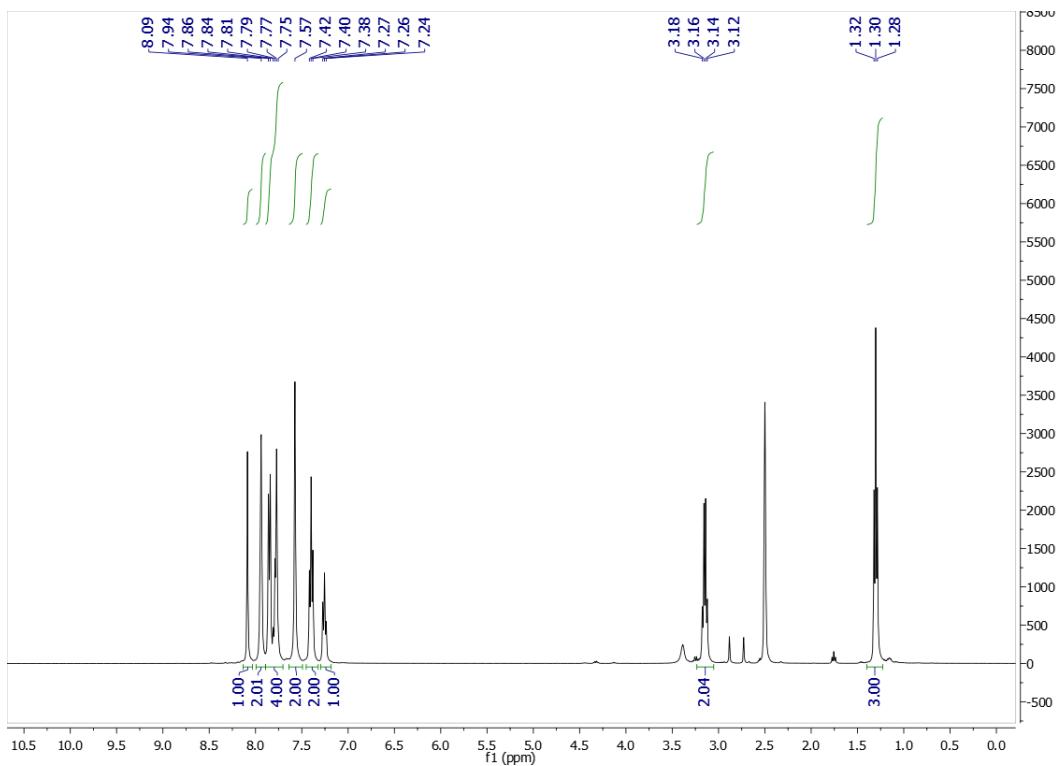
**Figure S8.**  $^{13}\text{C}$  NMR spectrum of compound **13** at 101 MHz (DMSO- $d_6$ )



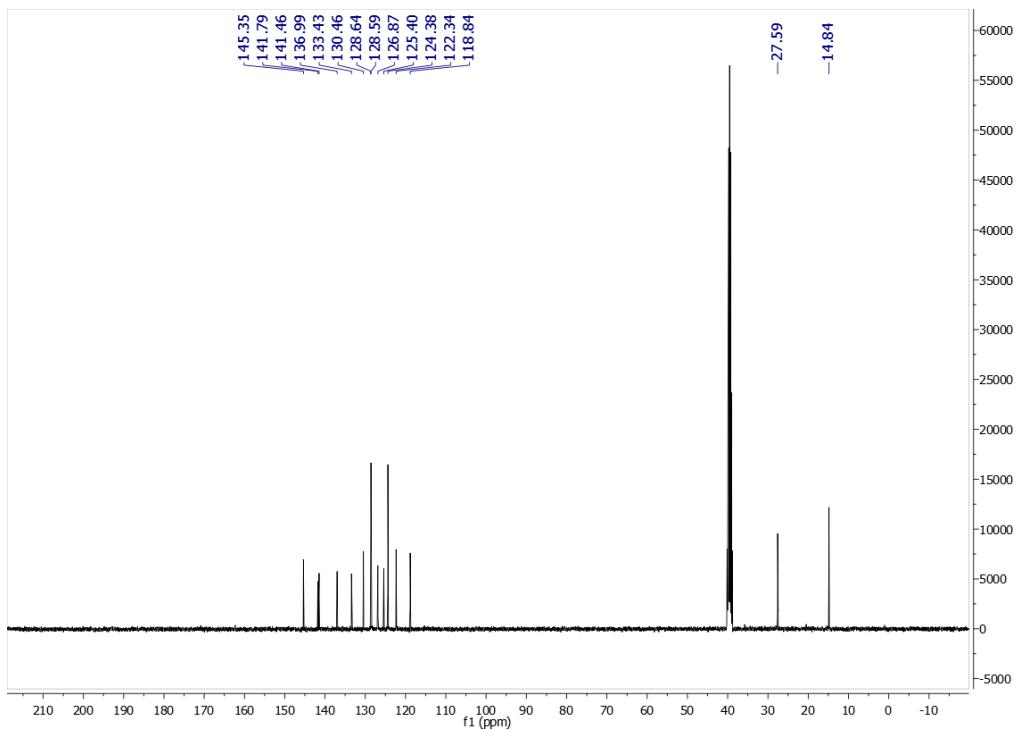
**Figure S9.**  $^1\text{H}$  NMR of compound 16a at 400 MHz (DMSO- $d_6$ )



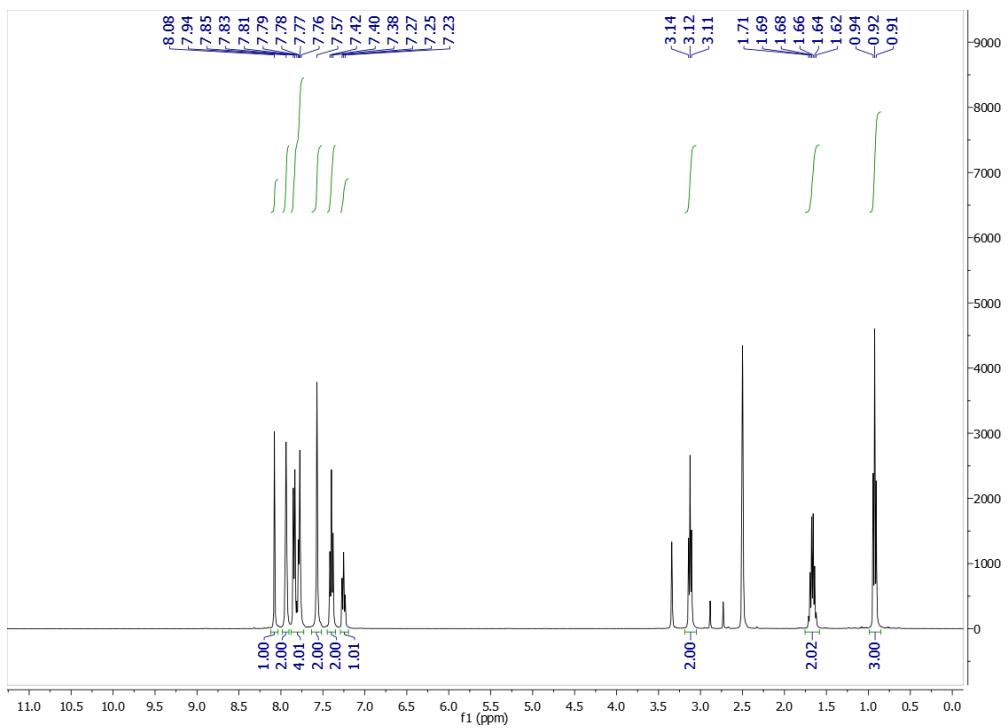
**Figure S10.**  $^{13}\text{C}$  NMR of compound **16a** at 101 MHz (DMSO- $d_6$ )



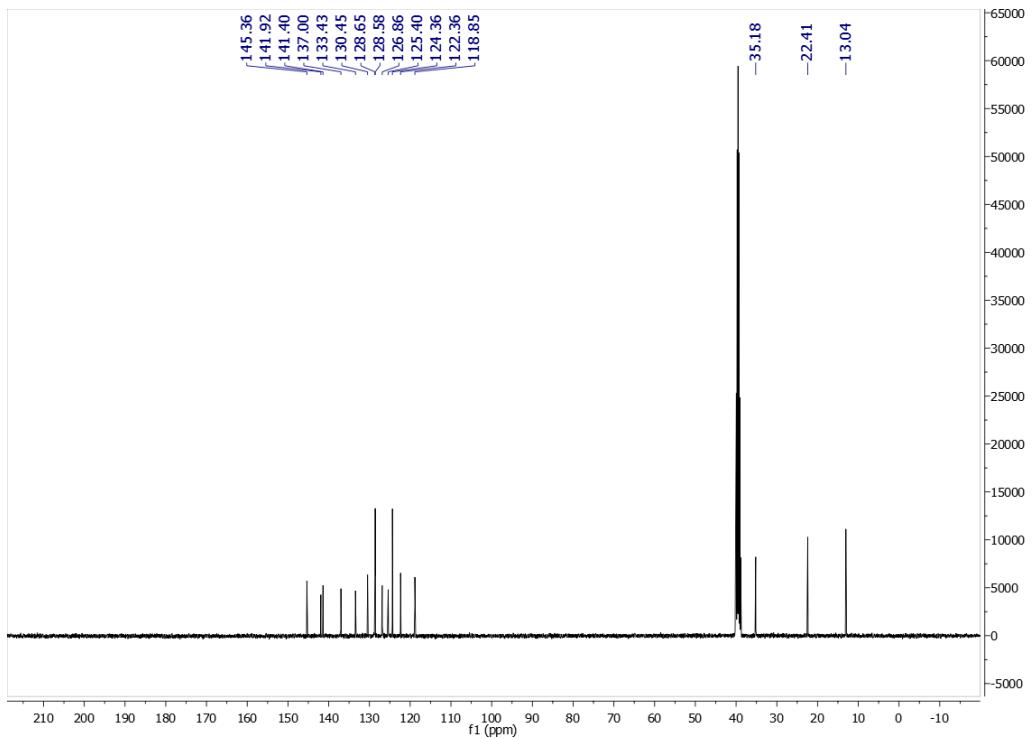
**Figure S11.**  $^1\text{H}$  NMR of compound **16b** at 400 MHz (DMSO- $d_6$ )



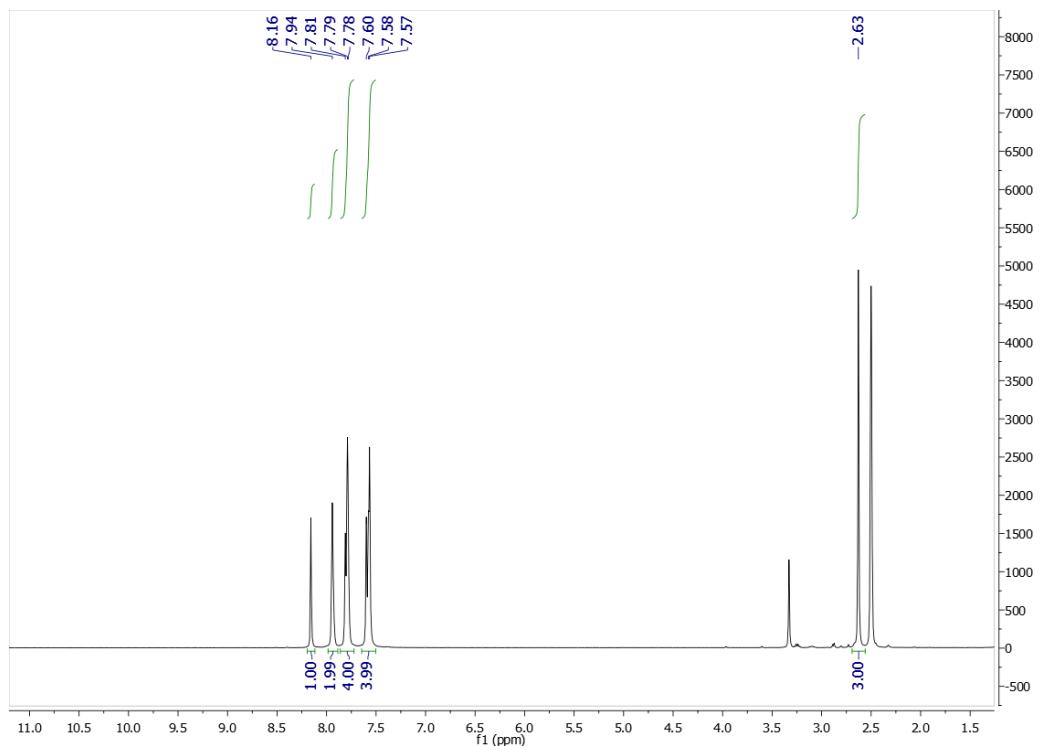
**Figure S12.**  $^{13}\text{C}$  NMR spectrum of compound **16b** at 101 MHz (DMSO- $d_6$ )



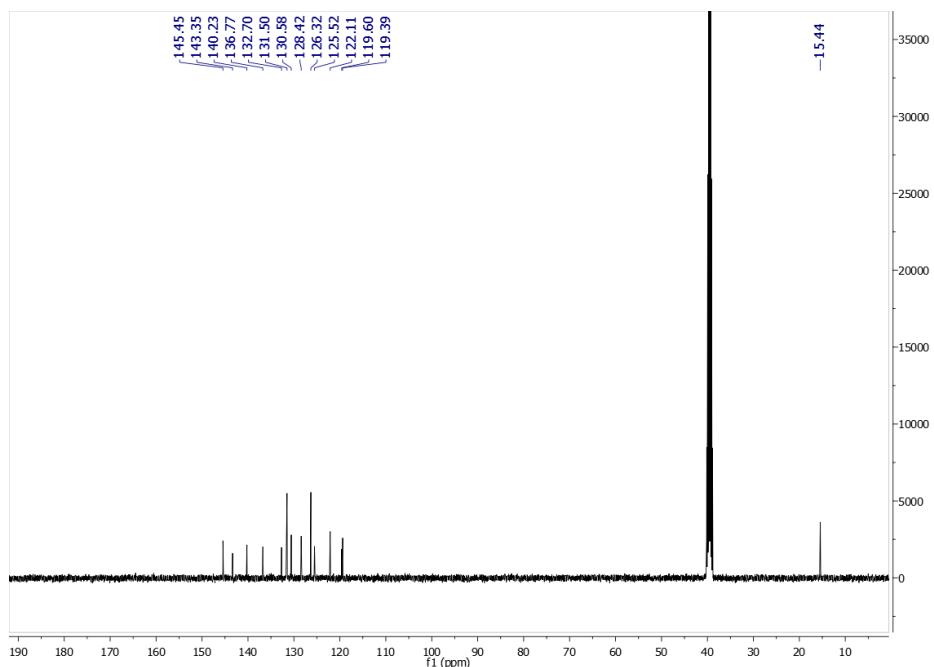
**Figure S13.**  $^1\text{H}$  NMR of compound **16c** at 400 MHz (DMSO- $d_6$ )



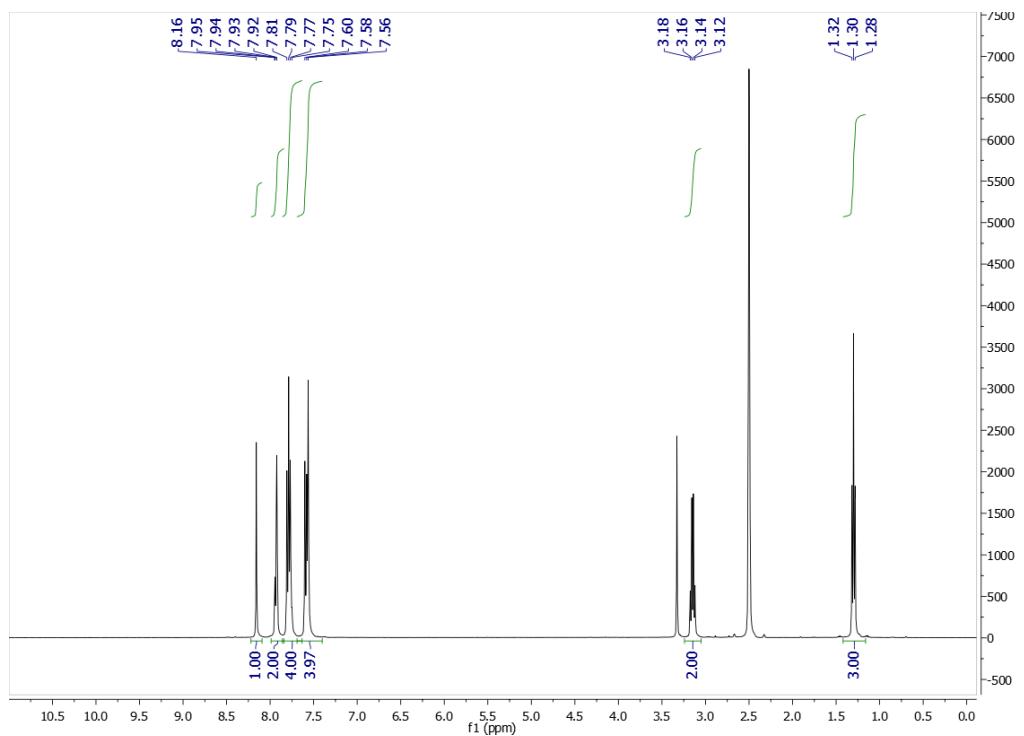
**Figure S14.**  $^{13}\text{C}$  NMR spectrum of compound **16c** at 101 MHz (DMSO- $d_6$ )



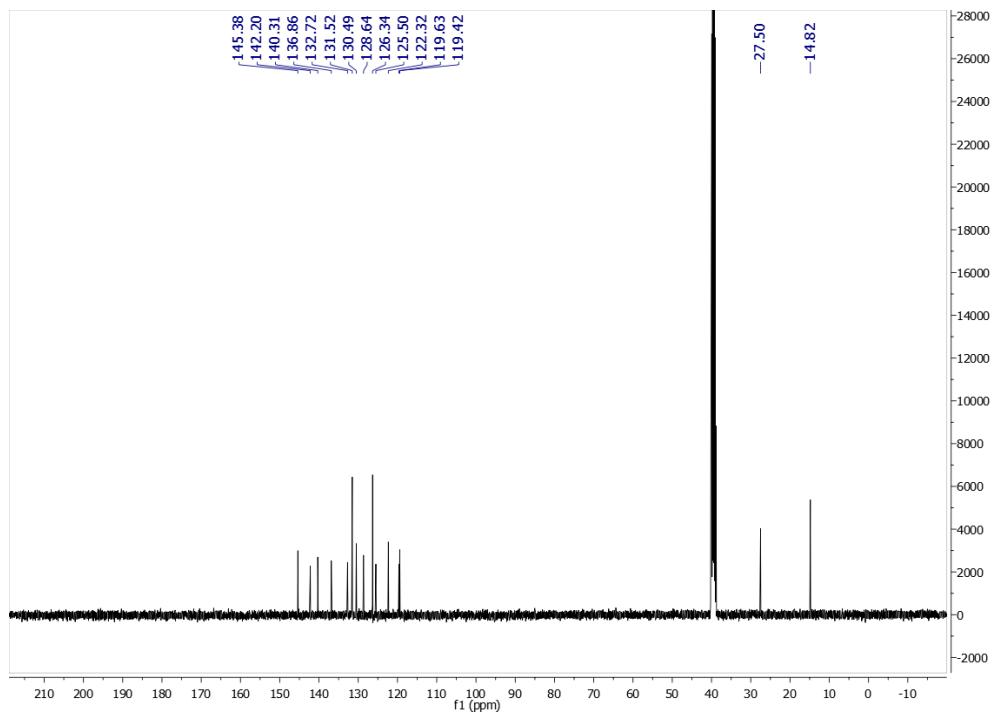
**Figure S15.** <sup>1</sup>H NMR of compound **17a** at 400 MHz (DMSO-*d*<sub>6</sub>)



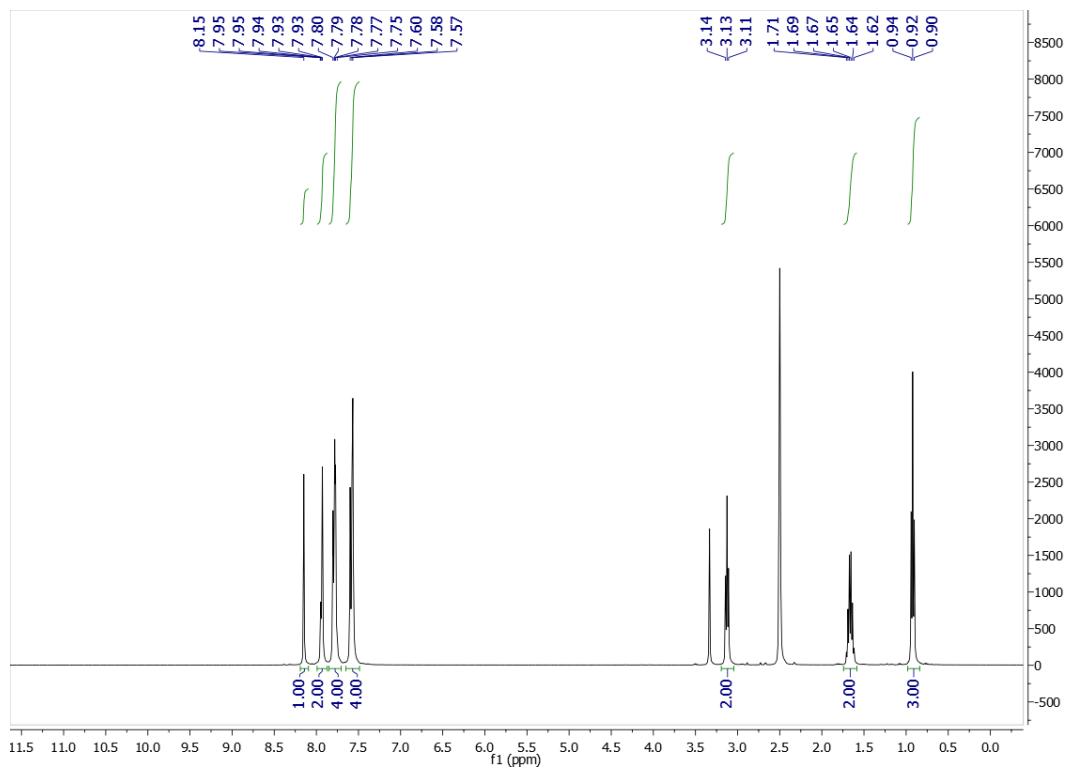
**Figure S16.** <sup>13</sup>C NMR spectrum of compound **17a** at 101 MHz (DMSO-*d*<sub>6</sub>)



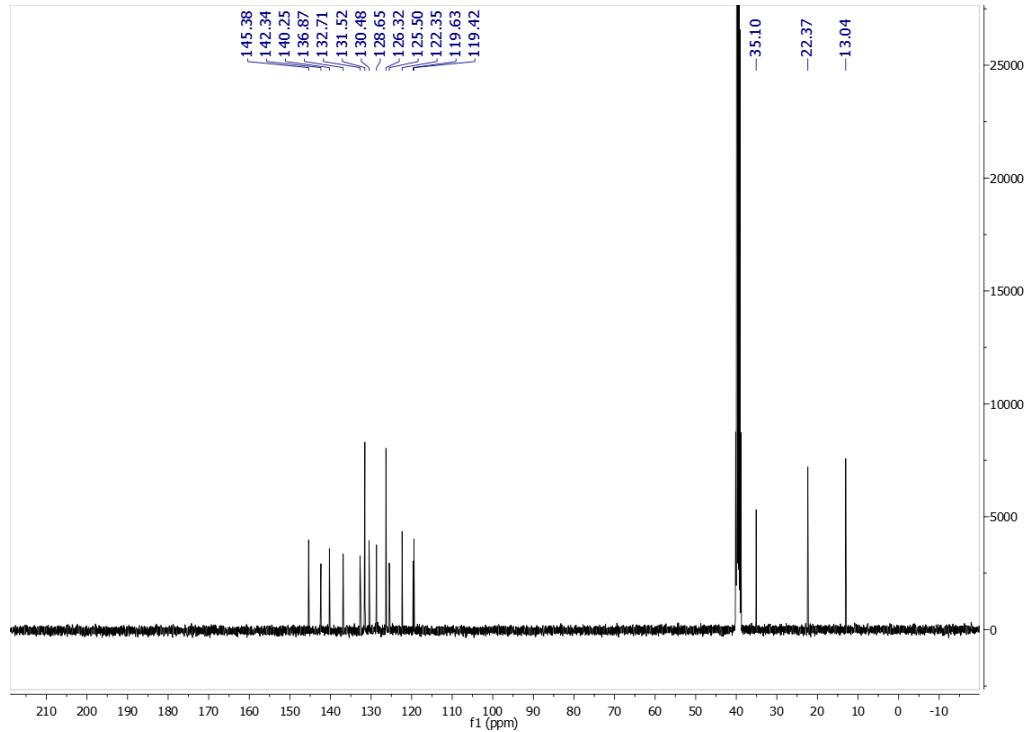
**Figure S17.** <sup>1</sup>H NMR of compound **17b** at 400 MHz (DMSO-*d*<sub>6</sub>)



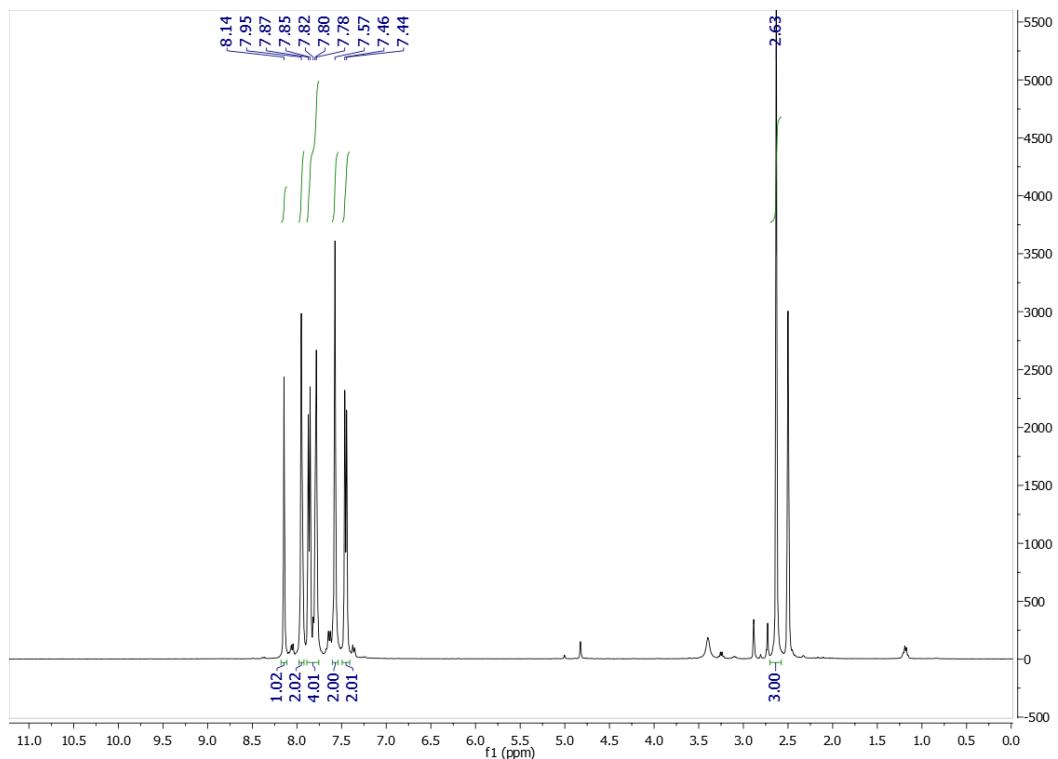
**Figure S18.** <sup>13</sup>C NMR spectrum of compound **17b** at 101 MHz (DMSO-*d*<sub>6</sub>)



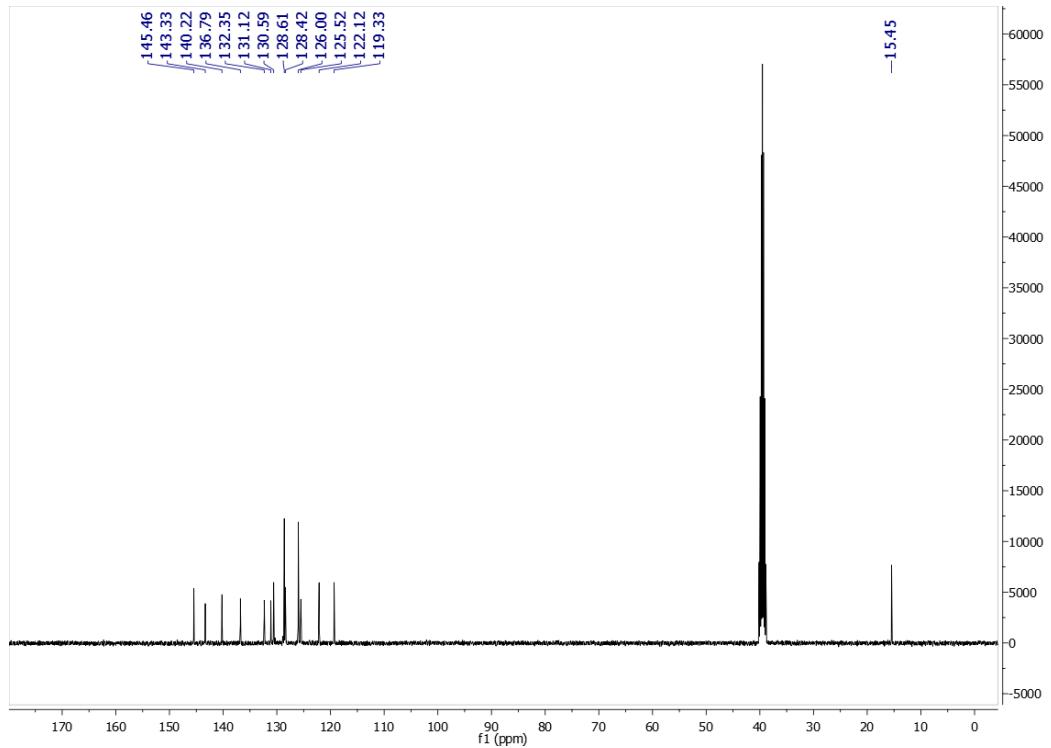
**Figure S19.**  $^1\text{H}$  NMR of compound **17c** at 400 MHz (DMSO- $d_6$ )



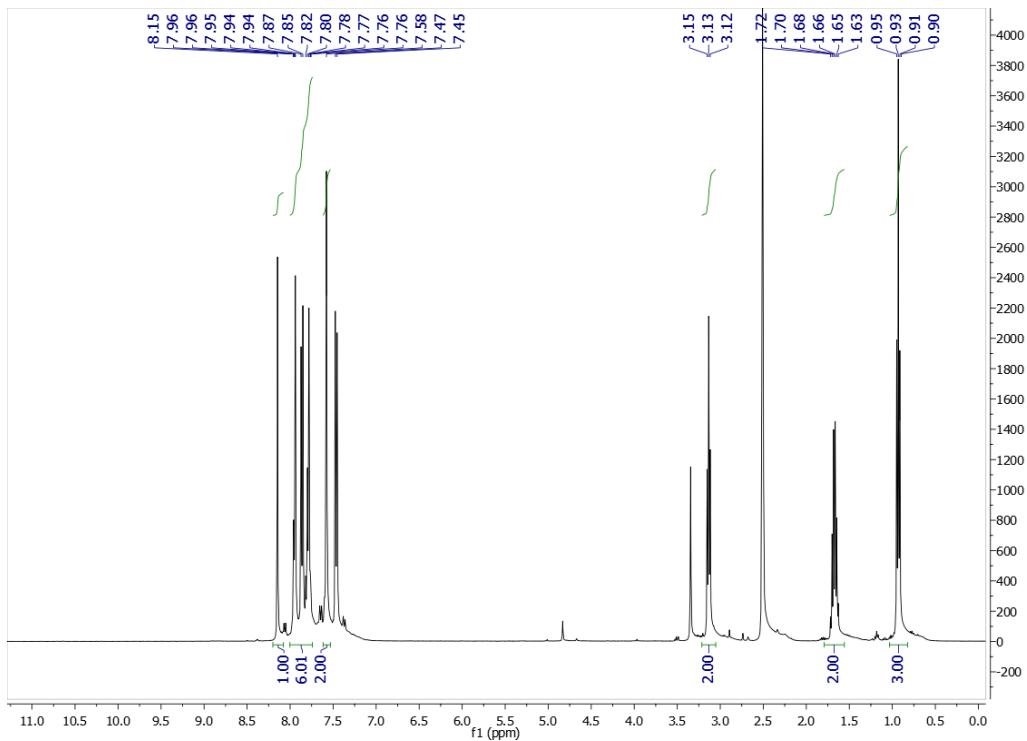
**Figure S20.**  $^{13}\text{C}$  NMR spectrum of compound **17c** at 101 MHz (DMSO- $d_6$ )



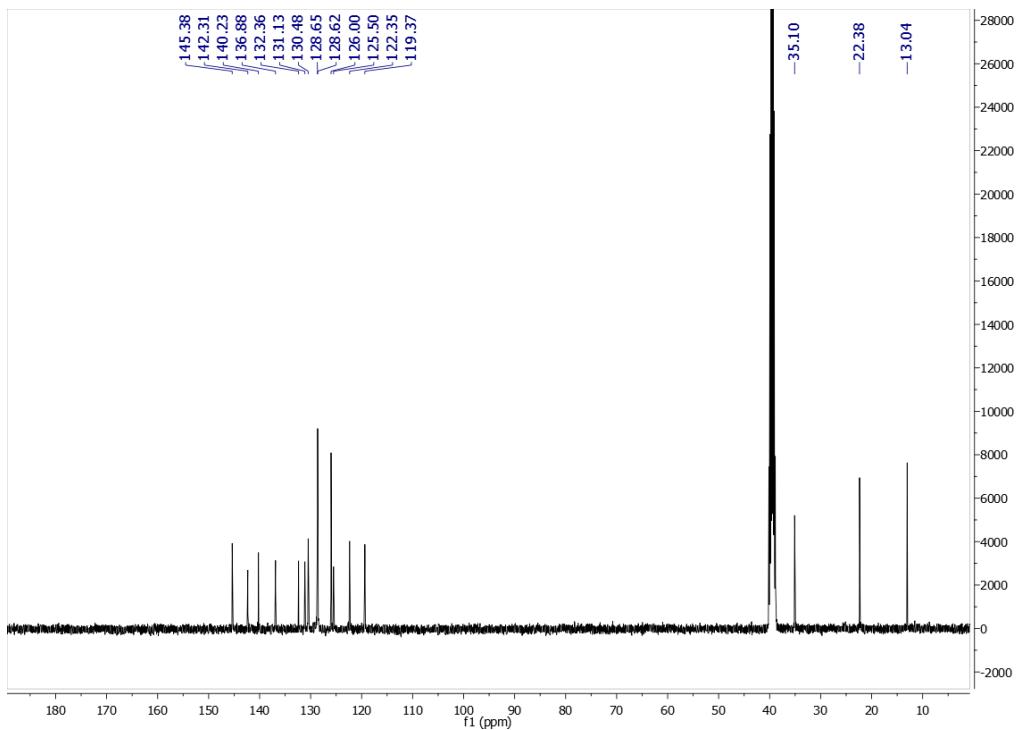
**Figure S21.** <sup>1</sup>H NMR of compound **18a** at 400 MHz (DMSO-*d*<sub>6</sub>)



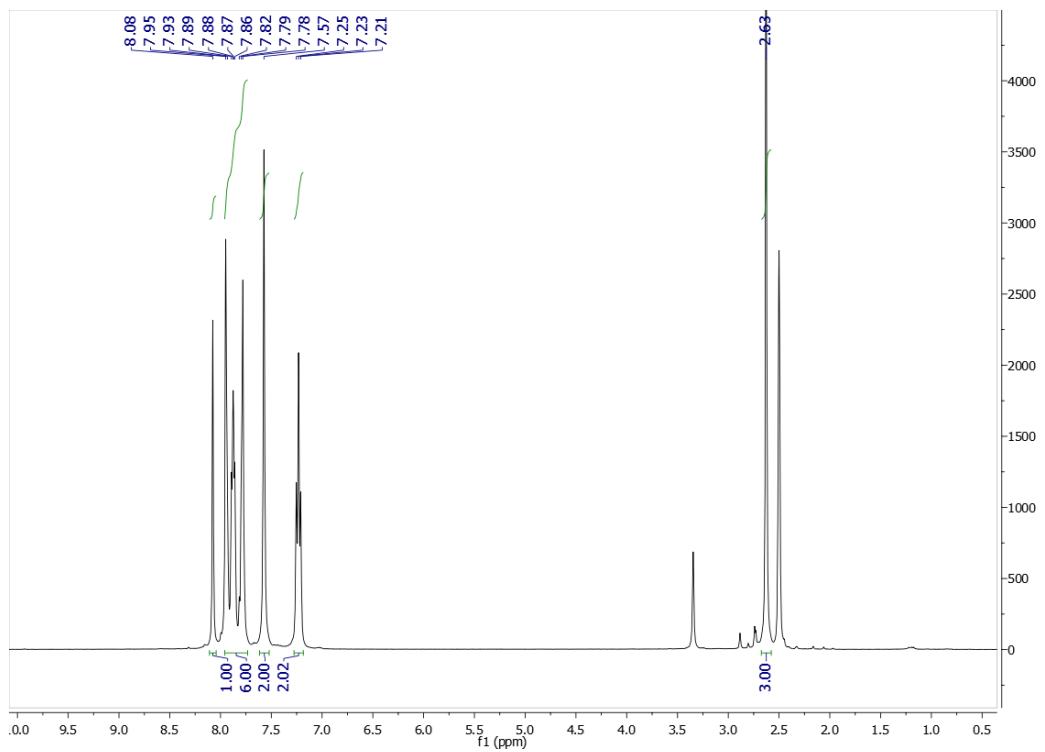
**Figure S22.** <sup>13</sup>C NMR spectrum of compound **18a** at 101 MHz (DMSO-*d*<sub>6</sub>)



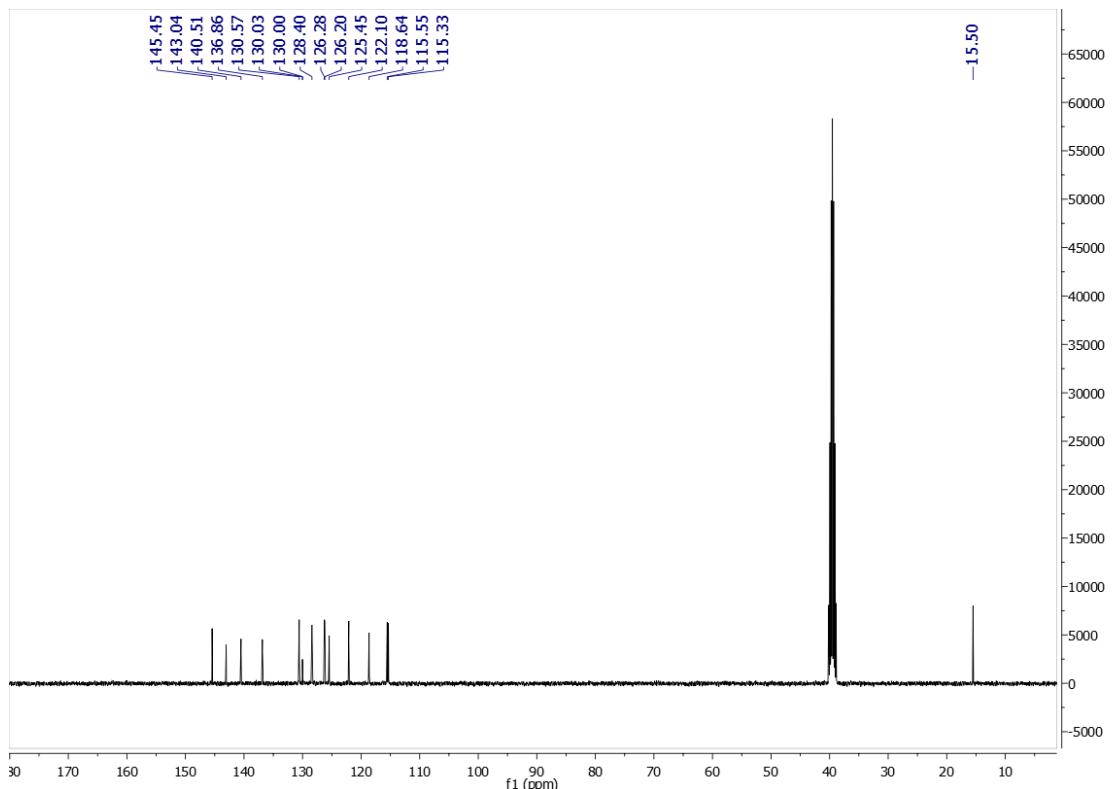
**Figure S23.** <sup>1</sup>H NMR of compound **18c** at 400 MHz (DMSO-*d*<sub>6</sub>)



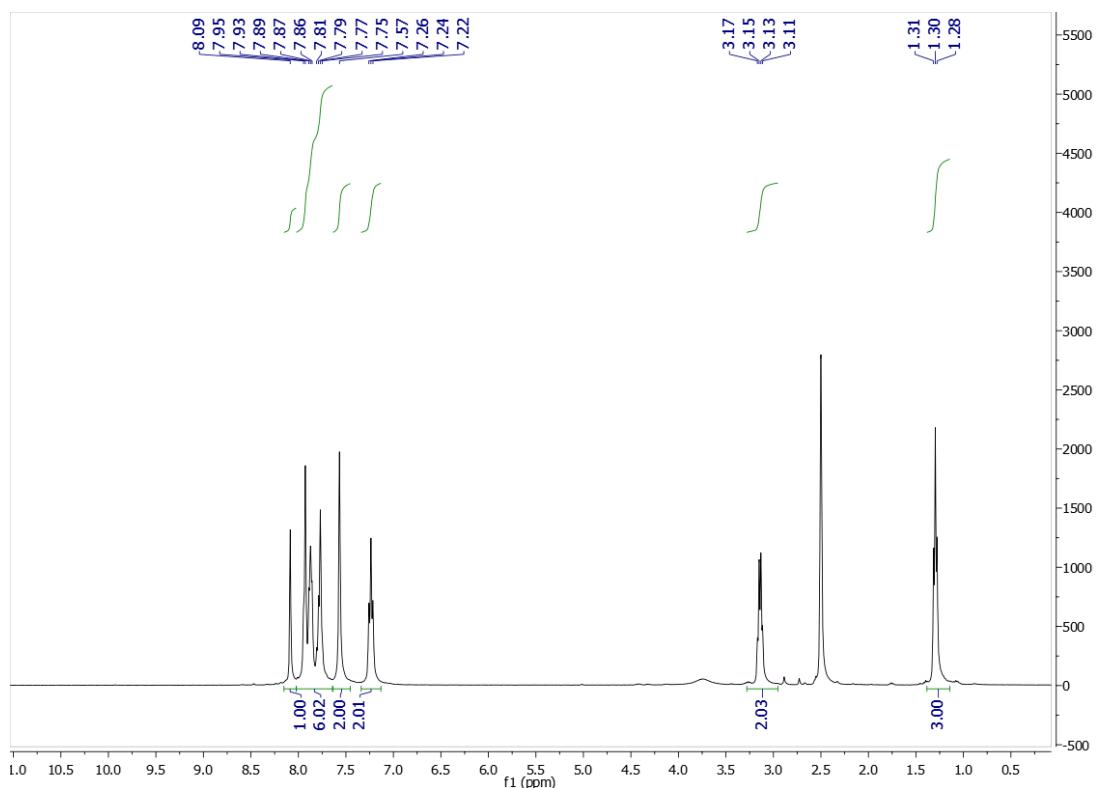
**Figure S24.** <sup>13</sup>C NMR spectrum of compound **18c** at 101 MHz (DMSO-*d*<sub>6</sub>)



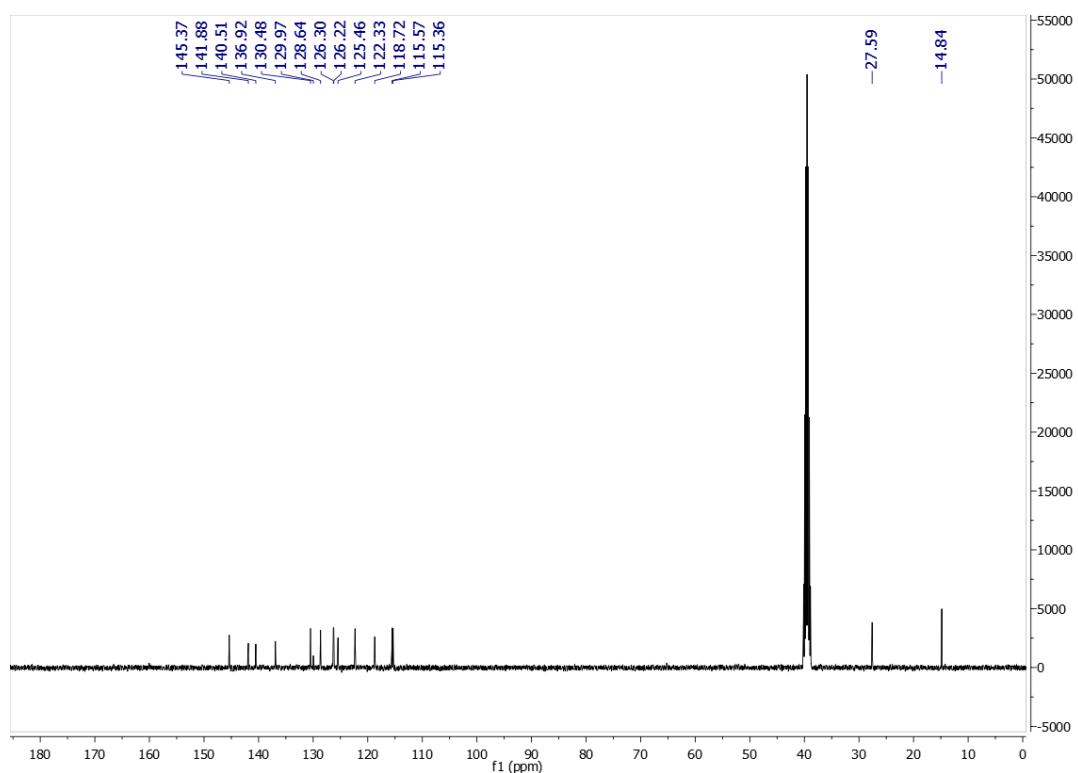
**Figure S25.** <sup>1</sup>H NMR of compound **19a** at 400 MHz (DMSO-*d*<sub>6</sub>)



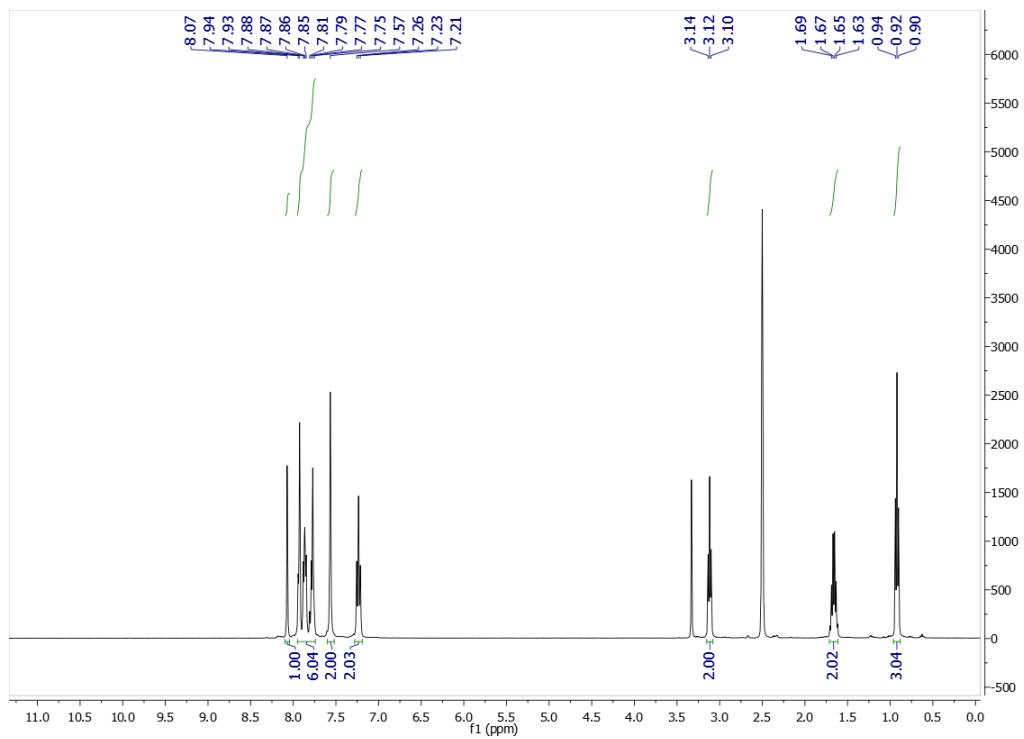
**Figure S26.** <sup>13</sup>C NMR spectrum of compound **19a** at 101 MHz (DMSO-*d*<sub>6</sub>)



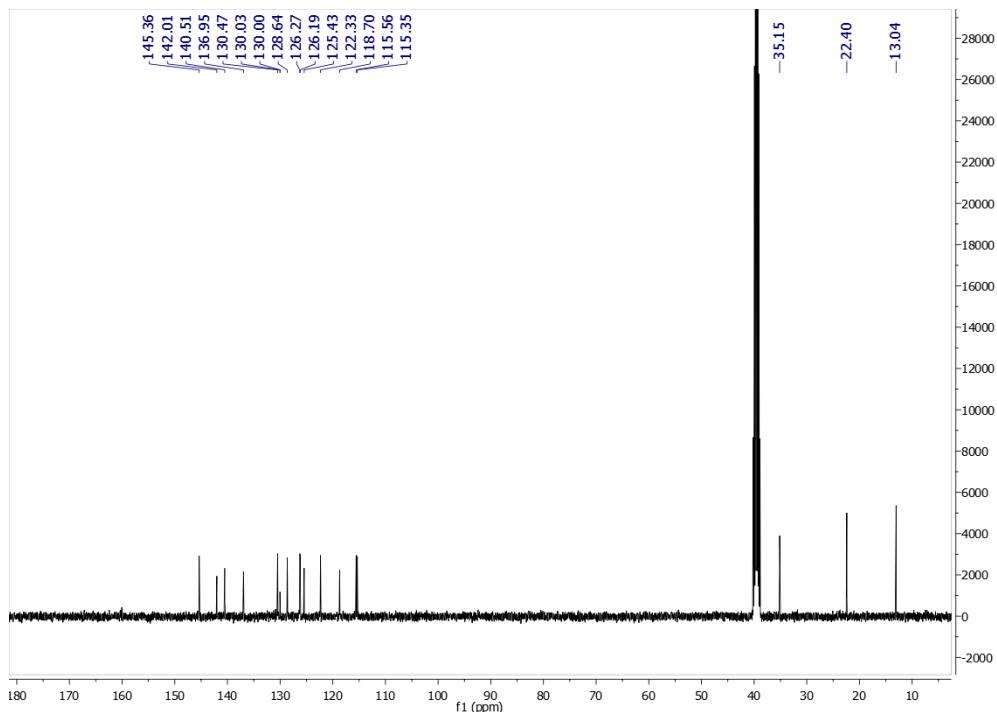
**Figure S27.**  $^1\text{H}$  NMR of compound **19b** at 400 MHz (DMSO- $d_6$ )



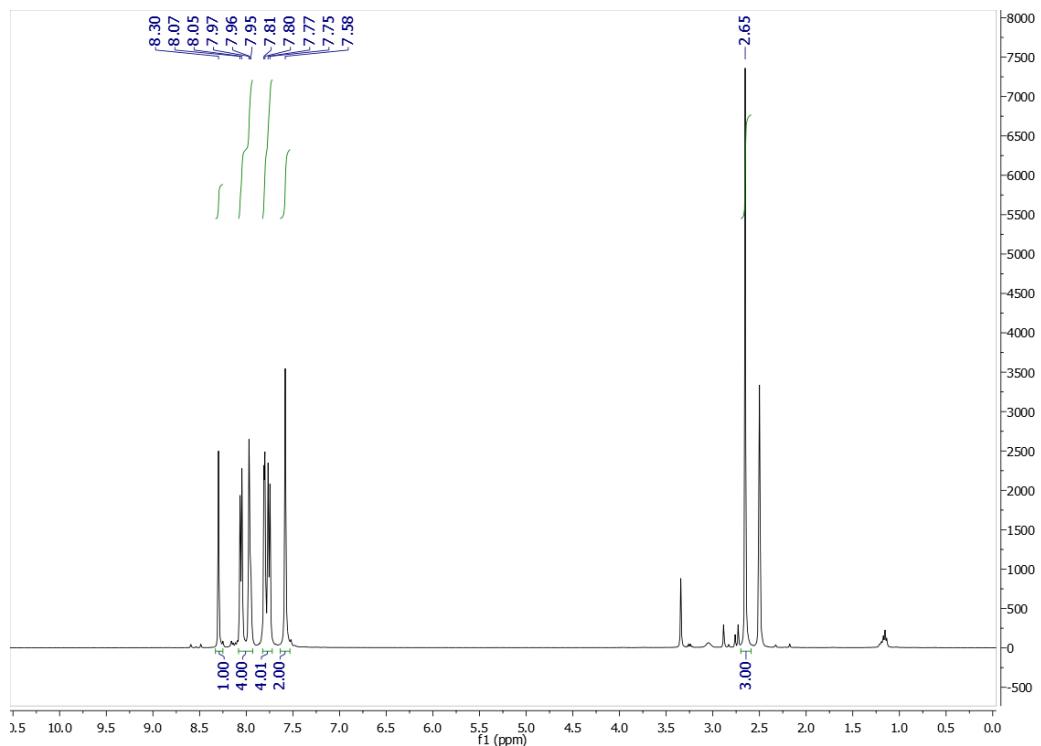
**Figure S28.**  $^{13}\text{C}$  NMR spectrum of compound **19b** at 101 MHz (DMSO- $d_6$ )



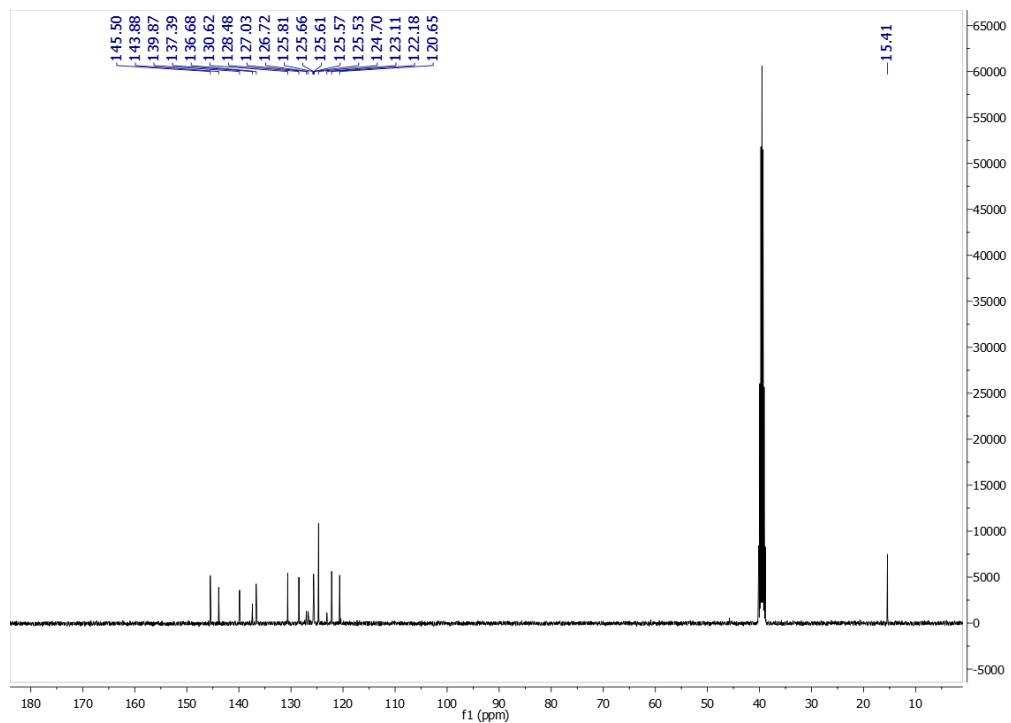
**Figure S29.** <sup>1</sup>H NMR of compound **19c** at 400 MHz (DMSO-*d*<sub>6</sub>)



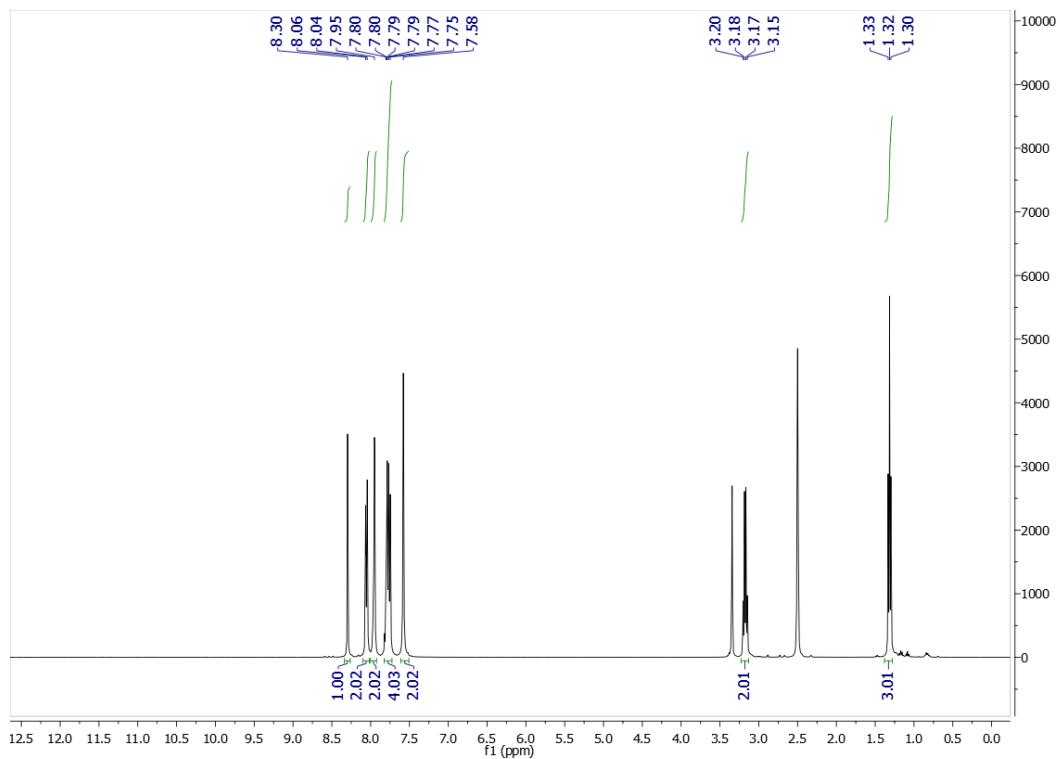
**Figure S30.** <sup>13</sup>C NMR spectrum of compound **19c** at 101 MHz (DMSO-*d*<sub>6</sub>)



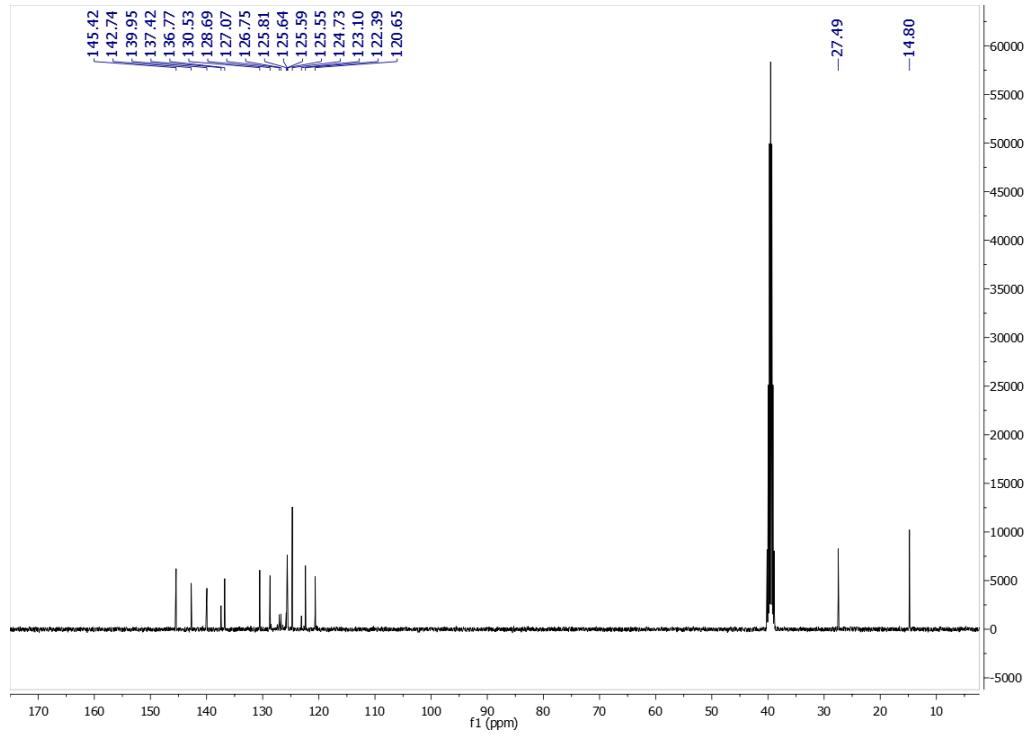
**Figure S31.** <sup>1</sup>H NMR of compound 20a at 400 MHz (DMSO- $d_6$ )



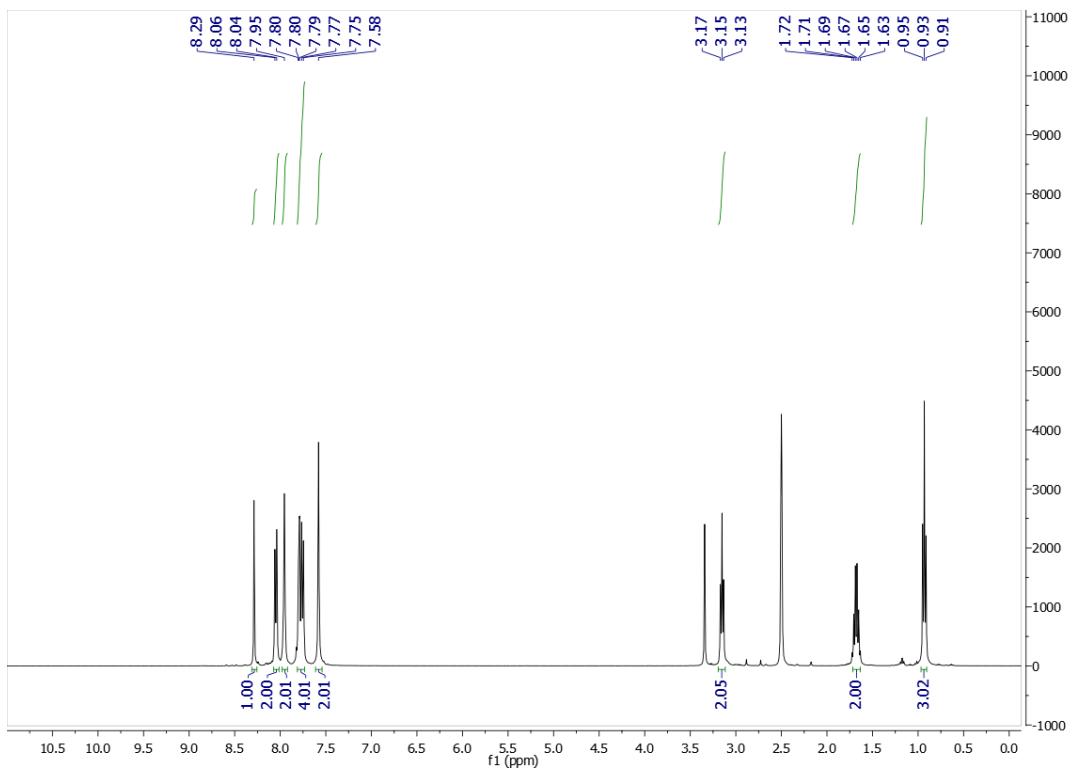
**Figure S32.** <sup>13</sup>C NMR spectrum of compound 20a at 101 MHz (DMSO- $d_6$ )



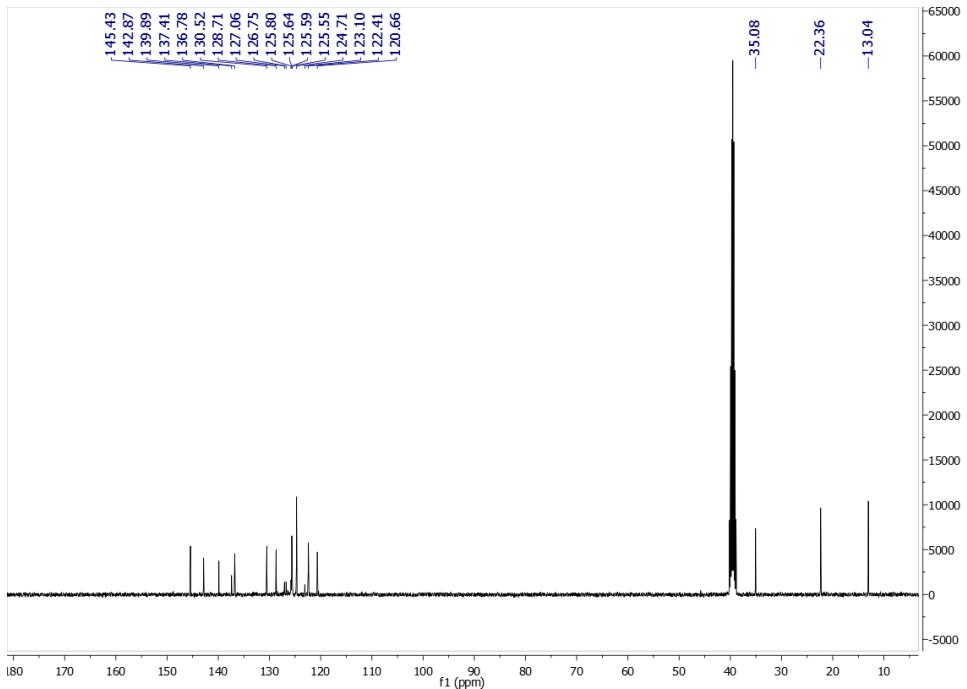
**Figure S33.** <sup>1</sup>H NMR of compound **20b** at 400 MHz (DMSO-*d*<sub>6</sub>)



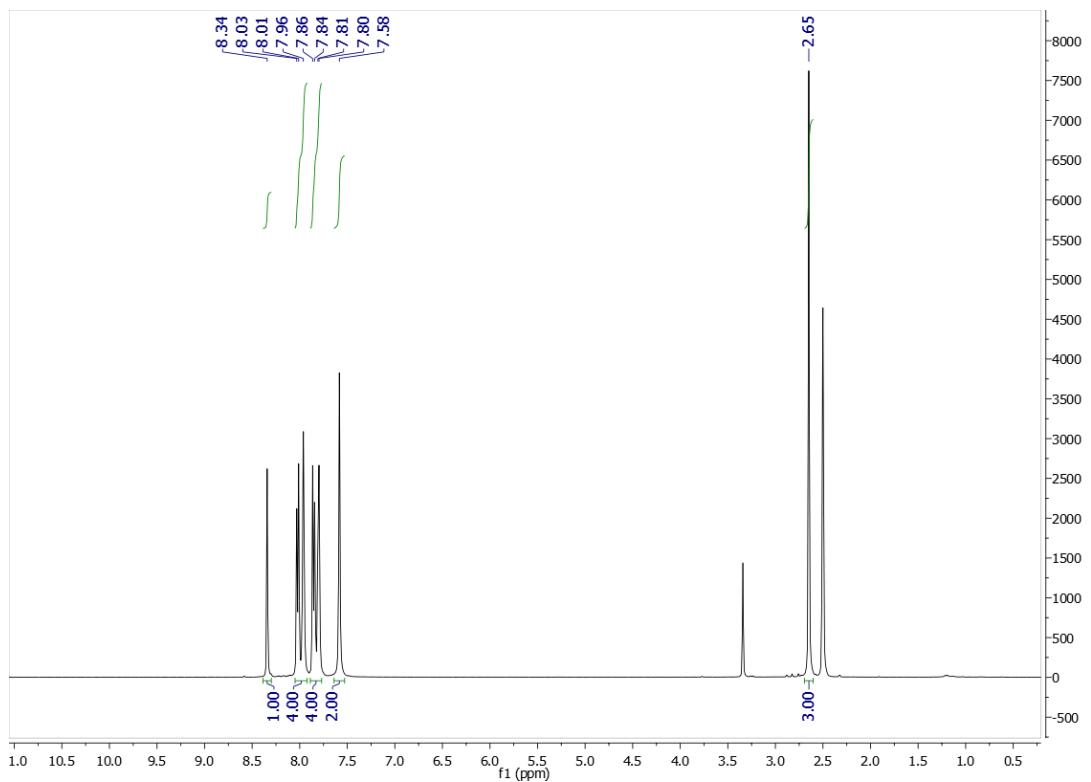
**Figure S34.** <sup>13</sup>C NMR spectrum of compound **20b** at 101 MHz (DMSO-*d*<sub>6</sub>)



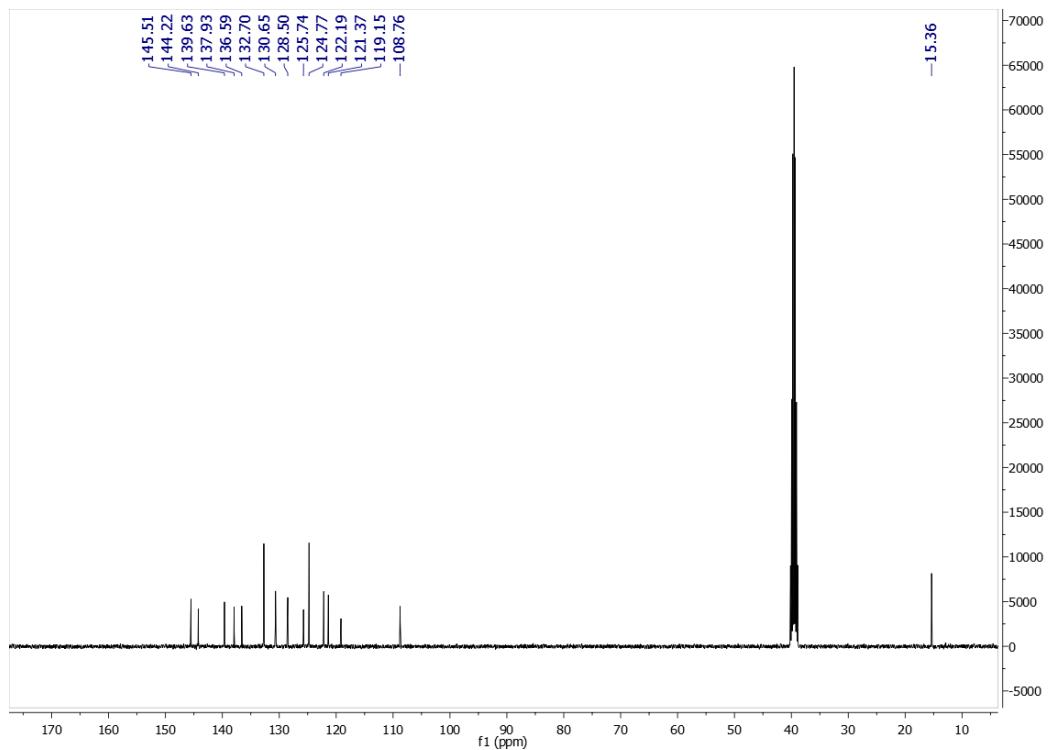
**Figure S35.** <sup>1</sup>H NMR of compound **20c** at 400 MHz ( $\text{DMSO}-d_6$ )



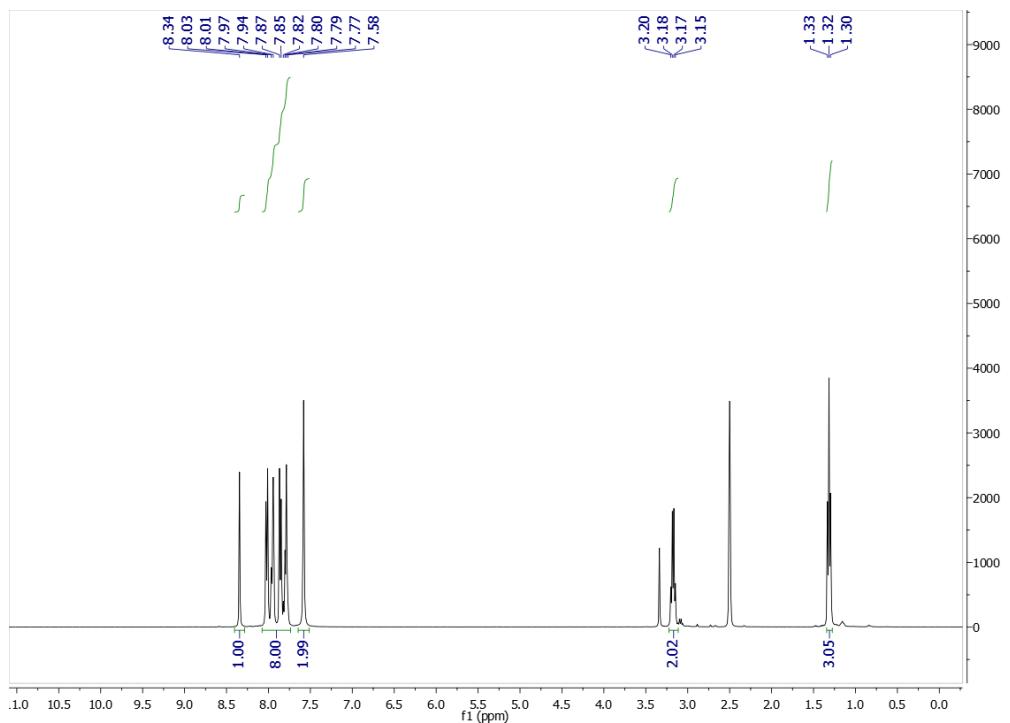
**Figure S36.** <sup>13</sup>C NMR spectrum of compound **20c** at 101 MHz ( $\text{DMSO}-d_6$ )



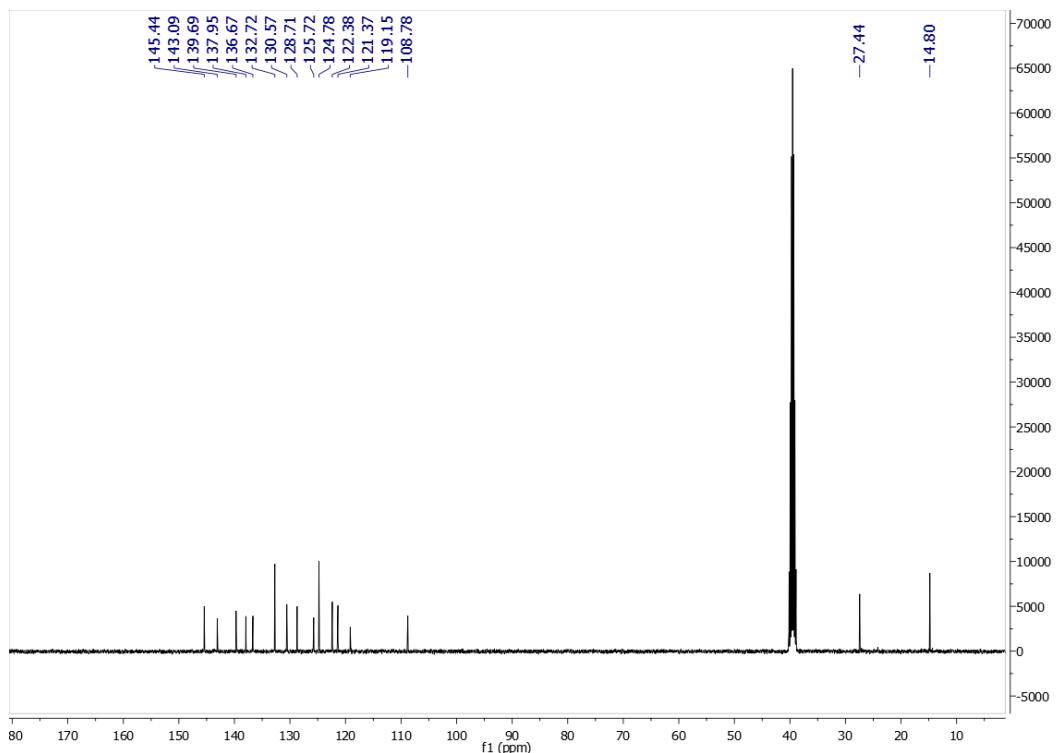
**Figure S37.** <sup>1</sup>H NMR of compound 21a at 400 MHz (DMSO-*d*<sub>6</sub>)



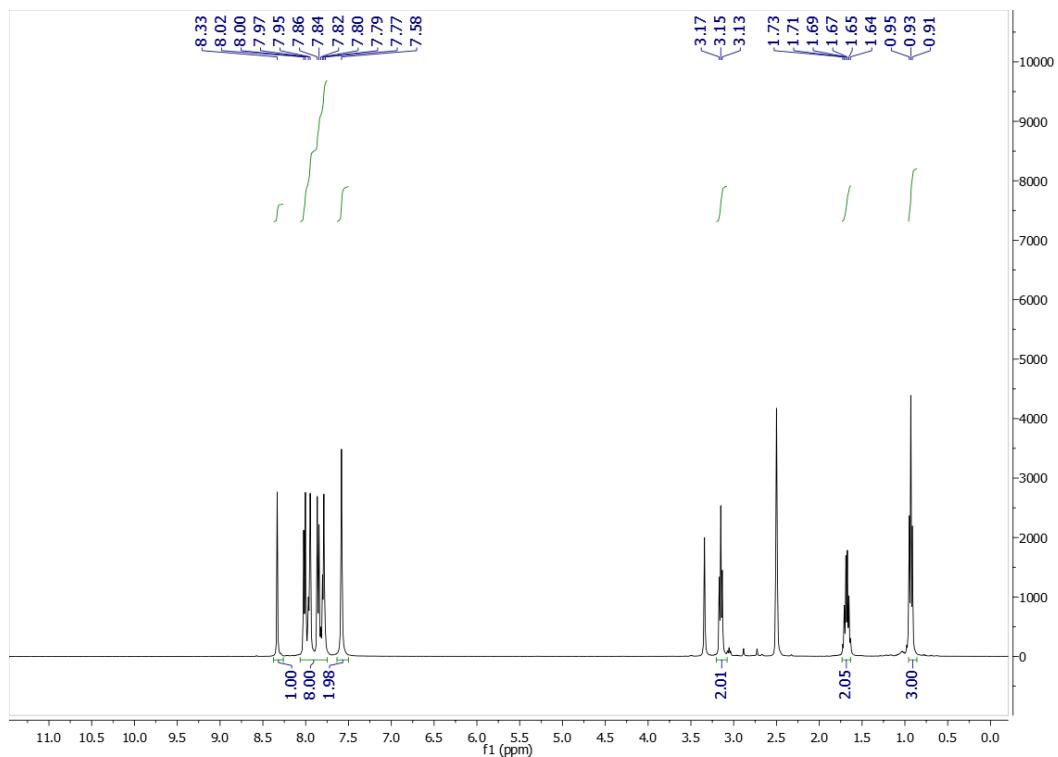
**Figure S38.** <sup>13</sup>C NMR spectrum of compound 21a at 101 MHz (DMSO-*d*<sub>6</sub>)



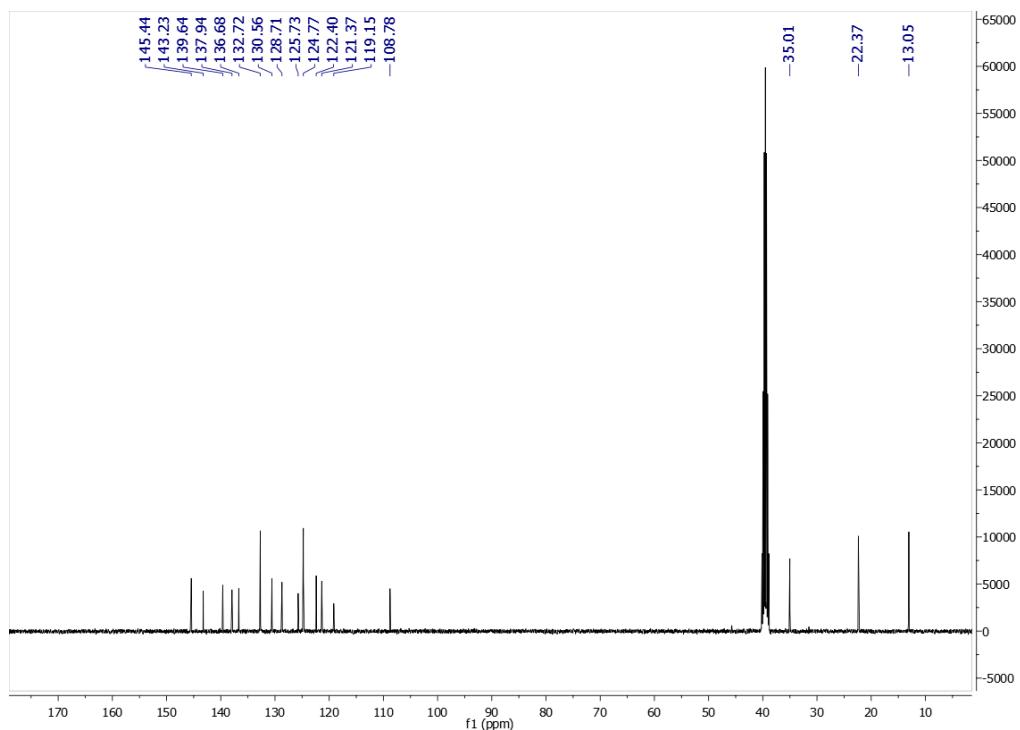
**Figure S39.** <sup>1</sup>H NMR of compound **21b** at 400 MHz (DMSO-*d*<sub>6</sub>)



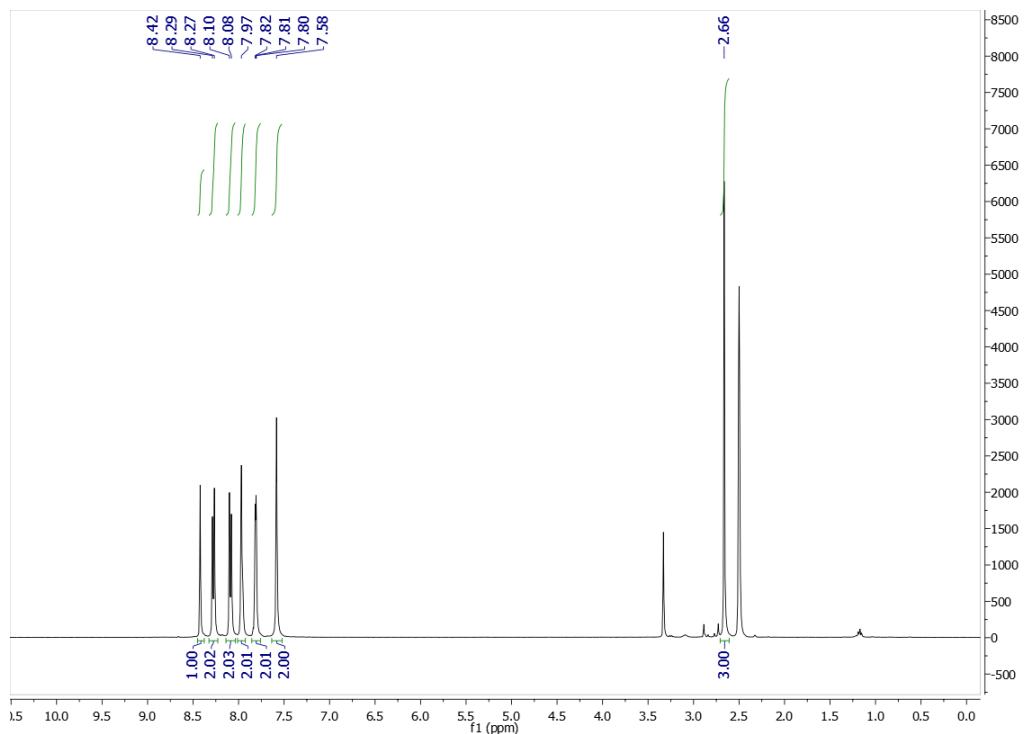
**Figure S40.** <sup>13</sup>C NMR spectrum of compound **21b** at 101 MHz (DMSO-*d*<sub>6</sub>)



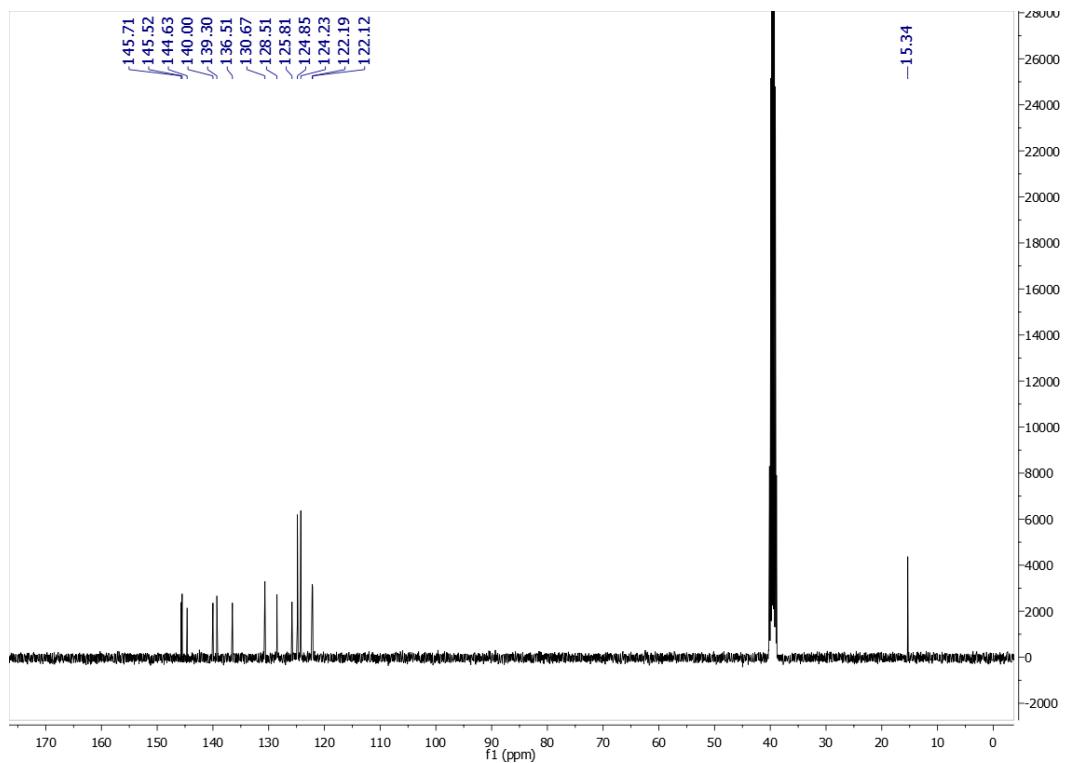
**Figure S41.**  $^1\text{H}$  NMR of compound **21c** at 400 MHz (DMSO- $d_6$ )



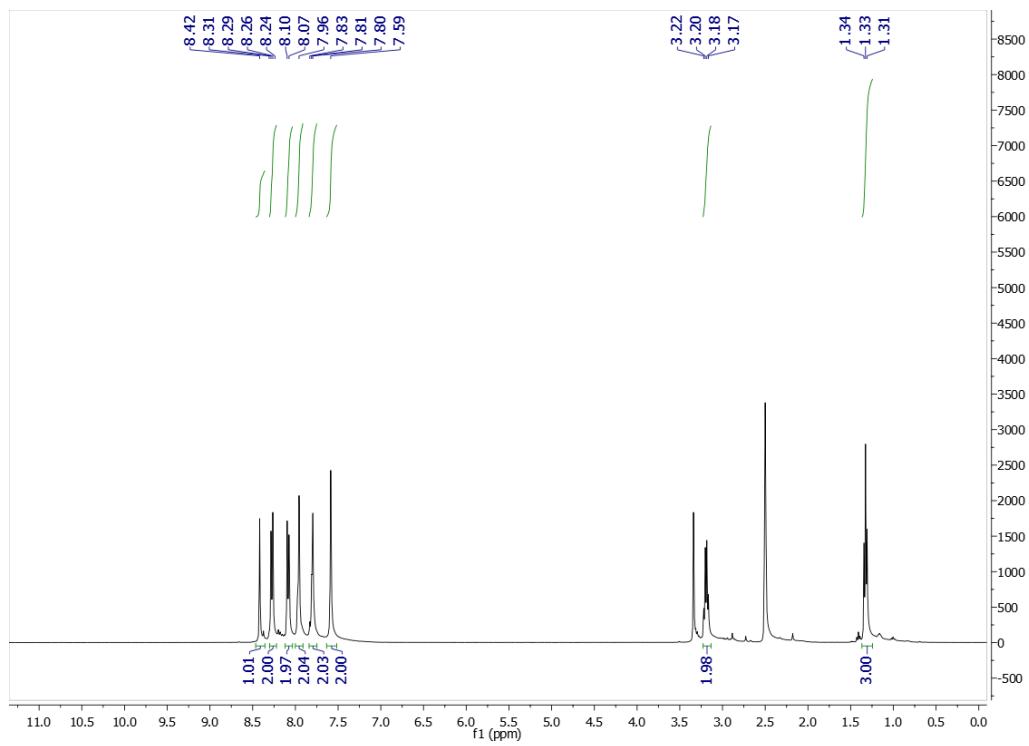
**Figure S42.**  $^{13}\text{C}$  NMR spectrum of compound **21c** at 101 MHz (DMSO- $d_6$ )



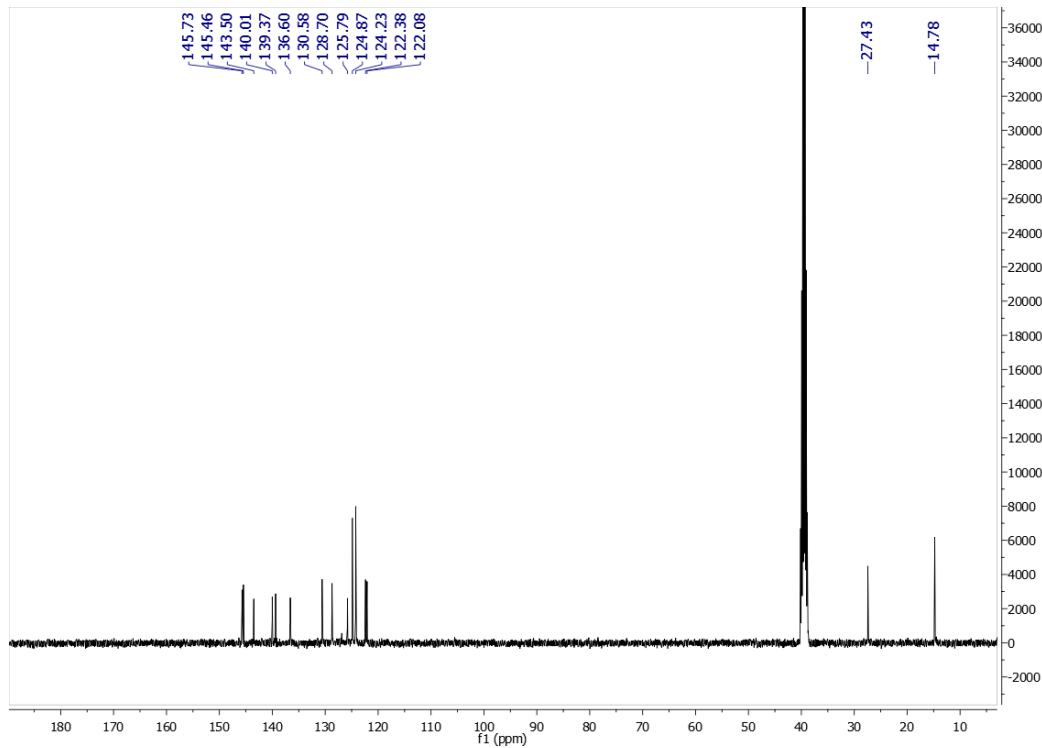
**Figure S43.** <sup>1</sup>H NMR of compound 22a at 400 MHz (DMSO-*d*<sub>6</sub>)



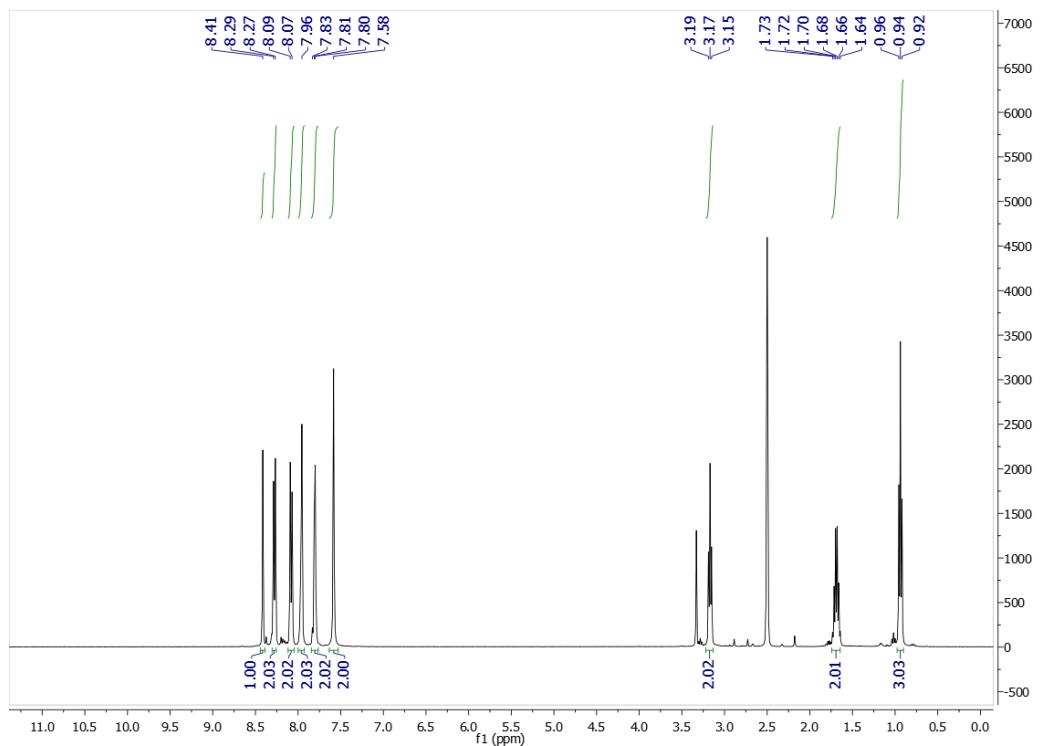
**Figure S44.** <sup>13</sup>C NMR spectrum of compound 22a at 101 MHz (DMSO-*d*<sub>6</sub>)



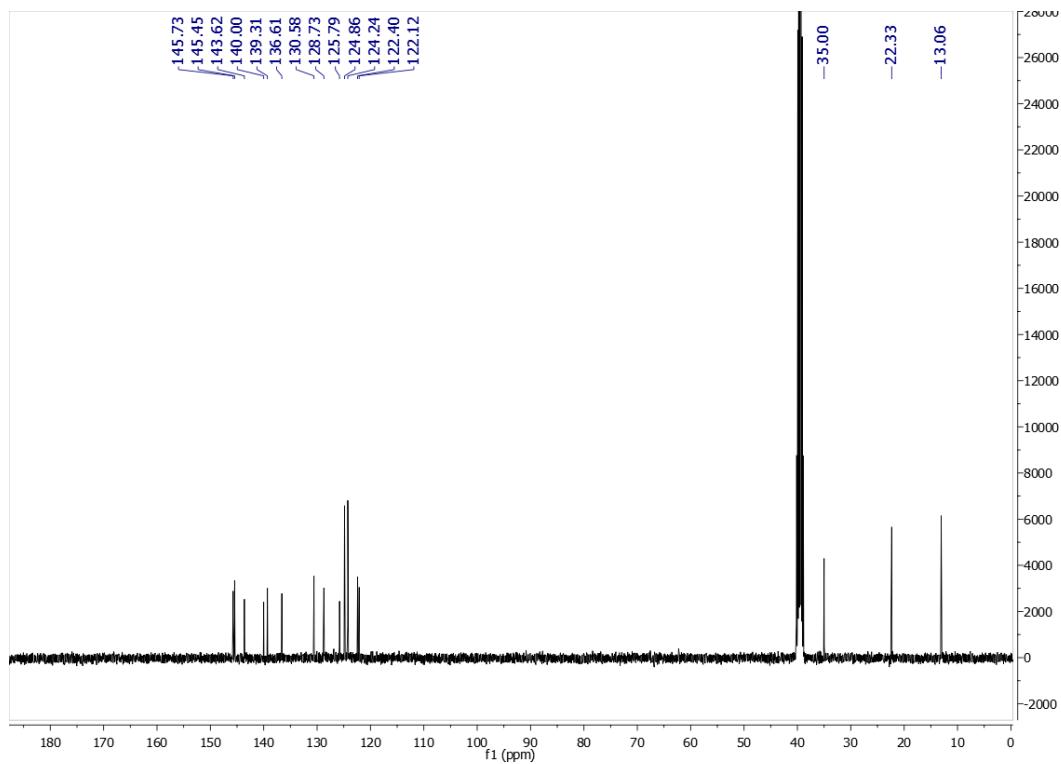
**Figure S45.**  $^1\text{H}$  NMR of compound **22b** at 400 MHz (DMSO- $d_6$ )



**Figure S46.**  $^{13}\text{C}$  NMR spectrum of compound **22b** at 101 MHz ( $\text{DMSO}-d_6$ )



**Figure S47.**  $^1\text{H}$  NMR of compound **22c** at 400 MHz (DMSO- $d_6$ )



**Figure S48.**  $^{13}\text{C}$  NMR spectrum of compound **22c** at 101 MHz (DMSO- $d_6$ )

**Table S1.** The *in vitro* antibacterial activity of compounds **2–22c** against multidrug-resistant bacterial strains. The minimal inhibitory concentration (MIC) values are provided as an average value obtained from three experimental replicas.

Compound	Minimal inhibitory concentration ( $\mu\text{g/ml}$ )			
	<i>S. aureus</i> TCH 1516	<i>K. pneumoniae</i> AR-0034	<i>A. baumannii</i> AR-0033	<i>P. aeruginosa</i> AR-0054
<b>2</b>	>64	>64	>64	>64
<b>3</b>	>64	>64	>64	>64
<b>4</b>	>64	>64	>64	>64
<b>5</b>	>64	>64	>64	>64
<b>5</b>	>64	>64	>64	>64
<b>7</b>	>64	>64	>64	>64
<b>8</b>	>64	>64	>64	>64
<b>9</b>	>64	>64	>64	>64
<b>10</b>	>64	>64	>64	>64
<b>11</b>	>64	>64	>64	>64
<b>12</b>	>64	>64	>64	>64
<b>13</b>	>64	>64	>64	>64
<b>14</b>	>64	>64	>64	>64
<b>15</b>	64	>64	>64	>64
<b>16</b>	>64	>64	>64	>64
<b>17</b>	>64	>64	>64	>64
<b>16a</b>	>64	>64	>64	>64
<b>16b</b>	>64	>64	>64	>64
<b>16c</b>	>64	>64	>64	>64
<b>17a</b>	>64	>64	>64	>64
<b>17b</b>	>64	>64	>64	>64
<b>17c</b>	>64	>64	>64	>64
<b>18a</b>	>64	>64	>64	>64
<b>18b</b>	>64	>64	>64	>64
<b>18c</b>	>64	>64	>64	>64
<b>19a</b>	>64	>64	>64	>64
<b>19b</b>	>64	>64	>64	>64
<b>19c</b>	>64	>64	>64	>64
<b>20a</b>	>64	>64	>64	>64
<b>20b</b>	>64	>64	>64	>64
<b>20c</b>	>64	>64	>64	>64
<b>21a</b>	>64	>64	>64	>64
<b>21b</b>	>64	>64	>64	>64
<b>21c</b>	>64	>64	>64	>64
<b>22a</b>	>64	>64	>64	>64
<b>22b</b>	>64	>64	>64	>64
<b>22c</b>	>64	>64	>64	>64
<b>Ceftazidime</b>	16	>64	>64	>64
<b>Ciprofloxacin</b>	8	2	32	64
<b>Levofloxacin</b>	4	1	32	64
<b>Meropenem</b>	2	32	>64	16

<b>Piperacillin/Tazobactam</b>	4	4	8	>64
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**Table S2.** The *in vitro* antifungal activity of compounds **2–22c** against multidrug-resistant *Candida auris* strains. The minimal inhibitory concentration (MIC) values are provided as an average value obtained from three experimental replicas.

Compound	Minimal inhibitory concentration ( $\mu\text{g/ml}$ )		
	<i>C. auris</i> AR-381	<i>C. auris</i> AR-382	<i>C. auris</i> AR-383
<b>2</b>	>64	>64	>64
<b>3</b>	>64	>64	>64
<b>4</b>	>64	>64	>64
<b>5</b>	>64	>64	>64
<b>6</b>	>64	>64	>64
<b>7</b>	>64	>64	>64
<b>8</b>	>64	>64	>64
<b>9</b>	>64	>64	>64
<b>10</b>	>64	>64	>64
<b>11</b>	>64	>64	>64
<b>12</b>	>64	>64	>64
<b>13</b>	32	16	32
<b>14</b>	>64	>64	>64
<b>15</b>	>64	>64	>64
<b>16a</b>	>64	>64	>64
<b>16b</b>	>64	>64	>64
<b>16c</b>	>64	>64	>64
<b>17a</b>	>64	>64	>64
<b>17b</b>	>64	>64	>64
<b>17c</b>	>64	>64	>64
<b>18a</b>	>64	>64	>64
<b>18b</b>	>64	>64	>64
<b>18c</b>	>64	>64	>64
<b>19a</b>	64	64	32
<b>19b</b>	>64	>64	>64
<b>19c</b>	>64	>64	>64
<b>20a</b>	>64	>64	>64
<b>20b</b>	>64	>64	>64
<b>20c</b>	>64	>64	>64
<b>21a</b>	>64	>64	>64
<b>21b</b>	>64	>64	>64
<b>21c</b>	>64	>64	>64
<b>22a</b>	>64	>64	>64
<b>22b</b>	>64	>64	>64
<b>22c</b>	>64	>64	>64
<b>Fluconazole</b>	8	32	>64
<b>Amfotericin B</b>	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$