

**Electronic Supplementary Information**

for

**Small change for big improvement in the preparation of the key intermediate**

***N<sup>1</sup>, N<sup>3</sup>-disubstituted 1,3,5-triazone of ensitrelvir***

Wei Hu,<sup>#a</sup> Yuanchang Liu,<sup>#a</sup> Xiang Zhang,<sup>a</sup> Panpan Zheng,<sup>a</sup> Feifei Yang,<sup>a</sup>

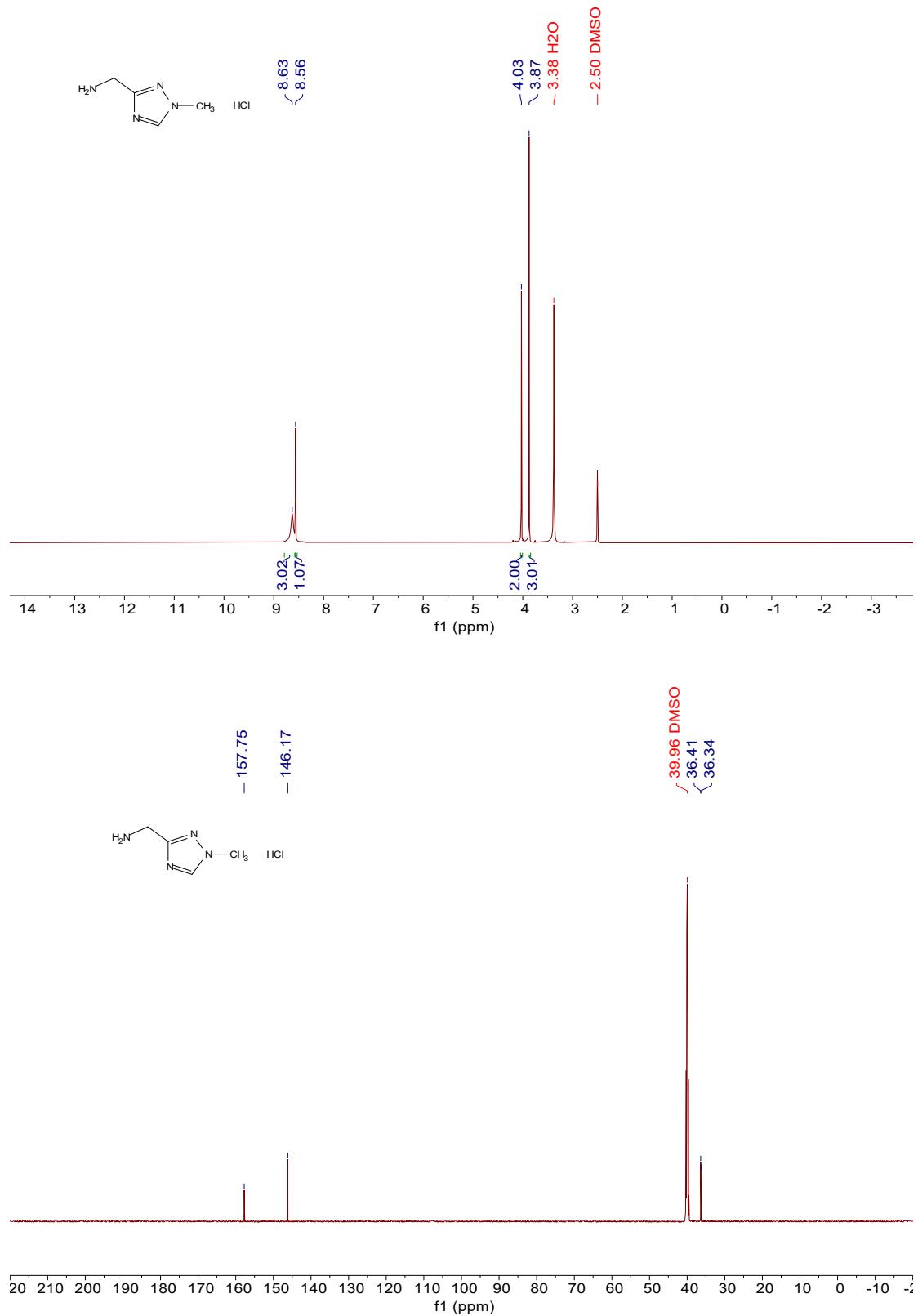
Guangyang Guo,<sup>a</sup> Xin Xie,<sup>ab</sup> Jiuzhong Huang,<sup>\*ab</sup> Weiming Chen<sup>\*ab</sup>

<sup>a</sup> School of Pharmaceutical Sciences; <sup>b</sup> Key Laboratory of Prevention and Treatment of  
Cardiovascular and Cerebrovascular Disease, Ministry of Education, Gannan Medical University,  
Ganzhou 341000, Jiangxi, P. R. China.

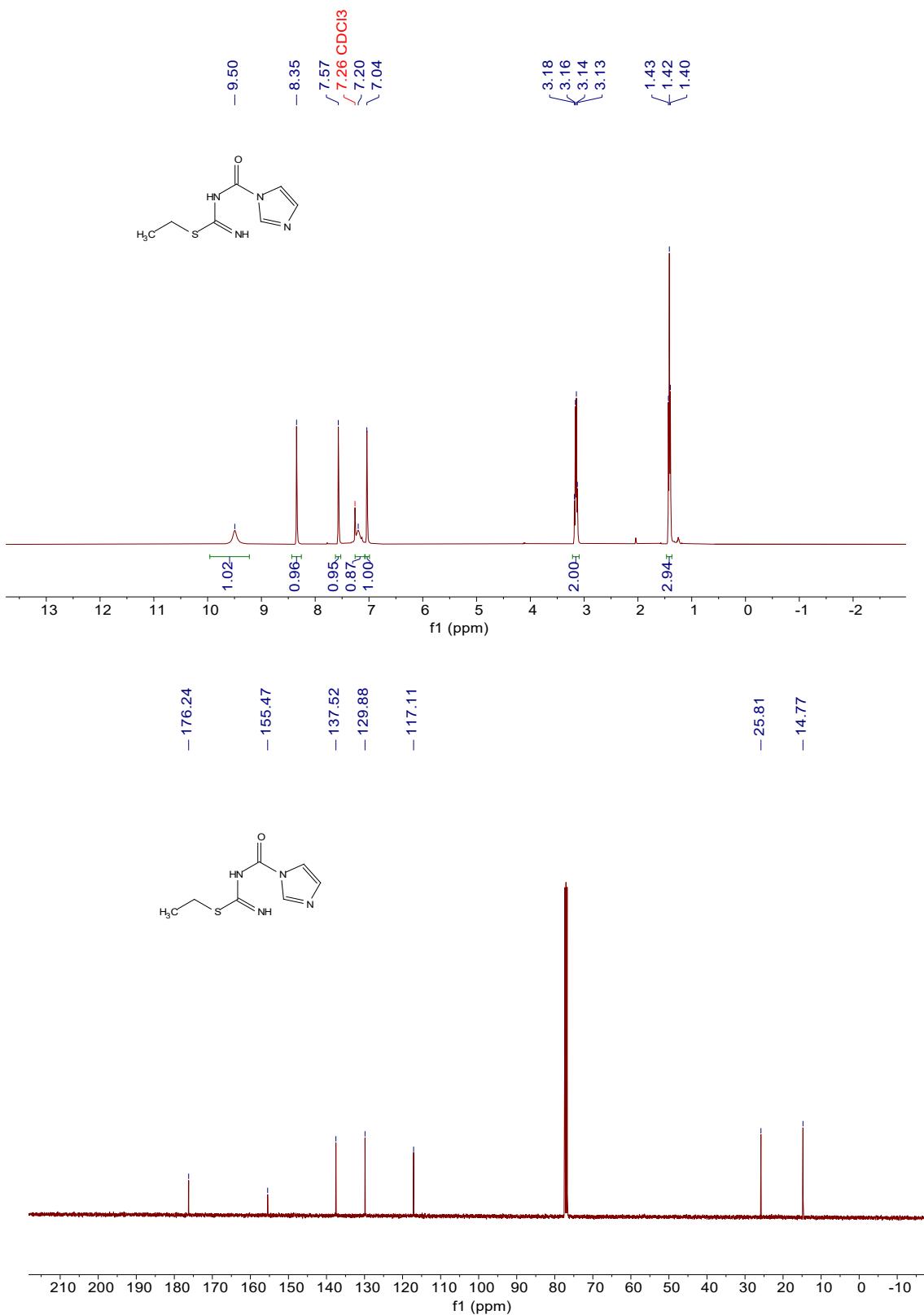
**SPECTROSCOPIC DATA**

|   |           |
|---|-----------|
| <sup>1</sup> H NMR and <sup>13</sup> C NMR of compound <b>10</b> .....  | <b>S2</b> |
| <sup>1</sup> H NMR and <sup>13</sup> C NMR of compound <b>13a</b> ..... | <b>S3</b> |
| <sup>1</sup> H NMR and <sup>13</sup> C NMR of compound <b>13</b> .....  | <b>S4</b> |
| <sup>1</sup> H NMR and <sup>13</sup> C NMR of compound <b>12</b> .....  | <b>S5</b> |
| <sup>1</sup> H NMR and <sup>13</sup> C NMR of compound <b>2</b> .....   | <b>S6</b> |
| HRMS of compound <b>13</b> and <b>12</b> .....                          | <b>S7</b> |

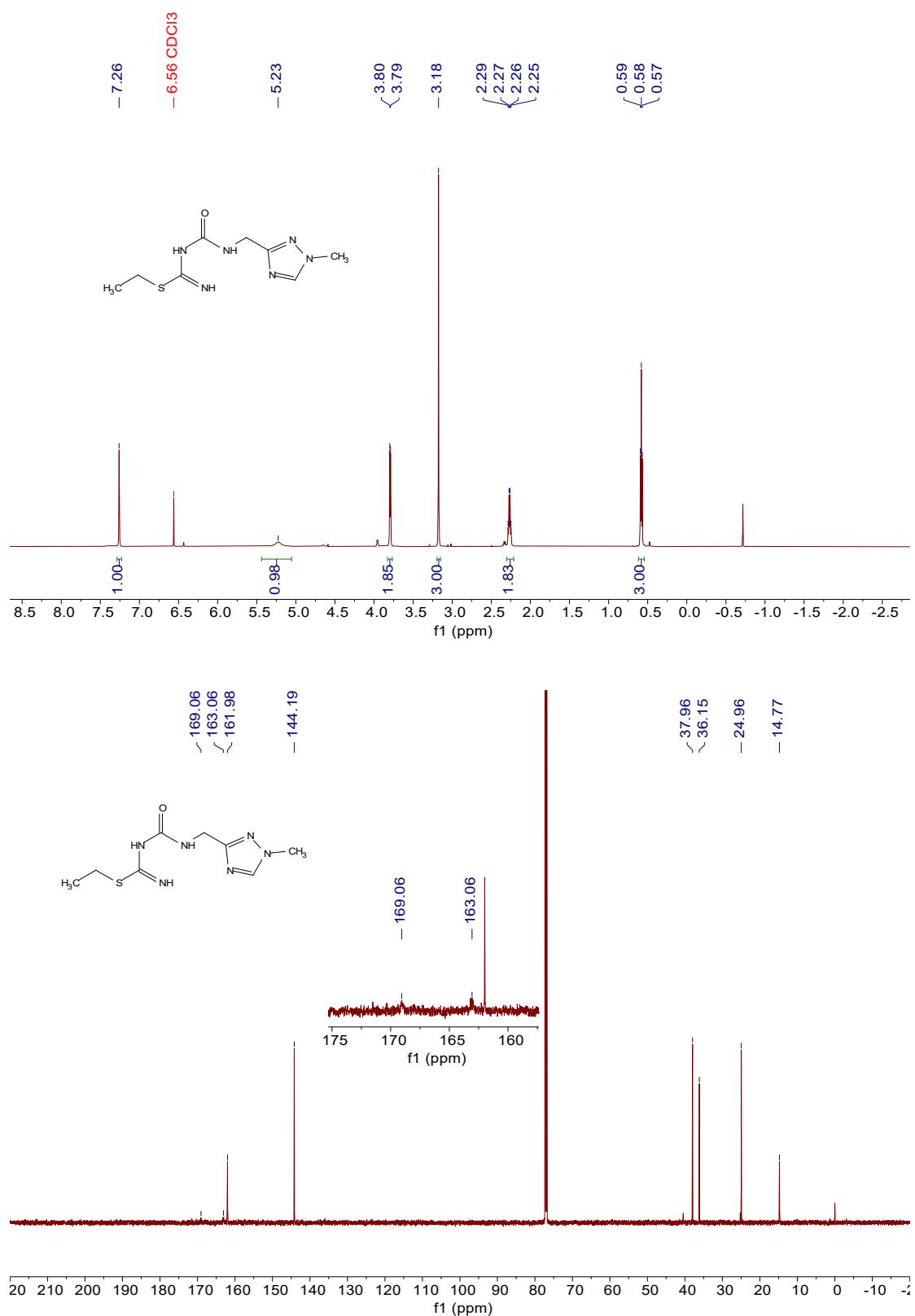
**<sup>1</sup>H NMR (600 MHz) and <sup>13</sup>C NMR (150 MHz) in DMSO-*d*<sub>6</sub> of compound 10**



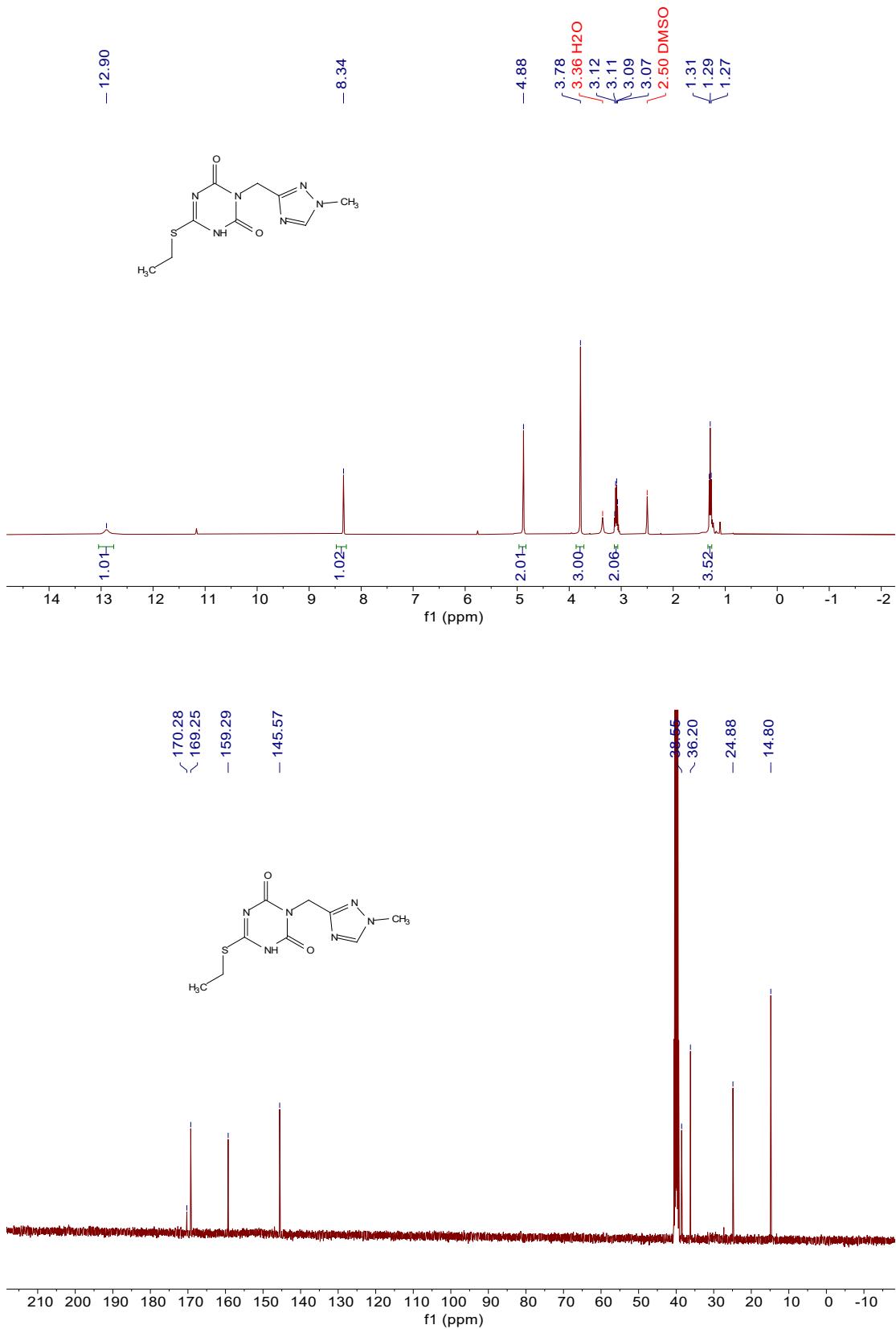
<sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) in CDCl<sub>3</sub> of compound **13a**



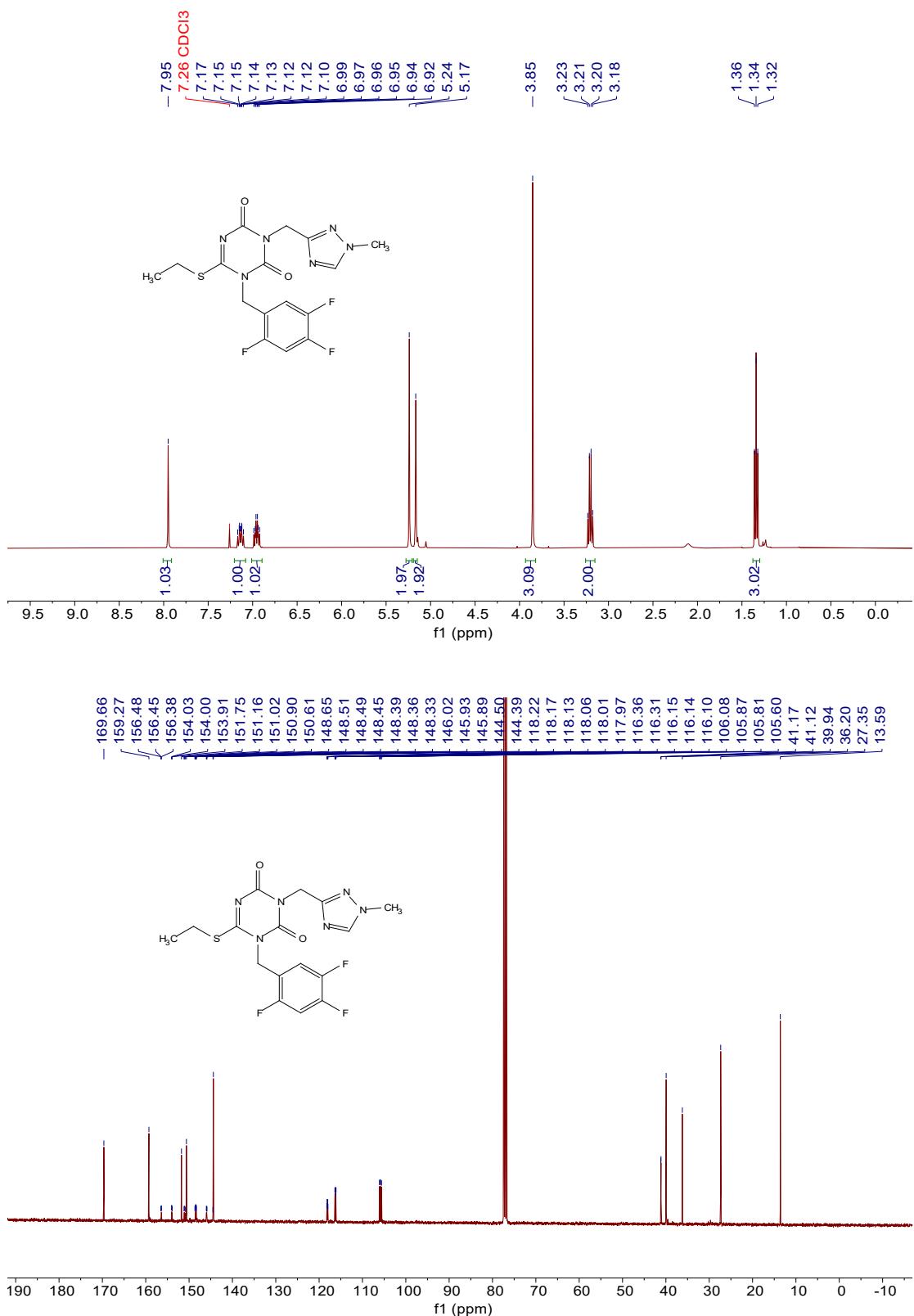
<sup>1</sup>H NMR (600 MHz) and <sup>13</sup>C NMR (150 MHz) in CDCl<sub>3</sub> of compound **13**



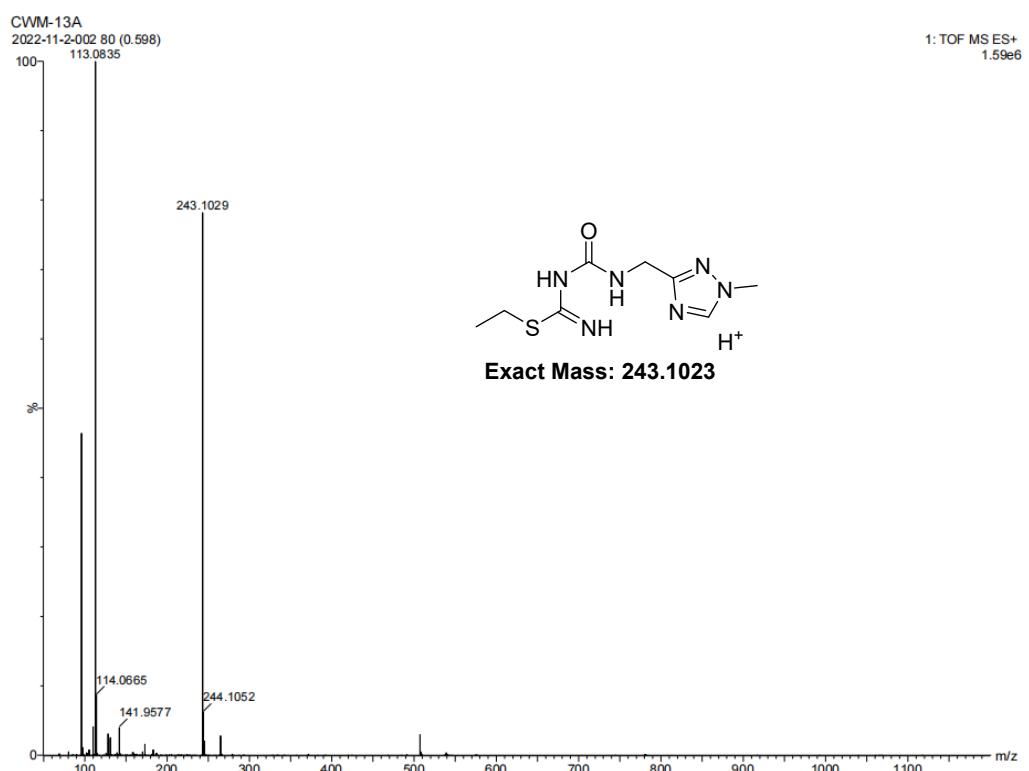
<sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) in DMSO-*d*<sub>6</sub> of compound **12**



$^1\text{H}$  NMR (400 MHz) and  $^{13}\text{C}$  NMR (100 MHz) in  $\text{CDCl}_3$  of compound 2



HRMS of compound **13**



HRMS of compound **12**

