

## Supporting Information for

### Original article

# Exploring the hydrophobic channel of NNIBP leads to the discovery of novel piperidine-substituted thiophene[3,2-*d*]pyrimidine derivatives as potent HIV-1 NNRTIs

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<sup>b</sup>*Rega Institute for Medical Research, Laboratory of Virology and Chemotherapy, K.U. Leuven, Leuven B-3000, Belgium*

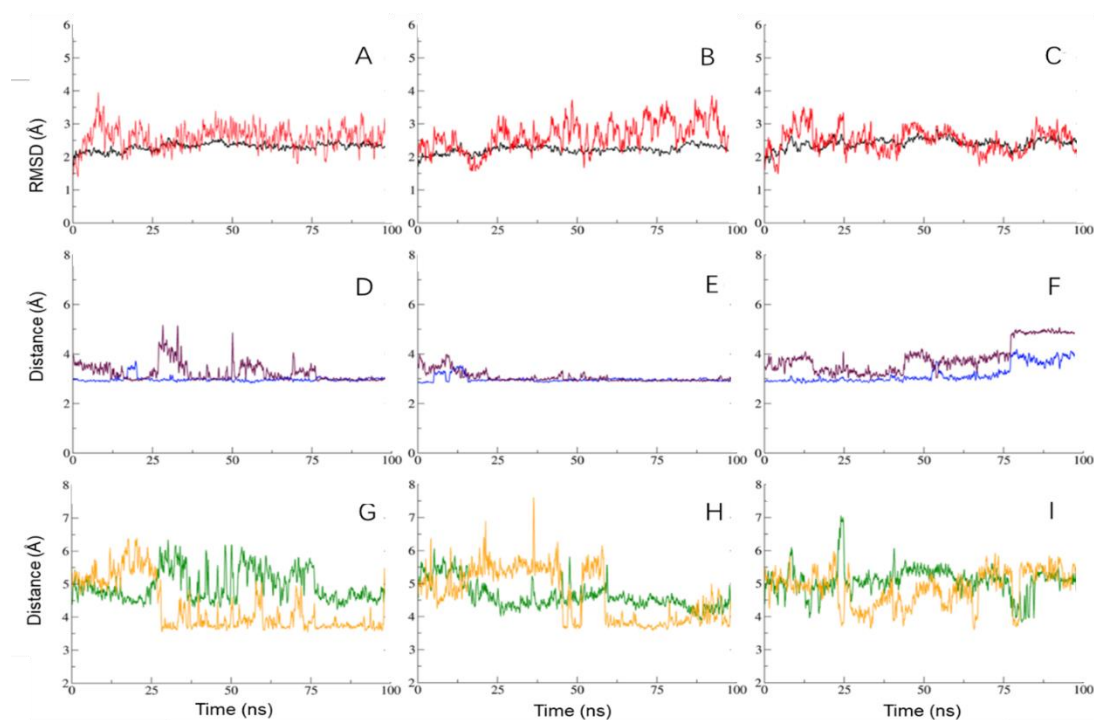
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## 1. Molecular modelling studies



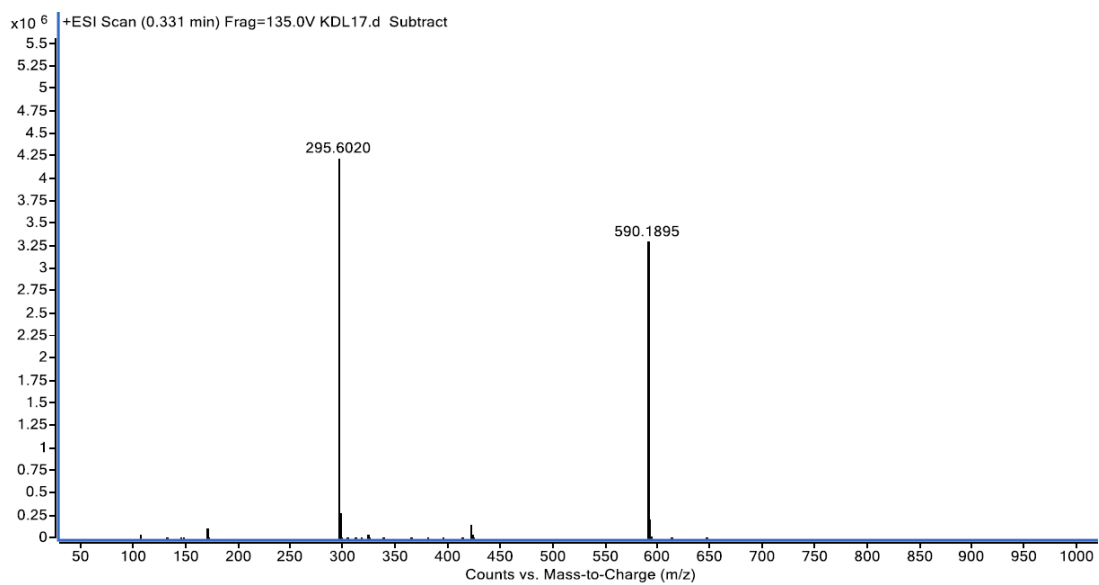
**Figure S1** Root mean square deviation (RMSD; Å) and distance (Å) analyses for **26** in complex with the WT (A, D, and G), the single K103N (B, E and H) and the double RES056 (C, F and I) RT. RMSD for the protein residues in close proximity of the ligand (8 Å), and for the ligand are shown respectively in black and red. Distances for the hydrogen-bonding (measured as N–O distance) interactions involving the –NH guanidine moiety of **26** and the backbone oxygen of K101, and for the protonated nitrogen of **26** and the backbone oxygen of K/N103 (measured as N–O distance) are highlighted in blue and brown, respectively. Finally, distances for the  $\pi$ -stacking formed between the benzonitrile moiety of **26** and residues Y181 (in green) and F227 (in orange) are also reported.

**Table S1** The corresponding list of compounds name in article and HPLC spectra.

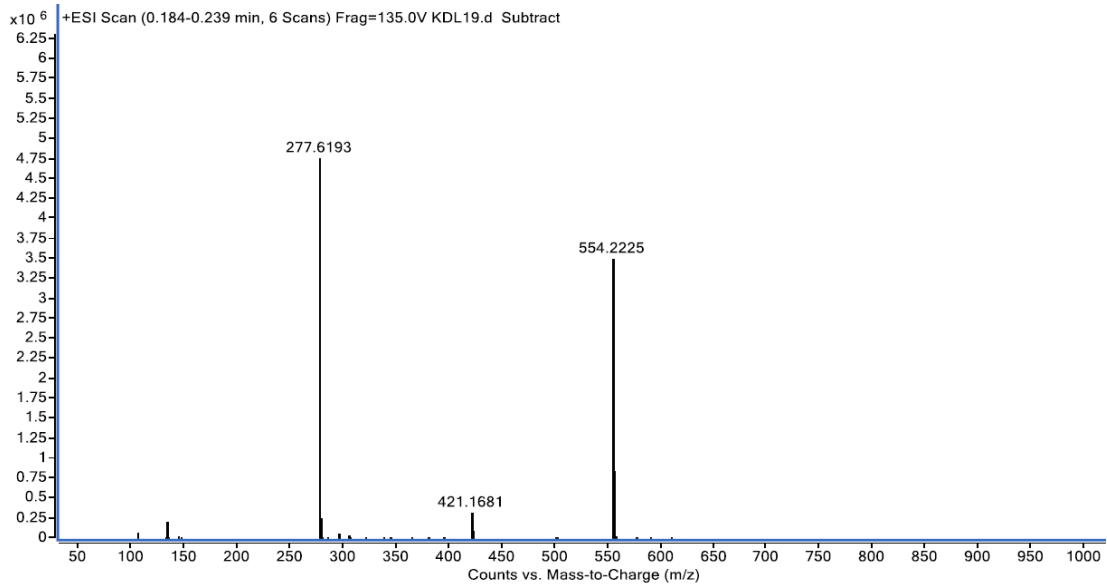
Compd.	Compd. ID in spectra	Compd.	Compd. ID in spectra
<b>11</b>	KDL17	<b>22</b>	KDL31
<b>12</b>	KDL19	<b>23</b>	KDL37
<b>13</b>	KDL33	<b>24</b>	KDL39
<b>14</b>	KDL35	<b>25</b>	KDL41
<b>15</b>	KDL79	<b>26</b>	KDL43
<b>16</b>	KDL81	<b>27</b>	KDL45
<b>17</b>	KDL25	<b>28</b>	KDL47
<b>18</b>	KDL27	<b>29</b>	KDL71
<b>19</b>	KDL21	<b>30</b>	KDL73
<b>20</b>	KDL23	<b>31</b>	KDL75
<b>21</b>	KDL29	<b>32</b>	KDL77

## 2. High resolution mass spectrum

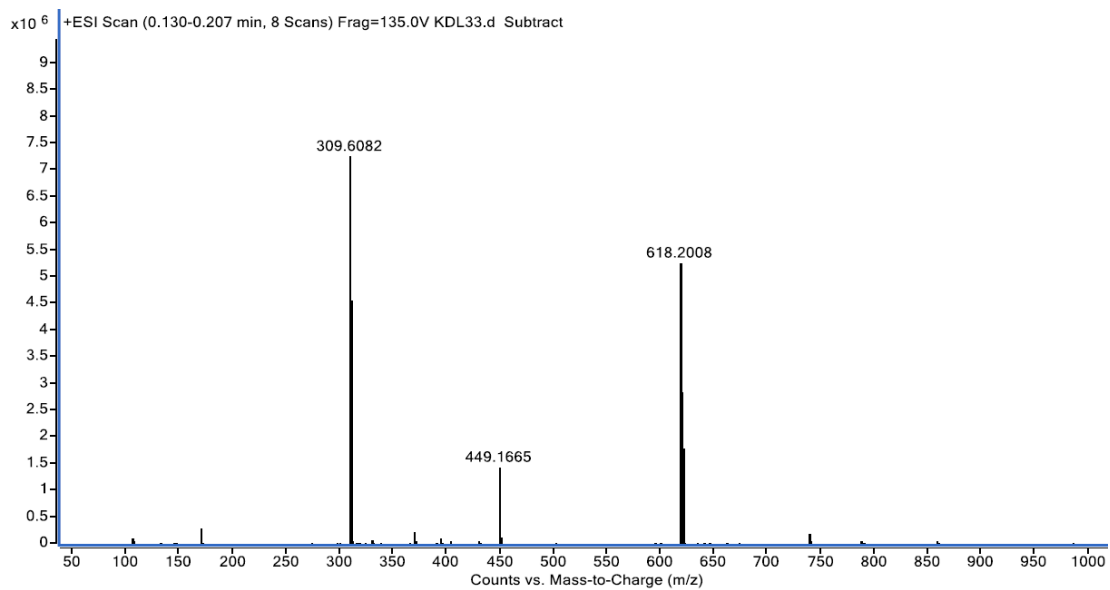
### Compound 11



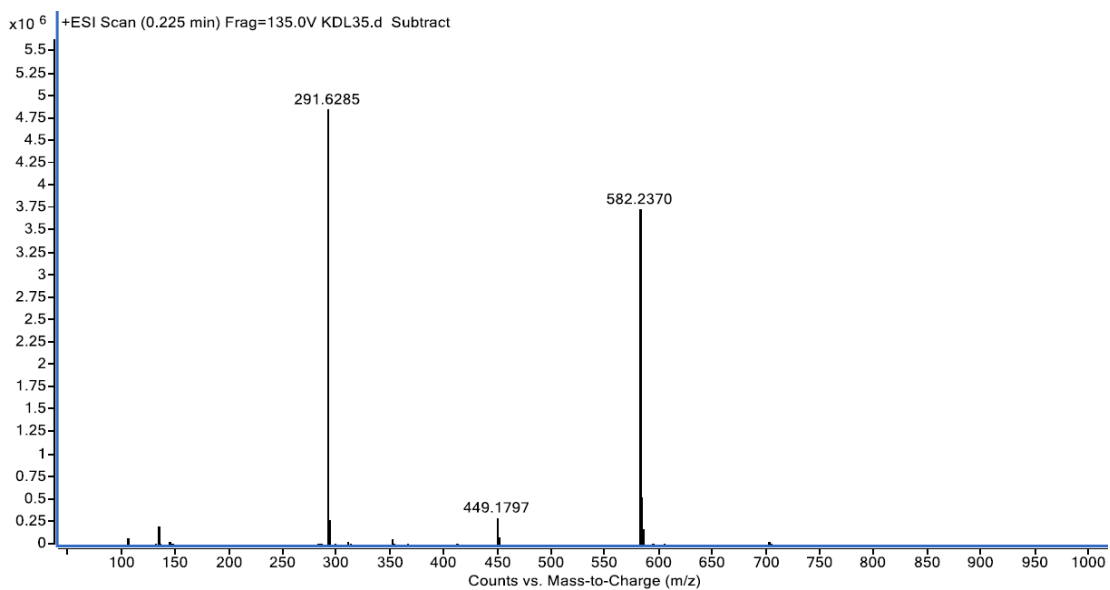
### Compound 12



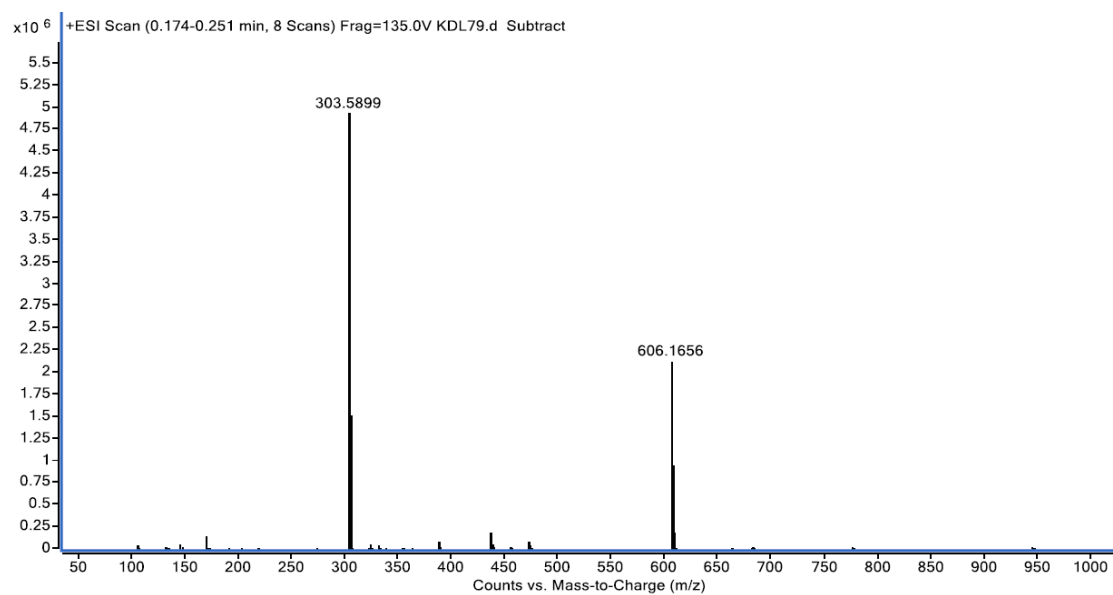
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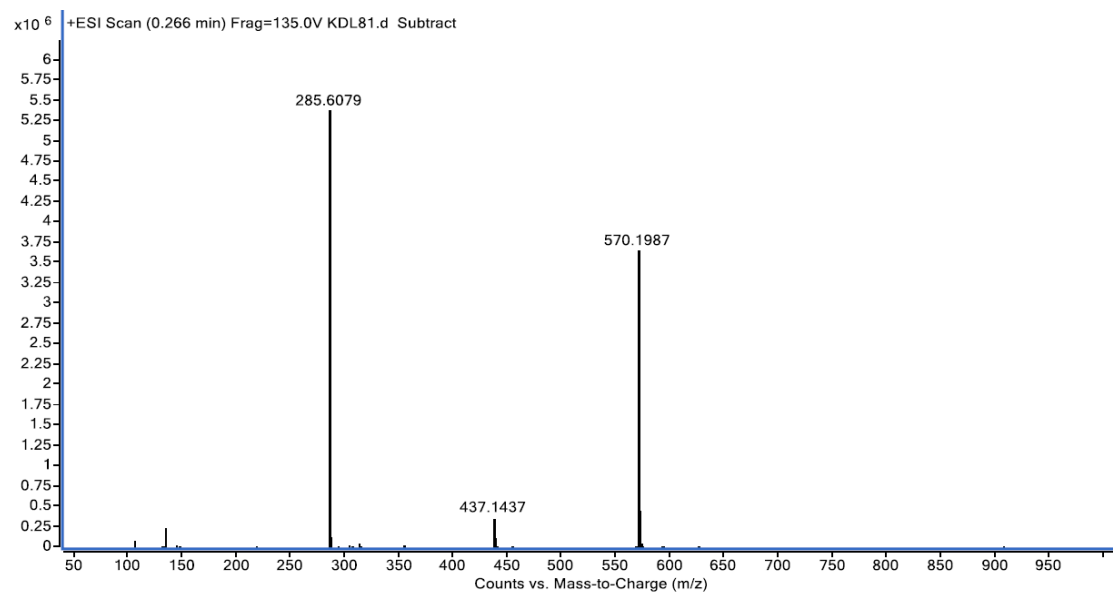
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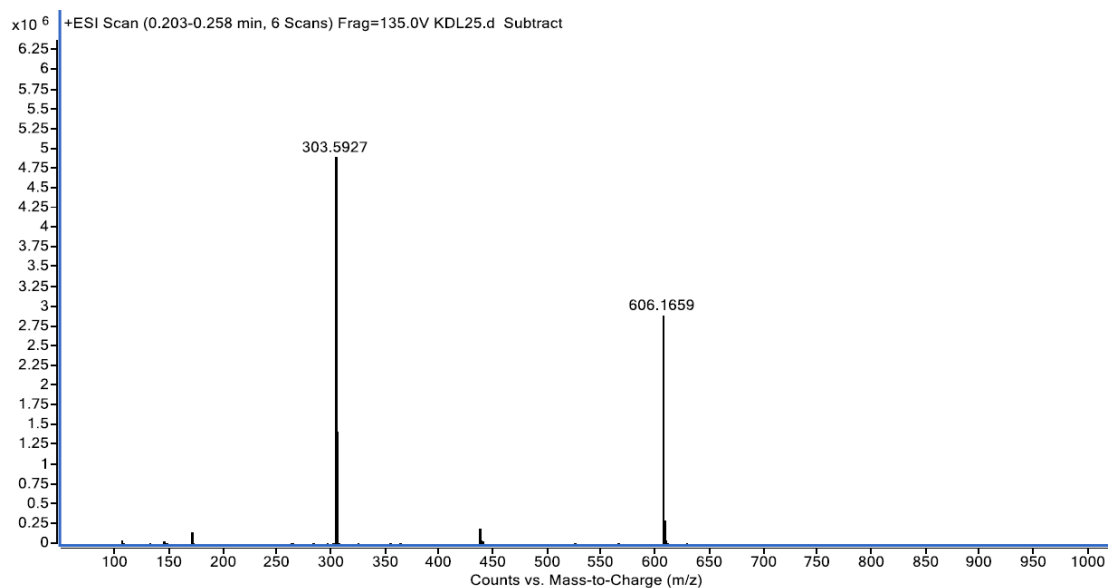
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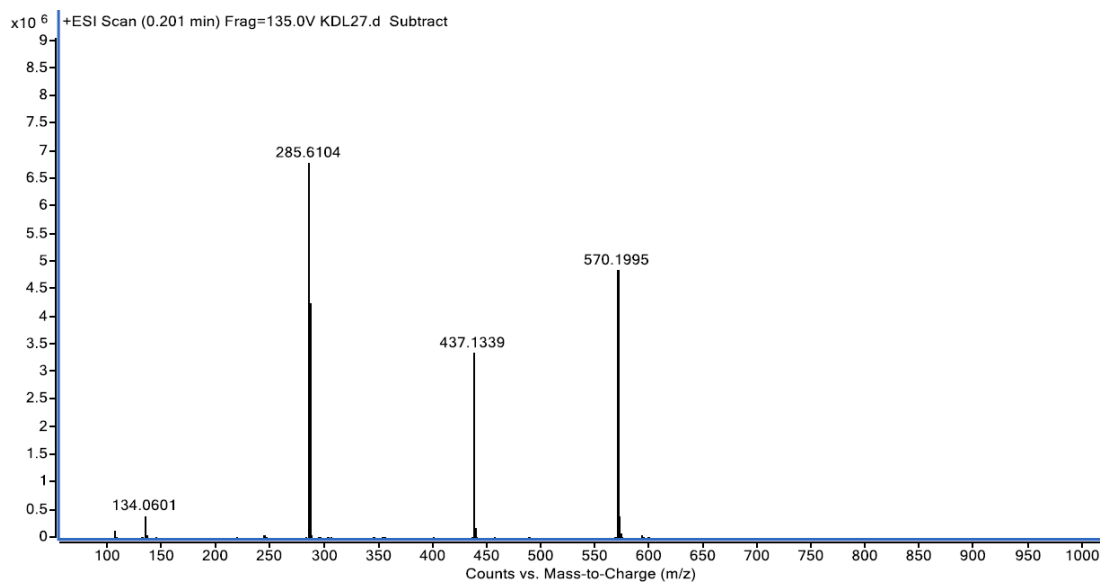
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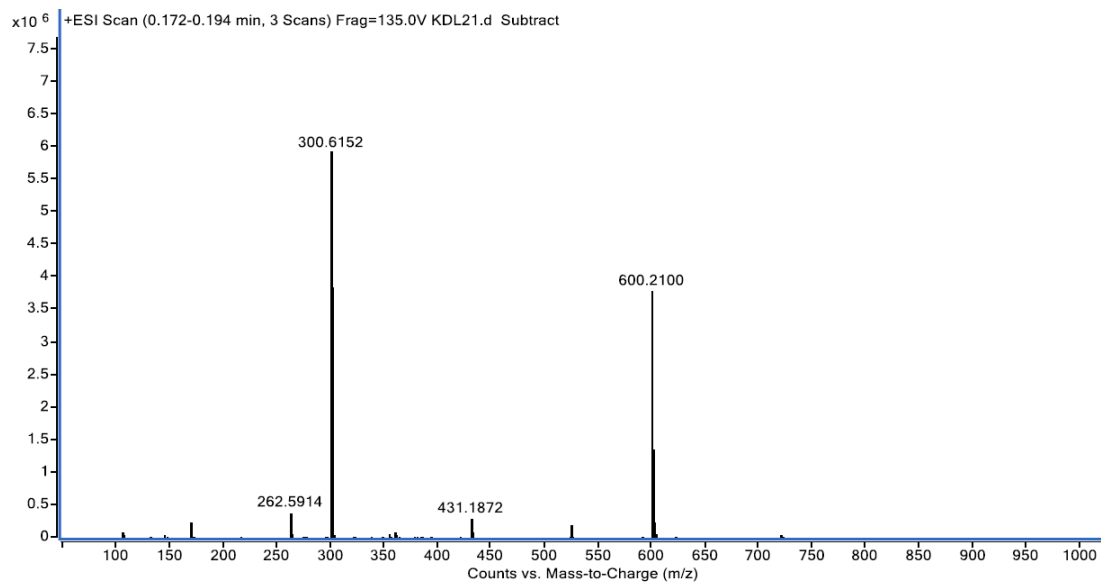
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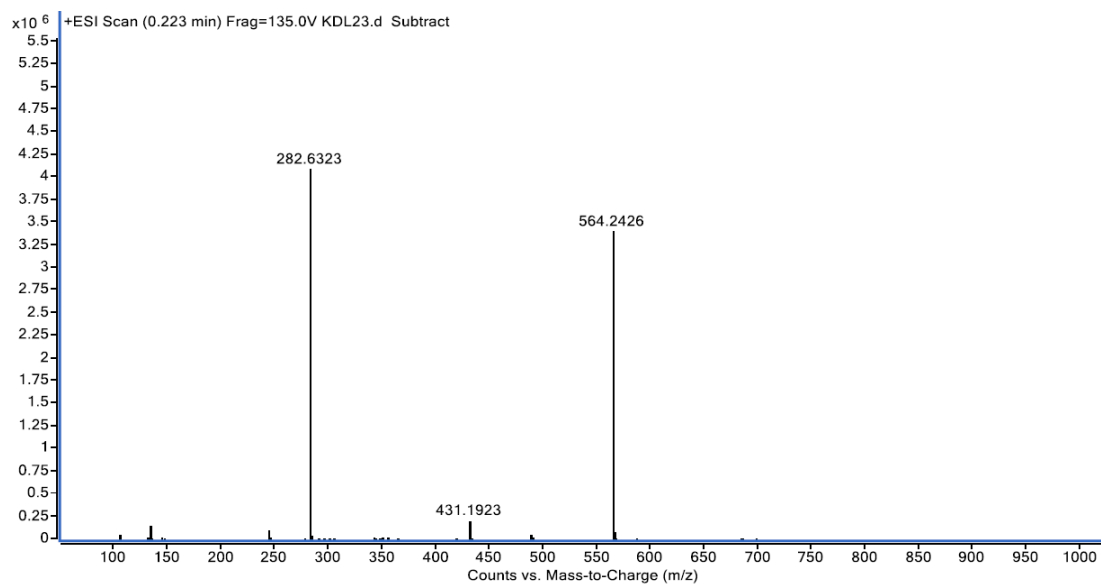
## Compound 18



## Compound 19

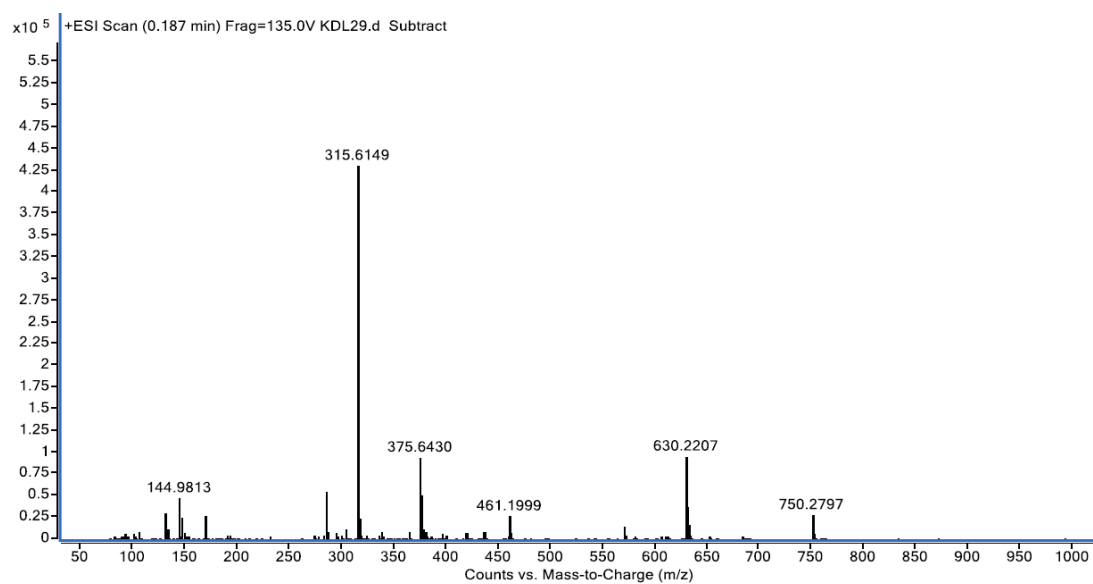


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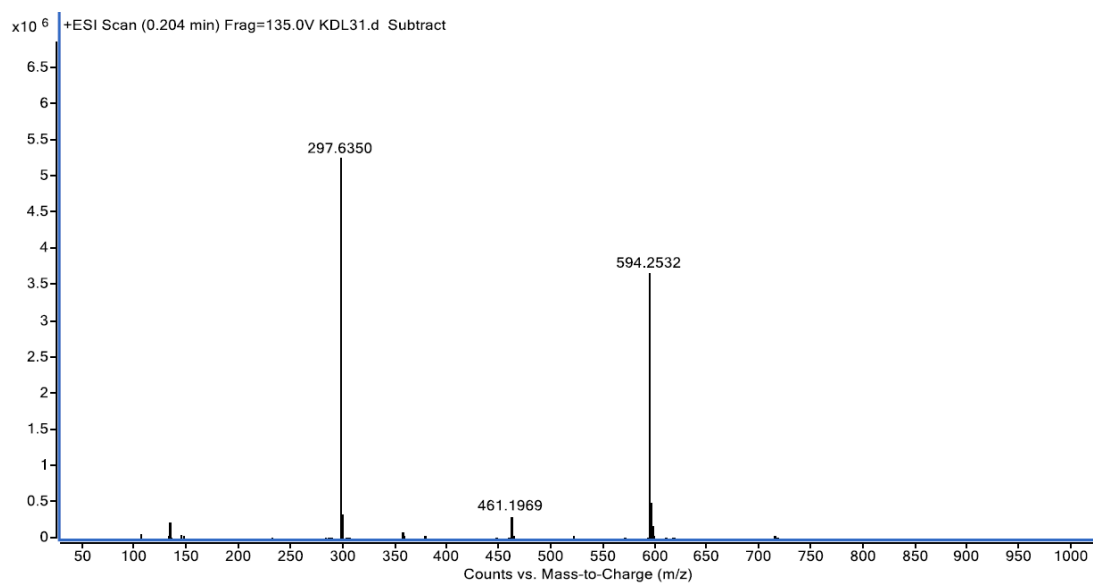




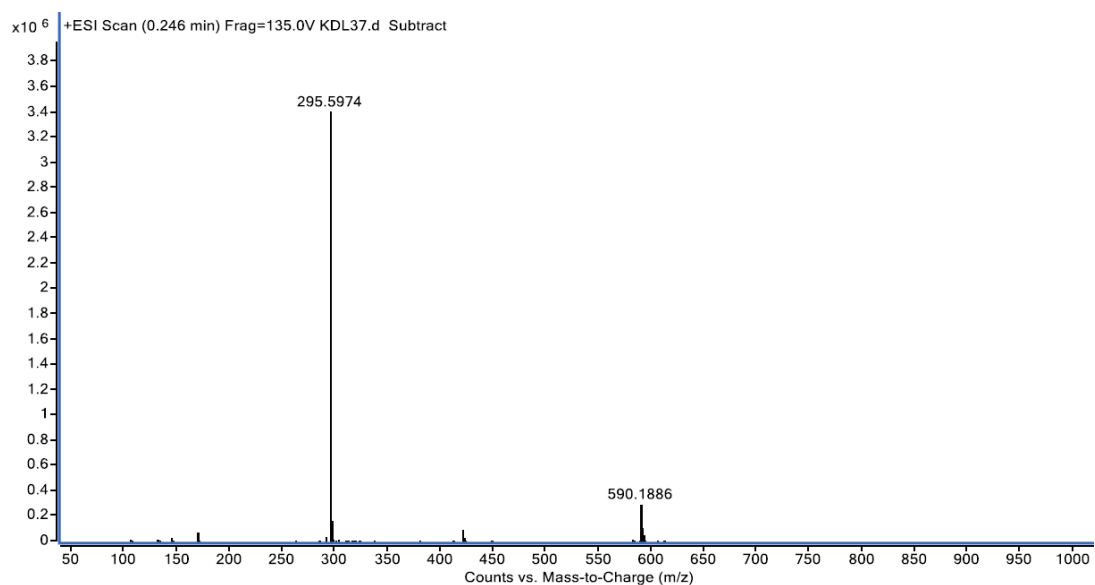
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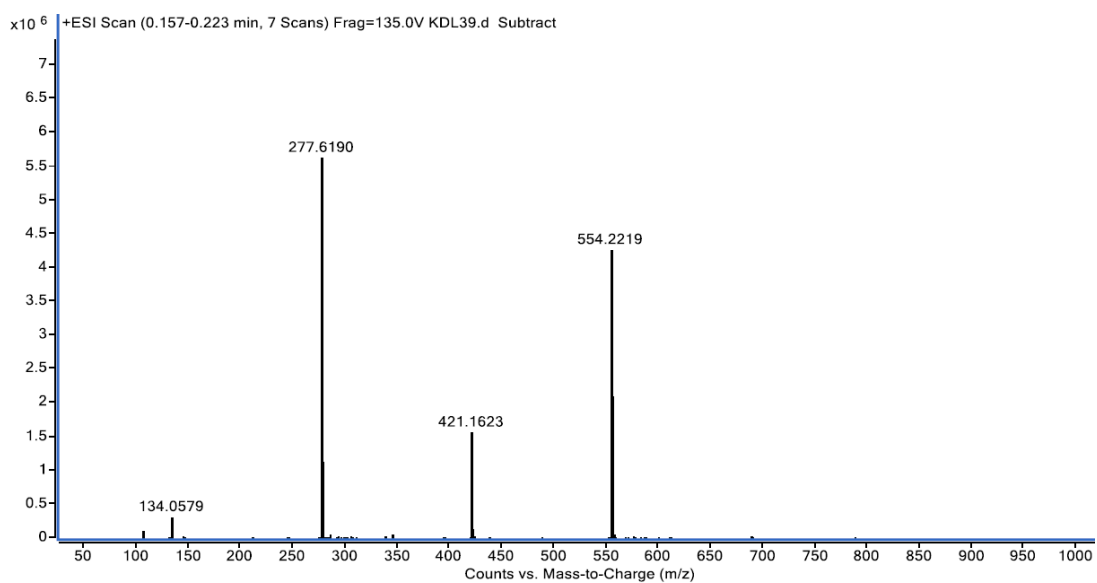
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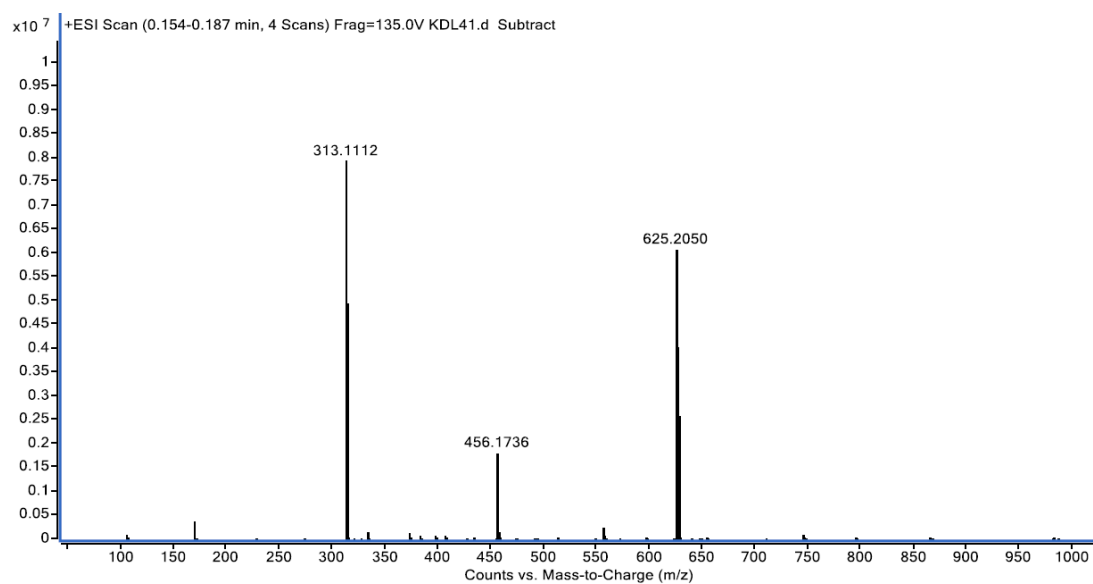
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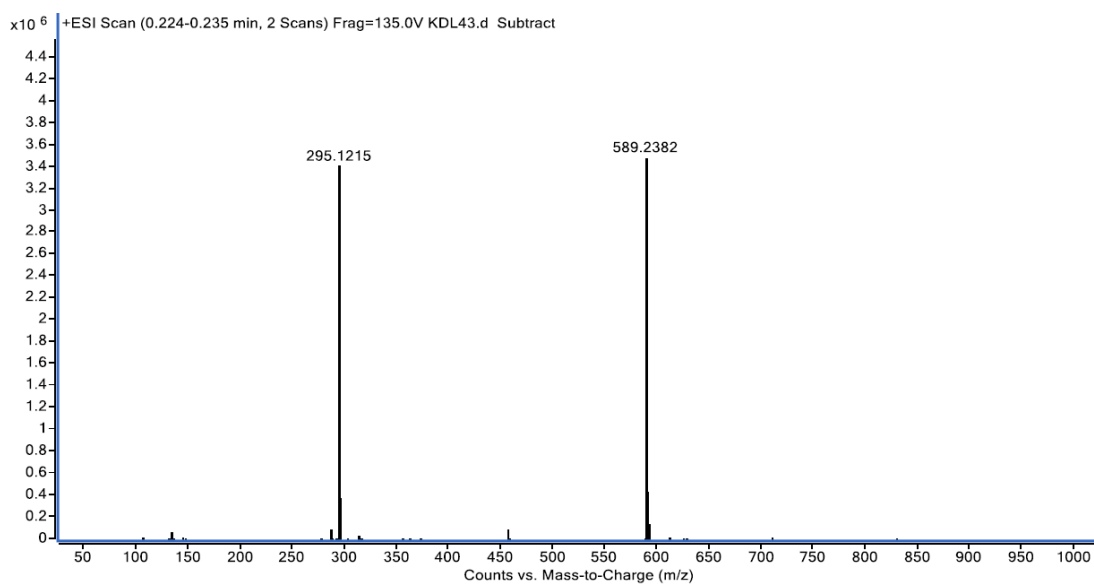
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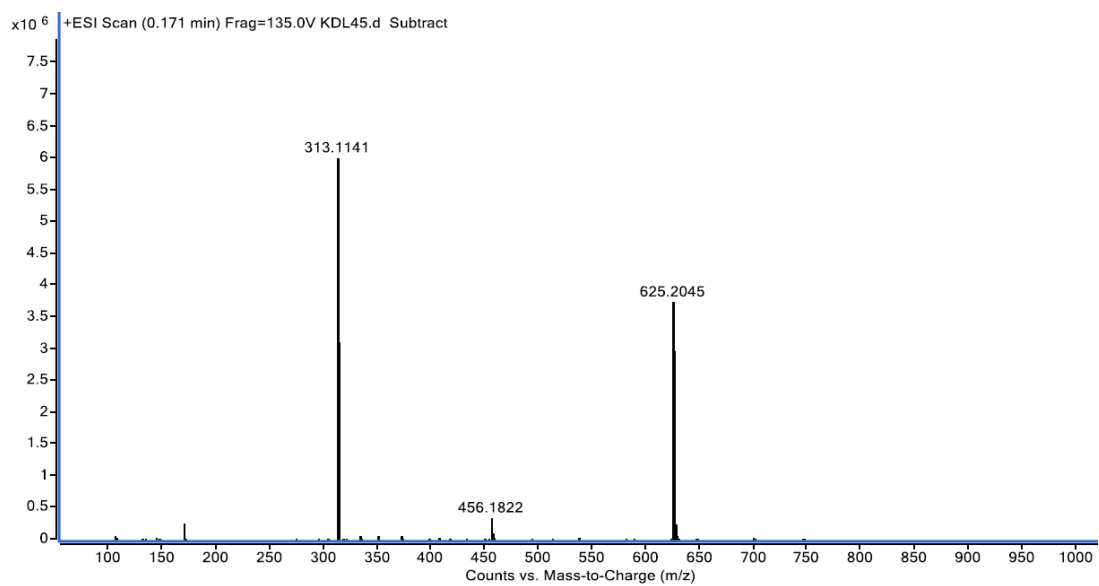
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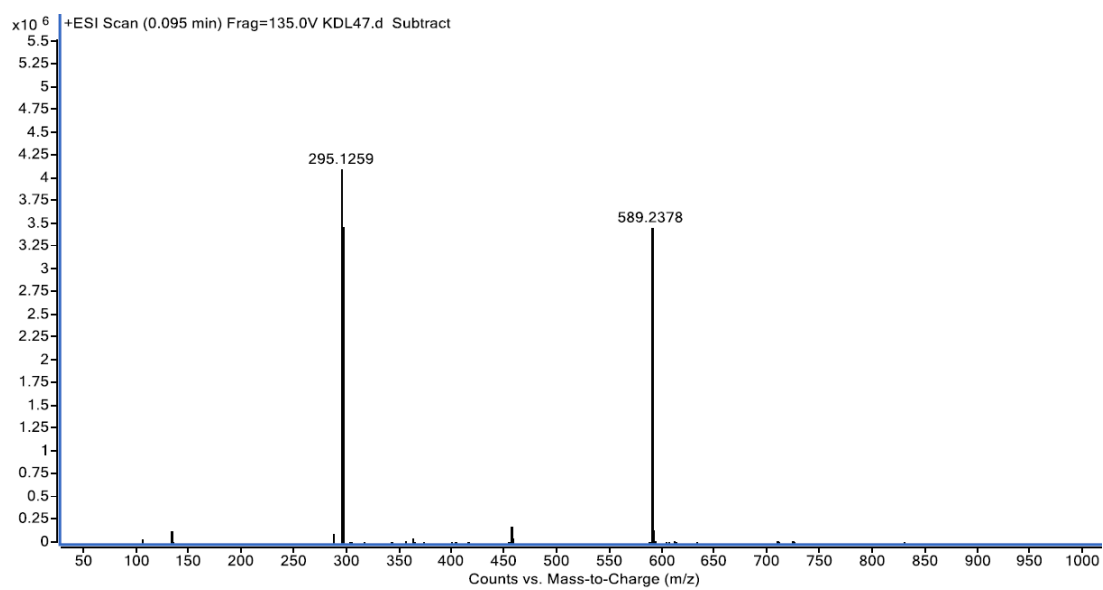
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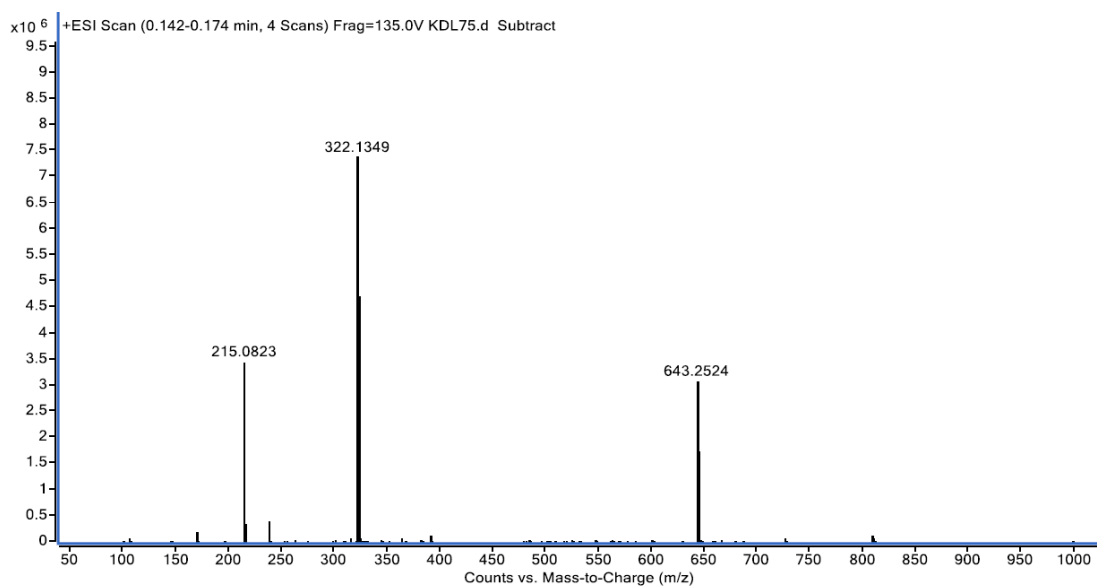
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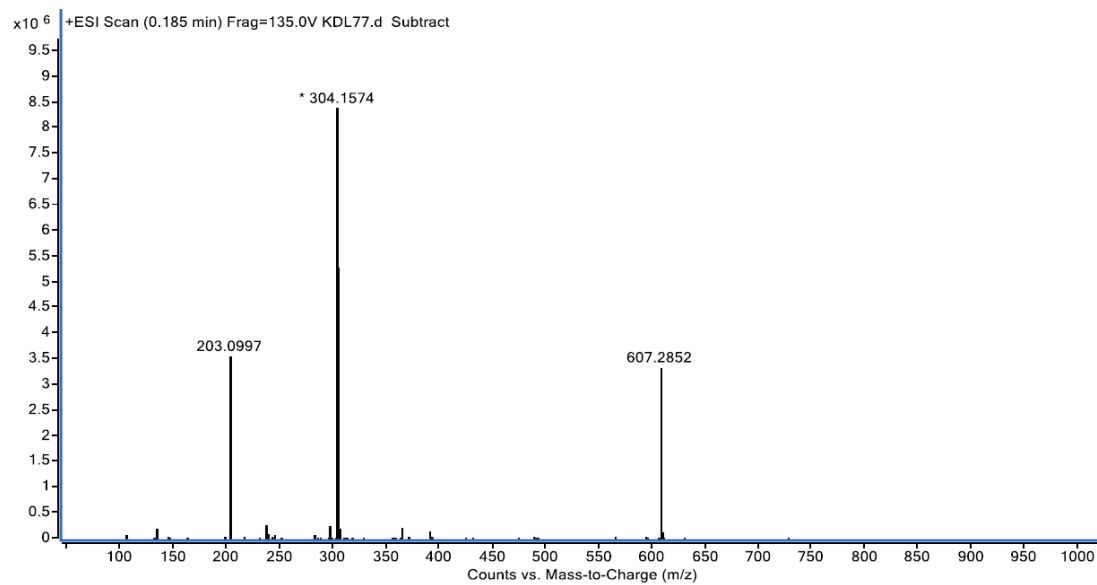
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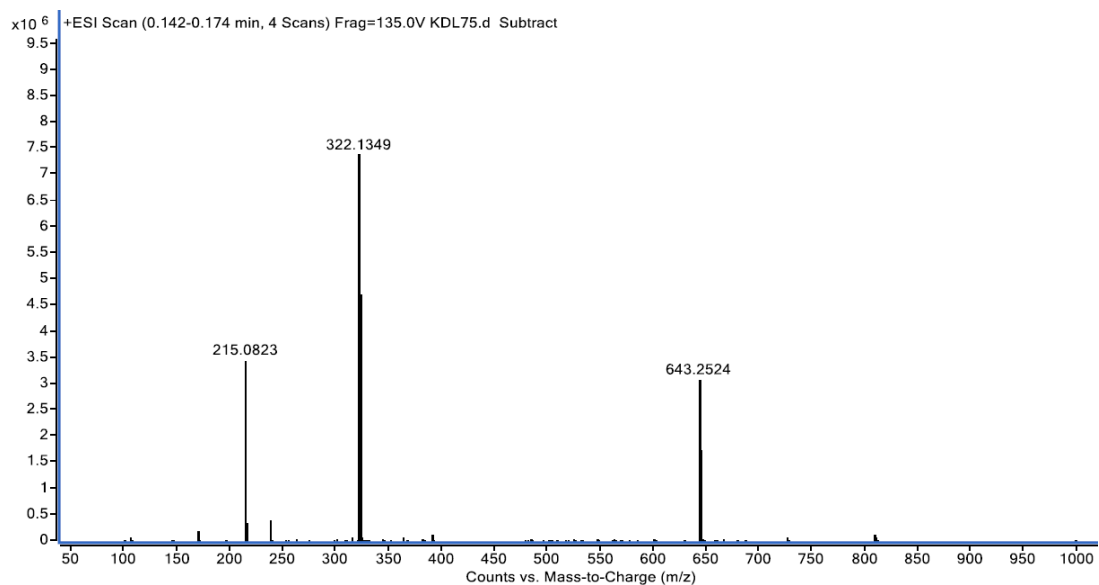
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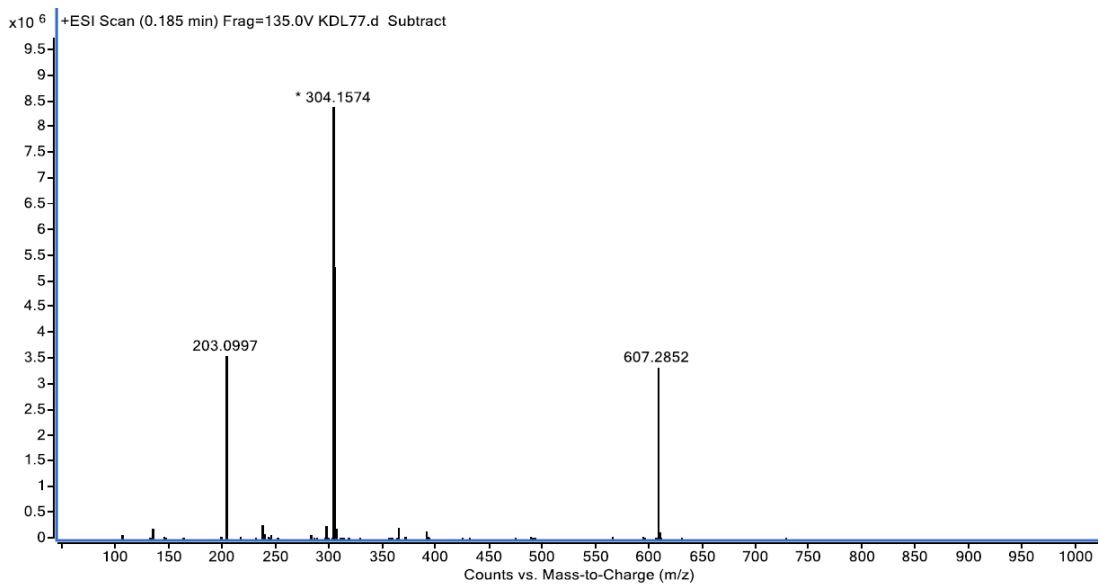
## Compound 30



## Compound 31

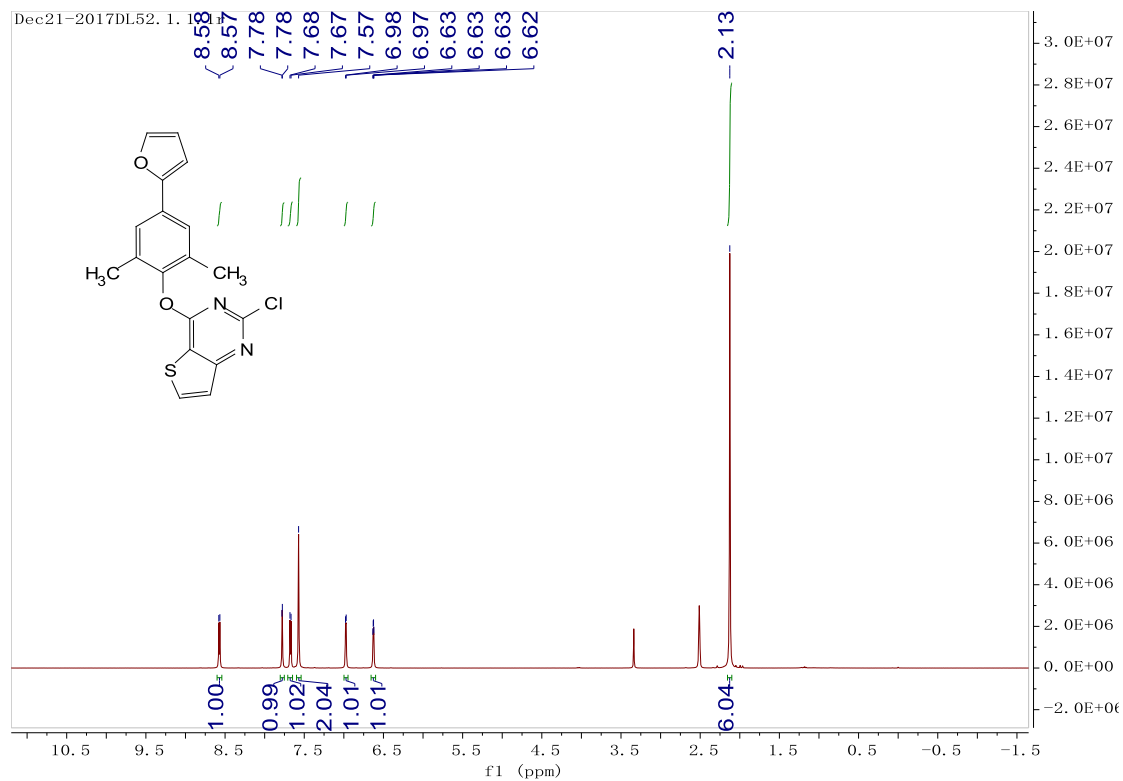


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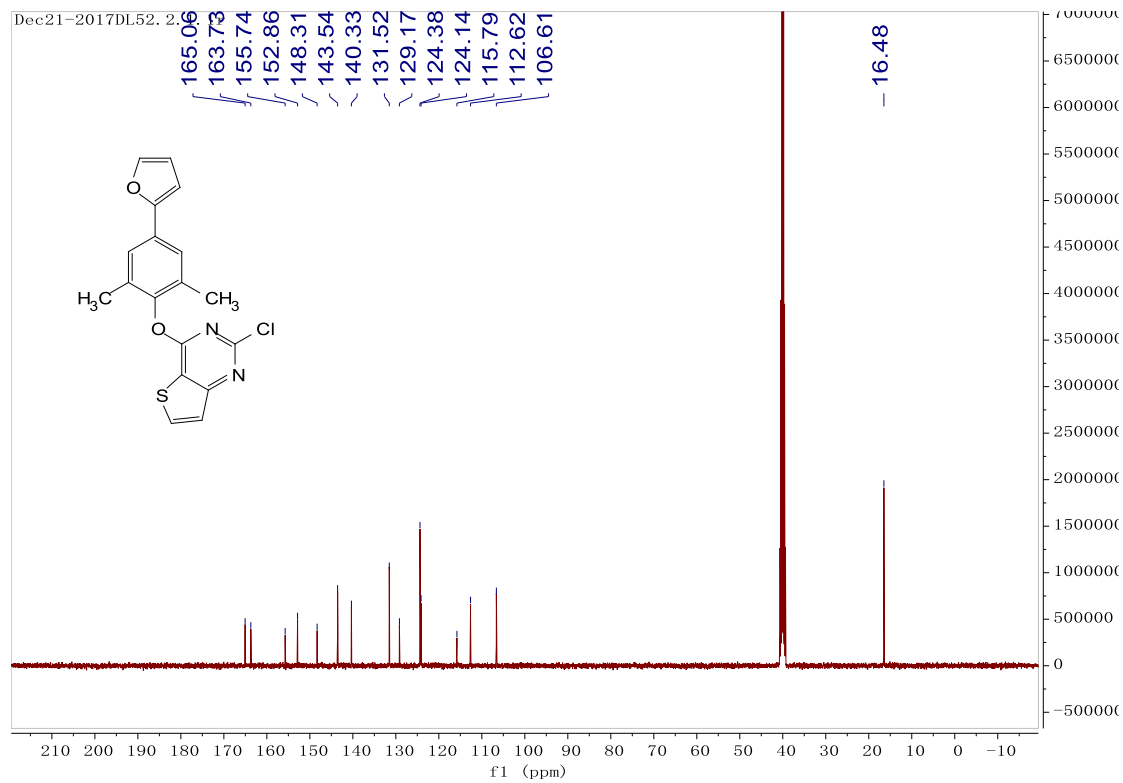


### 3. NMR spectrum

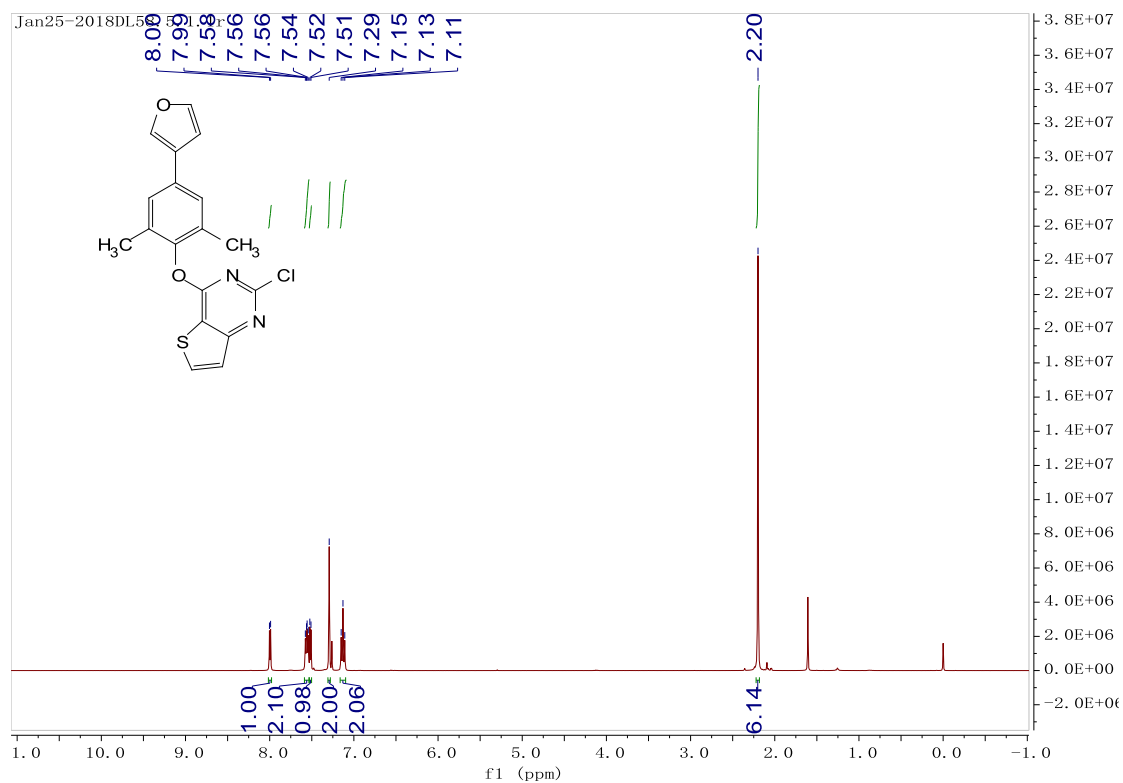
#### 8a <sup>1</sup>H NMR



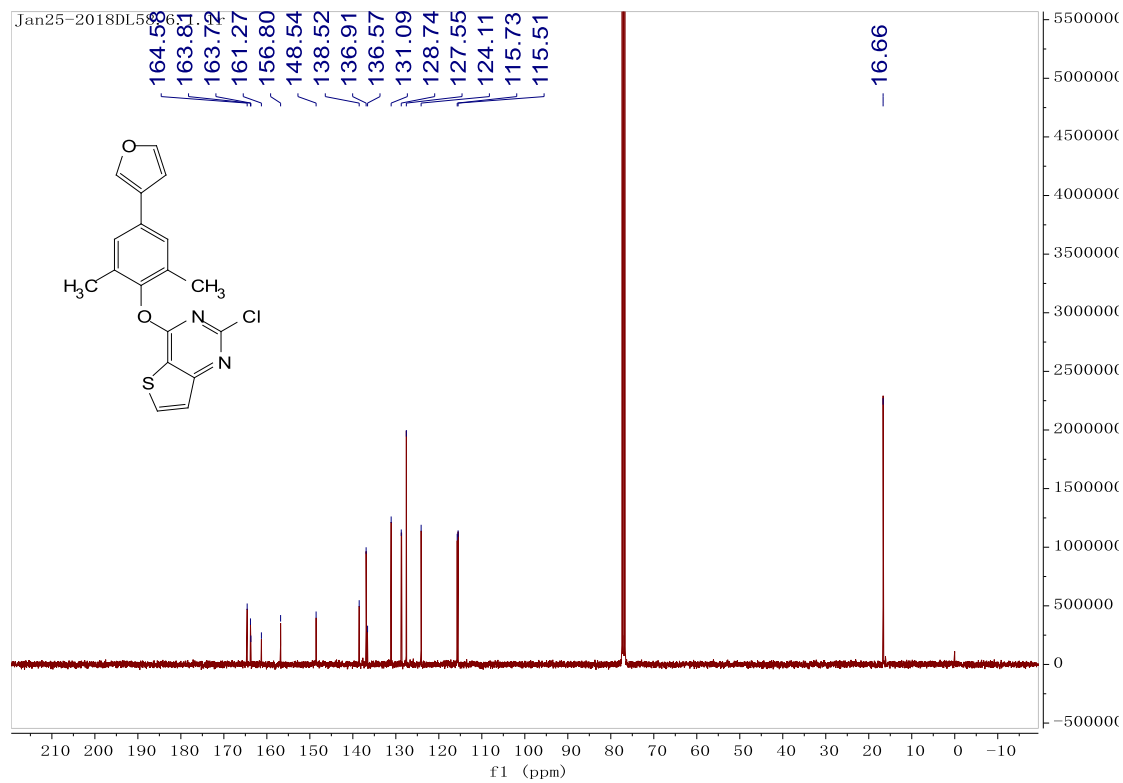
#### 8a <sup>13</sup>C NMR



### 8b <sup>1</sup>H NMR

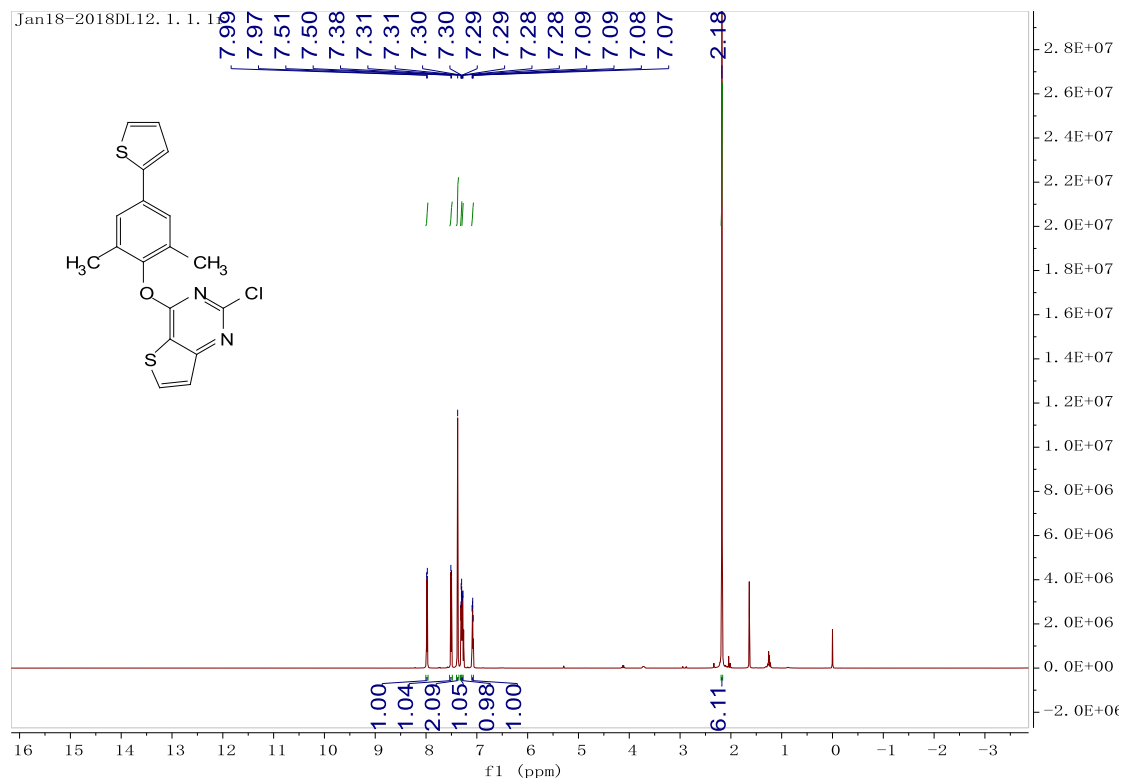


### 8b <sup>13</sup>C NMR

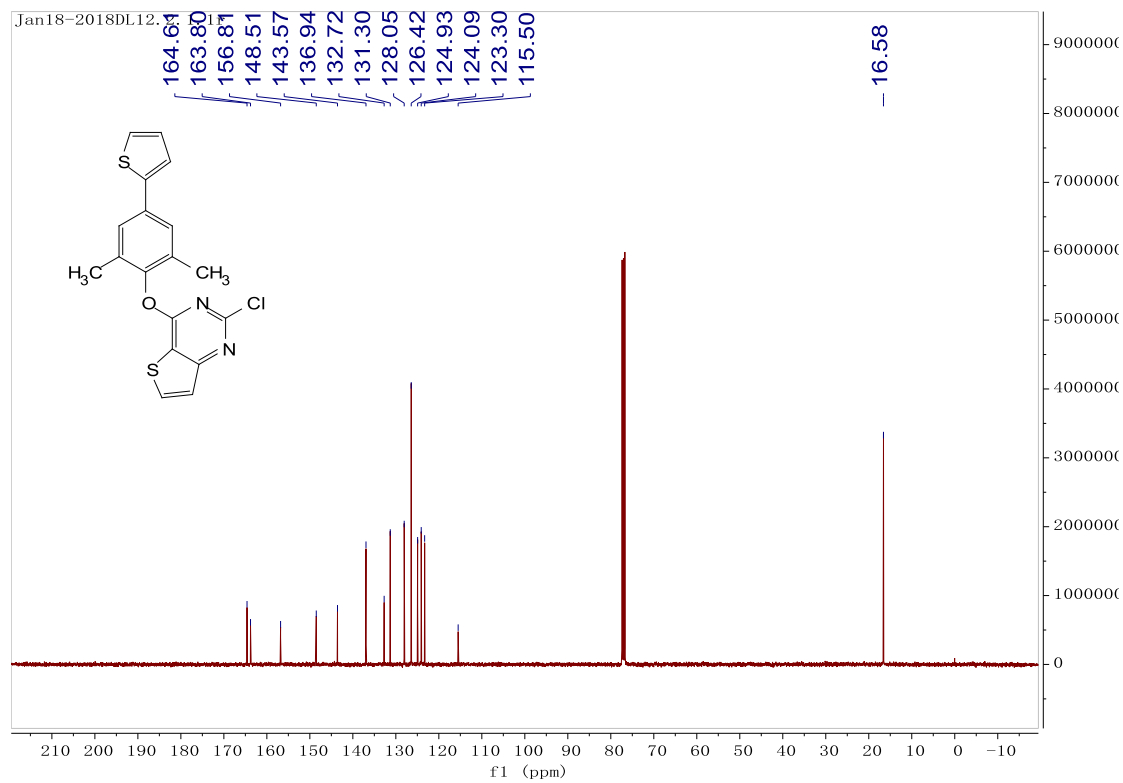




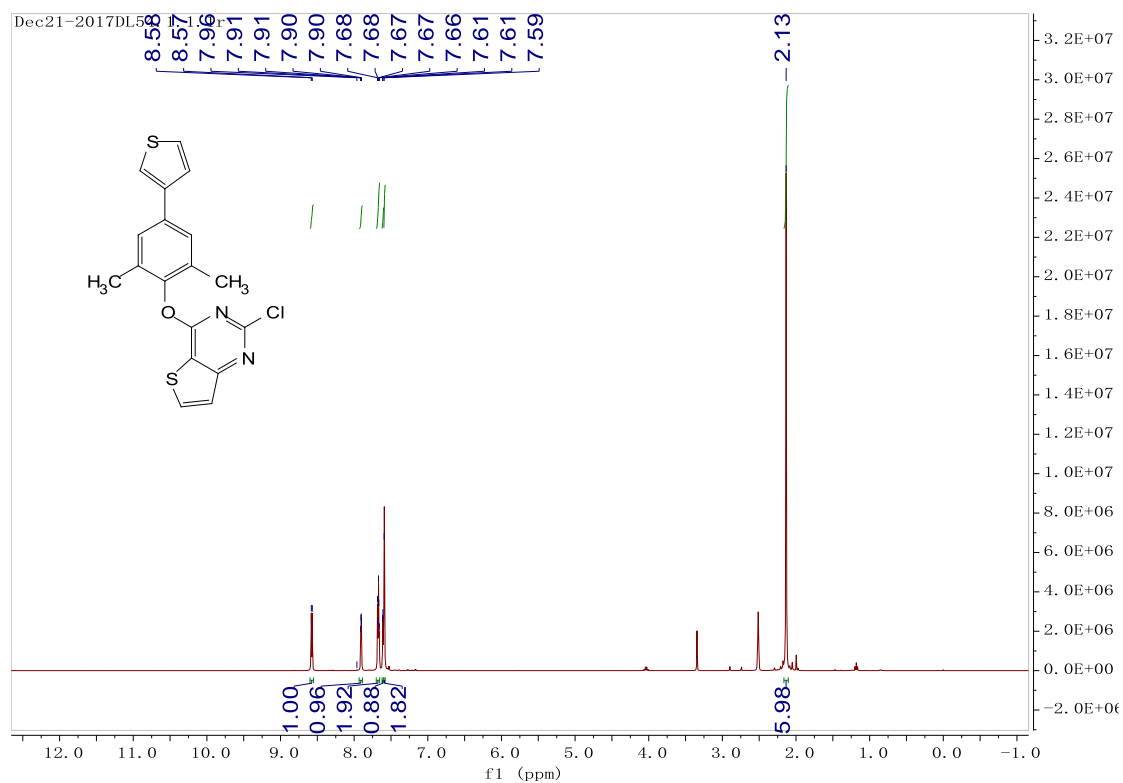
### 8c <sup>1</sup>H NMR



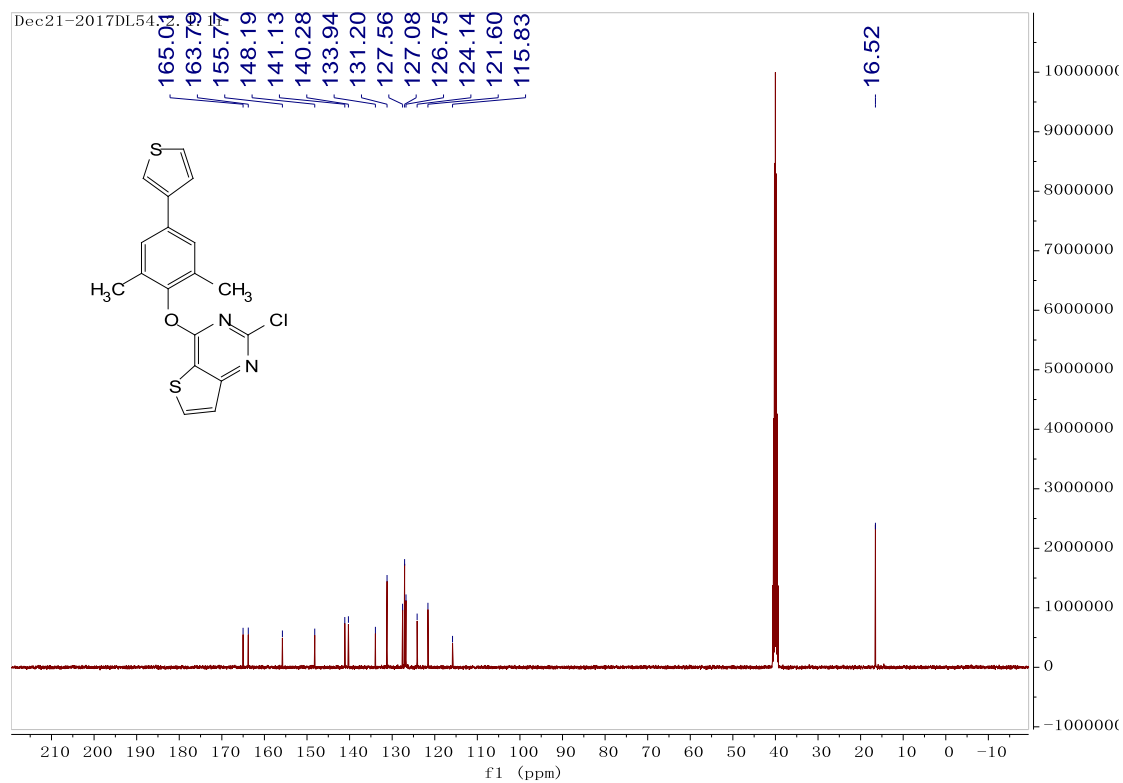
### 8c <sup>13</sup>C NMR



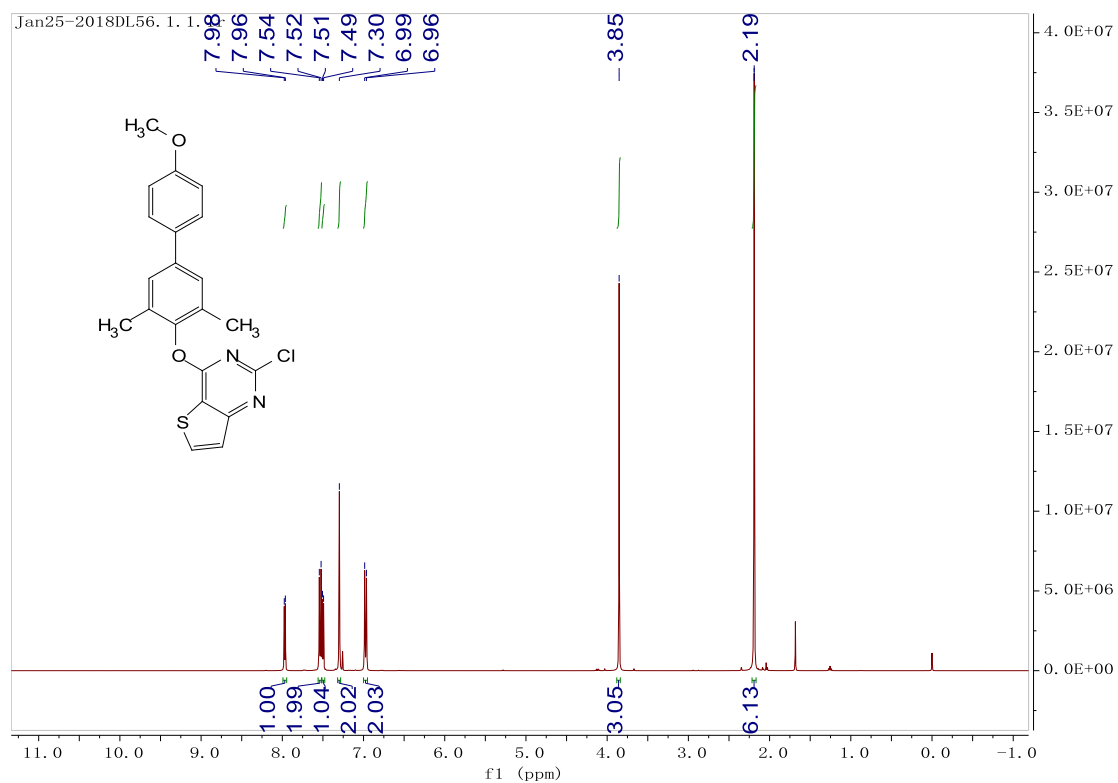
### 8d <sup>1</sup>H NMR



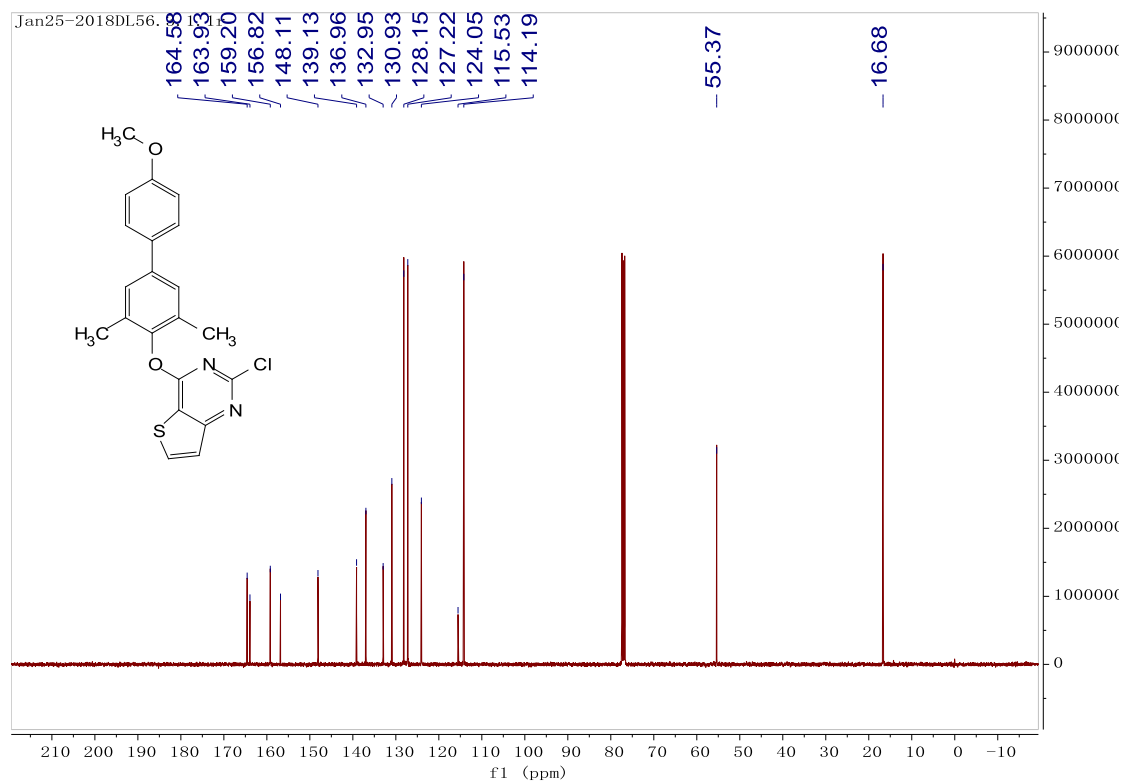
### 8d <sup>13</sup>C NMR



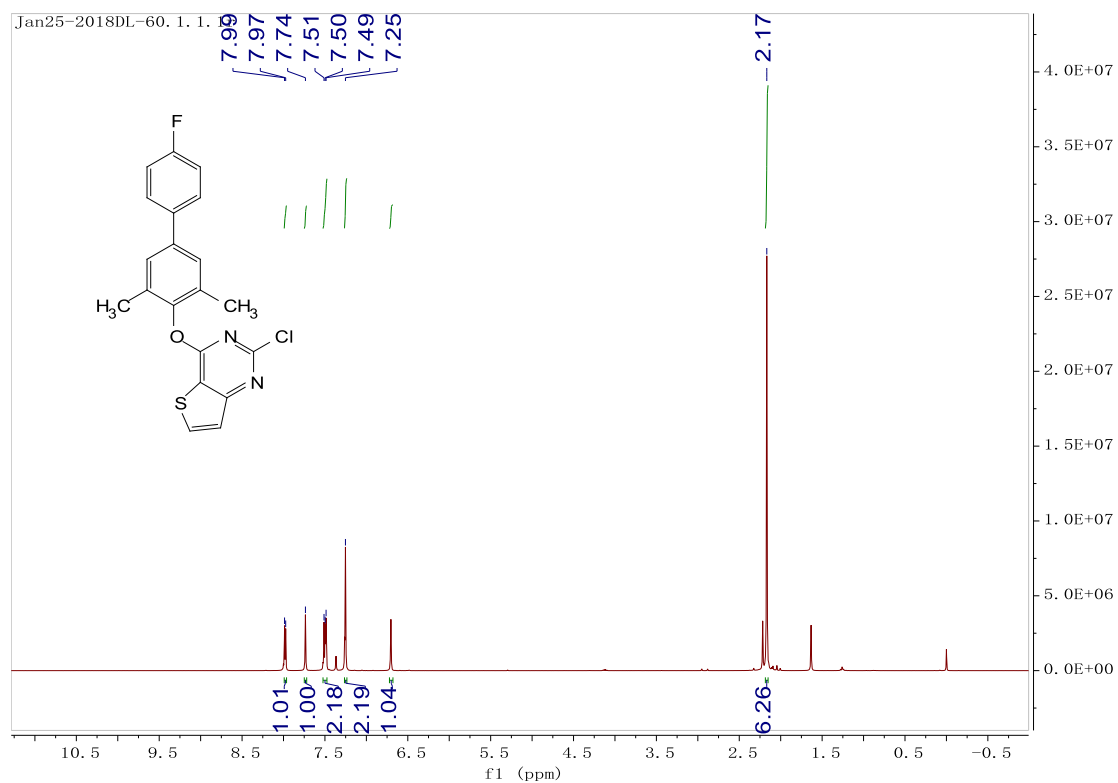
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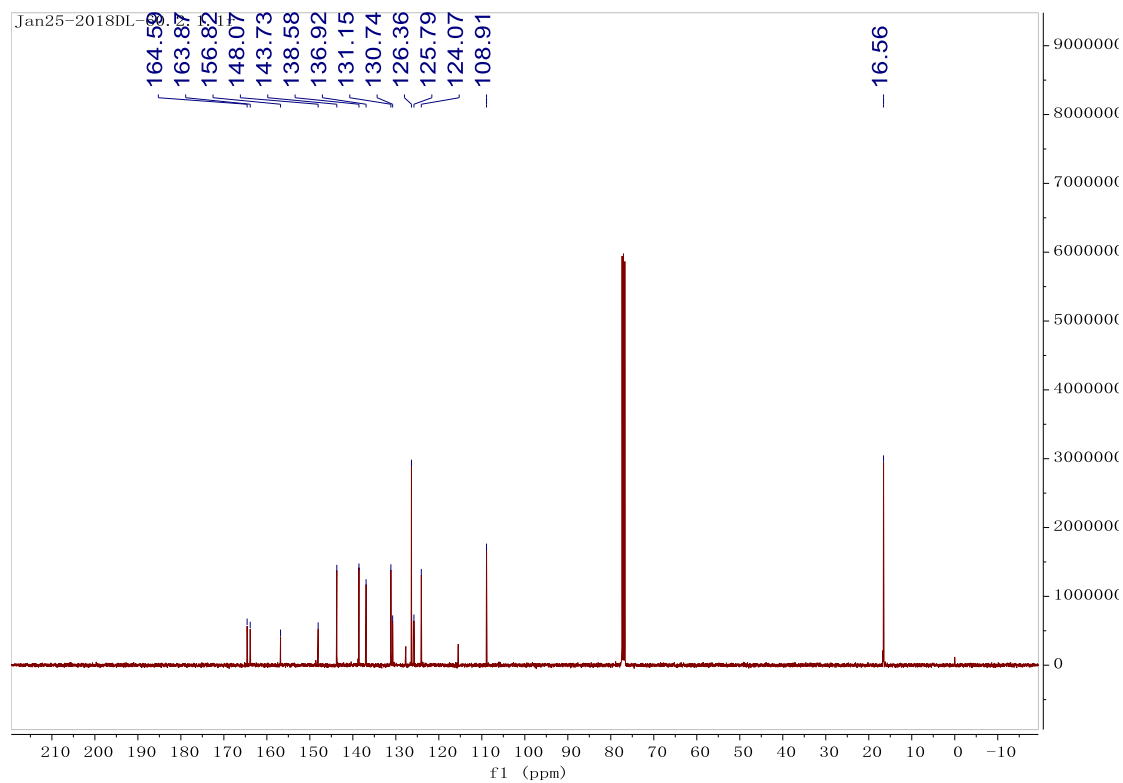
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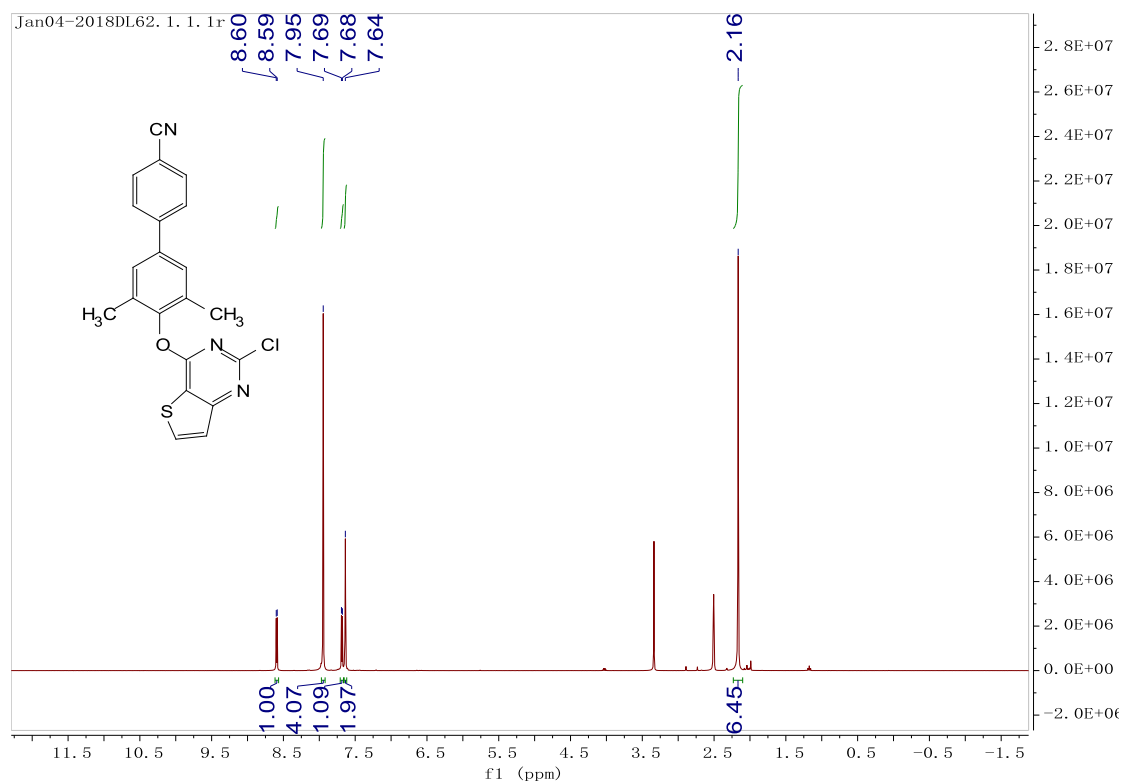
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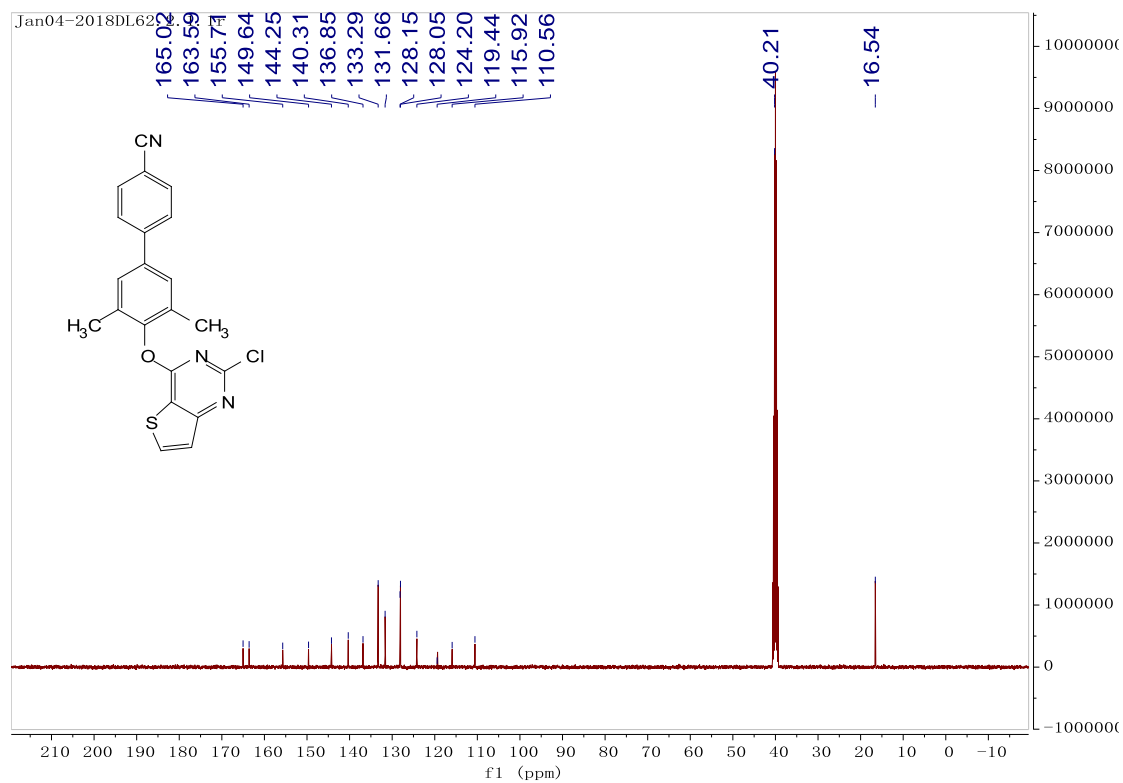
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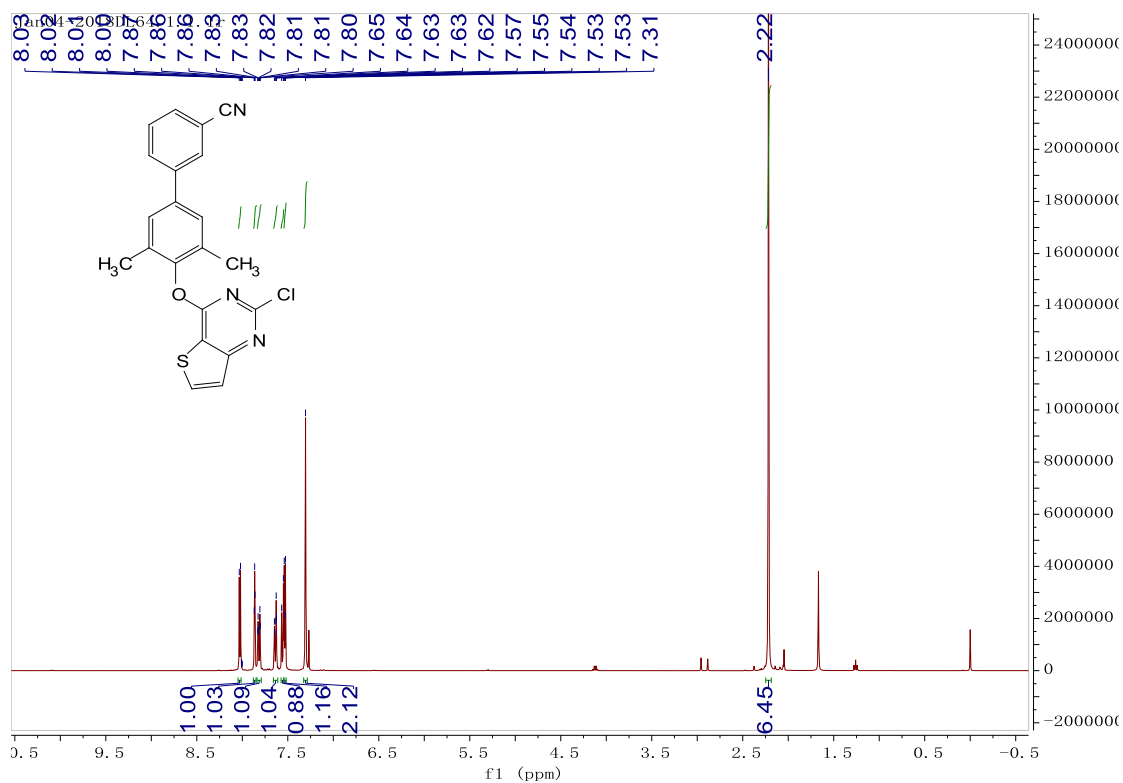
### 8h <sup>1</sup>H NMR



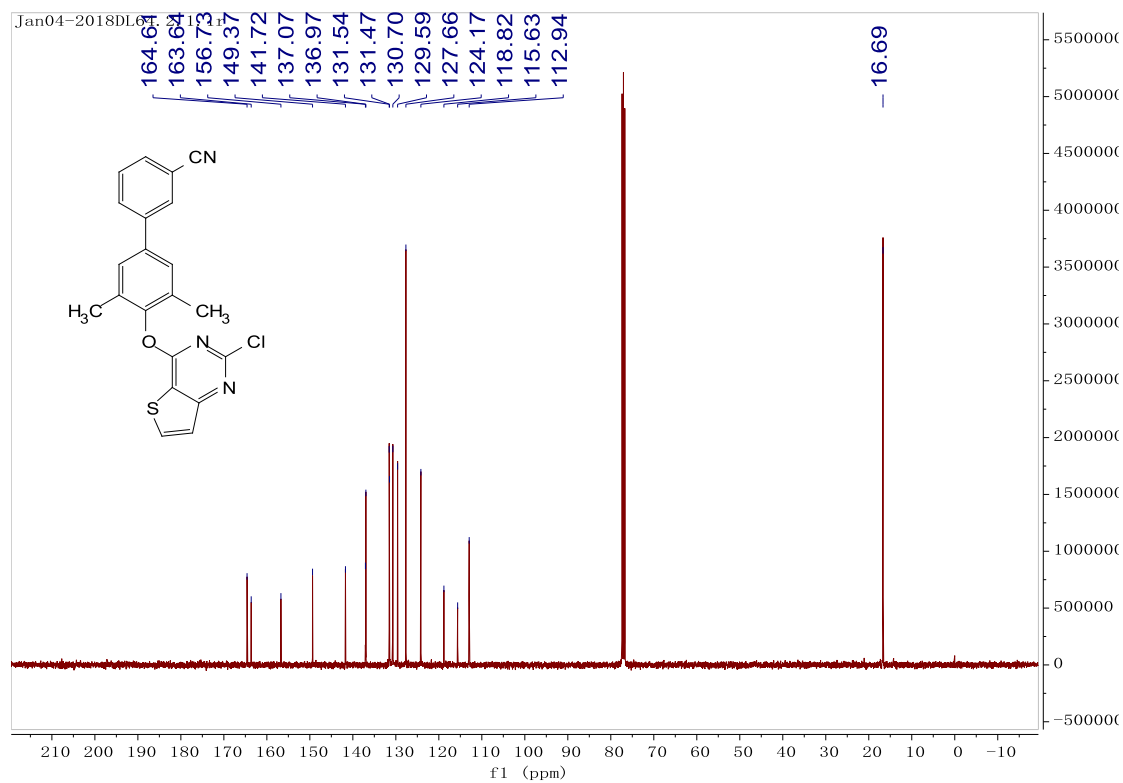
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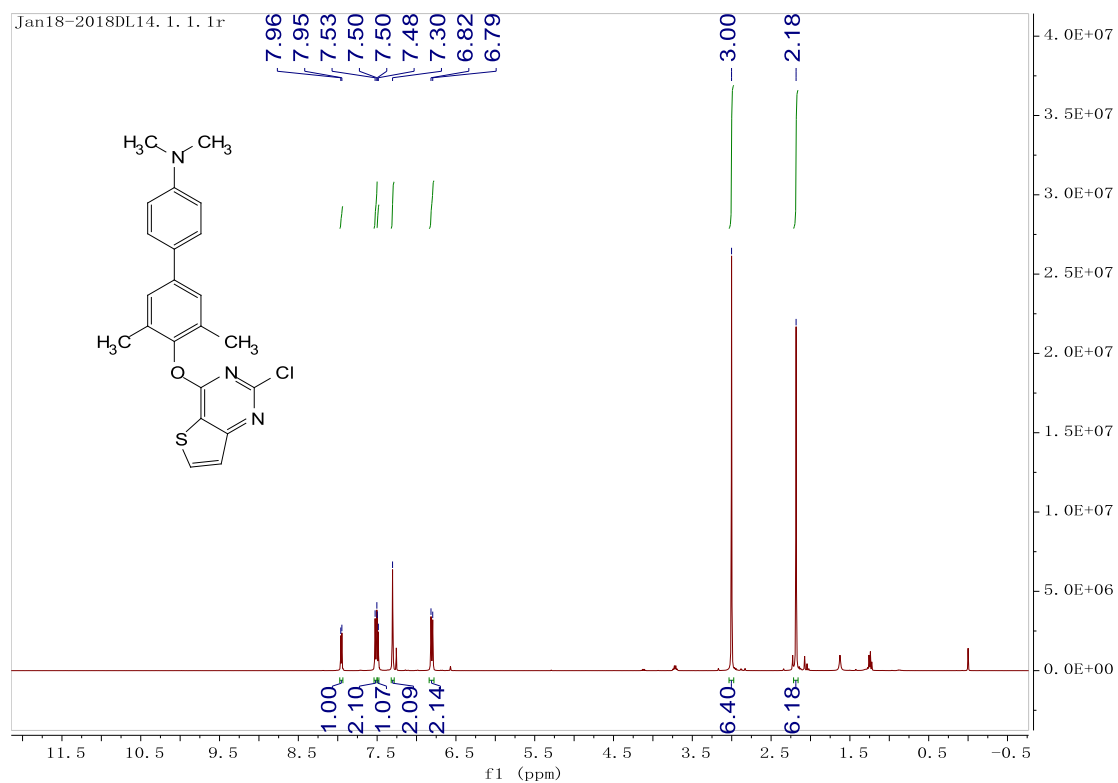
### 8i <sup>1</sup>H NMR



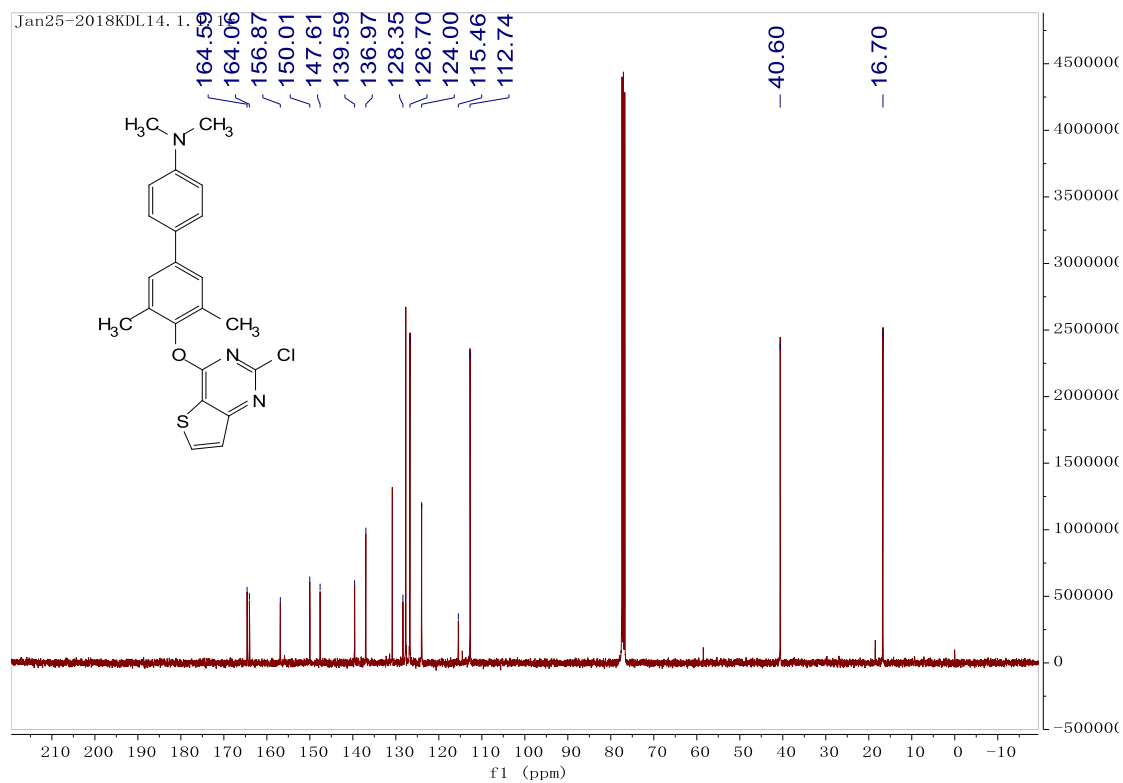
### 8i <sup>13</sup>C NMR



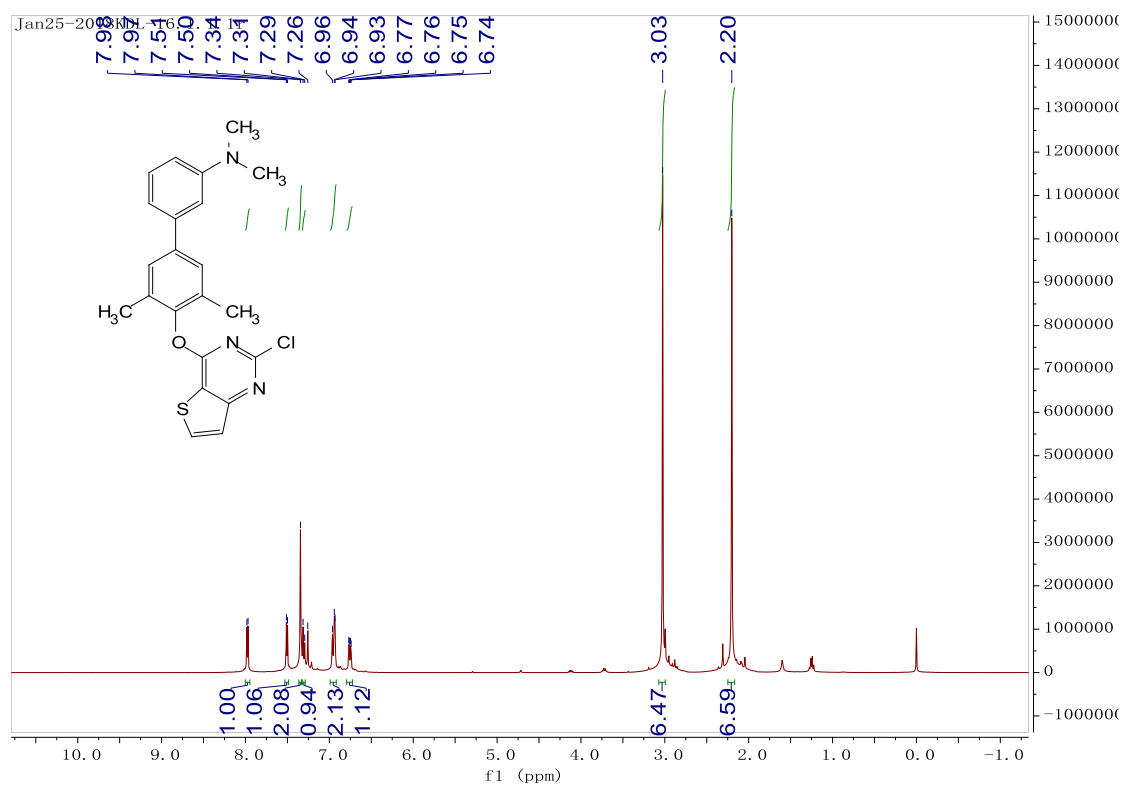
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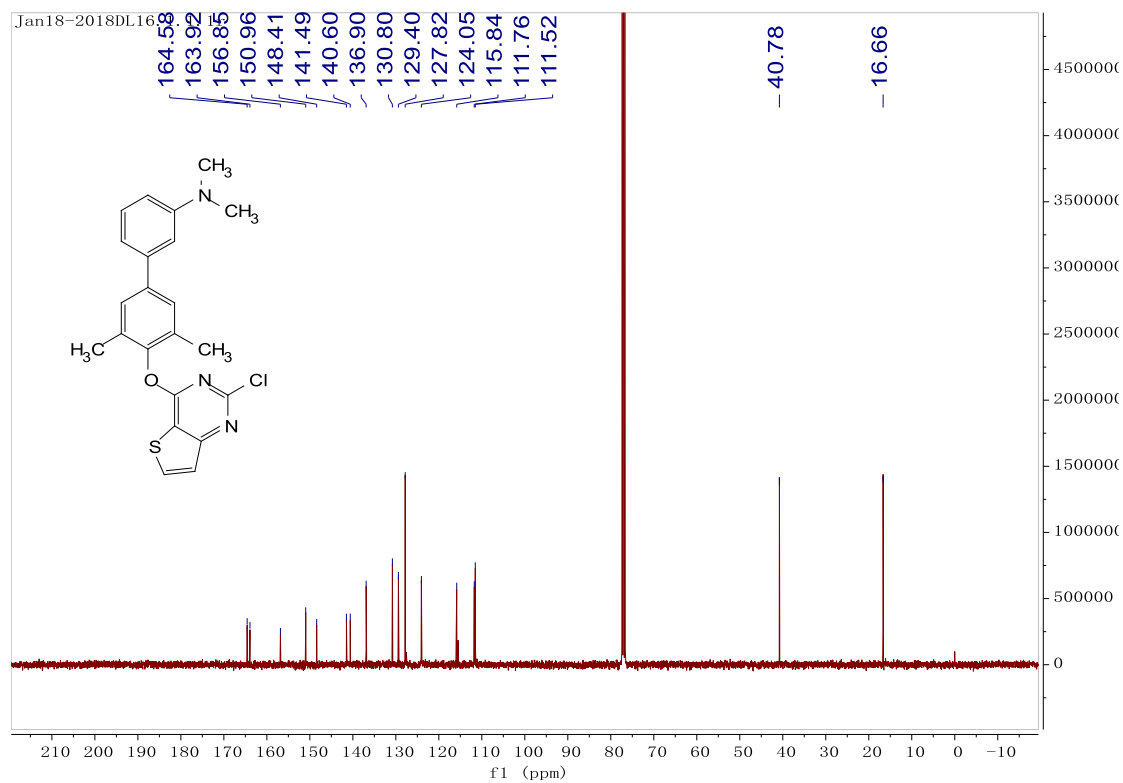
# 8j <sup>13</sup>C NMR



### 8k <sup>1</sup>H NMR

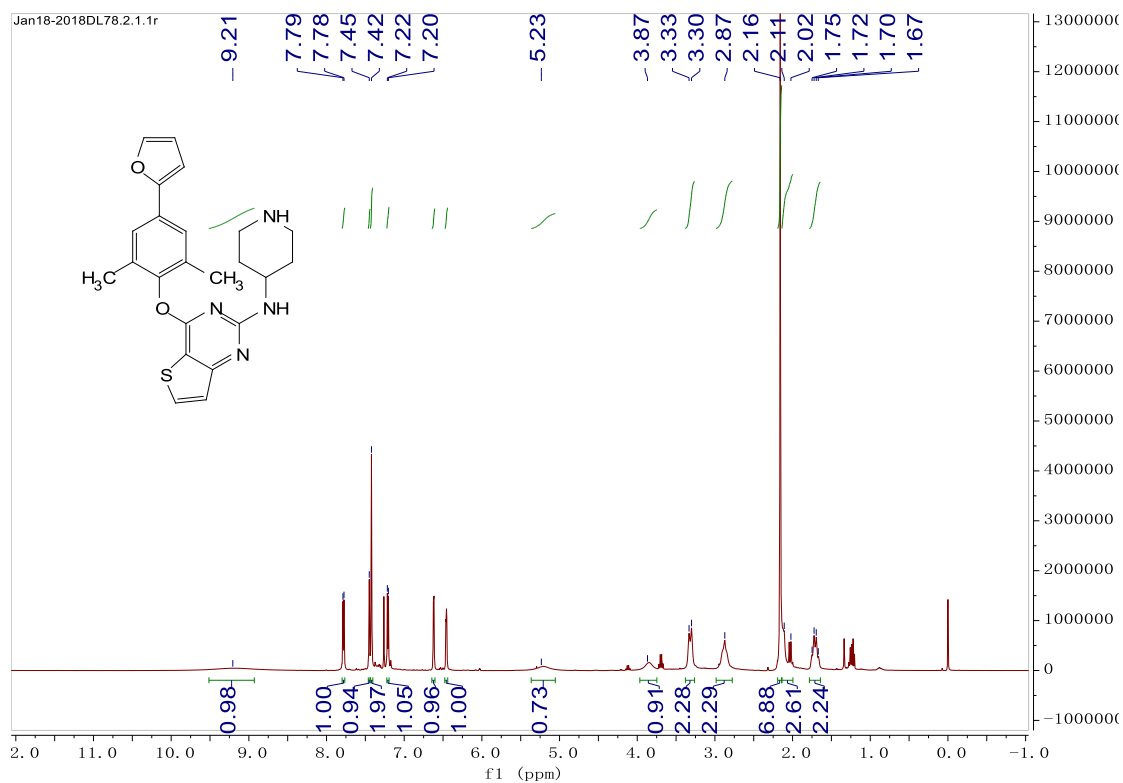


### 8k <sup>13</sup>C NMR

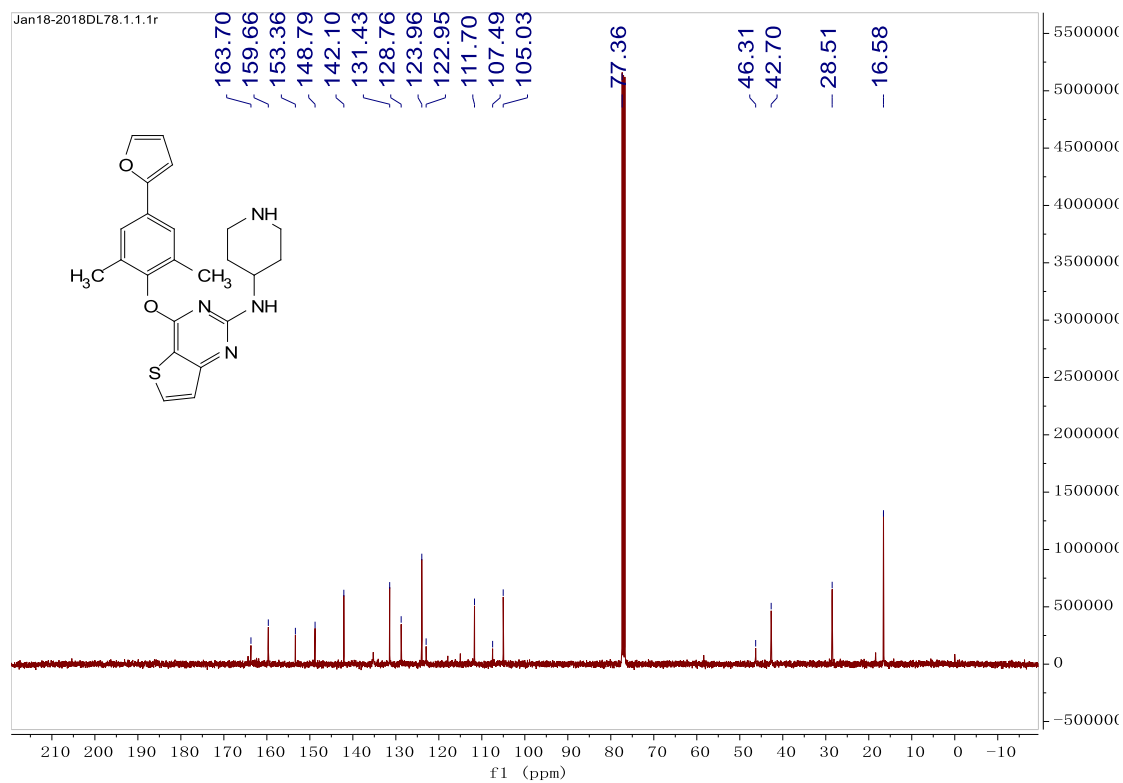




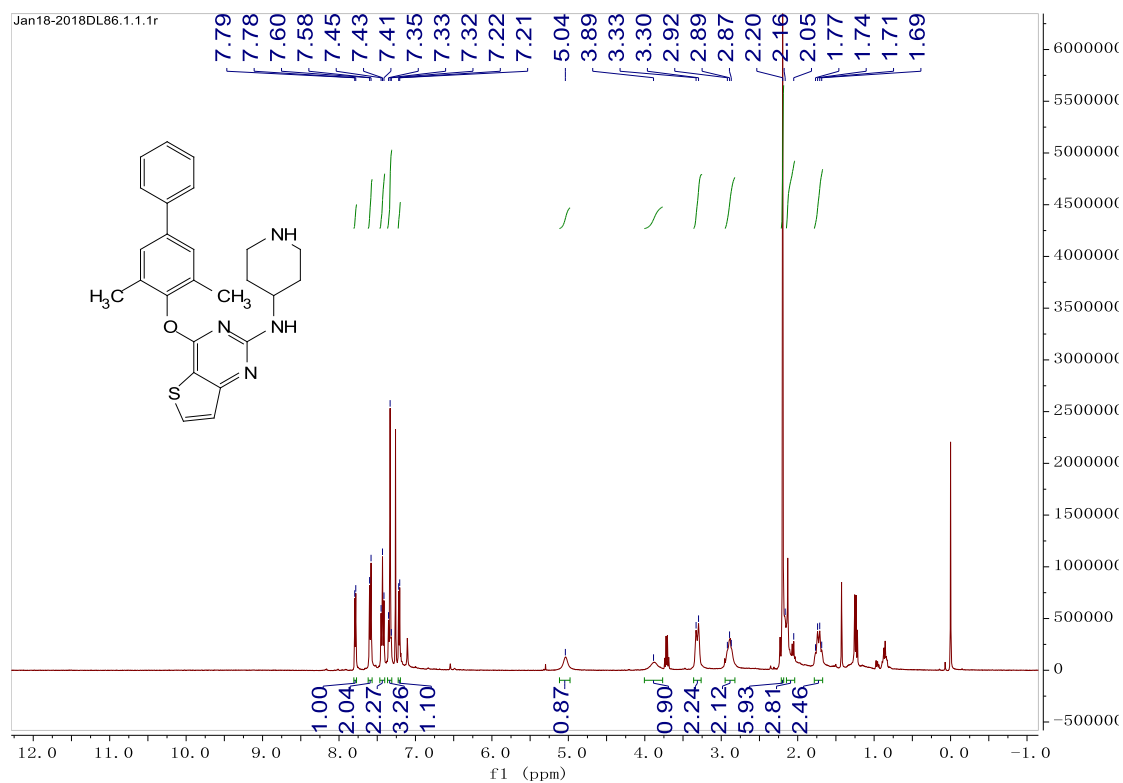
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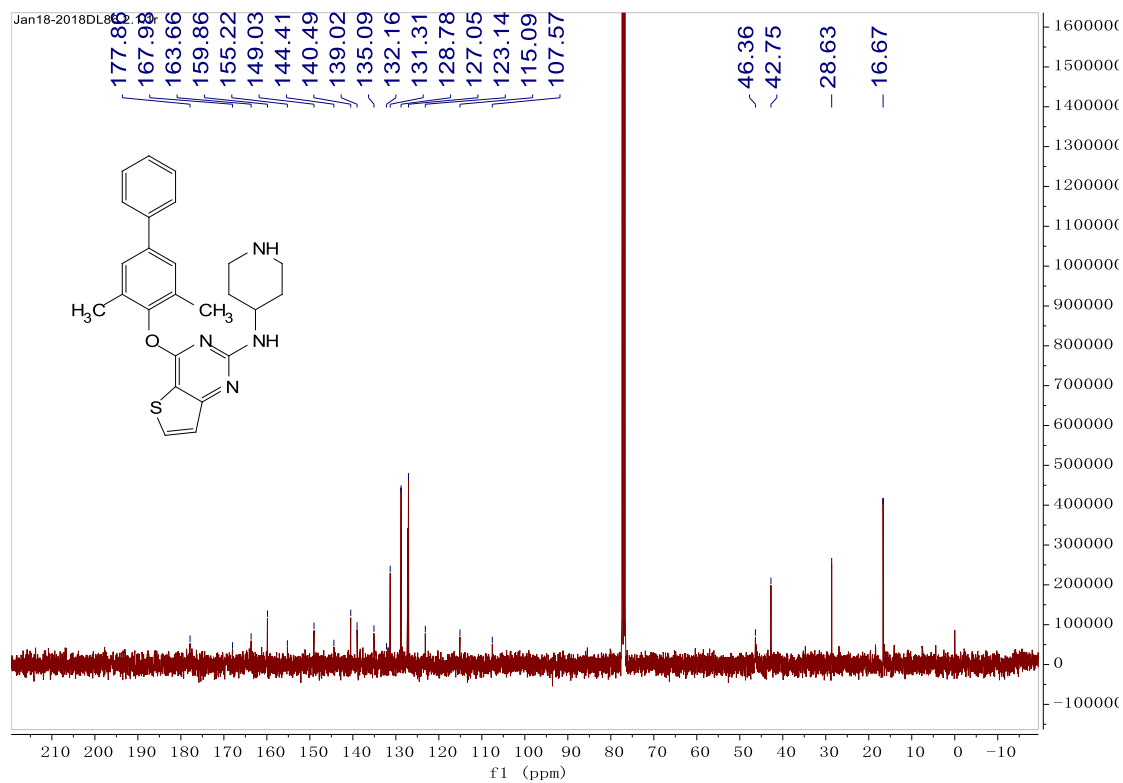
### 10a <sup>13</sup>C NMR



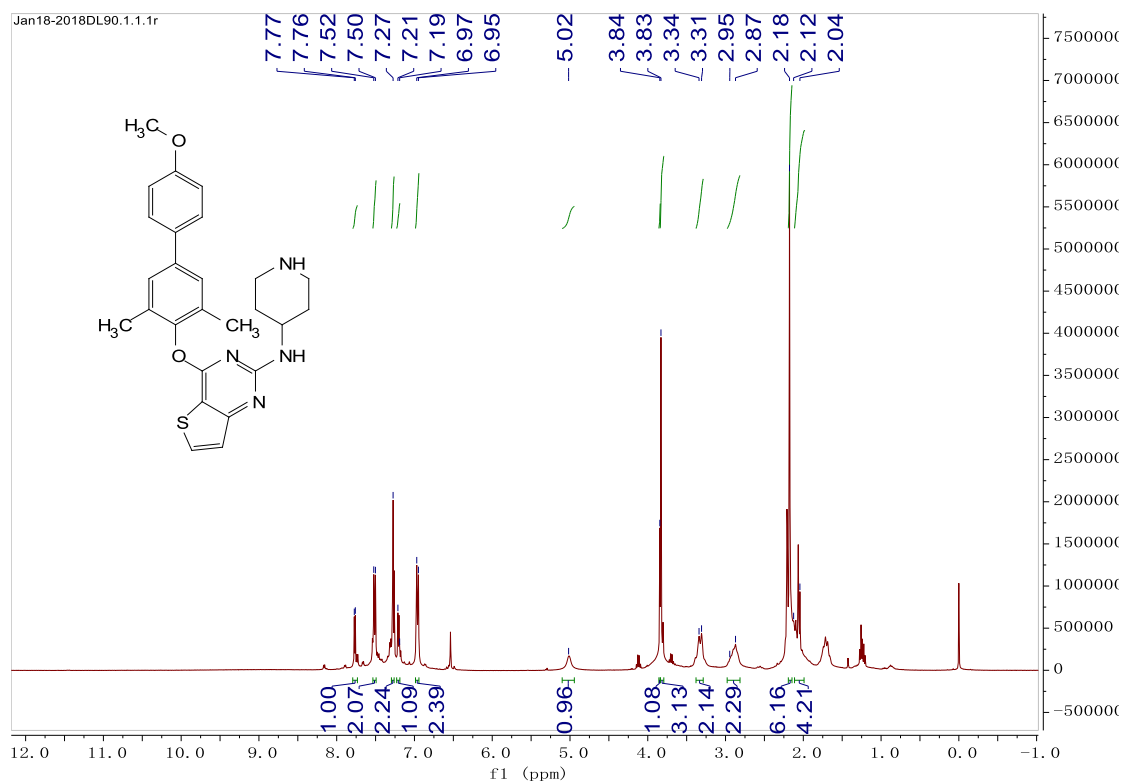
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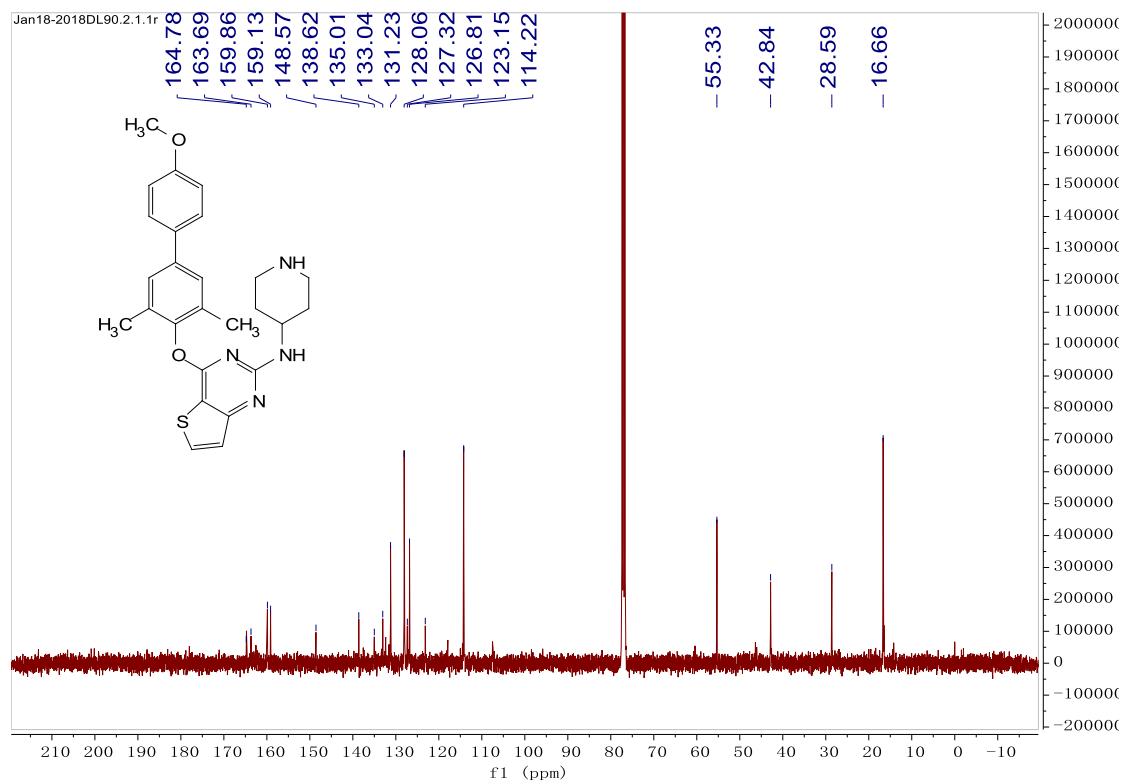
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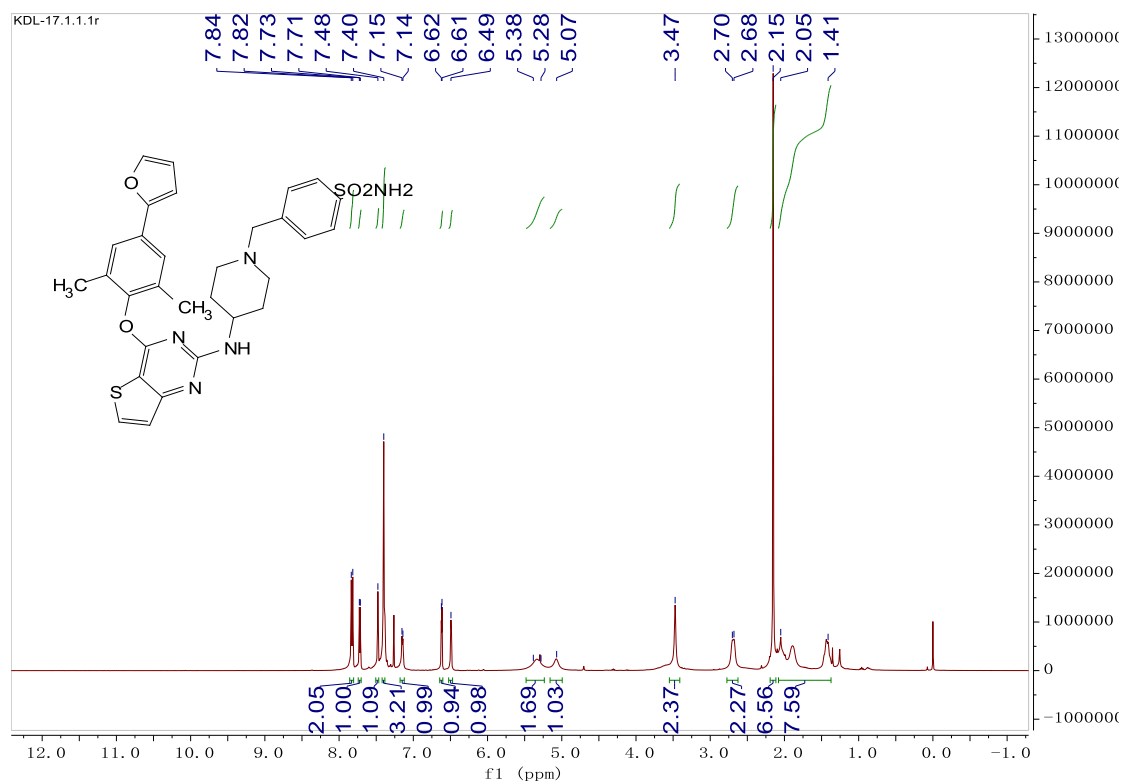
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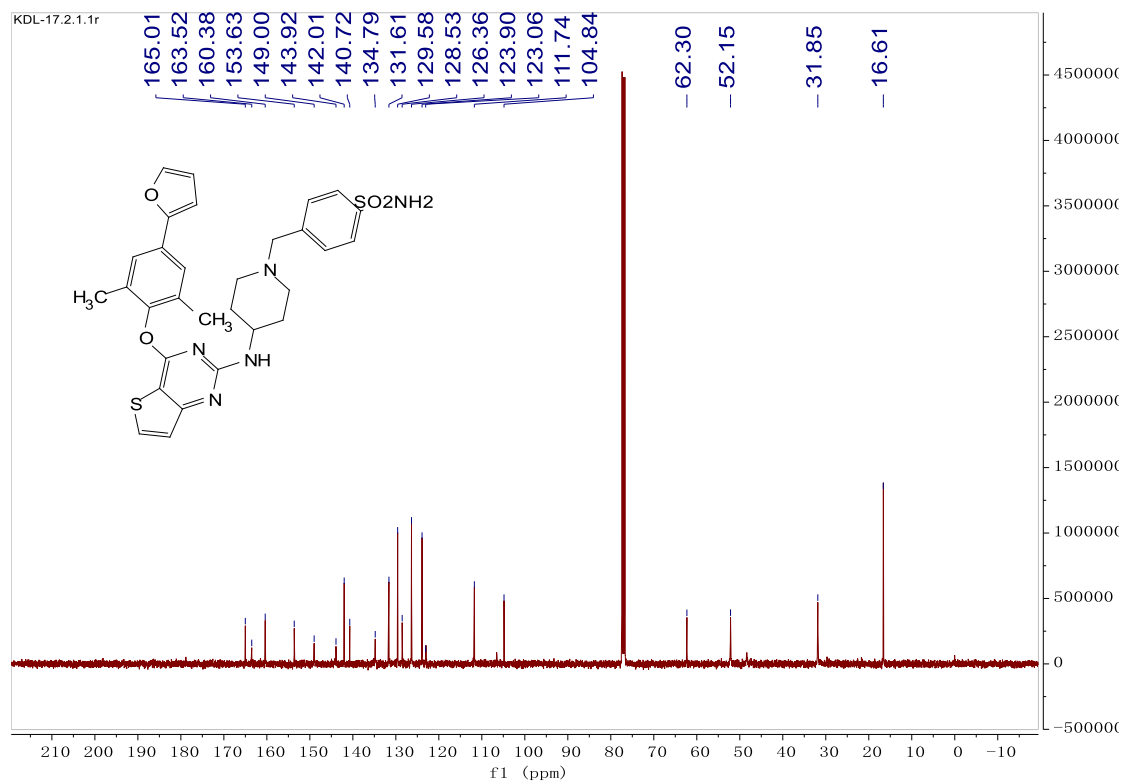
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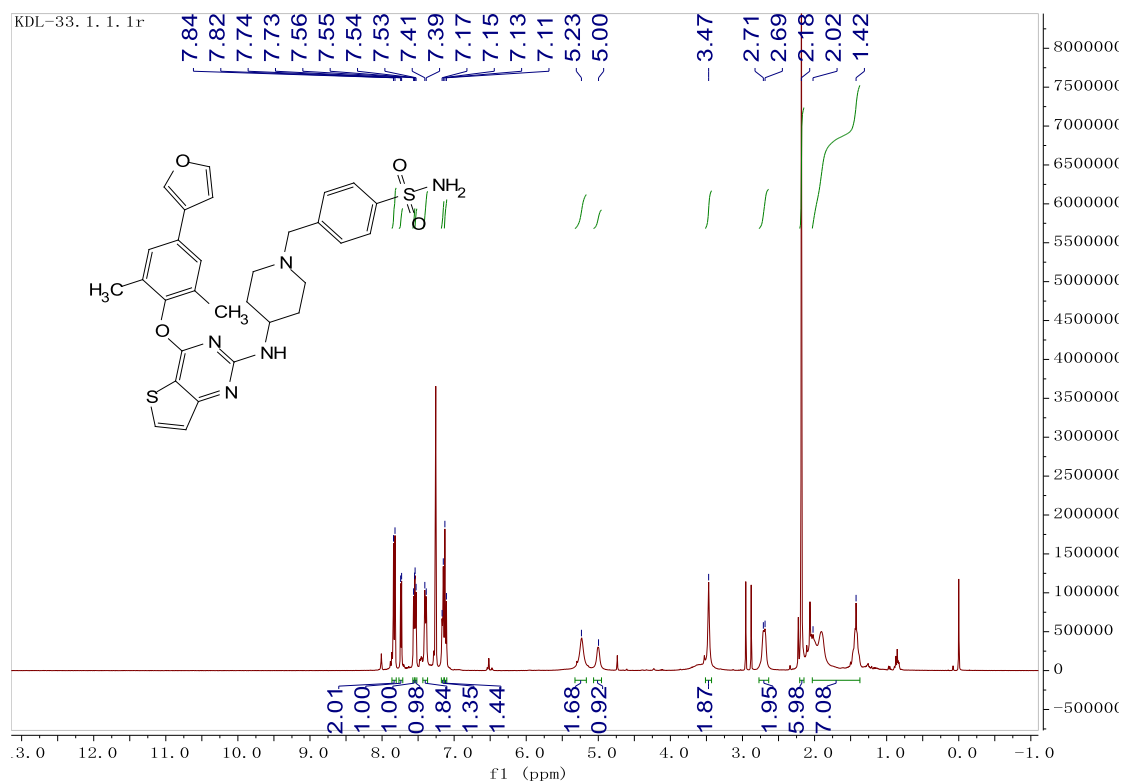
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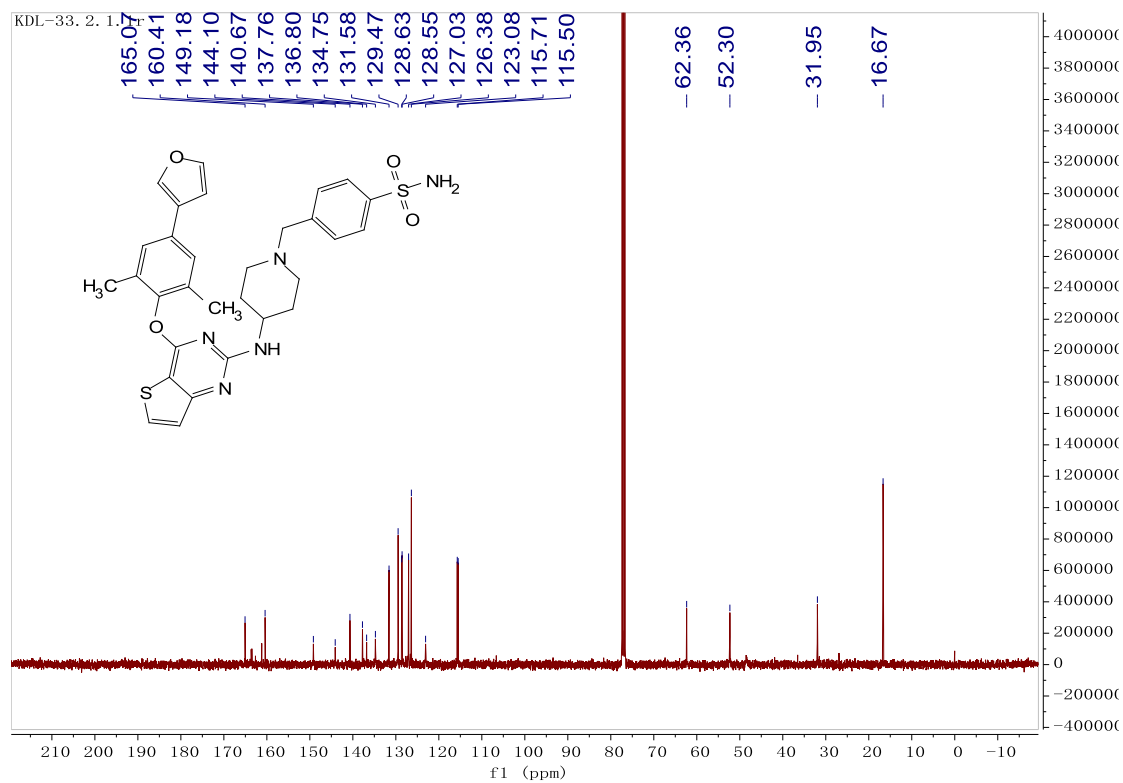
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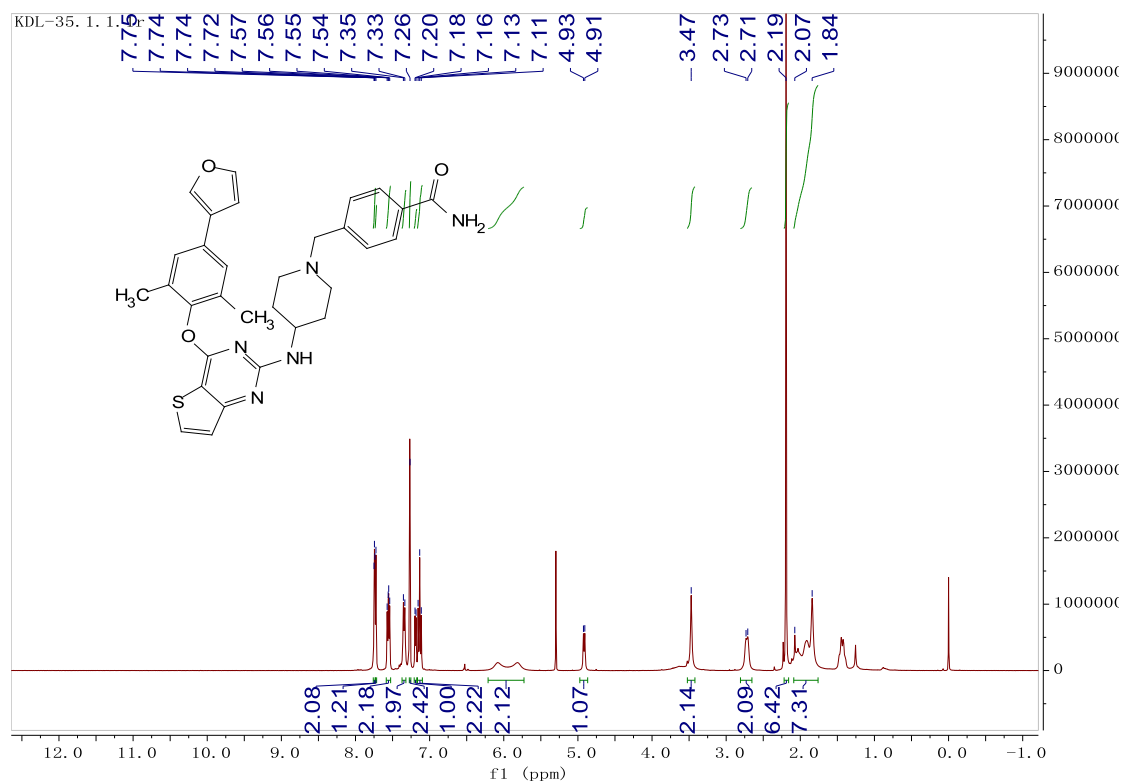
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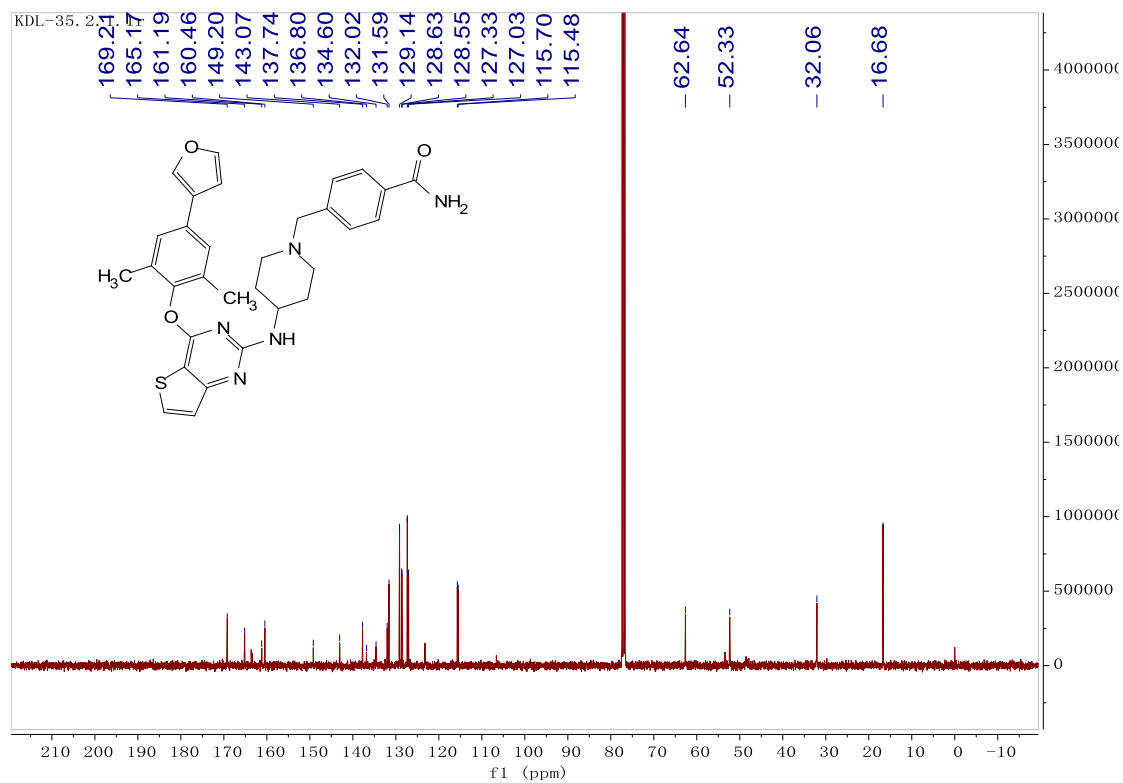
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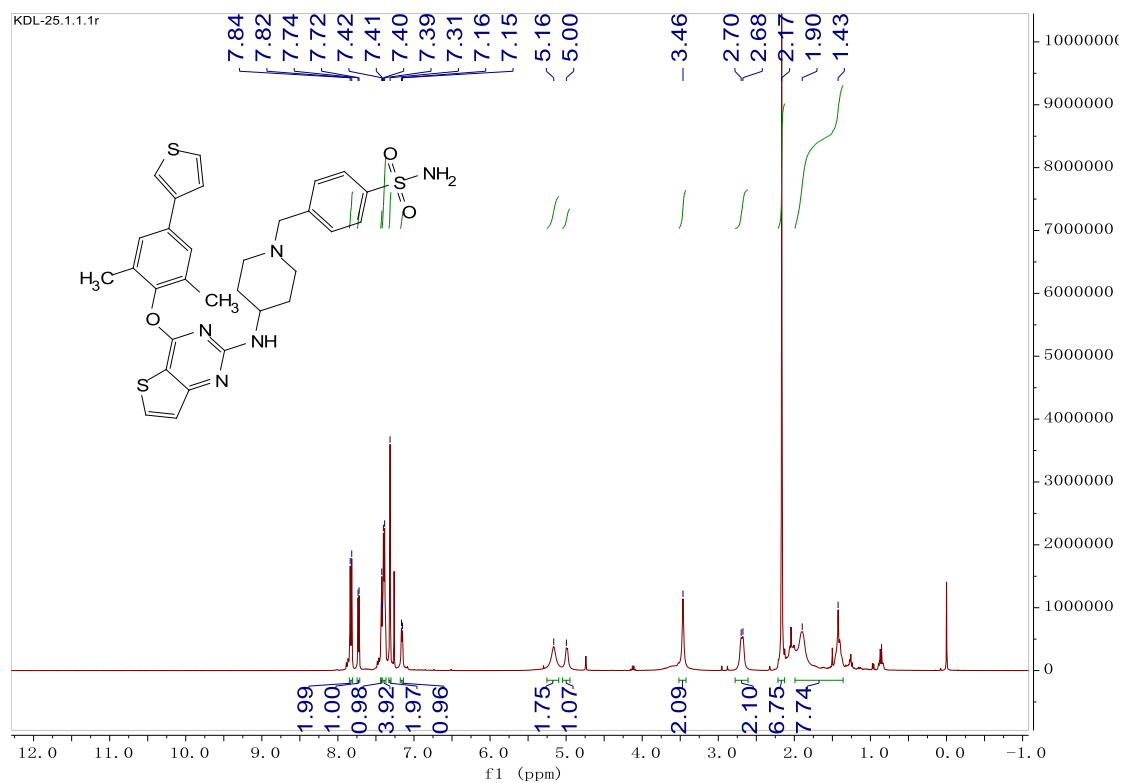
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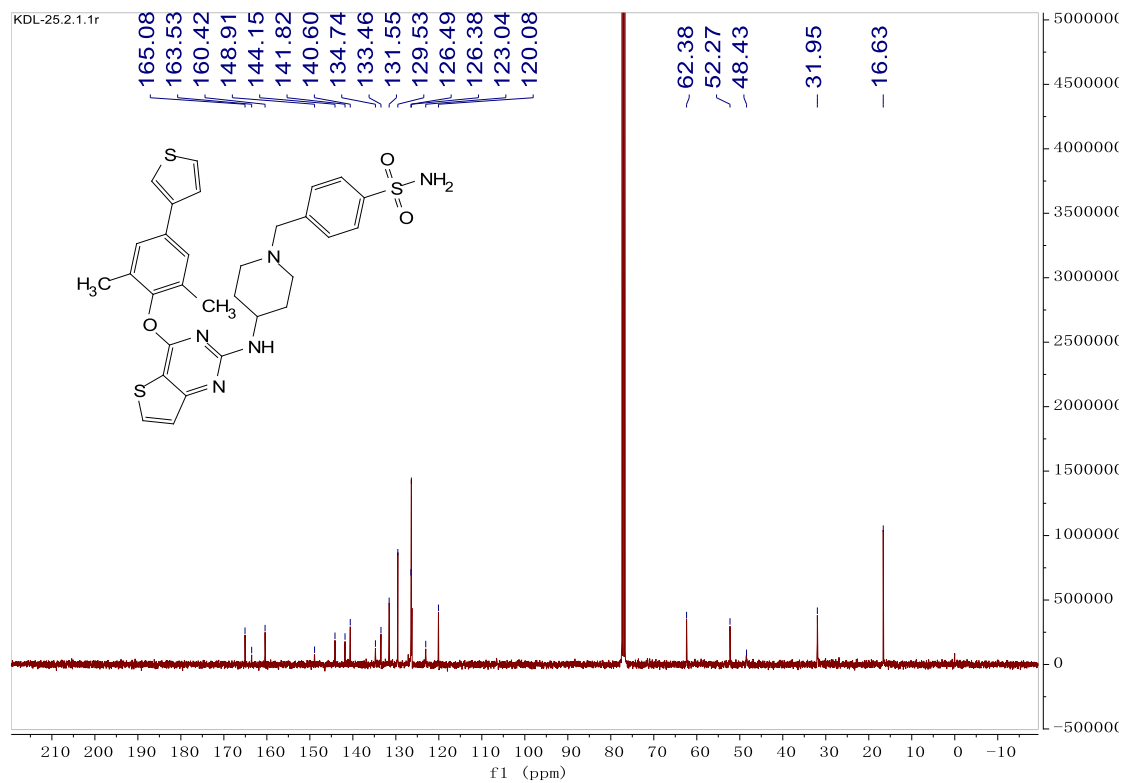
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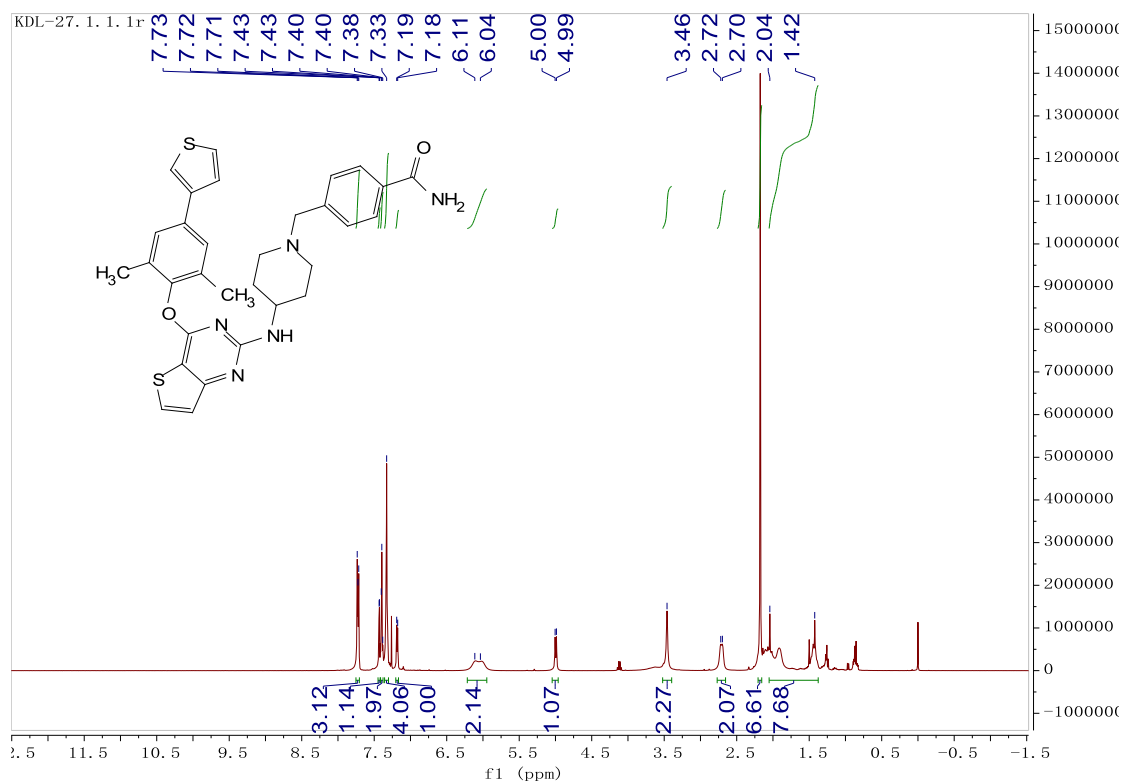
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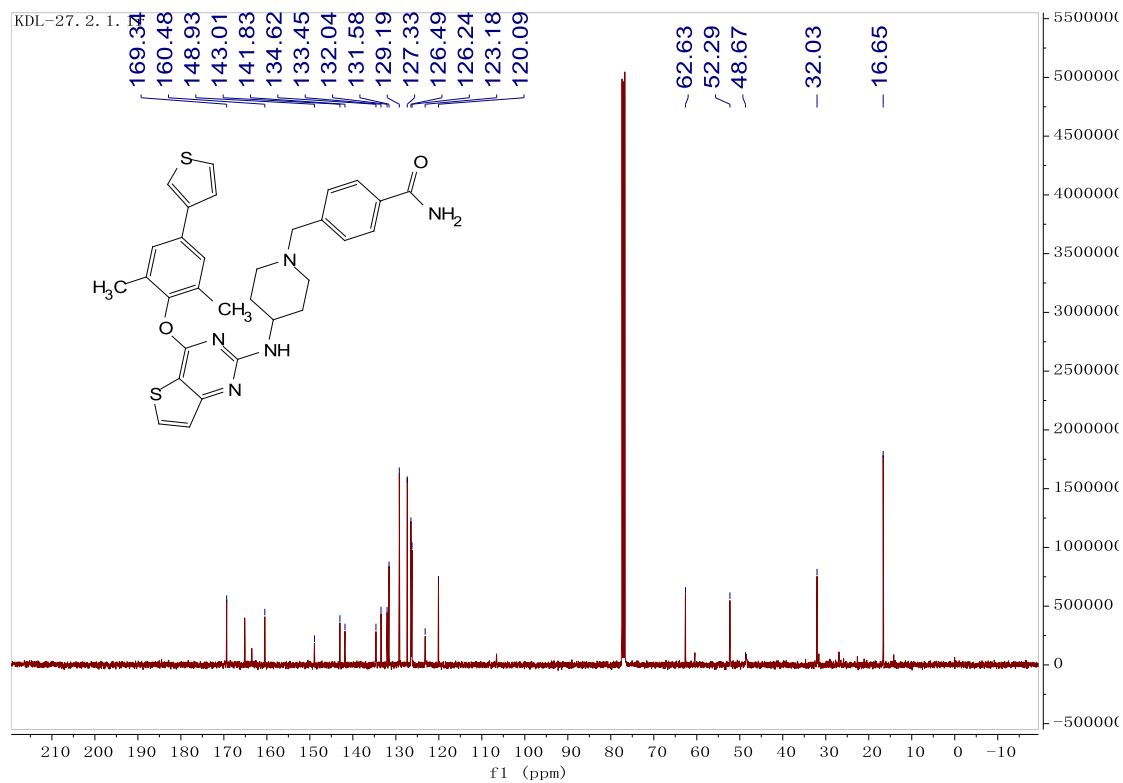
# 17 <sup>13</sup>C NMR



# 18 <sup>1</sup>H NMR

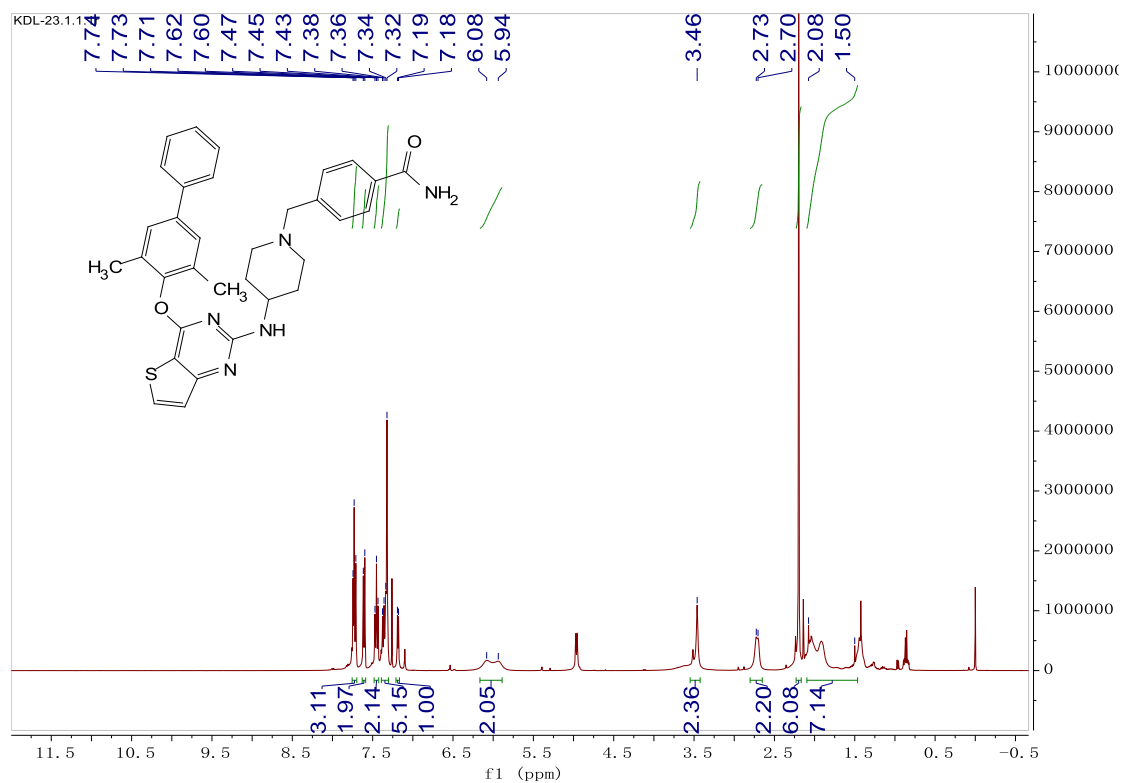


# 18 <sup>13</sup>C NMR

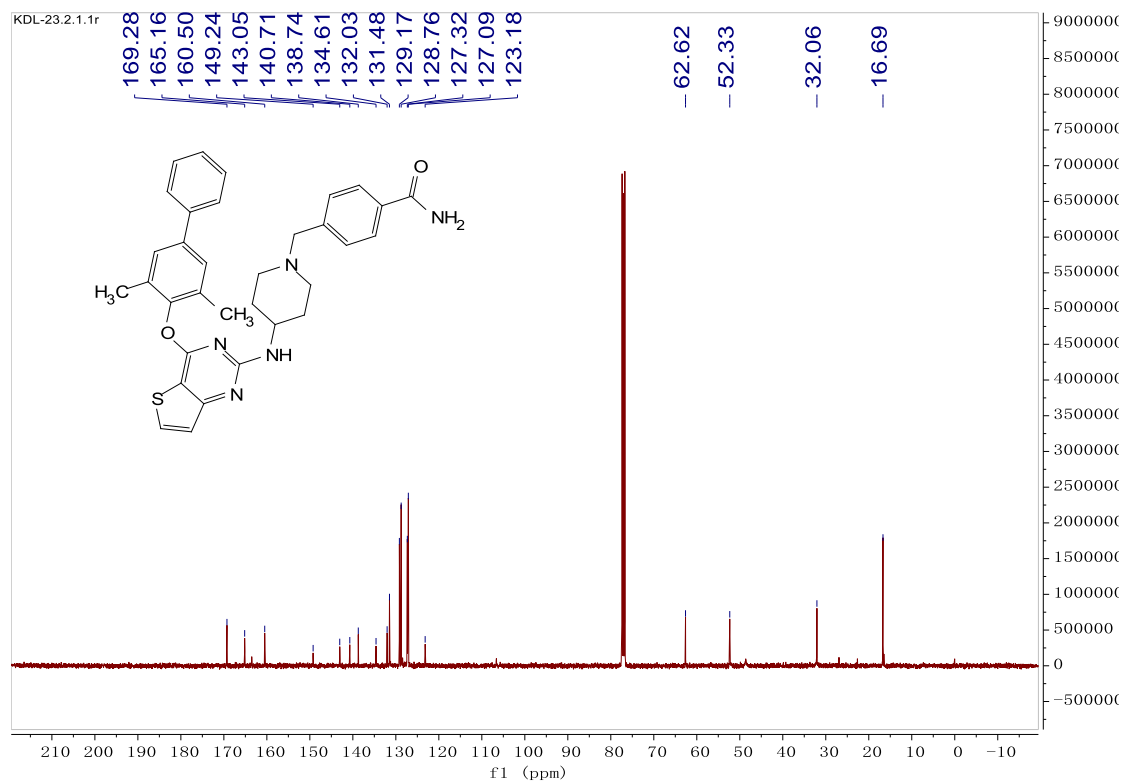




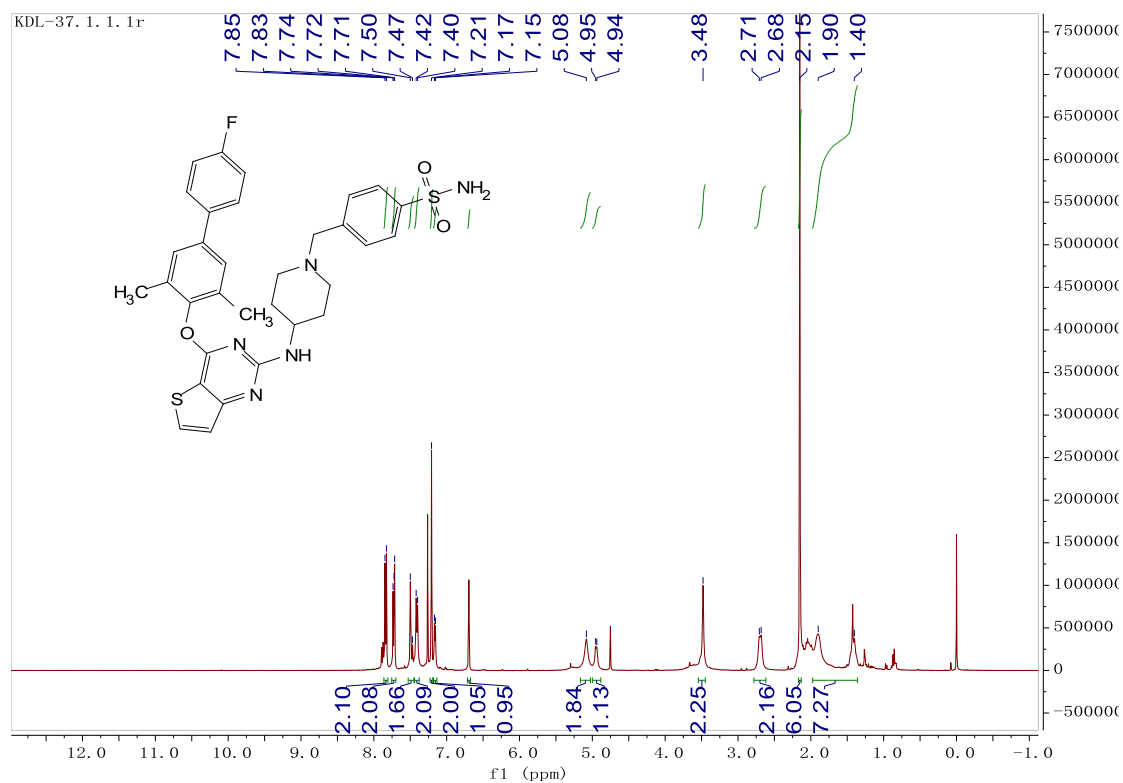
## 20 $^1\text{H}$ NMR



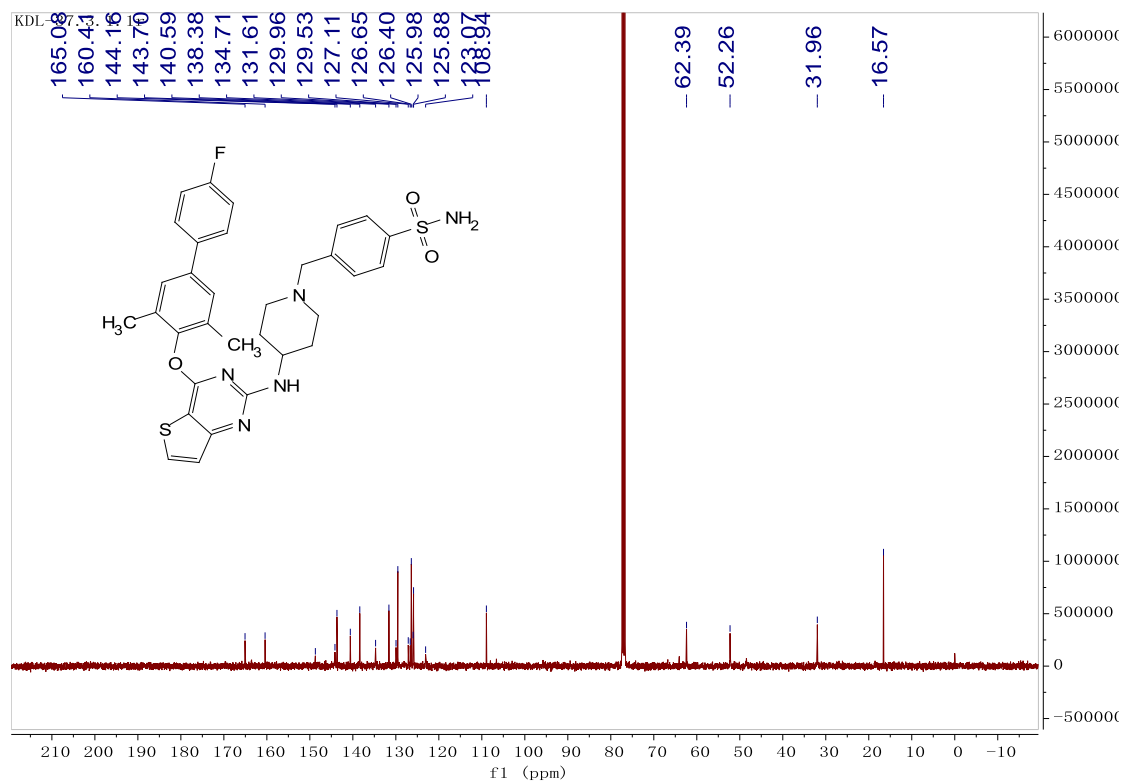
## 20 $^{13}\text{C}$ NMR



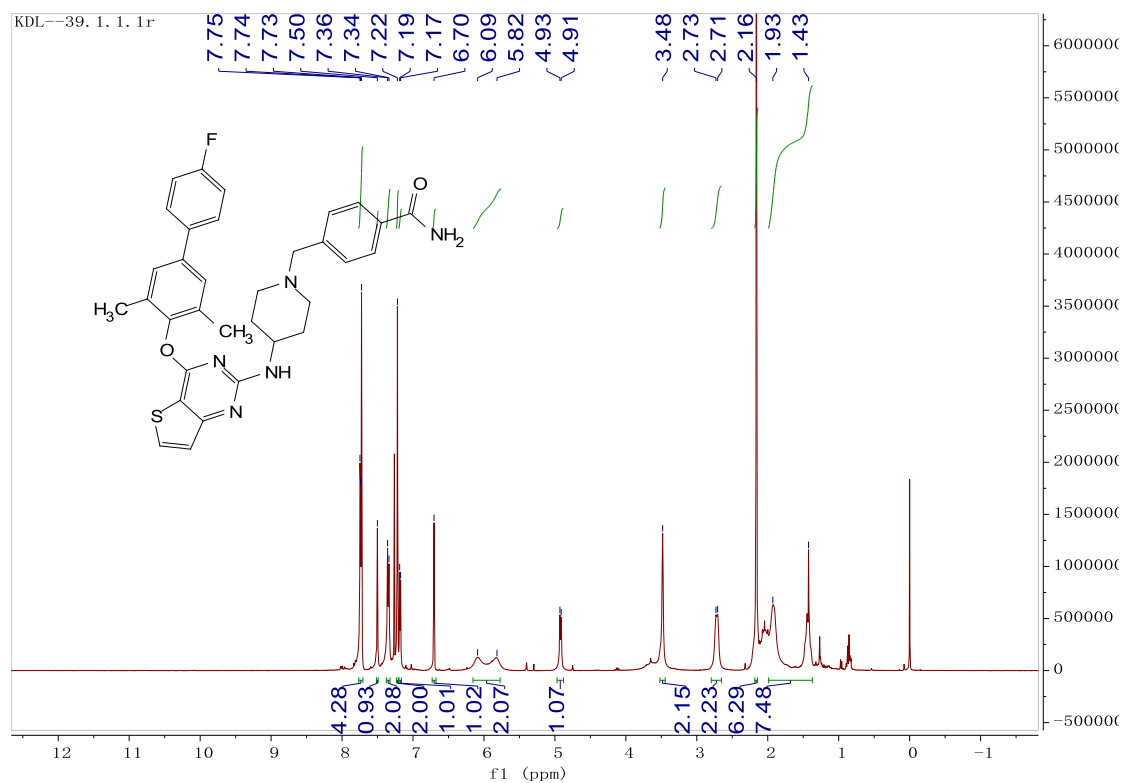
## 23 <sup>1</sup>H NMR



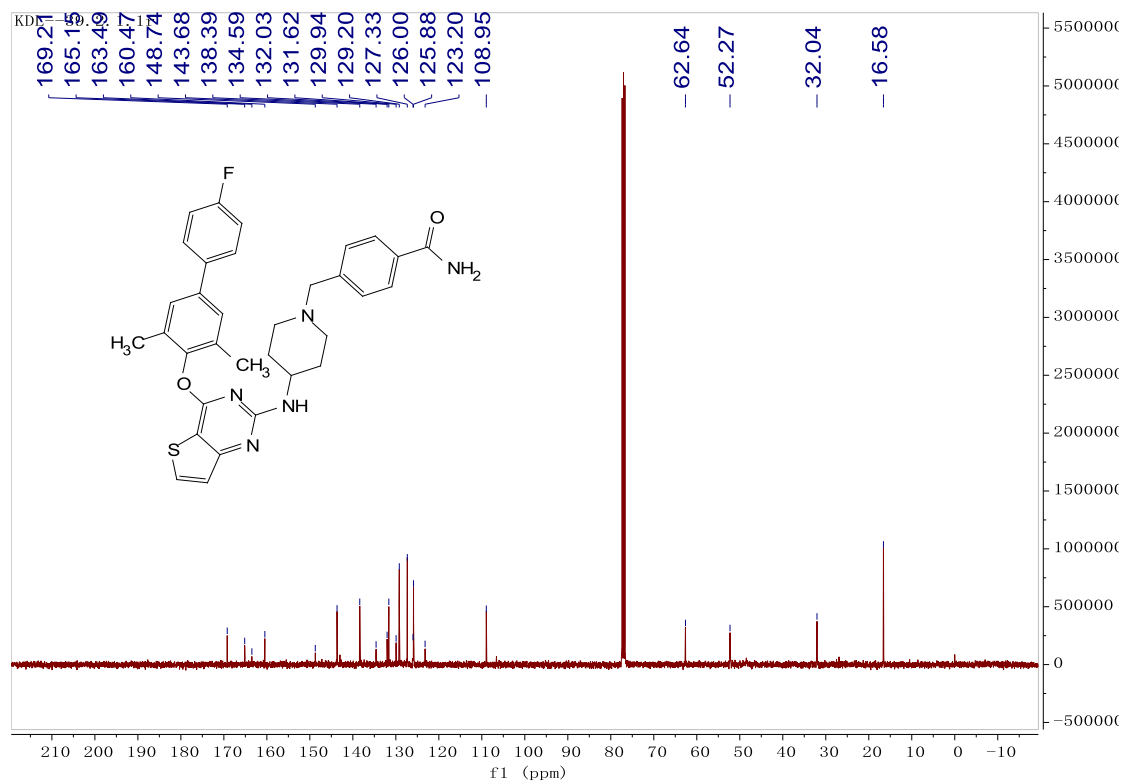
## 23 <sup>13</sup>C NMR



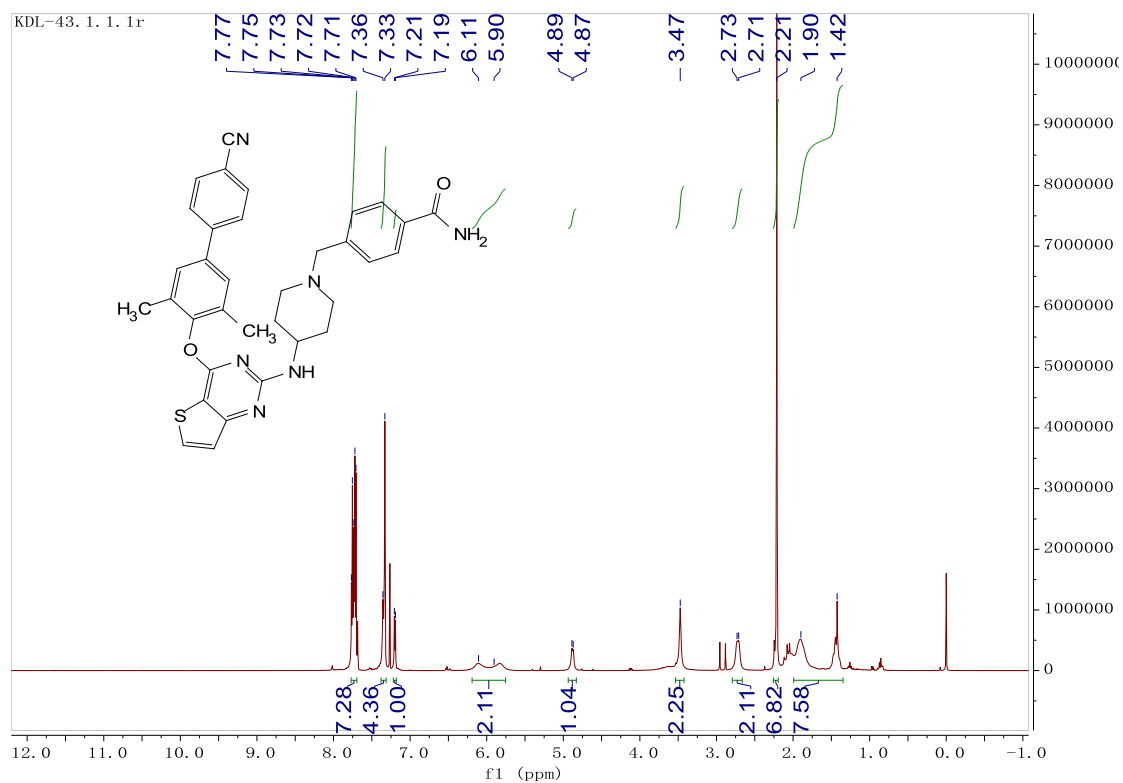
## 24 $^1\text{H}$ NMR



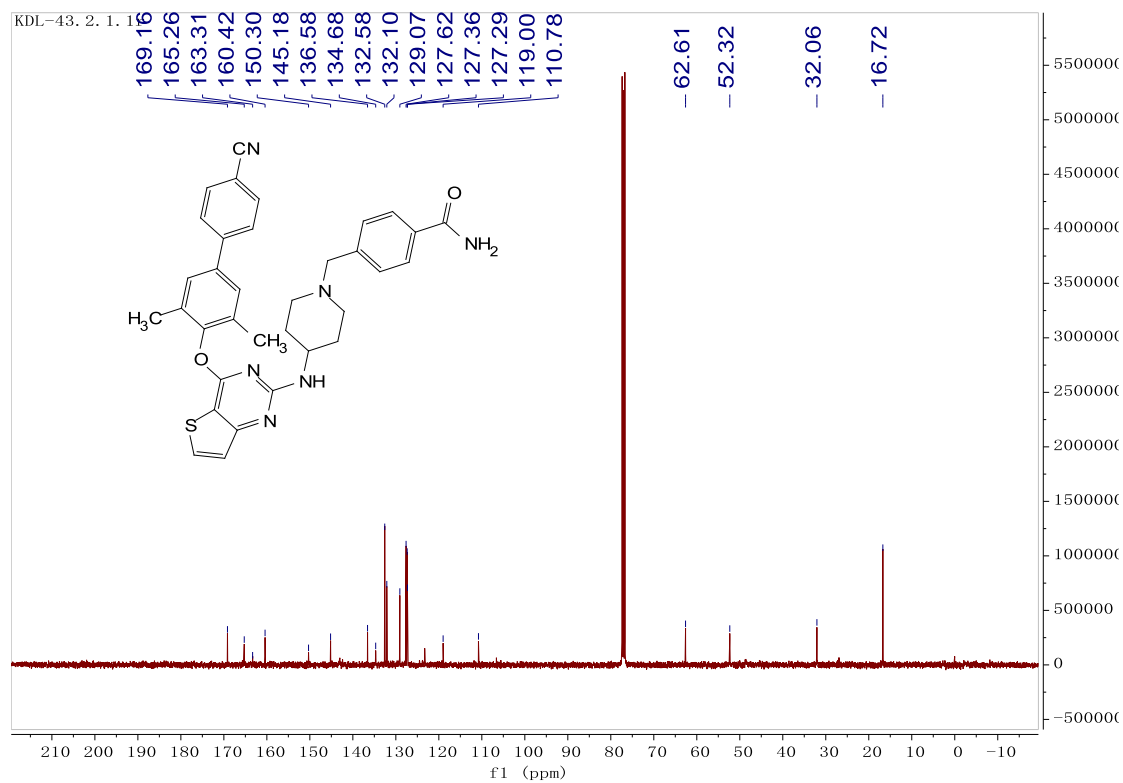
## 24 $^{13}\text{C}$ NMR



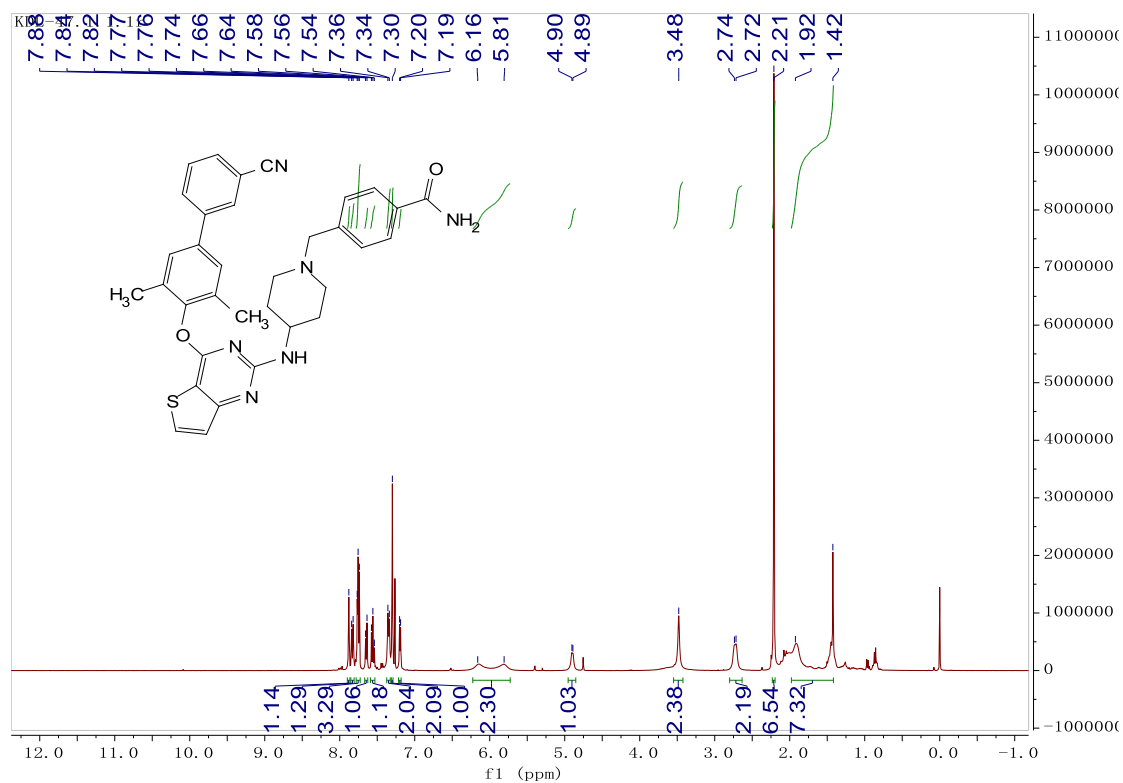
## 26 $^1\text{H}$ NMR



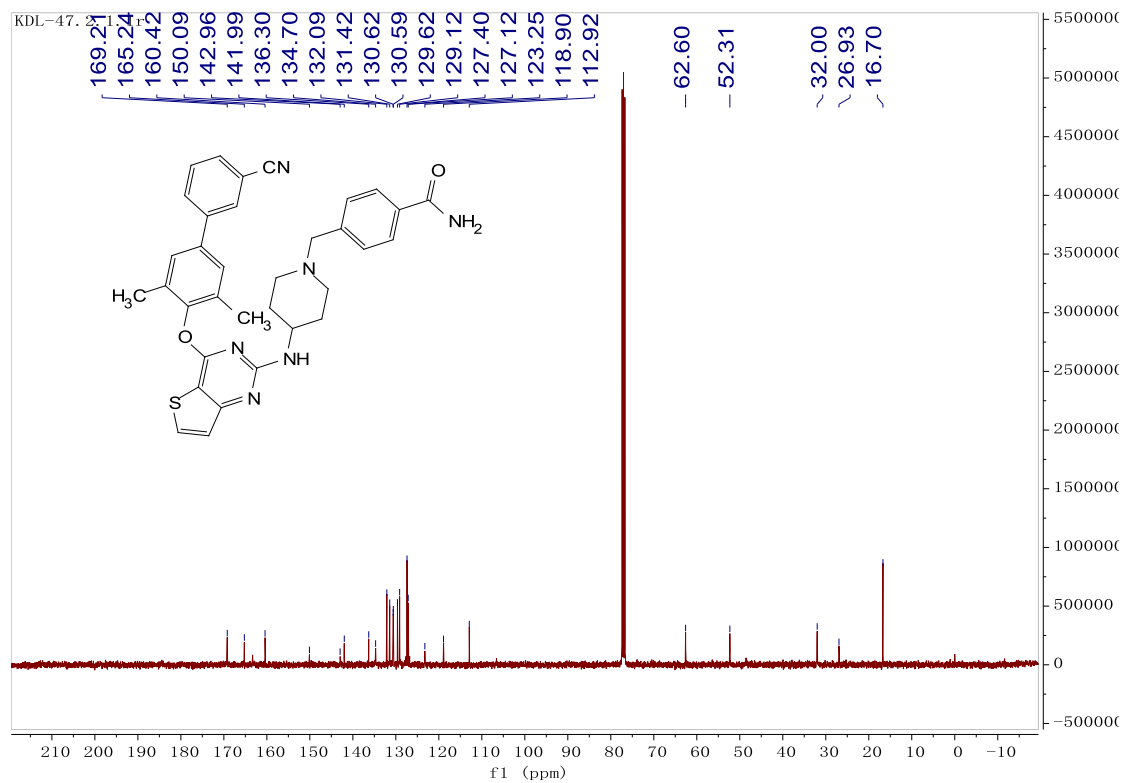
## 26 $^{13}\text{C}$ NMR



## 28 <sup>1</sup>H NMR

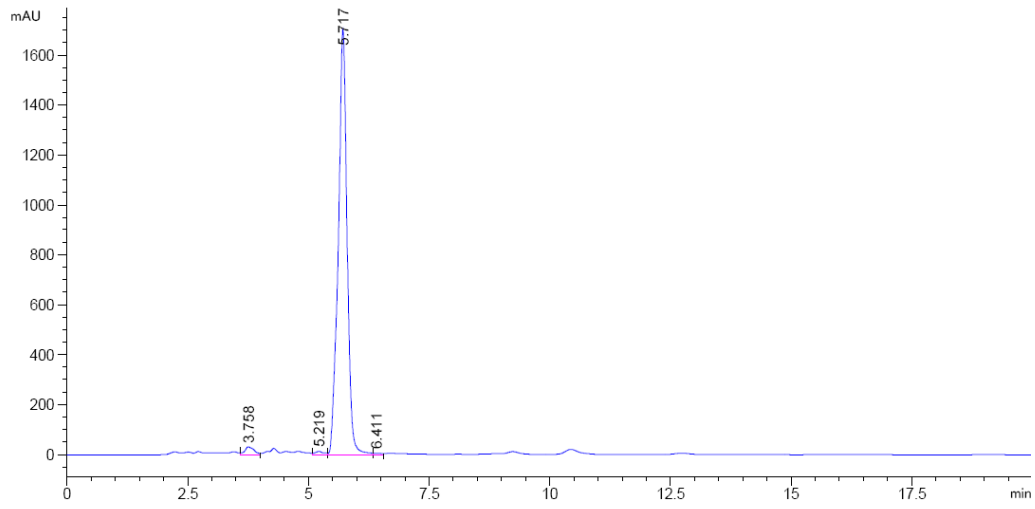


## 28 <sup>13</sup>C NMR

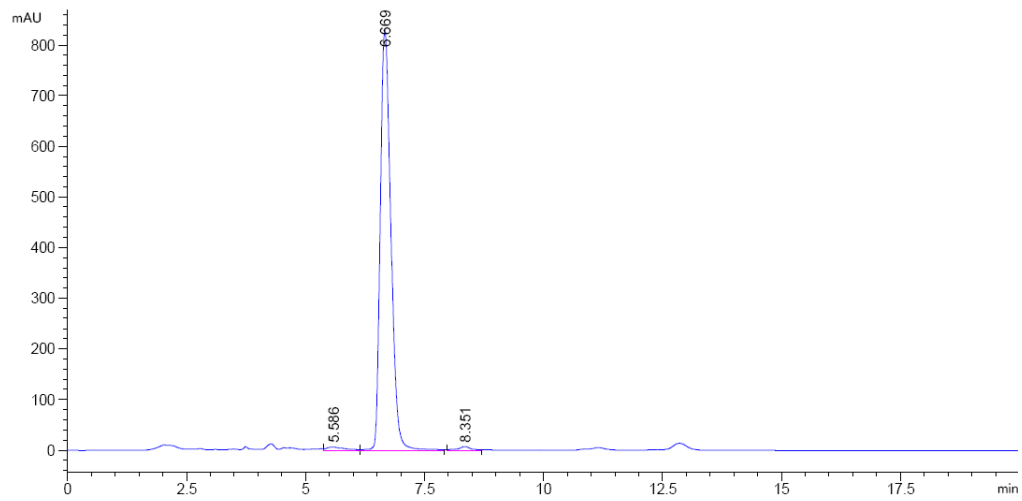


## 4. HPLC spectrum

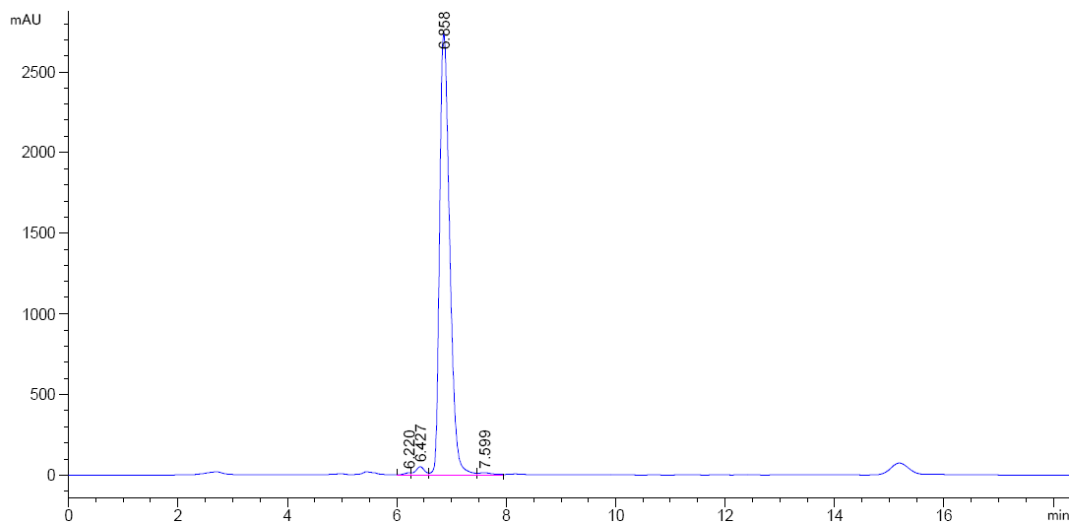
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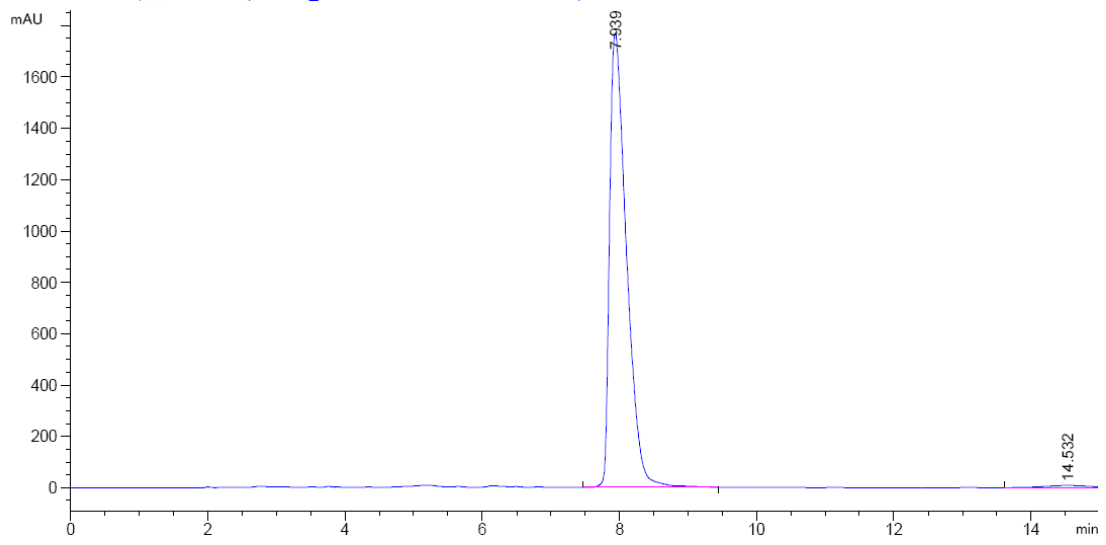
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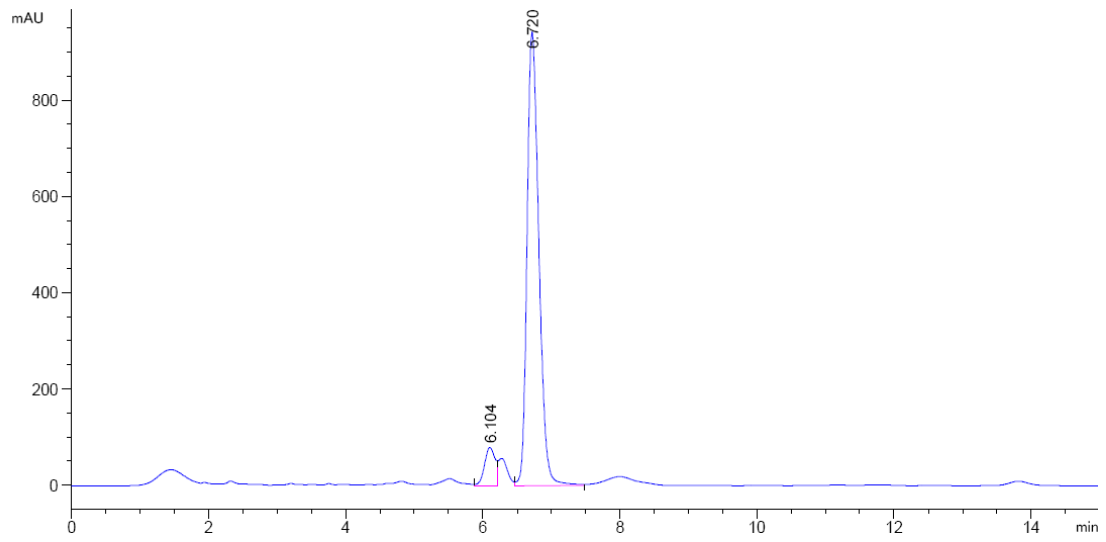
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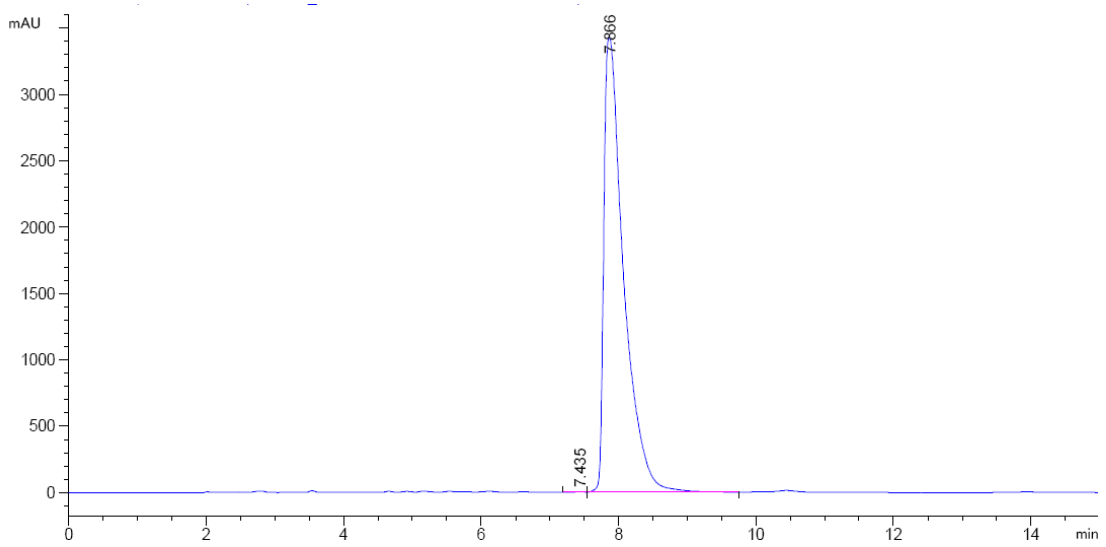
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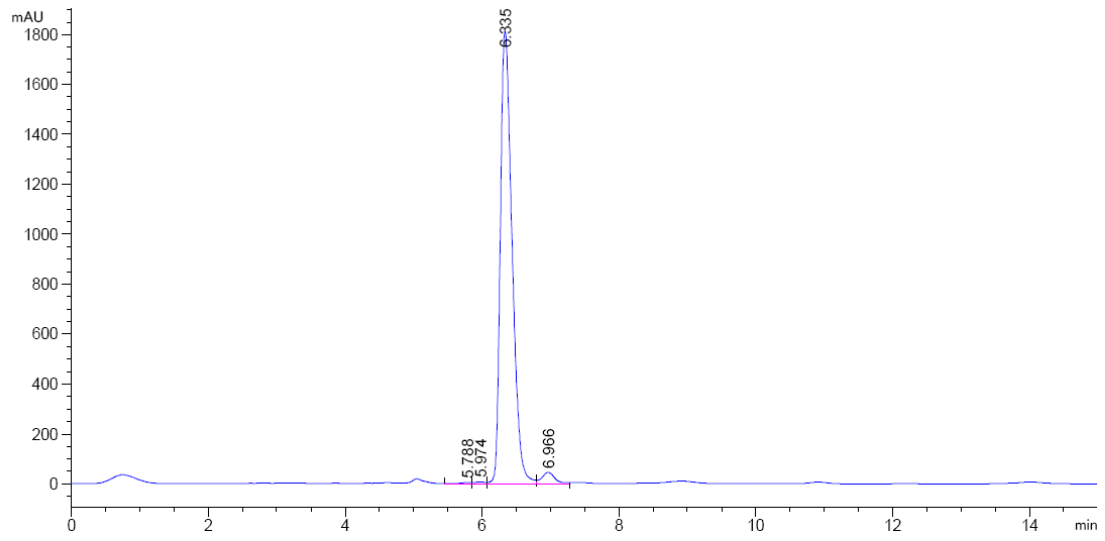
15



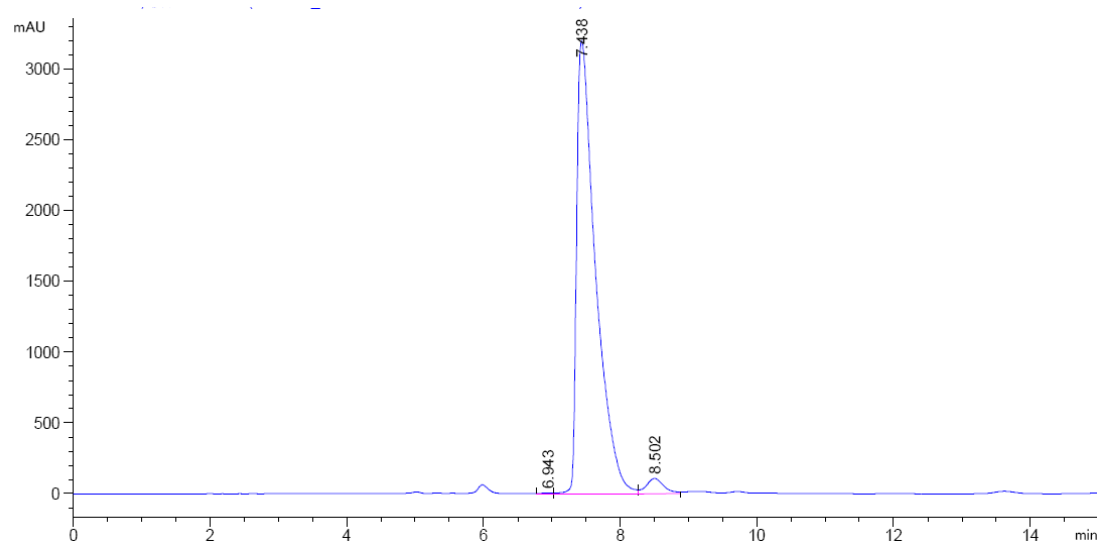
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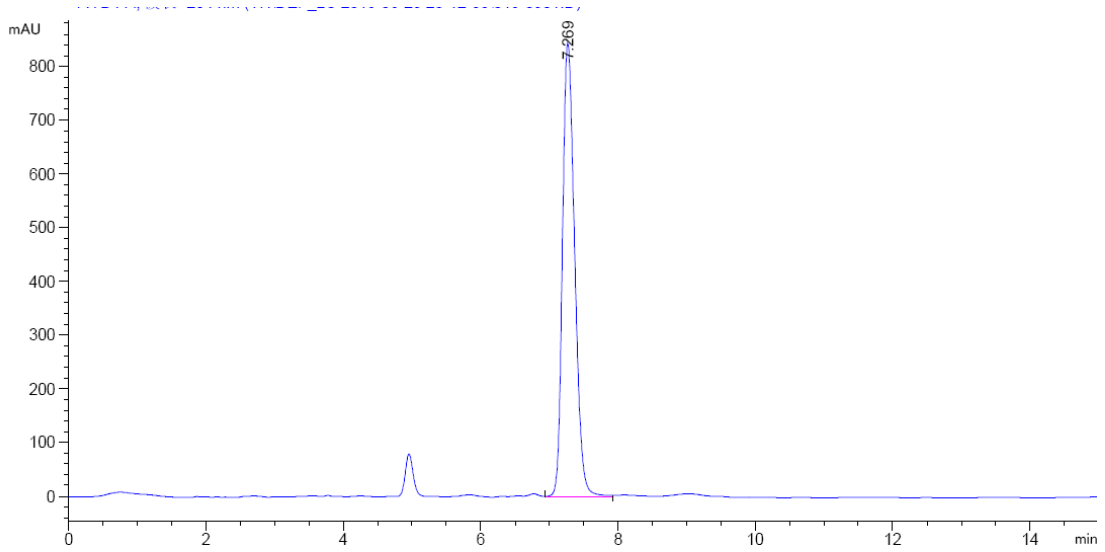
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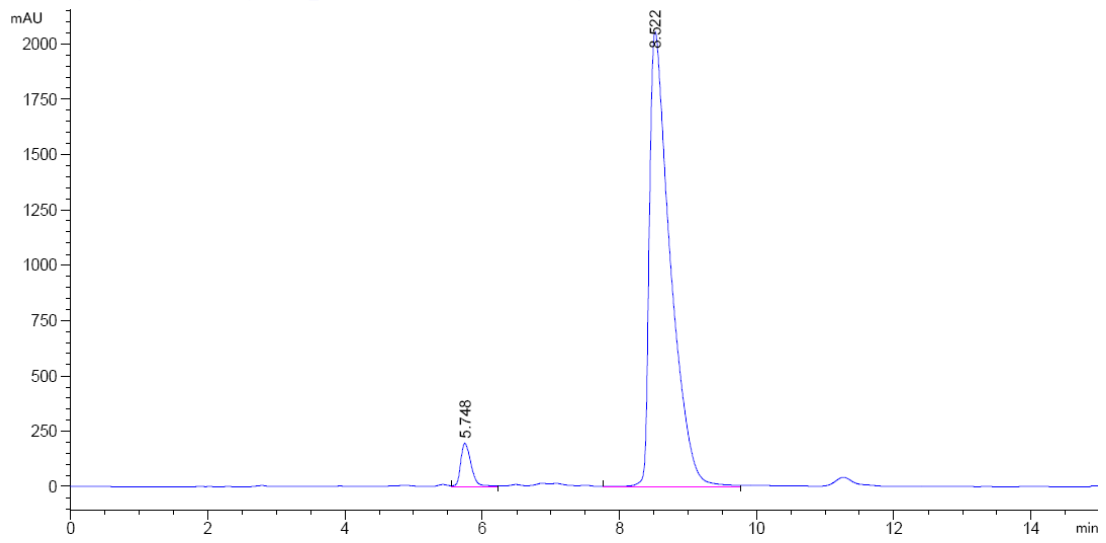


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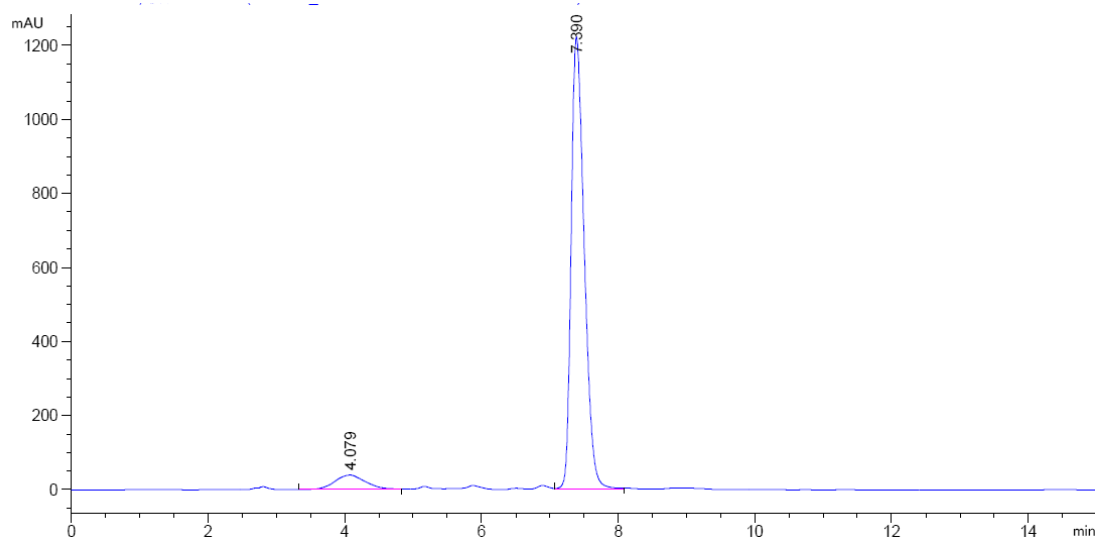




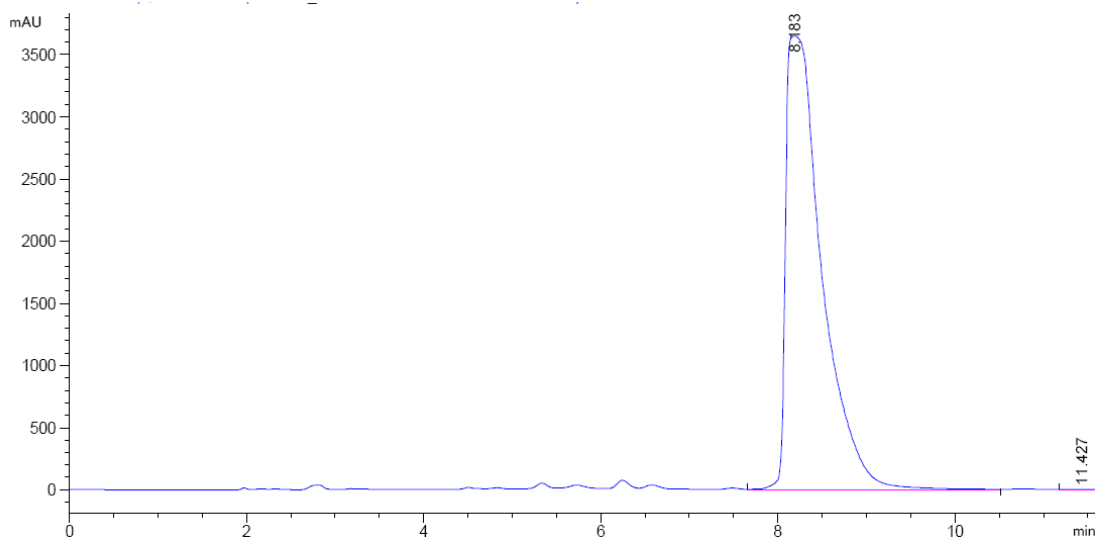
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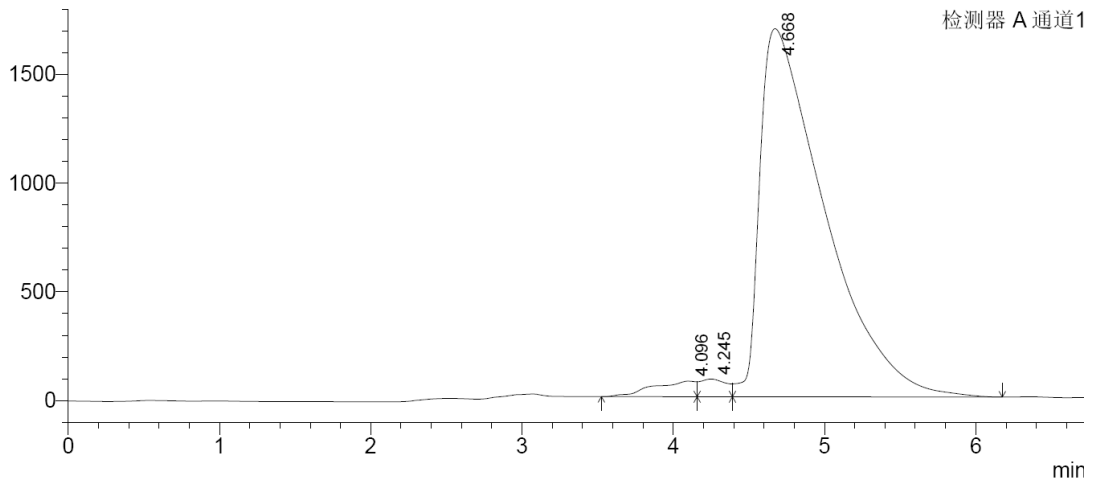
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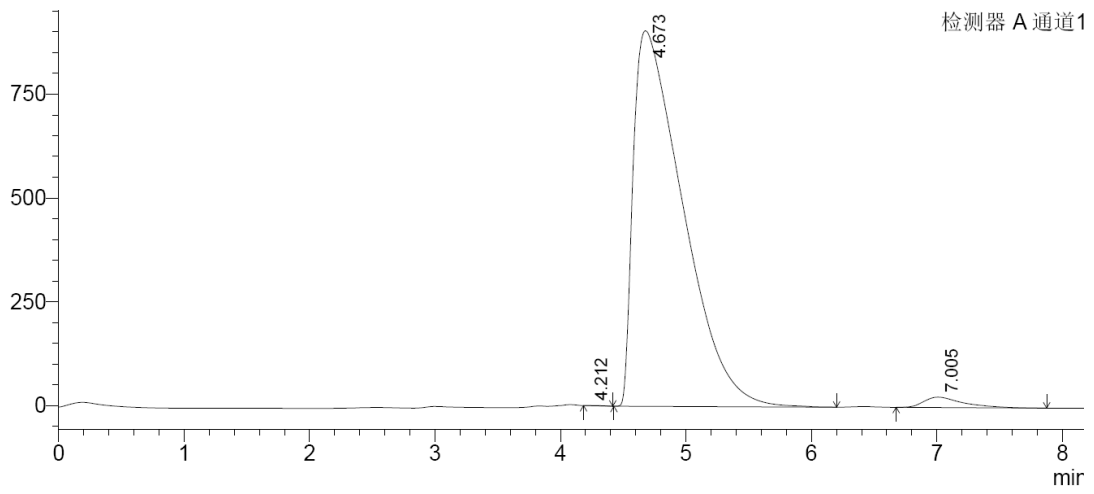
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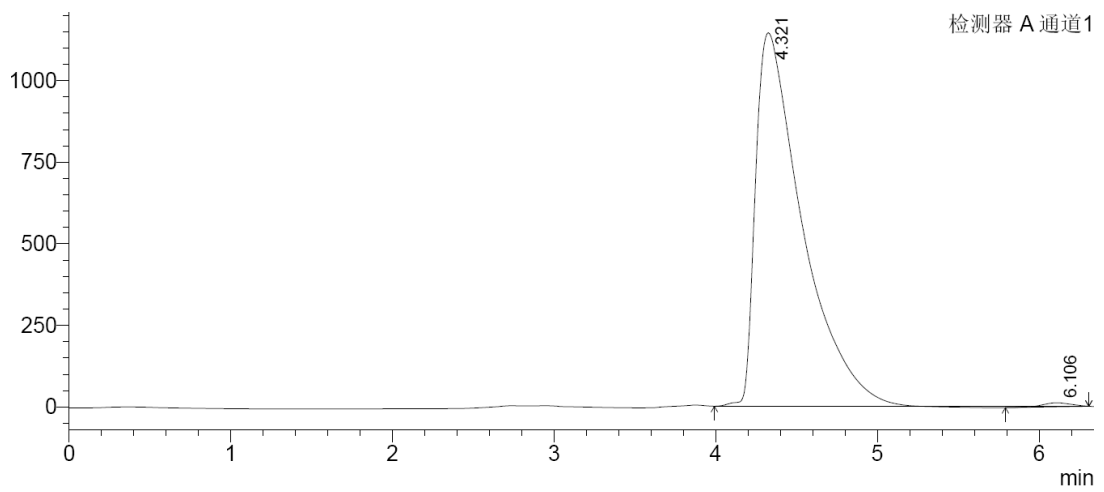
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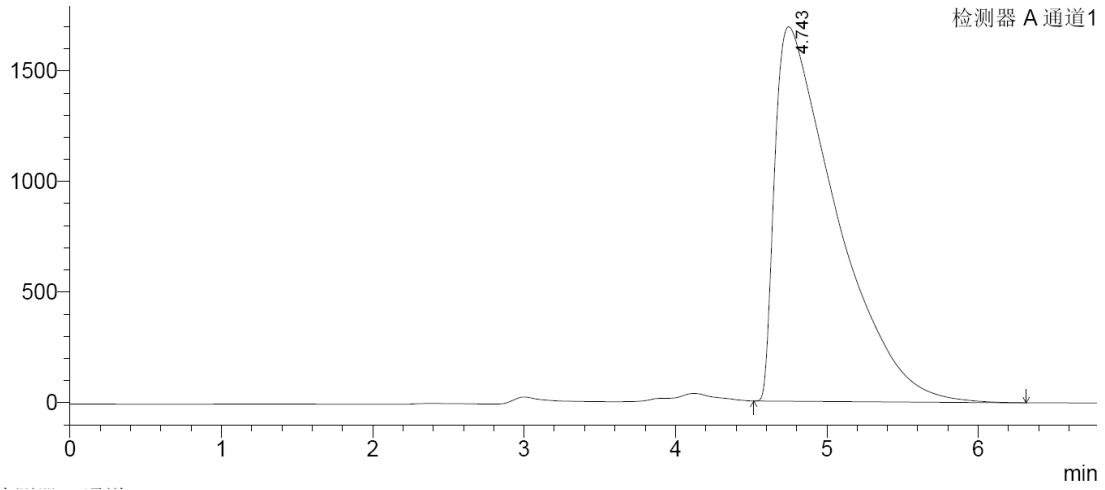
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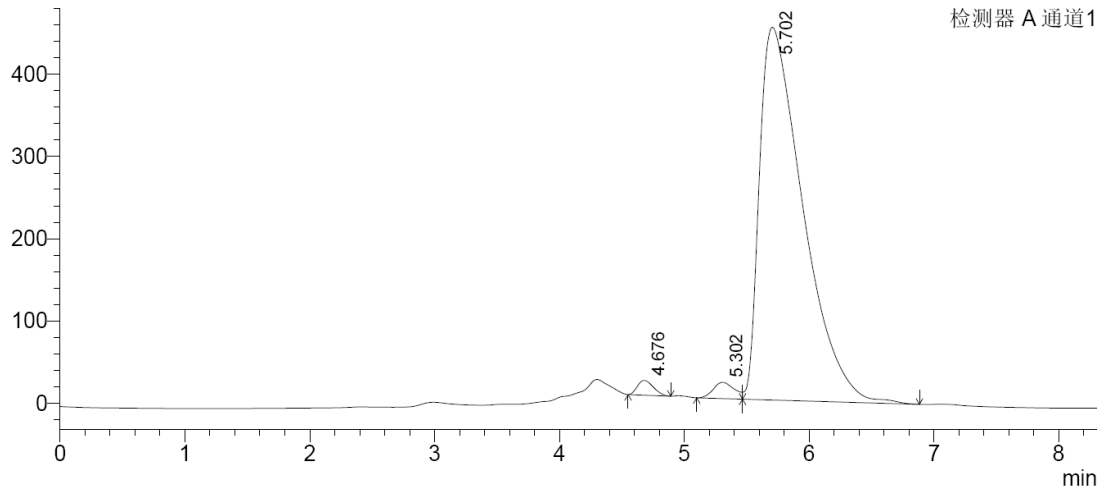
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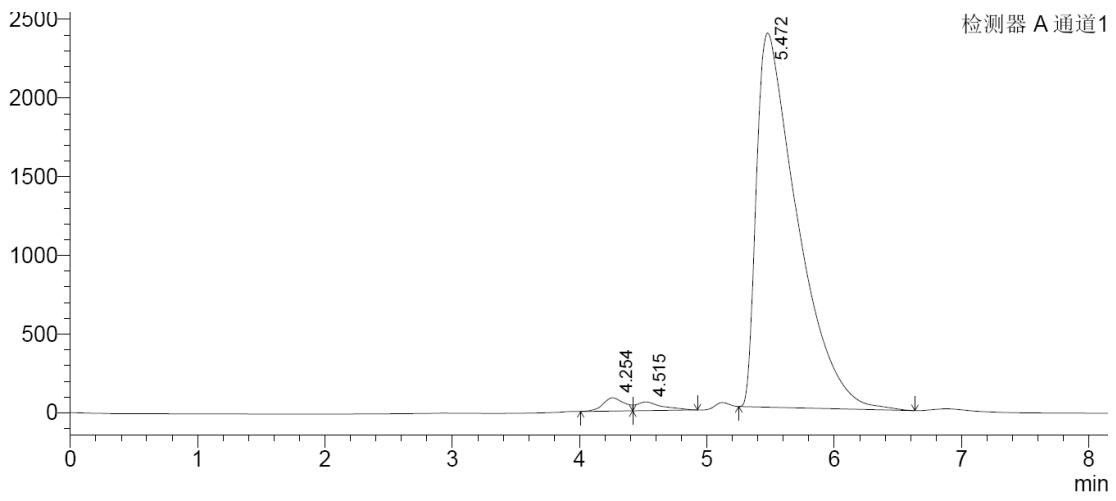
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