

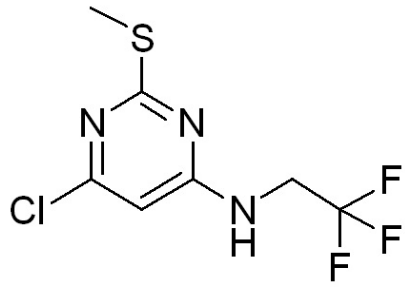
## Supplementary Information

**Title: Optimization of 6-heterocyclic-2-(1H-pyrazol-1-yl)-N-(pyridin-2-yl)pyrimidin-4-amine as Potent Adenosine A<sub>2A</sub> Receptor Antagonists for the Treatment of Parkinson's Disease**

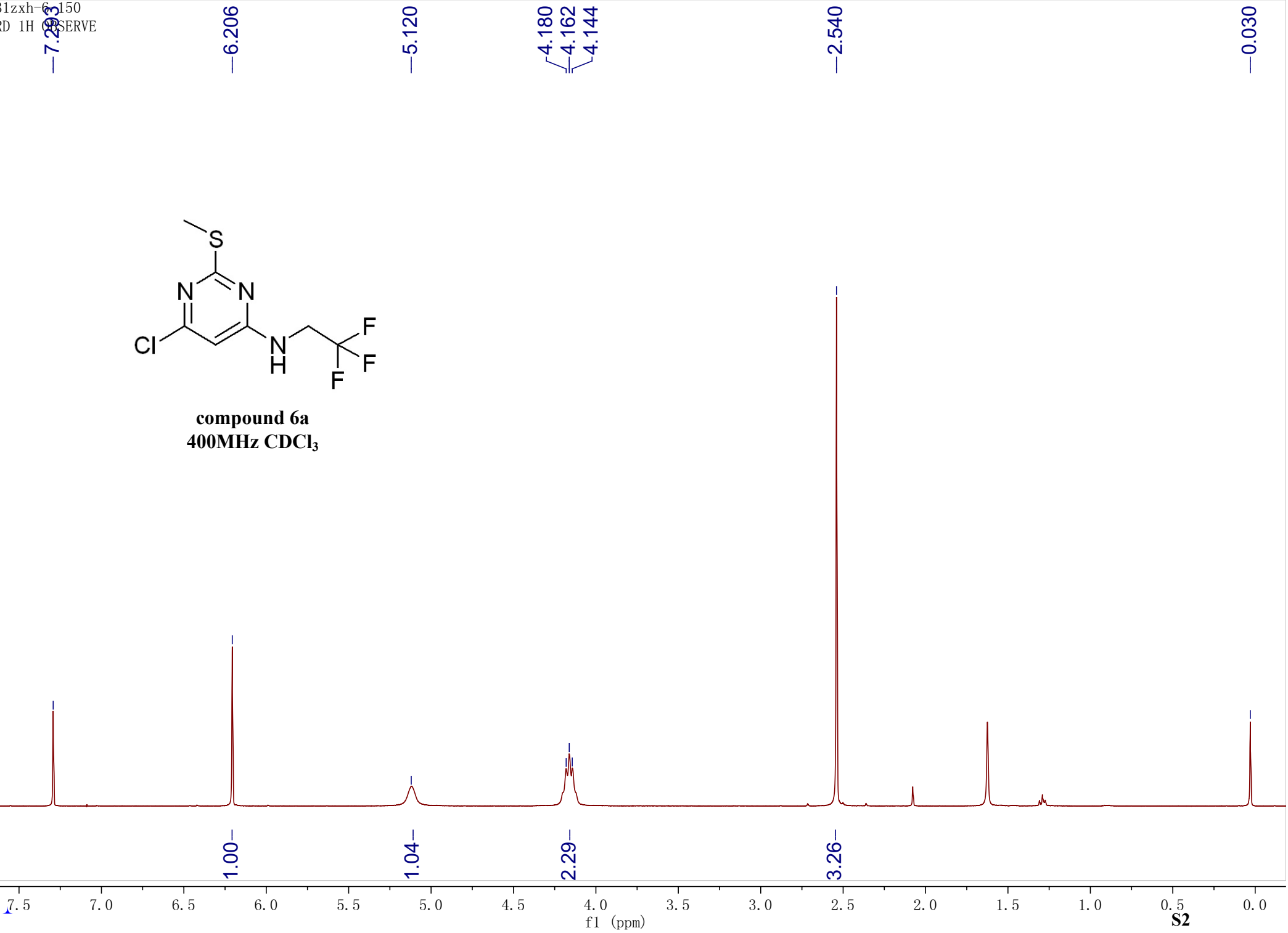
Jiyue Zheng,<sup>#</sup> Zhaohui Yang,<sup>#</sup> Xuan Li, Haikuo Ma, Meiyu Wang, Hongjian Zhang, Xuechu Zhen,<sup>\*</sup> and Xiaohu Zhang<sup>\*</sup>

Jiangsu Key Laboratory of Translational Research and Therapy for Neuro-Psycho-Diseases and College of Pharmaceutical Sciences, Soochow University, Su Zhou, Jiangsu 215021, P. R. China

<sup>#</sup> These authors contributed equally

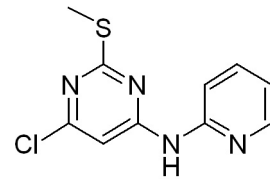


**compound 6a**  
400MHz CDCl<sub>3</sub>

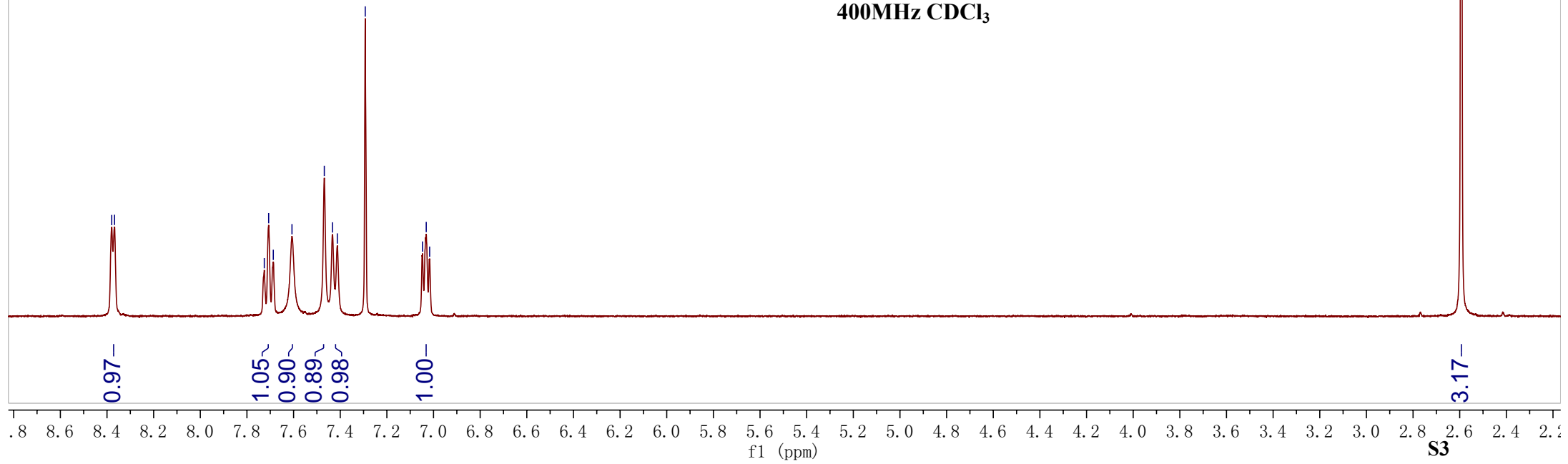


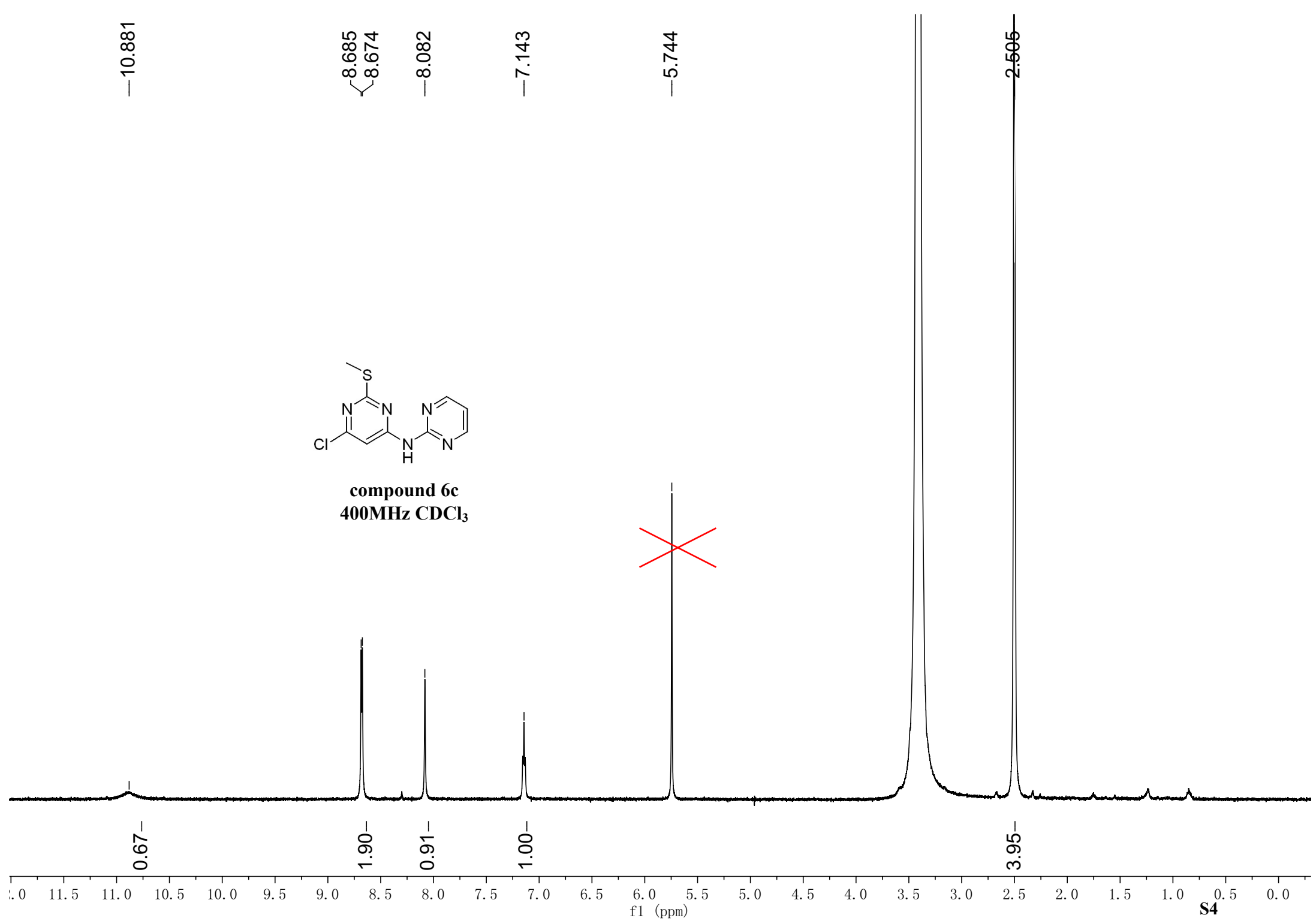
8.380  
8.368  
7.726  
7.707  
7.687  
7.607  
7.468  
7.433  
7.413  
7.293  
7.047  
7.031  
7.017

2.594



**compound 6b**  
400MHz CDCl<sub>3</sub>





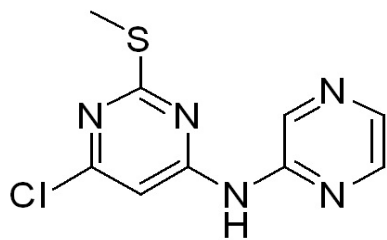
—8.853

8.285  
8.276

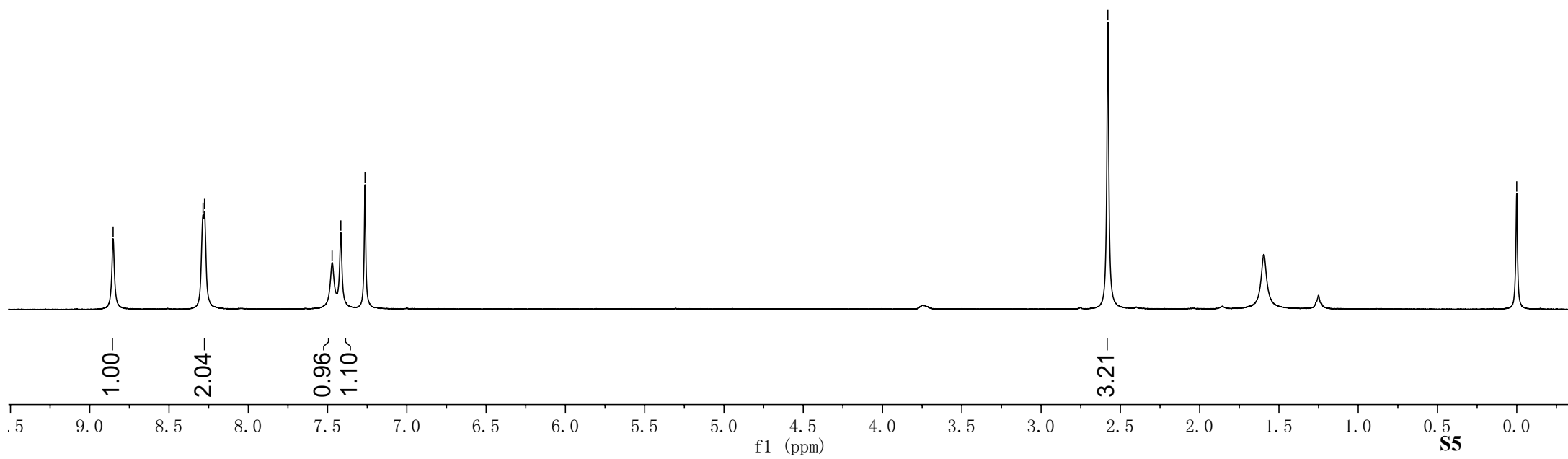
7.472  
7.416  
7.264

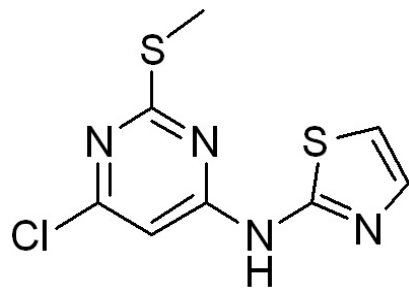
—2.579

—0.000

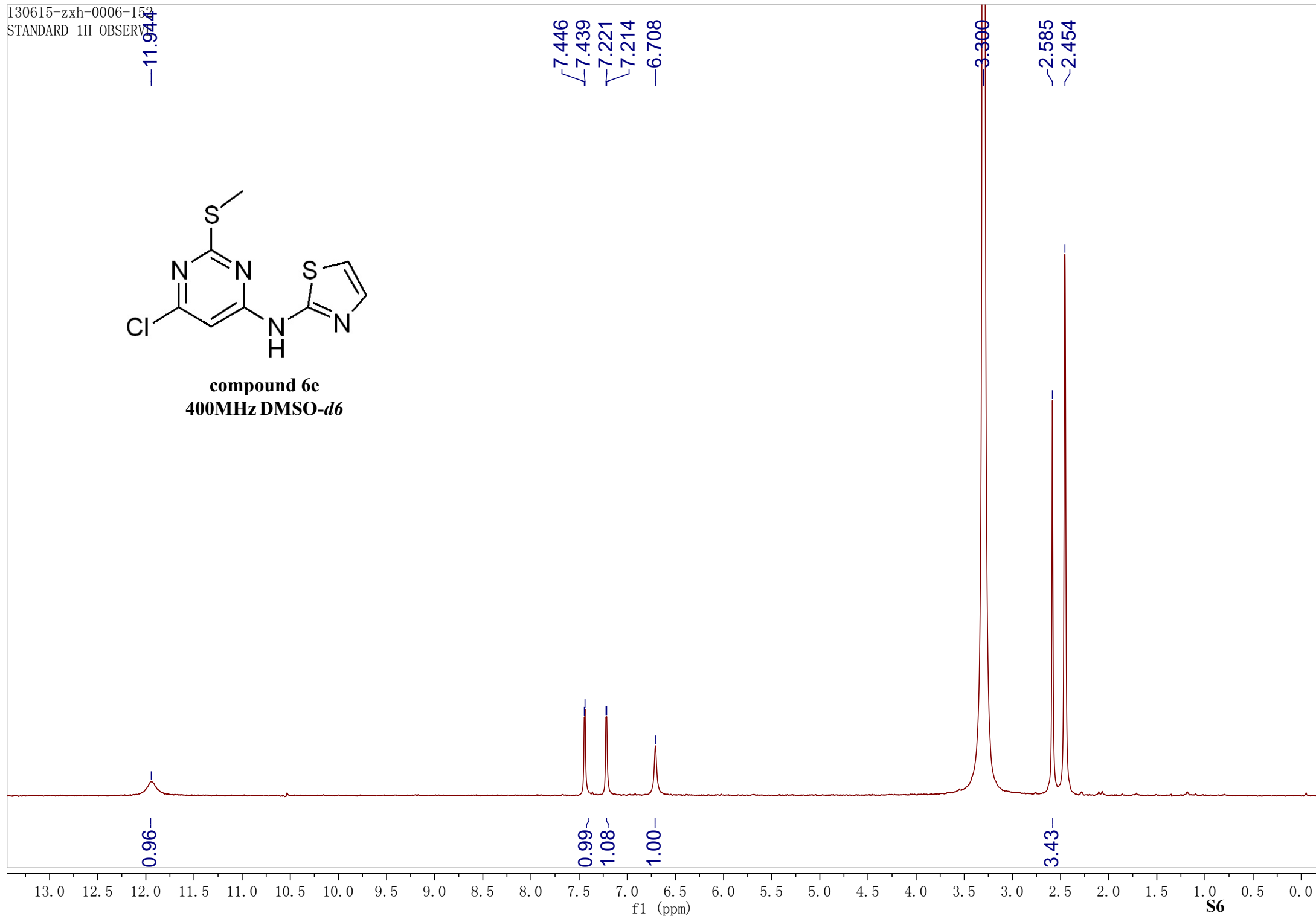


**compound 6d**  
400MHz CDCl<sub>3</sub>

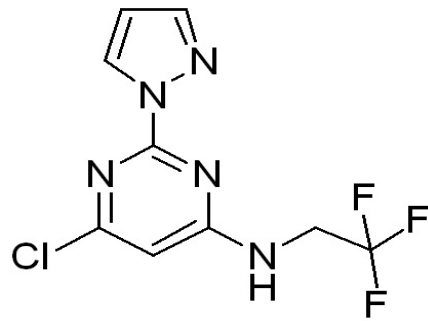




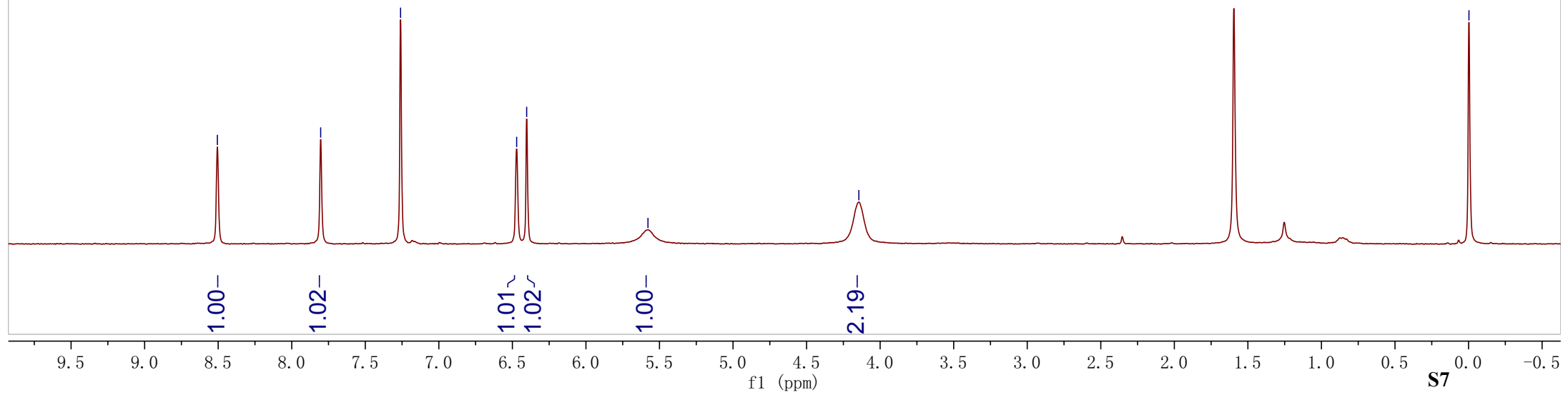
**compound 6e**  
**400MHz DMSO-d6**



8.506 7.803 7.260 6.471 6.403 5.578 4.145 -0.003



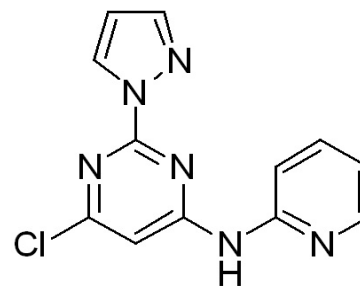
**compound 8a**  
400MHz CDCl<sub>3</sub>



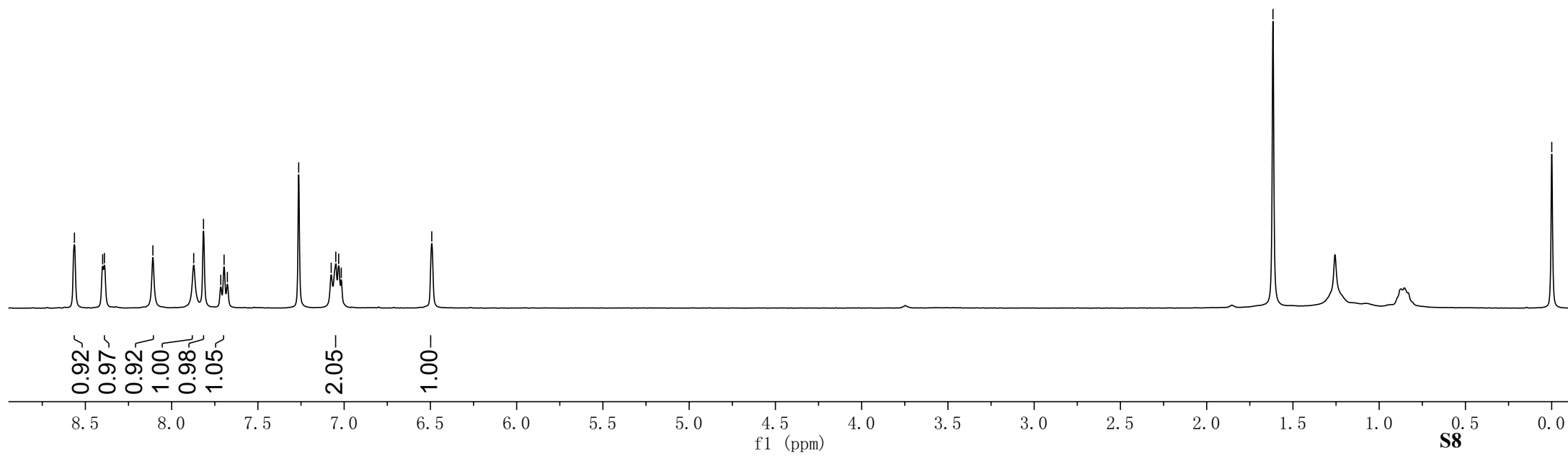
8.563  
8.400  
8.390  
8.109  
7.872  
7.815  
7.715  
7.696  
7.677  
7.263  
7.075  
7.048  
7.032  
7.017  
-6.492

-1.616

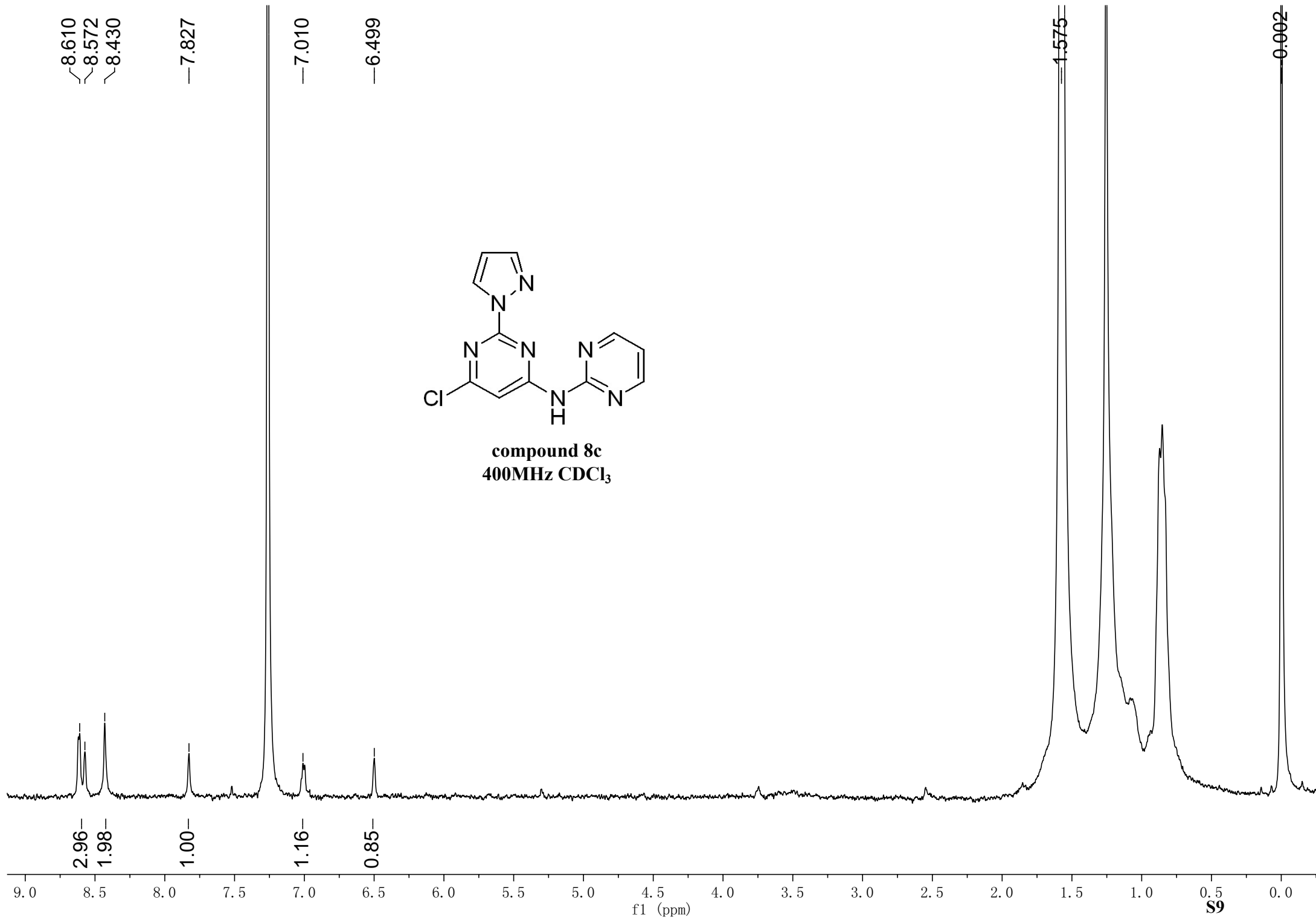
-0.000

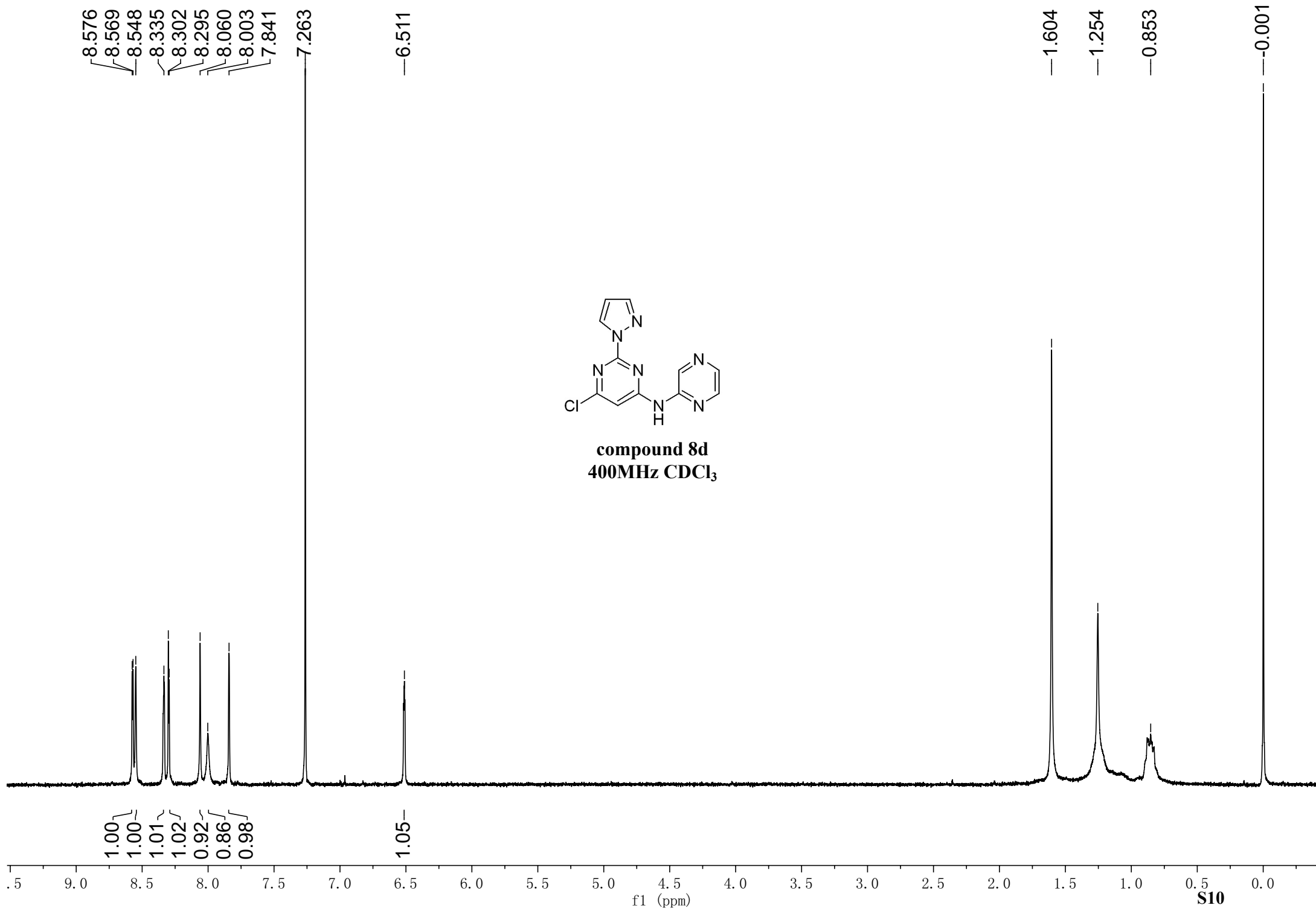


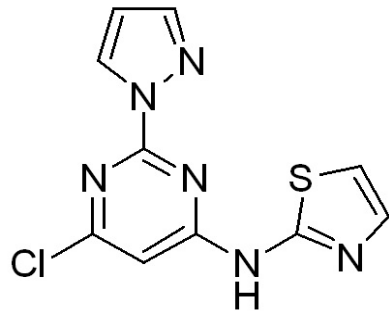
**compound 8b**  
400MHz CDCl<sub>3</sub>



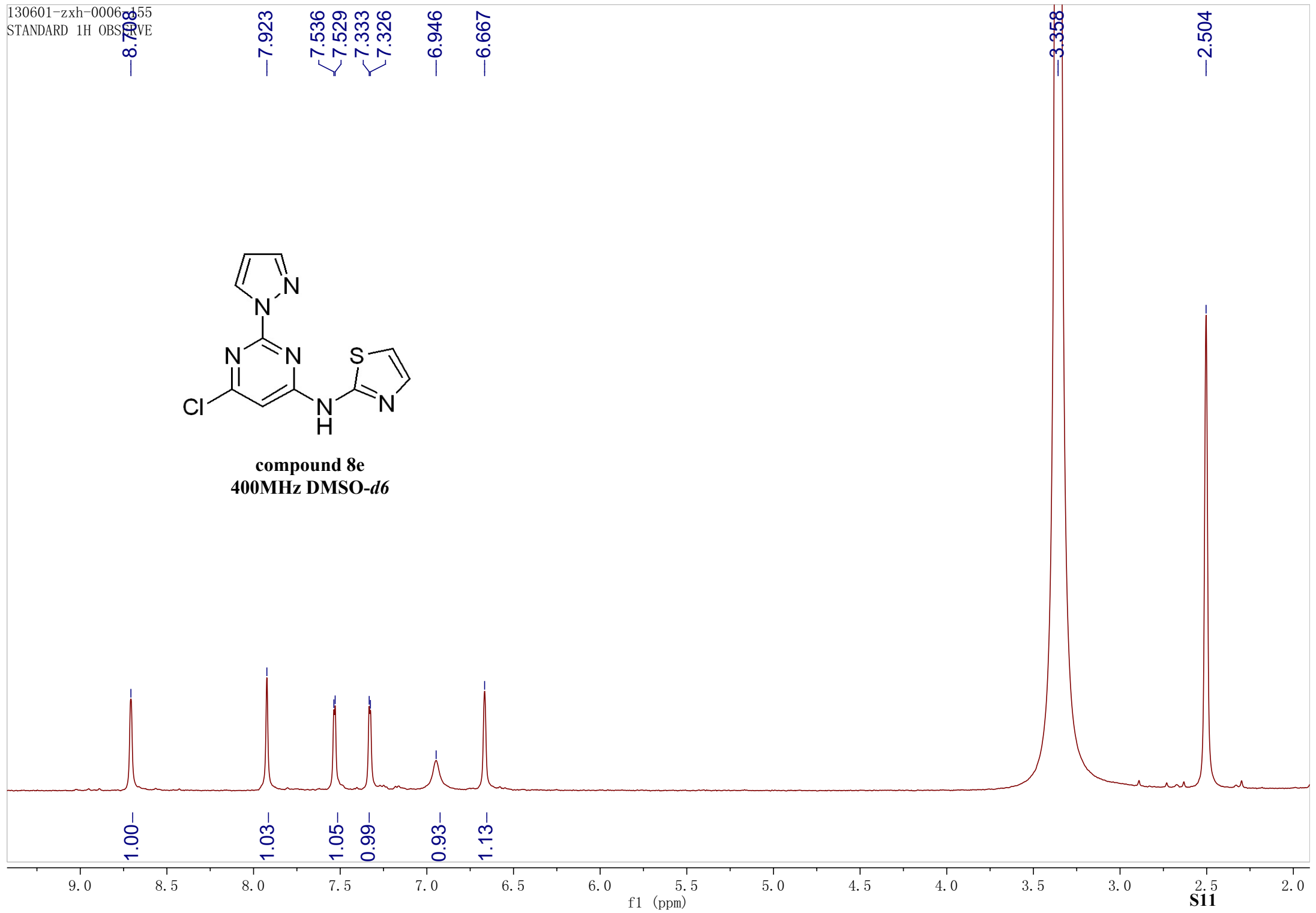


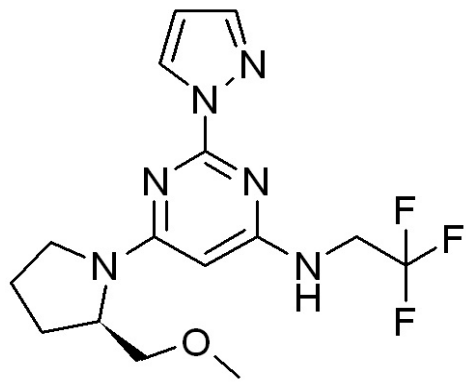




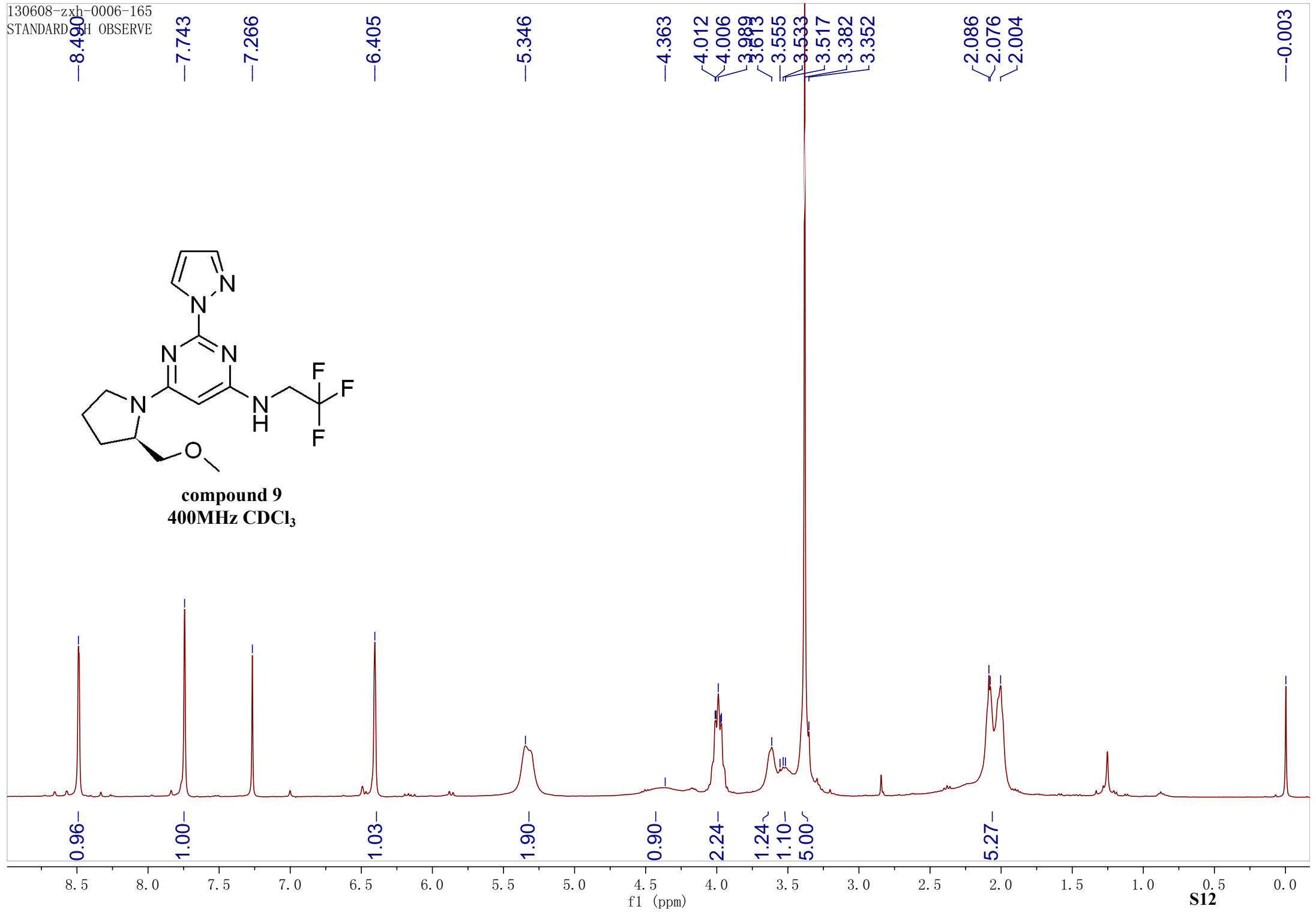


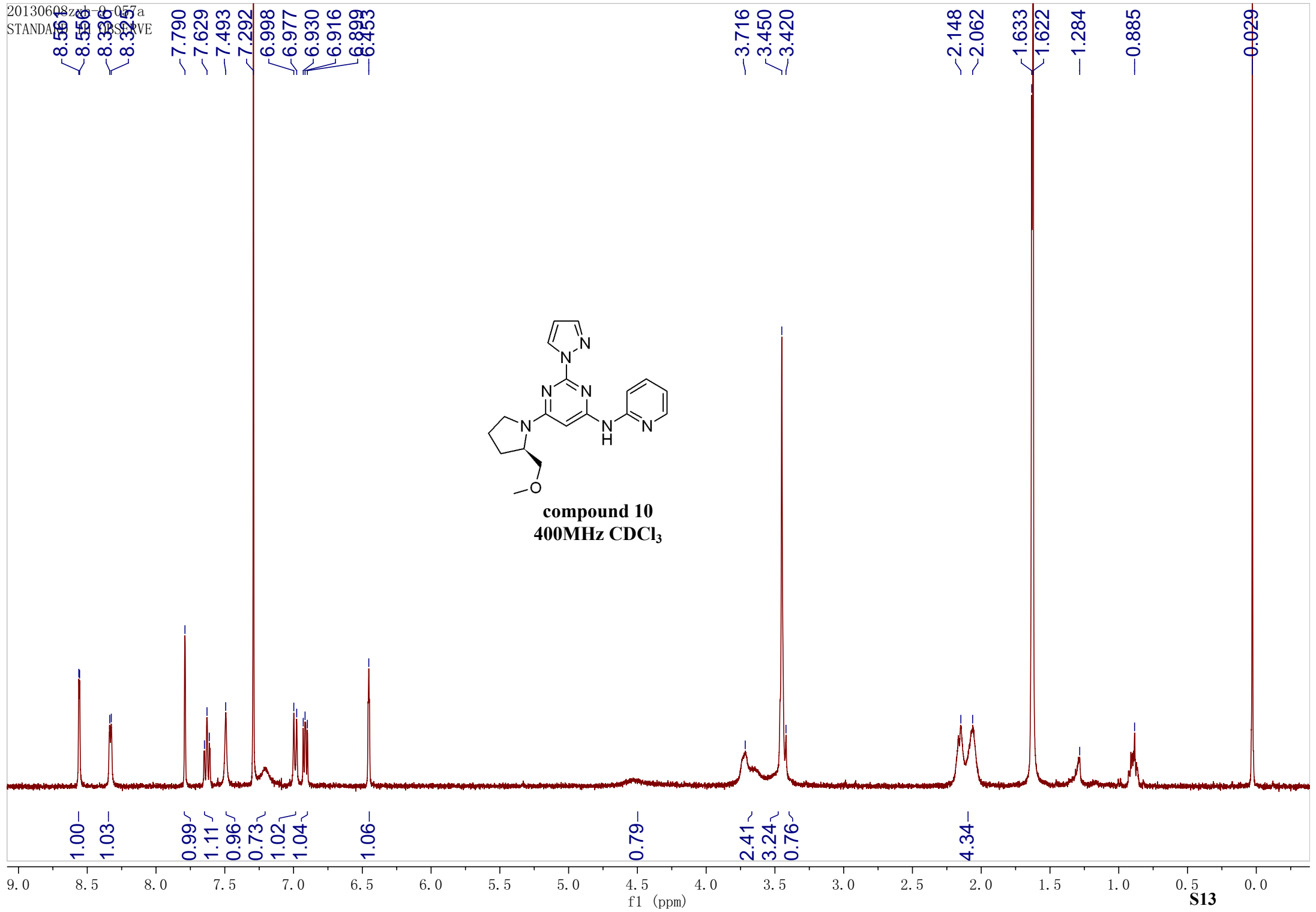
**compound 8e**  
**400MHz DMSO-d6**



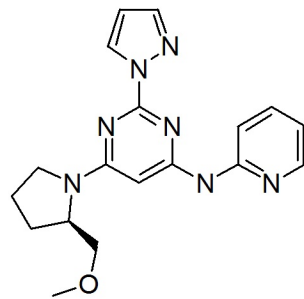


**compound 9**  
400MHz CDCl<sub>3</sub>

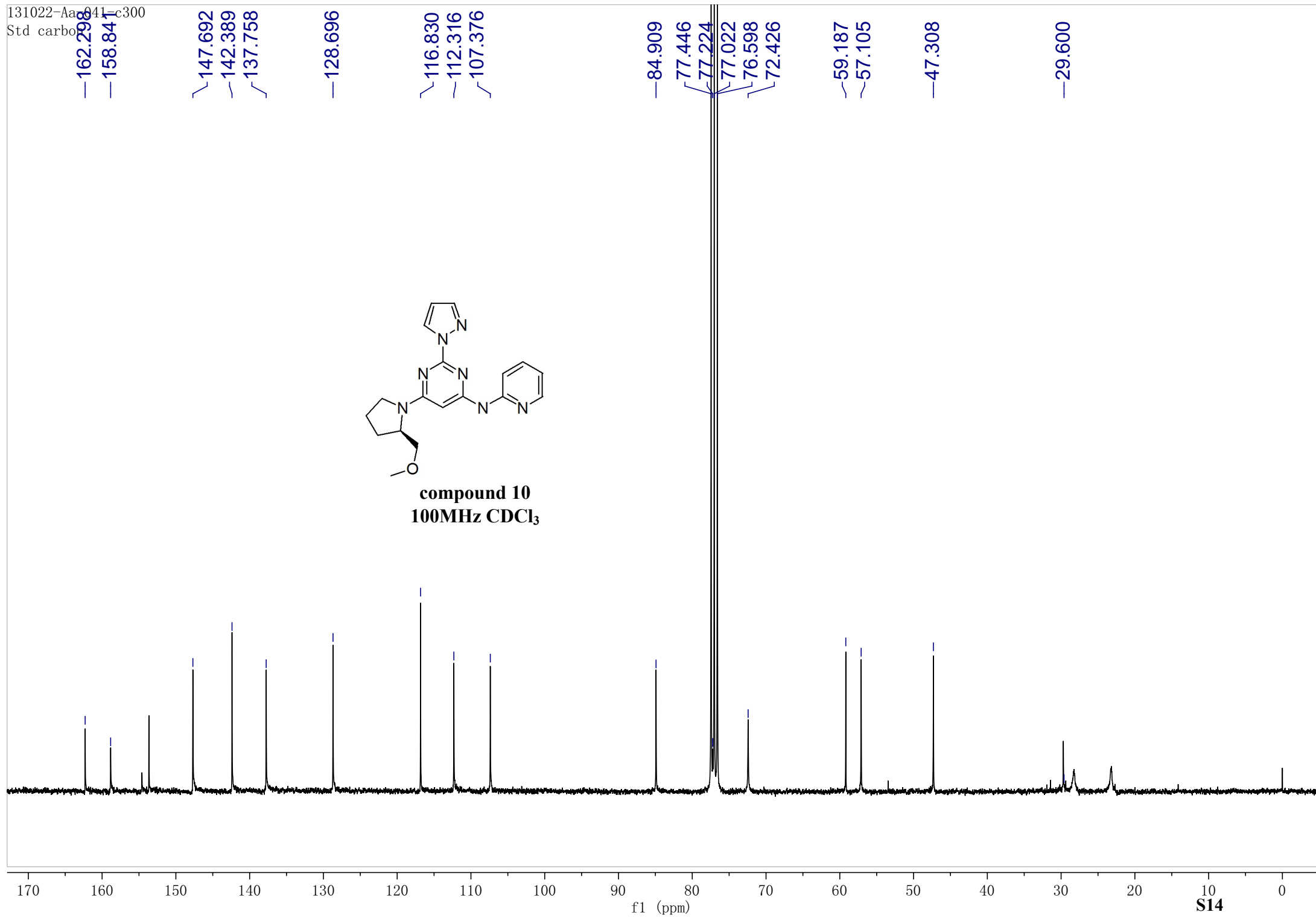




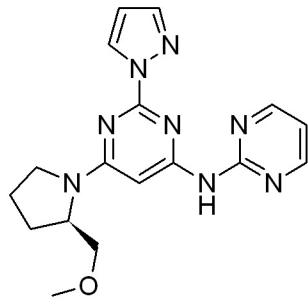
—162.298  
—158.841  
—147.692  
—142.389  
—137.758  
—128.696  
—116.830  
—112.316  
—107.376  
—84.909  
77.446  
77.224  
77.022  
76.598  
72.426  
—59.187  
—57.105  
—47.308  
—29.600



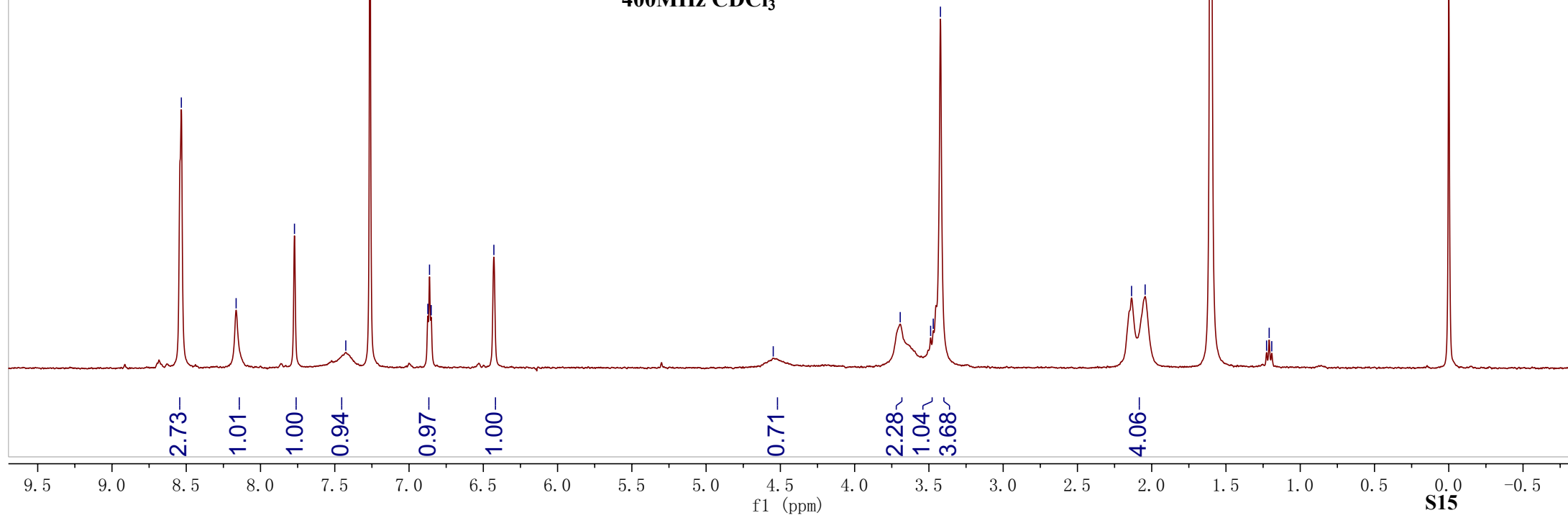
**compound 10**  
**100MHz CDCl<sub>3</sub>**



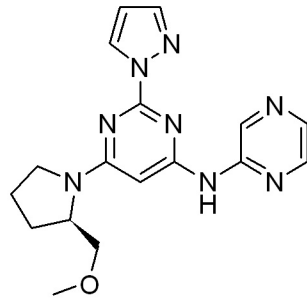
8.533 8.164 7.771 7.426 7.263 6.873 6.862 6.851 6.429 4.548 3.693 3.488 3.471 3.422 2.136 2.044 1.603 1.227 1.209 1.192 -0.000



**compound 11**  
400MHz CDCl<sub>3</sub>



8.530  
8.393  
8.221  
8.138  
8.133  
7.775  
7.599  
7.266  
6.440  
3.687  
3.420  
2.134  
2.049  
1.603  
0.860  
0.003



**compound 12**  
400MHz CDCl<sub>3</sub>

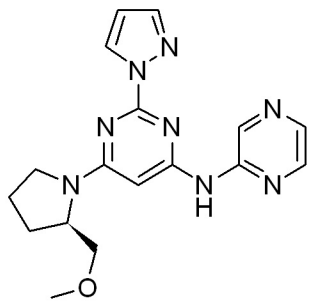
1.00  
1.06  
1.02  
0.98  
1.07  
0.98  
0.97  
1.02  
0.97  
2.71  
4.54  
3.99

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

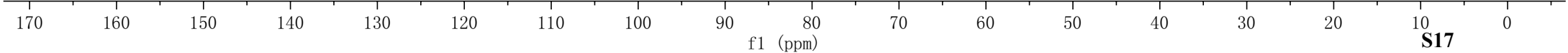
f1 (ppm)

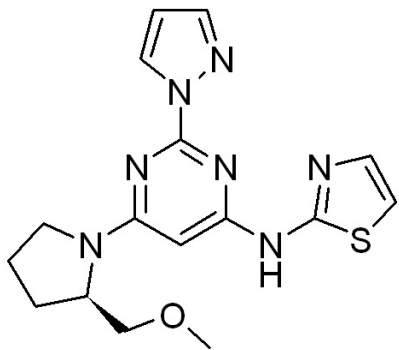


162.388  
158.236  
154.662  
150.392  
142.620  
141.345  
136.591  
135.682  
128.792  
107.592  
85.536  
77.357  
77.244  
77.039  
76.721  
72.453  
59.225  
57.296  
47.409

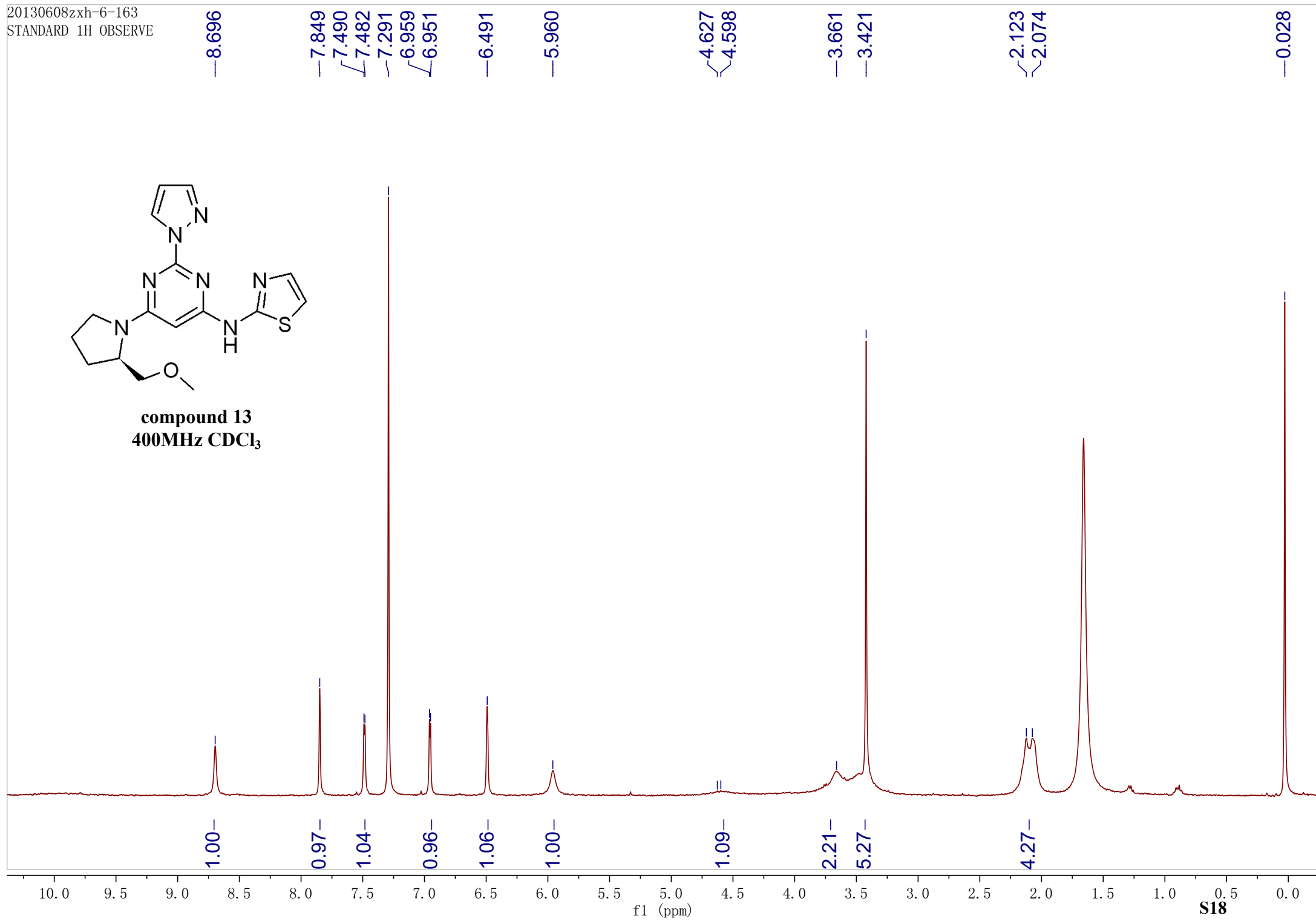


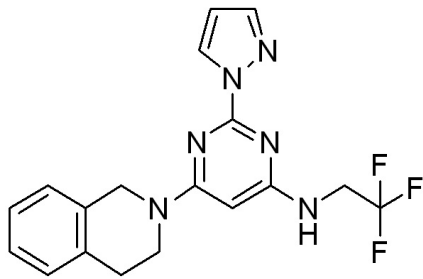
**compound 12**  
**100MHz CDCl<sub>3</sub>**



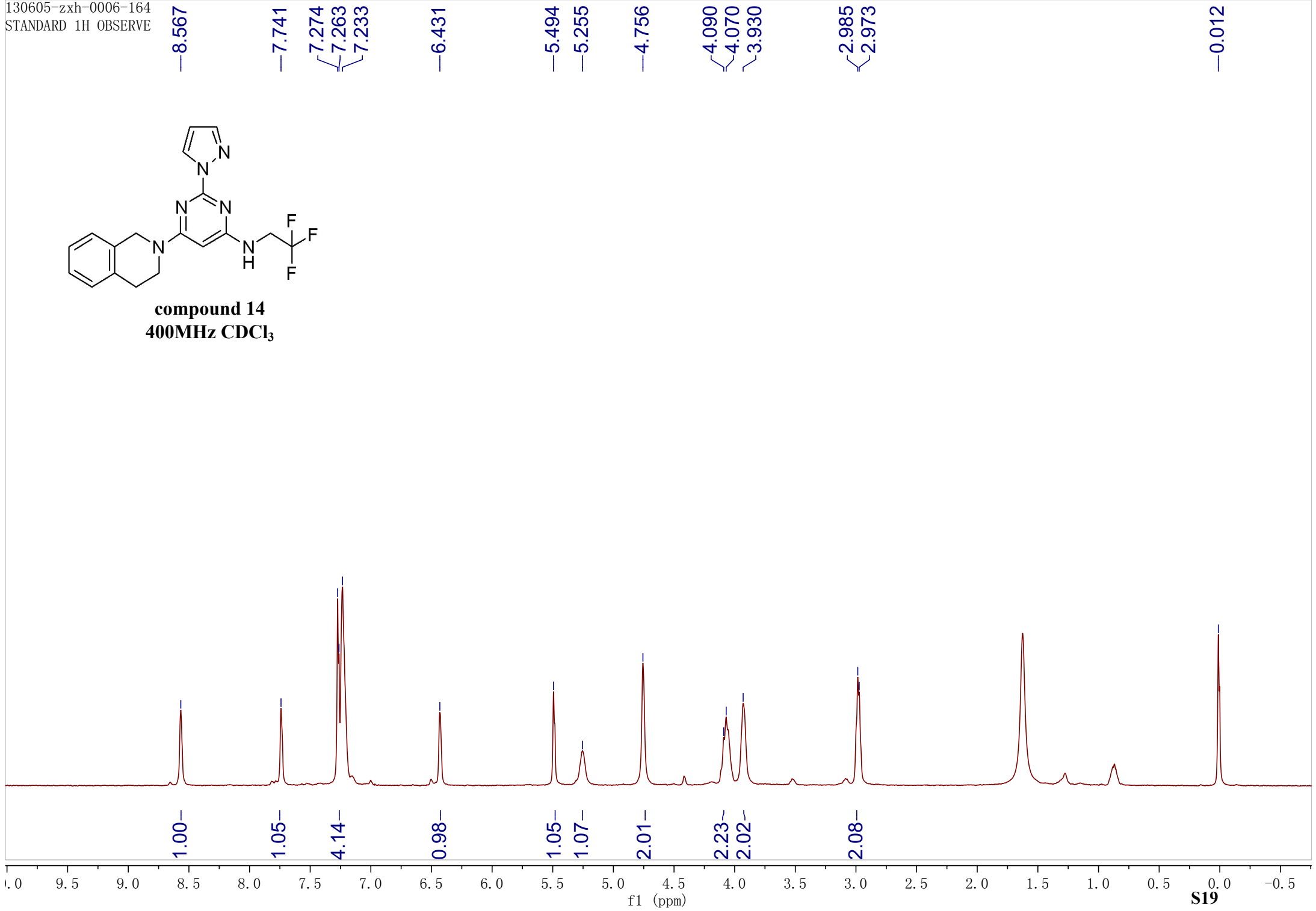


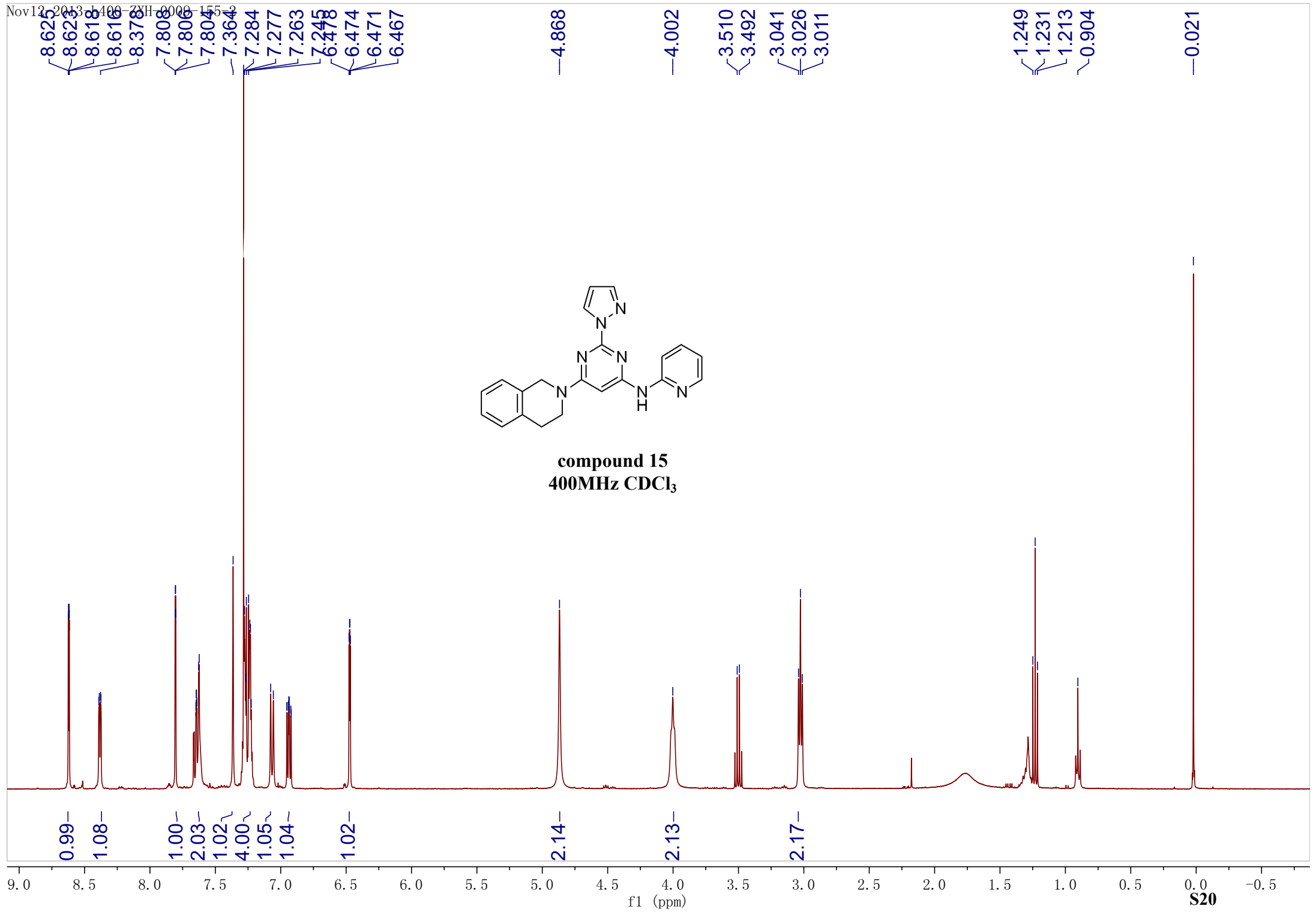
**compound 13**  
400MHz CDCl<sub>3</sub>

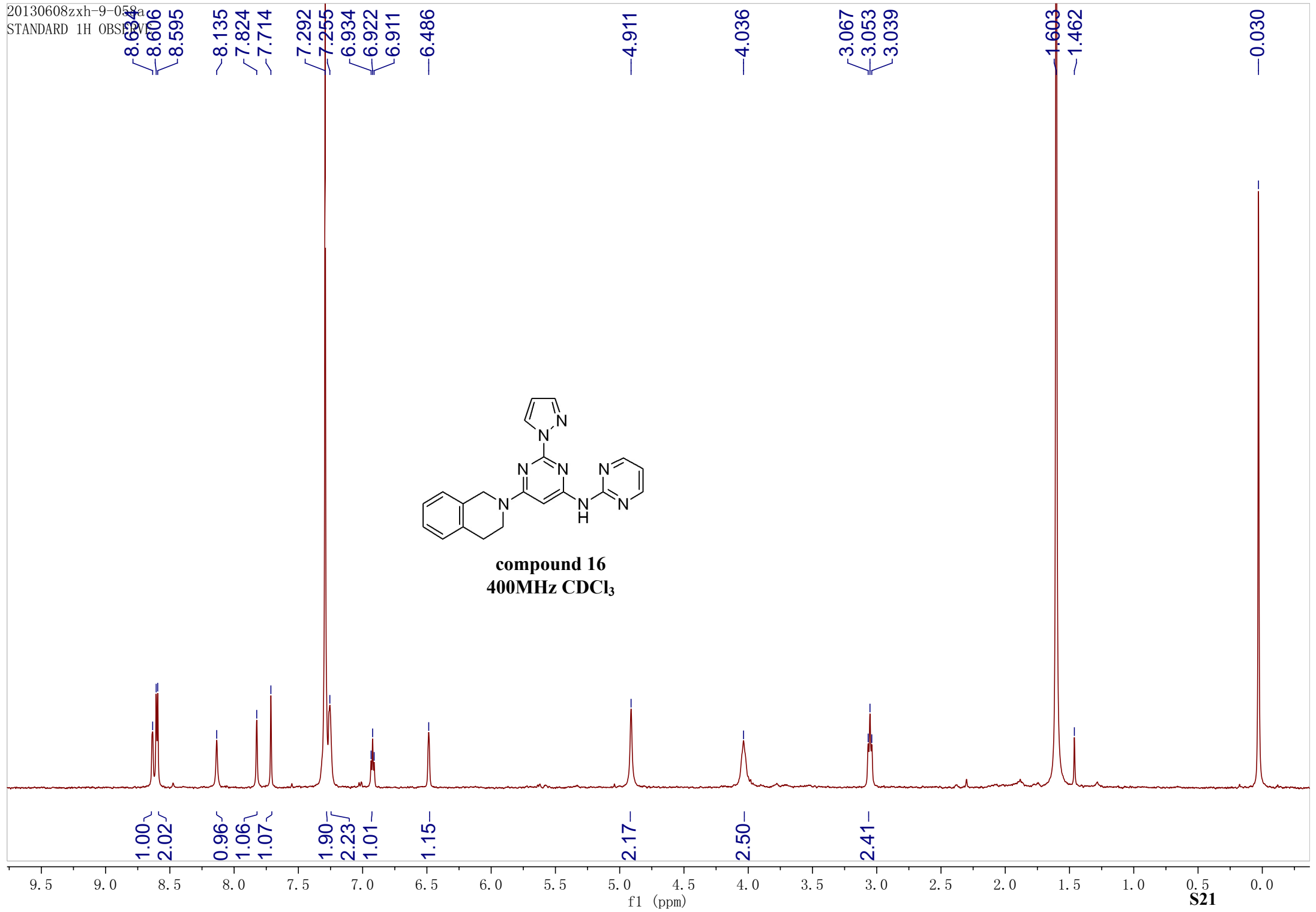


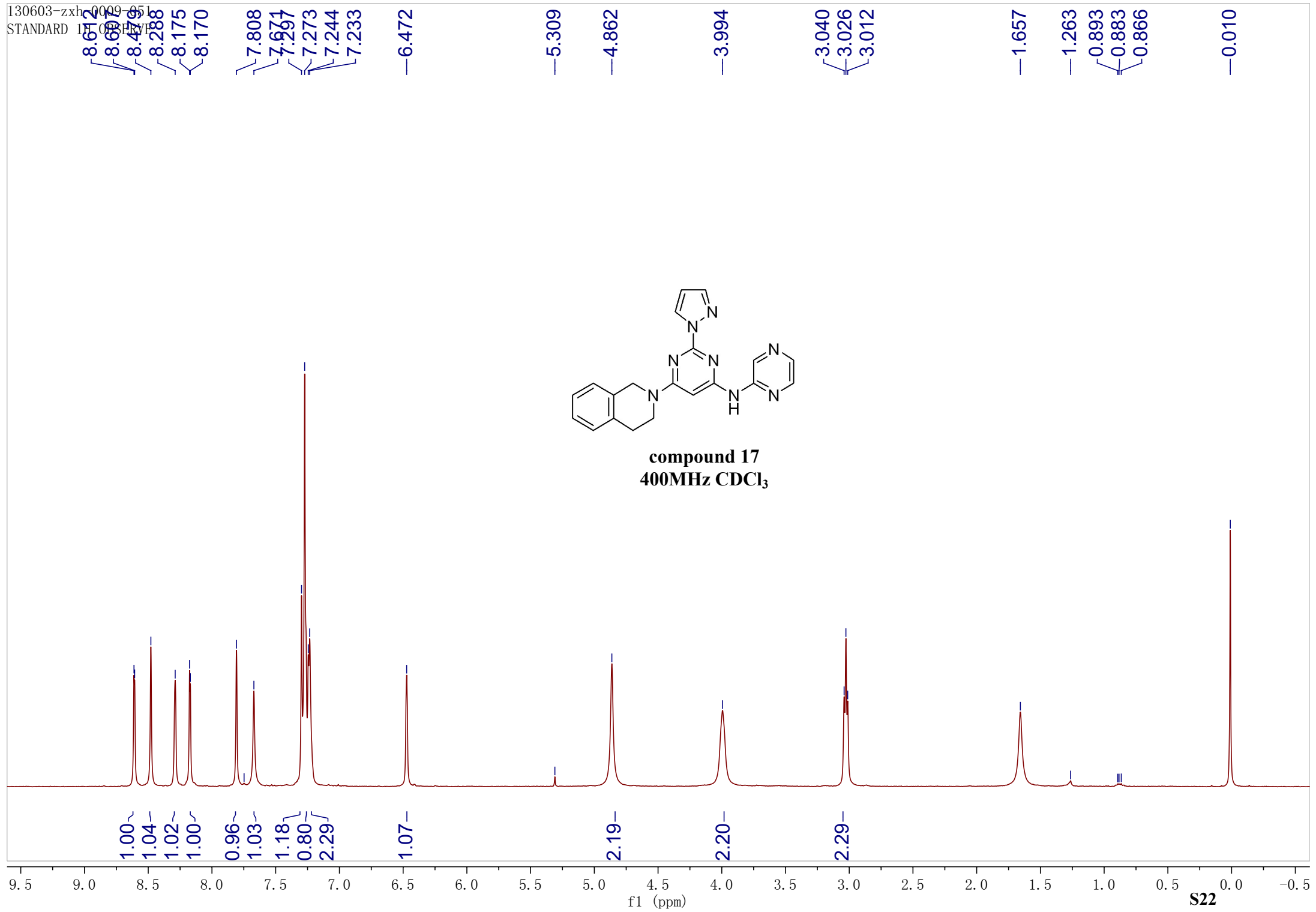


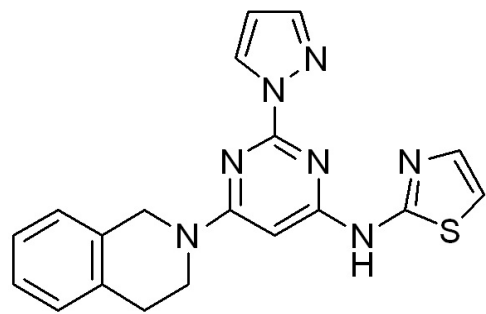
**compound 14**  
**400MHz CDCl<sub>3</sub>**



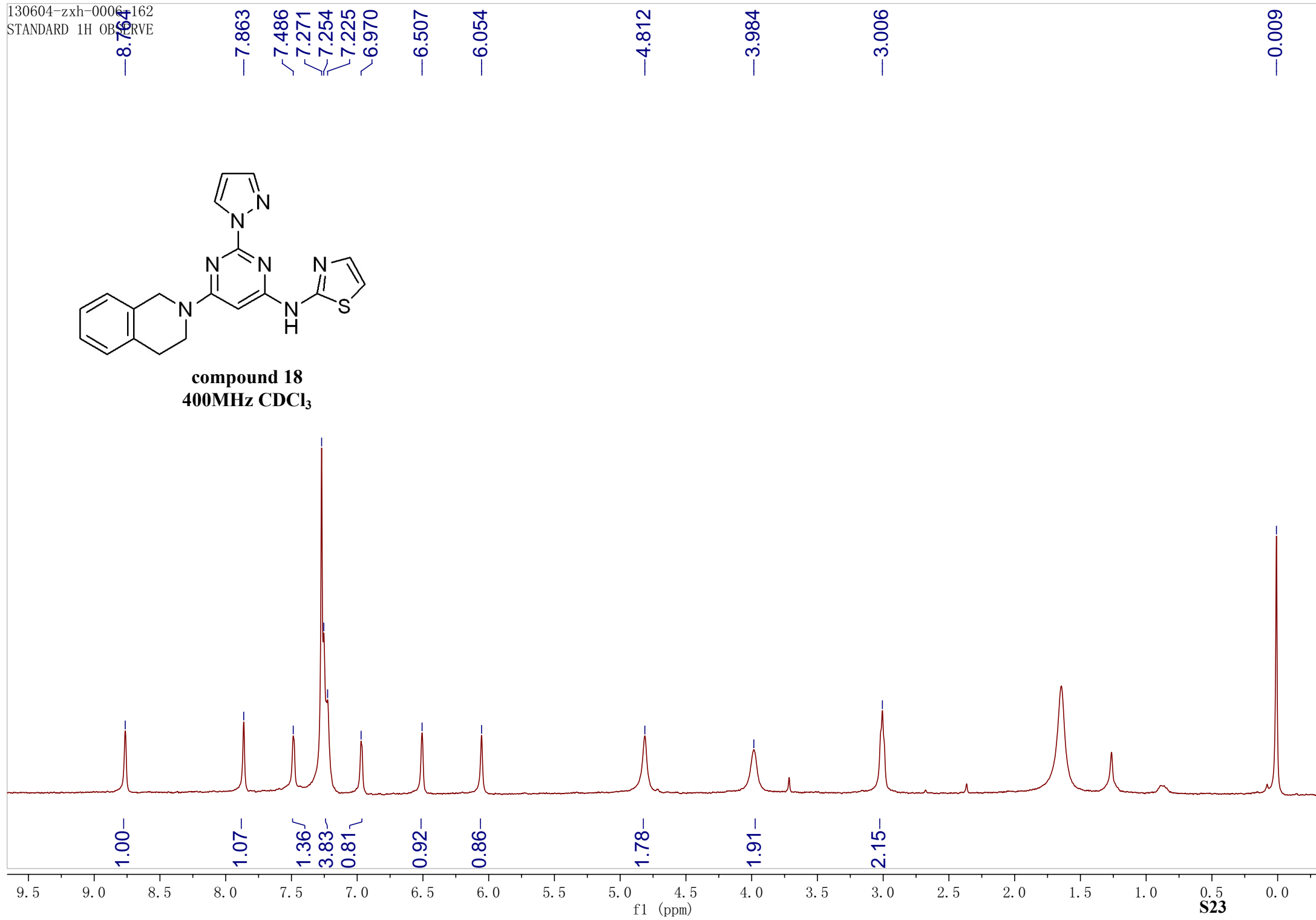








**compound 18**  
400MHz CDCl<sub>3</sub>



8.663  
8.588  
8.583

7.845  
7.784

7.273

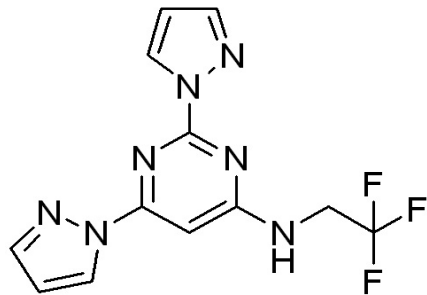
6.998

6.505

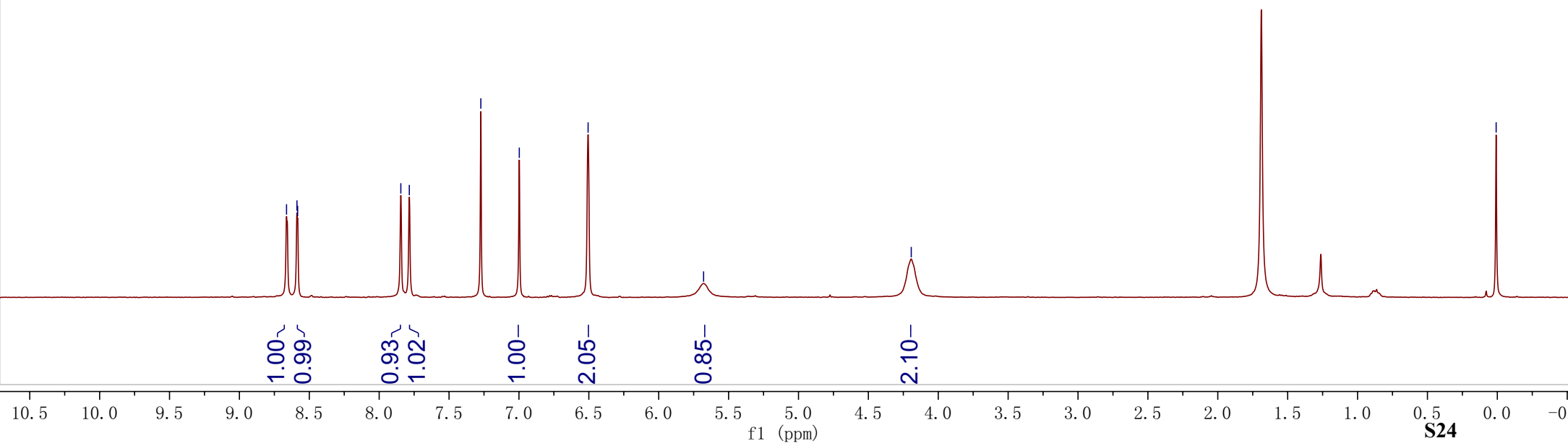
5.679

4.193

0.008

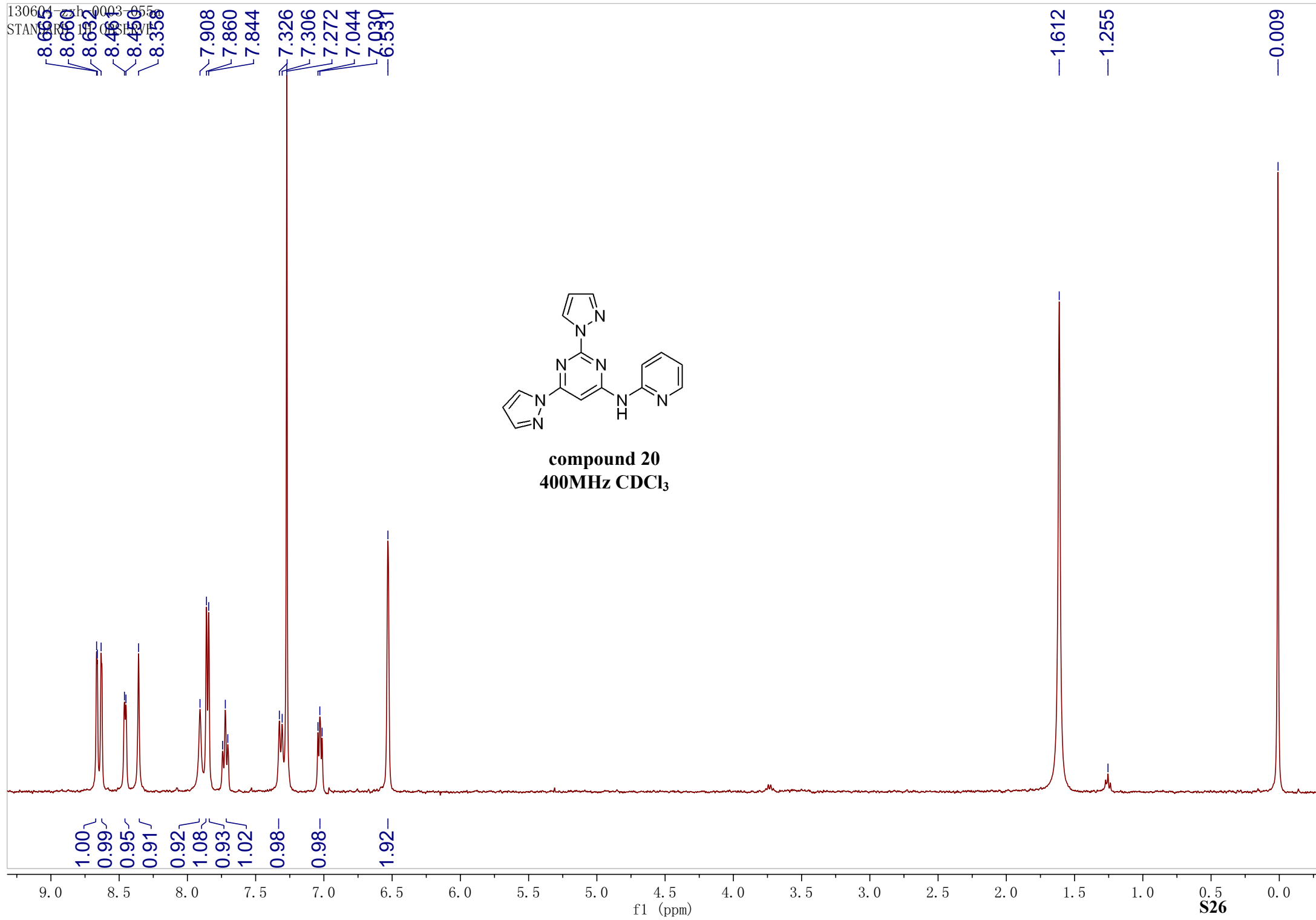


**compound 19**  
400MHz CDCl<sub>3</sub>









8.917  
8.688  
8.677  
8.633  
8.563

7.863

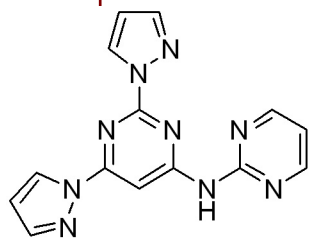
7.266

6.995

6.537

1.580

0.004



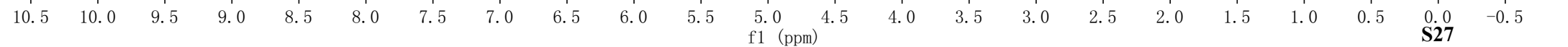
**compound 21**  
400MHz CDCl<sub>3</sub>

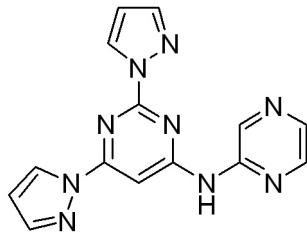
0.97  
1.62  
1.09  
1.09  
1.11

1.94

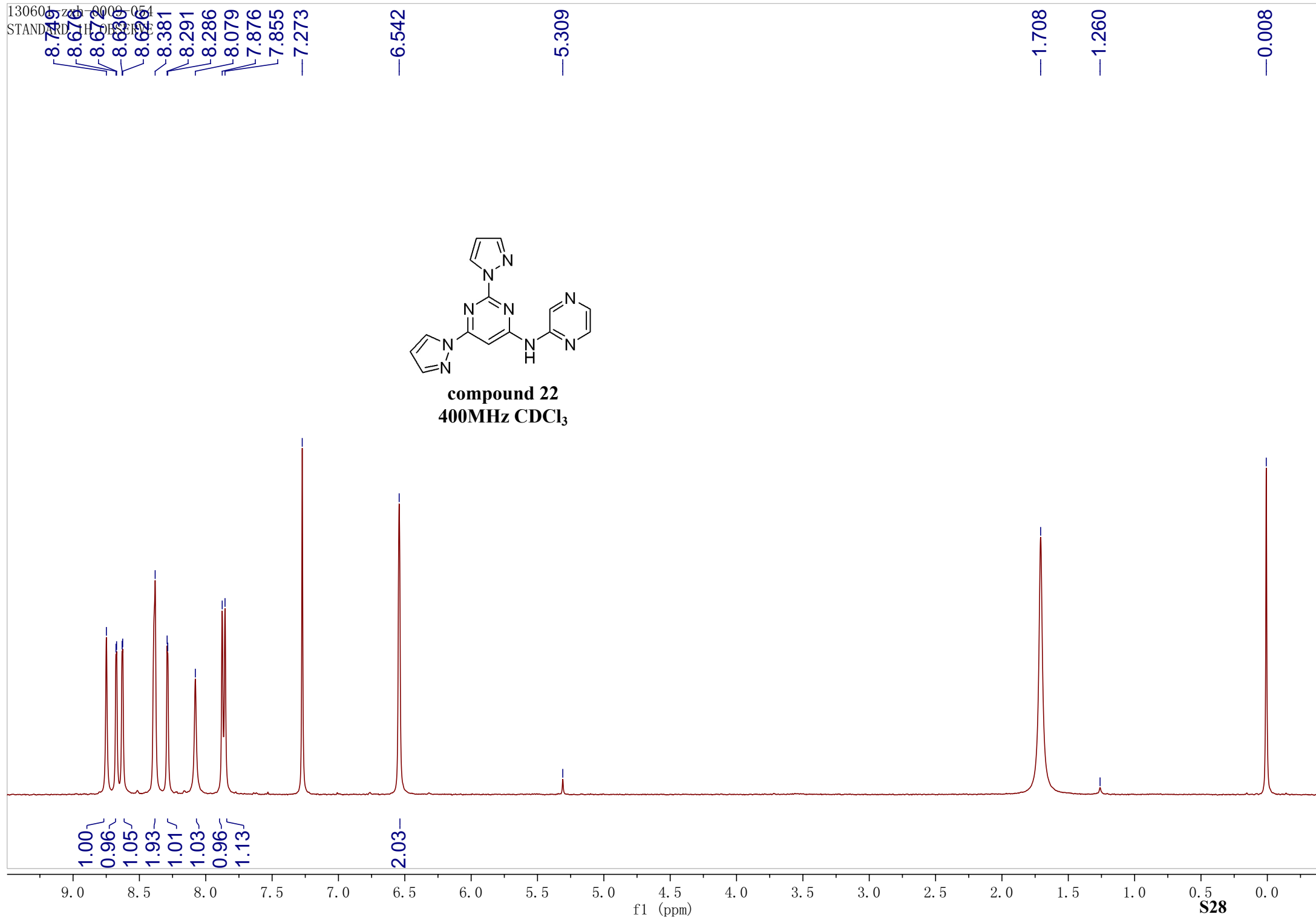
0.98

2.00





**compound 22**  
400MHz CDCl<sub>3</sub>



—12.214

~8.922

~8.809

~7.948

~7.520

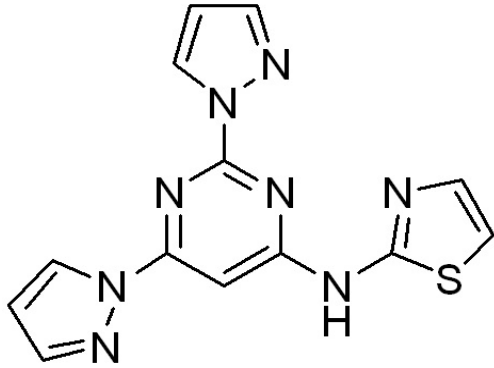
~7.387

~7.315

—6.673

—3.344

—2.500



**compound 23**  
**400MHz DMSO-d6**

1.00

0.98

1.01

2.02

1.15

0.80

1.06

2.17

