

Supporting Information

SAR study on N^2 , N^4 -disubstitued pyrimidine-2,4-diamines as effective CDK2/CDK9 inhibitors and antiproliferative agents

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1. Yields of target compounds

Compd.	Yield	Compd.	Yield
2a	50%	3d	22%
2b	46%	3e	47%
2c	20%	3f	55%
2d	24%	3g	40%
2e	53%	3h	68%
2f	57%	3i	36%
2g	38%	3j	51%
2h	42%	3k	74%
2i	20%	3l	28%
3a	52%	3m	51%
3b	53%	3n	34%
3c	61%	3o	57%

2. HPLC chromatogram for 2a, 2d and 3b

The compounds were analyzed on a Shimadzu LC-6AD instrument.

Column: (4.6*150mm, Shimadzu Shim-pack VP-ODS)

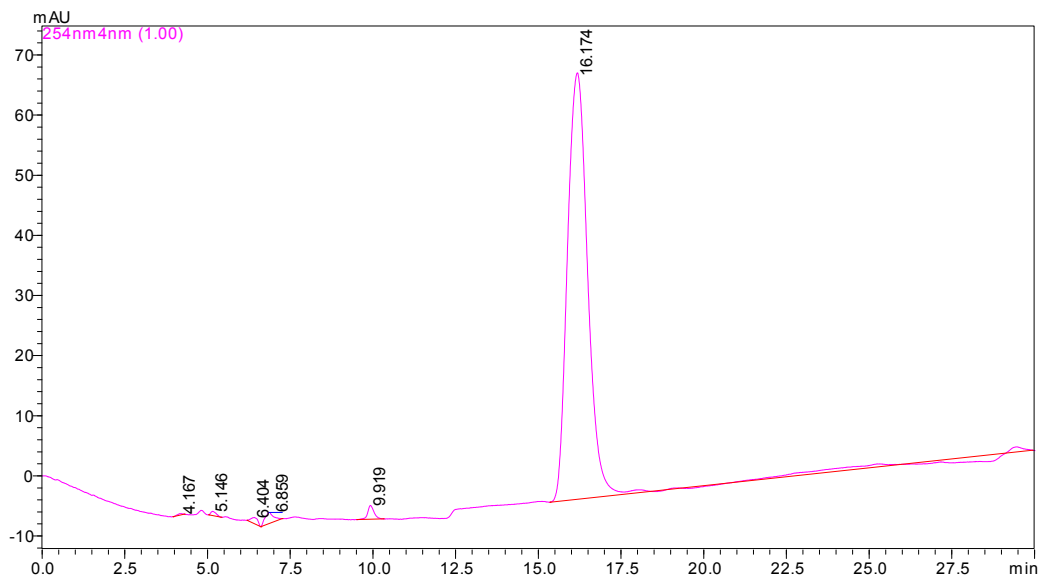
Column temperature: 40 °C

Mobile phase: methanol/water with 2% Et₃N (v/v, gradient elution method: from 70:30 to 100:0)

Elution time: 30 mins

Flow rate: 0.3 ml/min

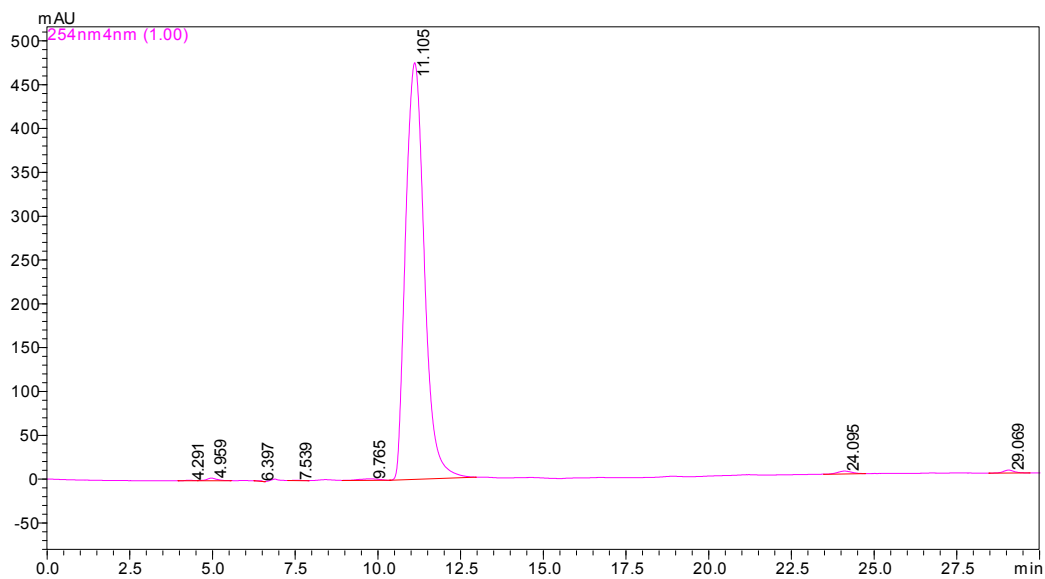
(1) For 2a:



Retention time	Area	Height	Proportion
4.167	2943	270	0.0950
5.146	7902	699	0.2551
6.404	14195	993	0.4582

6.859	33718	1871	1.0884
9.919	30677	2302	0.9903
16.174	3008464	70928	97.1130

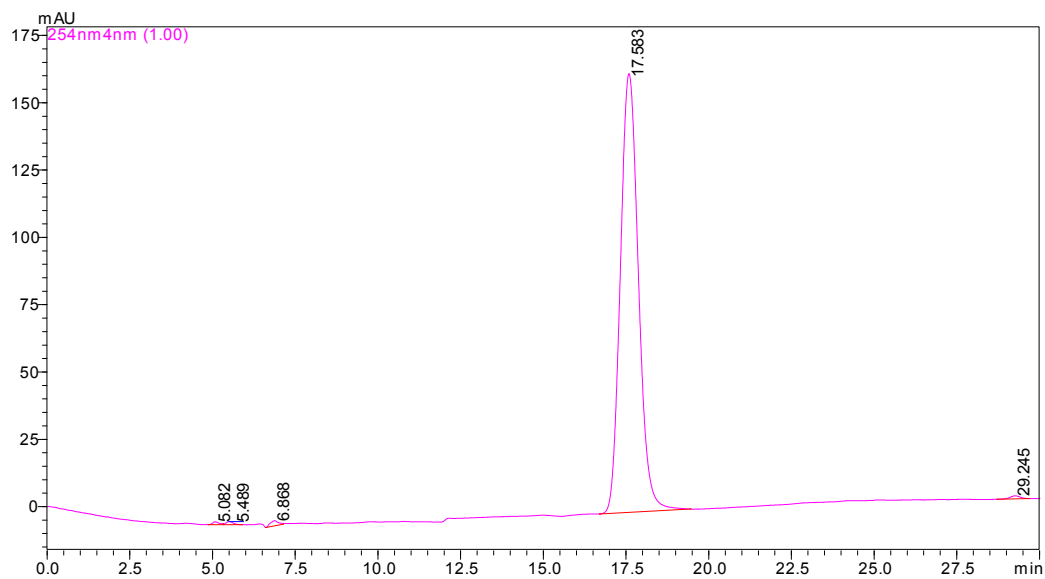
(2) For 2d:



Retention time	Area	Height	Proportion
4.291	12622	620	0.0663
4.959	63908	2987	0.3359
6.397	8337	699	0.0438
7.539	6348	378	0.0334
9.765	69941	1696	0.3676

11.105	18694153	475274	98.2547
24.095	94687	3181	0.4977
29.069	76218	3342	0.4006

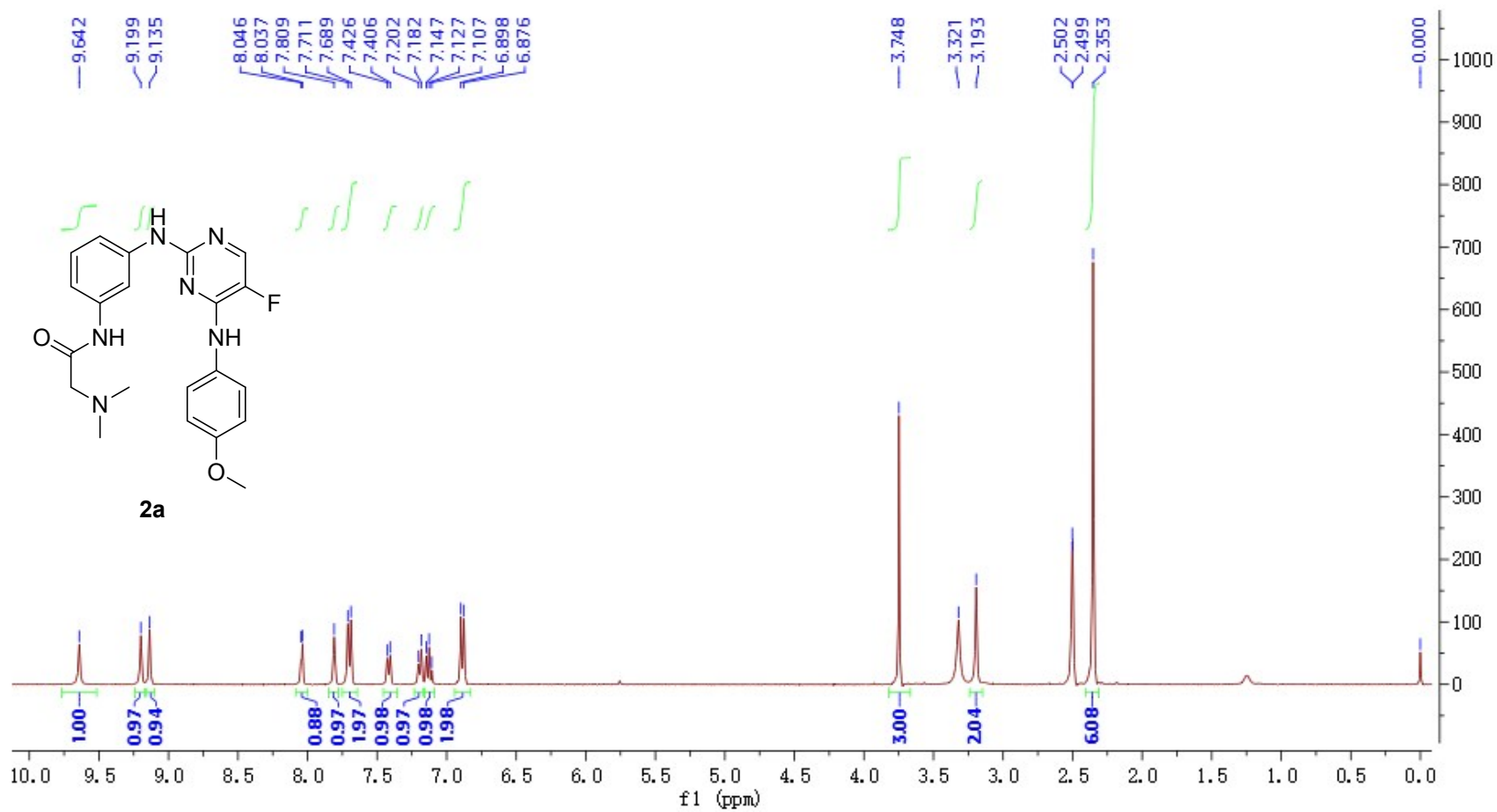
(3) For 3b:



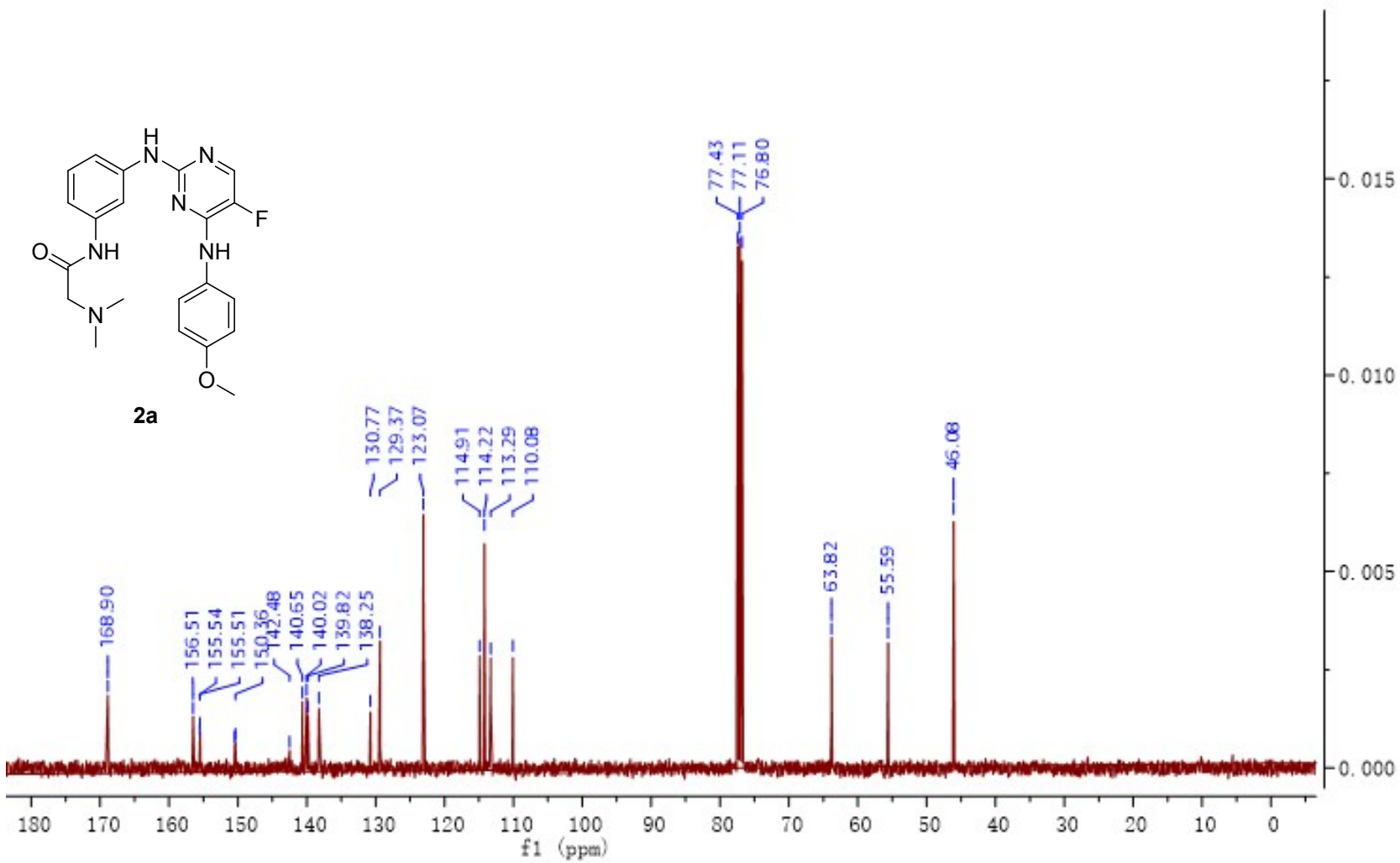
Retention time	Area	Height	Proportion
5.082	13819	1022	0.2203
5.489	17491	1125	0.2788
6.868	32959	1993	0.5254
17.583	6183849	162931	98.5839
29.245	24556	1148	0.3915

3. NMR spectra for target compounds

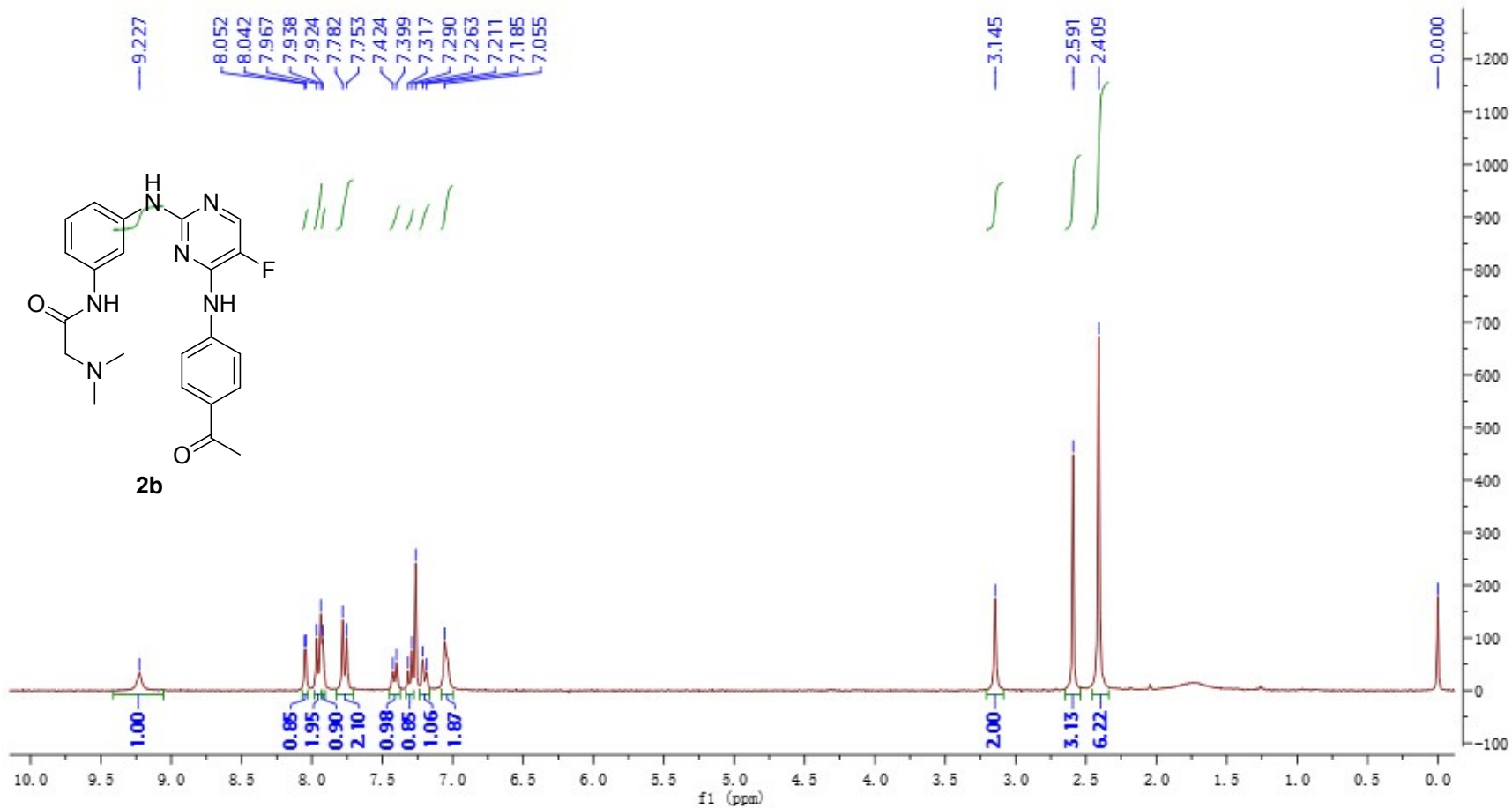
¹H NMR spectrum for Compound 2a:



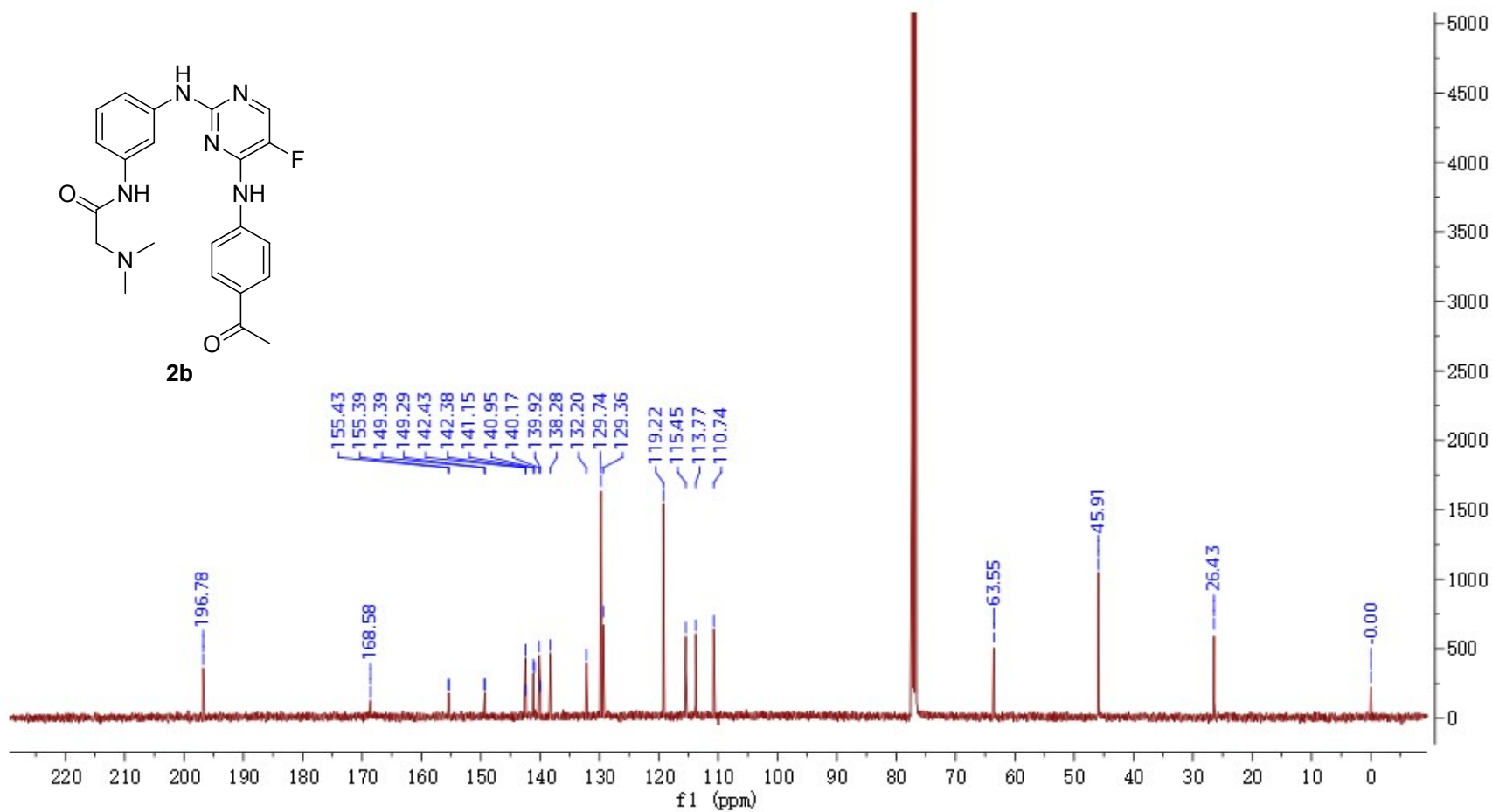
¹³C NMR spectrum for Compound 2a:



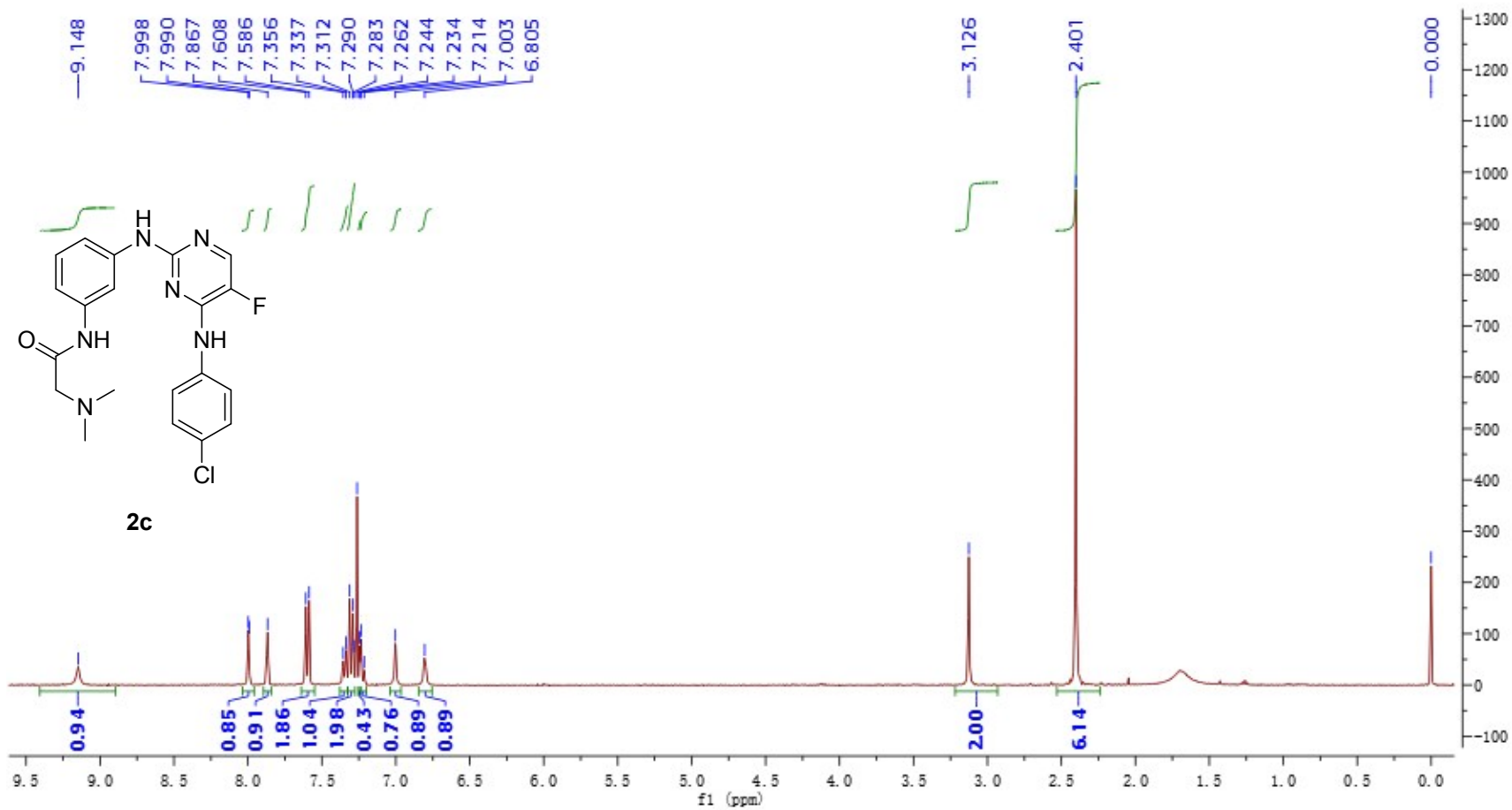
¹H NMR spectrum for Compound 2b:



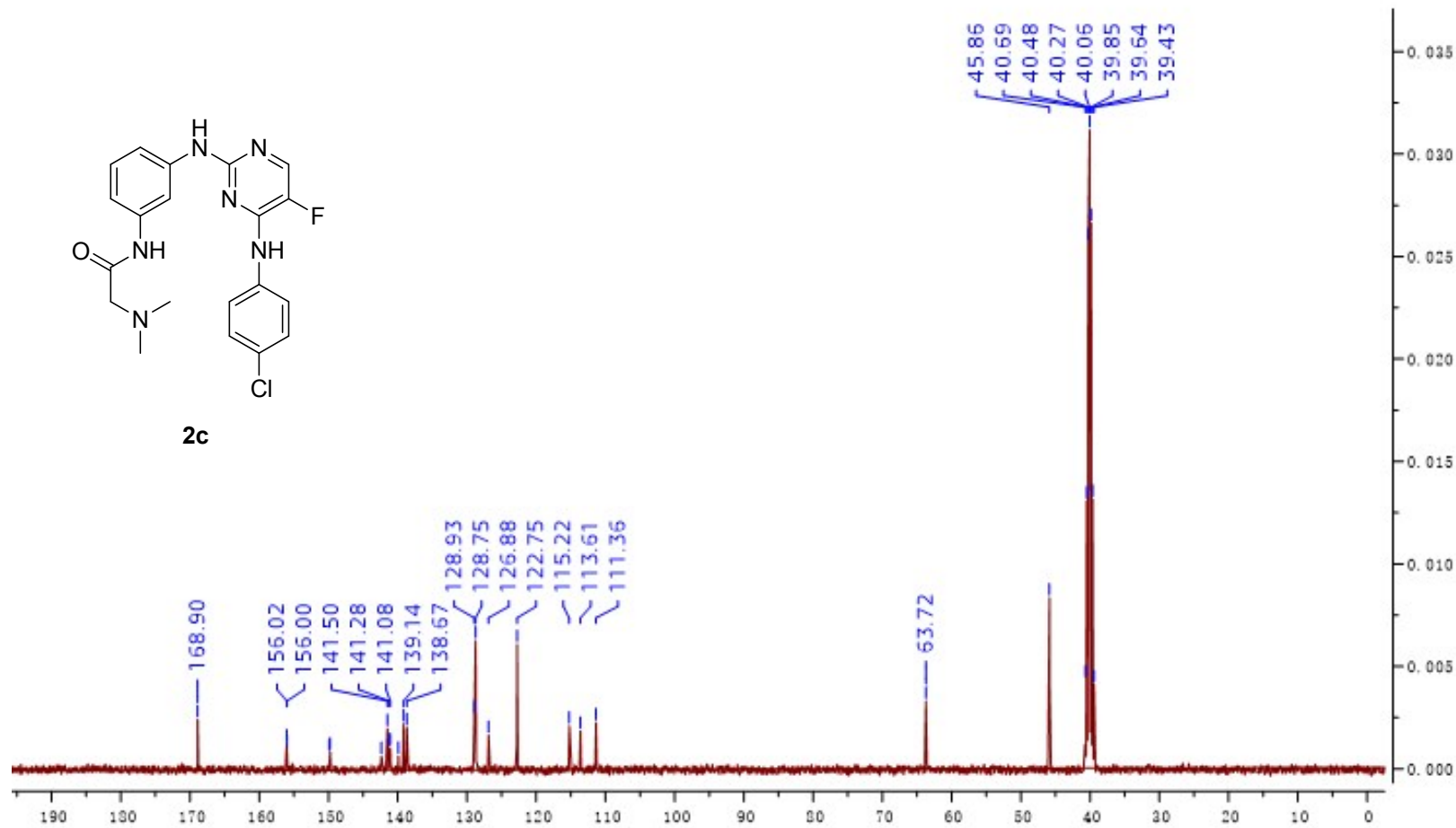
¹³C NMR spectrum for Compound 2b:



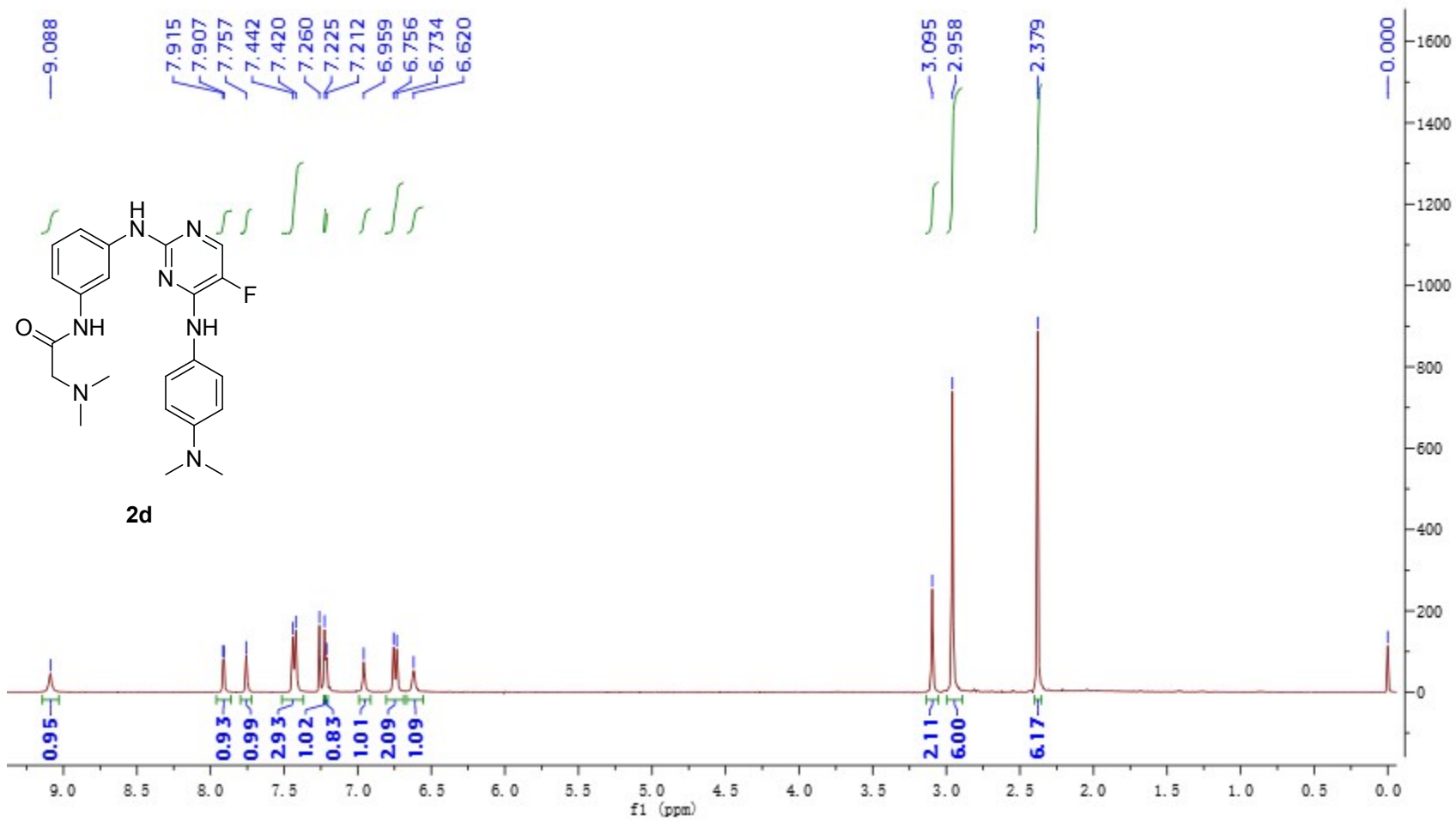
¹H NMR spectrum for Compound 2c:



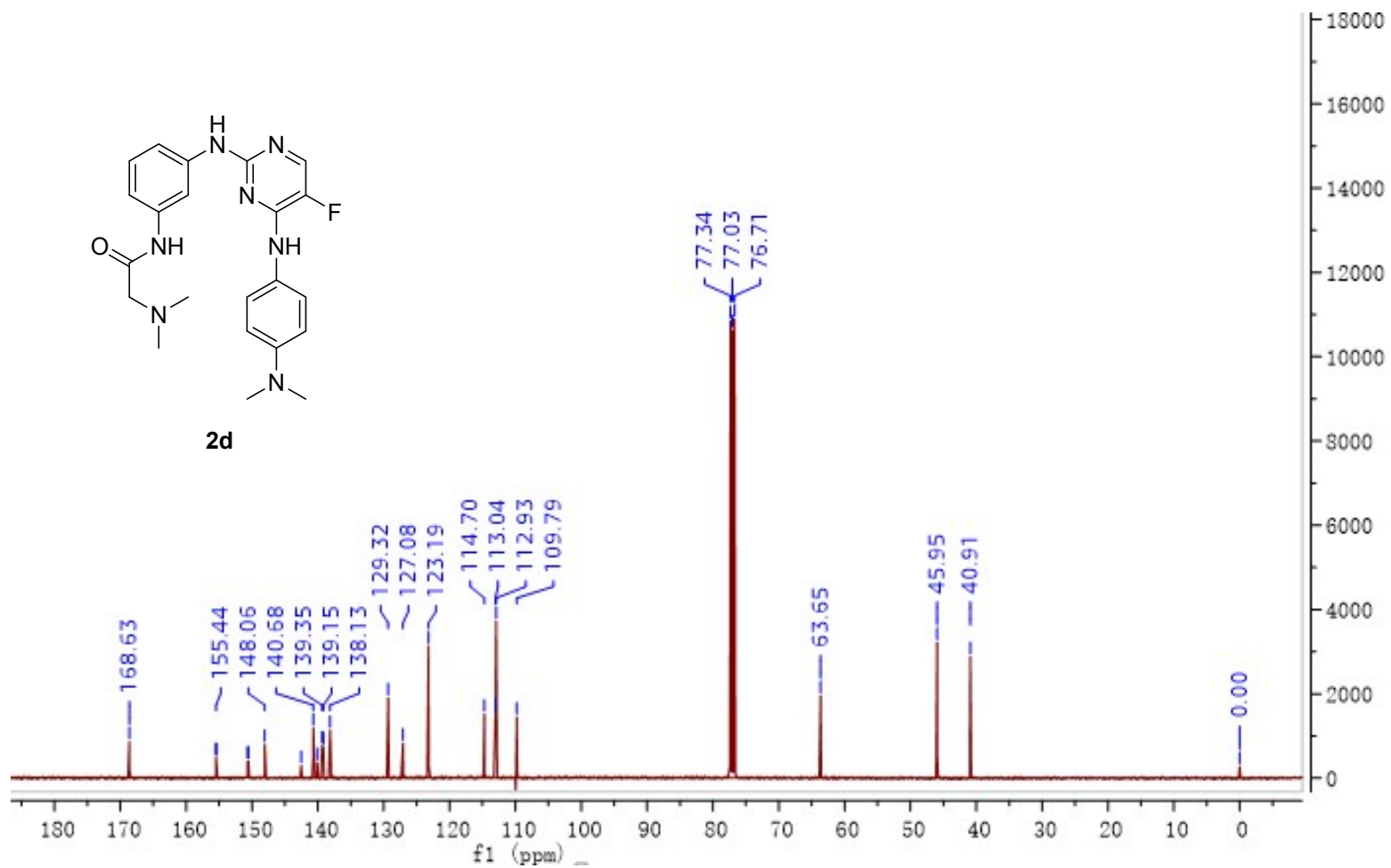
¹³C NMR spectrum for Compound **2c**:



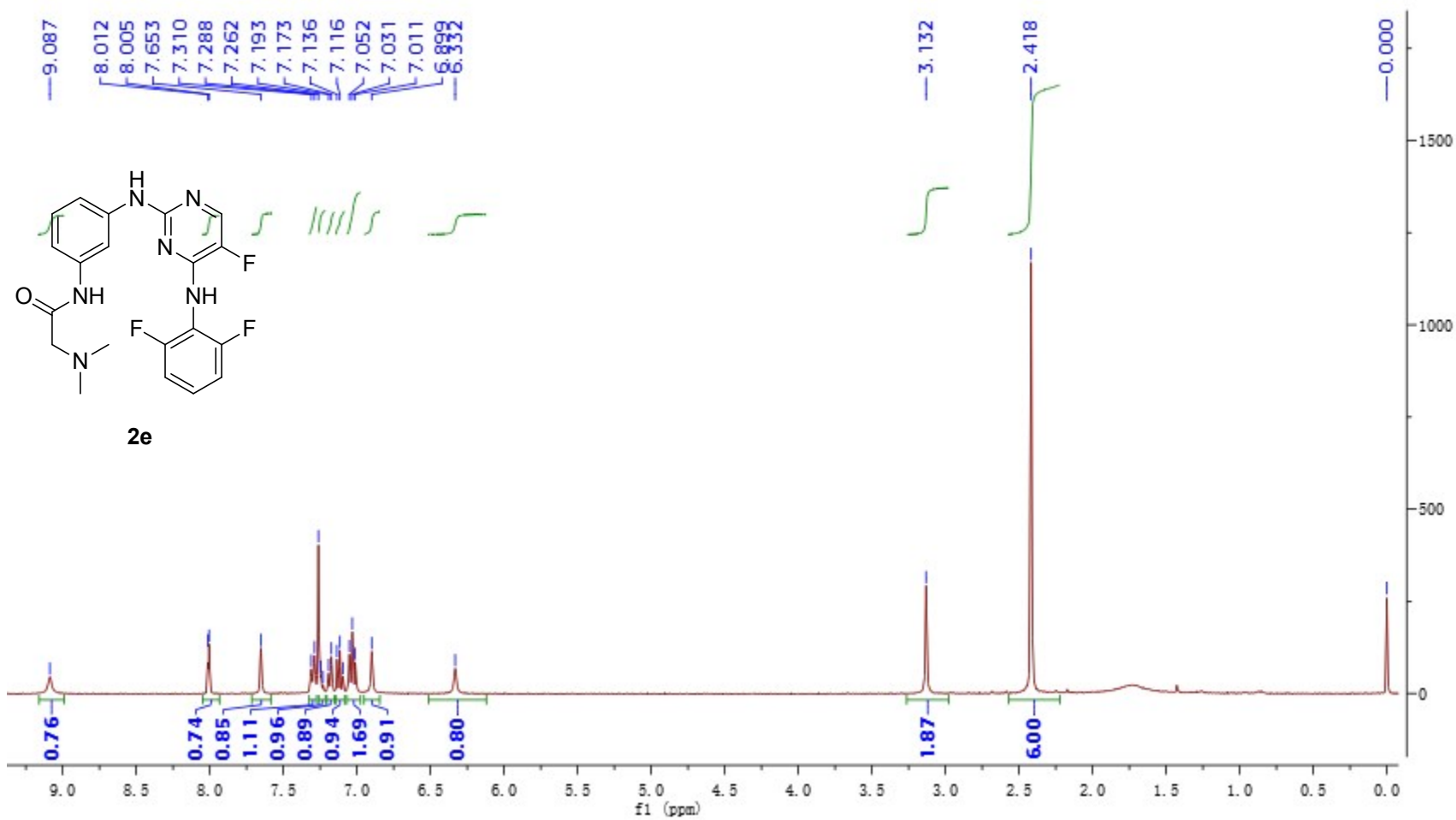
¹H NMR spectrum for Compound 2d:



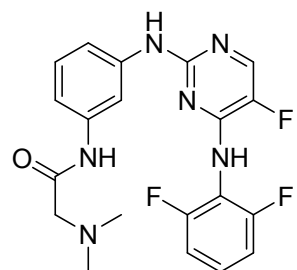
¹³C NMR spectrum for Compound 2d:



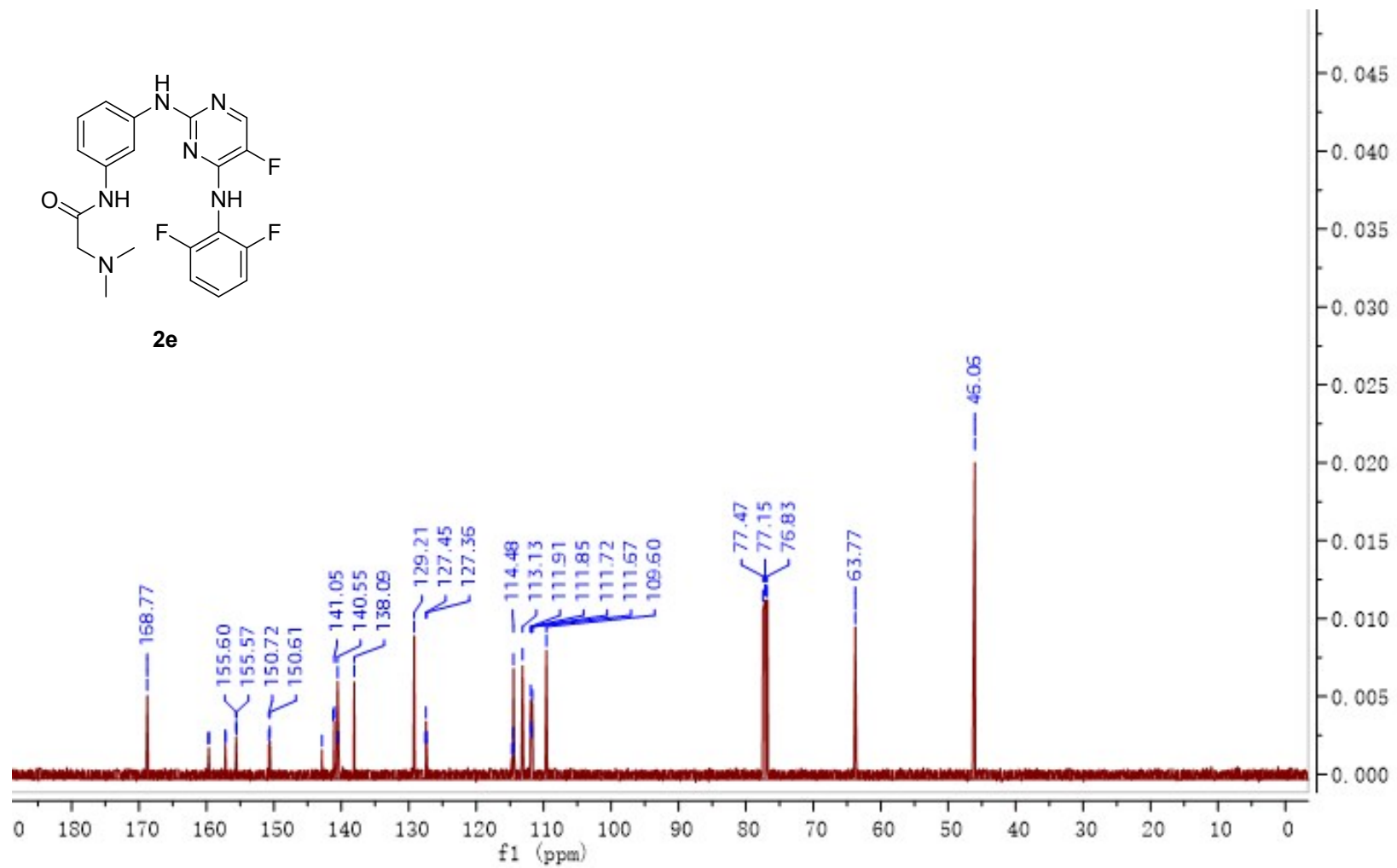
¹H NMR spectrum for Compound 2e:



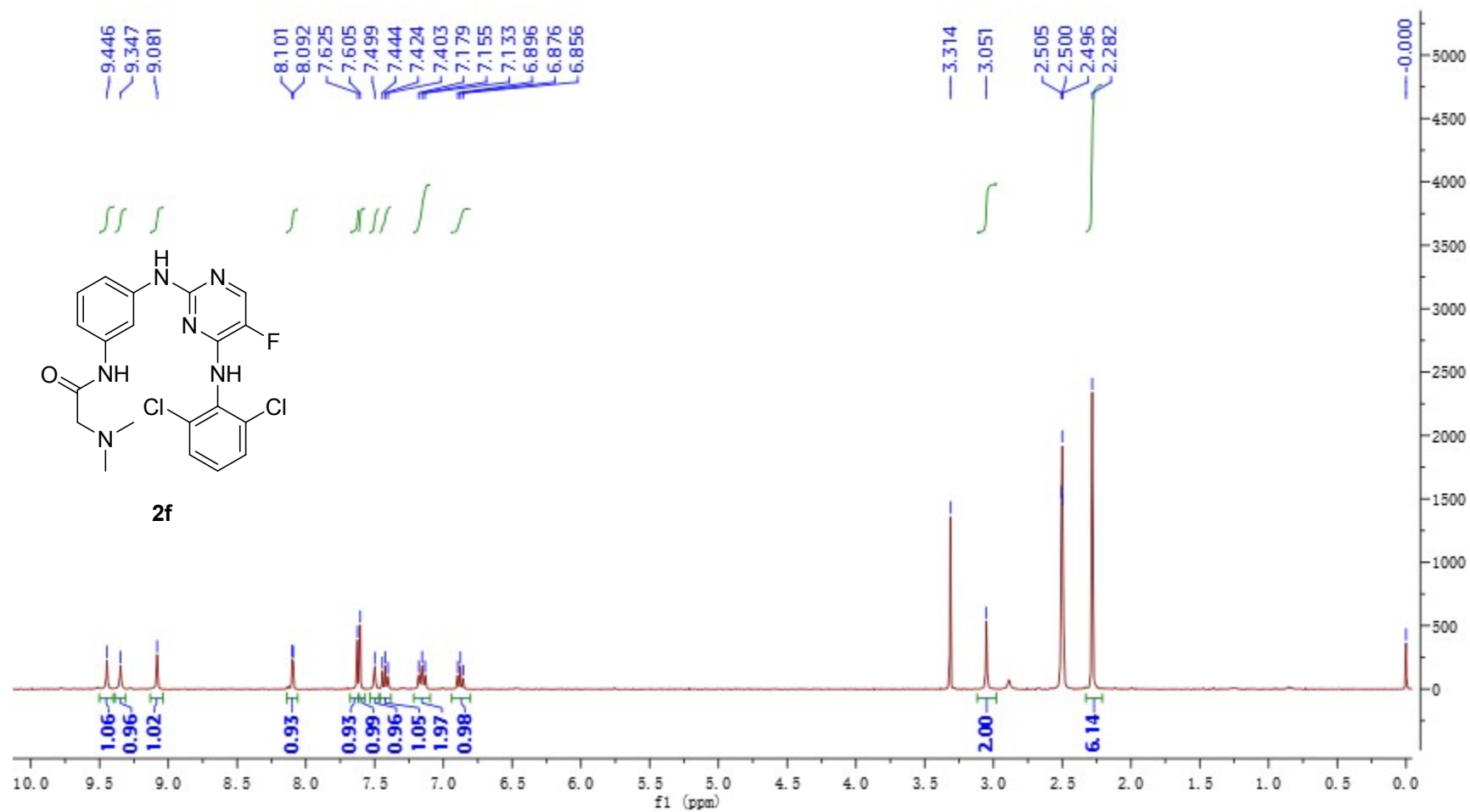
¹³C NMR spectrum for Compound 2e:



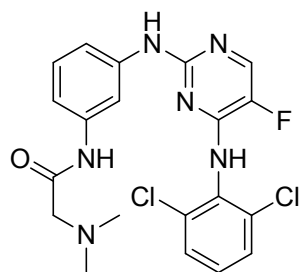
2e



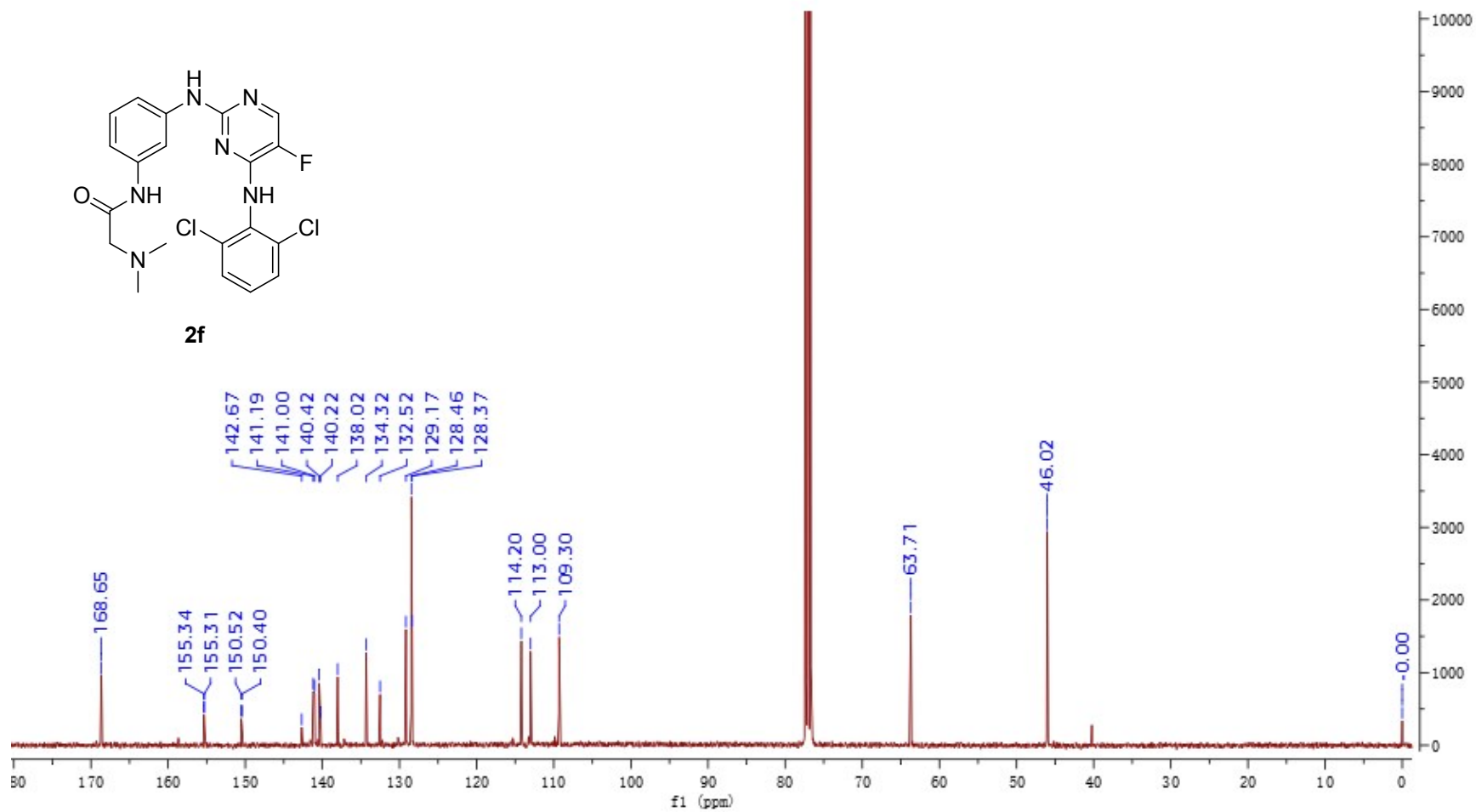
¹H NMR spectrum for Compound 2f:



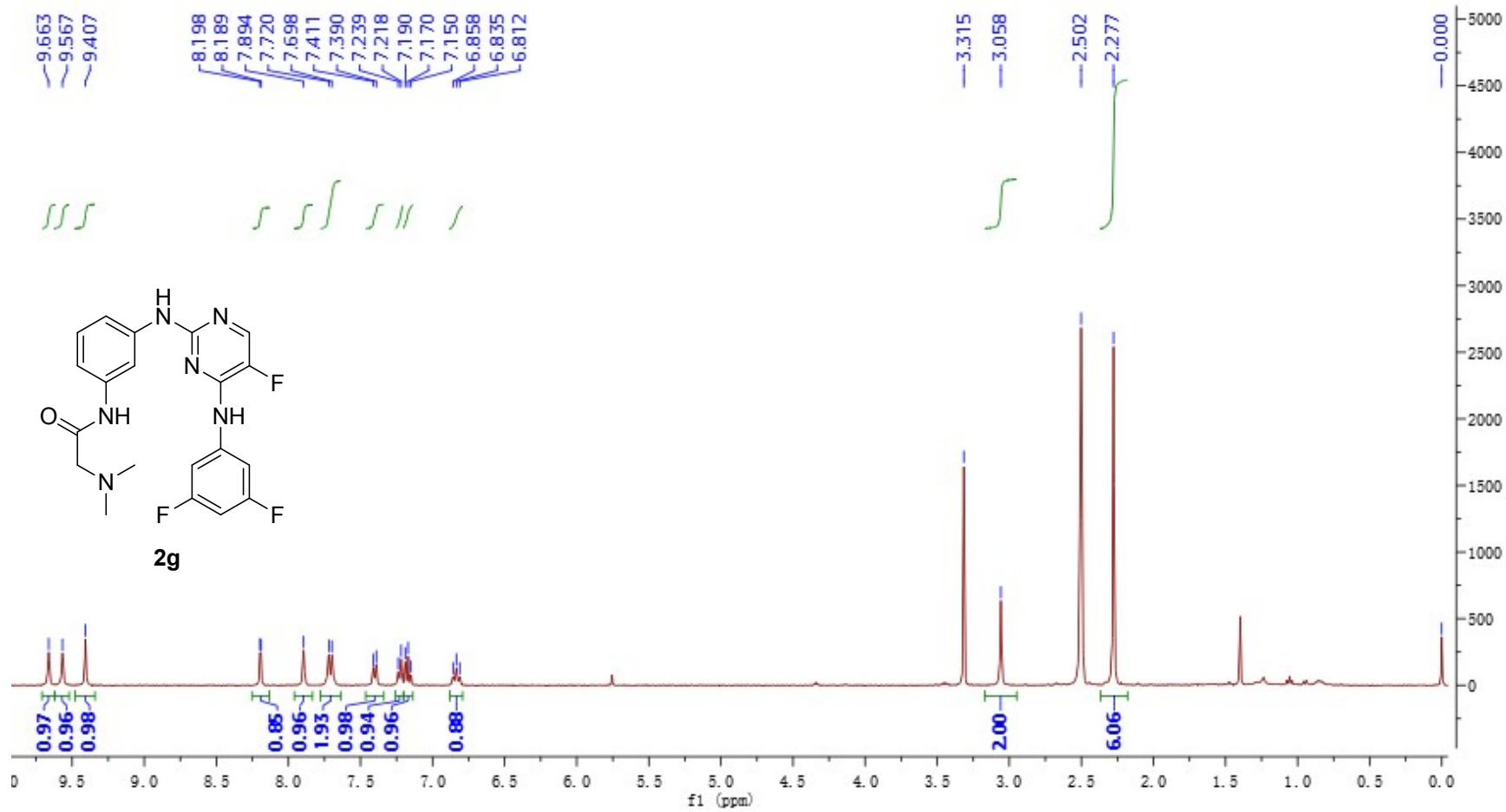
¹³C NMR spectrum for Compound 2f:



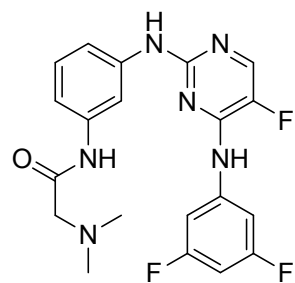
2f



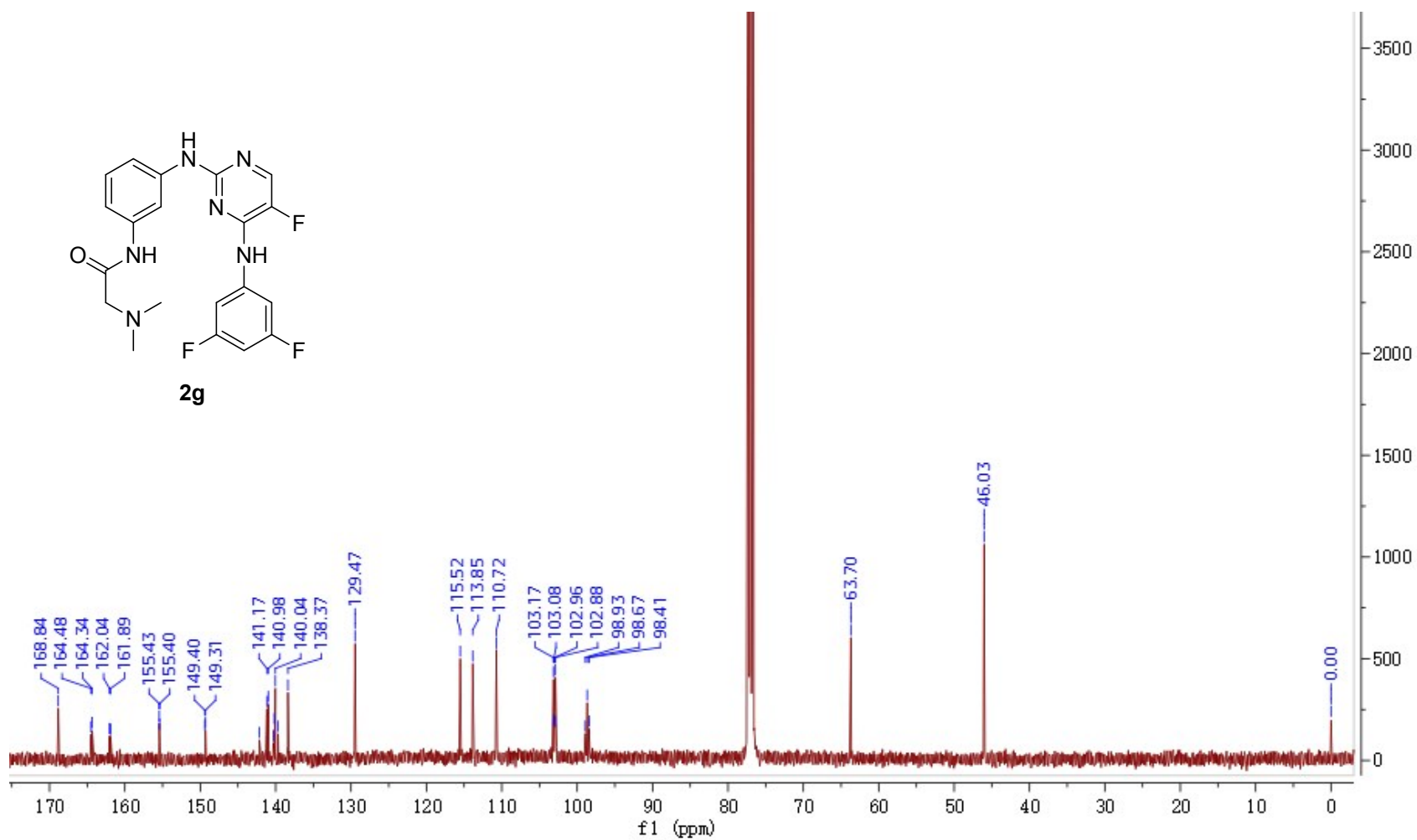
¹H NMR spectrum for Compound 2g:



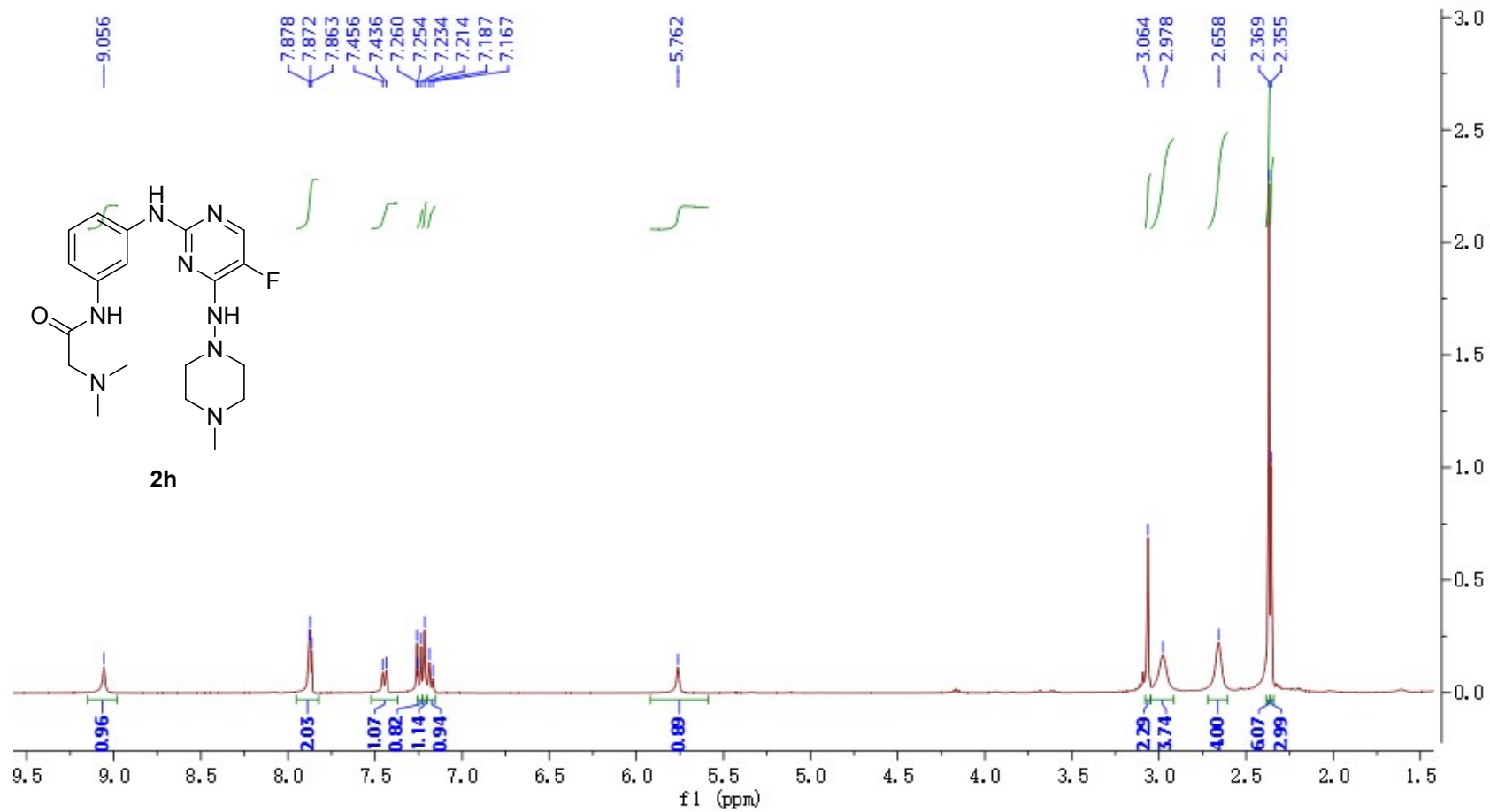
¹³C NMR spectrum for Compound 2g:



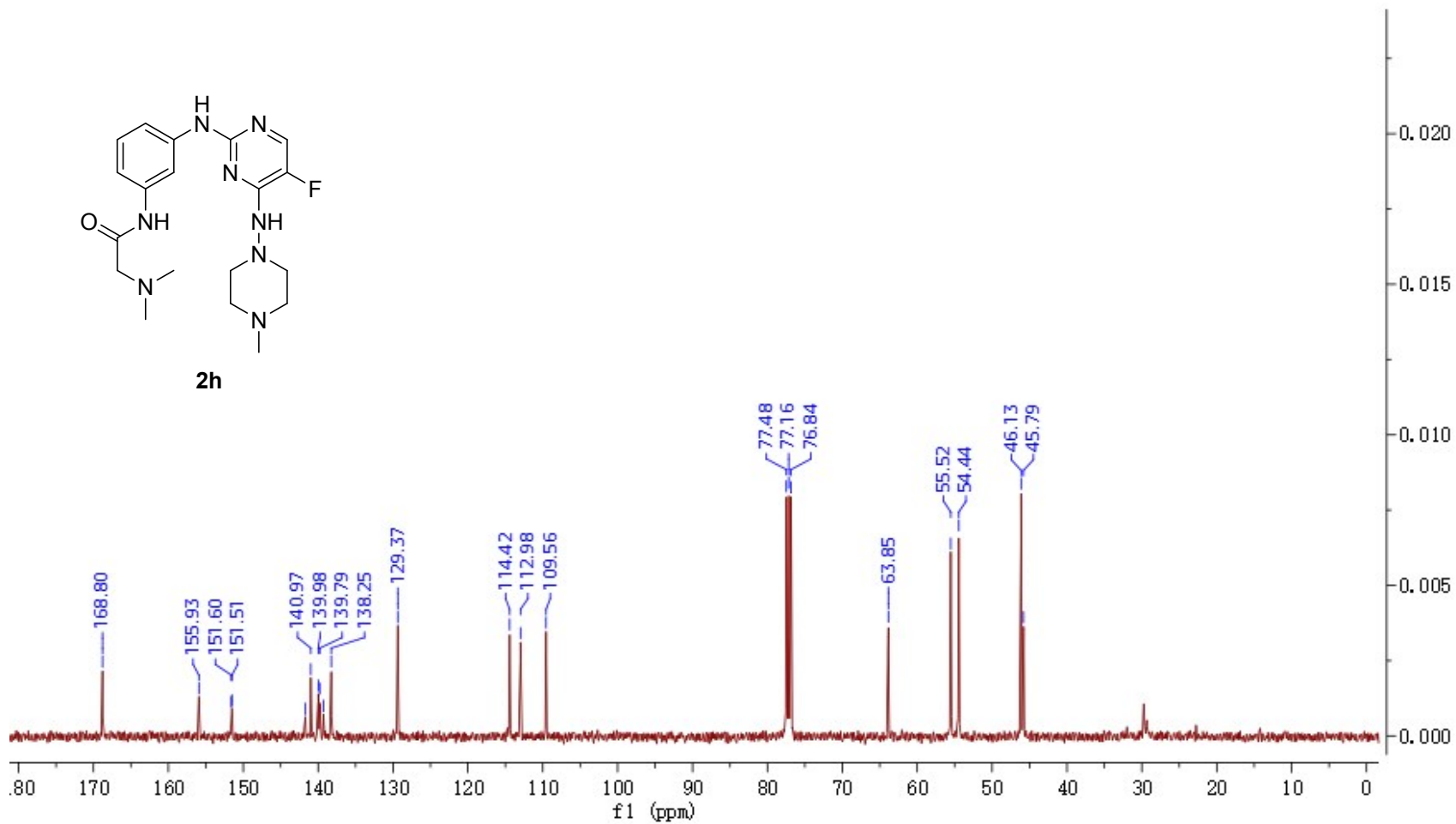
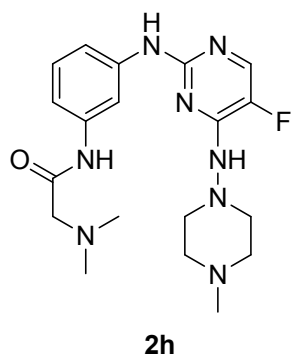
2g



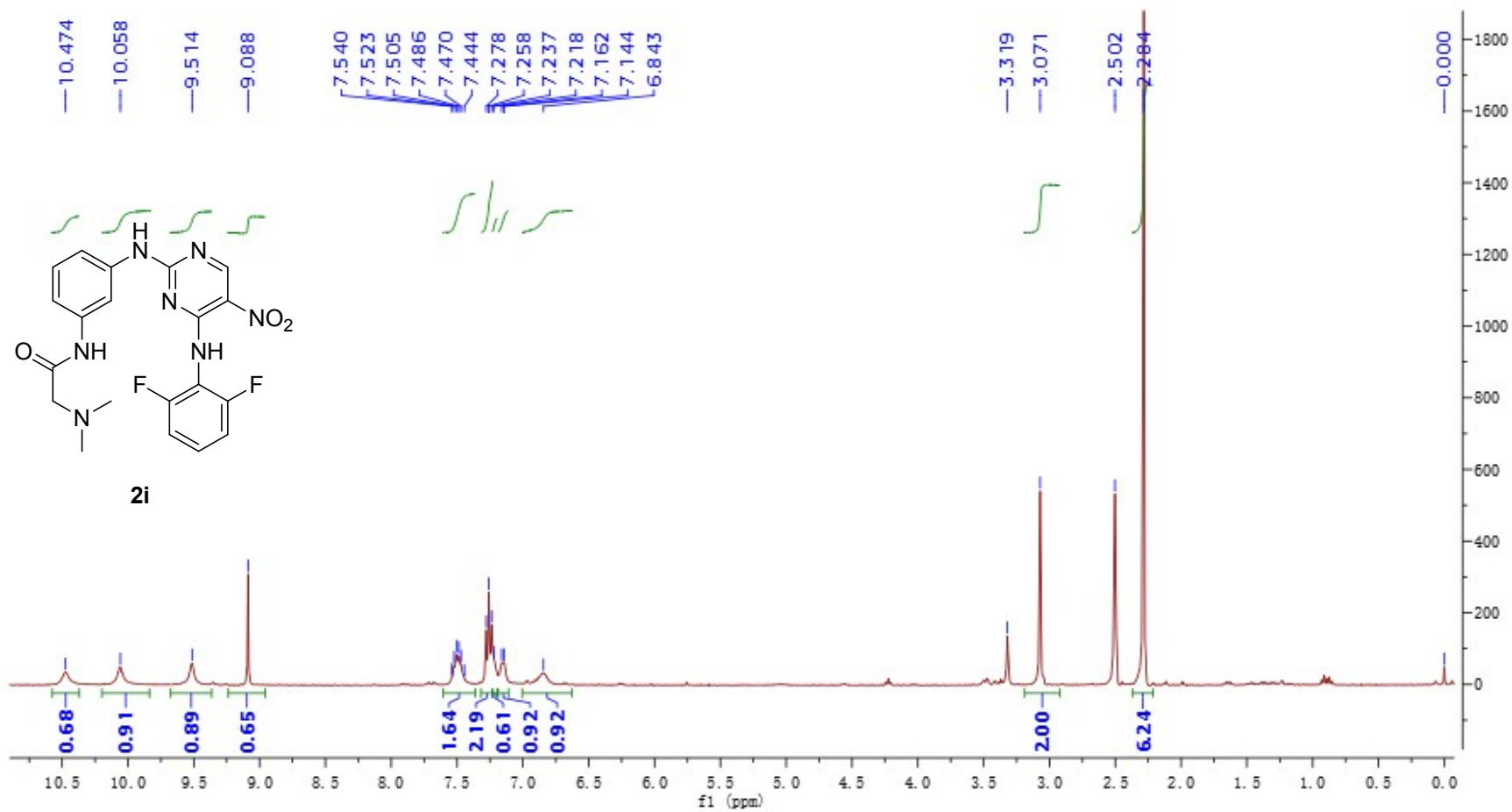
¹H NMR spectrum for Compound 2h:



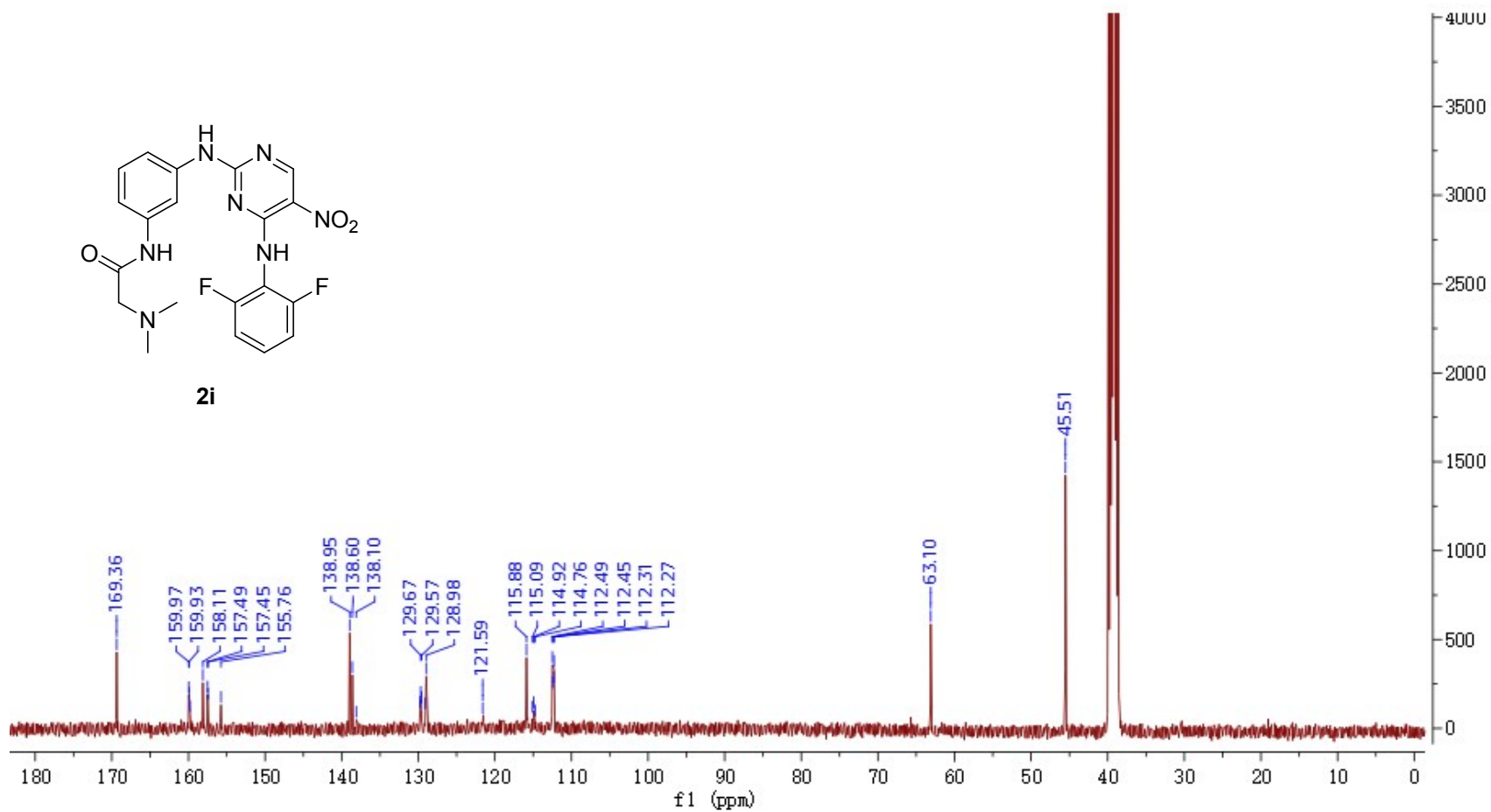
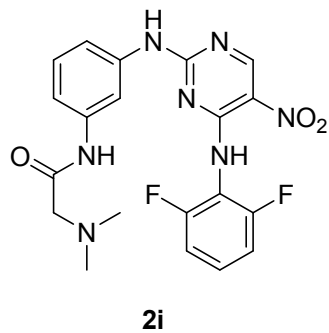
¹³C NMR spectrum for Compound 2h:



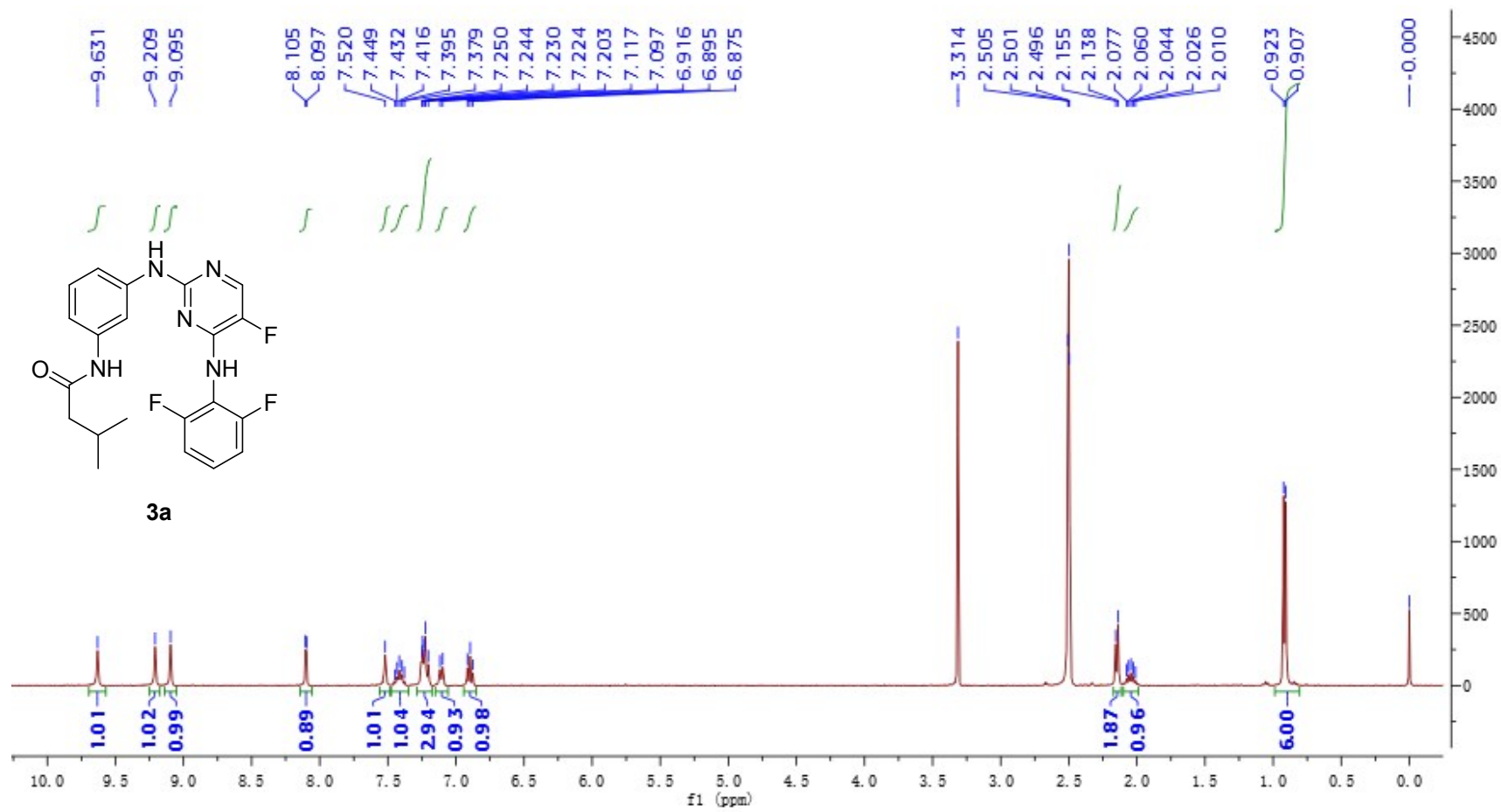
¹H NMR spectrum for Compound 2i:



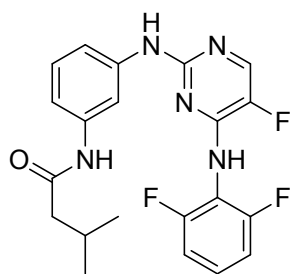
¹³C NMR spectrum for Compound 2i:



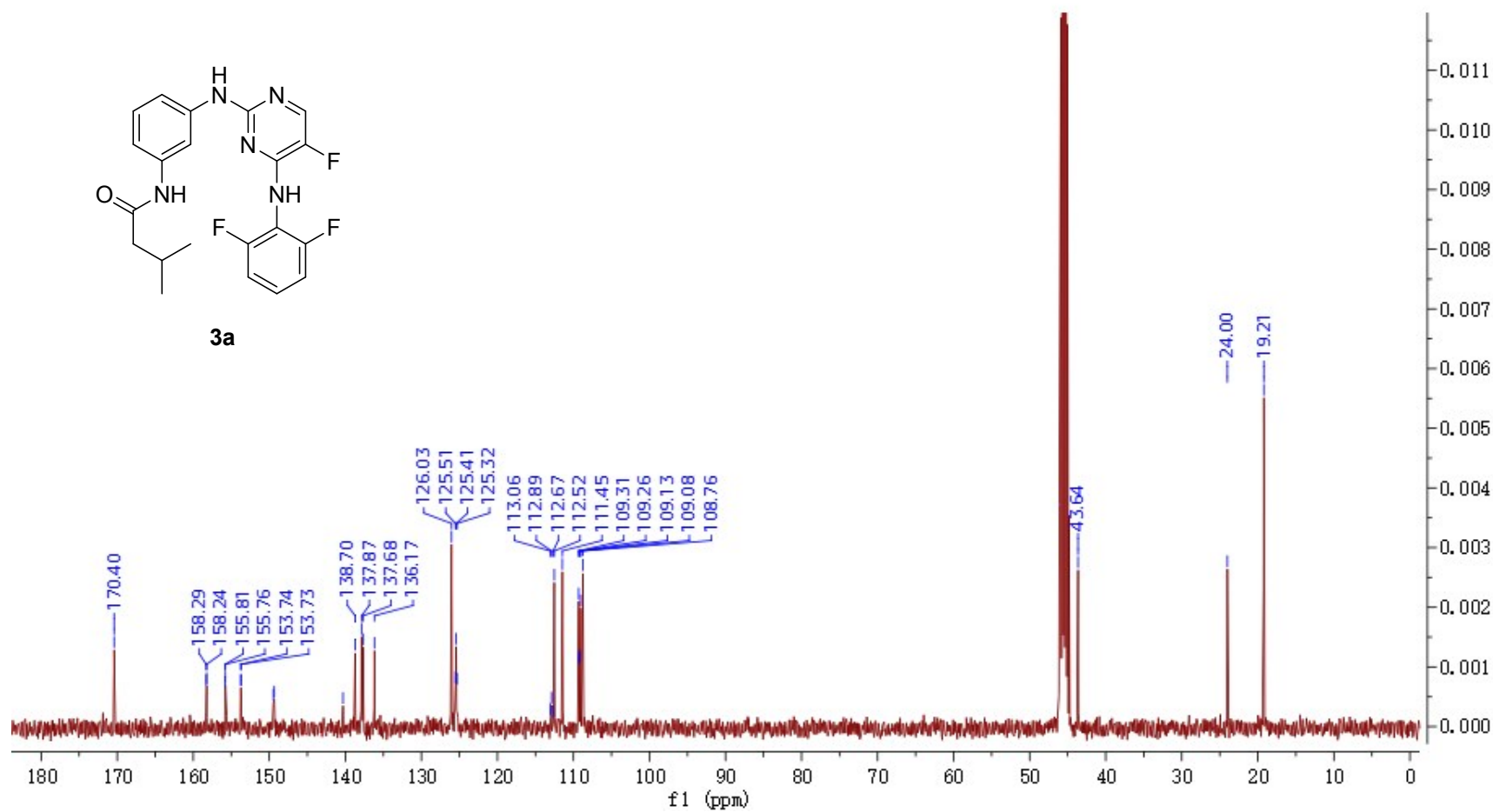
¹H NMR spectrum for Compound 3a:



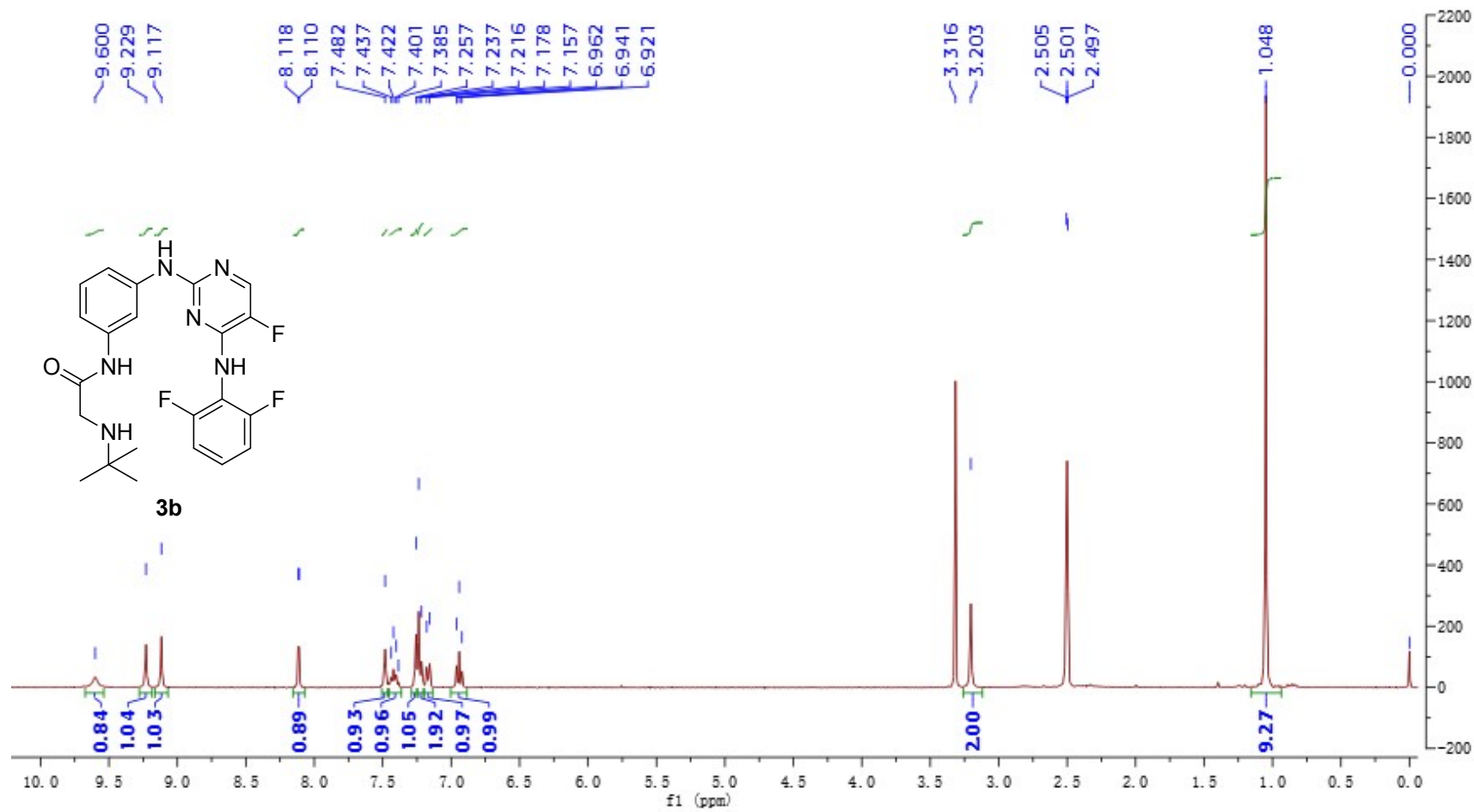
¹³C NMR spectrum for Compound 3a:



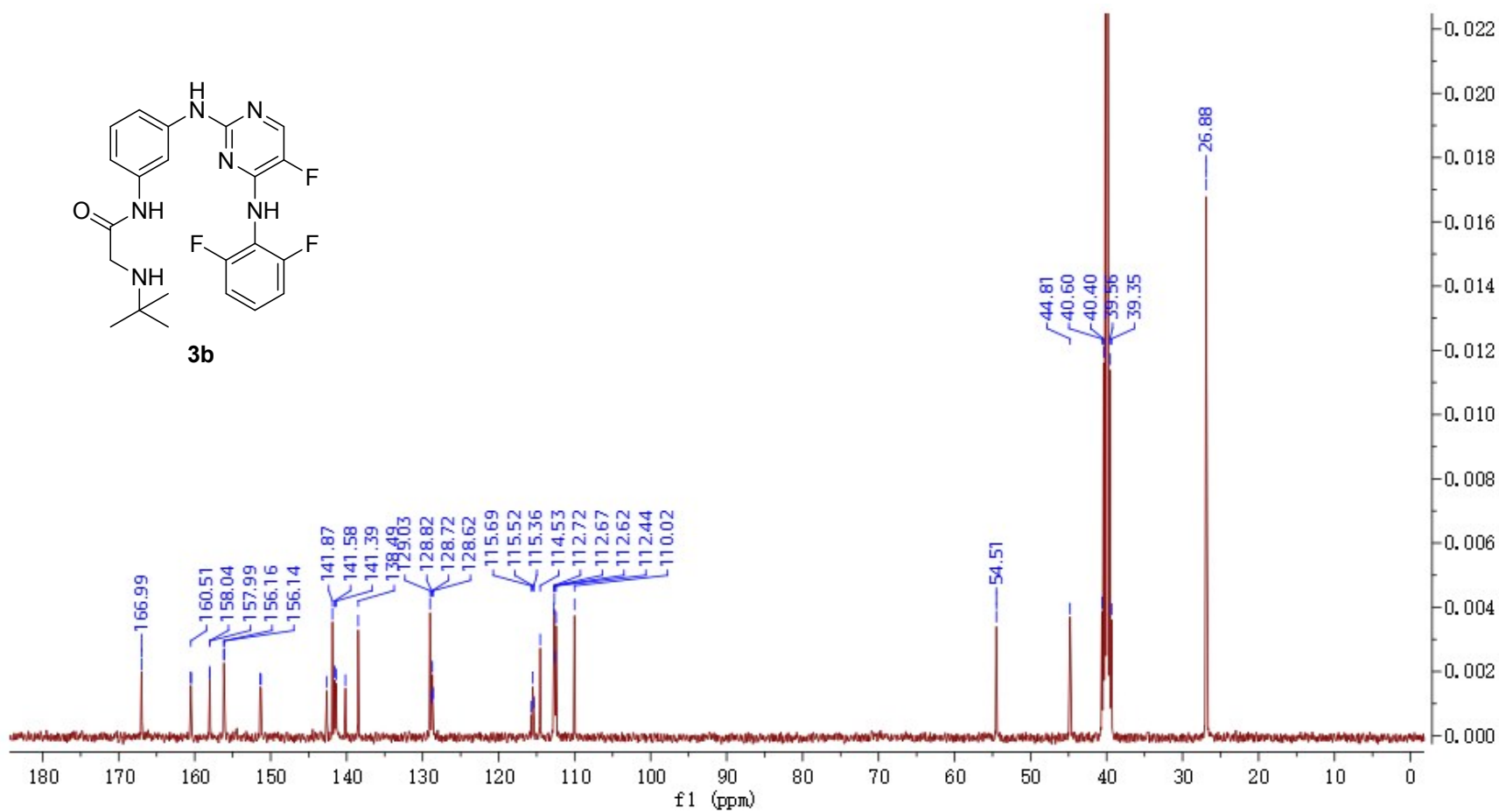
3a



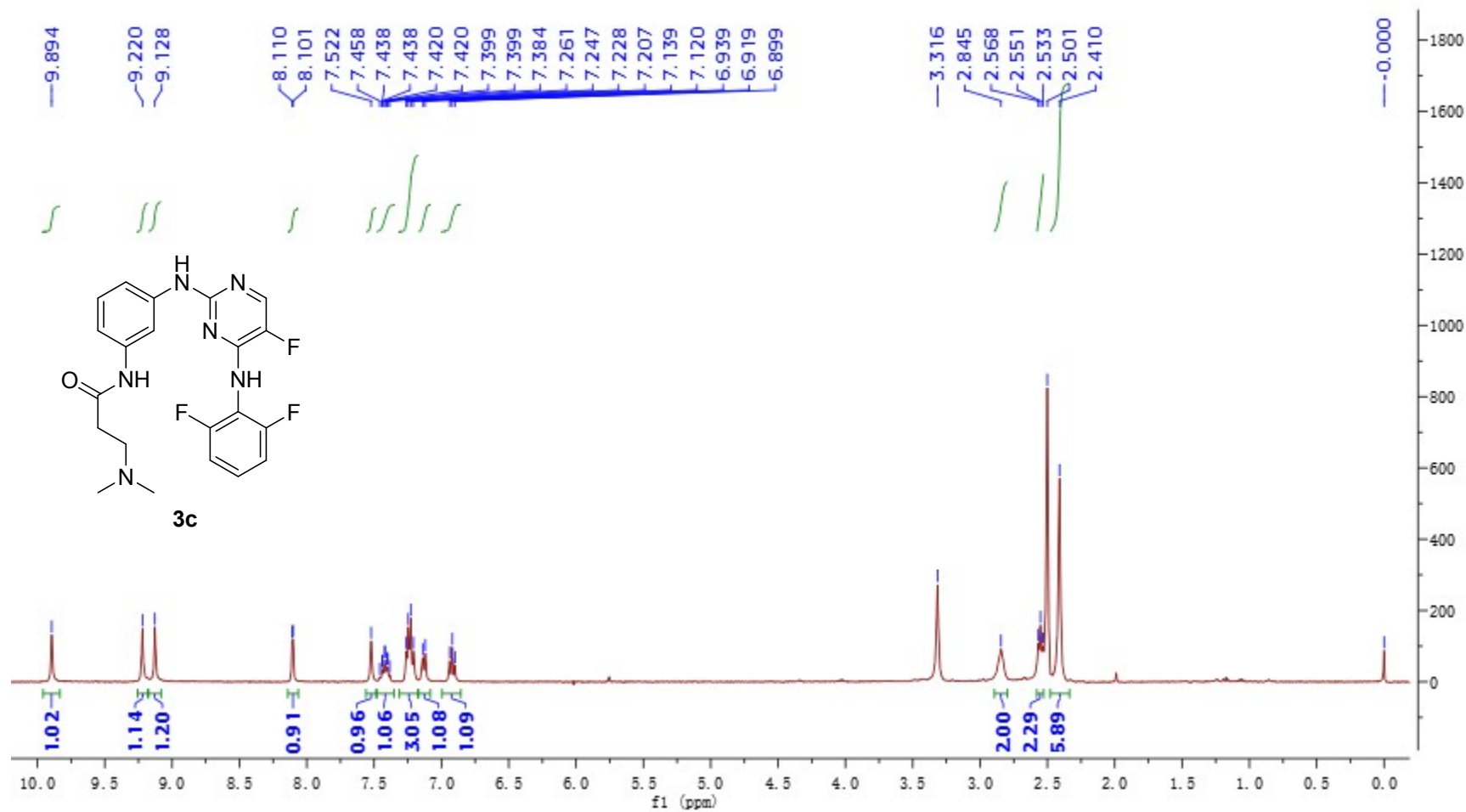
¹H NMR spectrum for Compound 3b:



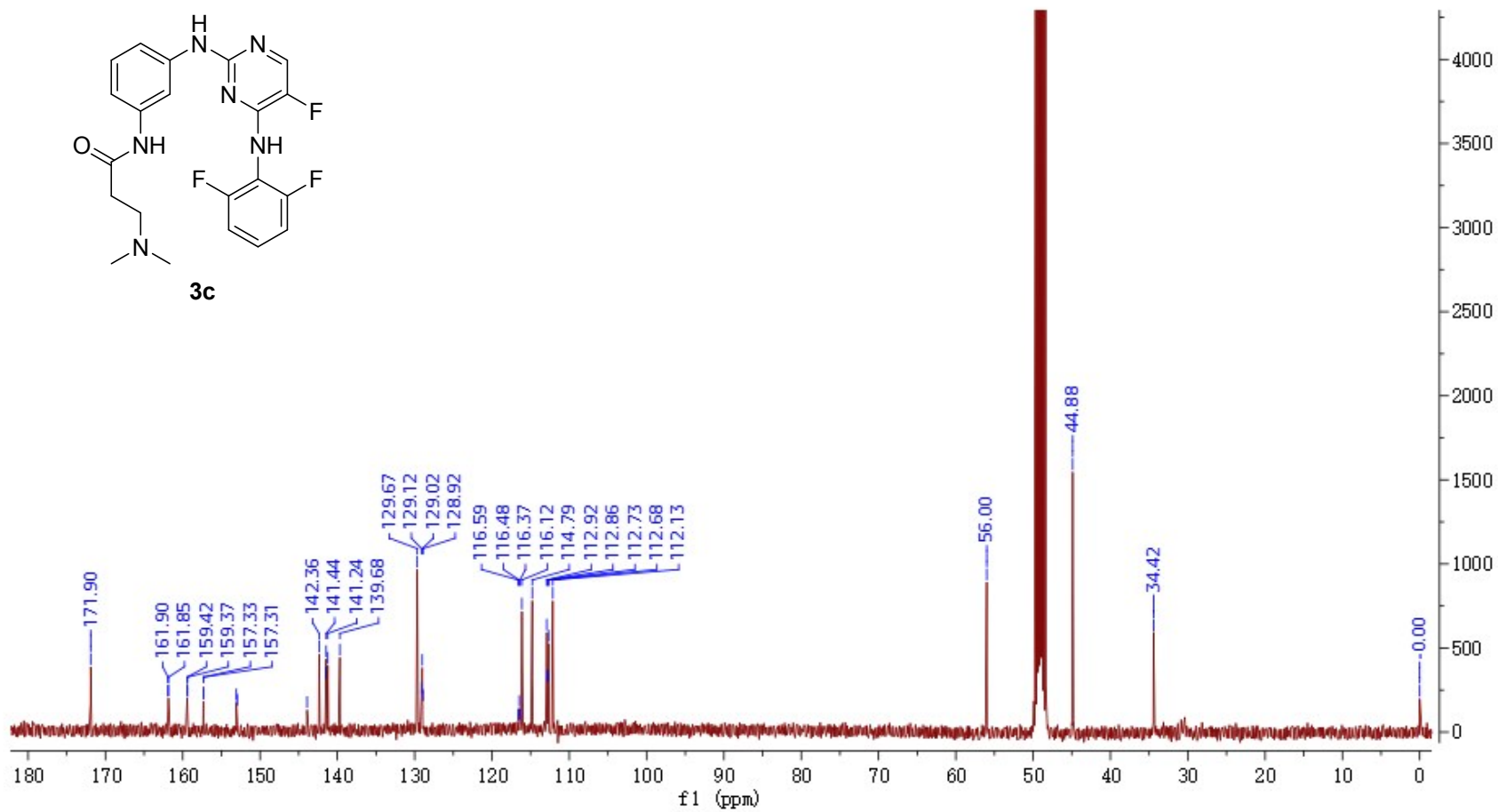
¹³C NMR spectrum for Compound 3b:



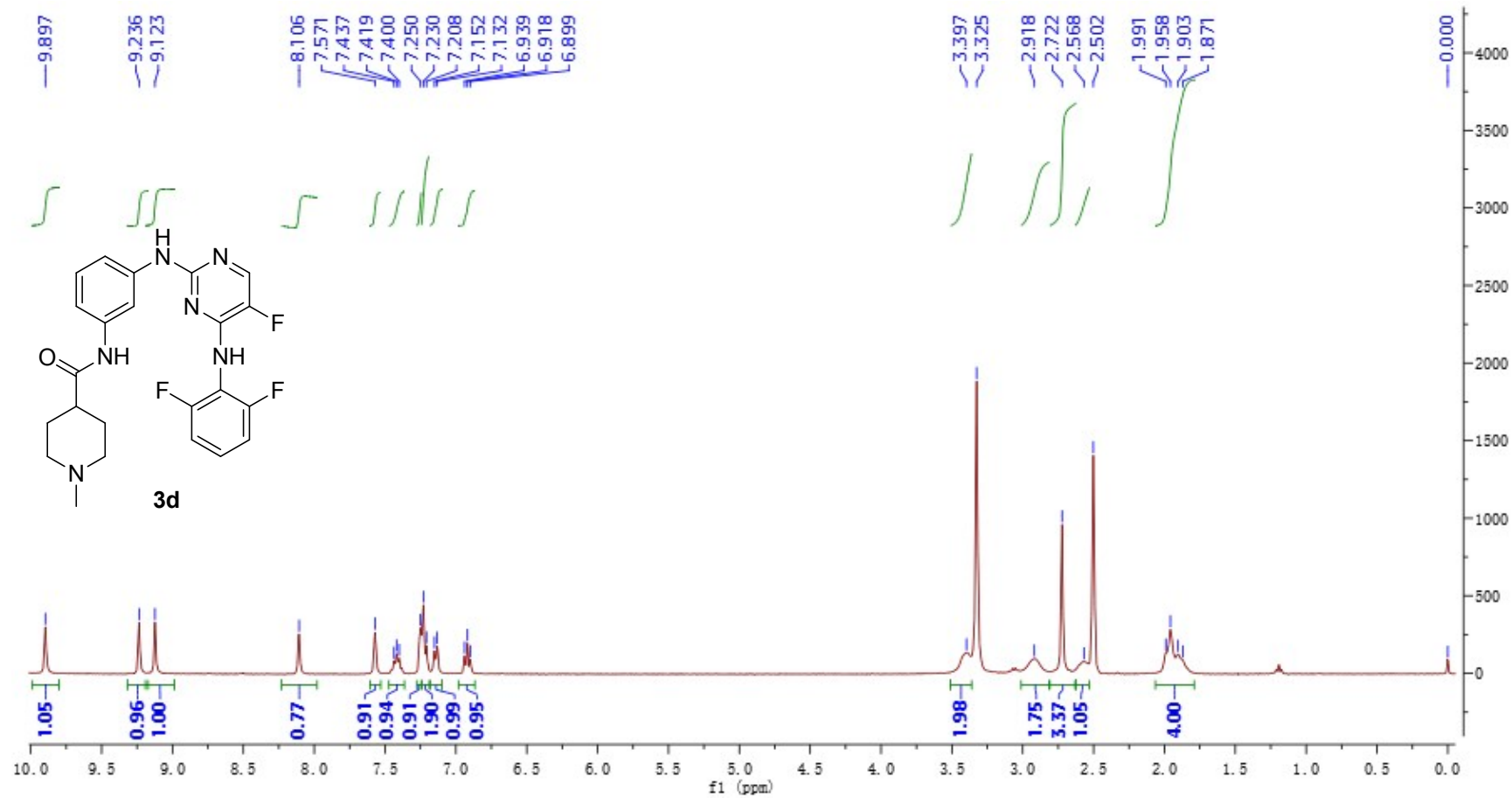
¹H NMR spectrum for Compound 3c:



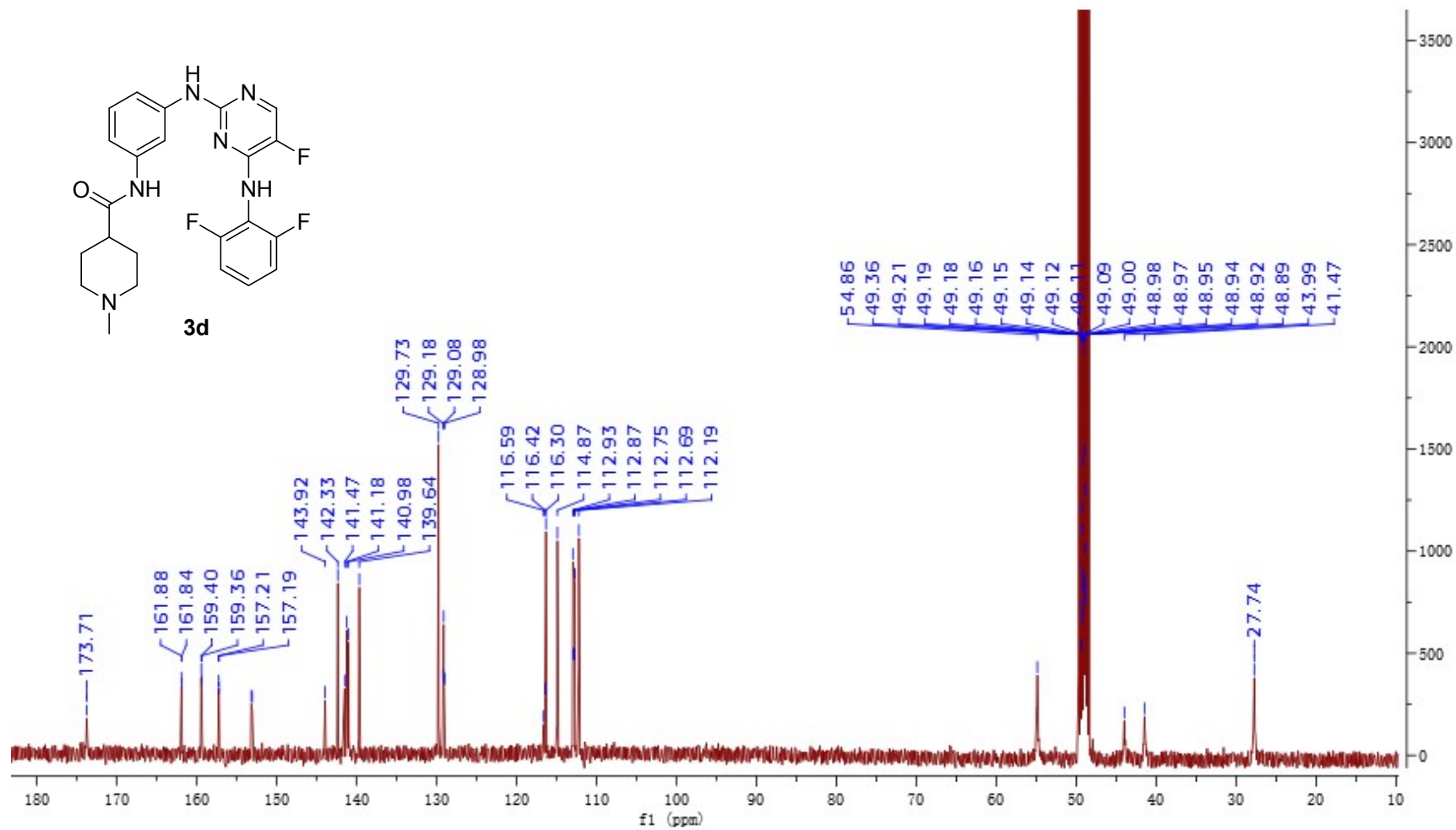
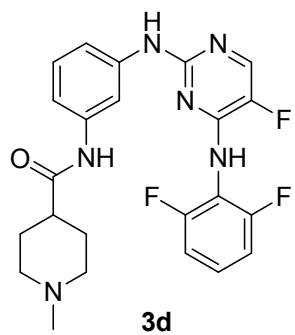
¹³C NMR spectrum for Compound 3c:



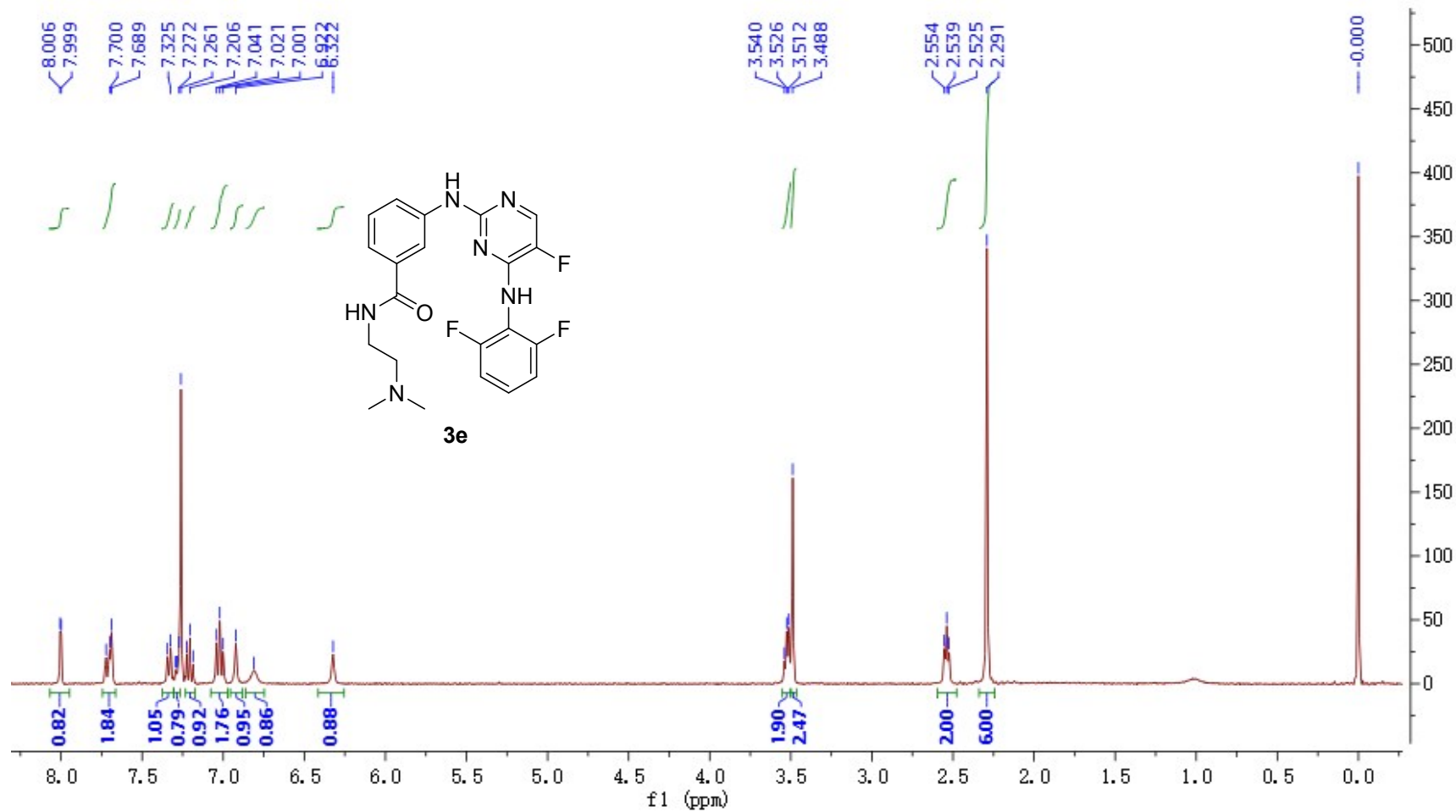
¹H NMR spectrum for Compound 3d:



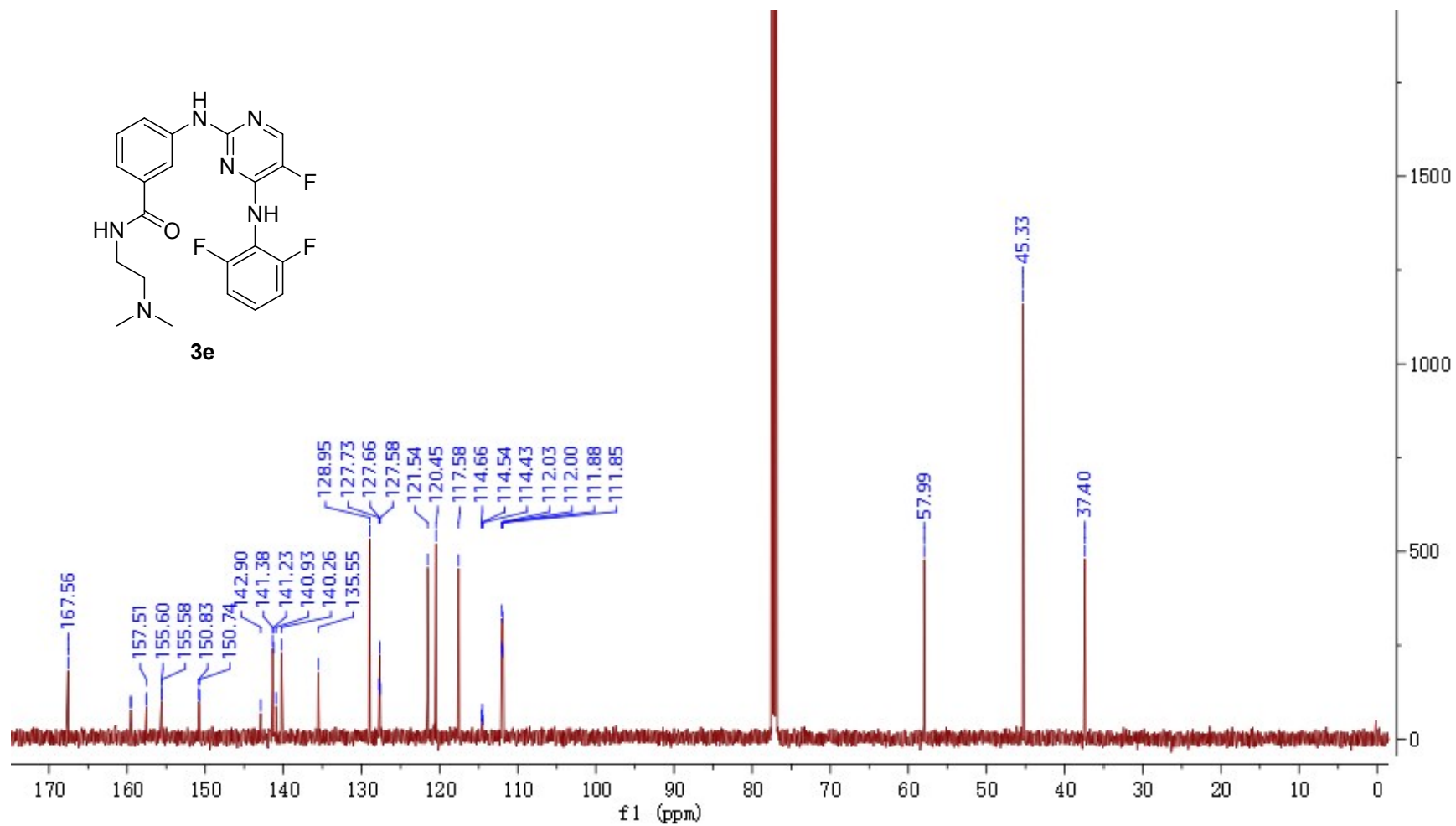
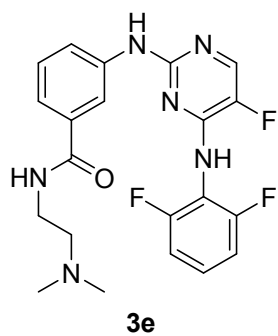
¹³C NMR spectrum for Compound 3d:



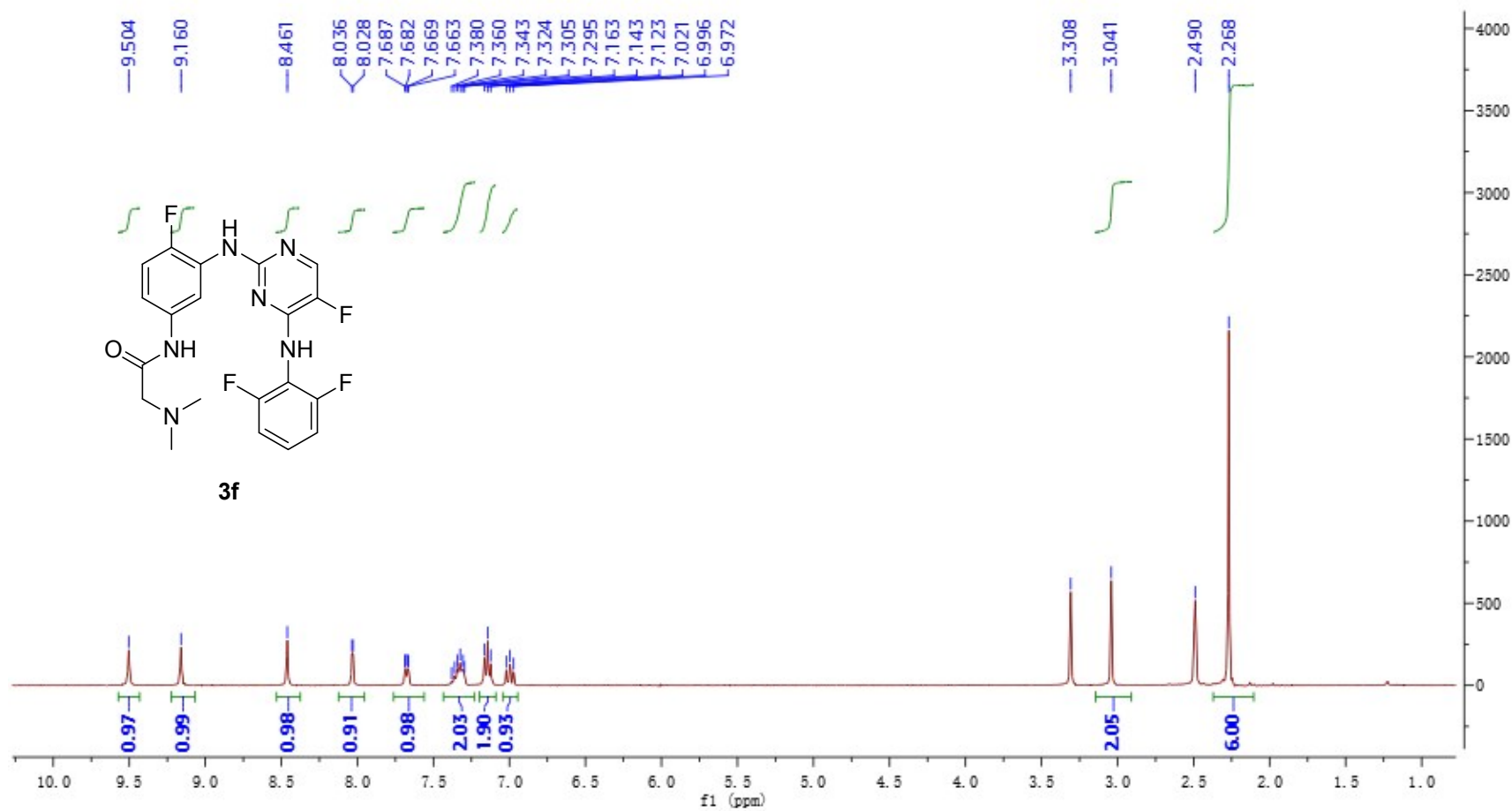
¹H NMR spectrum for Compound 3e:



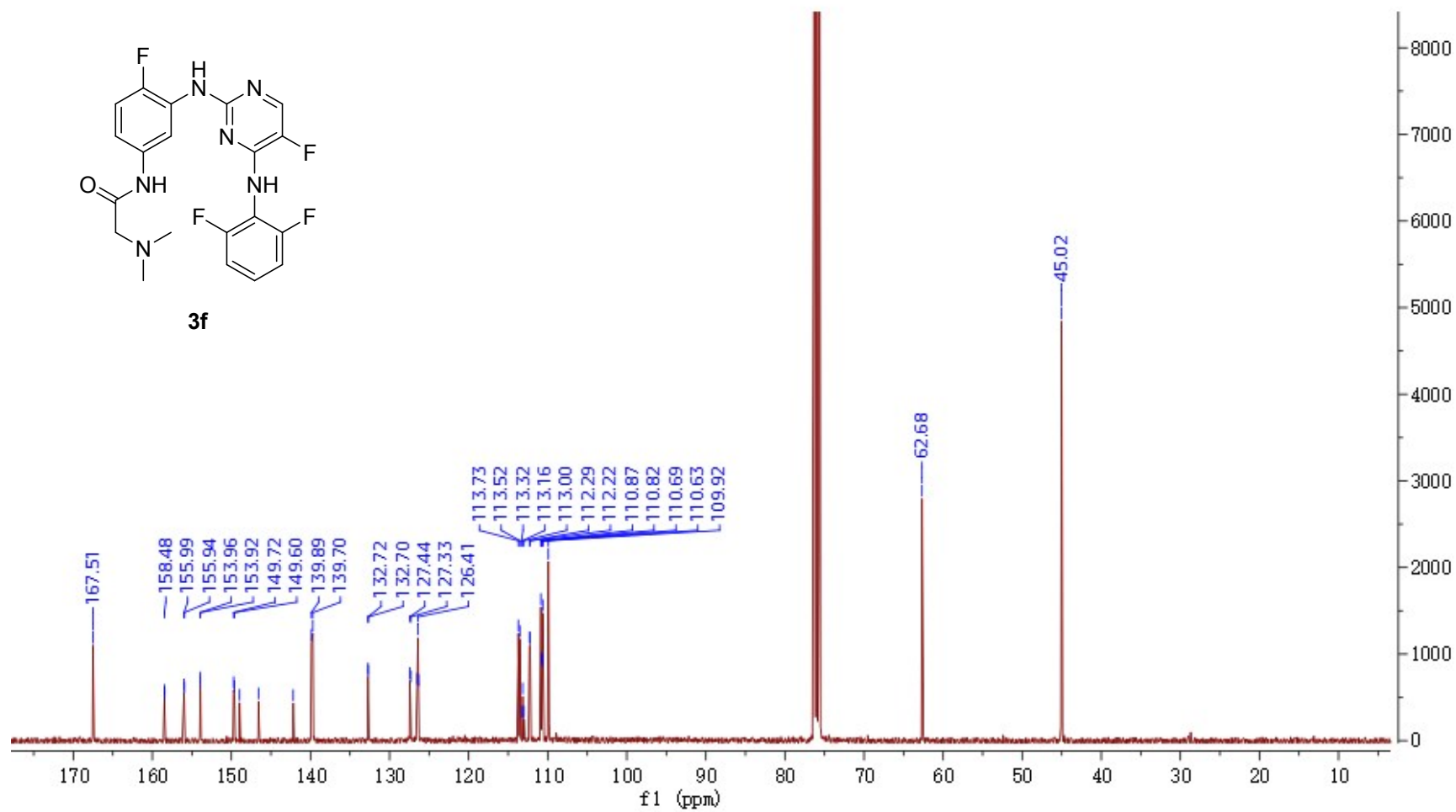
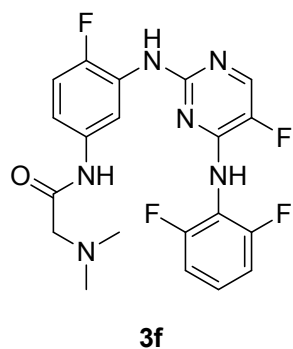
¹³C NMR spectrum for Compound 3e:



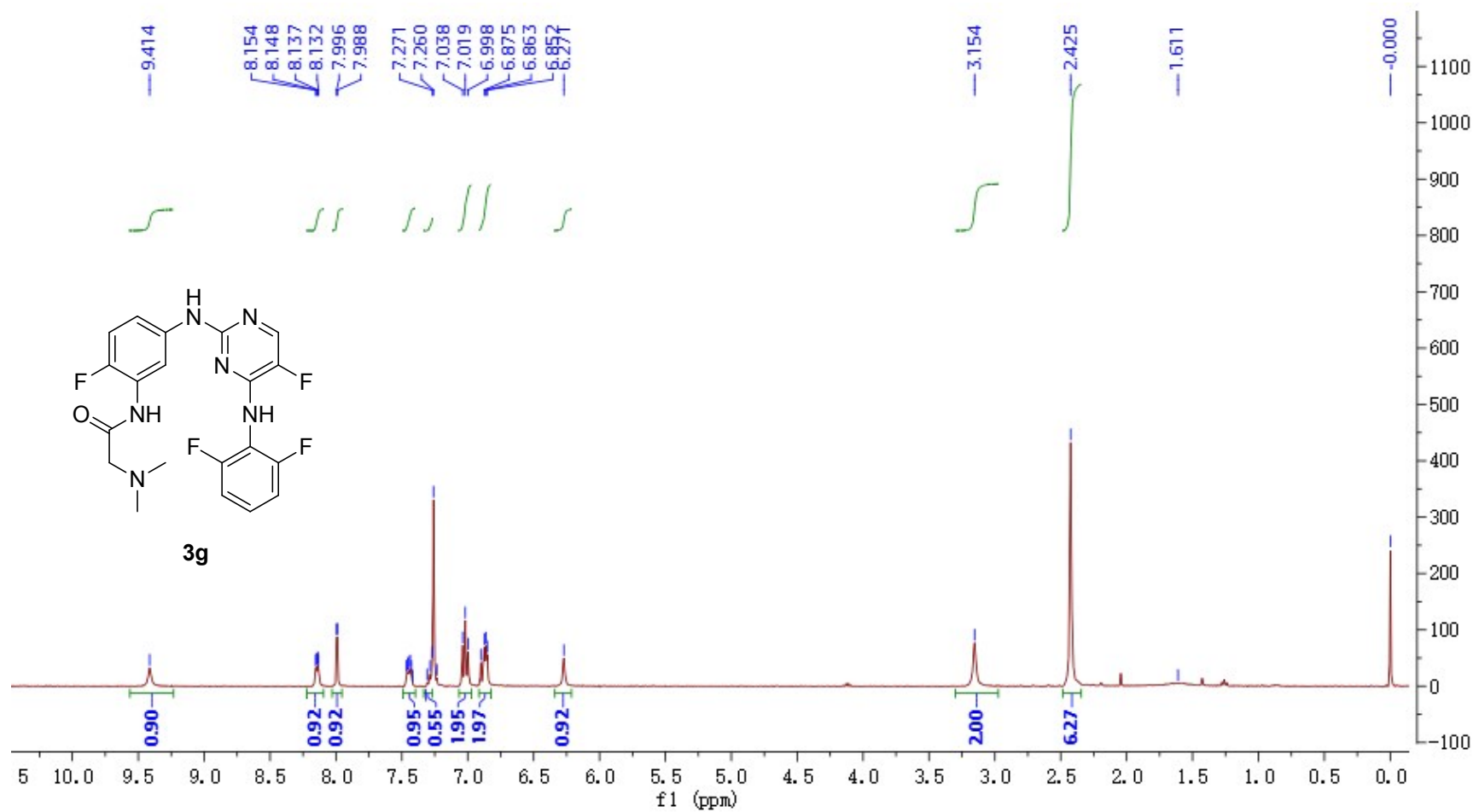
¹H NMR spectrum for Compound 3f:



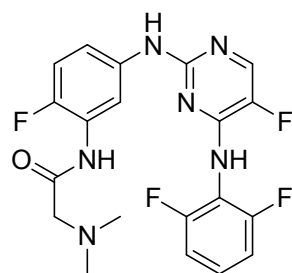
¹³C NMR spectrum for Compound 3f:



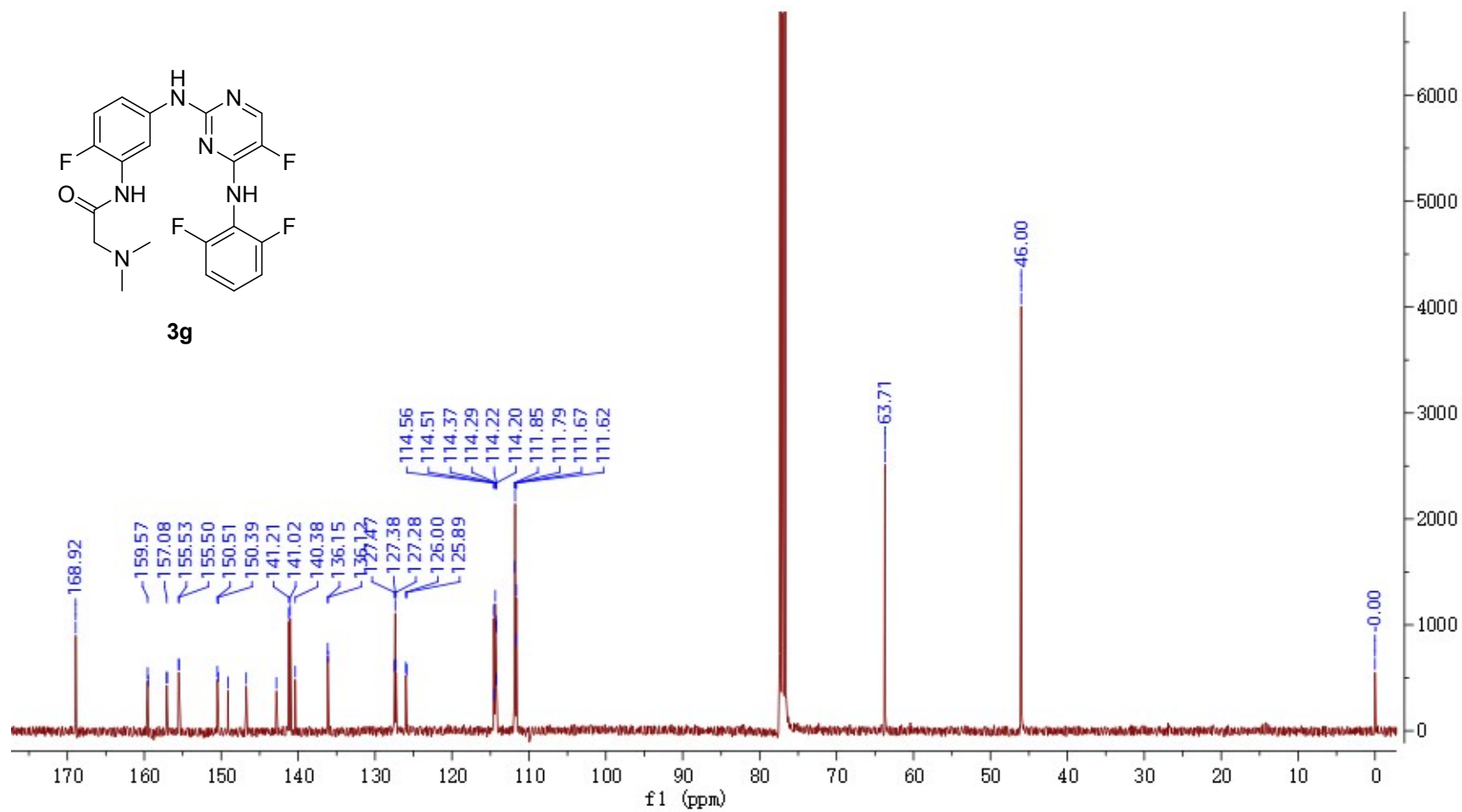
¹H NMR spectrum for Compound 3g:



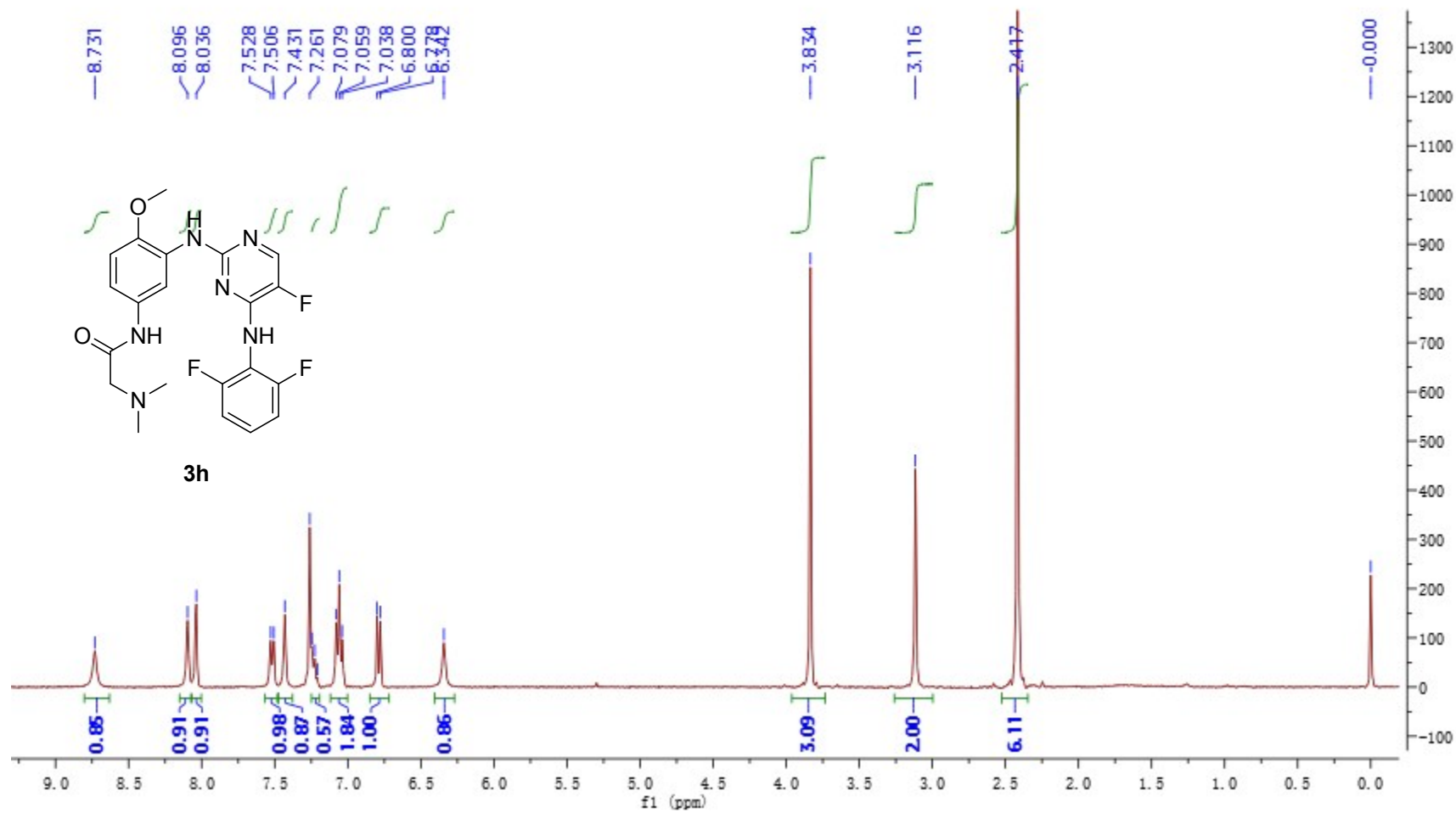
¹³C NMR spectrum for Compound 3g:



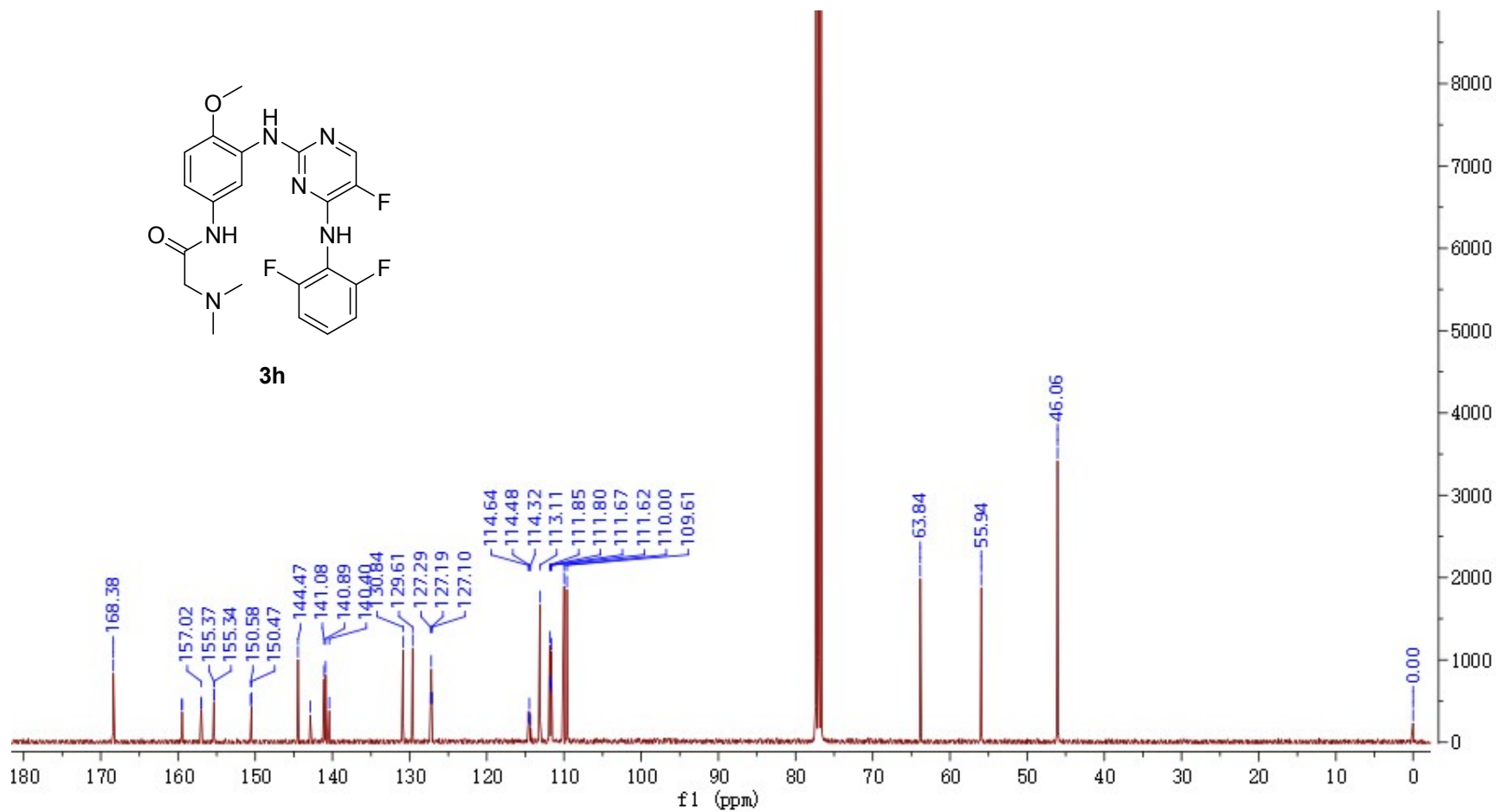
3g



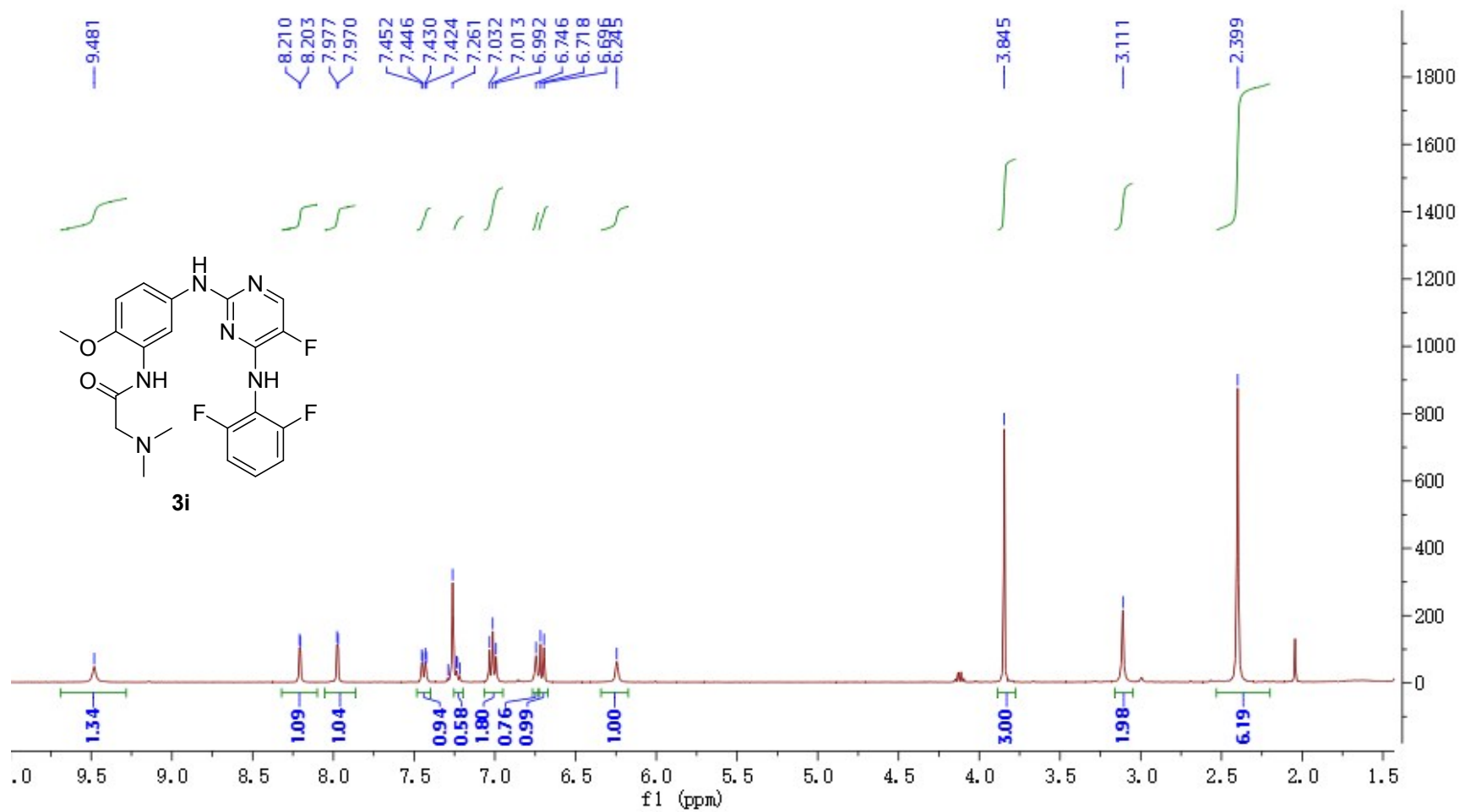
¹H NMR spectrum for Compound 3h:



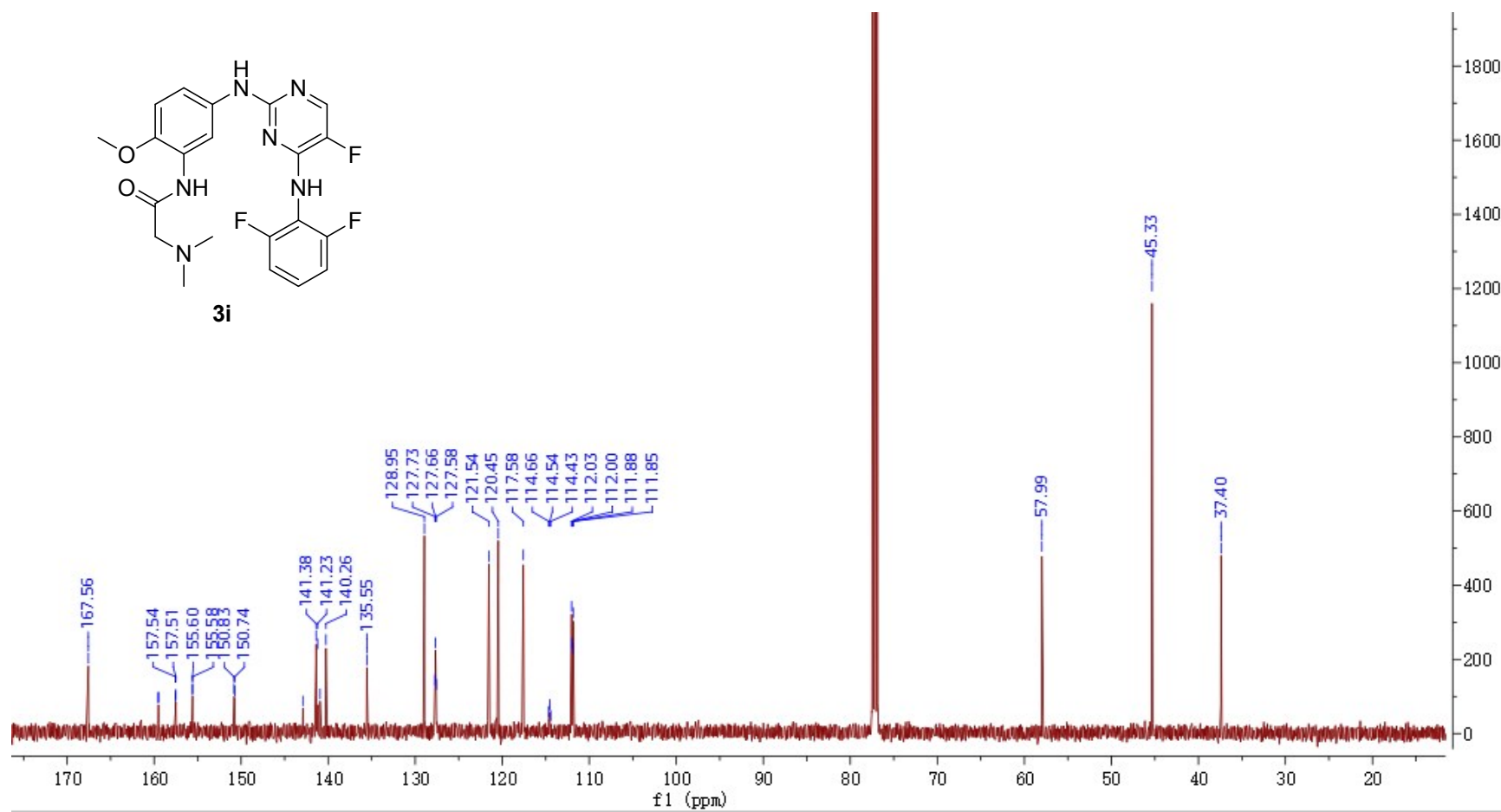
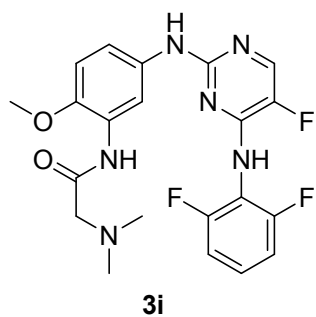
¹³C NMR spectrum for Compound 3h:



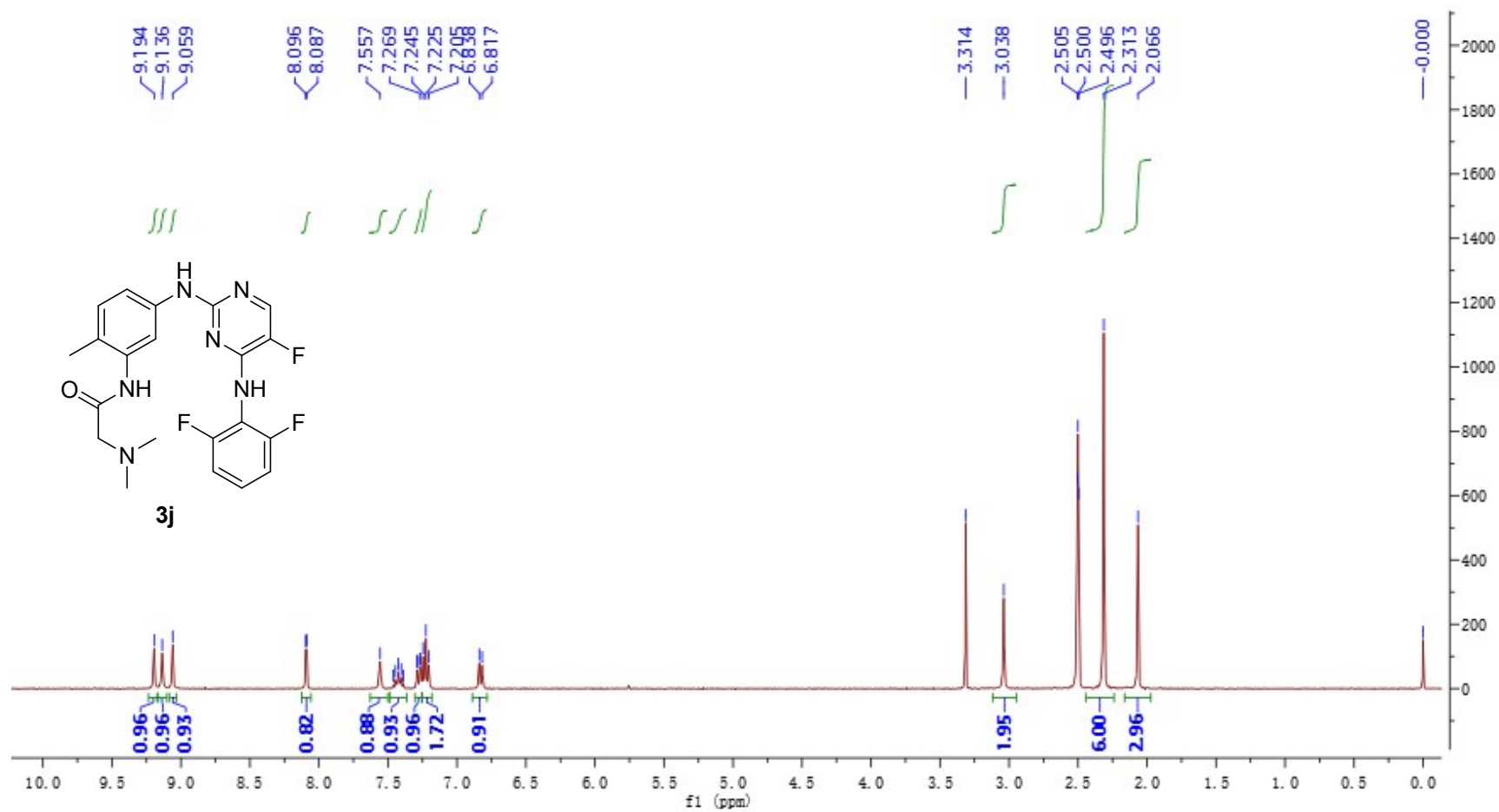
¹H NMR spectrum for Compound 3i:



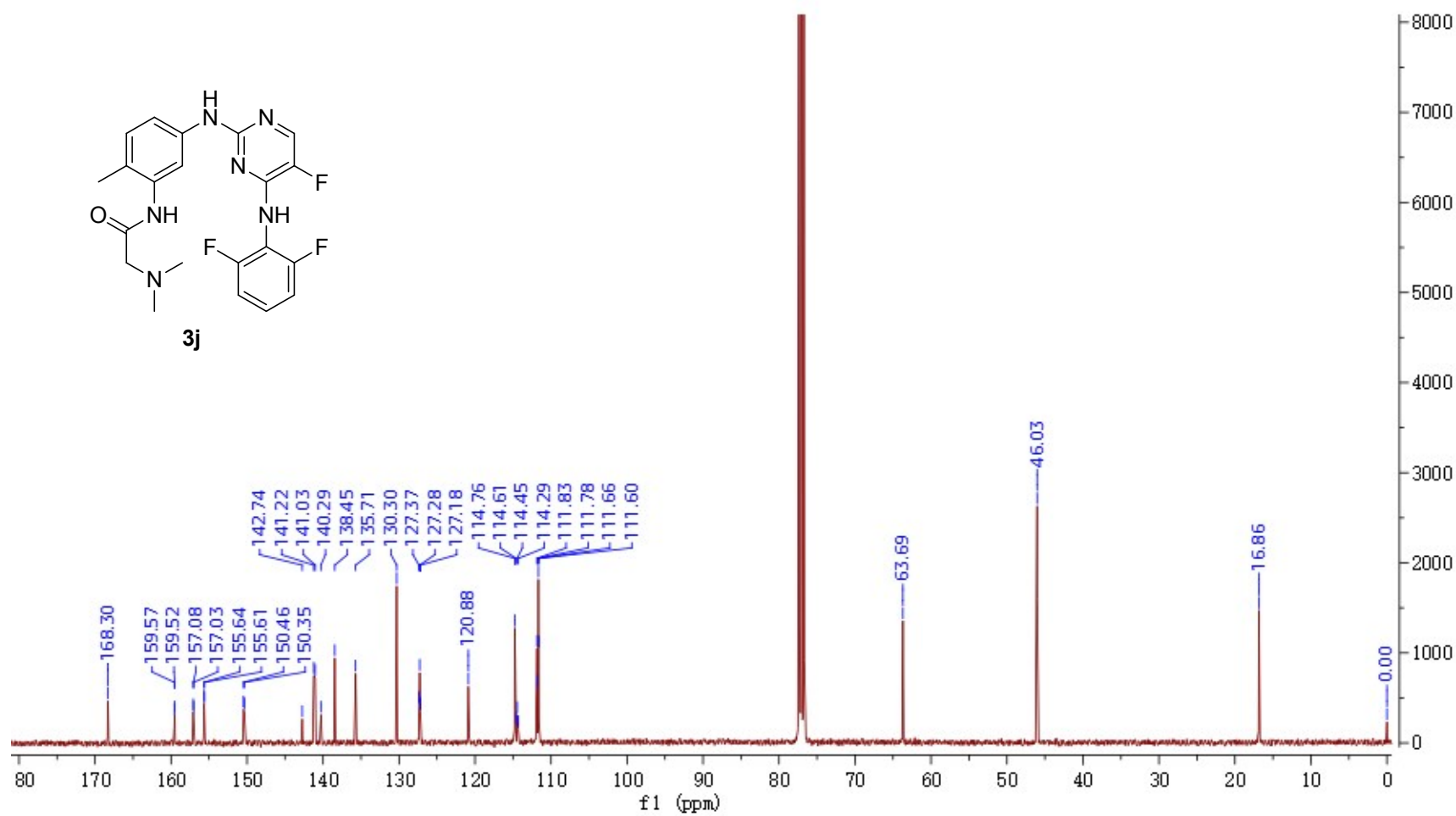
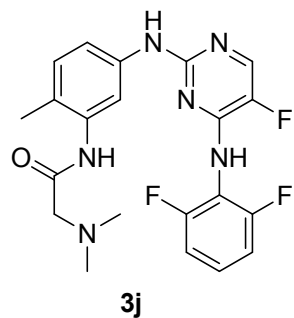
¹³C NMR spectrum for Compound 3i:



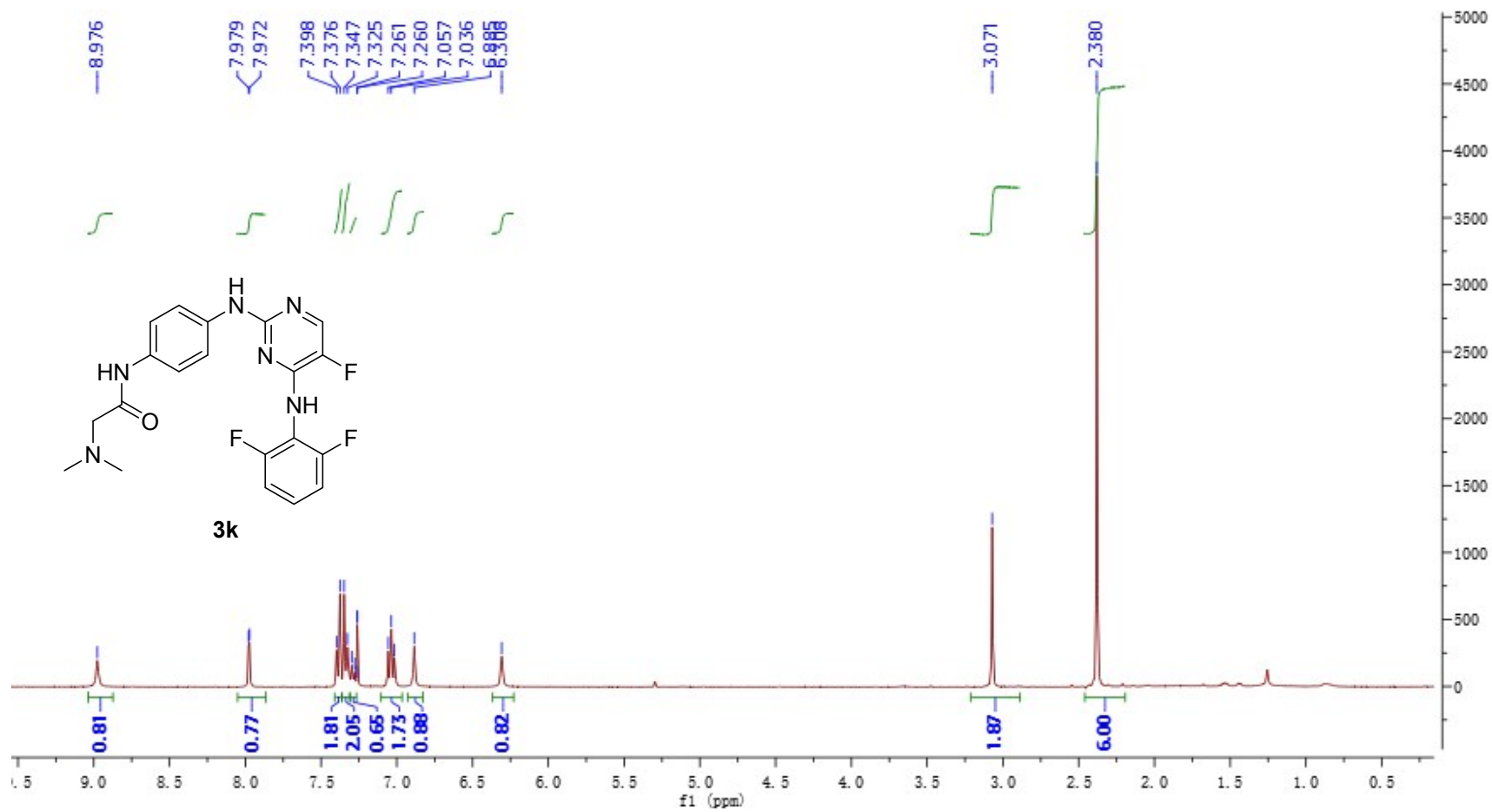
¹H NMR spectrum for Compound 3j:



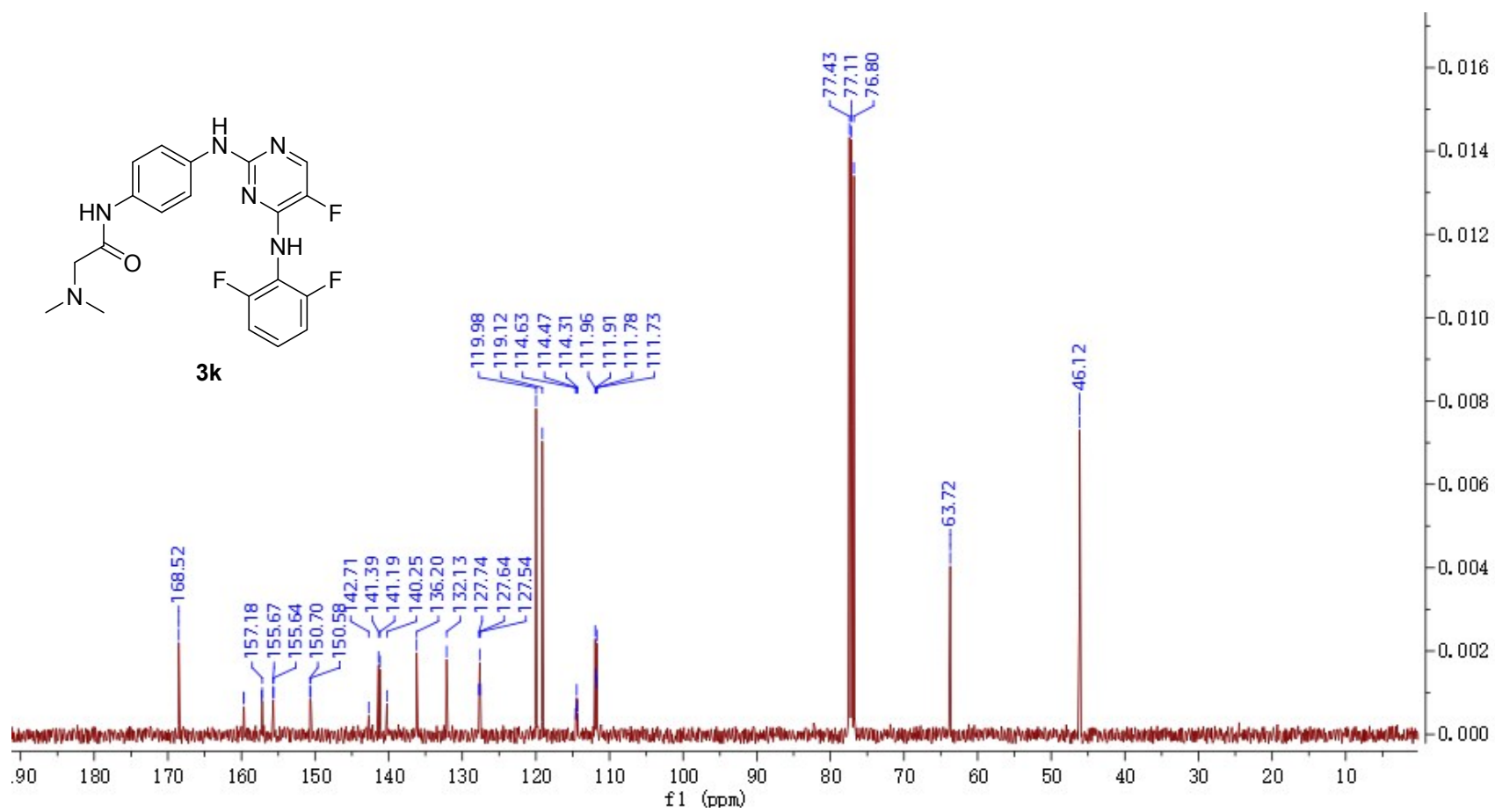
¹³C NMR spectrum for Compound 3j:



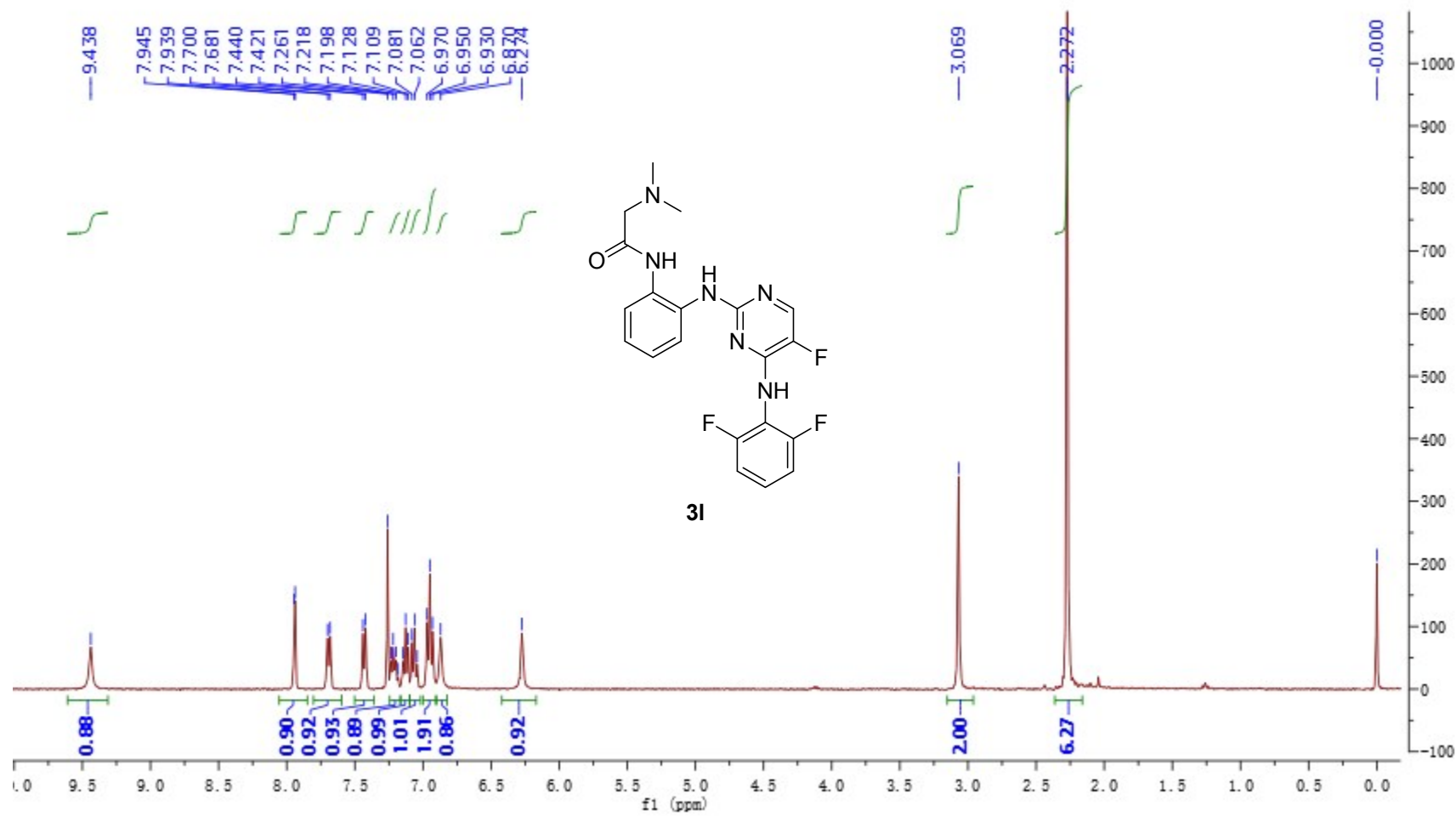
¹H NMR spectrum for Compound 3k:



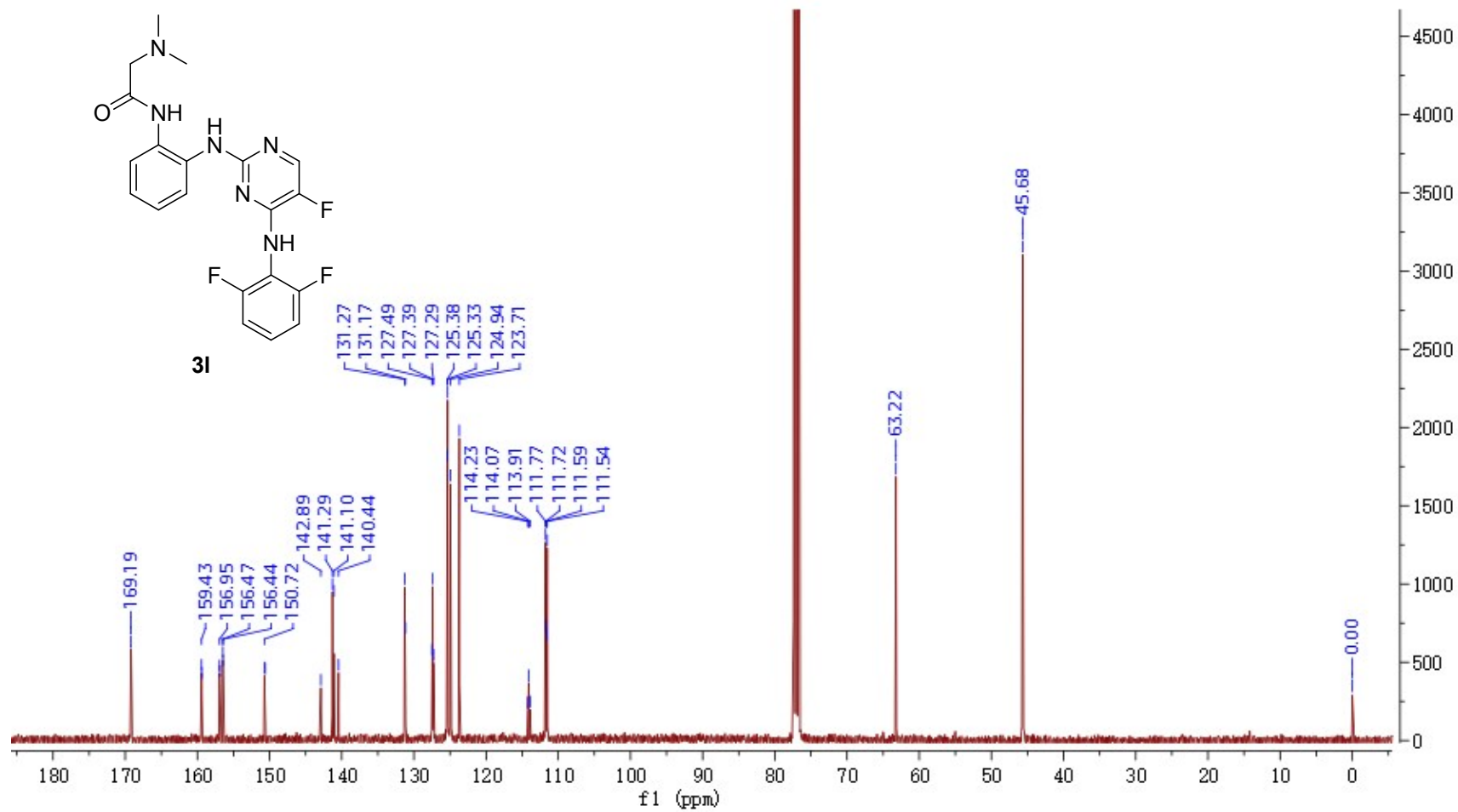
¹³C NMR spectrum for Compound 3k:



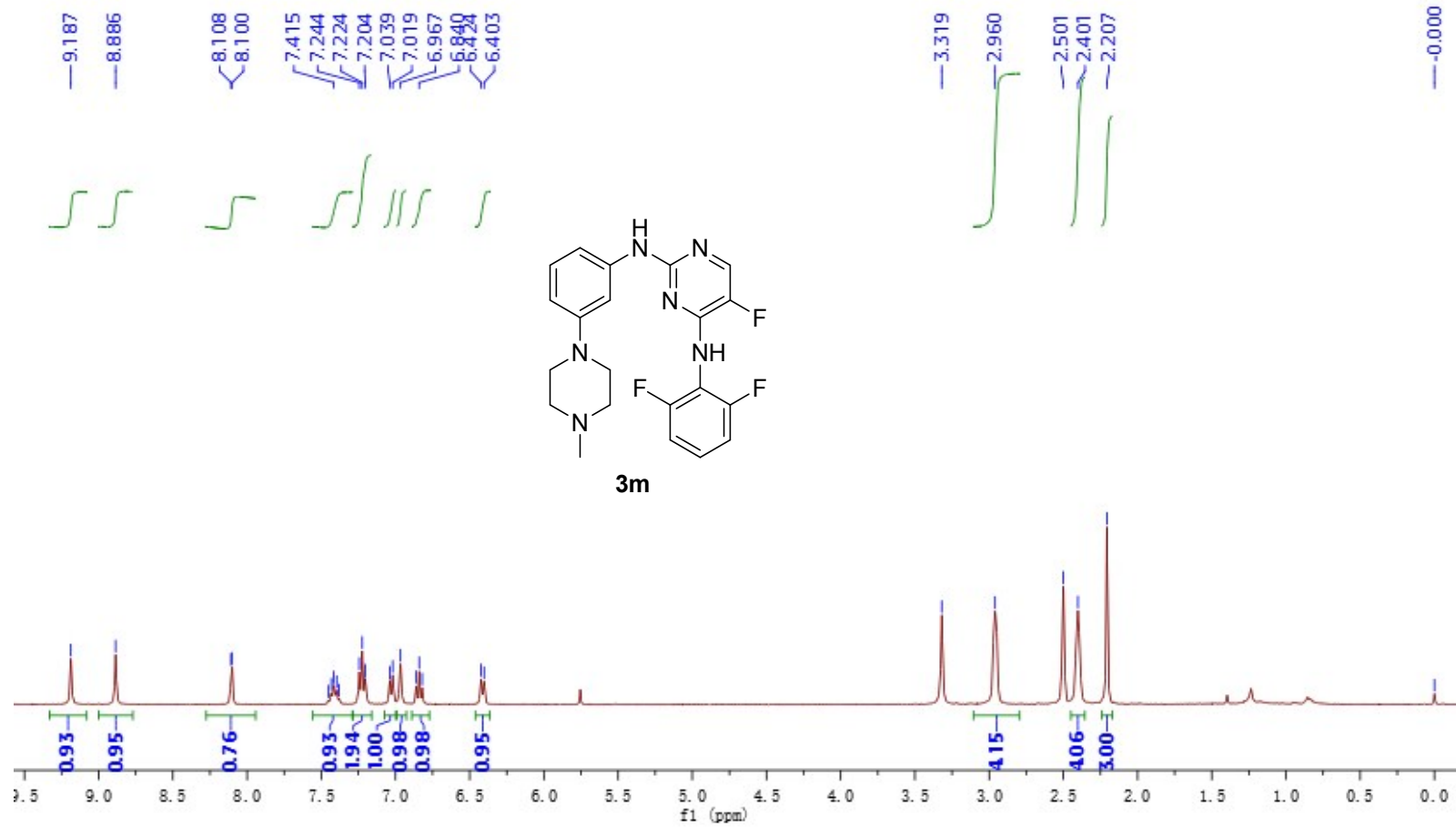
¹H NMR spectrum for Compound 3l:



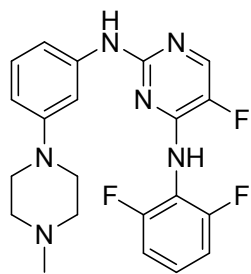
¹³C NMR spectrum for Compound 3l:



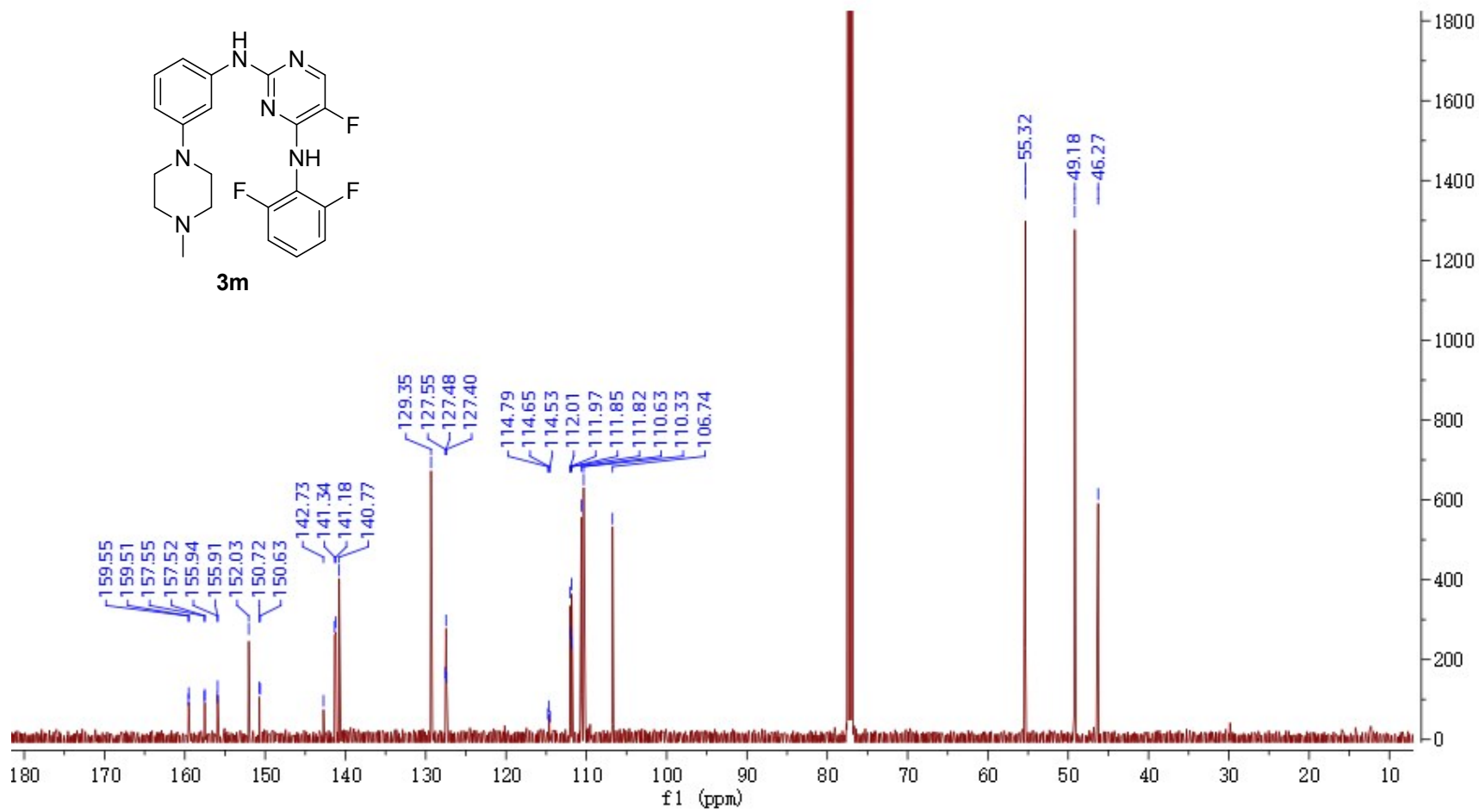
¹H NMR spectrum for Compound 3m:



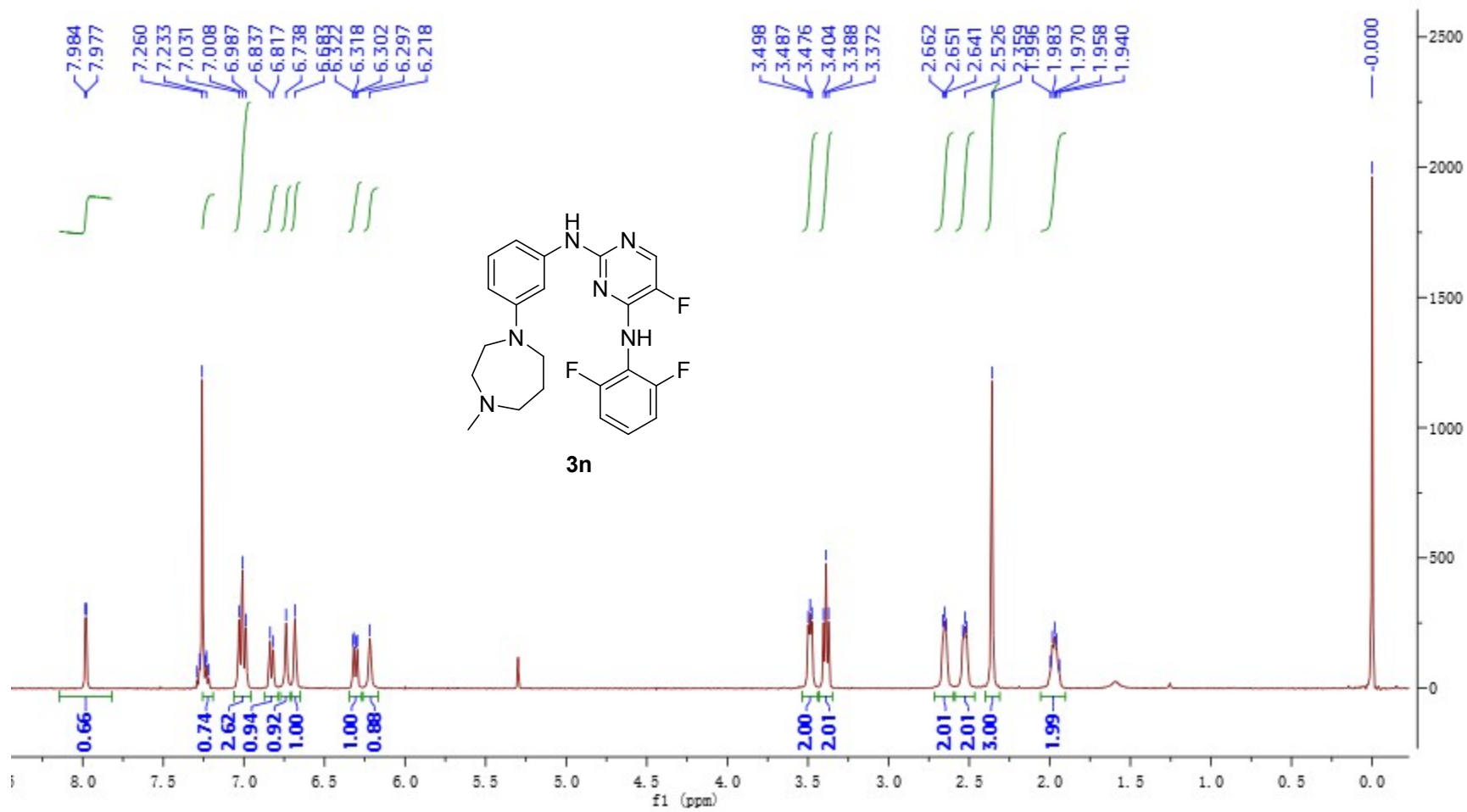
¹³C NMR spectrum for Compound 3m:



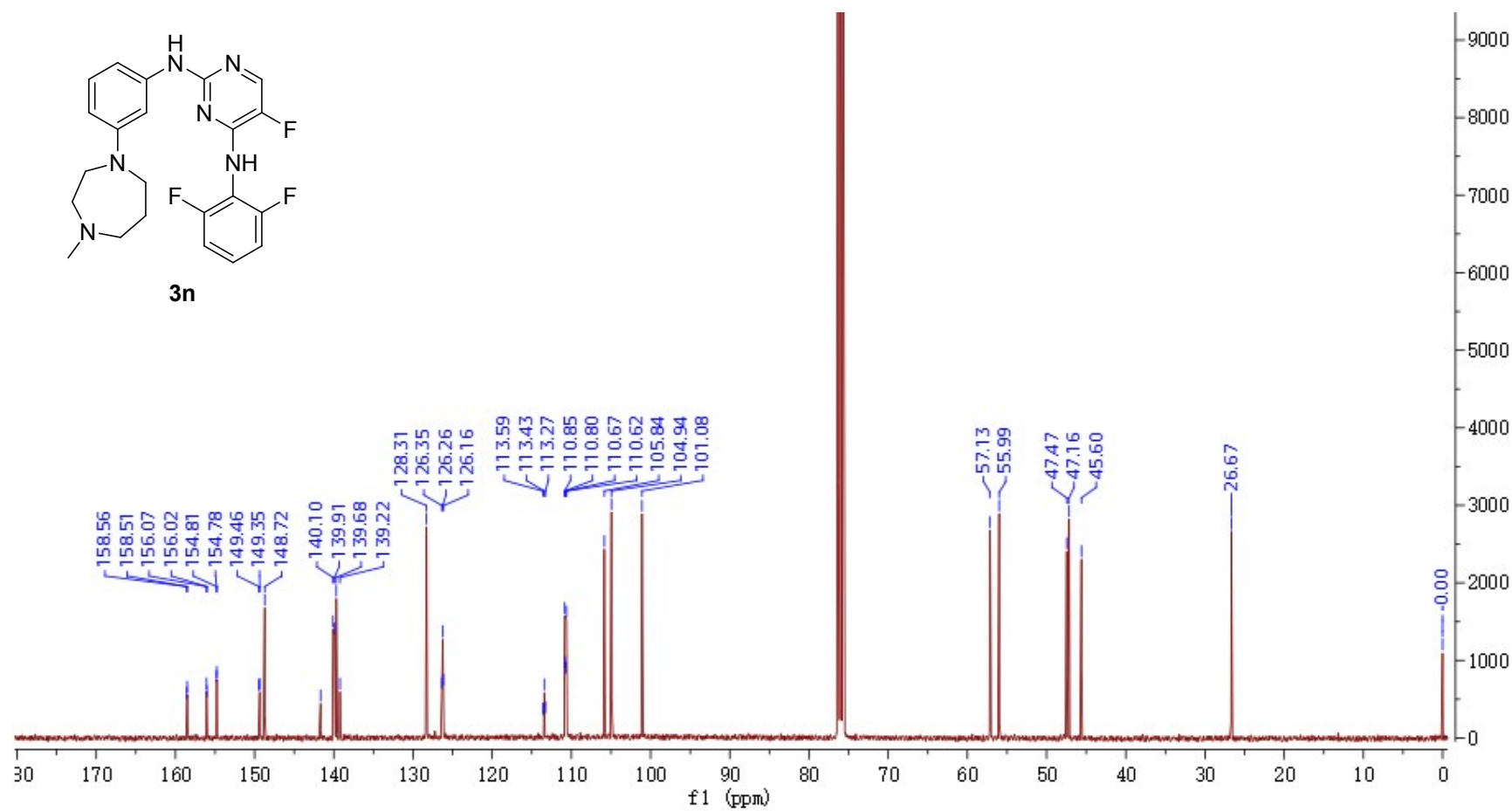
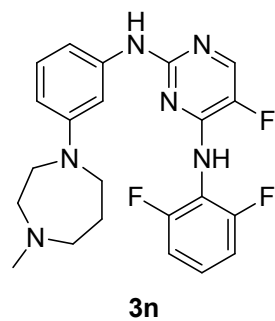
3m



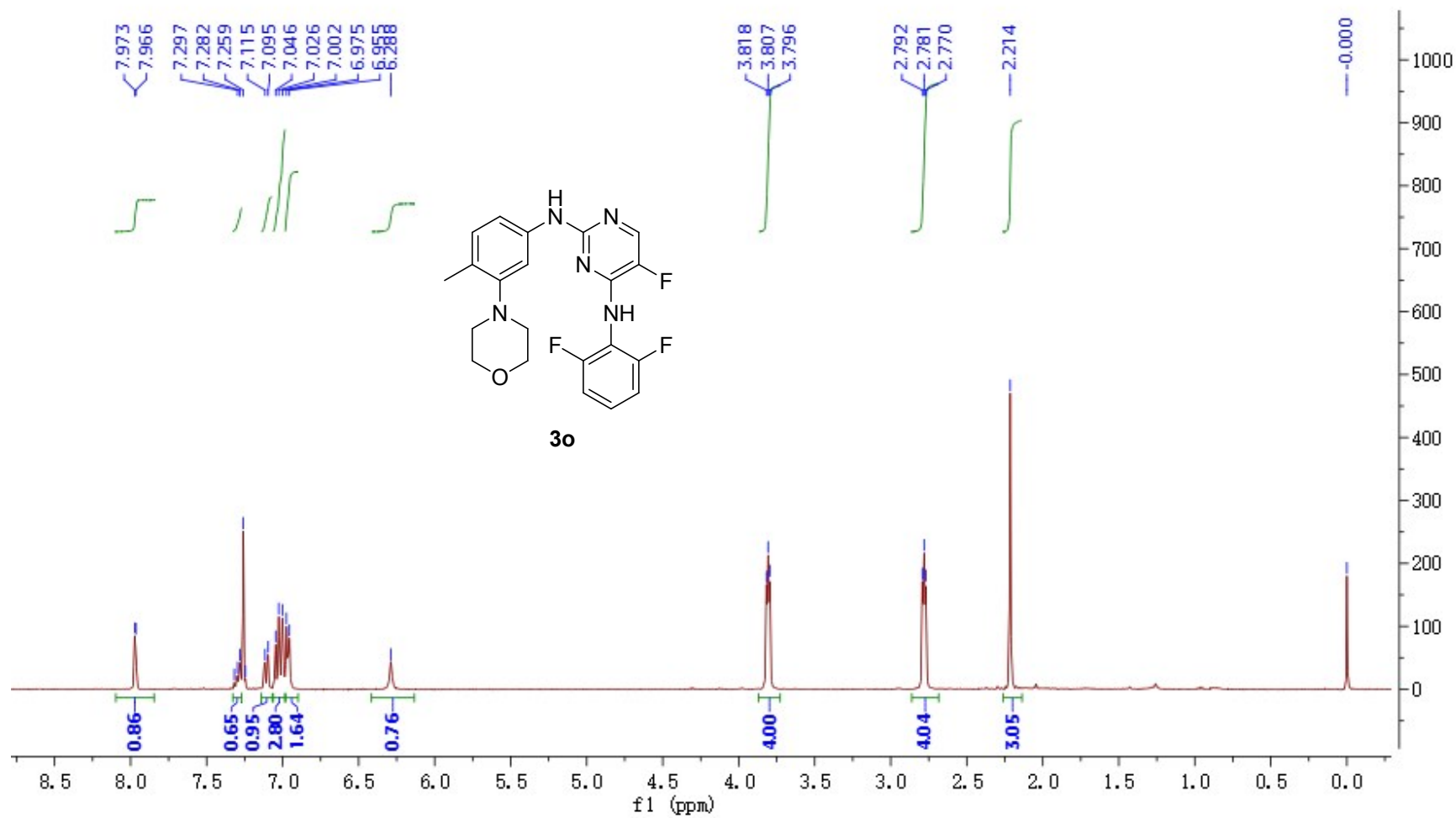
¹H NMR spectrum for Compound 3n:



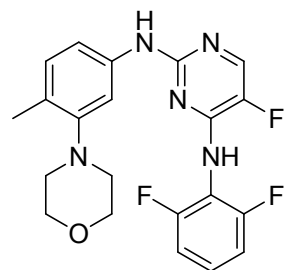
¹³C NMR spectrum for Compound 3n:



¹H NMR spectrum for Compound 3o:



¹³C NMR spectrum for Compound 3o:



3o

