

# Design, Synthesis and Biological Evaluation of Tetrahydroquinoxaline Sulfonamide Derivatives as Colchicine Binding Site Inhibitors

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<sup>3</sup> Jiangsu Key Laboratory of Drug Design and Optimization, Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 211198, China

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\* Corresponding authors

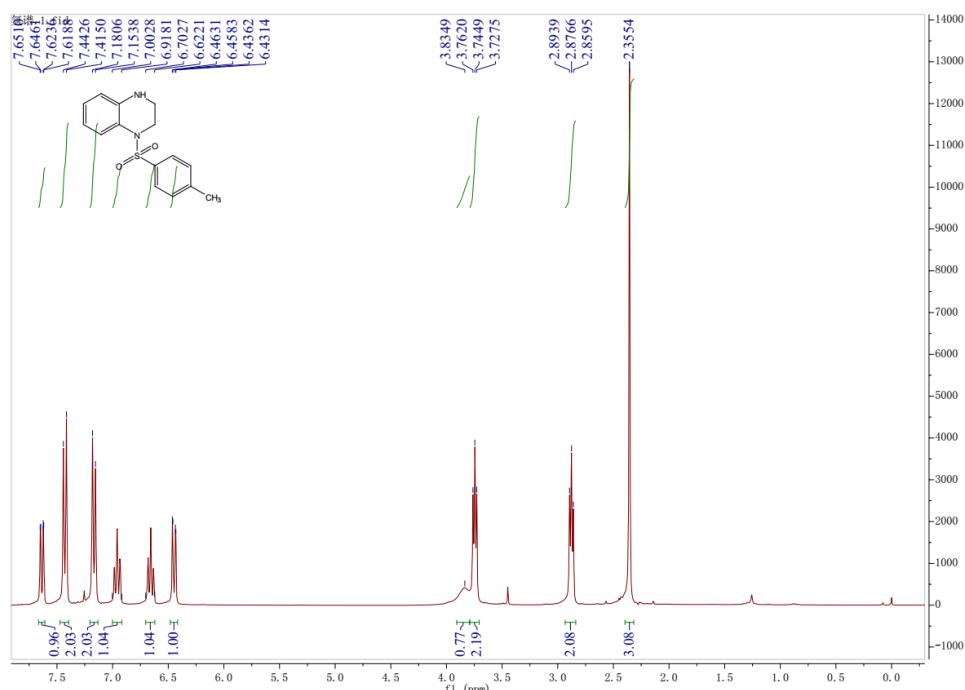
E-mail address: [liangting910710@126.com](mailto:liangting910710@126.com), jhworg@126.com

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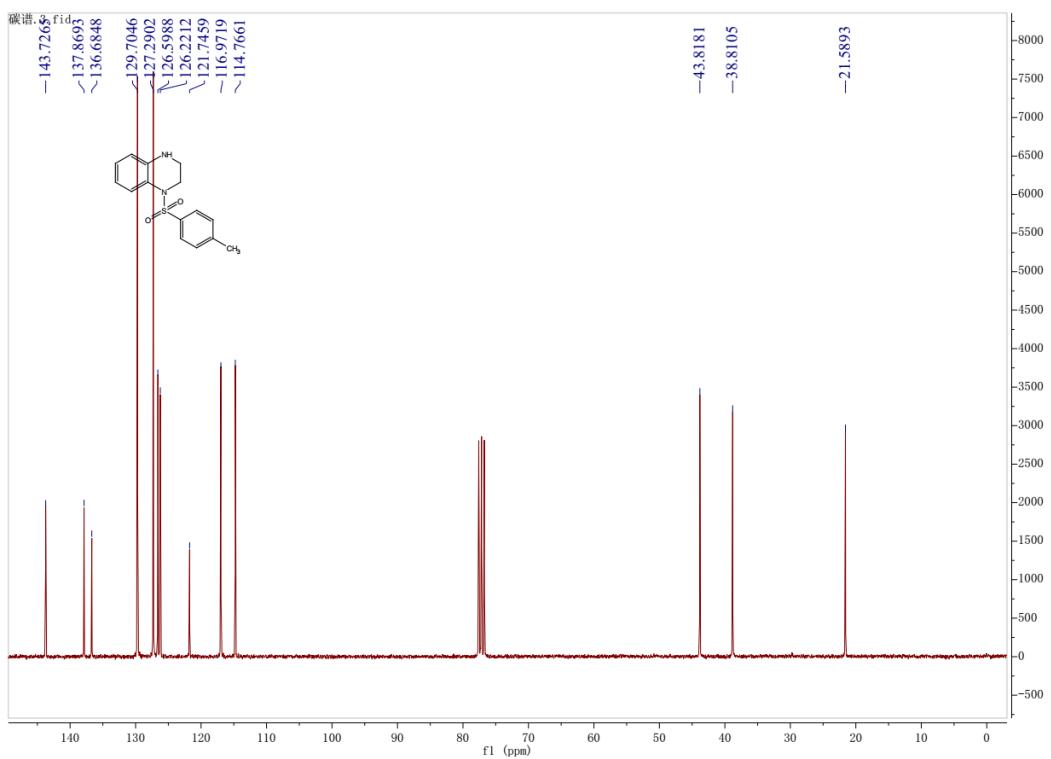
<sup>1</sup>H-NMR, <sup>13</sup>C-NMR, HRMS spectra and HPLC purity of target compounds

### I-1

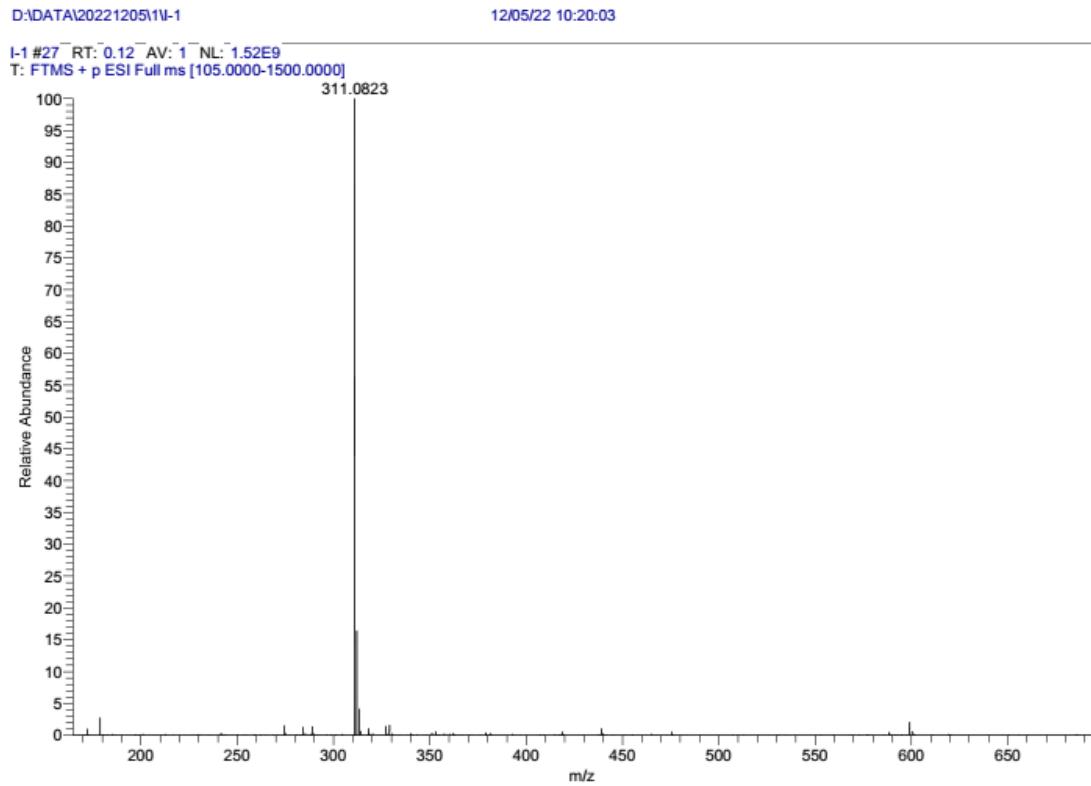
#### <sup>1</sup>H-NMR



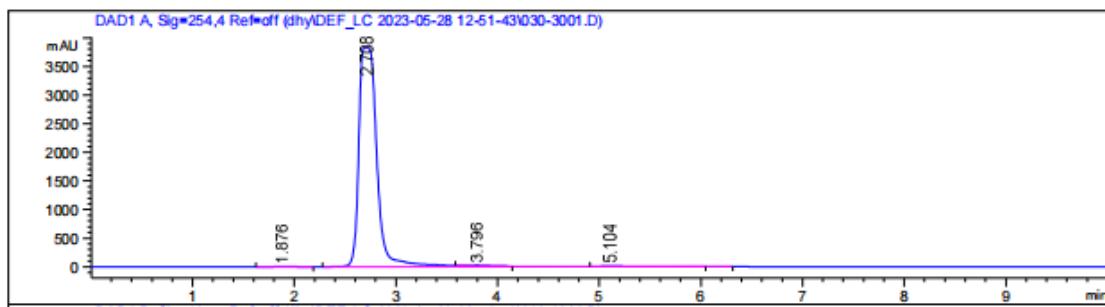
### <sup>13</sup>C-NMR



### HRMS

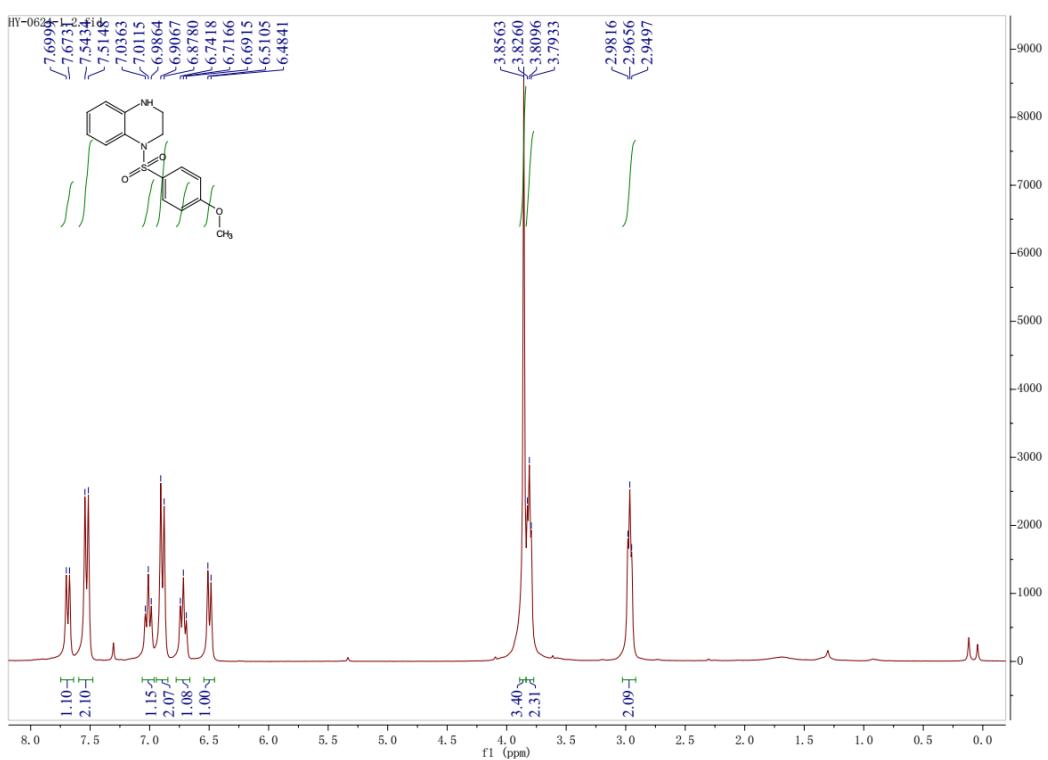


### HPLC purity

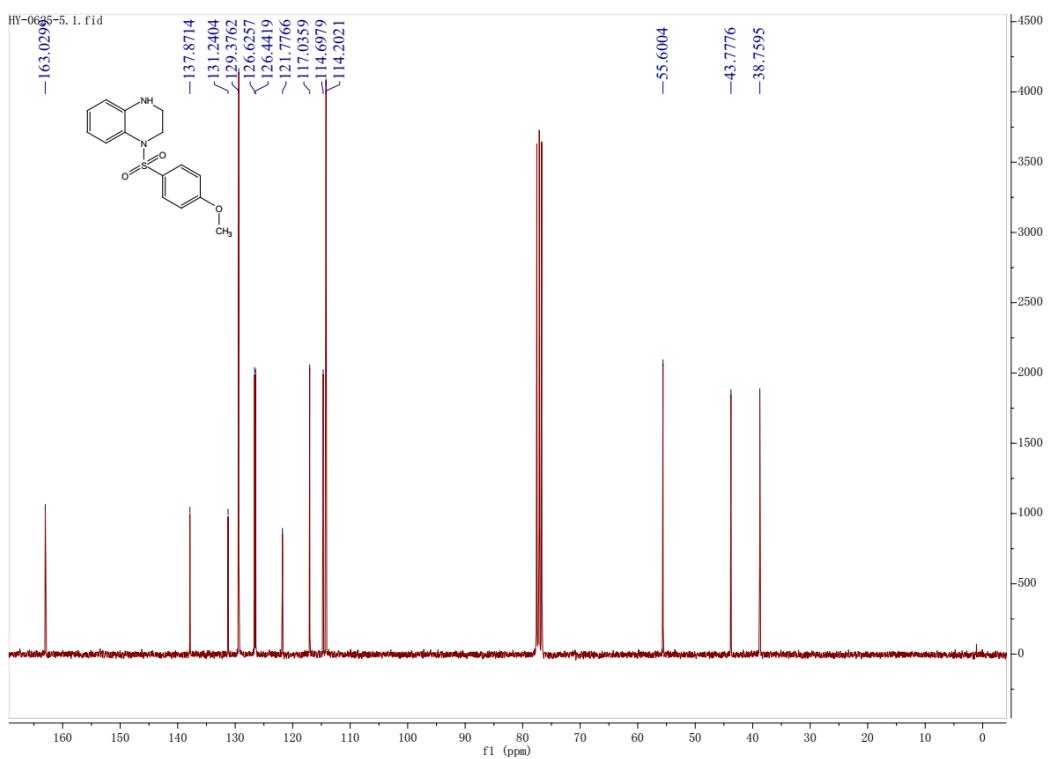


## I-2

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



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

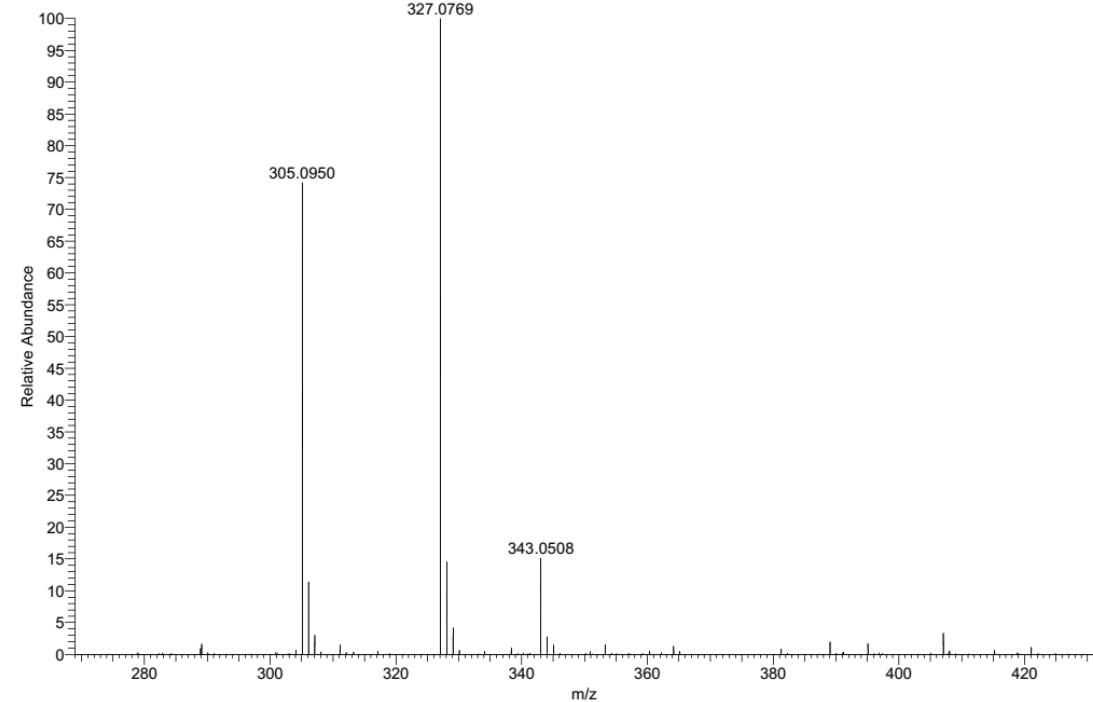


## HRMS

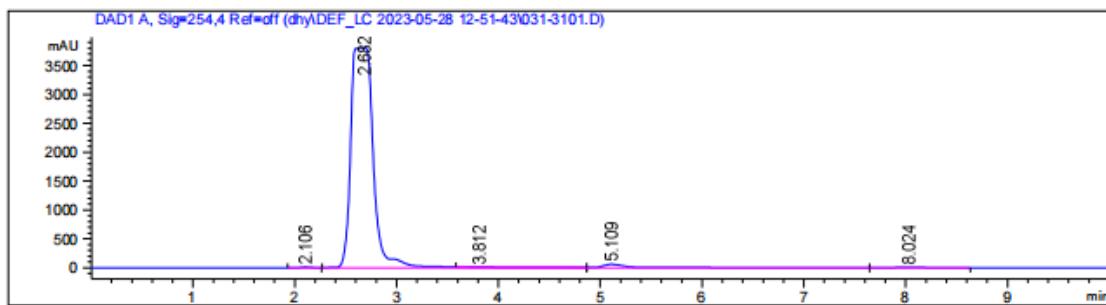
D:\DATA\20221205\1\I-2

12/05/22 10:23:13

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T: FTMS + p ESI Full ms [105.0000-1500.0000]



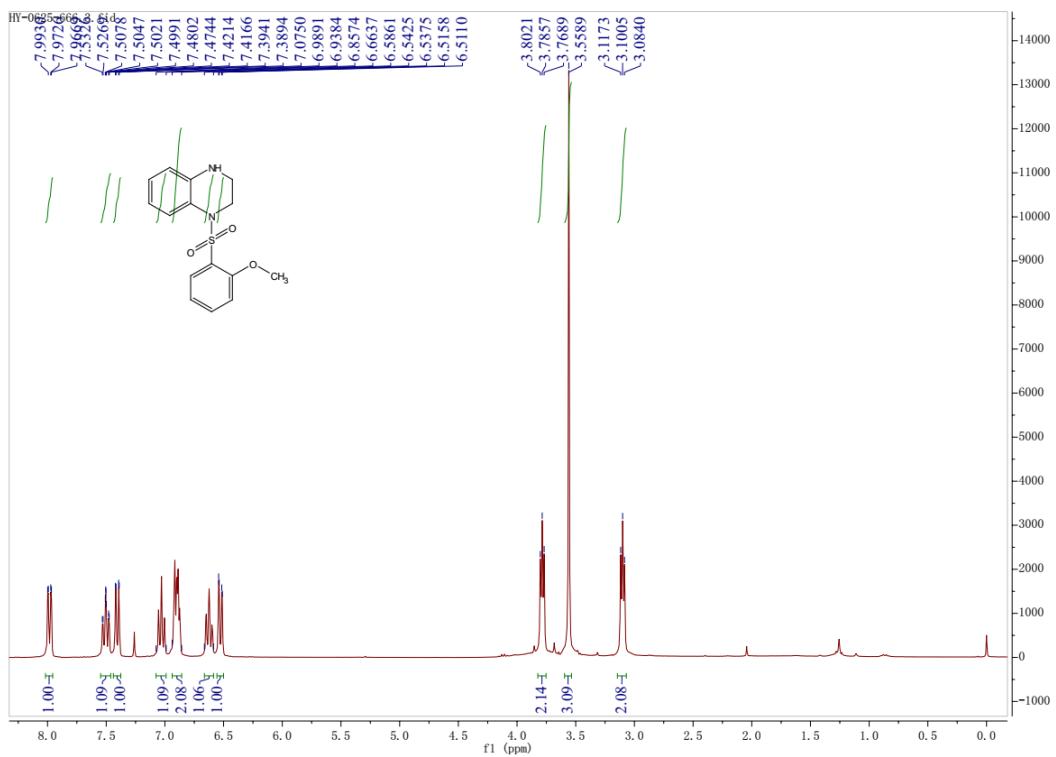
## HPLC purity



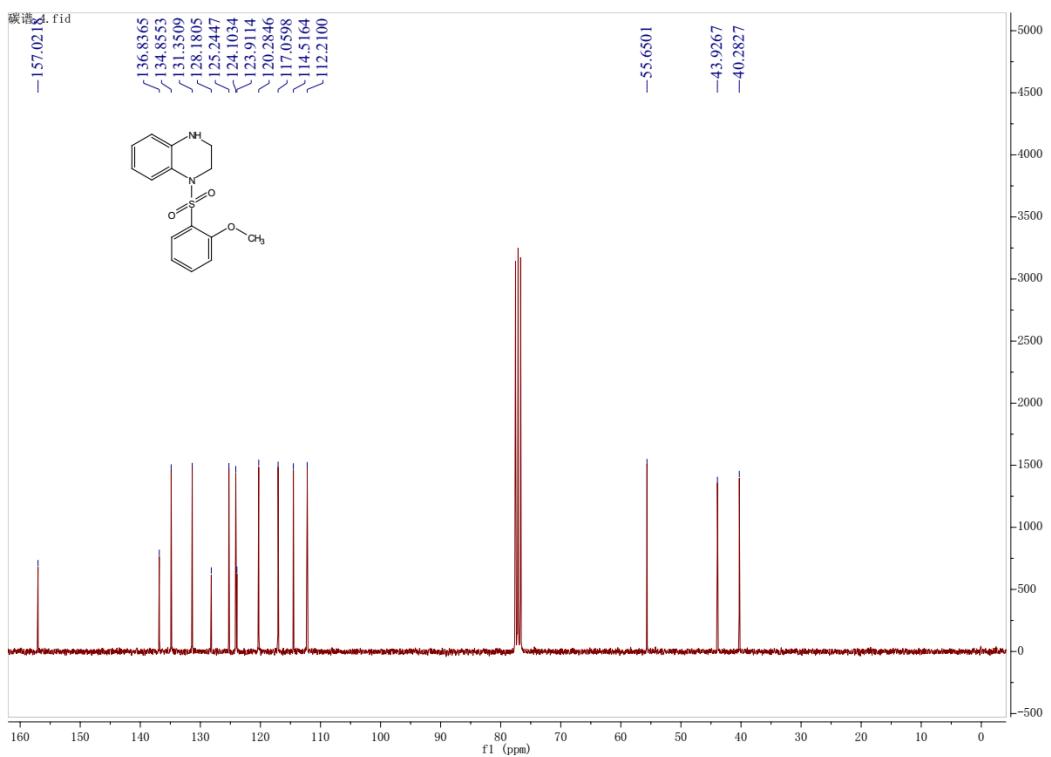
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1	2.106	BB	0.0758	46.87372	9.79933	0.0793
2	2.682	BV R	0.2400	5.79879e4	3800.25659	98.0913
3	3.812	VV E	0.3947	204.96324	6.85751	0.3467
4	5.109	VB	0.2236	850.55853	57.83422	1.4388
5	8.024	BB	0.3025	25.98289	1.33831	0.0440

### I-3

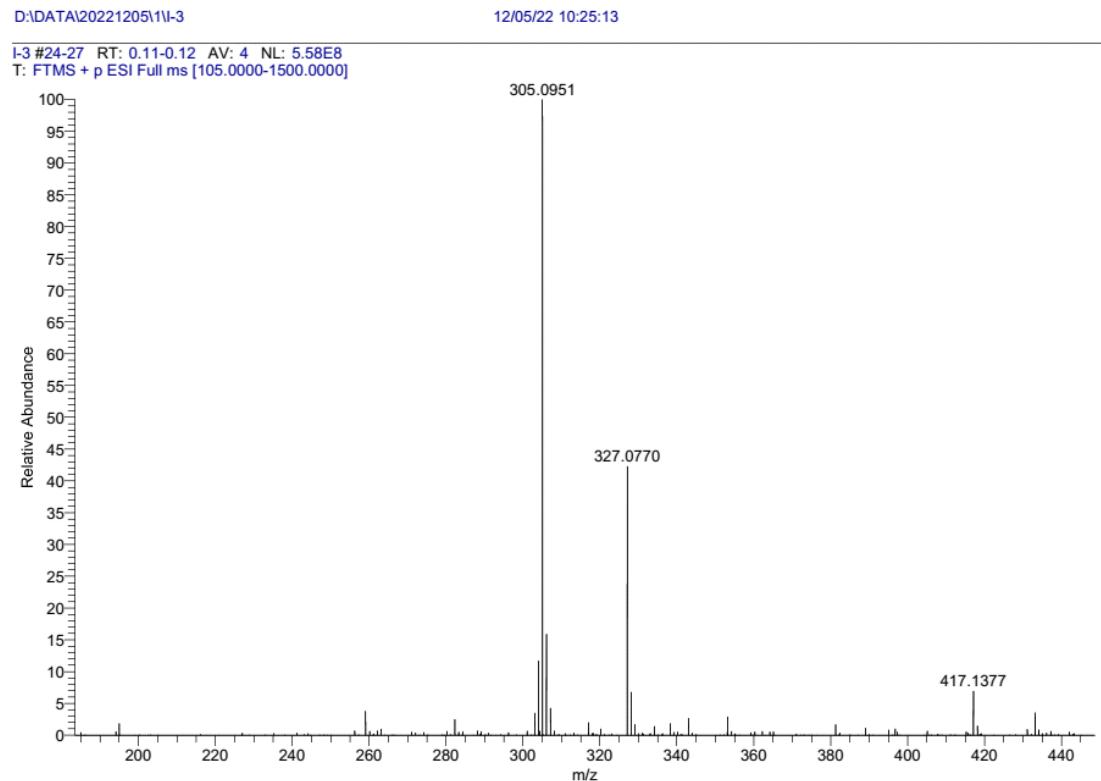
#### <sup>1</sup>H-NMR



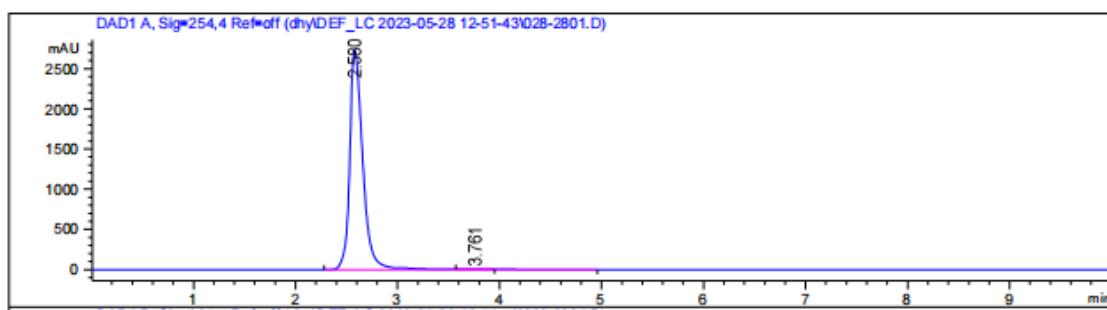
#### <sup>13</sup>C-NMR



## HRMS



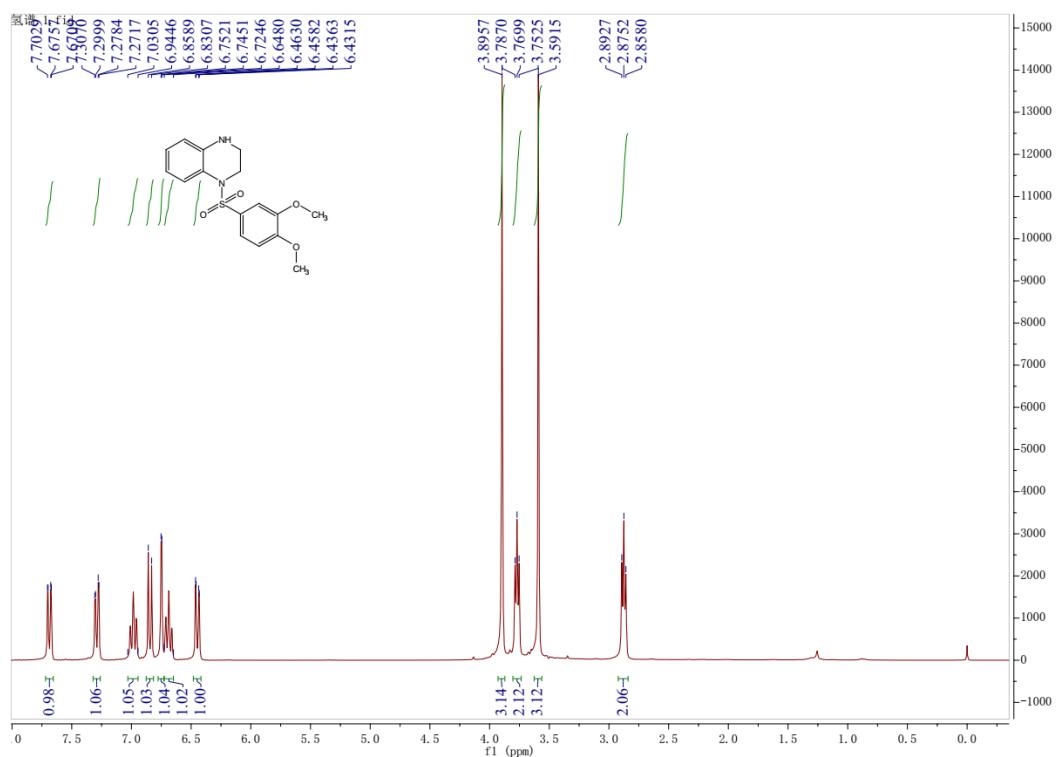
HPLC purity



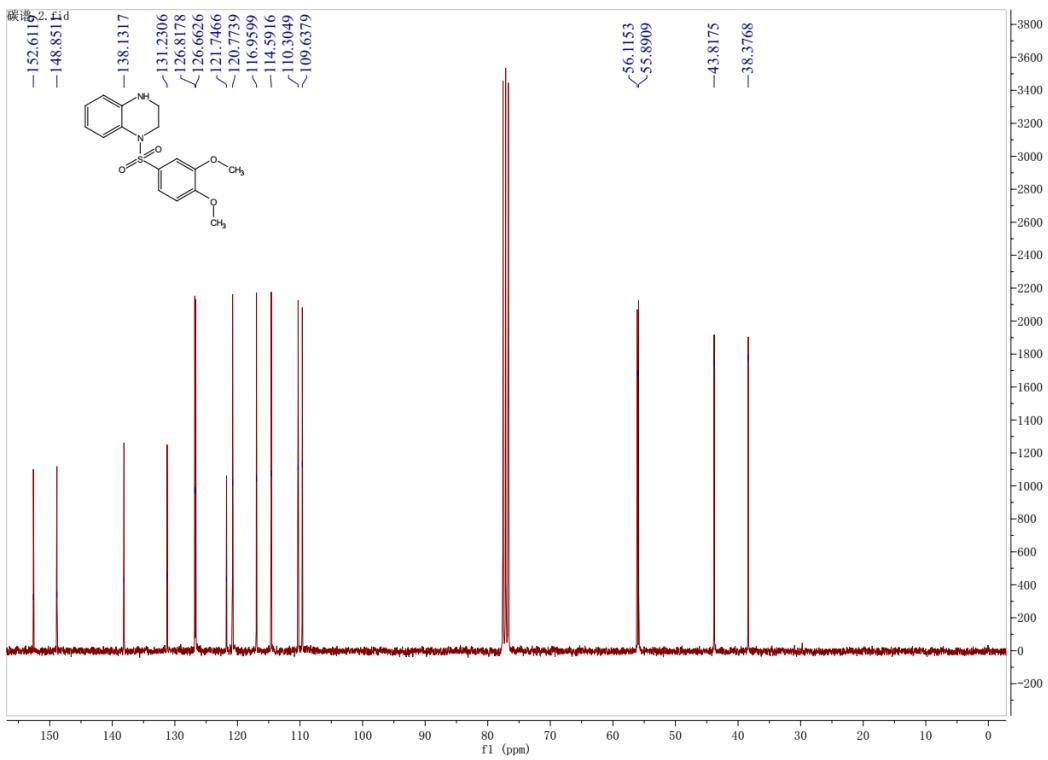
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1	2. 580	BV R	0. 1366	2. 44404e4	2726. 32520	99. 8812
2	3. 761	VB E	0. 1703	29. 06045	2. 72828	0. 1188

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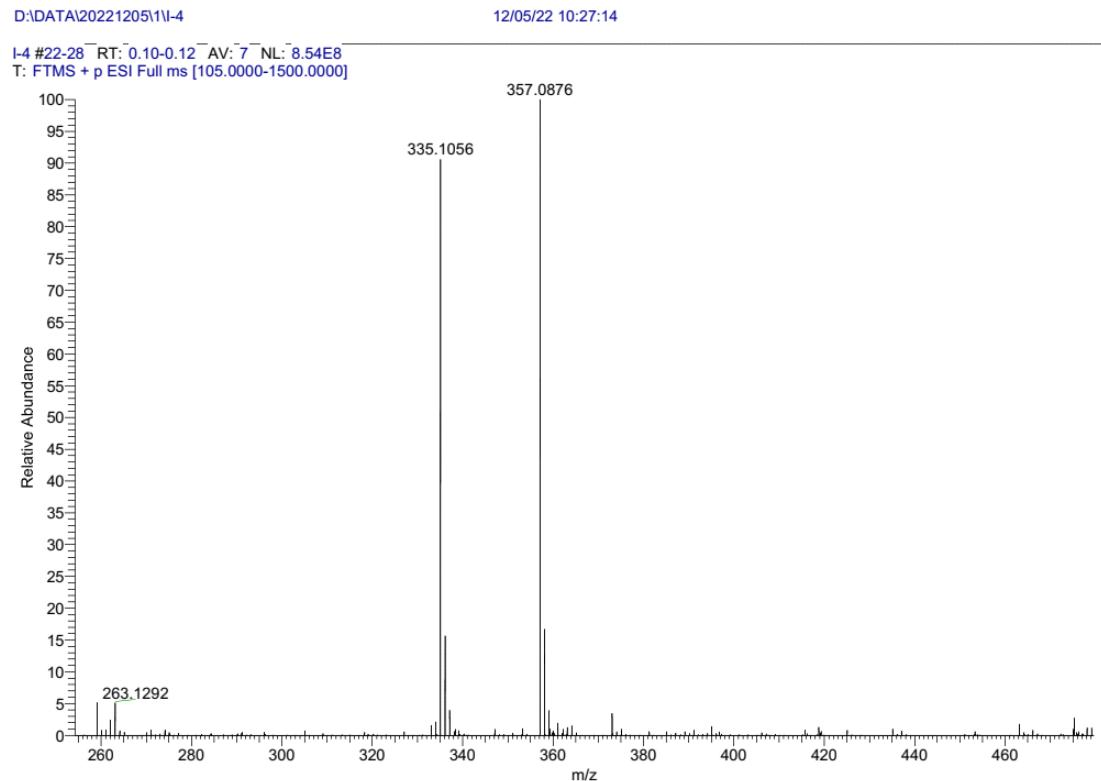
##### <sup>1</sup>H-NMR



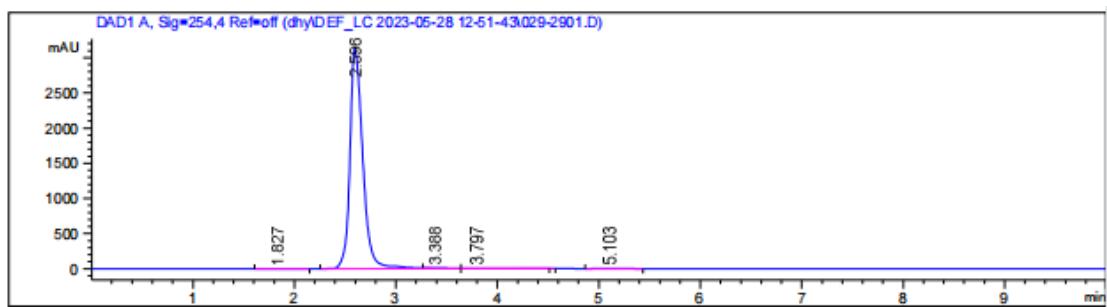
##### <sup>13</sup>C-NMR



## HRMS



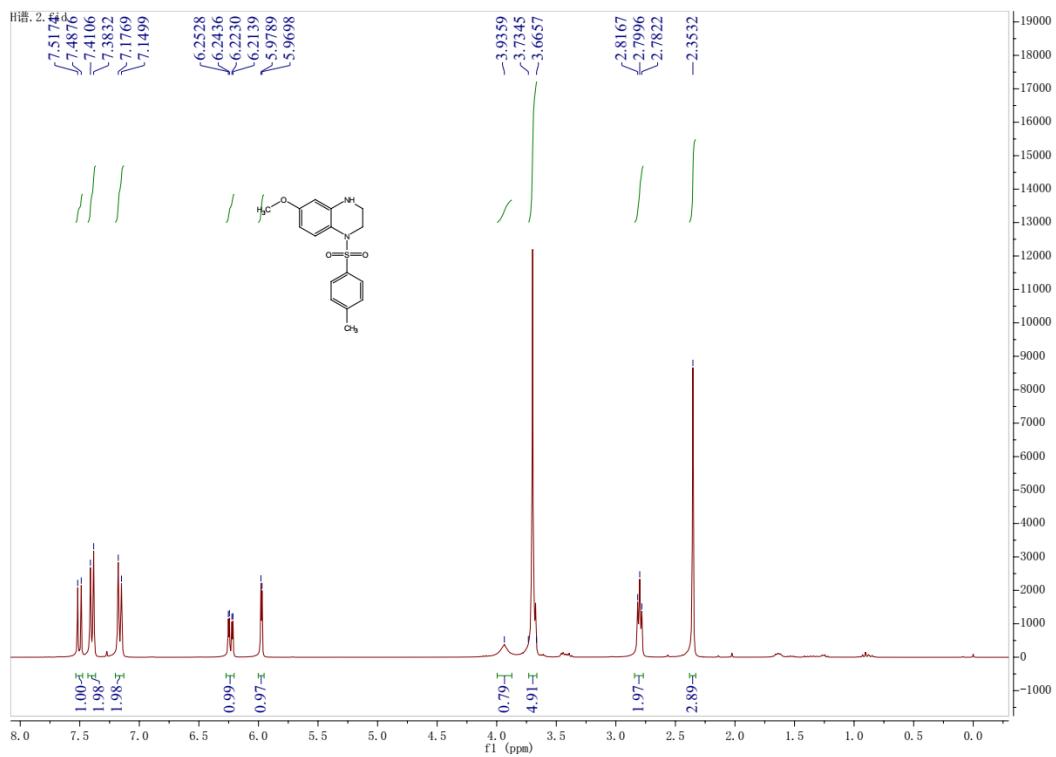
HPLC purity



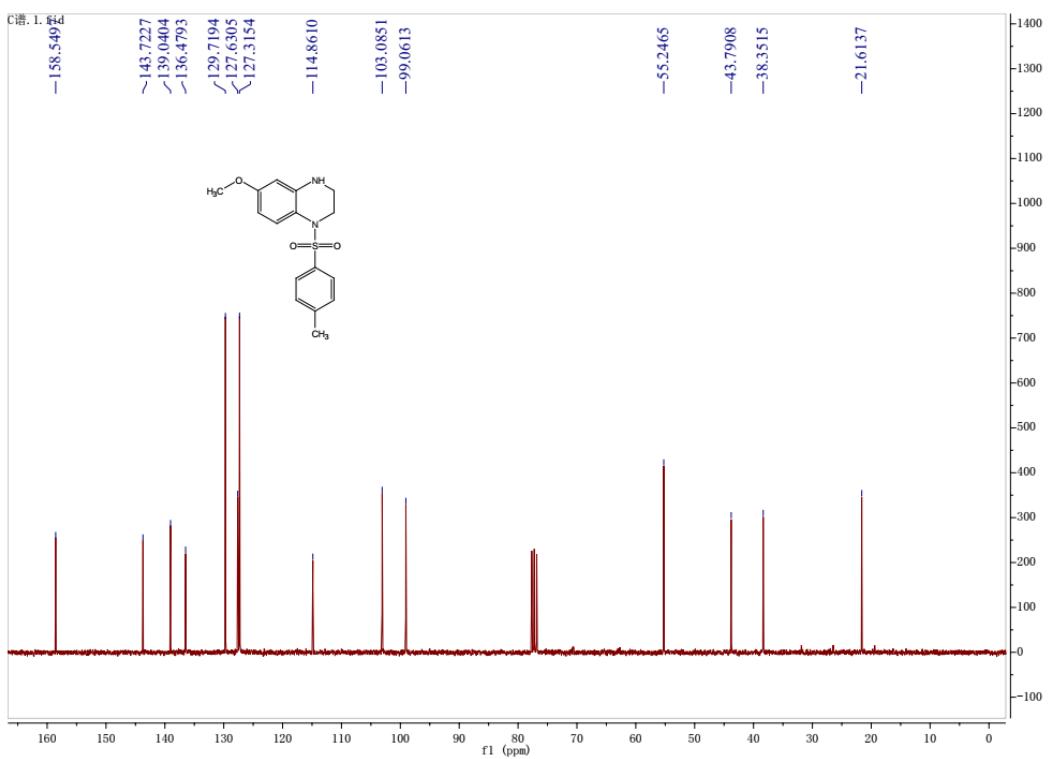
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1	1.827	BB		0.1563	15.19031	1.26285	0.0540
2	2.596	BV R		0.1364	2.78831e4	3116.74927	99.1785
3	3.388	VV E		0.2500	50.90475	2.93949	0.1811
4	3.797	VB E		0.2468	98.68674	5.67783	0.3510
5	5.103	BB		0.1928	66.18219	5.48524	0.2354

## I-5

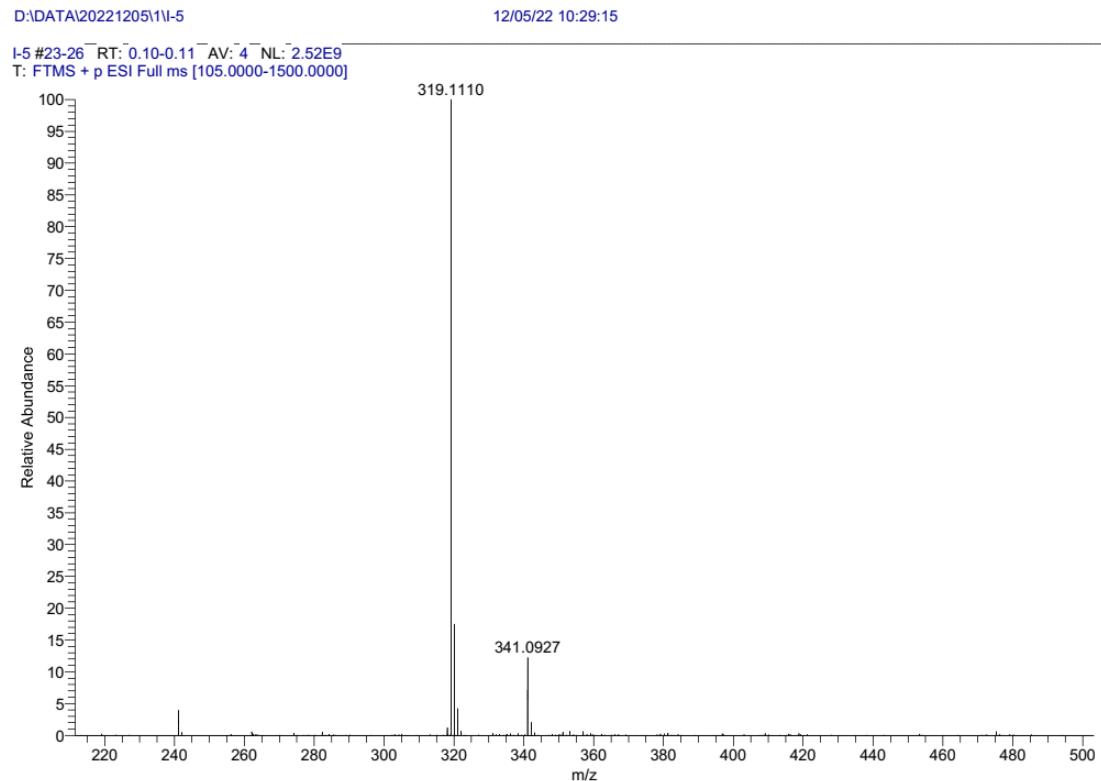
### <sup>1</sup>H-NMR



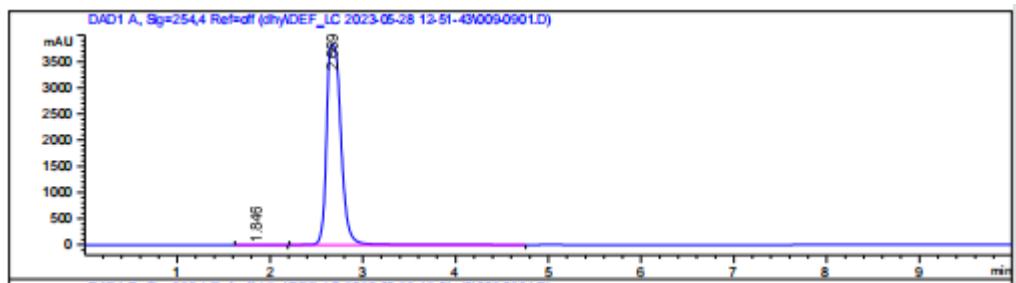
### <sup>13</sup>C-NMR



## HRMS



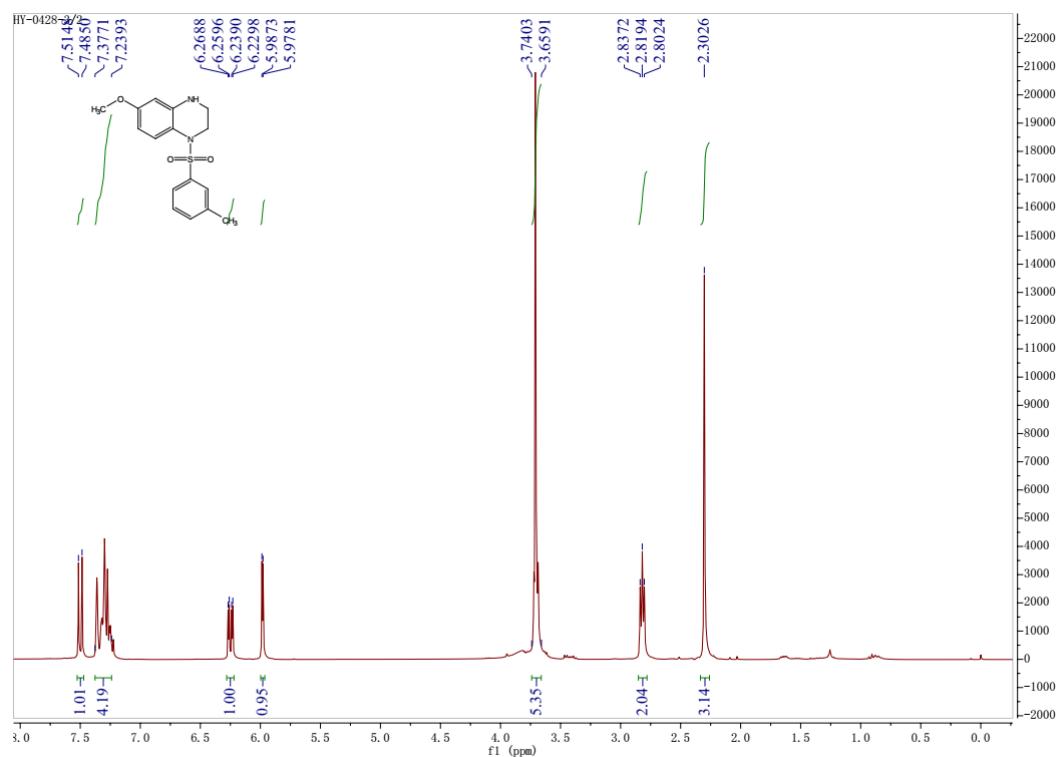
HPLC purity



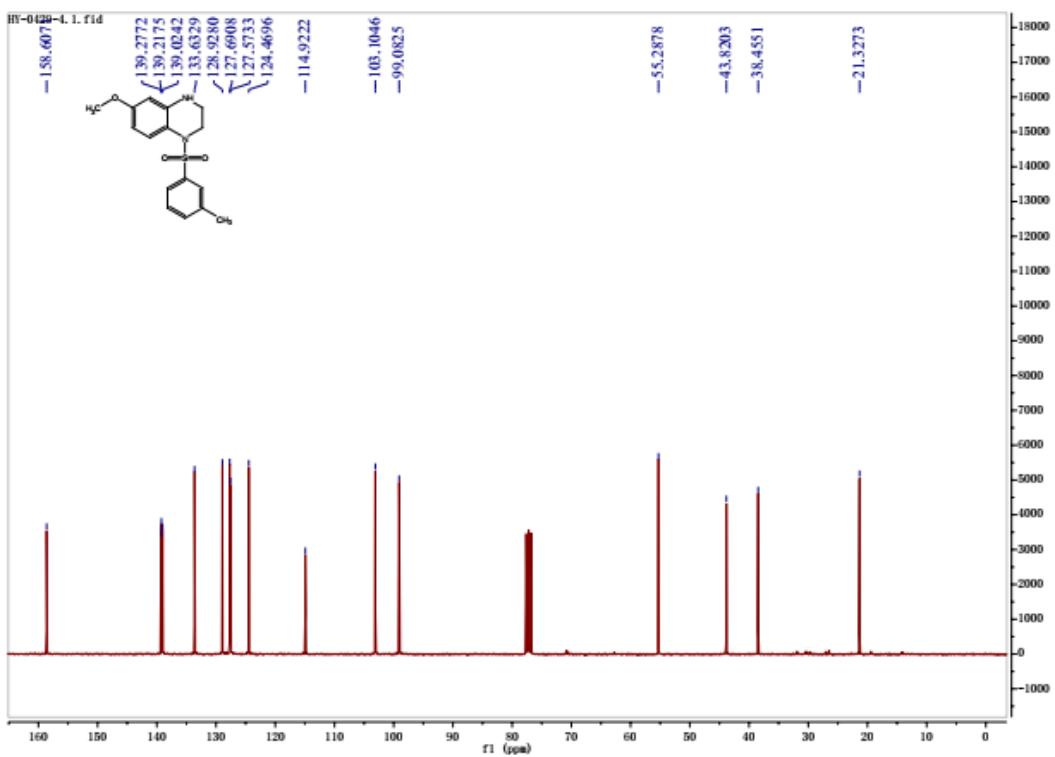
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1	1.846	BB	0.1410	12.63274	1.16048	0.0306
2	2.669	BV R	0.1681	4.12785e4	3819.05420	99.9694

## I-6

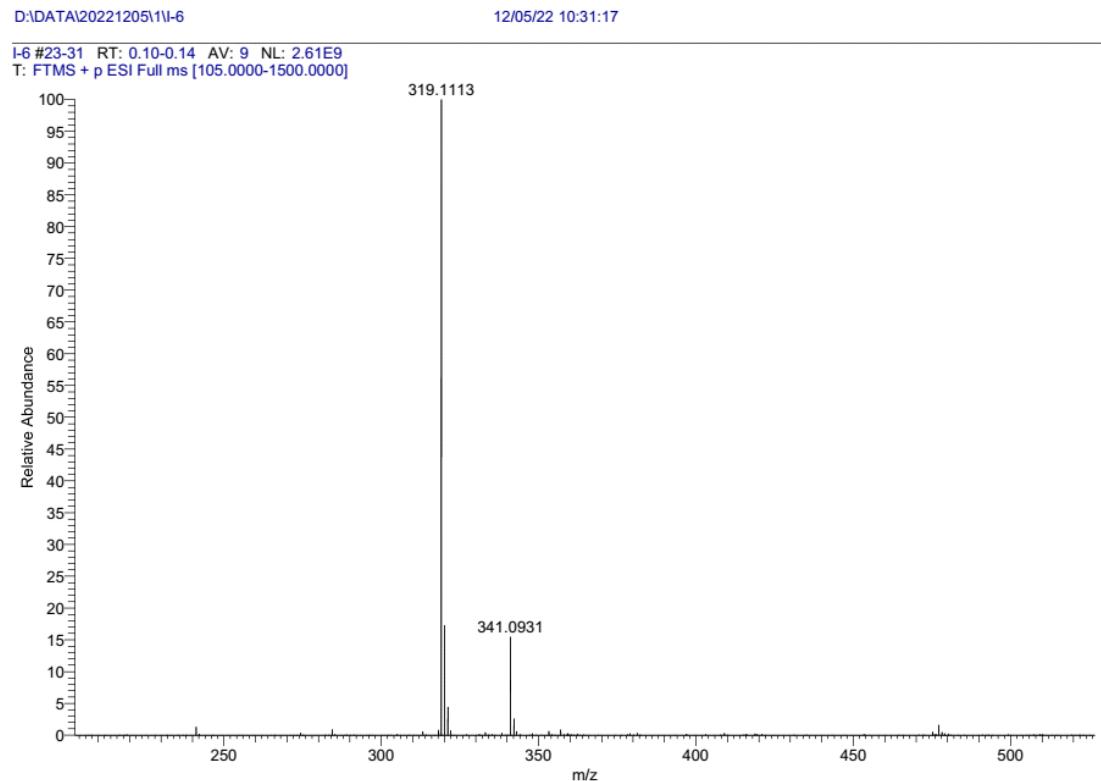
### <sup>1</sup>H-NMR



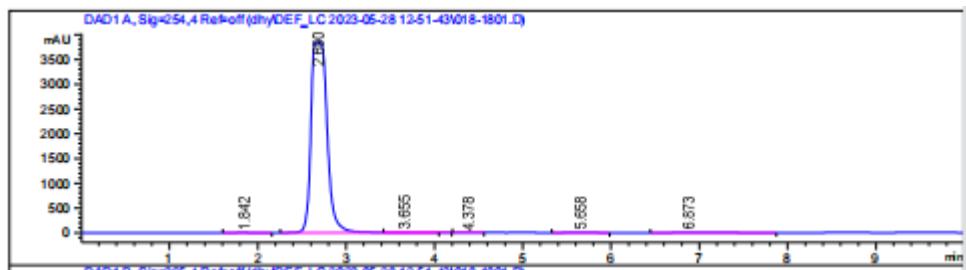
### <sup>13</sup>C-NMR



## HRMS



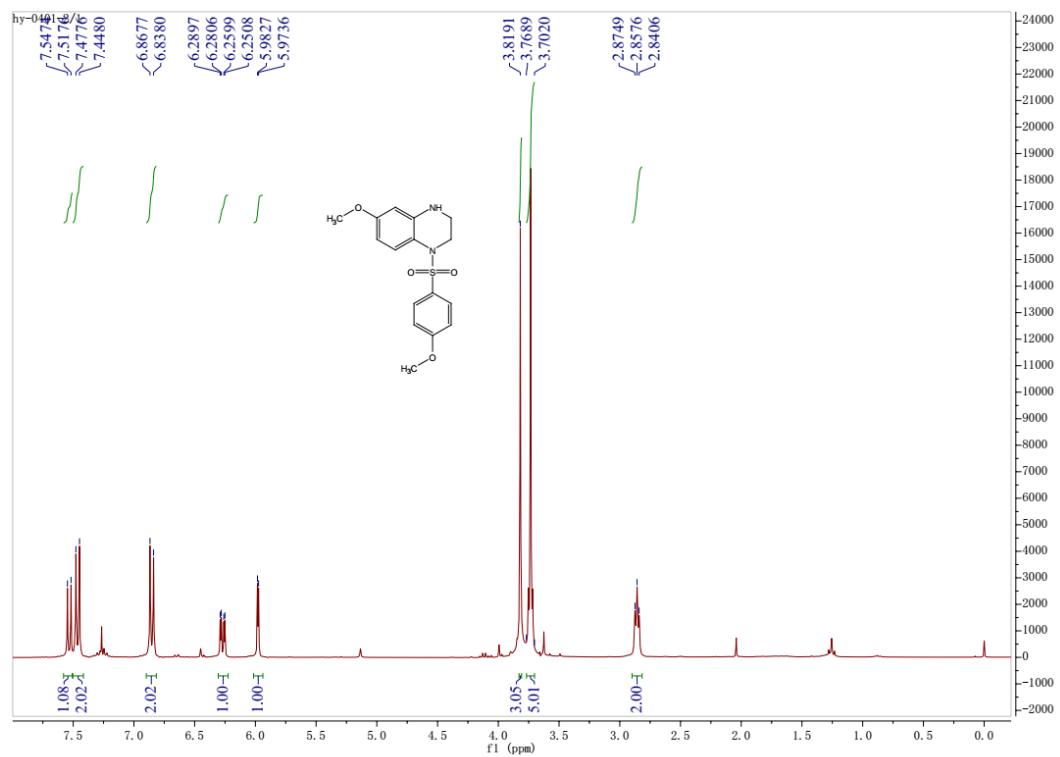
HPLC purity



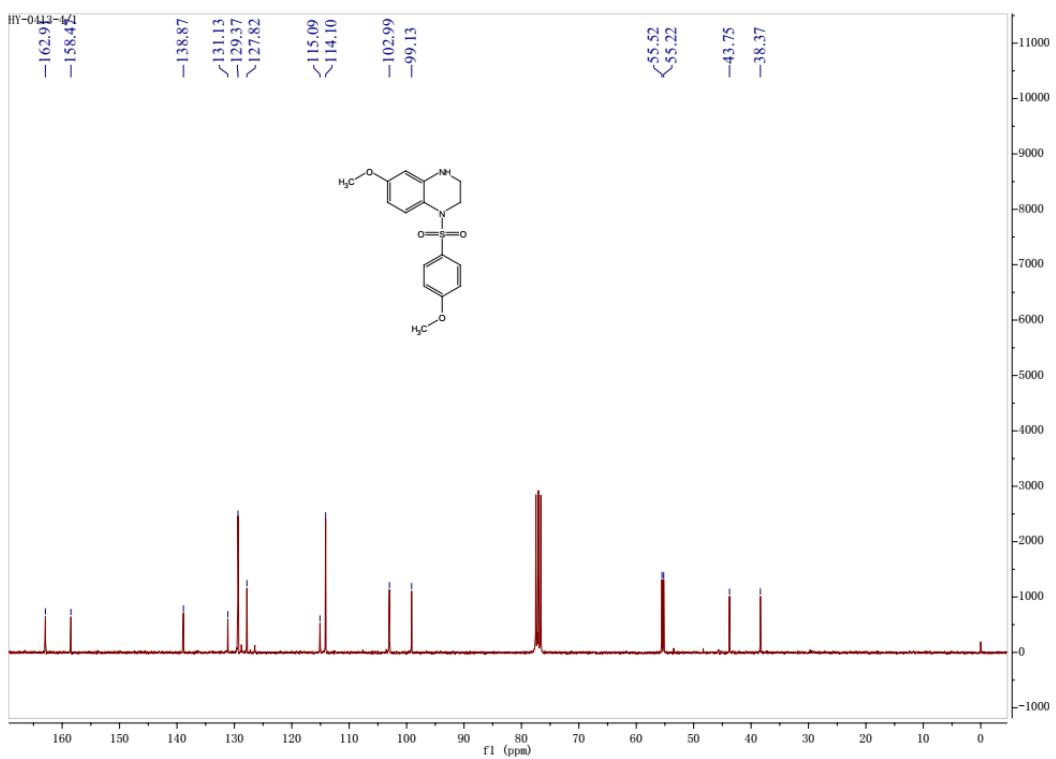
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							%
1	1.842	BB	0.1503	30.64877	2.74327	0.0626	
2	2.690	BV R	0.2002	4.87124e4	3833.69238	99.5411	
3	3.655	VB E	0.2686	80.24499	4.71499	0.1640	
4	4.378	BB	0.1583	19.44459	2.02010	0.0397	
5	5.658	BB	0.2522	35.94201	2.20410	0.0734	
6	6.873	BB	0.4421	58.27518	1.71636	0.1191	

## I-7

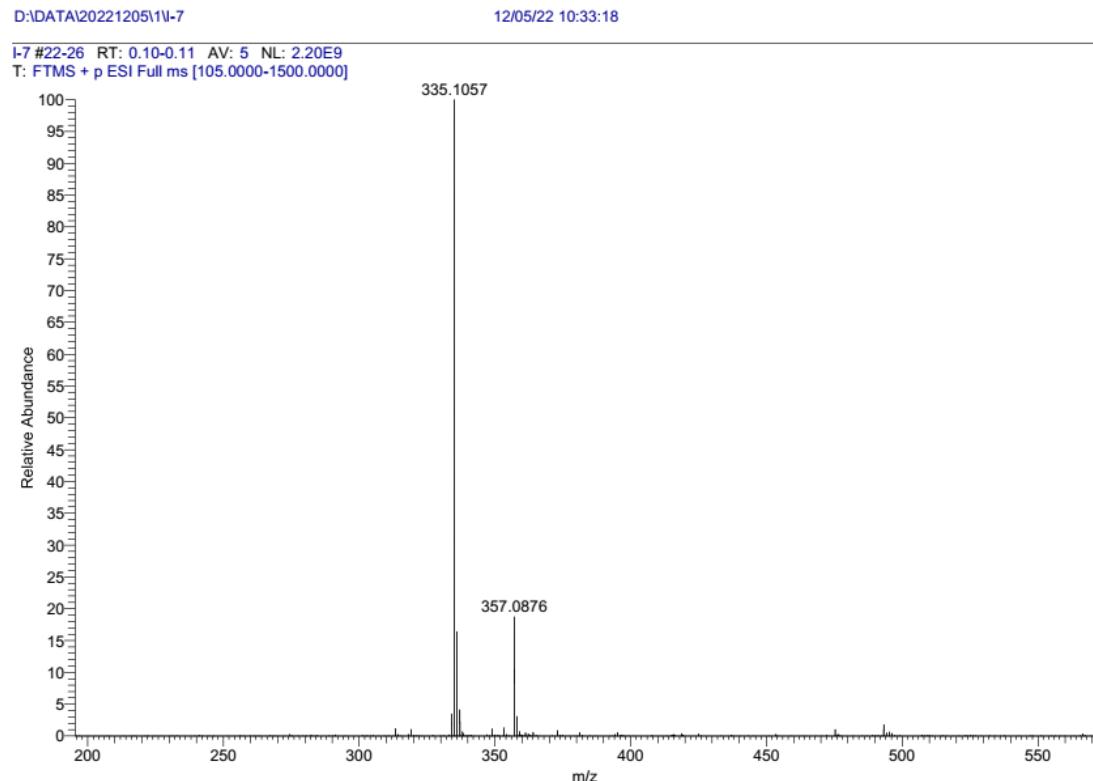
### <sup>1</sup>H-NMR



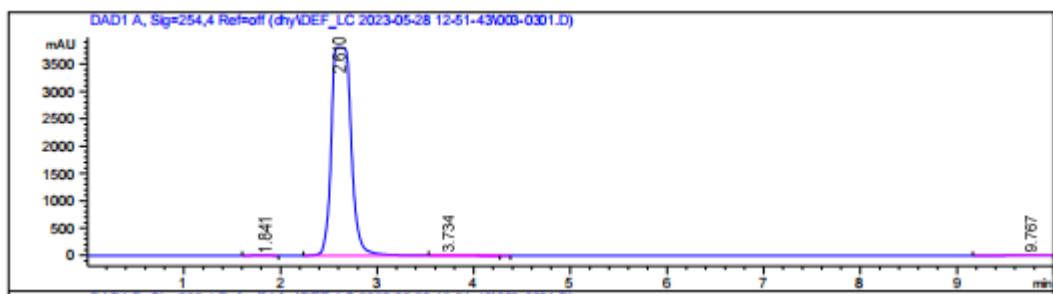
### <sup>13</sup>C-NMR



## HRMS

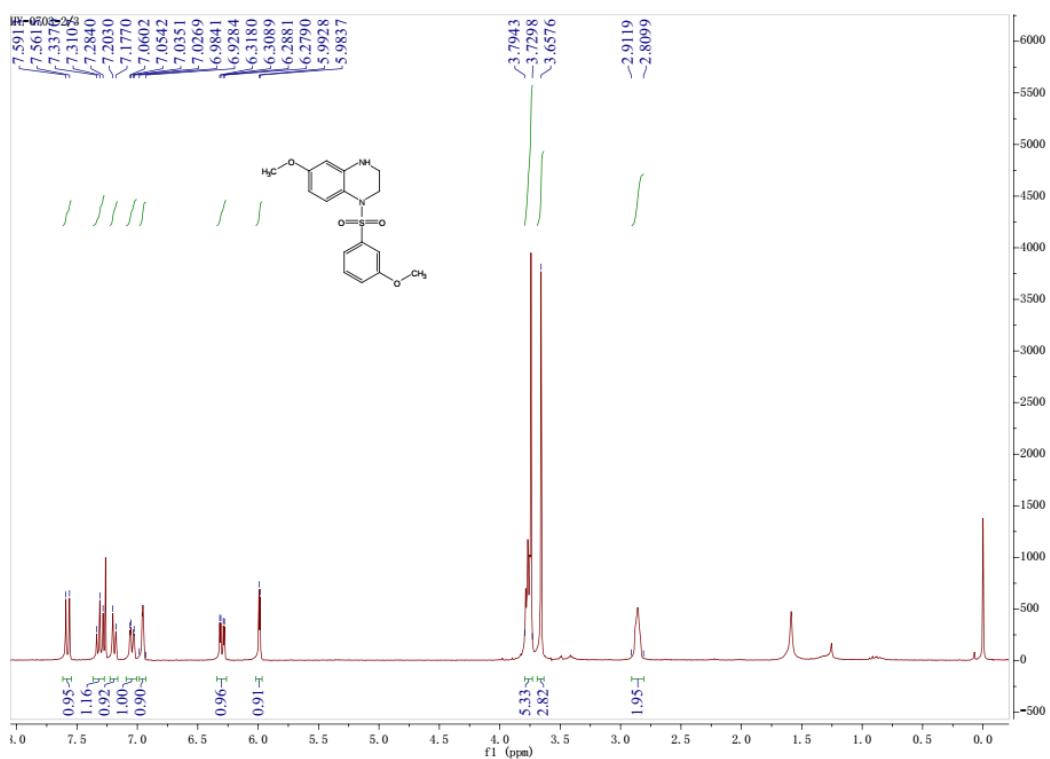


HPLC purity

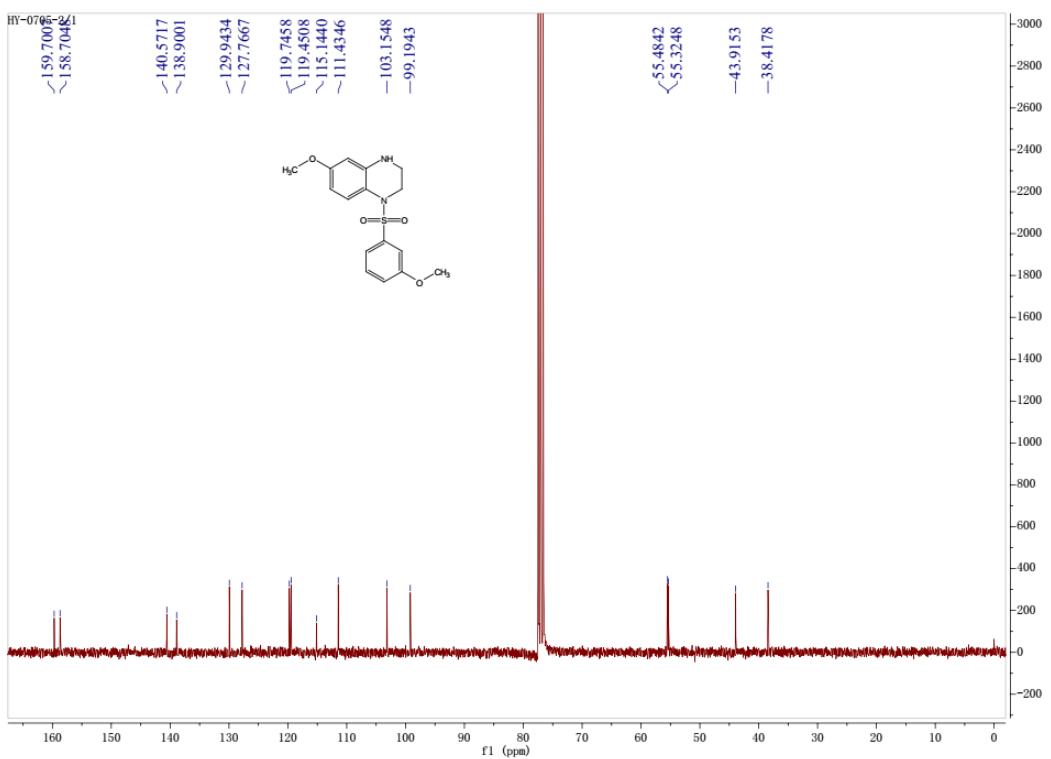


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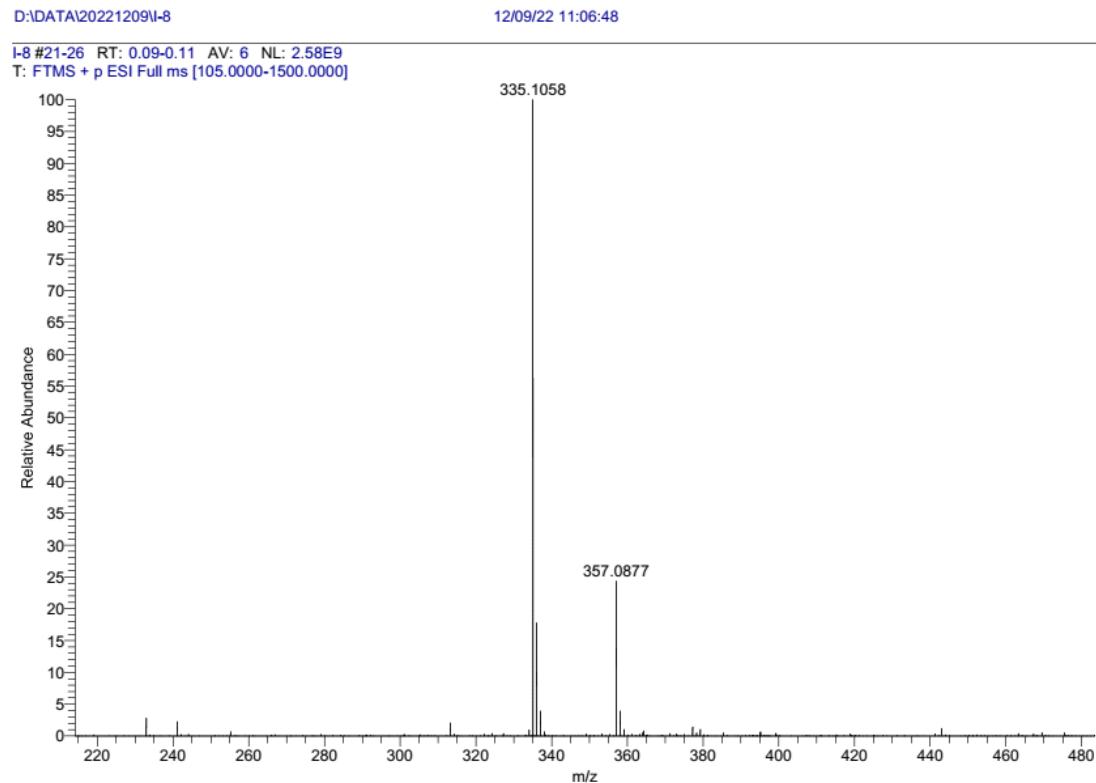
<sup>1</sup>H-NMR



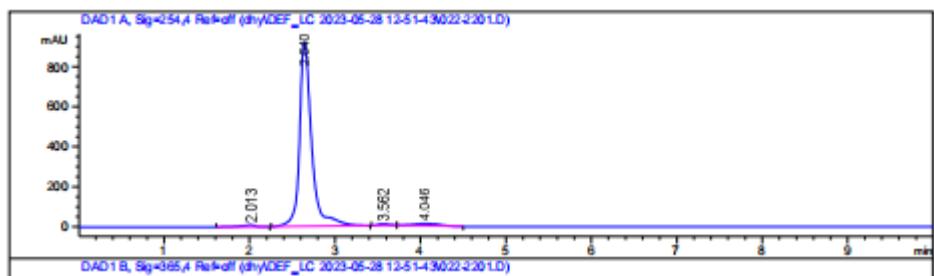
<sup>13</sup>C-NMR



## HRMS



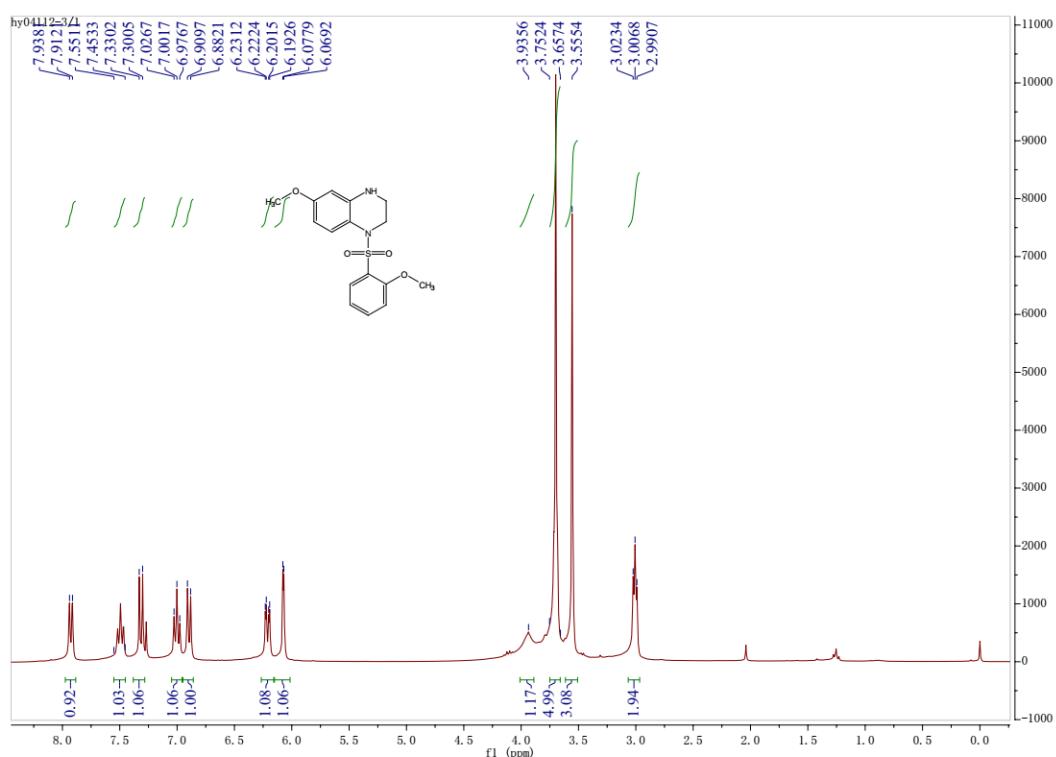
HPLC purity



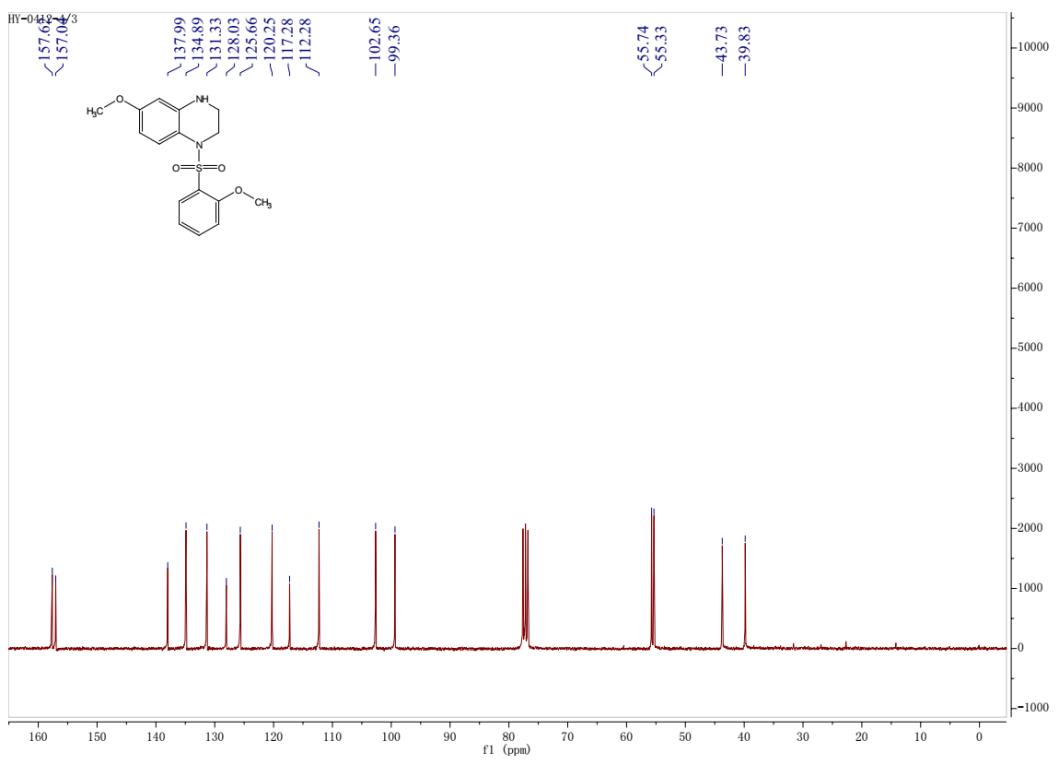
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1	2. 013	BB	0. 1475	105. 52792	9. 65779	1. 1173
2	2. 640	BB	0. 1474	9068. 36719	917. 02521	96. 0126
3	3. 562	BB	0. 1293	59. 13969	7. 39317	0. 6261
4	4. 046	BB	0. 2866	211. 94304	10. 19221	2. 2440

### I-9

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



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

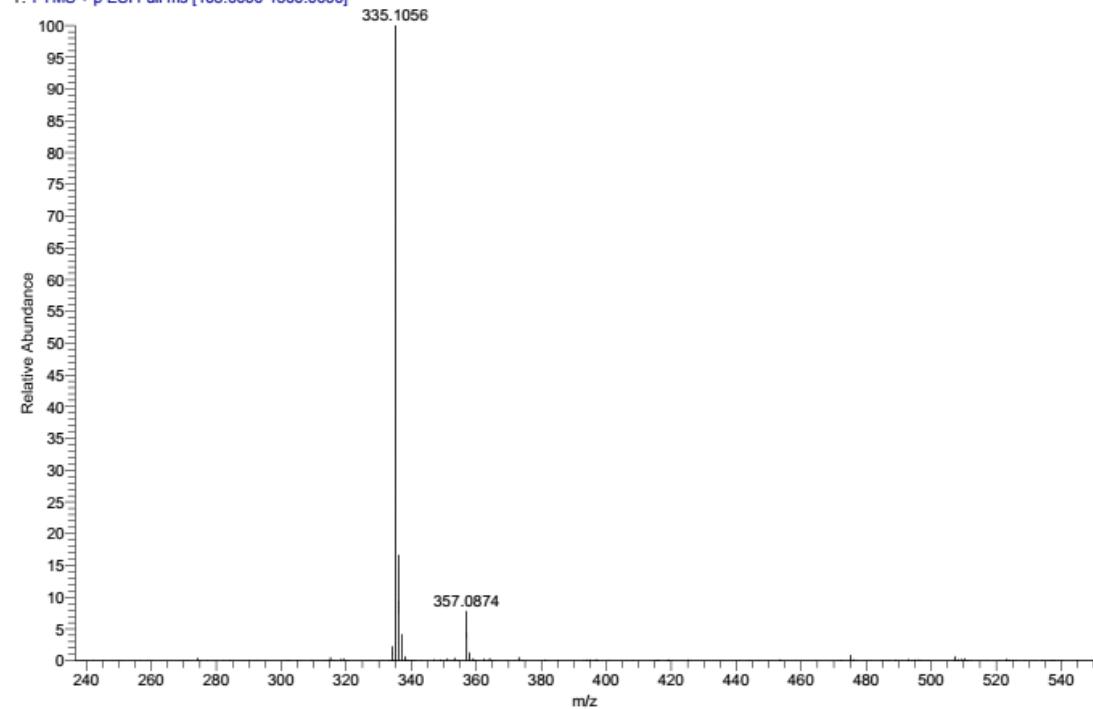


## HRMS

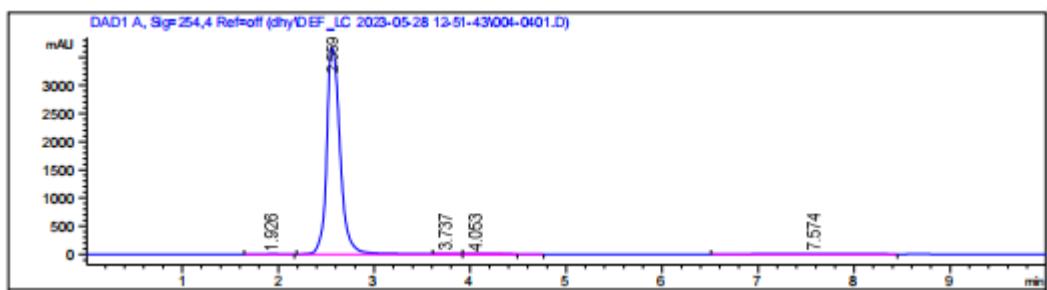
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12/05/22 10:37:20

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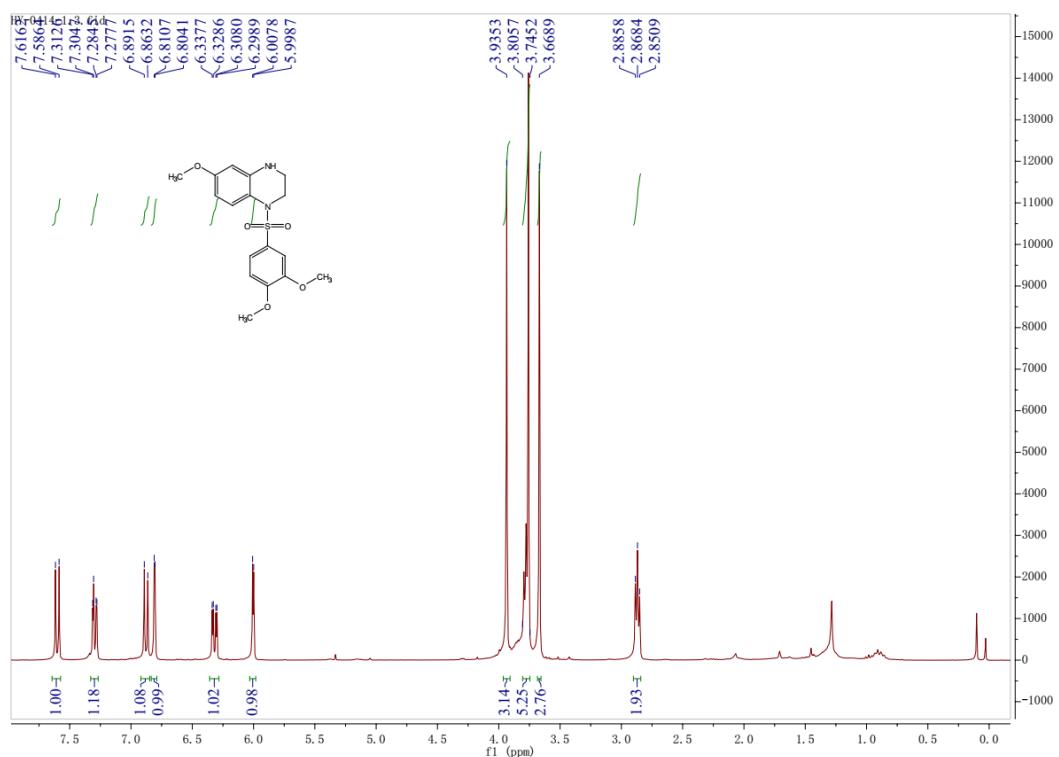
## HPLC purity



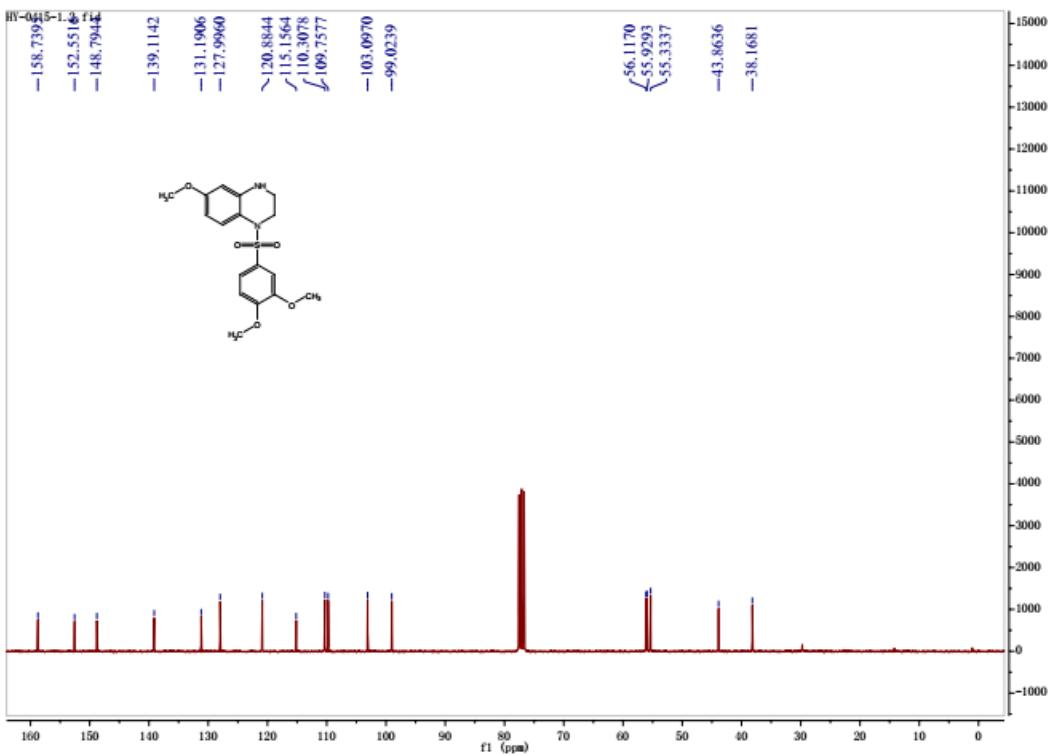
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1	1.926	BB	0.1216	22.68030	2.41377	0.0627
2	2.559	BV R	0.1479	3.58819e4	3676.13940	99.1342
3	3.737	VV E	0.1665	11.26871	1.03966	0.0311
4	4.053	VB E	0.2211	17.82541	1.22961	0.0492
5	7.574	BB	0.5721	261.59573	6.46458	0.7227

### I-10

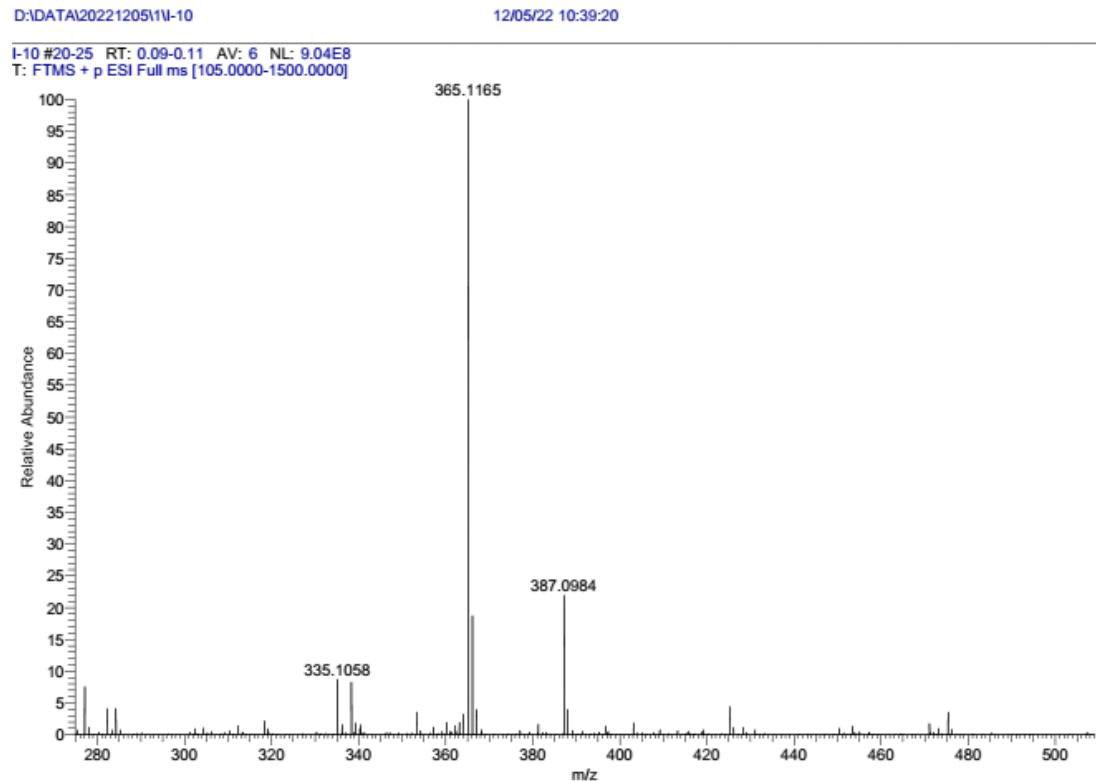
#### <sup>1</sup>H-NMR



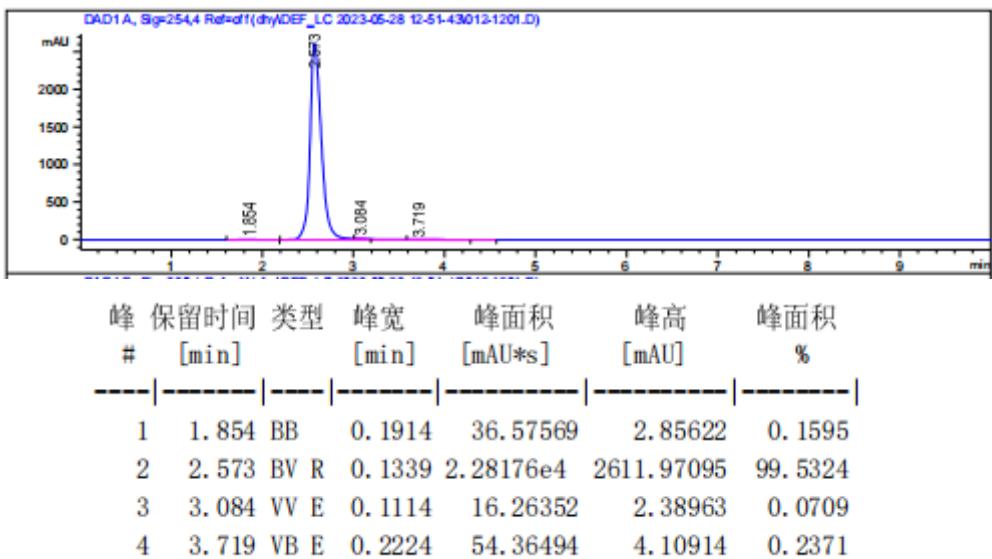
#### <sup>13</sup>C-NMR



## HRMS

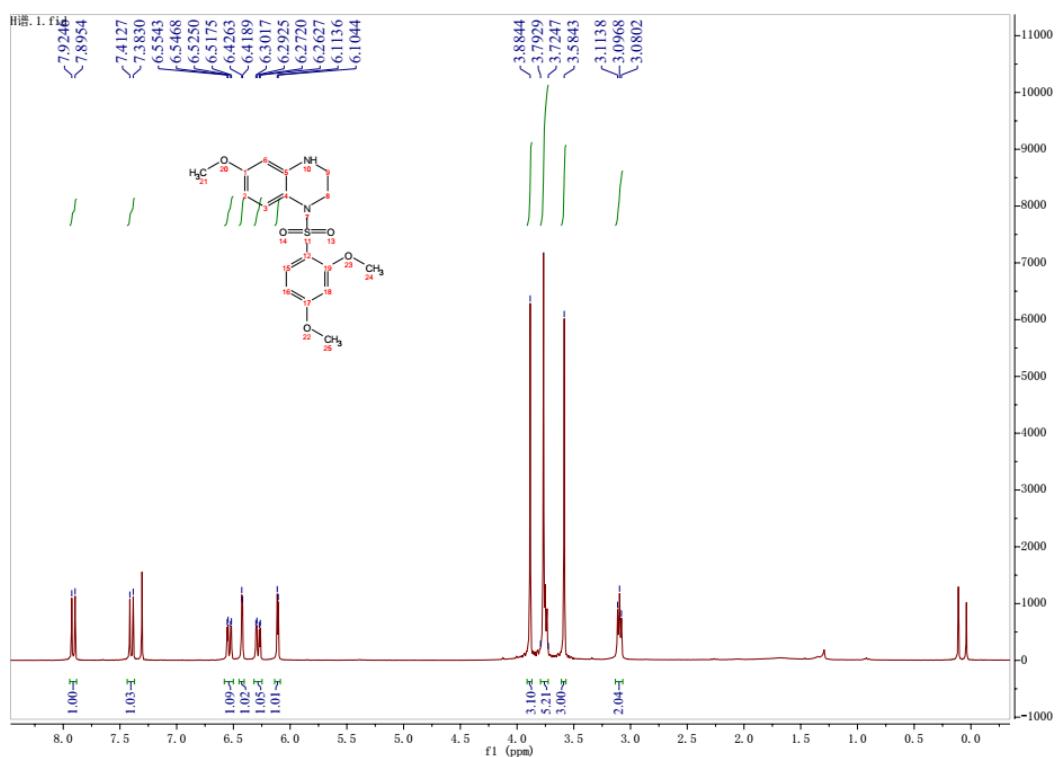


HPLC purity

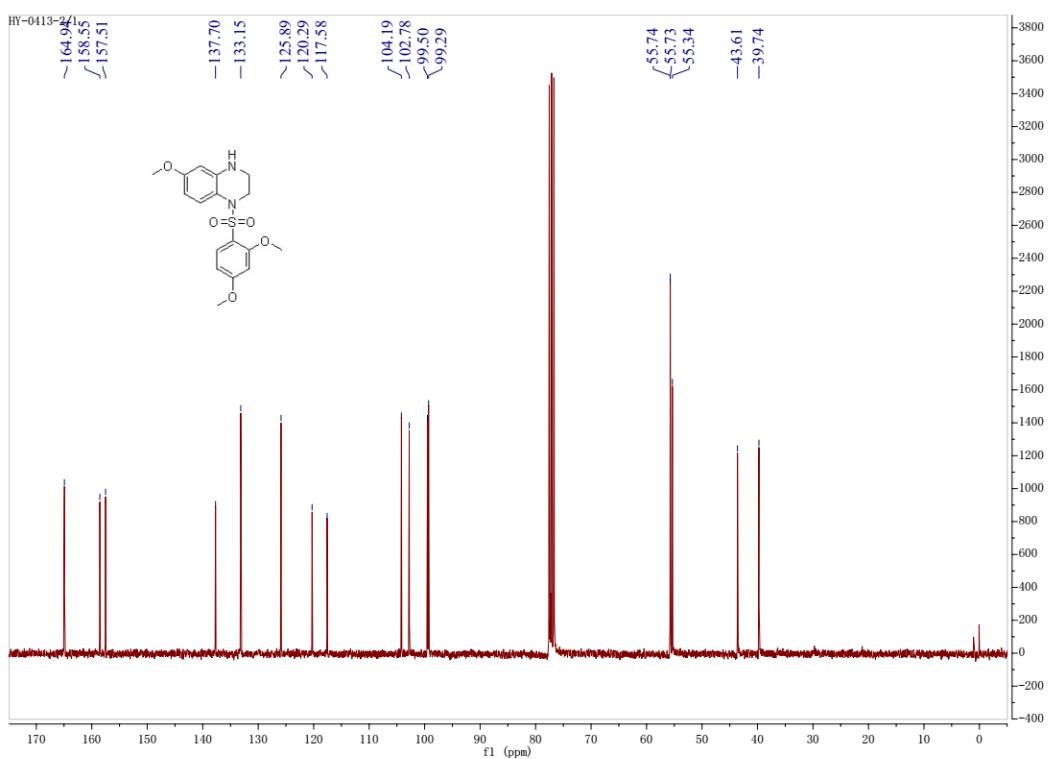


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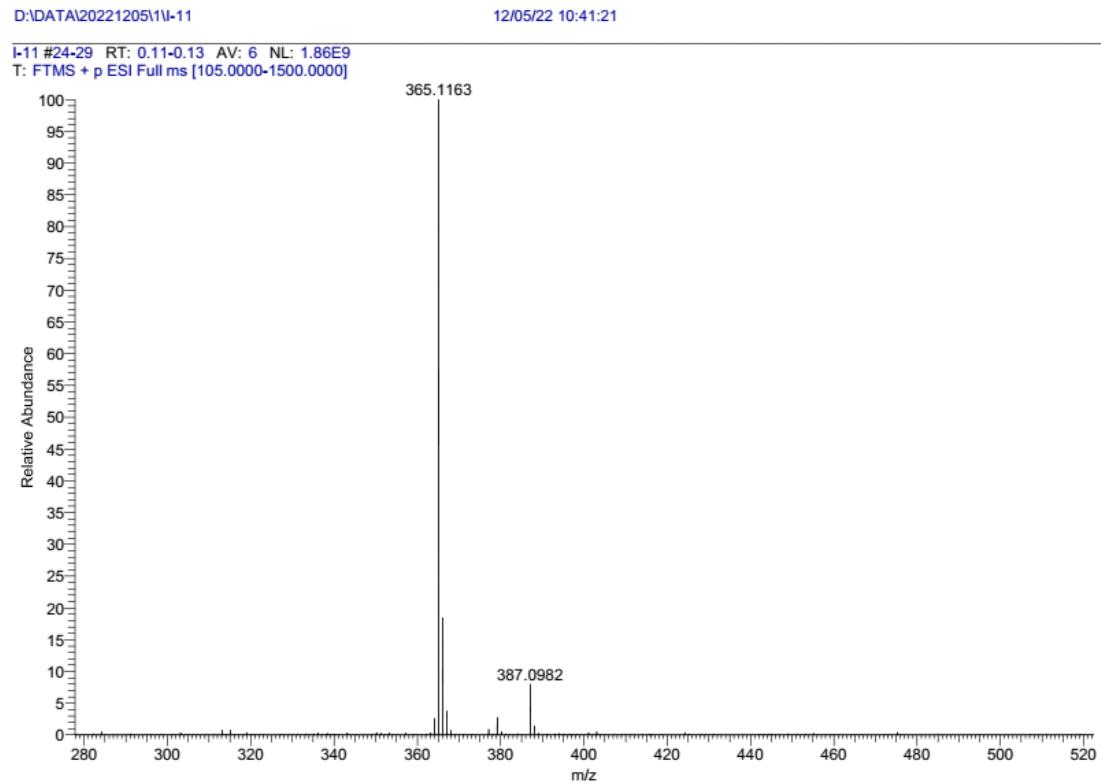
### <sup>1</sup>H-NMR



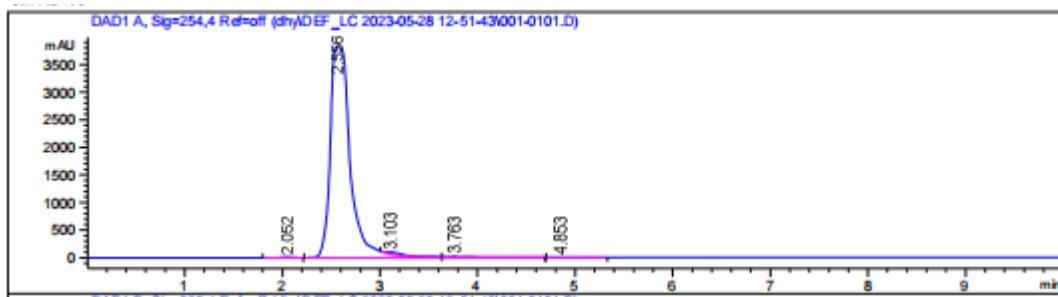
### <sup>13</sup>C-NMR



## HRMS



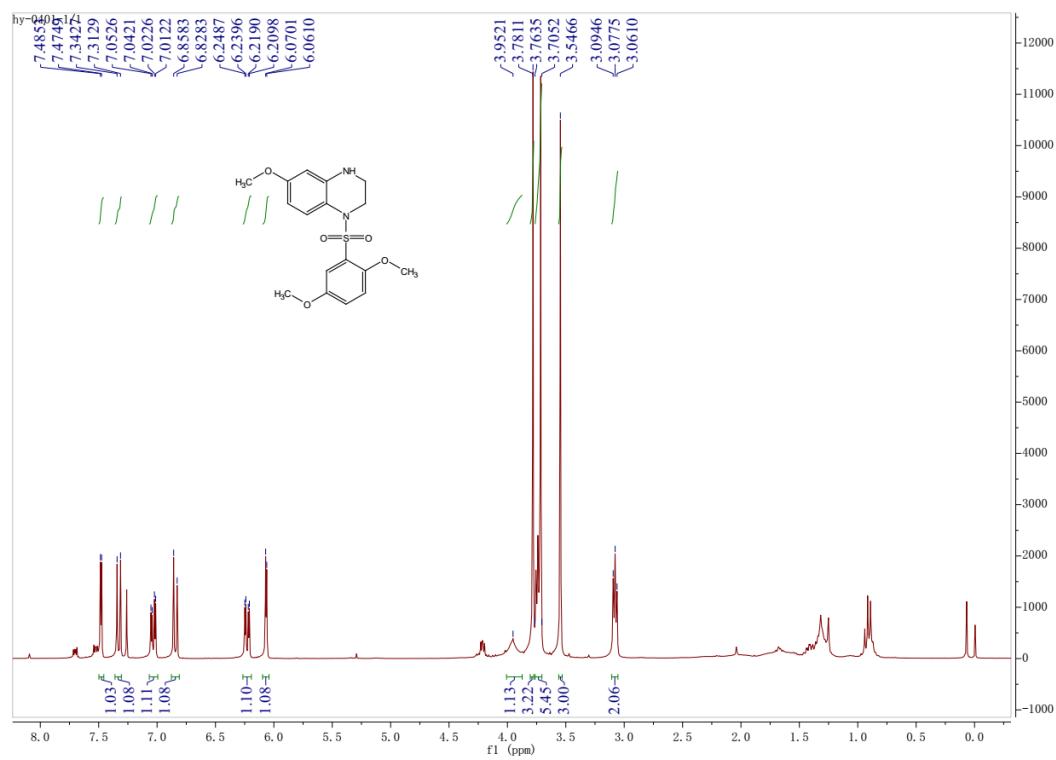
HPLC purity



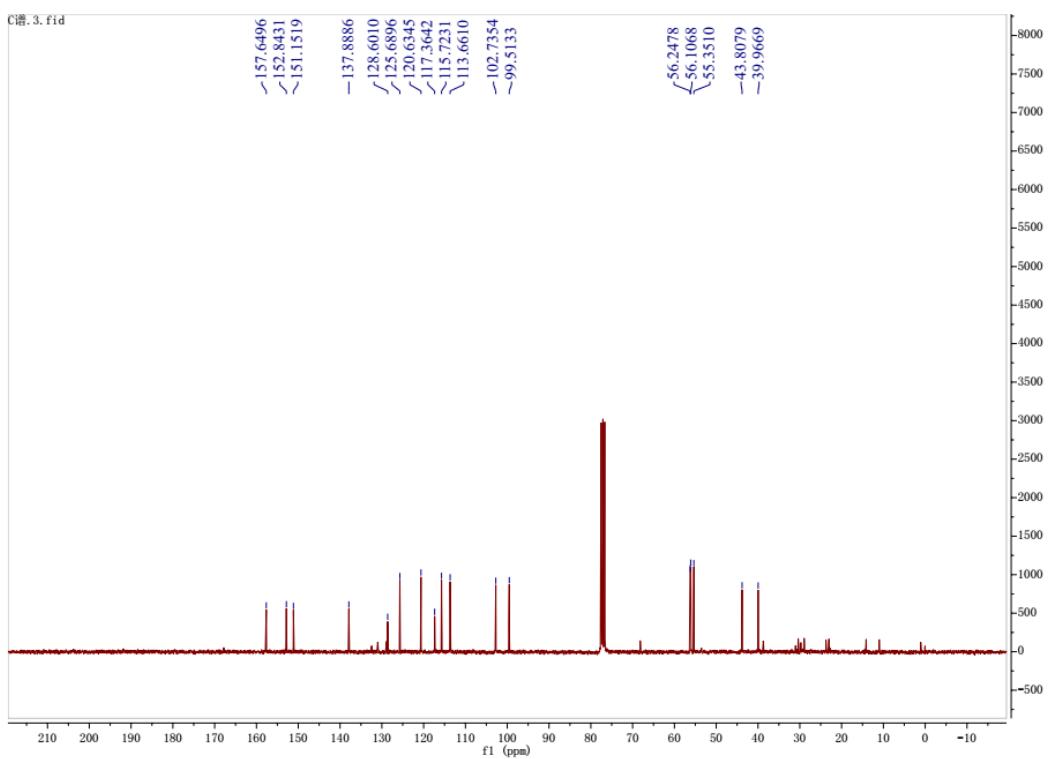
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1	2.052	BB	0.0852	76.75024	14.16857	0.1382
2	2.556	BV R	0.2192	5.45632e4	3806.43188	98.2834
3	3.103	VV E	0.2362	569.95819	33.55543	1.0267
4	3.763	VB E	0.3305	292.19229	12.33008	0.5263
5	4.853	BB	0.2045	14.08991	1.05013	0.0254

## I-12

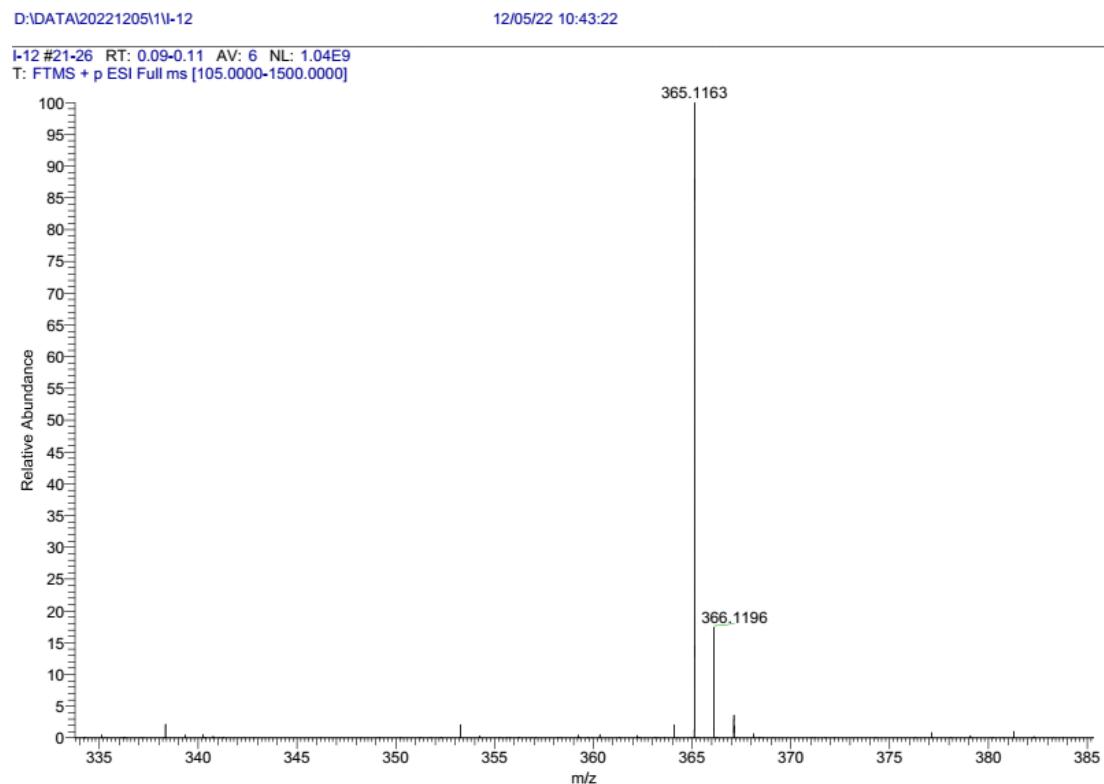
### <sup>1</sup>H-NMR



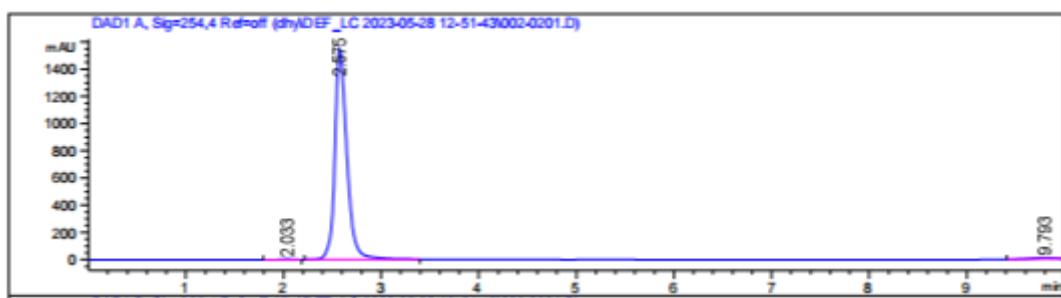
### <sup>13</sup>C-NMR



## HRMS



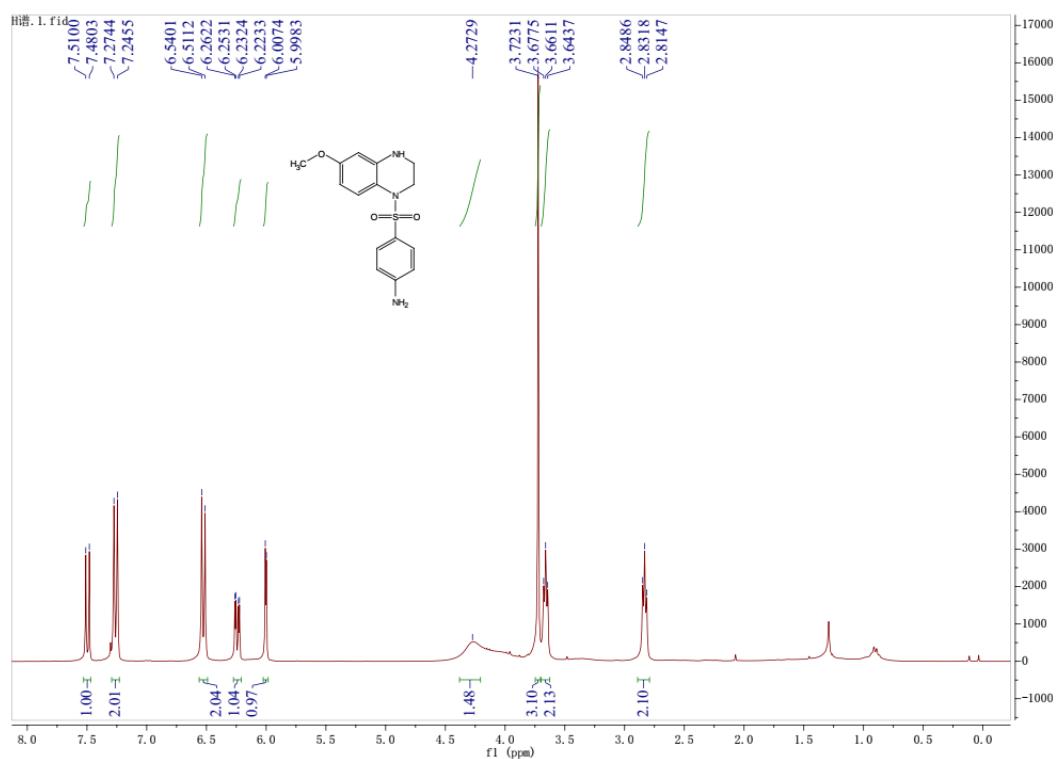
HPLC purity



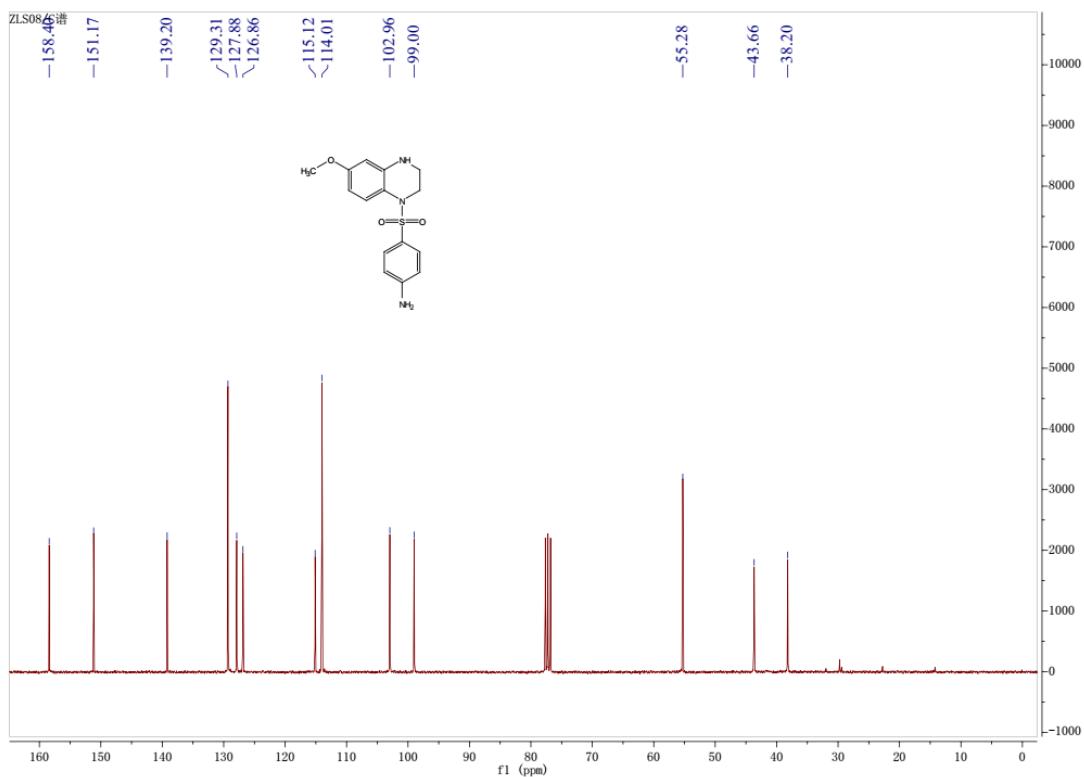
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1	2.033	BB	0.0937	29.02226	4.86083	0.2150
2	2.575	BB	0.1327	1.33359e4	1544.44434	98.7769
3	9.793	BBA	0.2642	136.10683	8.43682	1.0081

### I-13

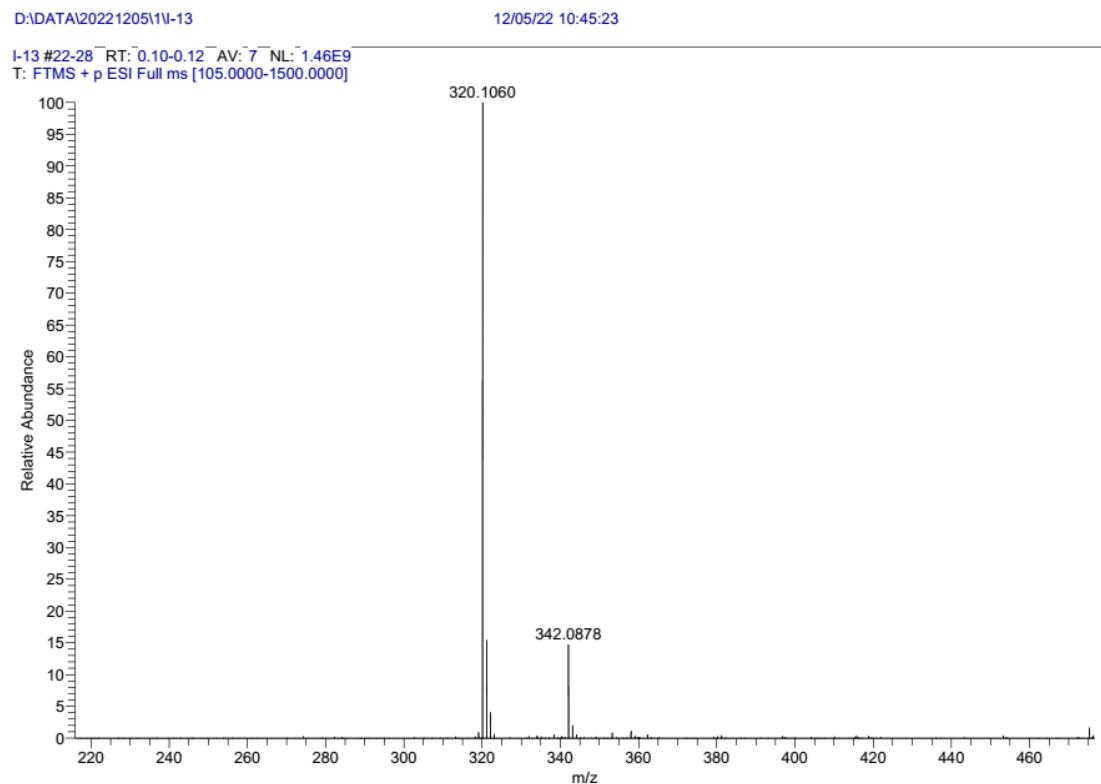
<sup>1</sup>H-NMR



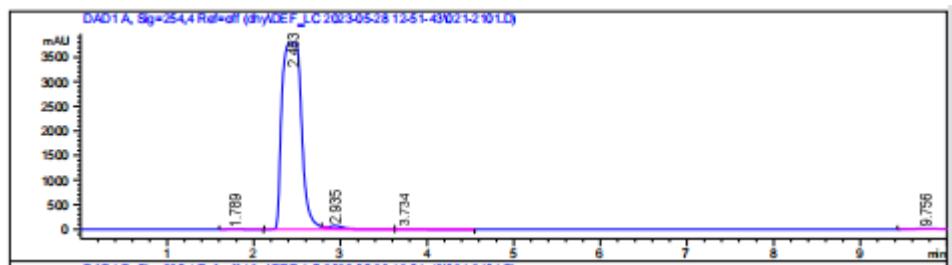
<sup>13</sup>C-NMR



## HRMS



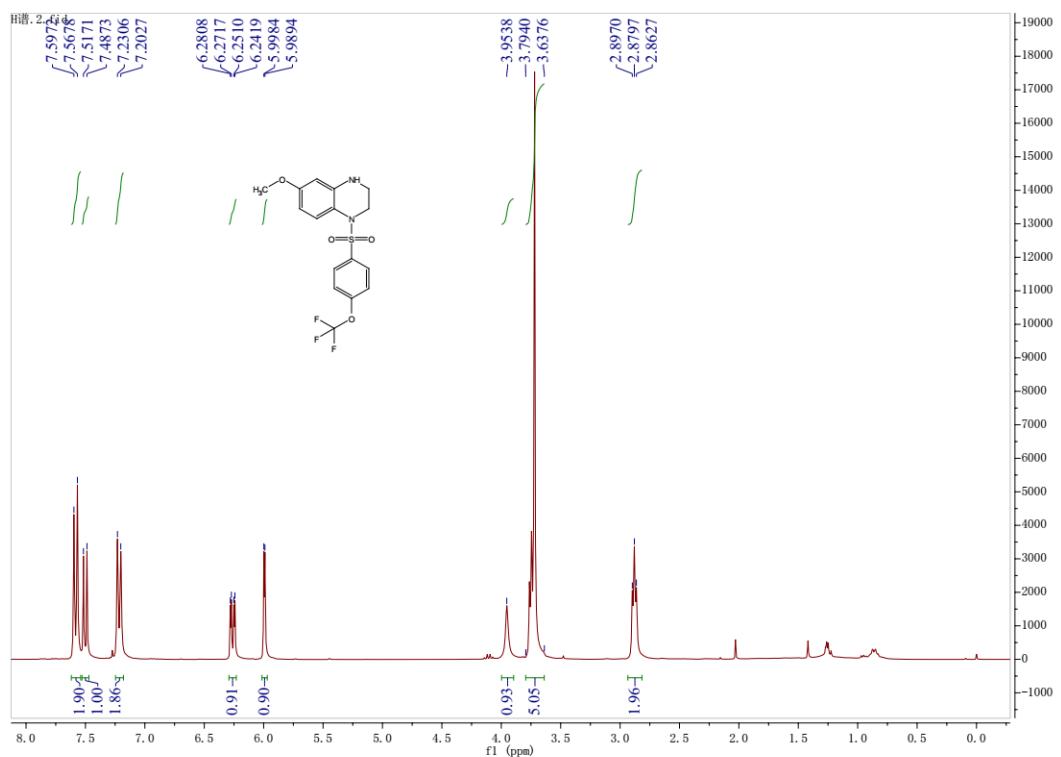
HPLC purity



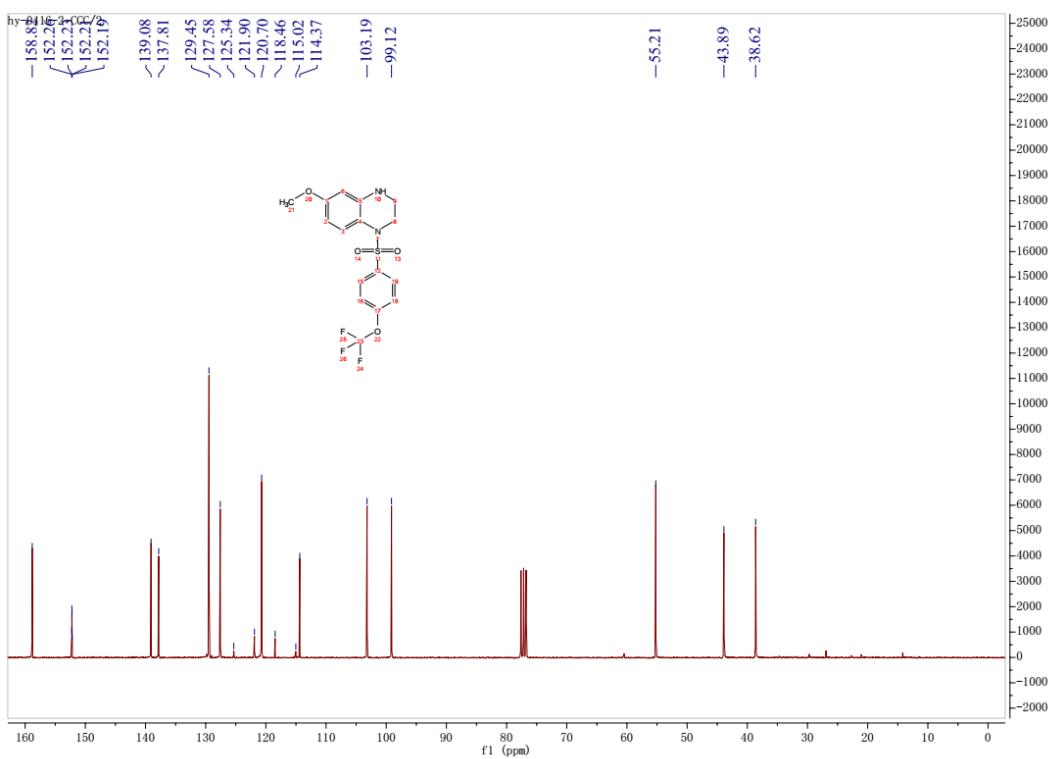
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1	1.789	BB	0.1867	48.39608	4.07015	0.0807
2	2.463	BV R	0.2113	5.89000e4	3790.66577	98.2586
3	2.935	VV E	0.1764	774.58685	64.37450	1.2922
4	3.734	VB E	0.2675	58.44681	3.02431	0.0975
5	9.756	BBA	0.2653	162.43475	9.80127	0.2710

## I-14

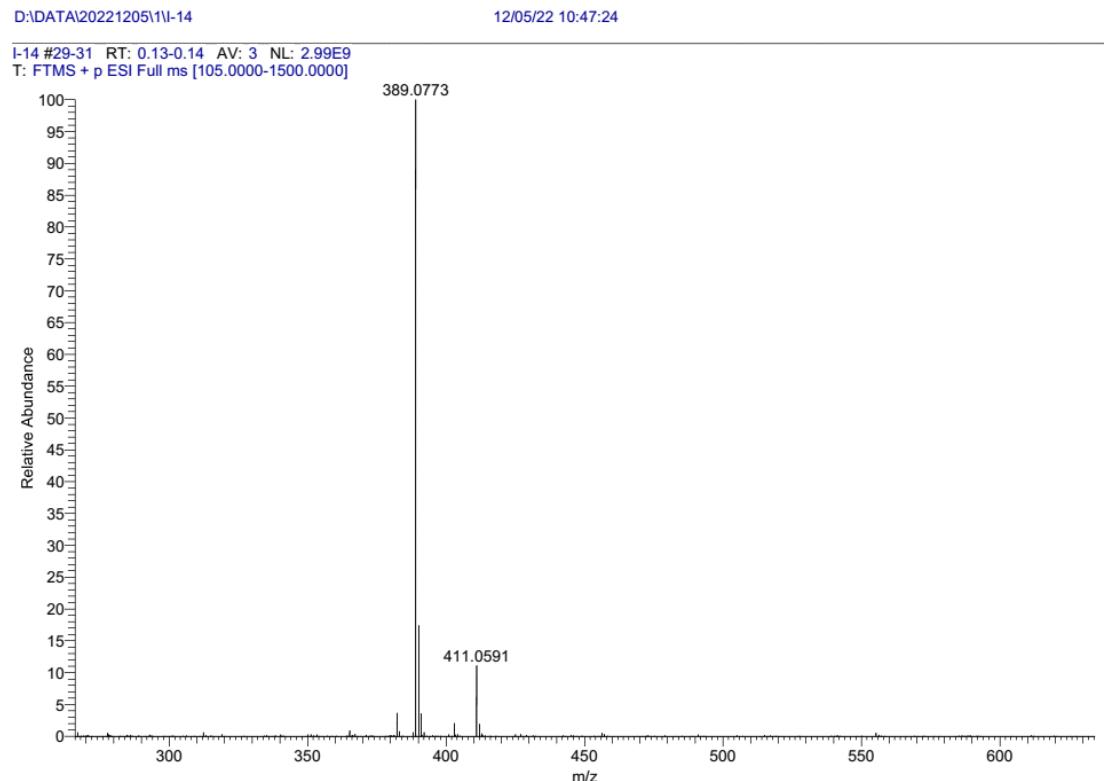
### <sup>1</sup>H-NMR



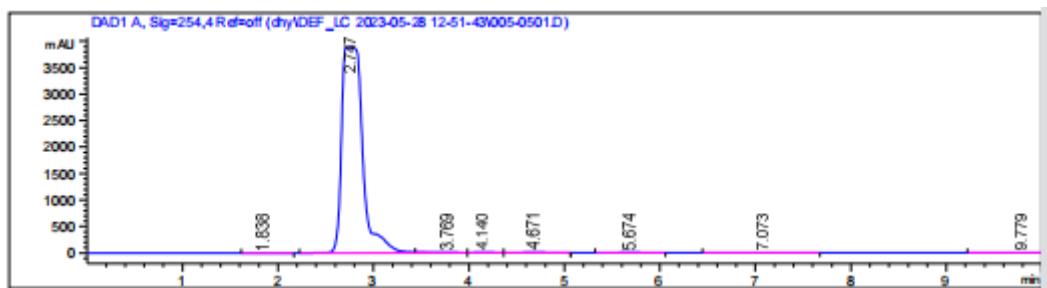
### <sup>13</sup>C-NMR



## HRMS



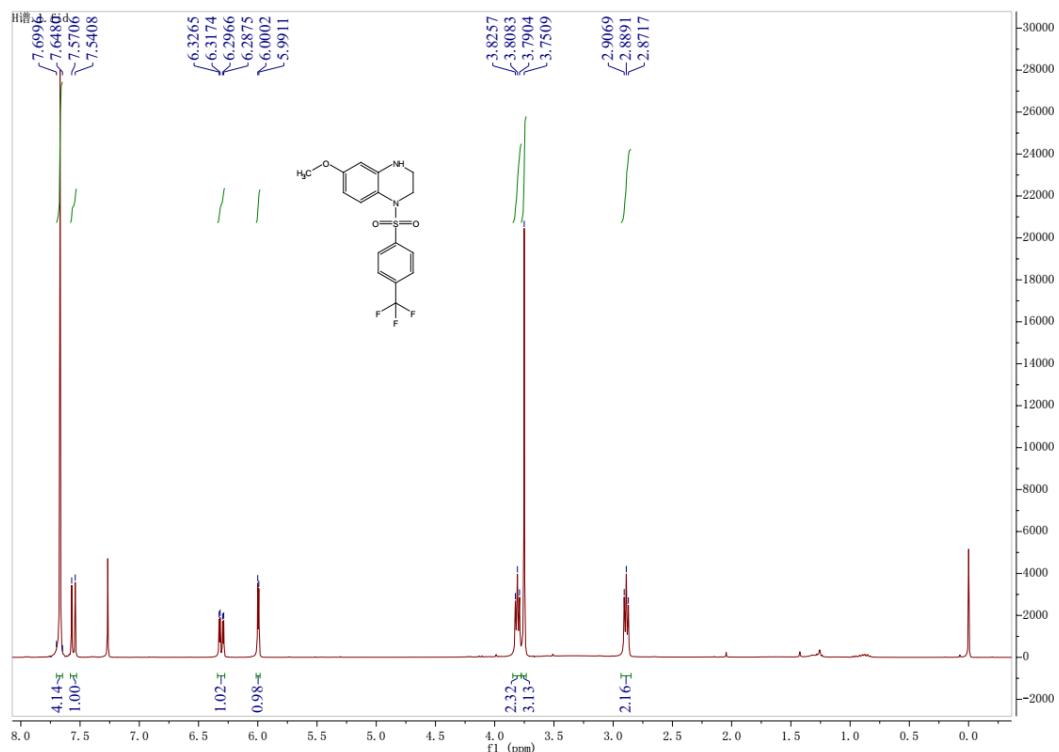
HPLC purity



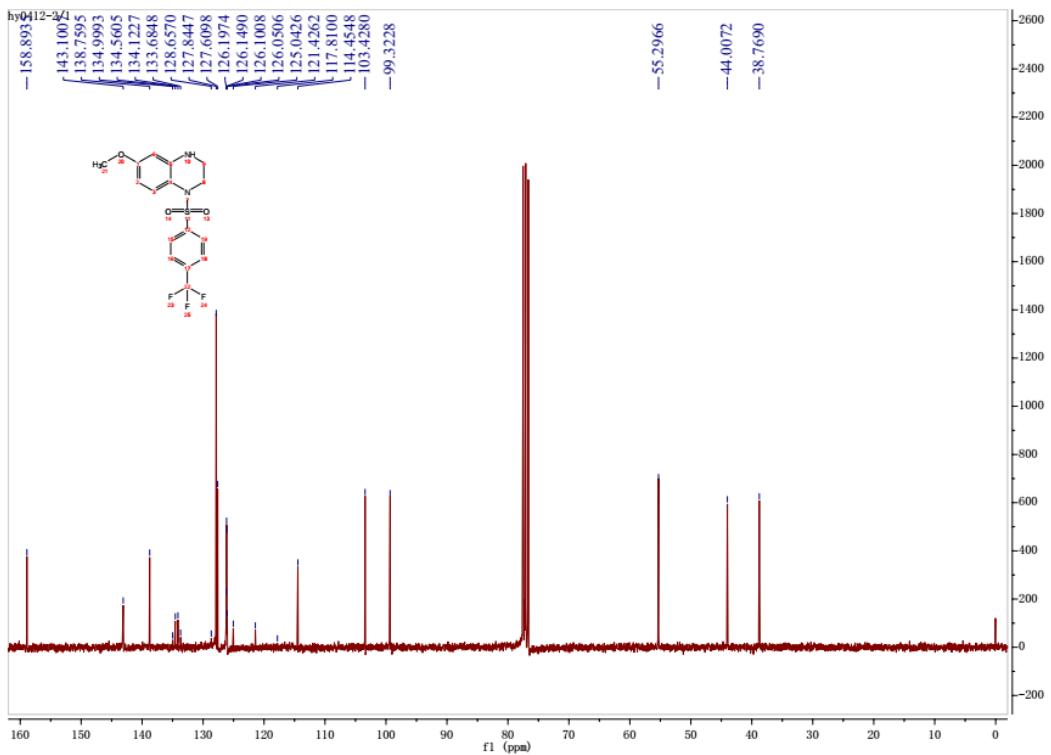
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.838	BB	0.1374	17.07867	1.66925	0.0282
2	2.747	BV R	0.2072	5.95669e4	3877.42114	98.4780
3	3.769	VV E	0.2367	153.20473	9.17975	0.2533
4	4.140	VV E	0.2187	171.62225	11.73210	0.2837
5	4.671	VB E	0.2509	213.46021	12.39488	0.3529
6	5.674	BB	0.2782	169.04475	9.20682	0.2795
7	7.073	BB	0.4226	159.88232	4.95259	0.2643
8	9.779	BBA	0.3884	36.34280	1.55939	0.0601

## I-15

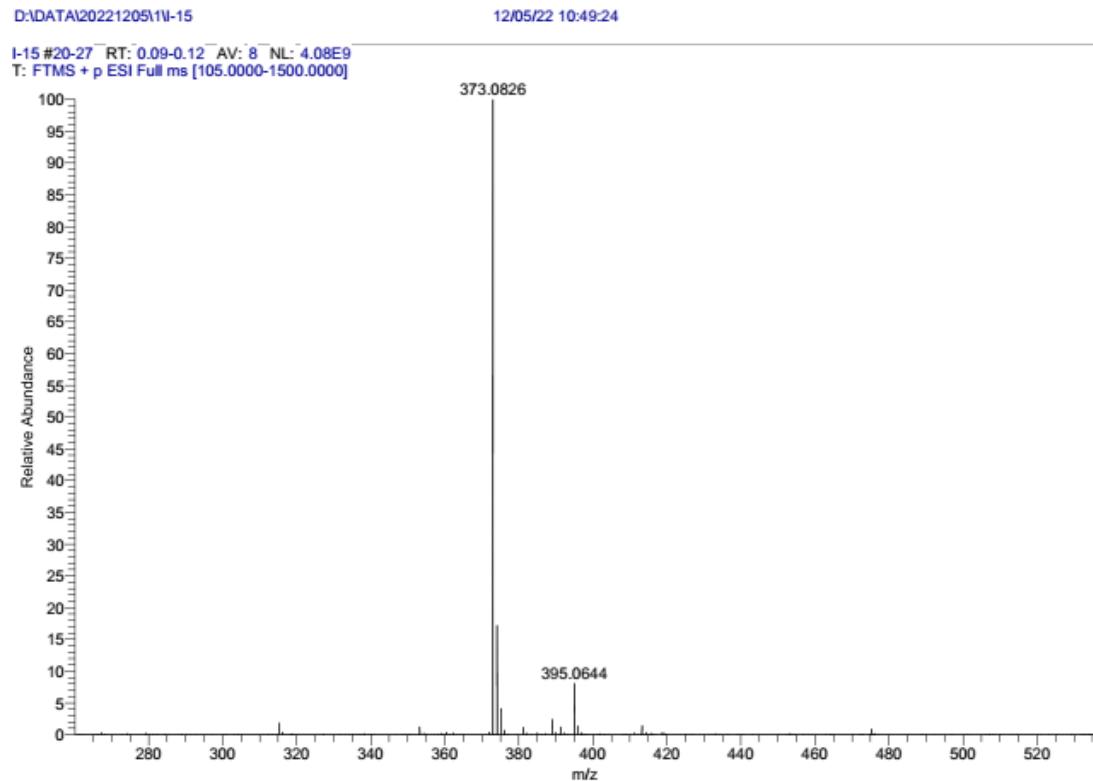
### <sup>1</sup>H-NMR



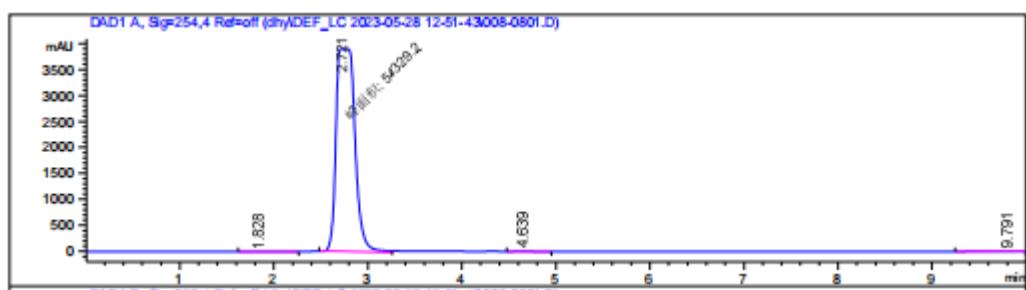
### <sup>13</sup>C-NMR



## HRMS



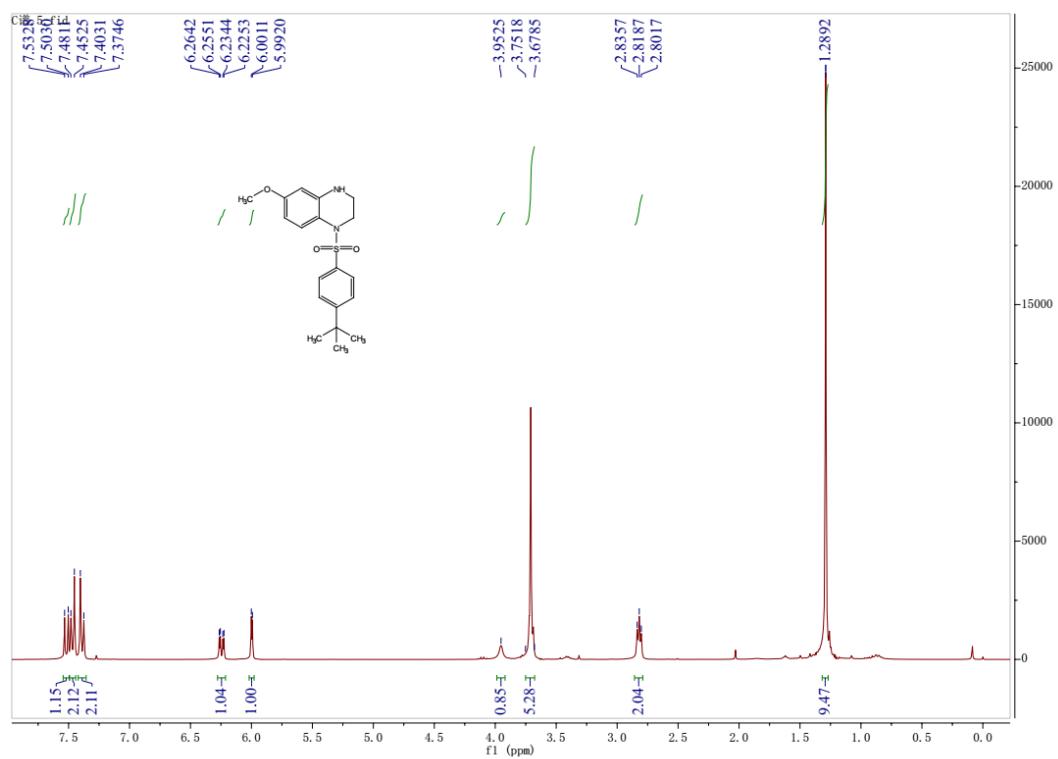
HPLC purity



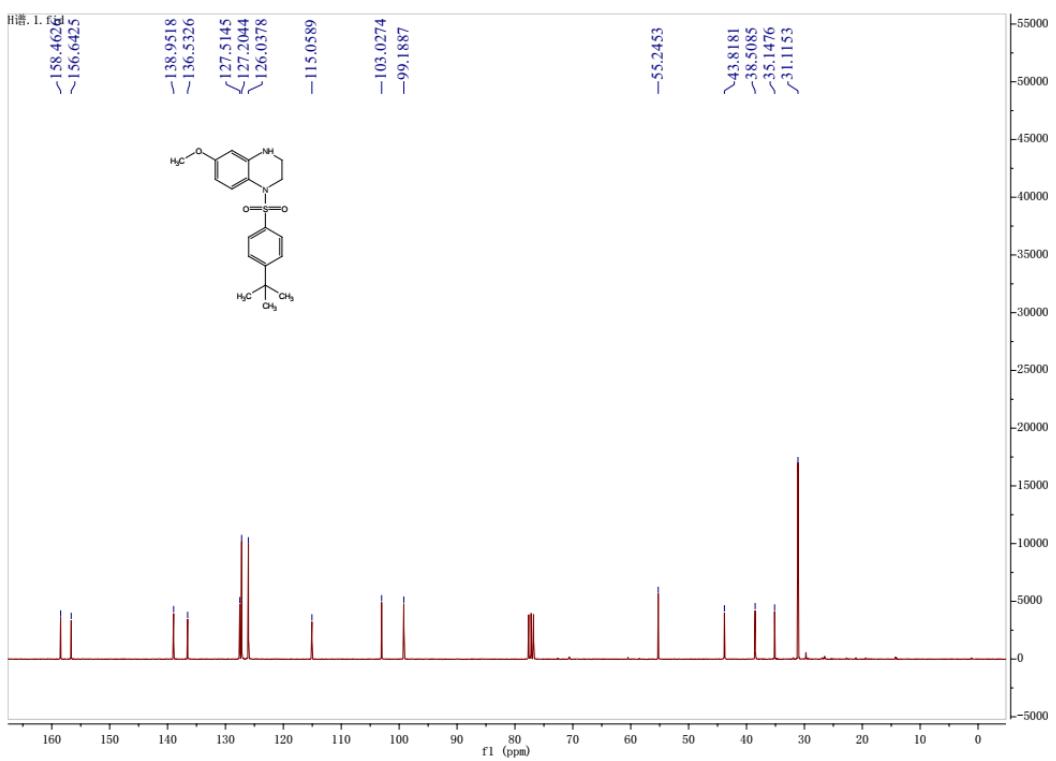
#	峰保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积	
						%	
1	1.828	BB	0.1409	10.76635	1.02194	0.0198	
2	2.721	MM	0.2324	5.43292e4	3895.61279	99.7702	
3	4.639	BB	0.1927	14.37638	1.20912	0.0264	
4	9.791	BBA	0.3545	100.01393	4.58464	0.1837	

## I-16

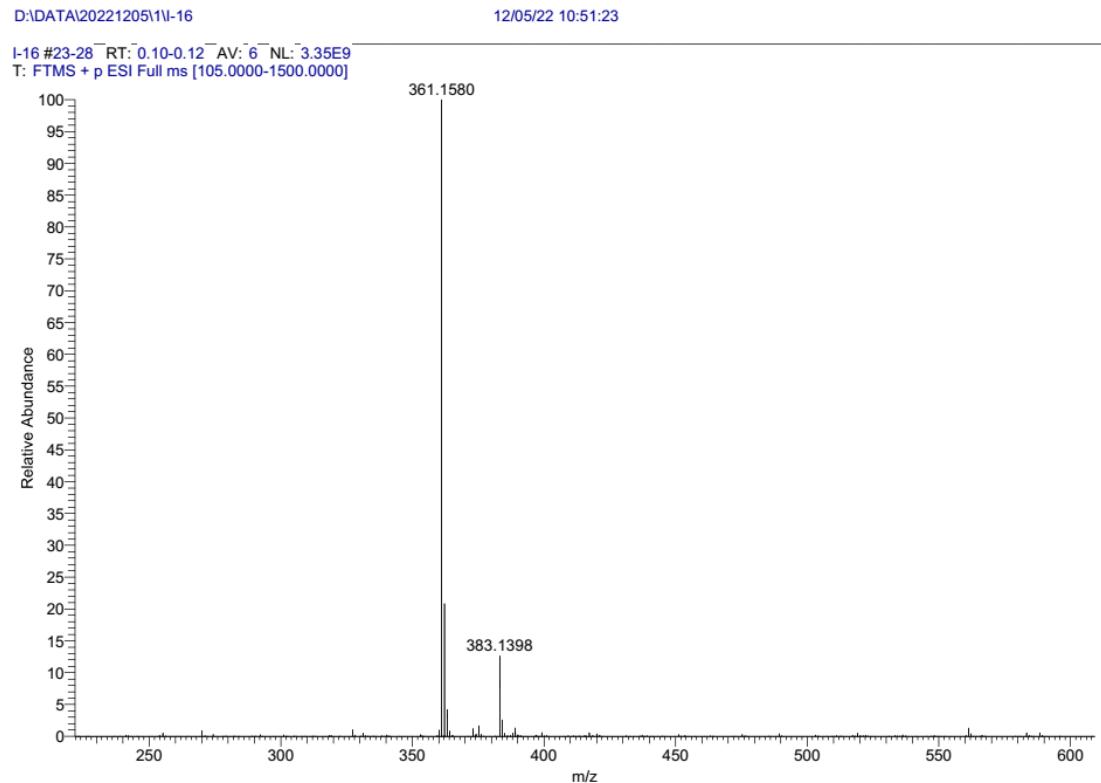
### <sup>1</sup>H-NMR



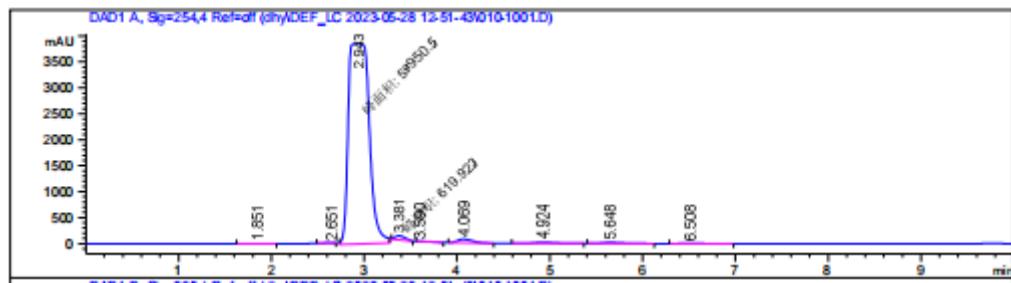
### <sup>13</sup>C-NMR



## HRMS



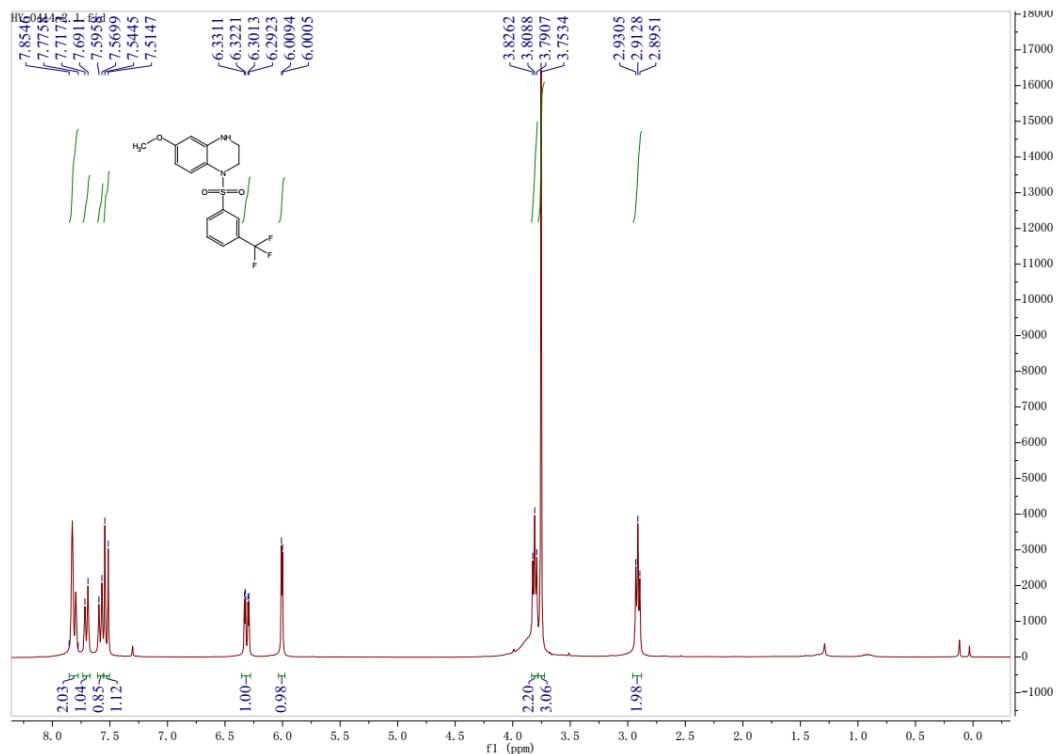
HPLC purity



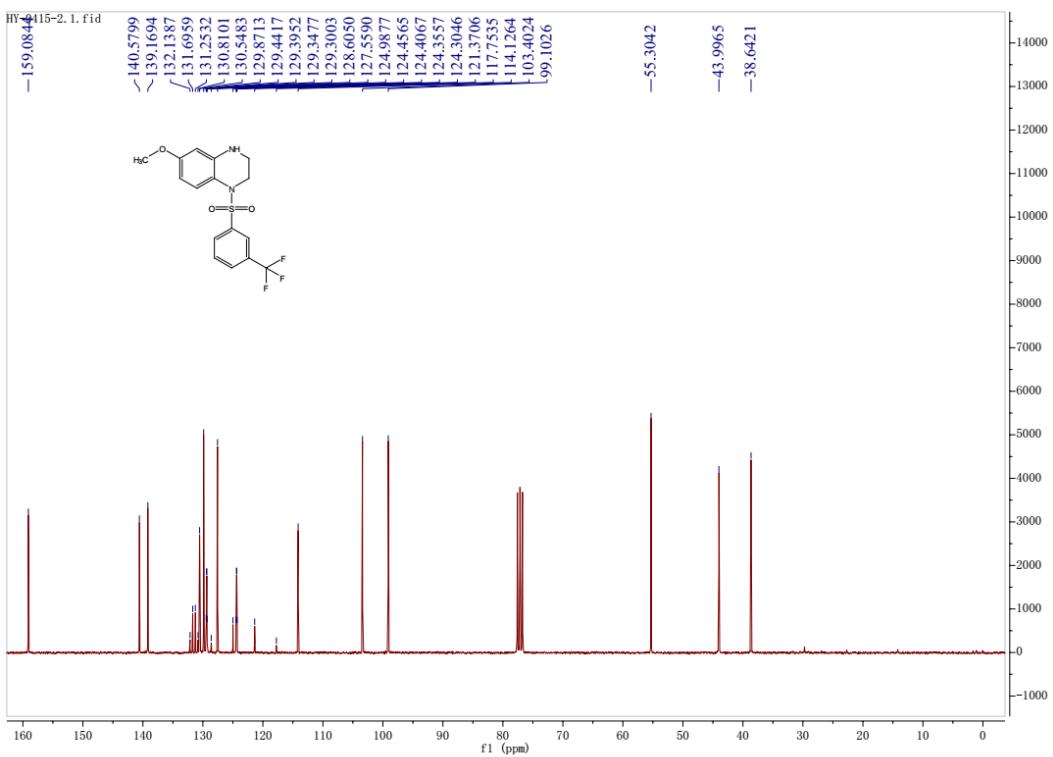
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %	
1	1.851	BB	0.1228	16.64512	1.81829	0.0268	
2	2.651	BB	0.1178	25.18689	2.88542	0.0406	
3	2.943	MM	0.2589	5.99505e4	3858.75757	96.6797	
4	3.381	MM	0.1300	619.92285	79.47868	0.9997	
5	3.590	BB	0.1930	40.83002	2.75287	0.0658	
6	4.069	BB	0.1751	767.74139	69.35452	1.2381	
7	4.924	BB	0.2341	303.18176	19.64463	0.4889	
8	5.648	BB	0.2289	267.14728	18.24235	0.4308	

### I-17

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



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

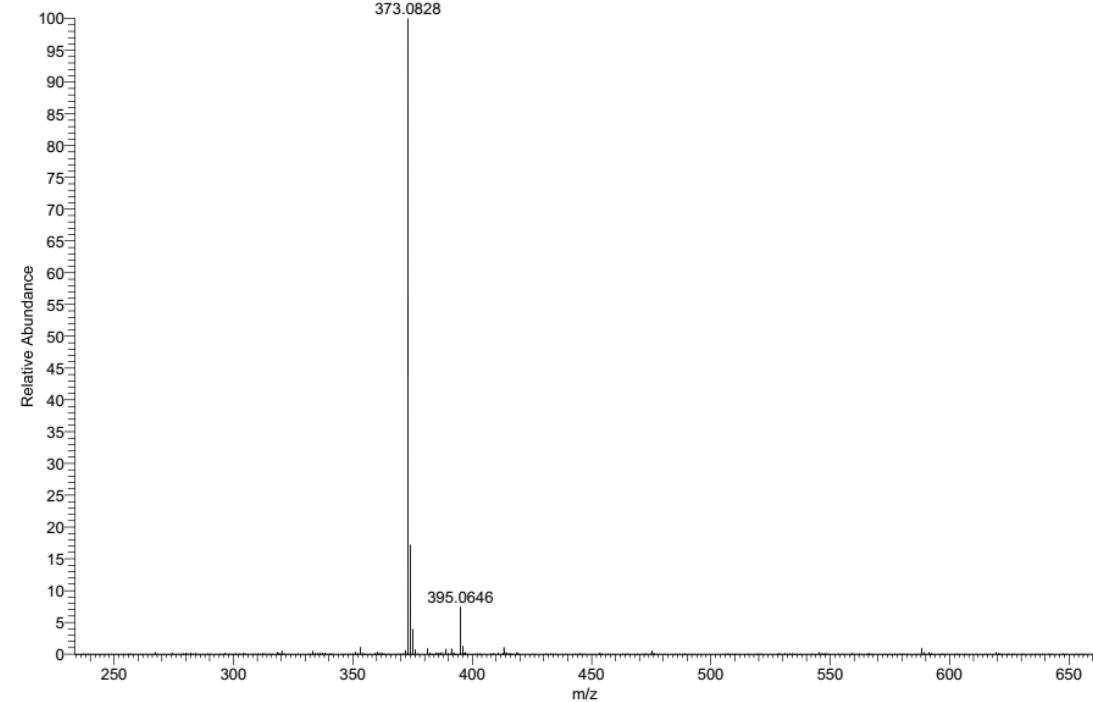


## HRMS

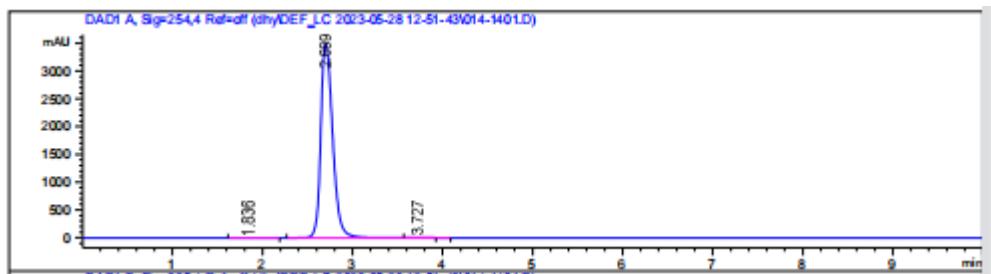
D:\DATA\20221205\1\I-17

12/05/22 10:53:24

I-17 #22-29 RT: 0.10-0.13 AV: 8 NL: 4.06E9  
T: FTMS + p ESI Full ms [105.0000-1500.0000]



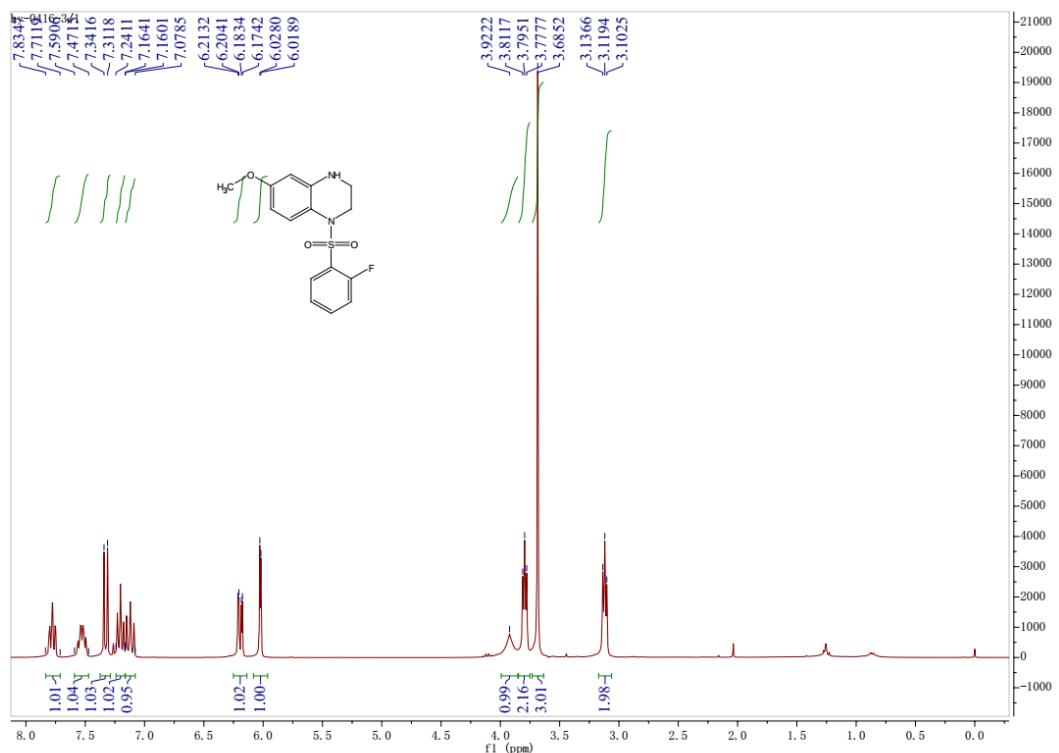
## HPLC purity



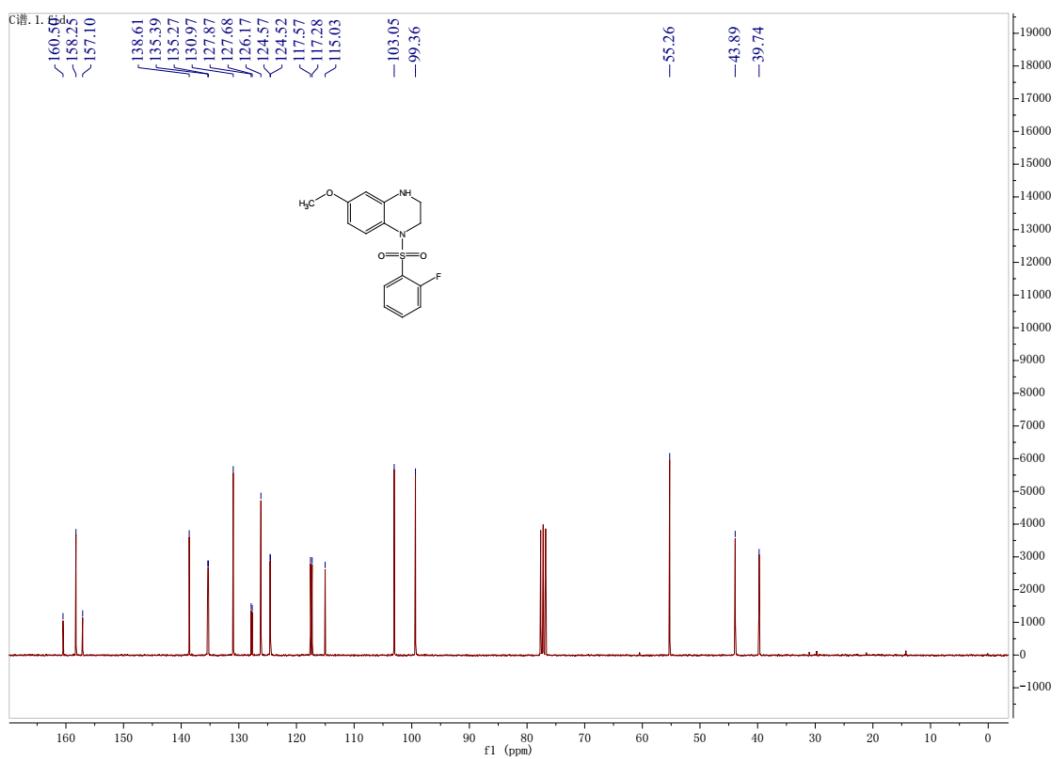
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1. 836	BB	0. 1487	13. 67305	1. 20227	0. 0424
2	2. 699	BV R	0. 1419	3. 22347e4	3486. 67798	99. 9252
3	3. 727	VB E	0. 1497	10. 44748	1. 07173	0. 0324

### I-18

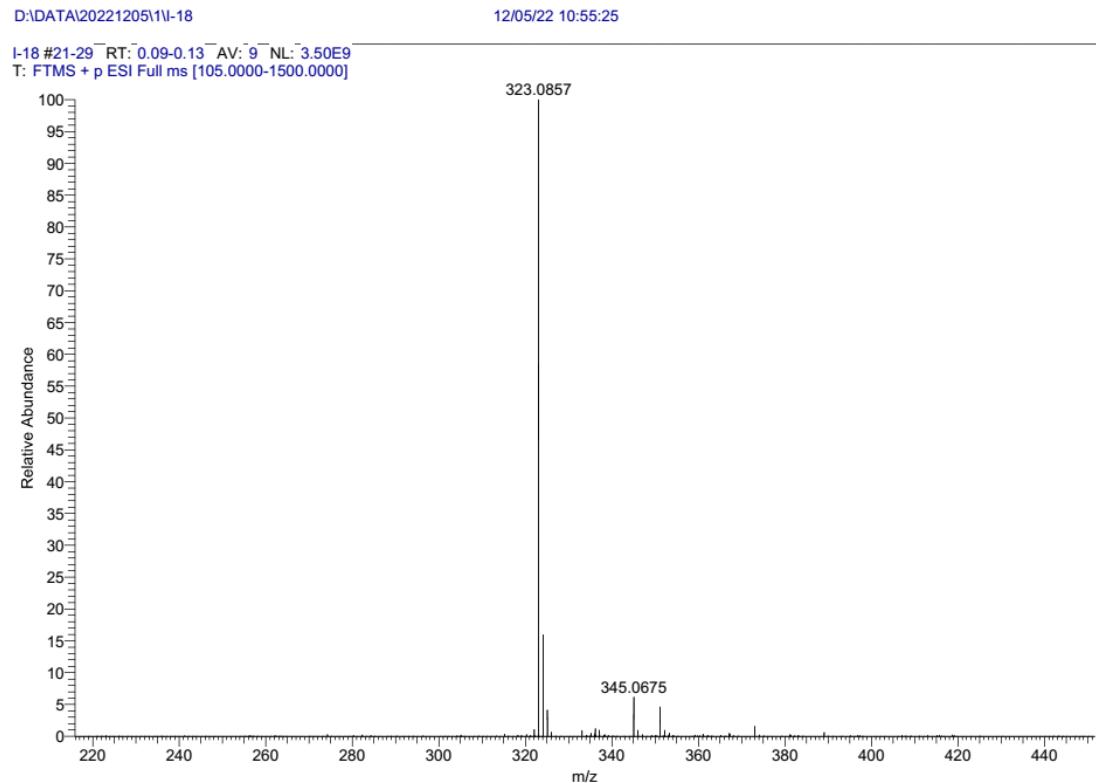
#### <sup>1</sup>H-NMR



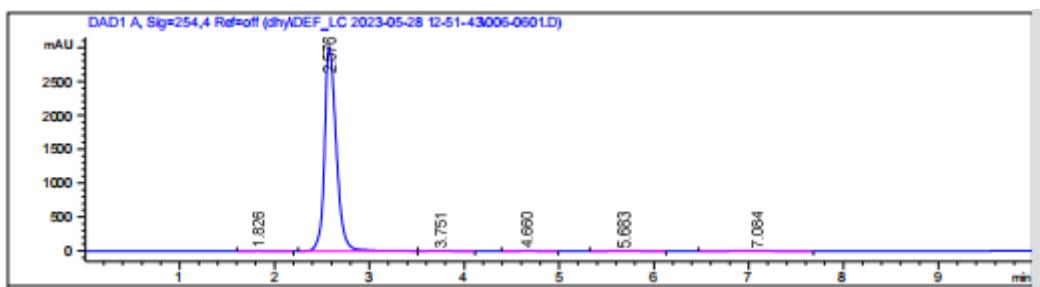
#### <sup>13</sup>C-NMR



## HRMS



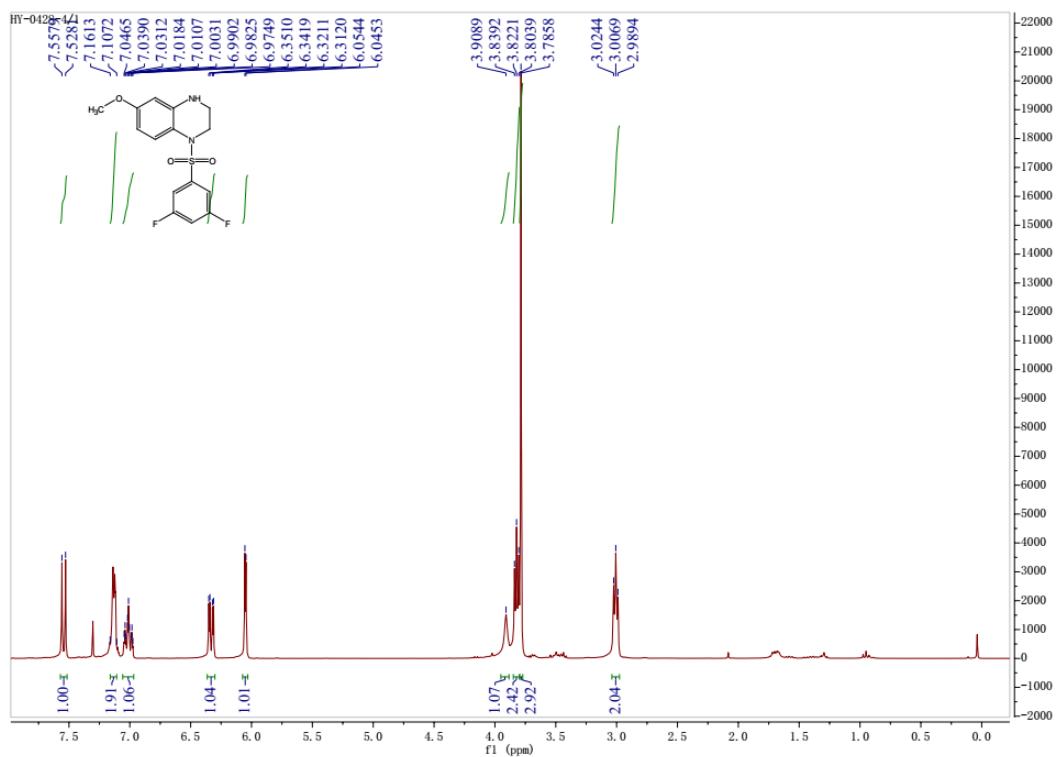
HPLC purity



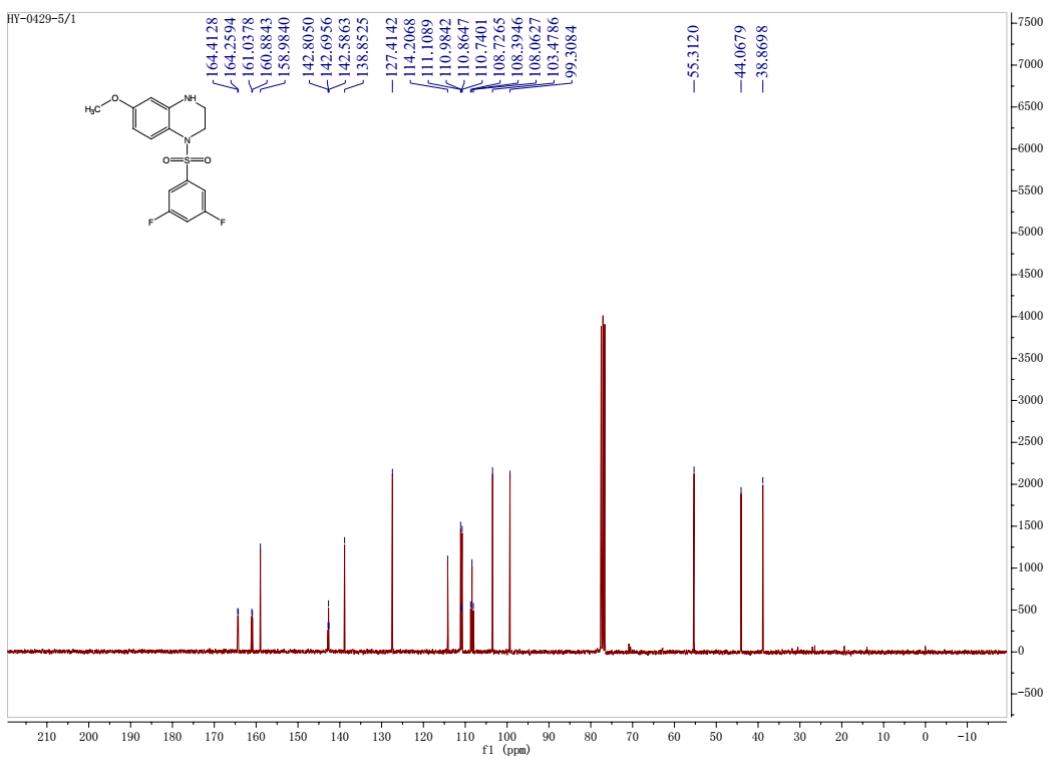
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.826	BB	0.1897	18.64995	1.57984	0.0716
2	2.576	BB	0.1324	2.58720e4	3006.13721	99.3715
3	3.751	BB	0.1760	17.49418	1.52353	0.0672
4	4.660	BB	0.2051	19.37649	1.45758	0.0744
5	5.683	BB	0.2755	54.87186	2.97003	0.2108
6	7.084	BB	0.4197	53.24213	1.64470	0.2045

## I-19

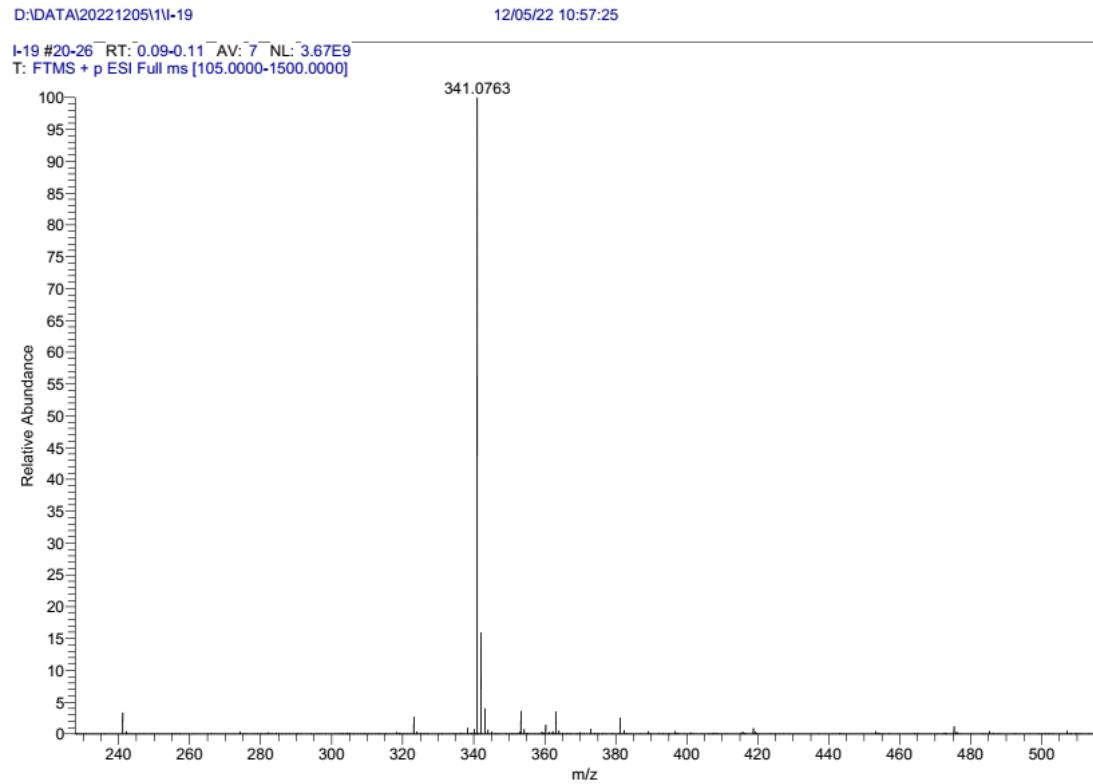
### <sup>1</sup>H-NMR



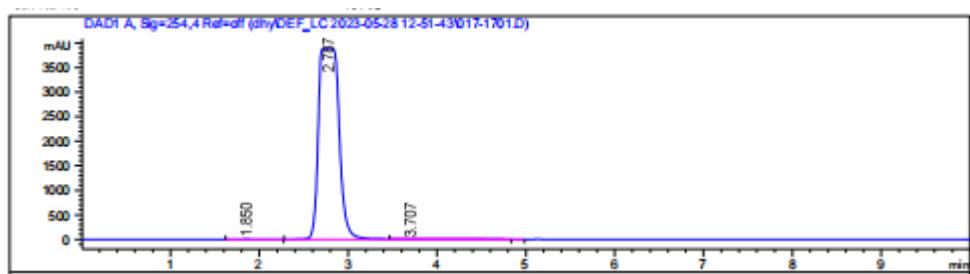
### <sup>13</sup>C-NMR



## HRMS



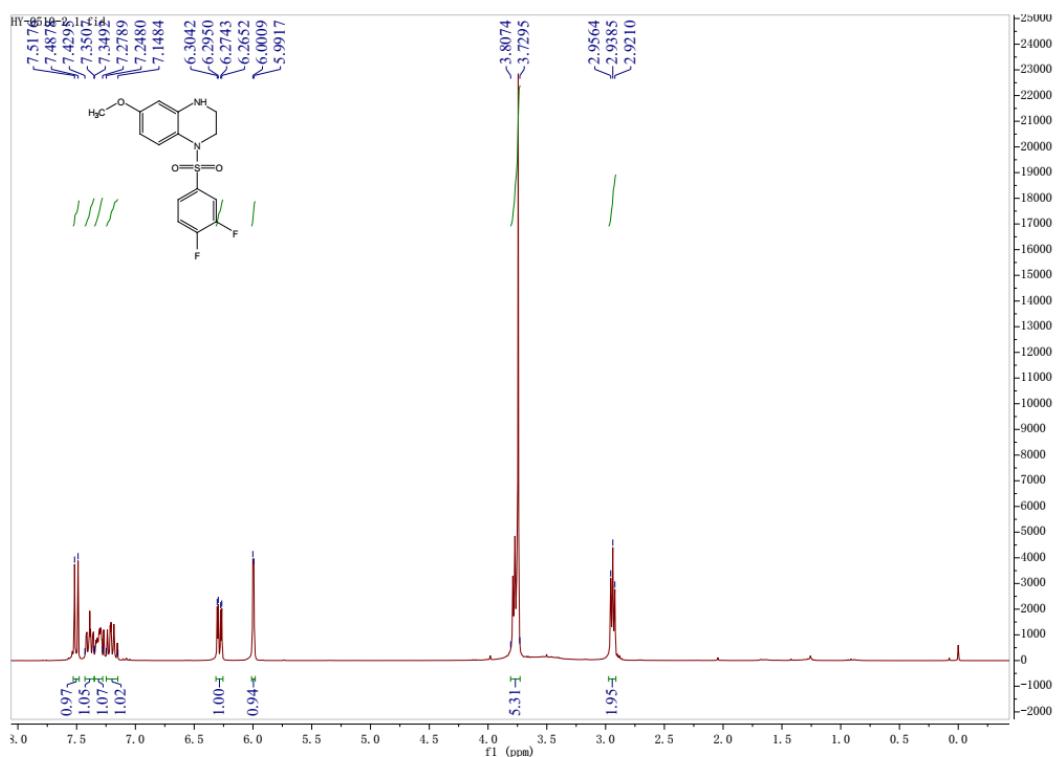
HPLC purity



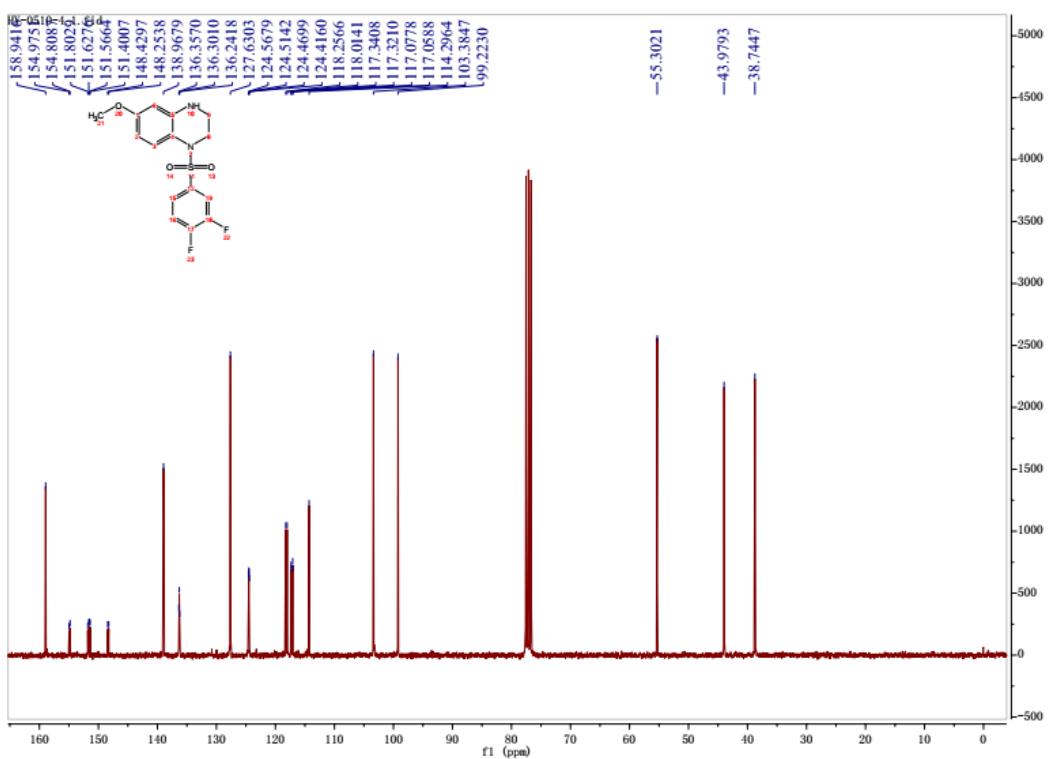
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.850	BB	0.1042	21.48151	2.84167	0.0344
2	2.787	BV R	0.2011	6.24416e4	3893.15405	99.8876
3	3.707	VB E	0.2580	48.80634	2.66085	0.0781

## I-20

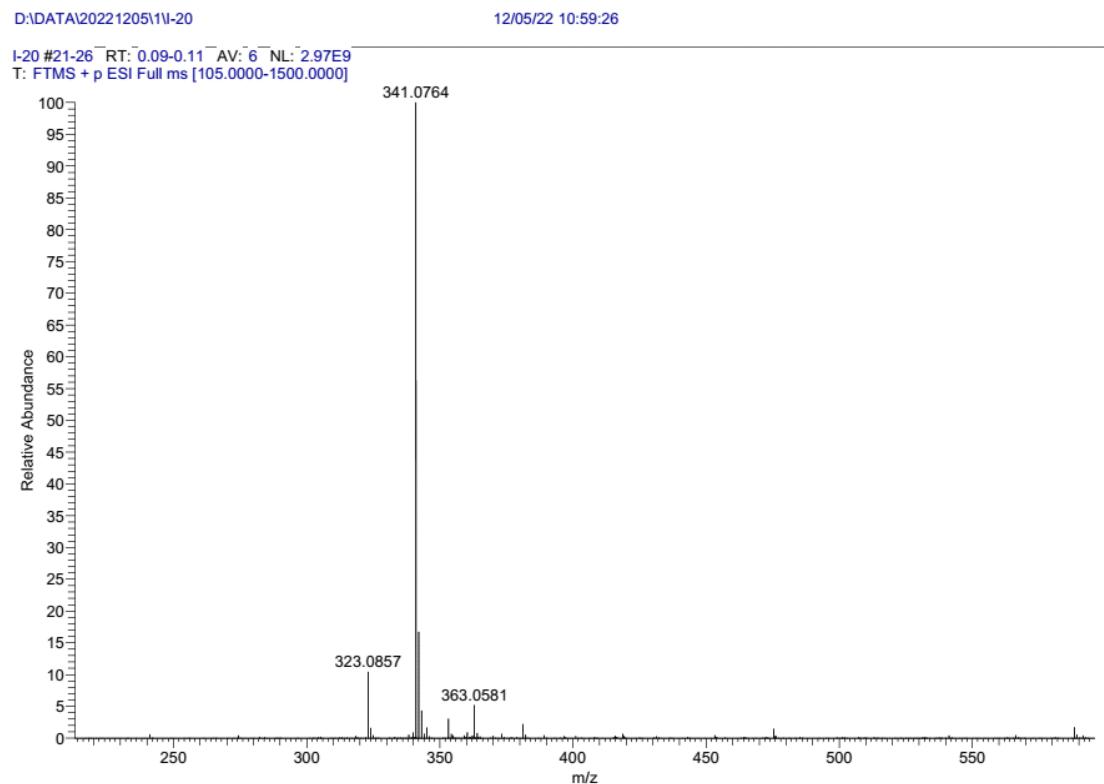
### <sup>1</sup>H-NMR



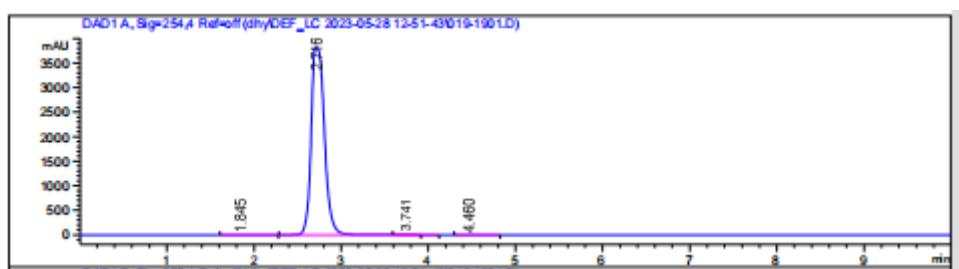
### <sup>13</sup>C-NMR



## HRMS



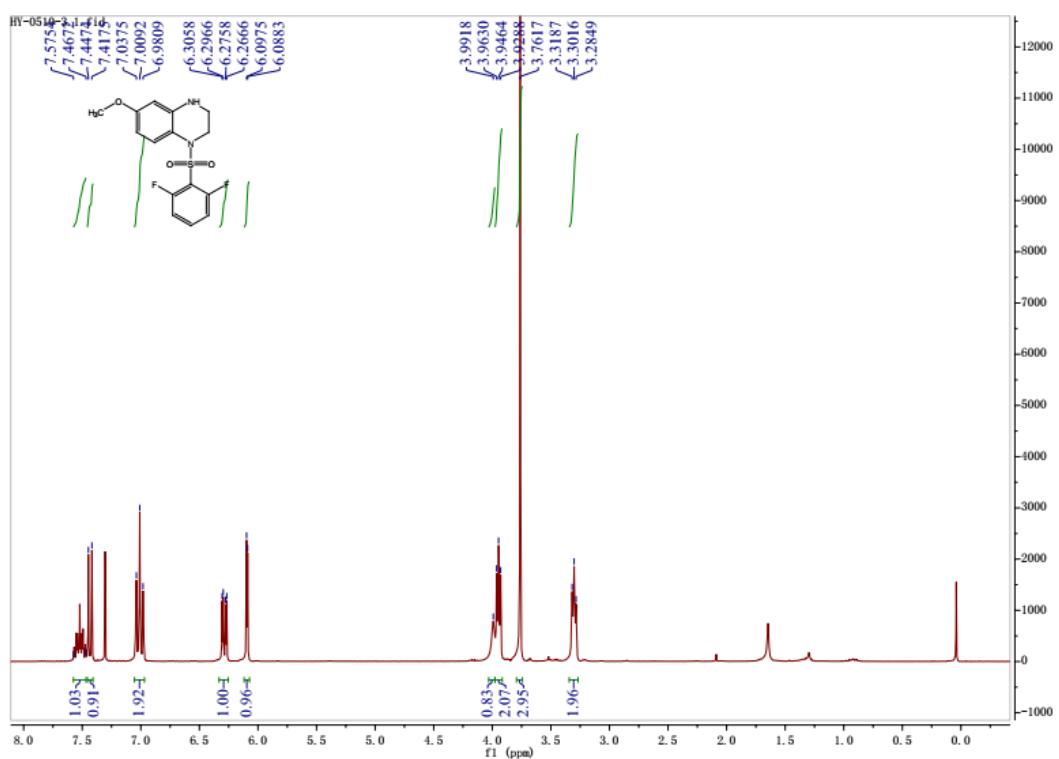
HPLC purity



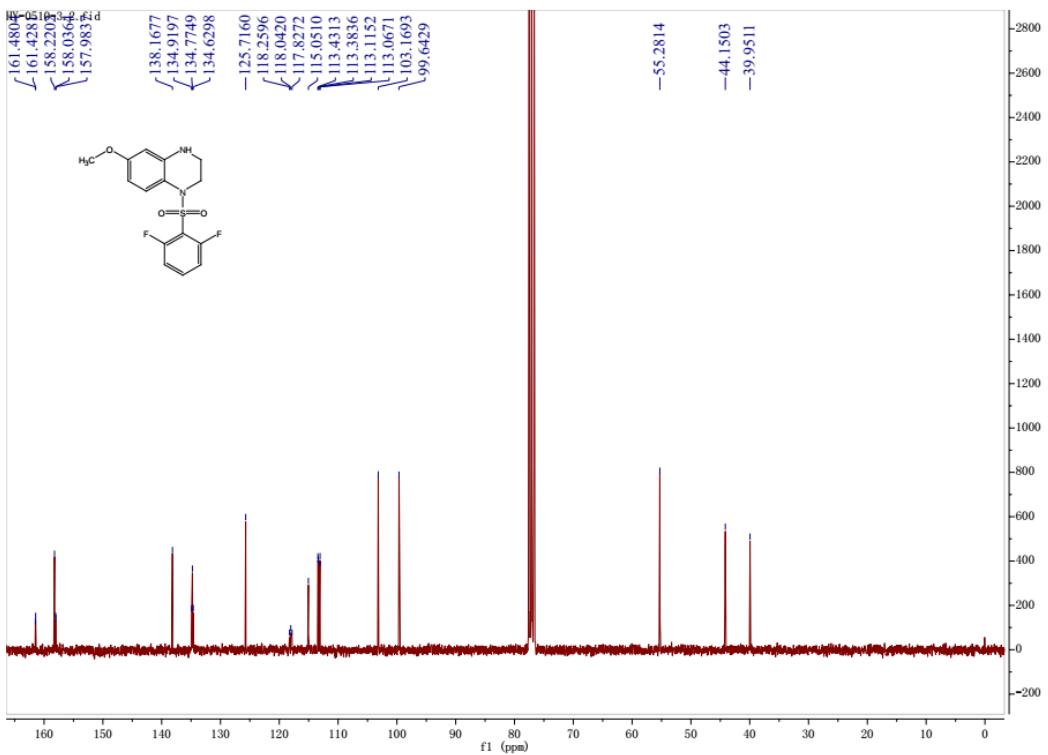
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.845	BB	0.1659	16.14899	1.29161	0.0398
2	2.716	BV R	0.1657	4.04873e4	3819.50977	99.9027
3	3.741	VB E	0.1507	10.80317	1.15950	0.0267
4	4.460	BB	0.1829	12.46189	1.06163	0.0307

## I-21

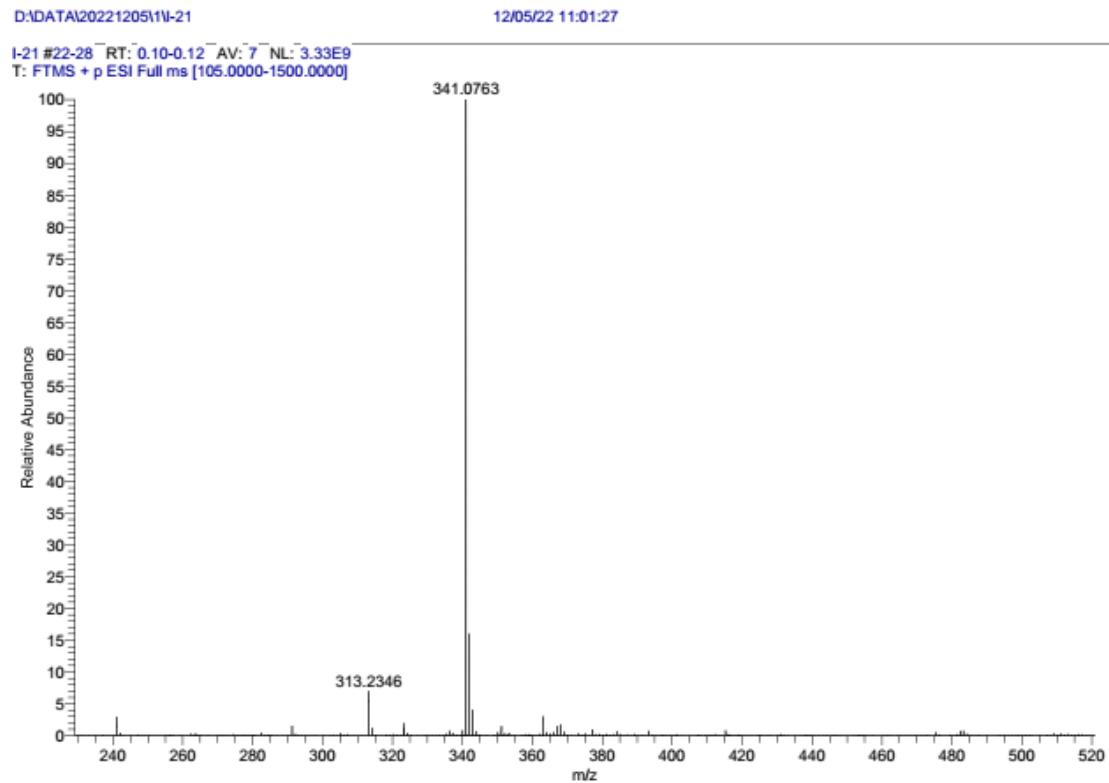
### <sup>1</sup>H-NMR



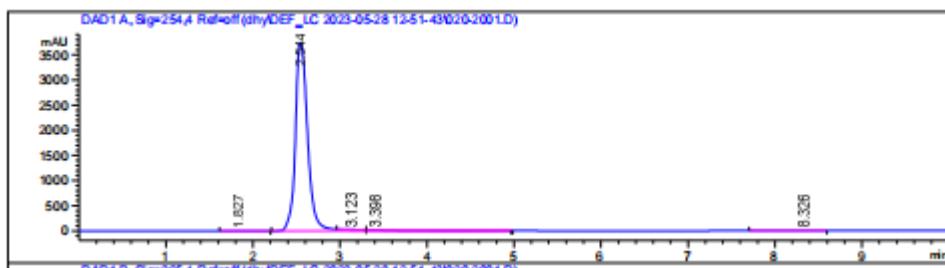
### <sup>13</sup>C-NMR



## HRMS



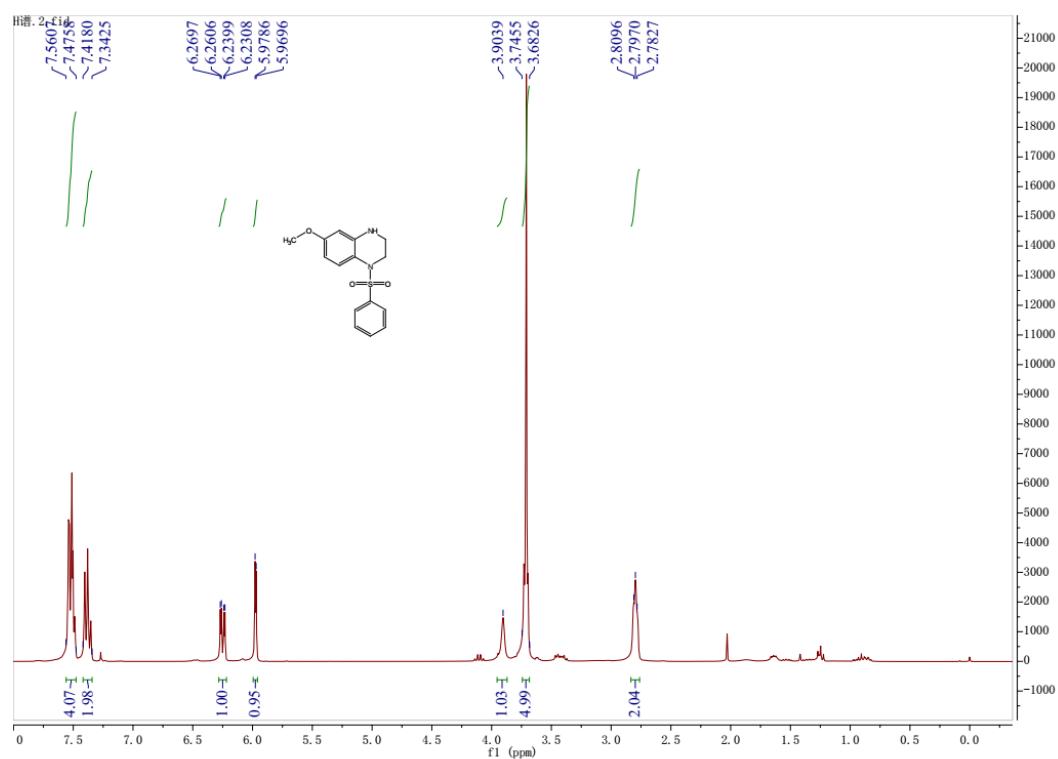
HPLC purity



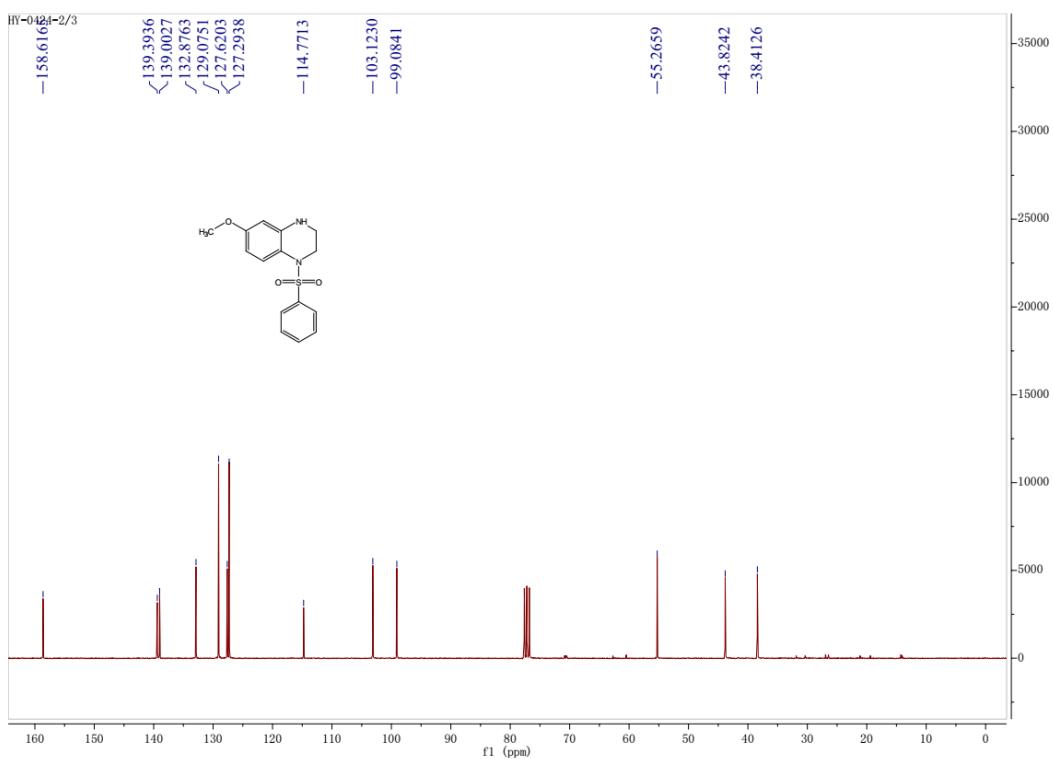
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.827	BB	0.1682	20.95062	1.62690	0.0558
2	2.544	BV R	0.1514	3.69006e4	3730.16089	98.3249
3	3.123	VV E	0.2078	142.99910	9.60058	0.3810
4	3.398	VB E	0.3223	429.64246	17.38570	1.1448
5	8.326	BB	0.3005	35.06787	1.75982	0.0934

## I-22

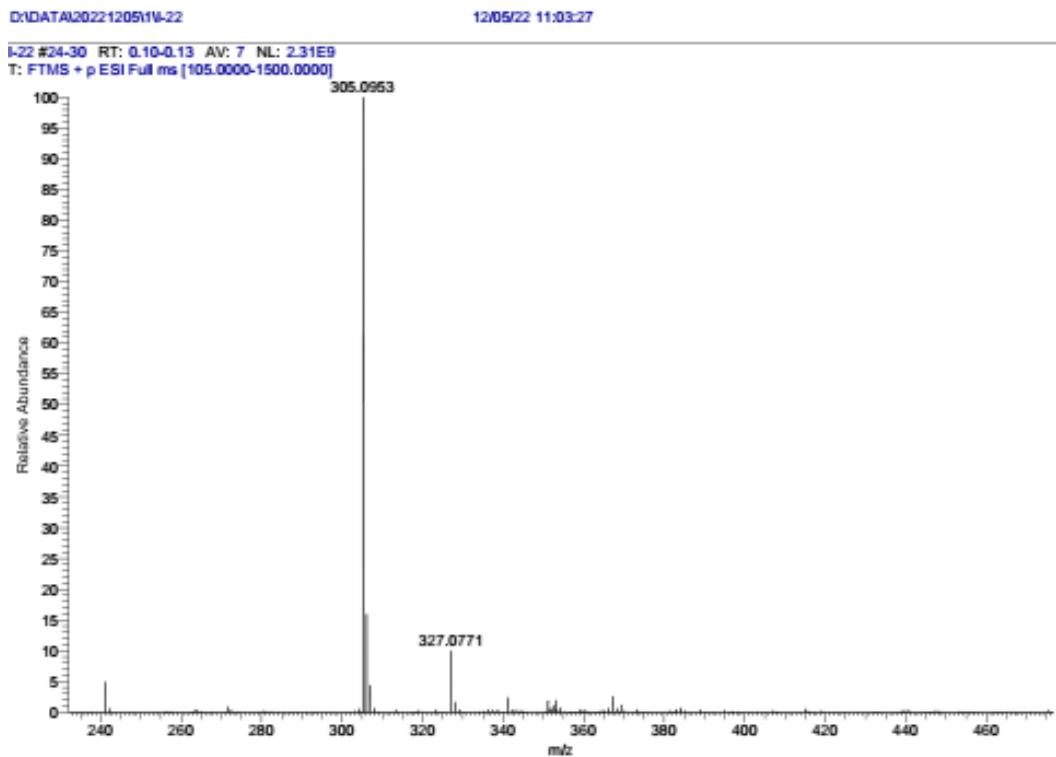
### <sup>1</sup>H-NMR



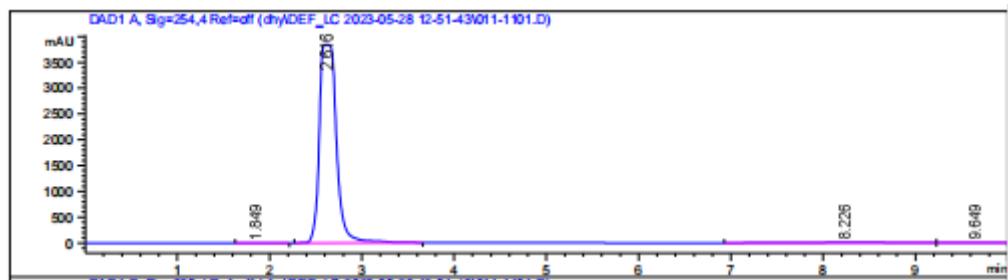
### <sup>13</sup>C-NMR



## HRMS



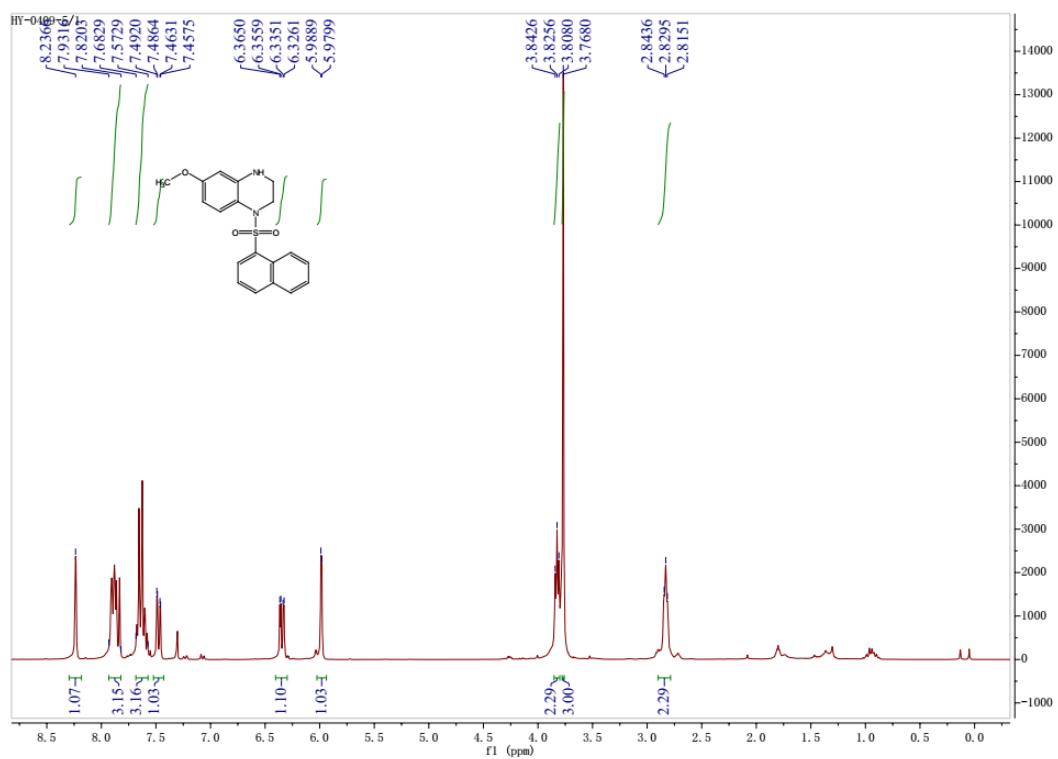
## HPLC purity



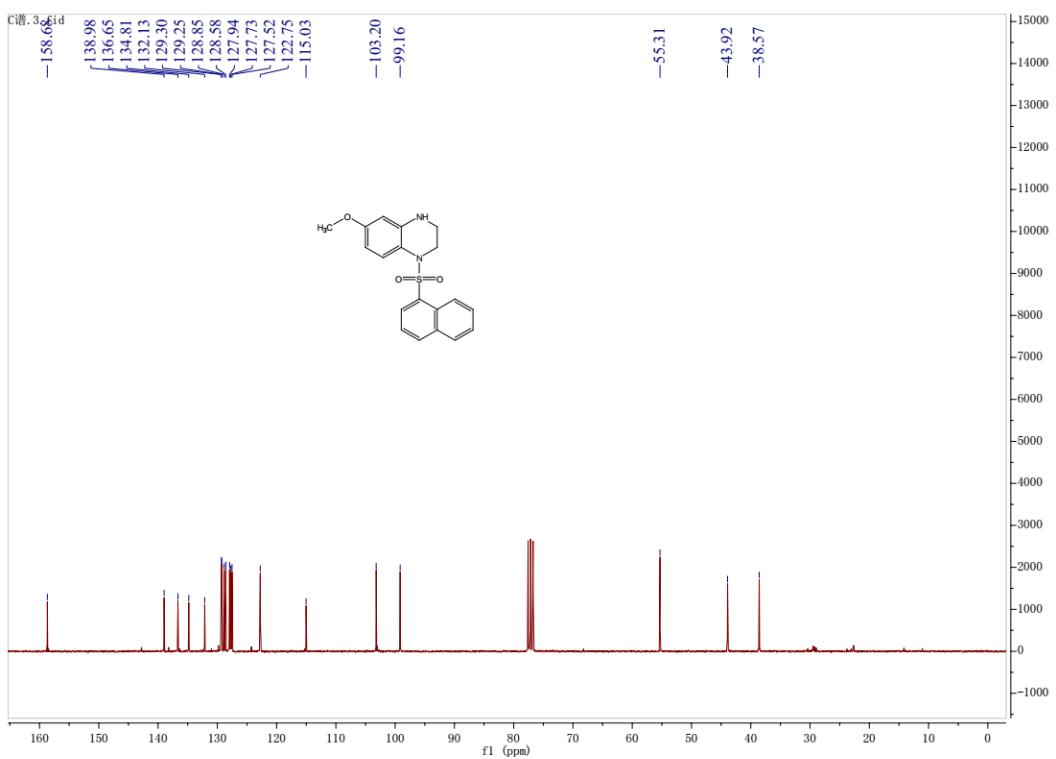
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.849	BB	0.1257	14.46094	1.53729	0.0288
2	2.616	BB	0.2024	4.95036e4	3839.62695	98.6978
3	8.226	BB	0.6719	592.69482	11.26432	1.1817
4	9.649	BBA	0.4046	45.97319	1.85833	0.0917

### I-23

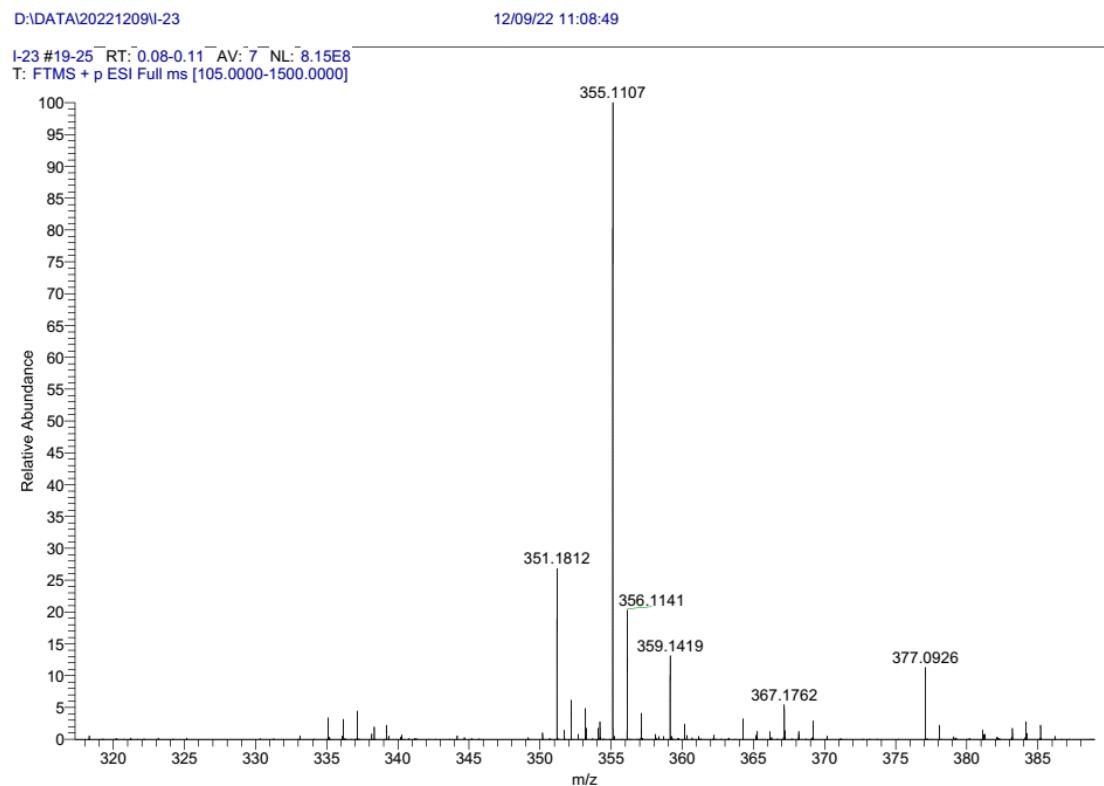
<sup>1</sup>H-NMR



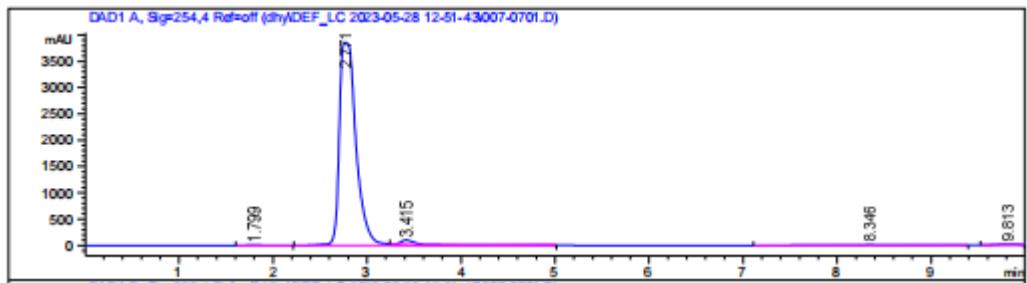
<sup>13</sup>C-NMR



## HRMS



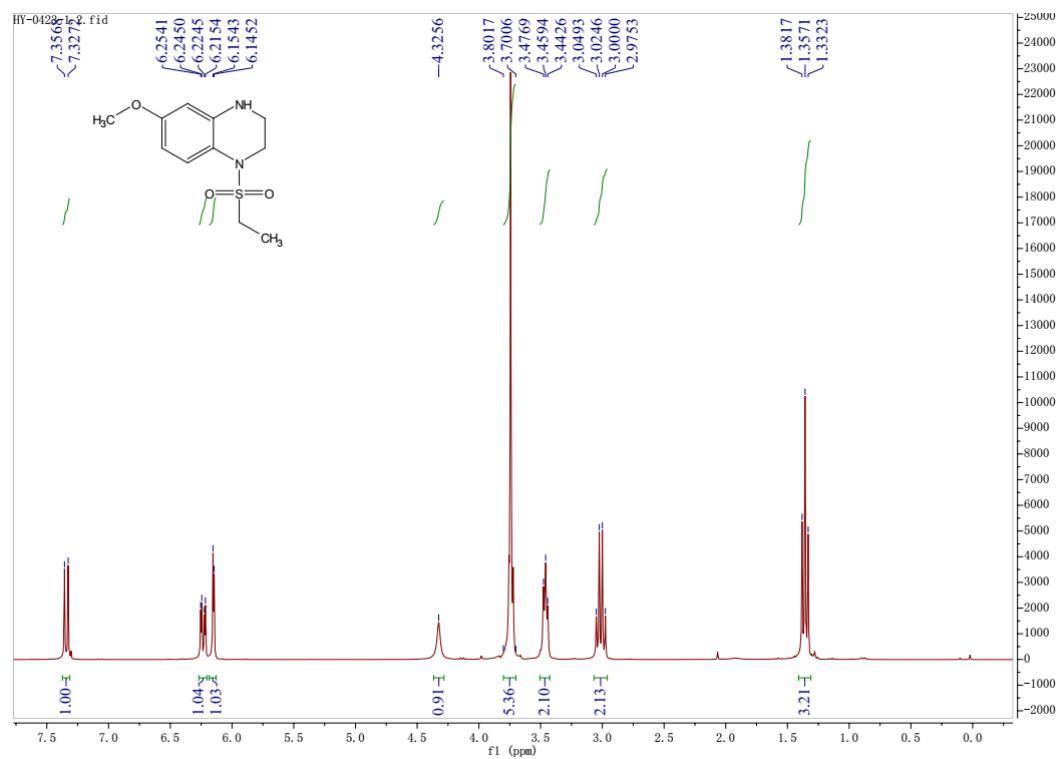
HPLC purity



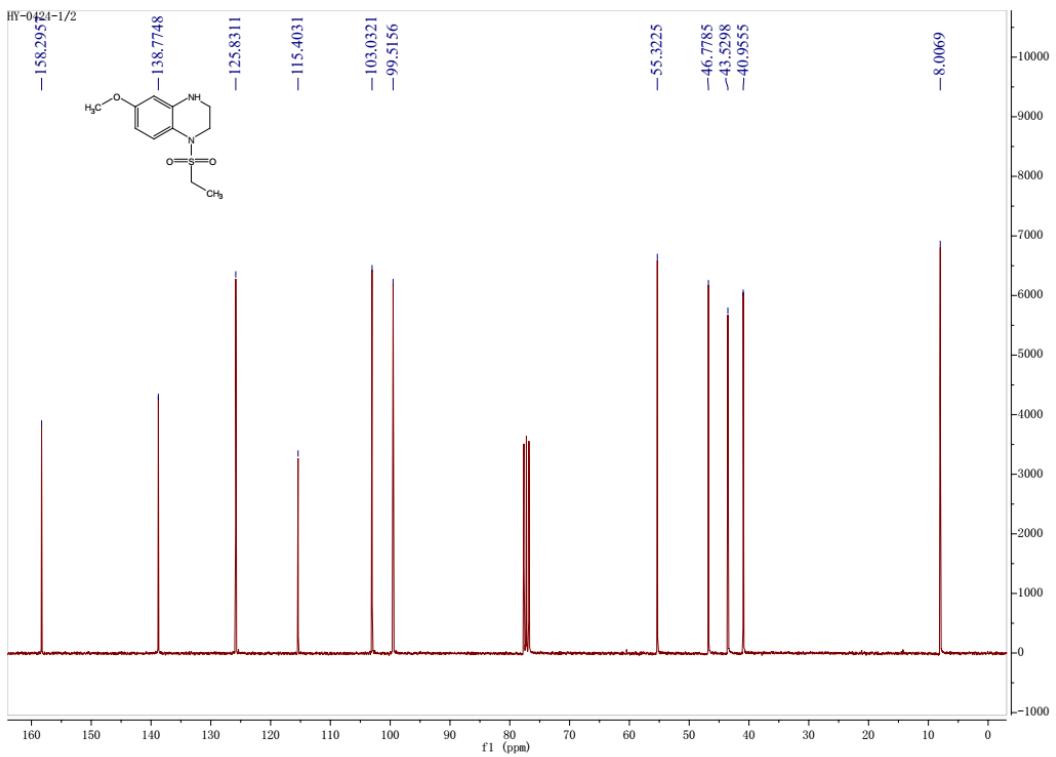
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积		峰面积 %
				[mAU*s]	[mAU]	
1	1.799	BB	0.1655	42.54476	3.95602	0.0862
2	2.771	BV R	0.1882	4.75982e4	3851.61743	96.4098
3	3.415	VB E	0.1895	1162.18054	89.48328	2.3540
4	8.346	BB	0.6051	376.77512	8.09414	0.7632
5	9.813	BBA	0.2460	190.98544	13.10363	0.3868

## I-24

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



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

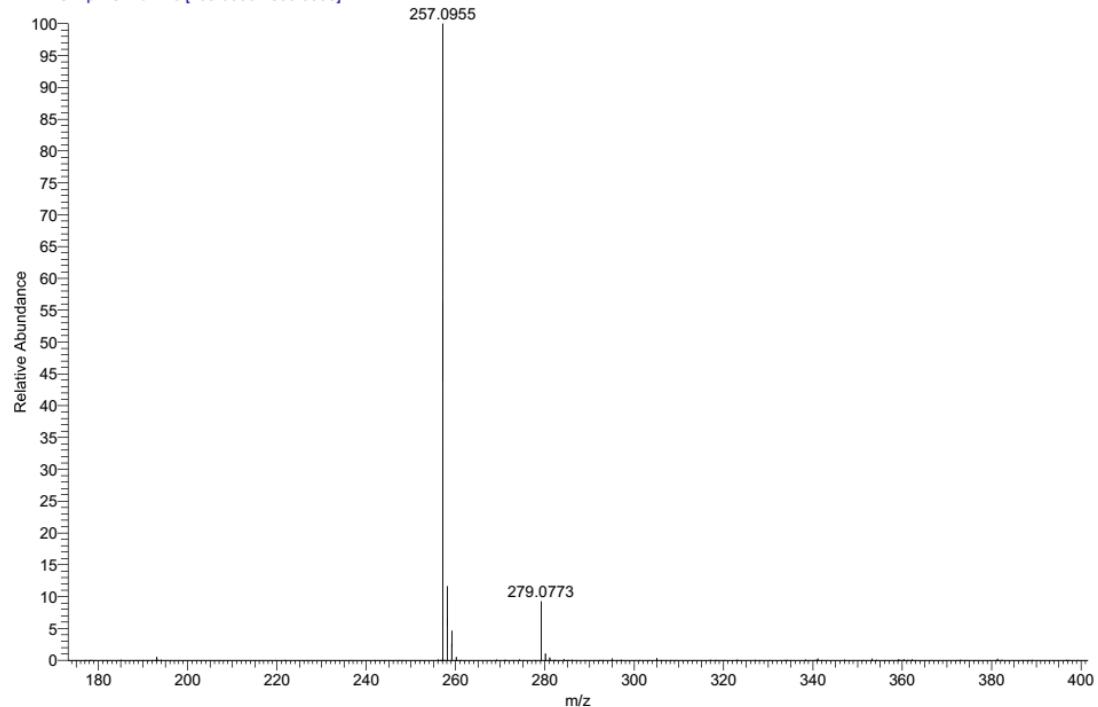


## HRMS

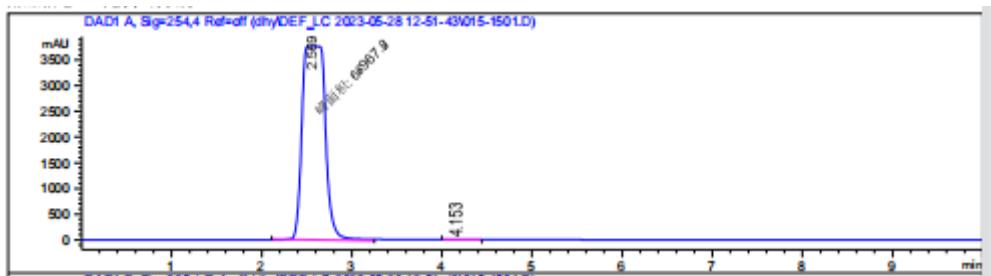
D:\DATA\20221205\1\I-24

12/05/22 11:07:29

I-24 #21-27 RT: 0.09-0.12 AV: 7 NL: 6.52E9  
T: FTMS + p ESI Full ms [105.0000-1500.0000]



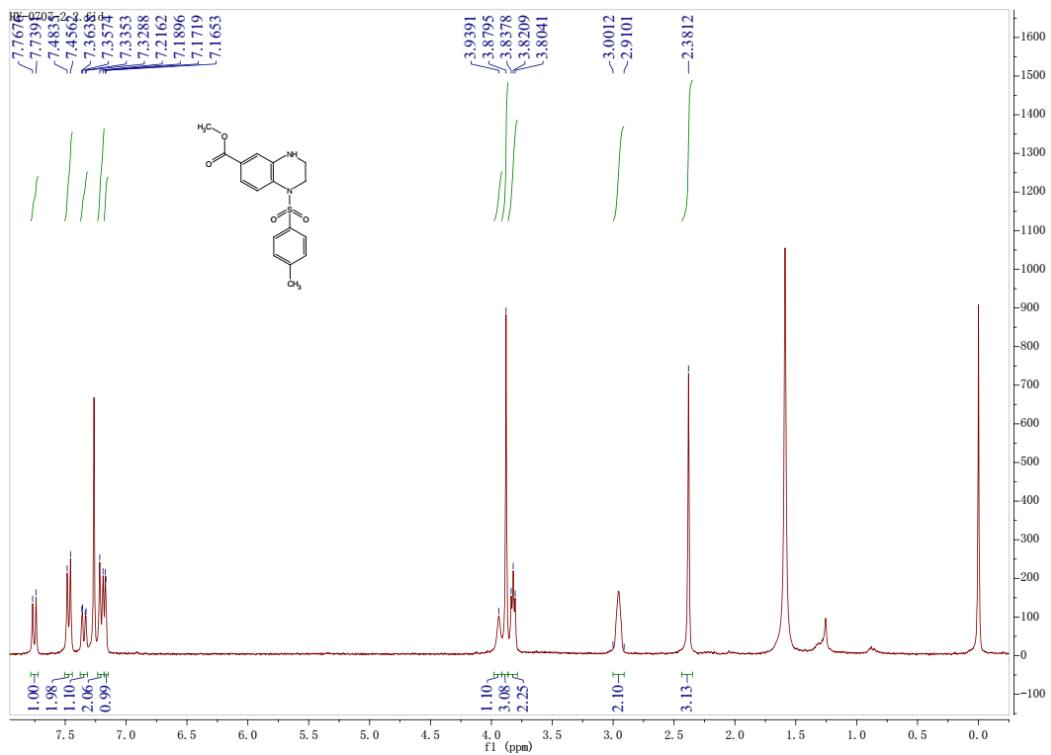
HPLC purity



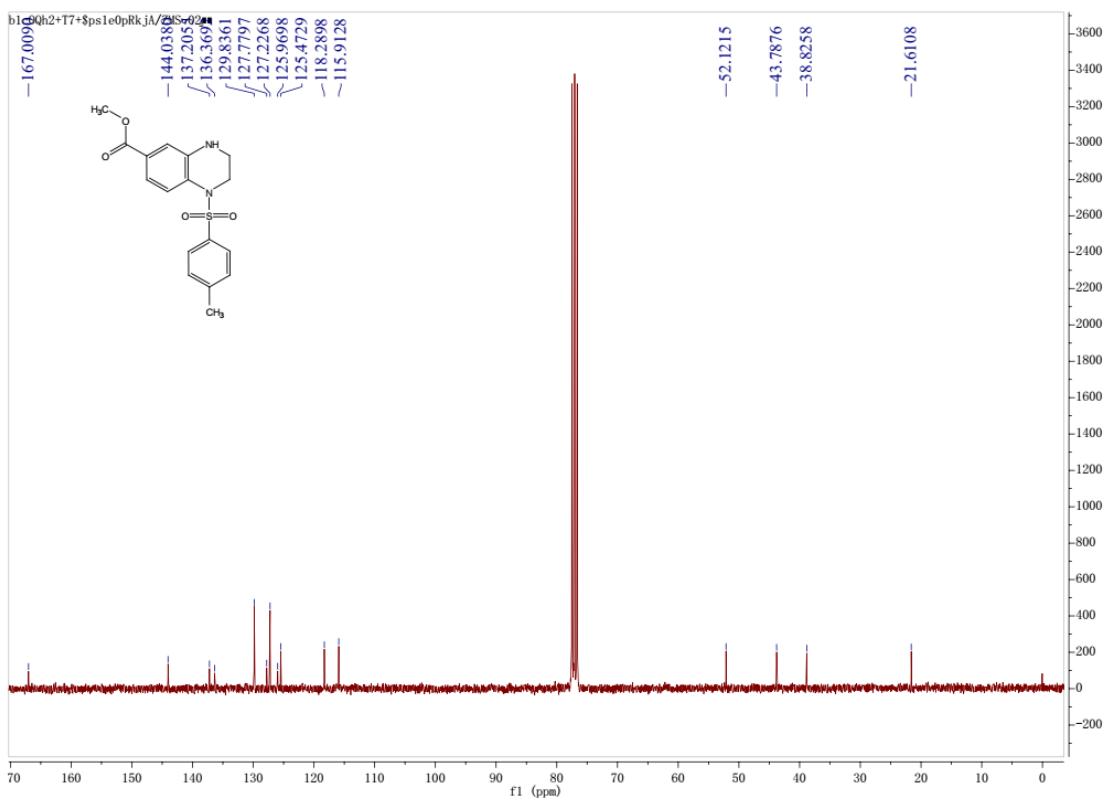
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	2.569	MM	0.2961	6.69678e4	3769.74097	99.9377
2	4.153	BB	0.1745	41.74950	3.85147	0.0623

### I-25

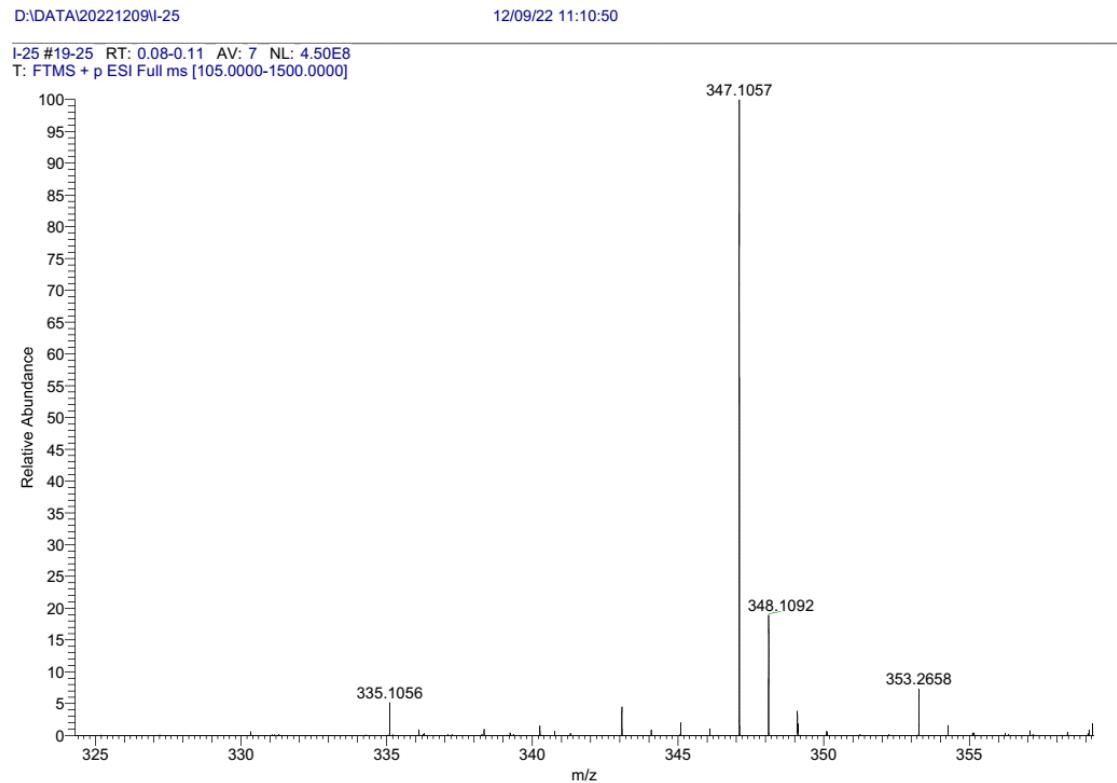
<sup>1</sup>H-NMR



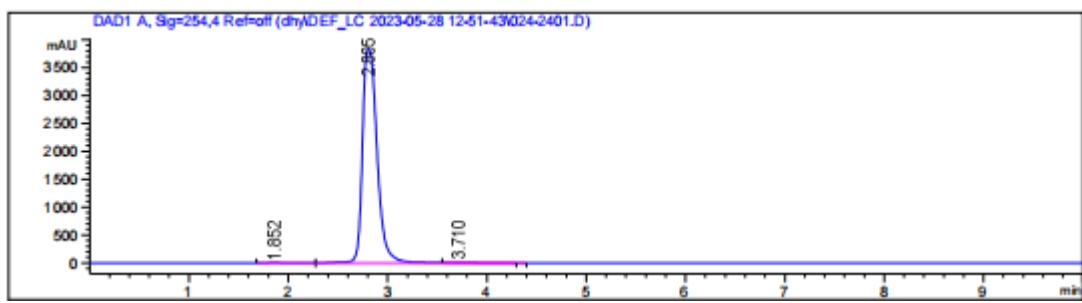
<sup>13</sup>C-NMR



## HRMS



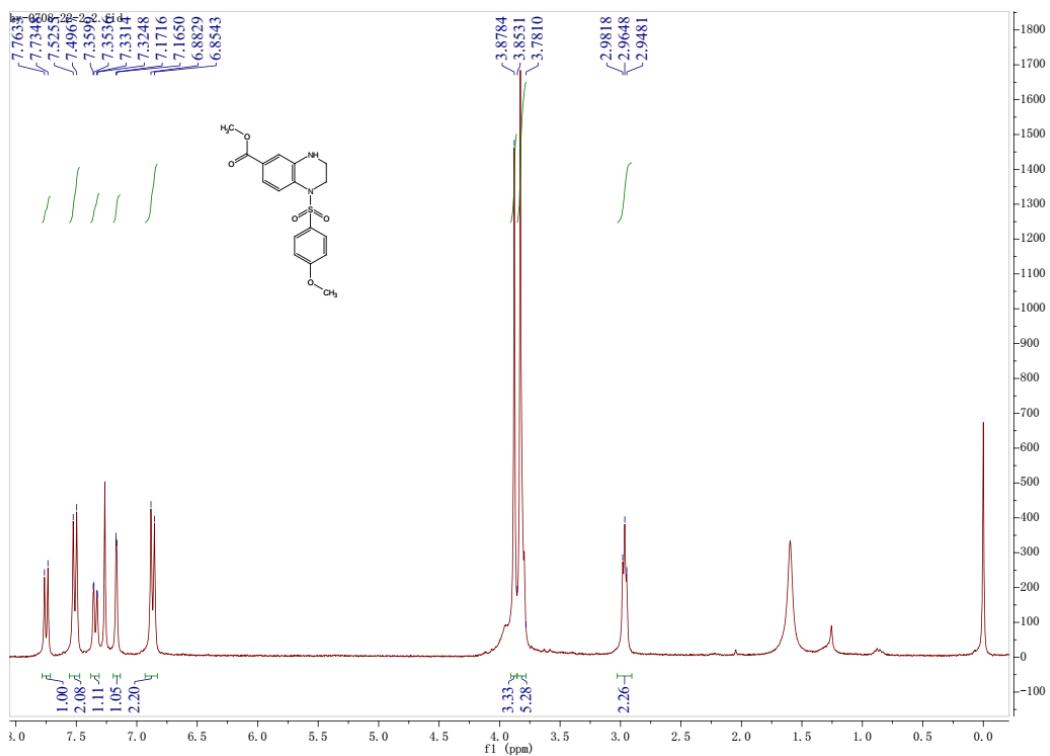
HPLC purity



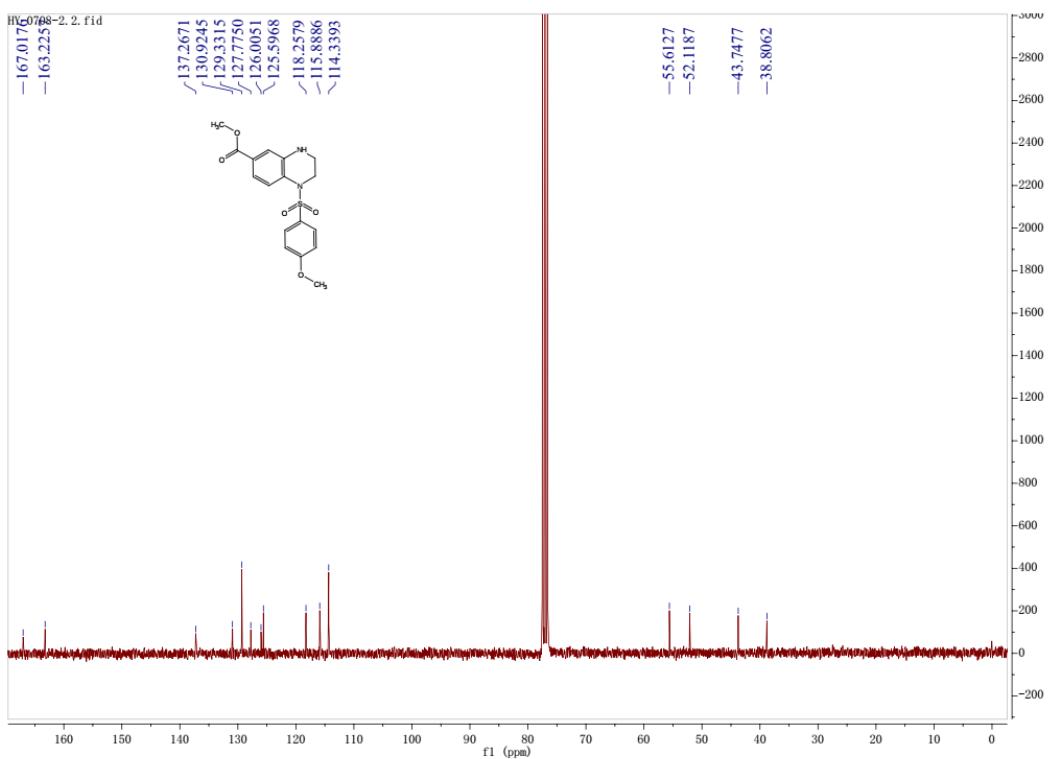
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1.852	BB	0.0862	38.39258	6.38451	0.0977
2	2.805	BV R	0.1593	3.92300e4	3837.58911	99.8214
3	3.710	VB E	0.2116	31.80025	2.13689	0.0809

## I-26

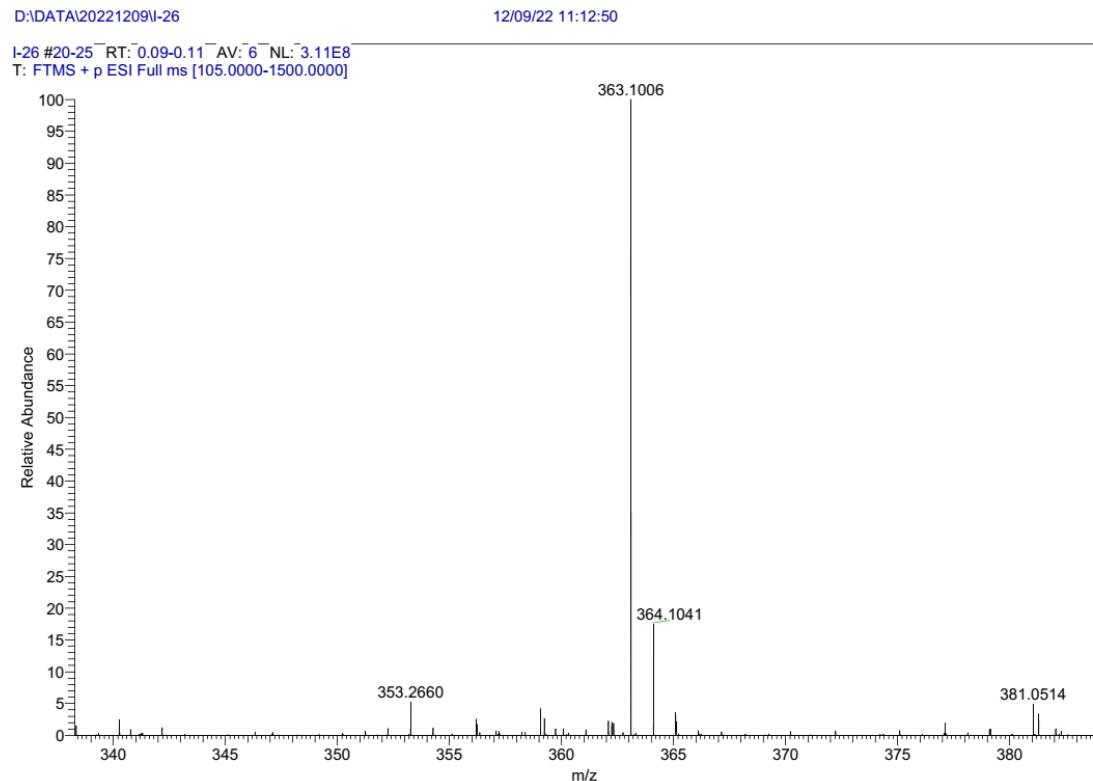
<sup>1</sup>H-NMR



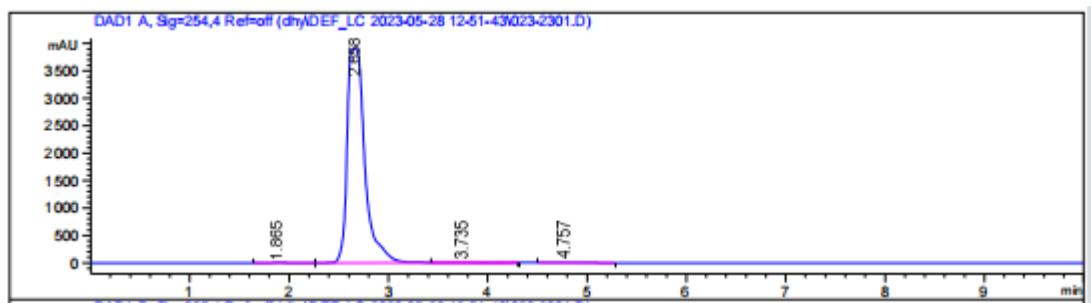
<sup>13</sup>C-NMR



## HRMS



HPLC purity



峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	1. 865	BV	0. 1677	30. 02051	2. 30833	0. 0615
2	2. 658	VV R	0. 1915	4. 86709e4	3902. 44629	99. 7257
3	3. 735	VB E	0. 2801	79. 69418	3. 65877	0. 1633
4	4. 757	BB	0. 2349	24. 16605	1. 41780	0. 0495