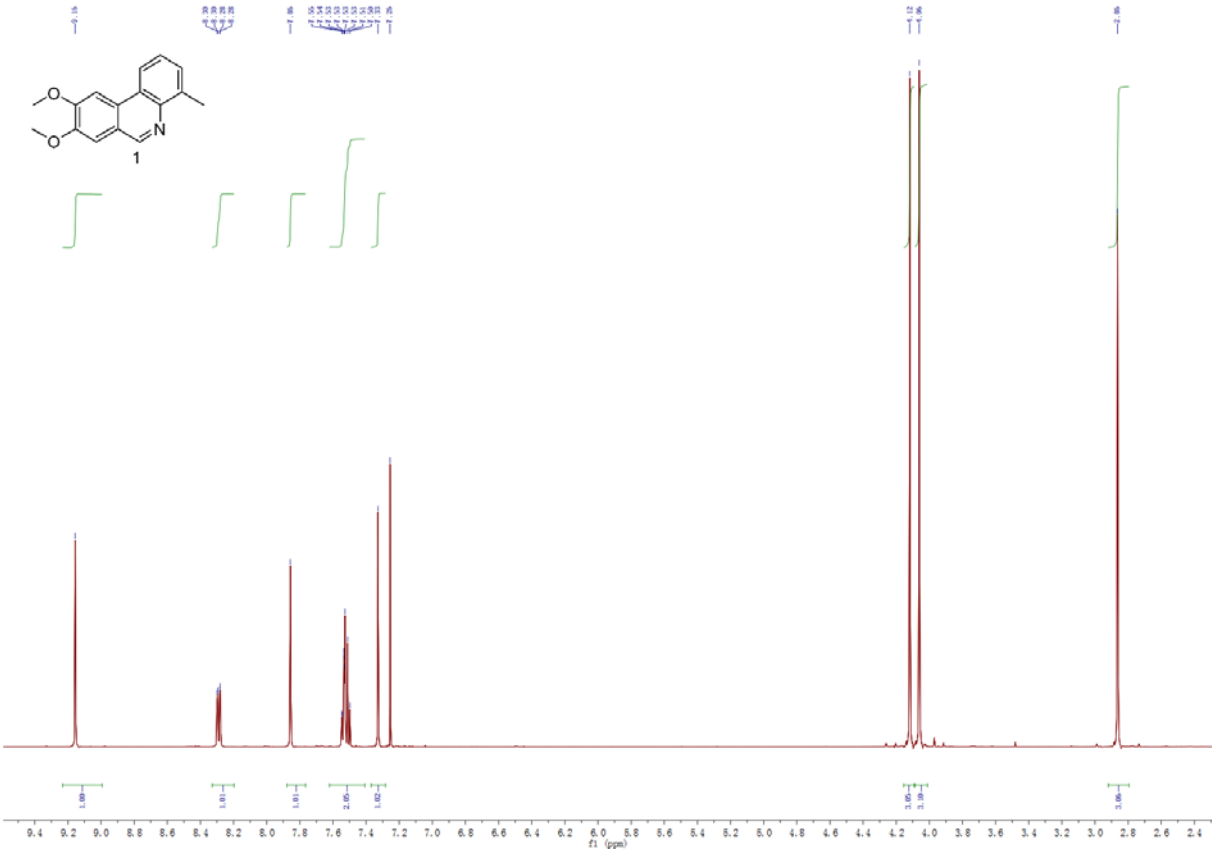
Supporting Information

Novel Nucleocapsid Protein-Targeting Phenanthridine inhibitors of SARS-CoV-2

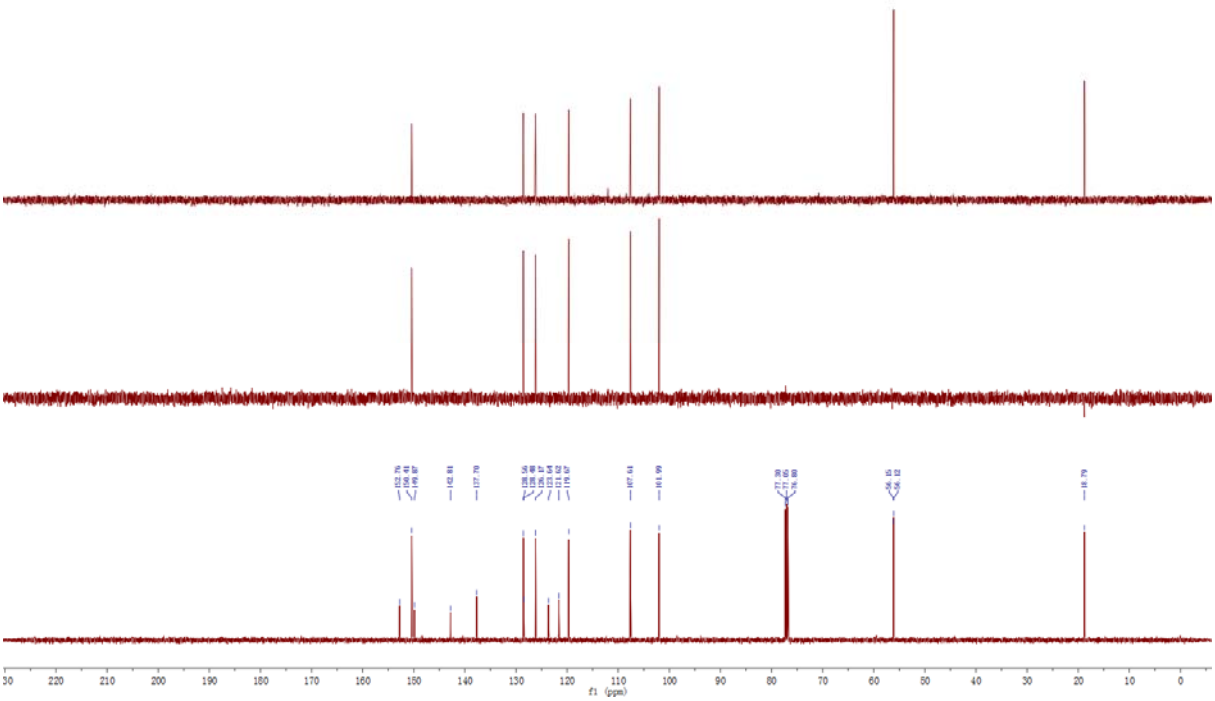
Yi-Ting Wang, Xin-Yan Long, Xiao Ding, Shi-Rui Fan, Jie-Yun Cai, Bi-Juan Yang, Xin-Fang Zhang, Lian Yang, Rong-hua Luo, Ting Ruan, Juan Ren, Chen-Xu Jing, Yong-Tang Zheng, Xiao-Jiang Hao, and Duo-Zhi Chen

Table of contents

^{1}H NMR, ^{13}C NMR and HRESIMS spectrums of compound 1-17



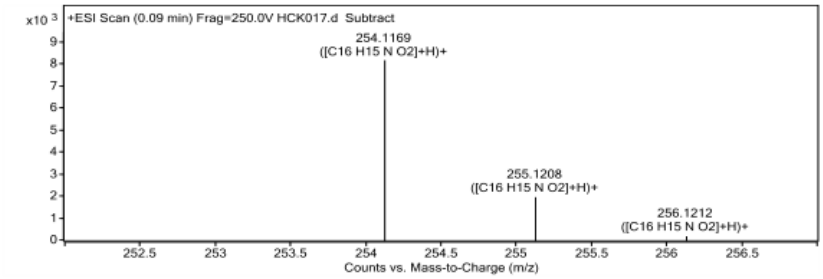
^{1}H NMR (500 MHz) spectrum of compound **1** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **1** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
250	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
180.0794		3579.74		
181.0875	1	11528.31		
182.0942	1	3539.19		
192.08		3003.92		
193.0874	1	3884.09		
209.083		8704.47		
210.0902	1	24065.34		
238.0853	1	35597		
239.0912	1	10833.75		
254.1169	1	8176.08	C16 H15 N O2	(M+H)+

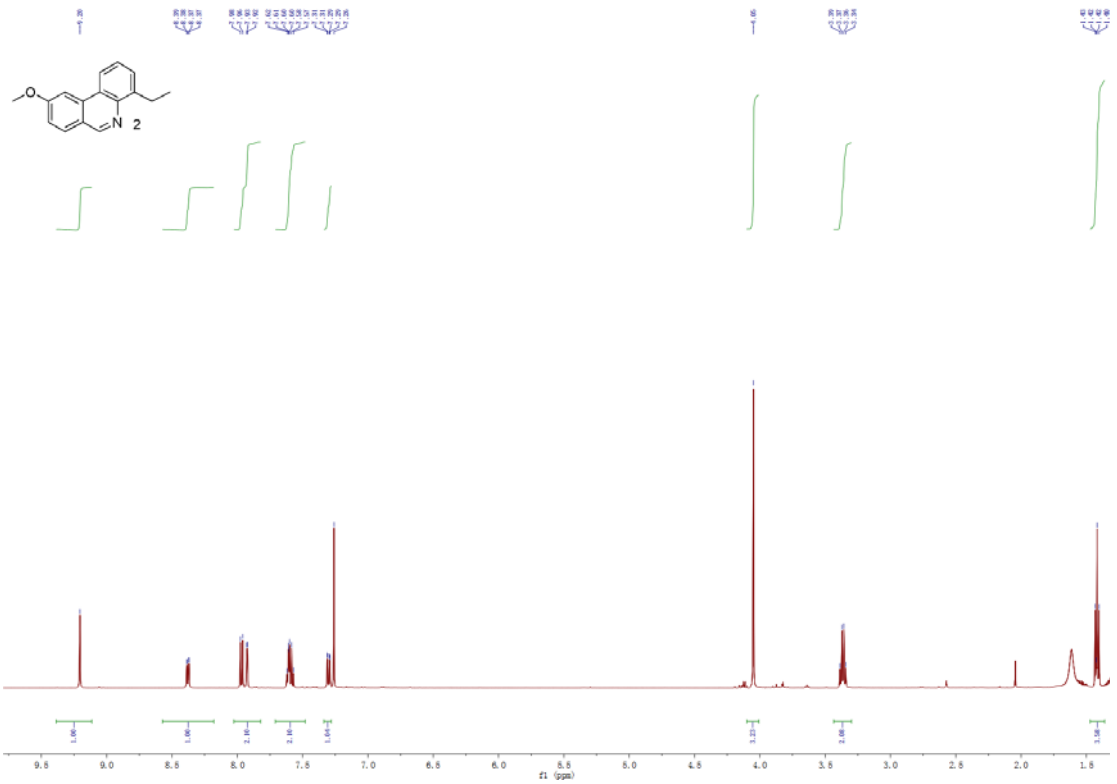
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

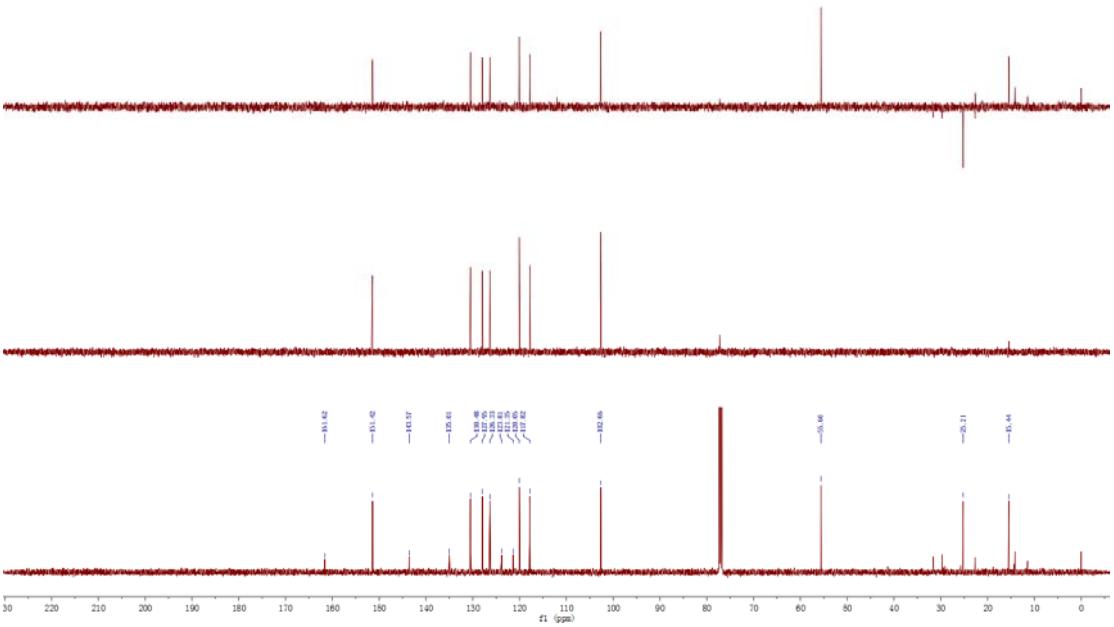
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C16 H15 N O2	253.1103	254.1176	254.1169	0.70	2.75	10.0000

HRESI (+) MS spectrum of compound **1**.



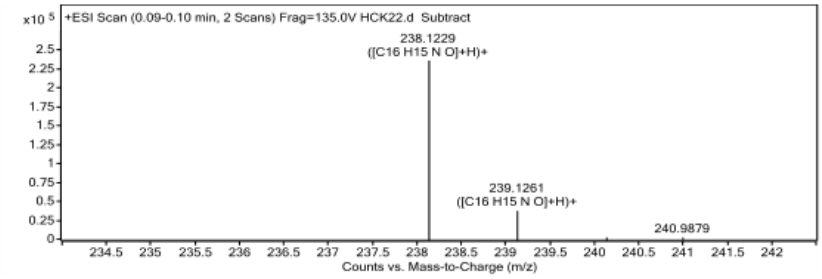
^{1}H NMR (500 MHz) spectrum of compound **2** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **2** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0216	1	533680.38		
80.0245	1	14673.11		
81.0176	1	18777.86		
118.5081	1	6143.02		
120.5277	2	5595.79		
137.0015	2	5016.08		
139.0209	2	5252.92		
157.0349	1	5778.03		
238.1229	1	236531.34	C16 H15 N O	(M+H)+
239.1261	1	39001.64	C16 H15 N O	(M+H)+

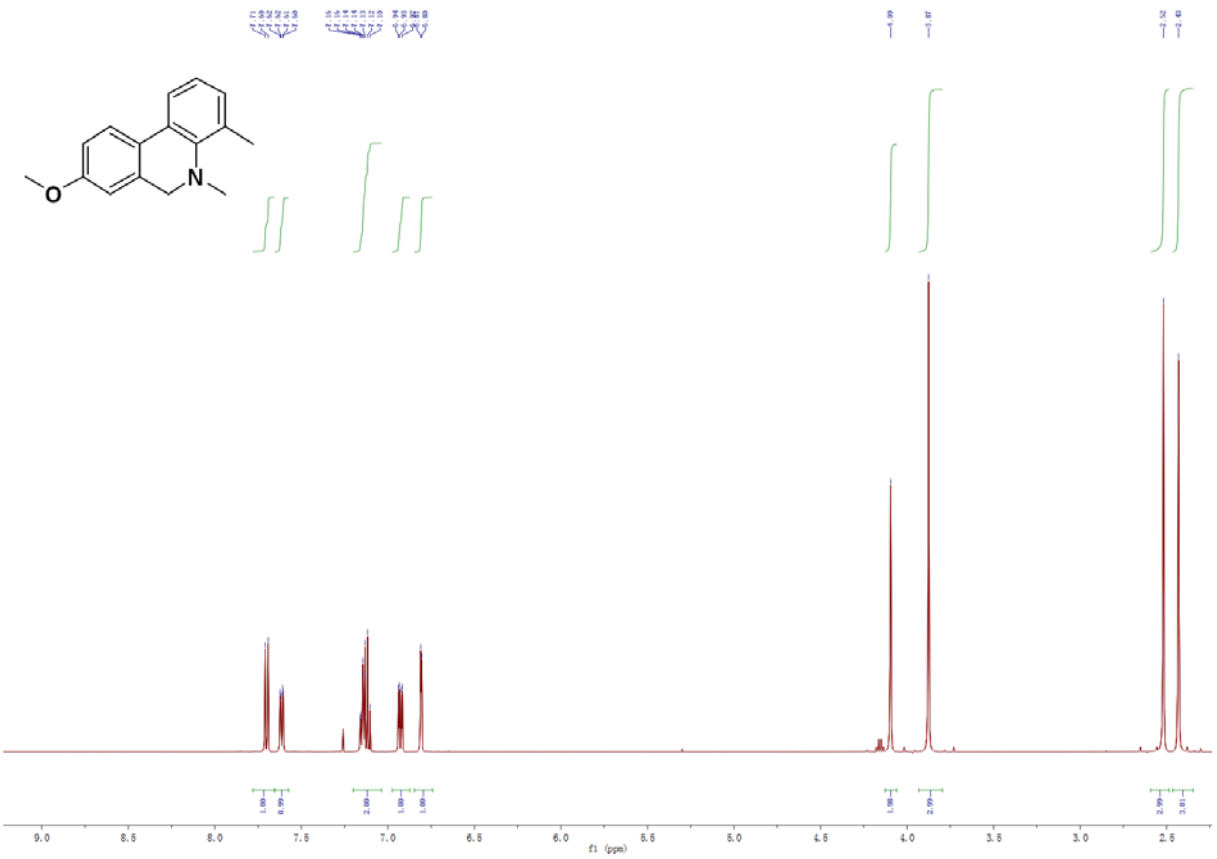
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

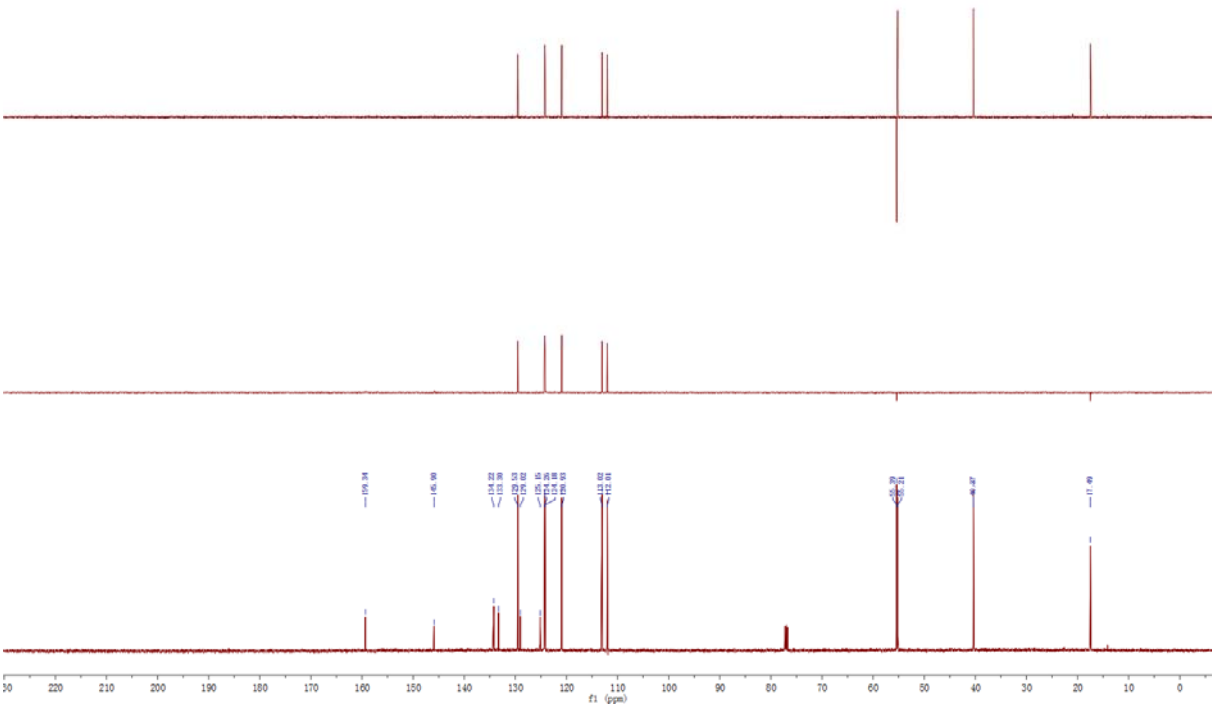
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C16 H15 N O	237.1154	238.1226	238.1229	-0.30	-1.26	10.0000

HRESI (+) MS spectrum of compound **2**.



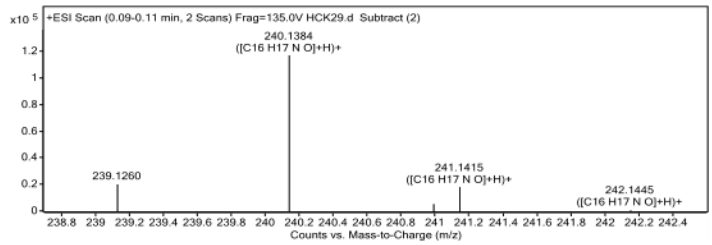
^{1}H NMR (500 MHz) spectrum of compound **3** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **3** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0215	1	548429.56		
80.0243	1	13939.46		
81.0174	1	22588.8		
118.508	2	10863.11		
137.0018	1	10705.78		
238.1227	1	122233.65		
239.126	1	21061.25		
240.1384	1	117358.68	C16 H17 N O	(M+H)+
241.1415	1	18467.42	C16 H17 N O	(M+H)+
254.1175	1	13652.38		

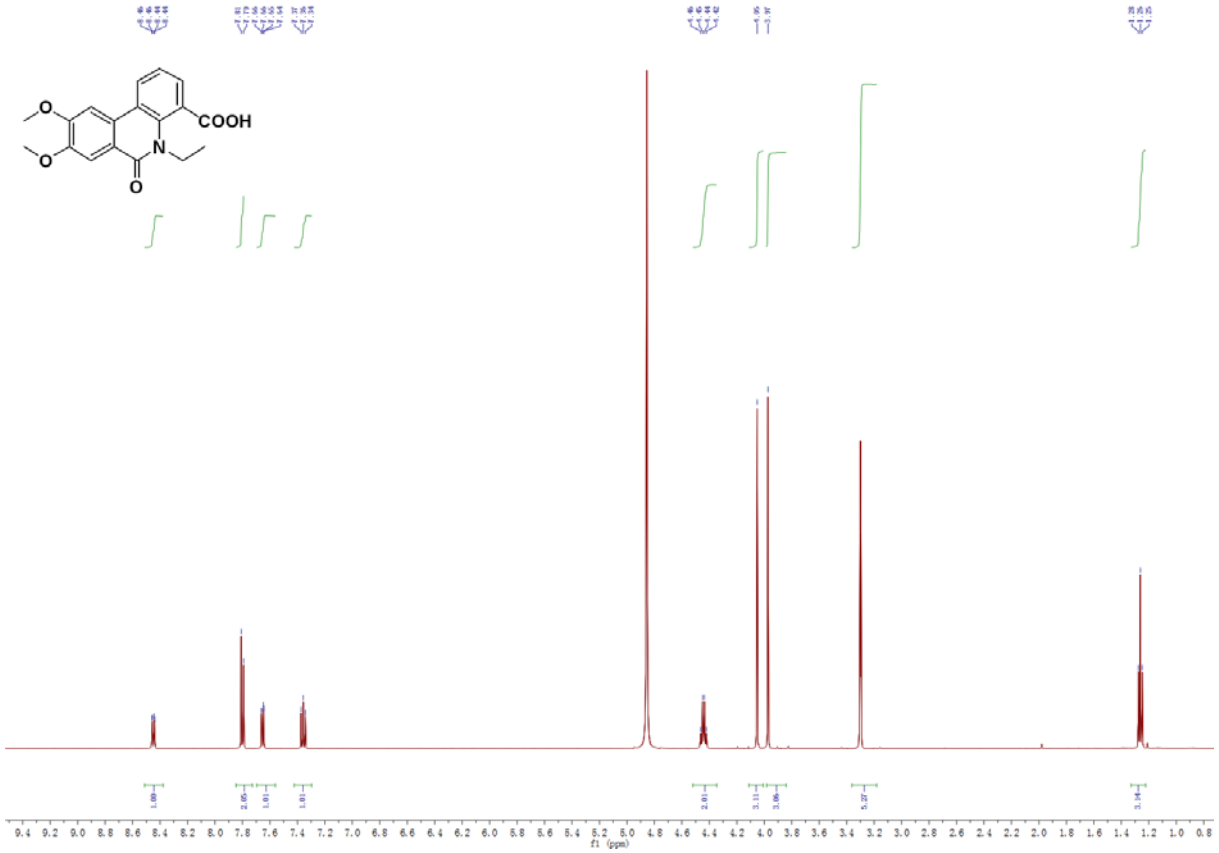
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

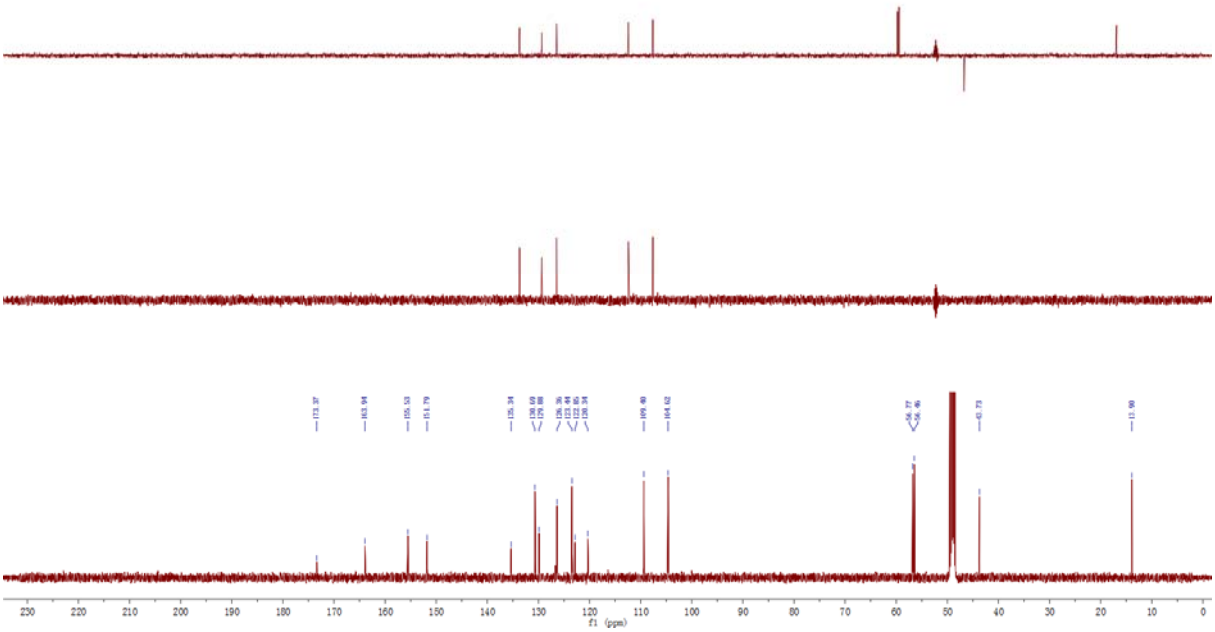
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C16 H17 N O	239.1310	240.1383	240.1384	-0.10	-0.42	9.0000

HRESI (+) MS spectrum of compound **3**.



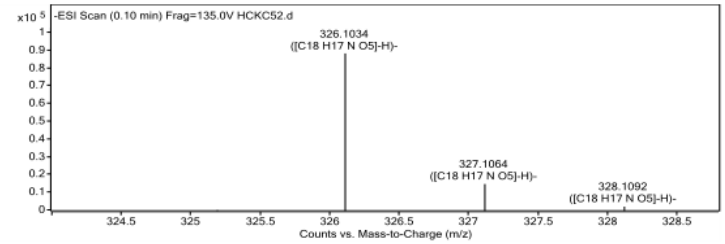
^{1}H NMR (500 MHz) spectrum of compound **4** in CD_3OD.



^{13}C NMR (125 MHz) spectrum of compound **4** in CD_3OD.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
112.9853	1	22211.83		
254.0822	1	254755.22		
255.0855	1	44261.14		
282.1135	1	86115.33		
326.1034	1	88347.26	C18 H17 N O5	(M-H)-
675.1967	1	21782.32		
966.001	1	84231.08		
982.9898	1	28748.19		
1033.9885	1	126847.33		
1034.9907	1	29190.7		

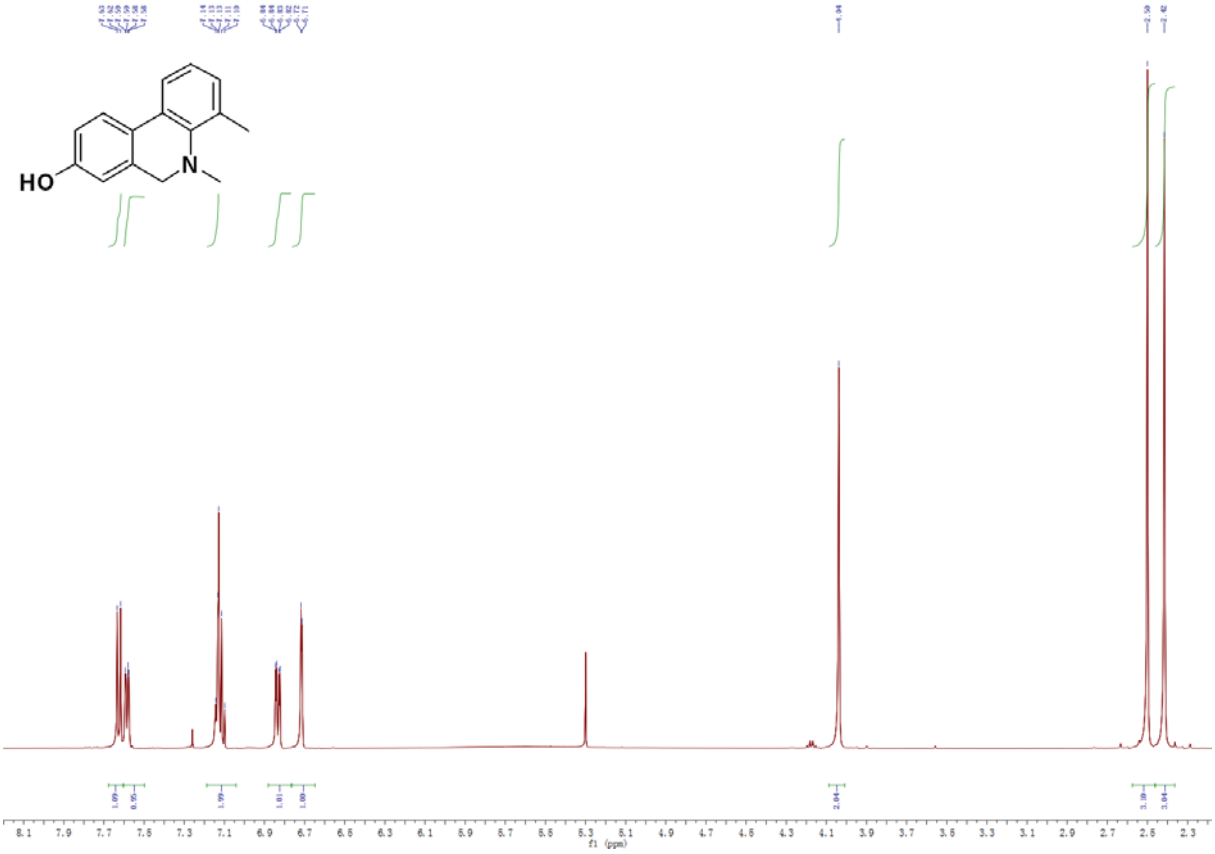
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

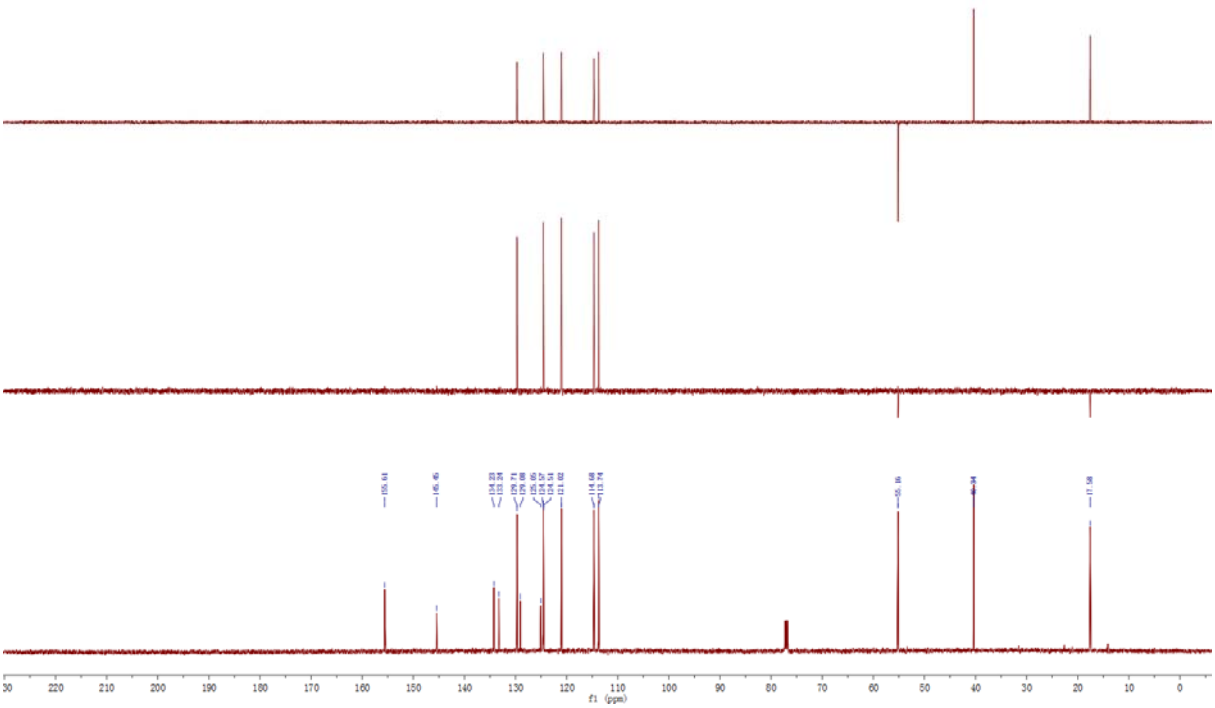
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C18 H17 N O5	327.1107	326.1034	326.1034	0.00	0.00	11.0000

HRESI (-) MS spectrum of compound **4**.



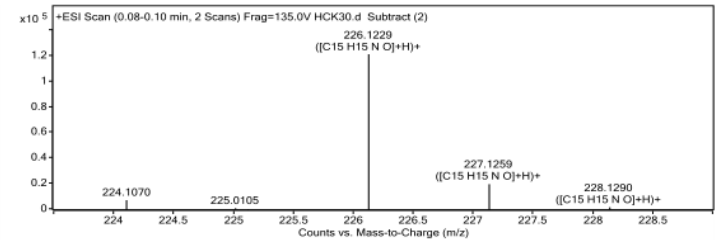
^{1}H NMR (500 MHz) spectrum of compound **5** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **5** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0214	1	224453.22		
80.0245	1	5156.44		
81.0175	1	7981.73		
118.5082	1	3935.15		
126.4941	1	4576.37		
137.0017	2	5591.59		
157.0355		3096.96		
224.107	1	7471.71		
226.1229	1	121178.08	C15 H15 N O	(M+H)+
227.1259	1	20205.18	C15 H15 N O	(M+H)+

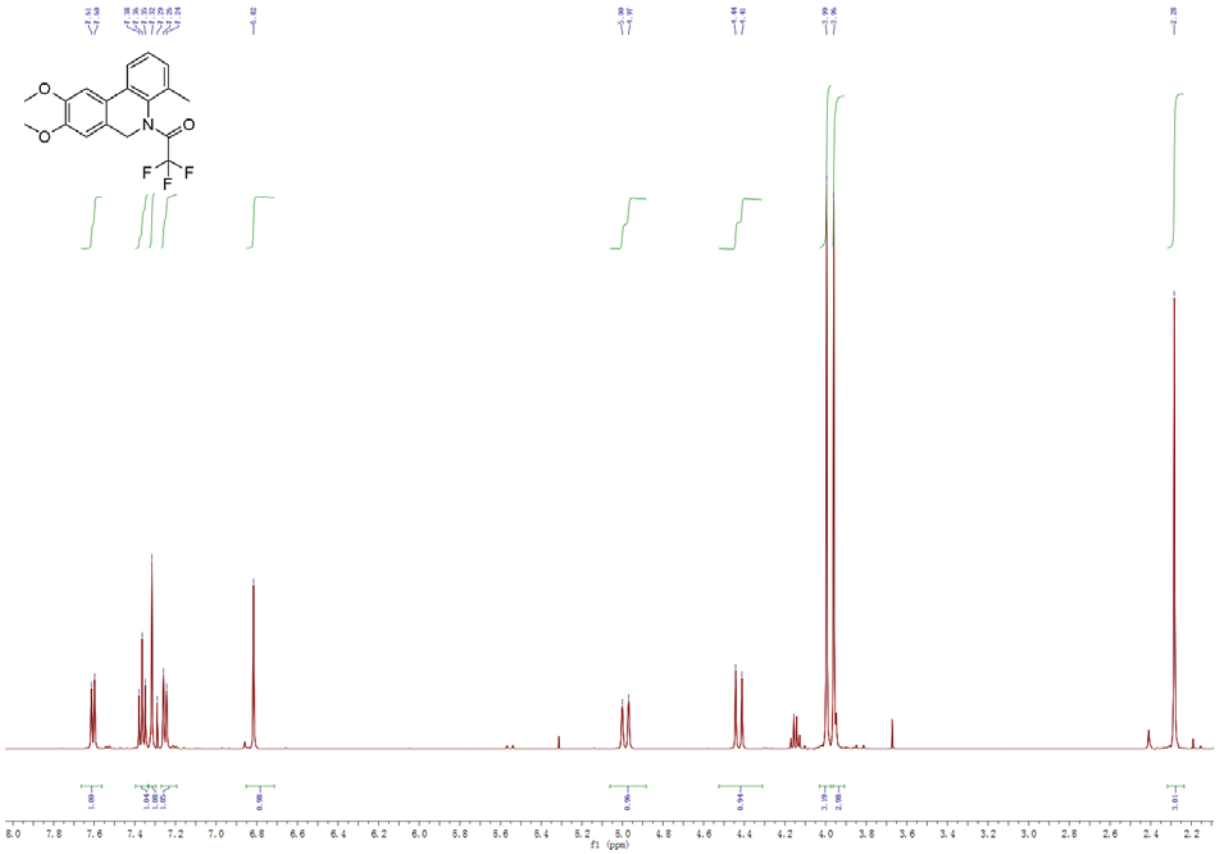
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

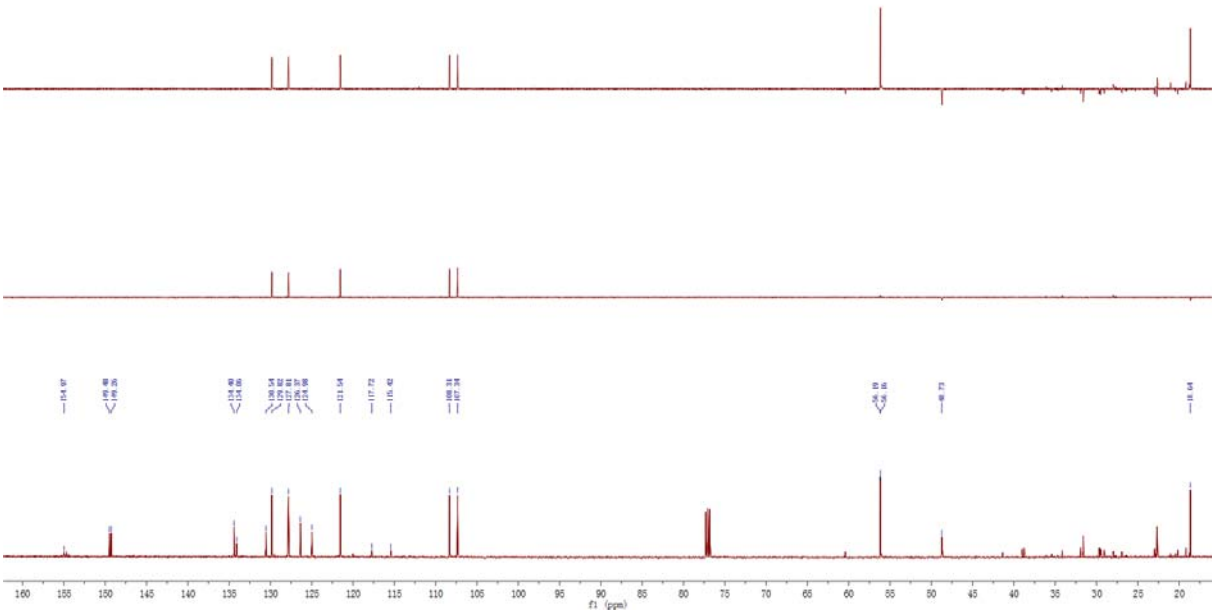
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C15 H15 N O	225.1154	226.1226	226.1229	-0.30	-1.33	9.0000

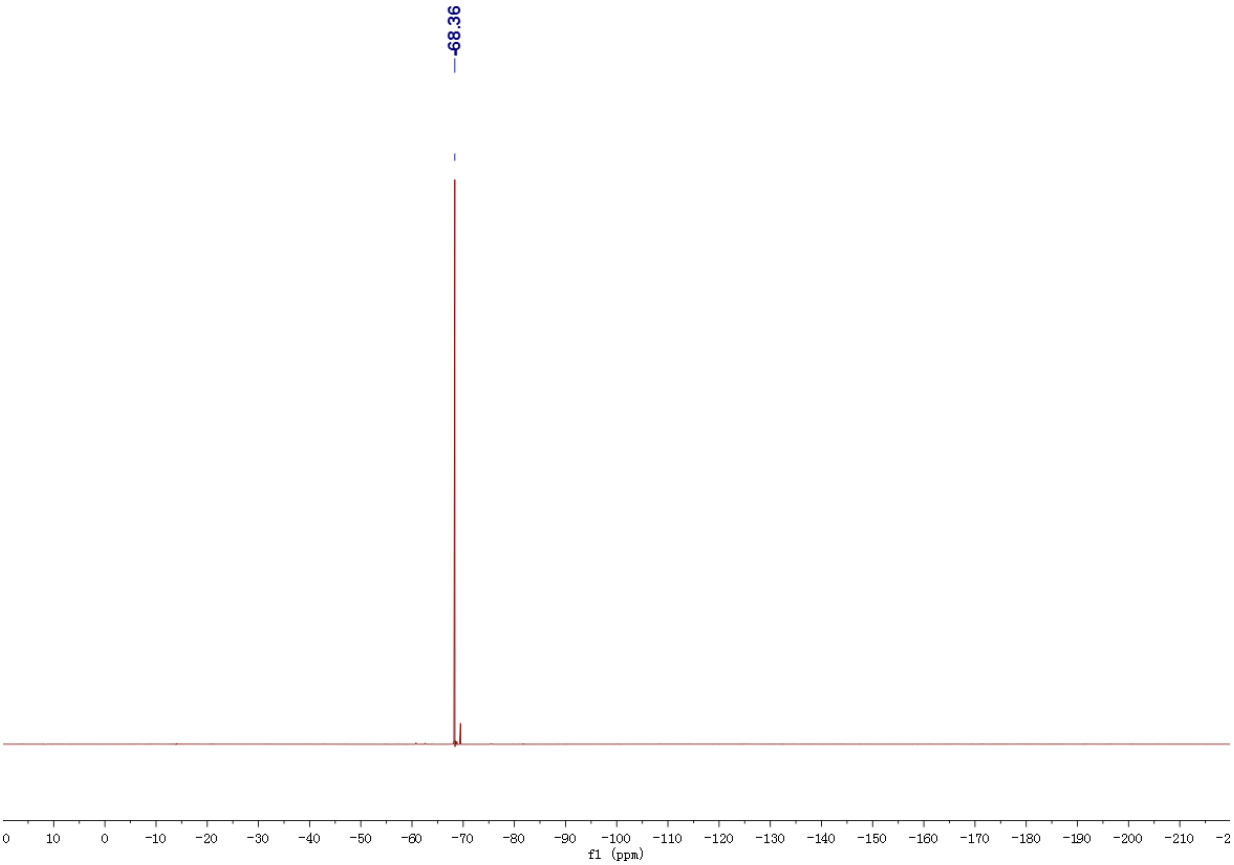
HRESI (+) MS spectrum of compound **5**.



^{1}H NMR (500 MHz) spectrum of compound **6** in $CDCl_3$



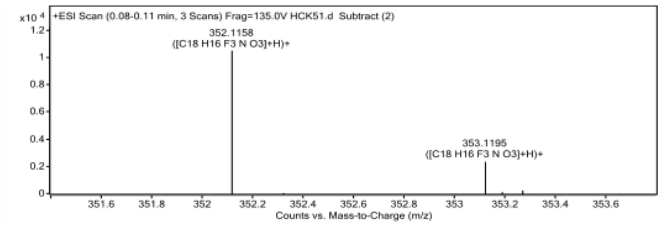
^{13}C NMR (125 MHz) spectrum of compound **6** in $CDCl_3$.



^{19}F NMR (125 MHz) spectrum of compound **6** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0218	1	360188.5		
80.0247	1	8136.17		
81.0174	1	14089.83		
157.0356		9547.31		
254.1181	1	12994.93		
274.2748	1	15350.48		
318.3012	1	9771.69		
351.1081		8455.11		
352.1158	1	10545.38	C18 H16 F3 N O3	(M+H)+
415.2122	1	7677.89		
449.1044	2	8340.18		
453.1681	1	7983.59		
474.2607	1	8300.38		

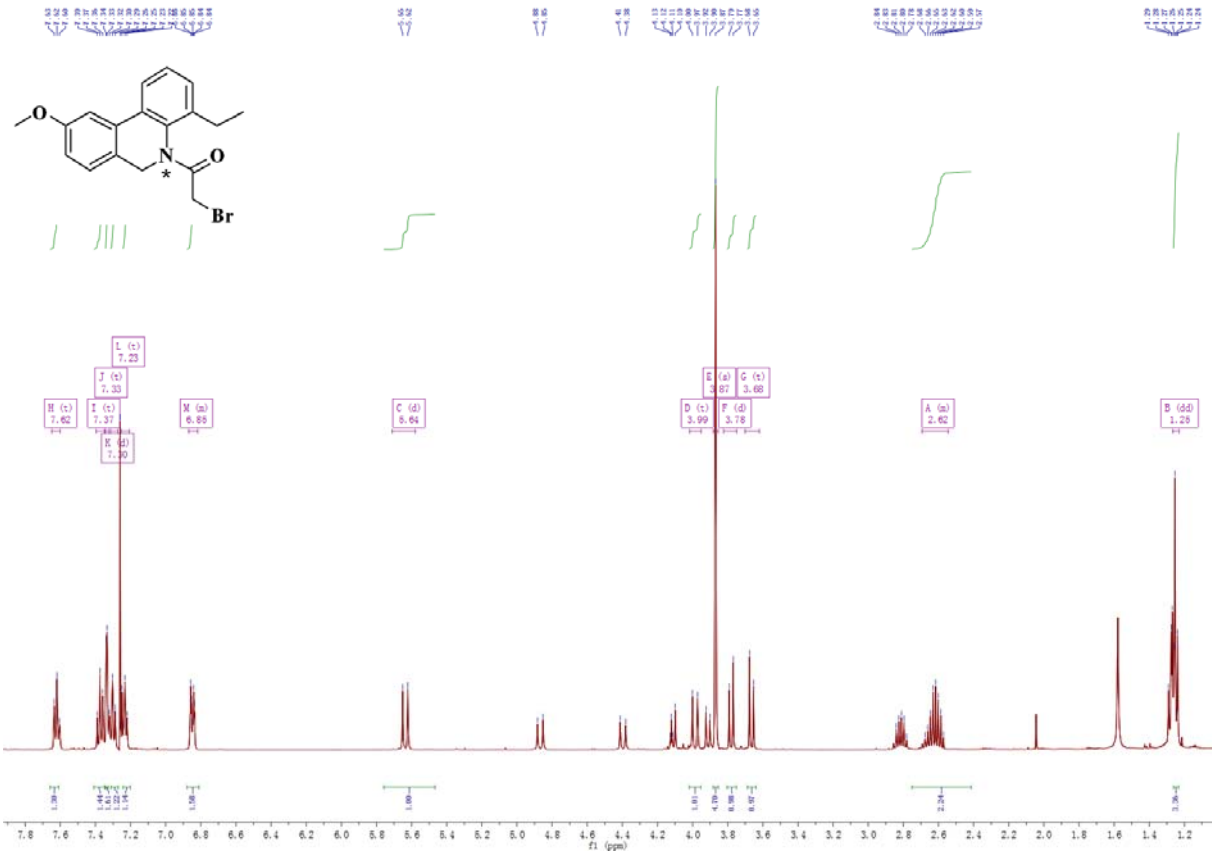
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5
F	0	5

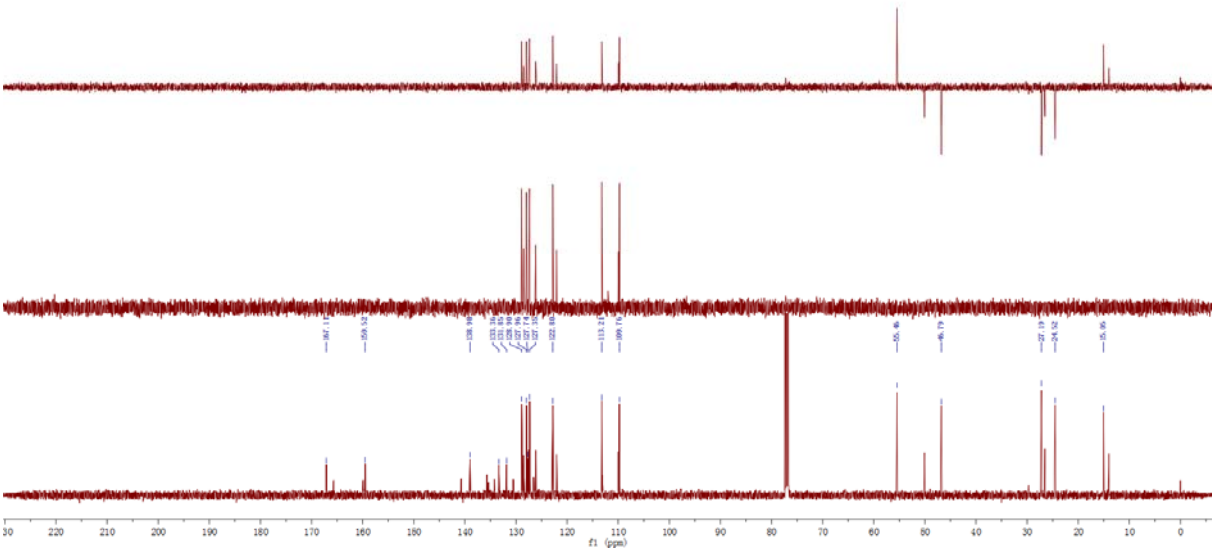
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C18 H16 F3 N O3	351.1082	352.1155	352.1158	-0.30	-0.85	10.0000

HRESI (+) MS spectrum of compound **6**.



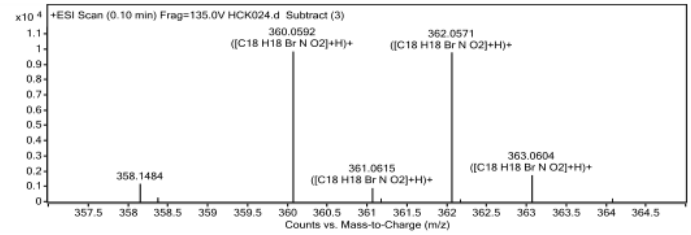
^{1}H NMR (500 MHz) spectrum of compound **7** in $CDCl_3$



^{13}C NMR (125 MHz) spectrum of compound **7** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0214	1	773002.75		
80.0244	1	19284.22		
81.0173	1	26284.11		
118.5076	2	12038.94		
126.494	1	11107.31		
137.0015	2	12762.64		
157.0345	1	12000.01		
240.9873		6747.39		
360.0592	1	9907.59	C18 H18 Br N O2	(M+H)+
362.0571	1	9825.67	C18 H18 Br N O2	(M+H)+

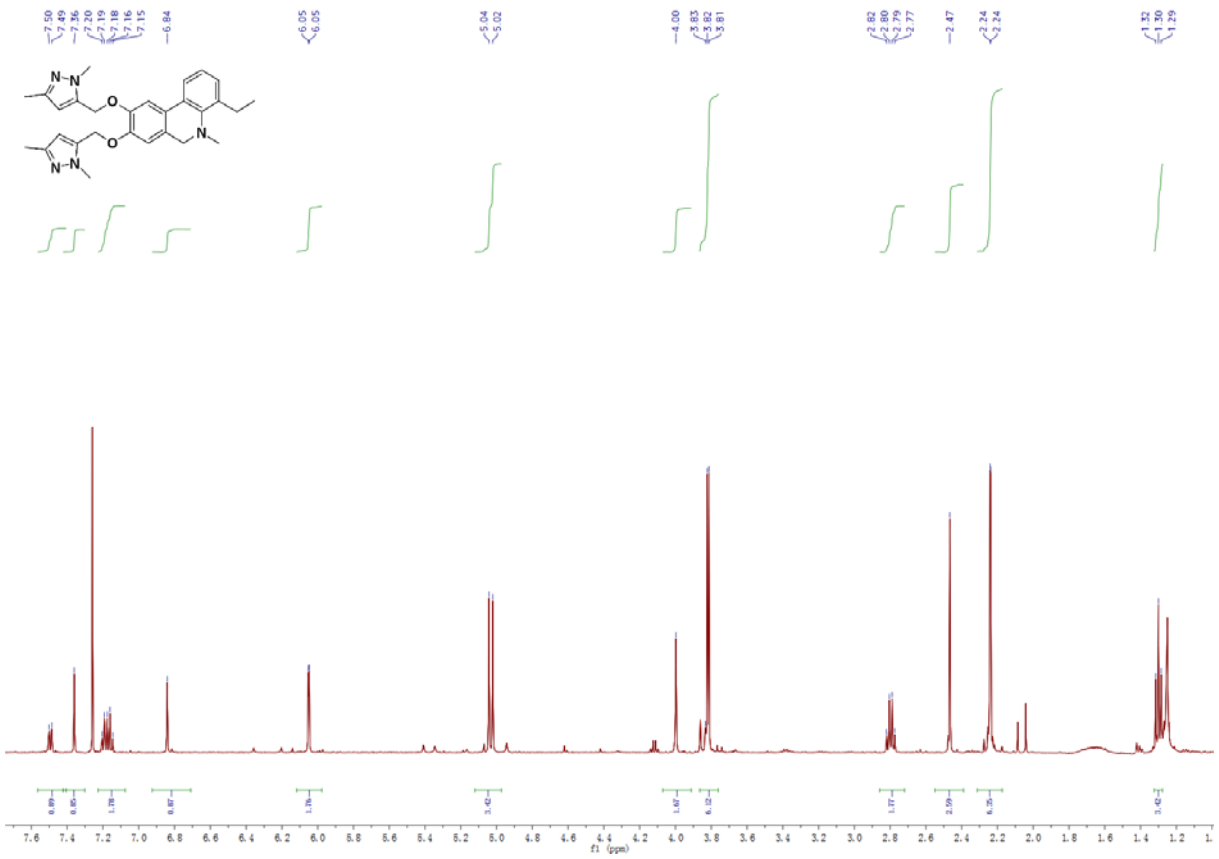
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3
Br	0	3

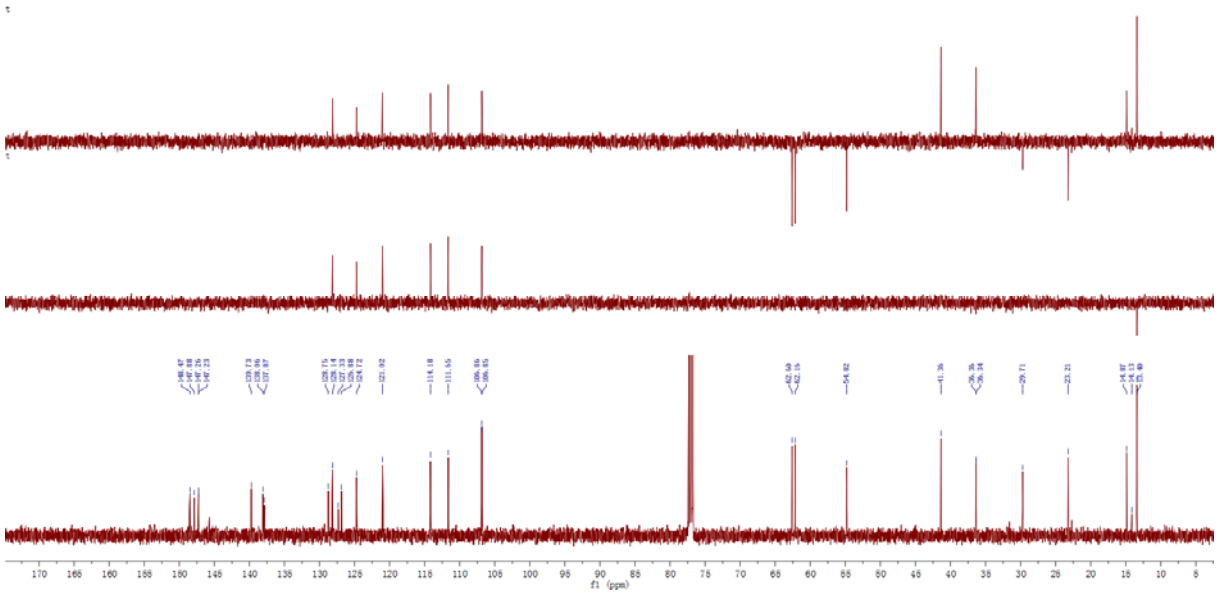
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C18 H18 Br N O2	359.0521	360.0594	360.0592	0.20	0.56	10.0000

HRESI (+) MS spectrum of compound **7**.



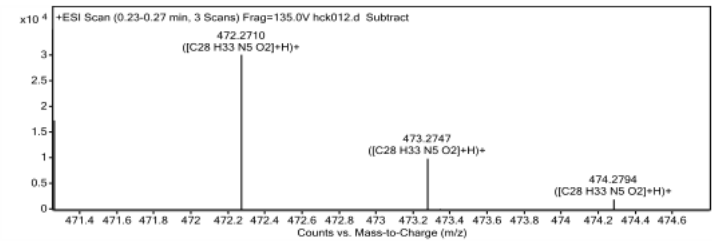
^{1}H NMR (500 MHz) spectrum of compound **8** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **8** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
63.9982		7257.3		
79.0217	1	410113.88		
80.0245	1	11367.56		
81.0174	1	19100.03		
97.995	2	7893.07		
109.0763	1	6452.35		
470.256	1	55268.95		
471.2592	1	17449.04		
472.271	1	30112.67	C28 H33 N5 O2	(M+H)+
473.2747	1	10034.47	C28 H33 N5 O2	(M+H)+

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

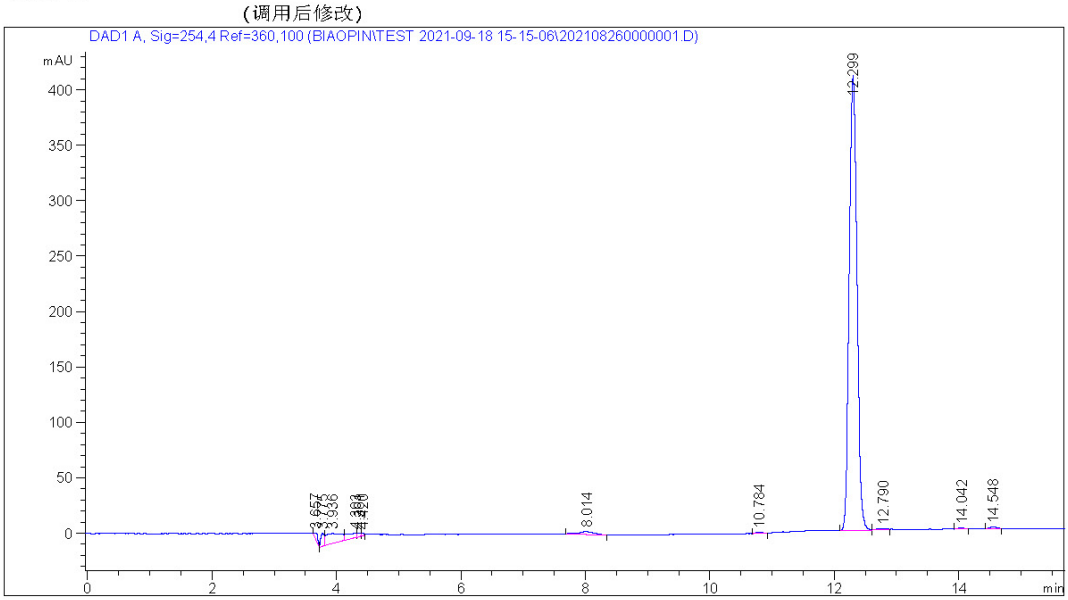
Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C28 H33 N5 O2	471.2634	472.2707	472.2710	-0.30	-0.64	15.0000

HRESI (+) MS spectrum of compound **8**.

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 15-15-06\202108260000001.D
样品名称: 5057

==========

操作者	: D-YI	序列行 :	1
仪器	: 仪器 1	位置 :	样品瓶 1
进样日期	: 2021-9-18 15:16:09	进样次数 :	1
		进样量 :	2.0 µl
采集方法	: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 15-15-06\YBJ_LC.M		
最后修改	: 2021-9-18 13:24:58 : D-YI		
分析方法	: C:\CHEM32\1\DATA\TEST.M		
最后修改	: 2021-9-18 15:02:17 : D-YI		
	(调用后修改)		



==========

面积百分比报告

==========

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=254,4 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	3.657	BB	0.0685	22.95609	5.10037	0.5832
2	3.775	BV	0.0621	47.55928	11.53565	1.2082
3	3.936	VV	0.2023	151.65434	9.10396	3.8527
4	4.303	VV	0.1746	55.99206	4.01626	1.4224
5	4.361	VV	0.0556	13.05810	3.20206	0.3317
6	4.420	VV	0.0493	6.21444	2.09939	0.1579
7	8.014	VV	0.2338	53.40079	2.71066	1.3566
8	10.784	BB	0.0937	8.22669	1.07043	0.2090

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 15-15-06\202108260000001.D
样品名称: 5057

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
9	12.299	BV	0.1367	3540.21826	410.13559	89.9368
10	12.790	VV	0.1580	15.62767	1.19942	0.3970
11	14.042	BV	0.0918	7.88112	1.18146	0.2002
12	14.548	BB	0.1166	13.55042	1.91488	0.3442
总量 :				3936.33925	453.27014	

==========

峰加和报告

==========

信号 1: DAD1 A, Sig=254,4 Ref=360,100

==========

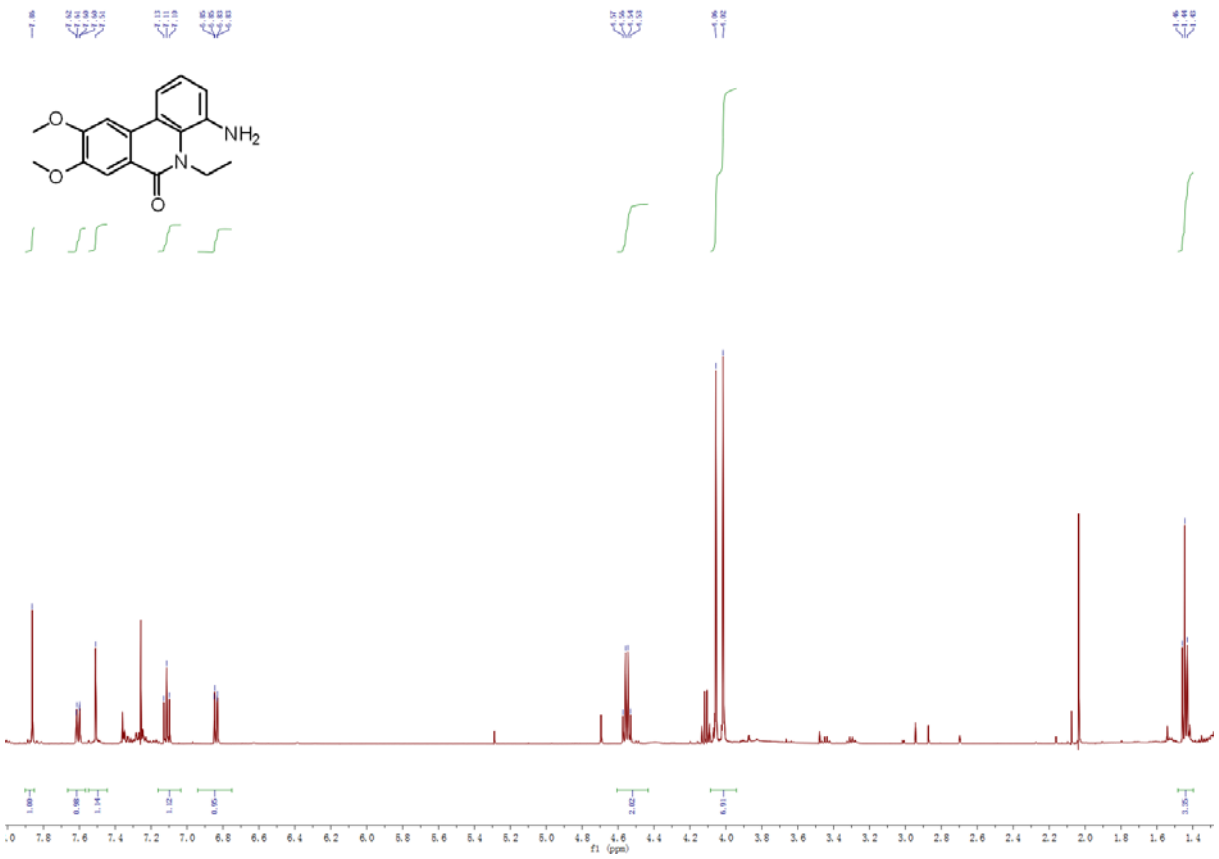
最终峰加和报告

==========

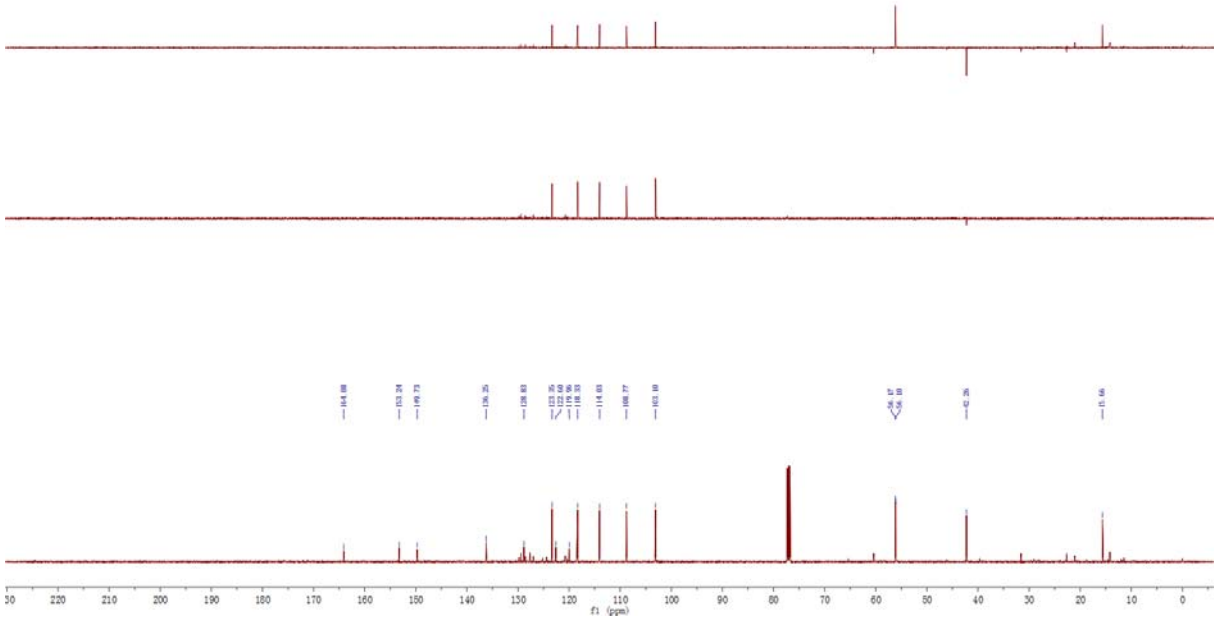
信号 1: DAD1 A, Sig=254,4 Ref=360,100

*** 报告结束 ***

HPLC spectrum of compound **8**.



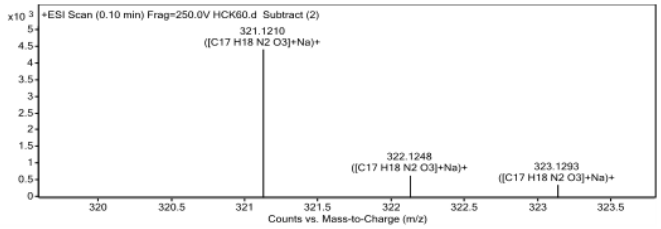
^{1}H NMR (500 MHz) spectrum of compound **9** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **9** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
250	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
225.0658		4932.8		
226.0736		3908.91		
227.0812	1	10012.33		
255.0767	1	11088.55		
256.0827	1	3001.08		
270.1		21964.9		
271.1067	1	12749.53		
321.121	1	4429.8	C17 H18 N2 O3	(M+Na)+
355.1185	1	11577.14		
908.3127	2	4567.79		
908.8137	2	6762.24		
909.3156	2	6663.43		
909.8164	2	6250.32		

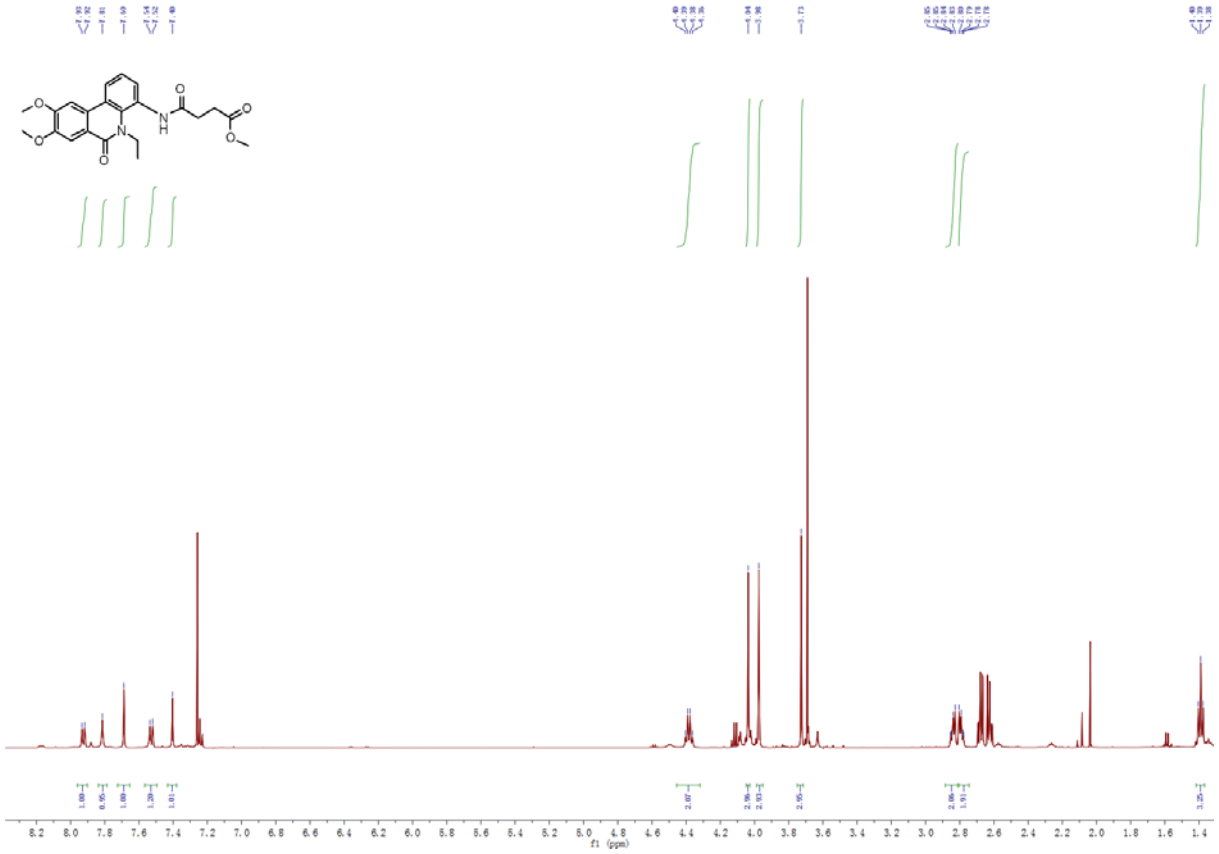
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

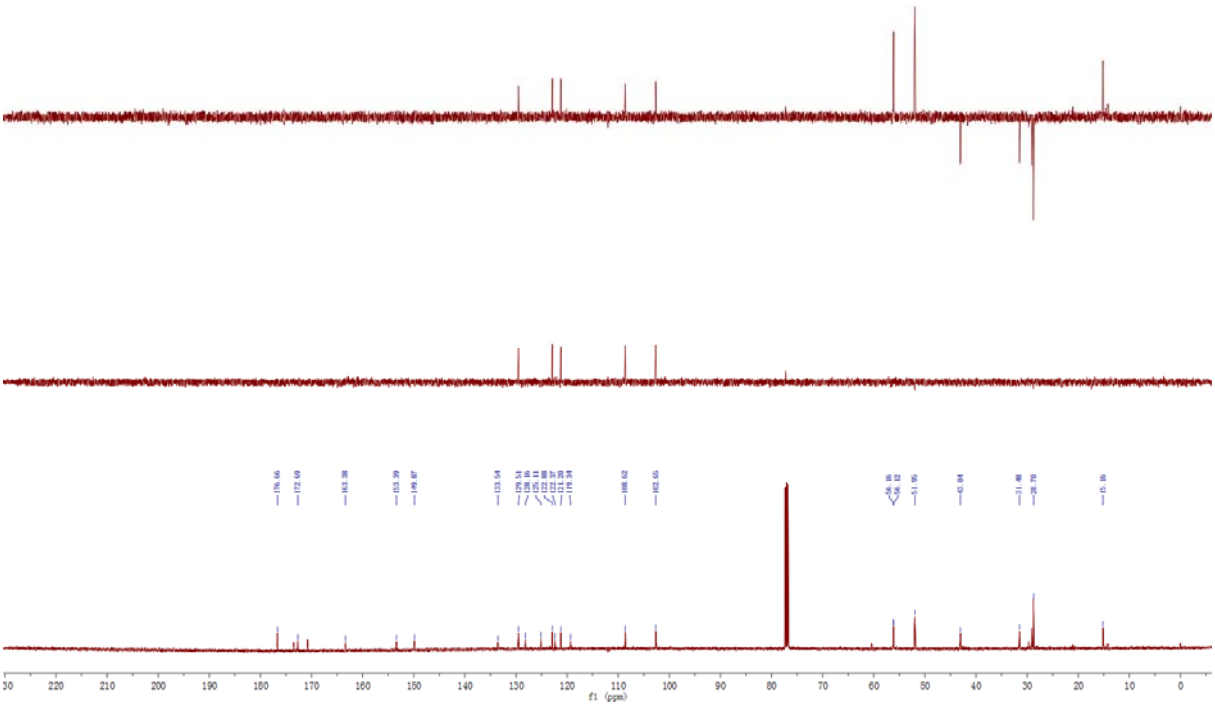
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C17 H18 N2 O3	298.1317	321.1210	321.1210	0.00	0.00	10.0000

HRESI (+) MS spectrum of compound **9**.



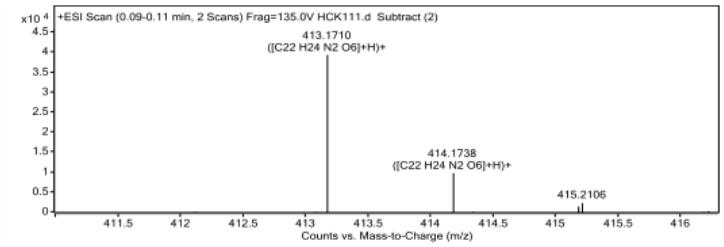
^{1}H NMR (500 MHz) spectrum of compound **10** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **10** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0215	1	574242.63		
80.0243	1	13763.79		
81.0174	1	22483.95		
137.0017	1	10087.71		
157.0349		10791.06		
413.171	1	39417.8	C22 H24 N2 O6	(M+H)+
414.1738	1	9856.41	C22 H24 N2 O6	(M+H)+
435.1524	1	20690.33		
451.1267	1	15604.35		
847.3163	1	15892.33		

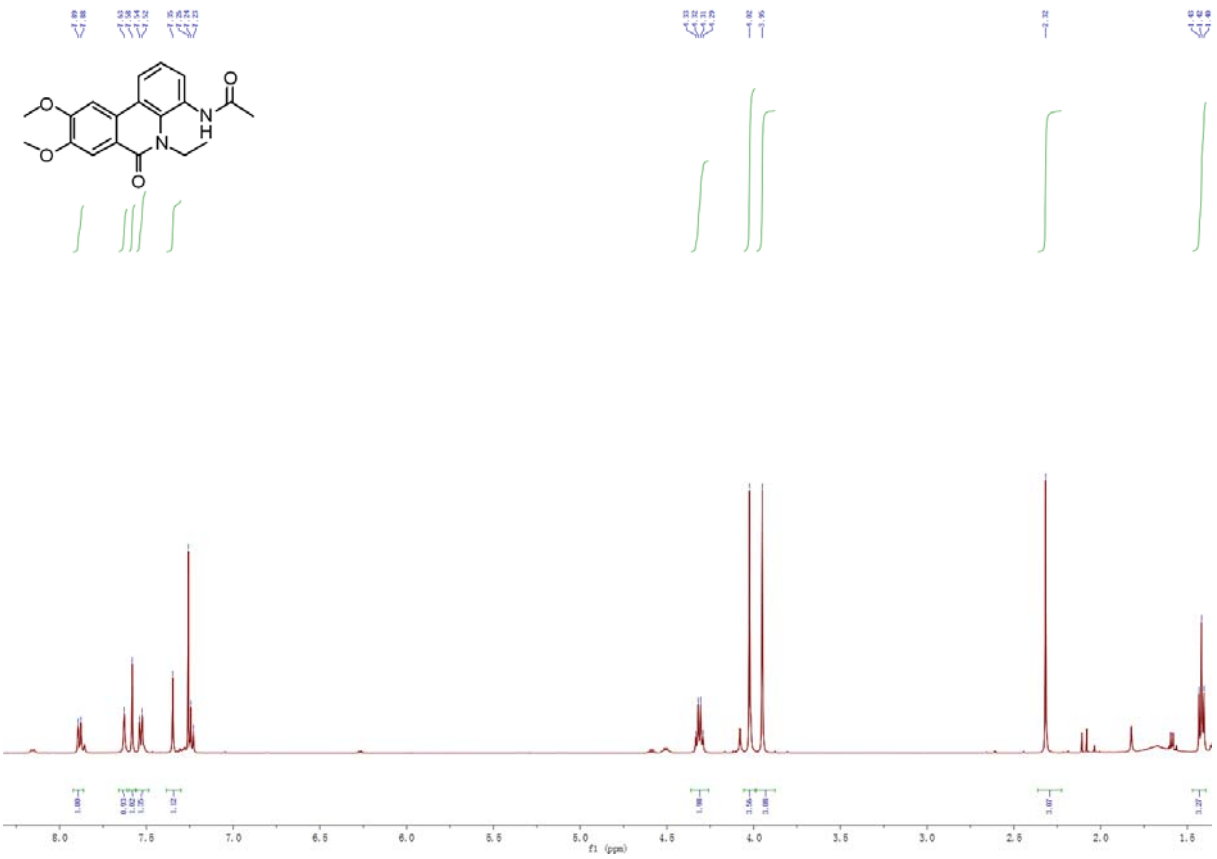
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

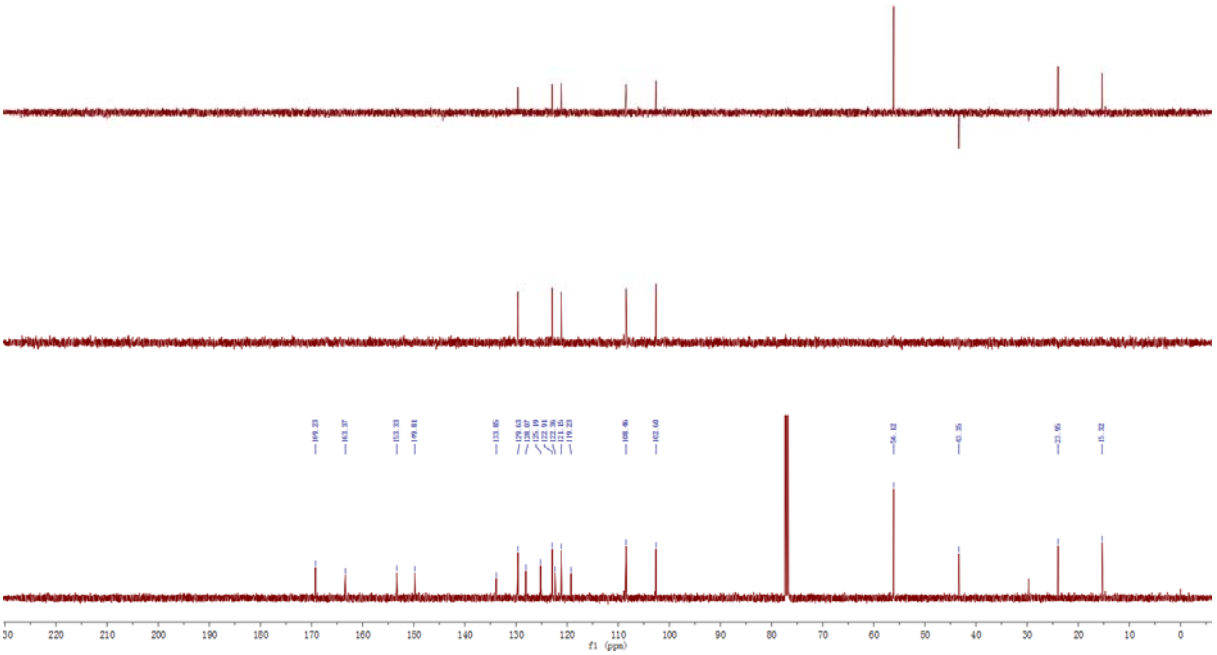
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C22 H24 N2 O6	412.1634	413.1707	413.1710	-0.30	-0.73	12.0000

HRESI (+) MS spectrum of compound **10**.



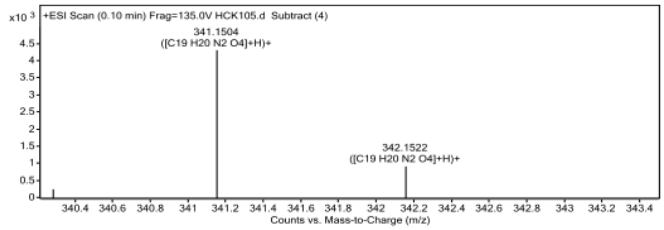
^{1}H NMR (500 MHz) spectrum of compound **11** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **11** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0216	1	58486.42		
80.0246	1	3081.91		
81.0172		5532.43		
118.5085	2	4106.84		
126.495	2	3322.92		
137.0024	2	8633.03		
139.0215	2	2231.9		
144.9866	2	2020.57		
157.0356	1	5327.9		
157.5149	1	4140.15		
341.1504	1	4331.65	C19 H20 N2 O4	(M+H)+
437.1942	1	2221.47		
453.1701	1	2923.89		

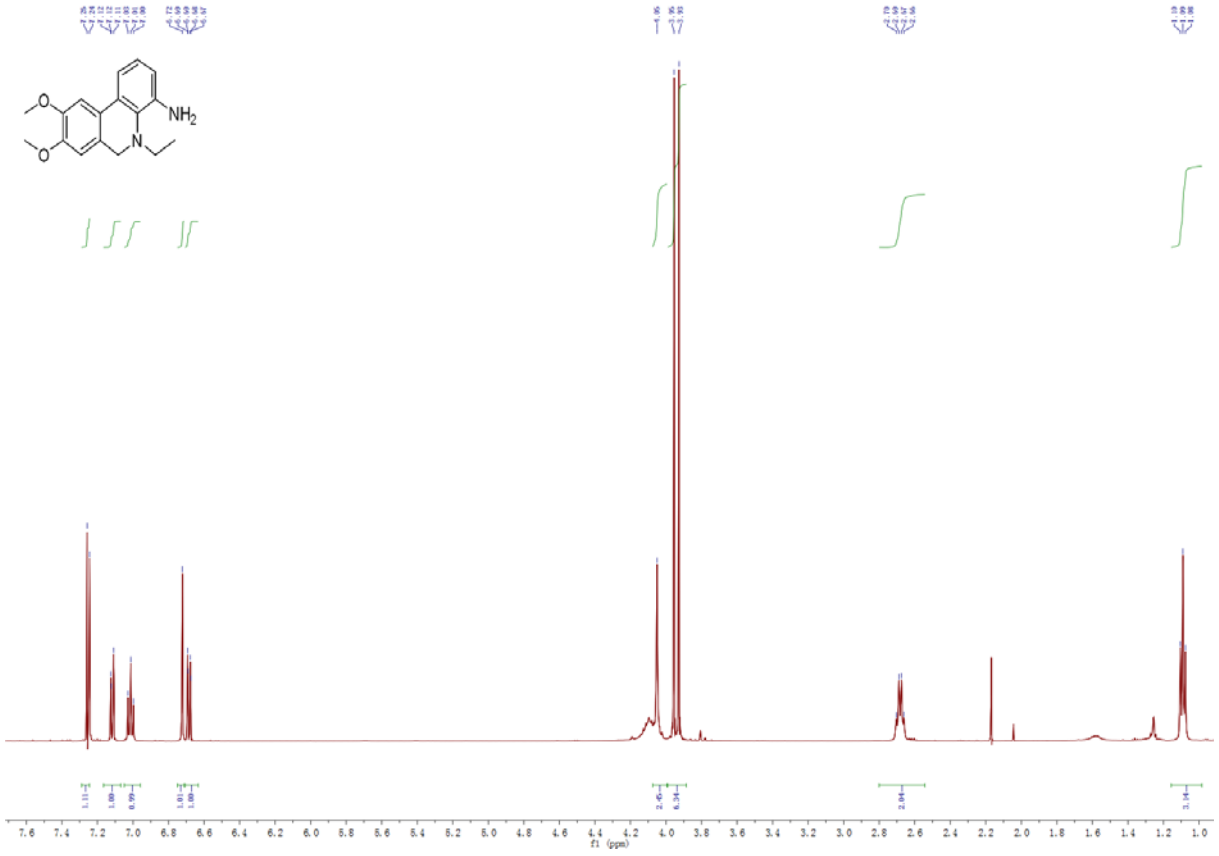
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

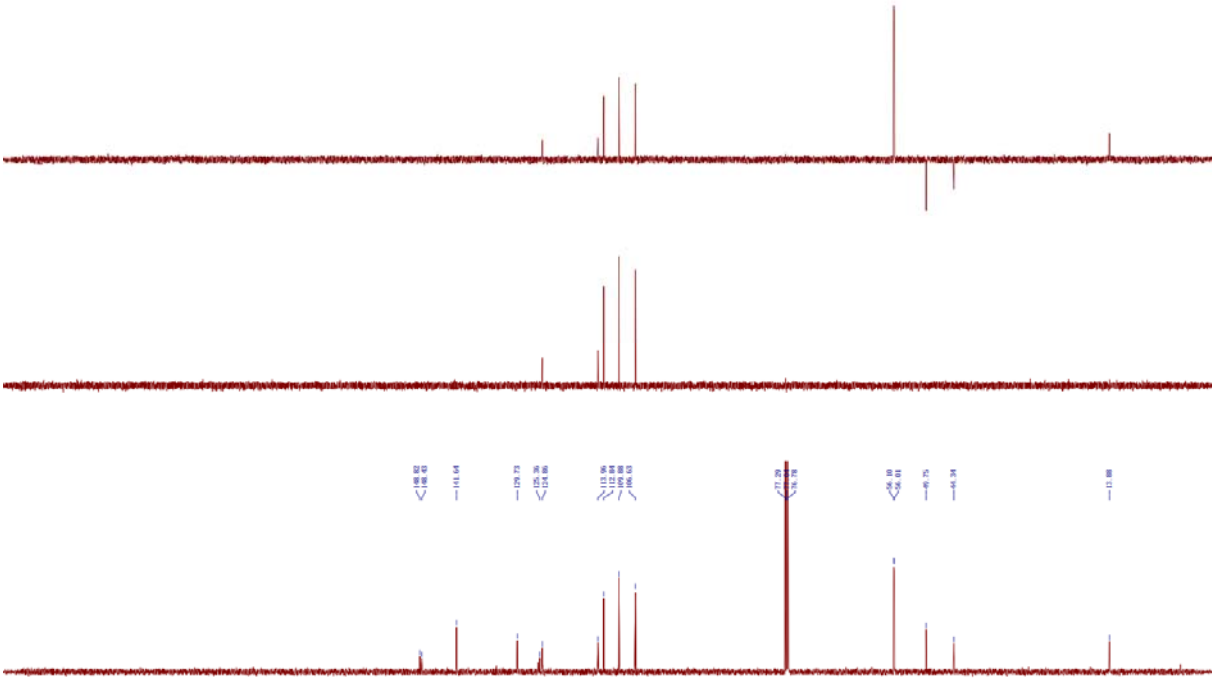
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C19 H20 N2 O4	340.1423	341.1496	341.1504	-0.80	-2.35	11.0000

HRESI (+) MS spectrum of compound **11**.



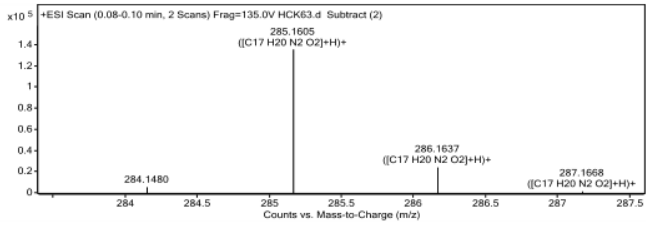
^{1}H NMR (500 MHz) spectrum of compound **12** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **12** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0217	1	92969.3		
80.0244	1	4093.57		
81.0173	1	6523.44		
126.4947		2456.28		
137.0022	2	1391.71		
139.0207	2	1802.08		
157.0353		2099.78		
283.1445	1	33563.22		
284.148	1	6490.26		
285.1605	1	135977.28	C17 H20 N2 O2	(M+H)+
286.1637	1	25069.22	C17 H20 N2 O2	(M+H)+
287.1668	1	2461.39	C17 H20 N2 O2	(M+H)+
343.1656	1	2293.99		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

Formula Calculator Results

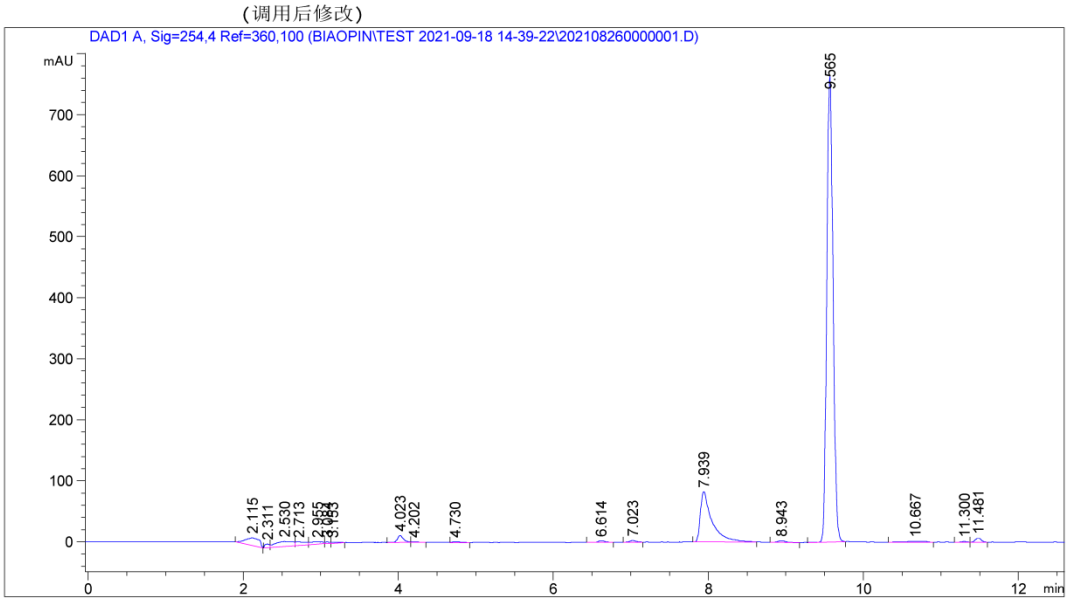
Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C17 H20 N2 O2	284.1525	285.1598	285.1605	-0.70	-2.45	9.0000

HRESI (+) MS spectrum of compound **12**.

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 14-39-22\202108260000001.D
样品名称: 5030

==========

操作者 : D-YI 序列行 : 1
仪器 : 仪器 1 位置 : 样品瓶 1
进样日期 : 2021-9-18 14:40:24 进样次数 : 1
进样量 : 2.0 µl
来自于序列的不同进样量! 实际进样量: 1.0 µl
采集方法 : C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 14-39-22\YBJ_LC.M
最后修改 : 2021-9-18 13:24:58 : D-YI
分析方法 : C:\CHEM32\1\DATA\TEST.M
最后修改 : 2021-9-18 14:35:44 : D-YI
(调用后修改)



==========

面积百分比报告

==========

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=254,4 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	2.115	BB	0.1640	157.07436	12.37888	2.7089
2	2.311	BV	0.0566	22.60004	5.66219	0.3898
3	2.530	VV	0.1978	129.55679	8.13571	2.2343
4	2.713	VV	0.1183	55.03342	6.04006	0.9491
5	2.955	VV	0.1432	47.47268	4.09617	0.8187
6	3.084	VV	0.0612	11.77315	2.68457	0.2030
7	3.153	VB	0.0688	9.57563	1.72337	0.1651

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 14-39-22\202108260000001.D
样品名称: 5030

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
8	4.023	VV	0.0836	62.73681	11.15264	1.0820
9	4.202	VV	0.1034	9.67289	1.38573	0.1668
10	4.730	VB	0.0983	9.97415	1.48610	0.1720
11	6.614	BV	0.1015	16.82634	2.53405	0.2902
12	7.023	BB	0.0856	15.39555	2.65823	0.2655
13	7.939	BV	0.1467	867.18610	82.45864	14.9554
14	8.943	BB	0.1087	19.81525	2.79574	0.3417
15	9.565	VV	0.0875	4288.22754	763.95282	73.9543
16	10.667	BV	0.2304	30.70580	1.67113	0.5295
17	11.300	BV	0.0860	7.85068	1.34721	0.1354
18	11.481	VB	0.0845	37.00320	6.90287	0.6382
总量 :				5798.48036	919.06612	

==========

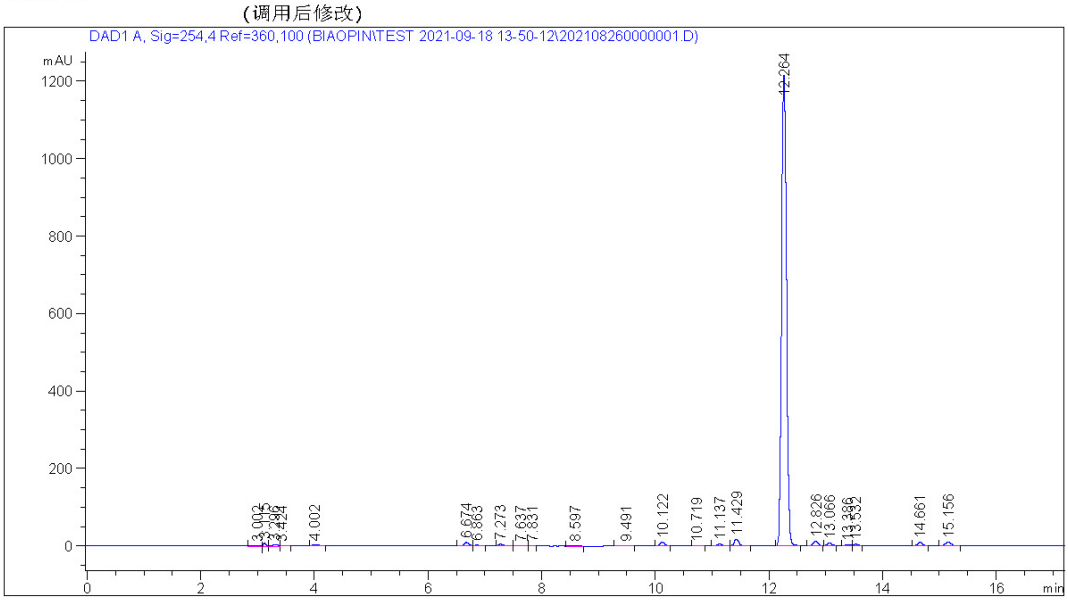
*** 报告结束 ***

HPLC spectrum of compound **12**

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 13-50-12\202108260000001.D
样品名称: 5005

操作者	: D-YI	序列行 :	1
仪器	: 仪器 1	位置 :	样品瓶 1
进样日期	: 2021-9-18 13:51:18	进样次数 :	1
		进样量 :	2.0 µl
采集方法	: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 13-50-12\YBJ_LC.M		
最后修改	: 2021-9-18 13:24:58 : D-YI		
分析方法	: C:\CHEM32\1\DATA\TEST.M		
最后修改	: 2021-9-18 15:02:17 : D-YI		

(调用后修改)



面积百分比报告

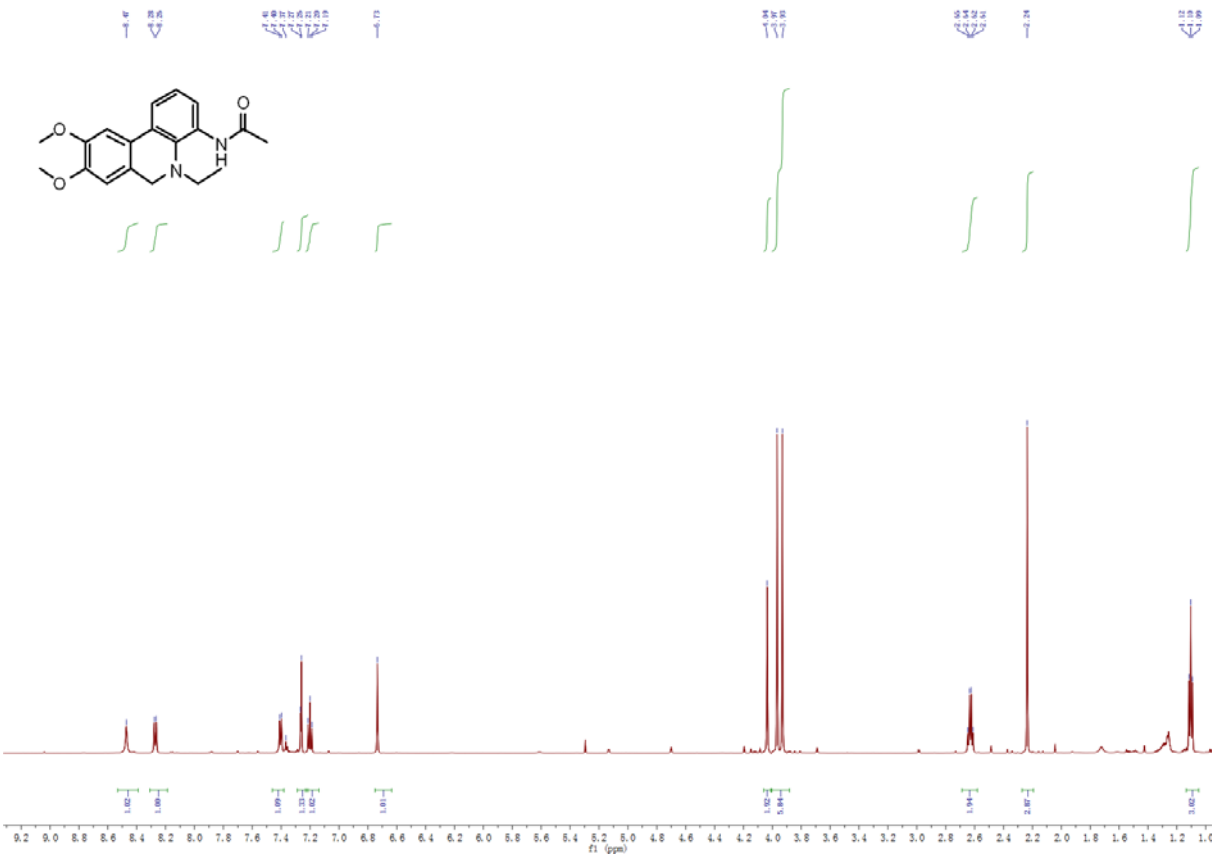
排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=254,4 Ref=360,100

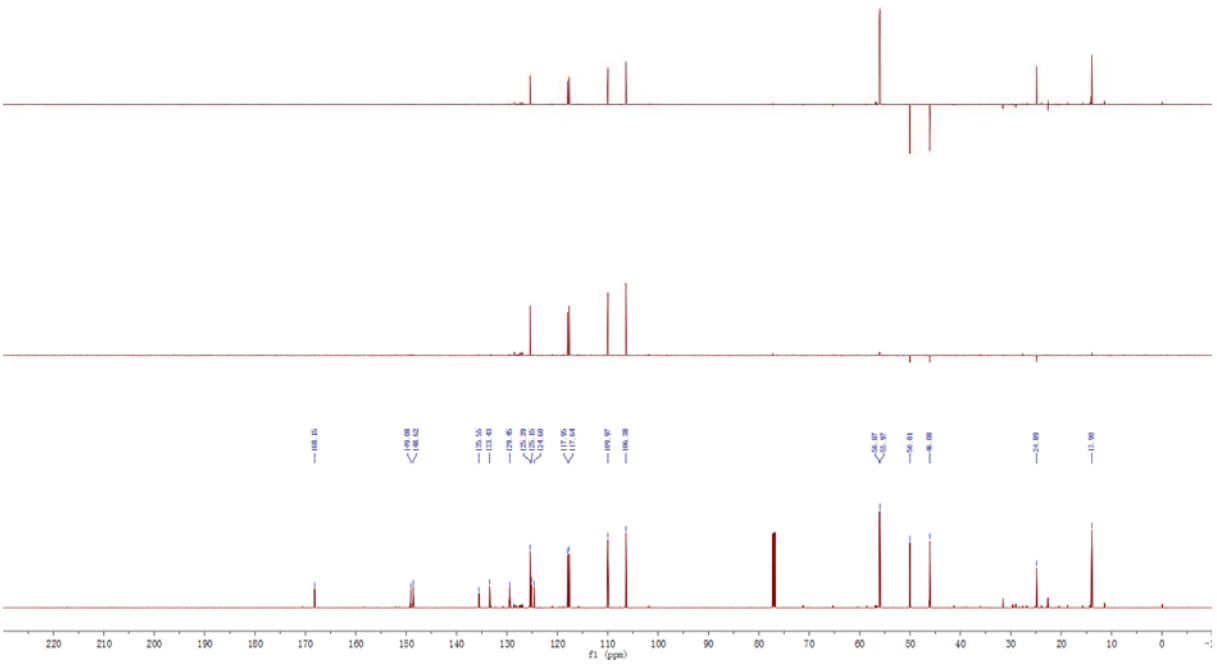
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	3.002	VB	0.1334	37.78116	3.75387	0.4785
2	3.115	BV	0.0462	35.35271	10.80508	0.4478
3	3.296	VV	0.1272	35.82769	3.62865	0.4538
4	3.424	VB	0.0922	15.83005	2.36059	0.2005
5	4.002	BV	0.1286	26.30930	2.93482	0.3332
6	6.674	VV	0.0860	49.78949	8.80485	0.6306
7	6.863	VB	0.1012	13.45195	1.88558	0.1704
8	7.273	VB	0.0902	25.09378	4.29224	0.3178

仪器 1 2021-9-18 15:04:08 D-YI 页 1/2

HPLC spectrum of compound **12**.



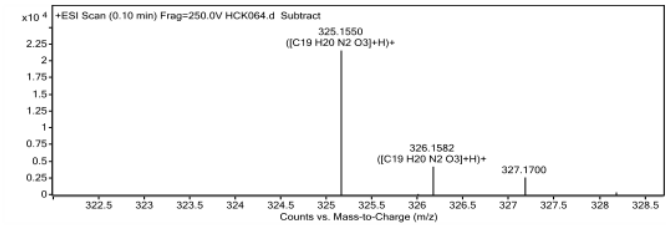
^{1}H NMR (600 MHz) spectrum of compound **13** in $CDCl_3$.



^{13}C NMR (150 MHz) spectrum of compound **13** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
250	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
137.9873	1	6913.56		
211.0865	1	6363.12		
239.0825		11894.25		
240.0949		5776.55		
254.105		11858.79		
255.1128	1	59133.37		
256.1173	1	11167.7		
279.1129	1	22177.55		
281.093	1	7425.93		
283.1445	1	11973.04		
285.1592	1	9491.42		
297.1235	1	17422.19		
325.155	1	21644.42	C19 H20 N2 O3	(M+H)+

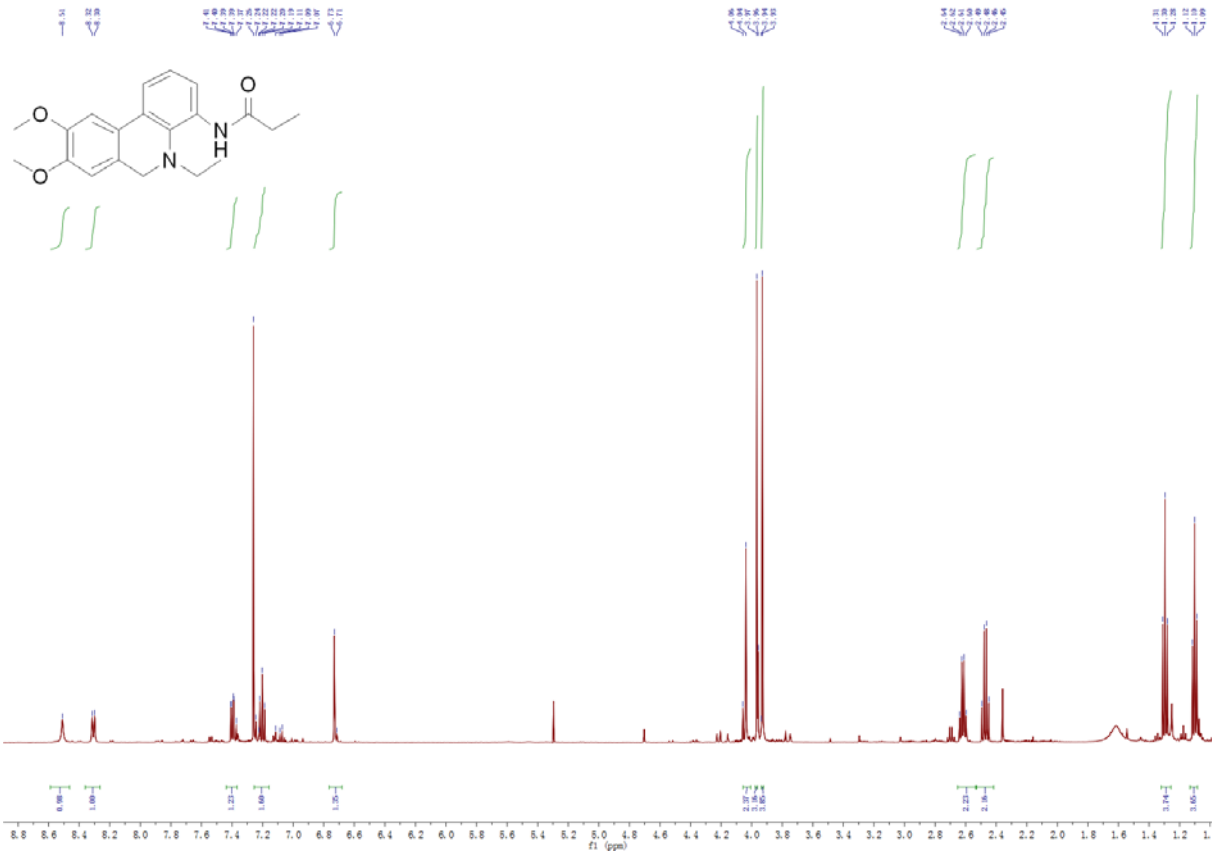
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

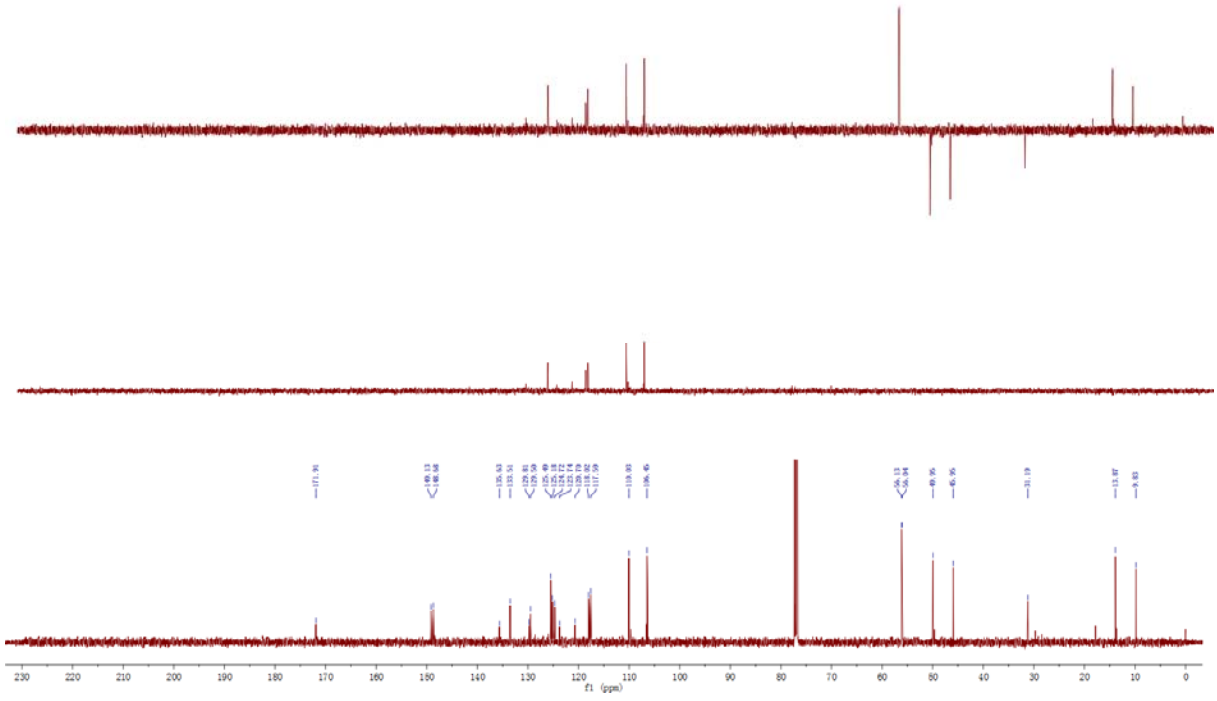
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C19 H20 N2 O3	324.1474	325.1547	325.1550	-0.30	-0.92	11.0000

HRESI (+) MS spectrum of compound **13**.



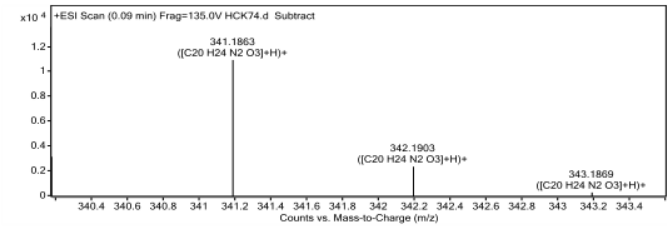
^{1}H NMR (500 MHz) spectrum of compound **14** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **14** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0216	1	83940.84		
80.0246	1	2629.93		
81.0172	1	4873.43		
100.0146		1472.98		
101.0037		2482.98		
118.5087		2800.06		
126.4943		1555.78		
137.0022		2779.41		
282.1491	1	3605.11		
339.17	1	11716.73		
340.1731	1	3229.81		
341.1863	1	10970.16	C20 H24 N2 O3	(M+H)+
342.1903	1	2408.18	C20 H24 N2 O3	(M+H)+

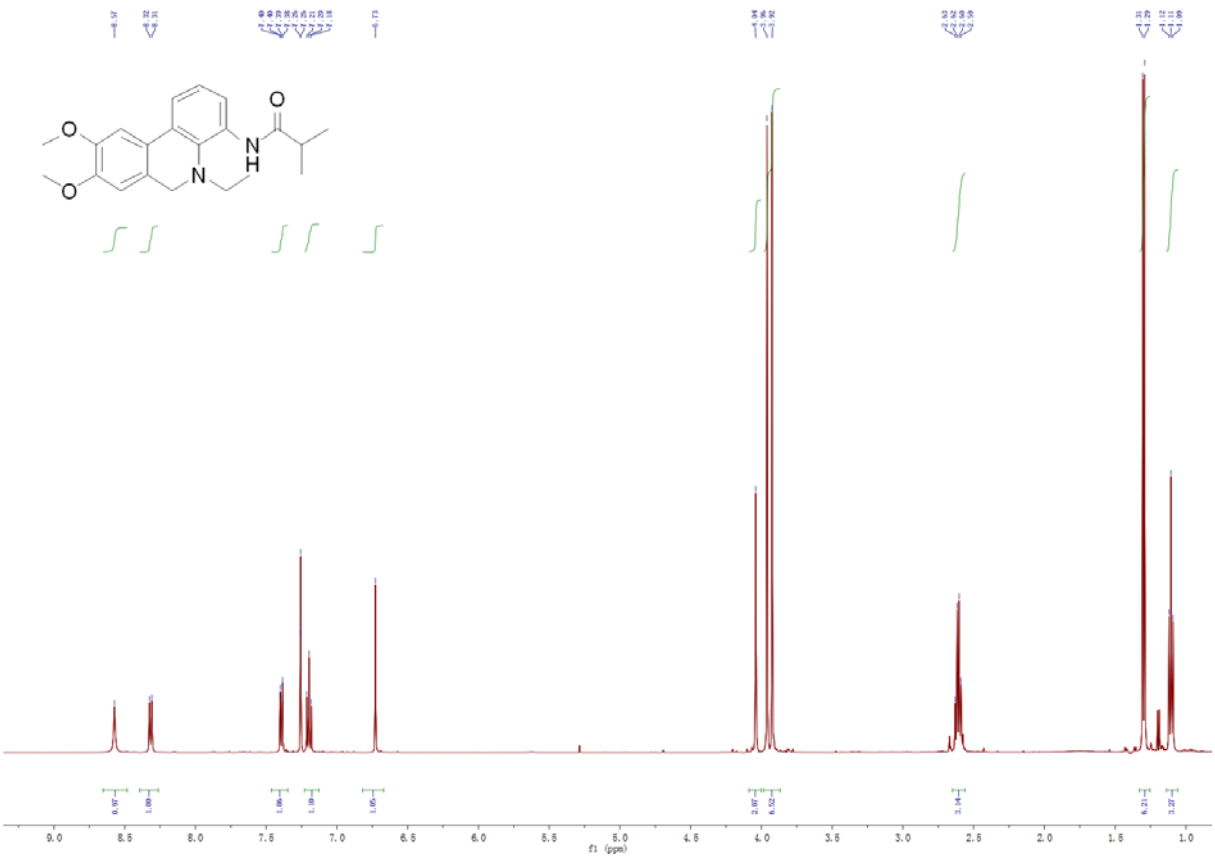
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

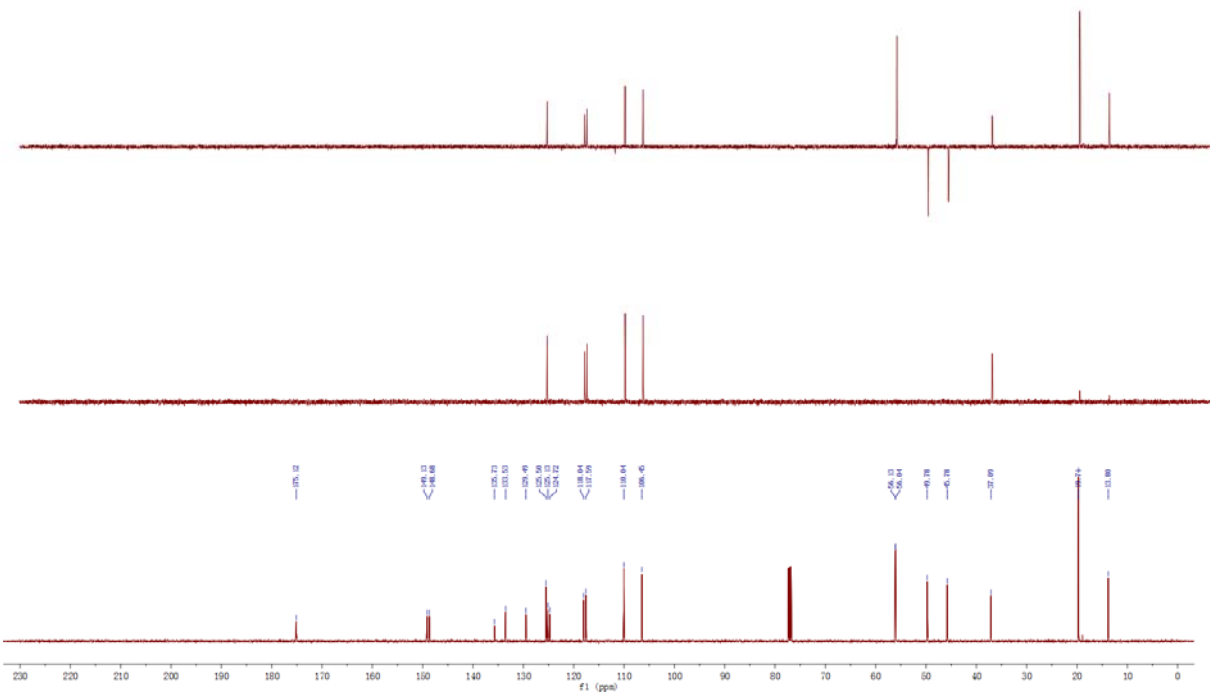
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C20 H24 N2 O3	340.1787	341.1860	341.1863	-0.30	-0.88	10.0000

HRESI (+) MS spectrum of compound **14**.



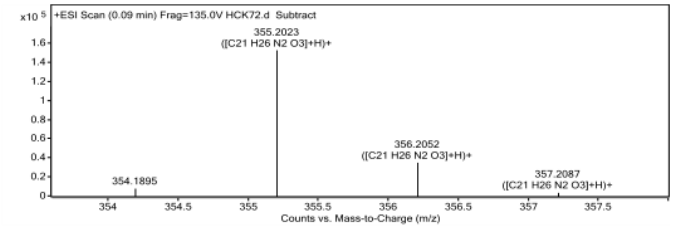
^{1}H NMR (500 MHz) spectrum of compound **15** in $CDCl_3$.



^{13}C NMR (125 MHz) spectrum of compound **15** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0217	1	117862.63		
80.0242	1	3772.56		
81.0175	1	5308.99		
100.015	2	3873.41		
118.5086	2	8151.94		
126.4948	1	2975.3		
137.0021	2	7013.4		
139.0206		3996.73		
353.1867	1	36857.39		
354.1895	1	8612.55		
355.2023	1	153102.02	C21 H26 N2 O3	(M+H)+
356.2052	1	35562.73	C21 H26 N2 O3	(M+H)+
357.2087	1	4462.73	C21 H26 N2 O3	(M+H)+

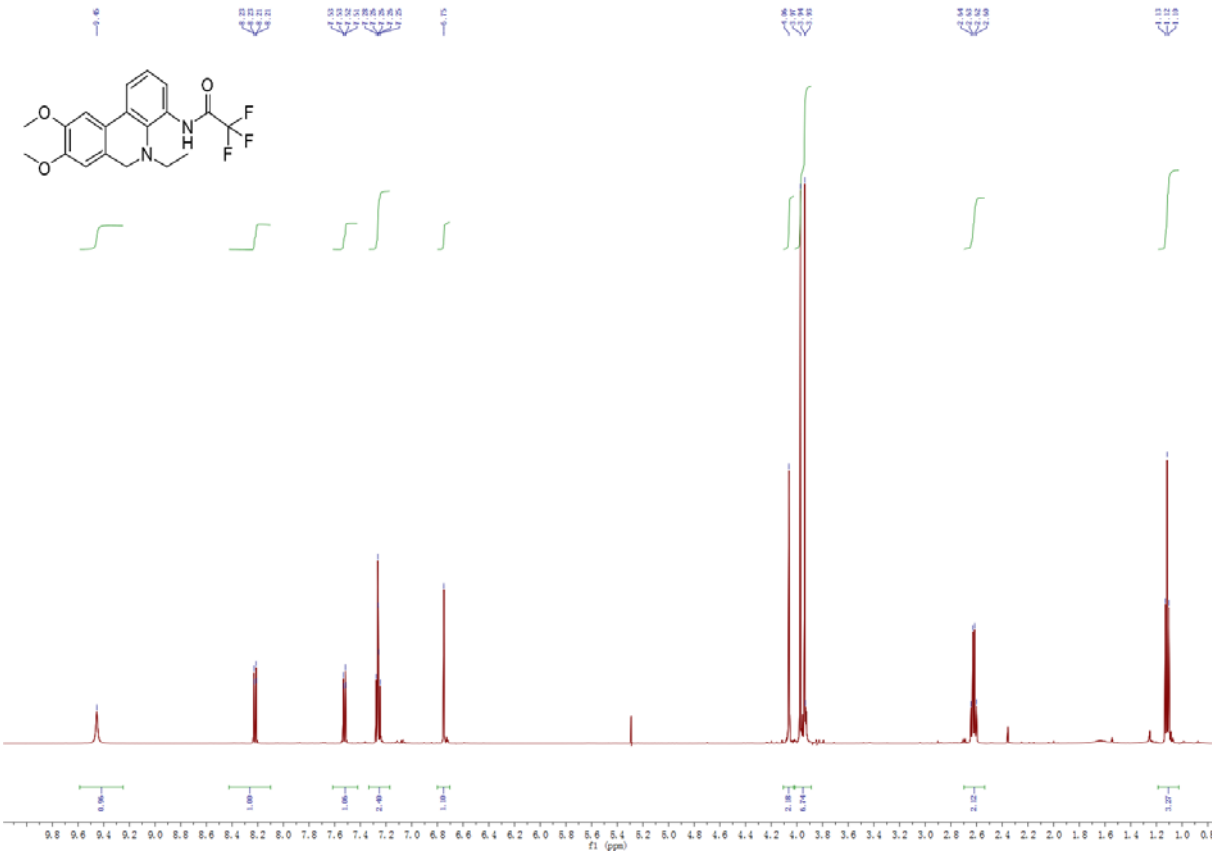
Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

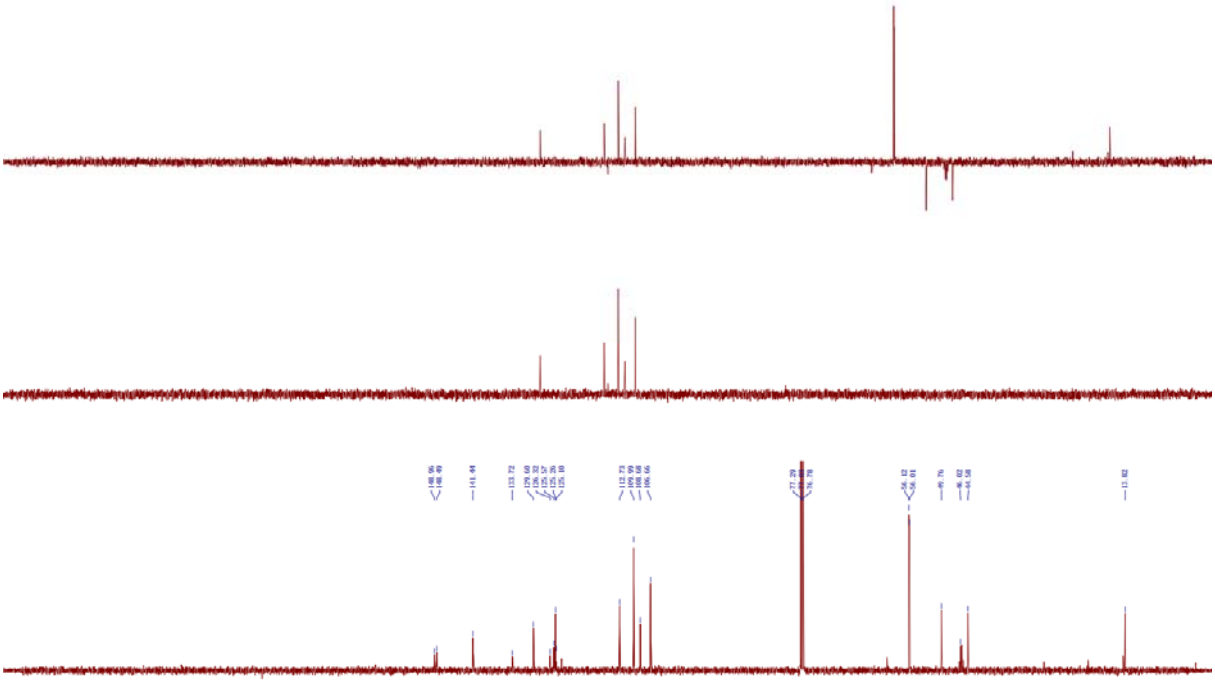
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C21 H26 N2 O3	354.1943	355.2016	355.2023	-0.70	-1.97	10.0000

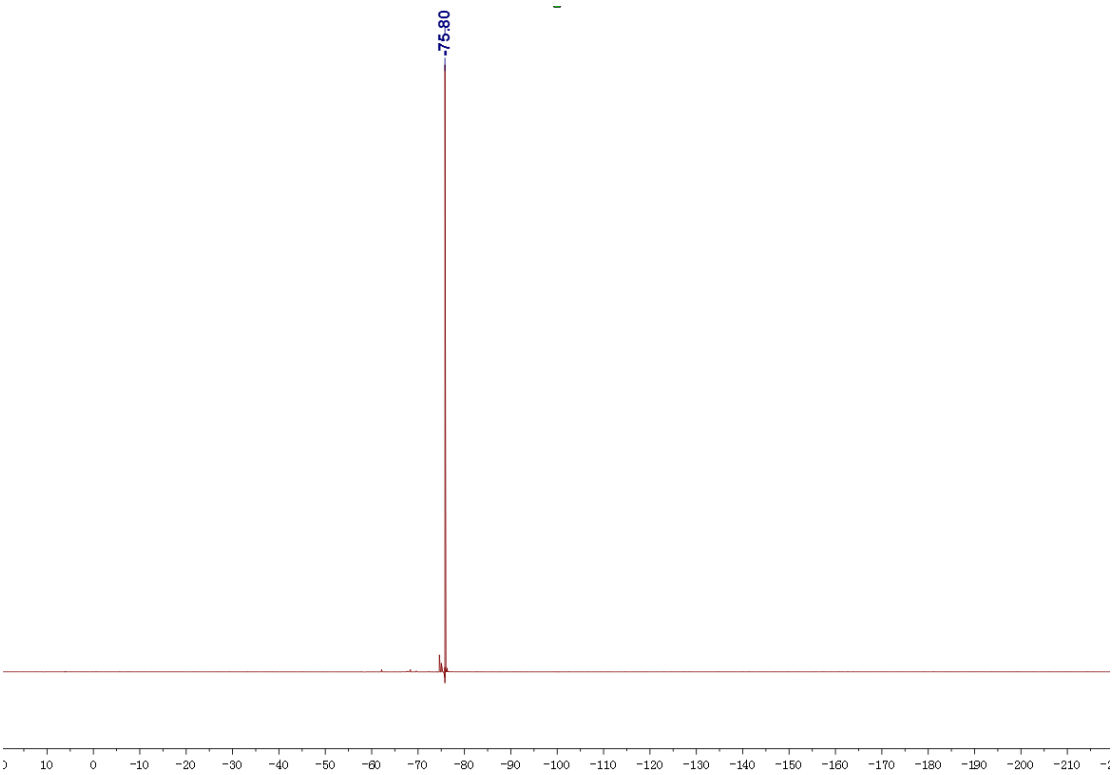
HRESI (+) MS spectrum of compound **15**.



^{1}H NMR (500 MHz) spectrum of compound **16** in $CDCl_3$.



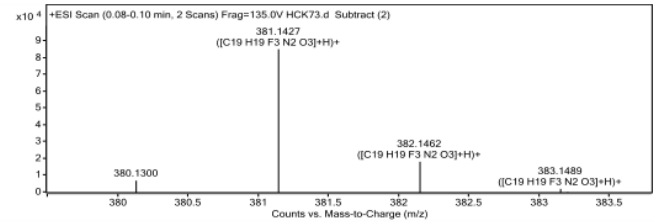
^{13}C NMR (125 MHz) spectrum of compound **16** in $CDCl_3$.



^{19}F NMR (125 MHz) spectrum of compound **16** in $CDCl_3$.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0218	1	91160.74		
80.0247	1	2724.77		
81.0175	1	4434		
118.5088	2	5275.65		
126.4947		4302.41		
137.0024	2	5592.55		
139.0211	2	2946.96		
157.5157	1	2555.25		
282.1494	1	7318.59		
379.1273	1	37916.16		
380.13	1	7319.82		
381.1427	1	85089.79	C19 H19 F3 N2 O3	(M+H)+
382.1462	1	18376.33	C19 H19 F3 N2 O3	(M+H)+

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5
F	0	5

Formula Calculator Results

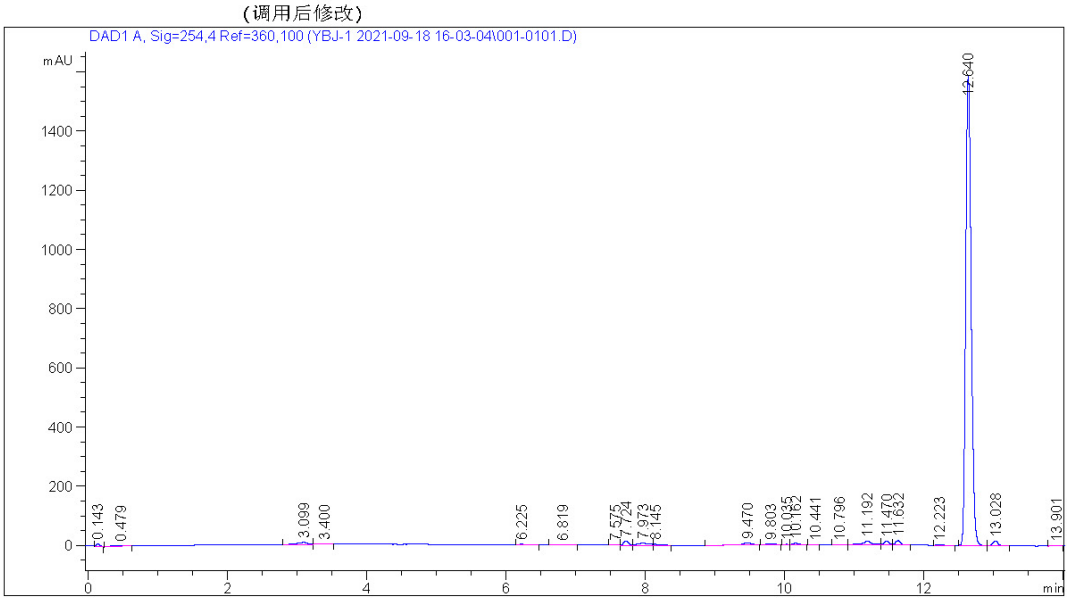
Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C19 H19 F3 N2 O3	380.1348	381.1421	381.1427	-0.60	-1.57	10.0000

HRESI (+) MS spectrum of compound **16**.

数据文件: C:\CHEM32\1\DATA\YBJ-1 2021-09-18 16-03-04\001-0101.D
样品名称: 5012

==========

操作者 : D-YI 序列行 : 1
仪器 : 仪器 1 位置 : 样品瓶 1
进样日期 : 2021-9-18 16:04:11 进样次数 : 1
进样量 : 4.0 µl
采集方法 : C:\CHEM32\1\DATA\YBJ-1 2021-09-18 16-03-04\YBJ_LC.M
最后修改 : 2021-9-18 15:42:55 : D-YI
分析方法 : C:\CHEM32\1\DATA\YBJ-1 2021-09-18 16-03-04\001-0101.D\DA.M (YBJ_LC.M, 从数据文件)
最后修改 : 2021-9-18 16:19:16 : D-YI
(调用后修改)



==========

面积百分比报告

==========

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=254,4 Ref=360,100

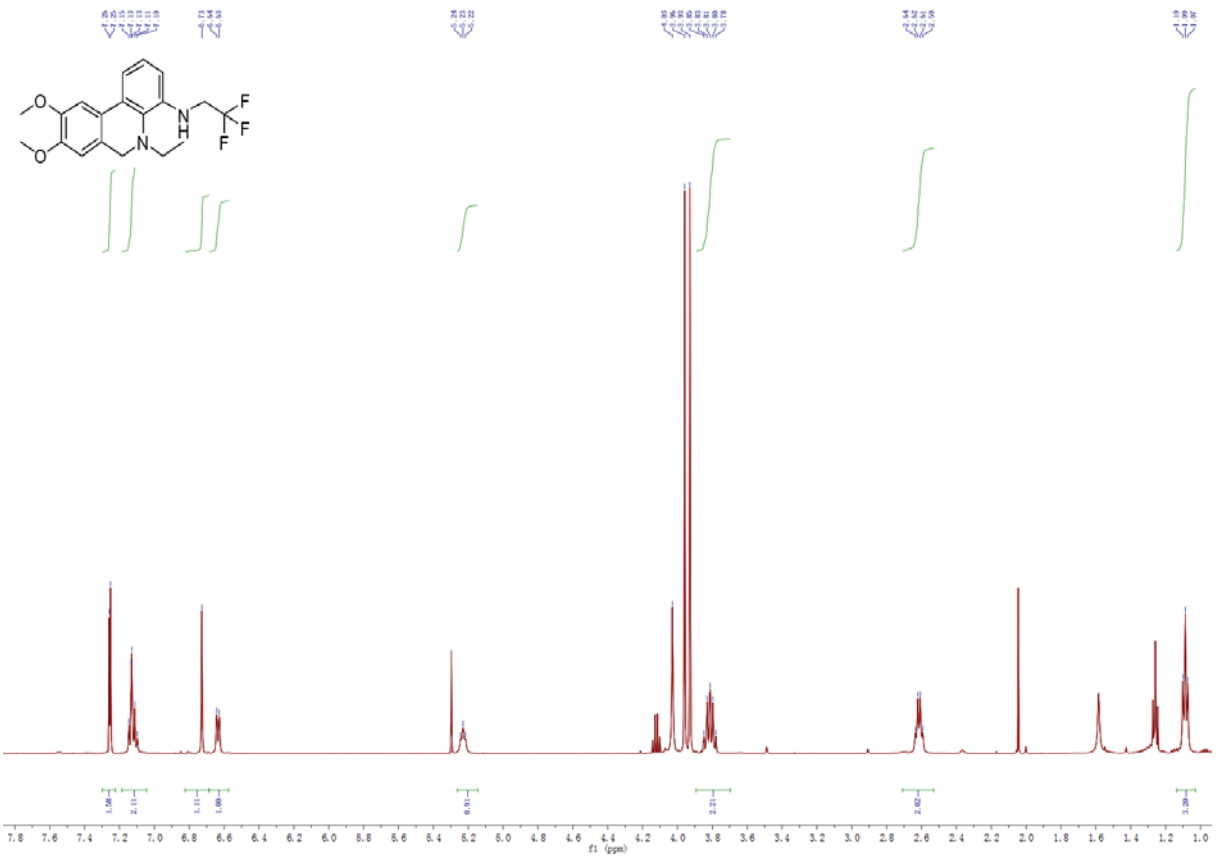
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	0.143	BB	0.0477	29.82464	9.74106	0.3091
2	0.479	BV	0.2087	56.26776	3.27111	0.5832
3	3.099	BV	0.1434	68.40977	6.57391	0.7090
4	3.400	VB	0.1376	11.51176	1.02073	0.1193
5	6.225	BB	0.1120	13.11769	1.59464	0.1360
6	6.819	VB	0.1363	15.30800	1.43634	0.1587
7	7.575	BV	0.0916	9.73285	1.63094	0.1009

数据文件: C:\CHEM32\1\DATA\YBJ-1 2021-09-18 16-03-04\001-0101.D
样品名称: 5012

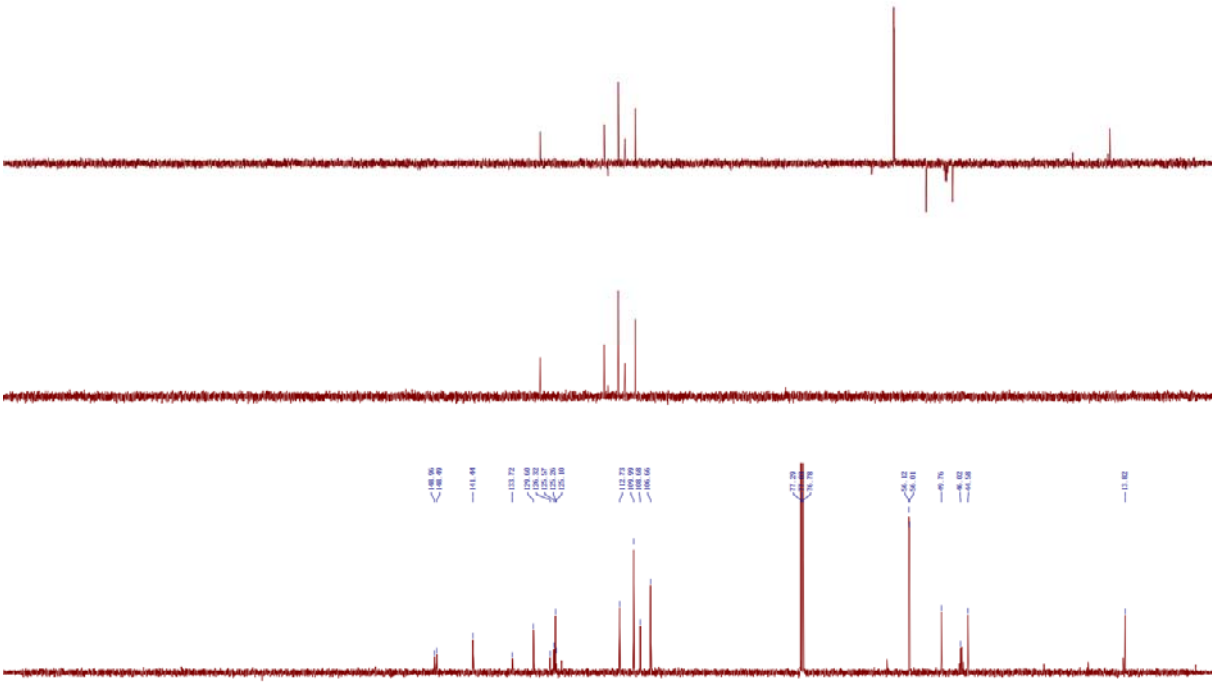
峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
8	7.724	VV	0.0703	63.62310	13.66659	0.6594
9	7.973	VV	0.1792	82.22714	6.89059	0.8522
10	8.145	VB	0.1072	26.65921	3.56869	0.2763
11	9.470	BB	0.1644	86.87325	7.43017	0.9004
12	9.803	BB	0.1213	18.40181	2.35121	0.1907
13	10.035	BV	0.0702	6.20205	1.38685	0.0643
14	10.162	VB	0.0941	31.34312	5.07455	0.3248
15	10.441	BV	0.0673	5.59819	1.27219	0.0580
16	10.796	BB	0.1074	10.04907	1.40584	0.1042
17	11.192	BV	0.1365	123.77792	12.39983	1.2829
18	11.470	VV	0.0851	66.07772	11.83873	0.6848
19	11.632	VB	0.0764	76.07918	15.20432	0.7885
20	12.223	BB	0.1036	16.41424	2.28993	0.1701
21	12.640	BV	0.0862	8734.36816	1588.40430	90.5243
22	13.028	VB	0.0783	84.52987	16.34697	0.8761
23	13.901	VBA	0.0903	12.24708	1.82472	0.1269
总量 :				9648.64359	1716.62421	

*** 报告结束 ***

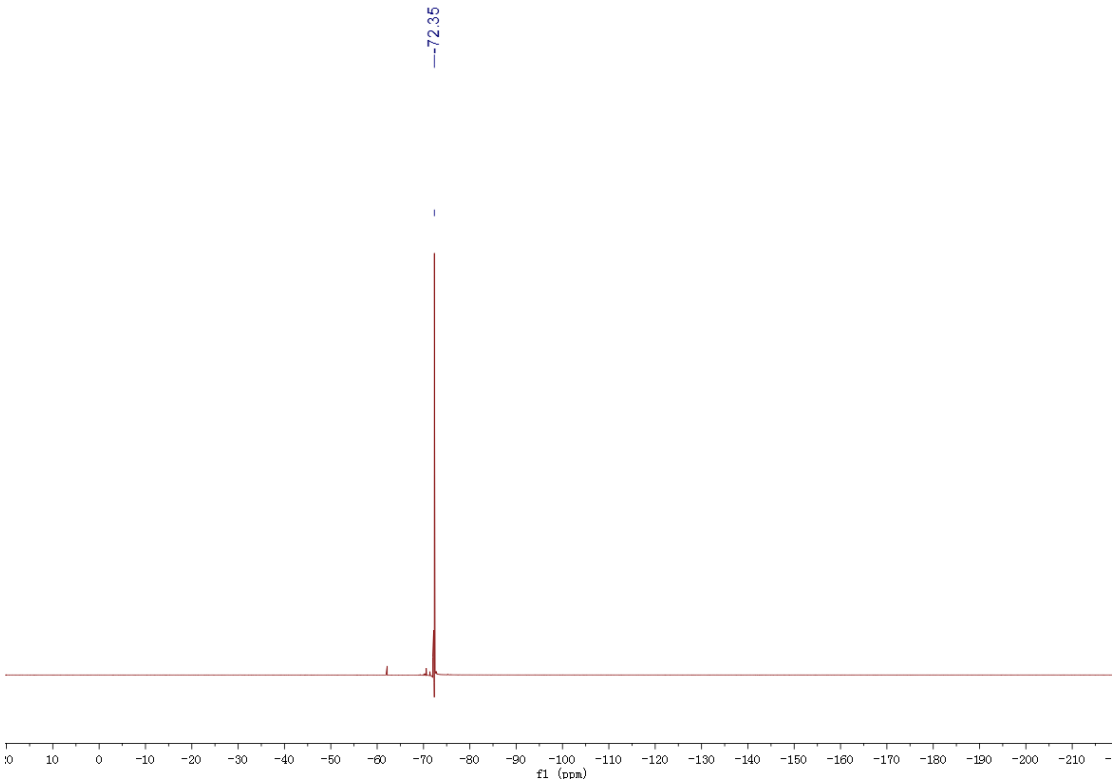
HPLC spectrum of compound **16**.



^{1}H NMR (500 MHz) spectrum of compound **17** in $CDCl_3$.



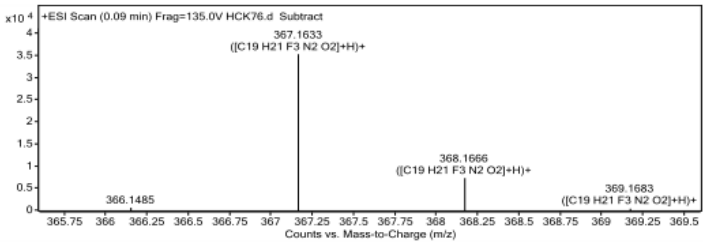
^{13}C NMR (125 MHz) spectrum of compound **17** in $CDCl_3$.



^{19}F NMR (125 MHz) spectrum of compound **17** in $CDCl_3$

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
79.0217	1	59457.6		
80.0244	1	2064.65		
118.5085	2	2079.85		
132.1021		1439.86		
137.0018	1	2398.7		
240.9873	1	1508.35		
282.1496	1	2098.28		
284.1645	1	4209.11		
365.146	1	4457.27		
367.1633	1	35396.29	C19 H21 F3 N2 O2	(M+H)+
368.1666	1	7429.36	C19 H21 F3 N2 O2	(M+H)+
399.1521		2188.59		
409.1738	1	2237.31		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5
F	0	5

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C19 H21 F3 N2 O2	366.1555	367.1628	367.1633	-0.50	-1.36	9.0000

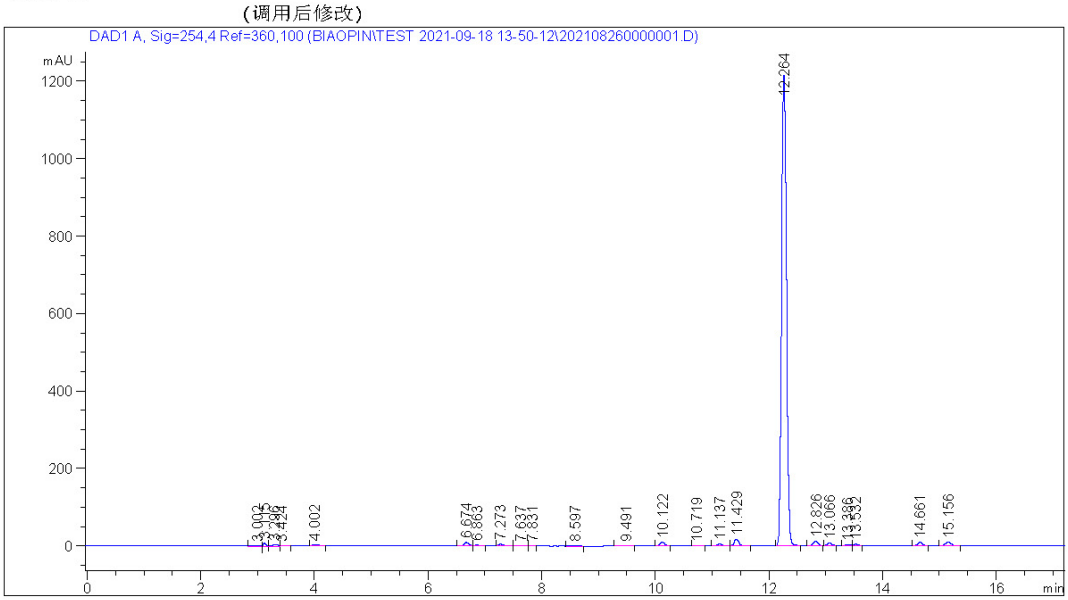
HRESI (+) MS spectrum of compound **17**.

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 13-50-12\202108260000001.D
样品名称: 5005

==========

操作者	: D-YI	序列行 :	1
仪器	: 仪器 1	位置 :	样品瓶 1
进样日期	: 2021-9-18 13:51:18	进样次数 :	1
		进样量 :	2.0 µl
采集方法	: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 13-50-12\YBJ_LC.M		
最后修改	: 2021-9-18 13:24:58 : D-YI		
分析方法	: C:\CHEM32\1\DATA\TEST.M		
最后修改	: 2021-9-18 15:02:17 : D-YI		

(调用后修改)



==========

面积百分比报告

==========

排序 : 信号
乘积因子: : 1.0000
稀释因子: : 1.0000
内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=254,4 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	3.002	VB	0.1334	37.78116	3.75387	0.4785
2	3.115	BV	0.0462	35.35271	10.80508	0.4478
3	3.296	VV	0.1272	35.82769	3.62865	0.4538
4	3.424	VB	0.0922	15.83005	2.36059	0.2005
5	4.002	BV	0.1286	26.30930	2.93482	0.3332
6	6.674	VV	0.0860	49.78949	8.80485	0.6306
7	6.863	VB	0.1012	13.45195	1.88558	0.1704
8	7.273	VB	0.0902	25.09378	4.29224	0.3178

数据文件: C:\CHEM32\1\DATA\BIAOPIN\TEST 2021-09-18 13-50-12\202108260000001.D
样品名称: 5005

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
9	7.637	BV	0.1186	9.56527	1.13223	0.1212
10	7.831	VB	0.0715	7.11381	1.44280	0.0901
11	8.597	BB	0.1090	11.34892	1.48797	0.1437
12	9.491	VB	0.1584	12.91430	1.10434	0.1636
13	10.122	BV	0.0839	52.46339	9.89437	0.6645
14	10.719	VB	0.1036	8.99609	1.09836	0.1139
15	11.137	BV	0.0995	33.73194	4.94880	0.4273
16	11.429	VB	0.0857	97.32494	17.81621	1.2327
17	12.264	BV	0.0951	7192.69775	1214.54956	91.1041
18	12.826	BB	0.0823	56.06670	10.49434	0.7102
19	13.066	BB	0.0852	37.60786	6.94115	0.4763
20	13.386	BV	0.0740	9.35492	1.81879	0.1185
21	13.532	VB	0.0624	15.65128	3.76991	0.1982
22	14.661	VB	0.0861	46.62008	8.48431	0.5905
23	15.156	BV	0.0962	64.13522	10.08231	0.8123
总量 :				7895.02861	1333.53112	

==========

峰加和报告

==========

信号 1: DAD1 A, Sig=254,4 Ref=360,100

==========

最终峰加和报告

==========

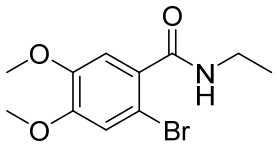
信号 1: DAD1 A, Sig=254,4 Ref=360,100

*** 报告结束 ***

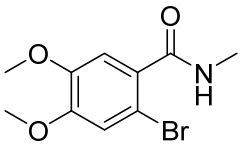
HPLC spectrum of compound **17**.

Preparation of intermediates

Synthesis of amide substrates

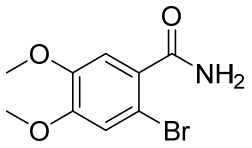


Amide 1

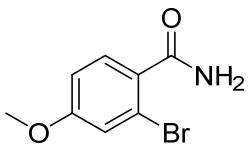


Amide 2

Amide 3



Amide 4



Amide 5

Synthetic procedures for these amides were already reported in the previous reports[1]. 2-bromo-4,5-dimethoxybenzoic acid, 2-bromo-4,5-dimethoxybenzoic acid, 2-bromo-5-methoxybenzoic acid, 2-bromo-4,5-dimethoxybenzoic acid or 2-bromo-4-methoxybenzoic acid (10 mmol) was dissolved in DCM (20 mL) respectively, to which $SOCl_2$ (10 mL) was added. The reaction solution was stirred for 6 h at 50°C, and then concentrated to remove DCM. The residue was then added to a solution of methylamine or ethylamine in water at 0°C and filtered. The cake was purified by column chromatography to give Amide 1-5 as a pale yellow solid (yield 80-90%).

Synthesis of intermediates 1a-1e

By referencing the synthesis method of 6-Phenanthridinones[2], amide substrates were coupled to 1-iodo-2-ethylbenzene or 1-iodo-2-methylbenzene to afford compound **1a-1e**. A flask was charged under nitrogen with $Pd(OAc)_2$ (0.5 mmol), tri(2-furyl) phosphine (1.1 mmol), K_2CO_3 (20 mmol), the amides 1-5 (10 mmol), a solution of norbornene (12 mmol) in anhydrous DMF (20 mL), and 1-iodo-2-methylbenzene or 1-iodo-2-ethylbenzene(11 mmol). The reaction mixture was heated with stirring at 105 °C for 8 h and then cooled to r.t. After the addition of saturated NH_4Cl (50 mL) and extraction with EtOAc (3×50 mL), the combined organic extracts were washed

with brine (30 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave the crude product, which was purified by flash chromatography on silica gel to furnish **1a-1e** as a colorless solid. (yield 75-85%).

Synthesis of intermediates 3a-3c

By referencing the synthesis method of dihydrophenanthridines[3], compounds **3a-3c** were synthesized through the reduction of compounds **1a-1c** in the presence of BH_3-THF. To a stirred solution of **1a-1c** (1 mmol) in THF (2 ml) was added 1M BH_3-THF (2 mL, 2 mmol) dropwise. After an 6 h stirring in an 60 ℃ oil bath and then quenched using H_2O (5 mL), phases were separated and aqueous phase was extracted with EtOAc (2×20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuum. Crude product was purified by flash chromatography on silica gel to give **3a-3c** as colorless oil.(yield 10-80%).

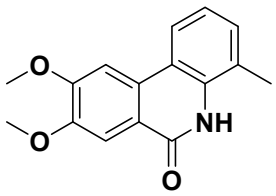
Compounds **3b** and **3c** could also be prepared through the reduction of compounds **1** and **2**. To a stirred solution of **1** or **2** (1 mmol) in MeOH (2 ml) was added $NaBH_4$ (5 mmol). After an 2 h stirring at r.t. and then quenched using H_2O (5 mL), the solvent was removed by evaporation. The residue was added H_2O and extracted with (2×20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuum. Crude product was purified by flash chromatography on silica gel to give **3b** or **3c** as colorless oil. (yield 55-60%).

Synthesis of intermediates 5a

Compound **3a** (1 mmol) was dissolved in CH_2Cl_2 (5 ml). The reaction solution was then cooled to -78 ℃ and BBr_3 (0.4 mL, 4 mmol) was added dropwise. After an 6 h stirring at room temperature and then quenched using saturated aqueous $NaHCO_3$ (10 mL), phases were separated and aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuum. Crude product was purified by flash chromatography on silica gel to give **5a** as a a yellow solid.(yield 65%).

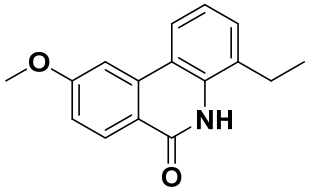
Characterization data of intermediates

8,9-dimethoxy-4-methylphenanthridin-6(5H)-one (1a)



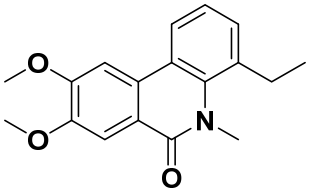
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.69 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.89 (s, 1H), 7.62 (s, 1H), 7.29 (dd, J = 10.0, 4.6 Hz, 1H), 7.19 – 7.12 (m, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 161.4 (C), 153.7 (C), 149.8 (C), 133.7 (C), 130.0 (CH), 129.9 (C), 123.0 (C), 122.3 (CH), 120.6 (CH), 119.3 (C), 118.3 (C), 108.4 (CH), 103.2 (CH), 56.3 (CH_3), 56.2 (CH_3), 17.0 (CH_3). ESI$^+$ *m/z*: 270 [*M*+H]$^+$.

4-ethyl-9-methoxyphenanthridin-6(5H)-one (1b)



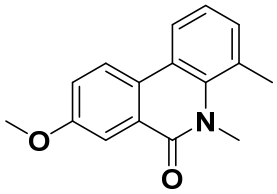
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.59 (s, 1H), 8.44 (d, J = 8.8 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.36 (dd, *J* = 9.5, 4.3 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.16 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.00 (s, 3H), 2.89 – 2.76 (m, 2H), 1.35 (t, 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 163.4 (C)), 162.0 (C), 137.2 (C), 134.0 (C), 130.5 (CH), 129.0 (CH), 128.8 (C), 122.4 (CH), 121.1 (CH), 119.1 (C), 118.4 (C), 115.7 (CH), 105.3 (CH), 55.6 (CH_3), 23.6 (CH_2), 13.6 (CH_3). ESI$^+$ *m/z*: 254 [*M*+H]$^+$.

4-ethyl-8,9-dimethoxy-5-methylphenanthridin-6(5H)-one (1c)



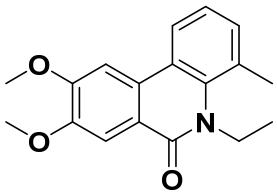
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.98 (d, *J* = 7.1 Hz, 1H), 7.89 (s, 1H), 7.56 (s, 1H), 7.35 (d, *J* = 6.8 Hz, 1H), 7.31 – 6.93 (m, 2H), 4.07 (s, 3H), 4.04 (s, 3H), 3.79 (s, 3H), 3.02 (q, *J* = 7.5 Hz, 2H), 1.50 – 1.06 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 163.9 (C), 153.3 (C), 149.7 (C), 138.7 (C), 132.8 (C), 131.1 (CH), 128.9 (C), 122.9 (CH), 121.3 (C), 120.3 (CH), 119.4 (C), 108.7 (CH), 102.9 (CH), 56.3 (CH_3), 56.1 (CH_3), 38.6 (CH_3), 28.3 (CH_2), 15.6 (CH_3). ESI$^+$ *m/z*: 298 [*M*+H]$^+$.

8-methoxy-4,5-dimethylphenanthridin-6(5H)-one (1d)



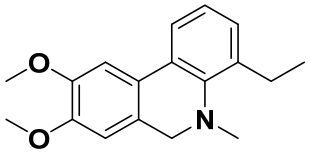
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.07 – 8.04 (m, 1H), 7.96 – 7.93 (m, 1H), 7.87 (t, J = 2.7 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.21 (dd, J = 7.4, 0.7 Hz, 1H), 7.14 (dd, J = 9.7, 5.6 Hz, 1H), 3.92 (s, 3H), 3.78 (s, 3H). 2.62 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 163.8 (C), 159.2 (C), 138.3 (C), 132.6 (CH), 127.4 (C), 126.5 (C), 125.9 (C), 123.6 (CH), 122.7 (CH), 122.1 (CH), 121.2 (C), 120.3 (CH), 108.7 (CH), 55.5 (CH_3), 38.3 (CH_3), 23.5 (CH_3). ESI$^+$ *m/z*: 254 [*M*+H]$^+$.

5-ethyl-8,9-dimethoxy-4-methylphenanthridin-6(5H)-one (1e)



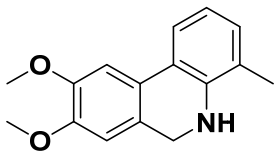
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 8.04 (t, J = 7.5 Hz, 1H), 7.89 (s, 1H), 7.56 (s, 1H), 7.28 (dt, J = 8.8, 4.4 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 4.50 (q, J = 7.0 Hz, 2H), 4.07 (s, 3H), 4.03 (s, 3H), 2.70 (s, 3H), 1.36 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 163.7 (C), 153.3 (C), 149.7 (C), 137.9 (C), 133.4 (CH), 128.8 (C), 126.0 (C), 122.5 (CH), 121.6 (C), 120.9 (CH), 119.7 (C), 108.8 (CH), 102.9 (CH), 56.2 (CH_3), 56.1 (CH_3), 42.5 (CH_2), 24.0 (CH_3), 15.0 (CH_3). ESI$^+$ *m/z*: 298 [*M*+H]$^+$.

4-ethyl-8,9-dimethoxy-5-methyl-5,6-dihydrophenanthridine (3a)



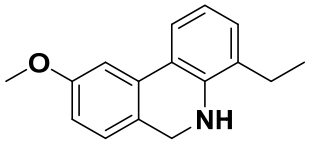
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.56 (dt, J = 8.7, 4.4 Hz, 1H), 7.26 (d, J = 5.4 Hz, 1H), 7.22 – 7.07 (m, 2H), 6.75 (s, 1H), 4.02(s,2H), 3.97 (s, 3H), 3.93 (s, 3H), 2.81 (q, J = 7.5 Hz, 2H), 2.48 (s, 3H), 1.43 – 1.16 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 148.9 (C), 148.5 (C), 145.6 (C), 139.6 (C), 129.3 (C), 127.7 (CH), 125.4 (C), 125.0 (C), 124.6 (CH), 120.9 (CH), 109.9 (CH), 106.6 (CH), 56.1 (CH_3), 56.0 (CH_3), 55.0 (CH_2), 41.3 (CH_3), 23.2 (CH_2), 14.9 (CH_3). ESI$^+$ *m/z*: 284 [*M*+H]$^+$.

8,9-dimethoxy-4-methyl-5,6-dihydrophenanthridine (3b)



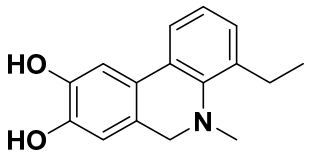
^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.47 (d, J = 7.9 Hz, 1H), 7.19 (s, 1H), 6.97 (d, J = 7.4 Hz, 1H), 6.76 (t, J = 7.6 Hz, 1H), 6.64 (s, 1H), 4.38 (s, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 148.6 (C), 148.4 (C), 143.0 (C), 129.4 (CH), 125.1 (C), 125.1 (C), 121.9 (C), 121.5 (C), 120.8 (CH), 118.3 (CH), 109.1 (CH), 106.3 (CH), 56.1 (CH_3), 56.0 (CH_3), 46.0 (CH_2), 17.1 (CH_3). ESI$^+$ *m/z*: 256 [*M*+H]$^+$.

4-ethyl-9-methoxy-5,6-dihydrophenanthridine (3c)



^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.56 (dd, J = 7.8, 1.1 Hz, 1H), 7.23 (d, J = 2.5 Hz, 1H), 7.06 (s, 1H), 7.04 (s, 1H), 6.86 – 6.80 (m, 1H), 6.80 – 6.73 (m, 1H), 4.34 (s, 2H), 3.85 (s, 3H), 2.54 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 159.3 (C), 143.5 (C), 143.3 (C), 133.7 (C), 128.2 (CH), 126.7 (CH), 125.3 (C), 121.7 (C), 121.7 (CH), 118.6 (CH), 112.5 (CH), 108.3 (CH), 55.4 (CH_3), 45.8 (CH_2), 23.9 (CH_2), 13.2 (CH_3). ESI$^+$ *m/z*: 240 [*M*+H]$^+$.

4-ethyl-5-methyl-5,6-dihydrophenanthridine-8,9-diol (5a)



^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.46 (d, J = 7.1 Hz, 1H), 7.27 (d, J = 2.7 Hz, 1H), 7.17 (dt, J = 15.0, 7.5 Hz, 1H), 7.00 (s, 1H), 6.75 (s, 1H), 3.96 (s, 2H), 2.82-2.76 (m, 2H), 2.31 (s, 3H), 1.28 (dd, J = 14.7, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 143.8 (C), 143.0 (C), 141.2(C), 139.4 (C), 128.8 (C), 127.6 (CH), 126.3(C), 125.1 (C), 124.6 (CH), 120.7 (CH), 113.8 (CH), 110.4 (CH), 53.6 (CH_2), 40.2 (CH_3), 23.3 (CH_2), 14.9 (CH_3).

Amino acid and nucleotide sequences in this study

>Amino acid_His$_6$-Wild type

MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQRRPQGLPNNTASW
FTALTQHGKEDLKFPRGQGVPINTNSSPDDQIGYYRRATRRIRGGDGKMKDLS
PRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTRNPANNAAI
VLQLPQGTTLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMA
GNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQK
RTATKAYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASA
FFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPT
EPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADST
QAHHHHHH

> Amino acid_ His_6-Mutant A

MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQRRPQGLPNNTASW
FTALTQHGKEDLKFPRGQGVPINTNSSPDDQIGYYRRATRRIRGGDGKMKDLS
PRWAFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTANPANNAAIV
LQLPQGTTLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMAG
NGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRT
ATKAYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFF
GMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEP
KKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA
HHHHHH

> Amino acid_ His_6-Mutant B

MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQRRPQGLPNNTASW
FTALTQHGKEDLKFPRGQGVPINTNSSPDDQIGYYRRATRRIRGGDGKMKDLS
PRWAFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIGTRNPANAAAIV
LQLPQGTTLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMAG
NGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQKRT
ATKAYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFF
GMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEP
KKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA
HHHHHH

> Amino acid_ His_6-Mutant C

MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQRRPQGLPNNTASW
FTALTQHGKEDLKFPRGQGVPINTNSSPDDQIGYYRRATRRIRGGDGKMKDLS
PRWYFYYLGTGPEAGLPYGAAADGIAWVATEGALNTPKDHIGTRNPANNAAI
VLQLPQGTTLPKGFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSRGTSPARMA
GNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAAEASKKPRQK
RTATKAYNVTQAFGRRGPEQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASA
FFGMSRIGMEVTPSGTWLTYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPT
EPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADST
QAHHHHHH

>Nucleotide_ His_6-Mutant A

ATGTCAGATAATGGACCCCAAAACCAGAGGAACGCACCGCGTATCACCTT
CGGCGGCCCGTCCGATTCTACGGGTTCCAACCAGAATGGTGAACGTTCCG
GTGCGCGTTCCAAGCAGAGACGTCCGCAGGGCCTGCCAAATAACACCGCA
AGCTGGTTTACCGCGTTAACCCAGCATGGTAAAGAAGATTTAAAATTCCC
GCGTGGTCAAGGTGTGCCGATTAACACCAATTCCTCGCCAGATGATCAGA
TCGGGTATTACCGCCGCGCAACCCGTCGTATCCGTGGCGGTGACGGCAAG
ATGAAAGACCTGAGCCCGCGTTGGGCTTTCTACTACCTGGGTACTGGTCC
GGAGGCCGGCCTGCCTTATGGTGCGAATAAGGACGGTATTATCTGGGTTG
CAACGGAAGGTGCTTTGAACACCCCGAAAGACCACATTGGTACTGCCAAC
CCGGCGAACAACGCCGCCATCGTGCTGCAGCTCCCGCAAGGCACGACCTT
GCCGAAGGGCTTTTATGCAGAGGGCAGCCGCGGTGGTTCTCAGGCGTCTT
CTCGCTCTAGCAGCAGATCACGCAACAGCTCTCGCAACAGCACCCCGGGT
AGCAGCCGTGGTACGAGCCCGGCGCGTATGGCTGGTAACGGTGGCGACGC
CGCTCTGGCTTTGTTGCTGCTGGATCGTCTGAATCAGCTGGAAAGCAAGAT
GTCCGGTAAAGGCCAACAACAACAGGGACAGACCGTCACCAAGAAAAGC
GCGGCGGAGGCGAGCAAGAAGCCGCGTCAAAAGCGCACCGCGACCAAAG
CGTACAATGTTACCCAAGCGTTTGGCCGTCGTGGCCCGGAGCAGACCCAG
GGCAACTTCGGCGATCAAGAACTGATTCGTCAGGGCACGGACTACAAACA
TTGGCCGCAGATTGCACAGTTTGCTCCGTCGGCGAGCGCGTTTTTCGGTAT
GTCCCGCATCGGCATGGAAGTTACCCCAAGTGGCACCTGGCTGACTTATA
CCGGAGCTATCAAACTGGACGATAAAGACCCGAATTTTAAGGACCAAGTT
ATTCTGCTGAACAAACACATCGATGCTTACAAAACCTTCCCTCCGACCGA
GCCGAAAAAGGACAAAAAGAAAAAGGCGGACGAGACGCAAGCCTTGCCC

CAACGTCAGAAAAAGCAACAGACGGTGACGCTGTTGCCGGCGGCCGATCT
CGACGACTTCAGCAAGCAGCTTCAGCAAAGCATGAGCAGCGCGGATAGC
ACCCAAGCTCATCATCATCATCATCATTAA

>Nucleotide_ His_6-Mutant B

ATGTCAGATAATGGACCCCAAAACCAGAGGAACGCACCGCGTATCACCTT
CGGCGGCCCGTCCGATTCTACGGGTTCCAACCAGAATGGTGAACGTTCCG
GTGCGCGTTCCAAGCAGAGACGTCCGCAGGGCCTGCCAAATAACACCGCA
AGCTGGTTTACCGCGTTAACCCAGCATGGTAAAGAAGATTTAAAATTCCC
GCGTGGTCAAGGTGTGCCGATTAACACCAATTCCTCGCCAGATGATCAGA
TCGGGTATTACCGCCGCGCAACCCGTCGTATCCGTGGCGGTGACGGCAAG
ATGAAAGACCTGAGCCCGCGTTGGGCTTTCTACTACCTGGGTACTGGTCC
GGAGGCCGGCCTGCCTTATGGTGCGAATAAGGACGGTATTATCTGGGTTG
CAACGGAAGGTGCTTTGAACACCCCGAAAGACCACATTGGTACTCGCAAC
CCGGCGAACGCTGCCGCCATCGTGCTGCAGCTCCCGCAAGGCACGACCTT
GCCGAAGGGCTTTTATGCAGAGGGCAGCCGCGGTGGTTCTCAGGCGTCTT
CTCGCTCTAGCAGCAGATCACGCAACAGCTCTCGCAACAGCACCCCGGGT
AGCAGCCGTGGTACGAGCCCGGCGCGTATGGCTGGTAACGGTGGCGACGC
CGCTCTGGCTTTGTTGCTGCTGGATCGTCTGAATCAGCTGGAAAGCAAGAT
GTCCGGTAAAGGCCAACAACAACAGGGACAGACCGTCACCAAGAAAAGC
GCGGCGGAGGCGAGCAAGAAGCCGCGTCAAAAGCGCACCGCGACCAAAG
CGTACAATGTTACCCAAGCGTTTGGCCGTCGTGGCCCGGAGCAGACCCAG
GGCAACTTCGGCGATCAAGAACTGATTCGTCAGGGCACGGACTACAAACA
TTGGCCGCAGATTGCACAGTTTGCTCCGTCGGCGAGCGCGTTTTTCGGTAT
GTCCCGCATCGGCATGGAAGTTACCCCAAGTGGCACCTGGCTGACTTATA
CCGGAGCTATCAAACTGGACGATAAAGACCCGAATTTTAAGGACCAAGTT
ATTCTGCTGAACAAACACATCGATGCTTACAAAACCTTCCCTCCGACCGA
GCCGAAAAAGGACAAAAAGAAAAAGGCGGACGAGACGCAAGCCTTGCCC
CAACGTCAGAAAAAGCAACAGACGGTGACGCTGTTGCCGGCGGCCGATCT
CGACGACTTCAGCAAGCAGCTTCAGCAAAGCATGAGCAGCGCGGATAGC
ACCCAAGCTCATCATCATCATCATCATTAA

>Nucleotide_ His_6-Mutant C

ATGTCAGATAATGGACCCCAAAACCAGAGGAACGCACCGCGTATCACCTT
CGGCGGCCCGTCCGATTCTACGGGTTCCAACCAGAATGGTGAACGTTCCG
GTGCGCGTTCCAAGCAGAGACGTCCGCAGGGCCTGCCAAATAACACCGCA
AGCTGGTTTACCGCGTTAACCCAGCATGGTAAAGAAGATTTAAAATTCCC
GCGTGGTCAAGGTGTGCCGATTAACACCAATTCCTCGCCAGATGATCAGA
TCGGGTATTACCGCCGCGCAACCCGTCGTATCCGTGGCGGTGACGGCAAG
ATGAAAGACCTGAGCCCGCGTTGGTATTTCTACTACCTGGGTACTGGTCCG
GAGGCCGGCCTGCCTTATGGTGCGGCCGCAGACGGTATTGCATGGGTTGC
AACGGAAGGTGCTTTGAACACCCCGAAAGACCACATTGGTACTCGCAACC
CGGCGAACAACGCCGCCATCGTGCTGCAGCTCCCGCAAGGCACGACCTTG
CCGAAGGGCTTTTATGCAGAGGGCAGCCGCGGTGGTTCTCAGGCGTCTTC
TCGCTCTAGCAGCAGATCACGCAACAGCTCTCGCAACAGCACCCCGGGTA
GCAGCCGTGGTACGAGCCCGGCGCGTATGGCTGGTAACGGTGGCGACGCC
GCTCTGGCTTTGTTGCTGCTGGATCGTCTGAATCAGCTGGAAAGCAAGAT
GTCCGGTAAAGGCCAACAACAACAGGGACAGACCGTCACCAAGAAAAGC
GCGGCGGAGGCGAGCAAGAAGCCGCGTCAAAAGCGCACCGCGACCAAAG
CGTACAATGTTACCCAAGCGTTTGGCCGTCGTGGCCCGGAGCAGACCCAG
GGCAACTTCGGCGATCAAGAACTGATTCGTCAGGGCACGGACTACAAACA
TTGGCCGCAGATTGCACAGTTTGCTCCGTCGGCGAGCGCGTTTTTCGGTAT
GTCCCGCATCGGCATGGAAGTTACCCCAAGTGGCACCTGGCTGACTTATA
CCGGAGCTATCAAACTGGACGATAAAGACCCGAATTTTAAGGACCAAGTT
ATTCTGCTGAACAAACACATCGATGCTTACAAAACCTTCCCTCCGACCGA
GCCGAAAAAGGACAAAAAGAAAAAGGCGGACGAGACGCAAGCCTTGCCC
CAACGTCAGAAAAAGCAACAGACGGTGACGCTGTTGCCGGCGGCCGATCT
CGACGACTTCAGCAAGCAGCTTCAGCAAAGCATGAGCAGCGCGGATAGC
ACCCAAGCTCATCATCATCATCATTAA

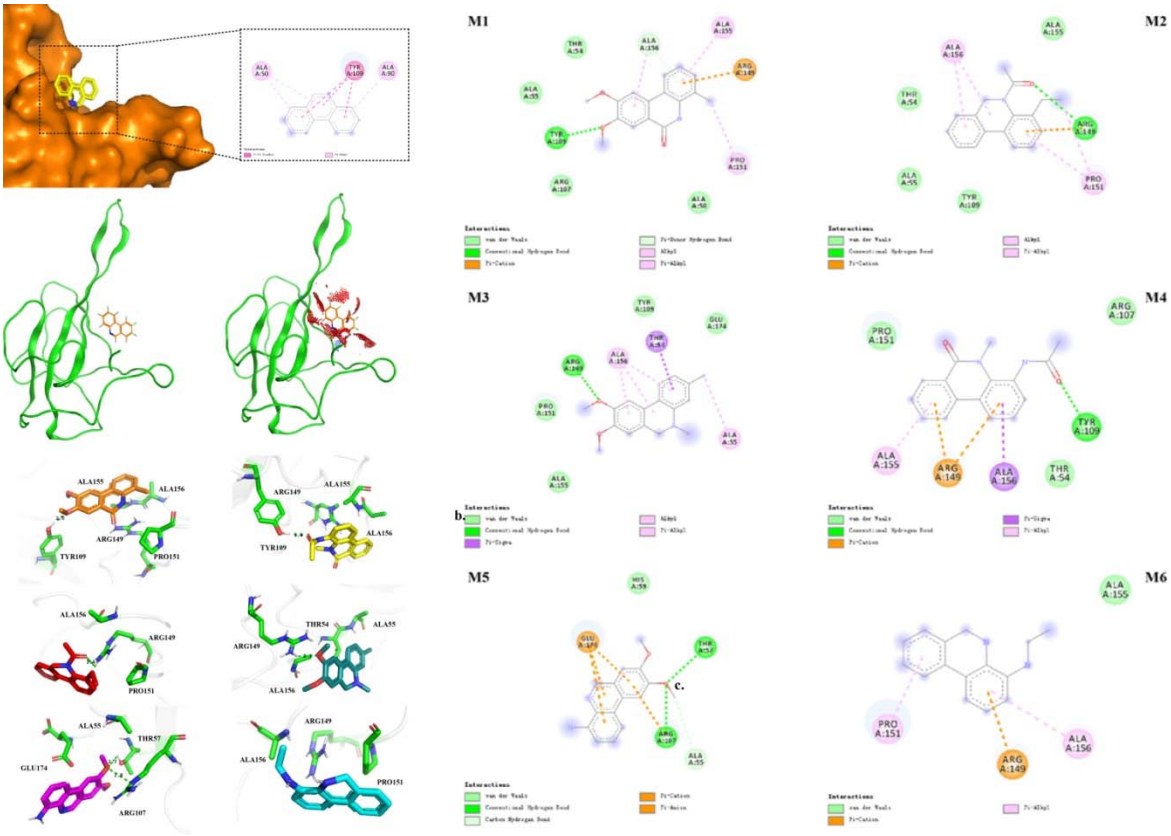


Figure S1: Two dimensional (2D) of binding modes of the six model moleculars (**M1-6**) with SARS-CoV-2 N-NTD. The estimated binding free energies are: -6.2 kcal/mol (**M1**), -5.6 kcal/mol (**M2**), -5.7 kcal/mol (**M3**), -5.8 kcal/mol (**M4**), -5.9 kcal/mol (**M5**), -5.2 kcal/mol (**M6**).

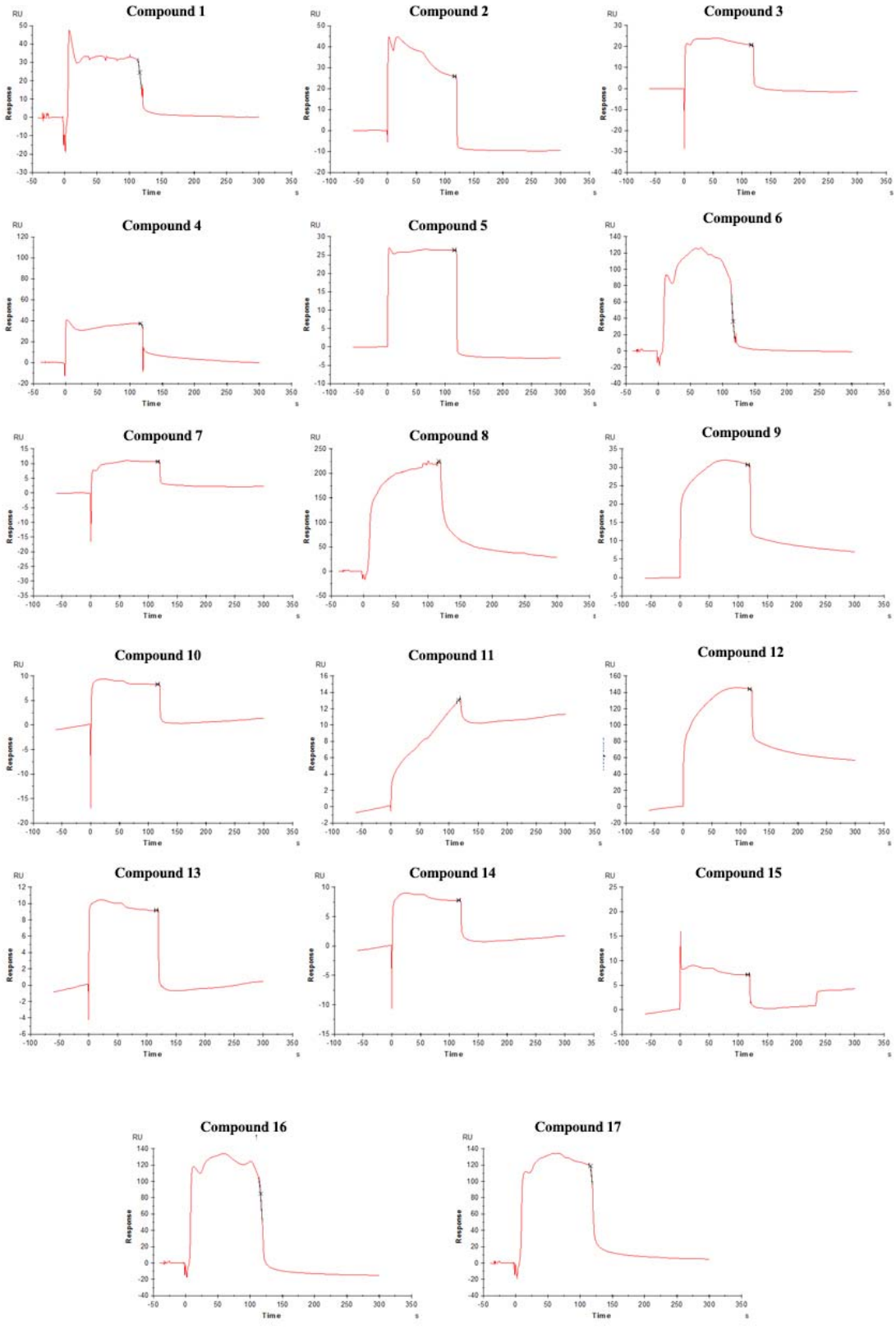


Figure S2: SARS-CoV-2 Npro binding level screening of compounds **1-17**. Binding curves of immobilized SARS-CoV-2 Npro. Data are shown as red lines. Top four compounds were chosen as the hits.

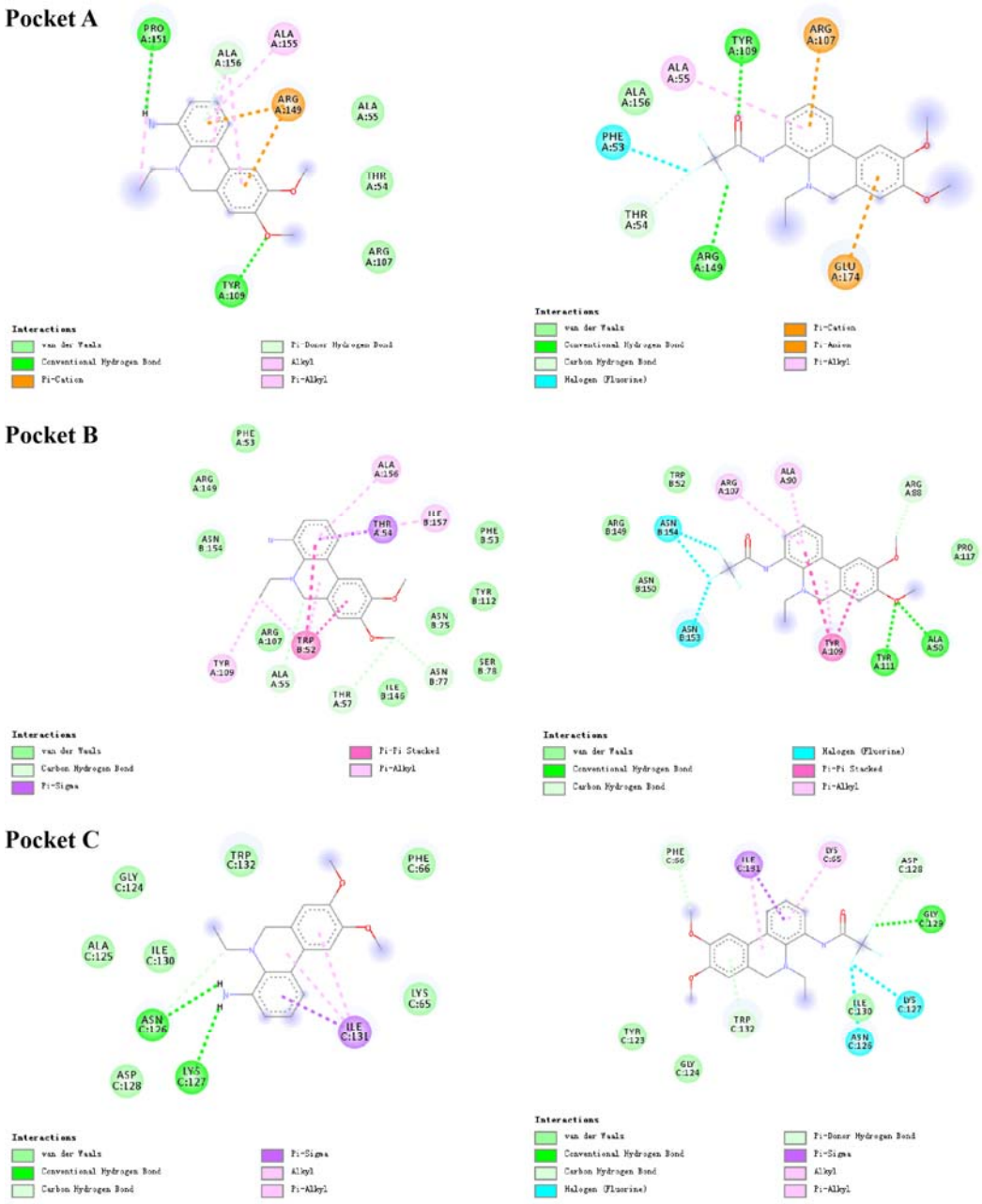


Figure S3: Docking modes of compound **12** (left) and **16** (right) with three potential pockets of SARS-CoV-2 Npro.

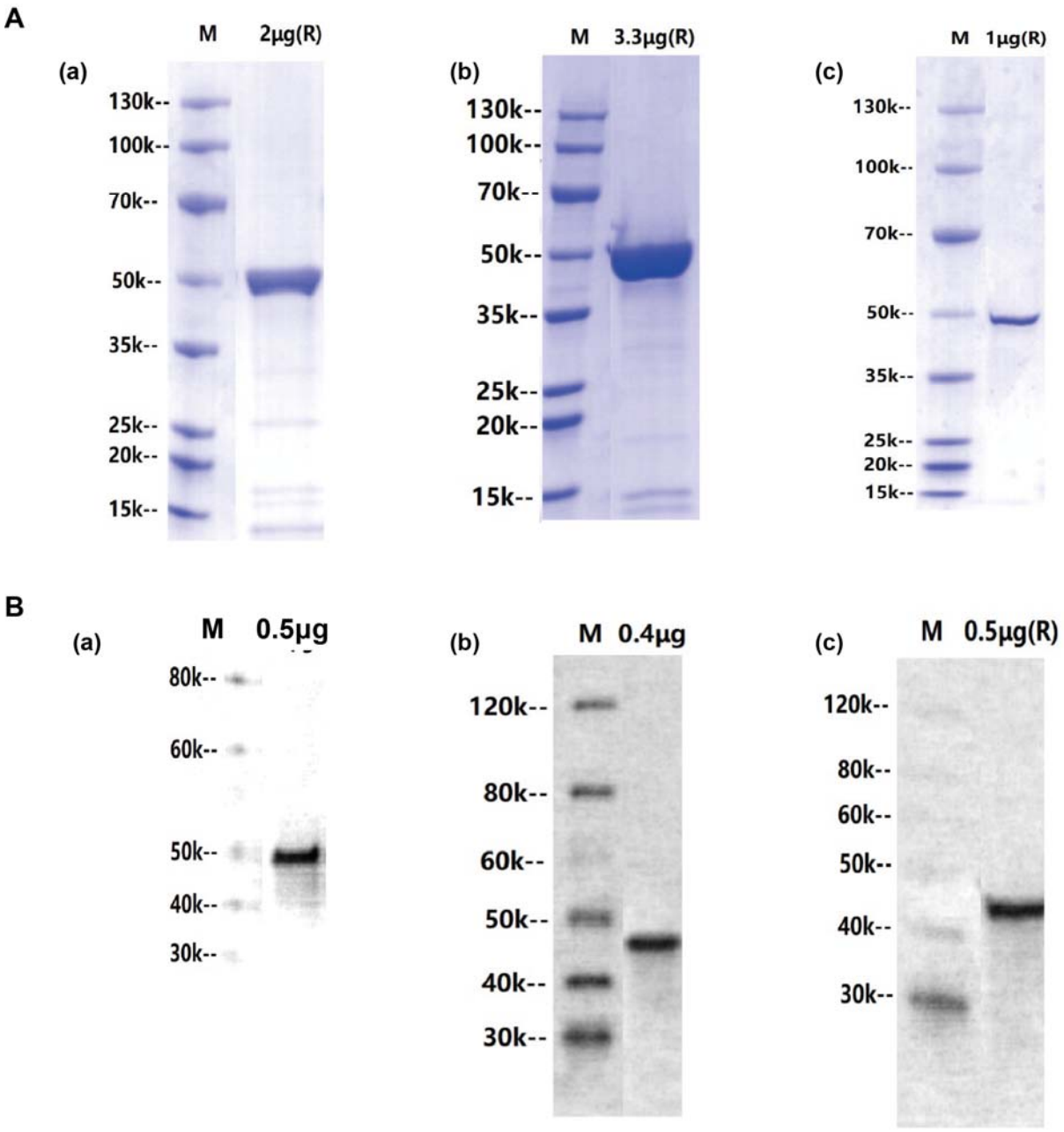


Figure S4: The analysis data of mutant A-C after purification. A: SDS-PAGE results. Lane M: Marker. Lane 1: purified protein. B: Western Blot results. Lane M: Marker (M00521, Genscript). Primary antibody: His-Tag Mouse Monoclonal Antibody (abs137964, absin). Second antibody: Goat Anti-Mouse (115-035-146, Jackson). (a): mutant A. (b): mutant B. (c): mutant C.

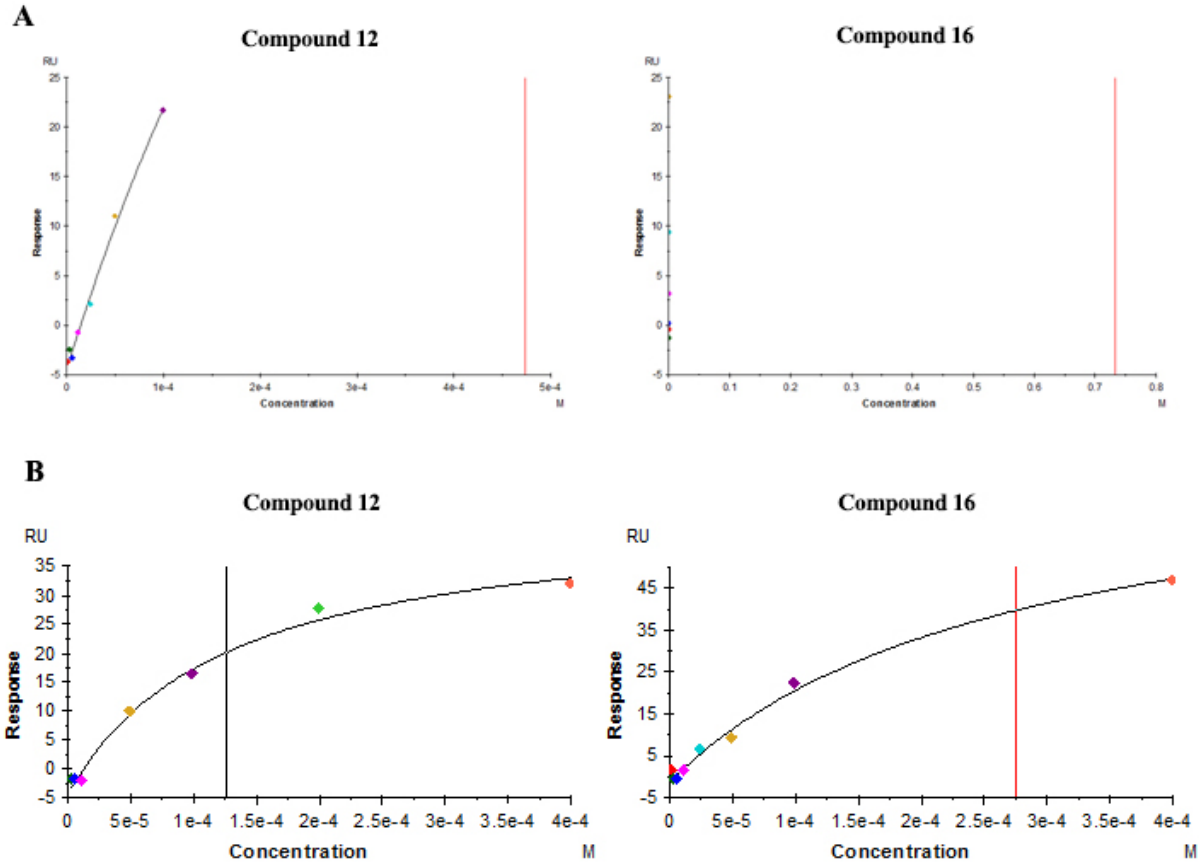


Figure S5: The affinity fitting curves of mutant A-B with compound **12** or **16**. A: Fitting curves of immobilized mutant A. B: Fitting curves of immobilized mutant B. When the affinity of the small molecule is weak, there is no kinetic curve, and the affinity model is used to fit, When the small molecule with strong affinity, the kinetics model is used to fit. (according to the GE Healthcare Laboratory Guideline).

Table S1. The SPR RU values of Phenanthridine Compounds.

	Mean	SD		Mean	SD
Compound **1**	29.45	2.05	Compound **10**	13.14	1.14
Compound **2**	30.7	4	Compound **11**	17.71	1.11
Compound **3**	34.9	5.3	Compound **12**	144.9	11.35
Compound **4**	33.45	3.85	Compound **13**	14.3	1.5
Compound **5**	34.95	0.25	Compound **14**	10.6	0.9
Compound **6**	57.5	4.8	Compound **15**	11.85	1.05
Compound **7**	22	2.5	Compound **16**	101	7.5
Compound **8**	210.7	10.58	Compound **17**	125.1	6.4
Compound **9**	23.14	0.96			

Table S2. The Viability of SARS-Cov-2 Infected Cell After Treatment of Phenanthridine Compounds

Consentration (μM)	Compound **12**		Compound **16**		Remdesivir	
	Mean	SD	Mean	SD	Mean	SD
0.064	42.07	0.5515	49.07	2.164	16.557	7.279
0.32	44.04	3.567	66.95	28.14	22.283	4.497
1.6	69.61	23.35	84.14	36.77	56.674	20.297
8	73.32	22.93	82.36	20.35	103.720	2.962
40	87.56	1.682	87.41	6.437	97.265	0.155
200	97.85	2.289	99.6	6.335	81.893	8.897

Table S3 The Inhibition of Phenanthridine Compounds on SARS-Cov-2

Concentration (μM)	Compound **12**		Compound **16**	
	Mean	SD	Mean	SD
3.125	45.99	17.76	56.23	24.35
6.25	53.79	23.2	54.85	18.31
12.5	61.27	32.45	68.79	13.71
50	76.41	15.07	68.9	1.378
100	72.33	12.93	97.83	2.39

Table S4. The EC_{50} Value of Compound **12** and **16**.

	EC_{50} (μM)	CC_{50} (μM)	[α] SI
Compound **12**	3.69	>200	>50
Compound **16**	2.18	>200	>90
Remdesivir	1.21	>200	>150

[α] SI= CC_{50} / EC_{50}

References

1. Chen, D. Z.; Zhang, H.; Jing, C. X.; He, X. L.; Yang, B. J.; Cai, J. Y.; Zhou, Y. F.; Song, X. M.; Li, L.; Hao, X. J., Efficient synthesis of new phenanthridine Wnt/beta-catenin signaling pathway agonists. *Eur J Med Chem* **2018,** *157*, 1491-1499.

2. Ferraccioli, R.; Carenzi, D.; Rombola, O.; Catellani, M., Synthesis of 6-phenanthridinones and their heterocyclic analogues through palladium-catalyzed sequential aryl-aryl and N-aryl coupling. *Org Lett* **2004,** *6* (25), 4759-4762.

3. Chen, D. Z.; Fan, S. R.; Yang, B. J.; Yao, H. C.; Wang, Y. T.; Cai, J. Y.; Jing, C. X.; Pan, Z. H.; Luo, M.; Yuze, Y. Q.; Liu, G. J.; Hao, X. J., Phenanthridine Derivative Host Heat Shock Cognate 70 Down-Regulators as Porcine Epidemic Diarrhea Virus Inhibitors. *J Nat Prod* **2021,** *84* (4), 1175-1184.