

# Design, Synthesis and Activity Evaluation of Dihydropyranopyrazole PDE2 inhibitors

Yan Zhou<sup>1</sup>, Jinjian Li<sup>1</sup>, Han Yuan<sup>1</sup>, Rui Su<sup>1</sup>, Yue Huang<sup>1</sup>, Yiyong Huang<sup>1</sup>,  
Zhe Li<sup>1</sup>, Yinuo Wu<sup>1</sup>, Hai-Bin Luo<sup>1,2</sup>, Chen Zhang<sup>1\*</sup>, Ling Huang<sup>1,2\*</sup>

<sup>1</sup> *School of Pharmaceutical Sciences, Sun Yat-Sen University, Guangzhou 510006, PR China*

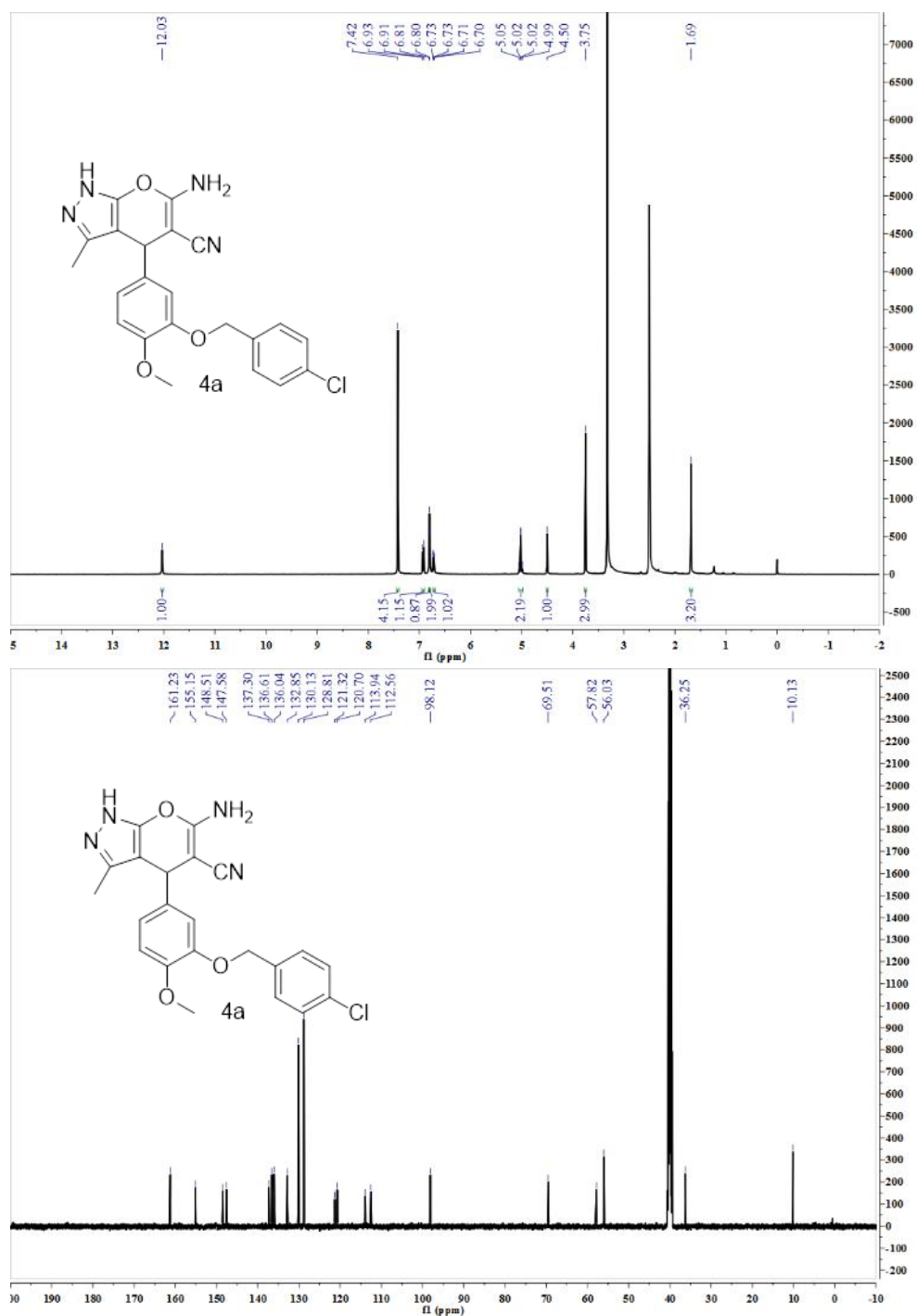
<sup>2</sup> *School of Pharmaceutical Sciences, Hainan University, Haikou, 510006, PR China*

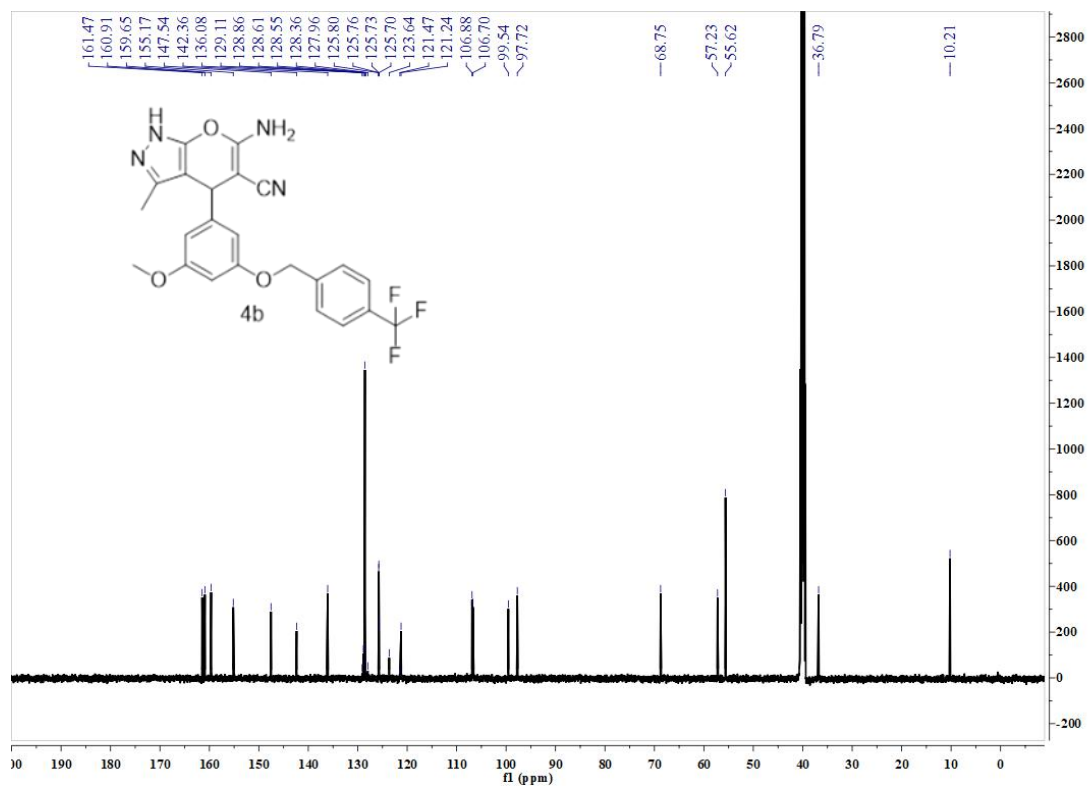
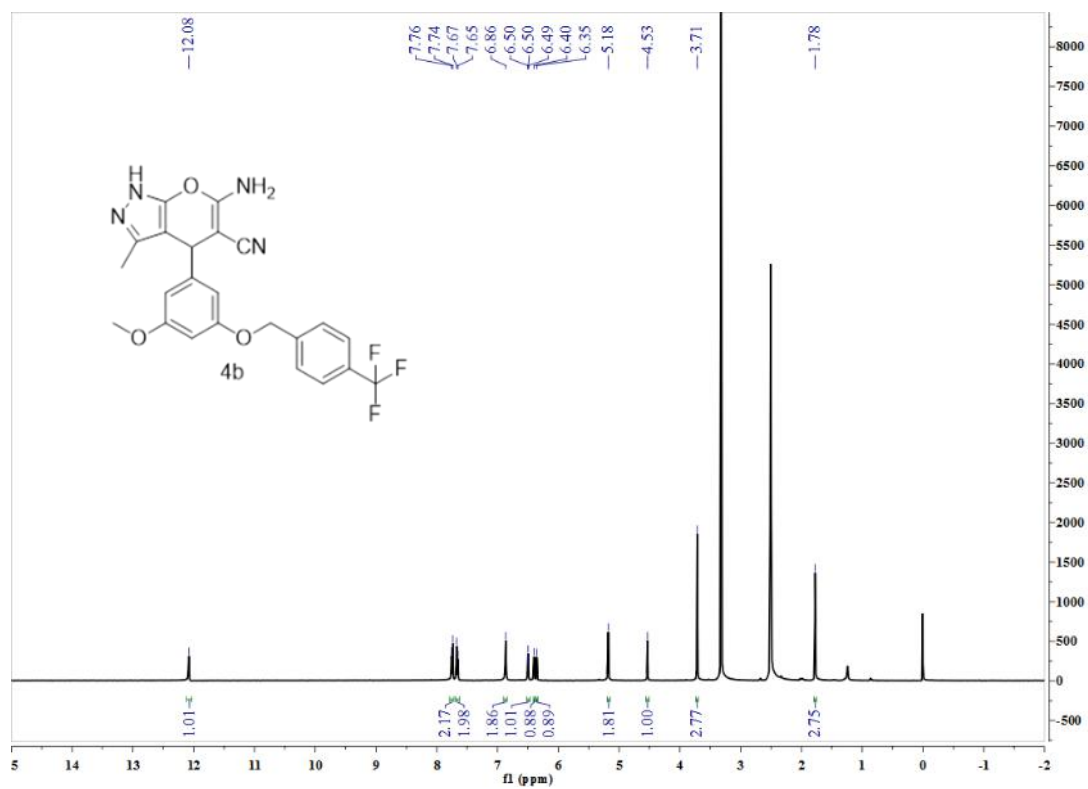
Corresponding author. E-mail address: [zhangch328@mail.sysu.edu.cn](mailto:zhangch328@mail.sysu.edu.cn) (C. Zhang), [huangl72@mail.sysu.edu.cn](mailto:huangl72@mail.sysu.edu.cn) (L. Huang).

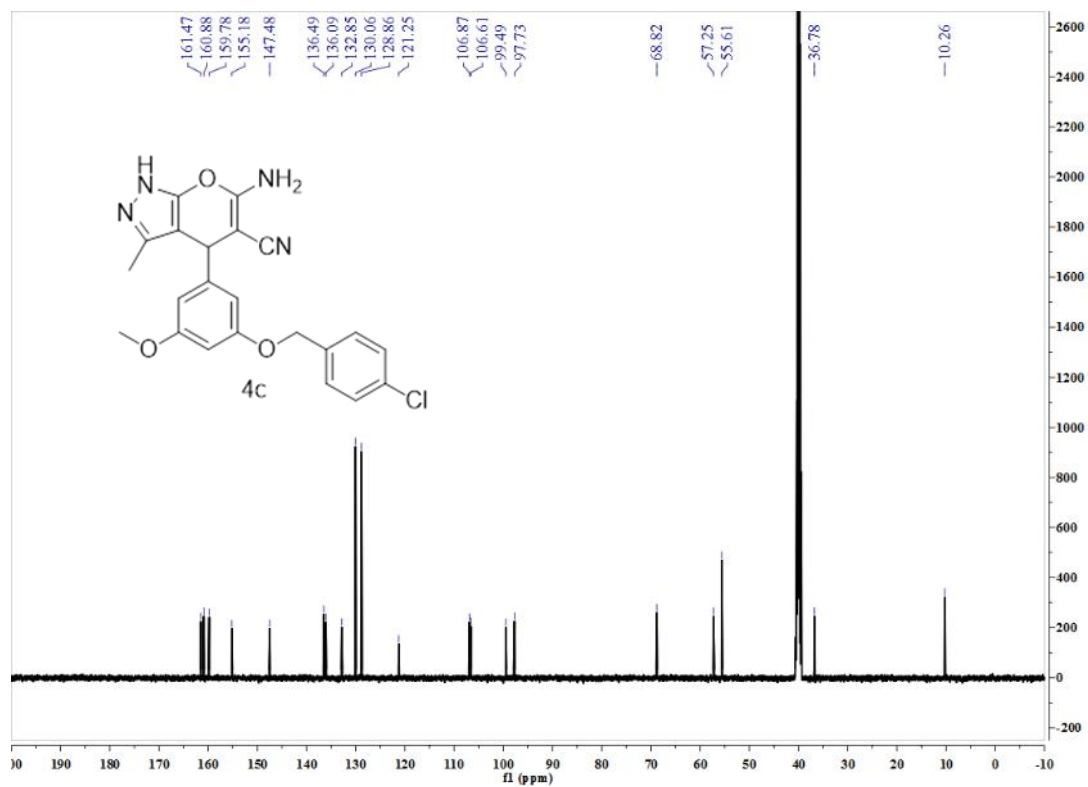
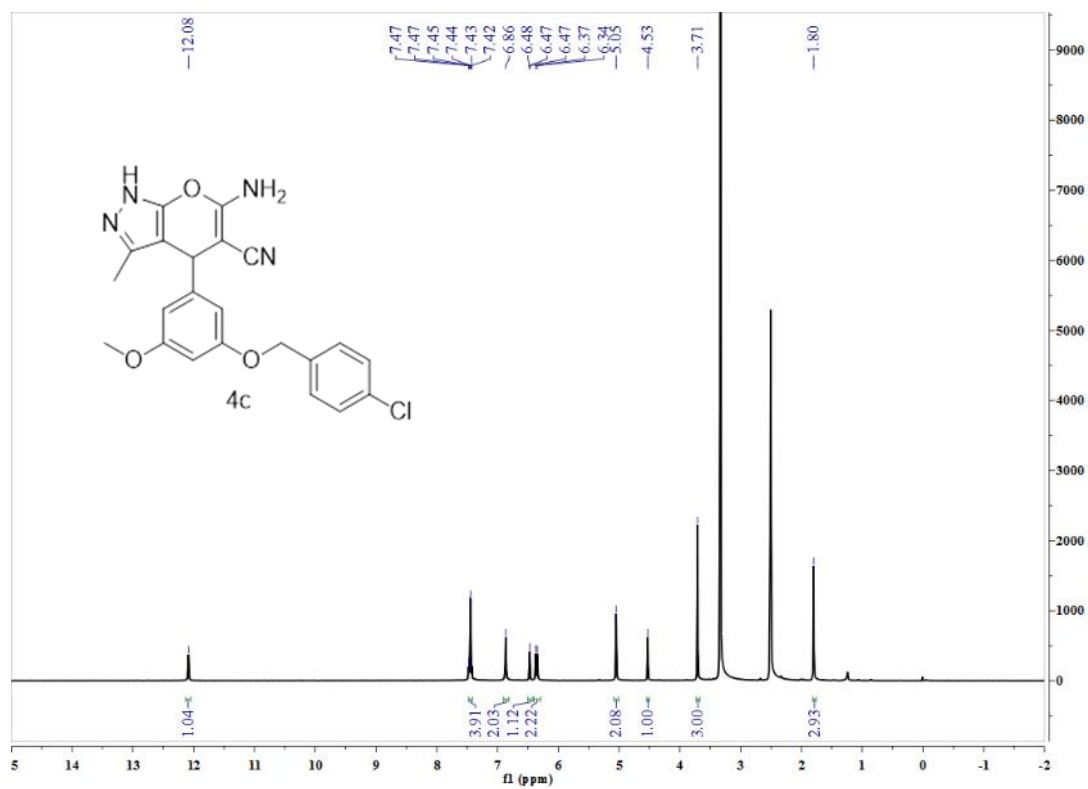
## Table of Contents:

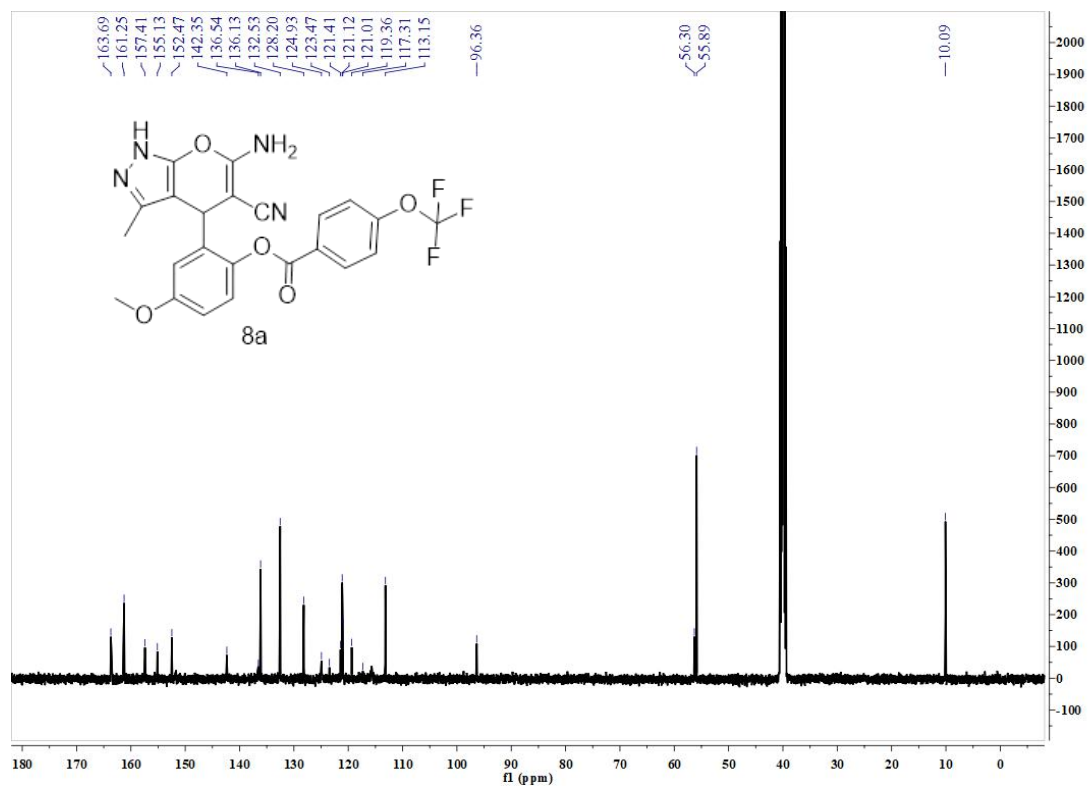
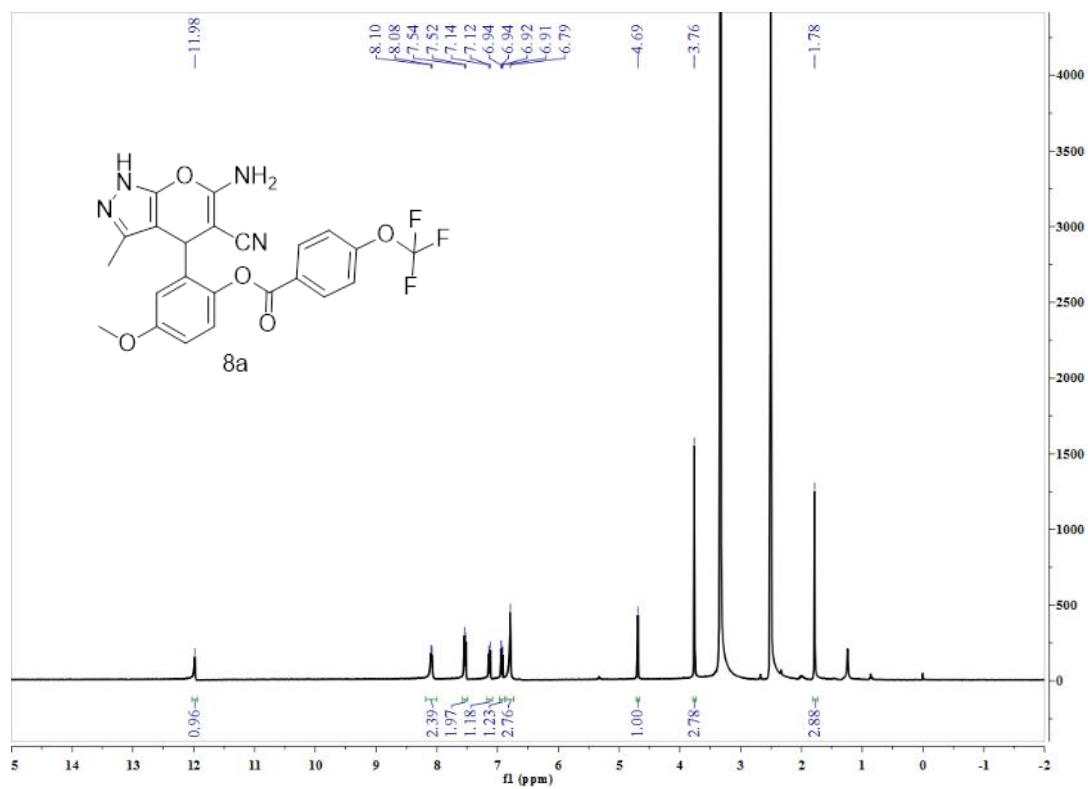
1. <sup>1</sup> HNMR and <sup>13</sup> CNMR spectrums of tested compounds.....	S2
2. HRMS spectra of target compounds.....	S32
3. Chiral Resolution of Compound <b>11h</b> .....	S60

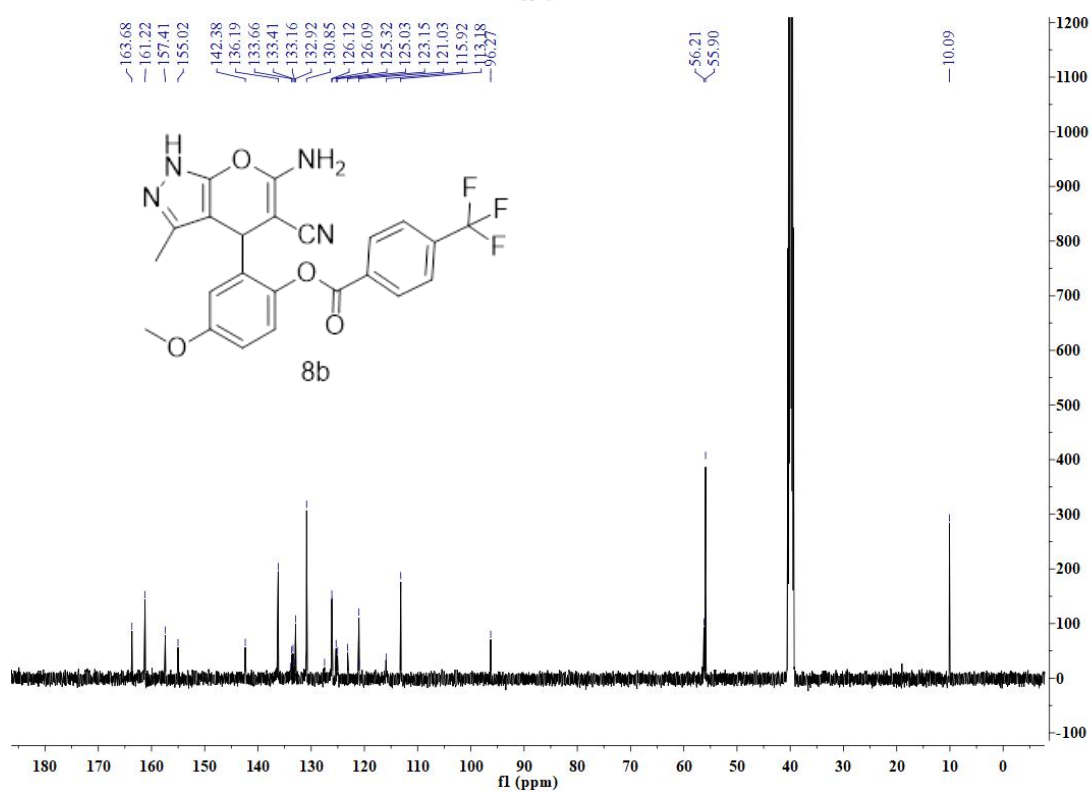
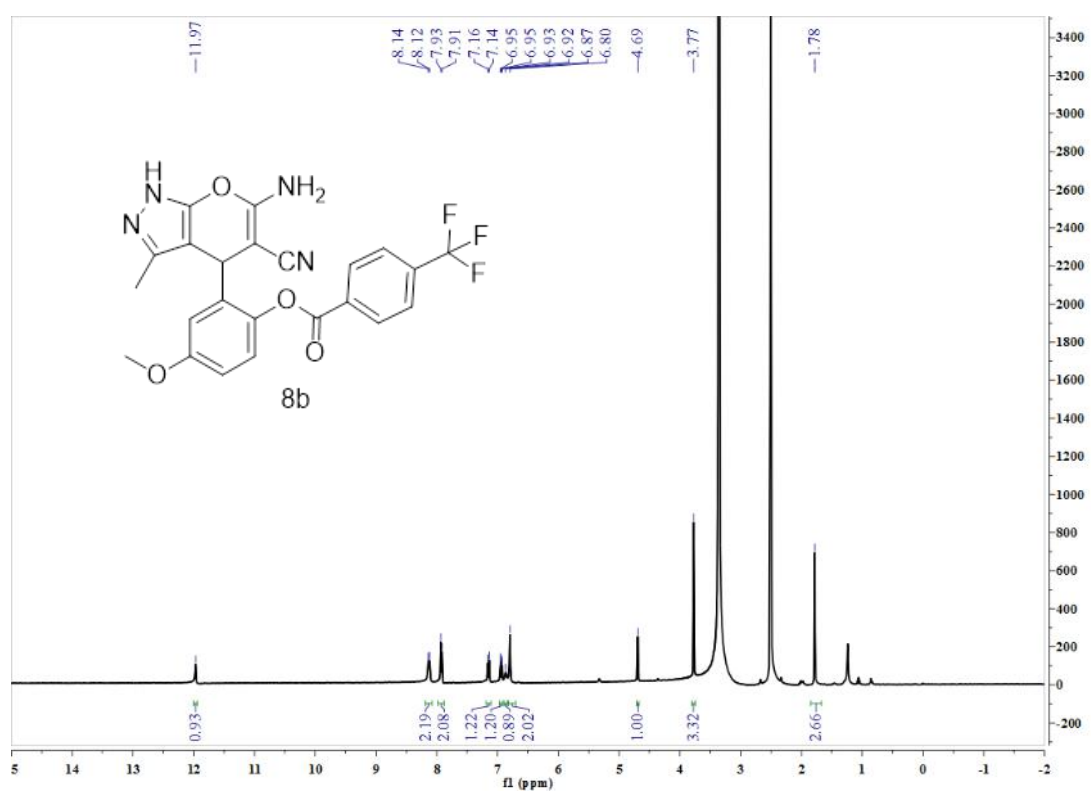
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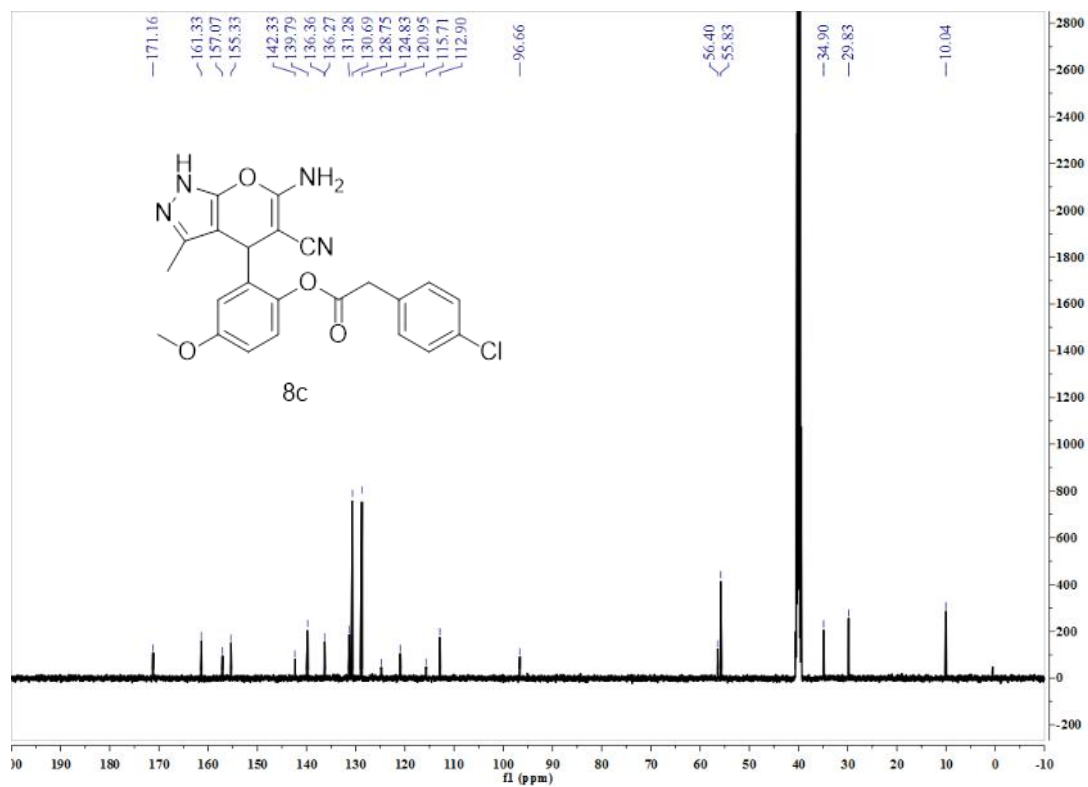
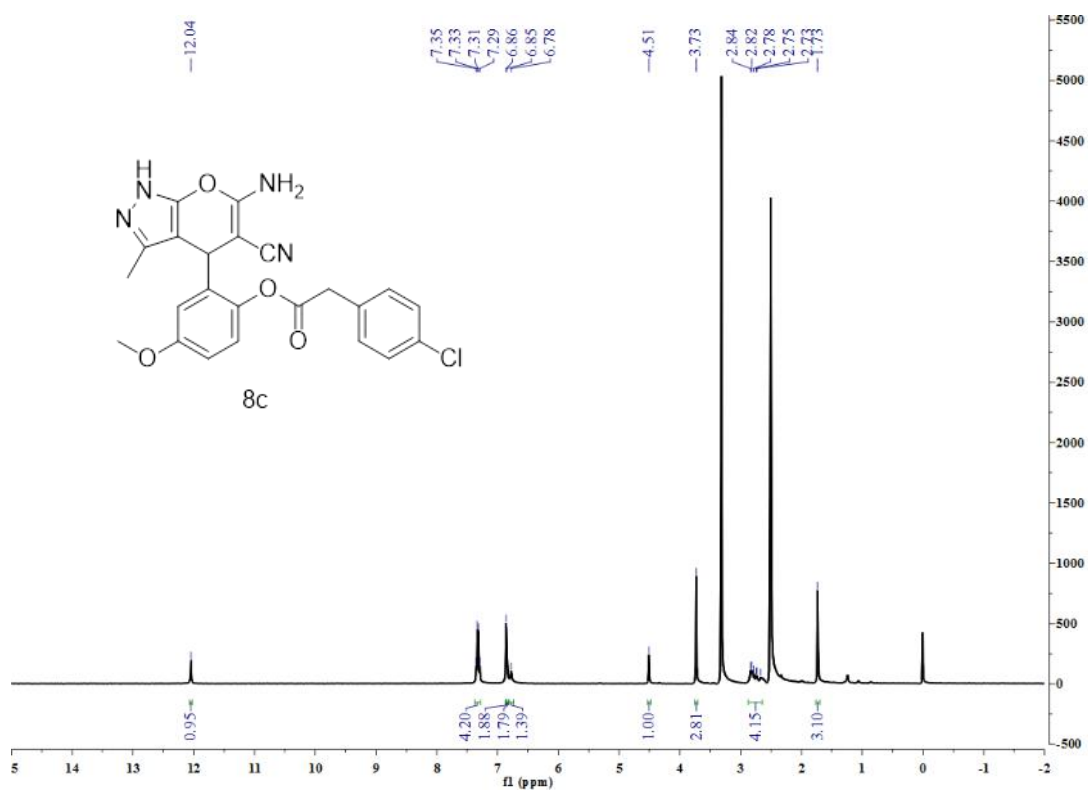


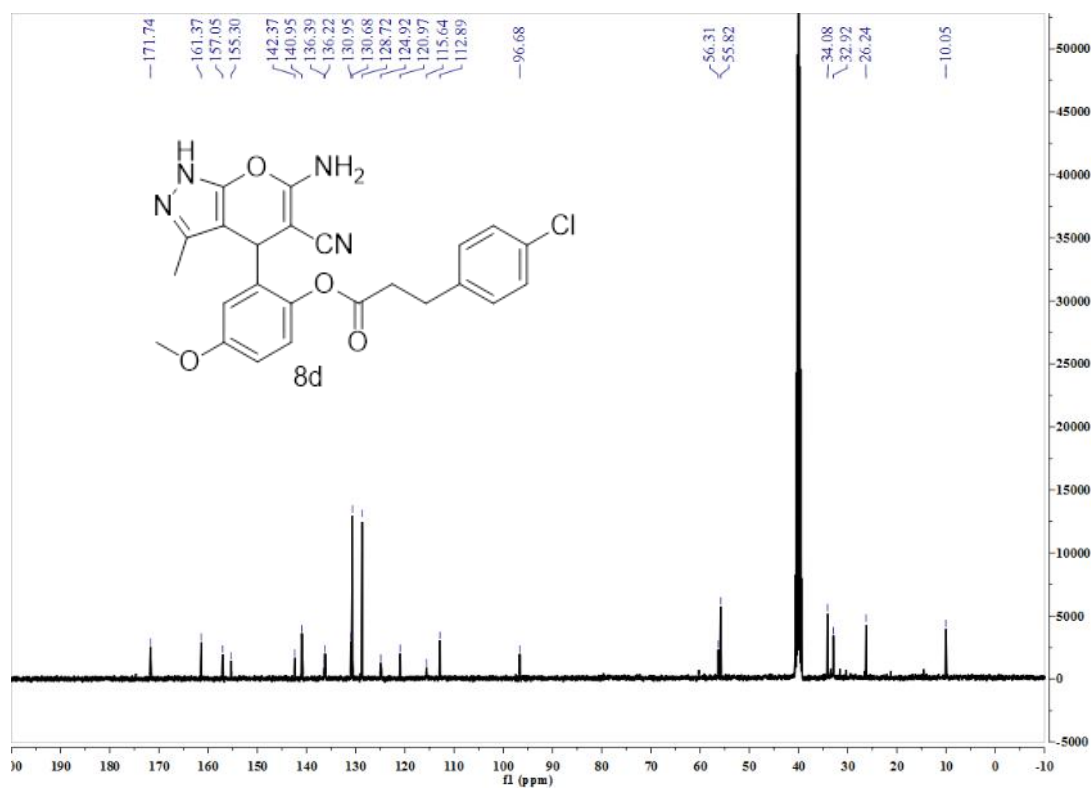
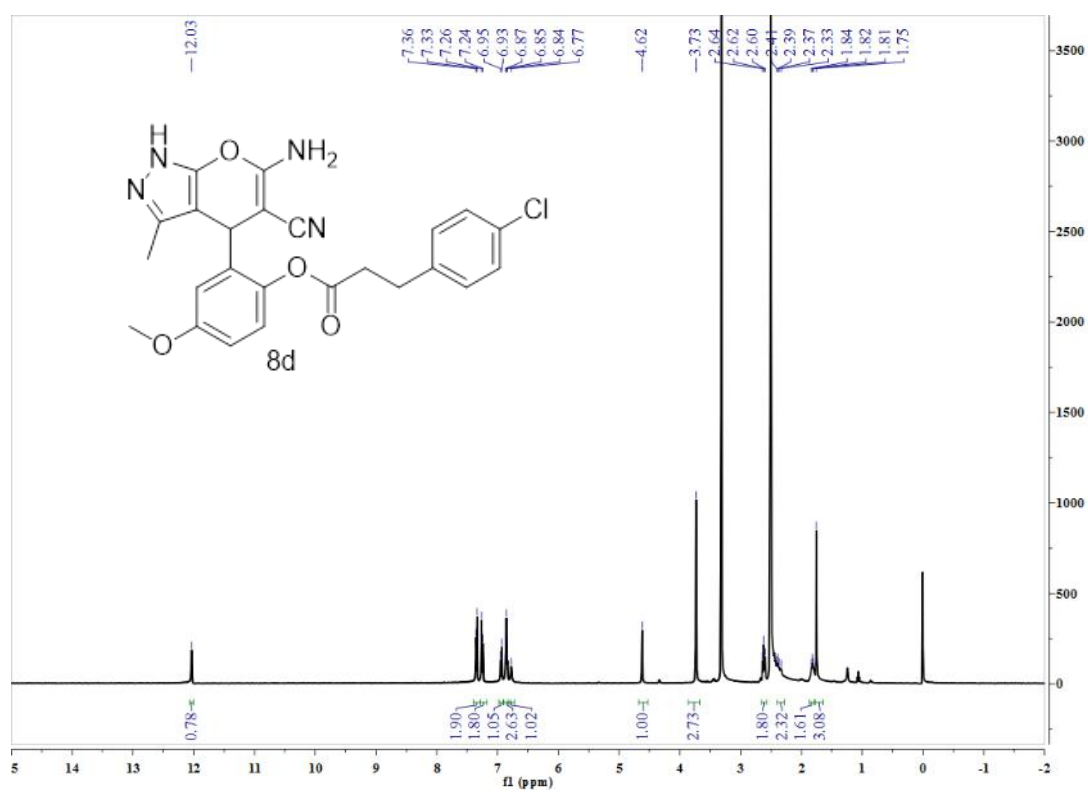




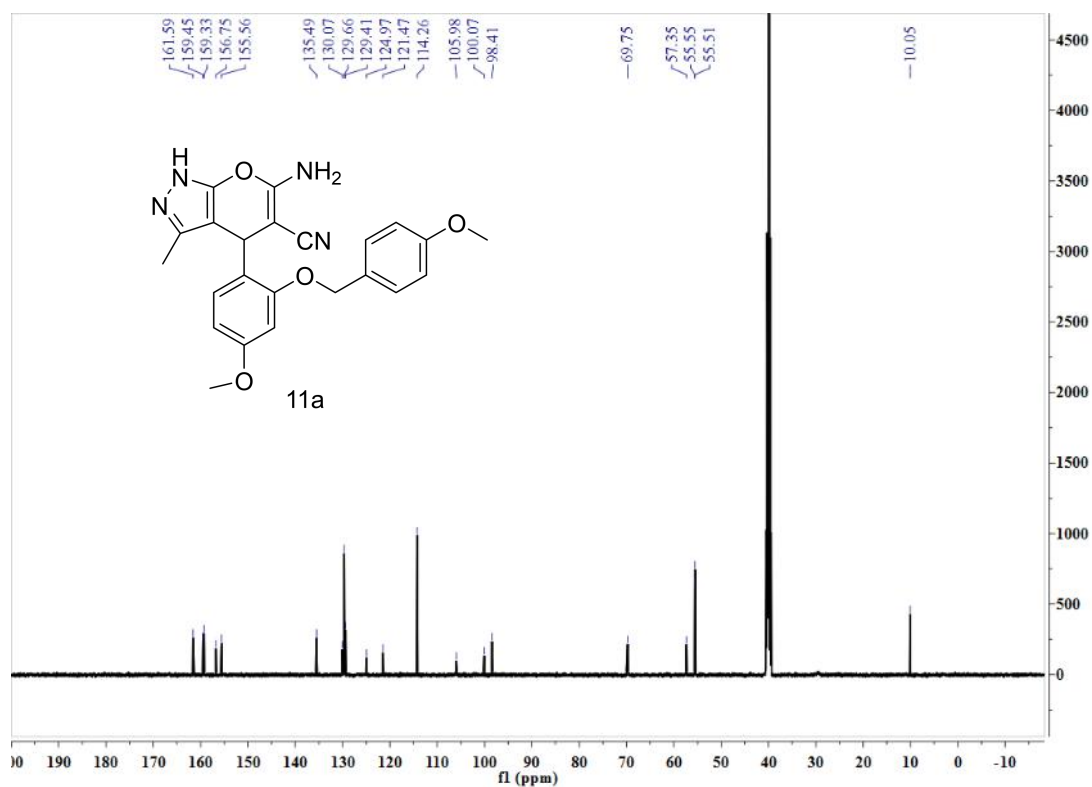
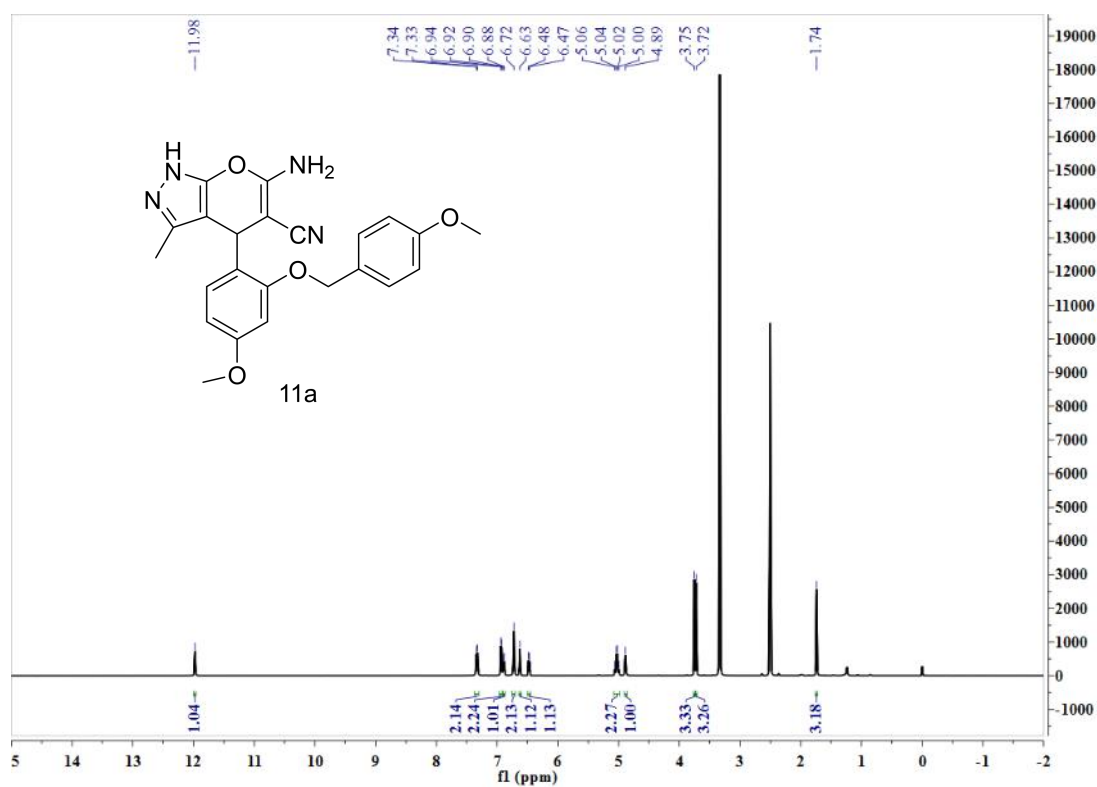


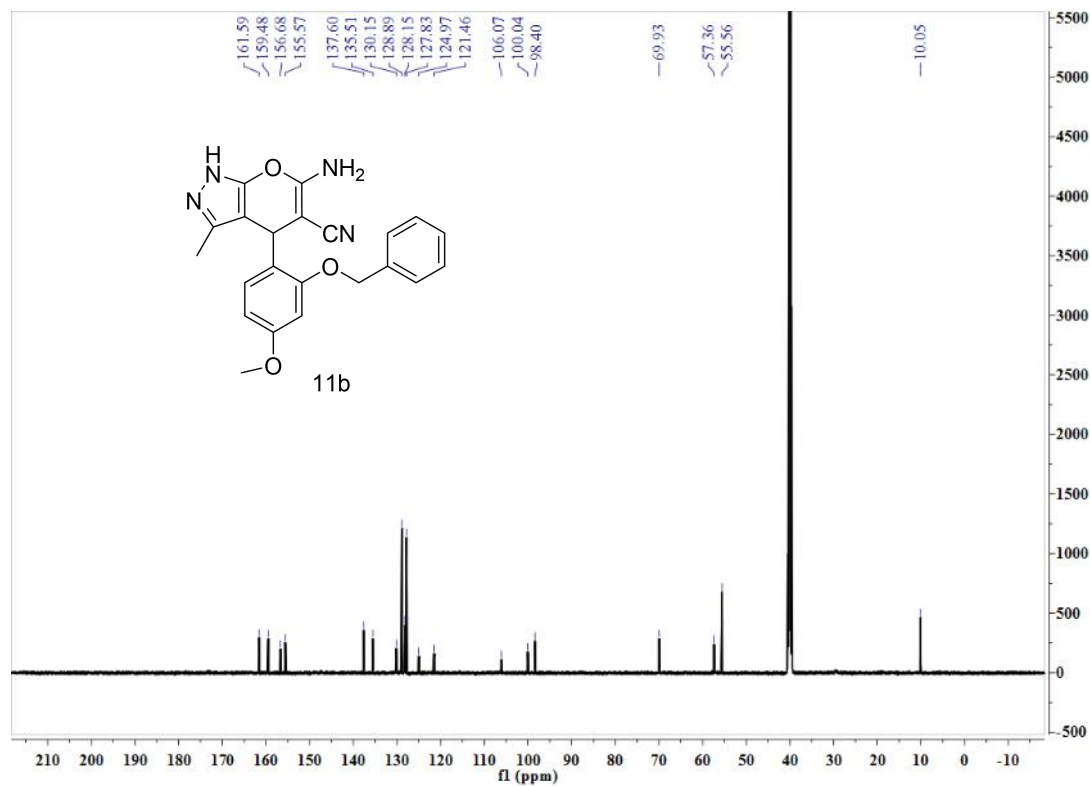
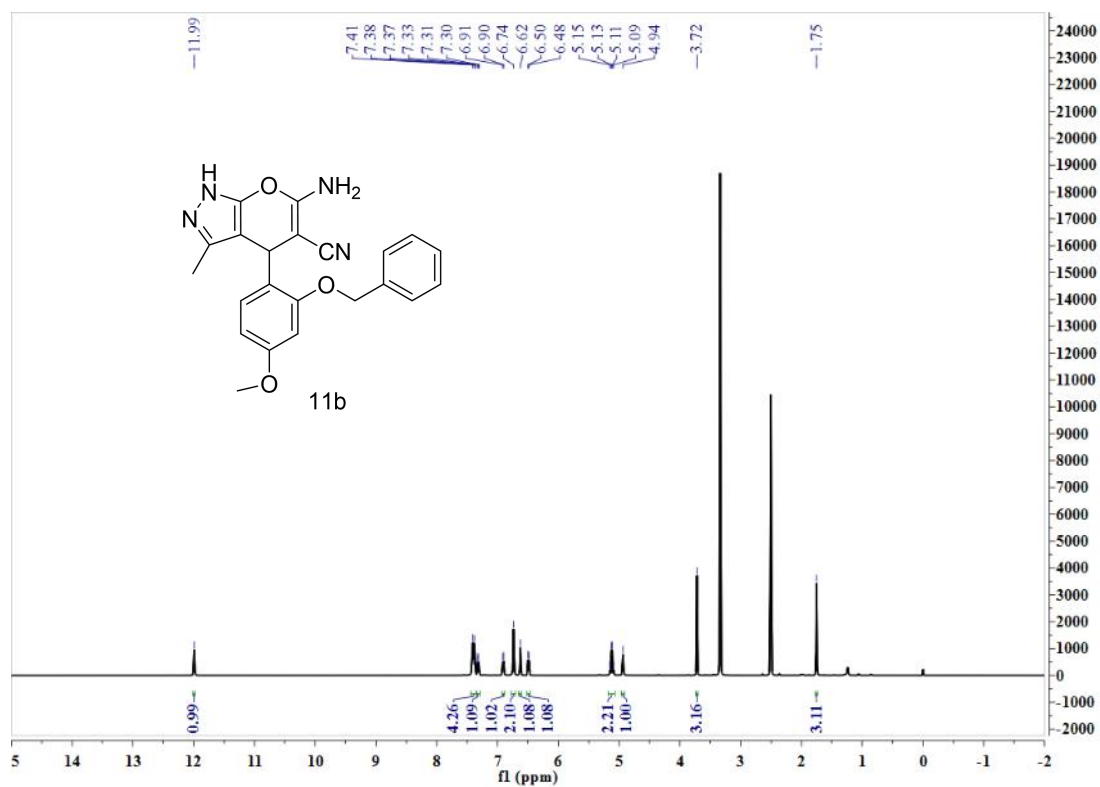


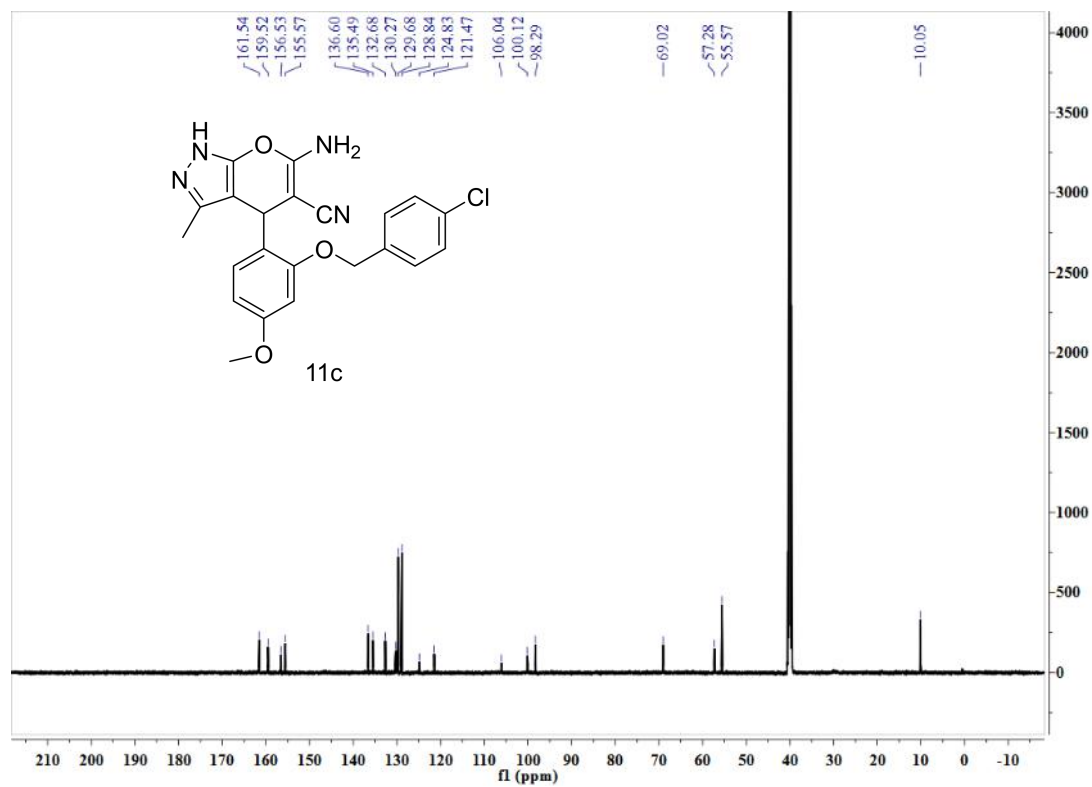
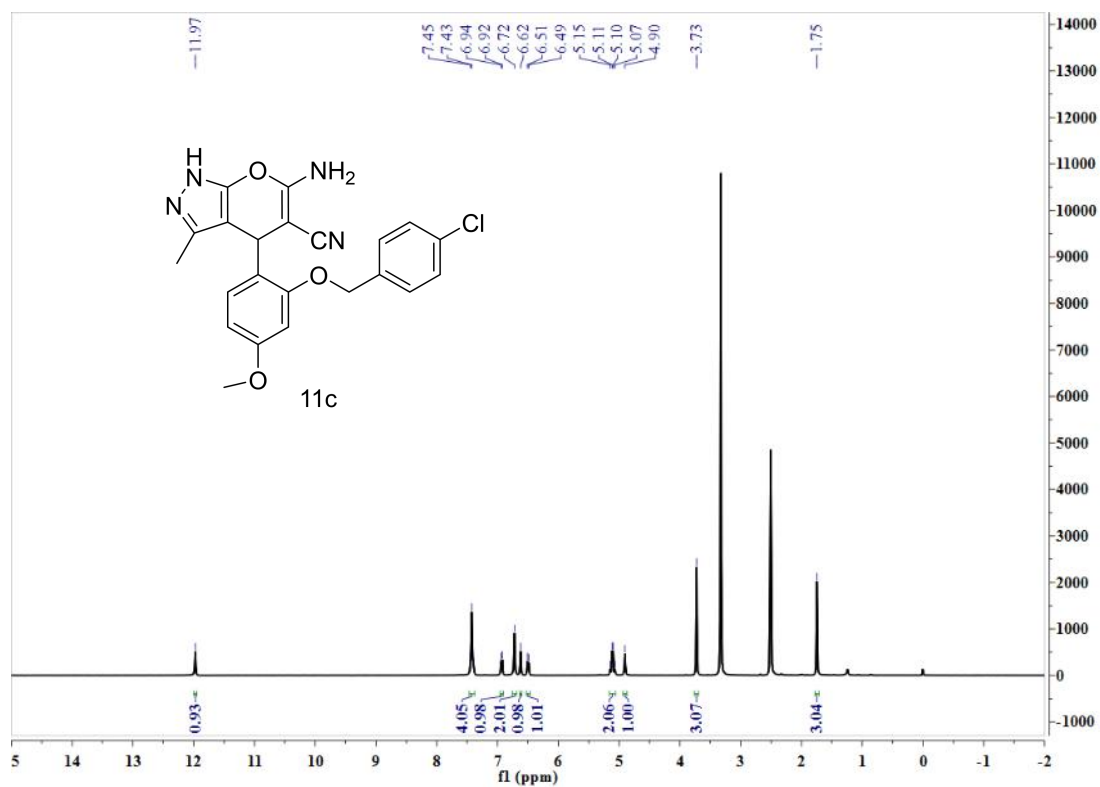


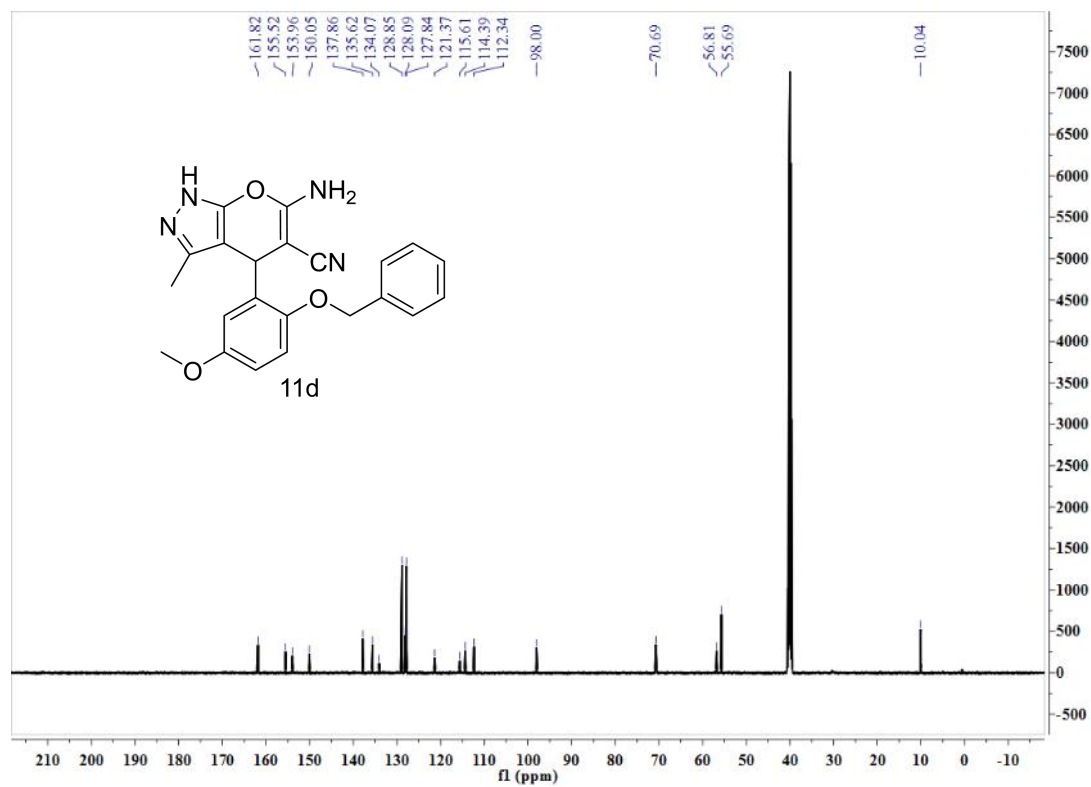
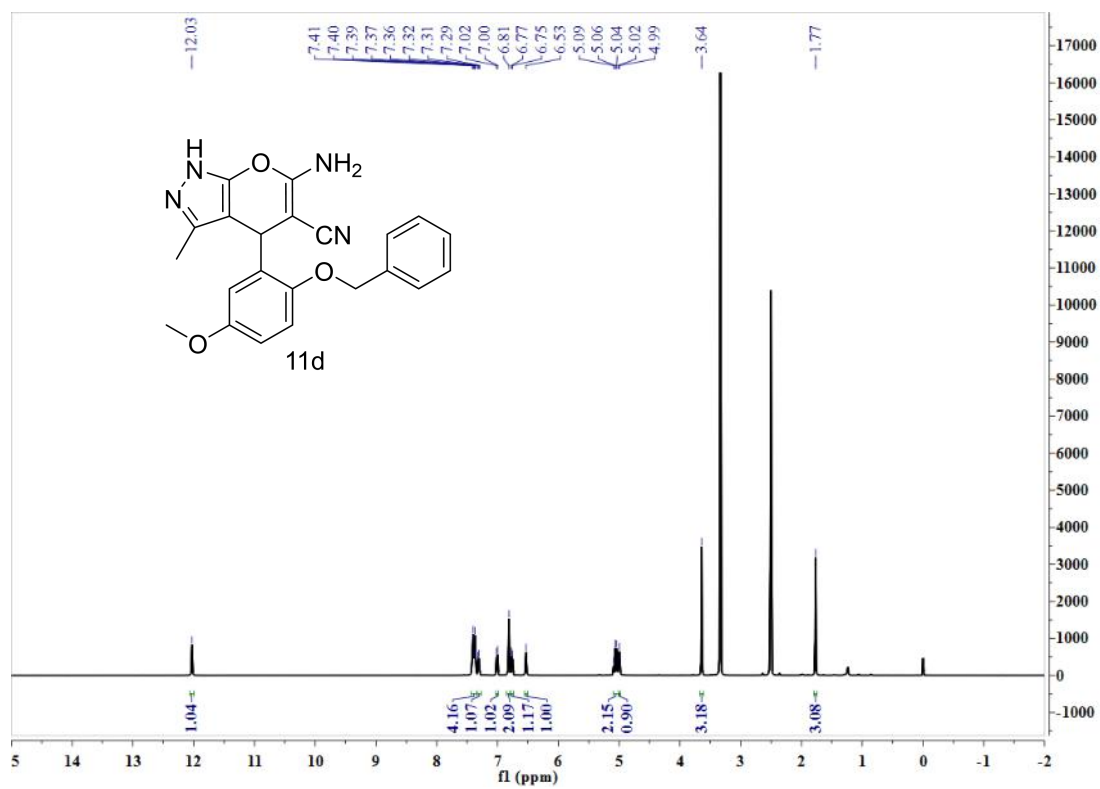


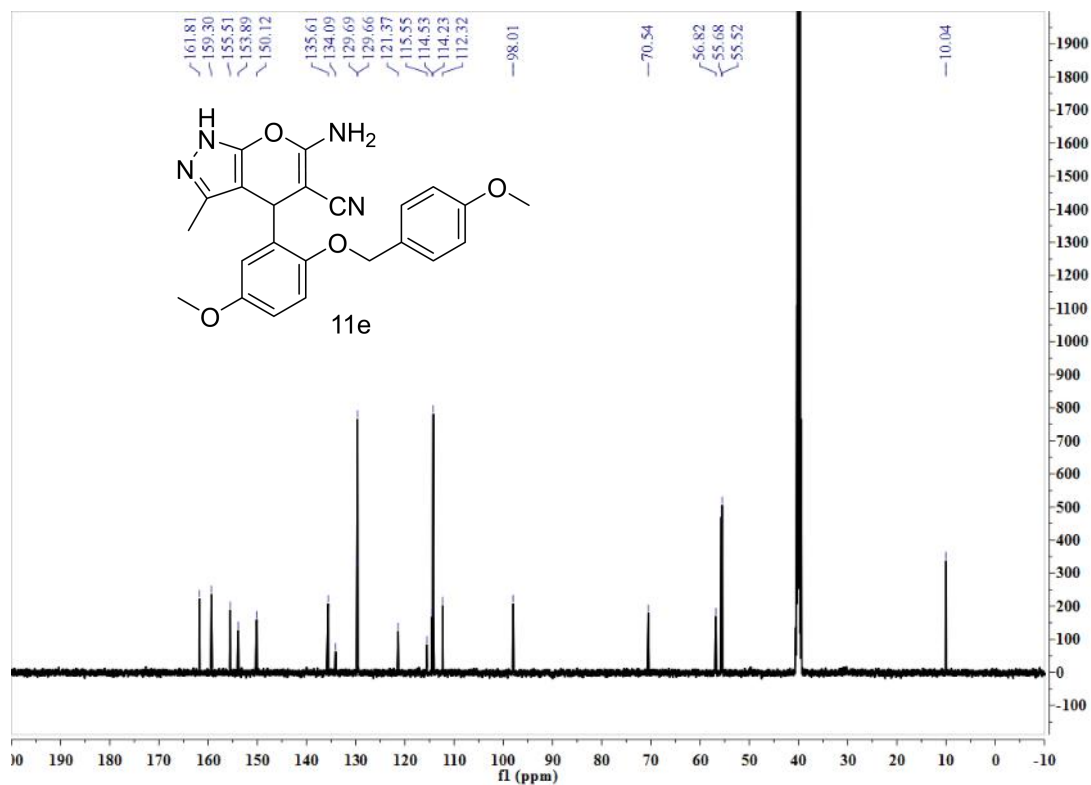
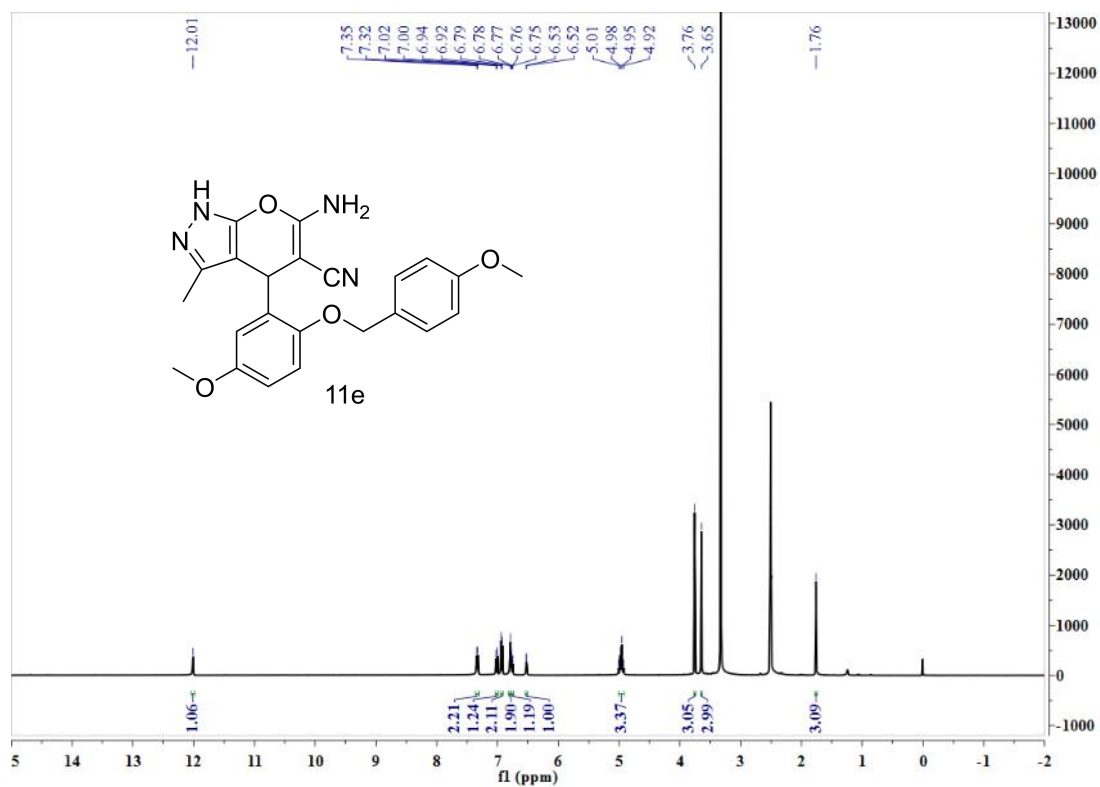


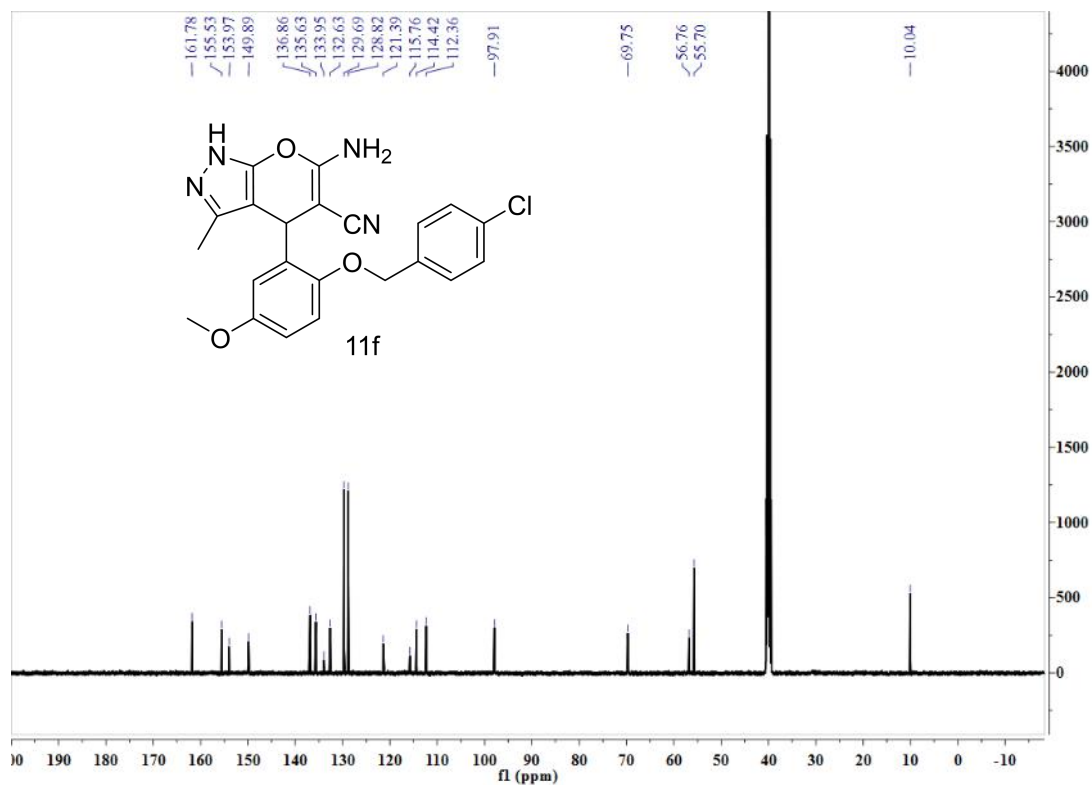
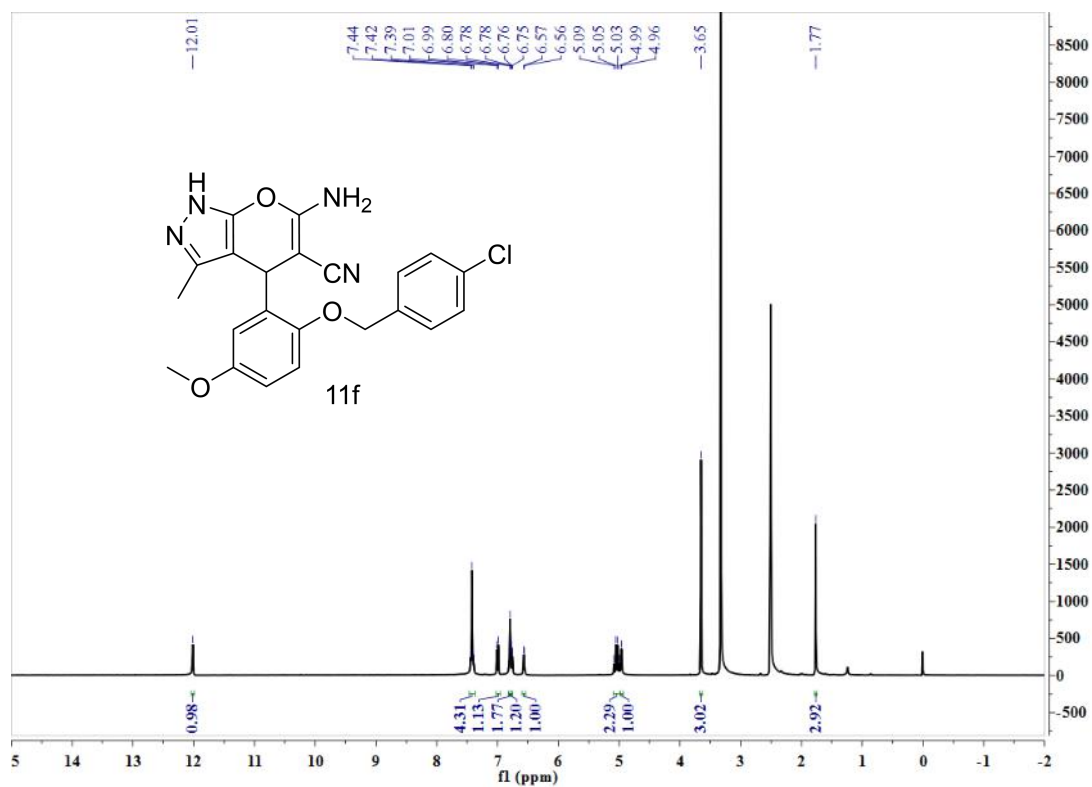


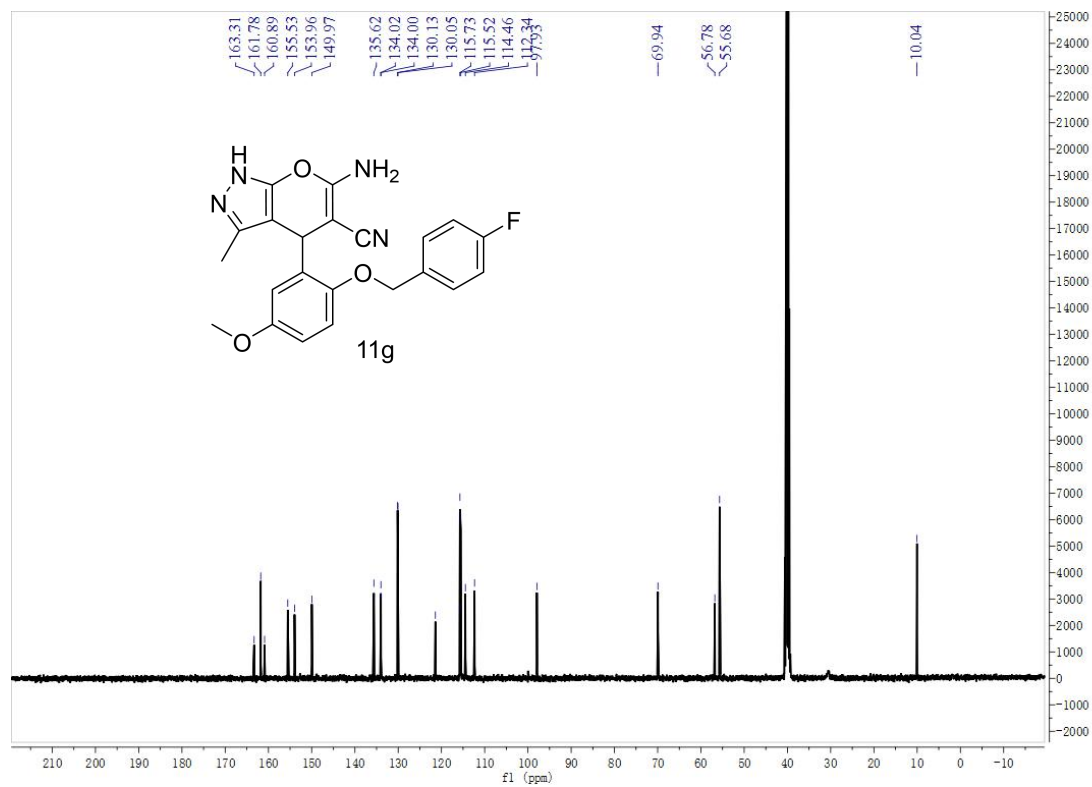
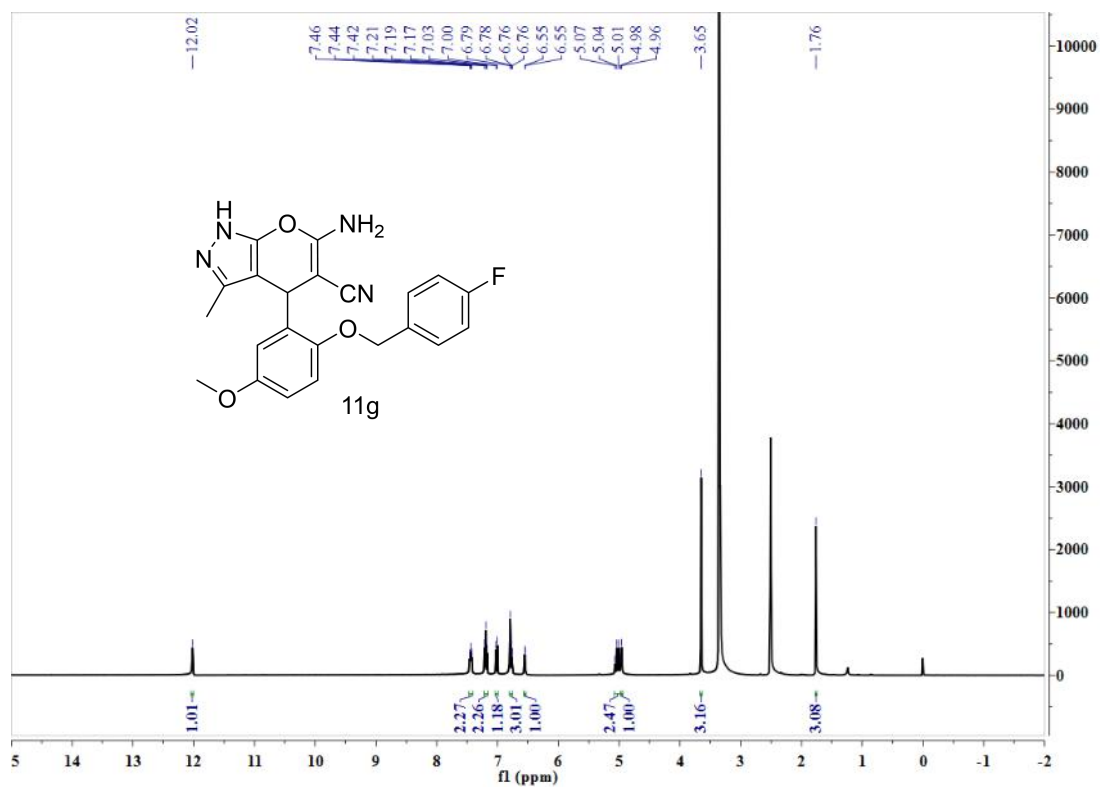


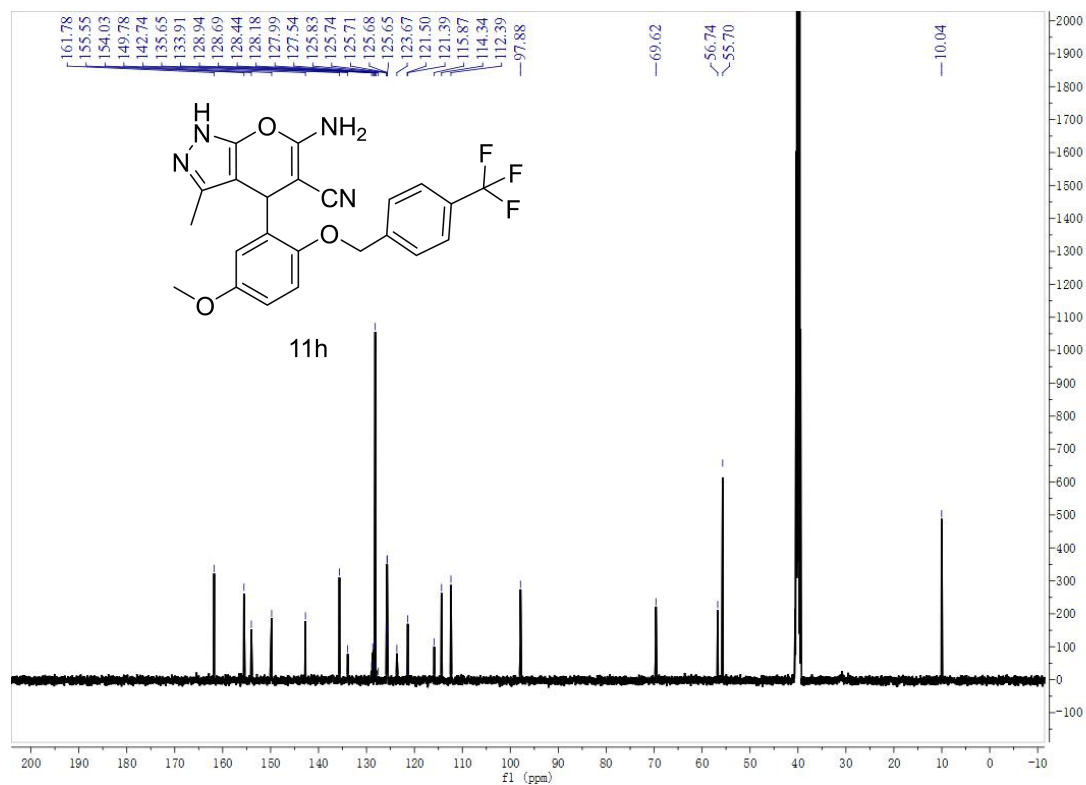
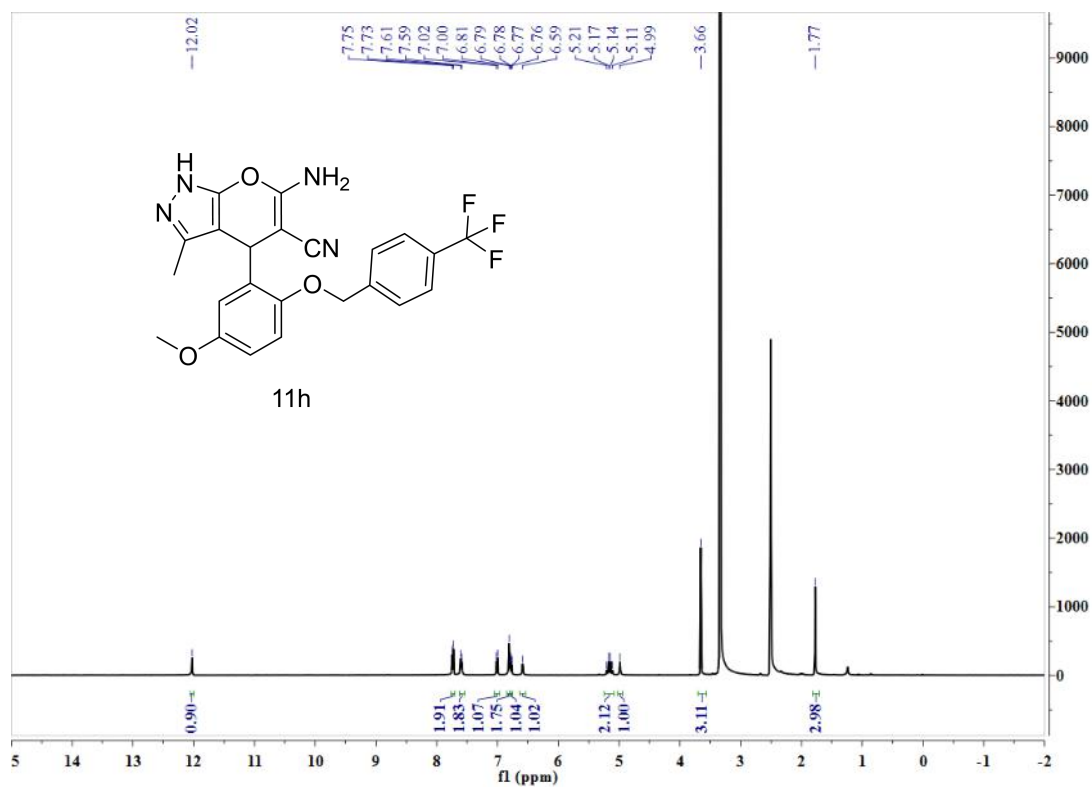




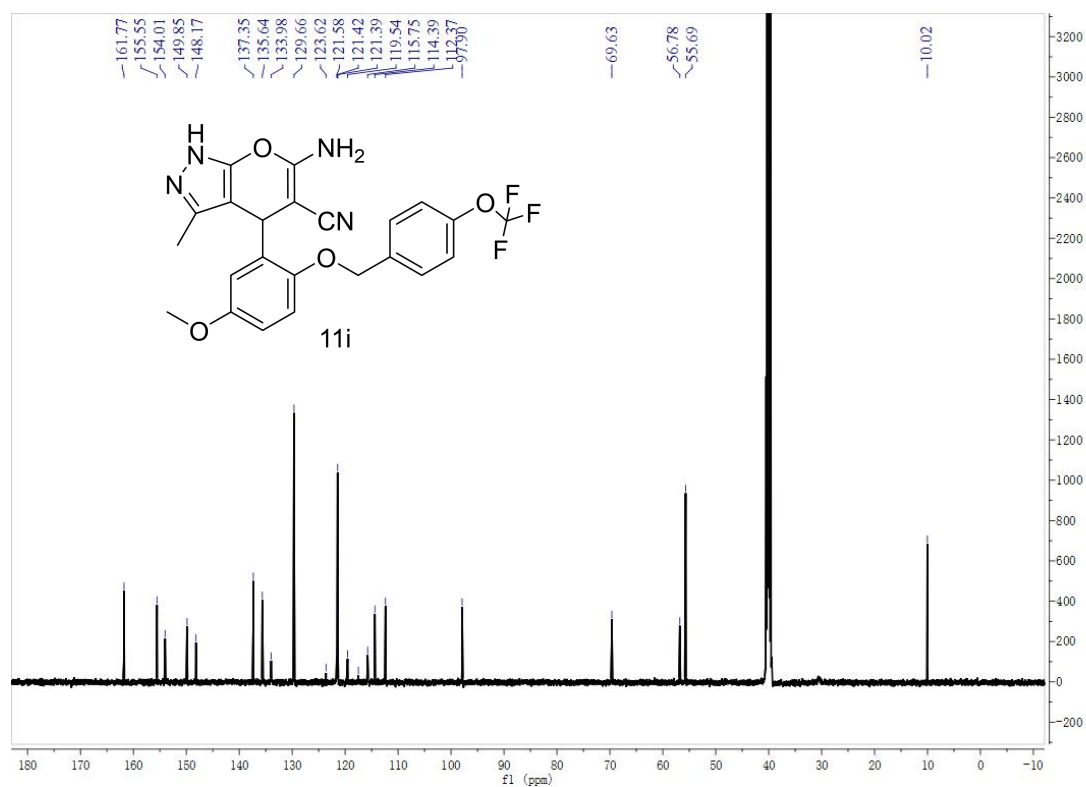
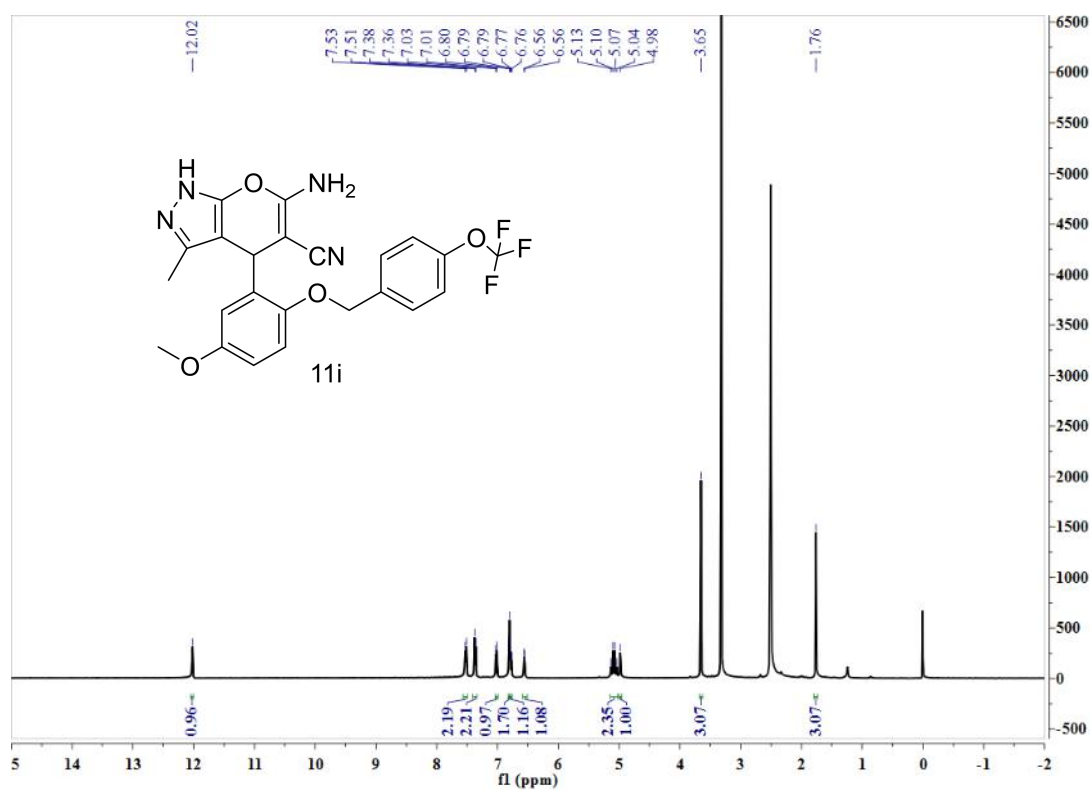


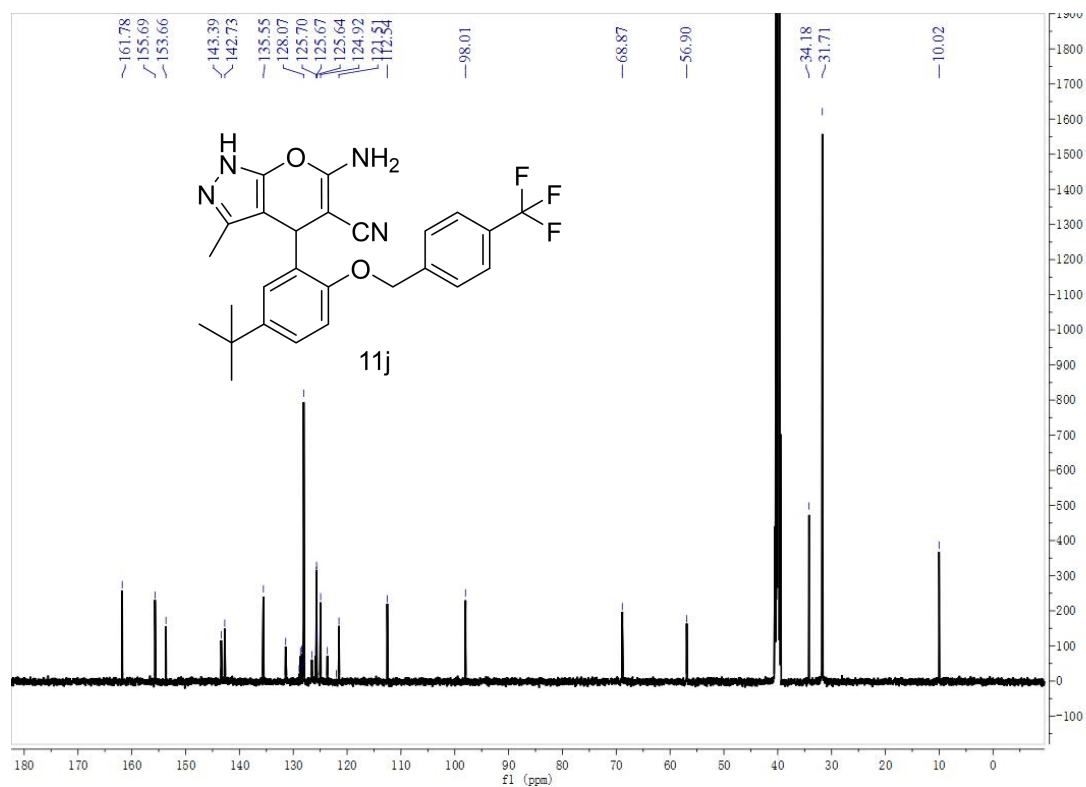
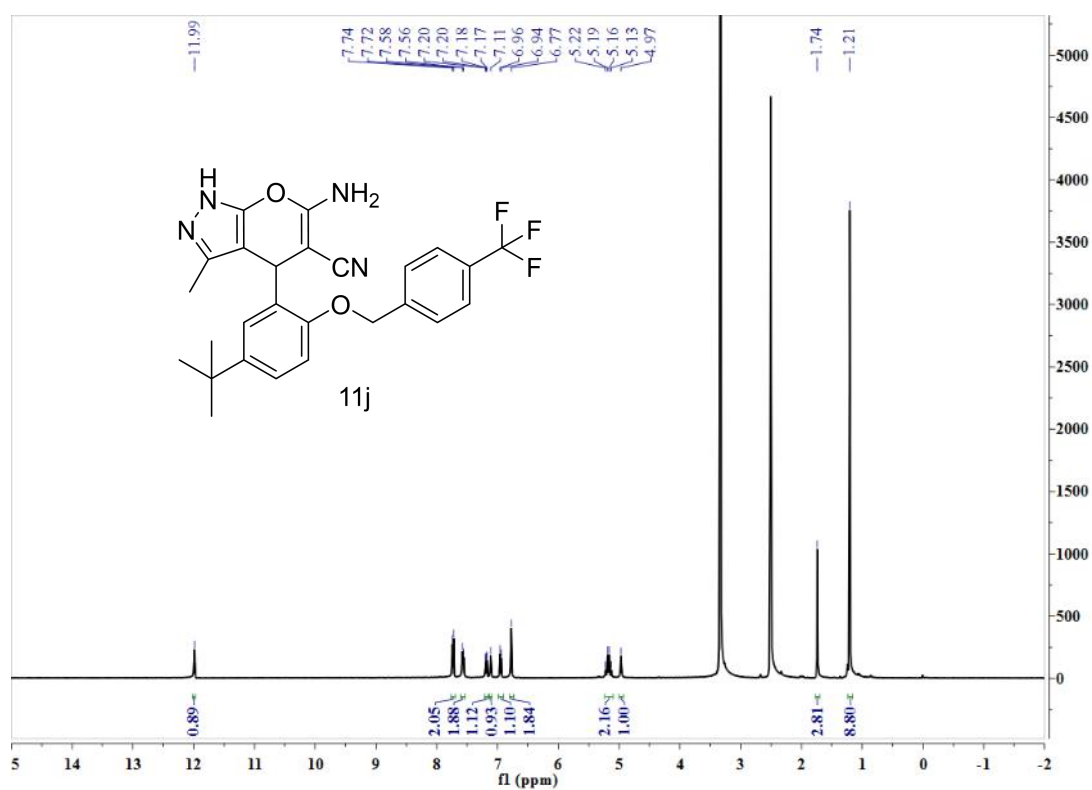


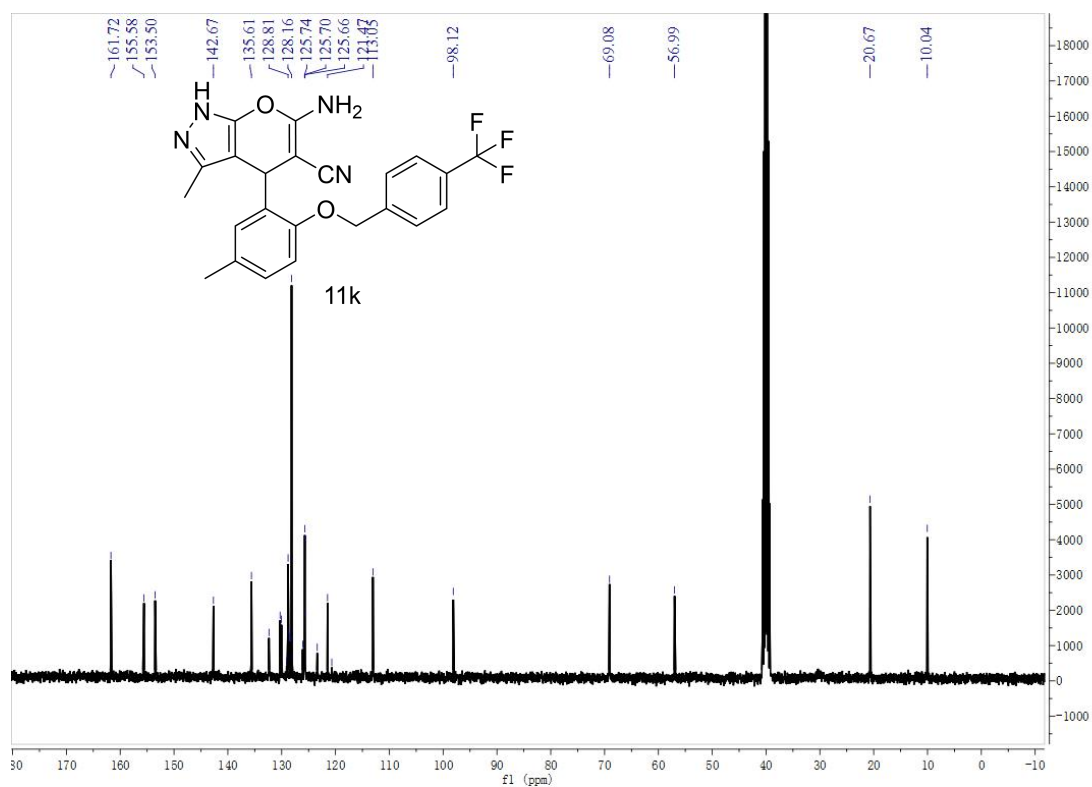
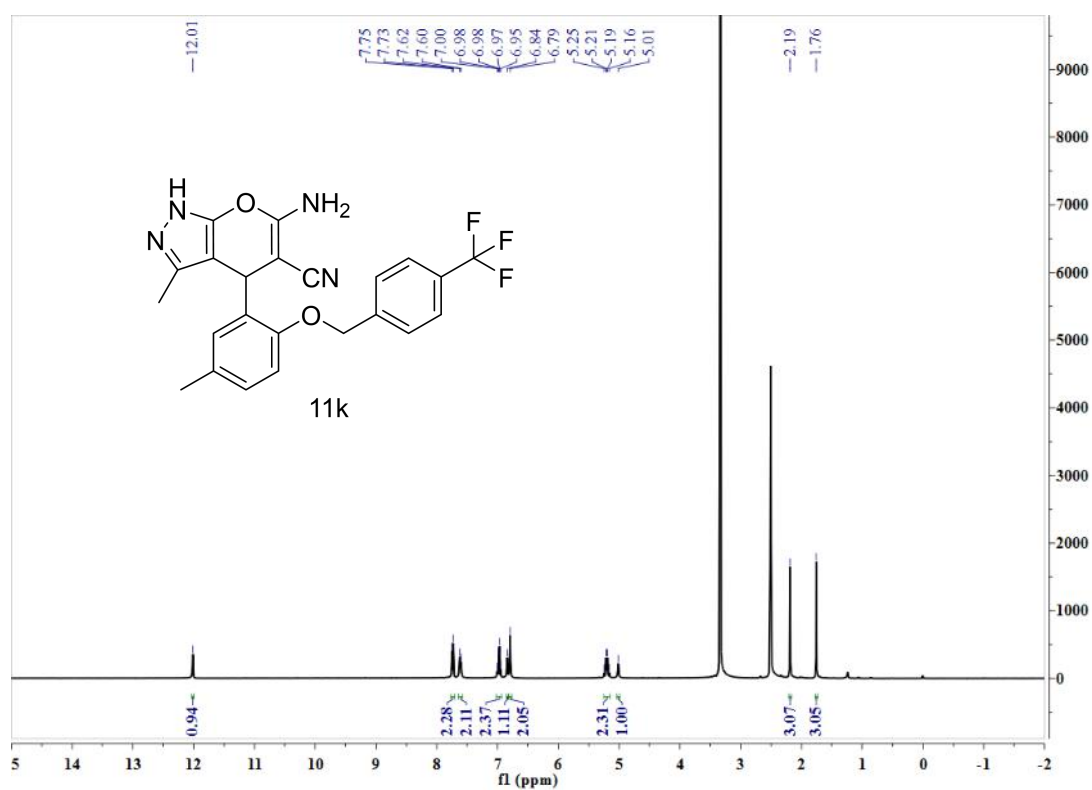


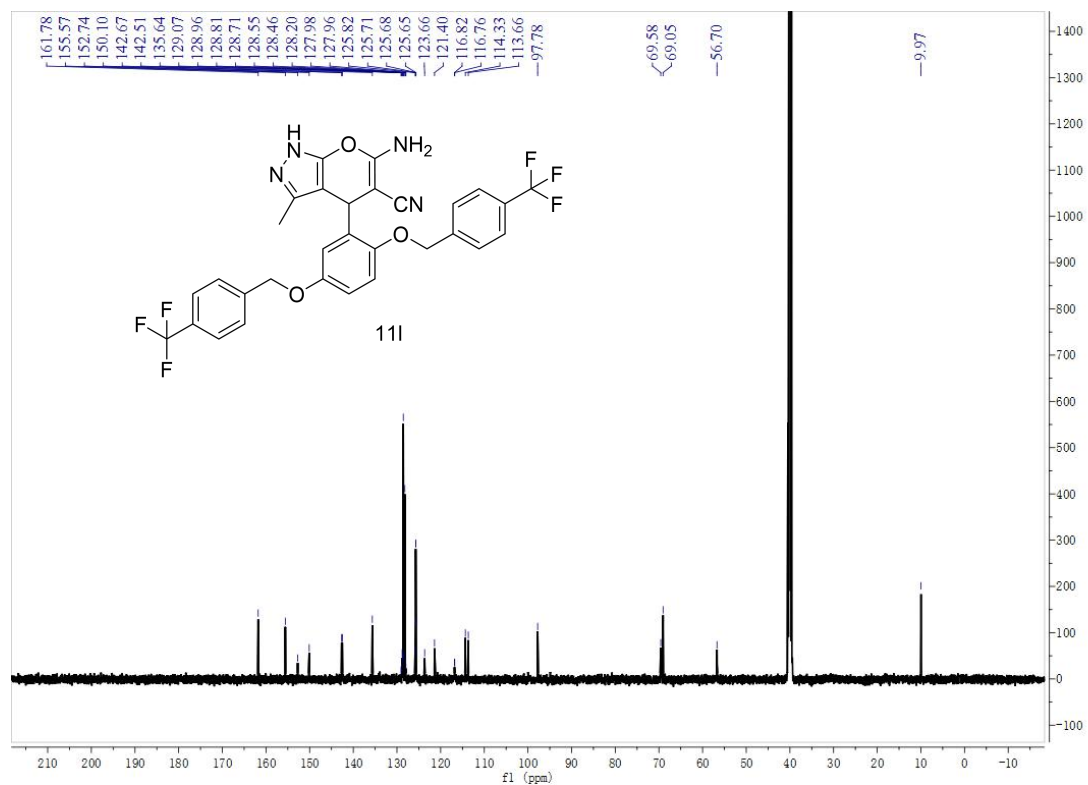
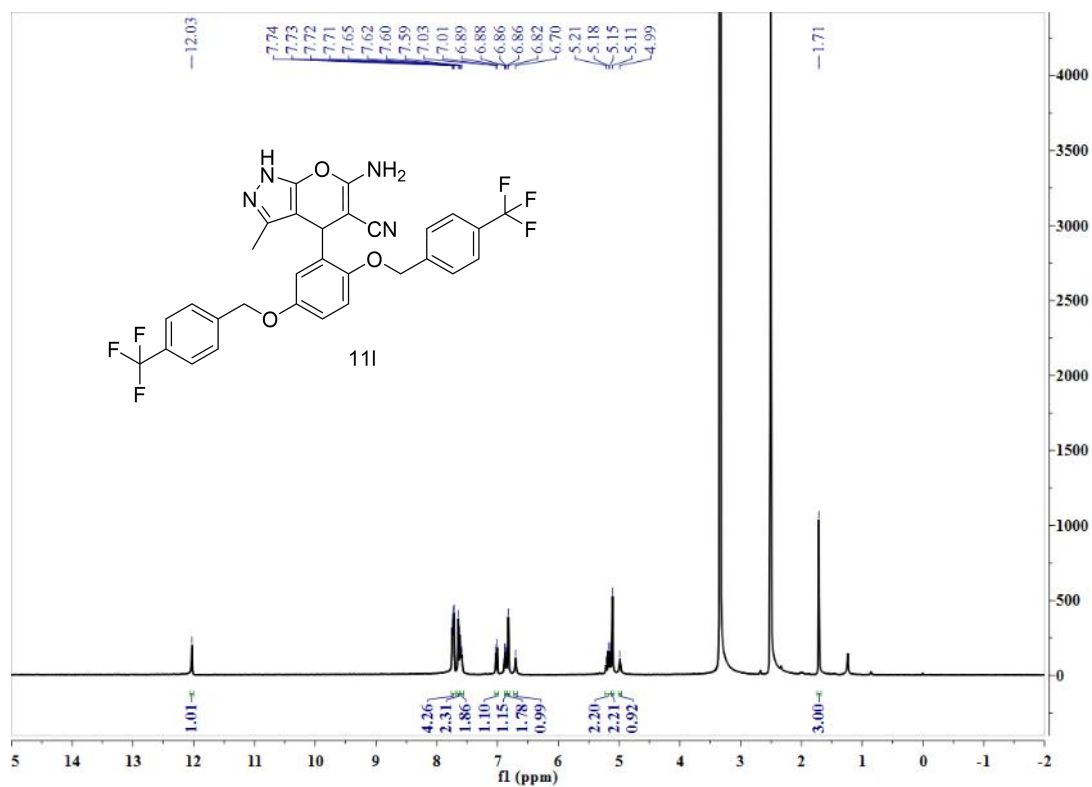


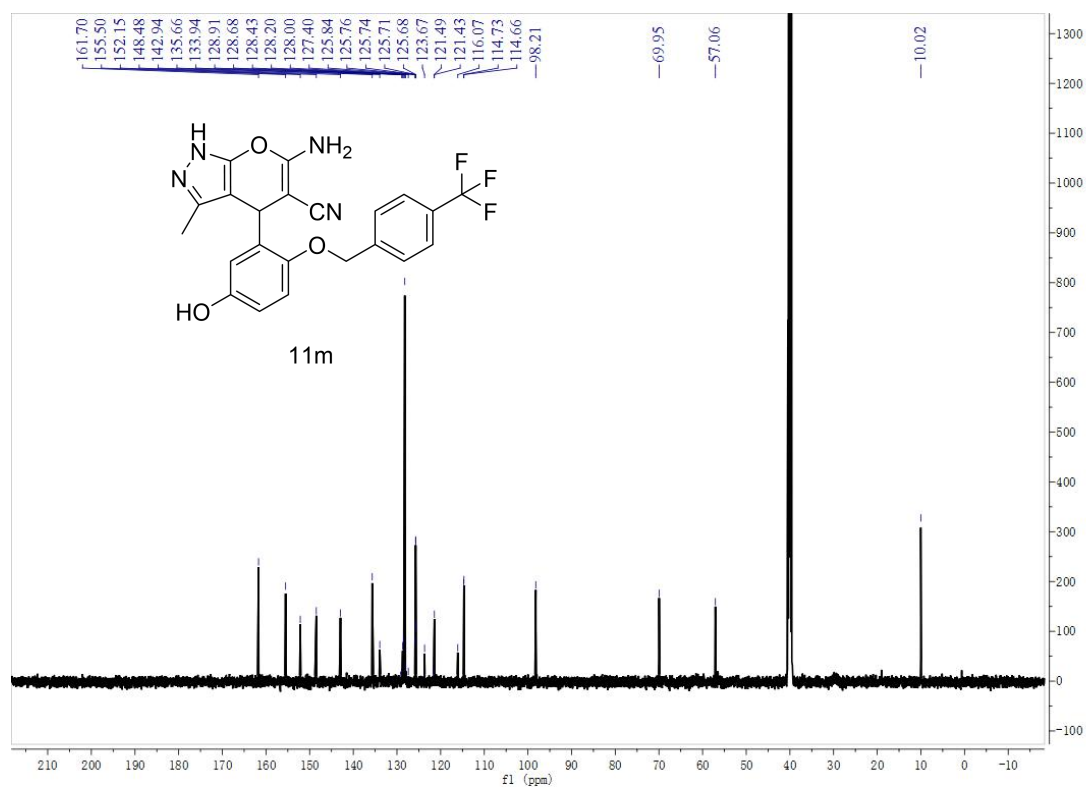
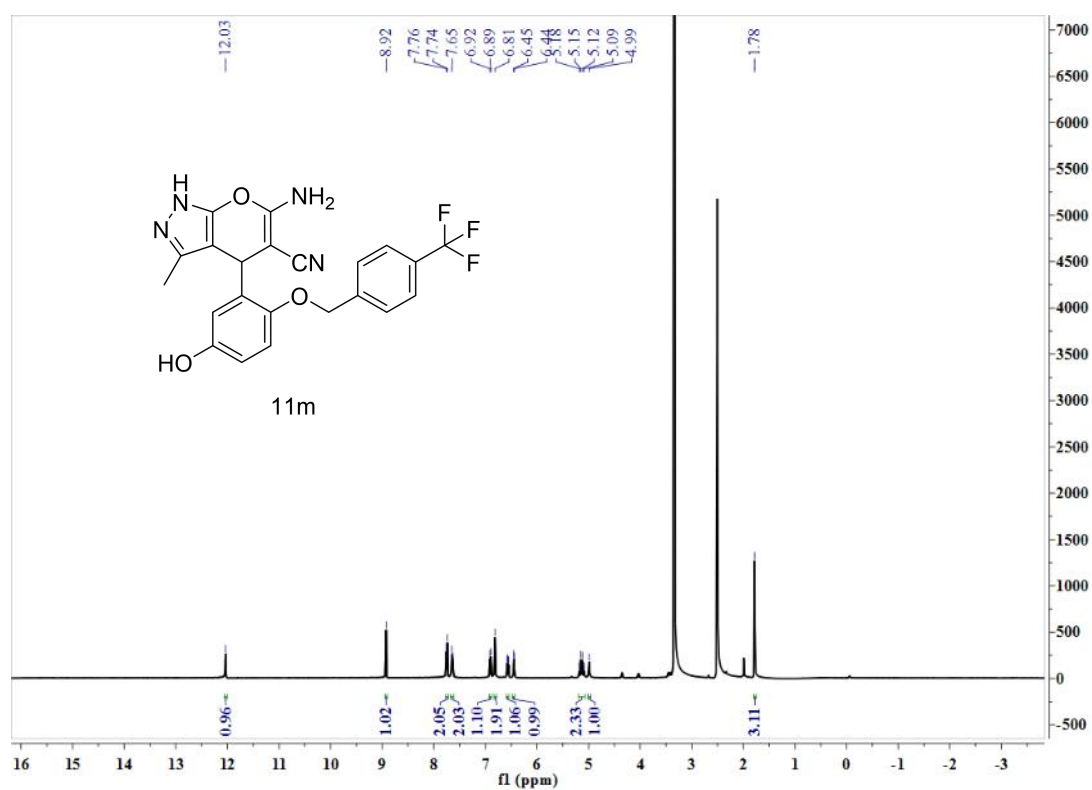


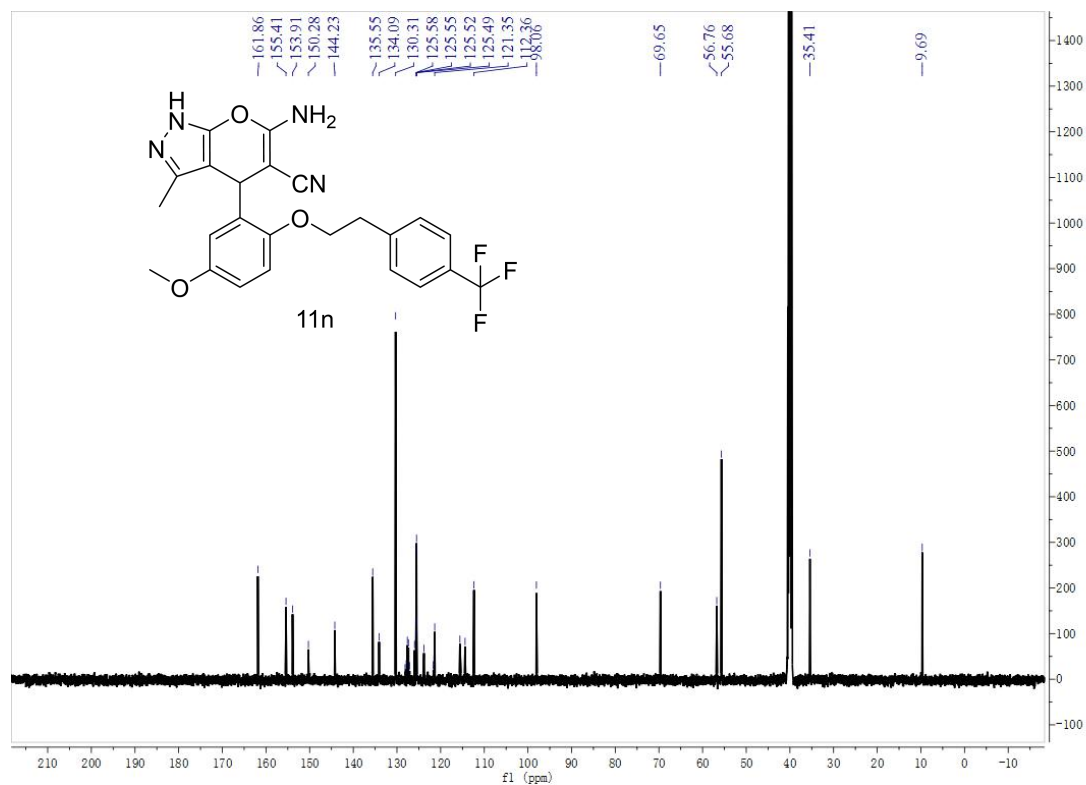
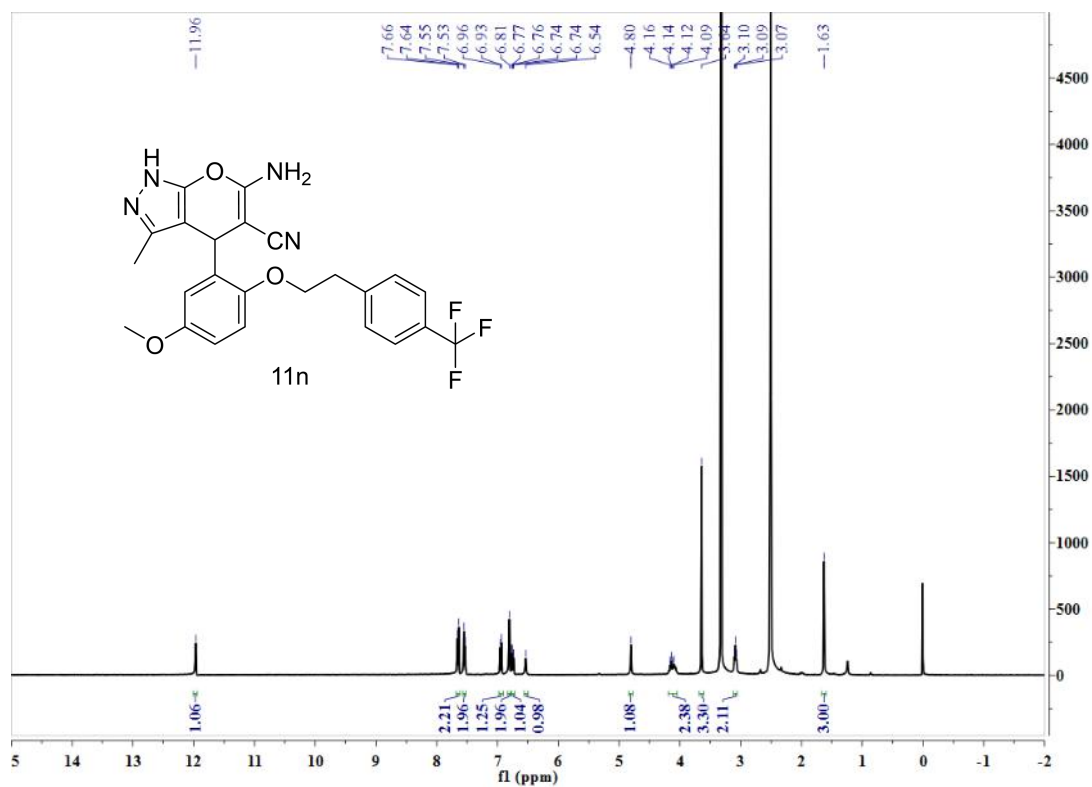


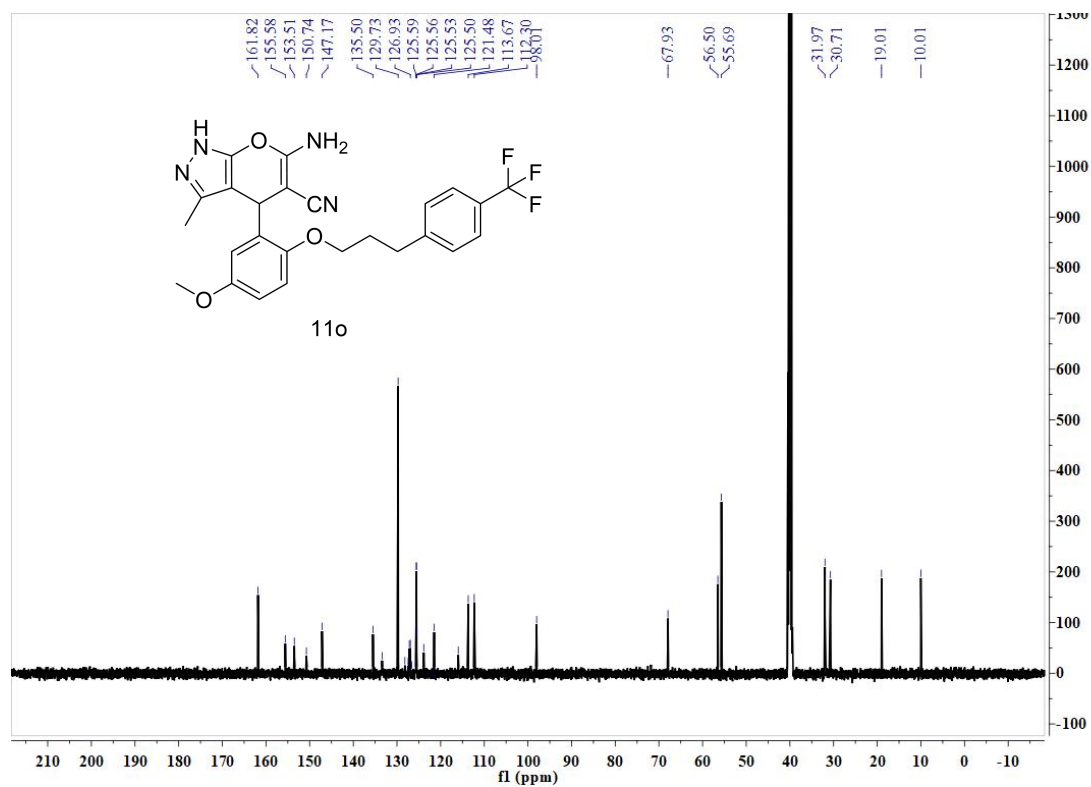
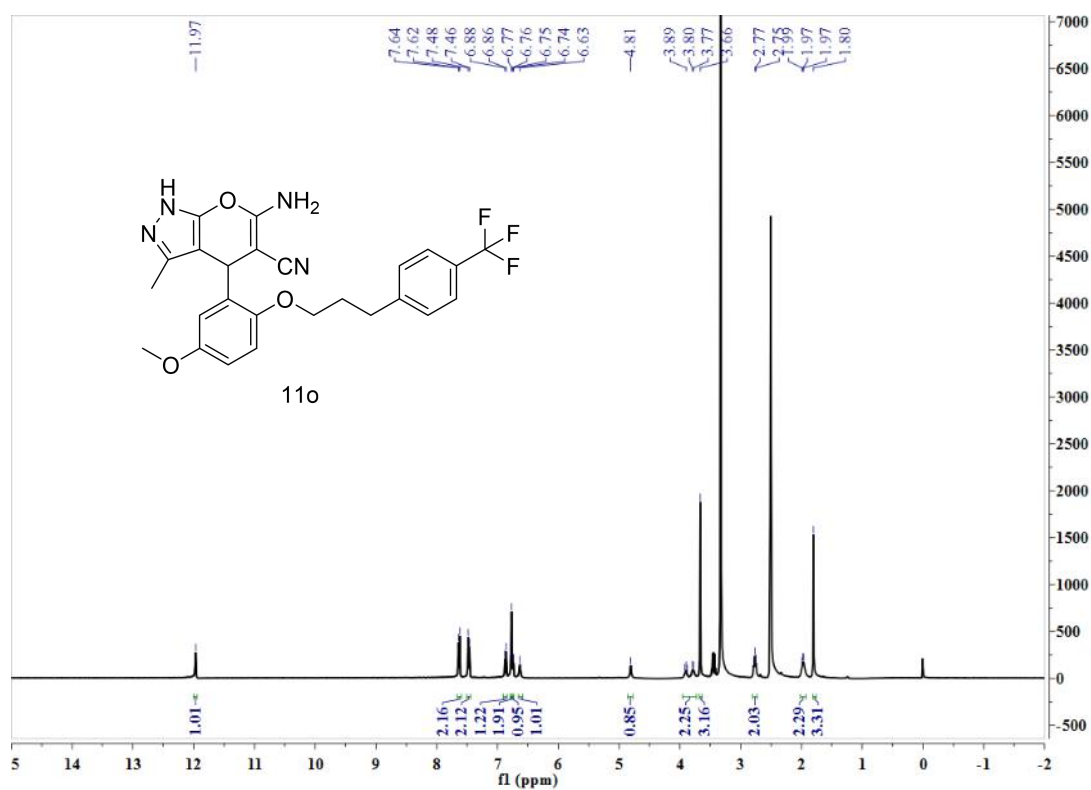


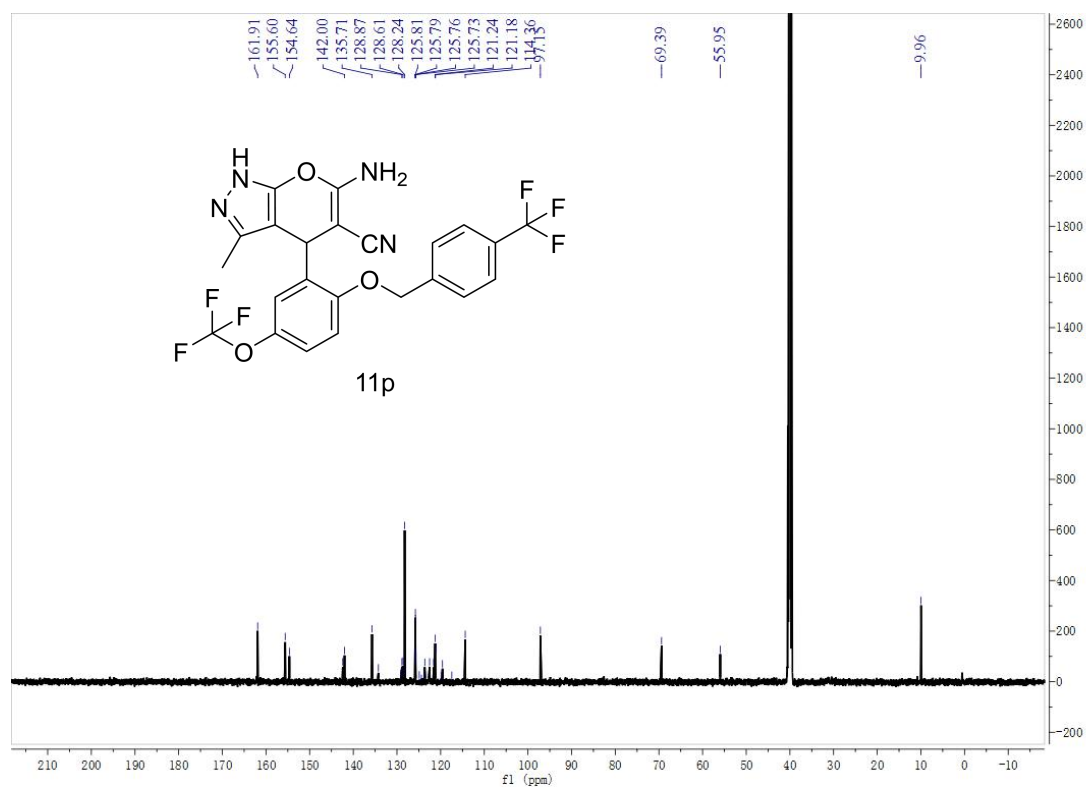
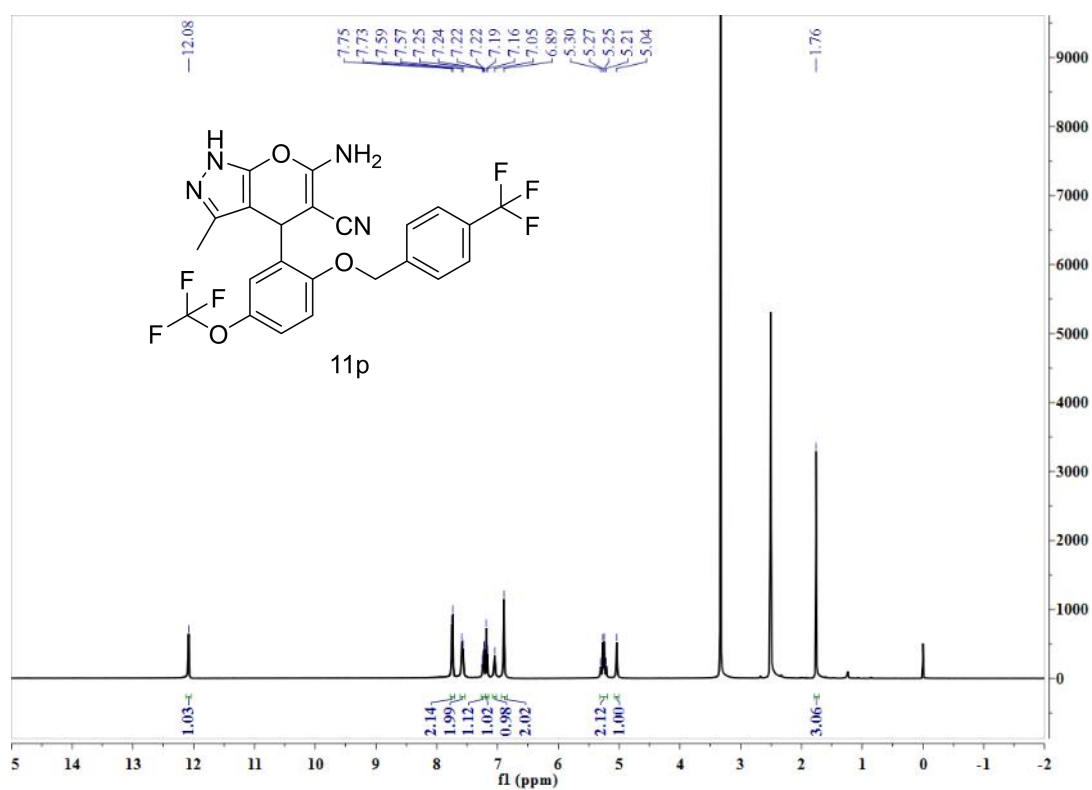




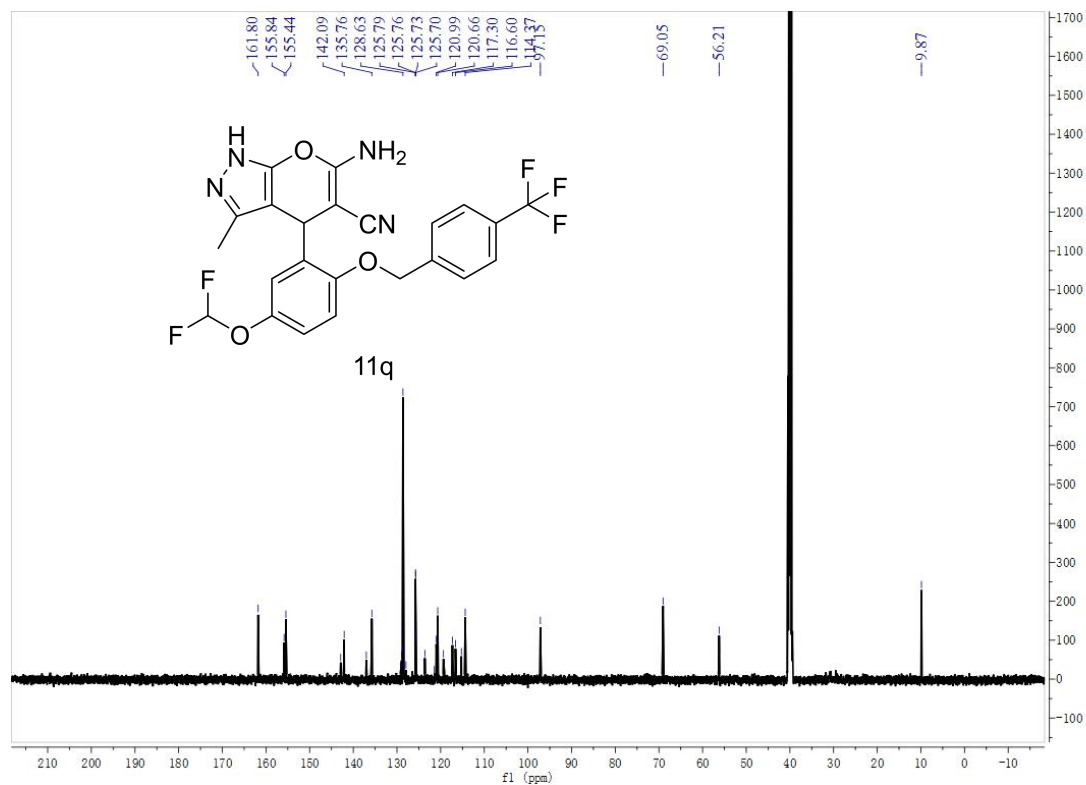
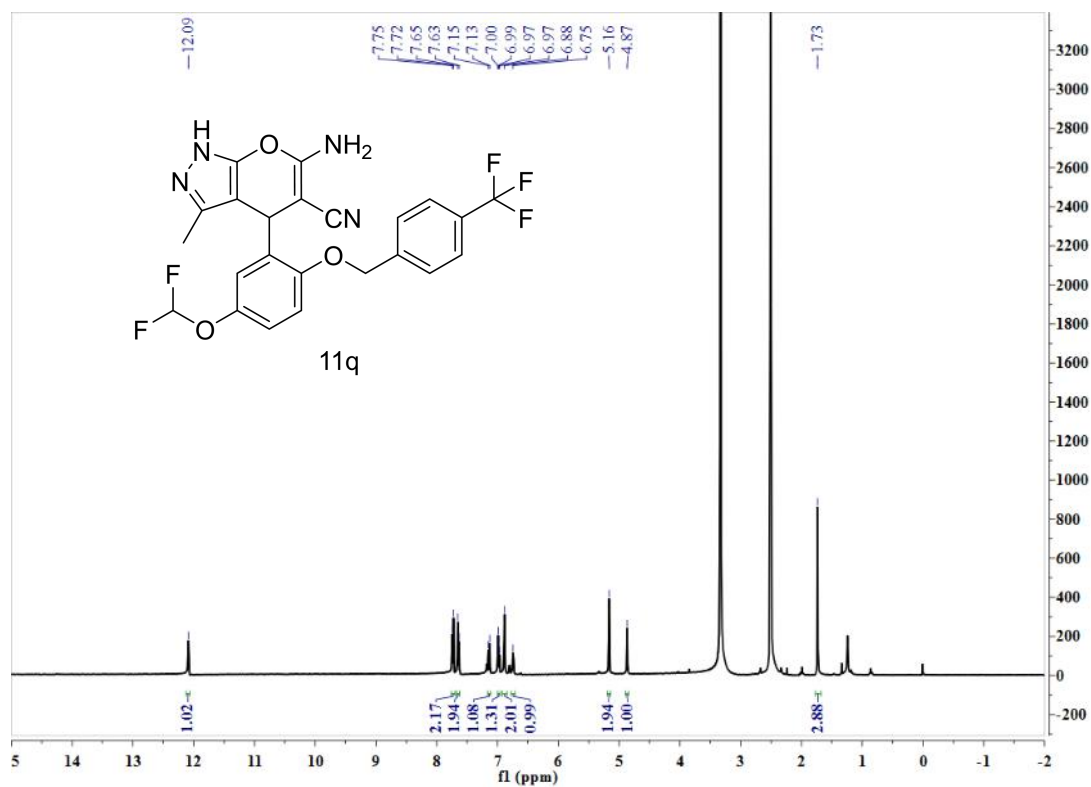


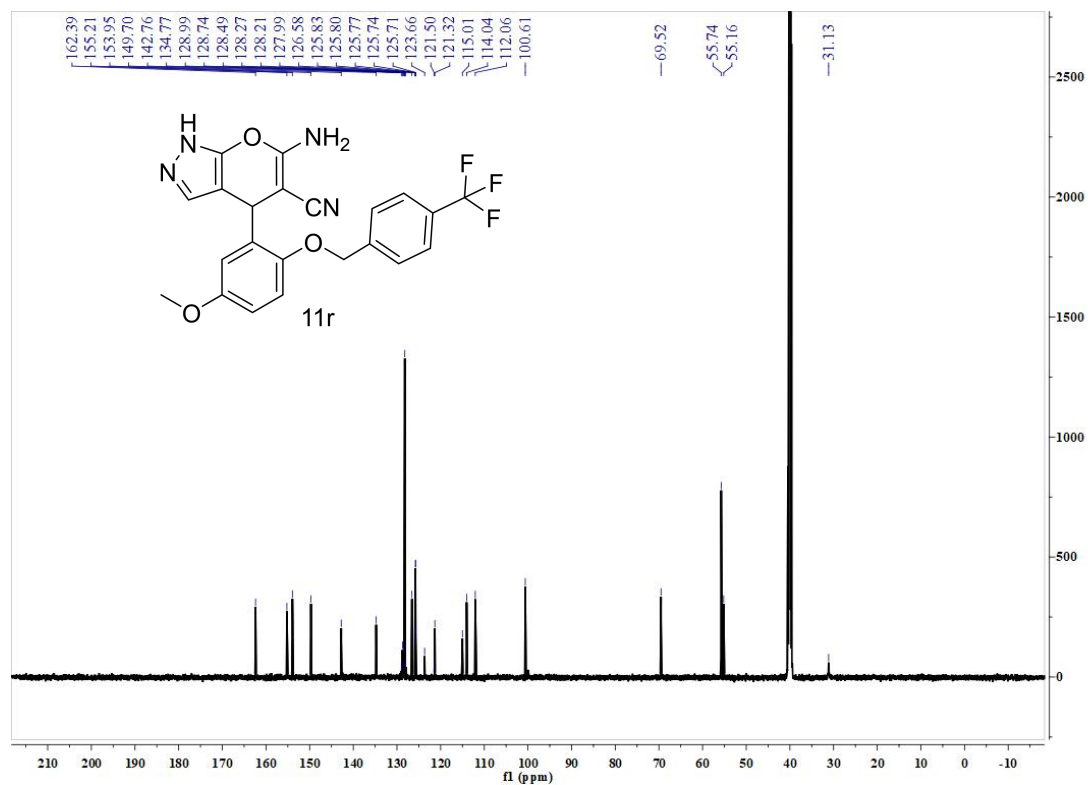
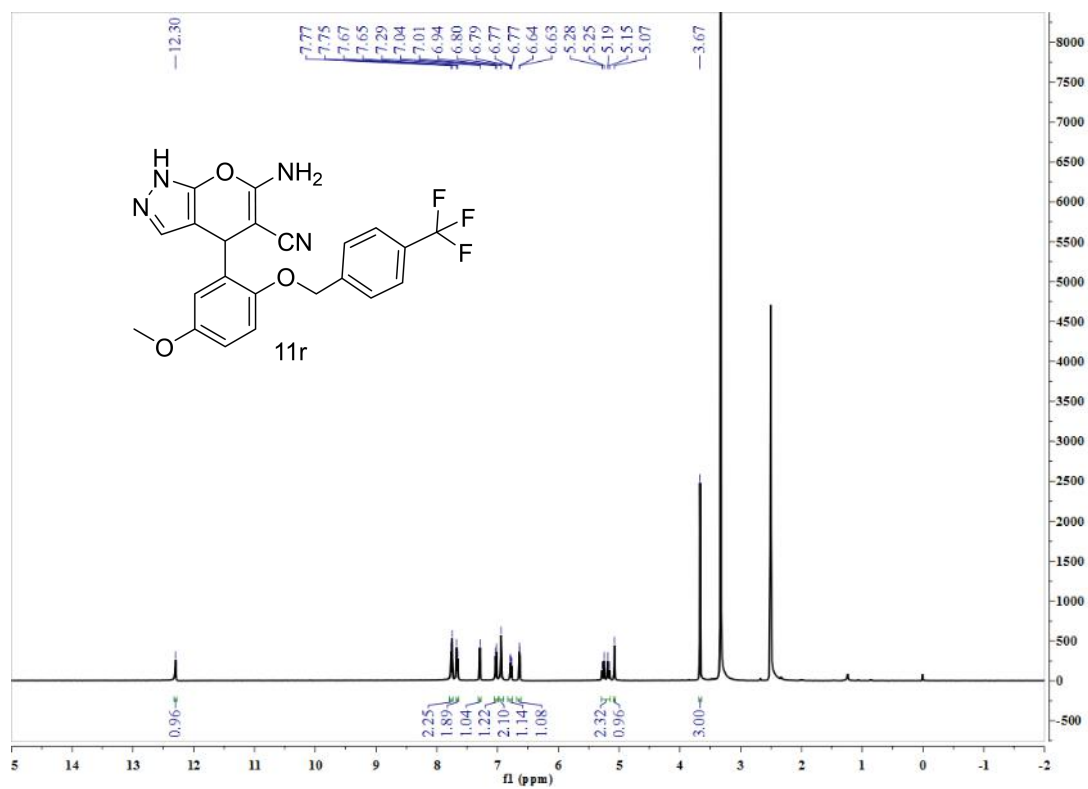


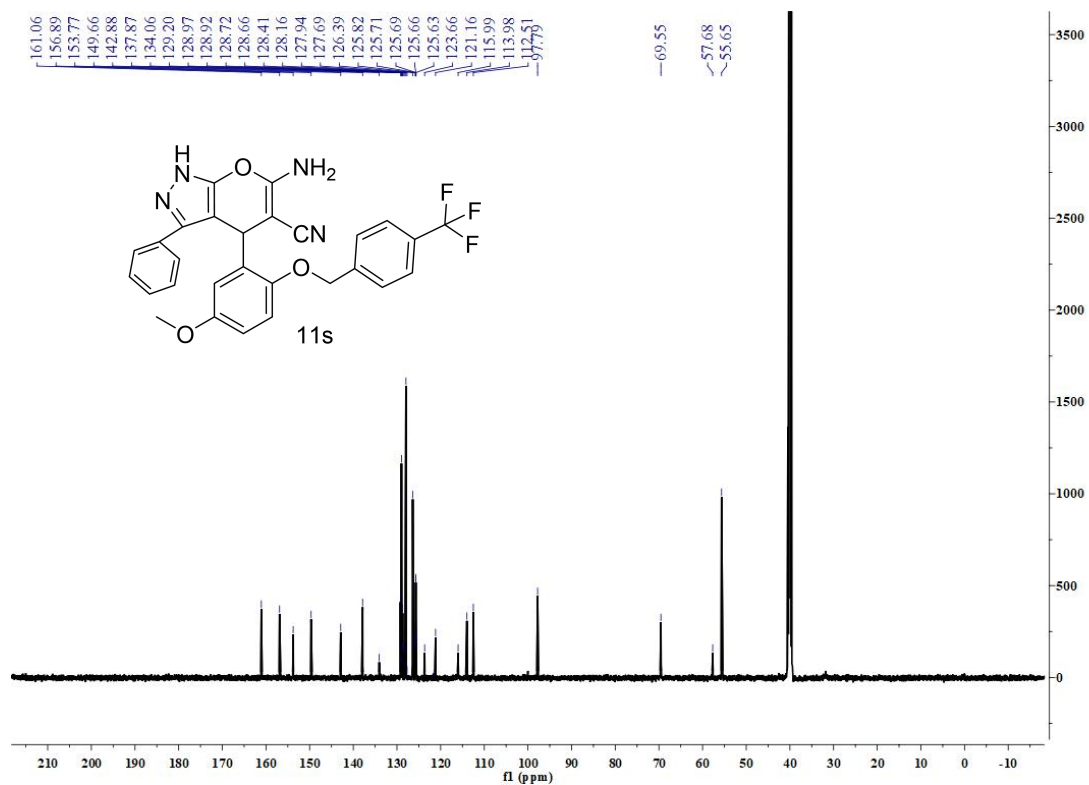
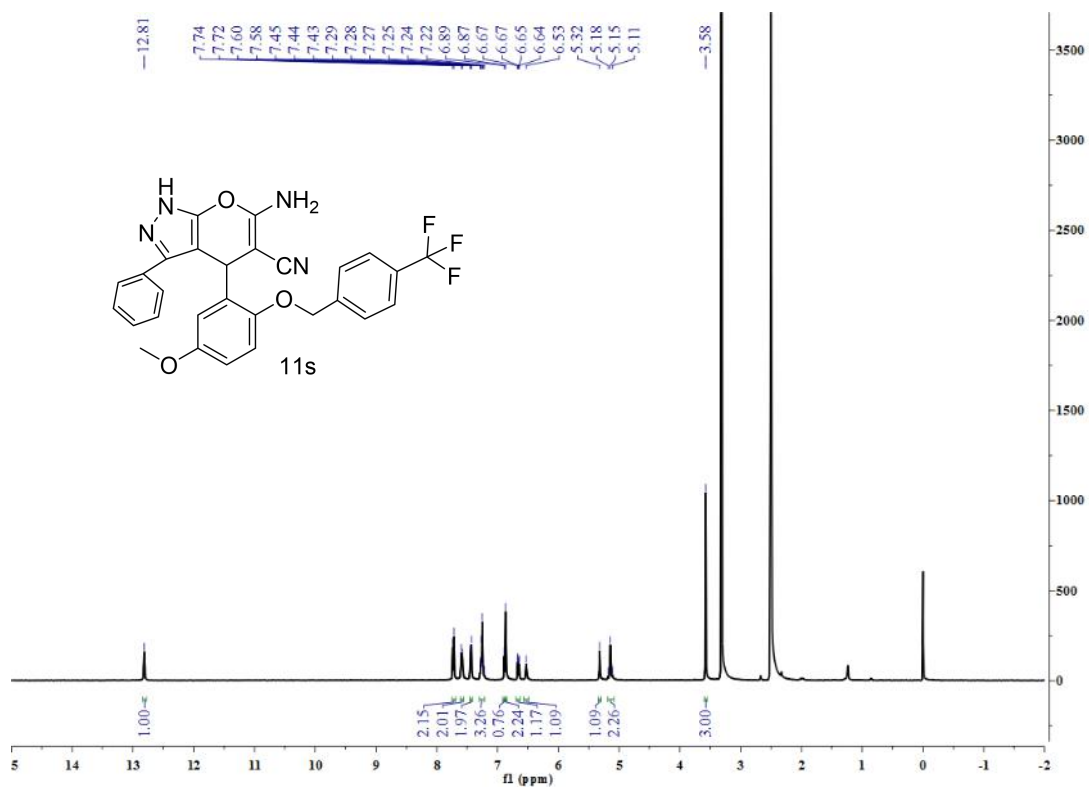


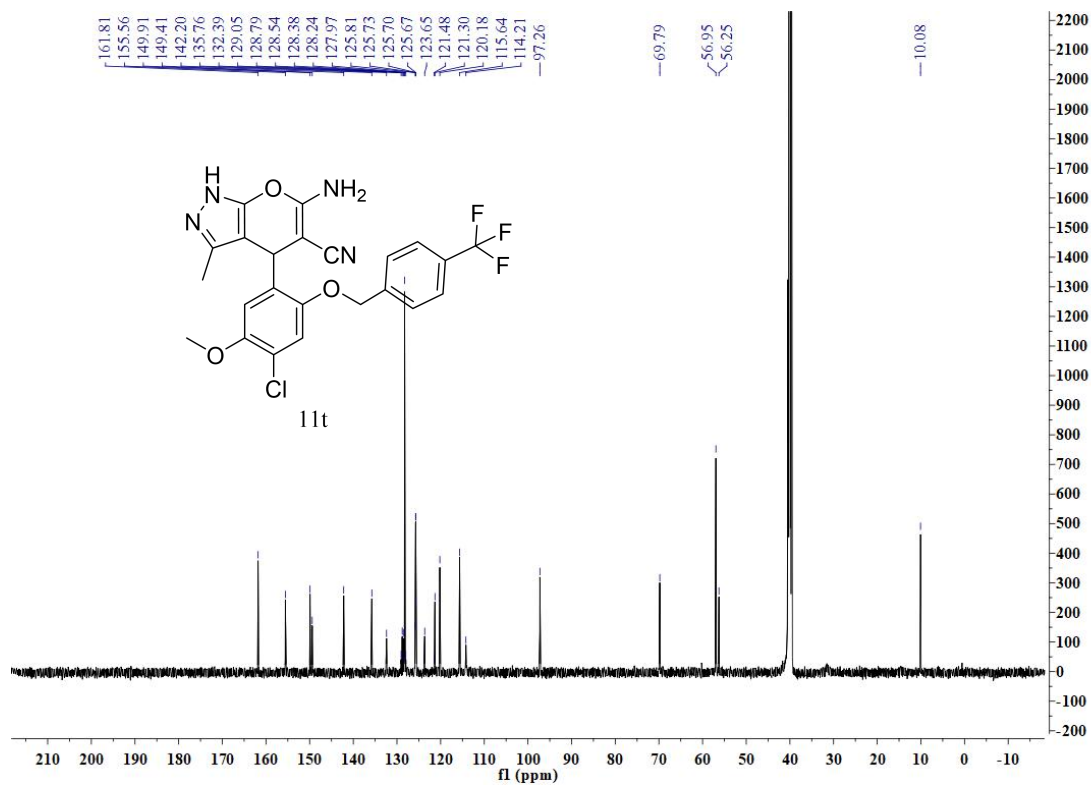
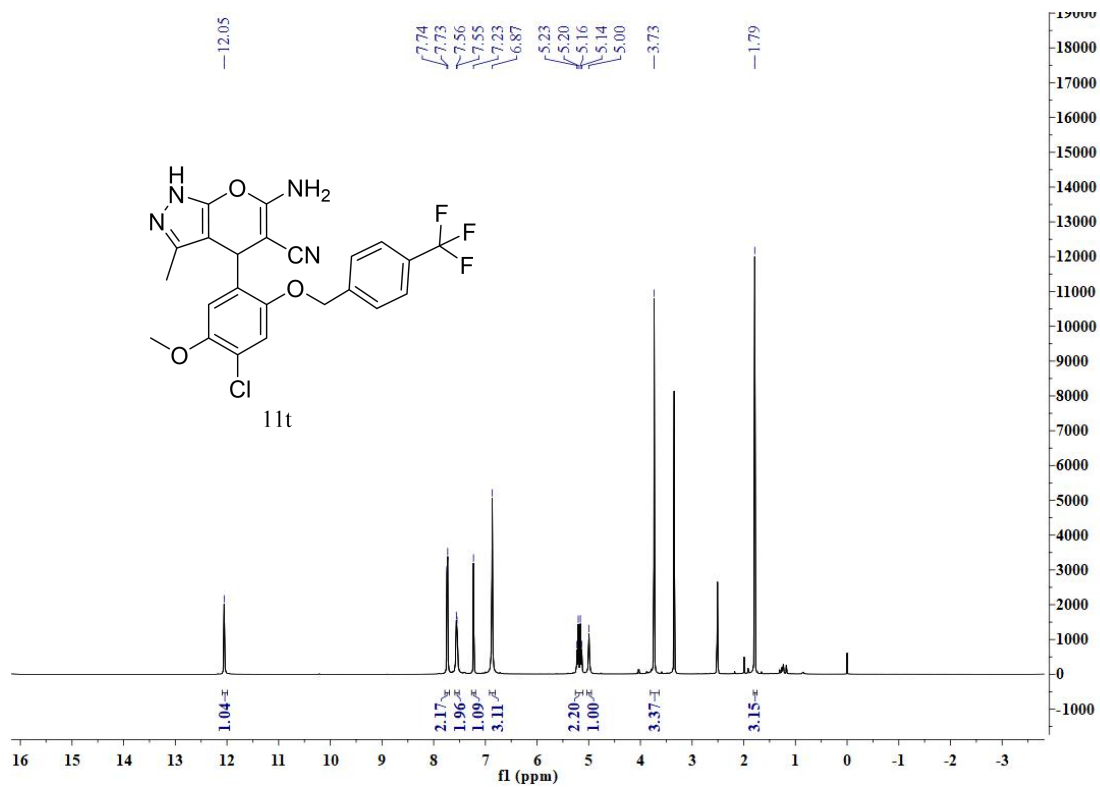


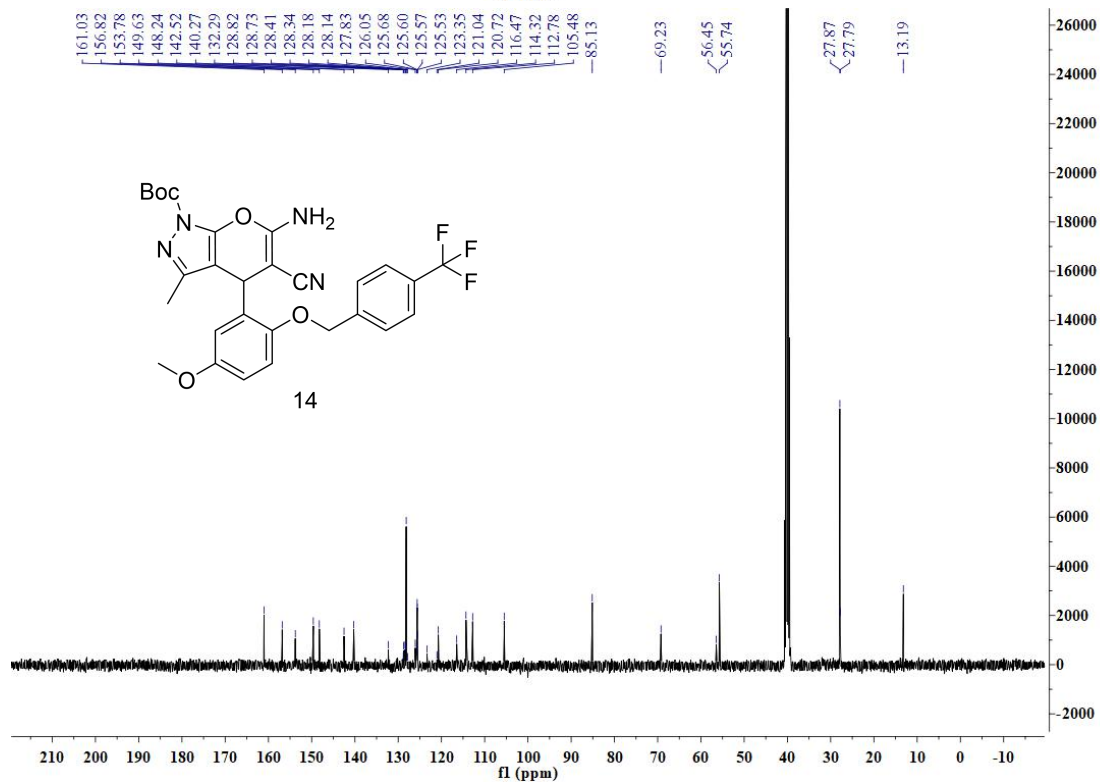
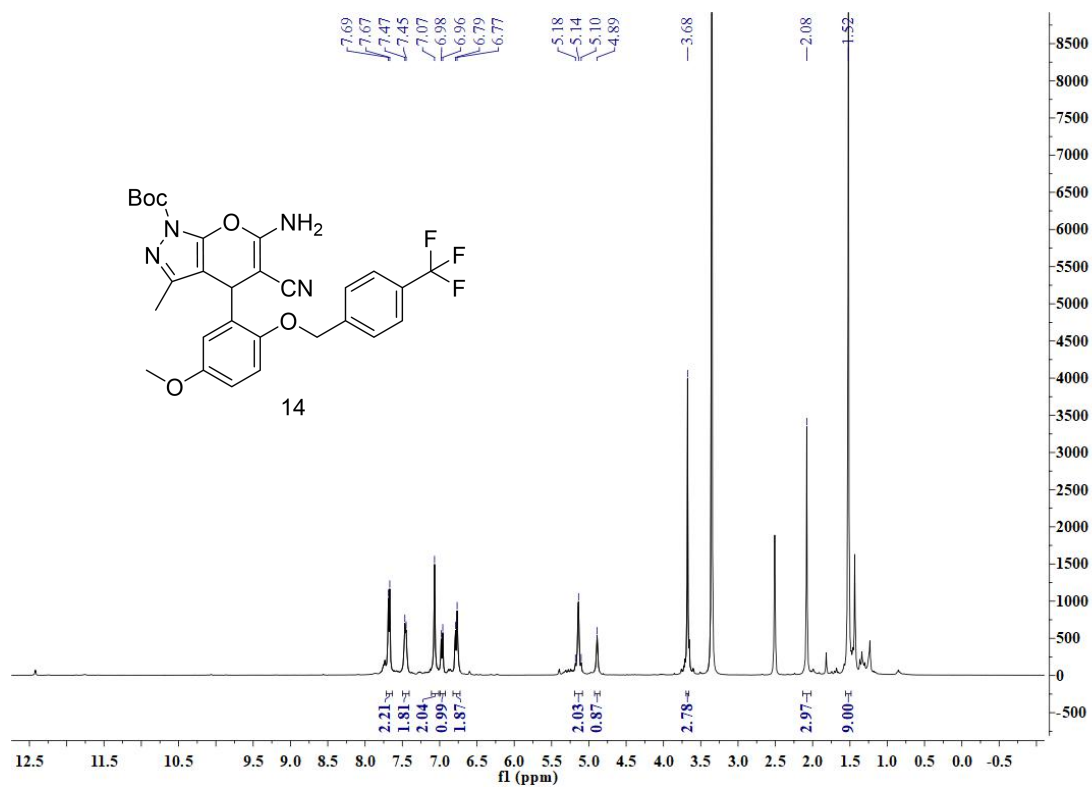


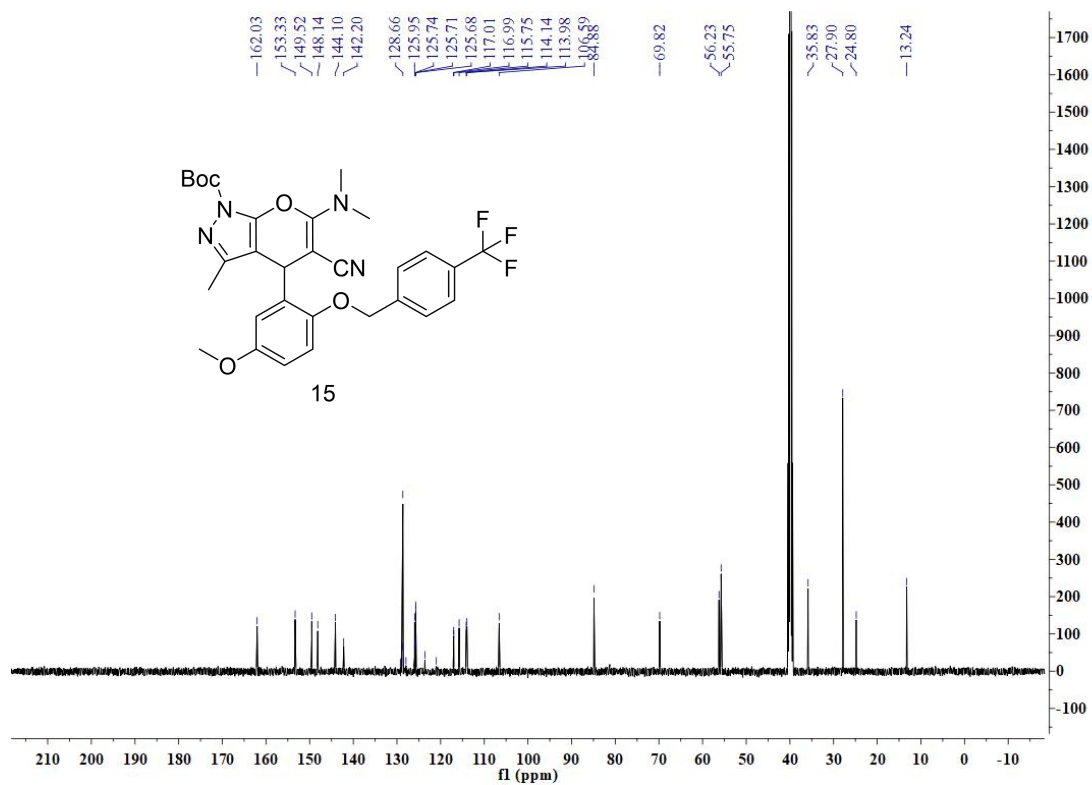
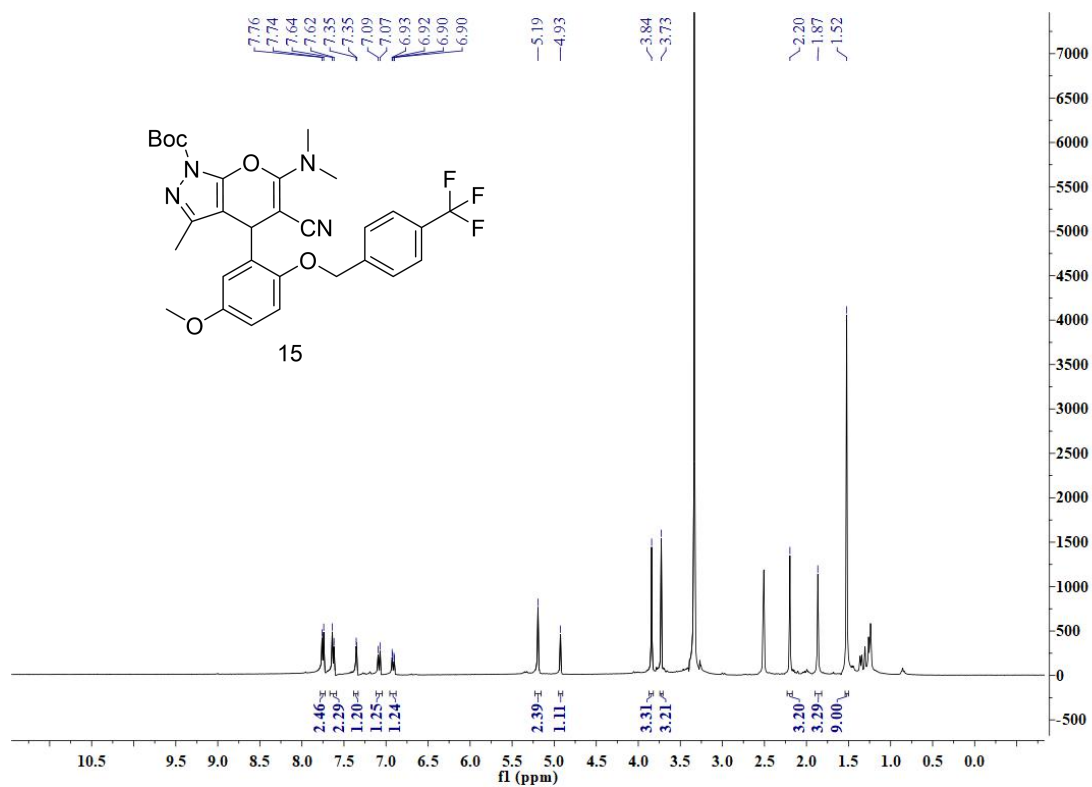


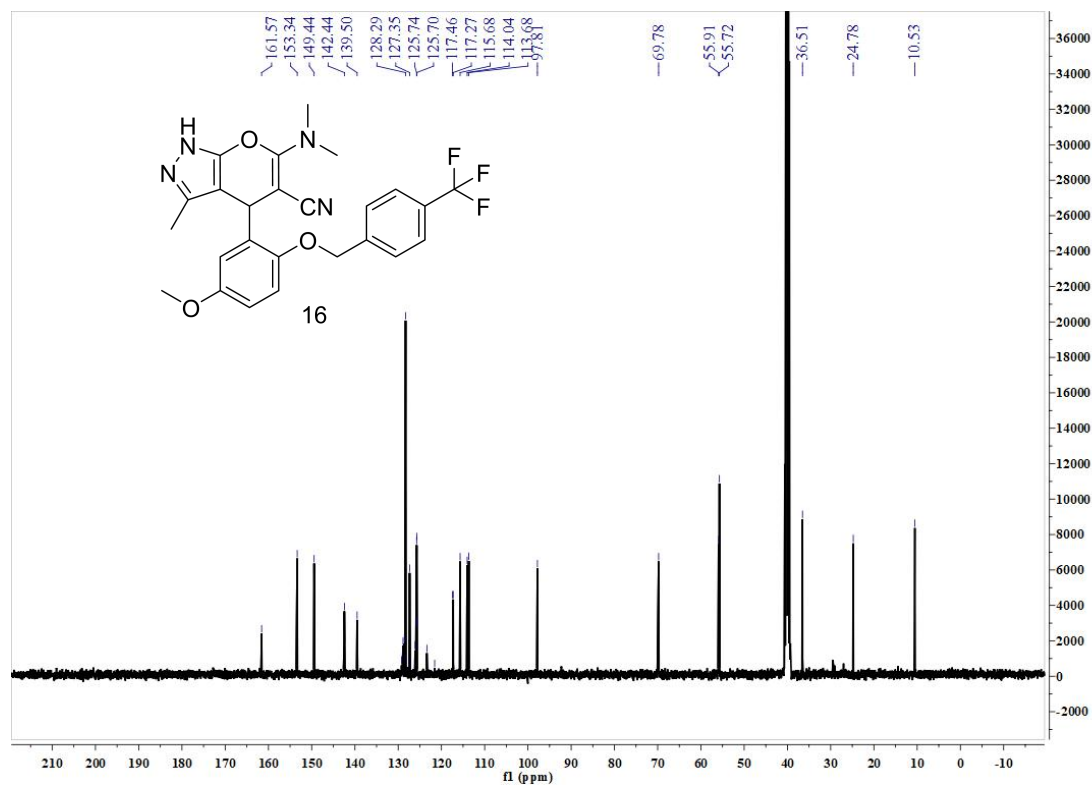
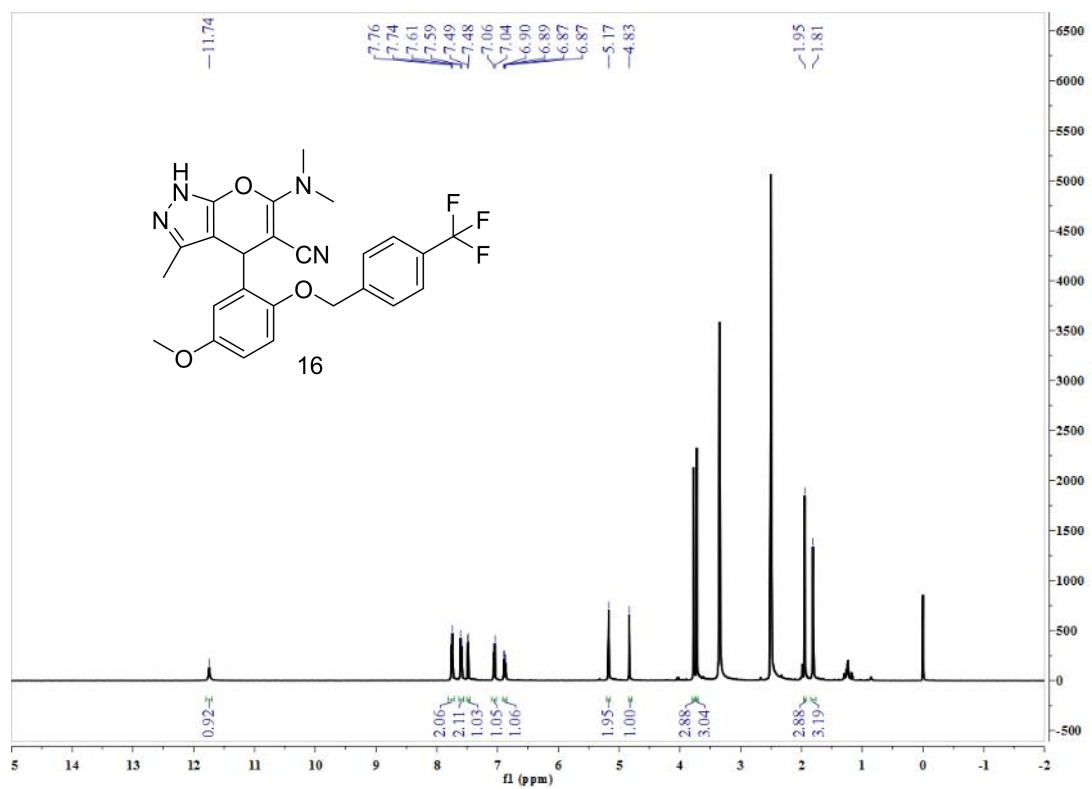












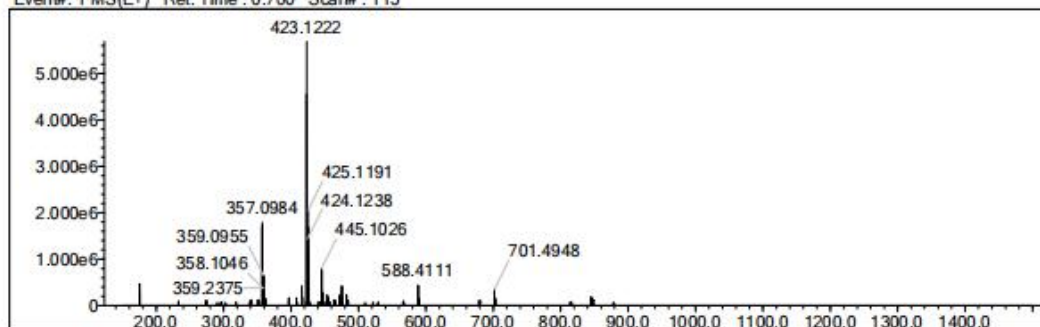
## 2. HRMS spectra of target compounds

### HRMS spectrum of 4a

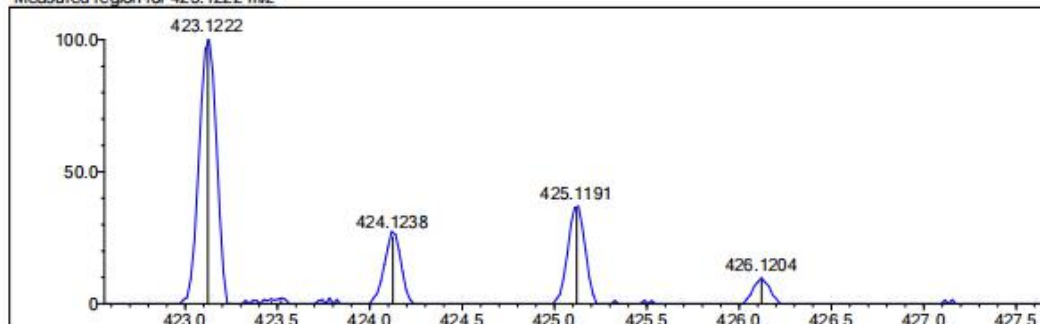
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B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	28	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
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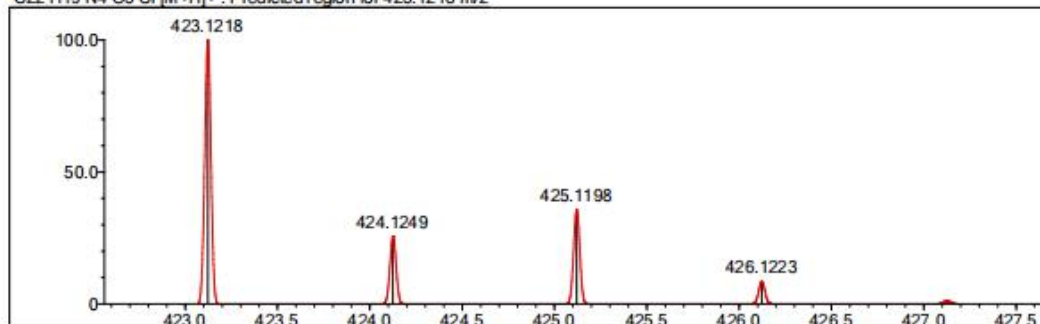
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Measured region for 423.1222 m/z



C22 H19 N4 O3 Cl [M+H]<sup>+</sup>: Predicted region for 423.1218 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	78.64	C22 H19 N4 O3 Cl	[M+H] <sup>+</sup>	423.1222	423.1218	0.4	0.95	78.64	15.0



# HRMS spectrum of **4b**

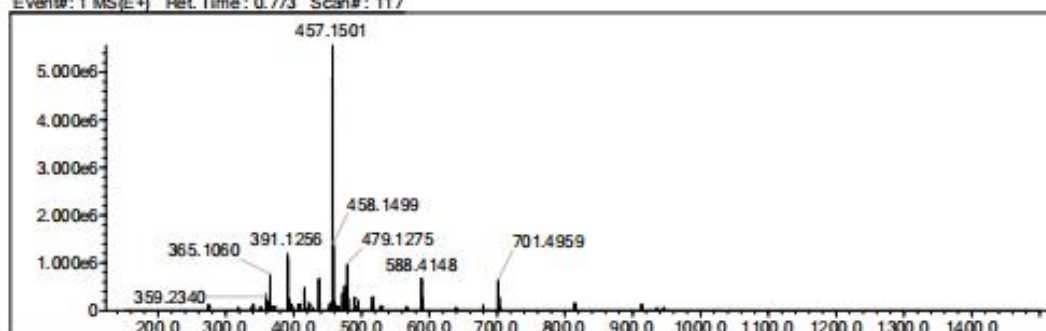
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B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	28	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

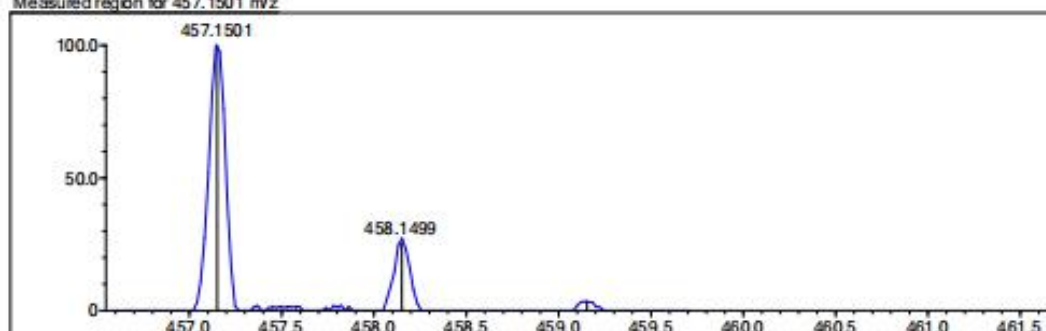
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Electron Ions: both  
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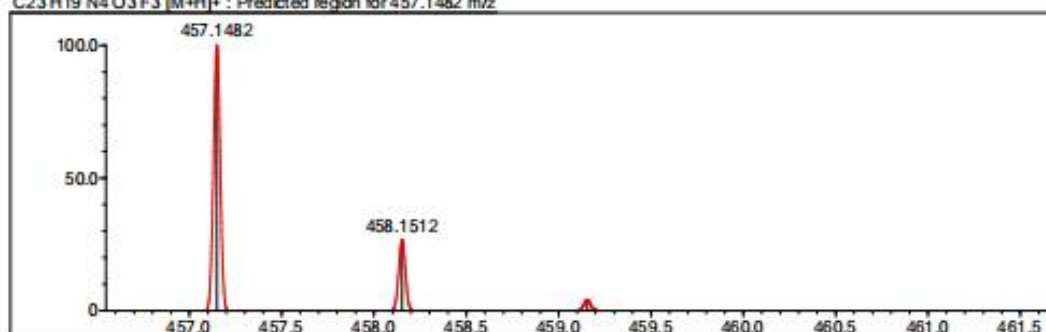
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Measured region for 457.1501 m/z



C23H19N4O3F3 [M+H]<sup>+</sup>: Predicted region for 457.1482 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isot	DBE
5	77.49	C23 H19 N4 O3 F3	[M+H] <sup>+</sup>	457.1501	457.1482	1.9	4.16	84.14	15.0

# HRMS spectrum of 4c

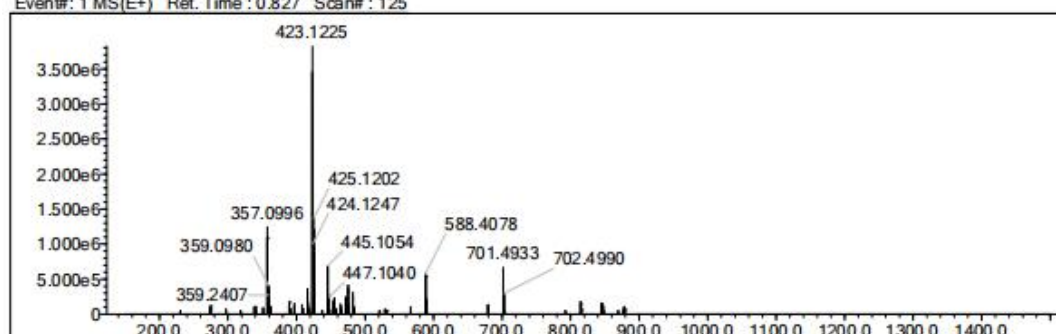
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2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	28	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

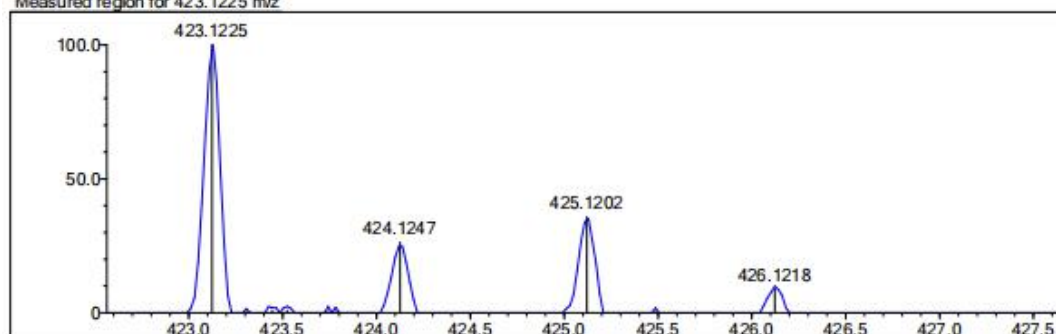
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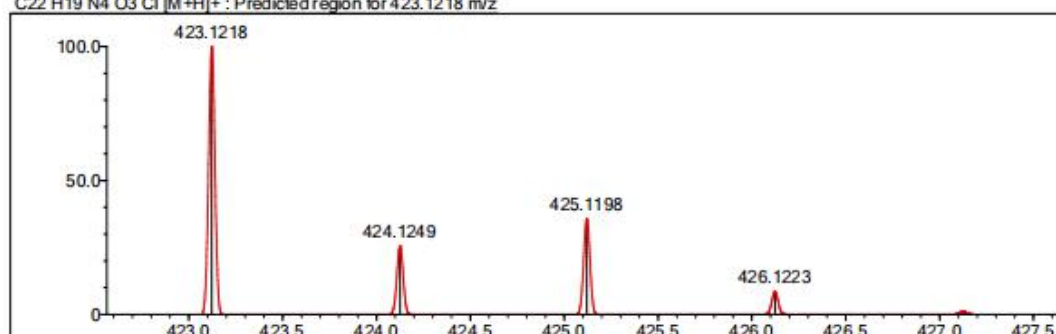
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Measured region for 423.1225 m/z



C22 H19 N4 O3 Cl [M+H]<sup>+</sup> : Predicted region for 423.1218 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	93.26	C22 H19 N4 O3 Cl	[M+H] <sup>+</sup>	423.1225	423.1218	0.7	1.65	94.80	15.0

# HRMS spectrum of 8a

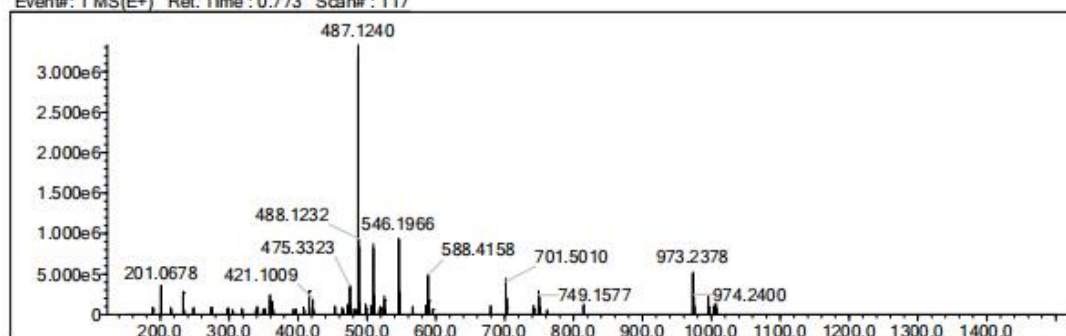
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2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	23	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
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Max Isotopes: all  
MSn Iso RI (%): 75.00

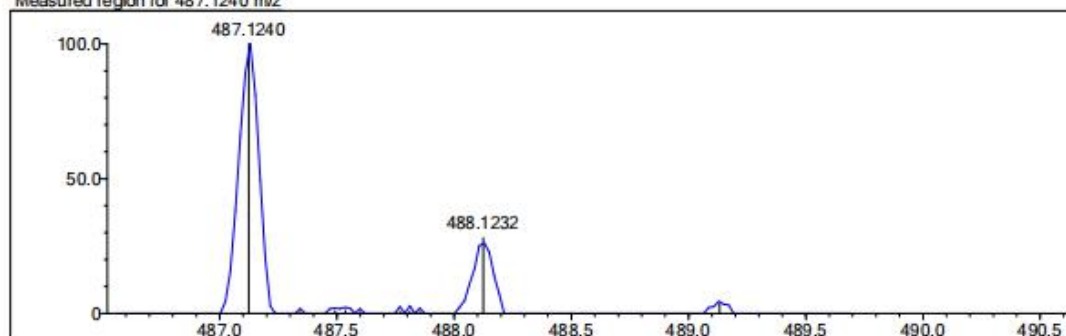
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MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

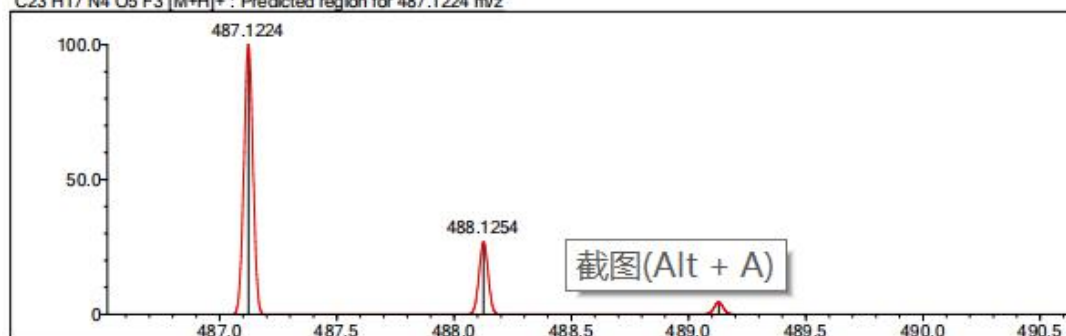
Event#: 1 MS(E+) Ret. Time : 0.773 Scan#: 117



Measured region for 487.1240 m/z



C23 H17 N4 O5 F3 [M+H]<sup>+</sup> : Predicted region for 487.1224 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	82.22	C23 H17 N4 O5 F3	[M+H] <sup>+</sup>	487.1240	487.1224	1.6	3.28	87.19	16.0

# HRMS spectrum of **8b**

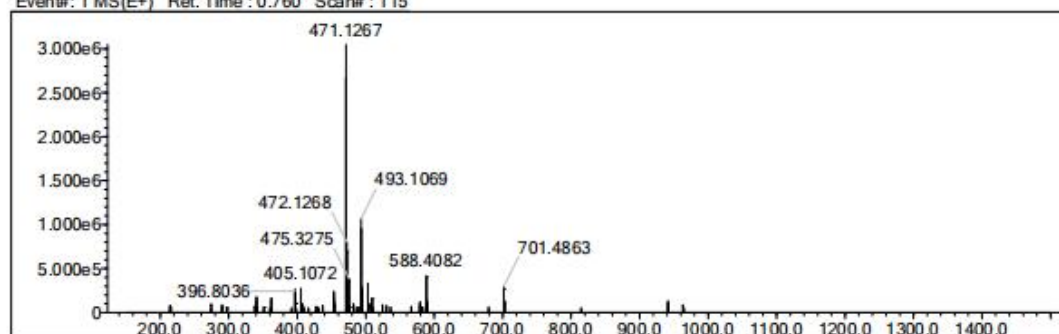
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

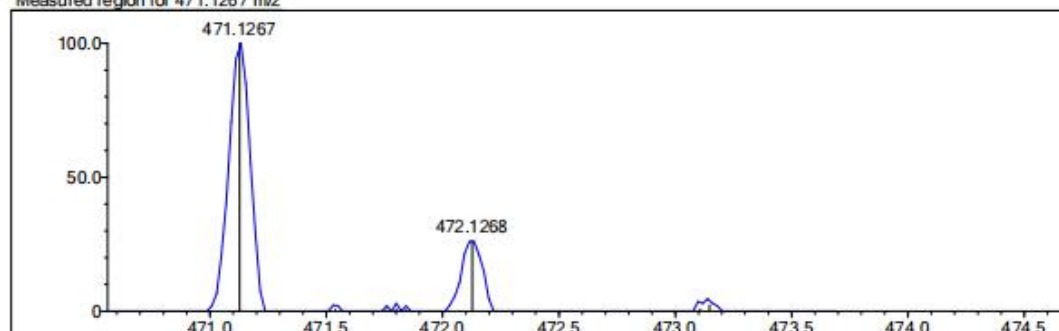
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

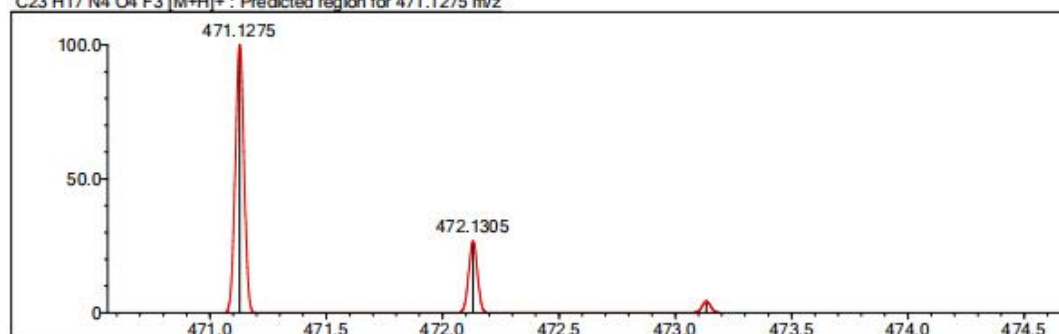
Event#: 1 MS(E+) Ret. Time : 0.760 Scan# : 115



Measured region for 471.1267 m/z



C23 H17 N4 O4 F3 [M+H]<sup>+</sup> : Predicted region for 471.1275 m/z



Rank	Score	Formula (M)	Ion	Mess. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
5	87.87	C23 H17 N4 O4 F3	[M+H] <sup>+</sup>	471.1267	471.1275	-0.8	-1.70	89.44	16.0

# HRMS spectrum of **8c**

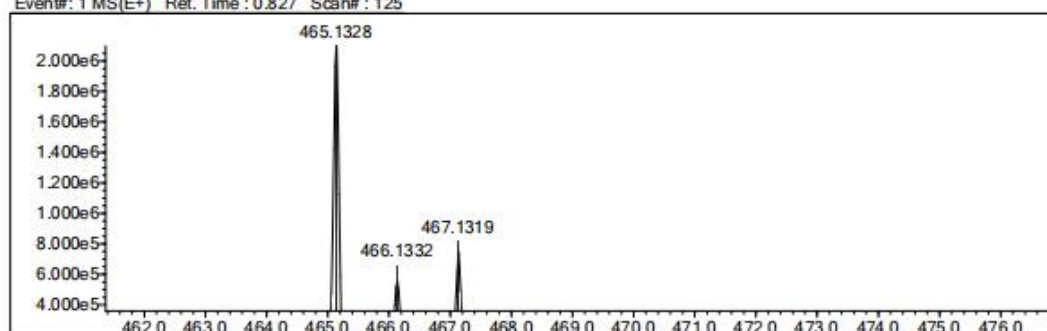
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

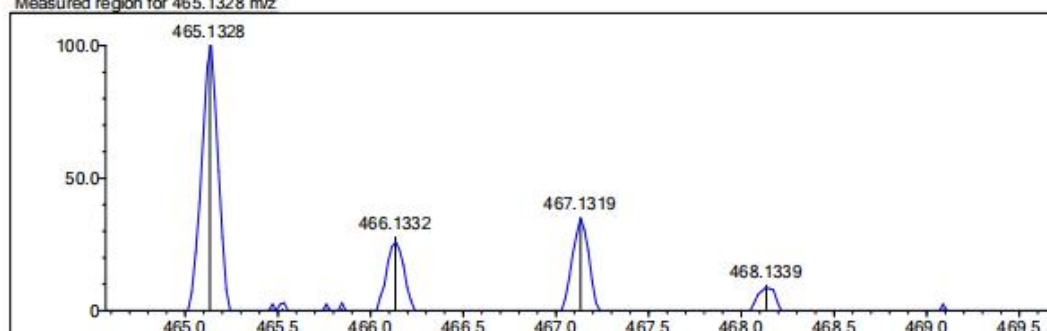
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

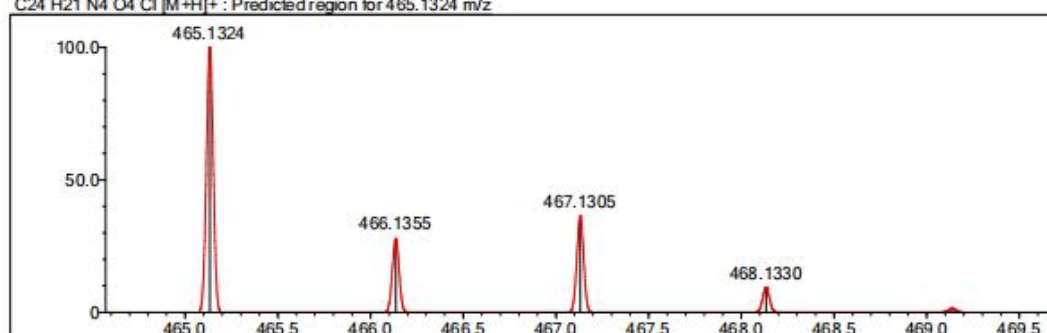
Event#: 1 MS(E+) Ret. Time : 0.827 Scan#: 125



Measured region for 465.1328 m/z



C24 H21 N4 O4 Cl [M+H]<sup>+</sup> : Predicted region for 465.1324 m/z



Rank	Score	Formula (M)	Ion	Mess. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
6	89.13	C24 H21 N4 O4 Cl	[M+H] <sup>+</sup>	465.1328	465.1324	0.4	0.86	89.13	16.0



# HRMS spectrum of **8d**

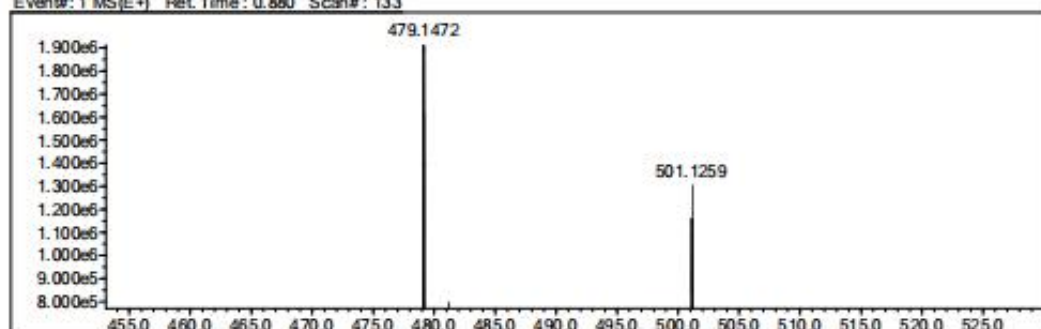
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

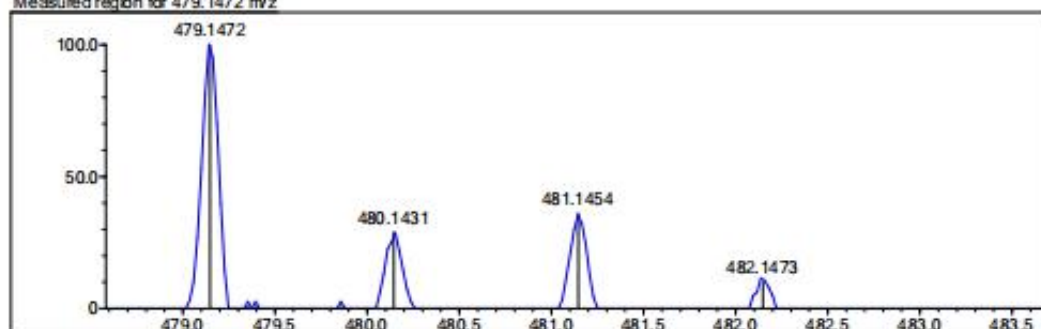
DBE Range: -100.0 - 100.0  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

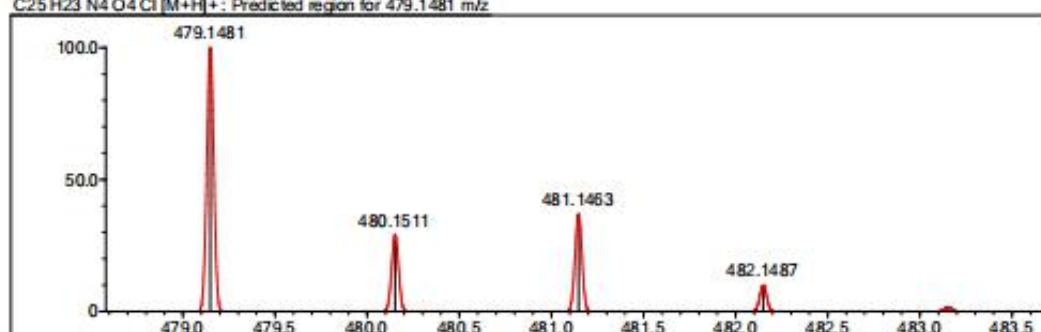
Event#: 1 MS(E+) Ret. Time: 0.880 Scan#: 133



Measured region for 479.1472 m/z



C25 H23 N4 O4 Cl [M+H]<sup>+</sup>: Predicted region for 479.1481 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isot	DBE
5	95.78	C25 H23 N4 O4 Cl	[M+H] <sup>+</sup>	479.1472	479.1481	-0.9	-1.88	97.94	16.0

# HRMS spectrum of 11a

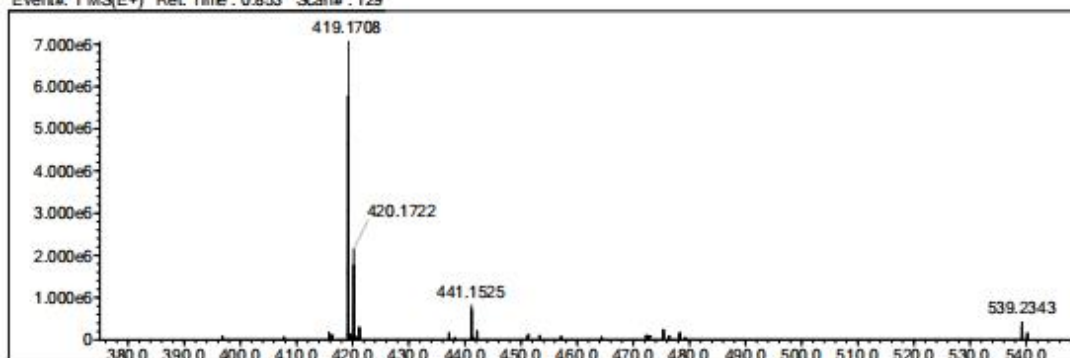
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	O	2	0	4	S	2	0	0	Br	1	0	0	H
2H	1	0	0	18O	2	0	0	Cl	1	0	0	Pd	2	0	0	
B	3	0	0	F	1	0	0	K	1	0	0	I	3	0	0	
C	4	0	25	Si	4	0	0	Mn	3	0	0	Pt	2	0	0	
N	3	0	4	P	3	0	0	Se	2	0	0					

Error Margin (ppm): 100  
HC Ratio: 0.0 - 10.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

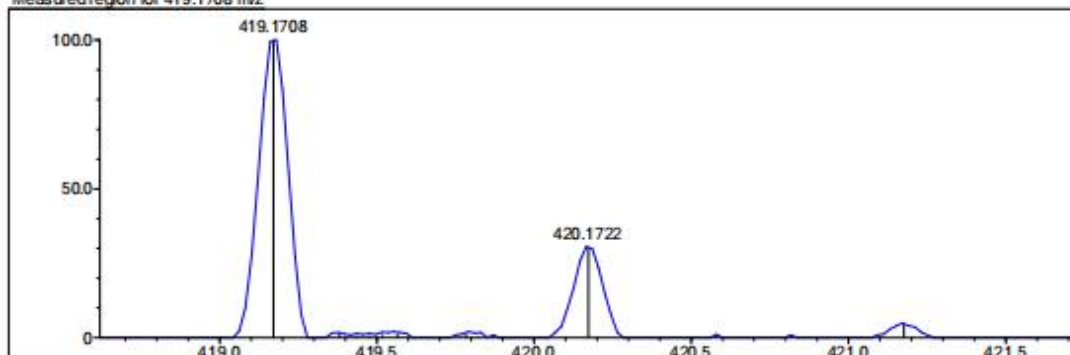
DBE Range: not fixed  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: AND

Electron Ions: both  
Use MSn Info: no  
Isotope Res: 10000  
Max Results: 100

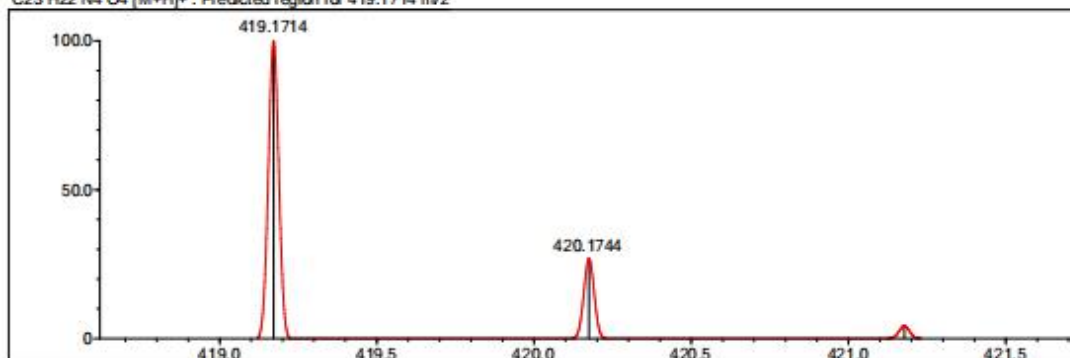
Event#: 1 MS(E+) Ret. Time : 0.853 Scan#: 129



Measured region for 419.1708 m/z



C23 H22 N4 O4 [M+H]<sup>+</sup> : Predicted region for 419.1714 m/z



Rank	Score	Formula (M)	Ion	Mass, m/z	Pred. m/z	Df, (mDa)	Df, (ppm)	Iso	DBE
1	72.95	C23H22N4O4	[M+H] <sup>+</sup>	419.1708	419.1714	-0.6	-1.43	73.74	15.0

# HRMS spectrum of **11b**

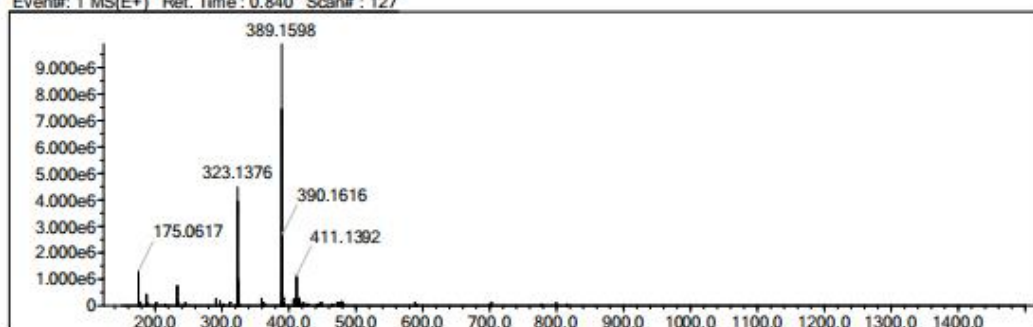
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	1	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

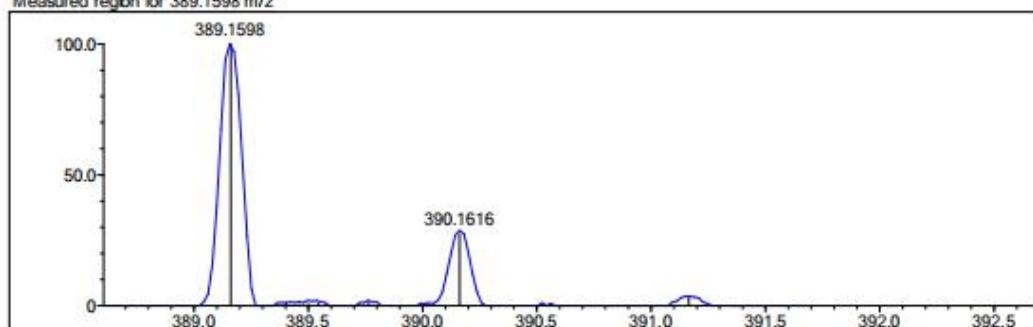
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

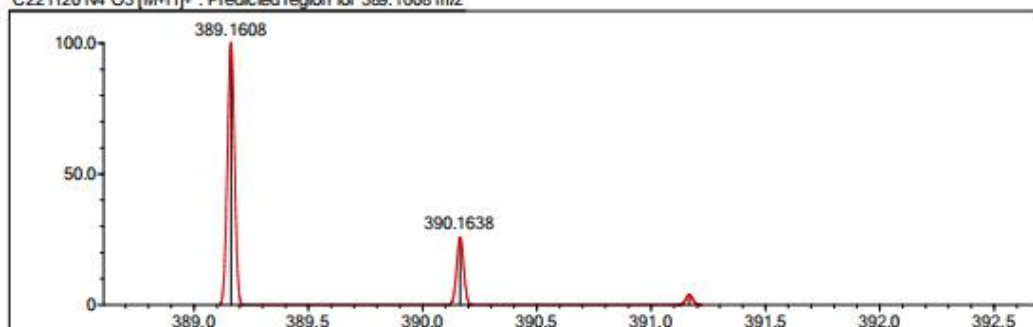
Event#: 1 MS(E+) Ret. Time: 0.840 Scan#: 127



Measured region for 389.1598 m/z



C22 H20 N4 O3 [M+H]<sup>+</sup> : Predicted region for 389.1608 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
4	73.41	C22 H20 N4 O3	[M+H] <sup>+</sup>	389.1598	389.1608	-1.0	-2.57	76.41	15.0



# HRMS spectrum of **11c**

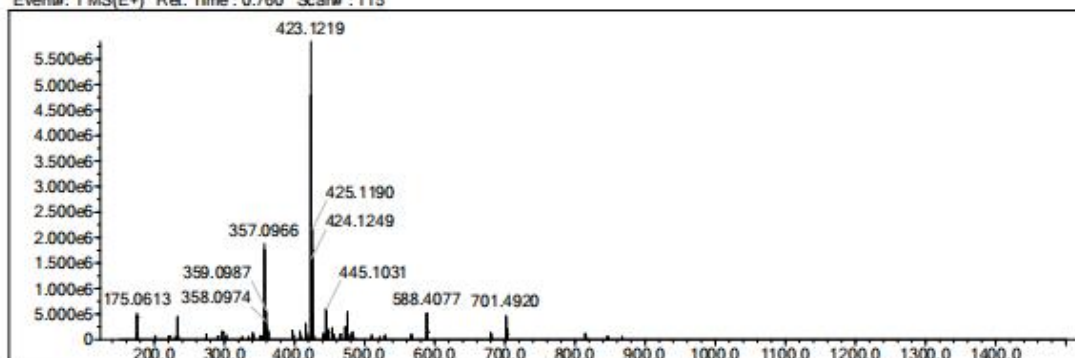
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	O	2	0	4	S	2	0	0	Br	1	0	0	H
2H	1	0	0	18O	2	0	0	Cl	1	0	1	Pd	2	0	0	
B	3	0	0	F	1	0	0	K	1	0	0	I	3	0	0	
C	4	0	25	Si	4	0	0	Mn	3	0	0	Pt	2	0	0	
N	3	0	4	P	3	0	0	Se	2	0	0					

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 10.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

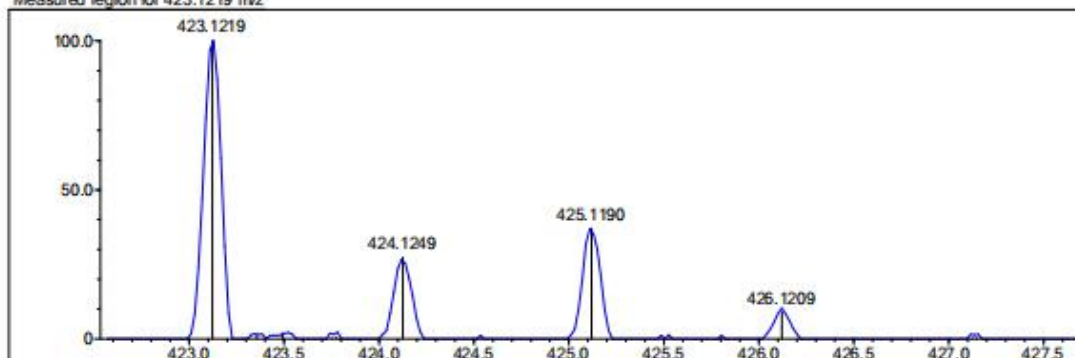
DBE Range: not fixed  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: AND

Electron Ions: both  
 Use MSn Info: no  
 Isotope Res: 10000  
 Max Results: 100

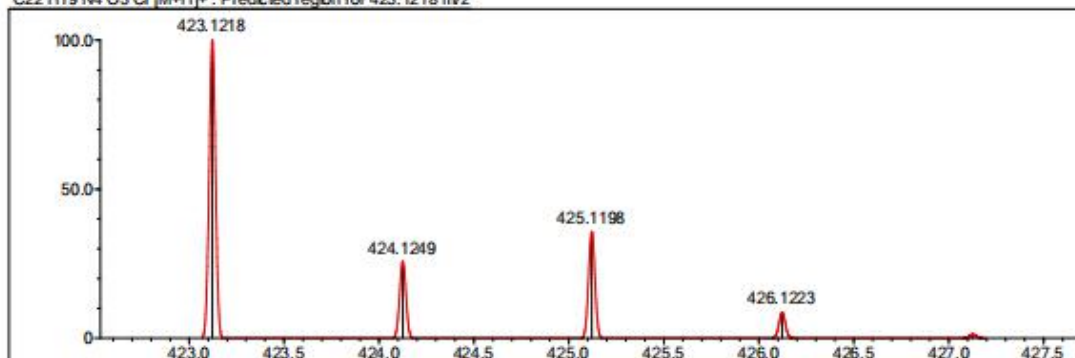
Event#: 1 MS(E+) Ret. Time: 0.760 Scan#: 115



Measured region for 423.1219 m/z



C22 H19 N4 O3 Cl [M+H]<sup>+</sup> : Predicted region for 423.1218 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	90.94	C22 H19 N4 O3 Cl	[M+H] <sup>+</sup>	423.1219	423.1218	0.1	0.24	90.94	15.0

# HRMS spectrum of **11d**

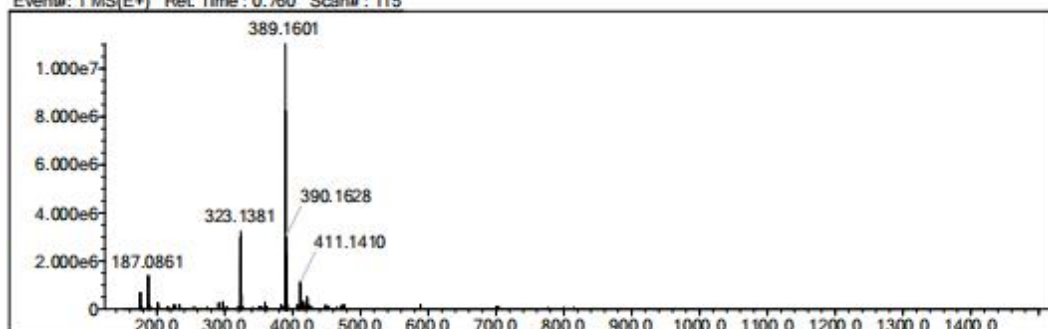
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	1	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

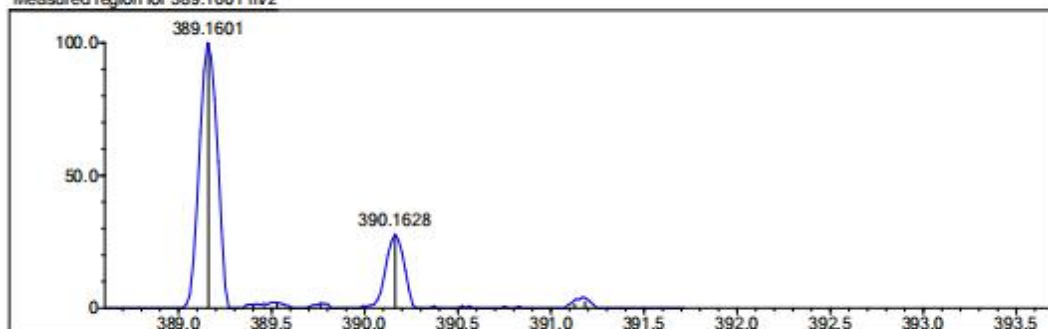
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

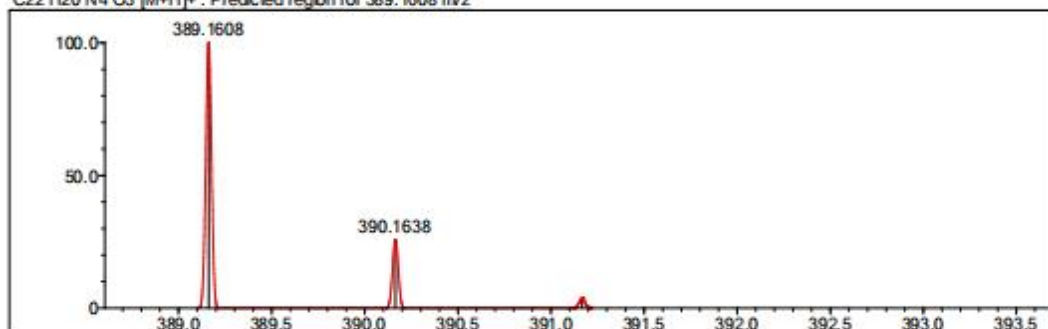
Event#: 1 MS(E+) Ret. Time : 0.760 Scan#: 115



Measured region for 389.1601 m/z



C22 H20 N4 O3 [M+H]<sup>+</sup> : Predicted region for 389.1608 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
4	70.11	C22 H20 N4 O3	[M+H] <sup>+</sup>	389.1601	389.1608	-0.7	-1.80	71.54	15.0

# HRMS spectrum of **11e**

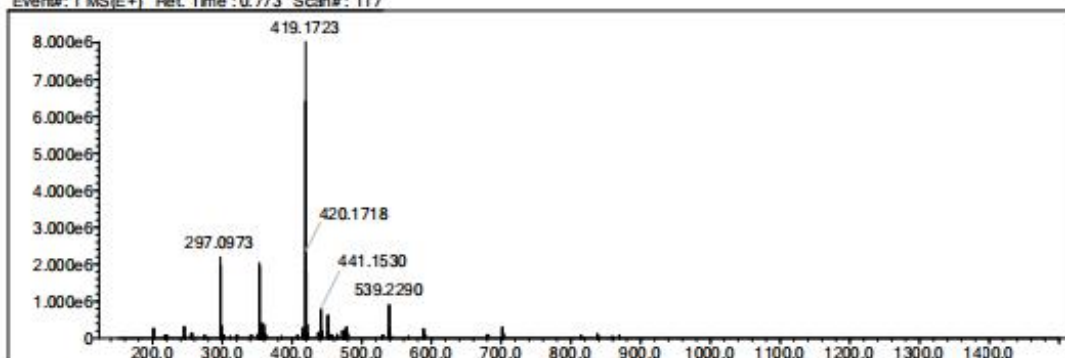
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	O	2	0	4	S	2	0	0	Br	1	0	0	H
2H	1	0	0	18O	2	0	0	Cl	1	0	1	Pd	2	0	0	
B	3	0	0	F	1	0	0	K	1	0	0	I	3	0	0	
C	4	0	25	Si	4	0	0	Mn	3	0	0	Pt	2	0	0	
N	3	0	4	P	3	0	0	Se	2	0	0					

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 10.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

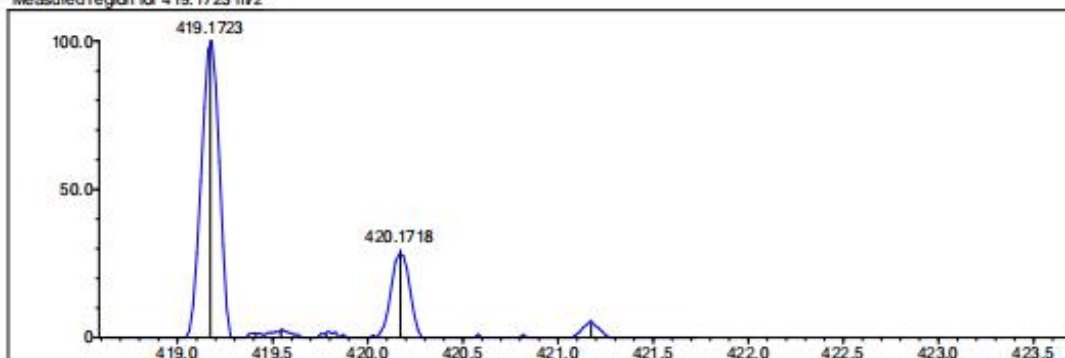
DBE Range: not fixed  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: AND

Electron Ions: both  
 Use MSn Info: no  
 Isotope Res: 10000  
 Max Results: 100

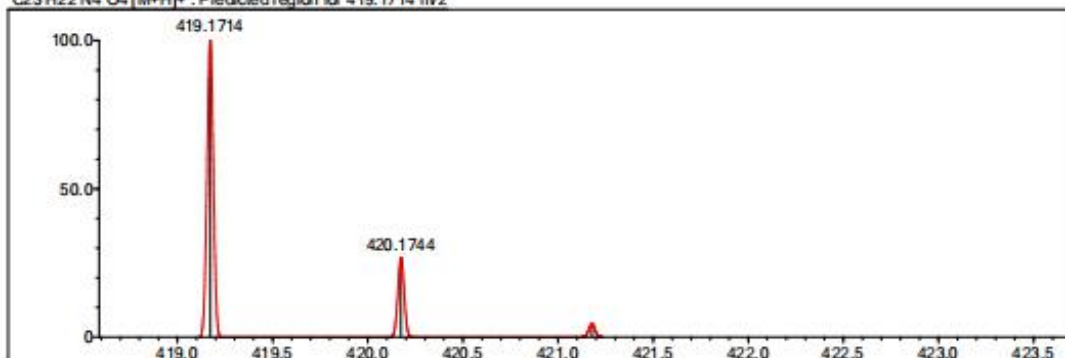
Event#: 1 MS(E+) Ret. Time: 0.773 Scan#: 117



Measured region for 419.1723 m/z



C23 H22 N4 O4 [M+H]<sup>+</sup> : Predicted region for 419.1714 m/z



Rank	Score	Formula (M)	Ion	Mass. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isc	DBE
1	71.53	C23 H22 N4 O4	[M+H] <sup>+</sup>	419.1723	419.1714	0.9	2.15	73.65	15.0

# HRMS spectrum of **11f**

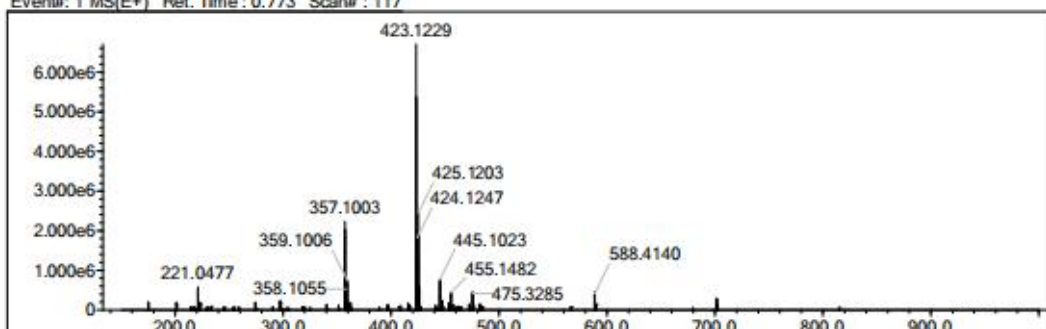
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	1	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

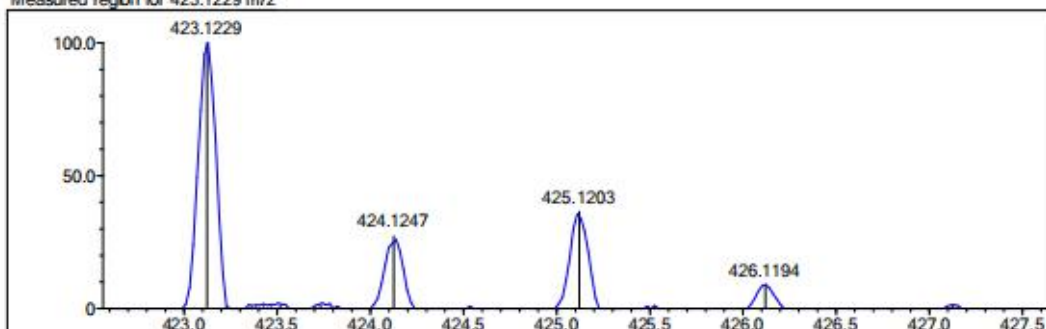
DBE Range: -100.0 - 100.0  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

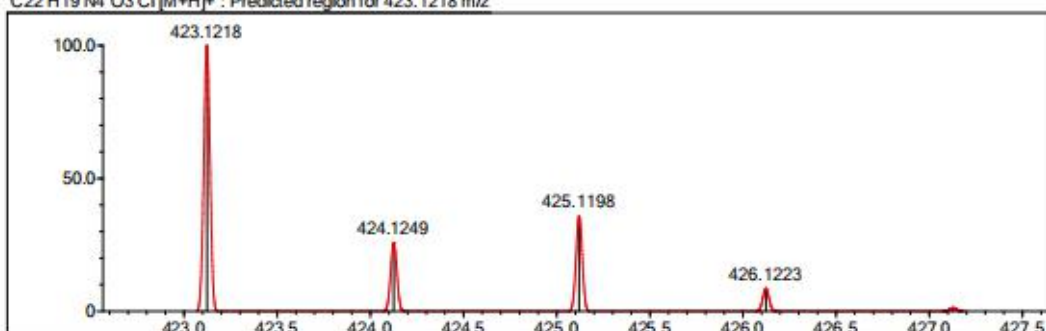
Event#: 1 MS(E+) Ret. Time: 0.773 Scan#: 117



Measured region for 423.1229 m/z



C22 H19 N4 O3 Cl [M+H]<sup>+</sup> : Predicted region for 423.1218 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
9	88.67	C22 H19 N4 O3 Cl	[M+H] <sup>+</sup>	423.1229	423.1218	1.1	2.60	92.36	15.0

# HRMS spectrum of **11g**

Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	1	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100

HC Ratio: 0.0 - 100.0

Max Isotopes: all

MSn Iso RI (%): 75.00

DBE Range: -100.0 - 100.0

Apply N Rule: no

Isotope RI (%): 1.00

MSn Logic Mode: OR

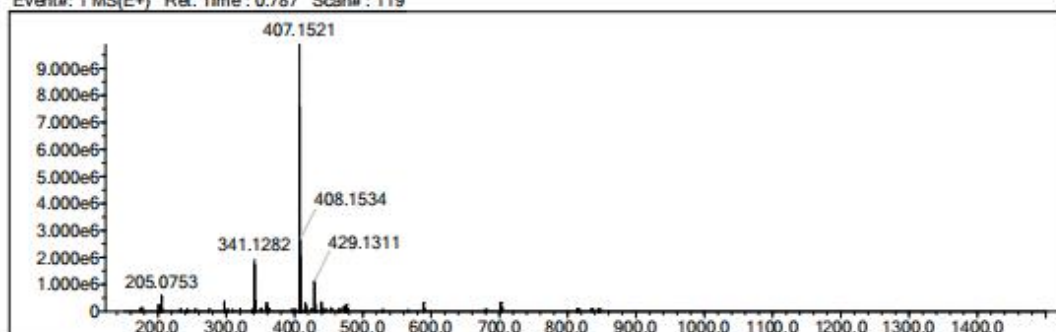
Electron Ions: both

Use MSn Info: yes

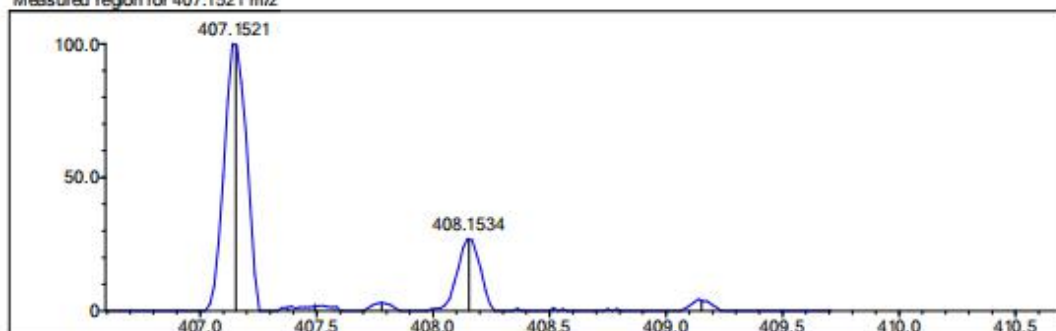
Isotope Res: 10000

Max Results: 100

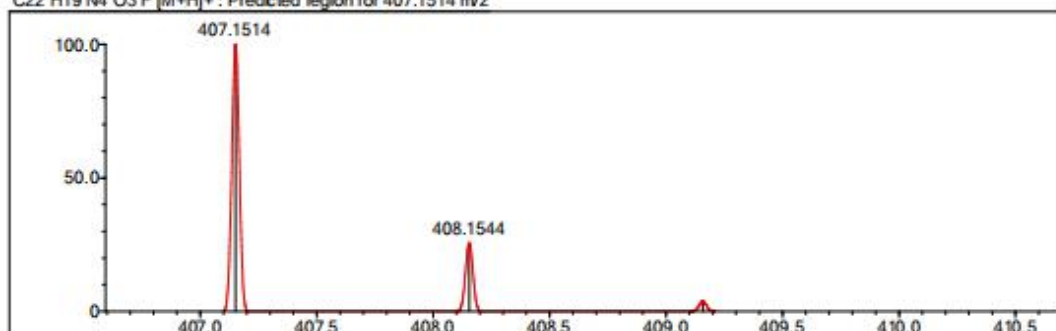
Event#: 1 MS(E+) Ret. Time: 0.787 Scan#: 119



Measured region for 407.1521 m/z



C22 H19 N4 O3 F [M+H]<sup>+</sup>: Predicted region for 407.1514 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
2	72.69	C22 H19 N4 O3 F	[M+H] <sup>+</sup>	407.1521	407.1514	0.7	1.72	74.03	15.0



# HRMS spectrum of **11h**

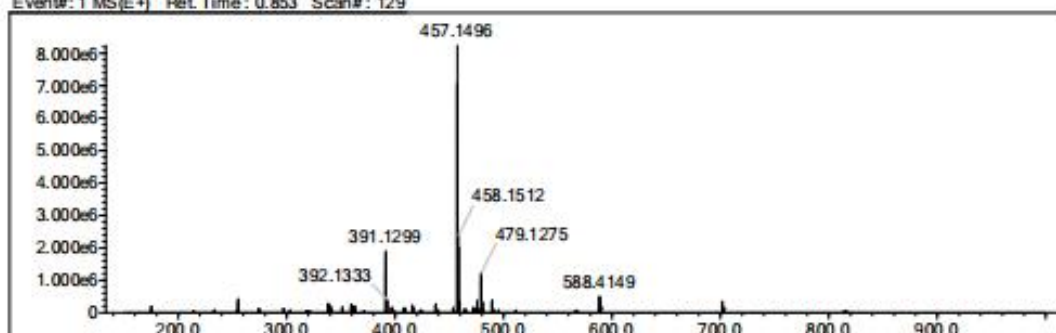
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

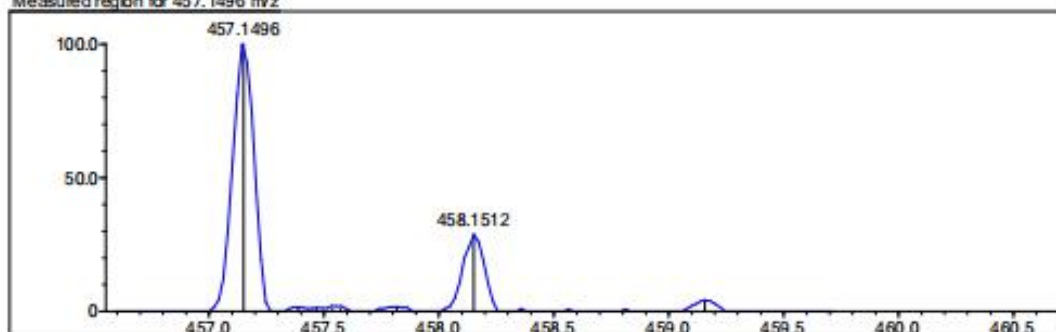
DBE Range: -100.0 - 100.0  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

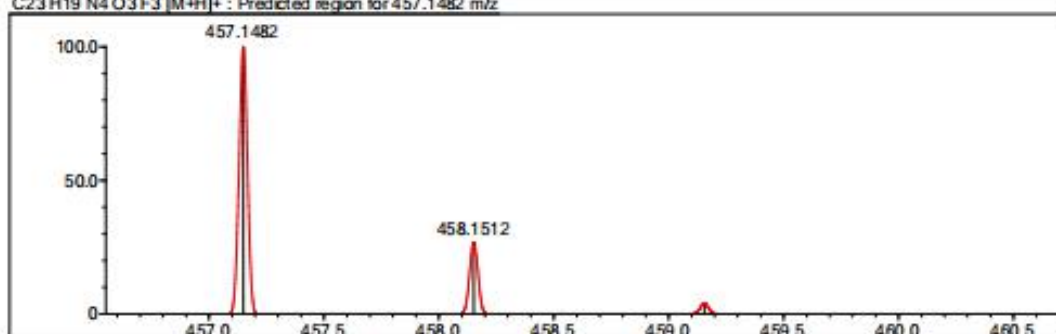
Event#: 1 MS(E+) Ret. Time: 0.853 Scan#: 129



Measured region for 457.1496 m/z



C23H19N4O3F3 [M+H]<sup>+</sup> : Predicted region for 457.1482 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isot	DBE
5	76.78	C23H19N4O3F3	[M+H] <sup>+</sup>	457.1496	457.1482	1.4	3.06	80.95	15.0

# HRMS spectrum of **11i**

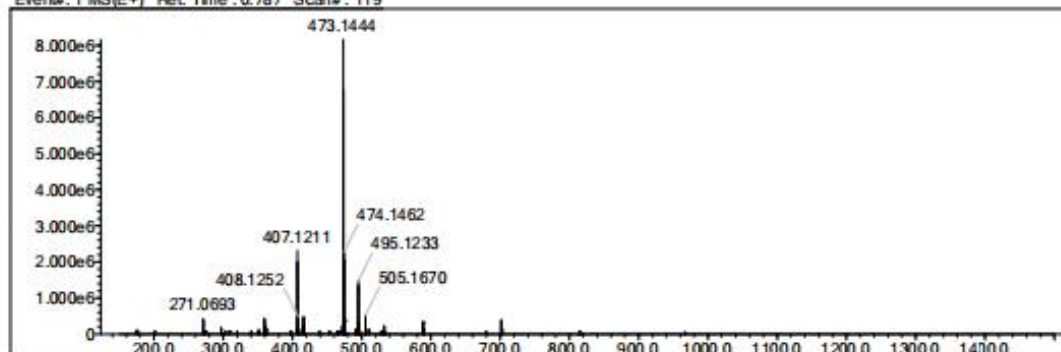
Elmt	Val	Min	Max	Elmt	Val	Min	Max	Elmt	Val	Min	Max	Elmt	Val	Min	Max	Use Adduct
H	1	0	19	O	2	0	4	S	2	0	0	Br	1	0	0	H
2H	1	0	0	18O	2	0	0	Cl	1	0	0	Pd	2	0	0	
B	3	0	0	F	1	0	3	K	1	0	0	I	3	0	0	
C	4	0	23	Si	4	0	0	Mn	3	0	0	Pt	2	0	0	
N	3	0	4	P	3	0	0	Se	2	0	0					

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 10.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

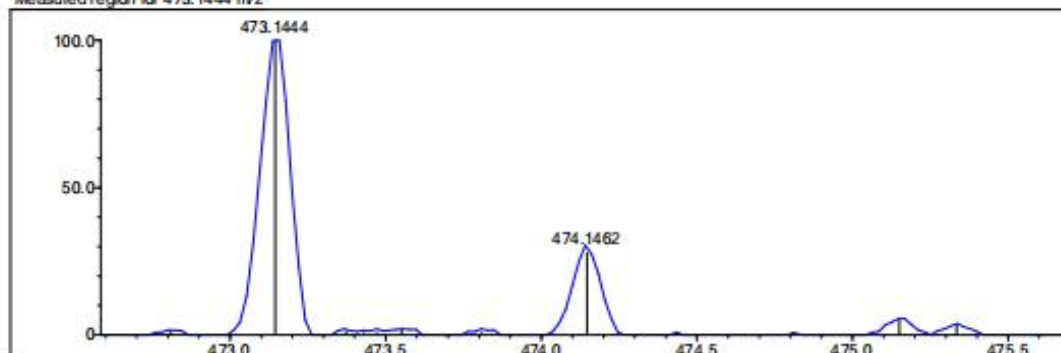
DBE Range: not fixed  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: AND

Electron Ions: both  
 Use MSn Info: no  
 Isotope Res: 10000  
 Max Results: 100

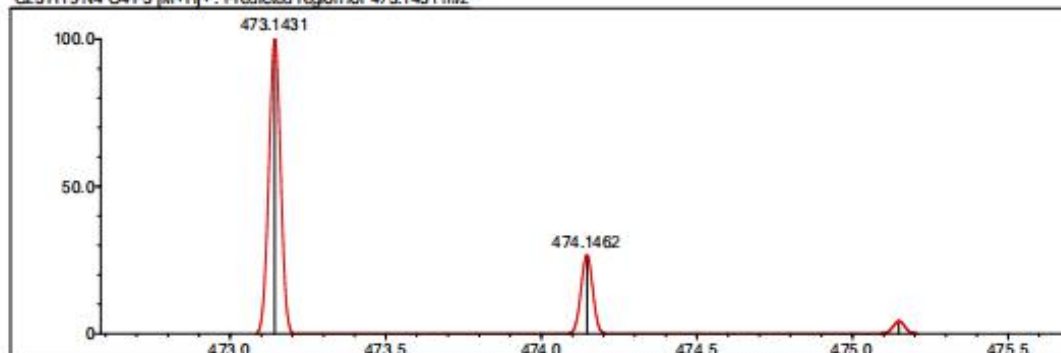
Event#: 1 MS(E+) Ret. Time : 0.787 Scan#: 119



Measured region for 473.1444 m/z



C23H19N4O4F3 [M+H]<sup>+</sup>: Predicted region for 473.1431 m/z



Rank	Score	Formula (M)	Ion	Mass, m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	73.86	C23H19N4O4F3	[M+H] <sup>+</sup>	473.1444	473.1431	1.3	2.75	77.23	15.0

# HRMS spectrum of **11j**

Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100

HC Ratio: 0.0 - 100.0

Max Isotopes: all

MSn Iso RI (%): 75.00

DBE Range: -100.0 - 100.0

Apply N Rule: no

Isotope RI (%): 1.00

MSn Logic Mode: OR

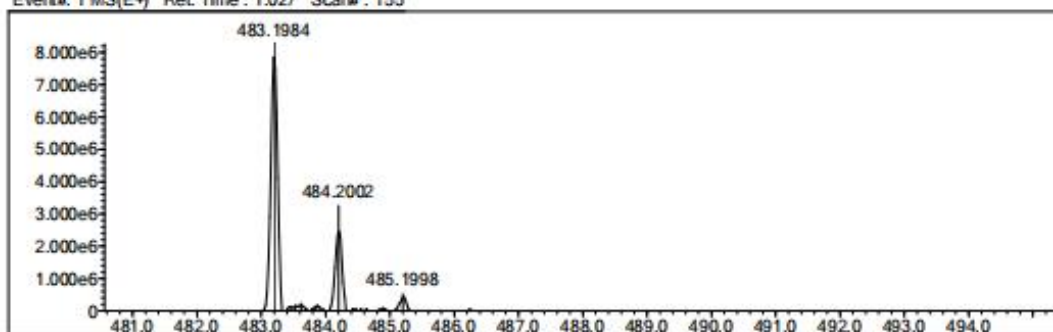
Electron Ions: both

Use MSn Info: yes

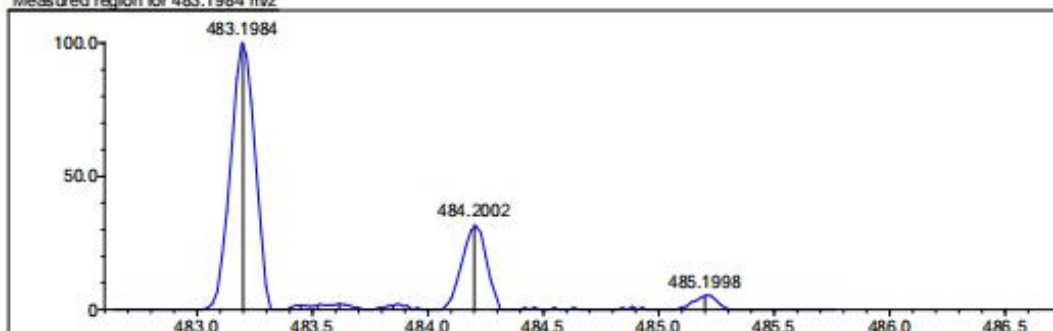
Isotope Res: 10000

Max Results: 100

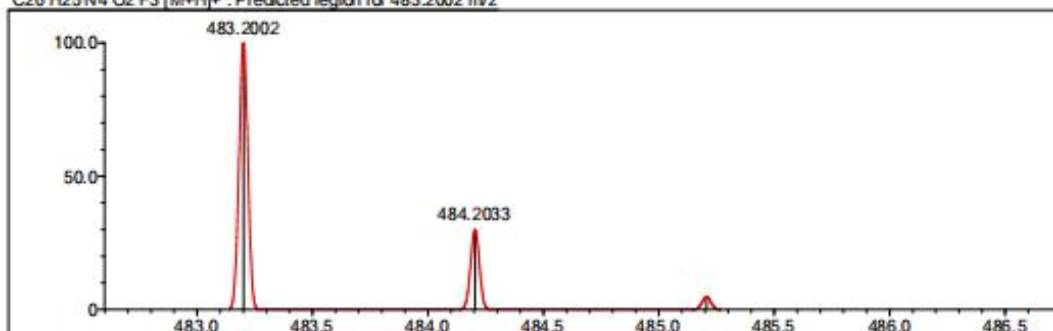
Event#: 1 MS(E+) Ret. Time: 1.027 Scan#: 155



Measured region for 483.1984 m/z



C26 H25 N4 O2 F3 [M+H]<sup>+</sup> : Predicted region for 483.2002 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	74.26	C26 H25 N4 O2 F3	[M+H] <sup>+</sup>	483.1984	483.2002	-1.8	-3.73	79.70	15.0



# HRMS spectrum of **11k**

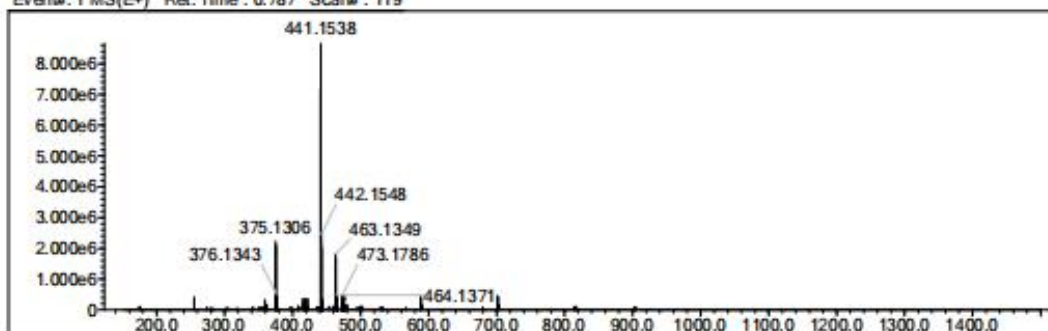
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

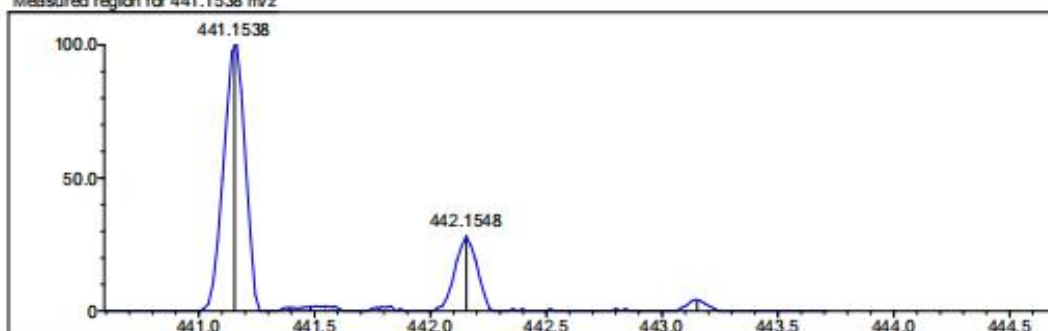
DBE Range: -100.0 - 100.0  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

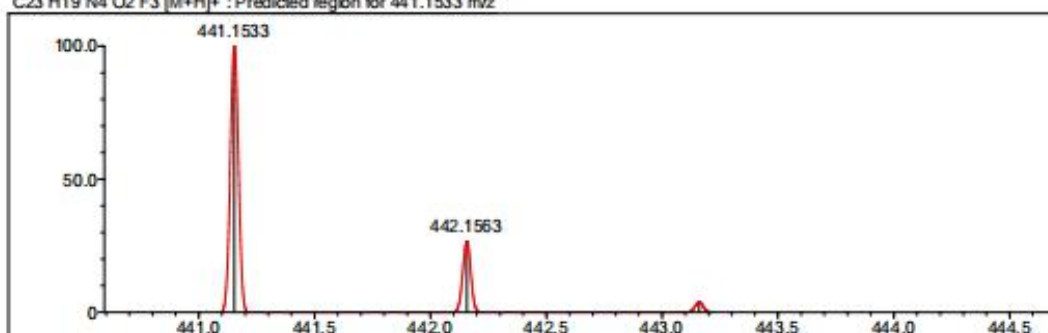
Event#: 1 MS(E+) Ret. Time : 0.787 Scan#: 119



Measured region for 441.1538 m/z



C23 H19 N4 O2 F3 [M+H]<sup>+</sup> : Predicted region for 441.1533 m/z



Rank	Score	Formula (M)	Ion	Mass. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isot	DBE
2	77.55	C23 H19 N4 O2 F3	[M+H] <sup>+</sup>	441.1538	441.1533	0.5	1.13	77.80	15.0

# HRMS spectrum of **111**

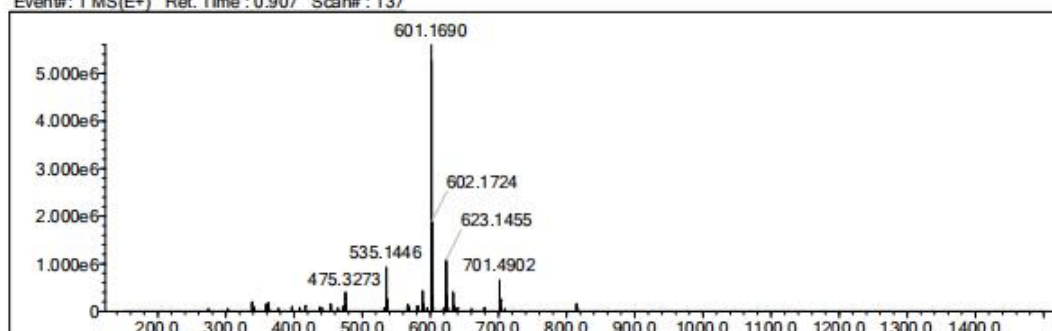
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

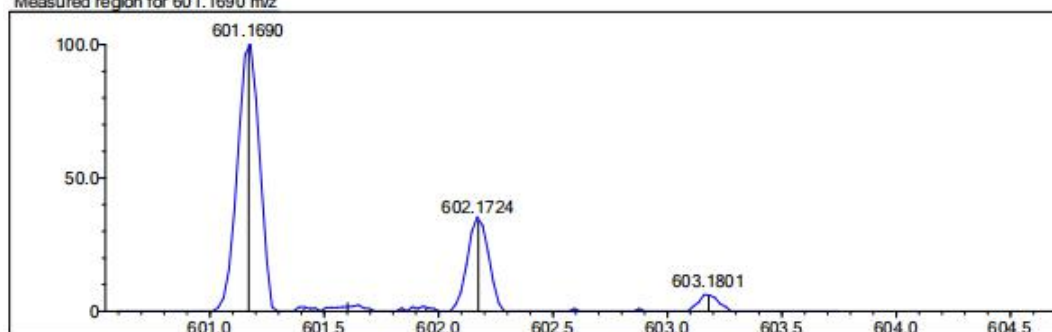
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

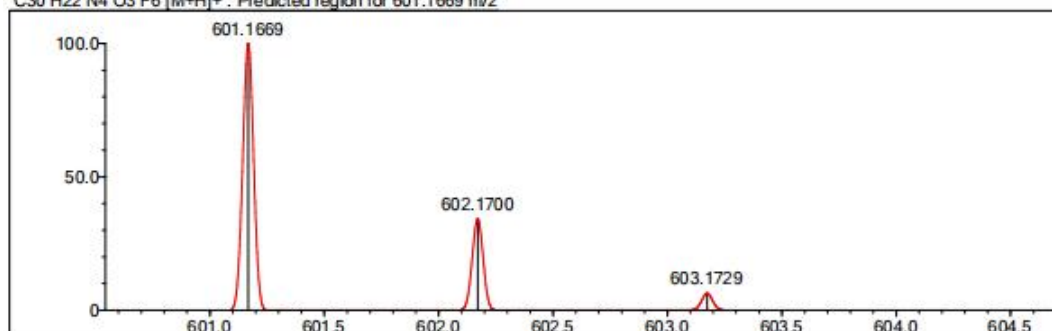
Event#: 1 MS(E+) Ret. Time : 0.907 Scan#: 137



Measured region for 601.1690 m/z



C30 H22 N4 O3 F6 [M+H]<sup>+</sup> : Predicted region for 601.1669 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	88.53	C30 H22 N4 O3 F6	[M+H] <sup>+</sup>	601.1690	601.1669	2.1	3.49	94.41	19.0

# HRMS spectrum of **11m**

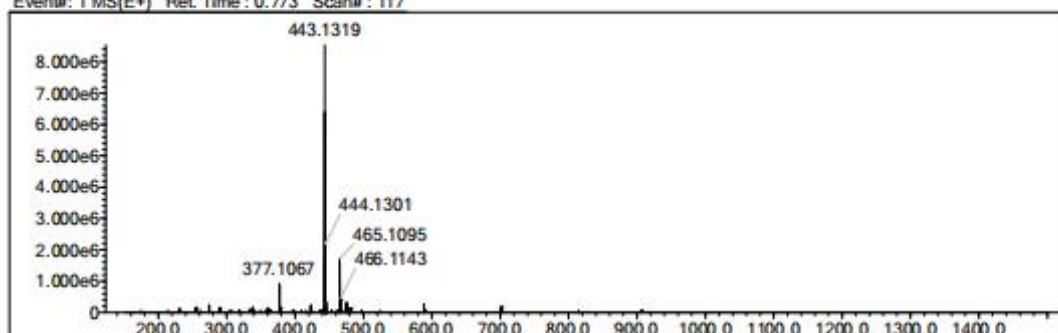
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

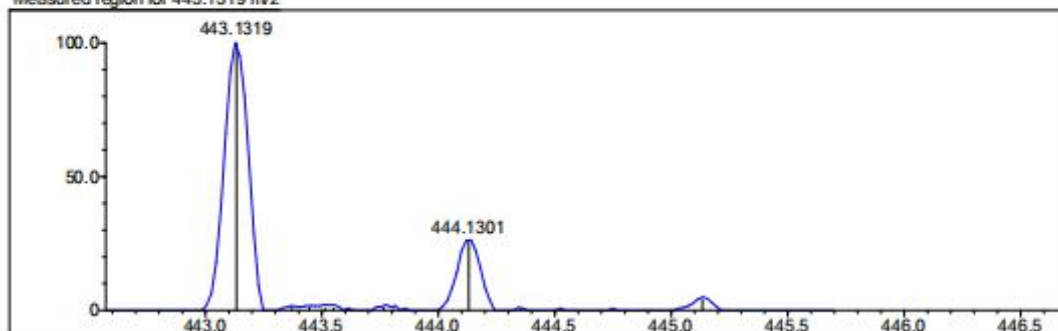
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

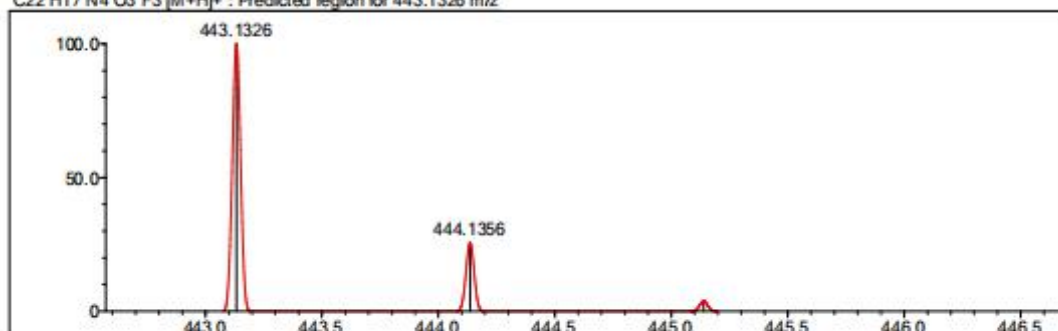
Event#: 1 MS(E+) Ret. Time : 0.773 Scan#: 117



Measured region for 443.1319 m/z



C22 H17 N4 O3 F3 [M+H]<sup>+</sup> : Predicted region for 443.1326 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
11	70.76	C22 H17 N4 O3 F3	[M+H] <sup>+</sup>	443.1319	443.1326	-0.7	-1.58	71.80	15.0

# HRMS spectrum of **11n**

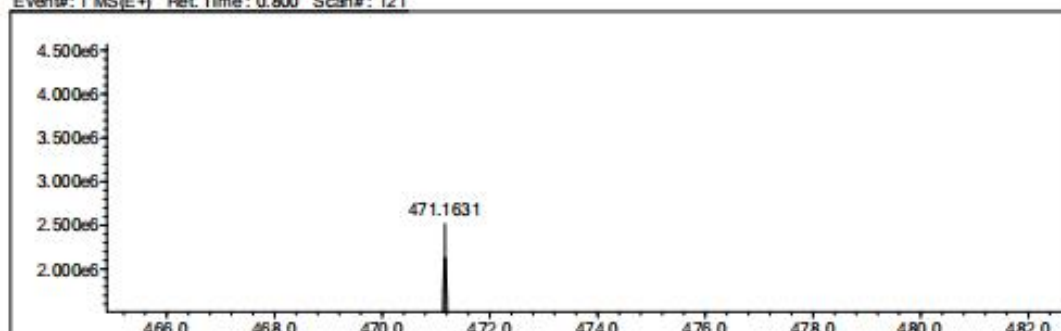
Elmt	Val	Min	Max	Elmt	Val	Min	Max	Elmt	Val	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
HC Ratio: 0.0 - 100.0  
Max Isotopes: all  
MSn Iso RI (%): 75.00

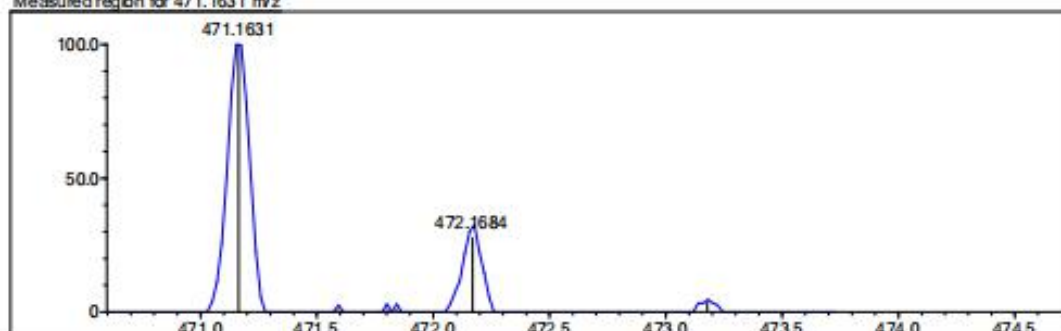
DBE Range: -100.0 - 100.0  
Apply N Rule: no  
Isotope RI (%): 1.00  
MSn Logic Mode: OR

Electron Ions: both  
Use MSn Info: yes  
Isotope Res: 10000  
Max Results: 100

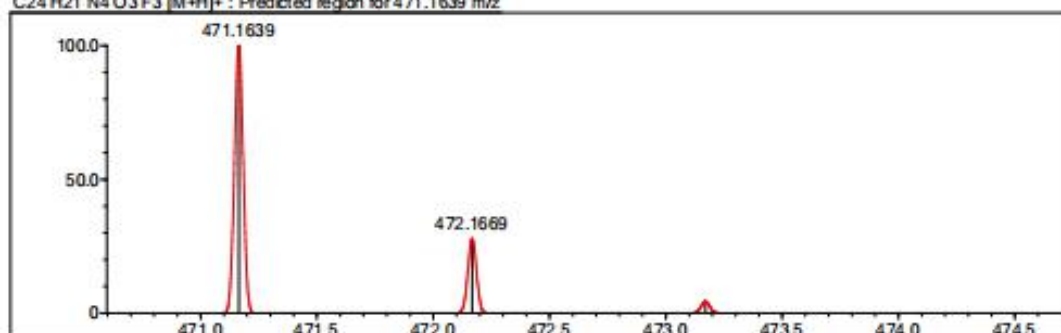
Event#: 1 MS(E+) Ret. Time: 0.800 Scan#: 121



Measured region for 471.1631 m/z



C24H21N4O3F3 [M+H]<sup>+</sup> : Predicted region for 471.1639 m/z



Rank	Score	Formula (M)	Ion	Mass, m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Isotope	DBE
4	90.05	C24H21N4O3F3	[M+H] <sup>+</sup>	471.1631	471.1639	-0.8	+1.70	91.66	15.0

# HRMS spectrum of **11o**

Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100

HC Ratio: 0.0 - 100.0

Max Isotopes: all

MSn Iso RI (%): 75.00

DBE Range: -100.0 - 100.0

Apply N Rule: no

Isotope RI (%): 1.00

MSn Logic Mode: OR

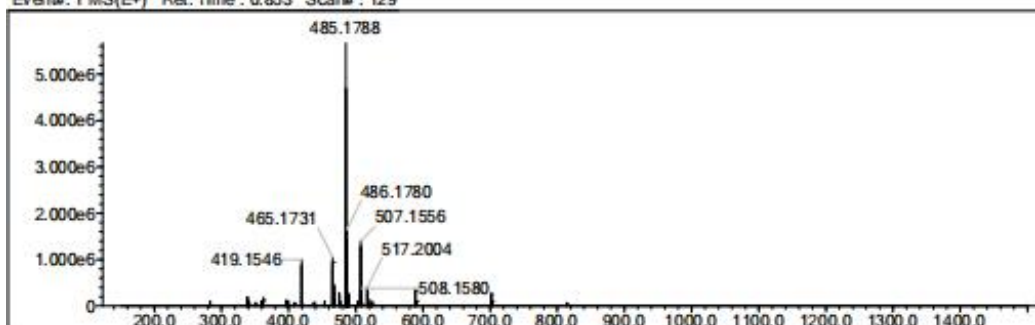
Electron Ions: both

Use MSn Info: yes

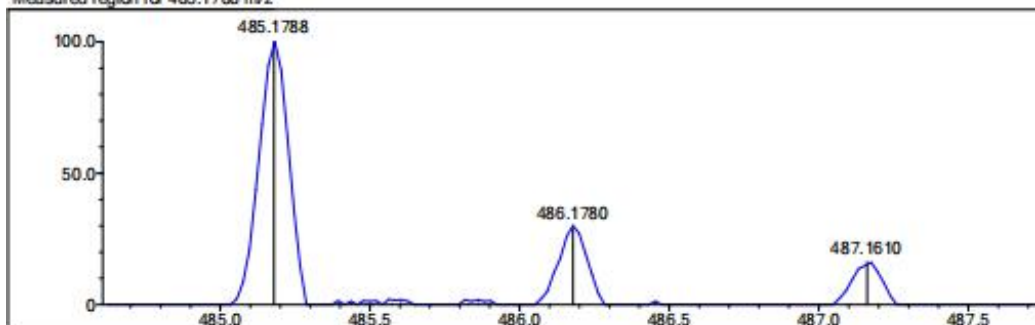
Isotope Res: 10000

Max Results: 100

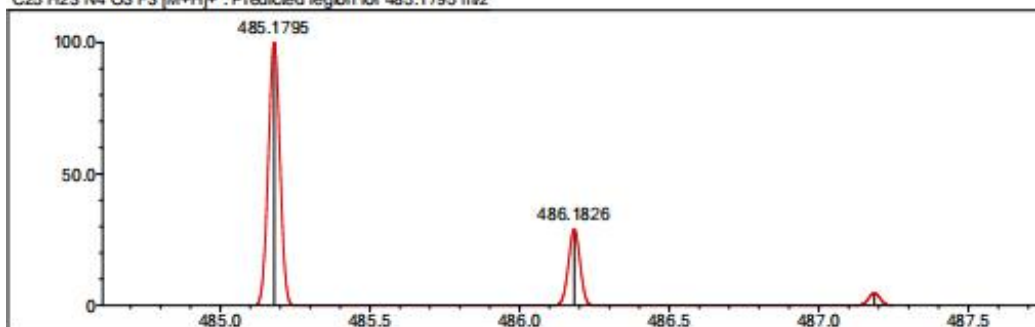
Event#: 1 MS(E+) Ret. Time : 0.853 Scan#: 129



Measured region for 485.1788 m/z



C25 H23 N4 O3 F3 [M+H]<sup>+</sup> : Predicted region for 485.1795 m/z



Rank	Score	Formula (M)	Ion	Mass. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
7	36.95	C25 H23 N4 O3 F3	[M+H] <sup>+</sup>	485.1788	485.1795	-0.7	-1.44	37.37	15.0



# HRMS spectrum of **11p**

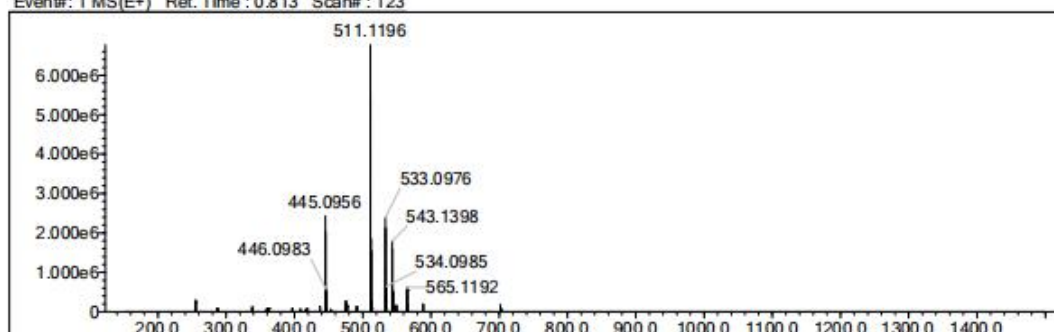
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

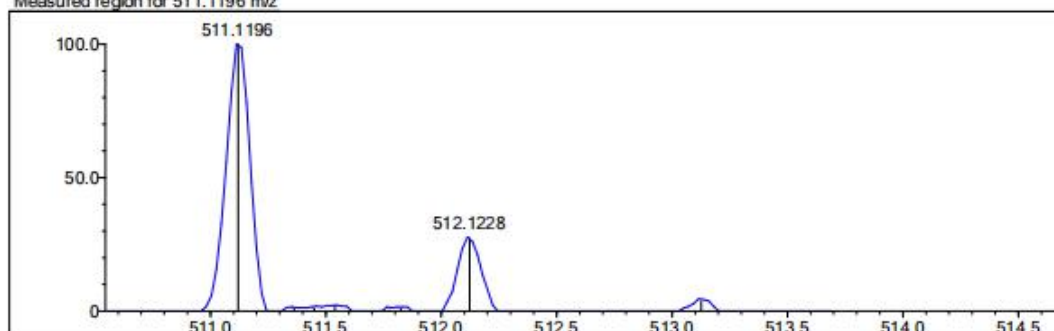
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

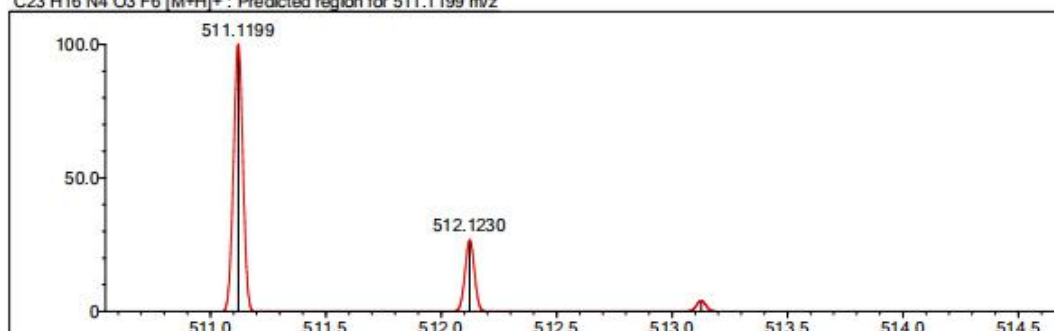
Event#: 1 MS(E+) Ret. Time : 0.813 Scan#: 123



Measured region for 511.1196 m/z



C23 H16 N4 O3 F6 [M+H]<sup>+</sup> : Predicted region for 511.1199 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDe)	Df. (ppm)	Iso	DBE
1	85.65	C23 H16 N4 O3 F6	[M+H] <sup>+</sup>	511.1196	511.1199	-0.3	-0.59	85.65	15.0

# HRMS spectrum of **11q**

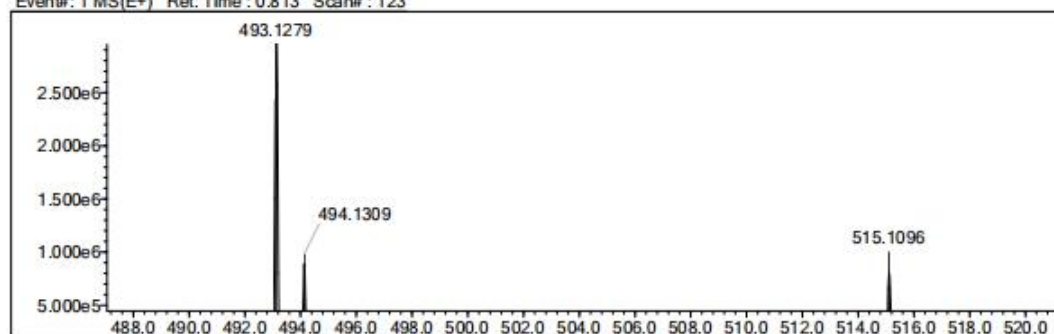
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

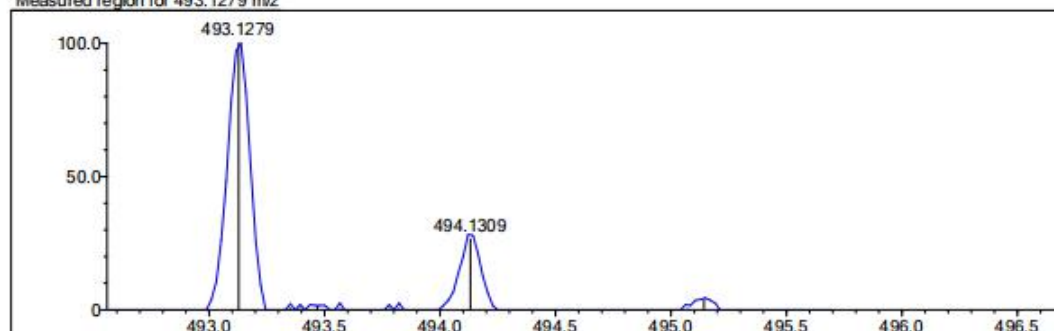
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

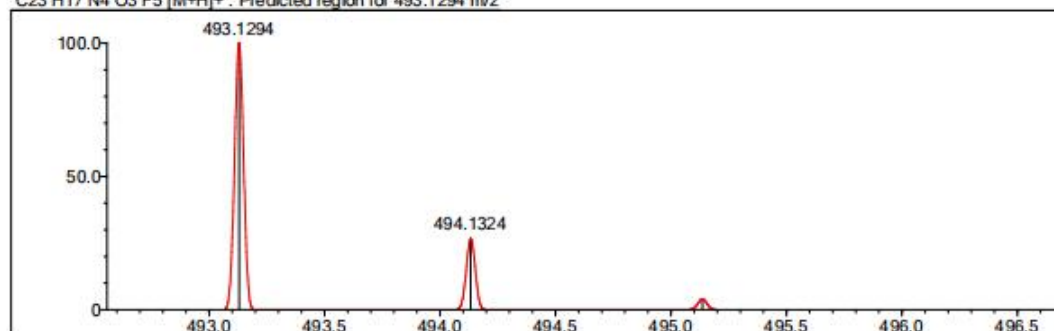
Event#: 1 MS(E+) Ret. Time : 0.813 Scan#: 123



Measured region for 493.1279 m/z



C23 H17 N4 O3 F5 [M+H]<sup>+</sup> : Predicted region for 493.1294 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
9	76.87	C23 H17 N4 O3 F5	[M+H] <sup>+</sup>	493.1279	493.1294	-1.5	-3.04	81.00	15.0

# HRMS spectrum of **11r**

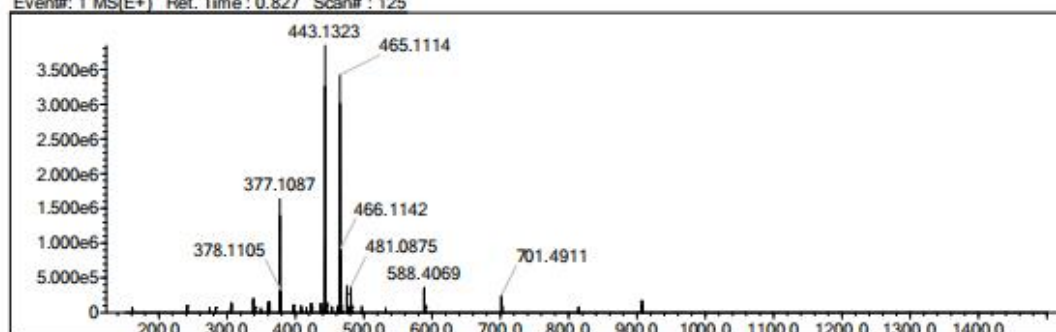
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	0	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

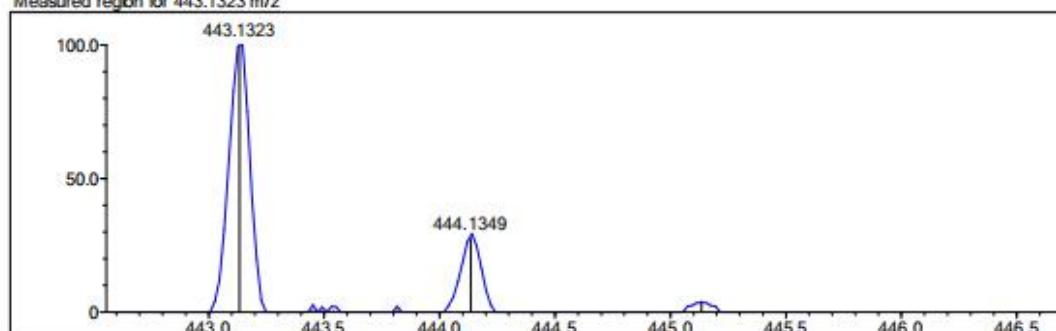
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

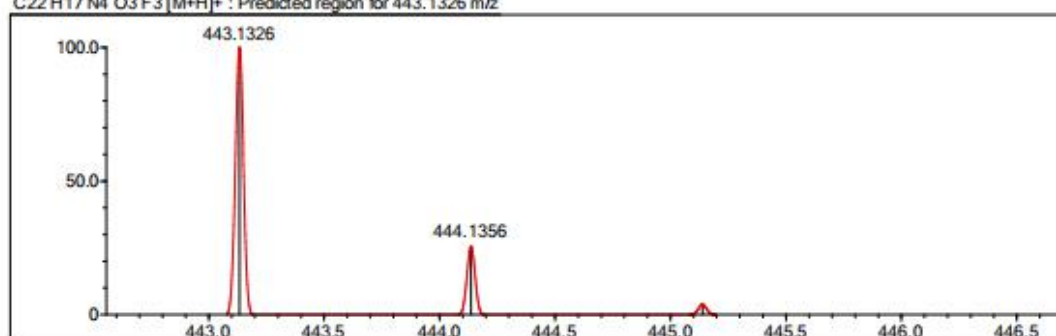
Event#: 1 MS(E+) Ret. Time: 0.827 Scan#: 125



Measured region for 443.1323 m/z



C22 H17 N4 O3 F3 [M+H]<sup>+</sup> : Predicted region for 443.1326 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
7	72.53	C22 H17 N4 O3 F3	[M+H] <sup>+</sup>	443.1323	443.1326	-0.3	-0.68	72.53	15.0



# HRMS spectrum of **11s**

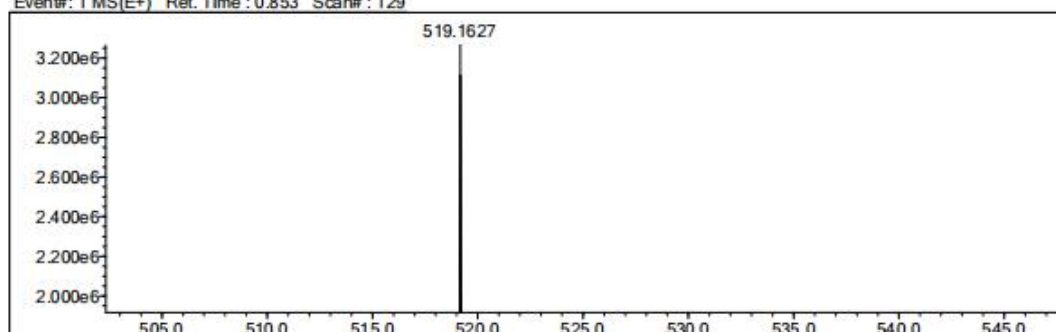
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	21	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	28	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	0	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

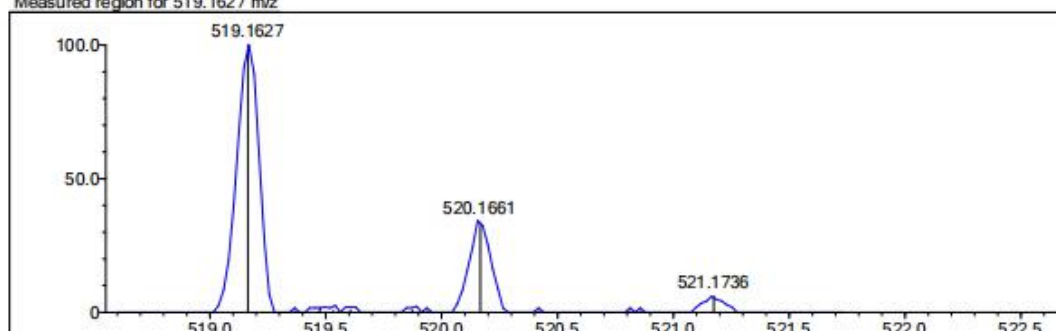
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

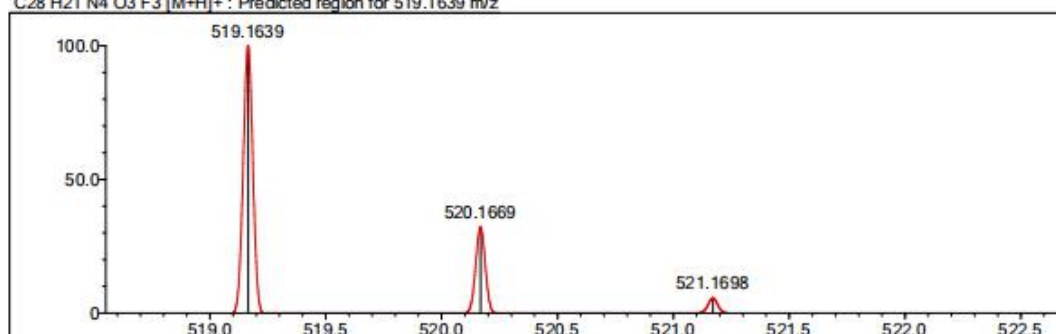
Event#: 1 MS(E+) Ret. Time : 0.853 Scan#: 129



Measured region for 519.1627 m/z



C28 H21 N4 O3 F3 [M+H]<sup>+</sup> : Predicted region for 519.1639 m/z



Rank	Score	Formula (M)	Ion	Mess. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	87.88	C28 H21 N4 O3 F3	[M+H] <sup>+</sup>	519.1627	519.1639	-1.2	-2.31	90.85	19.0

# HRMS spectrum of **11t**

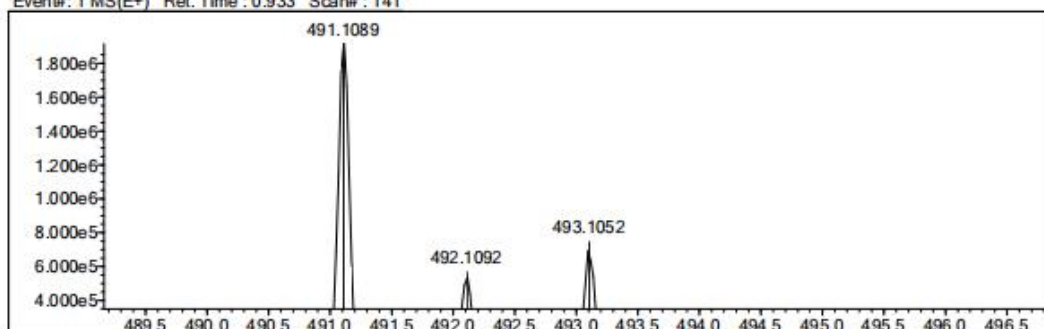
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	25	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	30	S	2	0	0	Ru	2	0	0	NH4
N	3	0	4	Cl	1	0	1	Sb	3	0	0	
O	2	0	4	Fe	2	0	0	I	3	0	0	
F	1	0	6	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

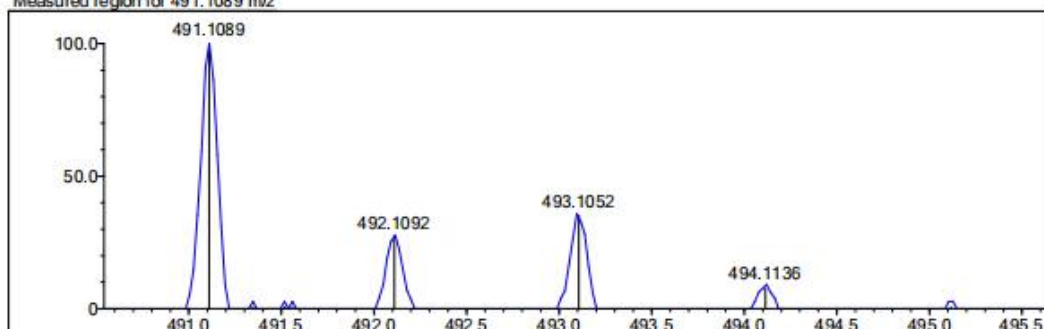
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

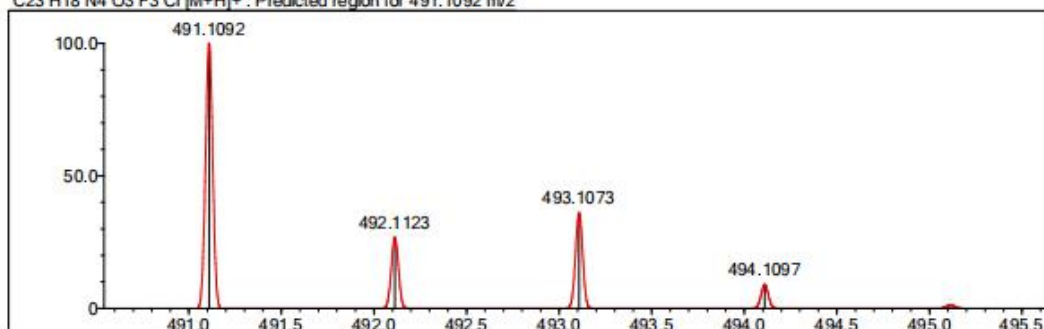
Event#: 1 MS(E+) Ret. Time : 0.933 Scan#: 141



Measured region for 491.1089 m/z



C23 H18 N4 O3 F3 Cl [M+H]<sup>+</sup>: Predicted region for 491.1092 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	94.98	C23 H18 N4 O3 F3 Cl	[M+H] <sup>+</sup>	491.1089	491.1092	-0.3	-0.61	94.98	15.0

# HRMS spectrum of 16

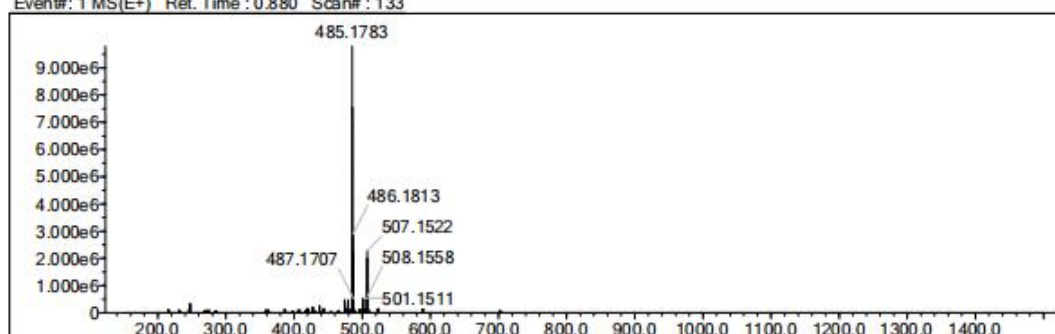
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	23	Al	3	0	0	Zn	2	0	0	K
2H	1	0	0	Si	4	0	0	Se	2	0	0	H
B	3	0	0	P	3	0	0	Br	1	0	0	Na
C	4	0	25	S	2	0	0	Ru	2	0	0	NH4
N	3	0	5	Cl	1	0	0	Sb	3	0	0	
O	2	0	5	Fe	2	0	0	I	3	0	0	
F	1	0	3	Ni	2	0	0	Ir	3	0	0	
Na	1	0	0	Cu	2	0	0	Pt	2	0	0	

Error Margin (ppm): 100  
 HC Ratio: 0.0 - 100.0  
 Max Isotopes: all  
 MSn Iso RI (%): 75.00

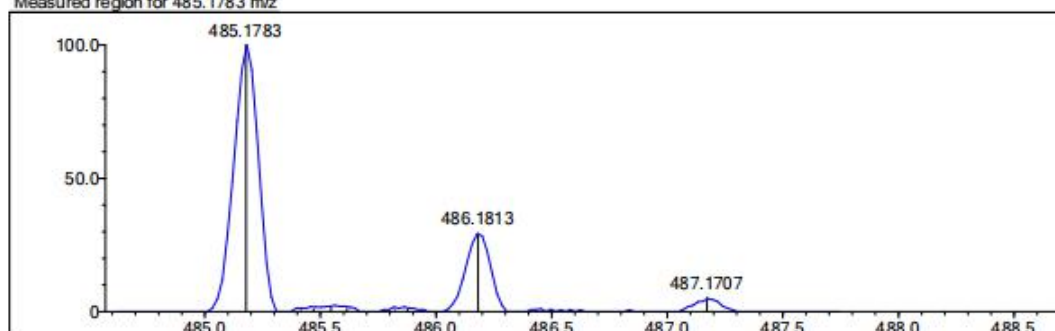
DBE Range: -100.0 - 100.0  
 Apply N Rule: no  
 Isotope RI (%): 1.00  
 MSn Logic Mode: OR

Electron Ions: both  
 Use MSn Info: yes  
 Isotope Res: 10000  
 Max Results: 100

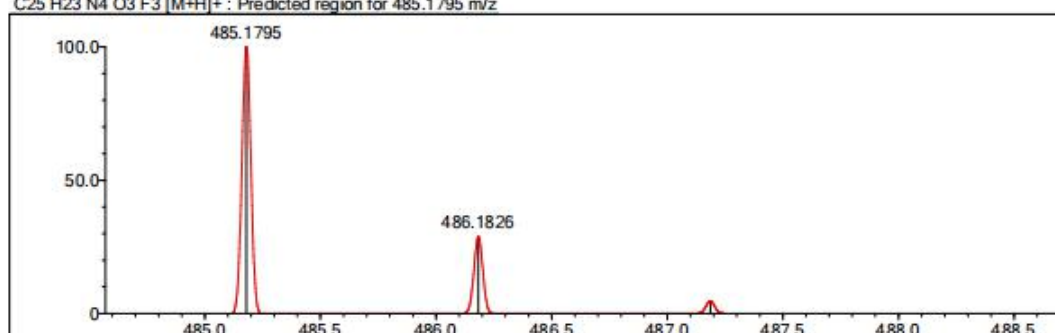
Event#: 1 MS(E+) Ret. Time : 0.880 Scan#: 133



Measured region for 485.1783 m/z



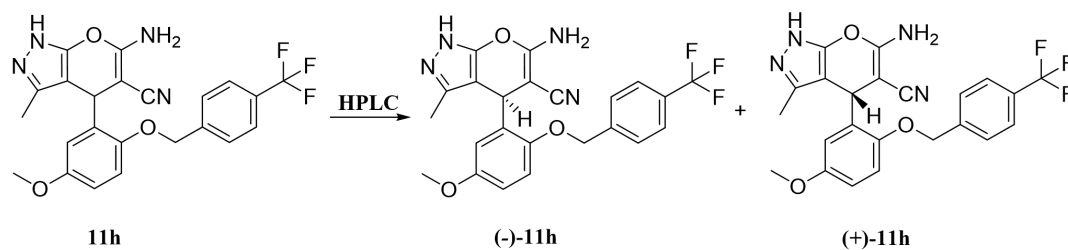
C25 H23 N4 O3 F3 [M+H]<sup>+</sup> : Predicted region for 485.1795 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
2	73.54	C25 H23 N4 O3 F3	[M+H] <sup>+</sup>	485.1783	485.1795	-1.2	-2.47	76.34	15.0

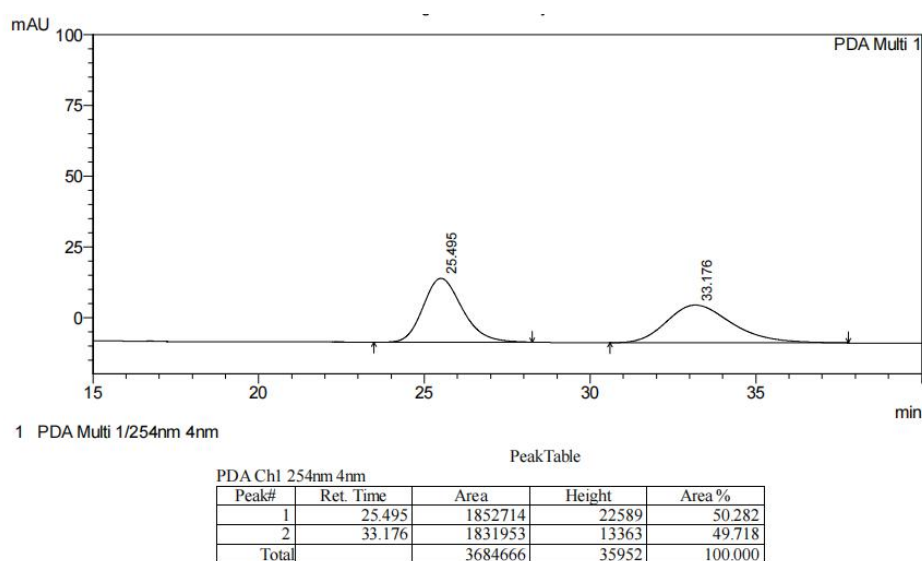
### 3. Chiral Resolution of Compound 11h

Considering the effect of chiral structure on the biological activity of compounds, the chiral isomers **(-)-11h** and **(+)-11h** were prepared by the separation of **11h** with chiral HPLC. The chiral resolution of compound **11h** was performed using Gilson instruments, and the chromatographic column was a CHIRALPAK®IF column (250 mm × 4.6 mm, 5 μm). The compound was filtered with a microporous membrane with an injection volume of 5 μL, and the mobile phase was Hex/EtOH = 80:20. The eluent was ultrasonically degassed for 30 min before use. Flow rate: 1 mL/min; Cycle time: 40 min. the chiral isomers **(-)-11h** ( $[\alpha]_D^{20} = -46.7$  (c 1.0, THF),  $t_R = 24.847$  min, ee value, > 99%) and **(+)-11h** ( $[\alpha]_D^{20} = +46.5$  (c 1.0, THF),  $t_R = 33.976$  min, ee value, > 99%) were prepared by the separation of **(±)-11h** with chiral HPLC.

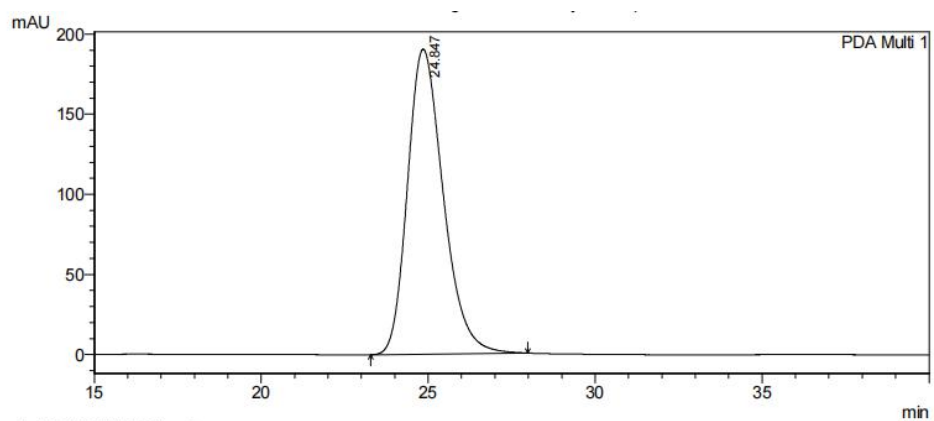


**Scheme 1.** Reagents and conditions: AD-H column. Mobile phase: hex: EtOH=80:20, flow rate: 1 mL/min.

**stereoisomers separation HPLC chromatogram.**



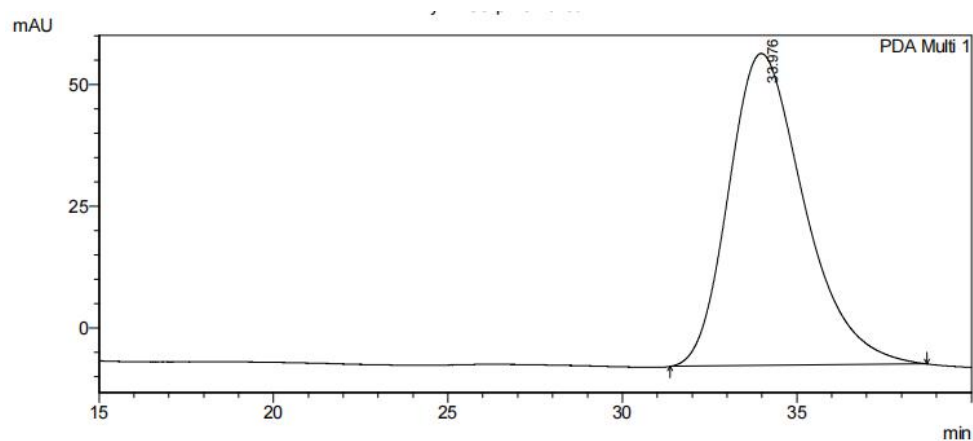
**HPLC chromatogram of (±)-11h**



PeakTable

Peak#	Ret. Time	Area	Height	Area %
1	24.847	14198971	190395	100.000
Total		14198971	190395	100.000

### HPLC chromatogram of (-)-11h



PeakTable

Peak#	Ret. Time	Area	Height	Area %
1	33.976	9647987	64117	100.000
Total		9647987	64117	100.000

### HPLC chromatogram of (+)-11h