Supporting Information

Cell origin and culture conditions.

Cell origin: H2228 cell line, a human non-small cell lung cancer cell line, was bought from Shanghai Cell Bank, Chinese Academy of Sciences. BaF_3/ALK cell line was from KYinno Biotechnology co.,LTD (Beijing, China). For human normal cell lines: EA.hy926, HK-2 and L02 were also obtained from Shanghai Cell Bank, Chinese Academy of Sciences.

Cell culture: For cell culture, H2228, HK-2, L02 and BaF_3/ALK cell lines were maintained in RPIM 1640 medium supplemented with 10% FBS (fetal bovine serum). Special for H2228 cell culture, we added 1% of sodium pyruvate (100mM, Gibco) and GlutaMAX (1X, Gibco) as a nutritional supplement. EA.hy926 cells were cultivated in DMEM medium, 10% FBS added. All above cell lines were in an atmosphere of 37 ℃, 5% CO_2 and saturated humidity.

Cytotoxicity assays

MTT assay: In vitro evaluation of antitumor cell proliferation for compounds were assessed by standard MTT method. In brief, each well of the 96-well plate was seeded in 5,000 H2228 cells, followed by incubation overnight. Then the former medium was discard and compounds of gradient concentration dissolved in a 1% FBS medium instead of it. After incubation for 48h, 10μL of MTT solution (5mg/mL) was added in each well followed by continued incubation for 4 hours. 150μL of DMSO was added in each well after removal of the medium, then, mixed thoroughly on the shaker for 10 min. Each plate was assayed on the microplate reader at 570nm. Each experiment was repeated at least three times respectively.

CCK8 assay: Wells of 96-well plates were seeded in 8000 Baf3/ALK cells, with the volume of 50uL for each. And then 50uL of the culture medium, containing different dilution of compounds, was added. Mixed softly and cell culture moved on in the incubator for 48h. Added and mixed 10uL of CCK8 solution (Beyotime, China) into each pole, incubated for another 4h at 37℃. Each plate was tested on the microplate reader at 450nm. Each experiment was repeated at least three times, respectively.

Kinase inhibition assay

Kinase inhibition assays were performed according to the literature and were conducted by Shanghai Bioduro-Sundia Biologics Co., Ltd.

The experiment protocol is as following, 1) Formulate 1×Assay buffer. 2) Dilute the compounds with DMSO when this solution at 100x final concentration in a 384-well plate, using the dispenser Echo 550 Transfer 100 nl of compounds at 100 times of the final concentration to a 384-well-plate. Use 1× Assay buffer Prepare 2x the final concentration of enzyme solution. 3) Add 5 uL of enzyme solution to the compound well and the max control well, respectively; Add 5 uL of 1x Assay buffer to the min control well. 4) 1000 rpm centrifugation for 60 seconds.5) Prepare 2x final concentration substrate solution with 1x Assay buffer, add 5 μL per well, and start the reaction. 6) Centrifuge at 1000 rpm for 60 sec and incubate at room temperature for appropriate time. 7) Configure the Detection Mix solution, add 10 μL per well to stop the reaction, centrifuge at 1,000 rpm for 60 sec, chambers incubated at R.T. for

appropriate time. 8) Envision reading. The statistics were analyzed by GraphPad Prism 8, using log (inhibitor) vs. response -Variable slope to fit the Dose-effect curve.

H2228 and BaF_3/ALK colony formation.

H2228 tablet colony: Prepared an H2228 cell suspension in the density of 300,000/mL, 1mL of this suspension was implanted in each well of a 6-well plate. Continue culturing for 24h, medium was changed as containing 5nM, 10nM and 15nM of compound **18d**, cells cultivated in blank medium as the control groups. After another 48h of culture with compound **18d**, collected each group of cells and seeded 1000 cells of different groups in a new 6-well plate. Kept 14 days of culture till colony formed, changed medium every 3 day. In the end, wash twice with PBS and 4% paraformaldehyde fixed for 30 min, then wash twice again and 0.5% crystal violet add stained the cells in dark for 30 min, then PBS eliminated the excess dye. Each well was photographed, then 1mL of 33% acetic acid was added in and shaken thoroughly to discolor. Each group was sampled 50 μL, diluted with 33% acetic acid to 200 μL, transferred to a 96-well plate and read under the 570 nm channel of microplate reader. This experiment was repeated at least three times respectively. The data was analyzed by GraphPad Prism 8 to generate the corresponding statistical graphs.

Baf3/ALK soft agar colony: Baf3 cells were seeded in 6-well plates at a density of 500,000 per well for 48 hours using blank medium and the medium containing 5 nM, 10 nM, and 15 nM of **18d**. 1.4% and 3% aqueous agarose (sterilized) (Beyotime, Low melting point agarose) solutions were prepared and kept in a water bath at 42°C. Mixed 3% agarose with medium containing 20% of the serum at the ratio of 1:1 to obtain 1.5% agarose medium, added 1 ml of 1.5% agarose medium to each well in a 6-well plate, and set aside until solidification. Mixed 1.4% agarose with 20% FBS medium with volume ratio of 1:1, to obtain 0.7% agarose medium, kept at 42°C for non-coagulated. Counted the number of cells in each group, then diluted and mixed each group of cells with 0.7% agarose medium according to the density of 1000 per well, added 1 ml of medium containing cell suspension into each well that has been coagulated. After the upper layer of agarose to solidify, add 2 ml of complete medium per well. Place in an incubator for 3 weeks and changed medium every three days. Remove the 6-well plate, randomly selected 10 fields of view under the microscope of a 20x objective, took photos of the cloned cell masses, calculated the cell mass area using image J, and analyzed them using GrapPad Prism 8.

Western Blots assays general method

Western Blots assays were performed according to references [28-29]. H2228 cells were incubated with **18d** for 48h, then, homogenized with lysis buffer. The protein concentrations were detected using a BCA Protein Assay Kit (Pierce BCA Protein Assay Kit 23227, Thermo, USA), and their extracts were mixed up with loading buffer (Beyotime, China) and inactivated for 5 min at 100 °C. Subsequently, proteins (20 μg) were fractionated by 5~12% SDS-PAGE, and transferred to PVDF membranes. Then, PVDF membranes were blocked in 10% skimmed milk and incubated with the expected dilution of primary antibodies, including ALK (Abcam), *p*-ALK (Abcam), STAT-3

(Abcam), p-STAT-3 (Abcam) and β-actin (SAB). The above primary antibodies were then reacted with HRP-conjugated secondary antibody, and immunoreactive bands were visualized by an ECL Detection Reagent (Yeasen) and were estimated through densitometry with a chemiluminescence imaging system (Tanon, China). Intensities of the blots were quantified with image J and analyzed by GraphPad Prism 8.

Cell apoptosis assay

JC-1 stained method: H2228 cells were seeded in a 24-well plate at a density of 30,000 per well. Switched to serum-free medium containing different concentrations of compound **18d** after 12 h later and continued incubation for 24 h. Stained each well with 10ug/mL of JC-1 for 30min in dark. Then collected the dye and stained with 10ug/mL of DAPI and kept in dark for 15 min. Washed twice with PBS. Finally, an inverted fluorescence microscope was used in the darkroom to observe and photograph the wells under UV, blue and green channel, respectively.

Western blots method: Most steps were same as western blots assays general method, specia**l** for bax and bcl-2, 12%SDS-PAGE was used at electrophoresis phase.

Annexin V-FITC/PI apoptosis experimental method

Seeded 200,000 of H2228 cells in each well of a 6-well plate, and after 24 hours, changed the medium by containing 5 nM, 10 nM, and 20 nM of compound **18a** respectively, while retained the blank medium group as a control. After another 48 hours, collected cells from each group using trypsin, free of EDTA and calcium ions, as well as cells floating in the supernatant in each group. After resuspending each sample 2-3 times by PBS, stained the samples using PI and Annexin V-FITC. Prepared a double-stained negative tube, two single-stained tubes and one double-stained positive tube for setting the gate. Operated all samples and collected data on the Beckman Coulter Flow Cytometer using the PE and FITC channels in a low-speed loading mode. The resulting data imaged by the instrument's own software and analyzed by GraphPad Prism 8.

Immunofluorescence staining

H2228 cells were seeded into 24-Well plate and then treated with control (1‰ DMSO) and compound **18d** (10, 20 nM). Cells were washed thrice with PBS, fixed with 4% paraformaldehyde for 15 min and punched with 0.2% triton X100 then blocked with 500 μL blocking buffer at room temperature for 1 h, Cells were incubated with a primary monoclonal antibody (ALK, and *p*ALK) at 4 ^{o}C overnight, then washed with PBS thrice and followed by incubation with the fluorescence secondary antibody (Cy3-labeled Goat Anti-rabbit IgG (H+L)-A0428) and labeling of nuclei by DAPI (Beyotime, China). The cells were finally visualized by a fluorescence microscope under 10X objective (M Shot, China).

Cell cycle assay

PI stained method: Seeded 100,000 of H2228 cells in each well of a 6-well plate, cultured for 24 hours, and then switched to medium containing 5 nM, 10 nM, and 20 nM of compound **18d** for another 48 hours. Collected each group of cells separately (it

was necessary to collect the floating cells in the supernatant of each group), resuspended it 2-3 times using PBS, removed the supernatant and mixed well with 70% cold ethanol, then fixed overnight in a 4 ℃ freezer. The 70% alcohol was then removed, washed 2-3 times using PBS, added a PI dye containing RNase A, stained at room temperature in the dark for 30 minutes, finally detected the samples in the PE channel of the Beckman coulter flow cytometer. The resulting data imaged by flow cytometer self-equipped software and analyzed by GraphPad Prism 8.

In vivo antitumor assay

Selected and collected H2228 cells of logarithmic growth phase and resuspended them 3 times with PBS to remove residual serum. After mixing the blank 1640 medium with Matrix in a 1:1 ratio, added H2228 cells and mixed them well so that the final cell concentration is 5×10^7/mL, placed the centrifuge tube with cell suspension on ice, sterilized and taked it into the animal room.

Mixed the cell suspension first, aspirated the cell suspension using a 1 mL sterile syringe, and injected 0.2 ml of the cell suspension at the right limb fossa of each nude mouse. The cell suspension should be well mixed prior before injected to each nude mouse and kept the cell suspension always on ice to prevent Matrix from coagulating. After injection, the physical condition of nude mice and tumor growth were observed regularly. When the tumor volume reached 200mm^3, the nude mice were divided into six groups, which contained 10 mice with similar average volume of tumores, and nude mice with too large or too small tumors were excluded. The blank group was administrated an aqueous solution of 0.5% CMC-Na, and the other five groups were given compound **18a-d** and the positive drug Ceritinib. All compounds were formulated with 0.5% CMC-Na aqueous solution, oral administration, and administered at a dose of 20 mg/kg.

After 14 days of continuous administration, the nude mice were euthanized by carbon dioxide asphyxiation. The tumors of each group of nude mice were peeled, photographed and weighed in turn. The resulting data was analyzed by GraphPad Prism 8.

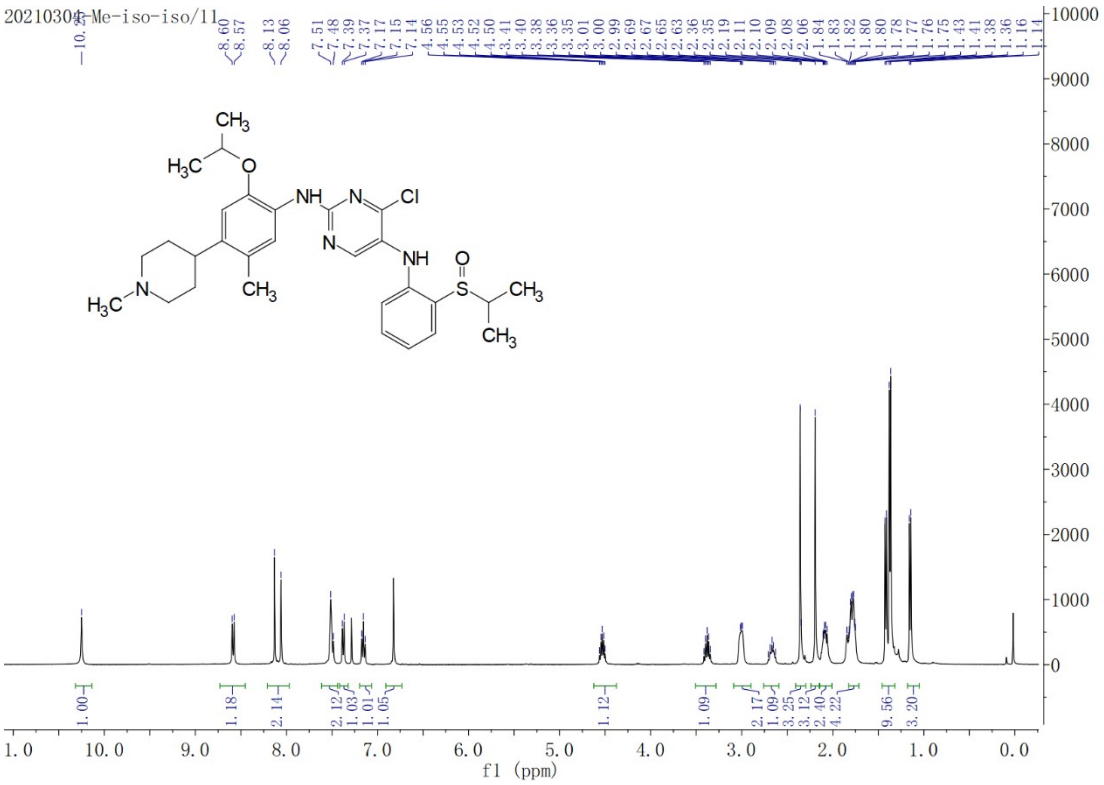
The nude mice used in the experiment were all 4-week old male nude mice, purchased from Guangdong Medical Animal Experiment Center. All experiments were carried out in accordance with the ethical requirements of laboratory animals. Laboratory animal use license number: SYXK (Guangdong) 2020-0102. Animal test certificate number: 00279323. After the end of the experiment, the animal carcasses were uniformly treated harmlessly.

Animal sacrifice images.

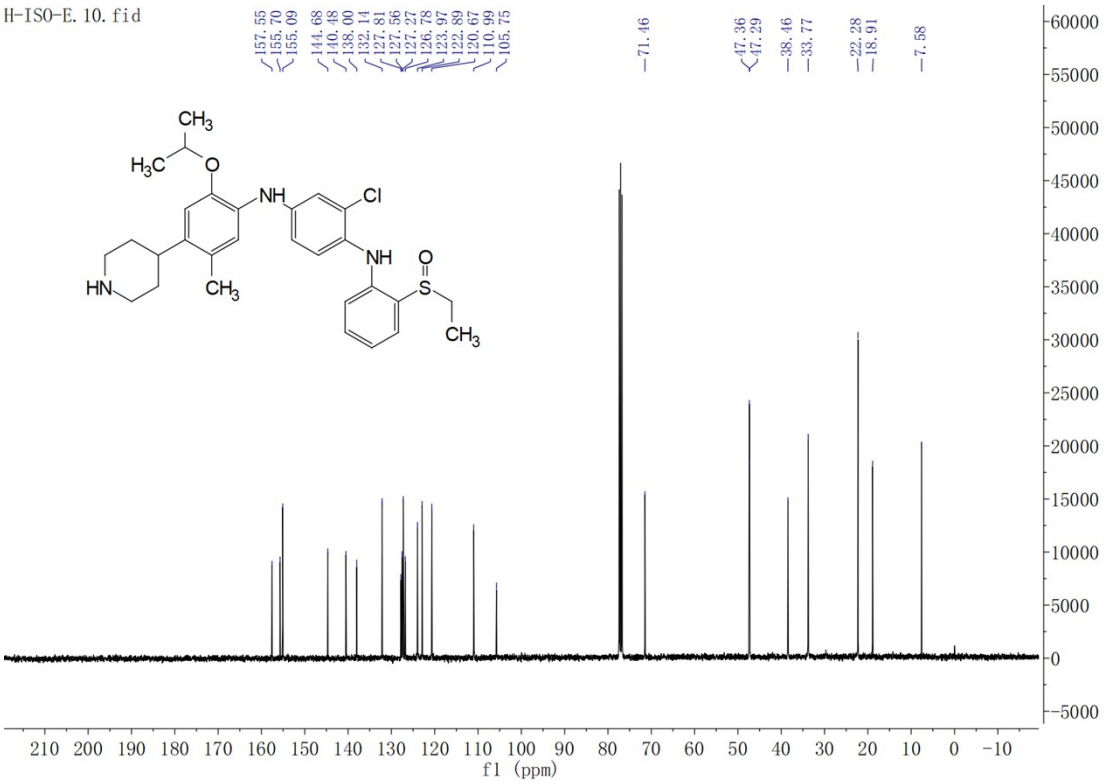
NMR

18a in $CDCl_3$

H^1 NMR

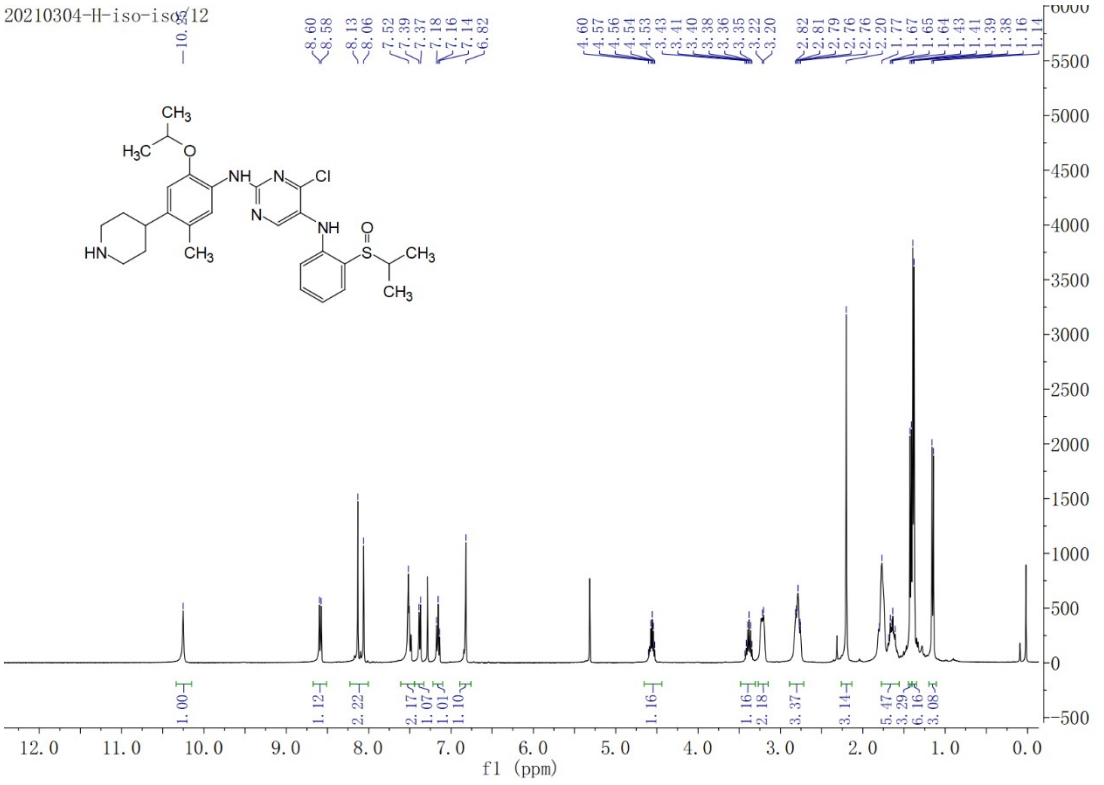


C^{13} NMR

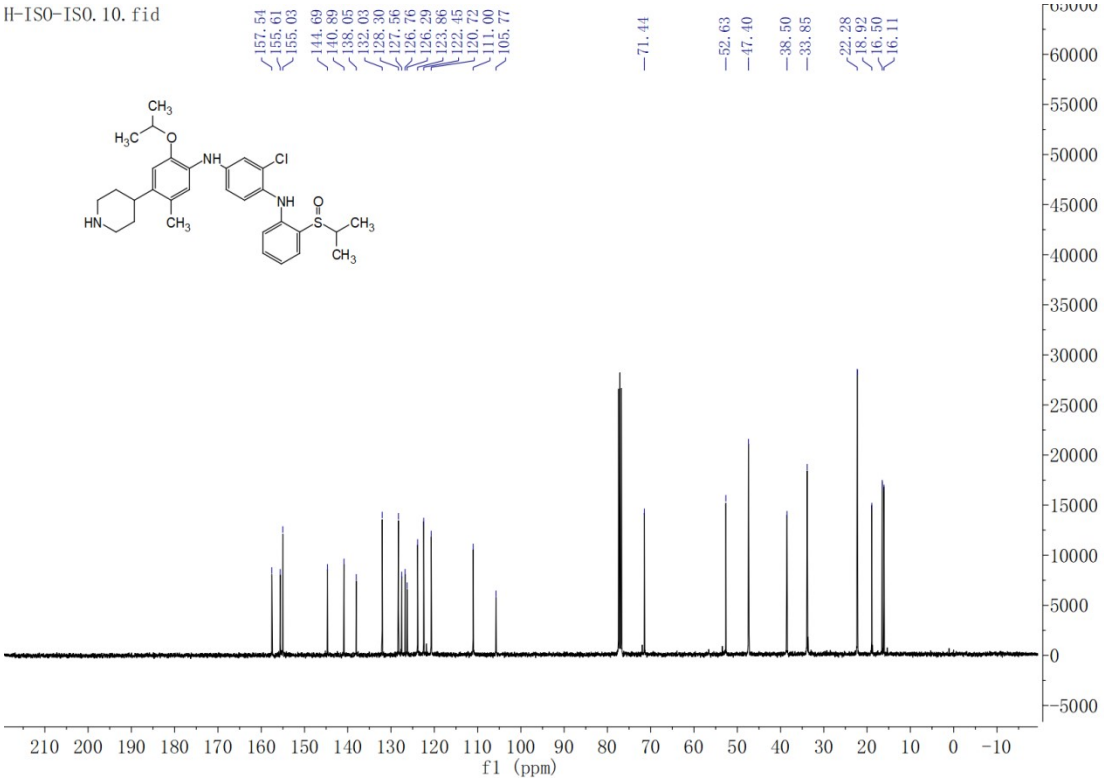


18b in $CDCl_3$

H^1 NMR

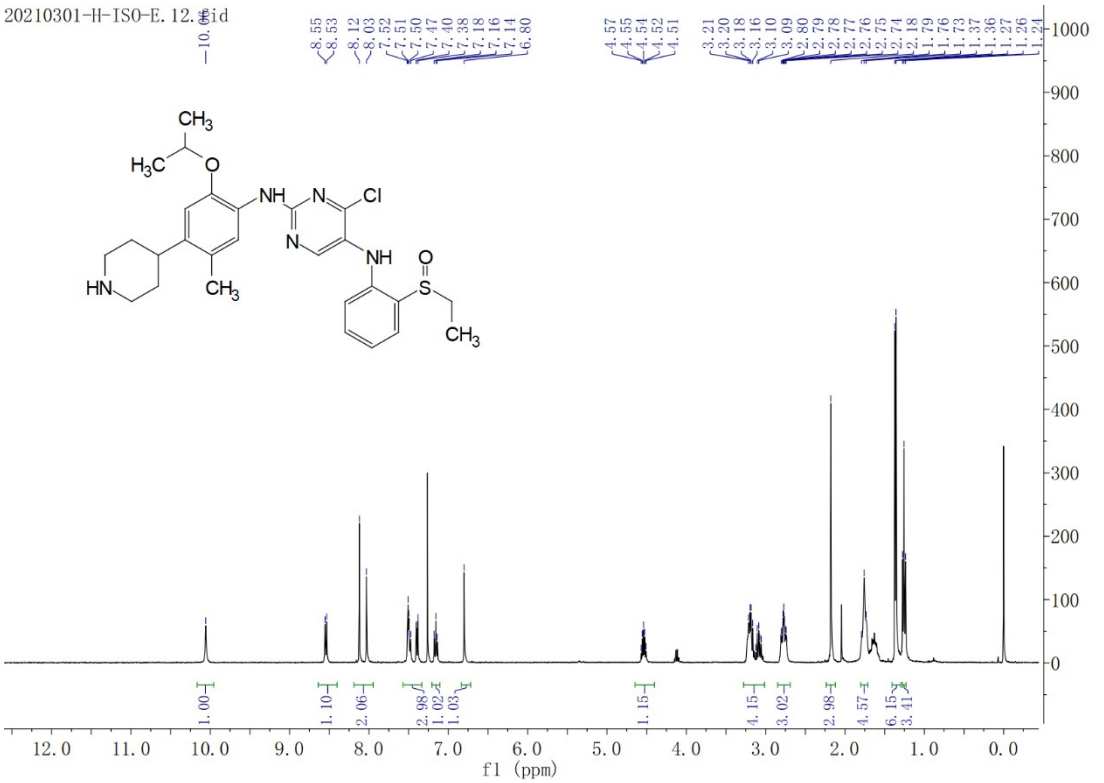


C[13] NMR

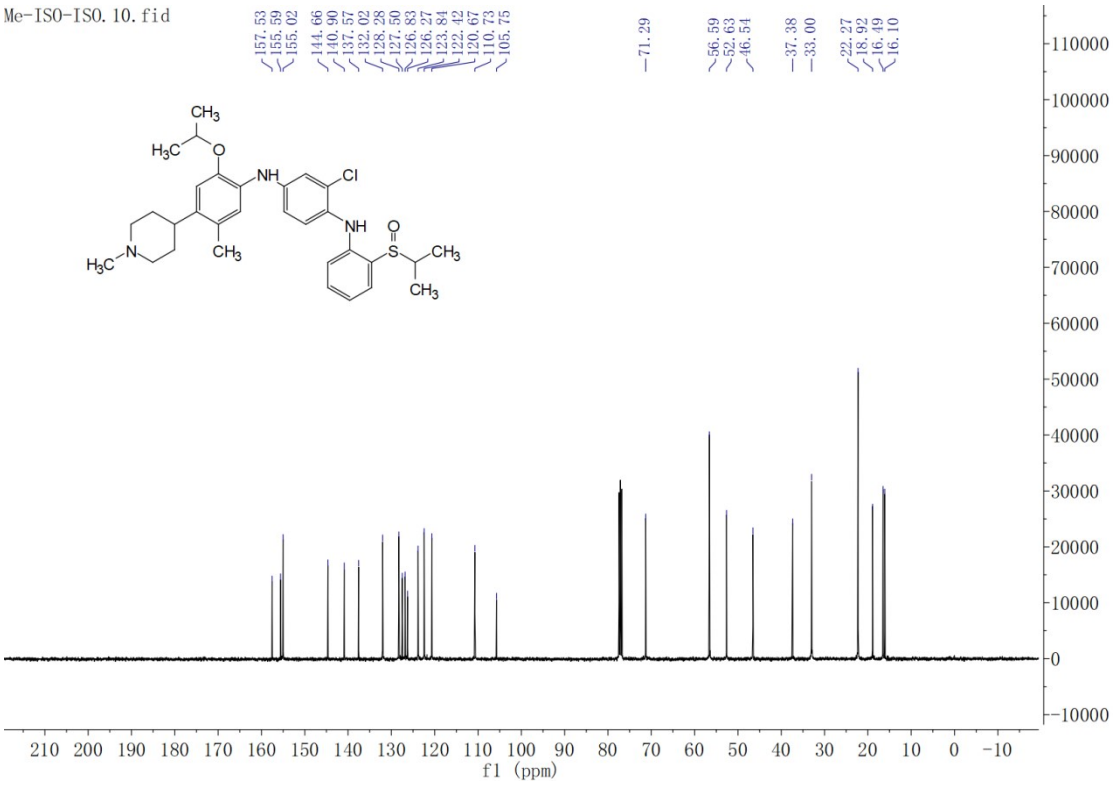


18c in $CDCl_3$

H[1] NMR

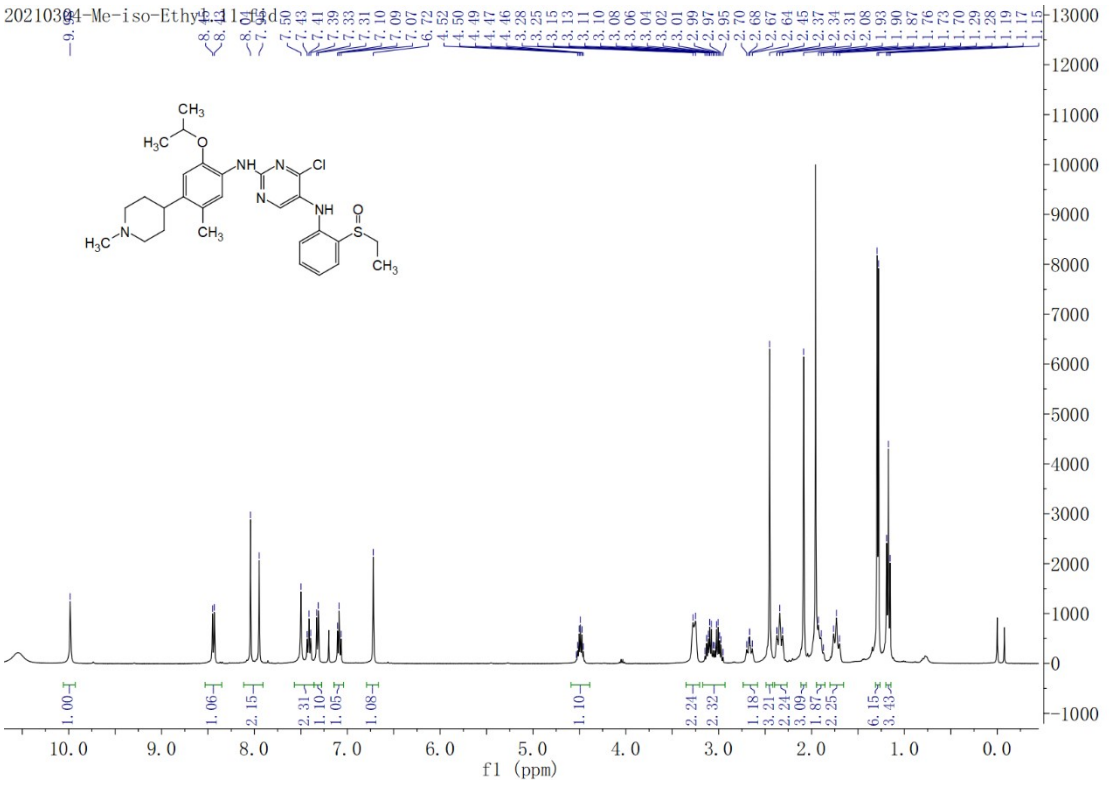


C[13] NMR



18d in $CDCl_3$

H^1 NMR



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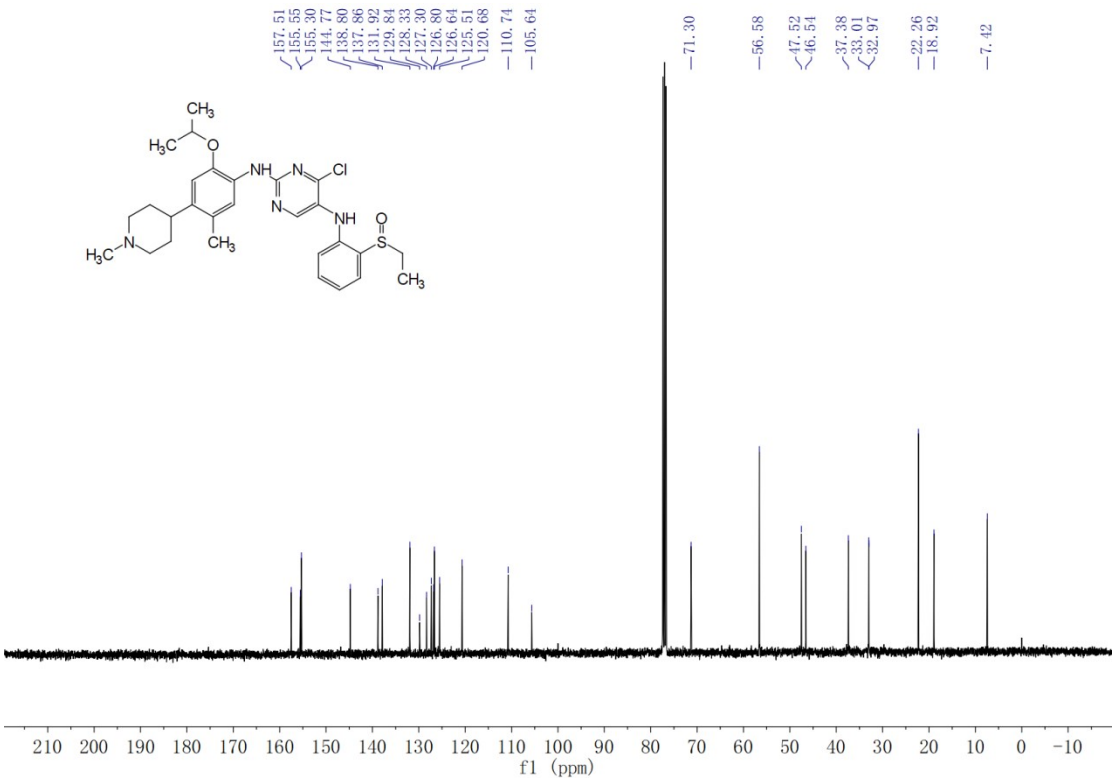

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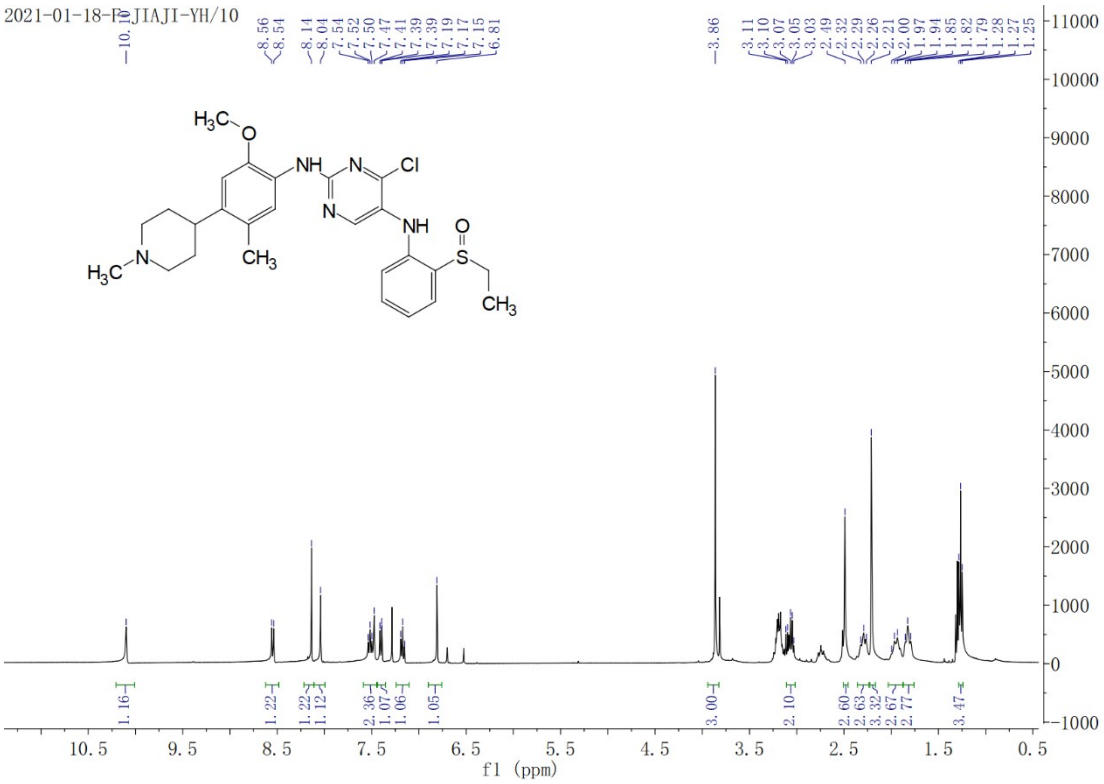

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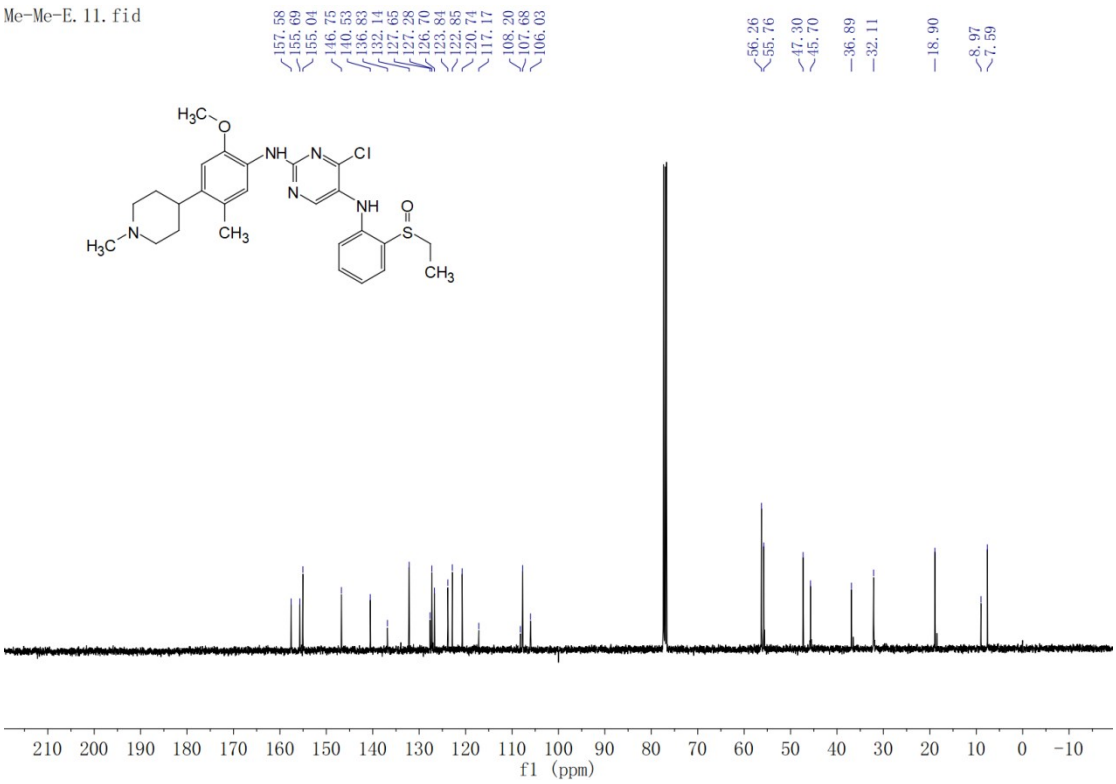
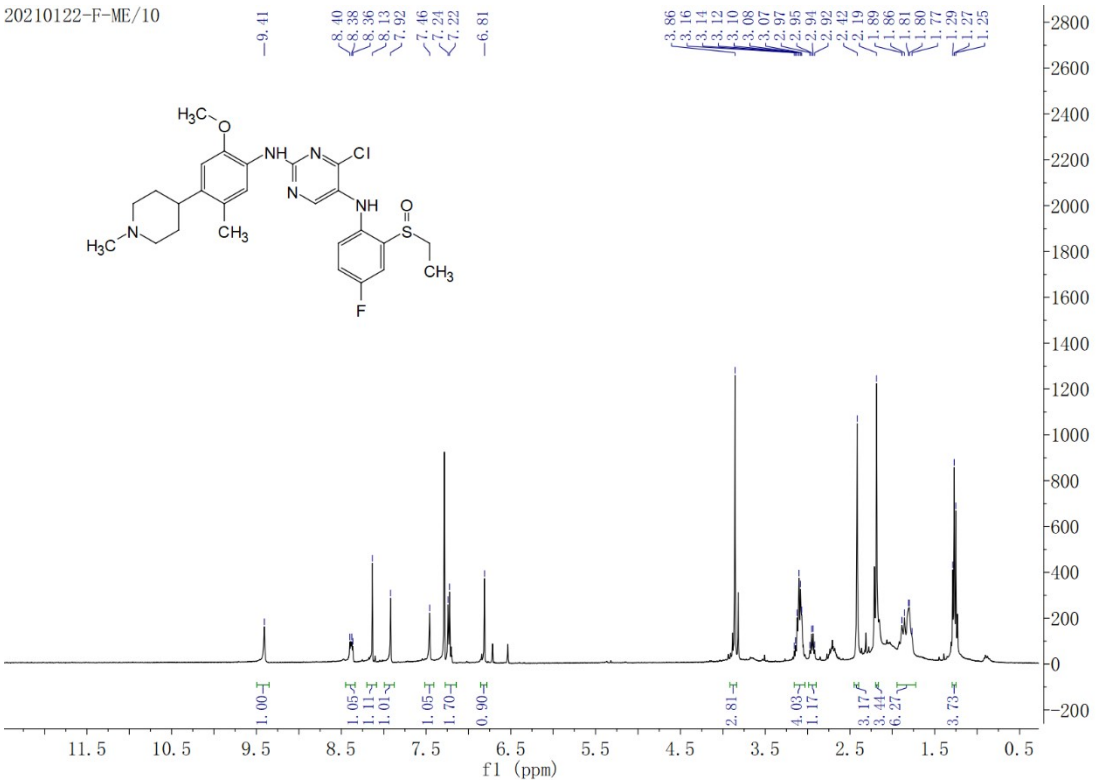
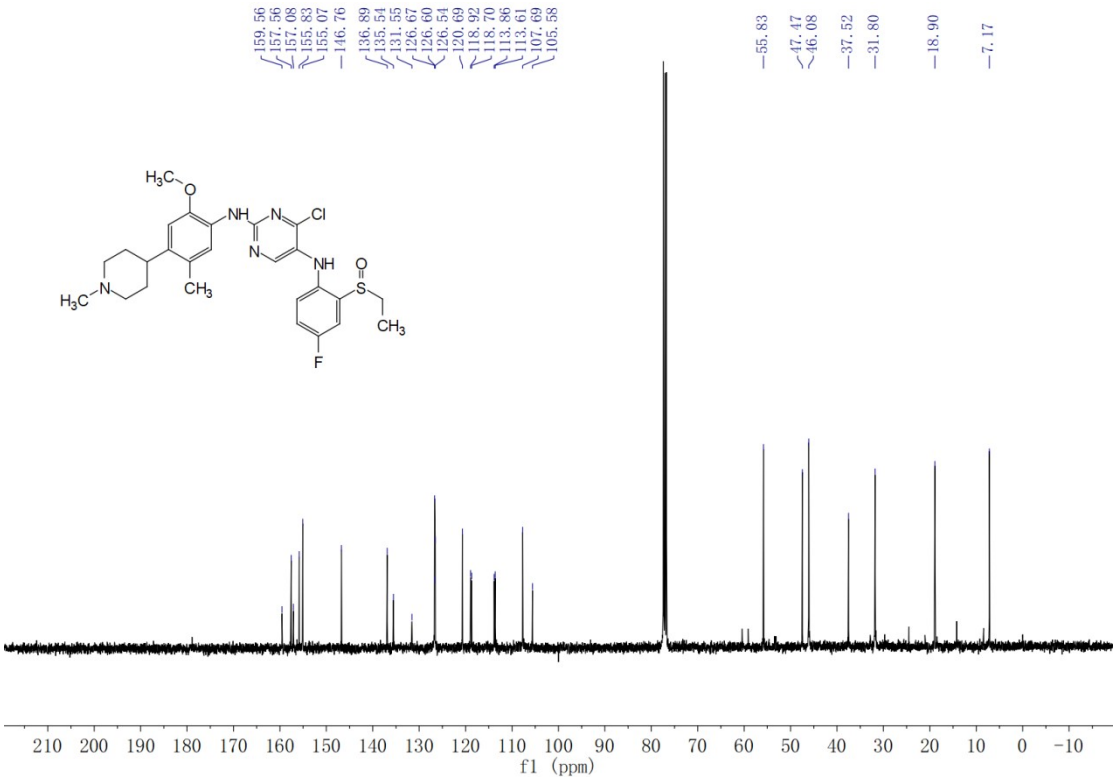


18f in $CDCl_3$

H[1] NMR

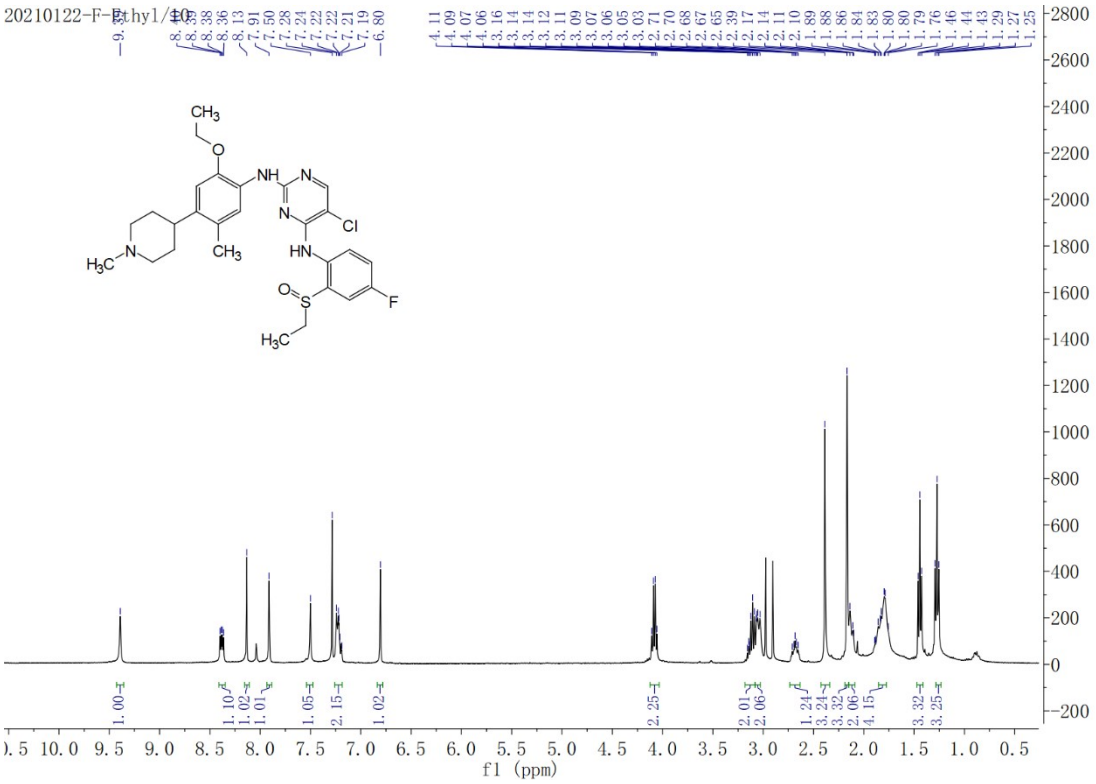


C[13] NMR

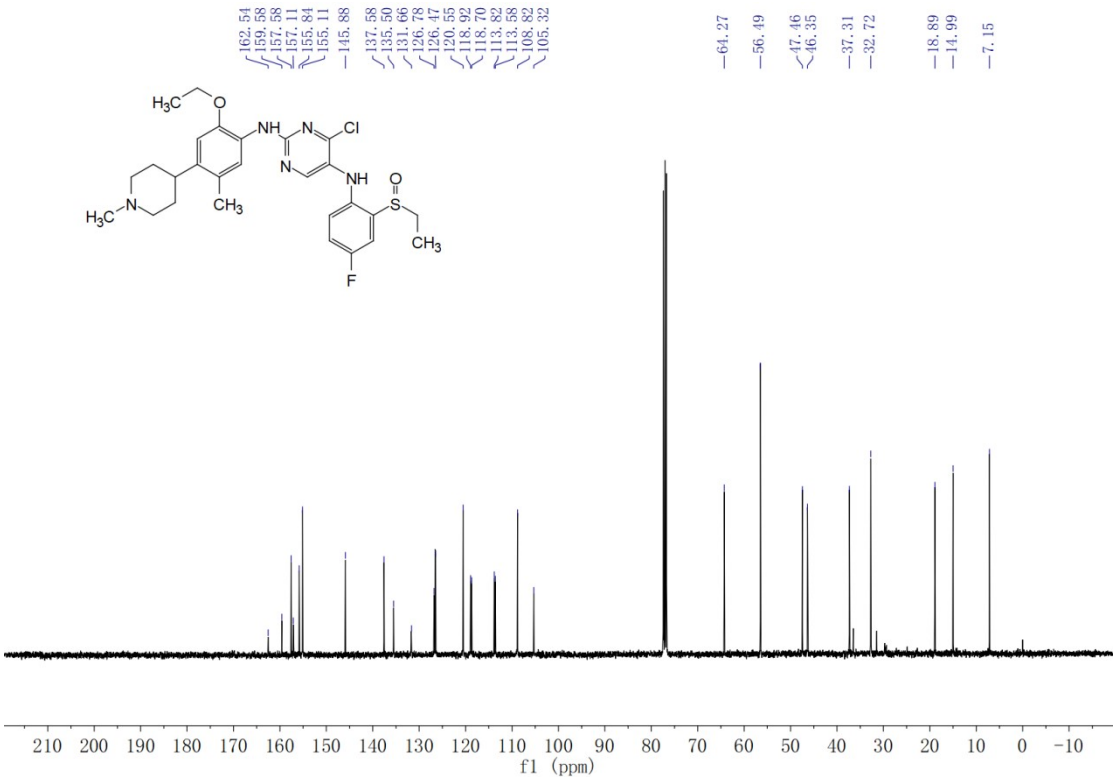


18g in $CDCl_3$

H[1] NMR

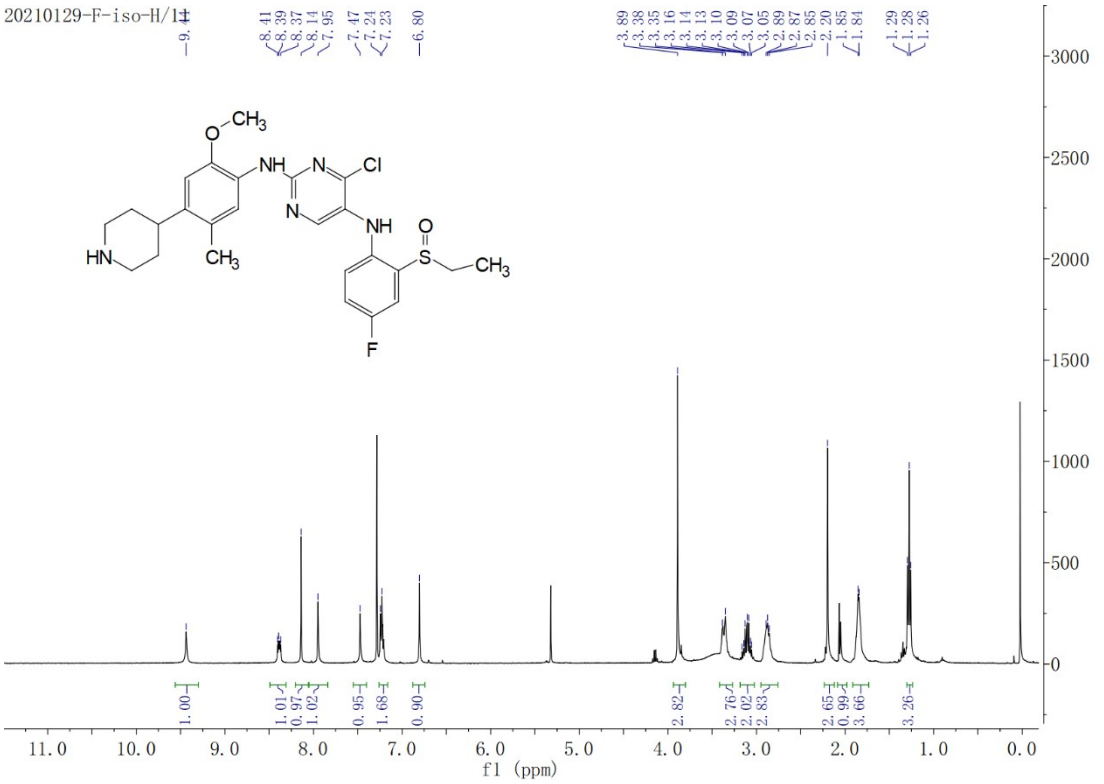


C[13] NMR

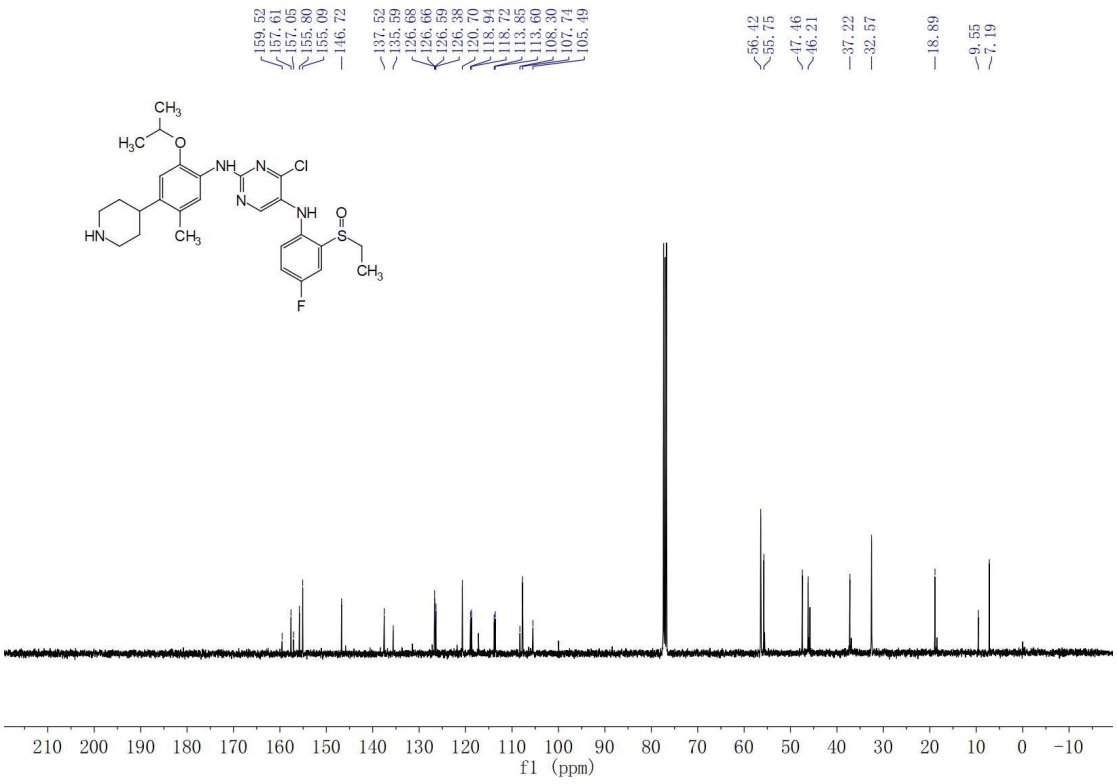


18h in $CDCl_3$

H[1] NMR

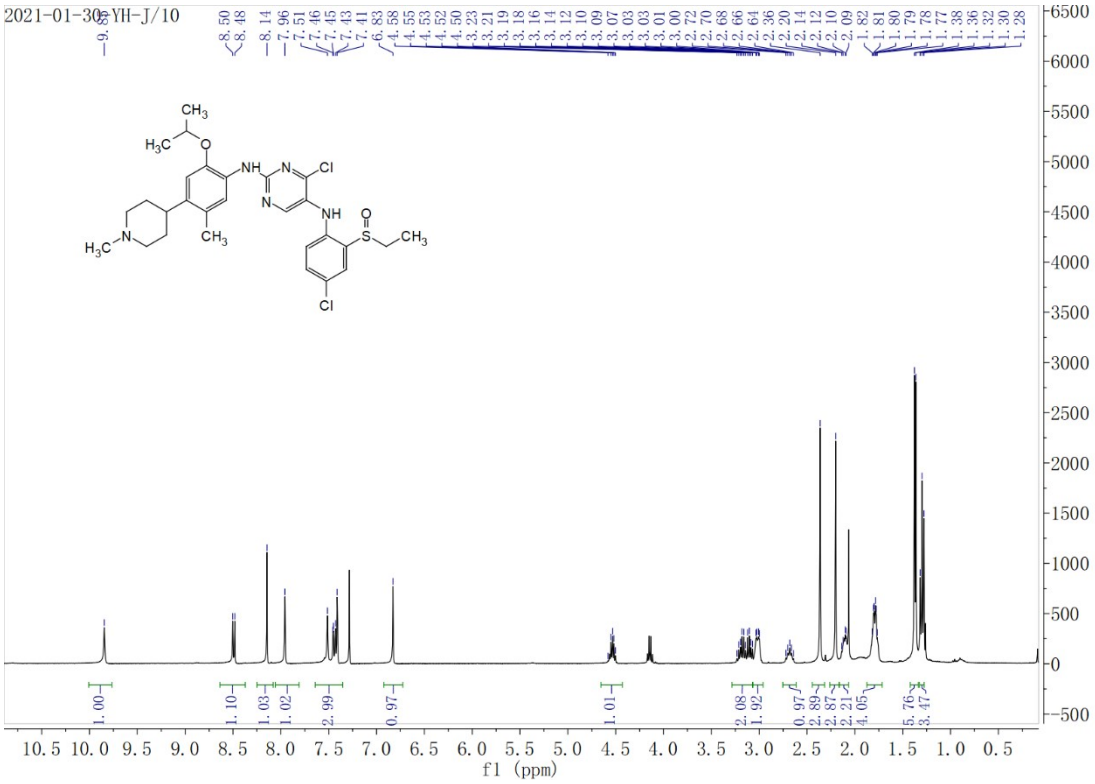


C[13] NMR

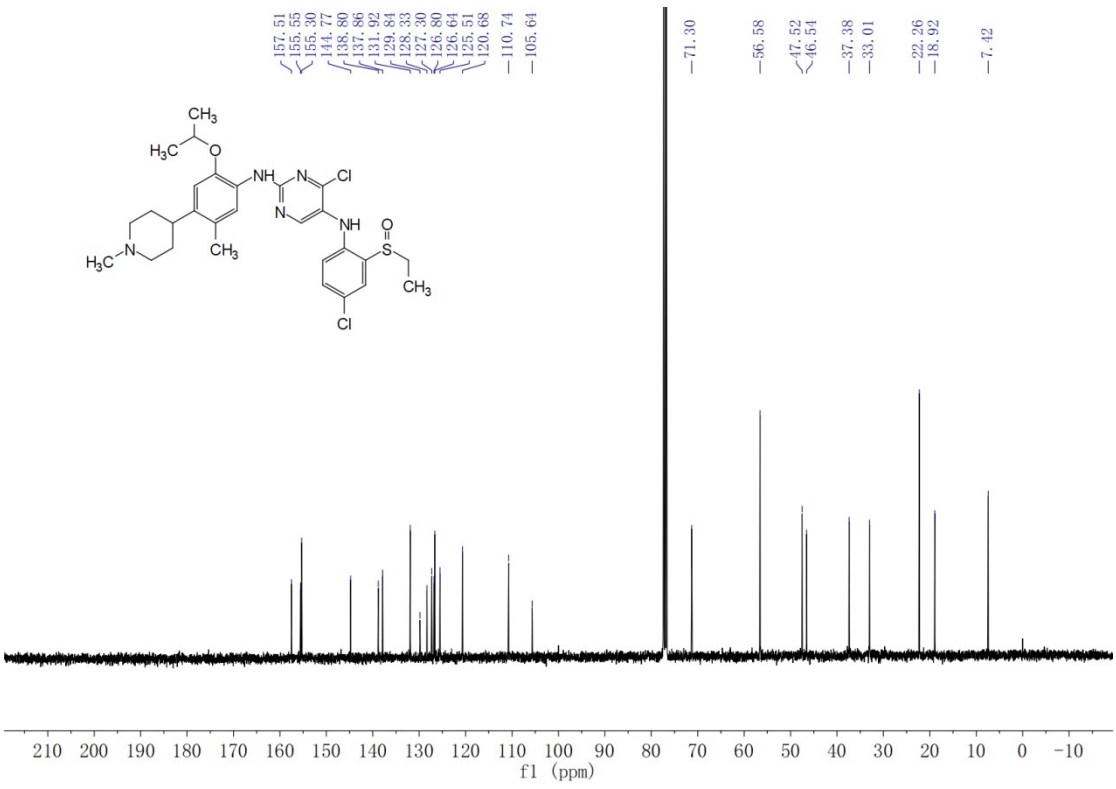


18i in $CDCl_3$

H[1] NMR



C[13] NMR



18j in $CDCl_3$

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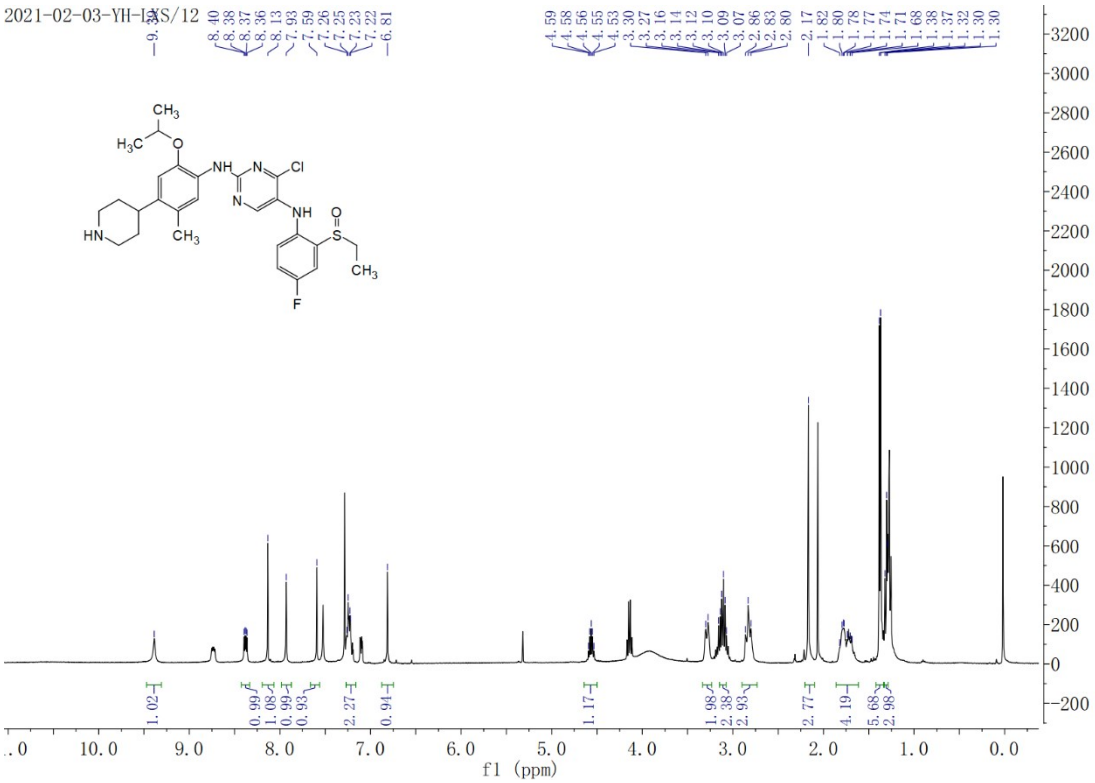
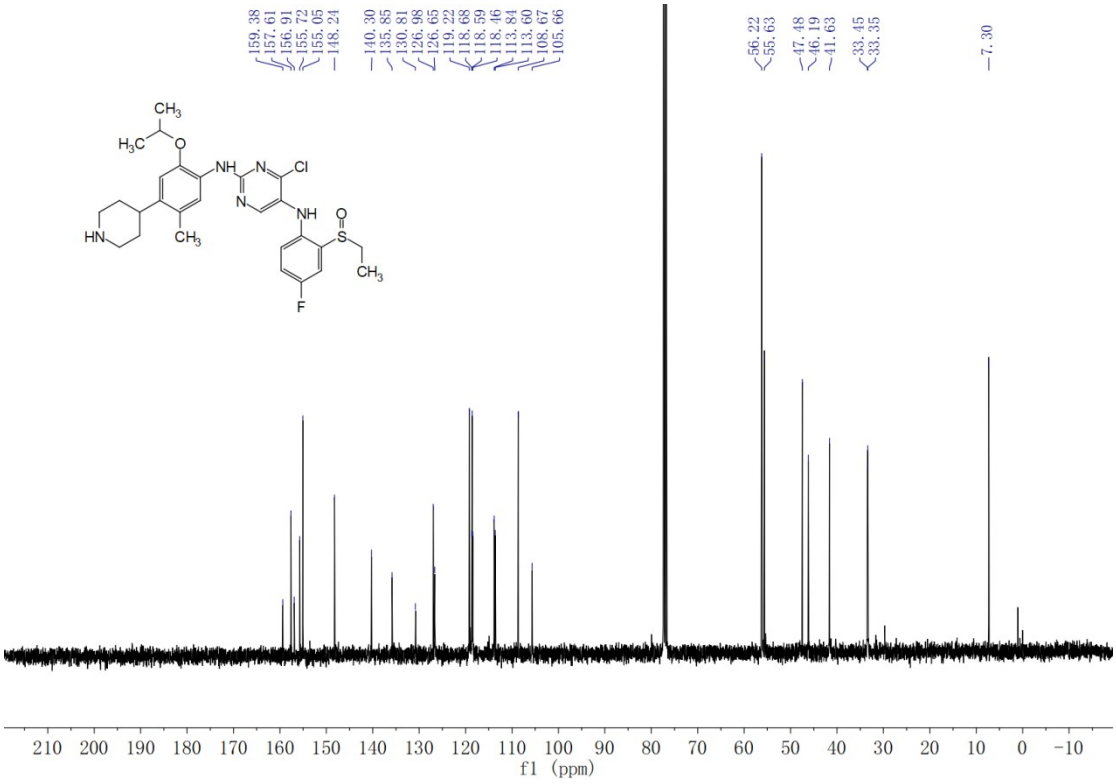


C[13] NMR



18k in $CDCl_3$

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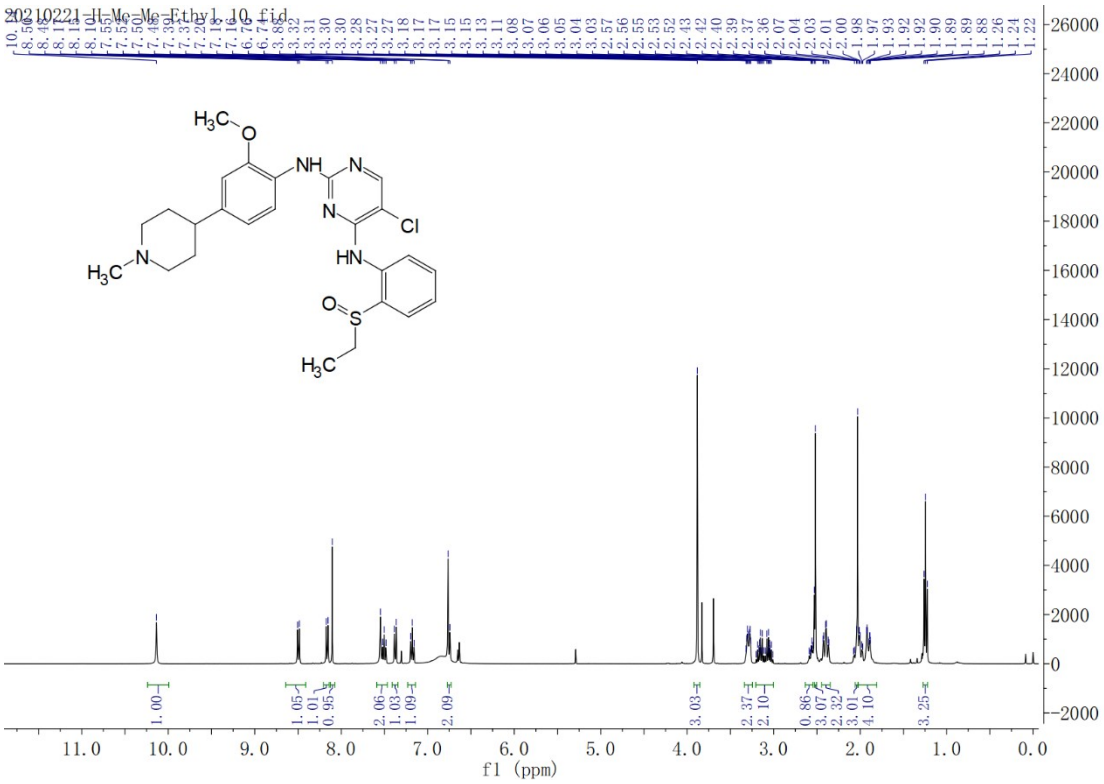
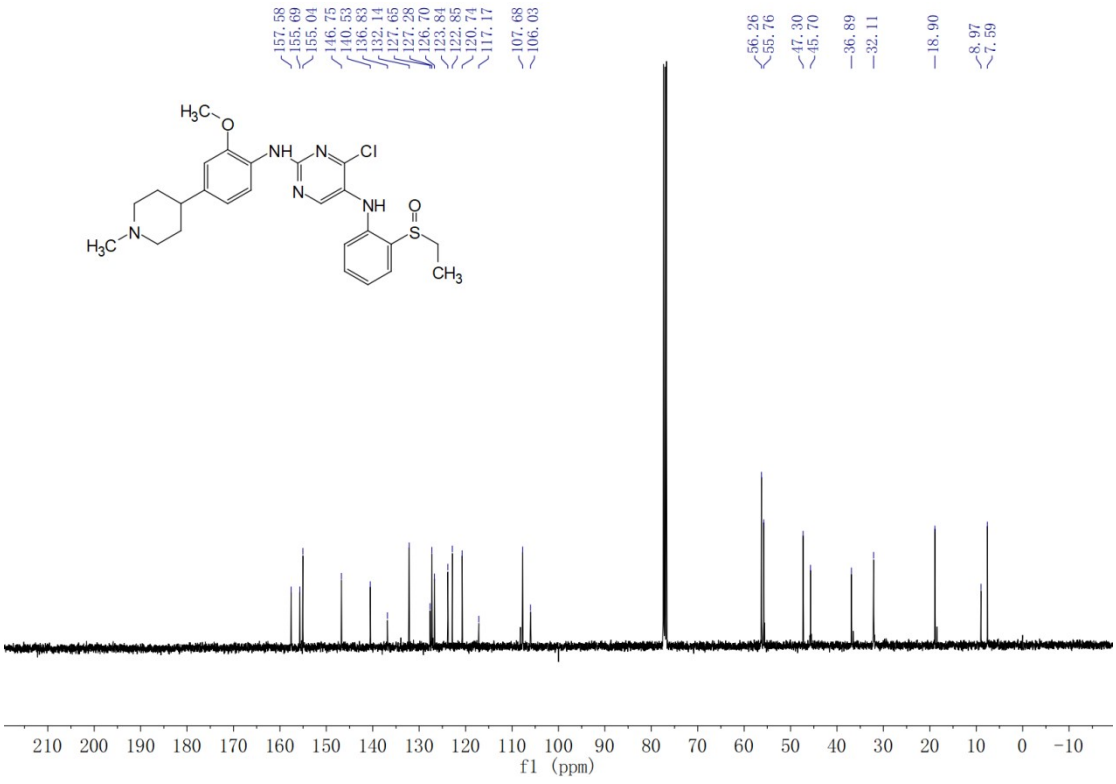
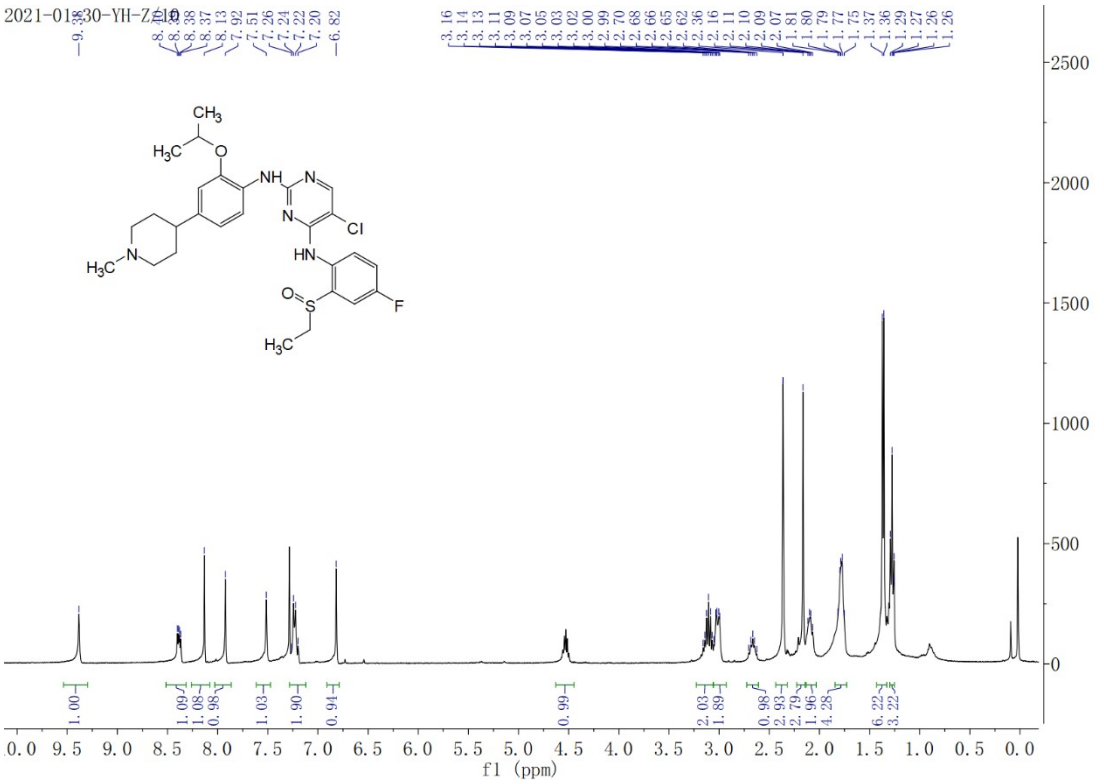


C[13] NMR

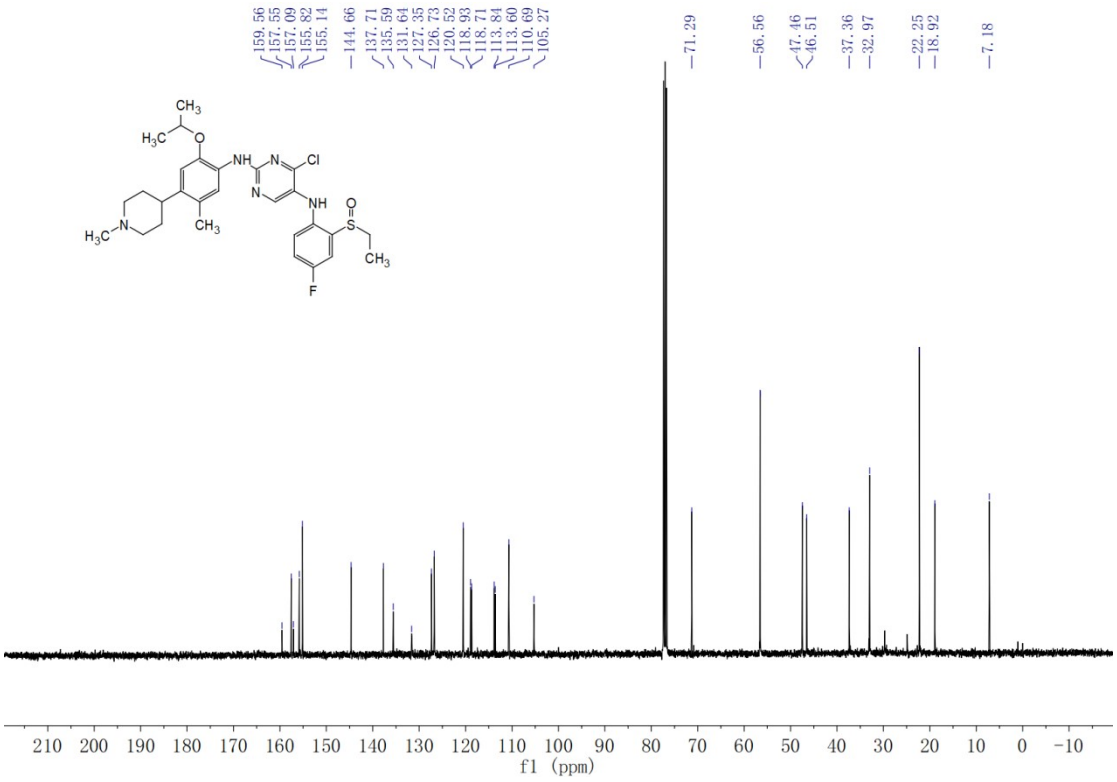


18l in $CDCl_3$

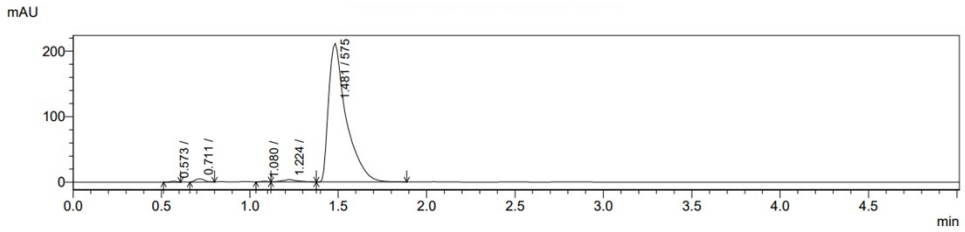
H[1] NMR



C[13] NMR



18a

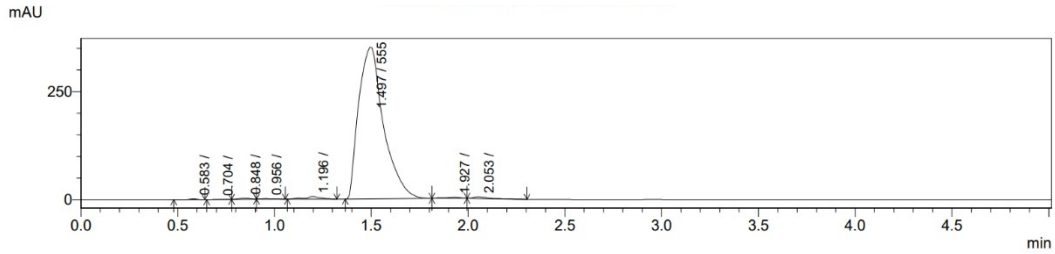


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.573		0.037	1382	3074	0.204	1092	0.906	---
0.711		0.058	4688	17280	1.144	744	1.277	1.588
1.080		0.041	1276	3283	0.217	2875	---	3.989
1.224		0.088	3725	22006	1.457	796	---	1.141
1.481	575	0.098	211459	1464964	96.978	947	1.904	1.403
			222529	1510607	100.000			

18b



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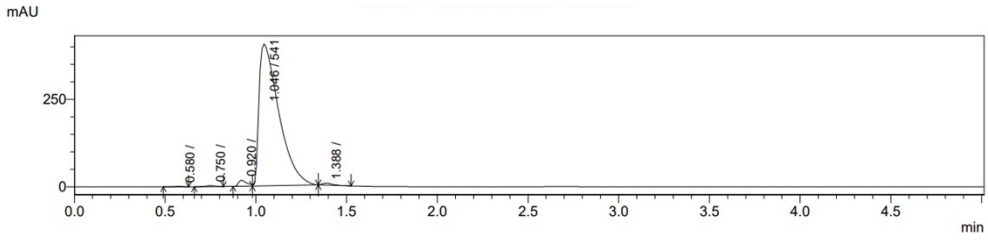
PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.583		0.045	1891	5419	0.168	722	0.904	---
0.704		0.060	669	2587	0.080	664	1.302	1.234
0.848		0.066	2346	9291	0.289	878	0.952	1.287
0.956		0.089	1056	4840	0.150	1426	1.522	1.000
1.196		0.062	6458	35362	1.098	1363	0.938	2.082
1.497	555	0.136	351007	3132217	97.262	627	1.396	1.631
1.927		0.068	2414	12832	0.398	2614	0.787	2.209
2.053		0.068	3804	17831	0.554	3723	2.543	0.880
			369646	3220379	100.000			

18c

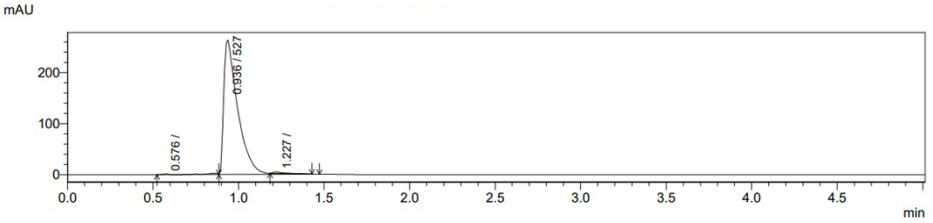


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.580		0.043	1805	4899	0.155	818	0.883	---
0.750		0.060	2885	11584	0.367	656	0.905	1.707
0.920		0.051	17412	56636	1.792	1234	---	1.539
1.046	541	0.116	405329	3067878	97.076	371	2.558	0.783
1.388		0.056	5622	19299	0.611	2552	1.578	2.085
			433054	3160296	100.000			

18d

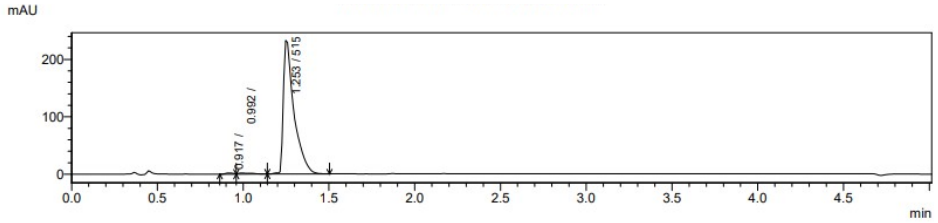


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.576		0.041	1662	18162	1.181	958	0.888	--
0.936	527	0.083	263191	1507381	98.004	590	2.602	3.147
1.227		0.053	2686	12534	0.815	2739	2.793	2.350
			267539	1538077	100.000			

18e



峰表

PDA Ch1 254nm

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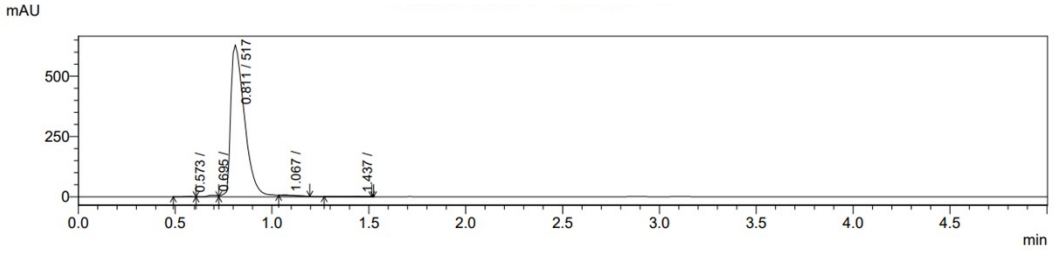
0.917		0.059	1838	6259	0.614	1156	--	--
0.992		0.099	2032	10631	1.042	587	--	0.550
1.253	515	0.059	232963	1003331	98.344	1794	2.336	1.849
			236833	1020221	100.000			

18f

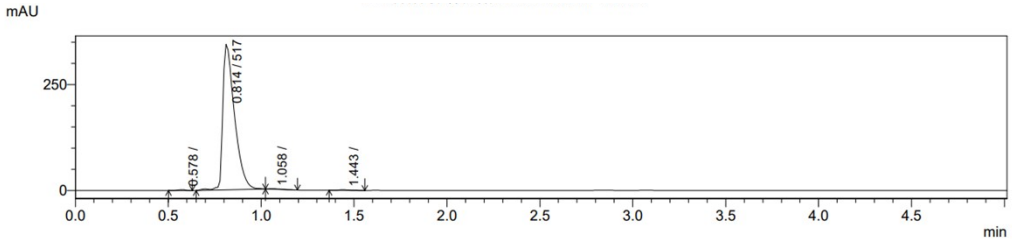


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.573		0.044	1912	5333	0.167	724	--	--
0.695		--	6662	24205	0.758	373	--	1.059
0.811	517	0.075	630918	3147733	98.623	511	1.960	0.809
1.067		0.084	2025	9148	0.287	1106	2.147	1.883
1.437		0.054	1507	5255	0.165	2792	1.208	3.128
			643023	3191672	100.000			

18g

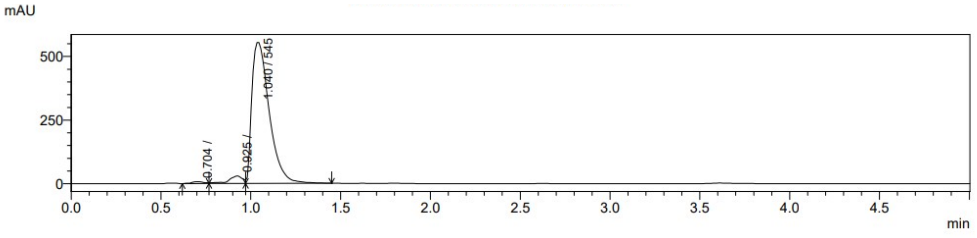


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.578		0.041	1939	5021	0.329	839	0.884	--
0.814	517	0.066	343644	1512102	98.995	615	1.953	2.239
1.058		0.086	1114	5355	0.351	949	2.225	1.815
1.443		0.053	1451	4980	0.326	2993	1.149	3.173
			348149	1527458	100.000			

18h

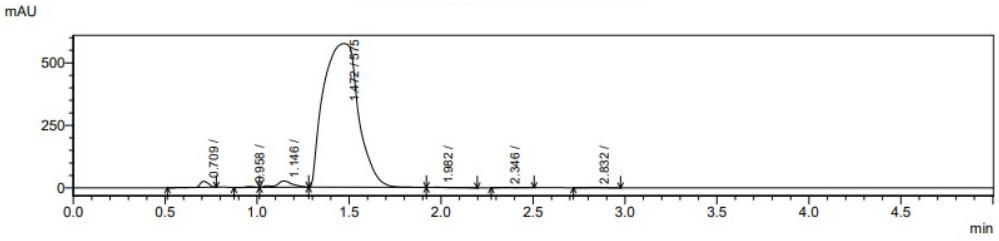


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.704		0.078	7203	35388	0.908	311	--	--
0.925		0.083	29443	156707	4.021	518	--	1.369
1.040	545	0.103	553759	3705249	95.071	535	1.884	0.671
			590405	3897345	100.000			

18i

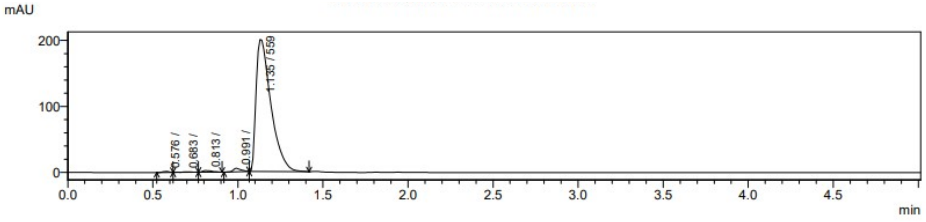


峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.709		0.053	23994	82674	1.053	902	1.297	--
0.958		0.047	3566	10543	0.134	1826	1.144	2.706
1.146		0.078	25166	148780	1.896	822	0.989	1.508
1.472	575	0.213	574847	7584036	96.624	345	1.076	1.367
1.982		0.065	1244	4575	0.058	3897	1.354	2.297
2.346		0.077	1764	9210	0.117	3792	1.541	2.606
2.832		0.098	1512	9171	0.117	3835	1.029	2.900
			632093	7848990	100.000			

18j



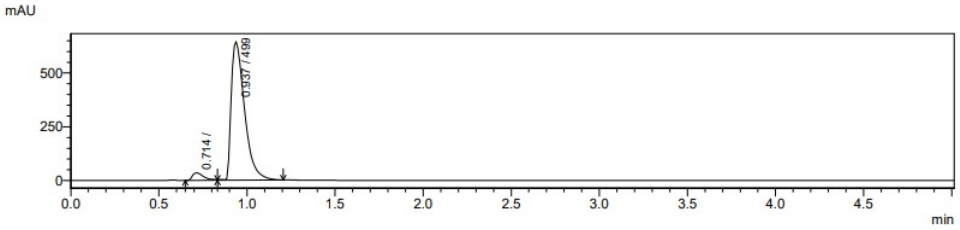
m/z

峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.576		0.040	1606	3999	0.319	923	0.908	—
0.683		0.070	613	3464	0.277	691	1.150	1.187
0.813		0.063	2405	9646	0.771	730	1.640	1.163
0.991		0.049	5267	17002	1.358	1663	1.391	1.639
1.135	559	0.092	200139	1217552	97.275	688	1.989	1.063
			210032	1251663	100.000			

18k



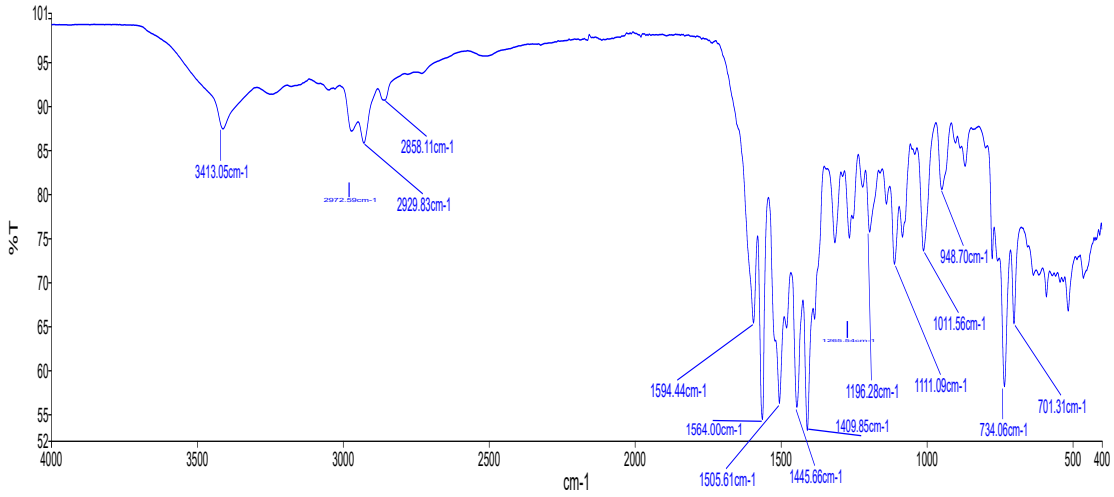
峰表

PDA Ch1 254nm

保留时间	化合物名	峰宽(高度 50%)	高度	面积	面积%	理论塔板数(USP)	拖尾因子	分离度(USP)
0.714		0.068	34817	159309	4.475	445	—	—
0.937	499	0.080	645144	3400341	95.525	579	1.860	1.536
			679961	3559650	100.000			

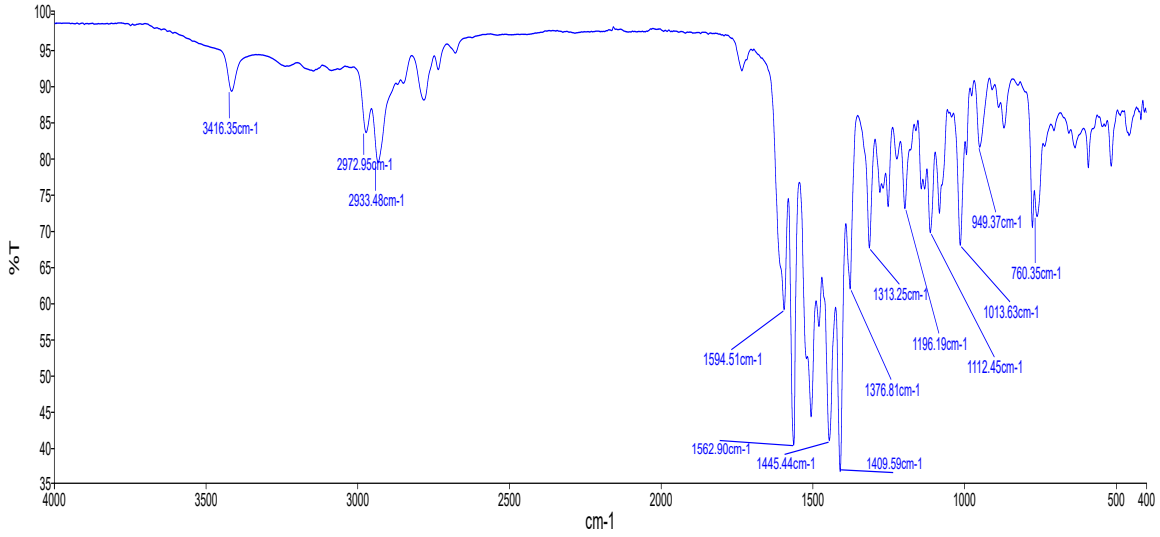
IR

18a

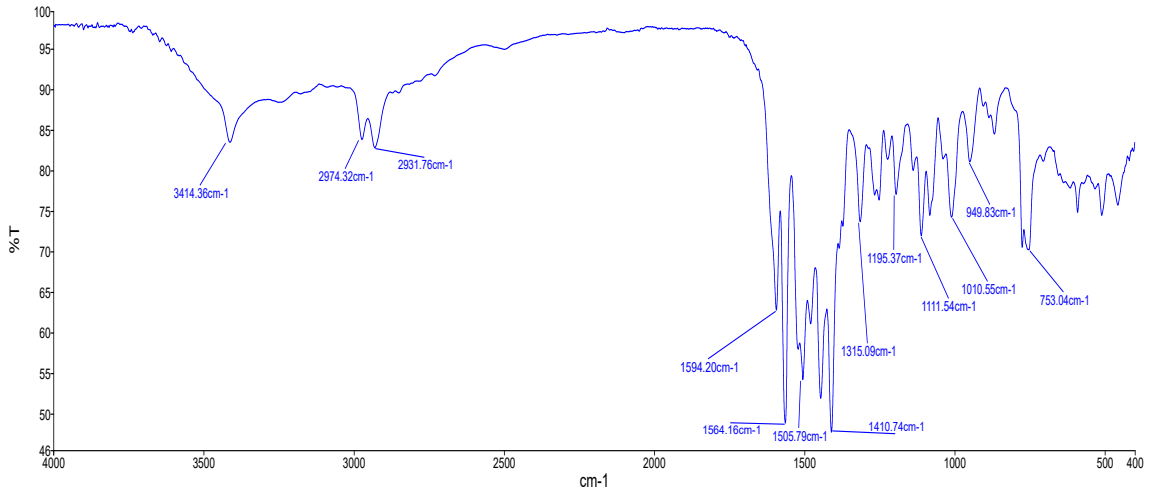


18b

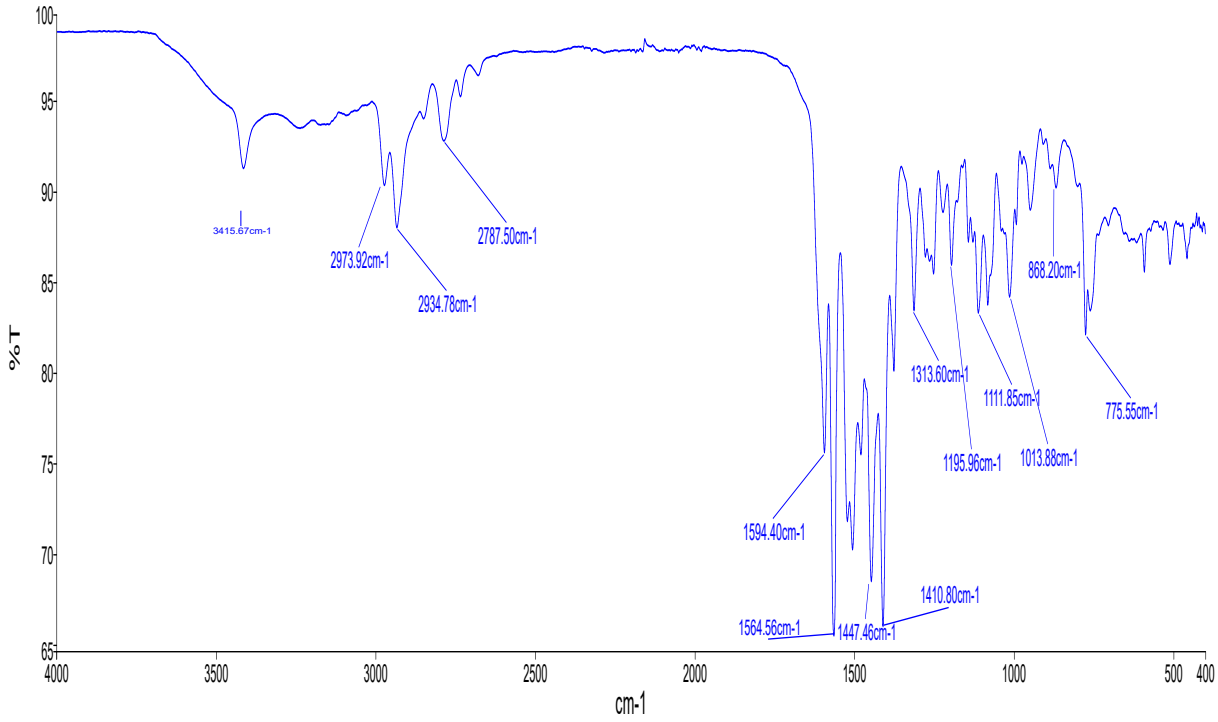
4



18c



18d


100
95
90
85
80
75
70
65
%T
4000
3500
3000
2500
2000
1500
1000
500
400
cm-1
3415.67cm-1
2973.92cm-1
2934.78cm-1
2787.50cm-1
1594.40cm-1
1564.56cm-1
1447.46cm-1
1410.80cm-1
1313.60cm-1
1195.96cm-1
1111.85cm-1
1013.88cm-1
868.20cm-1
775.55cm-1

HRMS

18a

Formula Predictor Report - 18A.lcd

Page 1 of 1

Data File: \\Deep-20160624ld\data1\新呈术\YH\18A.lcd

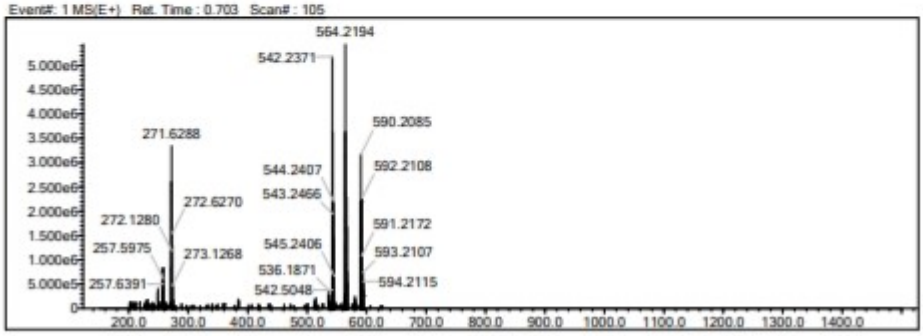
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	36	36	N	3	5	5	S	2	1	1	I	3	0	0	Na
B	3	0	0	O	2	2	2	Cl	1	1	1					
C	4	28	40	F	1	0	0	Br	1	0	0					

Error Margin (ppm): 50
HC Ratio: unlimited
Max Isotopes: all
MSn Iso RI (%): 75.00

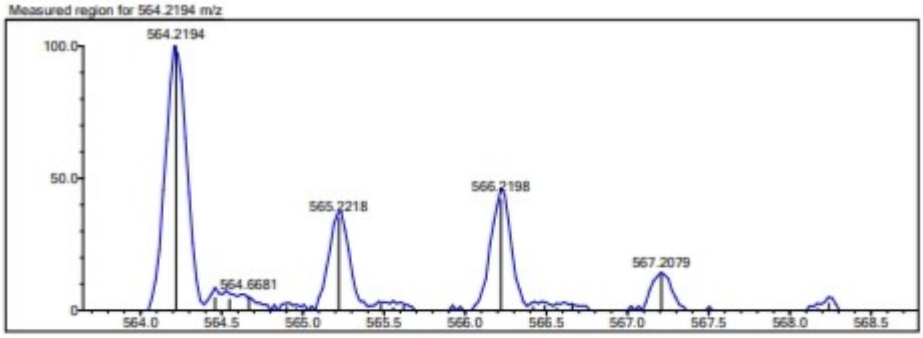
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

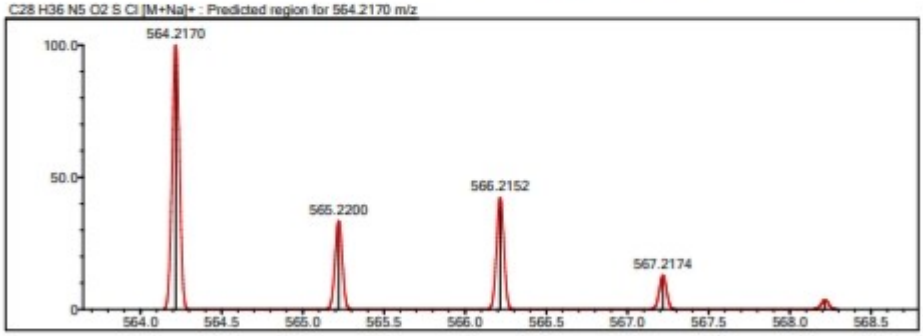
Event#: 1 MS(E+) Ret. Time : 0.703 Scan# : 105



Measured region for 564.2194 m/z



C28 H36 N5 O2 S Cl [M+Na]+ : Predicted region for 564.2170 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	64.25	C28 H36 N5 O2 S Cl	[M+Na]+	564.2194	564.2170	2.4	4.25	69.93	13.0

18b

Formula Predictor Report - 18B.lcd

Data File: H:\申-高分辨\18B.lcd

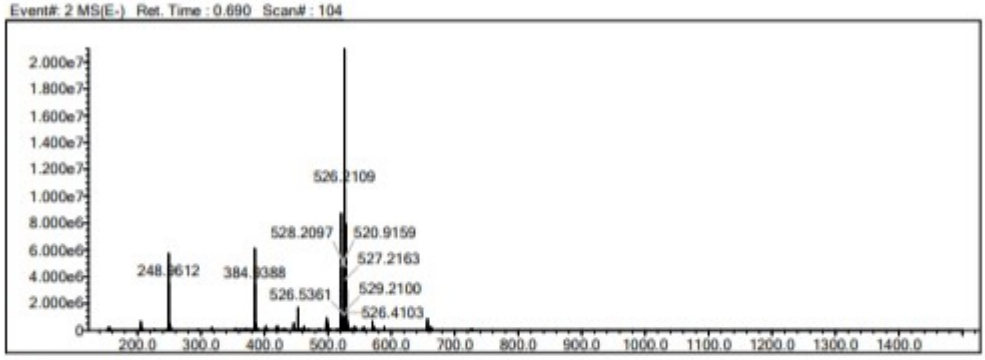
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	34	34	N	3	5	7	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					
C	4	27	27	F	1	0	0	Br	1	0	1					

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

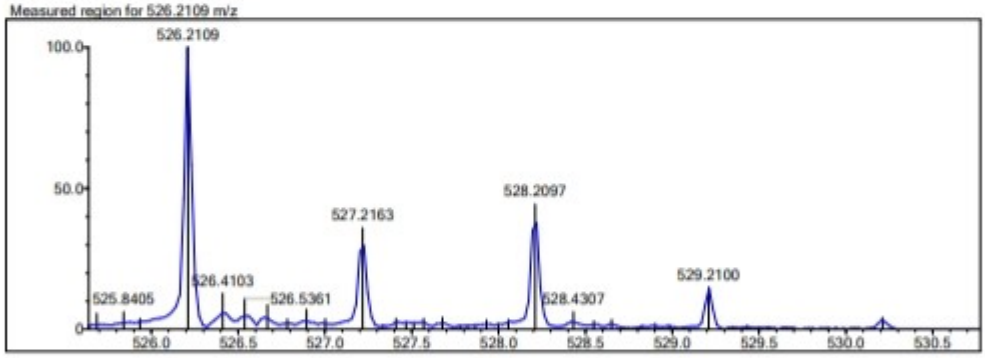
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

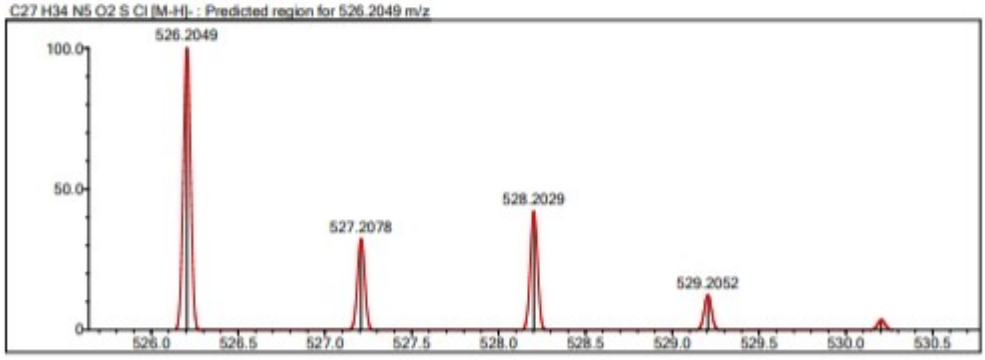
Event#: 2 MS(E-) Ret. Time : 0.690 Scan# : 104



Measured region for 526.2109 m/z



C27 H34 N5 O2 S Cl [M-H]- : Predicted region for 526.2049 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	26.97	C27 H34 N5 O2 S Cl	[M-H]-	526.2109	526.2049	6.0	11.40	74.38	13.0

18c

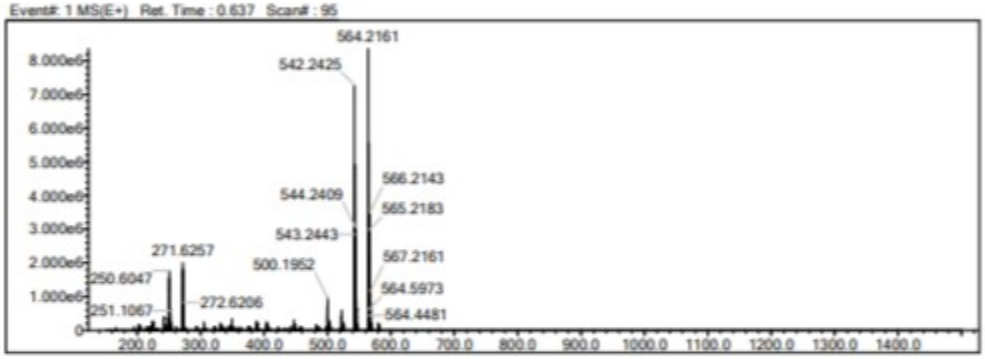
Formula Predictor Report - 18C.lcd

Data File: \\Deep-20160624kf\data1\新足长\YH\18C.lcd

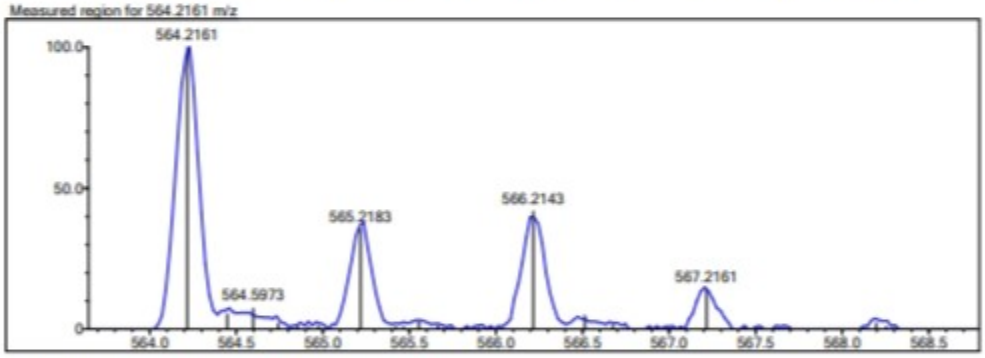
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	36	36	N	3	5	5	S	2	1	1	I	3	0	0	Na
B	3	0	0	O	2	2	2	Cl	1	1	1					
C	4	28	40	F	1	0	0	Br	1	0	0					

Error Margin (ppm):	50	DBE Range:	not fixed	Electron Ions:	both
HC Ratio:	unlimited	Apply N Rule:	yes	Use MSn Info:	no
Max Isotopes:	all	Isotope RI (%):	1.00	Isotope Res:	10000
MSn Iso RI (%):	75.00	MSn Logic Mode:	AND	Max Results:	10

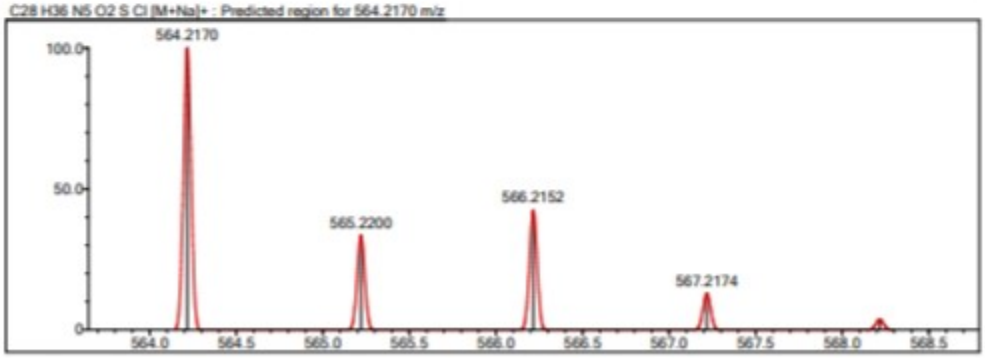
Event#: 1 MS(E+) Ret. Time : 0.637 Scan# : 95



Measured region for 564.2161 m/z



C28 H36 N5 O2 S Cl [M+Na]+ : Predicted region for 564.2170 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	55.64	C28 H36 N5 O2 S Cl	[M+Na]+	564.2161	564.2170	-0.9	-1.60	56.49	13.0

18d

Formula Predictor Report - 18D.lcd

Data File: H:\申-高分辨\18D.lcd

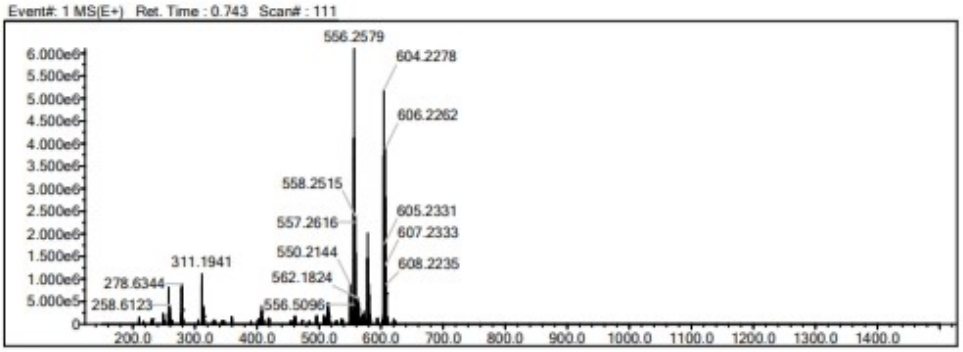
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	38	38	N	3	5	7	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	29	29	F	1	0	0	Br	1	0	1					NH4

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

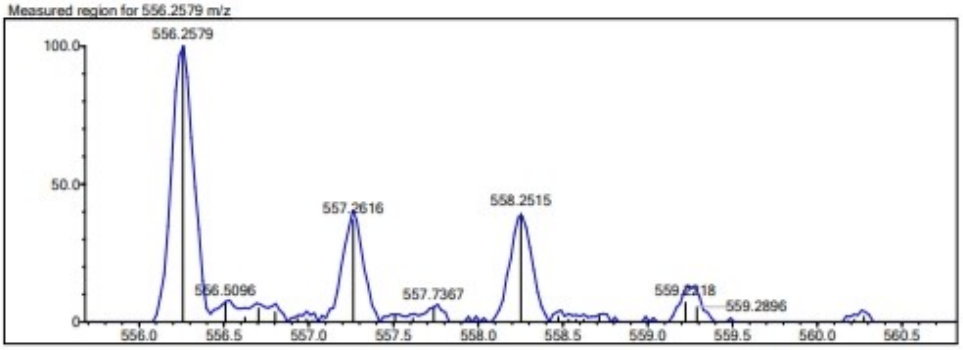
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

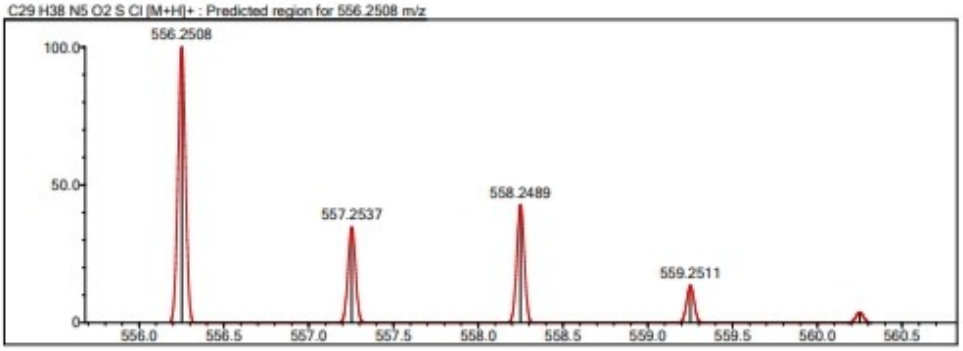
Event#: 1 MS(E+) Ret. Time : 0.743 Scan# : 111



Measured region for 556.2579 m/z



C29 H38 N5 O2 S Cl [M+H]+ : Predicted region for 556.2508 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	21.96	C29 H38 N5 O2 S Cl	[M+H]+	556.2579	556.2508	7.1	12.76	67.29	13.0

18f

Formula Predictor Report - 18F.lcd

Data File: H:\单-高分辨\18F.lcd

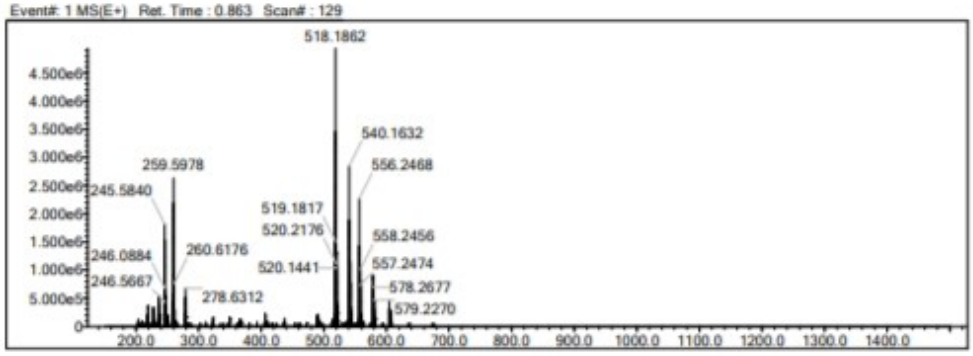
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	29	29	N	3	5	5	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	25	29	F	1	0	1	Br	1	0	0					NH4

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

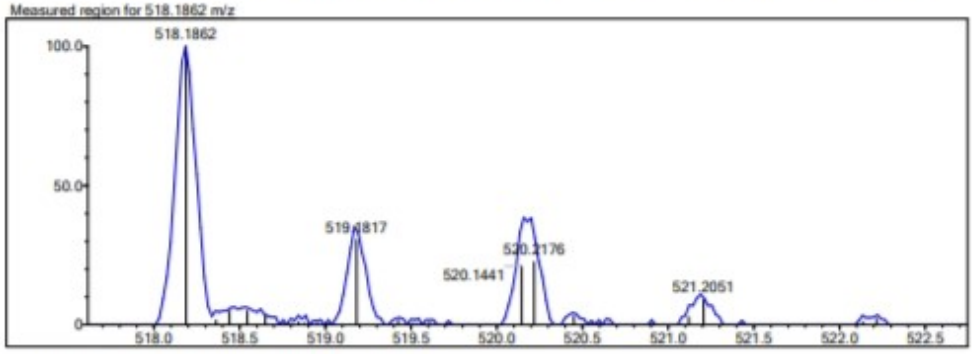
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

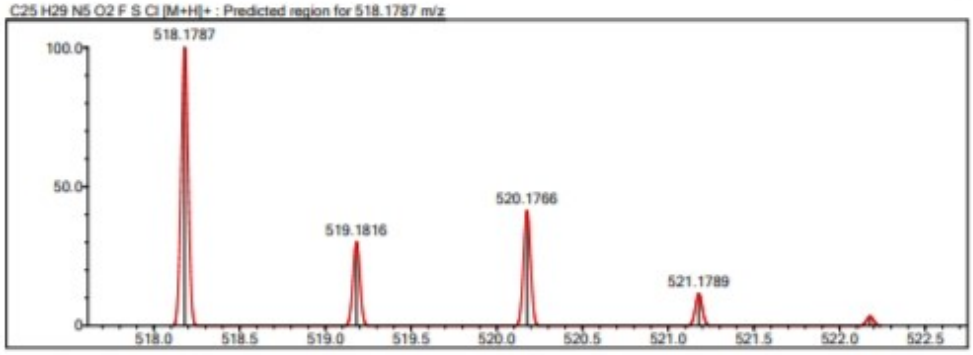
Event#: 1 MS(E+) Ret. Time : 0.863 Scan# : 129



Measured region for 518.1862 m/z



C25 H29 N5 O2 F S Cl [M+H]+ : Predicted region for 518.1787 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	12.09	C25 H29 N5 O2 F S Cl	[M+H]+	518.1862	518.1787	7.5	14.47	43.04	13.0

18g

Formula Predictor Report - 18G.lcd

Page 1 of 1

Data File: H:\甲-高分辨\18G.lcd

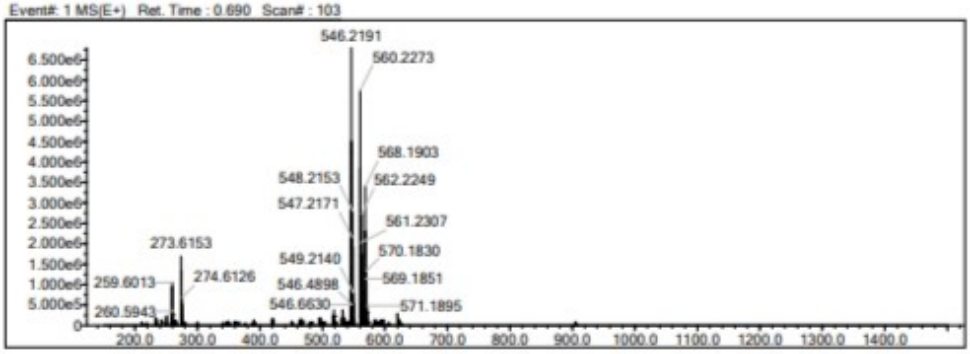
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	33	38	N	3	5	7	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	27	29	F	1	1	1	Br	1	0	1					NH4

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

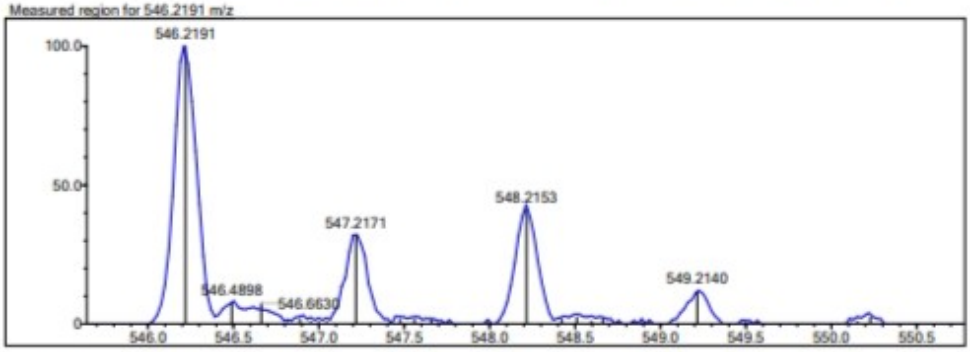
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

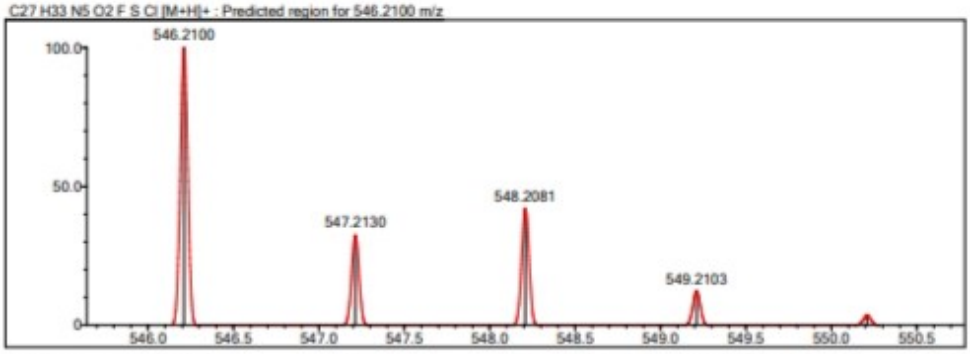
Event#: 1 MS(E+) Ret. Time : 0.690 Scan# : 103



Measured region for 546.2191 m/z



C27 H33 N5 O2 F S Cl [M+H]+ : Predicted region for 546.2100 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	17.41	C27 H33 N5 O2 F S Cl	[M+H]+	546.2191	546.2100	9.1	16.66	78.26	13.0

18h

Formula Predictor Report - 18E.lcd

Page 1 of 1

Data File: H:\研-高分辨\18E.lcd

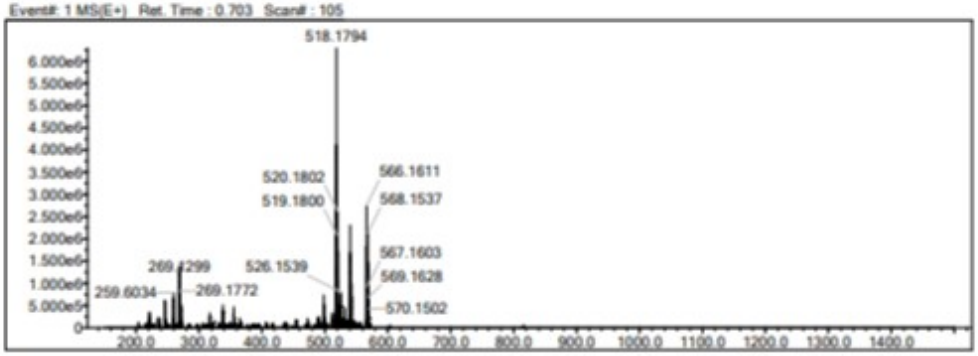
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	29	38	N	3	5	5	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	25	29	F	1	1	1	Br	1	0	1					NH4

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

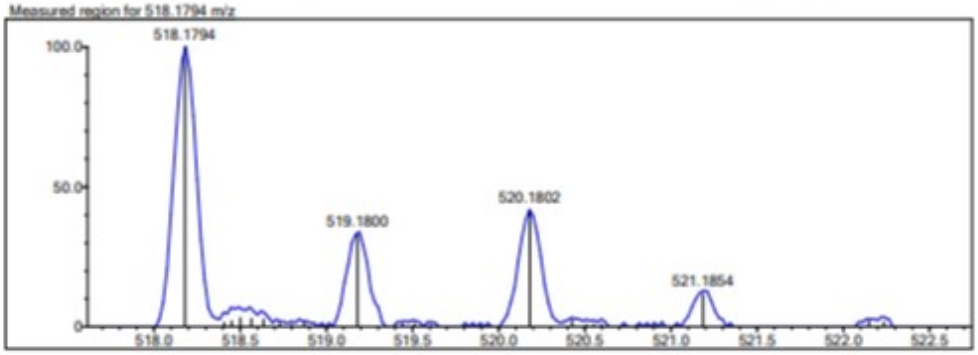
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

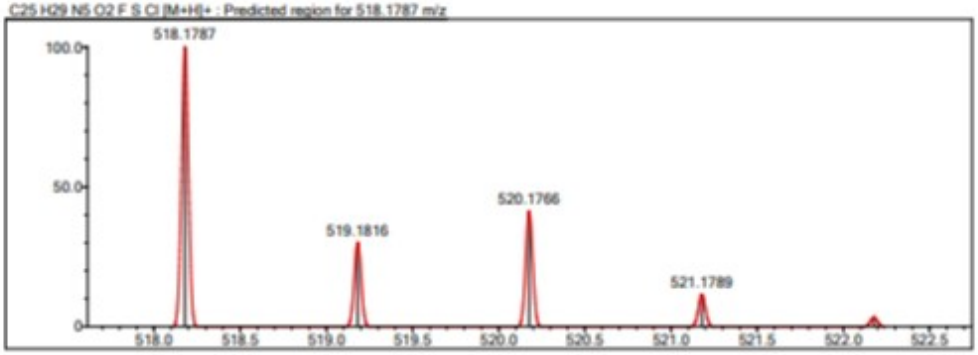
Event#: 1 MS(E+) Ret. Time : 0.703 Scan# : 105



Measured region for 518.1794 m/z



C25 H29 N5 O2 F S Cl [M+H]+ : Predicted region for 518.1787 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	70.65	C25 H29 N5 O2 F S Cl	[M+H]+	518.1794	518.1787	0.7	1.35	71.27	13.0

18i

Formula Predictor Report - 18l.lcd

Page 1 of 1

Data File: H:\单-高分辨\18l.lcd

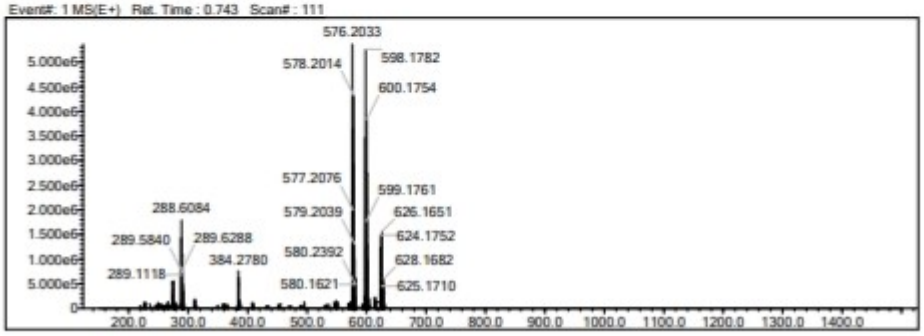
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	33	38	N	3	5	7	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	28	29	F	1	1	1	Br	1	0	1					NH4

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

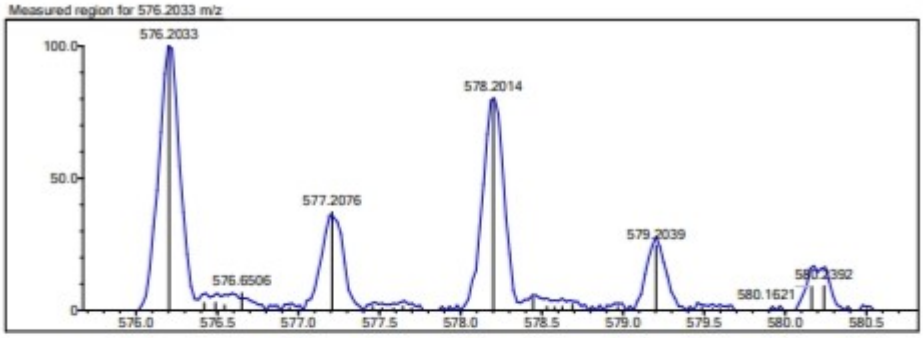
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

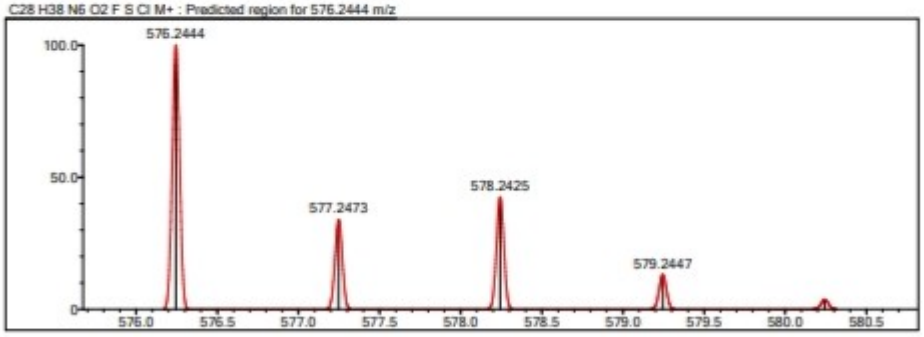
Event#: 1 MS(E+) Ret. Time : 0.743 Scan# : 111



Measured region for 576.2033 m/z



C28 H38 N6 O2 F S Cl M+ : Predicted region for 576.2444 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	0.00	C28 H38 N6 O2 F S Cl	M+	576.2033	576.2444	-41.1	-71.33	13.30	12.0

18j

Formula Predictor Report - 18H.lcd

Data File: H:\仲-高分辨\18H.lcd

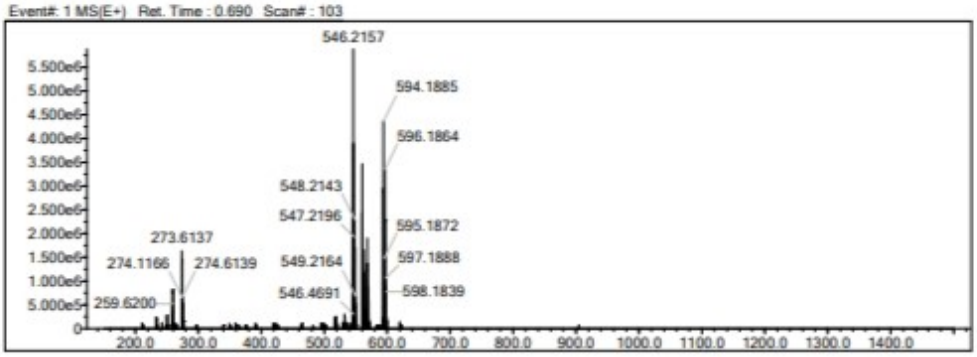
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	33	38	N	3	5	7	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	27	29	F	1	1	1	Br	1	0	1					NH4

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

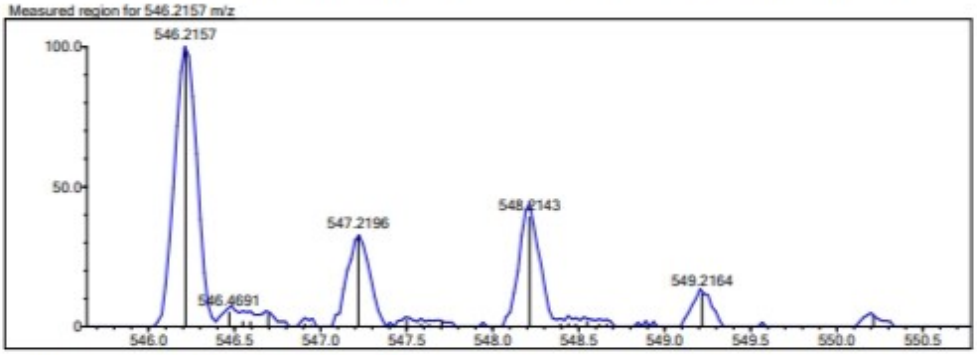
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

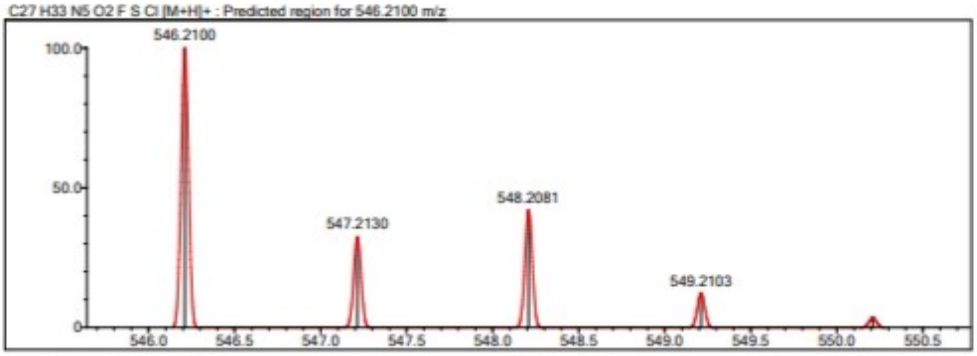
Event#: 1 MS(E+) Ret. Time : 0.690 Scan# : 103



Measured region for 546.2157 m/z



C27 H33 N5 O2 F S Cl [M+H]+ : Predicted region for 546.2100 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	31.62	C27 H33 N5 O2 F S Cl	[M+H]+	546.2157	546.2100	5.7	10.44	81.44	13.0

18k

Formula Predictor Report - 18K.lcd

Page 1 of 1

Data File: H:\单-高分辨\18K.lcd

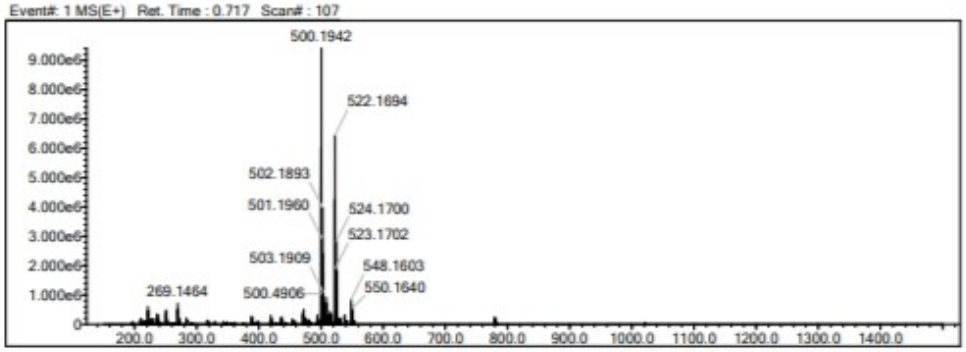
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	28	38	N	3	5	5	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	24	29	F	1	0	1	Br	1	0	1					NH4

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

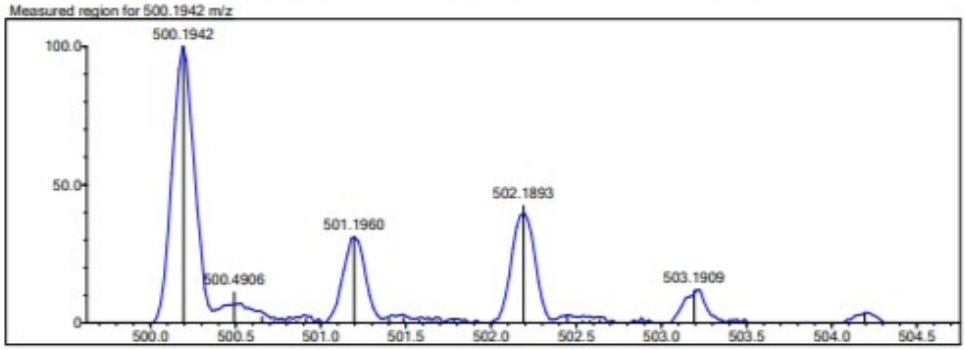
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

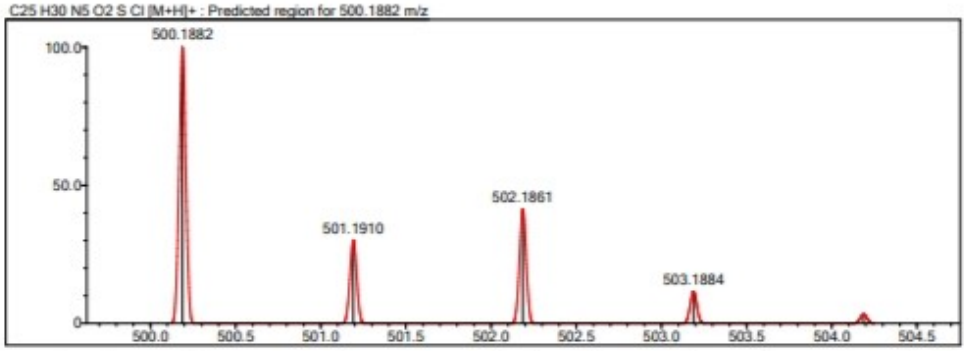
Event#: 1 MS(E+) Ret. Time : 0.717 Scan# : 107



Measured region for 500.1942 m/z



C25 H30 N5 O2 S Cl [M+H]+ : Predicted region for 500.1882 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	26.95	C25 H30 N5 O2 S Cl	[M+H]+	500.1942	500.1882	6.0	12.00	77.74	13.0

18l

Formula Predictor Report - 18J.lcd

Page 1 of 1

Data File: H:\伸-高分辨\18J.lcd

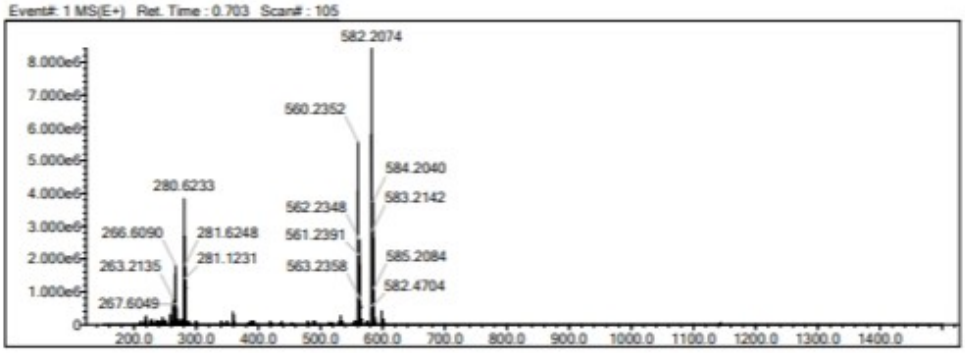
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	33	38	N	3	5	5	S	2	1	1	I	3	0	0	H
B	3	0	0	O	2	2	2	Cl	1	1	1					Na
C	4	27	29	F	1	1	1	Br	1	0	1					NH4

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

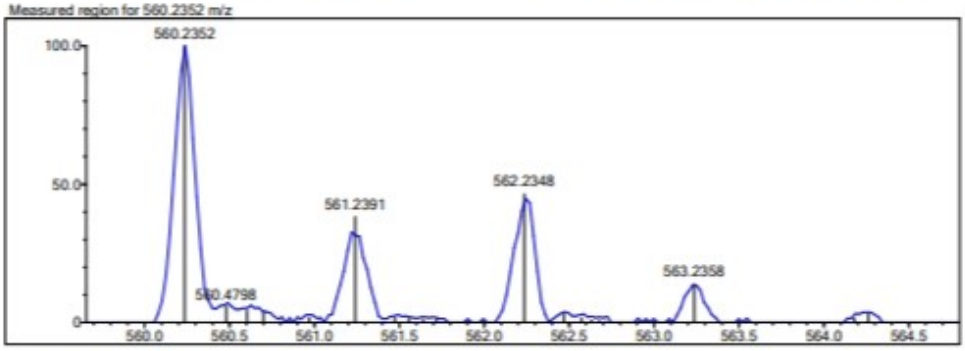
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 10

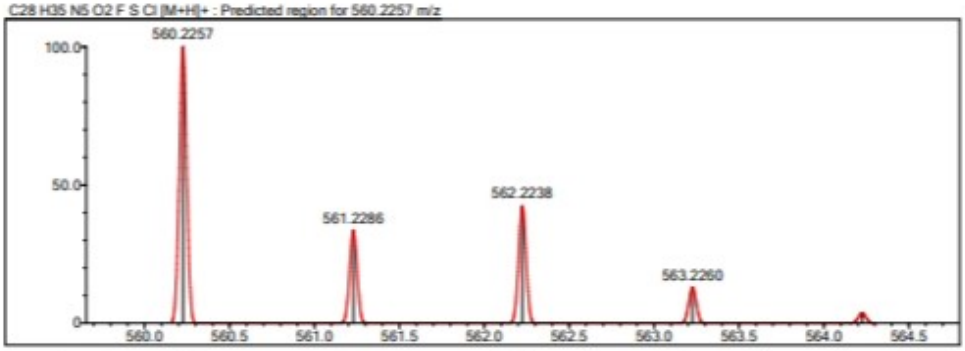
Event#: 1 MS(E+) Ret. Time : 0.703 Scan# : 105



Measured region for 560.2352 m/z



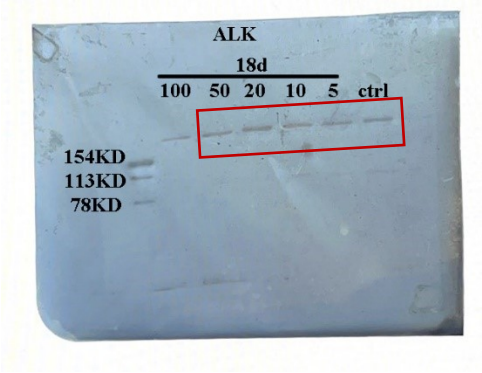
C28 H35 N5 O2 F S Cl [M+H]+ : Predicted region for 560.2257 m/z



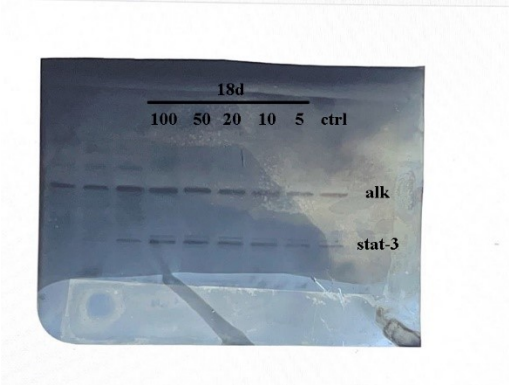
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	12.35	C28 H35 N5 O2 F S Cl	[M+H]+	560.2352	560.2257	9.5	16.96	57.62	13.0

Western Blots Original Images

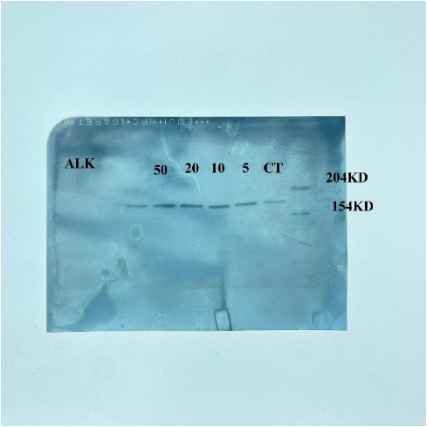
ALK Replicate 1 and cropped for Fig.5



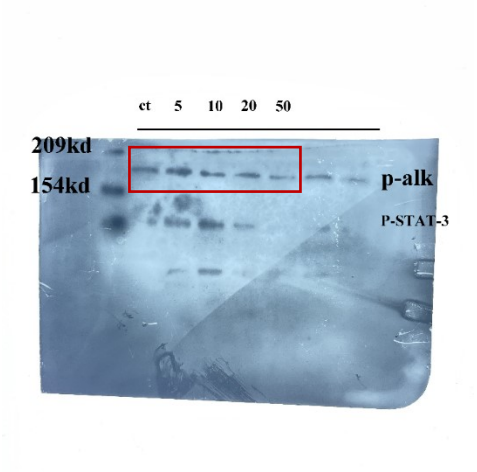
ALK Replicate 2



ALK Replicate 3



p-ALK Replicate 1 and cropped for Fig.5



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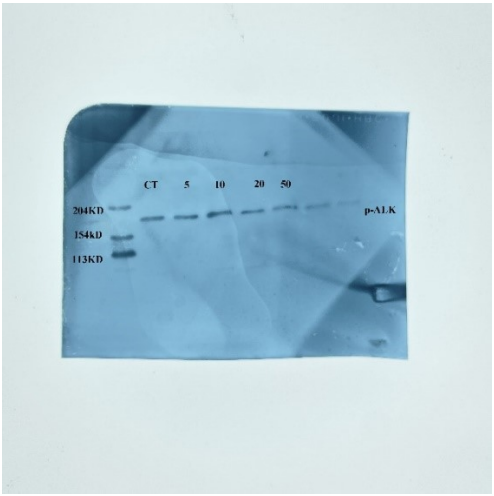

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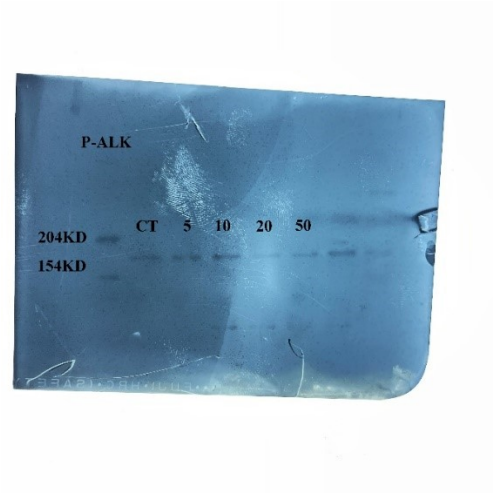
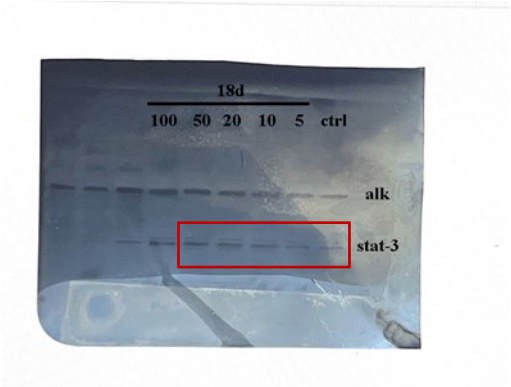
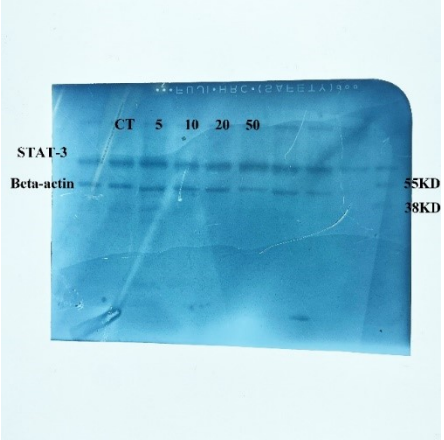


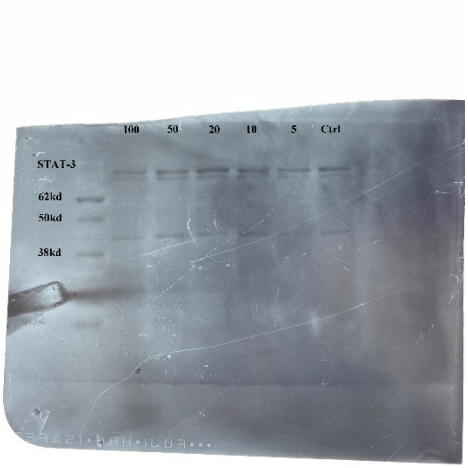
STAT-3 Replicate 1 and cropped for Fig.5



STAT-3 Replicate 2



STAT-3 Replicate 3



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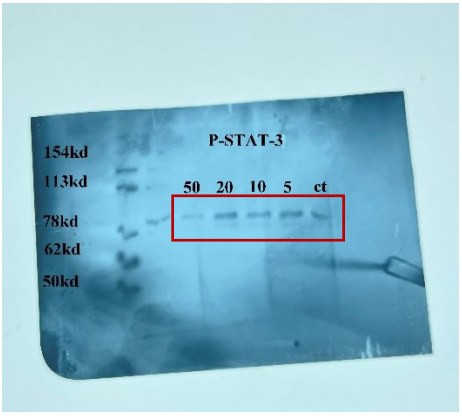
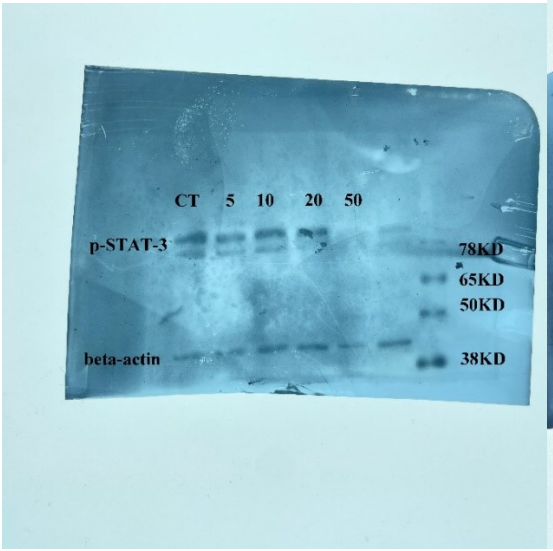
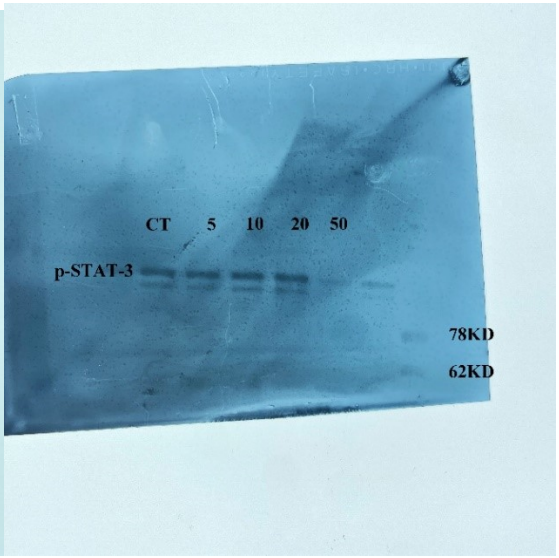
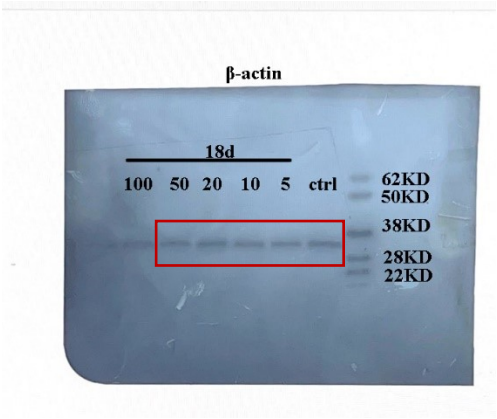


p-STAT-3 Replicate 2 **p-STAT-3 Replicate 3**

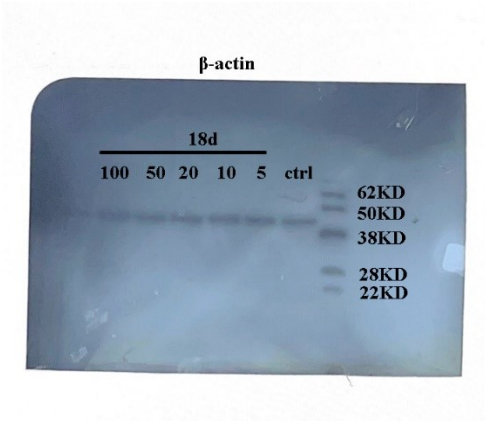




β-actin Replicate 1 and cropped for Fig.5



β-actin Replicate 2



β-actin Replicate 3