

Supporting Information

Synthesis and biological evaluation of Carabrol Derivatives

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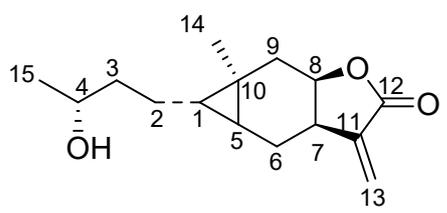
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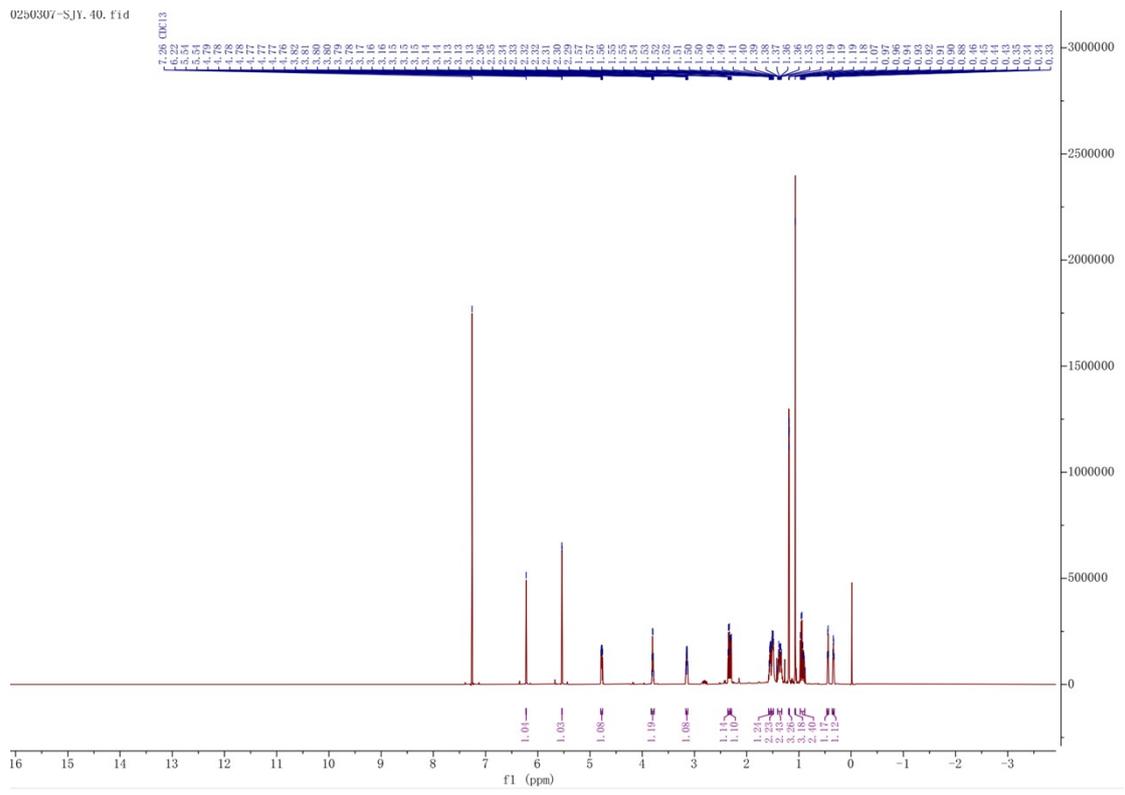
Fax: +86-531-59567077;

¹H-NMR , ¹³C-NMR spectra and HR-MS

1. Carabrol

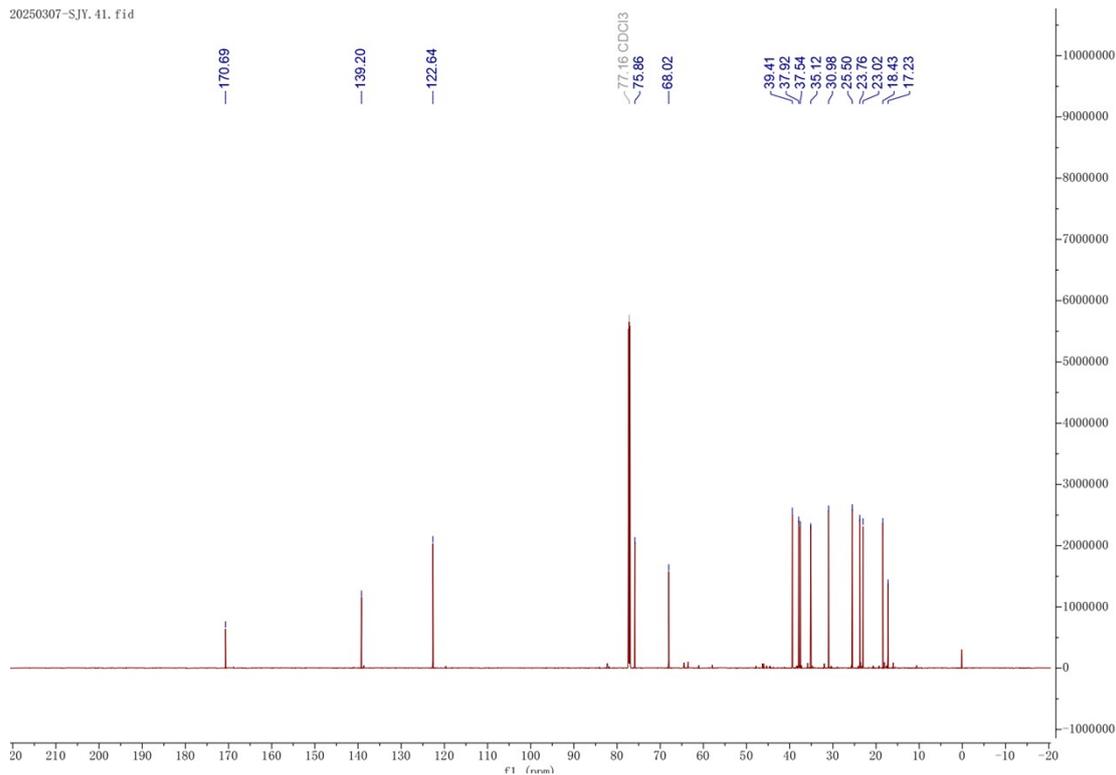


¹H-NMR



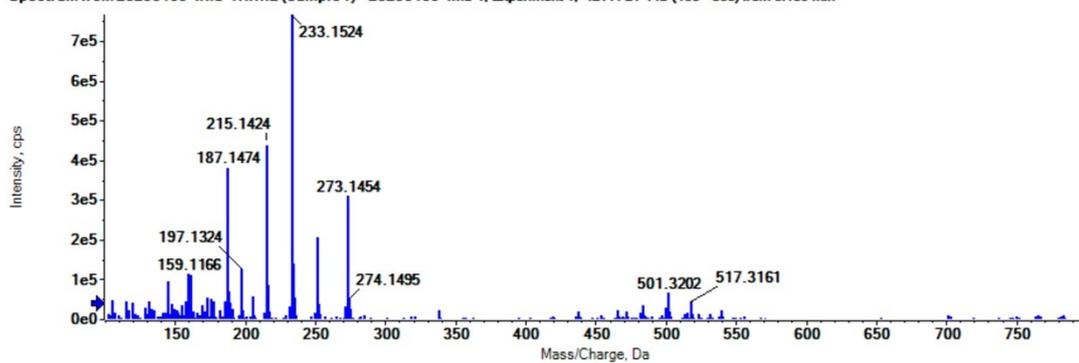
¹³C-NMR

20250307-SJY. 41. fid

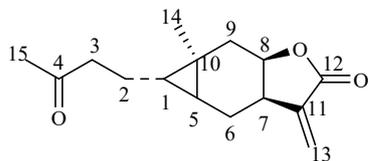


HR-MS

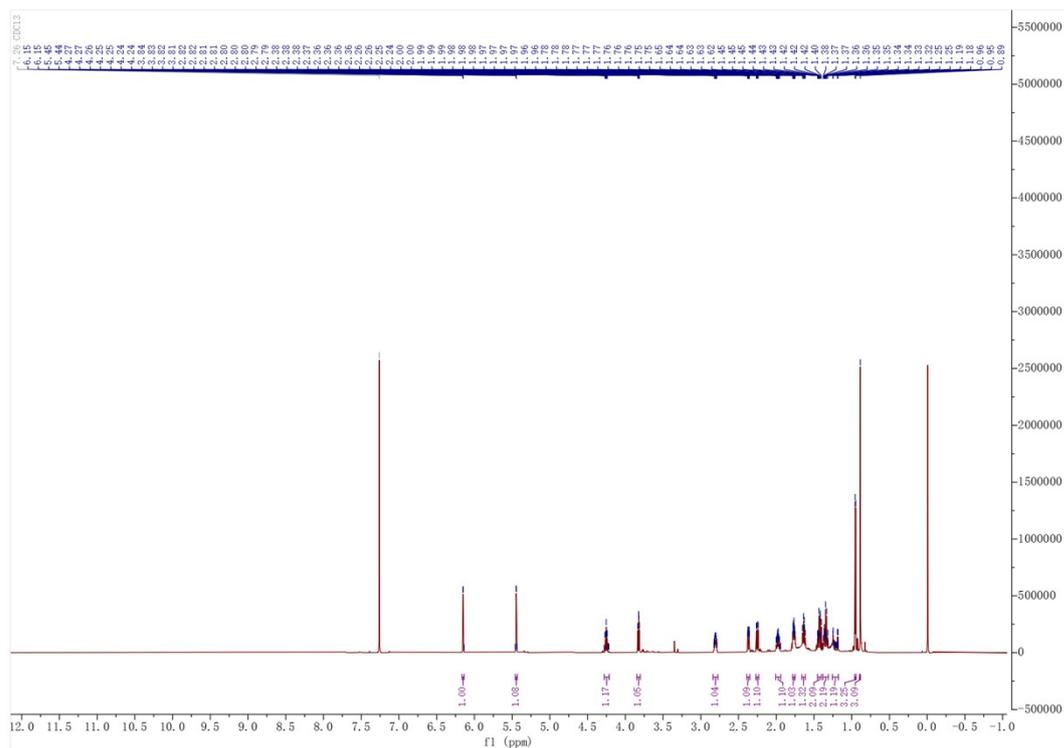
Spectrum from 20250405-whd-1.wiff2 (sample 1) - 20250405-whd-1, Experiment 1, -iDATOF MS (100 - 800) from 0.189 min



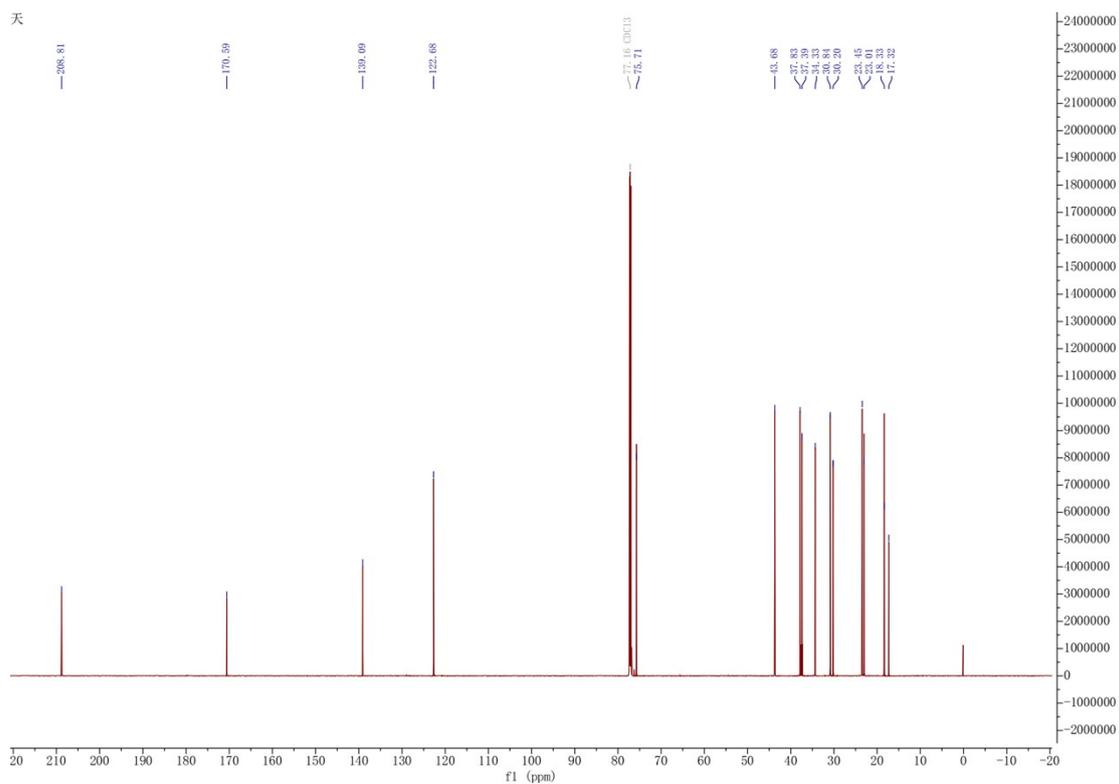
2.Carabrone z1



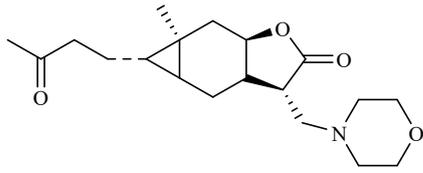
¹H-NMR



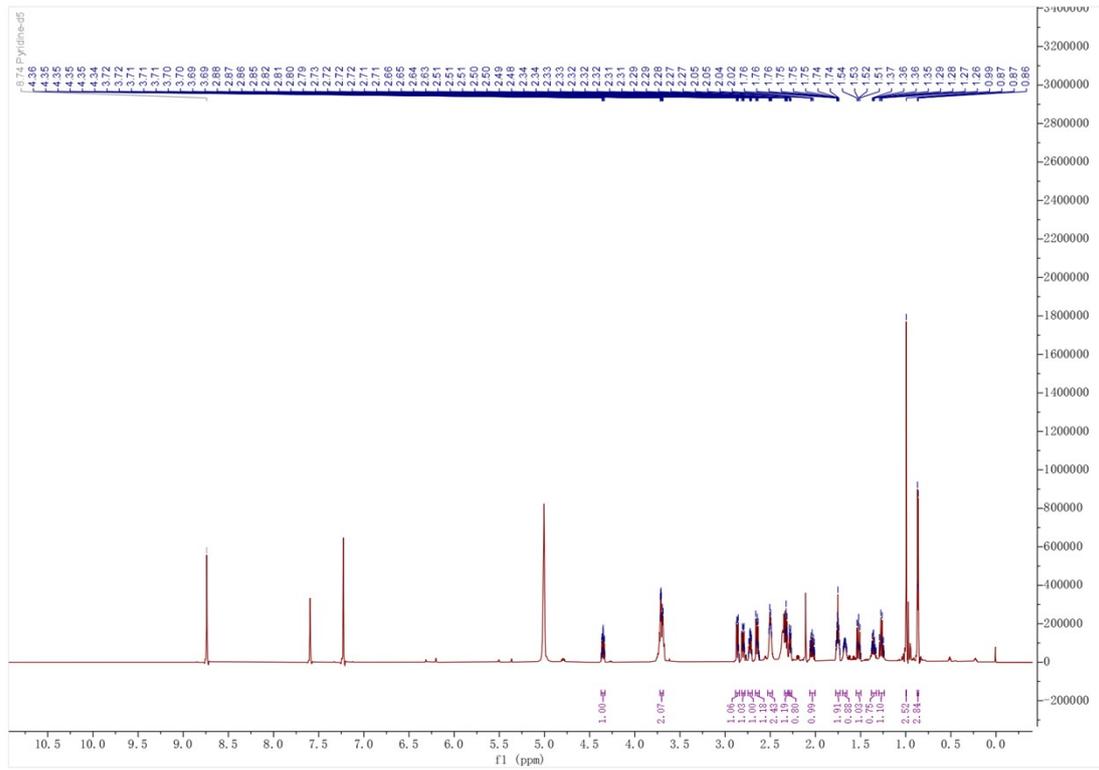
¹³C-NMR



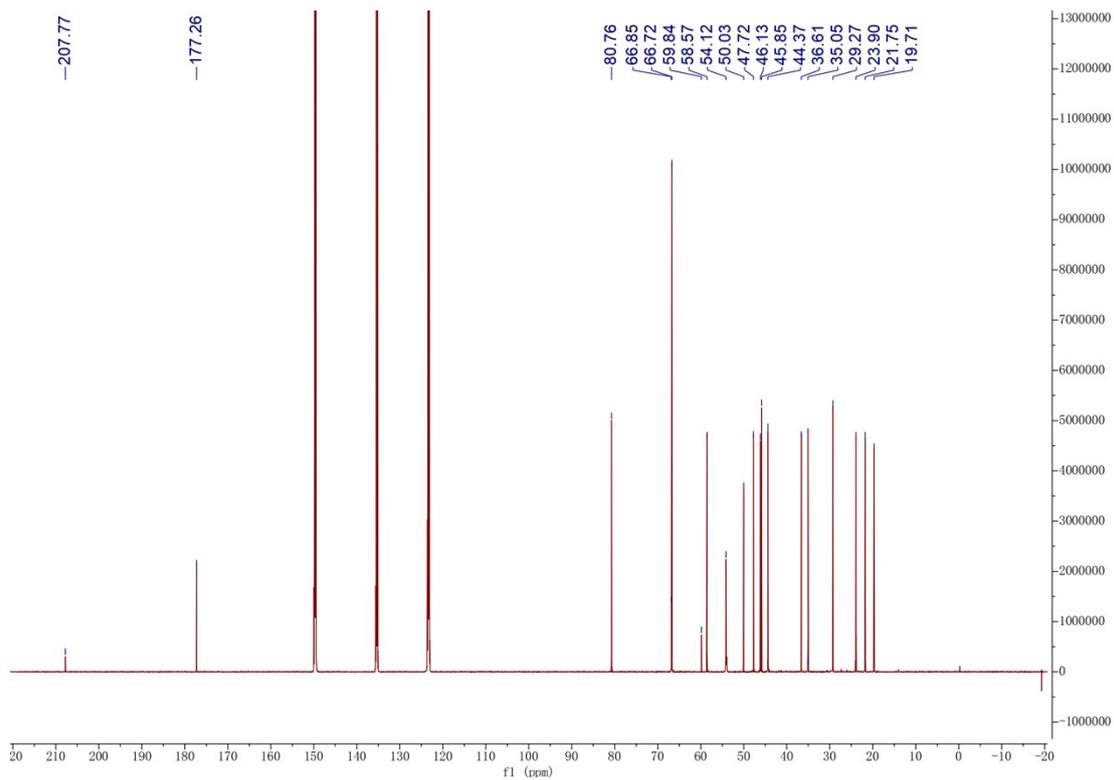
3.Compound Z2



¹H-NMR

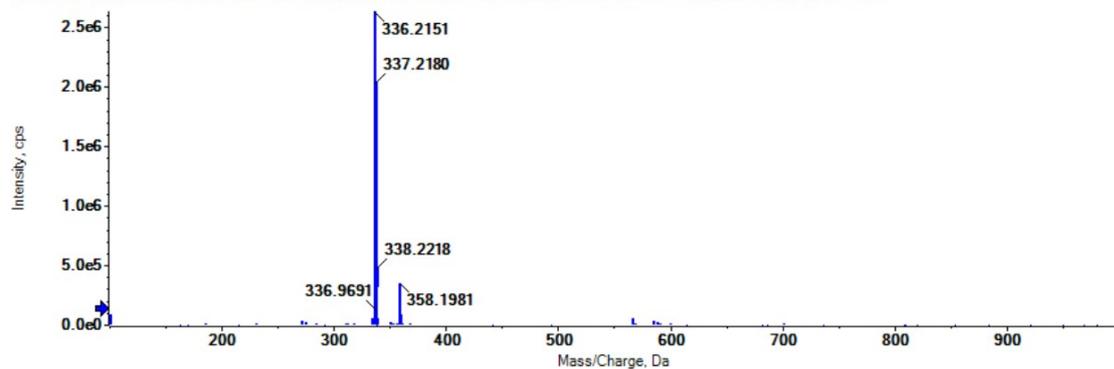


¹³C-NMR

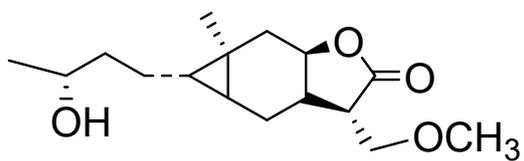


HR-MS

Spectrum from 20250426-whd-27.wiff2 (sample 1) - 20250426-whd-27, Experiment 1, +IDA TOF MS (100 - 1000) from 0.216 min

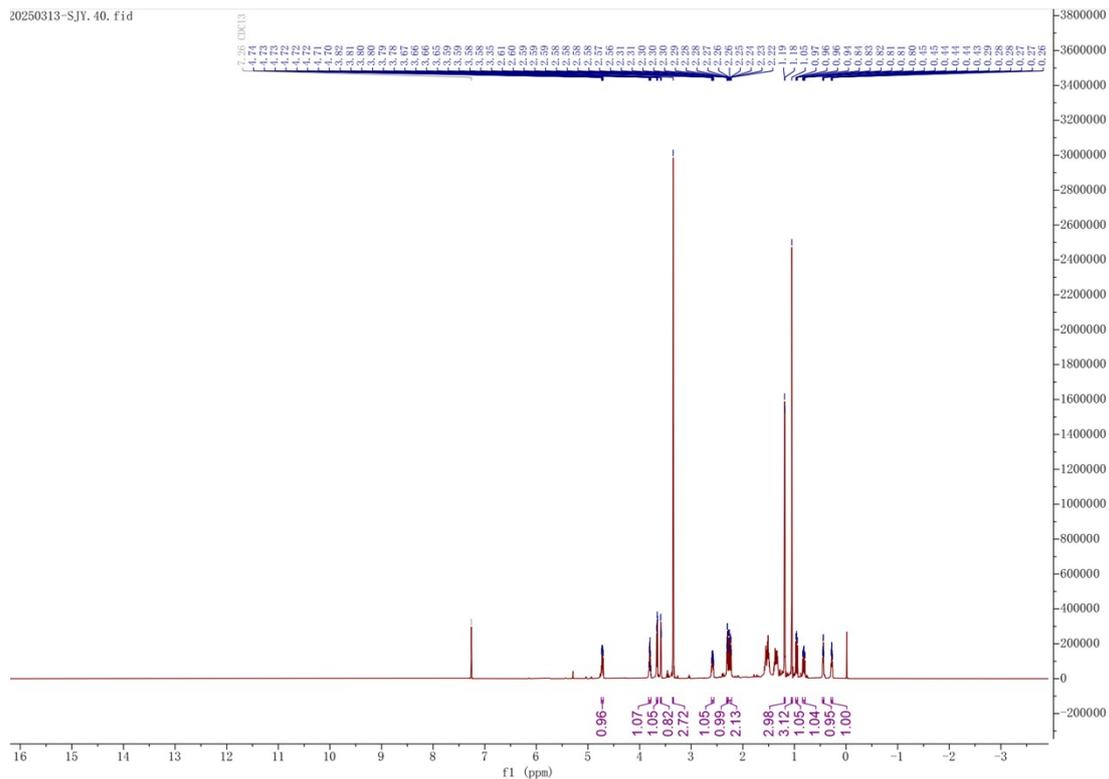


4. Compound z3



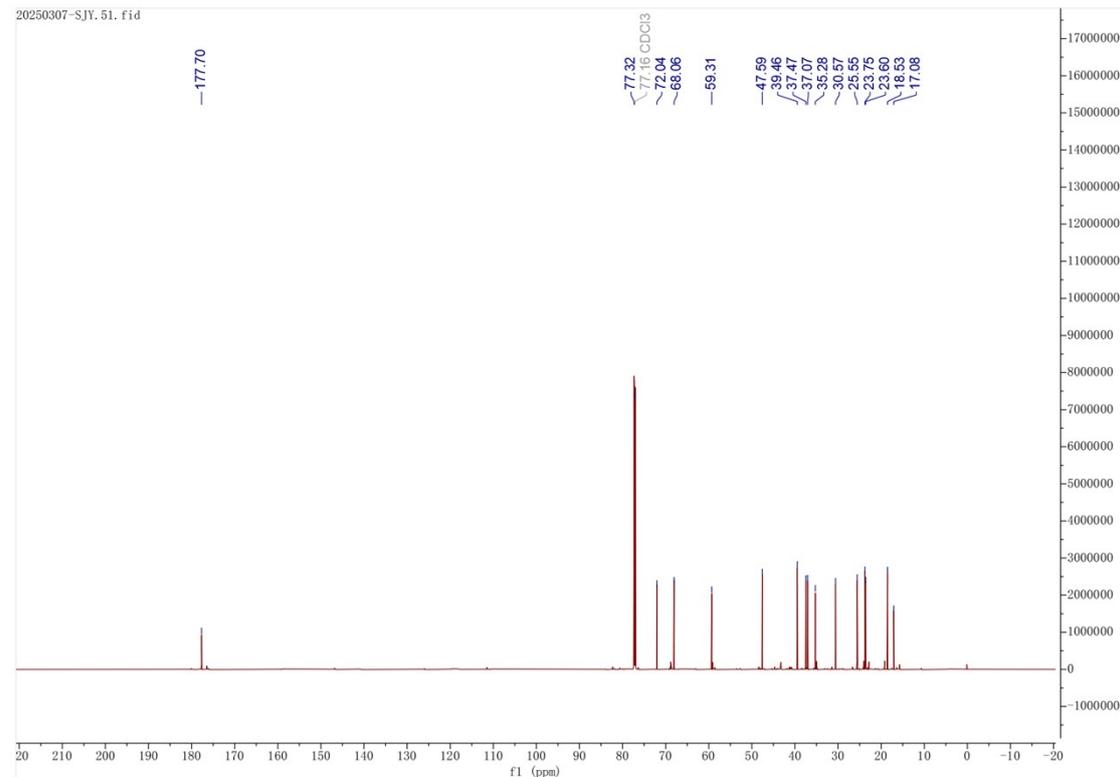
¹H-NMR

20250313-SJY.40.fid



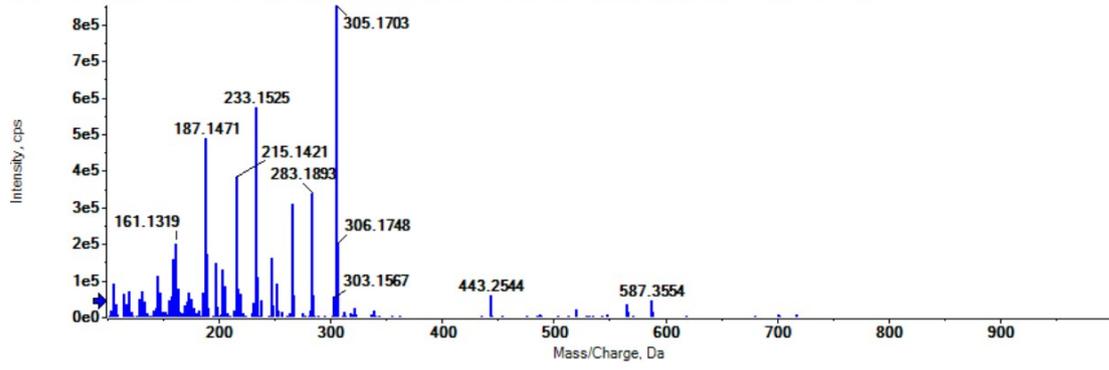
¹³C-NMR

20250307-SJY.51.fid

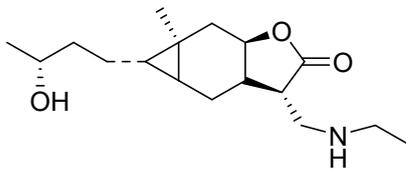


HR-MS

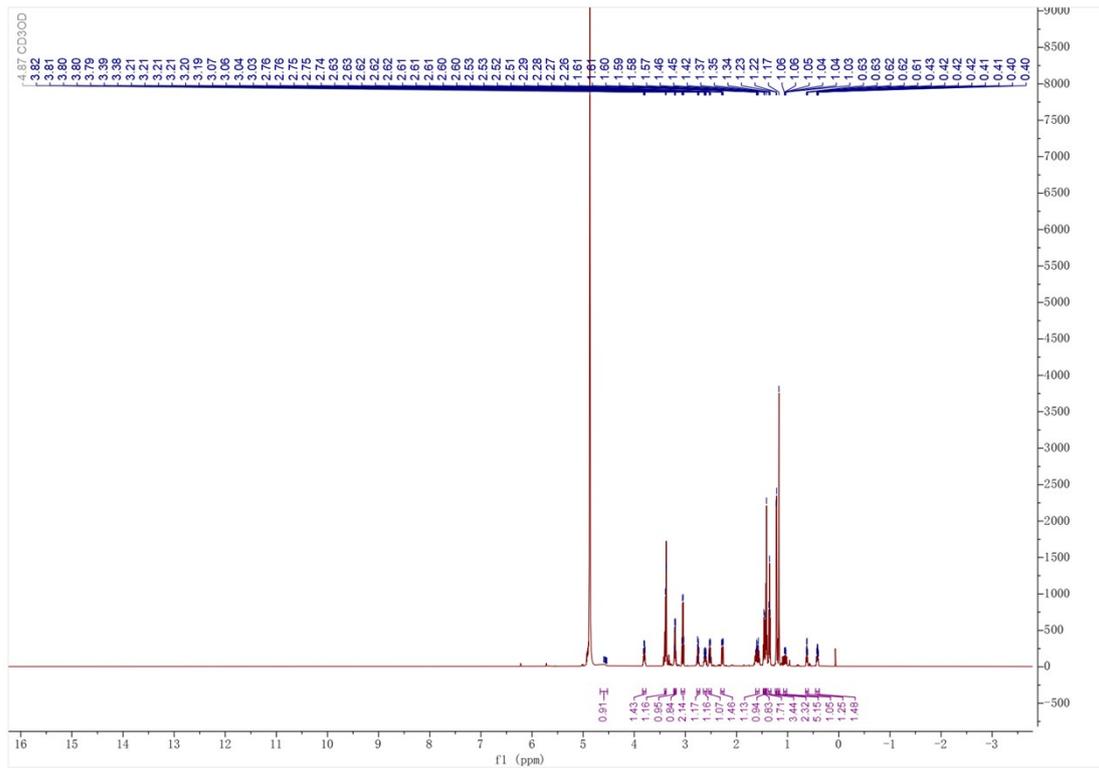
Spectrum from 20250426-whd-19.wiff2 (sample 1) - 20250426-whd-19, Experiment 1, +IDA TOF MS (100 - 1000) from 0.218 min



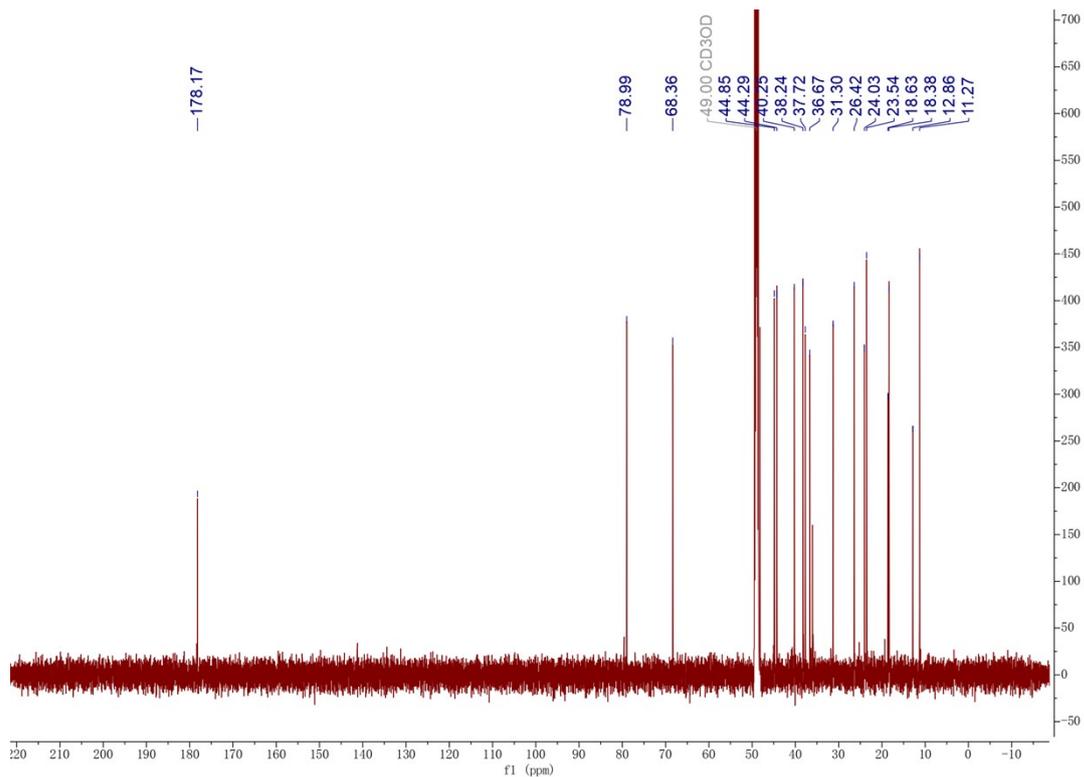
5. Compound a2



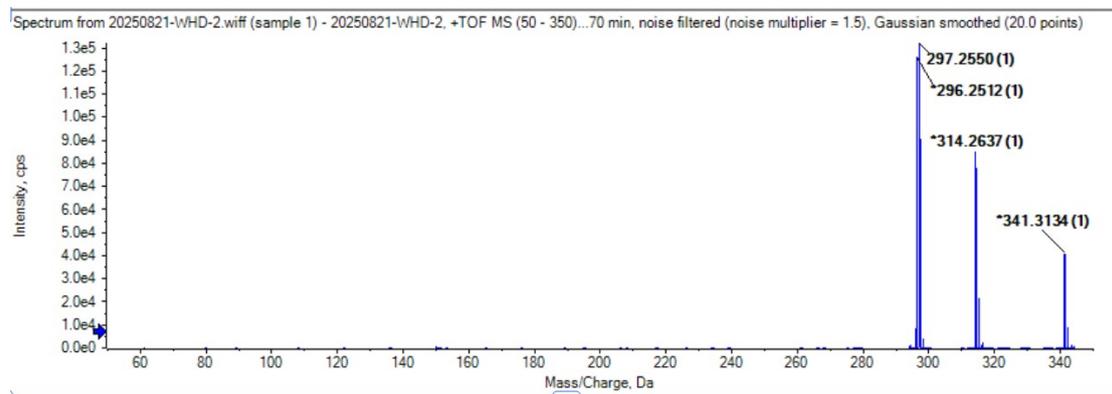
¹H-NMR



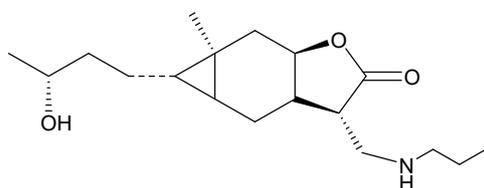
¹³C-NMR



HR-MS

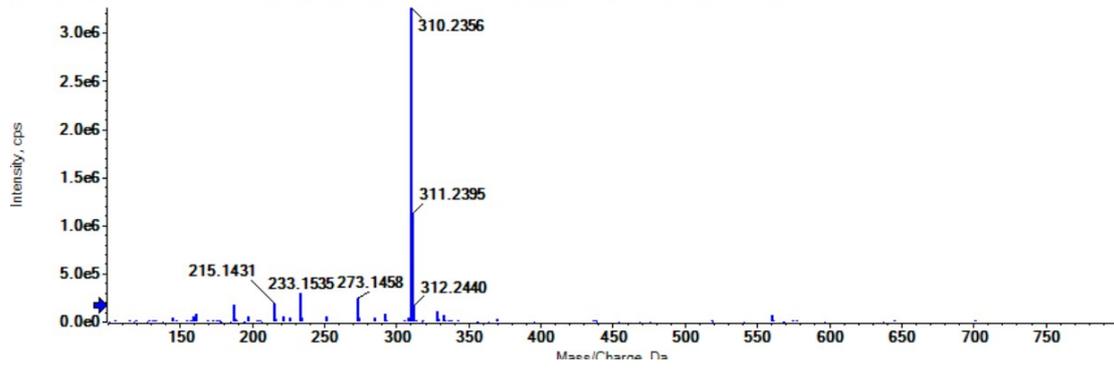


6.Compound a3

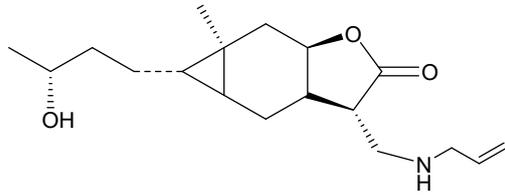


¹H-NMR

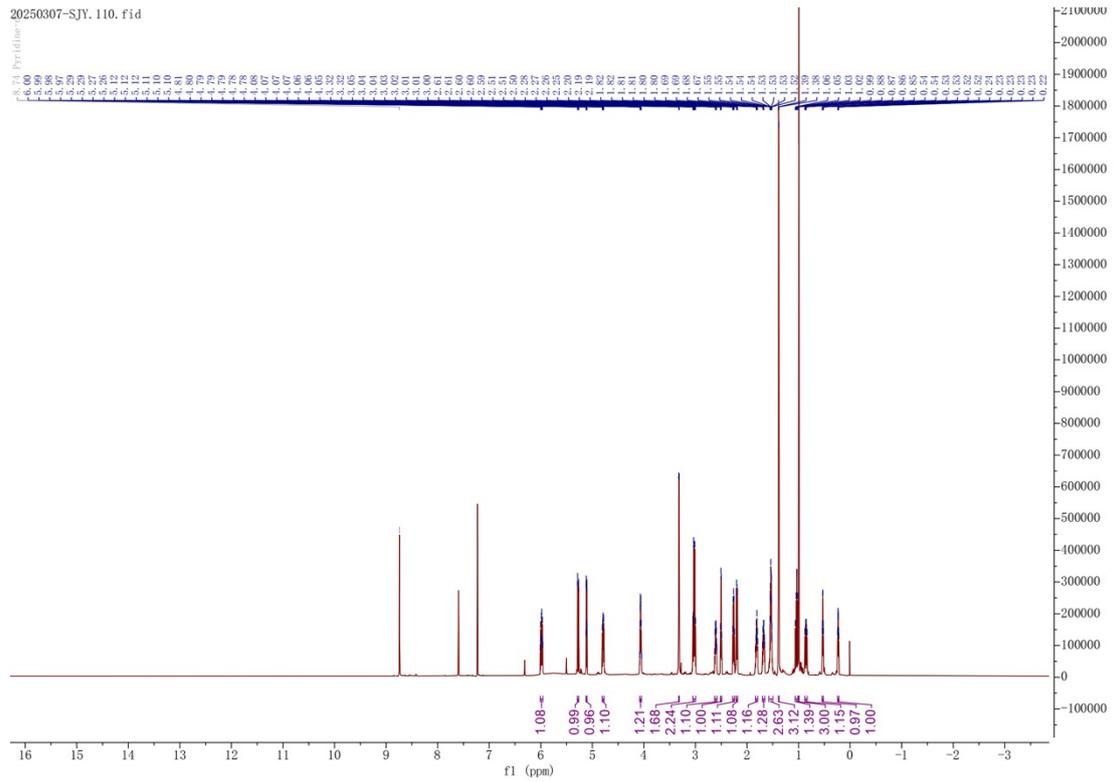
Spectrum from 20250426-whd-44.wiff2 (sample 1) - 20250426-whd-44, Experiment 1, +HDA TOF MS (100 - 800) from 0.109 min



7. Compound a4

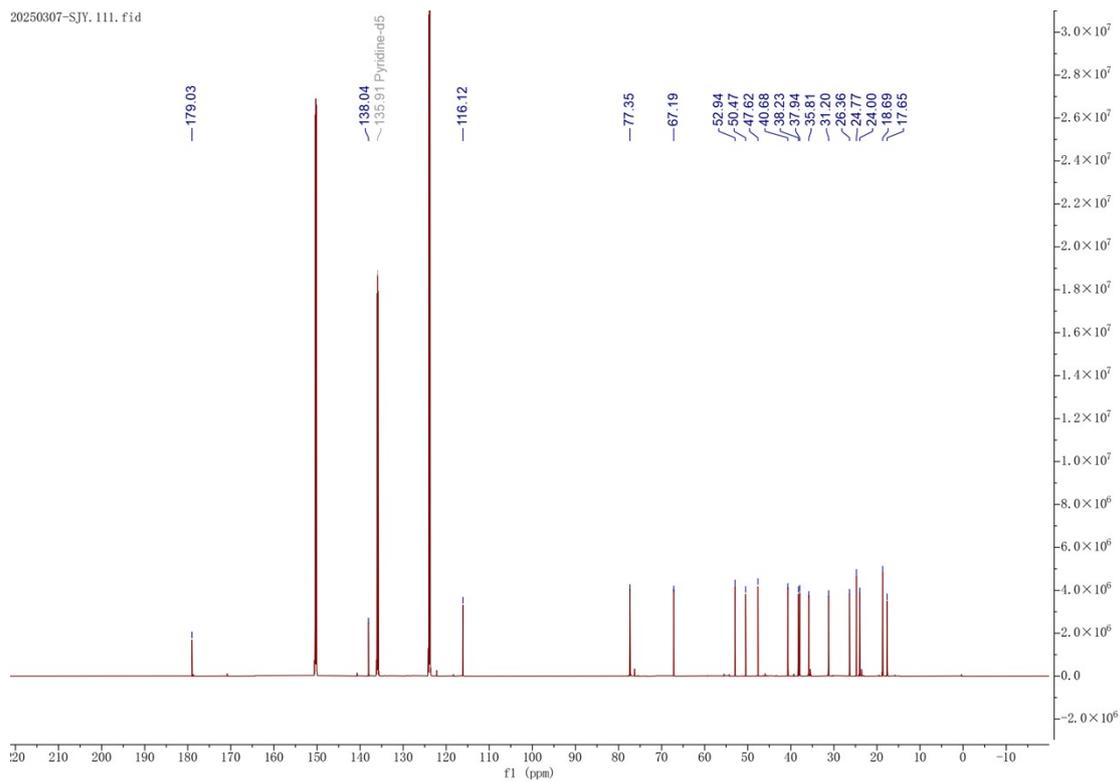


¹H-NMR



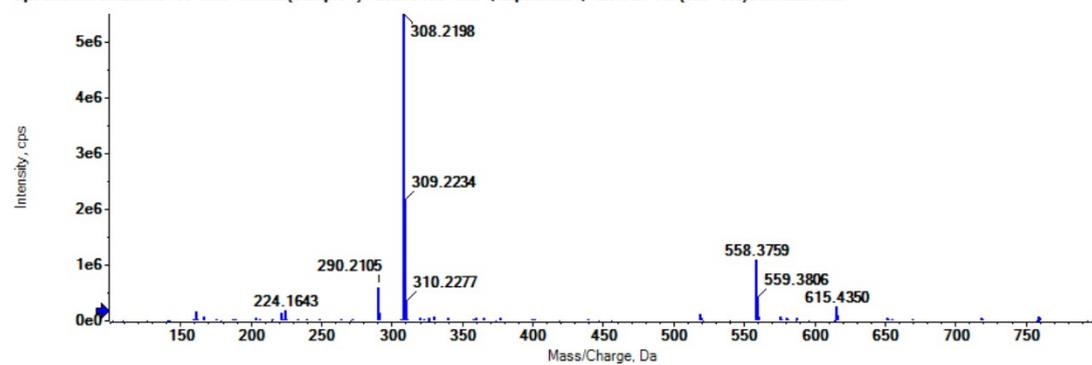
¹³C-NMR

20250307-SJV. 111. fid

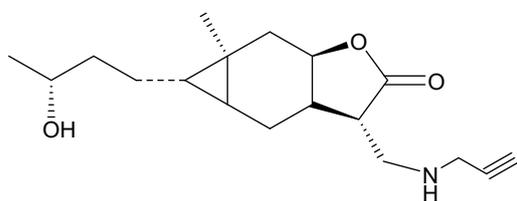


HR-MS

Spectrum from 20250405-whd-4. wiff2 (sample 1) - 20250405-whd-4, Experiment 1, +IDATOF MS (100 - 800) from 0.207 min

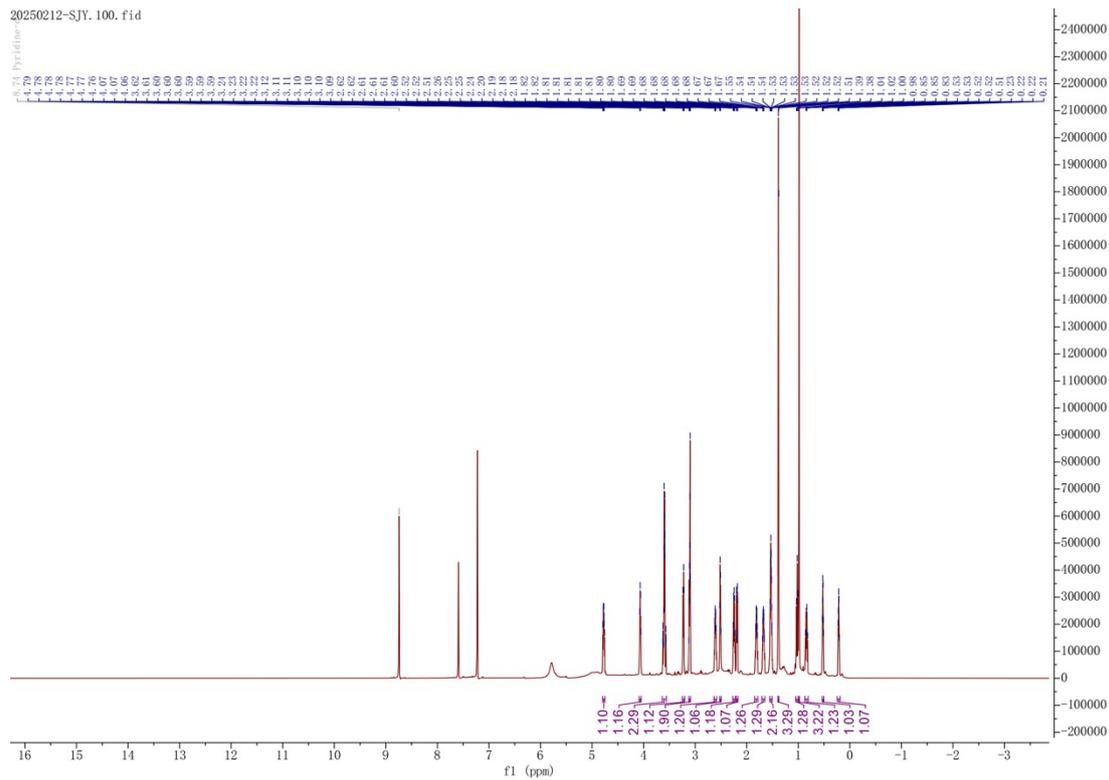


8.Compound a5

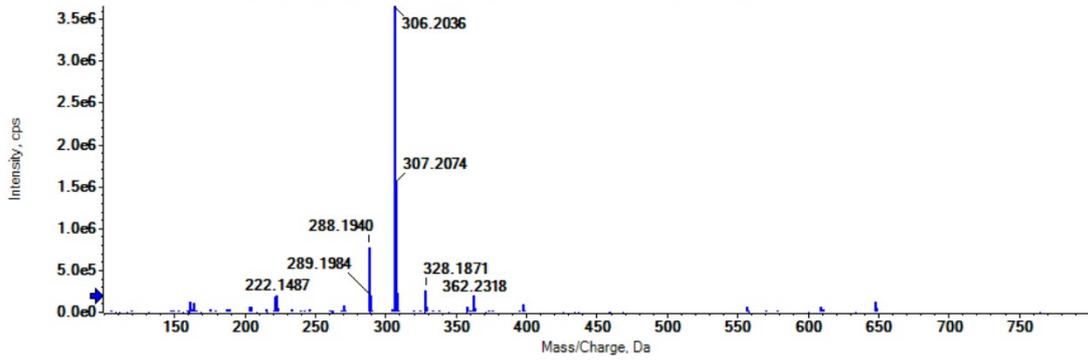


¹H-NMR

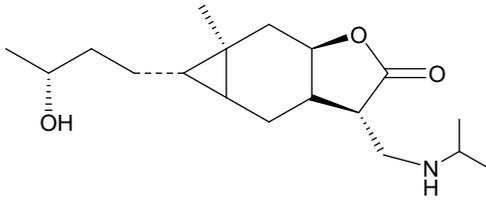
20250212-SJV. 100. fid



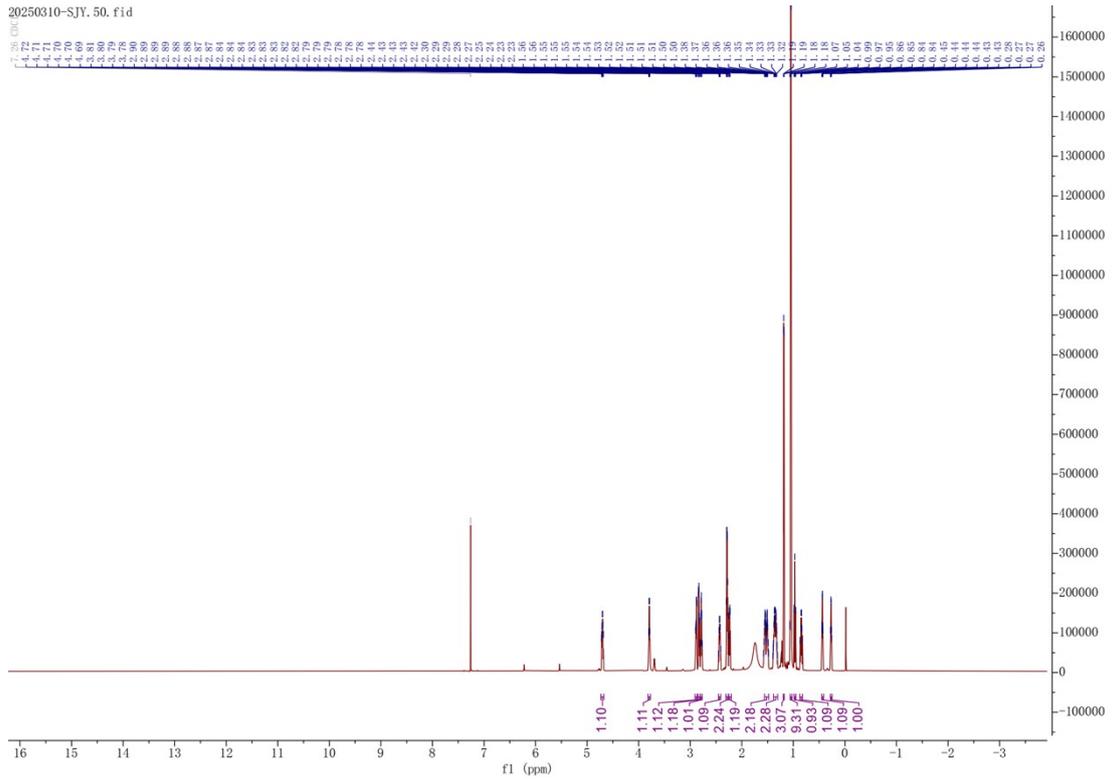
Spectrum from 20250405-whd-5.wiff2 (sample 1) - 20250405-whd-5, Experiment 1, +IDATOF MS (100 - 800) from 0.222 min



9. Compound a6

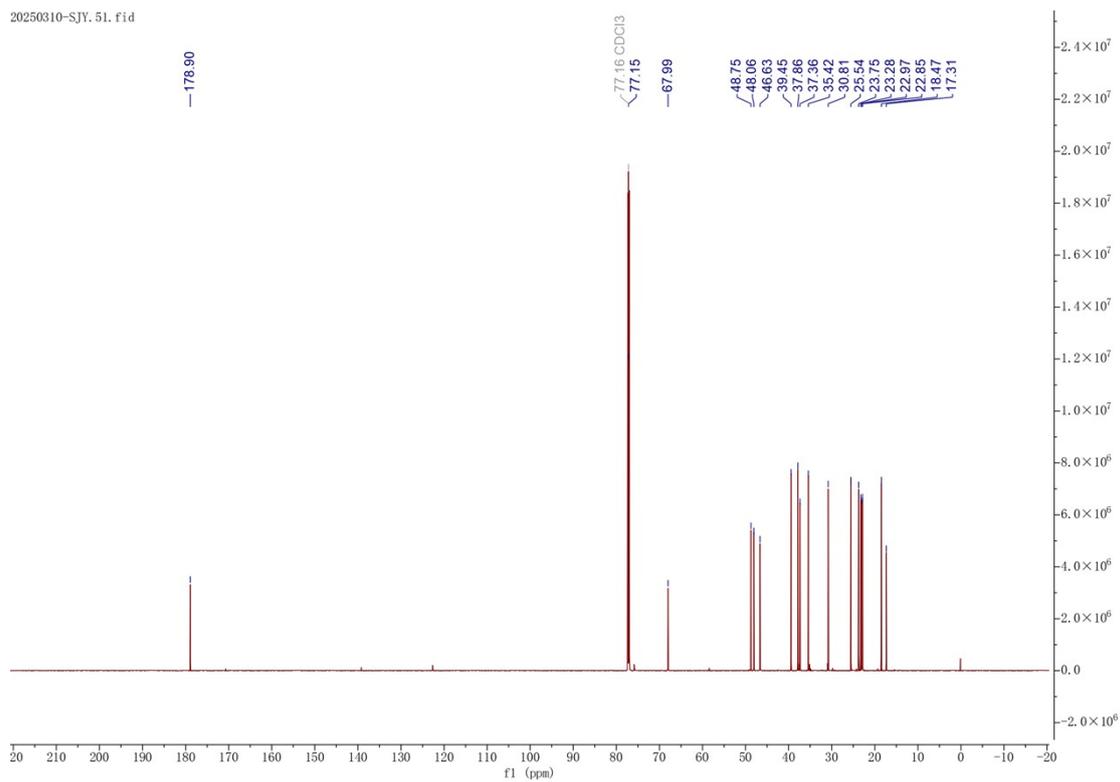


¹H-NMR



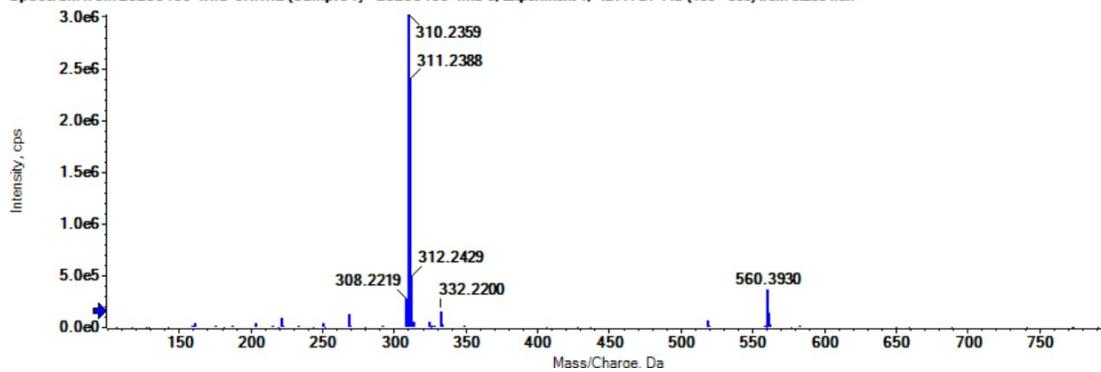
¹³C-NMR

20250310-SJY_51.fid

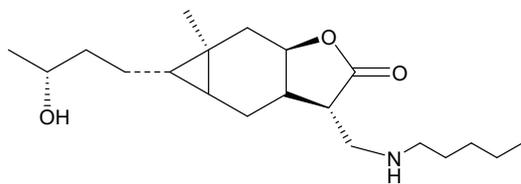


HR-MS

Spectrum from 20250405-whd-6.wiff2 (sample 1) - 20250405-whd-6, Experiment 1, +HDATAF MS (100 - 800) from 0.208 min

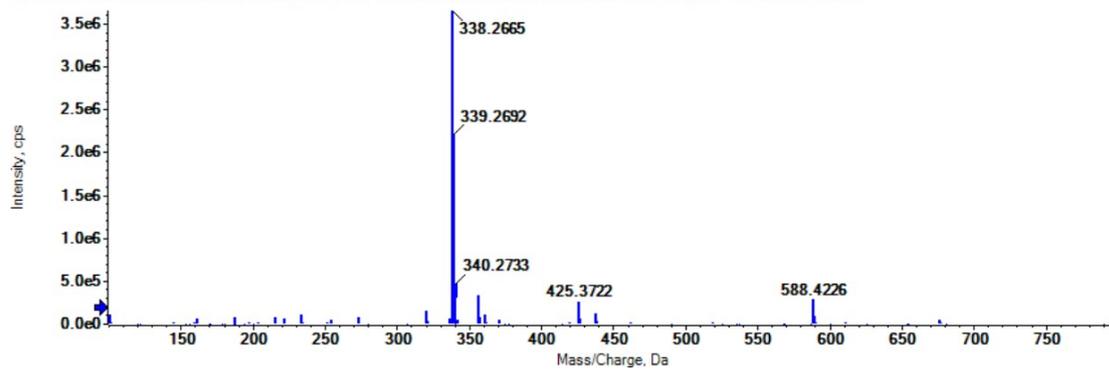


10. Compound a7

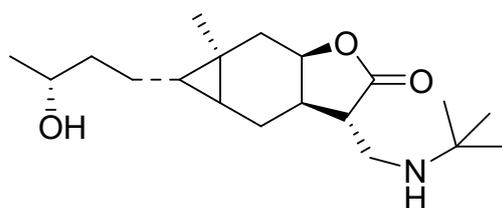


¹H-NMR

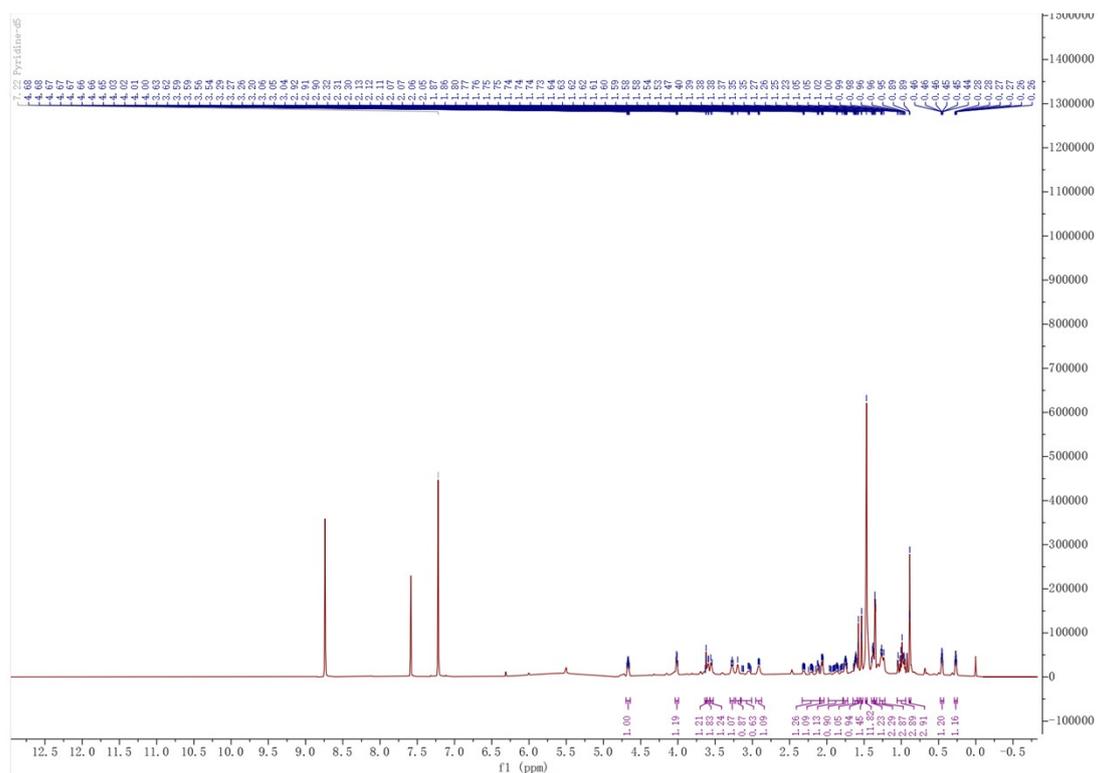
Spectrum from 20250405-whd-9.wiff2 (sample 1) - 20250405-whd-9, Experiment 1, +HDATA TOF MS (100 - 800) from 0.200 min



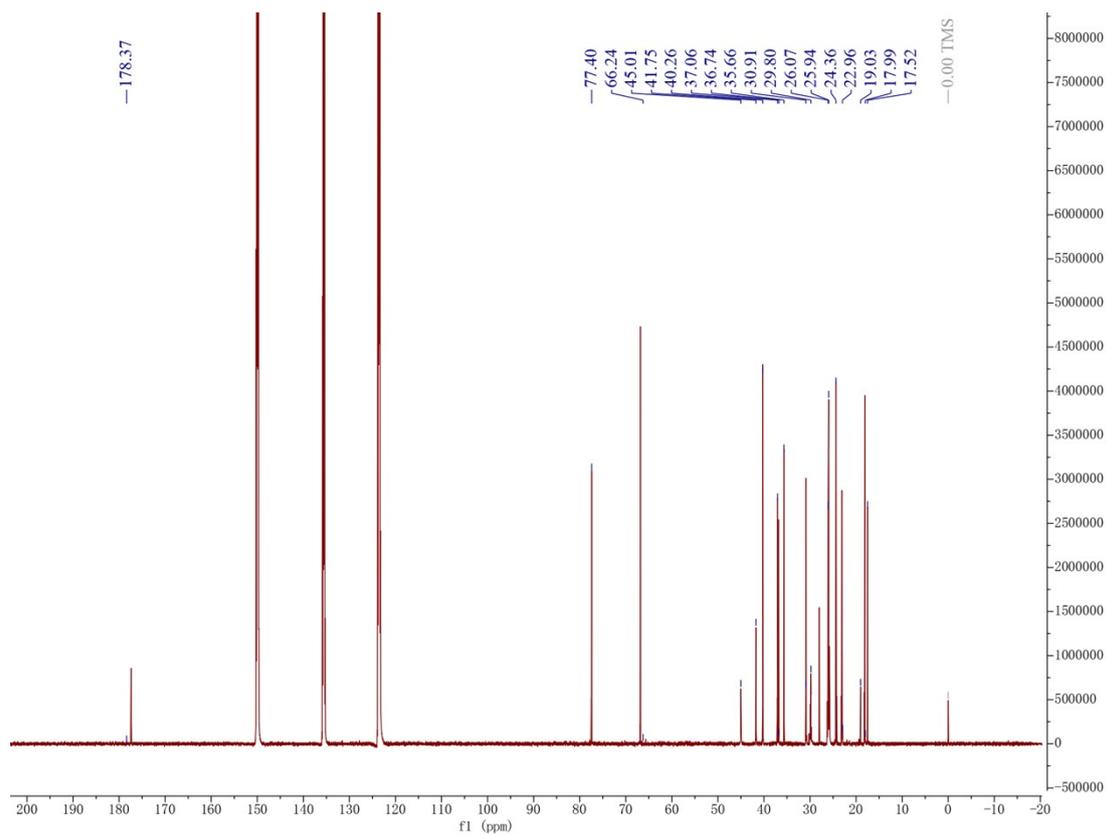
11. Compound a8



¹H-NMR

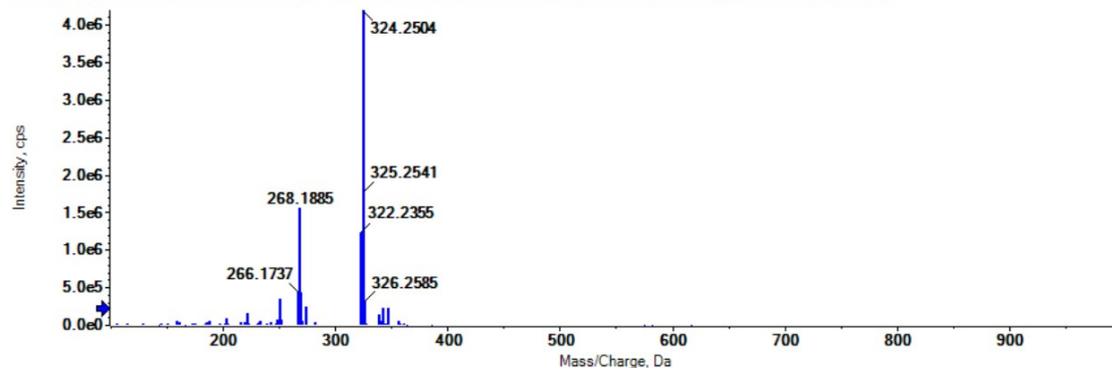


¹³C-NMR

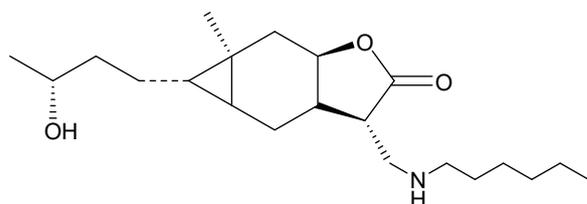


HR-MS

Spectrum from 20250426-whd-23.wiff2 (sample 1) - 20250426-whd-23, Experiment 1, +IDA TOF MS (100 - 1000) from 0.234 min

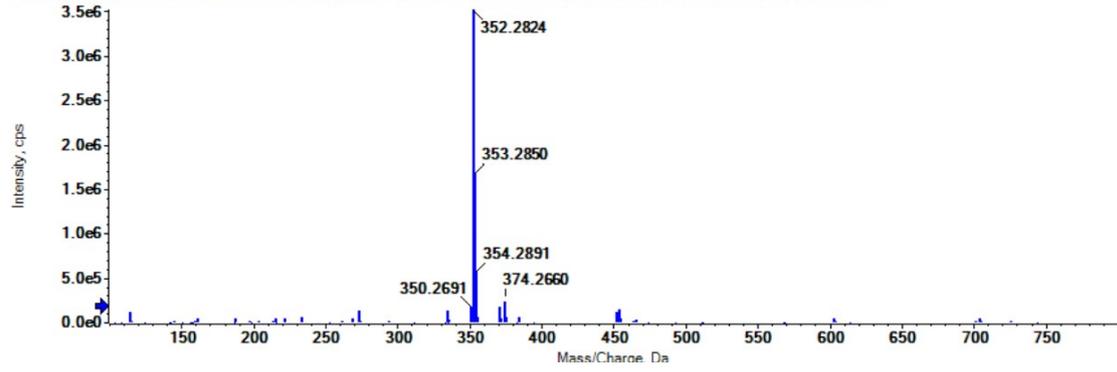


12. Compound a9

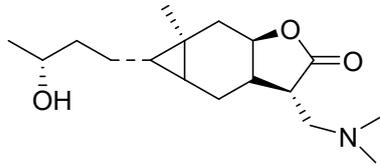


¹H-NMR

Spectrum from 20250405-whd-10.wiff2 (sample 1) - 20250405-whd-10, Experiment 1, +IDA TOF MS (100 - 800) from 0.239 min

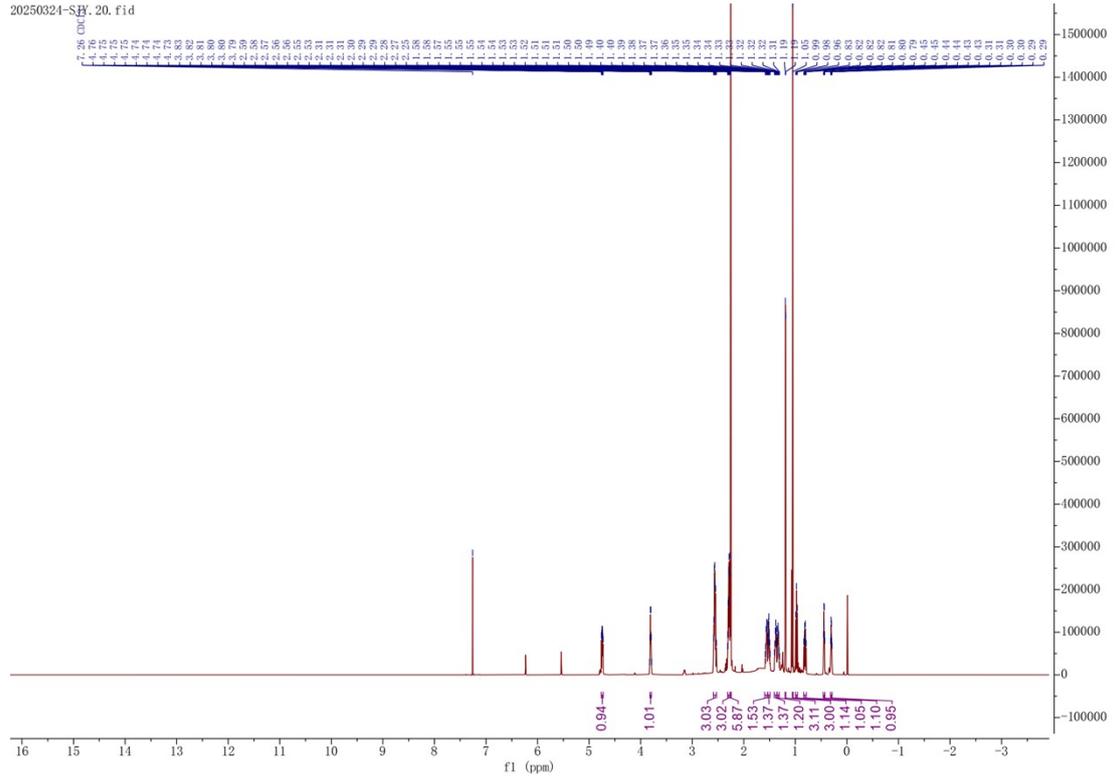


13.Compound a10



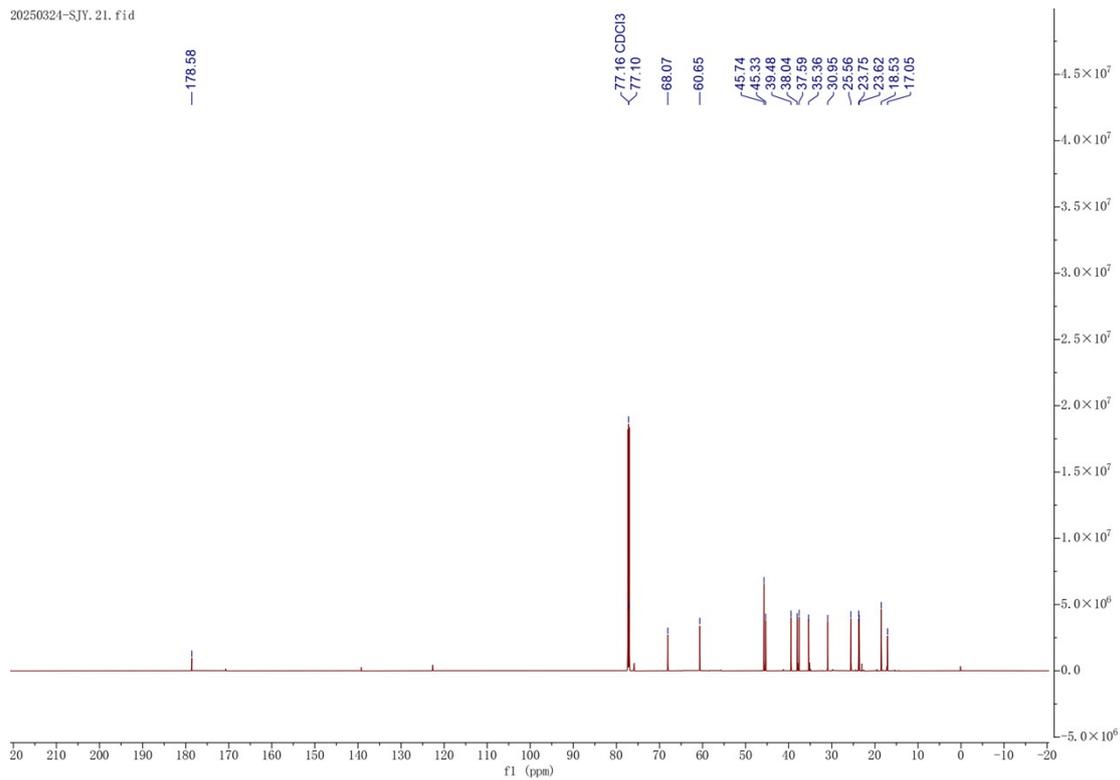
¹H-NMR

20250324-SH_20.fid



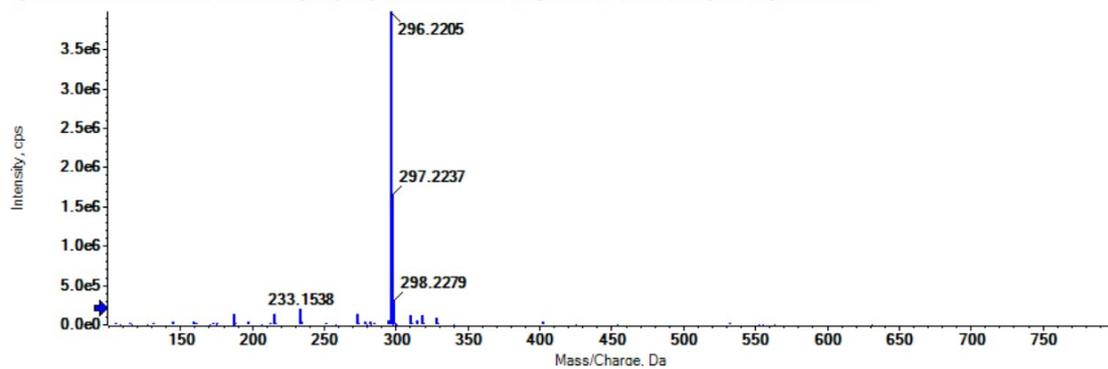
¹³C-NMR

20250324-SJV_21.fid

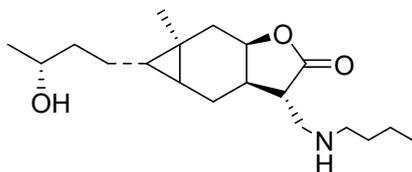


HR-MS

Spectrum from 20250425-whd-21.wiff2 (sample 1) - 20250425-whd-21, Experiment 1, +IDA TOF MS (100 - 800) from 0.193 min

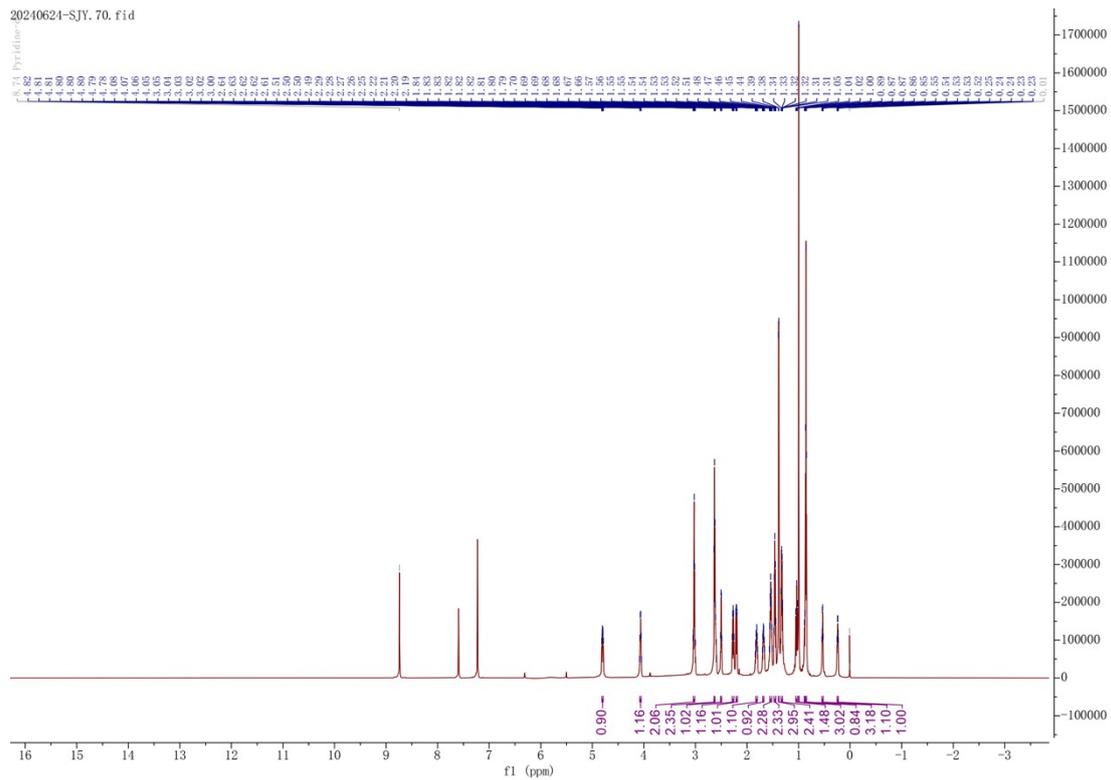


14. Compound a11



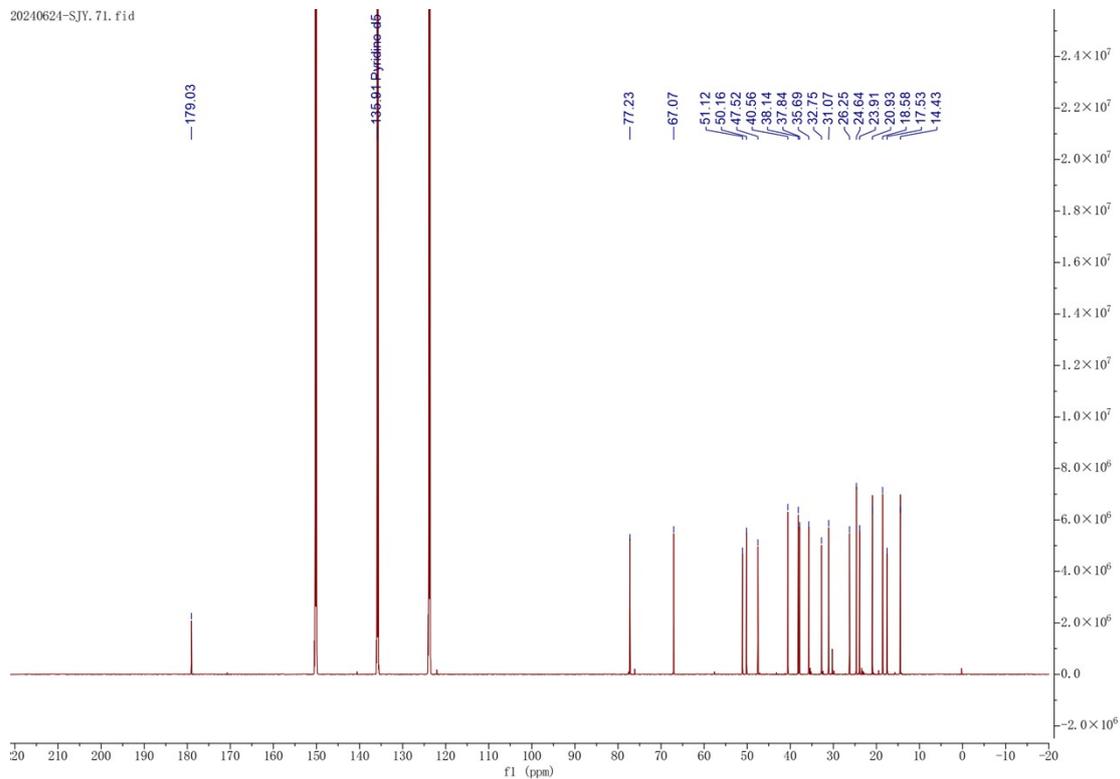
¹H-NMR

20240624-SJV. 70. fid



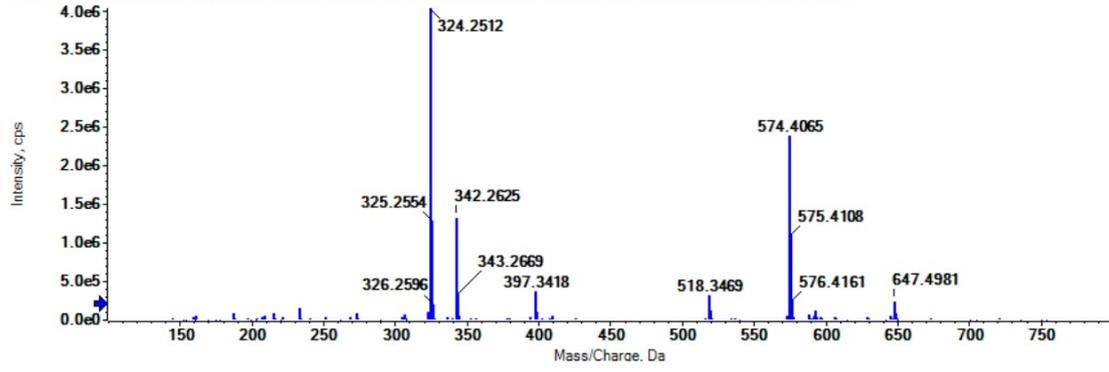
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20240624-SJV. 71. fid

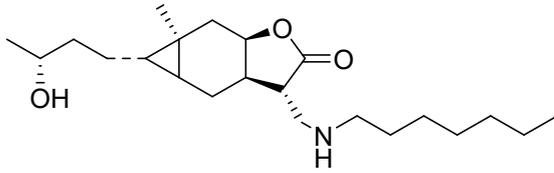


HR-MS

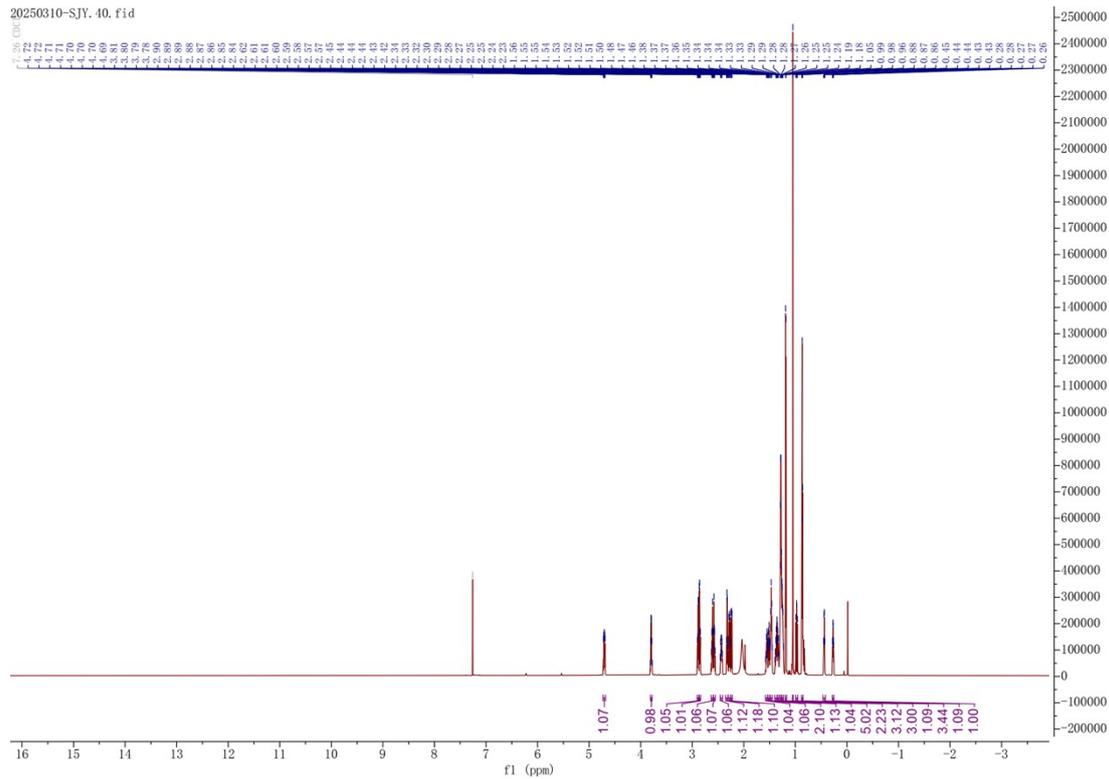
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15. Compound a12

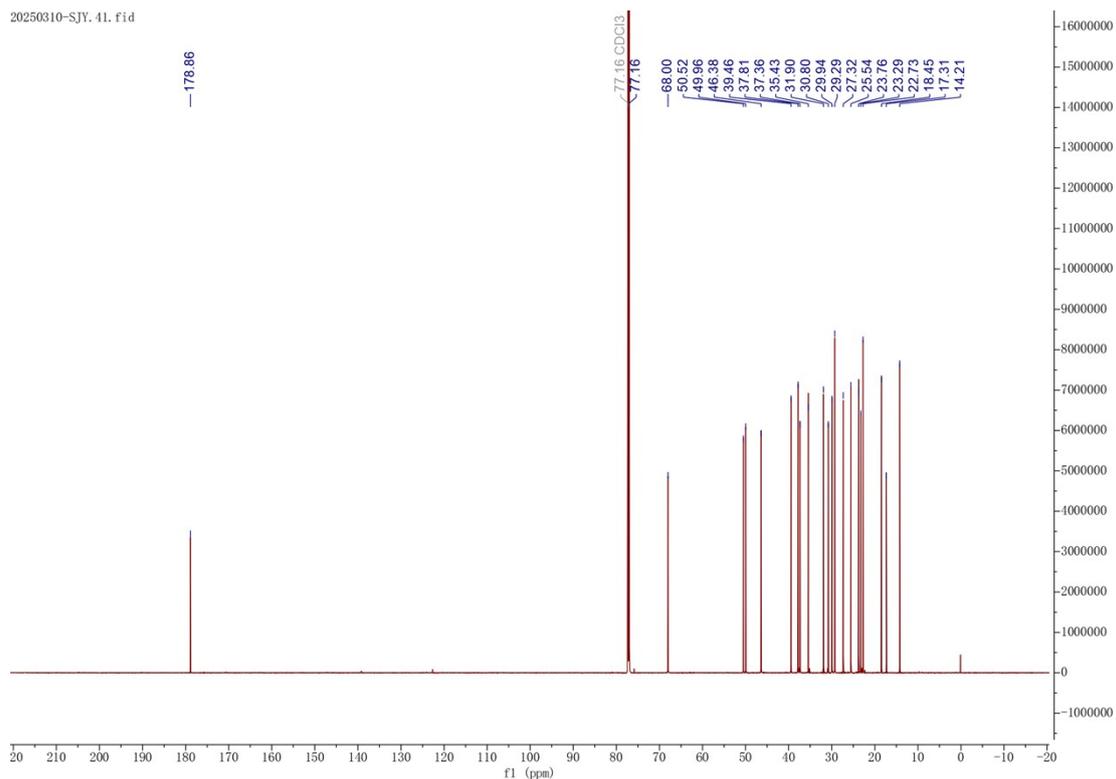


¹H-NMR



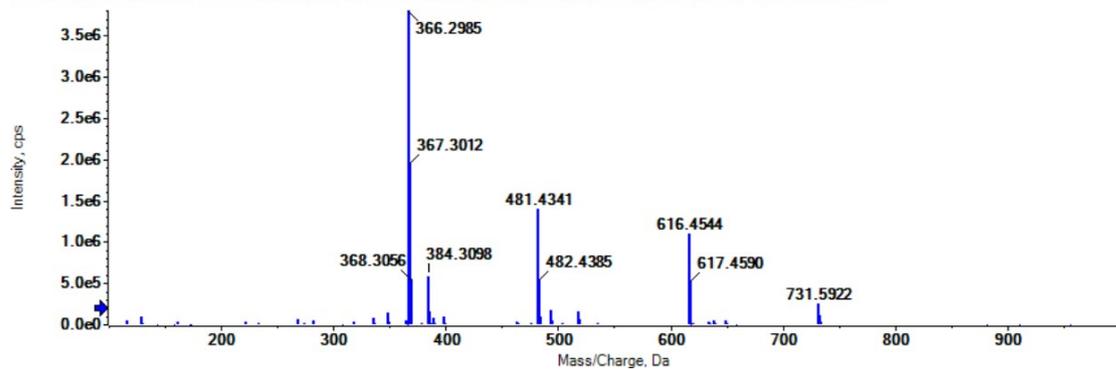
¹³C-NMR

20250310-SJY. 41. fid

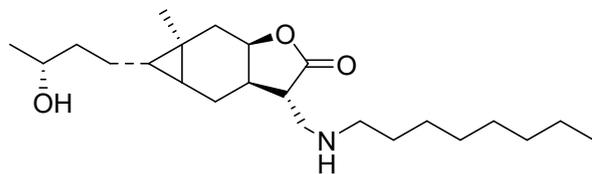


HR-MS

Spectrum from 20250426-whd-11.wiff2 (sample 1) - 20250426-whd-11, Experiment 1, -IDA TOF MS (100 - 1000) from 0.187 min

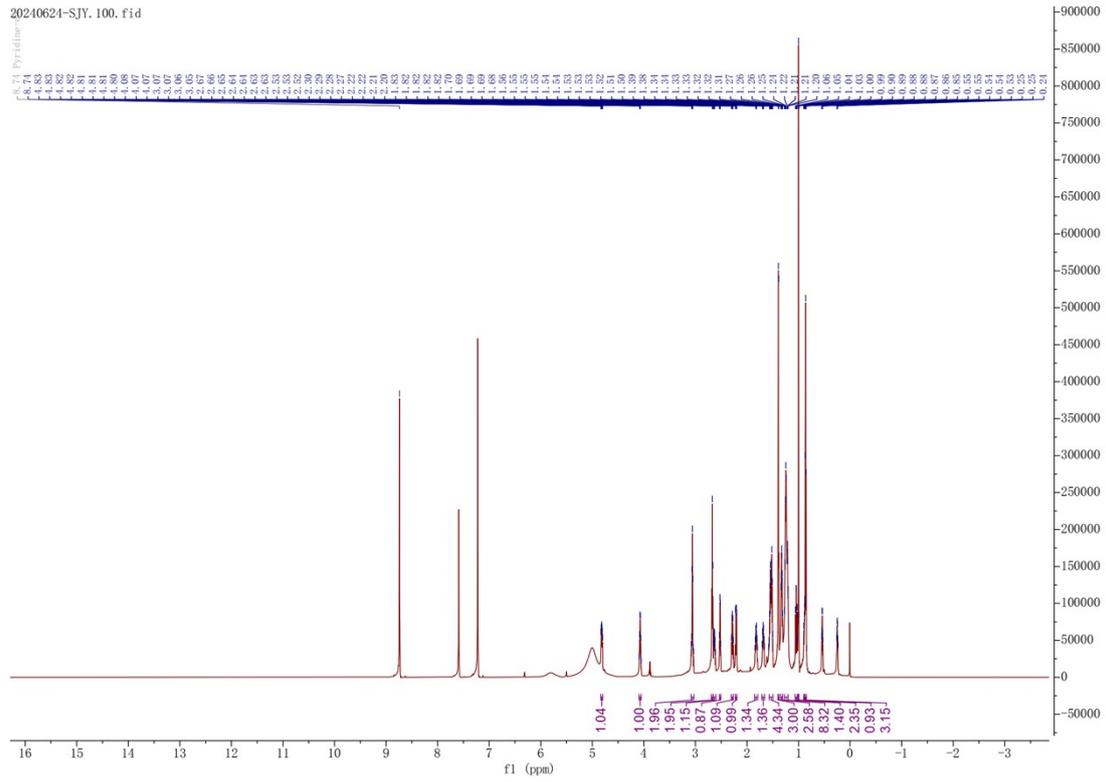


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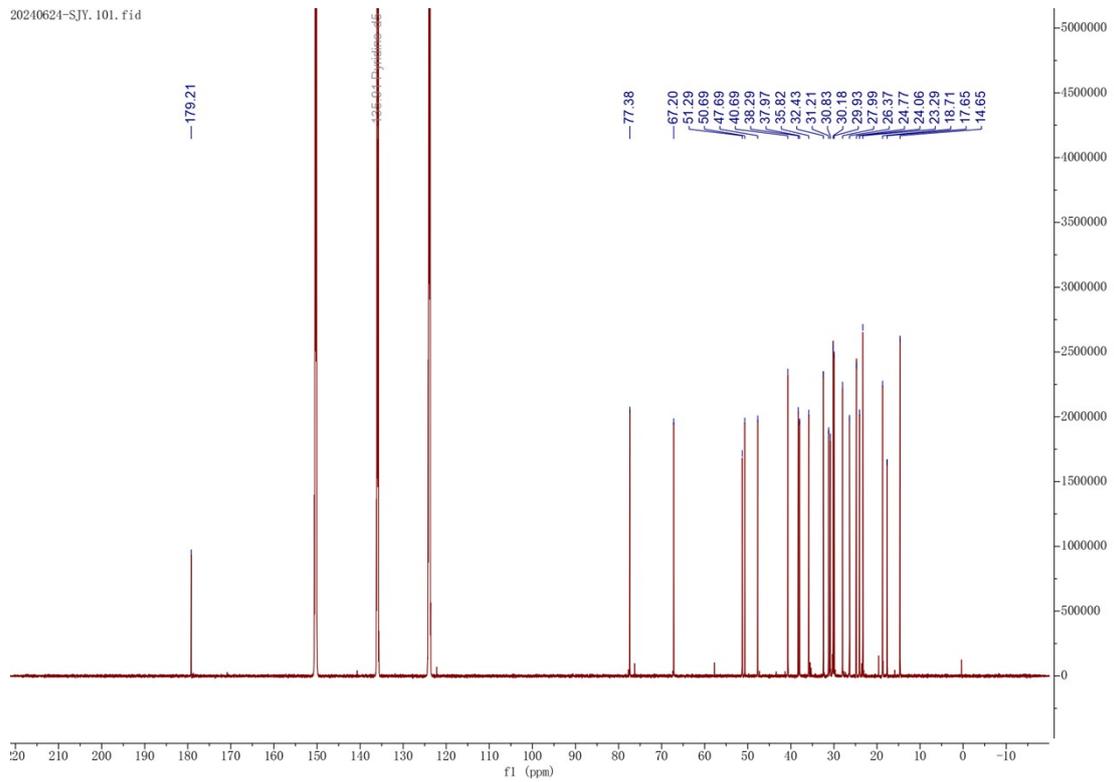
¹H-NMR

20240624-SJY. 100. fid



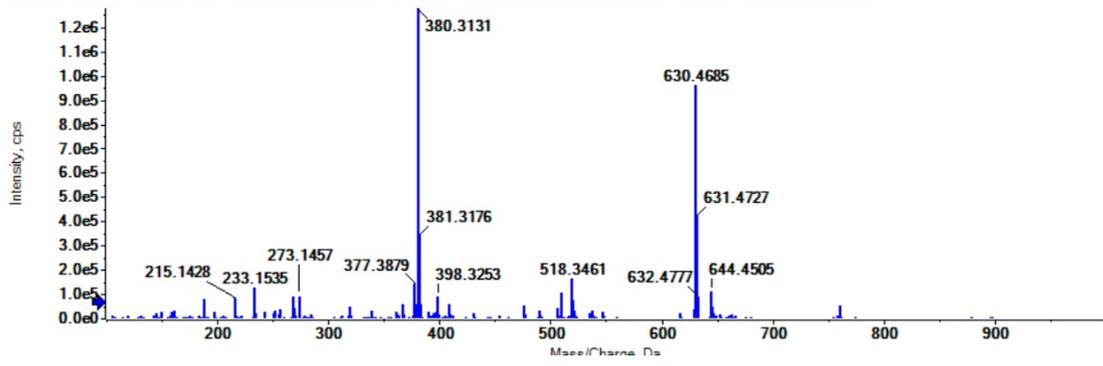
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20240624-SJY. 101. fid

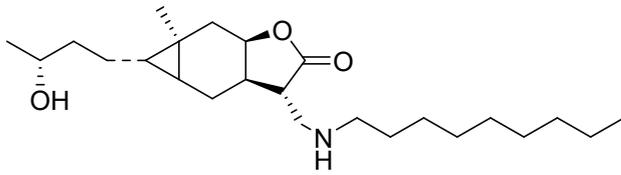


HR-MS

Spectrum from 20250426-whd-12.wiff2 (sample 1) - 20250426-whd-12, Experiment 1, +IDA TOF MS (100 - 1000) from 0.195 min

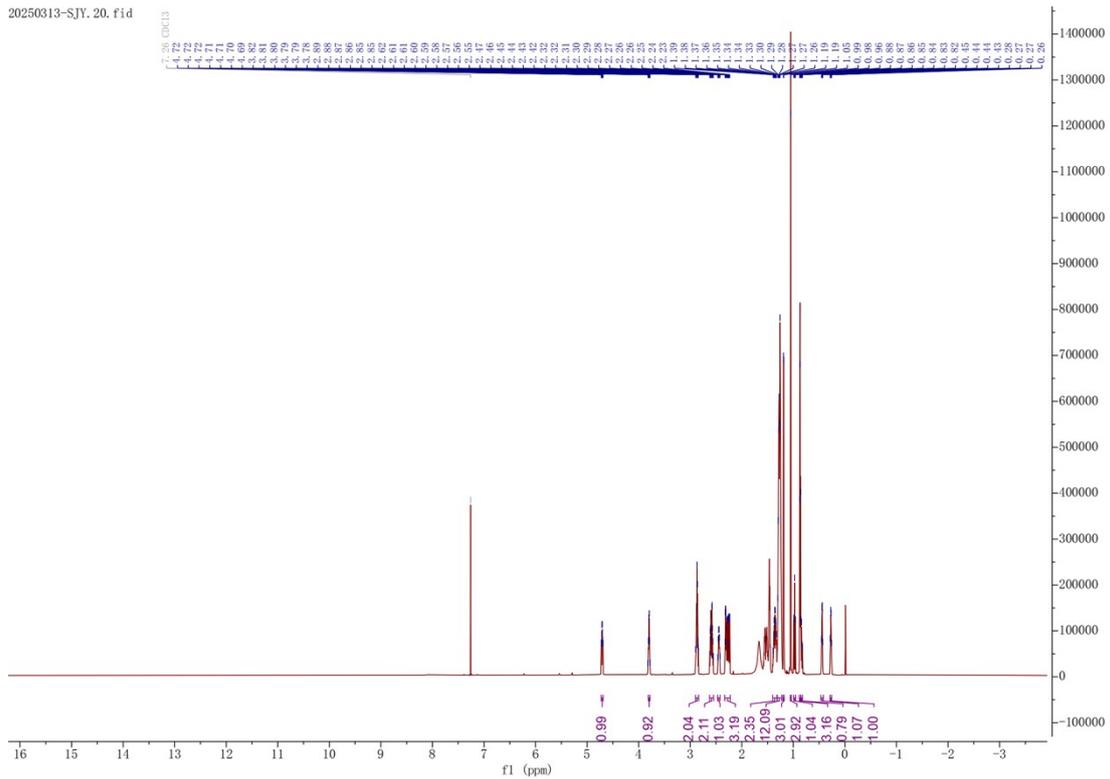


17.Compound a14



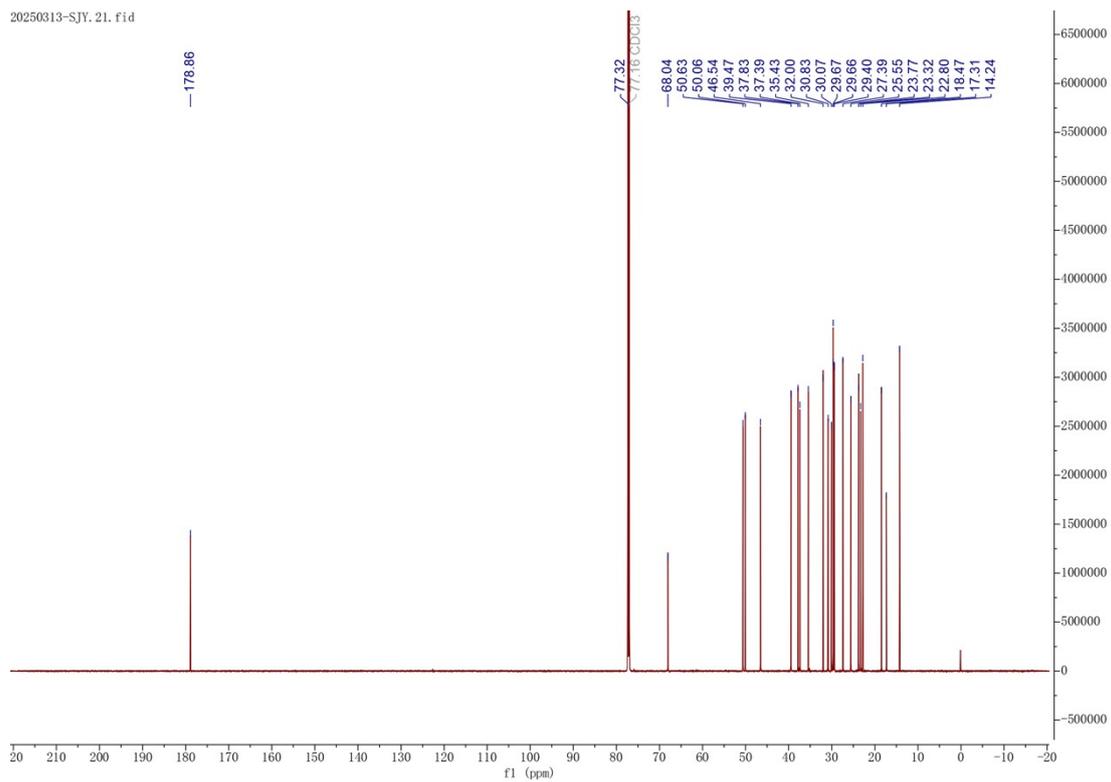
¹H-NMR

20250313-SJY_20.fid



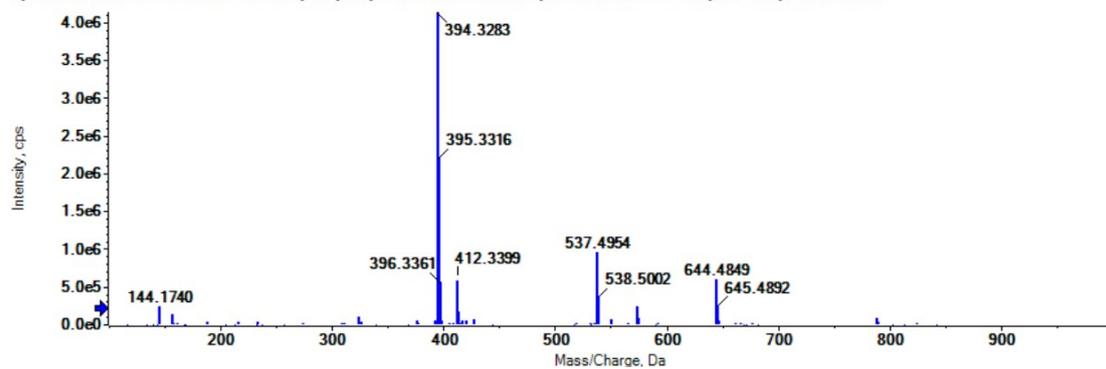
¹³C-NMR

20250313-SJV_21.fid

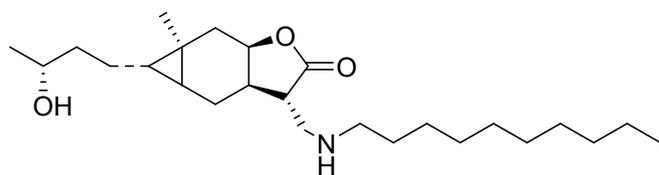


HR-MS

Spectrum from 20250426-whd-13.wiff2 (sample 1) - 20250426-whd-13, Experiment 1, +IDA TOF MS (100 - 1000) from 0.221 min

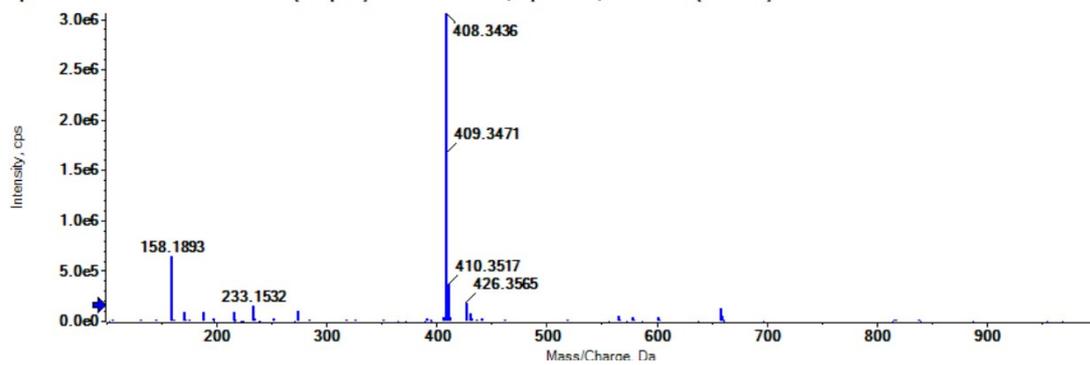


18. Compound a15

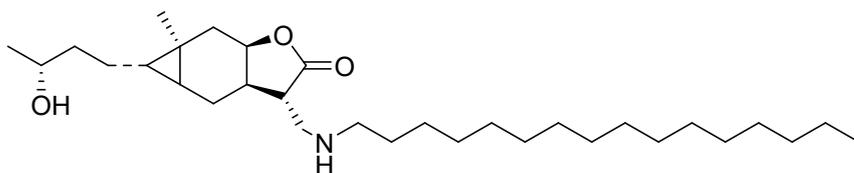


¹H-NMR

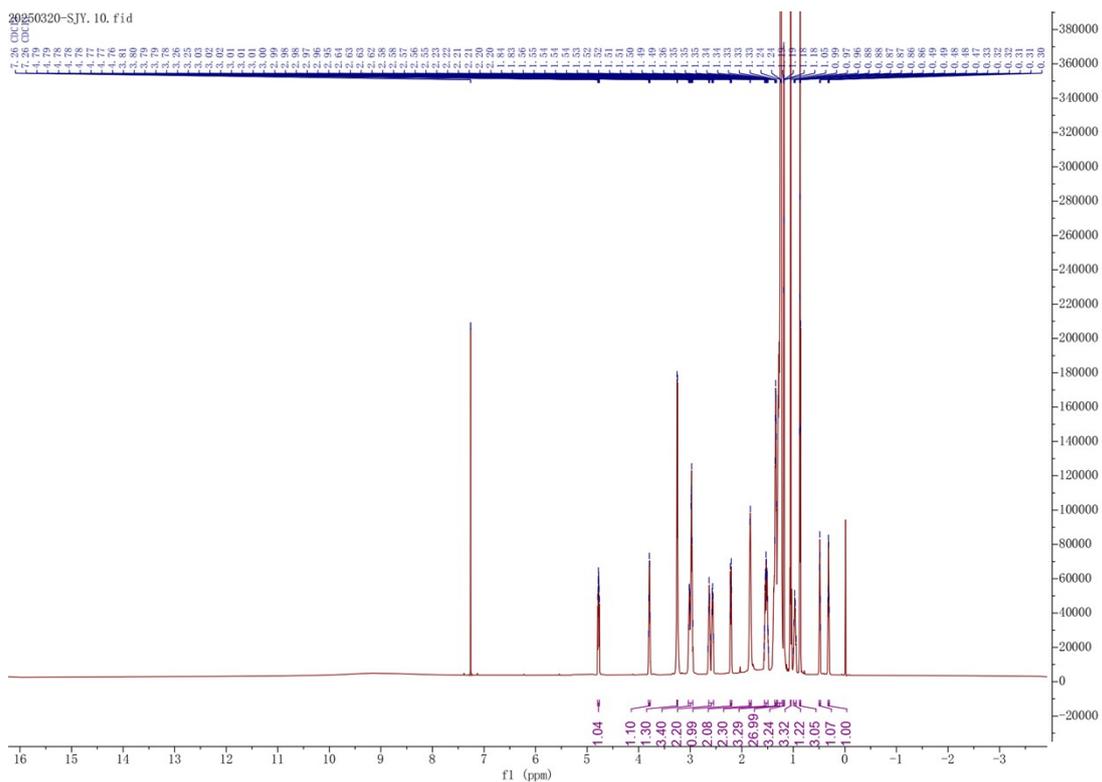
Spectrum from 20250426-whd-14.wiff2 (sample 1) - 20250426-whd-14. Experiment 1, +IDA TOF MS (100 - 1000) from 0.136 min



19. Compound a16

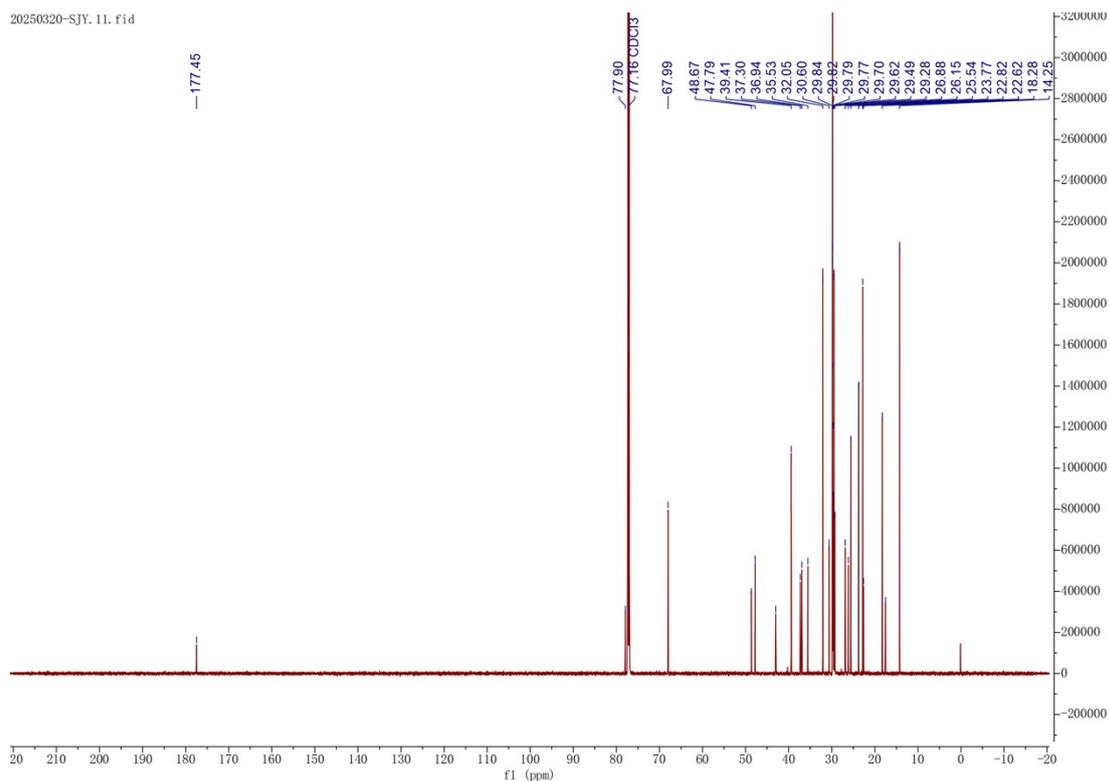


¹H-NMR



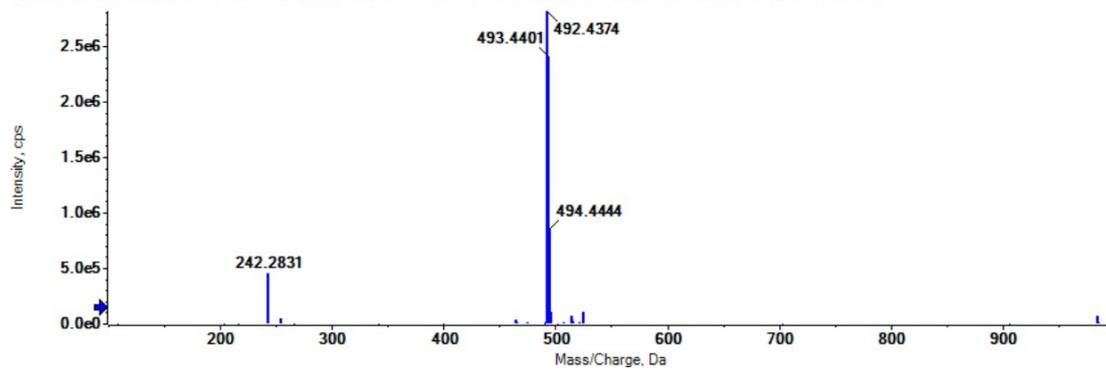
¹³C-NMR

20250320-SJY. 11. fid

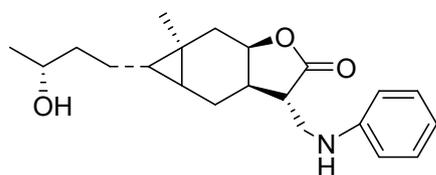


HR-MS

Spectrum from 20250426-whd-15.wiff2 (sample 1) - 20250426-whd-15, Experiment 1, +IDA TOF MS (100 - 1000) from 0.220 min

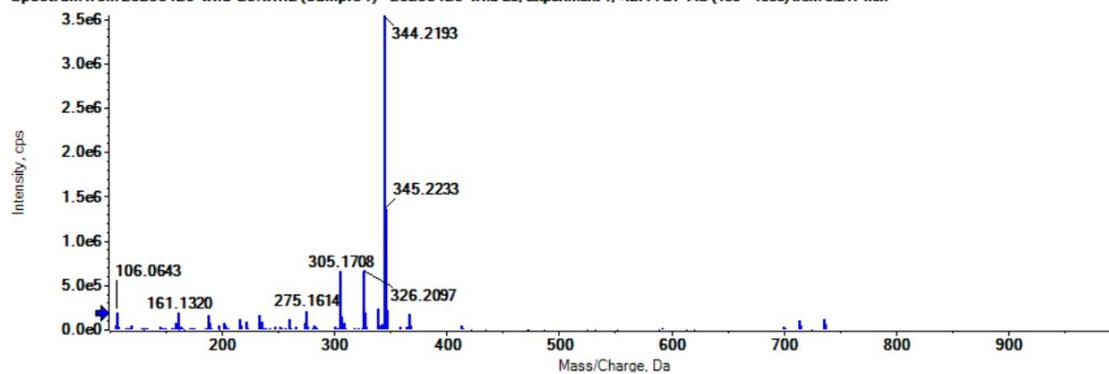


20. Compound a17

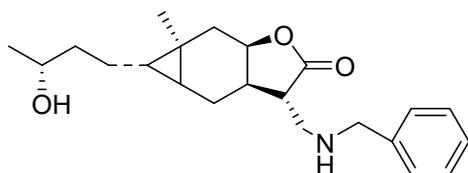


¹H-NMR

Spectrum from 20250426-whd-28.wiff2 (sample 1) - 20250426-whd-28, Experiment 1, +IDA TOF MS (100 - 1000) from 0.217 min

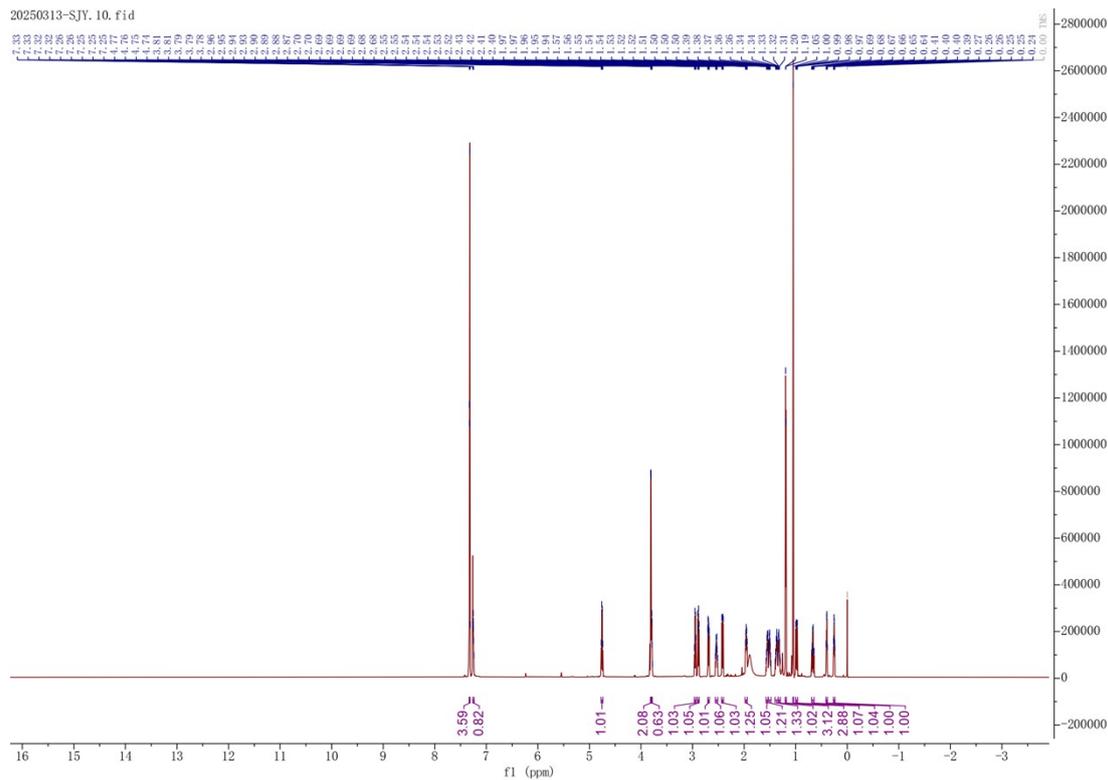


21. Compound a18



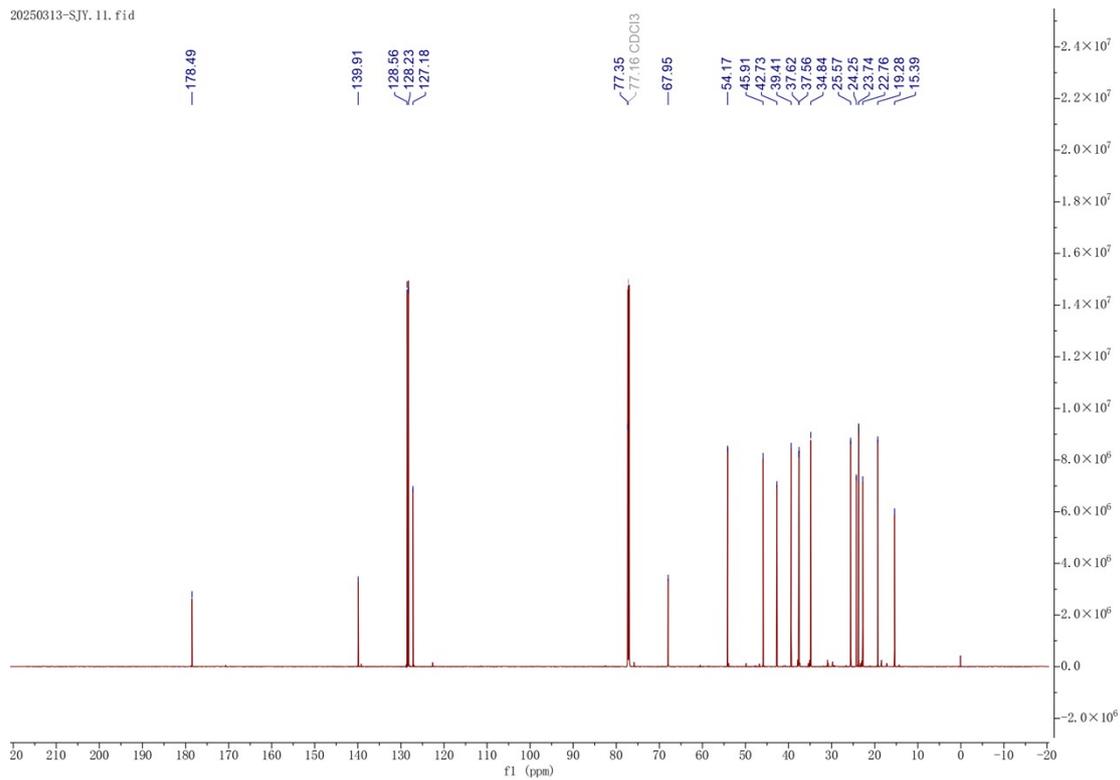
$^1\text{H-NMR}$

20250313-SJV. 10. F1d



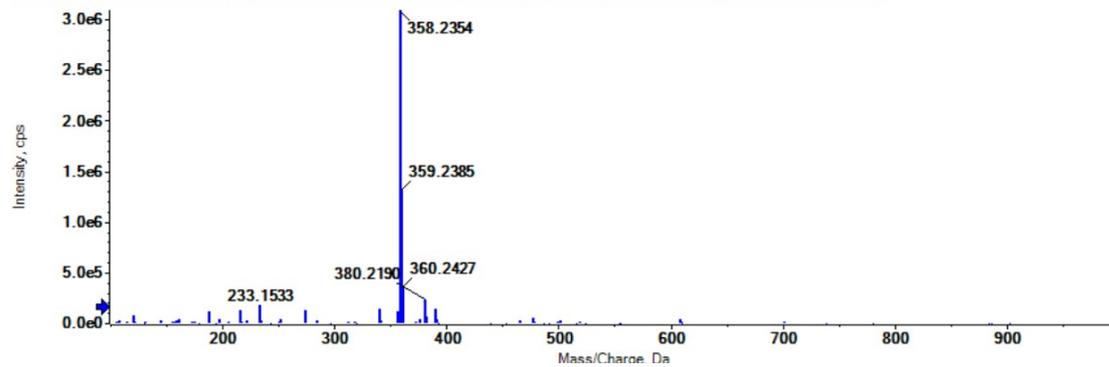
$^{13}\text{C-NMR}$

20250313-SJV. 11. fid

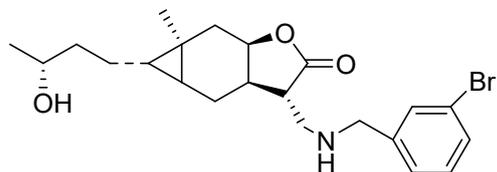


HR-MS

Spectrum from 20250426-whd-16.wiff2 (sample 1) - 20250426-whd-16, Experiment 1, +IDA TOF MS (100 - 1000) from 0.181 min

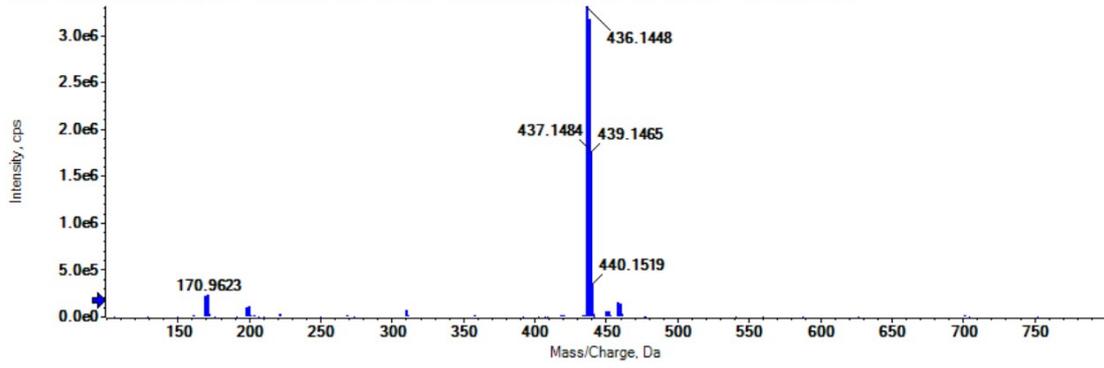


22. Compound a19

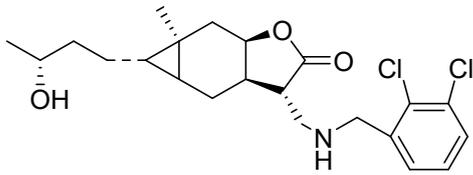


¹H-NMR

Spectrum from 20250405-whd-3.wiff2 (sample 1) - 20250405-whd-3, Experiment 1, +IDATOF MS (100 - 800) from 0.186 min

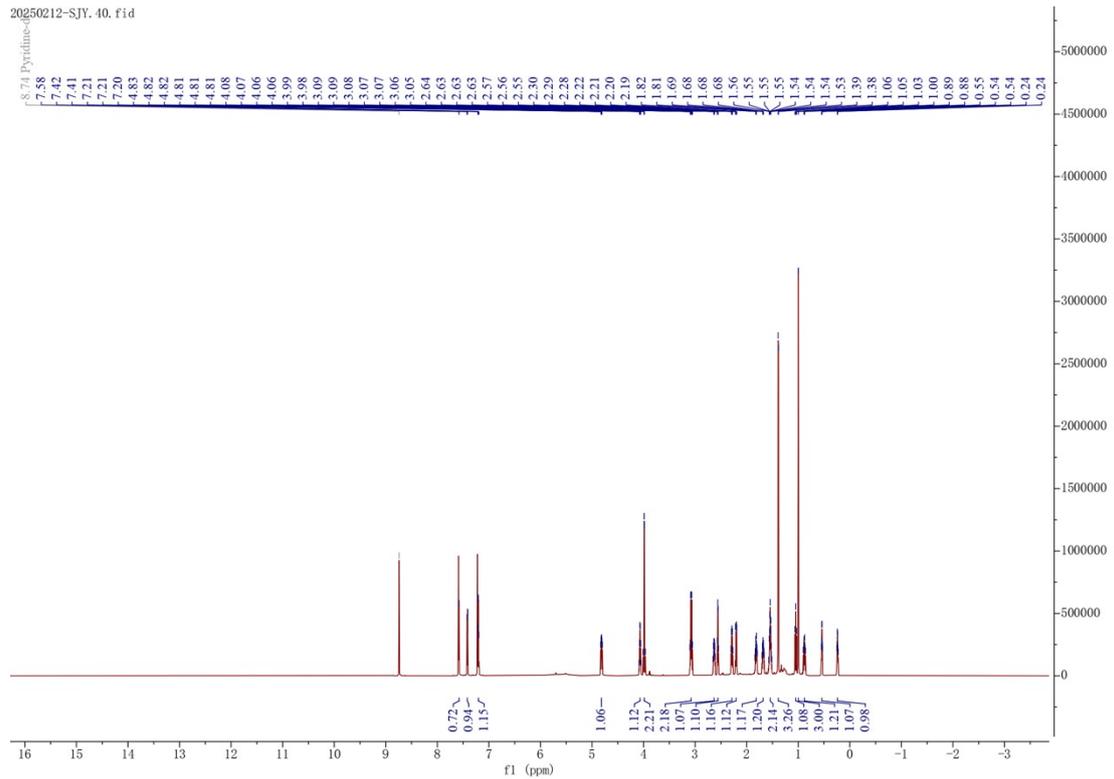


23. Compound a20



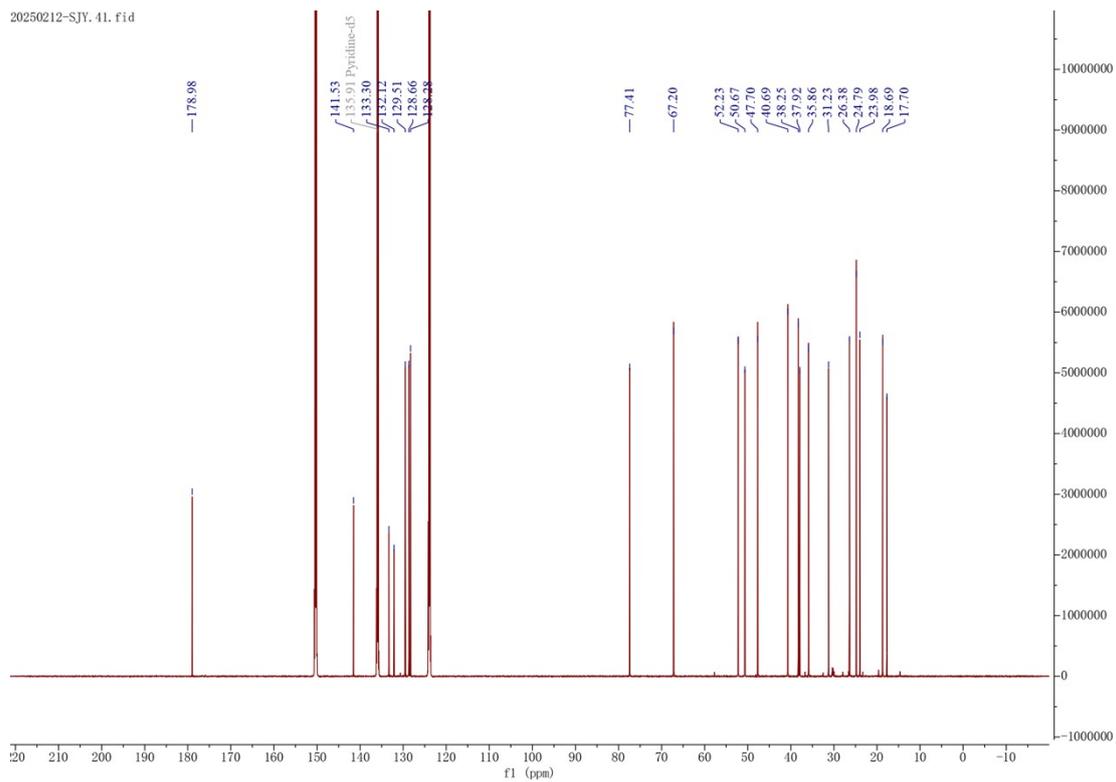
¹H-NMR

20250212-SJY, 40, fid



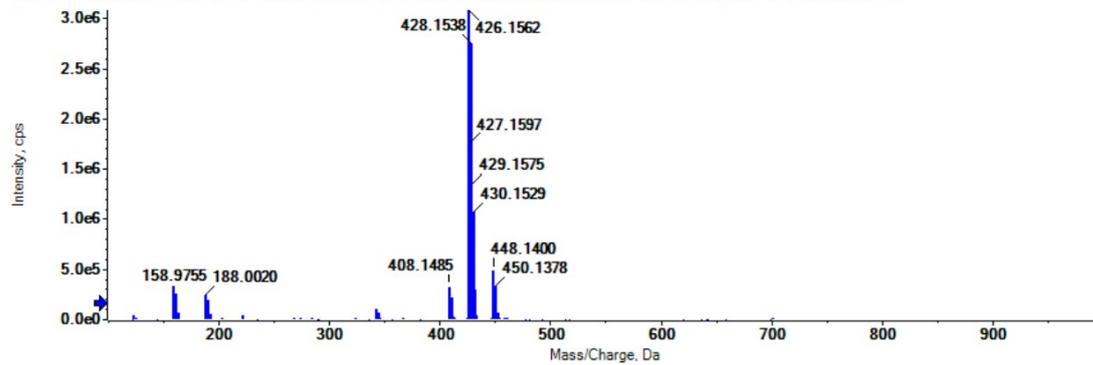
¹³C-NMR

20250212-SJV. 41. fid

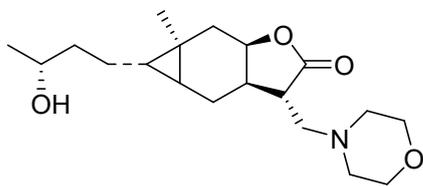


HR-MS

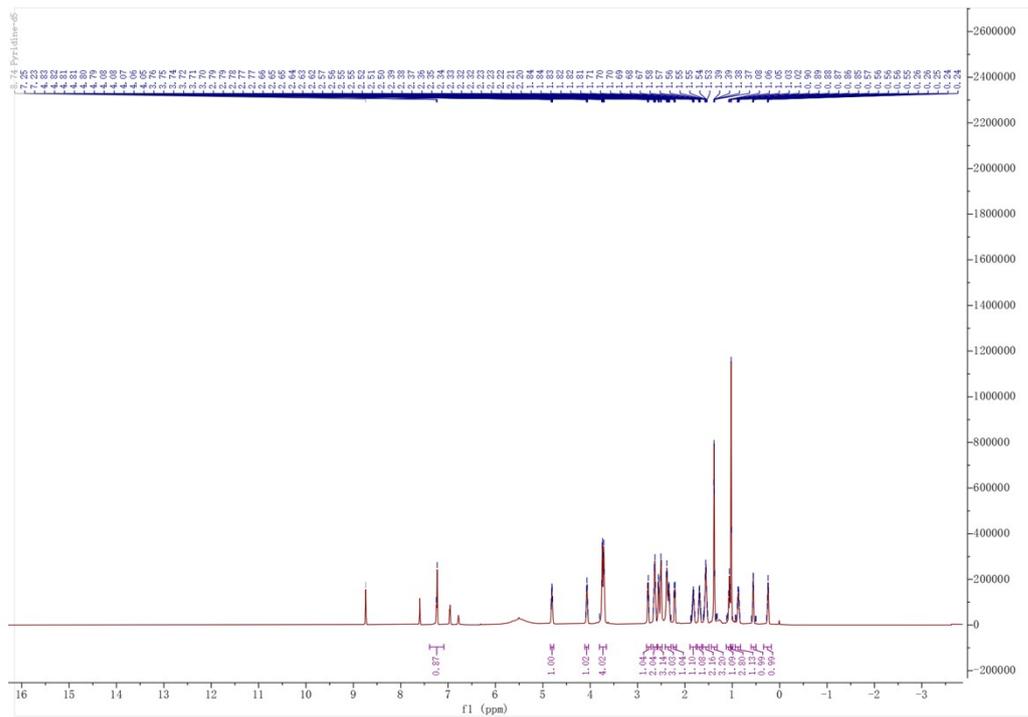
Spectrum from 20250426-whd-18-1.wiff2 (sample 1) - 20250426-whd-18-1, Experiment 1, +IDA TOF MS (100 - 1000) from 0.231 min



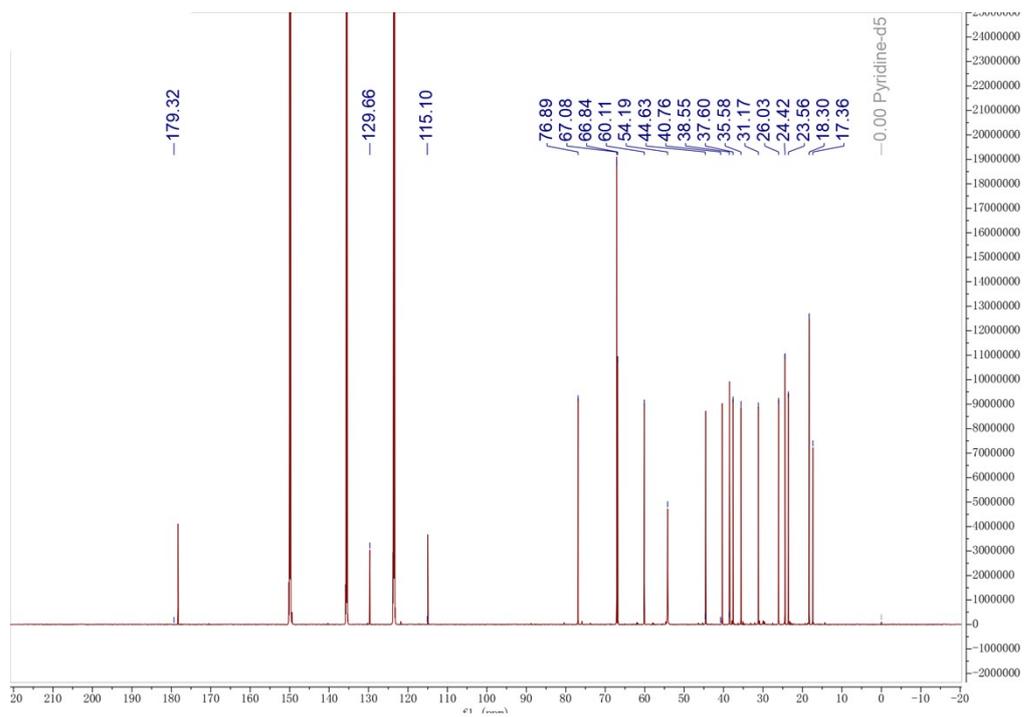
24. Compound a21



¹H-NMR

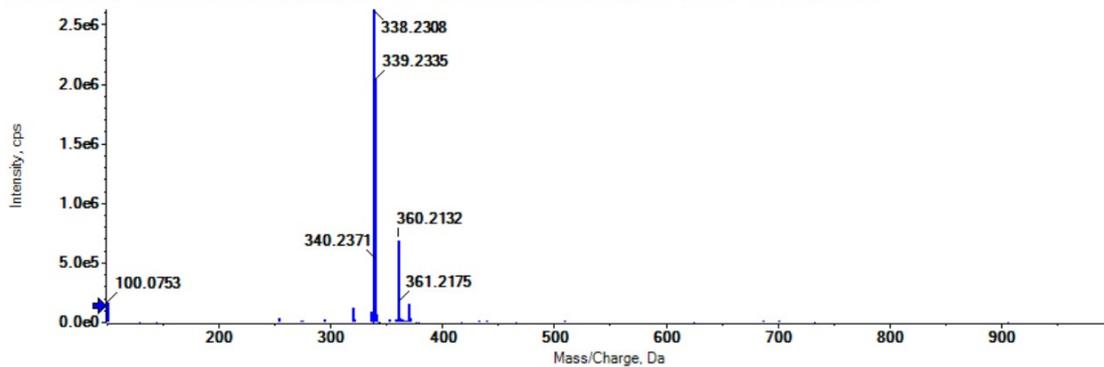


¹³C-NMR

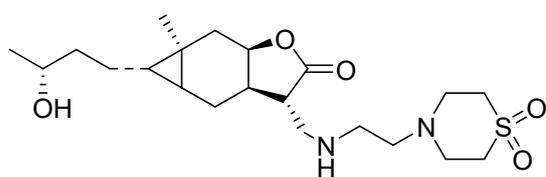


HR-MS

Spectrum from 20250426-whd-24.wiff2 (sample 1) - 20250426-whd-24, Experiment 1, +IDA TOF MS (100 - 1000) from 0.164 min

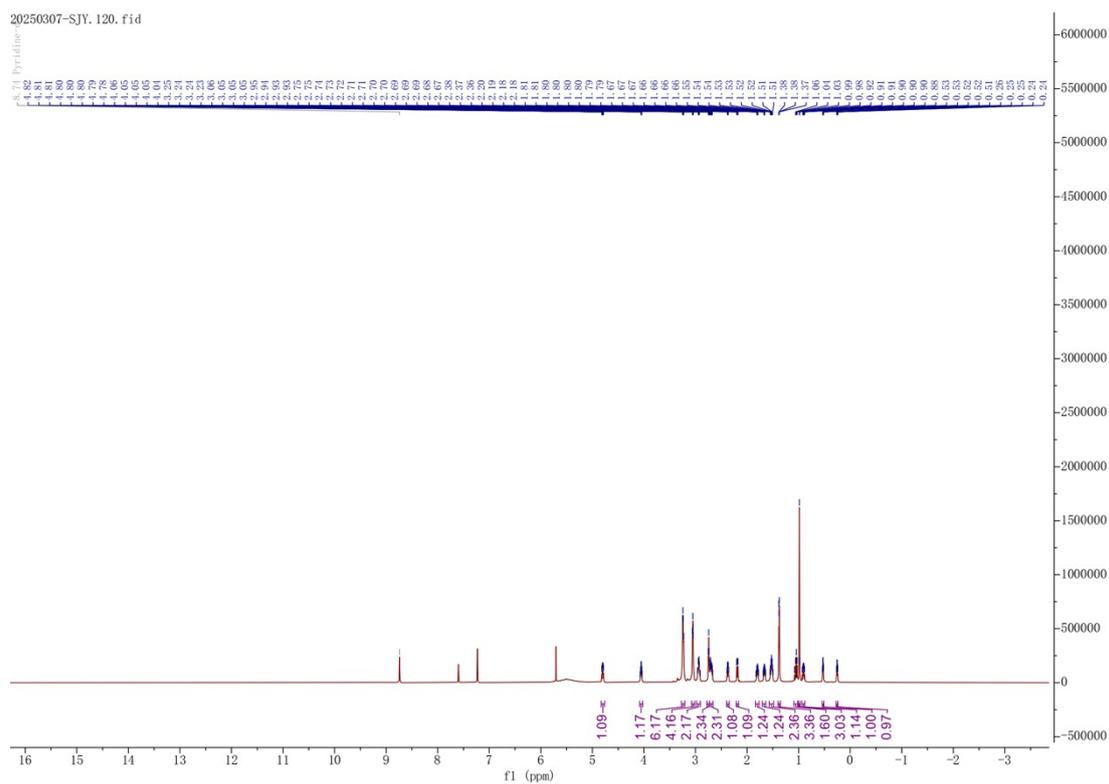


25. Compound a22



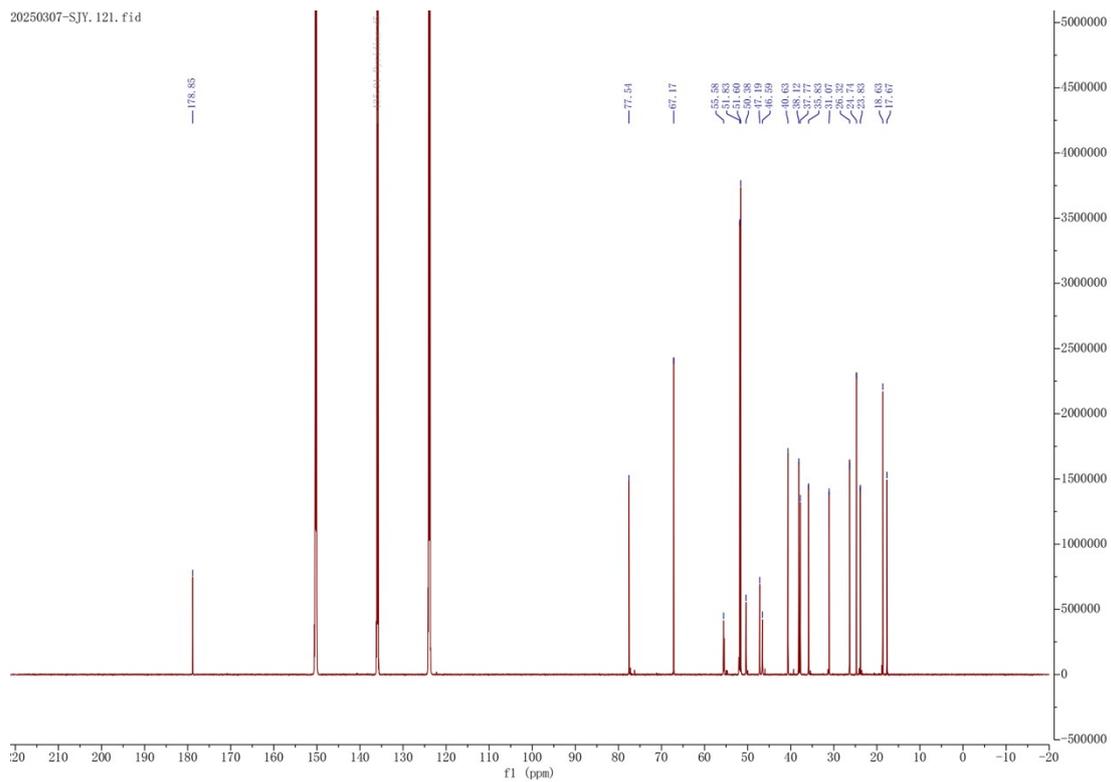
¹H-NMR

20250307-SJY, 120. f1d



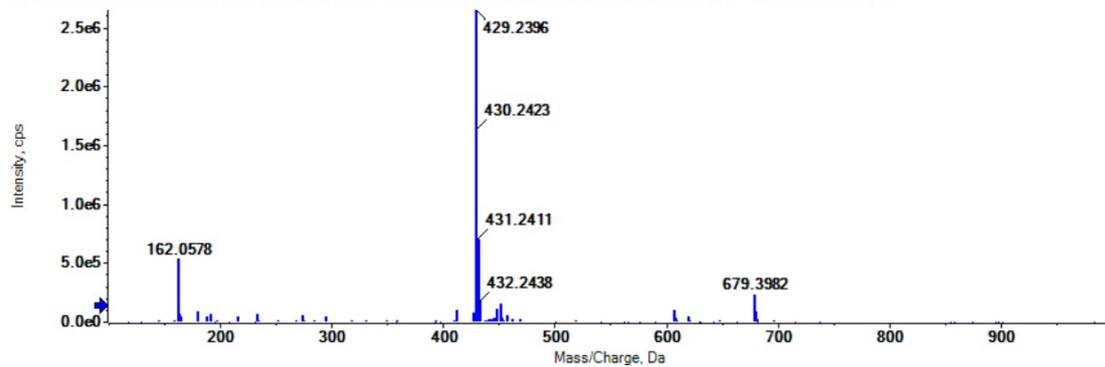
¹³C-NMR

20250307-SJY. 121. fid

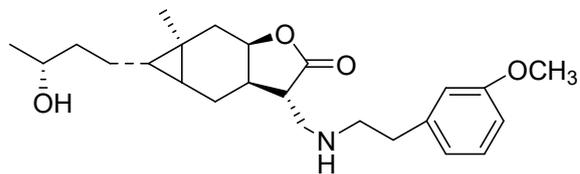


HR-MS

Spectrum from 20250426-whd-20.wiff2 (sample 1) - 20250426-whd-20, Experiment 1, +IDA TOF MS (100 - 1000) from 0.187 min

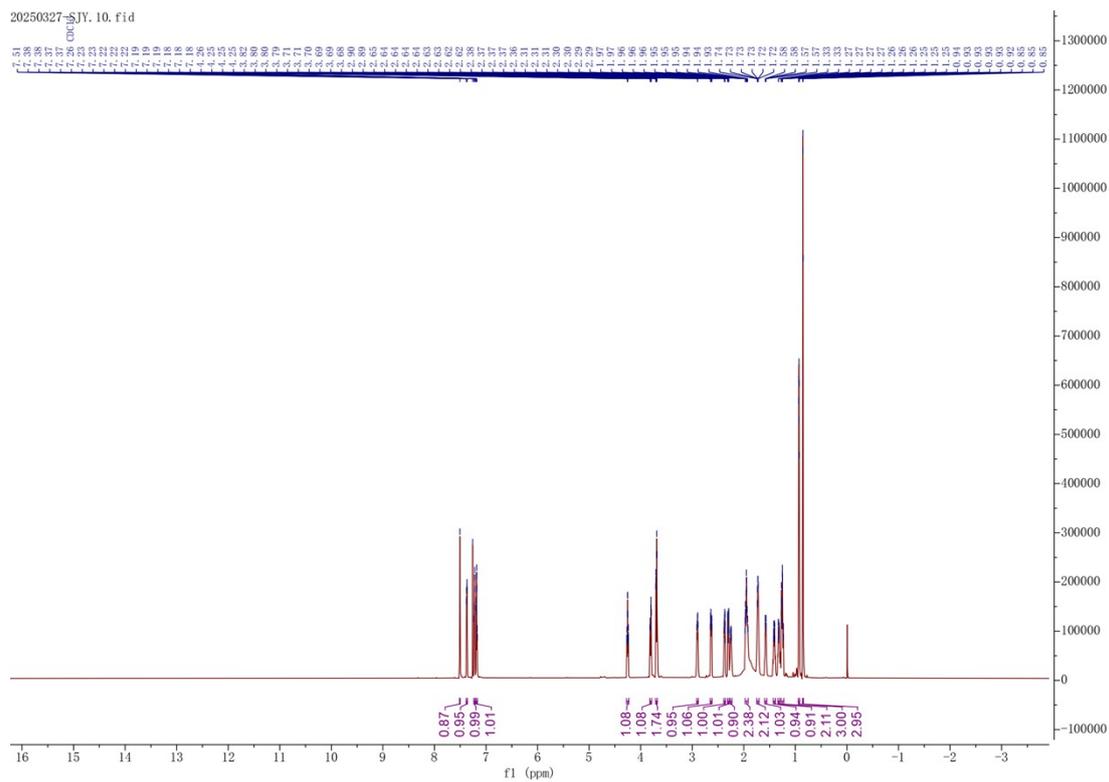


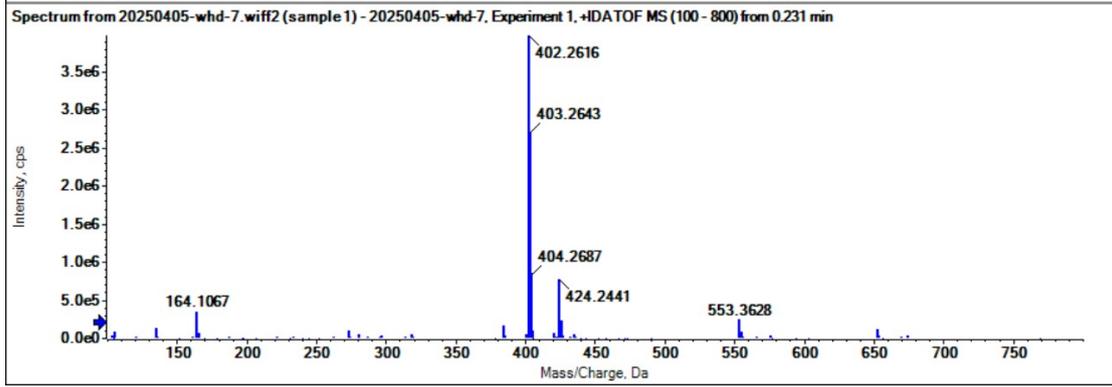
26.Compound a23



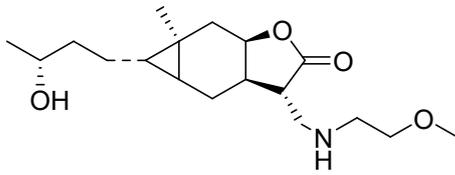
¹H-NMR

20250327-SJV. 10. fid

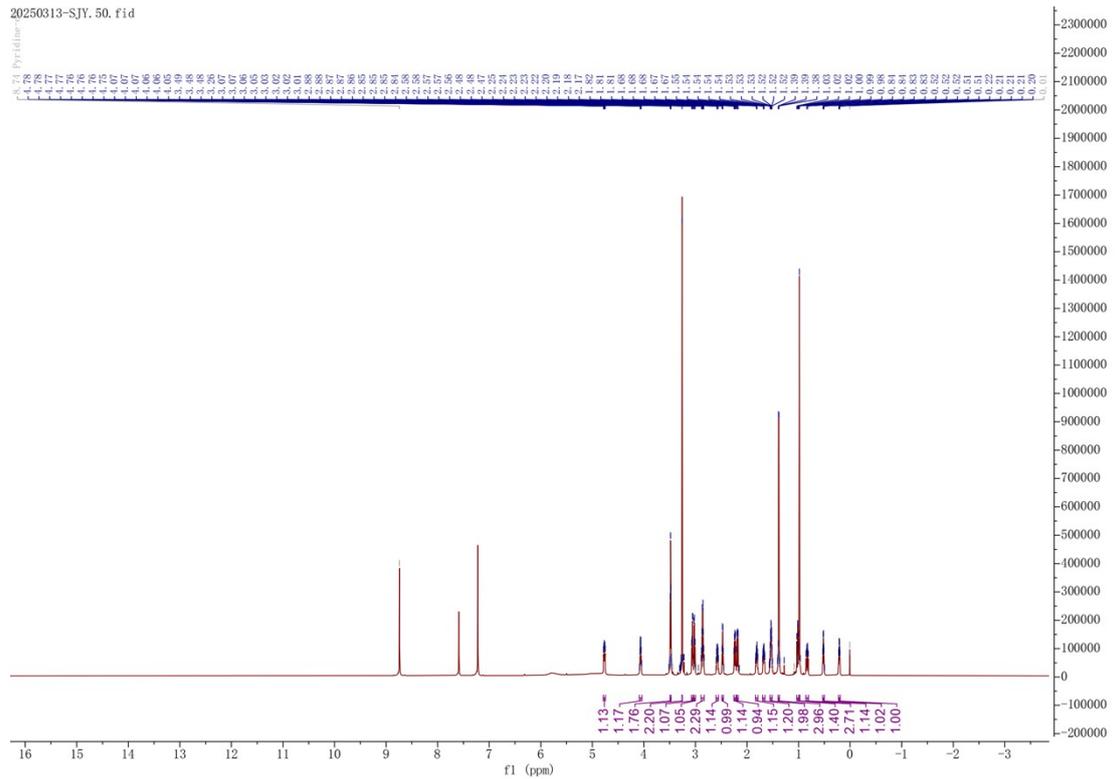




27. Compound a24

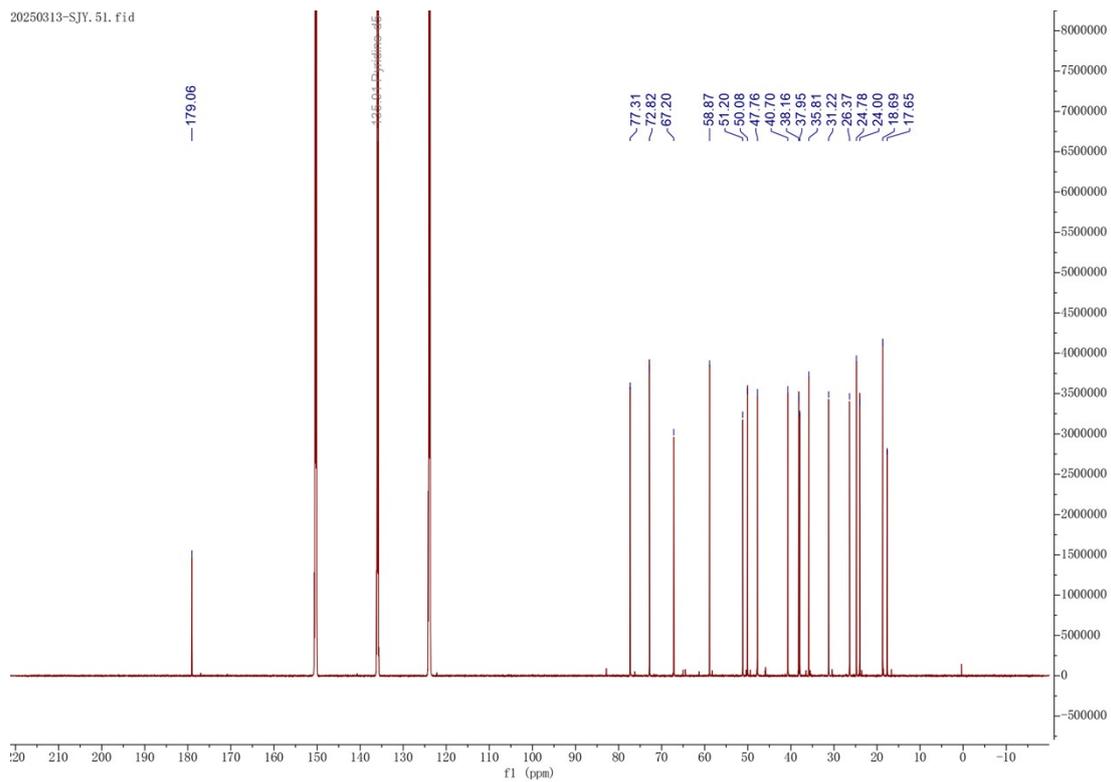


¹H-NMR



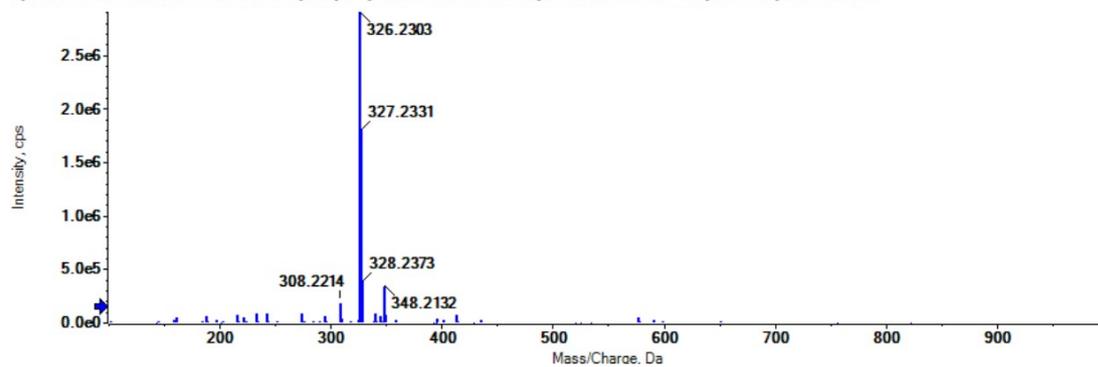
¹³C-NMR

20250313-SJV. 51. fid

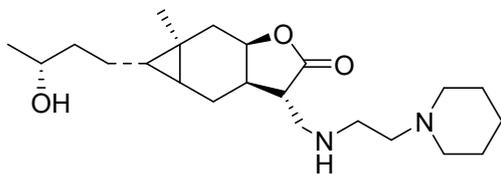


HR-MS

Spectrum from 20250426-whd-17.wiff2 (sample 1) - 20250426-whd-17, Experiment 1, +IDA TOF MS (100 - 1000) from 0.138 min

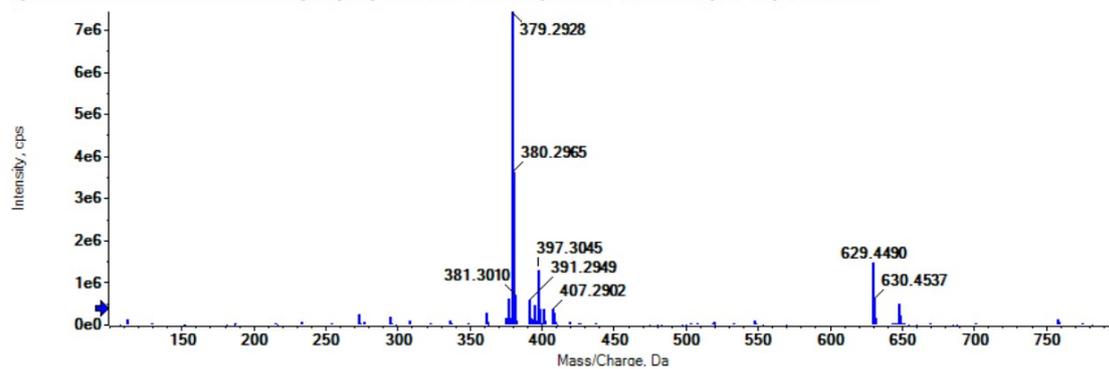


28. Compound a25



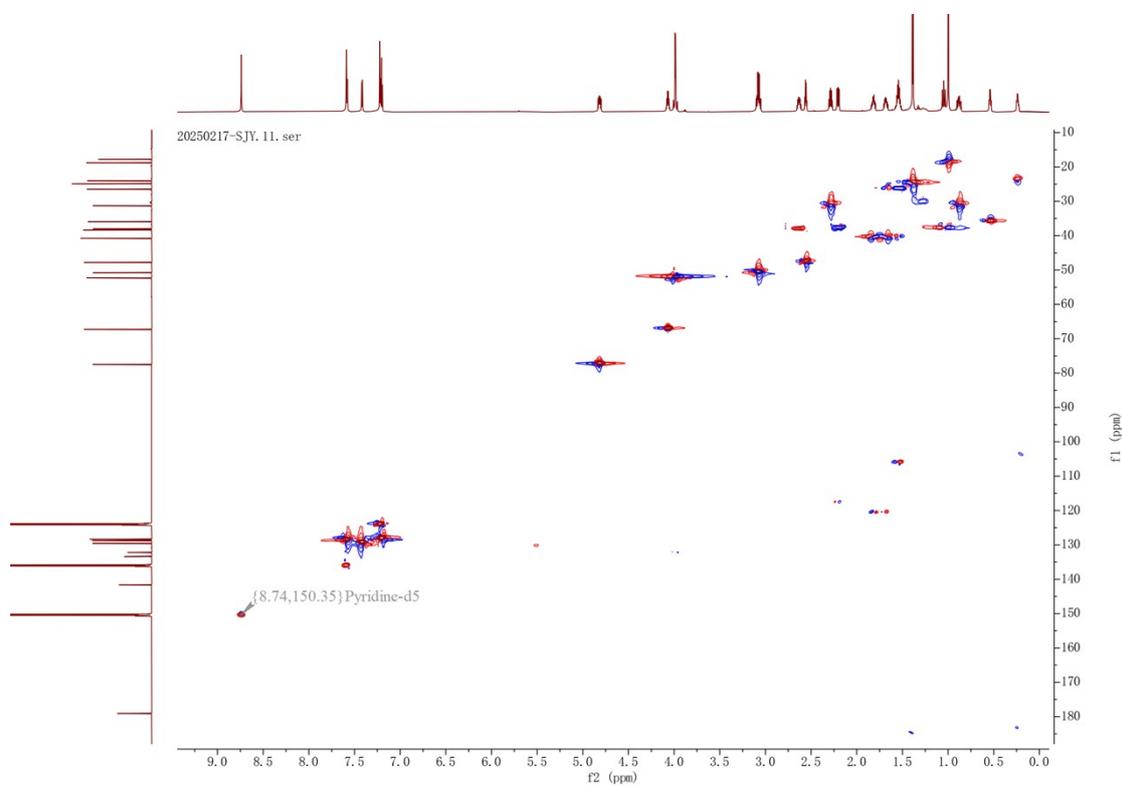
¹H-NMR

Spectrum from 20250425-whd-22.wiff2 (sample 1) - 20250425-whd-22, Experiment 1, +IDA TOF MS (100 - 800) from 0.206 min

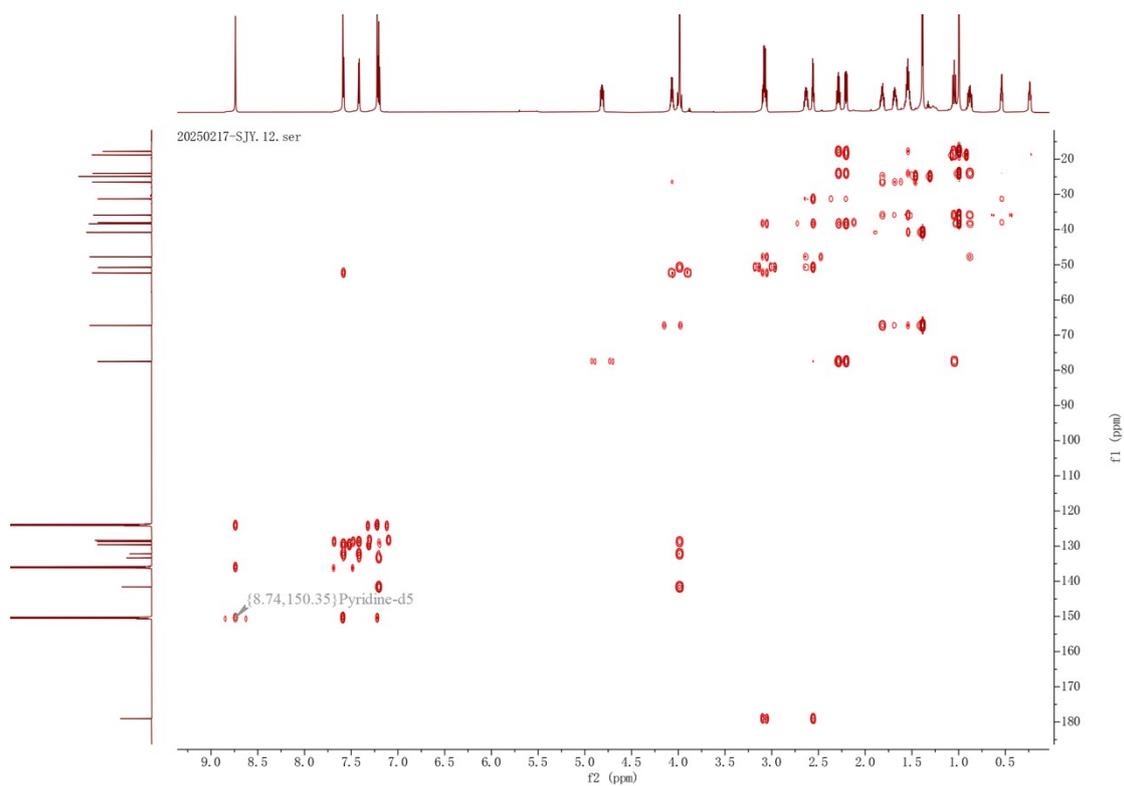


Compound a20

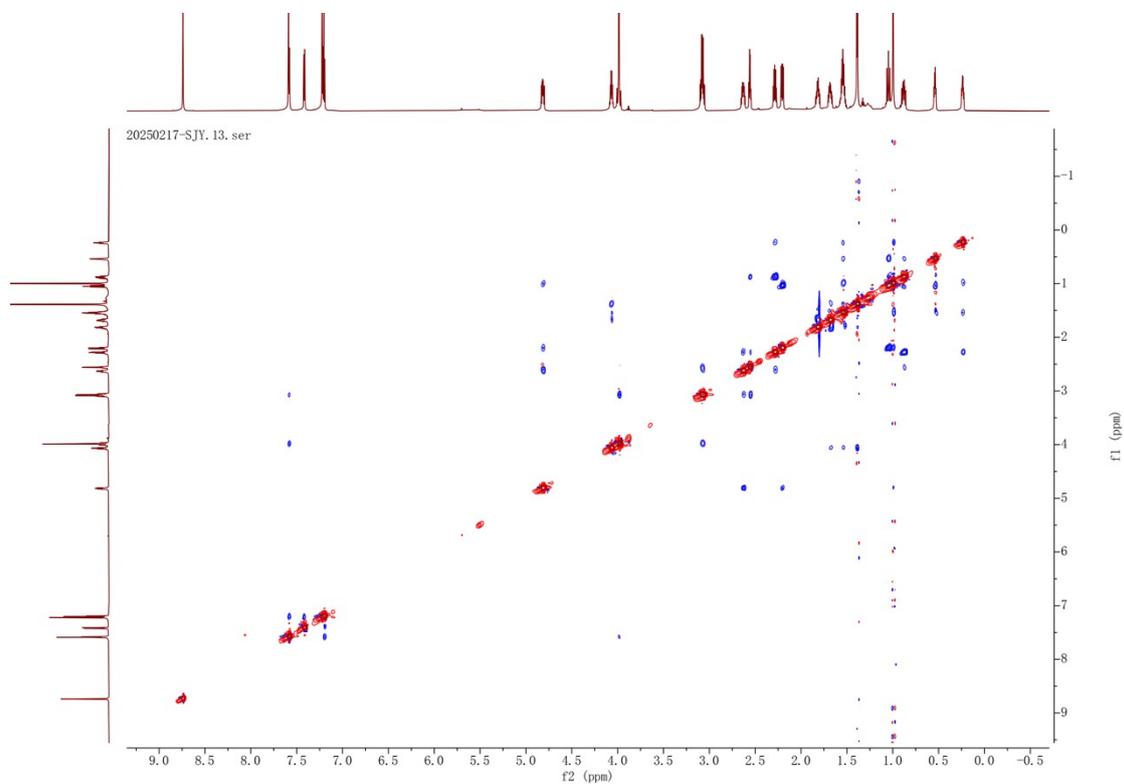
HSQC Spectrum of **Compound a20**



HMBC Spectrum of Compound a20

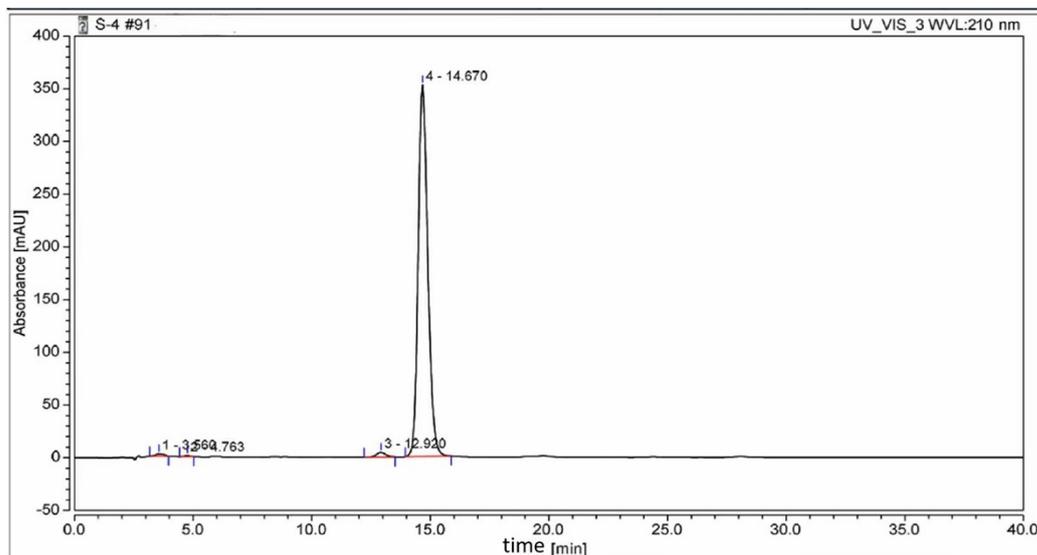


NOESY Spectrum of Compound a20



HPLC assessment of compound purity.

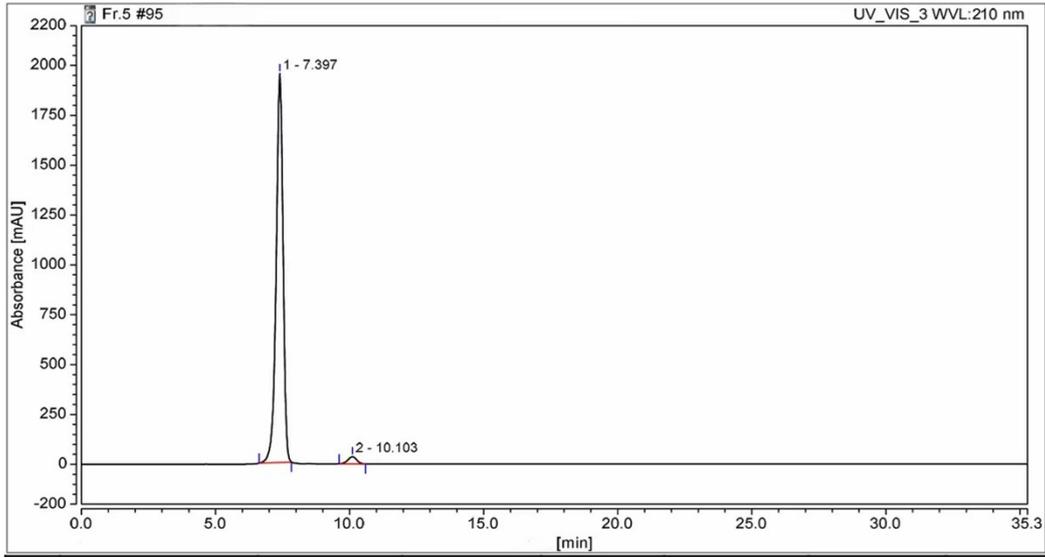
We provided the spectra of HPLC assays as below. Column: Inertex C18 (150 mm × 4.6 mm × 5 μm); Mobile phase: 80% Methanol, 20% Water; Wavelength: 210nm; Rate: 1 mL/min;



Compound a9 ,98.13%, tR = 14.670 min

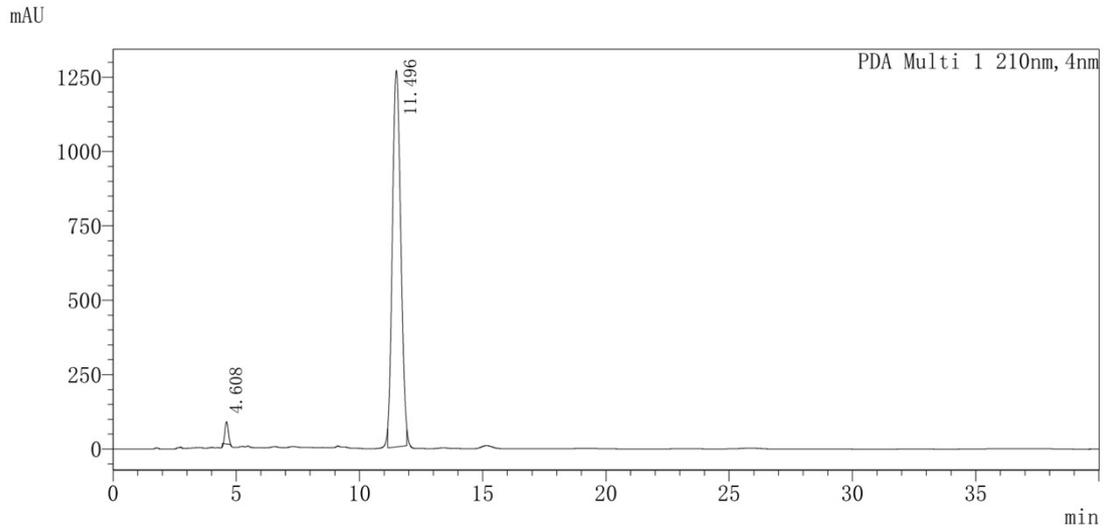
	Retention Time(min)	Peak Area(mAU*min)	% Peak Area
1	3.560	0.886	0.53
2	4.763	0.283	0.17
3	12.920	1.984	1.18
4	14.670	165.592	98.13

Compound a10,97.68%, tR = 7.397min



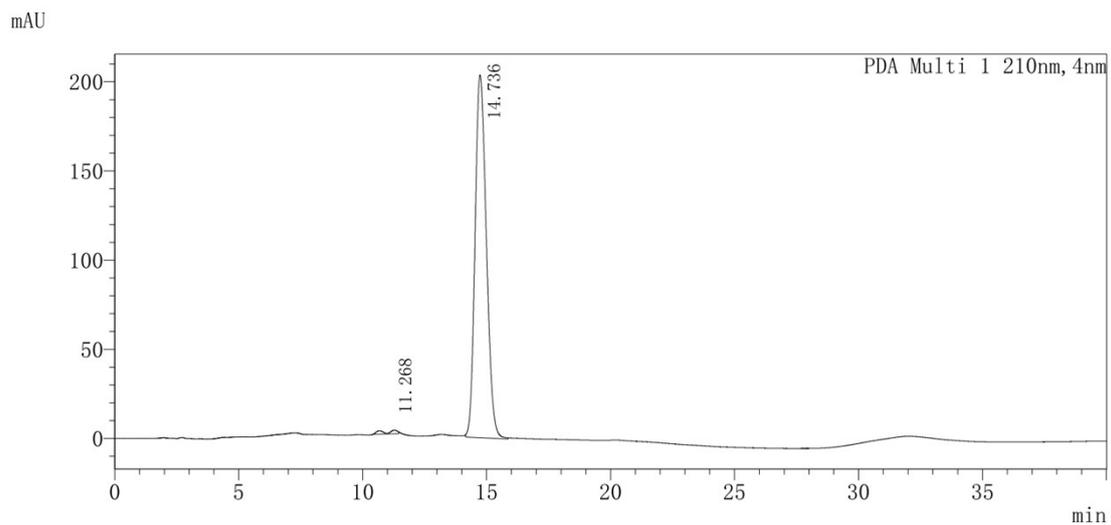
	Retention Time(min)	Peak Area(mAU*min)	% Peak Area
1	7.397	578.814	97.68
2	10.103	13.756	2.32

Carabrol



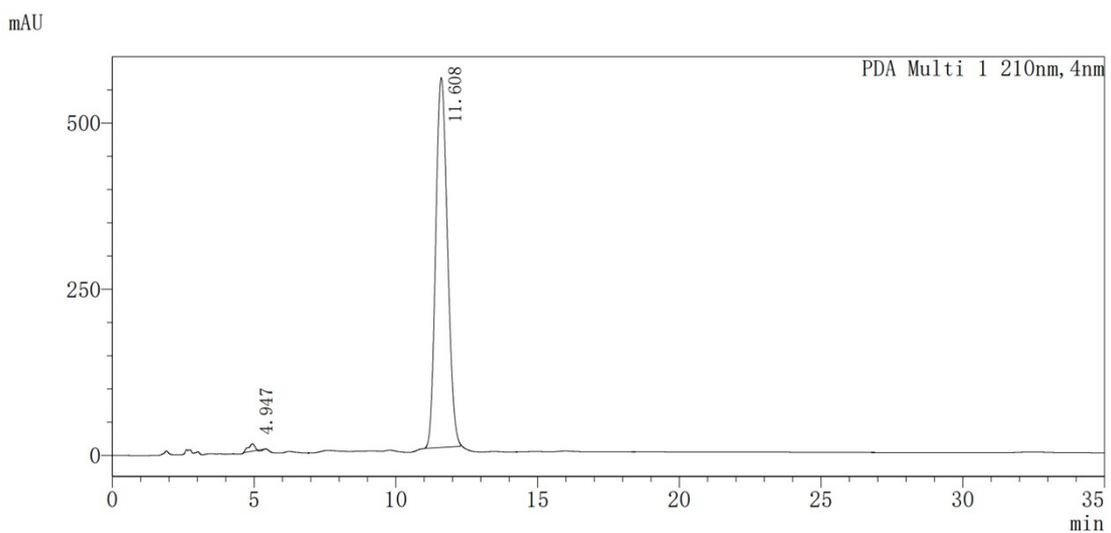
	Retention Time(min)	Peak Area	% Peak Area
1	4.608	675276	2.206
2	11.496	29930774	97.794

Carabrone



	Retention Time (min)	Peak Area	% Peak Area
1	11.268	203551	3.024
2	14.736	6528597	96.976

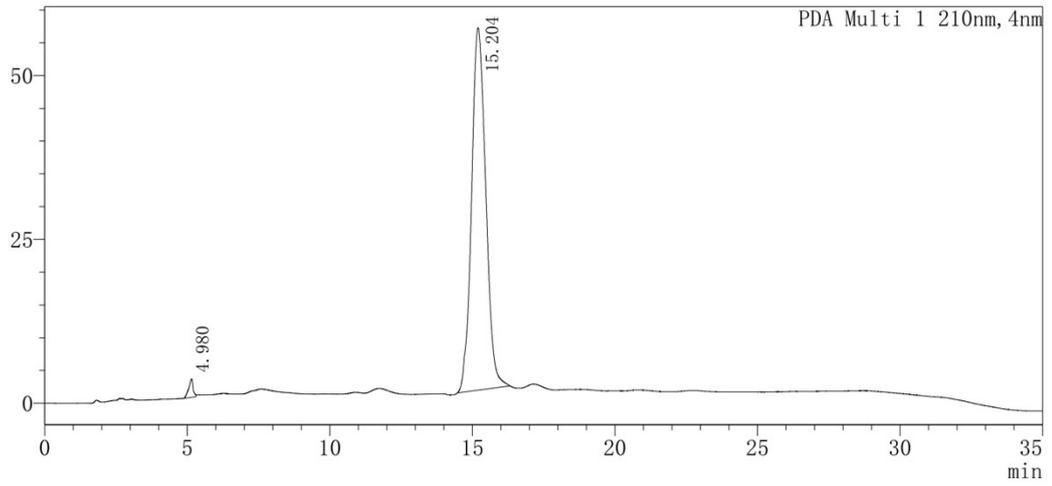
z2



	Retention Time (min)	Peak Area	% Peak Area
1	4.947	163156	1.005
2	11.608	16070932	98.995

a2

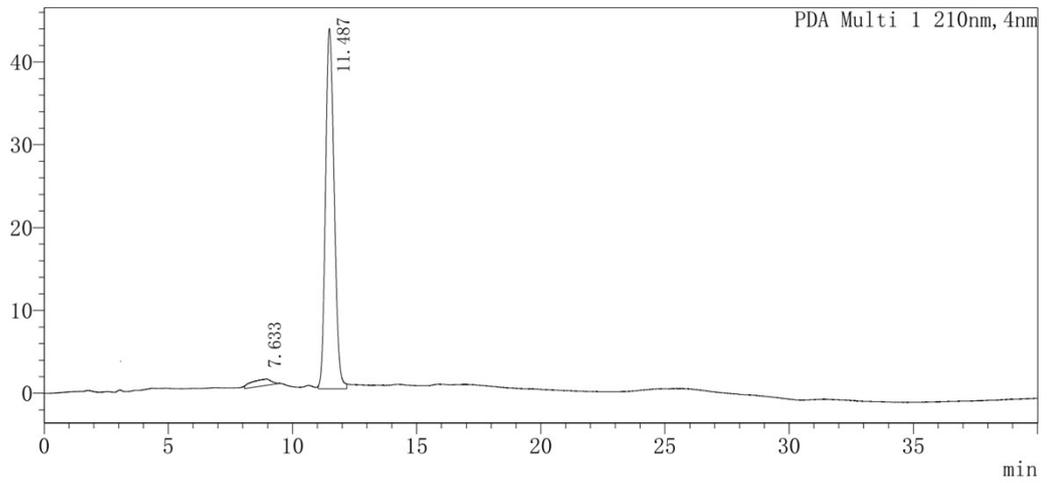
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	4.980	85714	4.557
2	15.204	1795365	95.443

a3

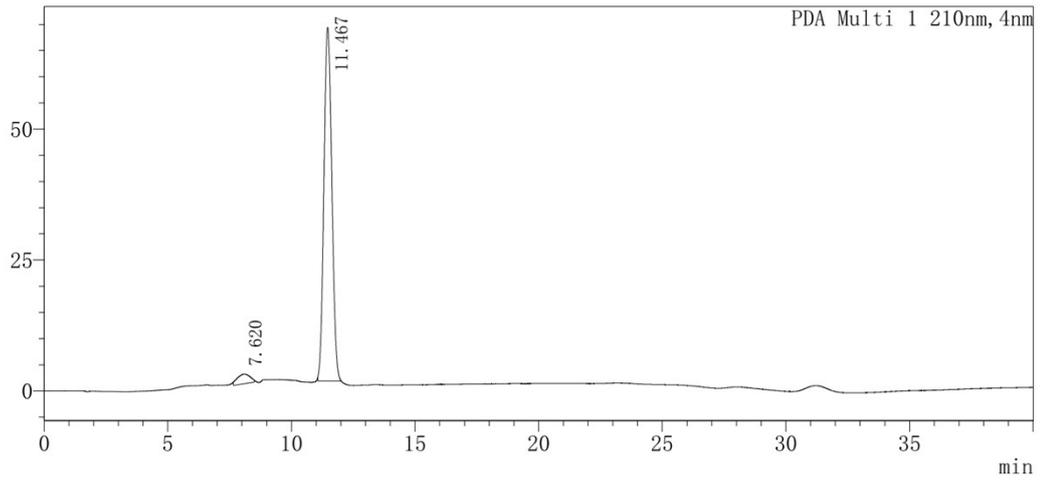
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	7.633	32824	2.752
2	11.487	1159791	97.248

a4

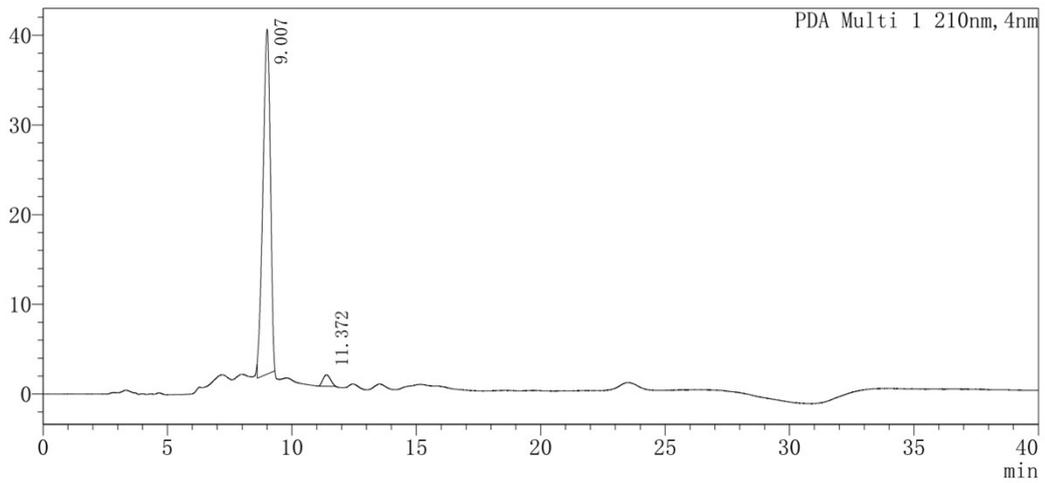
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	7.620	50265	2.447
2	11.467	2004096	97.553

a5

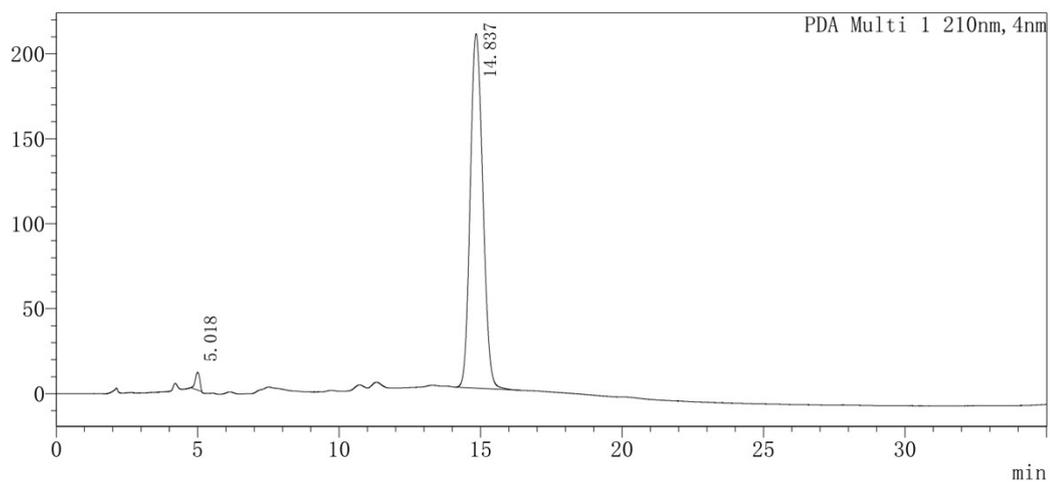
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	9.007	798116	96.181
2	11.372	31691	3.819

a6

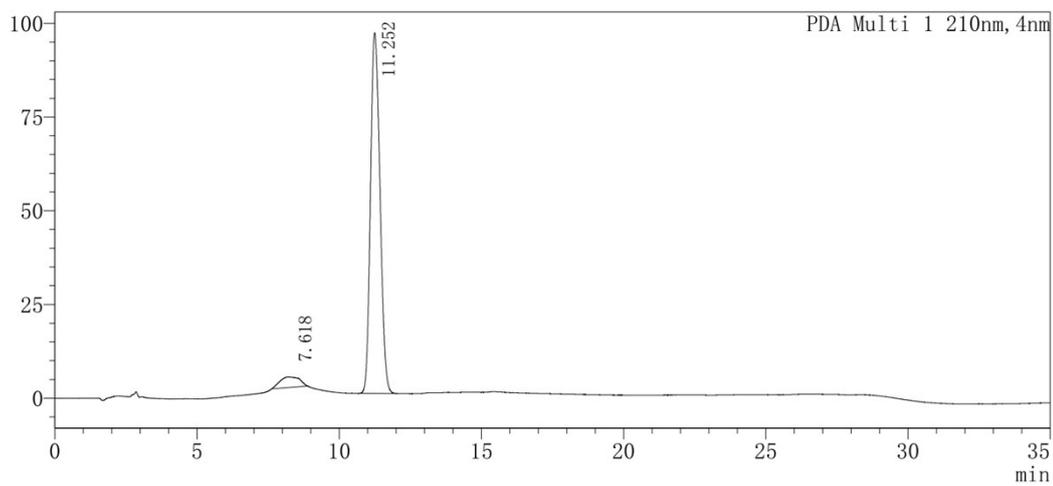
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	5.018	108803	1.658
2	14.873	6453494	98.342

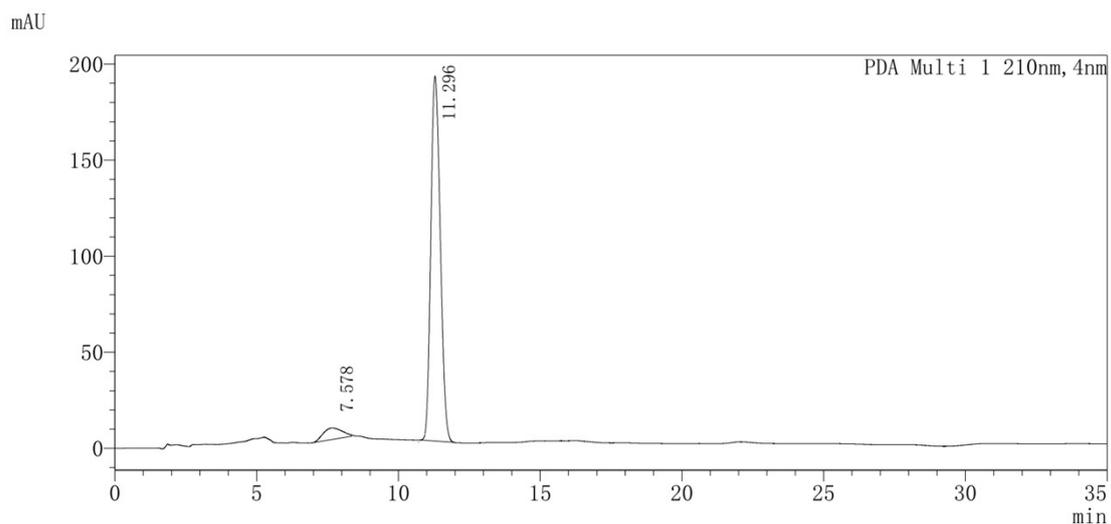
a7

mAU



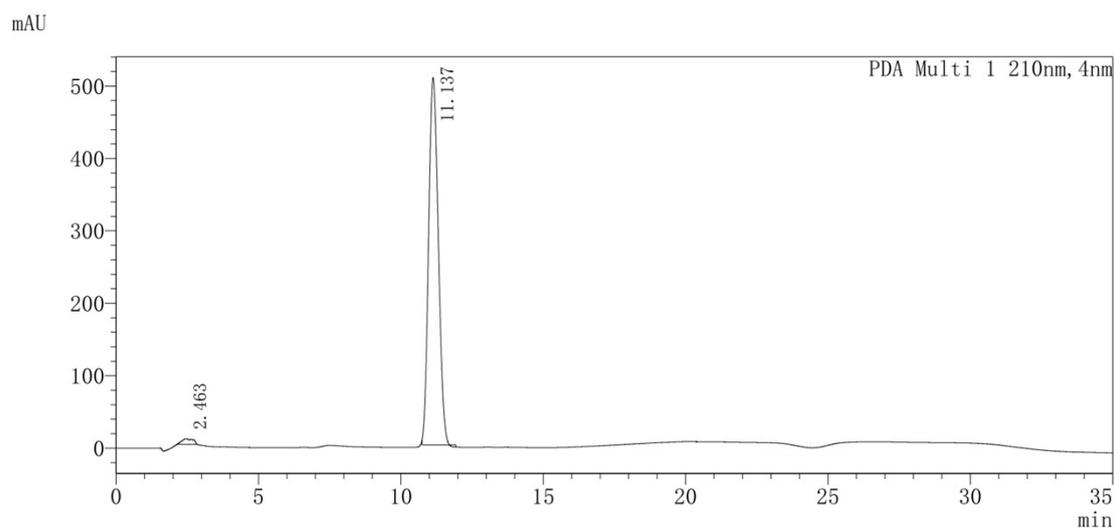
	Retention Time (min)	Peak Area	% Peak Area
1	7.618	93198	4.005
2	11.252	2233865	95.995

a8



	Retention Time (min)	Peak Area	% Peak Area
1	7.578	130194	2.619
2	11.296	4841253	97.381

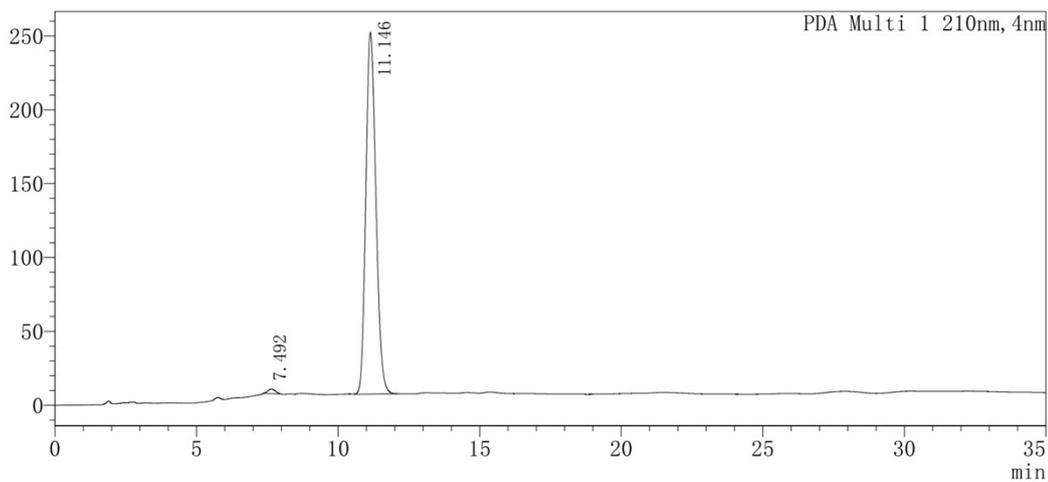
a11



	Retention Time (min)	Peak Area	% Peak Area
1	2.463	302964	1.981
2	11.137	14988799	98.019

a12

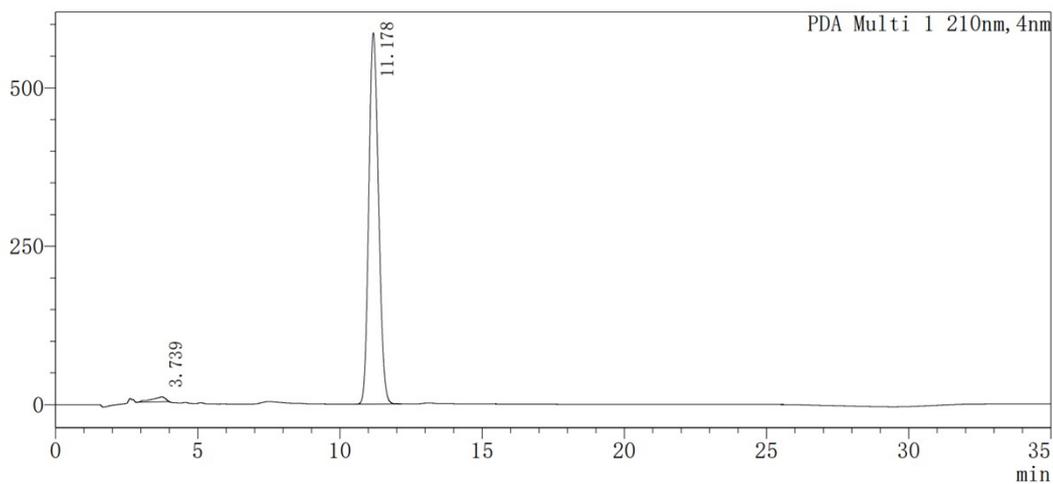
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	7.492	116778	1.892
2	11.146	6053917	98.108

a13

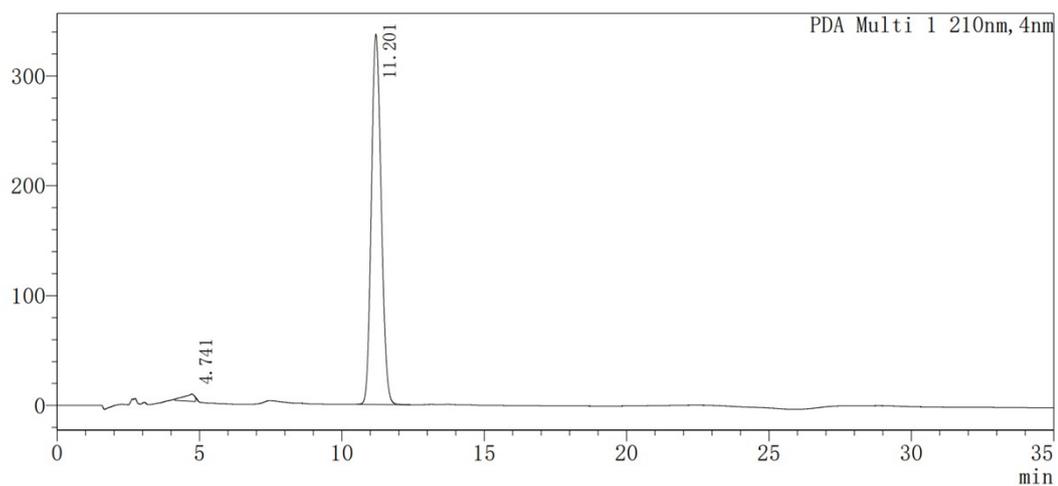
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	3.739	258594	1.826
2	11.178	13905802	98.174

a14

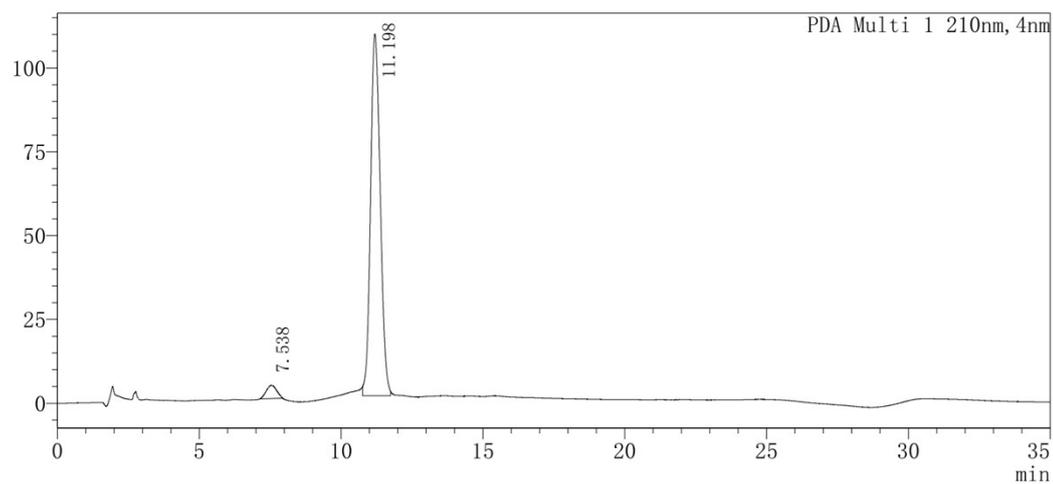
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	4.741	176492	2.130
2	11.201	8111292	97.870

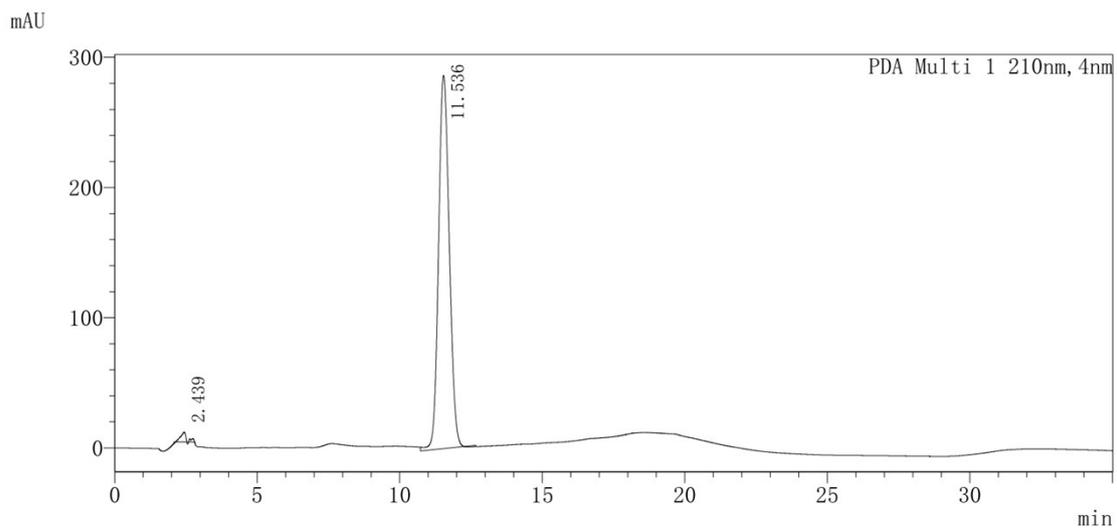
a15

mAU



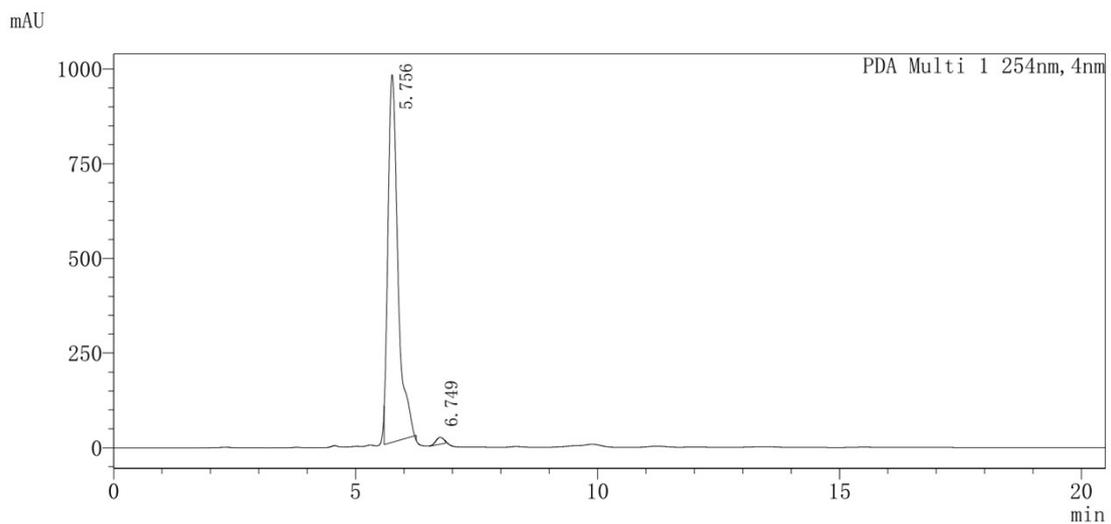
	Retention Time (min)	Peak Area	% Peak Area
1	7.538	69826	2.377
2	11.198	2867871	97.623

a16



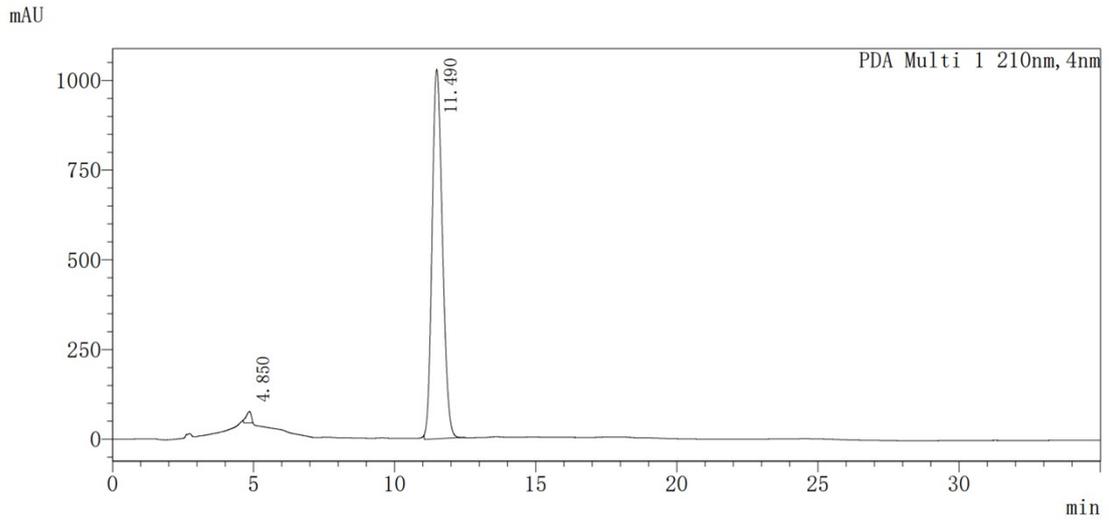
	Retention Time (min)	Peak Area	% Peak Area
1	2.439	106911	1.409
2	11.536	7483213	98.591

a17



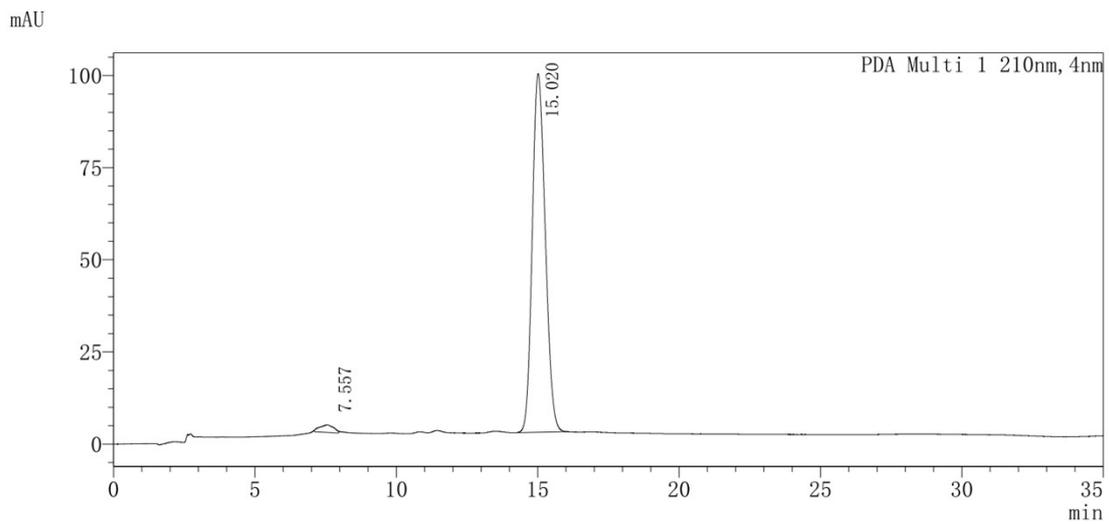
	Retention Time (min)	Peak Area	% Peak Area
1	5.756	13876426	98.604
2	6.749	196411	1.396

a18



	Retention Time (min)	Peak Area	% Peak Area
1	4.850	387964	1.460
2	11.490	26186841	98.540

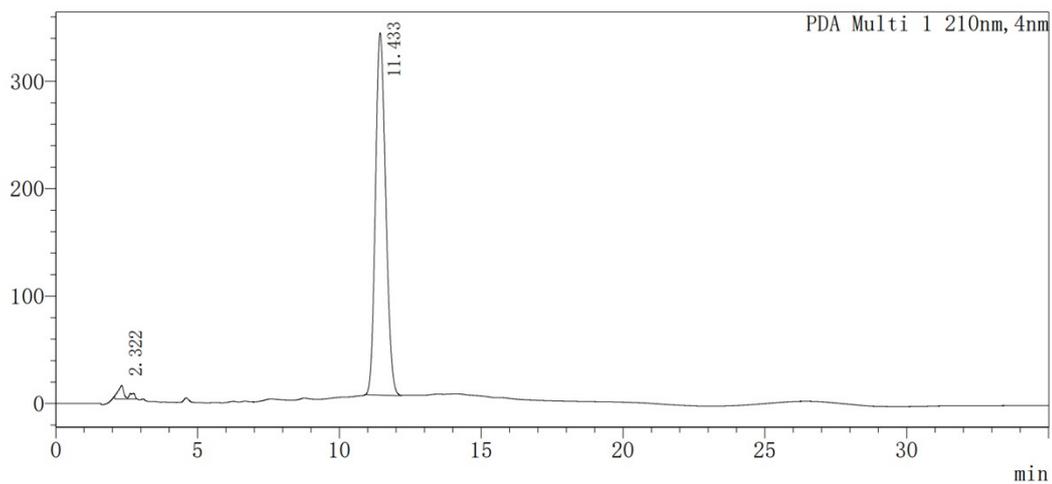
a19



	Retention Time (min)	Peak Area	% Peak Area
1	7.557	105602	3.206
2	15.020	3188334	96.794

a20

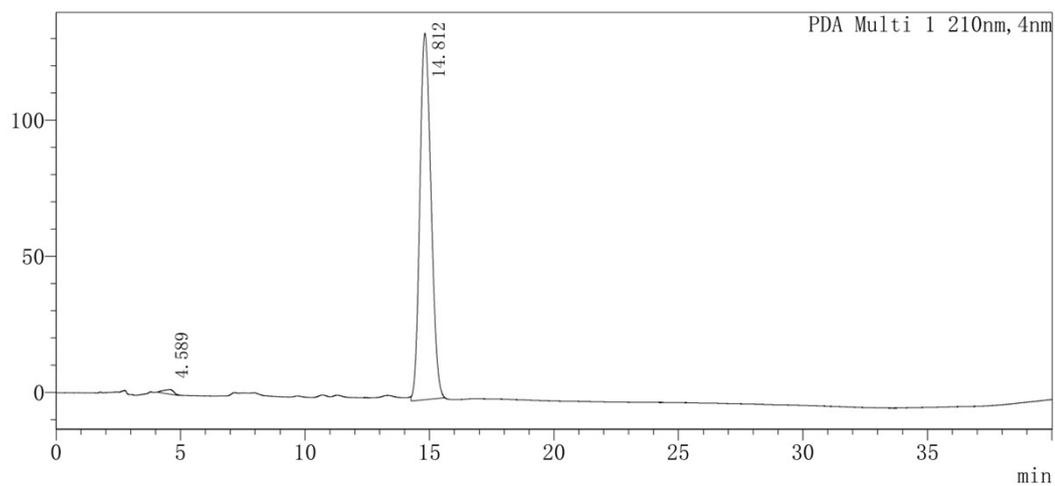
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	2.322	253090	2.898
2	11.433	8479788	97.102

a21

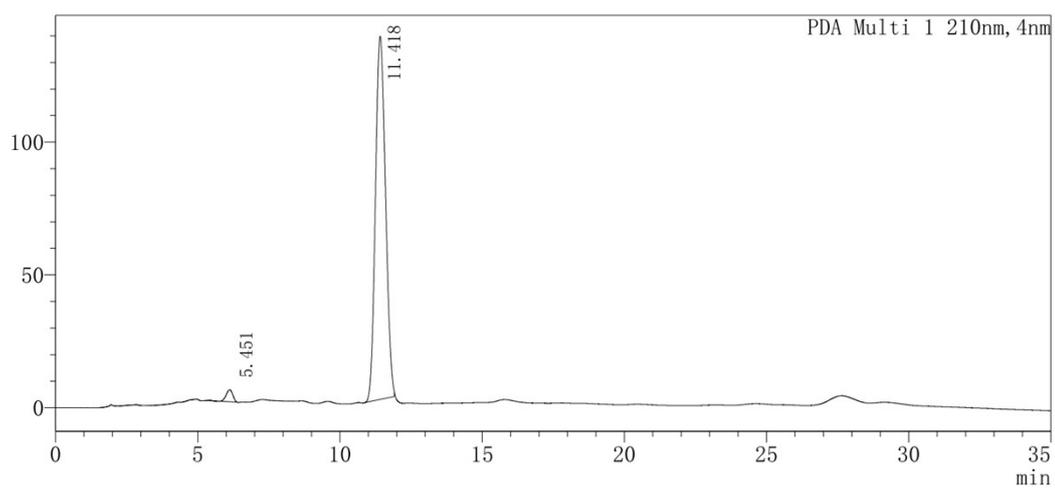
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	4.589	114497	2.606
2	14.812	4278722	97.394

a22

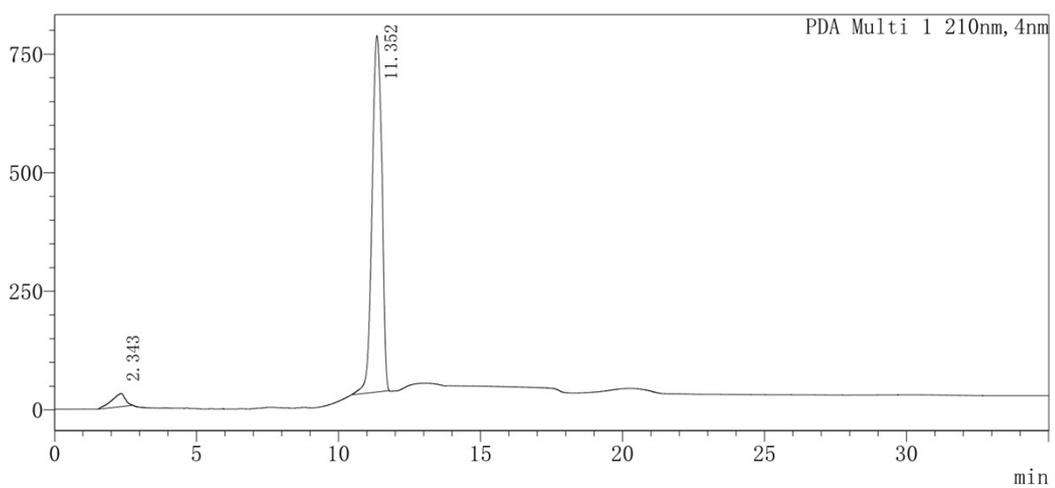
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	5.541	91086	2.235
2	11.418	3984149	97.765

a23

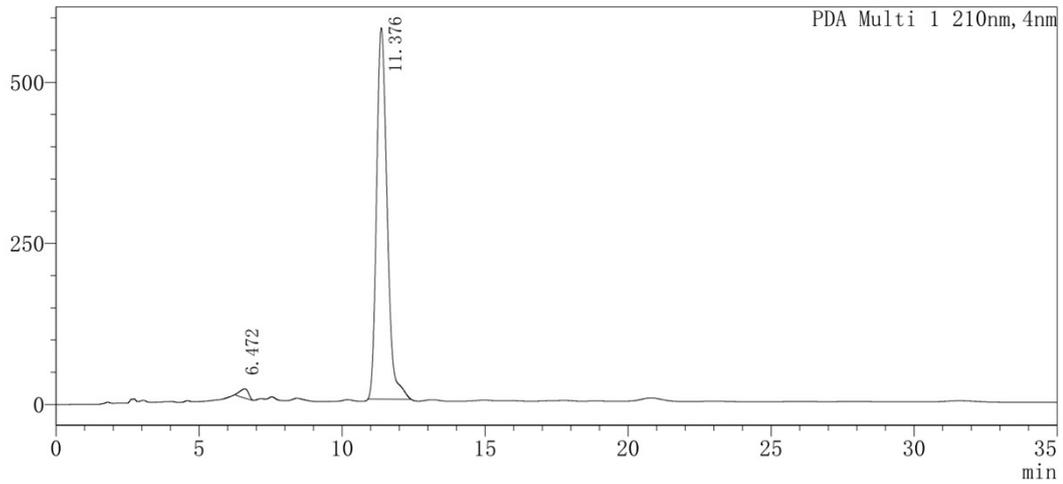
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	2.343	600239	2.928
2	11.352	19898104	97.072

a24

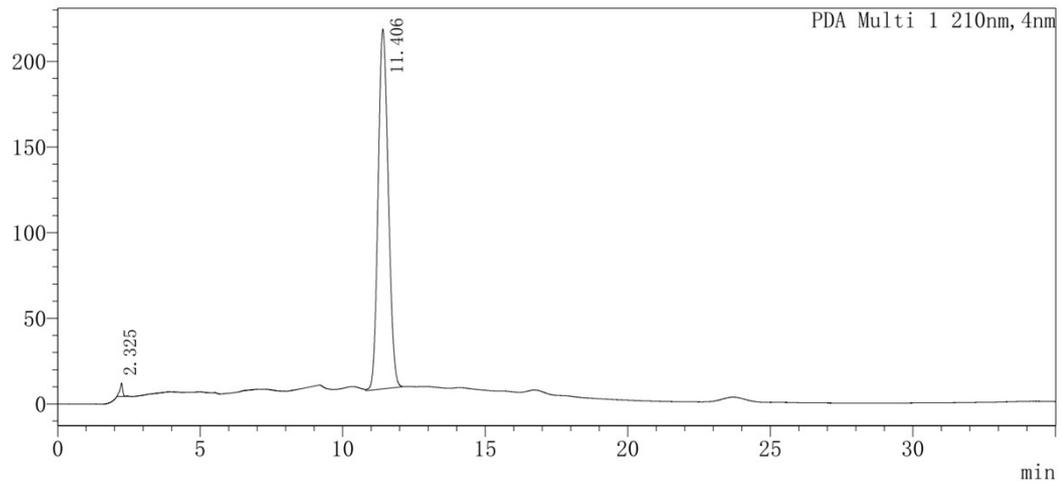
mAU



	Retention Time (min)	Peak Area	% Peak Area
1	2.343	440957	2.348
2	11.352	18781035	97.706

a25

mAU



	Retention Time (min)	Peak Area	% Peak Area
1	2.325	64853	1.277
2	11.409	5012801	98.723

The real time RT-PCR oligonucleotide primers.

Gene	Forward Prime	Reverse Primer
IL-1 β	5'-GCAACTGTTCTGAAGTCAACT-3'	5'-ATCTTTTGGGGTCCGTCAACT-3'
IL-6	5'-CTGCAAGAGACTTCCATCCAG-3'	5'- AGTGGTATAGACAGGTCTGTTGG-3'
COX-2	5'-TGAGCAACTATTCCAAACCAGC-3'	5'-GCACGTAGTCTTCGATCACTATC-3'

TNF- α	5'- CCCTCACACTCAGATCATCTTCT- 3'	5'- GCTACGACGTGGGCTACAG-3'
GAPDH	5'-AGGTCGGTGTGAACGGATTG-3'	5'-GGGGTCGTTGATGGCAACA-3'
