

Supporting Information

**Design, synthesis and biological evaluation of hydrogen sulfide releasing
derivatives of 3-*n*-butylphthalide as potential antiplatelet and antithrombotic
agents**

*Xiaoli Wang, Linna Wang, Xiao Sheng[#], Zhangjian Huang, Tingting Li, Ming Zhang, Jinyi Xu,
Hui Ji*, Jian Yin* and Yihua Zhang**

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1. HPLC assessment of compound purity

Target compounds **8a–g** and **9a–f** with a purity of > 95% (HPLC analysis) were used for subsequent experiments. We provided the spectra of HPLC assays as below.

Column: Inertex C₁₈ (150mm×4.6mm×5μm);

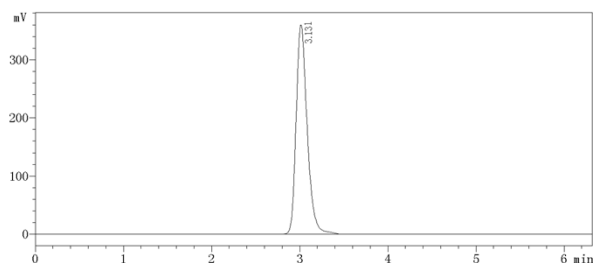
Mobile phase: methanol : H₂O = 90 : 10;

Wavelength: 254 nm;

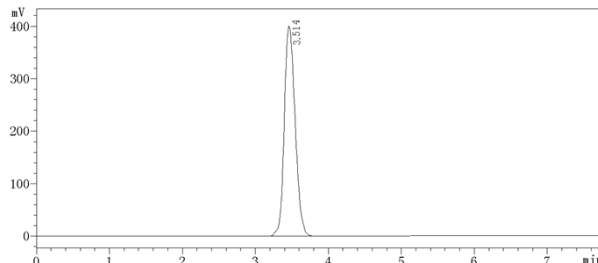
Rate: 1 mL/min;

Temperature: 25 °C

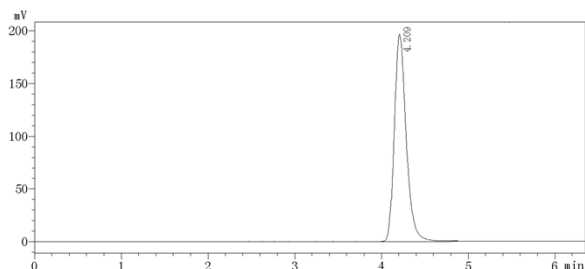
8a, 97.6%



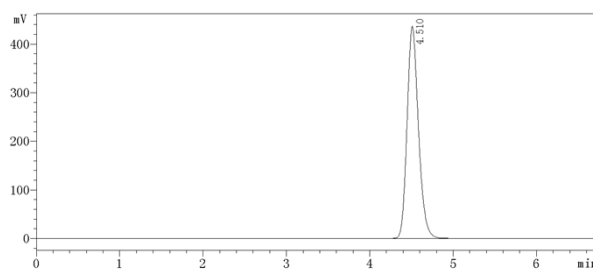
8b, 97.9%



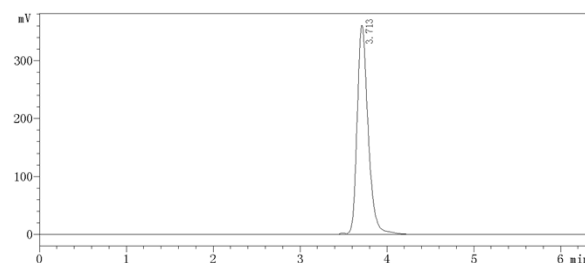
8c, 97.2%



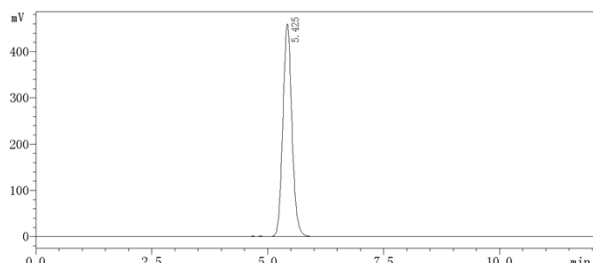
8d, 98.3%



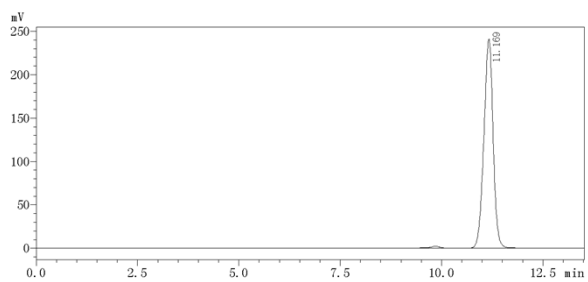
8e, 97.8%



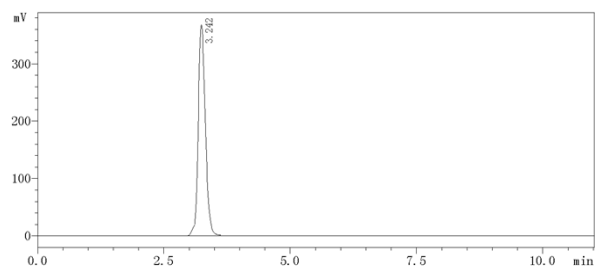
8f, 98.2%



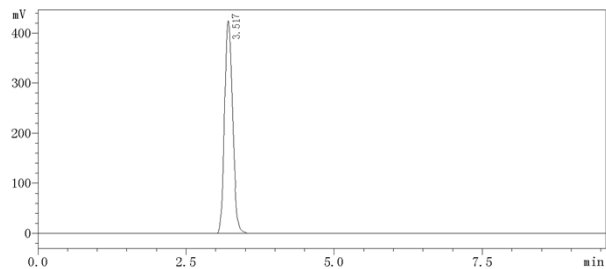
8g, 96.5%



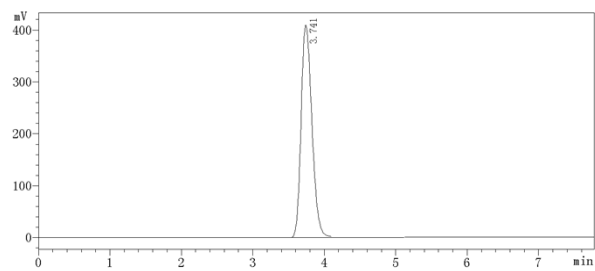
9a, 97.7%



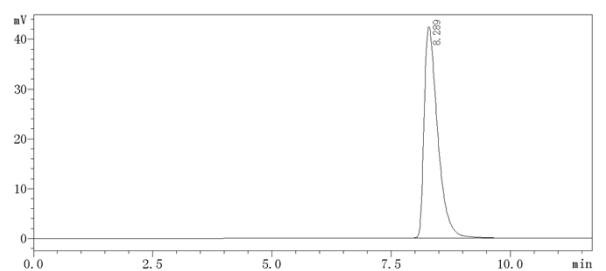
9b, 97.3%



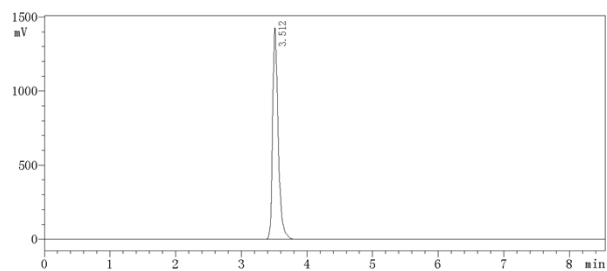
9c, 97.8%



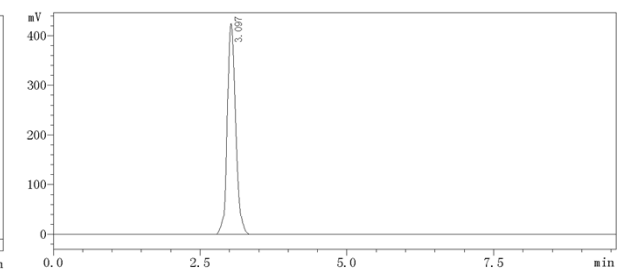
9d, 97.0%



9e, 98.5%

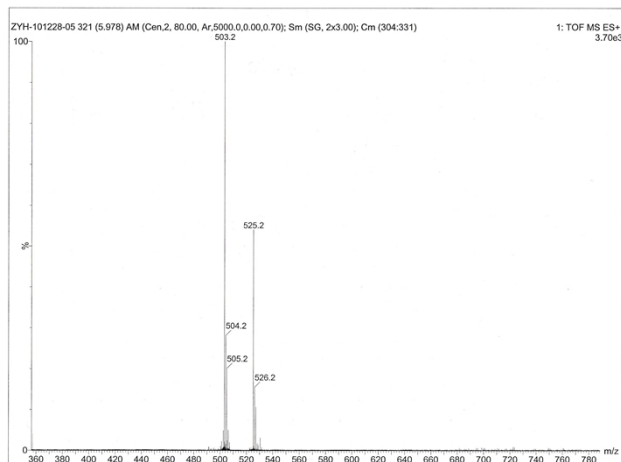


9f, 98.2%



2. The spectral data of new compounds

8a

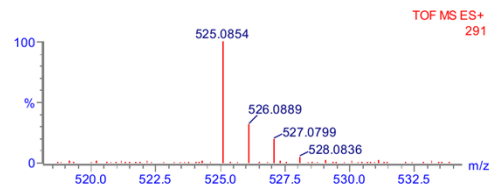


Elemental Composition Report

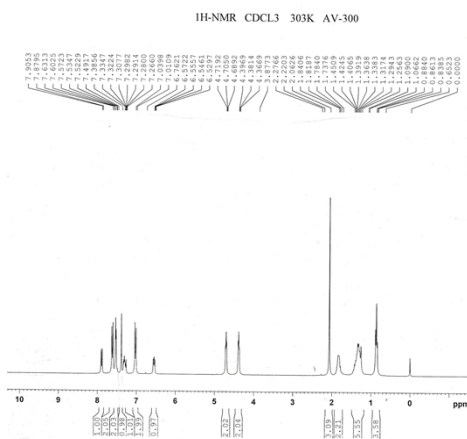
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 20.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
1619 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)

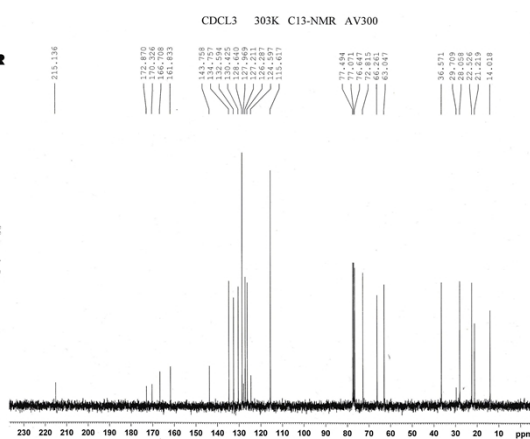
Elements Used:
C: 0-50 H: 0-100 N: 0-3 O: 0-8 S: 0-3 Na: 0-1



Minimum:	5.0	5.0	-1.5				
Maximum:	20.0	20.0	20.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula	
525.0854	525.0840	1.4	2.7	12.5	0.0	C25 H26 O5 S3 Na	
	525.0864	-1.0	-1.9	15.5	0.1	C27 H25 O5 S3	

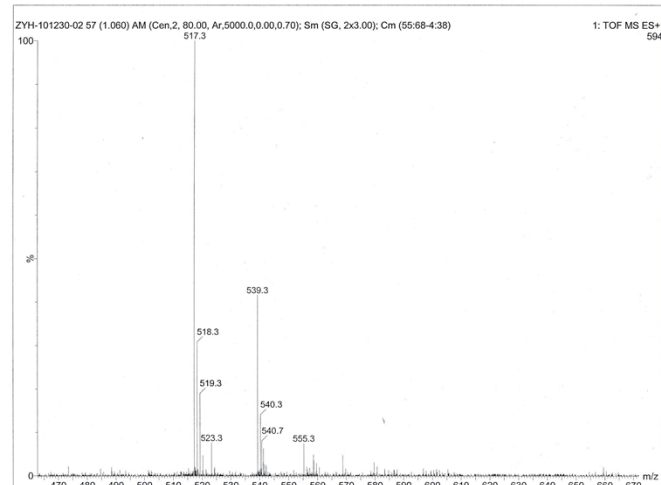


Current Data Parameters
NAME: 8a
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20121229
Time_: 18:47
INSTRUM: spect
PROBHD: 5 mm QNP 1H/13
PULPROG: zgpg30
TD: 65536
SOLVENT: CDCl3
NS: 180
DS: 4
SWH: 19511.250 Hz
FIDRES: 0.594046 Hz
AQ: 0.19000000 sec
RG: 320
DQ: 0.20000000 sec
TE: 300.2 K
T1: 2.00000000 sec
T2: 0.03000000 sec
T2RHO: 1.410200
MVIC: 130
PC: 1.00
SFO: 101.625310 MHz
SPFO: 300.1312000 MHz
F1 - Processing parameters
SI: 32768
SF: 300.1312000 MHz
WDW: EM
SSB: 0
LB: 0.20 Hz
GB: 0
PC: 1.00



Current Data Parameters
NAME: 8a
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20121229
Time_: 18:47
INSTRUM: spect
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F1 - Processing parameters
SI: 32768
SF: 300.1312000 MHz
WDW: EM
SSB: 0
LB: 0.20 Hz
GB: 0
PC: 1.00

8b

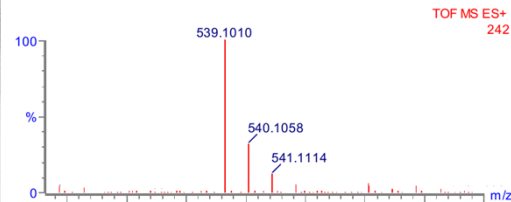


Elemental Composition Report

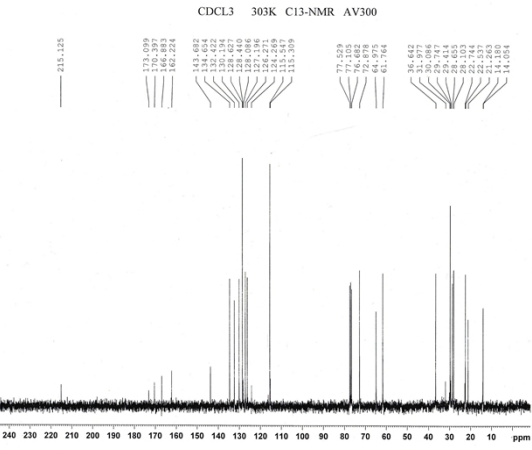
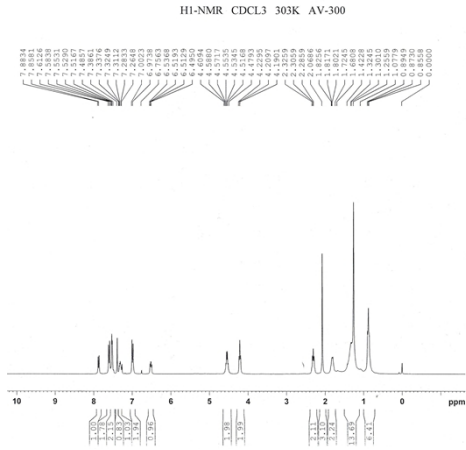
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 20.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
1667 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)

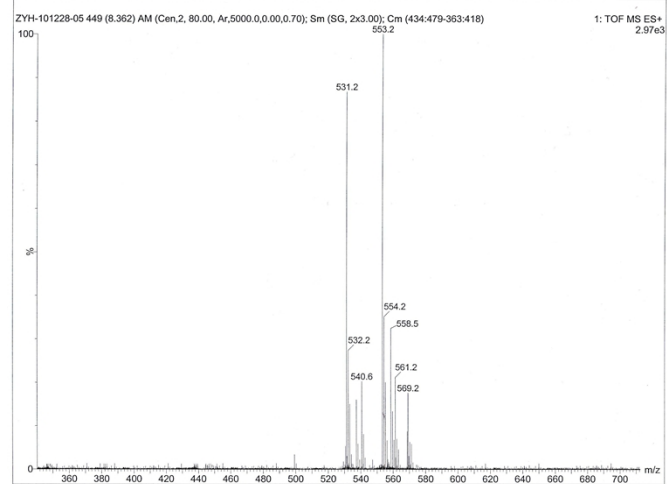
Elements Used:
C: 0-50 H: 0-100 N: 0-3 O: 0-8 Na: 0-1 S: 0-3



Minimum:	5.0	5.0	-1.5				
Maximum:	20.0	20.0	20.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula	
539.1010	539.0997	1.3	2.4	12.5	4.6	C26 H28 O5 Na S3	
	539.1021	-1.1	-2.0	15.5	5.2	C28 H27 O5 S3	



8c



Elemental Composition Report

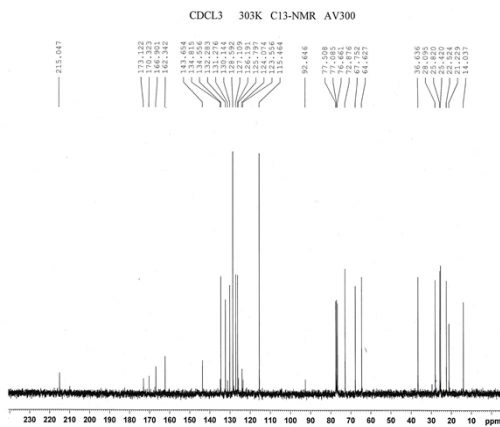
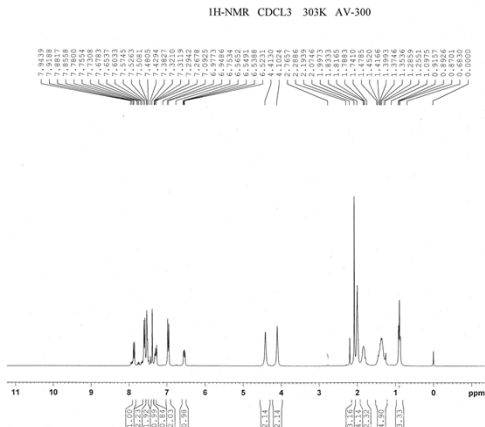
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 20.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
1715 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)

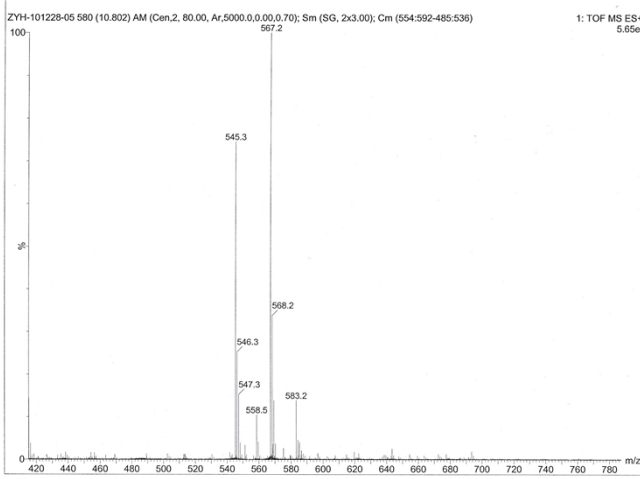
Elements Used:
C: 0-50 H: 0-100 N: 0-3 O: 0-8 Na: 0-1 S: 0-3

TOF MS ES+
585

Minimum Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
553.1167	553.1177	-1.0	-1.8	15.5	0.5	C29 H29 O5 S3
	553.1153	1.4	2.5	12.5	0.5	C27 H30 O5 Na S3



8d

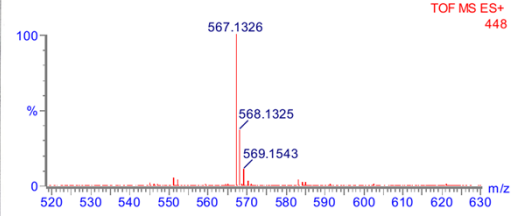


Elemental Composition Report

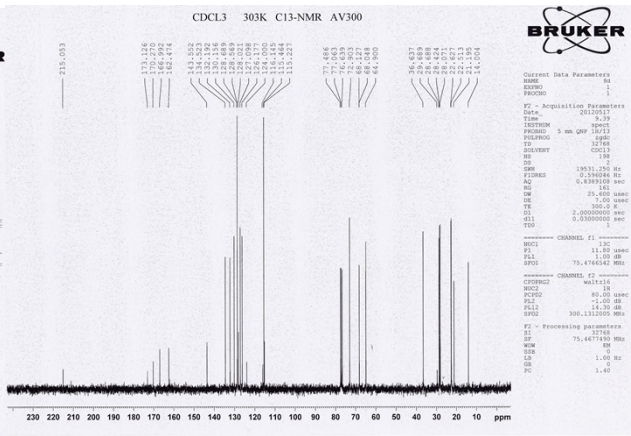
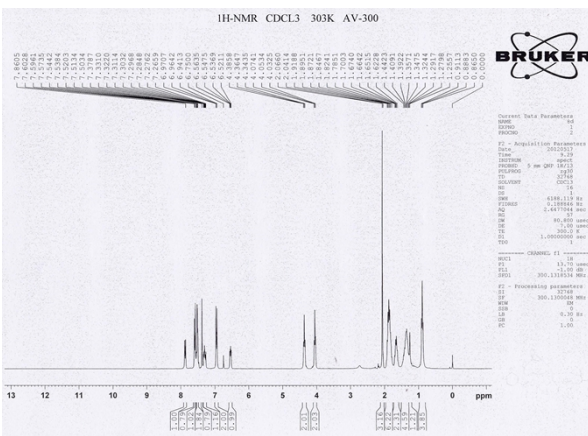
Single Mass Analysis
 Tolerance = 5.0 PPM / DBE: min = -1.5, max = 20.0
 Selected filters: None

Monoisotopic Mass, Even Electron Ions
 1763 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)

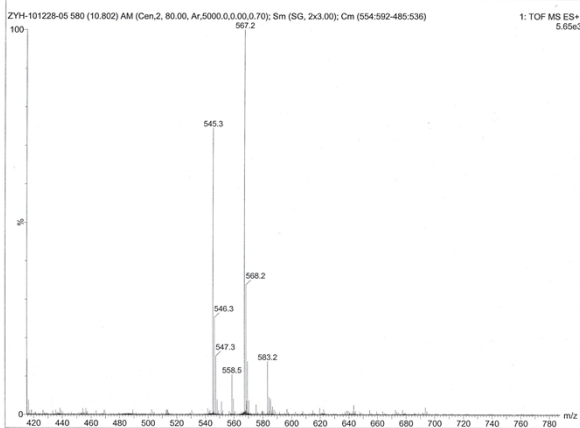
Elements Used:
 C: 0-50 H: 0-100 N: 0-3 O: 0-8 Na: 0-1 S: 0-3



Minimum:	Maximum:	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
567.1326	567.1310	5.0	1.6	2.8	12.5	16.2	C28 H32 O5 Na S3
	567.1334	-0.8	-1.4	15.5	17.3		C30 H31 O5 S3



8e



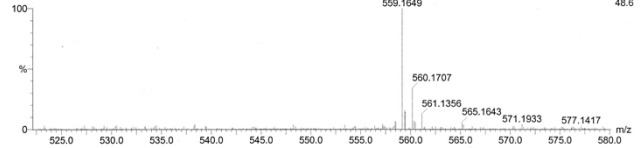
Elemental Composition Report

Single Mass Analysis
 Tolerance = 5.0 PPM / DBE: min = -1.5, max = 20.0
 Selected filters: None

Monoisotopic Mass, Even Electron Ions
 274 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

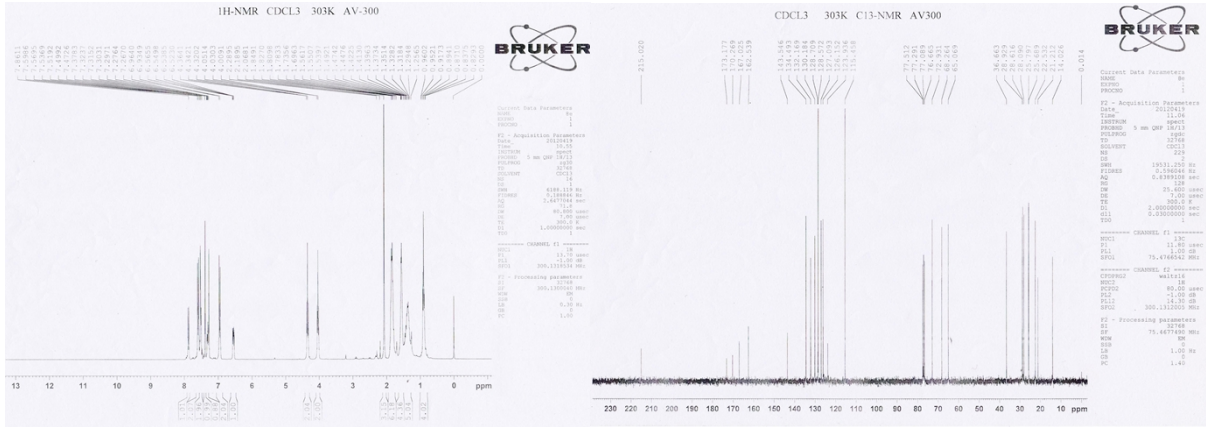
Elements Used:
 C: 0-50 H: 0-100 O: 0-10 S: 0-3

8e
 ZYH-120419-03 78 (1.453)

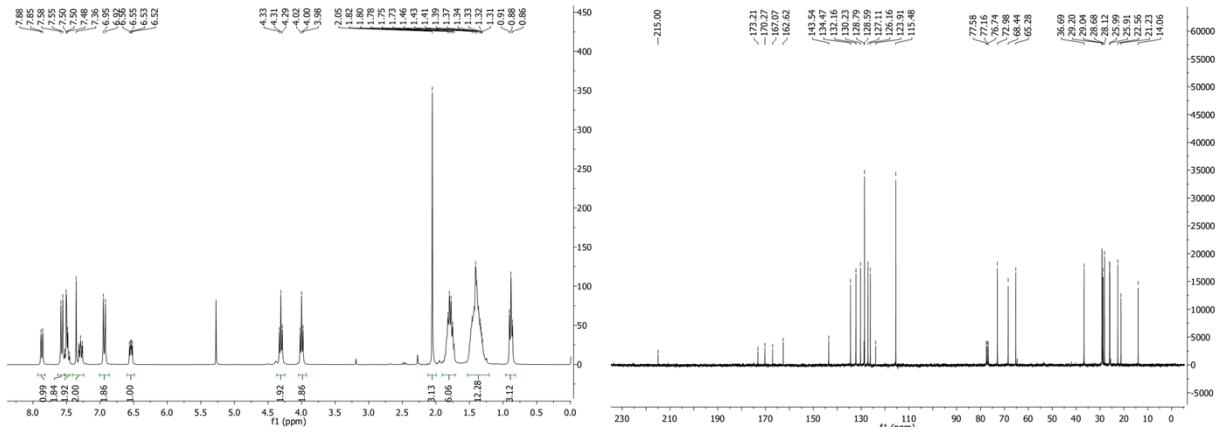


Minimum:	Maximum:	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
559.1649	559.1647	0.2	0.4	12.5	1.0		C29 H35 O5 S3
	559.1638	1.1	2.0	13.5	0.1		C28 H31 O10 S
	559.1672	-2.3	-4.1	8.5	0.3		C25 H35 O10 S2

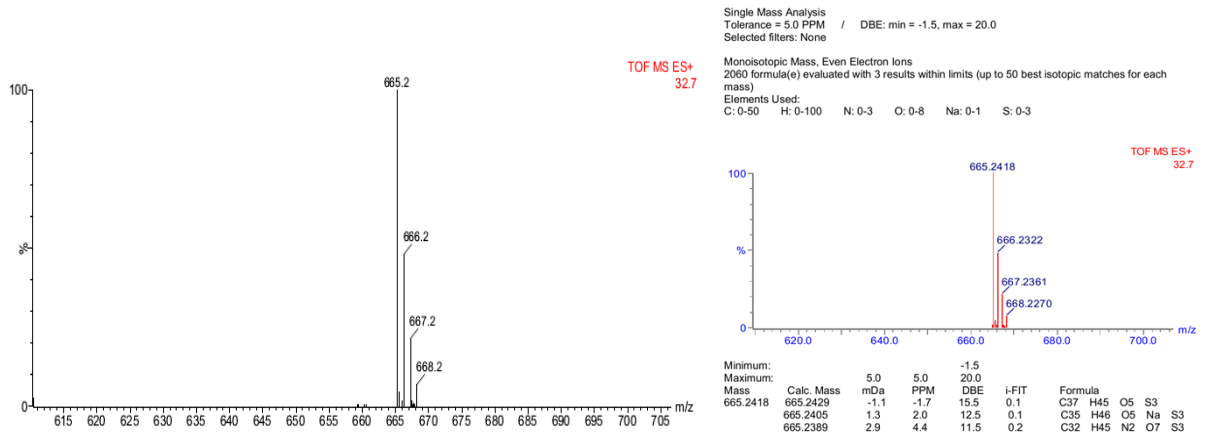
Page 1



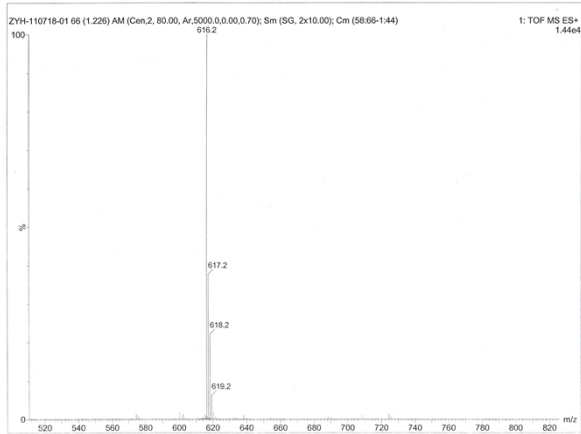
8f



8g



9b



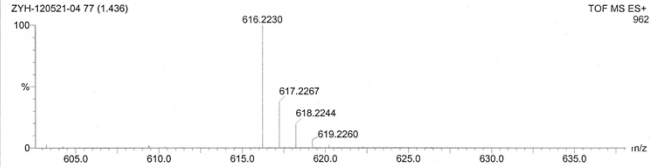
Elemental Composition Report

Page 1

Single Mass Analysis
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Selected filters: None

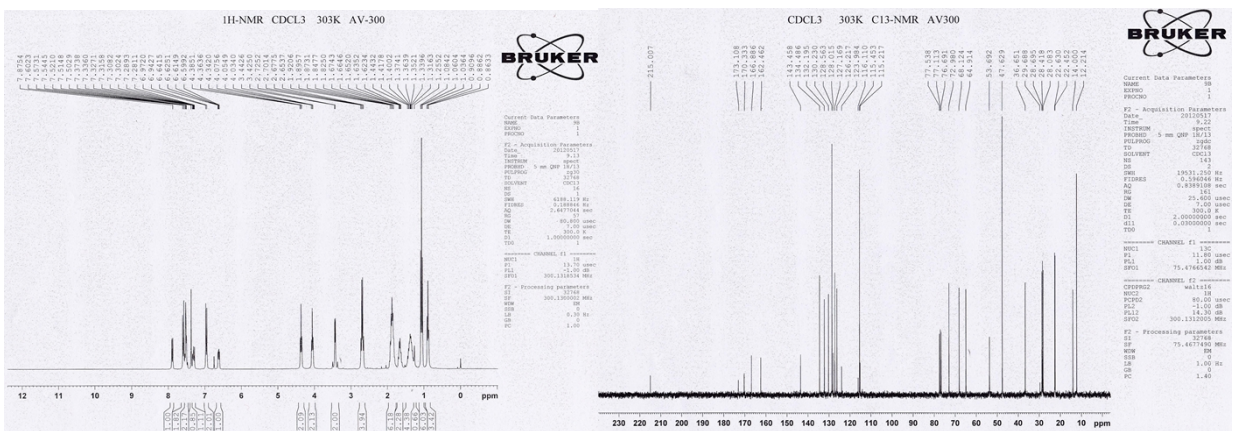
Monoisotopic Mass, Even Electron Ions
1729 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-5 O: 0-10 S: 0-3

TOF MS ES+
962

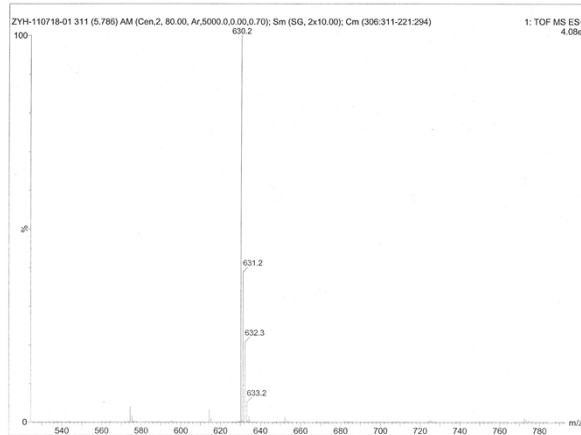


Minimum: -1.5
Maximum: 15.0

Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	Formula
616.2230	616.2225	0.5	0.8	12.5	1.2	C32 H42 N O5 S3
	616.2216	1.4	2.3	13.5	9.6	C31 H38 N O10 S
	616.2250	-2.0	-3.2	8.5	2.4	C28 H42 N O10 S2



9c



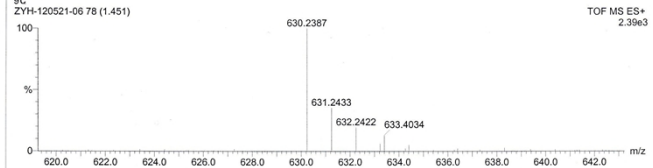
Elemental Composition Report

Page 1

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 15.0
Selected filters: None

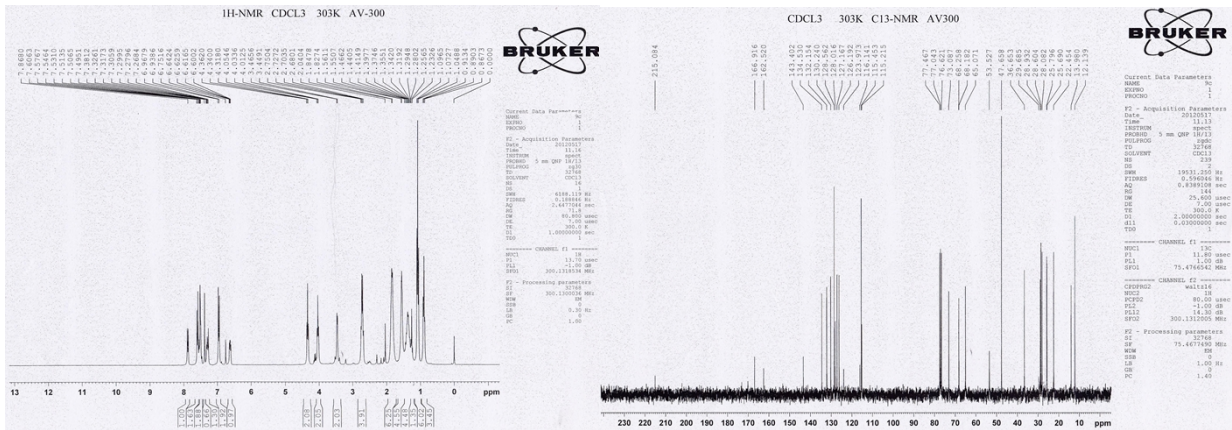
Monoisotopic Mass, Even Electron Ions
1770 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-5 O: 0-10 S: 0-3

TOF MS ES+
2.39e3

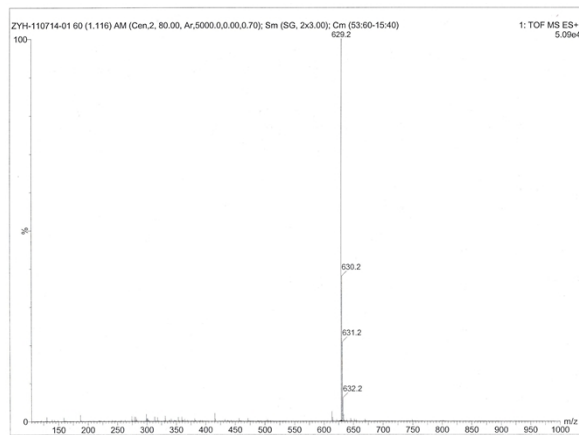


Minimum: -1.5
Maximum: 15.0

Mass	Calc. Mass	mDa	PPM	DBE	1-FIT	Formula
630.2387	630.2382	0.5	0.8	12.5	8.0	C33 H44 N O5 S3
	630.2373	1.4	2.2	13.5	23.7	C32 H40 N O10 S
	630.2407	-2.0	-3.2	8.5	3.3	C29 H44 N O10 S2



9d



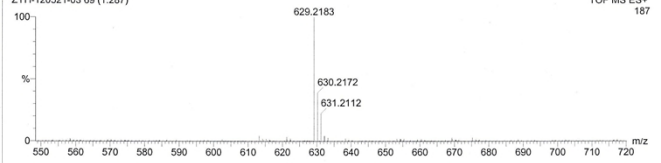
Elemental Composition Report

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Single Mass Analysis
 Tolerance = 5.0 PPM / DBE: min = -1.5, max = 15.0
 Selected filters: None

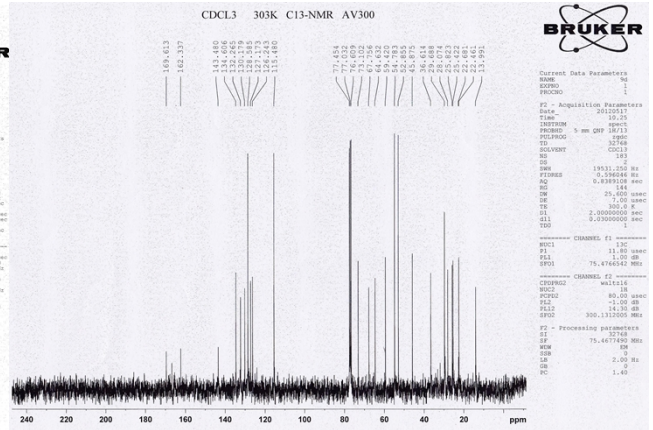
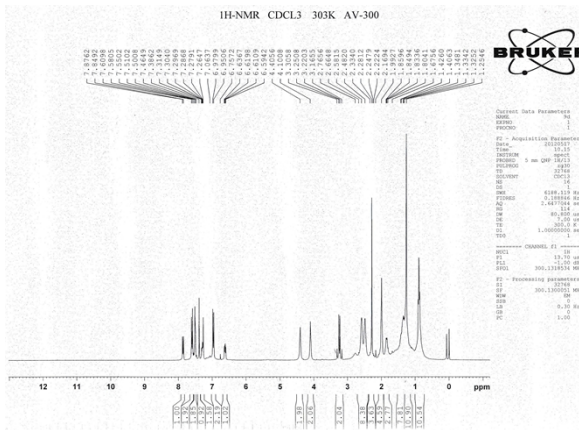
Monoisotopic Mass, Even Electron Ions
 1789 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
 Elements Used:
 C: 0-50 H: 0-100 N: 0-5 O: 0-10 S: 0-3

9d
 ZYH-120521-03 69 (1.287)

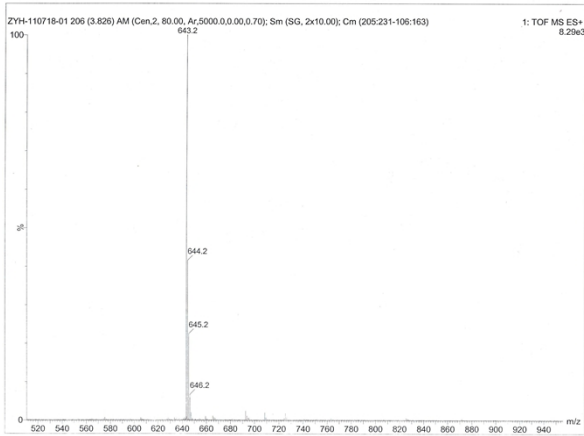


Minimum: -1.5
 Maximum: 5.0 5.0 15.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
629.2183	629.2178	0.5	0.8	13.5	0.0	C32 H41 N2 O5 S3
	629.2169	1.4	2.2	14.5	3.1	C31 H37 N2 O10 S
	629.2203	-2.0	-3.2	9.5	1.3	C28 H41 N2 O10 S2



9e



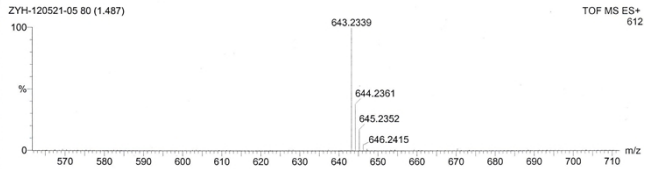
Elemental Composition Report

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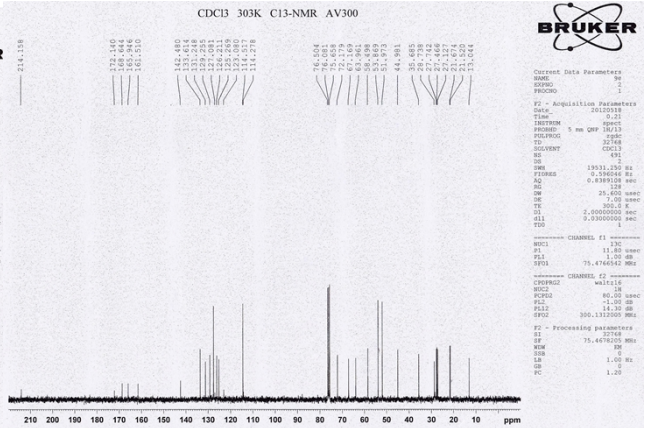
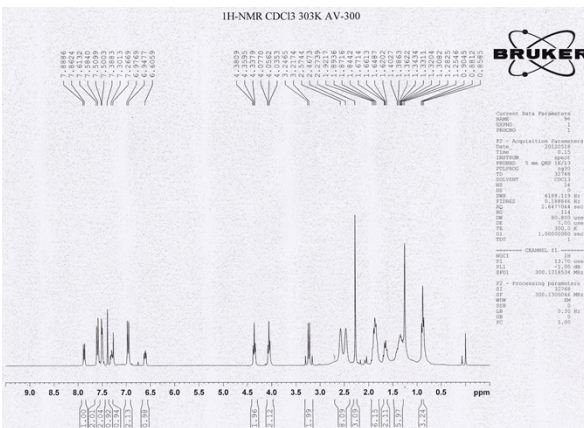
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 15.0
Selected filters: None

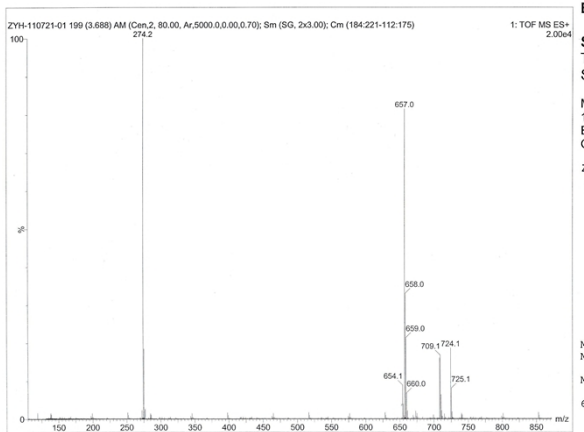
Monoisotopic Mass, Even Electron Ions
1826 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-5 O: 0-10 S: 0-3



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
643.2339	643.2334	0.5	0.8	13.5	3.8	C33 H43 N2 O5 S3
	643.2325	1.4	2.2	14.5	2.2	C32 H39 N2 O10 S
	643.2359	-2.0	-3.1	9.5	0.4	C29 H43 N2 O10 S2



9f



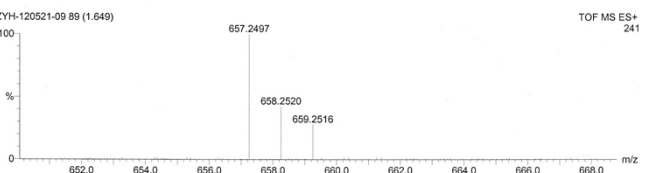
Elemental Composition Report

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Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 15.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
1858 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-5 O: 0-10 S: 0-3



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
657.2497	657.2491	0.6	0.9	13.5	0.9	C34 H45 N2 O5 S3
	657.2482	1.5	2.3	14.5	7.7	C33 H41 N2 O10 S
	657.2516	-1.9	-2.9	9.5	4.4	C30 H45 N2 O10 S2

