Electronic Supplementary Material (ESI) for RSC Advances.

Alkaloids from the Stems of *Clausena lansium* and their potential Neuroprotective Activity

Jie Liu,[1,2] Yi-Qian Du,[1] Chuang-Jun Li,[1] Li Li,[1] Fang-you Chen[1], Jing-Zhi Yang,[1]

Nai-Hong Chen,[1] and Dong-Ming Zhang[1]*

[1] State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China;

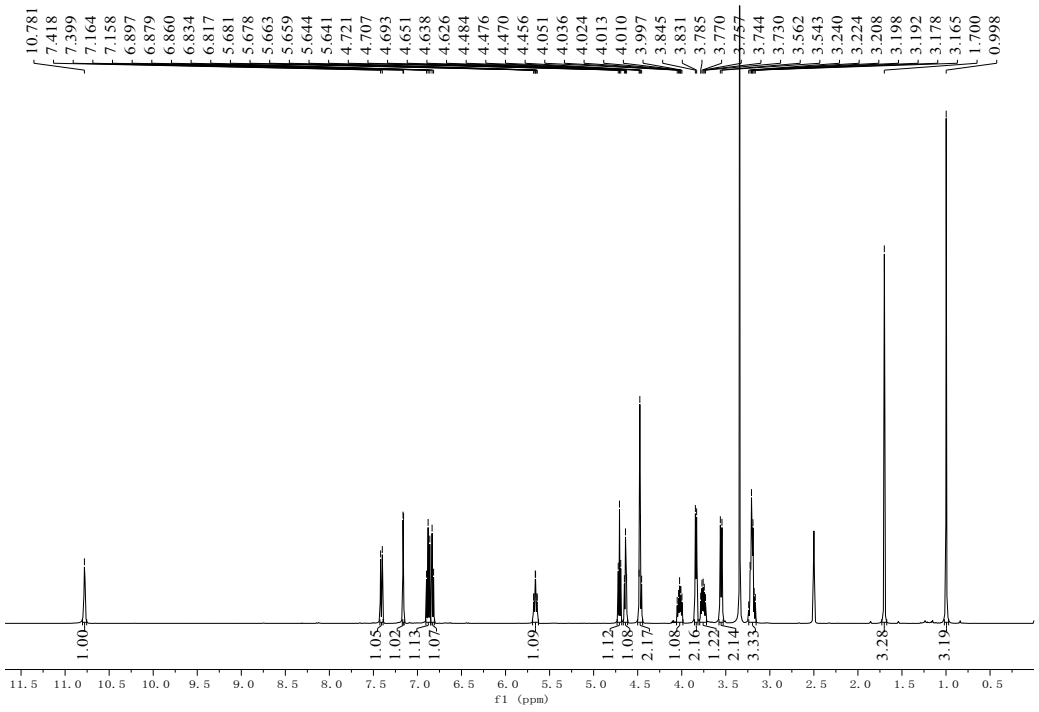
[2] Beijing Research Institute of Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, People's Republic of China

Supporting information

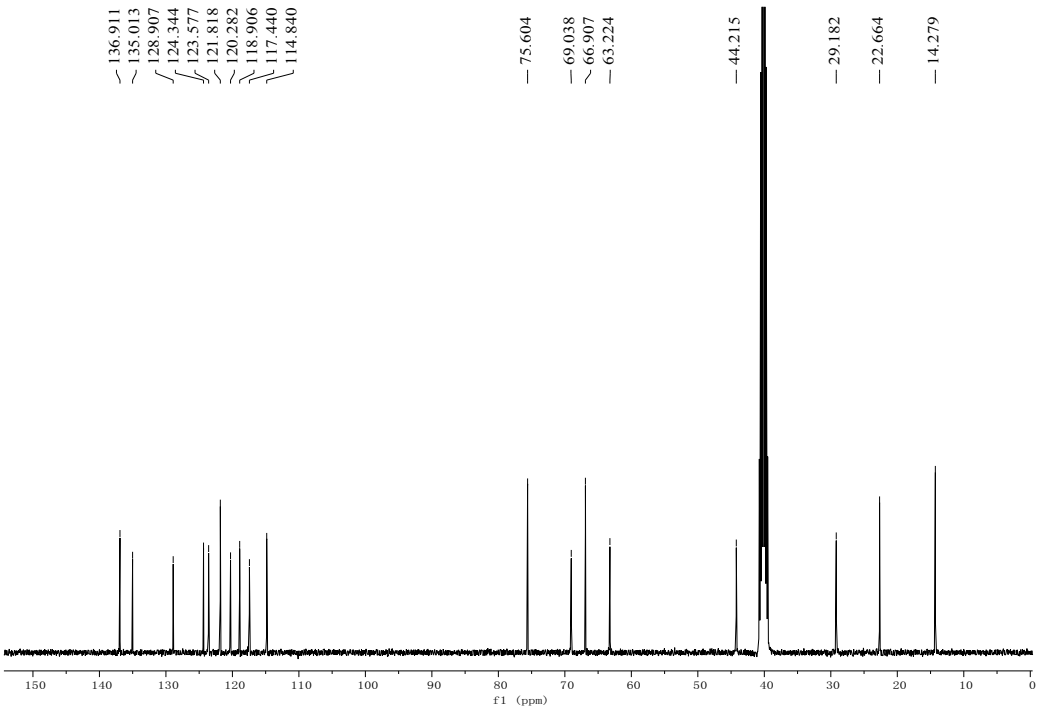
*To whom correspondence should be addressed. Tel./Fax: +86-10-63165227. E-mail: zhangdm@imm.ac.cn.

Index

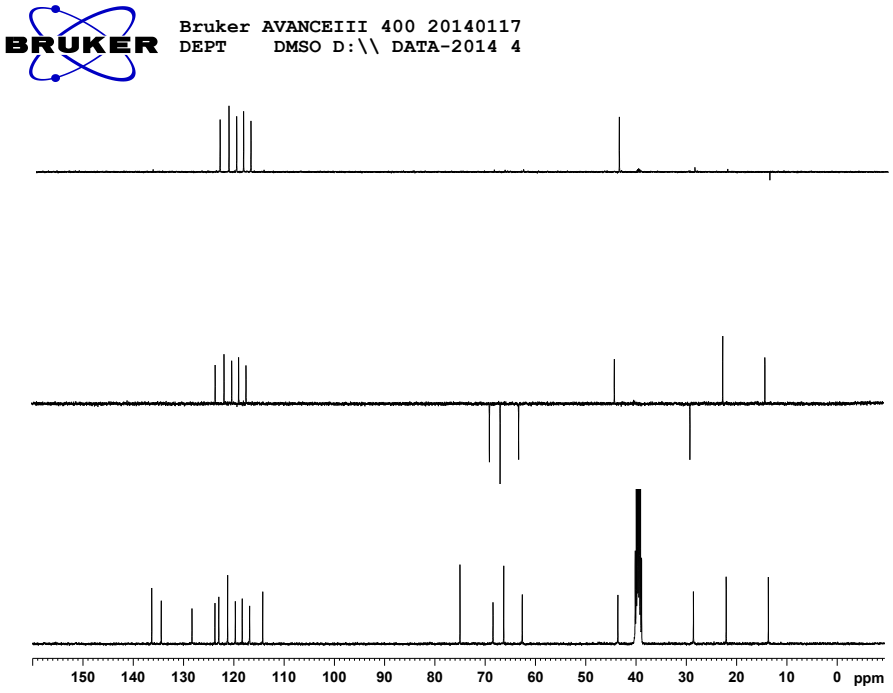
S1. The ^{1}H-NMR (400 MHz, DMSO-d_6) Spectrum of compound 1



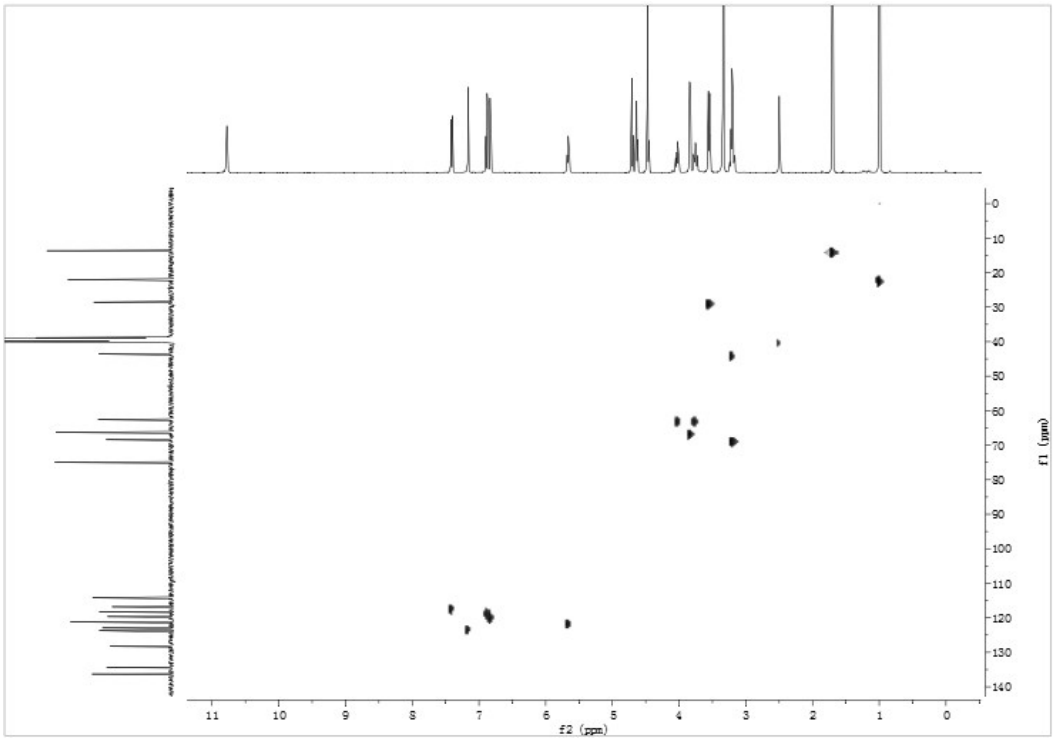
S2. The ^{13}C NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1



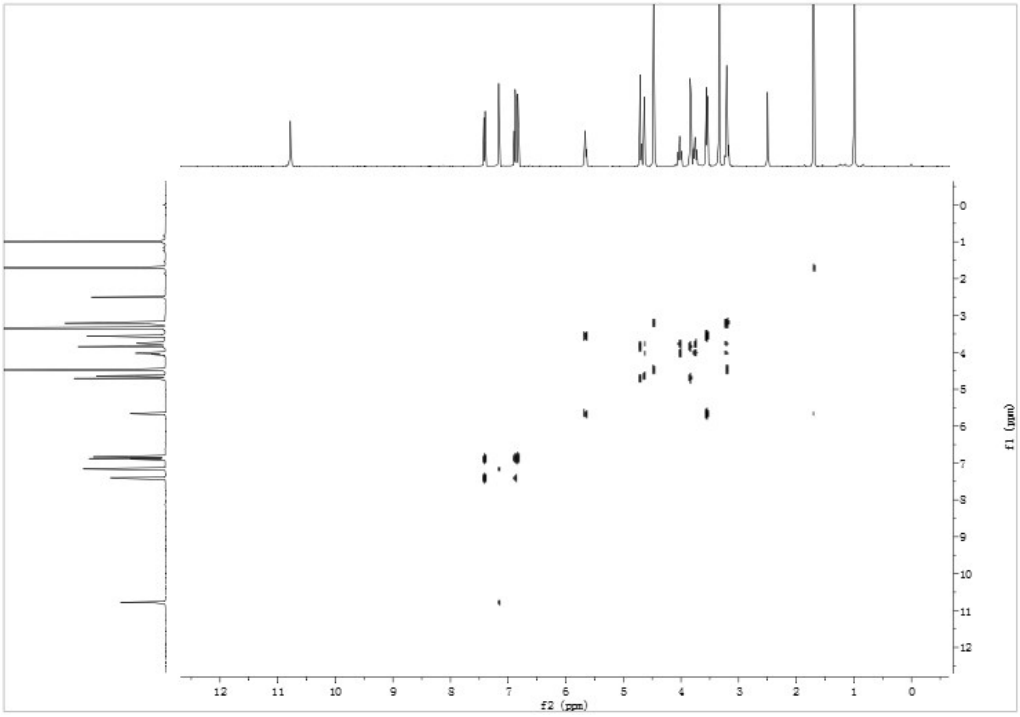
S3. The DEPT Spectrum of compound 1



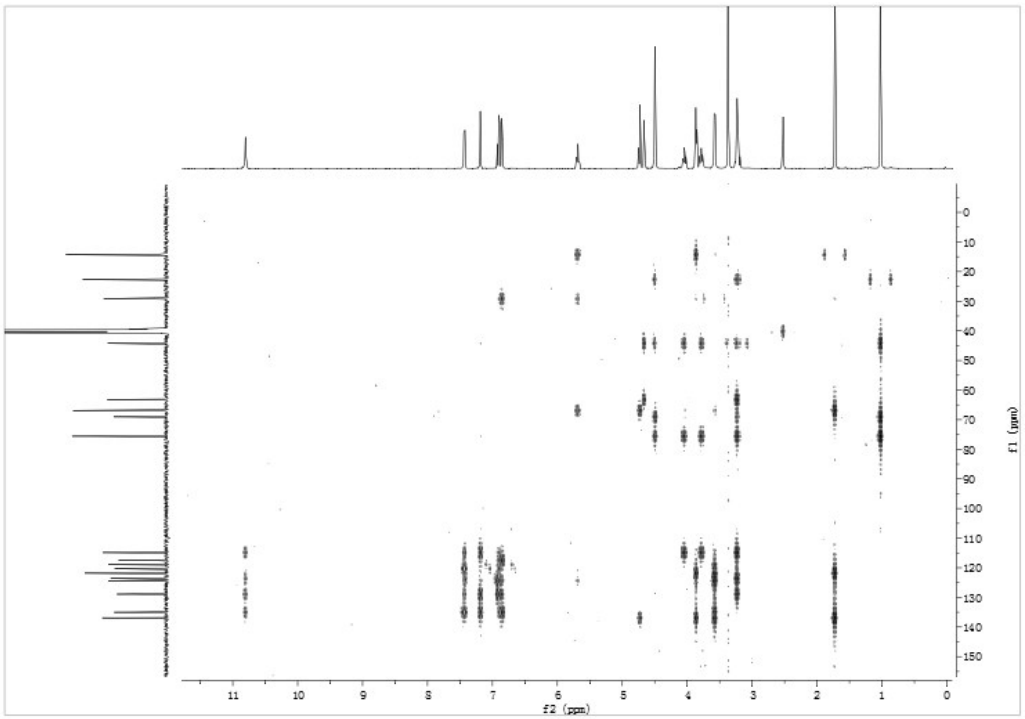
S4. The HSQC Spectrum of Compound 1



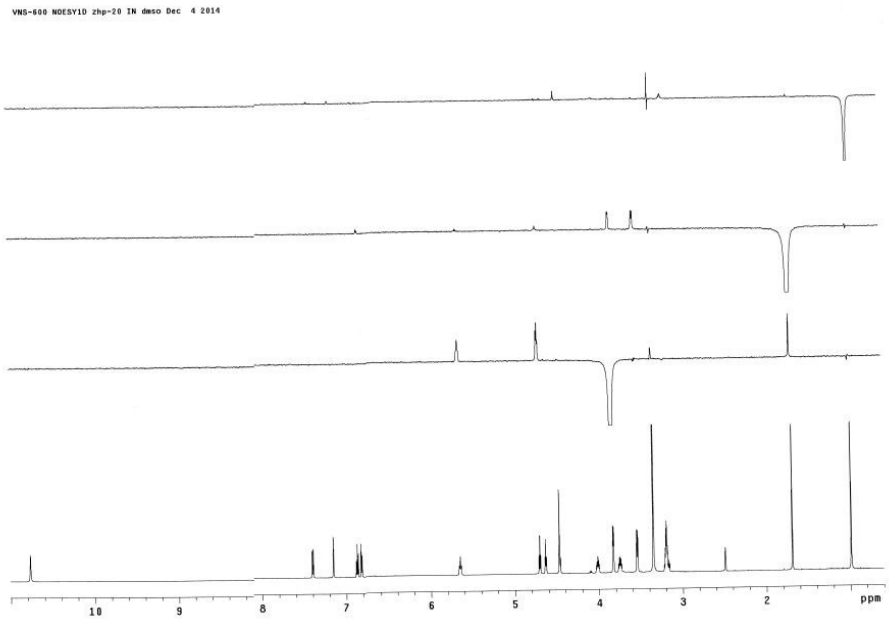
S5. The ^{1}H, ^{1}H-COSY Spectrum of compound 1



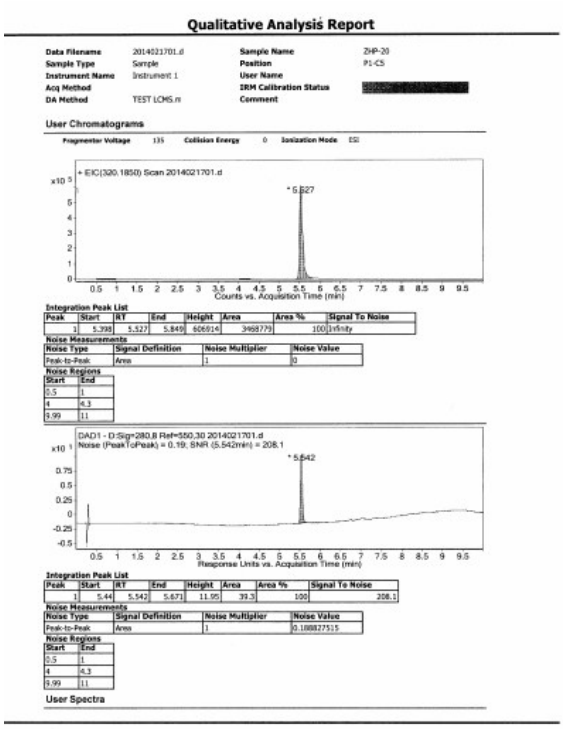
S6. The HMBC Spectrum of compound 1



S7. The NOE difference Spectrum of compound 1



S8. The HRESIMS Spectrum of Compound 1



Qualitative Analysis Report

Data Filename 2014021701.d Sample Name ZHP-20
Sample Type Sample Position P1-C5
Instrument Name Instrument 1 User Name
Acq Method IRM Calibration Status
DA Method TEST LCMS.m Comment

User Chromatograms

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI

+ EIC(320.1850) Scan 2014021701.d

* 5.527

Counts vs. Acquisition Time (min)

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	5.398	5.527	5.849	606914	3468779	100	Infinity

Noise Measurements

Noise Type	Signal Definition	Noise Multiplier	Noise Value
Peak-to-Peak	Area	1	0

Noise Regions

Start	End
0.5	1
4	4.3
9.99	11

DAD1 - D:\Sig=280,8 Ref=550,30 2014021701.d
Noise (Peak To Peak) = 0.19, SNR (5.542min) = 208.1

* 5.542

Response Units vs. Acquisition Time (min)

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	5.44	5.542	5.671	11.95	39.3	100	208.1

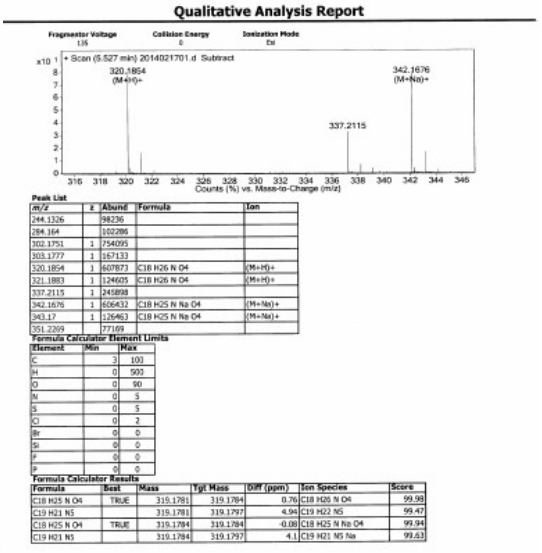
Noise Measurements

Noise Type	Signal Definition	Noise Multiplier	Noise Value
Peak-to-Peak	Area	1	0.188827515

Noise Regions

Start	End
0.5	1
4	4.3
9.99	11

User Spectra



Qualitative Analysis Report

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI

+ Scan (5.527 min) 2014021701.d Subtract

320.1854 (M+H)+
342.1676 (M+Na)+
337.2115

Counts (%) vs. Mass-to-Charge (m/z)

Peak List

m/z	z	Abund	Formula	Ion
244.1326		98236		
284.164		102286		
302.1751	1	754095		
303.1777	1	167133		
320.1854	1	607873	C18 H26 N O4	(M+H)+
321.1883	1	124605	C18 H26 N O4	(M+H)+
337.2115	1	245898		
342.1676	1	606432	C18 H25 N Na O4	(M+Na)+
343.17	1	126463	C18 H25 N Na O4	(M+Na)+
351.2209		77169		

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	900
O	0	90
N	0	5
S	0	5
Cl	0	2
Br	0	0
Si	0	0
F	0	0
P	0	0

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C18 H25 N O4	TRUE	319.1781	319.1784	0.76	C18 H26 N O4	99.98
C19 H21 N5		319.1781	319.1797	4.94	C19 H22 N5	99.47
C18 H25 N O4	TRUE	319.1784	319.1784	-0.08	C18 H25 N Na O4	99.94
C19 H21 N5		319.1784	319.1797	4.1	C19 H21 N5 Na	99.63

MS Formula Results: + Scan (5.527 min) Sub (2014021701.d)

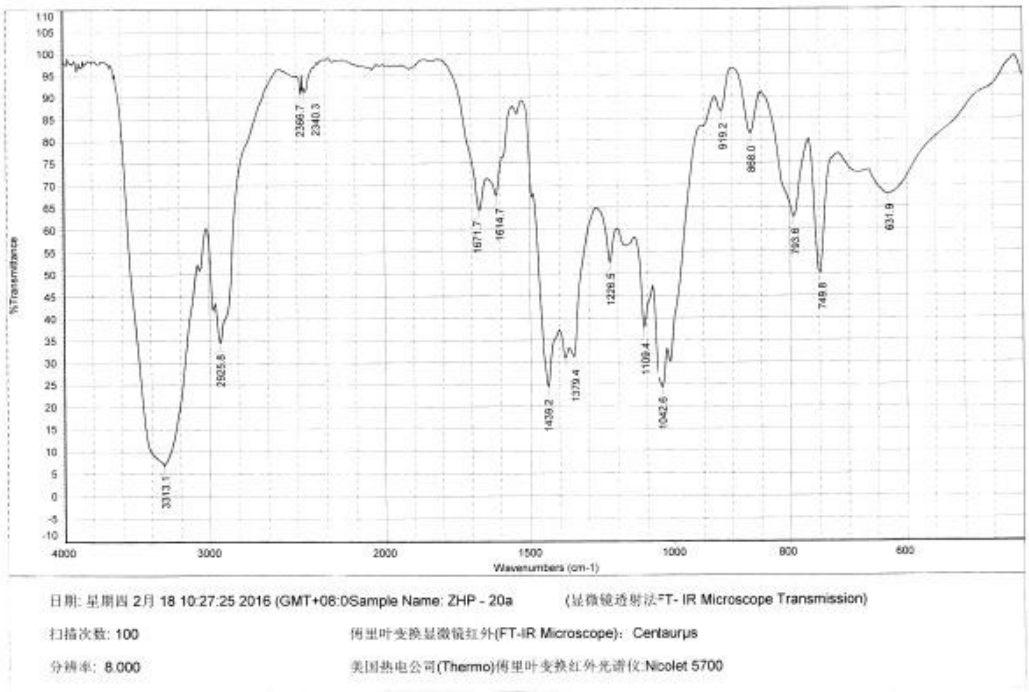
m/z	Ion	Formula	Abundance
320.1854	(M+H)+	C18 H26 N O4	607873.4

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross S	Mass	Calc Mass	Diff (ppm)	Abs Diff (ppm)	Abund Match	Spacing Mat	Mass Match	m/z	DBE
☑	C18 H25 N O4	C18 H26 N O4	320.1856	99.98		319.1781	319.1784	0.76	0.76	99.99	99.97	99.98	320.1854	7
☐	C19 H21 N5	C19 H22 N5	320.187	99.47		319.1781	319.1797	4.94	4.94	99.41	100	99.24	320.1854	12

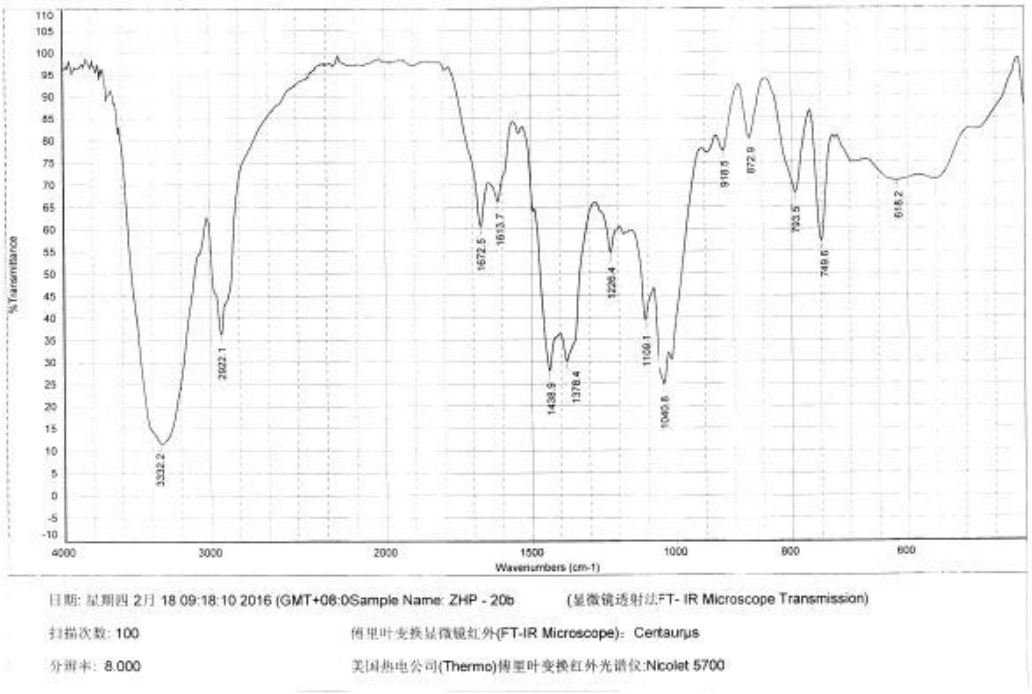
m/z	Ion	Formula	Abundance
342.1676	(M+Na)+	C18 H25 N Na O4	606432.1

Best	Formula (M)	Ion Formula	Calc m/z	Score	Cross S	Mass	Calc Mass	Diff (ppm)	Abs Diff (ppm)	Abund Match	Spacing Mat	Mass Match	m/z	DBE
☑	C18 H25 N O4	C18 H25 N Na O4	342.1676	99.94		319.1784	319.1784	-0.08	0.08	99.98	99.8	100	342.1676	7
☐	C19 H21 N5	C19 H21 N5 Na	342.1689	99.63		319.1784	319.1797	4.1	4.1	99.54	99.93	99.53	342.1676	12

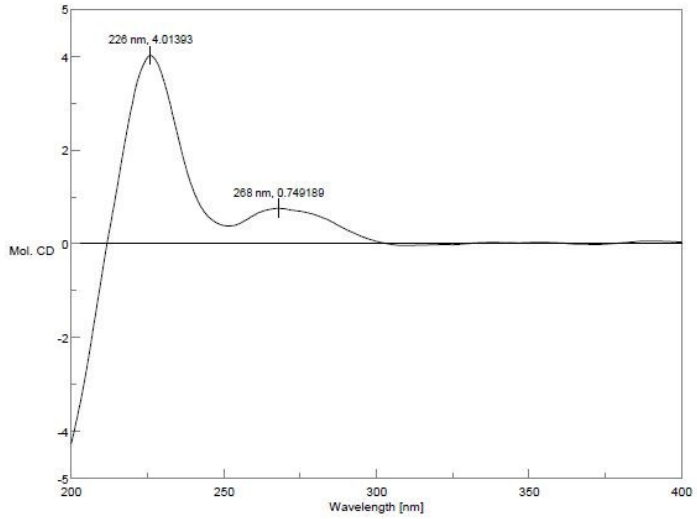
S9. The IR Spectrum of Compound 1a



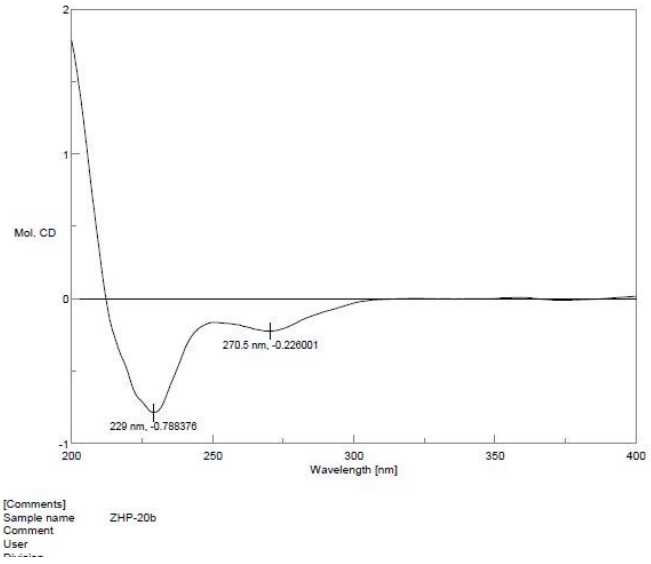
S10. The IR Spectrum of compound 1b



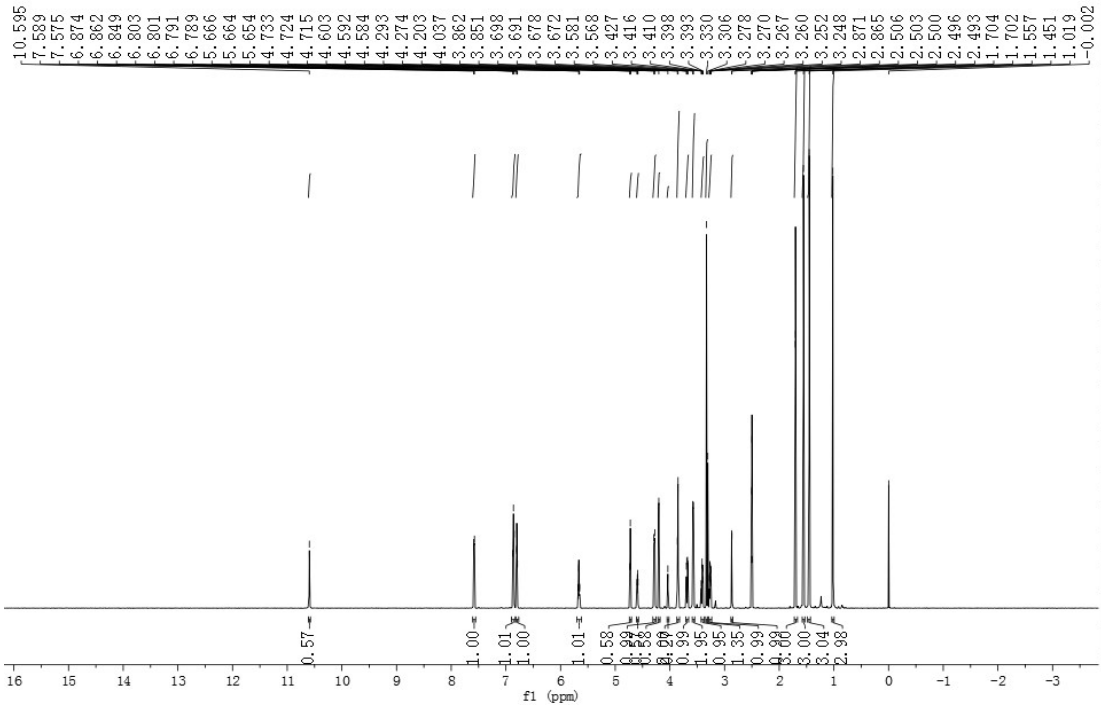
S11. The CD Spectrum of compound 1a



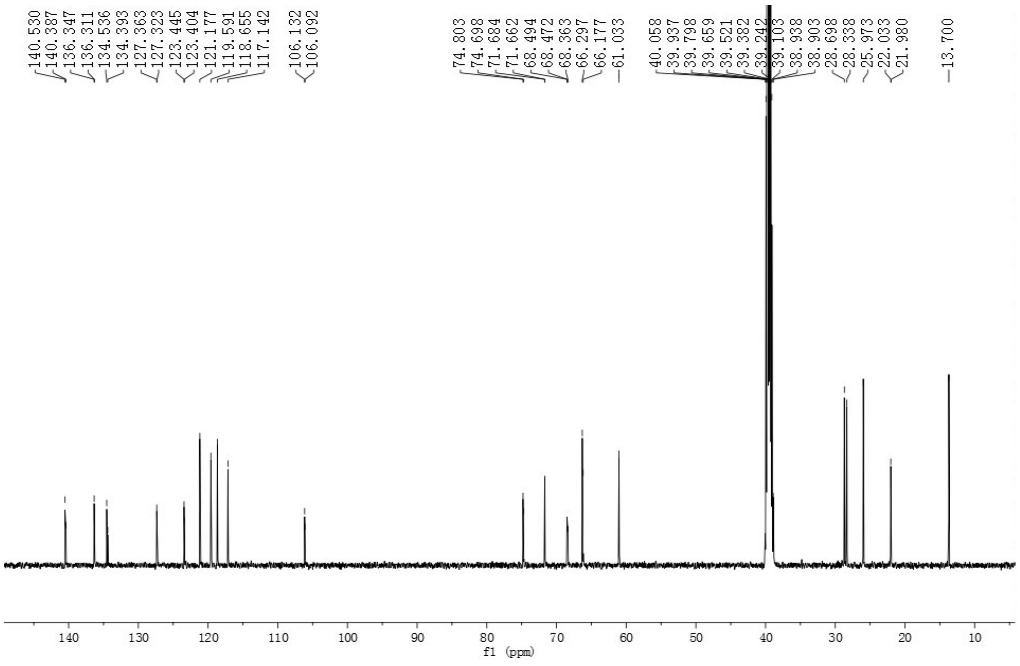
S12. The CD Spectrum of compound 1b



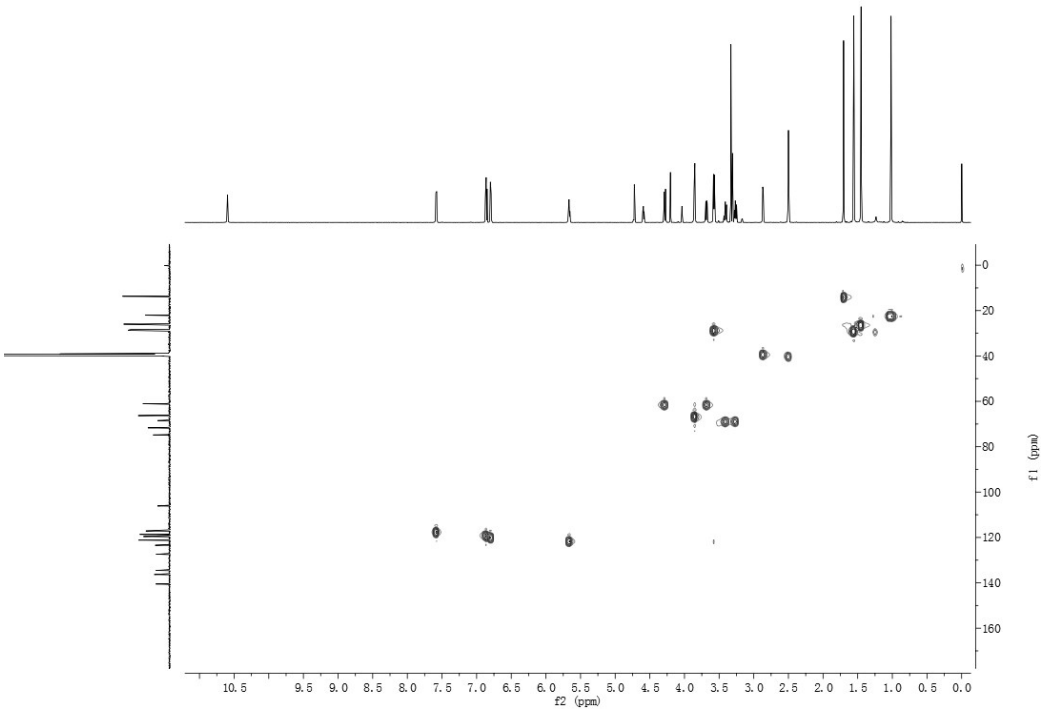
S13 The ^{1}H-NMR (600 MHz, DMSO-d_6) Spectrum of compound 1c


10.595
7.589
7.575
6.874
6.862
6.849
6.803
6.801
6.791
6.789
6.666
5.664
5.654
4.733
4.724
4.715
4.603
4.592
4.584
4.293
4.274
4.203
4.037
3.862
3.851
3.698
3.691
3.678
3.672
3.581
3.568
3.427
3.416
3.410
3.398
3.393
3.330
3.306
3.278
3.270
3.267
3.260
3.252
3.248
2.871
2.865
2.506
2.503
2.500
2.496
2.493
1.704
1.702
1.557
1.451
1.019
-0.002
0.57
1.00
1.01
1.00
1.01
0.58
0.99
0.99
0.99
1.35
0.95
1.35
0.99
3.00
3.04
2.98
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)

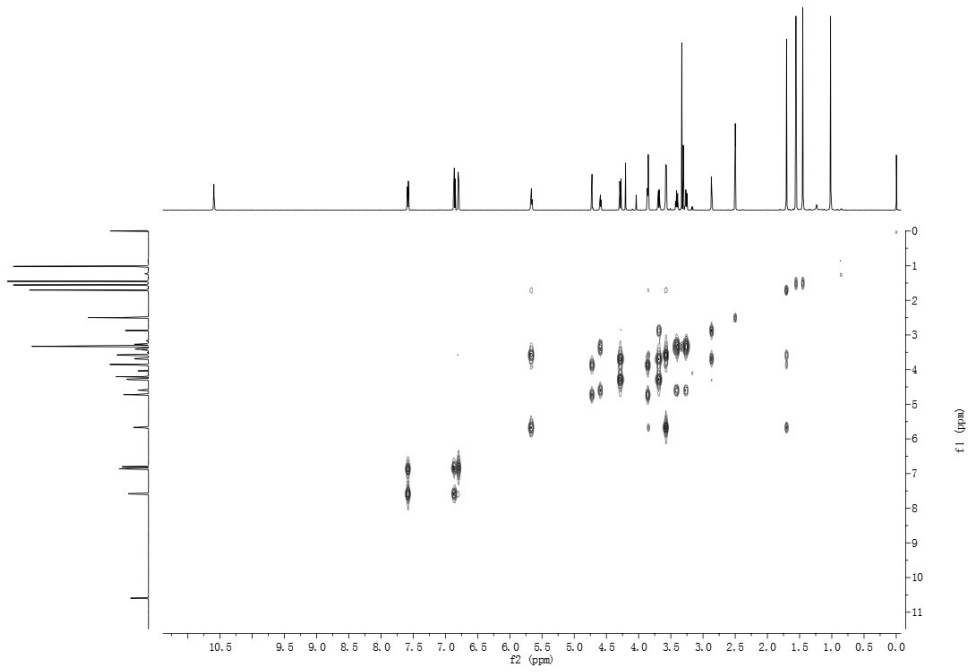
S14. The ^{13}C NMR Spectrum (150 MHz, DMSO-d_6) of Compound 1c



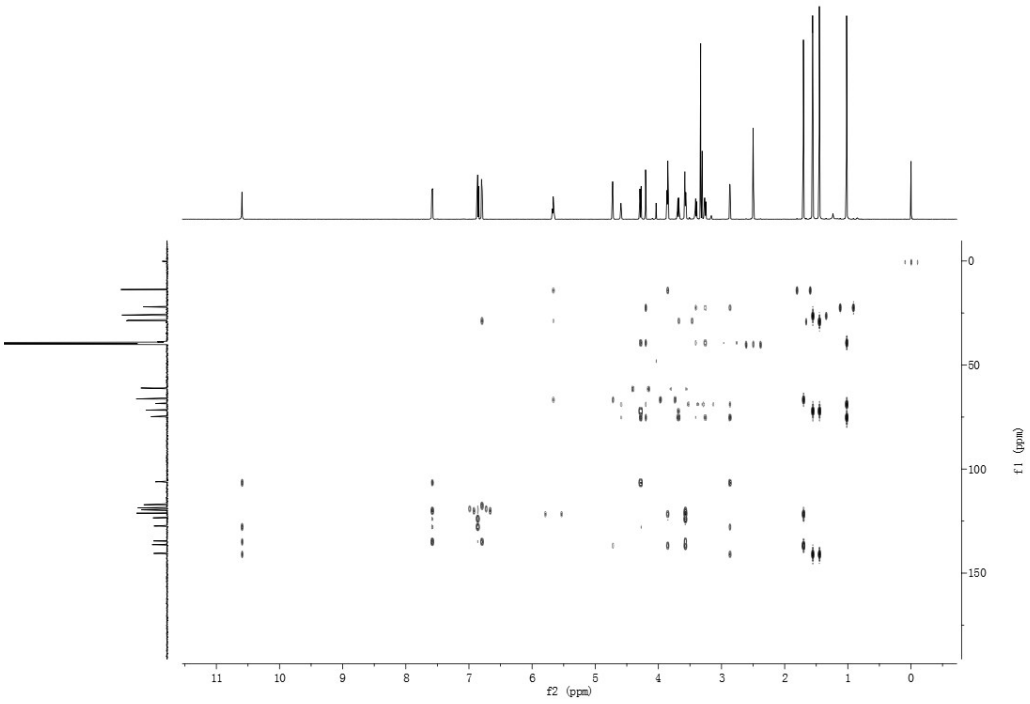
S15. The HSQC Spectrum of Compound 1c



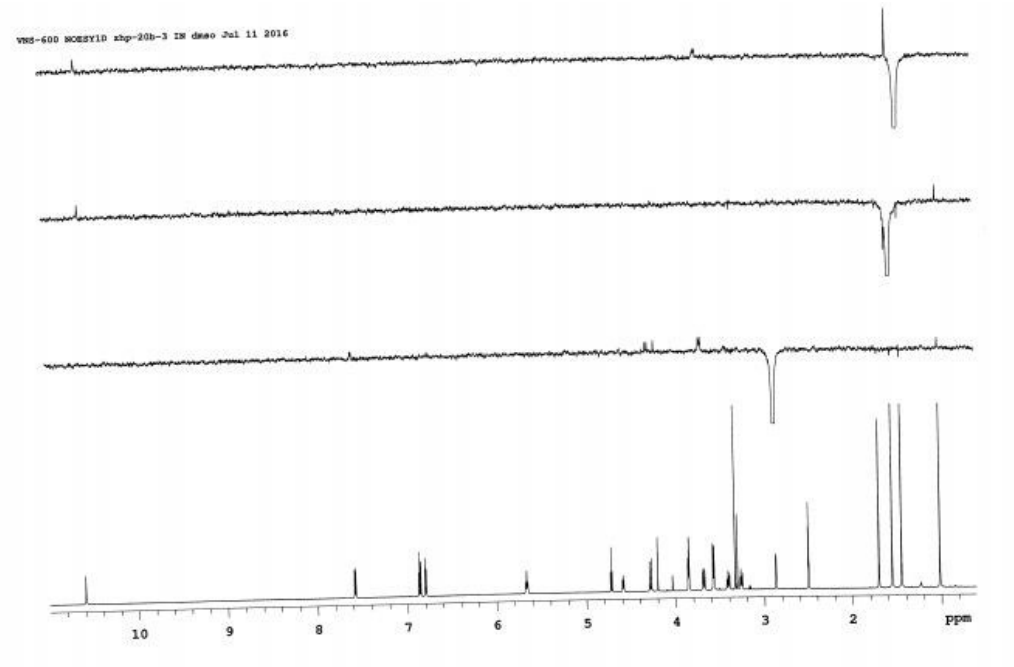
S16. The ^{1}H, ^{1}H-COSY Spectrum of compound 1c



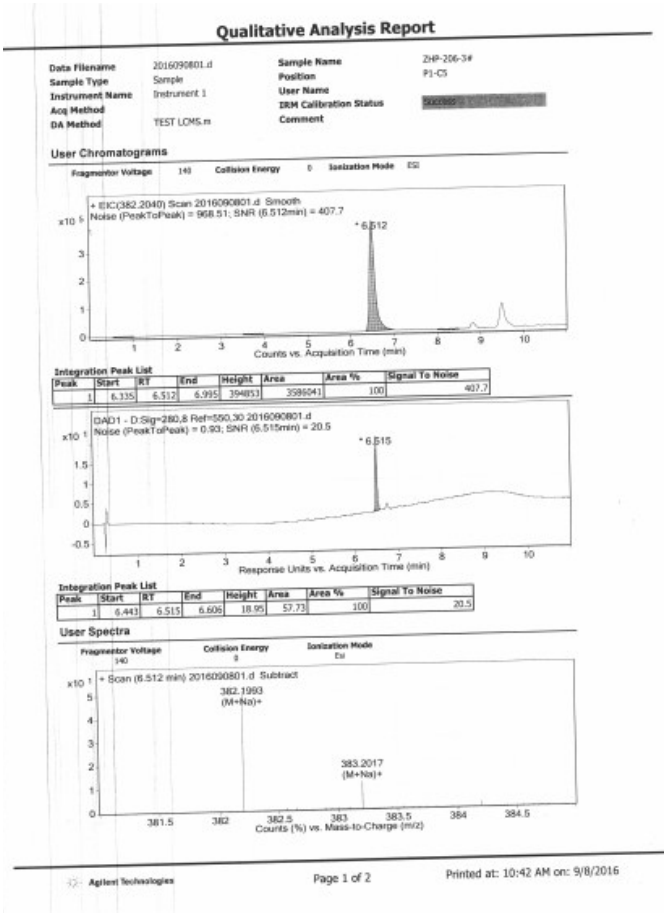
S17. The HMBC Spectrum of Compound 1c



S18. The NOE difference Spectrum of compound 1c



S19. The HREIMS Spectrum of compound 1c



Qualitative Analysis Report

Data Filename 2016090801.d
Sample Type Sample
Instrument Name Instrument 1
Acq Method
DA Method TEST LCMS.m
Sample Name ZHP-206-3#
Position P1-C5
User Name
IRM Calibration Status
Comment

User Chromatograms

Fragmentor Voltage 140 Collision Energy 0 Ionization Mode ESI

+ EIC(382.2040) Scan 2016090801.d Smooth
Noise (PeakToPeak) = 968.51; SNR (6.512min) = 407.7
* 6.512
Counts vs. Acquisition Time (min)

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.335	6.512	6.995	394853	3586041	100	407.7

DAD1 - D:Sig=280,8 Ref=550,30 2016090801.d
Noise (PeakToPeak) = 0.93; SNR (6.515min) = 20.5
* 6.515
Response Units vs. Acquisition Time (min)

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.443	6.515	6.606	18.95	57.73	100	20.5

User Spectra

Fragmentor Voltage 140 Collision Energy 0 Ionization Mode ESI

+ Scan (6.512 min) 2016090801.d Subtract
382.1993
(M+Na)+
383.2017
(M+Na)+
Counts (%) vs. Mass-to-Charge (m/z)

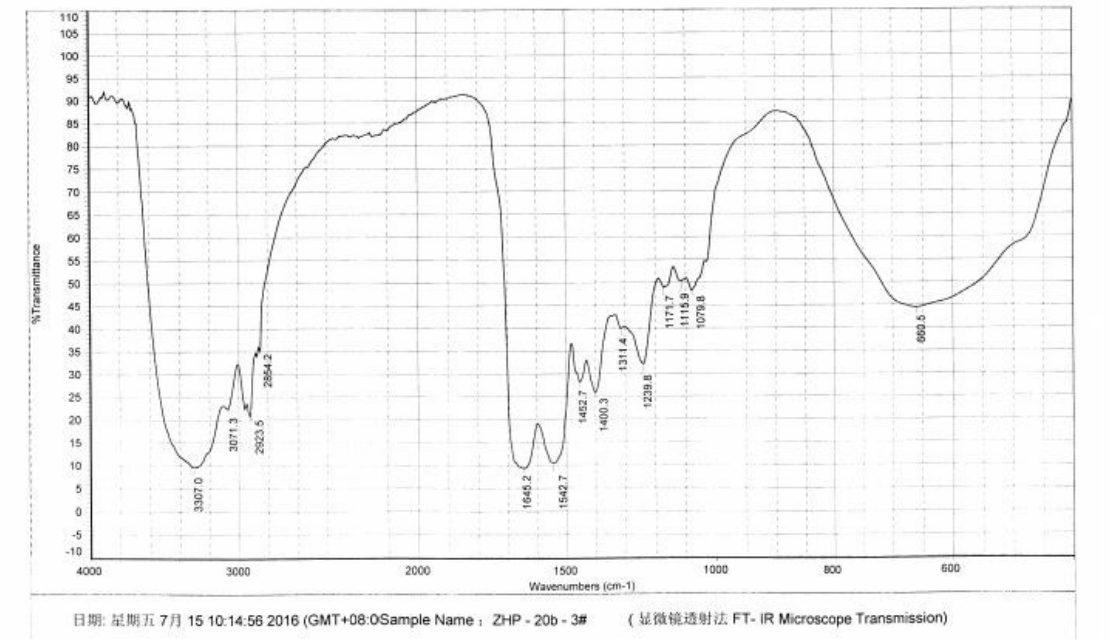
Agilent Technologies Page 1 of 2 Printed at: 10:42 AM on: 9/8/2016

MS Formula Results: + Scan (6.512 min) Sub (2016090801.d)

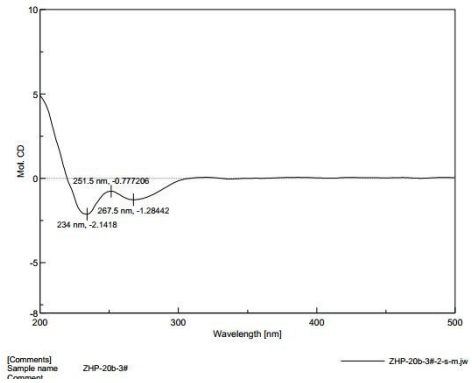
	m/z	Ion	Formula	Abundance
-	382.1993	(M+Na)+	C21 H29 N Na O4	497954.7

	Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
+	☑	C21 H29 N O4	C21 H29 N Na O4	99.93		359.21	359.2097	382.1989	-1.05	1.05	99.97	99.94	99.84	8

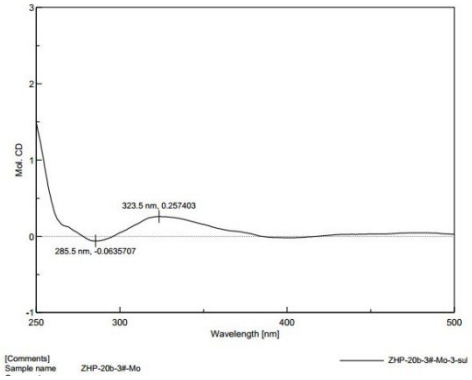
S20. The IR Spectrum of Compound 1c



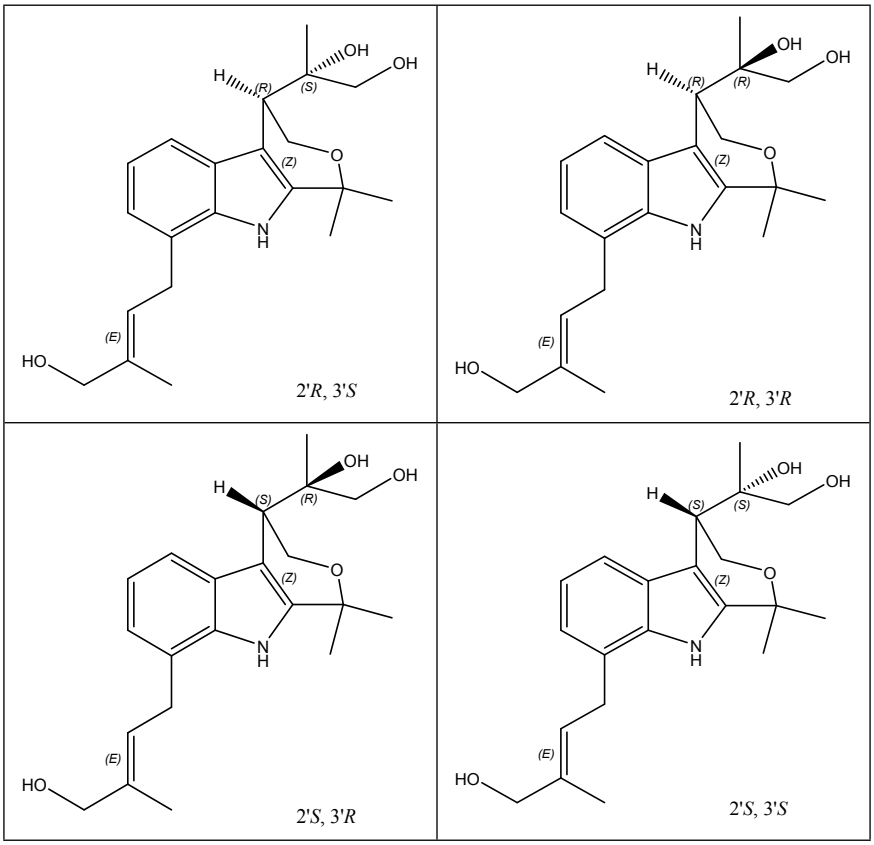
S21. The CD Spectrum of compound 1c

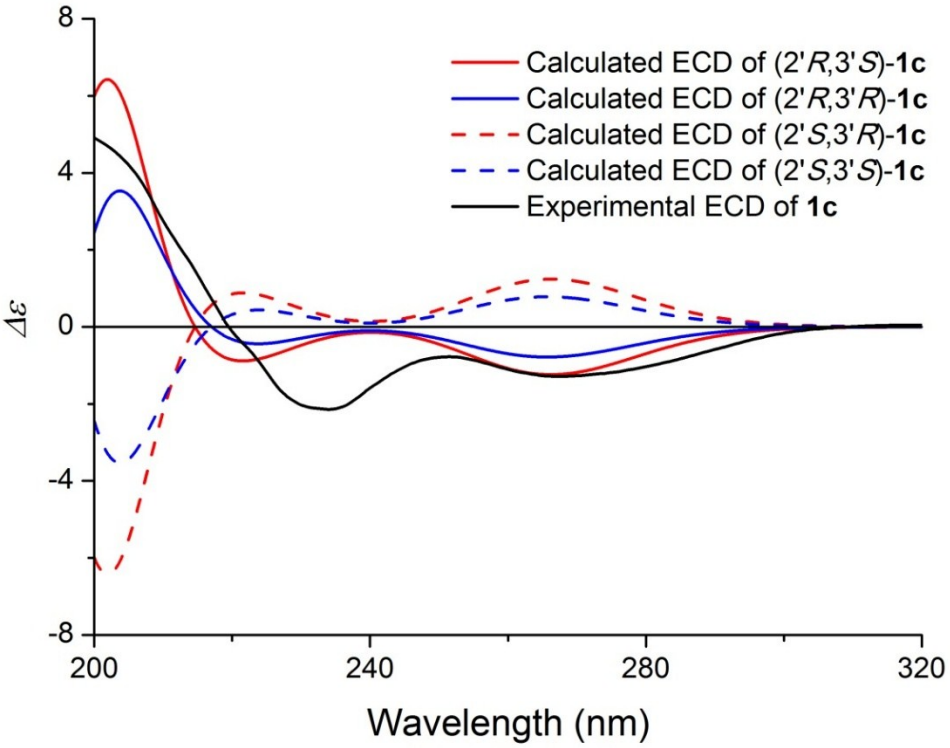


S22. The CD spectrum of compound 1c in a DMSO of dimolybdenum tetraacetate (the inherent CD of the diol was subtracted)

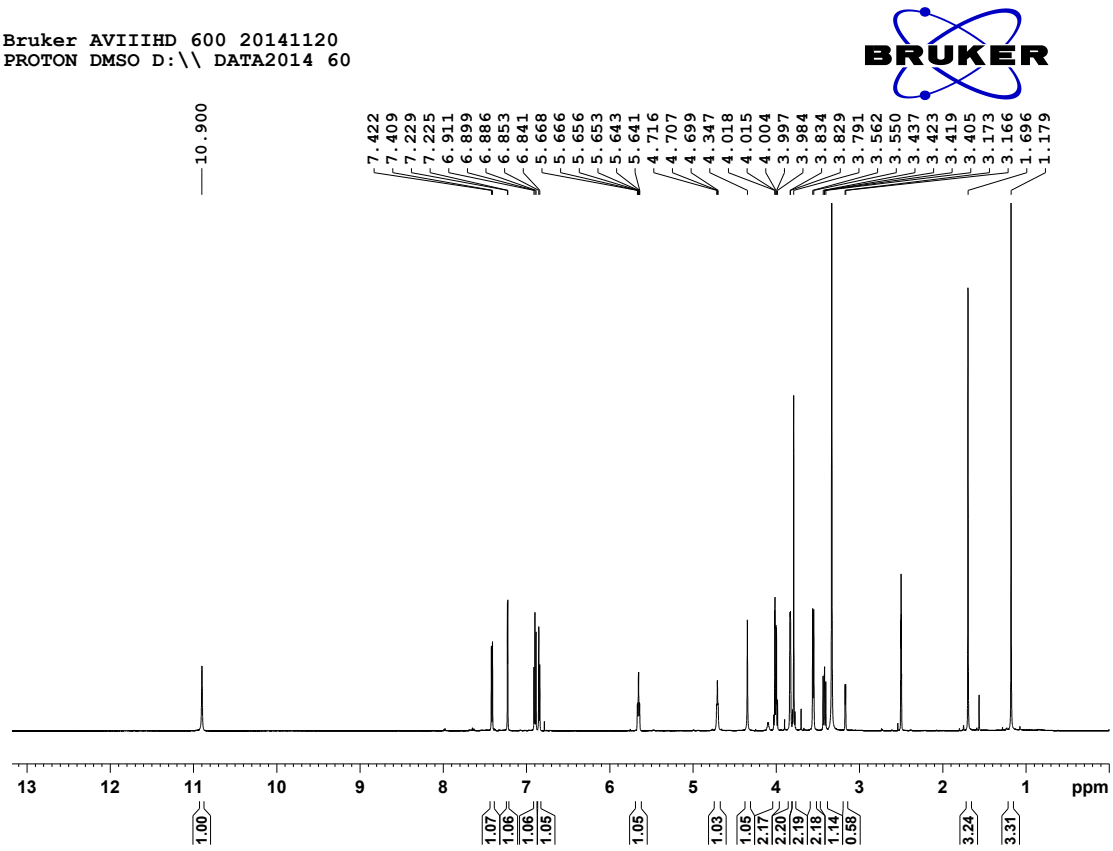


S23. The Calculated ECD spectra of (2'*R*, 3'*R*), (2'*R*, 3'*S*), (2'*S*, 3'*R*), (2'*S*, 3'*S*)-1c and the experimental ECD spectrum of 1c

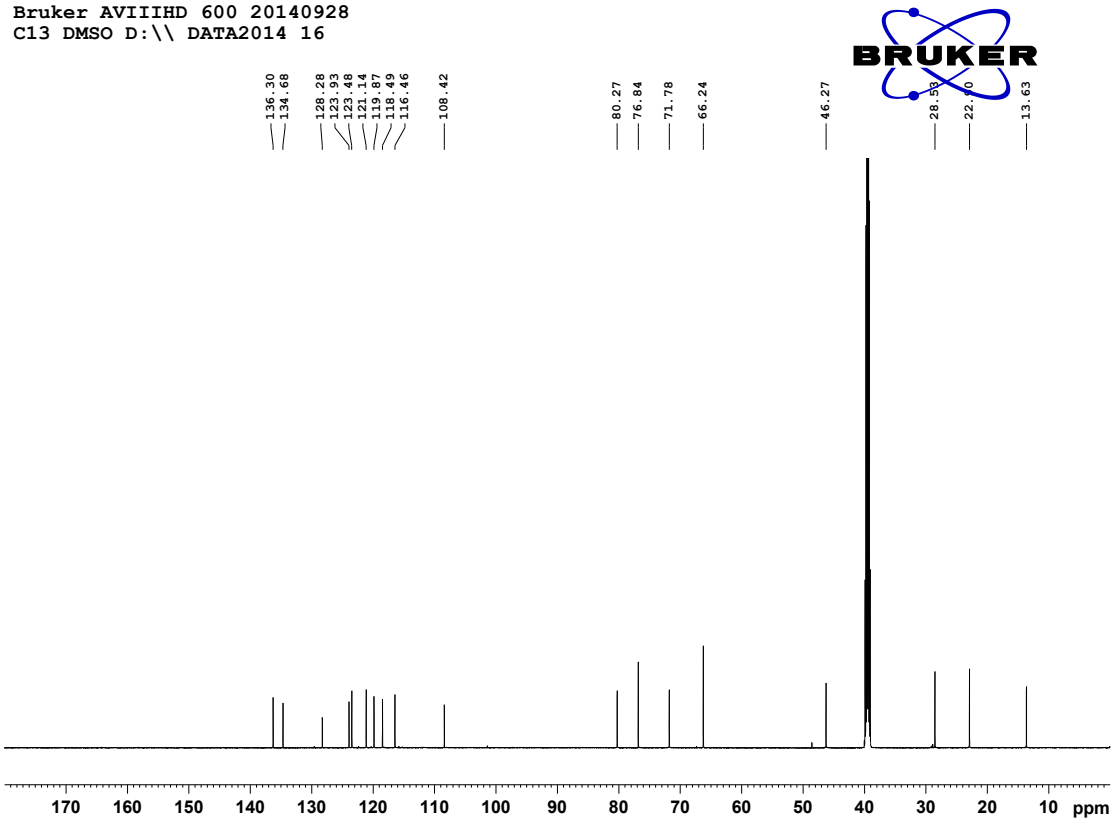



8
4
0
-4
-8
Δε
200
240
280
320
Wavelength (nm)
Calculated ECD of (2'R,3'S)-1c
Calculated ECD of (2'R,3'R)-1c
Calculated ECD of (2'S,3'R)-1c
Calculated ECD of (2'S,3'S)-1c
Experimental ECD of 1c

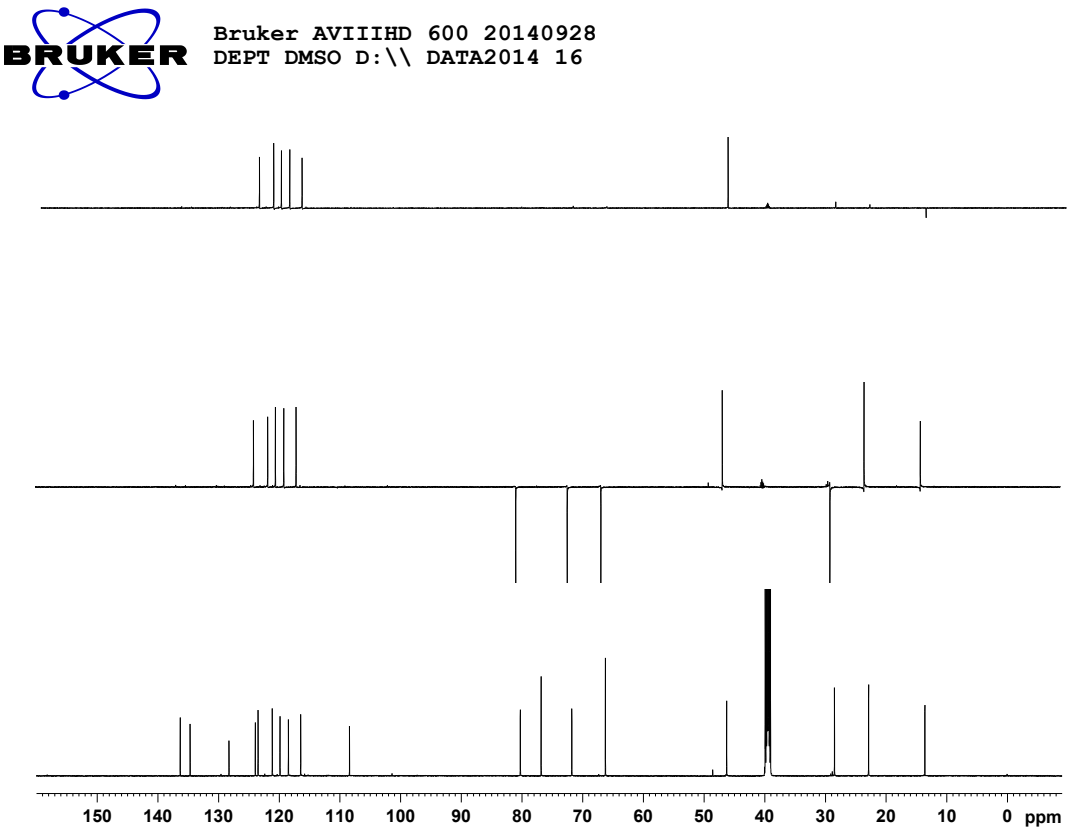
S24. The ^{1}H NMR Spectrum (600 MHz，DMSO-d_6) of compound 2



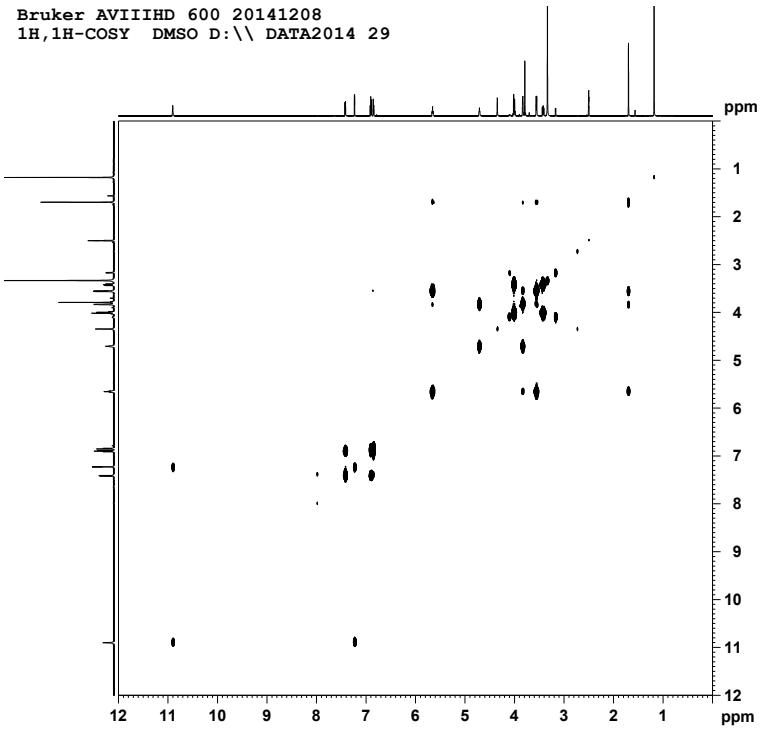
S25. The ^{13}C NMR Spectrum (150 MHz，DMSO-d_6) of compound 2



S26. The DEPT Spectrum of compound 2



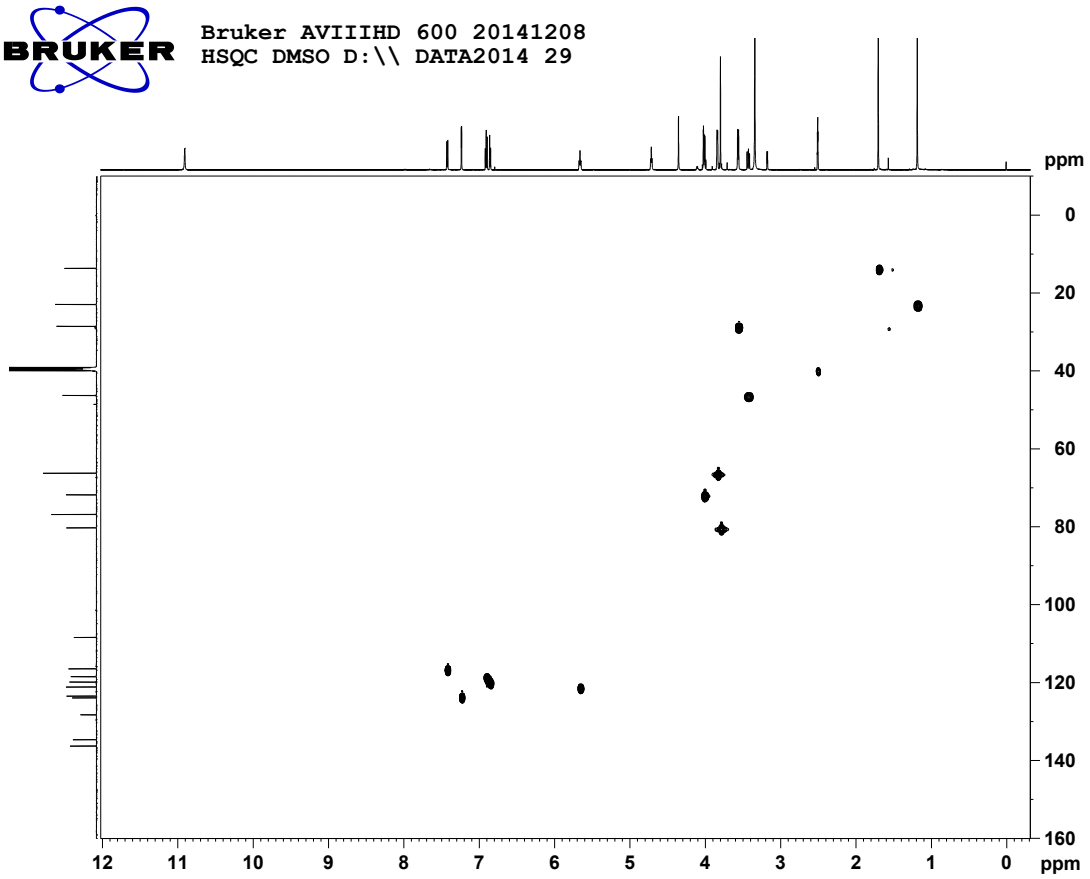
S27. The ^{1}H, ^{1}H-COSY Spectrum of compound 2



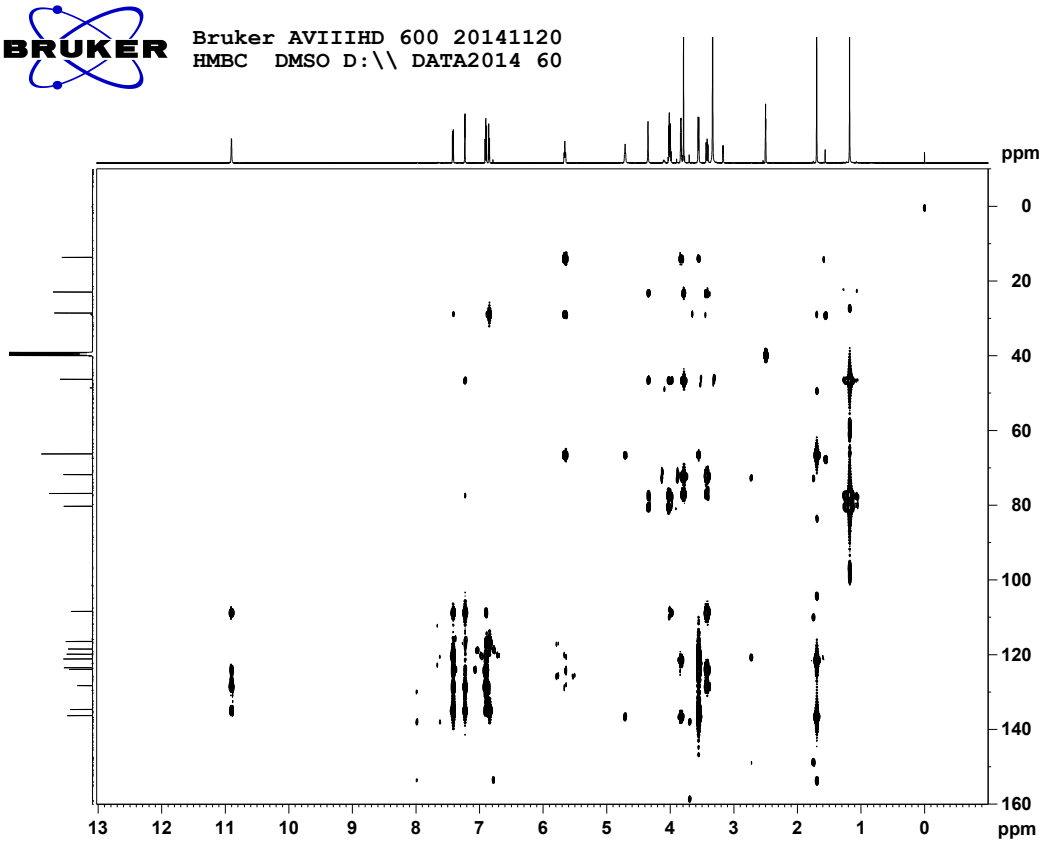

```
NAME      20141208  zhp-c22
EXPNO                2
PROCNO               1
Date_         20141222
Time             11.58
INSTRUM          spect
PROBHD   5 mm CPDCH 13C
PULPROG      cosygpmfqf
TD                2048
SOLVENT           DMSO
NS                   4
DS                  16
SWH           8417.509 Hz
FIDRES        4.110112 Hz
AQ            0.1217012 sec
RG                2050
DW              59.400 usec
DE              20.00 usec
TE              298.2 K
D0          0.00000300 sec
D1          2.00000000 sec
D13         0.00000400 sec
D16         0.00020000 sec
IN0         0.00011900 sec

======== CHANNEL f1 ========
SFO1       600.2540217 MHz
NUC1               1H
P1              11.50 usec
ND0                1
TD               128
SFO1          600.254 MHz
FIDRES       65.651260 Hz
SW              14.000 ppm
FnMODE              QF
SI                1024
SF         600.2500000 MHz
WDW              SINE
SSB                0
LB              0.00 Hz
GB                 0
PC              1.40
SI                1024
MC2                QF
SF         600.2500000 MHz
WDW              SINE
SSB                0
LB              0.00 Hz
GB                 0
```

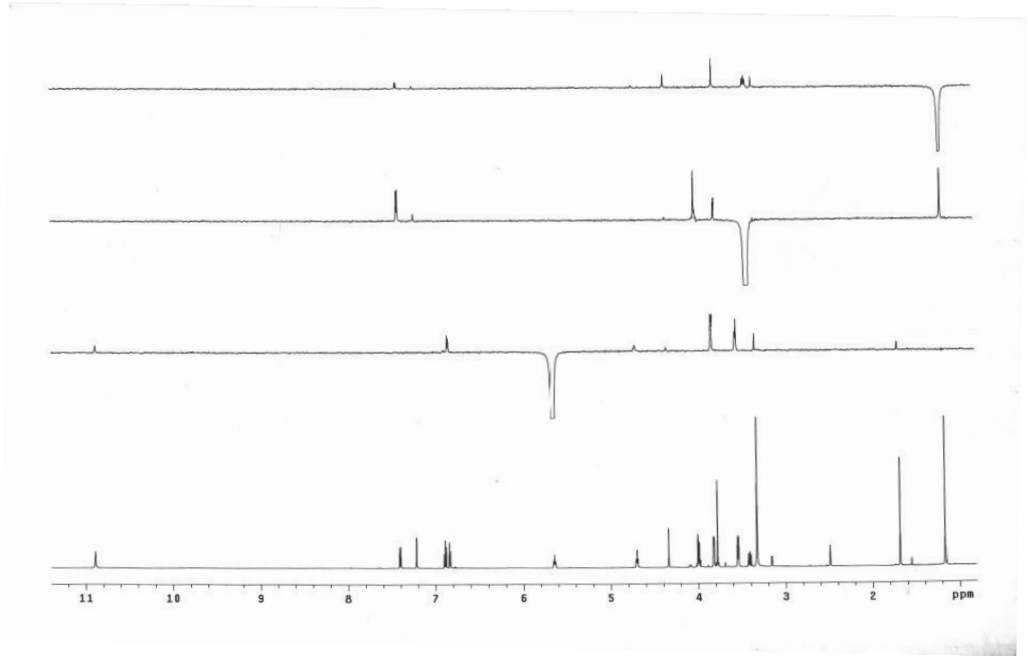
S28. The HSQC Spectrum of compound 2



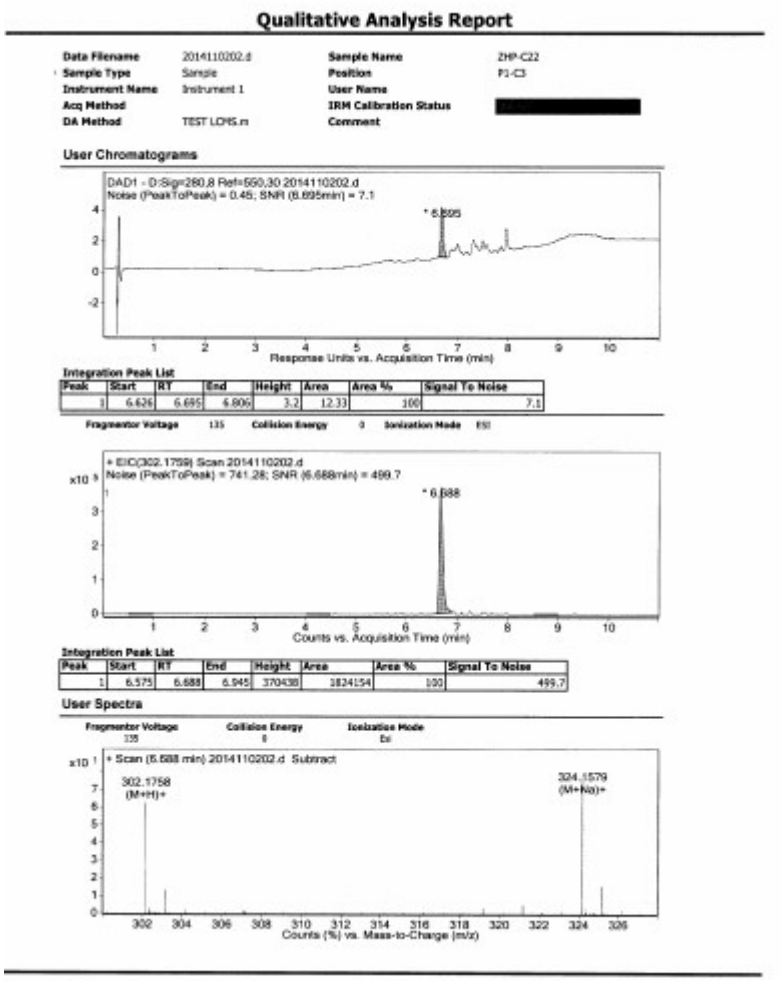
S29. The HMBC Spectrum of compound 2



S30. The NOE Spectrum of compound 2



S31. The HRESIMS Spectrum of compound 2



MS Formula Results: + Scan (6.688 min) Sub (20141102O2.d)

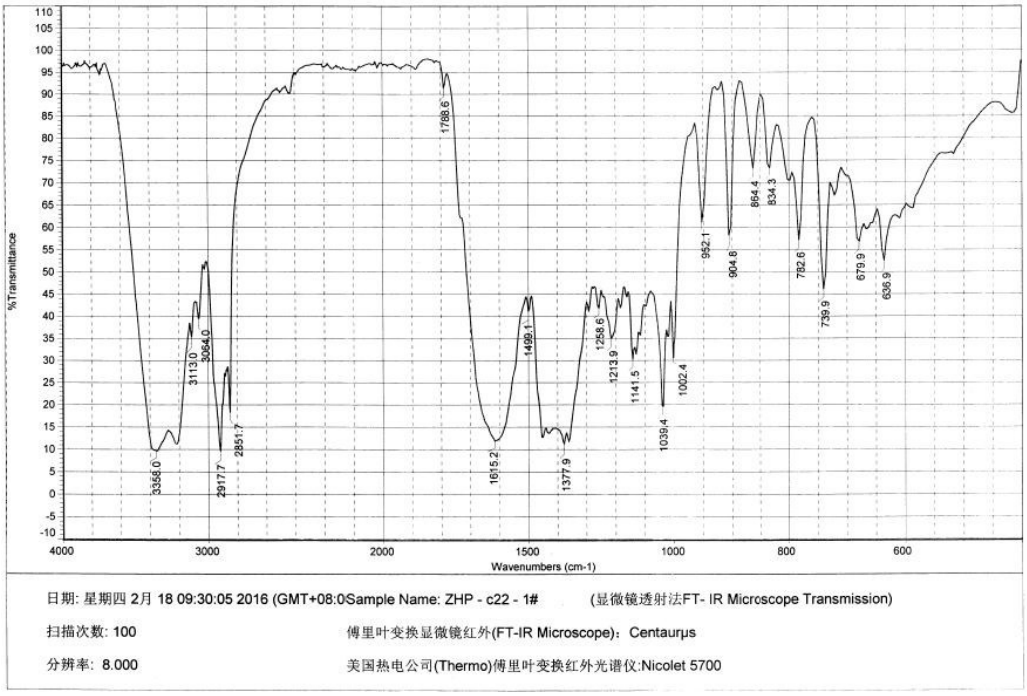
m/z	Ion	Formula	Abundance
302.1758	(M+H)+	C18 H24 N O3	373612

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
✓	C18 H23 N O3	C18 H24 N O3	99.81		301.1686	301.1678	302.1751	-2.57	2.57	99.8	99.77	99.87	8

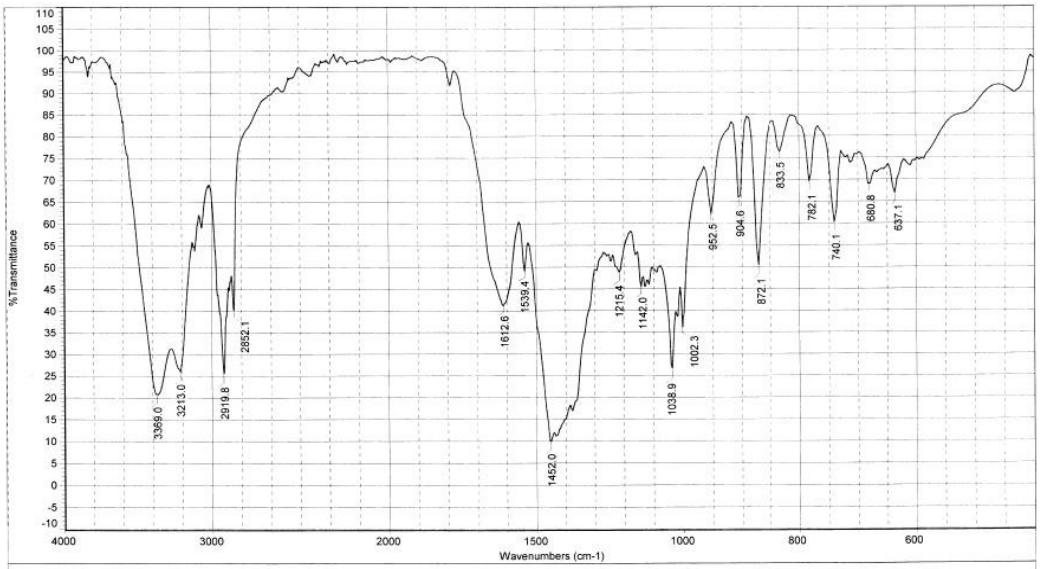
m/z	Ion	Formula	Abundance
324.1579	(M+Na)+	C18 H23 N Na O3	458262.4

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
✓	C18 H23 N O3	C18 H23 N Na O3	99.89		301.1687	301.1678	324.157	-2.86	2.86	99.78	99.98	100	8

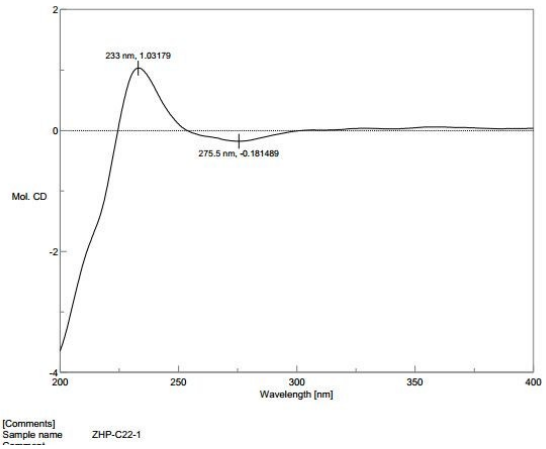
S32. The IR Spectrum of compound 2a



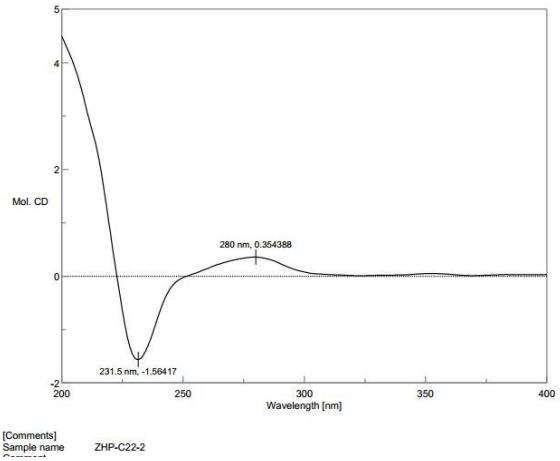
S33. The IR Spectrum of compound 2b



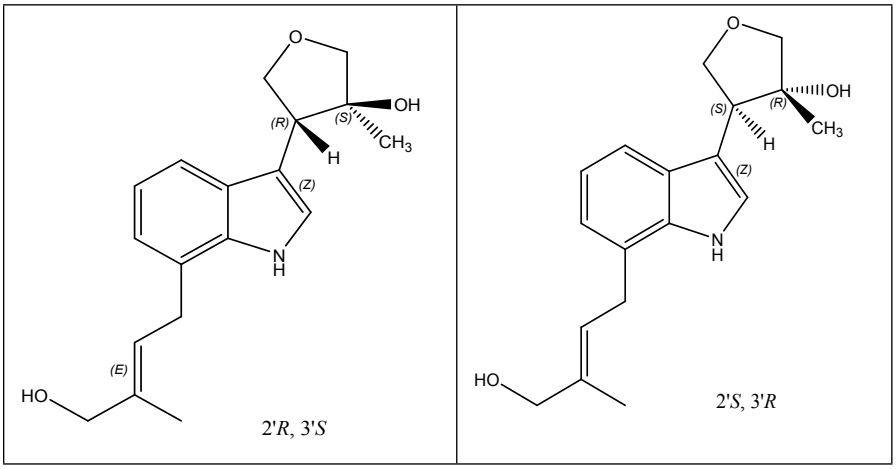
S34. The CD Spectrum of compound 2a

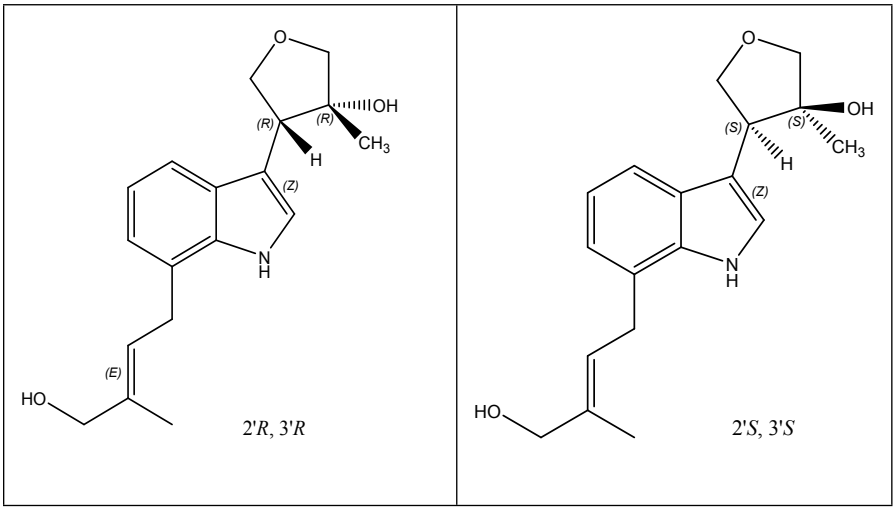


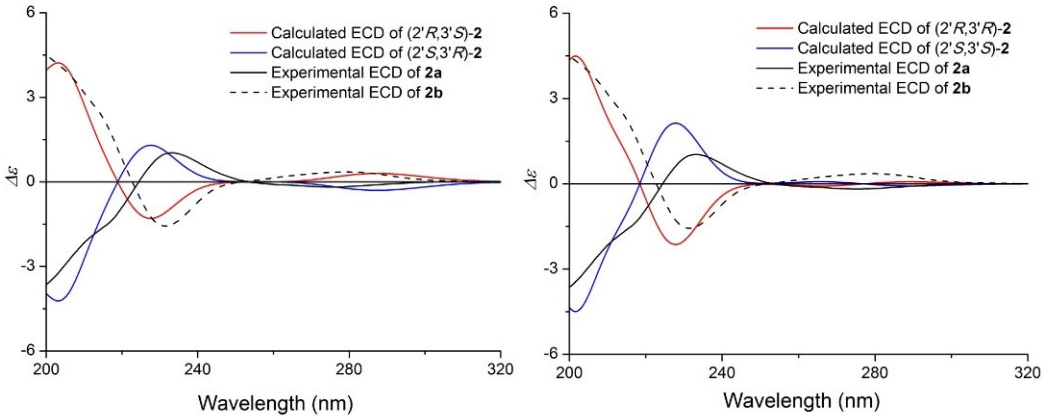
S35. The CD Spectrum of compound 2b



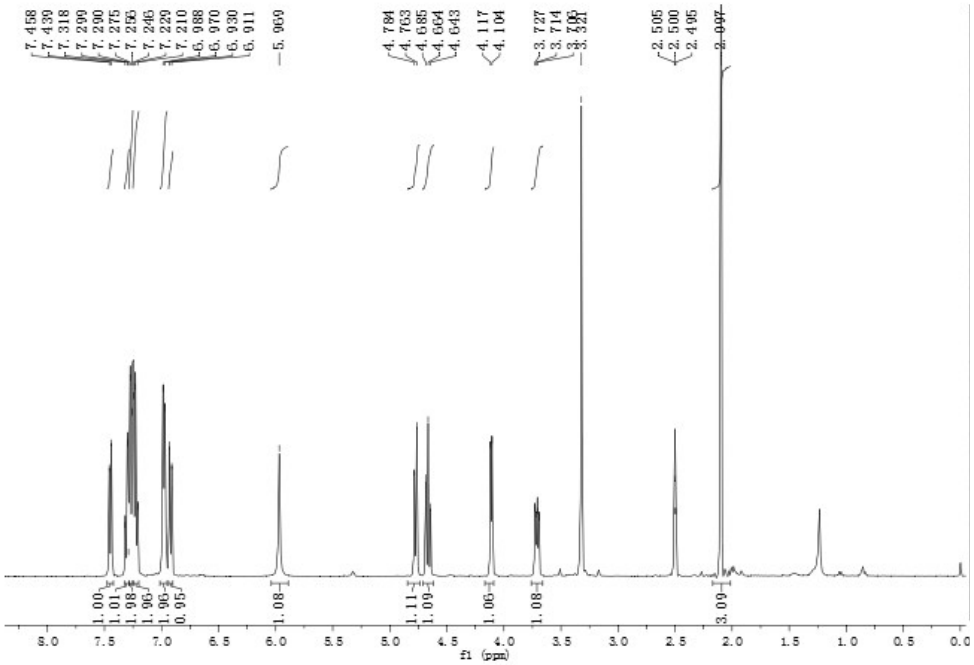
S36. Calculated ECD spectra of (2'*R*, 3'*S*), (2'*S*, 3'*R*), (2'*R*, 3'*R*), (2'*S*, 3'*S*)-2 and the experimental ECD spectrum of 2a and 2b



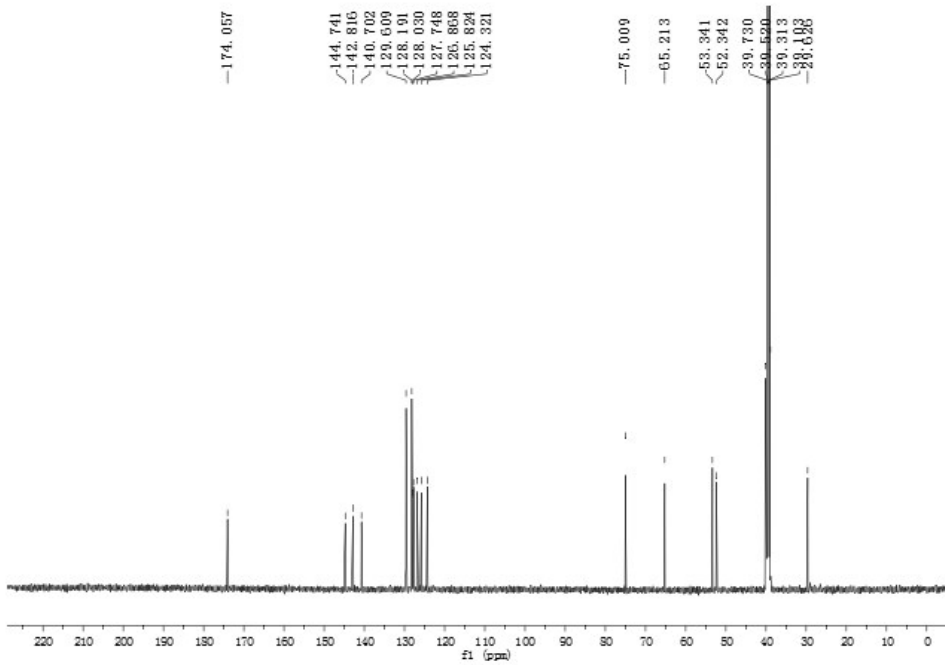

O
OH
(R)
(R)
CH3
H
(Z)
N
H
(E)
HO
2'R, 3'R
O
OH
(S)
(S)
CH3
H
(Z)
N
H
HO
2'S, 3'S


Calculated ECD of (2'R,3'S)-2
Calculated ECD of (2'S,3'R)-2
Experimental ECD of 2a
Experimental ECD of 2b
Δε
Wavelength (nm)
Calculated ECD of (2'R,3'R)-2
Calculated ECD of (2'S,3'S)-2
Experimental ECD of 2a
Experimental ECD of 2b
Δε
Wavelength (nm)

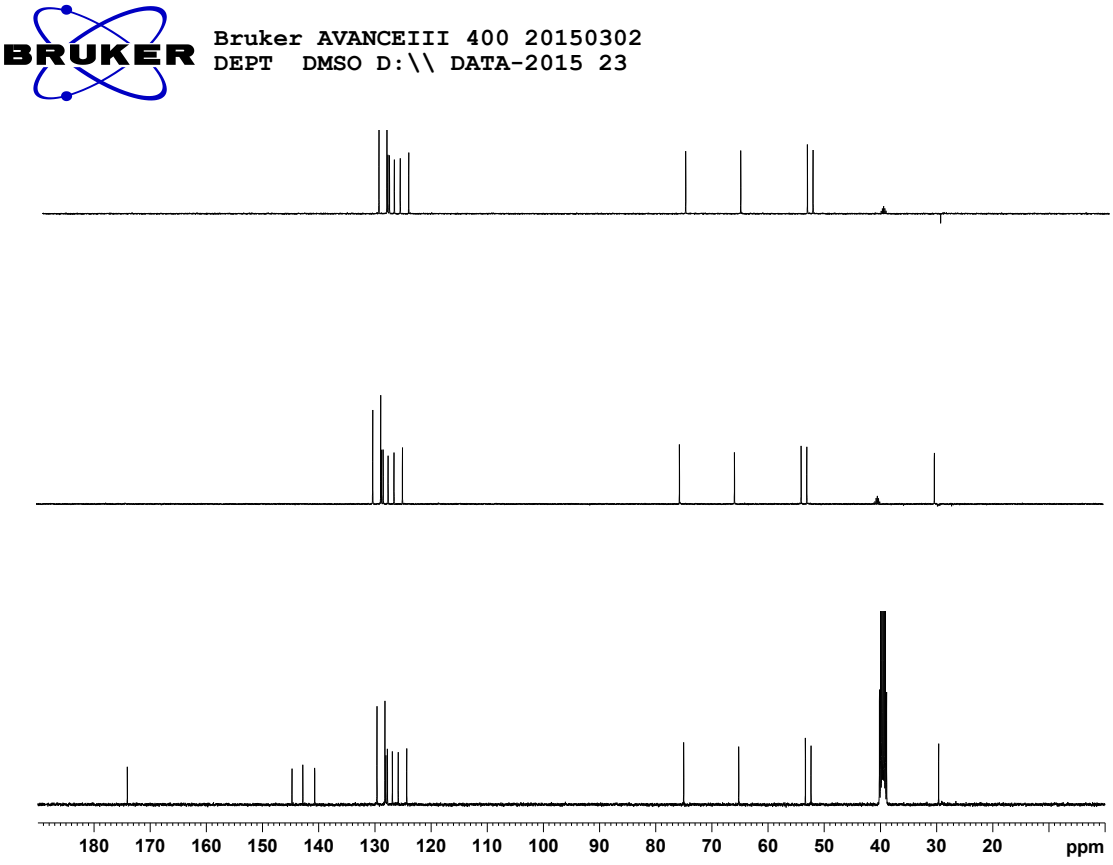
S37. The ^{1}H NMR Spectrum (400 MHz，DMSO-d_6) of compound 3



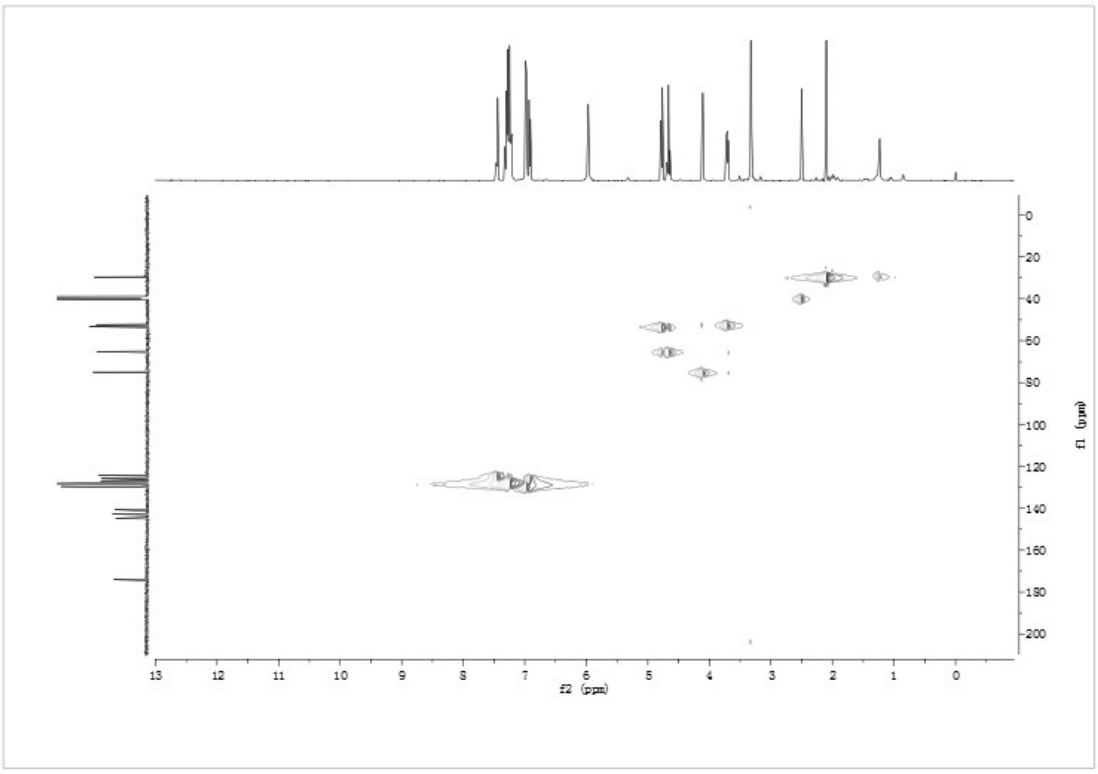
S38. The ^{13}C NMR Spectrum (100 MHz，DMSO-d_6)of compound 3



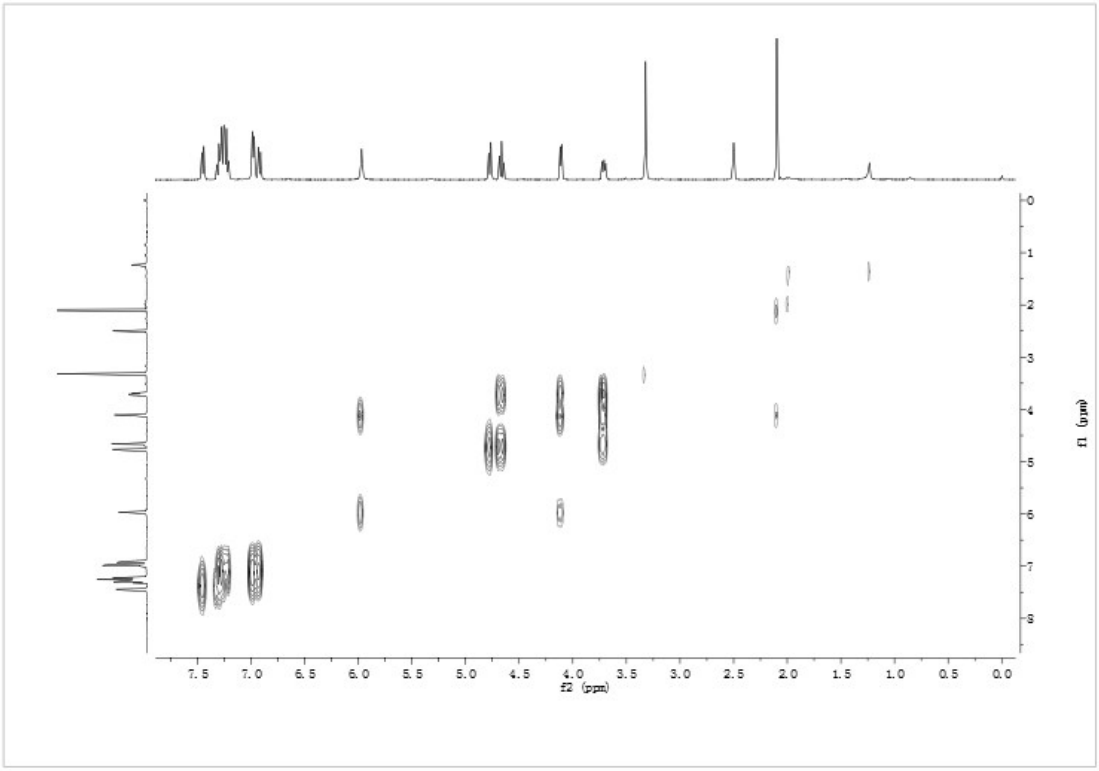
S39. The DEPT Spectrum of compound 3



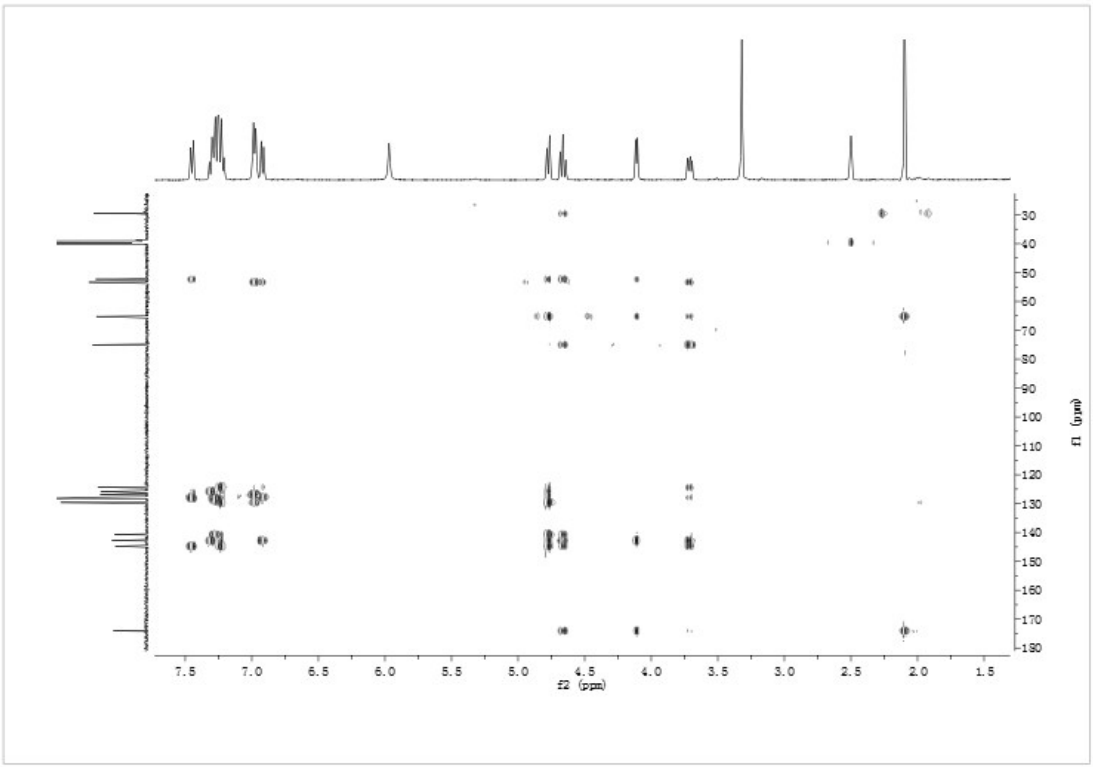
S40. The HSQC Spectrum of compound 3



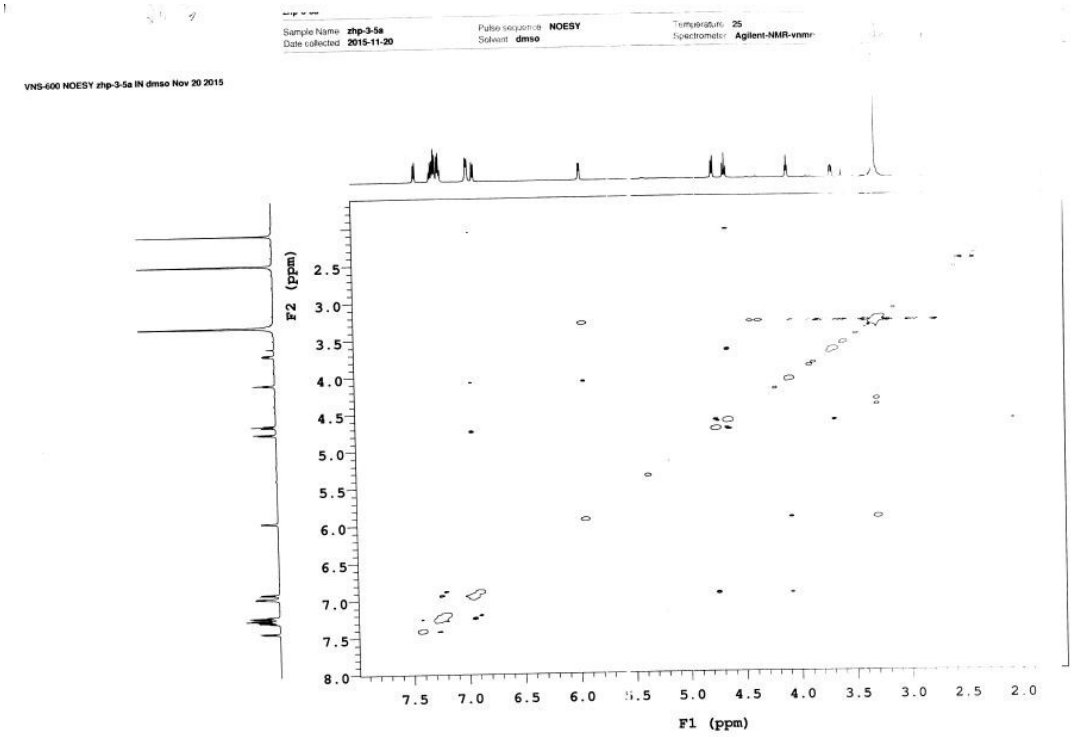
S41. The ^{1}H, ^{1}H-COSY Spectrum of compound 3



S42. The HMBC Spectrum of compound 3



S43. The NOESY Spectrum of compound 3

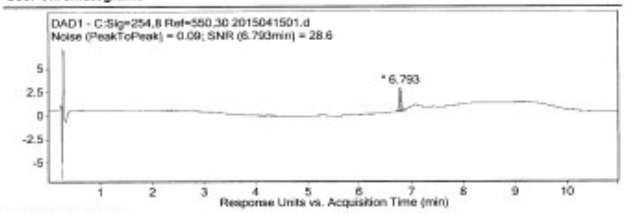


S44. The HRESIMS Spectrum of compound 3

Qualitative Analysis Report

Data Filename	2015041501.d	**Sample Name**	ZHP-3-5#
Sample Type	Sample	**Position**	P1-C6
Instrument Name	Instrument 1	**User Name**	
Acq Method	TEST LCMS.m	**IRM Calibration Status**	Success
DA Method	TEST LCMS.m	**Comment**	

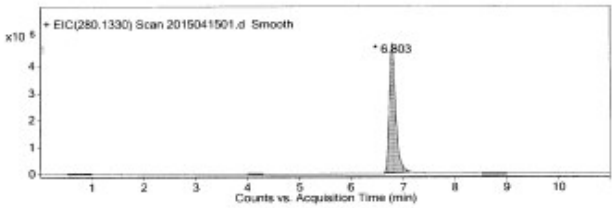
User Chromatograms



Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.731	6.793	6.908	2.5	7.36	100	28.6

Fragmentor Voltage 120 **Collision Energy** 0 **Ionization Mode** ESI

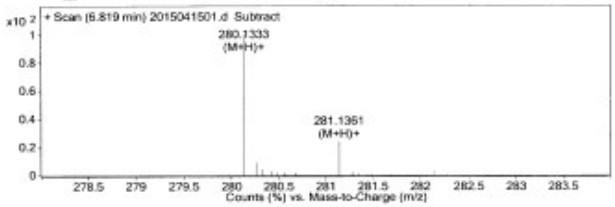


Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.642	6.803	7.157	4833693	41828871	100	Infinity

User Spectra

Fragmentor Voltage 120 **Collision Energy** 0 **Ionization Mode** Esi

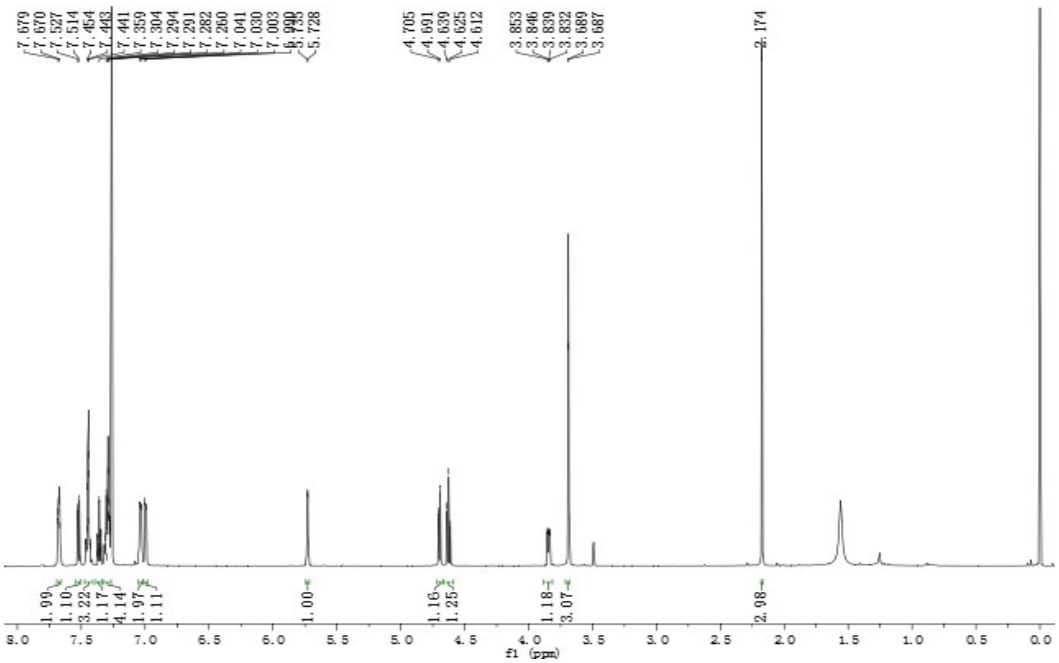


MS Formula Results: + Scan (6.819 min) Sub (2015041501.d)

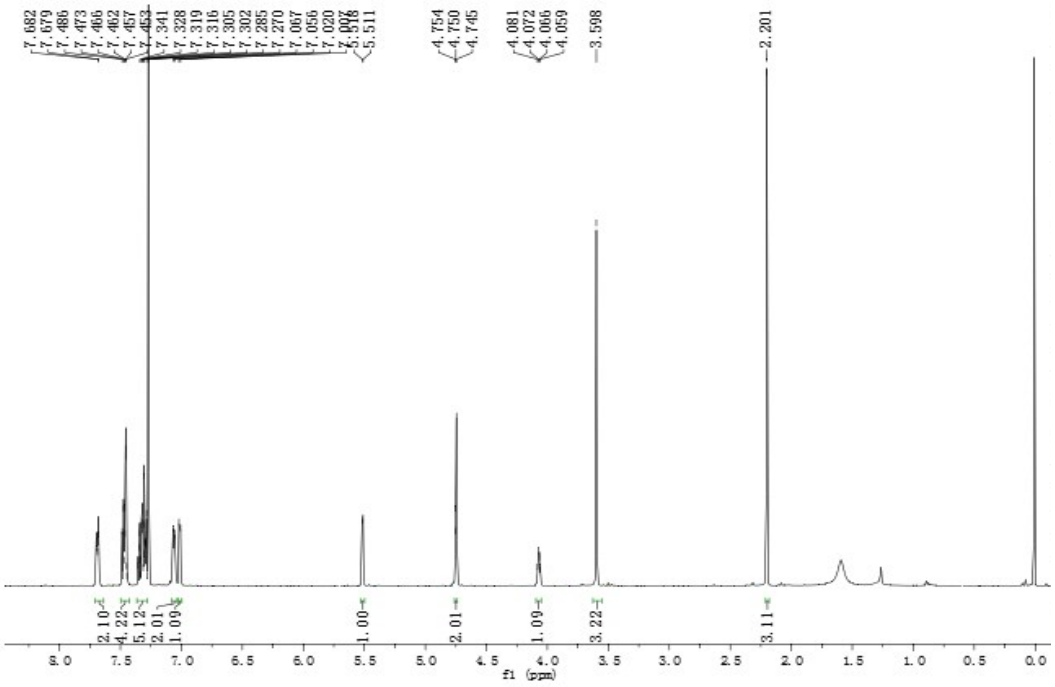
m/z	Ion	Formula	Abundance
280.1333	(M+H)+	C18 H18 N O2	5506573.5

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
✔	C18 H17 N O2	C18 H18 N O2	99.47		279.126	279.1259	280.1332	-0.4	0.4	100	98.23	99.91	11

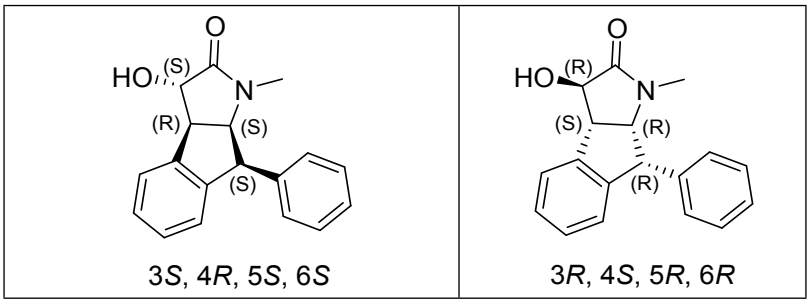
S45. The ^{1}H NMR Spectrum (600 MHz，$CDCl_3$) of compound 3aa

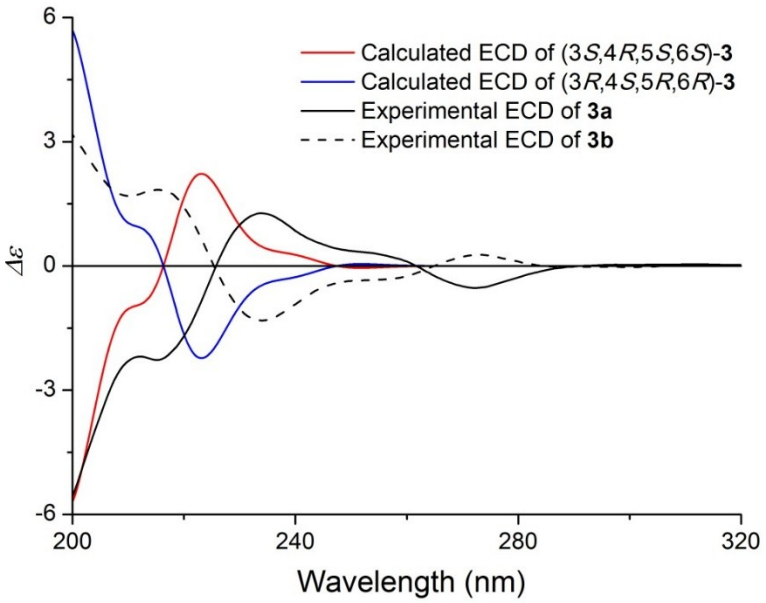


S46. The ^{1}H NMR Spectrum (600 MHz，$CDCl_3$)of compound 3ab

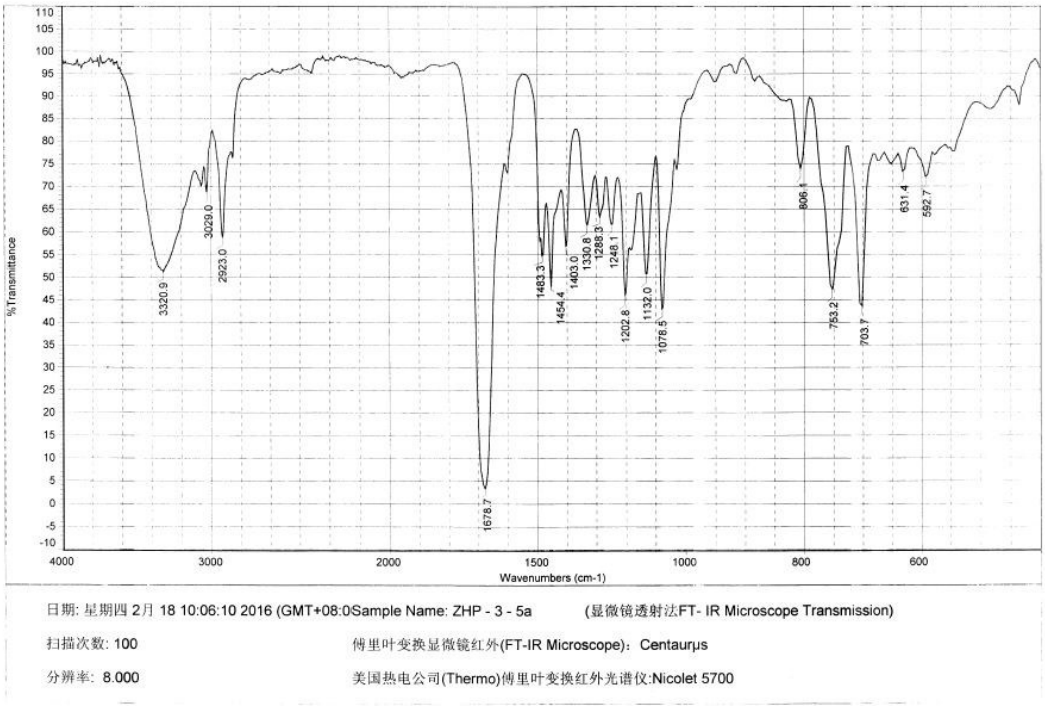


S47. The Calculated ECD spectra of (3*S*, 4*R*, 5*S*, 6*S*), (3*R*, 4*S*, 5*R*, 6*R*)-3 and the experimental ECD spectrum of 3a and 3b

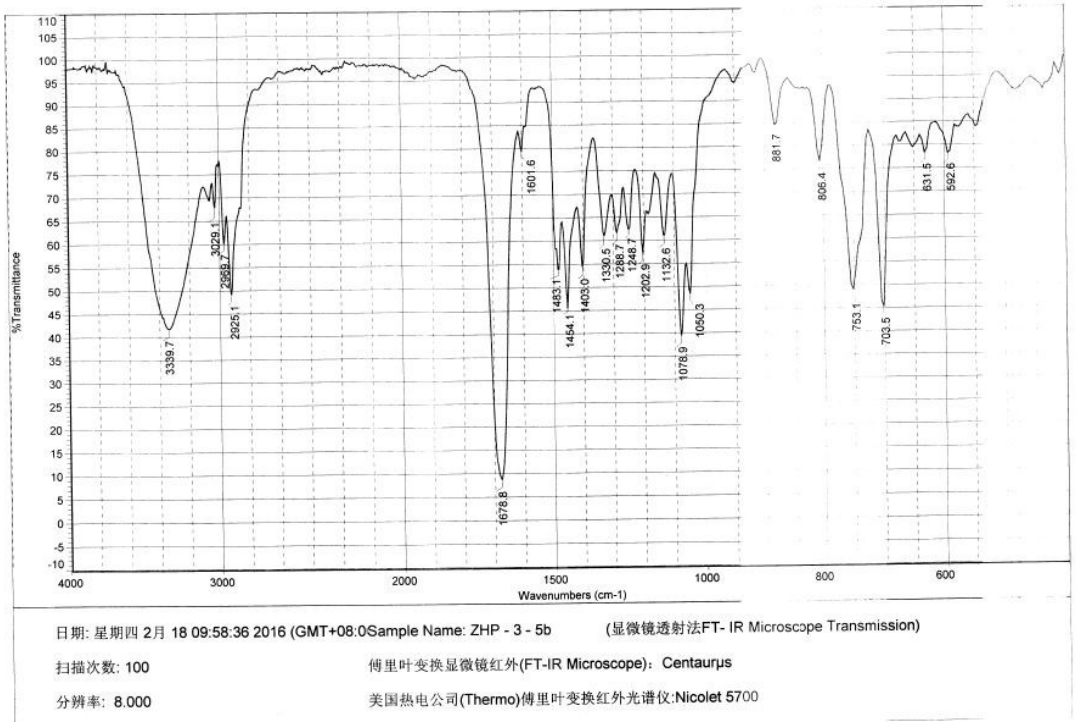




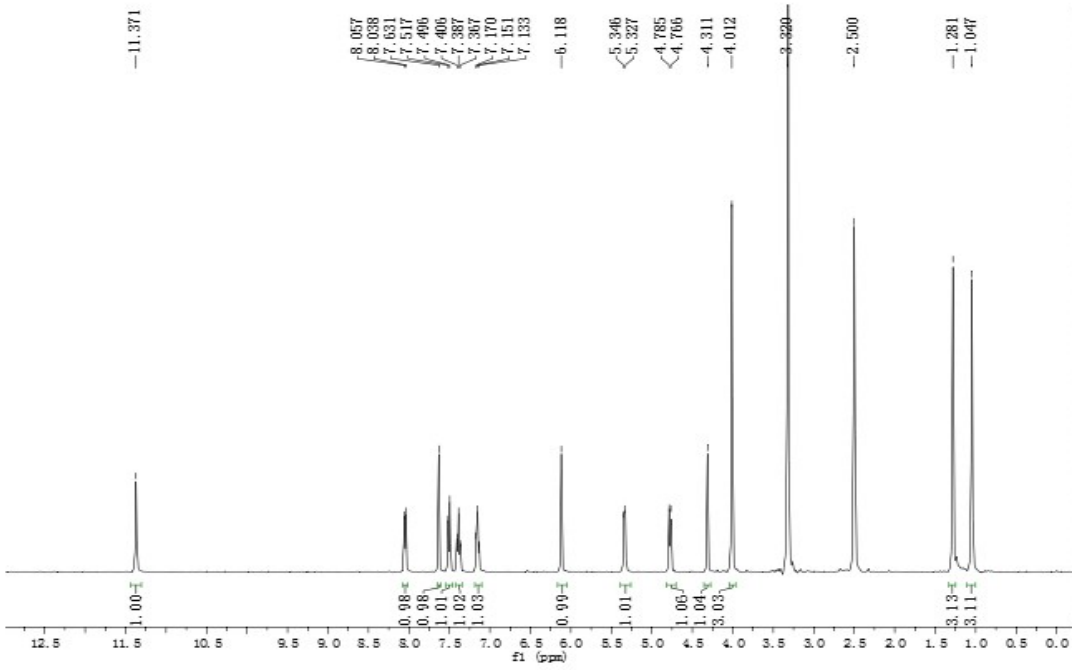
S48. The IR Spectrum of compound 3a



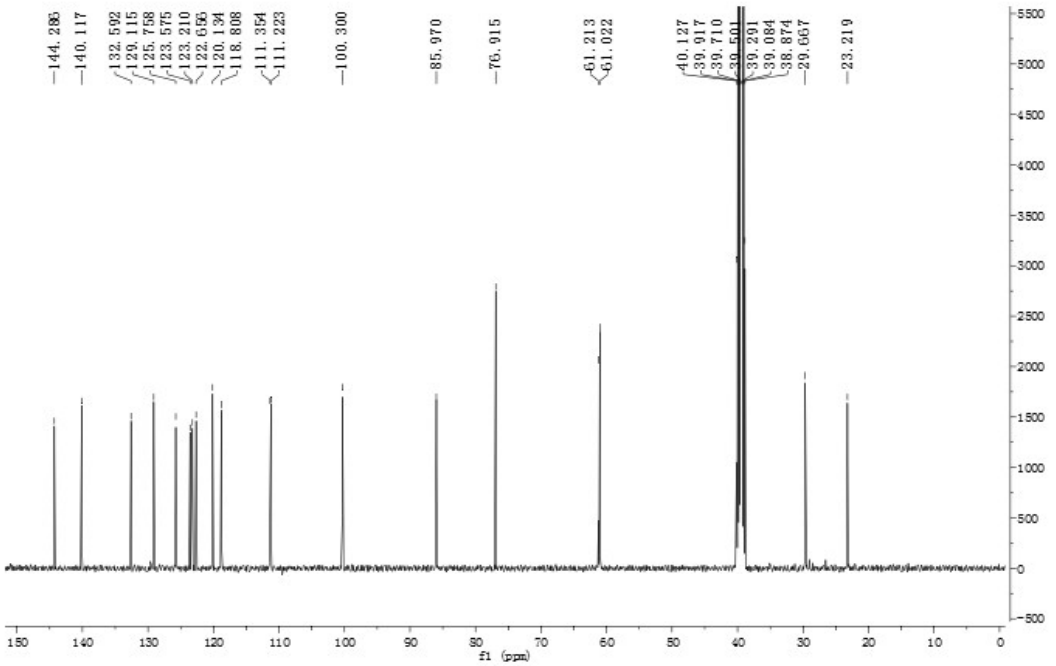
S49. The IR Spectrum of compound 3b



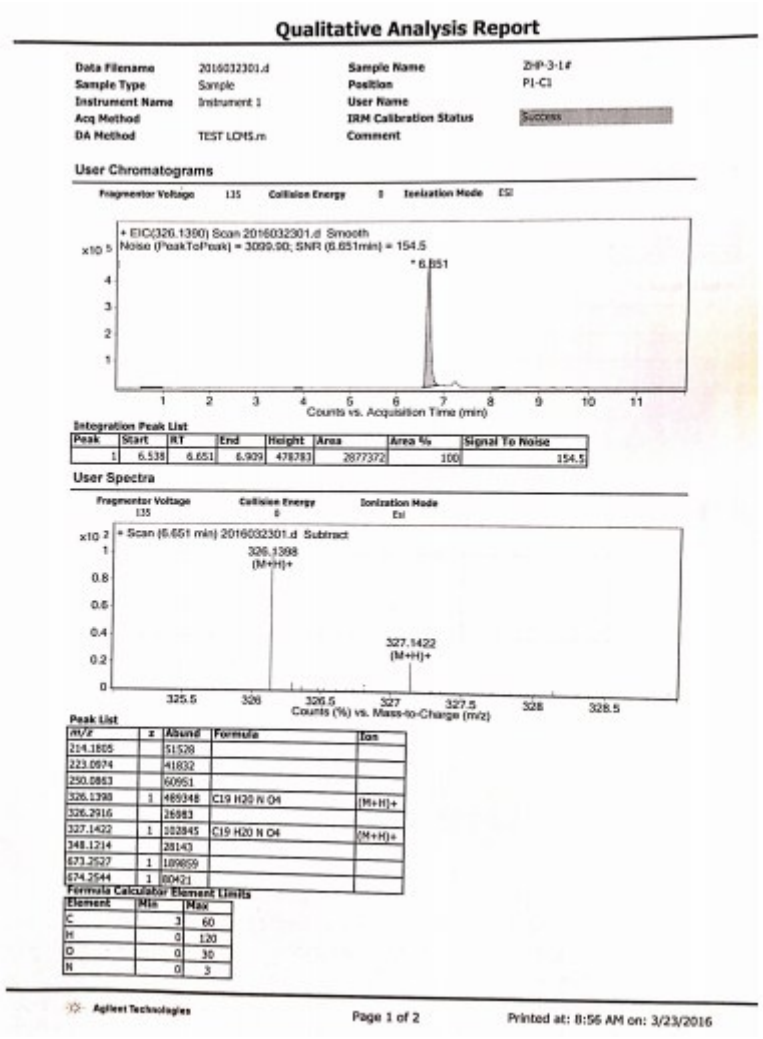
S50. The ^{1}H NMR Spectrum (600 MHz，DMSO-d_6) of compound 4



S51. The ^{13}C NMR Spectrum (150 MHz，DMSO-d_6) of compound 4



S52. The HRESIMS Spectrum of compound 4



Qualitative Analysis Report

Data Filename	2016032301.d	Sample Name	ZHP-3-1#
Sample Type	Sample	Position	P1-C3
Instrument Name	Instrument 1	User Name	
Acq Method		IRM Calibration Status	Success
DA Method	TEST LCMS.m	Comment	

User Chromatograms

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI

Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.538	6.651	6.909	478783	2877372	100	154.5

User Spectra

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI

Peak List

m/z	z	Abund	Formula	Ion
214.1805		51528		
223.0874		41832		
250.0863		60951		
326.1398	1	489348	C19 H20 N O4	(M+H)+
326.2916		26983		
327.1422	1	102845	C19 H20 N O4	(M+H)+
348.1214		28143		
673.2527	1	109859		
674.2544	1	60421		

Formula Calculator Element Limits

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

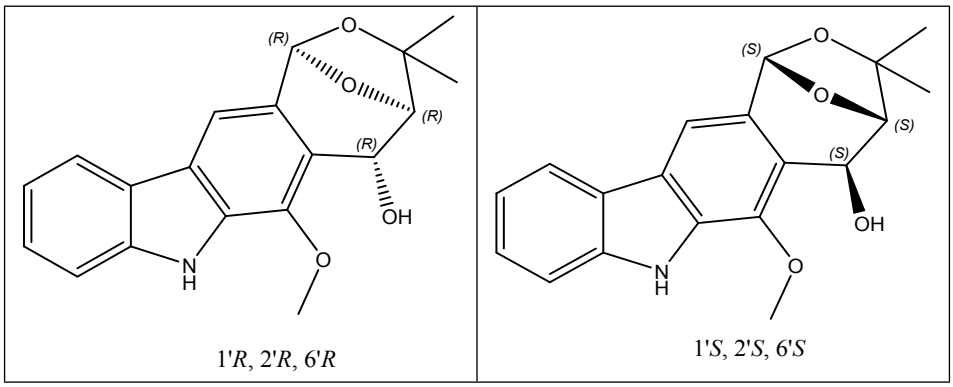
Agilent Technologies Page 1 of 2 Printed at: 8:56 AM on: 3/23/2016

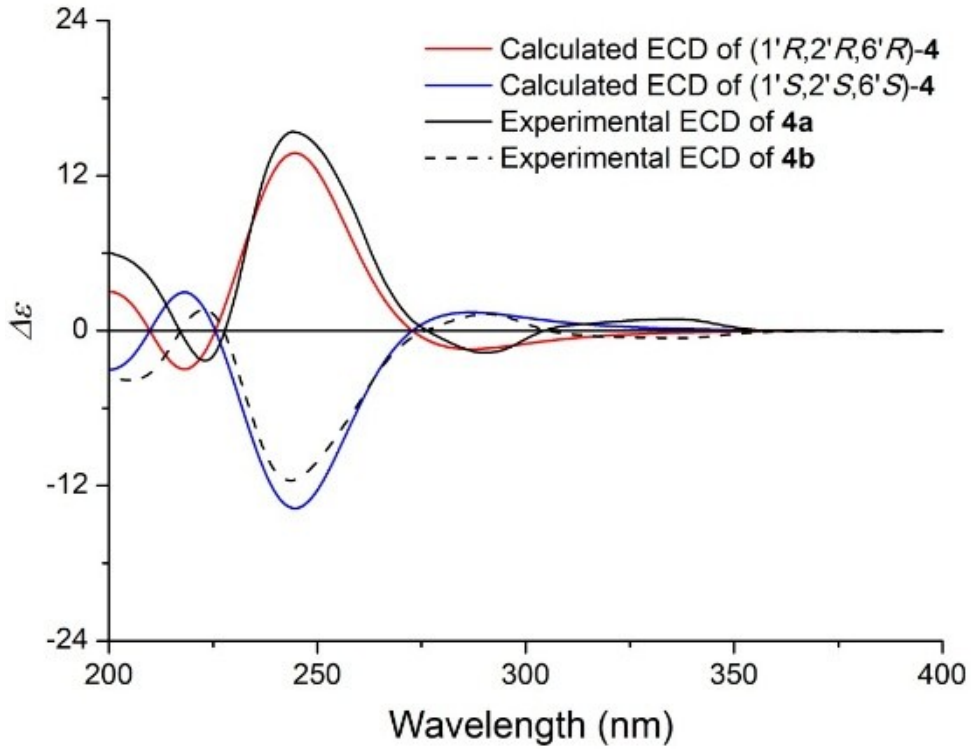
MS Formula Results: + Scan (6.651 min) Sub (2016032301.d)

m/z	Ion	Formula	Abundance
326.1398	(M+H)+	C19 H20 N O4	489347.8

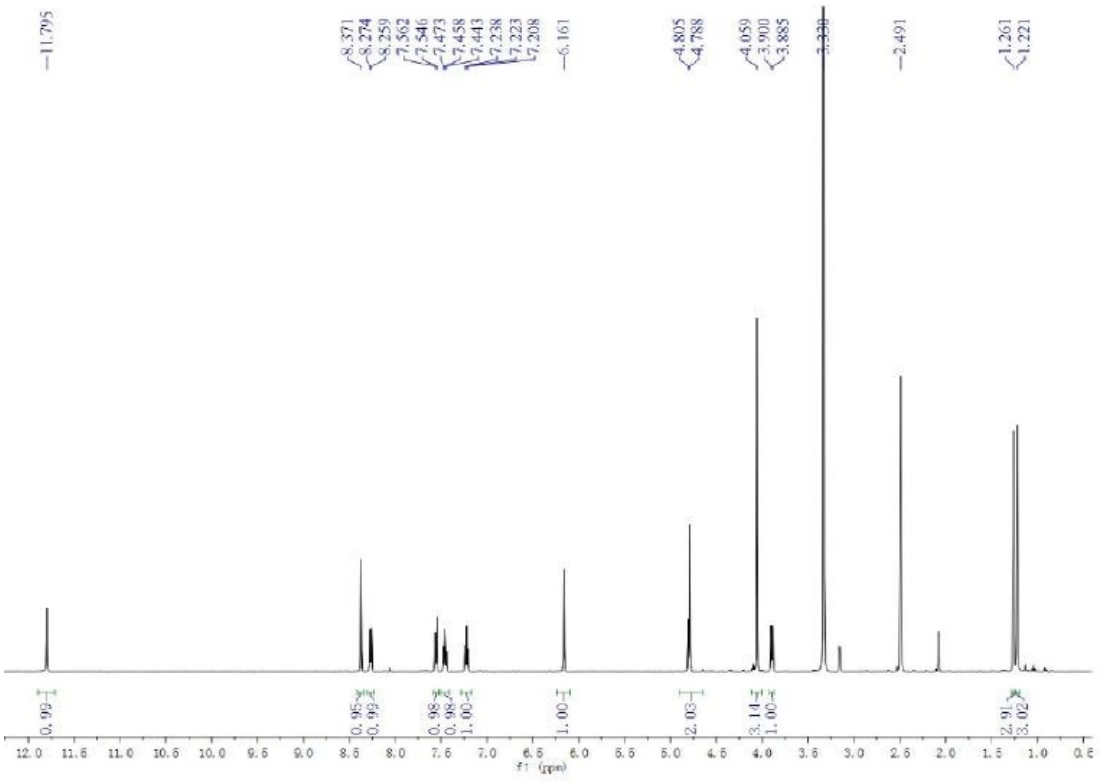
Best	Formula (M)	Ion Formula	Score	Cross Scc	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
✓	C19 H19 N O4	C19 H20 N O4	99.78		325.1325	325.1314	326.1387	-3.37	3.37	99.64	99.99	99.82	11
	C18 H23 N O Si2	C18 H24 N O Si2	96.69		325.1325	325.1318	326.1391	-2.15	2.15	99.85	89.01	99.58	10
	C9 H27 N3 O4 Si3	C9 H28 N3 O4 Si3	95.5		325.1325	325.1309	326.1382	-4.89	4.89	99.25	86.4	98.91	1
	C13 H25 Cl2 N3 O2	C13 H26 Cl2 N3 O2	73.39		325.1325	325.1324	326.1397	-0.39	0.39	100	7.58	99.16	2

S53. The Calculated ECD spectra of (1'*R*, 2'*R*, 6'*R*), (1'*S*, 2'*S*, 6'*S*)-isomers and the experimental ECD spectrum of 4a and 4b

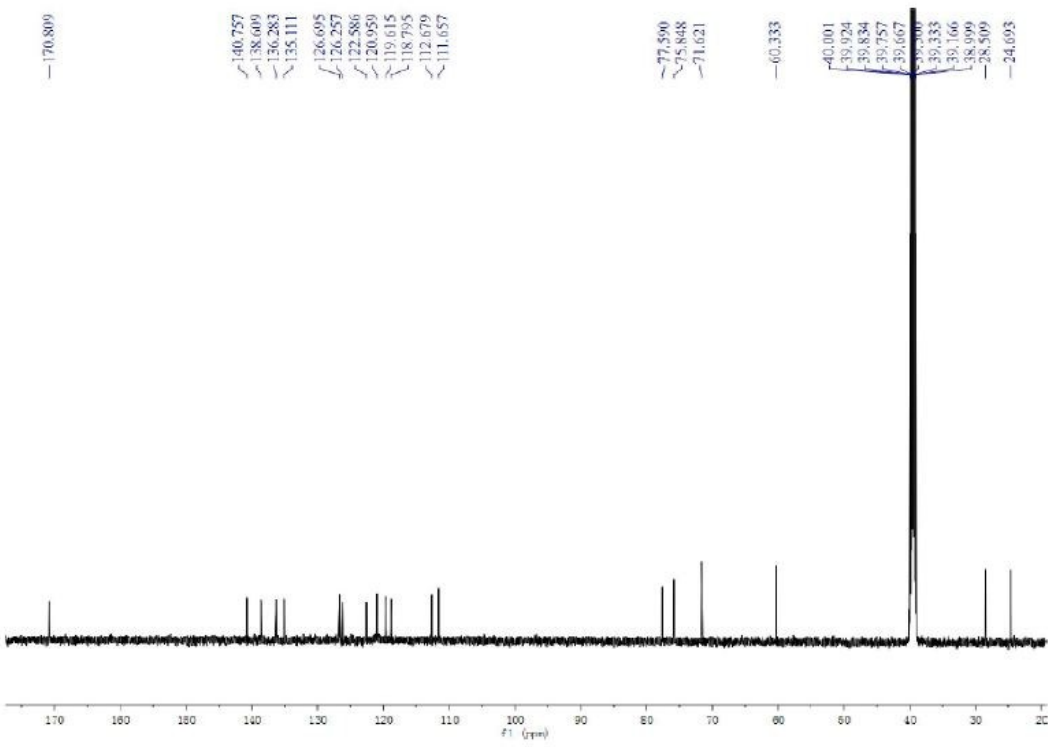




S54. The ^{1}H NMR Spectrum (600 MHz，DMSO-d_6) of compound 5



S55. The ^{13}C NMR Spectrum (150 MHz，DMSO-d_6) of compound 5



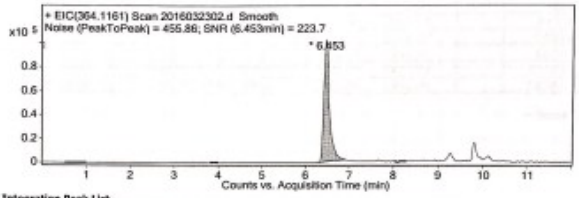
S56. The HRESIMS Spectrum of compound 5

Qualitative Analysis Report

Data Filename	2016032302.d	**Sample Name**	ZHP-C15
Sample Type	Sample	**Position**	P1-C2
Instrument Name	Instrument 1	**User Name**	
Acq Method		**IRM Calibration Status**	Success
DA Method	TEST LCMS.m	**Comment**	

User Chromatograms

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI

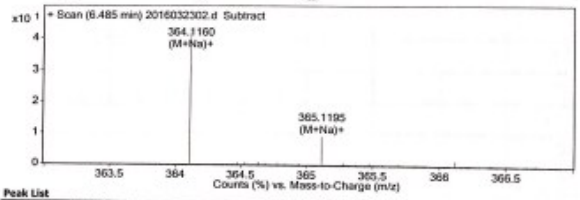


Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	6.292	6.453	6.92	101962	920921	100	223.7

User Spectra

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode Esi



Peak List

m/z	z	Abund	Formula	Ion
252.0648		63196		
266.0811	1	227533		
267.0842	1	39704		
324.1231		18831		
364.116	1	95228	C19 H19 N Na O5	(M+Na)+
365.1195	1	20401	C19 H19 N Na O5	(M+Na)+
380.0904		16856		
705.2417	1	186358		
706.2453	1	76502		
707.2466	1	20237		

Formula Calculator Element Limits

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

Agilent Technologies Page 1 of 2 Printed at: 9:12 AM on: 3/23/2016

MS Formula Results: + Scan (6.485 min) Sub (2016032302.d)

m/z	Ion	Formula	Abundance
364.116	(M+Na)+	C19 H19 N Na O5	95228

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
☑	C19 H19 N O5	C19 H19 N Na O5	99.96		341.1268	341.1263	364.1155	-1.37	1.37	99.95	99.97	99.97	11
☐	C10 H23 N3 O8 Si	C10 H23 N3 Na O8 Si	98.53		341.1268	341.1254	364.1147	-3.99	3.99	99.55	96.13	99.36	2
☐	C18 H23 N O2 Si2	C18 H23 N Na O2 Si2	96.82		341.1268	341.1267	364.116	-0.2	0.2	100	89.39	99.39	13
☐	C9 H27 N3 O5 Si3	C9 H27 N3 Na O5 Si3	95.71		341.1268	341.1259	364.1151	-2.82	2.82	99.77	86.66	98.42	1
☐	C13 H25 Cl2 N3 O3	C13 H25 Cl2 N3 Na O3	73.04		341.1268	341.1273	364.1165	1.48	1.48	99.94	6.19	99.46	2
☐	C12 H29 Cl2 N3 Si2	C12 H29 Cl2 N3 Na Si2	72.94		341.1268	341.1277	364.1169	2.64	2.64	99.8	6.63	98.77	1

S57. The Calculated ECD spectra of (1'*R*, 2'*R*), (1'*S*, 2'*S*)-5 and the experimental ECD spectrum of 5a and 5b