Supporting Information

Trinorlabdane diterpenoid alkaloids featuring an unprecedented skeleton with anti-inflammatory and anti-viral activities from *Forsythia suspensa*

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Contexts of Supporting Information

The elucidation of chemical structure

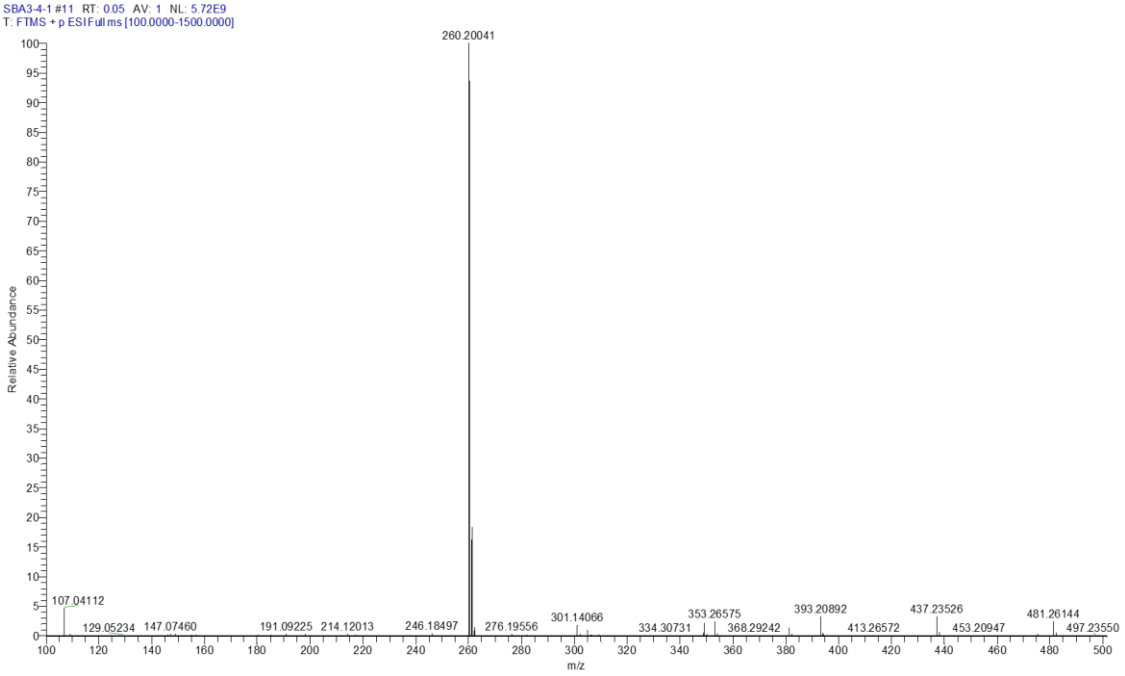
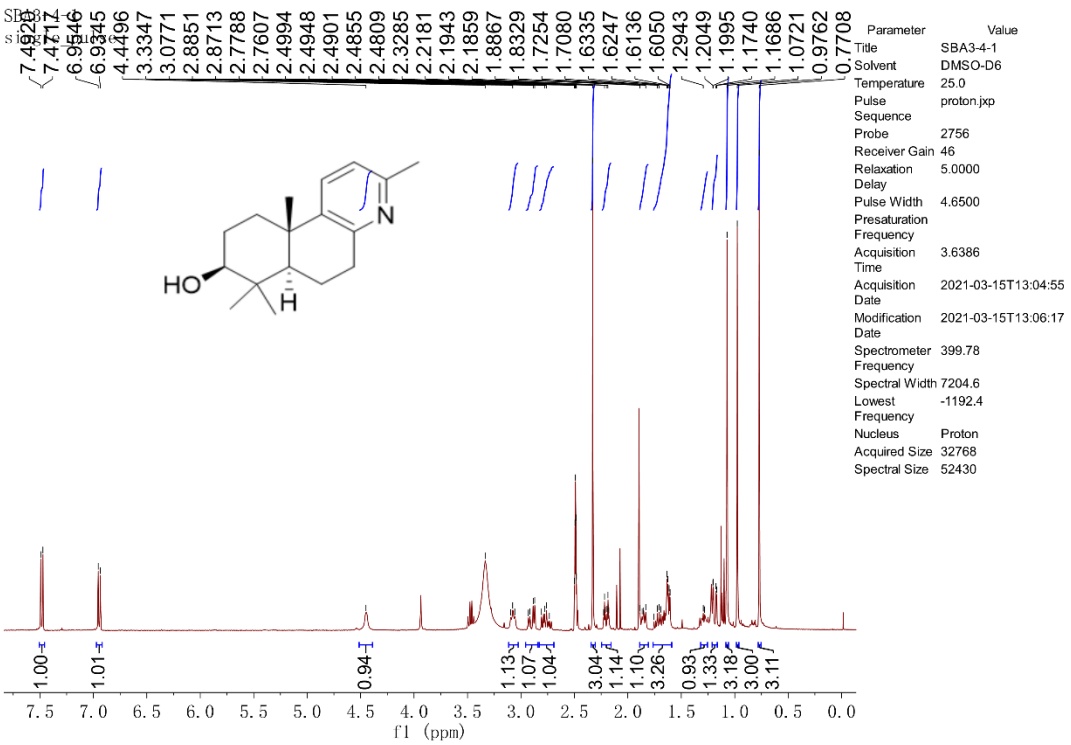
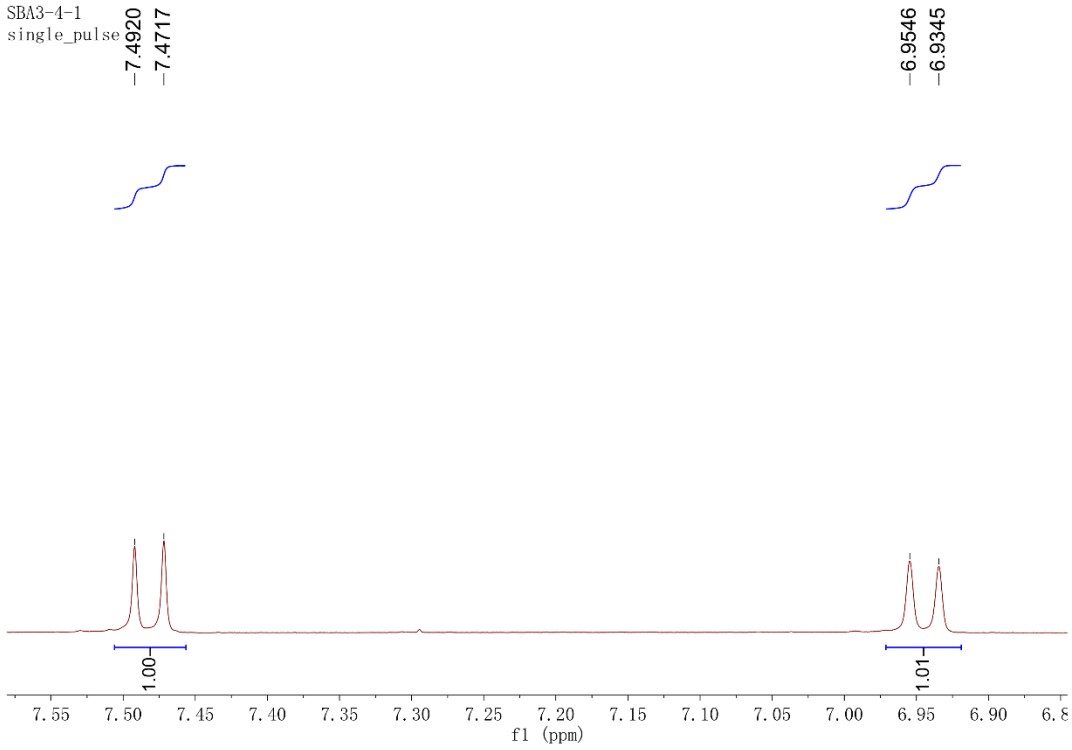


Figure S1. HR-ESI spectrum of 1

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6.9345
1.00
1.01
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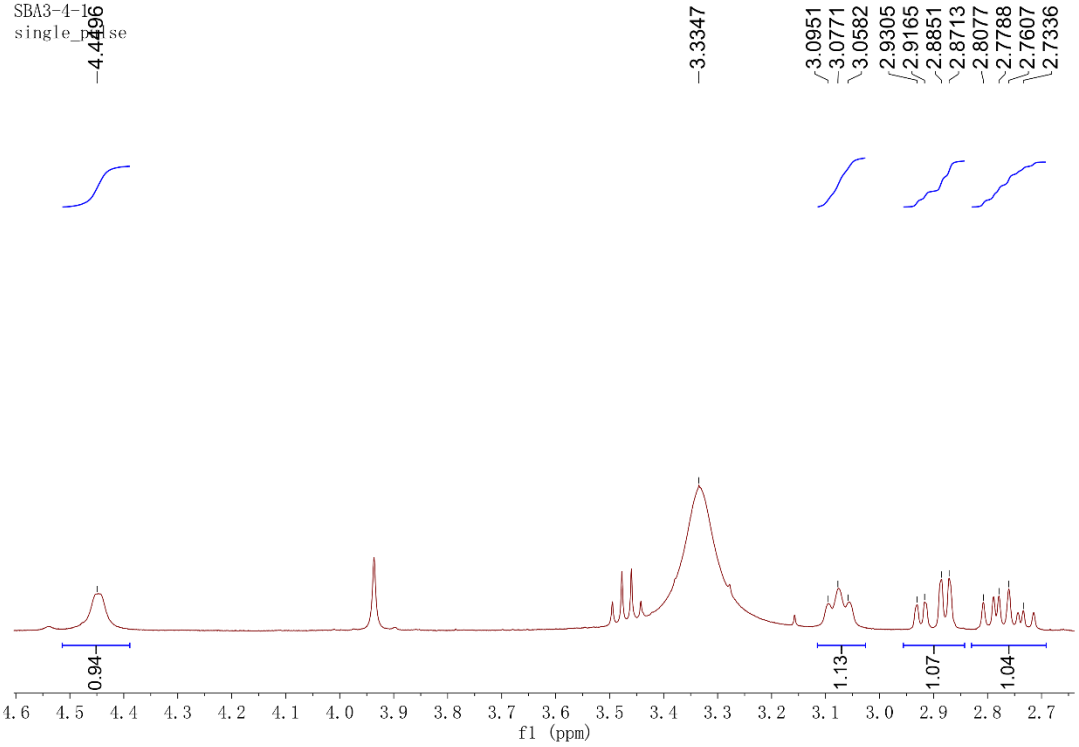
f1 (ppm)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3.0951
3.0771
3.0582
2.9305
2.9165
2.8851
2.8713
2.8077
2.7788
2.7607
2.7336
0.94
1.13
1.07
1.04
4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7
f1 (ppm)

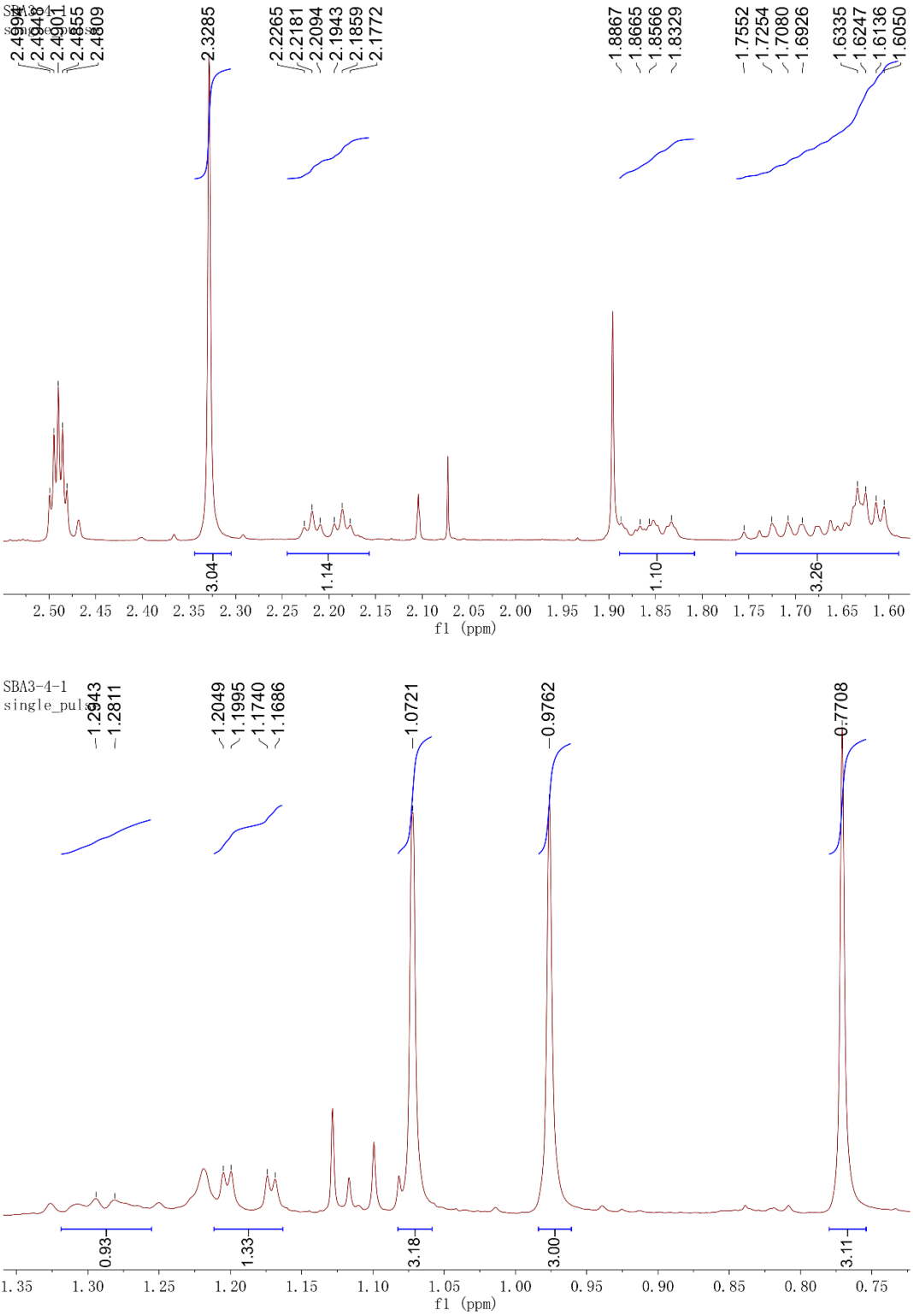
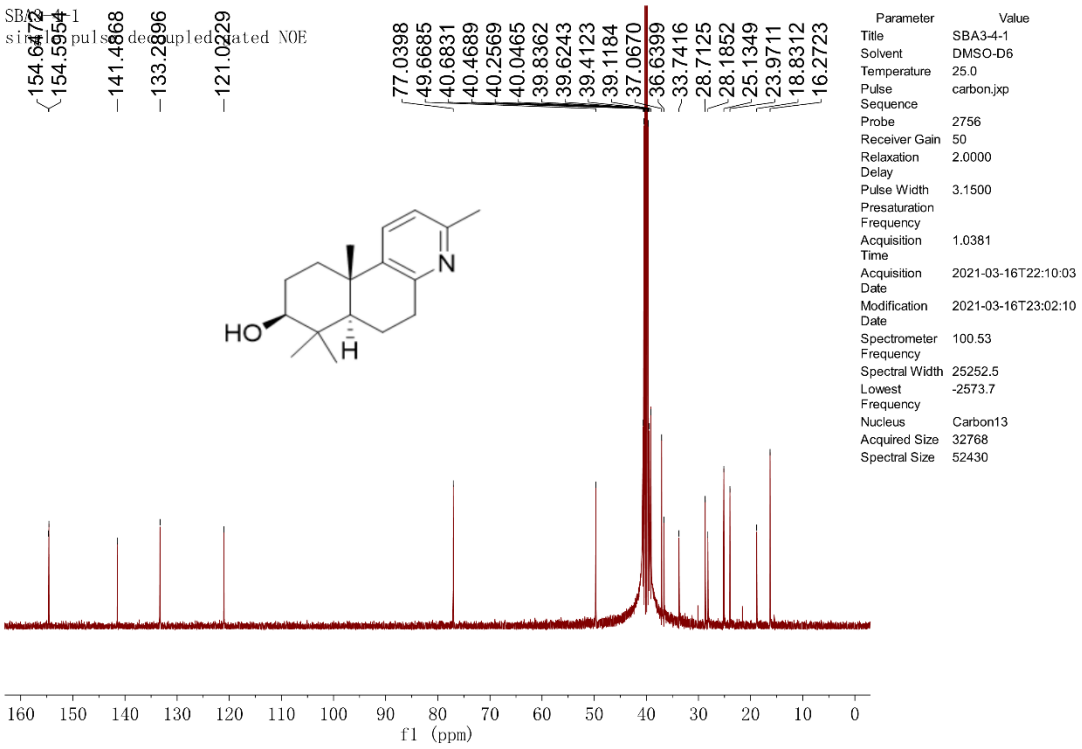


Figure S2. ^{1}H NMR spectrum of 1 in DMSO-d$_6$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154.5954
141.4868
133.2896
121.0229
77.0398
49.6685
40.6831
40.4689
40.2569
40.0465
39.8362
39.6243
39.4123
39.1184
37.0670
36.6399
33.7416
28.7125
28.1852
25.1349
23.9711
18.8312
16.2723
HO
N
H
Parameter Value
Title SBA3-4-1
Solvent DMSO-D6
Temperature 25.0
Pulse Sequence carbon.jxp
Probe 2756
Receiver Gain 50
Relaxation Delay 2.0000
Pulse Width 3.1500
Presaturation Frequency
Acquisition Time 1.0381
Acquisition Date 2021-03-16T22:10:03
Modification Date 2021-03-16T23:02:10
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Spectral Width 25252.5
Lowest Frequency -2573.7
Nucleus Carbon13
Acquired Size 32768
Spectral Size 52430
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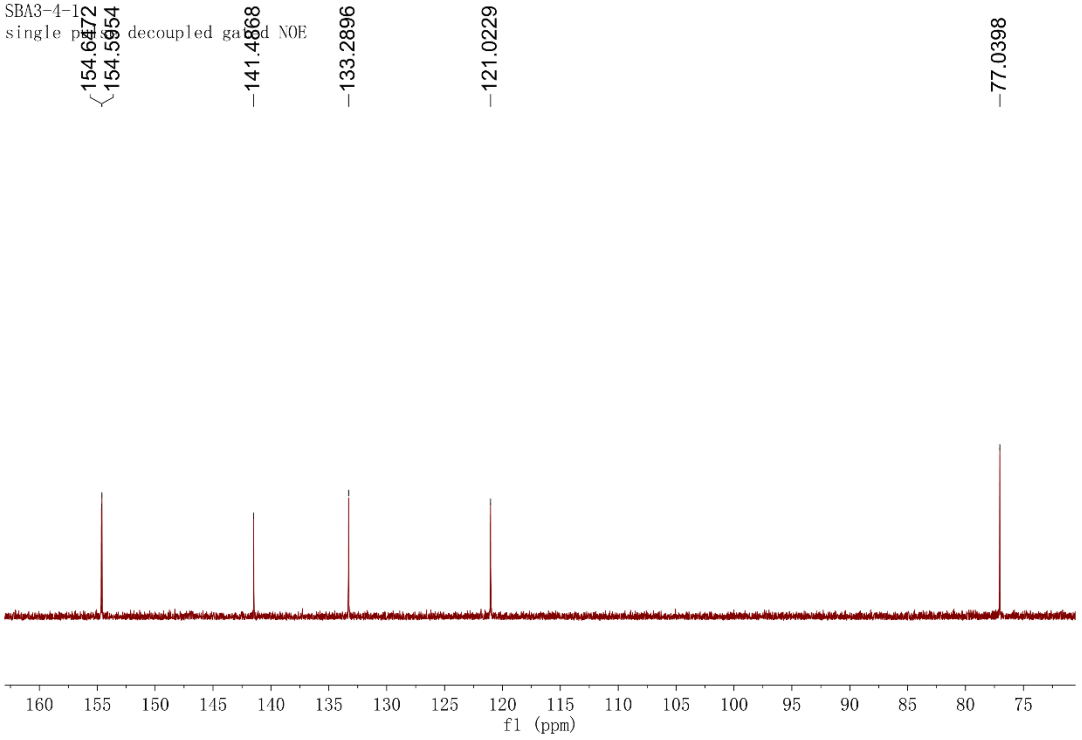
f1 (ppm)


SBA3-4-1
single puls decoupled gated NOE
154.6472
154.5954
141.4868
133.2896
121.0229
77.0398
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75
f1 (ppm)

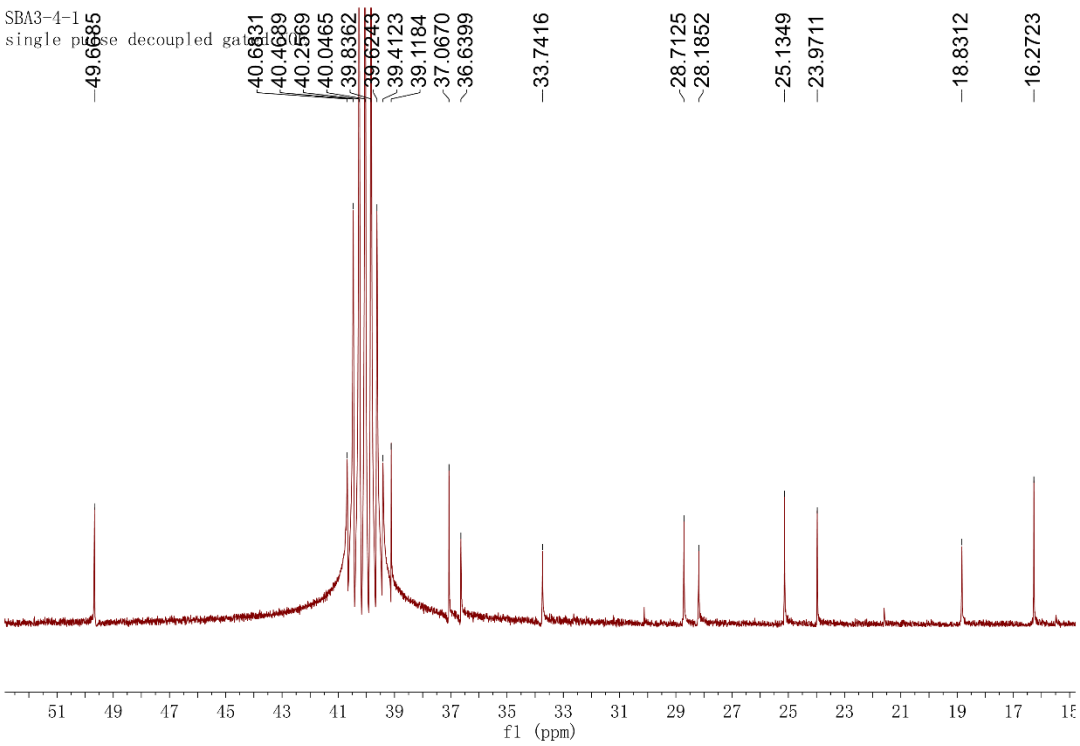
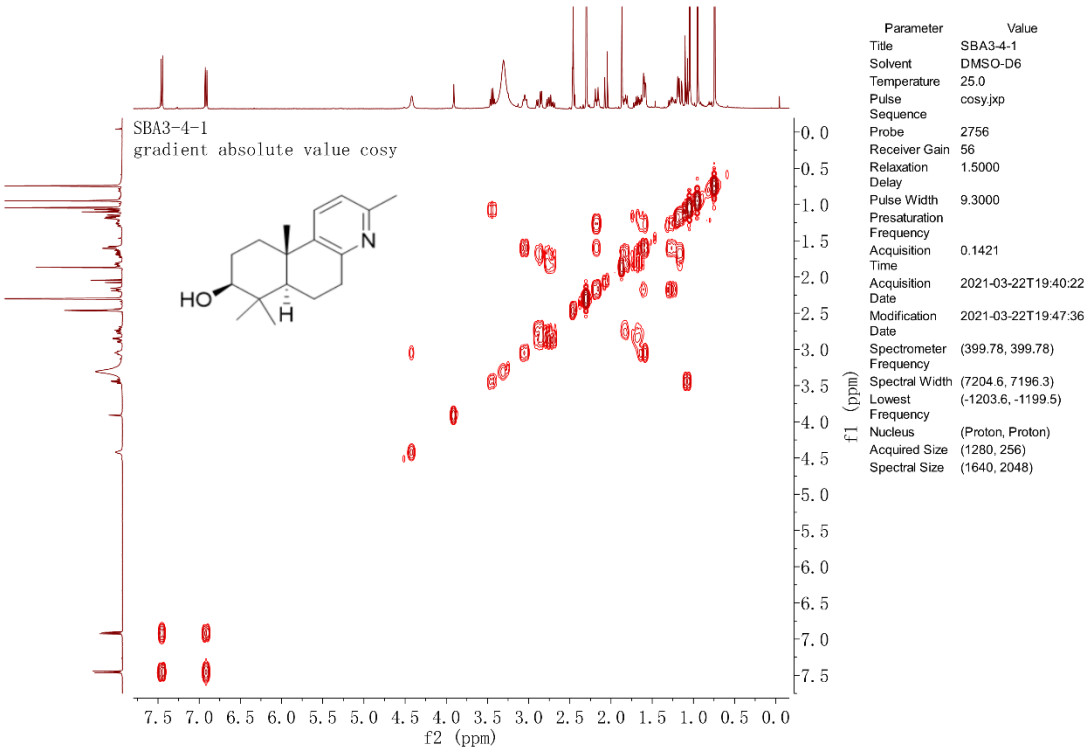


Figure S3. ^{13}C NMR spectrum of 1 in DMSO-d$_6$



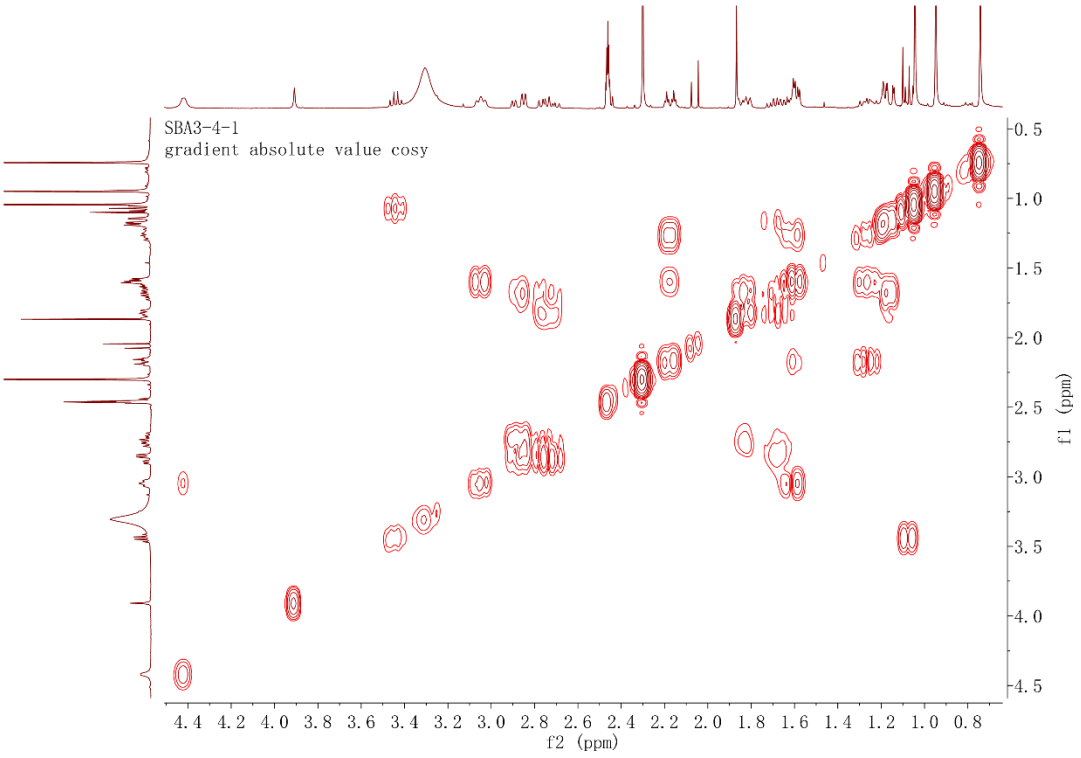
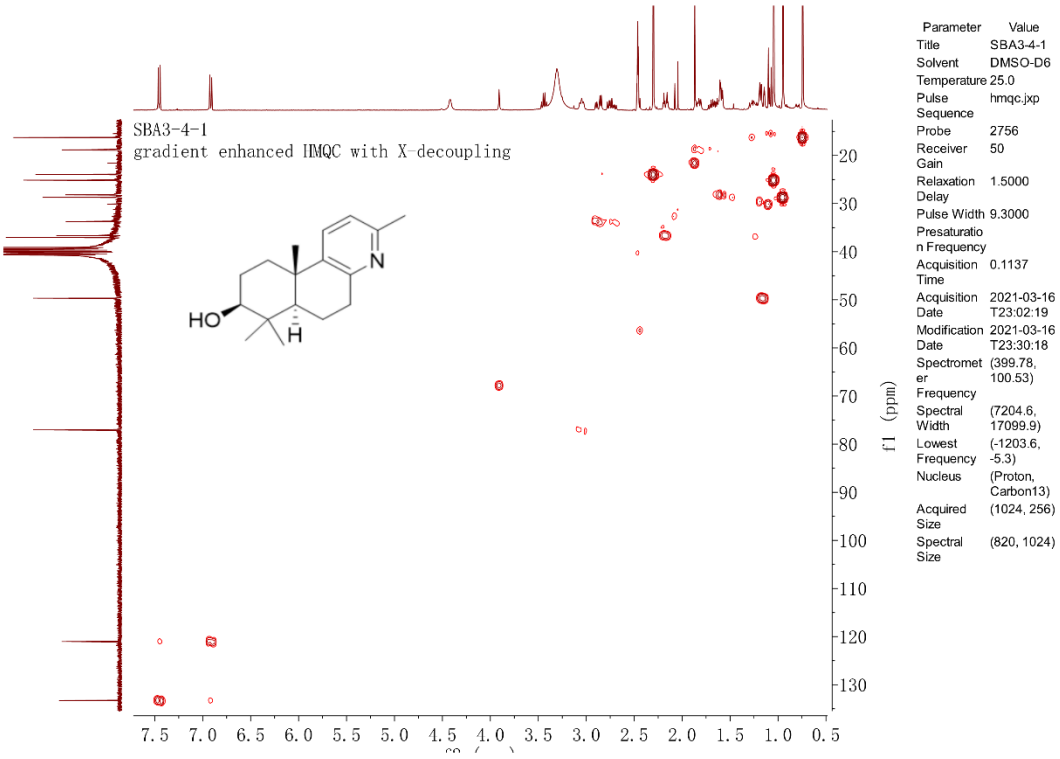


Figure S4. ^{1}H-^{1}H COSY spectrum of 1 in DMSO-d$_6$



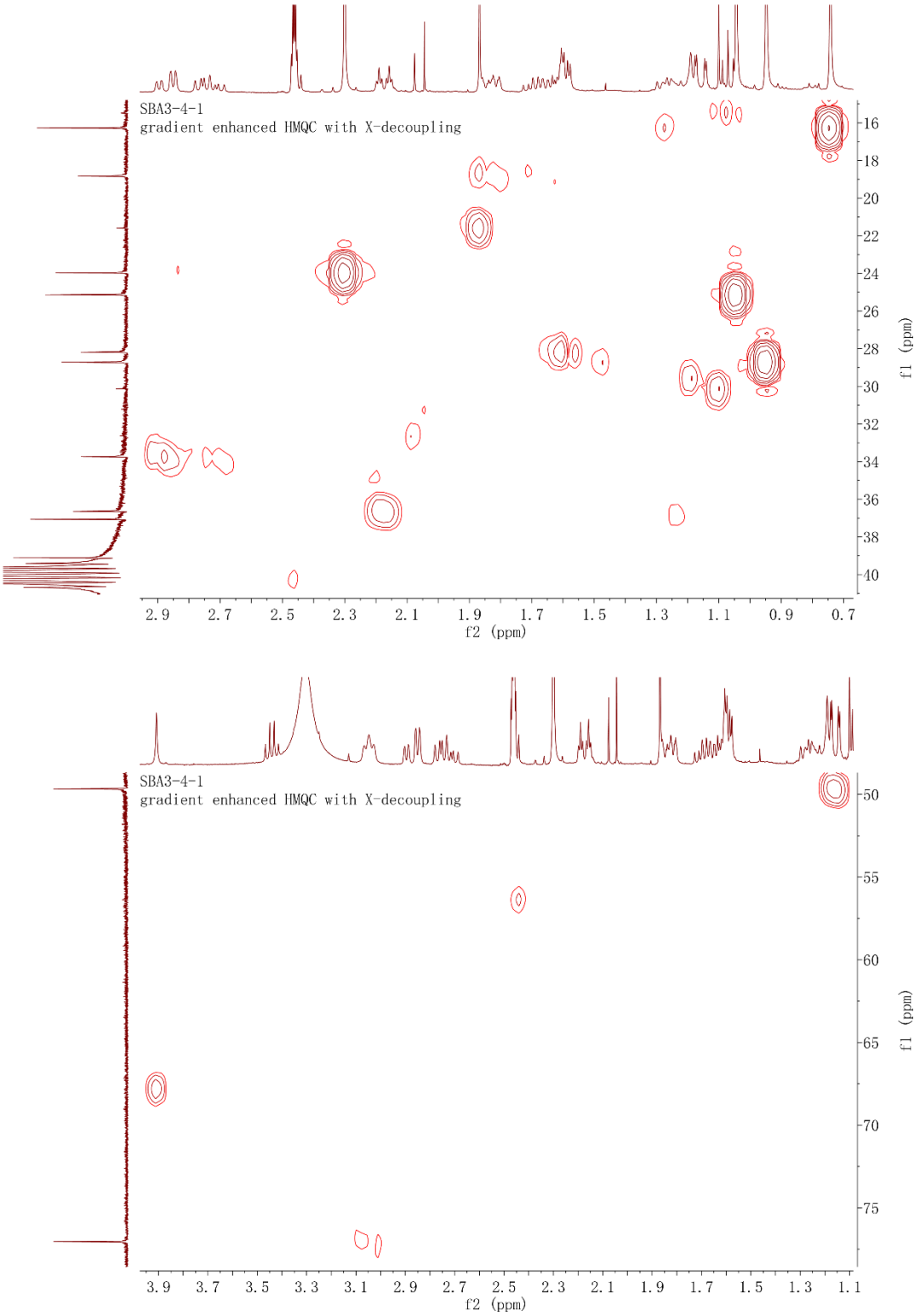
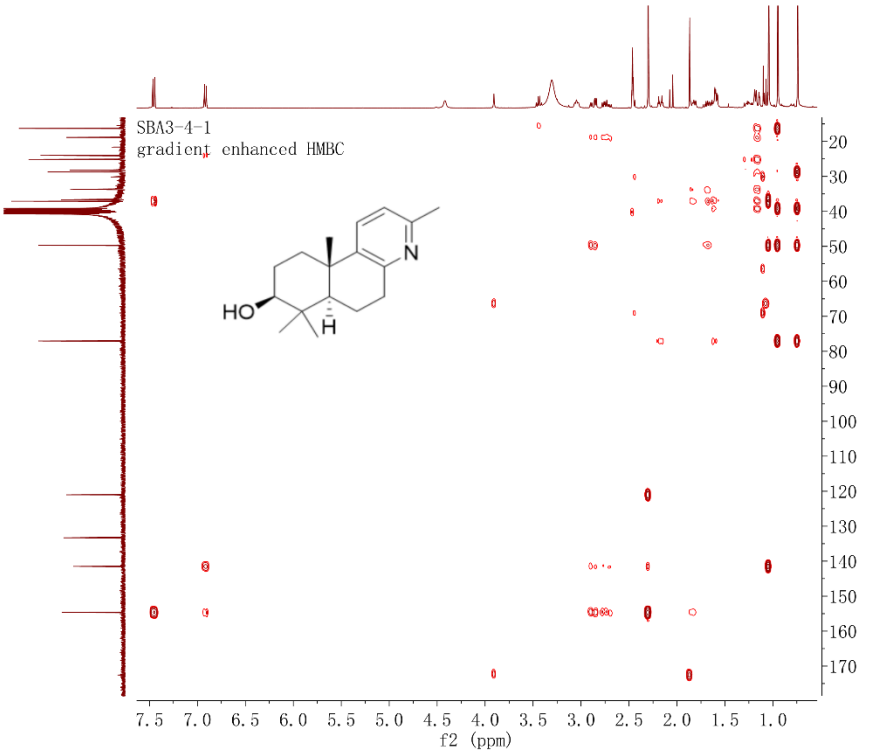
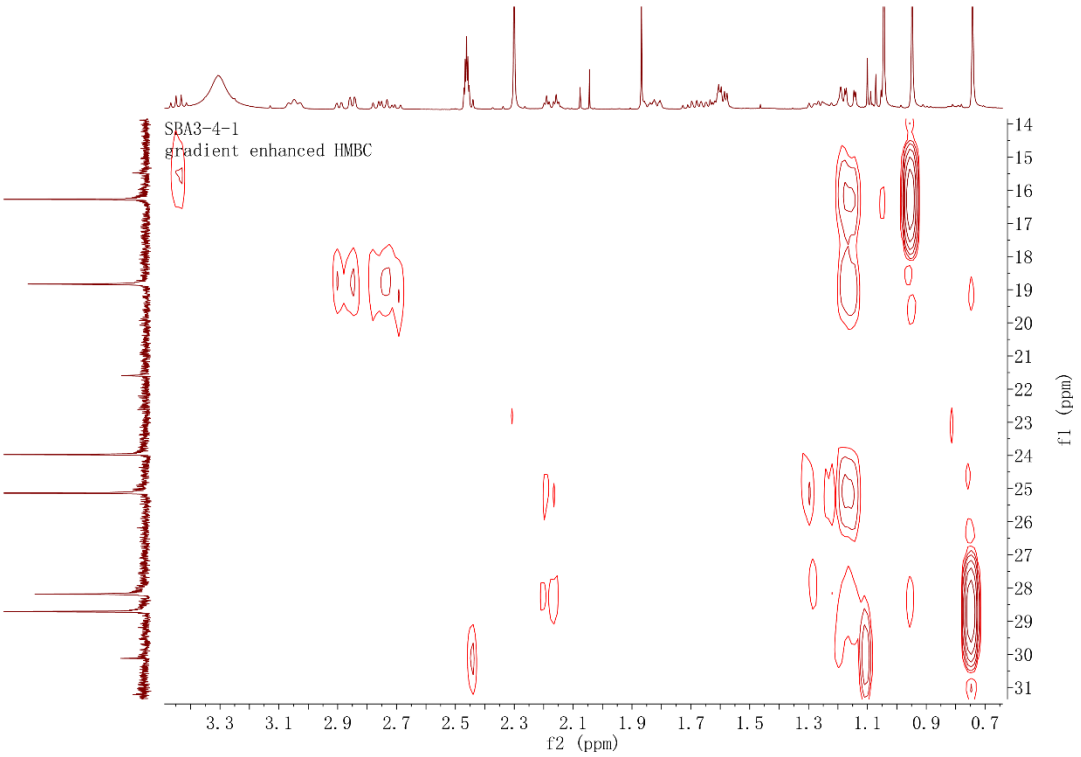


Figure S5. HMQC spectrum of 1 in DMSO-d_6



Parameter	Value
Title	SBA3-4-1
Solvent	DMSO-D6
Temperature	25.0
Pulse Sequence	hmbc.jxp
Probe	2756
Receiver Gain	50
Relaxation Delay	1.5000
Pulse Width	9.3000
Presaturation Frequency	
Acquisition Time	0.2274
Acquisition Date	2021-03-16T 16:49:57
Modification Date	2021-03-16T 17:20:48
Spectrometer Frequency	(399.78, 100.53)
Spectral Width	(7204.6, 25150.9)
Lowest Frequency	(-1203.6, -2522.9)
Nucleus	(Proton, Carbon13)
Acquired Size	(2048, 256)
Spectral Size	(1640, 1024)



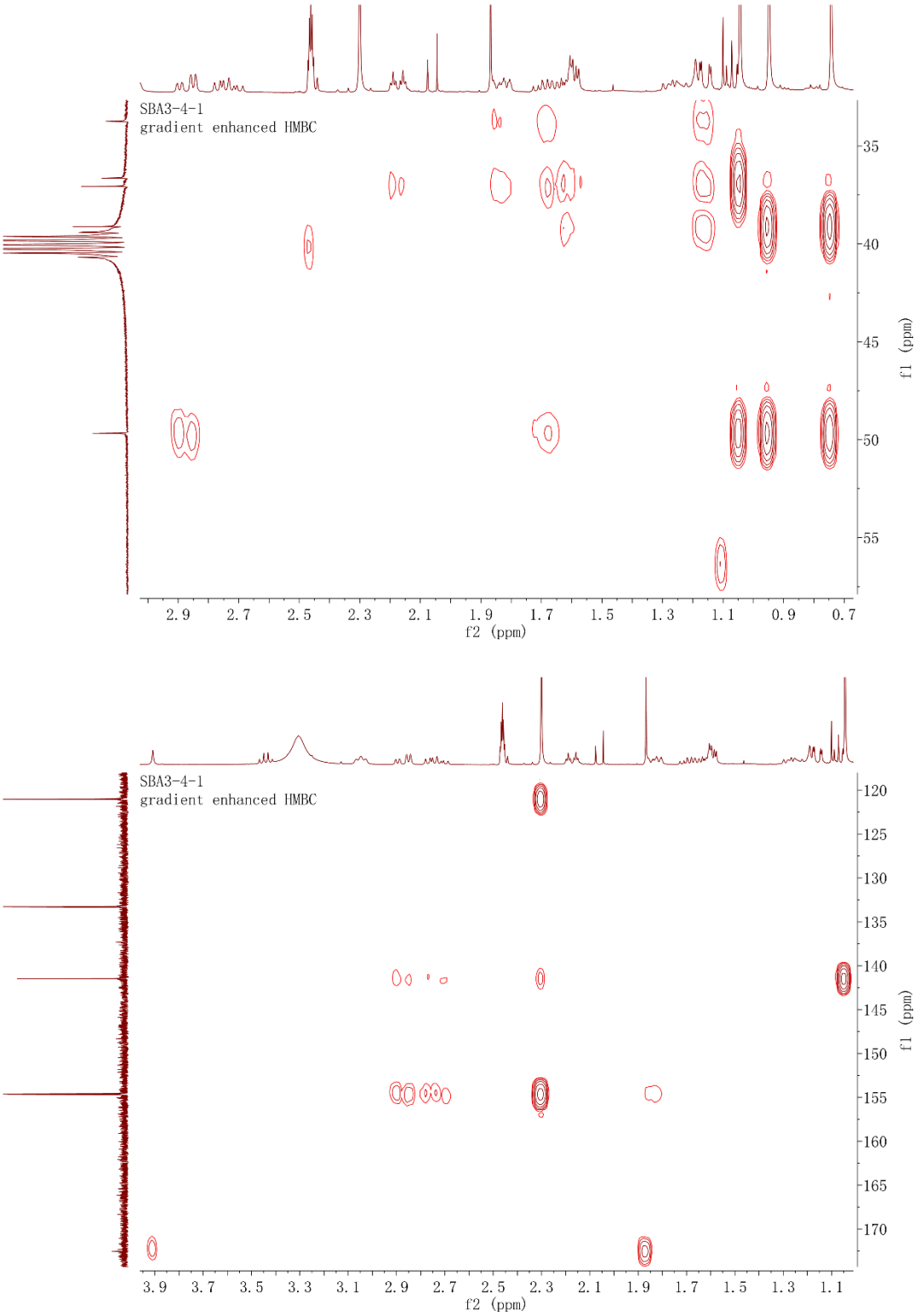
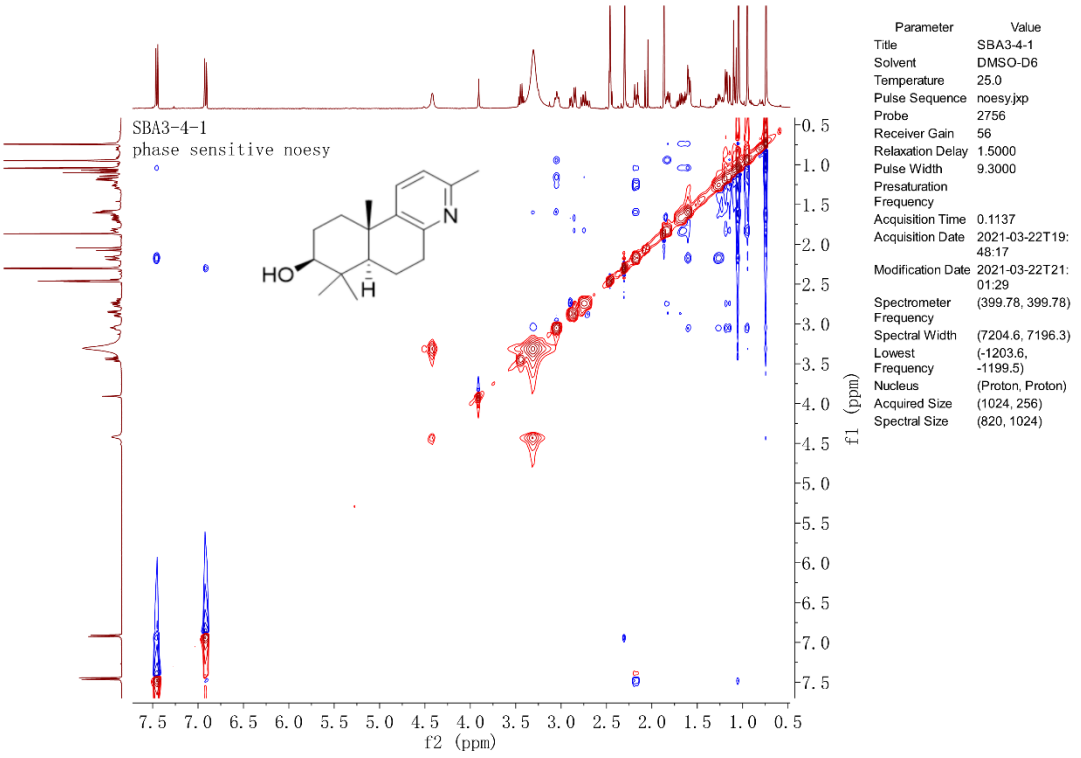
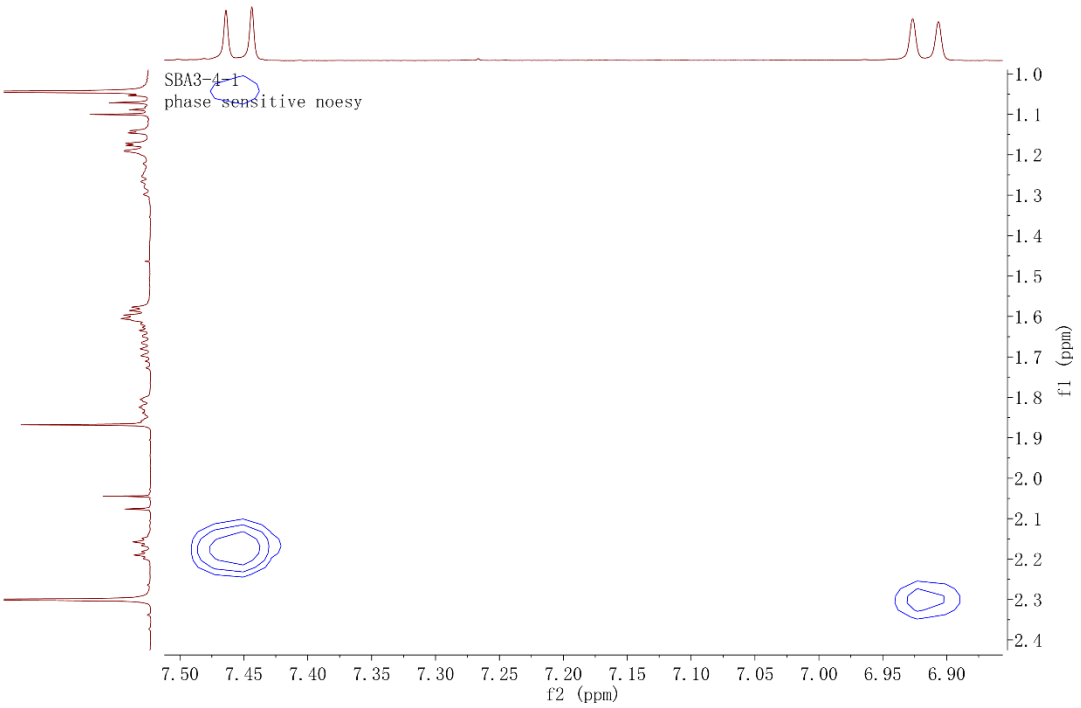


Figure S6. HMBC spectrum of 1 in DMSO-d_6



Parameter	Value
Title	SBA3-4-1
Solvent	DMSO-D6
Temperature	25.0
Pulse Sequence	noesy.jxp
Probe	2756
Receiver Gain	56
Relaxation Delay	1.5000
Pulse Width	9.3000
Presaturation Frequency	
Acquisition Time	0.1137
Acquisition Date	2021-03-22T19:48:17
Modification Date	2021-03-22T21:01:29
Spectrometer Frequency	(399.78, 399.78)
Spectral Width	(7204.6, 7196.3)
Lowest Frequency	(-1203.6, -1199.5)
Nucleus	(Proton, Proton)
Acquired Size	(1024, 256)
Spectral Size	(820, 1024)



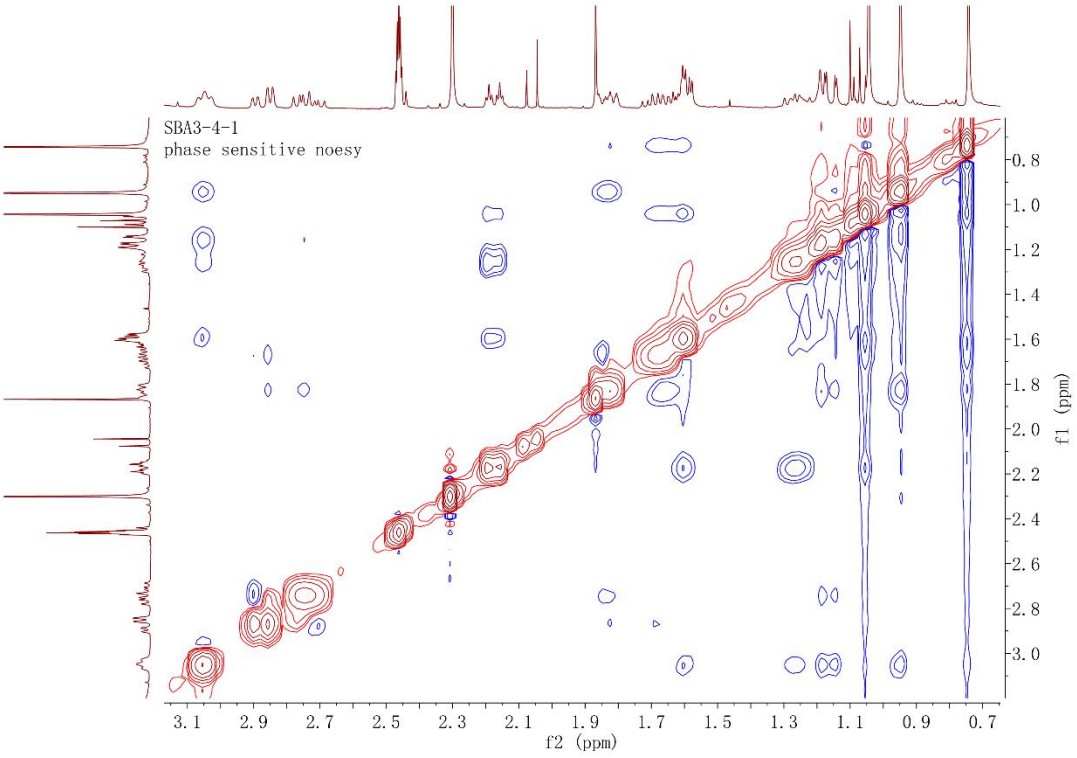
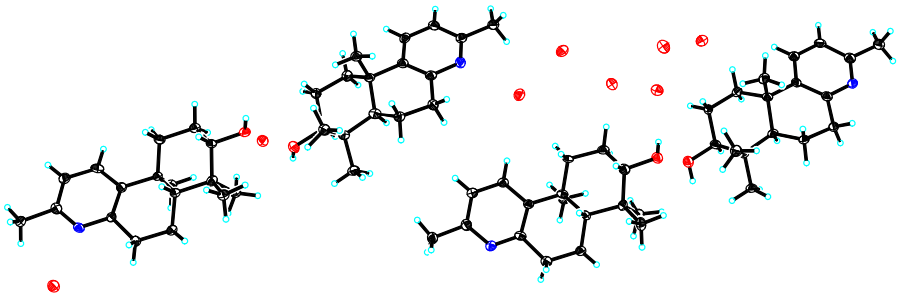


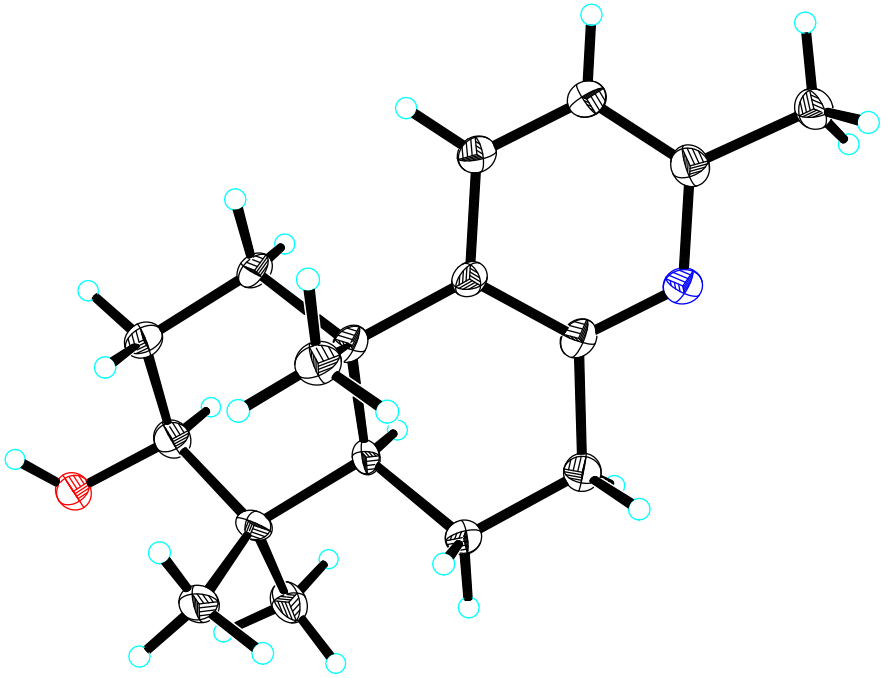
Figure S7. NOESY spectrum of 1 in DMSO-d6

Crystal data for yt_dsj2: $C_{17}H_{25}NO•2(H_2O)$, M = 295.41, a = 9.7060(9) Å, b = 24.576(2) Å, c = 14.6471(17) Å, α = 90°, β = 109.129(4)°, γ = 90°, V = 3300.9(6) Å^3, T = 100.(2) K, space group $P1211$, Z = 8, μ(Cu Kα) = 0.638 mm^{-1}, 47471 reflections measured, 12142 independent reflections (R_{int} = 0.1023). The final R_1 values were 0.1145 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.3024 ($I > 2\sigma(I)$). The final R_1 values were 0.1218 (all data). The final $wR(F^2)$ values were 0.3132 (all data). The goodness of fit on F^2 was 1.371. Flack parameter = -0.24(14).



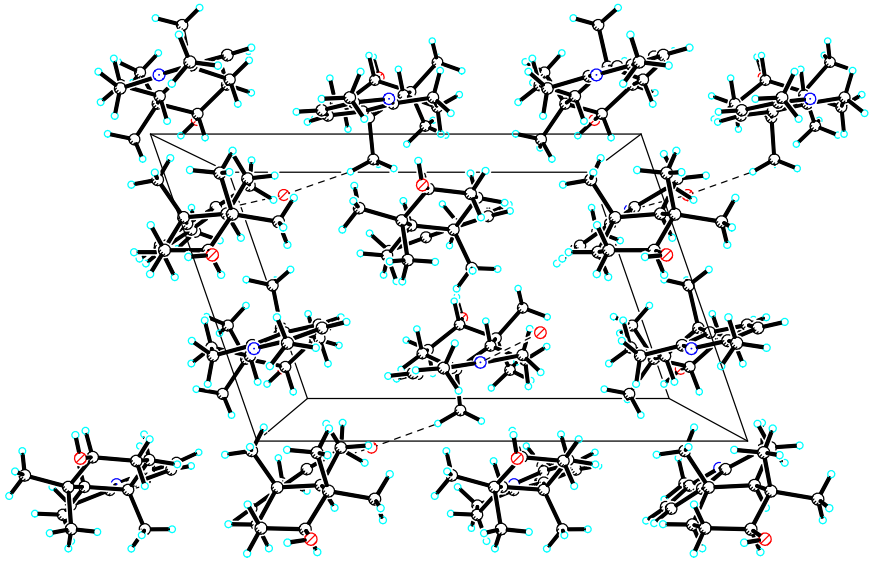
View of the molecules in an asymmetric unit.

Displacement ellipsoids are drawn at the 30% probability level.



View of a molecule of yt_dsj2 with the atom-labelling scheme.

Displacement ellipsoids are drawn at the 30% probability level.



View of the pack drawing of yt_dsj2.

Hydrogen-bonds are shown as dashed lines.

Table 1. Crystal data and structure refinement for yt_dsj2_0m.

Identification code	global	
Empirical formula	C17 H29 N O3	
Formula weight	295.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 9.7060(9) Å	α= 90°.
	b = 24.576(2) Å	β= 109.129(4)°.
	c = 14.6471(17) Å	γ = 90°.
Volume	3300.9(6) $Å^3$	
Z	8	
Density (calculated)	1.189 Mg/m^3	
Absorption coefficient	0.638 mm^{-1}	
F(000)	1296	
Crystal size	0.650 x 0.110 x 0.080 mm^3	
Theta range for data collection	3.19 to 73.50°.	
Index ranges	-11<=h<=10, -30<=k<=30, -18<=l<=18	
Reflections collected	47471	
Independent reflections	12142 [R(int) = 0.1023]	

Completeness to theta = 73.50°	98.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.95 and 0.33
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12142 / 1 / 776
Goodness-of-fit on F^2	1.371
Final R indices [I>2sigma(I)]	R1 = 0.1145, wR2 = 0.3024
R indices (all data)	R1 = 0.1218, wR2 = 0.3132
Absolute structure parameter	-0.24(14)
Largest diff. peak and hole	0.633 and -0.470 e.$Å^{-3}$

Figure S8. X-ray crystallographic data of 1

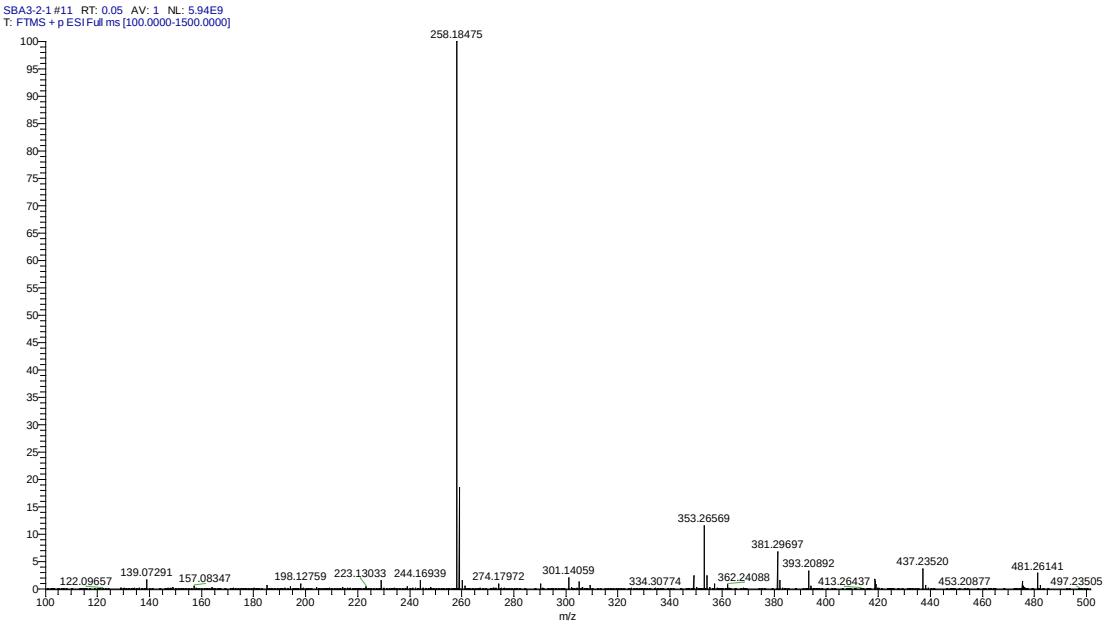
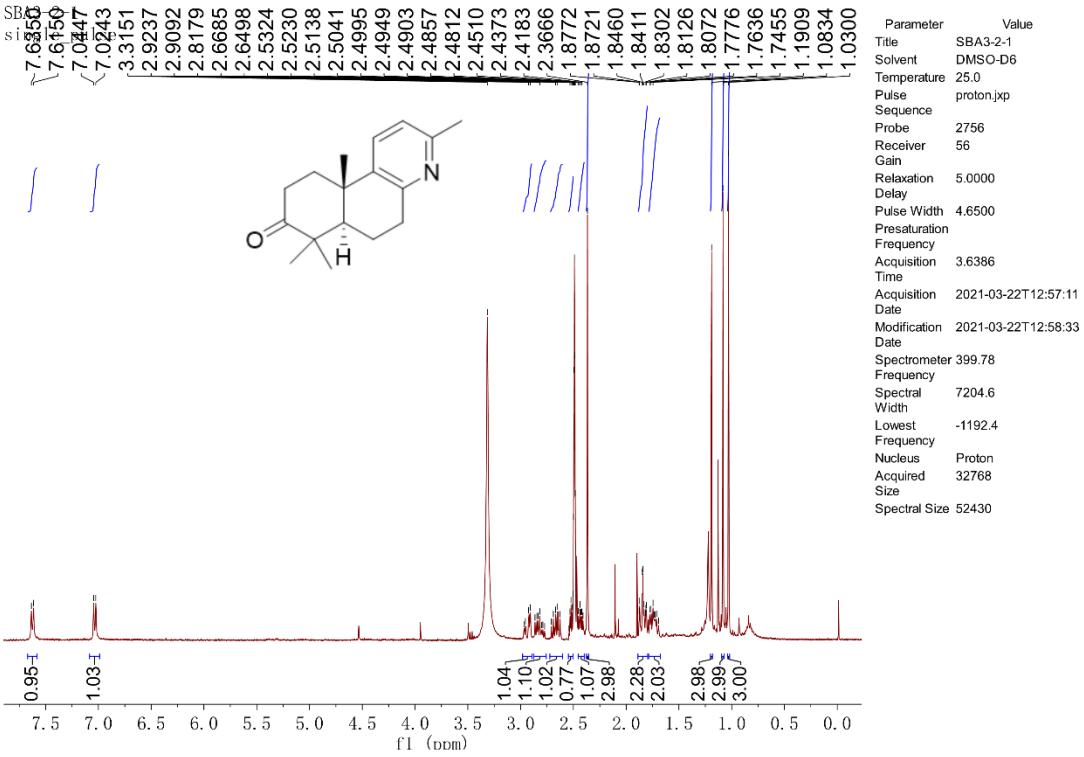


Figure S9. HR-ESI spectrum of 2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3.3151
2.9237
2.9092
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2.6498
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2.5230
2.5138
2.5041
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2.4949
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2.4812
2.4510
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1.8411
1.8302
1.8126
1.8072
1.7776
1.7636
1.7455
1.1909
1.0834
1.0300
O
N
H
0.95
1.03
1.04
1.10
1.02
0.77
1.07
2.98
2.28
2.03
2.98
2.99
3.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
Parameter Value
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Solvent DMSO-D6
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Pulse Sequence proton.jxp
Probe 2756
Receiver Gain 56
Relaxation Delay 5.0000
Pulse Width 4.6500
Presaturation Frequency
Acquisition Time 3.6386
Acquisition Date 2021-03-22T12:57:11
Modification Date 2021-03-22T12:58:33
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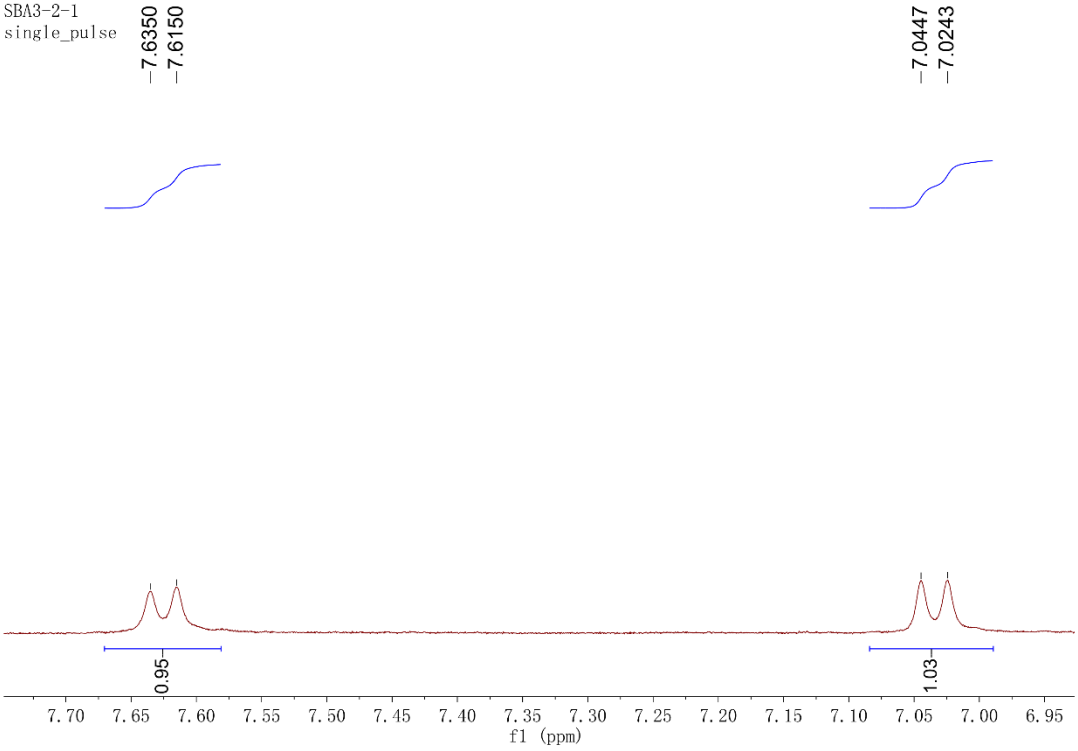
Spectral Width 7204.6
Lowest Frequency -1192.4
Nucleus Proton
Acquired Size 32768
Spectral Size 52430


SBA3-2-1
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7.6150
7.0447
7.0243
0.95
1.03
7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95
f1 (ppm)

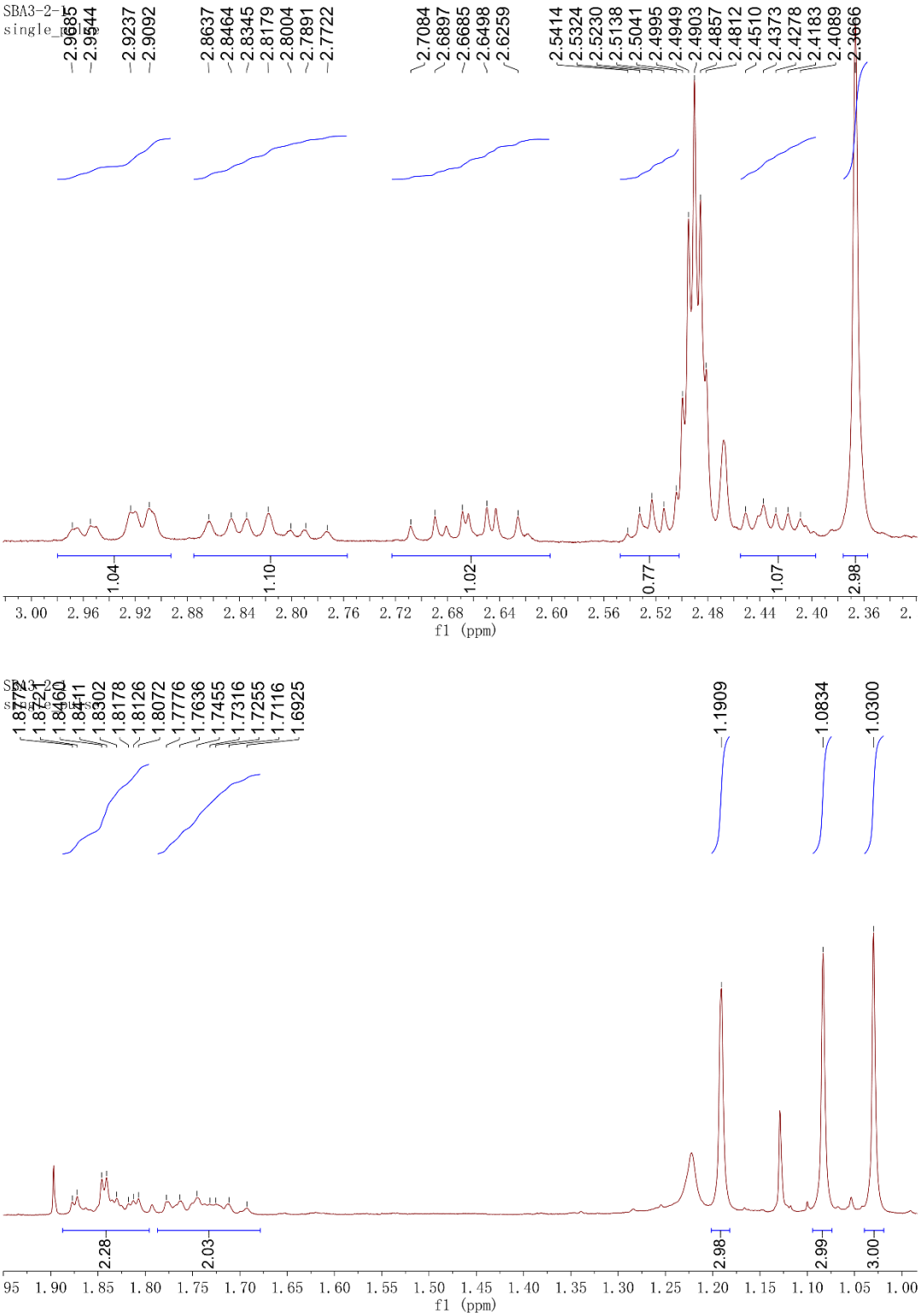
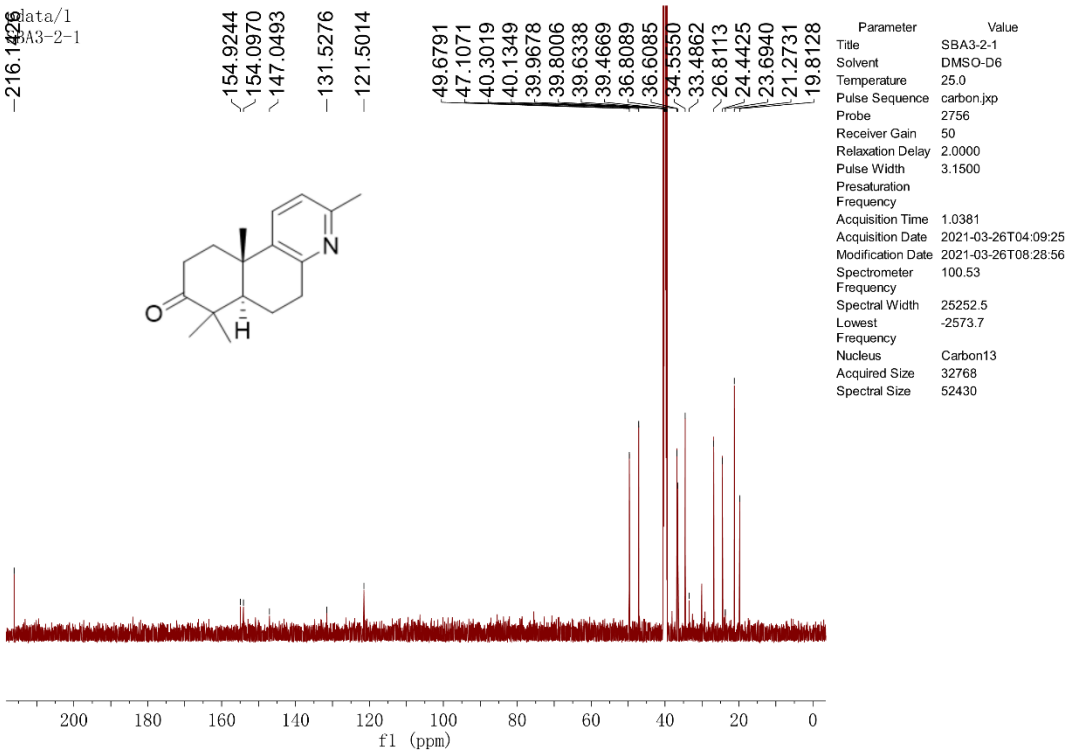


Figure S10. ^{1}H NMR spectrum of 2 in DMSO-d$_6$


216.1426
154.9244
154.0970
147.0493
131.5276
121.5014
49.6791
47.1071
40.3019
40.1349
39.9678
39.8006
39.6338
39.4669
36.8089
36.6085
34.5550
33.4862
26.8113
24.4425
23.6940
21.2731
19.8128
Parameter Value
Title SBA3-2-1
Solvent DMSO-D6
Temperature 25.0
Pulse Sequence carbon.jxp
Probe 2756
Receiver Gain 50
Relaxation Delay 2.0000
Pulse Width 3.1500
Presaturation Frequency
Acquisition Time 1.0381
Acquisition Date 2021-03-26T04:09:25
Modification Date 2021-03-26T08:28:56
Spectrometer Frequency 100.53
Spectral Width 25252.5
Lowest Frequency -2573.7
Nucleus Carbon13
Acquired Size 32768
Spectral Size 52430
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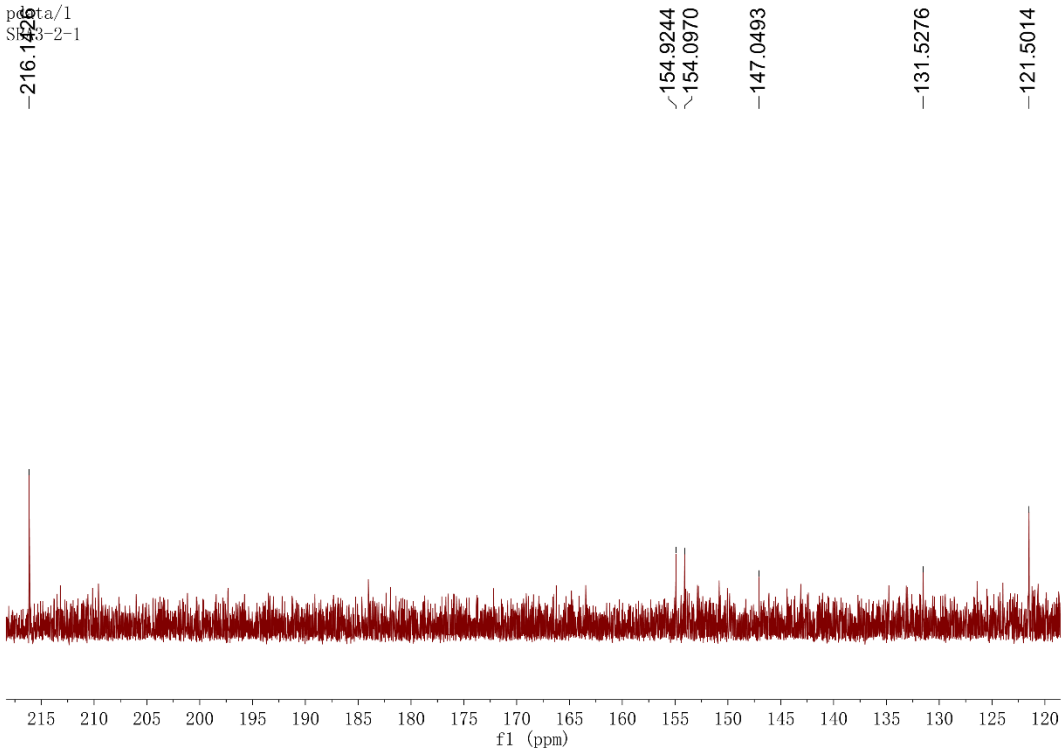
N
H
200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)


216.1426
154.9244
154.0970
147.0493
131.5276
121.5014
215 210 205 200 195 190 185 180 175 170 165 160 155 150 145 140 135 130 125 120
f1 (ppm)

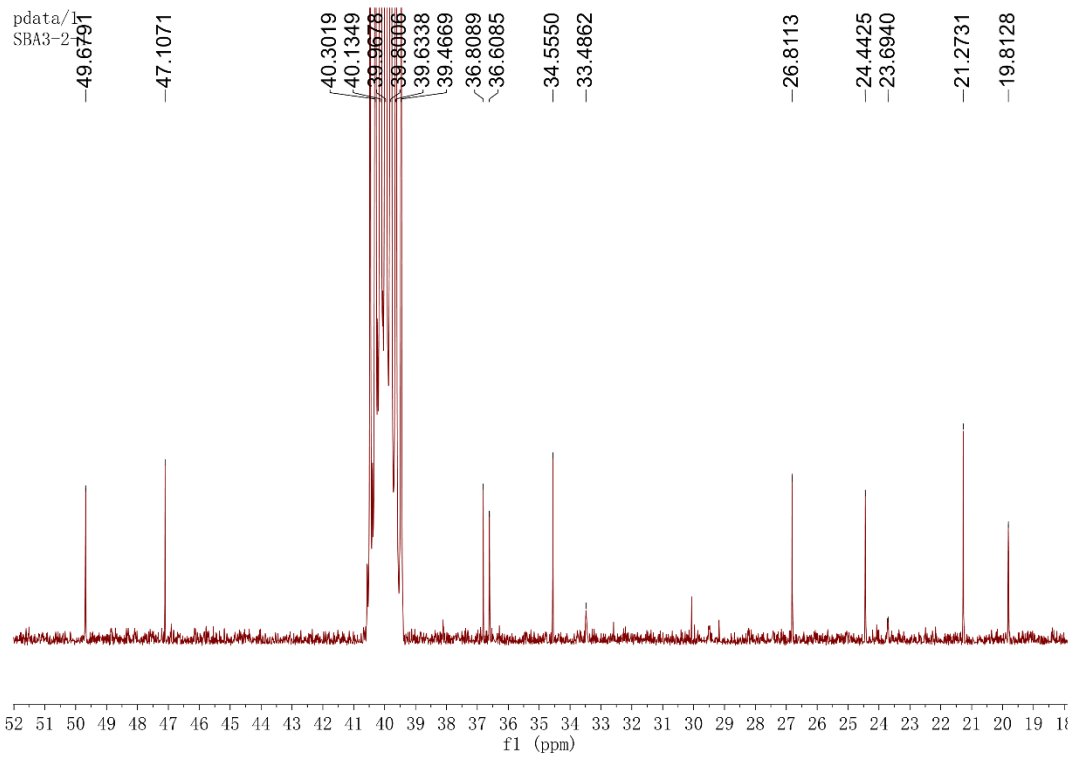
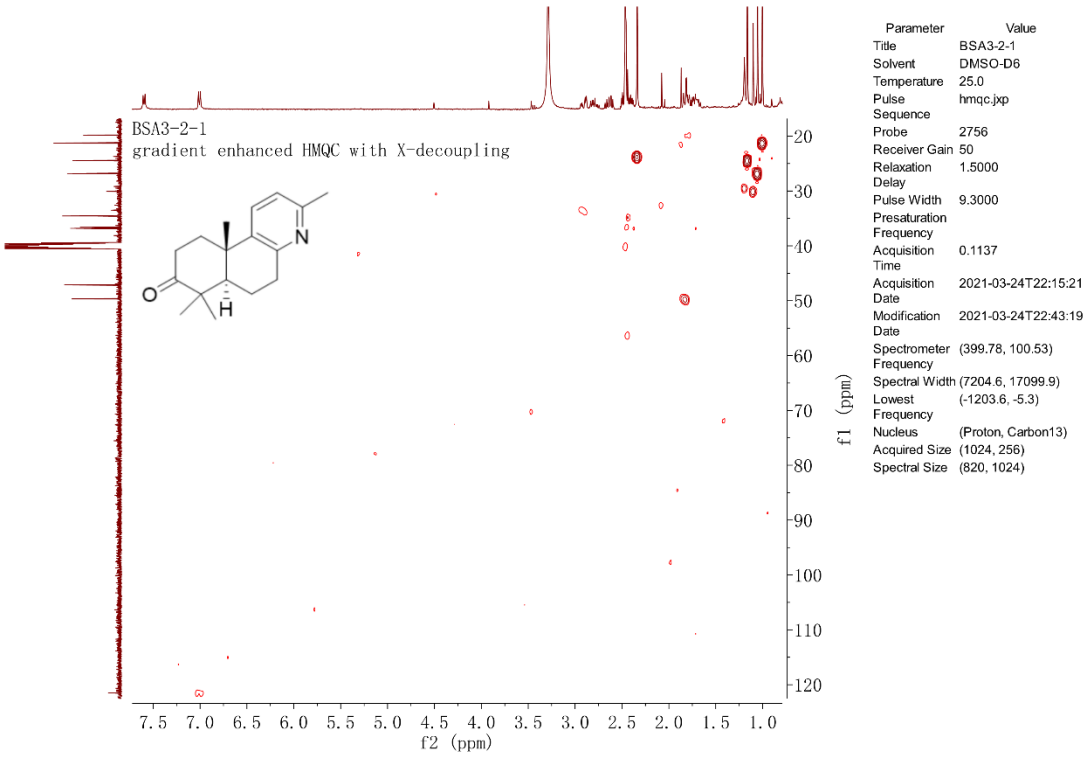


Figure S11. ^{13}C NMR spectrum of 2 in DMSO-d$_6$



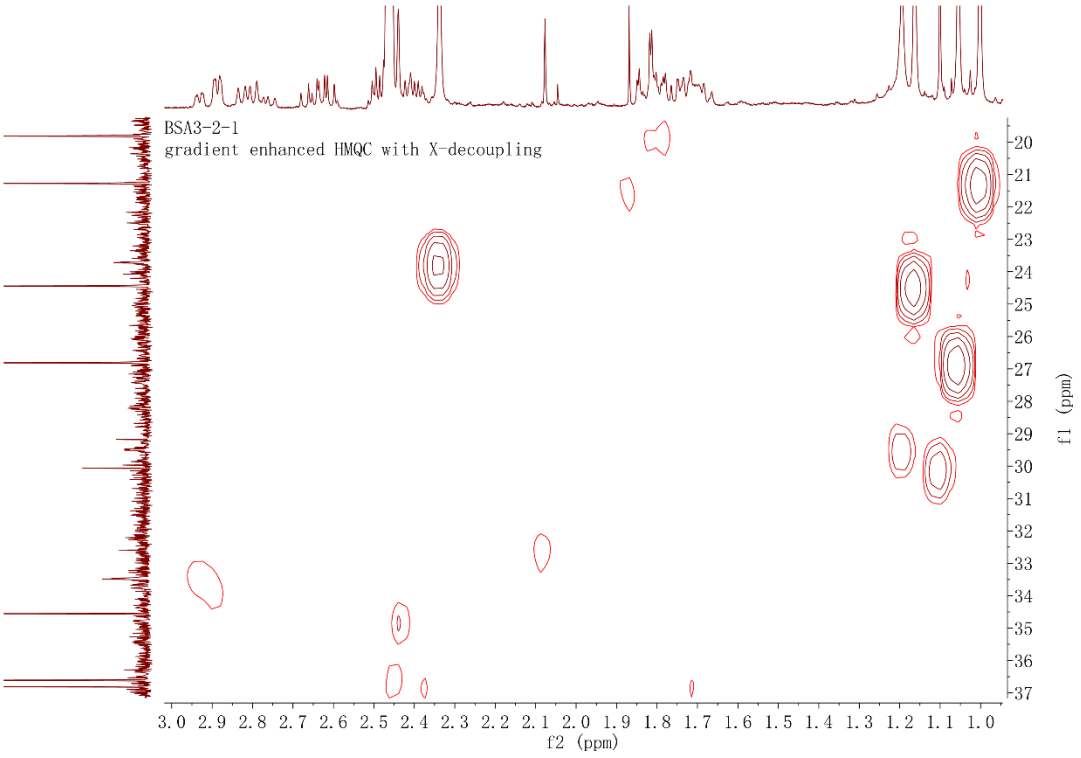
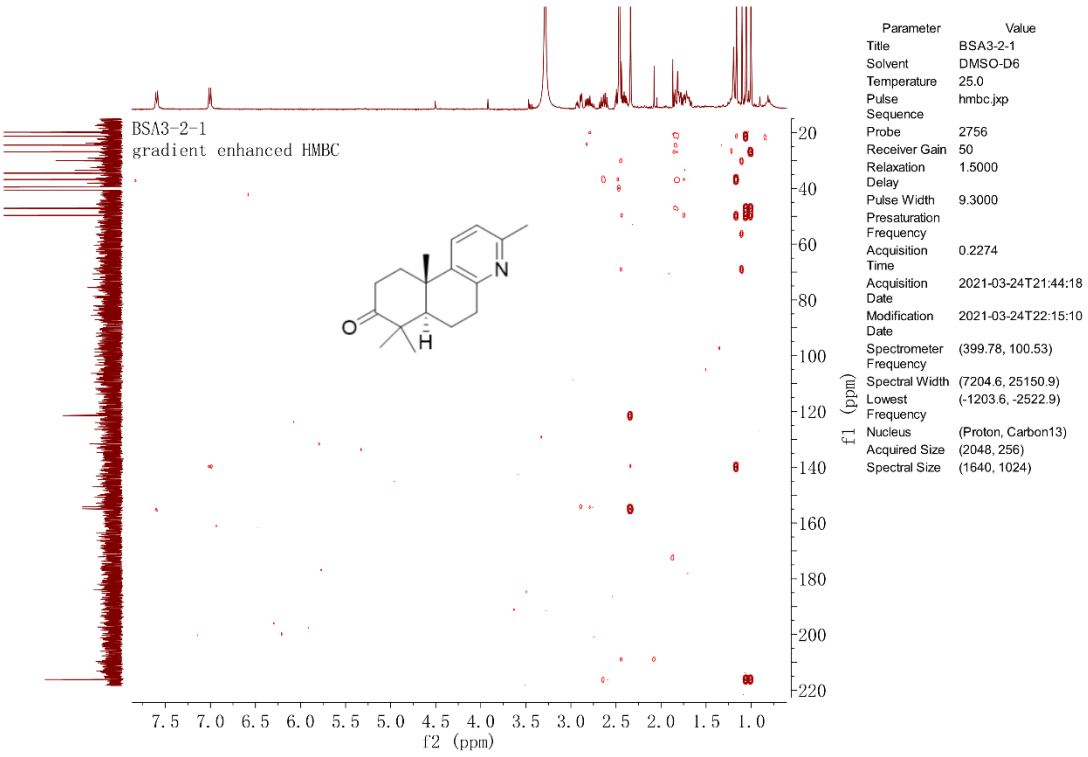


Figure S12. HMQC spectrum of 2 in DMSO-d_6



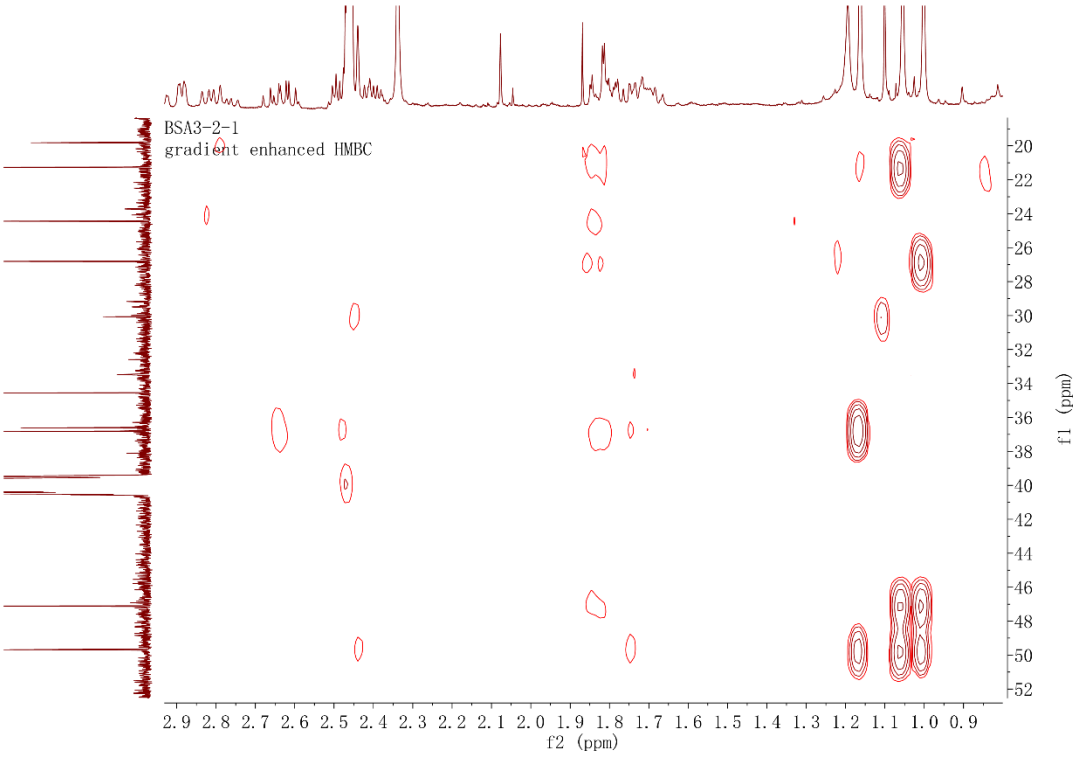
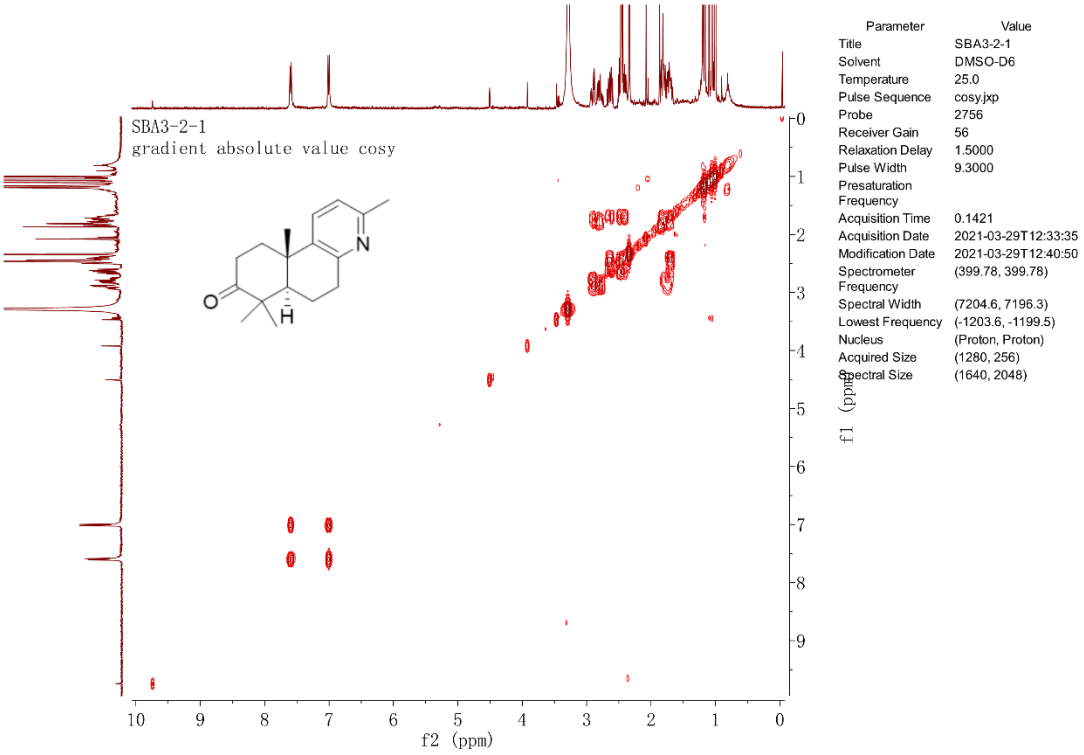


Figure S13. HMBC spectrum of 2 in DMSO-d_6



Parameter	Value
Title	SBA3-2-1
Solvent	DMSO-D6
Temperature	25.0
Pulse Sequence	cosy.jxp
Probe	2756
Receiver Gain	56
Relaxation Delay	1.5000
Pulse Width	9.3000
Presaturation Frequency	
Acquisition Time	0.1421
Acquisition Date	2021-03-29T12:33:35
Modification Date	2021-03-29T12:40:50
Spectrometer Frequency	(399.78, 399.78)
Spectral Width	(7204.6, 7196.3)
Lowest Frequency	(-1203.6, -1199.5)
Nucleus	(Proton, Proton)
Acquired Size	(1280, 256)
Spectral Size	(1640, 2048)

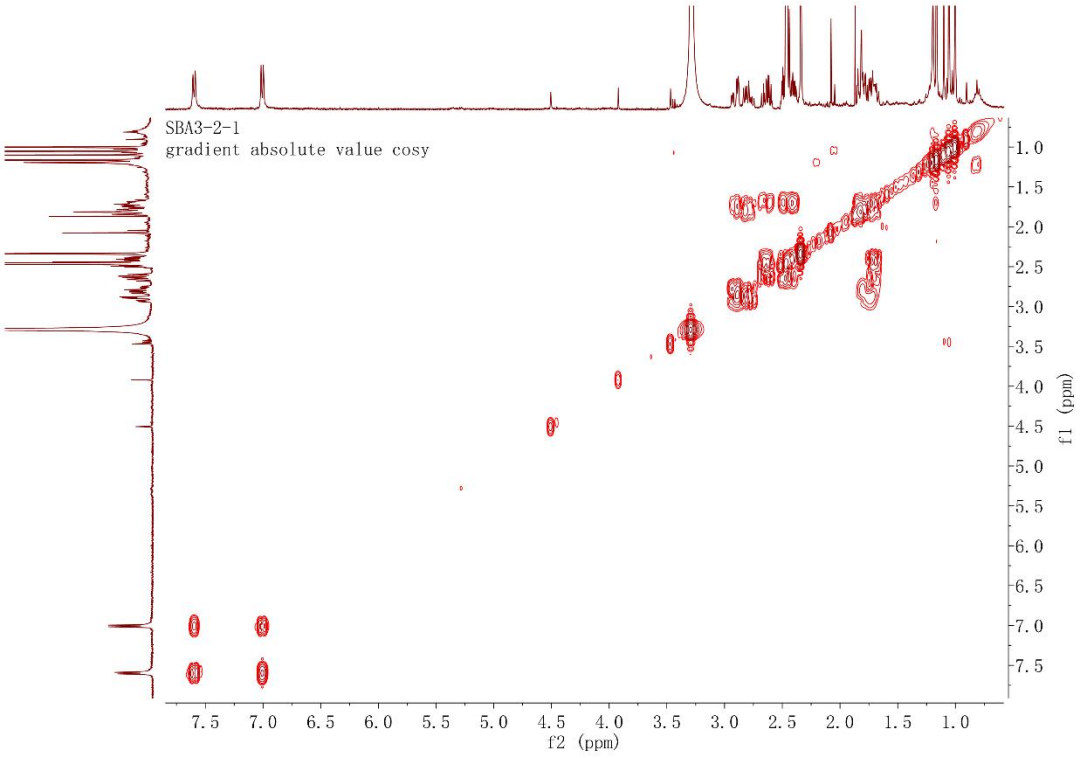
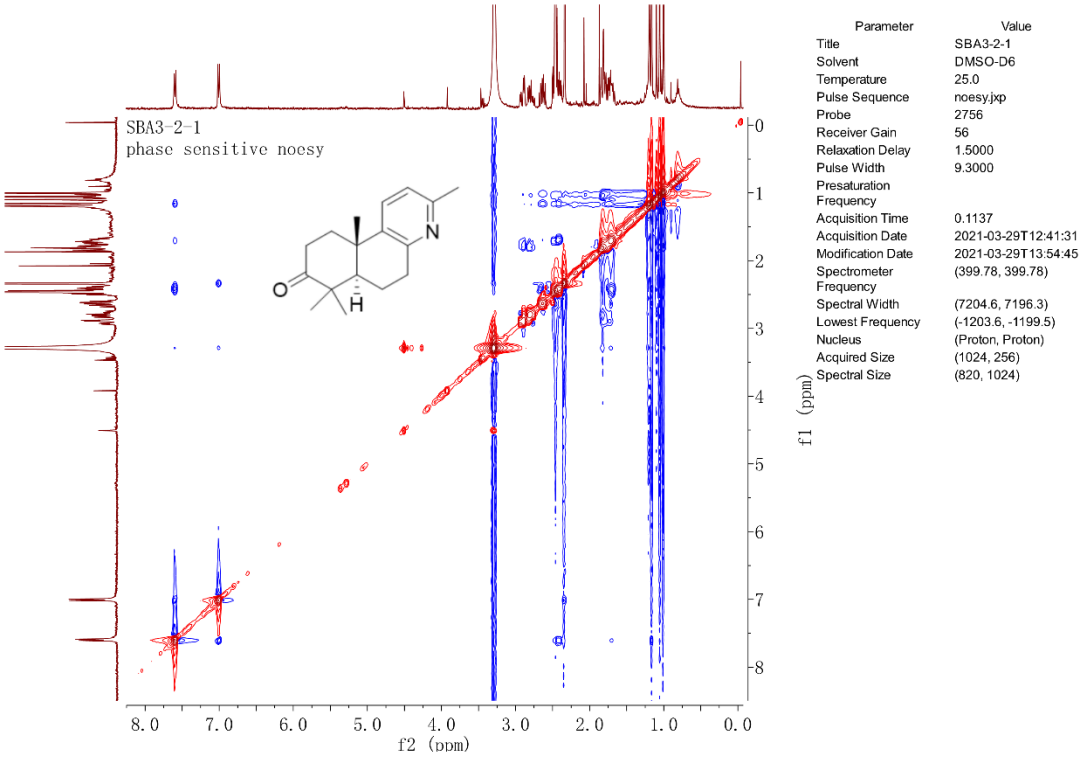


Figure S14. ^{1}H-^{1}H COSY spectrum of 2 in DMSO-d$_6$



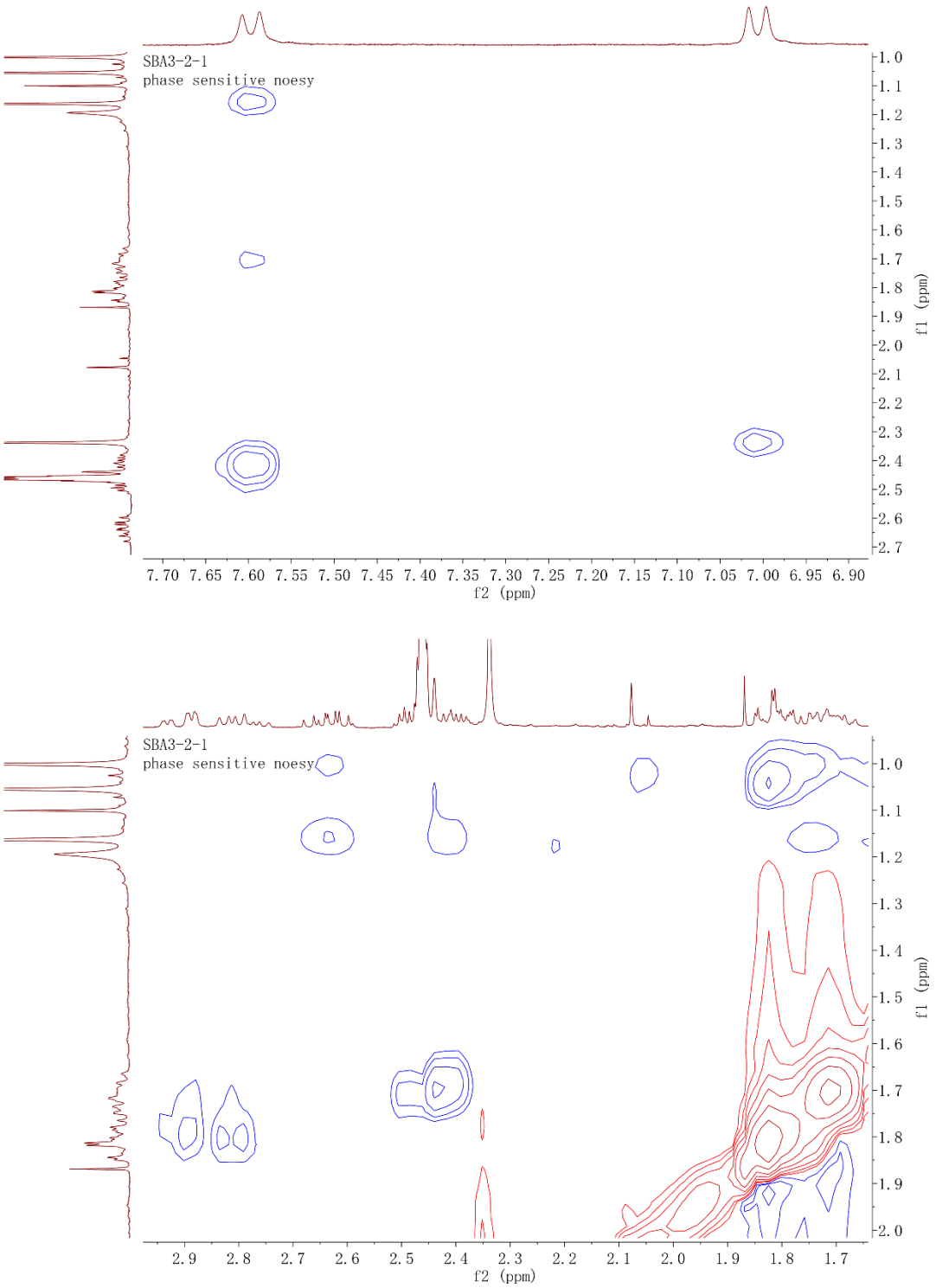
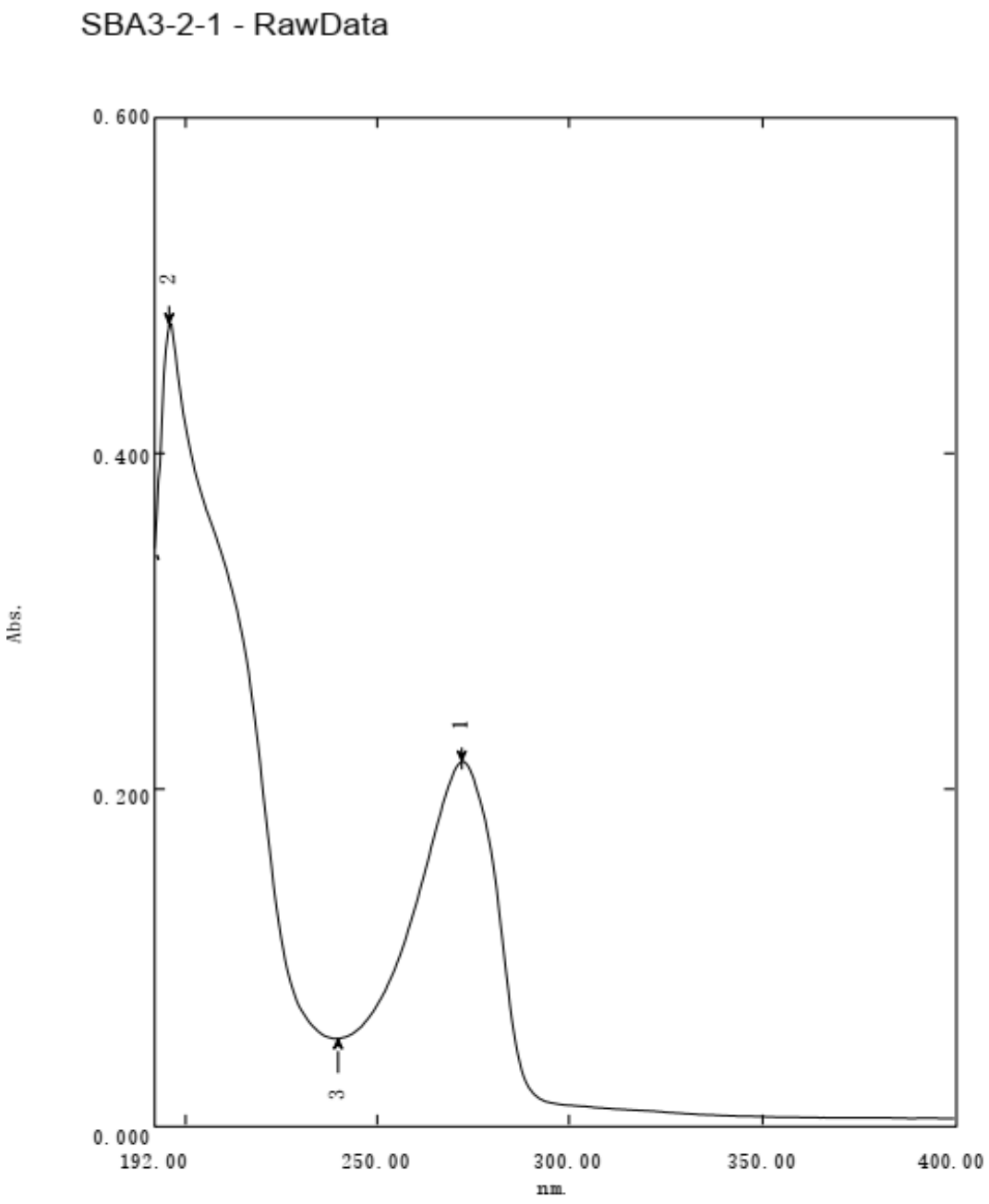


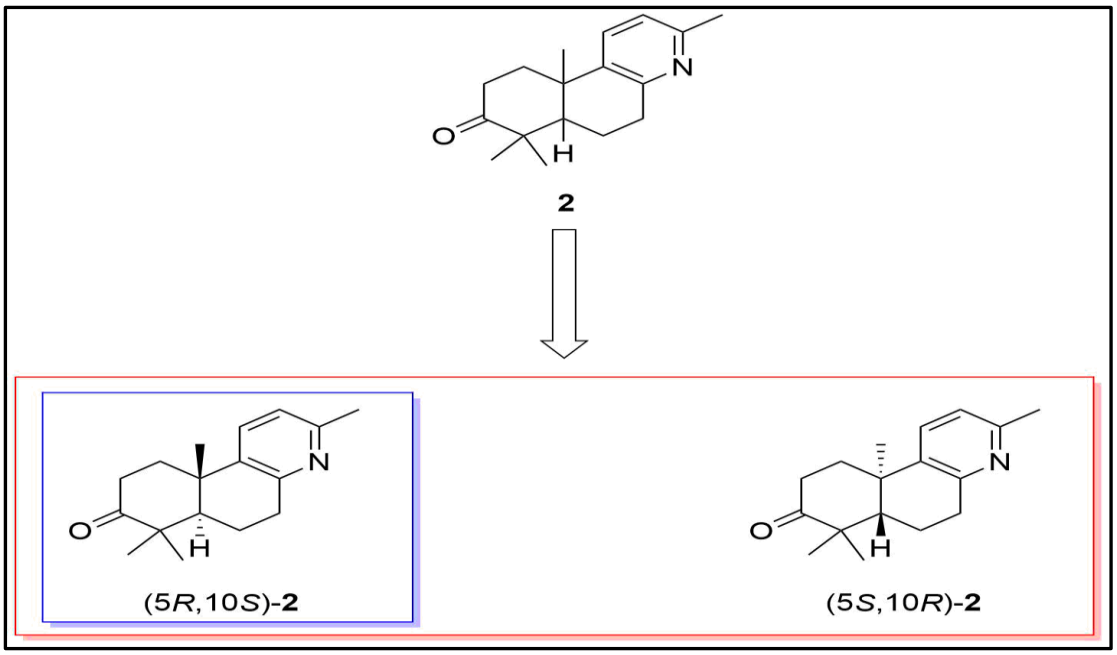
Figure S15. NOESY spectrum of 2 in DMSO-d_6



No.	P/V	波长(nm)	Abs.	描述
1	↑	272.00	0.216	
2	↑	196.00	0.477	
3	↓	239.50	0.051	
4	↓	192.00	0.343	

Figure S16. UV spectrum of 2 in MeOH

ECD results of 2



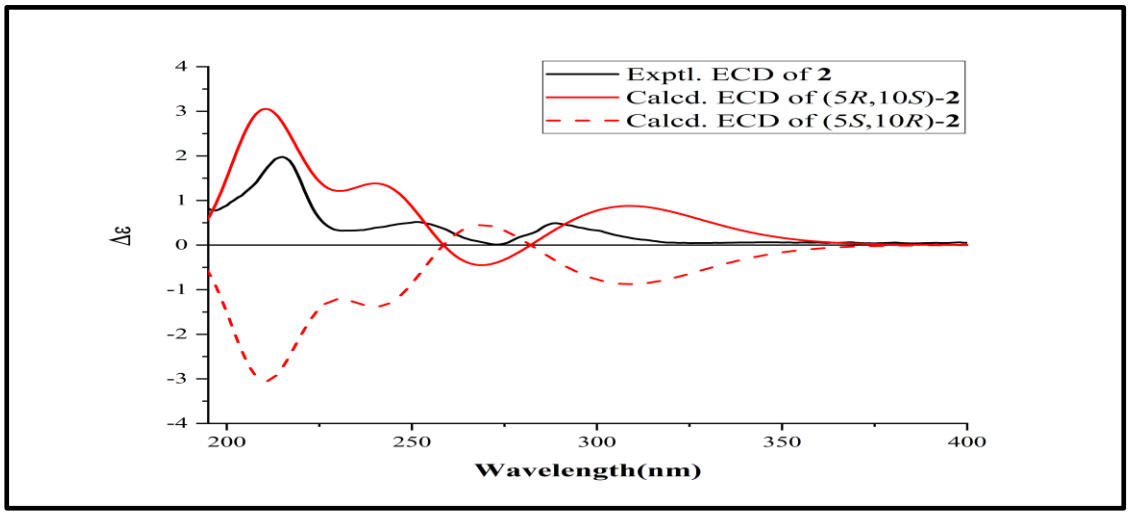


Fig.1. Experimental ECD curves of 2 (solid black line) and M062X/TZVP//B3LYP/6-31G(d) calculated ECD spectra of (5*R*,10*S*)-2 (solid red line) and (5*R*,10*S*)-2 (dash red line).

1. Conformer and energy analysis

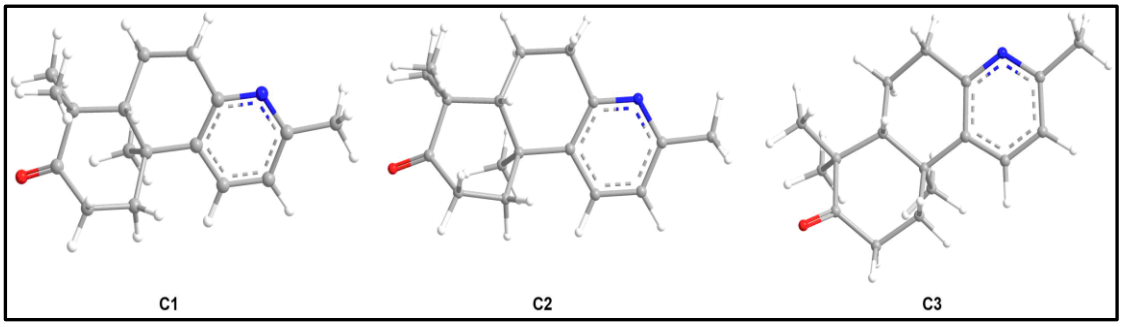


Fig. 2. B3LYP/6-31G(d) optimized lowest energy conformers for (5*R*,10*S*)-2

Table 1. Energy (298.15 K) analysis for (5*R*,10*S*)-2

Conf.	G (Hartree)	ΔG (Kcal/mol)	Boltzmann Distribution
C1	-791.748257	0	0.372244767
C2	-791.748106	0.09475401	0.317203515
C3	-791.748086	0.10730421	0.310551718

2. ECD data

2.1 ECD simulation

ECD spectrum of each conformation is simulated according to the overlapping Gaussian functions expressed as:

$$\Delta\varepsilon(E)=\frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{A}\Delta E_i R_i e^{[-(E-\Delta Ei)^2/\sigma^2]}$$

Where σ is half the bandwidth at 1/e peak height and expressed in energy units. The parameters ΔE_i and R_i are the excitation energies and rotational strengths for the transition *I*, respectively.

The above function is converted to Δε, λ (wavelength) correlations as:

$$\Delta\varepsilon(\lambda)=\frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{A}\Delta E_i R_i e^{[-(1240/\lambda-\Delta Ei)^2/\sigma^2]}$$

and then simulation were accomplished by using the Excel 2003 and the Origin 9.1 software.

2.2 Calculated ECD Data for (5*R*,10*S*)-2 in methanol

State	C1		C2		C3	
	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*
1	4.1507	12.5699	4.1502	12.7213	4.0895	-5.6649
2	4.9654	-10.1046	5.0535	-10.9946	4.966	-8.6865

3	5.2167	13.8661	5.2679	13.7566	5.2208	12.9665
4	5.7955	0.6318	5.7269	0.7583	5.7835	0.2888
5	6.2148	18.2291	6.1476	17.6158	6.2137	11.5167
6	6.8367	-46.5303	6.8514	-2.0703	6.8557	-16.743
7	6.8641	37.3614	6.9229	-47.8502	6.8883	-47.3199
8	6.9529	11.8963	6.9969	49.5532	6.9362	42.5042
9	7.1096	23.0774	7.0696	33.0483	7.0879	34.7899
10	7.1455	4.6031	7.2271	1.7447	7.1592	19.7376
11	7.3713	-5.5697	7.346	-25.362	7.2681	-0.5441
12	7.4405	-5.8241	7.4106	-6.2956	7.4132	-11.0651
13	7.4754	16.9848	7.4488	33.6945	7.4722	-10.6861
14	7.5926	5.3193	7.5619	4.0625	7.5474	10.874
15	7.7154	7.7292	7.6775	3.9771	7.7288	0.4758
16	7.76	-12.1662	7.7236	-9.3972	7.7749	1.9292
17	7.8033	2.9587	7.8004	-0.5982	7.9041	-1.3452
18	7.8693	13.7277	7.951	10.5599	7.9431	1.3306
19	7.9909	0.3687	7.9937	3.6218	7.9535	8.2621
20	8.109	-16.9228	8.0474	-19.7945	8.1347	-27.4753
21	8.1348	-11.3797	8.1605	-9.0723	8.1369	-17.7901
22	8.1612	-30.2039	8.2248	-46.9594	8.1614	-3.0874
23	8.265	-3.4795	8.2665	-0.0335	8.2321	2.0259
24	8.3093	-15.5442	8.3192	-9.177	8.2989	-10.9359
25	8.4194	3.1032	8.3783	14.9852	8.3559	1.2884
26	8.4396	10.4353	8.4518	-5.1363	8.4233	-1.3573
27	8.4744	-2.9899	8.4905	-0.1295	8.4561	11.3192
28	8.5423	9.5301	8.5457	26.9615	8.4865	-0.0122
29	8.566	-25.2745	8.5659	-14.2915	8.5157	14.2841
30	8.5907	48.6112	8.6041	-52.7682	8.6006	-67.0943
31	8.6091	-33.5327	8.6342	39.3095	8.6166	1.6128
32	8.6694	-24.6767	8.6985	26.003	8.6438	-30.1321
33	8.6949	38.0212	8.7045	-10.8051	8.6722	53.1564
34	8.7211	-81.8699	8.726	-49.2211	8.6781	13.494
35	8.7684	3.1443	8.7649	-4.7618	8.7393	-3.7035
36	8.7863	12.2685	8.7764	20.4338	8.7722	-7.3009
37	8.8333	38.8757	8.8277	62.3943	8.8145	17.2524
38	8.8584	-16.717	8.8449	-4.9717	8.8266	5.8313
39	8.8704	35.0945	8.8671	-51.597	8.8497	36.827
40	8.8972	-16.5842	8.8946	30.0902	8.8836	1.6127
41	8.9808	10.2452	8.9682	-4.2296	8.9386	10.0373
42	8.9942	-14.0926	8.9774	19.7253	8.9565	-1.6295
43	9.0052	24.3231	9.0111	-8.6635	9.0001	-17.5142
44	9.0383	2.8539	9.0279	9.4965	9.048	-0.8886
45	9.0696	-9.0273	9.0448	-7.5612	9.0762	11.4838

46	9.0792	-8.6556	9.0589	7.6623	9.1172	21.241
47	9.0946	2.1322	9.1036	-6.5861	9.1434	-2.2862
48	9.118	19.2625	9.1469	4.0987	9.1559	-19.1095
49	9.2122	6.1108	9.1792	2.5562	9.2109	-9.5425
50	9.2331	-15.1409	9.2086	12.8962	9.2482	-12.016
51	9.2644	-5.1269	9.2347	-16.8965	9.2717	-5.3903
52	9.2829	-2.868	9.2712	14.1253	9.3006	-8.5438
53	9.296	5.8033	9.3112	3.9362	9.3287	-19.5284
54	9.3215	30.0027	9.323	14.576	9.3441	-13.8939
55	9.392	0.3497	9.3891	1.3673	9.3554	5.9652
56	9.4123	-26.8713	9.4343	-21.1868	9.3965	6.7005
57	9.4251	9.2957	9.4479	0.5539	9.437	-8.1625
58	9.4606	40.9616	9.4713	14.1462	9.4402	-43.0164
59	9.5027	-2.6928	9.482	-18.4365	9.4802	-22.9911
60	9.5113	-4.0404	9.5007	18.8035	9.496	-39.5267

* R(velocity) 10**-40 erg-esu-cm

Figure S17. ECD data of 2