Electronic Supplementary Information

Identification and bioactivity evaluation of secondary metabolites from Antarctic-derived *Penicillium chrysogenum* CCTCC M 2020019

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Contents

I. Supplementary tables and Figures **S3**
Table S1. Bacterial inhibition zone diameter (mm) of the ethyl acetate extract obtained from *Penicillium chrysogenum* CCTCC M 2020019 ..... **S3**
Table S2. ^{1}H and ^{13}C NMR data of compound **9** **S3**
Table S3. Gibbs free energies[a] and equilibrium populations[b] of low-energy conformers of (6*R*)-**1** **S4**
Table S4. Energies of compound (6*R*)-**1** at B3LYP/6-31+G(d, p) in gas phase **S4**
Table S5. Cartesian coordinates for the low-energy reoptimized MMFF conformers of (6*R*)-**1** at B3LYP/6-311+G(d, p) level of theory in CH_3OH **S5**
Table S6. Crystal data and structure refinement for compound **2b** **S7**
Table S7. ^{1}H NMR data of reference **2b** **S8**
Table S8. Crystal data and structure refinement for compound **4** **S9**
Table S9. Alpha-glucosidase inhibitory activities of Compounds **1–9** **S10**
Fig. S1. Phylogenetic tree of *Penicillium chrysogenum* CCTCC M 2020019 based on neighbour-joining method **S11**
Fig. S2. Spectroscopic data of compound **1** **S12**
Fig. S3. ^{1}H and ^{13}C NMR spectra of compound **9** **S24**
Fig. S4. HPLC analysis of compound **1** using a chiral column **S26**
Fig. S5. Spectroscopic data of (6*S*)-chrysonin A (**1a**) **S27**
Fig. S6. Spectroscopic data of (6*R*)-chrysonin A (**1b**) **S29**
Fig. S7. Chemical Structure of (2*S*,3*R*)-2,3-dihydro-3-hydroxy-2-methyl-1,5-benzoxazepin-4(5*H*)-one (CAS number:1932813-80-3) **S31**
Fig. S8. Spectroscopic data of compound **2** **S31**
Fig. S9. ^{1}H NMR spectrum of reference **2b** **S42**
Fig. S10. Spectroscopic data of compound **3** **S43**
Fig. S11. Overlapping of ^{1}H-NMR spectra of compounds **2** and **3** **S45**
Fig. S12. HPLC analysis of compounds **2** and **3** **S46**
II. ECD calculations **S47**
III. Single crystal X-ray diffraction analysis for compounds 2b and 4 ..... **S47**
IV. Supplementary References **S48**

I. Supplementary tables and Figures

Table S1. Bacterial inhibition zone diameter (mm) of the ethyl acetate extracts obtained from *Penicillium chrysogenum* CCTCC M 2020019

Samples	*Acinetobacter baumannii*	*Pseudomonas aeruginosa*	Multi-drug resistant *Staphylococcus aureus*	*Vibrio alginolyticus*	*Staphylococcus aureus*
Extracts[a]	13	19	20	23	20
DMSO	ND	ND	ND	ND	ND
ampicillin	ND	ND	ND	ND	7

Note: [a] the crude ethyl acetate extracts. The crude acetate extracts were used herein at 100 μg/disc; ND means "not detected"; DMSO (dimethyl sulfoxide) and ampicillin were used as negative and positive controls, respectively.

Table S2. ^{1}H and ^{13}C-NMR data of compound **9** (reported by Zhaoling Pei, *et.al.*)[1]

No.	**9**[a]	
	δ_H(mult., *J*, Hz)	δ_C
1-O<u>H</u>	9.30,s	
2		147.9
3	6.85 (d, 7.9)	124.6
4	6.92 (t, 7.5)	118.9
5	6.74 (t, 7.7)	115.9
6	7.67 (d, 7.9)	122.3
7		126.4
8-N<u>H</u>	9.77, s	
9		168.9
10	2.09, s	23.6

Recorded in [a]DMSO-*d*6, ^{1}H at 500 MHz, ^{13}C at 125 MHz

Table S3. Gibbs free energies[a] and equilibrium populations[b] of low-energy conformers of (6*R*)-**1**.

Conformers	In MeOH	
	Δ*G*	*P* (%)
(6*R*)-**1**-1	0	99.85
(6*R*)-**1**-2	3.85	0.15

[a]B3LYP/6-31+G(d,p), in kcal/mol. [b]From Δ*G* values at 298.15K

Table S4. Energies of Compound (6*R*)-**1** at B3LYP/6-31+G(d,p) in gas phase.

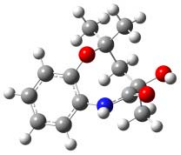
Configuration	Conformer	Structure	E (Hartree)	E (kcal/mol)	Populations (%)
(6*R*)-**1**	**1**-1		-786.12063340	-493361.8414	99.85

Table S5. Cartesian coordinates for the low-energy reoptimized MMFF conformers of (6*R*)-**1**-1 and (6*R*)-**1**-2 at B3LYP/6-311+G(d, p) level of theory in CH_3OH.

(6*R*)-**1**-1		Standard Orientation (Ångstroms)			
Center Number	Atomic Number	Atomic Type	X	Y	Z
1	6	0	3.672960	0.333663	0.276173
2	6	0	3.605672	-1.054335	0.373060
3	6	0	2.416510	-1.719485	0.067105
4	6	0	1.272281	-0.997629	-0.290664
5	6	0	1.349582	0.396634	-0.396367
6	6	0	2.553011	1.056401	-0.132523
7	7	0	0.135336	-1.732737	-0.658425
8	6	0	-1.180965	-1.382825	-0.601501
9	6	0	-1.751247	-0.569227	0.585025
10	6	0	-1.065234	0.718012	1.047446
11	6	0	-0.613595	1.696660	-0.056438
12	8	0	0.330153	1.107653	-0.970151
13	6	0	-1.789621	2.146254	-0.939491
14	6	0	-0.019152	2.962849	0.589855
15	8	0	-1.980620	-1.899270	-1.395581
16	8	0	-3.111249	-0.238868	0.240161
17	6	0	-1.852752	-1.533923	1.778370
18	1	0	4.605803	0.849766	0.487853
19	1	0	4.484676	-1.621324	0.669117
20	1	0	2.390089	-2.804692	0.129088
21	1	0	2.631579	2.130325	-0.275569
22	1	0	0.308338	-2.599280	-1.156229
23	1	0	-1.755740	1.257578	1.712305
24	1	0	-0.201689	0.458888	1.674059
25	1	0	-1.468607	2.923948	-1.643275
26	1	0	-2.163187	1.326033	-1.561399
27	1	0	-2.616055	2.546826	-0.343476
28	1	0	-0.783012	3.528743	1.134478
29	1	0	0.774131	2.716911	1.303448
30	1	0	0.425397	3.618477	-0.167424
31	1	0	-3.397735	-0.922765	-0.402127
32	1	0	-2.414003	-2.436364	1.507427
33	1	0	-0.864844	-1.846841	2.132751
34	1	0	-2.393459	-1.071487	2.612217

(6*R*)-**1**-2		Standard Orientation (Ångstroms)			
Center Number	Atomic Number	Atomic Type	X	Y	Z
1	6	0	3.611350	0.283002	0.283610
2	6	0	3.550084	-1.104673	0.368291
3	6	0	2.364614	-1.771005	0.050647
4	6	0	1.215155	-1.054002	-0.308453
5	6	0	1.286560	0.338554	-0.401142
6	6	0	2.489476	1.000469	-0.127214
7	7	0	0.082010	-1.806292	-0.651391
8	6	0	-1.245293	-1.535554	-0.521161
9	6	0	-1.801129	-0.509553	0.491179
10	6	0	-1.900800	0.923233	-0.038169
11	6	0	-0.623940	1.766506	-0.183566
12	8	0	0.296957	1.047500	-1.013418
13	6	0	-0.989614	3.013507	-1.022060
14	6	0	-0.096476	2.298167	1.162509
15	8	0	-2.055667	-2.225654	-1.159830
16	8	0	-3.200174	-0.917049	0.638908
17	6	0	-1.233310	-0.683421	1.894413
18	1	0	4.540346	0.802630	0.502758
19	1	0	4.429135	-1.670871	0.665456
20	1	0	2.343737	-2.856749	0.110074
21	1	0	2.564433	2.075243	-0.269333
22	1	0	0.255828	-2.712576	-1.072517
23	1	0	-2.627639	1.479590	0.571594
24	1	0	-2.373823	0.848765	-1.029735
25	1	0	-0.103354	3.634130	-1.200592
26	1	0	-1.364639	2.728618	-2.012352
27	1	0	-1.749488	3.628117	-0.527625
28	1	0	-0.890455	2.804661	1.722857
29	1	0	0.317940	1.521208	1.805794
30	1	0	0.709312	3.025169	1.007890
31	1	0	-3.405587	-1.461334	-0.153287
32	1	0	-1.434542	-1.696515	2.264968
33	1	0	-0.155381	-0.537624	1.956631
34	1	0	-1.718887	0.001820	2.598573

Table S6. Crystal data and structure refinement for **2b**

Empirical formula	$C_9H_9NO_2$
Formula weight	163.17
Temperature/K	105(8)
Crystal system	orthorhombic
Space group	Pbca
a/Å	12.9027(9)
b/Å	6.9592(4)
c/Å	18.0598(16)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1621.6(2)
Z	8
ρ_{calc}g/cm^3	1.337
μ/mm^{-1}	0.787
F(000)	688.0
Crystal size/mm^3	0.1 × 0.05 × 0.05
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.796 to 148.598
Index ranges	-9 ≤ h ≤ 15, -8 ≤ k ≤ 8, -22 ≤ l ≤ 19
Reflections collected	4560
Independent reflections	1609 [R_{int} = 0.0328, R_{sigma} = 0.0449]
Data/restraints/parameters	1609/0/110
Goodness-of-fit on F^2	1.068
Final R indexes [I>=2σ (I)]	R_1 = 0.0437, wR_2 = 0.1136
Final R indexes [all data]	R_1 = 0.0605, wR_2 = 0.1227
Largest diff. peak/hole / e Å^{-3}	0.21/-0.24

Table S7. ^{1}H-NMR data of reference **2b** (reported by Ting Jiang)[2]

No.	**2b**[a]
	δ_H (mult., *J* in Hz)
1	7.21 (dd, 9.9, 15)
2	6.13 (d, 15)
4	7.15 (d, 8.1)
5	6.70 (d, 8.1)
7	6.70 (d, 8.1)
8	7.15 (d, 8.1)
9	8.06 s
N<u>H</u>	10.11 (d, 9.9)
O<u>H</u>	9.80, brs

Recorded in [a]DMSO-*d*6, ^{1}H at 300 MHz

Table S8. Crystal data and structure refinement for compound **4**

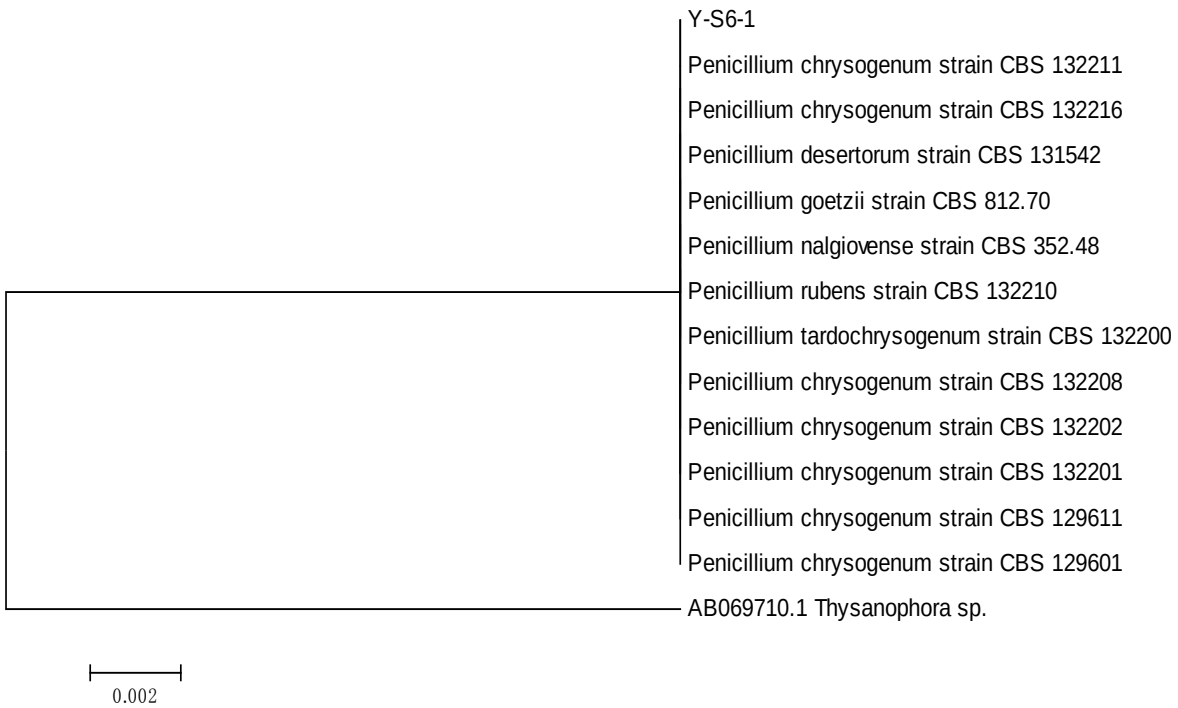
Empirical formula	$C_{11}H_{12}NO_2S$
Formula weight	206.25
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	6.4707(3)
b/Å	6.4978(2)
c/Å	13.6439(5)
α/°	96.434(3)
β/°	102.426(4)
γ/°	94.819(3)
Volume/Å^3	553.23(4)
Z	2
ρ_{calc}g/cm^3	1.238
μ/mm^{-1}	1.541
F(000)	218.0
Crystal size/mm^3	0.1 × 0.1 × 0.05
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	13.41 to 148.156
Index ranges	-8 ≤ h ≤ 8, -8 ≤ k ≤ 5, -16 ≤ l ≤ 16
Reflections collected	4537
Independent reflections	2136 [R_{int} = 0.0224, R_{sigma} = 0.0229]
Data/restraints/parameters	2136/0/139
Goodness-of-fit on F^2	1.100
Final R indexes [I>=2σ (I)]	R_1 = 0.0457, wR_2 = 0.1357
Final R indexes [all data]	R_1 = 0.0465, wR_2 = 0.1367
Largest diff. peak/hole / e Å^{-3}	0.60/-0.63

Table S9. Alpha-glucosidase inhibitory activity of compounds **1**–**9**

Compounds	Inhibition ratio (%)
1	54.46 ± 0.24 %
2	54.99 ± 0.59 %
3	35.68 ± 0.19 %
4	47.96 ± 0.68 %
5	64.34 ± 0.54 %
6	38.34 ± 0.68 %
7	85.38 ± 0.40 %
8	73.28 ± 0.28 %
9	82.43 ± 0.86 %
Control	99.29 ± 0.10 %

Acarbose was used as the positive control. Final concentrations of compounds **1**–**9** and acarbose were all set at 10 μM. Each value was represented as the mean value ± standard deviation of three replicates.

Fig. S1. Phylogenetic tree of *Penicillium chrysogenum* CCTCC M 2020019 based on neighbour-joining method



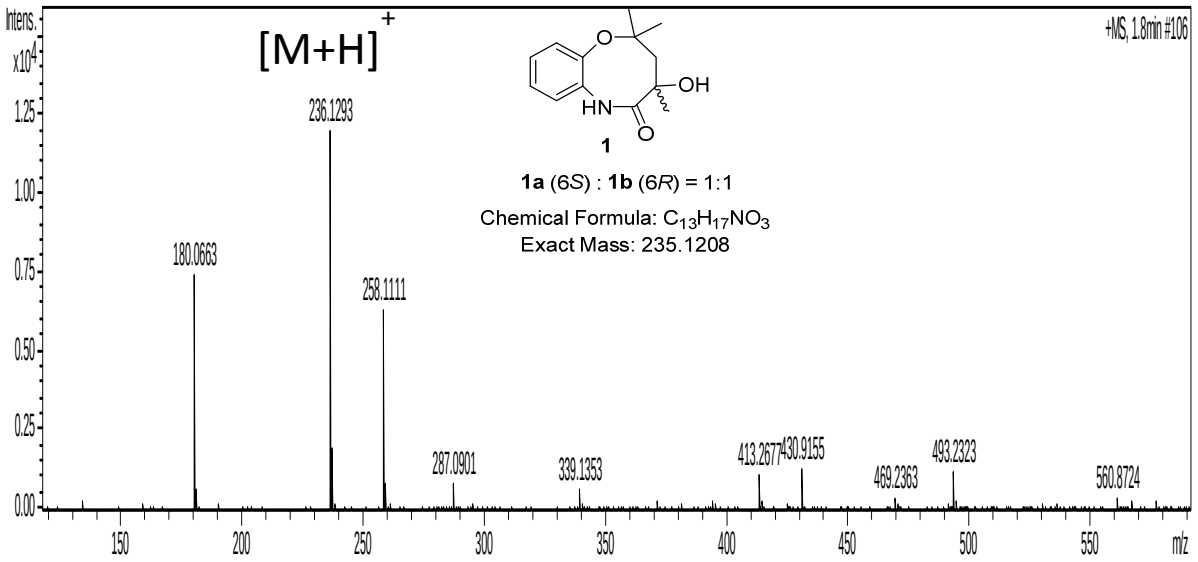
Note: Y-S6-1 is a nickname of *Penicillium chrysogenum* CCTCC M 2020019 in the above figure. Phylogenetic tree based on neighbour-joining method showing a 100% similarity between *Penicillium chrysogenum* CCTCC M 2020019 and *Penicillium chrysogenum*. Boot strap values of 50 and above alone are indicated.

28S rDNA sequence of *Penicillium chrysogenum* CCTCC M 2020019:

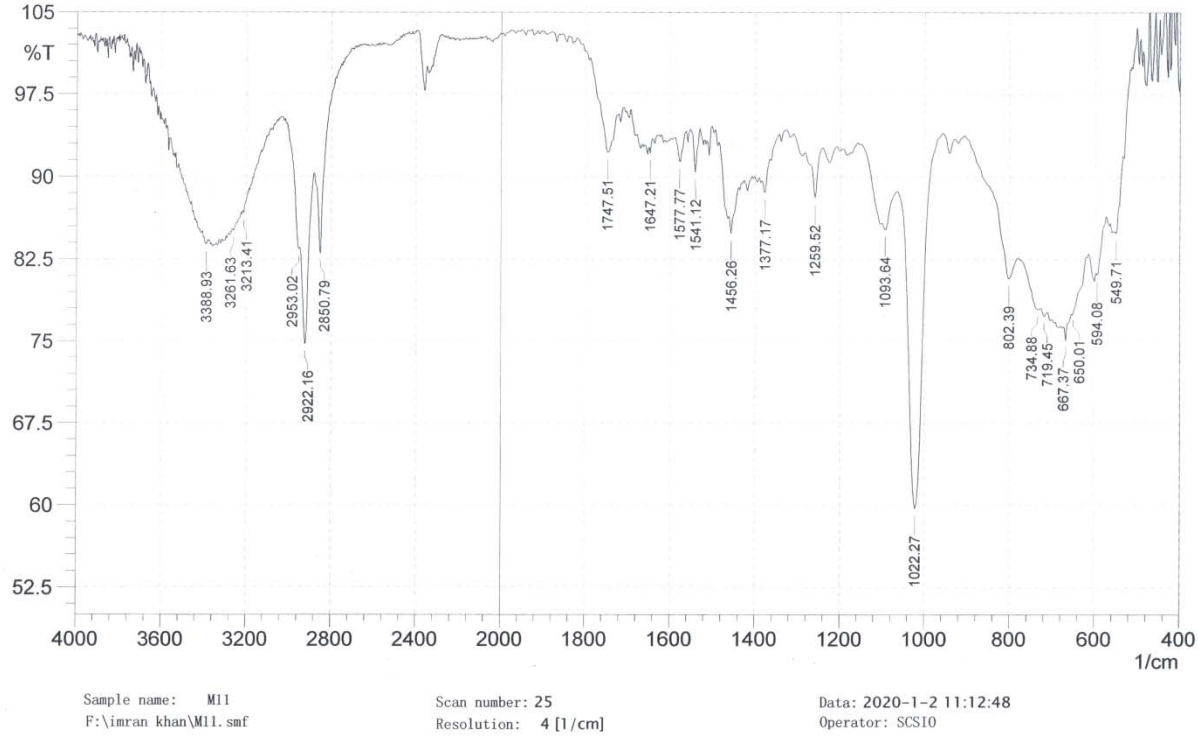
AGTAACGGCGAGTGAAGCGGCAAGAGCTCAAATTTGAAAGCTGGCTCCTTCGGGGTCCGCATTGTA
ATTTGTAGAGGATGCTTCGGGAGCGGTCCCCATCTAAGTGCCCTGGAACGGGACGTCATAGAGGGT
GAGAATCCCGTATGGGATGGGGTGTCCGCGCCCGTGTGAAGCTCCTTCGACGAGTCGAGTTGTTTG
GGAATGCAGCTCTAAATGGGTGGTAAATTTCATCTAAAGCTAAATATTGGCCGGAGACCGATAGCGC
ACAAGTAGAGTGATCGAAAGATGAAAAGCACTTTGAAAAGAGAGTTAAAAAGCACGTGAAATTGTT
GAAAGGGAAGCGCTTGCGACCAGACTCGCTCGCGGGGTTCAGCCGGCATTCGTGCCGGTGTACTTC
CCCGCGGGCGGGCCAGCGTCGGTTTGGGCGGTCGGTCAAAGGCCCTCGGAAGGTAACGCCCCTAG
GGGCGTCTTATAGCCGAGGGTGCAATGCGACCTGCCTAGACCGAGGAACGCGCTTCGGCTCGGACG
CTGGCATAATGGTCGTAAACGACCCGTCTTGAA

Fig. S2. Spectroscopic data for compound **1**.
(**A**): HR-ESI-MS (**a**), IR (**b**), and UV (**c**) spectra of compound **1a** and **1b**.

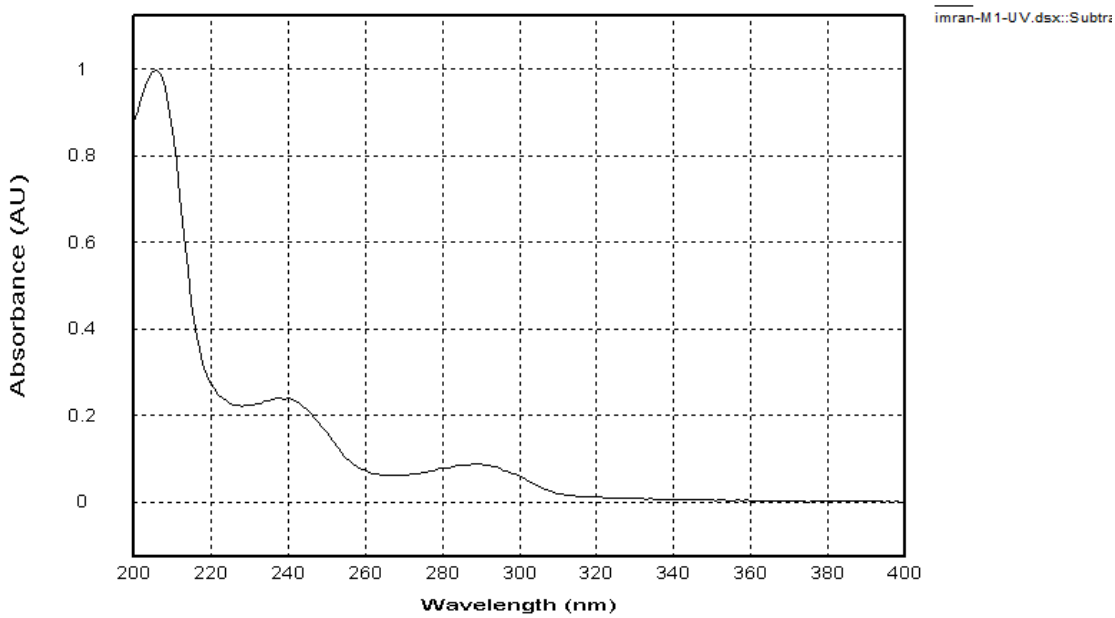
(**a**). HR-ESI-MS



(**b**). IR



(**c**). UV



No.	wavelength (nm)	absorbance
1	206	0.997
2	238	0.238
3	290	0.085

Fig. S2. Spectroscopic data for compound **1**. (continued)
(**B**) The ^{1}H NMR spectrum of compound **1** in $CDCl_3$.

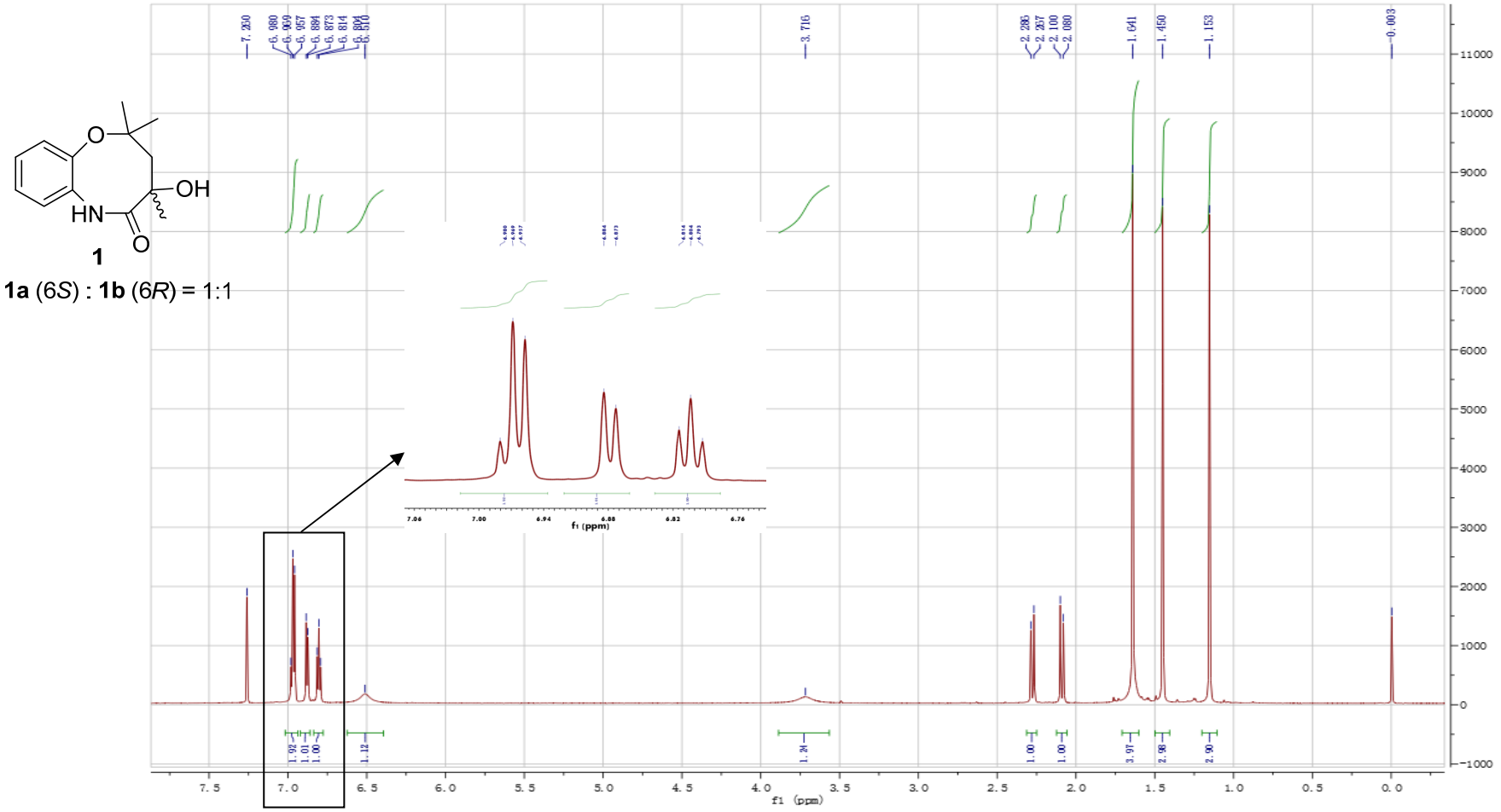


Fig. S2. Spectroscopic data for compound **1**. (continued)
(**C**) The ^{13}C NMR spectrum of compound **1** in $CDCl_3$.

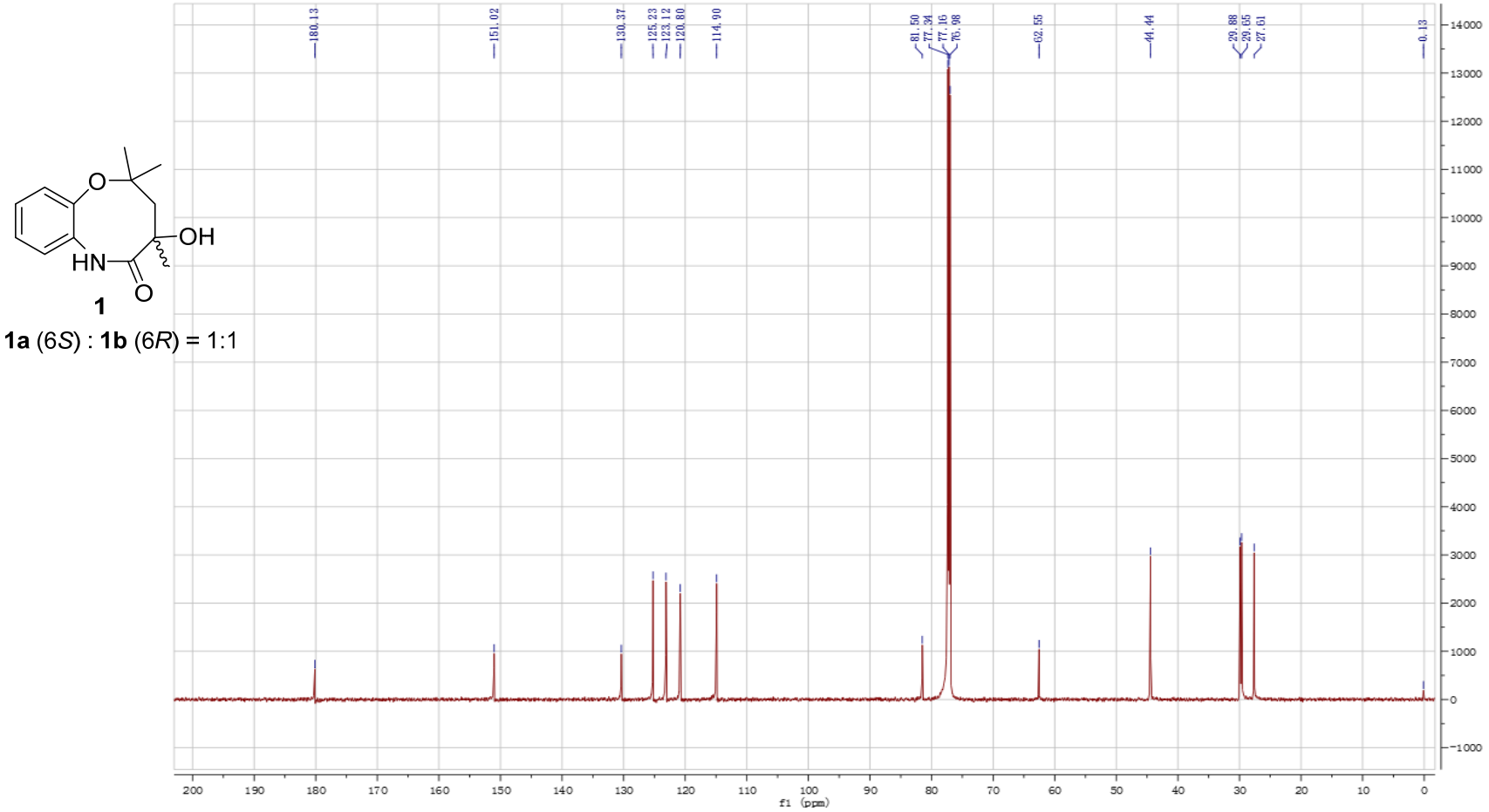


Fig. S2. Spectroscopic data for compound **1**. (continued)
(**D**) The DEPT 135 NMR spectrum of compound **1** in $CDCl_3$.

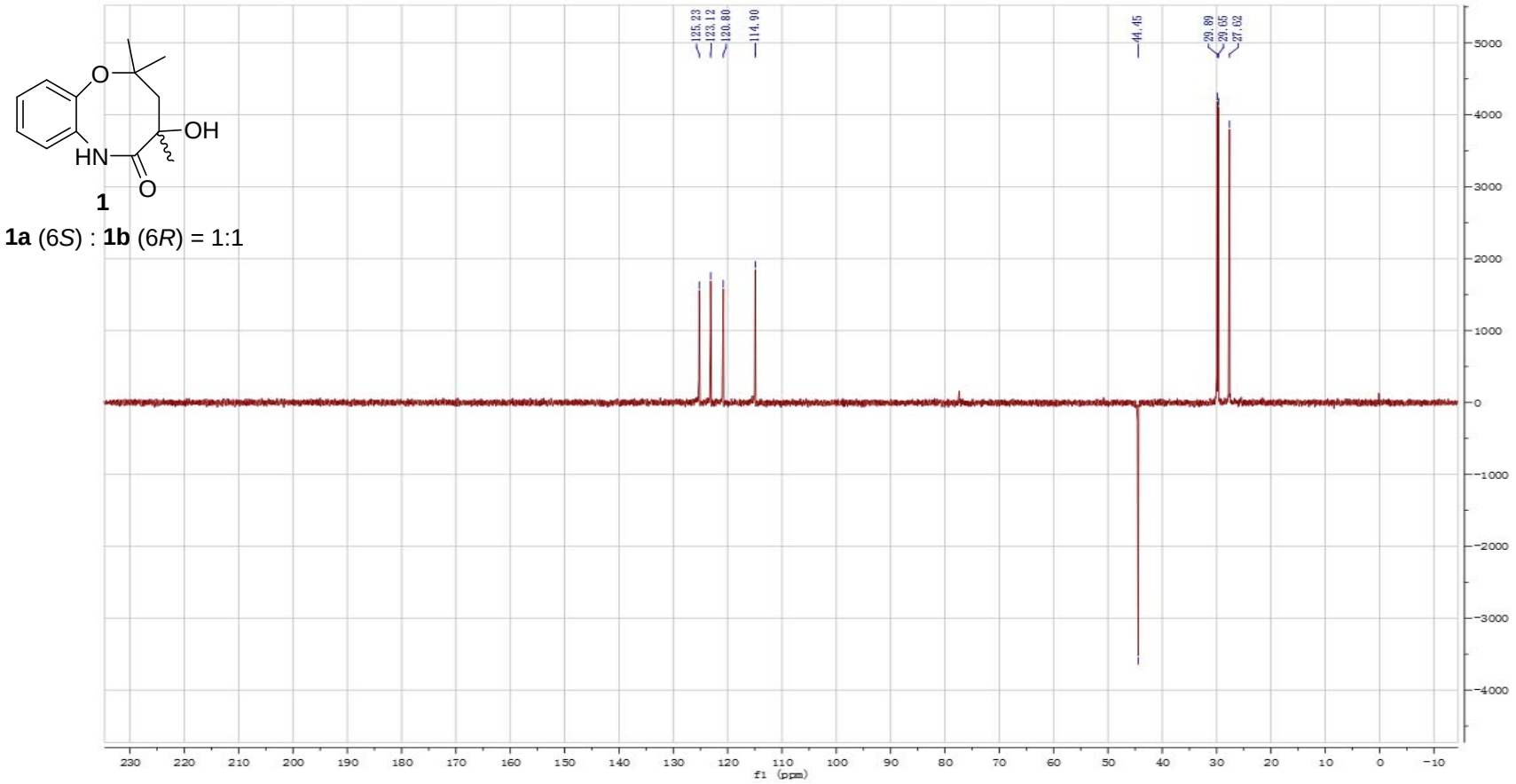
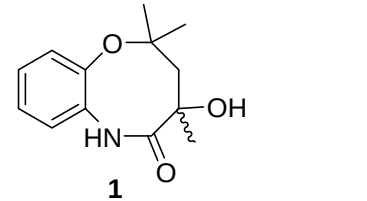


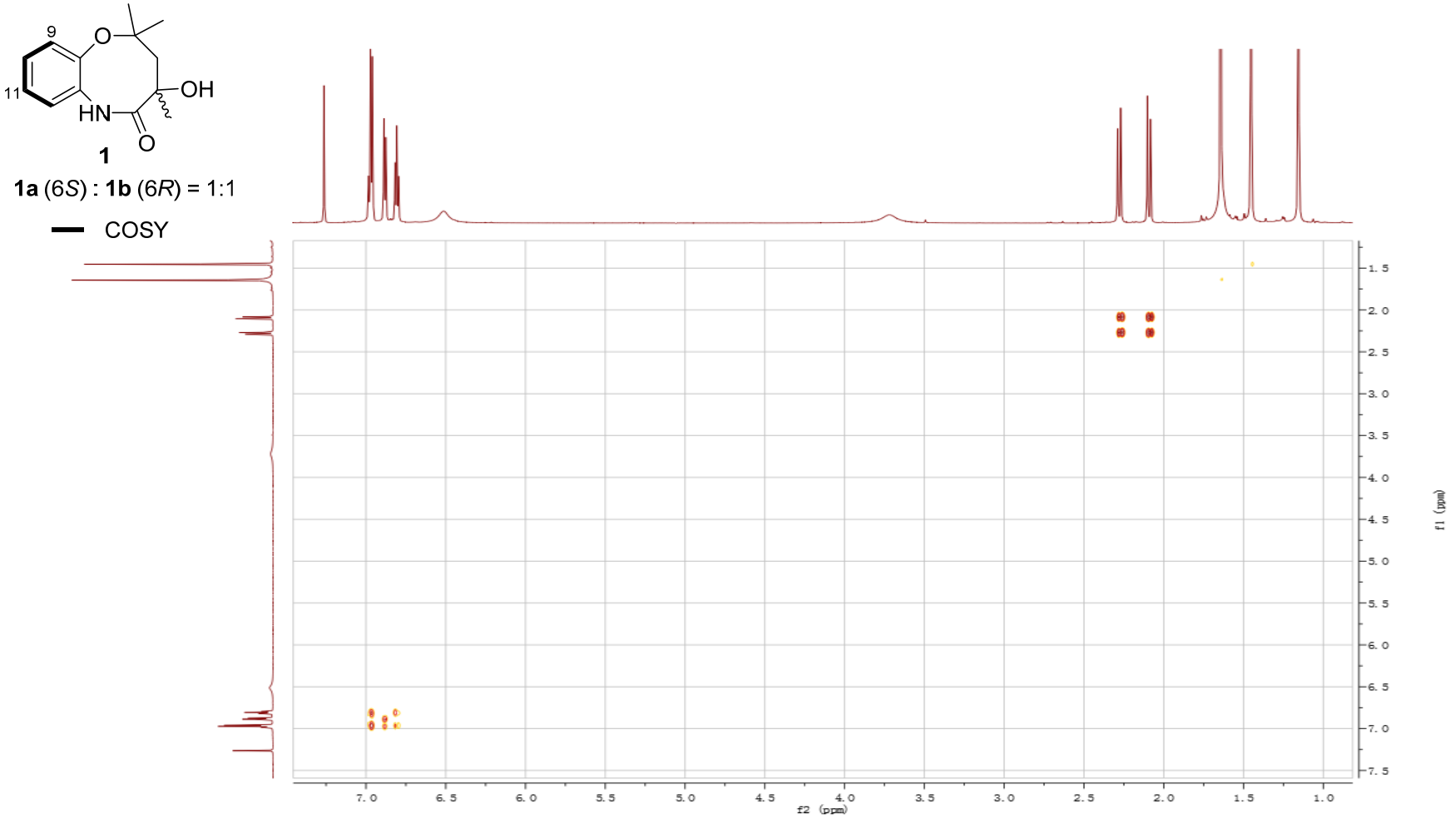
Fig. S2. Spectroscopic data for compound **1**. (continued)
(E) The HSQC spectrum of compound **1** in $CDCl_3$.



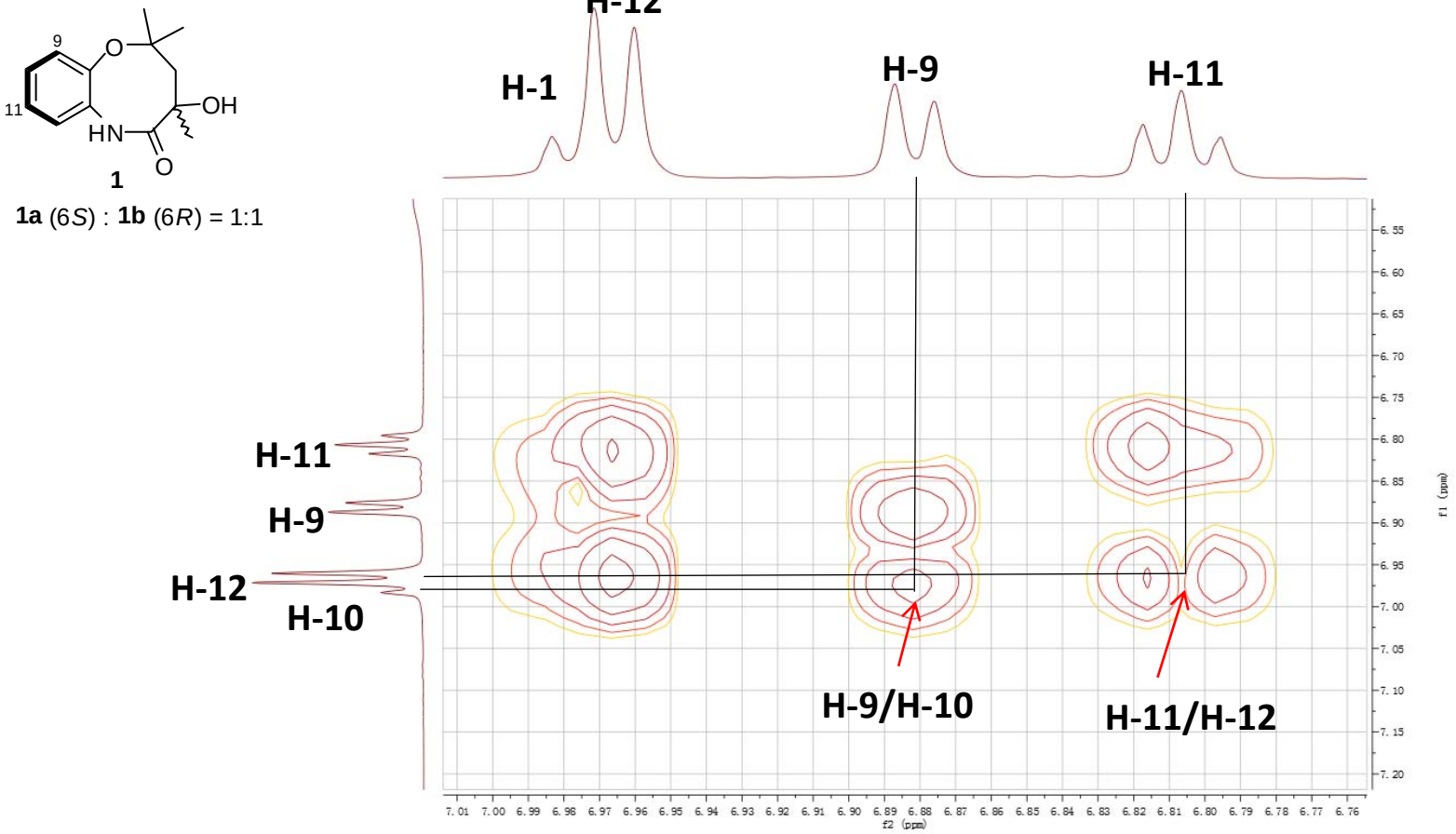
1

1a (6*S*) : **1b** (6*R*) = 1:1

Fig. S2. Spectroscopic data for compound **1**. (continued)
(F) The COSY spectrum of compound **1** in $CDCl_3$.

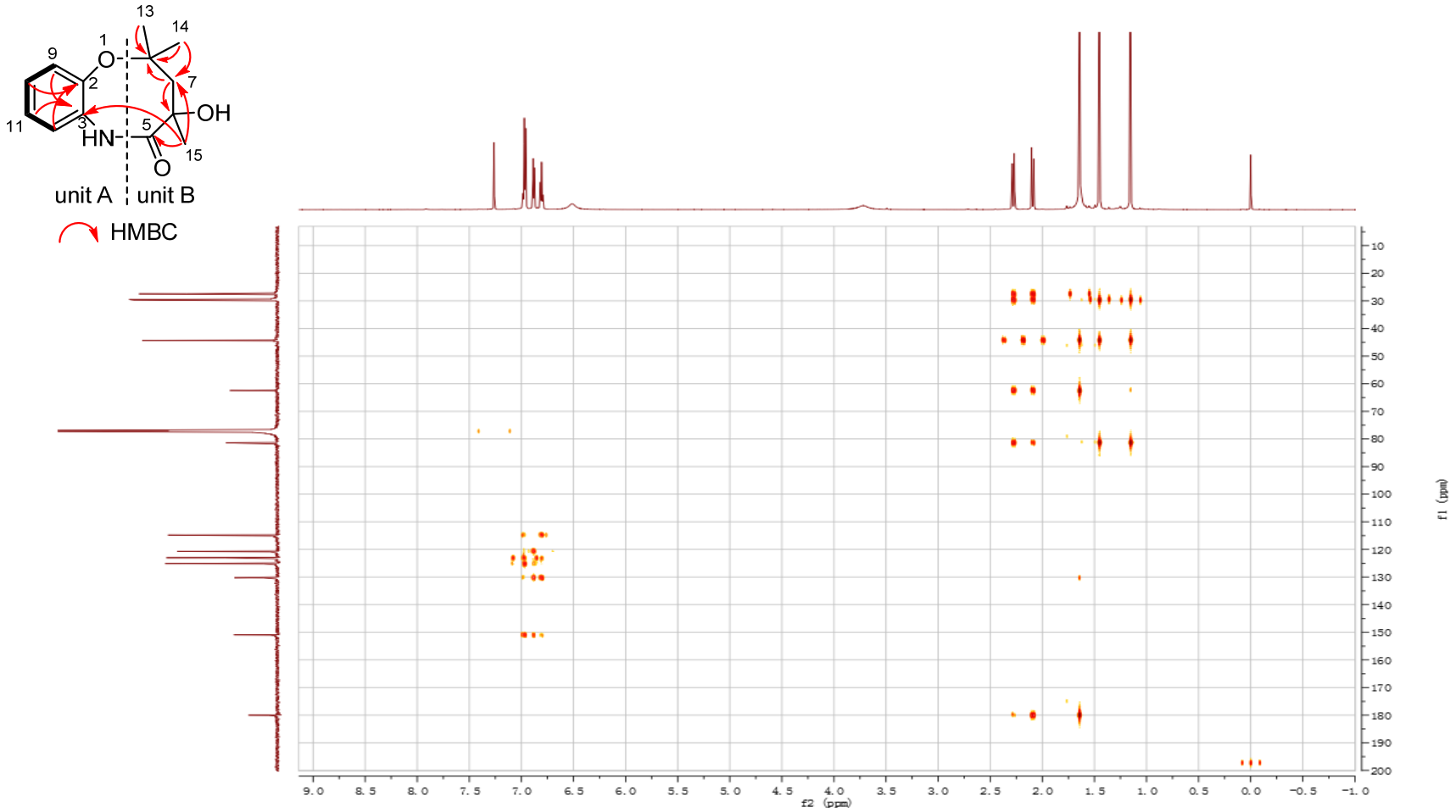


(G) Selected key COSY correlations of compound **1** in $CDCl_3$.



1a (6*S*) : **1b** (6*R*) = 1:1

Fig. S2. Spectroscopic data for compound **1**. (continued)
(H) The HMBC spectrum of compound **1** in $CDCl_3$.



(I) Selected key HMBC correlations of compound **1** in $CDCl_3$.

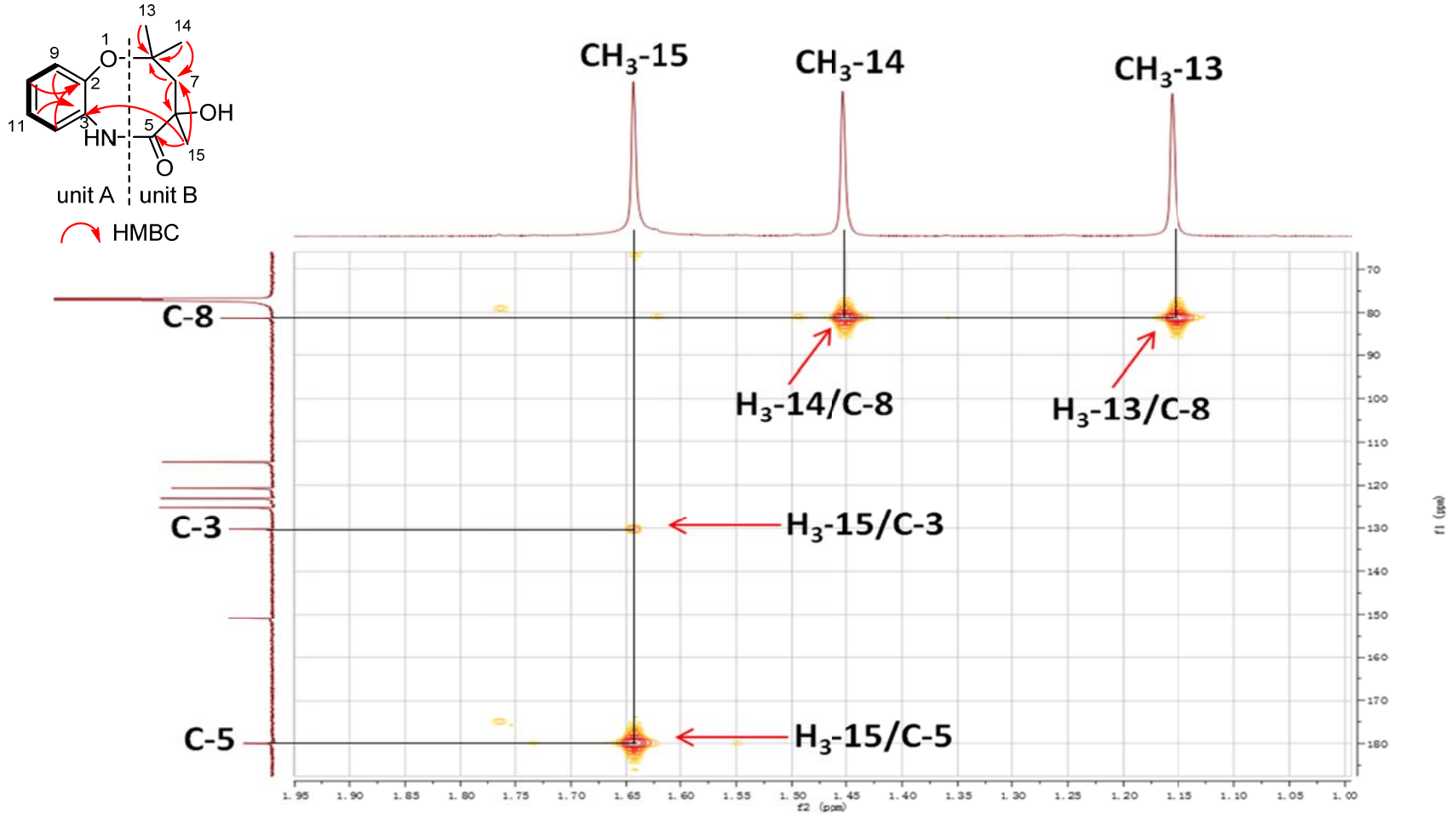
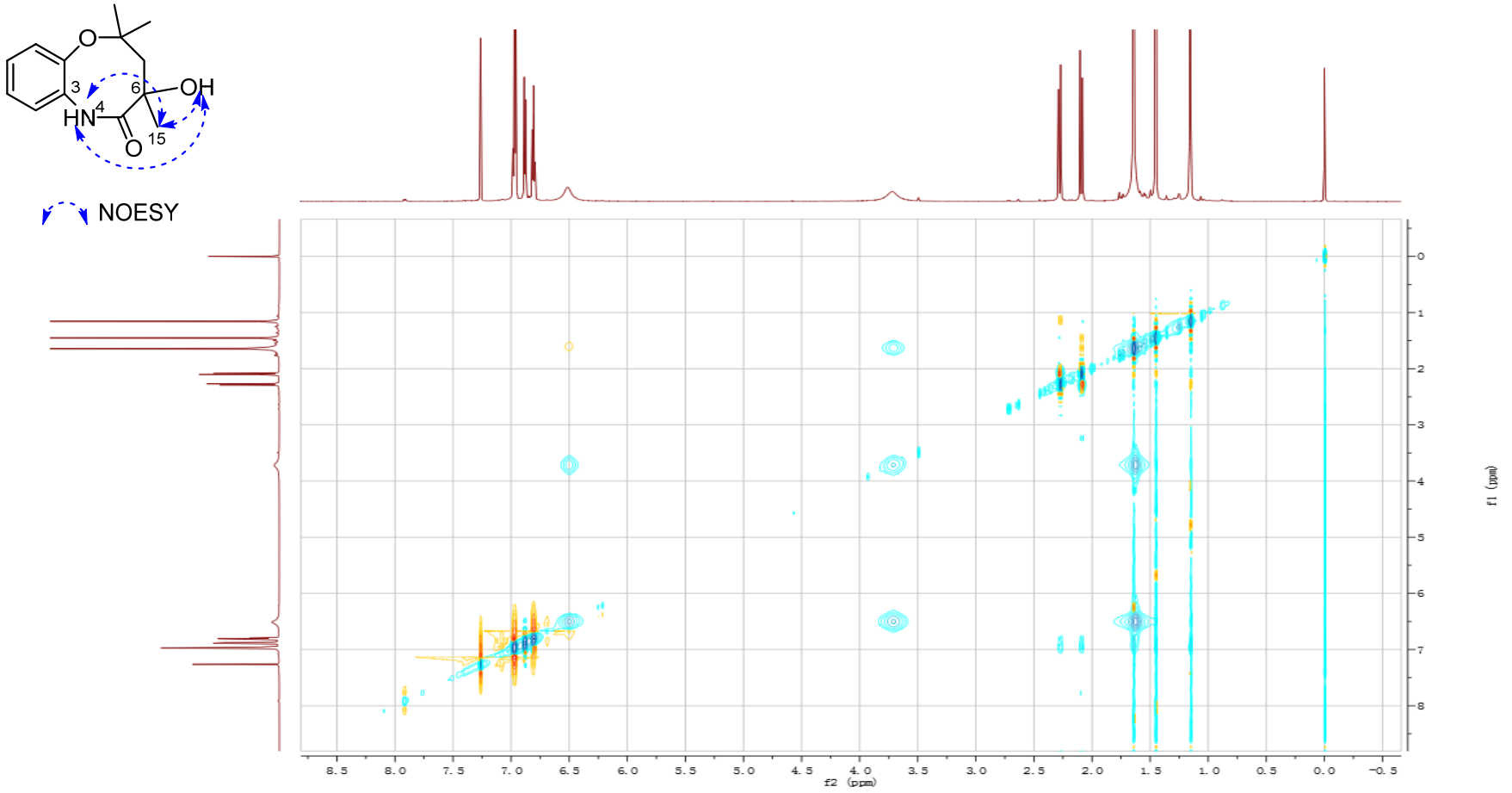


Fig. S2. Spectroscopic data for compound **1**. (continued)
(J) The NOESY spectrum of compound **1** in $CDCl_3$.



(K) Selected key NOESY correlations of compound **1** in $CDCl_3$.

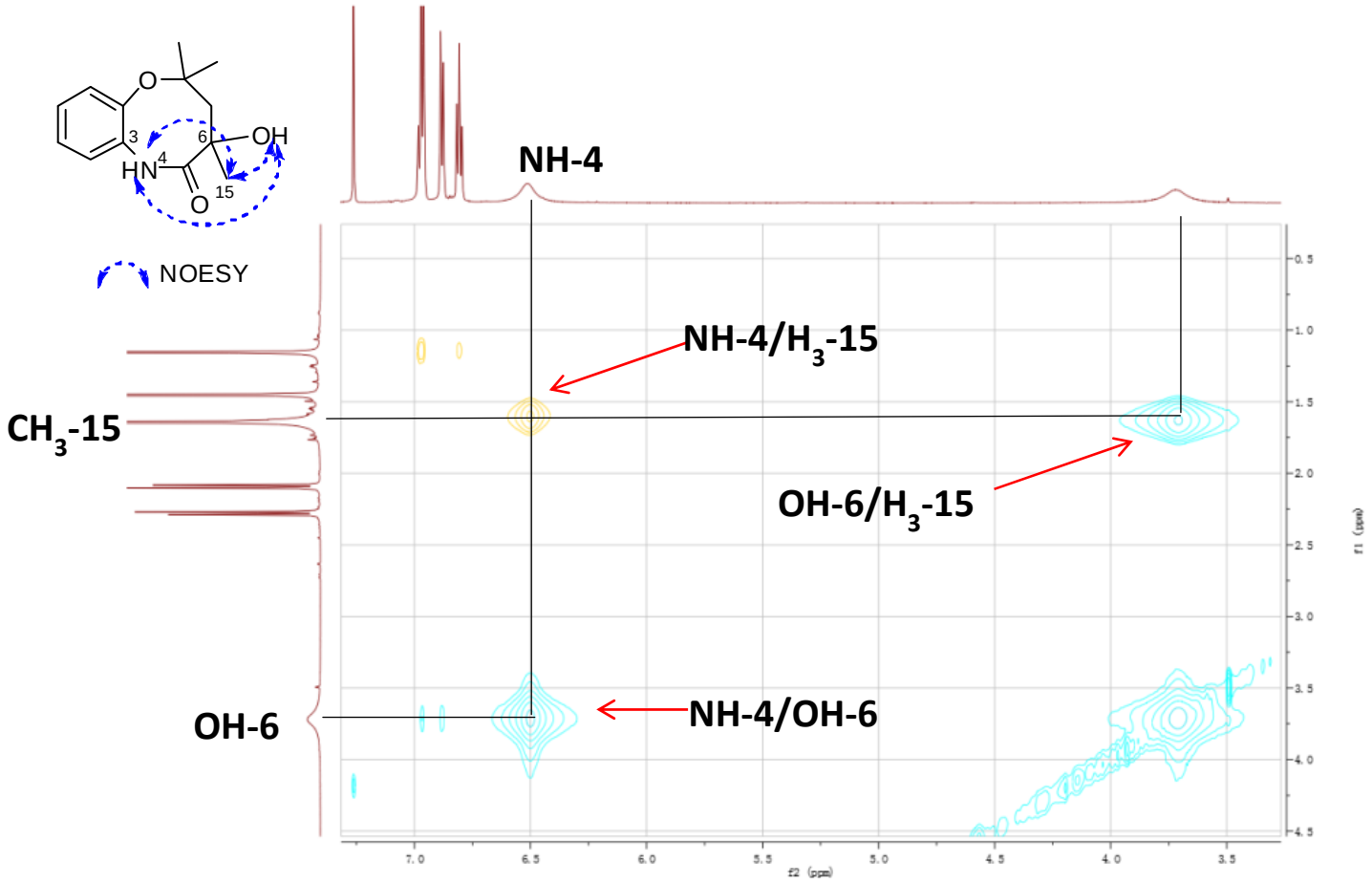


Fig. S3. Spectroscopic data for compound **9**

(**A**) The ^{1}H NMR spectrum of compound **9** in DMSO-d_6 (700 MHz).

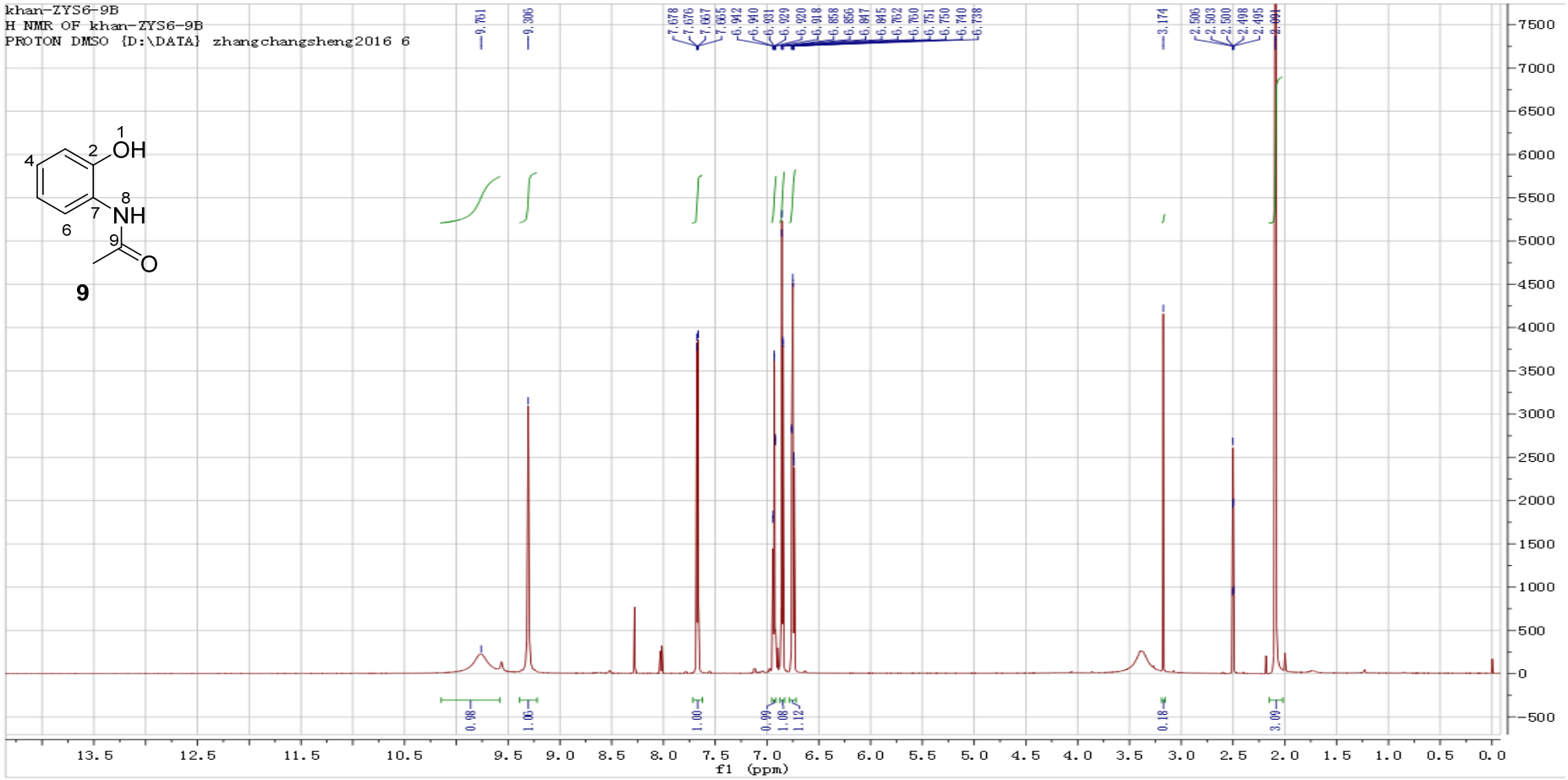


Fig. S3. Spectroscopic data for compound **9**

(B) The ^{13}C NMR spectrum of compound **9** in DMSO-d_6 (175 MHz).

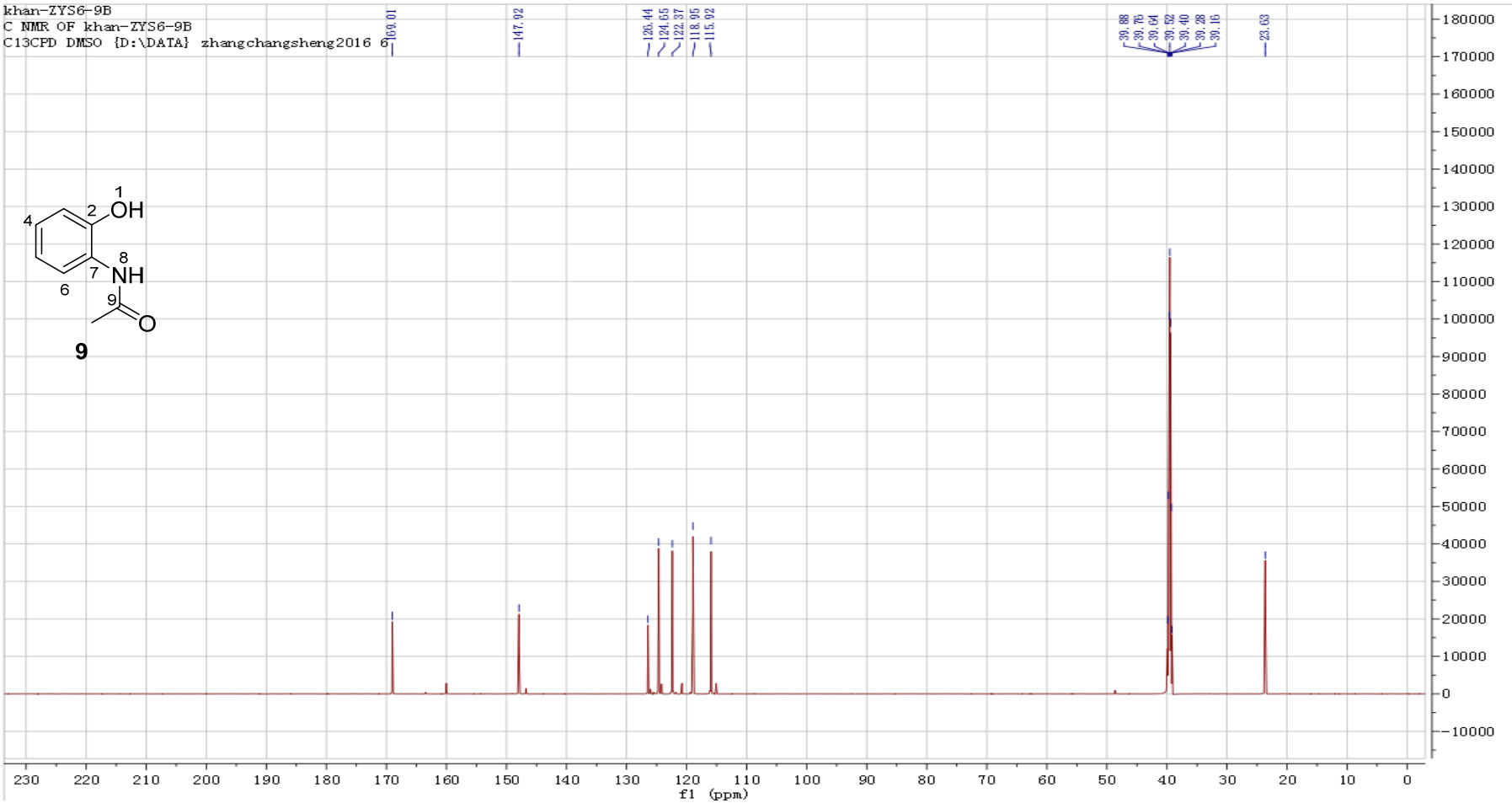
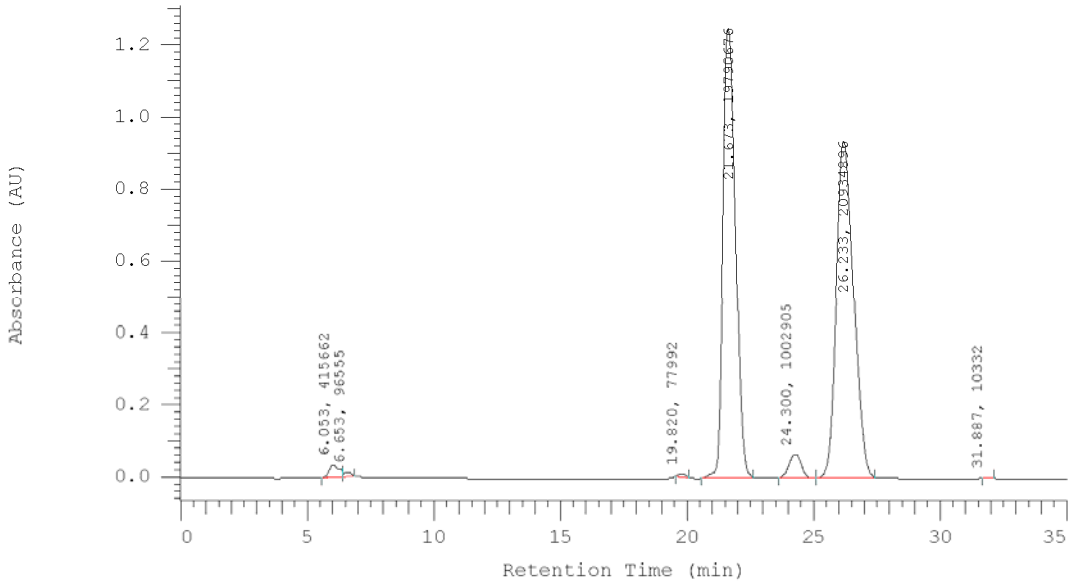


Fig. S4. HPLC analysis of compound **1** using a chiral column



Column: Lux® 5µm, i-cellulose-5 column, 250×4.6 mm, Phenomenex instrument Co., LTD.
Detection wavelength: 254 nm
Solvents, A: water, B: acetonitrile.
Isocratic elution: 0-35 min, A:73%; B:27%.
Compounds: **1a** [(6*S*)-chrysonin A], t_R=21.67 min, Peak area=19,790,676;
1b [(6*R*)-chrysonin A], t_R=26.23 min, Peak area=20,934,896;
Molar ratio of **1a**:**1b**=1:1.06

Fig. S5. Spectroscopic data of (6*S*)-chrysonin A (**1a**)
(**A**) The ^{1}H NMR spectrum of **1a** in $CDCl_3$.

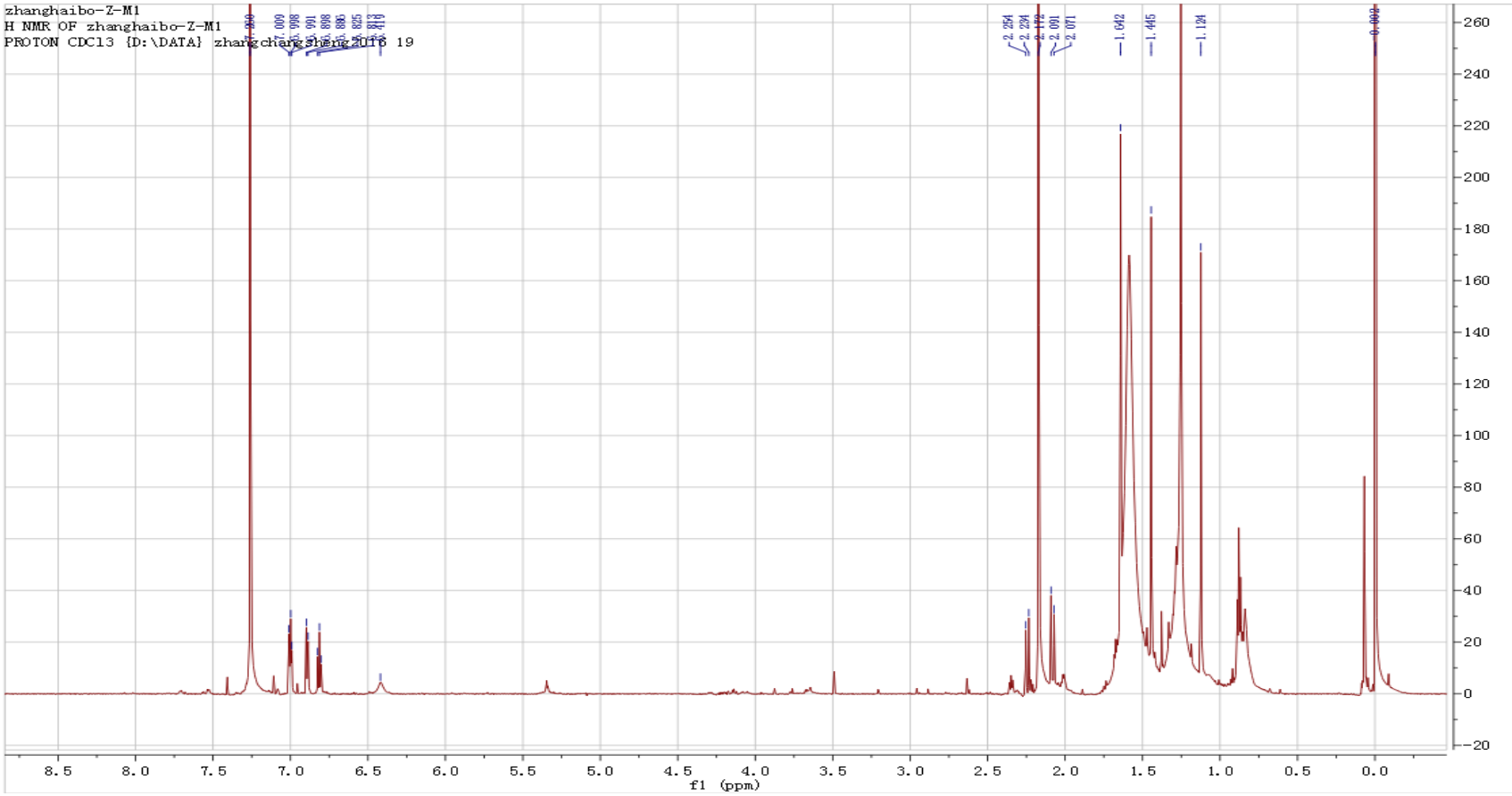


Fig. S5. Spectroscopic data of (6*S*)-chrysonin A (**1a**). (continued)
(**B**) The ^{13}C NMR spectrum of **1a** in $CDCl_3$.

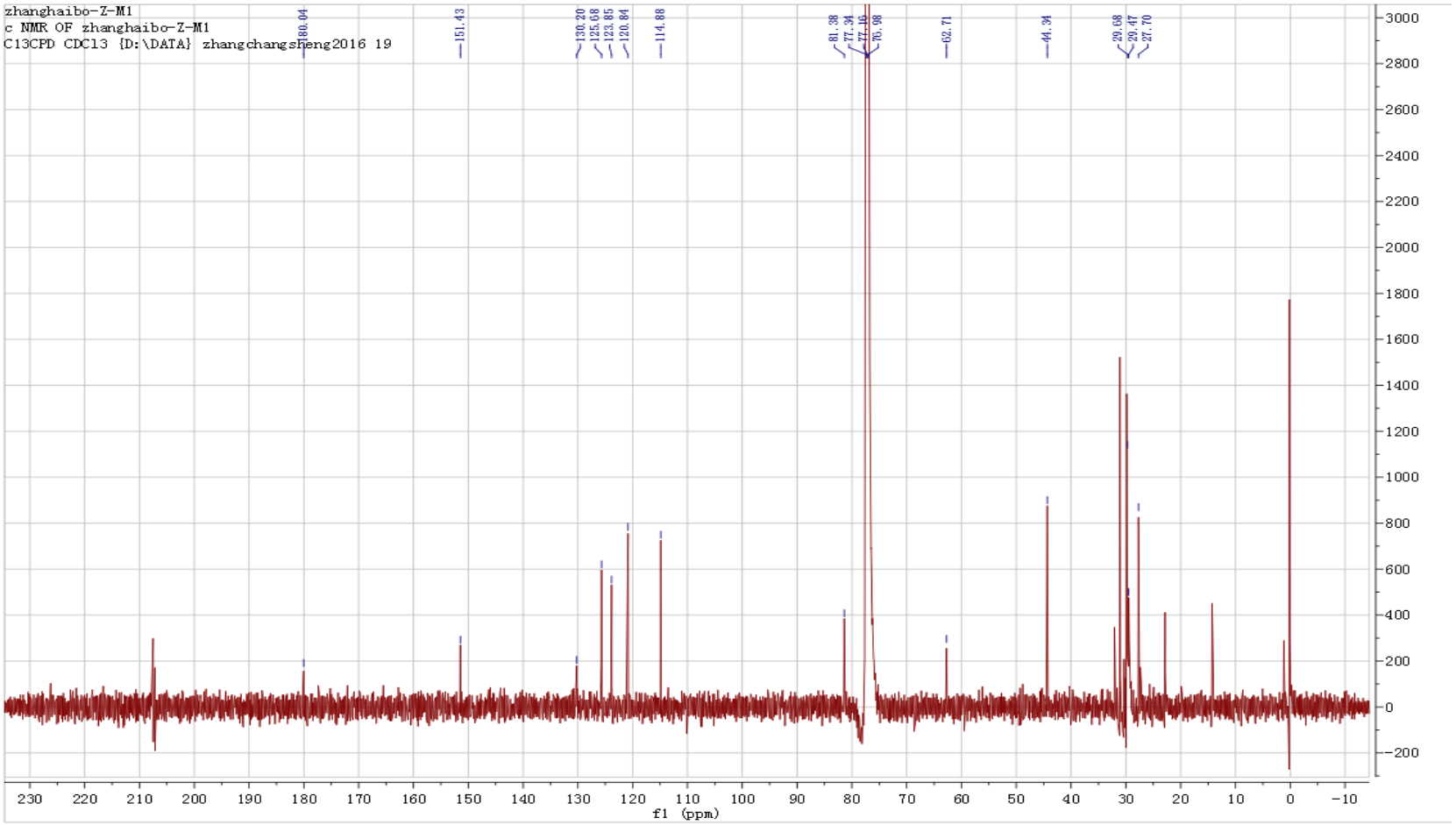


Fig. S6. Spectroscopic data of (6*R*)-chrysonin A (**1b**).
(**A**) The ^{1}H NMR spectrum of **1b** in $CDCl_3$.

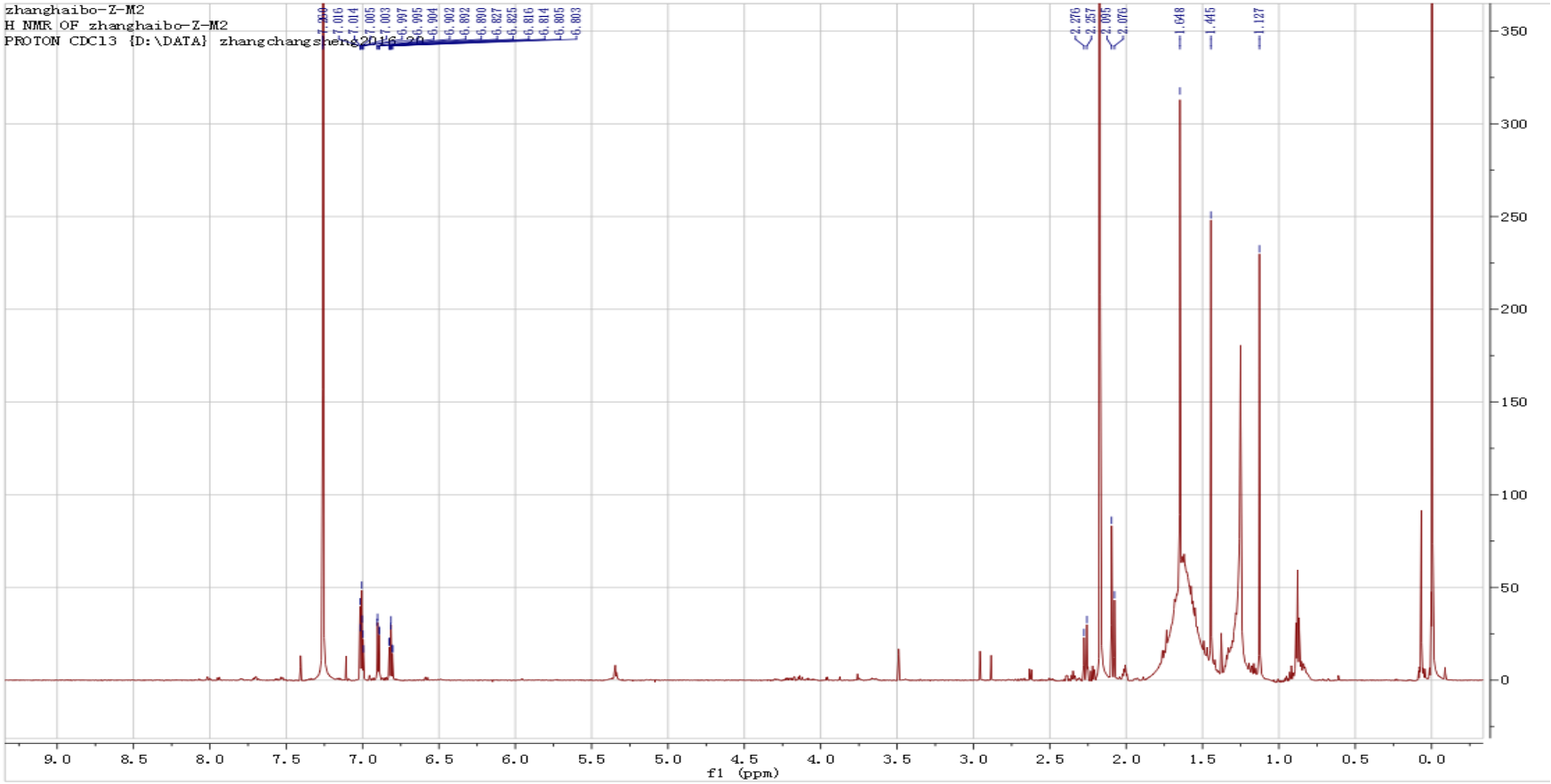


Fig. S6. Spectroscopic data of (6*R*)-chrysonin A (**1b**). (continued)
(**B**) The ^{13}C NMR spectrum of **1b** in $CDCl_3$.

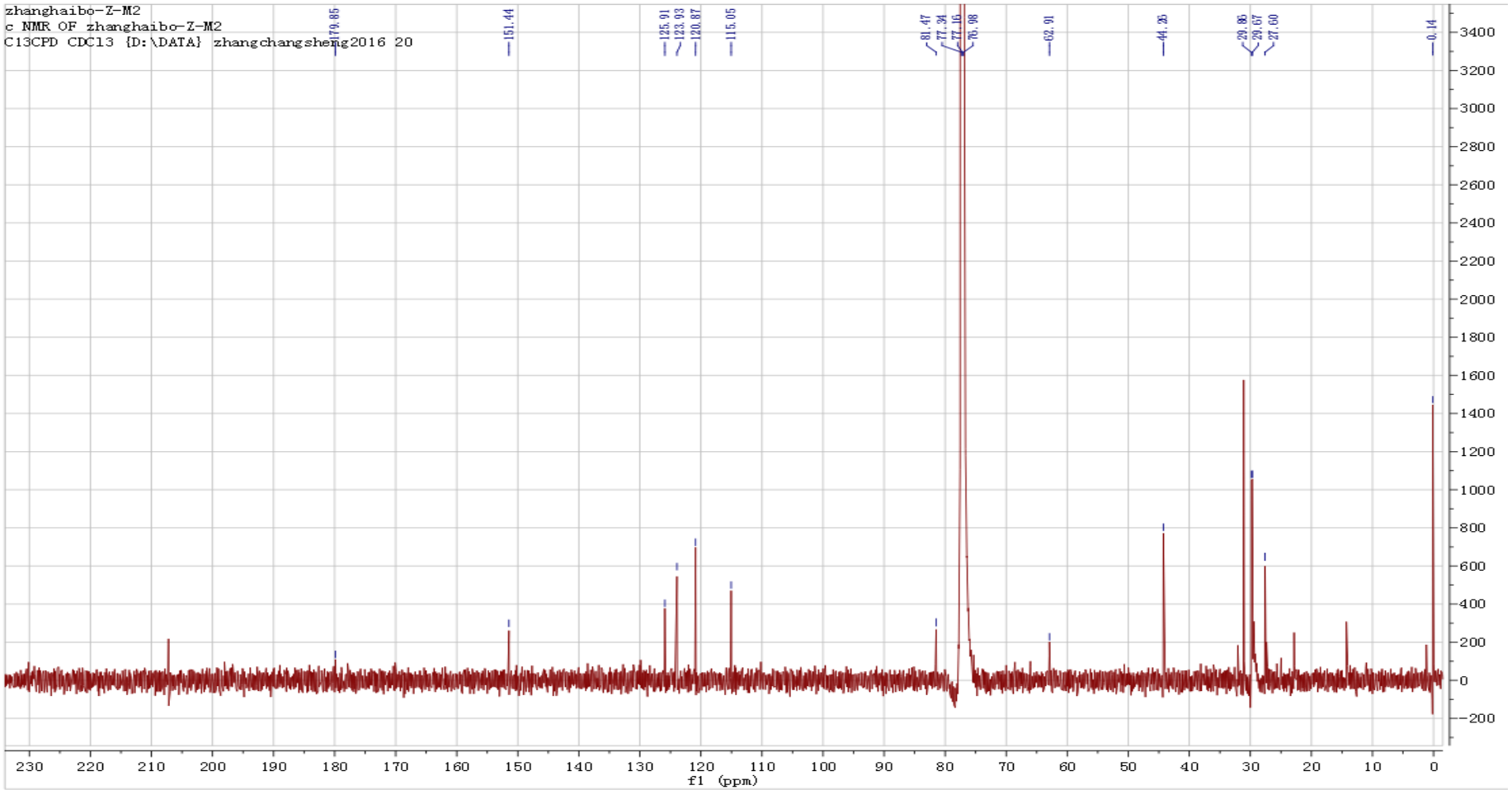
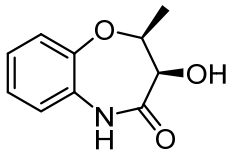


Fig. S7. Chemical Structure of compound 1932813-80-3 (CAS number)



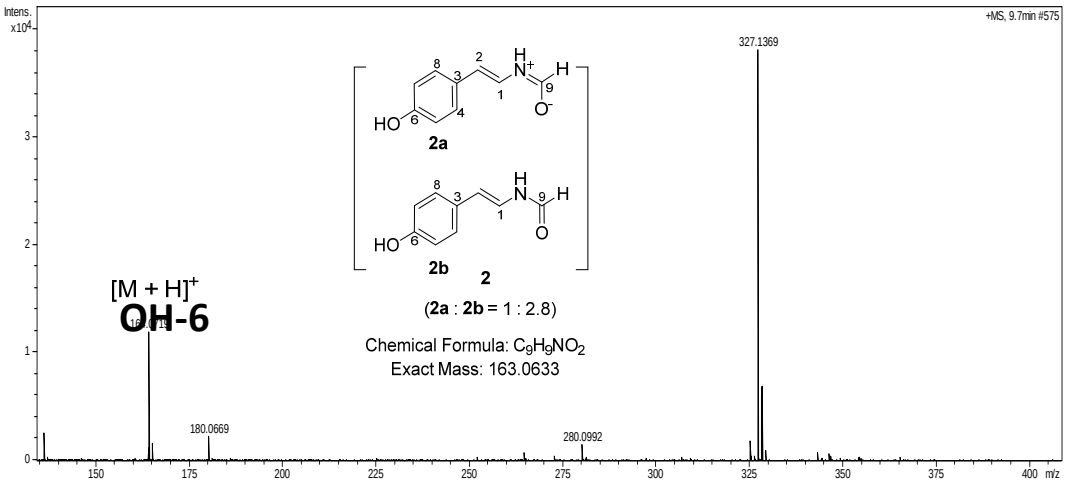
CAS number:1932813-80-3

No reference available for this compound: (2*S*,3*R*)-2,3-dihydro-3-hydroxy-2-methyl-1,5-benzoxazepin-4(5*H*)-one.

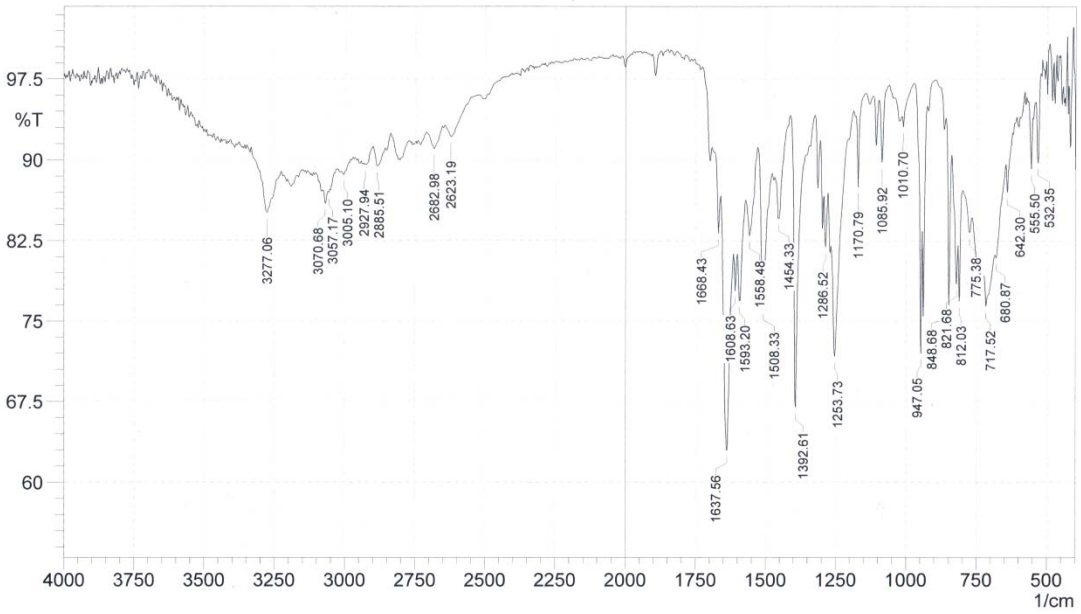
Fig. S8. Spectroscopic data of compound **2**

(**A**) : HR-ESI-MS (**a**), IR (**b**), and UV (**c**) spectra of compound **2**

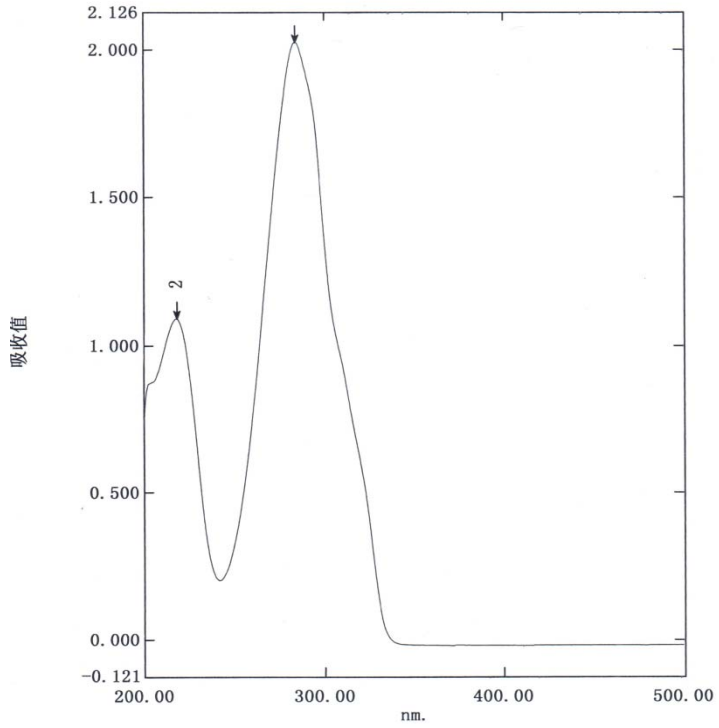
(**a**) HR-ESI-MS



(**b**). IR



(**c**). UV



No.	P/V	波长(nm)	吸收值	描述
1		284.00	2.024	
2		218.20	1.090	

Fig. S8. Spectroscopic data of compound **2**. (continued)
(**B**) The ^{1}H NMR spectrum of **2** in DMSO-d_6.

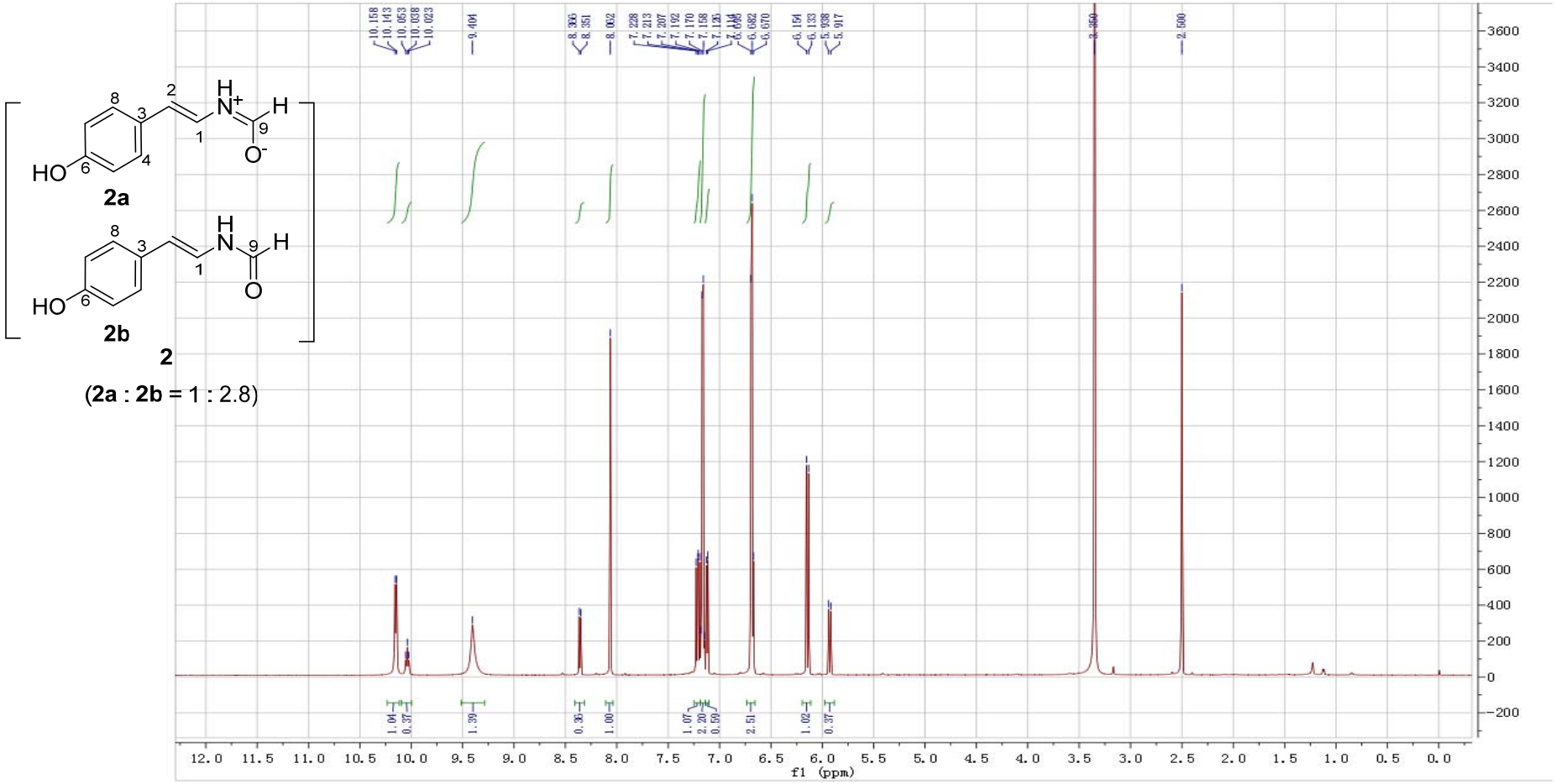


Fig. S8. Spectroscopic data of compound **2**. (continued)
(**C**) The ^{13}C NMR spectrum of **2** in DMSO-d_6.

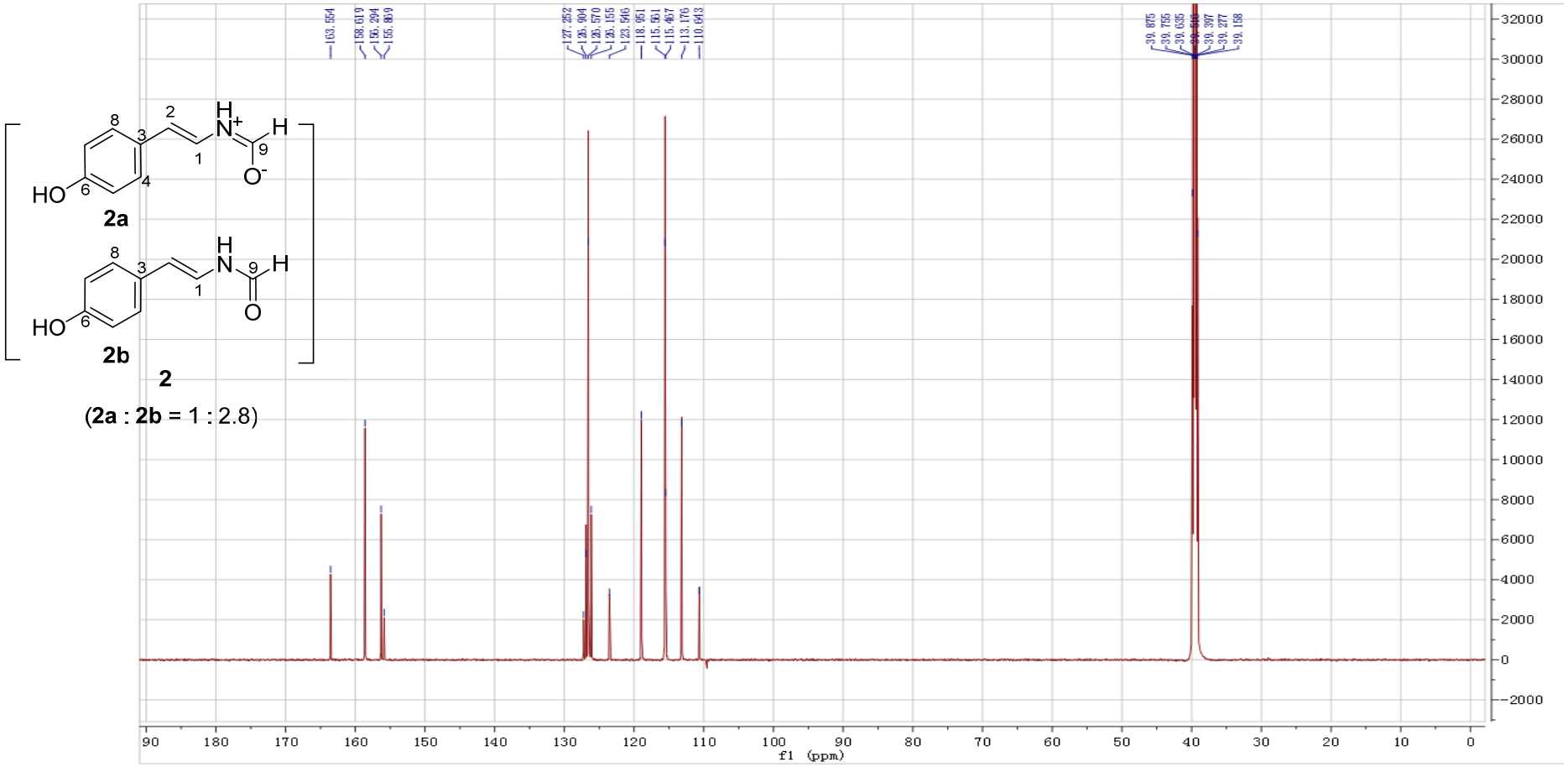


Fig. S8. Spectroscopic data of compound **2**. (continued)
(**D**) The DEPT 135 NMR spectrum of **2** in DMSO-d_6.

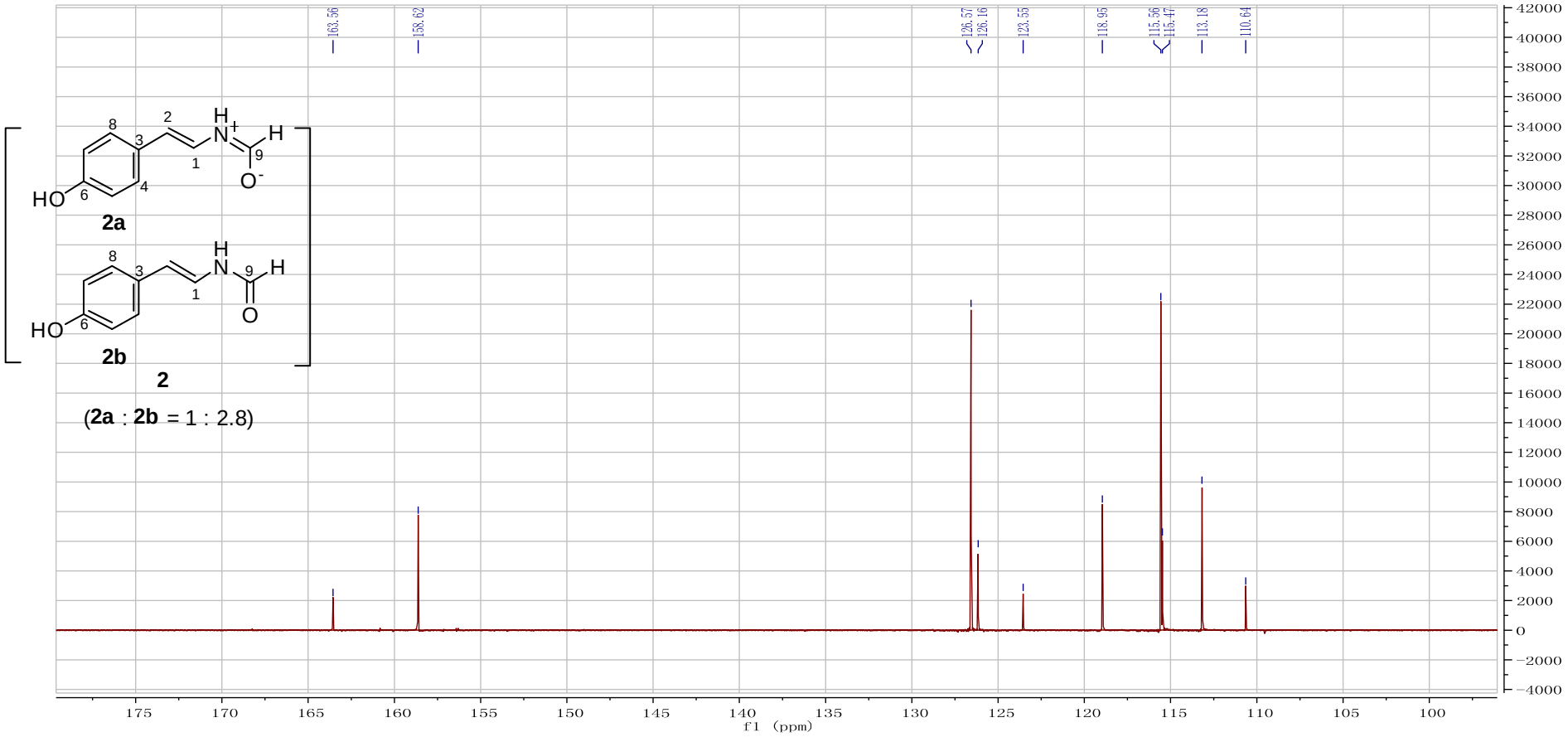


Fig. S8. Spectroscopic data of compound **2**. (continued)
(E) The HSQC spectrum of **2** in DMSO-d_6.

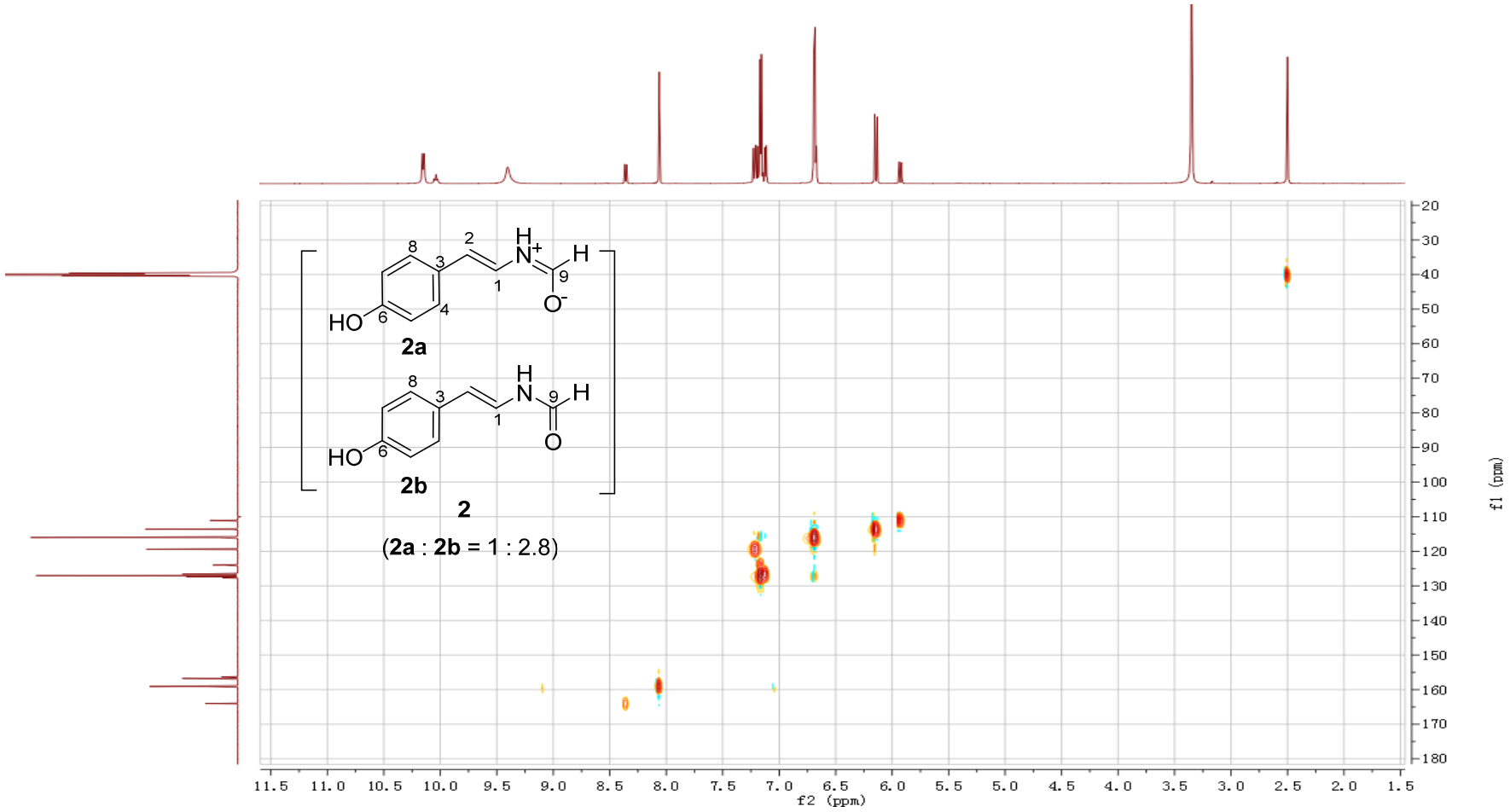
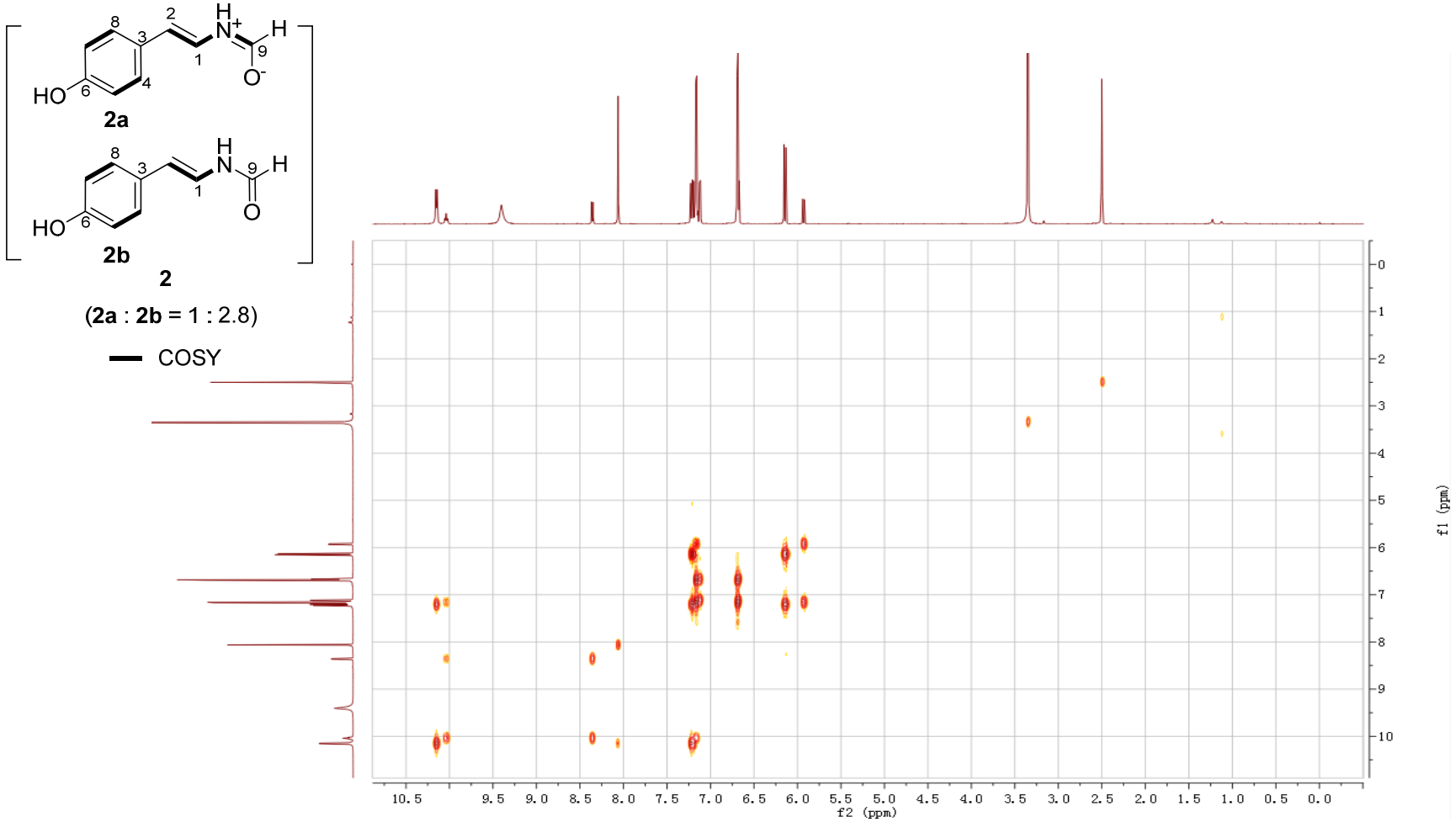


Fig. S8. Spectroscopic data of compound **2**. (continued)
(F) The COSY spectrum of **2** in DMSO-d_6.



(G) Selected key COSY correlations of compound **2** in DMSO-d_6.

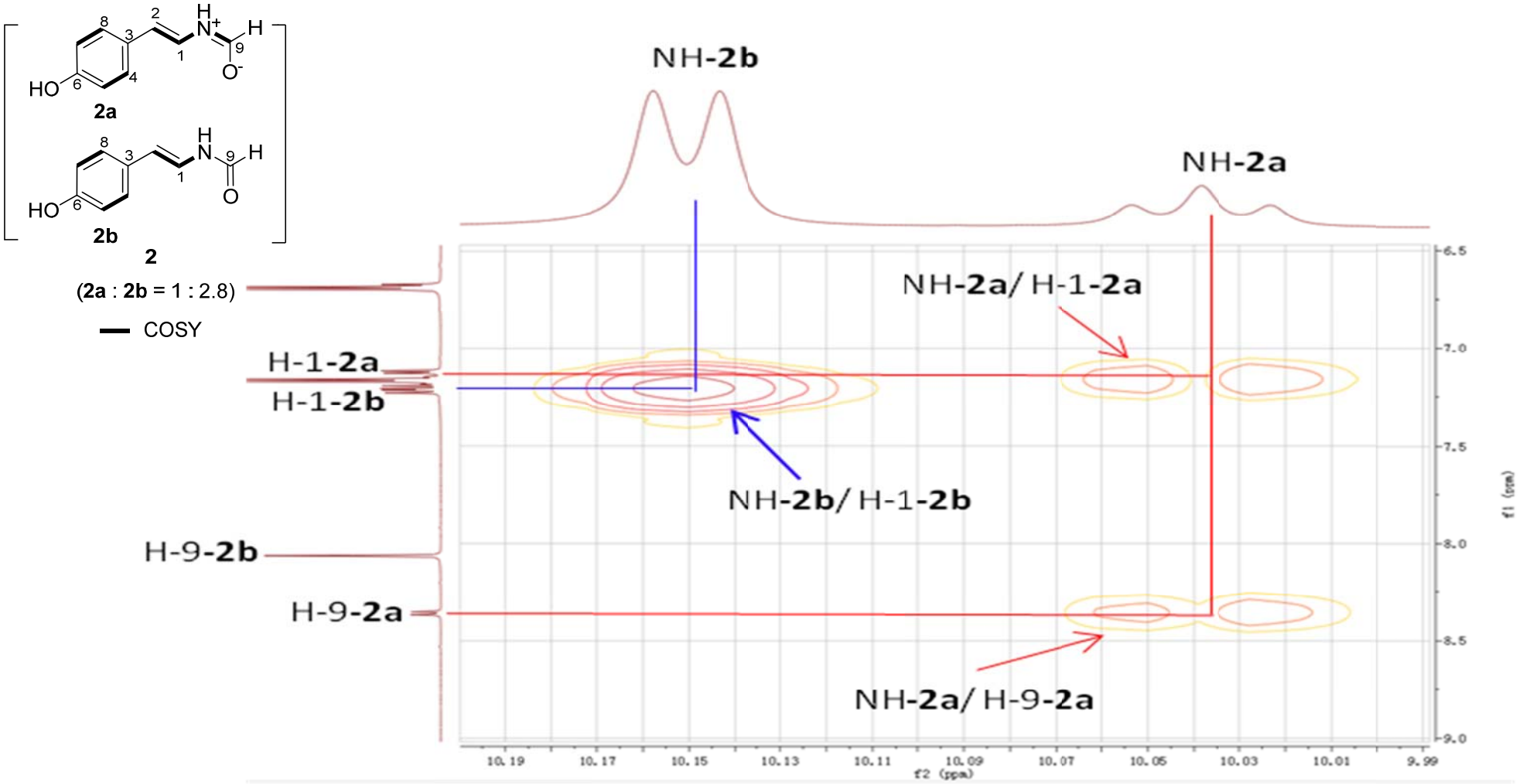


Fig. S8. Spectroscopic data of compound **2**. **(**continued)
(H) The HMBC spectrum of **2** in DMSO-d_6.

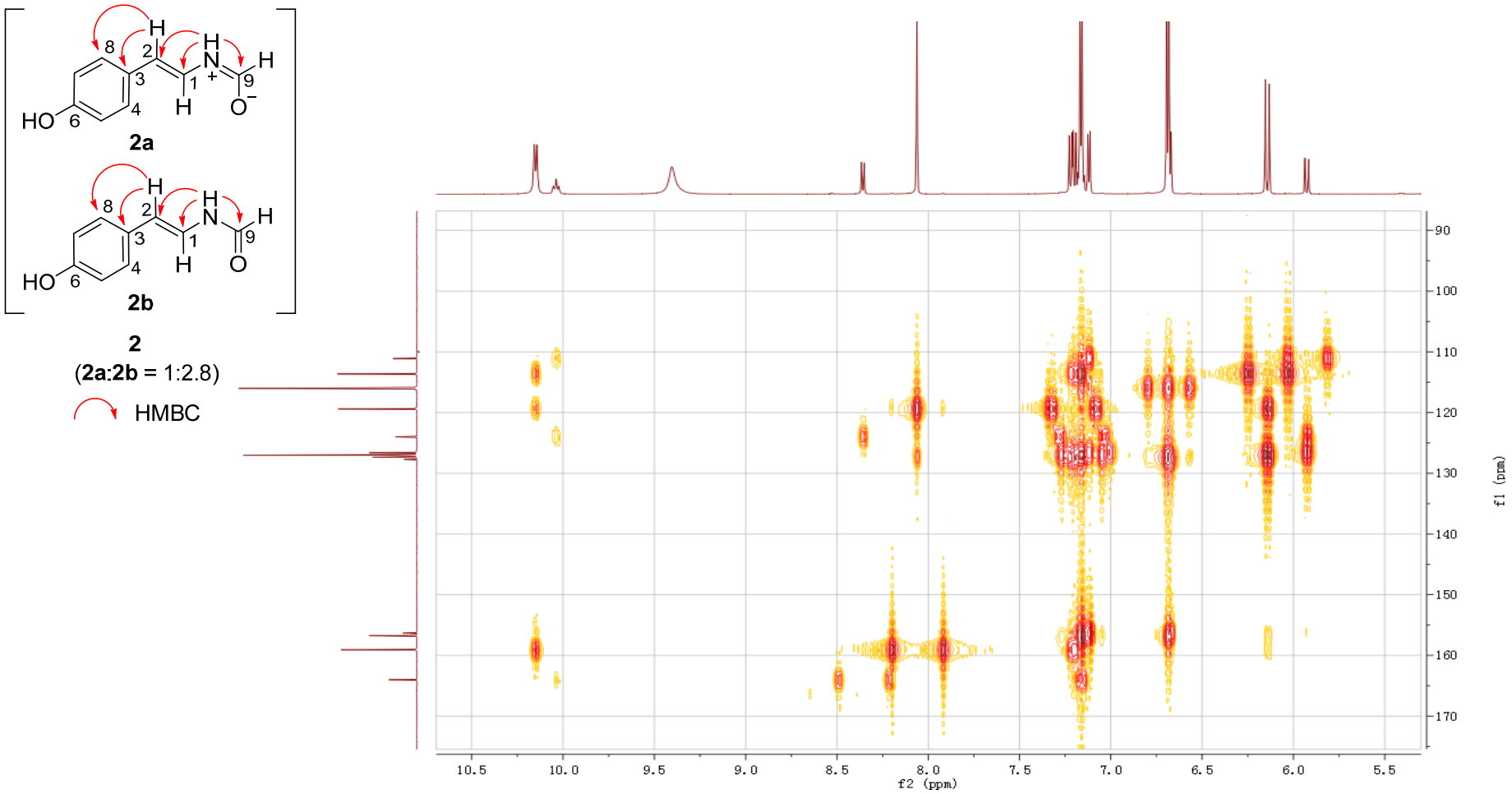
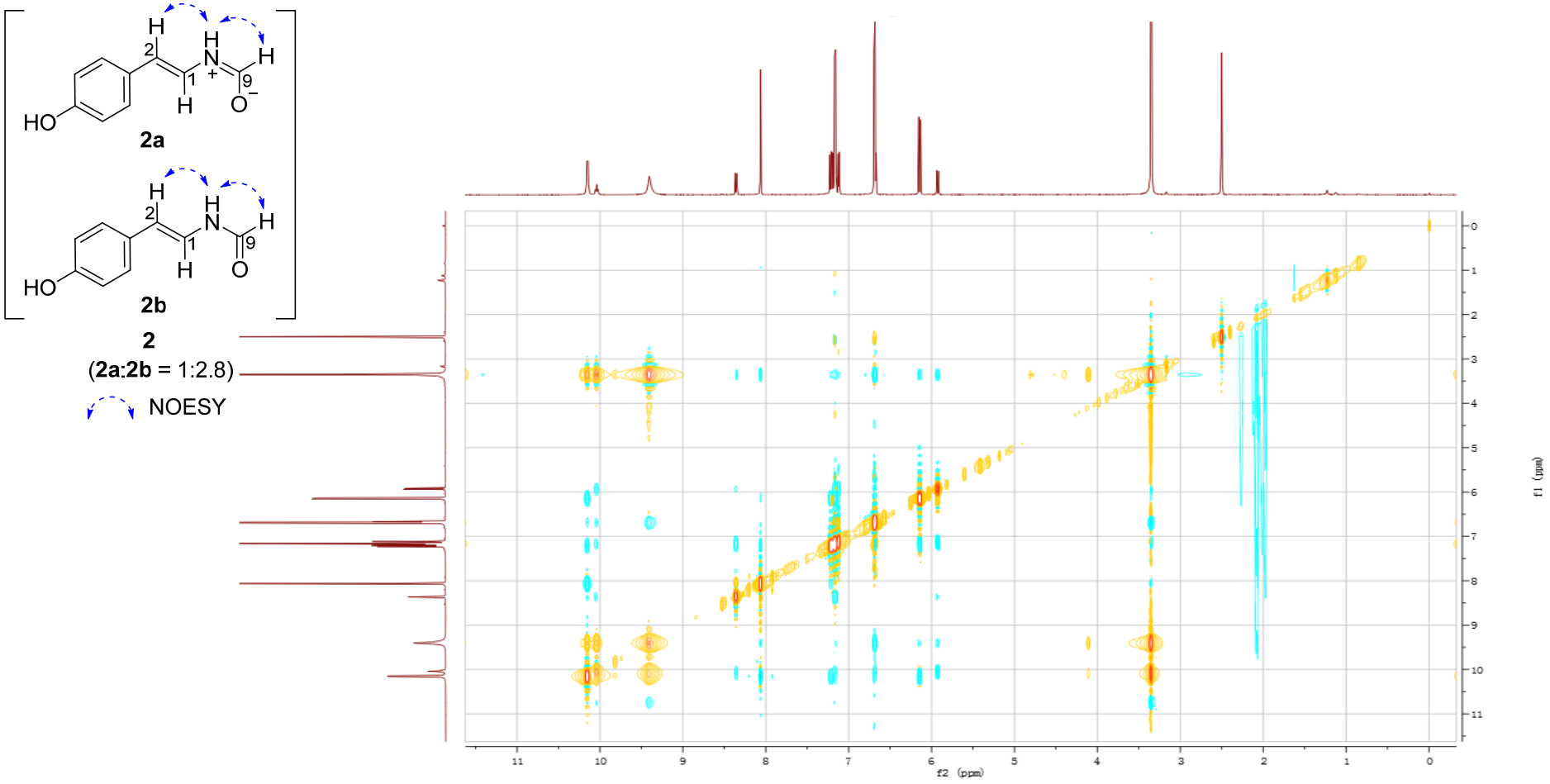


Fig. S8. Spectroscopic data of compound **2**. **(**continued)
(I) The NOESY spectrum of **2** in DMSO-d_6.



(J) Selected key NOESY correlations of compound **2** in DMSO-d_6.

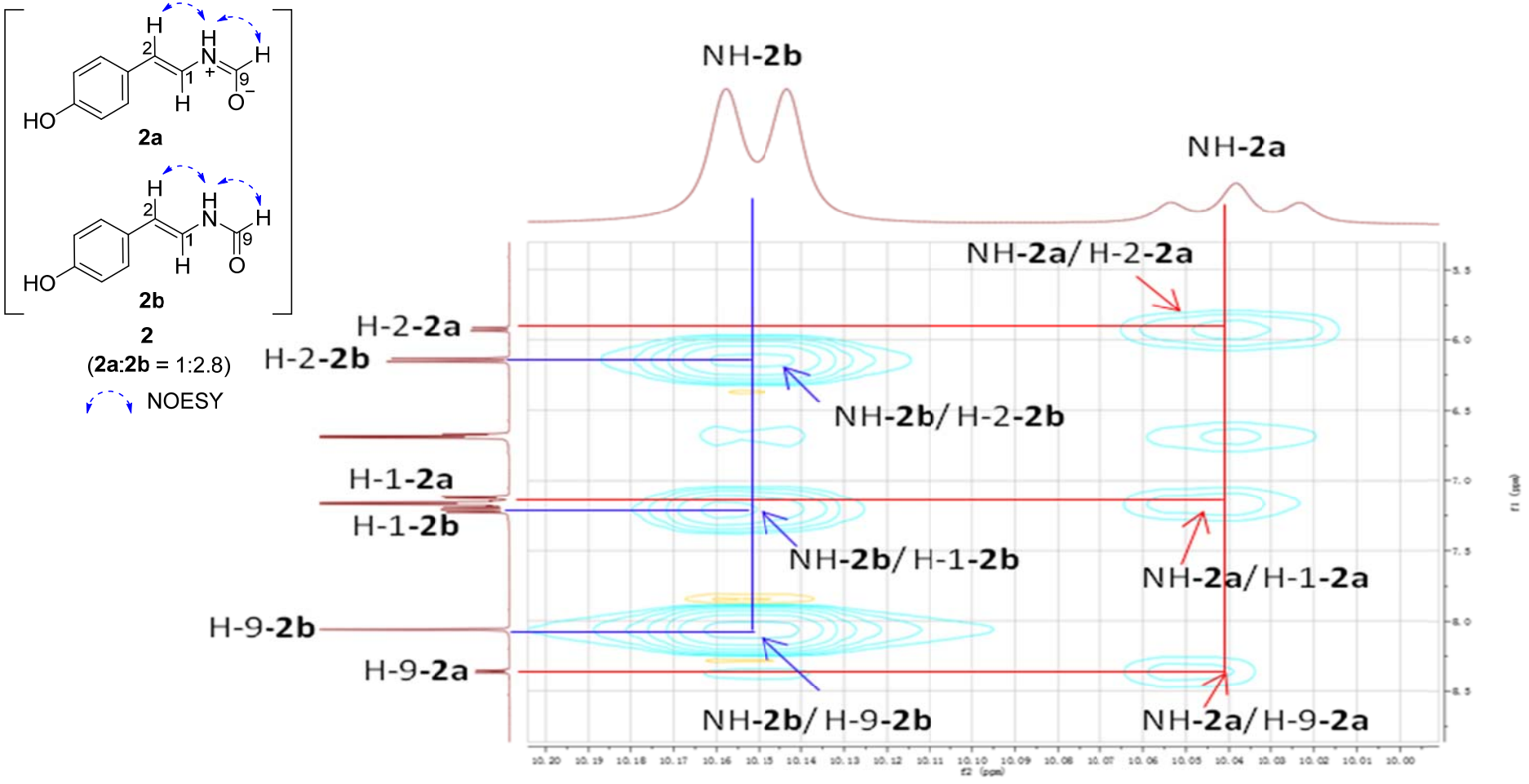


Fig. S9. ^{1}H NMR spectrum of reference **2b** (reported by Ting Jiang).[2]

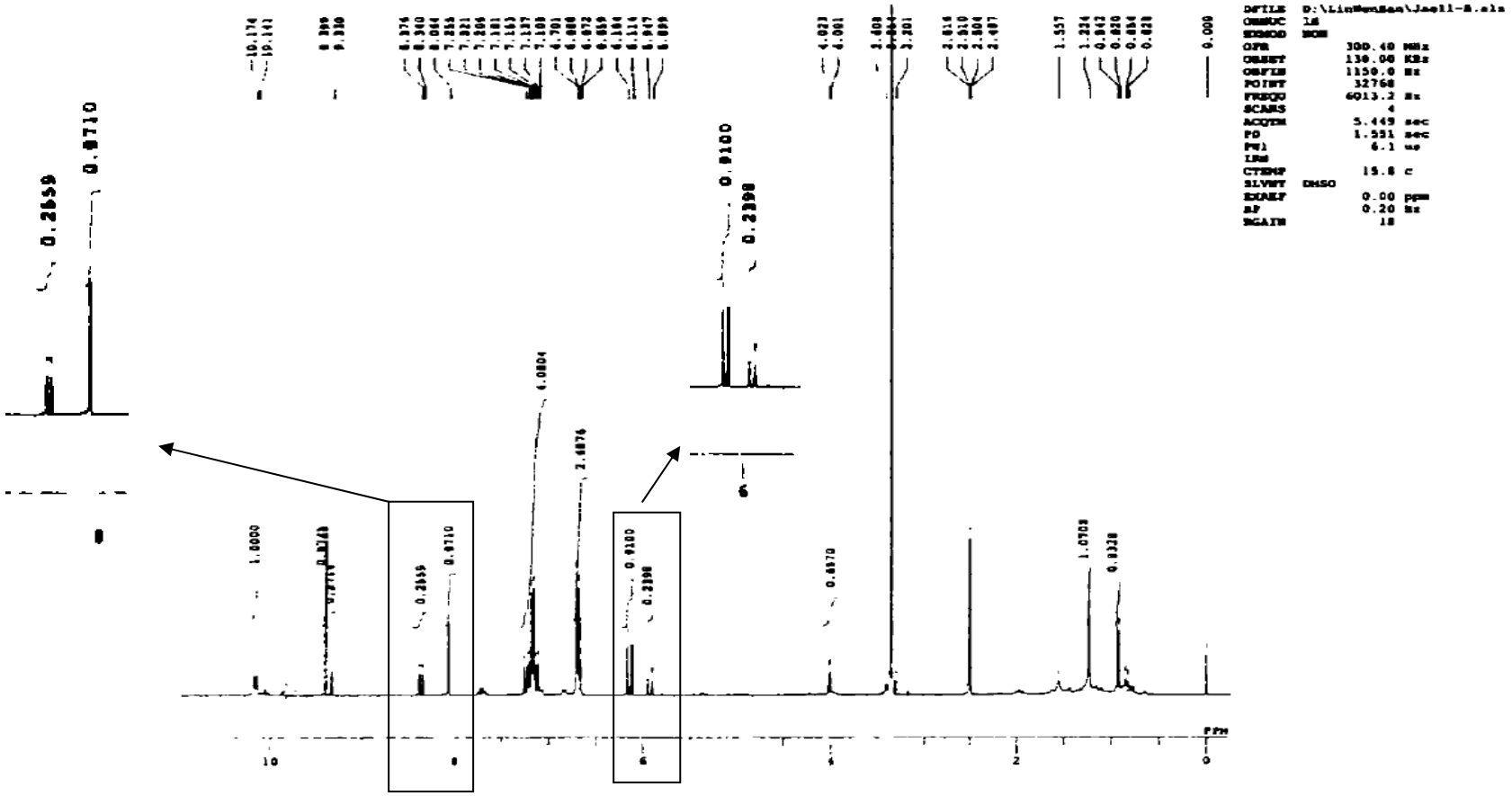


Fig. S10. Spectroscopic data of *N*-[2-*cis*-(4-hydroxyphenyl) ethenyl] formamide (**3**). (continued)
(**A**) The ^{1}H NMR spectrum of **3** in DMSO-d_6.

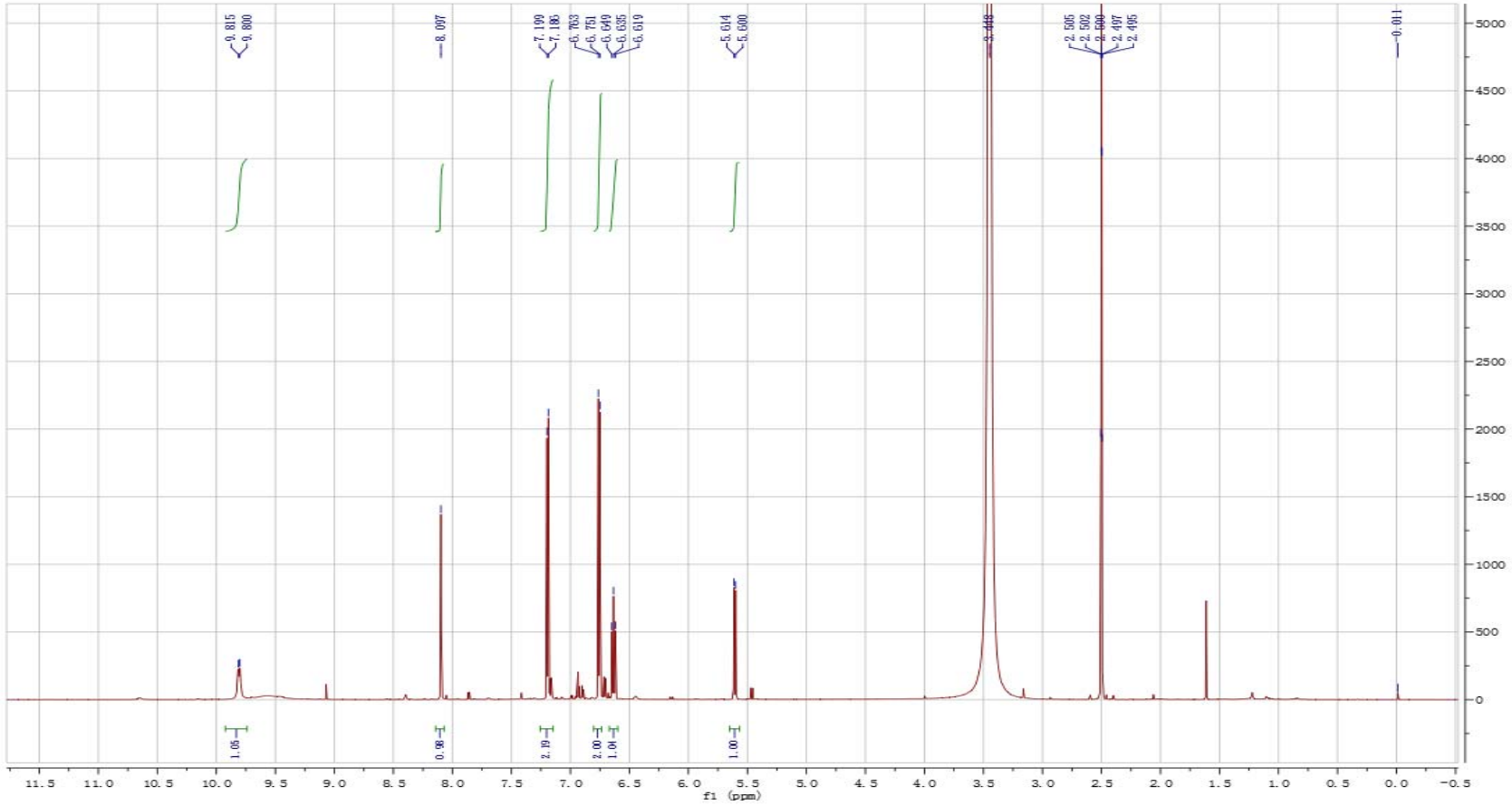


Fig. S10. Spectroscopic data of *N*-[2-*cis*-(4-hydroxyphenyl) ethenyl] formamide (**3**). (continued)
(**B**) The ^{13}C NMR spectrum of **3** in DMSO-d_6.

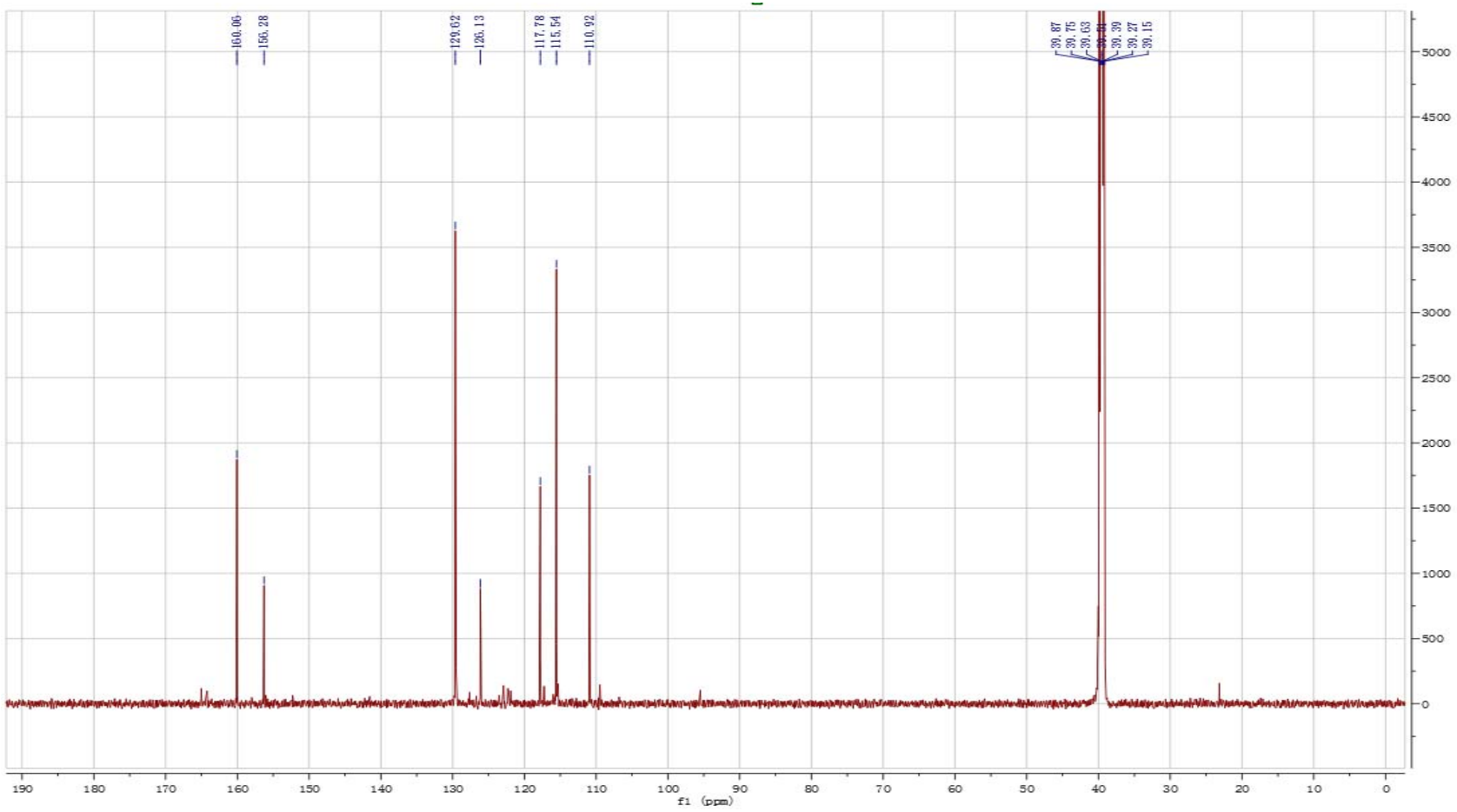


Fig. S11. Overlapping of ^{1}H-NMR spectra of compounds **2** (in maroon color) and **3** (in teal color).

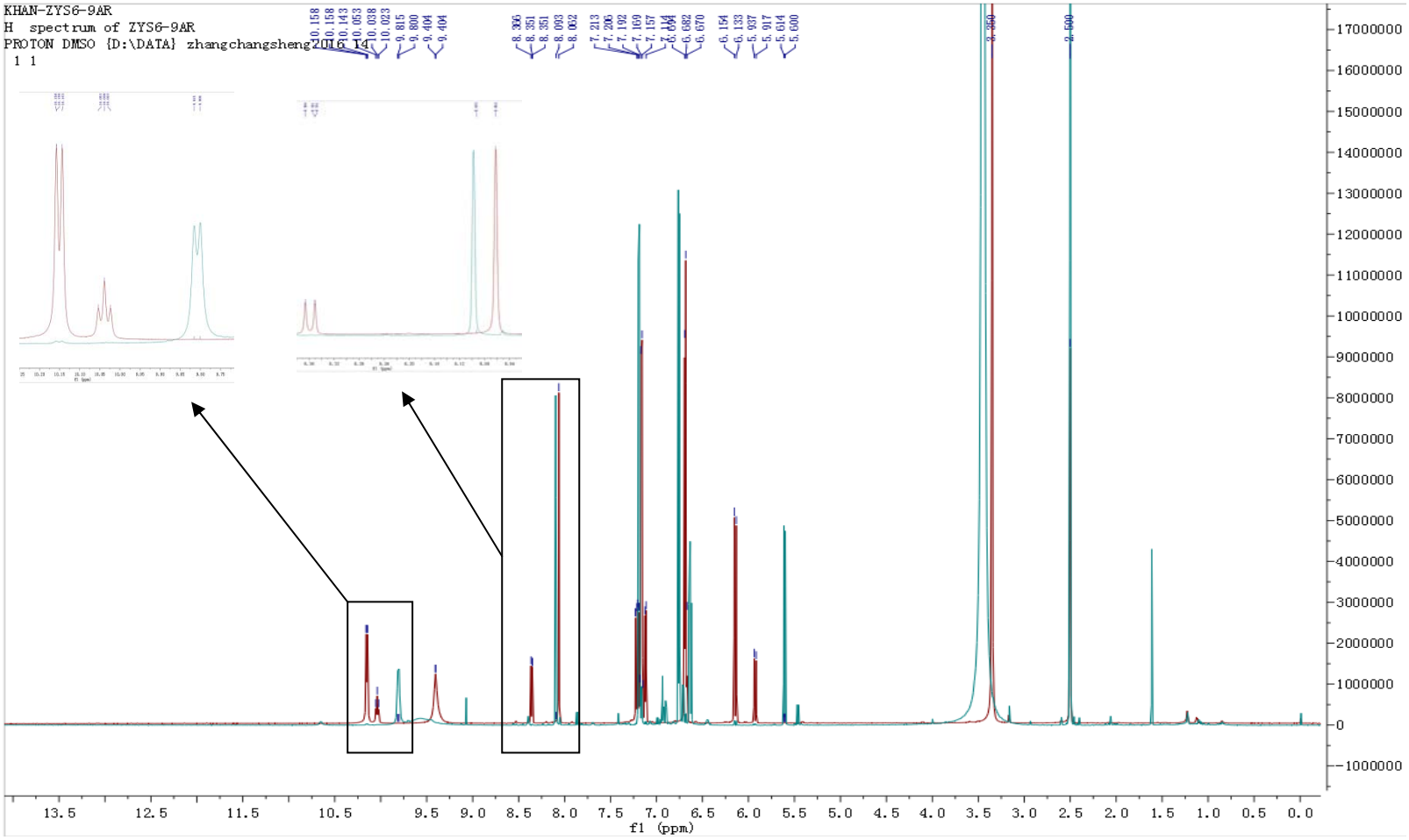
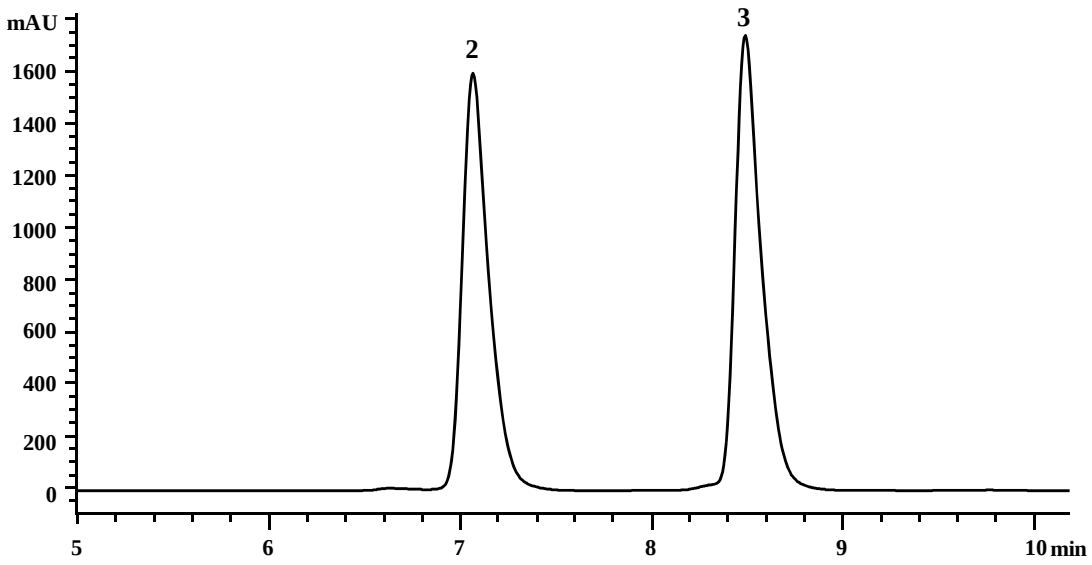


Fig. S12. HPLC analysis of compounds **2** and **3**



Column: Svea^{TM} HPLC column, C18, 5μm, 250×4.6 mm, Nanologica Co., LTD

Detection wavelength: 270 nm

Solvents, A: 10 % acetonitrile-water (0.1% formic acid), B: 90 % acetonitrile-water.

Gradient elution: 0-23 min, A: 95%-0%, B: 5 %-100%;

23-26 min, A: 0%; B: 100%;

26-28 min, A: 0%-95%; B: 100%-5%;

28-30 min, A: 95%; B: 5%.

Compounds: **2**, t_R = 7.1 min; **3**, t_R = 8.5 min.

II. ECD calculations

Calculation method of ECD

TDDFT-ECD calculation had been proven to be an efficient method for the stereochemisty study of the molecules which had achiral chromophores in a chiral environment.[3] To establish the absolute configuration of 1a and 1b, the ECD calculation of (6*R*)-**1** was carried out by application of the Boltzmann-weighted solution TDDFT-ECD protocol at the B3LYP/6-31+G(d, p) level (Tables S5-S7). Calculated ECD of (6*S*)-**1** was produced on the basis of the mirror-image ECD curves of (6*R*)-**1**.

The Conformational analysis of (6*R*)-**1** were performed in Sybyl 8.1 software using MMFF94s force field, which afforded the conformers for **1** with an energy cutoff of 10.0 kcal mol^{-1} to the global minima. All of the obtained conformers were optimized using the B3LYP/6-31+G(d, p) level in gas phrase by using Gaussian09 software.[4] TDDFT ECD calculations for the optimized conformers were performed at the B3LYP/6-31+G(d,p) level in methanol using the polarizable conductor calculation model (CPCM). The overall ECD curves of all the compounds were weighted by Boltzmann distribution after a UV correction of 0 nm. The ECD curves were produced by SpecDis 1.6 software with sigma =0.16 eV.[5]

III. Single crystal X-ray diffraction analysis for compounds 2b and 4

Colorless needle crystals of **2b** were obtained from the methanol solution of compound **2**. Brownish yellow crystals of **4** were crystallized in DMSO. Single crystals of comounds **2b** and **4** were respectively selected and placed on a Rigaku XtaLAB AFC12 (RINC): Kappa single diffractometer with Cu Kα radiation (λ=1.54184 Å). The

crystals were kept at 105(8) K during data collection. Using Olex2,[6] the structure was solved with the ShelXT[7] structure solution program using Intrinsic Phasing and refined with the ShelXL[8] refinement package using Least Squares minimisation. Crystallographic data of **2b** and **4** (Tables S8 and S9) were deposited in the Cambridge Crystallographic Data Center with the deposition numbers CCDC 1987282 and CCDC 1987281, respectively. A copy of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44(0)-1233-336033; e-mail: deposit@ccdc.cam.ac.uk).

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