Electronic Supporting Information (ESI) for

Denticulatains A and B: unique stilbene–diterpene heterodimers from *Macaranga denticulata*

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Detailed experimental procedures

1. General experimental procedures.

Optical rotations were measured with a JASCO P–1020 digital polarimeter. UV data were obtained on a Shimadzu UV–2401A spectrophotometer. A Bruker Tenor 27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on Bruker AM–400 and DRX–500 spectrometers. Chemical shifts (δ) were expressed in ppm with reference to the solvent signals. ESIMS spectra were performed on a Finnigan MAT 90 instrument, HRESIMS were performed on a VG Autospec–3000 spectrometer. Column chromatography was performed with silica gel (200–300 mesh; Qingdao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), and MCI gel CHP20P (75–150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). Semipreparative HPLC was performed on a Hewlett-Packard instrument (column: Zorbax SB–C_{18}, 250 × 9.4 mm; DAD detector). Fractions were monitored by TLC and spots were visualized by heating silica gel plates sprayed with 15% H_2SO_4 in EtOH.

2. Plant material.

The fronds of *Macaranga denticulata* were collected from Xishuangbanna of Yunnan province, PR China, in March 2008. A voucher specimen (Yangyp–20080316) was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences, which was identified by Prof. Yong-Ping Yang.

3. Antiangiogenesis assay.

Stock solutions (20 mg/mL) of all samples were prepared by dissolving the test compounds in 100% DMSO. These solutions were diluted in sterile salt water (5 mM NaCl, 0.17 mM KCl, 0.4 mM $CaCl_2$, 0.16 mM $MgSO_4$) to obtain final solutions of various concentrations in 0.2% DMSO. Aliquots were placed into 24-well plates, and embryos (TG[VEGFR2:GRCFP]) at 24 hpf (hours post-fertilization) were also transferred randomly into the above wells. Control embryos were treated with the

equivalent amount of DMSO solutions. All embryos were incubated at 28.5 ℃. After 48 h treatment, the intersegmental vessels of embryos were visualized with green fluorescent protein labeling and endogenous alkaline phosphatase staining. The antiangiogenic activities of compounds were calculated from the inhibition ratio of antiangiogenesis.

4. Acetylcholinesterase inhibitory activity.

Acetylcholinesterase inhibitory activity of the compounds isolated was assayed by the spectrophotometric method developed by Ellman with slightly modification. *S*-Acetylthiocholine iodide, *S*-butyrylthiocholine iodide, 5,5'-dithio-bis-(2-nitrobenzoic) acid (DTNB, Ellman's reagent), acetylcholinesterase derived from human erythrocytes were purchased from Sigma Chemical. Compounds were dissolved in DMSO. The reaction mixture (totally 200 μL) containing phosphate buffer (pH 8.0), test compound (50 μM), and acetylcholinesterase (0.02 U/mL), was incubated for 20 min (30 °C). Then, the reaction was initiated by the addition of 40 μL of solution containing DTNB (0.625 mM) and acetylthiocholine iodide (0.625 mM) for AChE inhibitory activity assay, respectively. The hydrolysis of acetylthiocholine was monitored at 405 nm every 3 minutes for one hour. Tacrine was used as positive control with final concentration of 0.333 μM. All the reactions were performed in triplicate. The percentage inhibition was calculated as follows: % inhibition = (E – S)/E × 100 (E is the activity of the enzyme without test compound and S is the activity of enzyme with test compound).

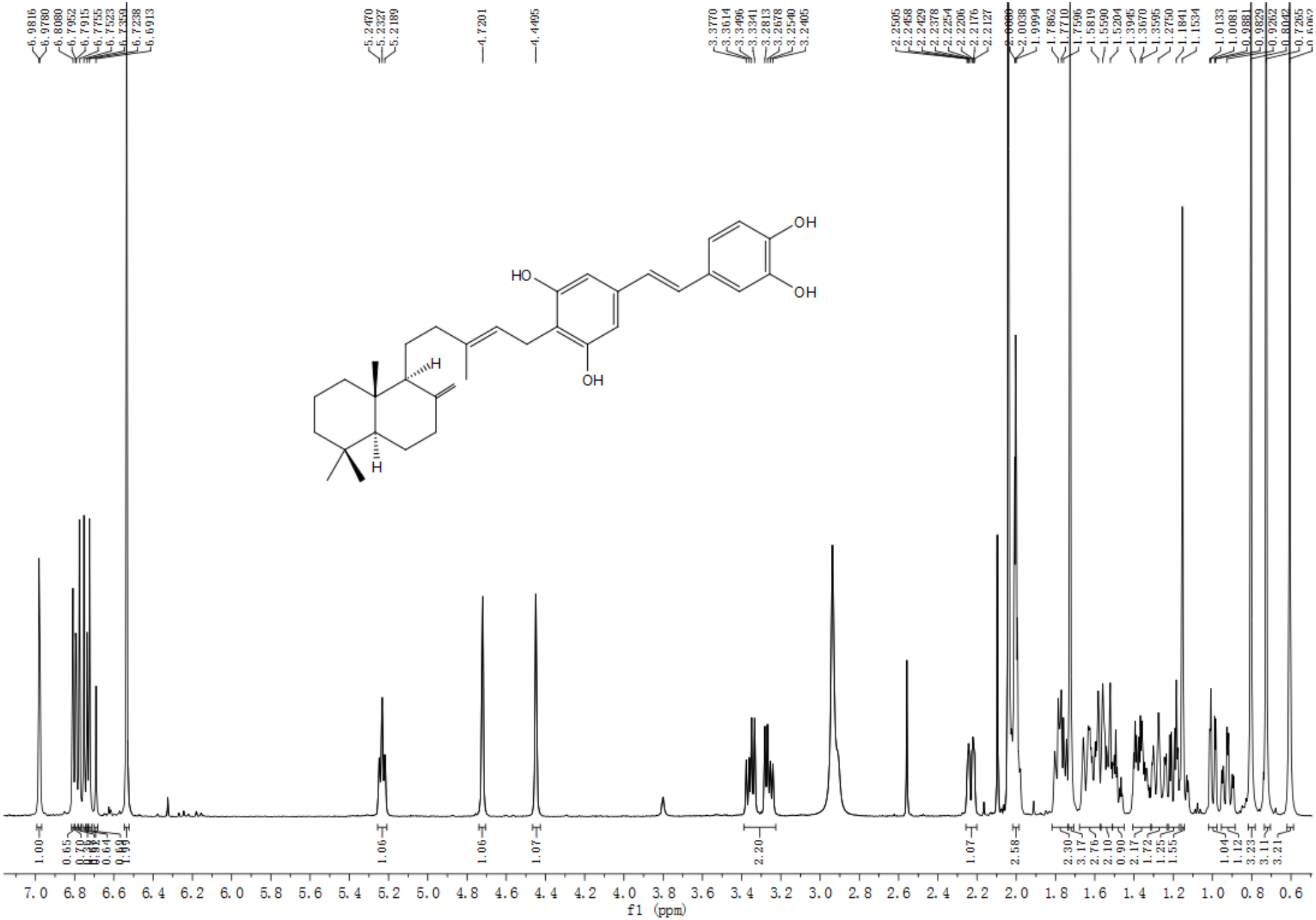


Figure S1. ^{1}H NMR spectrum of denticulatain A (**1**)

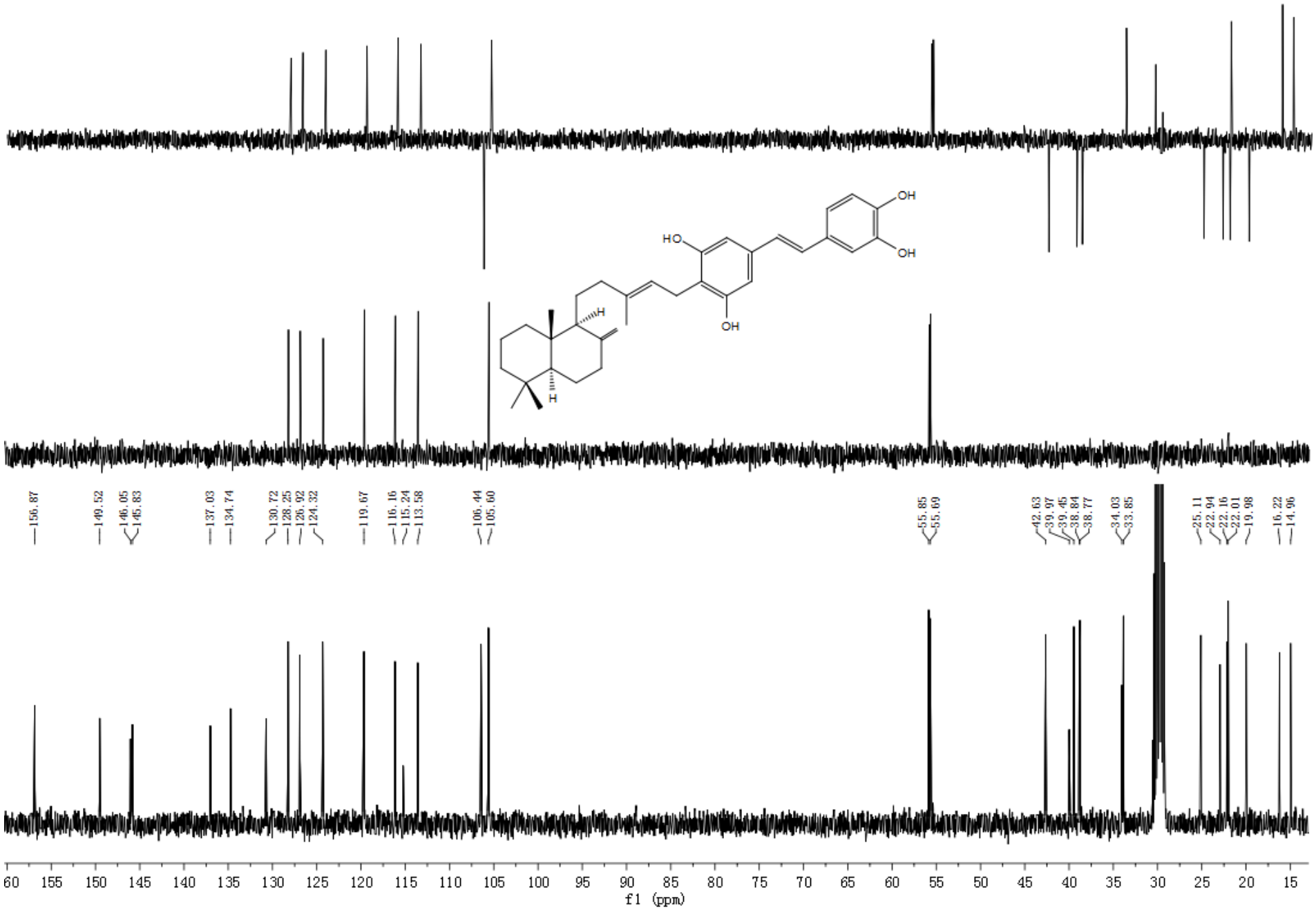


Figure S2. ^{13}C NMR spectrum of denticulatain A (**1**)

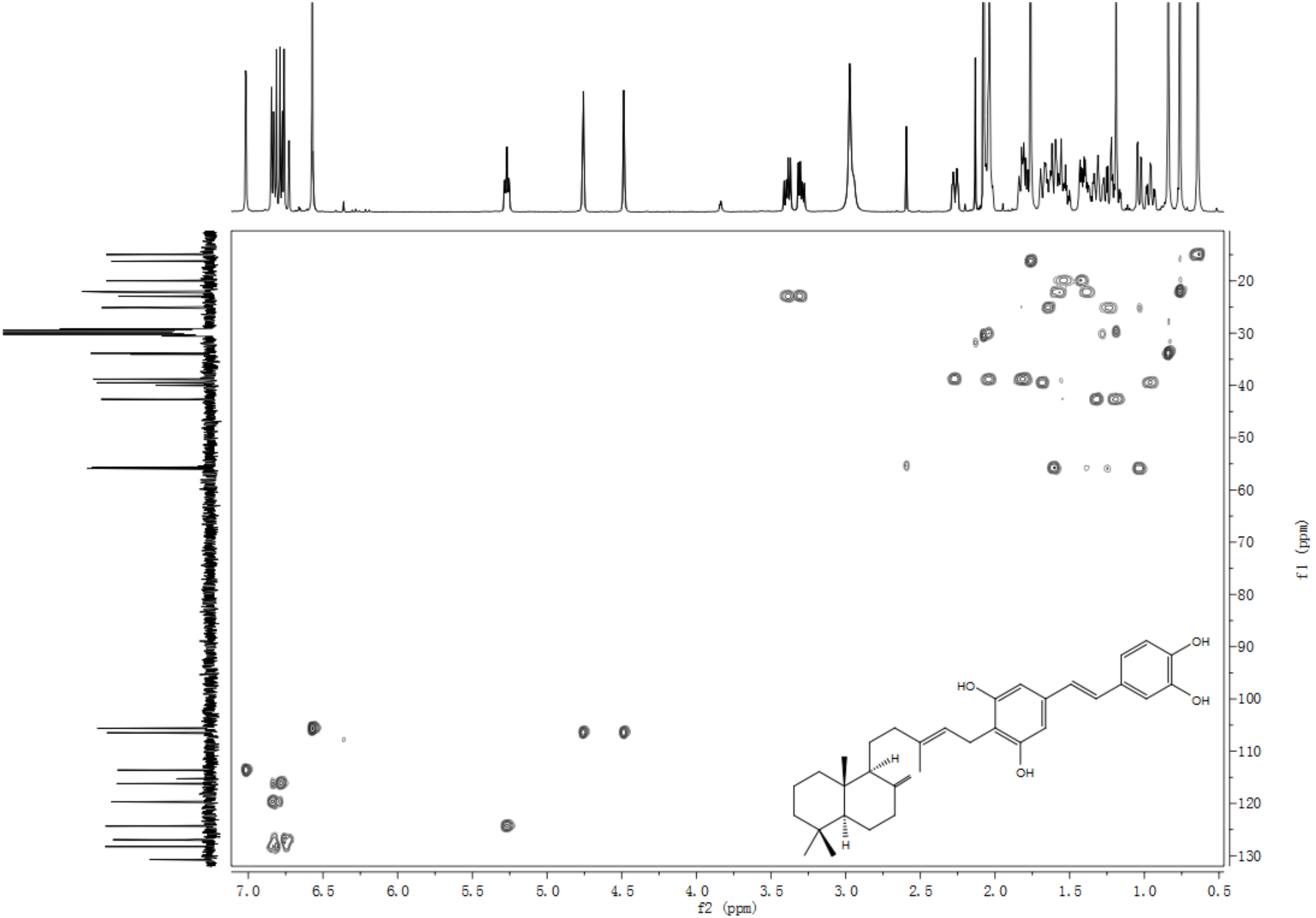


Figure S3. HSQC spectrum of denticulatain A (**1**)

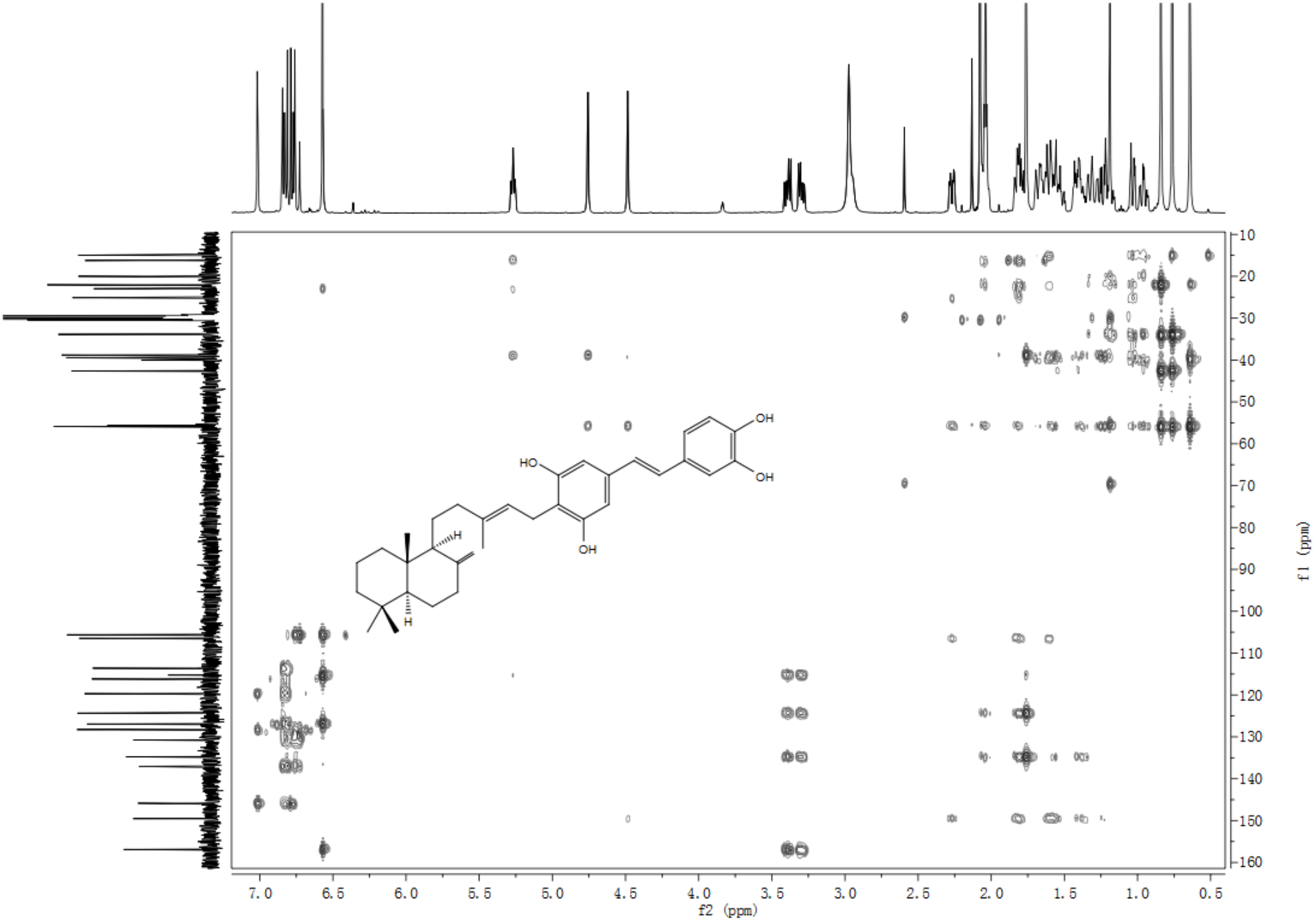


Figure S4. HMBC spectrum of denticulatain A (**1**)

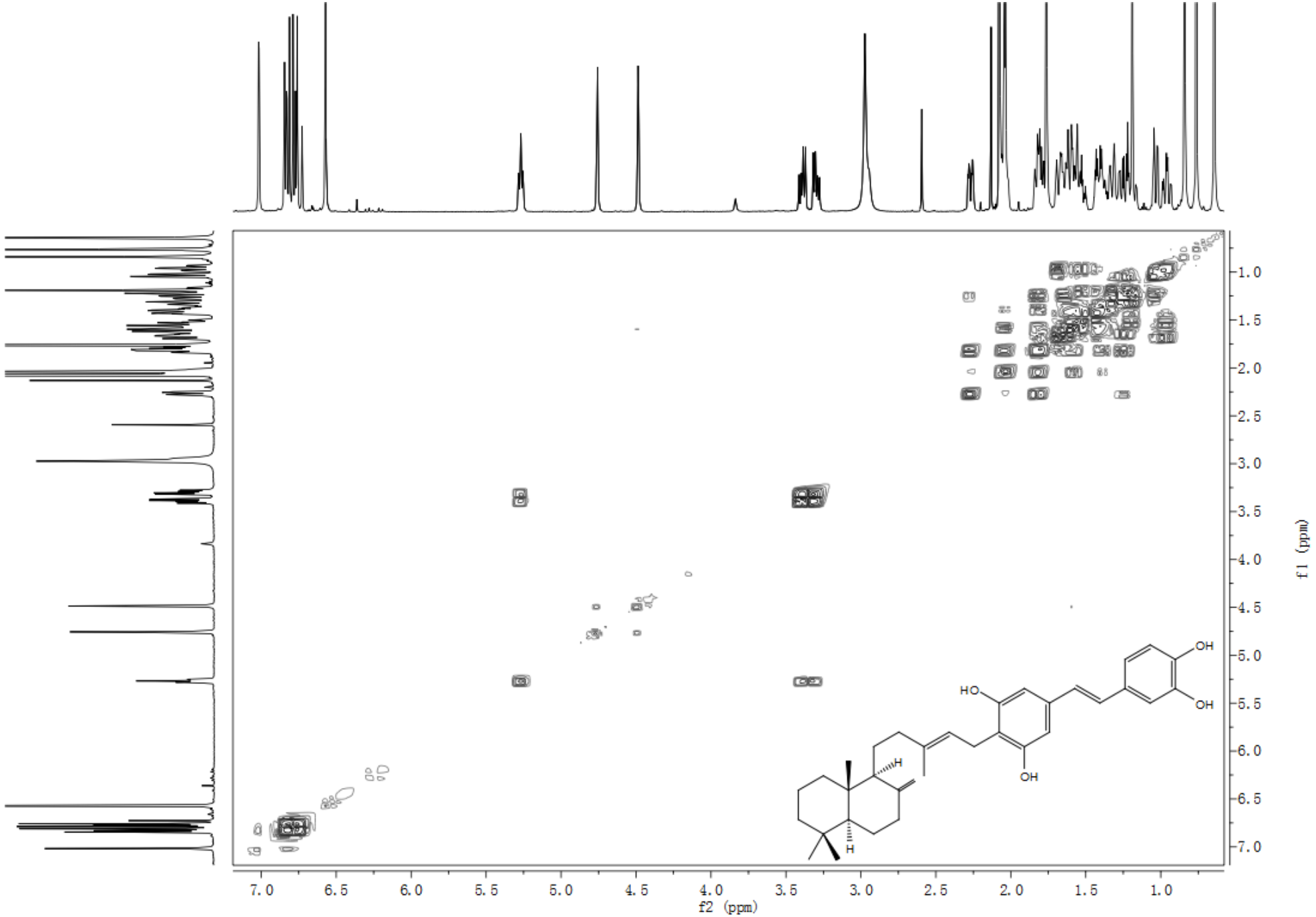


Figure S5. ^{1}H–^{1}H COSY spectrum of denticulatain A (**1**)

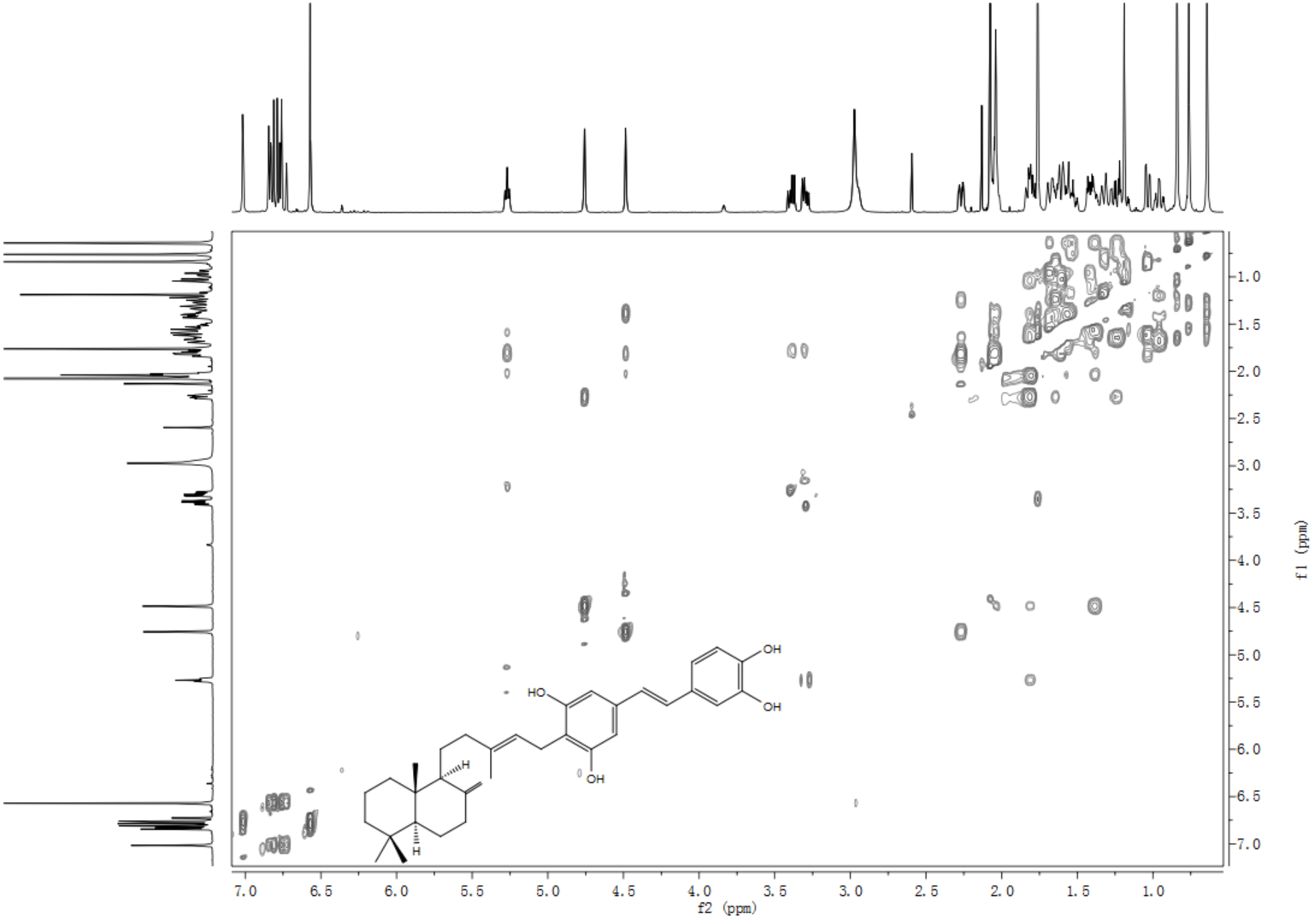


Figure S6. ROESY spectrum of denticulatain A (**1**)

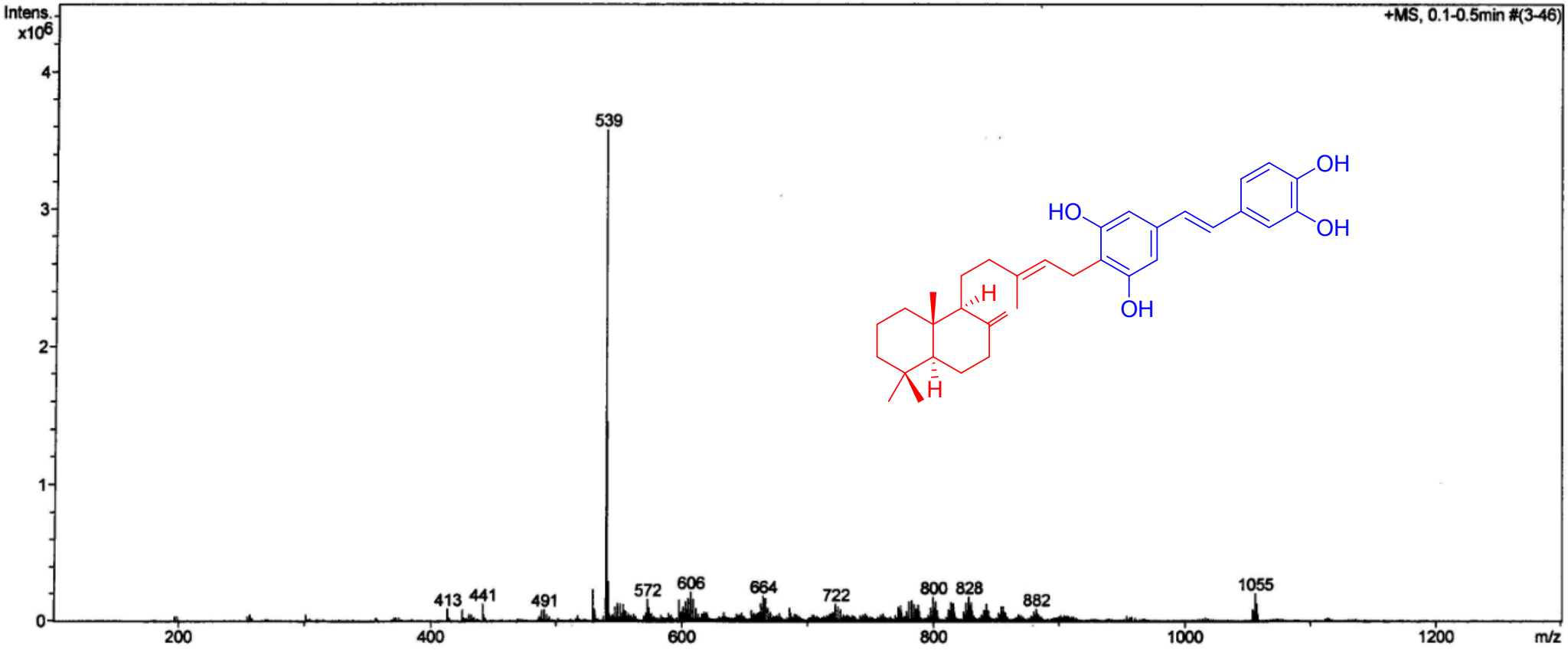
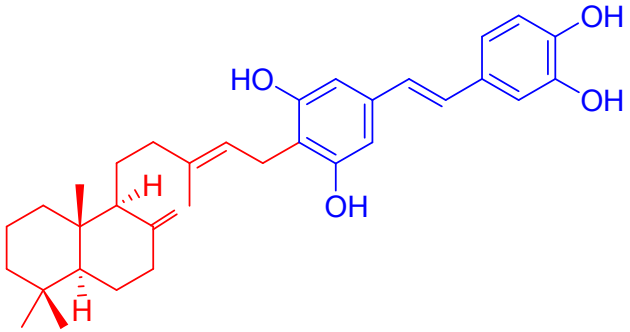


Figure S7. ESIMS of denticulatain A (**1**)

Elemental composition calculator



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Electron state: OddAndEven
Num of charges: 0
Add water: N/A
Add proton: N/A
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3	C	0	200
4	Cl	0	0
5	F	0	0
6	H	0	400
7	I	0	0
8	K	0	0
9	N	0	0
10	Na	1	1
11	O	2	5

12	P	0	0
13	Pt	0	0
14	S	0	0
15	Si	0	0

	Formula	Calculated m/z (amu)	mDa Error	PPM Error	DBE
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Figure S8. HRESIMS of denticulatain A (**1**)

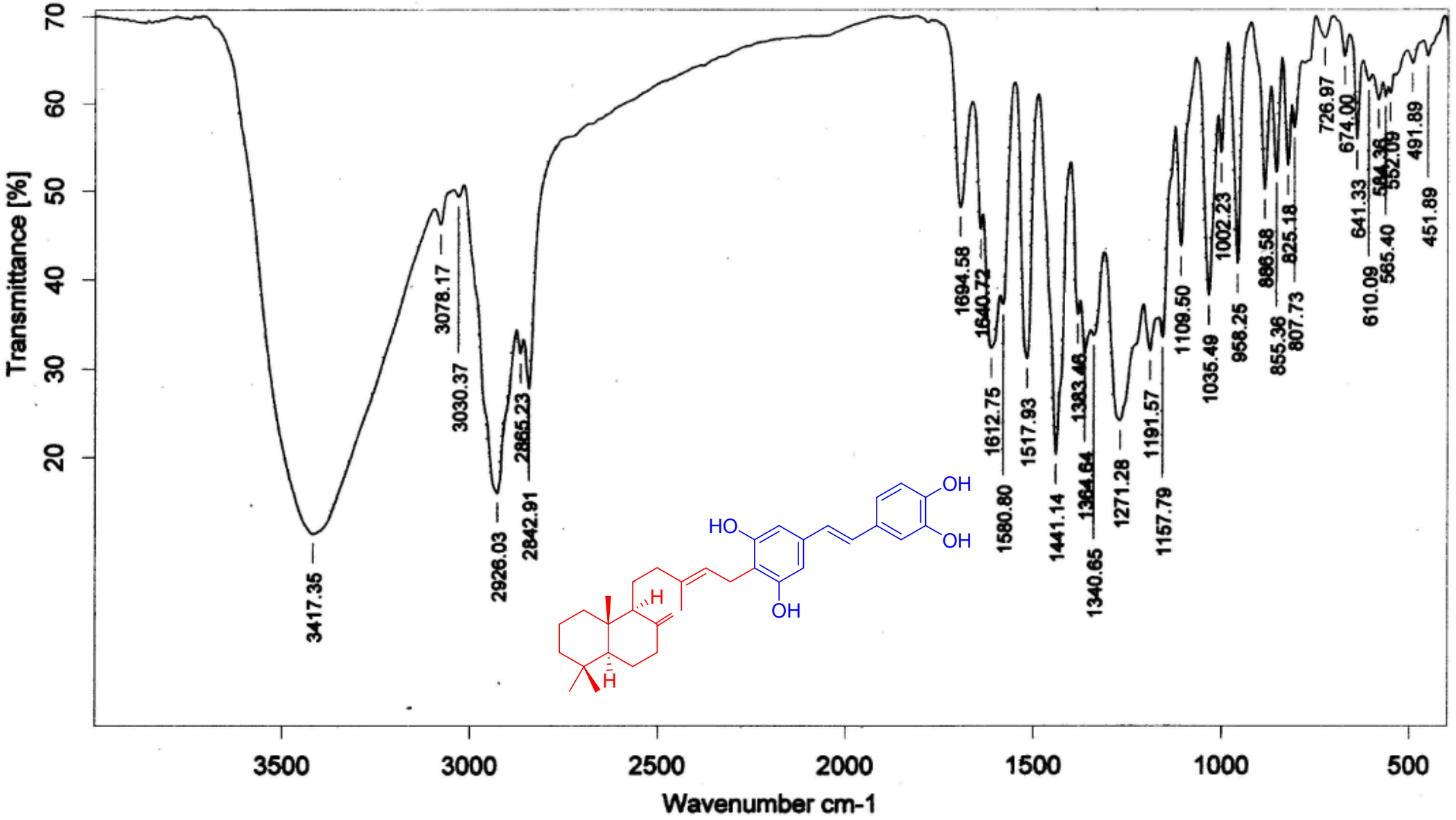
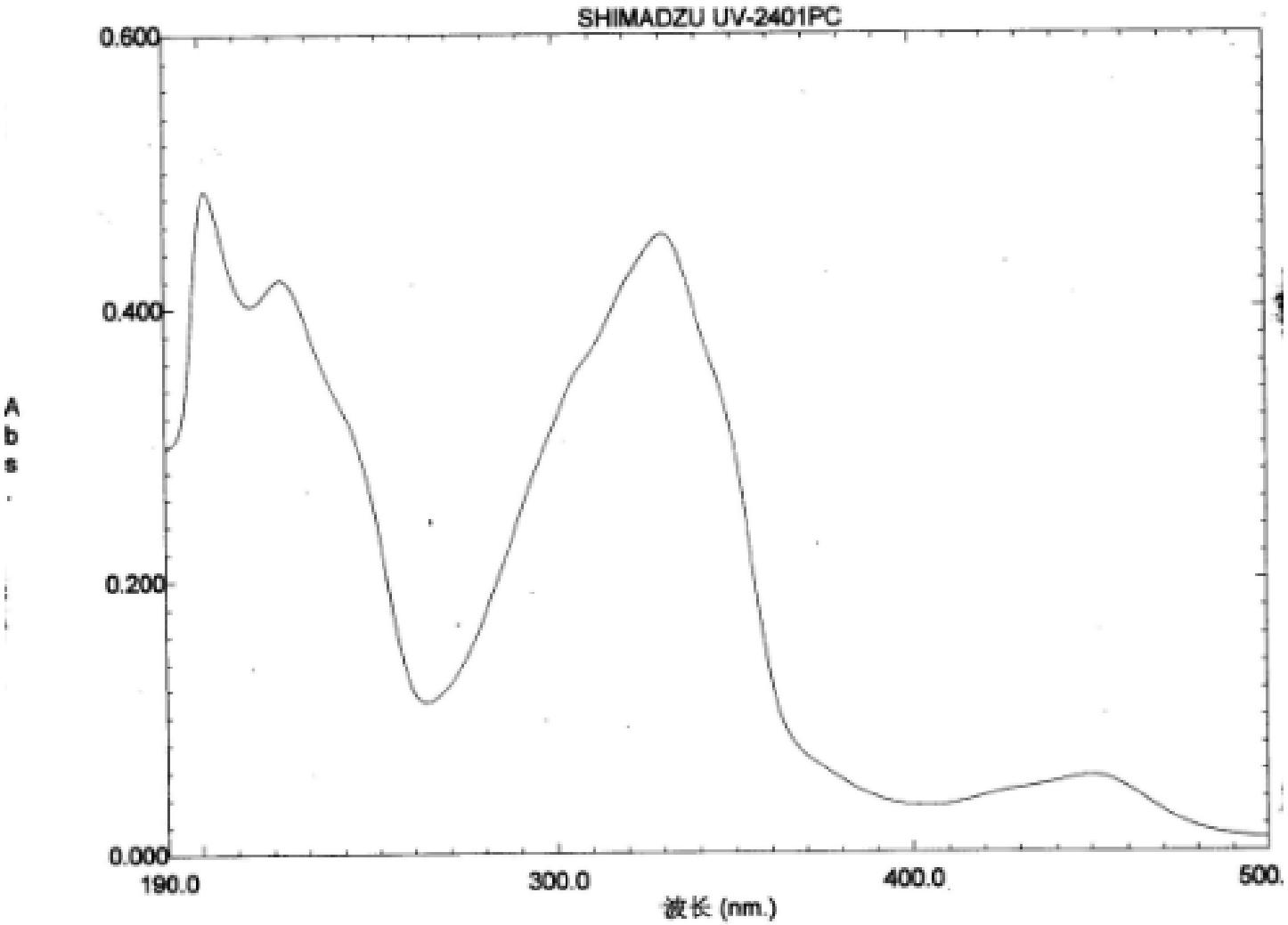


Figure S9. IR spectrum of denticulatain A (**1**)



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溶剂：甲醇

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采样间隔: 0.5

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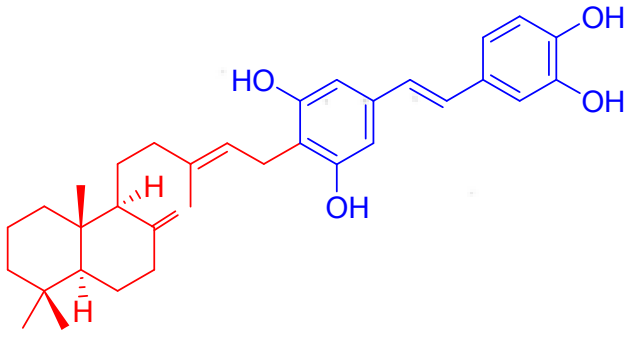

Figure S10. UV spectrum of denticulatain A (**1**)

Optical rotation measurement

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No.2	14 (2/3)	Sp.Rot	23.3330	0.0175 0.0000	13.2 10.00 Cell	Tue Dec 13 11:03:49 2011 0.00750g/mlMeOH SMDL-15A	Na 589nm	2 sec 10 sec
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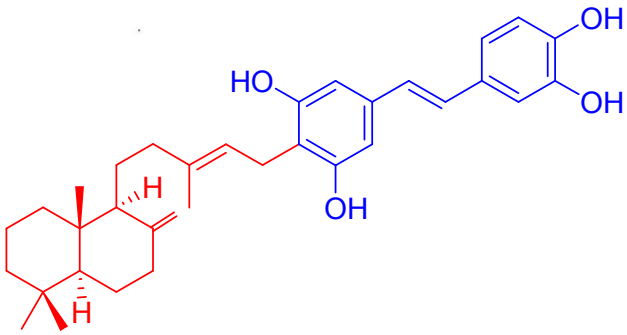


Figure S12. ORD spectrum of denticulatain A (**1**)

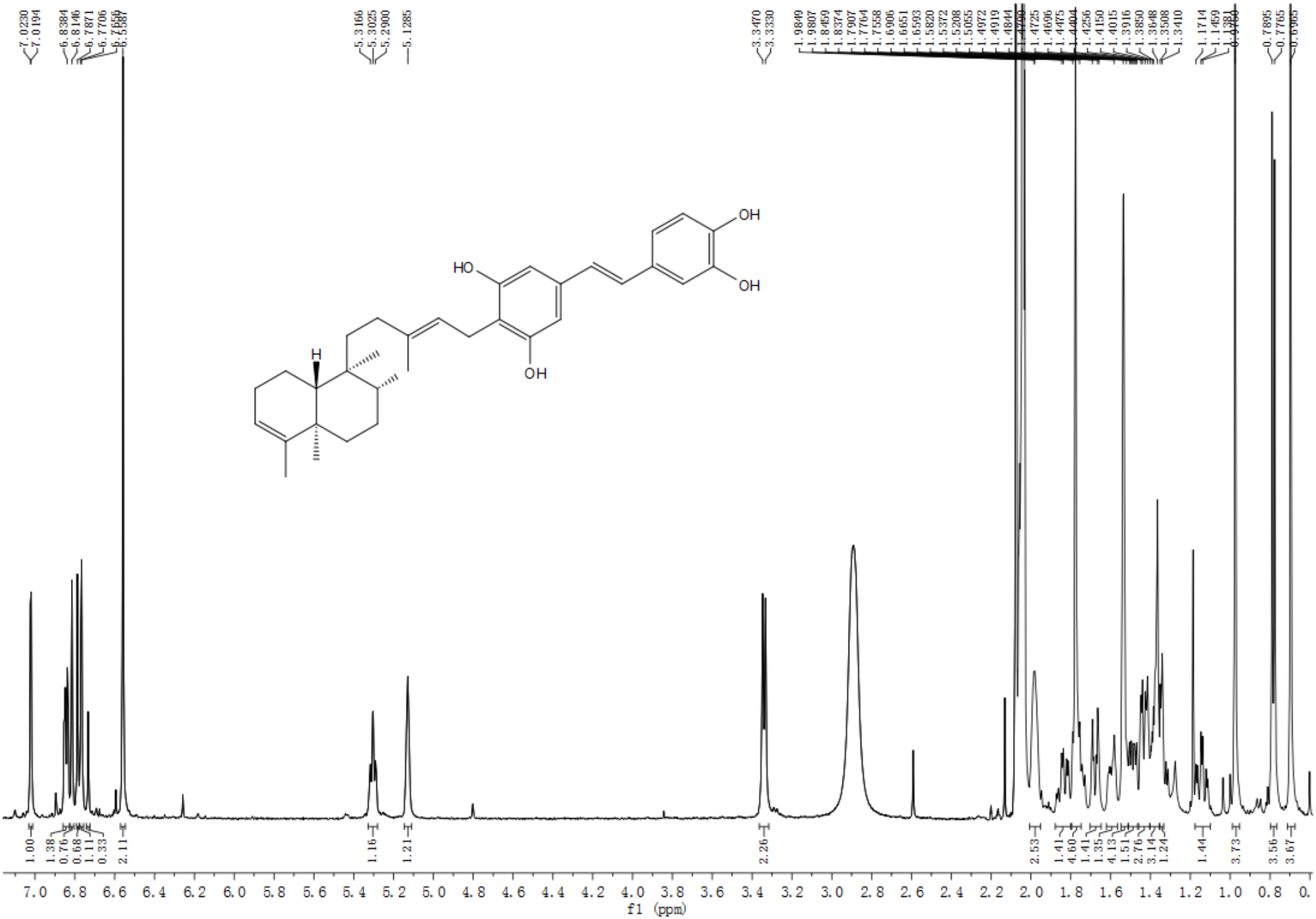


Figure S13. ^{1}H NMR spectrum of denticulatain B (**2**)

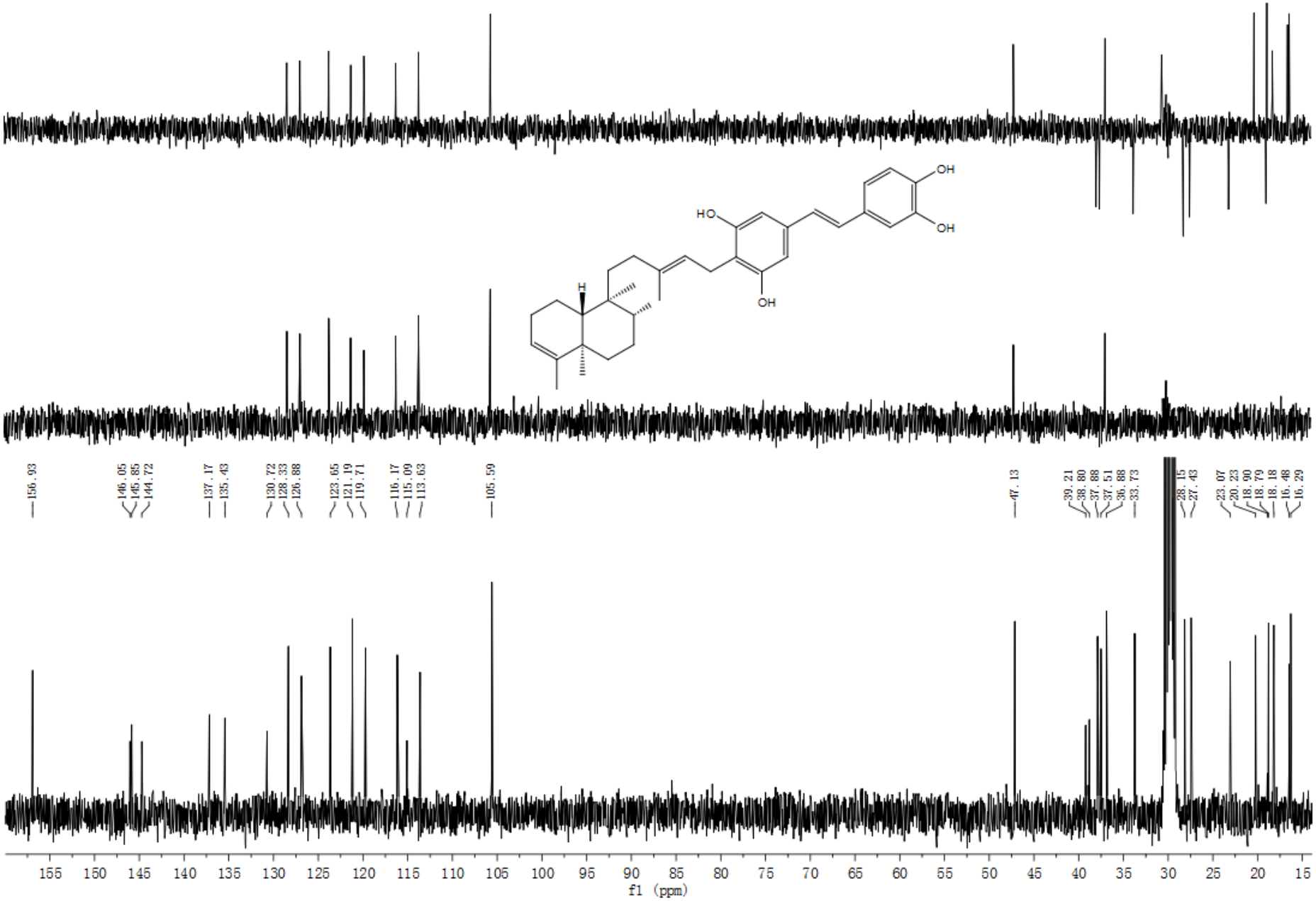


Figure S14. ^{13}C NMR spectrum of denticulatain B (**2**)

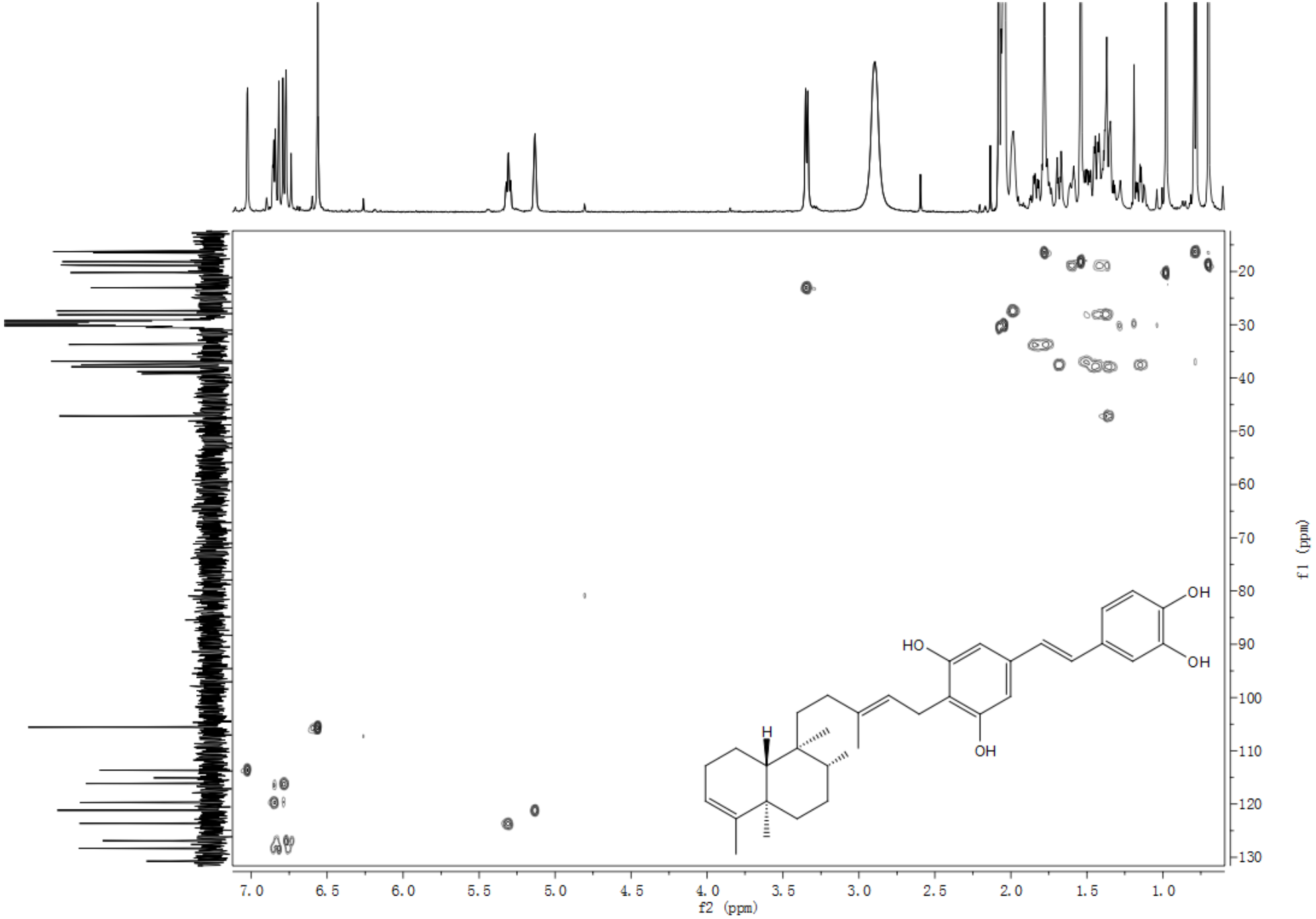


Figure S15. HSQC spectrum of denticulatain B (**2**)

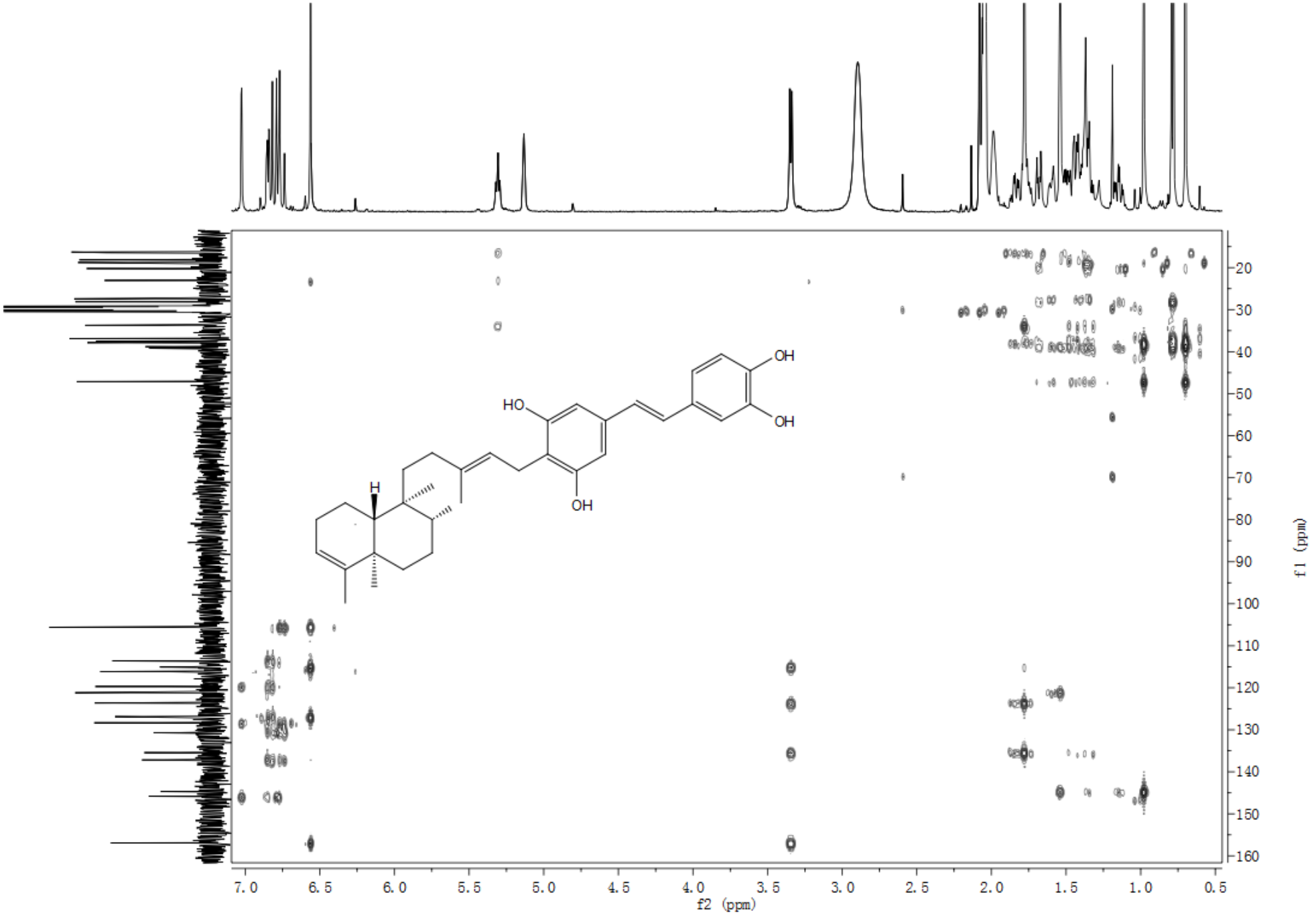


Figure S16. HMBC spectrum of denticulatain B (**2**)

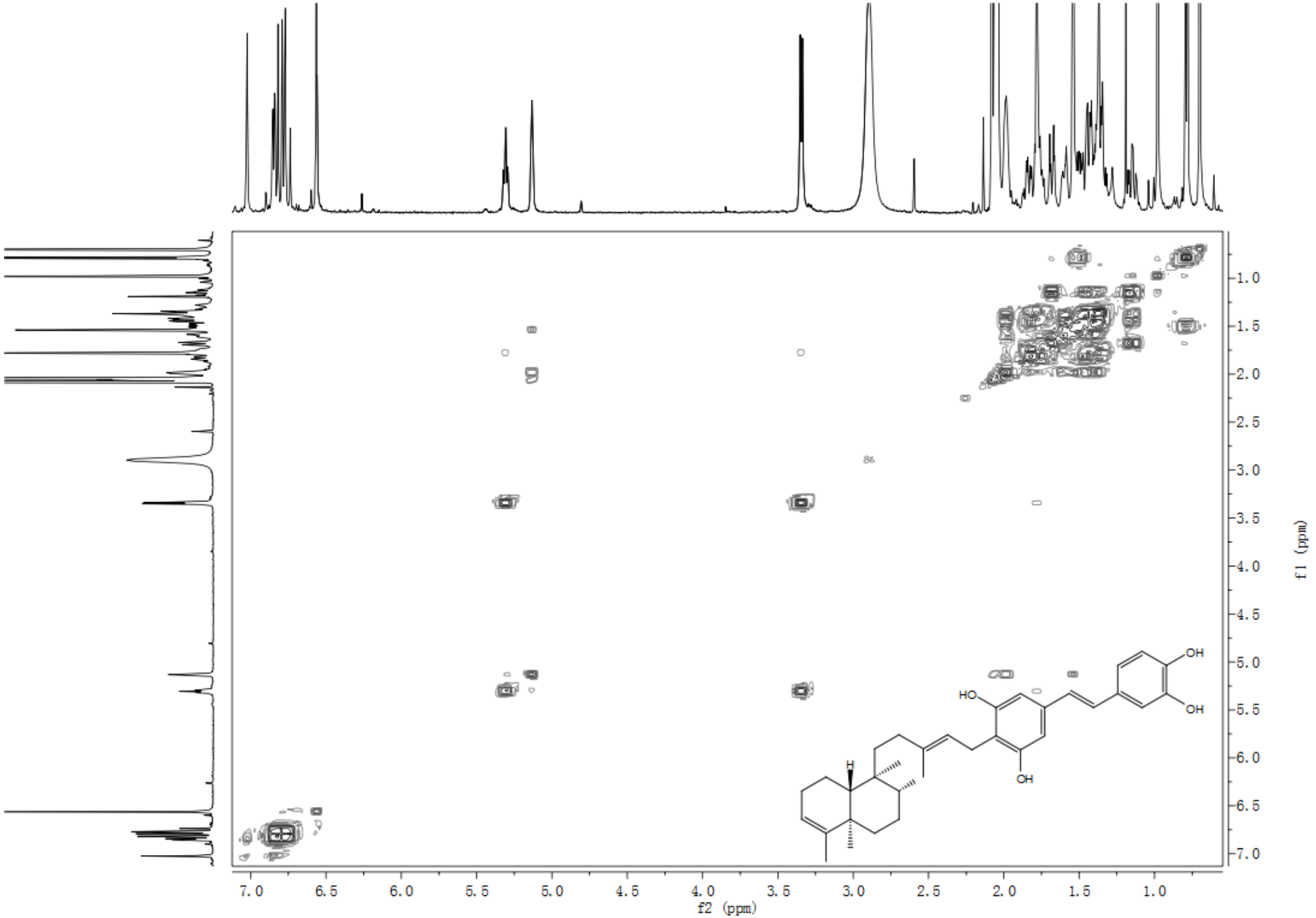


Figure S17. ^{1}H–^{1}H COSY spectrum of denticulatain B (**2**)

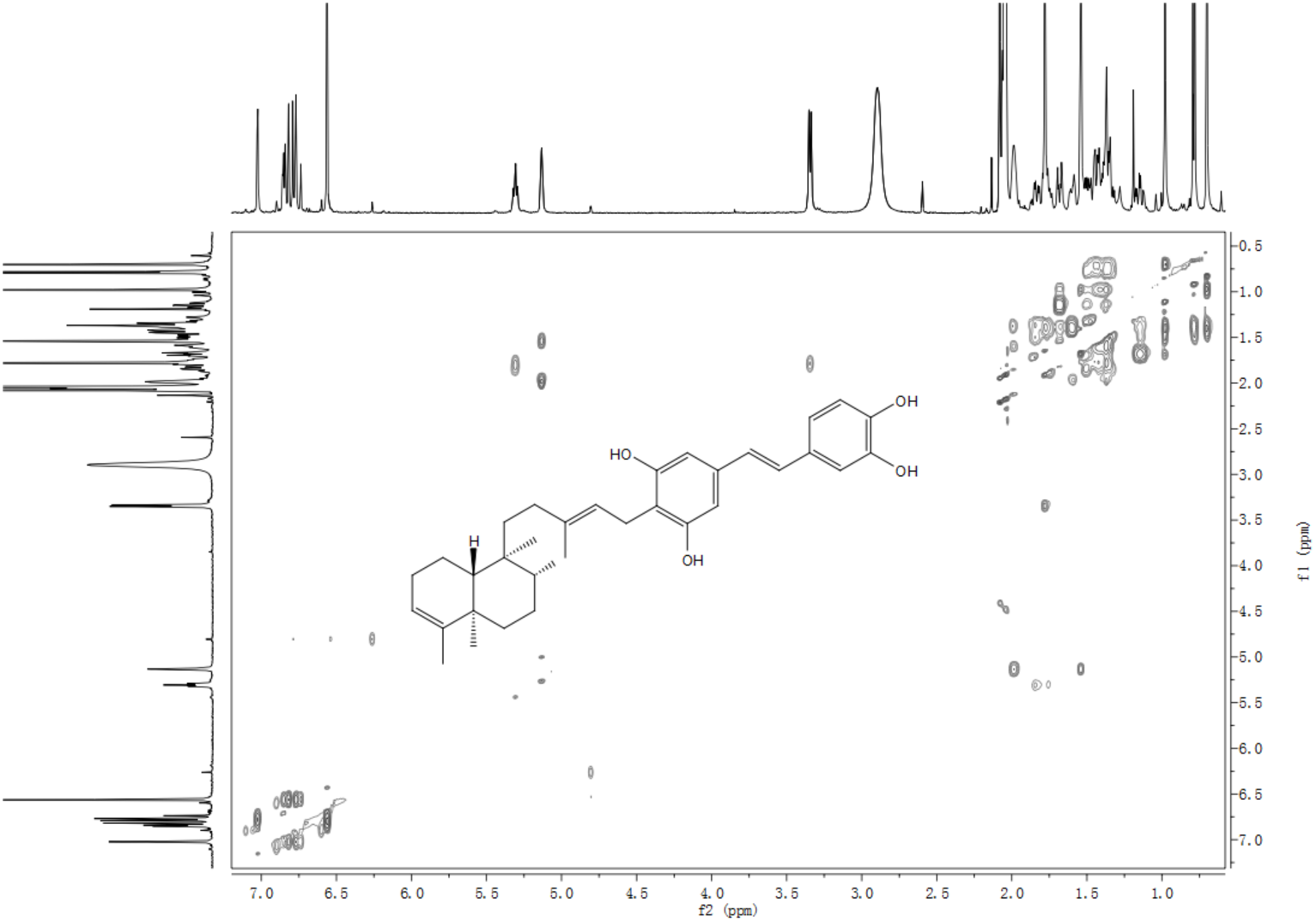


Figure S18. ROESY spectrum of denticulatain B (**2**)

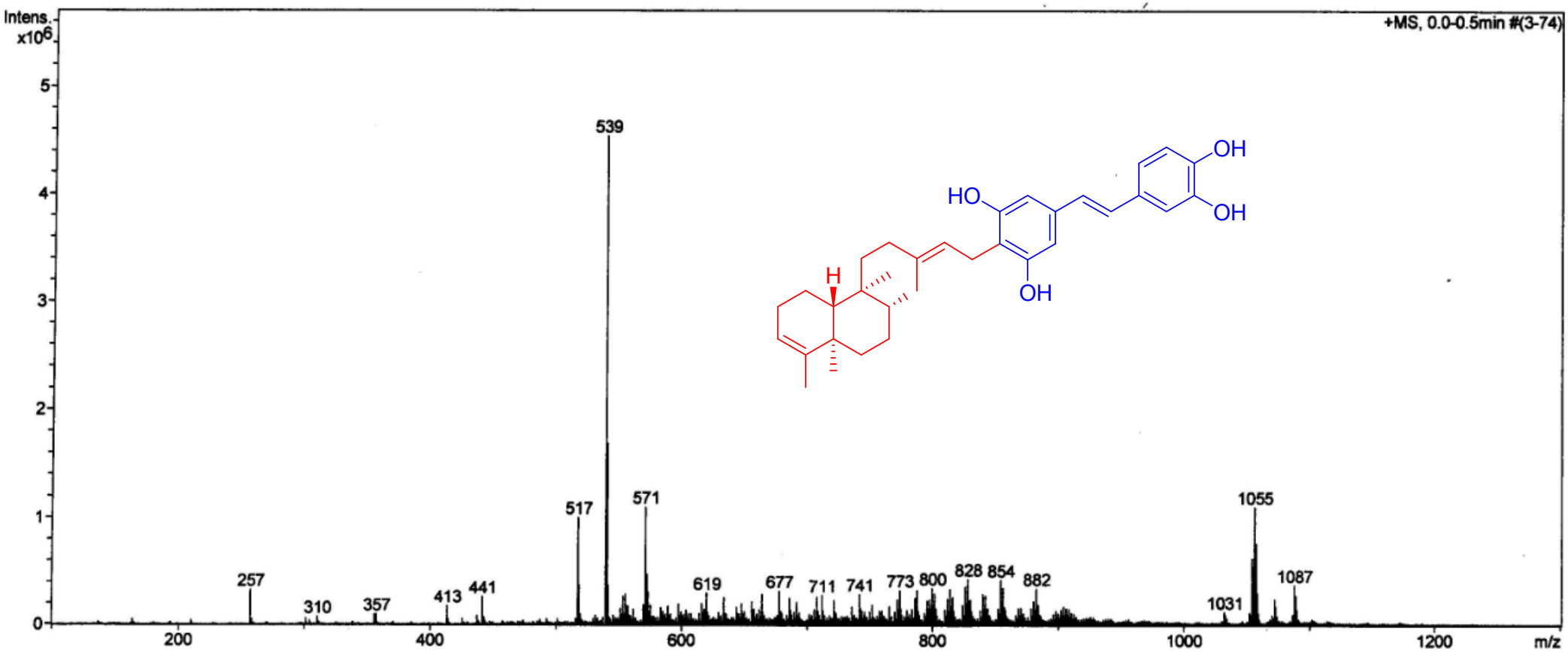
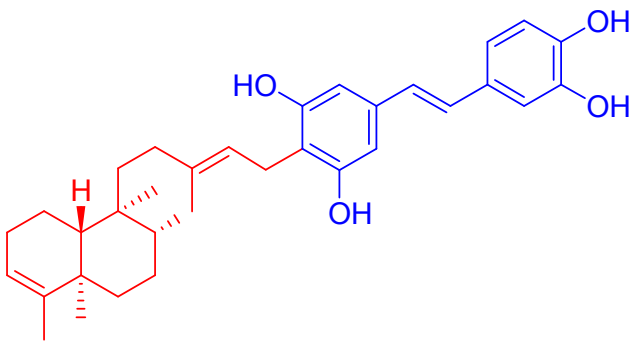


Figure S19. ESIMS of denticulatain B (**2**)

Elemental composition calculator



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Max num of results: 1000
Min DBE: -10.0000 Max DBE: +60.0000
Electron state: OddAndEven
Num of charges: 0
Add water: N/A
Add proton: N/A
File Name: 111206ESIA smdl-15b.wiff

	Elements	Min Number	Max Number
1	2H	0	0
2	Br	0	0
3	C	0	200
4	Cl	0	0
5	F	0	0
6	H	0	400
7	I	0	0
8	K	0	0
9	N	0	0
10	Na	1	1
11	O	2	5

12	P	0	0
13	Pt	0	0
14	S	0	0
15	Si	0	0

	Formula	Calculated m/z (amu)	mDa Error	PPM Error	DBE
1	C34 H44 O4 Na	539.3137	-0.7300	-1.3536	12.5

Figure S20. HRESIMS of denticulatain B (**2**)

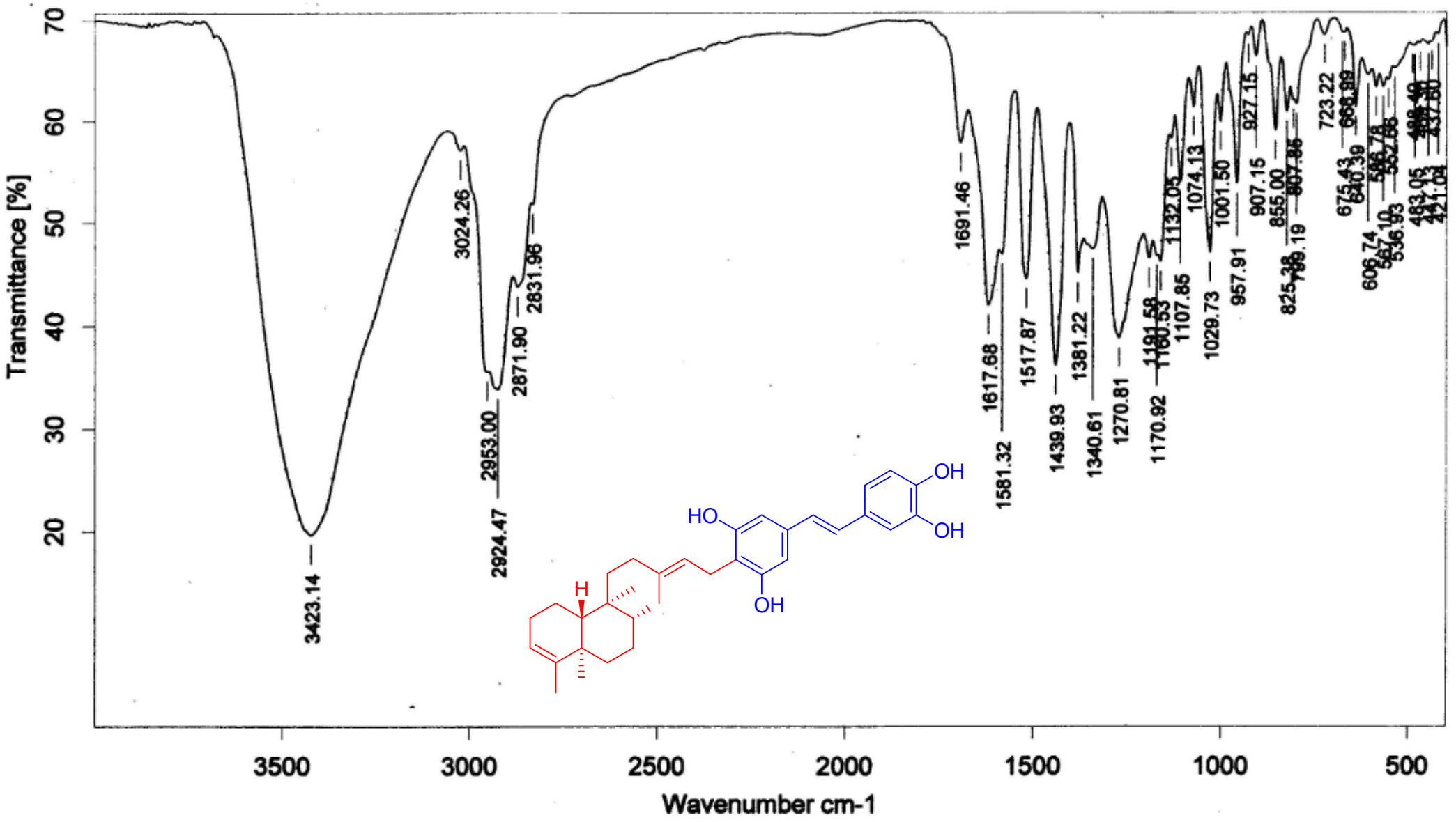
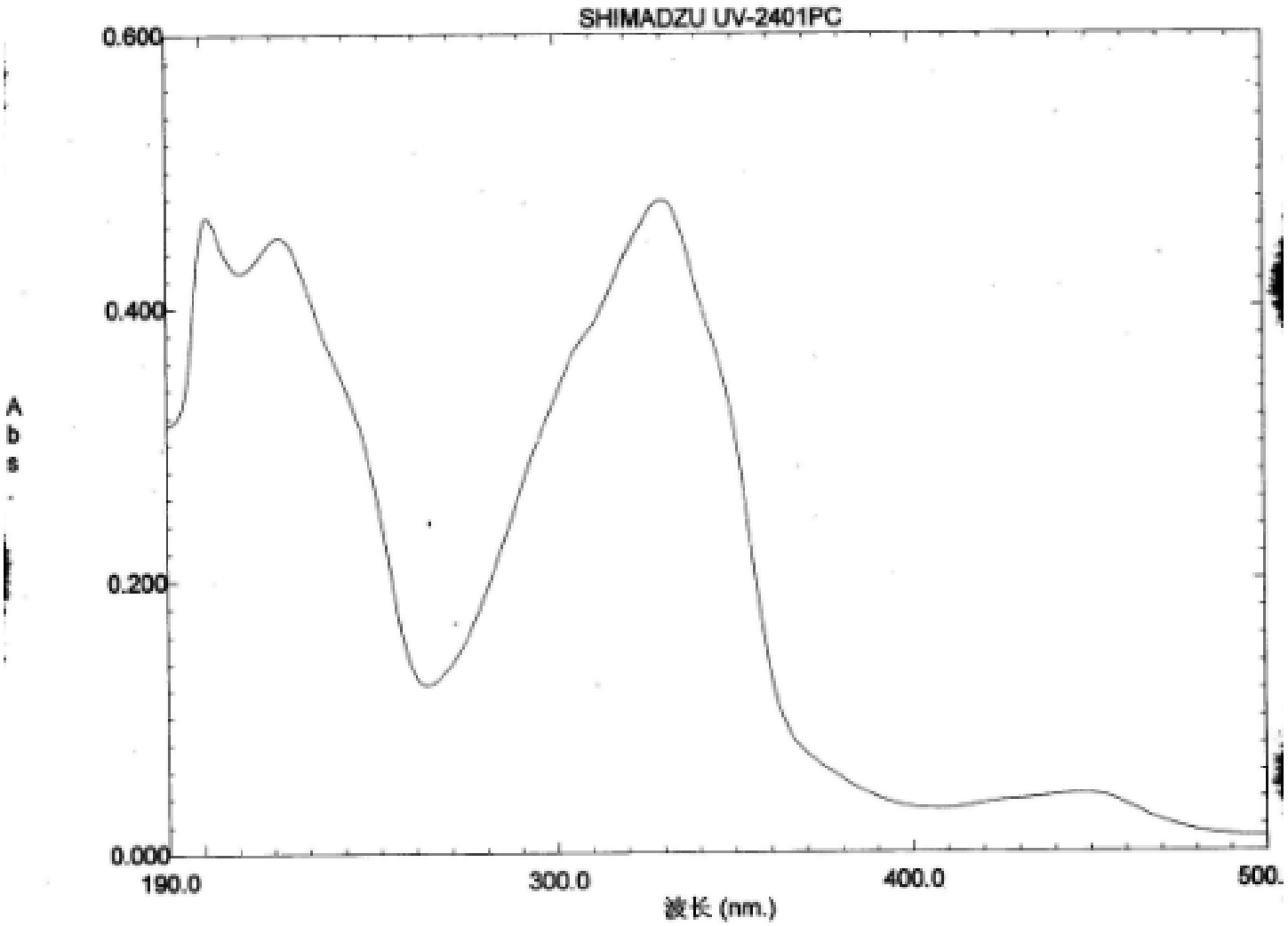


Figure S21. IR spectrum of denticulatain B (**2**)



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SMDL-15B

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扫描速度: 中速
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采样间隔: 0.5

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3	222.00	0.4519
4	201.50	0.4665

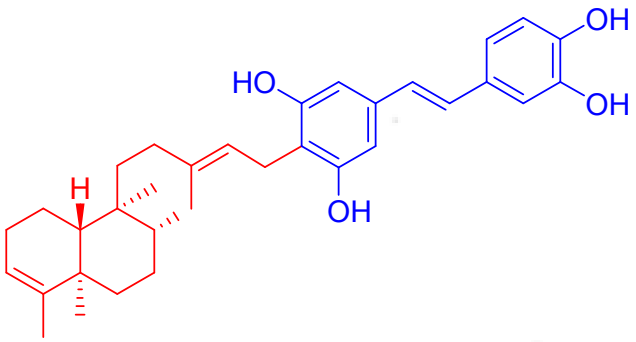

Figure S22. UV spectrum of denticulatain B (**2**)

Optical rotation measurement

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No.2	17 (2/3)	Sp.Rot	-29.7780	-0.0134 0.0000	13.5 10.00 Cell	Tue Dec 13 11:26:39 2011 0.00450g/mlMeOH SMDL-15B	Na 589nm	2 sec 10 sec
No.3	17 (3/3)	Sp.Rot	-29.3330	-0.0132 0.0000	13.5 10.00 Cell	Tue Dec 13 11:26:53 2011 0.00450g/mlMeOH SMDL-15B	Na 589nm	2 sec 10 sec

-29.1111°

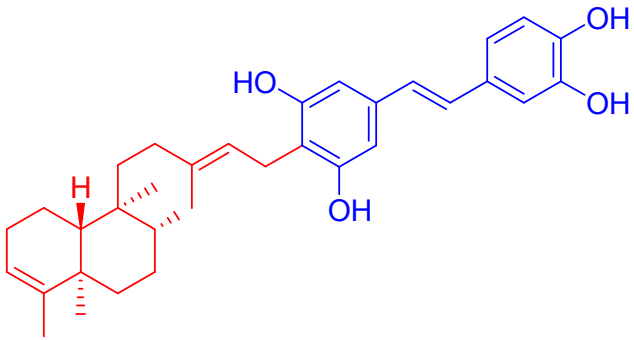

Figure S24. ORD spectrum of denticulatain B (**2**)