

Supporting Information

Heronamides D–F, Polyketide Macrolactams from Deep-Sea

Derived *Streptomyces* sp. SCSIO 03032

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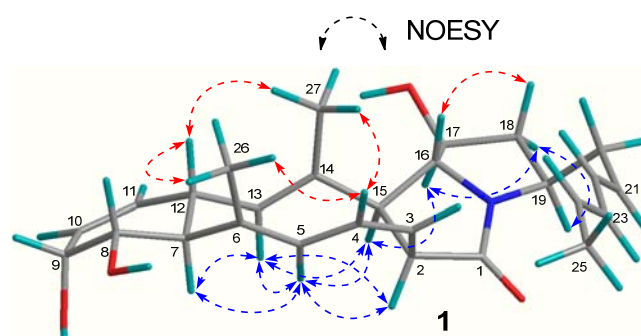
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Table S1. Determination of relative configurations of **1** by ^1H - ^1H coupling constants and NOESY correlations.

Position	configuration	<i>J</i> (Hz)	NOESY
$\Delta^{3,4}$	<i>Z</i>	10.4	
$\Delta^{5,6}$	<i>E</i>		from H-26 to H-4
$\Delta^{13,14}$	<i>E</i>		from H-27 to H-12
$\Delta^{21,22}$	<i>E</i>	14.5	
$\Delta^{21,22}$	<i>E</i>	14.5	
H-5/H-2	on the same side		between H-5 and H-2
H-5/H-7	on the same side		between H-5 and H-7
H-5/H-13	on the same side		between H-5 and H-13
H-5/H-15	on the same side		between H-5 and H-15
H-7/H-8	<i>trans</i>	10.5	
H-7/H-12	<i>trans</i>	10.5	
H-8/H-9	<i>cis</i>	4.1	



NOESY correlations from H-12 to H₃-26/H₃-27, and from H-4 to H₃-26/H₃-27 indicated that H-4, H-12, H₃-26, and H₃-27 were on the same face of the 10-membered ring, whereas the protons H-2, H-5, H-7, H-13, and H-15 were placed on the other face of the 10-membered ring on the basis of NOESY correlations from H-5 to H-2/H-7/H-13/H-15, and from H-13 to H-2/H-7/H-15. NOESY correlations from H-17 to H-15/H-18b, and between H-18b and H-19 suggested that the protons H-17, H-18b, and H-19 were on the same side as H-15.

Table S2. ¹H NMR spectroscopic data for **1a** (500 MHz, CDCl₃) and ¹H, NOESY NMR spectroscopic data for **1b** (500 MHz, pyridine-*d*₅).

Position	1a	1b		
	δ_{H} , mult (<i>J</i> in Hz)	δ_{H} , mult (<i>J</i> in Hz)	COSY	NOESY
2	3.86, ddd (9.0, 7.1, 1.7)	3.89, ddd (9.0, 7.1, 1.7)	3, 4, 15	
3	5.82, dd (10.0, 7.1)	5.77, m (10.0, 7.1)	2, 4	
4	6.73, ddd (10.0, 10.0, 1.7)	6.74, ddd (10.0, 10.0, 1.7)	2, 3, 5	
5	5.62, m	5.58, m ^a	4	7
7	2.03, dd (10.6, 10.6)	2.05, dd (10.6, 10.6)	8, 12	5
8	4.45, dd (10.6, 5.3)	4.49, dd (10.6, 5.3)	7, 9	
9	4.67, m	4.69, m	8, 10	
10	6.01, m	6.01, m ^a	9, 11	
11	6.21, m	6.17, m ^a	10, 12	
12	2.80, m	2.82, m	7, 11, 13	26
13	5.03, m	5.03, m ^a	12	
15	3.32, dd (9.0, 9.0)	3.47, dd (9.0, 9.0)	2, 16	
16	4.29, dd (9.0, 6.9)	4.41, dd (9.0, 6.9)	15, 17	26
17	4.21, m	5.40, m	16, 18a, 18b	15, 18a
18a	2.61, m	2.78, m	17, 18b, 19	
18b	2.17, m	1.97, m	17, 18a, 19	
19	4.21, m	4.29, m	18a, 18b, 20a, 20b	18a
20a	2.80, m	2.35, m	19, 20b, 21	
20b	2.66, m	2.61, m	19, 20a, 21	
21	5.62, m	5.62, m ^a	20a, 20b, 22	
22	6.24, dd (10.5, 15.1)	6.17, m ^a	21, 23	
23	6.10, m	6.10, m ^a	22, 24	
24	5.77, m	5.85, m ^a	23, 25	
25	1.63, d (6.7)	1.64, d (6.7)	24	
26	1.72, s	1.54, s		
27	1.54, s	1.32, s		12, 16
28	1.48, s	1.47, s		
29	1.46, s	1.76, s		

^aoverlapping signals

Table S3. $\Delta\delta^{SR}$ (ppm) data for 17-(*S*)- and 17-(*R*)-MTPA esters of heronamide D acetonides (**1b** and **1c**) in pyridine-*d*₅.

No.	<i>S</i> -MTPA (1b)	<i>R</i> -MTPA (1c)	$\Delta\delta^{SR}$ (ppm)
	δ_H	δ_H	$\Delta\delta$ ($\delta_S - \delta_R$)
2	3.89	3.88	0.01
4	6.74	6.71	0.03
5	5.58	5.56	0.02
12	2.82	2.81	0.01
13	5.13	5.09	0.04
15	3.47	3.44	0.03
16	4.41	4.30	0.11
17	5.40	5.47	-0.07
19	4.29	4.33	-0.04

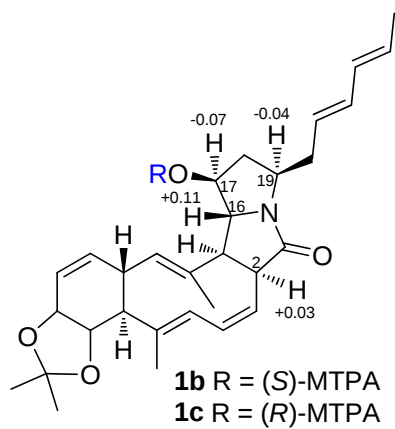


Table S4. $\Delta\delta^{SR}$ data (ppm) for the bis-9,17-(*S*)- and bis-9,17-(*R*)-MTPA esters of heronamide D (**1d** and **1e**) in CDCl_3 .

No.	<i>S</i> -MTPA (1d)	<i>R</i> -MTPA (1e)	$\Delta\delta^{SR}$ (ppm)
	δ_{H}	δ_{H}	$\Delta\delta$ ($\delta_{\text{S}} - \delta_{\text{R}}$)
3	5.51	5.49	0.02
4	6.62	6.61	0.01
5	5.34	5.32	0.02
7	1.912	1.913	-0.001
8	4.07	4.14	-0.07
9	5.59	5.56	0.03
10	6.00	5.95	0.05
11	6.09	6.06	0.03
12	2.81	2.77	0.04
13	4.92	4.85	0.07
15	3.16	3.12	0.04
16	4.11	4.02	0.09
17	5.06	5.10	-0.04
18a	1.85	1.94	-0.09
18b	2.61	2.57	0.04
20	2.44	2.57	-0.13
	2.23	2.25	-0.02
21	5.40	5.44	-0.04
25	1.742	1.746	-0.004
26	1.696	1.699	-0.003
27	1.28	1.13	0.15

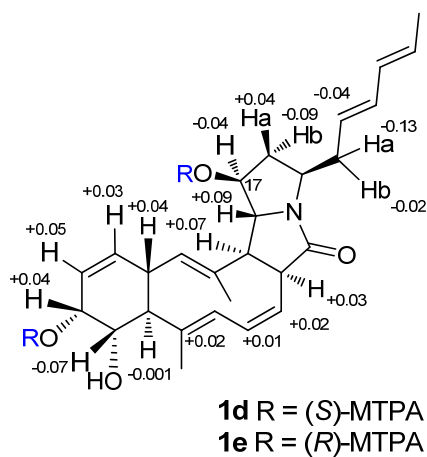
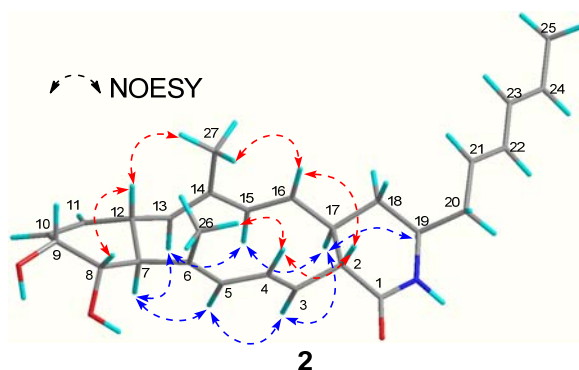
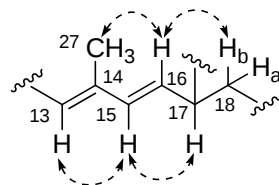


Table S5. Determination of relative configurations of **2** by ^1H - ^1H coupling constants and NOESY correlations.

Position	configuration	J (Hz)	NOESY
$\Delta^{3,4}$	E	15.0	
$\Delta^{5,6}$	E		from H-26 to H-4
$\Delta^{15,16}$	E	15.0	from H-27 to H-12
$\Delta^{21,22}$	E	15.0	
$\Delta^{23,24}$	E	15.0	
H-7/H-12	<i>trans</i>	10.5	
H-8/H-9	<i>cis</i>	4.0	
H-8/H-12	on the same side		between H-8 and H-12
H-2/H-17	<i>trans</i>	10.5	
H-17/H-19	on the same side		between H-17 and H-19
H ₃ -27/H-15	<i>anti</i>		



The protons H-2, H-4, H-12, H-16, H-26, and H-27 were placed on the same face of the 12-membered ring of **2**, on the basis of NOESY correlations from H-16 to H-2, from H-4 to H₃-26/H-2, and from H-12 to H₃-27; whereas the protons H-3, H-5, H-7, H-13, H-15, and H-17 were put on the other face of the 12-membered ring of **2**, on the basis of NOESY correlations from H-5 to H-3/H-7, between H-7 and H-13, and between H-3 and H-17.

Table S6. $\Delta\delta^{SR}$ data (ppm) for 8-(*S*)- and 8-(*R*)-MTPA ester of heronamide E (**2a** and **2b**) in CDCl₃.

No.	<i>S</i> -MTPA (2a)	<i>R</i> -MTPA (2b)	$\Delta\delta^{SR}$ (ppm)
	δ_H	δ_H	$\Delta\delta$ ($\delta_S - \delta_R$)
2	2.655	2.660	-0.005
3	5.12	5.17	-0.05
4	5.80	5.87	-0.07
5	5.62	5.69	-0.07
7	2.67	2.69	-0.02
8	5.33	5.43	-0.10
9	4.50	4.30	0.20
10	5.87	5.82	0.05
11	5.92	5.90	0.02
12	3.22	3.24	-0.02
13	4.832	4.836	-0.004
15	5.67	5.69	-0.02
16	4.89	4.91	-0.02
17	2.424	2.421	0.003
19	3.500	3.499	0.001
25	1.756	1.759	-0.003
27	1.62	1.65	-0.03
26	1.42	1.53	-0.11

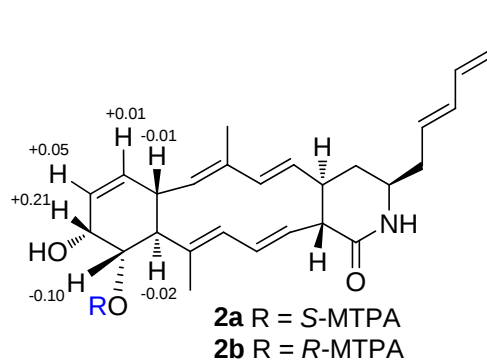


Table S7. Determination of relative configurations of **3** by ^1H - ^1H coupling constants and NOESY correlations in **3** or **3a**.

Position	configuration	J (Hz)	NOESY
$\Delta^{2,3}$	E^b	14.5	
$\Delta^{4,5}$	E^b	15.5	
$\Delta^{6,7}$	E^b		from H-26 to H-8
$\Delta^{10,11}$	Z^b	10.0	
$\Delta^{12,13}$	E^b	16.5	
$\Delta^{14,15}$	E^b		from H-27 to H-16
$\Delta^{16,17}$	E^a	15.0	
$\Delta^{21,22}$	E^a	15.0	
$\Delta^{23,24}$	E^a	15.0	
H-8/H-9	cis^b	2.8	
H-3/H-4	$anti^b$		between H-2 and H-4, and between H-3 and H-5
H-5/H-26	cis^b		between H-7 and H-4
H-13/H ₃ -27	cis^b		between H-13 and H ₃ -27
H-15/H-16	$anti^b$		between H-16 and H ₃ -27 and between H-15 and H-17

^aobserved in **3**, ^bobserved in **3a**.

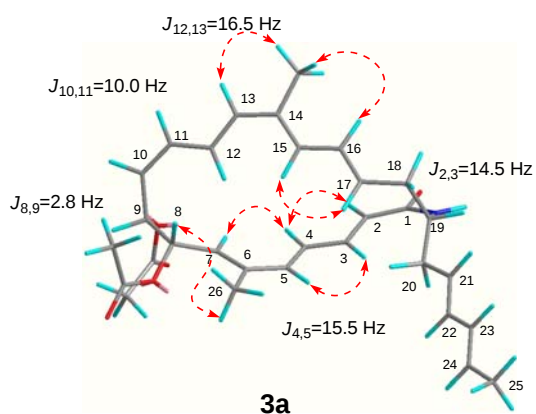
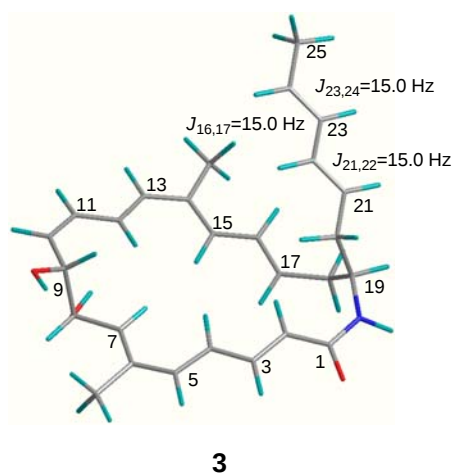
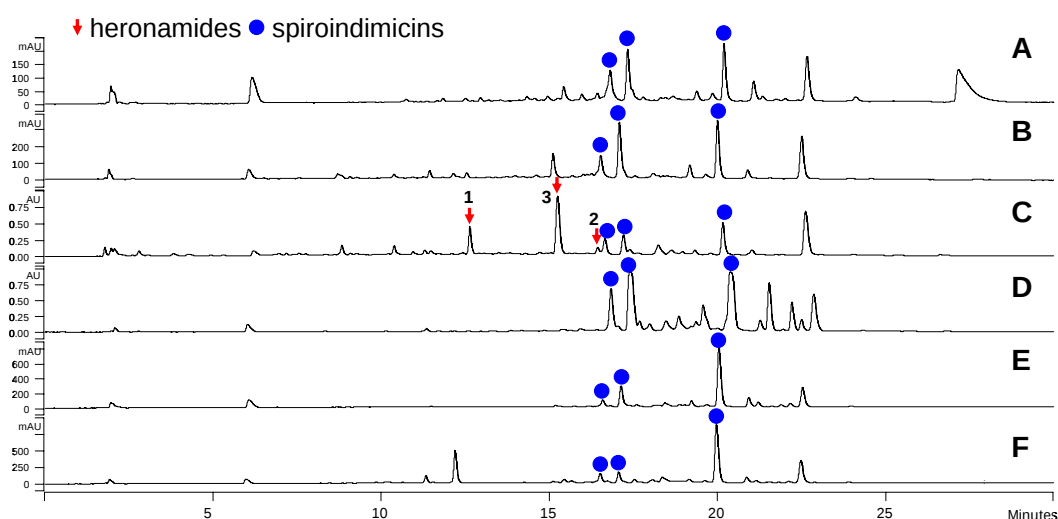


Table S8. NMR spectroscopic data (500 MHz, CDCl₃) for **3a**.

Position	δ_{H} , mult (<i>J</i> in Hz)	δ_{C} , type	COSY	HMBC	NOESY
1		167.5, C			
2	5.75, d (14.5)	123.0, CH	3	1, 4	NH, 4
3	6.94, ddd (1.5, 8.5, 14.5)	142.0, CH	2, 4, 5	1, 4, 5	5
4	6.17, dd (8.5, 15.5)	125.9, CH	3, 5	2, 6	2, 7
5	6.18, dd (1.5, 15.5)	143.4, CH	2, 4	3, 4, 26	
6		135.7, C			
	5.20, d (7.5)	131.6, CH	8, 27	5, 26	4
8	6.07, m	71.6, CH	9	7, 9	26
9	5.64, m	70.9, CH	8, 10	8, 10	
10	5.44, dd (10.0, 10.0)	122.7, CH	9, 11,	12	
11	6.26, dd (10.0, 10.0)	132.8, CH	10, 12	13	
12	5.95, dd (11.0, 16.5)	123.2, CH	11	13, 14	
13	6.17, m	138.7, CH			
14		133.3, C			
15	5.98, d (11.0)	131.4, CH		16, 27	17
16	6.06, m	133.7, CH	17	18a	27
17	5.62, m	131.3, CH	16, 18	16	15
18a	2.51, m	41.4, CH ₂	8b, 11, 17		
18b	1.81, m		18a, 19	19	
19	4.22, m	49.8, CH	18b, 20, NH		18a
20a	2.32, m	38.2, CH ₂	19, 21	18a, 19, 21	
20b	2.35, m	38.2, CH ₂	19, 21		
21	5.56, m	126.3, CH	20, 22	19, 20, 23	
22	6.08, m	130.4, CH	21, 23		
23	6.01, m	131.0, CH			
24	5.67, m	128.5, CH			
25	1.75, d (6.5)	18.0, CH ₃	24	23, 24	
26	1.96, s	12.7, CH ₃		5, 6, 7	
27	1.59, s	12.4, CH ₃	15	13, 14, 15	8
28*	2.06, s	21.0, CH ₃		30	16
29*	2.10, s	21.1, CH ₃		31	
30*		170.3, C			
31*		170.5, C			
NH	4.85, d (11.0)		19	1	

⁸, 9-OC (O) Me or 8, 9-OC (O) signals

Figure S1. HPLC analysis of metabolite profiles of *Streptomyces* sp. SCSIO 03032 cultured in different media.

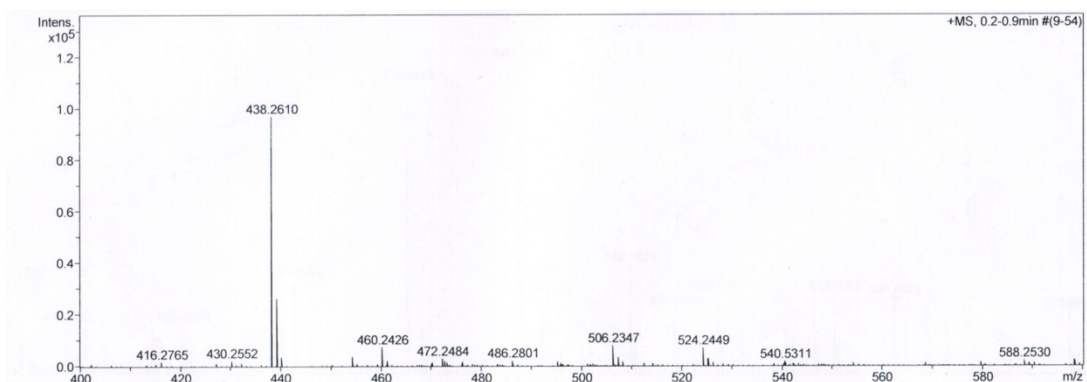


(A). AM1 medium (glucose 0.6 %, chitin 0.2 %, CaCO_3 0.2 %, sea salt 3 %, pH 7.2-7.4); (B). AM2 medium (l-Asn 0.2 %, trehalose 1 %, MgSO_4 0.1 %, CaCO_3 0.2 %, sea salt 3 %, pH 7.2-7.4); (C). Modified-ISP3 (oat meal 1.5 %, FeSO_4 0.0001 %, MnCl_2 0.0001 %, ZnSO_4 0.0001 %, sea salt 3 %, pH 7.2-7.4); (D). modified-A1BFe+C (starch 1 %, yeast extract 0.4 %, peptone 0.2 %, CaCO_3 0.2 %, sea salt 3 %, pH 7.2-7.4); (E). AM4 medium (l-Asn 0.2 %, K_2HPO_4 0.15 %, Glycerin 1 %, CaCO_3 0.2 %, sea salt 3 %, pH 7.2-7.4); (F). AM5 medium (starch 1.0 %, $(\text{NH}_2)_2\text{SO}_4$ 0.2 %, MgSO_4 0.1 %, K_2HPO_4 0.1 %, FeSO_4 0.0001 %, MnCl_2 0.0001 %, ZnSO_4 0.0001 %), sea salt 3%, pH 7.2-7.4.

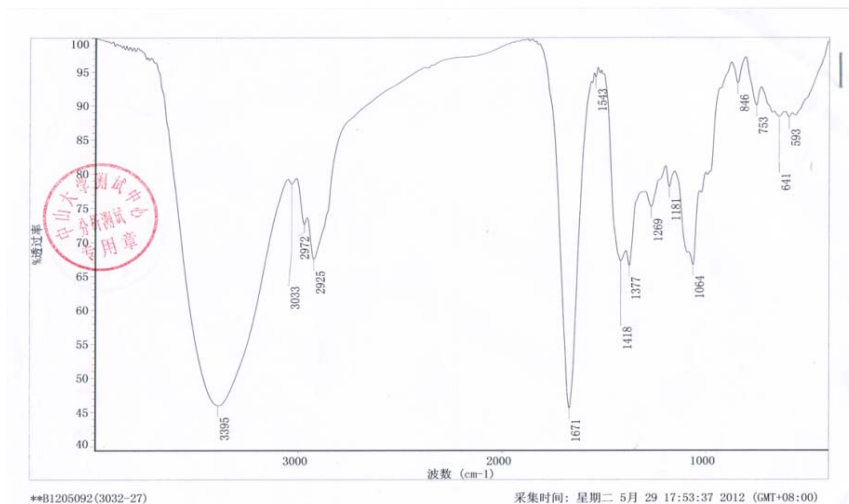
Figure S2. Spectroscopic data for heronamide D (**1**).

(A) HR-ESI-MS (**a**), IR (**b**), UV (**c**), and CD (**d**) spectra of heronamide D (**1**).

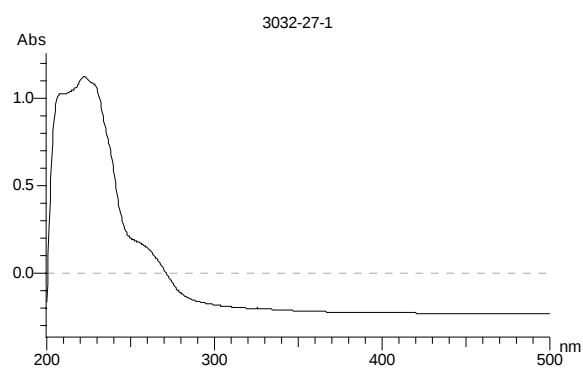
(a). HR-ESI-MS



(b). IR



(c). UV



(d). CD

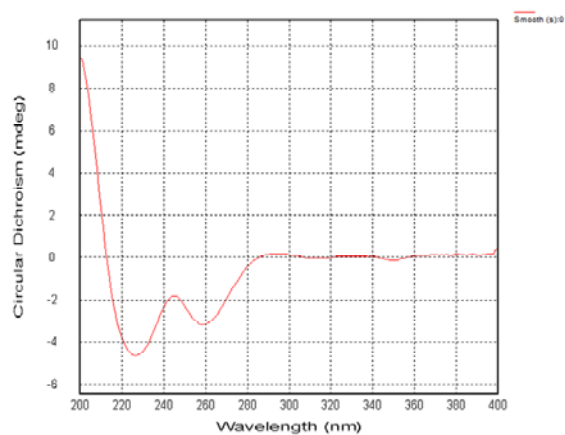


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(B) The ^1H NMR spectrum of heronamide D (**1**) in CDCl_3 .

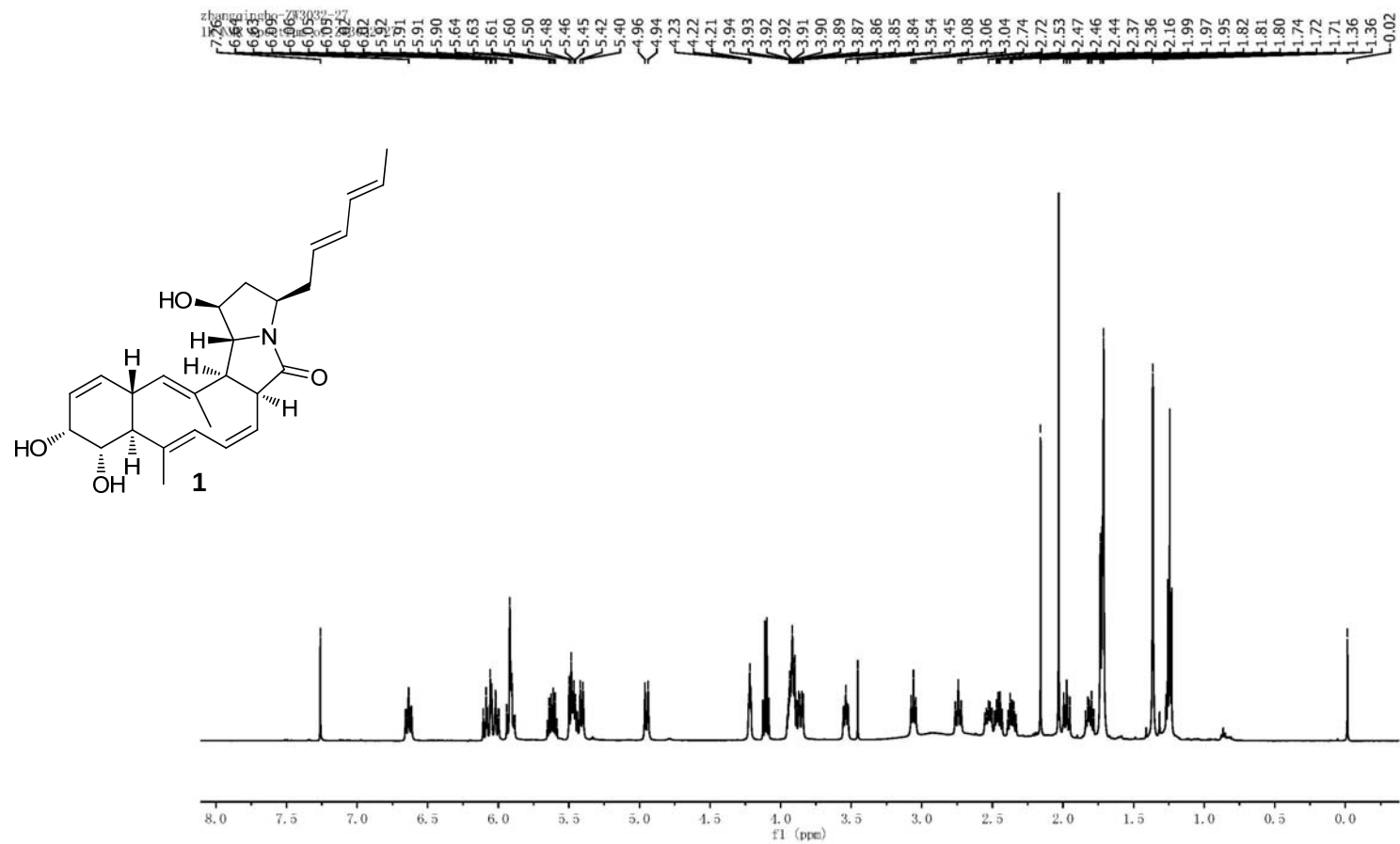


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(C) The ^{13}C and DEPT 135 NMR spectrum of heronamide D (**1**) in CDCl_3 .

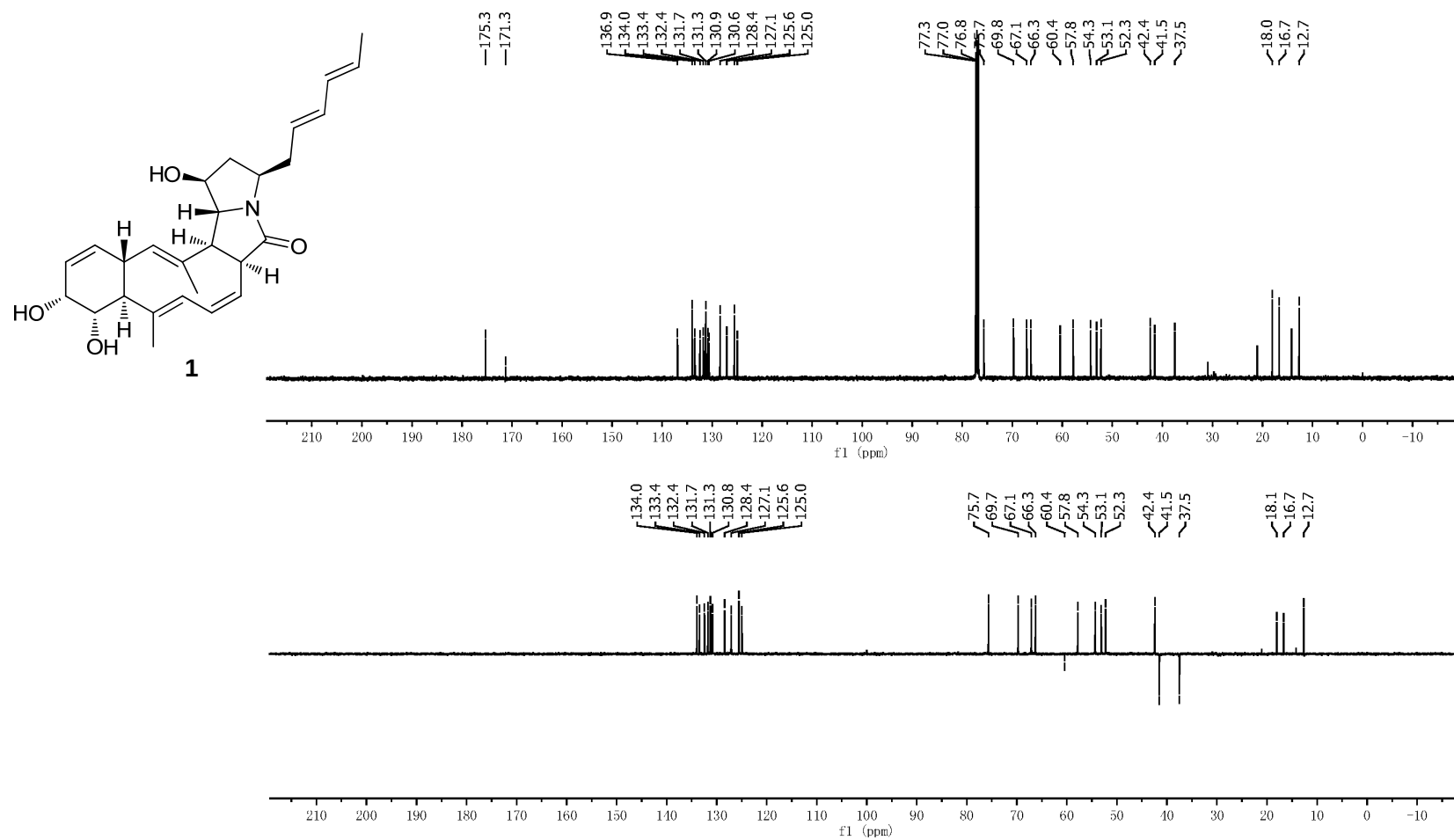


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(D) The HSQC spectrum of heronamide D (**1**) in CDCl₃.

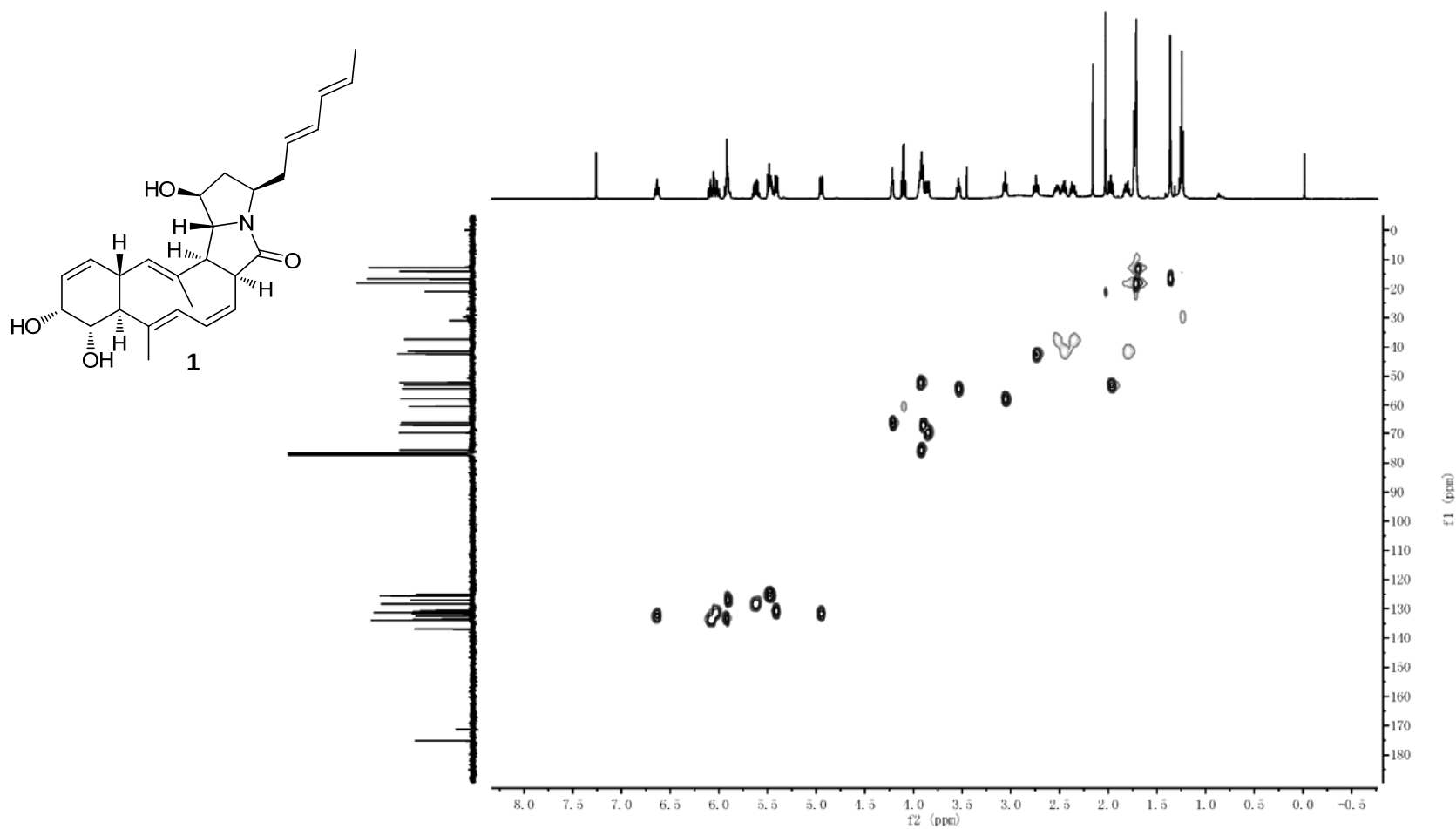


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(E) The COSY spectrum of heronamide D (**1**) in CDCl₃.

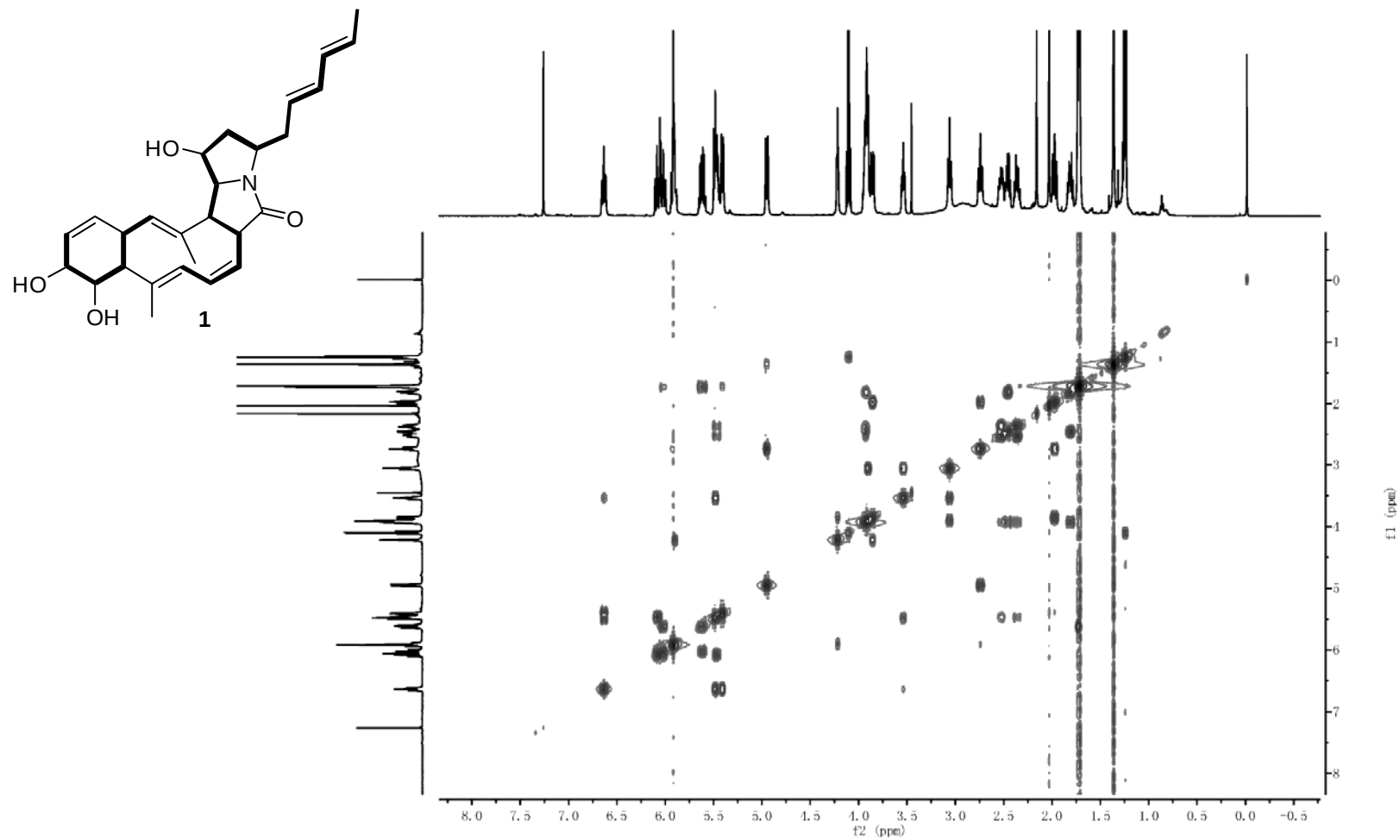


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(F) The HMBC spectrum of heronamide D (**1**) in CDCl₃.

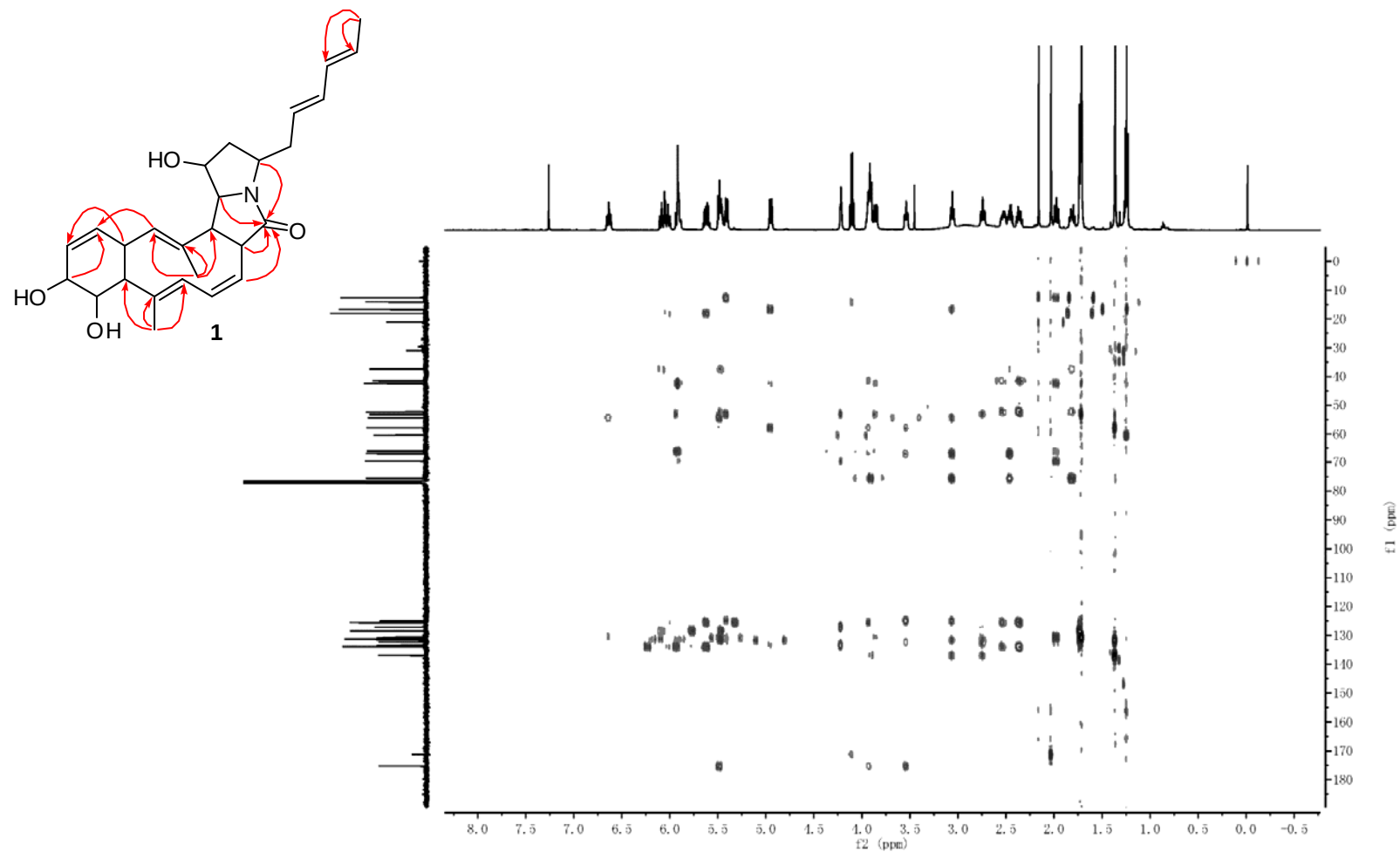


Figure S2. Spectroscopic data for heronamide D (**1**). (Continued)

(G) The NOESY spectrum of heronamide D (**1**) in CDCl₃.

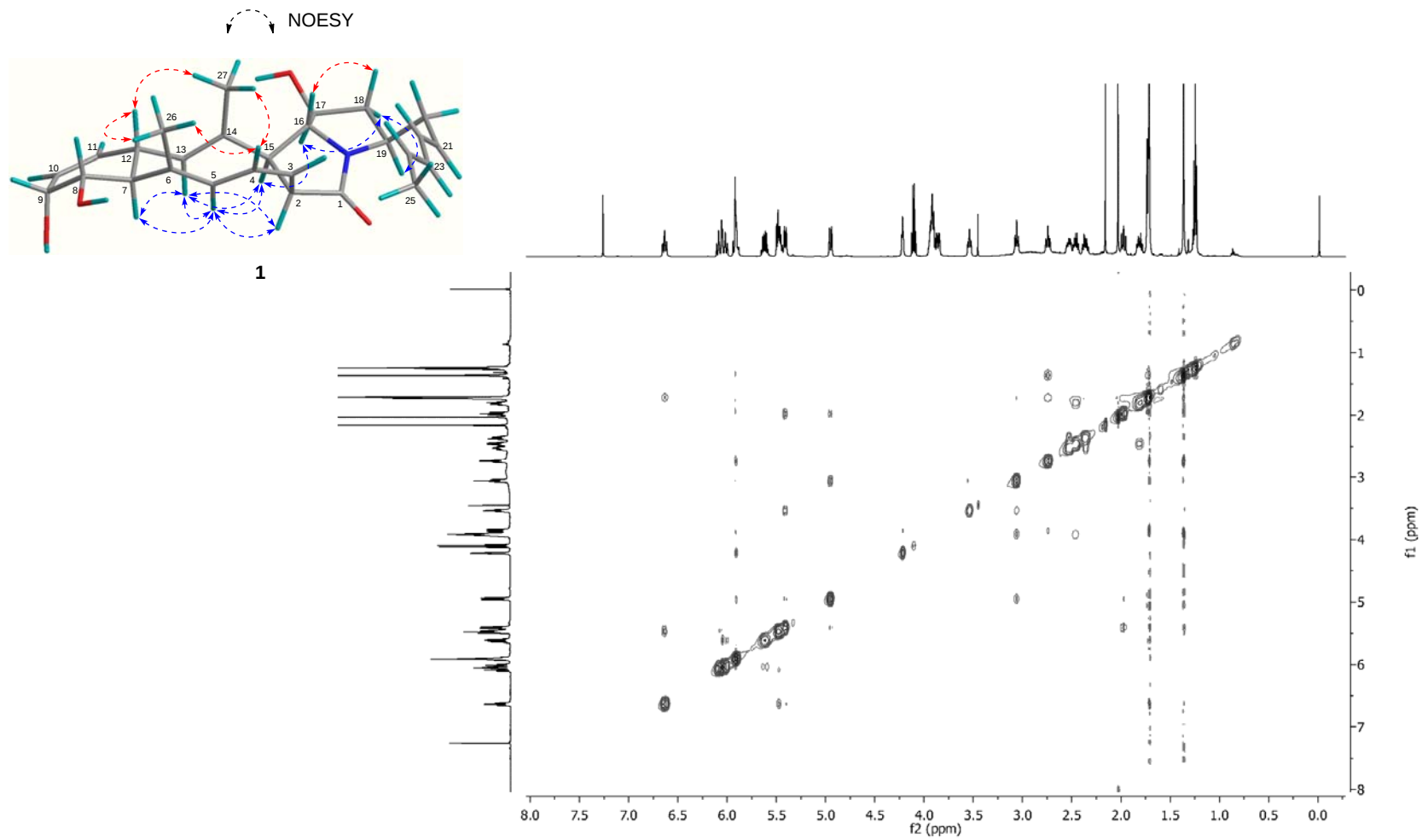
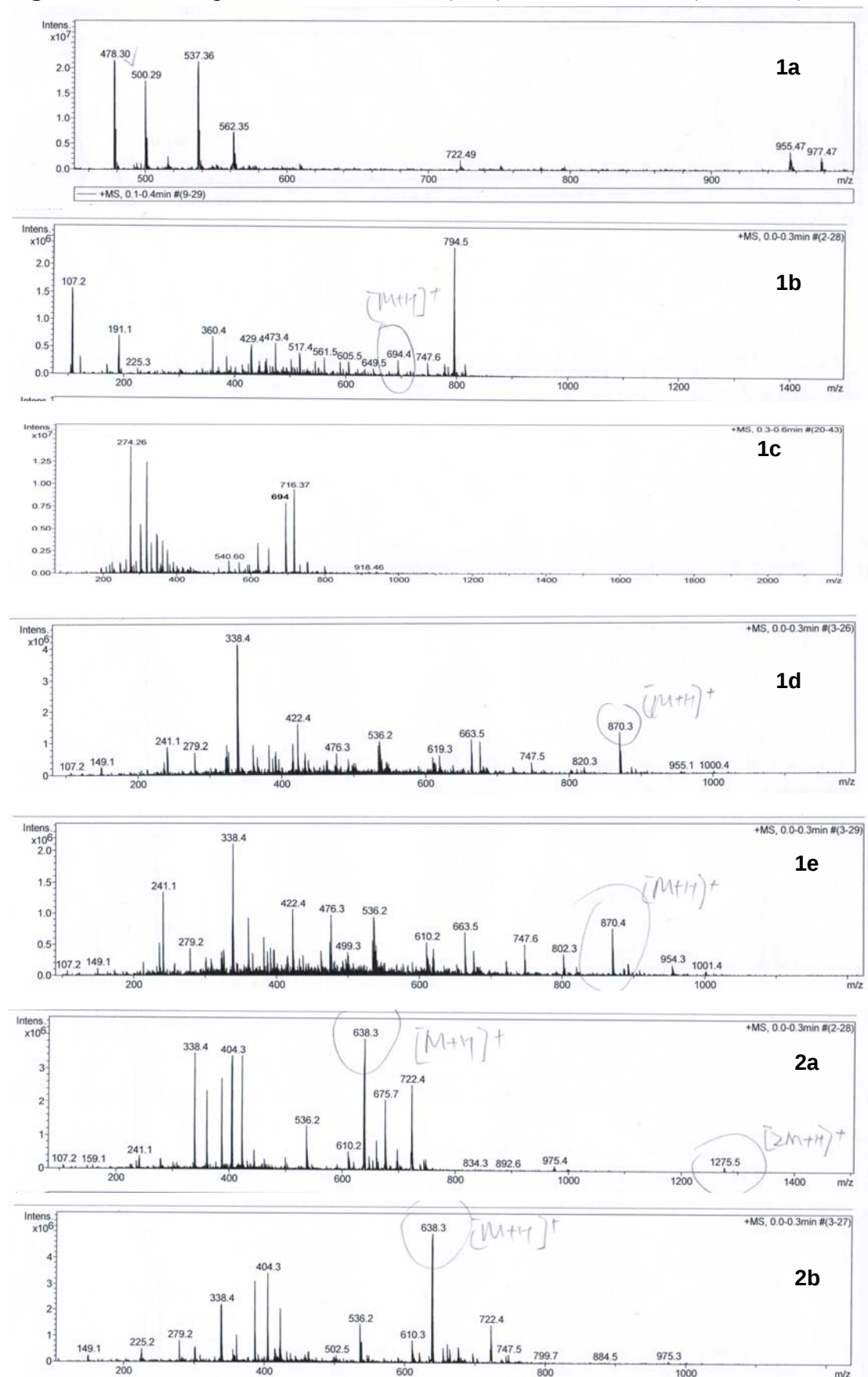


Figure S3. ESIMS spectra of **1** derivatives (**1a-e**) and **2** derivatives (**2a** and **2b**).



Chemical structure of compound **1a**, a complex polycyclic molecule. The structure features a tetracyclic core with a hydroxyl group (HO) and a carbonyl group (C=O). A long, unsaturated side chain is attached to the nitrogen atom of the carbonyl group. The molecule is labeled **1a**.



Figure S5. Spectroscopic data for **1b**.

(A) The ^1H NMR of **1b** in pyridine- d_5 .

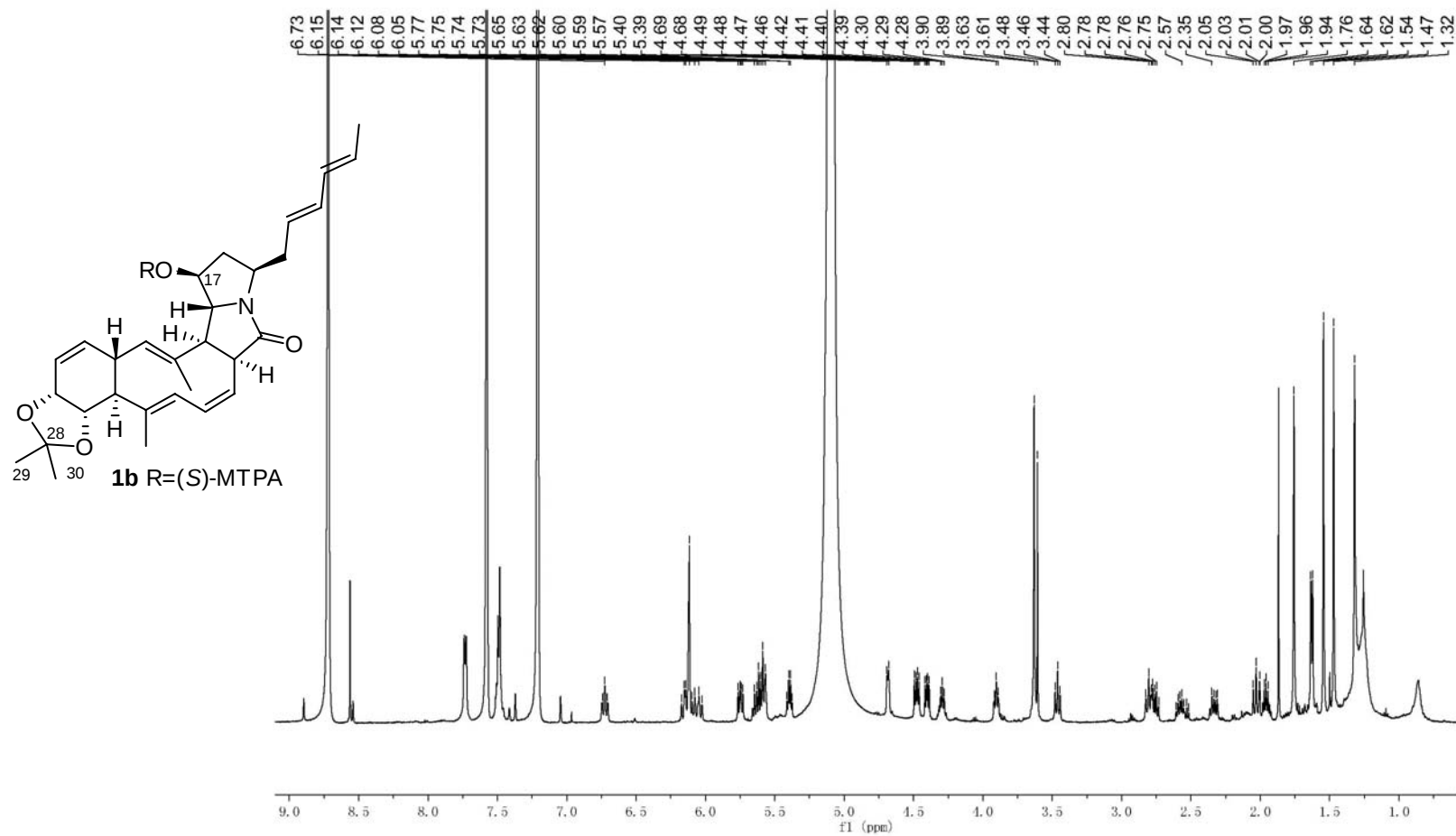


Figure S5. Spectroscopic data for **1b**. (Continued)

(B) The COSY spectrum of **1b** in pyridine- d_5 .

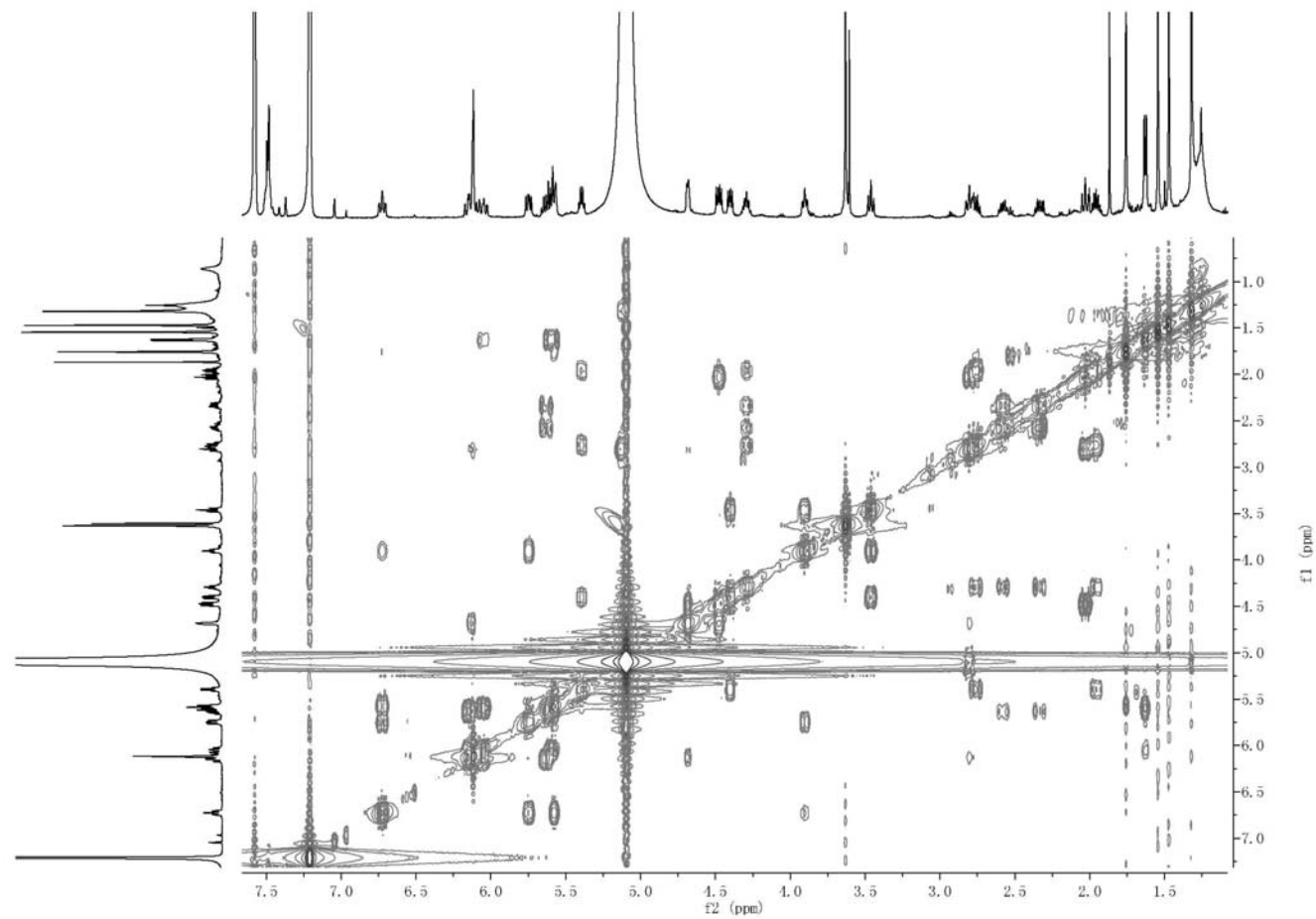


Figure S5. Spectroscopic data for **1b**. (Continued)

(B) The NOESY spectrum of **1b** in pyridine- d_5 .

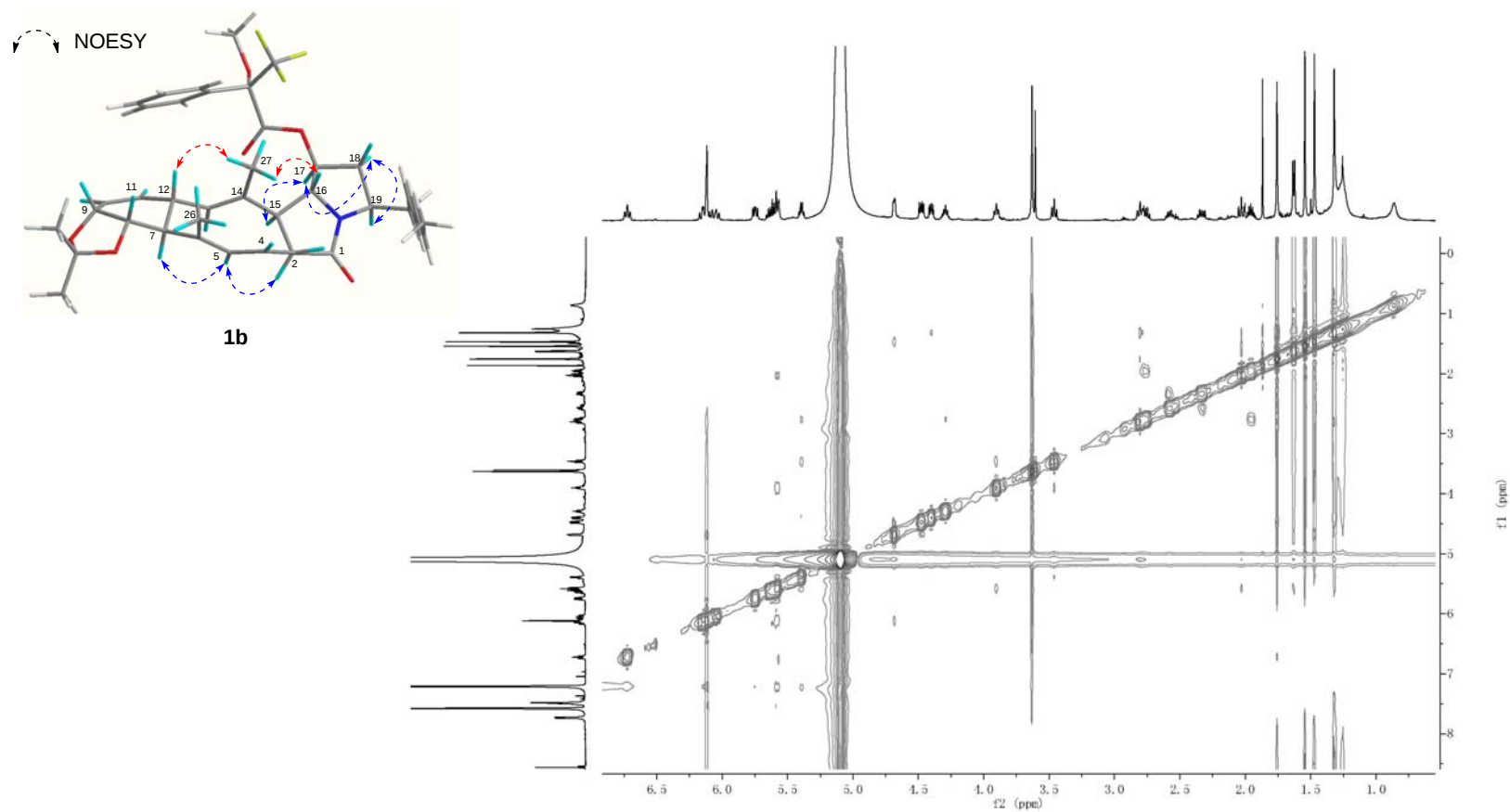


Figure S6. ^1H NMR spectroscopic data of *R*- and *S*-MTPA esters of heronamide D acetone (**1b** and **1c**) in CDCl_3 .

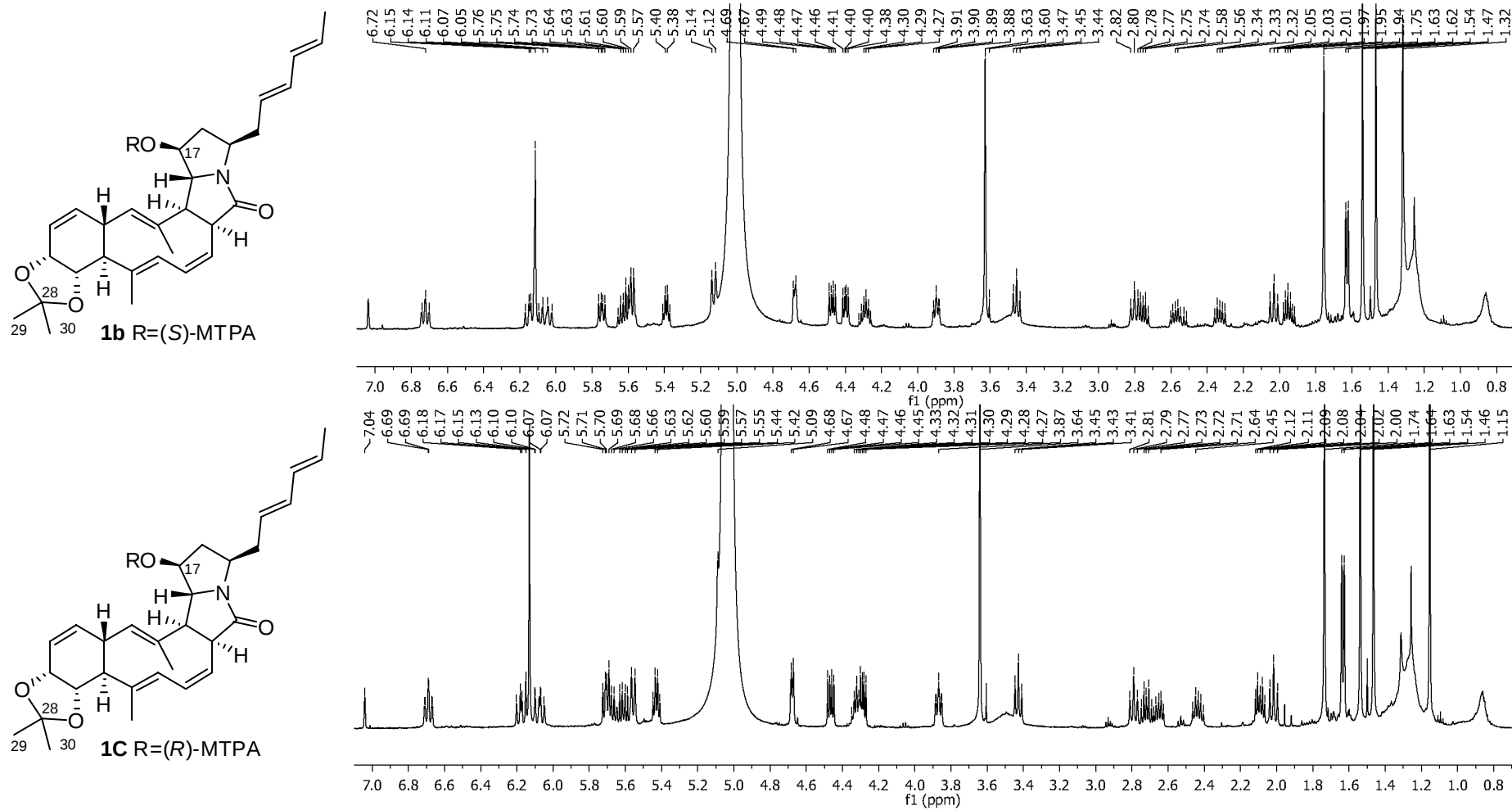


Figure S7. NMR spectroscopic data of bis-9,17-(*S*)- and bis-9,17-(*R*)-MTPA esters of heronamide D (**1d** and **1e**) in CDCl₃.

(A) The ¹H NMR spectrum of bis-9,17-(*S*)- and bis-9,17-(*R*)-MTPA esters of heronamide D (**1d** and **1e**) in CDCl₃.

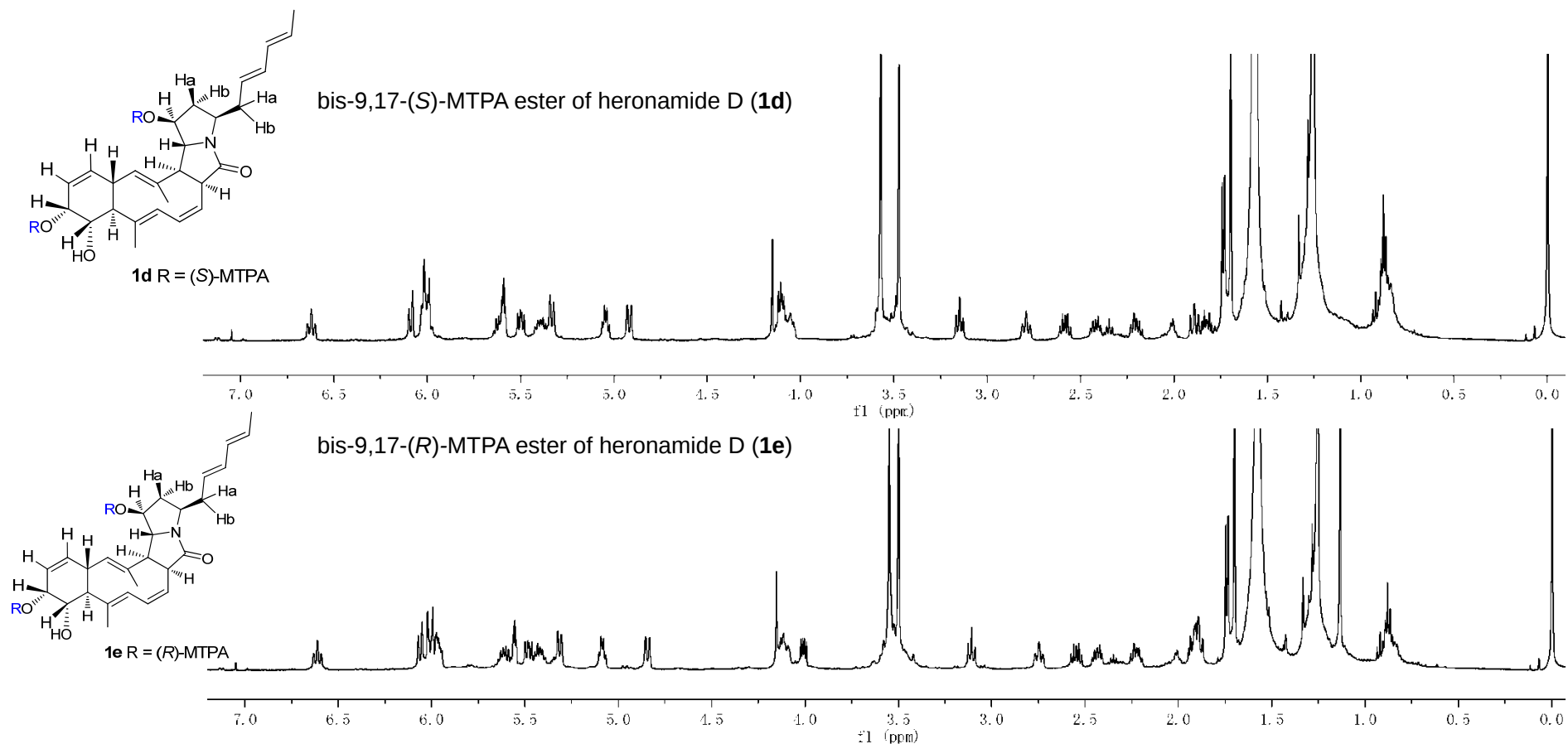


Figure S7. NMR spectroscopic data of bis-9,17-(*S*)- and bis-9,17-(*R*)-MTPA esters of heronamide D (**1d** and **1e**) in CDCl₃.

(B) The COSY spectrum of bis-9,17-(*S*)-MTPA ester of heronamide D (**1d**) in CDCl₃

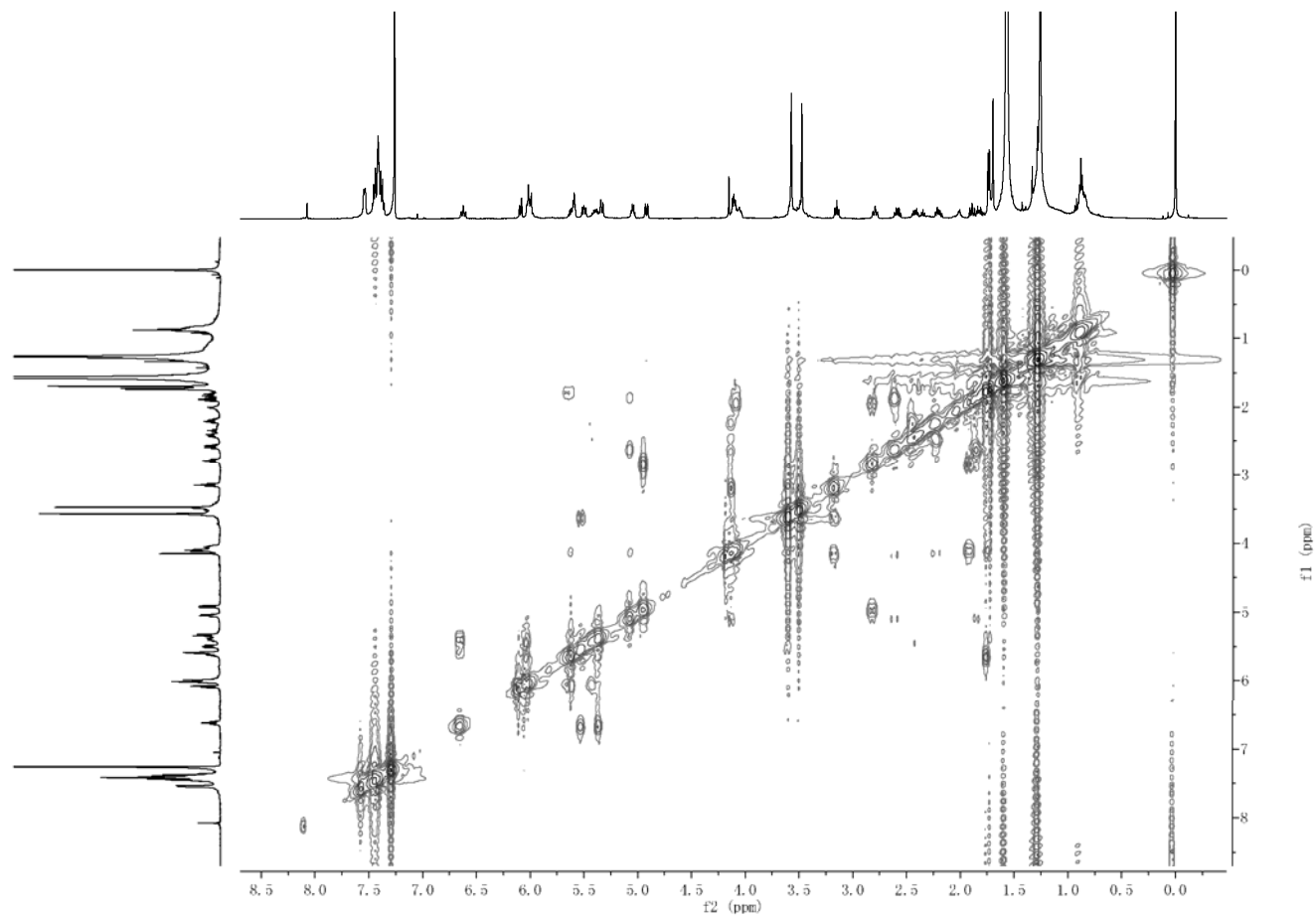


Figure S7. NMR spectroscopic data of bis-9,17-(*S*)- and bis-9,17-(*R*)-MTPA esters of heronamide D (**1d** and **1e**) in CDCl₃.
(C) The COSY spectrum of bis-9,17-(*S*)-MTPA ester of heronamide D (**1e**) in CDCl₃.

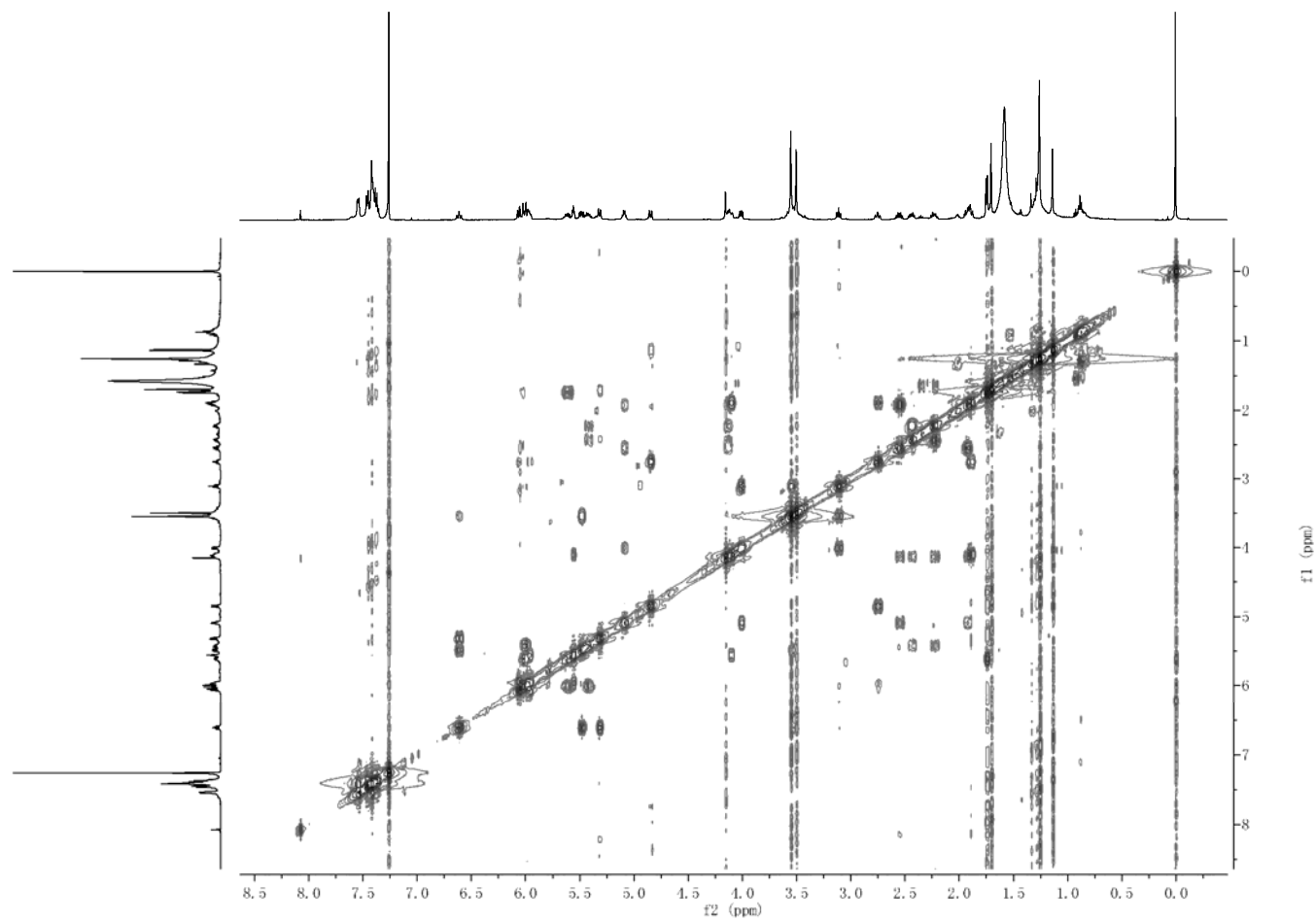
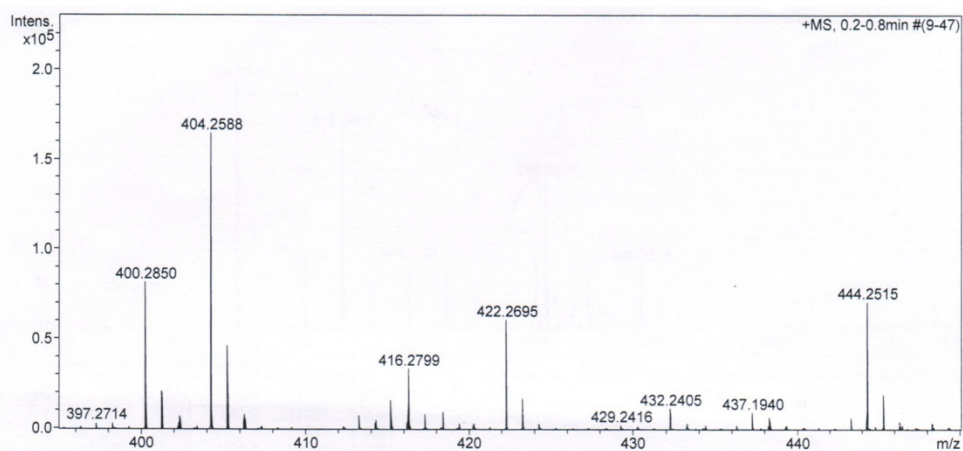


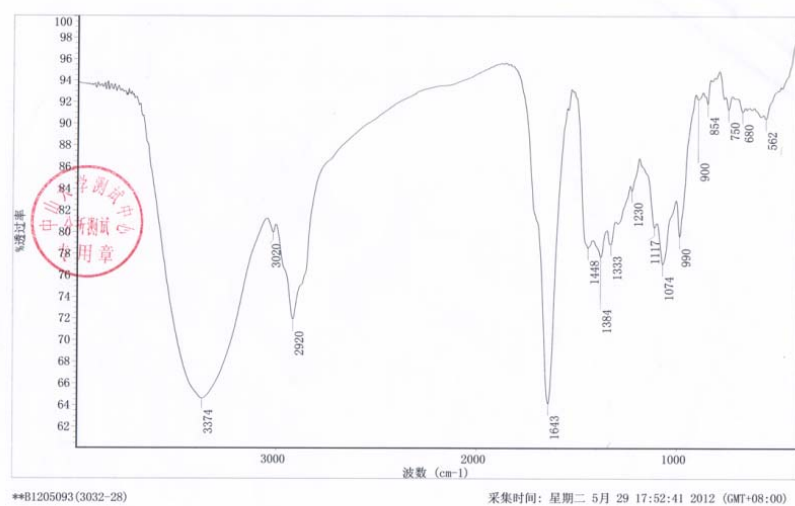
Figure S8. Spectroscopic data for heronamide E (**2**).

(A) HR-ESI-MS (**a**), IR (**b**) UV (**c**), and CD (**d**) spectra of heronamide E (**2**).

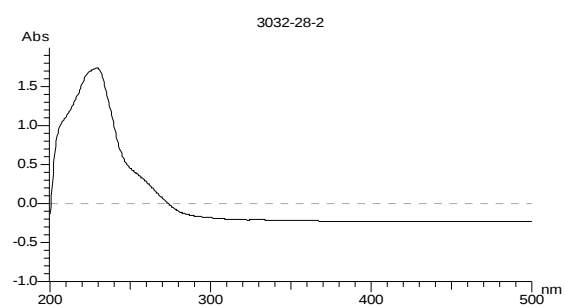
(a). HR-ESI-MS



(b). IR



(c). UV



(d). CD

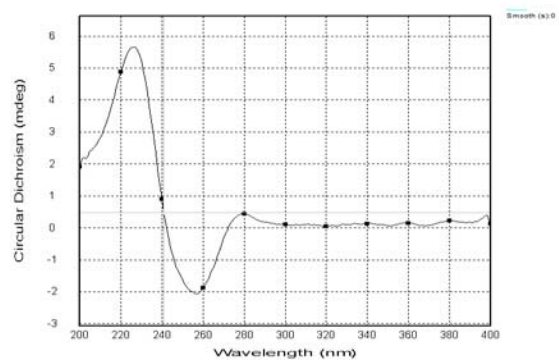


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(B) The ^1H NMR spectrum of heronamide E (**2**) in CDCl_3 .

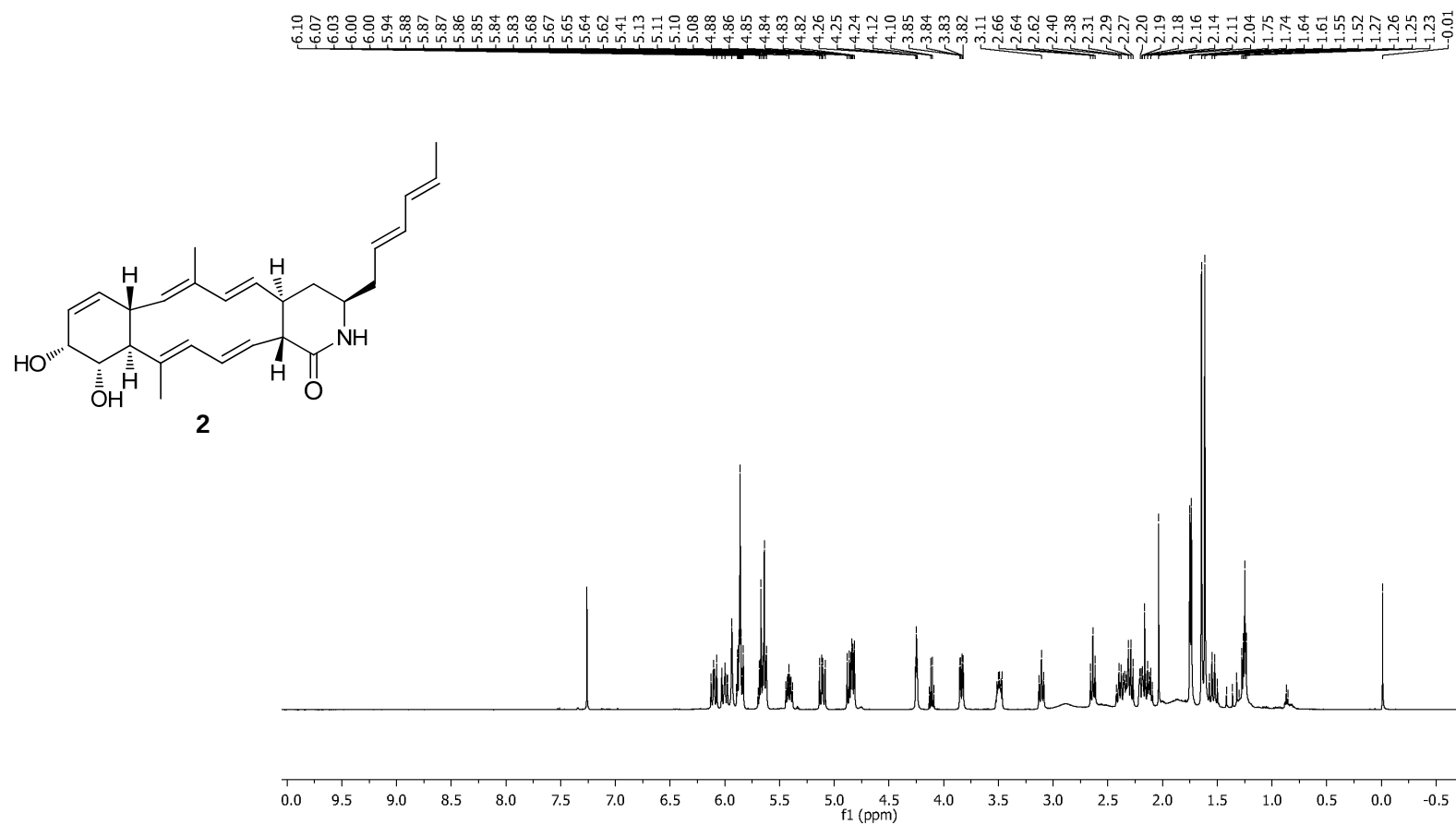


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(C) The ^{13}C NMR and DEPT 135 spectrum of heronamide E (**2**) in CDCl_3 .

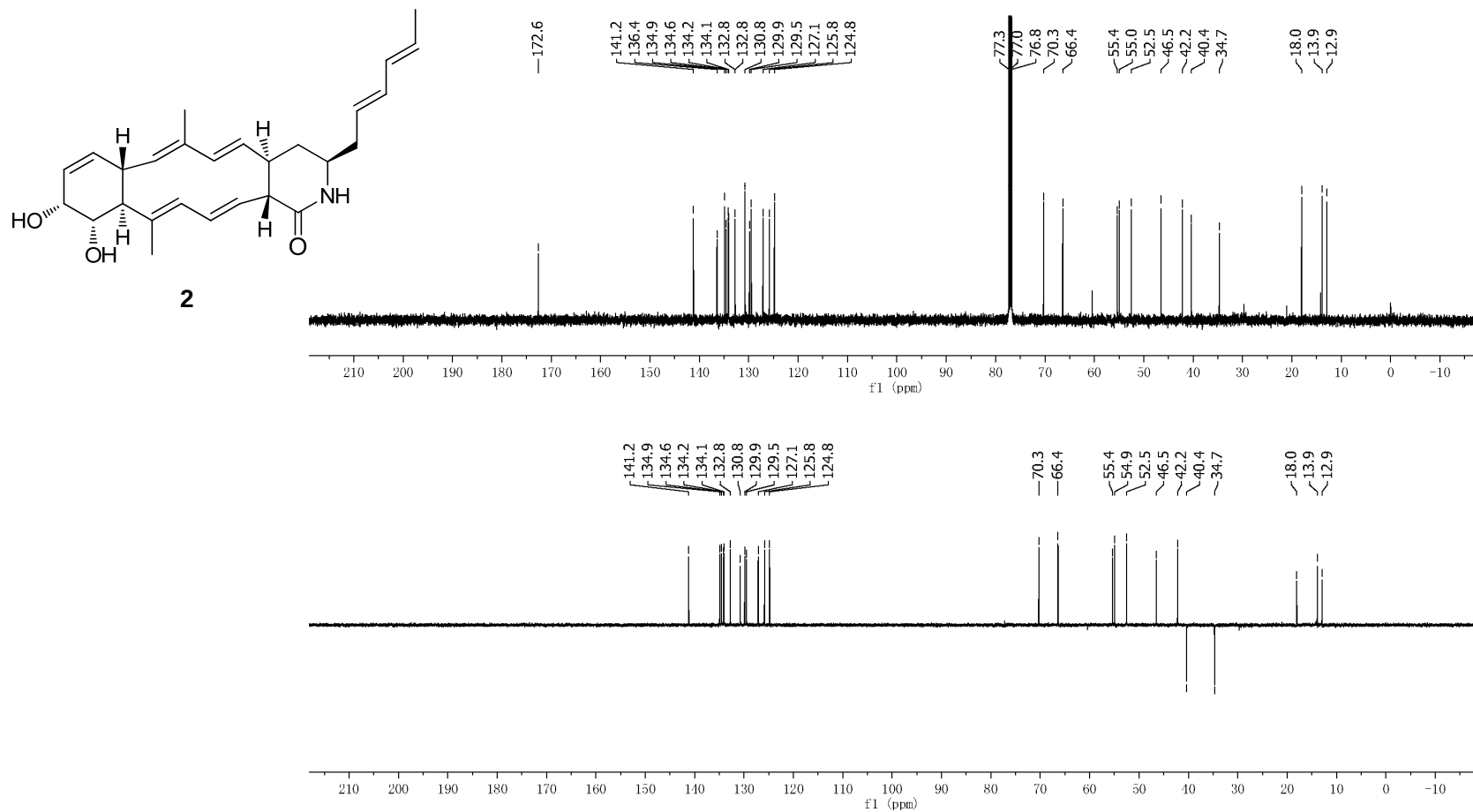


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(D) The HSQC spectrum of heronamide E (**2**) in CDCl₃.

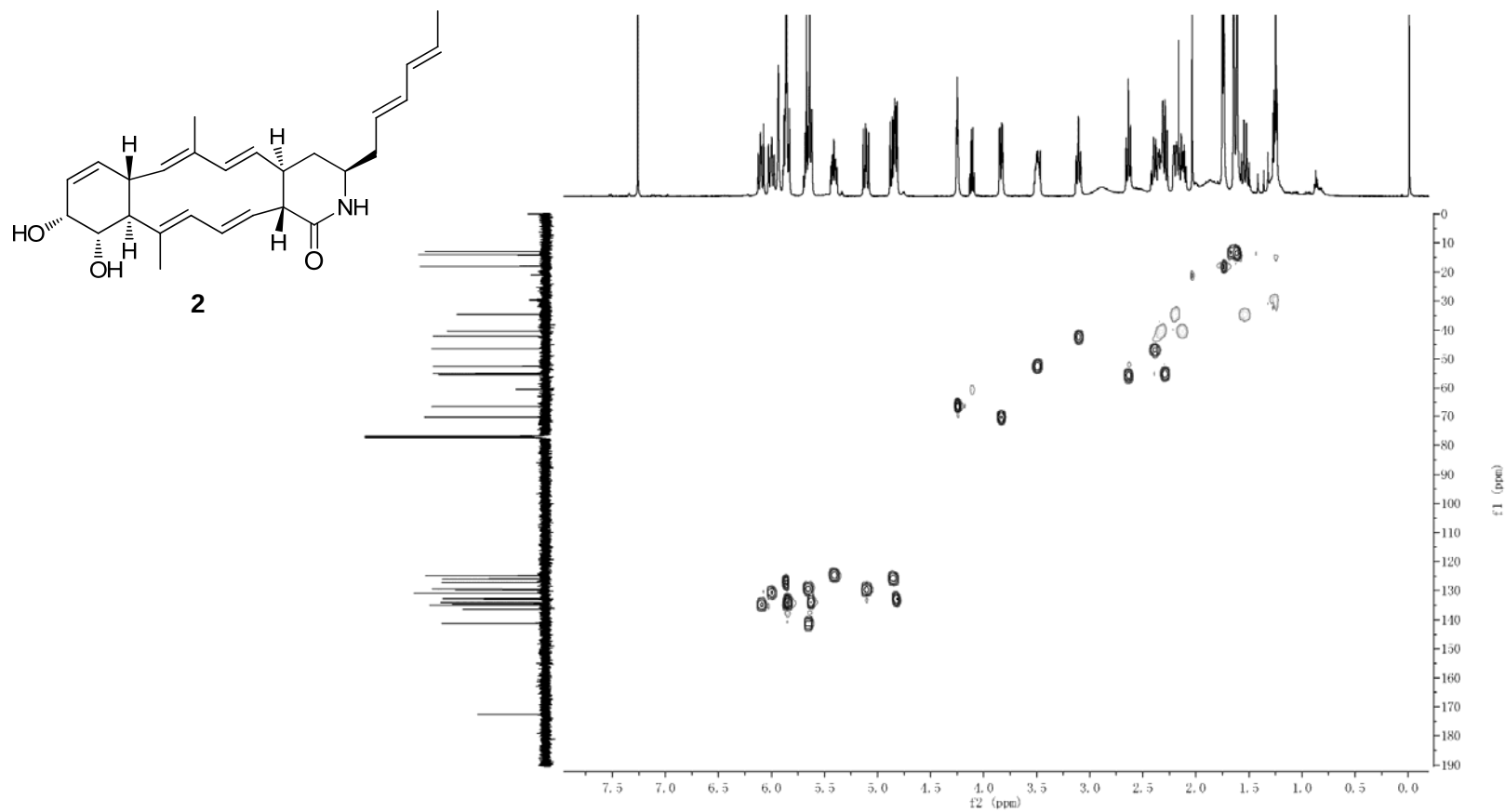


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(E) The COSY spectrum of heronamide E (**2**) in CDCl₃.

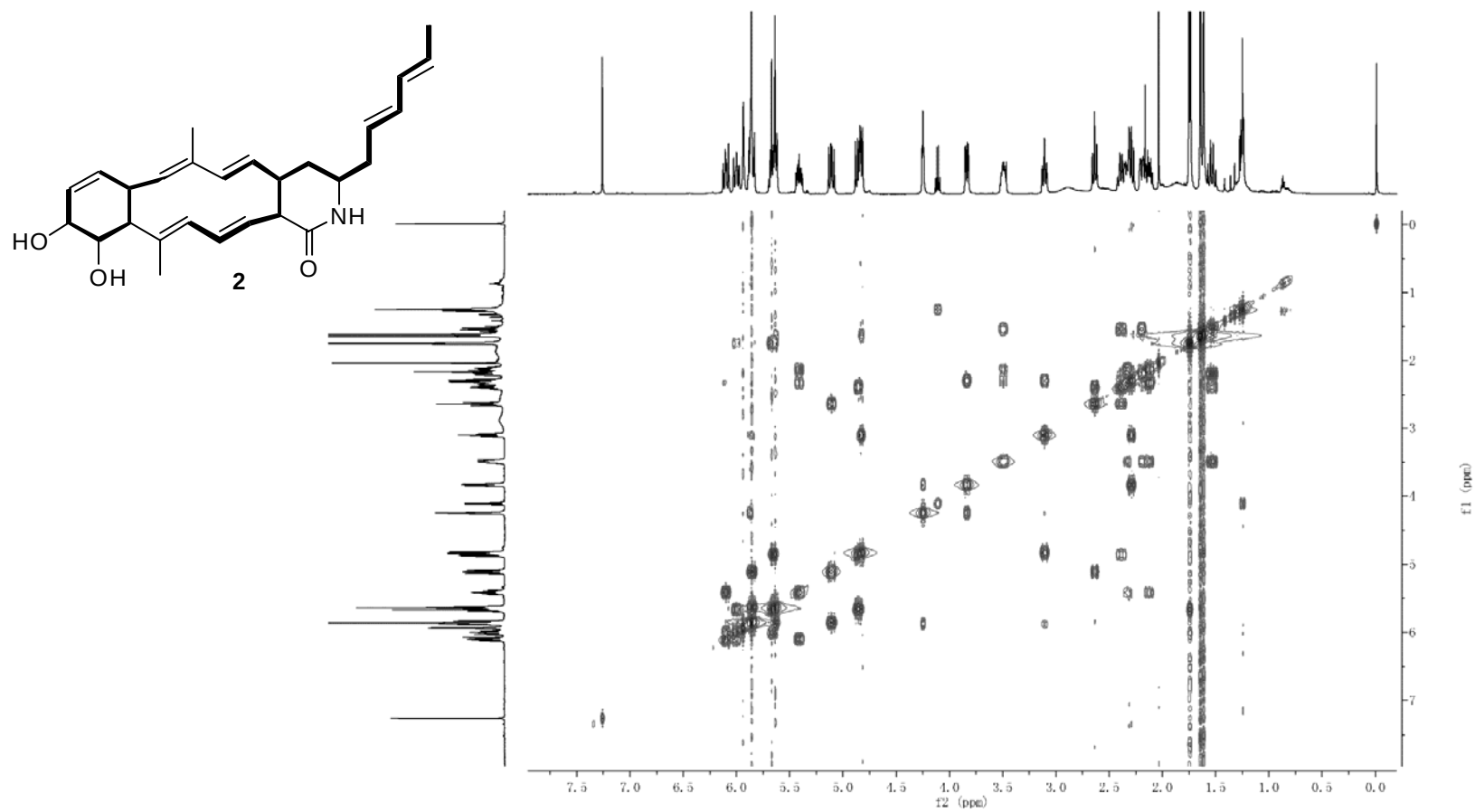


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(F) The HMBC spectrum of heronamide E (**2**) in CDCl₃.

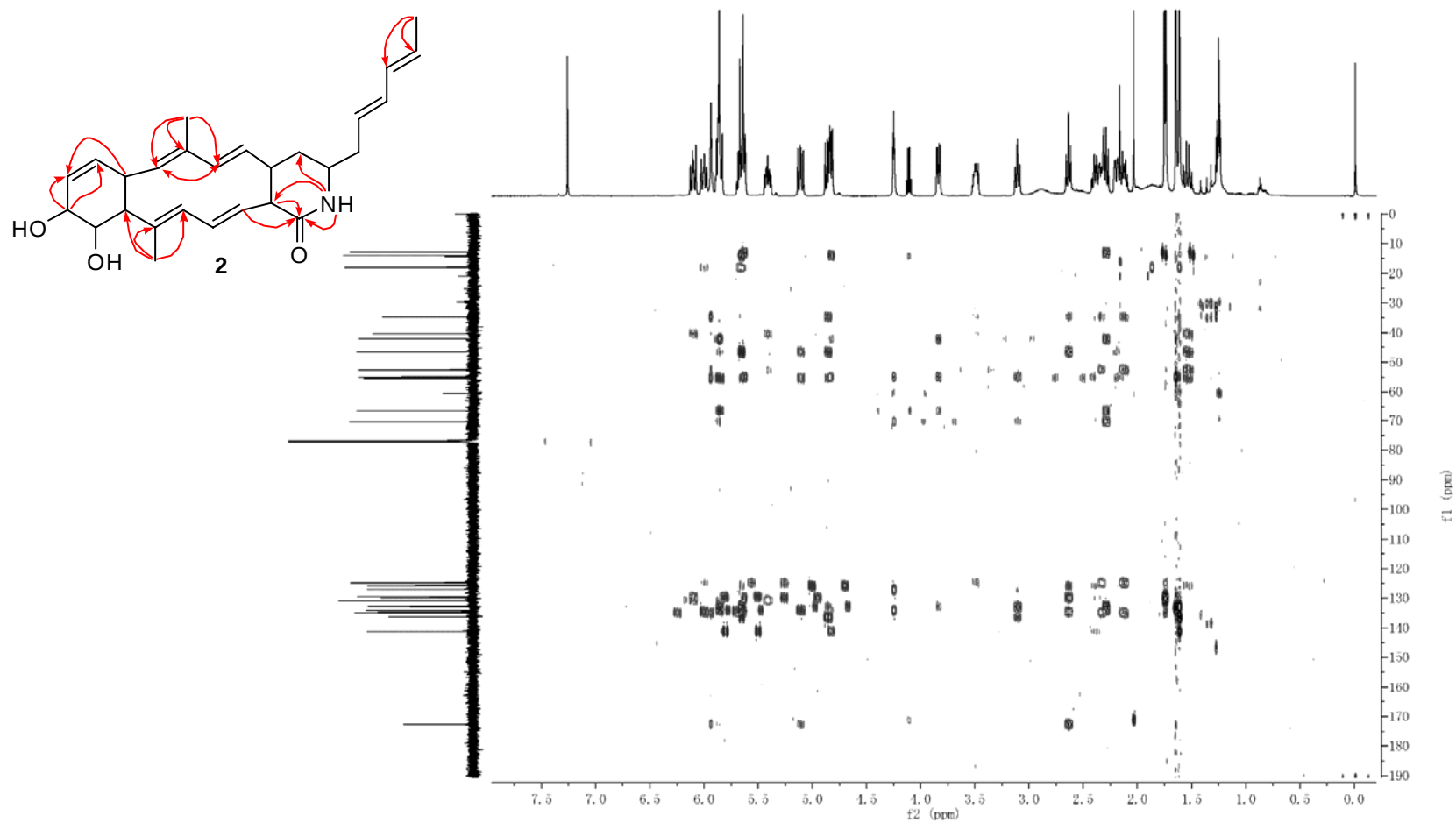


Figure S8. Spectroscopic data for heronamide E (**2**). (Continued)

(G) The NOESY spectrum of heronamide E (**2**) in CDCl_3 .

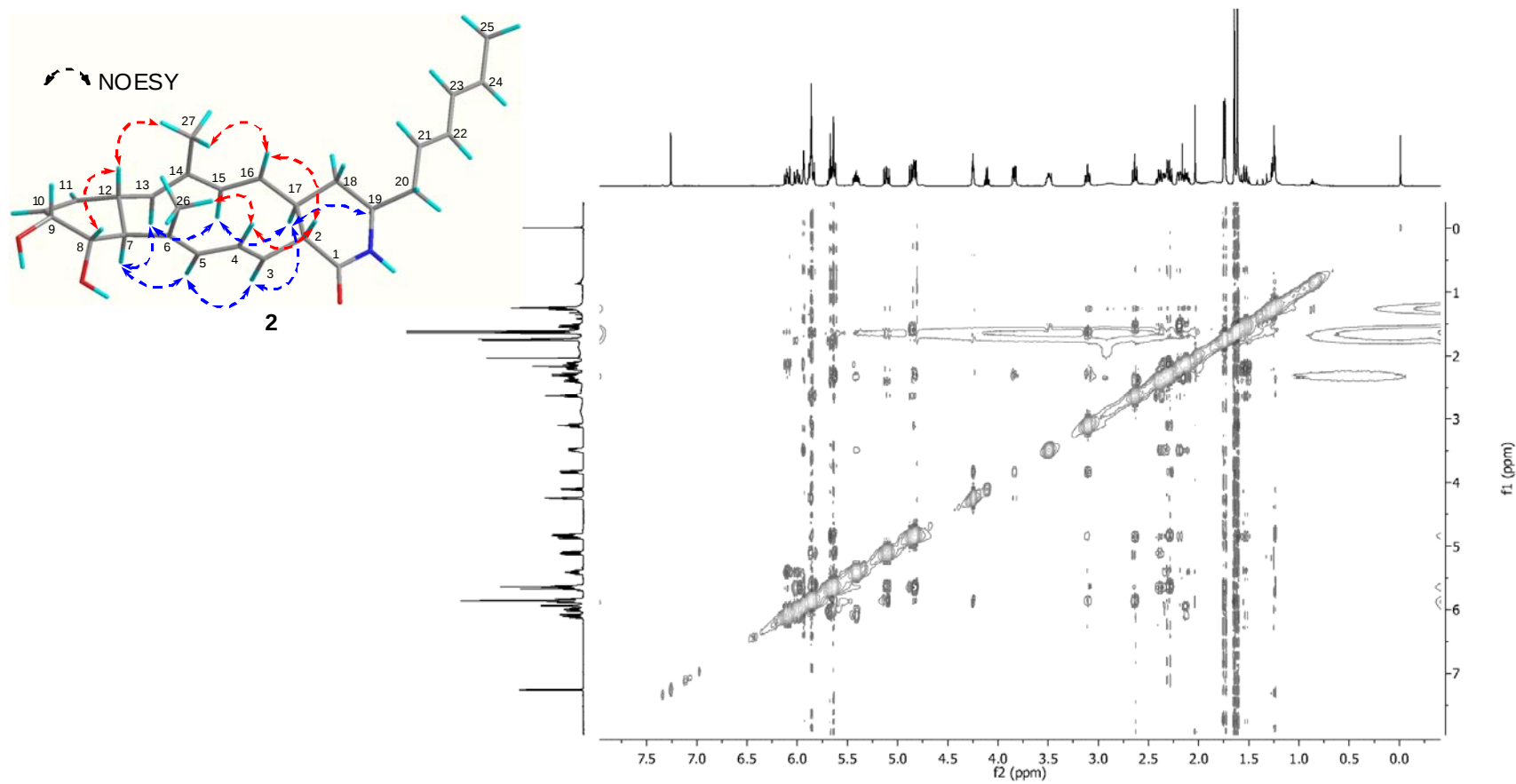


Figure S9. NMR spectroscopic data of 8-(*S*)- and 8-(*R*)-MTPA esters of heronamide E (**2a** and **2b**) in CDCl₃.

(A) The ¹H NMR spectrum of 8-(*S*)- and 8-(*R*)-MTPA esters of heronamide E (**2a** and **2b**) in CDCl₃.

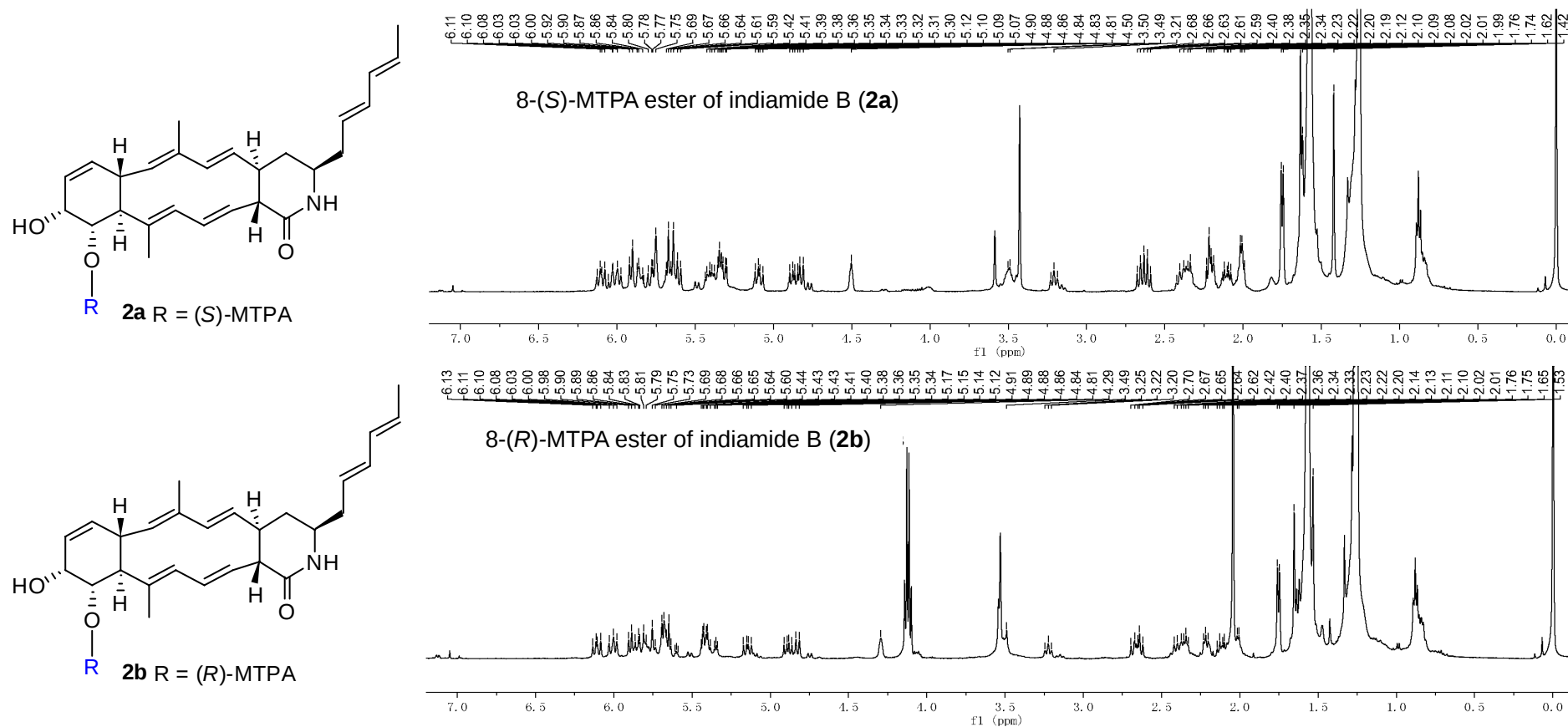


Figure S9. NMR spectroscopic data of 8-(*S*)- and 8-(*R*)-MTPA ester of heronamide E (**2a** and **2b**) in CDCl₃.

(B) The COSY spectrum of 8-(*S*)-MTPA ester of heronamide E (**2a**) in CDCl₃.

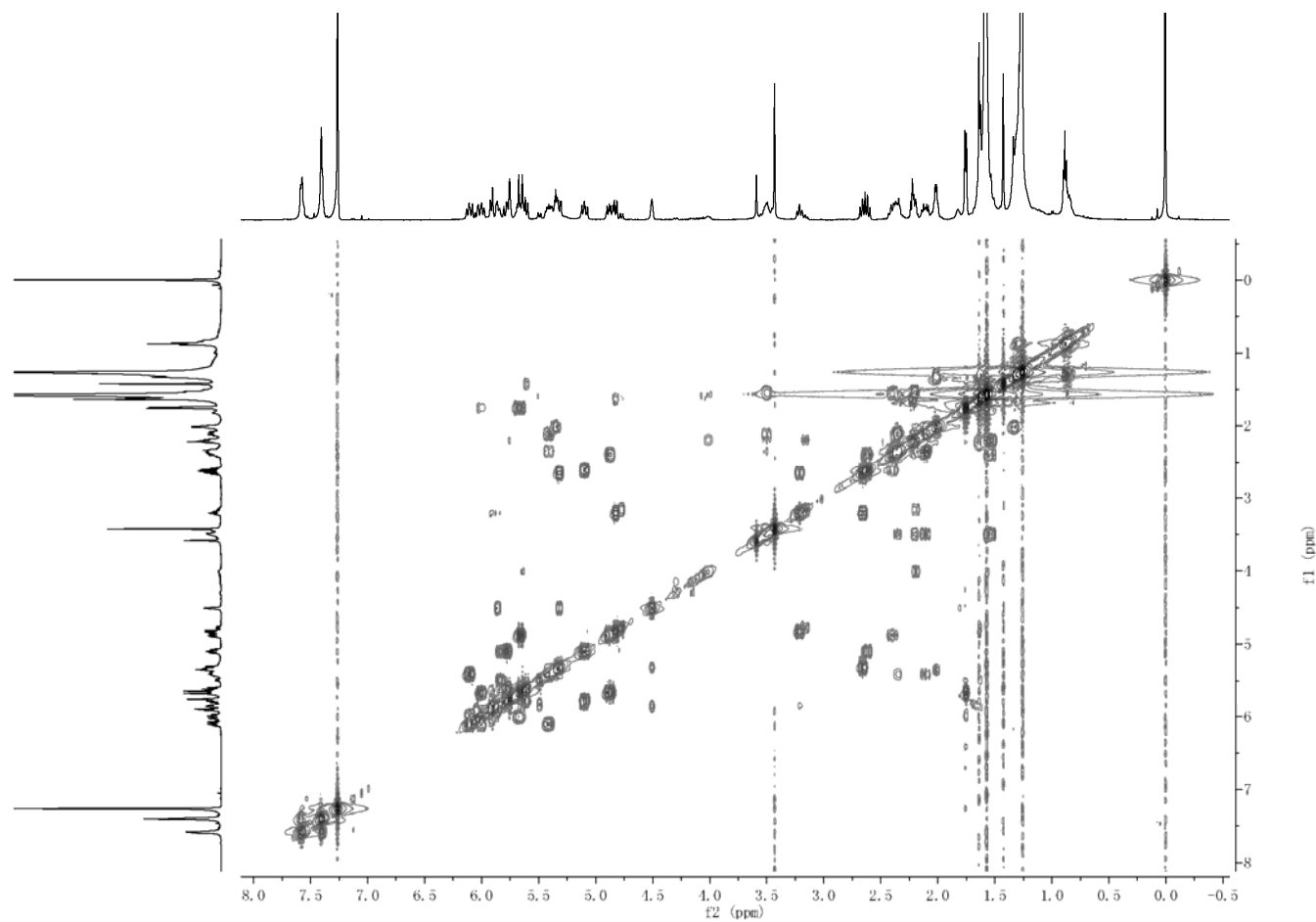


Figure S9. NMR spectroscopic data of *R* and *S* mosher ester of heronamide E (**2a** and **2b**) in CDCl₃.
(C) The COSY spectrum of 8-(*R*)-MTPA ester of heronamide E (**2b**) in CDCl₃.

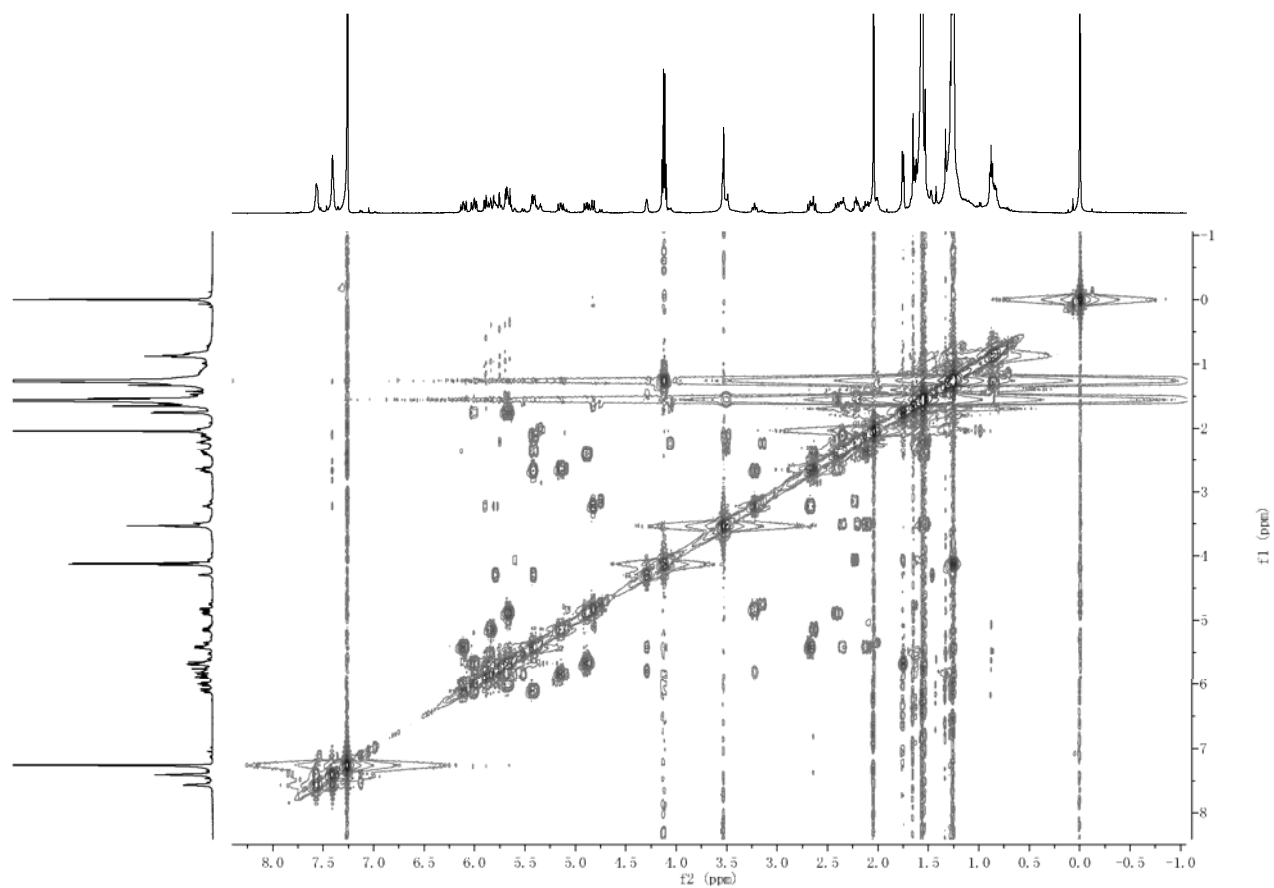
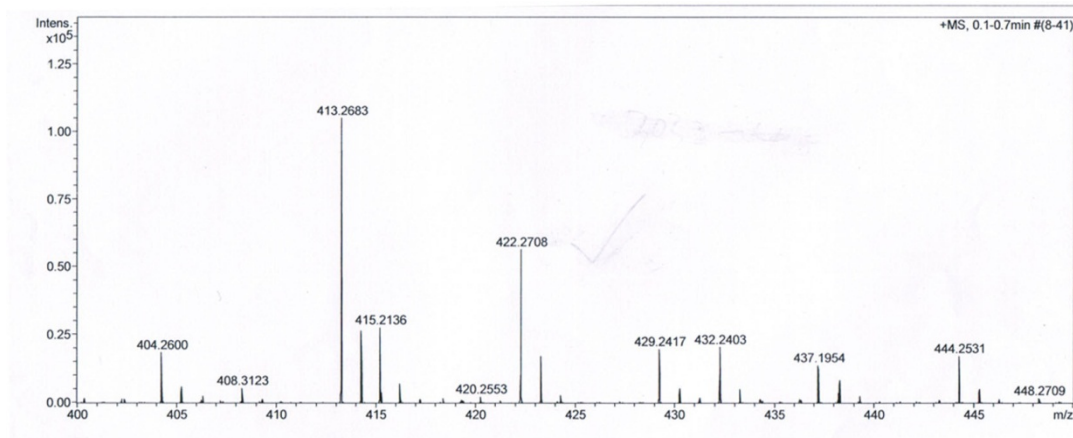


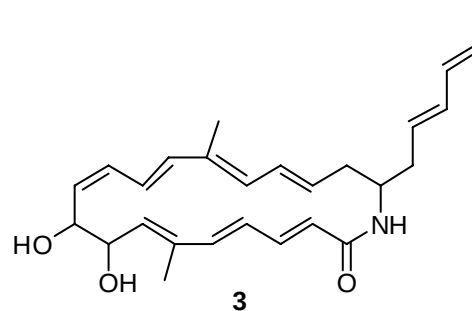
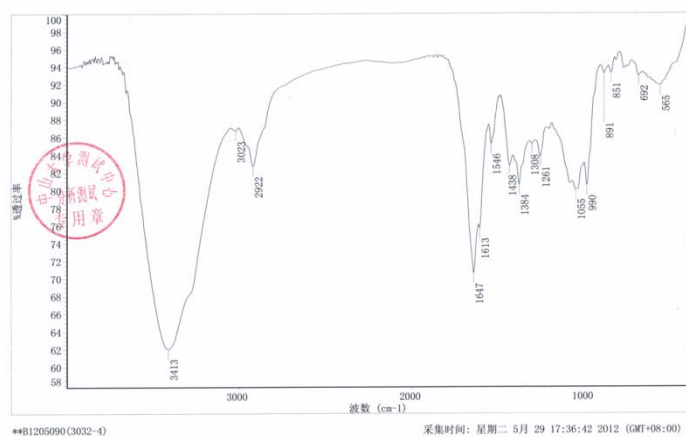
Figure S10. Spectroscopic data for heronamide F (**3**).

(A) HR-ESI-MS (a), IR (b), UV (c) and CD (d) spectra of heronamide F (**3**).

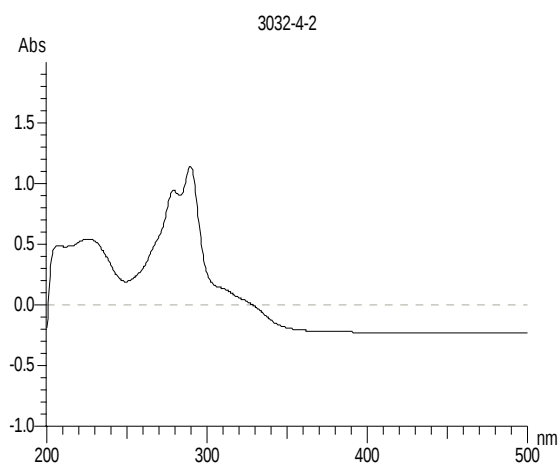
(a). HR-ESI-MS



(b). IR



(c). UV



(d). CD

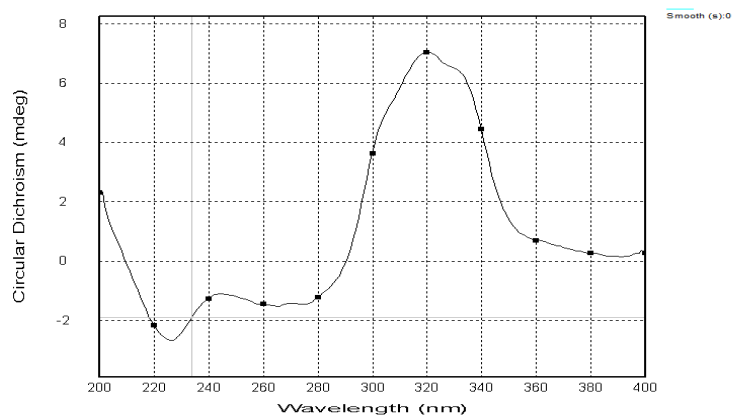


Figure S10. Spectroscopic data for heronamide F (**3**). (Continued)

(B) The ^1H NMR spectrum of heronamide F (**3**) in pyridine- d_5 .

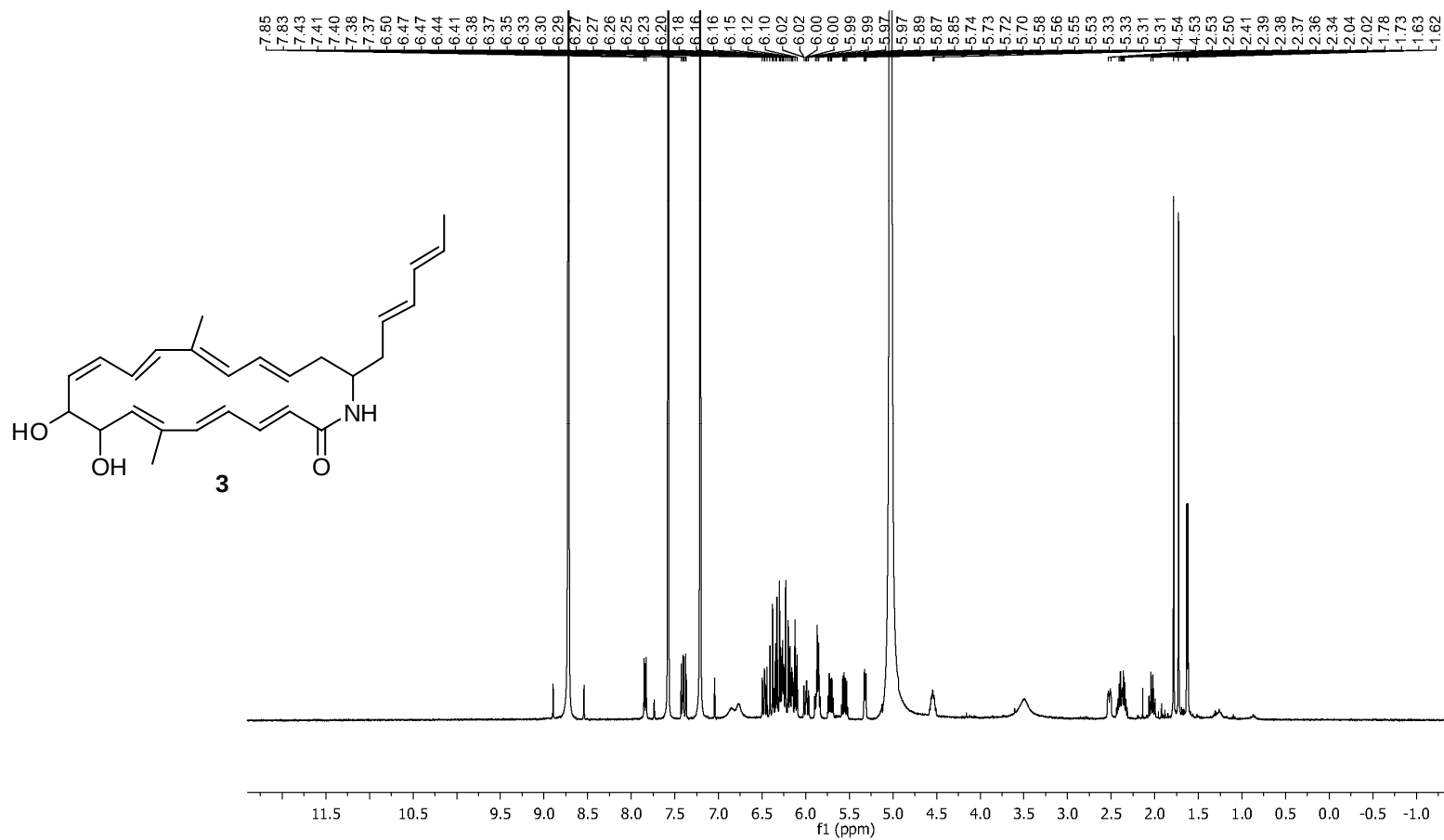


Figure S10. Spectroscopic data for heronamide F (**3**). (Continued)

(C) The ^{13}C NMR and DEPT 135 spectrum of heronamide F (**3**) in pyridine- d_5 .

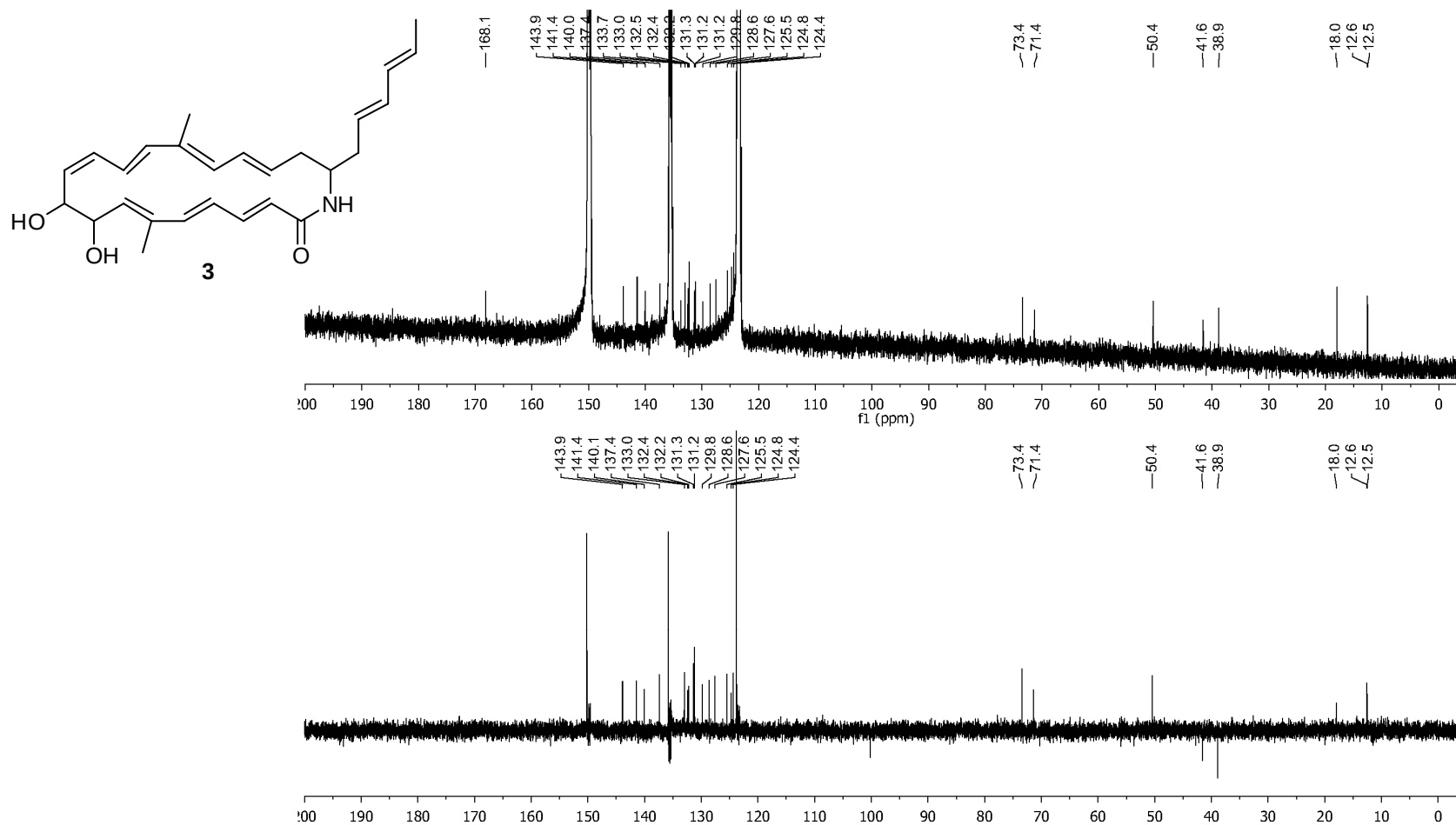


Figure S10. Spectroscopic data for heronamide F (**3**). (Continued)

(D) The HSQC spectrum of heronamide F (**3**) in pyridine- d_5 .

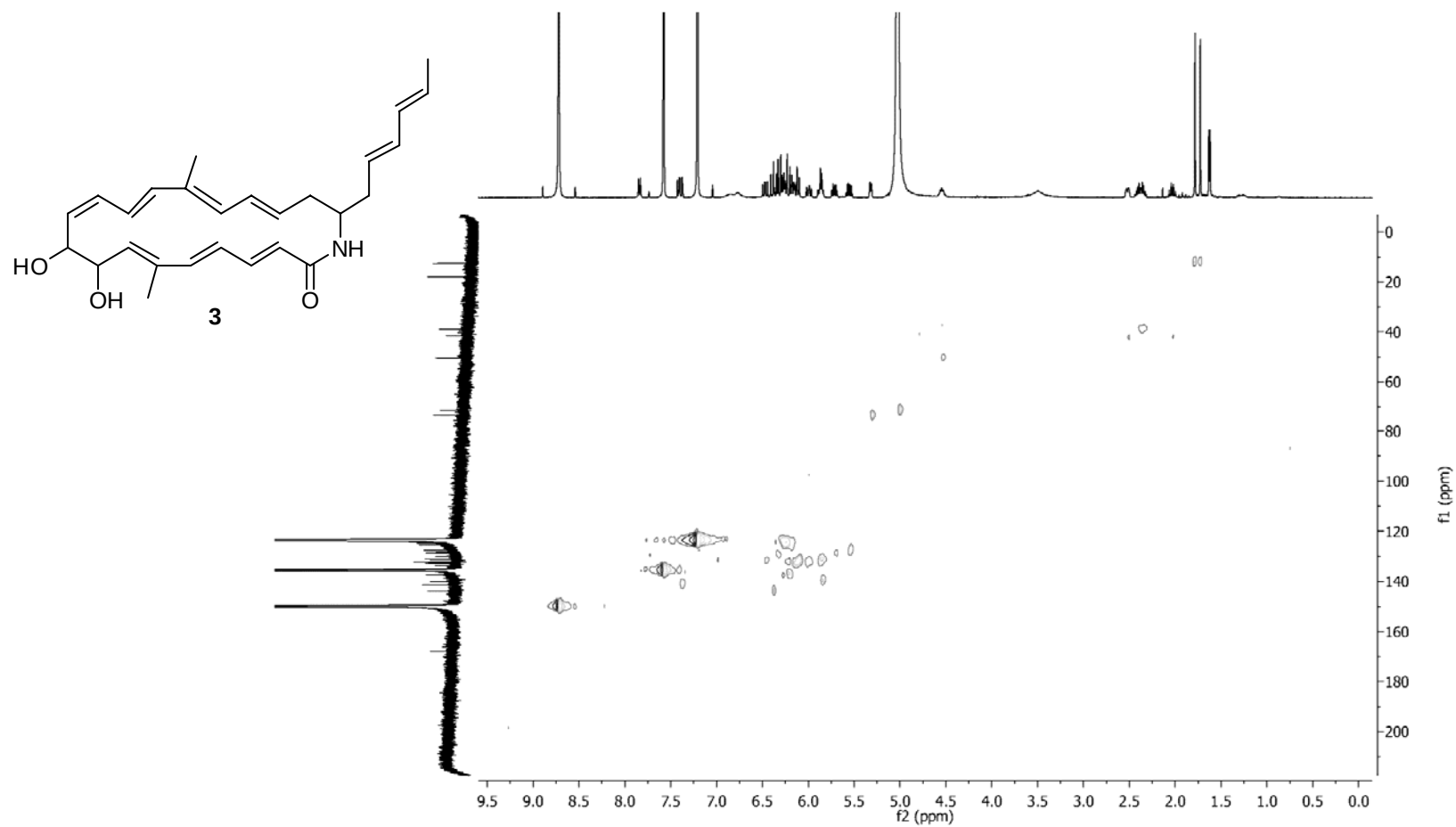


Figure S10. Spectroscopic data for heronamide F (**3**). (Continued)

(E) The COSY spectrum of heronamide F (**3**) in pyridine- d_5 .

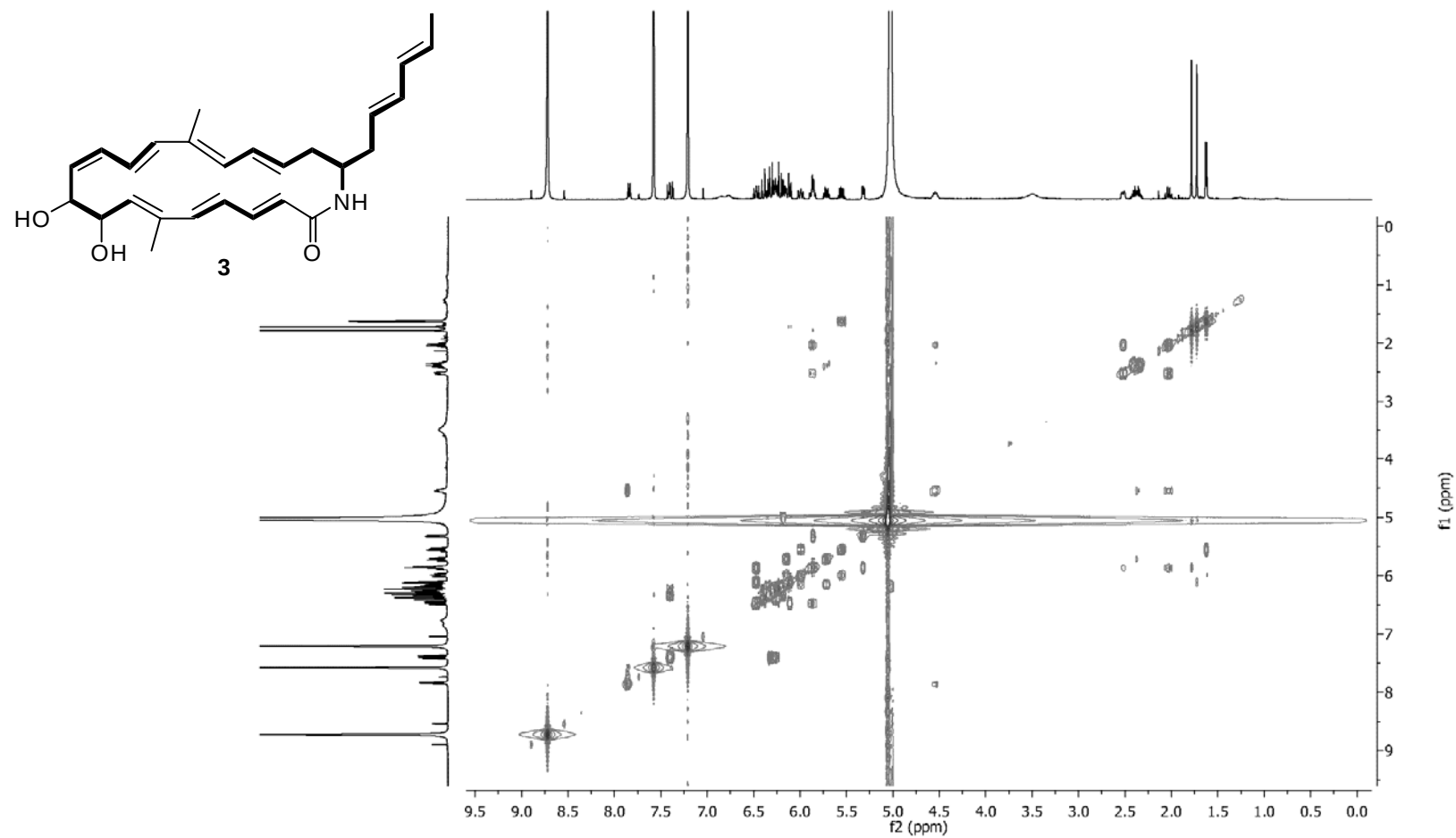


Figure S10. Spectroscopic data for heronamide F (**3**). (Continued)

(F) The HMBC spectrum of heronamide F (**3**) in pyridine- d_5 .

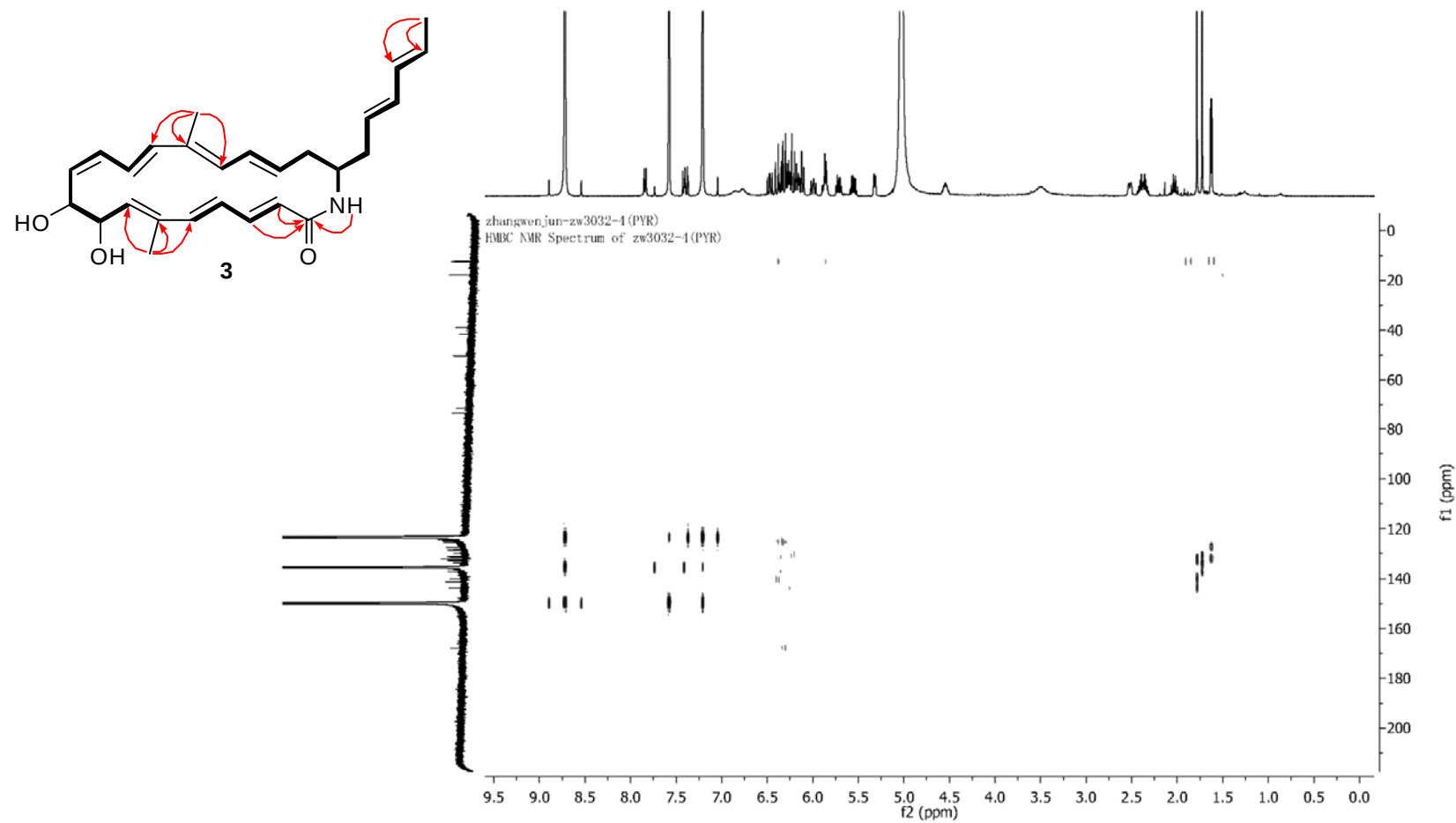
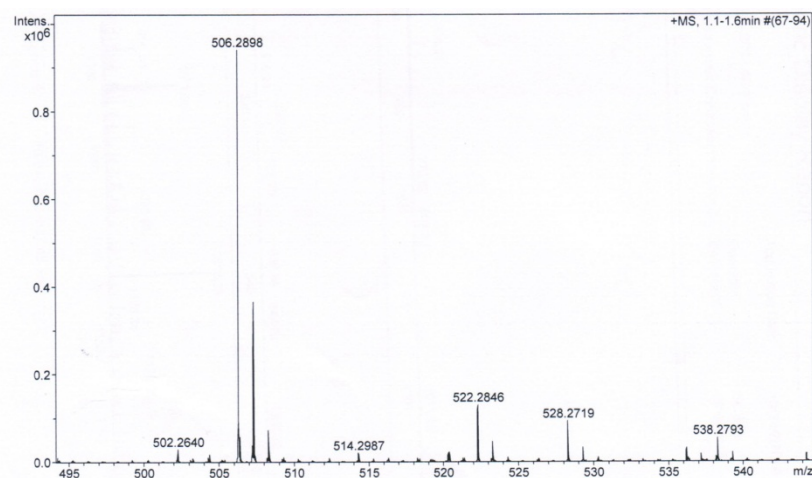


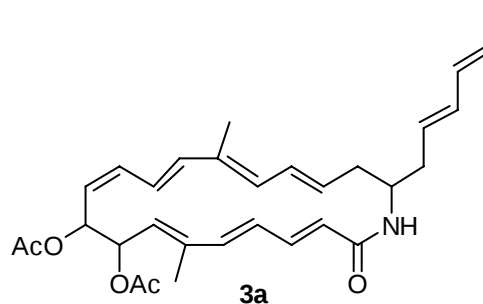
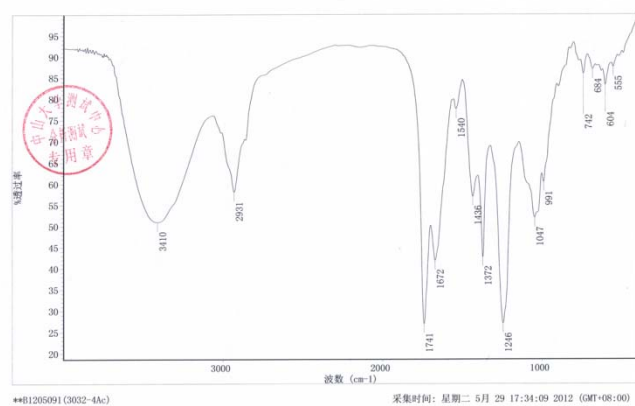
Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**).

(A) HR-ESI-MS , IR , UV , and CD spectra of diacetate of heronamide F (**3a**).

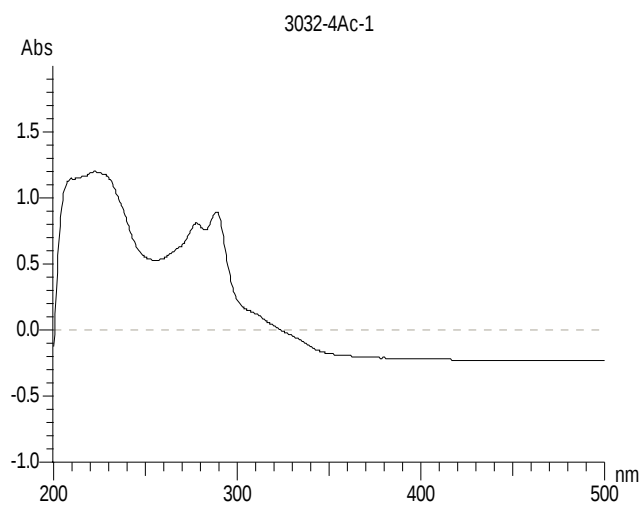
(a). HR-ESI-MS



(b). IR



(c). UV



(d). CD

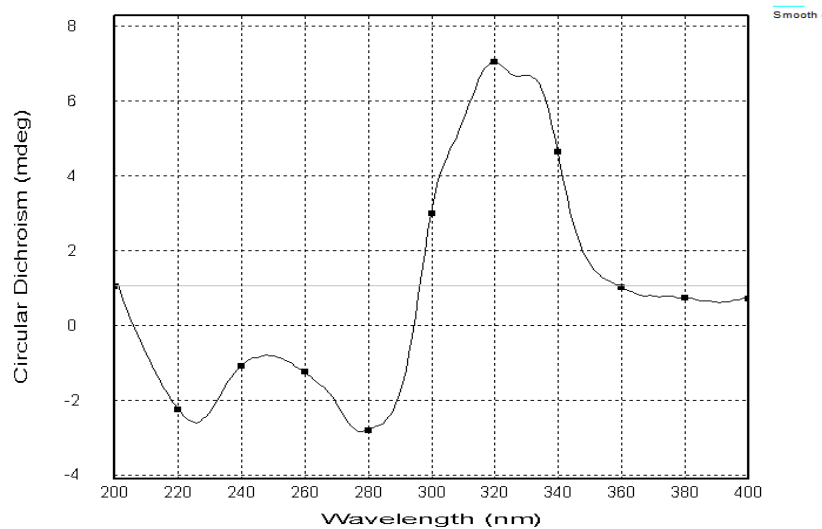


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(B) The ^1H NMR spectrum of diacetate of heronamide F (**3a**) in CDCl_3 .

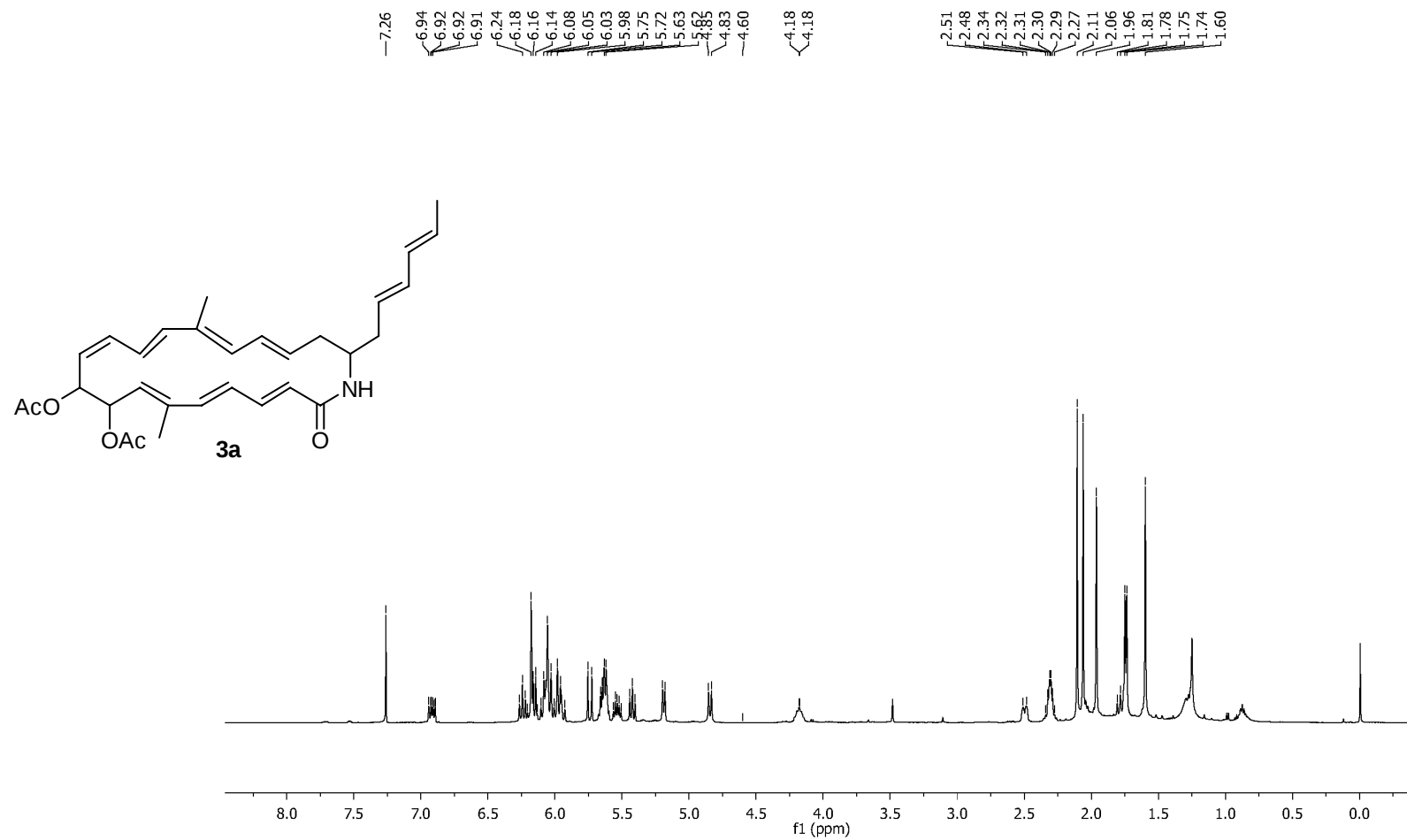


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(C) The ^{13}C NMR and DEPT 135 spectrum of diacetate of heronamide F (**3a**) in CDCl_3 .

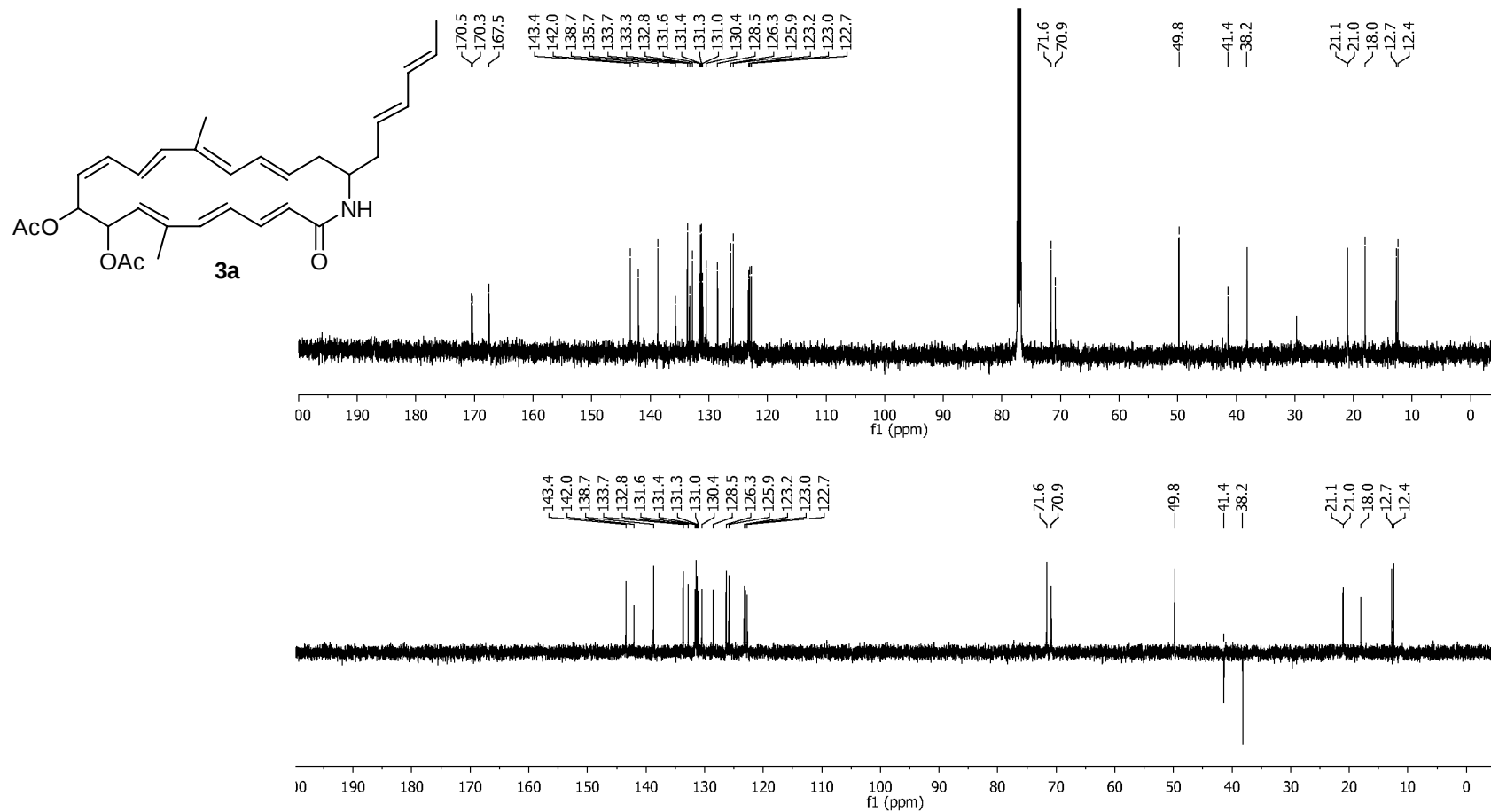


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(D) The HSQC spectrum of diacetate of heronamide F (**3a**) in CDCl₃.

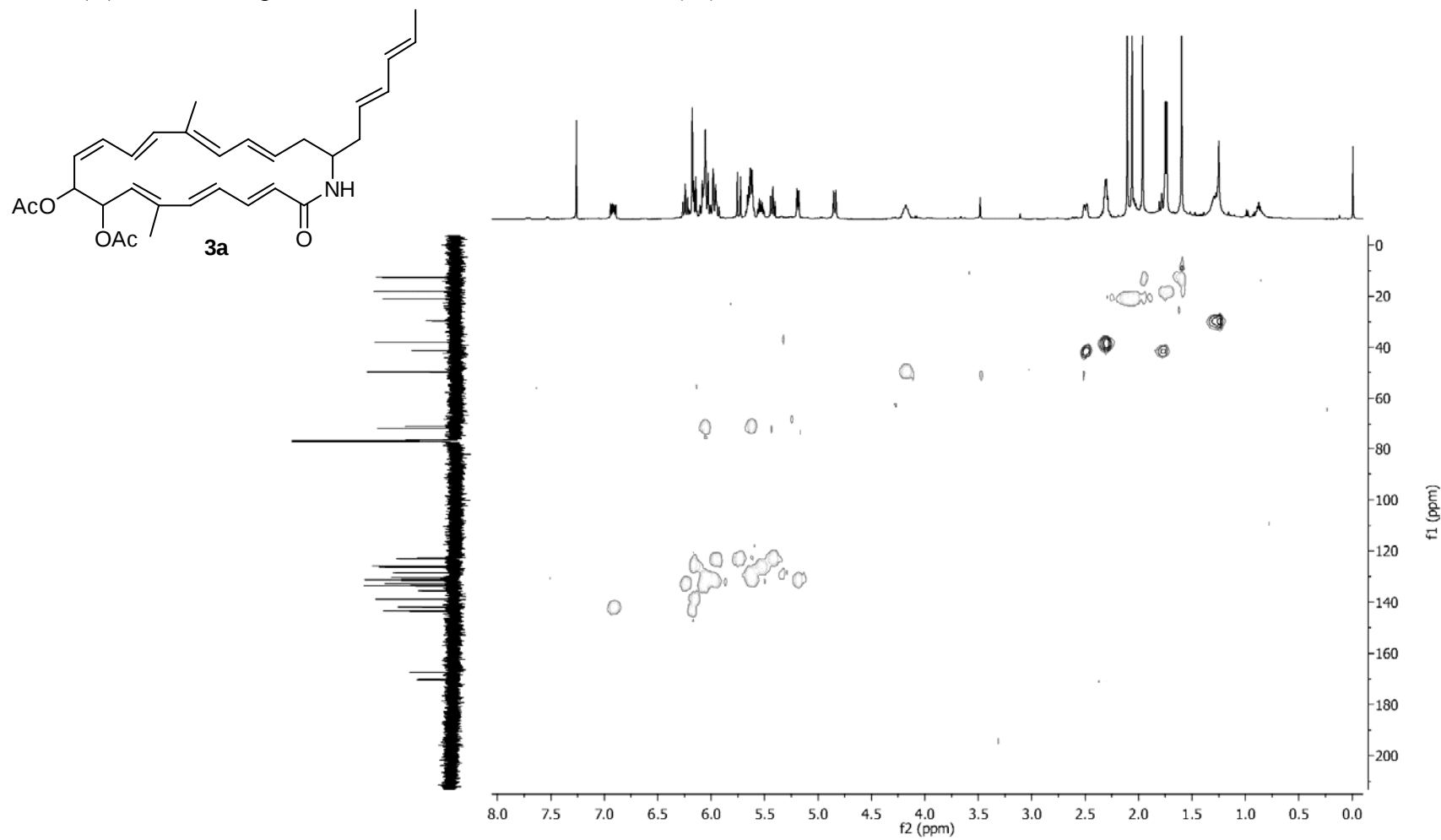


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(E) The COSY spectrum of diacetate of heronamide F (**3a**) in CDCl₃.

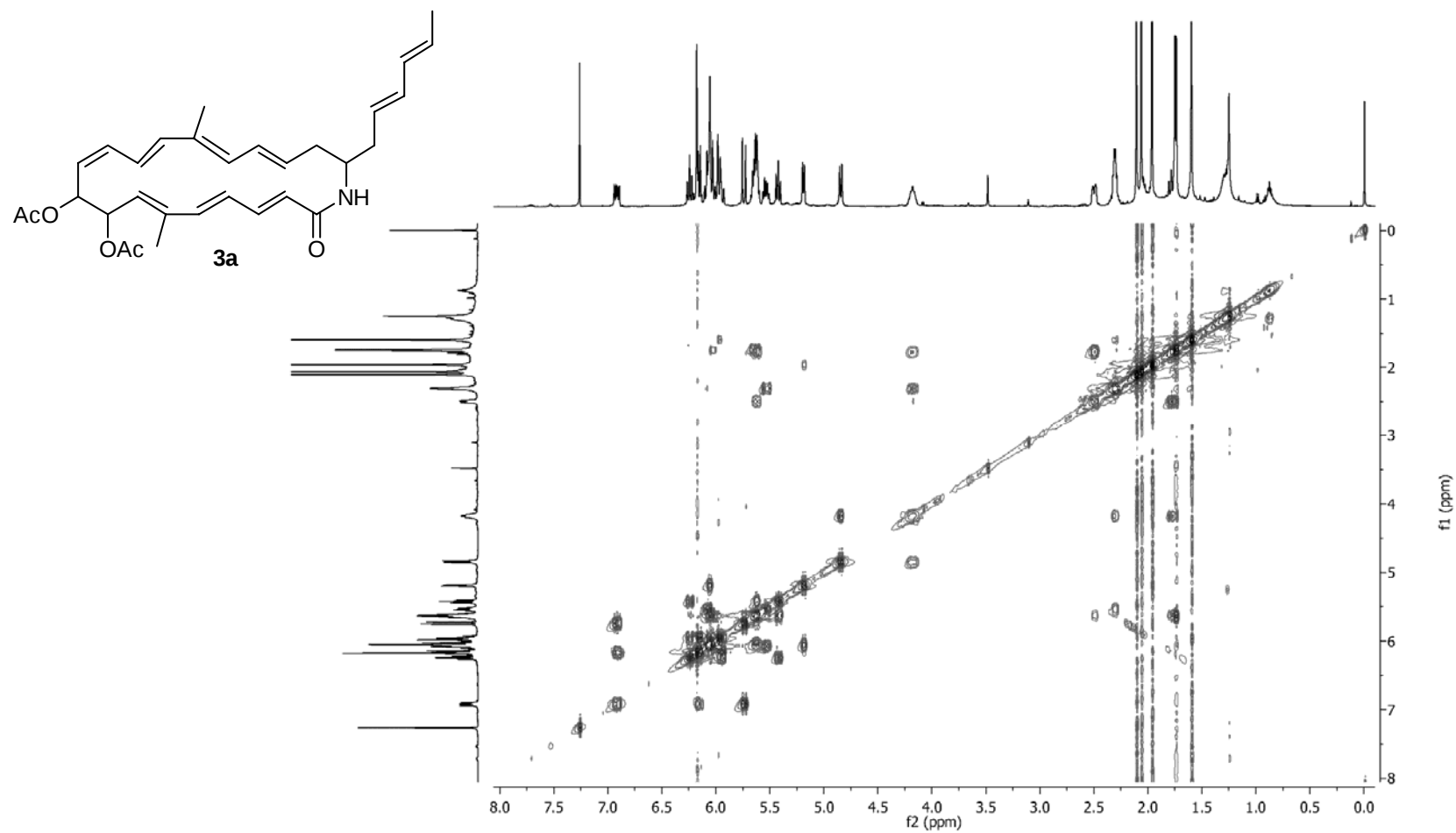


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(F) The HMBC spectrum of diacetate of heronamide F (**3a**) in CDCl₃.

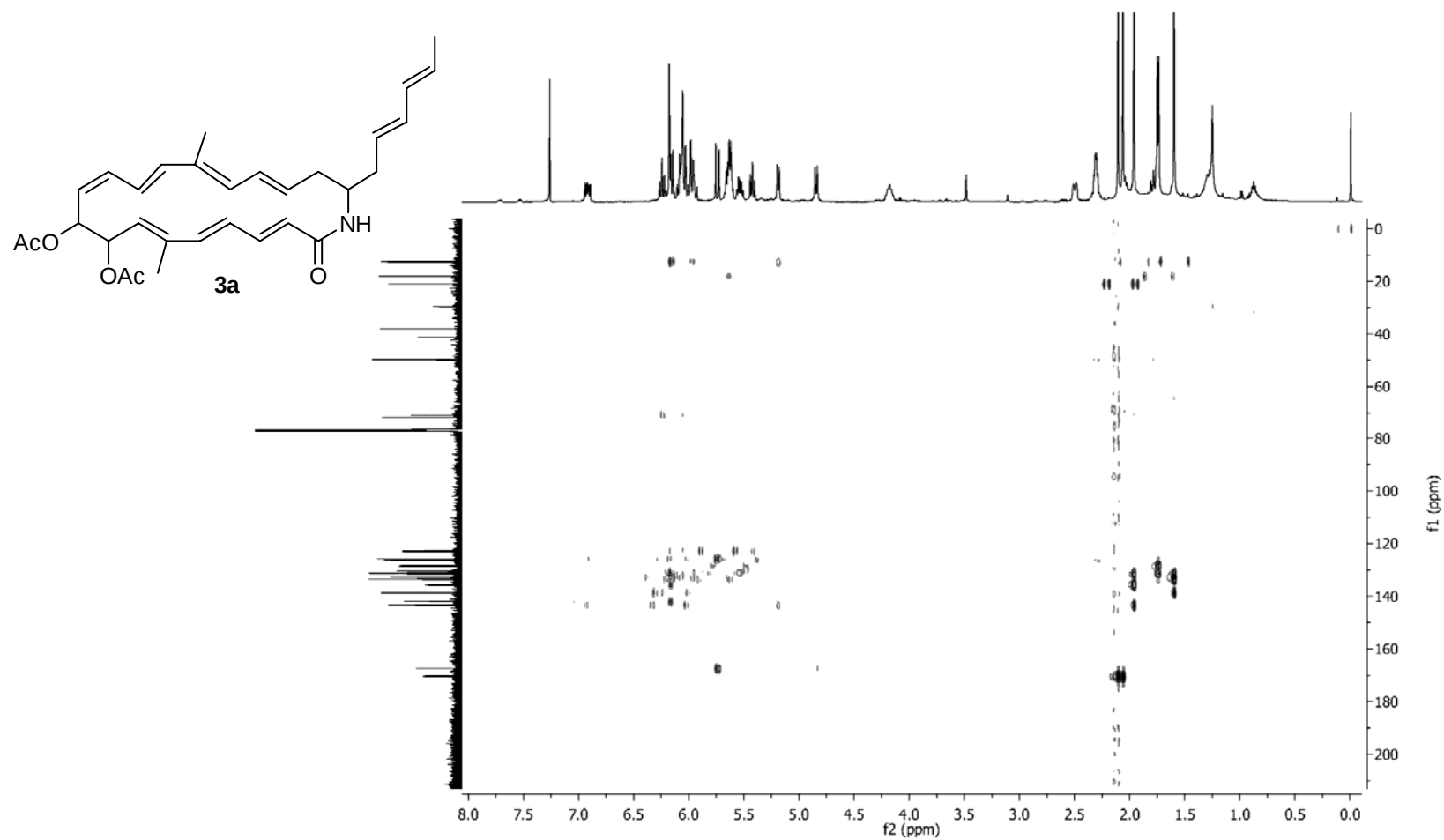


Figure S11. Spectroscopic data for diacetate of heronamide F (**3a**). (Continued)

(G) The NOESY spectrum of diacetate of heronamide F (**3a**) in CDCl_3 .

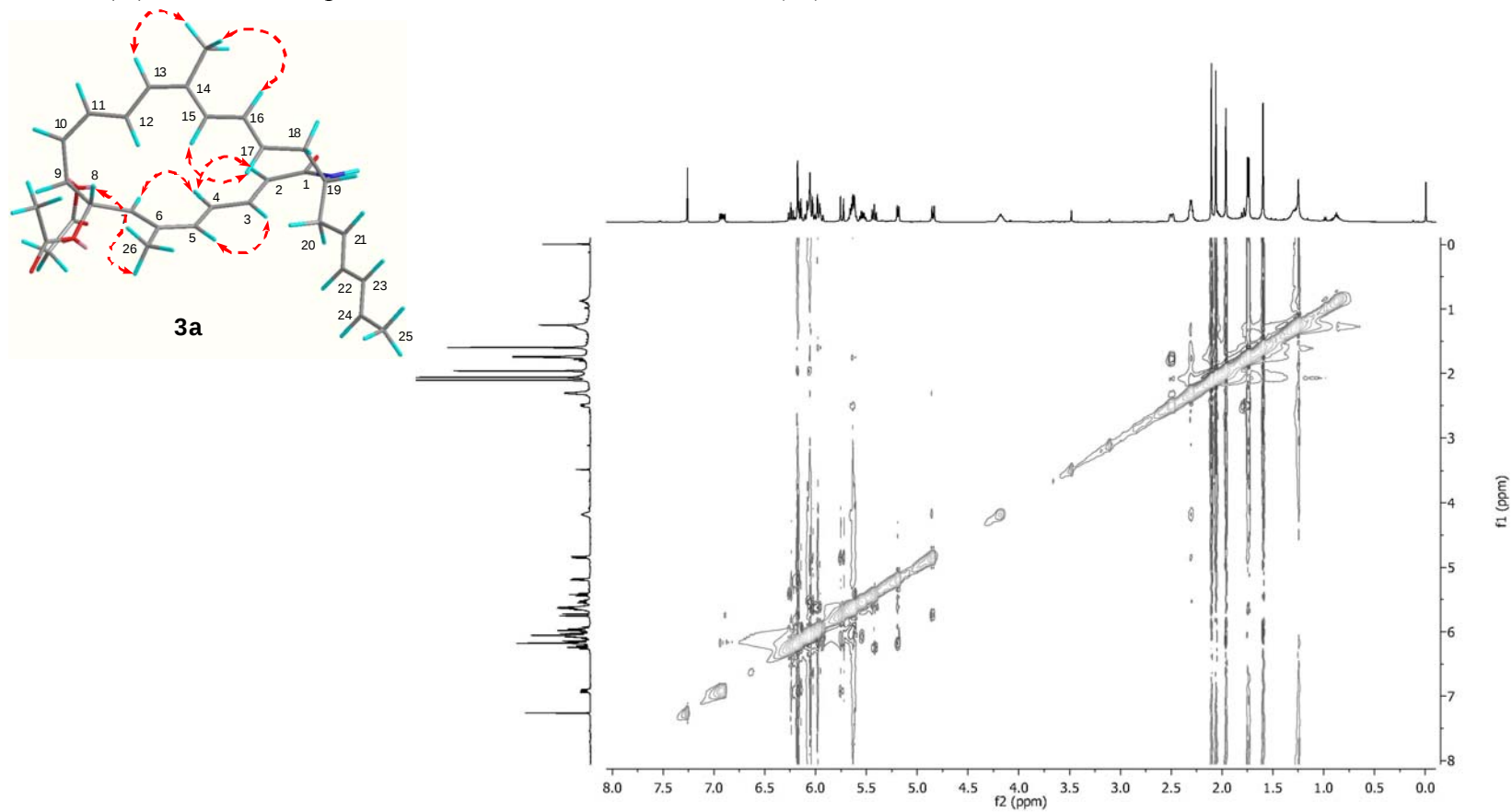
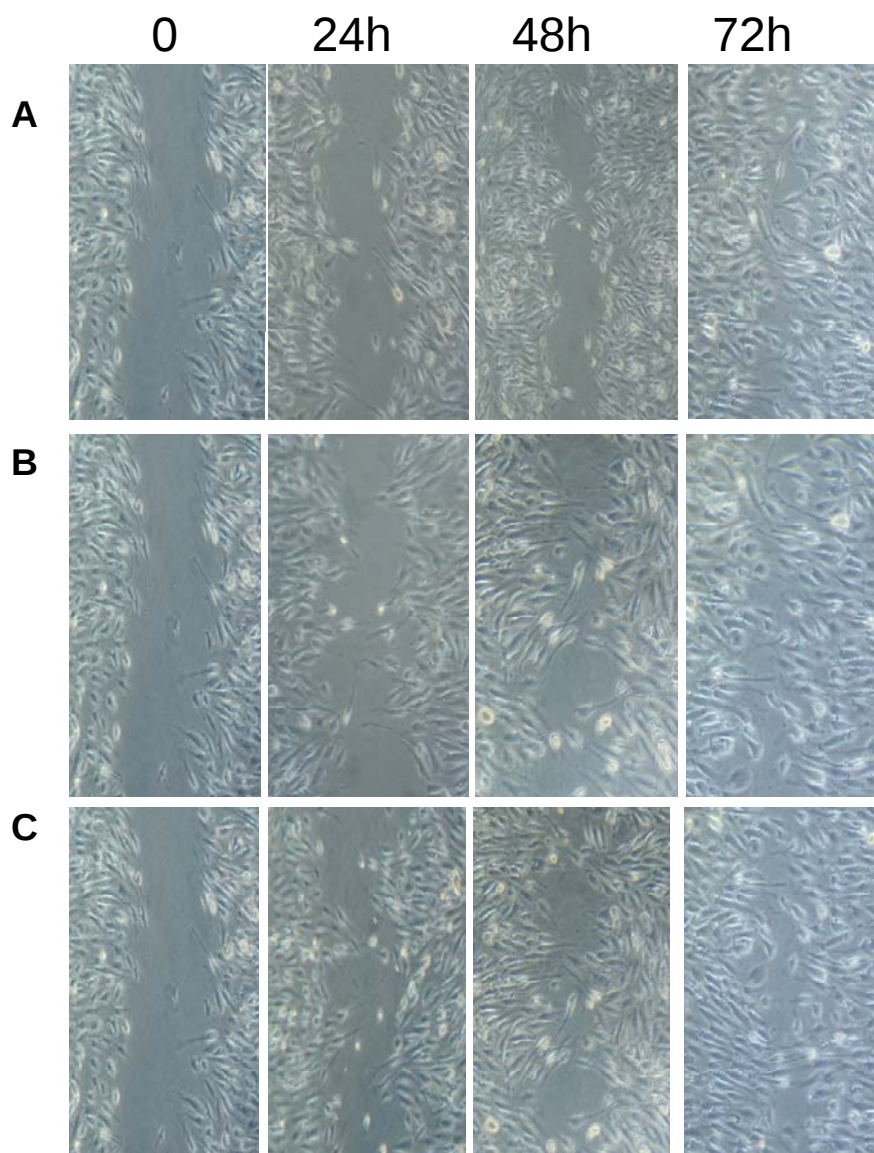


Figure S12. The effect of heronamides D (**1**) and F (**3**) on the migration of HUVEC cells.



The inhibitory effect of heronamides D (**1**) and F (**3**) on the migration capability of HUVEC cells was detected by wound healing assay, which was observed under an inverted-phase contrast microscope $\times 40$. (A) 1 % DMSO; (B) 17.1 μM **1** in 1 % DMSO; (C) 11.8 μM **3** in 1 % DMSO.