

SUPPORTING INFORMATION

Heronamides A – C, new polyketide macrolactams from an Australian marine-derived *Streptomyces* sp. A biosynthetic case for synchronized tandem electrocyclization.

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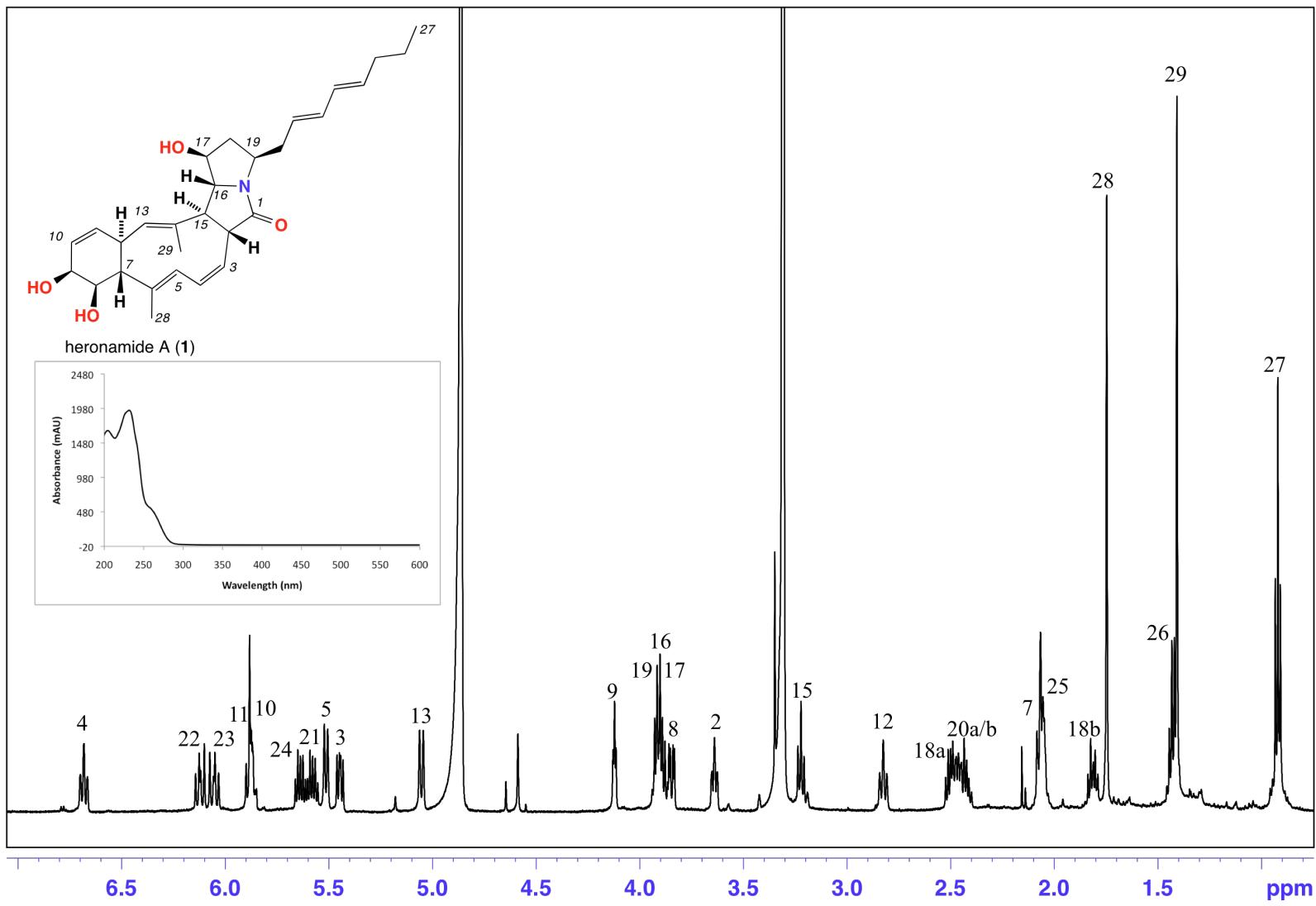


Figure S1a. ¹H NMR (600 MHz, methanol-*d*₄) and UV-vis (inset) spectrum of heronamide A (**1**)

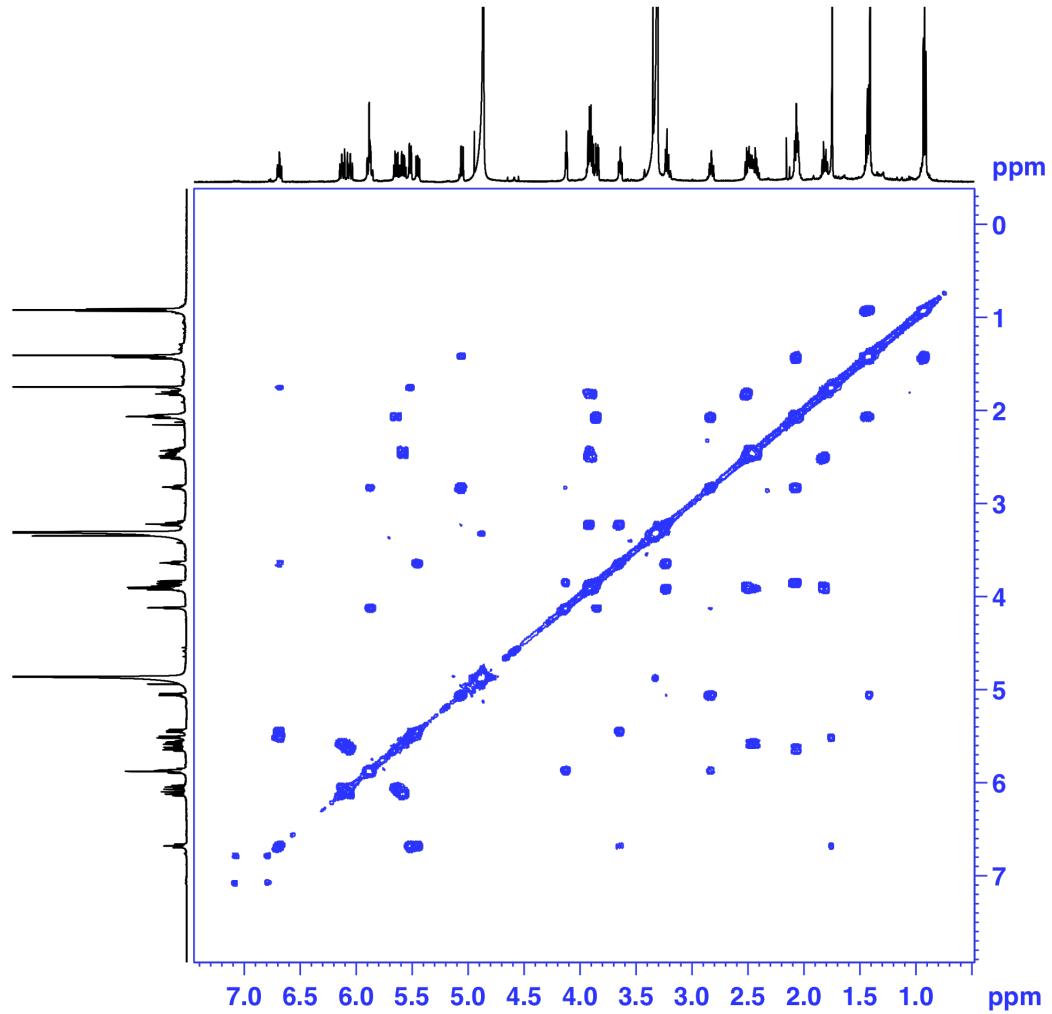


Figure S1b. COSY spectrum (600 MHz, methanol-*d*₄) of heronamide A (**1**)

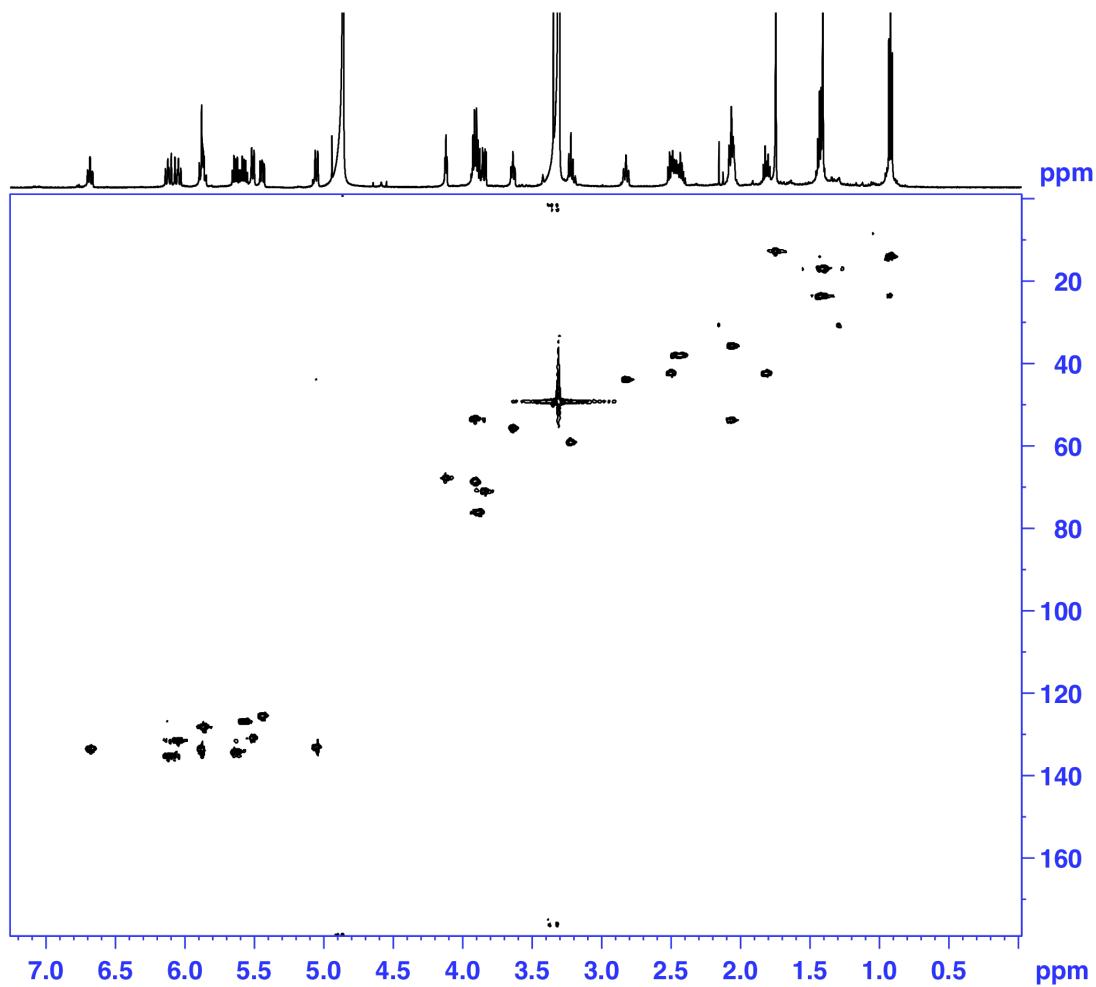


Figure S1c. HSQC spectrum (600 MHz, methanol-*d*₄) of heronamide A (**1**)

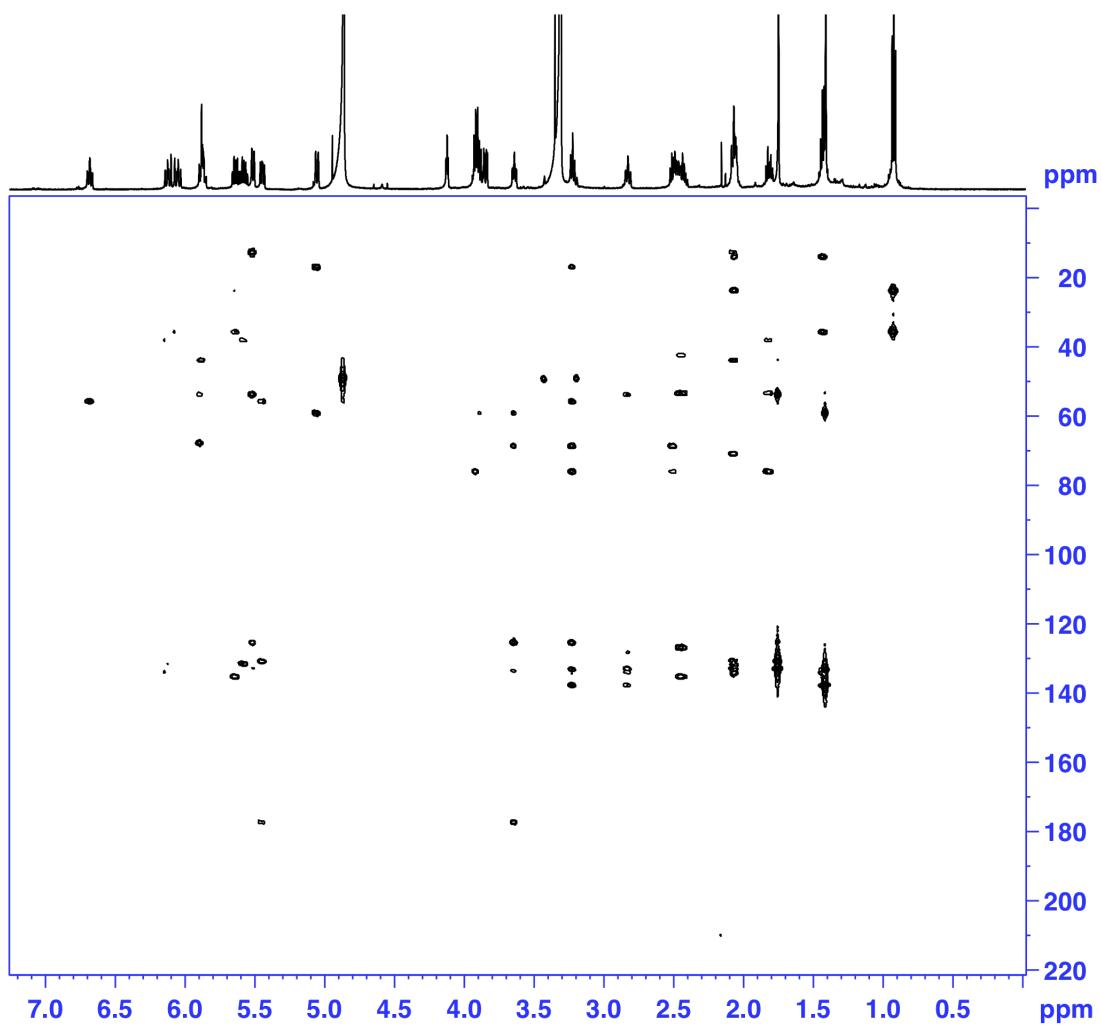


Figure S1d. HMBC spectrum (600 MHz, methanol-*d*₄) of heronamide A (**1**)

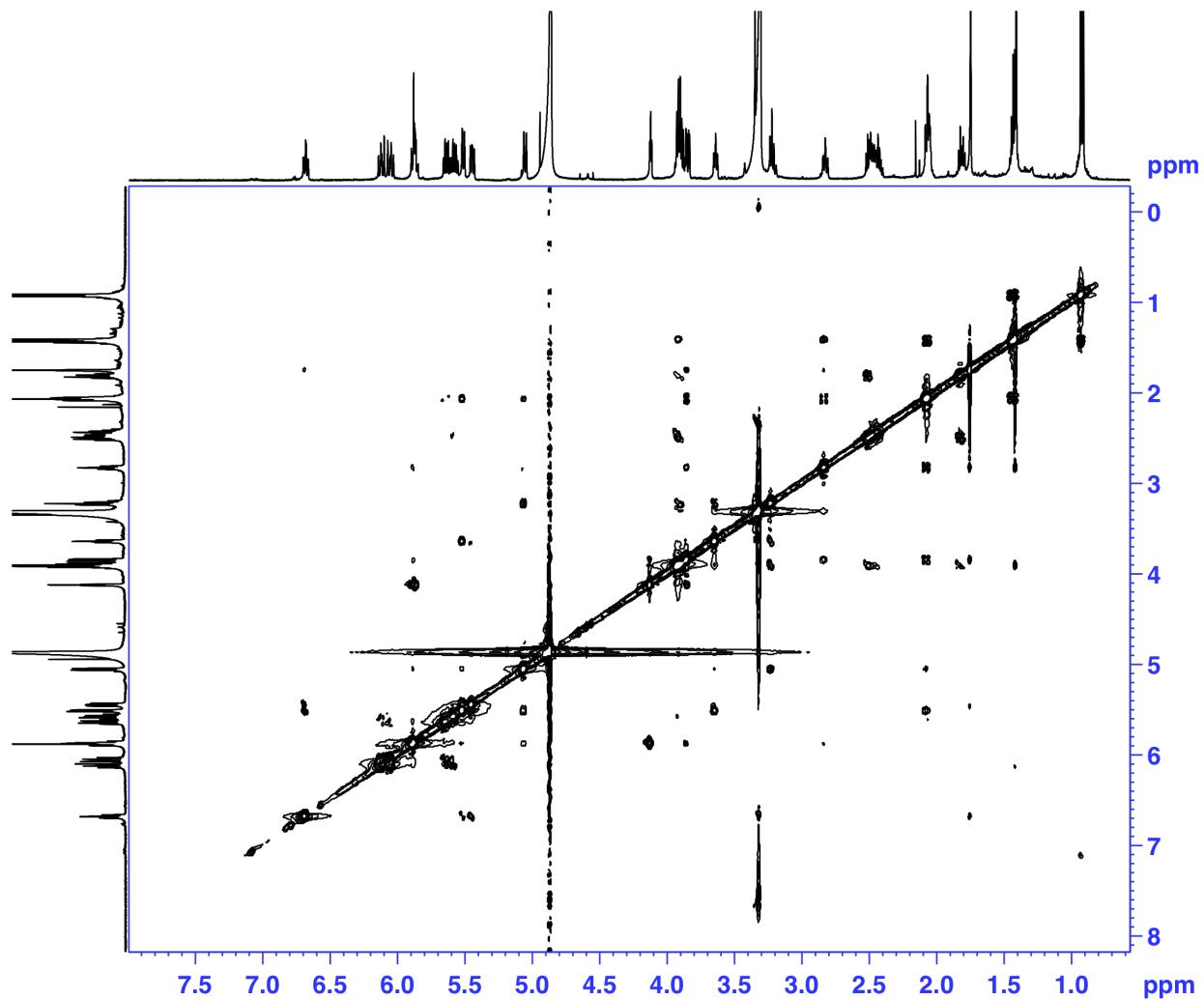


Figure S1e. ROESY spectrum (600 MHz, methanol- d_4) of heronamide A (**1**)

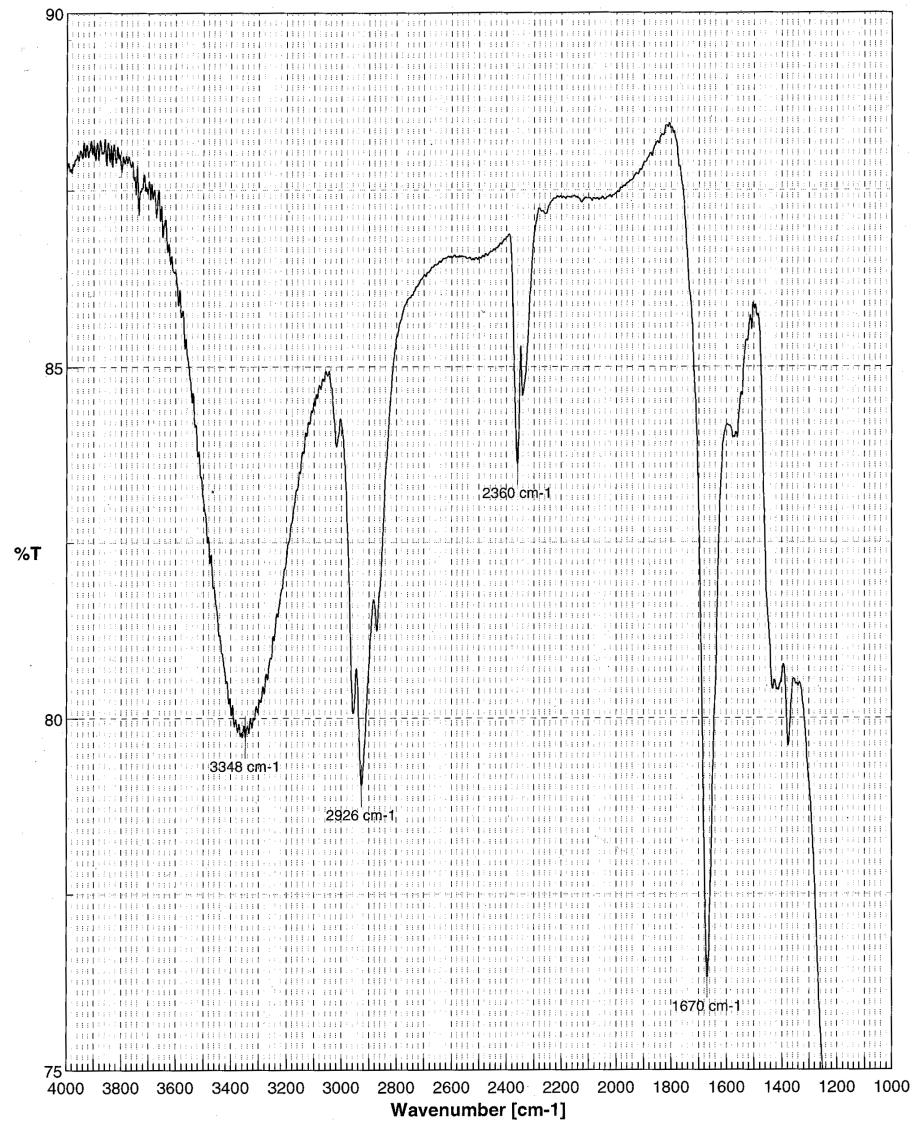


Figure S1f. IR spectrum of heronamide A (**1**)

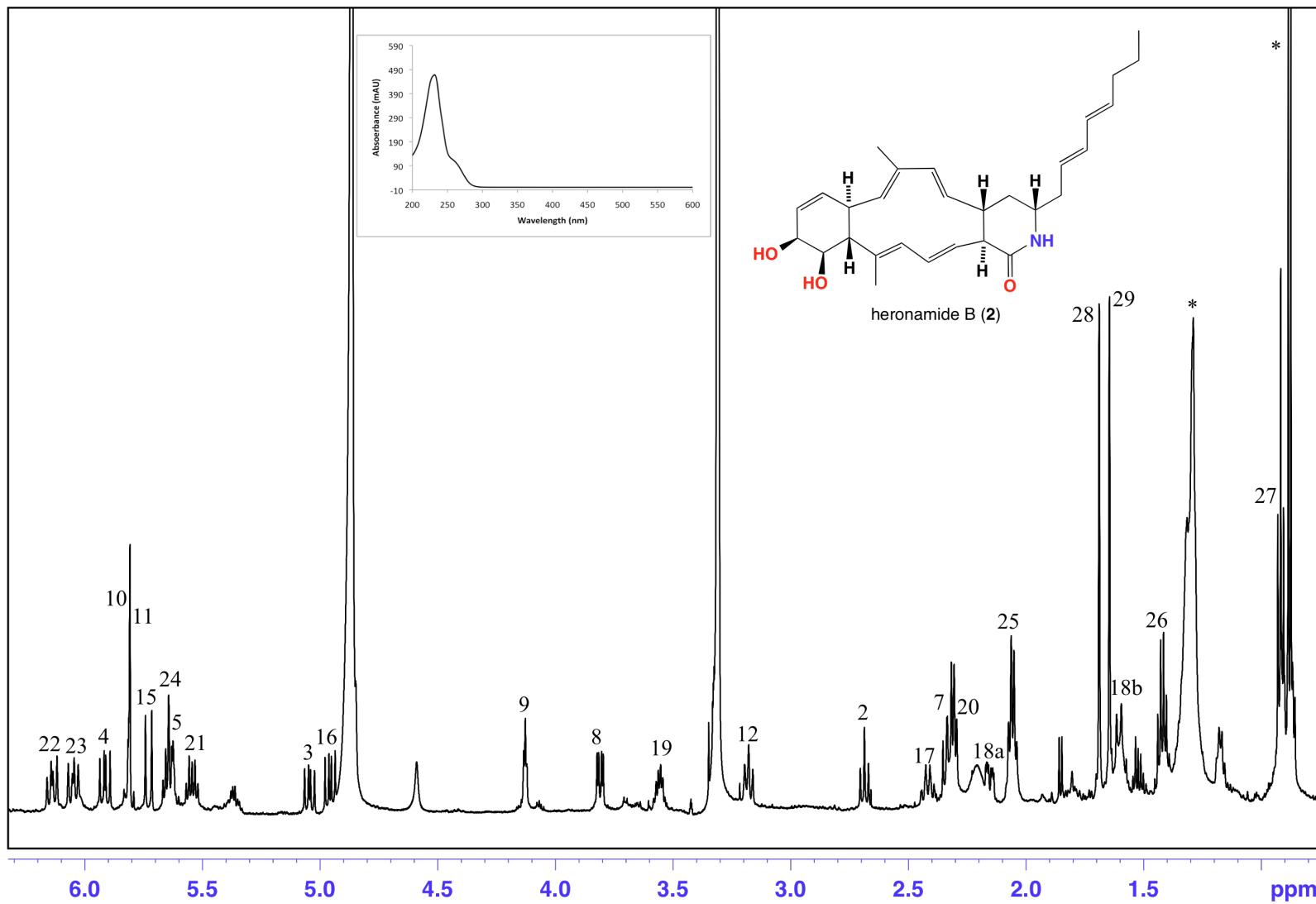


Figure S2a. ¹H NMR (600 MHz, methanol-*d*₄) and UV-vis (inset) spectrum of heronamide B (2)

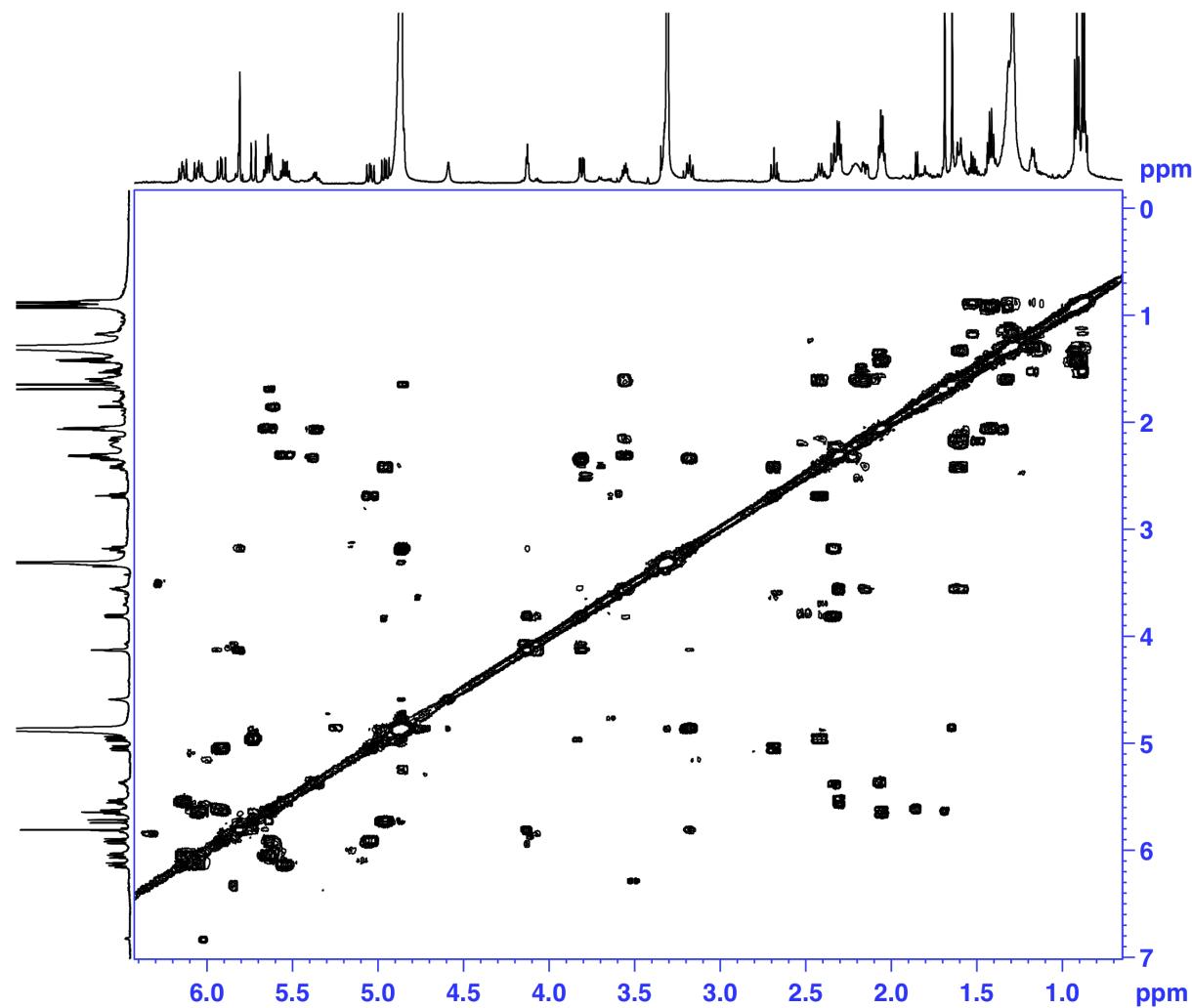


Figure S2b. COSY spectrum (600 MHz, methanol-*d*₄) of heronamide B (**2**)

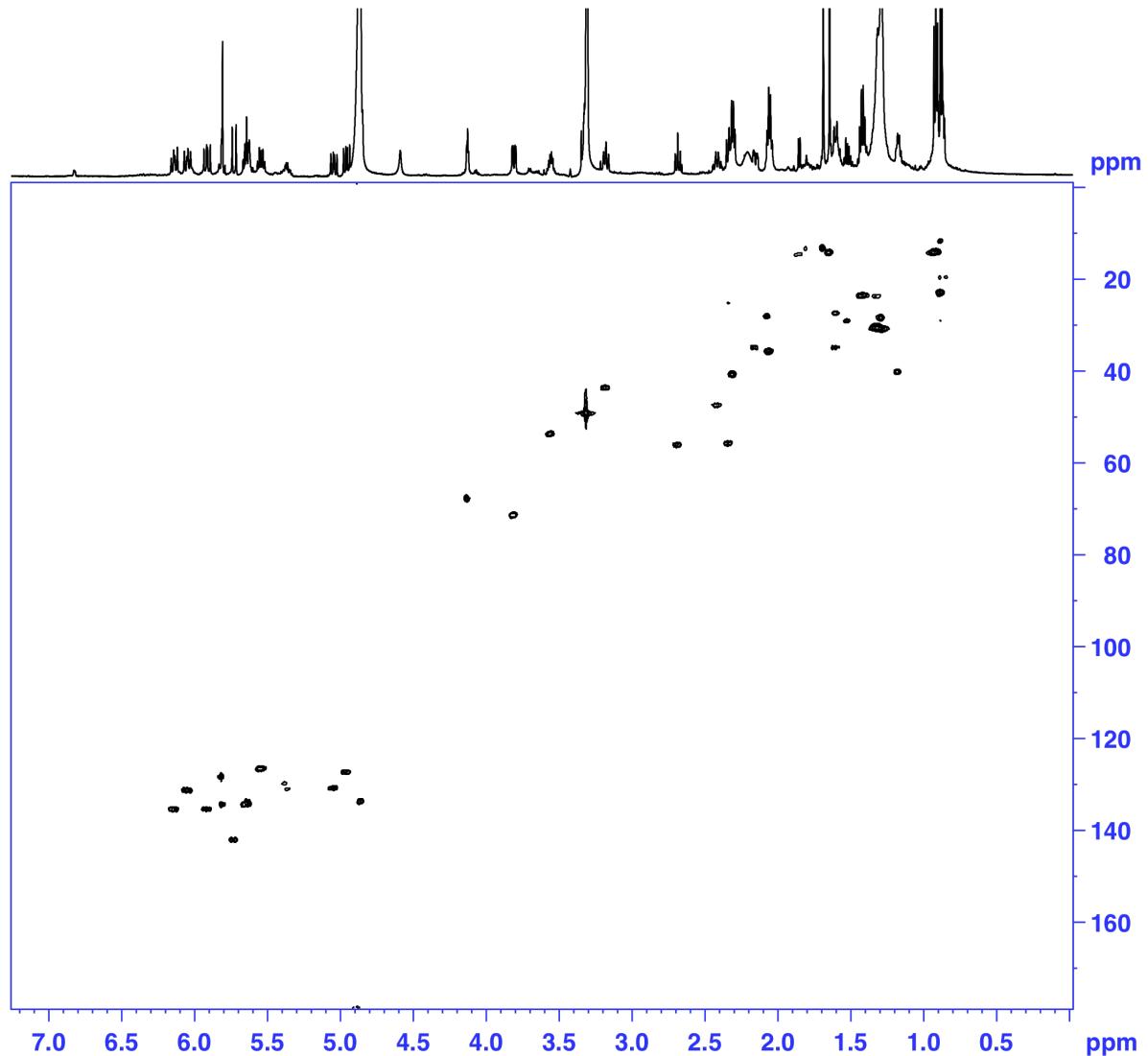


Figure S2c. HSQC spectrum (600 MHz, methanol- d_4) of heronamide B (**2**)

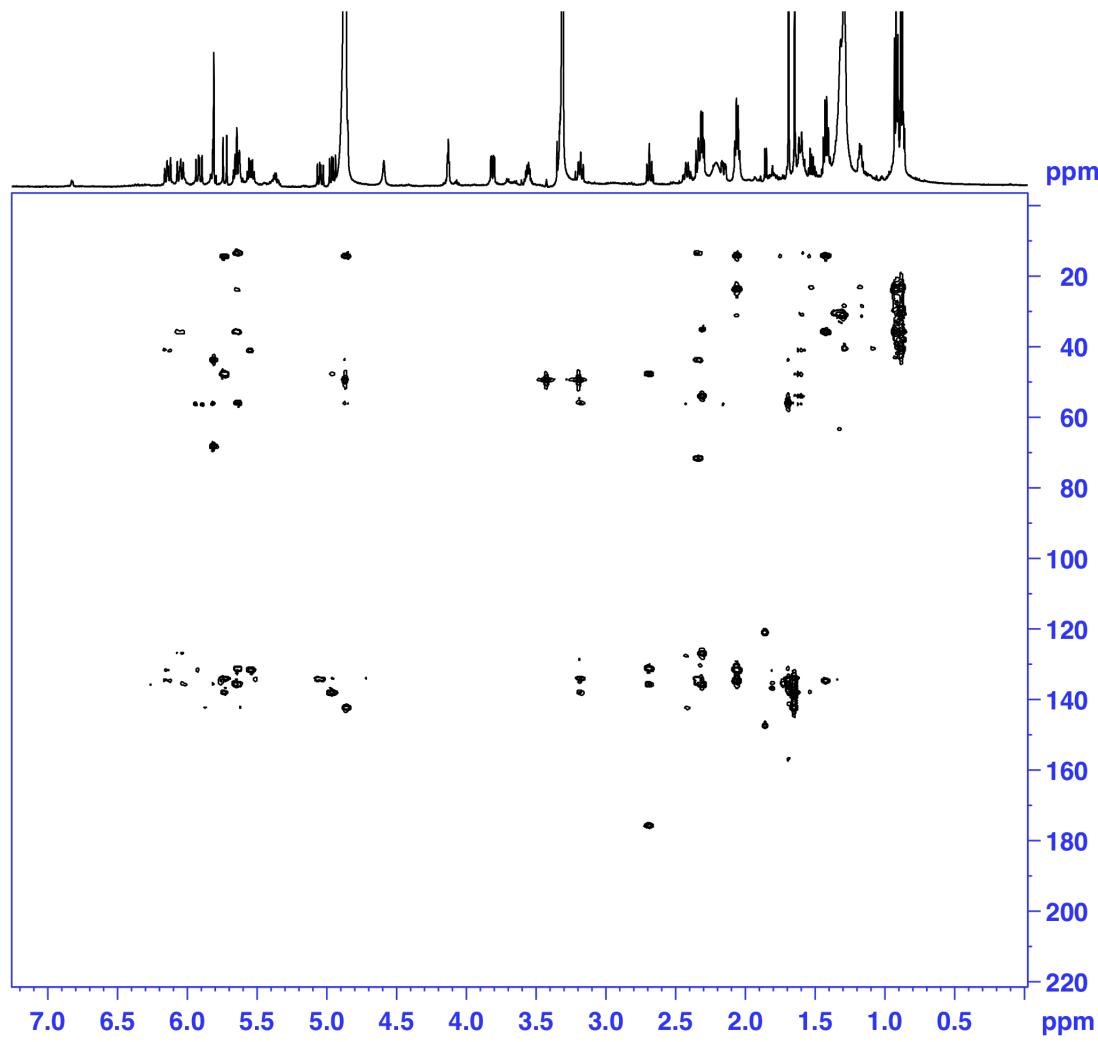


Figure S2d. HMBC spectrum (600 MHz, methanol-*d*₄) of heronamide B (**2**)

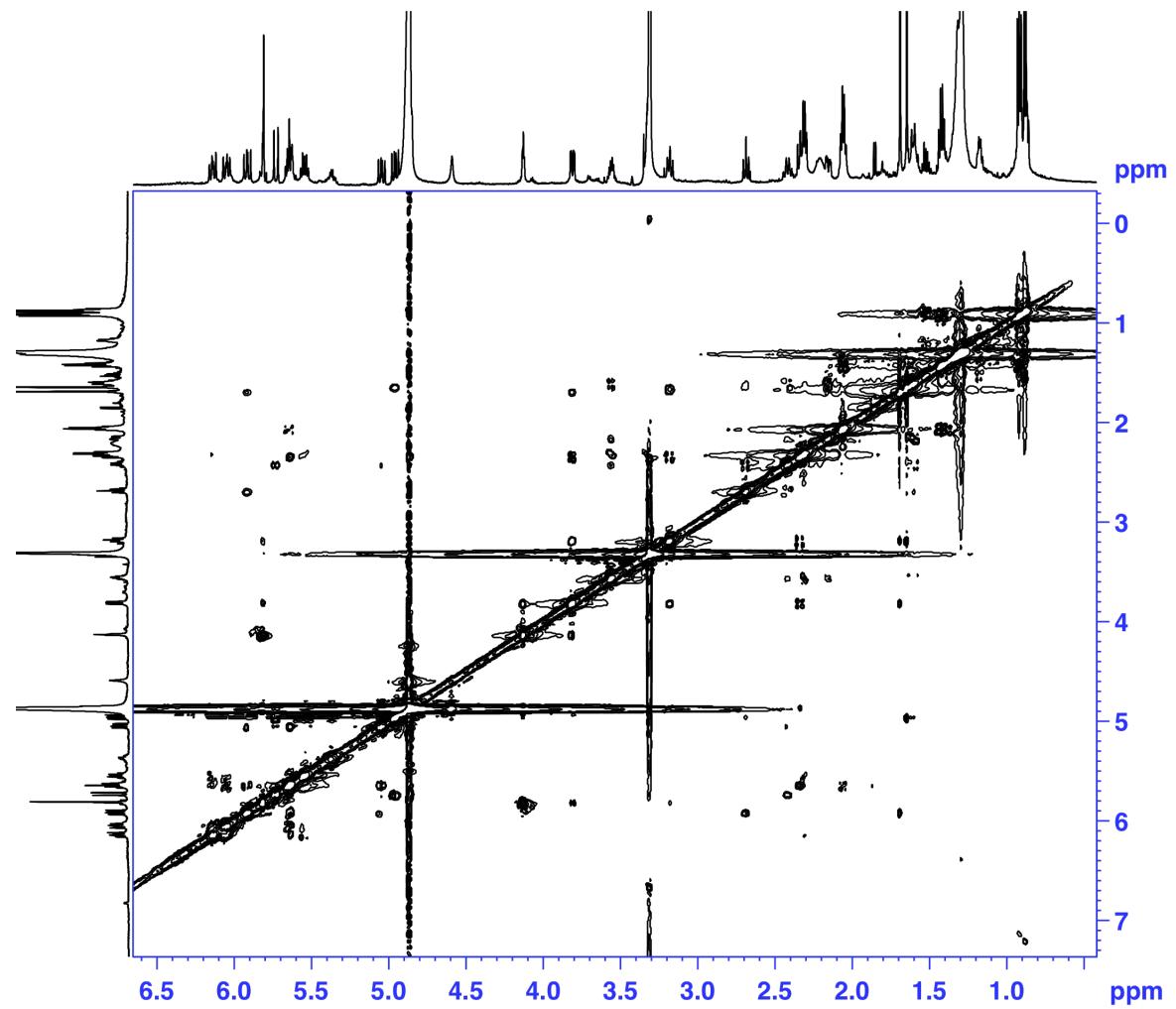


Figure S2e. ROESY spectrum (600 MHz, methanol- d_4) of heronamide B (**2**)

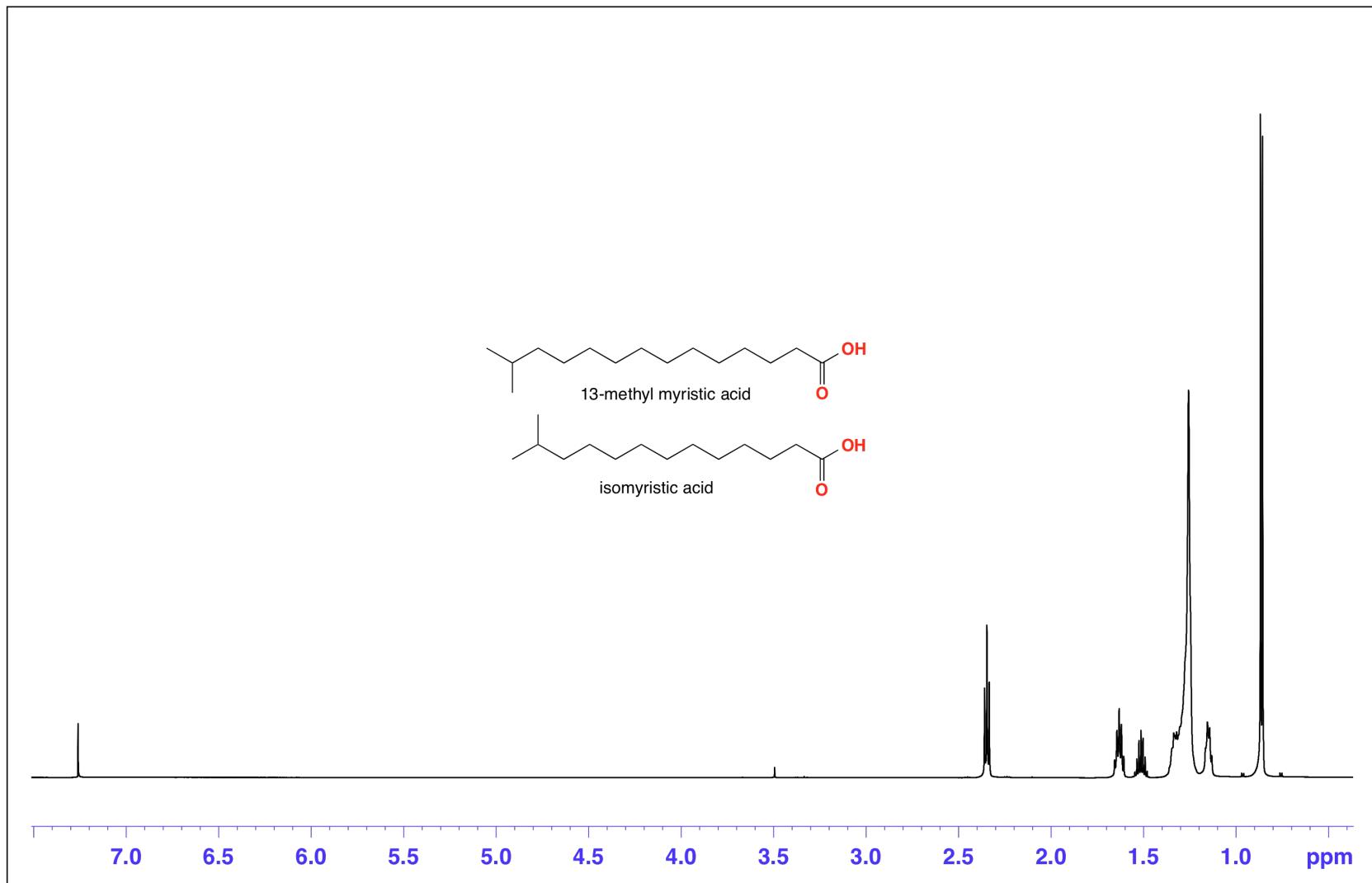


Figure S2f. ¹H NMR (600 MHz, CDCl₃) spectrum of 13-methylmyristic acid for comparison with isomyristic acid signals in NMR spectra of 2

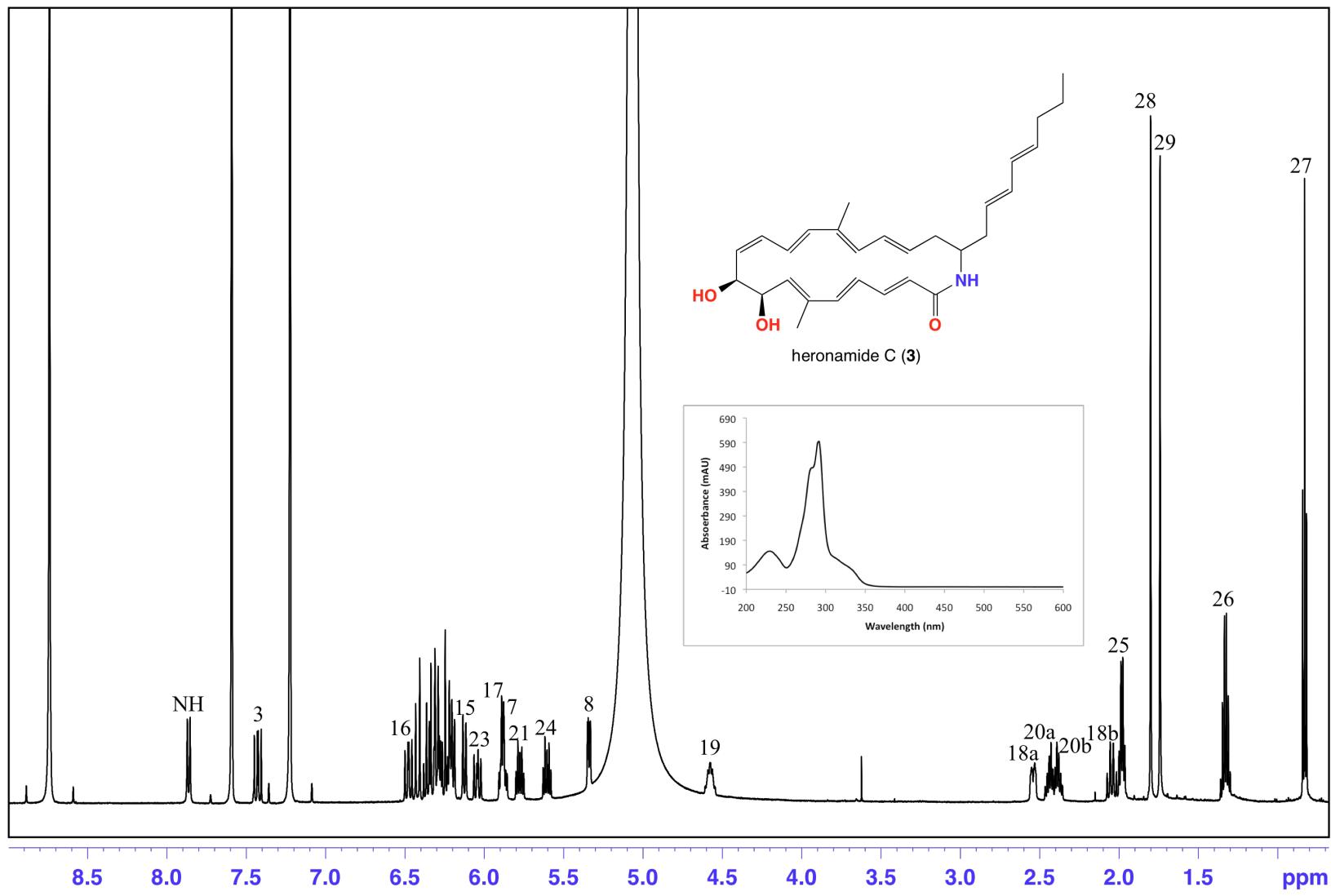


Figure S3a. ¹H NMR (600 MHz, pyridine-*d*₅) and UV-vis (inset) spectrum of heronamide C (3)

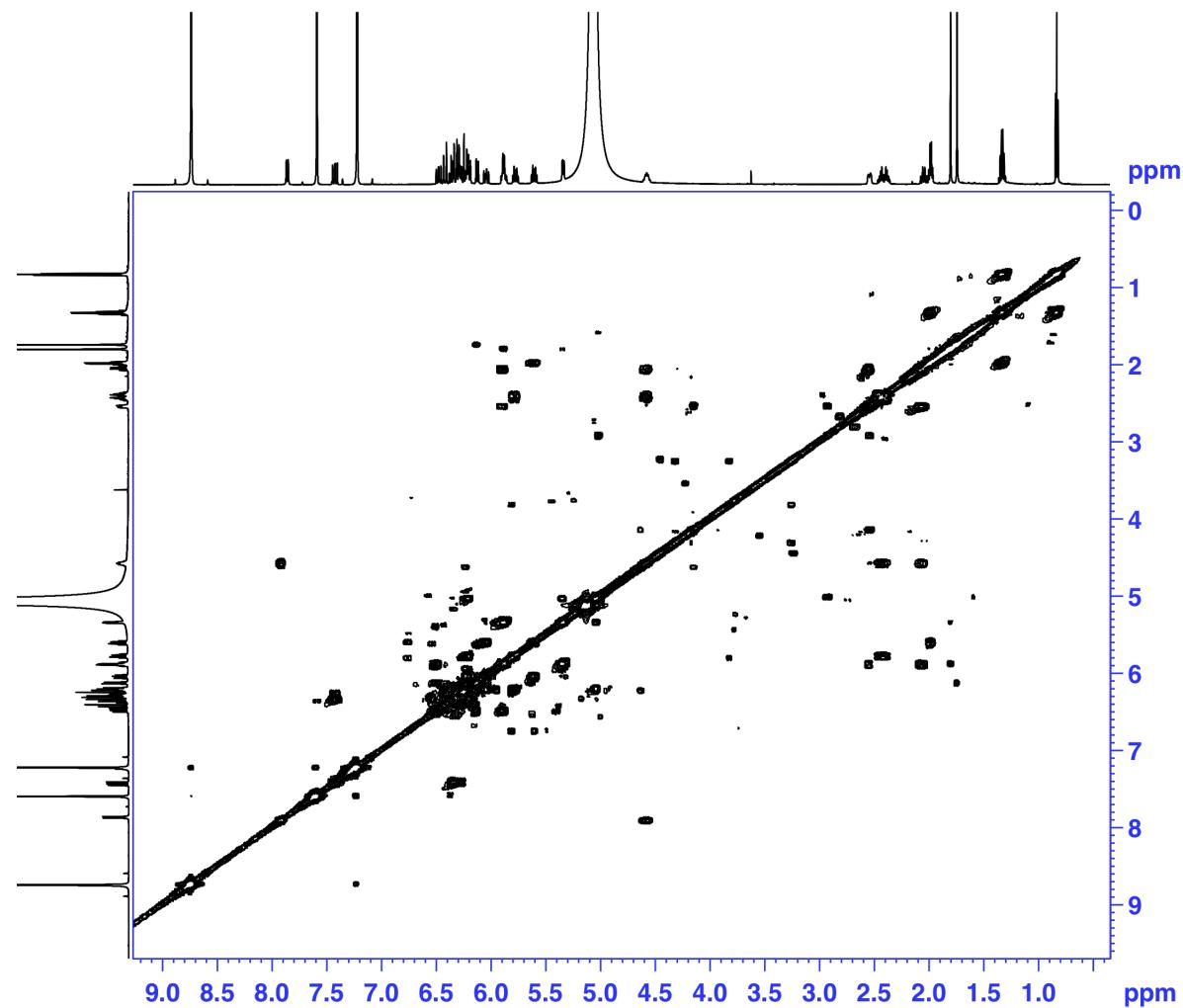


Figure S3b. COSY spectrum (600 MHz, methanol-*d*₄) of heronamide C (**3**)

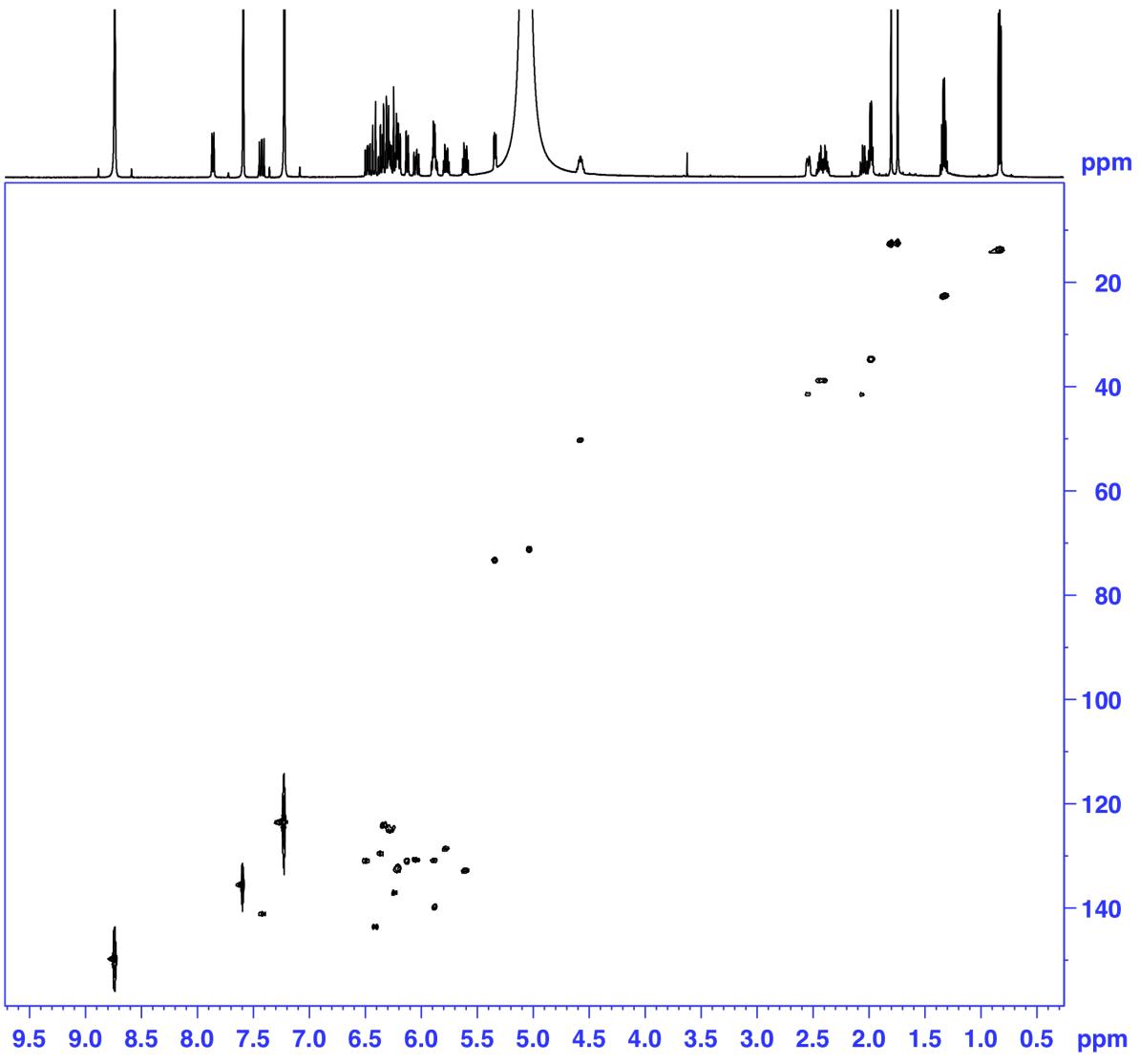


Figure S3c. HSQC spectrum (600 MHz, methanol- d_4) of heronamide C (3)

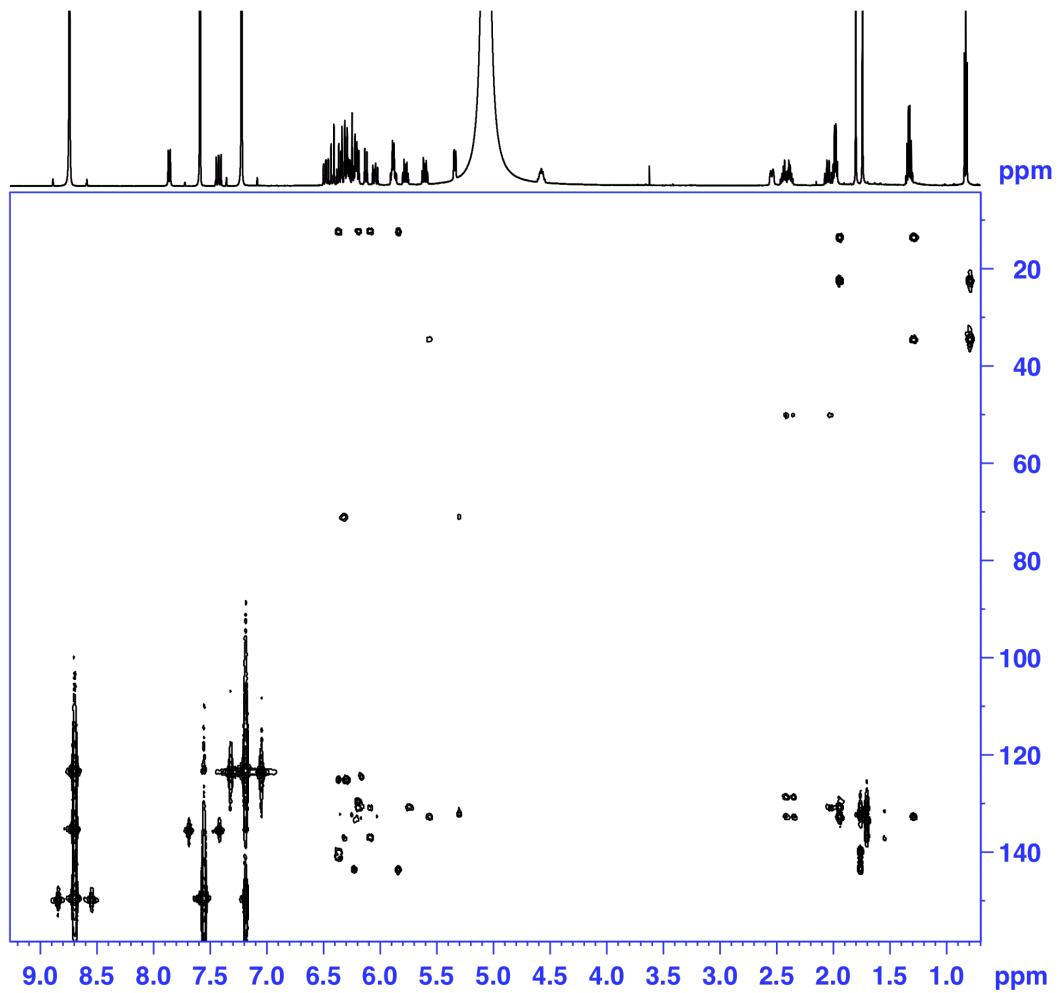


Figure S3d. HMBC spectrum (600 MHz, methanol- d_4) of heronamide C (**3**)

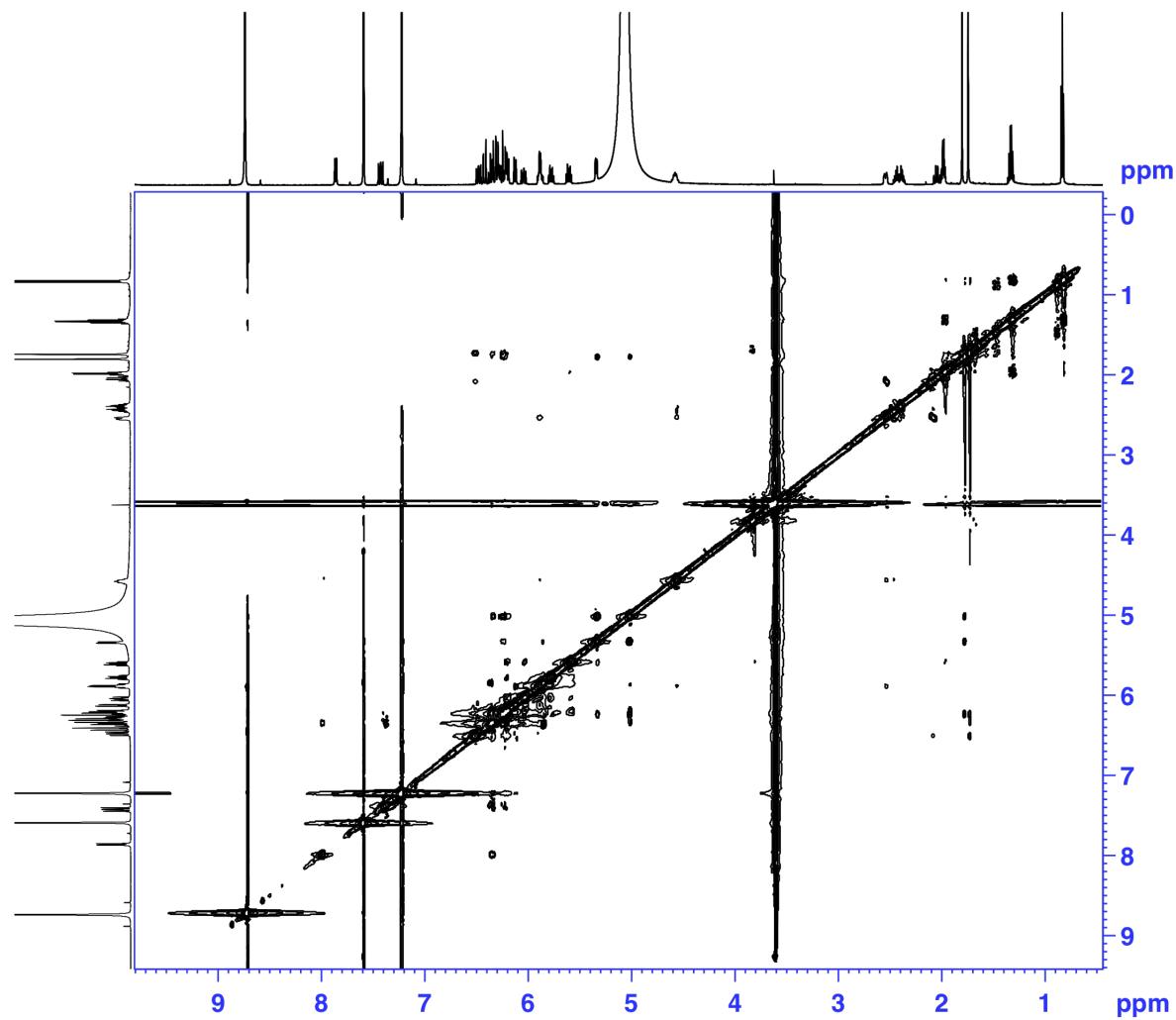


Figure S3e. ROESY spectrum (600 MHz, methanol- d_4) of heronamide C (**3**)

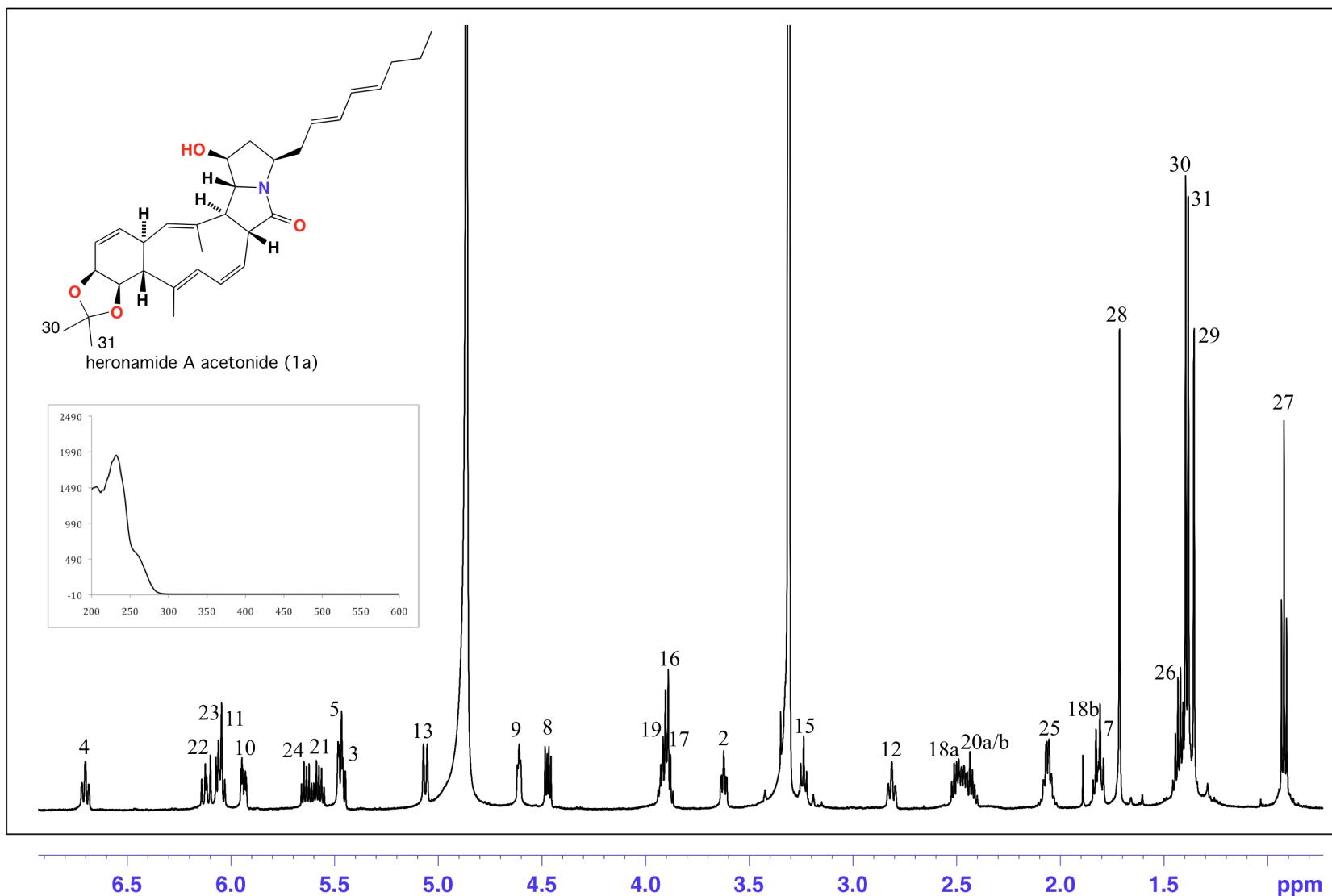


Figure S4. ¹H NMR (600 MHz, methanol-*d*₄) and UV-vis (inset) spectrum of heronamide A acetonide (**1a**)

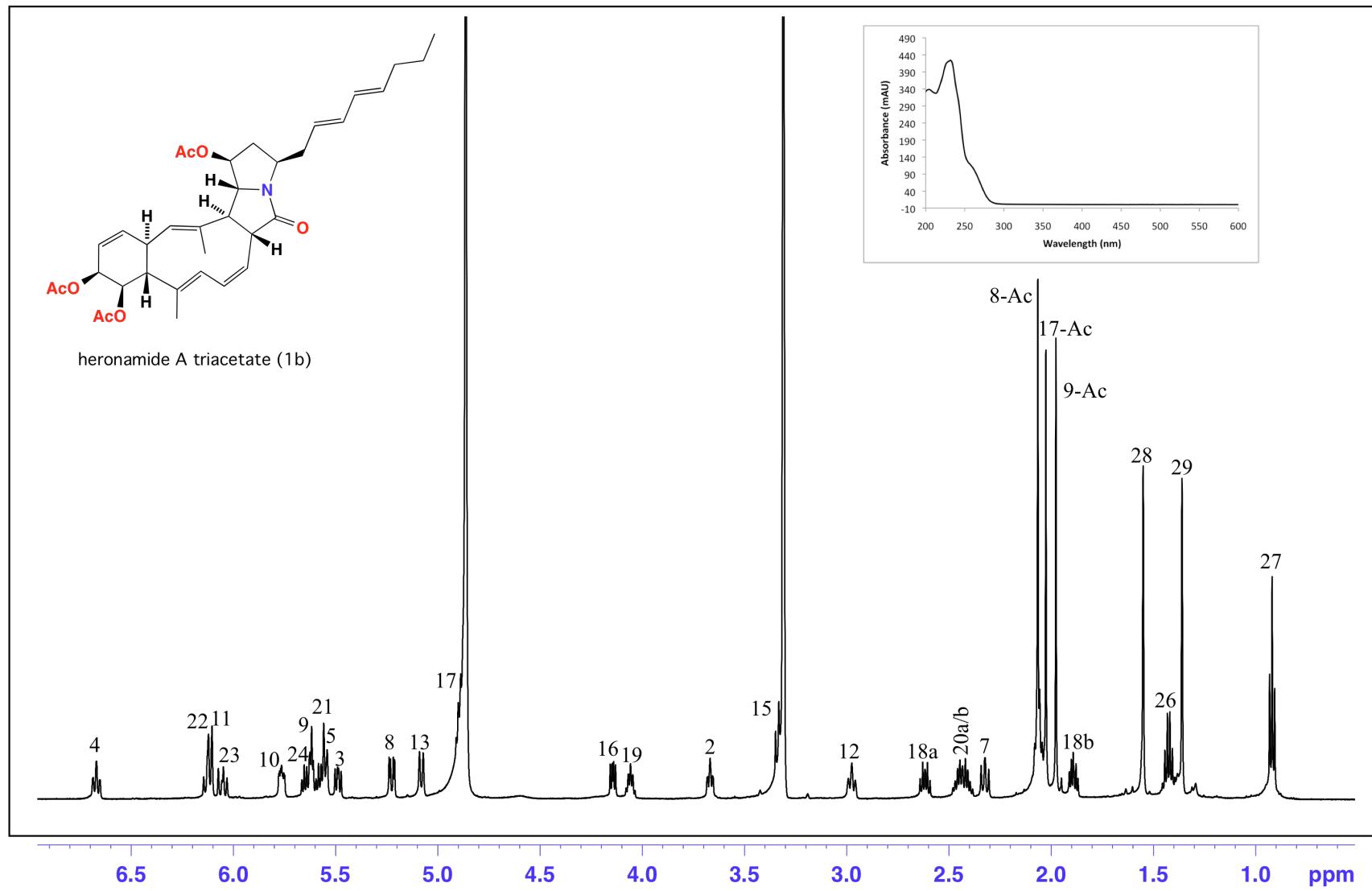


Figure S5a. ¹H NMR (600 MHz, methanol-*d*₄) and UV-vis (inset) spectrum of heronamide A triacetate (**1b**)

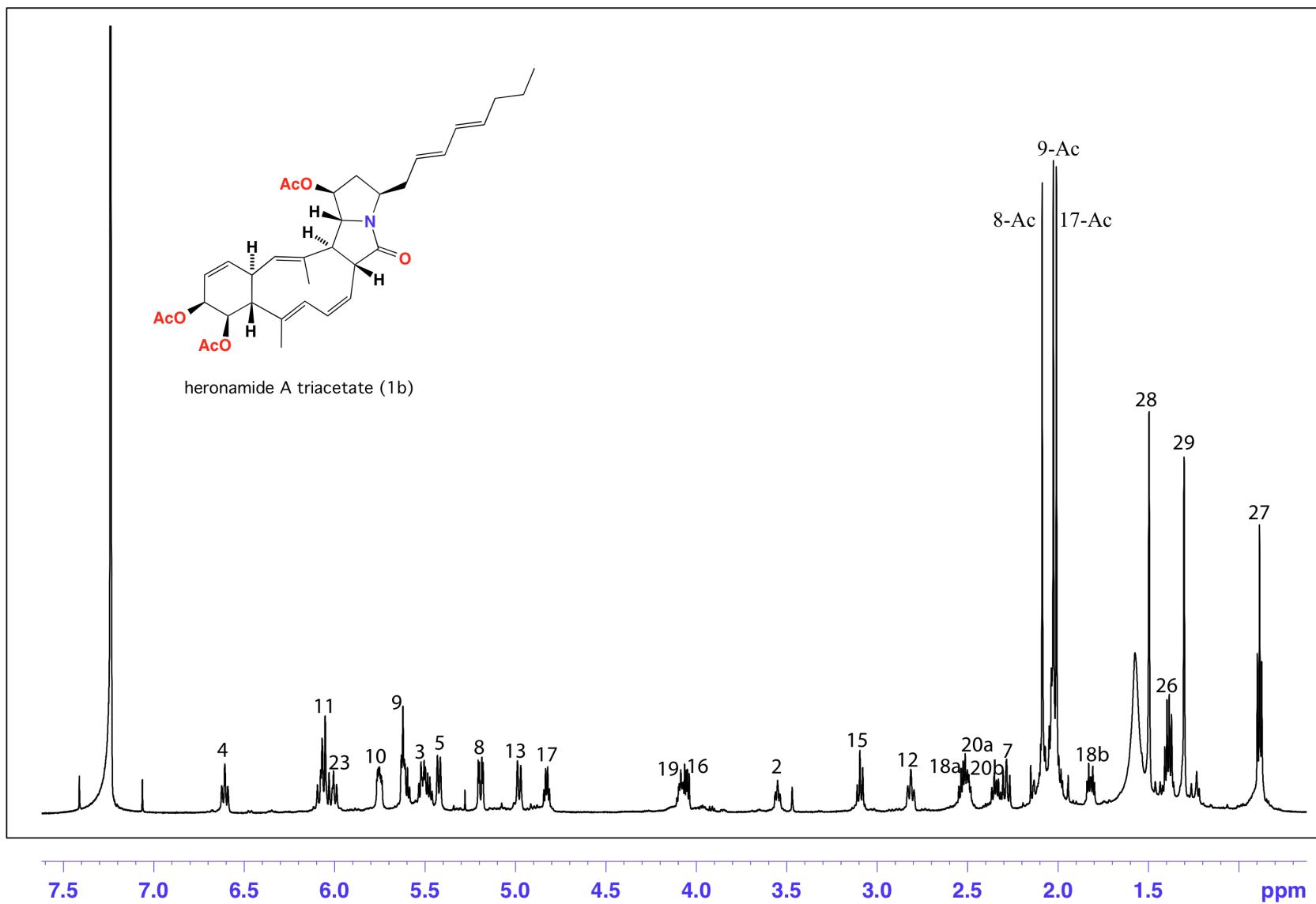


Figure S5b. ^1H NMR (600 MHz, CDCl_3) spectrum of heronamide A triacetate (**1b**)

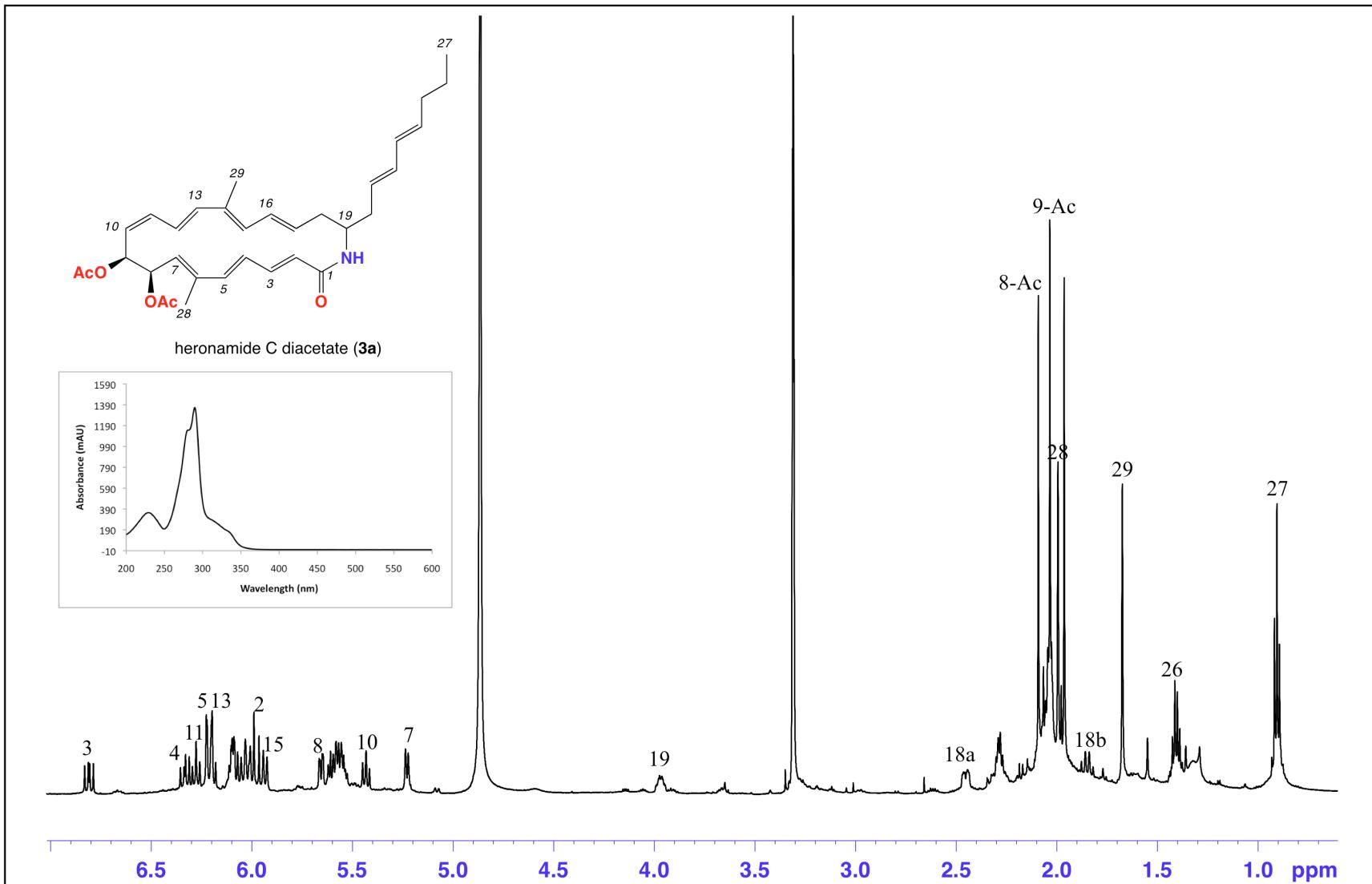


Figure S6. ¹H NMR (600 MHz, methanol-*d*₄) and UV-vis (inset) spectrum of heronamide C diacetate (**3a**)

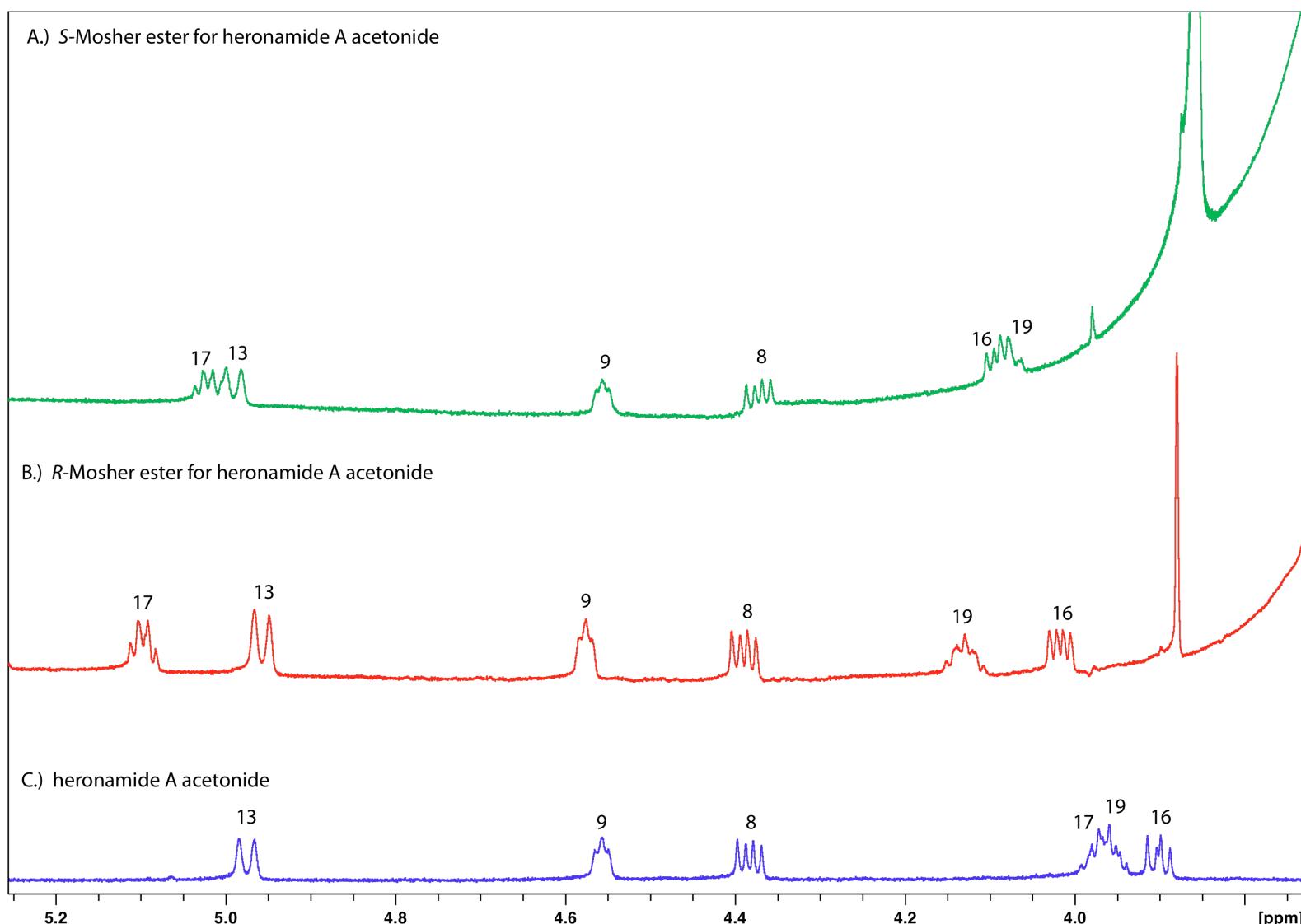


Figure S7a. ^1H NMR (600 MHz, CDCl_3) spectra of *R* and *S* Mosher esters of heronamide A acetonide (**1a**)

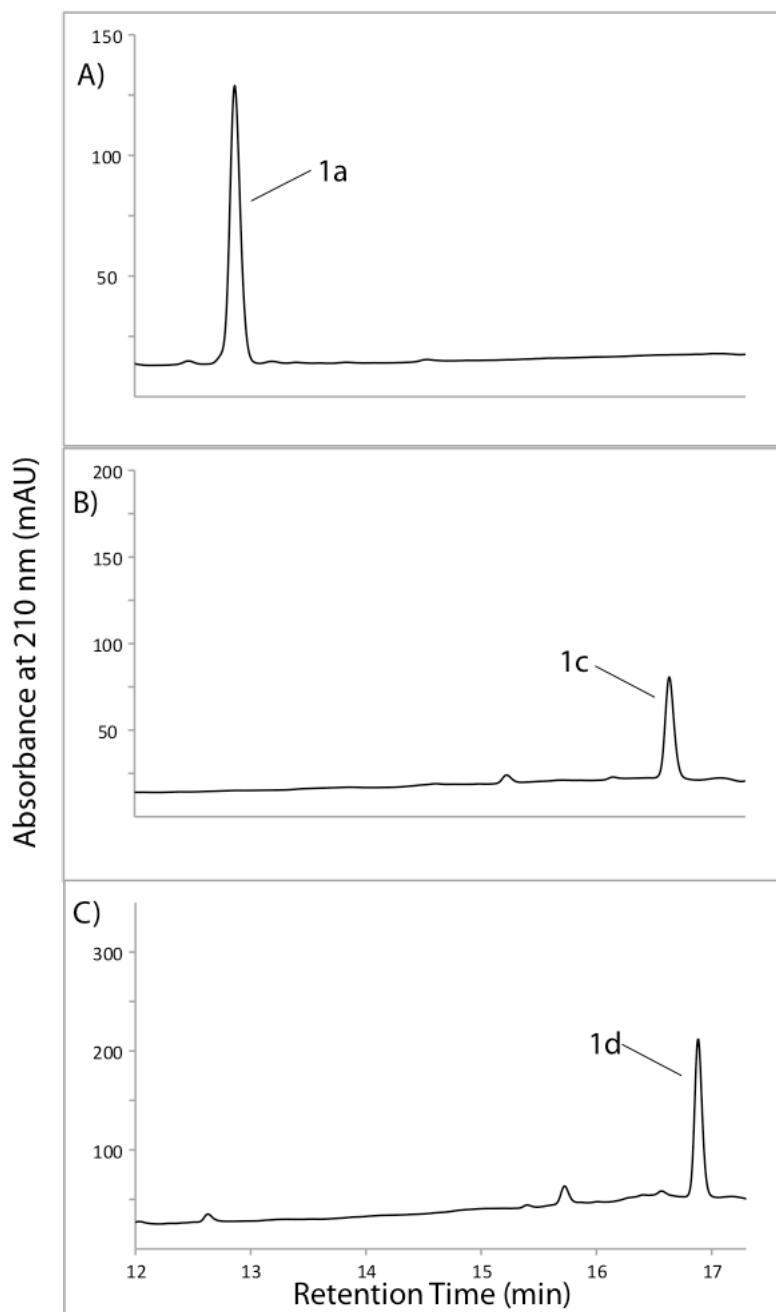


Figure S7b. HPLC trace analysis (210 nm) for A) heronamide A acetonide (**1a**), B) *S*-MTPA ester of heronamide A acetonide (**1c**), C) *R*-MTPA ester of heronamide A acetonide (**1d**). HPLC-DAD-ESI(\pm) MS conditions (Zorbax C₈ column, 150 \times 4.6 mm, 5 μ m, 1 mL/min, gradient from 10-100 % MeCN/H₂O (isocratic 0.05% formic acid) over 15 min, with a hold at 100 % MeCN for 5 min.

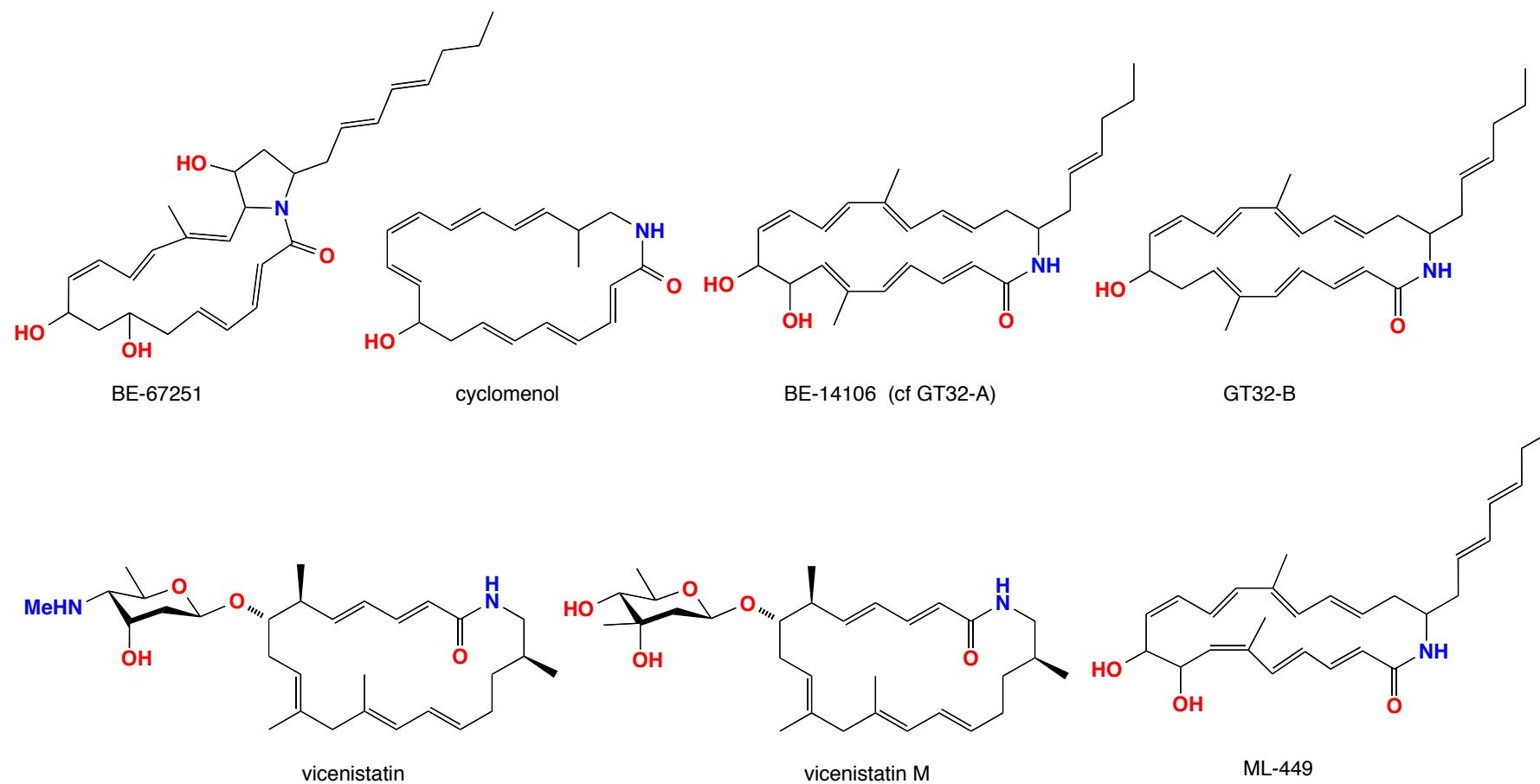
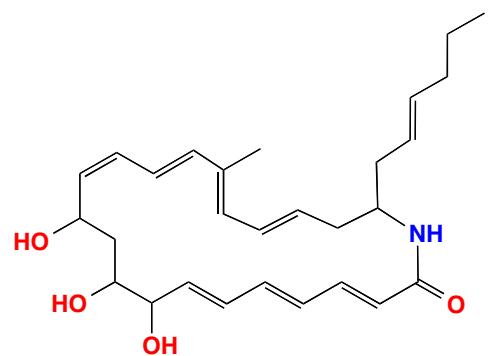
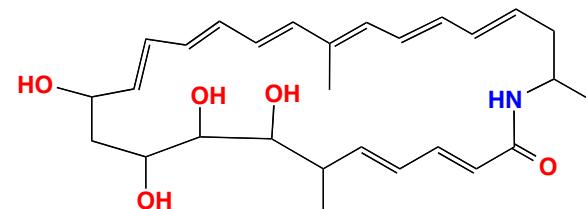


Figure S8. Reported *Streptomyces* polyketide 20-membered macrolactams



aureoverticillactam



salinilactam

Figure S9. Other reported polyketide macrolactams

Table S1. NMR (600 MHz, methanol-*d*₄) data for heronamide A (**1**)

pos	δ_{H} , mult (J in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		177.3			
2	3.64, ddd (9.2, 7.2, 2.4)	55.6	3, 15	5	1, 3, 4, 15, 16
3	5.45, dd (10.8, 7.2)	125.4	2, 4		1, 2, 5
4	6.68, ddd (10.8, 9.8, 2.4)	133.4	3, 5	28	2
5	5.51, d (9.8)	130.7	4	2, 7, 13	3, 7, 28
6		132.9			
7	2.07, m ^a	53.6	8, 12	5, 13	8, 9, 12
8	3.84, dd (11.4, 4.2)	70.8	7, 9	12, 28	7, 9, 12
9	4.12, dd (4.8, 4.2)	67.7	8, 10		7, 8, 10, 11
10	5.87, m ^b	128.1	9, 11	8	9, 12
11	5.88, m ^b	133.6	10, 12	13	7, 9, 13
12	2.82, m	43.7	7, 11, 13	8, 29	7, 13, 14
13	5.05, d (10.8)	133.1	12	5, 7, 11, 15	15, 29
14		137.8			
15	3.22, dd (9.2, 8.6)	59.0	2, 16	13	2, 3, 4, 14, 16, 17, 29
16	3.90, m ^c	68.5	15		14, 17
17	3.89, m ^c	76.0	18 α , 18 β		15
18 α	2.50, m ^d	42.3	17, 18 β , 19		16, 17
18 β	1.81, ddd (13.1, 7.8, 7.8)		17, 18 α , 19		17, 19, 20
19	3.91, m ^c	53.3	18a/b, 20a/b		
20a	2.46, m ^d	37.9	19, 20b, 21		19, 21, 22
20b	2.43, m ^d		19, 20a, 21		18, 19, 21, 22
21	5.57, dt (14.8, 7.5)	126.7	20a/b, 22		20, 23
22	6.12, dd (14.8, 10.4)	135.2	21, 23		20, 24
23	6.05, dd (14.5, 10.4)	131.4	22, 24	25	25
24	5.64, dt (14.5, 7.2)	134.1	23, 25		22, 25
25	2.06, m ^a	35.6	24, 26	23	23, 26, 27
26	1.42, sxt (7.4)	23.5	25, 27		25, 27
27	0.92, t (7.4)	13.9	26		25, 26
28	1.75, s	12.6		4, 8	5, 6, 7
29	1.41, s	16.8		12	13, 14, 15

[^{a-d}] overlapping signals

Table S2. NMR (600 MHz, methanol-*d*₄) data for heronamide B (**2**)

pos	δ_{H} , mult (J in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		175.5			
2	2.68, dd (10.5, 10.1)	56.0	3, 17	4, 16	1, 3, 4, 17
3	5.05, dd (15.1, 10.1)	130.8	2, 4	17	5
4	5.92, dd (15.1, 11.0)	135.4	3, 5	2, 28	2
5	5.63, m ^a	134.2	4	7	3, 7, 28
6		135.5			
7	2.33, m ^b	55.7	8, 12	5	8, 12, 28
8	3.81, dd (11.6, 4.2)	71.4	7, 9	12, 28	
9	4.13, m	67.9	8, 10		
10	5.81, m ^c	128.3	9, 11		9, 12
11	5.81, m ^c	134.4	10, 12		7, 9, 12
12	3.18, dd (10.5, 9.7)	43.6	7, 11, 13	8, 28, 29	7, 13, 14
13	4.86*	133.8	12		15, 29
14		137.8			
15	5.73, d (16.0)	142.1	16	17	13, 14, 17, 29
16	4.96, dd (16.0, 9.7)	127.3	15, 17	2, 18 α , 29	14, 17
17	2.42, m	47.4	2, 16, 18 α , 18 β	3, 15, 19	2, 15, 16
18 α	2.15, ddd (13.3, 4.8, 2.6)	34.8	17, 18 β , 19	16, 19	16, 17
18 β	1.60, m		17, 18 α , 19		17, 19, 20
19	3.56, m	53.7	18 α , 18 β , 20	17, 21	
20	2.31, m ^b	40.7	19, 21	22	18, 19, 21
21	5.54, dt (15.0, 7.4)	126.6	20, 22	19	20, 23
22	6.14, dd (15.0, 10.4)	135.5	21, 23	20	20, 23, 24
23	6.05, dd (15.0, 10.4)	131.3	22, 24	25	21, 25
24	5.65, m ^a	134.5	23, 25		22, 25
25	2.06, m	35.6	24, 26	23	23, 24, 26, 27
26	1.41, m	23.5	25, 27		24, 25, 27
27	0.92, t (7.4)	13.9	26		25, 26
28	1.69, s	13.1		4, 8, 12	5, 6, 7
29	1.64, s	14.1		12, 16	13, 14, 15

[^{a-c}] overlapping signals, * obscured by H₂O signal

Table S3. NMR (600 MHz, pyridine-*d*₅) data for heronamide C (**3**)

pos	δ_{H} , mult (J in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		168.3			
2	6.34, m ^a	129.9	3		1
3	7.38, dd (14.9, 11.0)	141.5	2, 4		1
4	6.22, m ^b	125.5	3, 5		5
5	6.36, m ^a	143.9	4		3, 7, 28
6		132.5			
7	5.84, br d (8.2)	140.0	8	5	5, 28
8	5.33, dd (8.2, 3.0)	73.4	7, 9	28	6, 7, 9
9	5.01, dd, (8.9, 3.0)	71.5	8, 10	28	
10	6.18, m ^b	132.6	9, 11		11
11	6.33, m ^a	124.4	10, 12		9
12	6.24, m ^b	124.7	11, 13		
13	6.21, m ^b	137.4	12		
14		133.7			
15	6.11, d (11.4)	131.3	16	17	13, 14, 17, 29
16	6.51, dd (14.9, 11.4)	131.3	15, 17	18 β , 29	
17	5.88, ddd (14.9, 10.5, 5.4)	131.2	16, 18 α , 18 β	15, 19	16
18 α	2.53, m	34.8	17, 18 β , 19	16	16, 17
18 β	2.07, dd (23.1, 10.5)		17, 18 α , 19	16	17, 19
19	4.56, m	50.4	18 α , 18 β , 20a/b	17, 21	
20a	2.45, ddd (14.3, 7.3, 7.1)	39.0	19, 20b, 21	19	18, 19, 21, 22
20b	2.39, ddd (14.3, 7.1, 6.7)		19, 20a, 21		18, 19, 21, 22
21	5.77, dt (15.1, 7.1)	128.9	20a/b, 22	19	20, 23
22	6.19, m ^b	133.2	21, 23		20
23	6.02, dd (14.8, 10.3)	131.1	22, 24		21, 24, 25
24	5.58, dt, (14.8, 6.9)	133.1	23, 25		22, 25, 26
25	1.96, td (7.5, 6.9)	34.8	24, 26		23, 24, 26, 27
26	1.30, sxt, (7.5)	22.7	25, 27		24, 25, 27
27	0.81, t (7.5)	13.8	26		25, 26
28	1.77, s	12.7		8, 9	5, 6, 7
29	1.72, s	12.5		16	13, 14, 15
NH	7.98, d (10.3)		19	2	1

[^{a,b}] overlapping signals

Table S4. NMR (600 MHz, methanol-*d*₄) data for heronamide A acetonide (**1a**)

pos	δ_{H} , mult (J in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		177.4			
2	3.62, ddd (9.2, 7.1, 2.3)	55.7	3, 15	5	1, 3, 4, 15, 16
3	5.47, m ^a	125.7	2, 4		1, 5
4	6.70, ddd (12.0, 10.2, 2.1)	133.4	3, 5	28	2
5	5.48, m ^a	131.3	4	2	3, 7, 28
6		132.0			
7	1.81, m ^b	55.0	8, 12	13	6, 12, 28
8	4.47, dd (11.1, 6.0)	76.0	7, 9	12, 28, 31	9, 32
9	4.61, dd (6.0, 3.8)	72.6	8, 10	12, 31	7, 8, 10, 11
10	5.94, ddd (9.8, 3.8, 2.8)	124.7	9, 11		8, 12
11	6.05, m ^c	136.5	10, 12		7, 9, 12, 13
12	2.81, br dd (10.9, 8.4)	41.2	7, 11, 13	8, 9	7, 10, 11, 13, 14
13	5.06, d (10.9)	132.9	12	7, 15	11, 15, 29
14		138.3			
15	3.24, dd (9.4, 8.6)	58.9	2, 16	2, 13	2, 3, 13, 14, 16, 17, 29
16	3.90, m ^d	68.4	15, 17		14, 17
17	3.89, m ^d	75.9	16, 18 α , 18 β		
18 α	2.50, m	42.3	17, 18 β , 19		16, 17
18 β	1.82, m ^b		17, 18 α , 19		
19	3.92, m ^d	53.3	18 α , 18 β , 20a/b		
20a	2.47, m ^e	37.9	19, 20b, 21		18, 19, 21, 22
20b	2.43, m ^e		19, 20a, 21		18, 19, 21, 22
21	5.57, dt (14.7, 7.5)	126.8	20a/b, 22		20, 23
22	6.12, dd (14.7, 10.4)	135.2	21, 23		20, 24
23	6.06, m ^c	131.6	22, 24	25	21, 25
24	5.64, dt (14.5, 7.0)	134.3	23, 25		22, 25, 26
25	2.06, m	35.6	24, 26	23	23, 24, 26, 27
26	1.42, sxt (7.4)	23.5	25, 27		25, 27
27	0.92, t (7.4)	13.9	26		25, 26
28	1.71, s	13.4		4, 8	6, 7
29	1.36, s	16.7		12, 16	13, 14, 15
30	1.40, s	28.7			31, 32
31	1.38, s	26.2		8, 9	30, 32
32		110.2			

[^{a-d} overlapping signals]

Table S5a. NMR (600 MHz, methanol-*d*₄) data for heronamide A triacetate (**1b**)

pos	δ_{H} , mult (<i>J</i> in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		177.7			
2	3.67, ddd (9.5, 7.2, 1.8)	54.9	3, 15	5	1, 3, 4, 15, 16
3	5.49, dd (10.6, 7.2)	126.0	2, 4		1, 2, 5
4	6.68, ddd (10.6, 10.0, 1.8)	133.2	3, 5	28	2, 5
5	5.55, d ^a (10.0)	130.9	4	2, 7	3, 7, 28
6		136.9			
7	2.32, m	51.7	8, 12	5, 13	5, 8, 12, 28
8	5.23, dd (12.3, 3.9)	71.6	7, 9	12, 28	7, 9, 12
9	5.62, m ^b	67.0	8, 10		
10	5.76, ddd (8.9, 5.4, 2.4)	123.6	9, 11	8	8, 9, 12
11	6.11, m ^c	136.6	10, 12		7, 9, 12
12	2.98, dd (10.4, 10.3)	43.4	7, 11, 13	8, 28, 29	6, 7, 10, 13, 14
13	5.08, d (10.9)	132.0	12	7, 15	15, 29
14		138.5			
15	3.33*	58.3	2, 16	13	2, 3, 13, 14, 16, 17, 29
16	4.14, dd (9.7, 5.7)	67.0	15, 17	18 β , 29	17
17	4.90*	77.3	16, 18 α , 18 β	18 α	15
18 α	2.62, ddd (13.8, 7.7, 7.2)	39.0	17, 18 β , 19	17, 19	16, 17, 19, 20
18 β	1.89, ddd (13.8, 11.4, 5.8)		17, 18 α , 19		17, 19, 20
19	4.06, dddd (7.2, 6.9, 6.4, 5.8)	54.0	18 α , 18 β , 20a/b	18 α , 20a	21
20a	2.45, m	37.9	19, 20b, 21	19	18, 19, 21, 22
20b	2.41, m		19, 20a, 21		18, 19, 21, 22
21	5.58, dt ^a (14.8, 7.4)	126.9	20a/b, 22		20, 23
22	6.12, m ^c	135.1	21, 23		
23	6.05, dd (14.9, 10.4)	131.5	22, 24		21, 25
24	5.64, dt ^b (14.9, 7.2)	134.3	23, 25		22, 25
25	2.06, m ^d	35.6	24, 26		23, 24, 26, 27
26	1.43, sxt (7.4)	23.4	25, 27		24, 25, 27
27	0.92, t (7.4)	13.8	26		25, 26
28	1.55, s	12.2		4, 8, 12	5, 7
29	1.36, s	16.5		12, 16	13, 14, 15
8-OC(O)Me	2.07, s ^d	20.7			8-OC(O)
9-OC(O)Me	1.98, s	20.7			9-OC(O)
17-OC(O)Me	2.03, s	20.7			17-OC(O)
8-OC(O)		172.1			
9-OC(O)		172.3			
17-OC(O)		171.8			

[^{a,b}] partially overlapping signals, [^{c,d}] overlapping signals, * obscured by solvent signal

Table S5b. NMR (600 MHz, CDCl₃) data for heronamide A triacetate (**1b**)

pos	δ_{H} , mult (J in Hz)	δ_{C}	COSY	ROESY	^1H - ^{13}C HMBC
1		174.9			
2	3.55, ddd (8.9, 7.5, 2.2)	53.5	3, 15	5, 15	1, 3, 4, 15, 16
3	5.52, m ^a	125.0	2, 4		2, 5
4	6.61, dd (10.4, 9.7)	132.0	3, 5	28	2
5	5.42, d (9.7)	130.1	4	2, 7	3, 7, 28
6		129.0			
7	2.28, dd (12.4, 9.8)	50.2	8, 12	5, 13	5, 8, 12, 28
8	5.19, dd (12.4, 4.0)	70.1	7, 9	12, 28	
9	5.62, m ^b	65.6	8, 10		
10	5.75, ddd (8.2, 5.5, 2.6)	123.1	9, 11		8, 9, 12
11	6.06, m ^c	135.0	10, 12	12, 13	7, 9, 12
12	2.81, dd, (11.0, 9.8)	42.3	7, 11, 13	8, 11, 29	7, 11, 13
13	4.98, d (11.0)	130.6	12	7, 15	15, 29
14		137.1			
15	3.10, dd (9.6, 8.9)	57.3	2, 16	2, 13, 17, 19	2, 3, 13, 14, 16, 17, 29
16	4.05, dd (9.6, 5.6)	65.1	15, 17	29	
17	4.83, ddd (13.9, 11.6, 5.6)	76.2	16, 18 α , 18 β	15, 18 α , 19	15
18 α	2.53, m ^d	38.0	17, 18 β , 19	17	16, 20
18 β	1.82, ddd (13.9, 12.0, 6.0)		17, 18 α , 19		17, 19, 20
19	4.09, m	52.6	18 α , 18 β , 20a/b	15, 17, 18 α , 20b	17
20a	2.50, m ^d	37.1	19, 20b, 21		21, 22
20b	2.35, ddd (15.0, 13.9, 7.9)		19, 20a, 21	19, 22	18, 19, 21, 22
21	5.48, ddd ^a (14.8, 7.9, 7.2)	125.5	20a/b, 22		20, 23
22	6.08, m ^c	133.8	21, 23	20b	20
23	6.01, dd (14.9, 10.6)	129.7	22, 24	25	25
24	5.61, m ^b	133.7	23, 25		22, 25, 26
25	2.03, m	34.5	24, 26	23	23, 26, 27
26	1.39, sxt (7.3)	22.3	25, 27		24, 25, 27
27	0.88, t (7.3)	13.6	26		25, 26
28	1.50, s	12.1		4, 8	5, 6, 7
29	1.30, s	16.1		12, 16	13, 14, 15
8-OC(O)Me	2.09, s	21.0			8-OC(O)
9-OC(O)Me	2.02, s	20.8			9-OC(O)
17-OC(O)Me	2.01, s	20.8			17-OC(O)
8-OC(O)		170.4			
9-OC(O)		170.2			
17-OC(O)		170.2			

[^{a-d}] overlapping signals

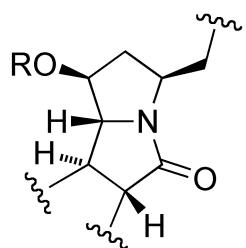
Table S6. NMR (600 MHz, methanol-*d*₄) data for heronamide C diacetate (**3a**)

pos	δ_{H} , mult (<i>J</i> in Hz)	δ_{C}	COSY	^1H - ^{13}C HMBC
1		170.2		
2	5.98, d (<i>15.1</i>)	124.5	3	1
3	6.81, dd (<i>15.1, 10.5</i>)	142.4	2, 4	1, 5
4	6.34, dd (<i>15.1, 10.5</i>)	127.6	3, 5	5
5	6.22, d ^a (<i>15.1</i>)	143.8	4	3, 4, 28
6		137.0		
7	5.23, br d (8.2)	132.4	8	5, 28
8	5.66, dd (9.3, 2.6)	72.0	7, 9	10, 8-OC(O)
9	6.09, m ^b	72.6	8, 10	8
10	5.43, dd (10.8, 9.3)	123.4	9, 11	12
11	6.28, dd (11.0, 10.8)	133.7	10, 12	8, 13
12	6.01, dd ^c (<i>15.1, 11.1</i>)	124.2	11, 13	
13	6.21, d ^a (<i>15.1</i>)	140.0	12	
14		134.5		
15	5.93, d (<i>11.0</i>)	132.6	16	13, 17, 29
16	6.20, m ^a	132.2	15, 17	
17	5.55, m ^d	131.4	16, 18 α , 18 β	
18 α	2.45, m	41.6	17, 18 β , 19	
18 β	1.85, m		17, 18 α , 19	
19	3.97, m	51.6	18 α , 18 β , 20	
20	2.29, m	39.0	19, 21	
21	5.57, m ^d	128.5	20, 22	
22	6.08, m ^b	134.0	21, 23	
23	6.03, m ^c	131.5	22, 24	
24	5.59, m ^d	133.9	23, 25	
25	2.04, m	35.7	24, 26	26, 27
26	1.41, sxt, (7.3)	23.6	25, 27	24, 25, 27
27	0.91, t (7.3)	13.9	26	25, 26
28	2.00, s	12.9		5, 6, 7
29	1.67, s	12.7		13, 14, 15
8-OC(O)Me	2.09, s	20.9		8-OC(O)
9-OC(O)Me	2.03, s	20.9		9-OC(O)
8-OC(O)		172.1		
8-OC(O)		172.1		

[^{a,c} partially overlapping signals] [^{b,d} overlapping signals]

Table S7. $\Delta\delta^{\text{SR}}$ ($= \delta_S - \delta_R$) data for the *S*- and *R*-MTPA-heronamide A acetonide Mosher esters

Proton	Chemical shift (δ)			$\Delta\delta^{SR}$ (Hz)
	Free alcohol (1a)	<i>S</i> -MTPA (1c)	<i>R</i> -MTPA (1d)	
16	3.90	4.09	4.02	+42
17	3.89	5.03	5.10	-42
19	3.92	4.08	4.13	-30



1c R = S(-)-MTPA
1d R = R(+)-MTPA