

Theonellamides J and K and 5-*cis*-Apoa-theopalauamide, Bicyclic Glycopeptides of the Red Sea Sponge *Theonella swinhoei*

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Supplementary Material

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S49 Figure S44. TOCSY spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 $\text{DMSO-}d_6\text{:H}_2\text{O}$ at 50 °C

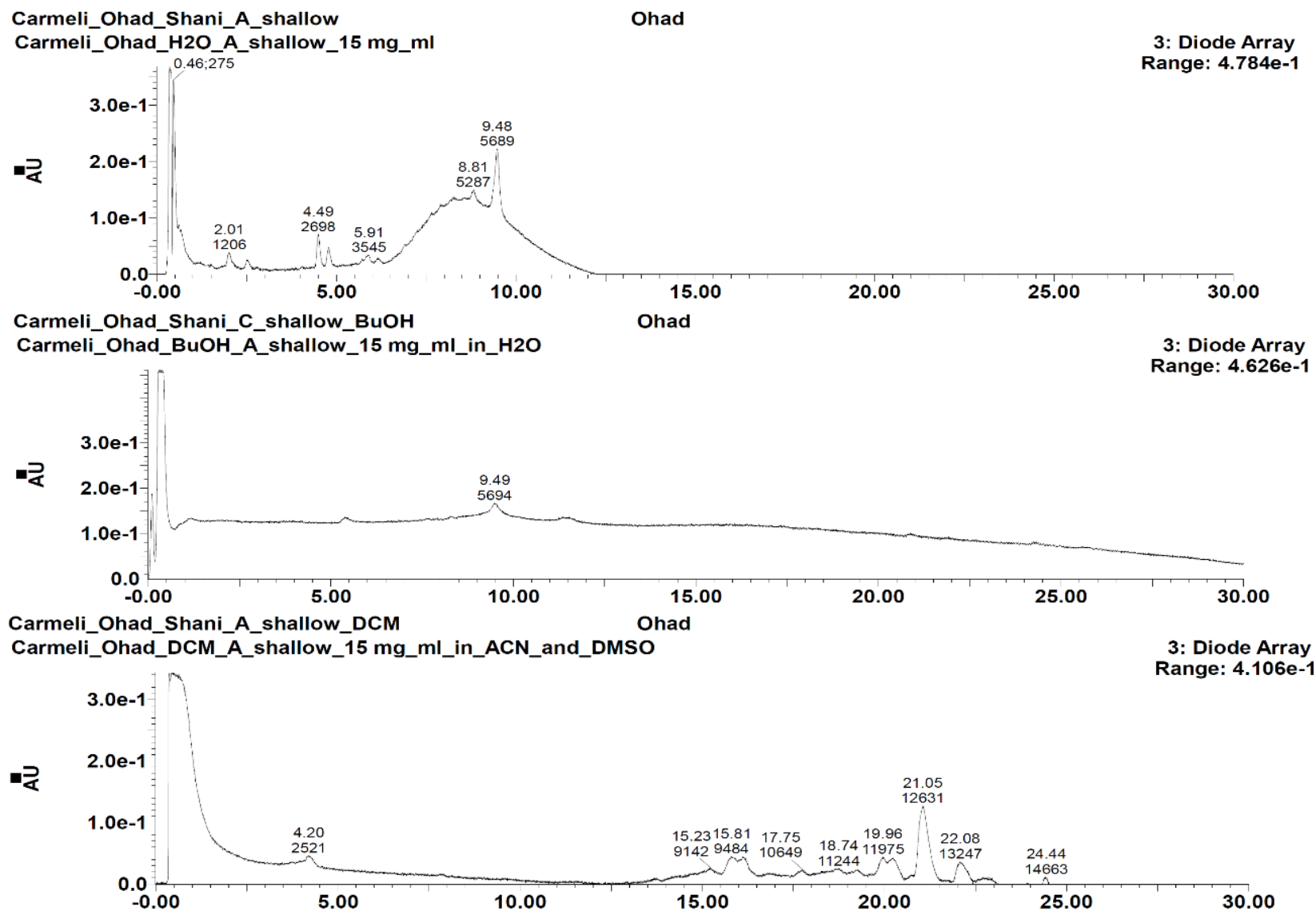
S50 Figure S45. ROESY spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 $\text{DMSO-}d_6\text{:H}_2\text{O}$ at 50 °C

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S1 Figure S1 LCMS chromatogram of *T. swinhoei* samples collected near Eilat at depths of 10 to 64 meters.

10 m sample

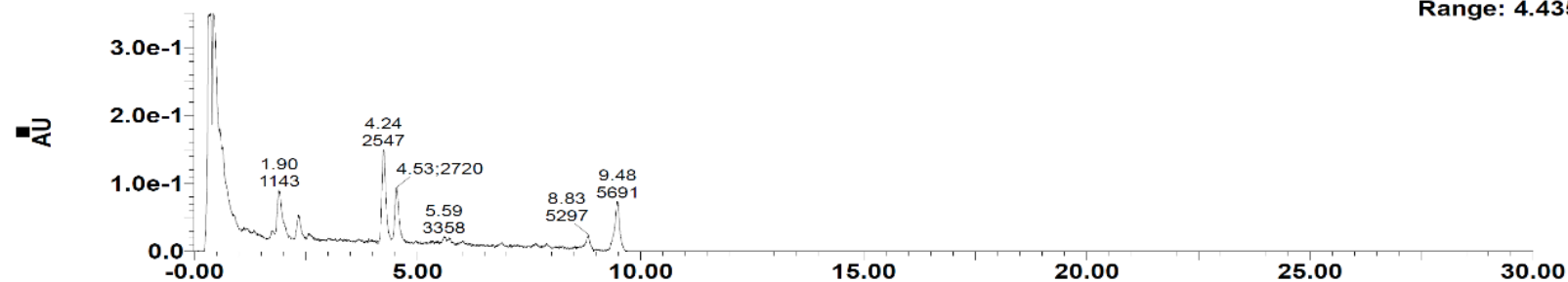


15 m sample

Carmeli_Ohad_Shani_B_shallow_H2O
Carmeli_Ohad_H2O_B_shallow_15 mg_ml_REP

Ohad

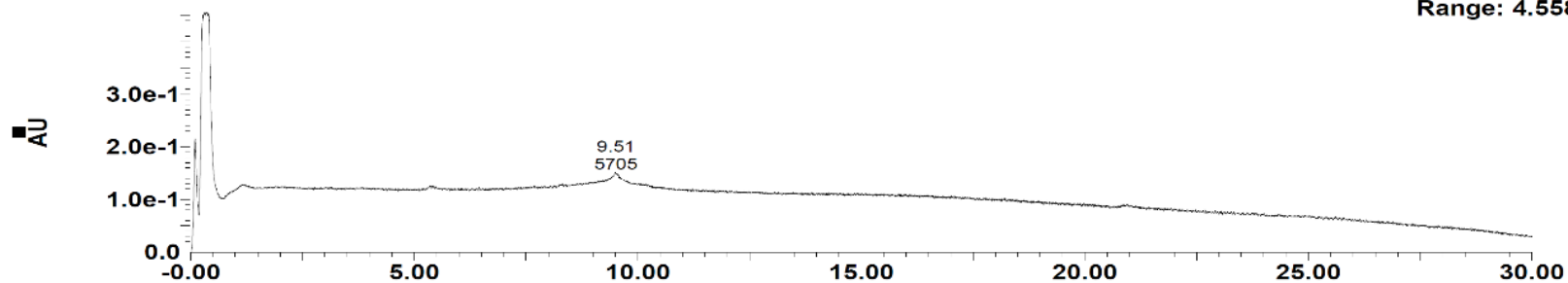
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Carmeli_Ohad_BuOH_B_shallow_15 mg_ml_in_H2O

Ohad

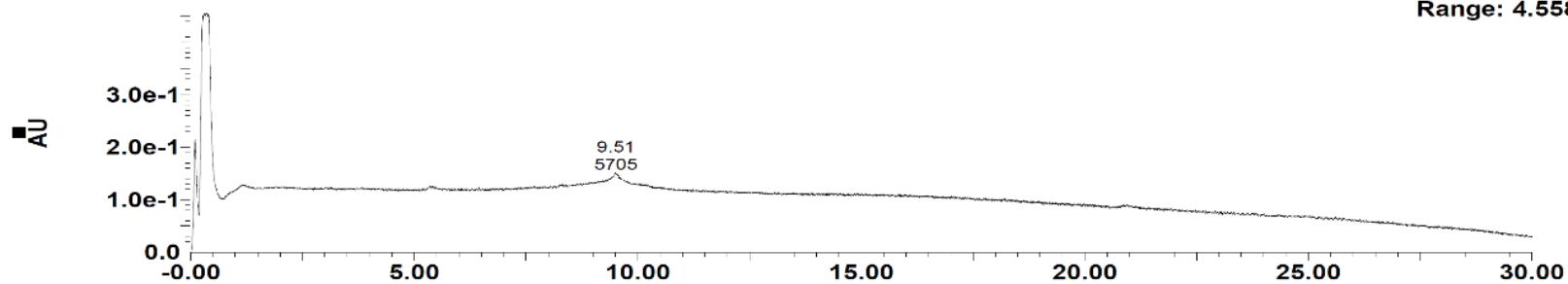
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Carmeli_Ohad_Shani_C_shallow_BuOH
Carmeli_Ohad_BuOH_B_shallow_15 mg_ml_in_H2O

Ohad

3: Diode Array
Range: 4.558e-1

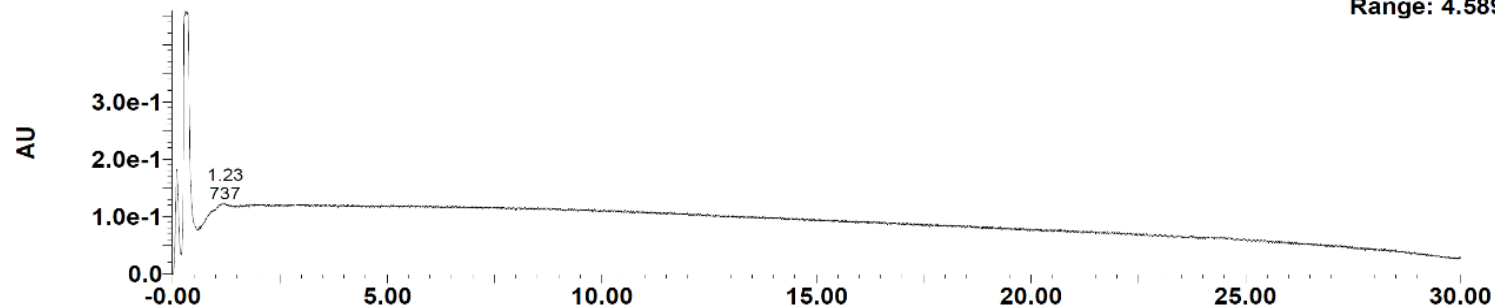


25 m sample

Carmeli_Ohad_Shani_C_shallow_H2O
Carmeli_Ohad_H2O_C_shallow_15 mg_ml_REP

Ohad

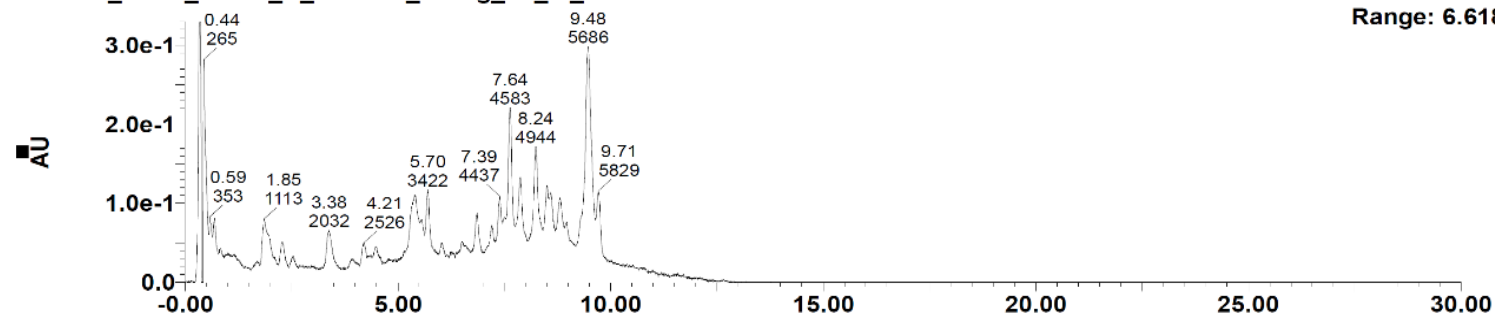
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Carmeli_Ohad_Shani_C_shallow_BuOH
Carmeli_Ohad_BuOH_C_shallow_15 mg_ml_in_H2O

Ohad

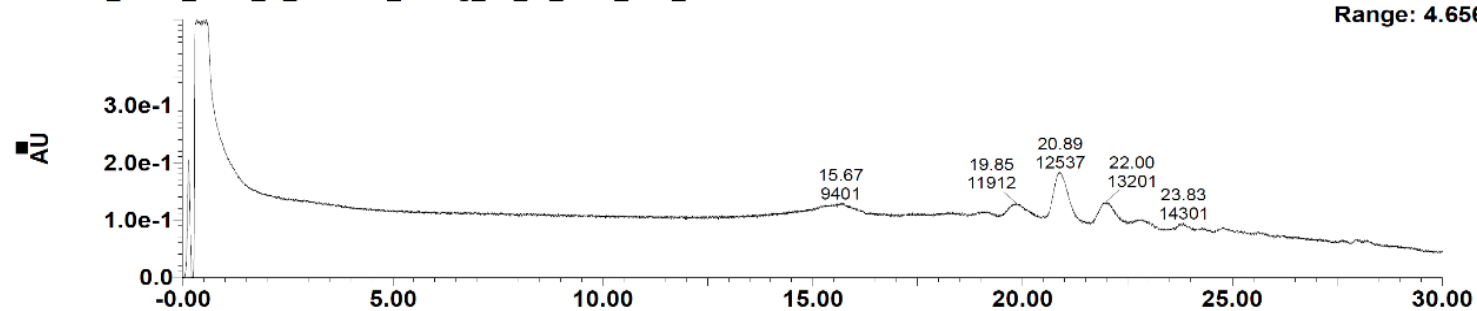
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Carmeli_Ohad_Shani_C_shallow_DCM
Carmeli_Ohad_DCM_C_shallow_15 mg_ml_in_ACN_and_DMSO

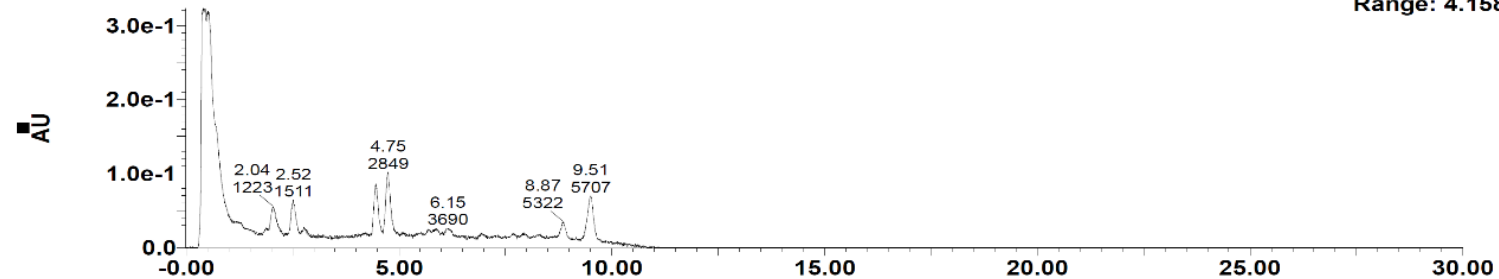
Ohad

3: Diode Array
Range: 4.656e-1

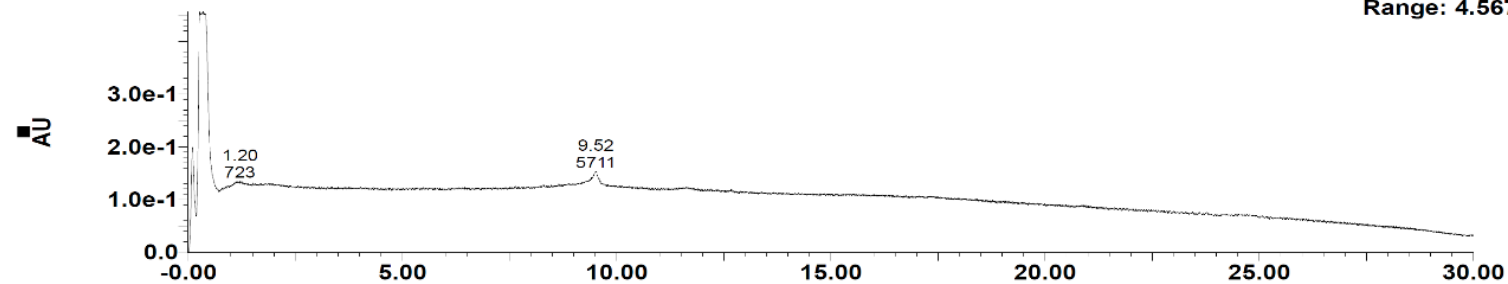


30m sample

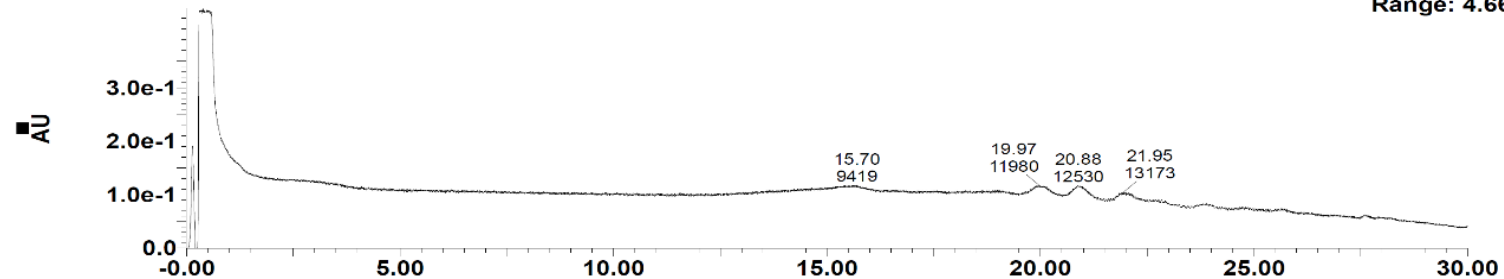
Carmeli_Ohad_Shani_D_shallow Ohad
Carmeli_Ohad_H2O_D_shallow 3: Diode Array
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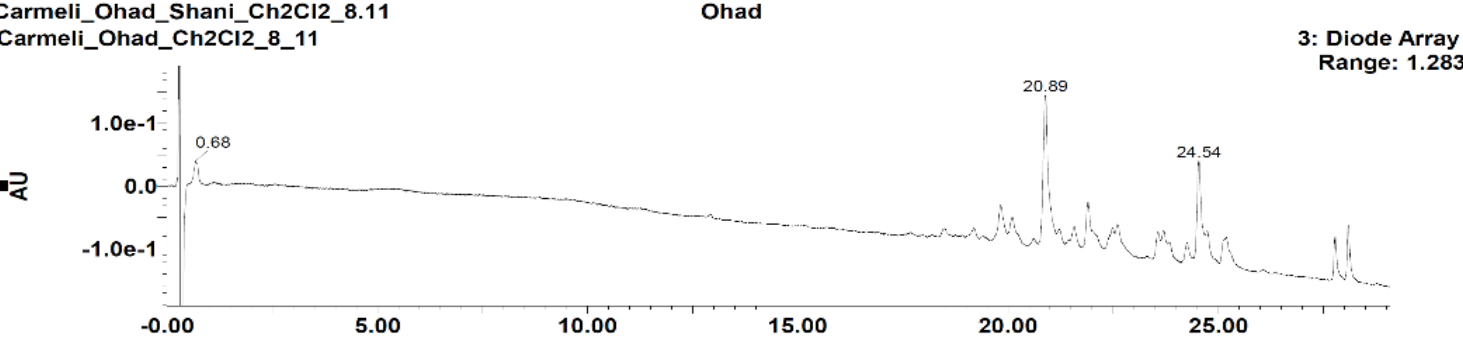
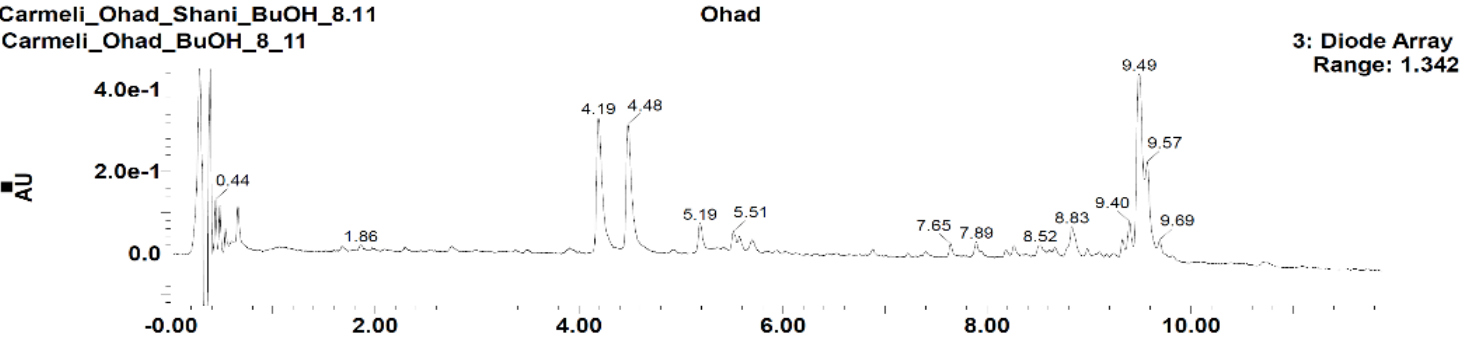
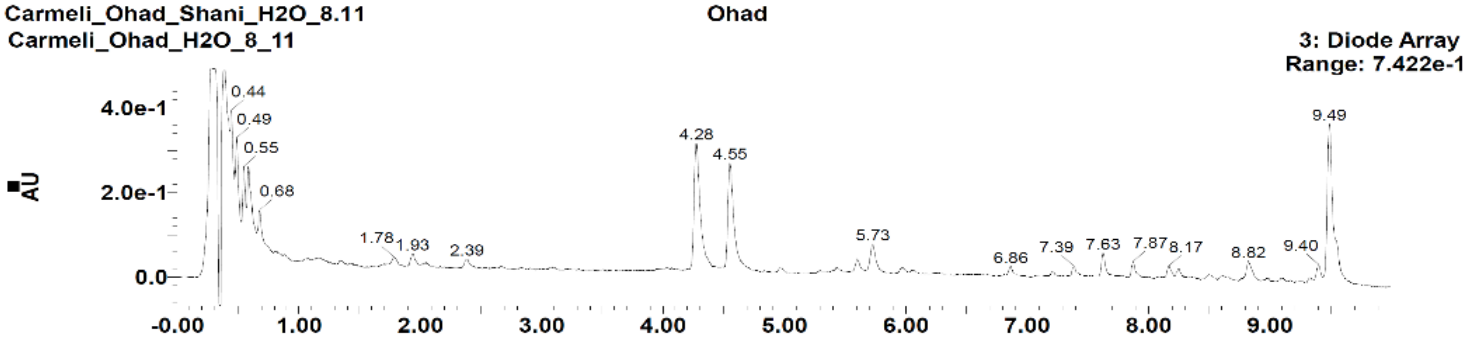
Carmeli_Ohad_Shani_C_shallow_BuOH Ohad
Carmeli_Ohad_BuOH_D_shallow_15 mg_ml_in_H2O 3: Diode Array
Range: 4.567e-1



Carmeli_Ohad_Shani_D_shallow_DCM Ohad
Carmeli_Ohad_DCM_D_shallow_15 mg_ml_in_ACN_and_DMSO 3: Diode Array
Range: 4.66e-1



59 m sample

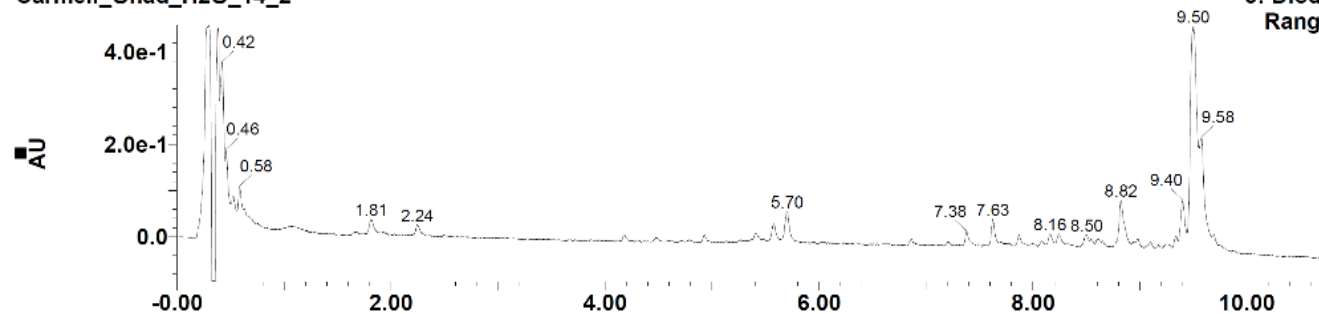


64 m sample

Carmeli_Ohad_Shani_H2O_14.2
Carmeli_Ohad_H2O_14_2

Ohad

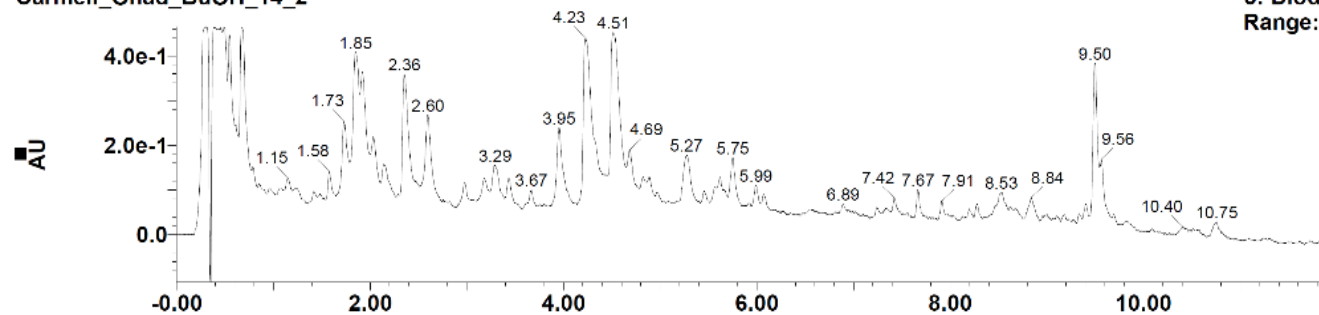
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Carmeli_Ohad_Shani_BuOH_14.2
Carmeli_Ohad_BuOH_14_2

Ohad

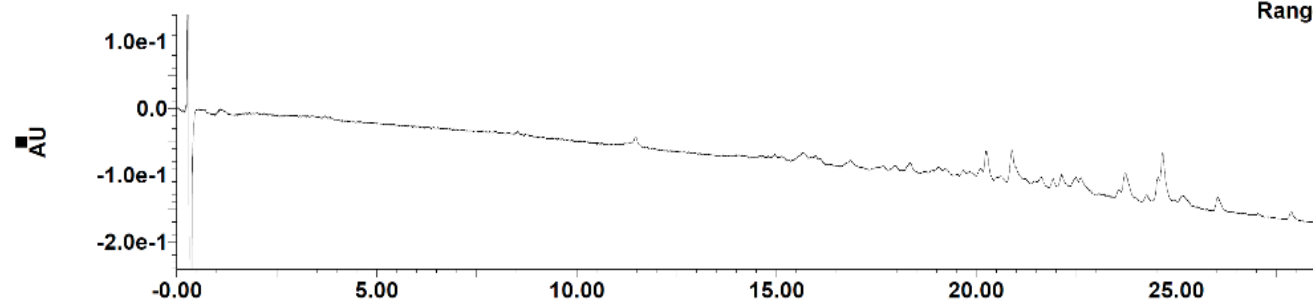
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Carmeli_Ohad_Shani_Ch2Cl2_4.12
Carmeli_Ohad_Ch2Cl2_4_12

Ohad

3: Diode Array
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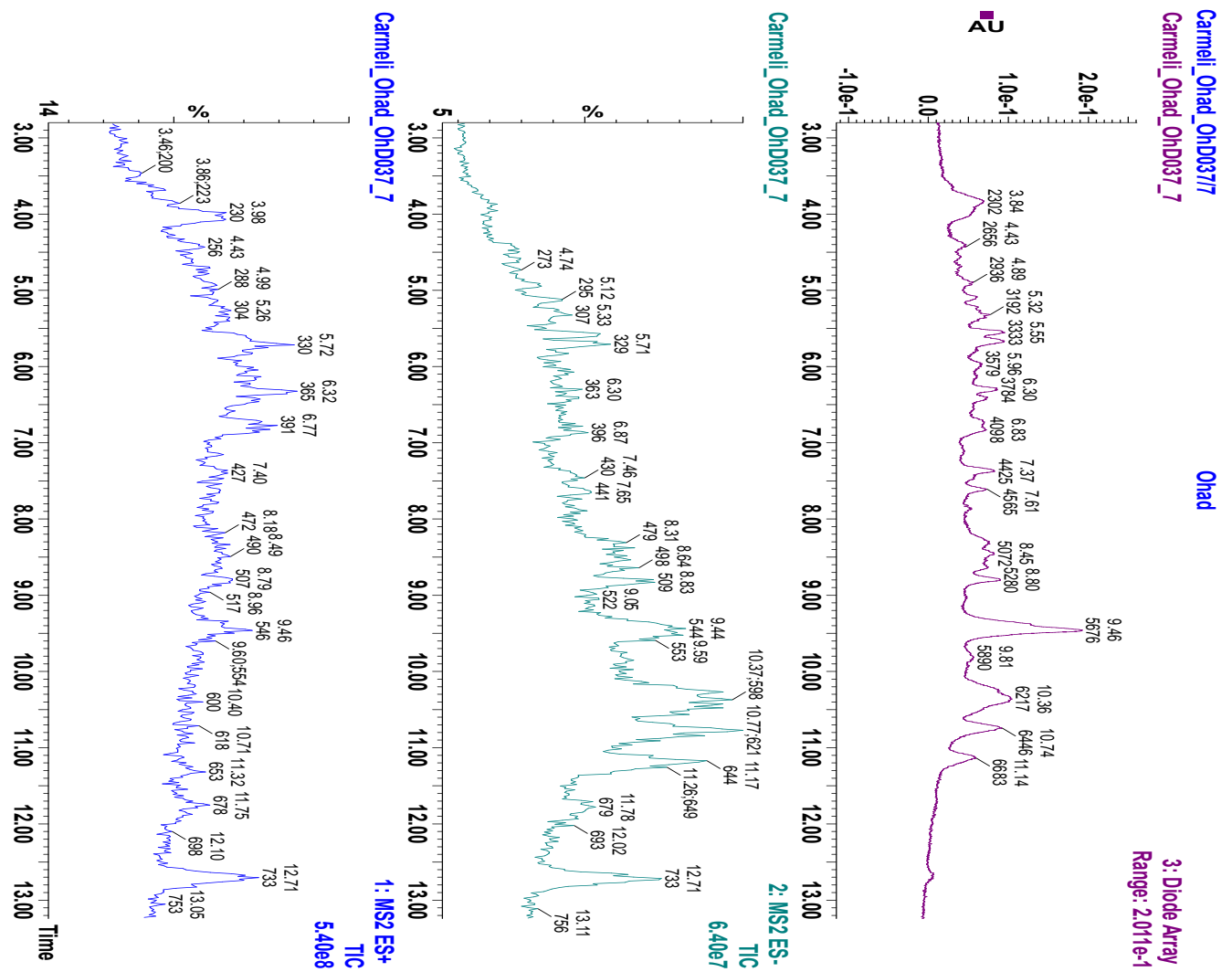


S2 Table S1. Molecular peaks (negative-ESI) and partial identifications of the theonellamides in the chromatograms.

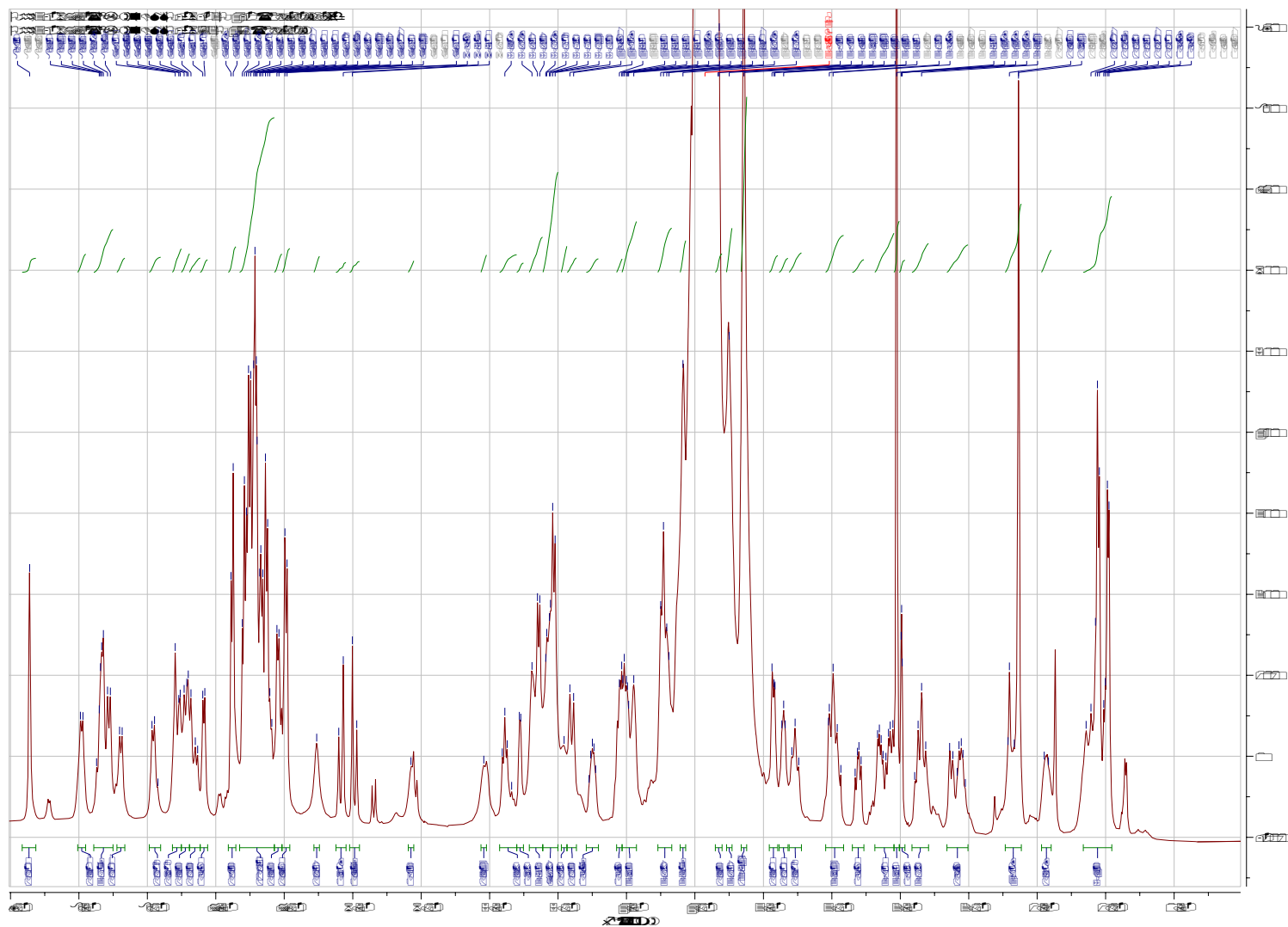
t_R min	10 m sample m/z (id)	15 m sample m/z (id)	25 m sample m/z (id)	30 m sample m/z (id)	59 m sample m/z (id)	64 m sample m/z (id)
9.7			1778, 1602		1778, 1602	1584, 1602
9.5	1746 (Tpl)	1746 (Tpl)	1746 (Tpl)	1746 (Tpl)	1746 (Tpl)	1746 (Tpl)
9.4					1716, 1730	1716, 1730
9.0			1762 (TnlA)			
8.9	1668 (TnlK)	1668 (TnlK)	1668 (TnlK)	1668 (TnlK)	1668 (TnlK)	1668 (TnlK)
8.7			1780 (TnlD*)		1778	
8.6			1780 (TnlD*)			
8.3			1780 (TnlD*)		1780 (TnlD*)	1780 (TnlD*)
8.2					1794	1794
8.0			1780 (TnlD*)		1780 (TnlD*)	1780 (TnlD*)
7.7			1780 (TnlD*), 1808,		1778, 1808	1780 (TnlD*), 1808
7.5			1808		1808, 1602	1808, 1602
7.3			1780 (TnlD*)			1780 (TnlD*)
6.9			1702, 1730		1780 (TnlD*)	1780 (TnlD*)
			1780 (TnlD*)			
6.6			1670			
6.1	1602		1602, 1678	1602		
5.8		1602, 1618	1618		1602, 1618	1602, 1618
5.6			1620, 1602, 1590		1602	1602
5.5			1620, 1602			

Tpl – theopalauamide; TnlA – theonellamide A; TnlK – theonellamide K, this study; TnlD* - theonellamide D or isomer of it.

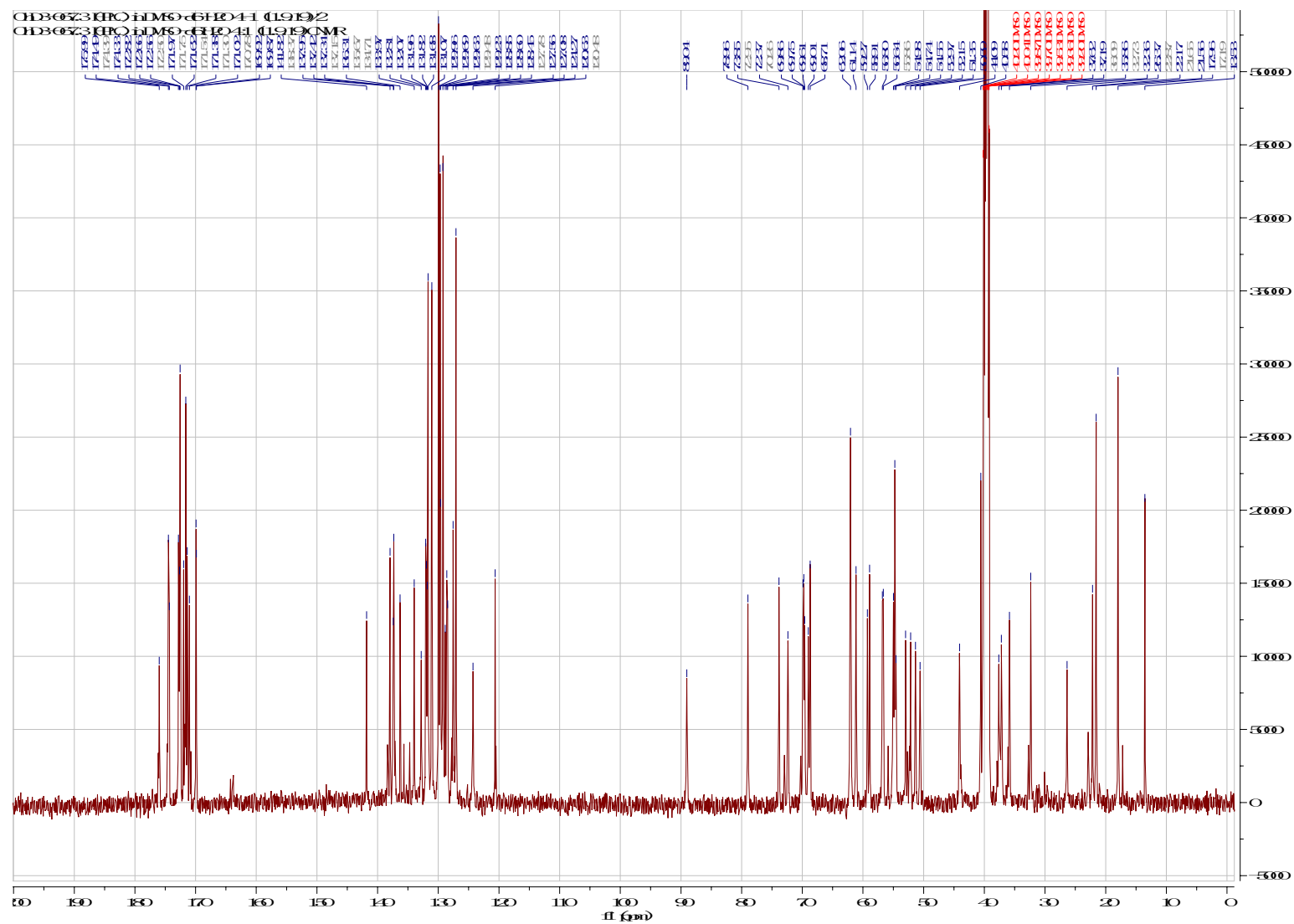
S3 Figure S2 LCMS chromatogram of *T. swinhoei* samples collected in the southern part of the Gulf of Aqaba during the 1980's.



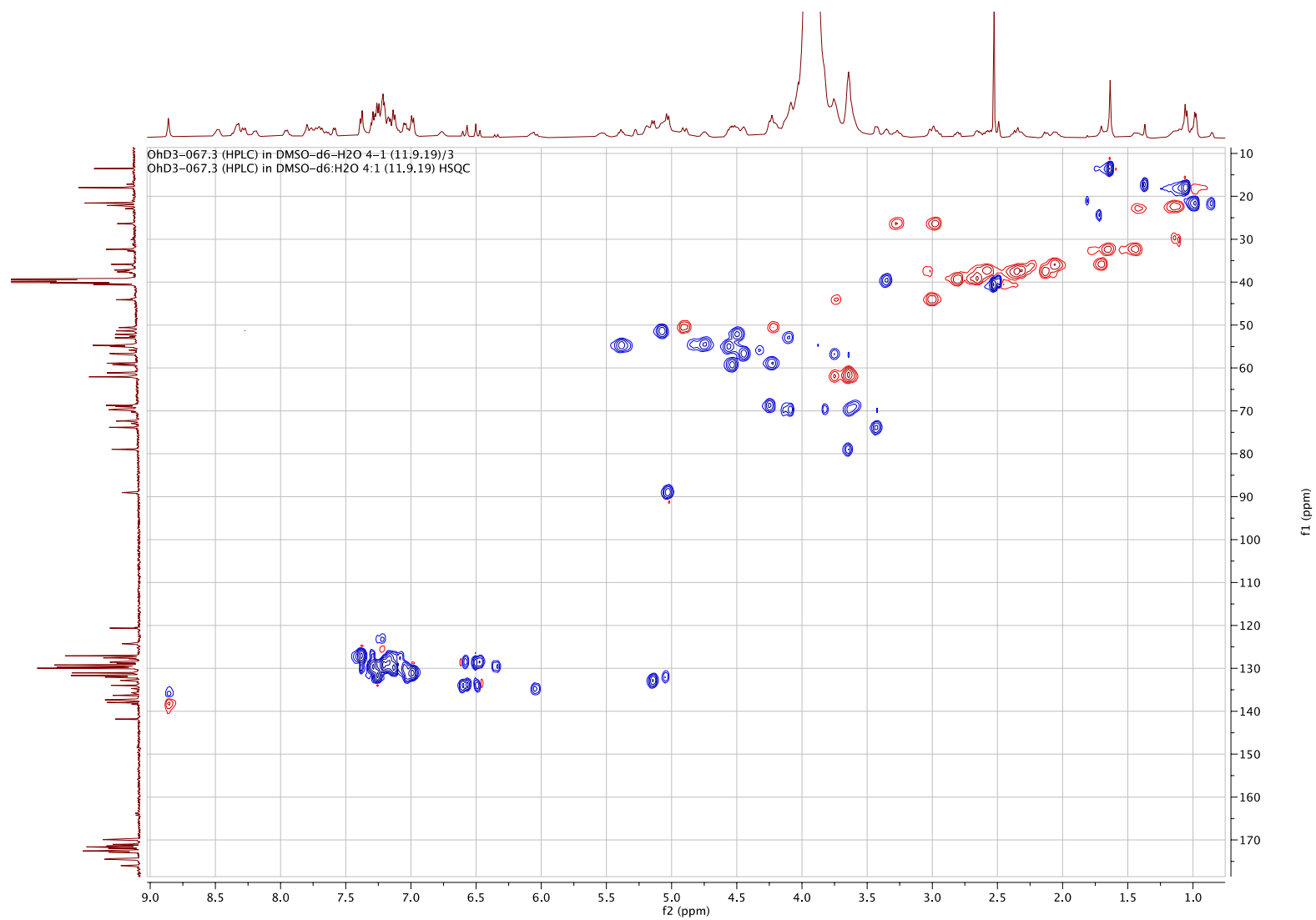
S4 Figure S3. ^1H NMR spectrum (500 MHz) of theopalauamide (**4**) in 4:1 $\text{DMSO-}d_6\text{:H}_2\text{O}$ at 50 °C



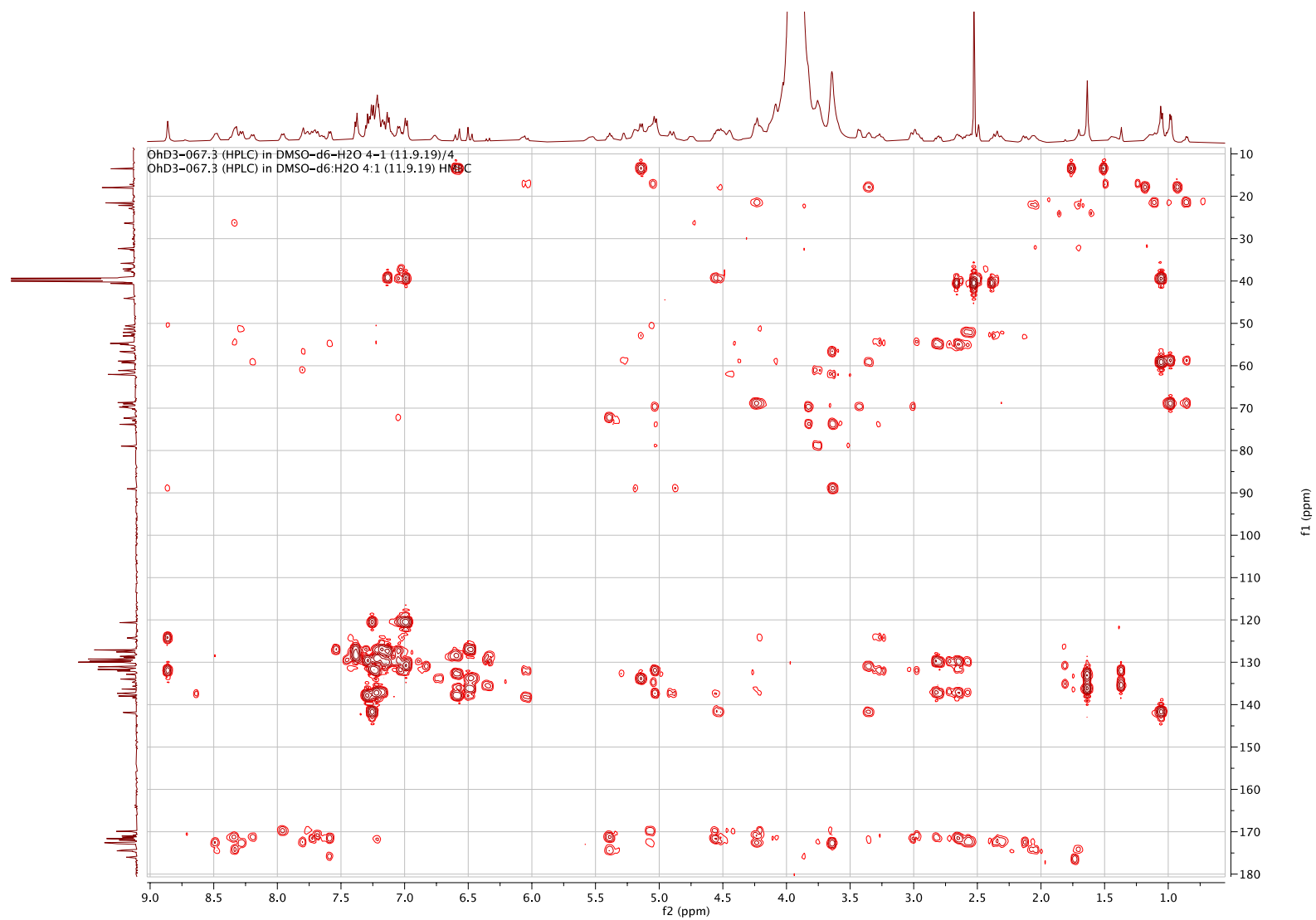
S5



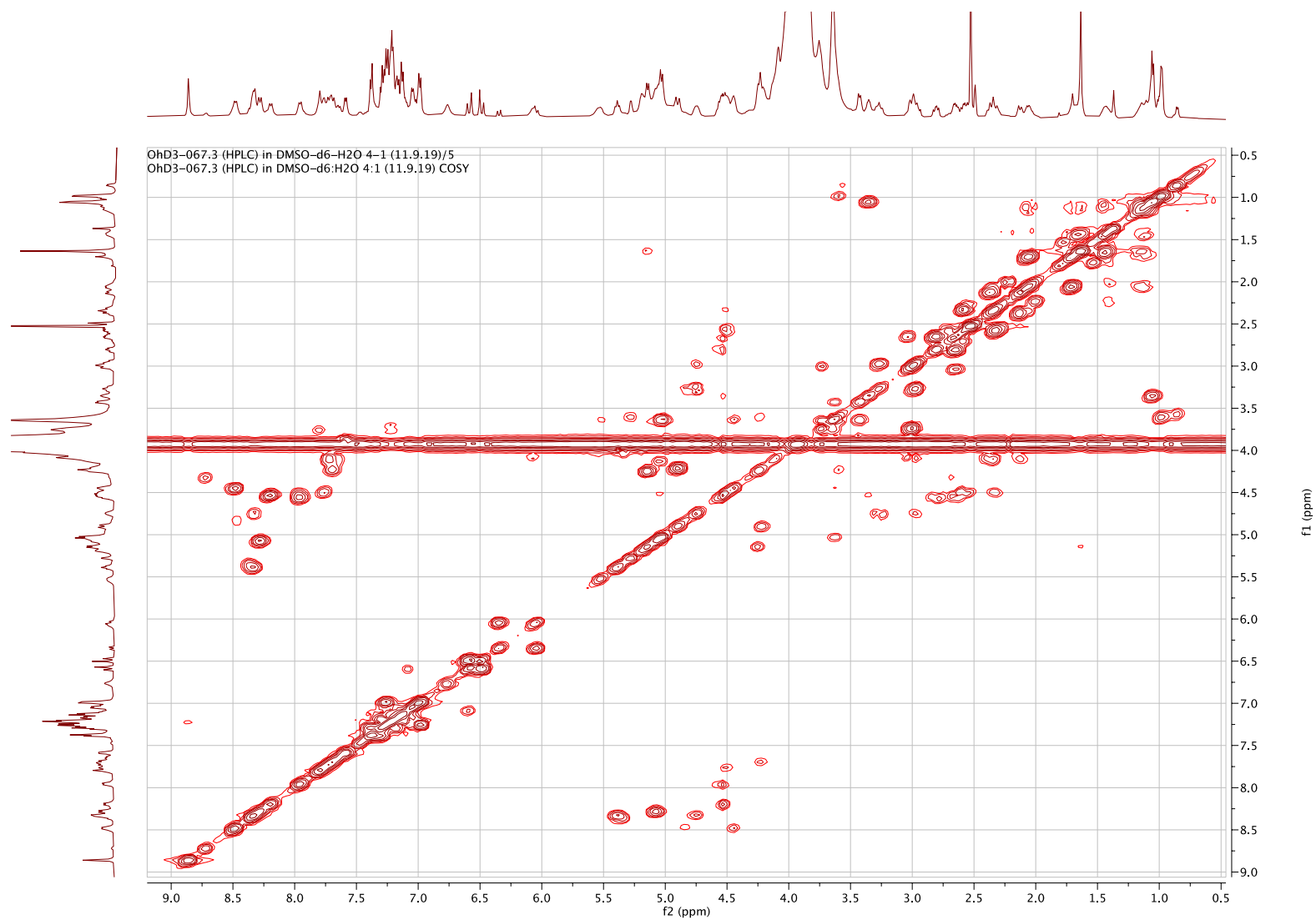
S6 Figure S5. HSQC spectrum of theopalauamide (**4**) in 4:1 DMSO- d_6 :H₂O at 50 °C



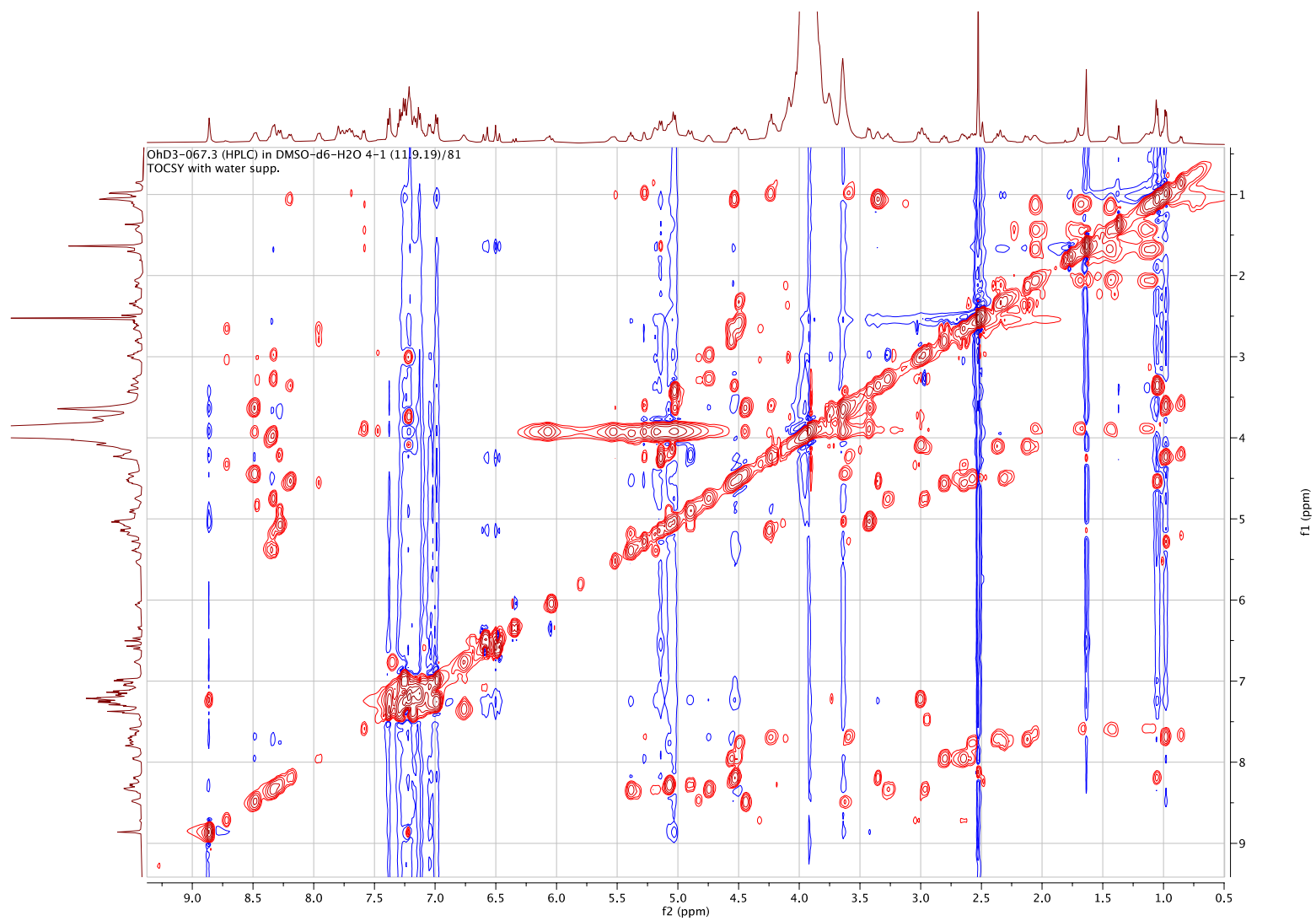
S7 Figure S6. HMBC spectrum of theopalauamide (**4**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



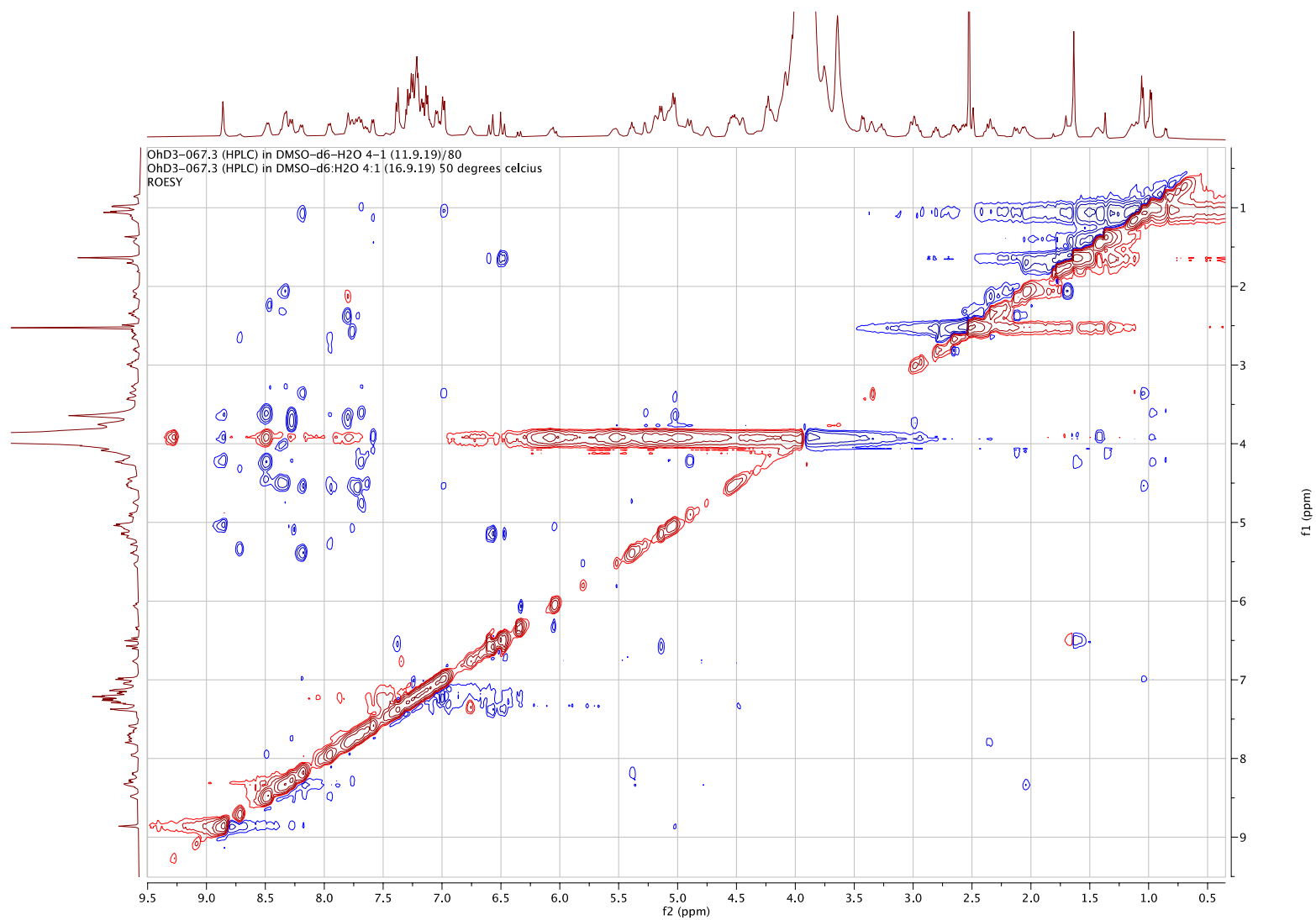
S8 Figure S7. COSY spectrum of theopalauamide (**4**) in 4:1 DMSO- d_6 :H₂O at 50 °C



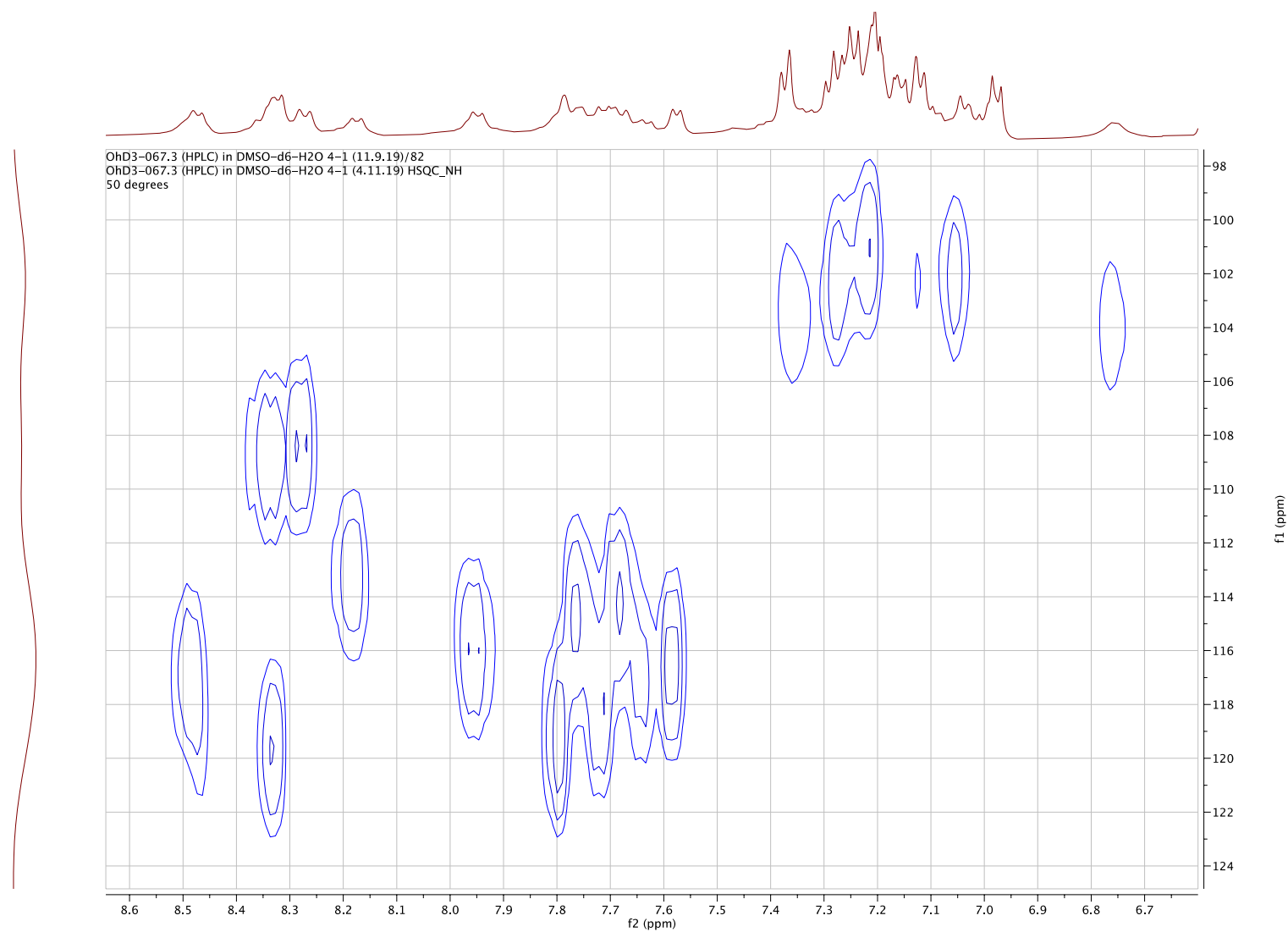
S9 Figure S8. TOCSY spectrum of theopalauamide (**4**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S10 Figure S9. ROESY spectrum of theopalauamide (**4**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S11 Figure S10. N-H HSQC spectrum of theopalauamide (**4**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



S12 Figure S11. N-H HMBC spectrum of theopalauamide (**4**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S13 Table S2. NMR data of theopalauamide (4) in 4:1 DMSO-*d*₆:H₂O at 50 °C^a

Position	$\delta_{C/N}^b$	δ_H^c	HMBC correlations ^d	COSY correlations	NOE correlations ^e
Apoa-1	172.6, C				
2a	37.6, CH ₂	2.37, m	Apoa-1,3	Apoa-2b,3	Ser ¹ -NH, Apoa-NH
b		2.10, brd (10.7)	Apoa-1,3	Apoa-2a,3	
3	53.0, CH	4.11, m		Apoa-2a,2b, NH	Apoa-NH
3-NH	117.7, NH	7.72, d (9.7)	Phe-1	Apoa-3	Apoa-2a,3,4, 5, Phe-2
4	68.7, CH	4.25, m	Apoa-5	Apoa-5	Phe-NH, Apoa-NH,4-OH
4-OH		5.28, d (4.4)	Apoa-5		Apoa-4,5
5	132.8, CH	5.14, brd (8.3)	Apoa-3,6-Me,7	Apoa-4,6-Me,	Apoa-NH, 7,8
6	136.3, C				
6-Me	13.5, CH ₃	1.64, brs	Apoa-5,6,7	Apoa-5	Apoa-7,8
7	134.0, CH	6.58, d (17.1)	Apoa-5,6,6-Me,8,9	Apoa-8	Apoa-5,6-Me
8	128.6, CH	6.49, d (17.1)	Apoa-6,7,9, 10,10'	Apoa-7	Apoa-5,6-Me
9	138.0, C				
10,10'	127.1, CH x 2	7.38, d (7.6)	Apoa-8,10', 10,12	Apoa-11,11'	
11,11'	129.7, CH x 2	7.29, t (7.6)	Apoa-9,10, 10',11',11	Apoa-10, 10',12	
12	128.9, CH	7.17, m	Apoa-10,10'	Apoa-11,11'	
Ser ¹ -1	172.8, C				
2	56.8, CH	3.76, m	Ser ¹ -3	Ser ¹ -3	sAla-NH
2-NH	114.9, NH	7.80, brs	Apoa-1, Ser ¹ -2,3	Ser ¹ -2	Apoa-2a, Ser ¹ -3
3	61.1, CH ₂	3.64, m	Ser ¹ -1,2	Ser ¹ -2	sAla-NH, Ser ¹ -NH
3-OH					
sAla-1	169.87, C				
2	51.4, CH	5.07, m	sAla-1	sAla-2-NH, 3a,3b	Asn-NH, sAla-NH,3b
2-NH	108.3, NH	8.28, d (10.3)	Ser ¹ -1	sAla-2	sAla-2,3b, Ser ¹ -2,3
3a	50.6, CH	4.90, brd (13.7)	sHis-6,8	sAla-2,3b	sHis-8
		4.21, m			
b			sAla-1, sHis-6,8	sAla-2,3a	sHis-6, sAla-NH,2
Asn-1	171.6, C				

2	52.2, CH	4.50, m	Asn-1,3	Asn-NH,3a, 3b	Asn-NH,3b
2-NH	119.2, NH	7.77, d (5.3)	sAla-1, Asn-2,3	Asn-2	sAla-2, Asn-2,3a
3a	37.2, CH ₂	2.58, dd (15.5, 9.5)	Asn-1,2,4	Asn-2,3b	Asn-N
b		2.35, dd (15.5, 12.9)	Asn-1,2,4	Asn-2,3a	Asn-2
4	172.5, C				
4-NH ₂	103.8, NH ₂	7.37, brs 6.76, brs			
Han-1	171.4, C				
2	54.7, CH	5.39, t (8.6)	Han-1,3,4	Han-NH,3	BrMePhe-NH, sHis-2
2-NH	108.7, NH	8.35, m	Han-1	Han-2	
3	72.4, CH	3.98, m		Han-2,3-OH	
3-OH		5.19, brd (4.1)		Han-3	
4	174.5, C				
4-NH ₂	102.1, NH ₂	7.05, m 7.28, m	Han-3		
BrMePhe-1	172.0, C				
2	59.3, CH	4.54, m	BrMePhe-1,3,3-Me,4	BrMePhe-NH,3	BrMePhe-NH,3,3-Me,5,5'
2-NH	113.1, NH	8.19, d (8.7)	Han-1, BrMePhe-2,	BrMePhe-2	Has-2, BrMePhe-2,3,3-Me
3	39.5, CH	3.35, qd (6.8,5.2)	BrMePhe-1,2,3-Me,4,5,5'	BrMePhe-2,3-Me	BrMePhe-NH,2
3-Me	18.0, CH ₃	1.05, d (6.8)	BrMePhe-2,3,4	BrMePhe-3	BrMePhe-NH,2,5,5'
4	141.8, C				
5,5'	131.1, CH x 2	6.99, d (8.1)	BrMePhe-3,5',5,7	BrMePhe-6,6'	BrMePhe-2,3-Me
6,6'	131.7, CH x 2	7.26, d (8.1)	BrMePhe-4,6',6,7	BrMePhe-5,5'	
7	120.6, C				
iSer-1	171.4, C				
2	69.8, CH	4.09, m	iSer-1	iSer-2-OH, 3a,3b	Aad-NH
2-OH		5.03 m	iSer-2	iSer-2	
3a	44.0, CH ₂	3.74, m	BrMePhe-1	iSer-2,3b, NH	
b		3.01, brd (14.1)	BrMePhe-1, iSer-1	iSer-2,3a, NH	
3-NH	101.2, NH	7.22, m	BrMePhe-1	iSer-3a,3b	
Aad-1	176.0, C				
2	54.7, CH	3.91, m	Aad-1,3,4		Aad-NH,3a, 3b, sHis-6,8

2-NH	116.5, NH	7.59, d (7.5)	iSer-1, Aad-1		Aad-2,3b,4, iSer-2
3a	32.4, CH ₂	1.65, m		Aad-3b	Aad-2
b		1.44, m	Aad-4	Aad-3a,4	Aad-NH,2
4	22.2, CH ₂	1.12, m		Aad-3b,5a,5b	Aad-NH
5a	35.9, CH ₂	2.06, m	Aad-3,4,6	Aad-4,5b	sHis-NH
b		1.70, m	Aad-3,4,6	Aad-4,5a	
6	174.3, C				
sHis-1	171.0, C				
2	54.6, CH	4.75, dt (13.0,6.5)	sHis-1,3	sHis-NH,3a,3b	Thr-NH, Han-2
2-NH	119.7, NH	8.33, m	Aad-6, sHis-1,2,3	sHis-2	Ada-2a
3a	26.4, CH ₂	3.27, t (13.0)	sHis-1,2,4,8	sHis-2,3b	Thr-NH
b		2.98, m	sHis-1,2,4	sHis-2,3a	Thr-NH
4	132.0, C				
5-N	180.9, N				
6	137.4, CH	8.86, s	sHis-5-N,7-N,4,8, Gal-1, sAla-3a,3b	sHis-8	Gal-1,2,5, sAla-3a, Ada-5
7-N	167.9, N				
8	124.3, CH	7.22, m	sHis-5-N,7-N,4,6 sAla-3	sHis-6	sAla-3a, Ada-5
Thr-1	172.7, C				
2	58.9, CH	4.23, m	Thr-1,3,4	Thr-NH,3	Ser ² -NH, Thr-NH,4
2-NH	114.3, NH	7.69, d (9.7)	sHis-1, Thr-2	Thr-2	sHis-2,3a,3b Thr-2,3,4,
3	69.0, CH	3.60, m	Thr-1	Thr-2,4	Thr-NH,4
3-OH		4.90, m		Thr-2,3	
4	21.6, CH ₃	0.98, d (5.3)	Thr-2,3	Thr-3	Thr-NH,2,3
Ser ² -1	169.92, C				
2	56.6, CH	4.45, m			Ser ² -NH
2-NH	117.0, NH	8.48, d (7.8)	Thr-1		Ser ² -2,3, Thr-2
3	62.1, CH ₂	3.64, m			Ser ² -NH
3-OH					
Phe-1	171.6, C				
2	55.0, CH	4.56, m	Ser ² -1		Phe-NH,5,5' Apoa-NH
2-NH	115.9, NH	7.96, d (8.7)	Ser ² -1		Phe-2,3a,3b, Apoa-4-OH

3a	39.4, CH ₂	2.81, dd (13.0,8.0)			Phe-NH
b		2.65, dd (13.0,5.6)			Phe-NH
4	137.3, C				
5,5'	130.0, CH x 2	7.13, d (7.5)			Phe-2
6,6'	129.2, CH x 2	7.21, m			
7	127.7, CH	7.14, m			
Gal-1	89.0, CH	5.03, d (9.3)	sAla-3, sHis-4, Gal-3,5	Gal-2	sHis-6, Gal-3,6b
2	69.9, CH	3.63, m		Gal-1,2-OH, 3	sHis-6
2-OH		5.53, brd (10.4)		Gal-2	
3	73.9, CH	3.43, brd (8.1)	Gal-4	Gal-2	Gal-1
4	69.6, CH	3.83, m	Gal-2,3		
5	79.0, CH	3.64, m	Gal-1,3,6		sHis-6
6a	62.0, CH ₂	3.75, m	Gal-5	Gal-6b	
b		3.64, m		Gal-6a	Gal-1

^a¹H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). ^bMultiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz). ^dHMBC correlations, optimized for 8 Hz. ^eSelected NOEs from ROESY experiment.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

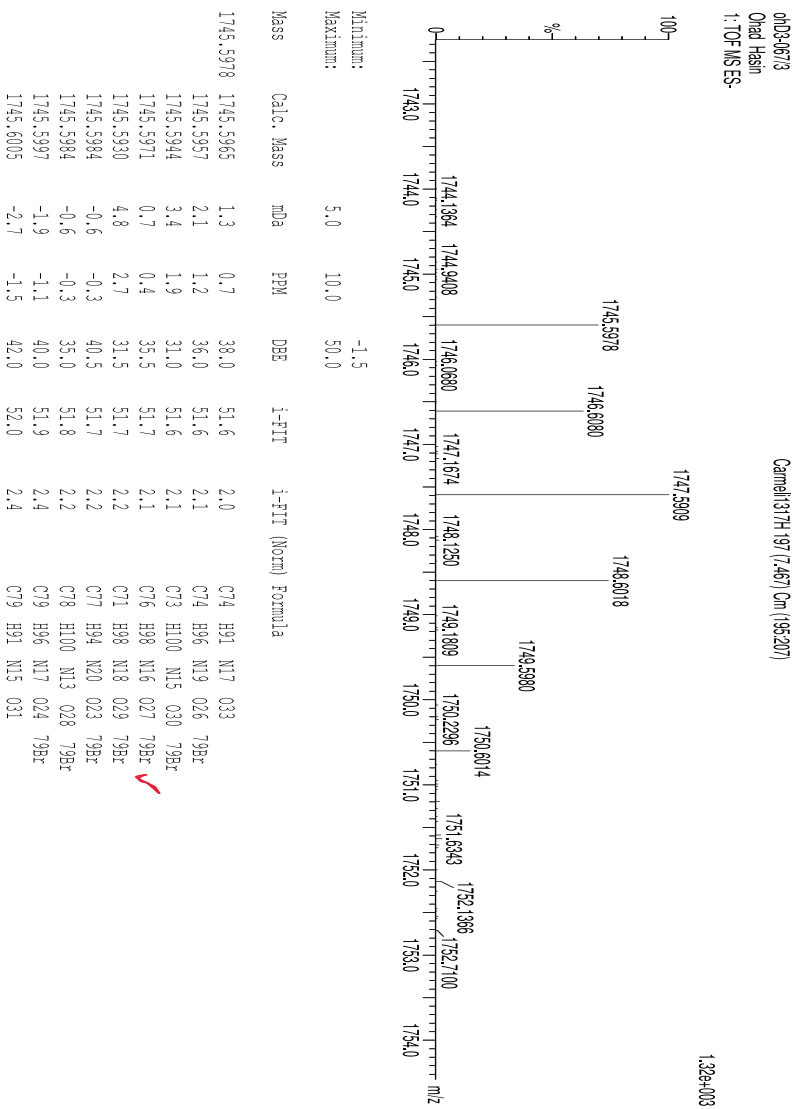
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions

114 formula(e) evaluated with 9 results within limits (up to 50 best isotopic matches for each mass)

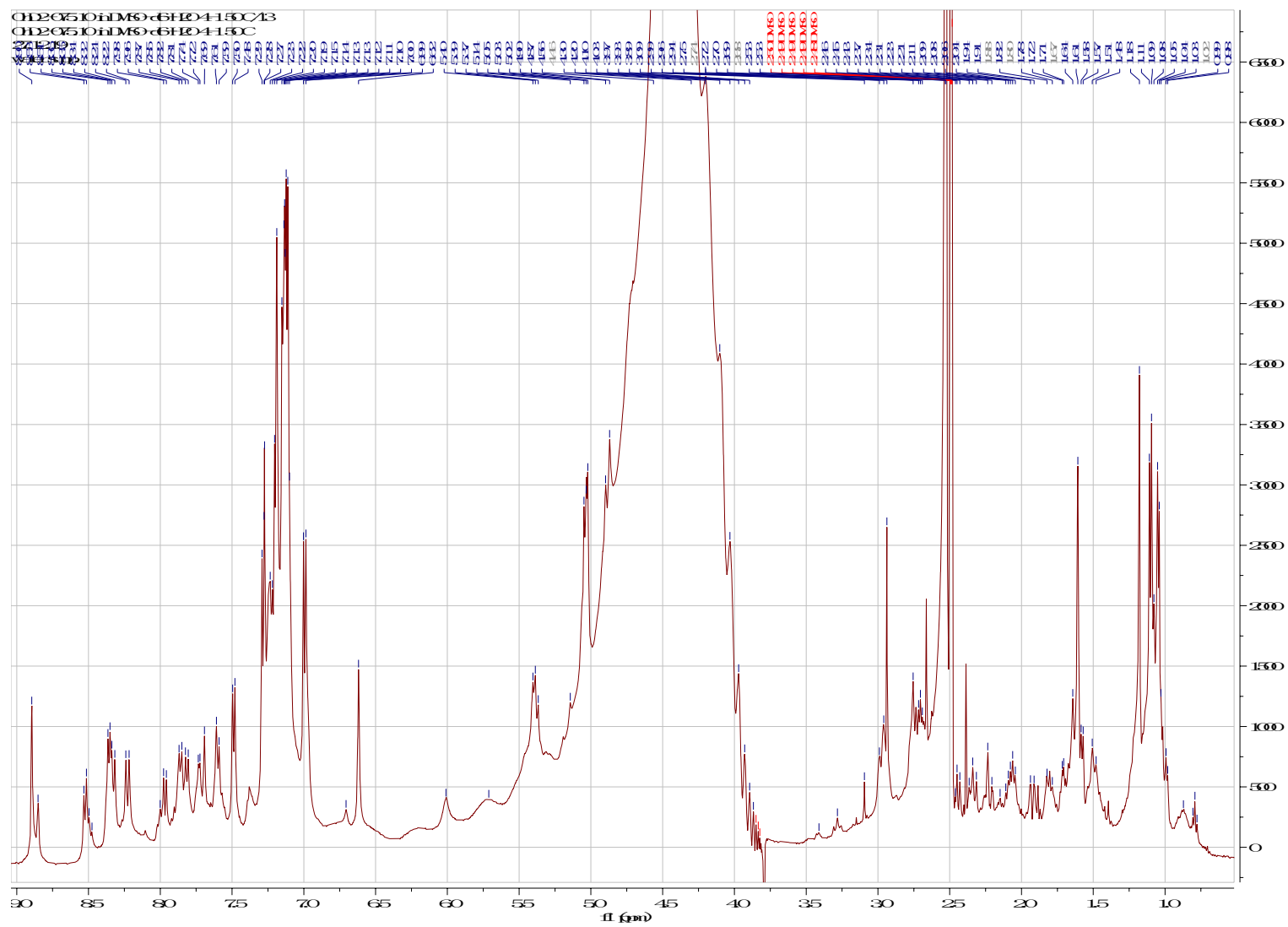
Elements Used:

C: 70-80 H: 90-100 N: 10-20 O: 23-33 79Br: 0-1

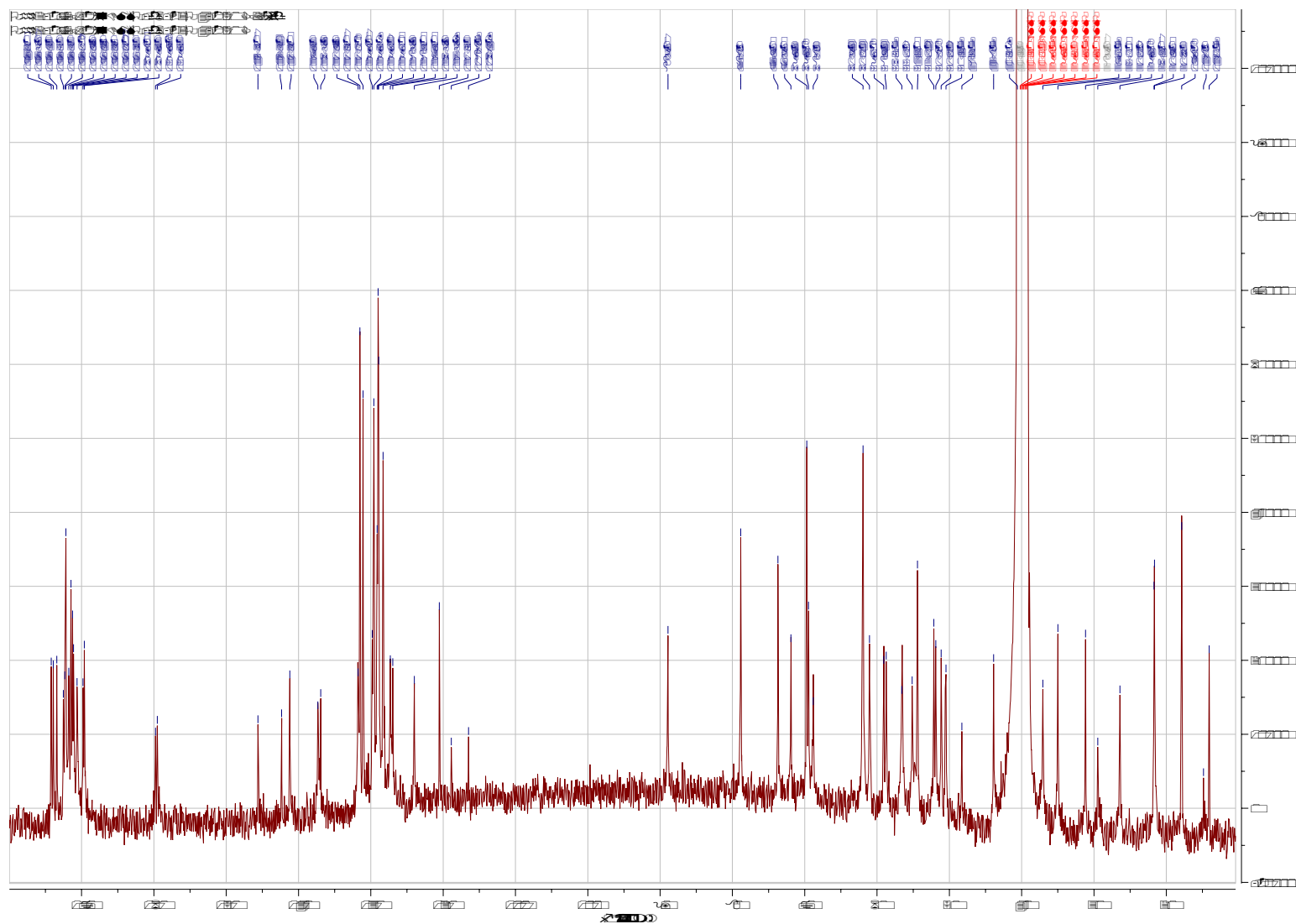


S14 Figure S12. (+)-HRESIMS data of theopalauamide (**4**)

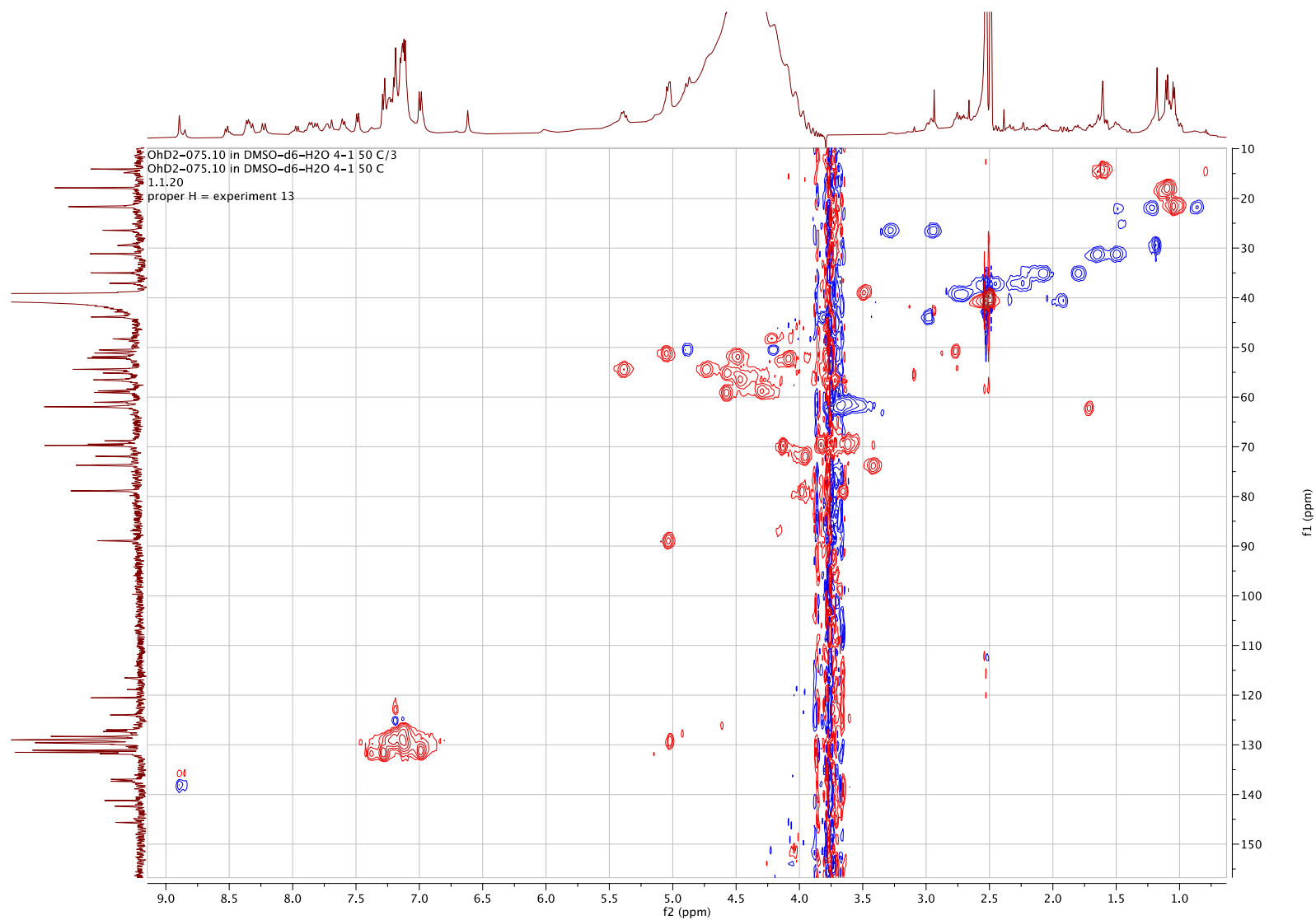
S15 Figure S13. ^1H NMR spectrum (500 MHz) of theonellamide J (**1**) in 4:1 $\text{DMSO}-d_6$: H_2O at 50 $^\circ\text{C}$



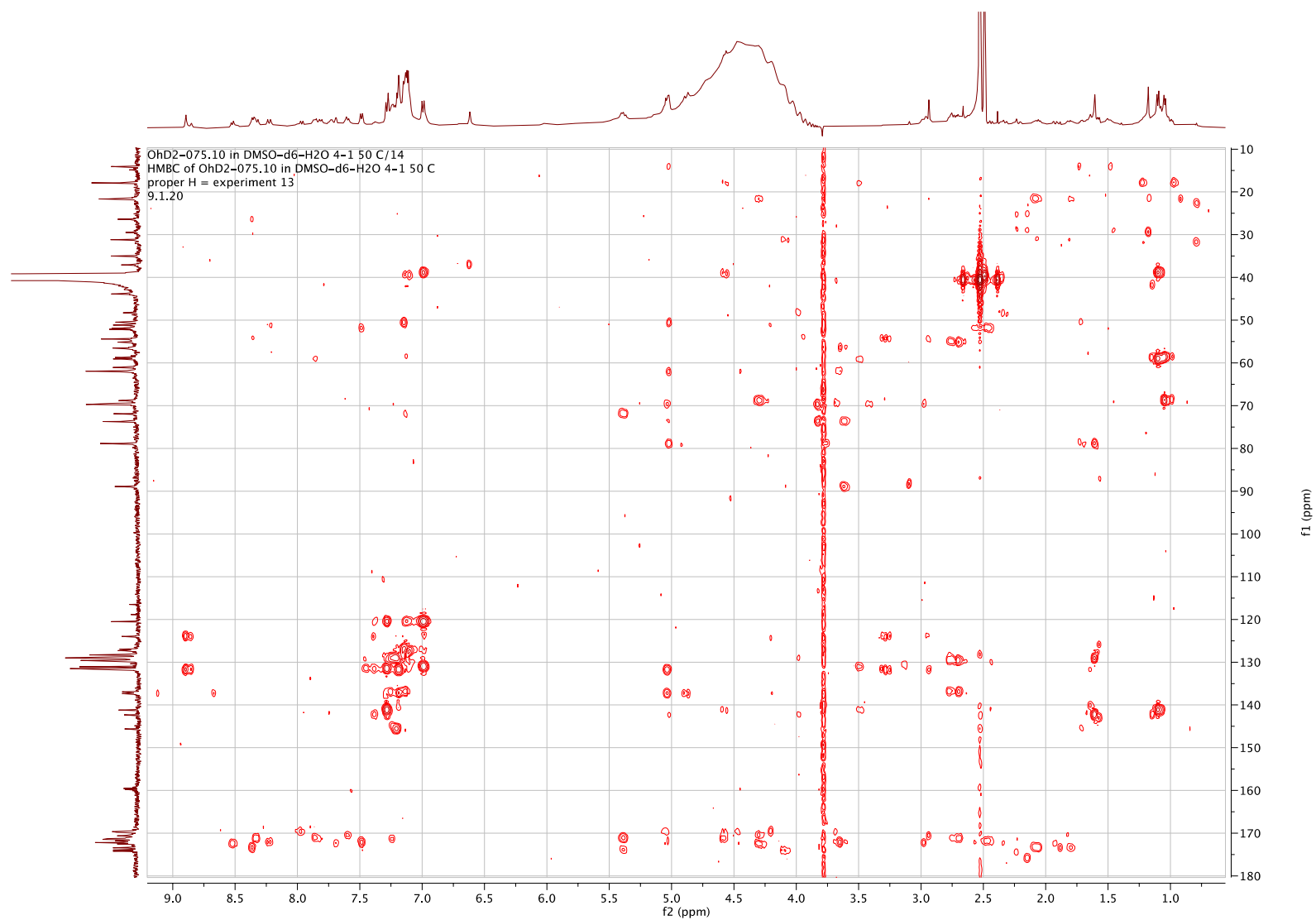
S16 Figure S14. ^{13}C NMR spectrum (125 MHz) of theonellamide J (**1**) in 4:1 DMSO- d_6 :H $_2$ O at 50 °C



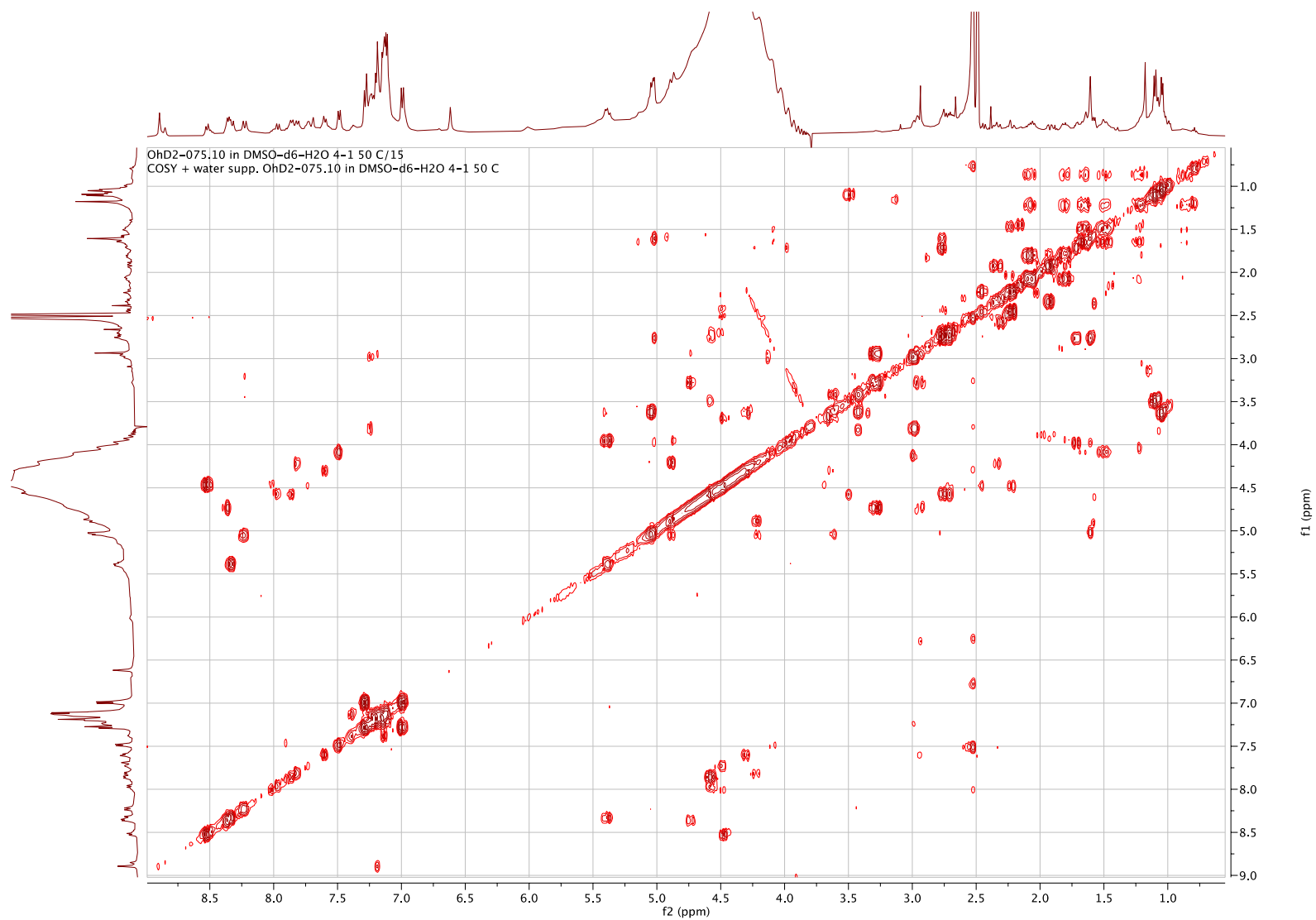
S17 Figure S15. HSQC spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C



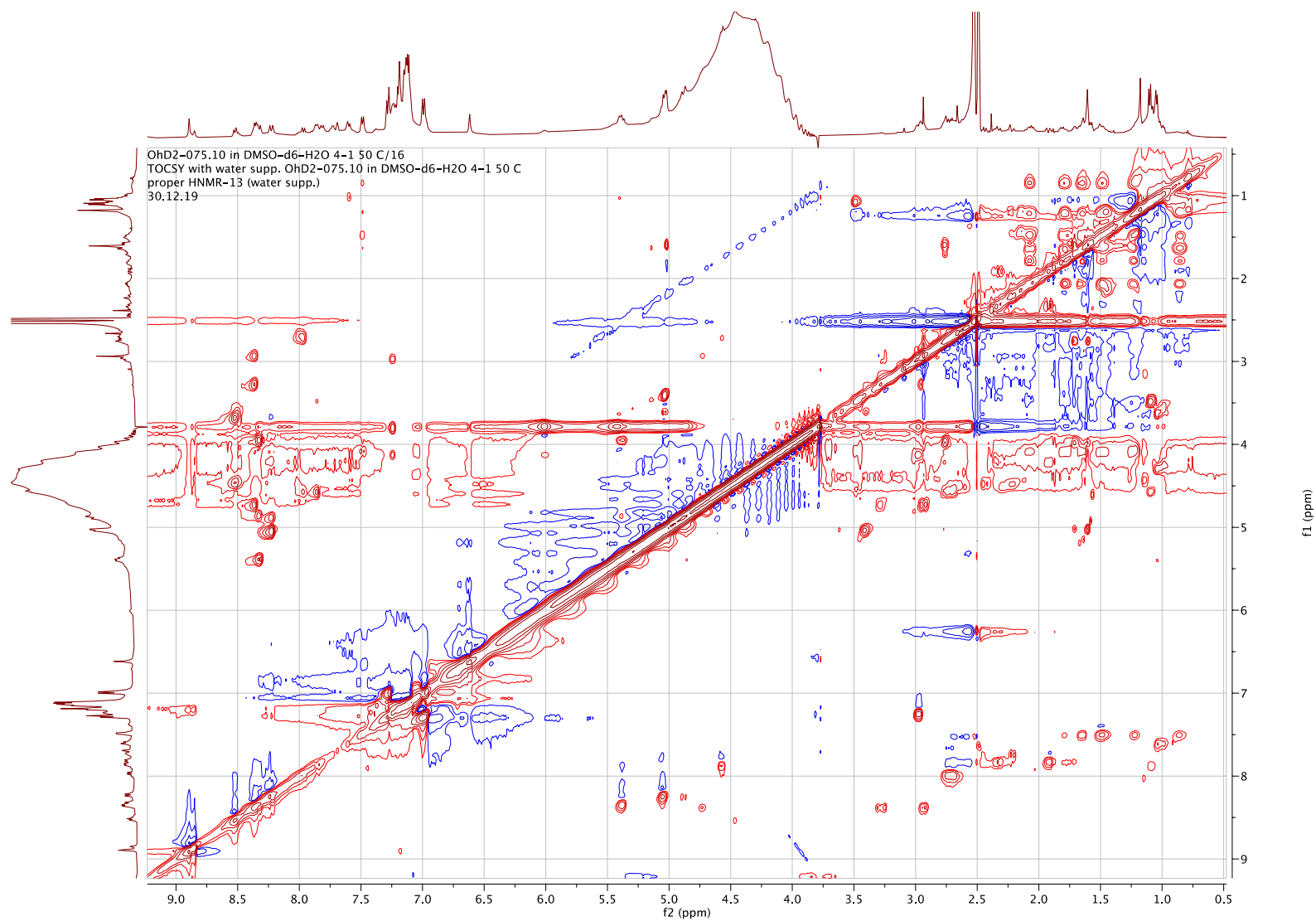
S18 Figure S16. HMBC spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C



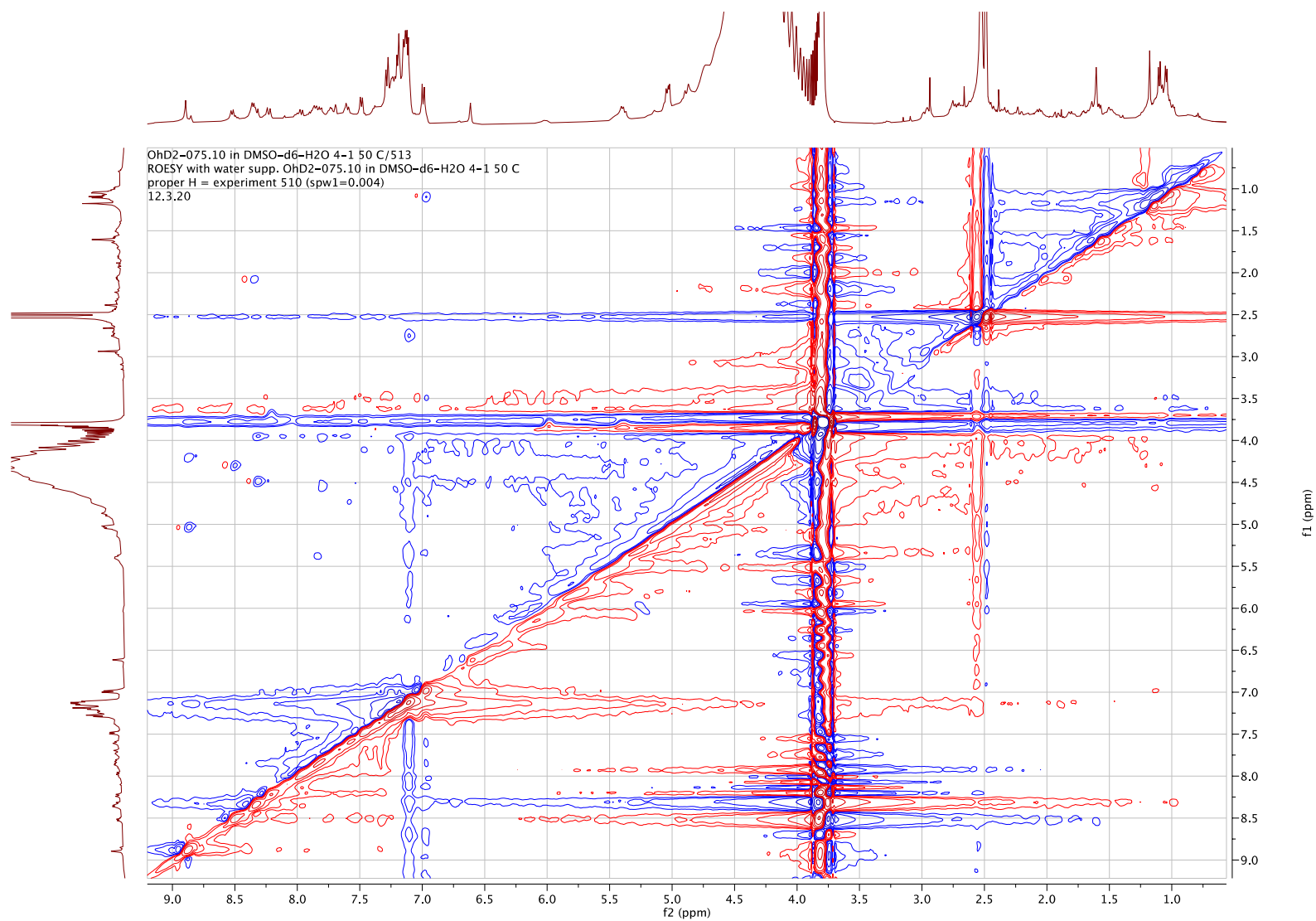
S19 Figure S17. COSY spectrum of theonellamide J (**1**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



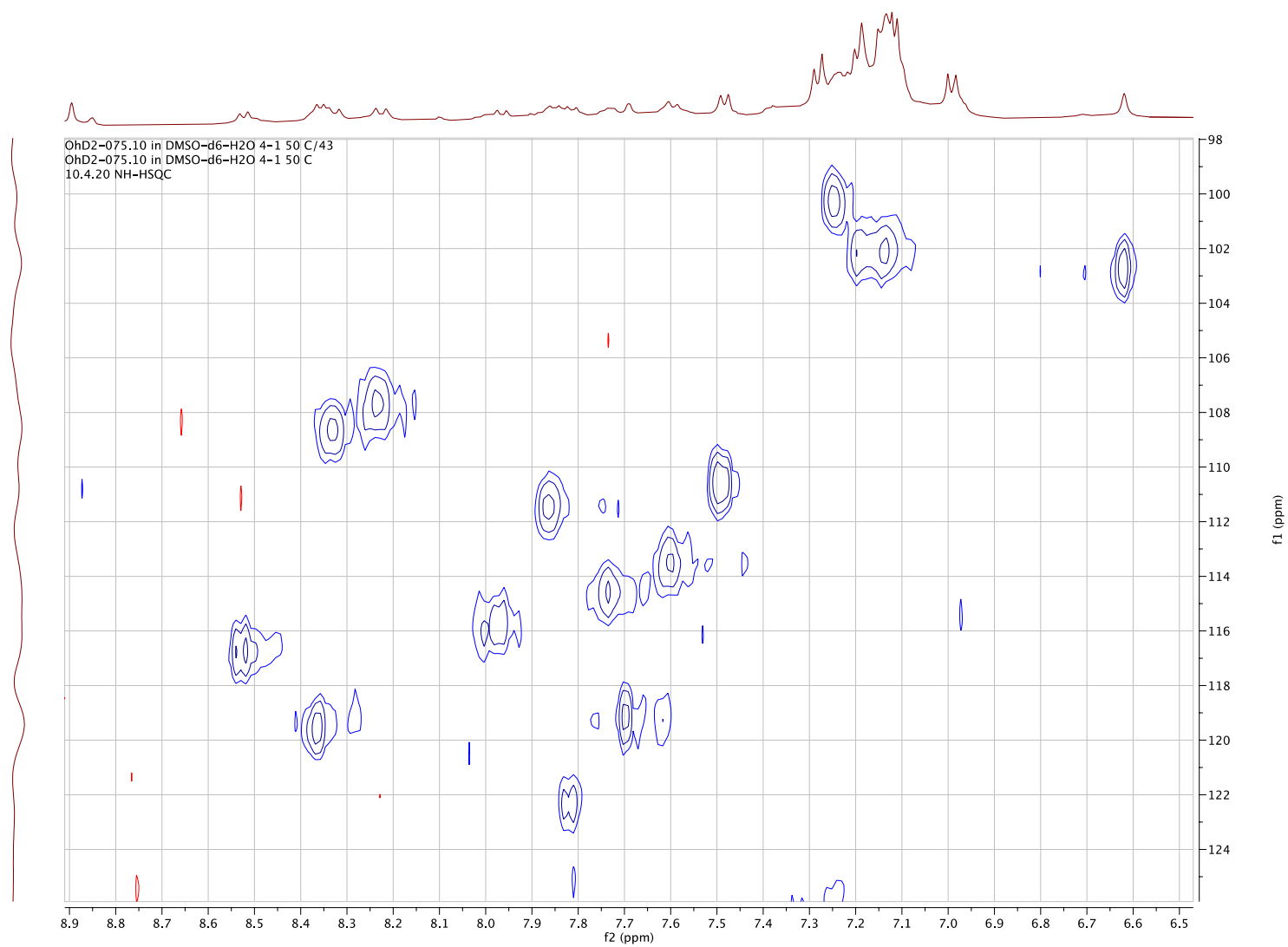
S20 Figure S18. TOCSY spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S21 Figure S19. ROESY spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S22 Figure S20. N-H HSQC spectrum theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S23 Figure S21. N-H HMBC spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :H₂O at 50 °C

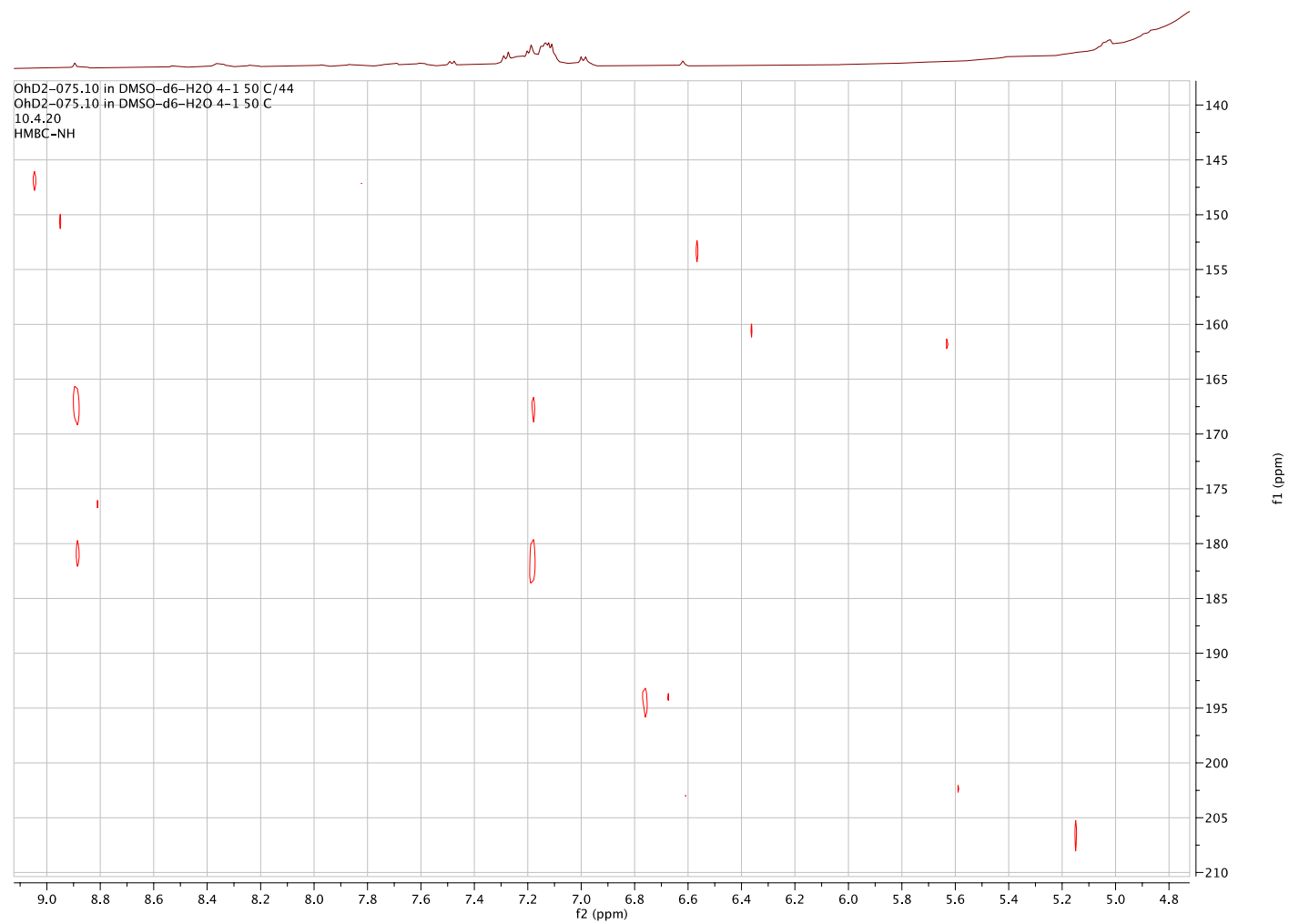


Table S3. NMR data of theonellamide J (**1**) in 4:1 DMSO-*d*₆:H₂O at 50 °C^a

Position	δ _{C/N} ^b	δ _H ^c	HMBC correlations ^d	COSY correlations	TOCSY correlations
Apcoa-1	171.8, C				
2a	40.4, CH ₂	2.33, t (13.1)	Apcoa-3	Apcoa-2b,3	Apcoa-2b,3
b		1.93, dd (13.1,3.0)	Apcoa-1	Apcoa-2a,3	Apcoa-2a,3
3	48.3, CH	4.22, m		Apcoa-2a,3-NH	Apcoa-NH-3
3-NH	122.3, NH	7.82, d (9.1)	Phe-1	Apcoa-3	Apcoa-2a,2b,3 ,4
4	62.1, CH	1.71, ddd (10.4, 6.6., 4.5)	Apcoa-5,6,7,9		Apcoa-3-NH,5,7,8
5	78.9, CH	3.98, m	Apcoa-3	Apcoa-6-Me	Apcoa-4,6-Me, 8
6	142.3, C				
6-Me	14.1, CH ₃	1.61, brs	Apcoa-5,6,7	Apcoa-7	Apcoa-5,7,8
7	129.1, CH	5.02, brs	Apcoa-4,6,8	Apcoa-5,6-Me	Apcoa-4,6-Me, 8
8	50.6, CH	2.76, m	Apcoa-10,10'	Apcoa-4,6-Me, 7	Apcoa-4,5,6-Me,7
9	145.6, C				
10,10'	128.3, CH x 2	7.14, d x 2 (7.6)	Apcoa-8,10',10,12		
11,11'	129.0, CH x 2	7.20, t x 2 (7.6)	Apcoa- 9,11',11		
12	127.0, CH	7.13, m			
Ser ¹ -1	172.3, C				
2	56.6, CH	3.71, m			
2-NH	119.2, NH	7.69, brs			
3	61.9, CH ₂	3.62, m 2H	Ser ¹ -1,3		
sAla-1	169.6, C				
2	51.1, CH	5.04, m	sAla-1	sAla-2-NH,3a, 3b	
2-NH	107.7, NH	8.23, d (11.1)	Ser ¹ -1, sAla-2	sAla-2,3a,3b	sAla-2,3a, 3b
3a	50.5, CH ₂	4.88, d (13.2)	sAla-2, sHis-6	sAla-2,3a,3b	
b		4.22, m	sAla-1,2, sHis-8		
Asn-1	171.5, C				
2	51.9, CH	4.48, brm	Asn-1	Asn-2-NH,3a,3b	Asn-2-NH
2-NH	114.6, NH	7.73, d (5.5)	Asn-1	Asn-2	Asn-2,3a,3b
3a	37.1, CH ₂	2.45, m	Asn-4,2	Asn-2,3b	Asn-2-NH,

b		2.24, m		Asn-2,3a	Asn-2-NH
4	172.2, C				
4-NH ₂	102.7, NH ₂	7.31, brs 6.62, s	Asn-3		
Han-1	171.5, C				
2	54.4, CH	5.39, m	Han-1,3,4	Han-2-NH,3	Han-2-NH,3
2-NH	108.7, <i>NH</i>	8.33, d (10.3)		Han-2	Han-2,3,3-OH
3	71.9, CH	3.95, m		Han-2,3-OH	Han-2,2-NH
3-OH		4.87, m			Han-2,2-NH
4	174.2, C				
4-NH ₂	102.2, <i>NH₂</i>	7.14, brs, 7.19, brs			
BrMePhe-1	171.1, C				
2	59.1, CH	4.58, m	BrMePhe-1	BrMePhe-2-NH,3	BrMePhe-2-NH
2-NH	111.5, <i>NH</i>	7.86, d (9.1)	Han-1	BrMePhe-2	BrMePhe-2,3-Me3
3	38.9, CH	3.49, m	BrMePhe-2,3,3-Me,4	BrMePhe-2	BrMePhe-2-NH, 3-Me
3-Me	17.9, CH ₃	1.10, d (7.2)	BrMePhe-2,3,4	BrMePhe-3	BrMePhe-2-NH, 3
4	141.2, C				
5,5'	131.1, CH x 2	6.99, d x 2 (8.4)	BrMePhe-3,5', 5,7	BrMePhe-6,6'	
6,6'	131.5, CH x 2	7.28, d x 2 (8.4)	BrMePhe-4,5, 5',6',6,7	BrMePhe-5,5'	
7	120.5, C				
iSer-1	172.2, C				
2	69.7, CH	4.13, m		iSer-3b	iSer-3b,3-NH
2-OH		5.42, brs	iSer-2		
3a	43.9, CH ₂	3.81, m	iSer-2	iSer-3b	iSer-3-NH
b		2.98, brd	BrMePhe-1, iSer-1,2	iSer-2,3a,3-NH	iSer-2,3-NH
3-NH	100.3, <i>NH</i>	7.24, m	BrMePhe-1	iSer-3a,3b	iSer-2,3a,3b
Ada-1	173.9, C				
2	52.2, CH	4.08, m	Ada-2	Ada-2-NH,3a, 3b	Ada-3a,3b,4a, 4b,5a,5b
2-NH	110.6, <i>NH</i>	7.49, d (7.2)	iSer-1, Ada-2	Ada-2	Ada-2,3a,3b, 4a,4b,5a,5b
3a	31.2, CH ₂	1.66, m		Ada-2,3b,4a, 4b	Ada-2,3b,4a, 4b,5a,5b

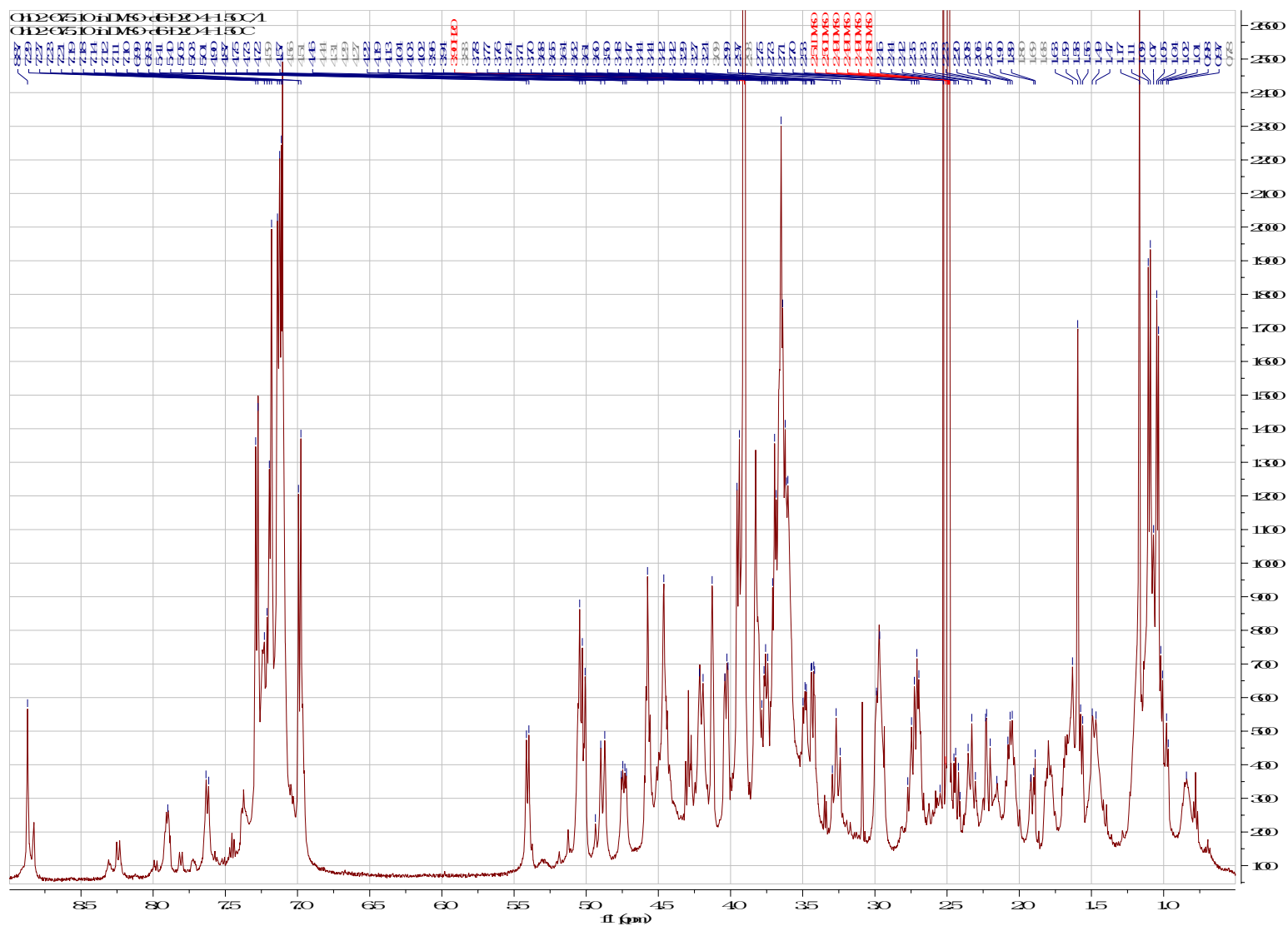
b		1.51, m	Ada-5	Ada-2,3a,3b, 4a	Ada-2,3a,4a, 4b,5a,5b
4a	21.7, CH ₂	1.22, m		Ada-3a,3b,4b, 5a,5b	Ada-2,3a,3b, 4b,5a,5b
b		0.88, m		Ada-3a,3b,4a, 5a,5b	Ada-2,3a,3b, 4a,5a,5b
5a	35.0, CH ₂	2.08, m	Ada-3,4,6	Ada-4a,4b,5b	Ada-2,3a,3b, 4a,4b,5b
b		1.80, m	Ada-4,6	Ada-4a,4b,5a	Ada-2,3a,3b, 4a,4b,5a
6	173.4, C				
sHis-1	170.6, C				
2	54.4, CH	4.73, m		sHis-2-NH, 3a,3b	sHis-2-NH, 3a,3b
2-NH	119.6, <i>NH</i>	8.36, d (7.2)	Ada-6	sHis-2	sHis-2,3a,3b
3a	26.4, CH ₂	3.28, brt (13.1)	sHis-2,4,8	sHis-2,3b	sHis-2,2-NH,3b
b		2.94, brd (13,1)	sHis-1	sHis-2,3a	sHis-2,2-NH,3a
4	131.9, C				
5-N	181.0, <i>N</i>				
6	137.3, CH	8.89, s	sHis-3,4,5,8,7-N, sAla-3	sHis-8	
7-N	167.4, <i>N</i>				
8	124.0, CH	7.19, s	sHis-4,5-N,6,7-N	sHis-6	
Thr-1	172.5, C				
2	58.7, CH	4.29, m	sHis-1, Thr-1,3, 4	Thr-2-NH,3	Thr-2-NH
2-NH	113.5, <i>NH</i>	7.60, d (9.7)	sHis-1	Thr-2	Thr-2,3,4
3	68.8, CH	3.63, m		Thr-2,3-OH,4	Thr-2-NH,4 7
3-OH		5.40, brs			Thr-4
4	21.6, CH ₃	1.04, d (6.0)	Thr-2,3	Thr-3	Thr-2-NH,3,3-OH
Ser ² -1	169.8, C				
2	56.5, CH	4.46, m	Ser ² -1	Ser ² -2-NH,3	Ser ² -2-NH
2-NH	116.7, <i>NH</i>	8.52, d (7.6)	Thr-1	Ser ² -2	Ser ² -2,3
3	62.0, CH ₂	3.68, m		Ser ² -2	Ser ² -2-NH
Phe-1	171.5, C				
2	55.2, CH	4.56, m		Phe-2-NH,3a, 3b	Phe-2-NH,3a, 3b
2-NH	115.8, <i>NH</i>	7.97, d (9.1)	Ser ² -1	Phe-2	Phe-2,3a,3b
		(8.01, d)			
3a	39.2, CH ₂	2.77, m	Phe-2,4,5,5'	Phe-2	Phe-2-NH
b		2.72, m	Phe-1,2,4,5,5'	Phe-2	Phe-2-NH,

4	136.9, C				Phe-2
5,5'	129.6, CH x 2	7.10, m	Phe-4,7		
6,6'	128.9, CH x 2	7.14, m	Phe-4,6',6		
7	127.3, CH	7.13, m			
Gal-1	88.9, CH	5.03, d (8.6)	Gal-2,5, sHis-4,6	Gal-2	Gal-2,3
2	69.5, CH	3.61, m	Gal-1,3	Gal-1,3	Gal-1,3
3	73.7, CH	3.41, brd (9.0)		Gal-2,4	Gal-1,2
4	69.7, CH	3.83, m	Gal-4	Gal-3	
5	78.9, CH	3.66, m	Gal-6		
6a	61.9, CH ₂	3.65, m			
b		3.58, m	Gal-4		

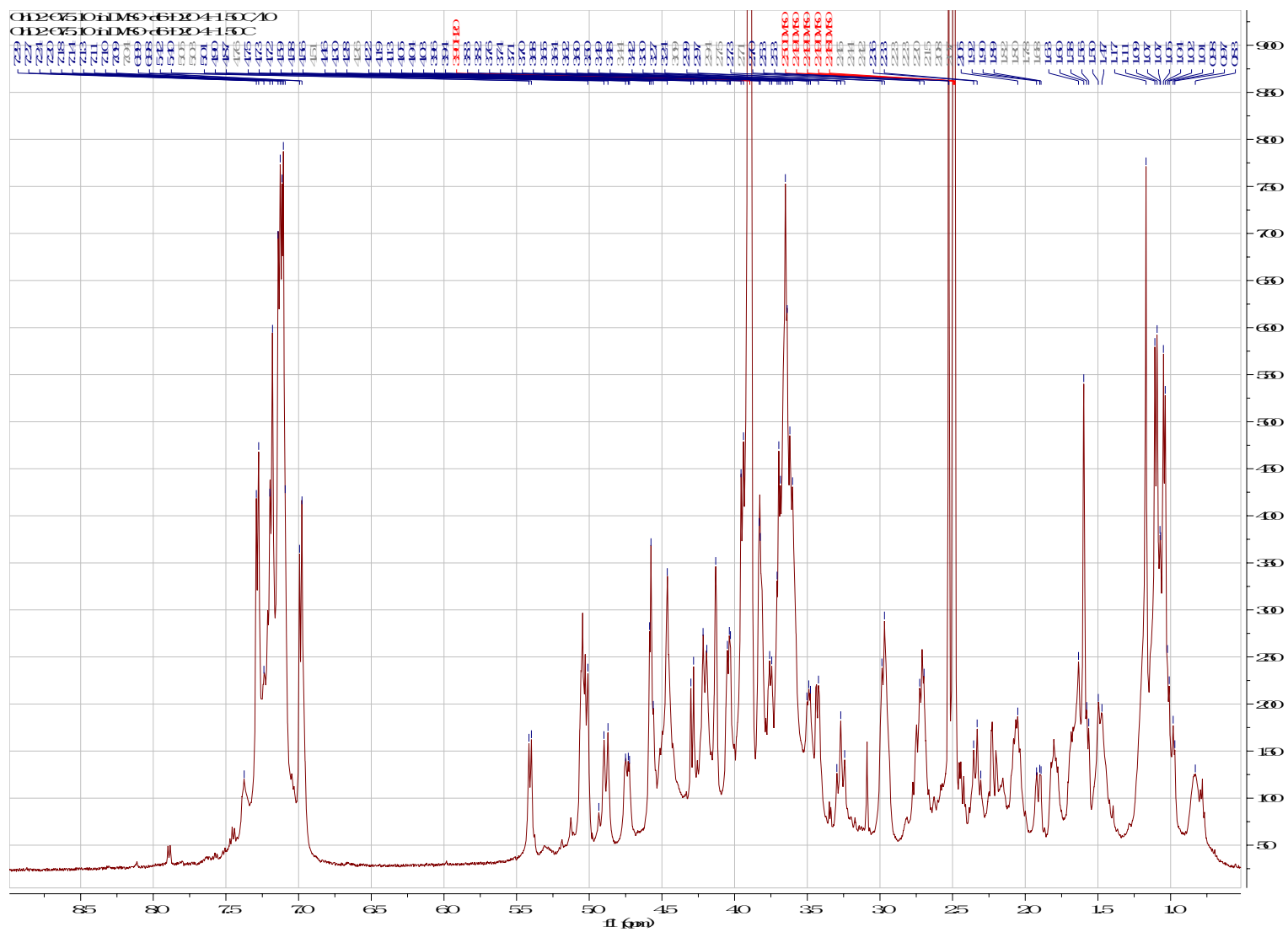
^a¹H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). Multiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz).

^dHMBC correlations, optimized for 8 Hz.

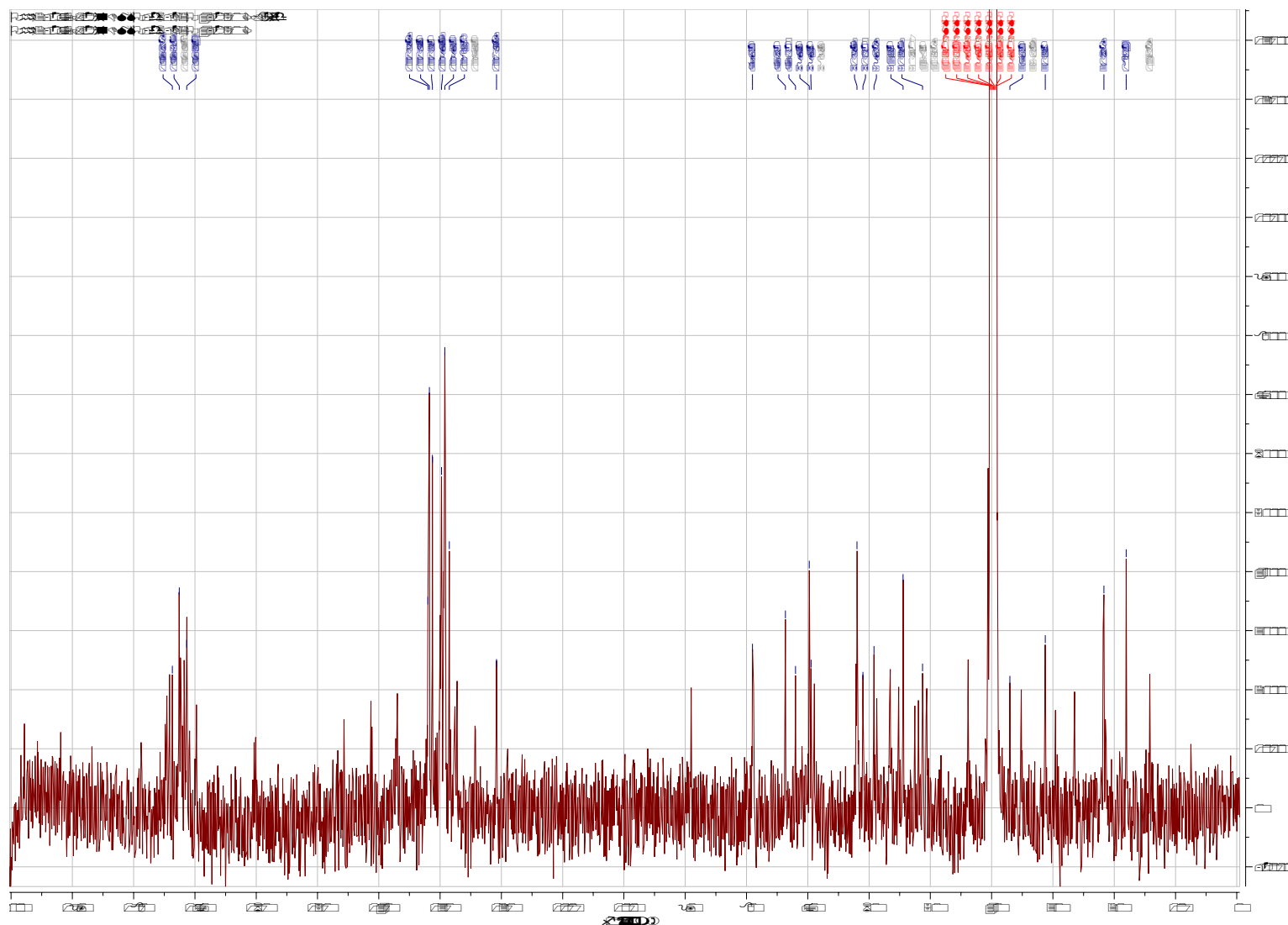
S25 Figure S22. ^1H NMR spectrum (500 MHz) of theonellamide J (**1**) after dissolving in 4:1 $\text{DMSO}-d_6$: D_2O at 50 $^\circ\text{C}$



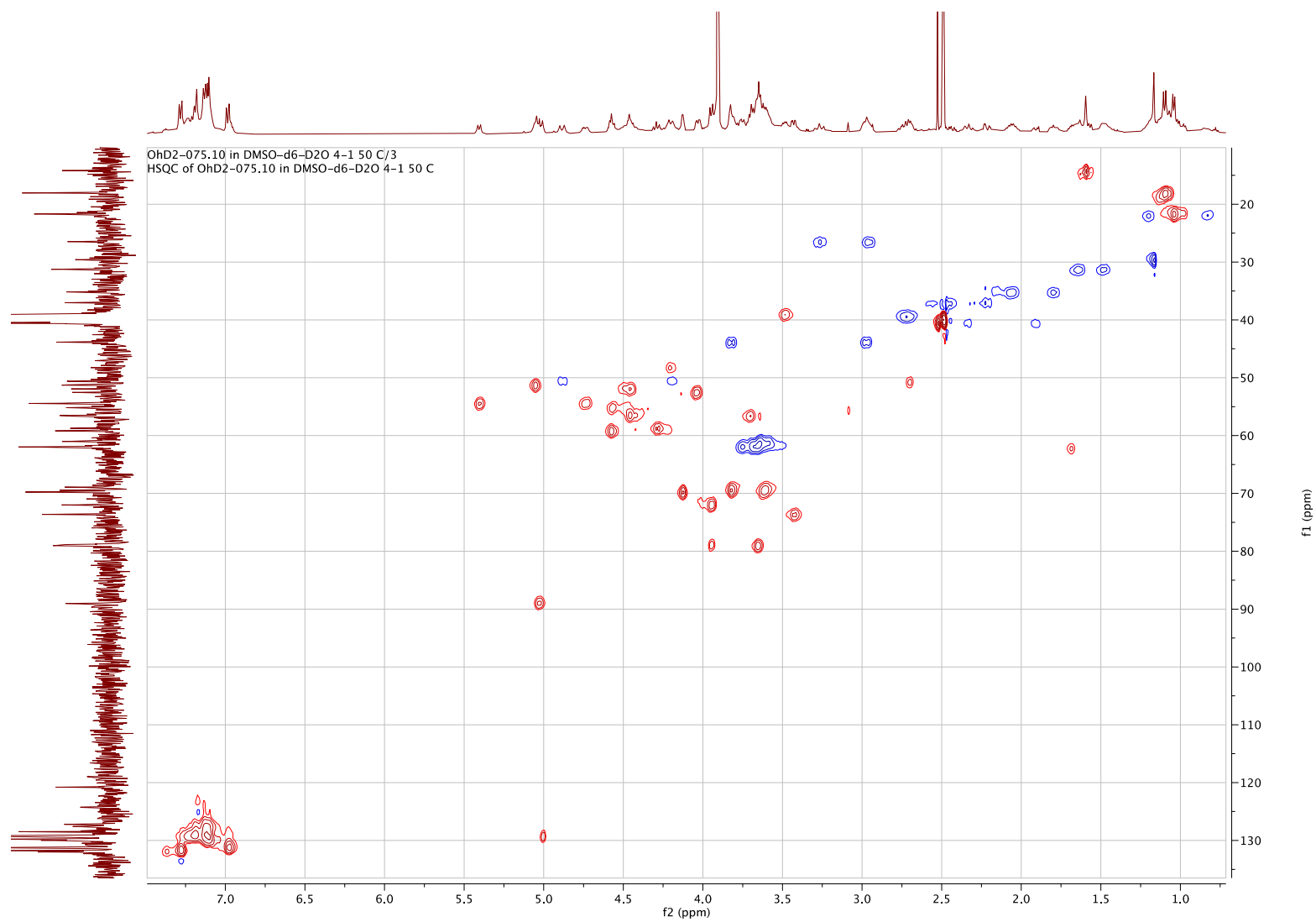
S26 Figure S23. ^1H NMR spectrum (500 MHz) of theonellamide J (**1**) 24 h after dissolving in 4:1 $\text{DMSO-}d_6$: D_2O at 50 $^\circ\text{C}$



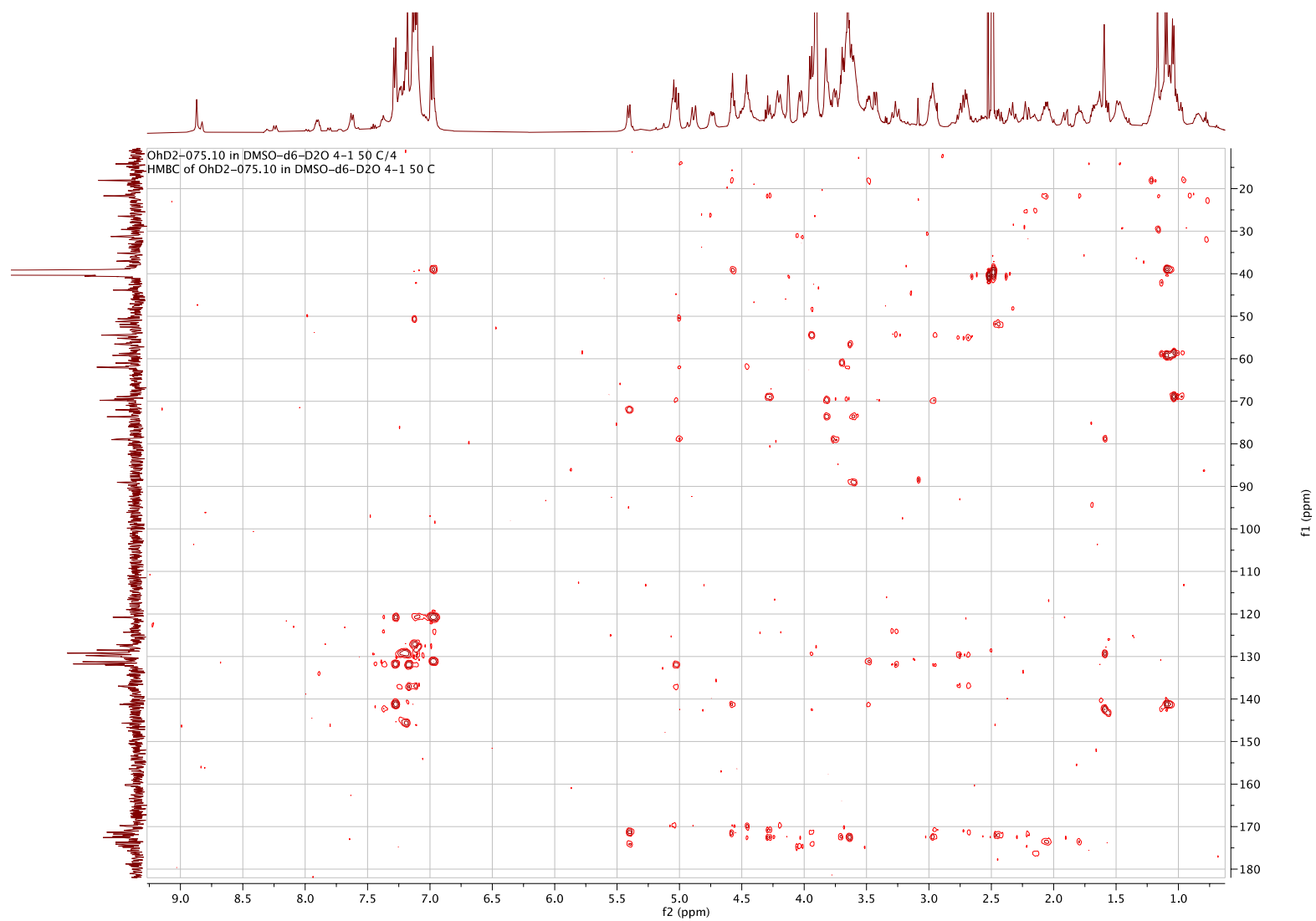
S27 Figure S24. ^{13}C NMR spectrum (125 MHz) of theonellamide J (**1**) in 4:1 DMSO- d_6 :D $_2$ O at 50 °C



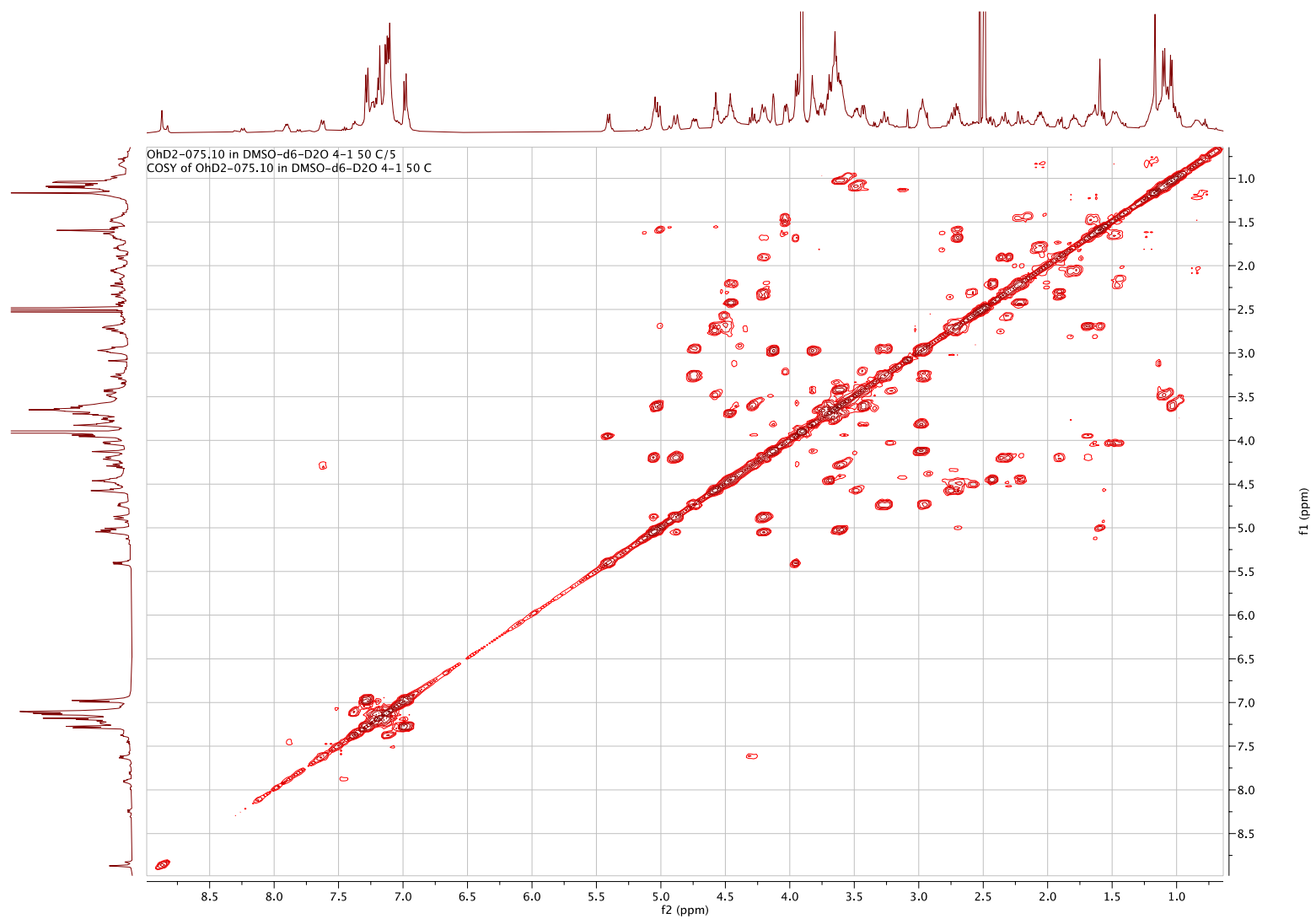
S28 Figure S245. HSQC spectrum of theonellamide J (**1**) in 4:1 DMSO-*d*₆:D₂O at 50 °C



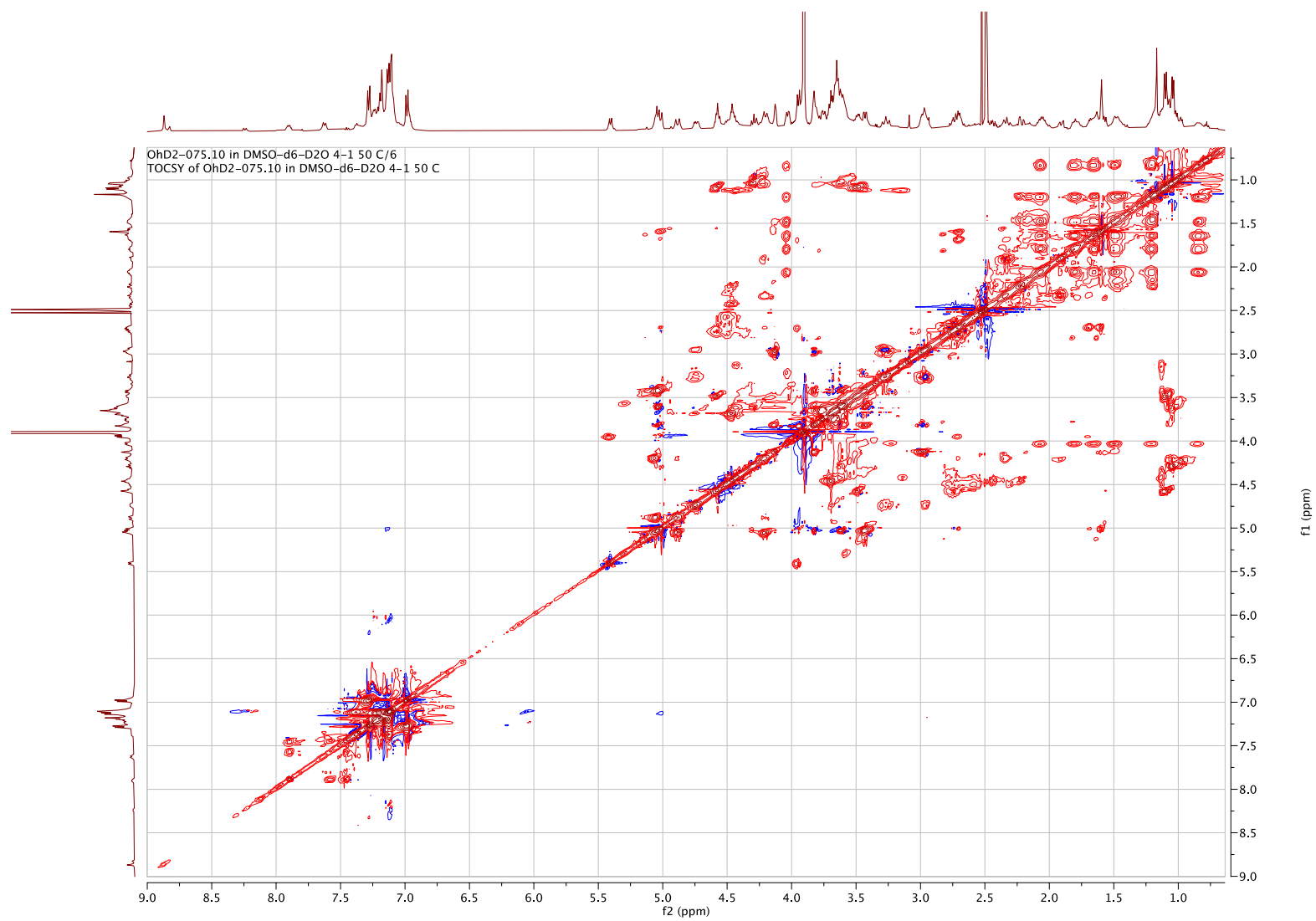
S29 Figure S26. HMBC spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :D₂O at 50 °C



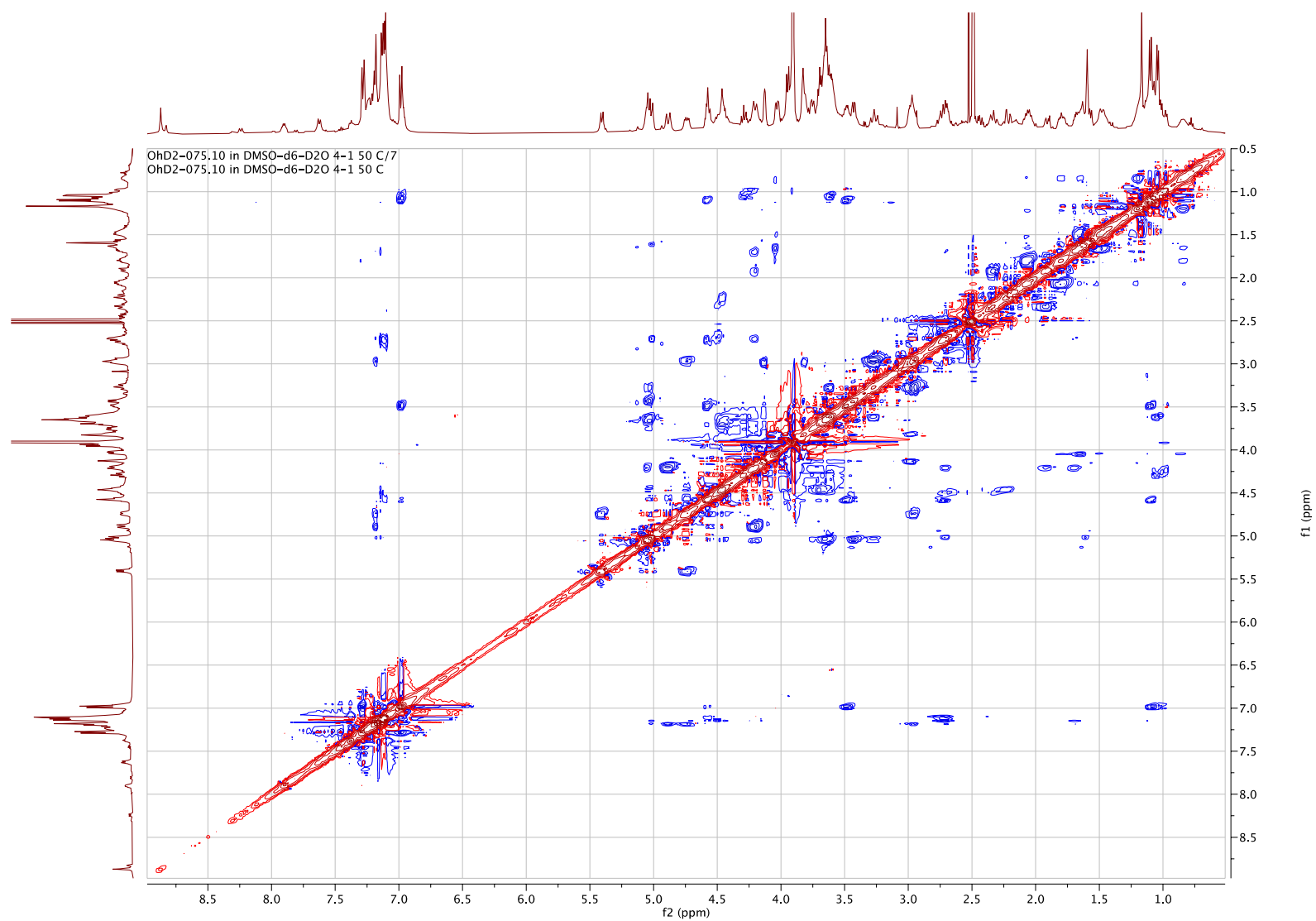
S30 Figure S27. COSY spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :D₂O at 50 °C



S31 Figure S28. TOCSY spectrum of theonellamide J (**1**) in 4:1 DMSO- d_6 :D₂O at 50 °C



S32 Figure S29. ROESY spectrum of theonellamide J (**1**) in 4:1 DMSO-*d*₆:D₂O at 50 °C



S33 Table S4. NMR data of theonellamide J (**1**) in 4:1 DMSO-*d*₆:D₂O at 50 °C^a

Position	δ_C^b	δ_H^c	HMBC correlations ^d	COSY correlations	TOCSY correlations	ROESY correlations ^e
Apcoa-1	172.6, C					
2a	40.4, CH ₂	2.33, dd (12.8, 12.3)	Apcoa-1,3	Apcoa-2b,3	Apcoa-2b,3	Apcoa-2b
b		1.91, d (12.8)	Apcoa-1	Apcoa-2a,3	Apcoa-2a,3	Apcoa-2a,3
3	48.3, CH	4.20, m		Apcoa-2a,2b,4	Apcoa-2a,2b, 8	Apcoa-2b,4,8,10,10'
4	62.1, CH	1.69, m		Apcoa-3,5,8	Apcoa-5,6-Me,7,8	Apcoa-3,8,10,10'
5	78.9, CH	3.95, m	Apcoa-3,6,6-Me,7	Apcoa-4,6-Me	Apcoa-4,6-Me,7,8	
6	142.4, C					
6-Me	14.2, CH ₃	1.59, brs	Apcoa-5,6, 7	Apcoa-7,8	Apcoa-4,5,7, 8	Apcoa-7, Phe-7
7	129.4, C	5.01, brs	Apcoa-4,5,6,6-Me,8	Apcoa-6-Me,7	Apcoa-4,5,6-Me,8	Apcoa-6-Me,8,10, 10'
8	50.7, CH	2.70, m		Apcoa-4,6-Me,7	Apcoa-3,4,5,6-Me,7	Apcoa-3,4,7,10,10'
9	145.7, C					
10,10'	129.1, CHx2	7.14, d (7.8)	Apcoa-8,10',10,12			Apcoa-3,4,7,8
11,11'	129.2, CHx2	7.20, t (7.8)	Apcoa-9,11',11	Apcoa-12		
12	127.2, CH	7.12, m		Apcoa-11,11'		
Ser ¹ -1	172.4, C					
2	56.6, CH	3.71, dd (6.6,5.9)	Ser ¹ -1	Ser ¹ -3		
3	62.0, CH ₂	3.62 m 2H	Ser ¹ -1,2	Ser ¹ -2		
sAla-1	169.8, C					
2	51.2, CH	5.06, m	sAla-1, Ser ¹ -1	sAla-3a,3b	sAla-3a,3b	sAla-3b
3a	50.6, CH ₂	4.88, d (14.0)	sAla-1	sAla-2,3b	sAla-2,3b	sAla-2,3b
b		4.20, m	sAla-1	sAla-2,3a	sAla-2,3a	sAla-2,3a, sHis-7
Asn-1	171.4, C					
2	52.0, CH	4.46, brm		Asn-3a,3b		Asn-3a,3b

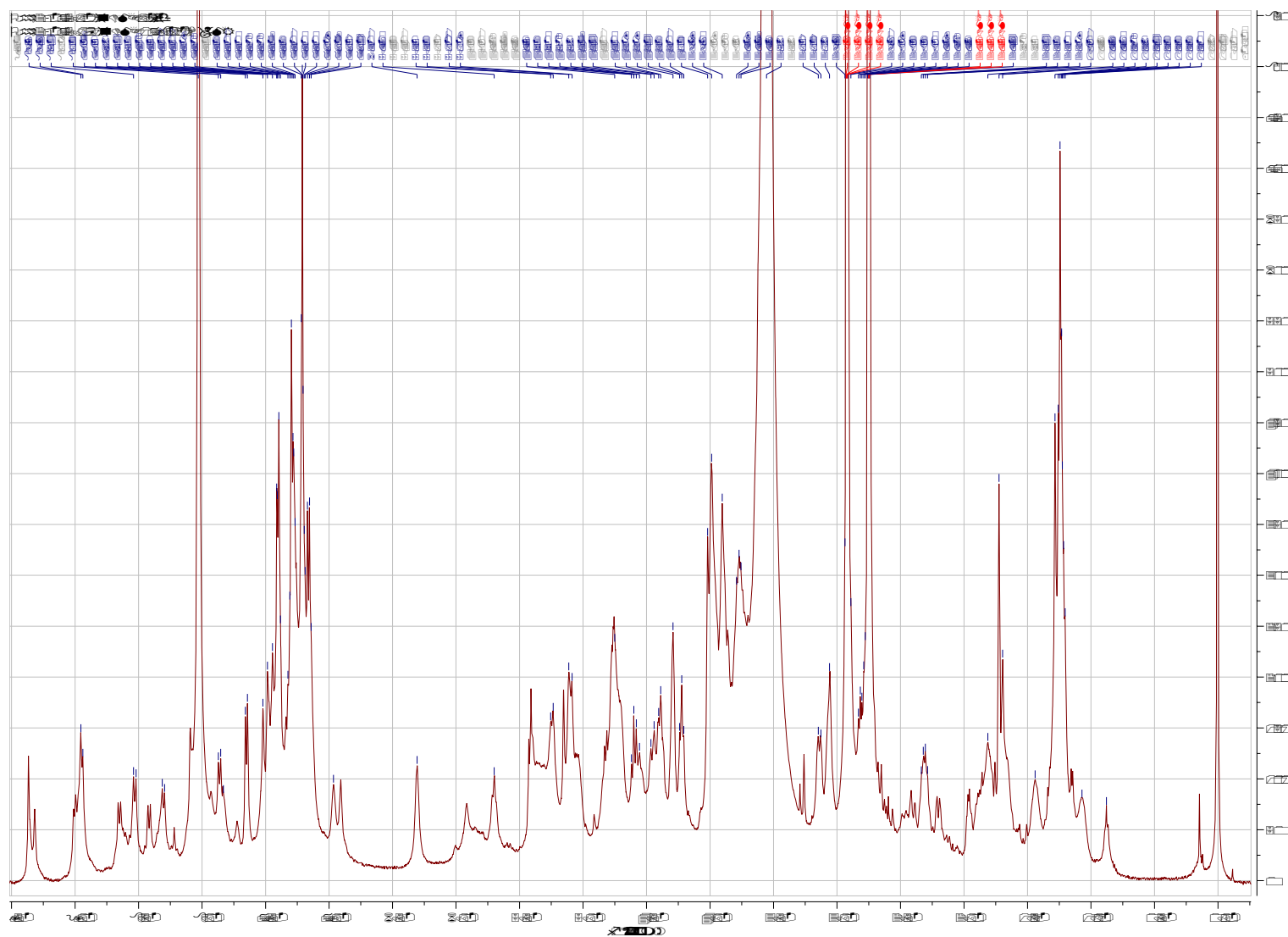
3a	37.0, CH ₂	2.45, dd (15.8,9.8)	Asn-2,4	Asn-2,3b	Asn-2,3b	Asn-2
b		2.21, dd (15.8,3.2)	Asn-1	Asn-2,3a	Asn-2,3a	Asn-2
4	172.1, C					
Han-1	171.3, C					
2	54.4, CH	5.41, d (8.6)	Han-1,3,4	Han-3	Han-3	Han-3, sHis-2, Thr-4
3	72.0, CH	3.95, d (8.6)	Han-1,2,4	Han-2	Han-2	Han-2
4	174.1, C					
BrMePhe-1	171.8, C					
2	59.2, CH	4.58, m	BrMePhe-1, 3-Me,4	BrMePhe-3	BrMePhe-3, 3-Me	BrMePh-3,3-Me,5,5
3	39.0, CH	3.49, dq (4.4,7.2)	BrMePhe-2,3-Me,4,5,5'	BrMePhe-2, 3-Me	BrMePhe-2, 3-Me	BrMePhe-2,3-Me,5,5'
3-Me	18.0, CH ₃	1.10, d (7.2)	BrMePhe-2, 3,4	BrMePhe-3	BrMePhe-2,3	BrMePhe-2, 3,5,5'
4	141.3, C					
5,5'	131.3, CHx2	6.99, d (8.3)	BrMePhe-3,5',5,7	BrMePhe-6,6'		BrMePhe-2, 3,3-Me
6,6'	131.8, CHx2	7.28, d (8.3)	BrMePhe-4, 6',6,7	BrMePhe-5,5'		
7	120.8, C					
iSer-1	172.6, C					
2	69.8, CH	4.13, brs	iSer-1	iSer-3a,3b	iSer-3a,3b	iSer-3b
3a	43.9, CH ₂	3.83, m	iSer-2	iSer-2,3b	iSer-2,3b	iSer-3b, Gal-3,5
b		2.98, m	iSer-1,2	iSer-2,3a	iSer-2,3a	iSer-2,3a
Ada-1	174.6, C					
2	52.5, CH	4.03, dd (9.7,3.5)	Ada-1,3, iSer-1	Ada-3a,3b	Ada-3a,3b,4a,4b,5a,5b	Ada-3a,3b, 4b
3a	31.3, CH ₂	1.65, m		Ada-2,3b,4a, 4b	Ada-2,3b,4a,4b,5a,5b	Ada-2, 3b
b		1.49, m		Ada-2,3a,4a, 4b	Ada-2,3a,4a, 4b,5a,5b	Ada-2, 3a
4a	21.8, CH ₂	1.20, m		Ada-3a,3b,4b,5a,5b	Ada-2,3a,3b,4b,5a,5b	Ada-3b
b		0.83, m		Ada-3a,3b,4a,5a,5b	Ada-2,3a,3b,4a,5a,5b	Ada-2,3a

5a	35.2, CH ₂	2.06, m	Ada-4,6	Ada-4a,4b,5b	Ada-2,3a,3b,4a,4b,5b	Ada-5b
b		1.79, m	Ada-3,4,6	Ada-4a,4b,5a	Ada-2,3a,3b,4a,4b,5a	Ada-5a
6	173.7, C					
sHis-1	170.9, C					
2	54.4, CH	4.74, dd (12.2,4.6)	sHis-3	sHis-3a,3b	sHis-3a,3b	Has-2, sHis-3b,7
3a	26.5, CH ₂	3.27, brt (13.5)	sHis-2,4,7	sHis-2,3b	sHis-2,3b	sHis-3b Gal-1,2
b		2.97, m	sHis-1,2,4	sHis-2,3a	sHis-2,3a	sHis-2,3a,7
4	132.0, C					
6	137.2, CH	8.88, s ^f				
8	124.3, CH	7.18, s	sHis-4,6		sHis-3a,3b	sHis-2,3b, sAla-3a
Thr-1	172.6, C					
2	58.7, CH	4.29, t (9.5)	Thr-1,3,4, sHis-1	Thr-3	Thr-3,4	Thr-3,4
3	68.9, CH	3.61, m	Thr-2	Thr-2,4	Thr-2,4	Thr-3,4, sHis-3a
4	21.7, CH ₃	1.04, d (6.1)	Thr-3	Thr-3	Thr-2,3	Has-2, Thr-2,3
Ser ² -1	170.0, C					
2	56.5, CH	4.46, m	Ser ² -1,3, Thr-1	Ser ² -3	Ser ² -3	Ser ² -3
3	62.0, CH ₂	3.69, m	Ser ² -1	Ser ² -2	Ser ² -2	Ser ² -2
Phe-1	171.3, C					
2	55.2, CH	4.57, m	Phe-3, Ser ² -1	Phe-3a,3b	Phe-3a,3b	Phe-3b,5,5'
3a	39.2, CH ₂	2.76, m	Phe-1,2,4, 5,5'	Phe-2	Phe-2,3b	Phe-5,5'
b		2.72, m	Phe-2,4,5, 5'	Phe-2	Phe-2,3a	Phe-2,5,5'
4	137.0, C					
5,5'	129.8, CHx2	7.11, m	Phe-6,6',7			Phe-2,3a,3b
6,6'	128.5, CHx2	7.12, m	Phe-4			Ser ² -2
7	127.6, CH	7.13, m				Apcoa-6-Me
Gal-1	89.0, CH	5.03, d (8.9)	sHis-4,6, Gal-4	Gal-2	Gal-2,3,4	Gal-2,3, sHis-3a
2	69.5, CH	3.62, m	Gal-1,3	Gal-1,3	Gal-1,3	
3	73.7, CH	3.43, dd (9.2,2.9)		Gal-2,4	Gal-1,2,4	Gal-1,4
4	69.8, CH	3.83, m	Gal-3	Gal-3,5	Gal-1,2,3,5,6	

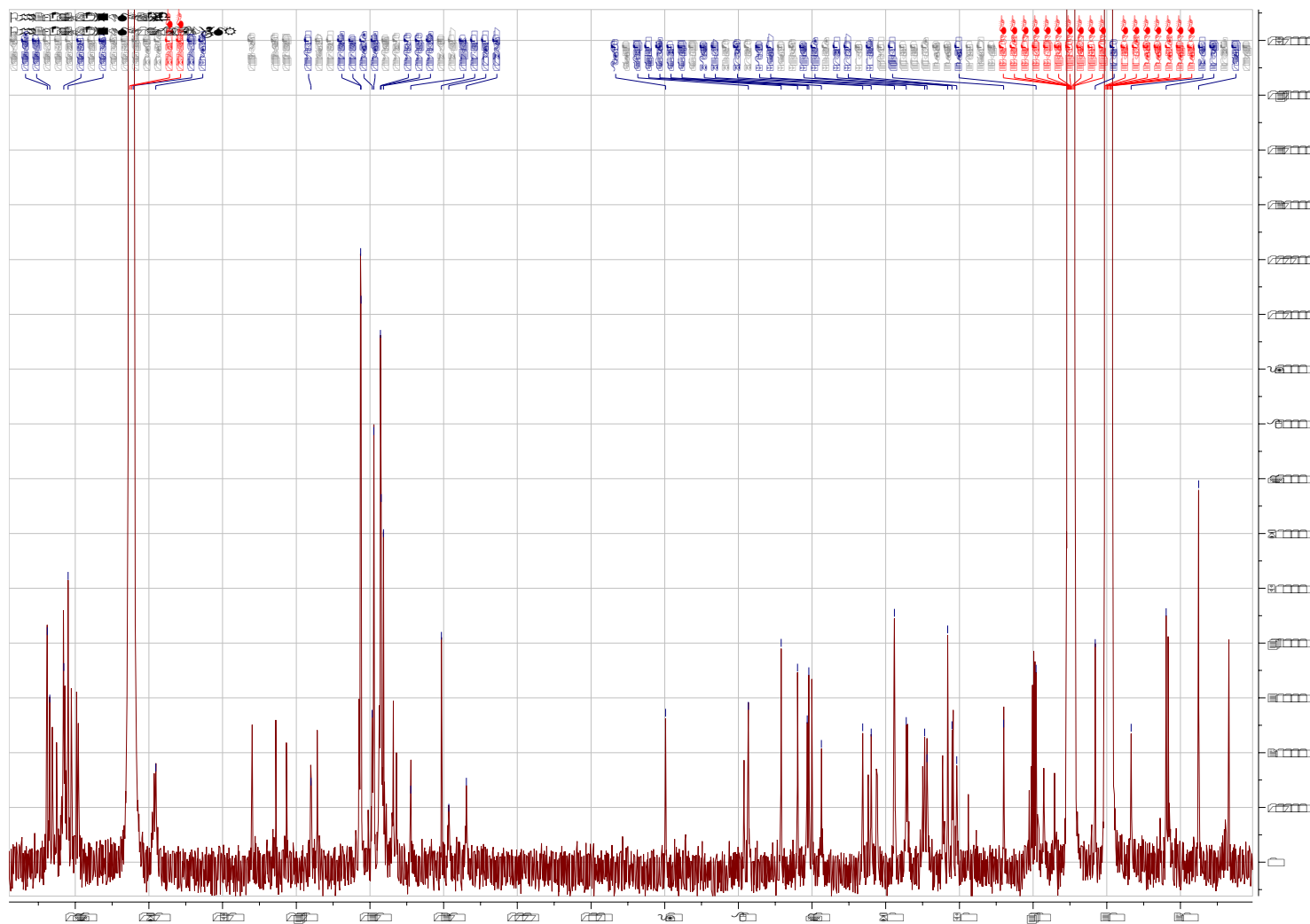
5	79.0, CH	3.66, m	Gal-2,6	Gal-4
6	62.0, CH ₂	3.75, m 3.58, m	Gal-5	Gal-4

^a¹H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). ^bMultiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz). ^dHMBC correlations, optimized for 8 Hz. ^eSelected NOEs from ROESY experiment. ^fExchanged with D₂O.

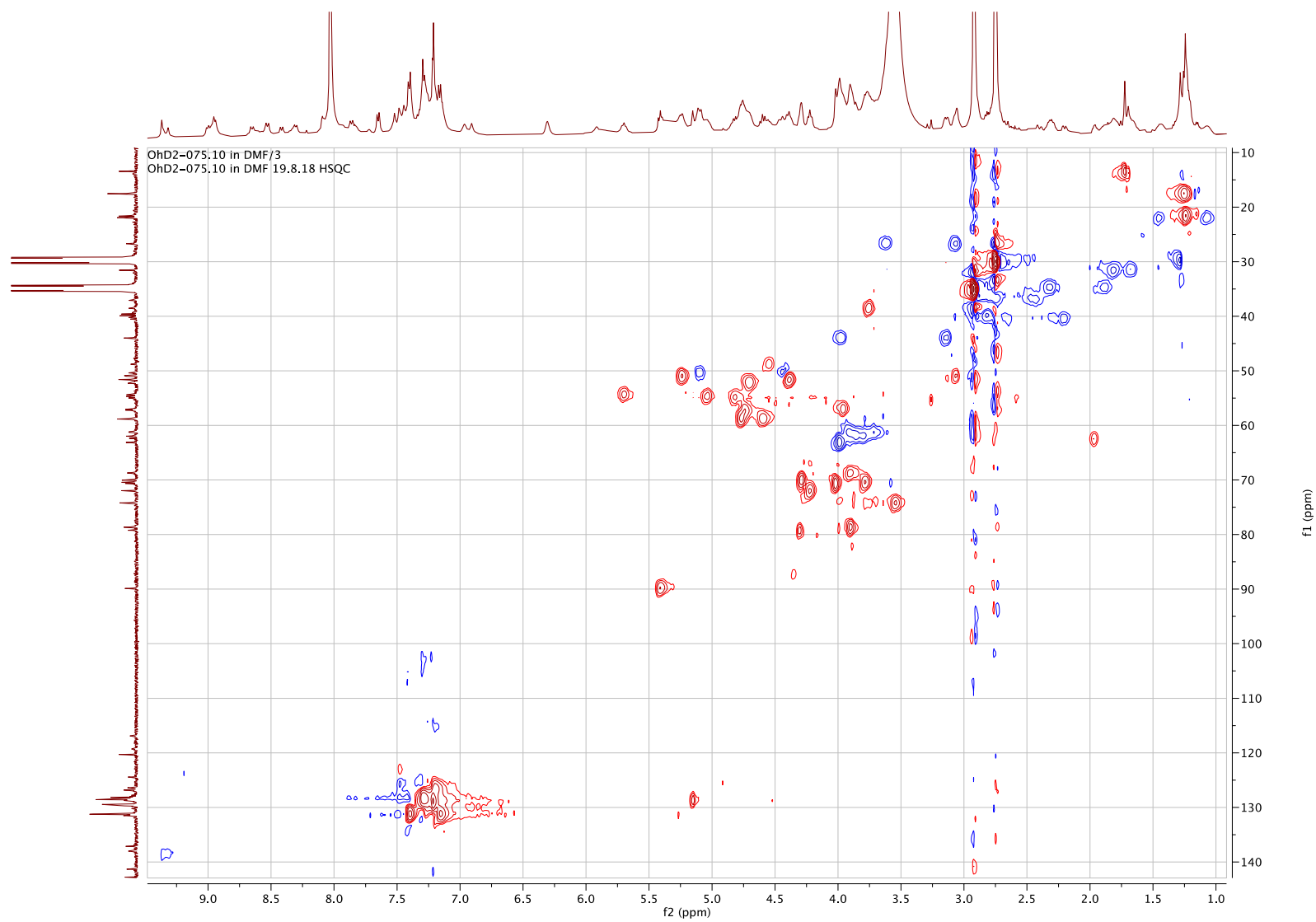
S34 Figure S30. ^1H NMR spectrum (500 MHz) of theonellamide J (**1**) in DMF-d_7



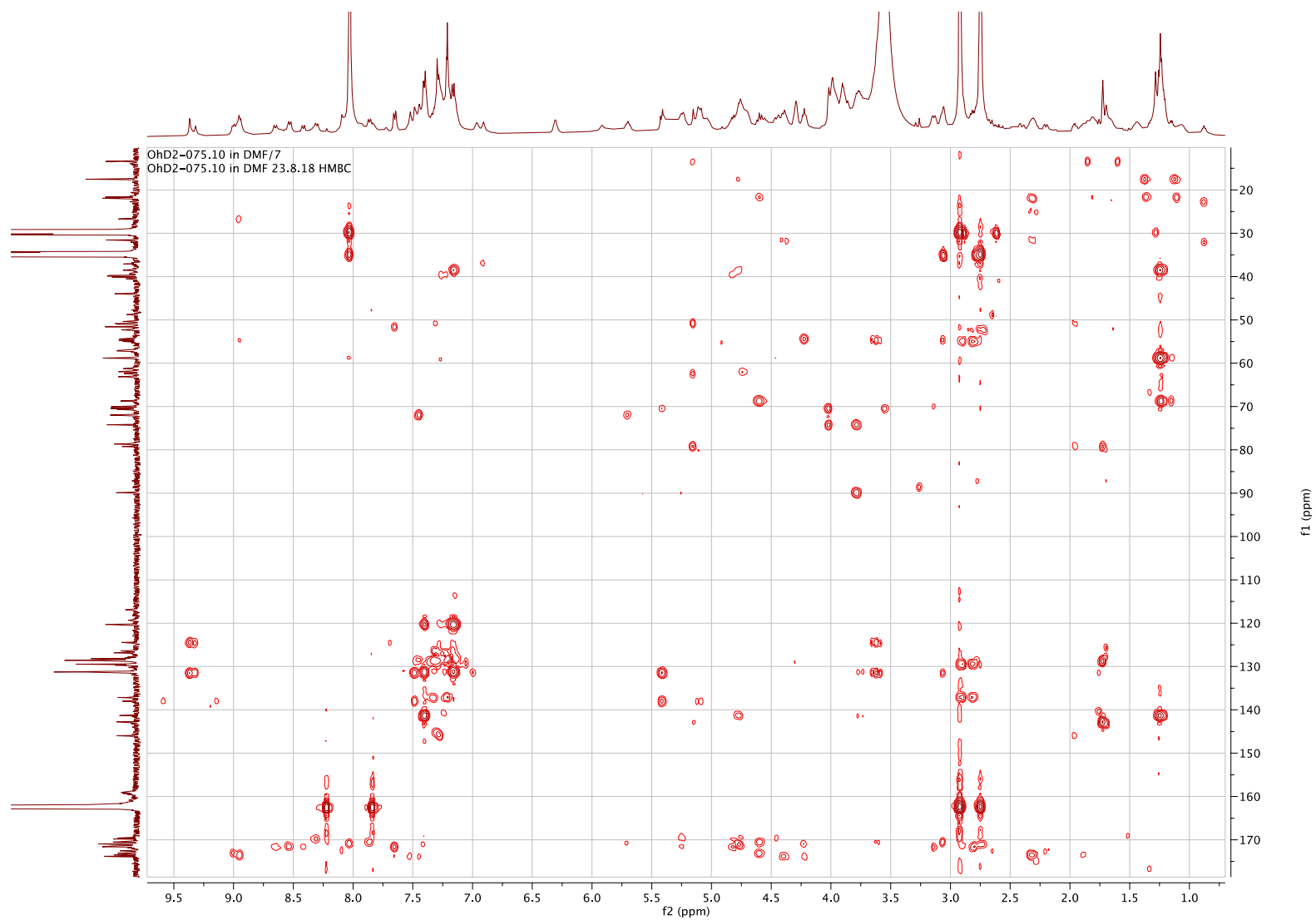
S35 Figure S31. ^{13}C NMR spectrum (125 MHz) of theonellamide J (**1**) in DMF- d_7



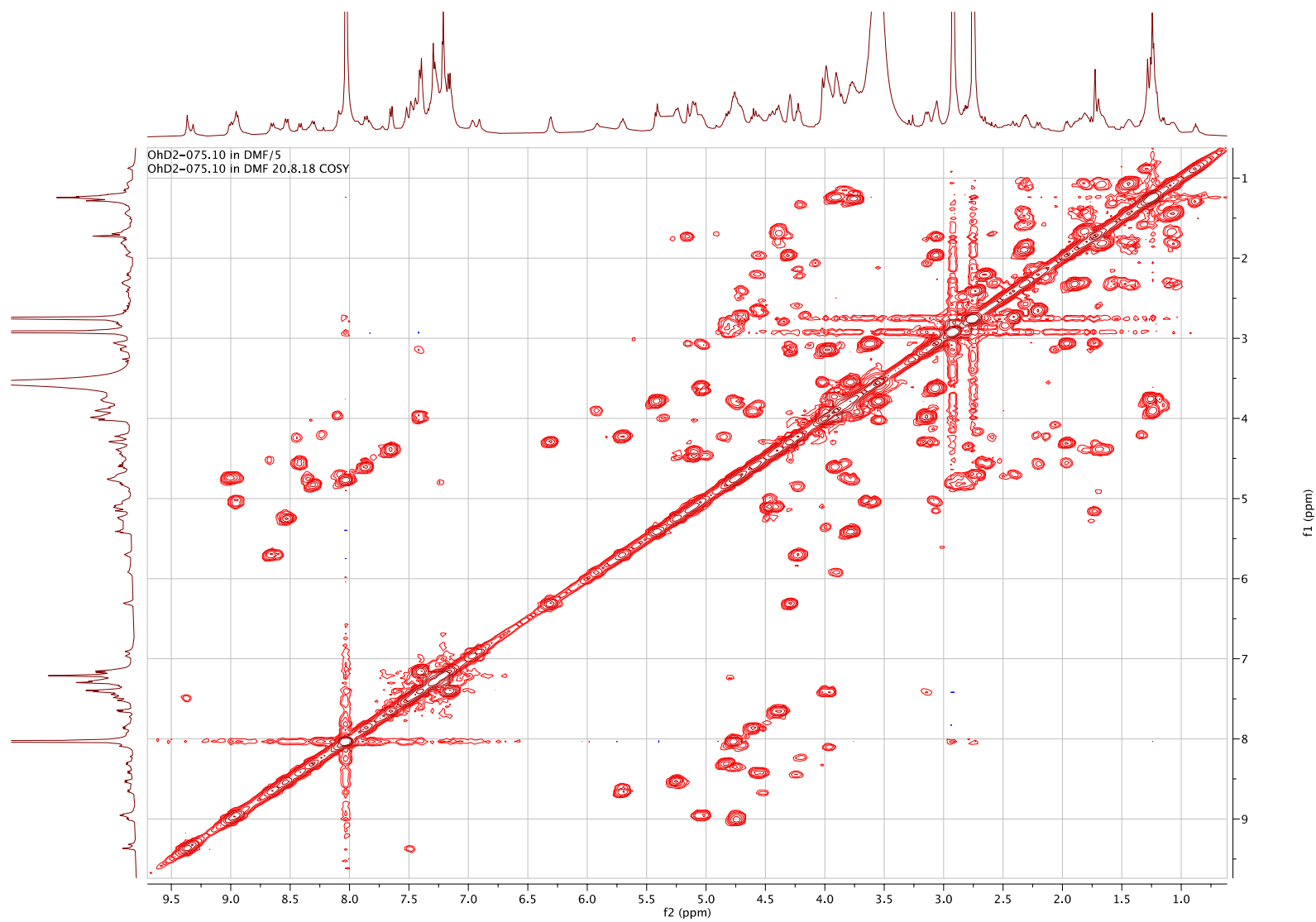
S36 Figure S32. HSQC spectrum of theonellamide J (**1**) in DMF-d₇



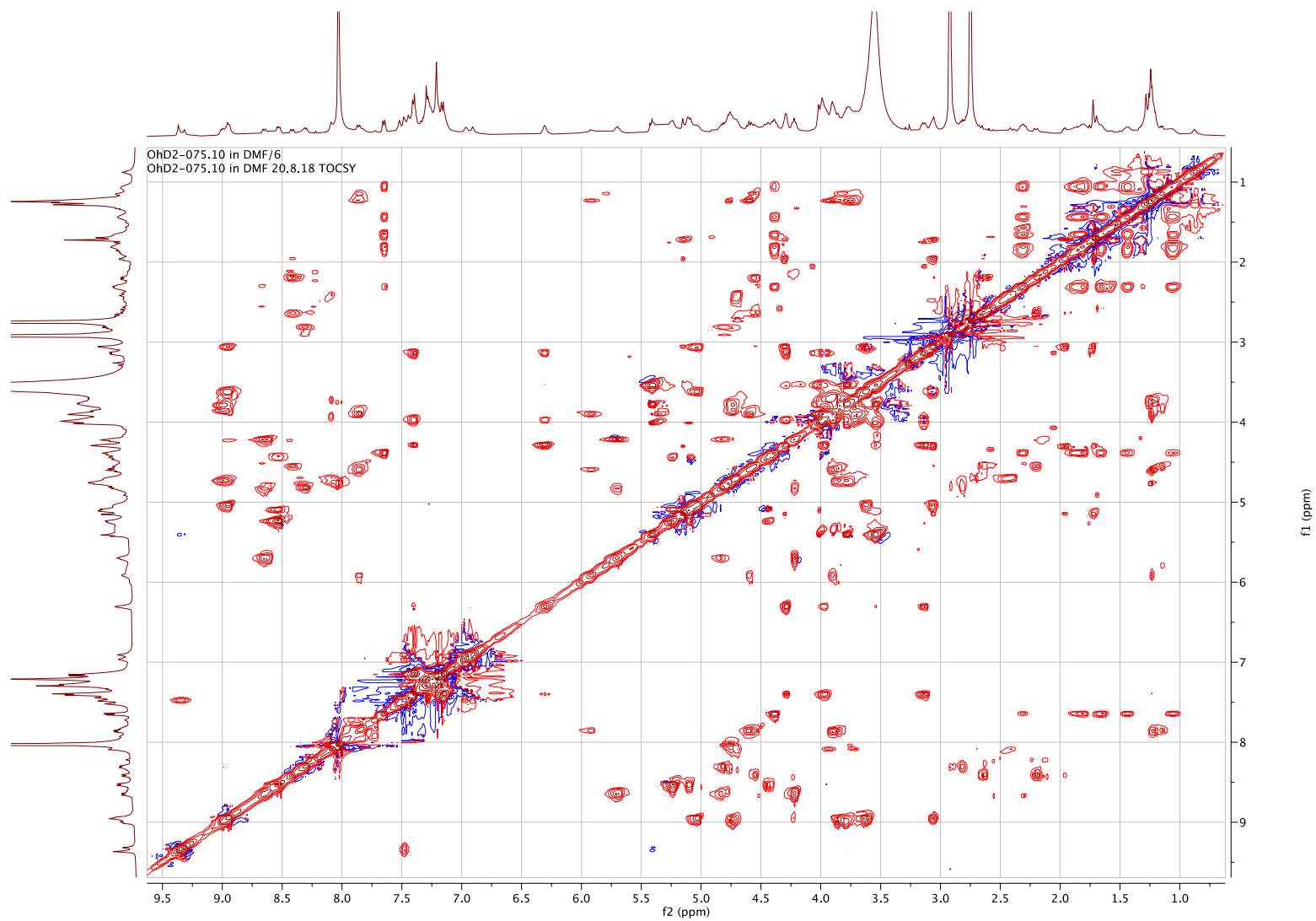
S37 Figure S33. HMBC spectrum of theonellamide J (1) in DMF-d₇



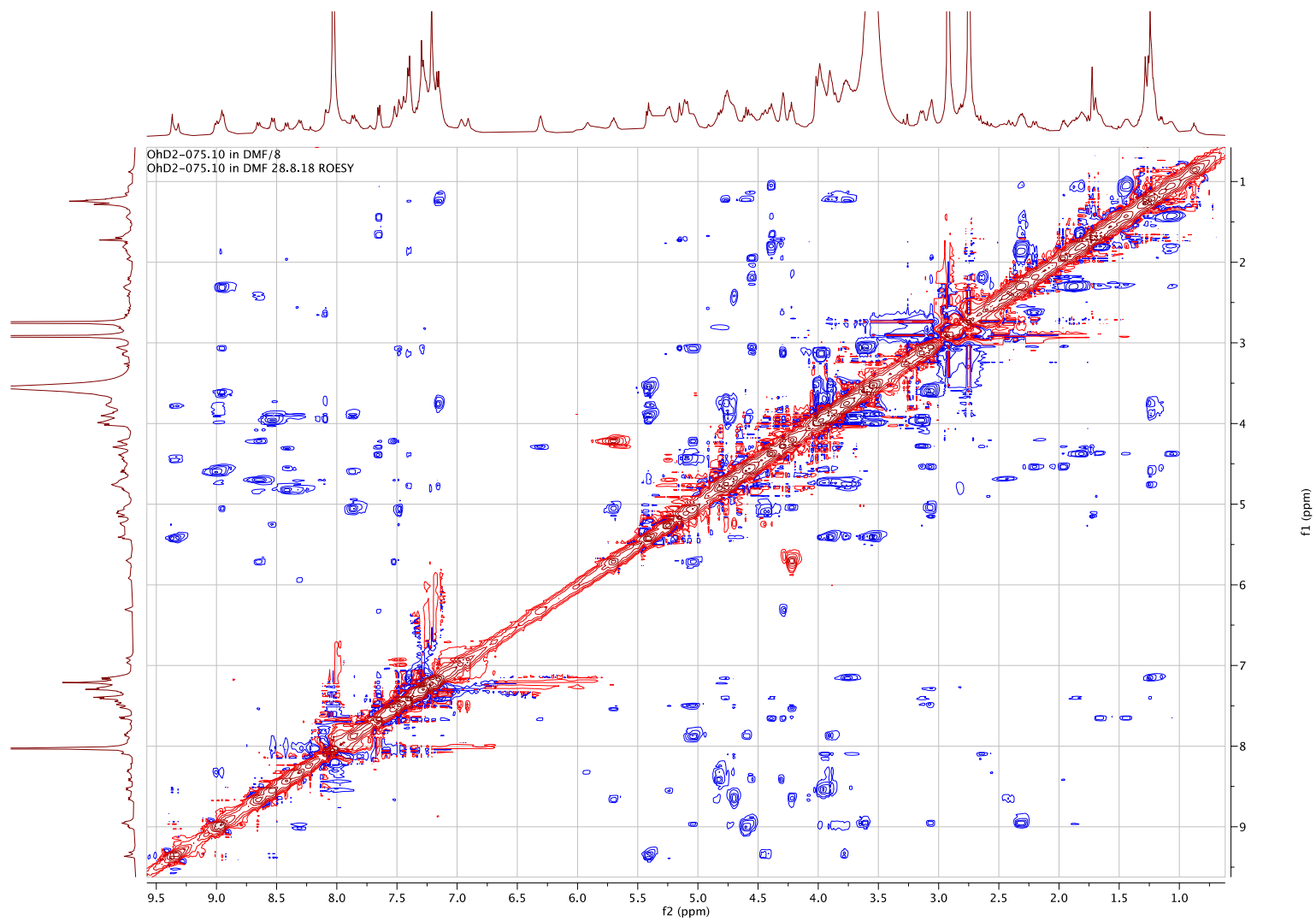
S38 Figure S34. COSY spectrum of theonellamide J (**1**) in DMF-d₇



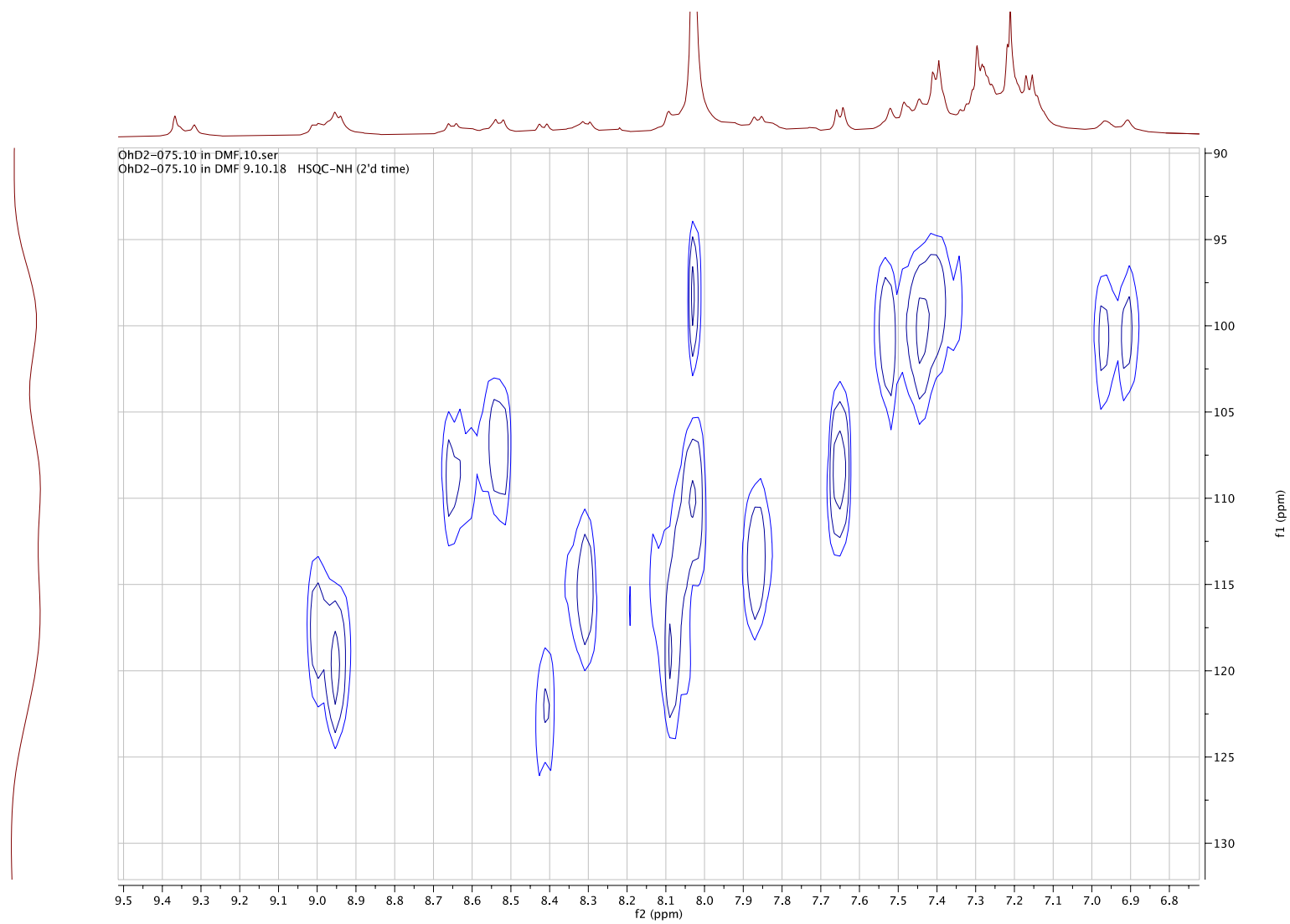
S39 Figure S35. TOCSY spectrum of theonellamide J (**1**) in DMF-d₇



S40 Figure S36. ROESY spectrum of theonellamide J (**1**) in DMF-d₇



S41 Figure S37. N-H HSQC spectrum theonellamide J (**1**) in DMF-d₇



S42 Table S5. NMR data of theonellamide J (**1**) in DMF-d₇^a

Position	δ_C^b	δ_H^c	HMBC correlations ^d	COSY correlations	TOCSY correlations	ROESY correlations ^e
Apcoa-1	172.5, C					
2a	40.6, CH ₂	2.66, t (12.5)	Apcoa-1,3	Apcoa-2b,3	Apcoa-2b,3,3-NH	Apcoa-2b,3-NH, Ser ¹ -2-NH
b		2.20, dd (12.5,3.3)	Apcoa-1,3	Apcoa-2a,3	Apcoa-2a,3,3-NH	Apcoa-2a,3,4,8
3	48.8, CH	4.56, m		Apcoa-2a,2b,3-NH,4	Apcoa-2a,2b,3-NH,4,8	Apcoa-2b,3-NH,4,8,10,10'
3-NH	122.3, NH	8.42, d (9.4)	Phe-1	Apcoa-3	Apcoa-2a,2b,3,4	Apcoa-2a,3,4,5, Phe-2
4	62.4, CH	1.96, dt (5.5,5.8)	Apcoa-5,8,9	Apcoa-3,5,8	Apcoa-2a, 2b,3,3-NH, 5,6-Me,7,8	Apcoa-2b,3,3-NH,5,6-Me, 7,8,10,10'
5	79.2, CH	4.30, brs ($\nu_{1/2}$ =12.9 Hz)	Apcoa-6,7	Apcoa-4,6-Me	Apcoa-4, 6-Me,7,8	Apcoa-3-NH,4,6-Me
6	142.8, C					
6-Me	13.4, CH ₃	1.72, s	Apcoa-5,6,7	Apcoa-5,7,8	Apcoa-4,5,7,8	Apcoa-4,5,7, Phe-5,5'
7	128.8, CH	5.15, brs	Apcoa-4,5,6,6-Me,8	Apcoa-6-Me,8		Apcoa-4,6-Me,8,10,10'
8	50.9, CH	3.06, brs ($\nu_{1/2}$ ~9 Hz)	Apcoa-4,6,9	Apcoa-4,7	Apcoa-4,5,6-Me	Apcoa-2b,3,4,7,10,10'
9	146.0, C					
10,10'	128.6, CH x 2	7.29, m	Apcoa-10',10, 11,11'			Apcoa-3,4,7,8
11,11'	128.2, CH x 2	7.21, m	Apcoa-9,11', 11,12			
12	126.4, CH	7.19, m				
Ser ¹ -1	171.4, C					

2	57.0, CH	3.96, m		Ser ¹ -2-NH,3a,3b	Ser ¹ -2-NH	Ser ¹ -3b, Ser ² -2, sAla-2,2-NH
2-NH	114.6, NH	8.09, s	Apcoa-1	Ser ¹ -2	Ser ¹ -2, 3a,3b	Ser ¹ -3a,3b
3	61.2, CH ₂	3.91, m 3.71, m	Ser ¹ -1	Ser ¹ -2,3b Ser ¹ -3,3a	Ser ¹ -2-NH Ser ¹ -2-NH	Ser ¹ -2-NH Ser ¹ -2-NH, sAla-2-NH
sAla-1	169.6, C					
2	51.0, CH	5.25, brd (9.9)	sAla-1	sAla-2-NH	sAla-2-NH, 3a,3b	sAla-2-NH, 3b(neg)
2-NH	107.0, NH	8.53, d (9.9)	Ser ¹ -1, sAla-2	sAla-2	sAla-2-NH, 3a,3b	sAla-2, sHis-6, Ser ¹ -2,3b, Thr-3
3a	50.4, CH ₂	5.11, brd (12.1)	sAla-2, sHis-6	sAla-3b	sAla-2,2-NH,3b	sAla-3b, sHis-3b,8 sHis-6,
b		4.45, brd (12.1)	sAla-1	sAla-3a	sAla-2,2-NH,3a	sAla-2(neg),3a, Ser ¹ -2
Asn-1	171.0, C					
2	52.3, CH	4.71, brm		Asn-2-NH,3a,3b		Has-2-NH
2-NH	118.9, NH	8.08, m		Asn-2	Asn-2-NH,3a,3b	
3a	37.1, CH ₂	2.73, m	Asn-1,2	Asn-2,3b	Asn-2,2-NH,3b	
b		2.41, dd (15.4,2.8)		Asn—2,3a	Asn-2,2-NH,3a	
4	173.9, C					
4-NH ₂	100.6, NH ₂	6.97, s 7.45, s	Asn-4			
Han-1	170.9, C					
2	54.4, CH	5.71, brdd (8.6,7.8)	Han-3	Han-2-NH,3	Han-2-NH, ,3-OH	sHis-2, Hans-3(neg), BrMePhe-2-NH, Thr-4
2-NH	108.3, NH	8.65, brd (8.6)		Han-2	Han-2,3,3-OH	Han-2,3, Asn-2,
3	72.0, CH	4.23, brt (7.8)	Han-1,2, 4	Han-2,3-OH	Han-2,2-NH,3,3-OH	sHis-2, Han-2(neg)
3-OH		4.83, m				
4	173.8, C					

4-NH ₂	100.4, NH ₂	6.91, s					Han-2,3
BrMePhe-1	171.0, C	7.52, s	Han-3,4				
2	58.8, CH	4.77, m	BrMePhe-1,3,3-Me,4	BrMePhe-2-NH,3	BrMePhe-2-NH,3,3-Me		BrMePhe-3,3-Me
2-NH	110.3, NH	8.03, m	Han-1, BrMePhe-2	BrMePhe-2	BrMePhe-2,3,3-Me		Has-2,3 BrMePhe-2,3
3	38.6, CH	3.76, m	BrMePhe-3-Me,4, 5,5'	BrMePhe-2,3-Me	BrMePhe-2,2-NH,3-Me		BrMePhe-2,3-Me
3-Me	17.5, CH ₃	1.25, d (7.1)	BrMePhe-1,2,3,4	BrMePhe-3	BrMePhe-2,3		
4	141.3, C						
5,5'	131.2, CH x 2	7.17, d x 2 (8.0)	BrMePhe-3,5',5,6,6',7	BrMePhe-6,6'			BrMePhe-3,3-Me
6,6'	131.3, CH x 2	7.41, d x 2 (8.0)	BrMePhe-4,5,5',6',6,7	BrMePhe-5,5'			
7	120.3, C						
iSer-1	171.6, C						
2	70.0, CH	4.29, brs		iSer-2-OH,3a,3b	iSer-3-NH		iSer-2-OH,3a, 3b, Ada-2-NH
2-OH		6.31, brs		iSer-2	iSer-2,3a, 3b		iSer-2
3a	44.0, CH ₂	3.98, m		iSer-2,3b	iSer-2,2-OH,3b,3-NH		iSer-2,3b,
b		3.14, brd (11.3)	iSer-1,2	iSer-2,3a	iSer-2,2-OH,3a,3-NH		iSer-2,3a,
3-NH	98.9, NH	7.42, m	BrMePhe-1	iSer-3a	iSer-2,3a, 3b		Ada-2,2-NH, iSer-3b
							BrMePhe-2,3-Me
Ada-1	173.8, C						
2	51.6, CH	4.39, ddd (12.2, 8.7, 2.8)	Ada-1,3	Ada-2-NH,3a, 3b	Ada-2-NH, 3a,3b,4a, 4b,5a,5b		Ada-3a, 3b,4a,4b
2-NH	108.2, NH	7.65, d (8.7)	iSer-1, Ada-1,2,3	Ada-2	Ada-2, 3a,3b,4a, 4b,5a,5b		iSer-2,3-NH, Ada-2,3b,4a,
3a	31.6, CH ₂	1.81, m		Ada-2,3b, 4a,4b	Ada-2,2-NH,3b, 4a,4b, 5a,5b		

b		1.68, m	Ada-2	Ada-2,3a, 4a,4b	Ada-2,2-NH,3a, 4a,4b, 5a,5b	
4a	21.9, CH ₂	1.44, m		Ada-3a, 3b,4b,5a,5b	Ada-2,2-NH,3a,3b, 4b,5a,5b	
b		1.07, m		Ada-3a, 3b,4a,5a,5b	Ada-2,2-NH,3a,3b, 4a,5a,5b	
5a	34.8, CH ₂	2.33 m	Ada-3,4,6	Ada-4a,4b, 5b	Ada-2,2-NH,3a,3b, 4a,4b,5b	
b		1.90, m	Ada-3,6	Ada-4a,4b, 5a	Ada-2,2-NH,3a,3b, 4a,4b,5a	
6 sHis-1 2	173.5, C 170.5, C 54.7, CH	5.04, brm		sHis-2- NH,3a,3b	sHis-2-NH,3a,3b	sHis-2-NH,3b Han-2,3
2-NH	119.8, NH	8.95, d (7.1)	Ada-6, sHis-2,3	sHis-2	sHis-2,3a,3b	sHis-2,3a,3b,
3a b	26.7, CH ₂	3.63, m 3.08, m	sHis-1,2,4,8 sHis-1,2,4	sHis-2,3b sHis-2,3a	sHis-2,2-NH,3b sHis-2,3a	sHis-2-NH,3b sHis-2,2-NH,3a,
4 6	131.5, C 138.0, CH	9.37, s	5.11, sHis-4,8	sHis-8	sHis-8	Gal-1,2, sAla-2-NH, 3b Ser ² -2
8	124.5, CH	7.48, brs	sHis-4,6	sHis-6	sHis-6	Gal-1, sHis-3b,
Thr-1 2	173.1, C 58.8, CH	4.60, t (9.4)	sHis-1, Thr-1,3,4	Thr-2-NH,3	Thr-2-NH,3,3-OH,4	Ser ² -2-NH, sHis-3b Thr-2-NH,4
2-NH	113.7, NH	7.86, d (9.6)	sHis-1	Thr-2	Thr-2,3,3-OH,4	sHis-2, Thr-2,3,4
3	68.7, CH	3.91, m		Thr-2,3-OH,4	Thr-2,2-NH,3-OH,4	Gal-1, Ser ² -2, sAla-2-NH, Thr-2,2-NH,4
3-OH 4		5.91, brs 1.24, d (6.1)	Thr-2,3	Thr-3 Thr-3	Thr-2,2-NH,3,4 Thr-2,2-NH,3,3-OH	Thr-4, Phe-2-NH Thr-2,2-NH,3, Ser ² -2, Han-2

Ser ² -1 2	169.8, C 57.2, CH	4.75, m	Ser ² -1,3	Ser ² -2-NH	Ser ² -2-NH, 3a,3b,3-OH	sHis-6 Ser ² -2-NH, 3a, Ser ¹ -2, Phe-2-NH
2-NH	117.9, NH	9.00, d (7.5)	Thr-1	Ser ² -2,	Ser ² -2,3a, 3b,3-OH	Phe-2-NH, Ser ² -2,3a, 3b, Thr-2
3a b 3-OH Phe-1 2	62.0, CH ₂ 171.6, C 55.0, CH	3.86, m 3.80, m 5.32, m 4.82, m	Ser ² -1 Phe-3	 Phe-2-NH, 3a,3b	Ser ² -3-OH Ser ² -3-OH Ser ² -2,2-NH,3a,3b Phe-2-NH,3a,3b	Ser ² -2-NH Apcoa-3-NH, Phe-3a, 3b,5,5'
2-NH	115.2, NH	8.30, d (9.6)	Ser ² -1	Phe-2	Phe-2,3a,3b	Ser ² -2,2-NH, Thr-3-OH, Phe- 3a,3b
3a b	40.2, CH ₂	2.91, m 2.81, dd (12.9,6.9)	Phe-1,2,4, Phe-1,2,4	Phe-2,3b Phe-2,3a	Phe-2,2-NH, 3b Phe-2,2-NH, 3a	Phe-2,2-NH, 3b Phe-2
4 5,5'	137.2, C 129.5, CH x 2	7.21, m	Phe-4,5',5, 6,6'			Phe-2, Apcoa-6-Me
6,6'	128.5, CH x 2	7.26, m	Phe-4			
7	126.8, CH	7.20, m				
Gal-1 2 3 4 5 6	89.9, CH 70.4, CH 74.2, CH 70.7, CH 78.6, CH 63.2, CH ₂	5.41, d (8.3) 3.78, brs 3.54, m 4.02, m 3.90, m 3.99, m	sHis-4,6, Gal-2,4 Gal1,3 Gal-2,4 Gal-2,3,5	Gal-2 Gal-1,3 Gal-2,4 Gal-3	Gal-2,3,4,5,6,6' Gal-1,3,4 Gal-1,2,4,5,6,6' Gal-1,2,3,4,5,6,6' Gal-4, 5,6,6' Gal-4, 5,6,6'	sHis-6, Gal-3,6a,6b sHis-6 Gal-1 Gal-1

^a1H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). ^bMultiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz). ^dHMBC correlations, optimized for 8 Hz. ^eSelected NOEs from ROESY experiment.

Elemental Composition Report

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 400.0

Element Prediction: Off

Number of isotope peaks used for iFIT = 5

Monoisotopic Mass, Even Electron Ions

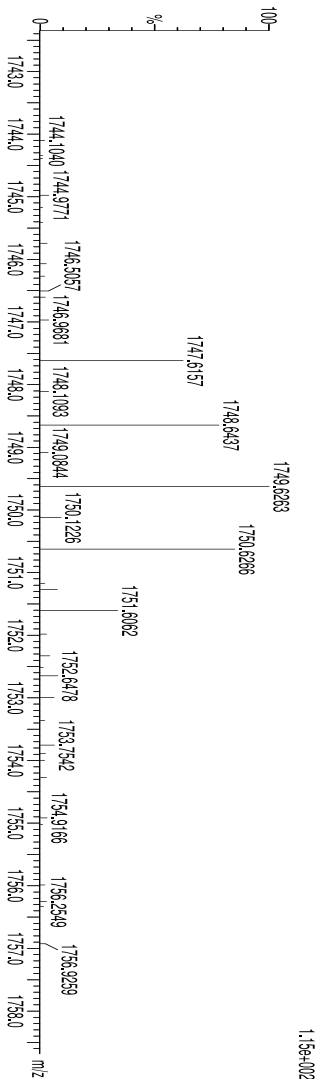
48 formulae evaluated with 11 results within limits (up to 3 closest results for each mass)

Elements Used:

C: 70-90 H: 90-100 N: 10-20 O: 25-30 S: 79Br: 1-1

OH247310
Oxid Hash
1: TOF MS ES+

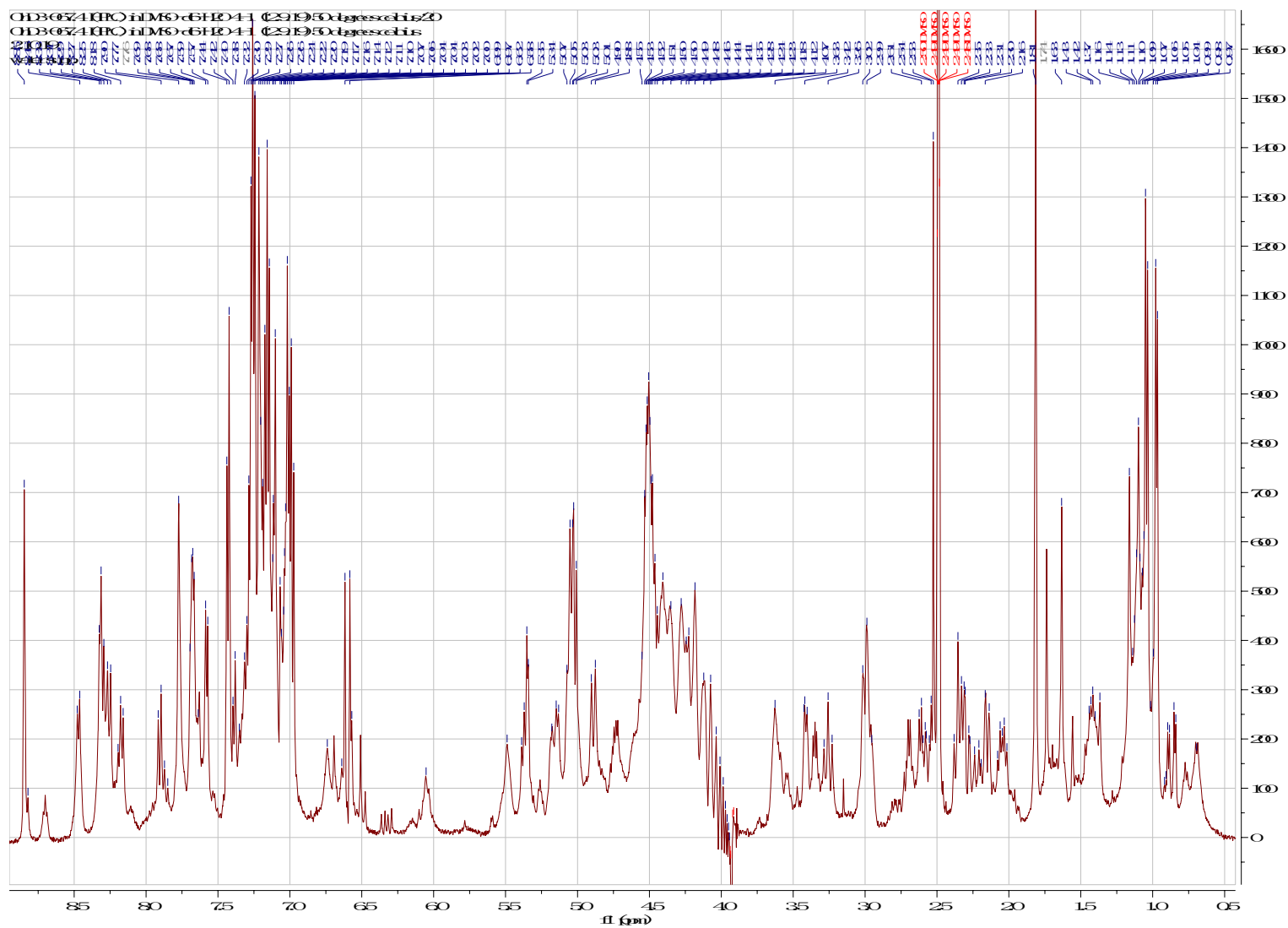
Camell1281 99 (2.513) Cm (99.60)



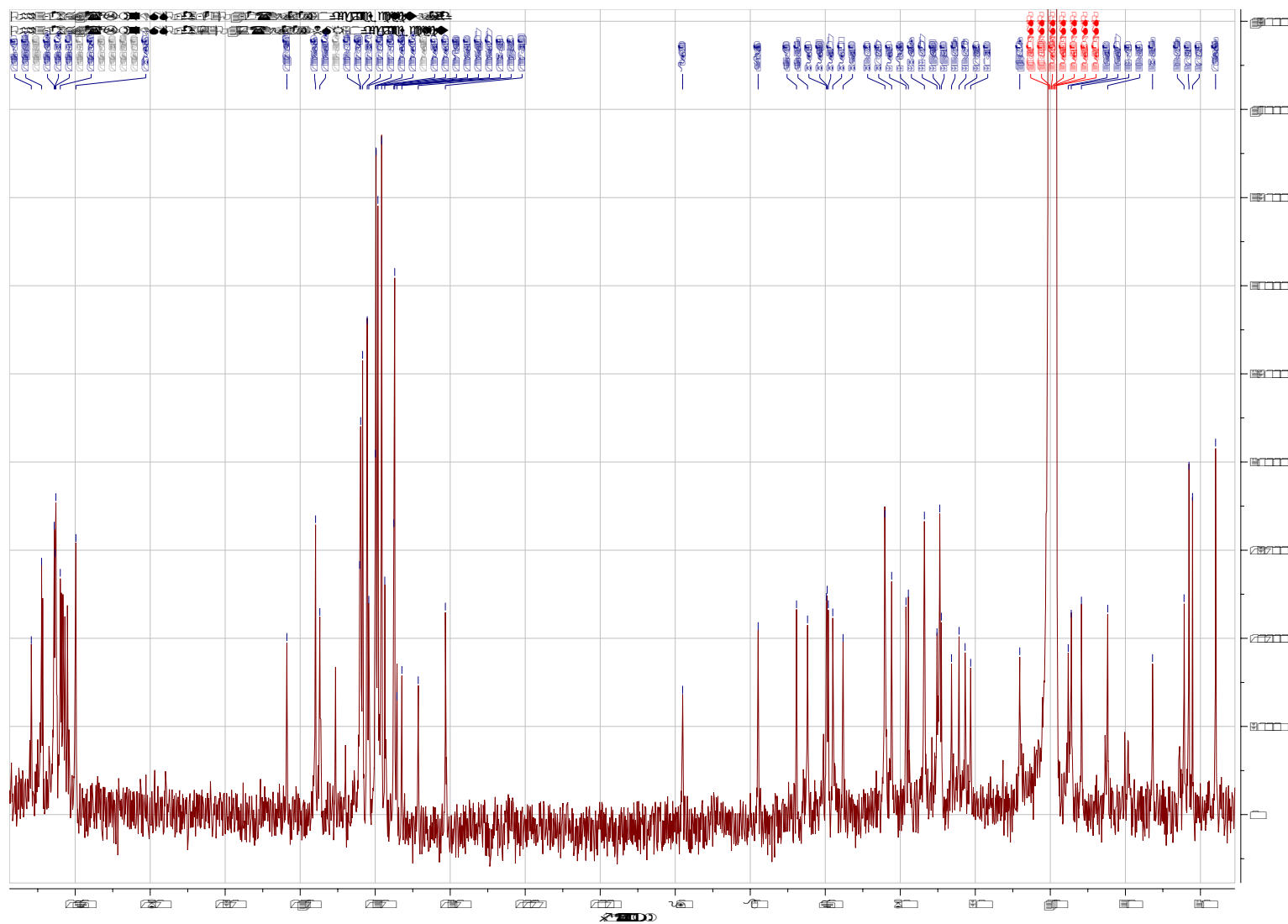
Minimum:	-1.5				
Maximum:	400.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT
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1747.6199	-4.2	-2.4	30.5	44.0	1.0
1747.6087	7.0	4.0	30.5	44.4	1.4
Formula					
C76 H100 N16 O27 79Br					
C70 H100 N20 O28 79Br					
C71 H100 N18 O29 79Br					

S43 Figure S38. (+)-HRESIMS data of theonellamide J (1)

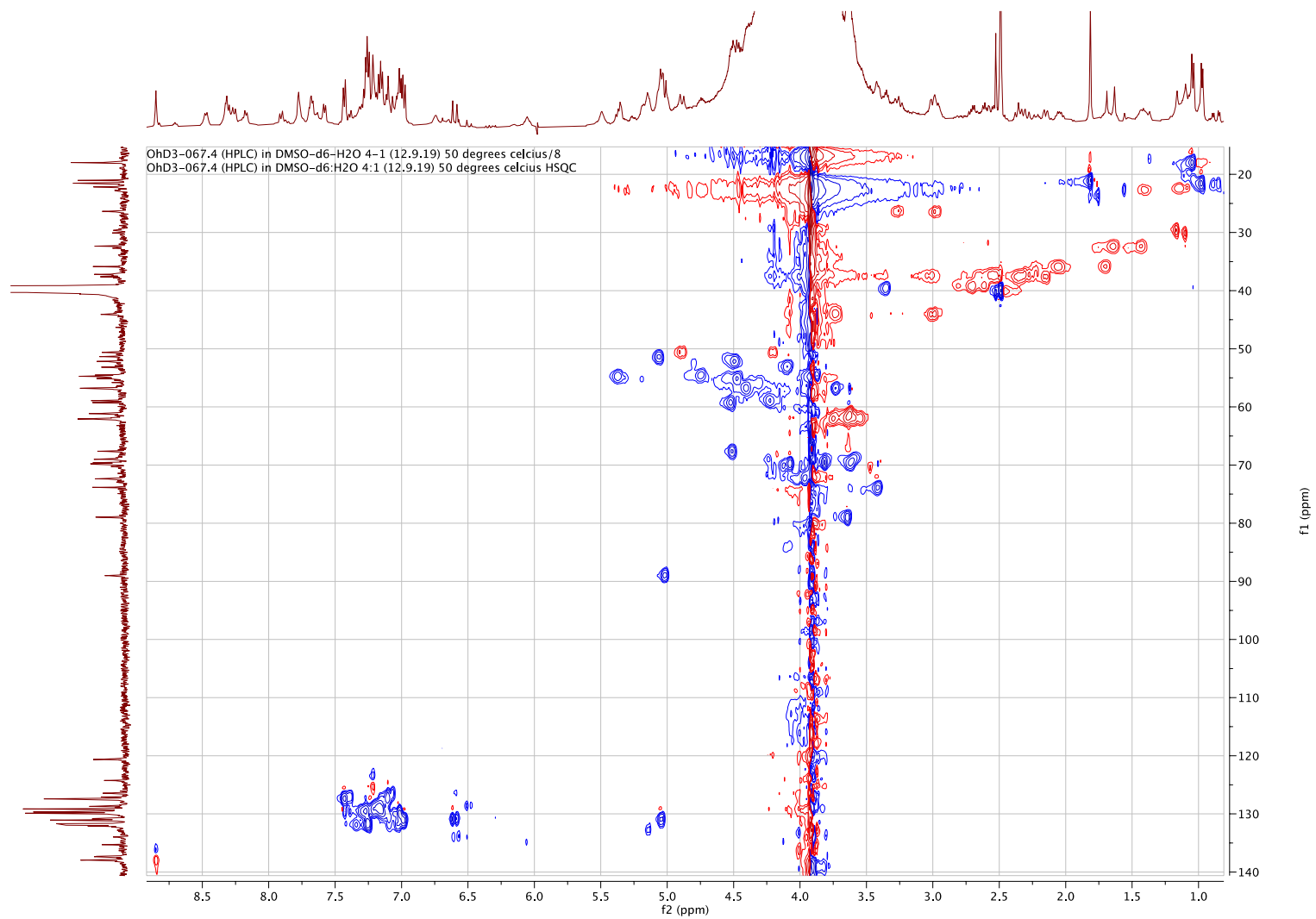
S44 Figure S39. ^1H NMR spectrum (500 MHz) of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO- d_6 :H $_2$ O at 50 °C



S45 Figure S40. ^{13}C NMR spectrum (125 MHz) of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO- d_6 :H $_2$ O at 50 °C



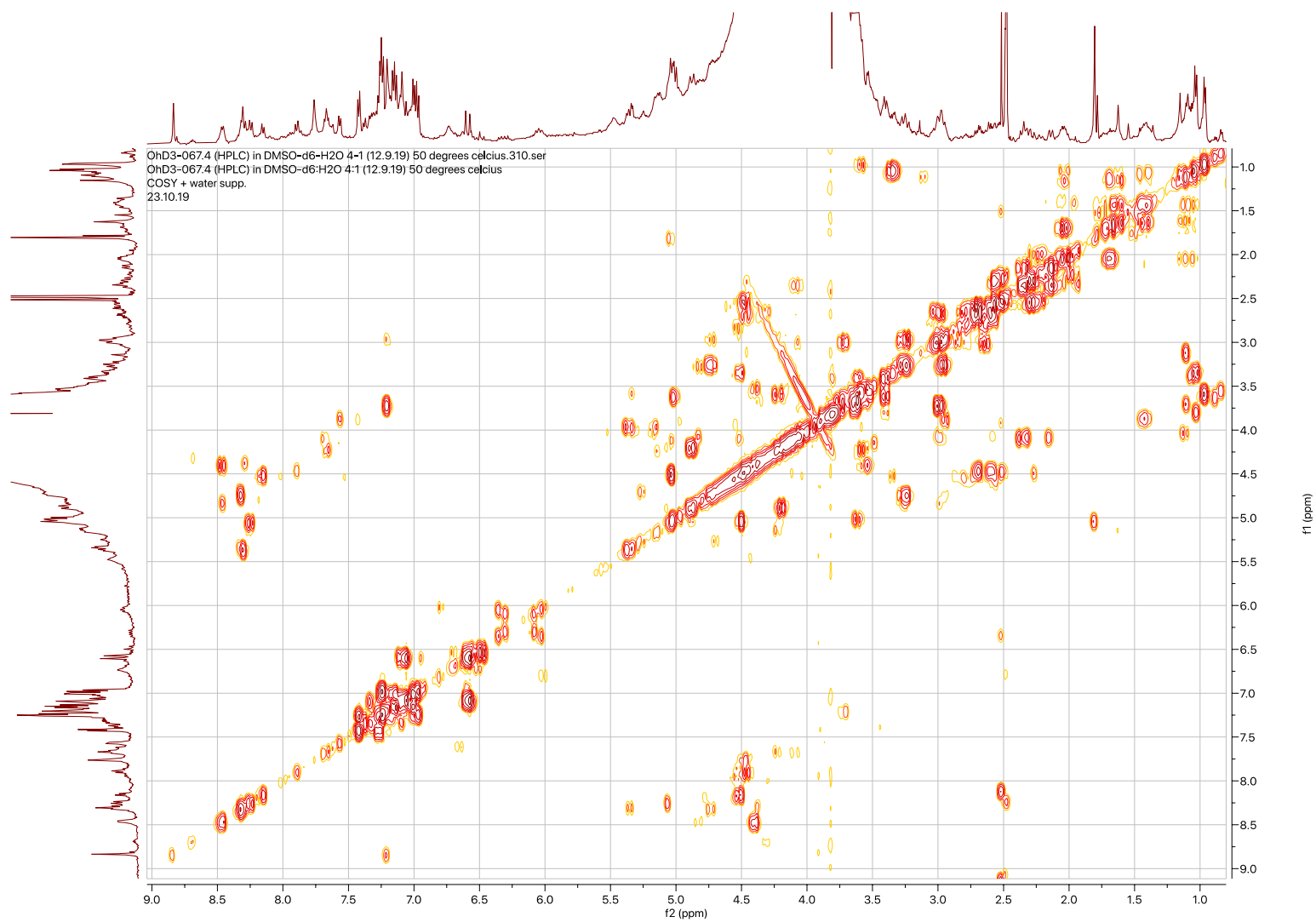
S46 Figure S41. HSQC spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



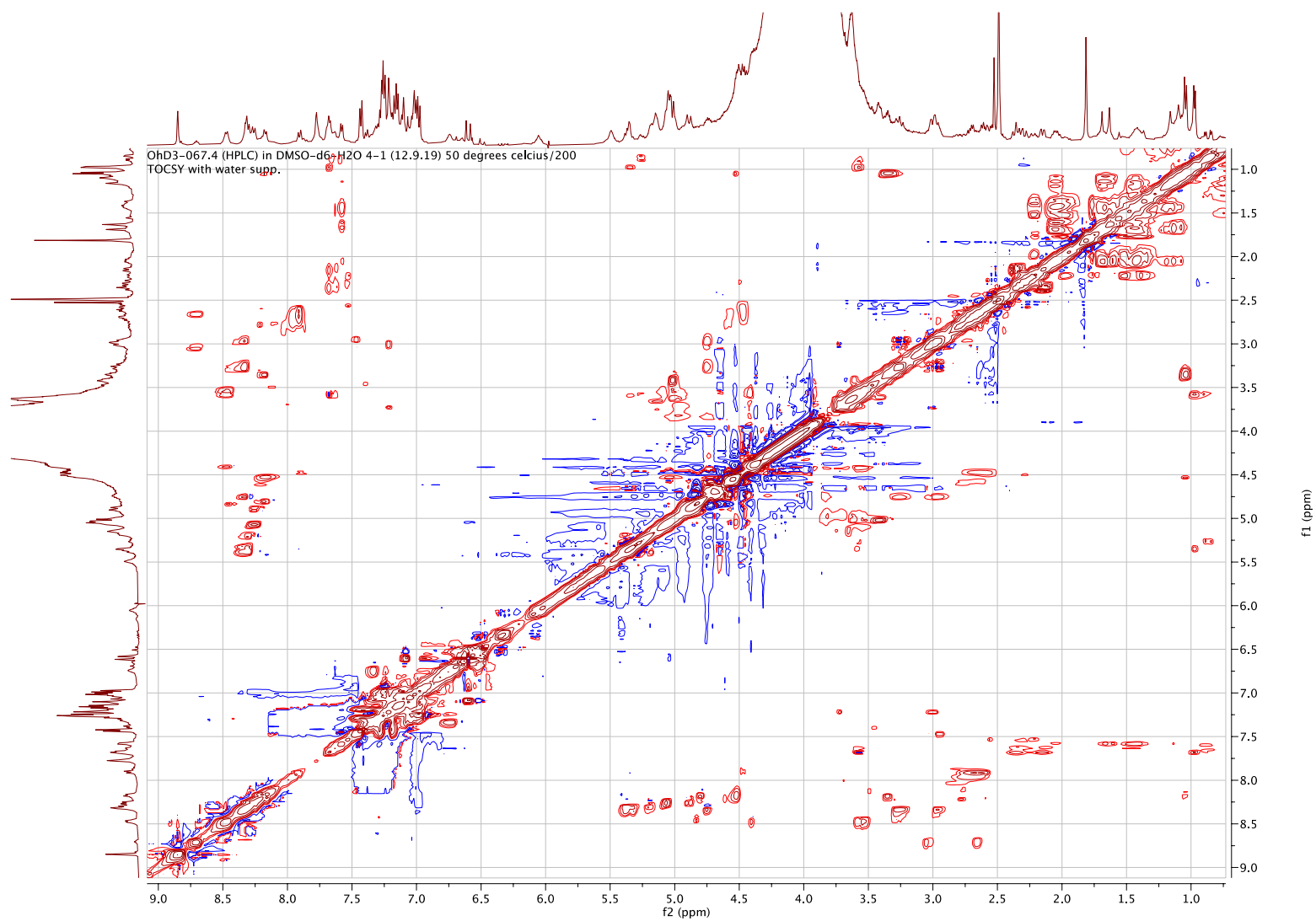
S47 Figure S42. HMBC spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



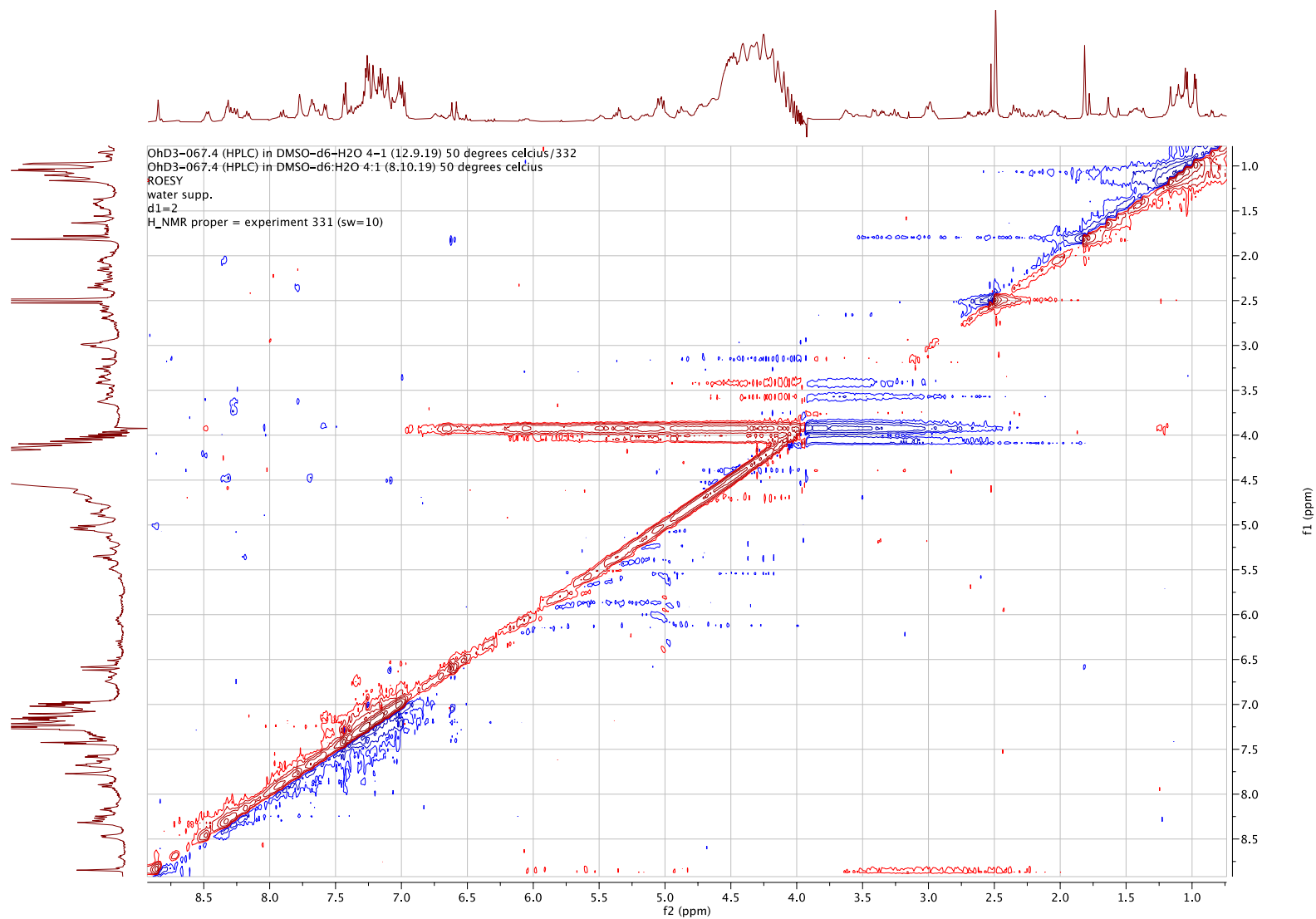
S48 Figure S43. COSY spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



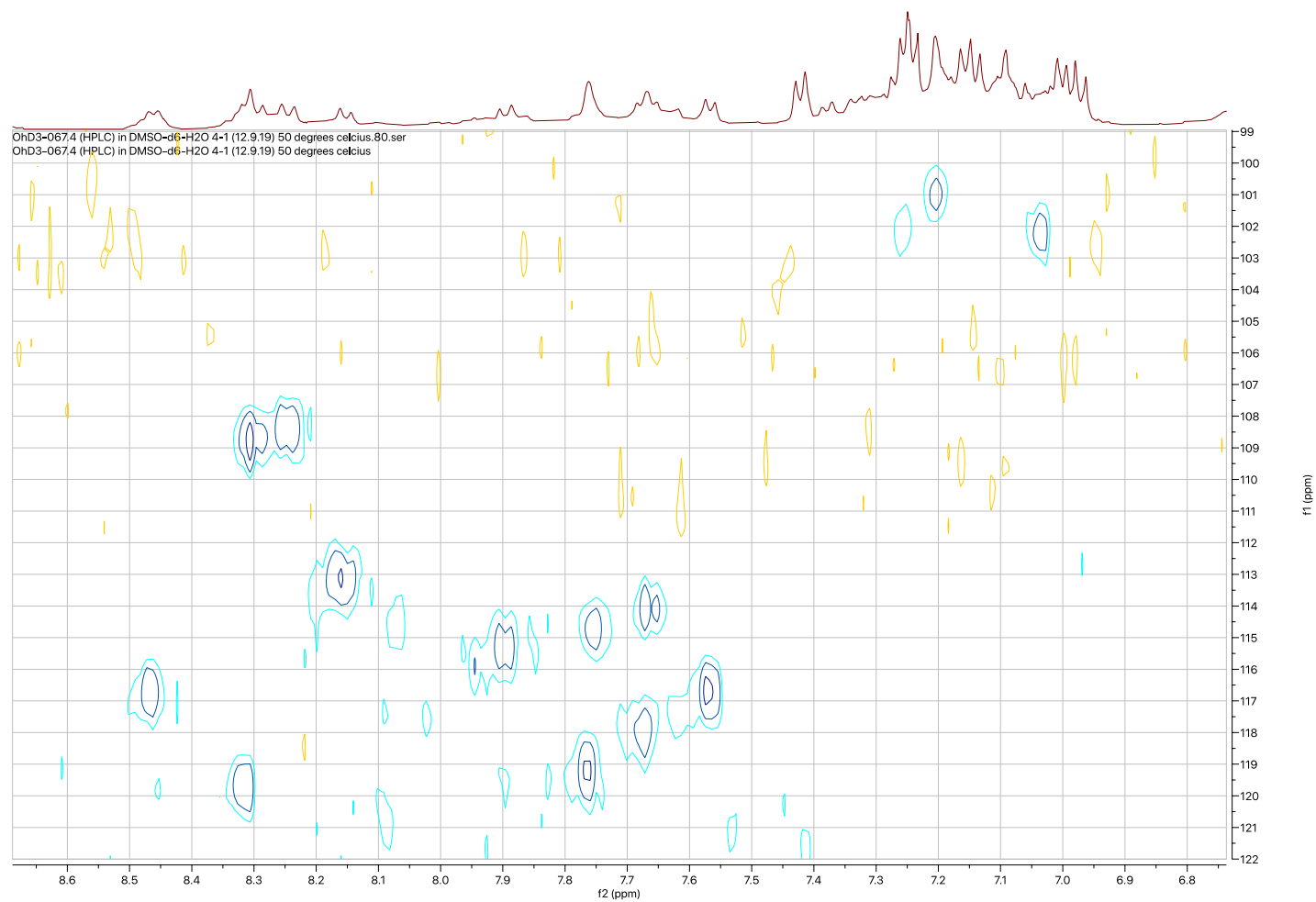
S49 Figure S44. TOCSY spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S50 Figure S45. ROESY spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



S51 Figure S46. N-H HSQC spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



S52 Figure S47. N-H HMBC spectrum of 5-*cis*-Apoa-theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C



Table S6. NMR data of theopalauamide (**2**) in 4:1 DMSO-*d*₆:H₂O at 50 °C^a

Position	$\delta_{C/N}^b$	δ_H^c	HMBC correlations ^d	COSY correlations	NOE correlations ^e
5-cis-Apoa-1	172.6, C				
2a	37.6, CH ₂	2.36, t (12.5)	Apoa-1,3	Apoa-2b,3	Ser ¹ -NH
b		2.15, dd (12.5,2.6)	Apoa-1,3	Apoa-2a,3	
3	53.2, CH	4.10, m		Apoa-2a,2b, NH	
3-NH	118.0, NH	7.69, d (8.1)	Phe-1	Apoa-3	Phe-2
4	67.7, CH	4.51, m		Apoa-5	
4-OH		5.28, d (5.0)			
5	130.9, CH	5.05, brd (10.1)	Apoa-3,6-Me,7	Apoa-4,6-Me,	Apoa-6-Me
6	135.3, C				
6-Me	21.1, CH ₃	1.82, brs	Apoa-5,6,7	Apoa-5	Apoa-5,8
7	126.5, CH	7.09, d (16.0)	Apoa-6,6-Me,8	Apoa-8	
8	130.8, CH	6.60, d (16.0)	Apoa-6,7,9, 10,10'	Apoa-7	Apoa-6-Me
9	138.1, C				
10,10'	127.6, CH x 2	7.43, d x 2 (8.1)	Apoa-8,10', 10,12	Apoa-11,11'	Apoa-11,11'
11,11'	129.7, CH x 2	7.27, dd (8.1,7.4)	Apoa-9,11', 11	Apoa-10,10',12	Apoa-10,10'
12	129.2, CH	7.17, t (7.4)	Apoa-10,10'	Apoa-11,11'	
Ser ¹ -1	172.8, C				
2	56.8, CH	3.74, m	Ser ¹ -3	Ser ¹ -NH,3	sAla-2-NH
2-NH	114.7, NH	7.77, m	Apoa-1,	Ser ¹ -2	Apoa-2a, Ser ¹ -3
3	61.2, CH ₂	3.62, m	Ser ¹ -1,2	Ser ¹ -2	Ser ¹ -NH, sAla-NH
3-OH					
sAla-1	169.88, C				
2	51.4, CH	5.06, m	sAla-1	sAla-2-NH, 3a,3b	
2-NH	108.5, NH	8.26, d (10.9)	Ser ¹ -1,	sAla-2	Ser ¹ -2
3a	50.6, CH	4.89, brd (13.4)	sHis-6	sAla-2,3b	
b		4.20, m	sAla-1	sAla-2,3a	sHis-6

Asn-1	171.4, C				
2	52.2, CH	4.49, m	Asn-1	Asn-NH,3a, 3b	Asn-2-NH
2-NH	119.2, NH	7.78, s	sAla-1	Asn-2	
3a	37.4, CH ₂	2.55, dd (16.0,5.9)	Asn-1,2,4	Asn-2,3b	Asn-4-NH ₂ b
b		2.30, dd (16.0,2.6)	Asn-1,4	Asn-2,3a	
4	172.5, C				
4-NH ₂ a	103.9, NH ₂	7.31, brs			Asn-3a
b		6.73, brs			
Han-1	171.3, C				
2	54.7, CH	5.37, t (9.1)	Han-1,3,4	Han-NH	BrMePhe-2-NH
2-NH	108.8, NH	8.30, d (9.2)	Asn-1	Han-2	Asn-3
3	72.4, CH	3.96, m			Asn-NH
3-OH		5.18, d (5.7)		Han-3	
4	174.5, C				
4-NH ₂	102.0, NH ₂	7.04, m			
		7.25, m			
BrMePhe-1	172.0, C				
2	59.2, CH	4.52, m	BrMePhe-1,3,3-Me,4	BrMePhe-NH,3	
2-NH	113.1, NH	8.17, d (9.2)	Has-1	BrMePhe-2	Asn-2
3	39.6, CH	3.35, m	BrMePhe-1, 2,3-Me,4,5,5'	BrMePhe-2,3-Me	BrMePhe-5,5'
			BrMePhe-2,3,4	BrMePhe-3	BrMePhe-5,5'
3-Me	18.0, CH ₃	1.04, d (7.2)			
4	141.8, C				
5,5'	131.1, CH x	6.98, d x 2 (8.4)	BrMePhe-3, 5',5,7	BrMePhe-6,6'	BrMePhe-3, 3-Me
	2				
6,6'	131.7, CH x	7.25, d x 2 (8.4)	BrMePhe-4,6',6,7	BrMePhe-5,5'	
	2				
7	120.6, C				
iSer-1	171.6, C				
2	69.9, CH	4.08, m	iSer-1	iSer-2-OH, 3a,3b	
2-OH		5.03 m		iSer-2	
3a	44.1, CH ₂	3.73, m	BrMePhe-1	iSer-2,3b,NH	

				iSer-2,3a,NH	
b		3.00, brd (14.4)	BrMePhe-1, iSer-1		
3-NH	101.0, NH	7.20, m	BrMePhe-1	iSer-3a,3b	
Aad-1	175.9, C				
2	54.7, CH	3.88, m	Aad-1	Aad-2-NH, 3a,3b	Aad-2-NH
2-NH	116.7, NH	7.58, d (8.0)	iSer-1, Aad-1	Aad-2	Aad-2
3a	32.4, CH ₂	1.65, m		Aad-2,4	
b		1.43, m		Aad-2,4	
4	22.2, CH ₂	1.11, m		Aad-3a,3b, 5a,5b	
5a	35.9, CH ₂	2.05, dt (13.3,7.5)	Aad-6,4	Aad-5b,4	sHis-NH
b		1.70, m	Aad-6	Aad-5a,4	
6	174.3, C				
sHis-1	171.0, C				
2	54.5, CH	4.74, ddd (12.8,7.3,5.7)		sHis-NH, 3a,3b	Thr-NH
2-NH	119.6, NH	8.32, d (5.9)	Aad-6, sHis-3	sHis-2	Aad-5a
3a	26.4, CH ₂	3.26, t (13.3)	sHis-1,2,4,8	sHis-2,3b	
b		2.96, m	sHis-1,2,8	sHis-2,3a	
4	132.0, C				
5-N	181.2, N				
6	137.4, CH	8.85, s	sHis-5-N,7-N,4,8, Gal-1,	sHis-8	sAla-3b, Gal-1
7-N	167.4, N				
8	124.3, CH	7.21, brs	sHis-5-N,7-N,4,6	sHis-6	
Thr-1	172.7, C				
2	58.9, CH	4.23, m	sHis-1, Thr-1,3,4	Thr-NH,3	Ser ² -2-NH
2-NH	114.1, NH	7.67, d (7.4)	sHis-1	Thr-2	sHis-2, Ser ² -3
3	68.9, CH	3.59, m		Thr-4	Ser ² -2-NH
3-OH		5.35, d (5.9)	Thr-2		
4	21.5, CH ₃	0.97, d (6.4)	Thr-3	Thr-3	
Ser ² -1	169.91, C				
2	56.8, CH	4.41, m	Ser ² -3	Ser ² -NH	

2-NH 3	116.6, NH 62.1, CH ₂	8.47, d (8.0) 3.57, m 3.64, m	Thr-1	Ser ² -2	Thr-2,3
3-OH Phe-1 2	171.8, C 55.1, CH	4.47, m	Ser ² -1, Phe-1,4	Phe-NH	Apoa-3-NH
2-NH 3	115.3, NH 39.2, CH ₂	7.91, d (10.2) 2.70, dd (12.7,7.2) 2.61, dd (12.7,7.7)	Ser ² -1 Phe-1,2,4,5 Phe-1,2,4,5	Phe-2,3a,3b Phe-2,3b Phe-2,3a	
4 5,5'	137.3, C 129.9, CH x 2	7.01, d x 2 (7.5)	Phe-5',5,7	Phe-6,6'	
6,6'	129.1, CH x 2	7.16, t x 2 (7.5)	Phe-4,6',6	Phe-5,5',7	
7 Gal-1 2	127.5, CH 89.0, CH 69.8, CH	7.10, t (7.5) 5.02, d (9.8) 3.62, m	sHis-4,6, Gal-3 Gal-3	Phe-6,6' Gal-2 Gal-1,2-OH, 3	sHis-6
2-OH 3	73.8, CH	5.53, m 3.41, m		Gal-2 Gal-2	
4	69.6, CH	3.81, m	Gal-2,3	Gal-5	
5	79.0, CH	3.64, m	Gal-1,6	Gal-4,6a	
6a	62.1, CH ₂	3.75, m	Gal-5	Gal-5,6b	
b		3.54, m		Gal-6a	

^a¹H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). ^bMultiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz). ^dHMBC correlations, optimized for 8 Hz. ^eSelected NOEs from ROESY experiment.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 400.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

82 formula(e) evaluated with 25 results within limits (up to 3 closest results for each mass)

Elements Used:

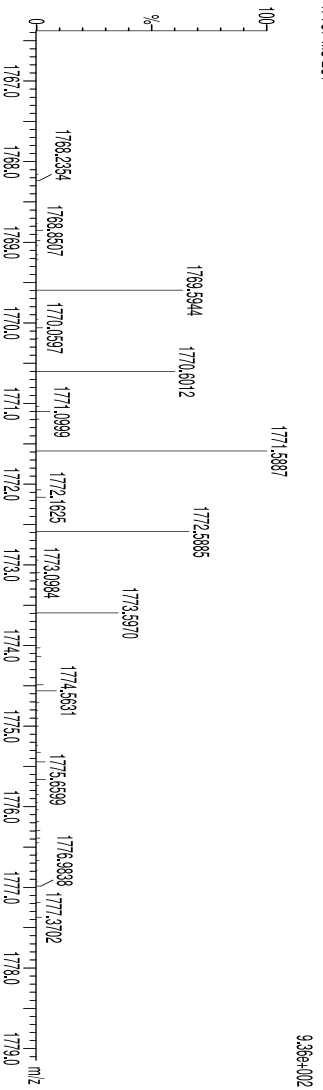
C: 70-80 H: 90-100 N: 10-20 O: 25-30 79Br: 1-1 Na: 0-1

ohD3-067/4

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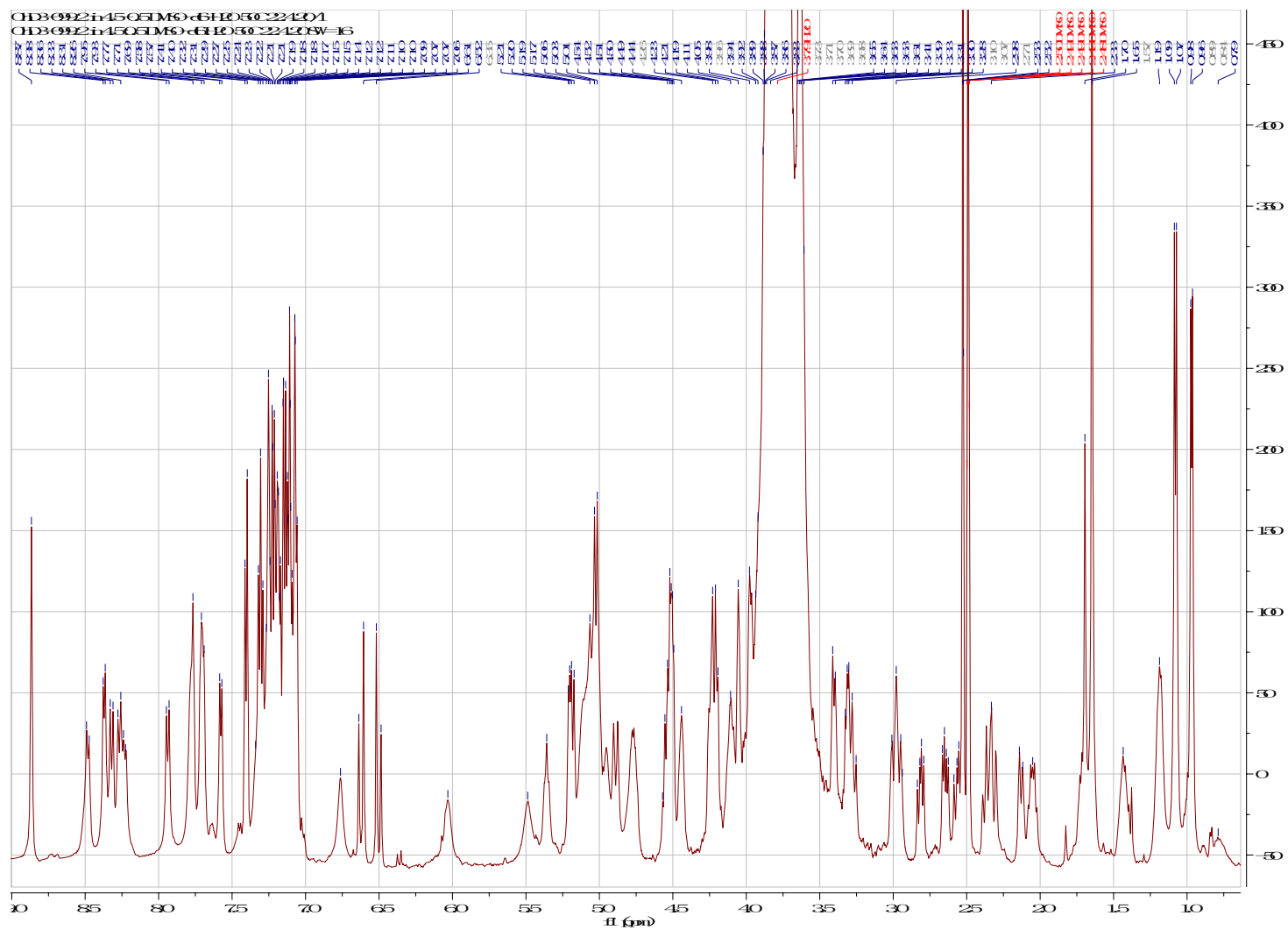
Ohad Hasin

1:TOF MS ES+

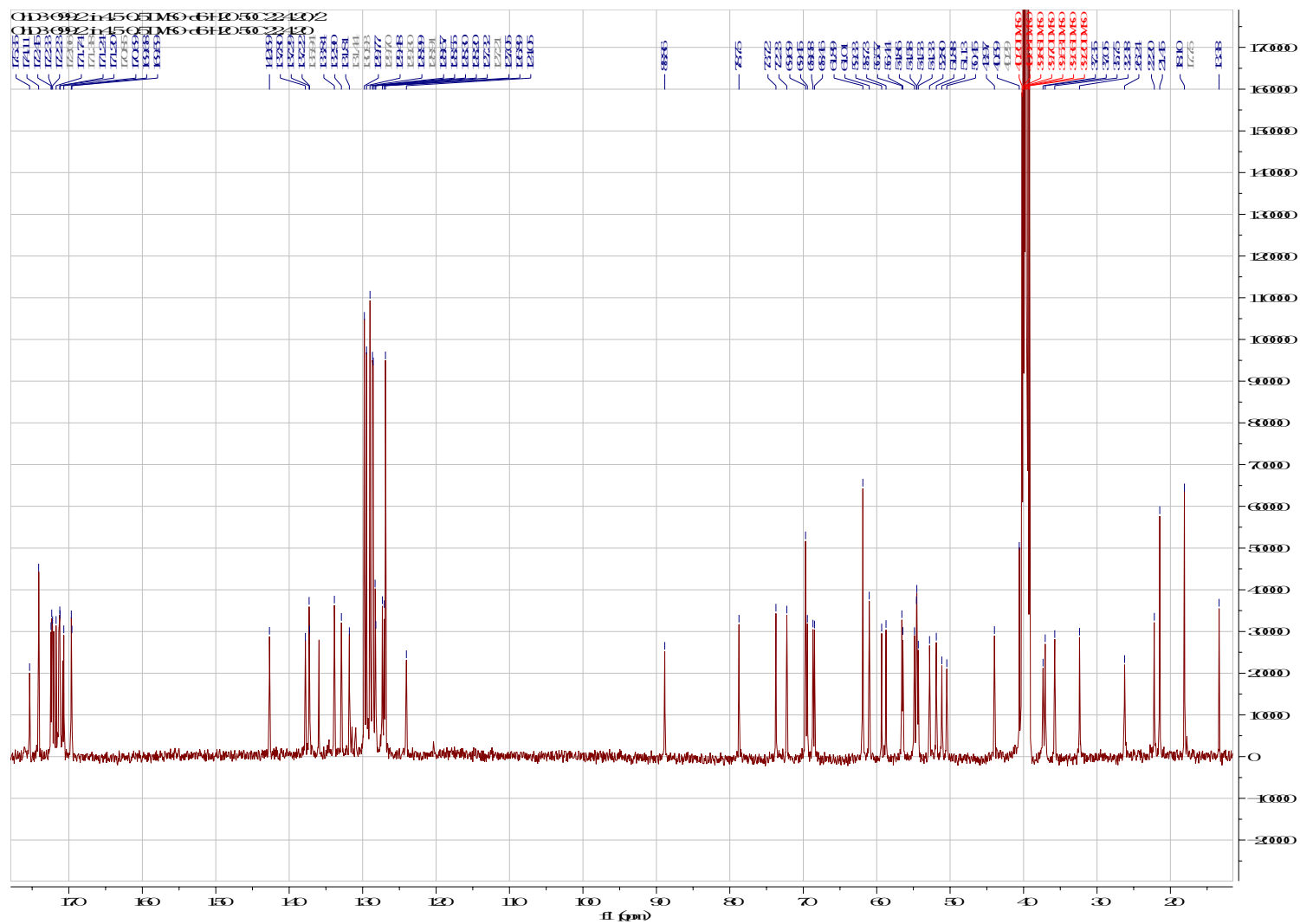


Minimum:						-1.5
Maximum:						400.0
		5.0	20.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)
						Formula
1769.5944	1769.5947	-0.3	-0.2	34.5	91.1	1.1
	1769.9920	1.4	0.8	33.5	91.1	1.1
1769.5911		-2.7	-1.5	37.5	91.0	1.1
						C76 H99 N16 O27 79Br Na
						C73 H98 N18 O29 79Br
						C78 H98 N16 O27 79Br

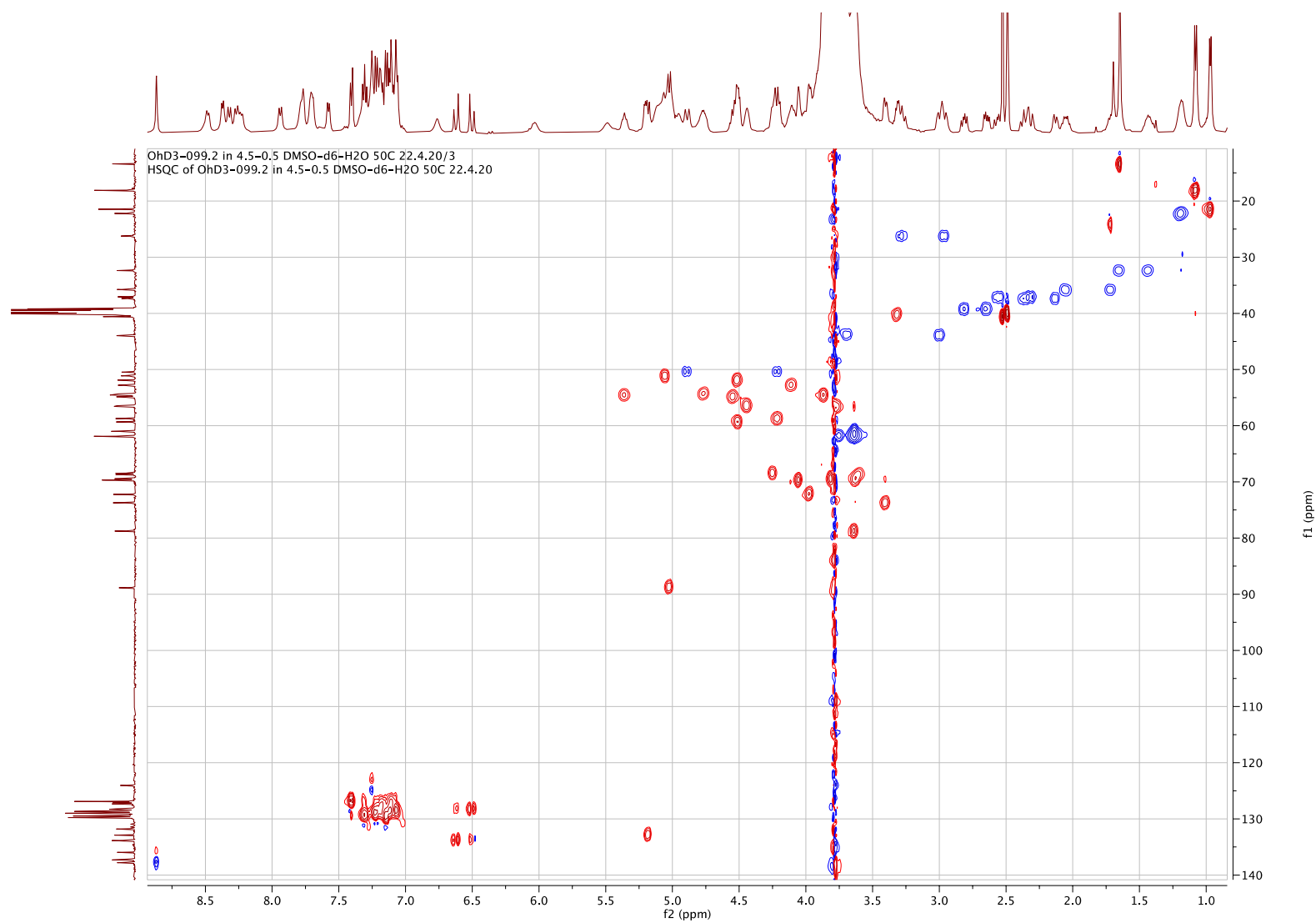
S55 Figure S49. ^1H NMR spectrum (500 MHz) of theonellamide K (**3**) in 4:1 $\text{DMSO}-d_6$: H_2O at 50 $^\circ\text{C}$



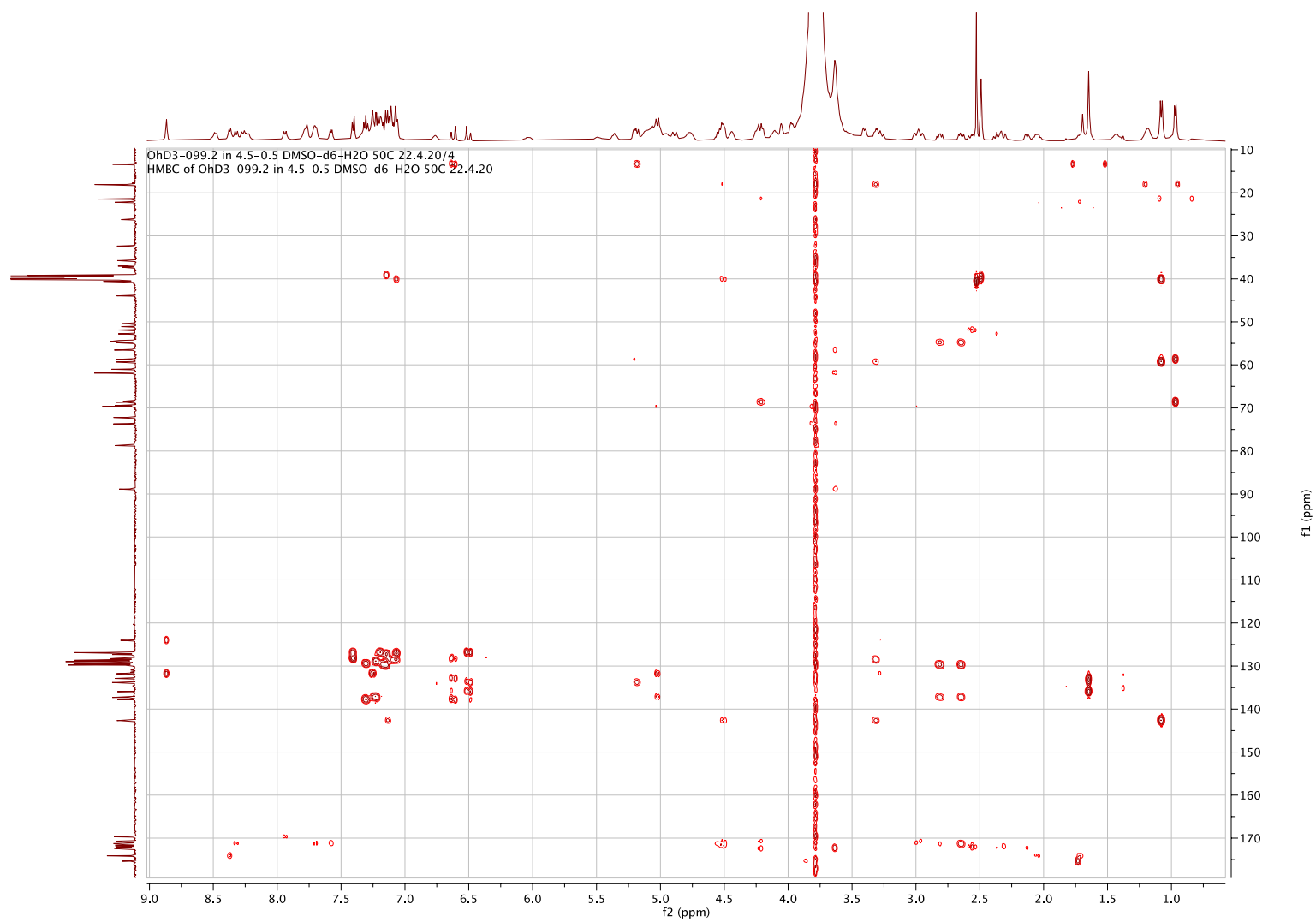
S56 Figure S50. ^{13}C NMR spectrum (125 MHz) of theonellamide K (**3**) in 4:1 $\text{DMSO-}d_6\text{:H}_2\text{O}$ at 50 $^\circ\text{C}$



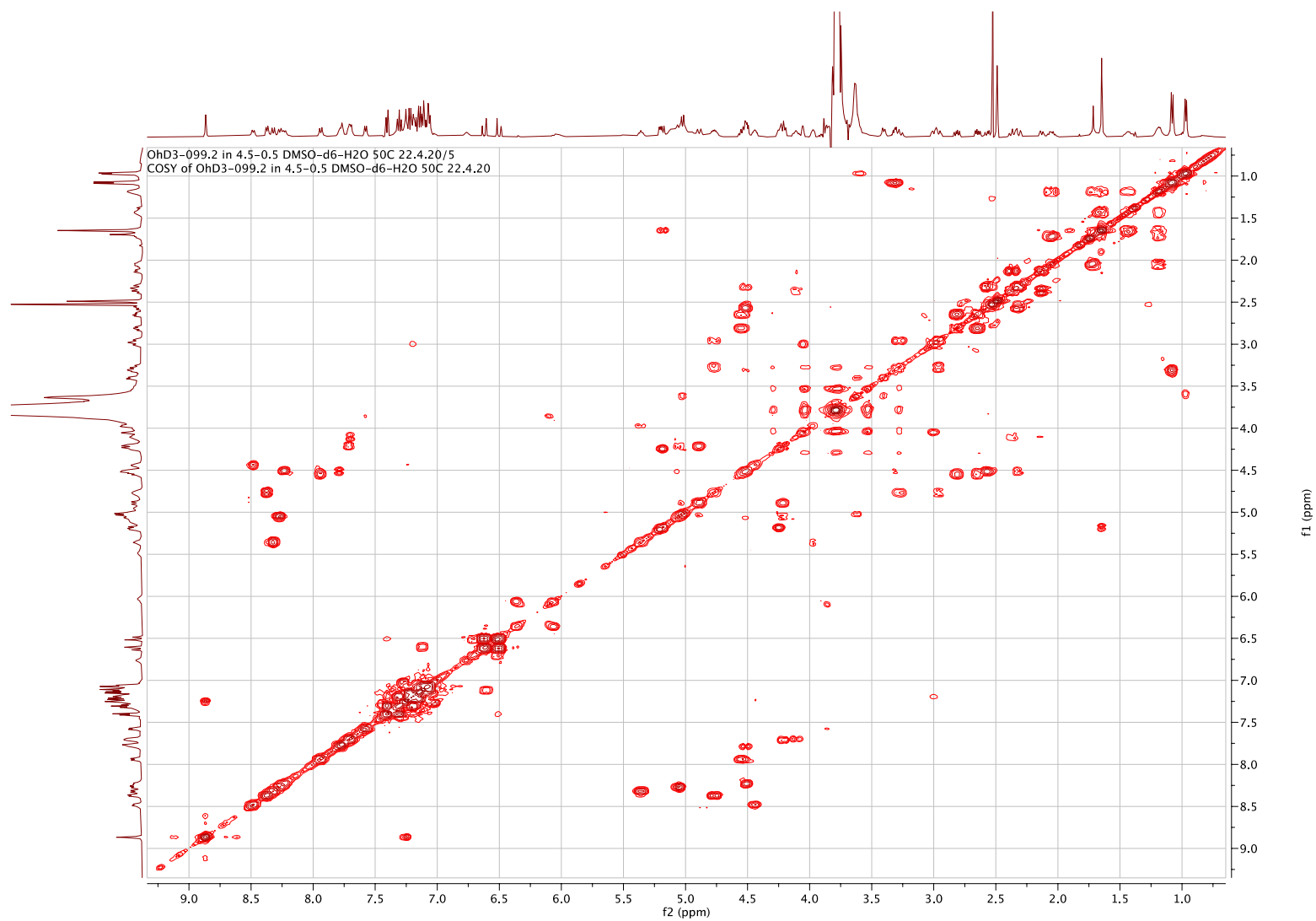
S57 Figure S51. HSQC spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



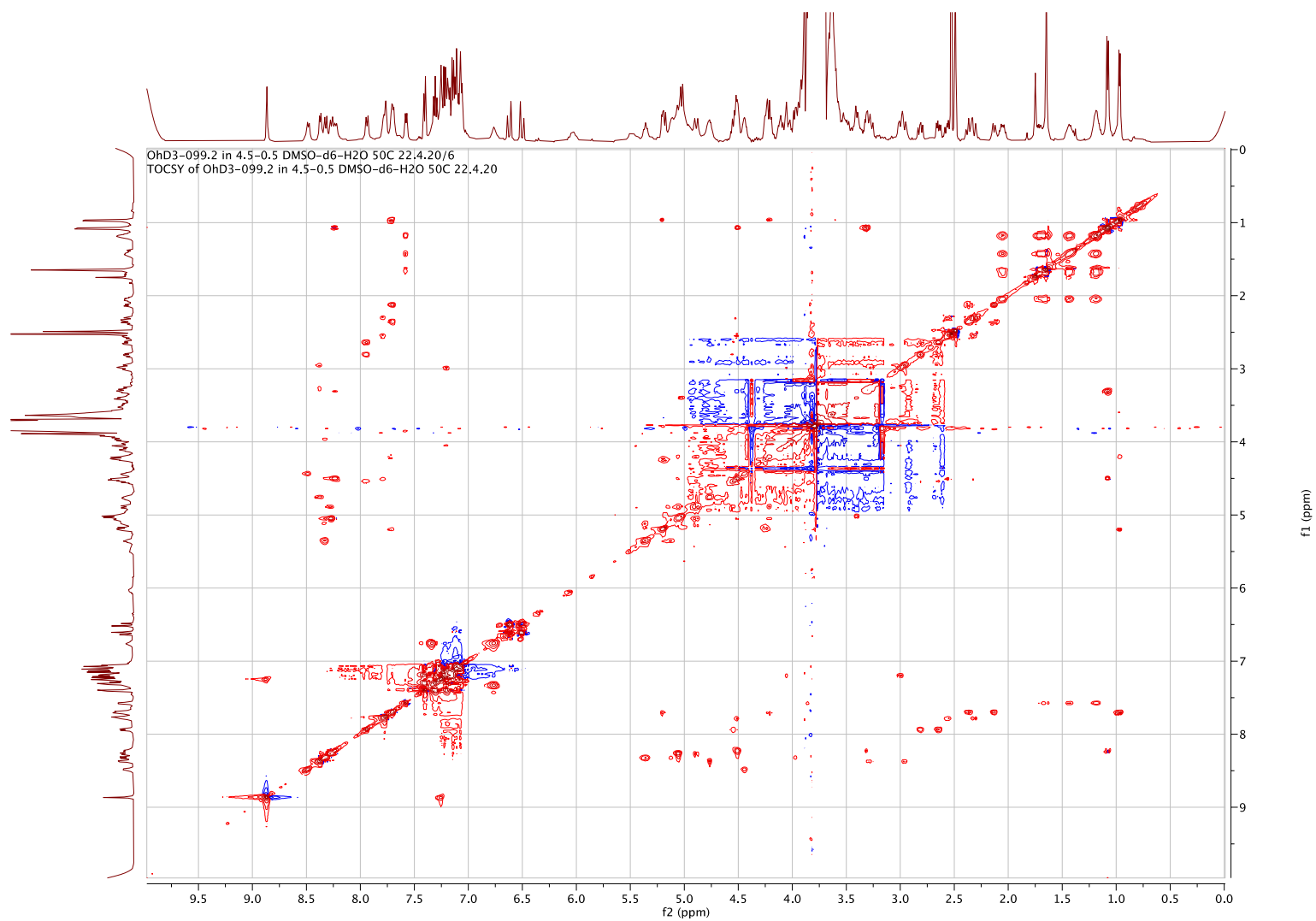
S58 Figure S52. HMBC spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



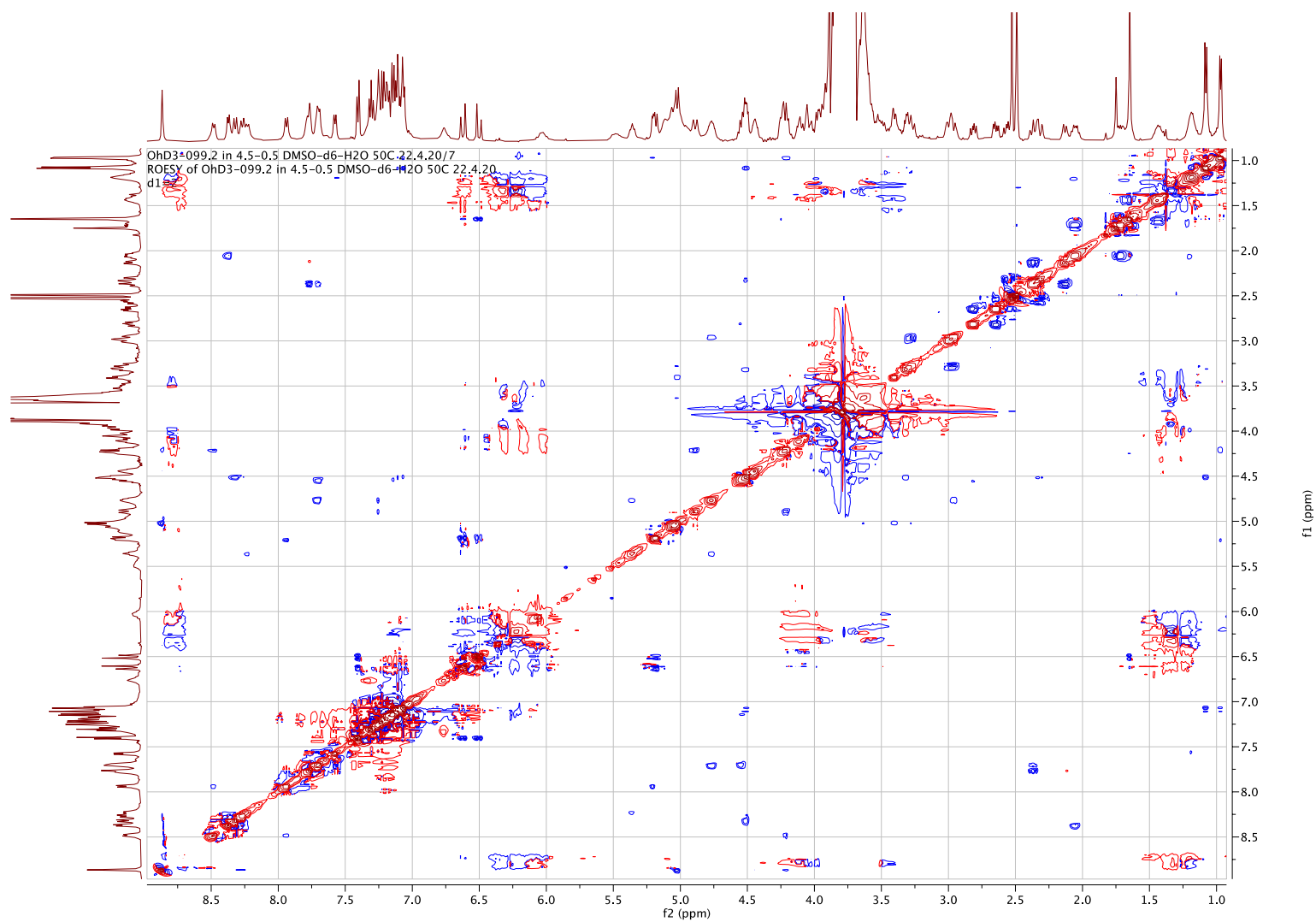
S59 Figure S53. COSY spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



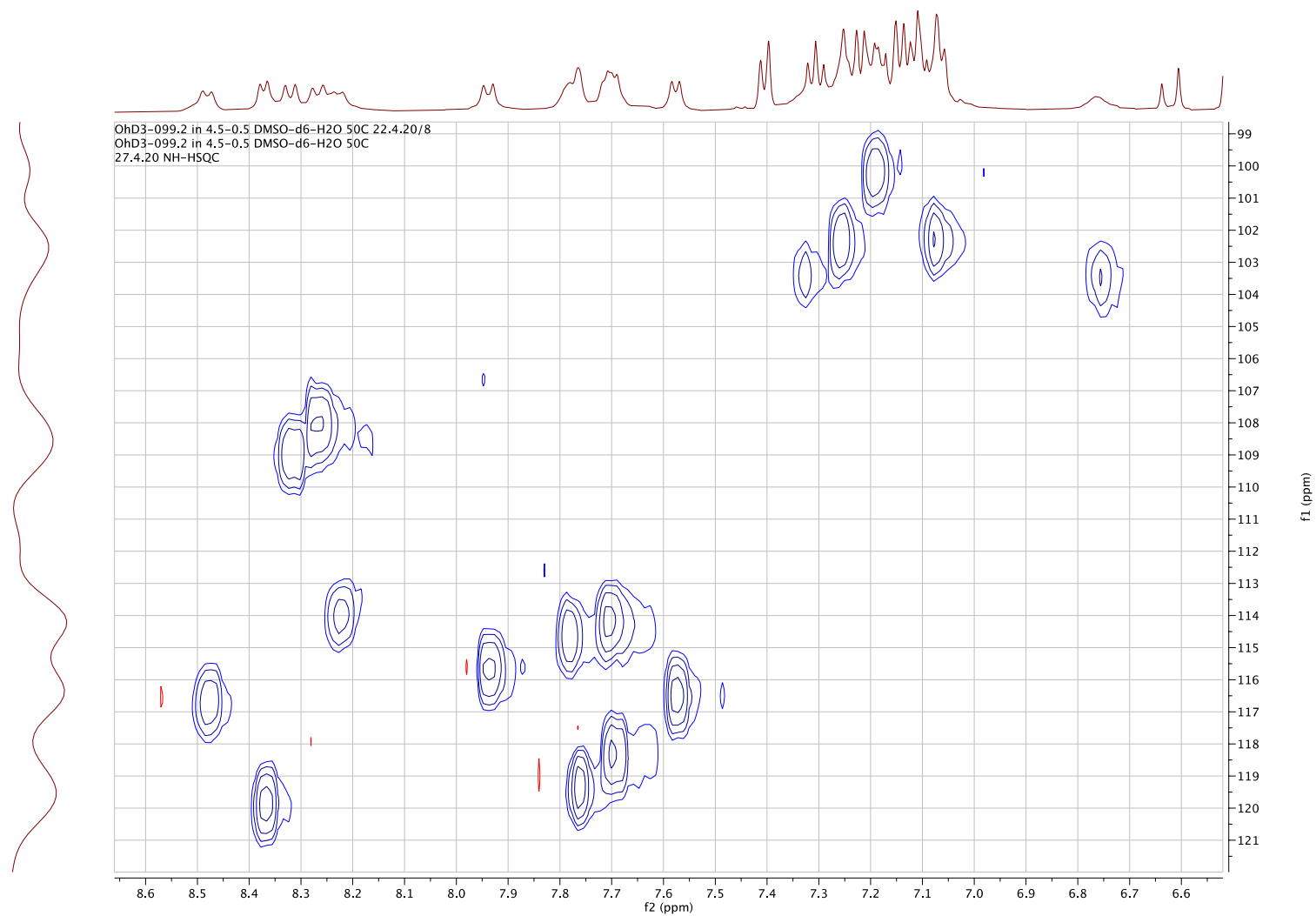
S60 Figure S54. TOCSY spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S61 Figure S55. ROESY spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S62 Figure S56. N-H HSQC spectrum theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C



S63 Figure S57. N-H HMBC spectrum of theonellamide K (**3**) in 4:1 DMSO- d_6 :H₂O at 50 °C

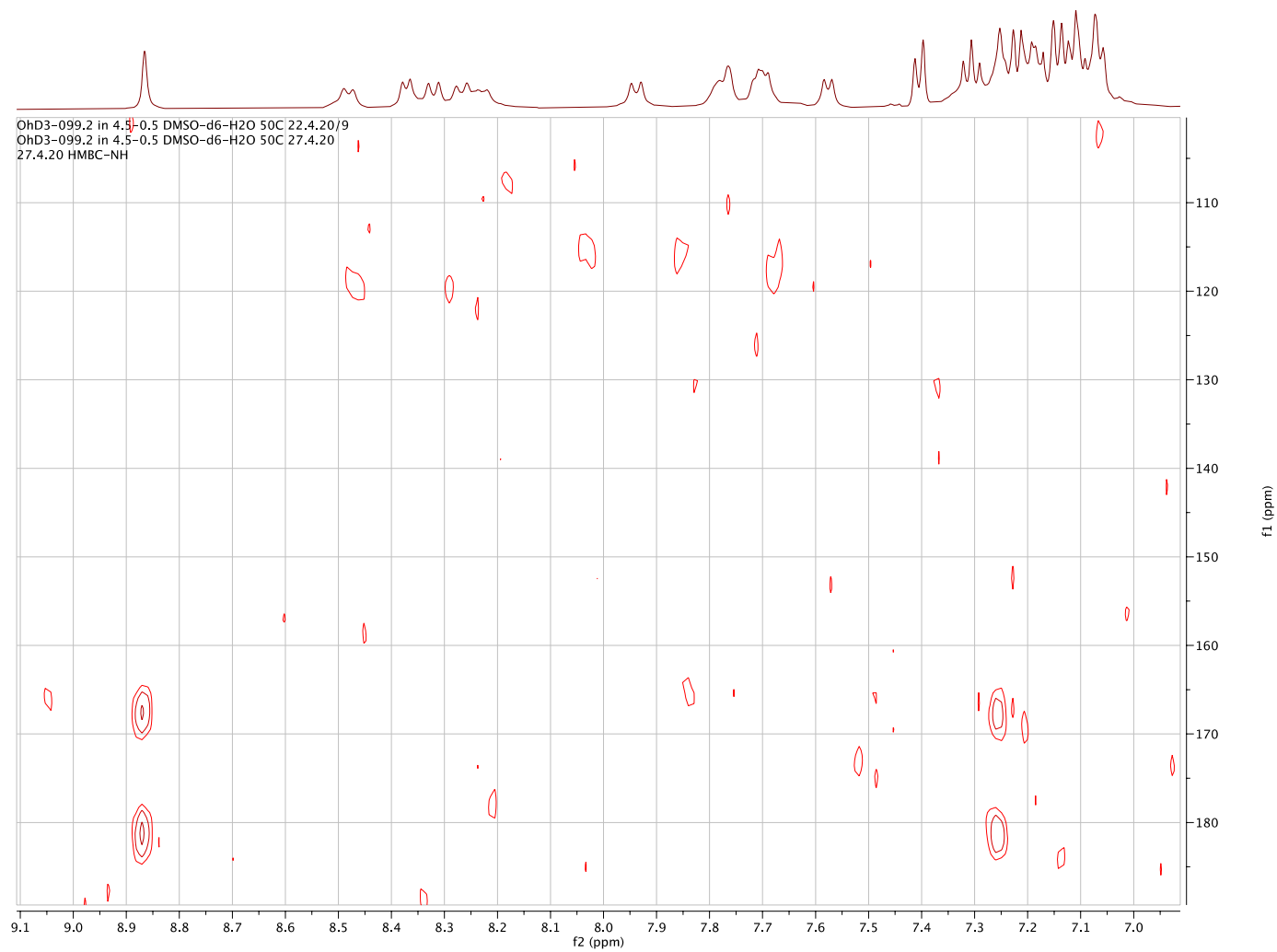


Table S7. NMR data of theonellamide K (**3**) in 4:1 DMSO-*d*₆:H₂O at 50 °C^a

Position	$\delta_{\text{C/N}}^{\text{b}}$	$\delta_{\text{H}}^{\text{c}}$	HMBC correlations ^d	COSY correlations	TOCSY correlations	NOE correlations ^e
Apoa-1	172.2, C					
2a	37.4, CH ₂	2.37, t (12.5)	Apoa-1,3	Apoa-2b,3	Apoa-3-NH,	Ser ¹ -2-NH, Apoa-2b, 2-NH
b		2.13, dd (12.5,2.8)	Apoa-1,3	Apoa-2a,3	Apoa-3-NH	Apoa-2a,3 ,4, Ser ¹ -2-NH(neg)
3	52.8, CH	4.11, m	Phe-1	Apoa-2a, 2b,3-NH	Apoa-3-NH	Apoa-2b, 3-NH,5
3-NH	118.4, NH	7.70, d (8.6)	Apoa-3	Apoa-3	Apoa-2a,2b,3	Apoa-3,5, Phe-2
4	68.5, CH	4.25, m		Apoa-5	Apoa-5	Apoa-2b,6-Me
5	132.9, CH	5.18, d (9.0)	Apoa-3,4, 6-Me,7	Apoa-4,6-Me	Apoa-4	Apoa-3,3-NH,7
6	135.9, C					
6-Me	13.4 CH ₃	1.65, s	Apoa-4,5, 6,	Apoa-5	Apoa-7,8	Apoa-4,7,8
7	133.8, CH	6.62, d (16.2)	Apoa-5,6,6-Me,8,9	Apoa-8	Apoa-6-Me,8	Apoa-5,6-Me,10,10'
8	128.2, CH	6.50, d (16.2)	Apoa-6,7,9,10,10'	Apoa-7	Apoa-6-Me,7	Apoa-5,6-Me,10,10'
9	137.8, C					
10,10'	126.9, CH	7.41, d (7.7)	Apoa-8,10', 10,12	Apoa-11,11'	Apoa-11,11'	Apoa-7,8
	x 2					
11,11'	129.5, CH	7.31, t (7.7)	Apoa-9,11', 11,	Apoa-10,10',12	Apoa-10,10',12	
	x 2					
12	128.3, CH	7.19, t (7.7)	Apoa-10, 10'	Apoa-11,11'	Apoa-11,11'	
Ser ¹ -1	172.3, C					
2	56.6, CH	3.78, m	Ser ¹ -1			
2-NH	119.4, NH	7.77, s	Apoa-1, Ser ¹ -2,3			Apoa-2a, 2b (neg)
3	61.0, CH ₂	3.64, m	Ser ¹ -1			sAla-2-NH
sAla-1	169.6, C					
2	51.1, CH	5.06, m	sAla-1,3,	sAla-2-NH,3a,3b	sAla-2-NH	sAla-2-NH,3b, Asn-2-NH, sHis-3a
2-NH	108.1, NH	8.27, d (9.9)	Ser ¹ -1, sAla-2	sAla-2	sAla-2,3a,3b	sAla-2, Ser ¹ -3
3a	50.5, CH ₂	4.89, d (13.6)	sAla-2,	sAla-2,3b	sAla-2-NH	sHis-8, sAla-3b
b		4.22, dd (13.6,10.0)	sHis-6, sAla-1,2	sAla-2,3a	sAla-2-NH	sAla-2,3a, sHis-6

Asn-1	171.2, C					
2	51.9, CH	4.52, m	Asn-3	Asn-2,3a,3b	Asn-2-NH	Has-2-NH Asn-2-NH,3b
2-NH	114.7, NH	7.78, brs	sAla-1	Asn-2	Asn-2,3a,3b	sAla-2 Asn-2,3a
3a	37.1, CH ₂	2.56, dd (16.2,9.9)	Asn-1,2,4	Asn-2,3b	Asn-2-NH	Asn-2-NH,3b
b		2.32, dd (16.2,2.4)	Asn-1,2,4	Asn-2,3a	Asn-2-NH	Asn-2,3a, Has-2-NH
4	172.1, C					
4-NH ₂	103.5, NH ₂	7.32, brs 6.76, brs		4-NHb 4-NHa	Asn-4-NHb Asn-4-NHa	Asn-4-NHb (ex) Asn-4-NHa (ex)
Han-1	170.9, C					
2	54.5, CH	5.36, dd (8.9,7.5)	Han-1,3,4	Han-2-NH,3	Han-2-NH	MePhe-2-NH, sHis-2, Han-3
2-NH	108.9, NH	8.32, d (9.6)	Asn-1	Han-2	Han-2,3,3-OH	Asn-2,3b, Han-3
3	72.2, CH	3.97, brd (7.5)	Han-1,2,4	Han-2,3-OH		Han-2,2-NH,4-NHa
3-OH		5.12, brs		Han-3		
4	174.1, C					
4-NH ₂	102.3, NH ₂	7.25, s 7.07, s	Han-3,4		Han-4-NHb Han-4-NHa	Han-3
MePhe-1	171.7, C					
2	59.3, CH	4.51, dd (8.2,4.8)	MePhe-1,3,3-Me,4	MePhe-2-NH,3	MePhe-2-NH,	MePhe-2-NH,3,3-Me,5,5'
2-NH	114.0, NH	8.23, d (8.5)	Han-1	MePhe-2	MePhe-2-NH,3,3-Me	Han-2, MePhe-2,3
3	40.1, CH	3.31, dq (4.8,7.1)	MePhe-1,2, 3-Me,4,5,5'	MePhe-2,3-Me	MePhe-2-NH,	MePhe-2,2-NH,3-Me,5,5'
3-Me	18.1, CH ₃	1.08, d (7.1)	MePhe-2,3,4	MePhe-3	MePhe-2-NH,	MePhe-2, 3,5,5'
4	142.4, C					
5,5'	128.6, CH x 2	7.07, d (7.2)	MePhe-3,4, 5',5,7	MePhe-6,6'		MePhe-2,3,3-Me
6,6'	128.7, CH x 2	7.12, m	MePhe-4,6',6	MePhe-5,5'		
7	127.1, CH	7.11, t (6.8)	MePhe-5,5'			
iSer-1	171.2, C					
2	69.7, CH	4.05, brs	iSer-1	iSer-3b	iSer-3-NH	iSer-3b, Ada-2-NH

3a	44.0, CH ₂	3.69, m	iSer-2	iSer-3b,	iSer-3-NH	iSer-3b
b		3.00, dd (11.8,3.5)	iSer-2	iSer-2,3a		iSer-2,3a
3-NH	100.2, NH	7.19, m	MePhe-1	iSer-3a,3b	iSer-2,3a	
Ada-1	175.4, C					
2	54.6, CH	3.87, m	Ada-1,4	Ada-2-NH,3b		
2-NH	116.5, NH	7.58, d (7.1)	iSer-1, Ada-1	Ada-2	Ada-2,3a, 3b,4	Ada-4, iSer-2
3a	32.4, CH ₂	1.66, m	Ada-1,2,4,5	Ada-3b,4	Ada-2-NH	
b		1.43, m	Ada-2,4,5	2,3a, 4		
4	22.2, CH ₂	1.19, m 2H	Ada-3,5,6	Ada-3a, 3b,5a,5b	Ada-2-NH	Ada-2-NH
5a	35.8, CH ₂	2.05, dt (13.5,8.5)	Ada-3,4,6	Ada-3b,4		sHis-2-NH, Ada-4,5b
b		1.72, m	Ada-3,4,6	Ada-3a,4		Ada-5a
6	174.1, C					
sHis-1	170.7, C					
2	54.3, CH	4.77, m	Ada-6, sHis-1,3,	sHis-2-NH,3a,3b	sHis-2-NH	sHis-2-NH,3b,8, sAla-2 Han-2, Thr-2-NH
2-NH	119.9, NH	8.37, d (6.6)	Ada-6, sHis-2,3,	sHis-2	sHis-2,3a, 3b	Ada-5a sHis-2,3a, 3b
3a	26.2, CH ₂	3.28, t (13.3)	sHis-1,2,4, 8	sHis-2,3b	sHis-2-NH	sAla-2, sHis-3b,2-NH, Gal-1
b		2.96, dd (13.3,4.0)	sHis-1,2,4,	sHis-2,3a	sHis-2-NH	sHis-2,2-NH,3a,8
4	131.8, C					
5	181.4, N					
6	137.2, CH	8.87, s	sAla-3, sHis-4,5,7, 8, Gal-1	sHis-8	sHis-8	Gal-1, sAla-3b
7	167.8, N					
8	124.1, CH	7.25, s	sHis-4,5,6	sHis-6	sHis-6	sHis-2,3b sAla-3a
Thr-1	172.5, C					
2	58.7, CH	4.22, m	Thr-1,3,3-OH,4 sHis-1	Thr-2-NH,3	Thr-2-NH	Ser ² -2-NH Thr-2-NH,4
2-NH	114.1, NH	7.71, d (8.4)	sHis-1	Thr-2	Thr-2,3-OH	sHis-2 Thr-2,3
3	68.7, CH	3.61, m	Thr-2	Thr-2,4		Thr-2-NH
3-OH		5.20, d (4.8)	Thr-2			Phe-2-NH, Thr-4
4	21.5, CH ₃	0.97, d (6.1)	Thr-2	Thr-3		Thr-2,3-OH
Ser ² -1	169.7, C					

2	56.4, CH	4.44, dt (8.9,3.3)	Thr-1, Ser ² -1,3	Ser ² -2-NH,3	Ser ² -2-NH	Phe-2-NH Ser ² -2-NH
2-NH	116.7, NH	8.48, d (8.1)	Thr-1	Ser ² -2	Ser ² -2,3	Phe-2-NH Thr-2-NH Ser ² -2,3
3	61.9, CH ₂	3.64, m	Ser ² -1,2	Ser ² -2	Ser ² -2-NH	Ser ² -2-NH
Phe-1	171.4, C					
2	54.9, CH	4.55, ddd (8.9,8.3,6.6)	Ser ² -1, Phe-1,3,4	Phe-2-NH, 3a,3b	Phe-2-NH	Phe-2-NH,3a,3b, Apoa-3-NH
2-NH	115.7	7.94, d (8.9)	Ser ² -1	Phe-2	Phe-2,3a, 3b	Ser ² -2,2-NH, Thr-3-OH, Phe-2,3a, 3b
3a	39.2, CH ₂	2.81, dd (13.5,8.3)	Phe-1,2,4,5, 5'	Phe-2,3b	Phe-2-NH	Phe-2,2-NH,3b
b		2.65, dd (13.5,6.6)	Phe-1,2,4,5, 5'	Phe-2,3a	Phe-2-NH	Phe-2,2-NH,3a, 5,5'
4	137.3, C					
5,5'	129.8, CH	7.14, m	Phe-3,7	Phe-6,6'		Phe-3b
	x 2					
6,6'	129.0, CH	7.22, d (7.4)	Phe-4,6',6	Phe-5,5',7		
	x 2					
7	127.3, CH	7.18, m	Phe-5,5'	Phe-6,6'		
Gal-1	88.9, CH	5.02, d (9.3)	sHis-4,6 Gal-2,3,5	Gal-2		sHis-3a,6 Gal-2,3
2	69.7, CH	3.63, m	Gal-1,	Gal-1,3		Gal-1
3	73.7, CH	3.40, brd (8.0)	Gal-2,	Gal-2		Gal-1
4	69.5, CH	3.81, m	Gal-3			
5	78.8, CH	3.64, m	Gal-3			
6	61.9, CH ₂	3.75, m 3.64, m	Gal-4,5, Gal-4			

^a¹H (500 MHz), ¹³C (125 MHz) and ¹⁵N (50 MHz). ^bMultiplicity and assignment from HSQC experiment. ^cMultiplicity (*J* in Hz). ^dHMBC correlations, optimized for 8 Hz. ^eSelected NOEs from ROESY experiment.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 400.0

Element prediction: Off

Number of isotope peaks used for i-FT = 5

Monoisotopic Mass, Even Electron Ions

211 formulae) evaluated with 22 results within limits (up to 3 closest results for each mass)

Elements Used:

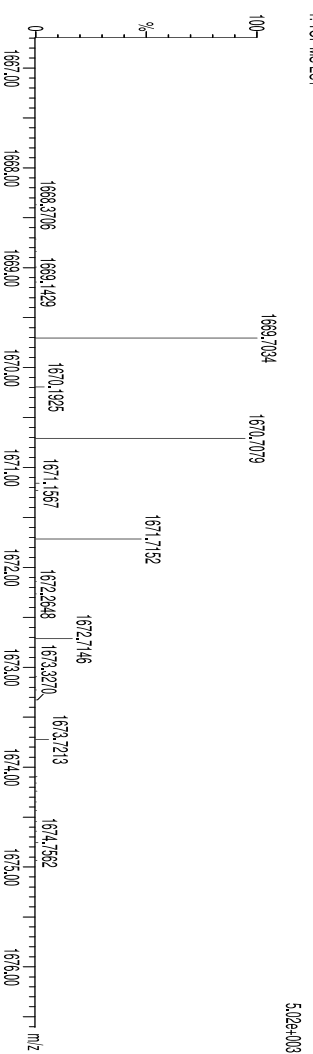
C: 70-80 H: 90-120 N: 0-20 O: 20-30

OhD3-099/2

Ohad Hasin

1:TOF MS ES+

Carmeli 1335 81 (3.577) Gm (76:81)



Minimum:							-1.5
Maximum:			5.0	20.0	400.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
1669.7034	1669.7022	1.2	0.7	34.5	77.0	0.4	C76 H101 N16 O27
1669.7035	1669.7025	-0.1	-0.1	39.5	77.7	1.2	C77 H97 N20 O23
1669.7049	1669.7049	-1.5	-0.9	33.5	79.7	3.1	C80 H105 N10 O29

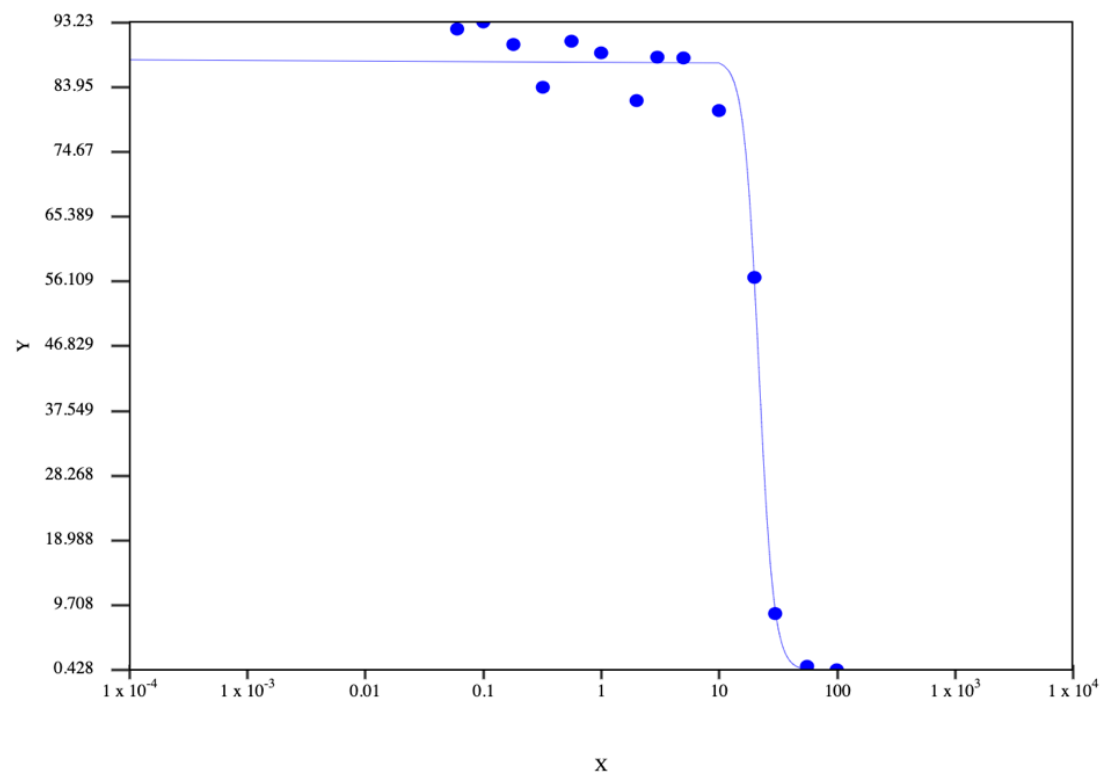
S65 Figure S58. (+)-HRESIMS data of theonellamide K (**3**)

S66 Table S8. Calculated survival percentage compare to DMSO and IC₅₀ of HCT-116 Colon Carcinoma cell line by compounds **1-4**

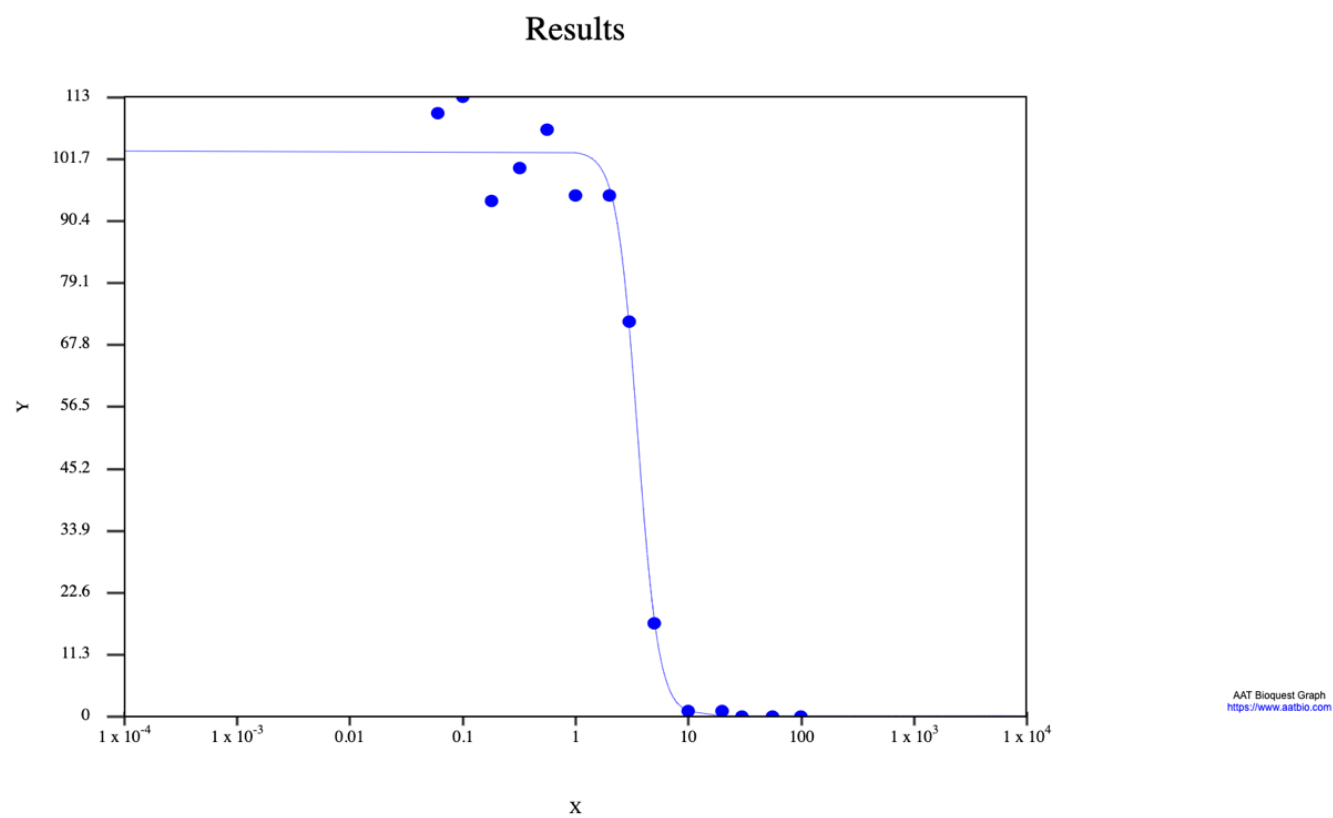
Concentration(μM)	Theonellamide J (1)	5- <i>cis</i> -Apoa- theopalauamide (2)	Theonellamide K (3)	Theopalauamide (4)
100.00	92	0	0	0
56.00	105	1	0	0
30.00	104	8	0	1
20.00	94	57	1	2
10.00	101	81	1	2
5.00	97	88	17	4
3.00	93	88	72	35
2.00	107	82	95	76
1.00	107	89	95	84
0.56	89	90	107	95
0.32	84	84	100	90
0.18	101	90	94	86
0.10	95	93	113	83
0.06	91	92	110	96
IC ₅₀ (SEM)	>100	21.8 (+/-0.7)	3.5 (+/-0.2)	2.8 (+/-0.9)

S67 Figure S59. Inhibition curve of HCT-116 Colon Carcinoma cell line by 5-*cis*-Apoa-theopalauamide (**2**)

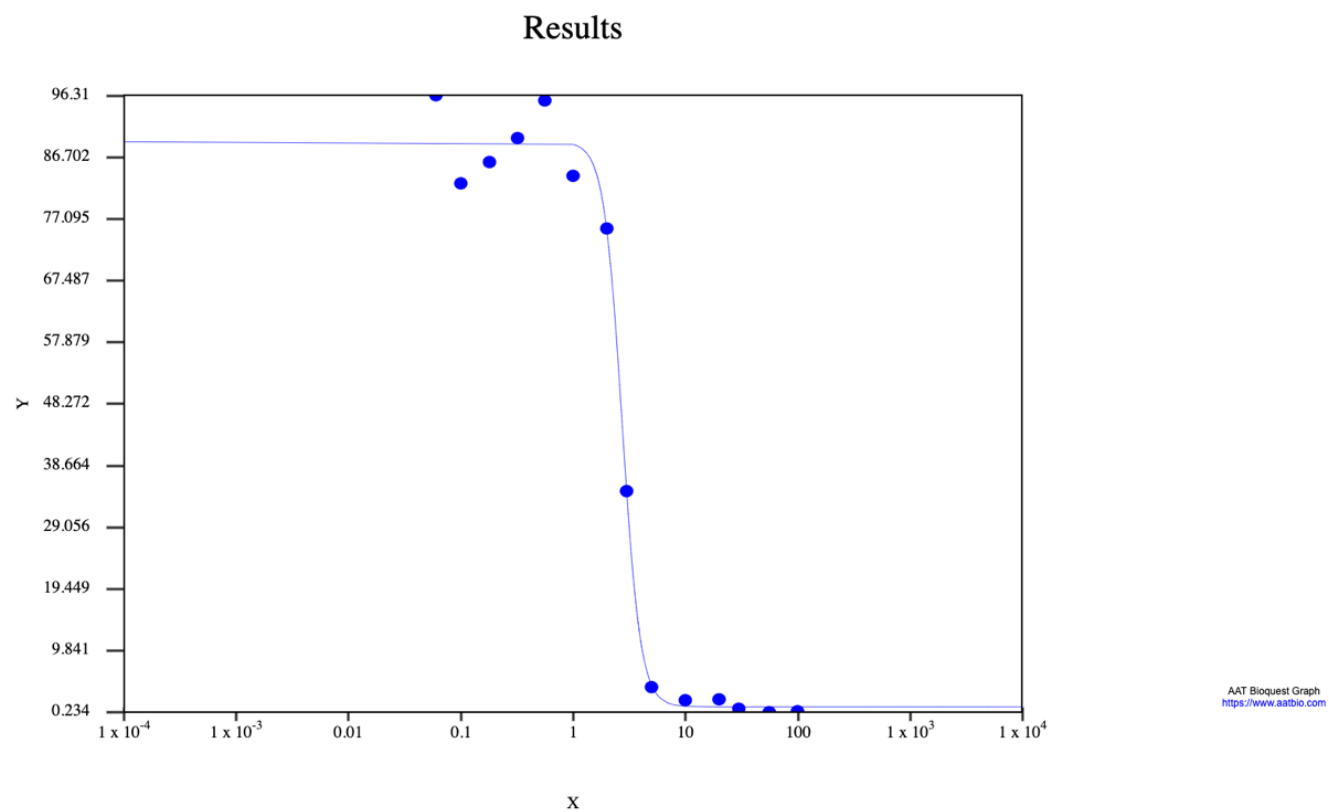
Results



S68 Figure S60. Inhibition curve of HCT-116 Colon Carcinoma cell line by theonellamide K (**3**)



S69 Figure S61. Inhibition curve of HCT-116 Colon Carcinoma cell line by theopalauamide (4)



S70 Figure S62. Under water photograph of *Theonella swinhoei*

