Supplementary material

Microbiota of Healthy Corals are Active Against Fungi in a Light Dependent Manner

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9) To whom the correspondence should be addressed regarding the mass spectrometry, studies on light dependence and isolation and characterization of the molecules. pdorrestein@ucsd.edu

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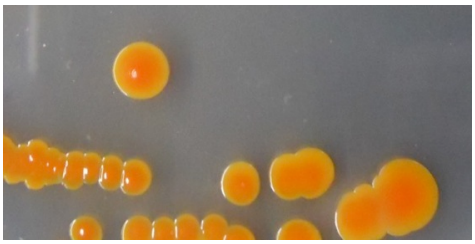
a

Soft coral - *Leptogorgia alba*
(Isla Otoque, Panama)



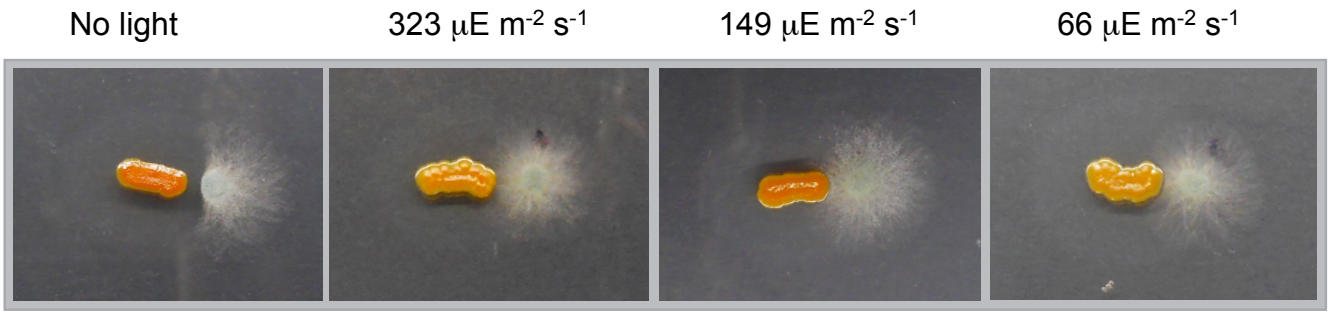
OT59 *Pseudoalteromonas*

b

Diseased octocoral - *Eunicea sp.*
(Isla grande, Colon, Panama)

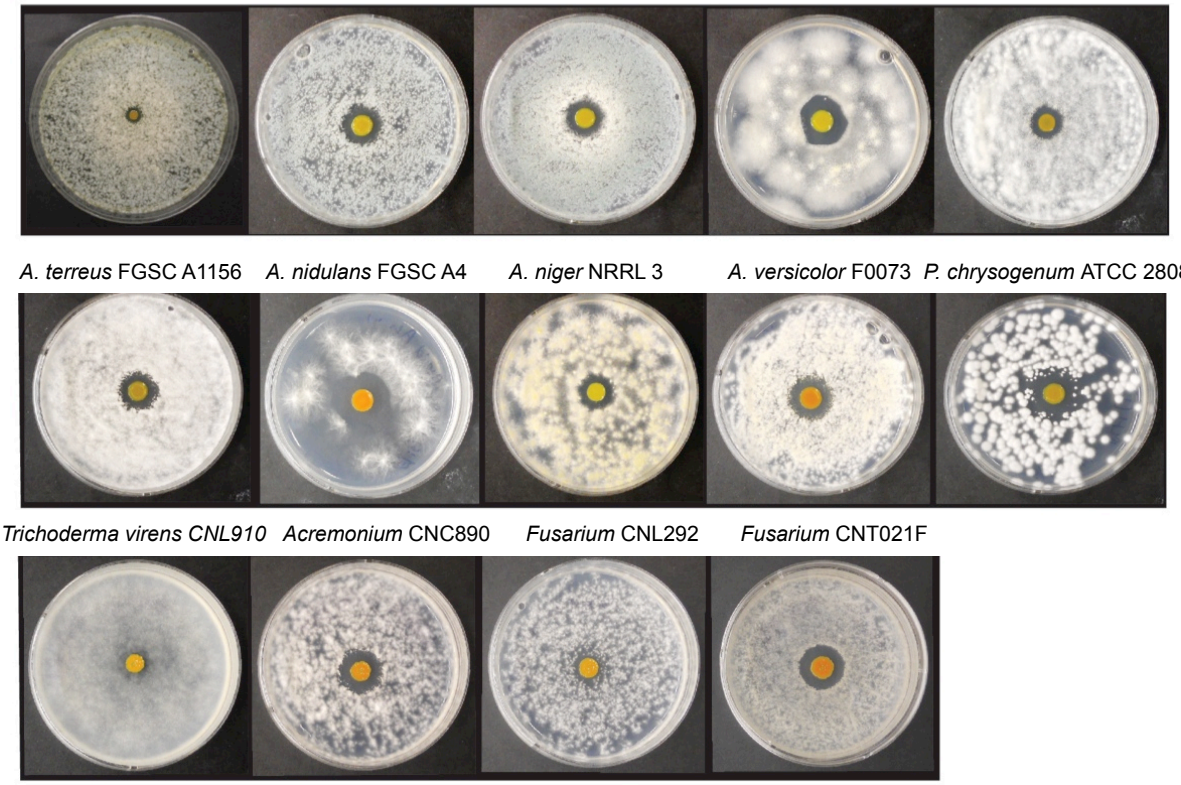
GLIG-280911-10-PGY-A
Penicillium citrinum

Supplement Figure 1. Corals from Panama waters as source of OT59 and *P. citrinum*



Supplement Figure 2. Interaction of OT59 (left) and *A. fumigatus (right)* at various irradiance levels

a



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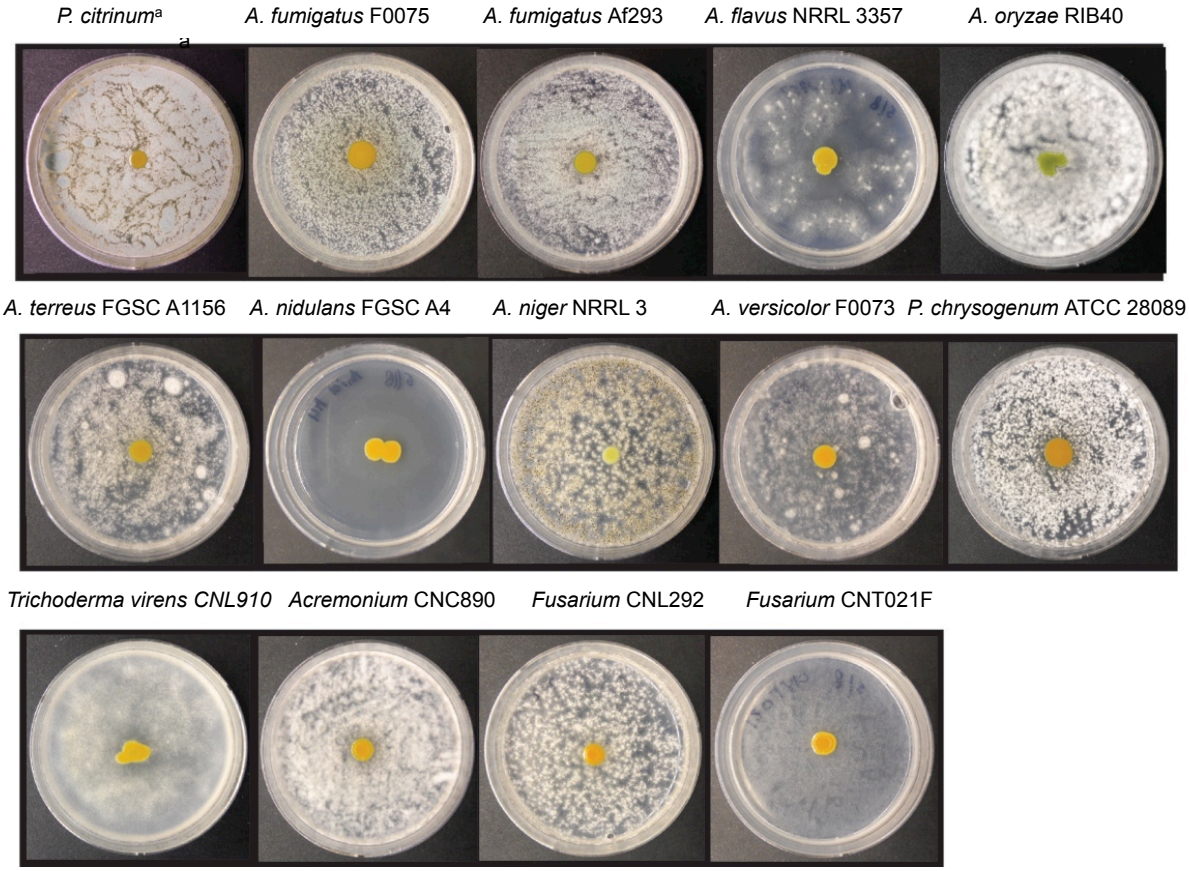
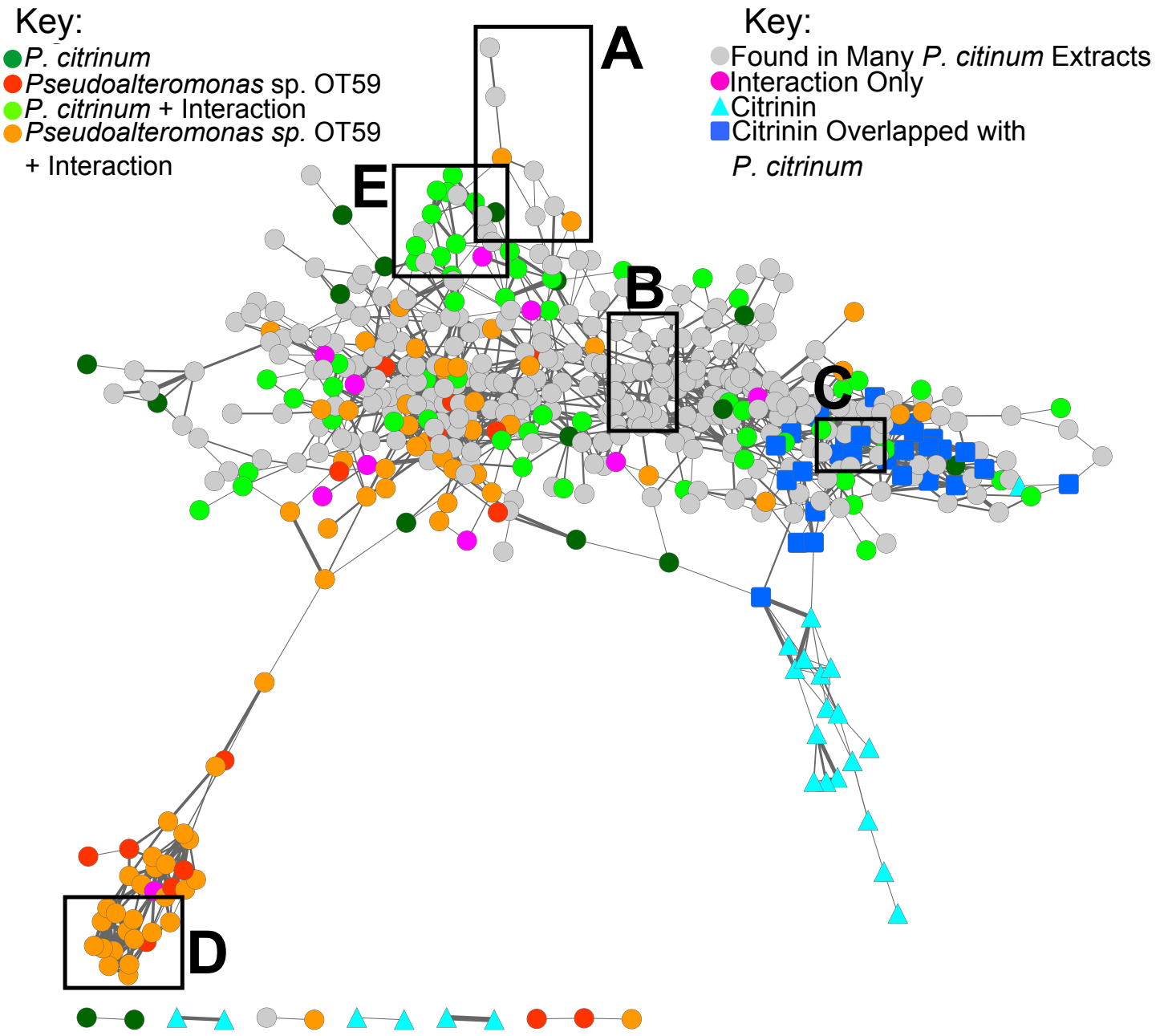


[a] Petridish with OD of 10 cm, all others 5 cm

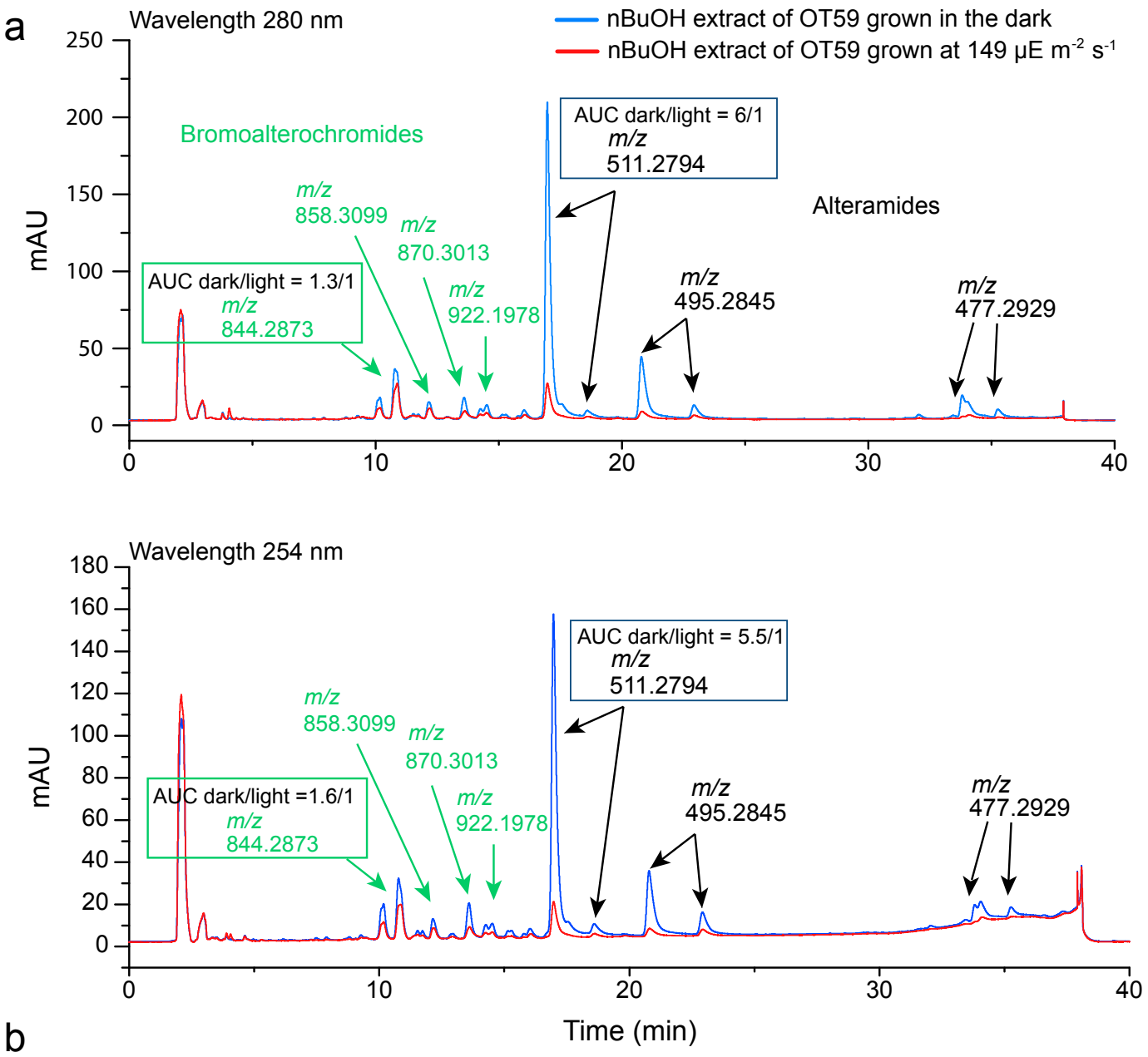
Supplement Figure 3. Fungal inhibition by OT59 in (a) dark and (b) under light exposure (149 μE m^{-2} s^{-1})



Supplement Figure 4. MS/MS network analysis of OT59 and *P. citrinum* extracts. In MS/MS networking molecules are subjected to fragmentation and visualized as nodes (circles) while the relatedness of each node is defined by an edge (lines). The thickness of the edge defines the degree of similarity of the MS/MS spectra. Compounds that belong to the same molecular family will have very similar MS/MS fragmentation patterns and will form a cluster in the network. For details on this technology see Watrous et al. [1]

Nodes in dark green represent metabolites only found in extract of *P. citrinum*; in light green are metabolites found in both the side-by-side growth of *P. citrinum* and *Pseudoalteromonas* as well as the *P. citrinum* grown alone; red nodes represent metabolites found only in *Pseudoalteromonas;* in orange metabolites found in *Pseudoalteromonas* and it's side-by-side interaction with *P. citrinum*. Grey nodes represent metabolites found in any combination of 2 or more extracts; pink nodes relate to metabolites that are only found in the side-by-side interaction of *Pseudoaltermonas* and *P. citrinum*; light blue nodes correspond to purchased citrinin; and dark blue nodes represent metabolites found in both the crude extract of the side-by side interaction of *Pseudoaltermonas* and *P. citrinum* and commercial citrinin. The various metabolite classes are boxed and indicated with a letter. (A) alteramides (B) estatins (C) citrinin (D) bromoalterochromides (E) citrinadins

Supplement Figure 5. (a) HPLC comparison at 280 and 254 nM of extract from OT59 grown in dark vs under constant light exposure at 149 μE m^{-2} s^{-1} (b) UV chromatograms of alteramides A (*m/z* 511),alteramide B (*m/z* 495) and alteramide congener (*m/z* 477)



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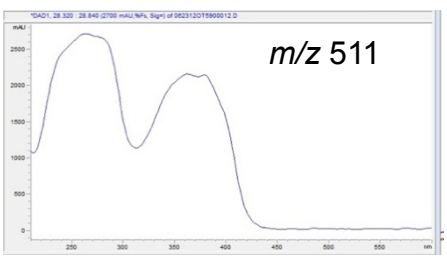
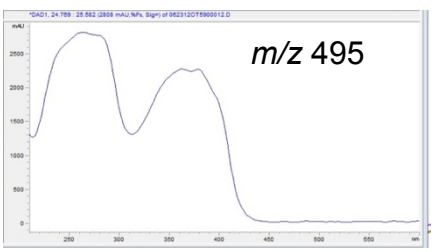
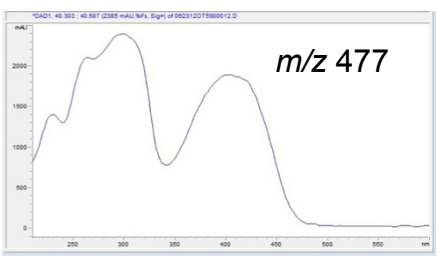
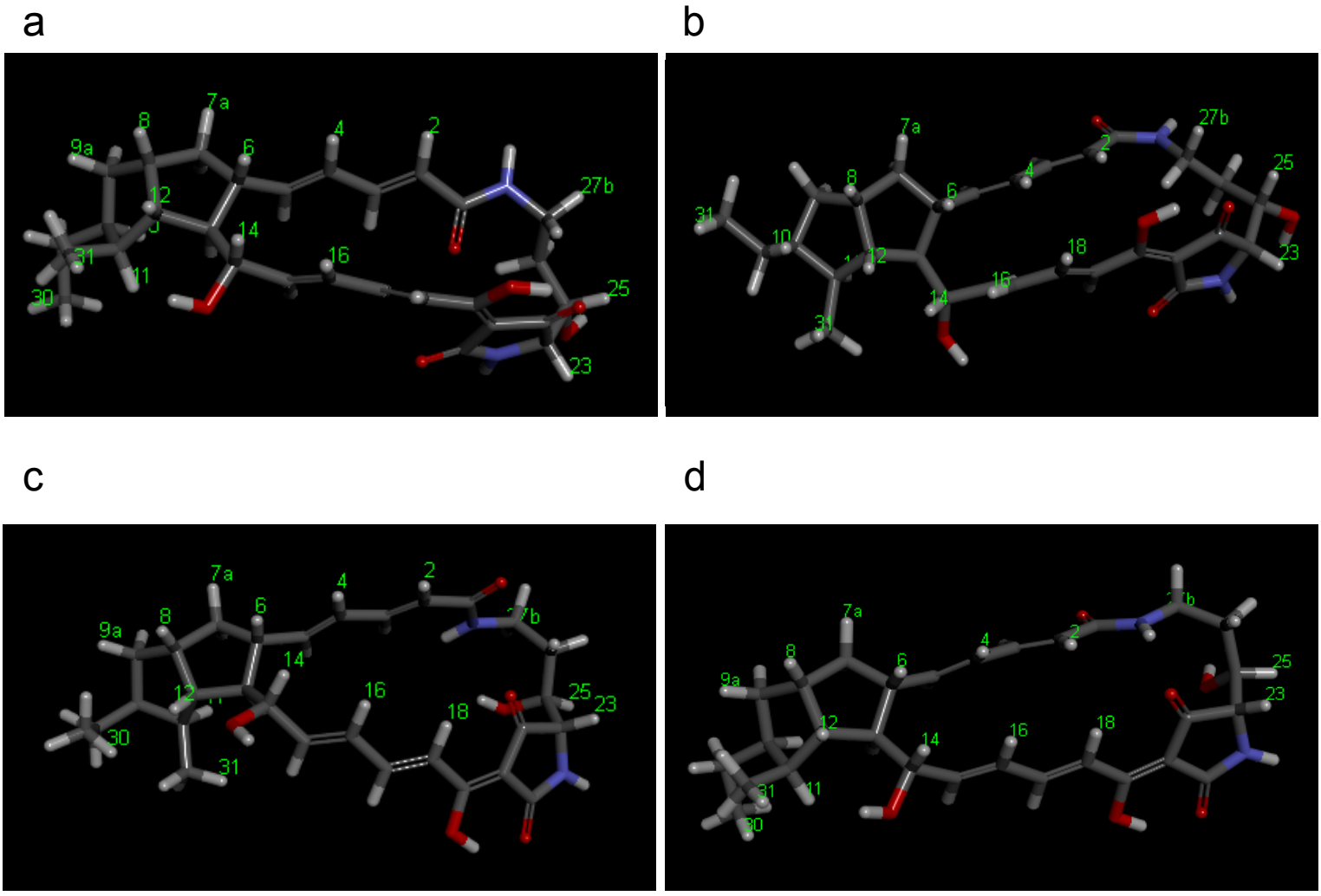


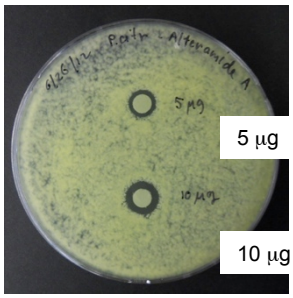


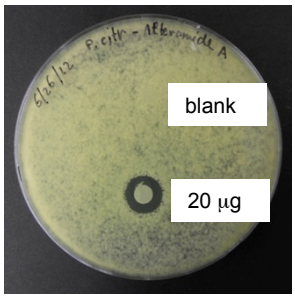




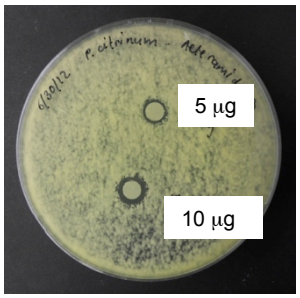
Supplement Figure 6. Example pairs of minimized conformations of alteramide A (**3**) that correlate with the NOEs observed in NMR. (a) and (b) minimized conformations associated with alteramide A (**3**) in the *E* tautomer that together account for NOEs observed and (c) and (d) minimized conformations associated with alteramide A (**3**) in the *Z* tautomer that together account for NOEs observed. Many additional conformations were found within 20 Kcal mol^{-1} energy threshold. (see Supplemental Methods)

Alteramide A (**3**)

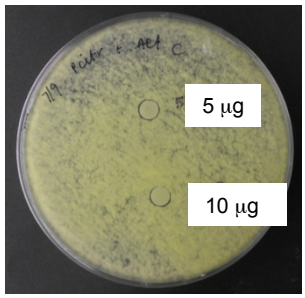


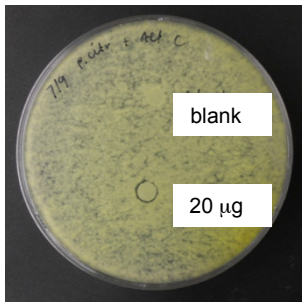


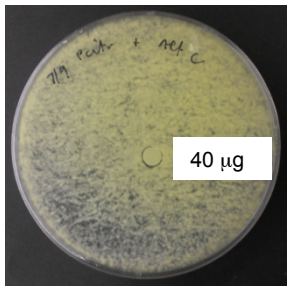
Alteramide B (**4**)



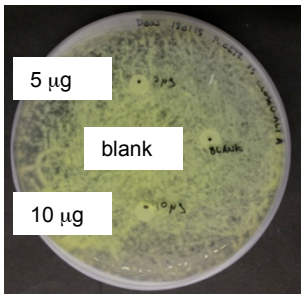
m/z 477 alteramide congener

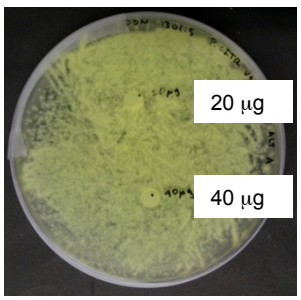




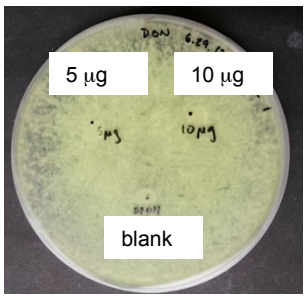


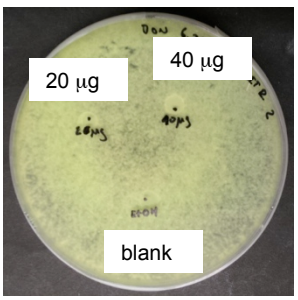
Intramolecular cyclized Alteramide A (**5**)



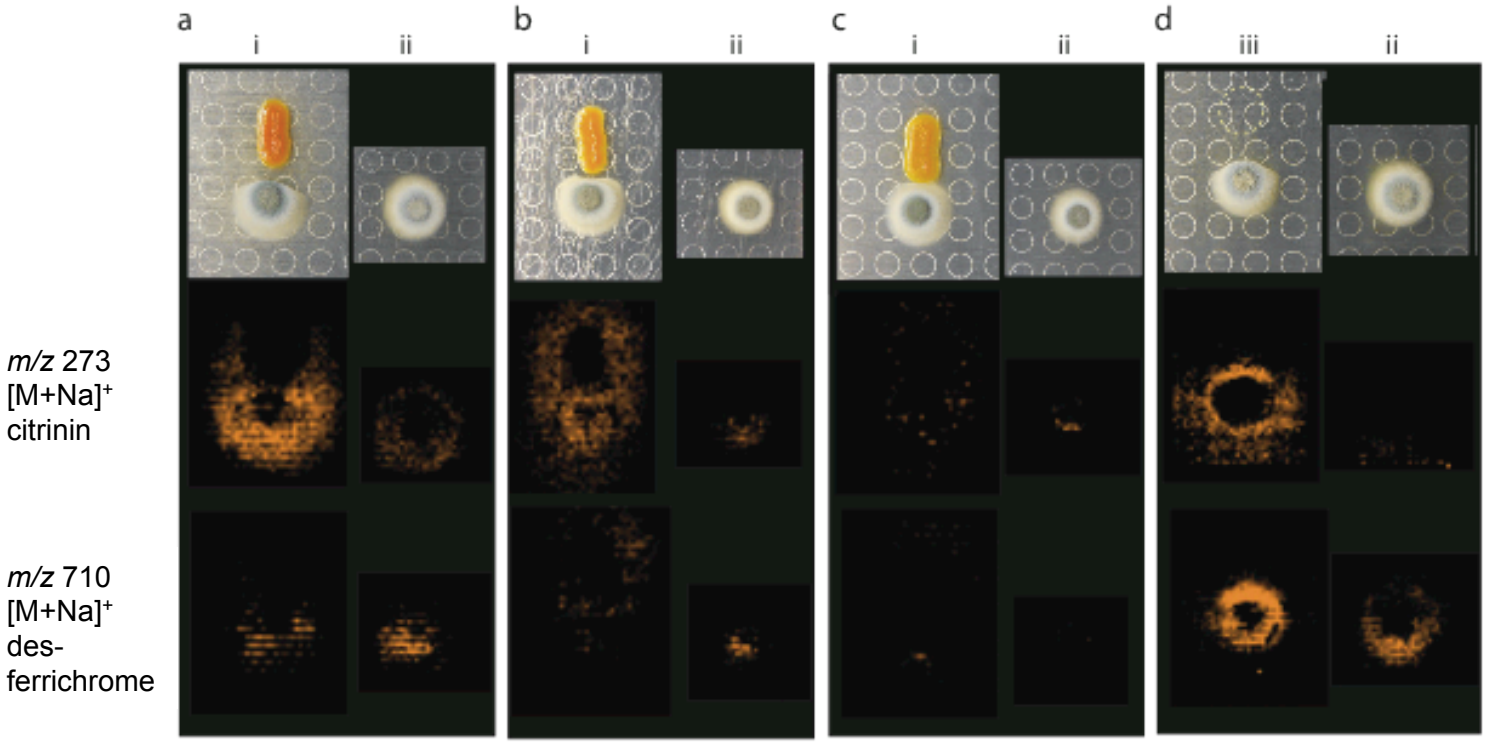


Intramolecular cyclized Alteramide B (**6**)

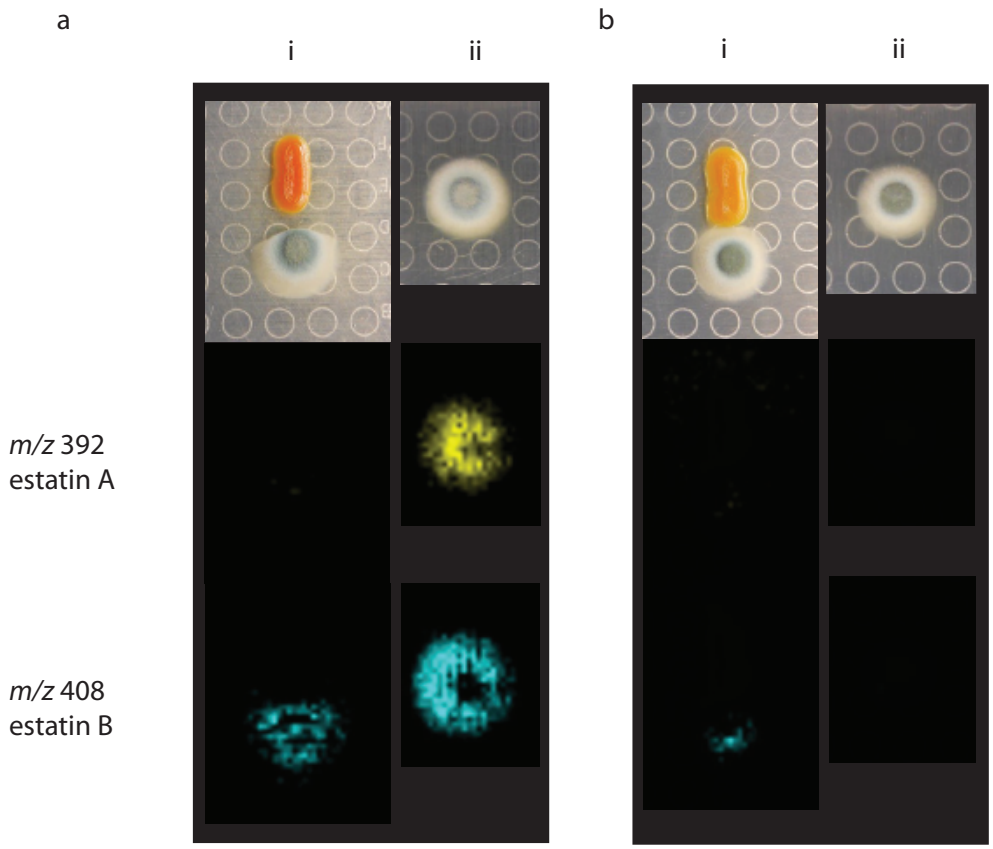




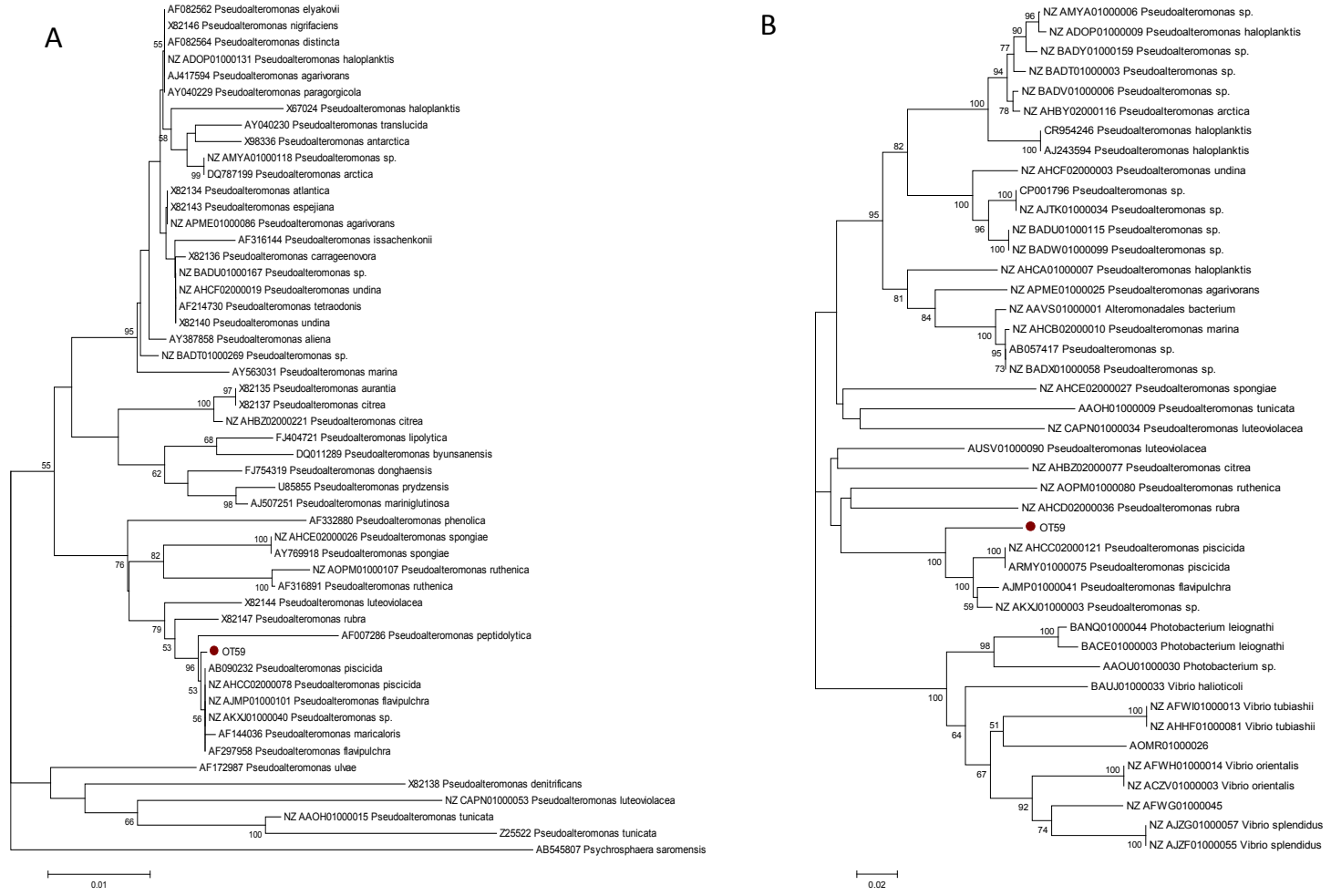
Supplement Figure 7. Lawn assay assessing inhibition of *P. citrinum* by purified alteramides



Supplement Figure 8. Comparison of citrinin and desferrichrome produced by (i) *P. citrinum (bottom)* in interaction with *Peudoaltermonas* OT59 (top), (ii) *P. citrinum* control, or (iii) *P. citrinum* in interaction with alteramide A (indicated as a dashed circle). Tested in the (a) dark, (b)12 h dark / 12 h light cycle, (c) light (149 μE m^{-2} s^{-1}), (d) dark.

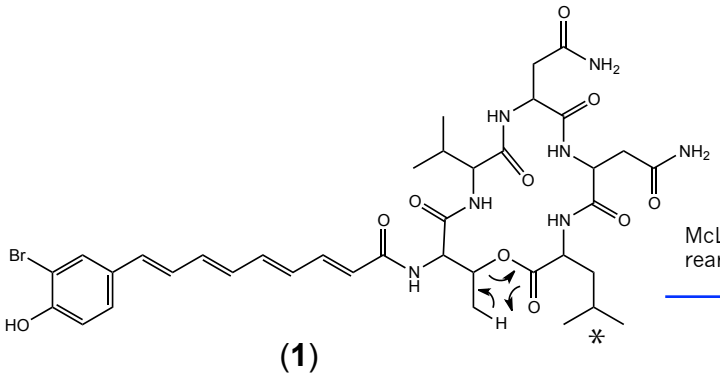


Supplement Figure 9. Comparison of estatin fungal ions produced by (i) *P. citrinum* (bottom) in interaction with *Pseudoaltermonas* OT59 (top) or (ii) *P. citrinum* control. Tested in the (a) dark or (b) under light exposure (149 μE m^{-2} s^{-1})

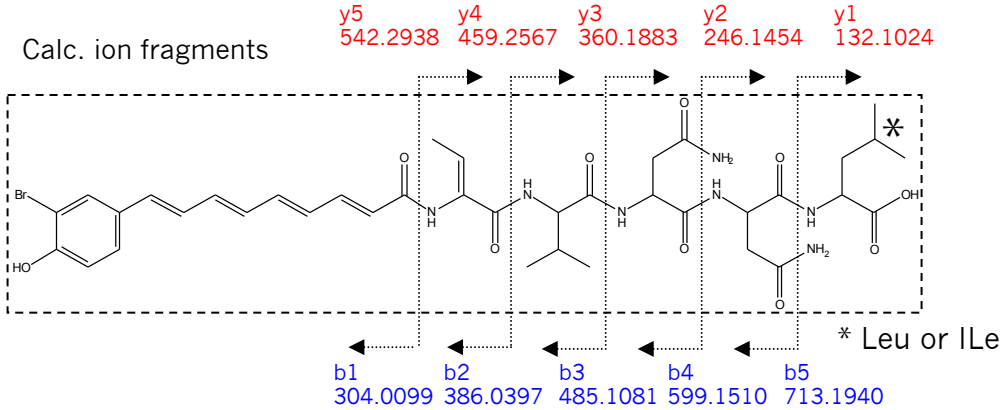


Supplement Figure 10. Evolutionary realtionships of 16S rRNA gene (A) and 60 kDa chaperonin gene (B) OT59 strain. The evolutionary history was inferred using the Neighbor-Joining method.[2] The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches. The evolutionary distances were computed using the Kimura 2-parameter method.[3] The scale bar represents the number of nucleotide substitutions per site. Evolutionary analyses were conducted in MEGA5.[4]

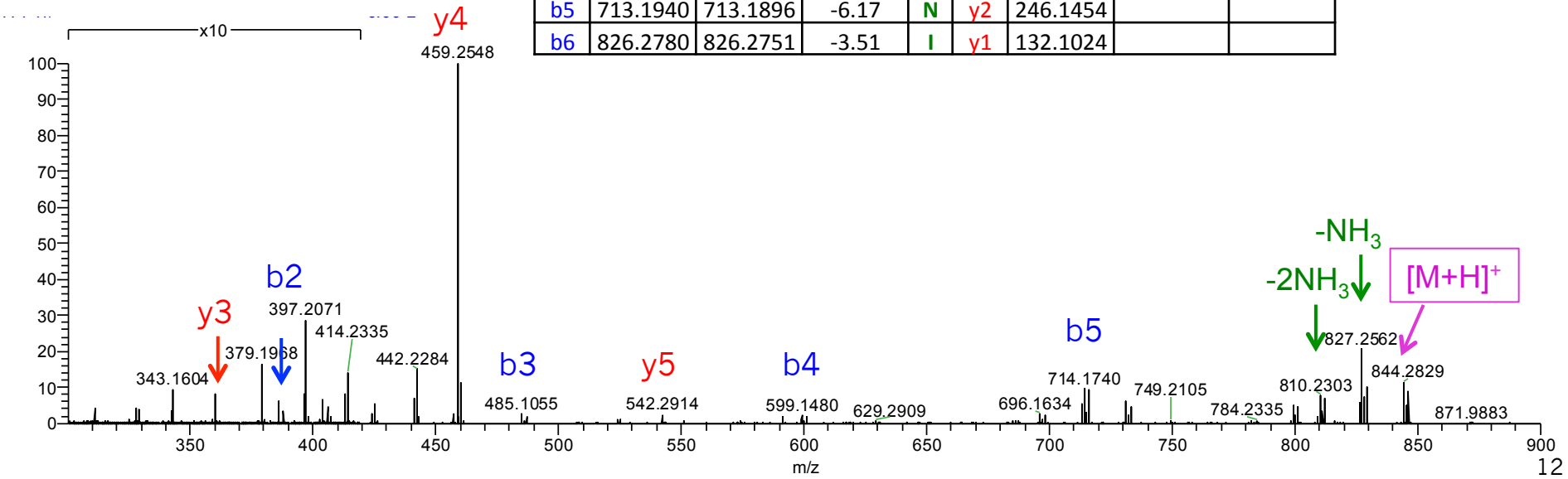
Supplement Figure 11. FT- MS2 of bromoalterochromide A/A' (**1**) *m/z* 844[5]



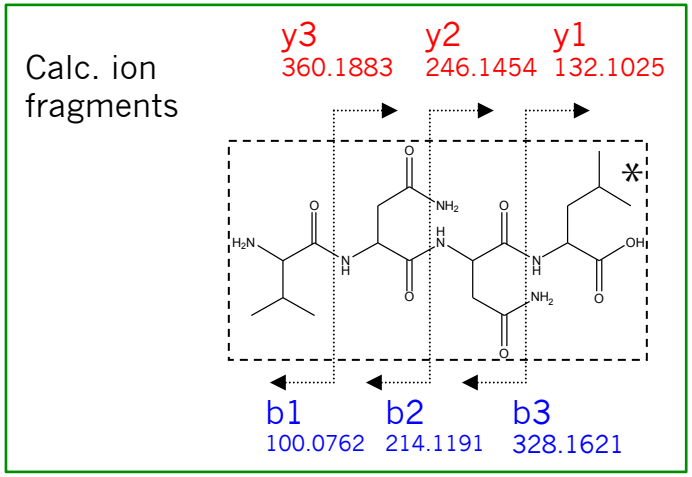
McLafferty-type rearrangement



	Calc ion	obs ion	error (ppm)			calc ion	obs ion	error (ppm)
b1	304.0099			a	y6	844.2881	844.2829	-6.13
b2	386.0397	386.0383	-3.63	b	y5	542.2938	542.2914	-4.43
b3	485.1081	485.1050	-6.39	V	y4	459.2567	459.2548	-4.10
b4	599.1510	599.1480	-5.01	N	y3	360.1883	360.1870	-3.61
b5	713.1940	713.1896	-6.17	N	y2	246.1454		
b6	826.2780	826.2751	-3.51	I	y1	132.1024		

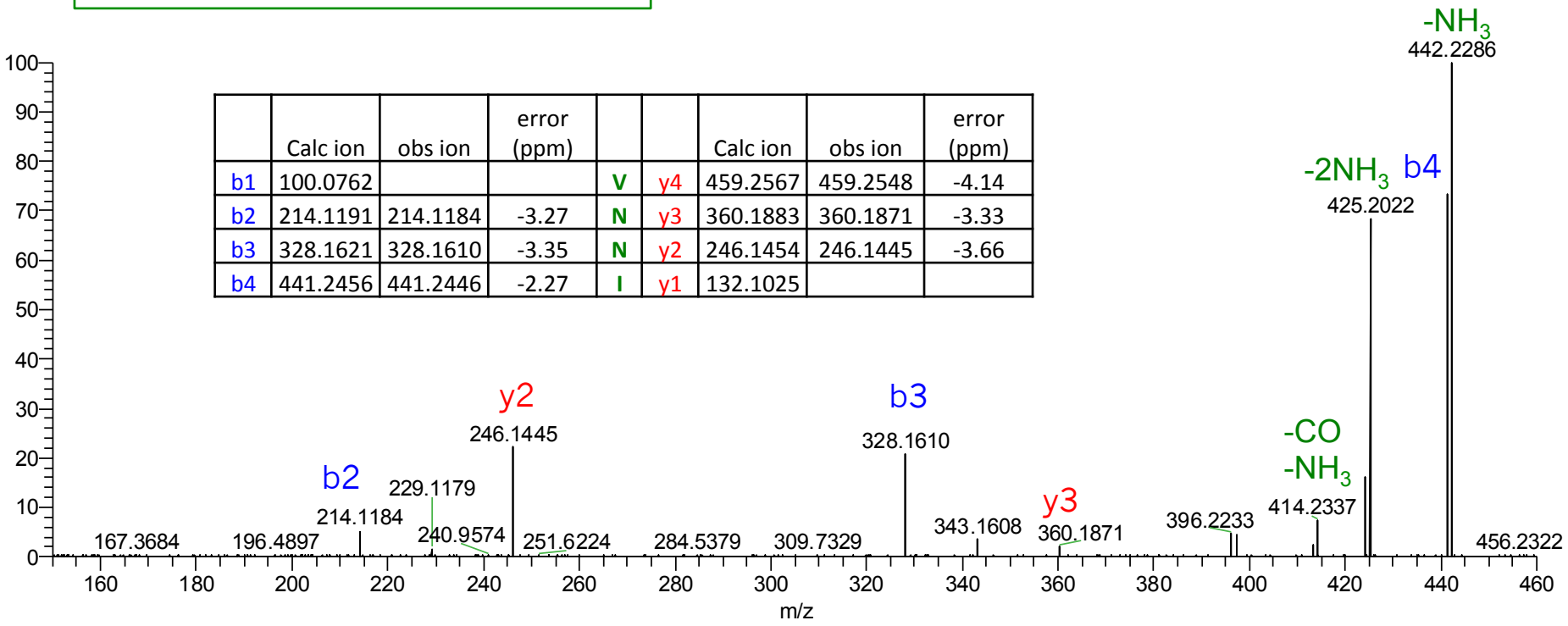


Supplement Figure 12. FT- MS3 of fragment *m/z* 459 from bromoalterochromide A/A' (**1**)

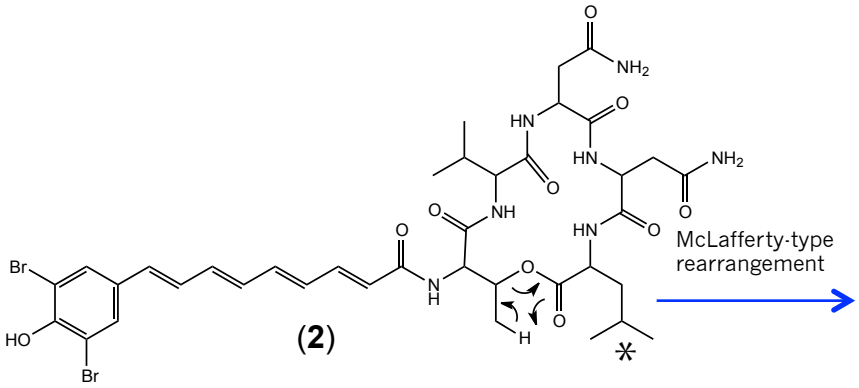


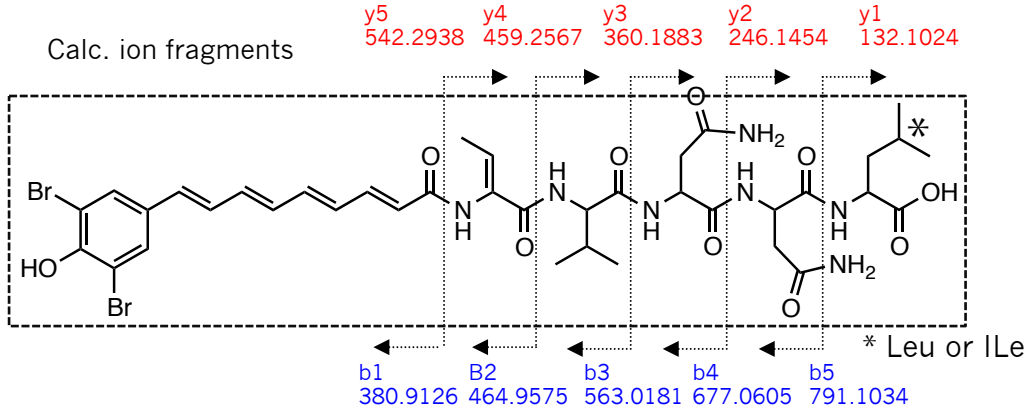
* Leu or ILe

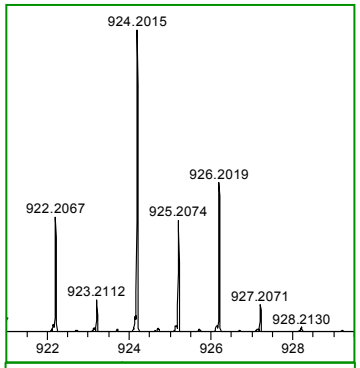
	Calc ion	obs ion	error (ppm)			Calc ion	obs ion	error (ppm)
b1	100.0762			V	y4	459.2567	459.2548	-4.14
b2	214.1191	214.1184	-3.27	N	y3	360.1883	360.1871	-3.33
b3	328.1621	328.1610	-3.35	N	y2	246.1454	246.1445	-3.66
b4	441.2456	441.2446	-2.27	I	y1	132.1025		



Supplement Figure 13. FT- MS2 of dibromoalterochromide A/A' [5] (**2**)

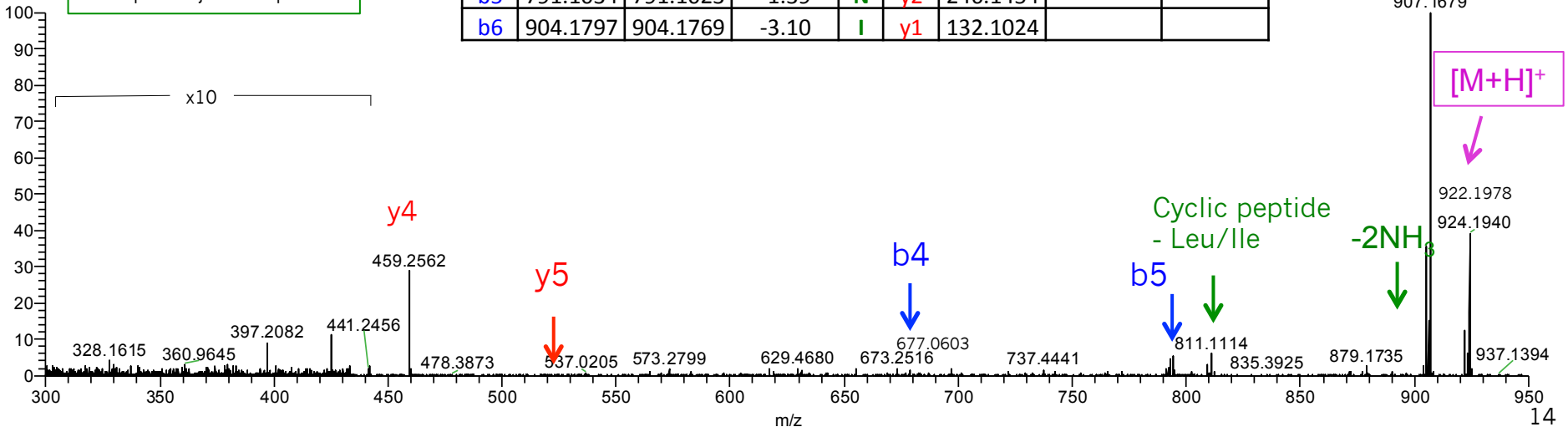




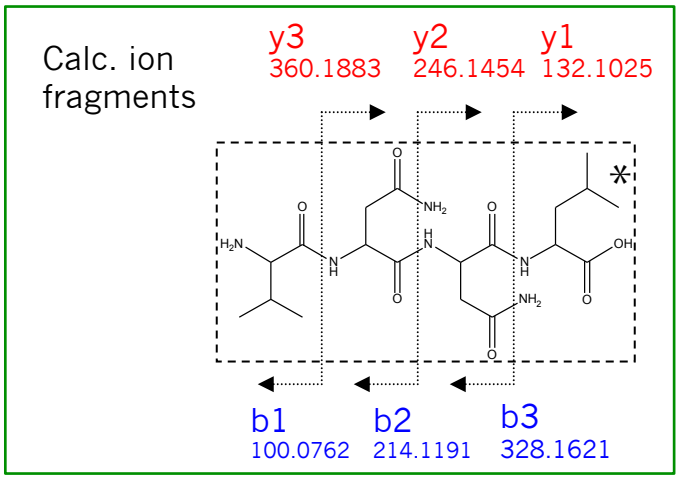


Dibromo substituent yields multiple major isotopes

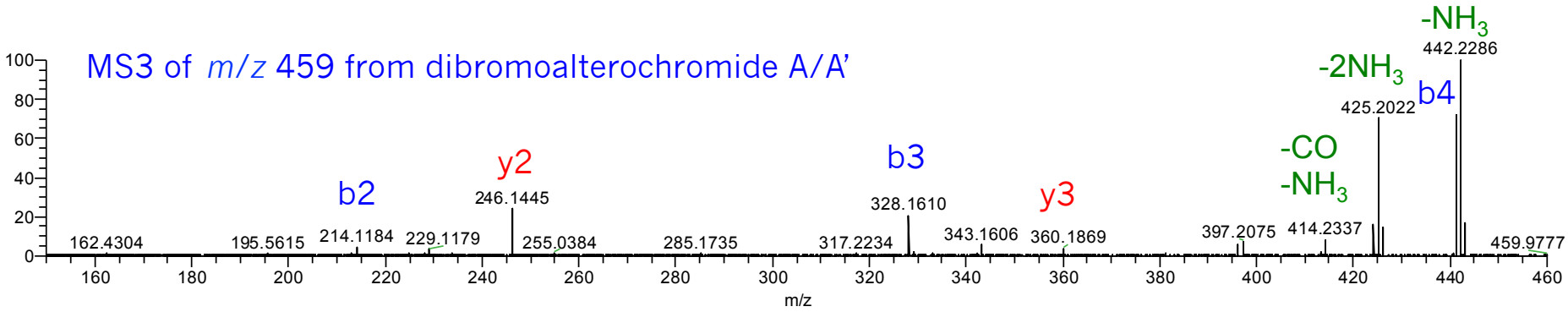
	Calc Ion	obs ion	error (ppm)			Calc ion	obs ion	error (ppm)
b1	380.9126			a	y6	922.1986	922.1978	-0.87
b2	464.9575	464.9566	-1.94	b	y5	542.2938	542.2914	-4.43
b3	563.0181	563.0151	-5.33	V	y4	459.2567	459.2548	-4.14
b4	677.0605	677.0603	-0.30	N	y3	360.1883		
b5	791.1034	791.1023	-1.39	N	y2	246.1454		
b6	904.1797	904.1769	-3.10	I	y1	132.1024		



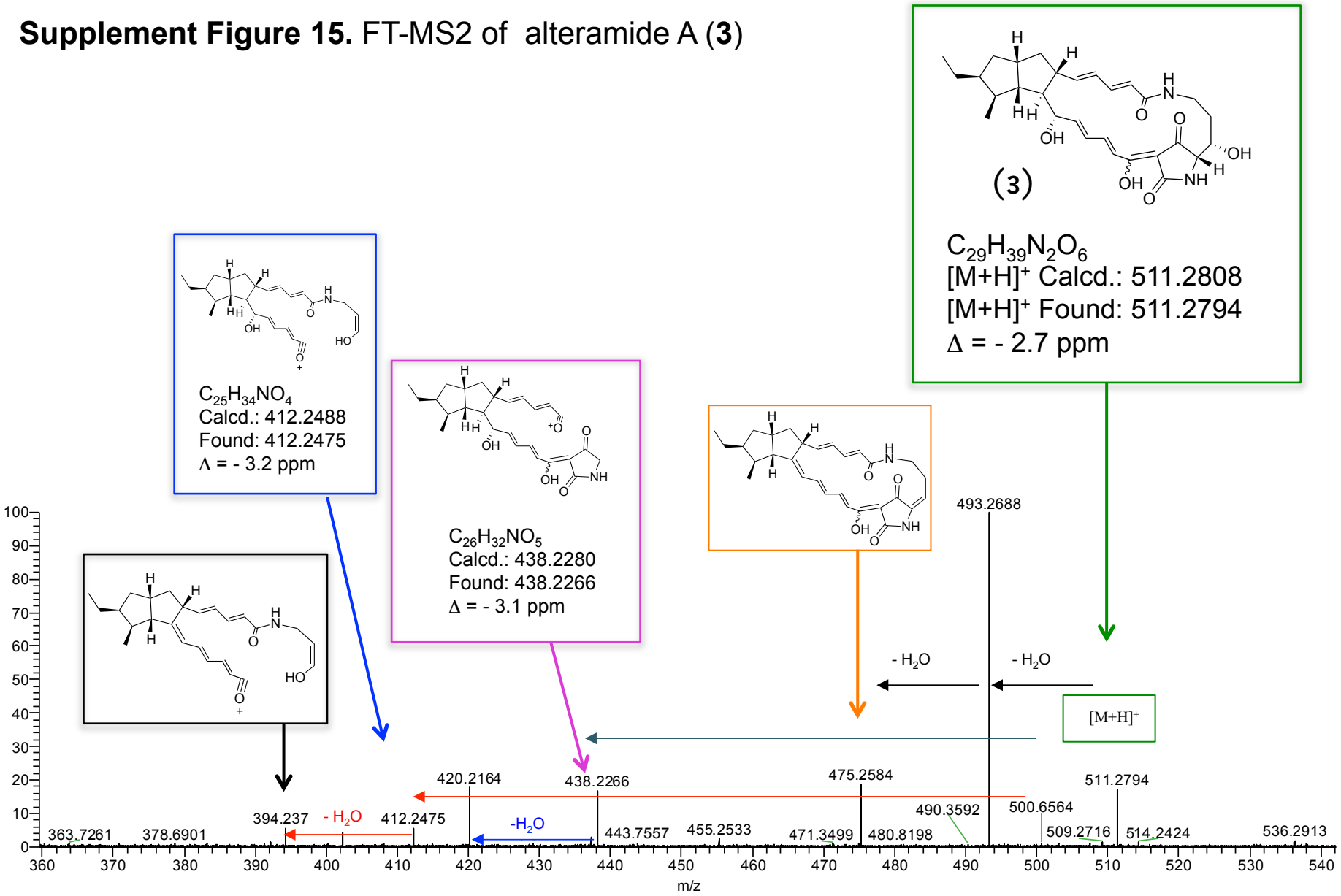
Supplement Figure 14. FT- MS3 of fragment *m/z* 459 from dibromoalterochromide A/A' (**2**)



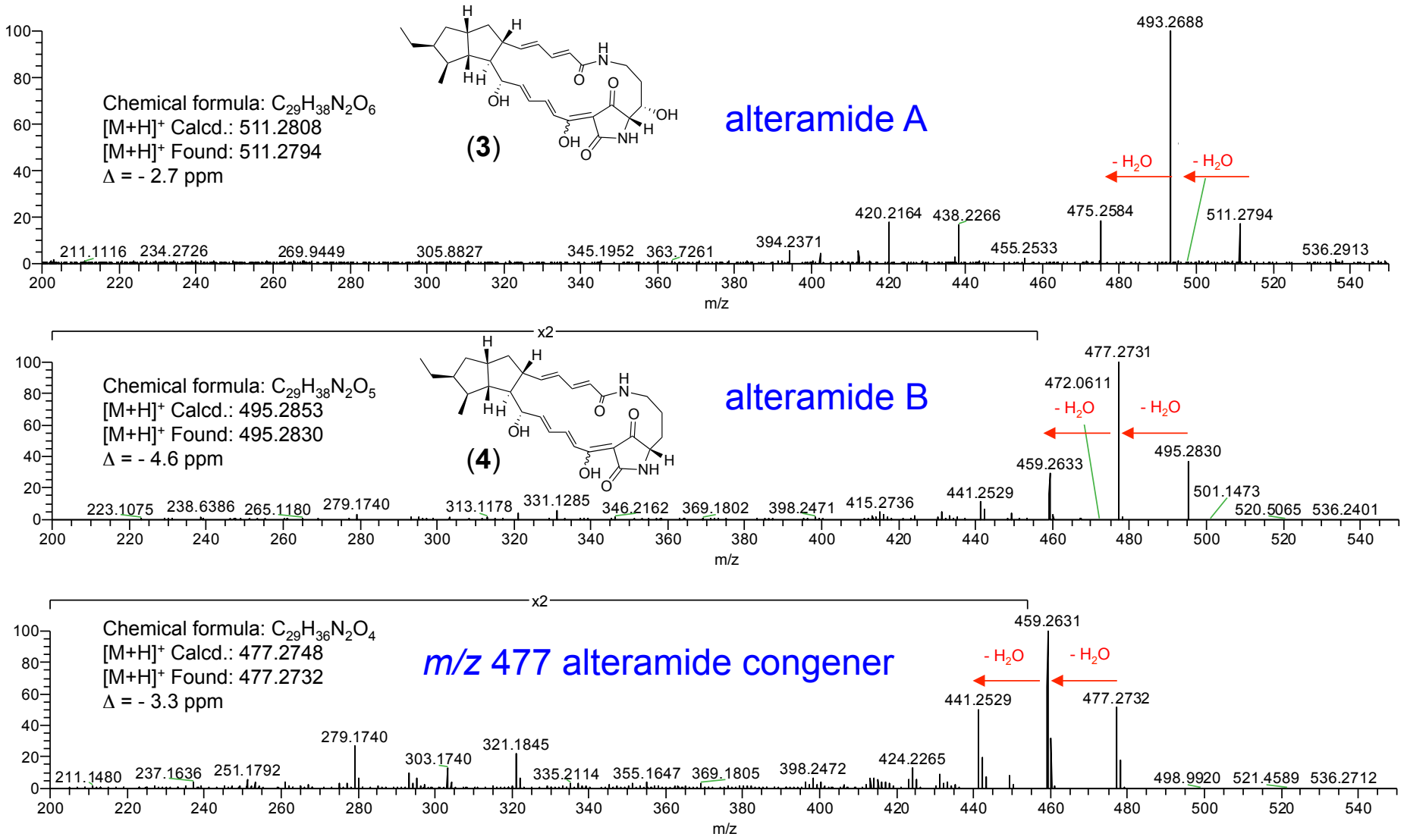
	calc Mw	obs ion	error (ppm)			calc Mw	obs ion	error (ppm)
b1	100.0762			V	y4	459.2567	459.2548	-4.14
b2	214.1191	214.1184	-3.27	N	y3	360.1883	360.1869	-3.89
b3	328.1621	328.1610	-3.35	N	y2	246.1454	246.1445	-3.66
b4	441.2456	441.2444	-2.72	I	y1	132.1025		



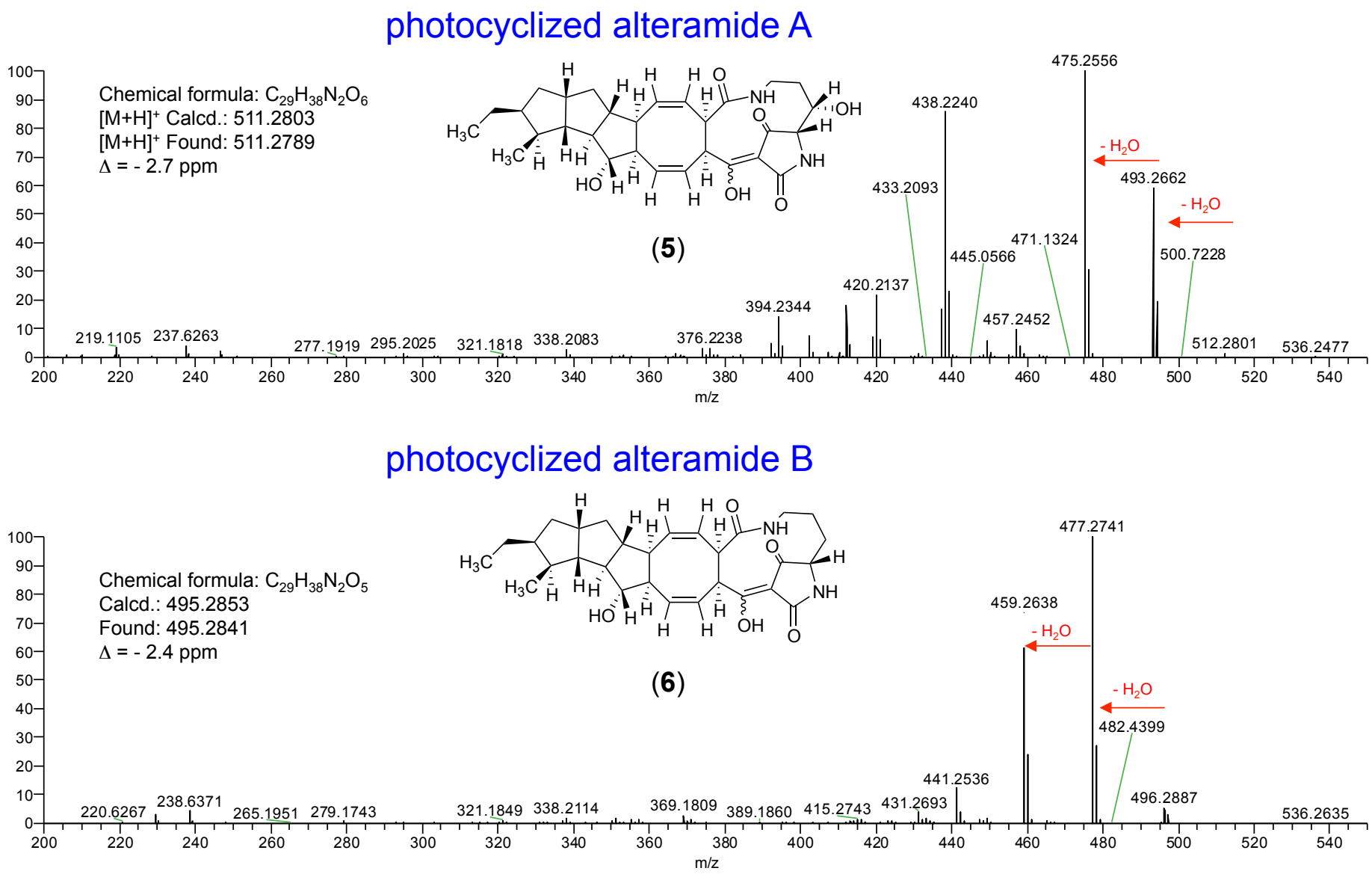
Supplement Figure 15. FT-MS2 of alteramide A (**3**)



Supplement Figure 16a. Comparison of FT-MS2 spectra of alteramides in OT59 extract

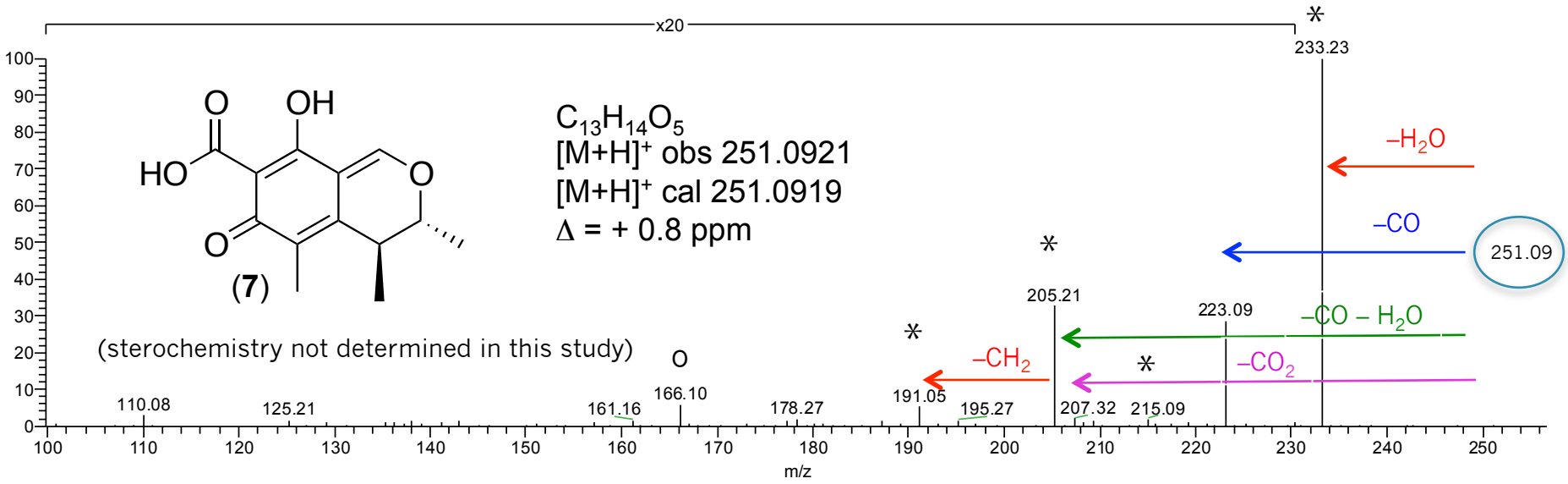


Supplement Figure 16b. Comparison of FT-MS2 spectra of photocyclized alteramide A (**5**) and alteramide B (**6**)

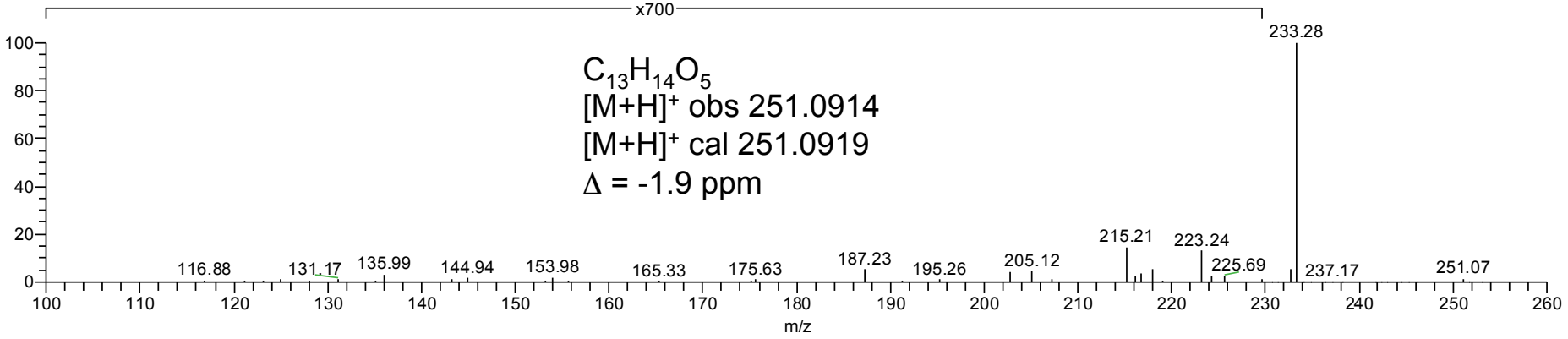


Supplement Figure 17a. IT-MS2 of citrinin[6] (**7**)

Citrinin detected in *n*BuOH extract of *P. citrinum*

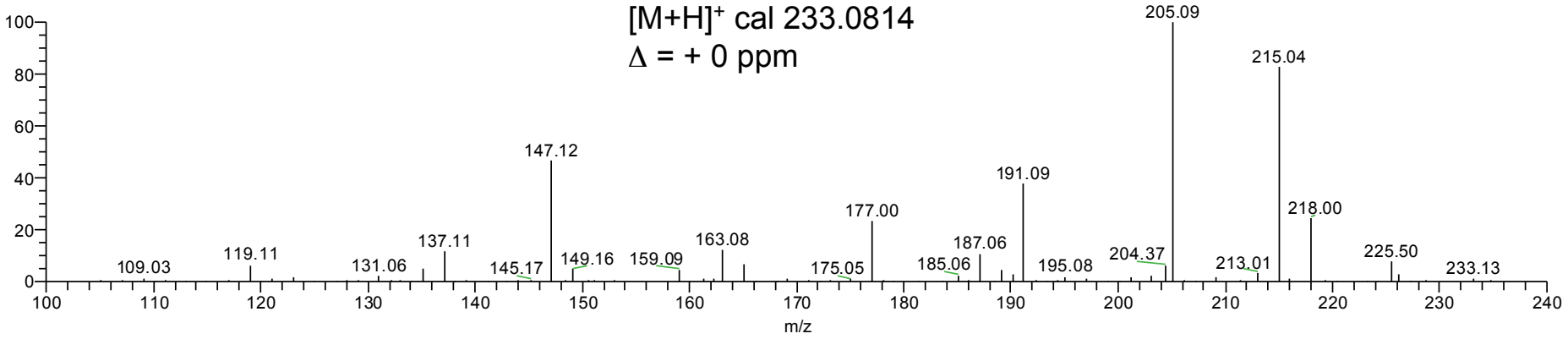


Standard citrinin (Sigma-Aldrich)

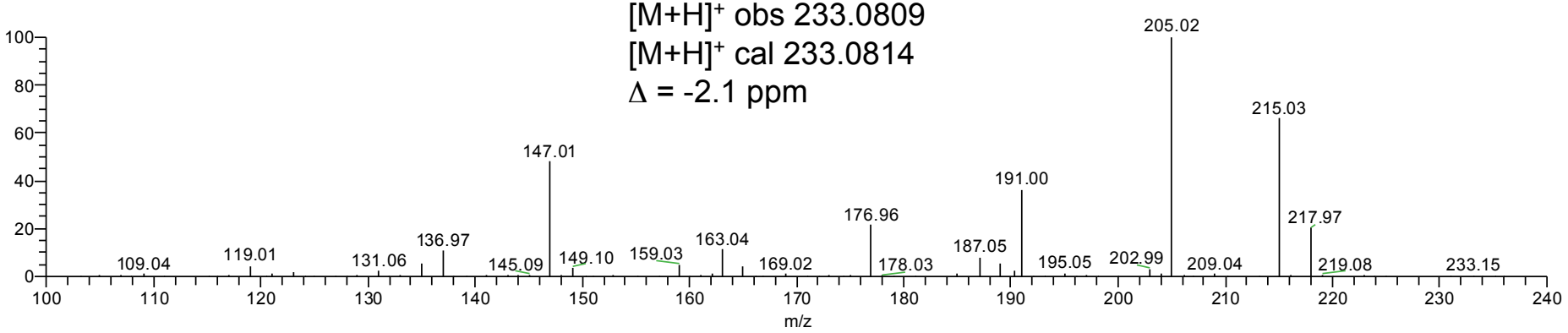


Supplement Figure 17b. IT-MS3 of *m/z* 233 fragment of citrinin (**7**)

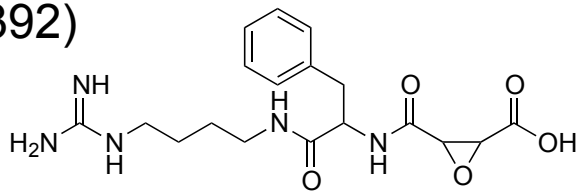
IT-MS3 of citrinin detected in *n*BuOH extract of *P. citrinum*



IT-MS3 of standard citrinin (Sigma-Aldrich)

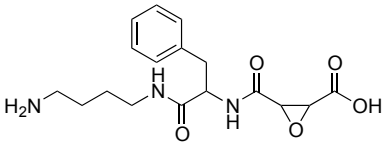


Supplement Figure 18a. FT-MS2 of estatin A (**8**) (*m/z* 392)

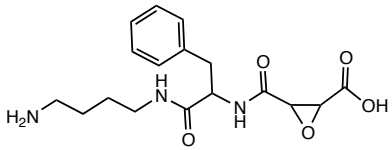


estatin A (**8**)

$C_{18}H_{25}N_5O_5$
$[M+H]^+$ obs 392.1923
$[M+H]^+$ cal 392.1928
Δ = - 1.3 ppm

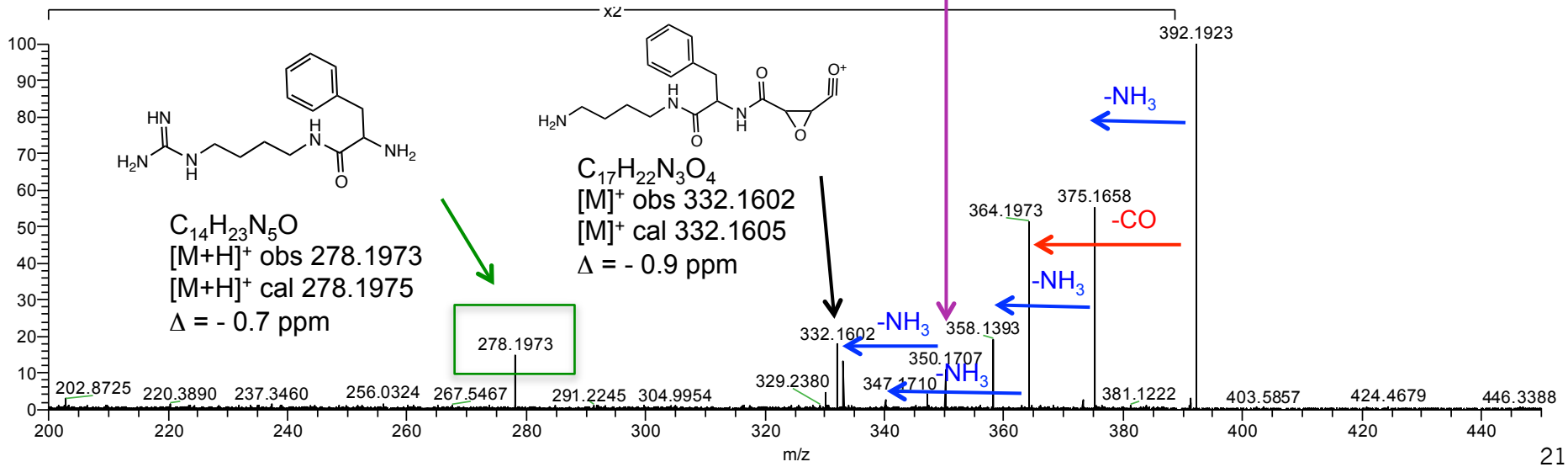


Related Cathestatin A
Isolated from *P. citrinum*[8]



$C_{17}H_{24}N_3O_5$
$[M+H]^+$ obs 350.1707
$[M+H]^+$ cal 350.1710
Δ = - 0.9 ppm

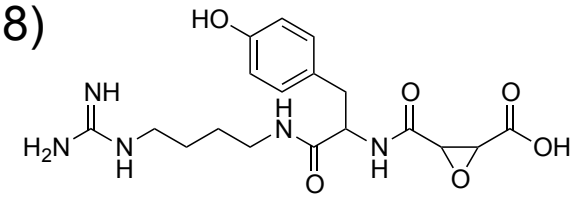
Estatins isolated from:
Myceliophthora thermophila[7]



$C_{14}H_{23}N_5O$
$[M+H]^+$ obs 278.1973
$[M+H]^+$ cal 278.1975
Δ = - 0.7 ppm

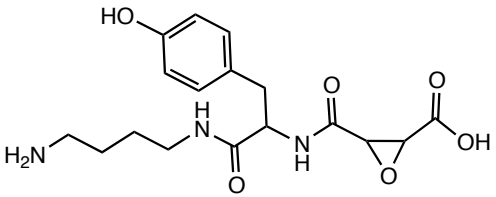
$C_{17}H_{22}N_3O_4$
$[M]^+$ obs 332.1602
$[M]^+$ cal 332.1605
Δ = - 0.9 ppm

Supplement Figure 18b. FT-MS2 of estatin B (**9**) (*m/z* 408)

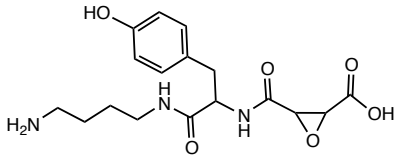


estatin B (**9**)

$C_{18}H_{25}N_5O_6$
$[M+H]^+$ obs 408.1872
$[M+H]^+$ cal 408.1878
Δ = - 1.5 ppm

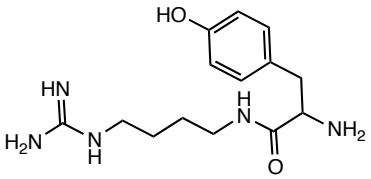


Related Cathestatin A
Isolated from *P. citrinum*[8]

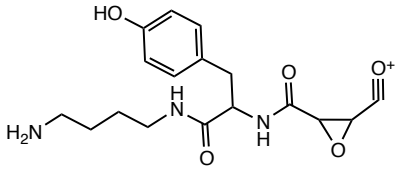


$C_{17}H_{24}N_3O_5$
$[M+H]^+$ obs 366.1655
$[M+H]^+$ cal 366.1660
Δ = - 1.4 ppm

Estatins isolated from:
Myceliophthora thermophila[7]



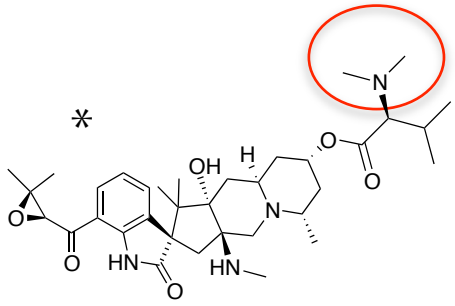
$C_{14}H_{23}N_5O$
$[M+H]^+$ obs 294.1922
$[M+H]^+$ cal 294.1925
Δ = - 1.0 ppm



$C_{17}H_{22}N_3O_4$
$[M]^+$ obs 348.1547
$[M]^+$ cal 348.1554
Δ = - 2.0 ppm

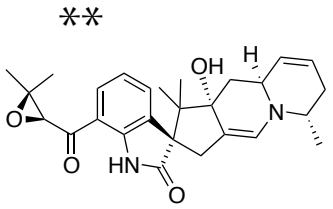
Supplement Figure 19a. FT- MS2 fragmentation of citrinadin A[9] (**10**)

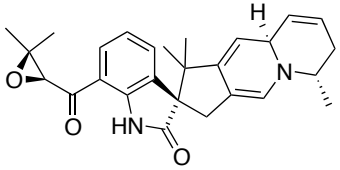
citrinadin A

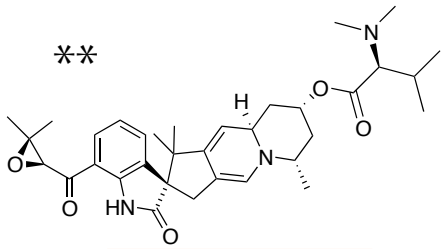


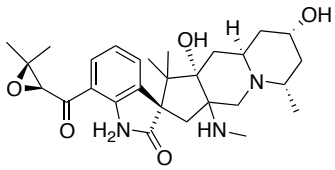
(**10**)

$C_{35}H_{52}N_4O_6$
$[M+H]^+$ obs 625.3946
$[M+H]^+$ cal 625.3960
Δ = - 2.2 ppm







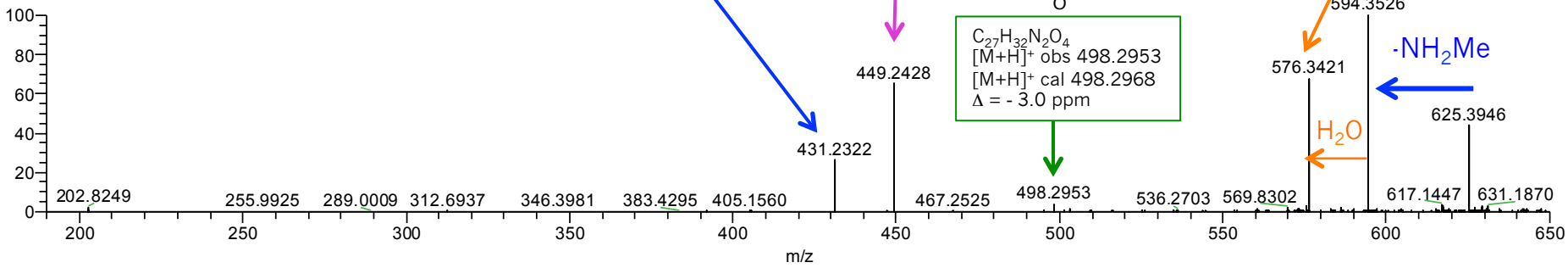


$C_{27}H_{32}N_2O_4$
$[M+H]^+$ obs 449.2428
$[M+H]^+$ cal 449.2440
Δ = - 2.7 ppm

$C_{27}H_{32}N_2O_4$
$[M+H]^+$ obs 431.2322
$[M+H]^+$ cal 431.2335
Δ = - 3.0 ppm

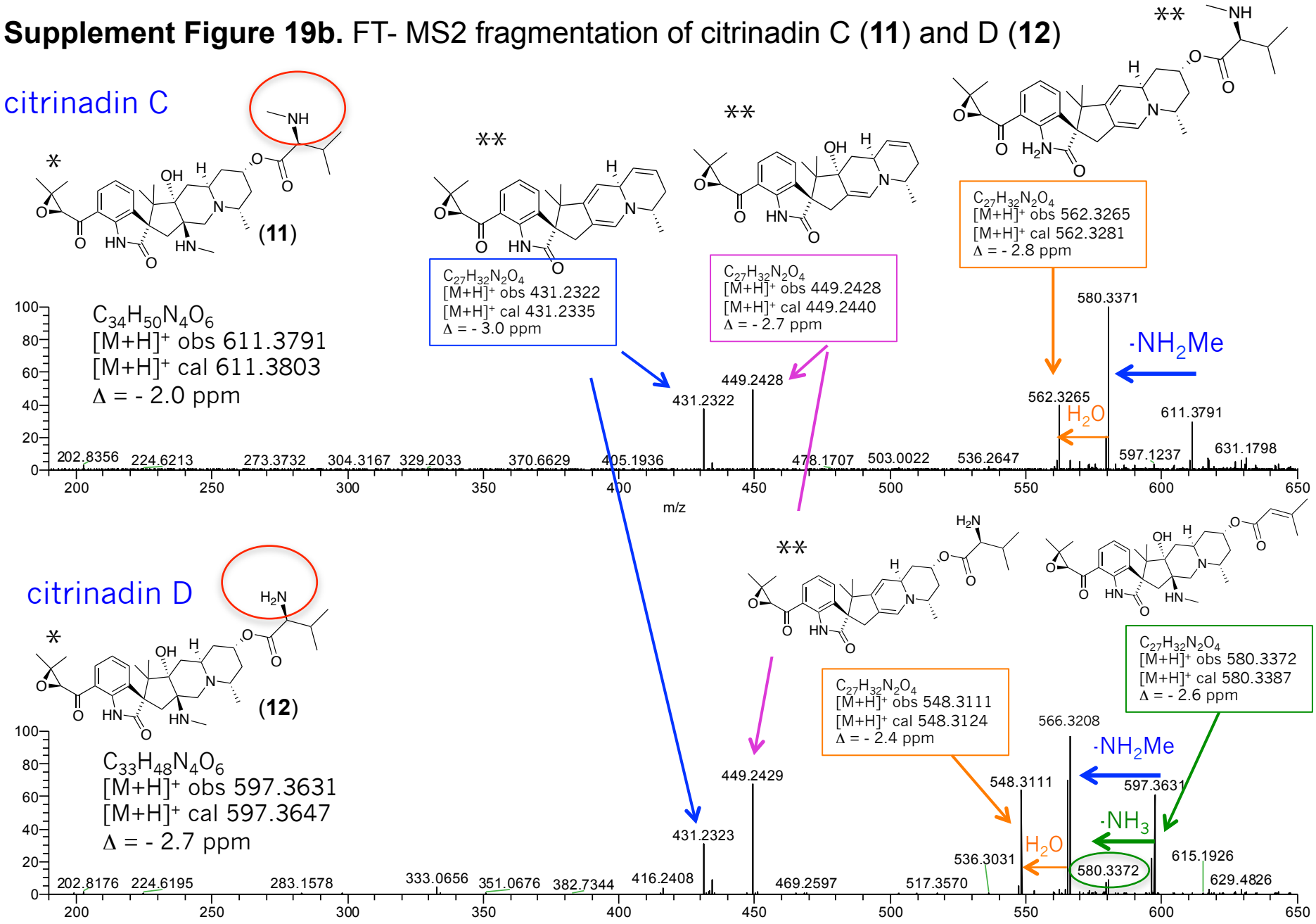
$C_{27}H_{32}N_2O_4$
$[M+H]^+$ obs 498.2953
$[M+H]^+$ cal 498.2968
Δ = - 3.0 ppm

$C_{27}H_{32}N_2O_4$
$[M+H]^+$ obs 576.3421
$[M+H]^+$ cal 576.3437
Δ = - 2.8 ppm



* Stereochemistry was not determined in this study and is displayed as published for citrinadin A and B. [9,10]
** It was not determined to which position the -NMe moiety and the -OH group eliminated in the ring systems

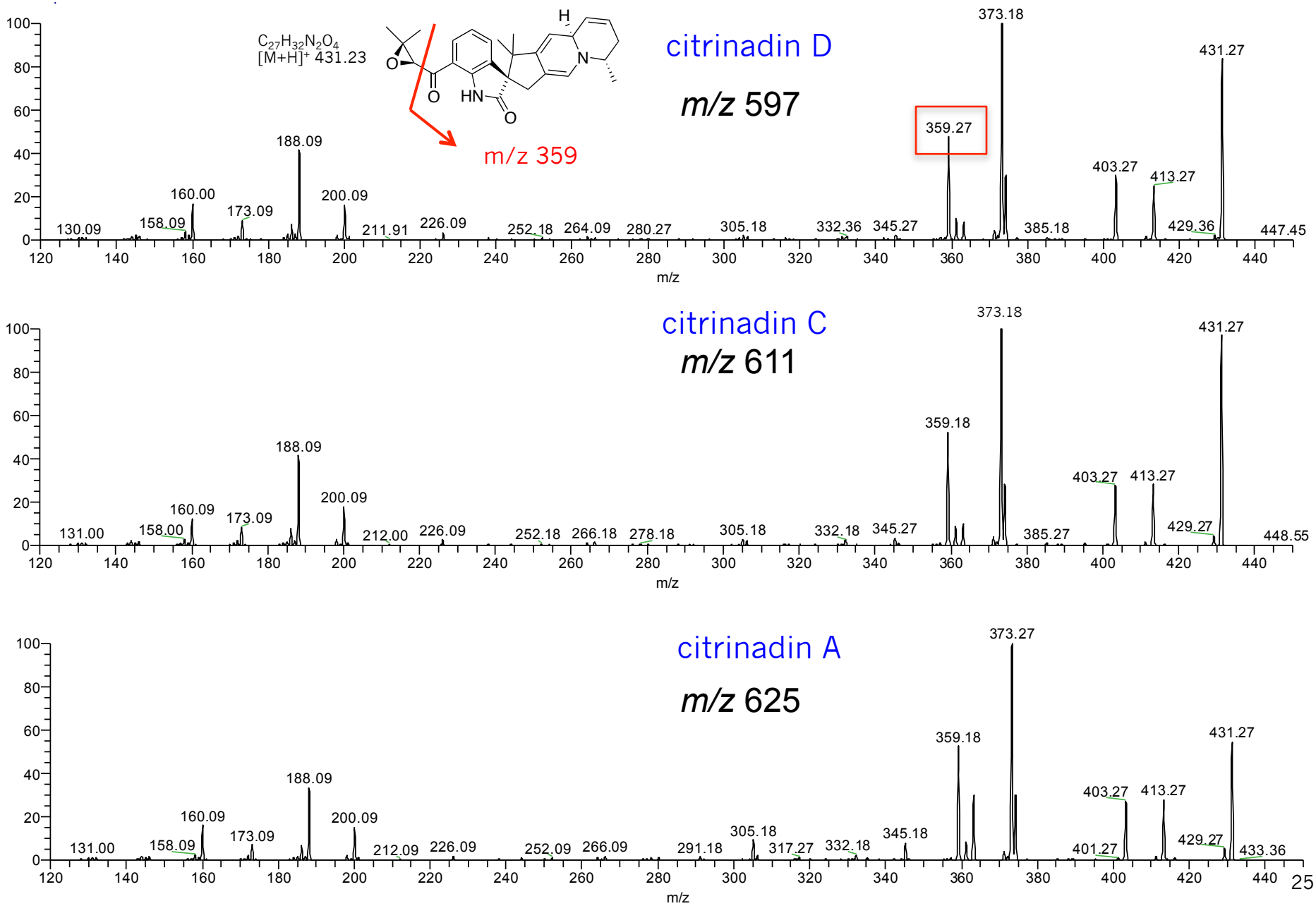
Supplement Figure 19b. FT- MS2 fragmentation of citrinadin C (**11**) and D (**12**)



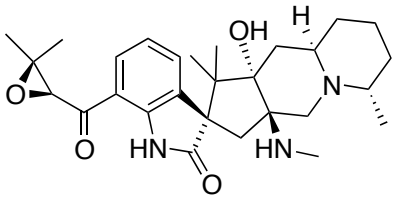
* Stereochemistry was not determined in this study and displayed based on published citrinadin A and B. [9,10]

** It was not determined to which position the NMe moiety and the OH group eliminated in the ring systems.

Supplement Figure 20. Comparison of IT-MS3 (*m/z* 431) of citrinadin A , C and D



Supplement Figure 21a. FT fragmention of *m/z* 466, deoxygenated citrinadin B (**13**)



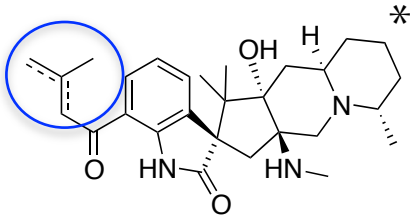
(**14**)

Citrinadin B[10]

$C_{28}H_{39}N_3O_4$

Exact mass 481.2941

contains 1 double bond



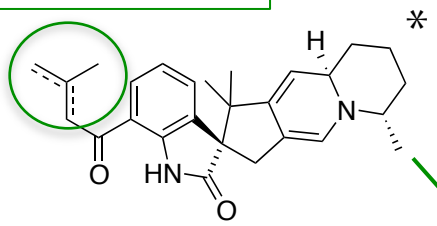
$C_{28}H_{40}N_3O_3$

$[M+H]^+$ obs 466.3052

$[M+H]^+$ cal 466.3064

Δ = - 2.6 ppm

contains 1 double bond



$C_{28}H_{40}N_3O_3$

$[M+H]^+$ obs 417.2530

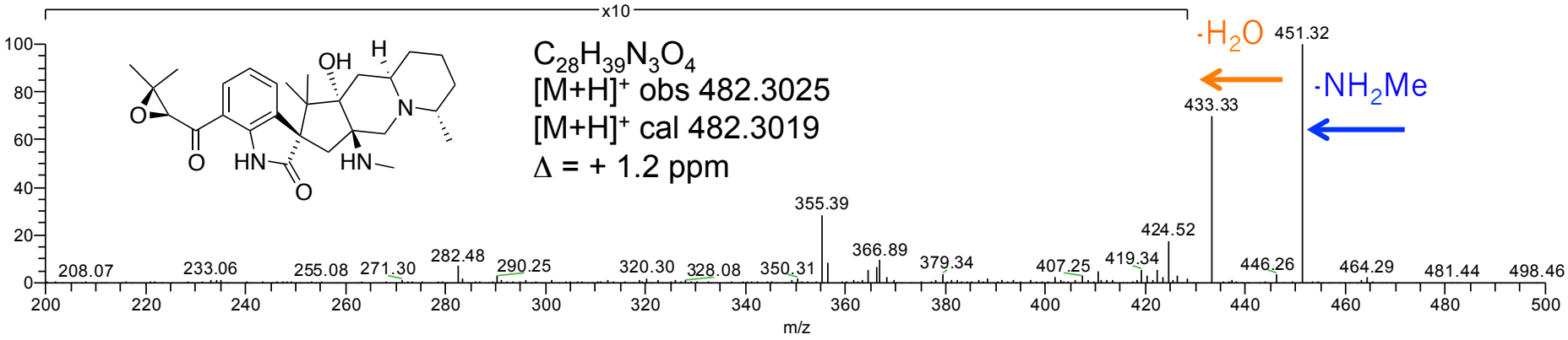
$[M+H]^+$ cal 417.2542

Δ = - 2.9 ppm

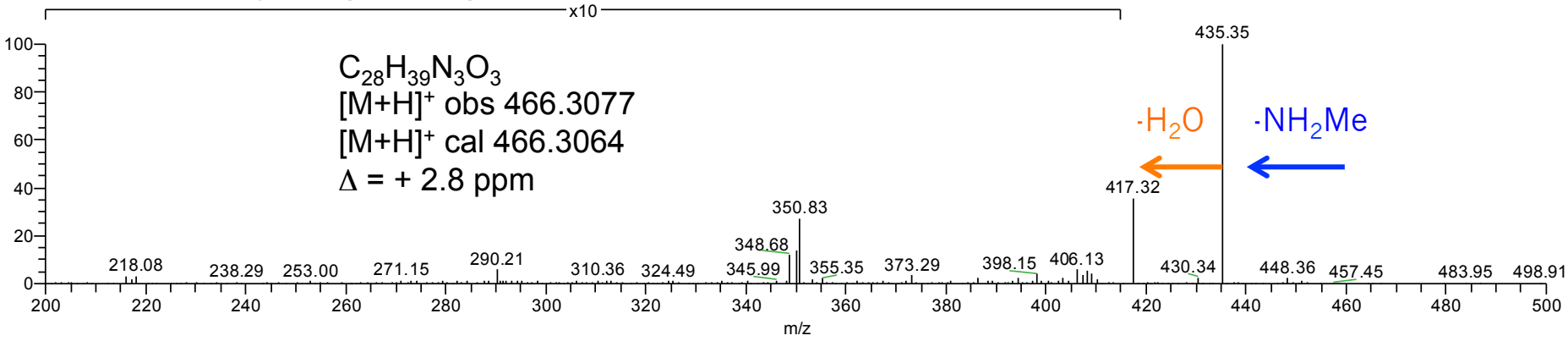
*Spectrum shown to illustrate similarity with other citrinidin analogs. Structures depicted here are speculative and further analyses would be required for full annotation.

Supplement Figure 21b. IT MS2 fragmention of *m/z* 466 compared to *m/z* 482 (citrinadin B)

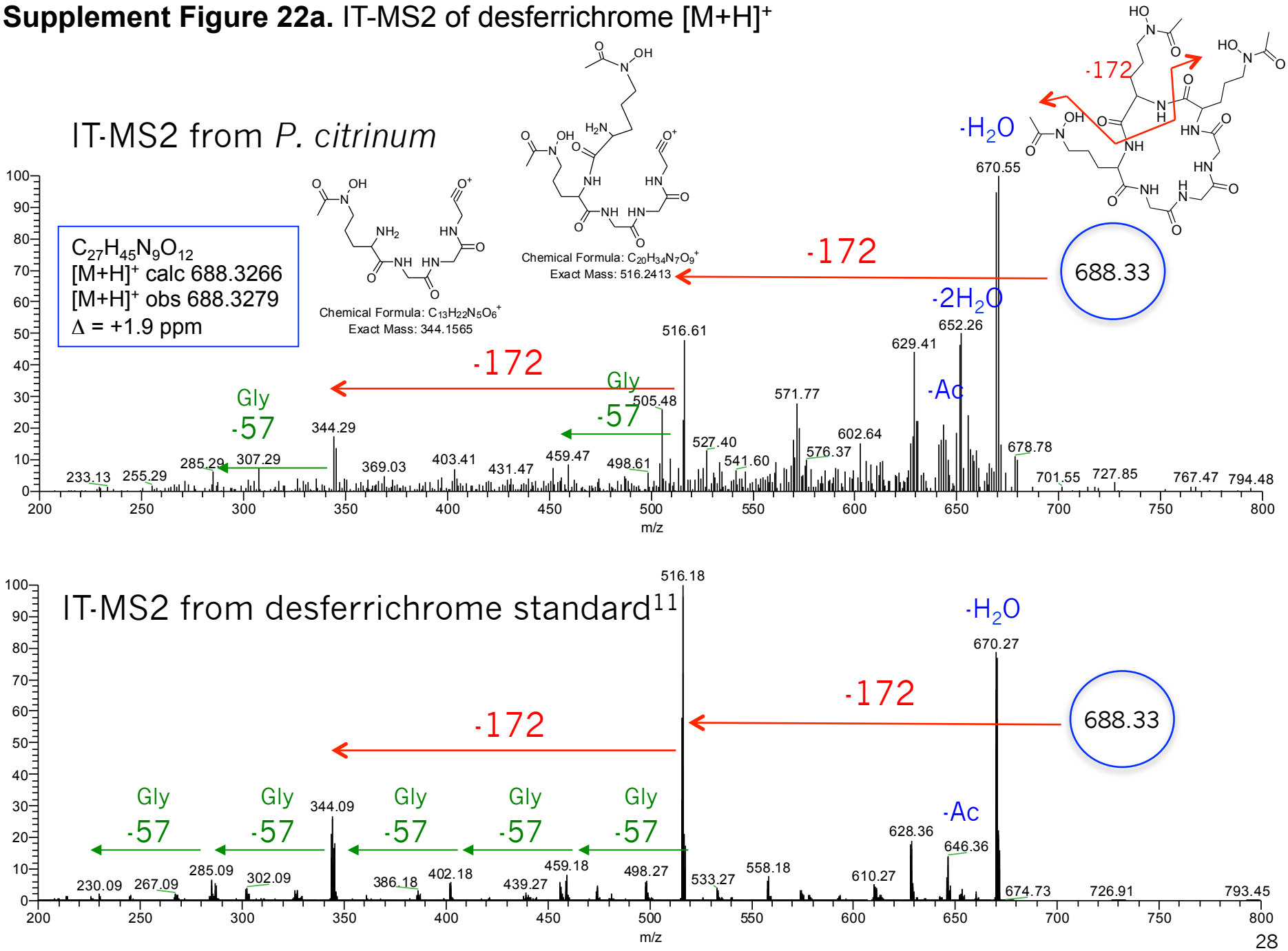
IT MS2 fragmention of *m/z* 482 (citrinadin B (**14**))



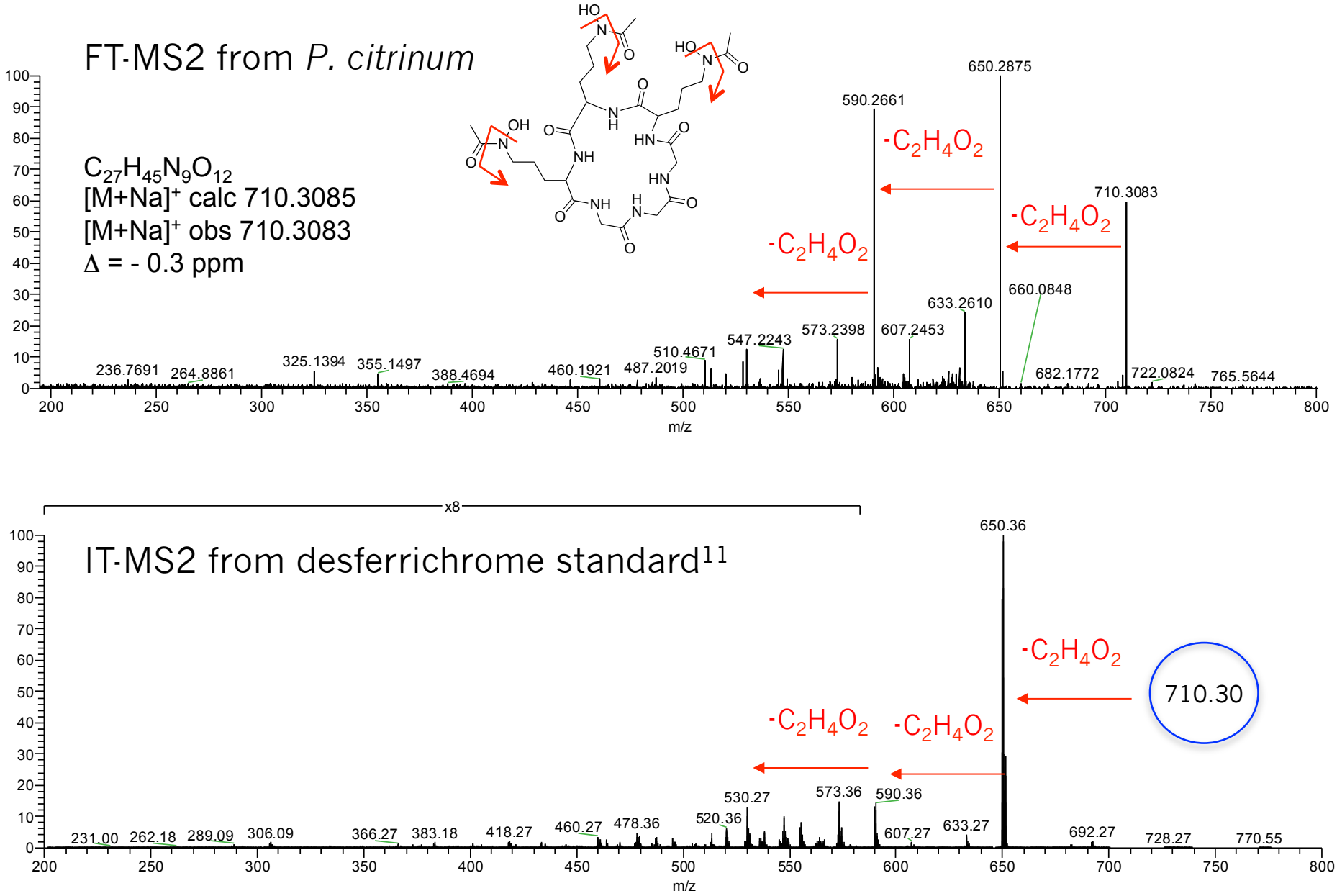
IT MS2 fragmention of *m/z* 466 (**13**)



Supplement Figure 22a. IT-MS2 of desferrichrome $[M+H]^+$



Supplement Figure 22b. MS2 of desferrichrome [M+Na]⁺ from *P. citrinum* vs standard



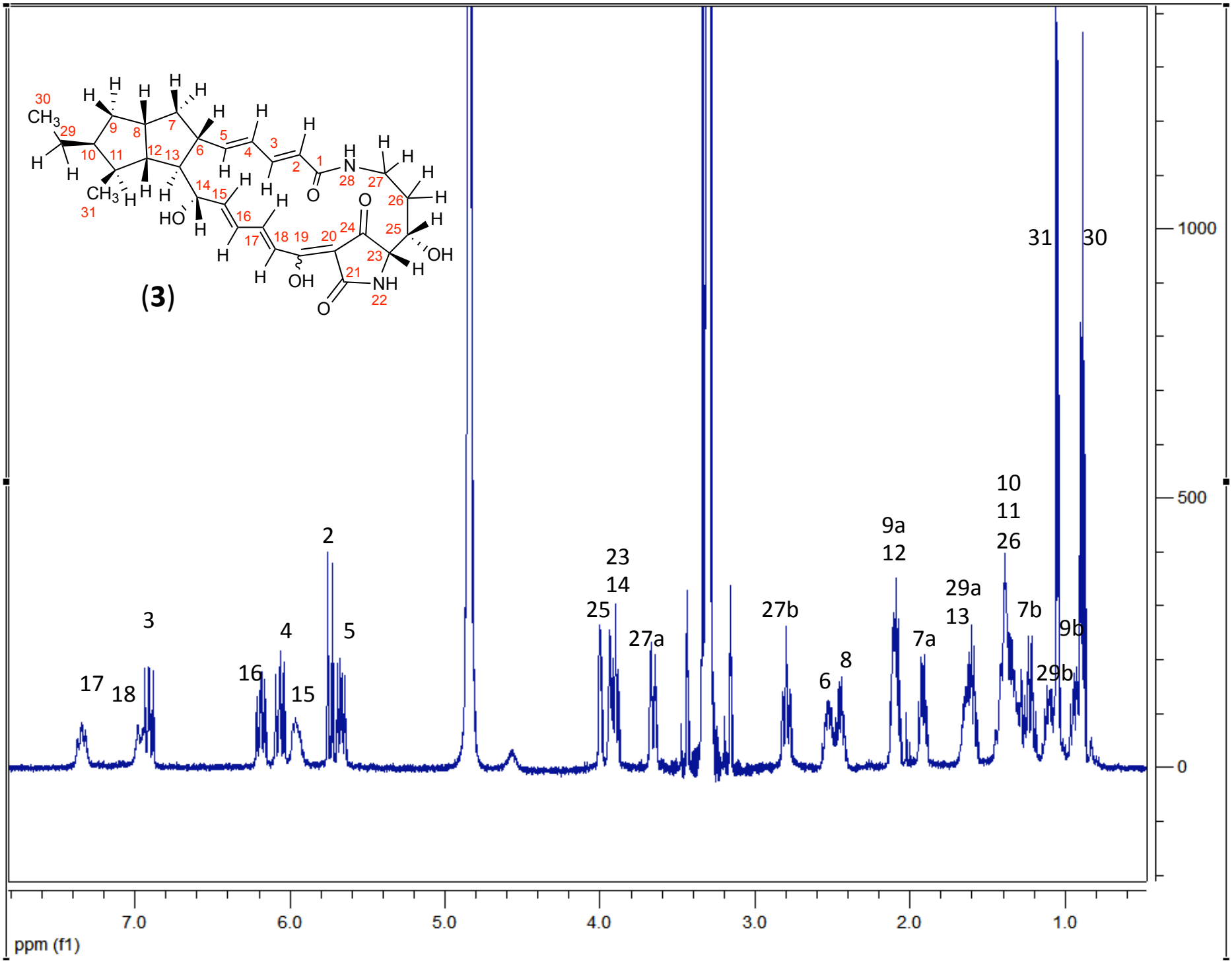
Supplemental Table 1. ^{1}H and ^{13}C NMR data of alteramide A (**3**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	168.3	-	
2	122.9	5.75, d (14.9)	C-1, C-4
3	141.9	6.90, dd (11.2, 14.6)	C-1, C-4, C-5
4	129.6	6.05, dd (11.3, 14.7)	C-2, C-3, C-6
5	148.1	5.66, dd (9.5, 14.9)	C-3, C-6, C-13
6	54.0	2.51, m	
7a	44.1	1.92, m	C-6, C-8, C-12, C-13
7b		1.22, m	C-5, C-6, C-8, C-9
8	42.5	2.45, m	
9a	39.8	2.10, m	C-7, C-8, C-10, C-11, C-12
9b		0.93, m	C-7, C-8, C-10, C-29
10	54.3	1.38, m	C-11, C-30
11	48.3	1.33, m	C-10, C-12
12	58.6	2.08, m	C-6, C-7, C-8, C-10, C-11, C-14, C-31
13	57.5	1.59, m	C-6, C-8, C-11, C-12, C-14, C-15
14	78.5	3.88, br t (8.5)	
15	144.4	5.90, br m	
16	132.6	6.16, dd (11.1, 14.1)	
17	nd	7.29, m	
18	128.6	7.06, br m	
19	nd	-	
20	nd	-	
21	nd	-	
22	-	-	
23	nd	3.88, m	
24	nd	-	
25	72.3	3.99, br d (5.1)	C-27
26a	32.6	1.44, m	
26b		1.37, m	
27a	37.9	3.66, m	
27b		2.80, t (12.5)	C-1, C-25, C-26
28	-	-	
29a	27.6	1.63, m	C-9, C-10, C-11, C-30
29b		1.10, m	C-9, C-10, C-11 (weak), C-30
30	12.6	0.89, t (7.0)	C-10, C-29
31	17.9	1.05, d (6.2)	C-10, C-11, C-12
nd = not detected			

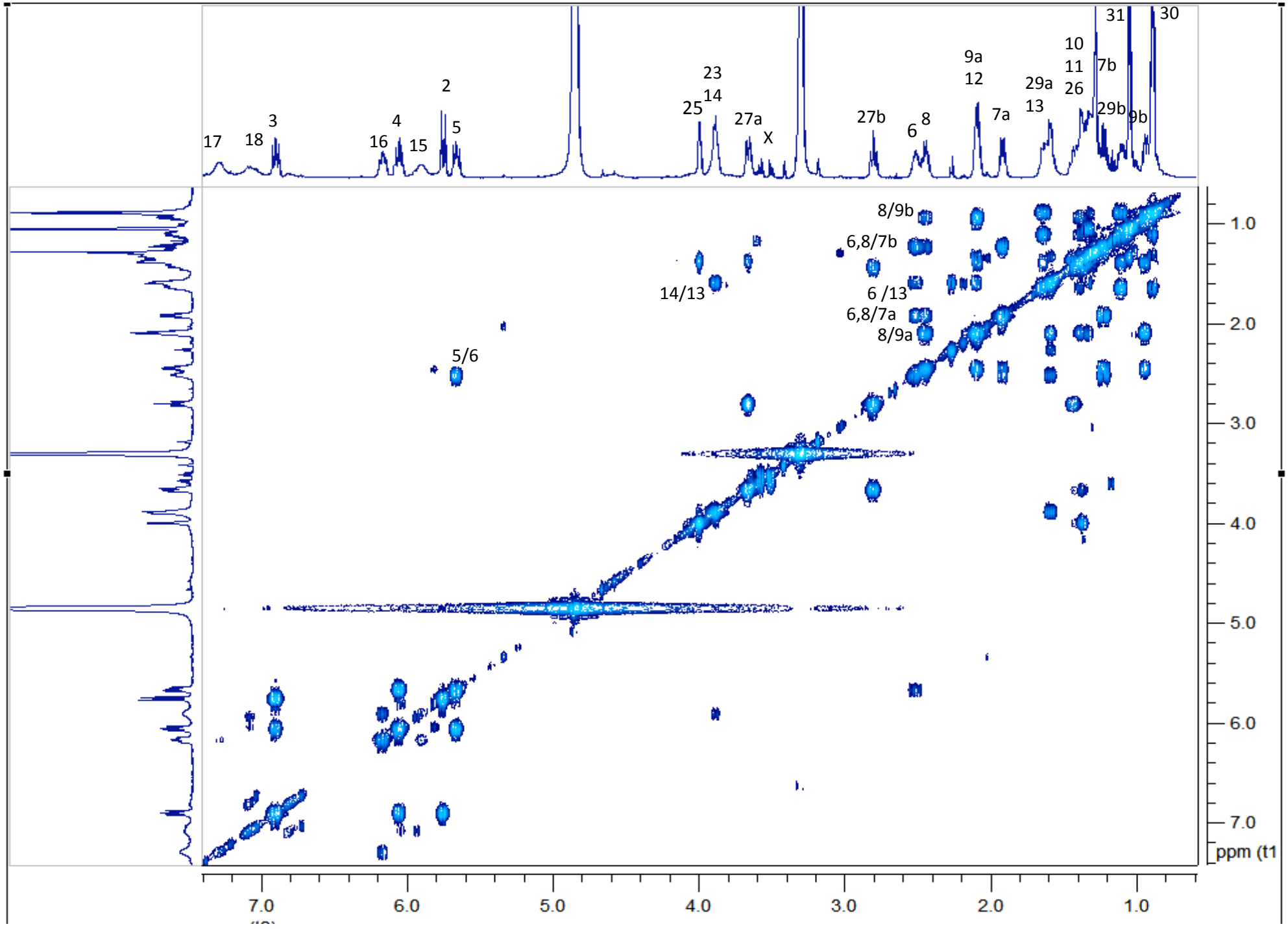
Supplemental Table 2. ^{1}H and ^{13}C NMR Data and NOEs - alteramide A (**3**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H - ^{1}H NOE (NOESY)
1	168.3	-	-
2	122.9	5.75, d (14.9)	H-4
3	141.9	6.90, dd (11.2, 14.6)	H-5
4	129.6	6.05, dd (11.3, 14.7)	H-2, H-6
5	148.1	5.66, dd (9.5, 14.9)	H-3, H-7b (weak), H-13,
6	54.0	2.51, m	H-4, H-7a, H-14
7a	44.1	1.92, m	H-6, H-8
7b		1.22, m	H-5 (weak), H-13 (weak)
8	42.5	2.45, m	H-7a, H-12
9a	39.8	2.09, m	
9b		0.93, m	
10	54.3	1.38, m	H-30, H-31
11	48.3	1.33, m	H-13 (weak)
12	58.6	2.09, m	H-6 (weak), H-8, H-14, H-31
13	57.5	1.59, m	H-5, H-7b (weak), H-11 (weak)
14	78.5	3.88, br t (8.5)	H-6, H-12, H-16
15	144.4	5.90, br m	
16	132.6	6.16, dd (11.1, 14.1)	H-14
17	nd	7.29, m	
18	128.6	7.06, br m	
19	nd	-	
20	nd	-	
21	nd	-	
22	-	-	
23	nd	3.88, m	
24	nd	-	
25	72.3	3.99, br d (5.1)	H-27b
26a	32.6	1.44, m	
26b		1.37, m	
27a	37.9	3.66, m	
27b		2.80, t (12.5)	H-25
28	-	-	
29a	27.6	1.63, m	
29b		1.10, m	
30	12.6	0.89, t (7.0)	H-10, H-11
31	17.9	1.05, d (6.2)	H-10 (weak), H-12, H-29a (weak)
nd = not detected			

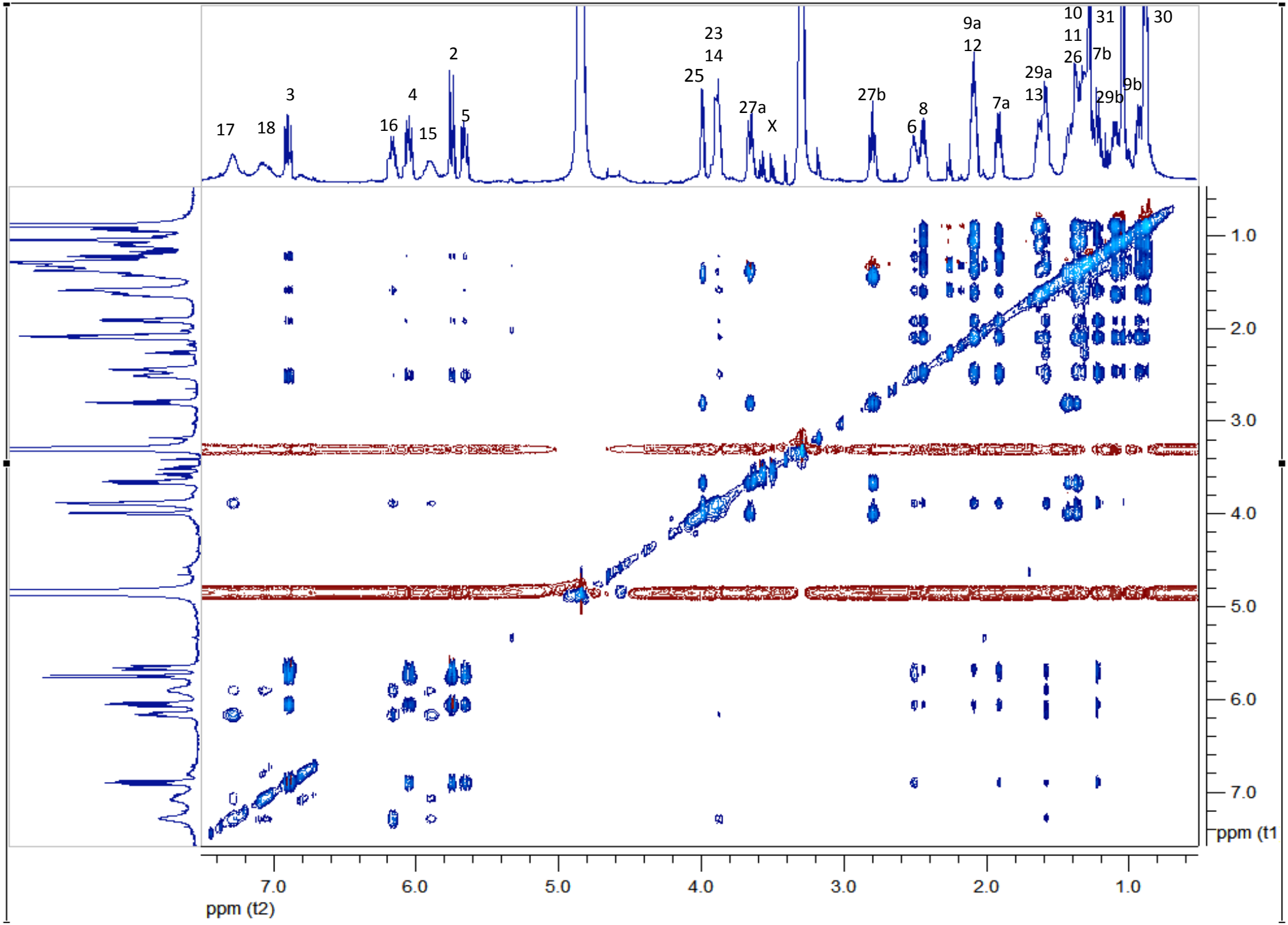
Supplement Figure 23. ^{1}H NMR (600 MHz, CD_3OD) spectra of alteramide A (**3**)



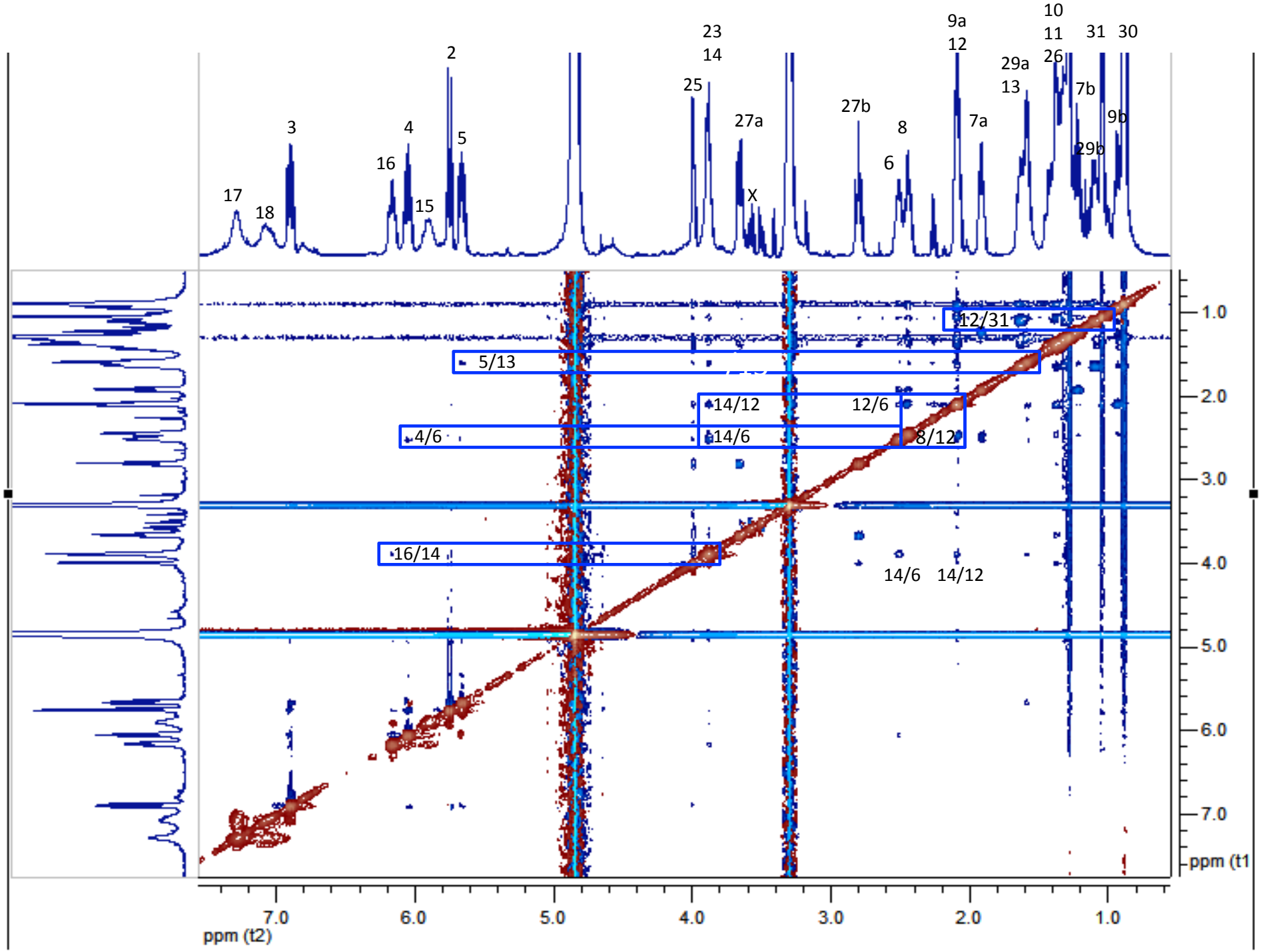
Supplement Figure 24. COSY(600 MHz, CD_3OD) spectrum of alteramide A (**3**)



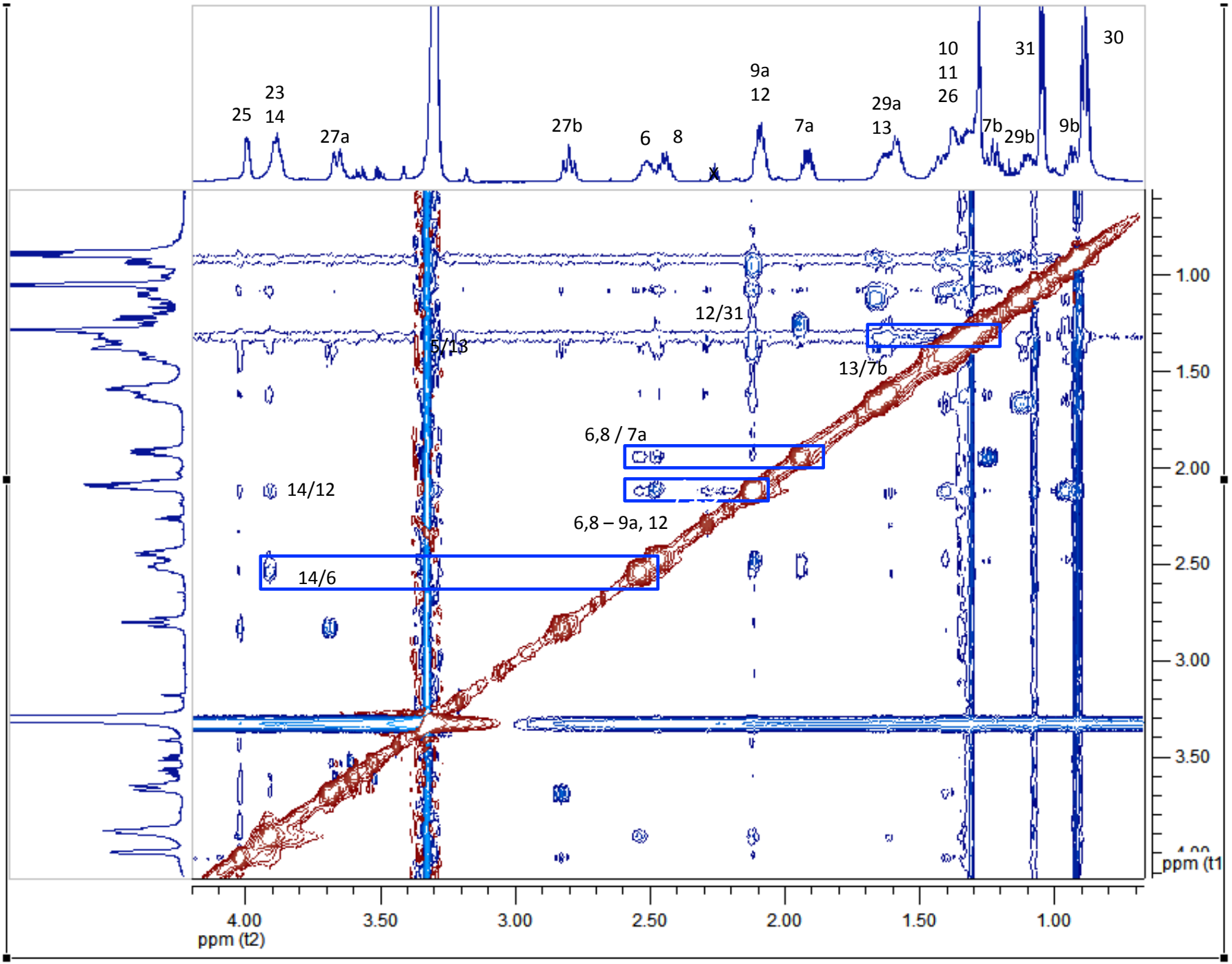
Supplement Figure 25. TOCSY(600 MHz, CD_3OD) of alteramide A (**3**)



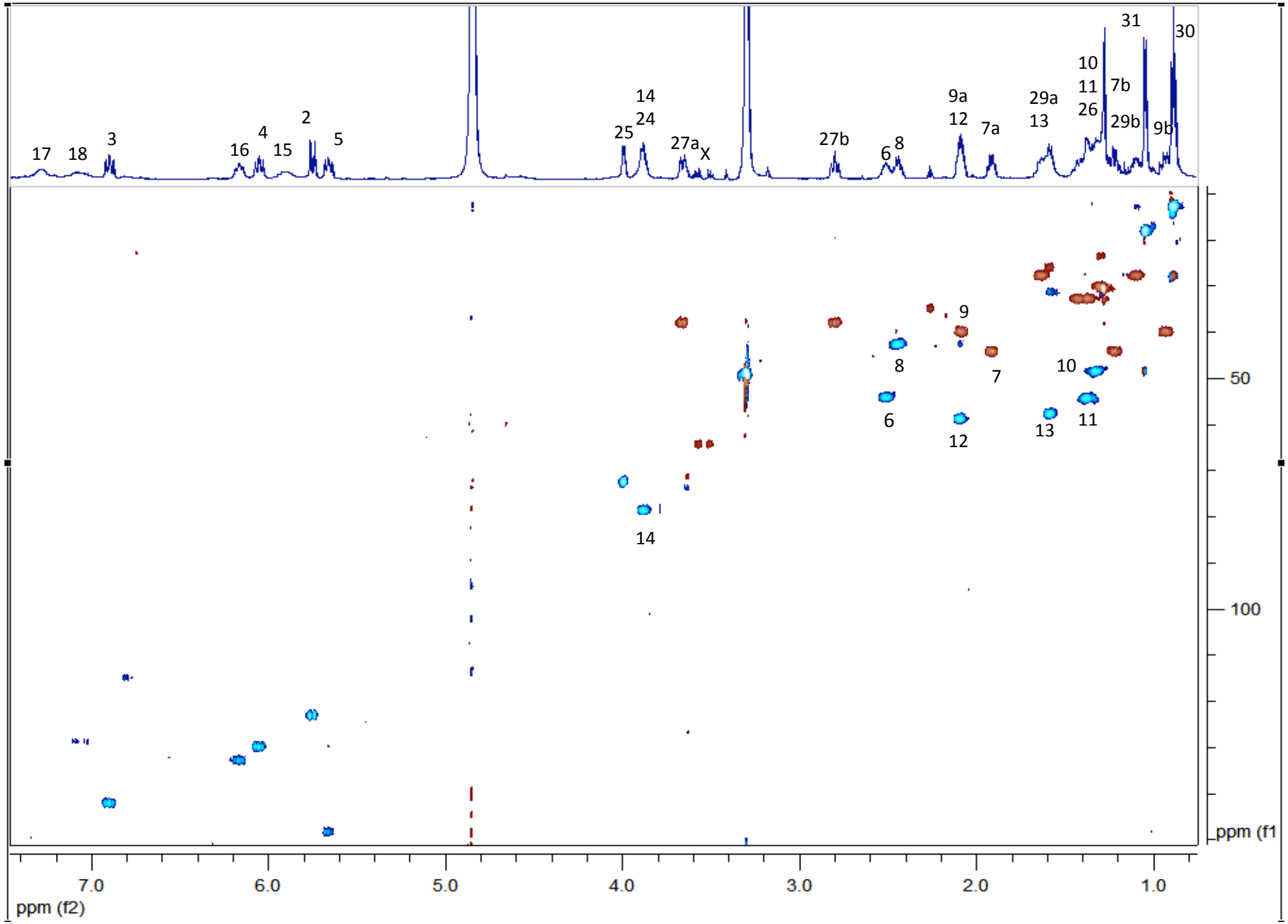
Supplement Figure 26a. NOESY(600 MHz, CD_3OD, 600 ms) of alteramide A (**3**)



Supplement Figure 26b. NOESY zoom-in (600 MHz, CD_3OD, 600 ms) of alteramide A (**3**)



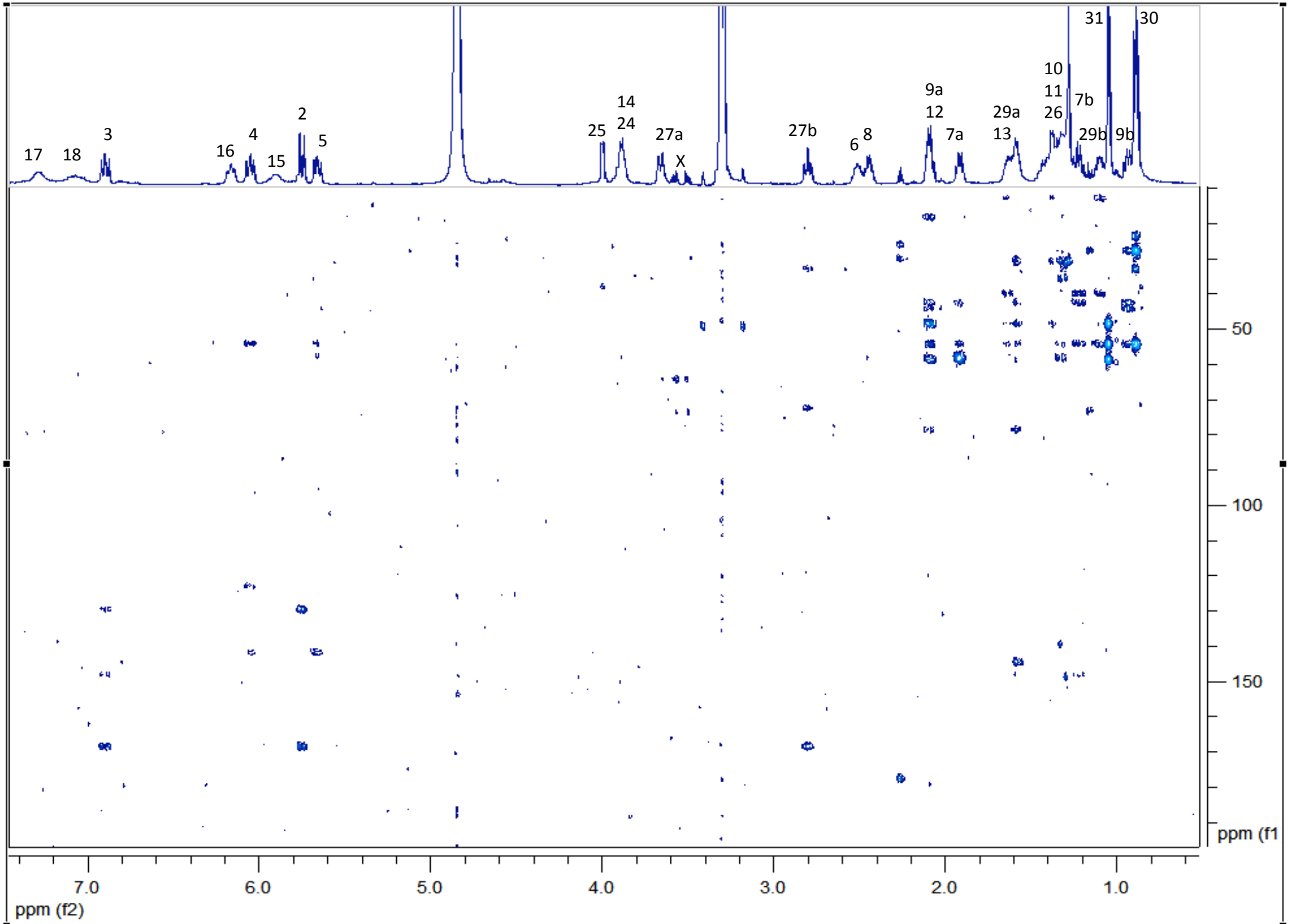
Supplement Figure 27. HSQC (600 MHz, CD_3OD) of alteramide A (**3**)



Supplement Table 3. HMBC (600 MHz, CD_3OD, 8 Hz) of alteramide A (**3**)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	168.3	-	
2	122.9	5.75, d (14.9)	C-1, C-4
3	141.9	6.90, dd (11.2, 14.6)	C-1, C-4, C-5
4	129.6	6.05, dd (11.3, 14.7)	C-2, C-3, C-6
5	148.1	5.66, dd (9.5, 14.9)	C-3, C-6, C-13
6	54.0	2.51, m	
7a	44.1	1.92, m	C-6, C-8, C-12, C-13
7b		1.22, m	C-5, C-6, C-8, C-9
8	42.5	2.45, m	
9a	39.8	2.10, m	C-7, C-8, C-10, C-11, C-12
9b		0.93, m	C-7, C-8, C-10, C-29
10	54.3	1.38, m	C-11, C-30
11	48.3	1.33, m	C-10, C-12
12	58.6	2.08, m	C-6, C-7, C-8, C-10, C-11, C-14, C-31
13	57.5	1.59, m	C-6, C-8, C-11, C-12, C-14, C-15
14	78.5	3.88, br t (8.5)	
15	144.4	5.90, br m	
16	132.6	6.16, dd (11.1, 14.1)	
17	nd	7.29, m	
18	128.6	7.06, br m	
19	nd	-	
20	nd	-	
21	nd	-	
22	-	-	
23	nd	3.88, m	
24	nd	-	
25	72.3	3.99, br d (5.1)	C-27
26a	32.6	1.44, m	
26b		1.37, m	
27a	37.9	3.66, m	
27b		2.80, t (12.5)	C-1, C-25, C-26
28	-	-	
29a	27.6	1.63, m	C-9, C-10, C-11, C-30
29b		1.10, m	C-9, C-10, C-11 (weak), C-30
30	12.6	0.89, t (7.0)	C-10, C-29
31	17.9	1.05, d (6.2)	C-10, C-11, C-12
		-	
nd = not detected			

Supplement Figure 28. HMBC (600 MHz, CD_3OD, 8 Hz) of alteramide A (**3**)



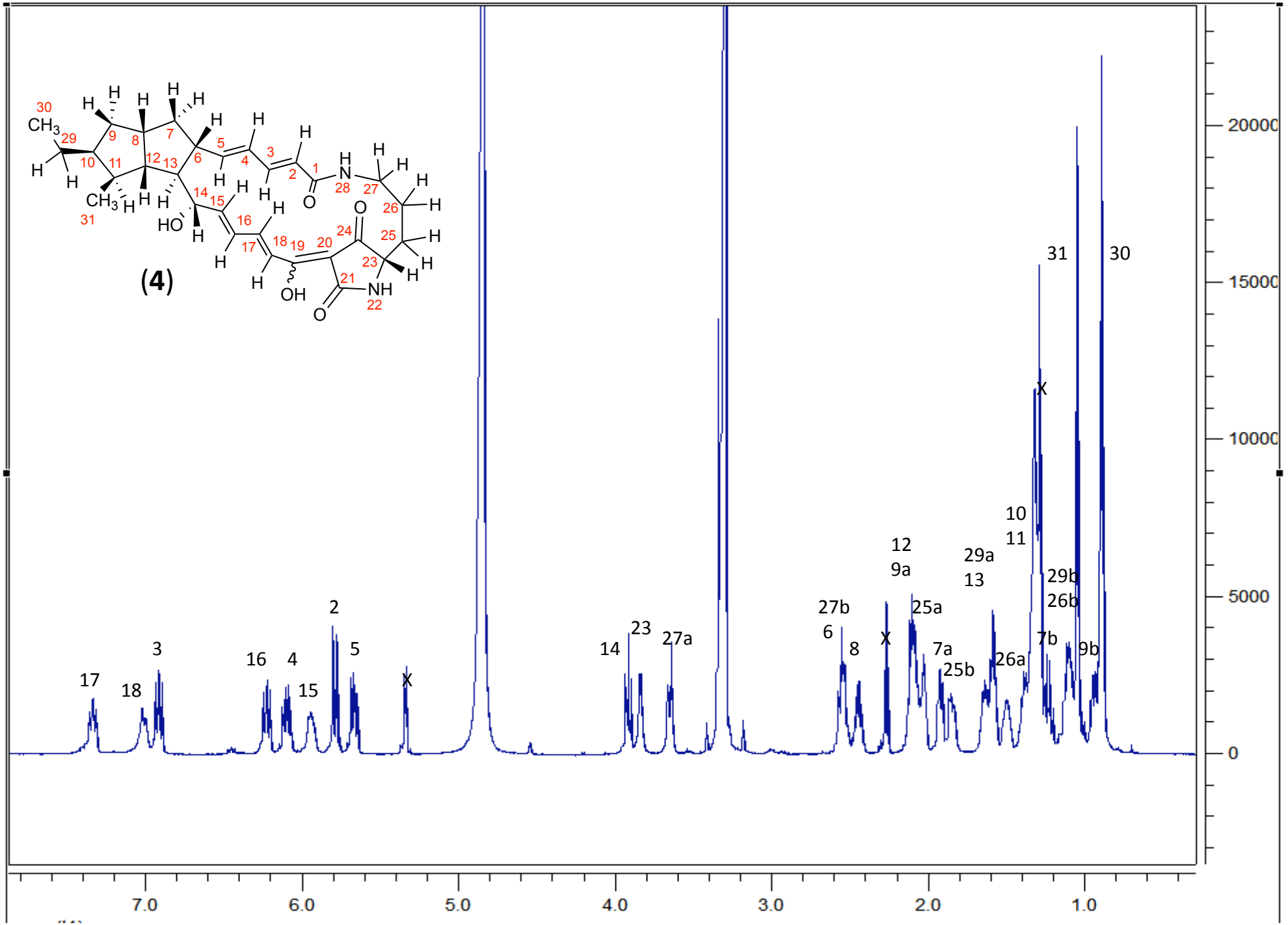
Supplemental Table 4. ^{1}H and ^{13}C NMR data of alteramide B (**4**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	168.0	-	-
2	122.5	5.74, d (16.0)	C-1 (168.0), C-4 (129.3)
3	141.0	6.85, dd (12.2, 16.0)	C-1 (168.0), C-2 (122.5), C-4 (129.3), C-5 (147.2)
4	129.3	6.04, dd (12.0, 15.8)	C-2 (122.5), C-3 (141.0), C-6 (53.3)
5	147.2	5.62, dd (10.0, 15.8)	C-3 (141.0), C-6 (53.3), C-7 (43.5), C-13 (56.5)
6	53.3	2.48, m	C-4 (129.2), C-5 (147,2), C-7 (43.5) (w), C-13 (56.5), C-14 (77.7)
7a	43.5	1.87, m	C-6 (53.3), C-8 (41.7), C-12 (57.9), C-13 (56.5)
7b		1.18, m	C-5 (147.2), C-6 (53.3) C-8 (41.7), C-9 (38.7)
8	41.7	2.40, m	C-7 (43.5), C-11 (47.7) (w), C-12 (57.9)
9a	38.7	2.04, m	C-8 (41.7), C-10 (53.5), C-11 (47.7), C-12 (57.9)
9b		0.89 m	C-7 (43.5), C-8 (41.8), C-10 (53.5), C-29 (27.0)
10	53.5	1.33, m	C-9 (38.7), C-11 (47.7), C-29 (27.0) (weak), C-30 (11.9), C-31 (17.2)
11	47.7	1.27, m	C-10 (53.5), C-12 (57.9), C-13 (56.5), C-29 (27.0), C-31 (17.2)
12	57.9	2.06, m	C-7 (43.5), C-8 (41.7), C-11 (47.7), C-13 (56.5), C-14 (77.7), C-31 (17.2)
13	56.5	1.53, m	C-5 (147.2), C-6 (53.3), C-11 (47.7), C-12 (57.9), C-14 (77.7)
14	77.7	3.86, m	C-6 (53.3), C-13 (56.5), C-16 (131.9)
15	146.9	5.86, m	C-17 (143.7) (weak)
16	131.9	6.17, dd (12.0, 16.6)	C-14 (77.7), C-17 (143.7)
17	143.7	7.27, dd (12.0, 16.6)	C-15 (146.9) (weak), C-16 (131.9) (weak)
18	nd	7.02, bd (16.6)	
19	nd	-	-
20	nd	-	-
21	nd	-	-
22	-	-	
23	61.6	3.77, brs	C-24 (197.0) (very weak)
24	197.0	-	-
25a	26.7	2.03, m	
25b		1.79, m	C-26 (21.4), C-27 (39.1)
26a	21.4	1.46, m	
26b		1.06, m	
27a	39.1	3.59, m	
27b		2.52, m	C-1 (168.0)
28	-	-	-
29a	27.0	1.58, m	C-9 (38.7), C-10 (53.5), C-11 (47.7), C-30 (11.9)
29b		1.05, m	C-9 (38.7), C-10 (53.5), C-11 (47.7) (weak), C-30 (11.9)
30	11.9	0.84, t (7.0)	C-10 (53.5), C-29 (27.0)
31	17.2	0.99, d (7.0)	C-10 (53.5), C-11 (47.7), C-12 (57.9)
nd = not detected			

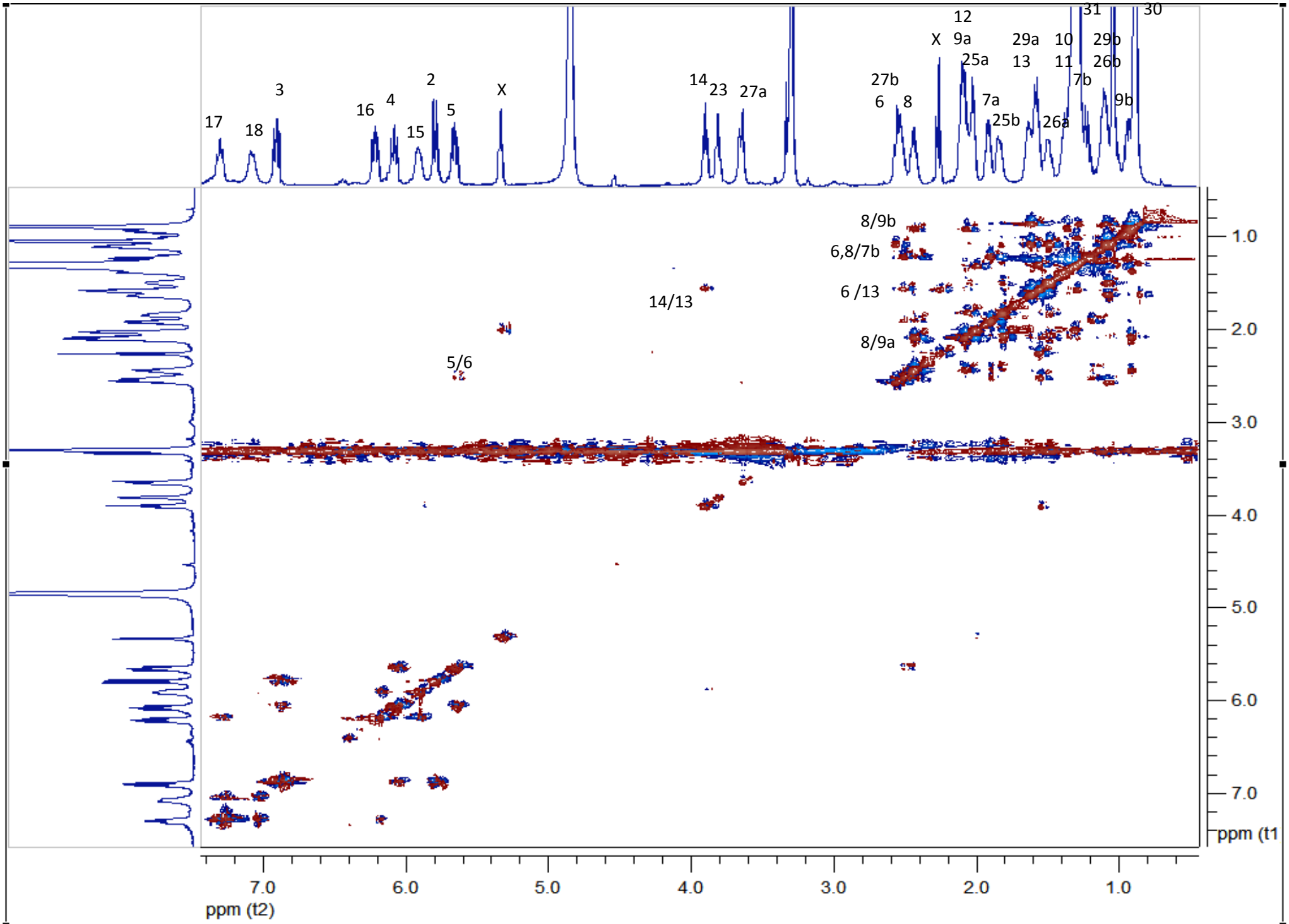
Supplemental Table 5. ^{1}H and ^{13}C NMR Data and NOEs - alteramide B (**4**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H - ^{1}H NOE (NOESY)
1	168.0	-	-
2	122.5	5.74, d (16.0)	H-4
3	141.0	6.85, dd (12.2, 16.0)	H-5
4	129.3	6.04, dd (12.0, 15.8)	H-2, H-6
5	147.2	5.62, dd (10.0, 15.8)	H-3, H-13, H-7b
6	53.3	2.48, m	H-4, H-12 (weak), H-14
7a	43.5	1.87, m	H-6, H-8
7b		1.18, m	H-5 (weak)
8	41.7	2.40, m	H-7a, H-12
9a	38.7	2.04, m	H-30
9b		0.89 m	
10	53.5	1.33, m	H-31 (weak)
11	47.7	1.27, m	H-13, H-30 (weak)
12	57.9	2.06, m	H-6 (weak), H-8, H-14, H-31
13	56.5	1.53, m	H-5, H-11, H-15
14	77.7	3.86, m	H-6, H-12, H-16
15	146.9	5.86, m	H-13, H-17
16	131.9	6.17, dd (12.0, 16.6)	H-14, H-18
17	143.7	7.27, dd (12.0, 16.6)	H-15
18	nd	7.02, bd (16.6)	H-16
19	nd	-	
20	nd	-	
21	nd	-	
22	-	-	
23	61.6	3.77, brs	H-25a, H-25b
24	197.0	-	
25a	26.7	2.03, m	H-23
25b		1.79, m	H-23, H-27b
26a	21.4	1.46, m	H-27a, H-27b
26b		1.06, m	H-27a
27a	39.1	3.59, m	H-26a, H-26b
27b		2.52, m	H-25b, H-26a
28	-	-	
29a	27.0	1.58, m	H-31
29b		1.05, m	
30	11.9	0.84, t (7.0)	H-9a, H-11 (weak)
31	17.2	0.99, d (7.0)	H-10 (weak), H-12, H-29a
nd = not detected			

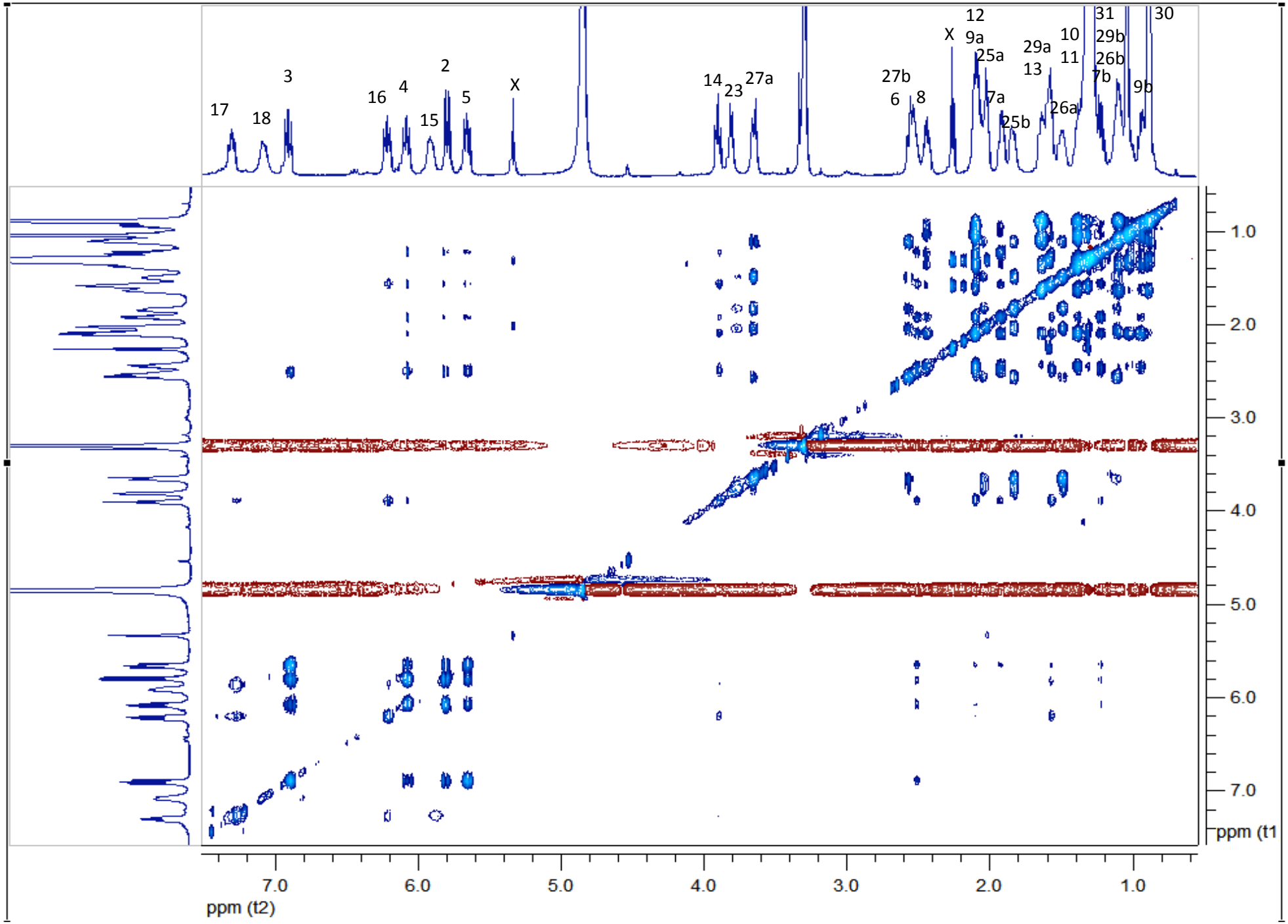
Supplement Figure 29. ^{1}H NMR (600 MHz, CD_3OD) spectrum of alteramide B (**4**)



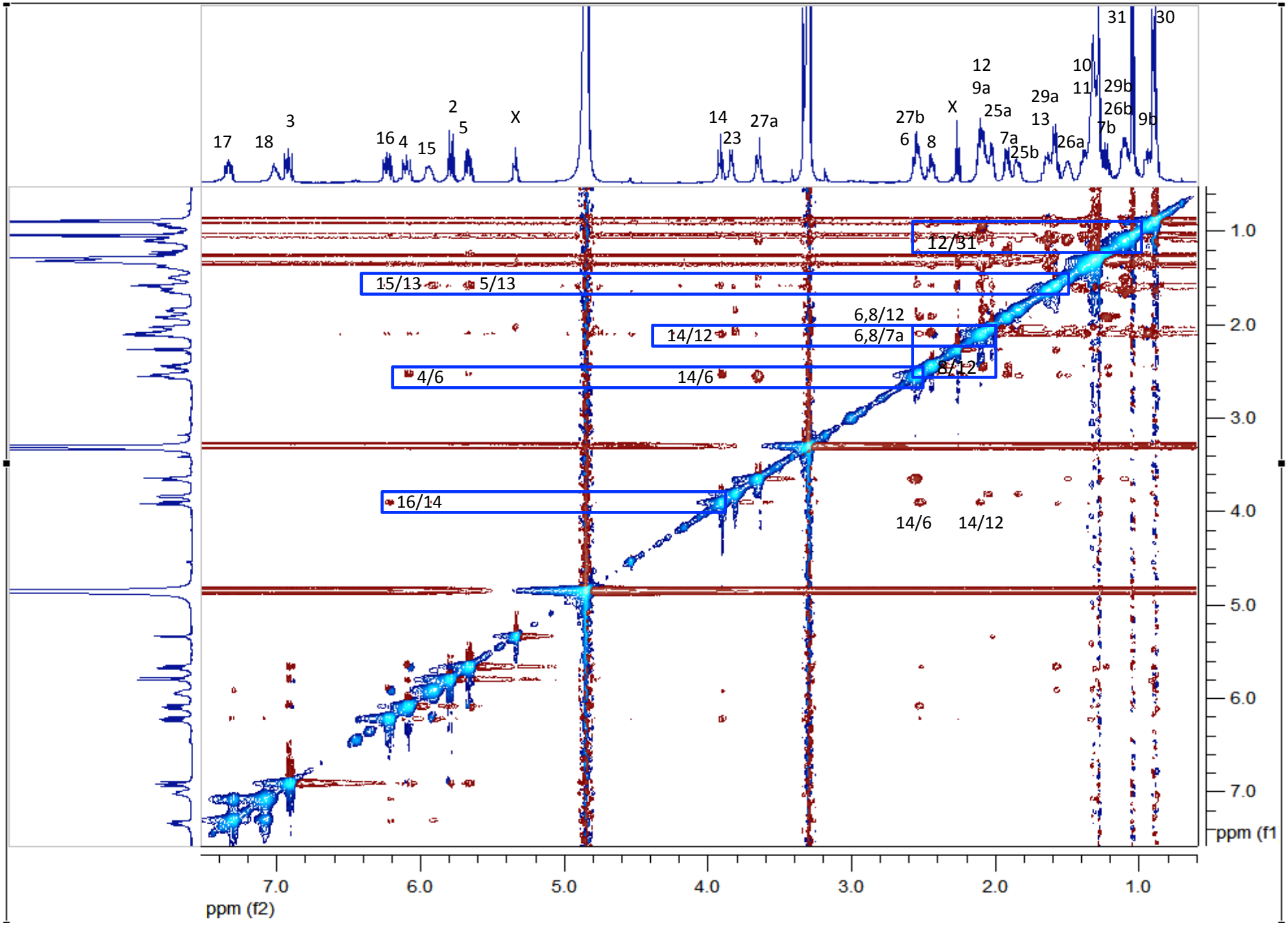
Supplement Figure 30. COSY (600 MHz, CD_3OD, DQF, phase sens.) alteramide B (**4**)



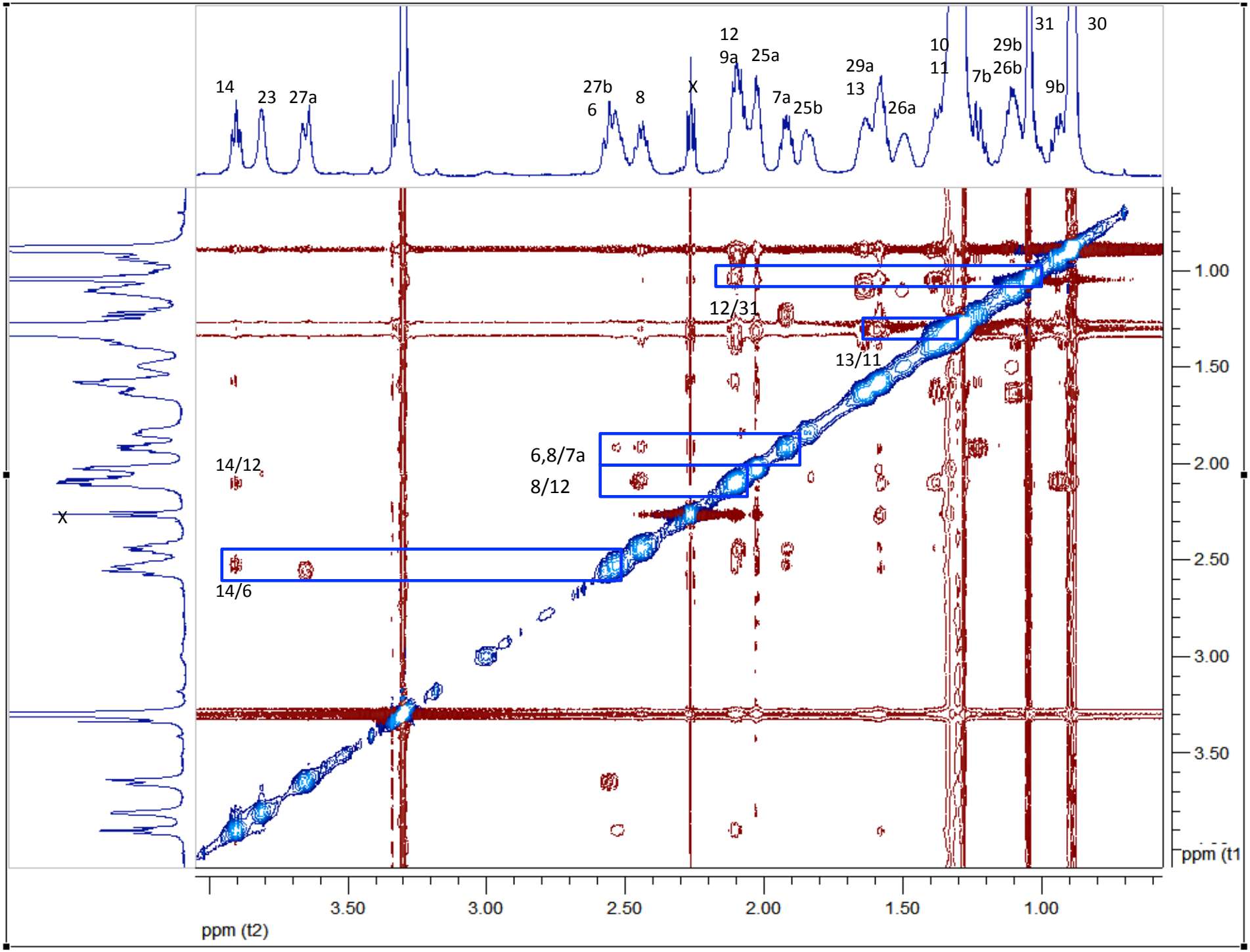
Supplement Figure 31. TOCSY (600 MHz, CD_3OD) of alteramide B (**4**)



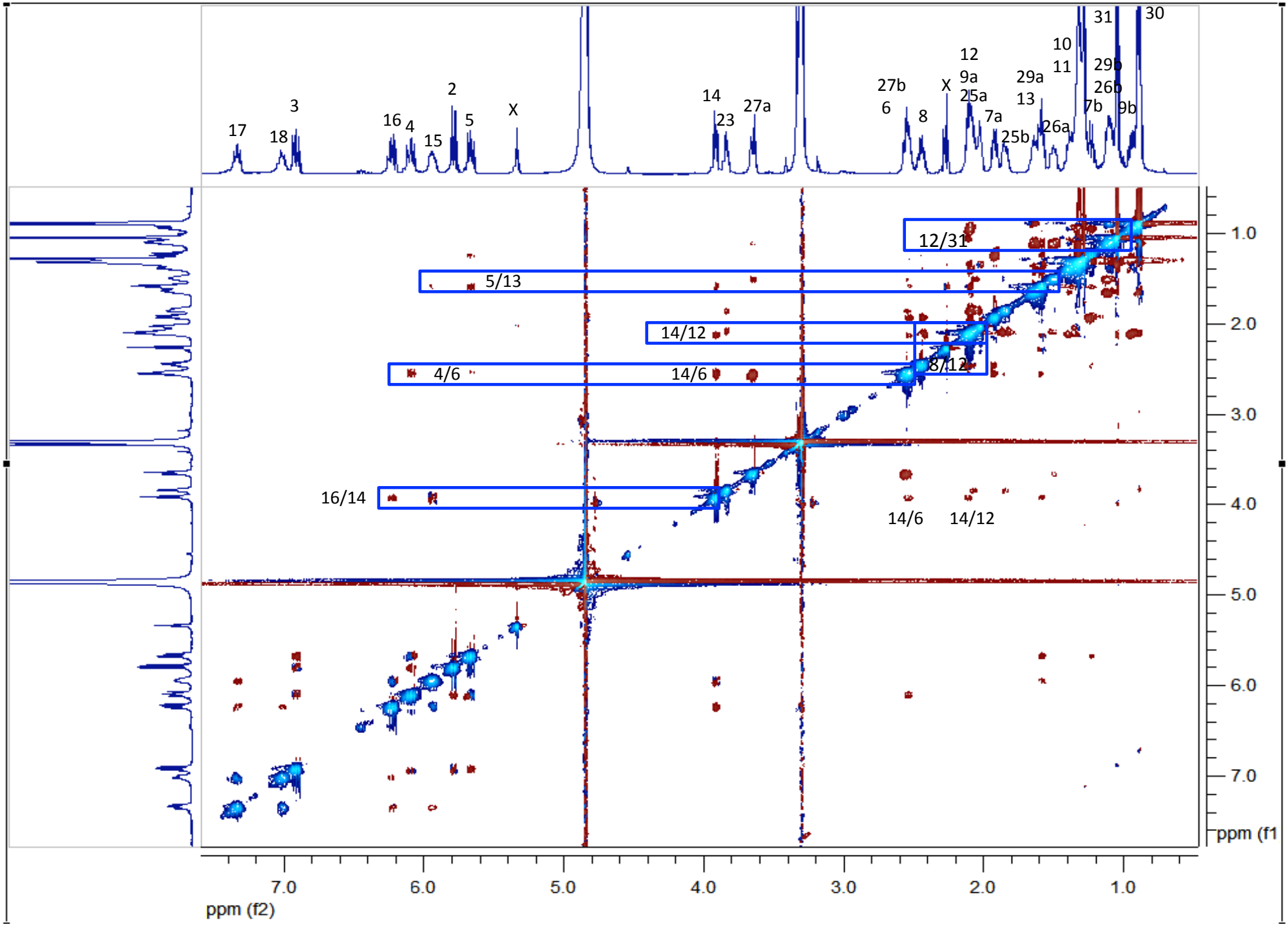
Supplement Figure 32a. NOESY(600 MHz, CD_3OD, 600 ms) of alteramide B (**4**)



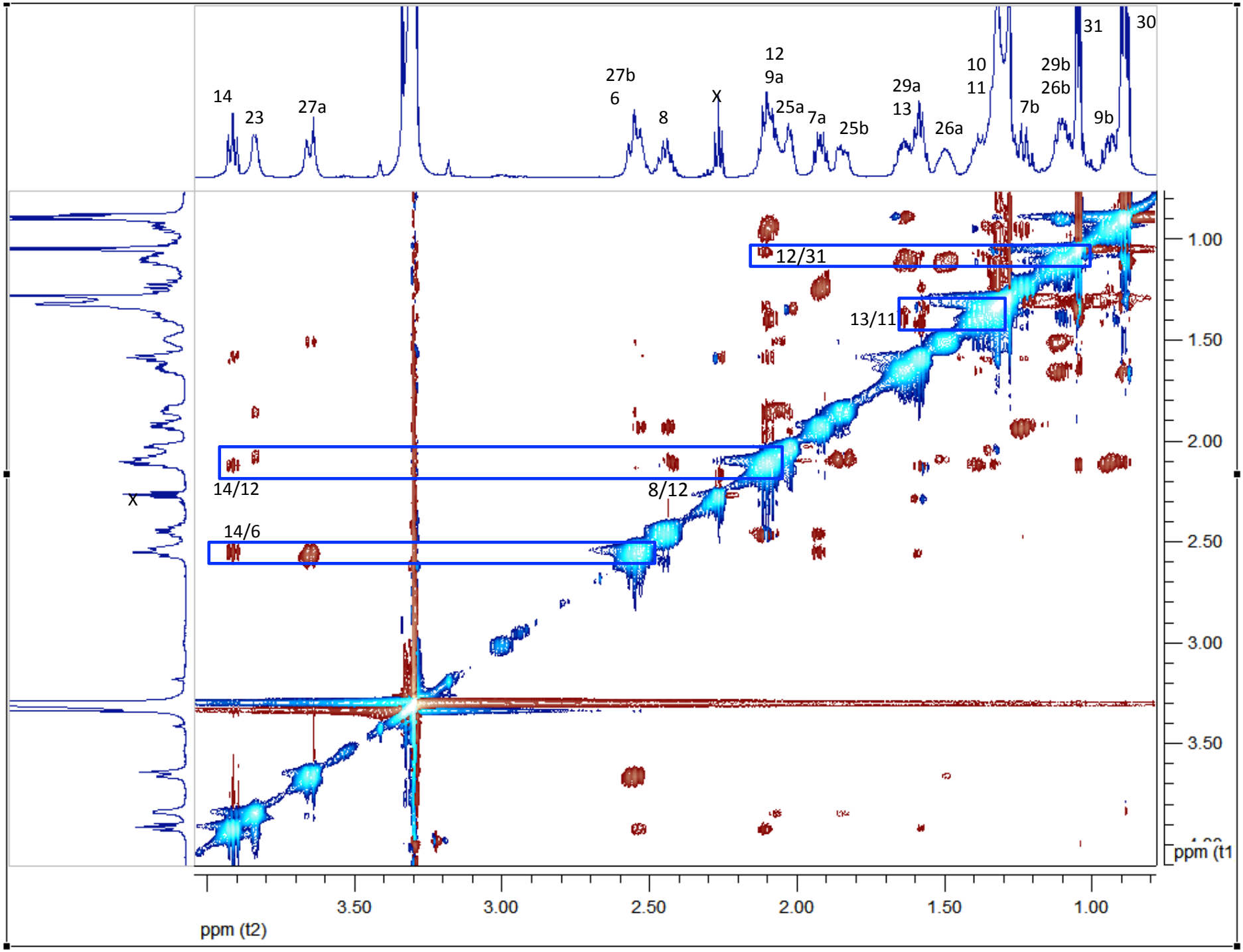
Supplement Figure 32b. NOESY zoom-in (600 MHz, CD_3OD) of alteramide B (**4**)



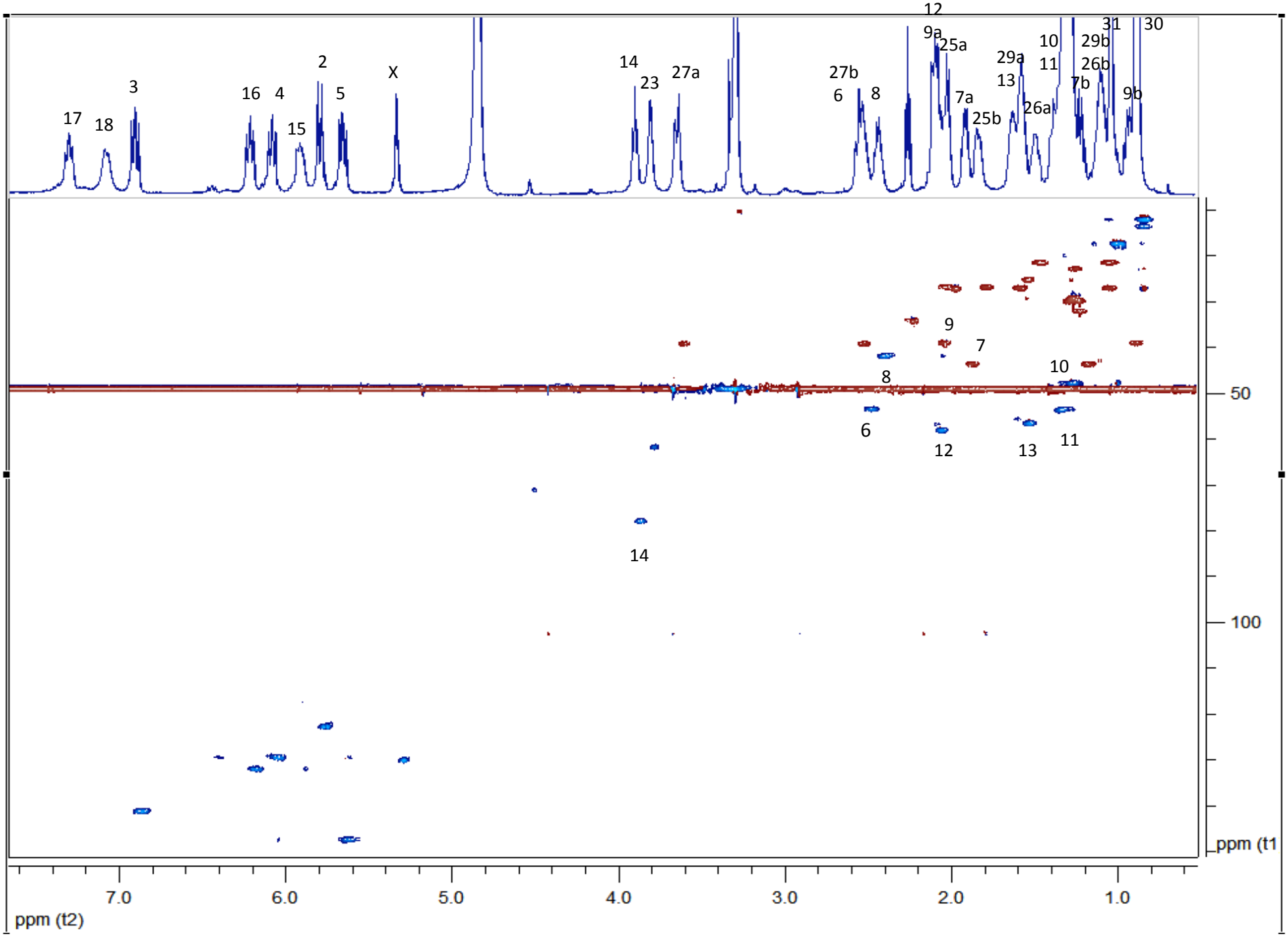
Supplement Figure 33a. ROESY (600 MHz, CD_3OD) of alteramide B (**4**)



Supplement Figure 33b. ROESY zoom-in (600 MHz, CD_3OD) of alteramide B (**4**)



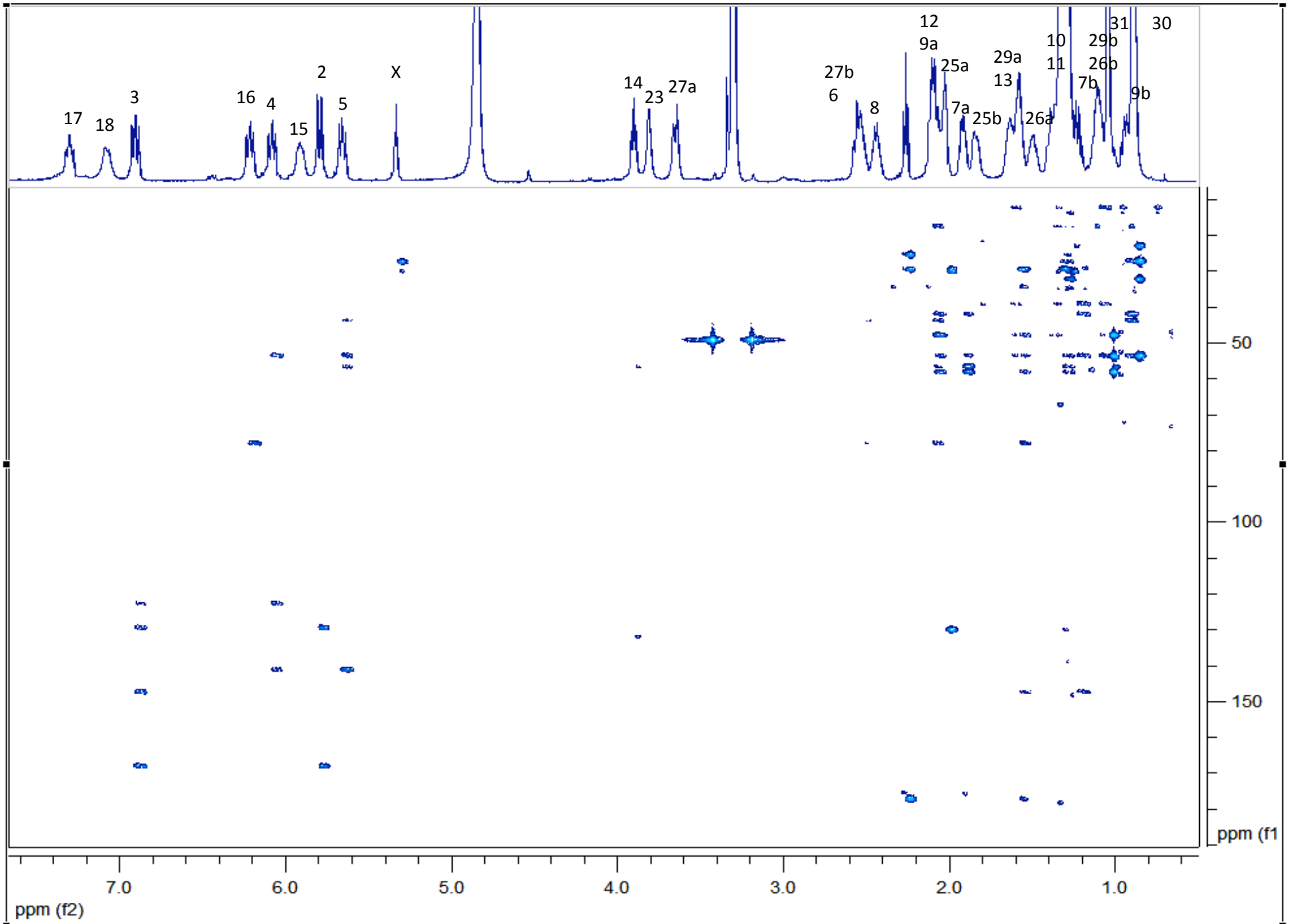
Supplement Figure 34. HSQC (600 MHz, CD_3OD) of alteramide B (**4**)



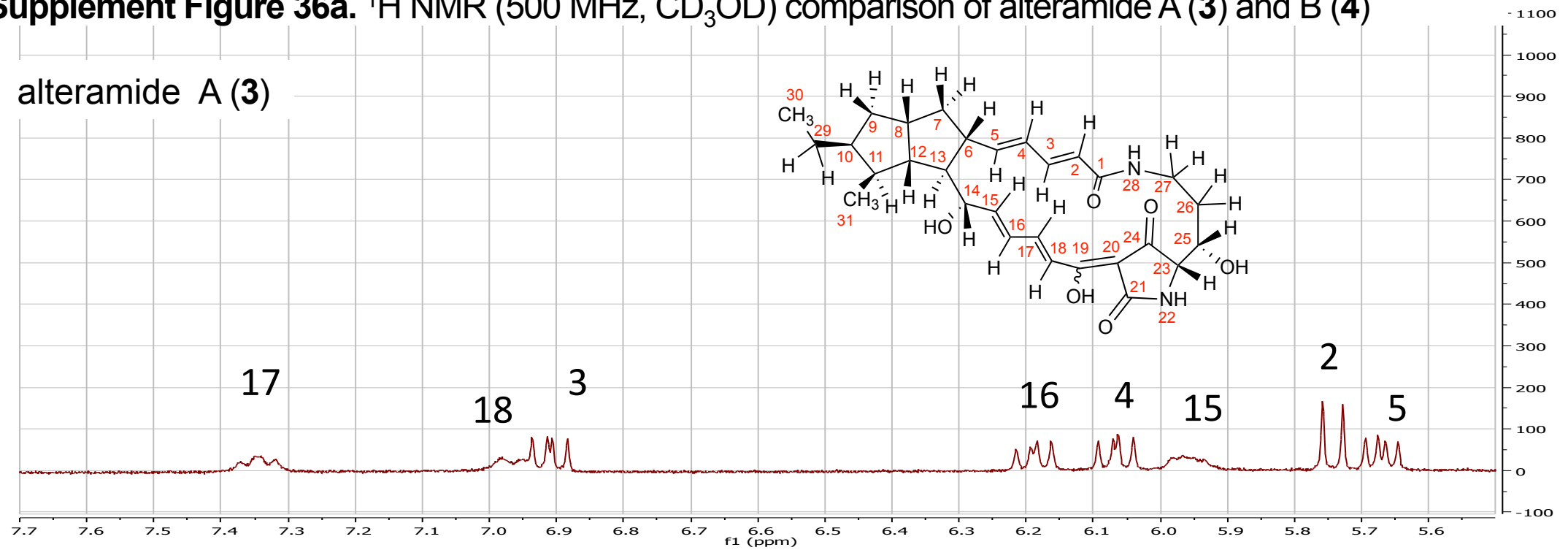
Supplement Table 6. HMBC (600 MHz, CD_3OD, 8 Hz) of alteramide B (**4**)

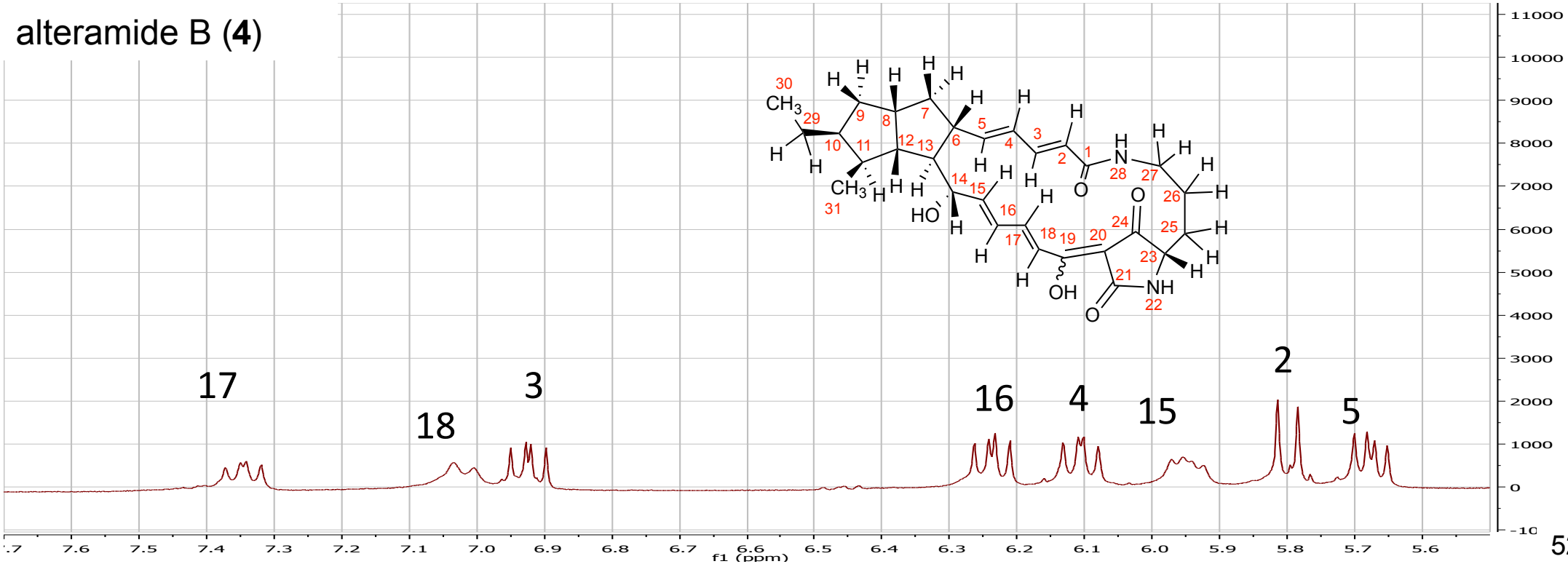
Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	168.0	-	-
2	122.5	5.74, d (16.0)	C-1 (168.0), C-4 (129.3)
3	141.0	6.85, dd (12.2, 16.0)	C-1 (168.0), C-2 (122.5), C-4 (129.3), C-5 (147.2)
4	129.3	6.04, dd (12.0, 15.8)	C-2 (122.5), C-3 (141.0), C-6 (53.3)
5	147.2	5.62, dd (10.0, 15.8)	C-3 (141.0), C-6 (53.3), C-7 (43.5), C-13 (56.5)
6	53.3	2.48, m	C-4 (129.2), C-5 (147,2), C-7 (43.5) (w), C-13 (56.5), C-14 (77.7)
7a	43.5	1.87, m	C-6 (53.3), C-8 (41.7), C-12 (57.9), C-13 (56.5)
7b		1.18, m	C-5 (147.2), C-6 (53.3) C-8 (41.7), C-9 (38.7)
8	41.7	2.40, m	C-7 (43.5), C-11 (47.7) (w), C-12 (57.9)
9a	38.7	2.04, m	C-8 (41.7), C-10 (53.5), C-11 (47.7), C-12 (57.9)
9b		0.89 m	C-7 (43.5), C-8 (41.8), C-10 (53.5), C-29 (27.0)
10	53.5	1.33, m	C-9 (38.7), C-11 (47.7), C-29 (27.0) (weak), C-30 (11.9), C-31 (17.2)
11	47.7	1.27, m	C-10 (53.5), C-12 (57.9), C-13 (56.5), C-29 (27.0), C-31 (17.2)
12	57.9	2.06, m	C-7 (43.5), C-8 (41.7), C-11 (47.7), C-13 (56.5), C-14 (77.7), C-31 (17.2)
13	56.5	1.53, m	C-5 (147.2), C-6 (53.3), C-11 (47.7), C-12 (57.9), C-14 (77.7)
14	77.7	3.86, m	C-6 (53.3), C-13 (56.5), C-16 (131.9)
15	146.9	5.86, m	C-17 (143.7) (weak)
16	131.9	6.17, dd (12.0, 16.6)	C-14 (77.7), C-17 (143.7)
17	143.7	7.27, dd (12.0, 16.6)	C-15 (146.9) (weak), C-16 (131.9) (weak)
18	nd	7.02, bd (16.6)	
19	nd	-	-
20	nd	-	-
21	nd	-	-
22	-	-	
23	61.6	3.77, brs	C-24 (197.0) (very weak)
24	197.0	-	-
25a	26.7	2.03, m	
25b		1.79, m	C-26 (21.4), C-27 (39.1)
26a	21.4	1.46, m	
26b		1.06, m	
27a	39.1	3.59, m	
27b		2.52, m	C-1 (168.0)
28	-	-	-
29a	27.0	1.58, m	C-9 (38.7), C-10 (53.5), C-11 (47.7), C-30 (11.9)
29b		1.05, m	C-9 (38.7), C-10 (53.5), C-11 (47.7) (weak), C-30 (11.9)
30	11.9	0.84, t (7.0)	C-10 (53.5), C-29 (27.0)
31	17.2	0.99, d (7.0)	C-10 (53.5), C-11 (47.7), C-12 (57.9)
nd = not detected			

Supplement Figure 35. HMBC (600 MHz, CD_3OD, 8 Hz) of alteramide B (**4**)

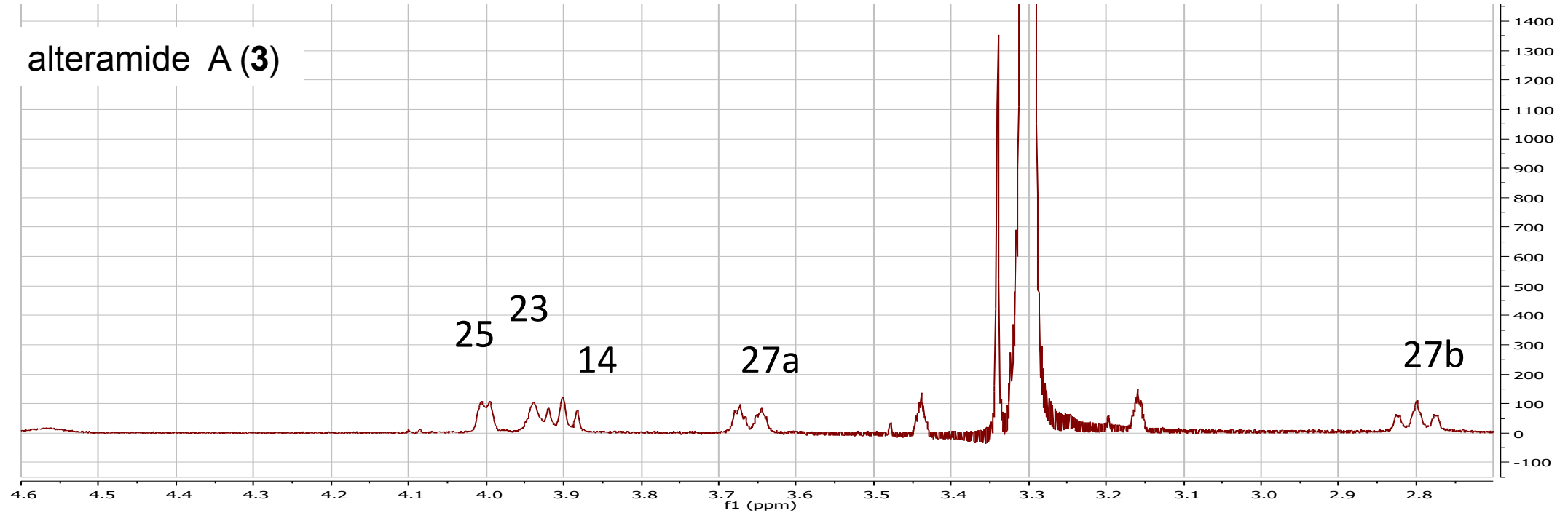


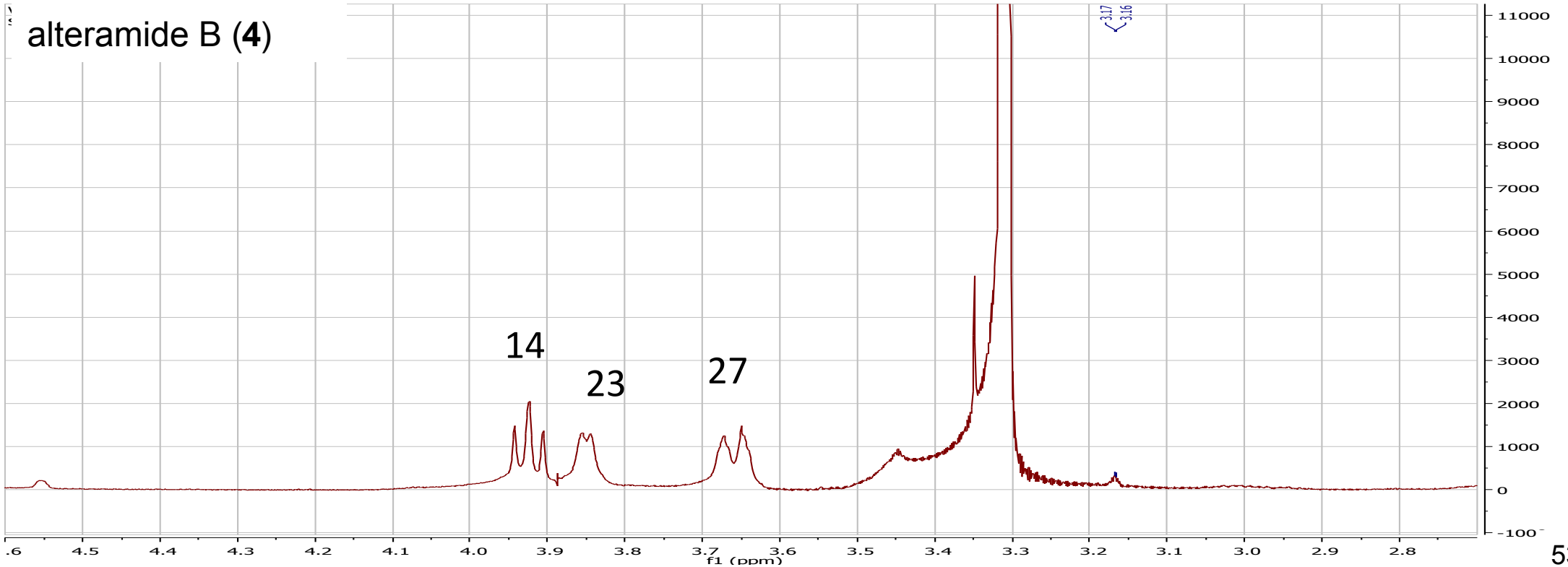
Supplement Figure 36a. ^{1}H NMR (500 MHz, CD_3OD) comparison of alteramide A (**3**) and B (**4**)



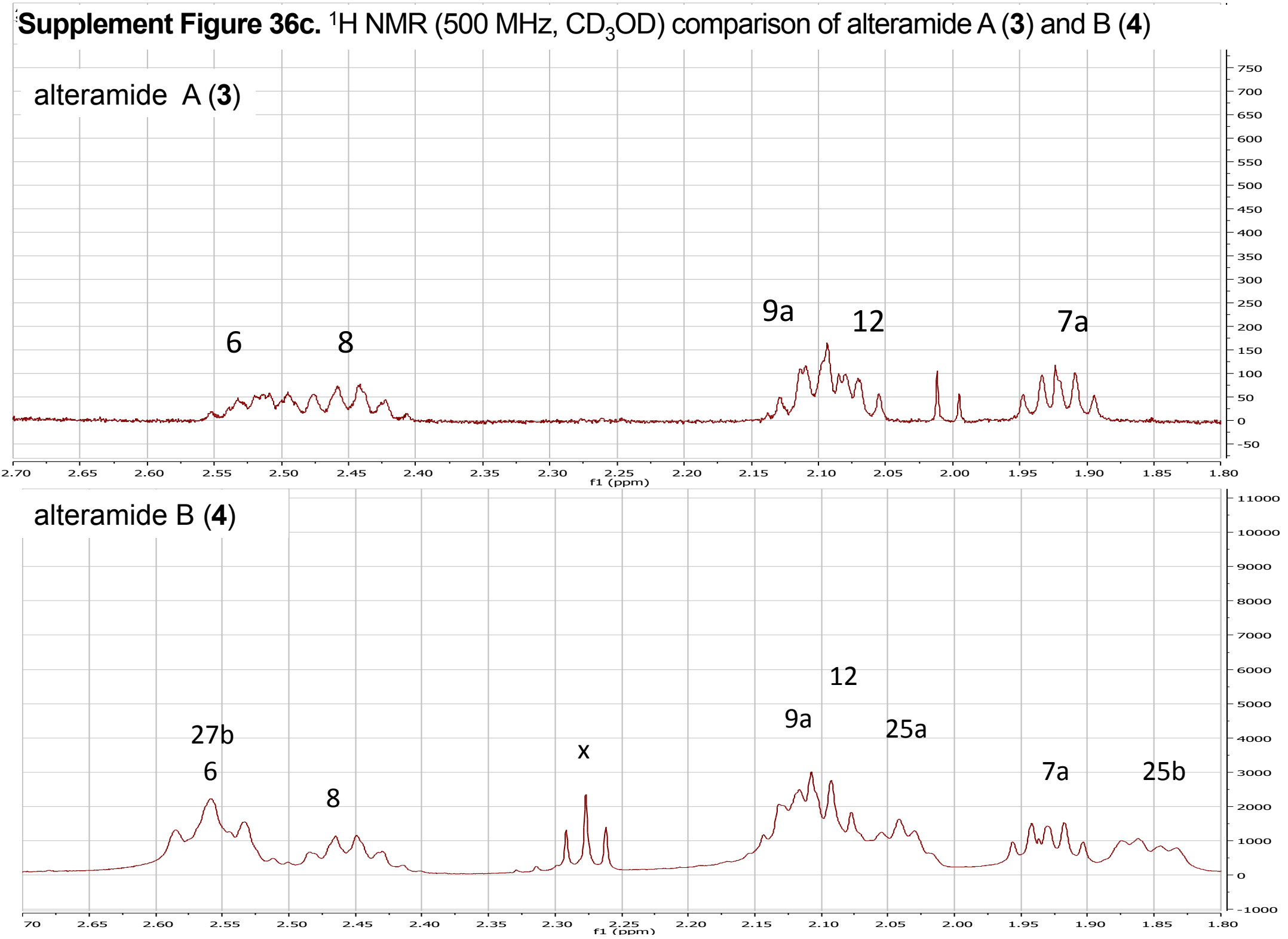


Supplement Figure 36b. ^{1}H NMR (500 MHz, CD_3OD) comparison of alteramide A (**3**) and B (**4**)

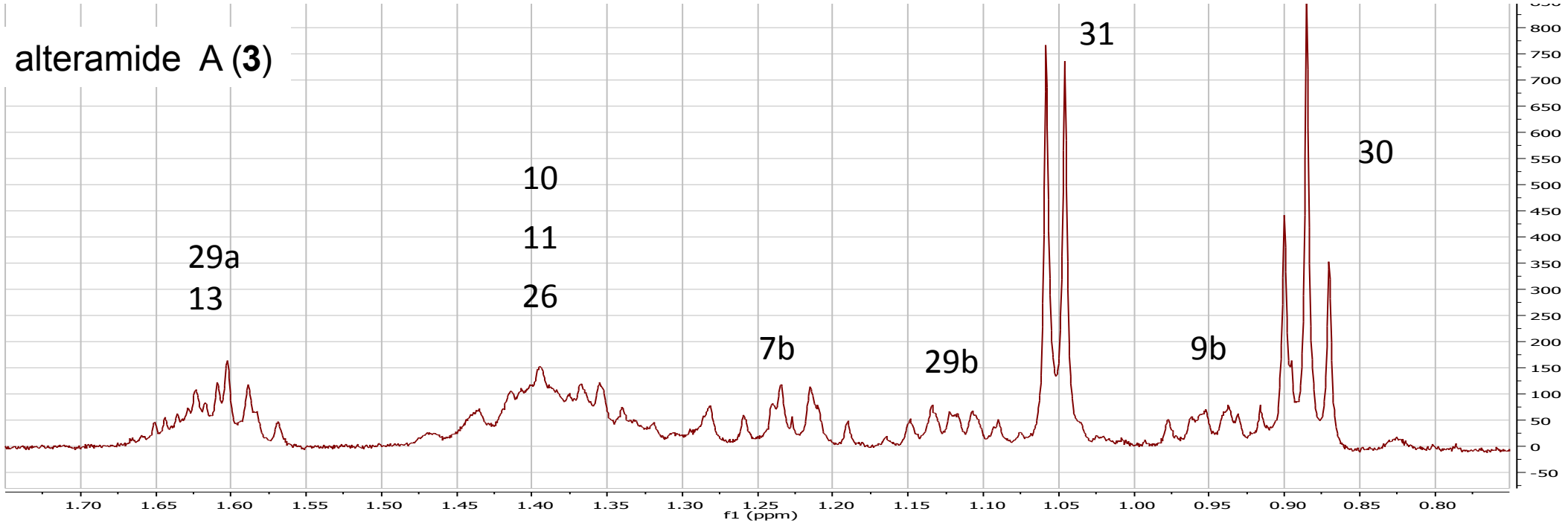


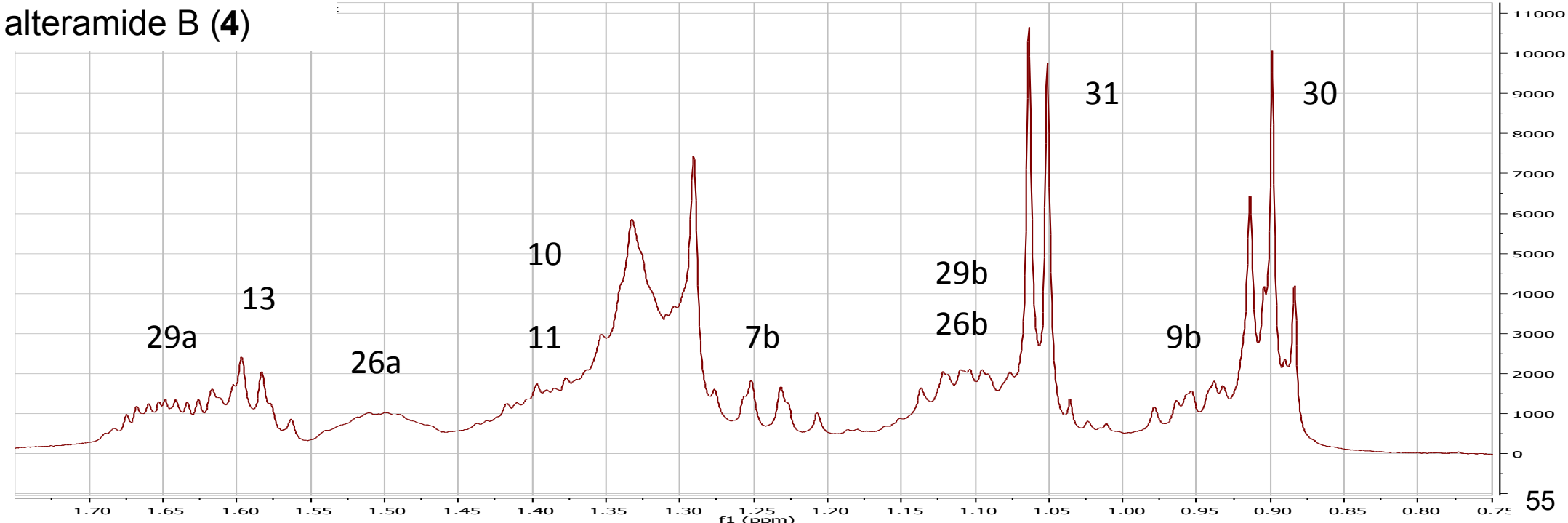


Supplement Figure 36c. ^{1}H NMR (500 MHz, CD_3OD) comparison of alteramide A (**3**) and B (**4**)



Supplement Figure 36d. ^{1}H NMR (500 MHz, CD_3OD) comparison of alteramide A (**3**) and B (**4**)





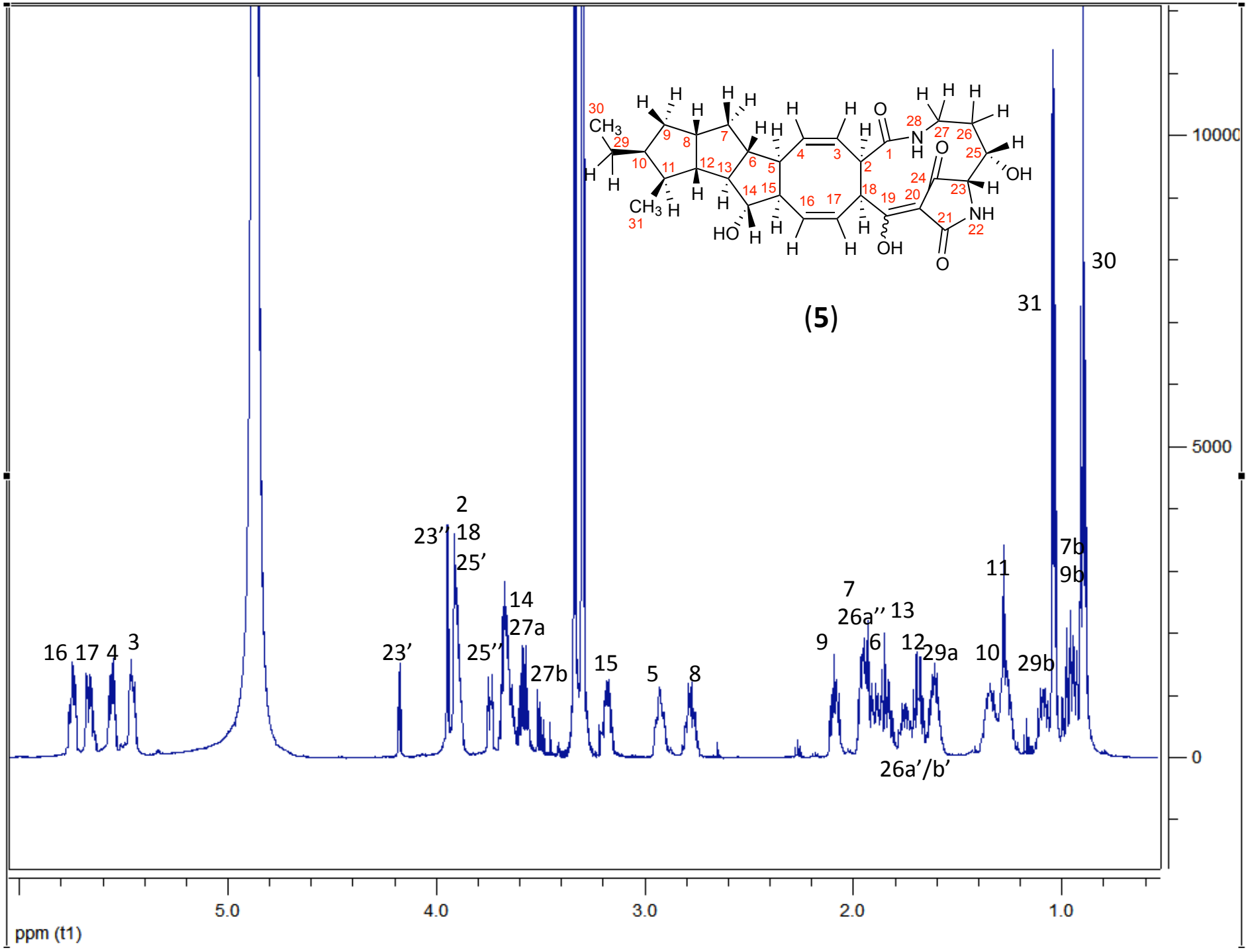
Supplemental Table 7. ^{1}H and ^{13}C NMR data of photocyclized alteramide A (**5**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	180.5	-	-
2	46.5	3.89, m	C-1 (180.5), C-3 (125.7), C-4 (138.2), C-18 (46.3)
3	125.7	5.45, m	C-1 (180.5), C-2 (46.6)
4	138.2	5.56, m	C-5 (46.2), C-6 (58.1), C-15 (59.4)
5	46.2	2.93, m	C-3 (125.7), C-6 (58.1), C-7 (36.3), C-15 (59.4), C-16 (138.1)
6	58.1	1.88, m	C-4 (138.2), C-5 (46.2), C-7 (36.2), C-12 (54.0) (weak), C-13 (65.2), C-14 (81.9)
7a	36.3	1.95, m	C-6 (58.1), C-8 (50.3), C-12 (54.0), C-13 (65.2)
7b	-	0.94, m	C-5 (46.1), C-6 (58.0), C-8 (50.2), C-9 (41.3)
8	50.3	2.78, m	C-7 (36.3), C-9 (41.3), C-12 (54.0), C-13 (65.2)
9a	41.3	2.09, m	C-8 (50.3), C-11 (47.6), C-12 (54.0)
9b	-	0.97, m	C-7 (36.2), C-8 (50.2), C-10 (54.6), C-11 (47.6) (weak), C-29 (27.0)
10	54.7	1.35, m	C-9 (41.3), C-11 (47.6), C-29 (26.9) (weak), C-30 (12.7), C-31 (18.1)
11	47.6	1.26, m	C-10 (54.7), C-12 (54.0), C-13 (65.2), C-29 (26.9), C-31 (18.1)
12	54.0	1.69, m	C-8 (50.3), C-9 (41.3), C-10 (54.7), C-11 (47.6), C-13 (65.2), C-14 (81.9), C-31 (18.1)
13	65.2	1.84, m	C-5 (46.1) (weak), C-6 (58.1), C-7 (36.3), C-11 (47.6), C-12 (54.0), C-14 (81.9), C-15 (59.4)
14	81.9	3.67, m	C-12 (54.0), C-13 (65.2), C-15 (59.4), C-16 (138.0)
15	59.4	3.18, m	C-5 (46.2), C-6 (58.1), C-14 (81.9), C-16 (138.0), C-17 (125.9)
16	138.0	5.75, m	C-15 (59.4), C-14 (81.9), C-18 (46.3), C-19 (180.3)
17	125.9	5.67, m	C-15 (59.4) (weak), C-18 (46.3), C-19 (180.3)
18	46.3	3.91, m	C-2(46.5), C-16 (138.0), C-17 (125.9), C-19 (180.3)
19	180.3	-	-
20	nd	-	-
21' (Z)	176.3 & 178.7	-	-
21'' (E)	174.5		-
22	-	-	-
23' (Z)	64.5	4.18, d (3.4)	C-21' (176.3 & 178.7), C-25' (69.7), C-26' (Z) (28.9)
23'' (E)	69.6	3.95, d (2.7)	C-21'' (174.5), C-25''(E) (71.0), C-26''(E) (31.1), C-24 (207.3)
24 (E / Z)	207.3	-	
25' (Z)	69.7	3.89, m	
25''(E)	71.0	3.74, dt (7.2, 2.7)	C-23'' (E) (69.6), C-24 (207.3), C-26'' (E) (31.1), C-27 (37.0) (weak)
26a' (Z)	28.9	1.72, m	C-25' (Z) (69.7)
26b' (Z)	-	1.60, m	C-27 (37.0)
26a'' (E)	31.1	1.94, m	C-25'' (E) (71.0), C-27 (37.0)
26b'' (E)	-	1.75, m	C-23'' (E) (69.6), C-25'' (E) (71.0), C-27 (37.0)
27a	37.0	3.66, m	C-1 (180.5), C-25'' (E) (71.0),), C-26'' (31.1)
27b		3.58, m	C-1 (180.5), C-25'' (E) (71.0), C-26'' (31.1)
28	-	-	-
29a	27.0	1.62, m	C-9 (41.3), C-10 (54.6), C-11 (47.6), C-30 (12.7)
29b		1.09, m	C-9 (41.3), C-10 (54.7), C-11 (47.6), C-30 (12.7)
30	12.7	0.90, t (7.4)	C-10 (54.7), C-29 (27.0)
31	18.1	1.04, d (6.4)	C-10 (54.6), C-11 (47.6), C-12 (54.0)

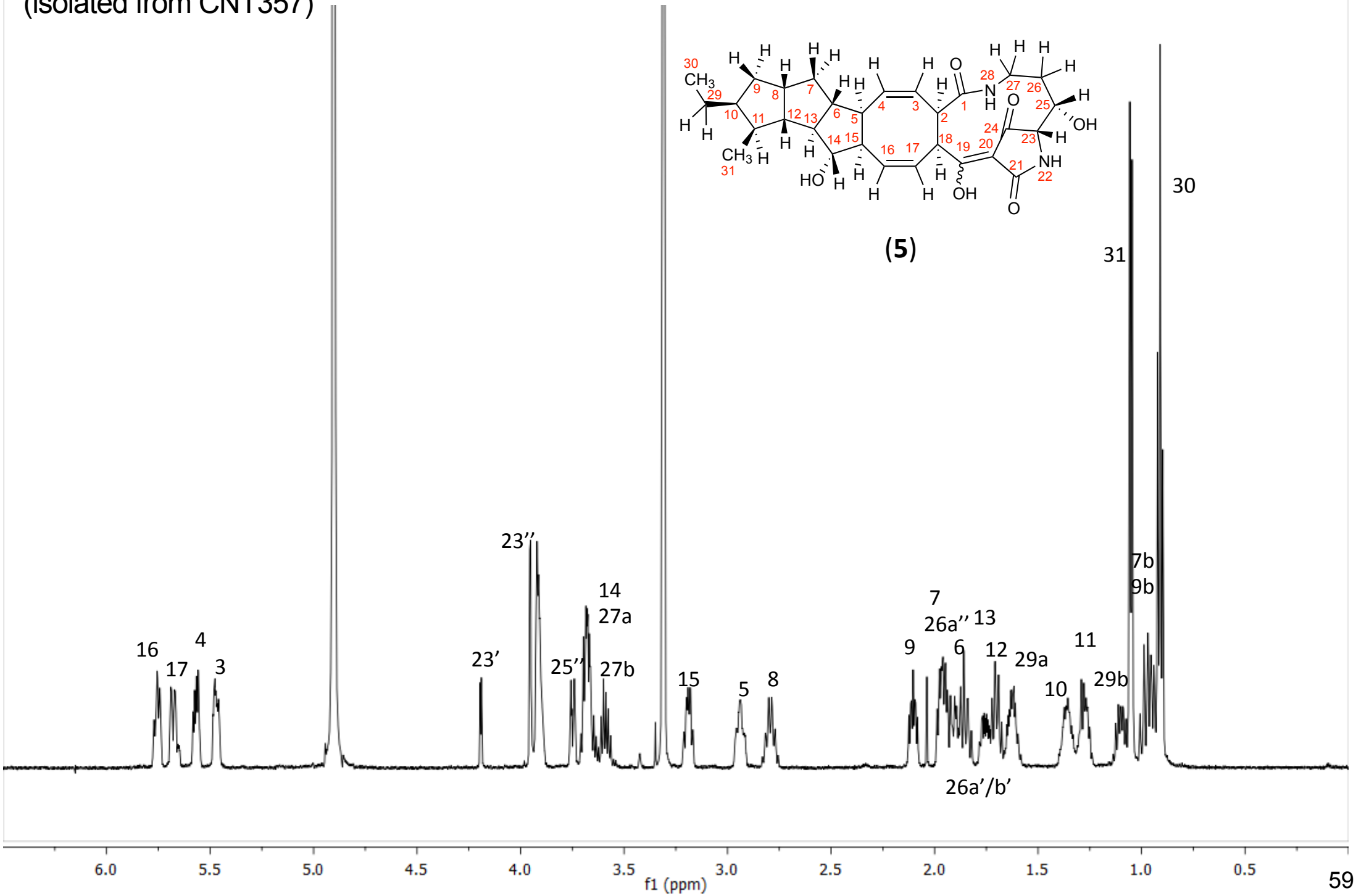
Supplemental Table 8. ^{1}H and ^{13}C NMR Data and NOEs - photocyclized alteramide A (**5**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H - ^{1}H NOE (NOESY)
1	180.3	-	-
2	46.5	3.93, m	H-5
3	125.6	5.45, m	
4	138.2	5.56, m	H-6
5	46.1	2.93, m	H-2, H-7b, H-13, H-15
6	58.0	1.88, m	H-4, H-8 (weak), H-12 (weak), H-14
7a	36.2	1.96, m	
7b	-	0.94, m	H-5, H-13
8	50.2	2.78, m	H-6 (weak), H-12
9a	41.3	2.09, m	
9b	-	0.97, m	
10	54.6	1.35, m	H-30, H-31
11	47.6	1.26, m	H-13, H-30 (weak)
12	54.0	1.69, m	H-6 (weak), H-8, H-14, H-31
13	65.2	1.84, m	H-5, H-7b, H-11, H-15
14	81.9	3.67, t (8.0)	H-6, H-12, H-16
15	59.4	3.19, m	H-5, H-13, H-18
16	138.1	5.75, t (8.0)	H-14
17	125.86	5.65, m	
18	46.5	3.93, m	H-15
19	180.1	-	
20	-	-	
21’ (Z)	179.0	-	
21’’ (E)	173.6		
22	-	-	
23’ (Z)	64.5	4.18, d (3.4)	H-26a/b’ (Z)
23’’ (E)	69.6	3.95, d (2.7)	H-26a/b’’ (E)
24 (E / Z)	207.3	-	
25’ (Z)	69.7	3.89, m	
25’’(E)	71.0	3.74, dt (7.2, 2.7)	
26a’ (Z)	28.9	1.72, m	H-23’ (Z)
26b’ (Z)	-	1.60, m	H-23’ (Z)
26a’’ (E)	31.1	1.94, m	H-23’’ (E)
26b’’ (E)	-	1.75, m	H-23’’ (E)
27a	37.0	3.66, m	H-23’’ (E)
27b		3.58, m	
28	-	-	
29a	27.0	1.62, m	H-31
29b		1.09, m	
30	12.7	0.90, t (7.4)	H-10, H-11 (weak)
31	18.1	1.04, d (6.4)	H-10, H-12, H-29a

Supplemental Figure 37. ^{1}H NMR (600 MHz, CD_3OD) spectra of photocyclized alteramide A (**5**)

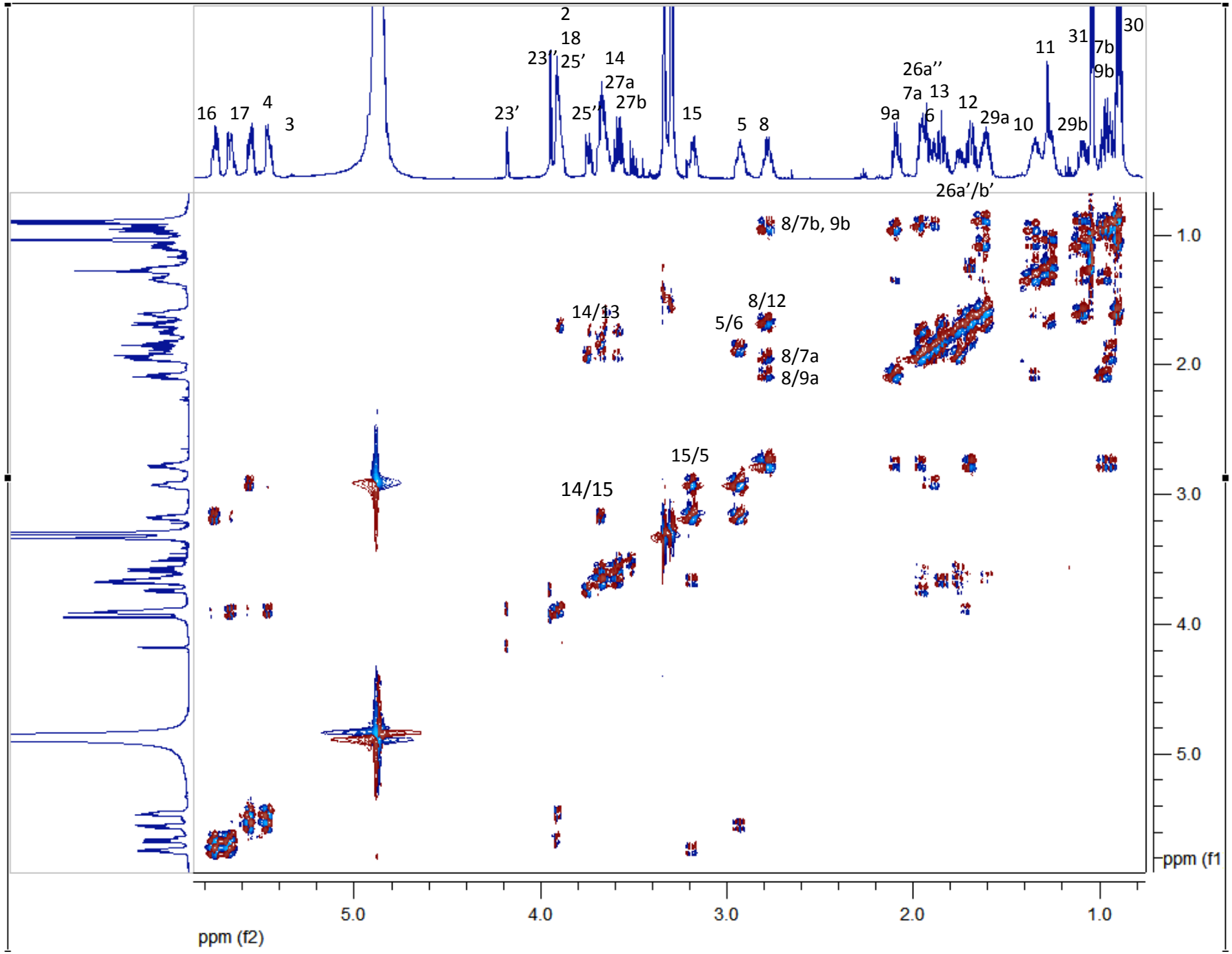


Supplemental Figure 38. ^{1}H NMR (600 MHz, CD_3OD) spectra of photocyclized alteramide A (**5**) (isolated from CNT357)

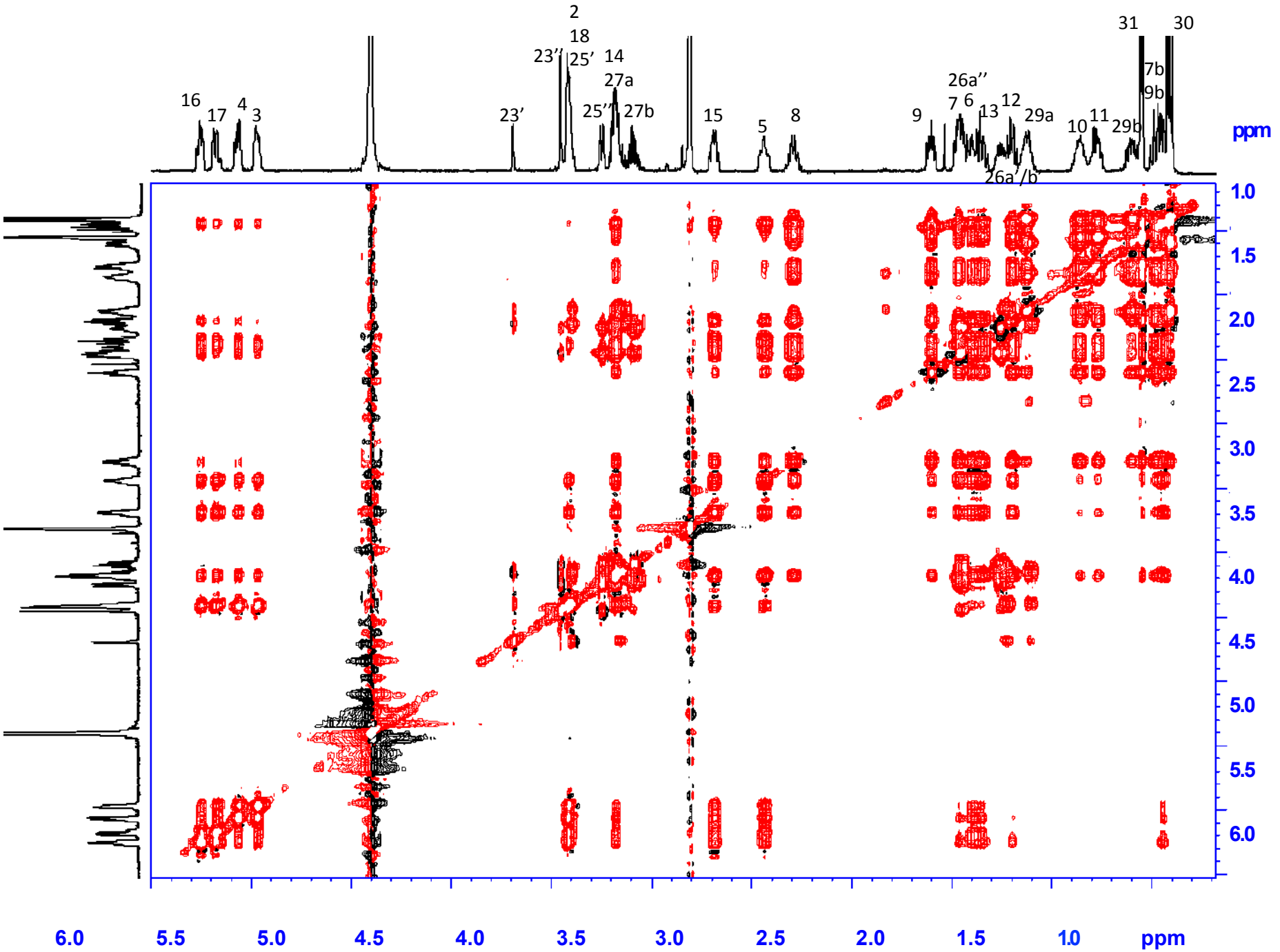


(5)

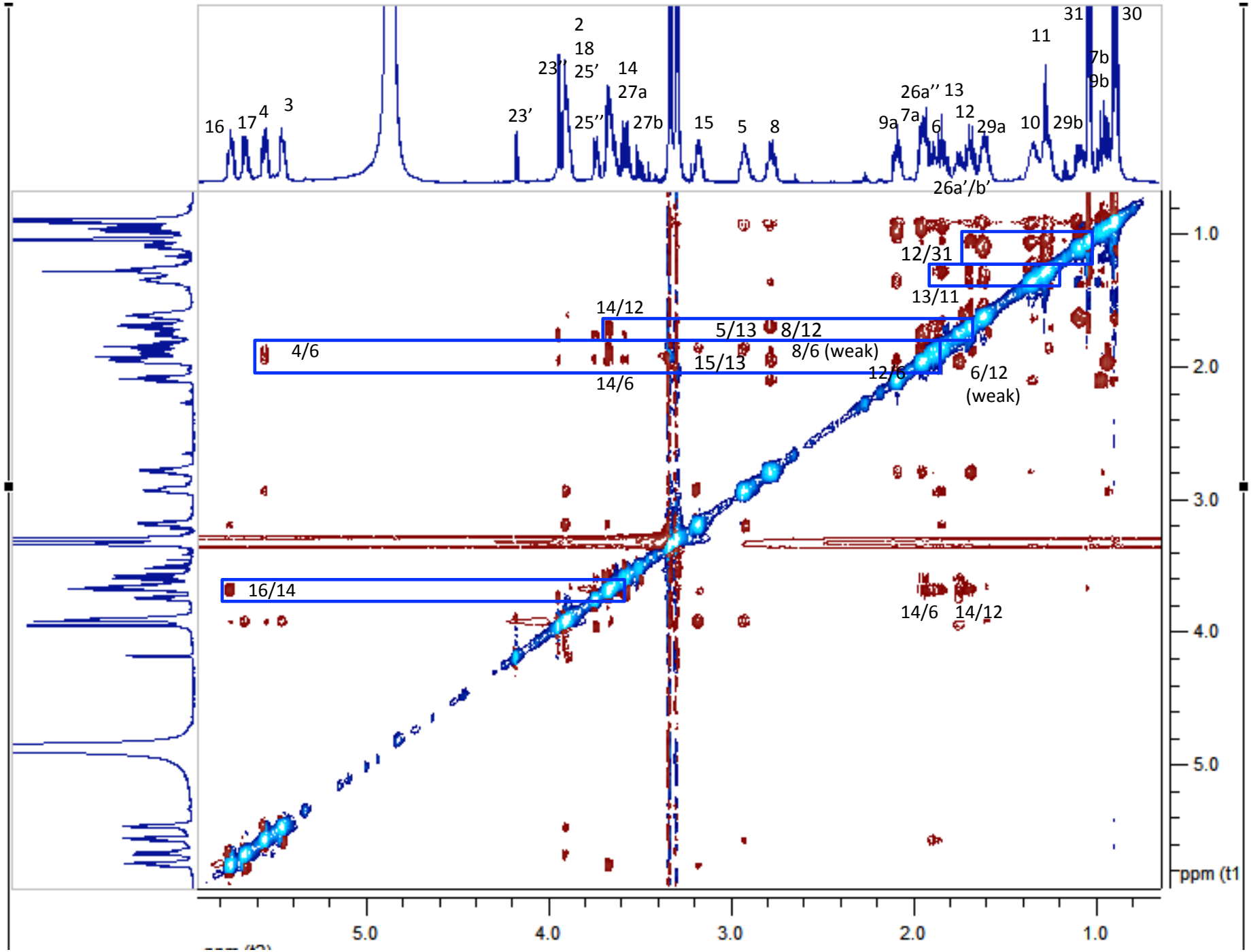
Supplemental Figure 39. COSY (600 MHz, CD_3OD, 600 ms) of photocyclized alteramide A (**5**)



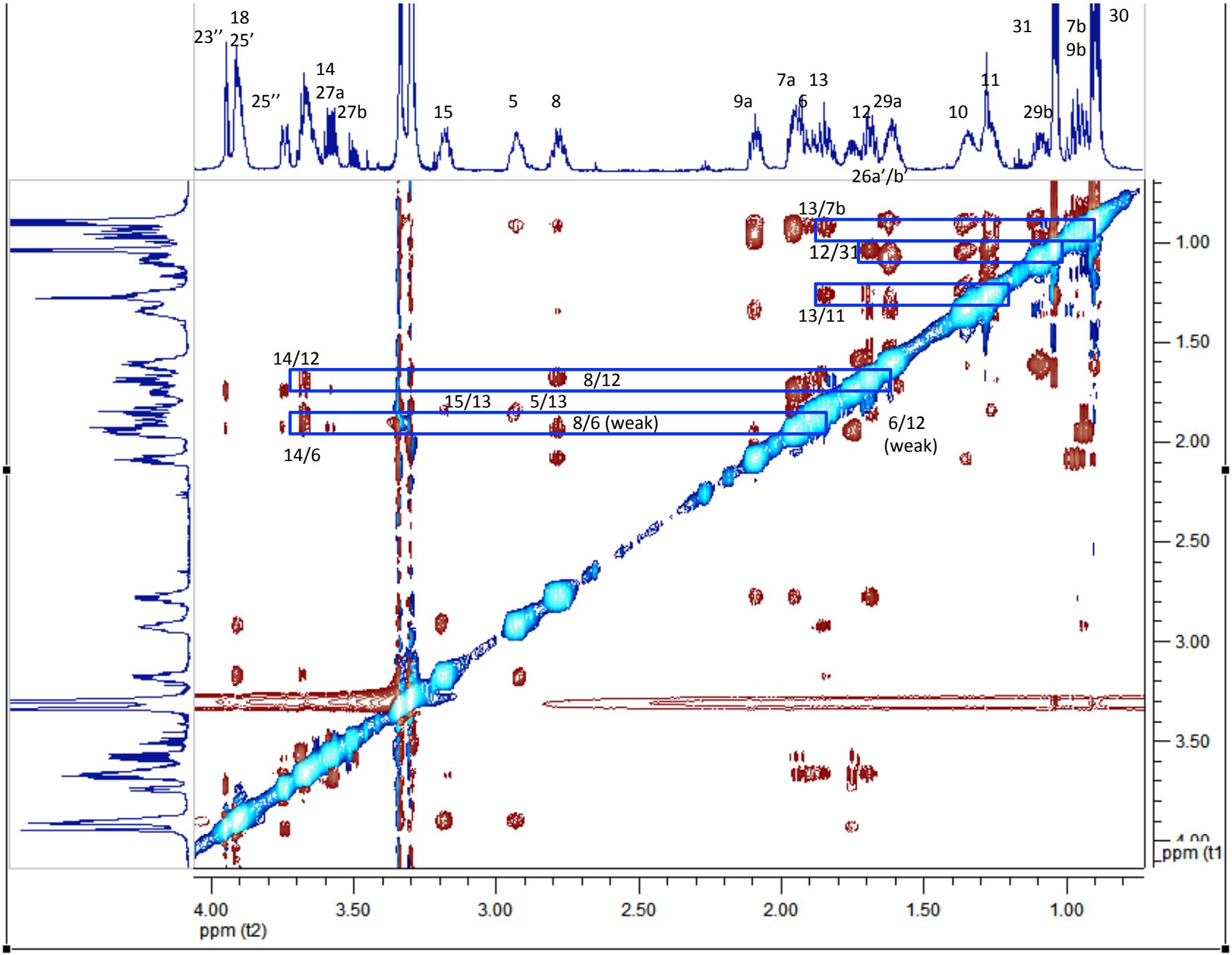
Supplemental Figure 40. TOCSY (600 MHz, CD_3OD, 75 ms) spectrum of photocyclized alteramide A (**5**)



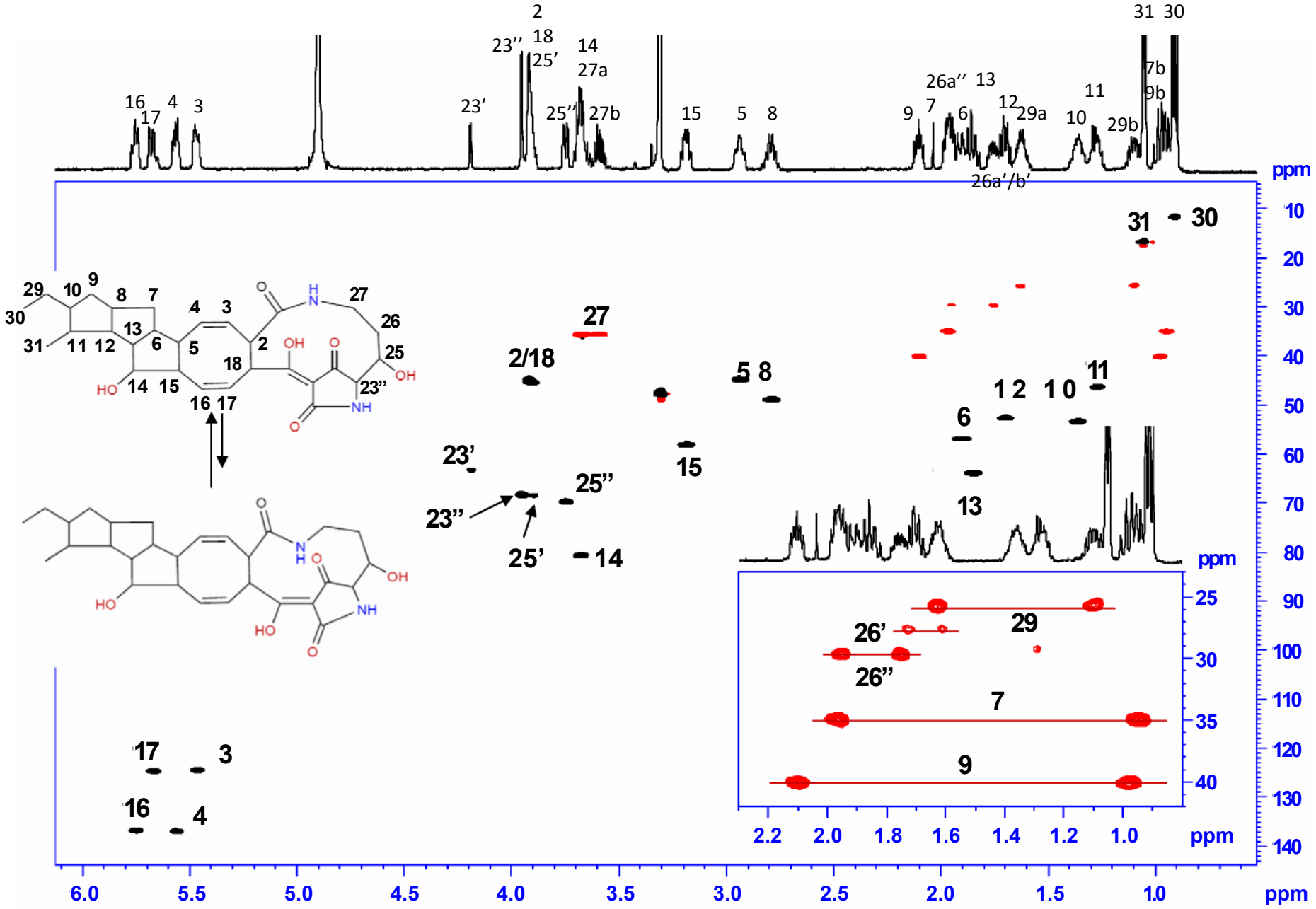
Supplemental Figure 41a. NOESY(600 MHz, CD_3OD, 600 ms) of photocyclized alteramide A (**5**)



Supplemental Figure 41b. NOESY zoom-in(600 MHz, CD_3OD, 600 ms, gradient) of photocyclized alteramide A (**5**)



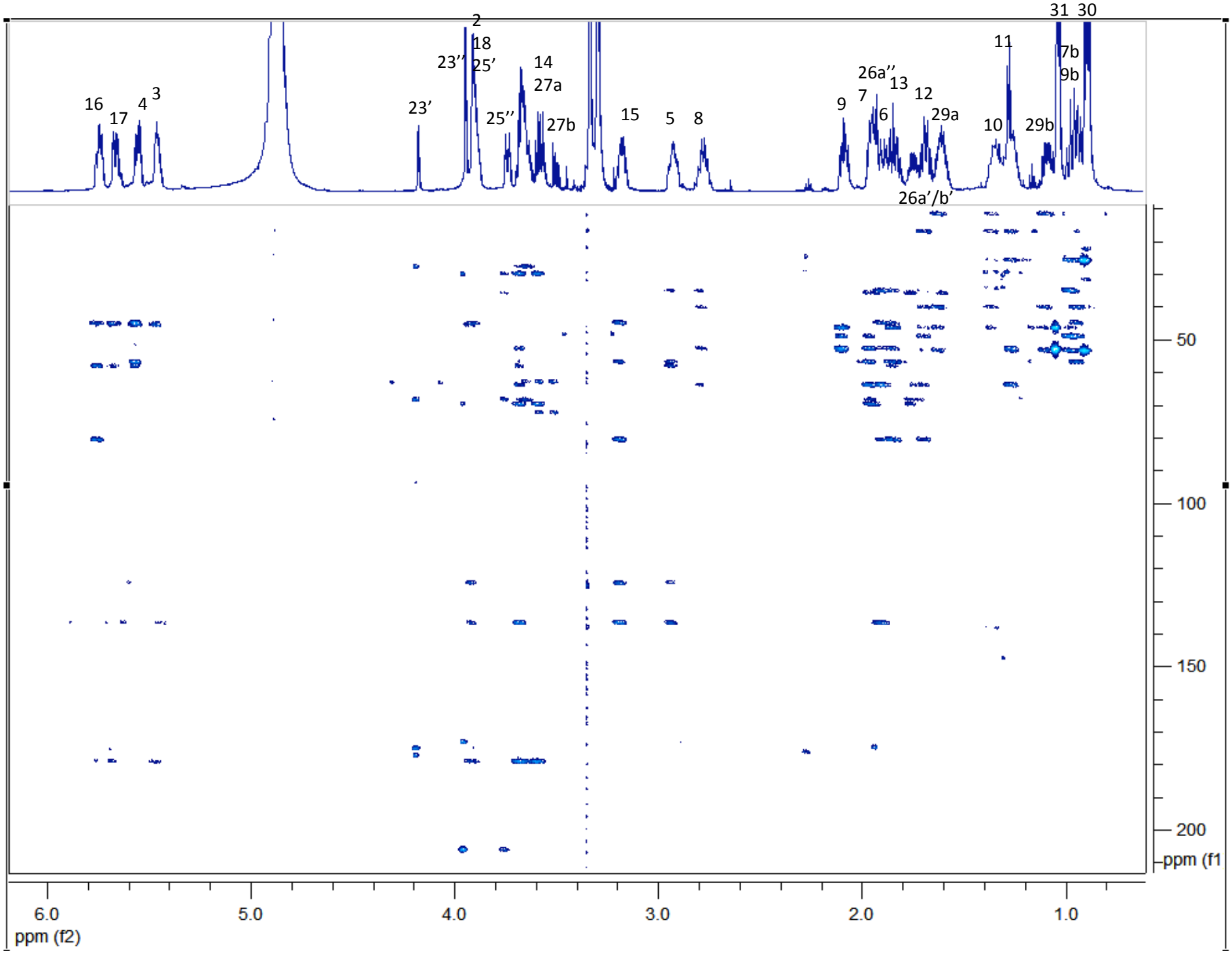
Supplement Figure 42. HSQC (600 MHz, CD_3OD) spectrum and annotation of photocyclized alteramide A (**5**)



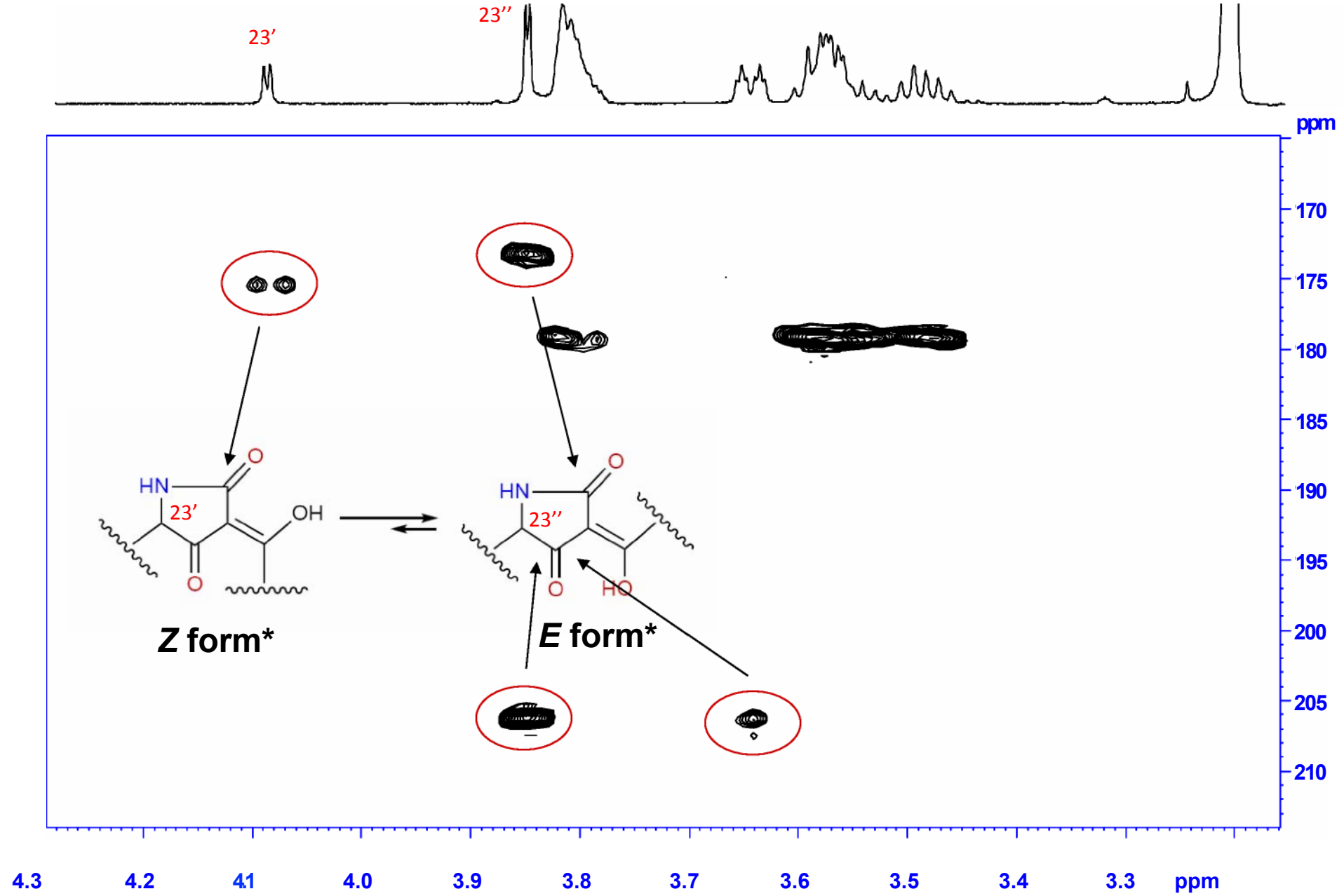
Supplement Table 9. HMBC (600 MHz, CD_3OD) spectrum of photocyclized alteramide A (**5**)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	180.5	-	-
2	46.5	3.89, m	C-1 (180.5), C-3 (125.7), C-4 (138.2), C-18 (46.3)
3	125.7	5.45, m	C-1 (180.5), C-2 (46.6)
4	138.2	5.56, m	C-5 (46.2), C-6 (58.1), C-15 (59.4)
5	46.2	2.93, m	C-3 (125.7), C-6 (58.1), C-7 (36.3), C-15 (59.4), C-16 (138.1)
6	58.1	1.88, m	C-4 (138.2), C-5 (46.2), C-7 (36.2), C-12 (54.0) (weak), C-13 (65.2), C-14 (81.9)
7a	36.3	1.95, m	C-6 (58.1), C-8 (50.3), C-12 (54.0), C-13 (65.2)
7b	-	0.94, m	C-5 (46.1), C-6 (58.0), C-8 (50.2), C-9 (41.3)
8	50.3	2.78, m	C-7 (36.3), C-9 (41.3), C-12 (54.0), C-13 (65.2)
9a	41.3	2.09, m	C-8 (50.3), C-11 (47.6), C-12 (54.0)
9b	-	0.97, m	C-7 (36.2), C-8 (50.2), C-10 (54.6), C-11 (47.6) (weak), C-29 (27.0)
10	54.7	1.35, m	C-9 (41.3), C-11 (47.6), C-29 (26.9) (weak), C-30 (12.7), C-31 (18.1)
11	47.6	1.26, m	C-10 (54.7), C-12 (54.0), C-13 (65.2), C-29 (26.9), C-31 (18.1)
12	54.0	1.69, m	C-8 (50.3), C-9 (41.3), C-10 (54.7), C-11 (47.6), C-13 (65.2), C-14 (81.9), C-31 (18.1)
13	65.2	1.84, m	C-5 (46.1) (weak), C-6 (58.1), C-7 (36.3), C-11 (47.6), C-12 (54.0), C-14 (81.9), C-15 (59.4)
14	81.9	3.67, m	C-12 (54.0), C-13 (65.2), C-15 (59.4), C-16 (138.0)
15	59.4	3.18, m	C-5 (46.2), C-6 (58.1), C-14 (81.9), C-16 (138.0), C-17 (125.9)
16	138.0	5.75, m	C-15 (59.4), C-14 (81.9), C-18 (46.3), C-19 (180.3)
17	125.9	5.67, m	C-15 (59.4) (weak), C-18 (46.3), C-19 (180.3)
18	46.3	3.91, m	C-2(46.5), C-16 (138.0), C-17 (125.9), C-19 (180.3)
19	180.3	-	-
20	nd	-	-
21’ (Z)	176.3 & 178.7	-	-
21’’ (E)	174.5		-
22	-	-	-
23’ (Z)	64.5	4.18, d (3.4)	C-21’ (176.3 & 178.7), C-25’ (69.7), C-26’ (Z) (28.9)
23’’ (E)	69.6	3.95, d (2.7)	C-21’’ (174.5), C-25’’(E) (71.0), C-26’’(E) (31.1), C-24 (207.3)
24 (E / Z)	207.3	-	
25’ (Z)	69.7	3.89, m	
25’’(E)	71.0	3.74, dt (7.2, 2.7)	C-23’’ (E) (69.6), C-24 (207.3), C-26’’ (E) (31.1), C-27 (37.0) (weak)
26a’ (Z)	28.9	1.72, m	C-25’ (Z) (69.7)
26b’ (Z)	-	1.60, m	C-27 (37.0)
26a’’ (E)	31.1	1.94, m	C-25’’ (E) (71.0), C-27 (37.0)
26b’’ (E)	-	1.75, m	C-23’’ (E) (69.6), C-25’’ (E) (71.0), C-27 (37.0)
27a	37.0	3.66, m	C-1 (180.5), C-25’’ (E) (71.0),), C-26’’ (31.1)
27b		3.58, m	C-1 (180.5), C-25’’ (E) (71.0), C-26’’ (31.1)
28	-	-	-
29a	27.0	1.62, m	C-9 (41.3), C-10 (54.6), C-11 (47.6), C-30 (12.7)
29b		1.09, m	C-9 (41.3), C-10 (54.7), C-11 (47.6), C-30 (12.7)
30	12.7	0.90, t (7.4)	C-10 (54.7), C-29 (27.0)
31	18.1	1.04, d (6.4)	C-10 (54.6), C-11 (47.6), C-12 (54.0)

Supplement Figure 43a. HMBC (600 MHz, CD_3OD) spectrum of photocyclized alteramide A (**5**)



Supplemental Figure 43b. HMBC (600 MHz, CD_3OD) spectrum (extended) of photocyclized alteramide A (**5**)



* The identification of *E* and *Z* form was followed according to the model reported by Michael et al.[12]

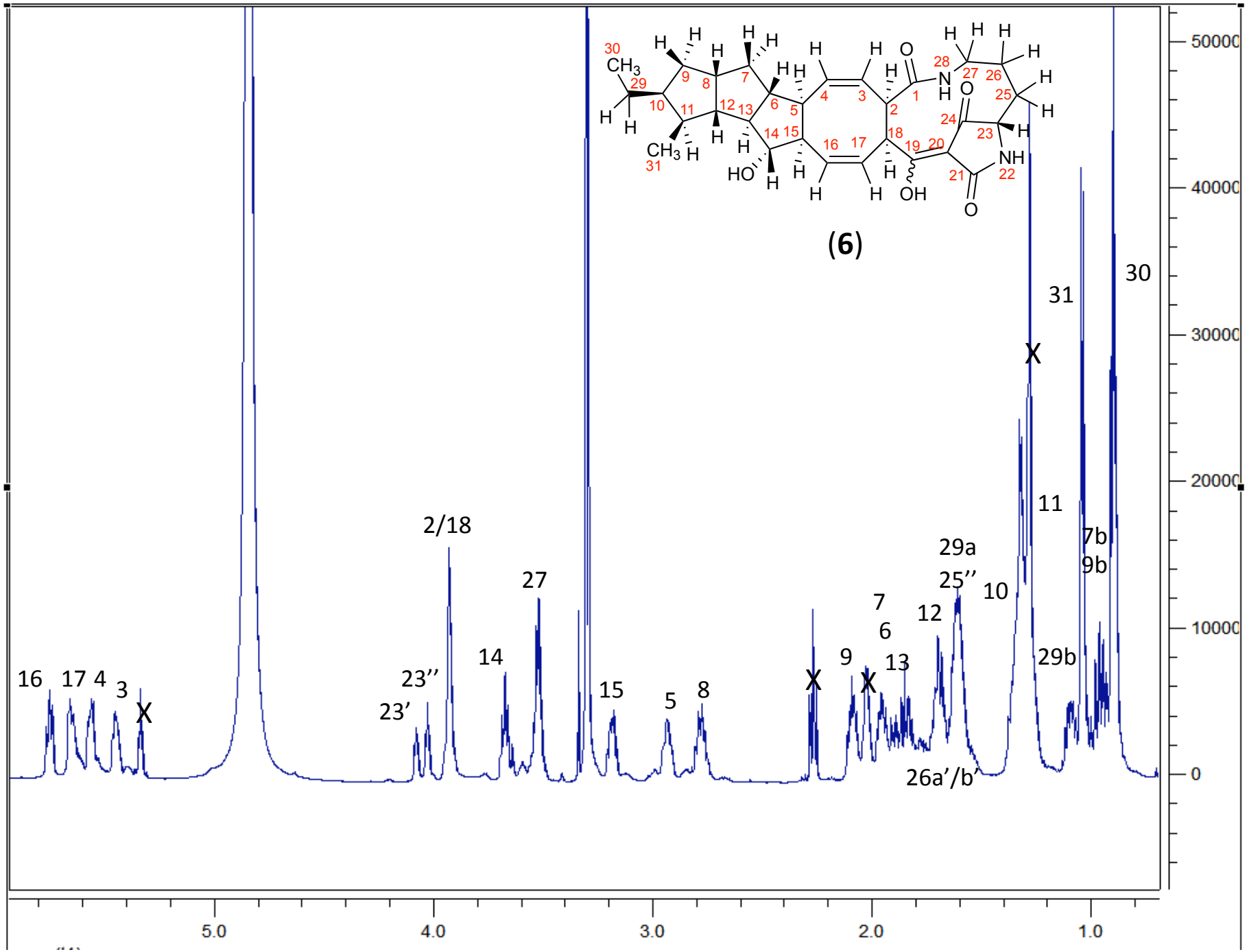
Supplemental Table 10. ^{1}H and ^{13}C NMR data of photocyclized alteramide B (**6**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	180.3	-	-
2	46.5	3.93, m	C-1 (180.2), C-3 (125.6), C-4 (138.1)
3	125.6	5.45, m	C-1 (180.3), C-2 (46.5), C-4 (138.1)
4	138.1	5.56, m	C-2 (46.5), C-3 (125.7), C-5 (46.1), C-6 (58.0), C-15 (59.4)
5	46.1	2.93, m	C-3 (125.6), C-6 (58.0), C-7 (36.2), C-15 (59.4), C-4 / C-16 (138.1)
6	58.0	1.88, m	C-4 (138.4), C-5 (46.1), C-7 (36.2), C-12 (54.0) (weak), C-13 (65.2), C-14 (81.9)
7a	36.2	1.96, m	C-6 (58.0), C-8 (50.2), C-12 (54.0), C-13 (65.2)
7b	-	0.94, m	C-5 (46.1), C-6 (58.0), C-8 (50.2), C-9 (41.3)
8	50.2	2.78, m	C-7 (36.2), C-9 (41.3), C-12 (54.0), C-13 (65.2)
9a	41.3	2.09, m	C-8 (50.2), C-10 (54.6), C-11 (47.6), C-12 (54.0)
9b	-	0.97, m	C-7 (36.2), C-8 (50.2), C-10 (54.6), C-11 (47.6) (weak), C-29 (26.9)
10	54.6	1.35, m	C-9 (41.3), C-11 (47.6), C-30 (12.7), C-31 (18.1)
11	47.6	1.26, m	C-10 (54.6), C-12 (54.0), C-13 (65.2), C-29 (26.9), C-31 (18.1)
12	54.0	1.69, m	C-8 (50.2), C-9 (41.3), C-11 (47.6), C-13 (65.2), C-14 (81.9), C-31 (18.1)
13	65.2	1.84, m	C-5 (46.1) (weak), C-6 (58.0), C-7 (36.2) (weak), C-11 (47.6), C-12 (54.0), C-14 (81.9)
14	81.9	3.67, t (8.0)	C-12 (54.0), C-13 (65.2), C-15 (59.4), C-16 (138.1)
15	59.4	3.19, m	C-5 (46.1), C-6 (58.0), C-14 (81.9), C-16 (138.1), C-17 (125.9)
16	138.1	5.75, t (8.0)	C-15 (59.4), C-14 (81.9), C-18 (46.5)
17	125.9	5.65, m	C-15 (59.4), C-18 (46.5),C-16 (138.1), C-19 (180.1)
18	46.5	3.94, m	C-16 (138.1), C-17 (125.9), C-19 (180.2)
19	180.1	-	-
20	nd	-	-
21' (Z)	179.0	-	-
21'' (E)	173.6		-
22	-	-	-
23' (Z)	58.4	4.08, t (4.6, 5.8)	C-21'(Z) (179.0), C-25'(Z) (23.6), C-26' (Z) (29.1)
23'' (E)	64.6	4.03, t (5.6)	C-21''(E) (173.6), C-25''(E) (24.1), C-26''(E) (29.7), C-24 (209.0)
24 (E / Z)	209.0	-	
25' (Z)	23.6	1.62, m	C-23'(Z) (58.4), C-24 (209.0)
25''(E)	24.1	1.70, m	C-24 (209.0)
26a' (Z)	29.1	1.79, m	C-23' (Z) (58.4), C-25' (Z) (23.6), C-27 (39.0)
26b' (Z)	-	1.54, m	C-23' (Z) (58.4), C-25' (Z) (23.6), C-27 (39.0)
26a'' (E)	29.7	1.72, m	C-23'' (E) (64.6), C-25' (E)'(24.1), C-27 (39.0)
26b'' (E)	-	1.61, m	C-23'' (E) (64.6), C-27 (39.0)
27	39.0	3.52, m	C-1 (180.3), C-25 (Z) (23.6), C-25''(E) (24.1), C-26' (Z) (29.1), C-26''(E) (29.7)
28	-	-	-
29a	26.9	1.61, m	C-9 (41.3), C-10 (54.6), C-11 (47.6), C-30 (12.7)
29b		1.09, m	C-9 (41.3), C-10 (54.6), C-11 (47.6) (weak),, C-30 (12.7)
30	12.7	0.90, t (7.4)	C-10 (54.6), C-29 (26.9)
31	18.1	1.04, d (6.4)	C-10 (54.6), C-11 (47.6), C-12 (54.0)

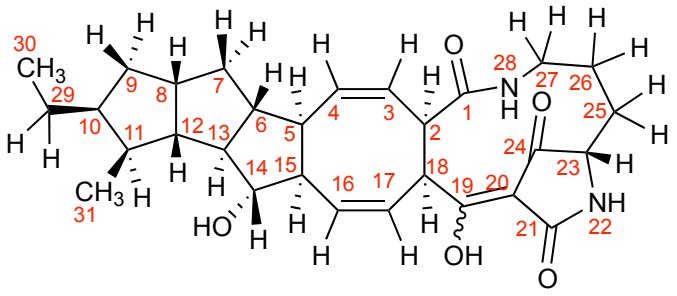
Supplemental Table 11. ^{1}H and ^{13}C NMR Data and NOEs – photocyclized alteramide B (**6**) (d_4-MeOH)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H - ^{1}H NOE (NOESY)
1	180.3	-	-
2	46.5	3.93, m	H-5
3	125.6	5.45, m	
4	138.2	5.56, m	H-6
5	46.1	2.93, m	H-2, H-7b weak), H-13, H-15
6	58.0	1.88, m	H-4, H-8 (weak), H-12 (weak), H-14
7a	36.2	1.96, m	
7b	-	0.94, m	H-5, H-13
8	50.2	2.78, m	H-6 (weak), H-12
9a	41.3	2.09, m	
9b	-	0.97, m	
10	54.6	1.35, m	
11	47.6	1.26, m	H-13, H-30 (weak)
12	54.0	1.69, m	H-6 (weak), H-8, H-14, H-31
13	65.2	1.84, m	H-5, H-7b, H-11, H-15
14	81.9	3.67, t (8.0)	H-6, H-12, H-16
15	59.4	3.19, m	H-5, H-13, H-18
16	138.1	5.75, t (8.0)	H-14
17	125.86	5.65, m	
18	46.5	3.94, m	H-15
19	180.1	-	
20	-	-	
21’ (Z)	179.0	-	
21’’ (E)	173.6		
22	-	-	
23’ (Z)	58.4	4.08, t (4.6, 5.8)	H-26a/b’ (Z), H-27 (weak)
23’’ (E)	64.6	4.03, t (5.6)	H-26a/b’’ (E), H-27
24 (E / Z)	209.0	-	
25’ (Z)	23.6	1.62, m	
25’’(E)	24.1	1.70, m	
26a’ (Z)	29.1	1.79, m	H-23’ (Z)
26b’ (Z)	-	1.54, m	H-23’ (Z)
26a’’ (E)	29.7	1.72, m	H-23’’ (E)
26b’’ (E)	-	1.61, m	H-23’’ (E)
27	39.0	3.52, m	H-23’’ (E)
28	-	-	
29a	26.9	1.61, m	H-31
29b		1.09, m	
30	12.7	0.90, t (7.4)	H-10, H-11 (weak)
31	18.1	1.04, d (6.4)	H-10, H-12, H-29a

Supplemental Figure 44. ^{1}H NMR (600 MHz, CD_3OD) spectra of photocyclized alteramide B (**6**)

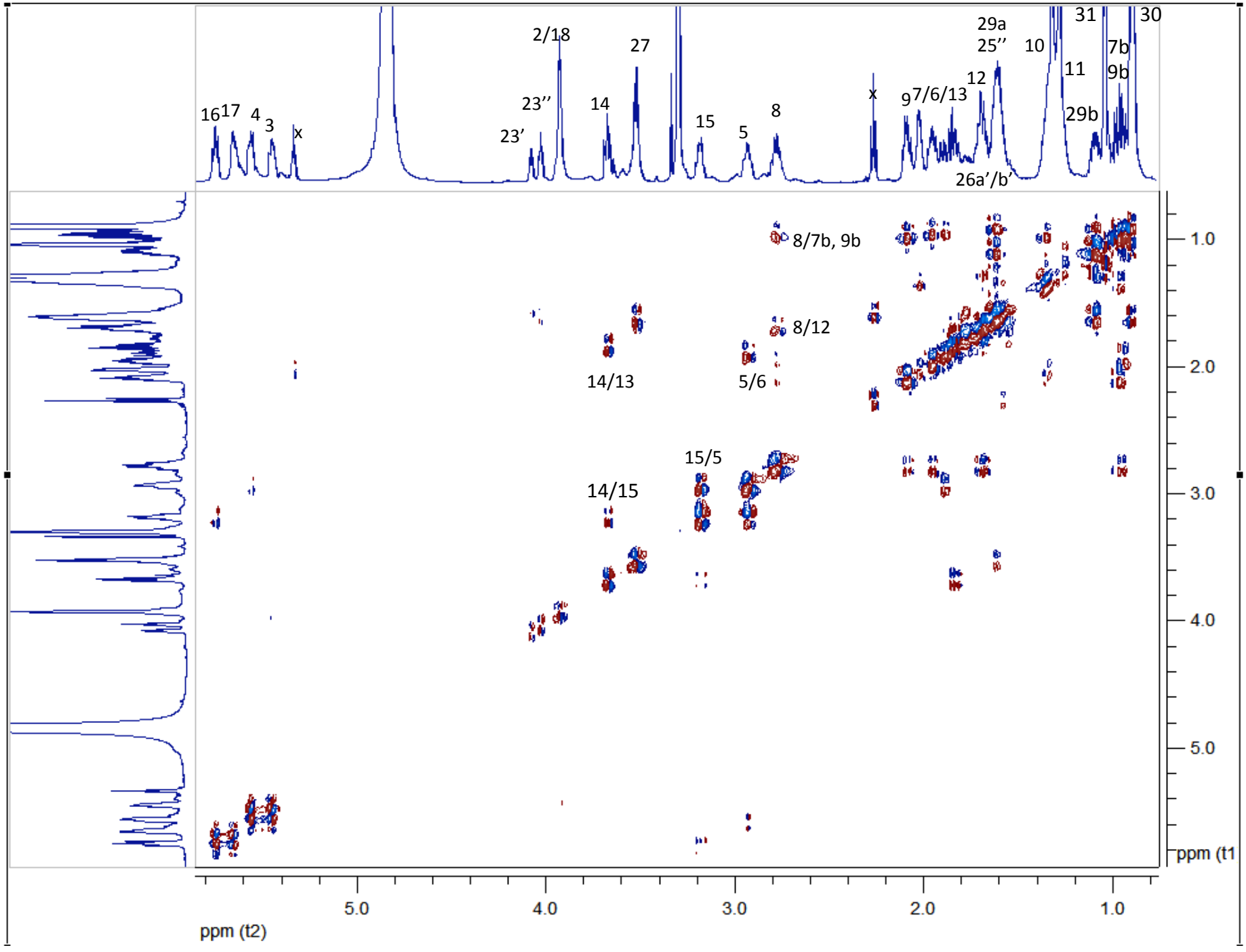


Supplemental Figure 45. ^{1}H NMR (600 MHz, CD_3OD) spectra of photocyclized alteramide B (**6**) (isolated from CNT357)

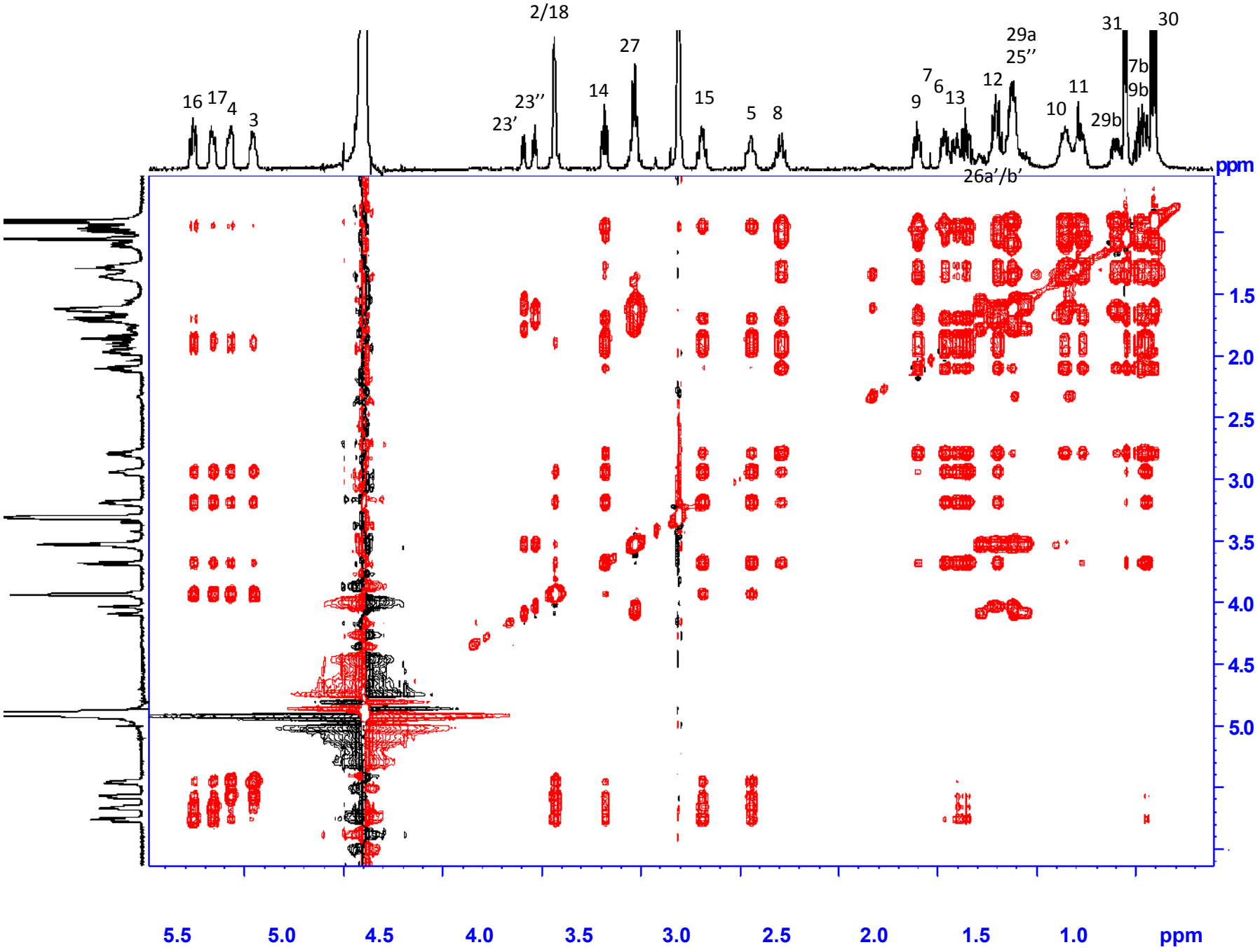


(6)

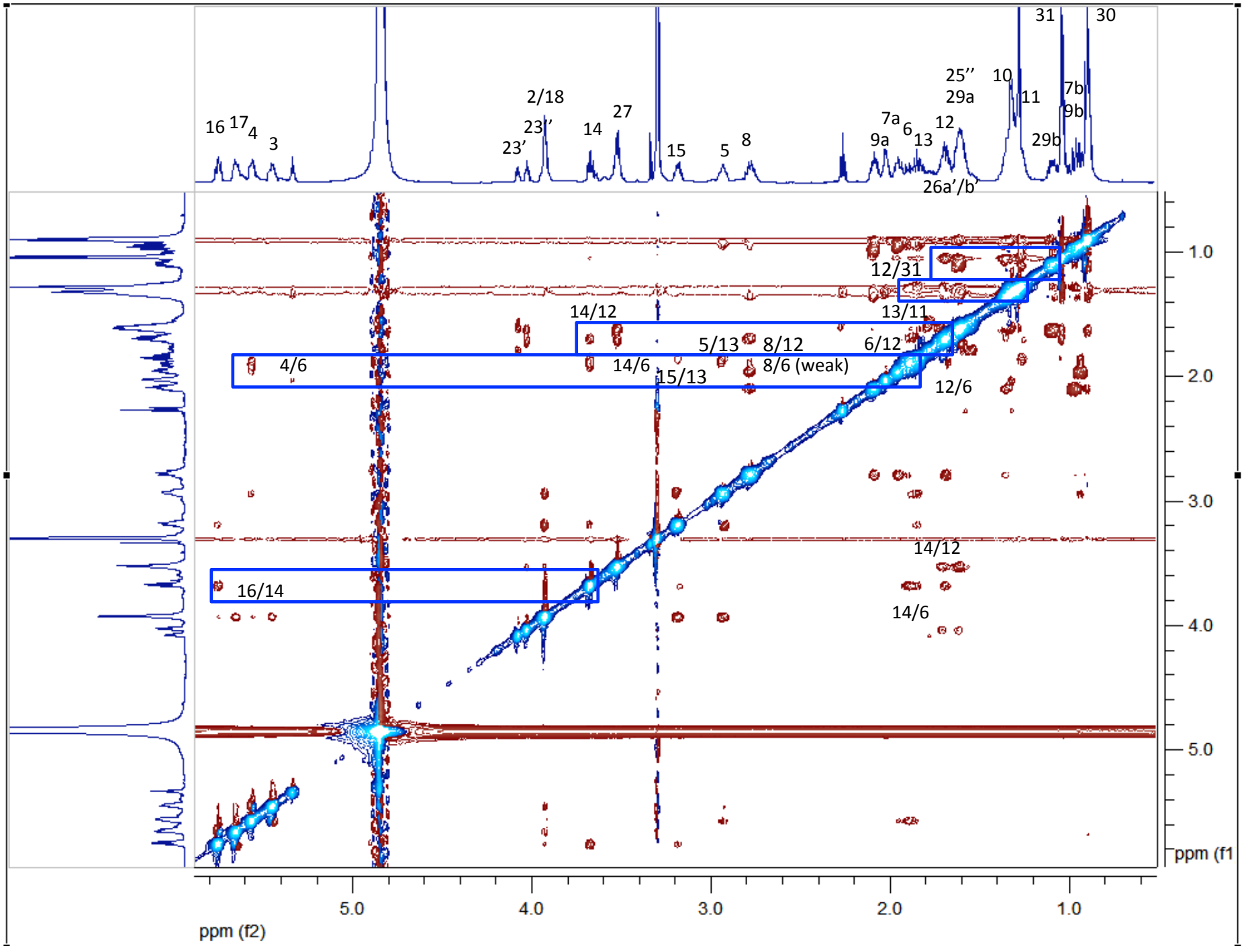
Supplemental Figure 46. COSY(600 MHz, CD_3OD, grad. phase sens.) of photocyclized alteramide B (**6**)



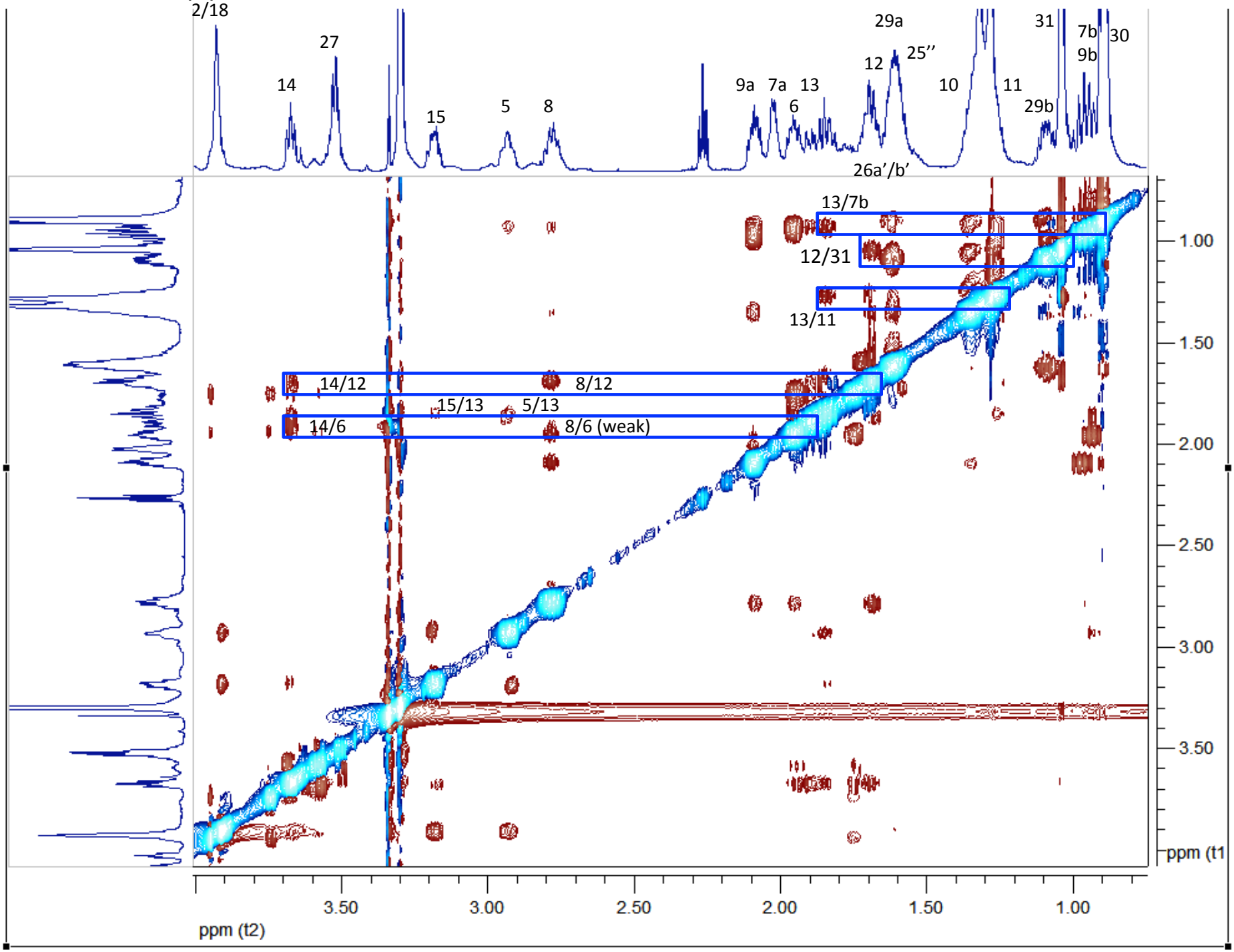
Supplemental Figure 47. TOCSY (600 MHz, CD_3OD, 75 ms) spectrum of photocyclized alteramide B (**6**)



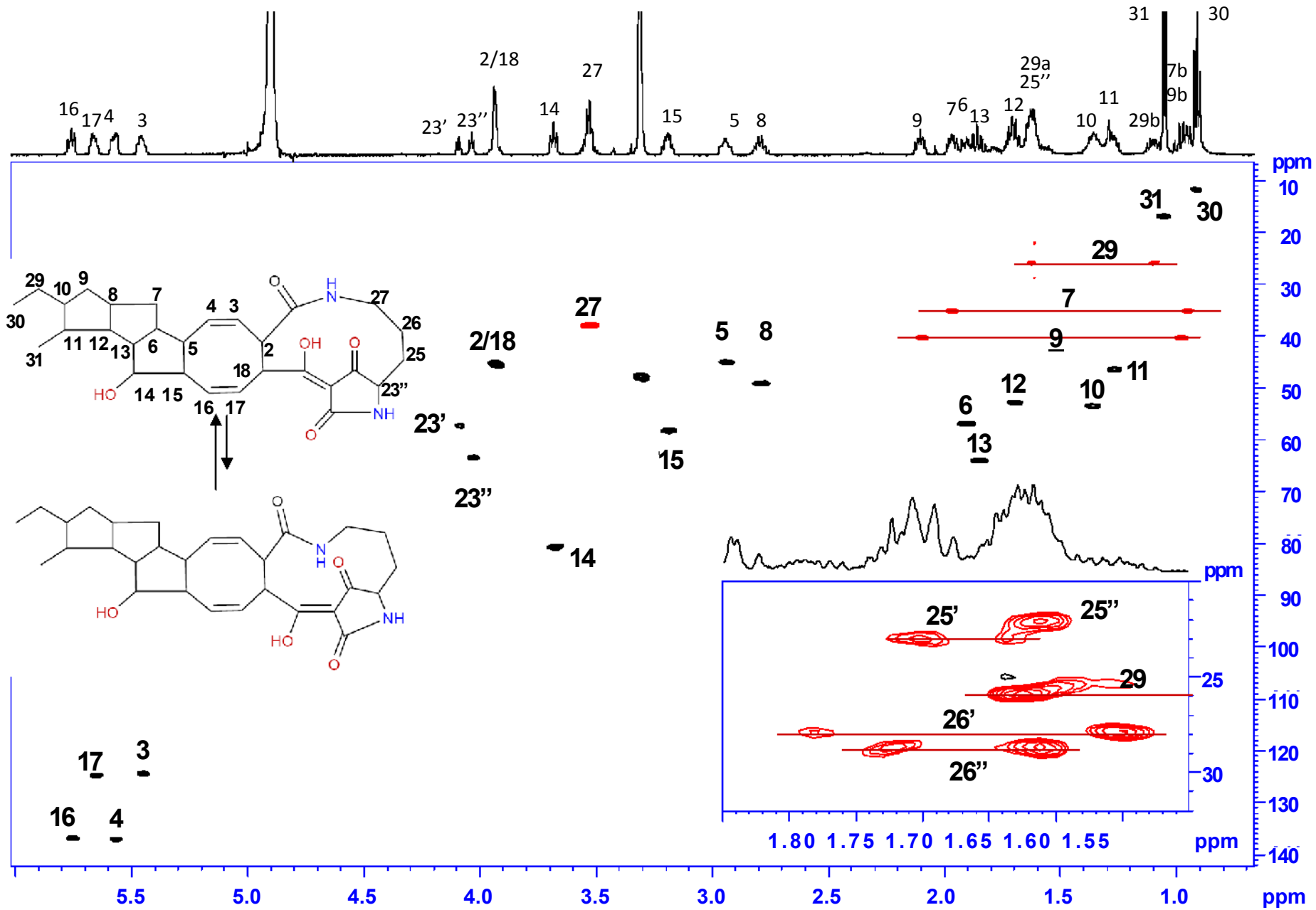
Supplemental Figure 48a. NOESY(600 MHz, CD_3OD, 600 ms, gradient) of photocyclized alteramide B (**6**)



Supplemental Figure 48b. NOESY zoom-in (600 MHz, CD_3OD, 600 ms, gradient) of photocyclized alteramide B (**6**)



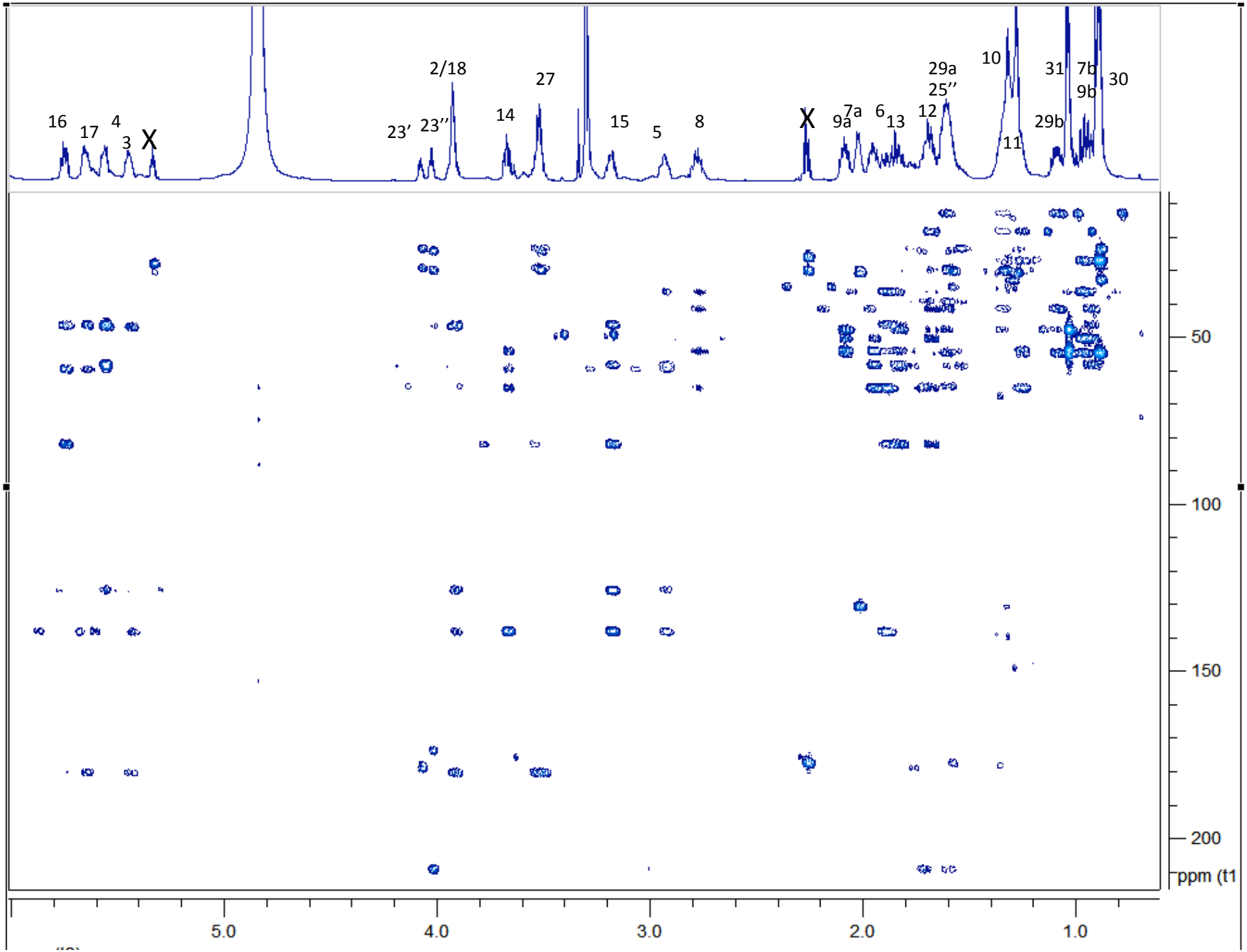
Supplemental Figure 49. HSQC (600 MHz, CD_3OD) spectrum and annotation of photocyclized alteramide B (**6**)



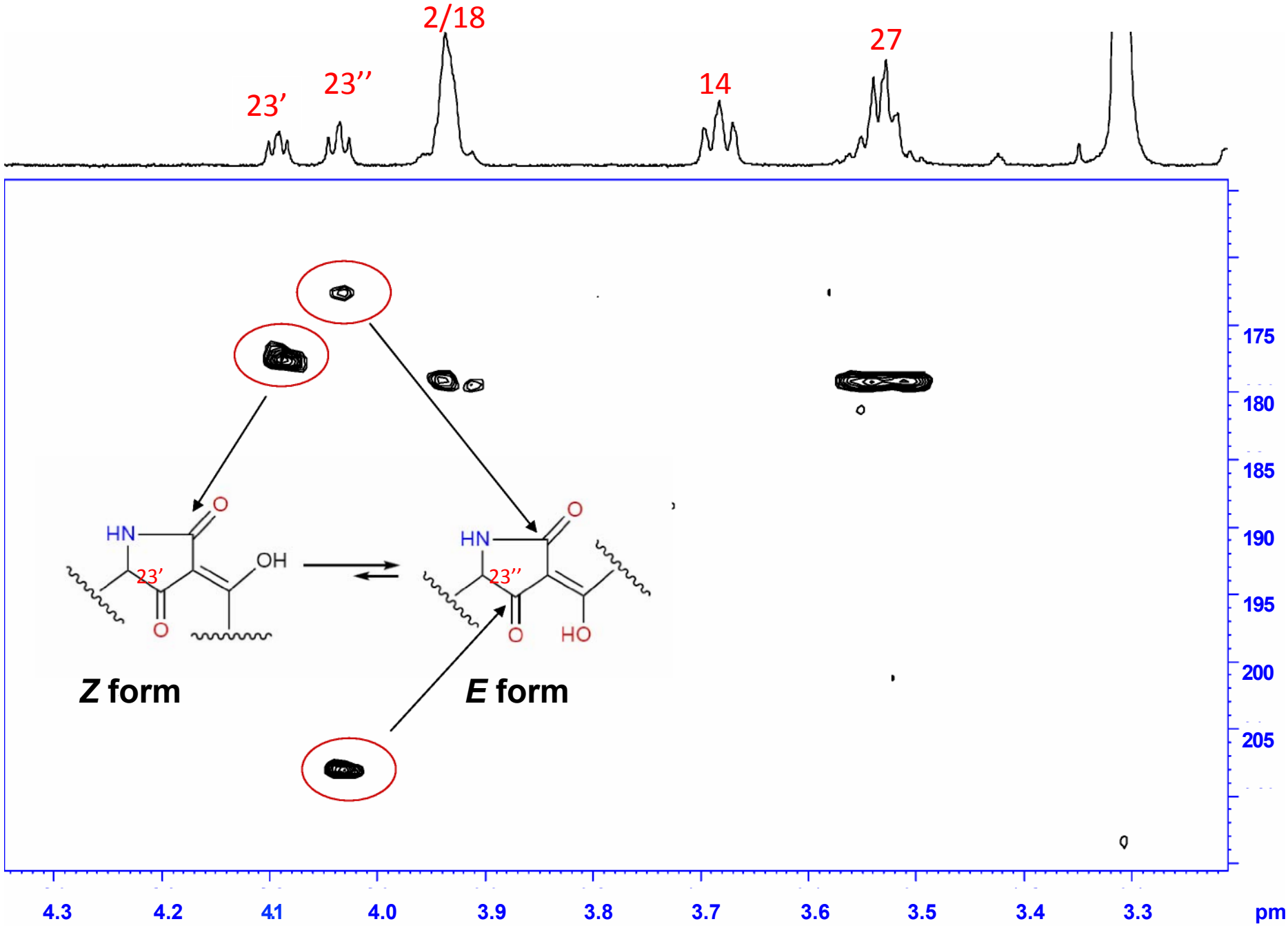
Supplement Table 11. HMBC (600 MHz, CD_3OD) spectrum of photocyclized alteramide B (**6**)

Position	^{13}C (ppm)	^{1}H (ppm), mult (J (Hz))	^{1}H coupled with ^{13}C (HMBC)
1	180.3	-	-
2	46.5	3.93, m	C-1 (180.2), C-3 (125.6), C-4 (138.1)
3	125.6	5.45, m	C-1 (180.3), C-2 (46.5), C-4 (138.1)
4	138.1	5.56, m	C-2 (46.5), C-3 (125.7), C-5 (46.1), C-6 (58.0), C-15 (59.4)
5	46.1	2.93, m	C-3 (125.6), C-6 (58.0), C-7 (36.2), C-15 (59.4), C-4 / C-16 (138.1)
6	58.0	1.88, m	C-4 (138.4), C-5 (46.1), C-7 (36.2), C-12 (54.0) (weak), C-13 (65.2), C-14 (81.9)
7a	36.2	1.96, m	C-6 (58.0), C-8 (50.2), C-12 (54.0), C-13 (65.2)
7b	-	0.94, m	C-5 (46.1), C-6 (58.0), C-8 (50.2), C-9 (41.3)
8	50.2	2.78, m	C-7 (36.2), C-9 (41.3), C-12 (54.0), C-13 (65.2)
9a	41.3	2.09, m	C-8 (50.2), C-10 (54.6), C-11 (47.6), C-12 (54.0)
9b	-	0.97, m	C-7 (36.2), C-8 (50.2), C-10 (54.6), C-11 (47.6) (weak), C-29 (26.9)
10	54.6	1.35, m	C-9 (41.3), C-11 (47.6), C-30 (12.7), C-31 (18.1)
11	47.6	1.26, m	C-10 (54.6), C-12 (54.0), C-13 (65.2), C-29 (26.9), C-31 (18.1)
12	54.0	1.69, m	C-8 (50.2), C-9 (41.3), C-11 (47.6), C-13 (65.2), C-14 (81.9), C-31 (18.1)
13	65.2	1.84, m	C-5 (46.1) (weak), C-6 (58.0), C-7 (36.2) (weak), C-11 (47.6), C-12 (54.0), C-14 (81.9)
14	81.9	3.67, t (8.0)	C-12 (54.0), C-13 (65.2), C-15 (59.4), C-16 (138.1)
15	59.4	3.19, m	C-5 (46.1), C-6 (58.0), C-14 (81.9), C-16 (138.1), C-17 (125.9)
16	138.1	5.75, t (8.0)	C-15 (59.4), C-14 (81.9), C-18 (46.5)
17	125.9	5.65, m	C-15 (59.4), C-18 (46.5),C-16 (138.1), C-19 (180.1)
18	46.5	3.94, m	C-16 (138.1), C-17 (125.9), C-19 (180.2)
19	180.1	-	-
20	nd	-	-
21’ (Z)	179.0	-	-
21’’ (E)	173.6		-
22	-	-	-
23’ (Z)	58.4	4.08, t (4.6, 5.8)	C-21’(Z) (179.0), C-25’(Z) (23.6), C-26’ (Z) (29.1)
23’’ (E)	64.6	4.03, t (5.6)	C-21’’(E) (173.6), C-25’’(E) (24.1), C-26’’(E) (29.7), C-24 (209.0)
24 (E / Z)	209.0	-	
25’ (Z)	23.6	1.62, m	C-23’(Z) (58.4), C-24 (209.0)
25’’(E)	24.1	1.70, m	C-24 (209.0)
26a’ (Z)	29.1	1.79, m	C-23’ (Z) (58.4), C-25’ (Z) (23.6), C-27 (39.0)
26b’ (Z)	-	1.54, m	C-23’ (Z) (58.4), C-25’ (Z) (23.6), C-27 (39.0)
26a’’ (E)	29.7	1.72, m	C-23’’ (E) (64.6), C-25’ (E)’(24.1), C-27 (39.0)
26b’’ (E)	-	1.61, m	C-23’’ (E) (64.6), C-27 (39.0)
27	39.0	3.52, m	C-1 (180.3), C-25 (Z) (23.6), C-25’’(E) (24.1), C-26’ (Z) (29.1), C-26’’(E) (29.7)
28	-	-	-
29a	26.9	1.61, m	C-9 (41.3), C-10 (54.6), C-11 (47.6), C-30 (12.7)
29b		1.09, m	C-9 (41.3), C-10 (54.6), C-11 (47.6) (weak),, C-30 (12.7)
30	12.7	0.90, t (7.4)	C-10 (54.6), C-29 (26.9)
31	18.1	1.04, d (6.4)	C-10 (54.6), C-11 (47.6), C-12 (54.0)

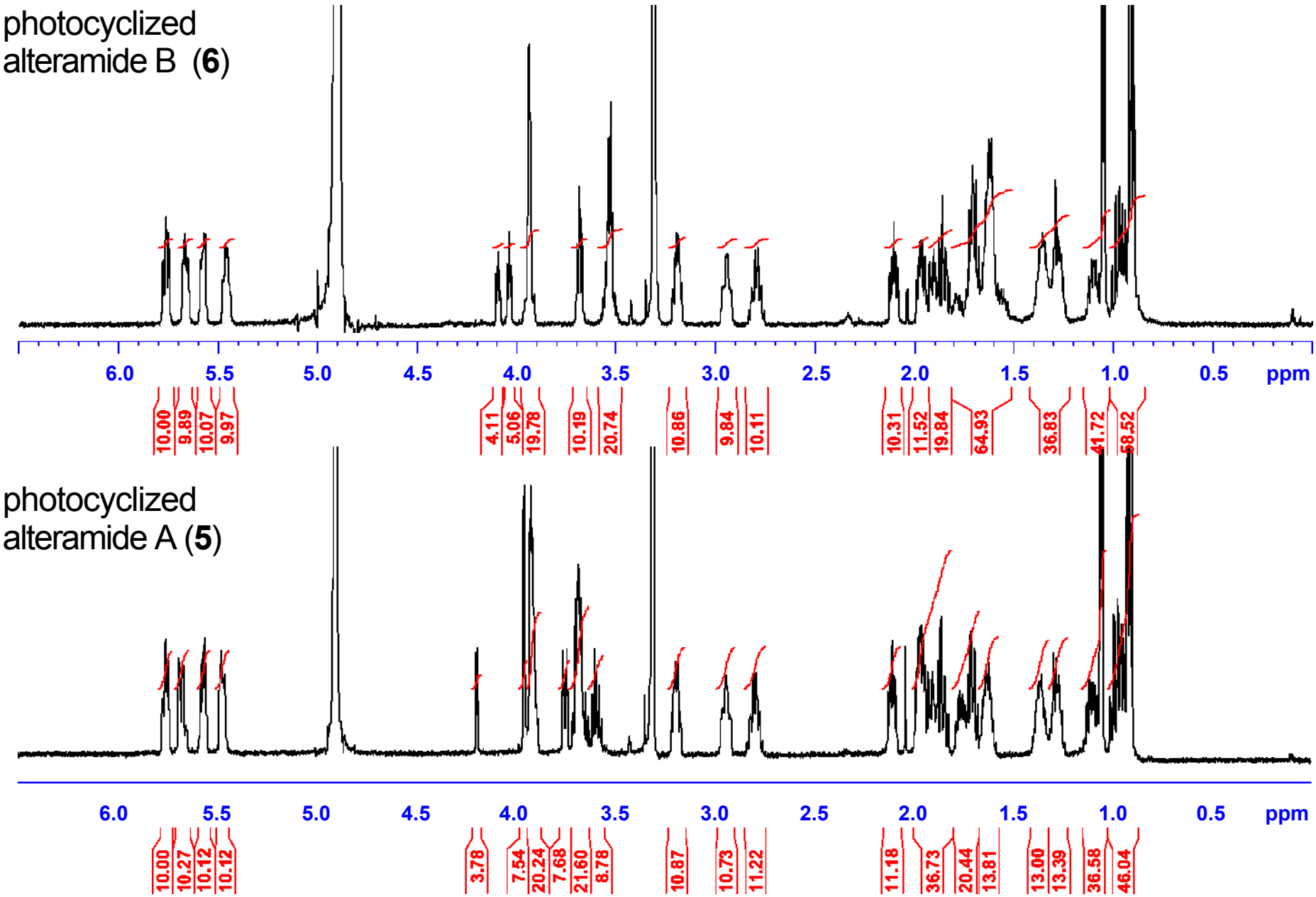
Supplement Figure 50a. HMBC (600 MHz, CD_3OD) spectrum of photocyclized alteramide B (**6**)



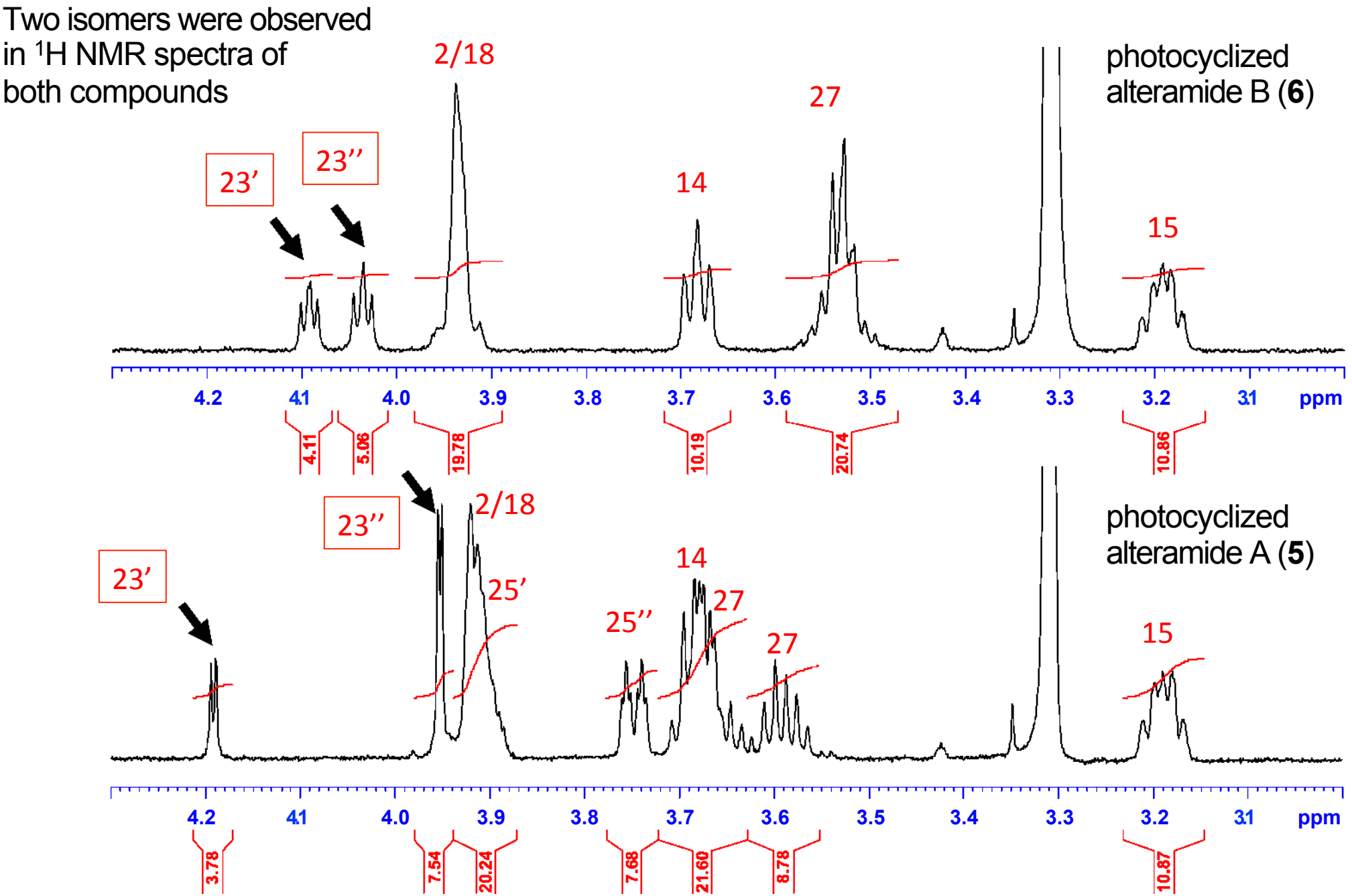
Supplemental Figure 50b. HMBC (600 MHz, CD_3OD) spectrum (extended) of photocyclized alteramide B (**6**)



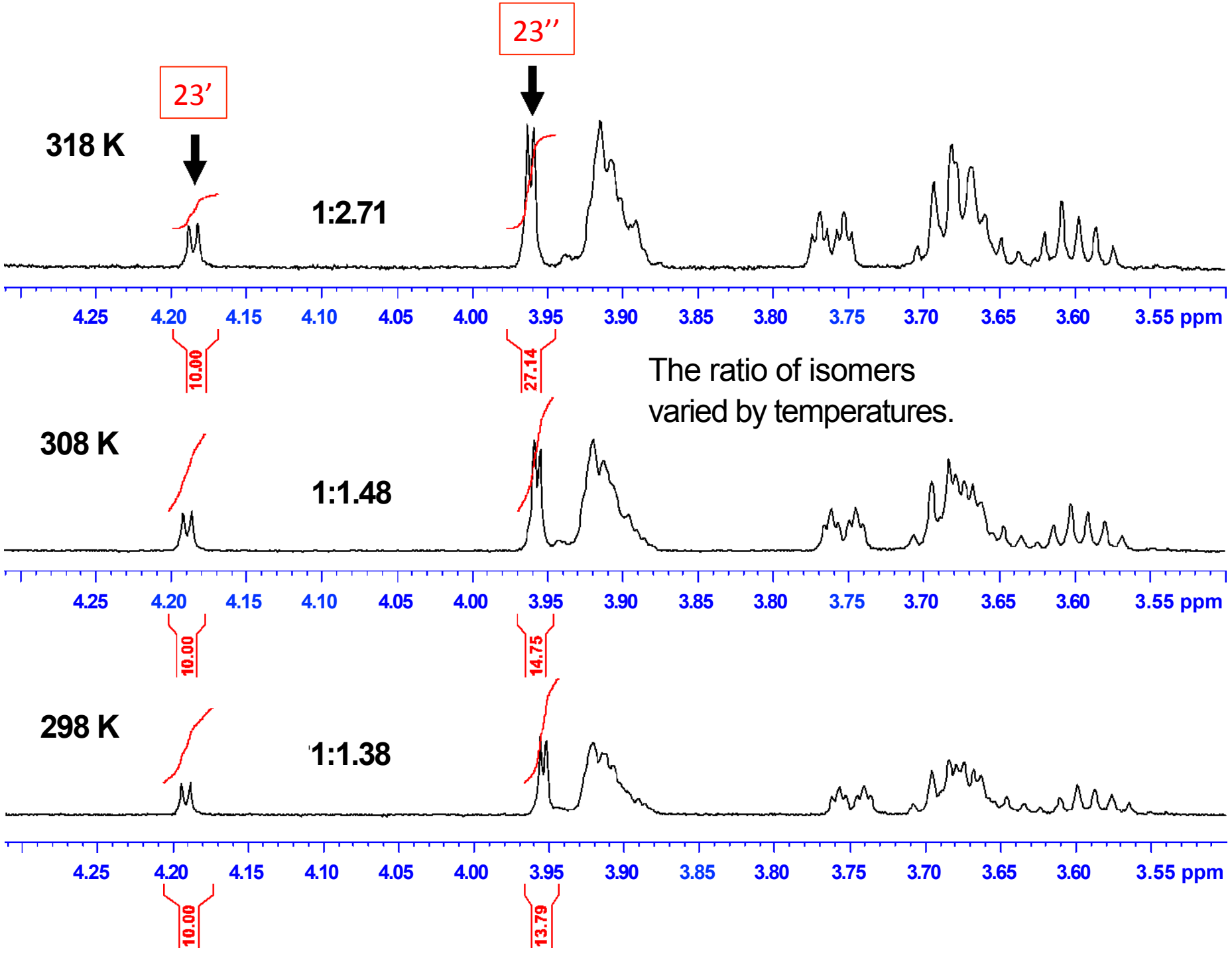
Supplemental Figure 51a. ^{1}H NMR (600 MHz, CD_3OD) spectra of photocyclized alteramides A (**5**) and B (**6**)



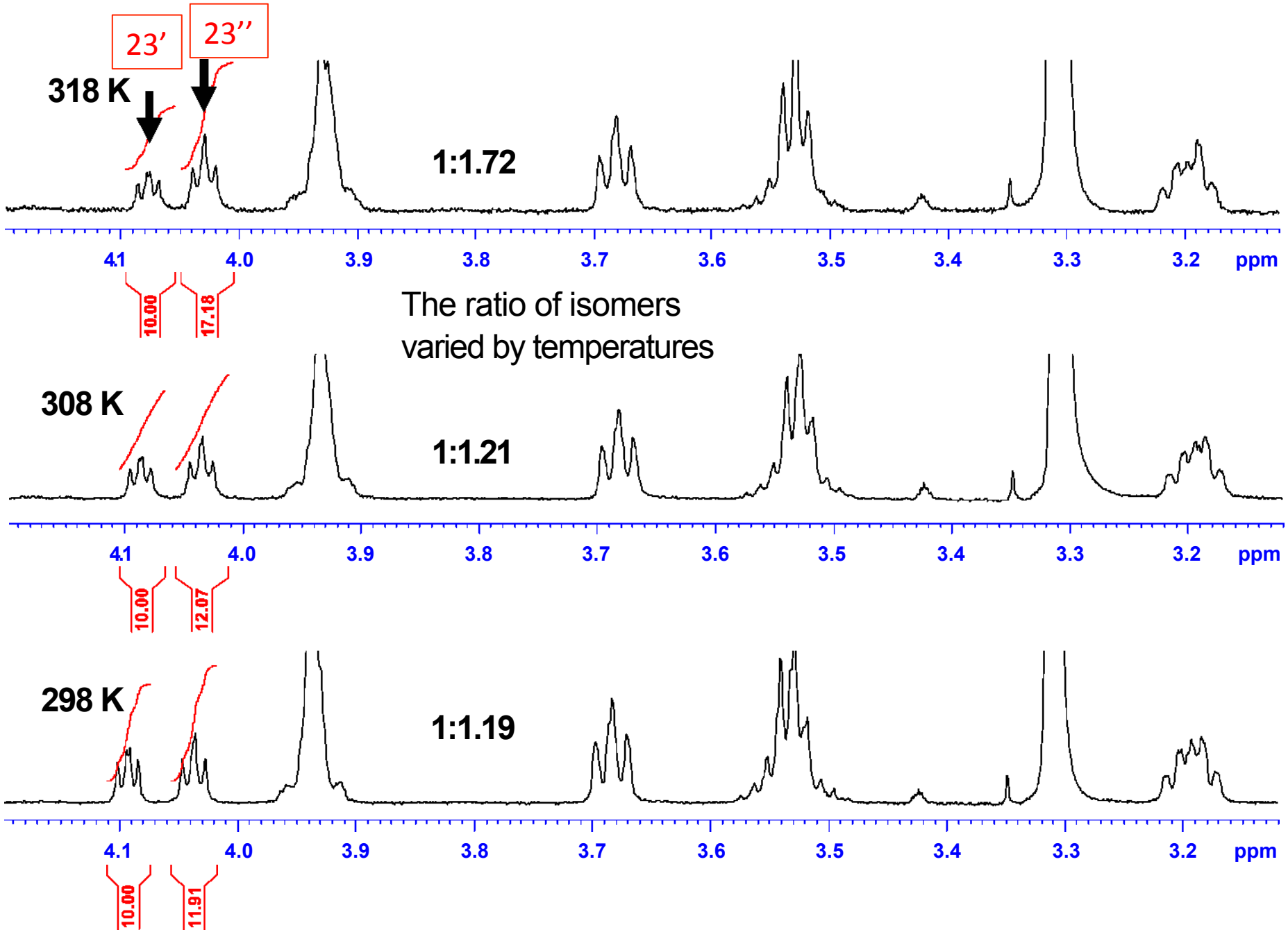
Supplemental Figure 51b. ^{1}H NMR (600 MHz, CD_3OD) extended spectra of photocyclized alteramide A (**5**) and alteramide B (**6**)



Supplemental Figure 52a. ^{1}H NMR (600 MHz, CD_3OD) extended spectra of photocyclized alteramide A (**5**) at various temperatures.



Supplemental Figure 52b. ^{1}H NMR (600 MHz, CD_3OD) extended spectra of photocyclized alteramide B (**6**) at various temperatures



Supplementary Methods

Isolation of intramolecular cyclized alteramides A (5) and B (6) from *Streptomyces* CNT 357

Streptomyces CNT357[13], was cultured in 4L of A1 medium (10 g soluble starch, 4 g yeast extract, 2 g peptone, 21 g seasalts, 1L deionized water) at 27 ^{o}C for one week. 25 g/L of Amberlite XAD-16 was used to harvest the secreted natural products from the A1 broth. Light exposure was not excluded during this isolation protocol. The resin was extracted with MeOH and acetone, respectively. The acetone extract was subjected to Sephadex LH-20 chromatography eluting with MeOH and further fractionated using HPLC (C-18, 250 X 4.6 mm, 5 μm) with a mobile phase gradient of 5% to 100% CH_3N/H_2O (0.1% TFA) in 30 min with a 1.0 mL/min flow rate. Intramolecular cyclized alteramide A (**5**) with observed *m/z* 511.2815 (calcd. *m/z* 511.2808, Δ=+1.4 ppm) (~ 500 μg) and intramolecular cyclized alteramide B (**6**) with *m/z* 495.2866 (calcd. *m/z* 495.2853, Δ=+2.6 ppm) (~500 μg) were both obtained with NMRs identical to the NMRs of the intramolecular cyclized alteramides A (**5**) and B (**6**) from OT59.

In silico conformation generation

Discovery Studio™ (version 3.5) software (Accelrys, San Diego, CA, USA) was used to generate the conformations for the open alteramide A as both *E* and Z tautomers with CAESAR (Conformer Algorithm based on Energy Screening and Recursive Buildup) algorithm.[14] Prior to generating conformations for each alteramide, the structure was examined for chemical correctness. Both polar and non-polar hydrogen atoms were added explicitly for each structure and then the structure was submitted to the conformation generation calculations. Conformations were generated using the following parameters – each structure was allowed to generate a maximum of 255 conformations each of which had to be within a 20 Kcal mol^{-1} energy threshold. Conformations were then minimized with a simple steepest descent method and the results analyzed.

Conformations were superposed within each molecule to facilitate with the analysis and to readily visualize the main clusters of conformations present within the ensemble of structures generated for each alteramide. Evaluation of the conformations were performed based on the proton – proton distances that relate to each molecule and its NMR spectrum.

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