

The Hoiamides, Structurally Intriguing Neurotoxic Lipopeptides from Papua New Guinea Marine Cyanobacteria

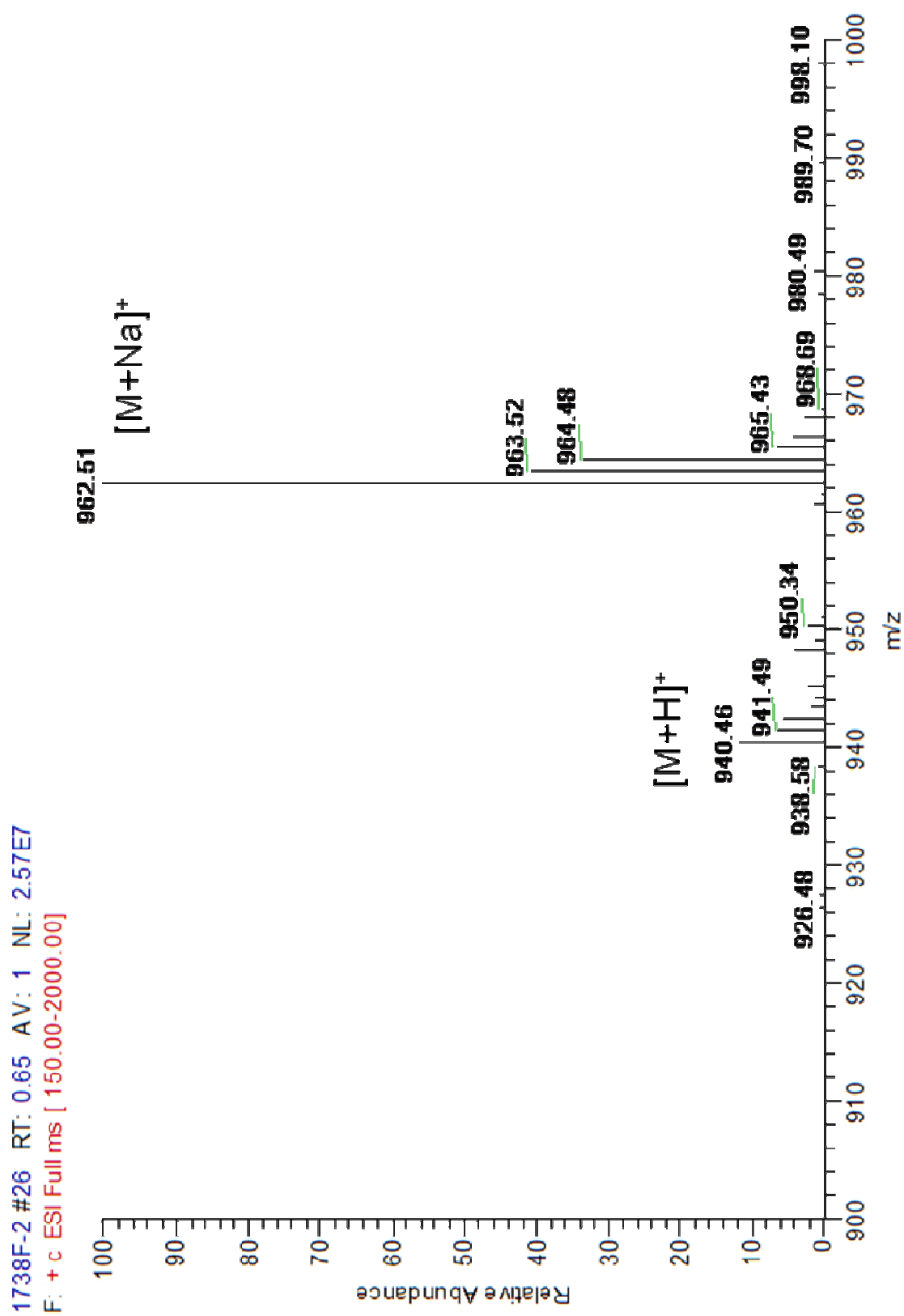
Hyukjae Choi, Alban R. Pereira, Zhengyu Cao, Cynthia F. Shuman, Niclas Engene, Tara Byrum,
Teatulohi Matainaho, Thomas F. Murray, Alfonso Mangoni* and William H. Gerwick*

Supporting Information

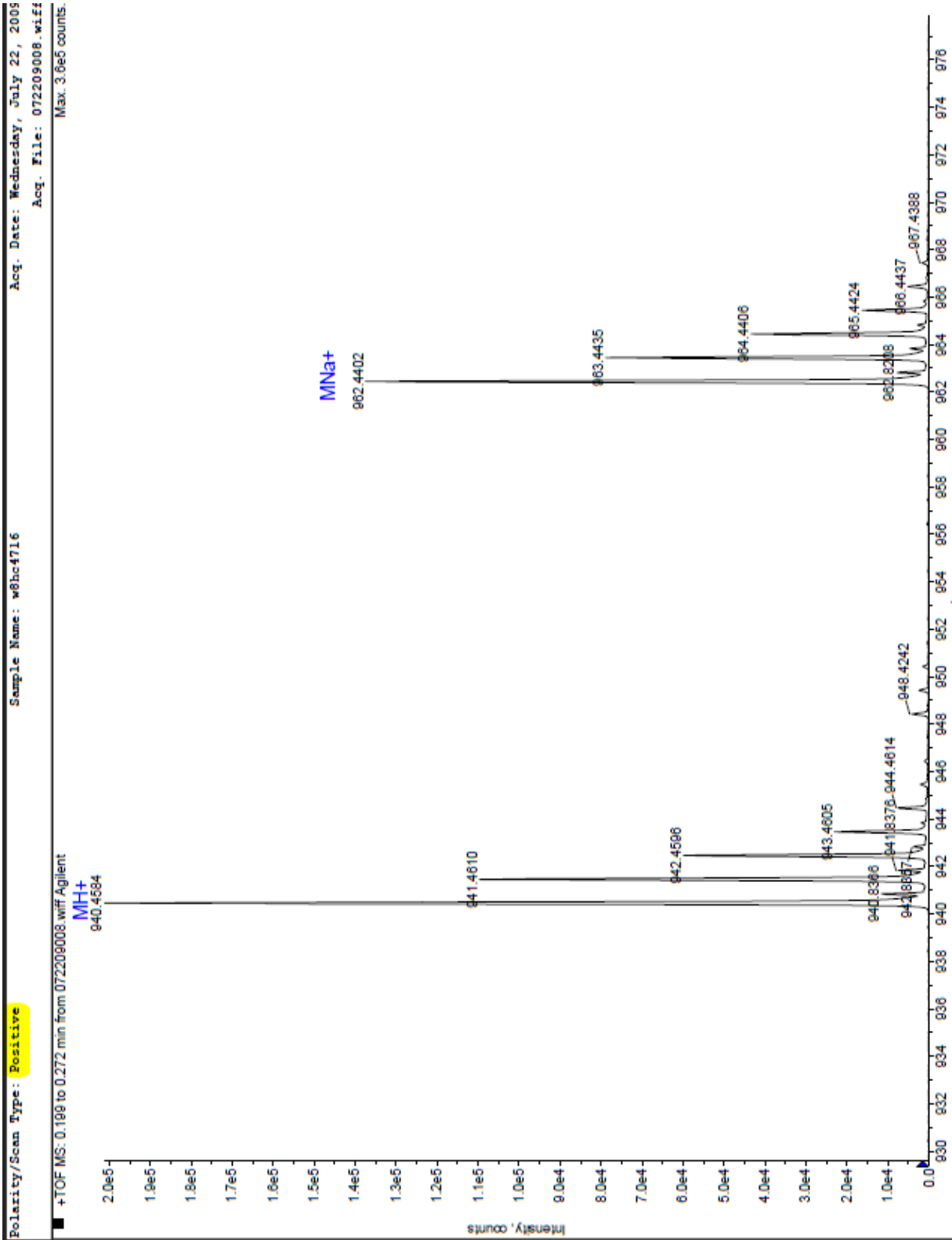
Index	S1–S2
LR ESIMS of hoiamide B (2)	S3
HR ESITOFMS of hoiamide B (2)	S4
¹ H NMR spectrum of hoiamide B (2)	S5
¹³ C NMR spectrum of hoiamide B (2)	S6
COSY spectrum of hoiamide B (2)	S7
TOCSY spectrum of hoiamide B (2)	S8
HSQC spectrum of hoiamide B (2)	S9
HMBC spectrum of hoiamide B (2)	S10
ROESY spectrum of hoiamide B (2)	S11
HETLOC spectrum of hoiamide B (2)	S12
HSQMBC spectrum of hoiamide B (2)	S13

LR ESIMS of 37-(<i>S</i>)-MTPA ester of 2,3-dehydrated hoiamide B (6)	S14
¹ H NMR spectrum of 37-(<i>S</i>)-MTPA ester of 2,3-dehydrated hoiamide B (6)	S15
LR ESIMS of 37-(<i>R</i>)-MTPA ester of 2,3-dehydrated hoiamide B (7)	S16
¹ H NMR spectrum of 37-(<i>R</i>)-MTPA ester of 2,3-dehydrated hoiamide B (7)	S17
HR EIMS of hoiamide C (3)	S18
¹ H NMR spectroscopic data table of natural hoiamide C (3) in pyridine- <i>d</i> ₅ at 700 MHz and ¹ H- ¹ H coupling constants based on spectral simulation	S19
NMR spectroscopic data table of natural hoiamide C (3) in CDCl ₃	S20
¹ H NMR spectrum of natural hoiamide C (3)	S21–S22
¹³ C NMR spectrum of natural hoiamide C (3)	S23
zTOCSY spectrum of natural hoiamide C (3)	S24
TOCSY spectrum of natural hoiamide C (3)	S25
COSY spectrum of natural hoiamide C (3)	S26–S27
HMBC spectrum of natural hoiamide C (3)	S28–S31
HSQC spectrum of natural hoiamide C (3)	S32–S33
¹⁵ N HMBC spectrum of hoiamide C (3)	S34
ROESY spectrum of hoiamide C (3)	S35
¹ H NMR spectrum of semisynthetic hoiamide C (3)	S36
¹³ C NMR spectrum of semisynthetic hoiamide C (3)	S37–S38
LCMS comparison of natural and semisynthetic hoiamide C (3)	S39
Circular dichroism and UV curves for natural and semisynthetic hoiamide C (3)	S40
Sodium influx stimulation of hoiamide B (2) in neocortical neurons	S41
Time- and concentration-response data for hoiamide A-induced suppression of spontaneous Ca ²⁺ oscillations in neocortical neurons	S42

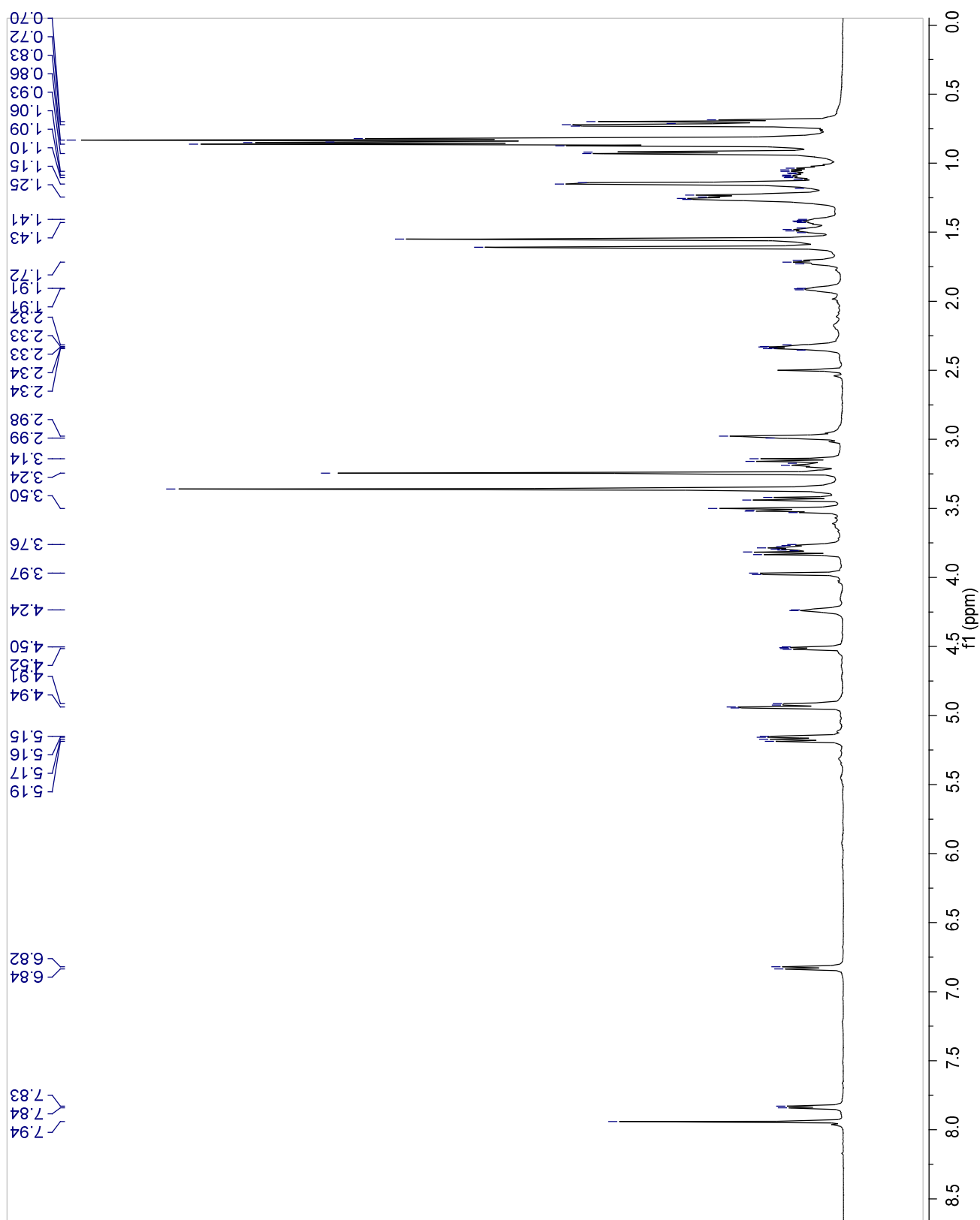
S3. LR ESIMS of hoiamide B (2).



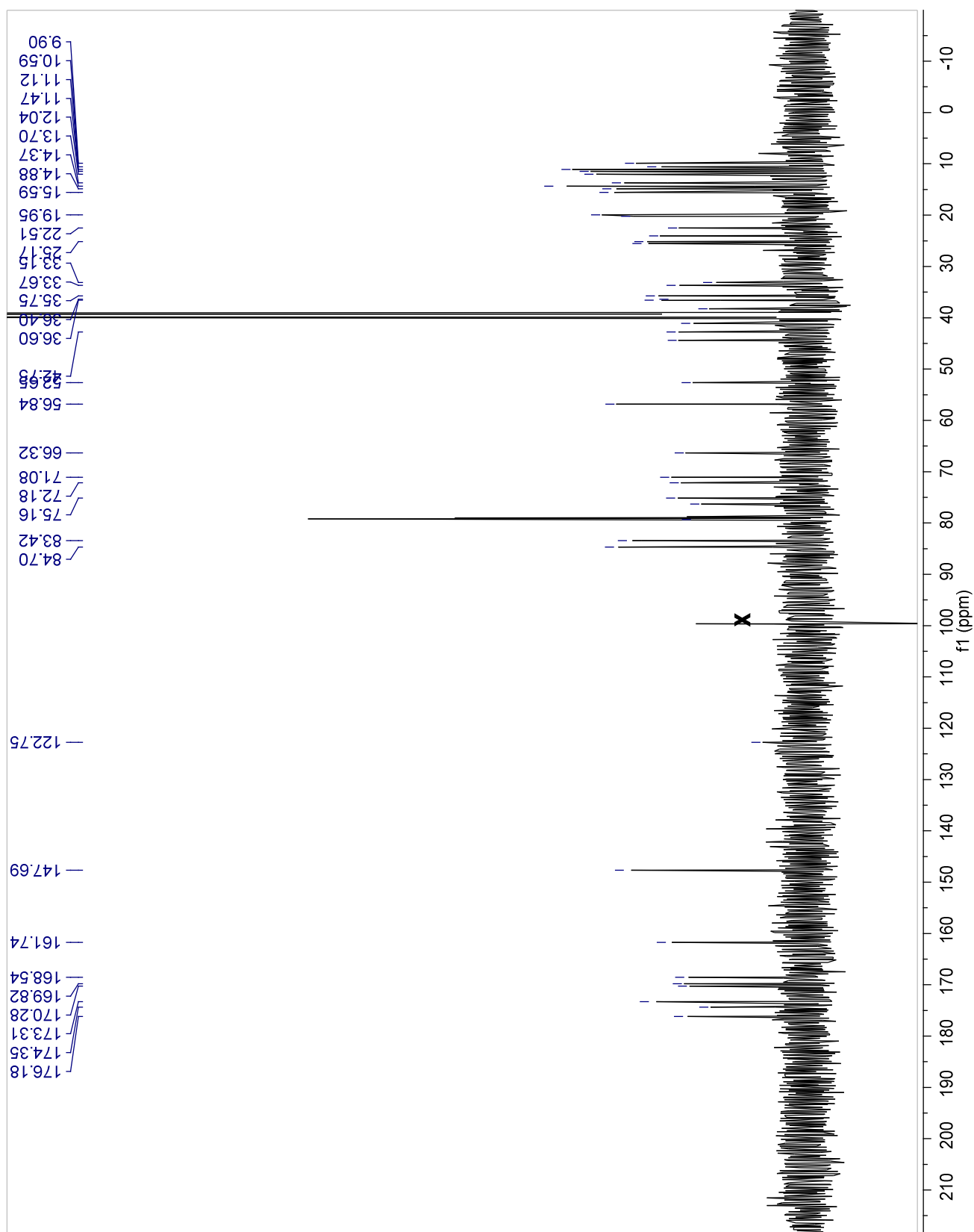
S4. HR ESITOFMS of hoiamide B (2).



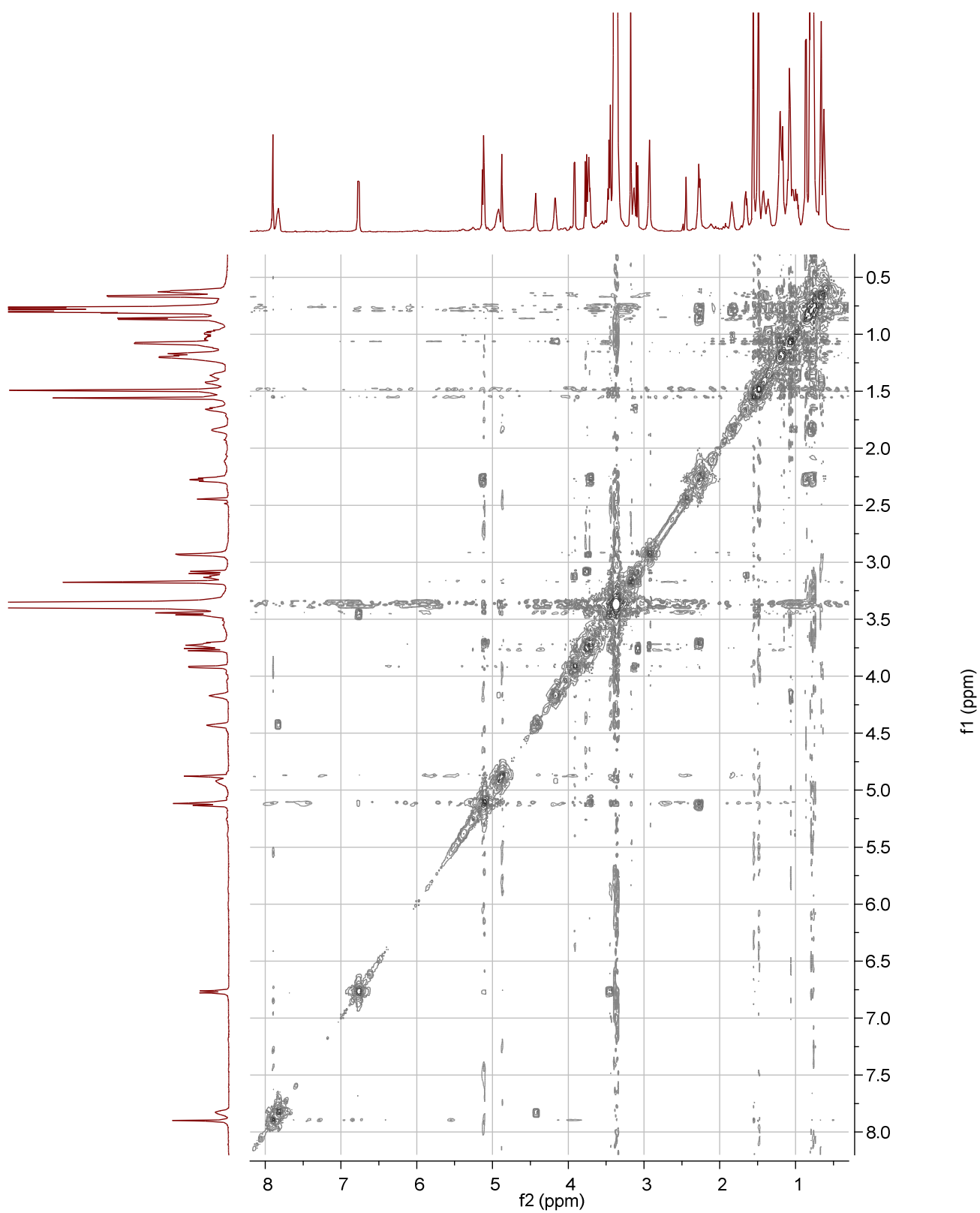
S5. ^1H NMR spectrum of hoiamide B (**2**) (recorded in $\text{DMSO}-d_6$ at 600 MHz).



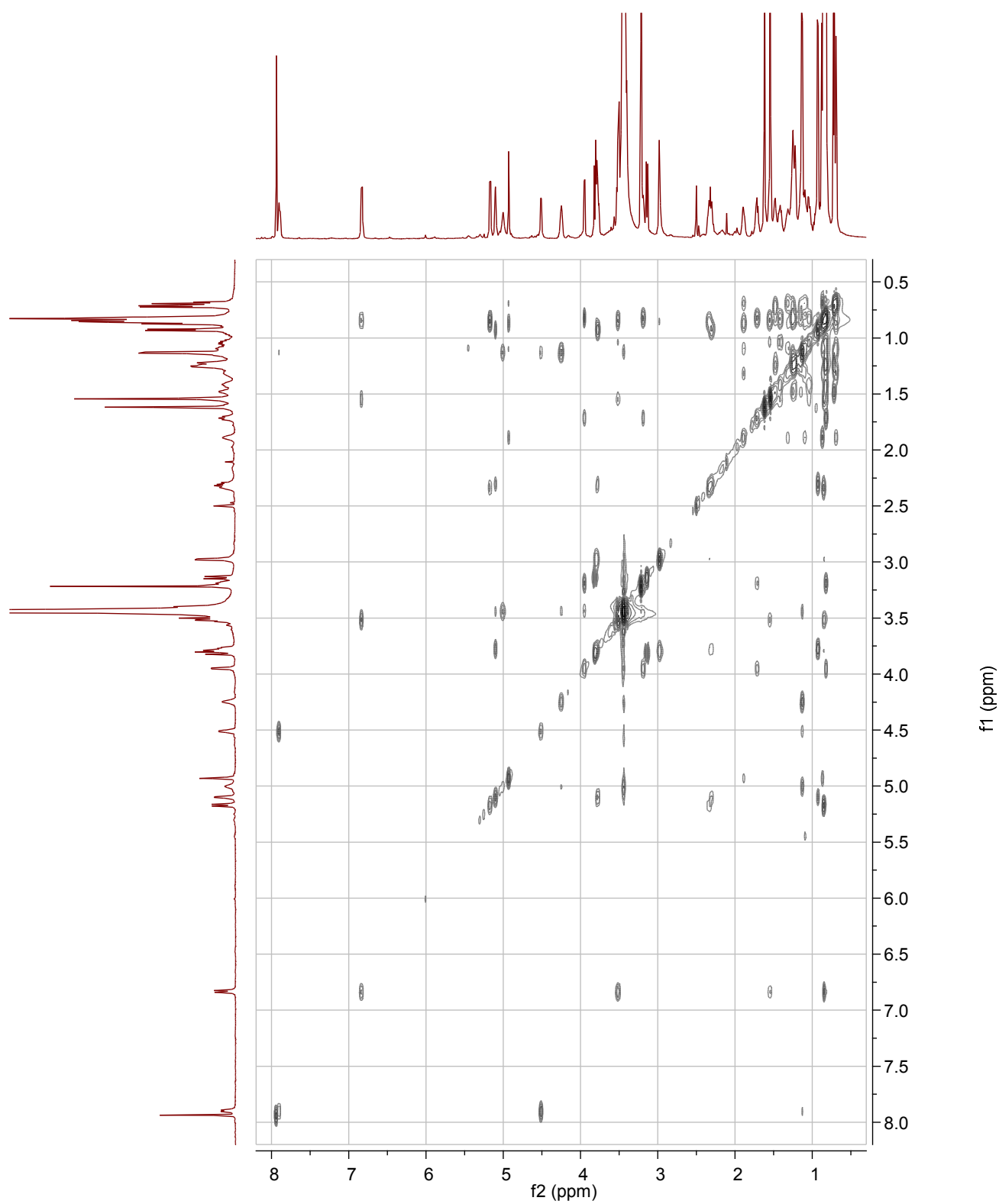
S6. ^{13}C NMR spectrum of hoiamide B (**2**) (recorded in $\text{DMSO}-d_6$ at 150 MHz).



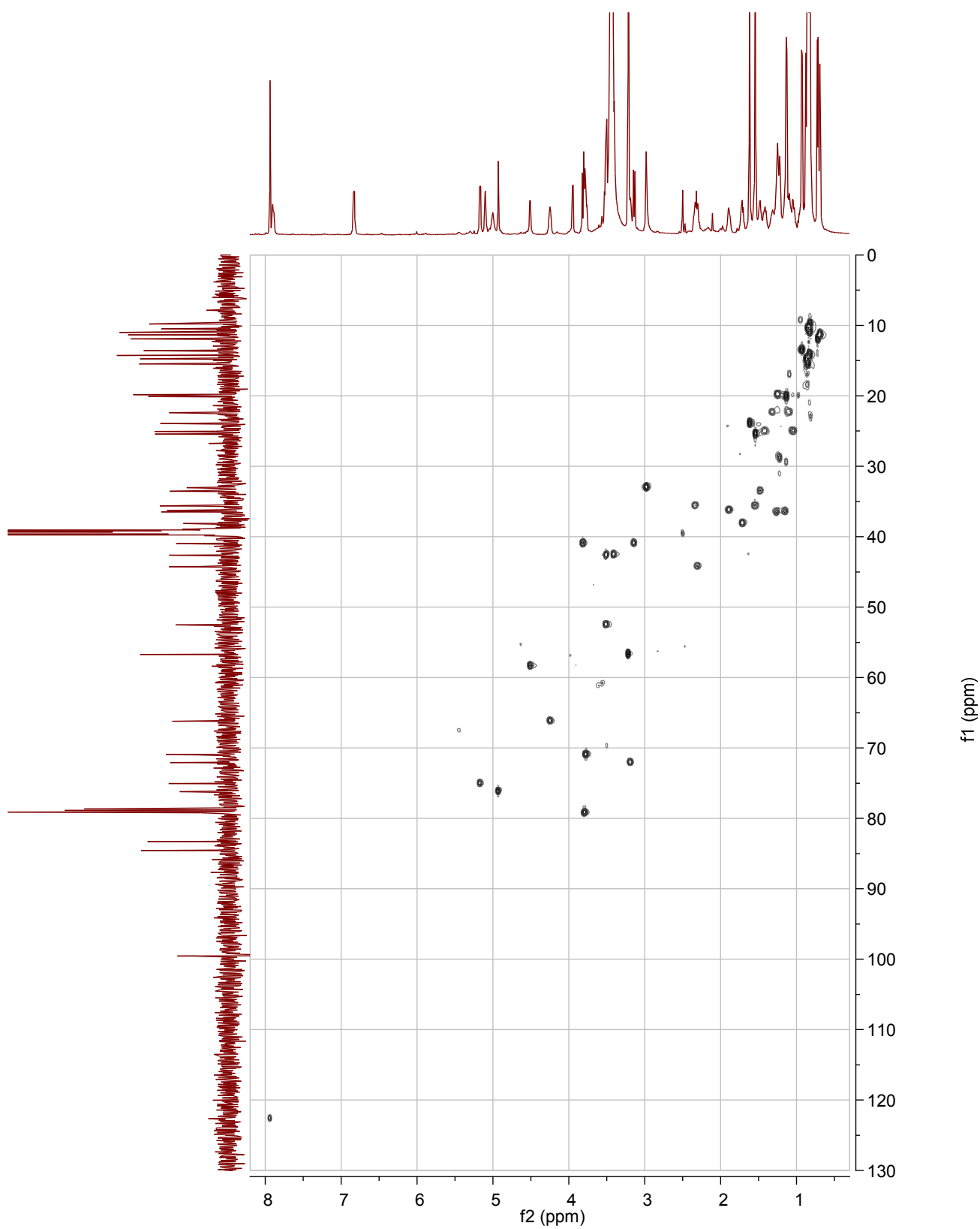
S7. COSY spectrum of hoiamide B (**2**) (recorded in DMSO-*d*₆ at 600 MHz).



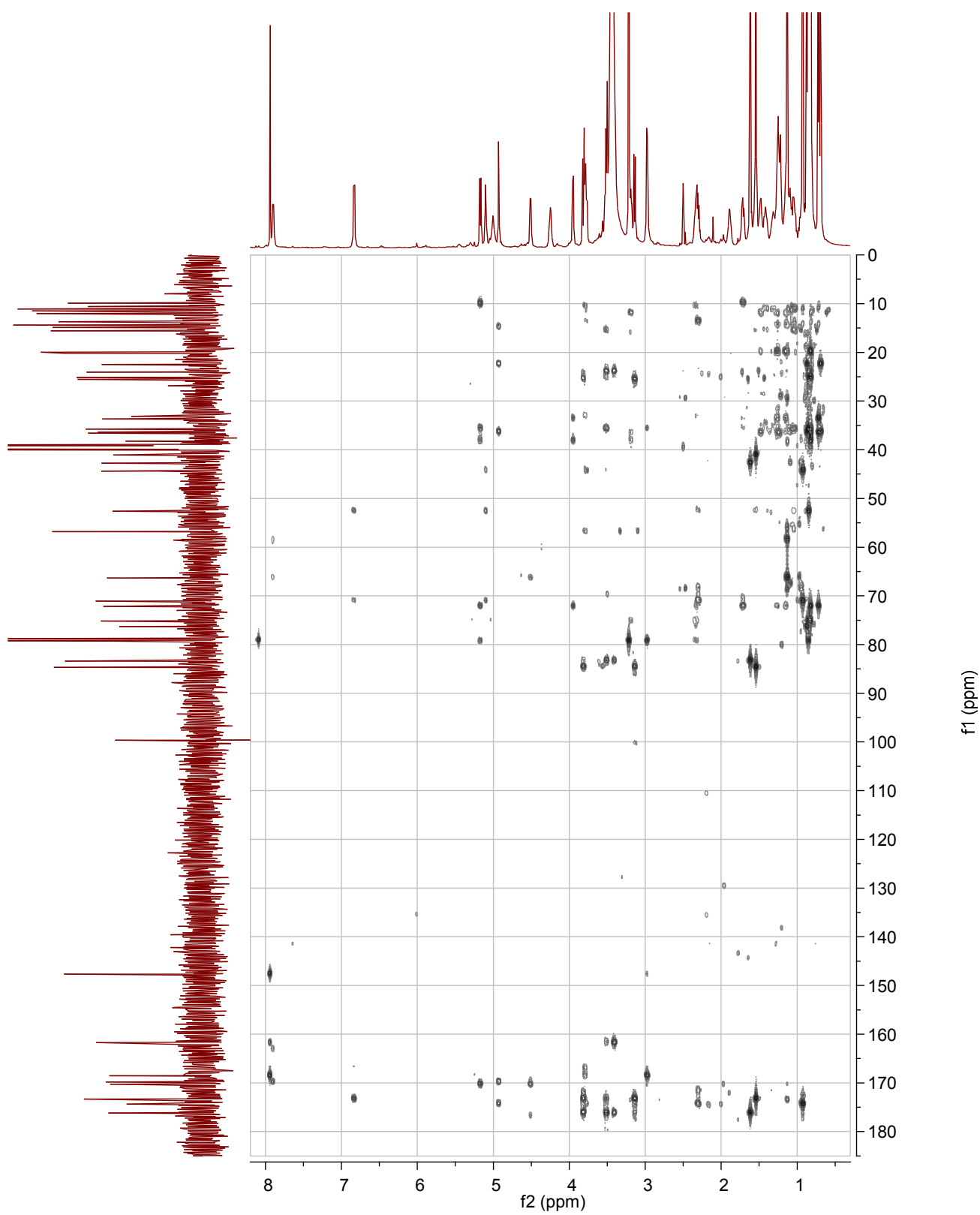
S8. TOCSY spectrum of hoiamide B (**2**) (recorded in DMSO-*d*₆ at 600 MHz).



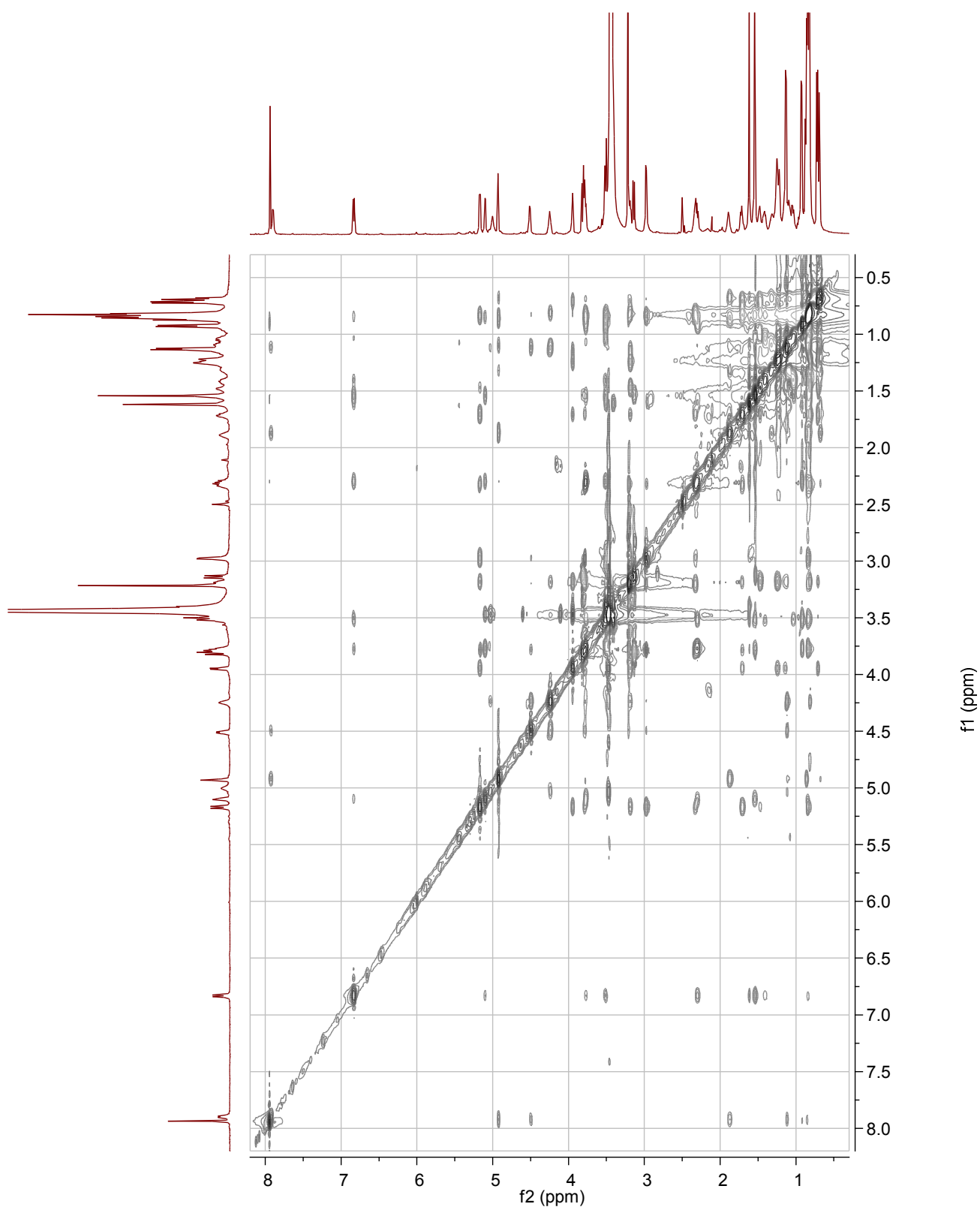
S9. HSQC spectrum of hoiamide B (**2**) (recorded in DMSO- d_6 at 600 MHz).



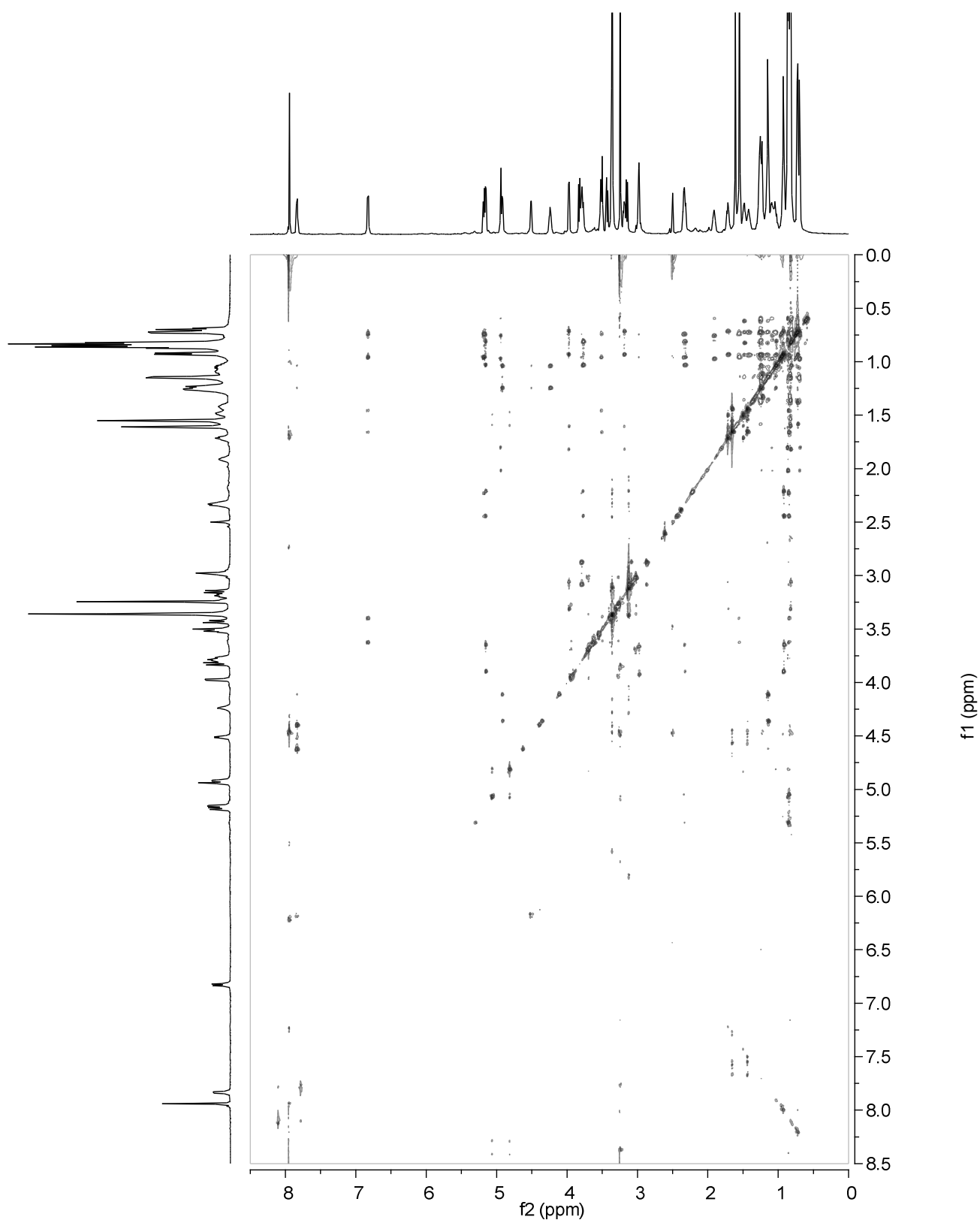
S10. HMBC spectrum of hoiamide B (**2**) (recorded in DMSO- d_6 at 600 MHz).



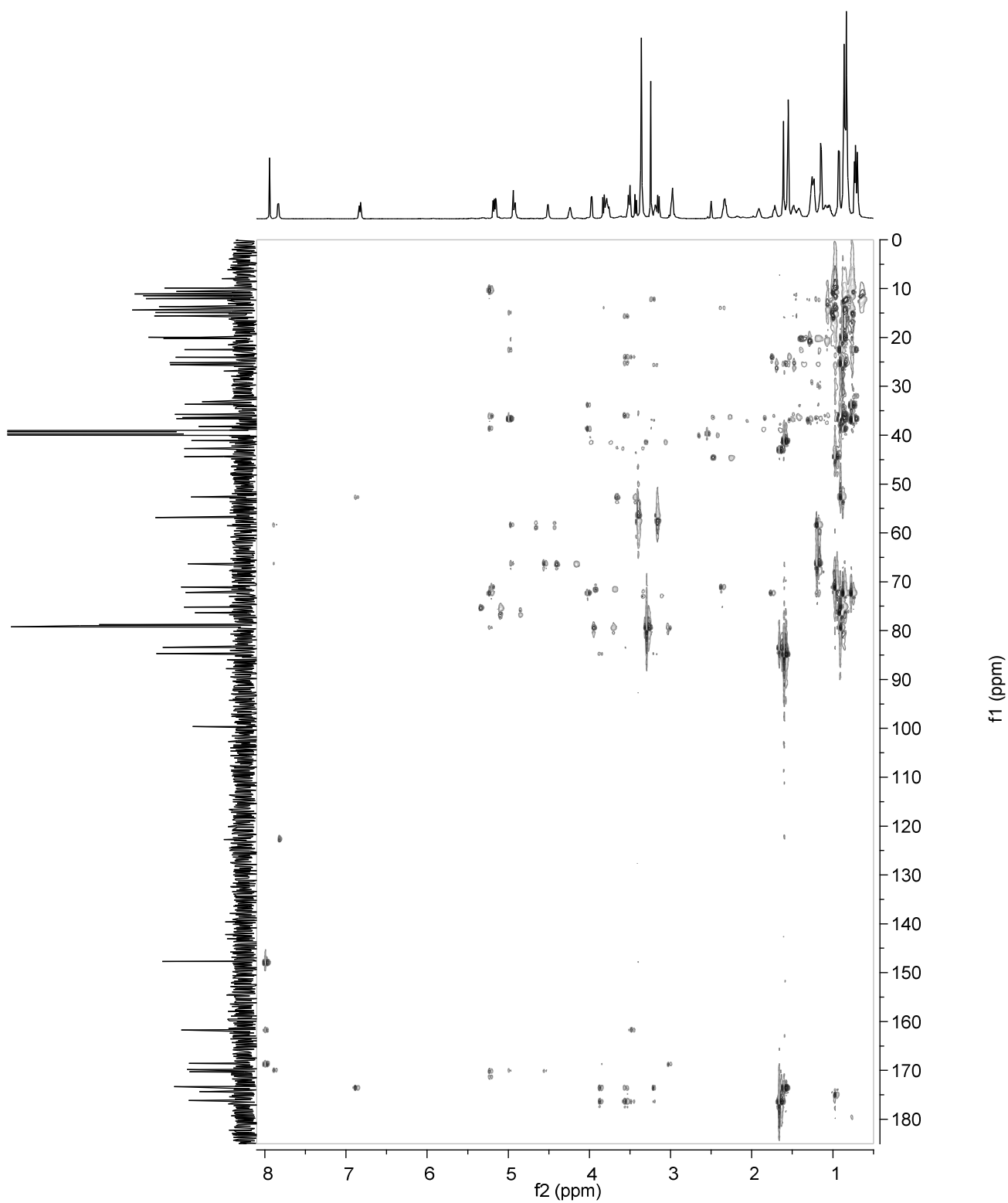
S11. ROESY spectrum of hoiamide B (**2**) (recorded in DMSO-*d*₆ at 600 MHz).



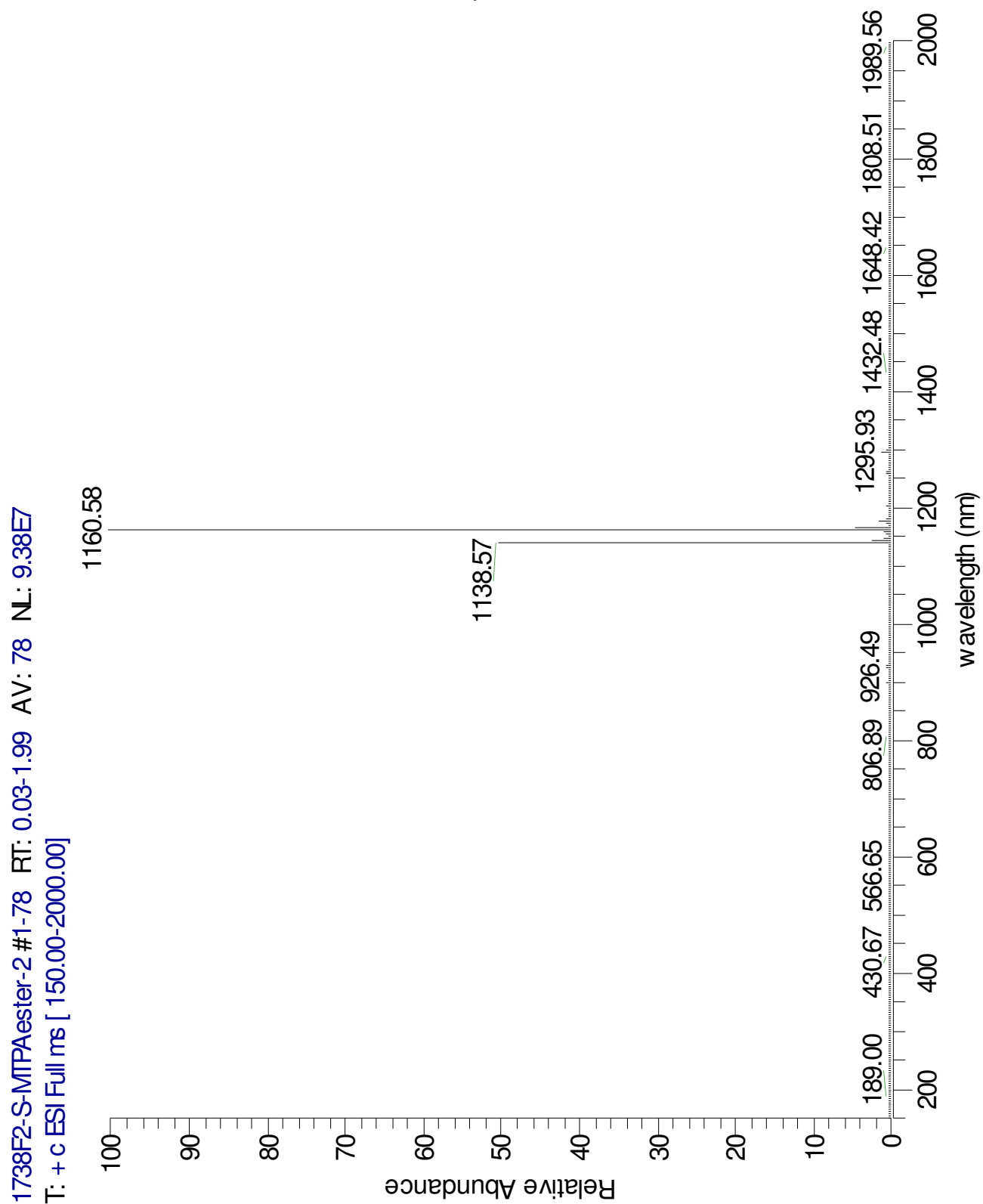
S12. HETLOC spectrum of hoiamide B (**2**) (recorded in DMSO- d_6 at 600 MHz).



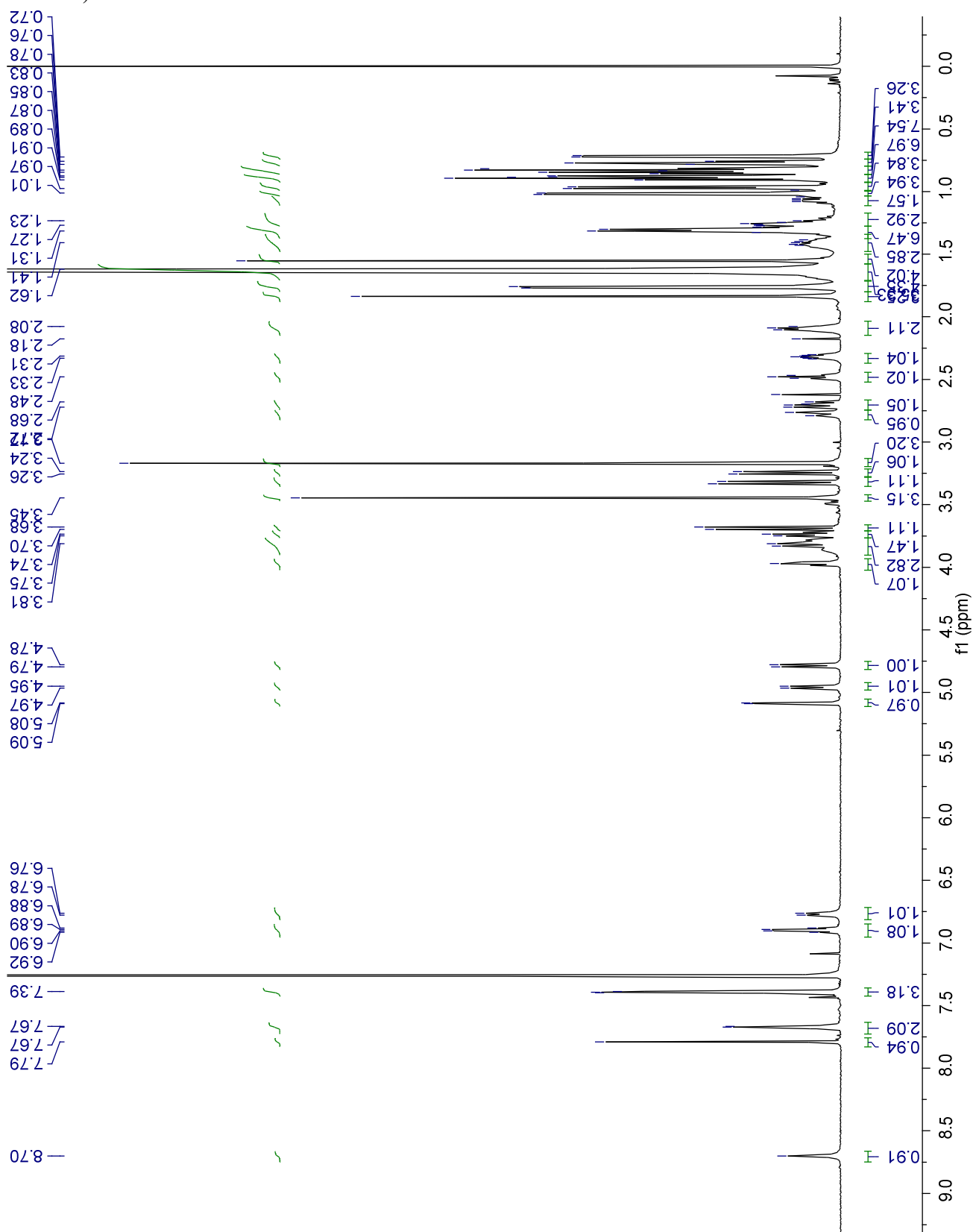
S13. HSQMBBC spectrum of hoiamide B (**2**) (recorded in DMSO-*d*₆ at 600 MHz).



S14. LR ESIMS of 37-(*S*)-MTPA ester of 2,3-dehydrated hoiamide B (**6**).



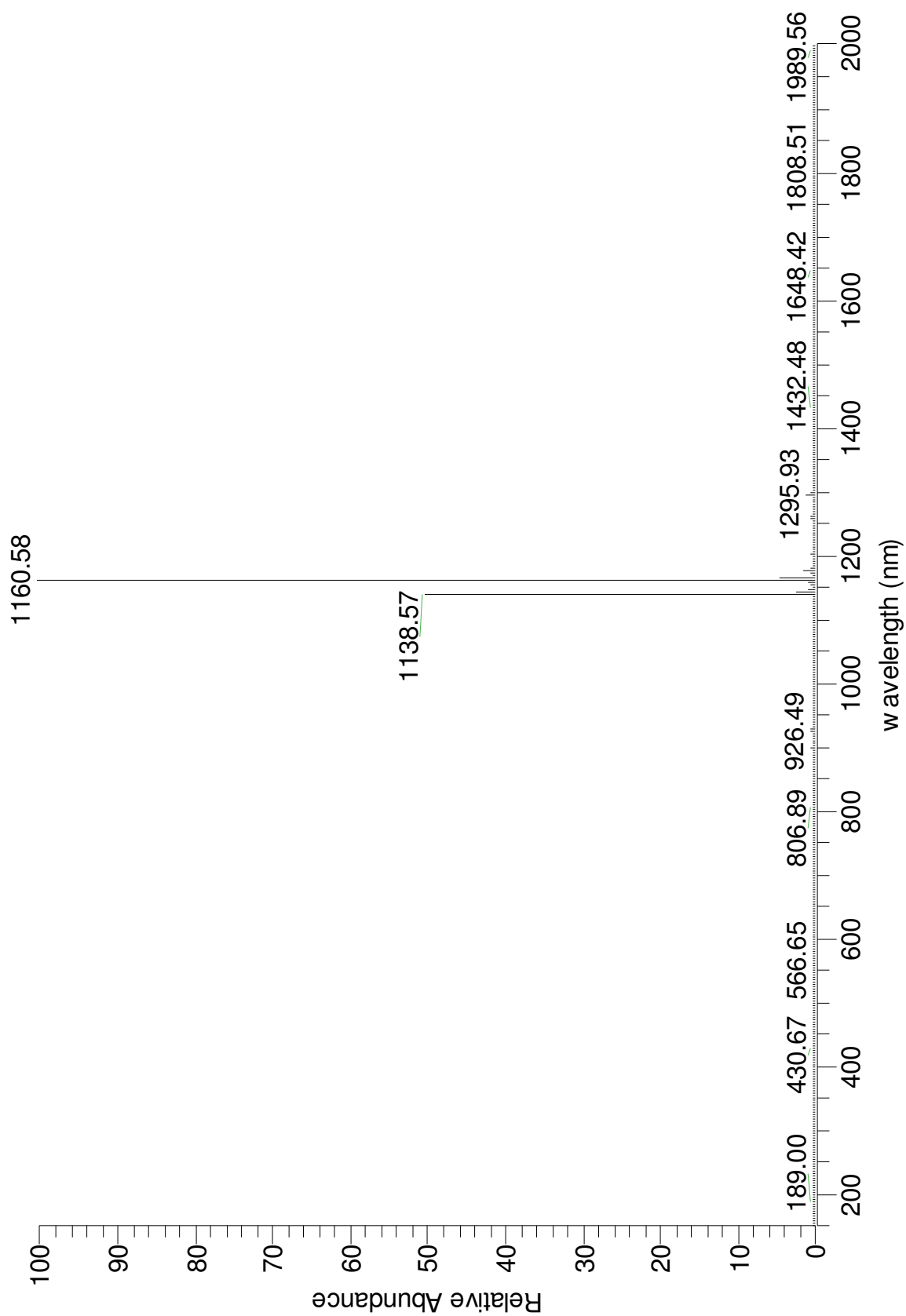
S15. ^1H NMR spectrum of 37-(*S*)-MTPA ester of 2,3-dehydrated hoiamide B (**6**) (recorded in $\text{DMSO}-d_6$ at 600 MHz).



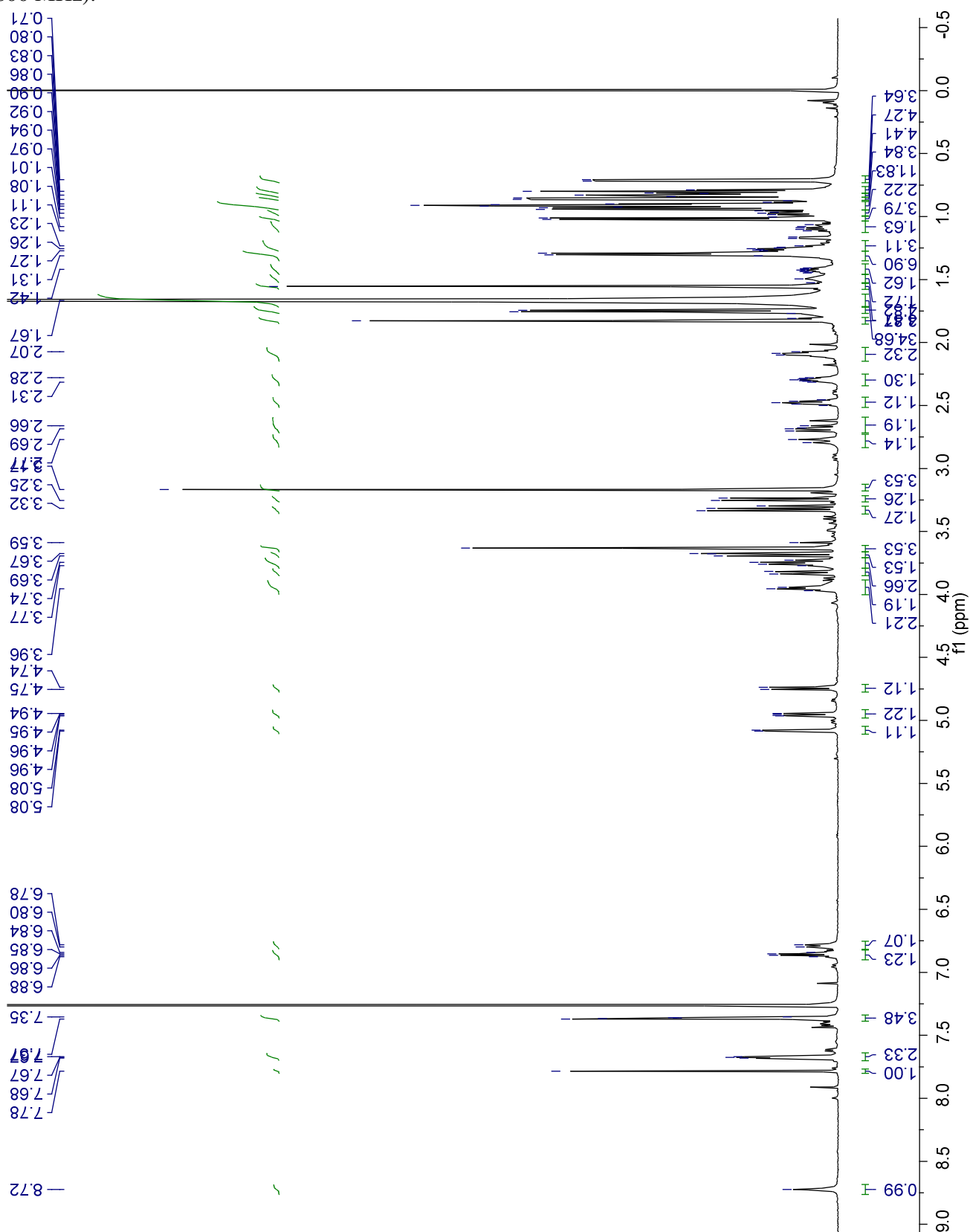
S16. LR ESIMS of 37-(*R*)-MTPA ester of 2,3-dehydrated hoiamide B (7).

1738F2-S-MTPAester-2 #1-78 RT: 0.03-1.99 AV: 78 NL: 9.38E7

T: + c ESI Full ms [150.00-2000.00]

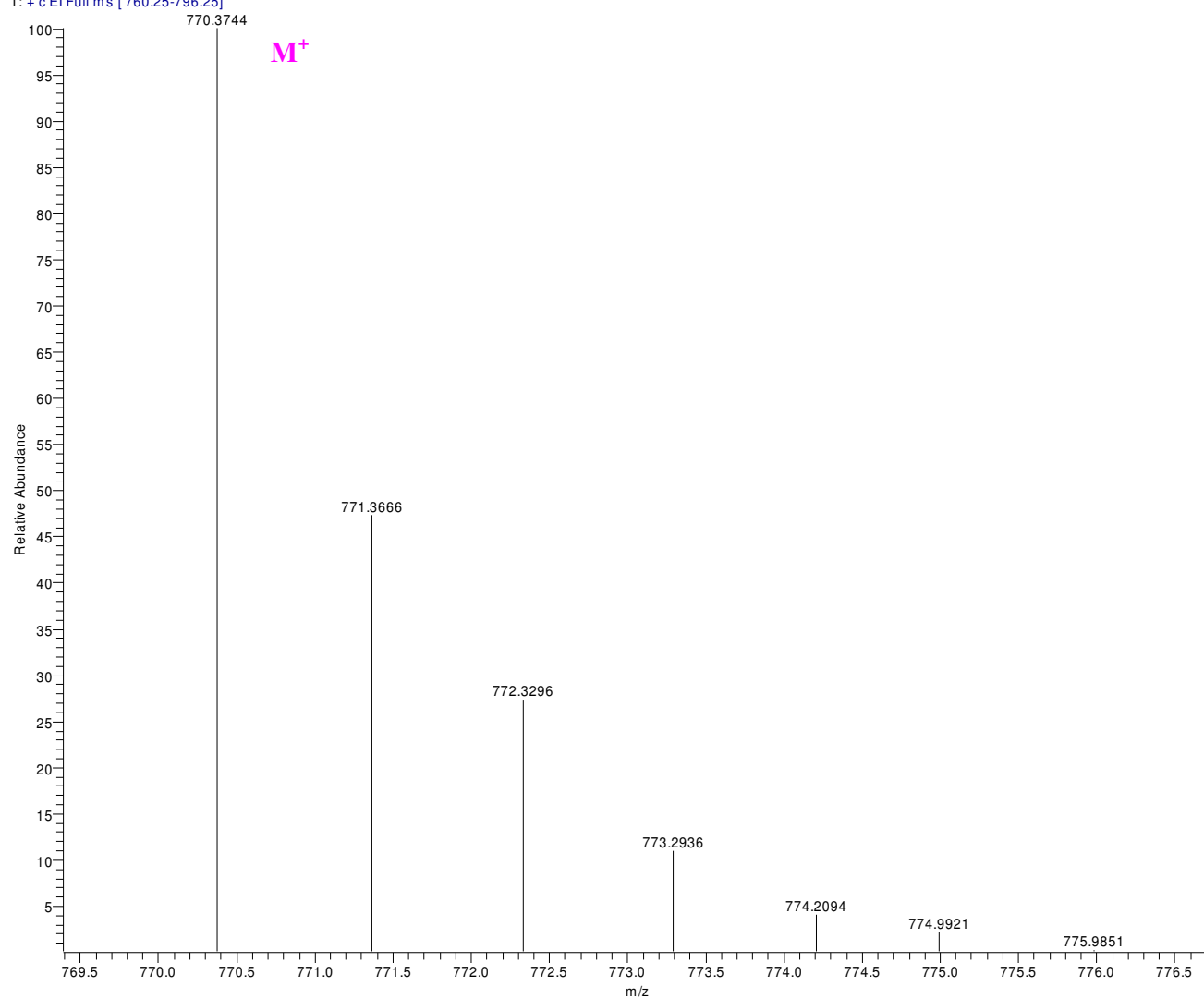


S17. ^1H NMR spectrum of 37-(*R*)-MTPA ester of 2,3-dehydrated hoiamide B (**7**) (recorded in $\text{DMSO}-d_6$ at 600 MHz).



S18. HR EIMS of hoiamide C (3)

07_10_2006-cfs01-b-c1 #70-76 RT: 5.63-5.71 AV: 7 NL: 9.02E5
T: + c EI Full ms [760.25-796.25]



S19. ^1H NMR spectroscopic data table of natural hoiamide C (**3**) in pyridine- d_5 at 700 MHz and ^1H - ^1H coupling constants based on spectral simulation .

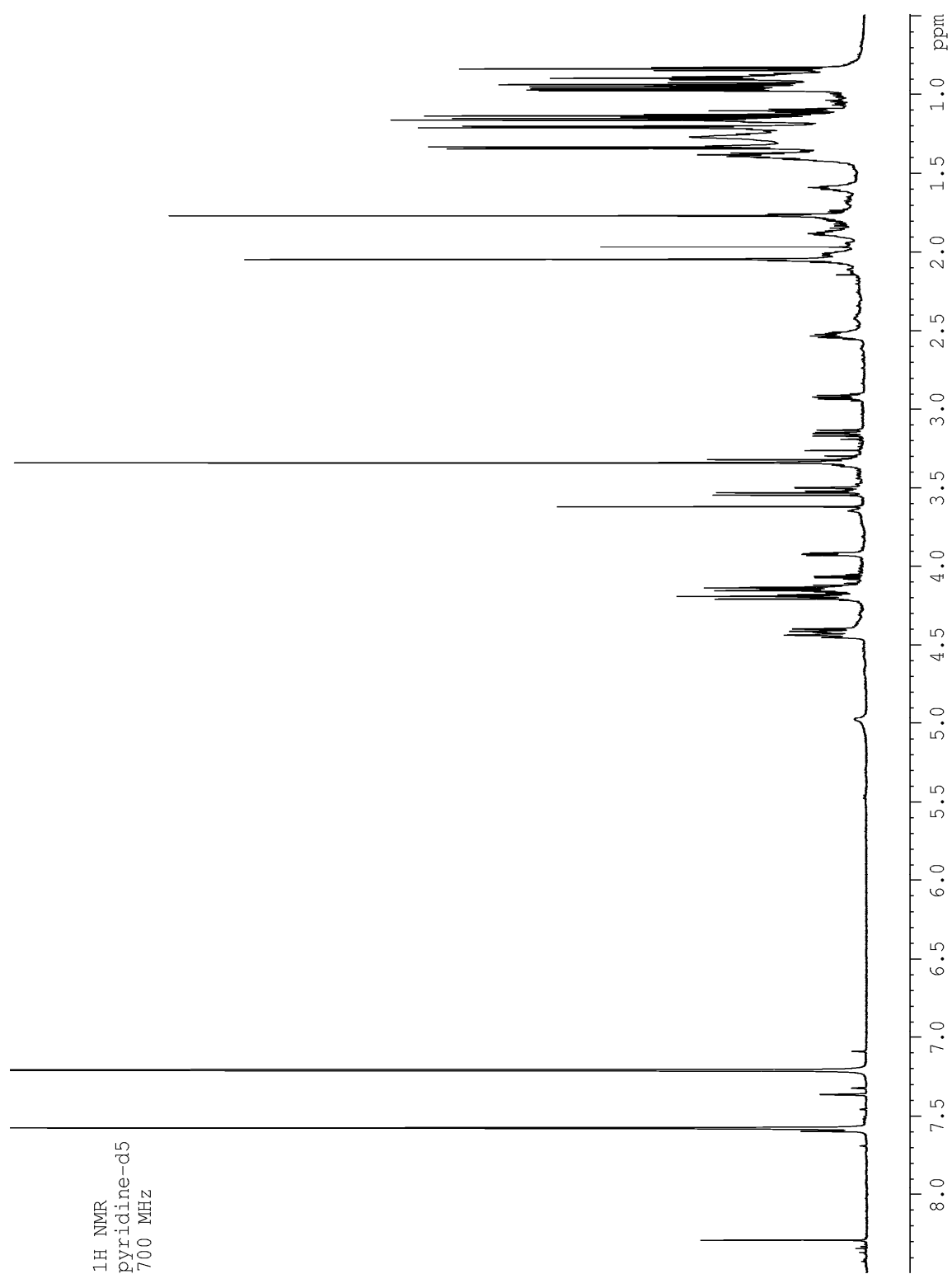
Residue	Position	δ_H multi (J in Hz)
Ahdhe	1	
	2	2.90, dddd (9.7, 7.1, 7.1, 7.1)
	3	4.43, br d (9.7)
	4	4.13, br t (9.7)
		NH 7.57, d (9.7)
	5	2.00, ddddd (8.8, 6.7, 6.7, 6.7, 3.5)
	6a	1.76, ddddd (13.3, 7.5, 7.5, 7.5, 3.5)
	6b	1.37, ddddd (13.3, 8.8, 7.5, 7.5, 7.5)
	7	0.91, t (7.5)
	8	0.95, d (6.7)
MoCys1	9	1.32, d (7.0)
	10	
	11	
	12a	4.18, d (11.5)
	12b	3.31, d (11.5)
MoCys2	13	1.75, s
	14	
	15	
	16a	4.13, d (11.3)
	16b	3.52, d (11.3)
MoCys3	17	2.03, s
	18	
	19	
Dmetua	20	8.27, s
	21	
	22a	3.49, dd (15.4, 2.2)
	22b	3.13, dd (15.4, 10.6)
	23	4.41, ddd (10.6, 3.5, 2.2)
	24	2.50, ddddd (10.3, 7.0, 7.0, 7.0, 3.5)
	25	4.39, dd (10.3, 1.3)
	26	2.03, ddddd (7.1, 6.9, 6.9, 6.9, 1.2)
	27	3.90, dd (7.1, 4.5)
	28	1.86, quintet (6.0)
	29a	1.57, m
	29b	1.36, m
	30	1.37, m
	31	0.87, t (7.0)
	32	1.14, d (6.7)
	33	1.19, d (6.9)
	34	0.93, d (7.0)
	35	3.32, s
	36a	4.17, dddd (10.8, 7.1, 7.1, 7.1, 7.1)
	36b	4.11, dddd (10.8, 7.1, 7.1, 7.1, 7.1)
	37	1.11, t (7.1)

S20. NMR spectroscopic data table of natural hoiamide C (**3**) in CDCl₃ at 500 MHz (¹H) and 125 MHz (¹³C).

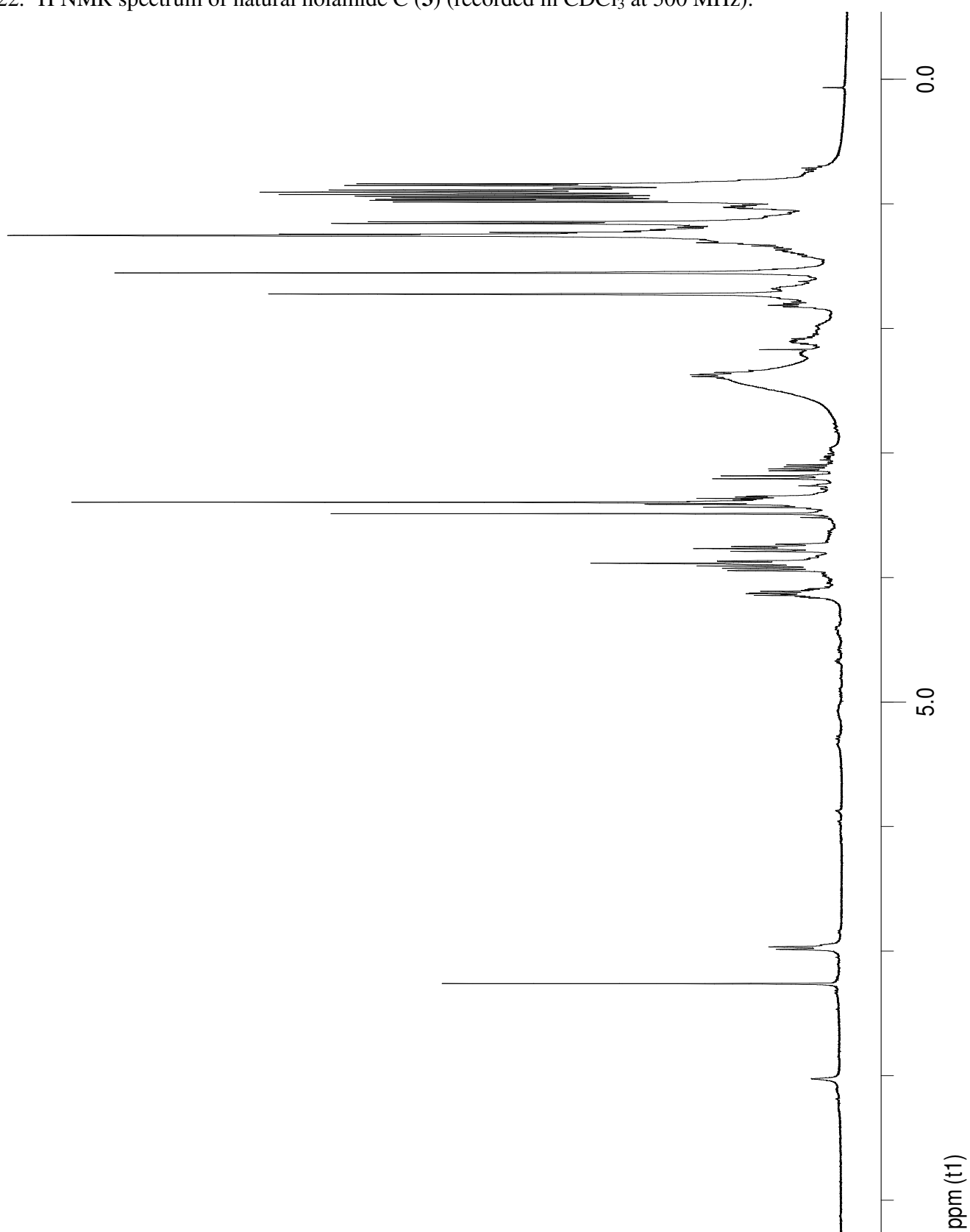
Residue	Position	δ_C	δ_H multi (<i>J</i> in Hz)	HMBC ^a	COSY
Ahdhe	1	176.5			
	2	43.5	2.37, dddd (9.2, 7.2, 7.2, 7.2)	1, 3, 4, 9	3, 9
	3	72.1	3.93, d (9.3)	1, 2, 9	2, 4
	4	53.6	3.75, t (8.5)	2, 5, 6, 8, 10	3, 5, NH
			NH 6.95, d (9.8)	4, 10	4
	5	36.2	1.75, m	3, 4, 6, 7, 8	4, 6a, 6b, 8
	6a	25.6	1.17, m	4, 8, 7	5, 6b, 7
	6b		1.54, m	4, 8, 7	5, 6a, 7
	7	11.1	0.90, t (8.0)	6,	6a, 6b
MoCys1	8	15.8	0.98, d (6.7)	4, 6	5
	9	14.0	1.15, d (7.1)	1, 2, 3	2
	10	174.3			
	11	84.8			
	12a	41.7	3.20, d (11.6)	10, 11, 13, 14	12b
MoCys2	12b		3.77, d (11.5)	10, 11, 13, 14	12a
	13	25.3	1.55, s	11, 10	
	14	177.6			
	15	83.4		16, 17	
	16a	42.9	3.42, d (11.4)	14, 17, 18	16b
MoCys3	16b		3.89, m	14, 17, 18	16a
	17	25.7	1.72, s	14	
	18	164.4			
	19	147.1			
	20	122.0	7.95, s	21	
Dmetua	21	169.0			
	22a	34.0	3.12, dd (15.8, 7.5)	21, 23, 24	22b, 23
	22b		3.36, dd (15.8, 3.8)	21, 23, 24	22a, 23
	23	82.2	3.89, m	21, 22, 24, 25, 34, 35	22a, 22b, 24, 35
	24	37.7	2.10, ddddd (9.9, 6.8, 6.8, 6.8, 5.2) ^b	22, 23, 25, 34	23, 25, 34
	25	72.4	3.87, m	23, 24, 33, 34	24, 26
	26	35.6	1.81, m	25, 27, 33	25, 27, 33
	27	78.6	3.39, m	25, 26, 32, 33	26, 28
	28	35.2	1.67, m	26, 27, 32, 29	27, 29a, 29b, 32
	29a	36.1	1.15, m	27, 28, 30, 31, 32	28, 30a, 30b, 31
	29b		1.30, m	27, 28, 30, 31, 32	28, 30a, 30b, 31
	30a	20.0	1.32, m	28, 29, 31	29a, 29b, 30b, 31
	30b		1.38, m	28, 29, 31	29a, 29b, 30a, 31
	31	14.4	0.89, t (7.3)	30	30a, 30b
	32	14.2	0.93, d (6.8)	27	28
	33	10.1	0.96, d (7.0)	25, 26, 27	26
	34	10.8	0.85, d (6.9)	23, 24	24
	35	57.2	3.39, s	23	23
	36	60.9	4.12, m	1, 37	37
	37	14.1	1.24, t (7.0)	36	36

^aProton showing long-range correlation to indicated carbon. ^bObtained by spectral simulation.

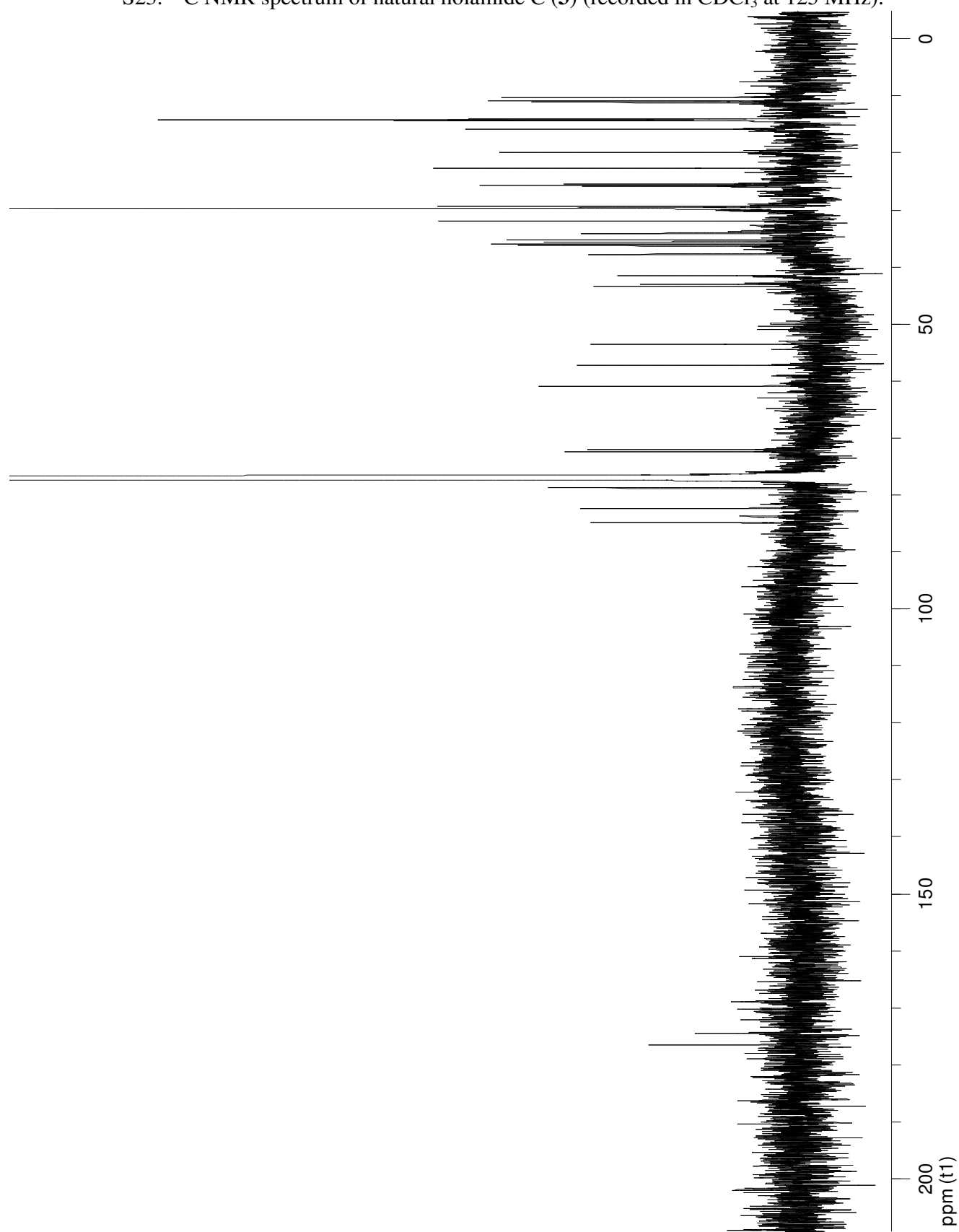
S21. ^1H NMR spectrum of natural hoiamide C (**3**) (recorded in pyridine- d_5 at 700 MHz).



S22. ^1H NMR spectrum of natural hoiamide C (**3**) (recorded in CDCl_3 at 500 MHz).

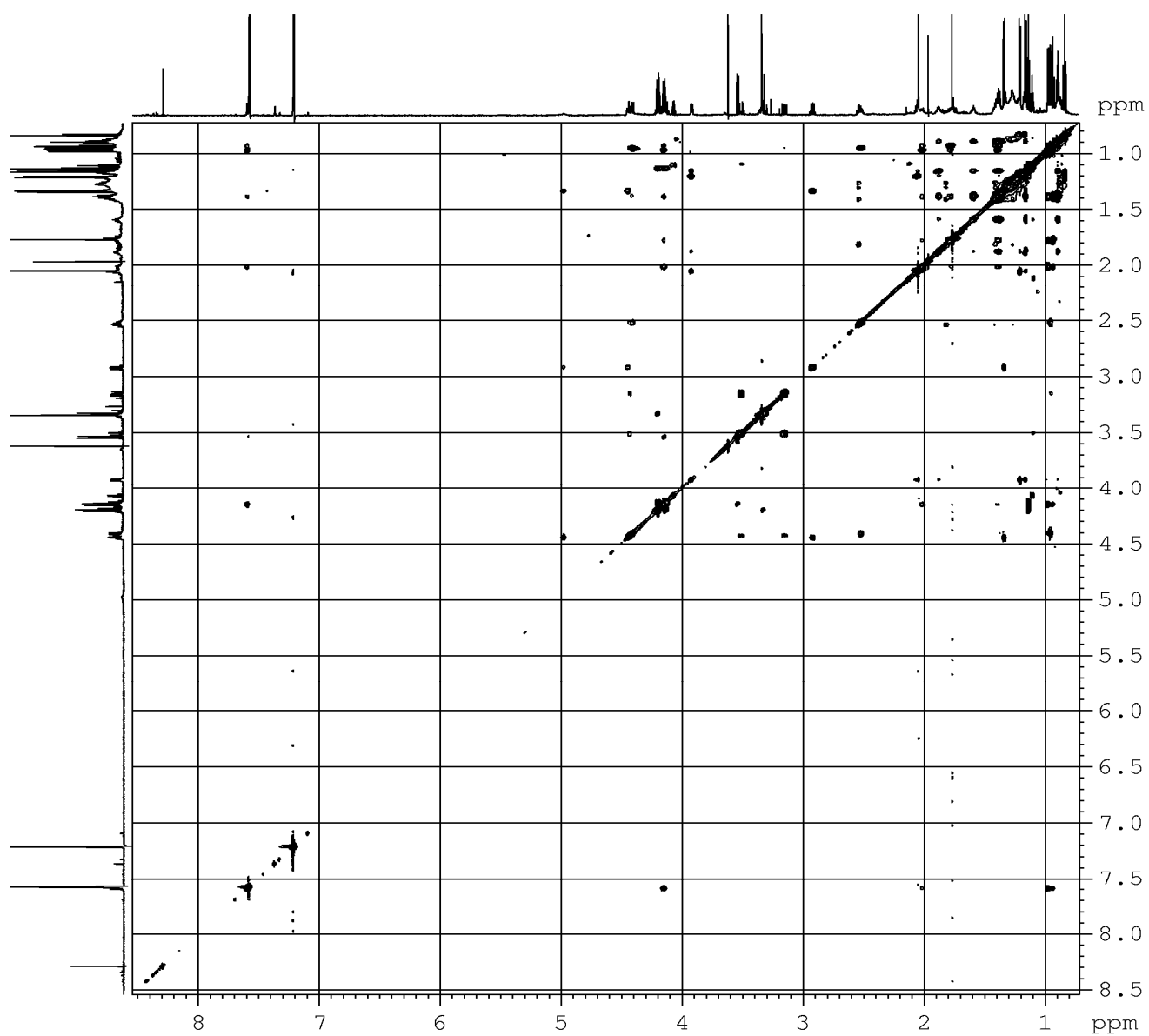


S23. ^{13}C NMR spectrum of natural hoiamide C (**3**) (recorded in CDCl_3 at 125 MHz).

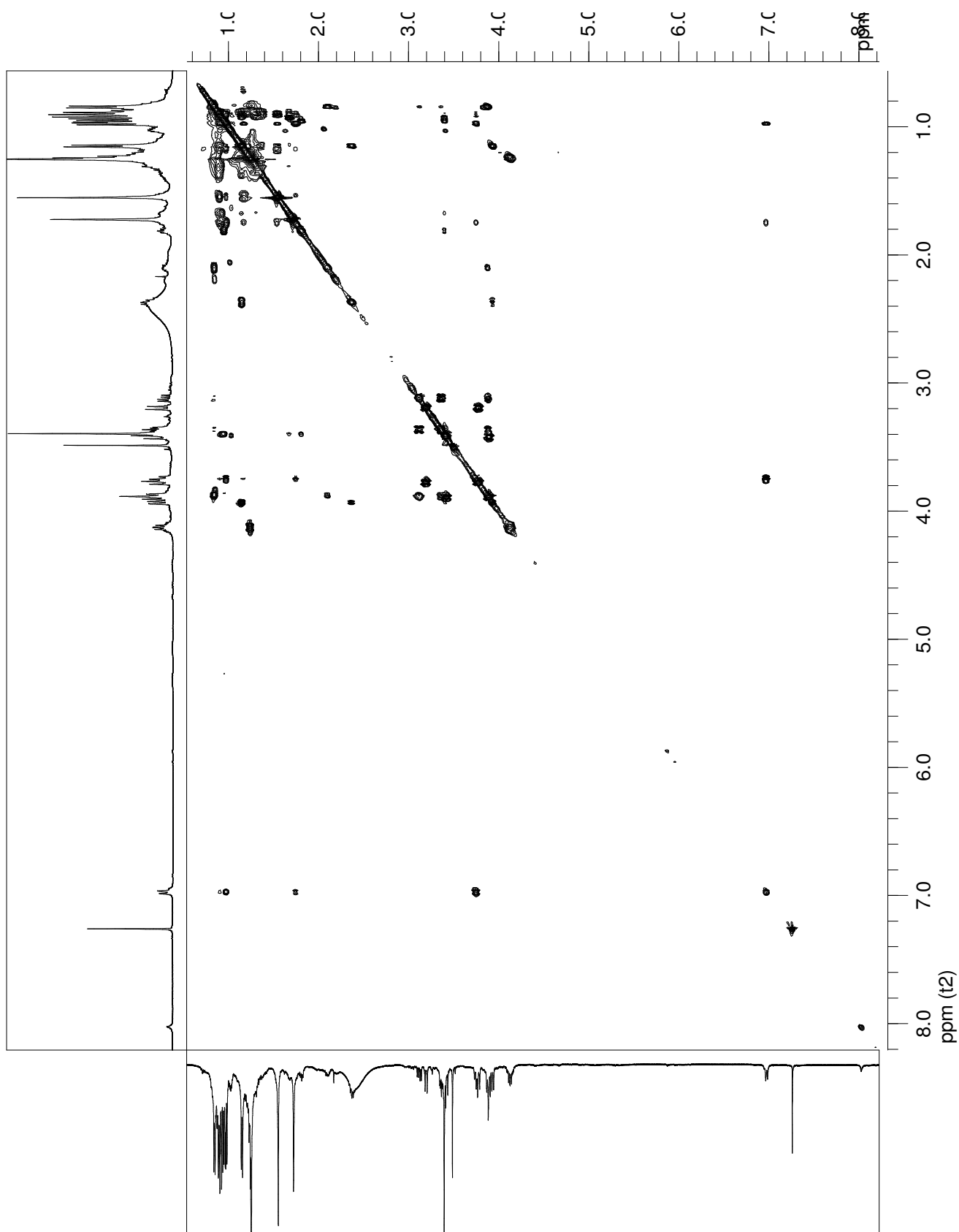


S24. zTOCSY spectrum of natural hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz).

zTOCSY
pyridine-*d*₅
700 MHz

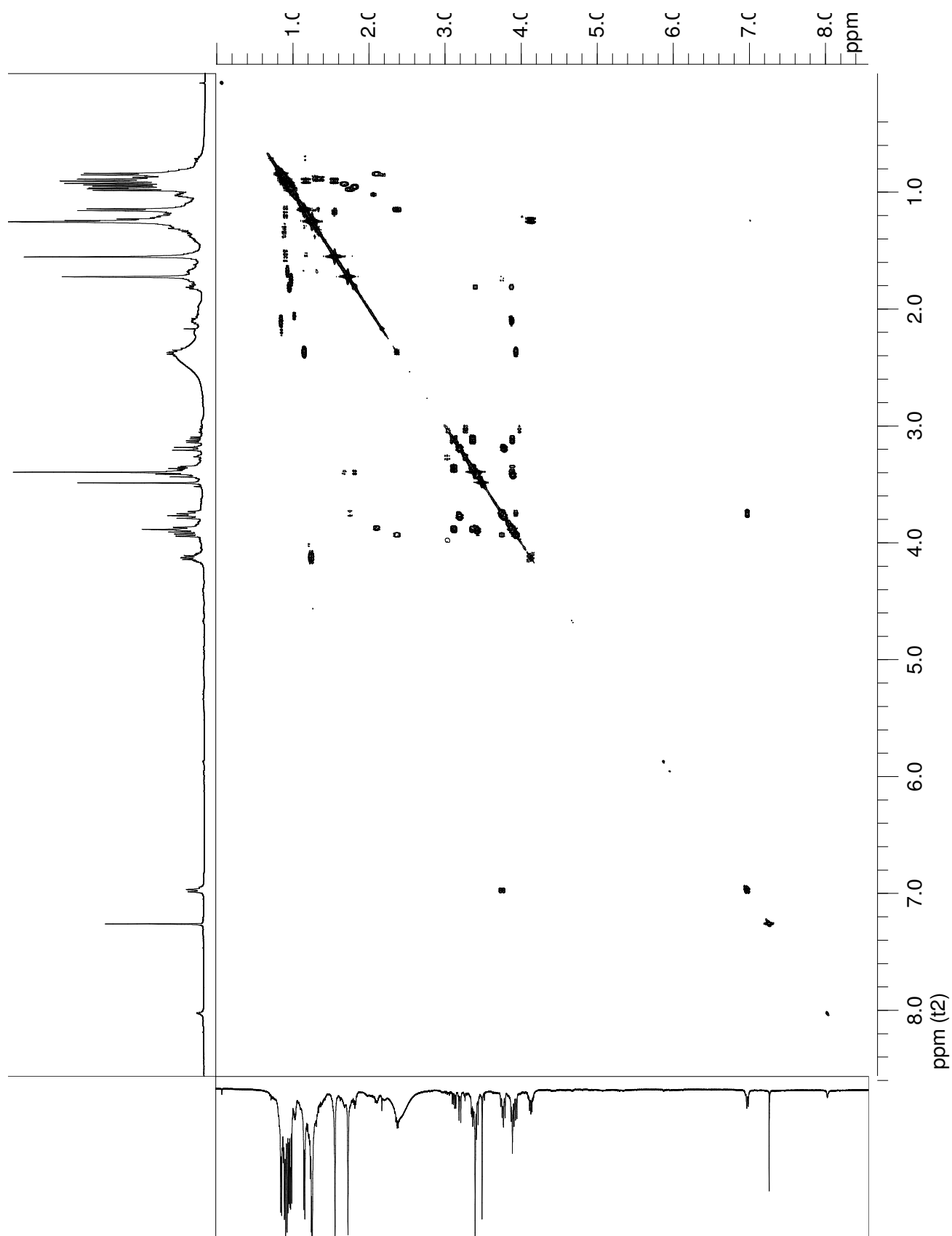


S25. TOCSY spectrum of natural hoiamide C (**3**) (recorded in CDCl₃ at 500 MHz).



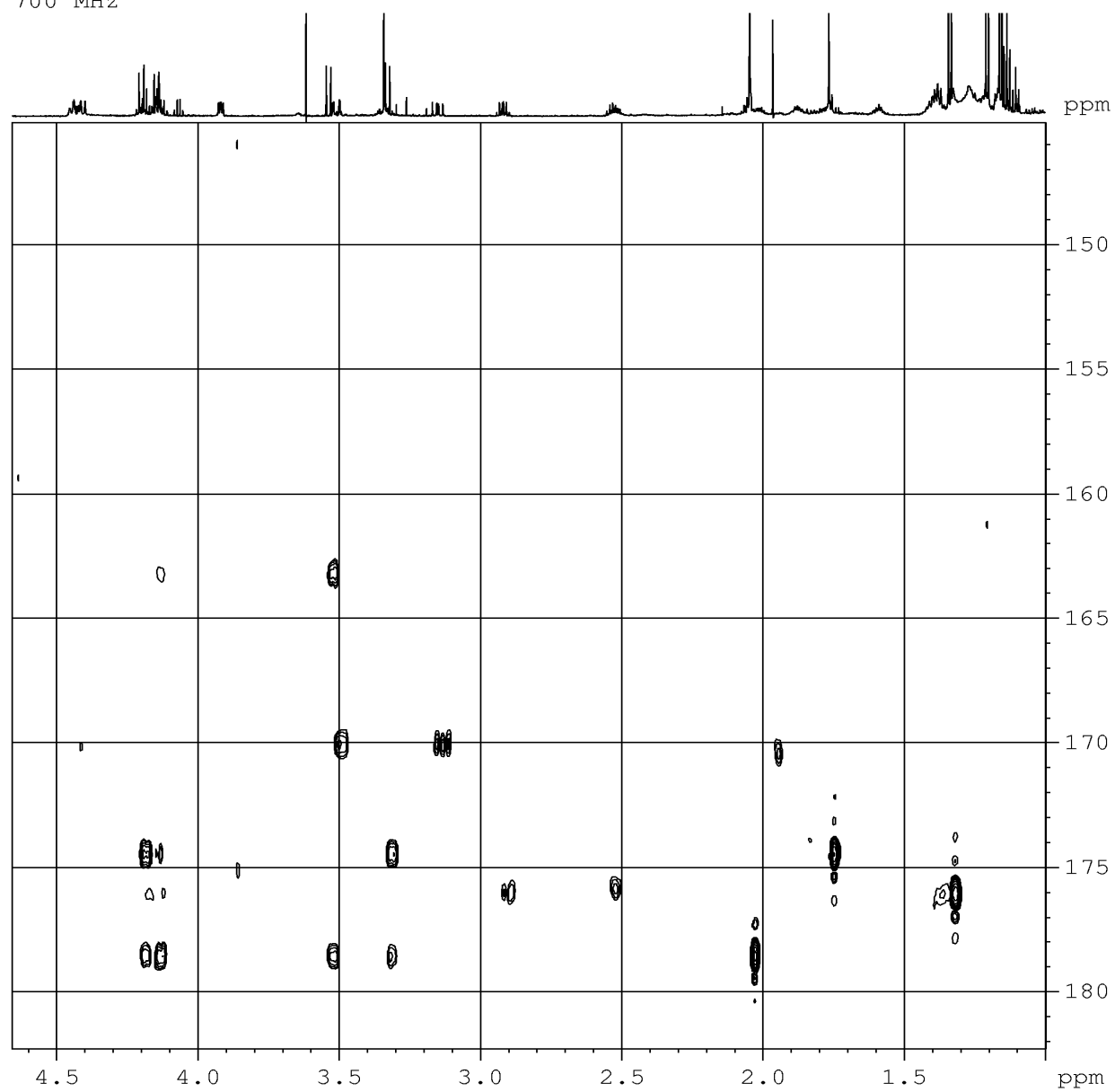
COSY
 pyridine- d_5
 700 MHz

S27. COSY spectrum of natural hoiamide C (**3**) (recorded in CDCl₃ at 500 MHz).



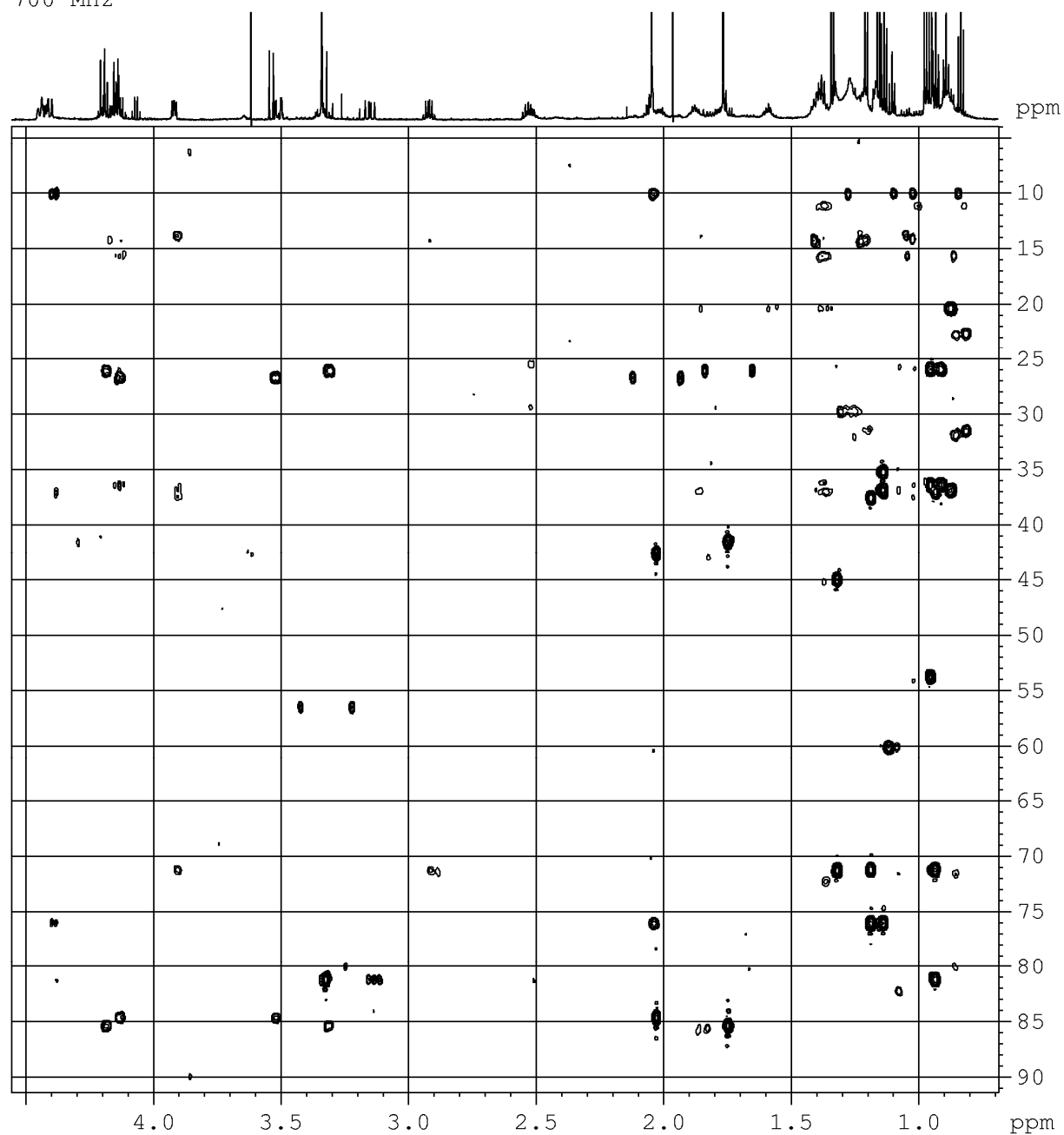
S28. HMBC spectrum of natural hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz).

gHMBC
pyridine-*d*₅
700 MHz



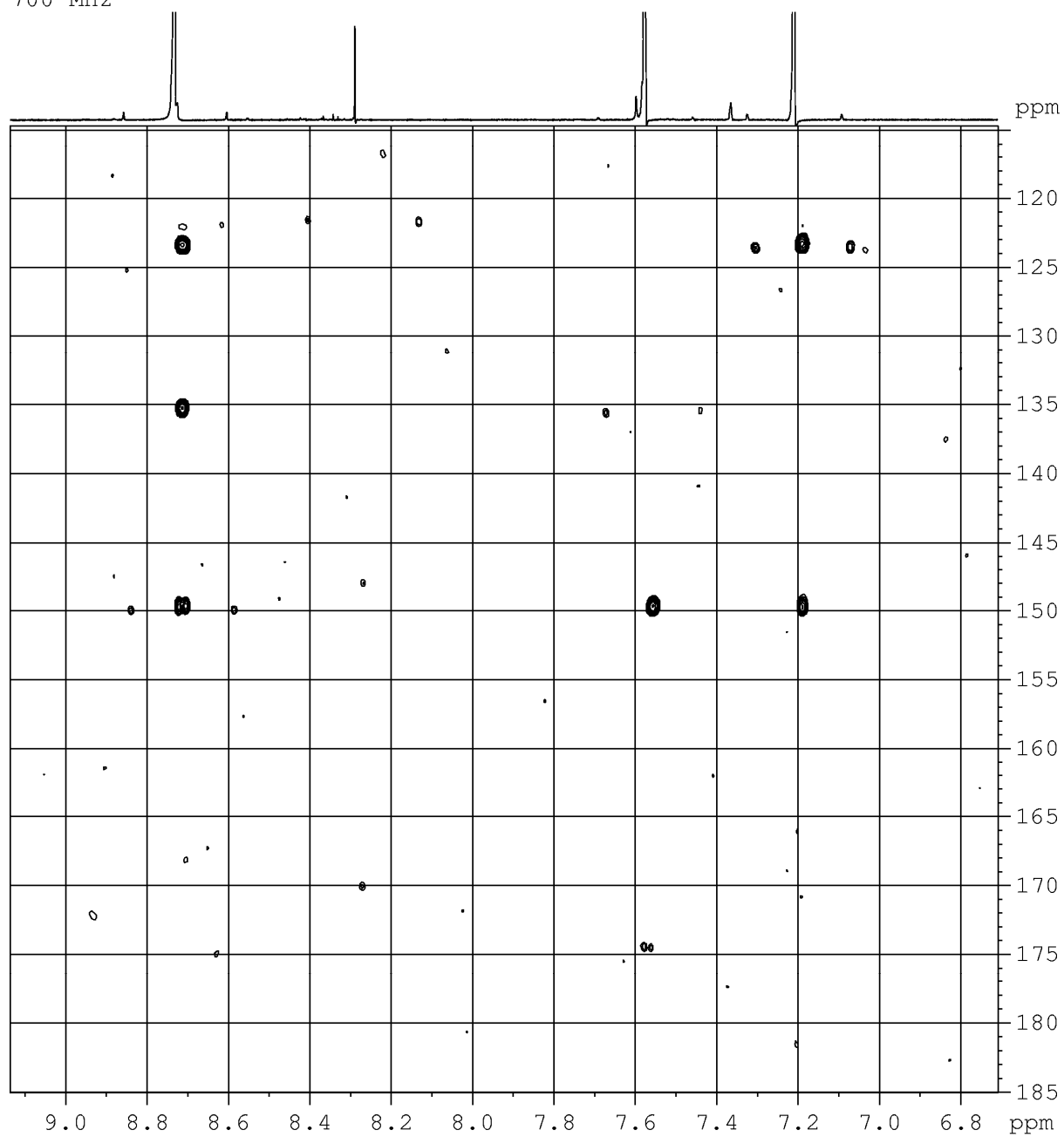
S29. HMBC spectrum of natural hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz) (Cont.).

gHMBC
pyridine-*d*₅
700 MHz

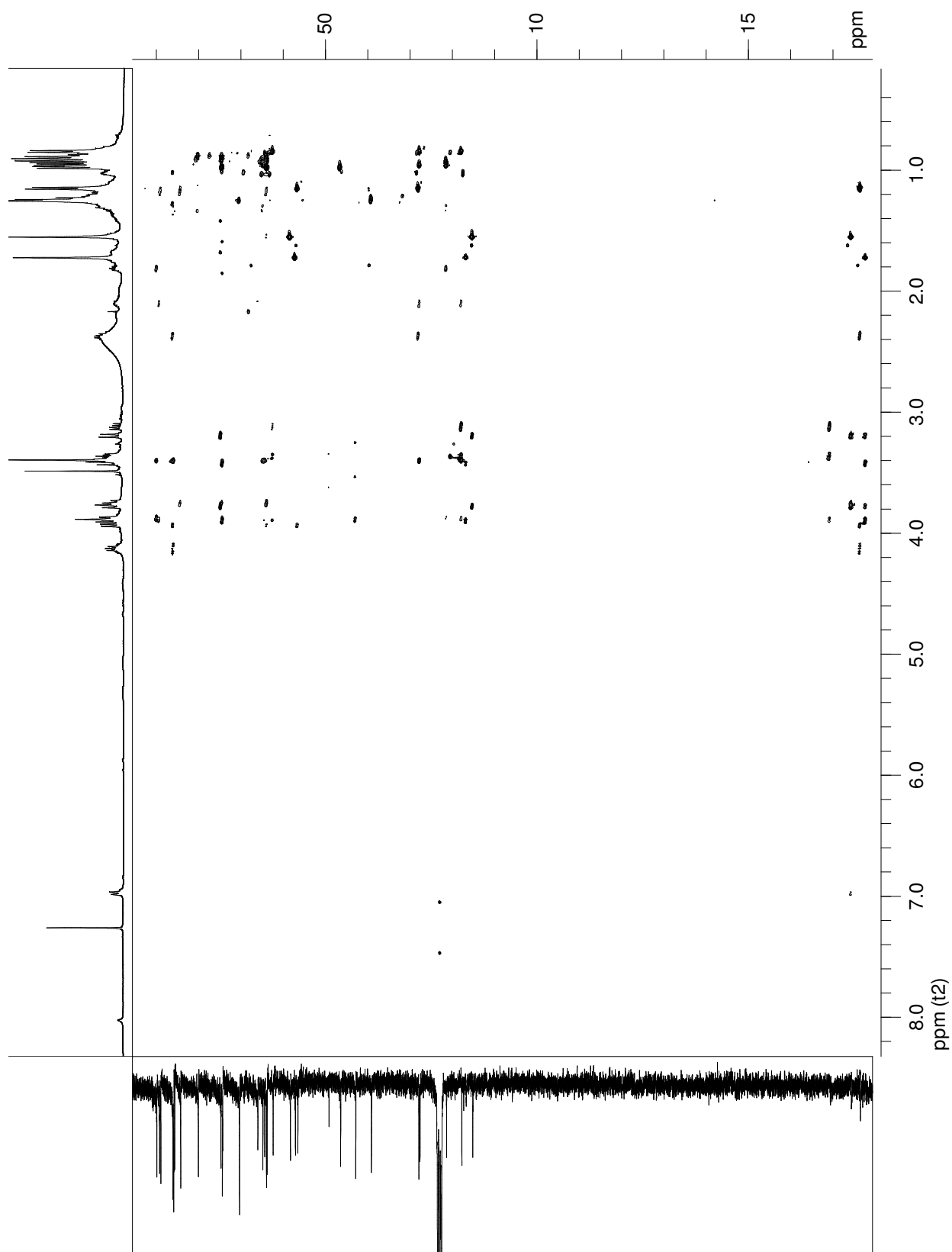


S30. HMBC spectrum of natural hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz) (Cont.).

gHMBC
pyridine-*d*₅
700 MHz

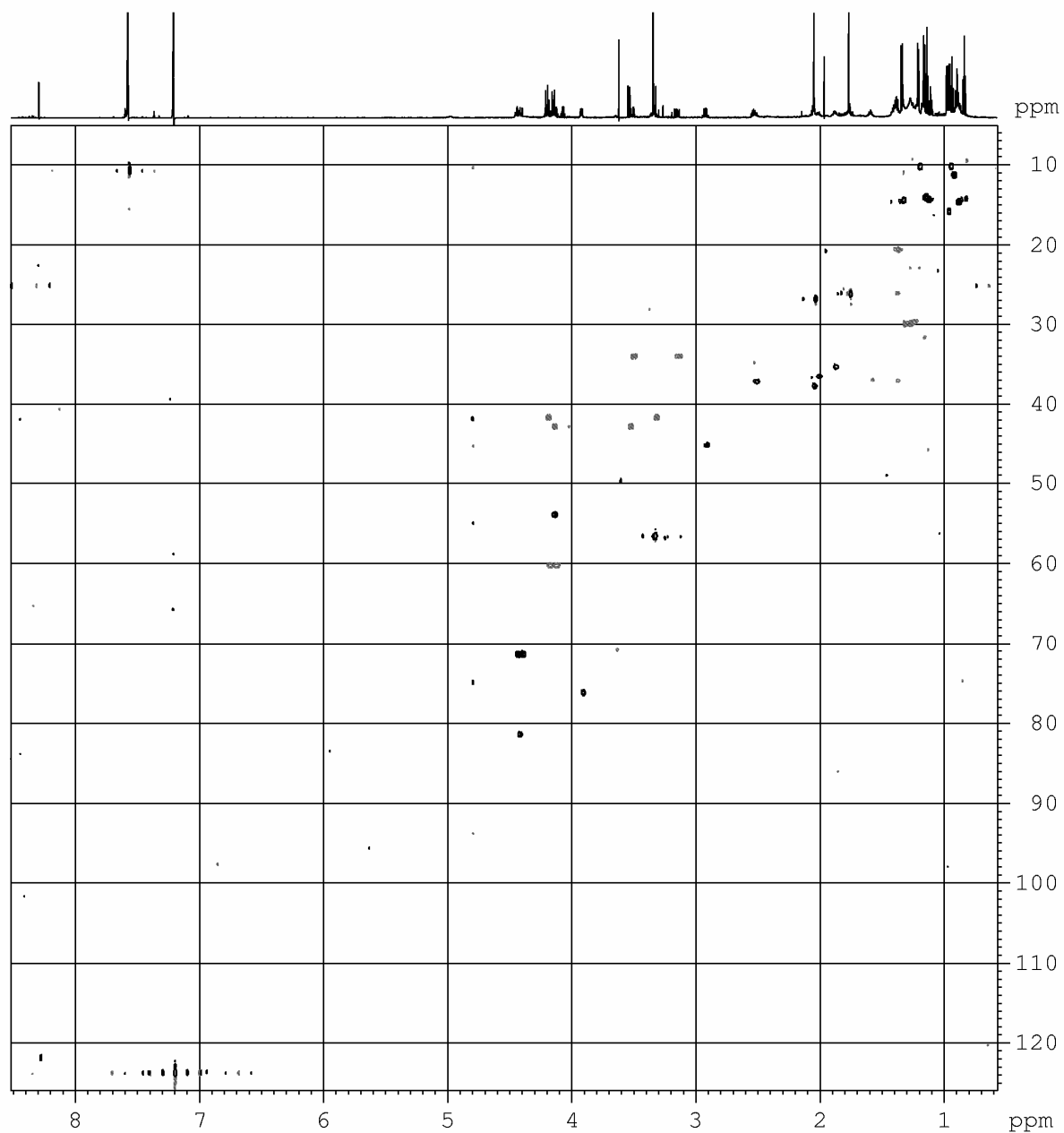


S31. HMBC spectrum of natural hoiamide C (**3**) (recorded in CDCl₃ at 500 MHz).



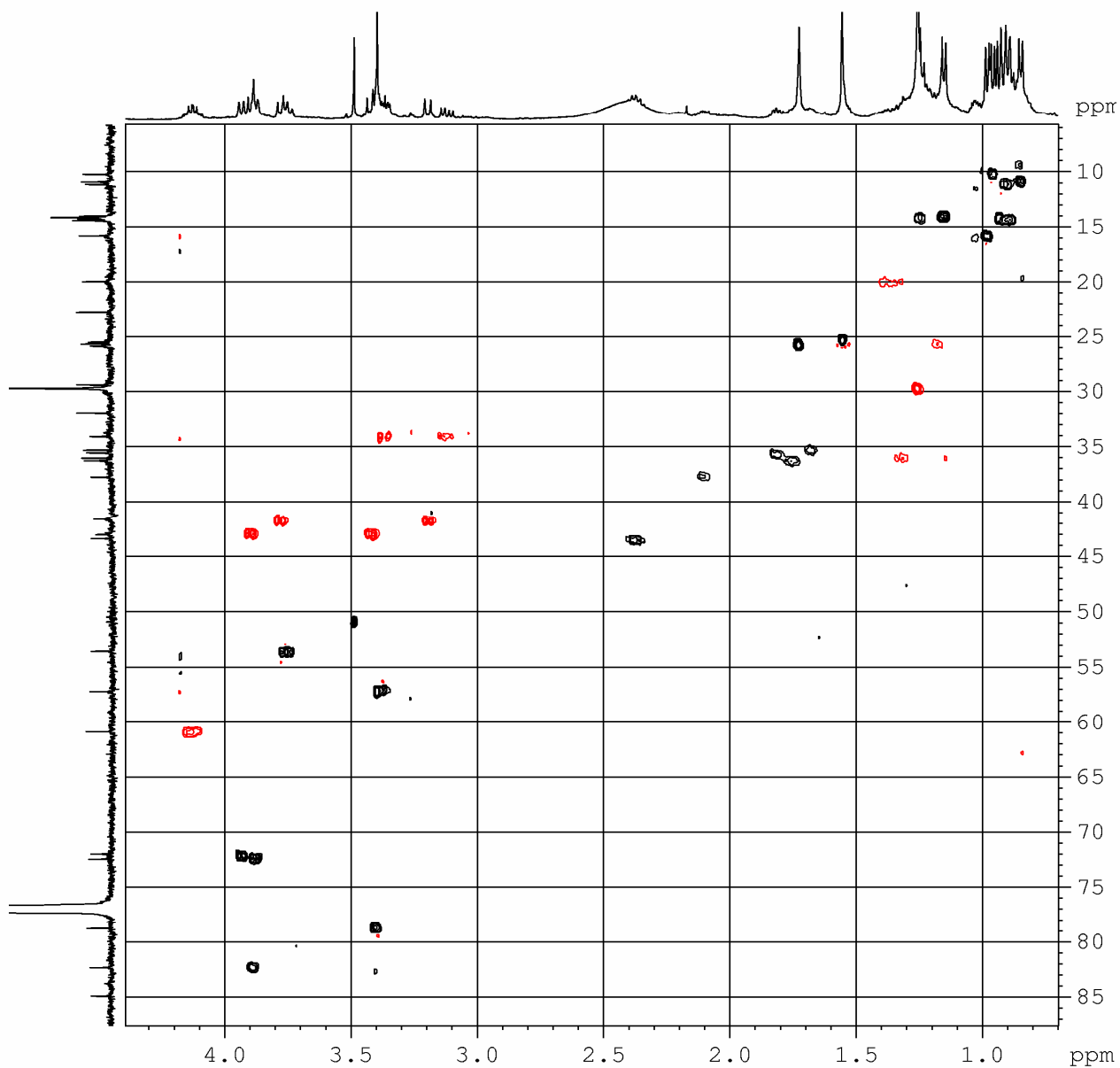
S32. HSQC spectrum of natural hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz).

gHSQC
pyridine-*d*₅
700 MHz

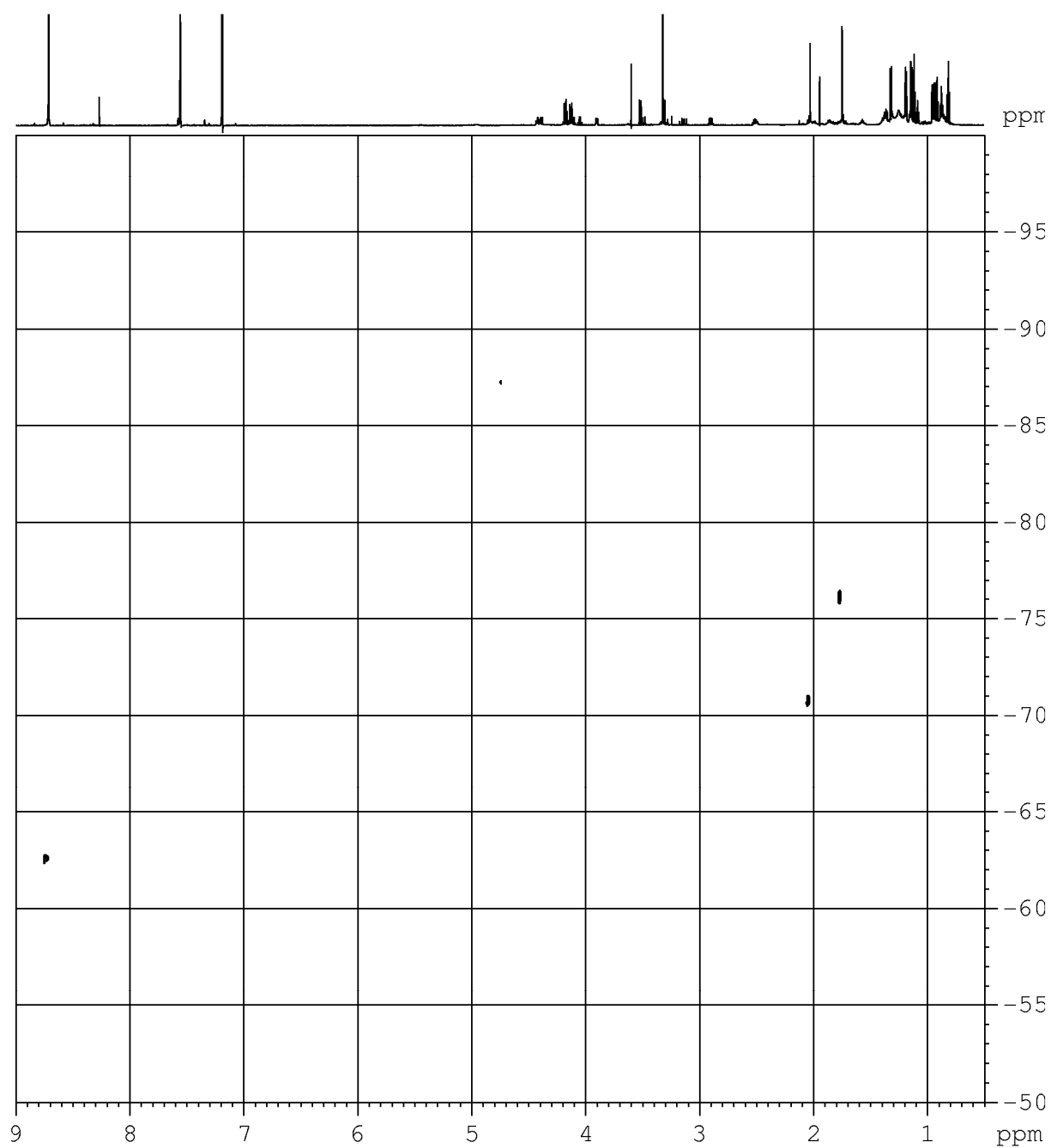


S33. HSQC spectrum of natural hoiamide C (**3**) (recorded in CDCl₃ at 500 MHz).

gHSQC
500 MHz
CDCl₃

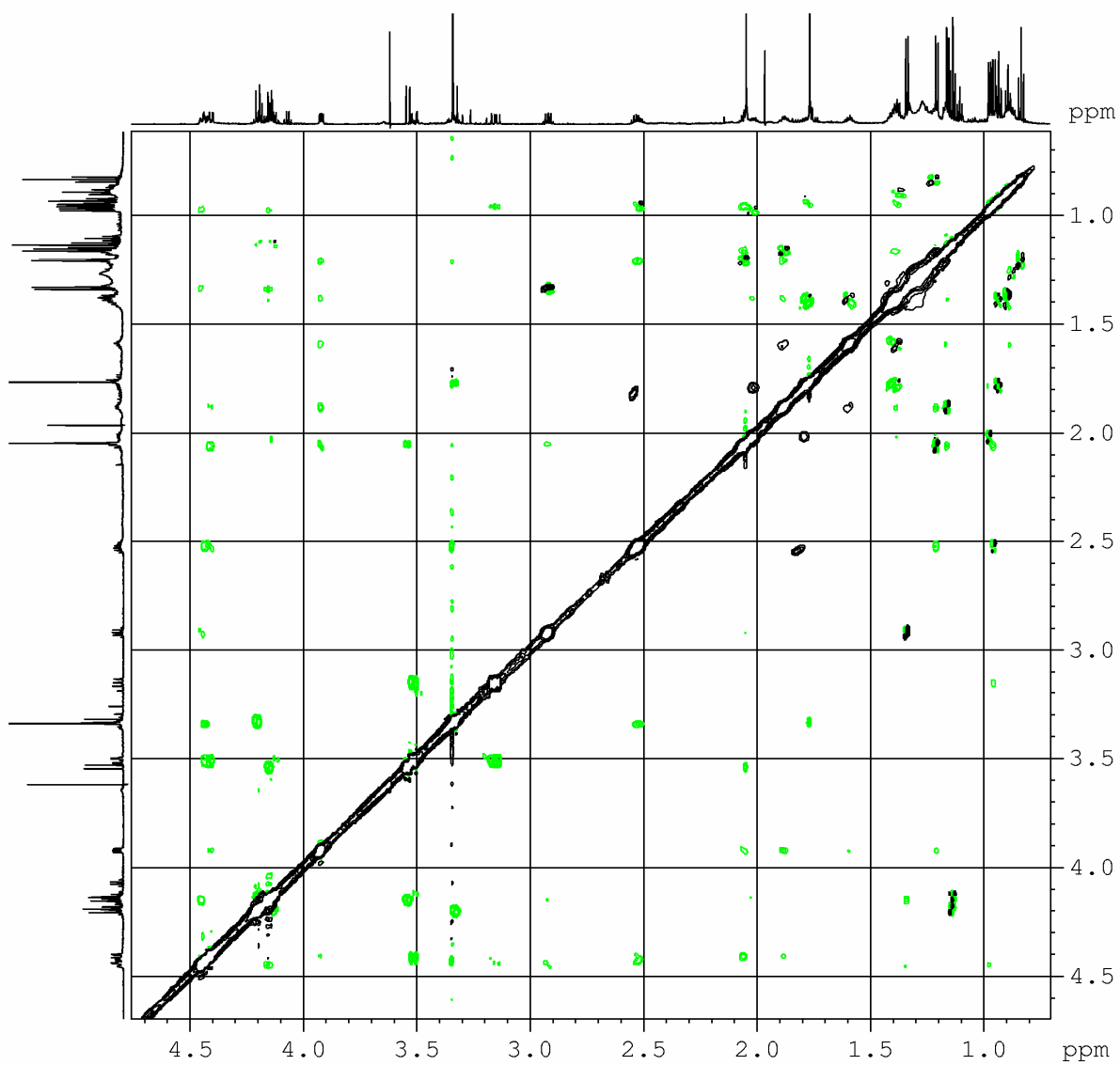


S34. ^{15}N HMBC spectrum of hoiamide C (**3**) (recorded in pyridine- d_5 at 700 MHz).

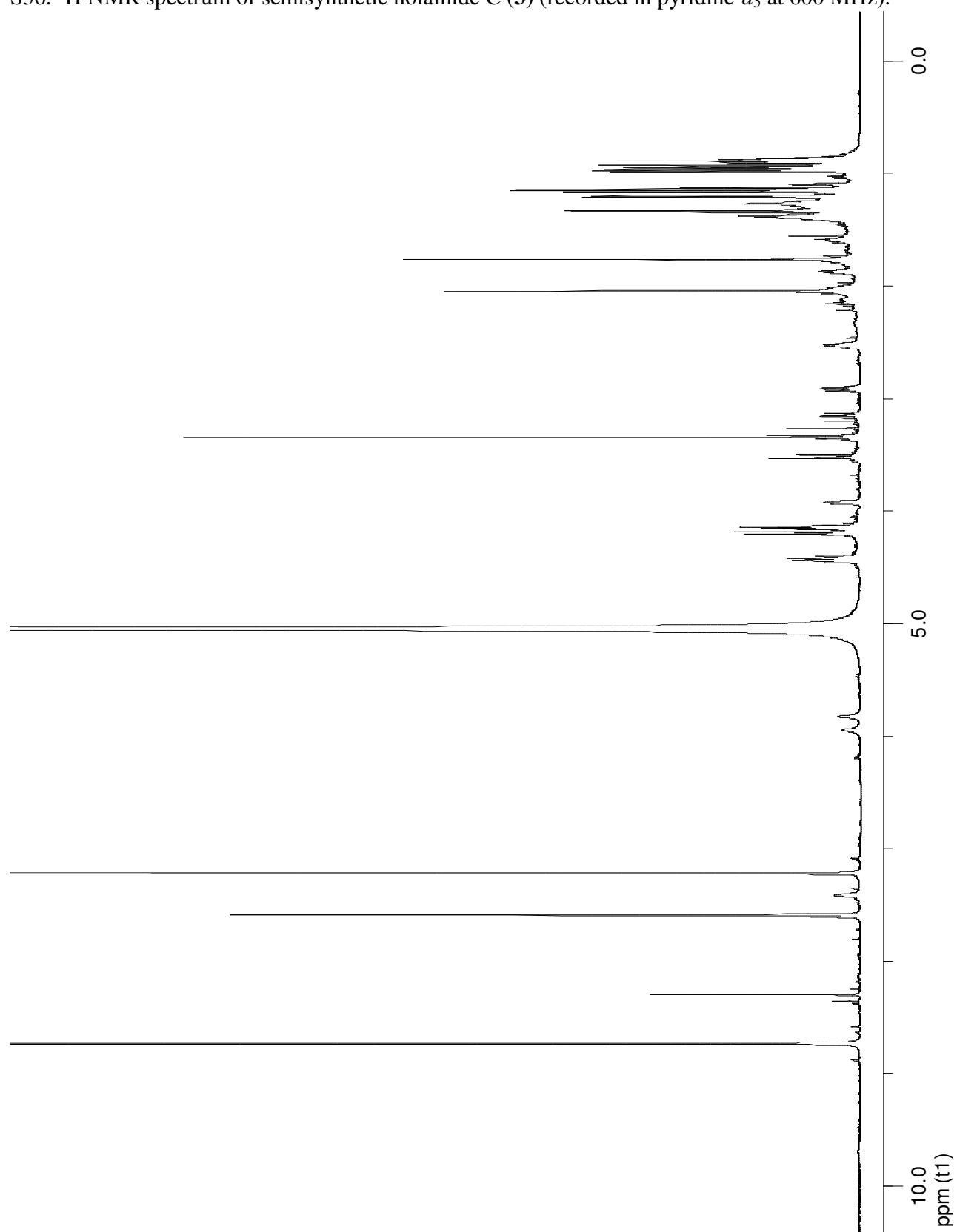


S35. ROESY spectrum of hoiamide C (**3**) (recorded in pyridine-*d*₅ at 700 MHz).

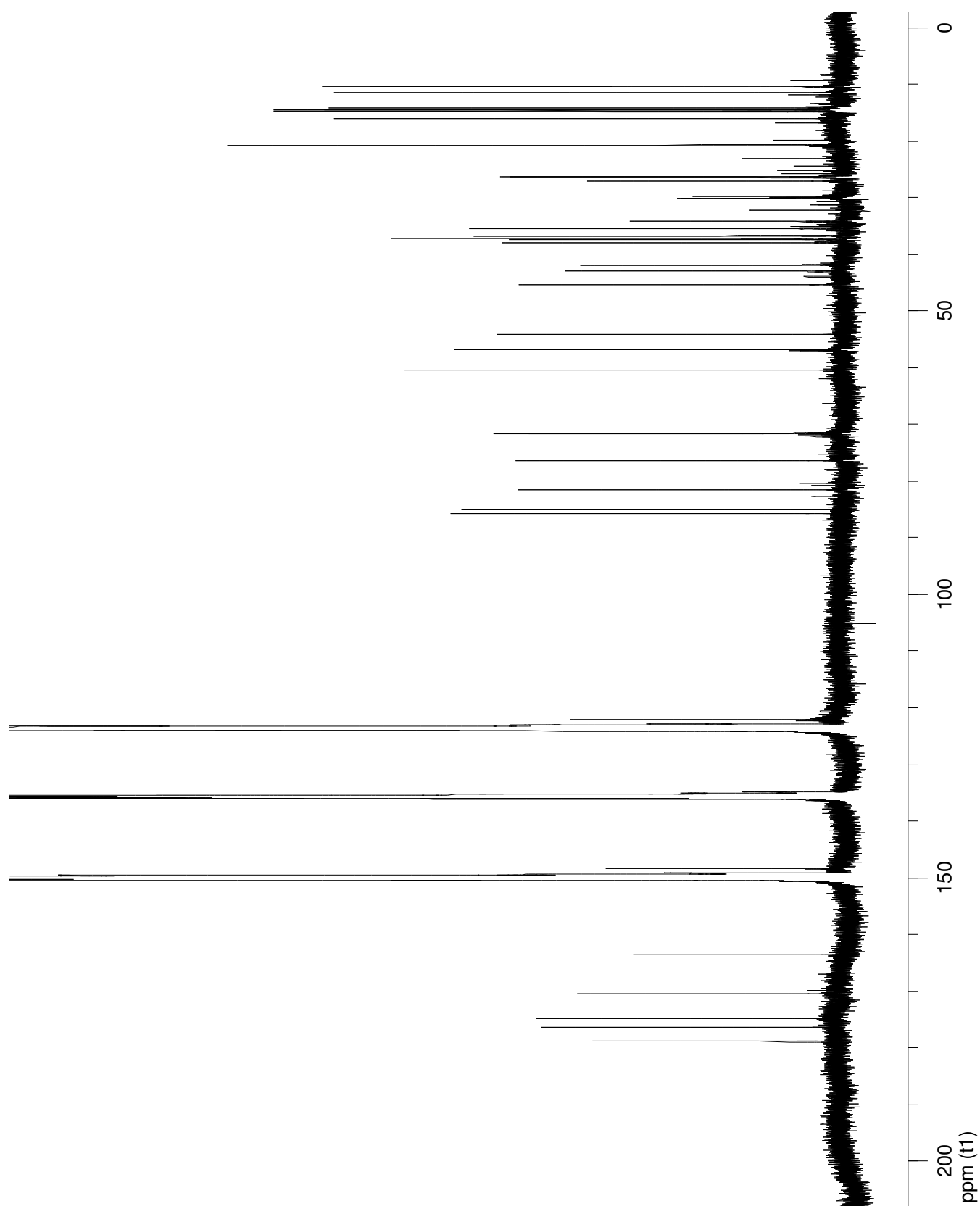
ROESY
pyridine-*d*₅
700 MHz



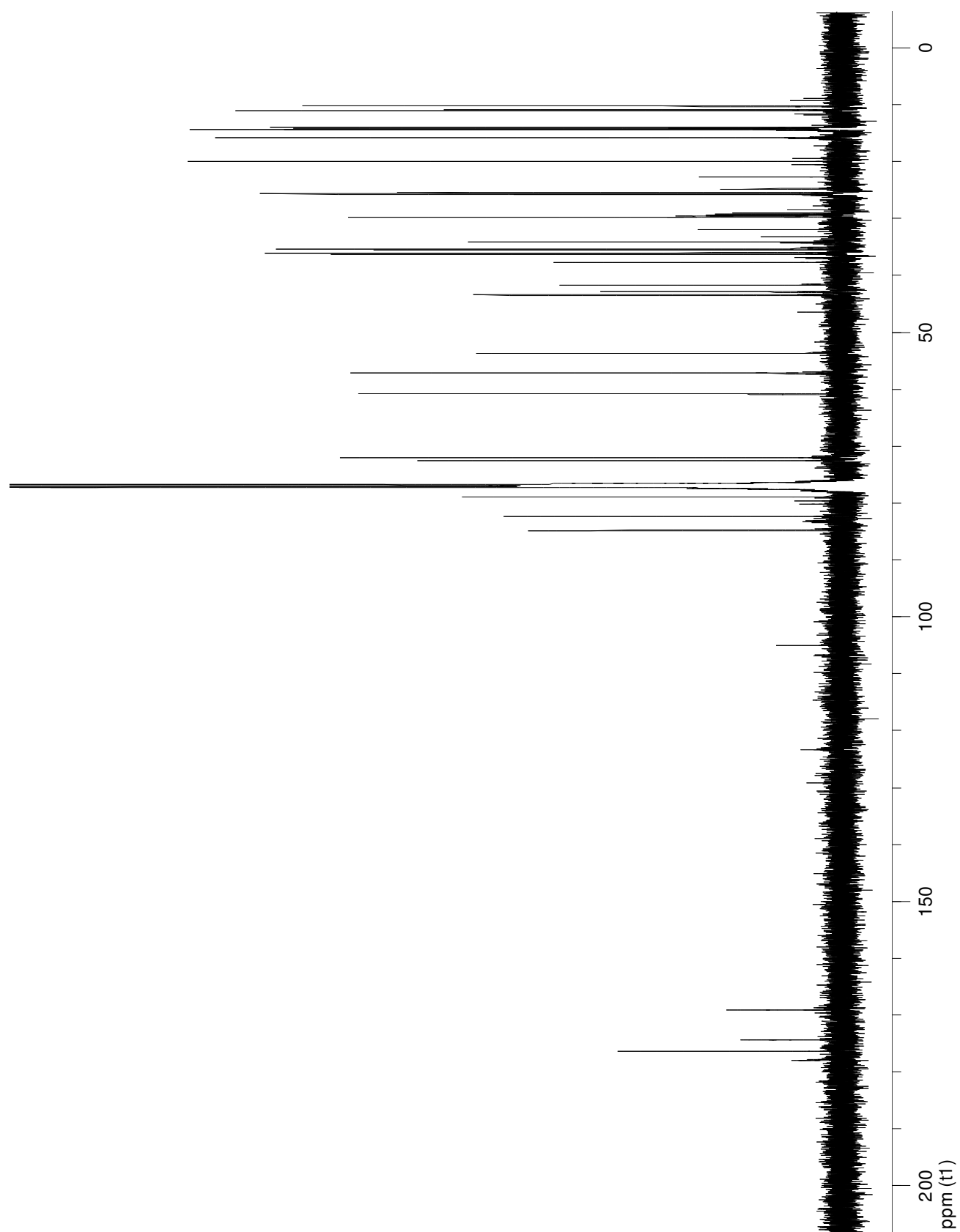
S36. ¹H NMR spectrum of semisynthetic hoiamide C (**3**) (recorded in pyridine-*d*₅ at 600 MHz).



S37. ^{13}C NMR spectrum of semisynthetic hoiamide C (**3**) (recorded in pyridine- d_5 at 125 MHz).

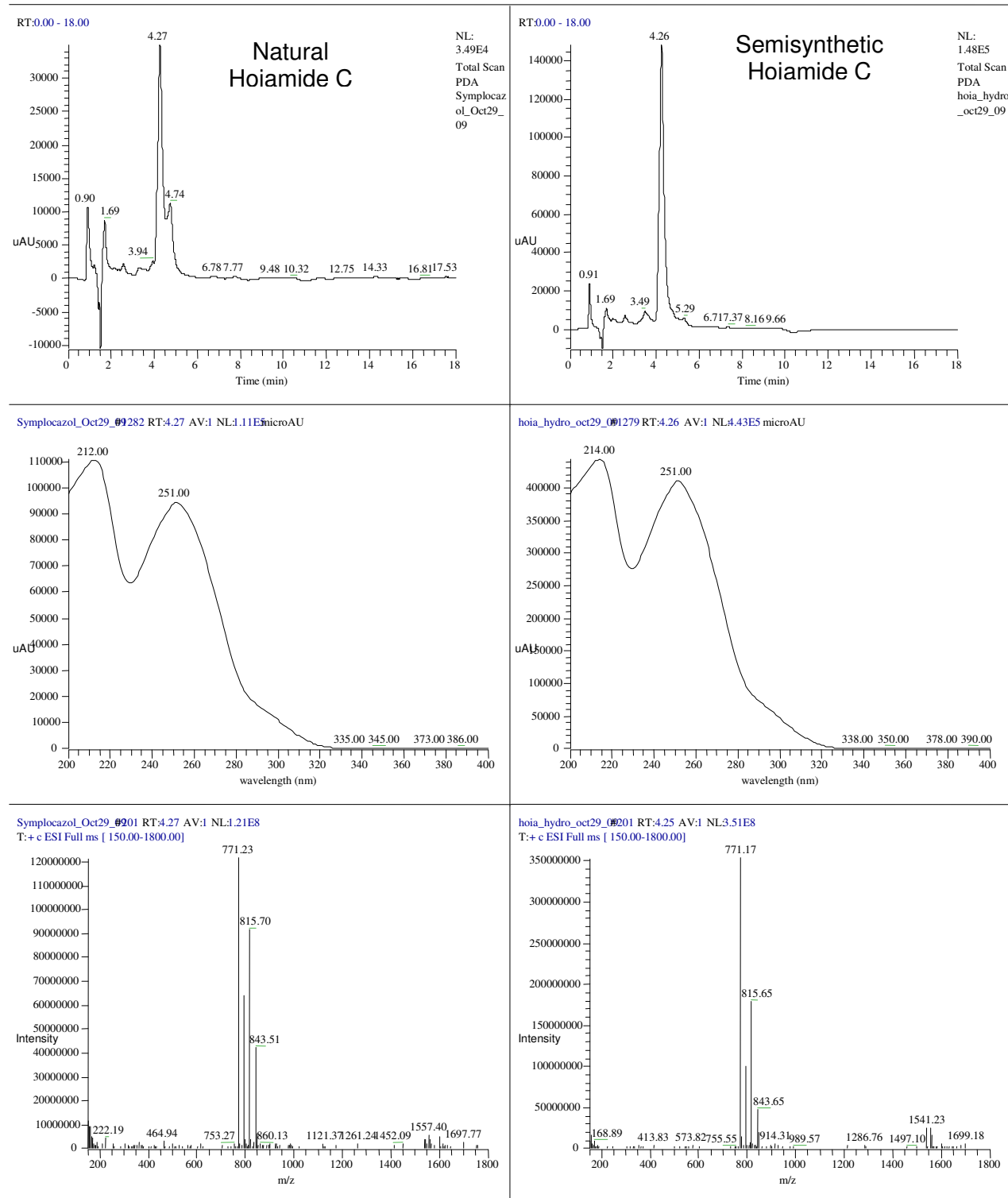


S38. ^{13}C NMR spectrum of semisynthetic hoiamide C (**3**) (recorded in CDCl_3 at 125 MHz).



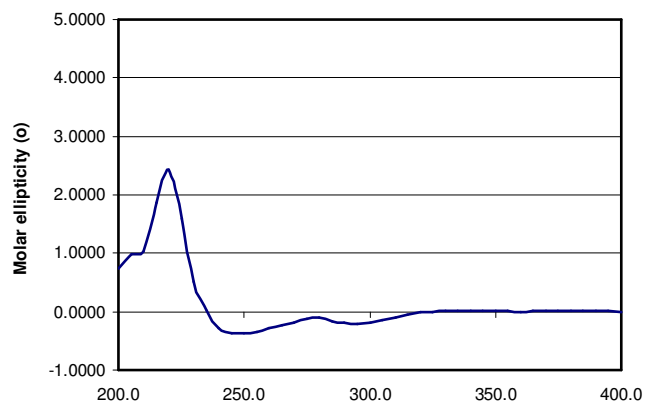
S39. LCMS comparison of natural and semisynthetic hoiamide C (**3**) (Conditions: LiChrosphere 100 RP-18 5 μm , 125 x 4 mm, gradient 70% MeCN/H₂O to 100% MeCN for 25 min at 0.7 mL/min).

d:\data\alban\hoia_hydro_oct29_0 10/29/2009 10:43:20

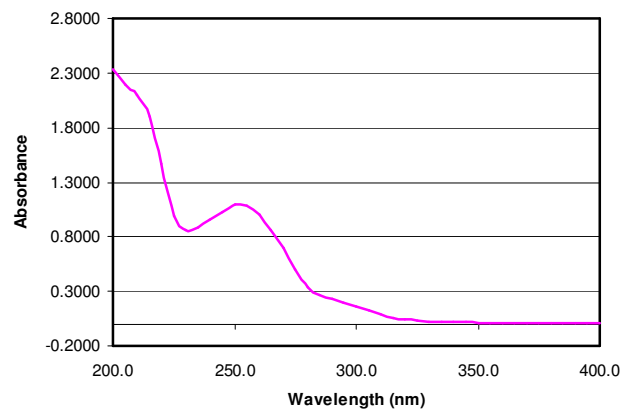
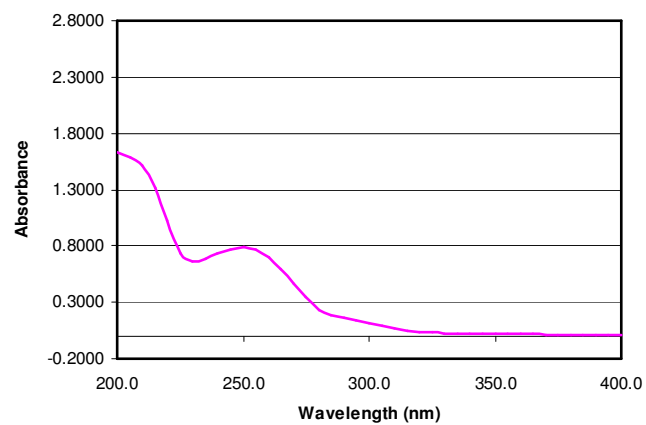
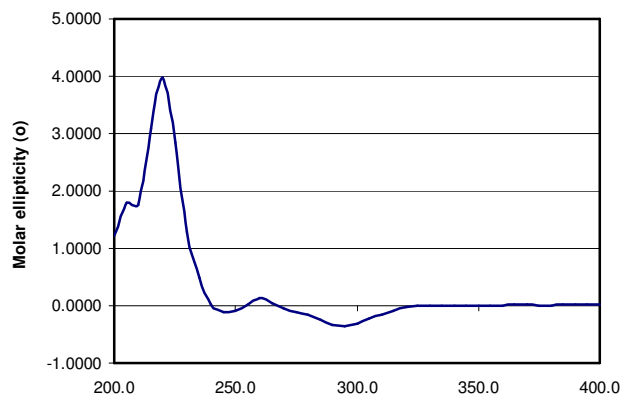


S40. Circular dichroism and UV curves for natural and semisynthetic hoiamide C (**3**) (Solvent: MeCN).

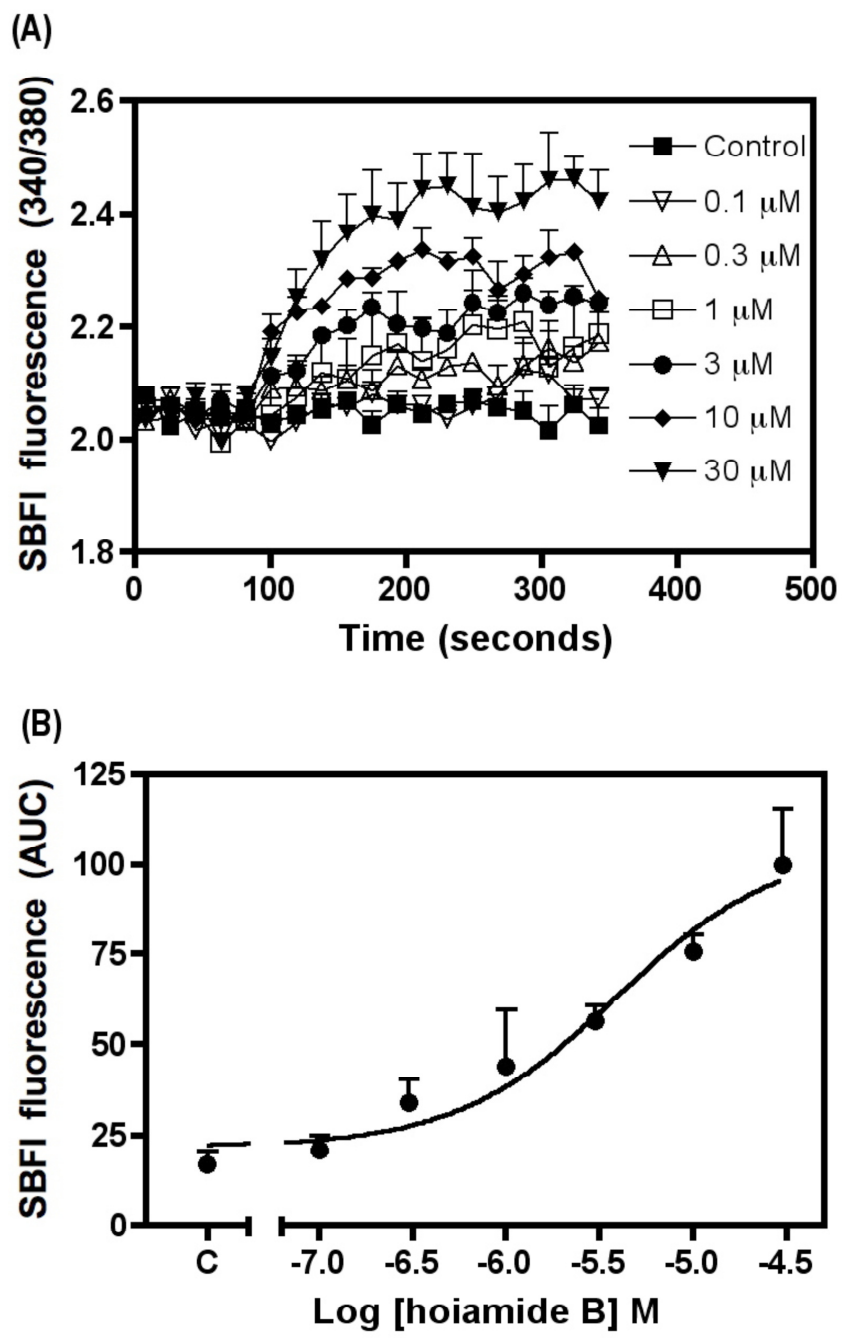
Natural Hoiamide C



Semisynthetic Hoiamide C



S41. Stimulation of sodium influx by hoiamide B (2) in neocortical neurons. (A) Time-response relationships for hoiamide B-induced elevation in neuronal $[Na^+]_i$ in neocortical neurons. (B) Concentration-response relationships for hoiamide B-induced elevation in neuronal $[Na^+]_i$ in neocortical neurons.



S42. Time- and concentration-response data for hoiamide A-induced suppression of spontaneous Ca^{2+} oscillations in neocortical neurons.

