

Phorbasides A-E, Cytotoxic Chlorocyclopropane Macrolide Glycosides from the Marine Sponge *Phorbas* sp. CD Determination of C-Methyl Sugar Configurations

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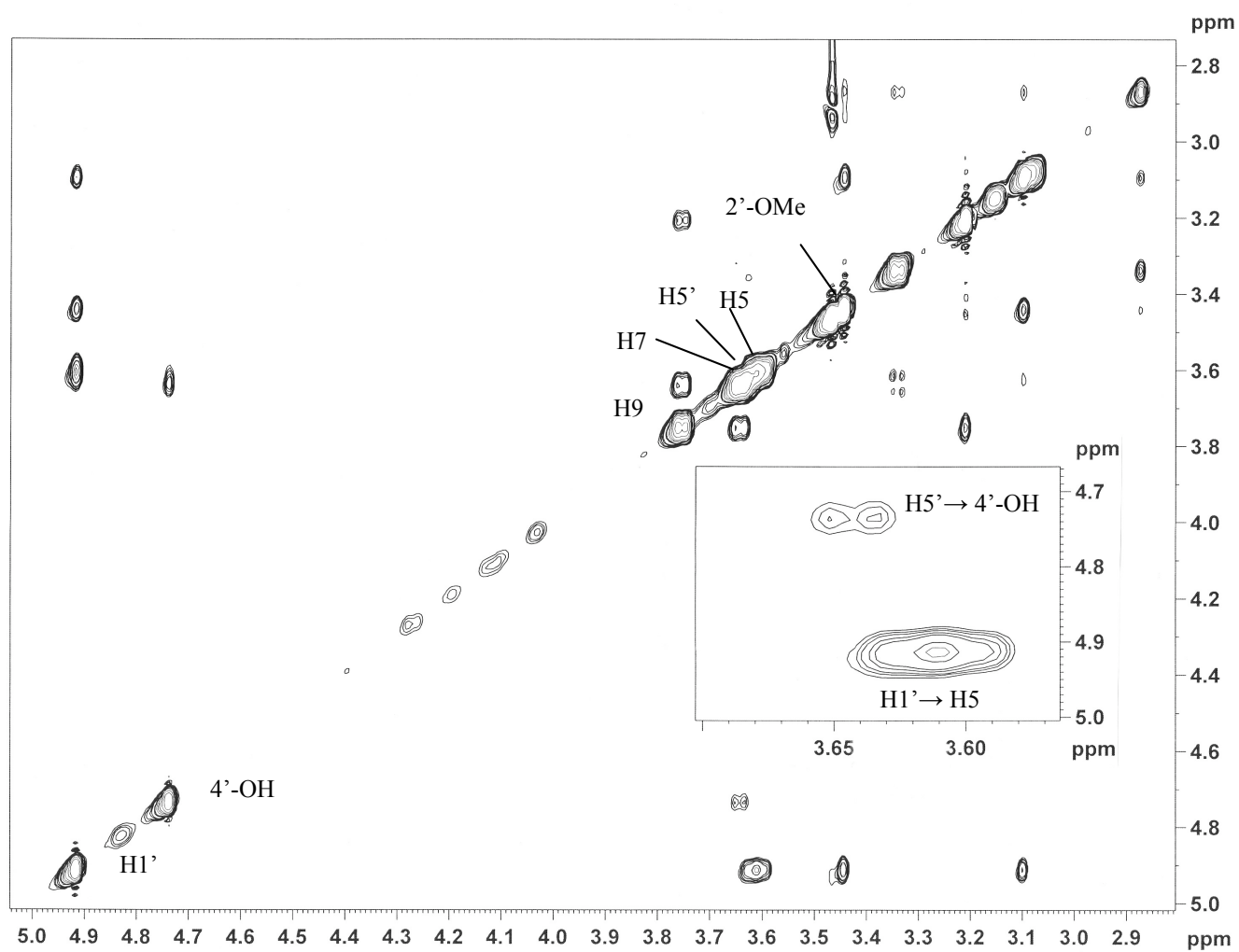
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<i>Content</i>	<i>Page</i>
<i>Table of Contents</i>	<i>S1</i>
<i>General Procedures</i>	<i>S2</i>
Fig. S1 ROESY spectrum, phorbaside A (3) (CDCl ₃ , 600 MHz)	S3
Table S1: ¹ H & ¹³ C NMR data phorbaside C (5) (CDCl ₃)	S4
Table S2: ¹ H & ¹³ C NMR data phorbaside D (6) (CDCl ₃)	S5
Table S3: ¹ H & ¹³ C NMR data phorbaside E (7) (CDCl ₃)	S6
Fig. S2: ¹ H NMR spectrum, phorbaside C (5) (CDCl ₃ , 600 MHz)	S7
Fig. S3: DQFCOSY, phorbaside C (5) (CDCl ₃ , 600 MHz)	S8
Fig. S4: HSQC-TOCSY, phorbaside C (5) (CDCl ₃ , 600 MHz)	S9
Fig. S5: ¹ H NMR spectrum, phorbaside D (6) (CDCl ₃ , 600 MHz)	S10
Fig. S6: ROESY spectrum, phorbaside D (6) (CDCl ₃ , 600 MHz)	S11
Fig. S7: gHMBC spectrum, phorbaside D (6) (CDCl ₃ , 600 MHz)	S12
Fig. S8: gHSQC spectrum, phorbaside D (6) (CDCl ₃ , 600 MHz)	S13
Fig. S9: ¹ H NMR spectrum, phorbaside E (7) (CDCl ₃ , 600 MHz)	S14
Fig. S10: DQFCOSY spectrum, phorbaside E (7) (CDCl ₃ , 600 MHz)	S15
Fig. S11: gHSQC spectrum, phorbaside E (7) (CDCl ₃ , 600 MHz)	S16
Fig. S12: gHMBC spectrum, phorbaside E (7) (CDCl ₃ , 600 MHz)	S17

General Procedures: 1 and 2D NMR spectra for phorbasides A-E were measured on NMR spectrometer equipped with a 14 T superconducting magnet and a $\{^{13}\text{C}\}\text{-}^1\text{H}/^{15}\text{N}$ 'cryo-probe' with a preamplifier cooled to $T = 20$ K. NMR spectra of synthetic compounds were acquired on a NMR spectrometer equipped with a 7T cryomagnet and a $\{^1\text{H}, ^{13}\text{C}\}$ dual-tuned probe. References were as follows, for $\text{CH}(\text{D})\text{Cl}_3$, ^1H , 400 MHz, ref. δ 7.26 ppm; ^{13}C , 75 MHz, δ 77.00 ppm. FTIR spectra were acquired on thin films dispersed on NaCl or ZnSe plates. Circular dichroism (CD) spectra were measured using a grating spectropolarimeter equipped with a photoelastic modulator. All solvents were HPLC grade or distilled from glass.



ROESY spectrum of phorbaside A (**3**, 93-054-C3-1-3a, 600 MHz, CDCl₃, t_m = 400 mS, ref. CHCl₃, δ = 7.24 ppm). Apodization: $\sin^2$ (F1 and F2), zero-filled to 2048 F2 x 1024 F1.

No.	¹³ C	¹ H (m, <i>J</i> (Hz))	HMBC (<i>J</i> = 8Hz)
1	176.4		H-2, H-13, H-24
2	47.3	2.50 (q, 7.2)	H-4b, H-24
3	97.7		3-OH, H-2, H-4a, H-4b, H-24
4	39.4	1.14 (dd, 7.2) 2.29 (dd, 12.0, 4.8)	3-OH
5	79.8	3.60 (dd, 10.8, 4.8)	H-1', H-2', H-23
6	38.6	1.45 (m)	H-4b, H-23
7	74.9	3.65 (dd, 10.2, 1.8)	H-22, H-23
8	36.8	2.18 (m)	H-22
9	79.7	3.75 (dd, 9.0, 1.8)	11-OMe, H-8, H-22
10	127.7	5.28 d (9.6)	H-12, H-21
11	132.5		H-9, H-12, H-21
12	46.6	2.23 (d, 7.2)	H-10, H-13, H-21
13	71.0	5.70 (q, 6.6)	H-12, H-14, H-15,
14	140.1	6.06 (dd, 16.2, 6.3)	H-12, H-13, H-15
15	111.3	5.66 (bd, 16.2)	H-13
16	91.0		H-15, H-20
17	75.9		H-14, H-19, H-20
18	11.8	1.77 (brt, 5.6)	H-20
19	34.1	3.15 (m, 9.6, 6), 3.0)	
20	19.2	1.25 (m)	H-19
21	16.5	1.71 (s)	H-10, H-12
22	6.6	0.98 (d, 7.2)	H-7, H-8, H-9
23	12.4	0.90 (d, 6.6)	
24	12.5	1.14 (d, 7.2)	H-2
9-OMe	55.3	3.23 (s)	H-9
1'	98.5	4.90 (br s)	2'-OMe, H-1', H-7'
2'	85.4	3.22 (s)	H-1', 2'-OMe, H-4', H-7'
3'	70.1		H-2', H-4', H-7'
4'	72.0	3.78 (d, 9.3)	H-2', H-6', H-7', H-1''
5'	70.0	3.97 (dq, 9.3, 6.6)	H-1', H-4', H-6'
6'	19.1	1.27 (d, 6.6)	H-4'
7'	18.0	1.44 (s)	H-2'
3'-OH		2.28	
OMe	57.8	3.38 (s)	H-2',
1''	92.7	5.43 (s)	H-3'', H-5'', H-4''
2''	79.1	3.58 (s)	H-1'', H-7''
3''	80.5	3.97	H-2'', H-7'', 3''-OH
4''	69.7	3.97 (dd, 9.3, 2.3)	H-5'', H-6''
5''	67.3	3.72 (dq, 9.3, 6.6)	H-1'', H-4'', H-6''
6''	18.6	1.25 (d, 6.6)	H-4'', H-5'',
7''	19.0	1.46 (s)	H-2'', 3''-OH

Table S1. NMR data for phorbaside C (**5**) (600 MHz, CDCl₃)

No.	¹³ C	¹ H (m, <i>J</i> (Hz))	HMBC (<i>J</i> = 8Hz)
1	176.4		H-2, H-13, H-24
2	47.1	2.50 (q, 7.2)	H-4b, H-24
3	97.4		3-OH, H-2, H-4a, H-4b, H-24
4	39.9	1.10 (dd, 7.2) 2.28 (dd, 12.0, 4.2)	3-OH
5	77.7	3.72 (ddd, 12, 7.2, 4.2)	H-1', H-2', H-23
6	38.4	1.50 (m)	H-4b, H-23
7	74.6	3.67 (dd, 10.2, 1.8)	H-22, H-23
8	36.4	2.18 (m)	H-22
9	79.5	3.77 (dd, 9.6, 1.8)	11-OMe, H-8, H-22
10	128.0	5.28 (d, 9.6)	H-12, H-21
11	132.4		H-9, H-12, H-21
12	46.5	2.23 (m)	H-10, H-13, H-21
13	70.5	5.72 (q, 6.6)	H-12, H-14, H-15,
14	140.0	6.05 (dd, 16.0, 6.6)	H-12, H-13, H-15
15	111.0	5.66 (d, 16.0)	H-13
16	90.5		H-15, H-20
17	75.8		H-14, H-19, H-20
18	12.1	1.77 (dt, 7.8)	H-20
19	35.6	3.18 (dt, 9.0, 6.6, 3.6)	
20	19.0	1.29 (m)	H-19
21	15.9	1.71 (s)	H-10, H-12
22	6.5	0.96 (d, 7.2)	H-7, H-8, H-9
23	13.9	0.87 (d, 6.6)	
24	12.4	1.1 (d, 7.2)	H-2
9-OMe	55.8	3.23 (s)	H-9
OH		4.71 (d, 1.8)	
1'	101.3	4.87 (d, 6.0)	2'-OMe, H-1', H-7'
2'	81.6	3.22 (d, 6.0)	H-1', 2'-OMe, H-4', H-7'
3'	70.3		H-2', H-7'
4'	60.9	3.35 (s)	H-2', H-6', H-7', H-1''
5'	63.1	3.91 (q, 6.0)	H-1', H-4', H-6'
6'	15.5	1.10(d, 6.6)	H-4'
7'	19.6	1.27 (s)	H-2'
O(CO)	158.0		H-4'
NH			
2'-OMe	61.5	3.61 (s)	
NH		5.10	

Table S2. NMR data for phorbaside D (**5**) (600 MHz, CDCl₃)

No.	¹³ C	¹ H (m, <i>J</i> (Hz))	HMBC (<i>J</i> = 8 Hz)
1	176.6		H-2, H-13, H-24
2	47.2	2.50 (q, 7.2)	H-4b, H-24
3	132.5		3-OH, H-2, H-4a, H-4b, H-24
4	39.2	1.13 (dd, 12.0, 7.2) 2.29 (dd, 12.0, 4.8)	H-2, H-5, H-6, 3-OH
5	79.3	3.60 (dd, 10.2, 4.8)	H-1', H-4b, H-6, H-7, H-23
6	38.4	1.45 (m, 10.2, 6.6)	H-23
7	74.7	3.64 (dd, 10.2, 1.8)	H-22, H-23
8	36.9	2.18 (m)	H-22, H-9
9	79.4	3.76 (dd, 9.6, 1.8)	H-8, H-10, H-22, 9-OMe
10	127.4	5.27 (d, 9.0)	H-8, H-9, H-12, H-21
11	132.6		H-12, H-13, H-21
12	46.4	2.23 (d, 7.2)	H-10, H-13, H-15
13	70.9	5.71 (dd, 7.2, 7.2)	H-12, H-15
14	139.9	6.03 (dd, 15.6, 6.0)	H-12, H-13, H-15
15	111.2	5.65 (d, 15.6)	H-13
16	90.4		H-15, H-20
17	75.8		H-19
18	11.3	1.76 (ddd, 8.4, 5.4, 3.0)	H-19, H-20
19	34.0	3.17 (m)	H-18, H-20
20	19.2	1.25 (m)	H-19
21	16.0	1.71 (s)	H-10, H-12
22	6.2	0.96 (d, 7.2)	H-7, H-9
23	12.2	0.89 (d, 6.6)	H-5, H-7
24	12.3	1.12 (d, 7.2)	H-2
9-OMe	54.8	3.22 (s)	H-9
1'	99.2	4.83 (s)	H-5
2'	75.7	3.57 (s)	H-1', H-7', H-1''
3'	72.3		H-1', H-3', H-7'
4'	72.5	3.5 (d, 9.6)	H-2', H-3', H-5',
5'	67.5	3.75 (m)	H-1', H-6'
6'	18.0	1.28 (d, 6.6)	H-4', H-5'
7'	18.8	1.38 (s)	H-2', H-4'
1''	95.6	5.60 (s)	H-2', H-3'', H-5''
2''	85.6	3.17 (s)	H-1'', H-3'', H-4''
3''	80.1		H-2'', H-4'', H-7''
4''	70.5	3.85 (d, 9.6)	H-3'', H-5''
5''	66.5	3.71 (dq, 9.6, 6.6)	H-4'', H-6''
6''	18.8	1.30 (d, 6.6)	H-4'', H-5'',
7''	18.9	1.37 (s)	H-2'', H-4''
C-2''-OMe	58.0	3.39 (s)	H-2''

Table S3. NMR data for phorbaside E (**7**) (600 MHz, CDCl₃)

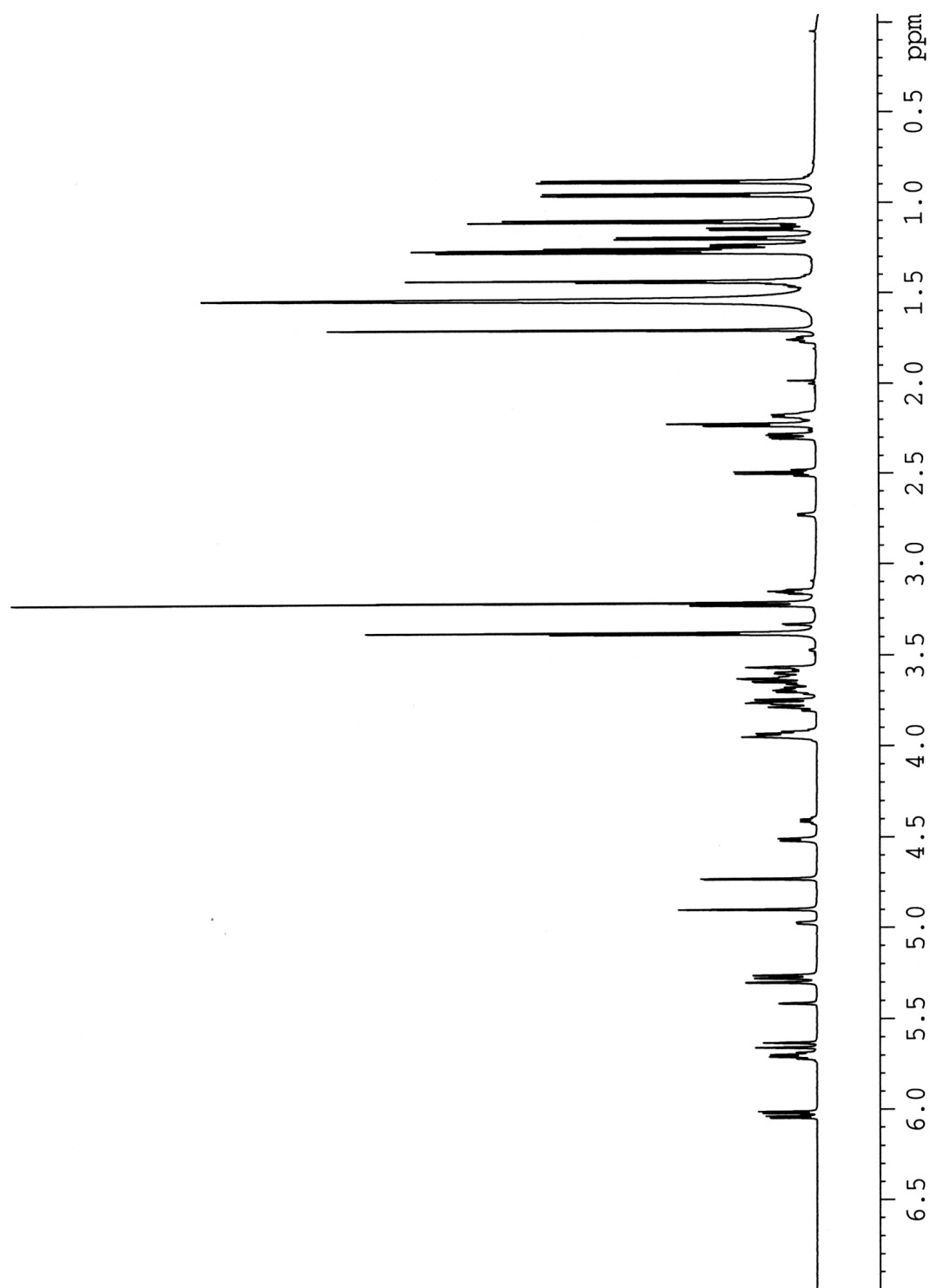


Figure S2. ^1H NMR of phorbaside C (**5**) in CDCl_3 at 600 MHz

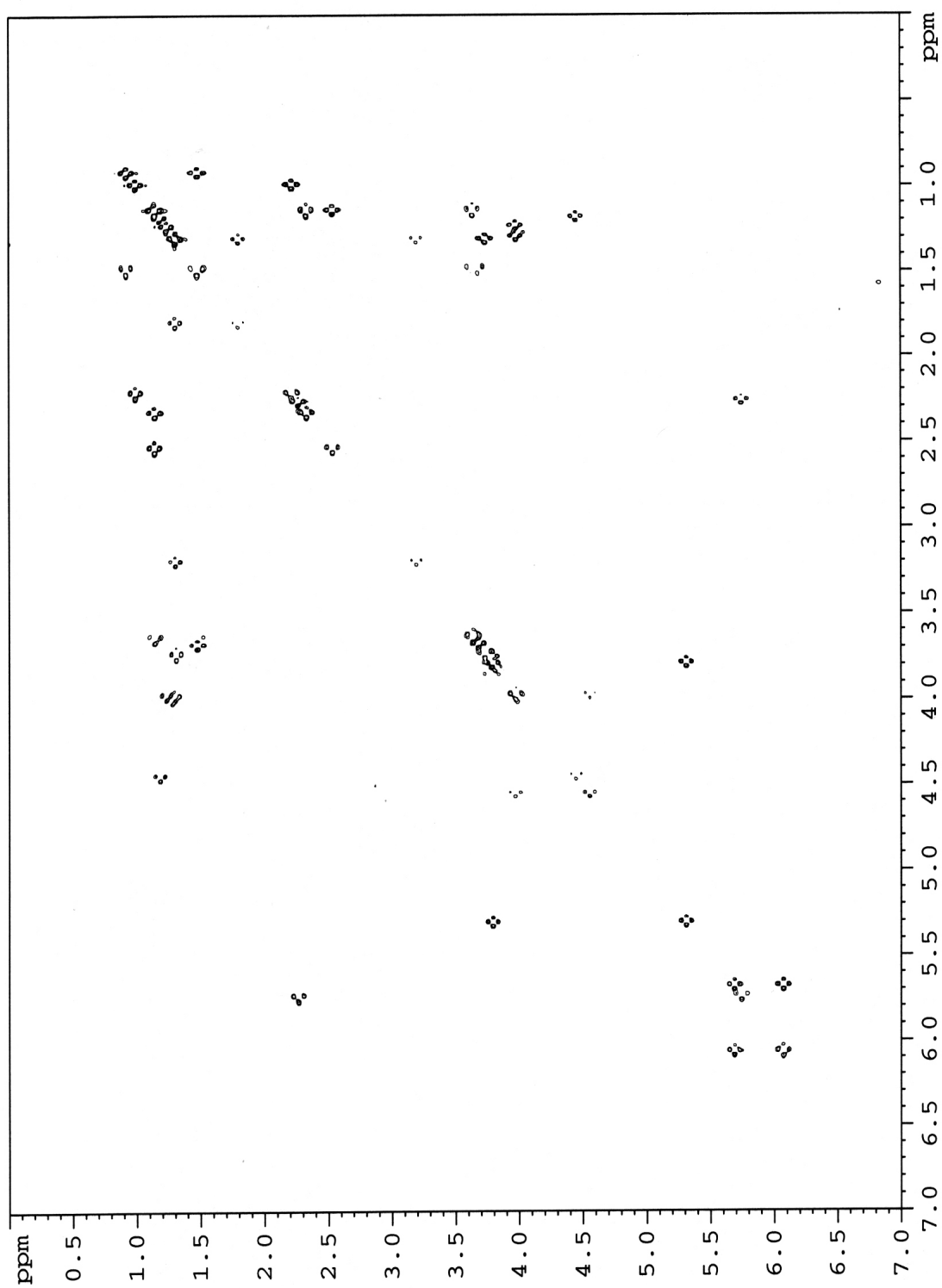


Figure S3. DQFCOSY of phorbaside C (**5**) (600 MHz, CDCl₃)

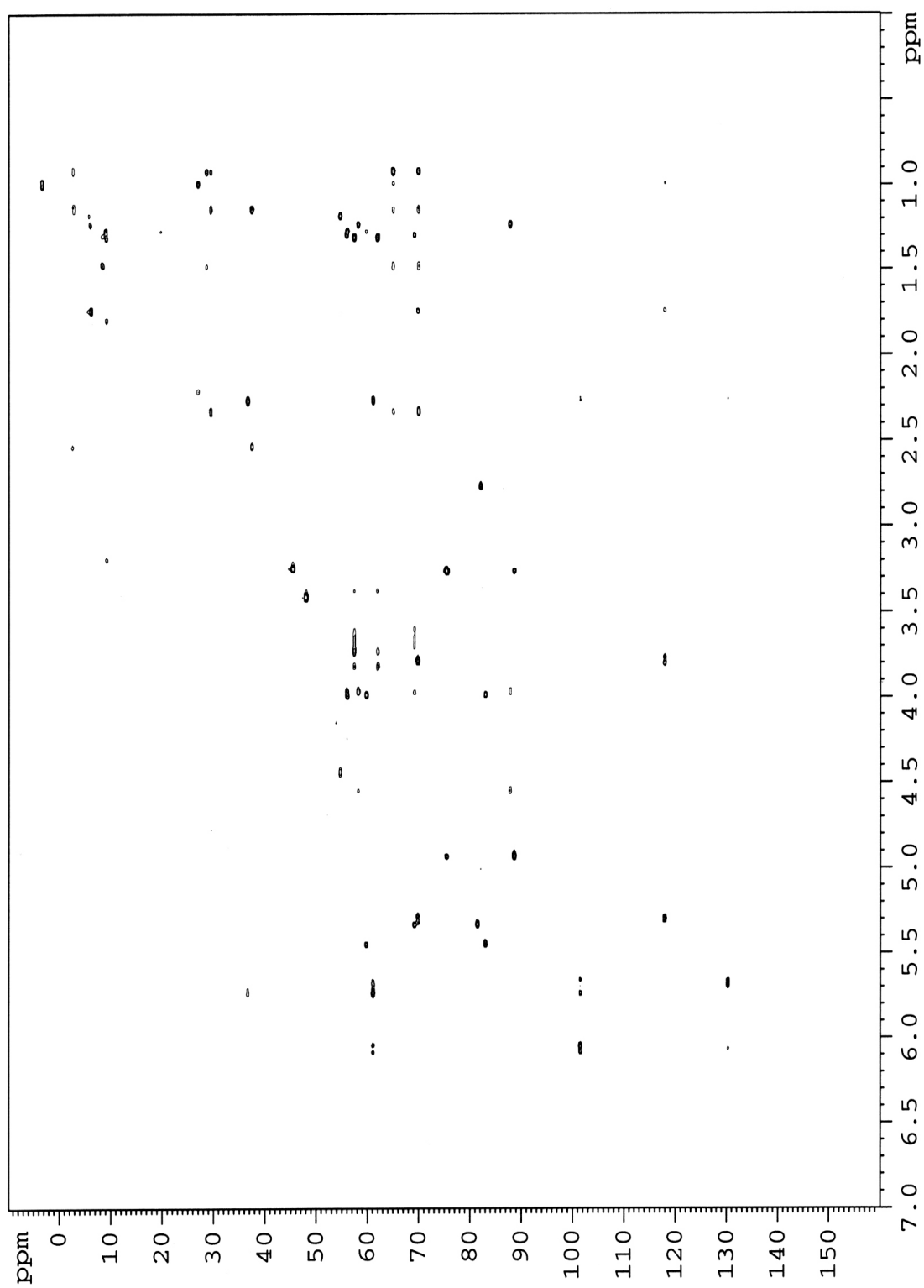


Figure S4. HSQC-TOCSY of phorbaside C (**5**) (600 MHz, CDCl_3)

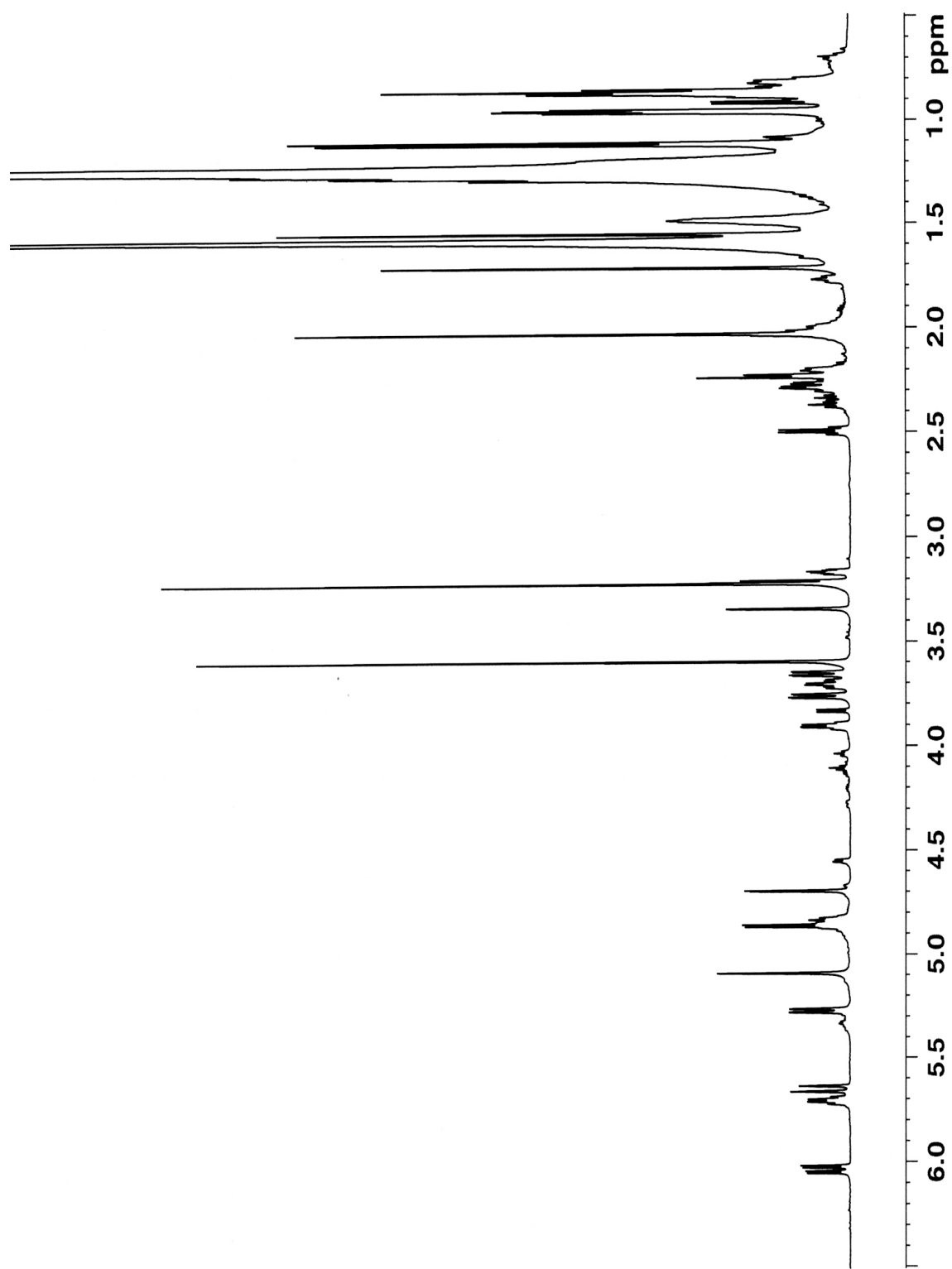


Figure S5. ^1H NMR of phorbaside D (**6**) (600 MHz, CDCl_3)

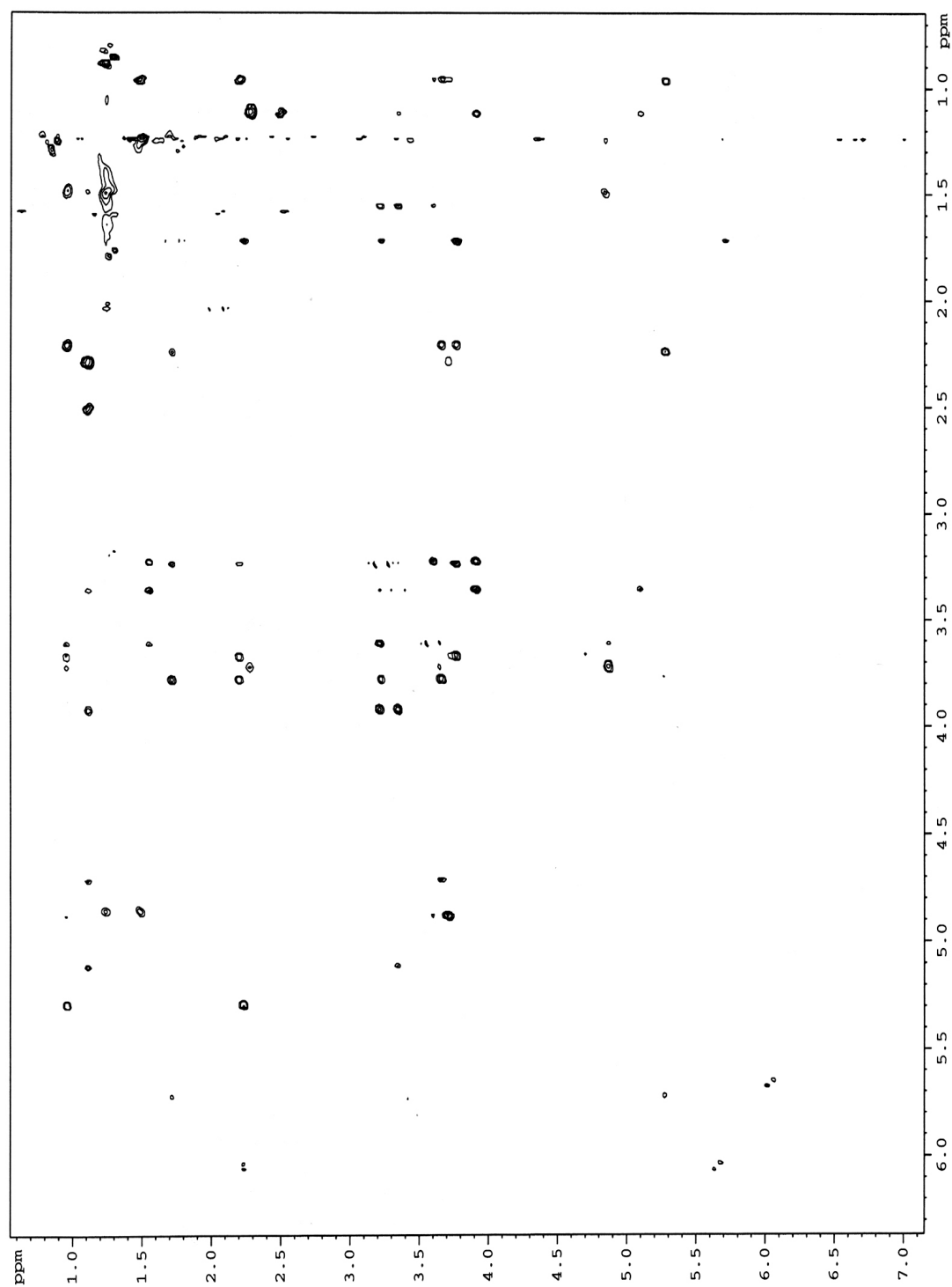


Figure S6. ROESY of phorbaside D (**6**) (600 MHz, CDCl₃, mixing time, $t_m = 400$ ms)

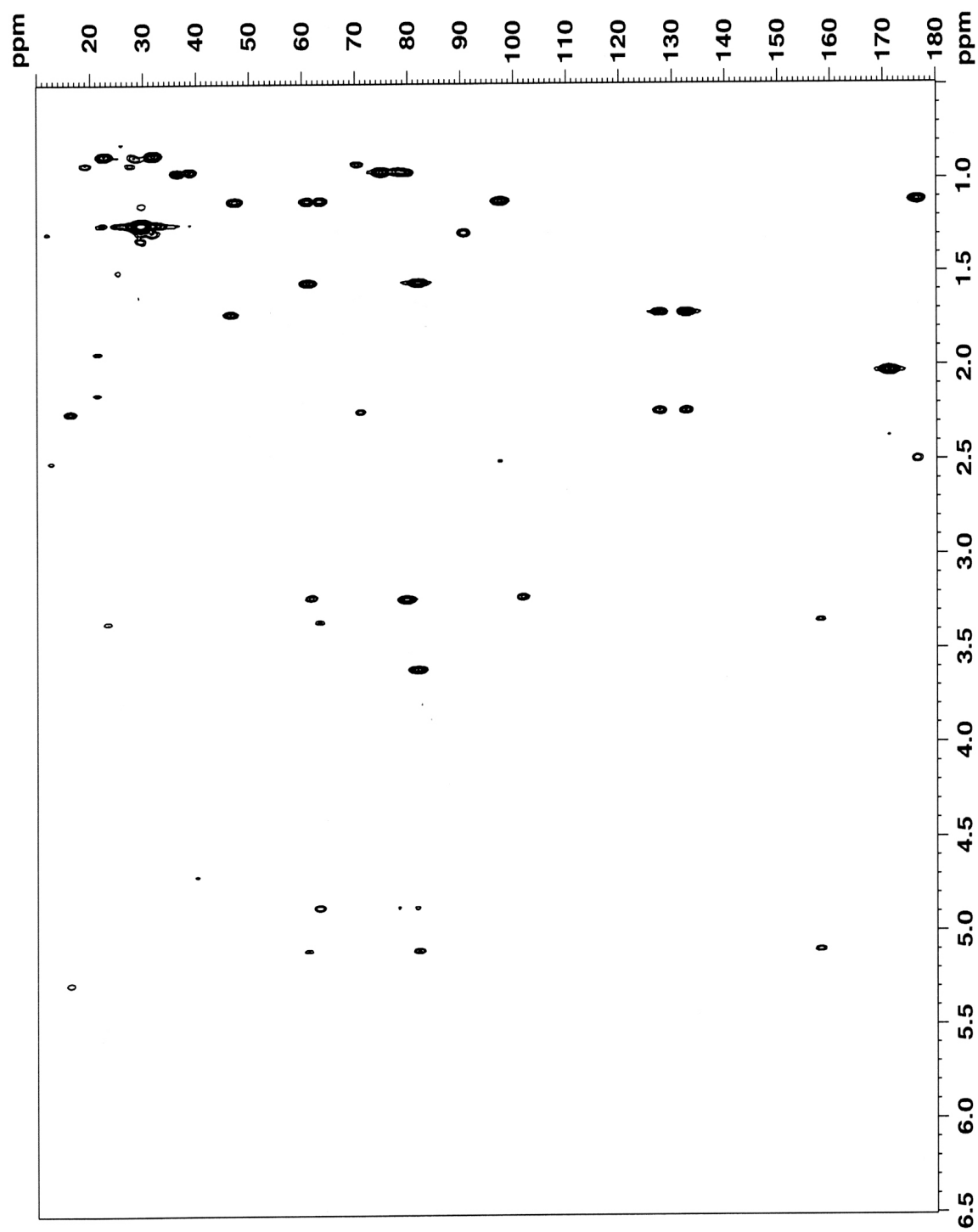


Figure S7. gHMBC of phorbaside D (**6**) (600 MHz, CDCl₃)

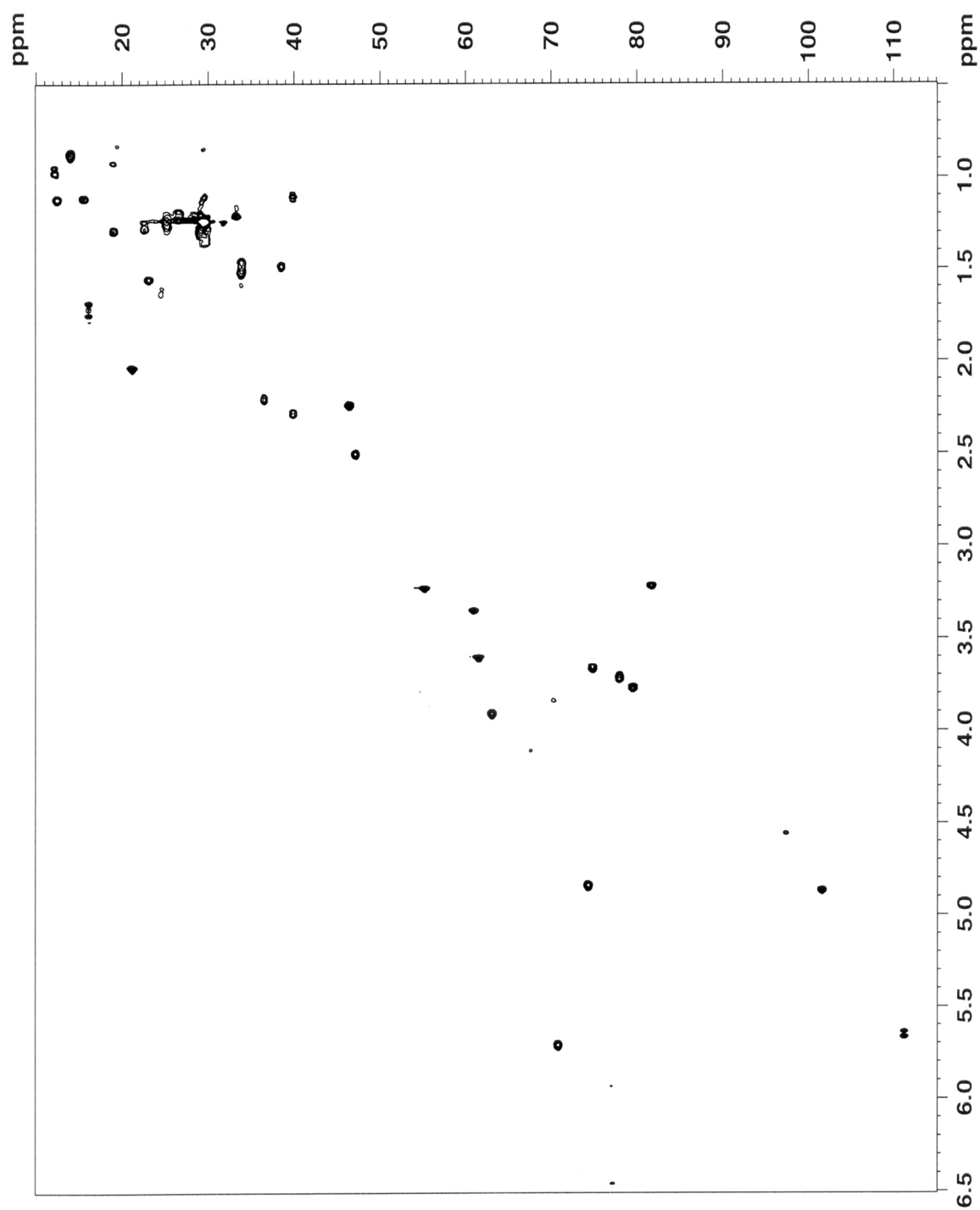


Figure S8. gHSQC of phorbaside D (**6**) (600 MHz, CDCl₃)

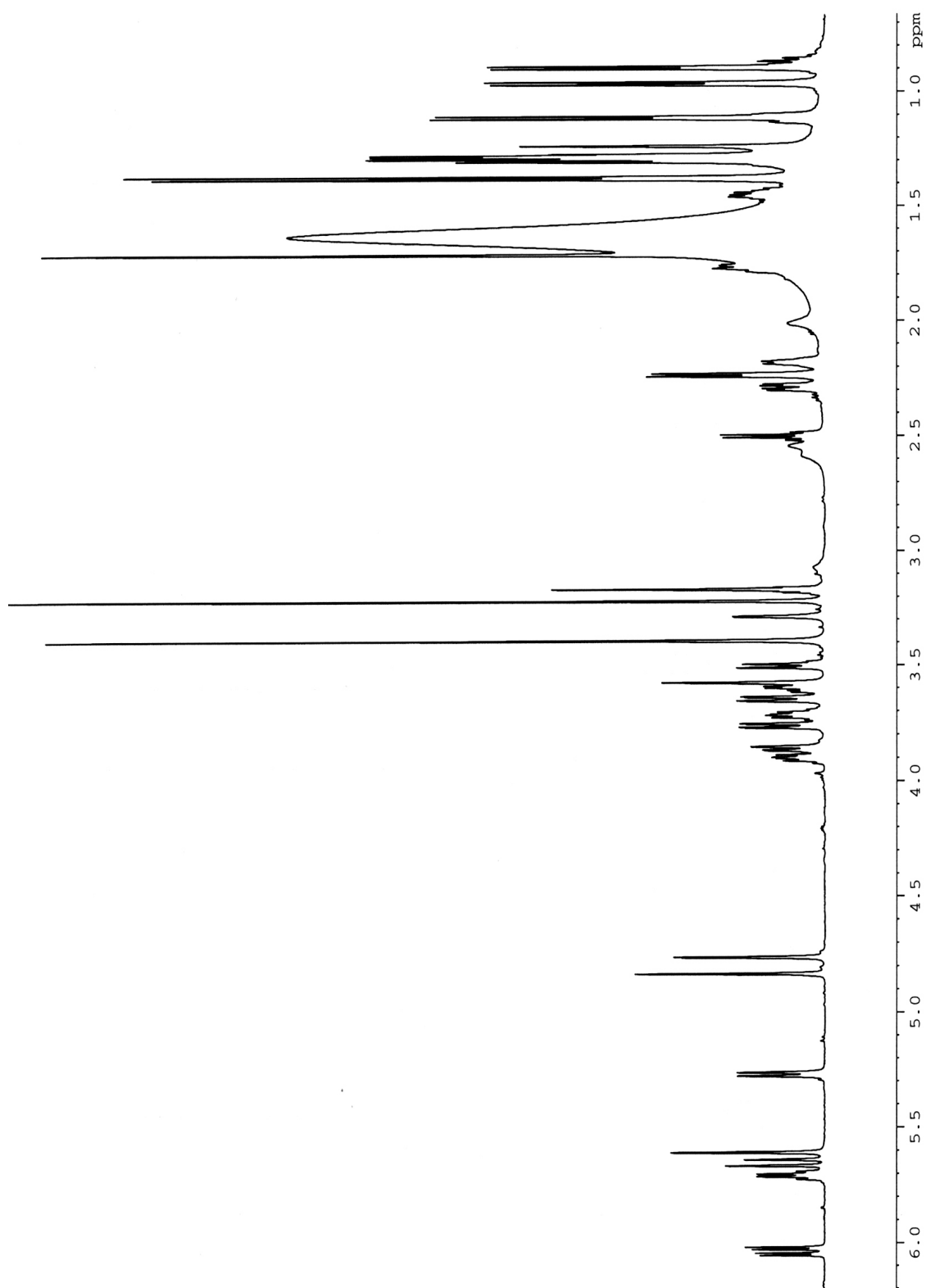


Figure S9. ^1H NMR of phorbaside E (**7**) (600 MHz, CDCl_3)

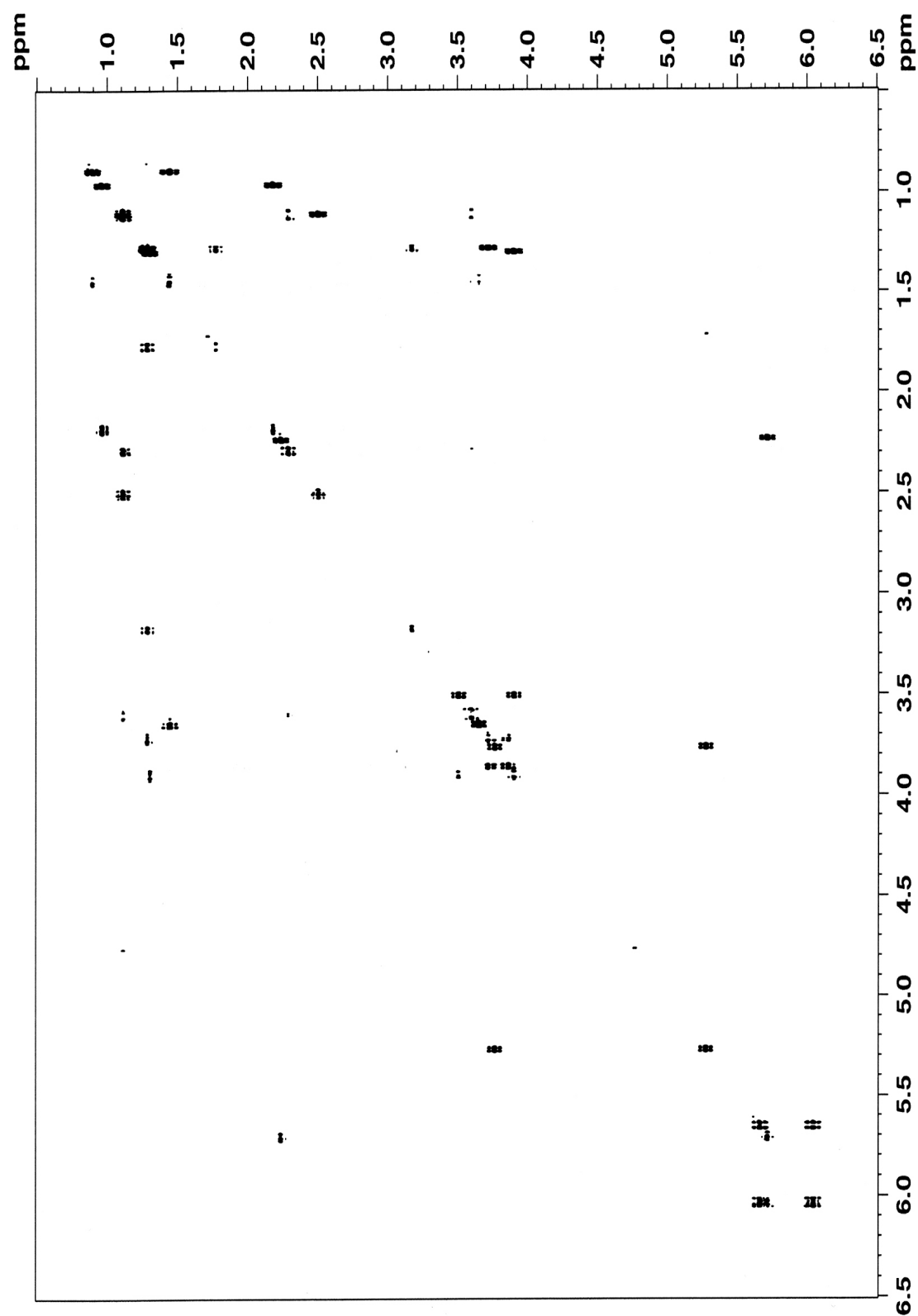


Figure S10. DQFCOSY of phorbaside E (**7**) (600 MHz, CDCl₃)

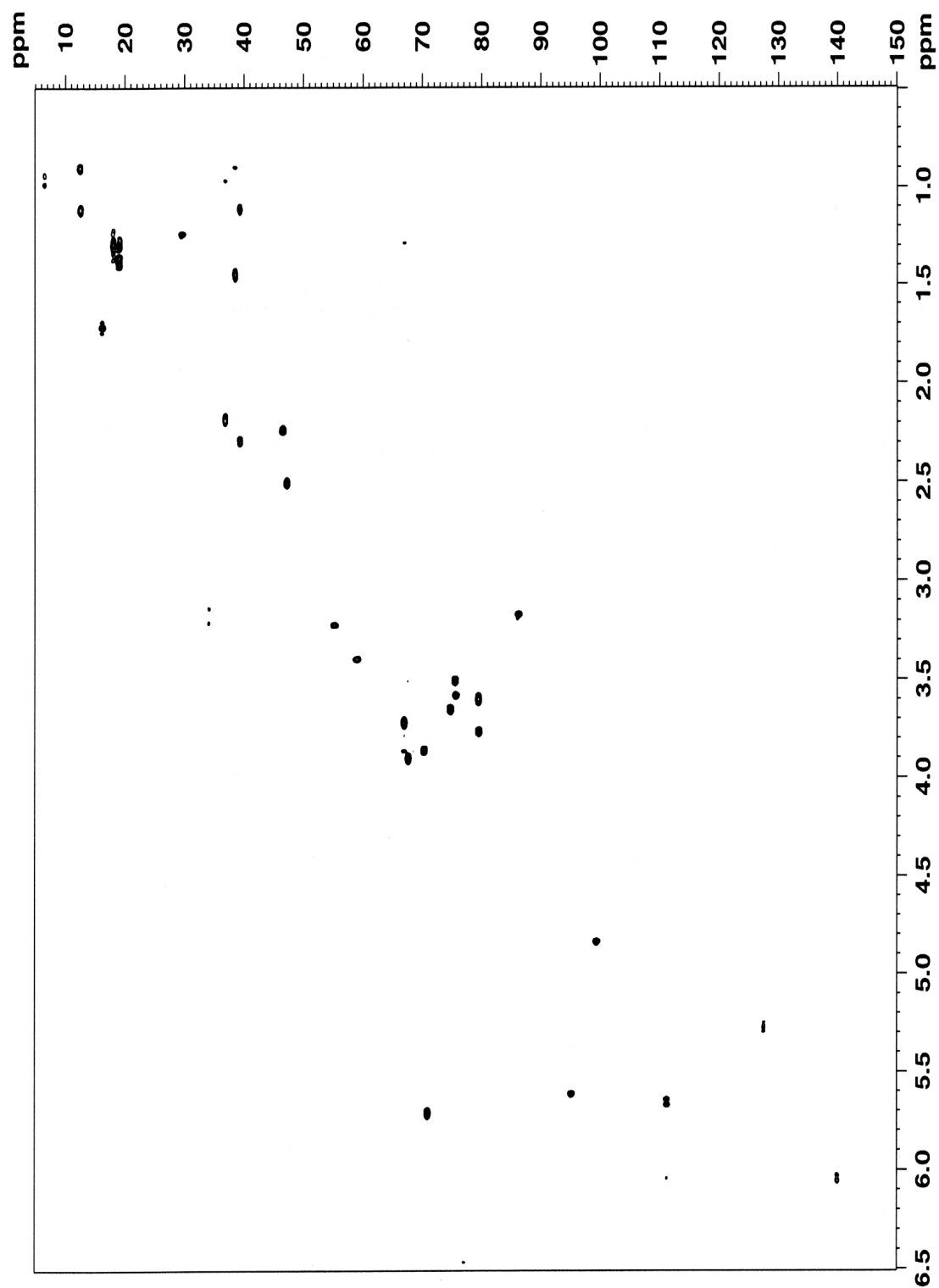


Figure S11. gHSQC of phorbaside E (**7**) (600 MHz, CDCl₃).

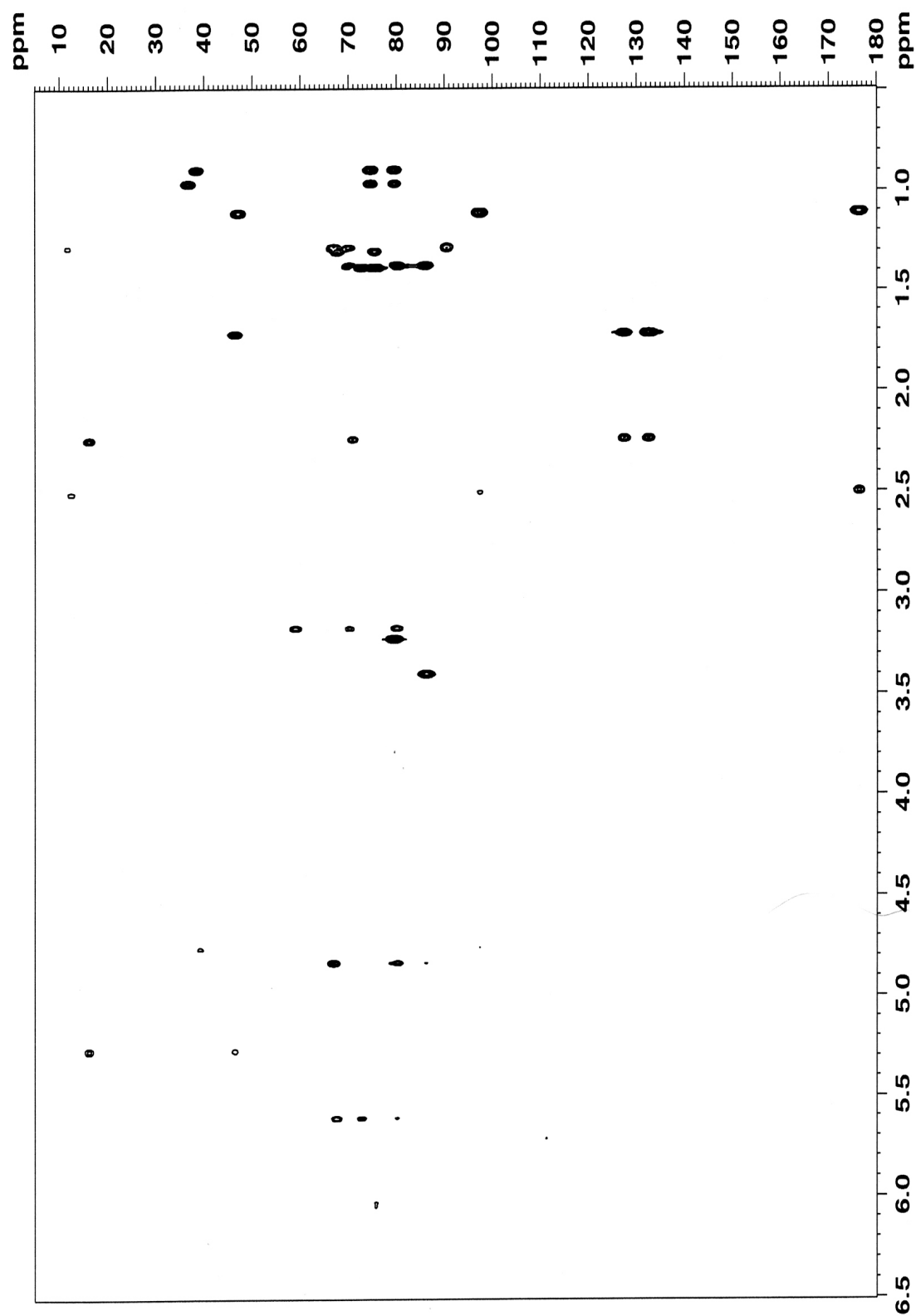


Figure S12. gHMBC of phorbaside E (**7**) (600 MHz, CDCl₃).