Supporting Information

Nocapyrones A – D, γ-Pyrones from a *Nocardiopsis* Strain Isolated from the Marine Sponge *Halichondria panicea*

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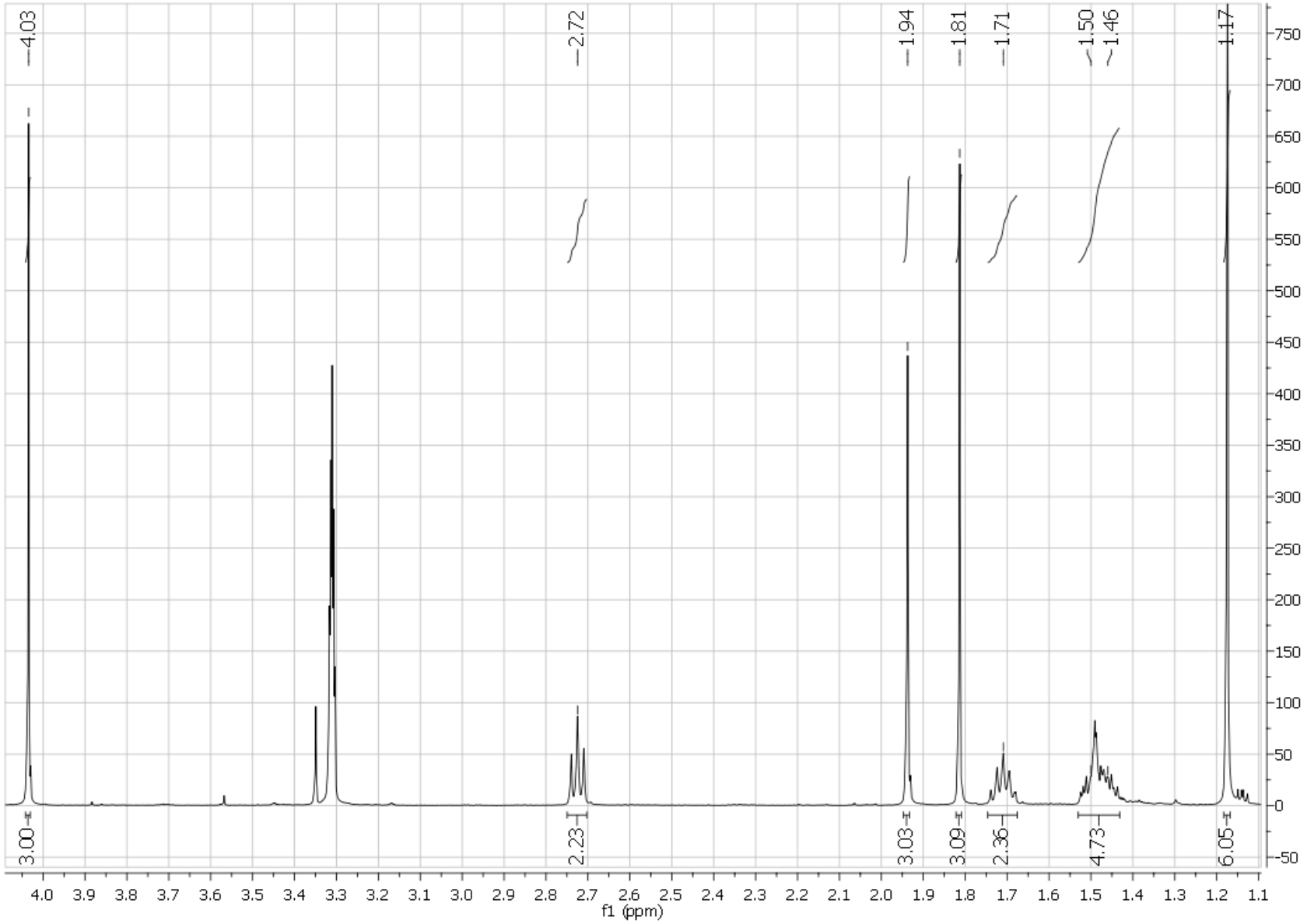
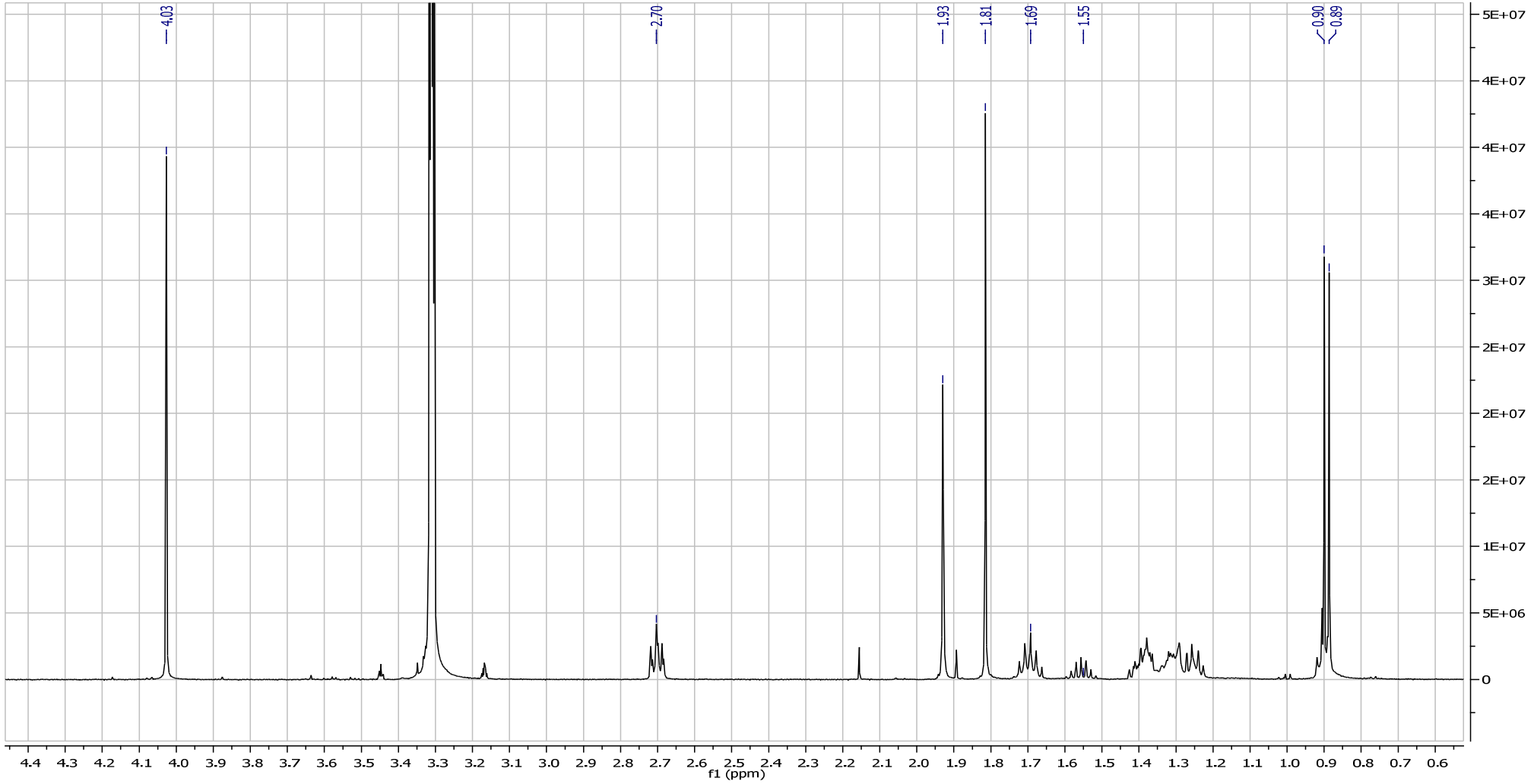
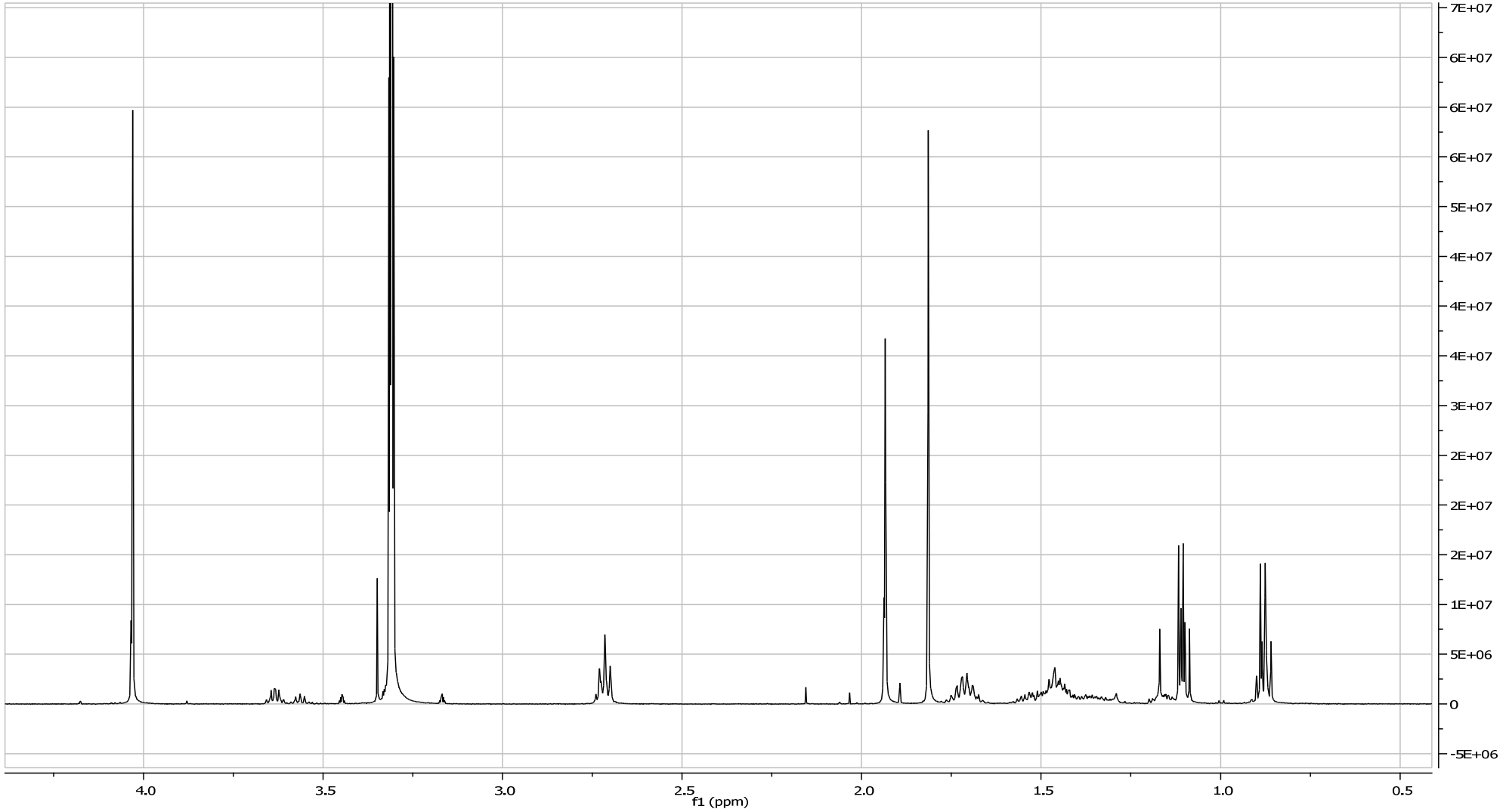
S1. ^{1}H NMR (500 MHz, CD_3OD) spectrum of nocapyrone A (**1**)



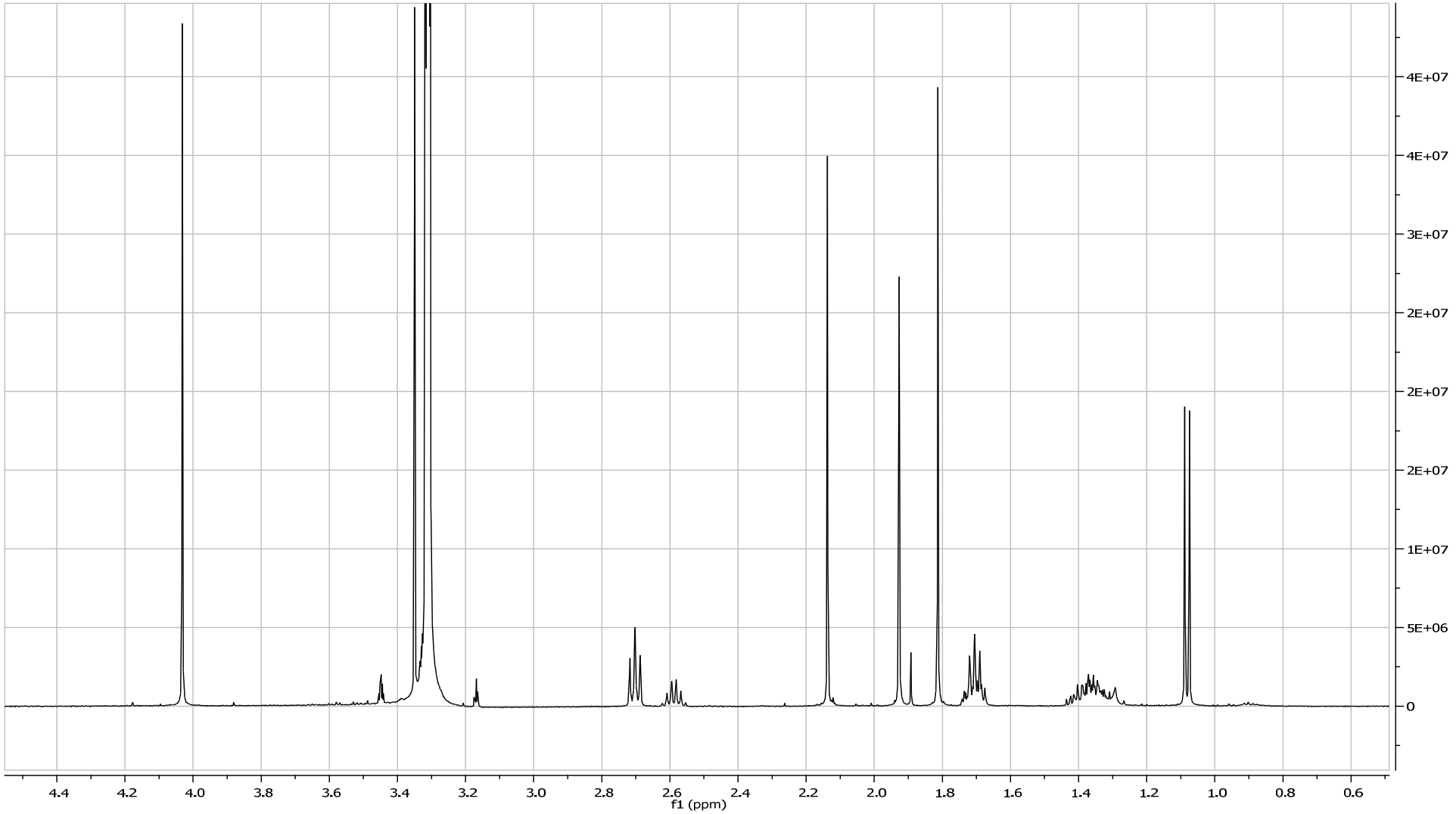
S2. ^{1}H NMR (500 MHz, CD_3OD) spectrum of nocapyrone B (**2**)



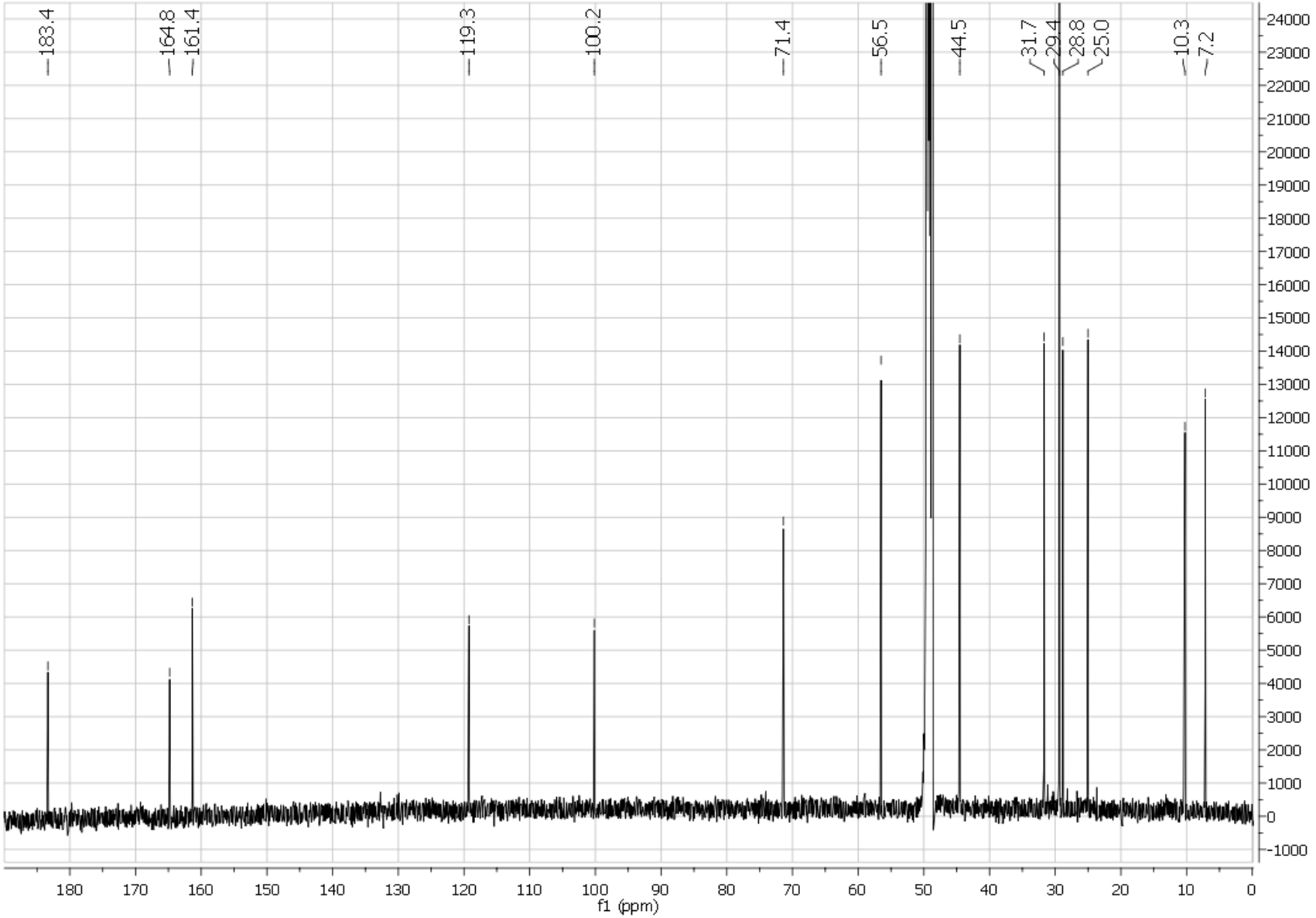
S3. ^{1}H NMR (500 MHz, CD_3OD) spectrum of nocapyrone C (**3**)



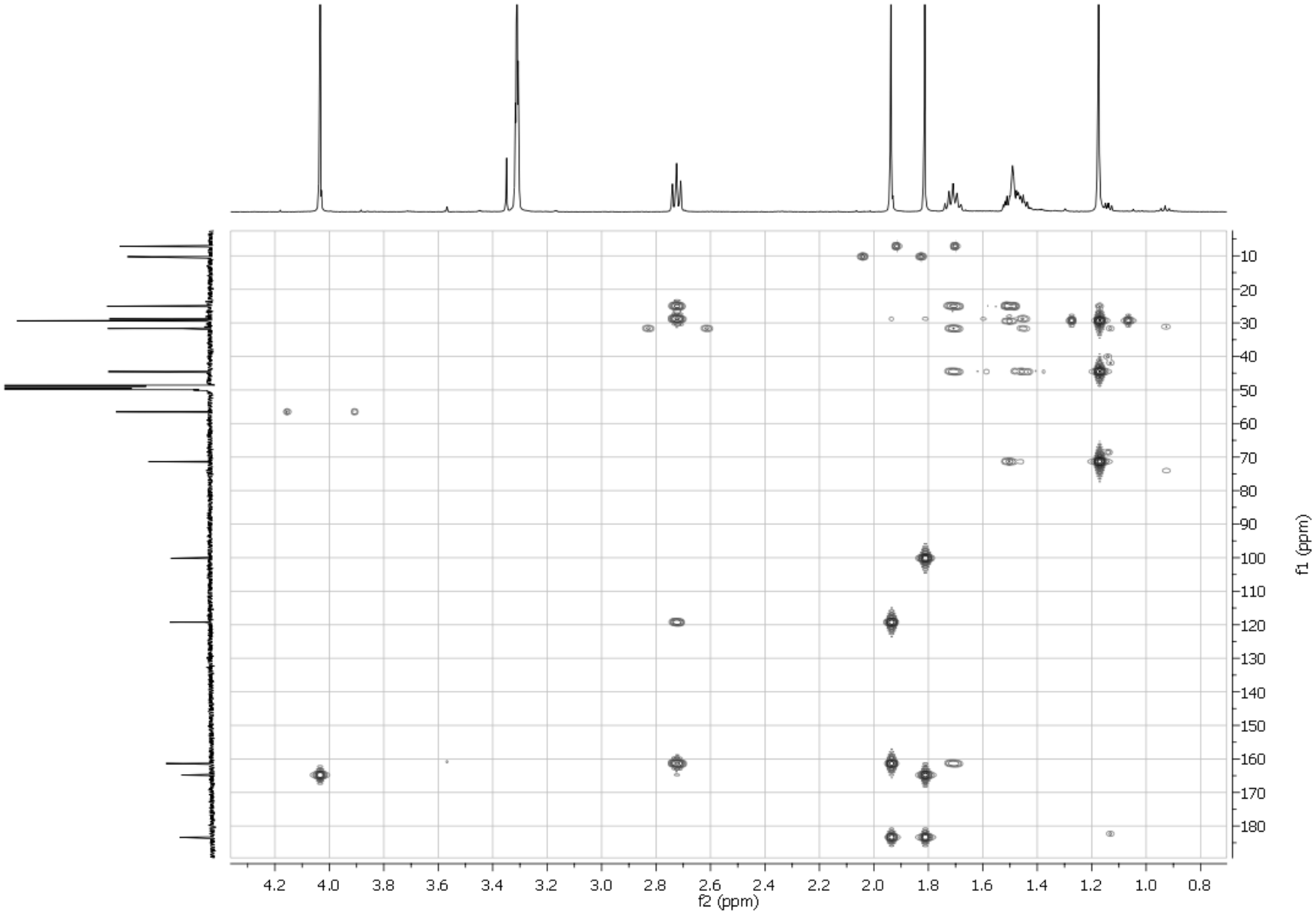
S4. ^{1}H NMR (500 MHz, CD_3OD) spectrum of nocapyrone D (**4**)



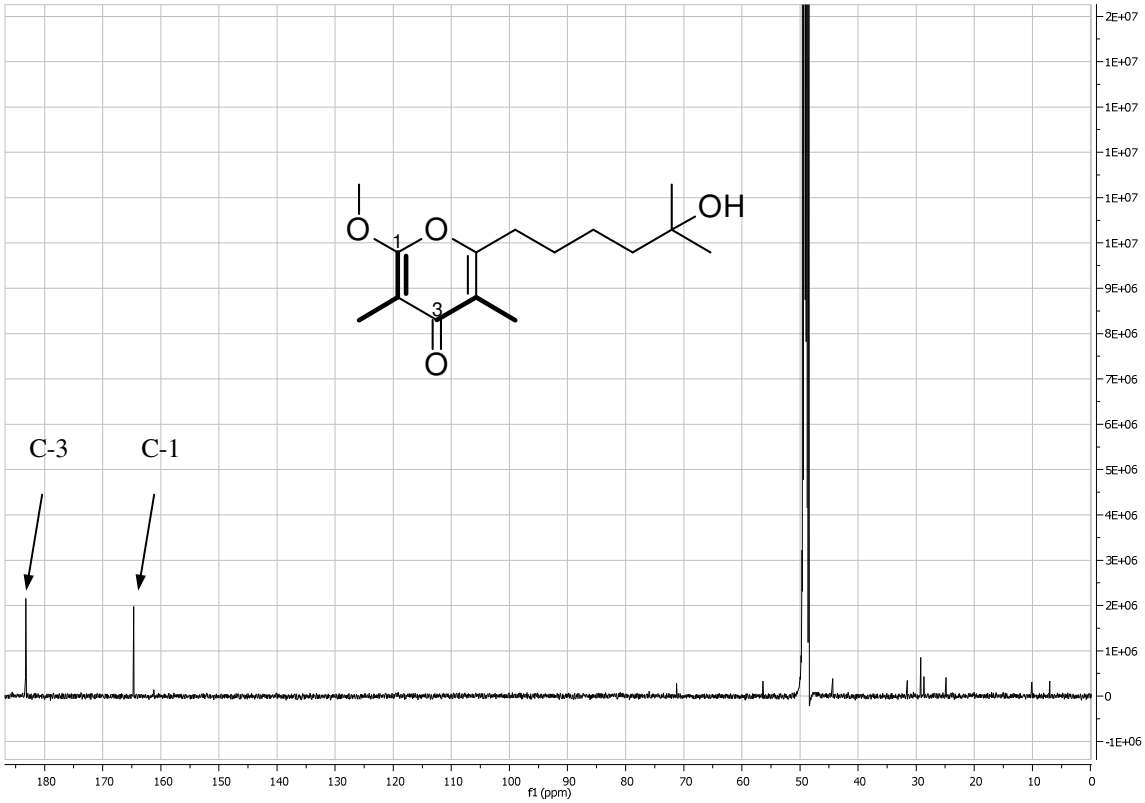
S5. ^{13}C NMR (125 MHz, CD_3OD) spectrum of nocayprone A (**1**)



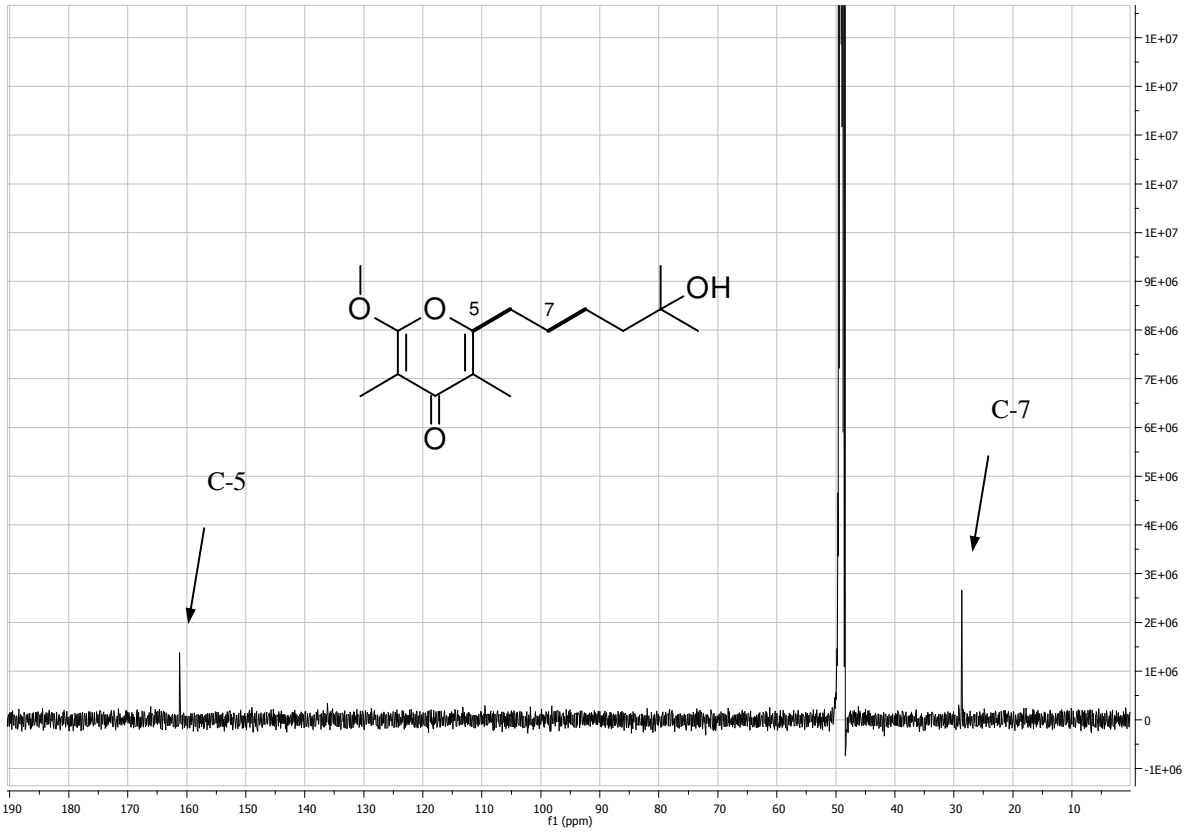
S6. ^{1}H-^{13}C HMBC NMR (500 MHz, 125 MHz, CD_3OD) spectrum of nocapyrone A (**1**)



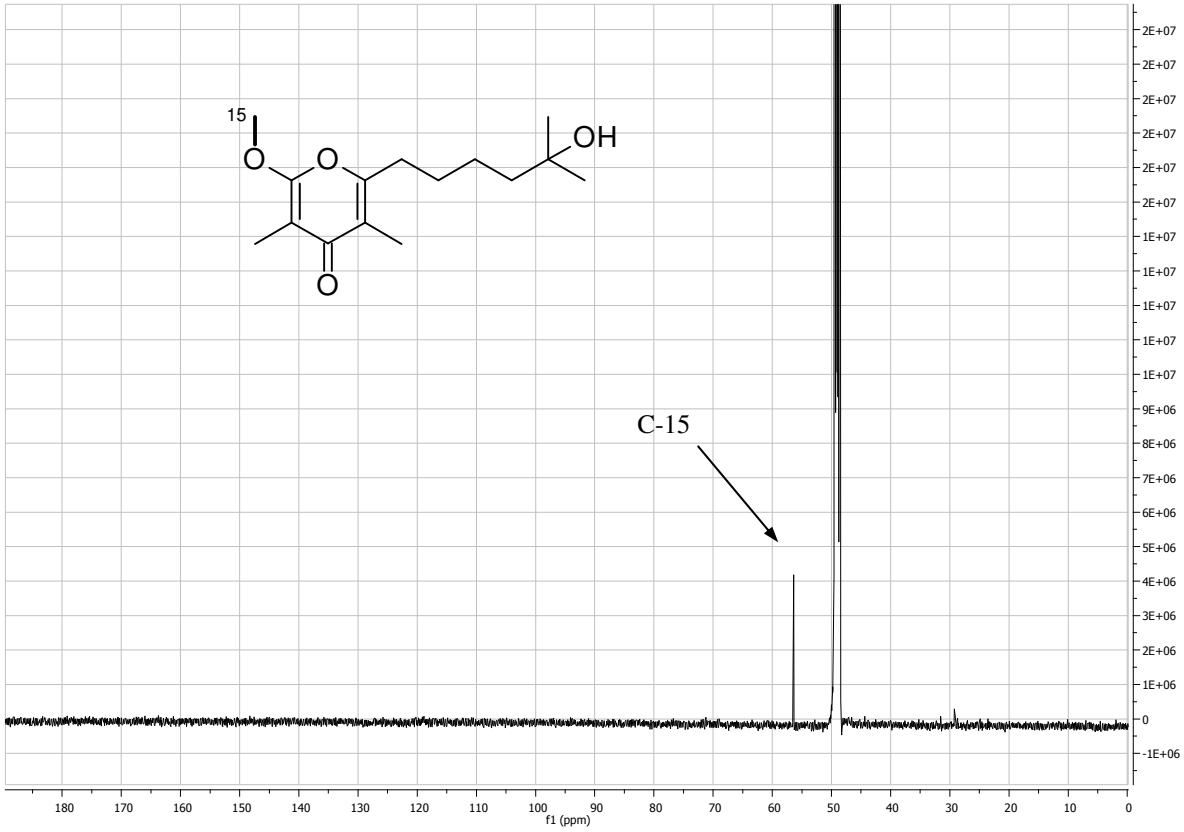
S7. ^{13}C NMR spectrum of **1** after feeding experiments with labelled proprionate



S8. ^{13}C NMR spectrum of **1** after feeding experiments with labelled acetate (1-^{13}C-acetate)



S9. ^{13}C NMR spectrum of **1** after feeding experiments with labelled methionine ([Me-^{13}C] methionine)



S10. NMR Spectroscopic Data (500 MHz, CD_3OD) for nocapyrone B (**2**)

nocapyrone B (**2**)				
position	δ_C, mult.	δ_H (*J* in Hz)	HMBC	COSY
1	164.9, C			
2	100.0, C			
3	183.3, C			
4	119.2, C			
5	161.8, C			
6	31.5, CH_2	2.70, t (7.5)	4, 5, 7, 8	7
7	27.9, CH_2	1.69,quint. (7.5)	5, 6, 8, 9	6, 8
8	30.2, CH_2	1.42, m	7, 9	7, 9
9	39.7, CH_2	1.31, m	8, 10, 11/12	8
10	29.2, CH	1.55, septett (6.8)	11/ 12	9, 11/ 12
11/ 12	22.9, CH_3	0.90, d (6.8)	9, 10, 11/12	10
13	10.2, CH_3	1.93, s	3, 4, 5	
14	7.0, CH_3	1.81, s	1, 2, 3	
15	56.3, CH_3	4.03, s	1	

S11. NMR Spectroscopic Data (500 MHz, CD_3OD) for nocapyrone C (**3**)

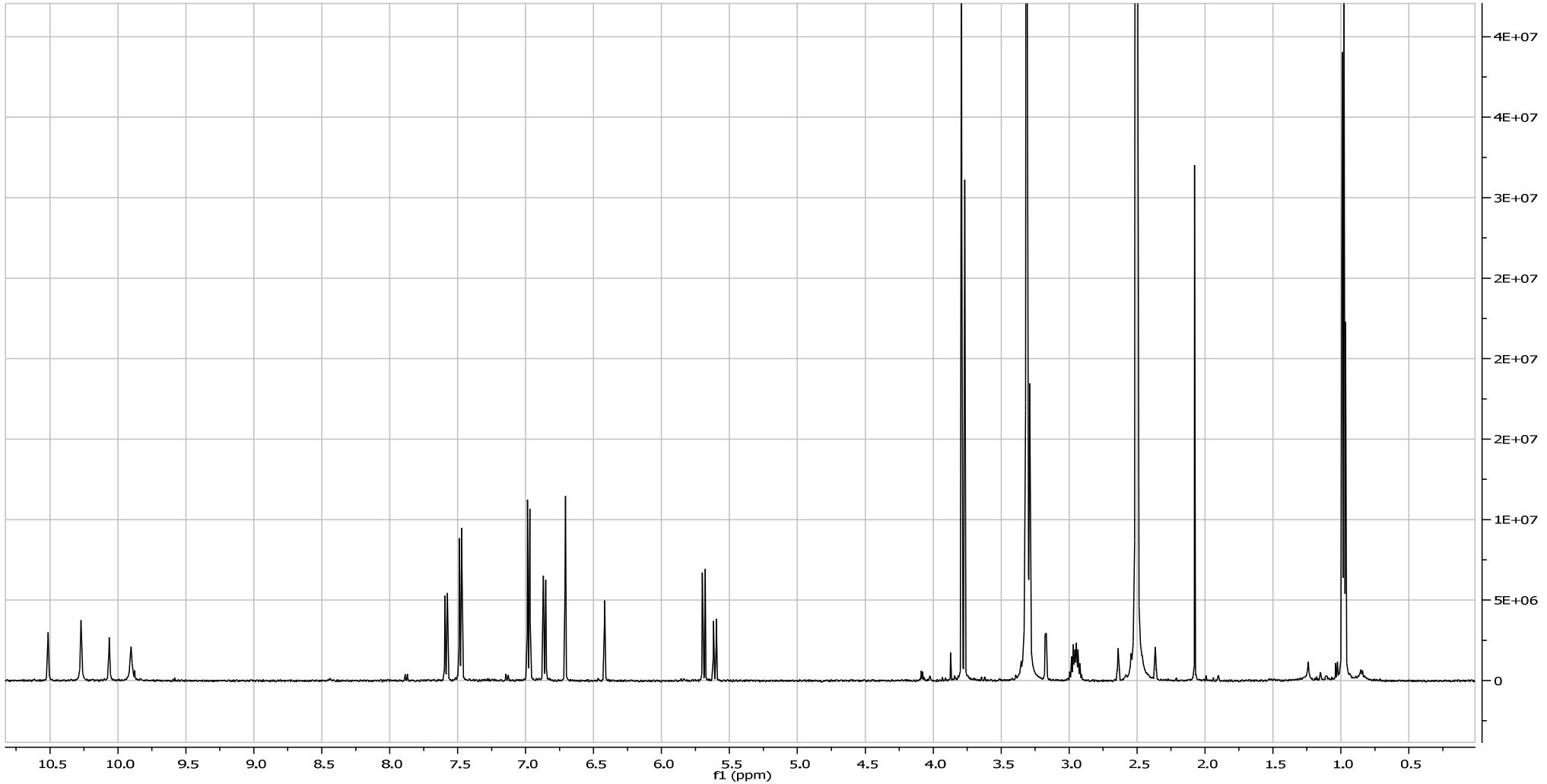
nocapyrone C (**3**)				
position	δ_C, mult.	δ_H (*J* in Hz)	HMBC	COSY
1	164.6, C			
2	100.1, C			
3	183.2, C			
4	119.2, C			
5	161.3, C			
6	31.5, CH_2	2.72, t (7.5)	4, 5	7
7	27.7, CH_2	1.71, m (7.5)	6	6, 8
8	33.5, CH_2	1.3 - 1.5, m		
9	33.3, CH_2	1.3 - 1.5, m		
10	40.8, CH	1.45, m		11, 16
11	71.8, CH	3.62, dq (6.2, 4.6)		10, 11
12	20.0, CH_3	1.11, d (6.2)	10, 11	11
13	10.1, CH_3	1.93, s	3, 4, 5	
14	7.0, CH_3	1.81, s	1, 2, 3	
15	56.4, CH_3	4.03, s	1	
16	14.9, CH_3	0.88, d (6.9)	9, 10, 11	10

S12. NMR Spectroscopic Data (500 MHz, CD_3OD) for nocapyrone D (**4**)

nocapyrone D (**4**)				
position	δ_C, mult.	δ_H (*J* in Hz)	HMBC	COSY
1	164.8[a], C			
2	99.8[a], C			
3	182.7[a], C			
4	119.0[a], C			
5	161.0[a], C			
6	31.4, CH_2	2.70, t (7.5)	4, 5, 7	7
7	27.7, CH_2	1.71, quint. (7.5)	5, 8, 9	6, 8
8	31.2, CH_2	1.28-1.45, m		
9	33.4, CH_2	1.70, 1.40, m	7	
10	47.4, CH	2.59, sextett (6.8)		9, 16
11	215.3[a], C			
12	28.3, CH_3	2.14, s	10, 11	
13	10.1, CH_3	1.93, s	3, 4, 5	
14	7.0, CH_3	1.81, s	1, 2, 3	
15	56.3, CH_3	4.03, s	1	
16	16.5, CH_3	1.08, d (7.0)	9, 10, 11	10

[a]shifts of the quaternary carbons were deduced from the ^1H-^{13}C HMBC spectrum

S13. ^{1}H NMR (500 MHz, DMSO-d6) of (2*E*/5*Z*)- and (2*Z*/5*Z*)-2-[(4-methoxyphenyl)methylene]-5-(2-methylpropylidene)-3,6-piperazinedione (**5**)



S14. Chemical data of (2*E*/5*Z*)-2-[(4-methoxyphenyl)methylene]-5-(2-methylpropylidene)-3,6-Piperazinedione (**5**)

White amorphous solid, UV (MeOH) λ_{max} (log ε) 339 (4.19), 239 (3.84) nm; ^{1}H NMR (500 MHz, DMSO-d6) δ 10.27 (1H, s, H-1), 9.90 (1H, s, H-4), 7.47 (2H, d, *J* = 8.9 Hz, H-13, H-17), 6.98 (2H, d, *J* = 8.9 Hz, H-14, H-16), 6.70 (1H, s, H-11), 5.68 (1H, d, *J* = 10.5 Hz, H-7), 3.79 (3H, s, OCH_3-18), 2.95 (1H, m, H-8), 0.97 (6H, d, *J* = 6.25 Hz, CH_3-9, CH_3-10); ^{13}C NMR (125 MHz, DMSO-d6) δ 159.2 (C-15), 158.1 (C-3), 157.6 (C-6), 132.2 (C-5), 131.0 (C-13, C-17), 125.5 (C-2), 125.4 (C-12), 124.9 (C-7), 114.3 (C-14, C-16), 113.2 (C-11), 55.4 (C-18), 24.0 (C-8), 22.4 (C-9, C-10); **(2*Z*/5*Z*) isomer:** ^{1}H NMR of (500 MHz, DMSO-d6) δ 10.27 (1H, s, H-4), 10.06 (1H, s, H-1), 7.58 (2H, d, *J* = 8.6 Hz, H-13, H-17), 6.86 (2H, d, *J* = 8.6 Hz, H-14, H-16), 6.41 (1H, s, H-11), 5.60 (1H, d, *J* = 11.4 Hz, H-7), 3.76 (3H, s, OCH_3-18), 2.95 (1H, m, H-8), 0.97 (6H, d, *J* = 3.9 Hz, CH_3-9, CH_3-10); ^{13}C NMR (125 MHz, DMSO-d6) δ 158.9 (C-15), 158.8 (C-3), 157.0 (C-6), not determined (C-5), 132.1 (C-13, C-17), 125.1 (C-2), 126.5 (C-12), 123.8 (C-7), 113.1 (C-14, C-16), 120.4 (C-11), 55.1 (C-18), 24.2 (C-8), 22.3 (C-9, C-10); HRESIMS *m/z* 309.1219 $[M + Na]^+$ (calcd. for $C_{16}H_{18}N_2O_3$, 309.1210).

S15. Enzyme Inhibitory Activity

To uncover specific enzyme inhibitory activities, compound **1** was screened in several enzyme activity tests including prominent drug targets such as phosphodiesterase 4 (PDE4), protein tyrosine phosphatase 1B (PTP1B) and acetylcholine esterase (AchE). AchE activity was measured using adaptations of the colorimetric assay described by Ellman *et al*. 1961 for a microplate test system.[1] Putative inhibitory activities against human recombinant protein tyrosin phosphatase 1B were tested using the Biomol Green PTP1B tyrosin phosphatase drug discovery kit (catalogue number BML-AK822, *Enzo Life Sciences GmbH*, Lörrach, Germany). Reverse transcriptase activity was assayed using a colorimetric reverse transcriptase enzyme-linked immunosorbent assay (ELISA) kit (catalogue number 11468120910, *Roche*, Mannheim, Germany) according to the manufacturer's instructions. The activity of phosphodiesterase 4 (PDE4) was measured using the PDE Light HTS cAMP phosphodiesterase kit (catalogue number LT07-600, *Lonza*, Rockland, USA) according to the manufacturer's instructions. Enzyme assays to determine GSK-3β activity were carried out as described by Baki *et al.* 2007.[2] In addition, **2** was tested against PTB1B and **5** against AchE.

(1) Ellman, G. L.; Courtney, K. D.; Andres, V.; Featherstone, R. M. *Biochem. Pharmacol.* **1961**, *7*, 88-95.

(2) Baki, A.; Bielik, A.; Molnár, L.; Szendrei, G.; Keserü, G. M. *Assay. Drug Dev. Technol.* **2007**, *5*, 75-83.

S16. Photograph and description of colony morphology of the investigated bacterium

Isolation: The strain HB383 was obtained from the marine sponge *Halichondria panicea*, collected in the Kiel Fjord, Baltic Sea, Germany, in February 2004.

Colony morphology: Colony diameter 19 to 44 mm on Gym4 medium after 10 d incubation at 28°C. Colonies greenish, later whitish, bold to powdery.

Agar colony of HB383, grown on Gym4 medium for 10 d