Antifungal and Cytotoxic *β*-Resorcylic Acid Lactones from *Paecilomyces* sp.

Liangxiong Xu,[†] Ping Wu,[†] Jinghua Xue,[†] Istvan Molnar,[‡] Xiaoyi Wei[*,†]

[†] Key Laboratory of Plant Resources Conservation and Sustainable Utilization / Guangdong Provincial Key Laboratory of Applied Botany, South China Botanical Garden, Chinese Academy of Sciences, Guangzhou 510650, P. R. China

[‡] Natural Products Center, School of Natural Resources and the Environment, University of Arizona, Tucson, AZ 85706, United States of America

*Corresponding author. E-mail: wxy@scbg.ac.cn; Tel: +86-20-37252538; Fax: +86-20-37252537.

Supporting Information

Table of Contents

1. Computational Results

2. NMR Spectra and HRESIMS of Compounds 1–8

3. Comparison between ECD Spectra of 7 and 8

Table S1. Relative and free energies[a] and equilibrium populations[b] of low-energy conformers of **1**–**3**, **5**, and **6** in MeOH

conformer	Δ*E*	Δ*G*	P (%)
compound **1**			
1a	0.0	0.0	69.2
1b	0.50	0.48	30.8
compound **2**			
2a	0.00	0.00	71.3
2b	0.52	0.54	28.7
compound **3**			
3a	0.0	0.0	35.3
3b	0.04	0.09	30.3
3c	0.91	0.70	10.8
3d	0.99	0.93	7.3
3e	0.90	1.02	6.3
3f	1.51	1.32	3.8
3g	1.51	1.48	2.9
3h	2.39	1.96	1.3
3i[c]	2.19	2.10	1.0
3j[c]	2.68	2.19	0.9
compound **5**			
5a	0.00	0.00	87.2
5b	1.15	1.51	6.8
5c	2.07	2.06	2.7
5d	2.02	2.13	2.4
5e[c]	2.35	2.71	0.9
compound **6**			
6a	0.0	0.0	65.9
6b	0.16	0.39	34.1
6c[c]	4.41	4.13	0.1

[a] At the B3LYP/6-311+G(d,p) (**1** and **2**) or B3LYP/def2-TZVP (others) level, in kcal/mol.

[b] From Δ*G* values at 298.15 K.

[c] Conformer not used for ECD/ TDDFT calculations.

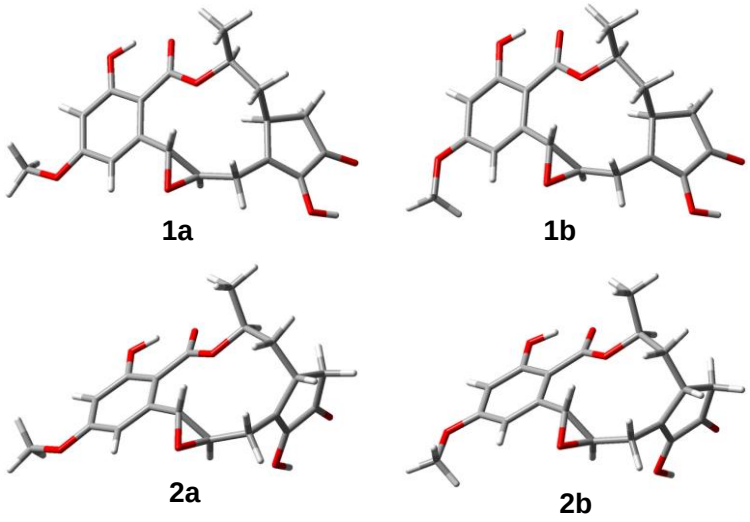


Figure S1. Conformations of low-energy conformers of **1** and **2**.

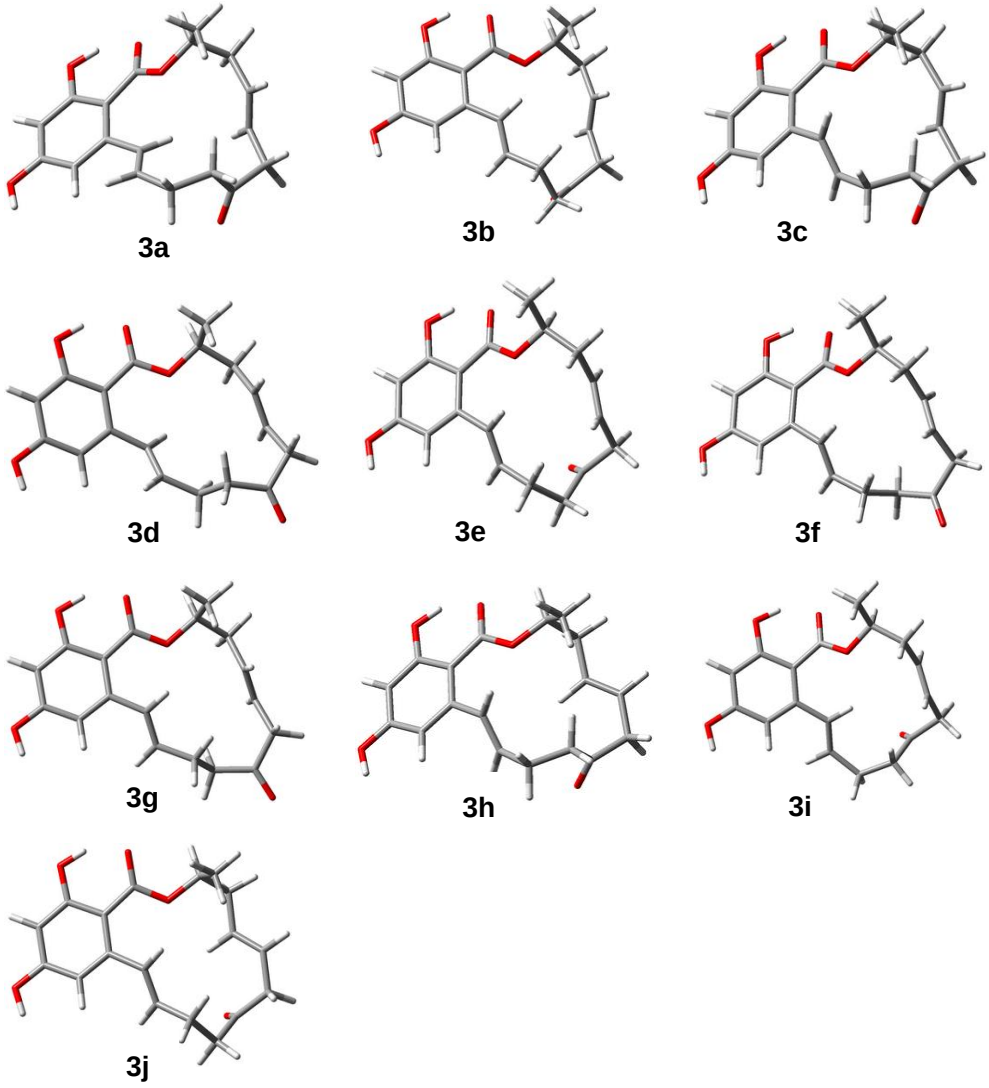


Figure S2. Conformations of low-energy conformers of **3**.

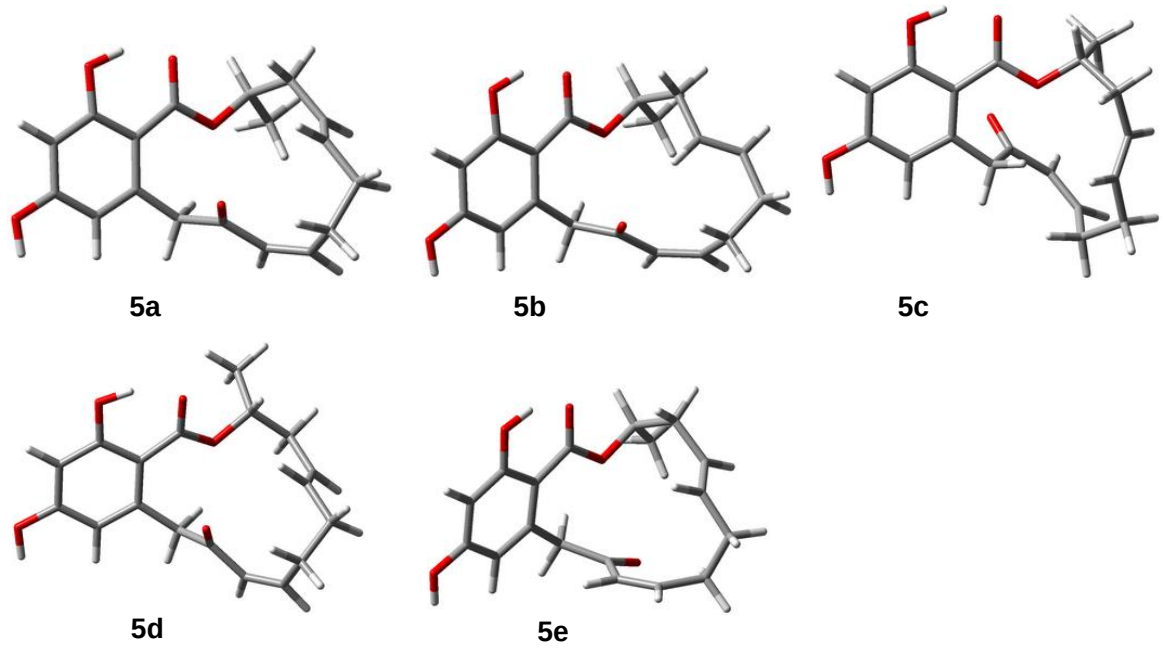


Figure S3. Conformations of low-energy conformers of **5**.

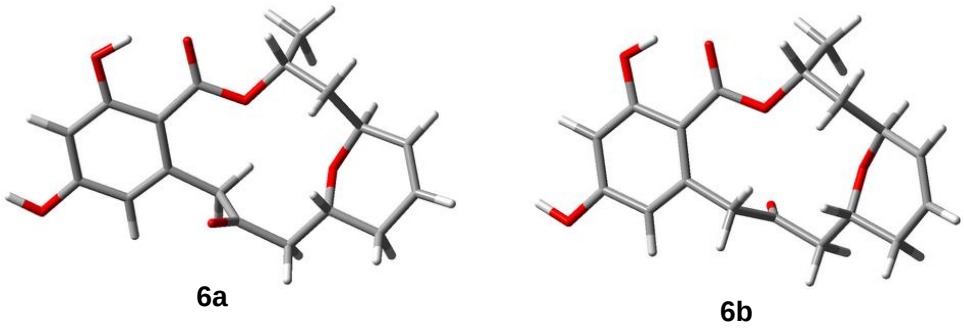


Figure S4. Conformations of low-energy conformers of **6**.

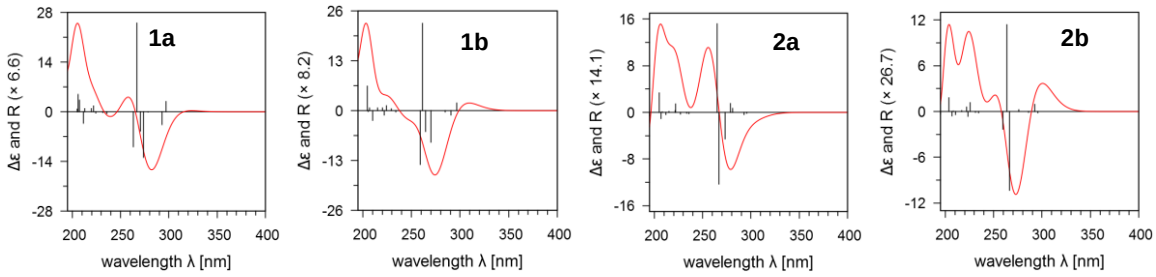


Figure S5. B3LYP/TZVP calculated ECD spectra of the low-energy conformers of **1** and **2** in MeOH. Vertical bars represent rotational strengths *R*. σ = 0.29 eV; shift = ±0 nm.

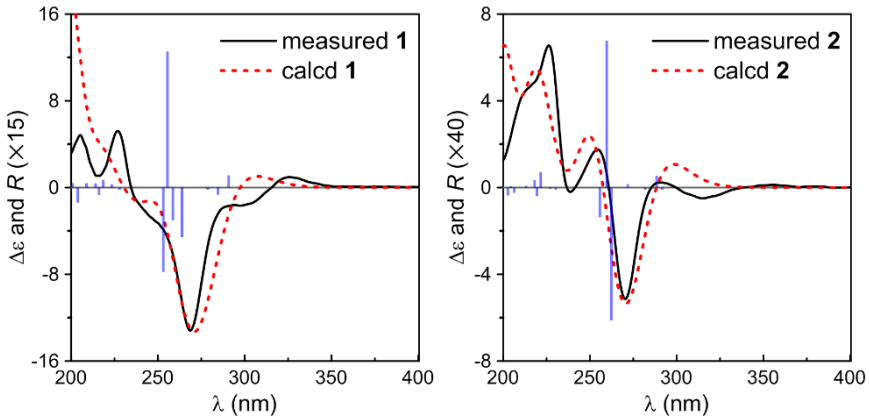


Figure S6. Comparison between B3LYP/TZVP calculated and experimental ECD spectra of **1** and **2** in MeOH. Vertical bars represent rotational strengths *R* of the global energy minima). Parameters for calculated ECD spectra: σ = 0.29 eV (for both), shift = –6 (for **1**) / –4 (for **2**) nm, and scaling factor = 0.85 (for **1**) / 0.53 (for **2**).

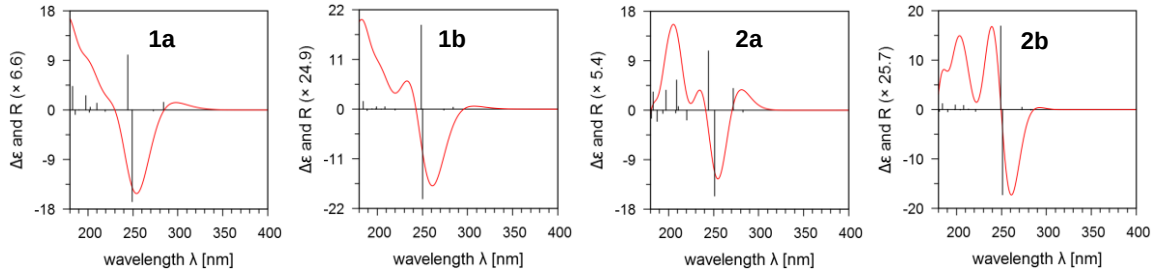


Figure S7. CAM-B3LYP/TZVP calculated ECD spectra of the low-energy conformers of **1** and **2** in MeOH. Vertical bars represent rotational strengths *R*. 0.40 (for **1**) or 0.32 (for **2**) eV; shift = ±0 nm.

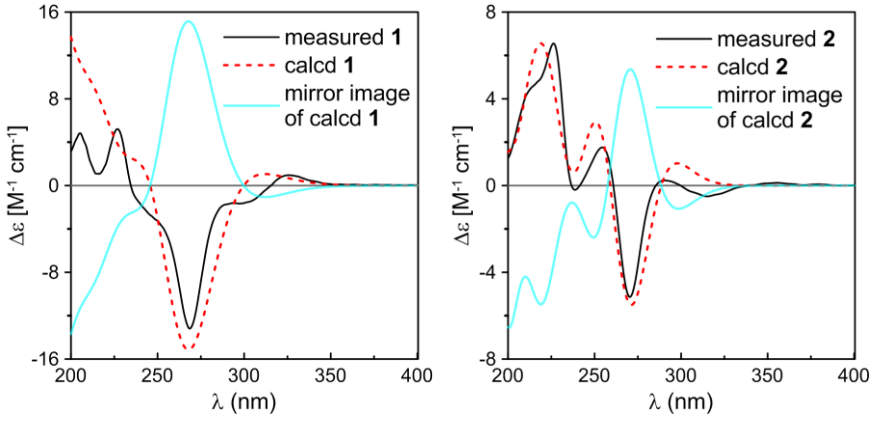


Figure S8. Comparison between CAM-B3LYP/TZVP calculated and experimental ECD spectra of **1** and **2** in MeOH. σ = 0.40 (for **1**) or 0.32 (for **2**) eV; shift = +11 (for **1**) or +14 (for **2**) nm.

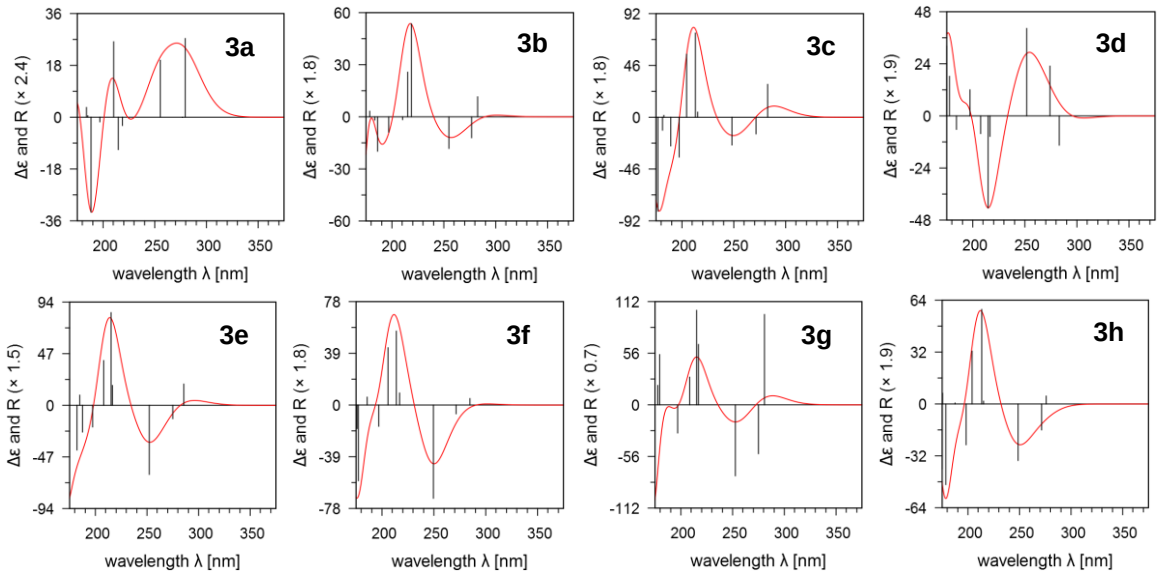


Figure S9. Calculated ECD spectra of the low-energy conformers of **3** in MeOH using the ωB97X /TZVP method. Vertical bars represent rotational strengths *R*. σ = 0.35 eV; shift = ±0 nm.

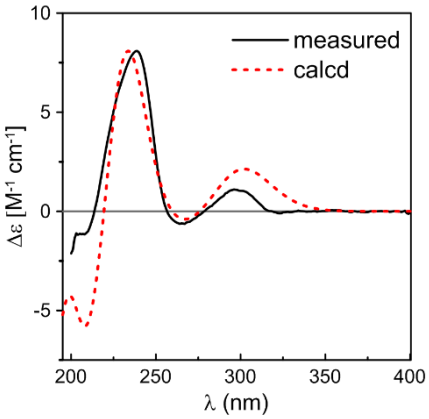


Figure S10. Comparison between the ωB97X/TZVP calculated and the measured ECD spectra of **3** in MeOH. Parameters for calculated ECD spectrum: σ = 0.35 eV, shift = +20 nm, and scaling factor = 0.24.

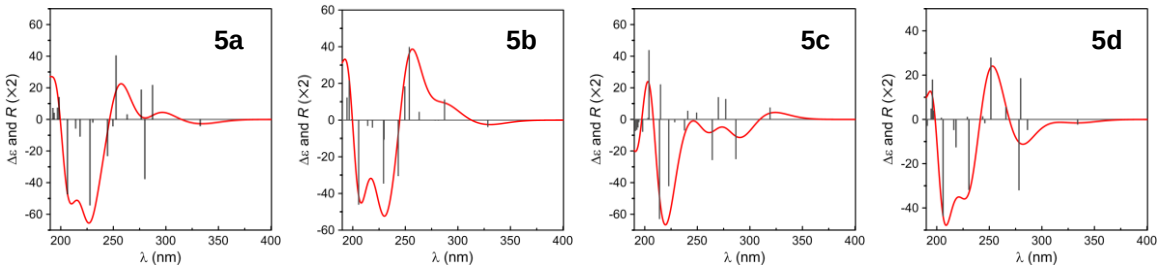


Figure S11. Calculated ECD spectra of the low-energy conformers of **5** in MeOH using the PBE1PBE /TZVP method. Vertical bars represent rotational strengths *R*. σ = 0.27 eV; shift = ±0 nm.

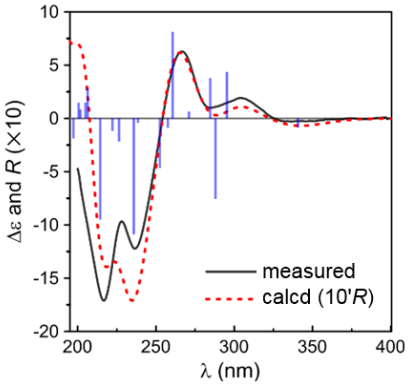


Figure S12. Comparison between the PBE1PBE/TZVP calculated and the measured ECD spectra of **5** in MeOH. Vertical bars represent rotational strengths *R* of the lowest-energy conformer. Parameters for calculated ECD spectrum: σ = 0.27 eV, shift = +8 nm, and scaling factor = 0.27.

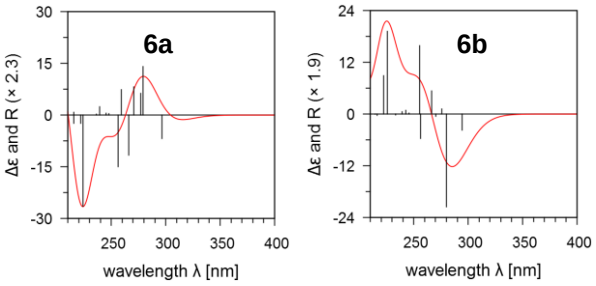


Figure S13. Calculated ECD spectra of the low-energy conformers of **6** in MeOH using the TPSSh /TZVP method. Vertical bars represent rotational strengths *R*. σ = 0.33 eV; shift = ±0 nm.

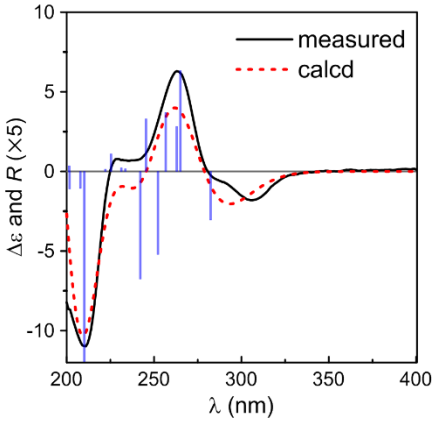


Figure S14. Comparison between the TPSSh/TZVP calculated and experimental ECD spectra of **6** in MeOH. Vertical bars represent rotational strengths *R* of the lowest-energy conformer. Parameters for calculated ECD spectrum: σ = 0.33 eV, shift = -14 nm, and scaling factor = 0.40.

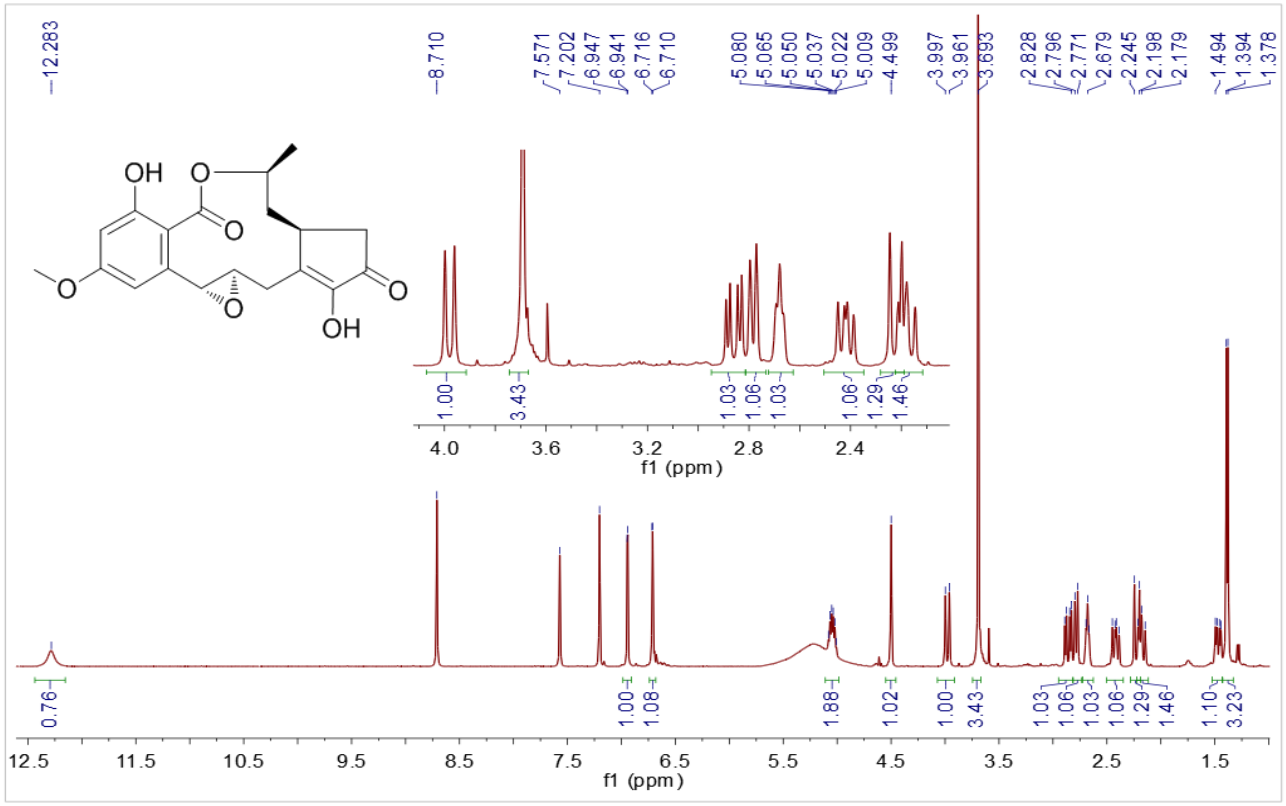


Figure S15. ^{1}H NMR (400 MHz) spectrum of paecilomycin N (**1**) in C_5D_5N.

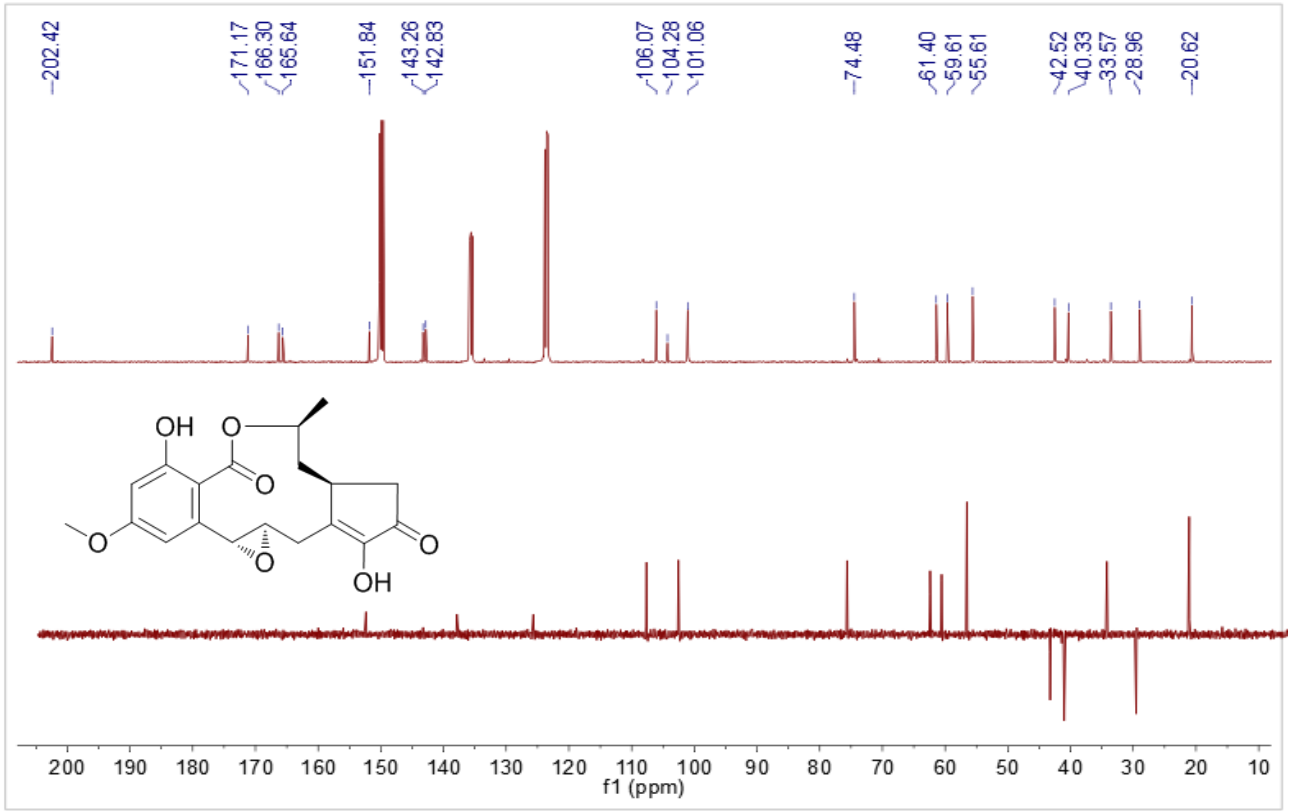


Figure S16. ^{13}C NMR (100 MHz) and DEPT spectra of paecilomycin N (**1**) in C_5D_5N.

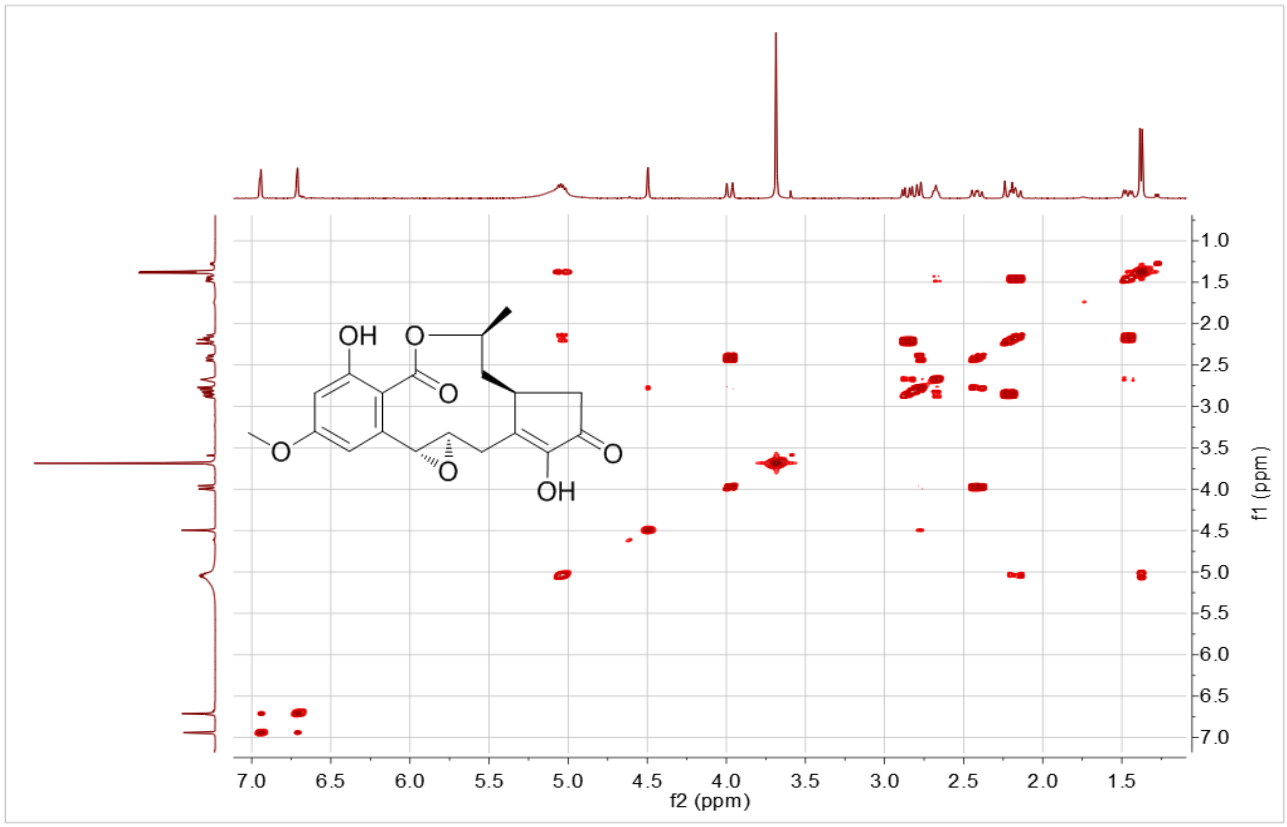


Figure S17. ^{1}H-^{1}H COSY spectrum of paecilomycin N (**1**) in C_5D_5N.

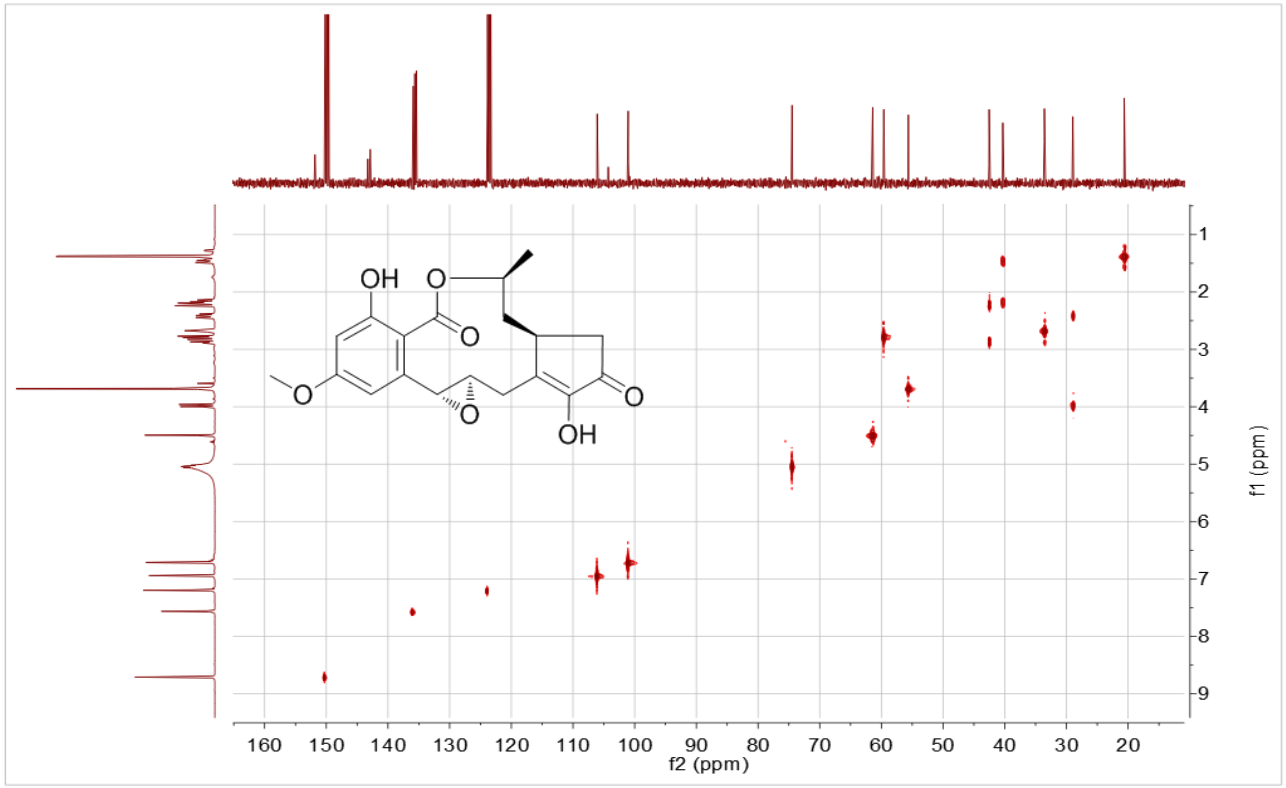


Figure S18. HSQC spectrum of paecilomycin N (**1**) in C_5D_5N.

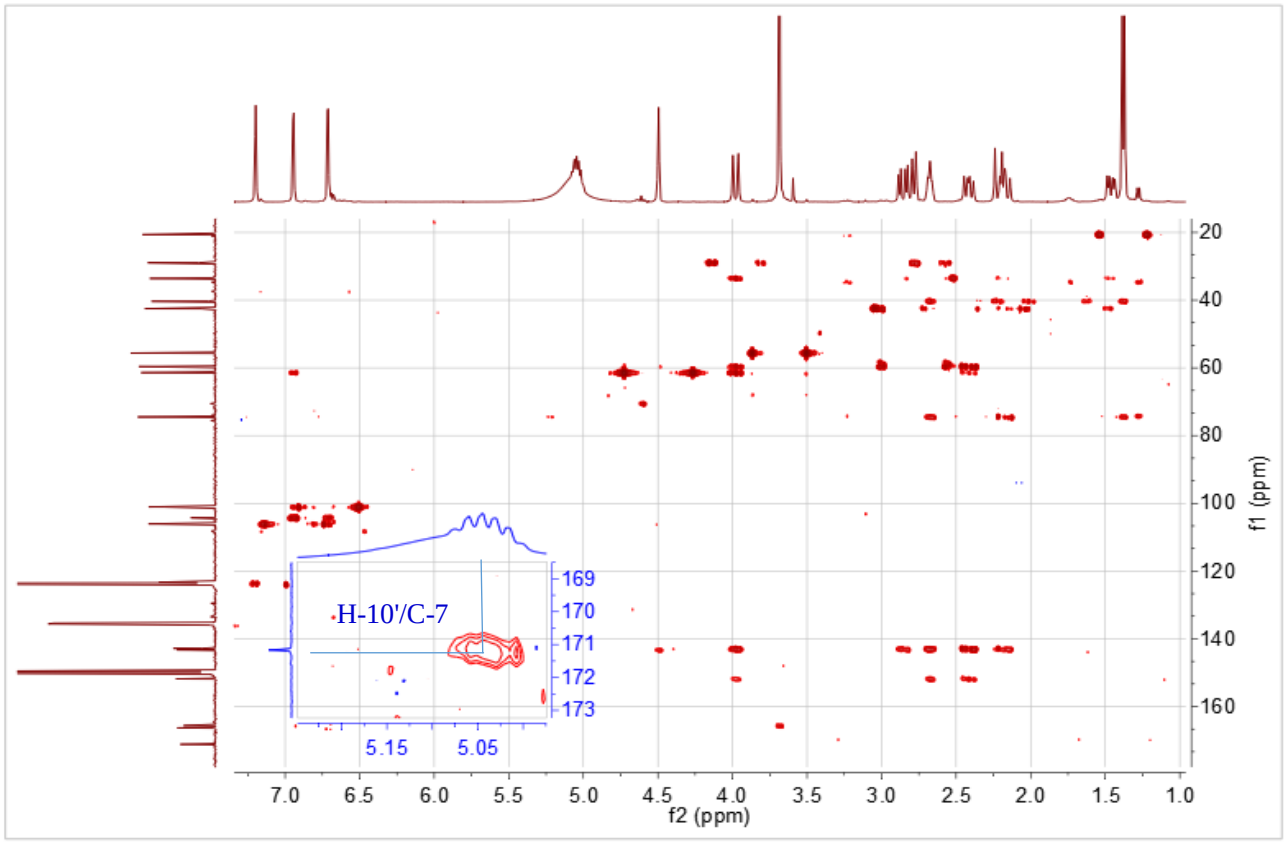


Figure S19. HMBC spectrum of paecilomycin N (**1**) in C_5D_5N.

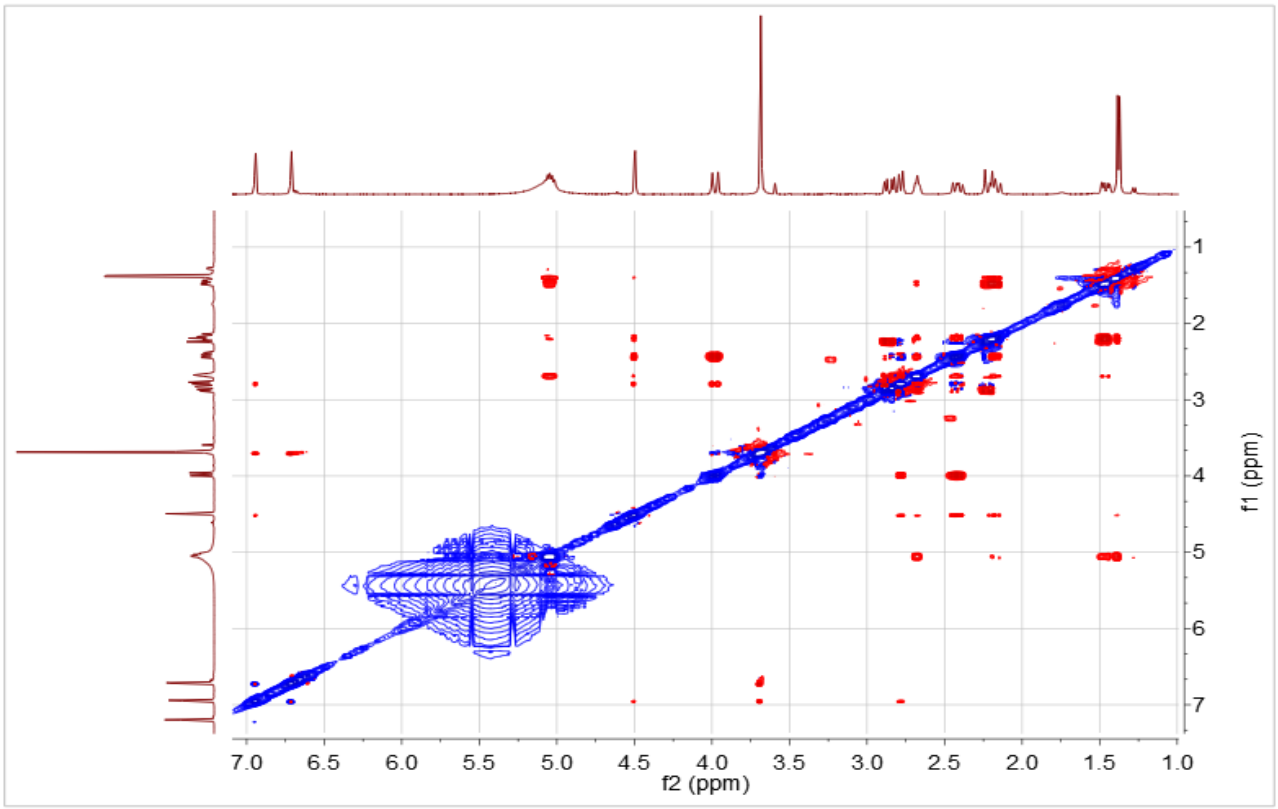


Figure S20. NOESY spectrum of paecilomycin N (**1**) in C_5D_5N.

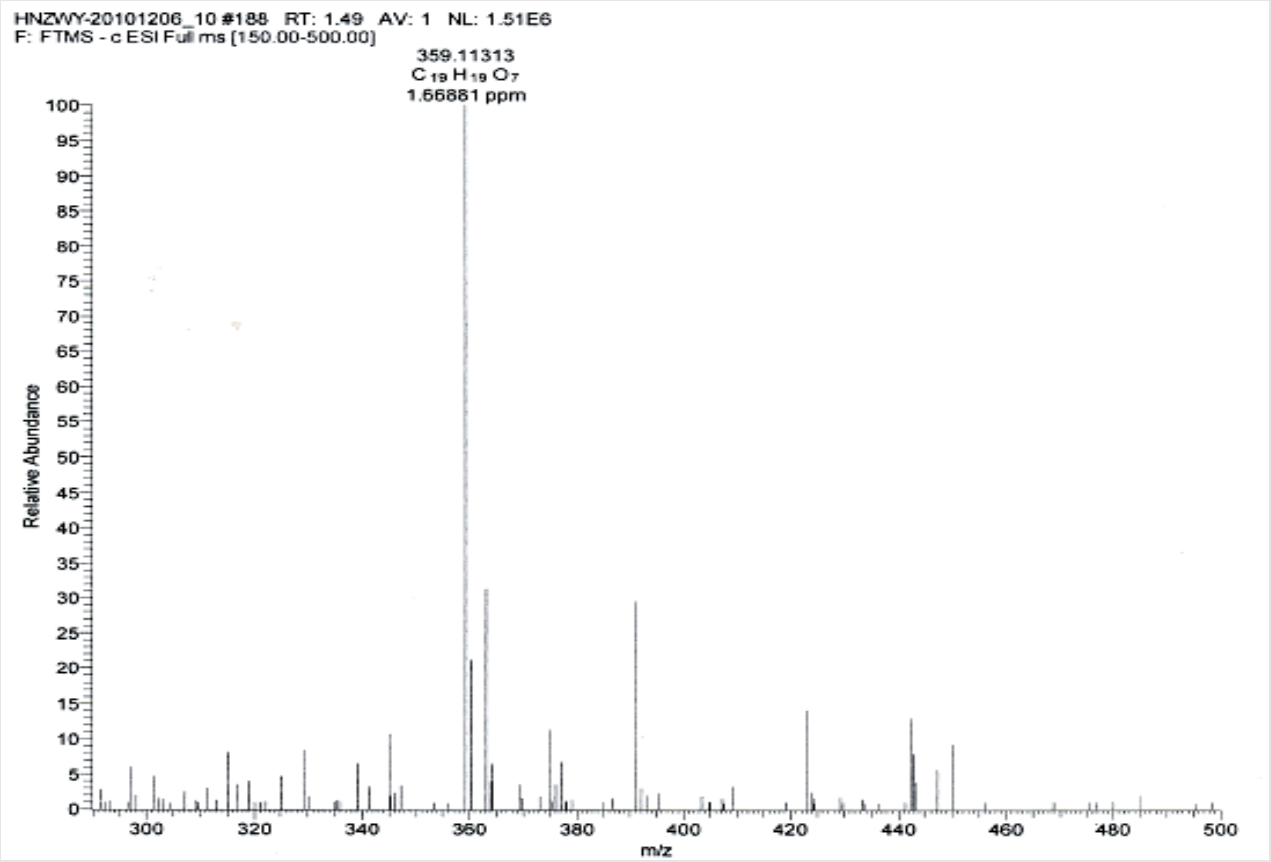


Figure S21. (-)-HRESIMS of paecilomycin N (**1**).

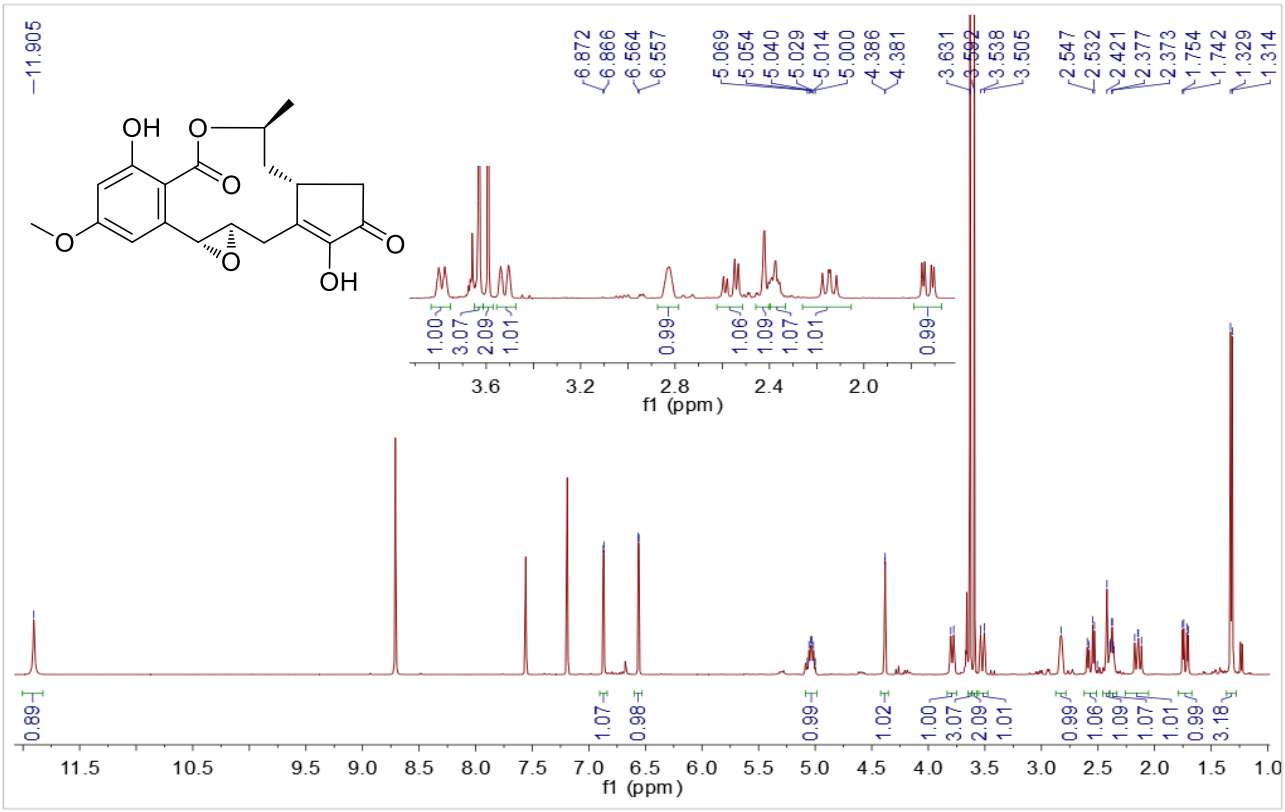


Figure S22. ^{1}H NMR (400 MHz) spectrum of paecilomycin O (**2**) in C_5D_5N.

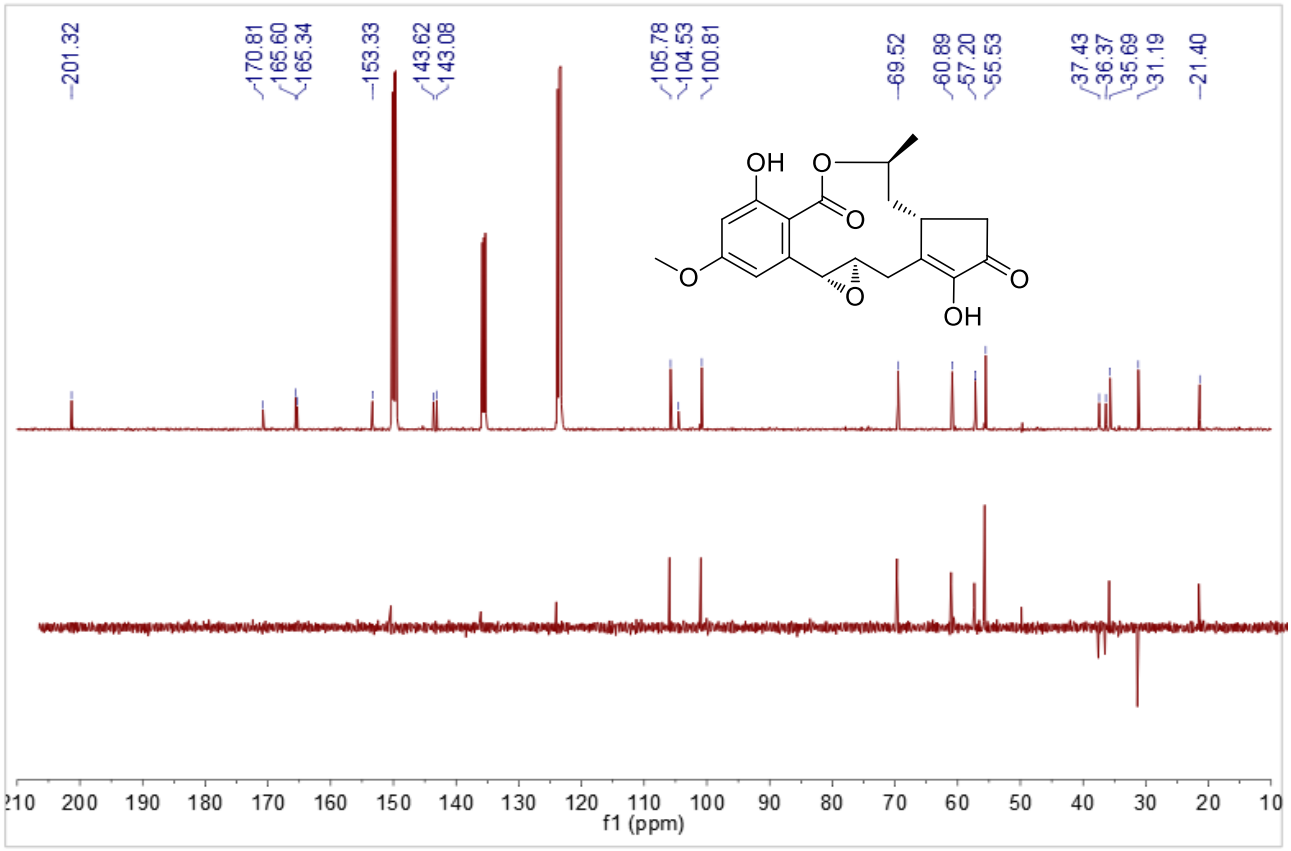


Figure S23. ^{13}C NMR (100 MHz) and DEPT spectra of paecilomycin O (**2**) in C_5D_5N.

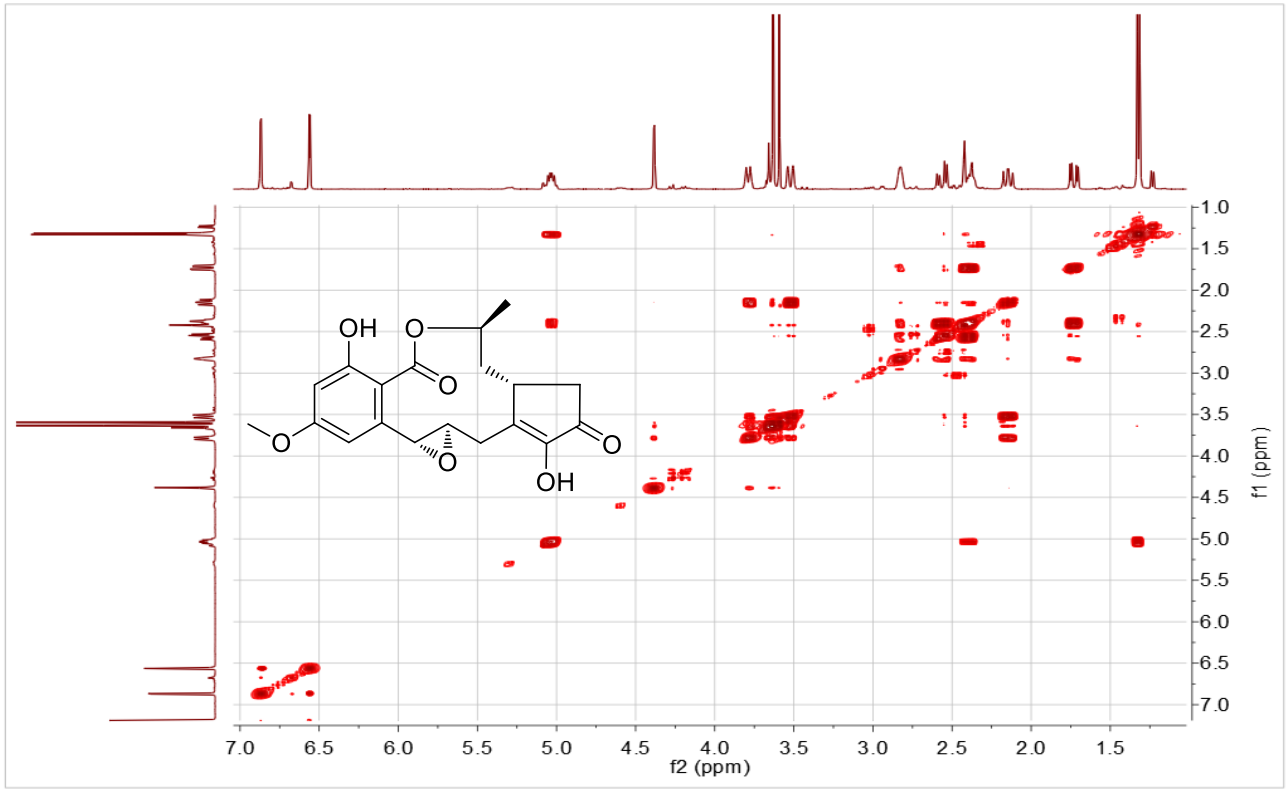


Figure S24. ^{1}H-^{1}H COSY spectrum of paecilomycin O (**2**) in C_5D_5N.

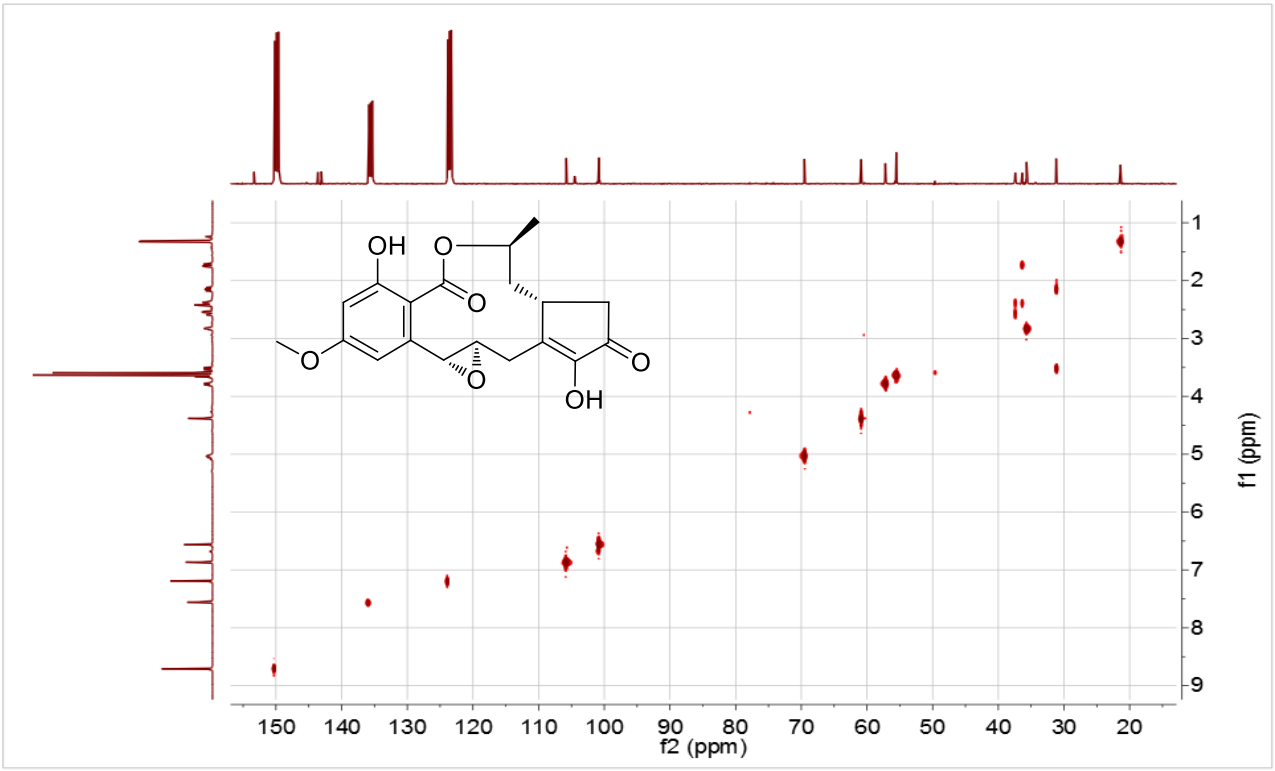


Figure S25. HSQC spectrum of paecilomycin O (**2**) in C_5D_5N.

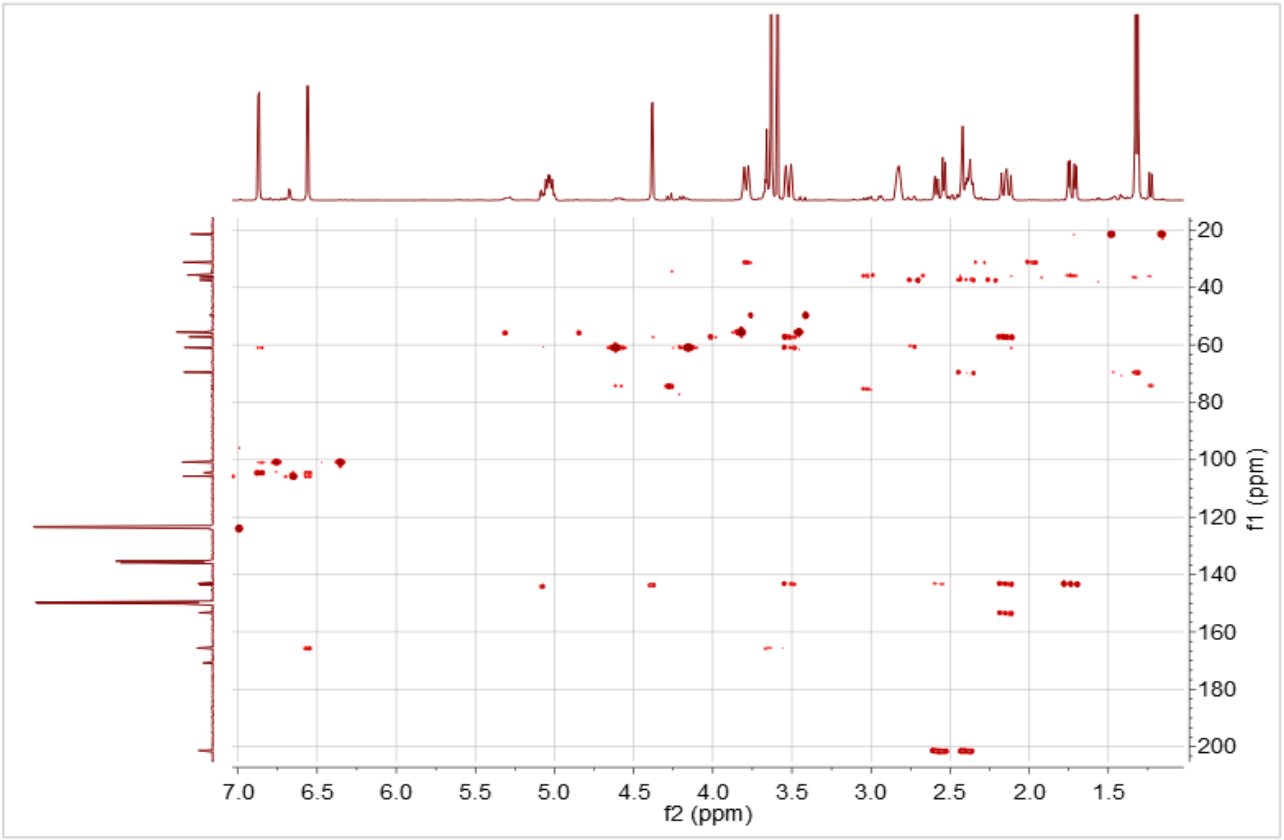


Figure S26. HMBC spectrum of paecilomycin O (**2**) in C_5D_5N.

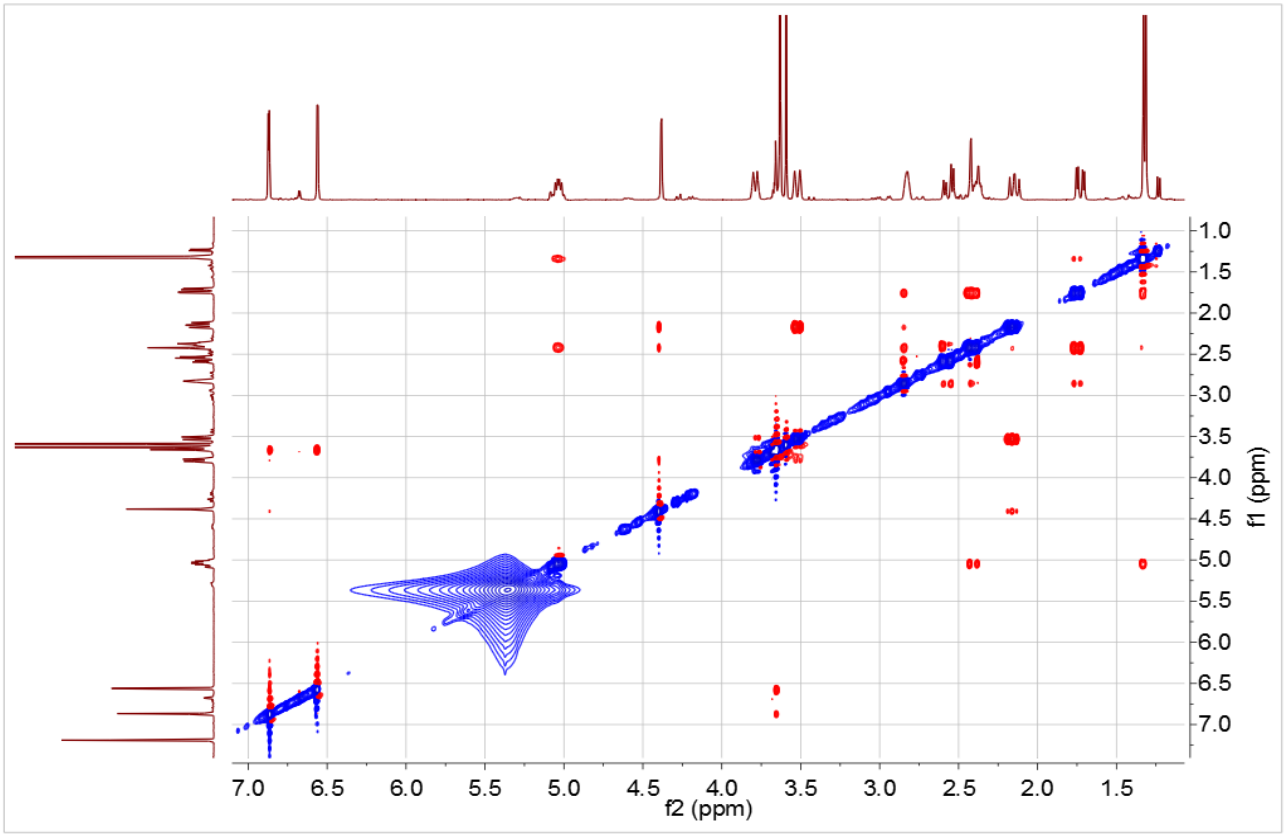


Figure S27. NOESY spectrum of paecilomycin O (**2**) in C_5D_5N.

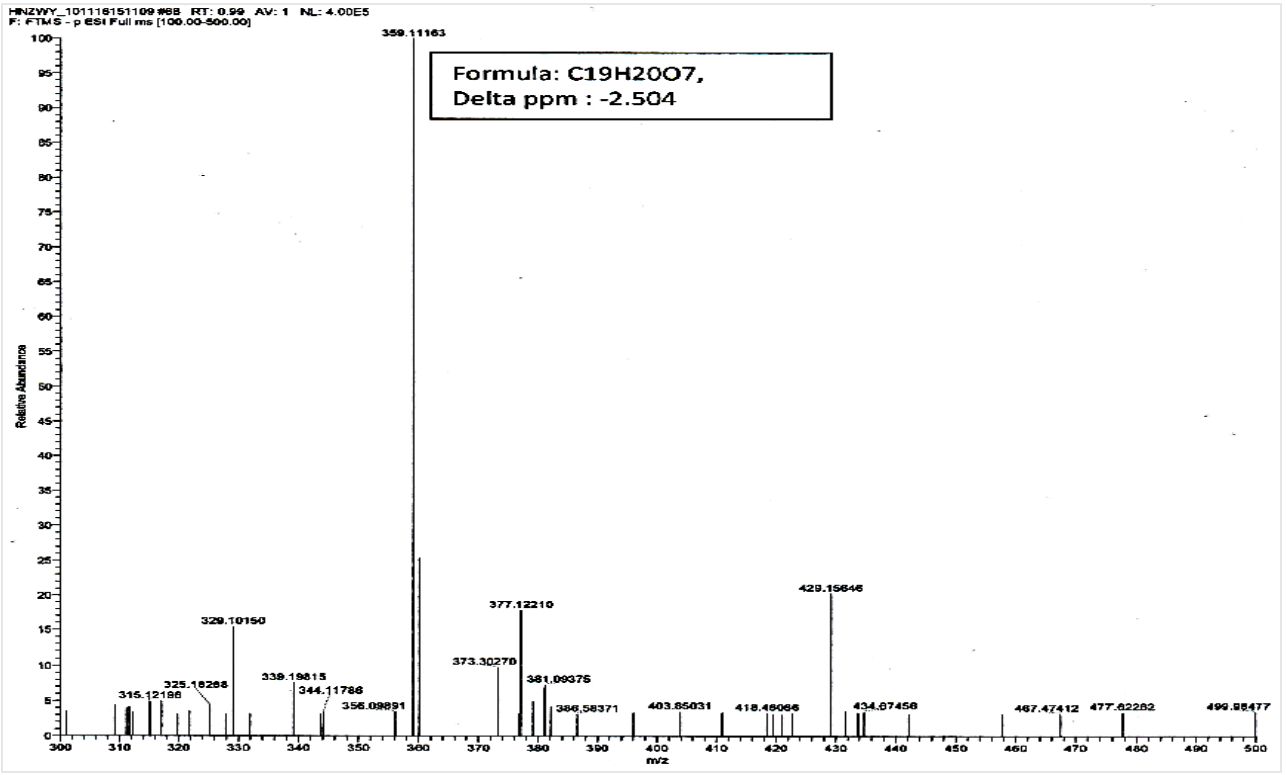


Figure S28. (-)-HRESIMS of paecilomycin O (**2**).

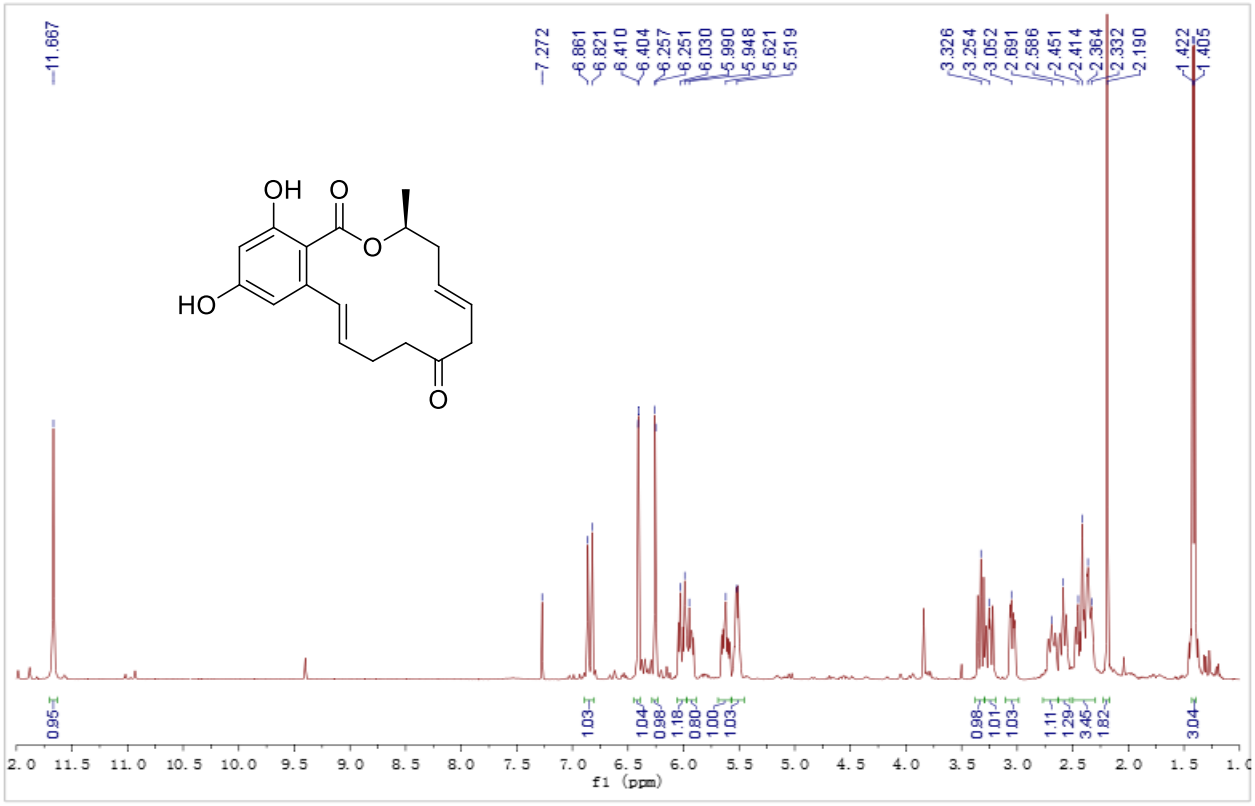


Figure S29. ^{1}H NMR (400MHz) spectrum of paecilomycin P (**3**) in $CDCl_3$.

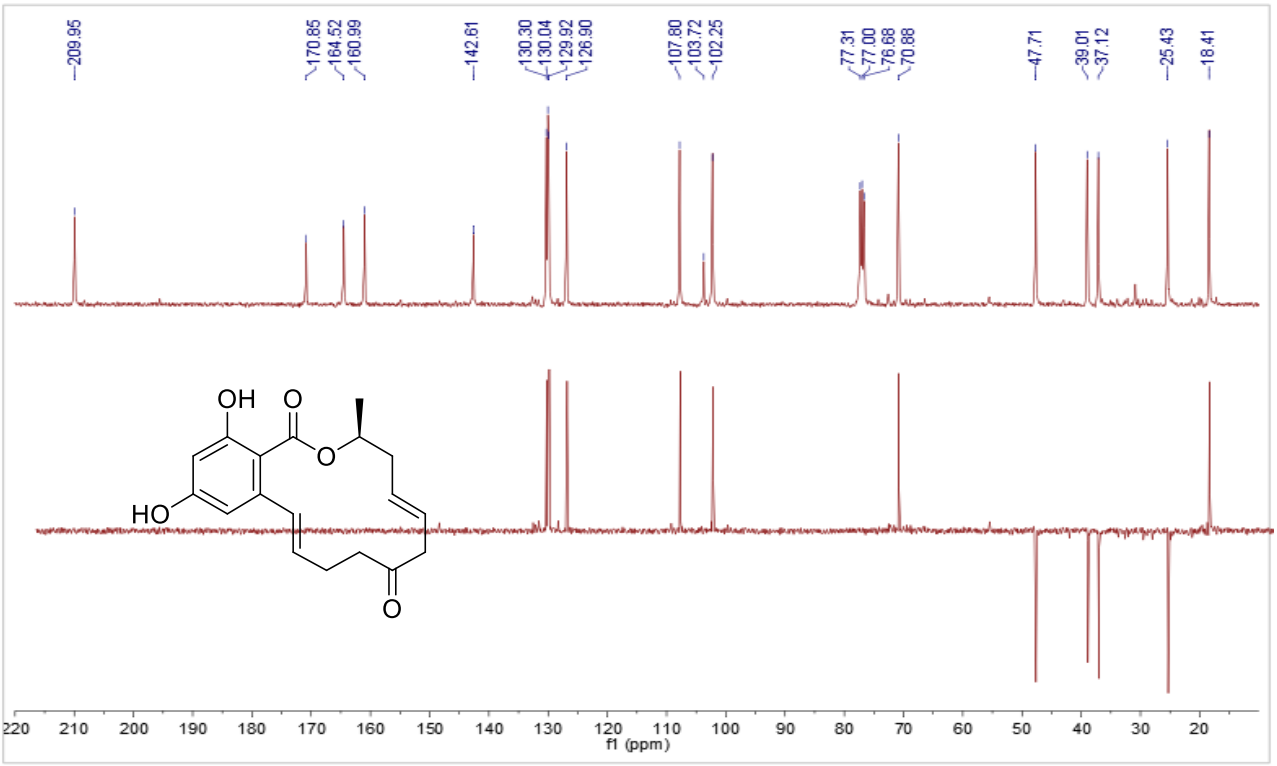


Figure S30. ^{13}C NMR and DEPT (100MHz) spectra of paecilomycin P (**3**) in $CDCl_3$.

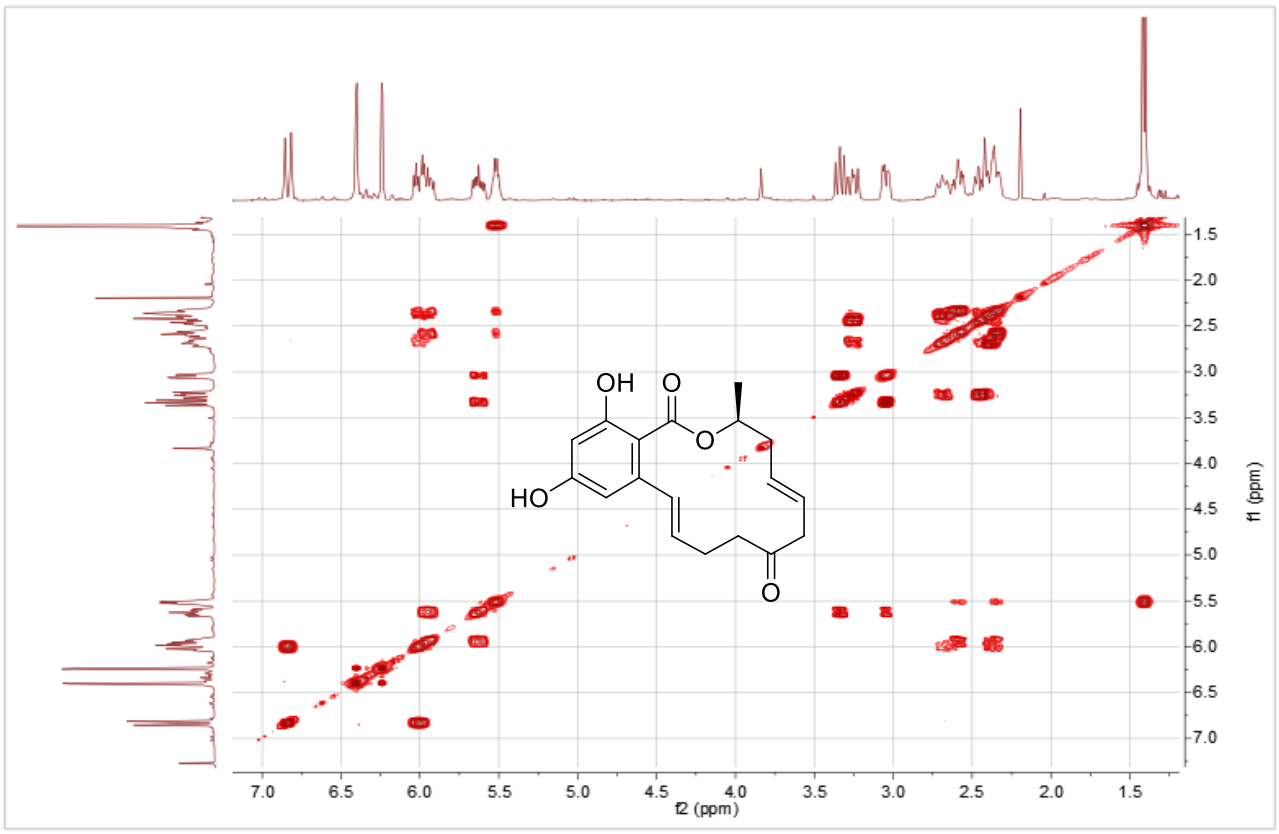


Figure S31. ^{1}H-^{1}H COSY spectrum of paecilomycin P (**3**) in $CDCl_3$.

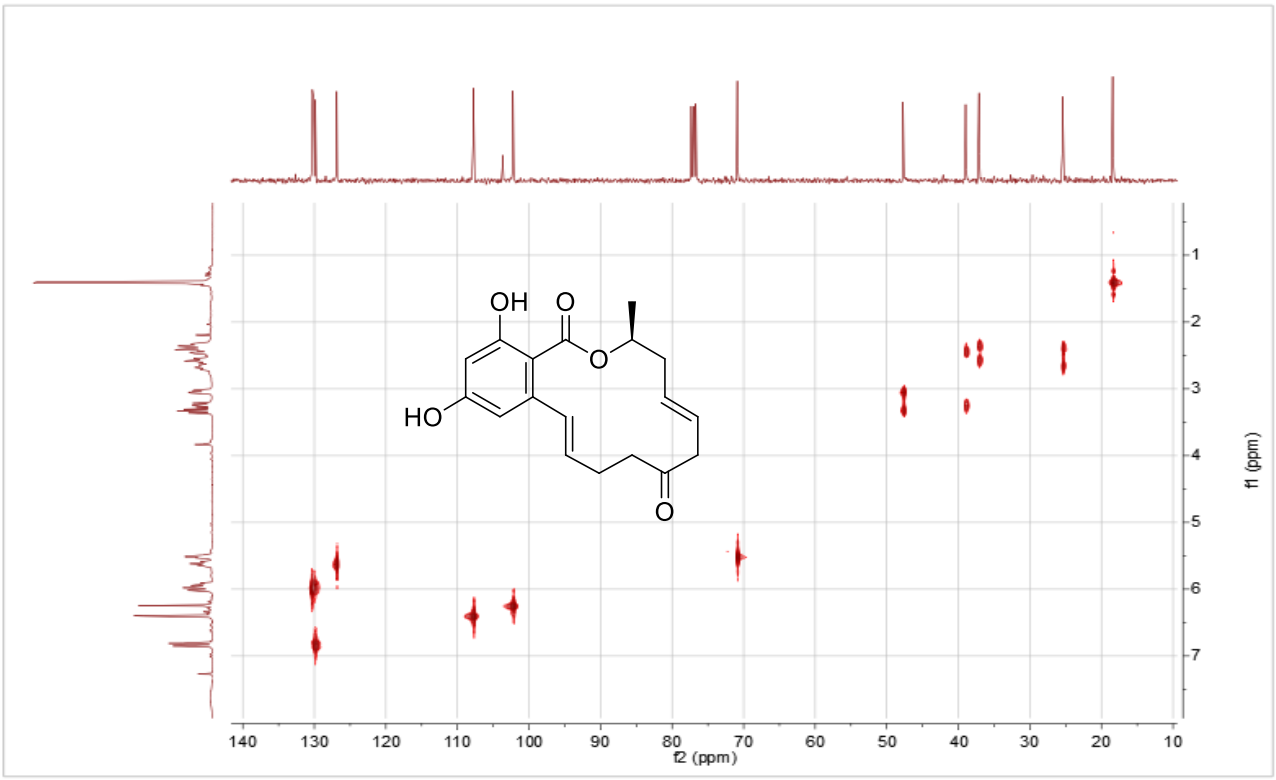


Figure S32. HSQC spectrum of paecilomycin P (**3**) in $CDCl_3$.

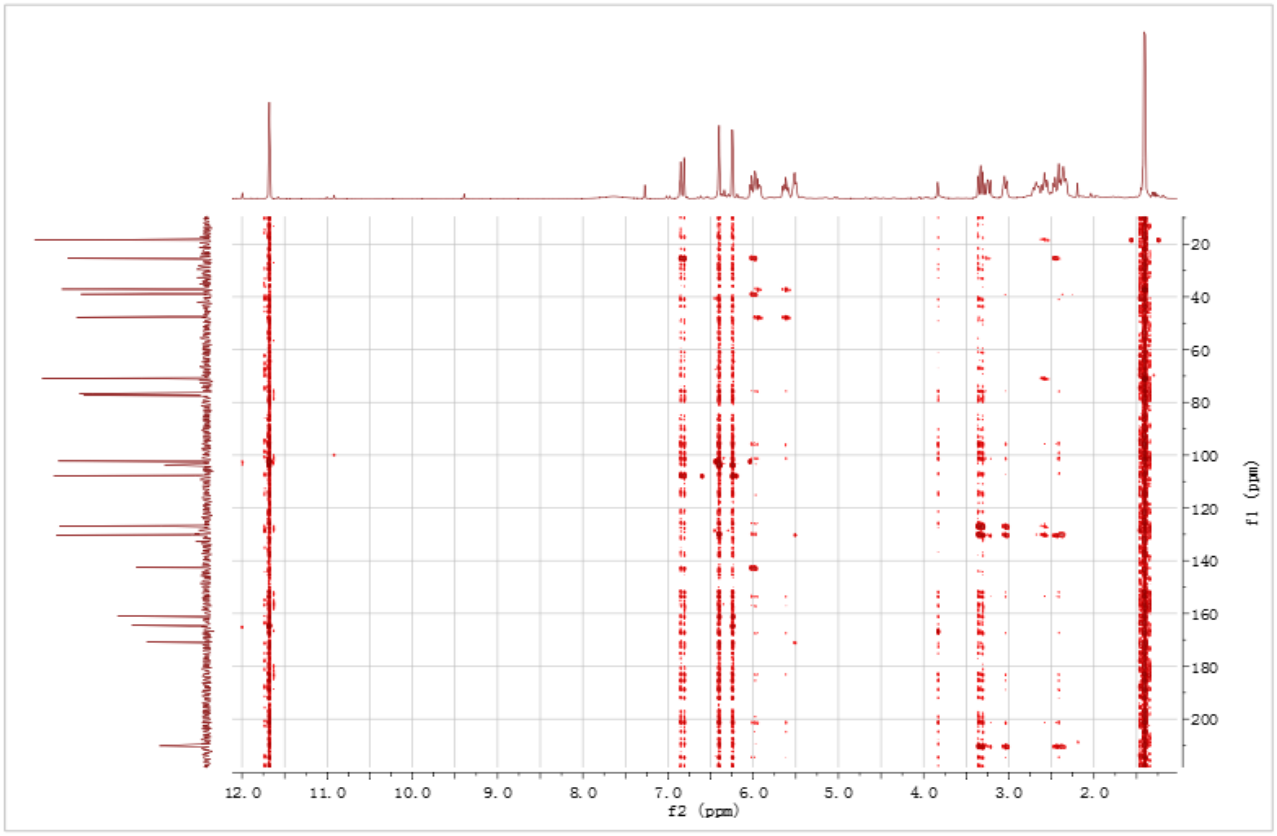


Figure S33. HMBC spectrum of paecilomycin P (**3**) in $CDCl_3$.

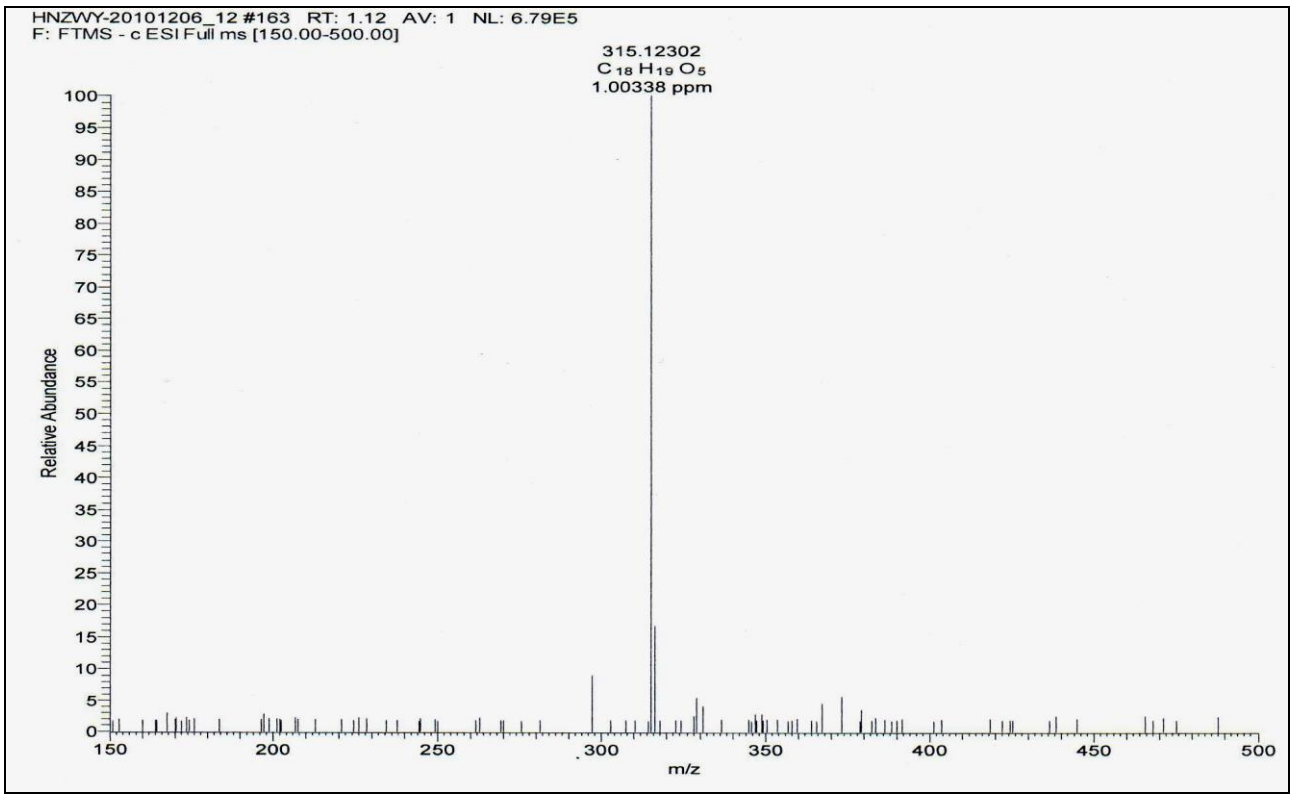


Figure S34. (-)-HRESIMS spectrum of paecilomycin P (**3**)

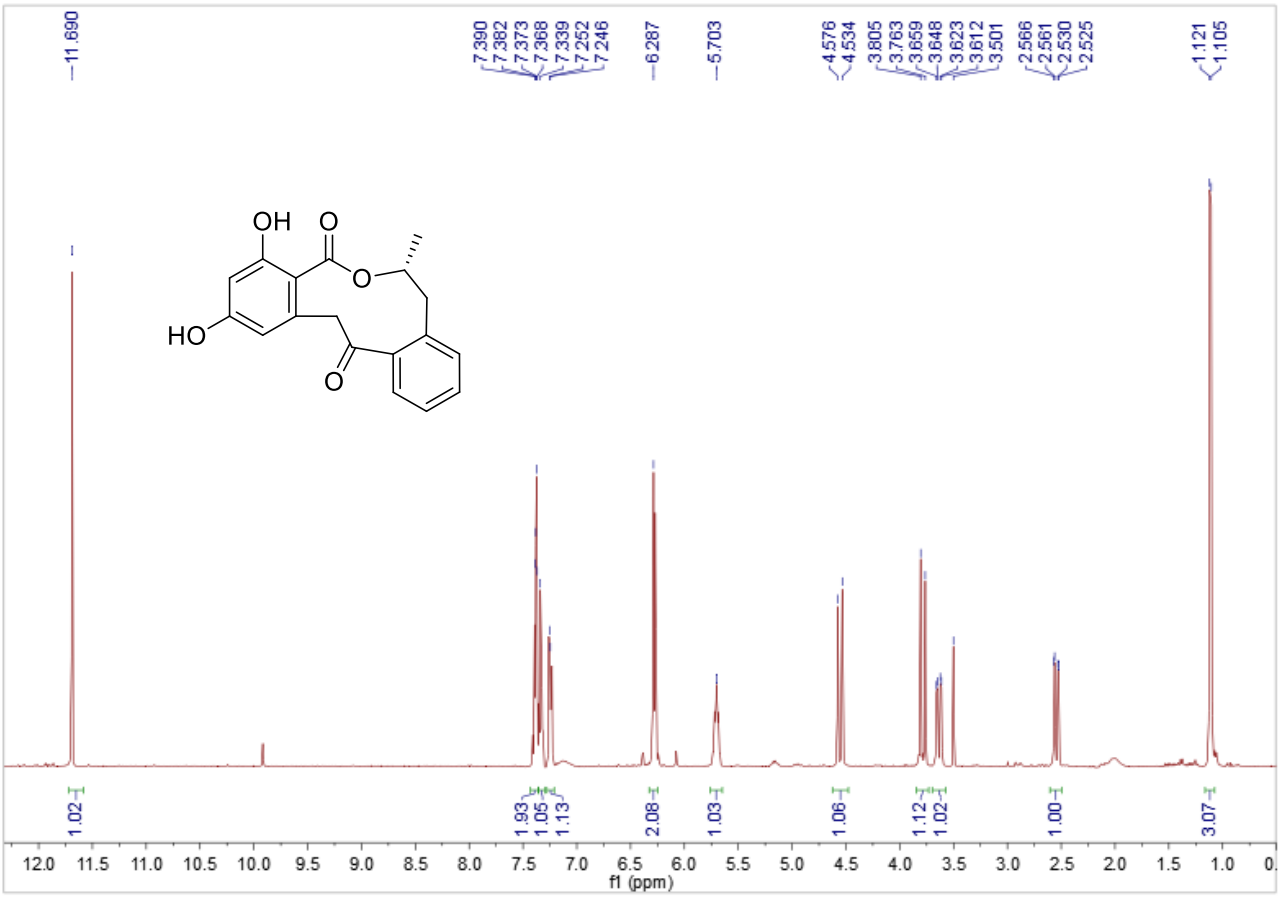


Figure S35. ^{1}H NMR (400MHz) spectrum of dechloropochonin I (**4**) in $CDCl_3$.

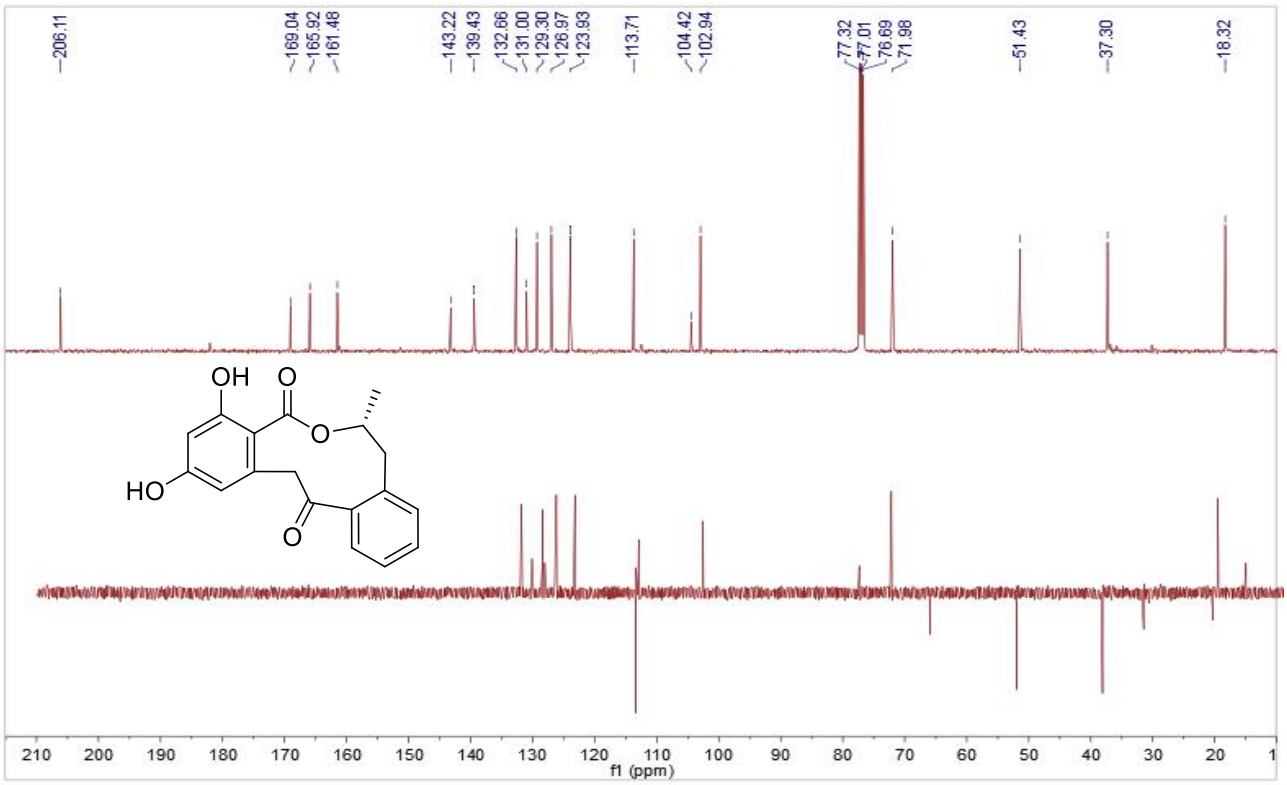


Figure S36. ^{13}C NMR (100MHz) spectrum of dechloropochonin I (**4**) in $CDCl_3$.

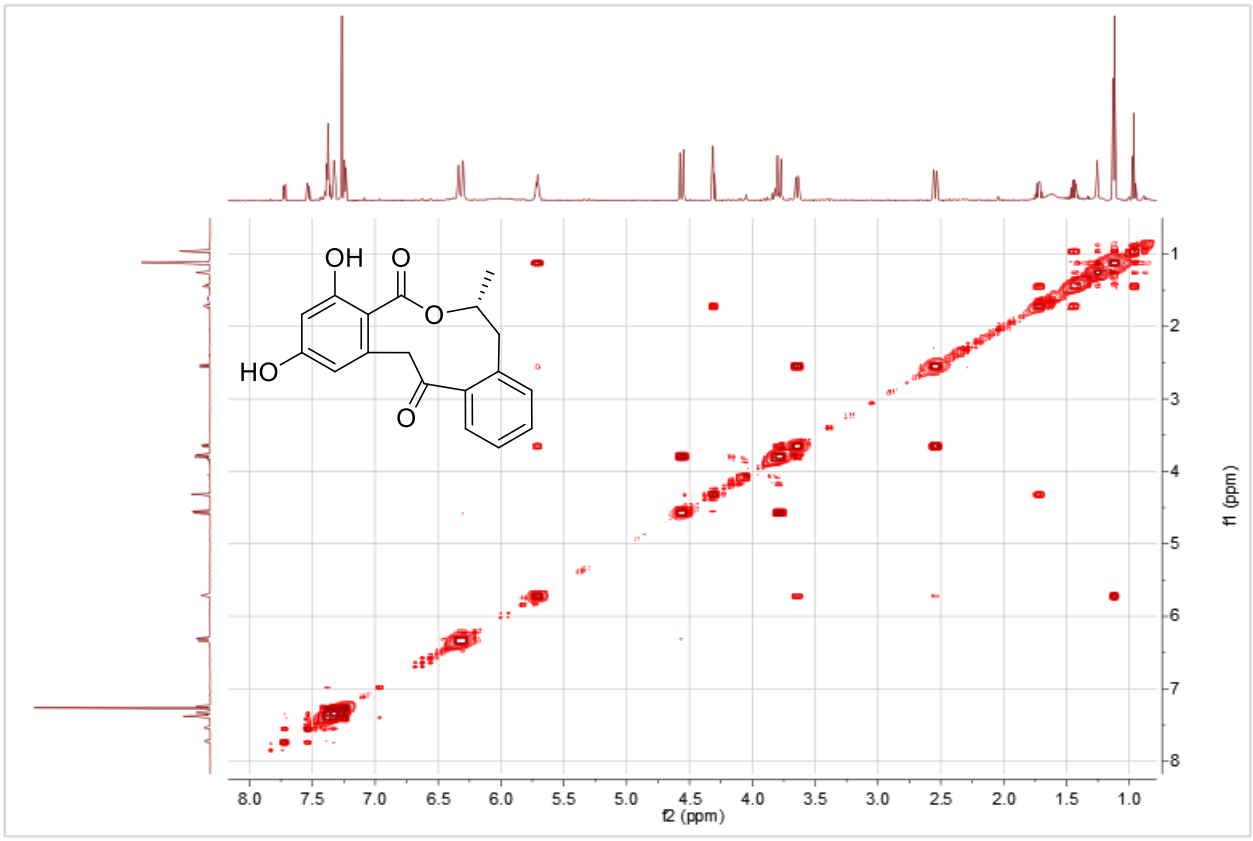


Figure S37. ^{1}H-^{1}H COSY spectrum of dechloropochonin I (**4**) in $CDCl_3$

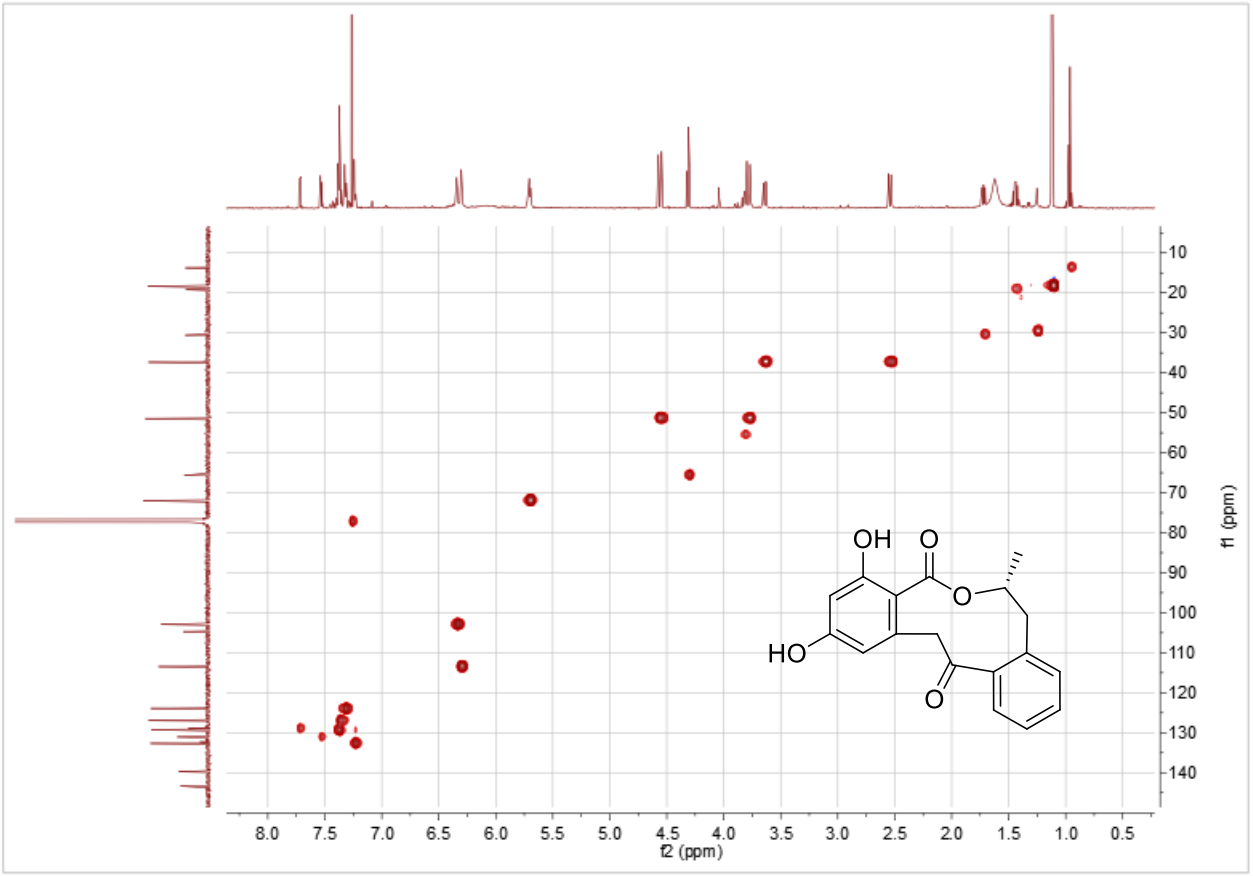


Figure S38. HSQC spectrum of dechloropochonin I (**4**) in $CDCl_3$

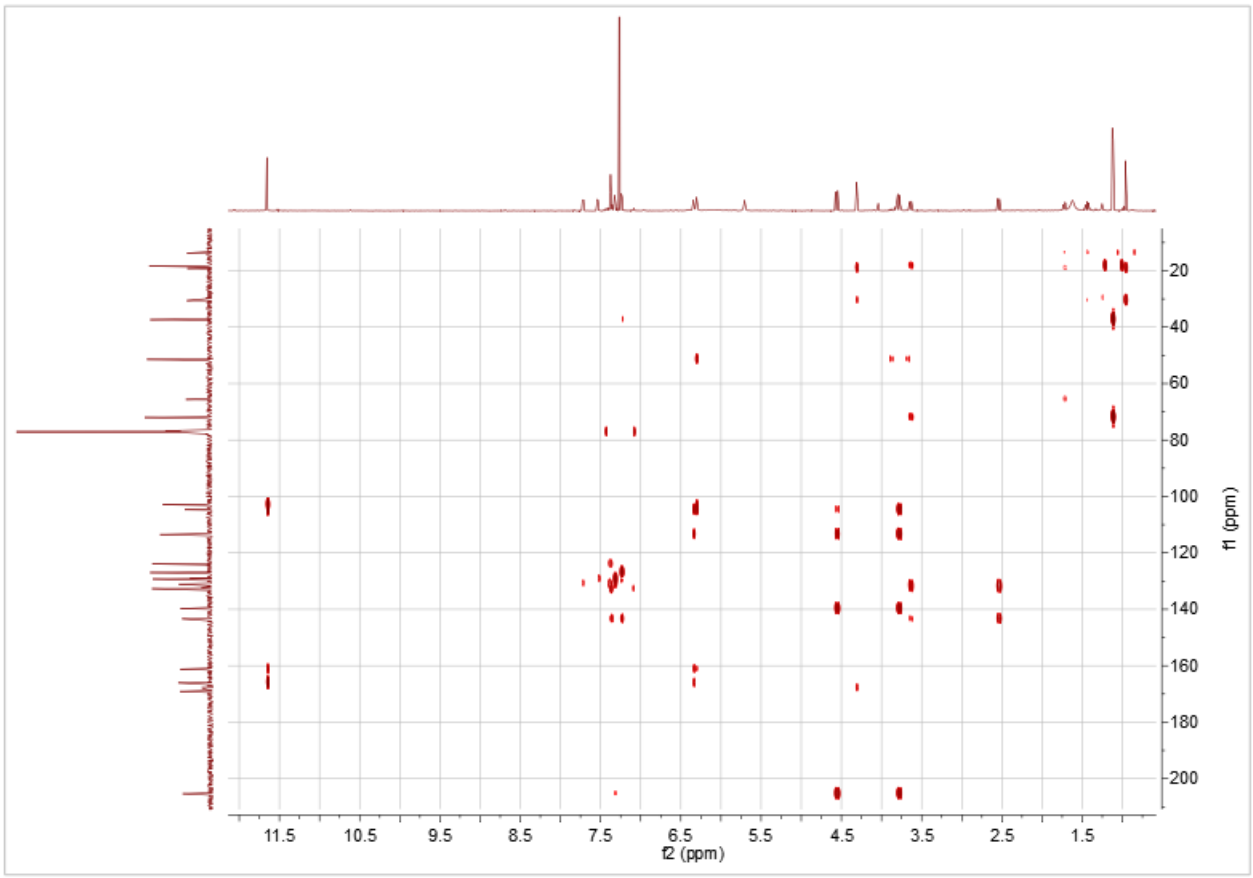
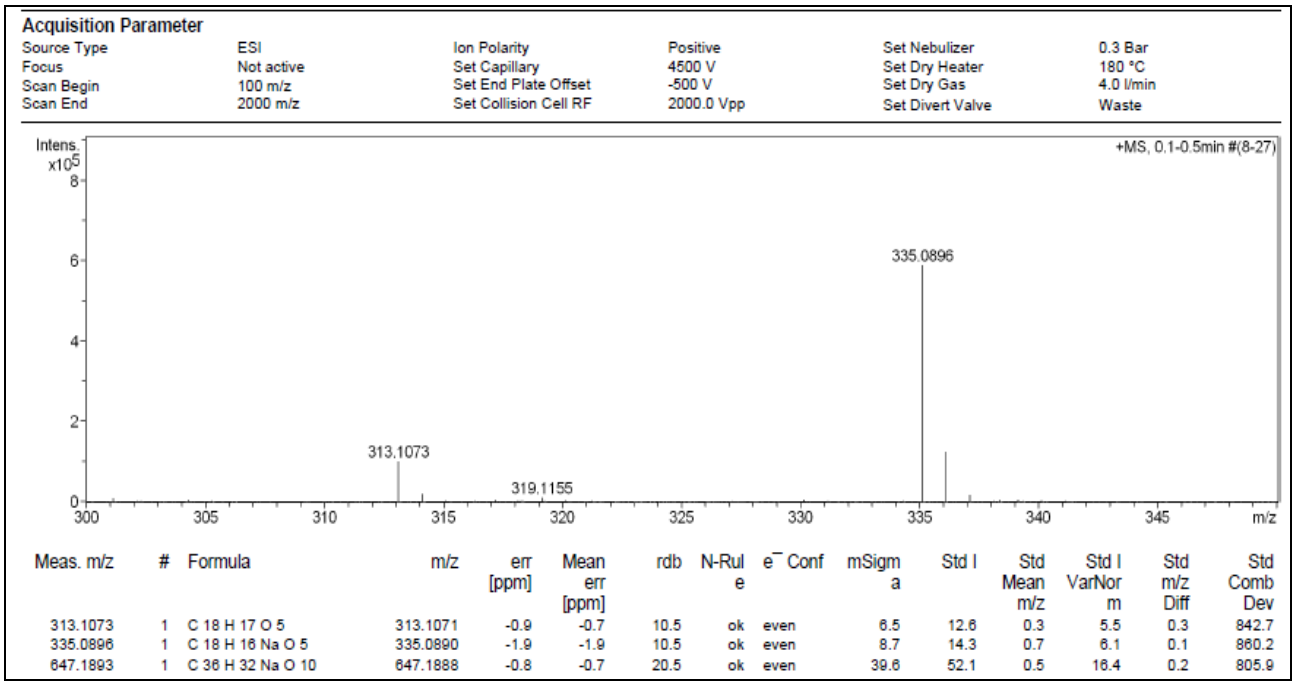


Figure S39. HMBC spectrum of dechloropochonin I (**4**) in $CDCl_3$



Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
313.1073	1	C 18 H 17 O 5	313.1071	-0.9	-0.7	10.5	ok	even	6.5	12.6	0.3	5.5	0.3	842.7
335.0896	1	C 18 H 16 Na O 5	335.0890	-1.9	-1.9	10.5	ok	even	8.7	14.3	0.7	6.1	0.1	860.2
647.1893	1	C 36 H 32 Na O 10	647.1888	-0.8	-0.7	20.5	ok	even	39.6	52.1	0.5	16.4	0.2	805.9

Figure S40. (+)-HRESIMS spectrum of dechloropochonin I (**4**)

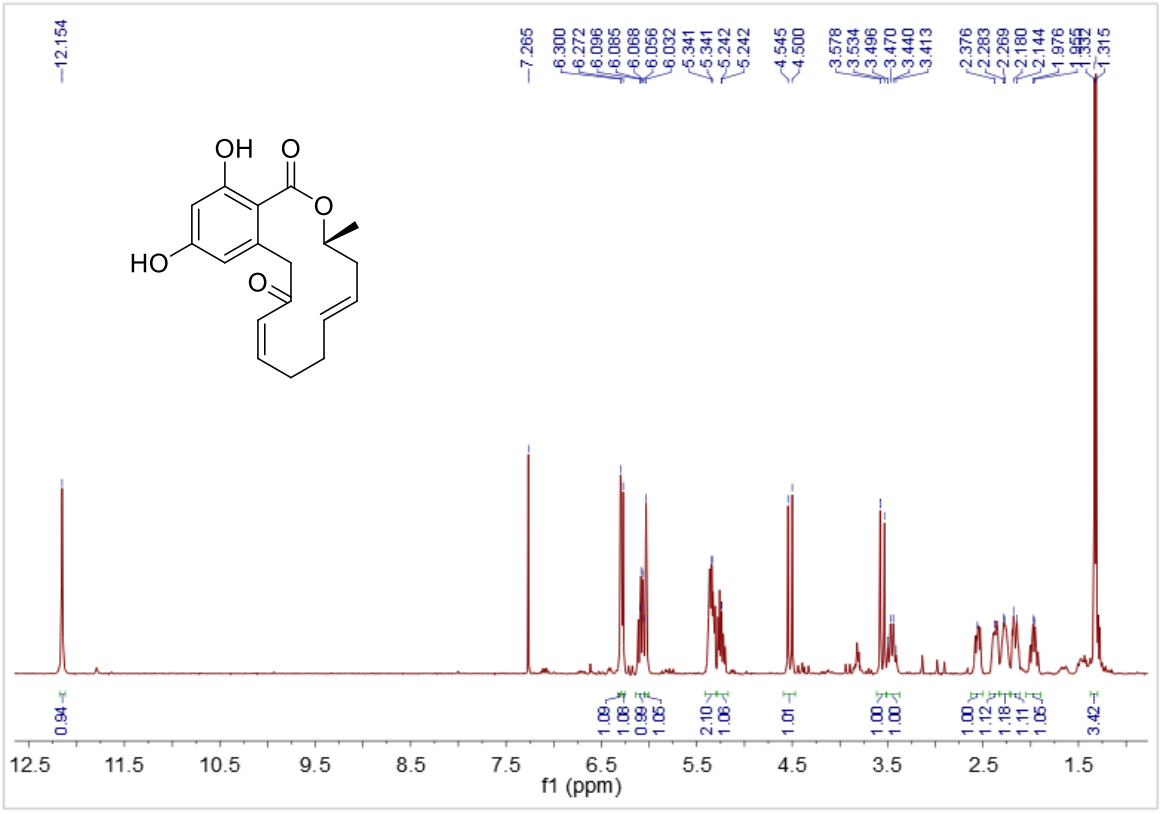


Figure S41. ^{1}H NMR (400MHz) spectrum of monocillin VI (**5**) in $CDCl_3$.

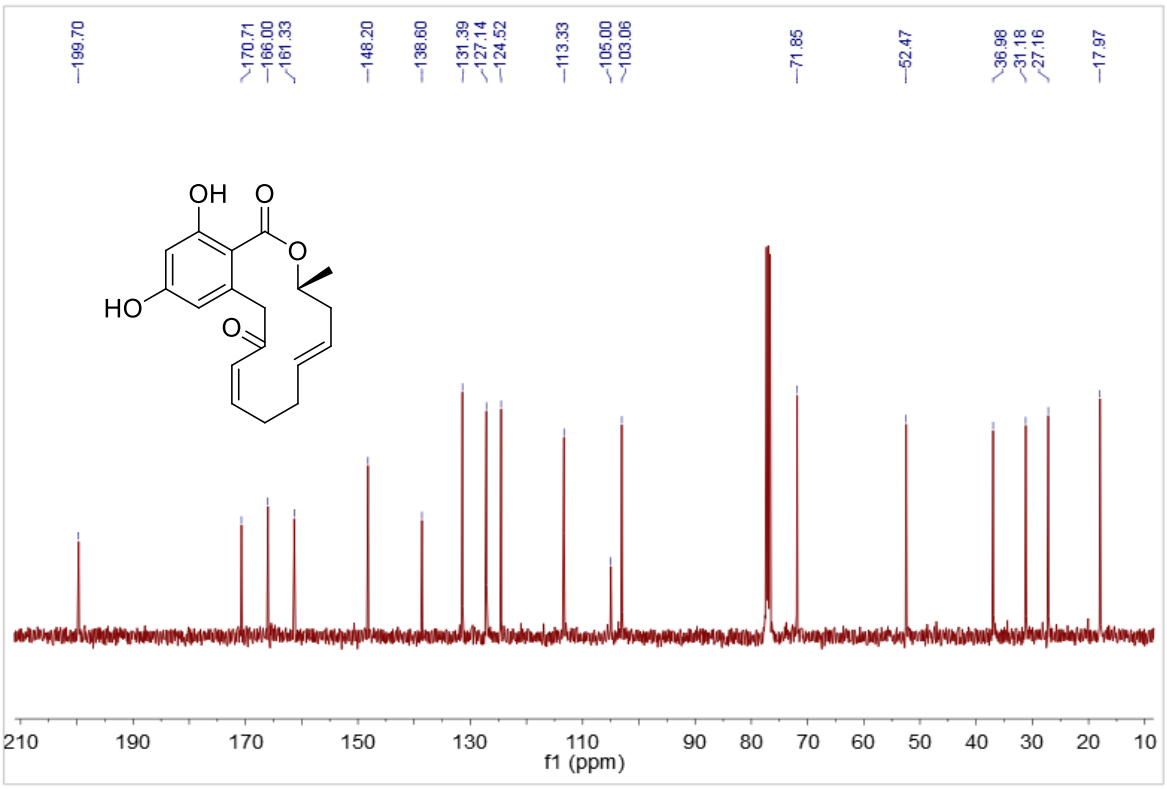


Figure S42. ^{13}C NMR (100MHz) spectrum of monocillin VI (**5**) in $CDCl_3$.

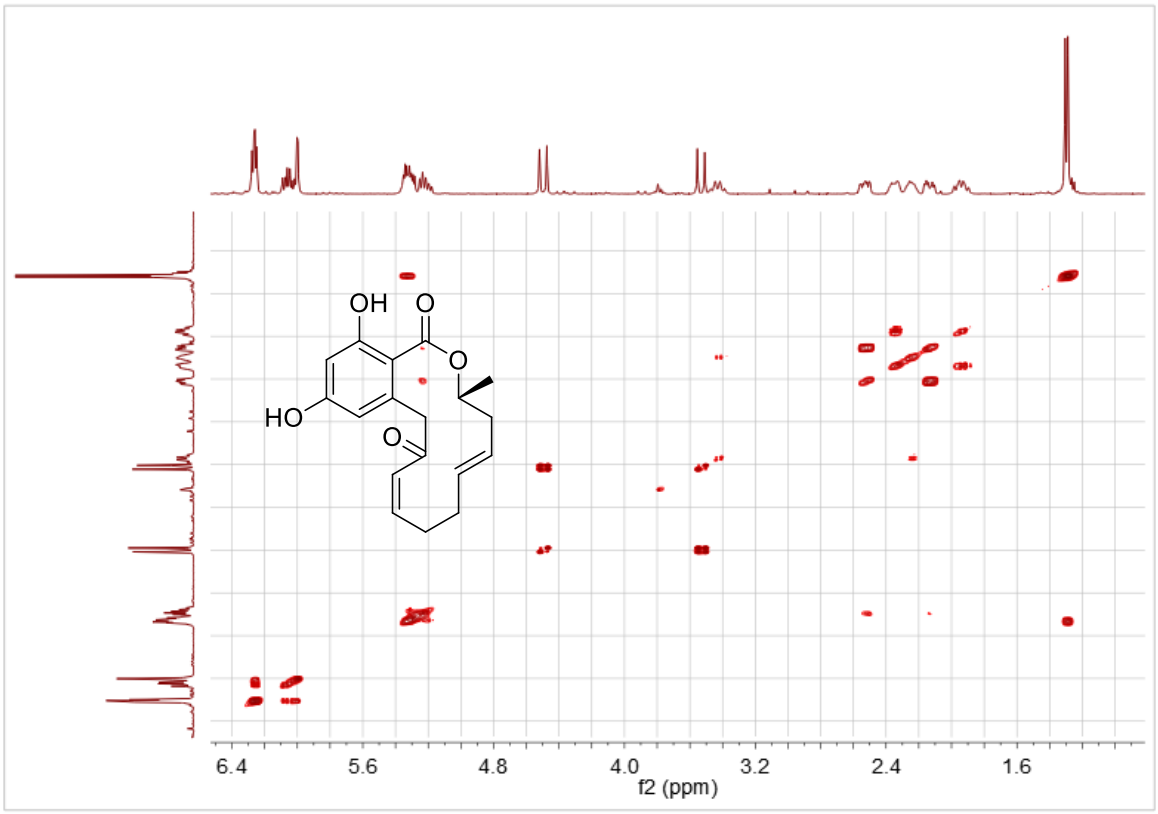


Figure S43. ^{1}H-^{1}H COSY spectrum of monocillin VI (**5**) in $CDCl_3$.

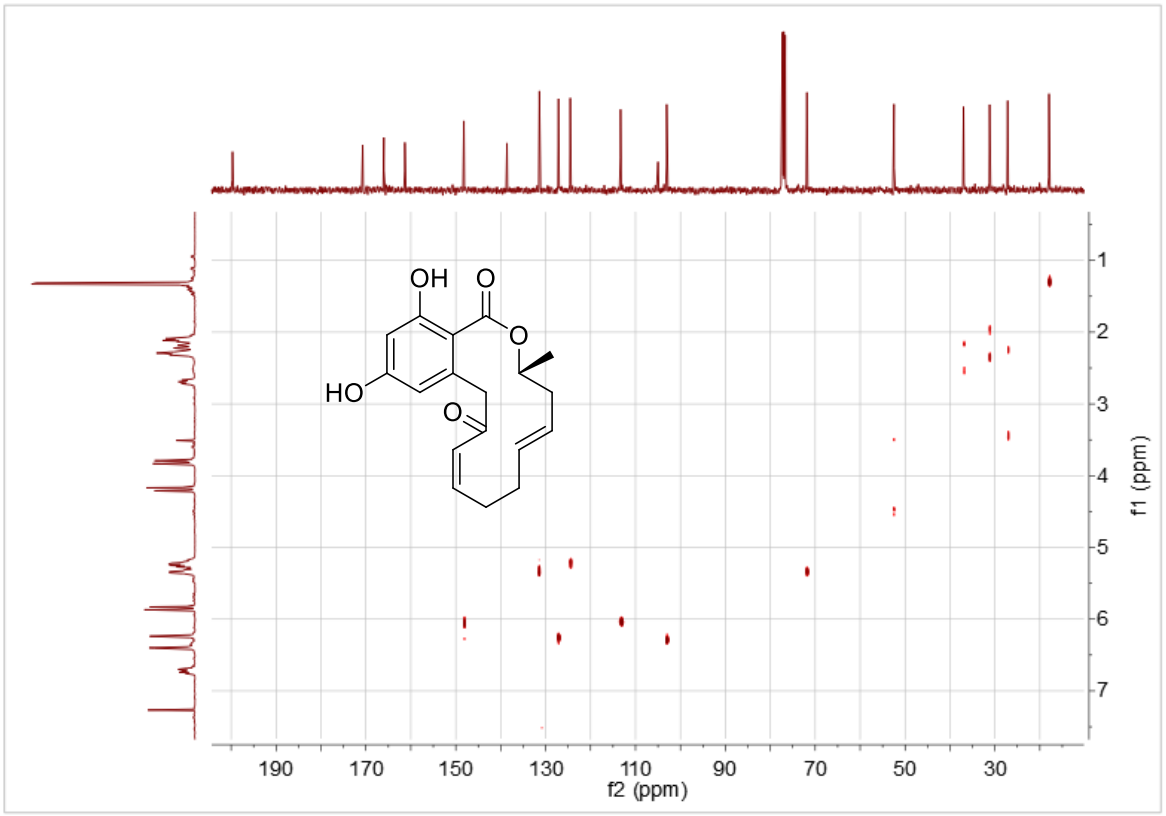


Figure S44. HSQC spectrum of monocillin VI (**5**) in $CDCl_3$.

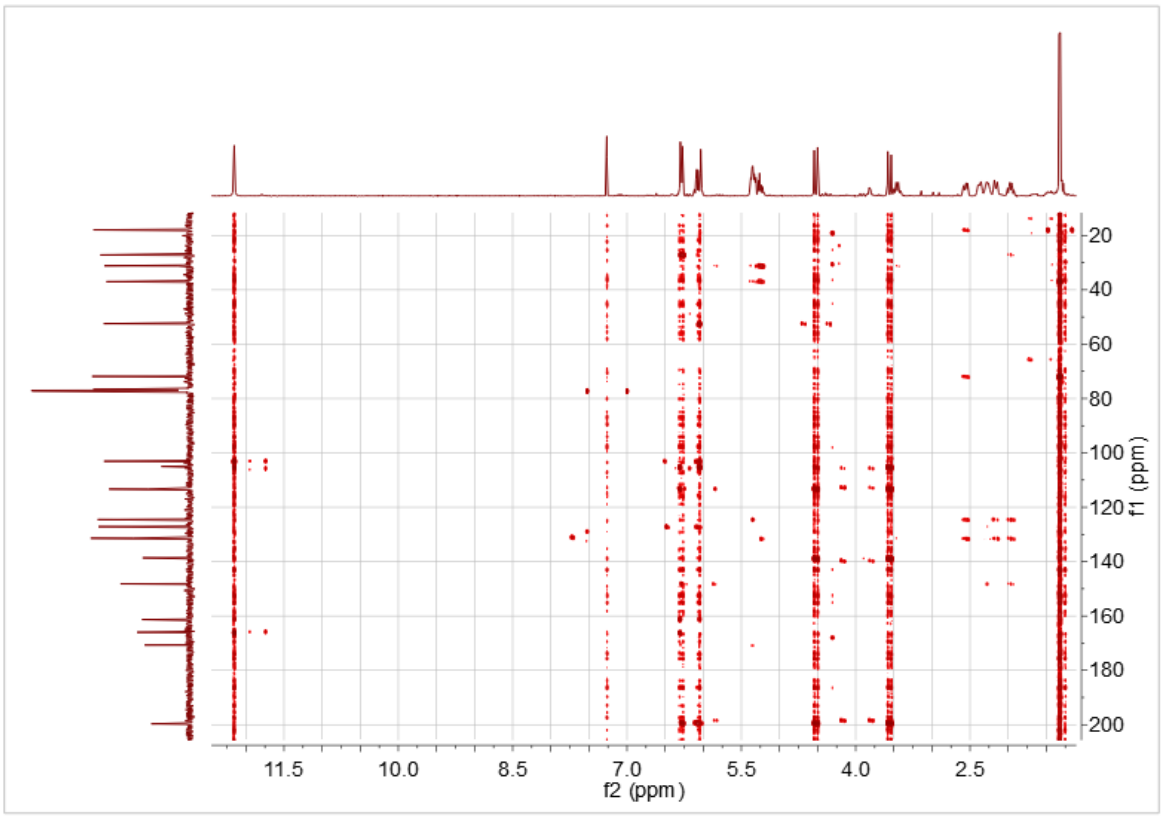
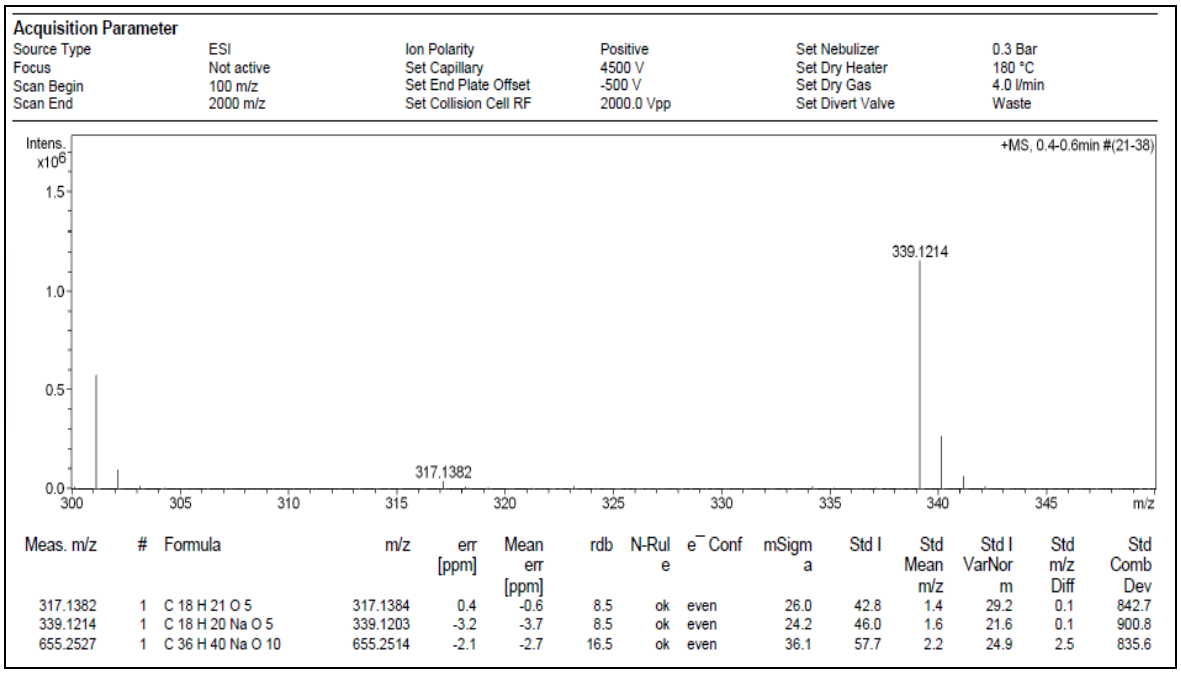


Figure S45. HMBC spectrum of monocillin VI (**5**) in $CDCl_3$.



Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
317.1382	1	C 18 H 21 O 5	317.1384	0.4	-0.6	8.5	ok	even	26.0	42.8	1.4	29.2	0.1	842.7
339.1214	1	C 18 H 20 Na O 5	339.1203	-3.2	-3.7	8.5	ok	even	24.2	46.0	1.6	21.6	0.1	900.8
655.2527	1	C 36 H 40 Na O 10	655.2514	-2.1	-2.7	16.5	ok	even	36.1	57.7	2.2	24.9	2.5	835.6

Figure S46. (+)-HRESIMS spectrum of monocillin VI (**5**).

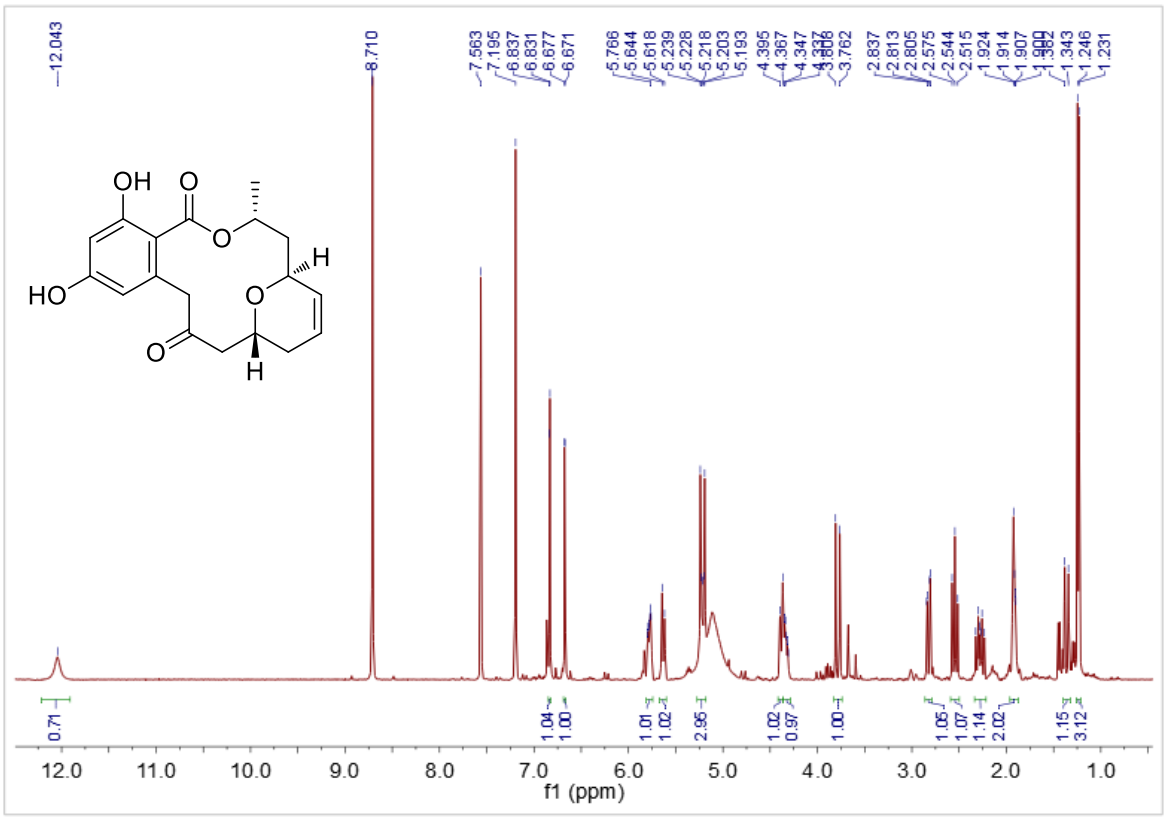


Figure S47. ^{1}H NMR (400MHz) spectrum of monocillin VII (**6**) in C_5D_5N.

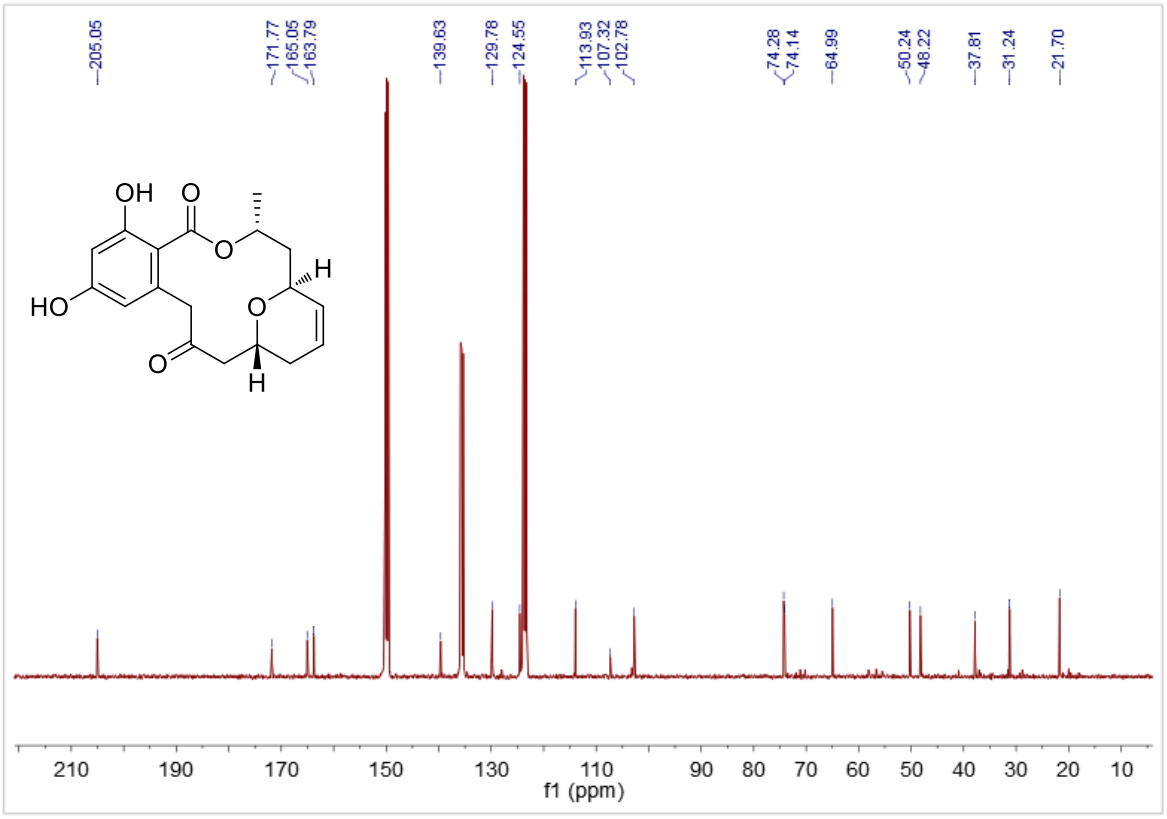


Figure S48. ^{13}C NMR (100MHz) spectrum of monocillin VII (**6**) in C_5D_5N.

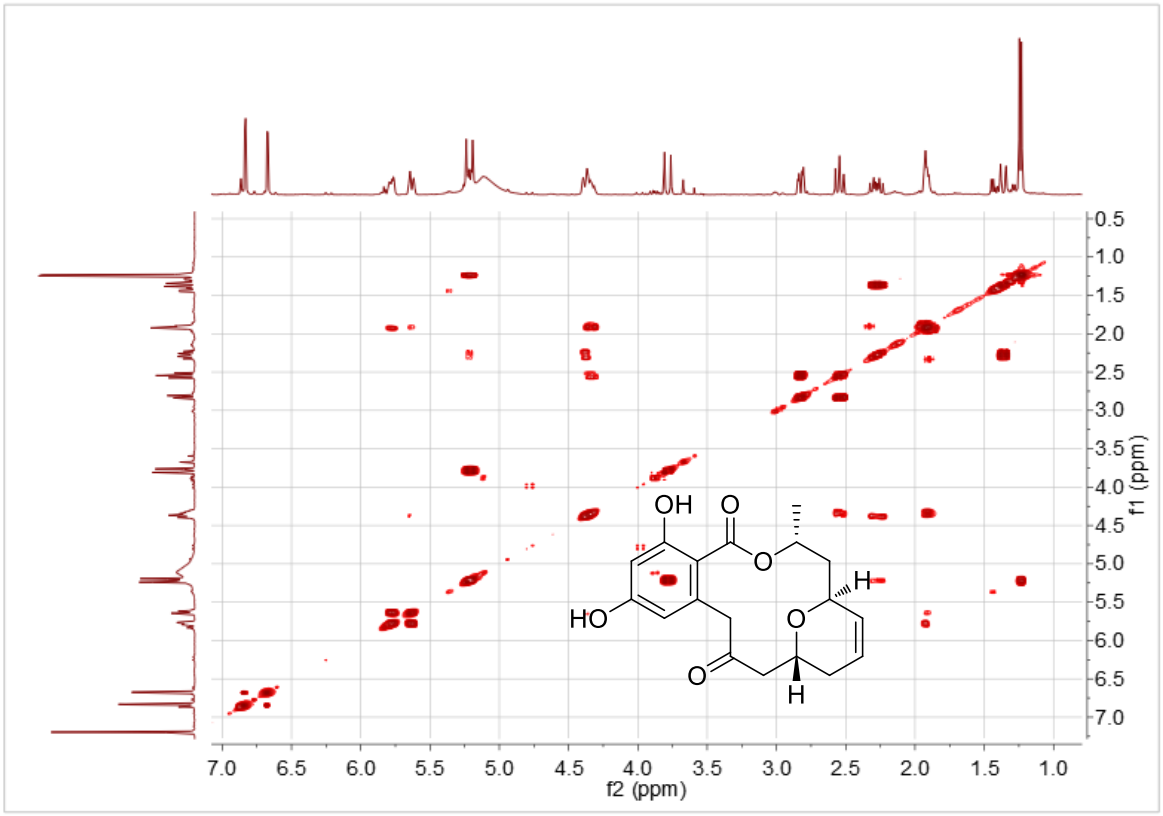


Figure S49. ^{1}H-^{1}H COSY spectrum of monocillin VII (**6**) in C_5D_5N.

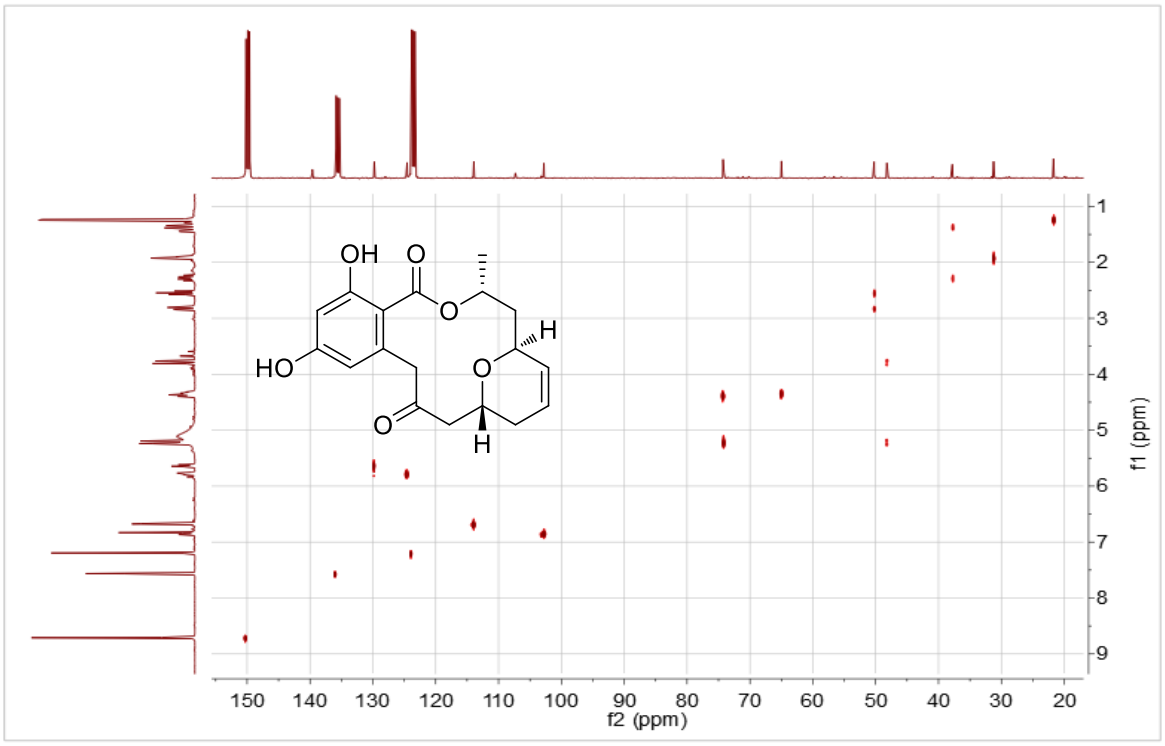


Figure S50. HSQC spectrum of monocillin VII (**6**) in C_5D_5N.

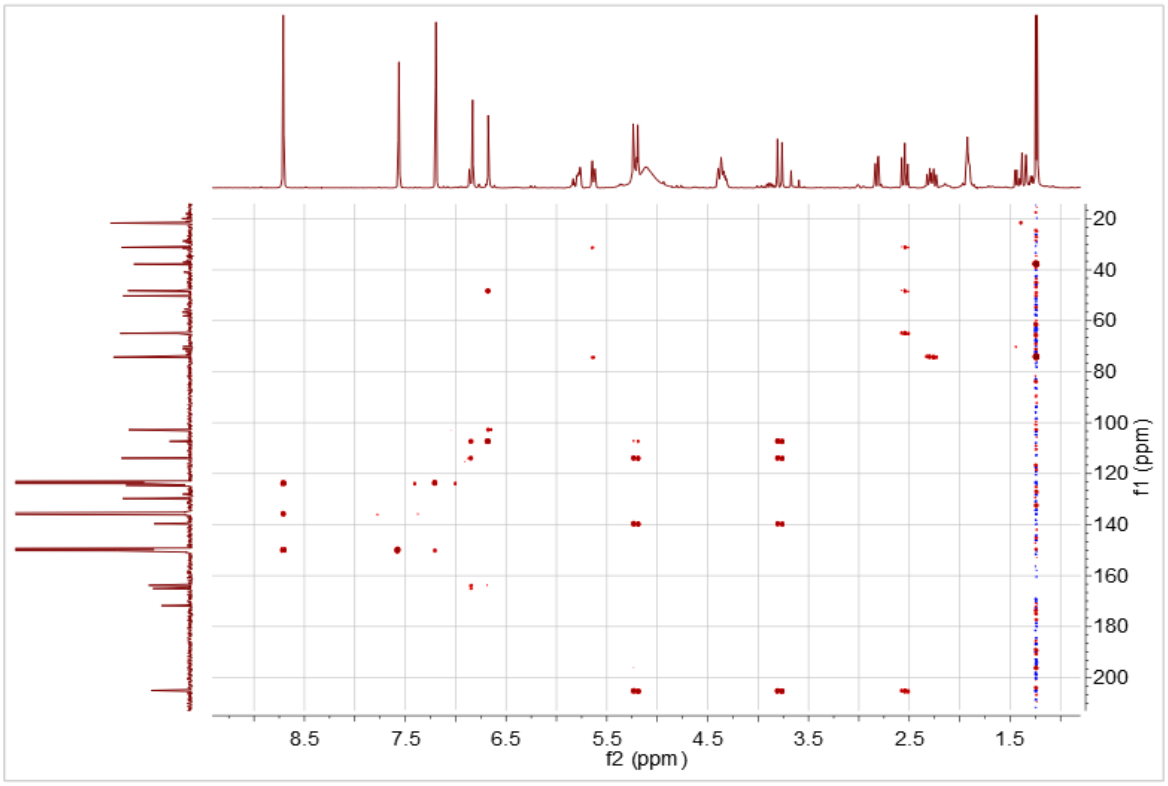


Figure S51. HMBC spectrum of monocillin VII (**6**) in C_5D_5N.

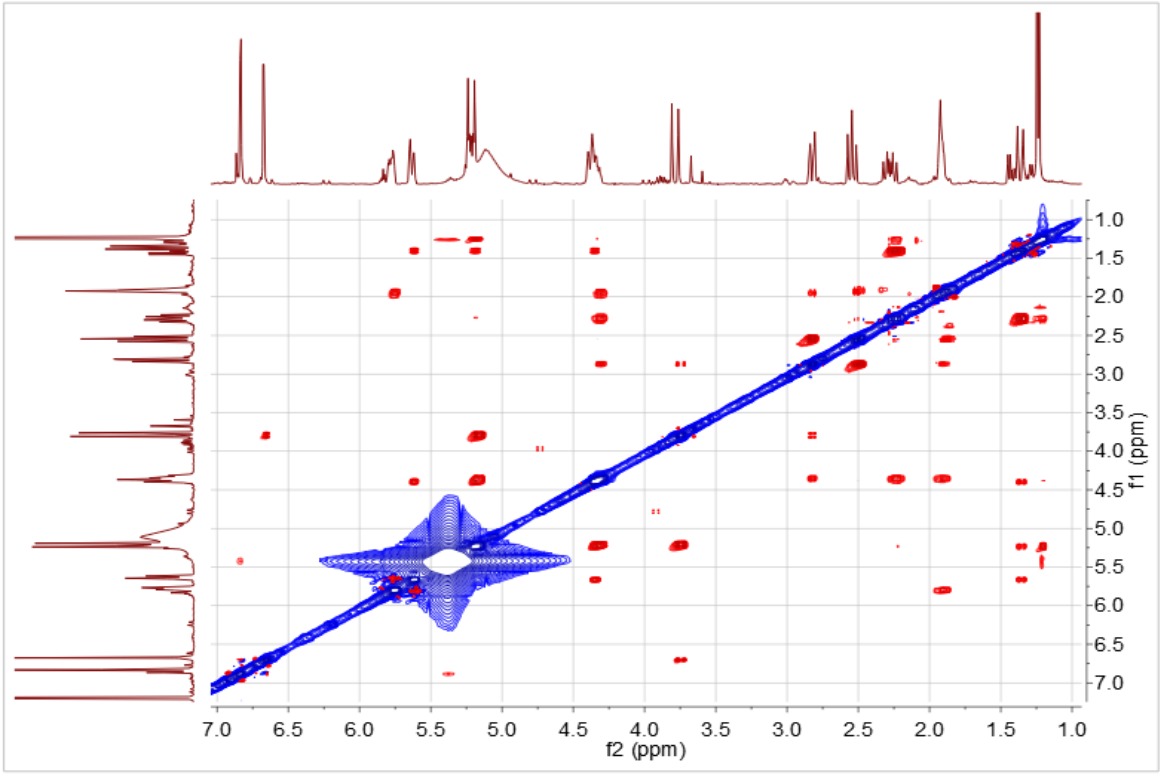
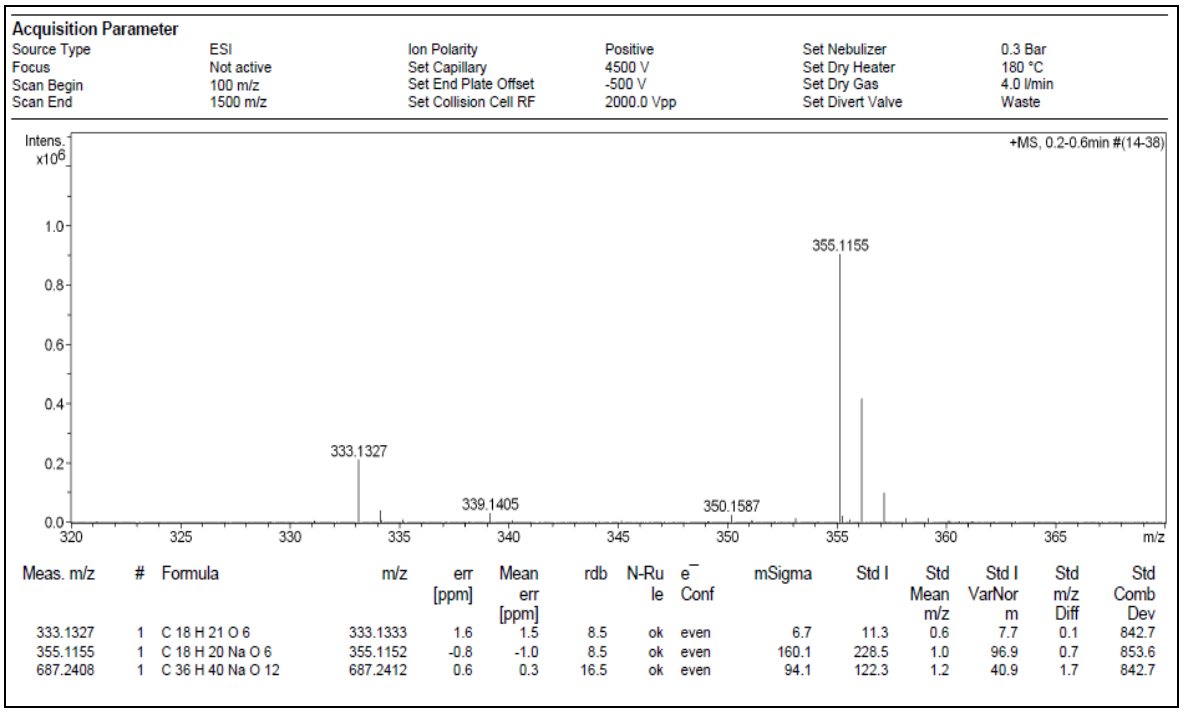


Figure S52. NOESY spectrum of monocillin VII (**6**) in C_5D_5N.



Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
333.1327	1	C 18 H 21 O 6	333.1333	1.6	1.5	8.5	ok	even	6.7	11.3	0.6	7.7	0.1	842.7
355.1155	1	C 18 H 20 Na O 6	355.1152	-0.8	-1.0	8.5	ok	even	160.1	228.5	1.0	96.9	0.7	853.6
687.2408	1	C 36 H 40 Na O 12	687.2412	0.6	0.3	16.5	ok	even	94.1	122.3	1.2	40.9	1.7	842.7

Figure S53. (+)-HRESIMS spectrum of monocillin VII (**6**).

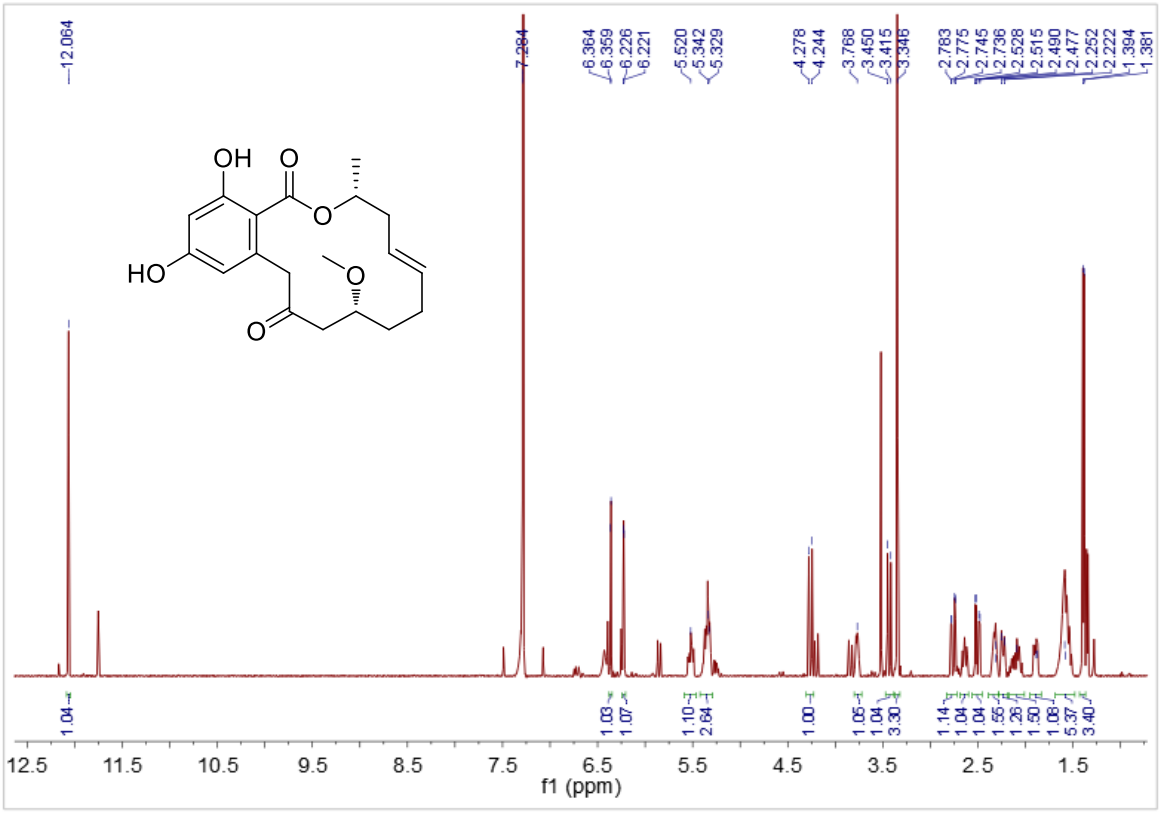


Figure S54. ^{1}H NMR (500 MHz) spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.

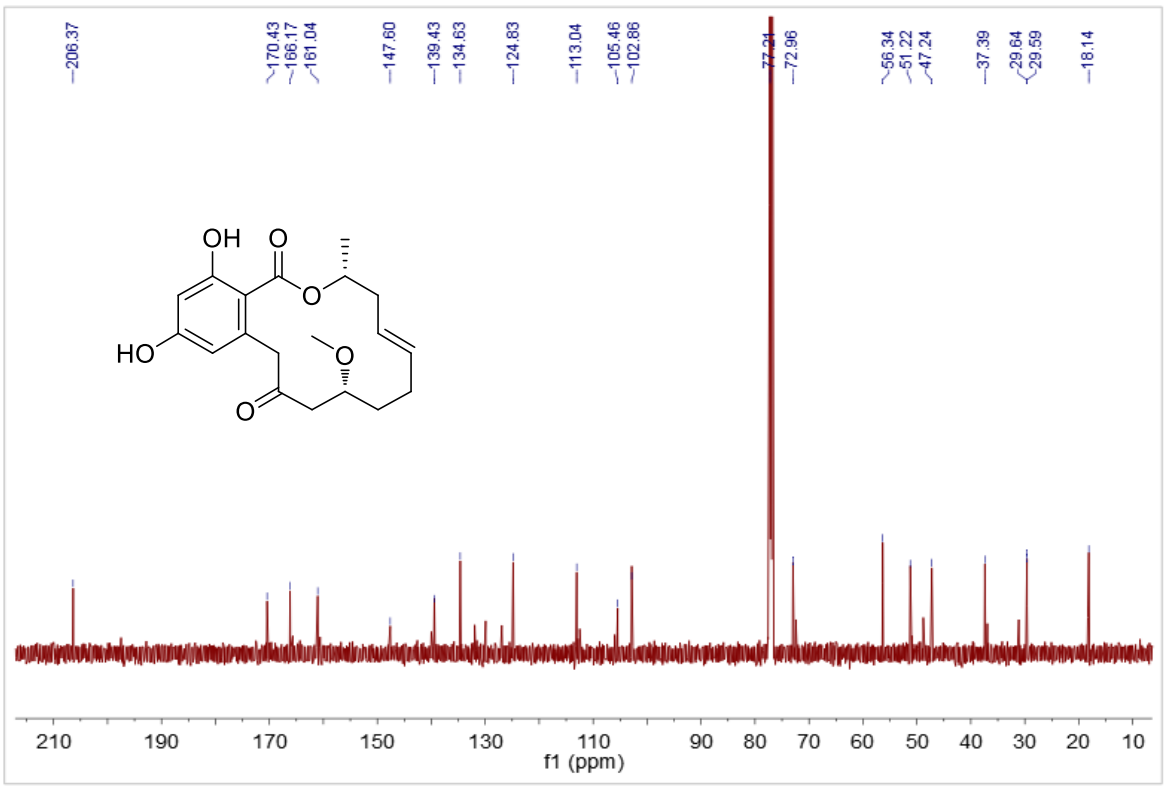


Figure S55. ^{13}C NMR (125 MHz) spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.

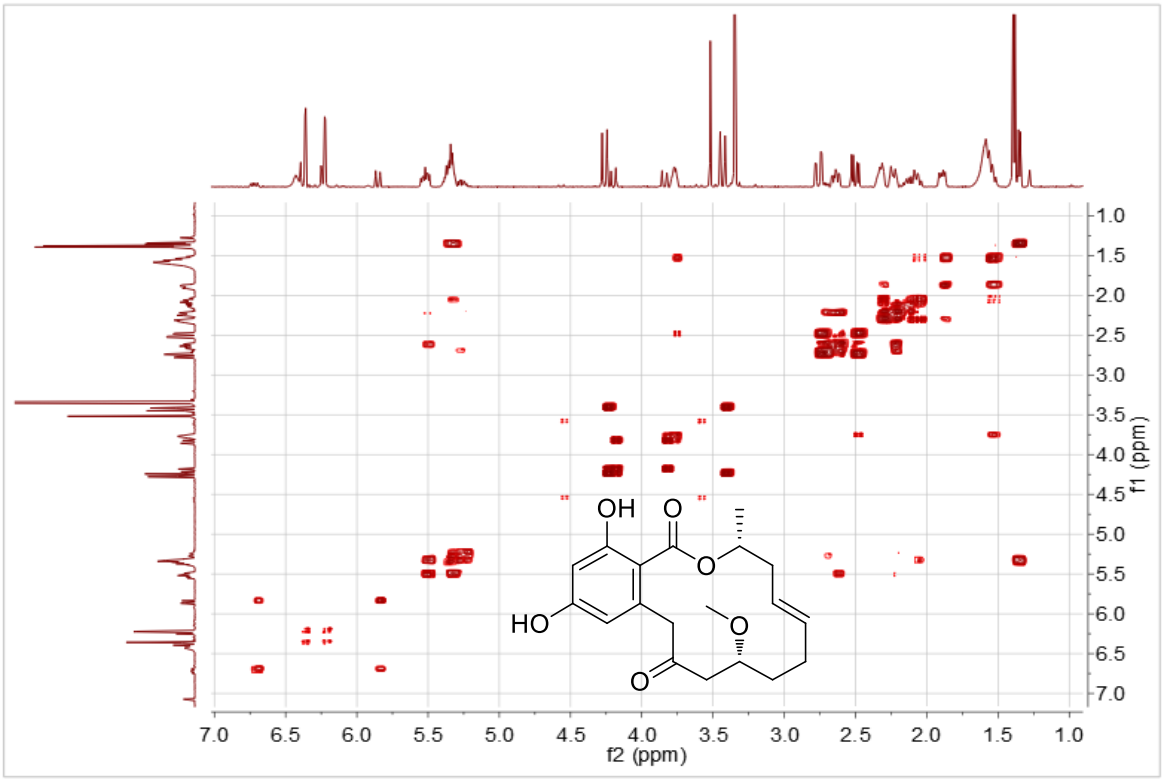


Figure S56. ^{1}H-^{1}H COSY spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.

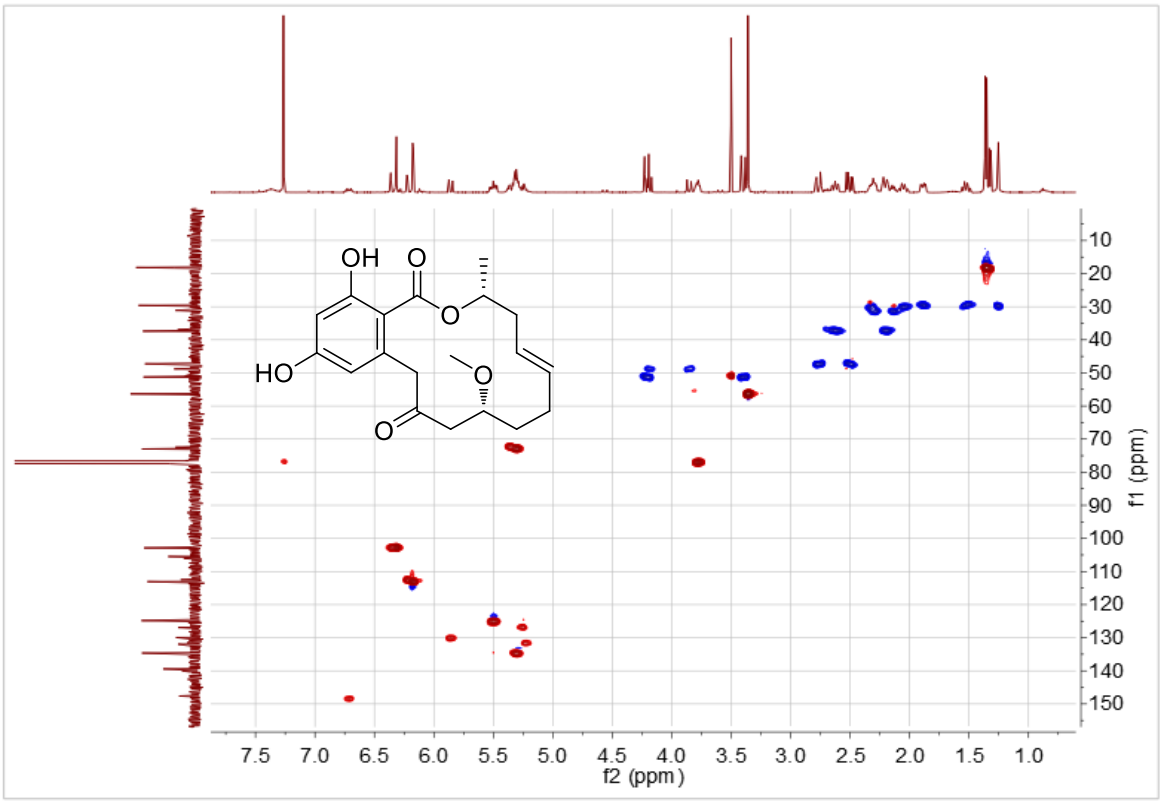


Figure S57. HSQC spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.

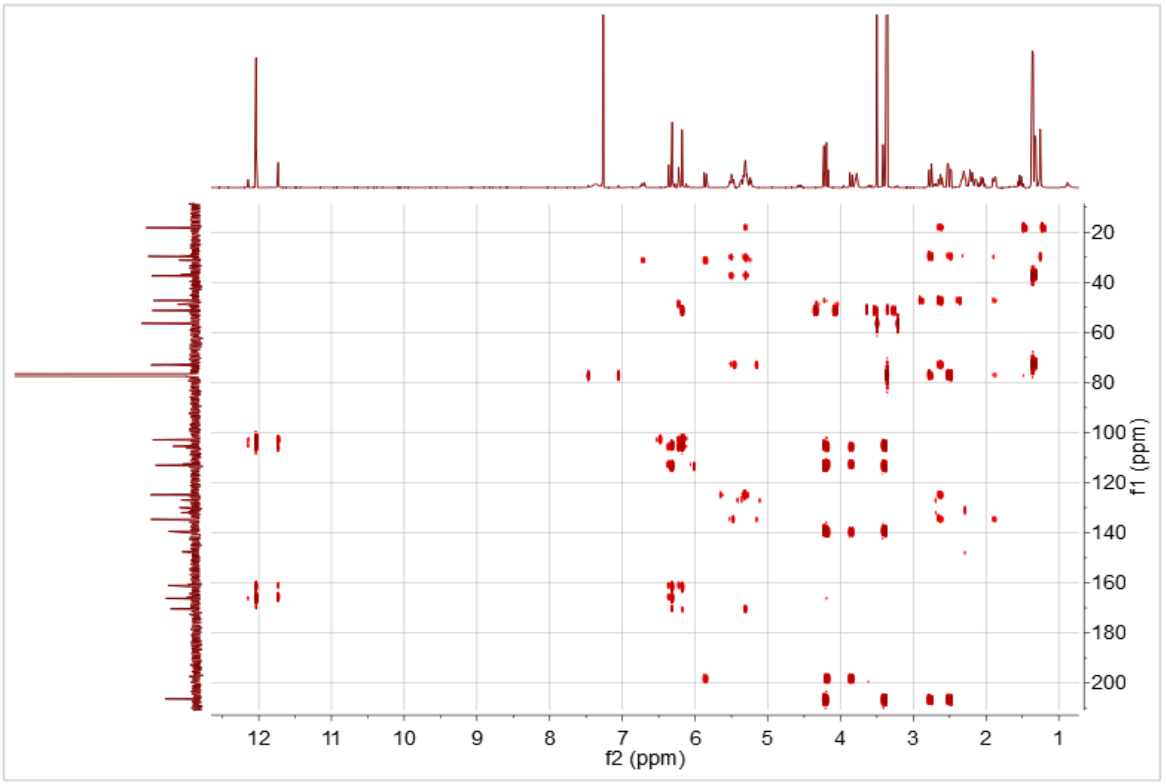


Figure S58. HMBC spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.

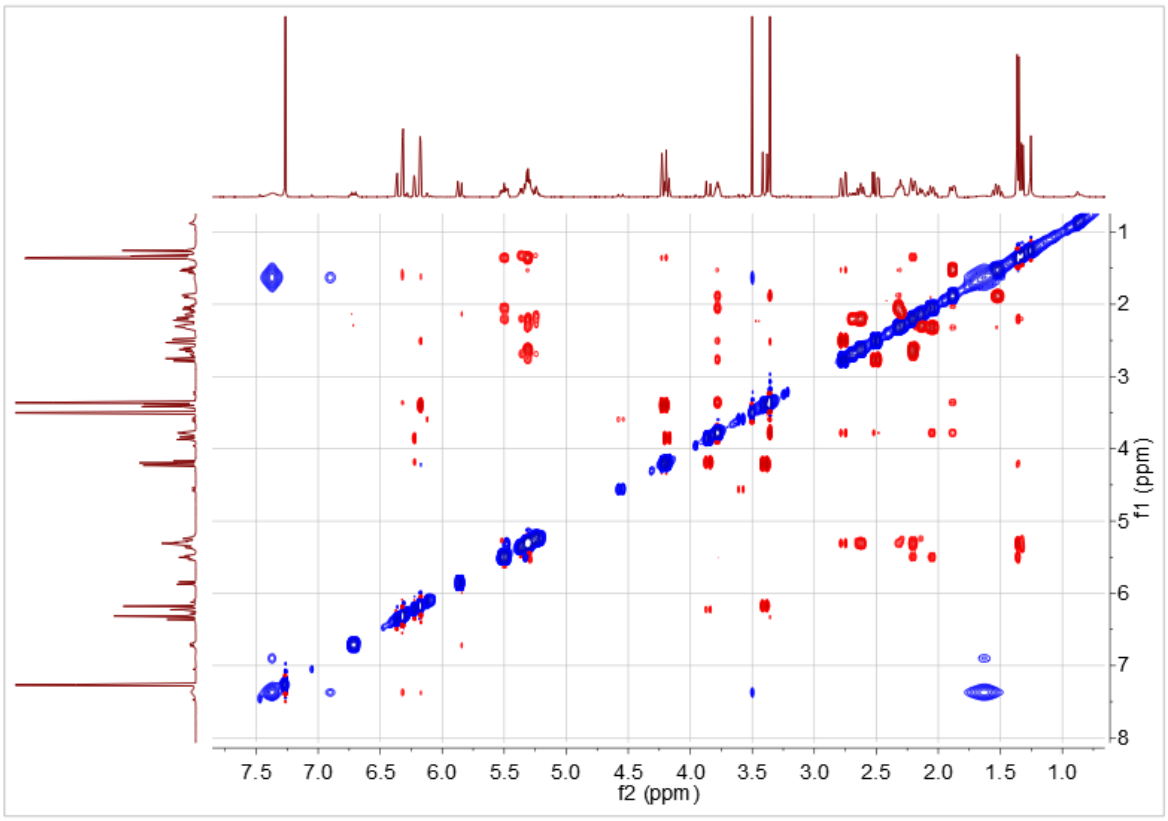
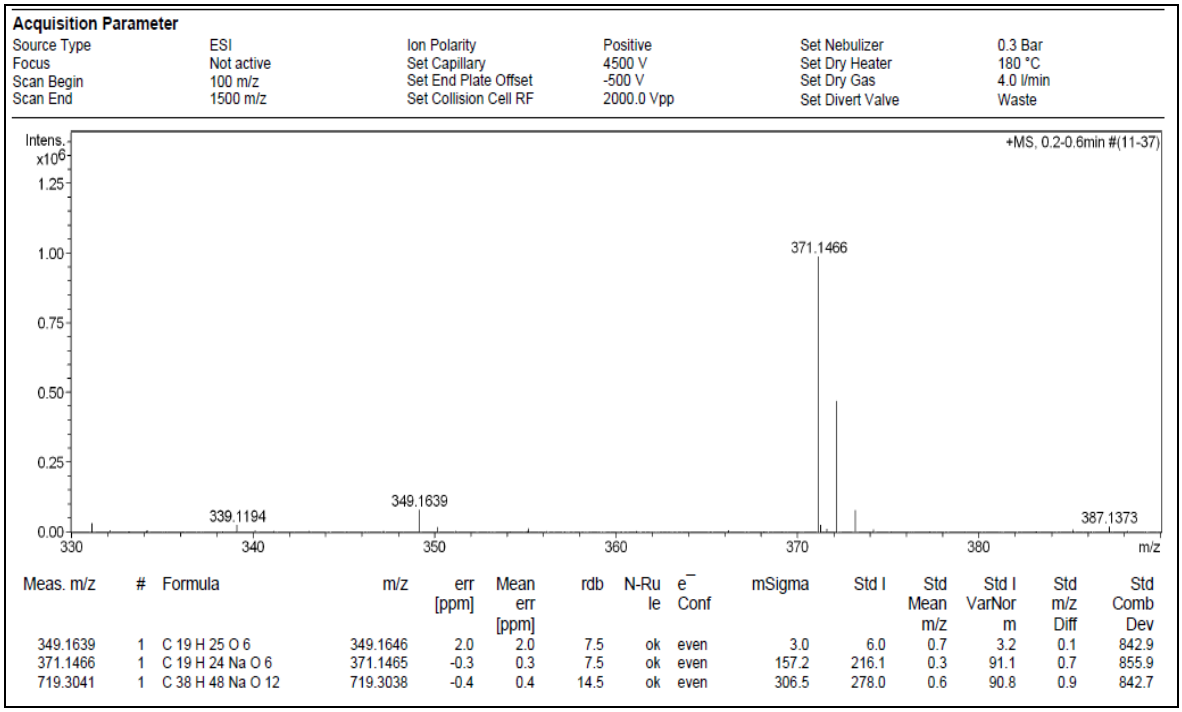


Figure S59. NOESY spectrum of 4'-methoxymonocillin IV (**7**) in $CDCl_3$.



Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
349.1639	1	C 19 H 25 O 6	349.1646	2.0	2.0	7.5	ok	even	3.0	6.0	0.7	3.2	0.1	842.9
371.1466	1	C 19 H 24 Na O 6	371.1465	-0.3	0.3	7.5	ok	even	157.2	216.1	0.3	91.1	0.7	855.9
719.3041	1	C 38 H 48 Na O 12	719.3038	-0.4	0.4	14.5	ok	even	306.5	278.0	0.6	90.8	0.9	842.7

Figure S60. (+)-HRESIMS spectrum of 4'-methoxymonocillin IV (**7**).

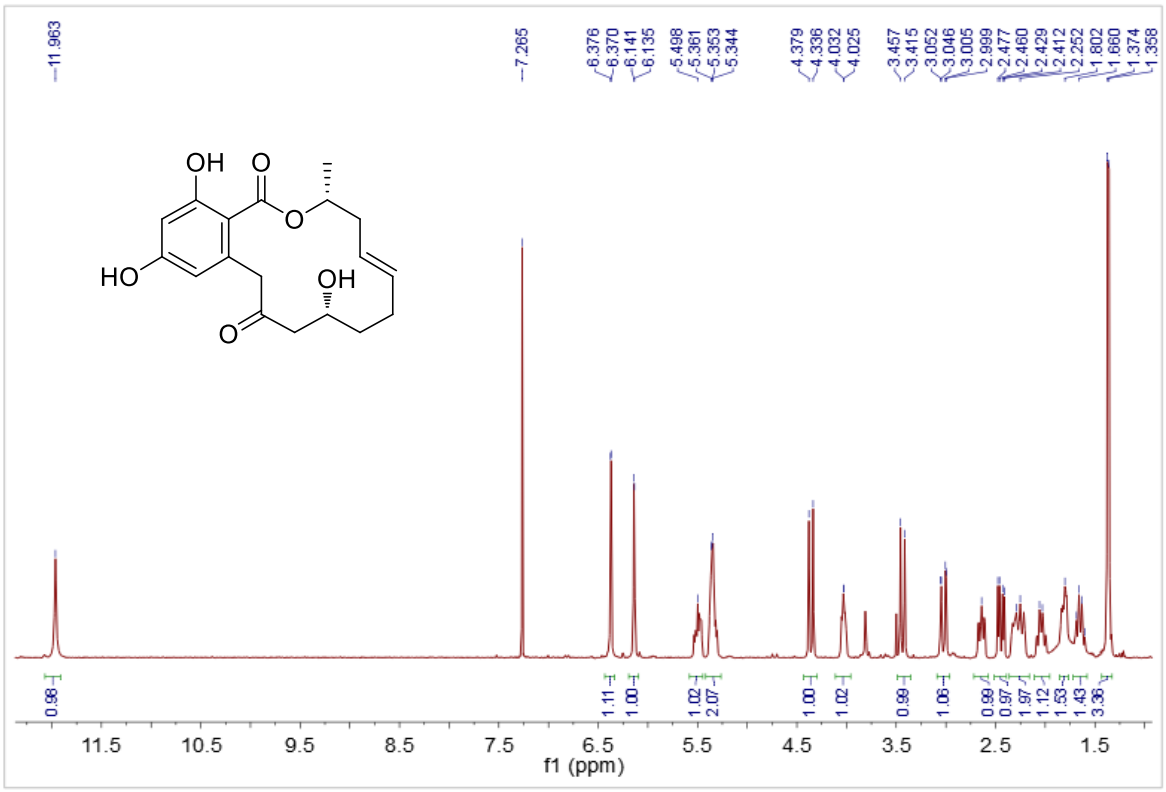


Figure S61. ^{1}H NMR (400 MHz) spectrum of 4'-hydroxymonocillin IV (**8**) in $CDCl_3$.

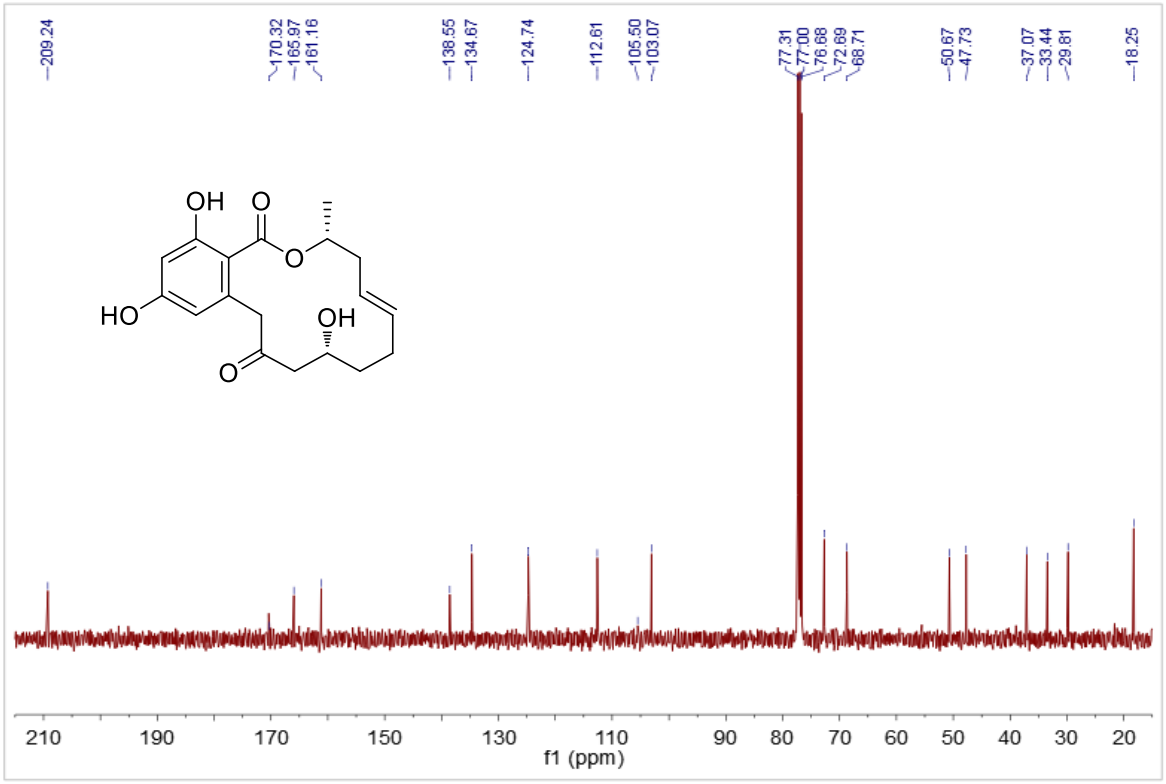


Figure S62. ^{13}C NMR (100 MHz) spectrum of 4'-hydroxymonocillin IV (**8**) in $CDCl_3$.

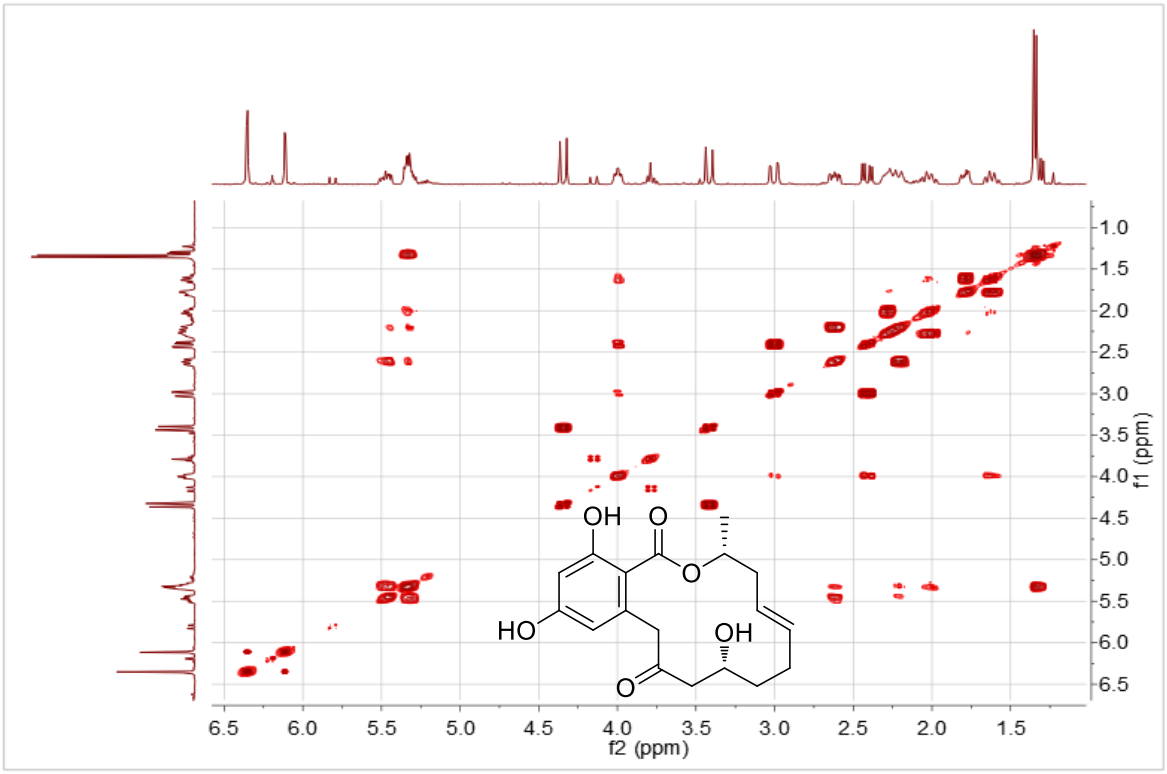


Figure S63. ^{1}H-^{1}H COSY spectrum of 4'-hydroxymonocillin IV (**8**) in $CDCl_3$.

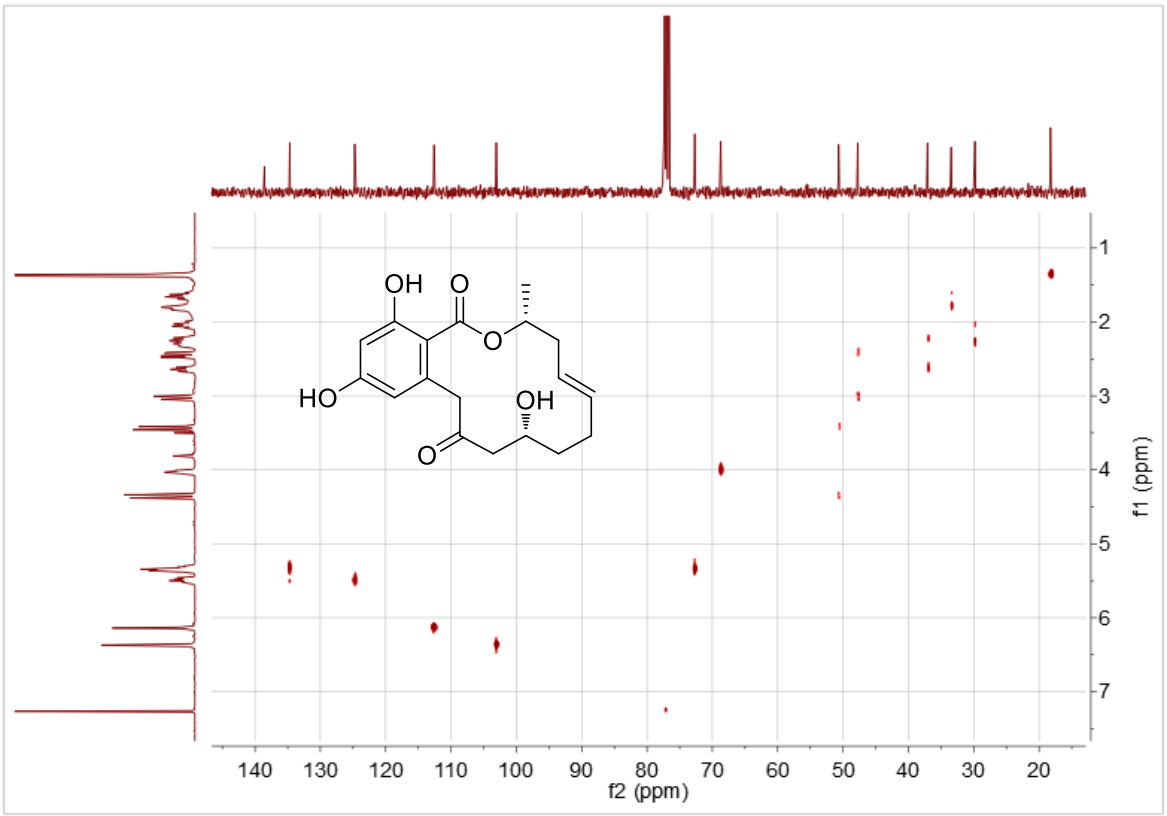


Figure S64. HSQC spectrum of 4'-hydroxymonocillin IV (**8**) in $CDCl_3$.

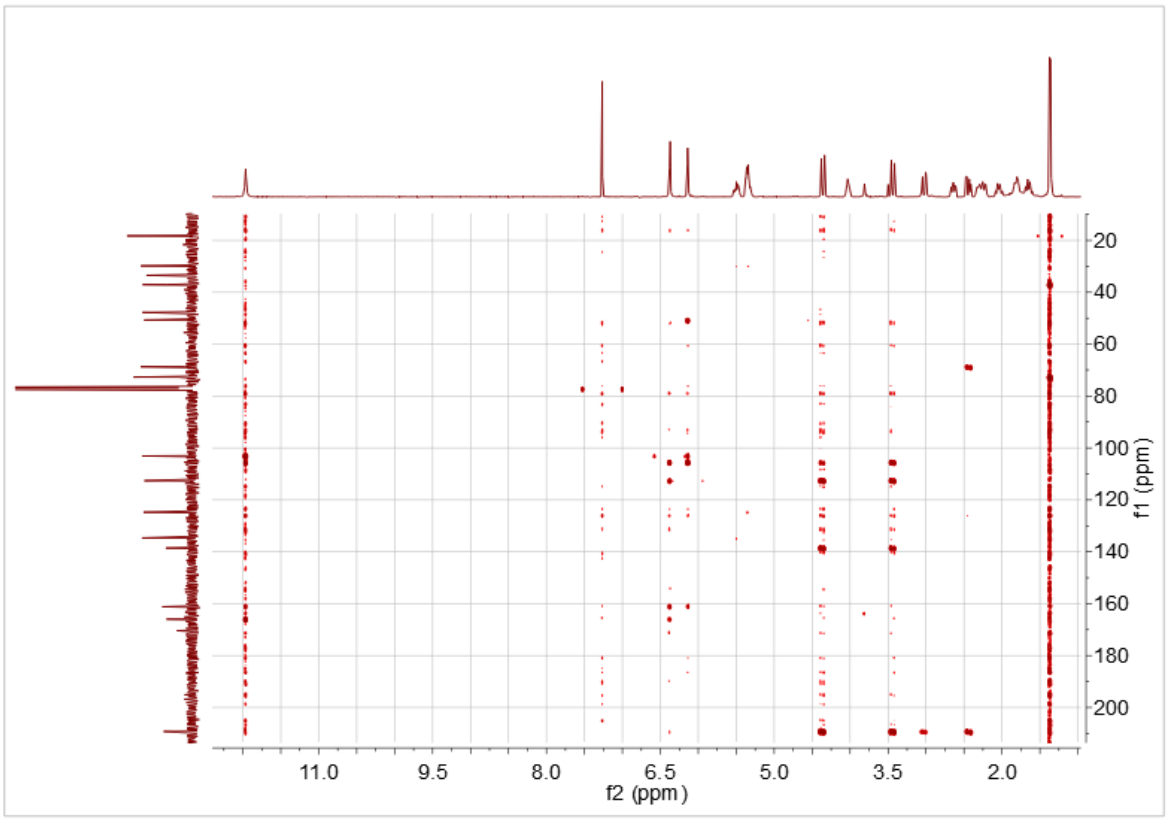
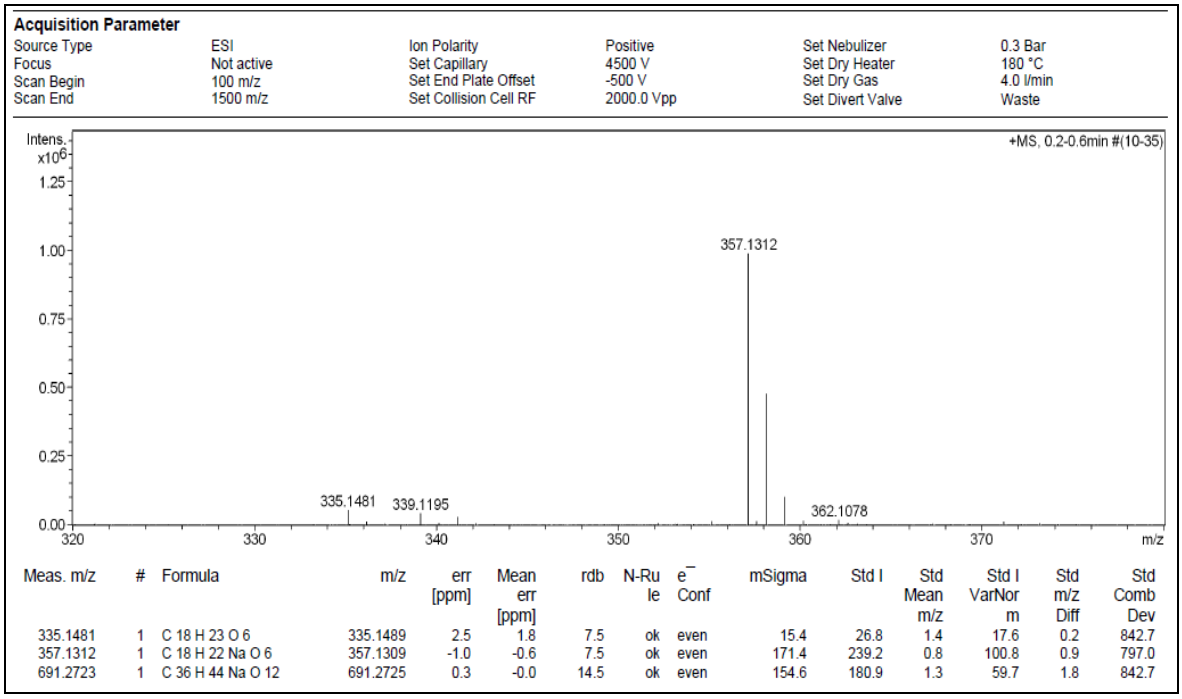


Figure S65. HMBC spectrum of 4'-hydroxymonocillin IV (**8**) in $CDCl_3$.



Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I VarNorm	Std m/z Diff	Std Comb Dev
335.1481	1	C 18 H 23 O 6	335.1489	2.5	1.8	7.5	ok	even	15.4	26.8	1.4	17.6	0.2	842.7
357.1312	1	C 18 H 22 Na O 6	357.1309	-1.0	-0.6	7.5	ok	even	171.4	239.2	0.8	100.8	0.9	797.0
691.2723	1	C 36 H 44 Na O 12	691.2725	0.3	-0.0	14.5	ok	even	154.6	180.9	1.3	59.7	1.8	842.7

Figure S66. (+)-HRESIMS spectrum of 4'-hydroxymonocillin IV (**8**).

Table S2. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR data of 2'α-hydroxymonocillin II (**9**).

position	δ_H mult. (*J* in Hz)		δ_C in $CDCl_3$, type
	in $CDCl_3$	in acetone-d_6	
1			107.1, C
2			164.6, C
3	6.82 d (2.6)	6.52 d (2.5)	102.0, CH
4			163.1, C
5	7.20 d (2.6)	6.25 d (2.5)	111.9, CH
6			144.5, C
7			171.6, C
1'	3.95 dd (13.5, 6.9)	3.73 dd (13.3, 7.6)	43.0, CH_2
	3.35 dd (13.5, 6.2)	2.86 dd (13.3, 6.3)	
2'	4.70 td (6.3, 6.2)	4.17 m	74.2, CH
3'	5.74 dd (15.5, 5.8)	5.33 dd (15.5, 4.5)	135.2, CH
4'	5.64 dt (15.5, 6.3)	5.36 m	127.9, CH
5'	2.03 m	2.10 m	30.5, CH_2
	1.95 d (9.0)	1.95 m	
6'	2.10 m	2.14 m	31.5, CH_2
7'	5.23 dd (14.2, 7.0)	5.22 m	133.0, CH
8'	5.40 dt (14.2, 6.8)	5.44 m	125.9, CH
9'	2.61 ddd (14.4, 6.8, 2.5)	2.69 ddd (15.0, 7.6, 3.6)	37.6, CH_2
	2.21 dt (13.8, 6.2)	2.31 dt (15.0, 5.7)	
10'	5.27 m	5.24 m	72.3, CH
11'	1.30 d (6.4).	1.40 d (6.4).	19.2, CH_3
2-OH	12.50 br s	11.90 br s	

3. Comparison between ECD Spectra of 7 and 8

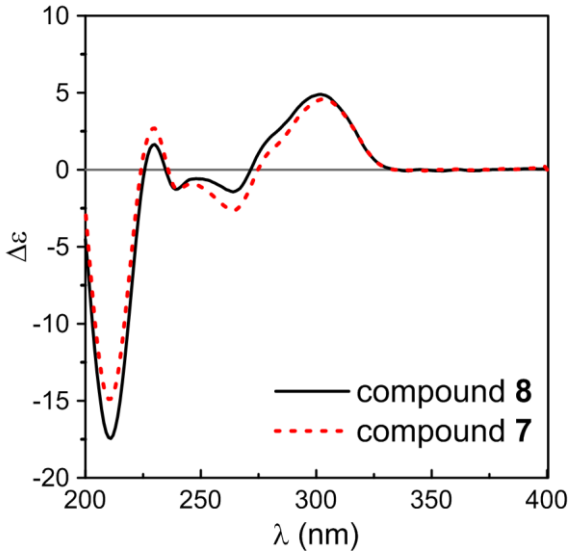


Figure S67. Comparison between ECD spectra of **7** and **8** in MeOH.