Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

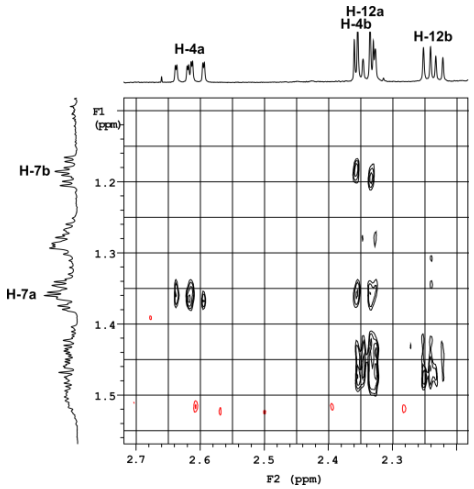
Supplementary Electronic Information

A joint molecular networking study of a *Smenospongia* sponge and a cyanobacterial bloom revealed new antiproliferative chlorinated polyketides

Roberta Teta, Gerardo Della Sala, Germana Esposito, Christopher W. Via, Carmela Mazzoccoli, Claudia Piccoli, Matthew J. Bertin, Valeria Costantino, and Alfonso Mangoni

Appendix A. Demonstration of the relative configuration of C-5 and C-6/C-8 of smenolactone C (**3**)

The NOESY spectrum of compound **3** shows correlation peaks of similar intensities between H-4a and H-7a, between H-4a and H-7b, between H-4b and H-7b, but there is no correlation peak at all between H-4b and H-7a.



The conformational analysis described in the main text demonstrated that a largely predominant conformation of the C-5/C-9 segment of compound **3** exists (shown in Figure 3E).

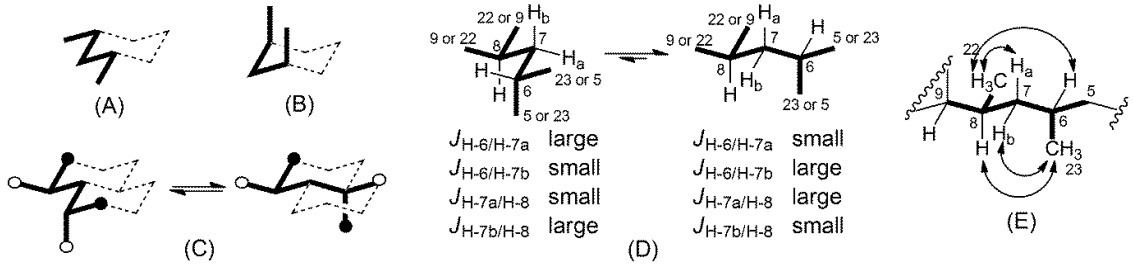
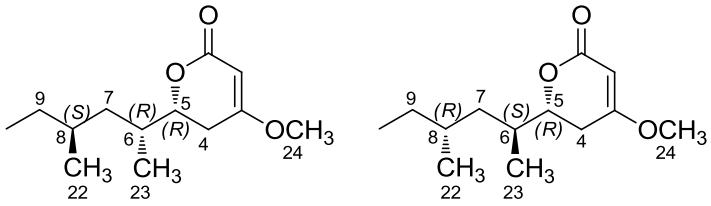


Figure 3 (from the main text)

Of the three possible rotamers around the C-5/C-6 bonds built starting from the conformation in Figure 5e (conformers **A**-**C** in the Figure below), none has unfavorable *syn*-pentane interactions, so they are expected to be all significantly populated. The intermediate value (5.8 Hz) of the coupling constant between H-5 and H-6 is in accordance with this.

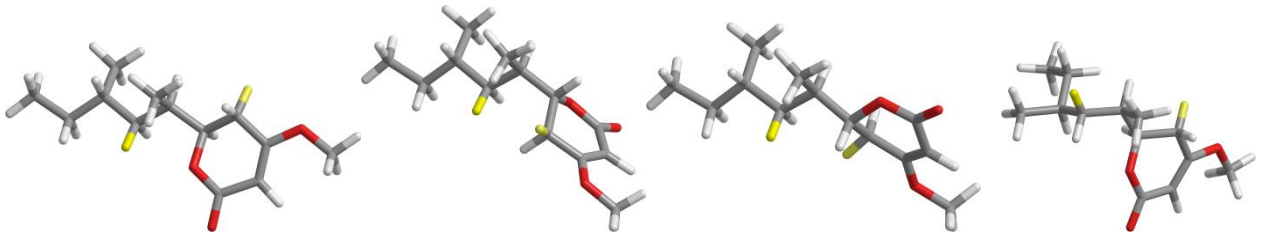
Even though coupling constants of H-7a and H-7b showed (as discussed in the main text) that the alternative conformation of the C-5/C-9 segment of compound **3** (on the left in Figure 5d) is not favored, this conformation can still be populated to some extents and needs to be considered. For this conformation, there is only one possible rotamer around the C-5/C-6 bonds devoid of *syn*-pentane interactions, i.e. the conformer **D** in the Figure below.

Models were prepared for each conformer A-D of the two diastereomeric simplified model of smenolactone C, namely (5*R*,6*R*,8*S*)-**24** and (5*R*,6*S*,8*R*)-**24**:



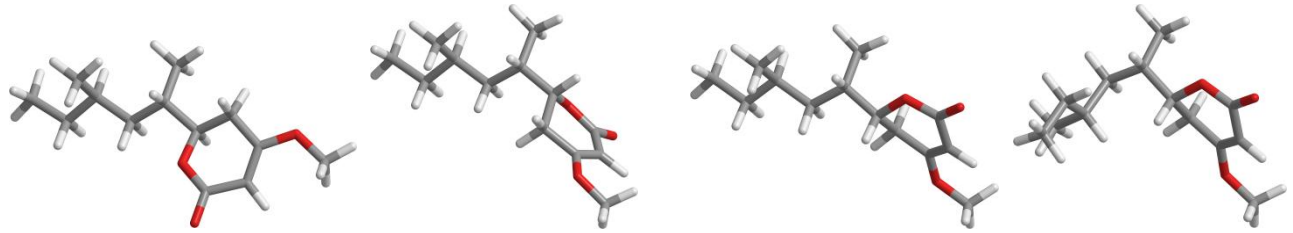
The models were optimized in the MMFF94 force field and inter-atomic distances were measured:

(5*R*,6*R*,8*S*)-**24**



	A	**B**	**C**	**D**	
H7a (δ 1.36)-H4a (δ 2.62)	4.71 Å	**2.86 Å**	**2.82 Å**	4.52 Å	NOESY
H7a (δ 1.36)-H4b (δ 2.34)	4.25 Å	4.01 Å	**2.17 Å**	4.83 Å	NOESY
H7b (δ 1.18)-H4a (δ 2.62)	4.53 Å	**2.25 Å**	3.94 Å	4.97 Å	no NOESY
H7b (δ 1.18)-H4b (δ 2.34)	4.97 Å	3.15 Å	2.98 Å	4.89 Å	NOESY

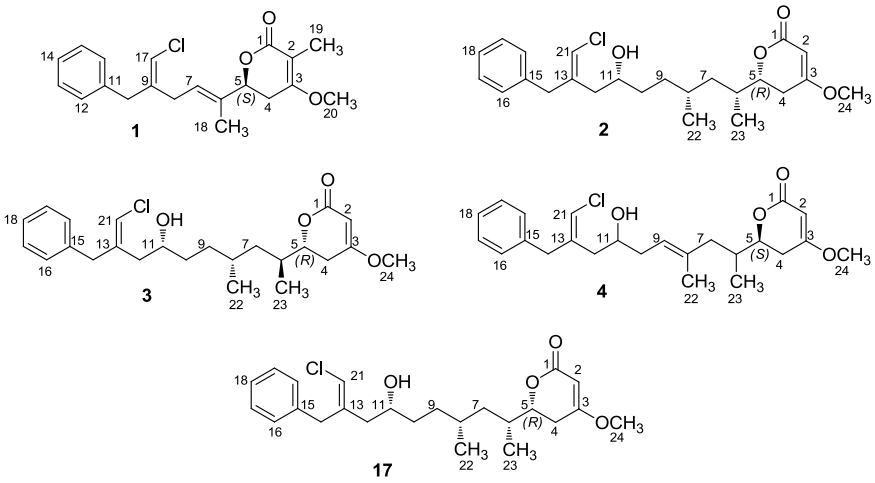
(5*R*,6*S*,8*R*)-**24**



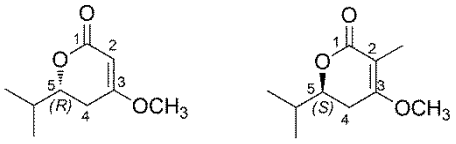
	A	**B**	**C**	**D**	
H7a (1.36)-H4a (2.62)	4.42 Å	**2.14 Å**	4.03 Å	3.00 Å	NOESY
H7a (1.36)-H4b (2.34)	4.77 Å	3.13 Å	3.01 Å	**2.33 Å**	NOESY
H7b (1.18)-H4a (2.62)	4.71 Å	3.05 Å	3.01 Å	4.27 Å	no NOESY
H7b (1.18)-H4b (2.34)	4.39 Å	4.13 Å	**2.24 Å**	3.88 Å	NOESY

It is apparent that is no way to rationalize the observed NOESY interactions for (5*R*,6*R*,8*S*)-**24**, whatever the population of each conformer may be; in contrast, for (5*R*,6*S*,8*R*)-**24** each of the observed NOESY corresponds to a very short distance between the involved protons in one of the four conformers.

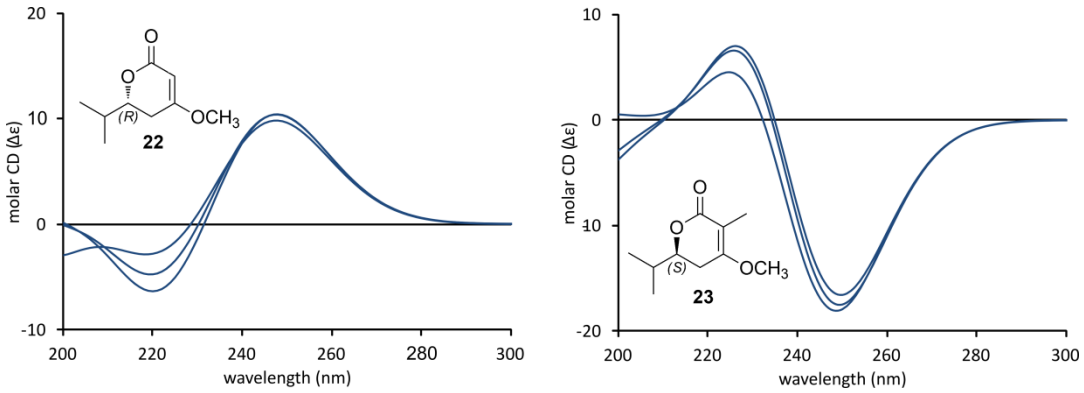
Appendix B. Quantum mechanical prediction of ECD spectra of smenolactones A-D (**1**-**4**) and trichophycin B (**17**)



Determination of the geometry and relative energies of conformers is the most demanding part of ECD prediction of a flexible molecule. Simplified model compounds are often used in quantum mechanical calculations on relatively large and flexible molecule. When using model compounds, it is important to make sure that the part of the molecule that is removed in a model compound has a negligible effect on the property of interest. The CD spectrum of compounds **1**-**4** and **17** is dominated by the skewed enone in the lactone ring, which is an inherently chiral chromophore. However, all compounds possess additional chromophores: a phenyl ring, a chlorinated double bond, and (for compounds **1** and **4**) an isolated double bond. The two alkene functions do not absorb in the UV range of interest (230-260 nm); the benzene ring is apart from the asymmetric portion of the molecule, so it is not expected to contribute significantly to the ECD spectrum. However, the possible interaction of these three chromophores with the enone system can potentially give rise to Cotton effects due to exciton coupling. In this scenario, quantum mechanical calculations were performed in two steps.

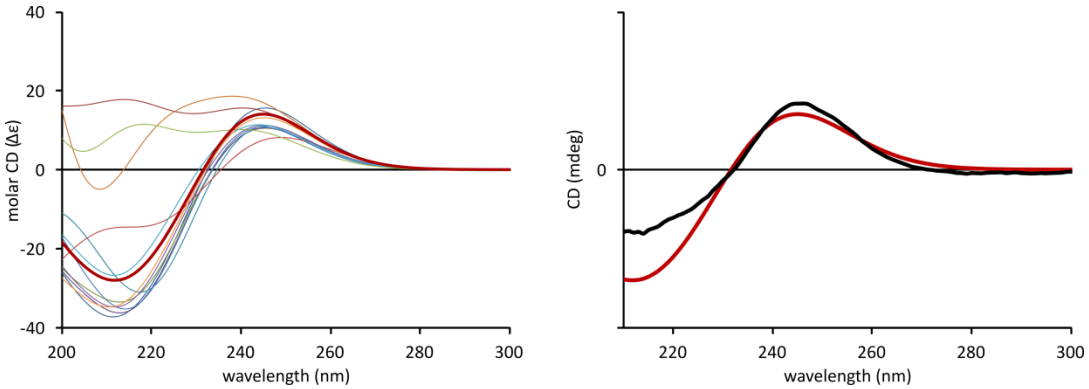


In the first step, model compounds were used. Compound (*R*)-**22** was used to study the lactone chromophore present in smenolactones B-D (**2**-**4**) (but also in trichophycin B, **17**, whose absolute configuration was determined by empirical correlation of ECD spectra as well).[1] Compound (*R*)-**22** may exist in six conformations, with two possible half-chair conformation of the lactone ring and three possible rotamers around the bond C5/C6. Only the three conformers with axial H-5 were considered for ECD prediction, because proton-proton coupling constants of H-5 with H-4a (in the range 12-13.5 Hz for all compounds **2**-**4** and **17**) clearly showed that the contribution of the conformers with equatorial H-5 was very low. The geometry of the three conformers was optimized, and their ECD spectrum calculated with Gaussian 16[2] using the TDDFT theory at the B3LYP/6-31G(d,p) level and the SMD model[3] for the solvent, methanol. The three spectra, obtained using the program SpecDis[4] with the half-width parameters σ set to 0.35 eV, were nearly identical in the region of interest, and showed the expected positive Cotton effect in the 230-260 nm region. Likewise, compound (*S*)-**23** was used to study the lactone chromophore of smenolactone A (**1**). Geometry optimization and ECD prediction of the three predominant conformers with axial H-5 was performed at the same B3LYP/6-31G(d,p)/SMD(MeOH) level of theory. The three spectra were again very similar and showed the expected negative Cotton effect in the 230-260 nm region.



Predicted ECD spectra of the three conformers of model compounds (*R*)-**22** and (*S*)-**23**. Calculation were performed at the B3LYP/6-31G(d,p)/SMD(MeOH) level of theory.

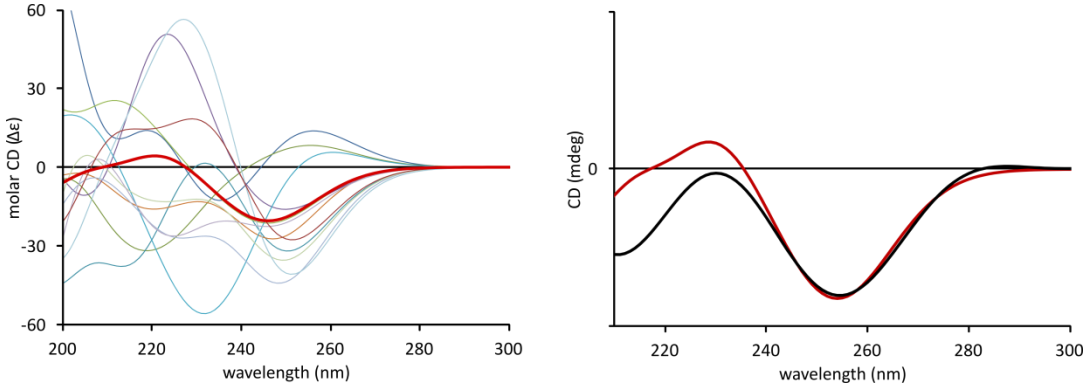
In the second step, the possible influence on the ECD spectrum of the other chromophores present in compounds **1**-**4** and **17** was evaluated by performing the calculations on the entire molecules of trichophycin A (**17**) and smenolactone A (**1**). Trichophycin B (**17**) was chosen because the Cartesian coordinates and populations of the 12 lowest energy conformers, optimized and validated by comparison with NMR data, were available from a previous study;[1] therefore no conformational search was needed. It should be noted that the published coordinates refer to the enantiomer of natural trichophycin B (**17**) (calculations were only used to determine the relative configuration of **17**); therefore, the molecule was reflected through the *xy* plane before starting the calculation. The ECD spectrum of each conformer was calculated at the B3LYP/6-31G(d,p)/SMD level, and the ECD curve generated with σ = 0.35 eV. The spectra were very similar to each other, and all of them showed a positive Cotton effect between 240 and 260 nm. The Boltzmann-averaged spectrum, calculated according to the populations reported in ref. 1, is very similar to the experimental ECD spectrum of compound **17**, as well as to the spectrum of model compound (*R*)-**22**. Therefore, compound (*R*)-**22** is a suitable model compound for compound **17** and, by extension, also for compounds **2**–**4**.



Predicted and experimental ECD spectra of trichophycin B (**17**). All calculations were performed at the B3LYP/6-31G(d,p)/SMD(MeOH) level of theory. (Left) Predicted ECD spectra of individual conformers (thin curves) and their Boltzman-weighted mean (red bold curve). (Right) Predicted (red curve; σ = 0.35 eV, UV shift = 0 nm) and experimental (black curve) ECD spectra.

Smenolactone A (**1**) required a separate analysis, because the phenyl ring and the chlorovinylidene group are closer to the lactone ring than in the other smenolactones, and a double bond is directly linked to it. The conformational space of compound **1** was explored using molecular dynamics (MD). A conformational search was performed using a 10-ns molecular MD simulation at 300 K in the CVFF force field using the InsightII/Discover package.[5] The coordinates were saved every 50 ps, giving 200 structures, which were optimized in the same force field. The search produced 28 unique

conformers, showing a high degree of conformational mobility for **1**. The geometry of the conformers was optimized quantum mechanically at the B3LYP/6-311G+(d,p)/SMD(MeOH) level of theory; during this step, four couples of conformers converged to the same conformer, reducing the total number of conformers to 24. Vibrational frequency analysis found no imaginary frequencies for any conformer, showing them to be true minima and not saddle points. Conformer populations were calculated using Boltzmann statistics and the internal energies as determined by the calculation. The resulting conformational ensemble was in good agreement with NMR data: the lactone ring was almost exclusively (99.3% population) in the half-chair conformation with axial H-5, in agreement with the large coupling constant of H-5 with H-4a (12.1 Hz); conformers with syn-oriented H-5 and H-7 were also predominant (77.8%), in accordance with the strong ROESY cross peak between H-5 and H-7 and, conversely, with the absence of a cross peak between H-5 and H_3-18. The ECD spectra of the 12 conformers populated more than 1% were then calculated. While most conformers showed the same negative Cotton effect at 240–259 nm as model compound (*S*)-**23**, three of them (accounting for 22.1% population) showed a positive, although weak, Cotton effect.



Predicted and experimental ECD spectra of smenolactone A (**1**). All calculations were performed at the B3LYP/6-311+G(d,p)/SMD(MeOH) level of theory. (Left) Predicted ECD spectra of individual conformers (thin curves) and their Boltzman-weighted mean (red bold curve). (Right) Predicted (red curve; σ = 0.35 eV, UV shift = +8 nm) and experimental (black curve) ECD spectra.

In spite of this, the Boltzmann-averaged ECD spectrum, calculated based on free energies of conformers corrected for low vibrational frequencies as proposed by Grimme,[6,7] was very similar to that of model compound (*S*)-**23**, and in good agreement with the experimental spectrum. This showed that the relationship between the configuration of the lactone and the sign of the Cotton effect at 240–260 nm also holds for smenolactone A (**1**). The 5*S* configuration of smenolactone A (**1**) was therefore confirmed.

References of Appendix B

1 M. J. Bertin, J. Saurí, Y. Liu, C. W. Via, A. F. Roduit and R. T. Williamson, *J. Org. Chem.*, 2018, **83**, 13256−13266.

2 Gaussian 16, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

3 A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. B*, 2009, **113**, 6378–6396.

4 T. Bruhn, A. Schaumlöffel, Y. Hemberger, G. Pescitelli, SpecDis version 1.71, Berlin, Germany, 2017, http:/specdis-software.jimdo.com.
5 BIOVIA, 5005 Wateridge Vista Drive, San Diego, CA 92121, USA.
6 S. Grimme, *Chem. - A Eur. J.*, 2012, **18**, 9955–9964.
7 Funes-Ardoiz, I.; Paton, R. S. (2016). GoodVibes: GoodVibes v1.0.2. http://doi.org/10.5281/zenodo.595246

Table S1. NMR data for smenolactone A (**1**) (700 MHz, CD_3OD).

Pos.	δ_C, type	δ_H, mult (*J* in Hz)	HMBC [a]	ROESY
1	171.7 (C)	-		
2	102.4 (C)	-		
3	169.9 (C)	-		
4a	28.7 (CH_2)	2.68 (ddq, 17.3,12.1, 2.0)	3	18,20
4b		2.63 (ddq, 17.3, 4.4, 1.1)	2,3,5	7,18,20
5	81.3 (CH)	4.69 (dd, 12.1, 4.4)	6,7,18	7
6	135.3 (C)	-		
7	126.2 (CH)	5.49 (tqd, 7.4, 1.4, 1.0)	5,18	4b,5,10
8	29.5 (CH_2)	2.96 (br. ABX, J_{AB}=15.7, J_{AX}= J_{BX}=7.4)	6,7,9,10,17	10,18
9	142.0 (C)	-		
10	41.8 (CH_2)	3.41 (br. AB, J_{AB}=15.2)	8,9,11,12/16,17	7,8,12/16,17
11	139.7 (C)	-		
12/16	130.1 (CH)	7.18 (br. d, 7.6)	10,14,16/12	10
13/15	129.6 (CH)	7.30 (br. t, 7.6)	11,12/16,15/13	
14	127.7 (CH)	7.22 (br. t, 7.6)	12/16	
17	115.5 (CH)	6.08 (br. s)	8,9,10	10
18	12.3 (CH_3)	1.66 (br. s)	5,6,7	4a,4b,8
19	8.8 (CH_3)	1.72 (br. s) (dd, 2.0, 1.1)	1,2,3	
20	56.4 (CH_3)	3.85 (s)	3	4a,4b

[a] HMBC correlations from proton stated to the indicated carbon.

Table S2. NMR data for smenolactone B (**2**) (700 MHz, CD_3OD).

Pos.	δ_C, type	δ_H, mult (*J* in Hz)	HMBC [a]	ROESY
1	170.9 (C)	-		
2	90.2(CH)	5.18 (d, 1.6)	1,3,4	24
3	176.6 (C)	-		
4a	31.2 (CH_2)	2.66 (ddd, 17.1, 13.0, 1.8)	3,5	5,6,7b,23
4b		2.33 (br. d, 17.1, 3.6)	5	5,7a,22,23,24
5	81.1 (CH)	4.33 (ddd, 12.8, 4.0, 4.0)		4a,4b,6,7a,7b,8,23
6	35.2 (CH)	1.88 (m)		4a,5,7a,8,9a,22,23
7a	41.1 (CH_2)	1.47 (ddd, 13.5, 8.7, 6.2)	5,6,8,23	4b,5,6
7b		1.11 (ddd, 13.5, 7.8, 5.5)	8,9,10,23	4a,5,8,22,23
8	30.9 (CH)	1.54 (m)		5,6,7b,9a, 22,23
9a	33.0 (CH_2)	1.37 (m)	10	6,8,22
9b		1.23 (m)	8	22,23
10a	35.2 (CH_2)	1.44 (ddd, 11.7, 9.8, 4.6)	9,11	12a,12b,22,23
10b		1.41 (m)		
11	70.8 (CH)	3.75 (m)		12a,12b,14,21
12a	38.9 (CH_2)	2.34 (br. dd, 13.3, 5.8)	11,13,14,21	10a,11,14
12b		2.24 (br. dd, 13.3, 7.6)	11,13,14,21	10a,11,14
13	141.5 (C)	-		
14	42.8 (CH_2)	3.48 (br. s)	12,15,16/20,21	11,12a,12b,16/20,21
15	139.8 (C)	-		
16/20	130.0 (CH)	7.19 (br. d, 7.6)	14,18	14
17/19	129.4 (CH)	7.29 (br. t, 7.6)	15,19/17	
18	127.5 (CH)	7.20 (br. t, 7.6)		
21	116.4 (CH)	6.05 (br. s)	12,13	11,14
22	20.7 (CH_3)	0.90 (d, 6.6)	7,8,9	4b,6,7b,8,9a,9b,10a
23	15.2 (CH_3)	1.00 (d, 6.8)	5,6,7	4a,4b,5,6,7b,8,9b,10a
24	57.1 (CH_3)	3.80 (s)	3	2,4b

[a] HMBC correlations from proton stated to the indicated carbon.

Table S3. NMR data for smenolactone C (**3**) (700 MHz, CD_3OD).

Pos.	δ_C, type	δ_H, mult (*J* in Hz)	HMBC [a]	ROESY
1	170.9 (C)	-		
2	90.1 (CH)	5.18 (d, 1.6)	1,3,4	24
3	176.7 (C)	-		
4a	30.7 (CH_2)	2.62 (ddd, 17.2, 12.9, 1.6)	2,3,5,6	6,7a,23
4b		2.34 (br. dd, 17.2, 3.7)	2,3	5,6,7a,7b,23,24
5	82.2 (CH)	4.26 (ddd, 12.8, 5.8, 3.7)	23	4b,6,23
6	35.4 (CH)	1.94 (ddq, 12.1, 6.8, 3.7)		4a,4b,5,7a,9b,22,23
7a	40.5 (CH_2)	1.37 (ddd, 13.3, 10.3, 3.7)	5,6,8,22,23	4a,4b,6,8,9a,22
7b		1.18 (ddd, 13.3, 10.3, 4.0)	5,6,8,22,23	4b,8,9b,23
8	31.1 (CH)	1.51 (ddd, 6.6, 3.7, 3.7)		7a,7b,9a,22,23
9a	35.2 (CH_2)	1.36 (ddd, 13.6, 12.7, 6.6)	8,22	7a,8,11,22
9b		1.27 (m)	8,11,22	6,7b,10,11,22
10	35.8 (CH_2)	1.46 (m)	9,11	9b,11,14,12a,12b
11	71.0 (CH)	3.76 (ddd, 12.7, 7.8, 4.4)		9a,9b,10,12a,12b,14
12a	38.9 (CH_2)	2.34 (br. dd, 13.5, 5.7)	10,11,13,14,21	10,11,14
12b		2.24 (br. dd, 13.5, 7.8)	10,11,13,14,21	10,11,14
13	141.7 (C)	-		
14	42.8 (CH_2)	3.48 (br. s)	12,13,15,16/20,21	6,10,11,12a,12b,16/20,21
15	140.0 (C)	-		
16/20	130.0 (CH)	7.19 (br. d, 7.4)	14,18	14,17/19,21
17/19	129.5 (CH)	7.29 (br. t, 7.4)	15,16/20	16/20
18	127.5 (CH)	7.21 (br. t, 7.4)	16/20	
21	116.4 (CH)	6.06 (br. s)	12,13,14	14,16/20
22	19.6 (CH_3)	0.87 (d, 6.6)	4,6,7	6,7a,8,9a,9b
23	15.1 (CH_3)	0.96 (d, 6.8)	5,6,7	4a,4b,5,6,7b,8
24	57.1 (CH_3)	3.80 (s)	3	4b,2

[a] HMBC correlations from proton stated to the indicated carbon.

Table S4. NMR data for smenolactone D (**4**) (700 MHz, CD_3OD).

Pos.	δ_C, type	δ_H, mult (*J* in Hz)	HMBC [a]
1	170.9 (C)	-	
2	90.2 (CH)	5.19 (d, 1.6)	1,3,4
3	176.5 (C)	-	
4a	31.3 (CH_2)	2.68 (ddd, 17.2, 13.2, 1.7)	2,3,4,5
4b		2.30 (br. dd (17.2, 3.5)	2,4
5	80.4 (CH)	4.35 (ddd, 13.1, 3.7, 3.7)	
6	35.4 (CH)	1.93 (m)	
7a	44.0 (CH_2)	2.25 (m)	6,8,9,23
7b		1.93 (m)	6,8,9
8	136.2 (C)		
9	124.3 (CH)	5.25 (br. t, 7.0)	7,8,10,22
10a	37.2 (CH_2)	2.19 (m)	8,9,11,12
10b		2.19 (m)	
11	71.1 (CH)	3.84 (m)	
12a	38.1 (CH_2)	2.33 (m)	11,13,14,21
12b		2.22 (m)	11,13,14,21
13	142.1 (C)		
14	42.6 (CH_2)	3.48 (br. s)	12,13,15,16/20,21
15	140.0 (C)		
16/20	130.1 (CH)	7.18 (br. d, 7.6)	14,18
17/19	129.5 (CH)	7.29 (br. t, 7.6)	15,19/17
18	127.7 (CH)	7.20 (br. t, 7.6)	
21	116.2 (CH)	6.04 (br. s)	12,13,14
22	16.1 (CH_3)	1.61 (br. s)	7,8,9
23	14.9 (CH_3)	0.92 (d, 6.8)	5,6,7
24	57.4 (CH_3)	3.80 (s)	3

[a] HMBC correlations from proton stated to the indicated carbon.

Table S5. NMR data for isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).

Pos.	δ_C, type	δ_H, mult (*J* in Hz)	HMBC [a]	COSY
1	142.8 (CH)	7.73 (d, 3.2)	3	
2	120.1 (CH)	7.60 (d, 3.2)	1,3	
3	175.0 (C)			
4	47.3 (CH)	5.29 (m)	3,5,6	5, NH
5	20.6 (CH_3)	1.55 (d, 7.2)	3,4	4
NH		8.39 (d, 8.0)	4,6	4
6	169.0 (C)			
7	130.5 (C)			
8	15.3 (CH_3)	1.73 (s)	6,7,9,11,12	9
9	141.0 (CH)	6.07 (d, 9.7)	6,8,10,11,12	8,10
10	32.3 (CH)	2.38 (m)		9,11,12
11a	34.7 (CH_2)	1.47 (m)	9,10,11,13,14	10,12b,13
11b		1.39 (m)	9,10,11,13,14	10,12a,13
12	32.2 (CH_2)	1.96 (t, 8.2)	10,12,14,15,16	12a,12b
13	142.0 (C)			
14	113.0 (CH)	6.19 (s)	13,14,16	
15	35.9 (CH_2)	3.55 (d, 10.5)	13,14,15,17,18/22	
16	138.7 (C)			
17/21	128.9 (CH)	7.20 (d, 7.5)	16,19,20,21	19/21
18/20	129.0 (CH)	7.30 (t, 7.5)	17,18,22	18/22
19	126.8 (CH)	7.22 (t, 7.5)	18,22	
22	20.5 (CH_3)	0.93 (d, 6.6)	9,10,12	10

[a] HMBC correlations from proton stated to the indicated carbon.

Table S6. NMR data for conulothiazole C (**6**) (500 MHz, DMSO-d_6).

Pos.	δ_H, mult (*J* in Hz)	COSY
1	7.70 (d, 3.3)	2
2	7.57 (d, 3.3)	1
3	-	
4	5.27 (t, 7.4)	25
NH	8.37 (d, 8.0)	4
5	-	
6	-	
7	6.07 (d, 9.8)	8,24
8	2.54 (m)	23
9	1.12	10
10	1.30 (m)	22
11	1.46 (m)	12
12	2.06 (m)	11
13	-	
14	3.36 (s)	21
15	-	
16/20	7.19 (d, 7.5)	
17/19	7.30 (t, 7.4)	
18	7.22 (t, 7.5)	
21	6.14 (s)	14
22	0.80 (d, 6.0)	10
23	0.93 (d, 6.5)	8
24	1.78 (s)	7
25	1.53 (d, 7.0)	4

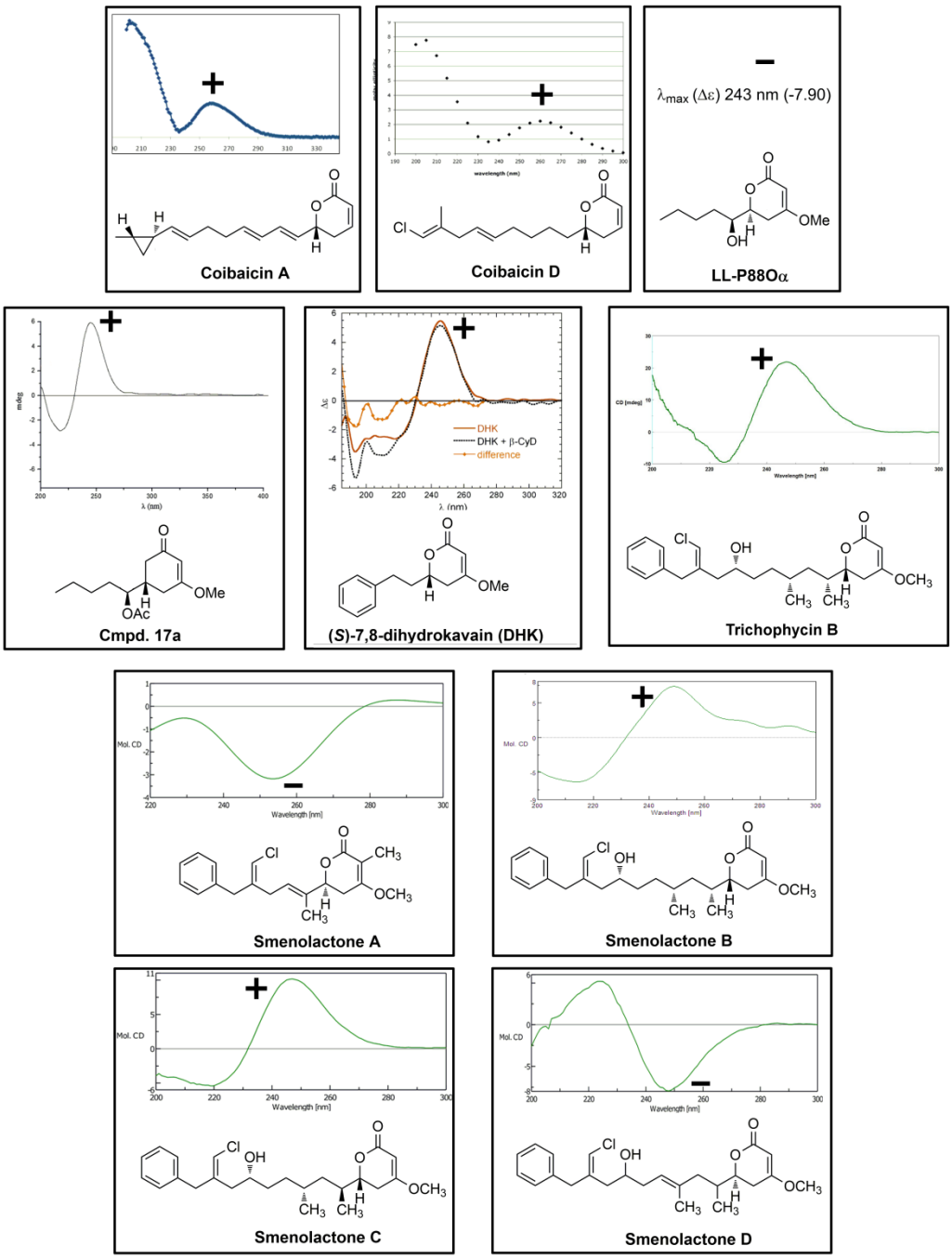


Figure S1. ECD spectra of reference chiral α,β-unsaturated δ-lactones: Coibaicin A,[1] Coibaicin D,[1] LL-P88Oα,[2] Compound 17a from Ref. 3, (*S*)-7,8-dihydrokavain (DHK),[4] tricophycin B,[5] and of smenolactones A-D.

References

1 V. M. T. Carneiro, C. M. Avila, M. J. Balunas, W. H. Gerwick and R. A. Pilli, *J. Org. Chem.*, 2014, **79**, 630–642.
2 G. A. Ellestad, W. J. McGahren and M. P. Kunstmann, *J. Org. Chem.*, 1972, **37**, 2045–2047.
3 J.-F. Tian, R.-J. Yu, X.-X. Li, H. Gao, L.-D. Guo, J.-S. Tang and X.-S. Yao, *Magn. Reson. Chem.*, 2015, **53**, 866–871.
4 G. Pescitelli, A. R. Bilia, M. C. Bergonzi, F. F. Vincieri and L. Di Bari, *J. Pharm. Biomed. Anal.*, 2010, **52**, 479–483.
5 M. J. Bertin, J. Saurí, Y. Liu, C. W. Via, A. F. Roduit and R. T. Williamson, *J. Org. Chem.*, 2018, **83**, 13256-13266.

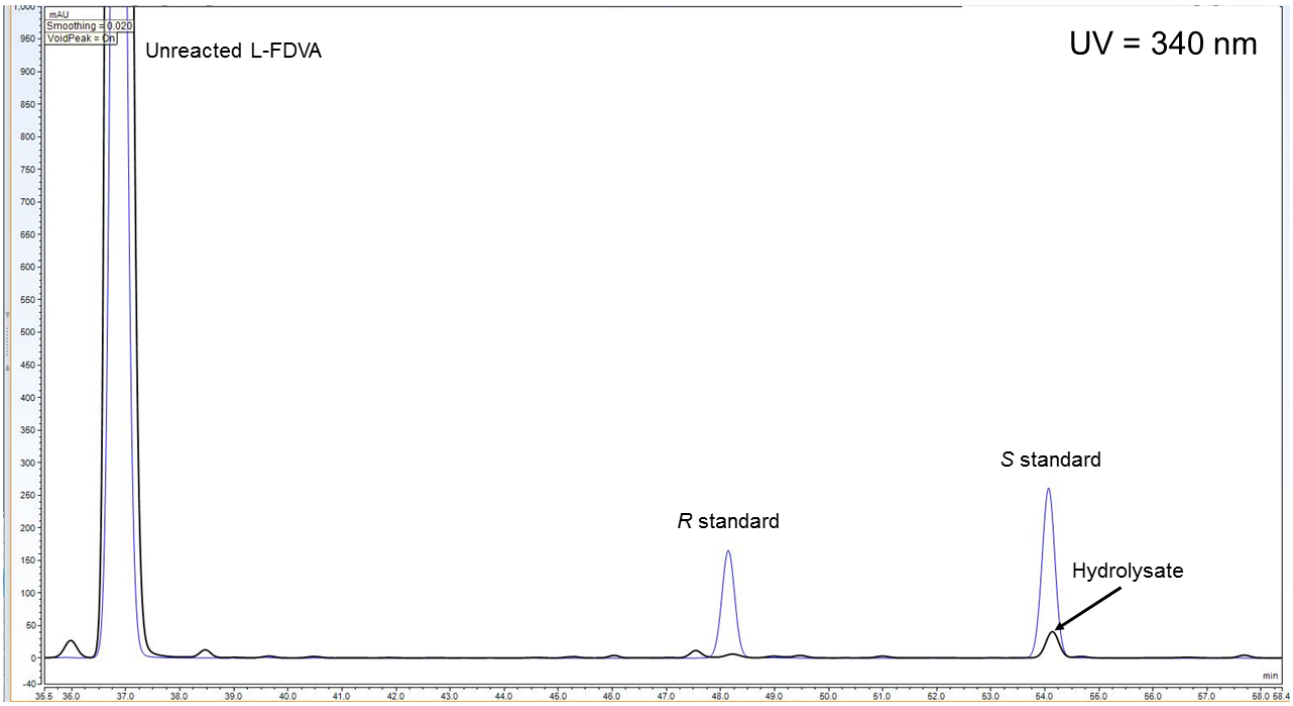


Figure S2. Marfey's analysis of the hydrolysate of **5** and *R* and *S* 2-thiazolemethanamine standards.

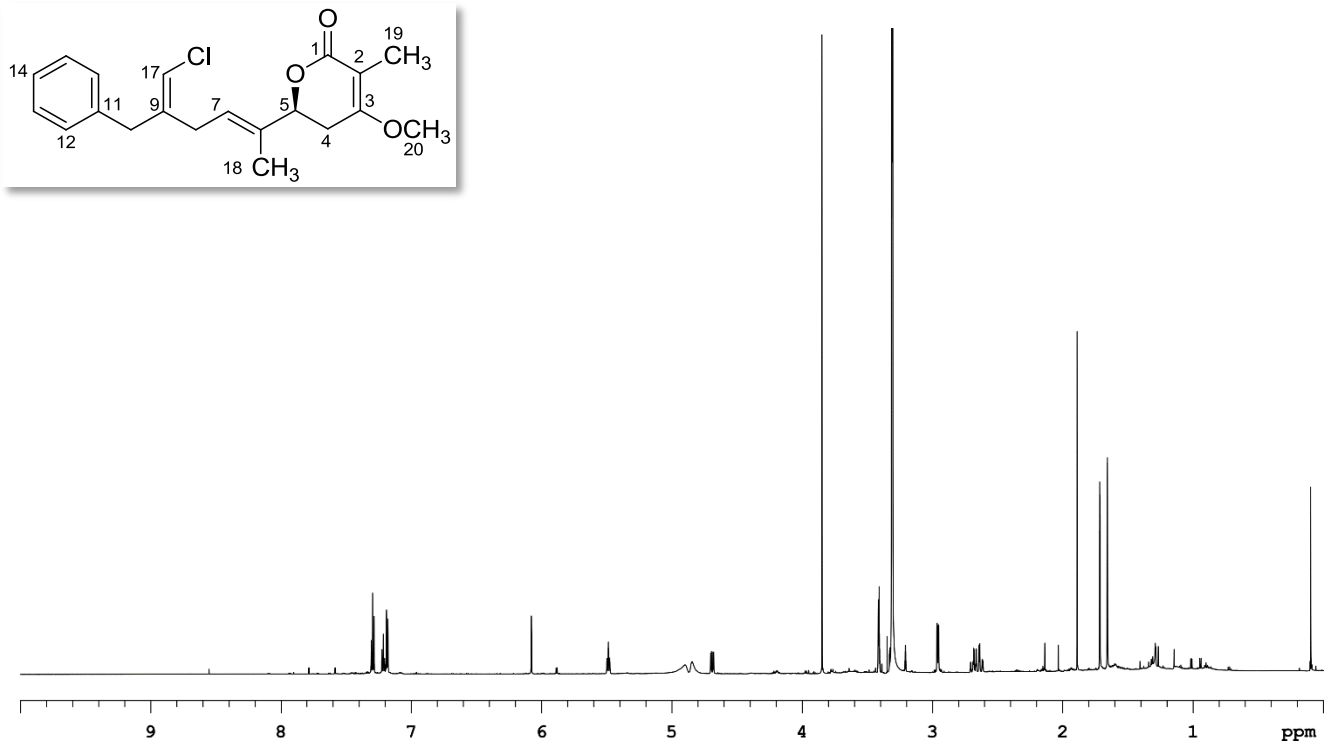


Figure S3. ^{1}H NMR spectrum of smenolactone A (**1**) (700 MHz, CD_3OD).

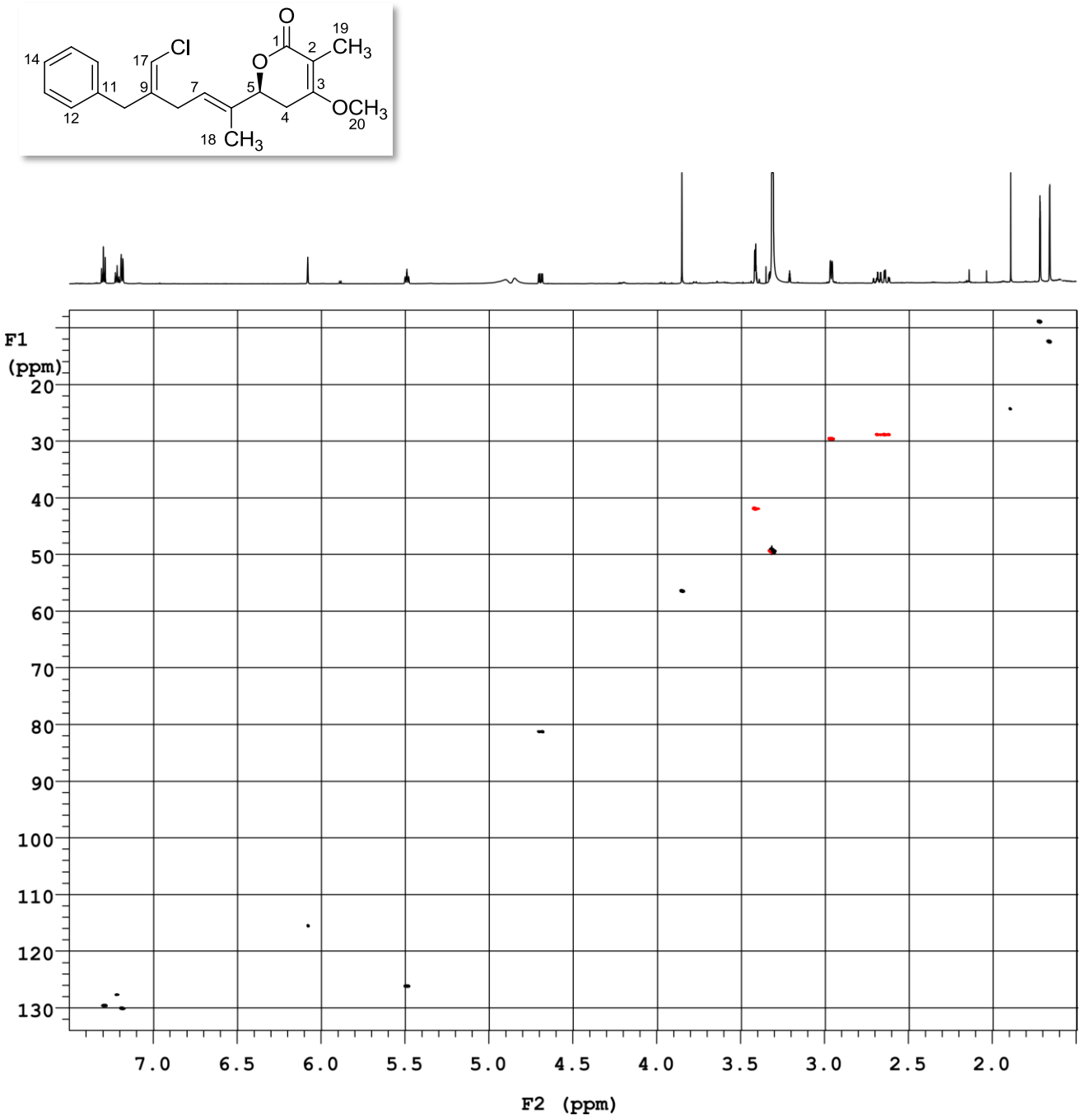


Figure S4. HSQC spectrum of smenolactone A (**1**) (700 MHz, CD_3OD).

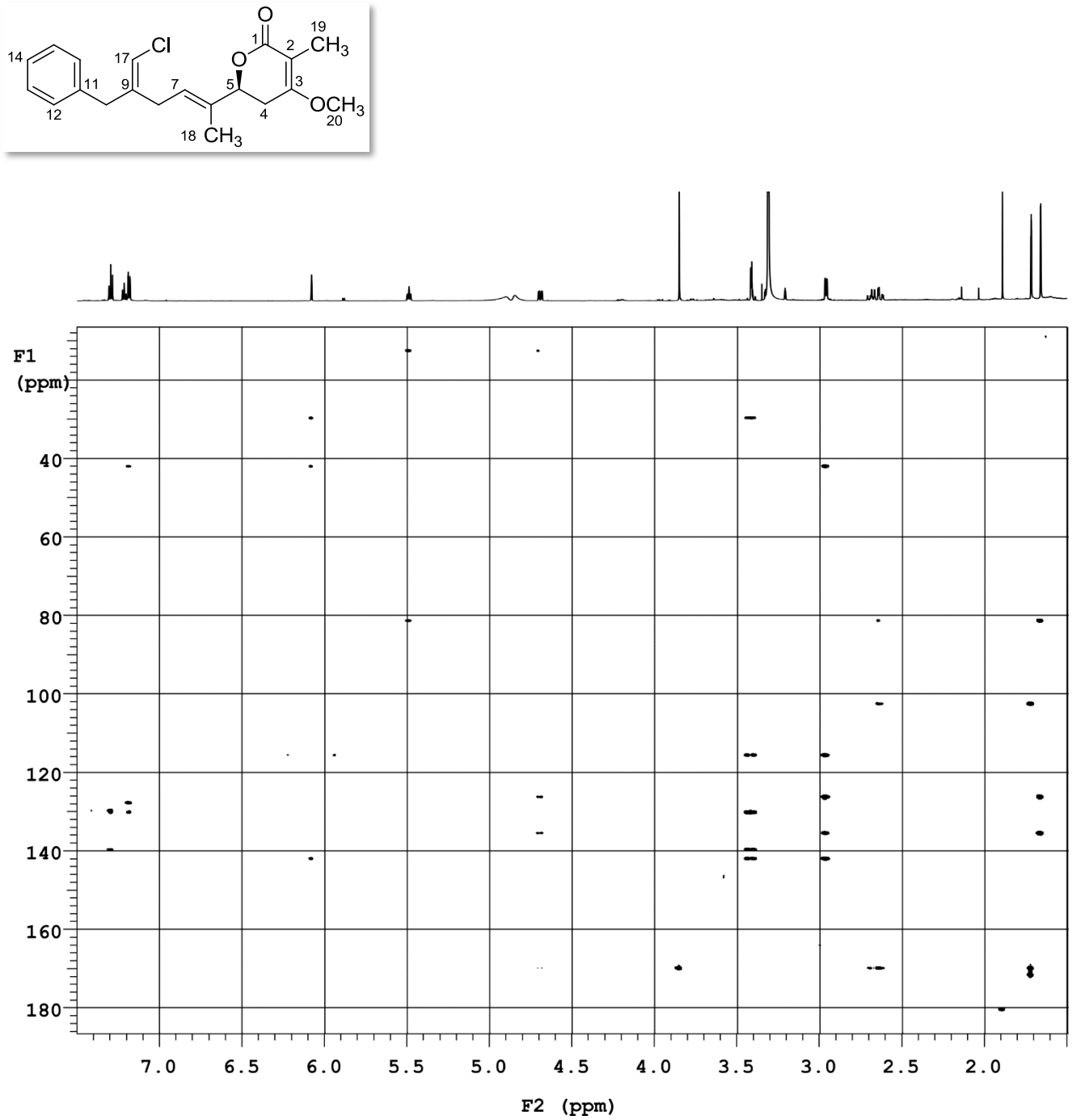


Figure S5. HMBC spectrum of smenolactone A (**1**) (700 MHz, CD_3OD).

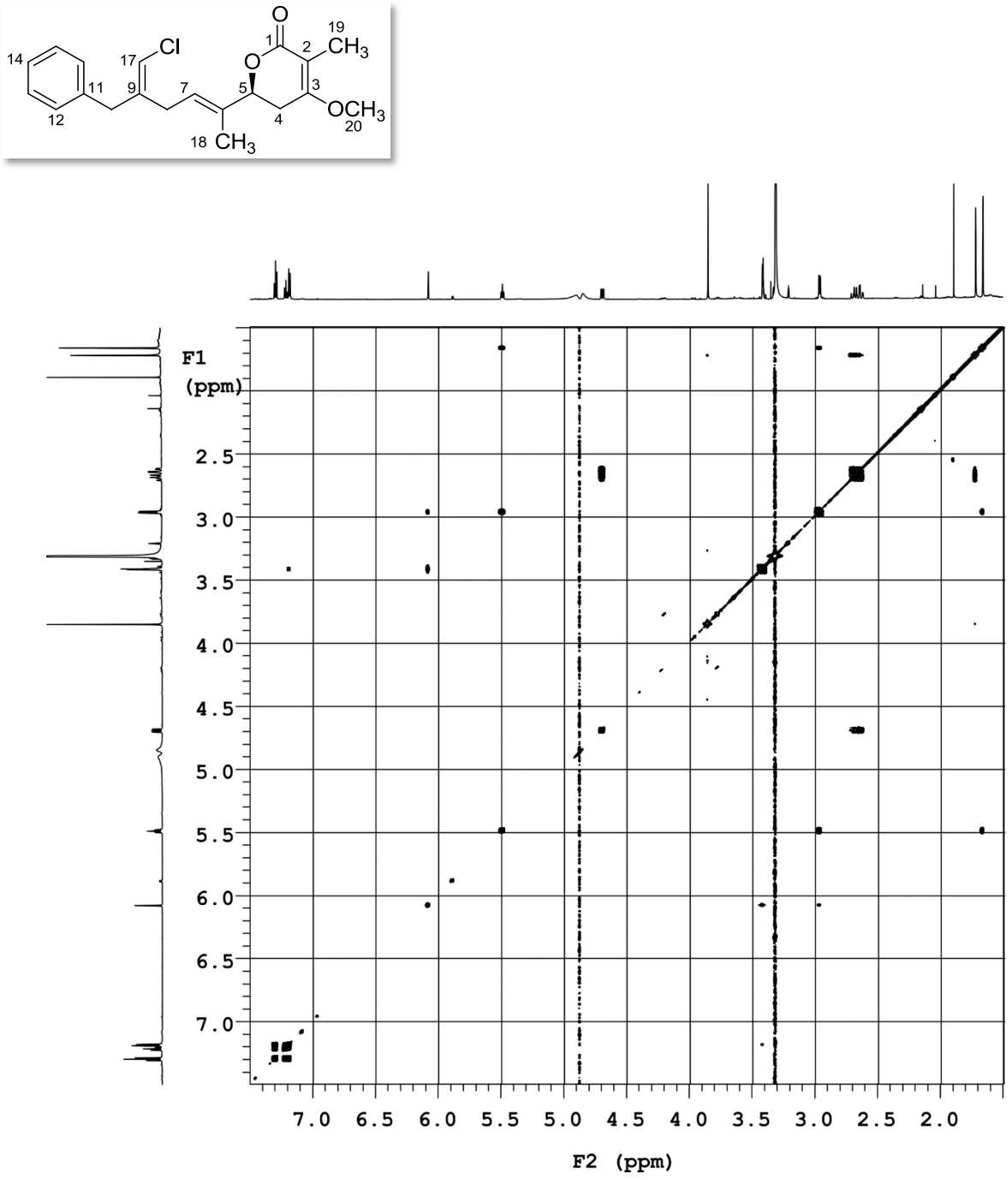
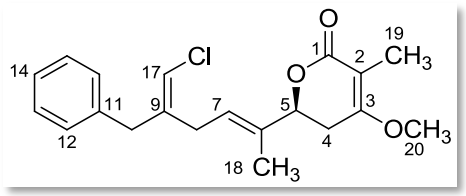


Figure S6. COSY spectrum of smenolactone A (**1**) (700 MHz, CD_3OD).



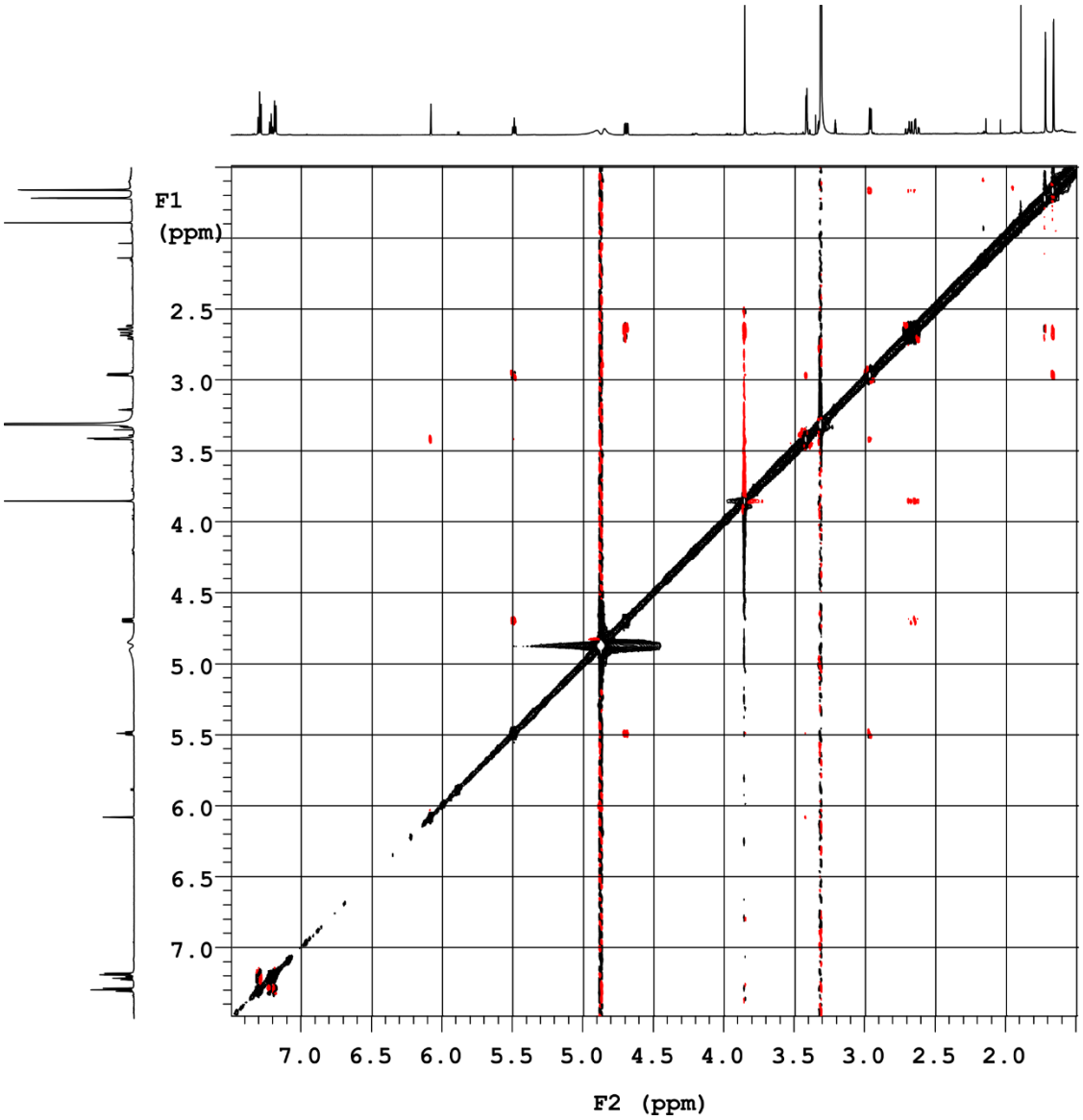
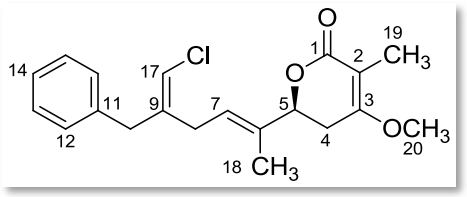


Figure S7. ROESY spectrum of smenolactone A (**1**) (700 MHz, CD_3OD).



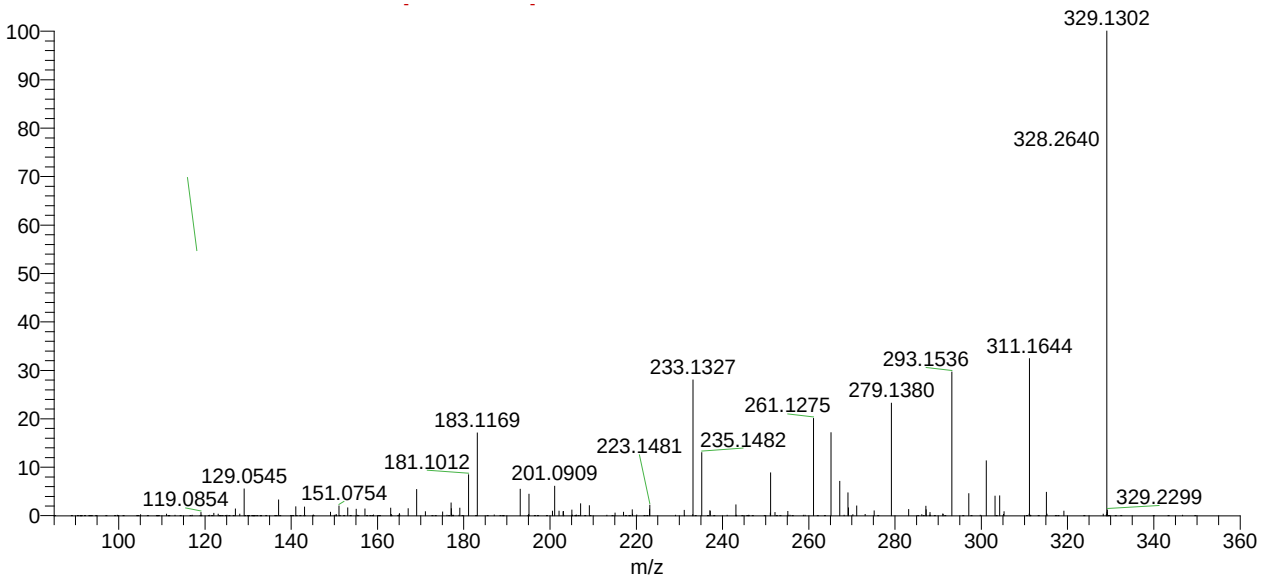


Figure S8. MS2 spectrum of smenolactone A (**1**)

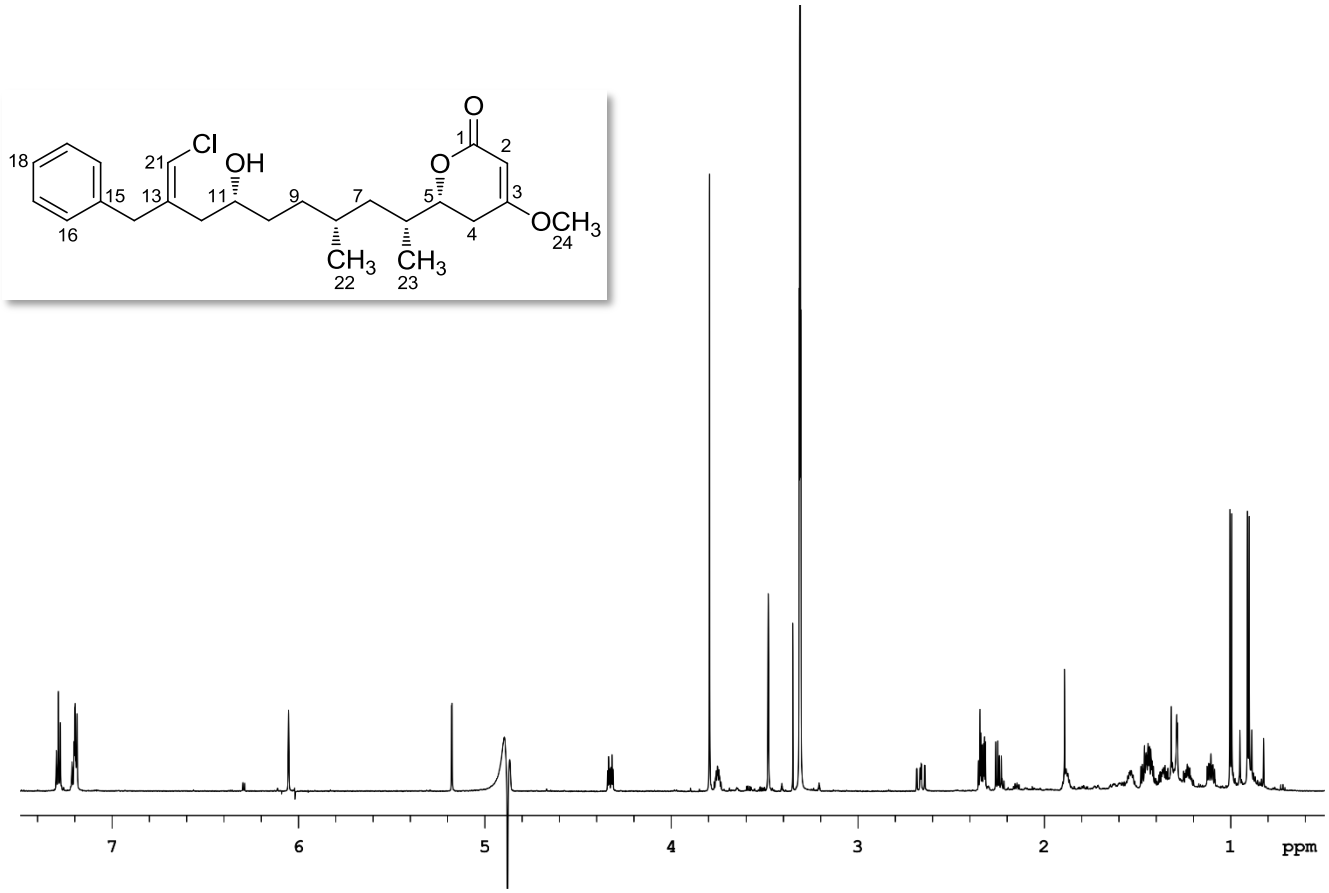


Figure S9. ^{1}H NMR spectrum of smenolactone B (**2**) (700 MHz, CD_3OD).

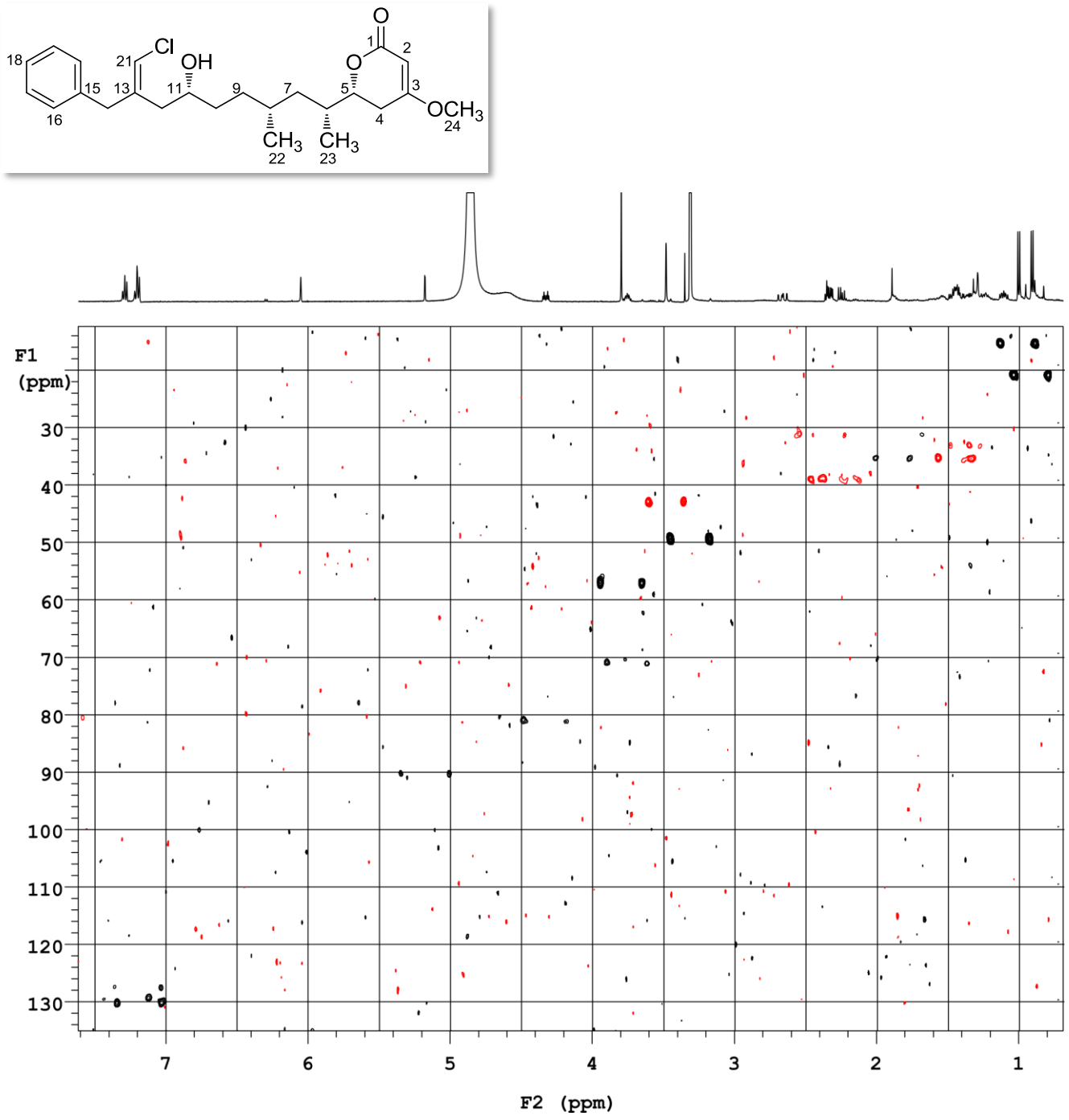


Figure S10. ^{13}C coupled HSQC spectrum of smenolactone B (**2**) (500 MHz, CD_3OD).

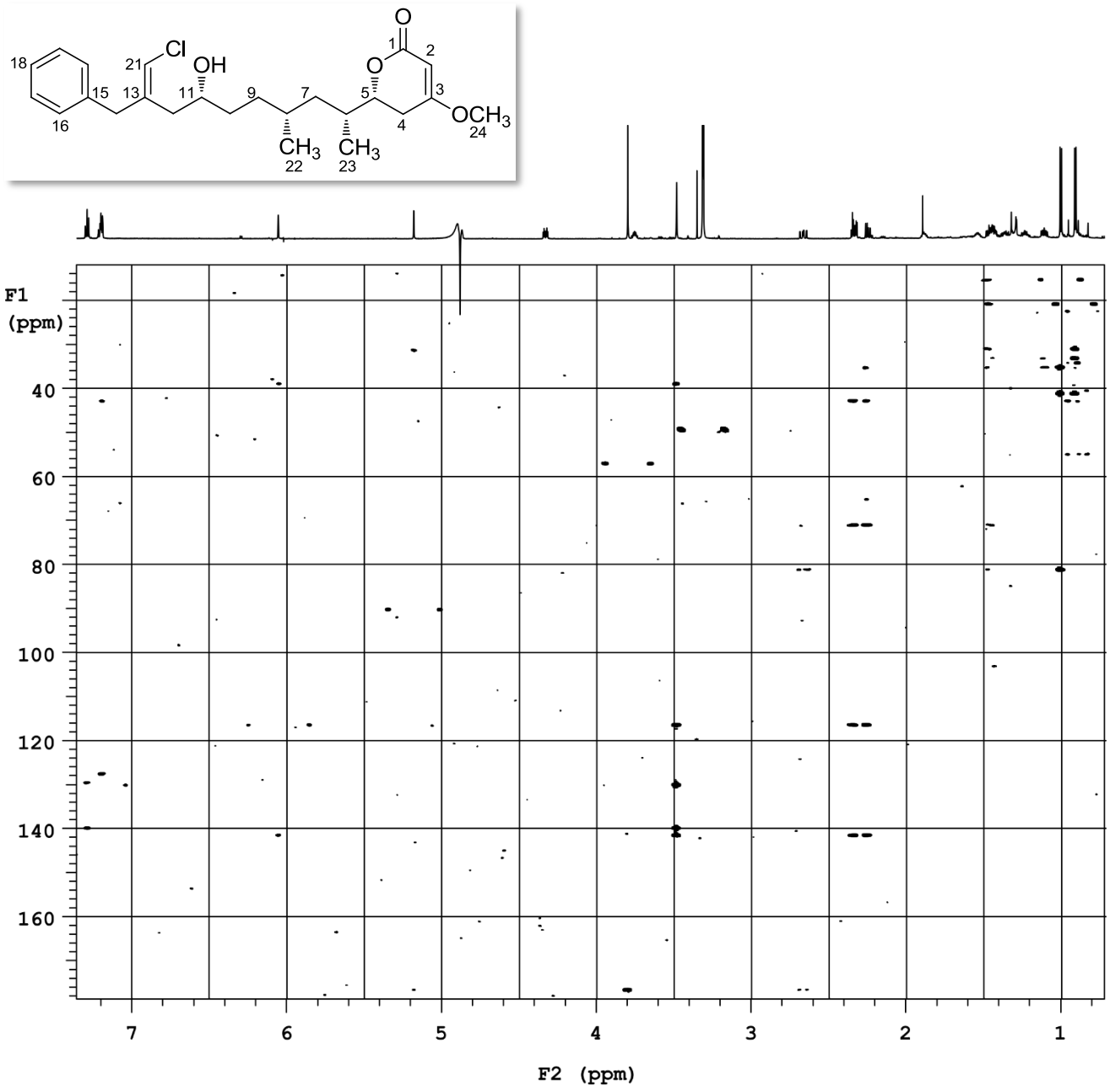


Figure S11. HMBC spectrum of smenolactone B (**2**) (500 MHz, CD_3OD).

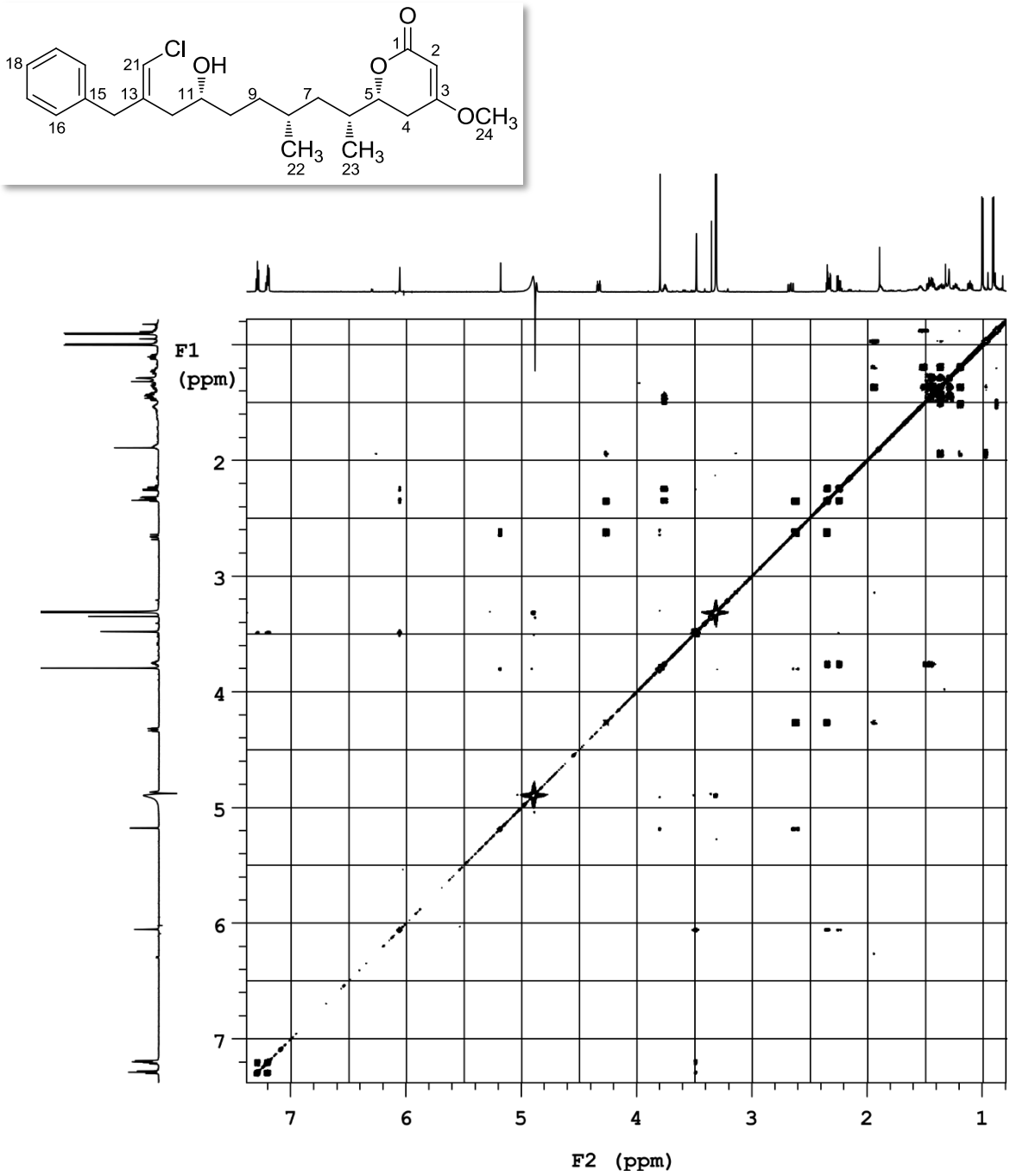
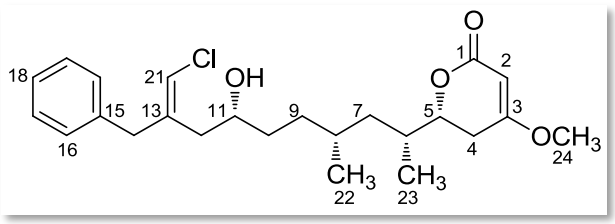


Figure S12. COSY spectrum of smenolactone B (**2**) (700 MHz, CD_3OD).



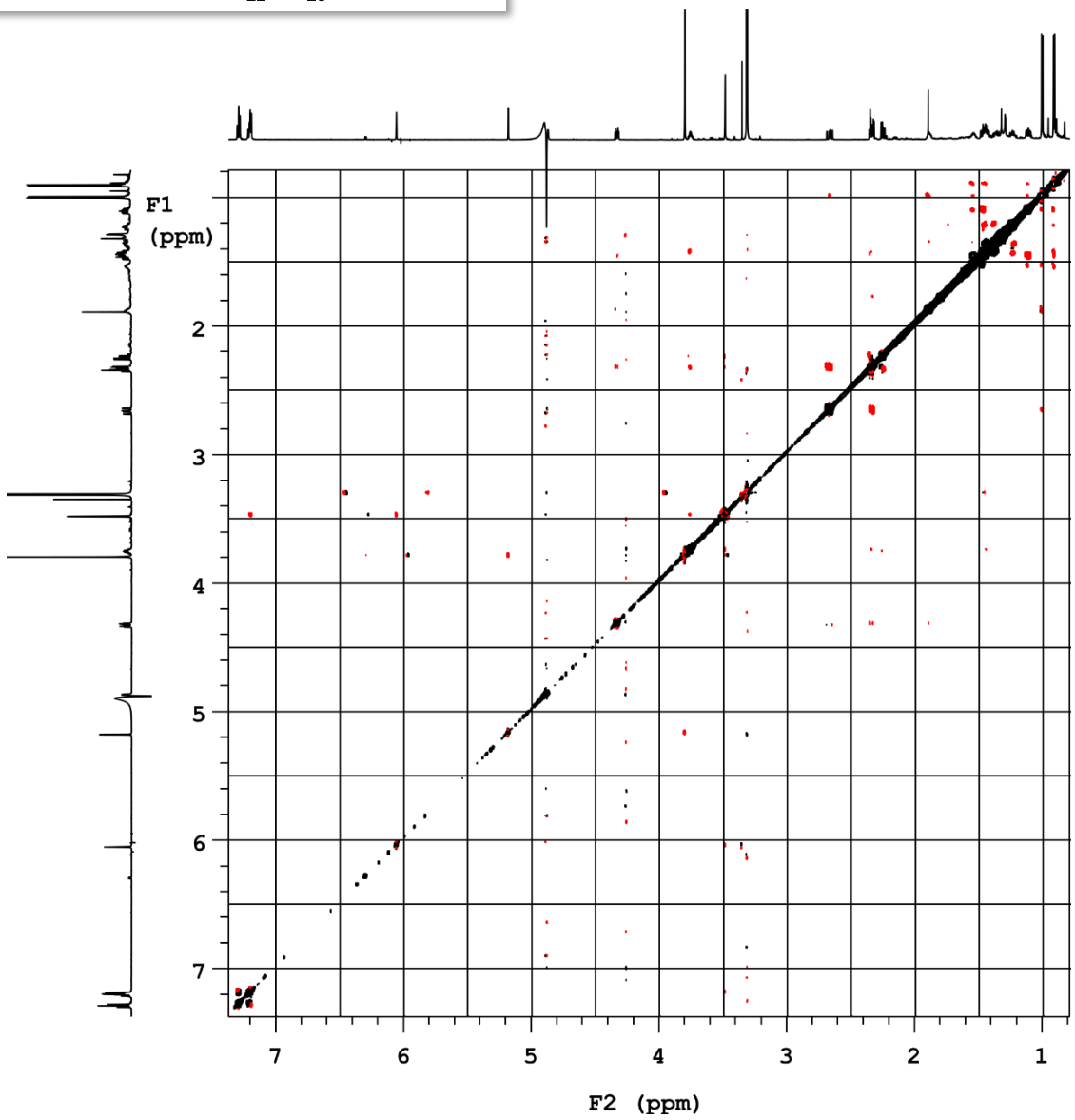
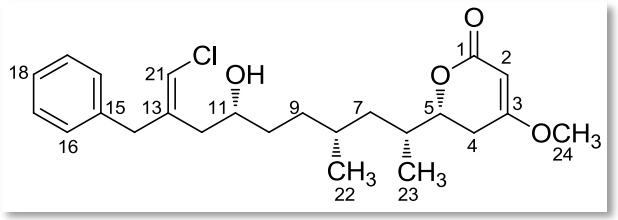


Figure S13. ROESY spectrum of smenolactone B (**2**) (700 MHz, CD_3OD).



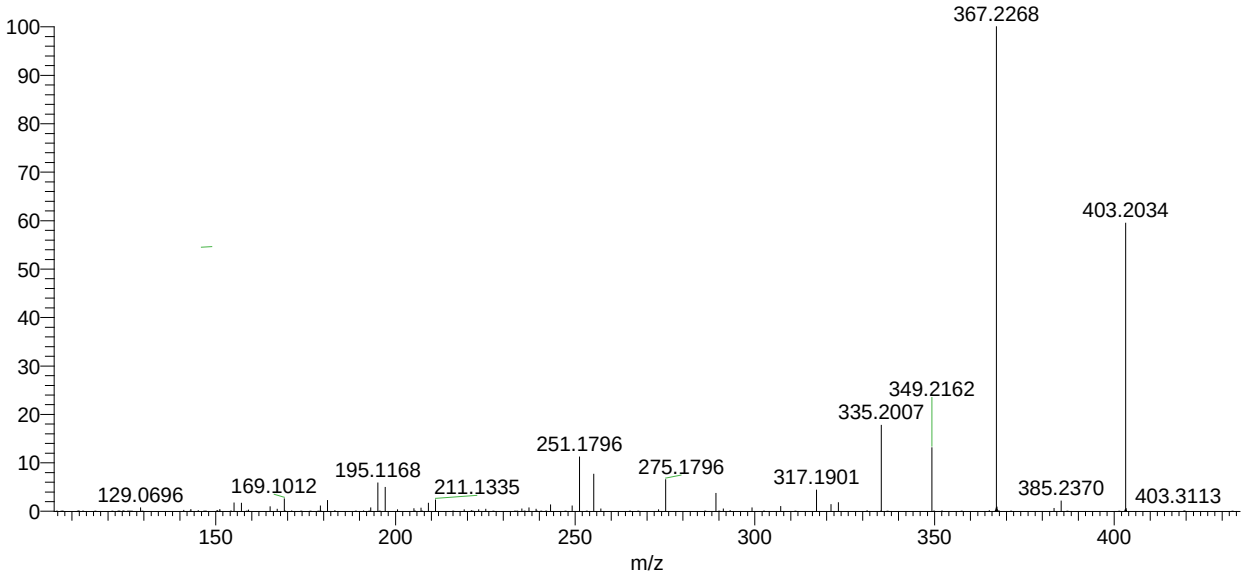


Figure S14. MS2 spectrum of smenolactone B (**2**)

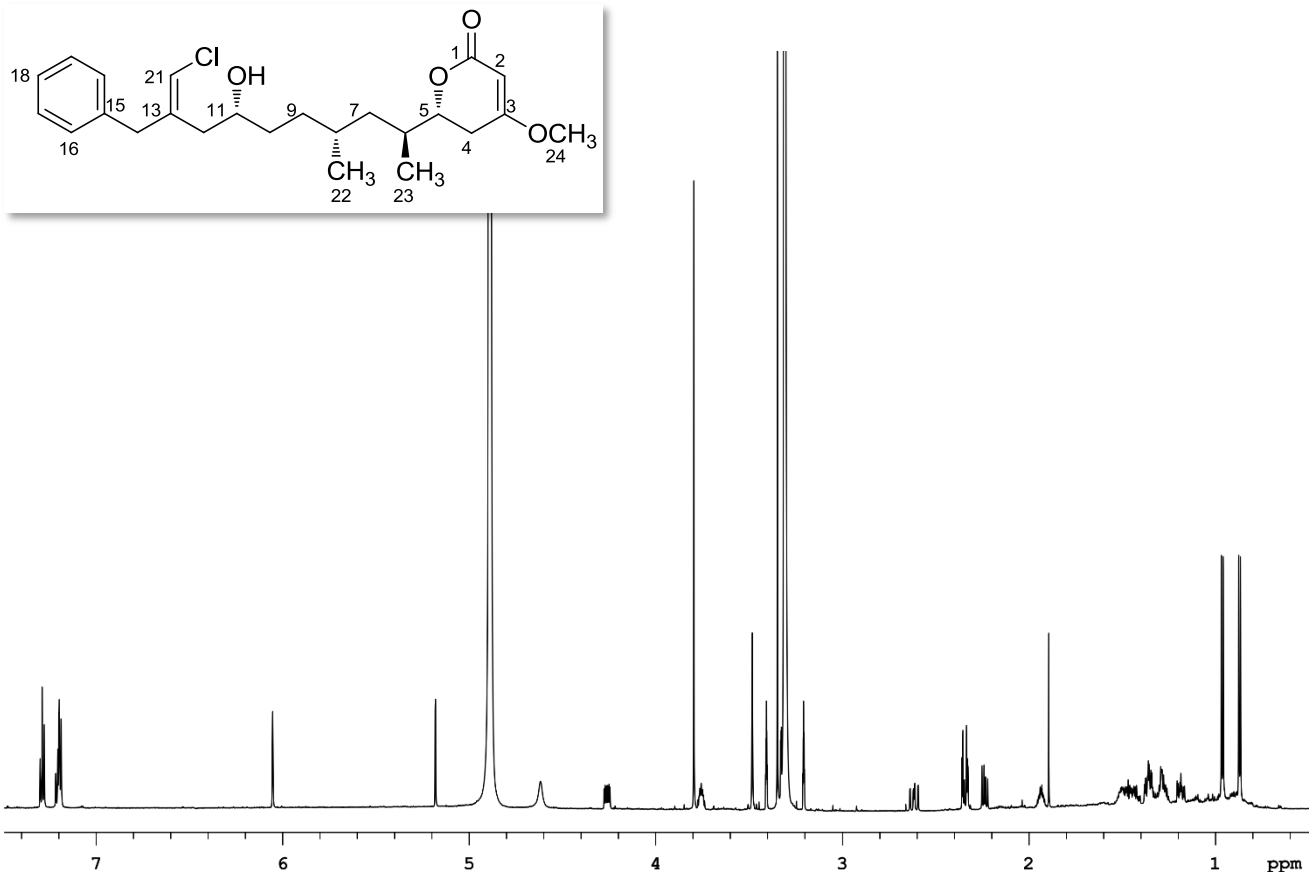


Figure S15. ^{1}H NMR spectrum of smenolactone C (**3**) (700 MHz, CD_3OD).

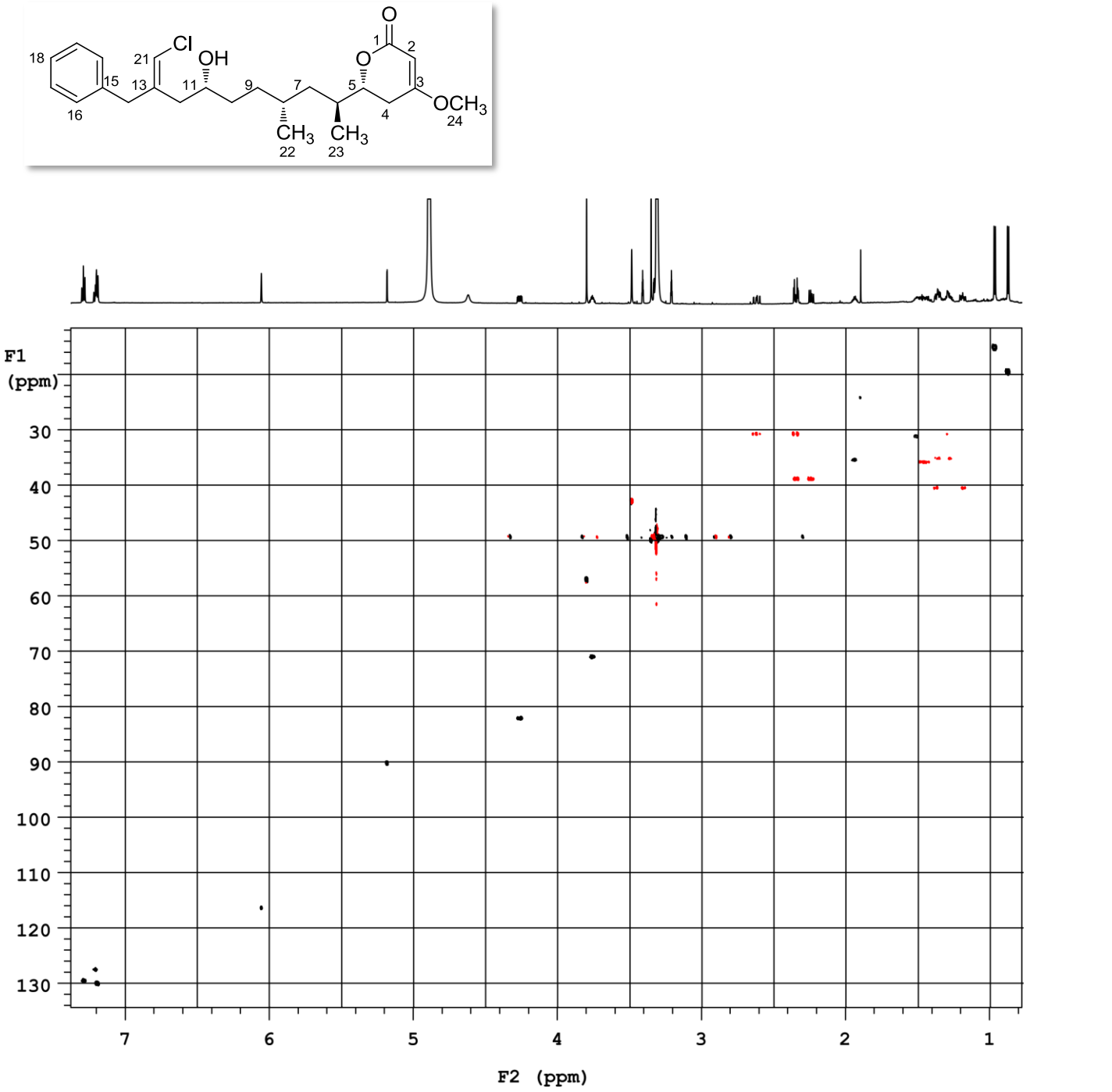


Figure S16. HSQC spectrum of smenolactone C (**3**) (700 MHz, CD_3OD).

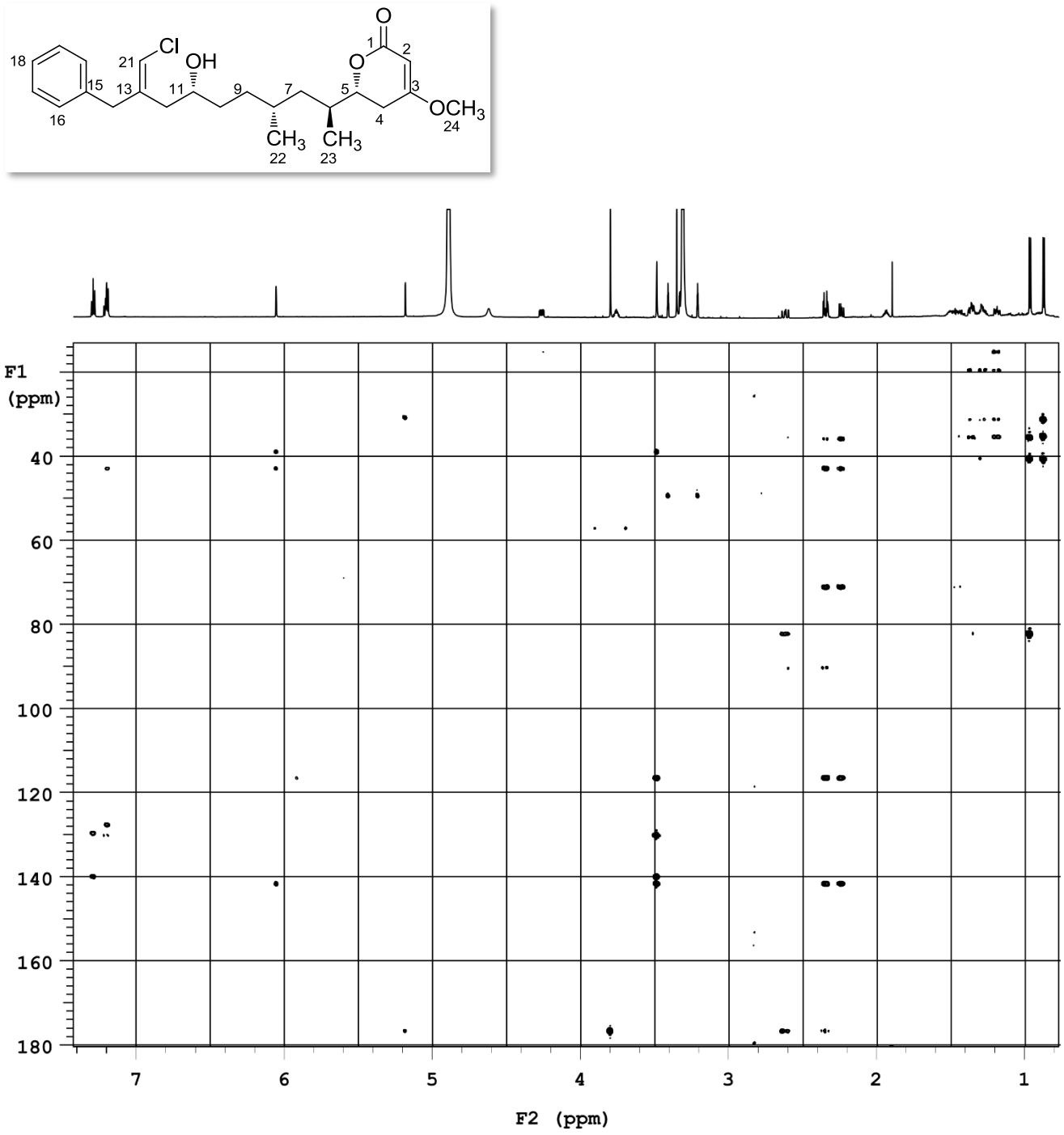


Figure S17. HMBC spectrum of smenolactone C (**3**) (700 MHz, CD_3OD).

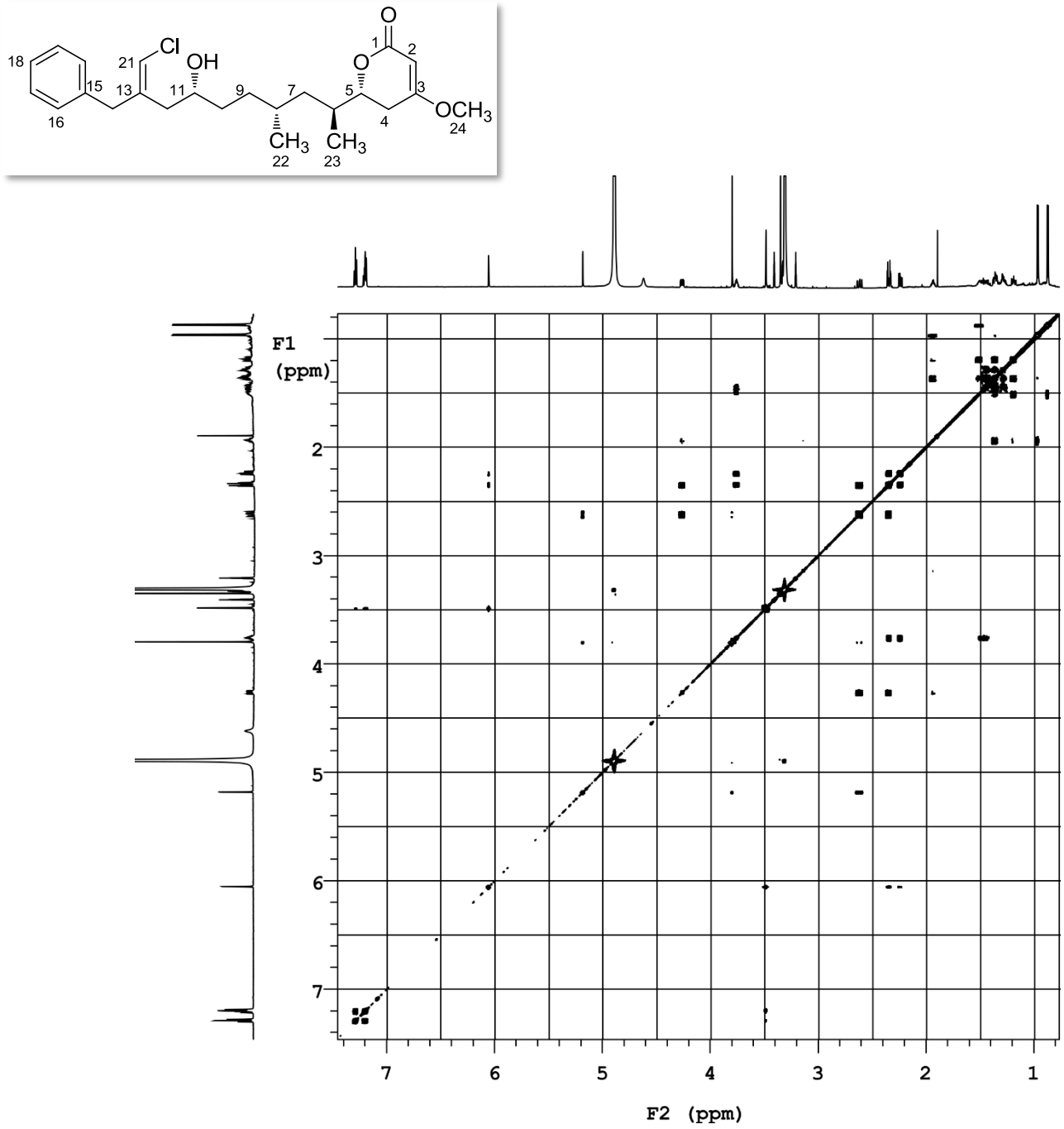


Figure S18. COSY spectrum of smenolactone C (**3**) (700 MHz, CD_3OD).

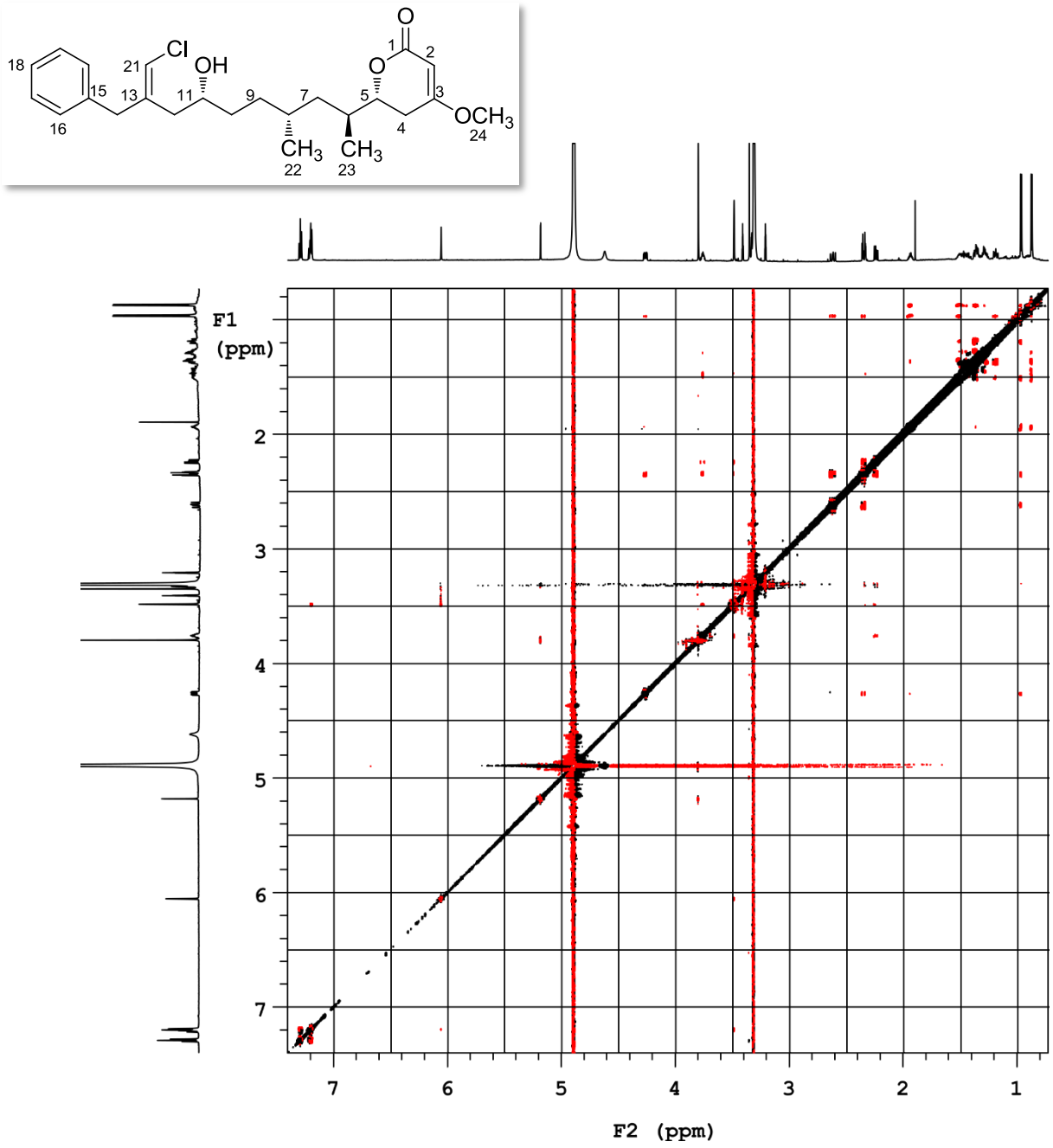
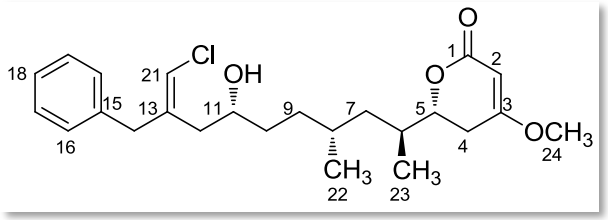


Figure S19. ROESY spectrum of smenolactone C (**3**) (700 MHz, CD_3OD).



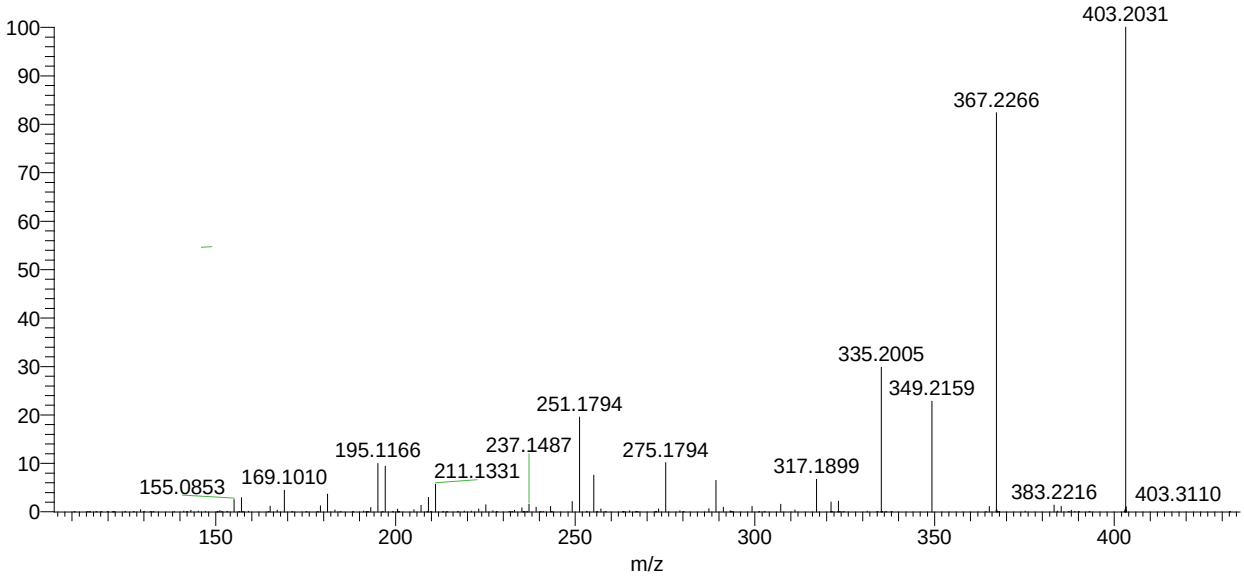


Figure S20. MS2 spectrum of smenolactone C (**3**)

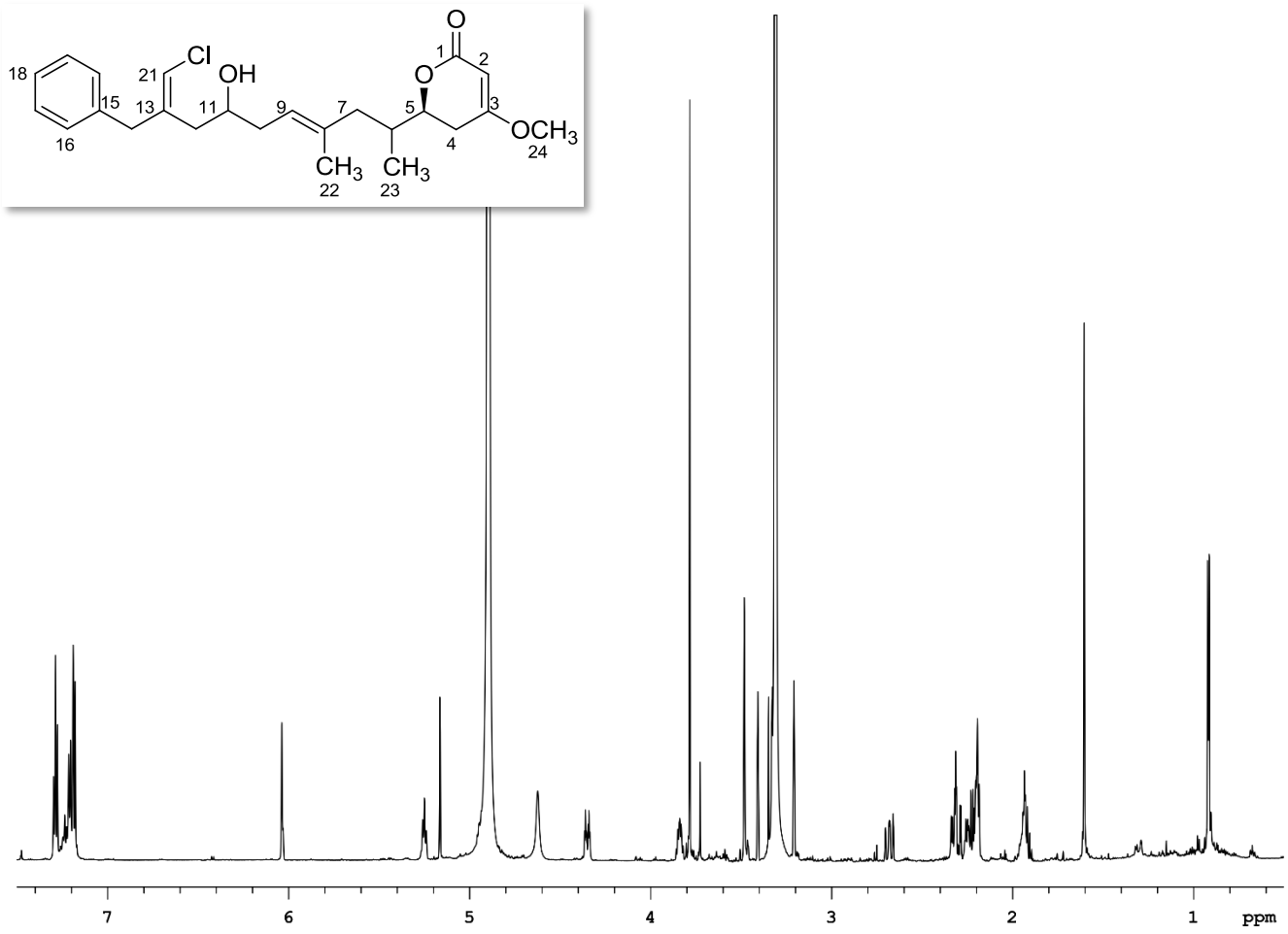


Figure S21. ^{1}H NMR spectrum of smenolactone D (**4**) (700 MHz, CD_3OD).

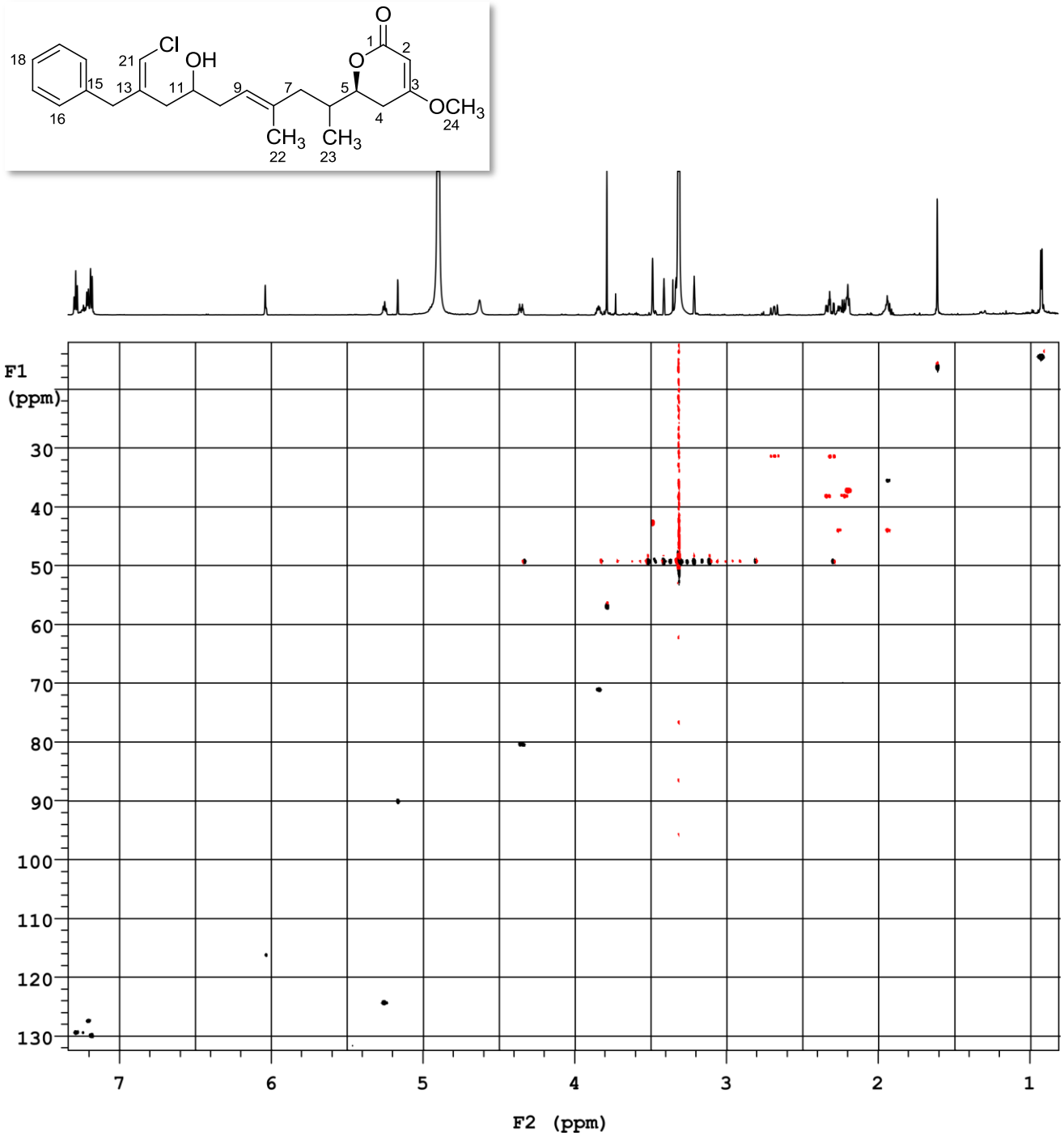


Figure S22. HSQC spectrum of smenolactone D (**4**) (700 MHz, CD_3OD).

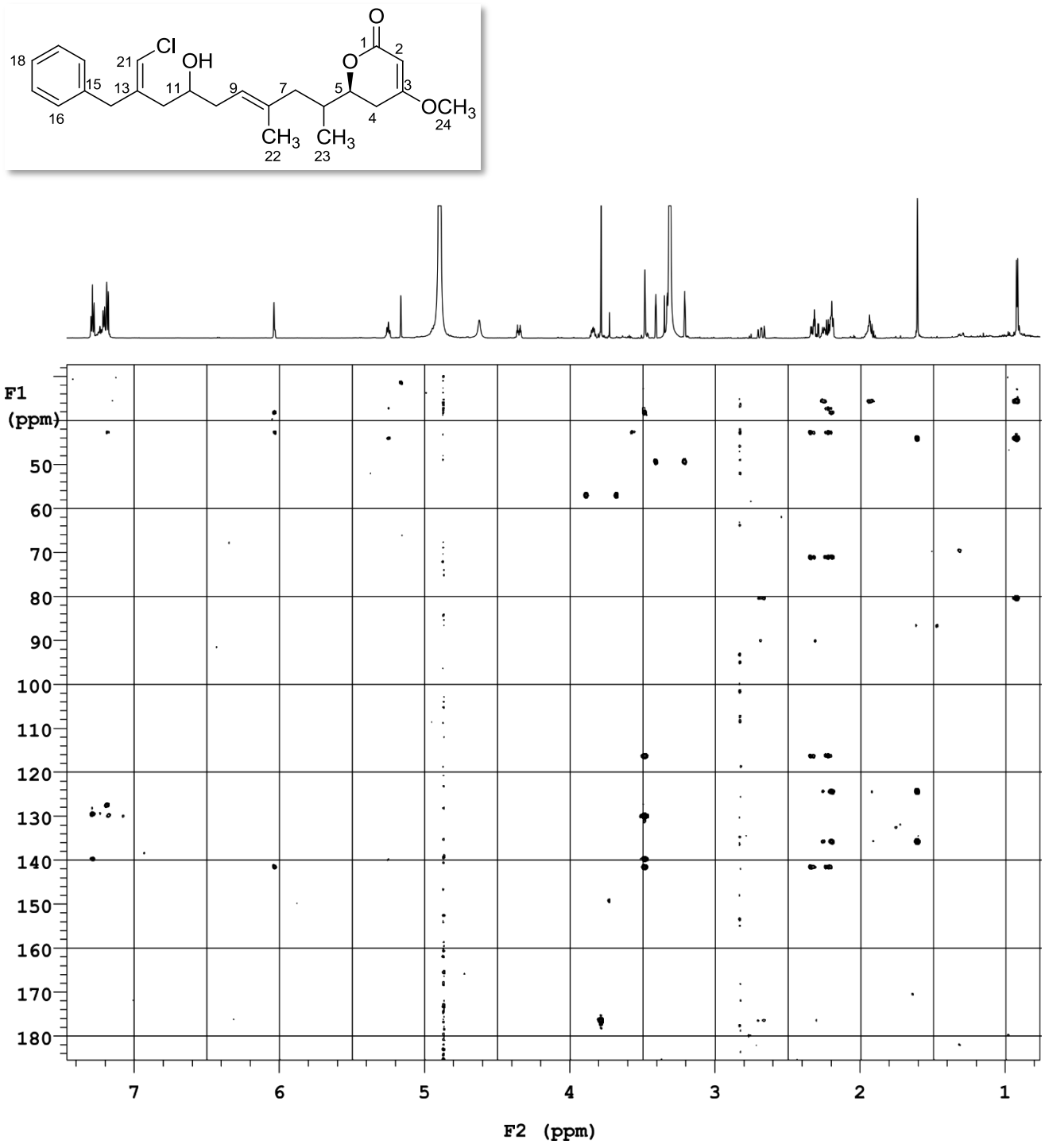


Figure S23. HMBC spectrum of smenolactone D (**4**) (700 MHz, CD_3OD).

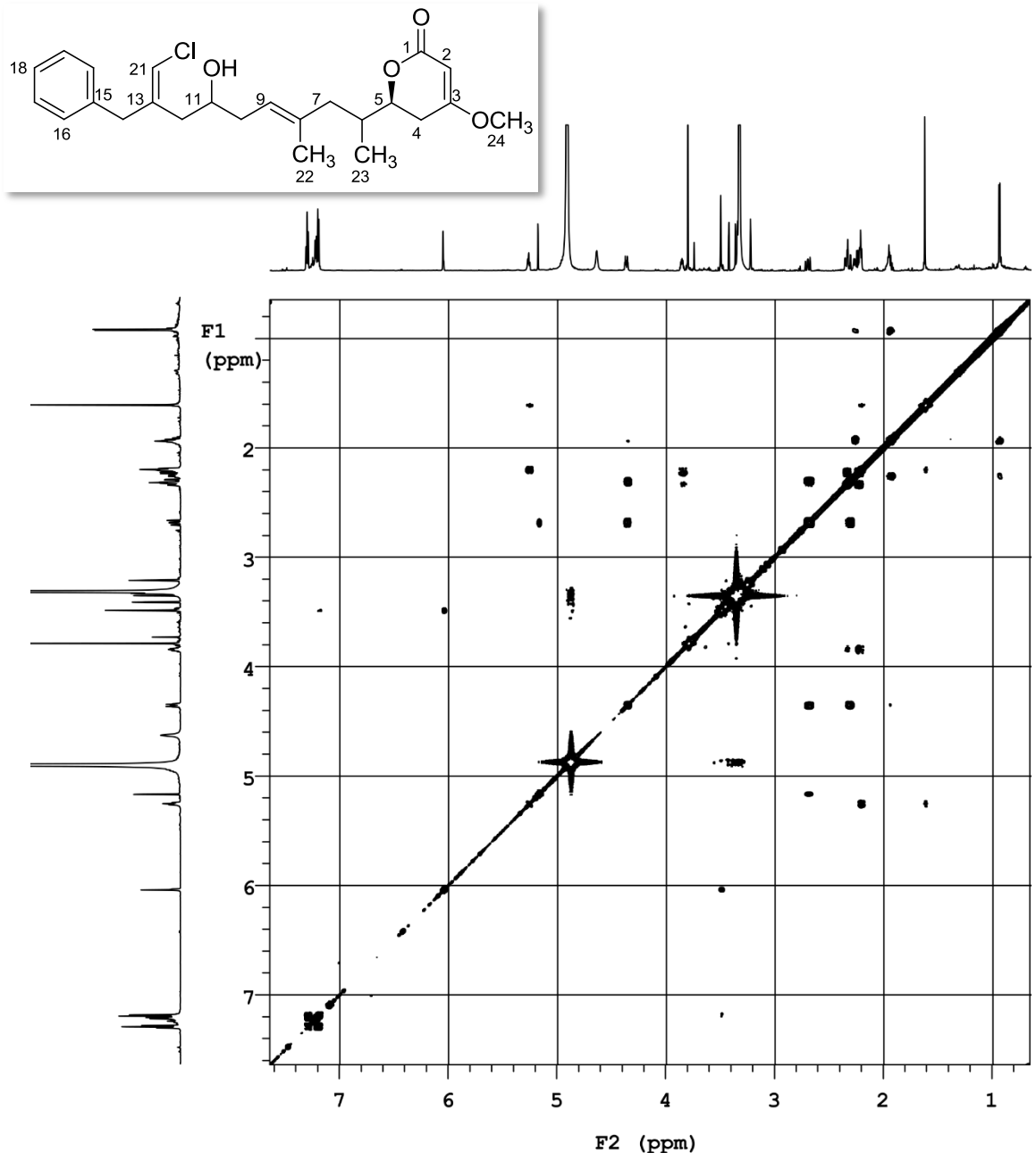


Figure S24. COSY spectrum of smenolactone D (**4**) (700 MHz, CD_3OD).

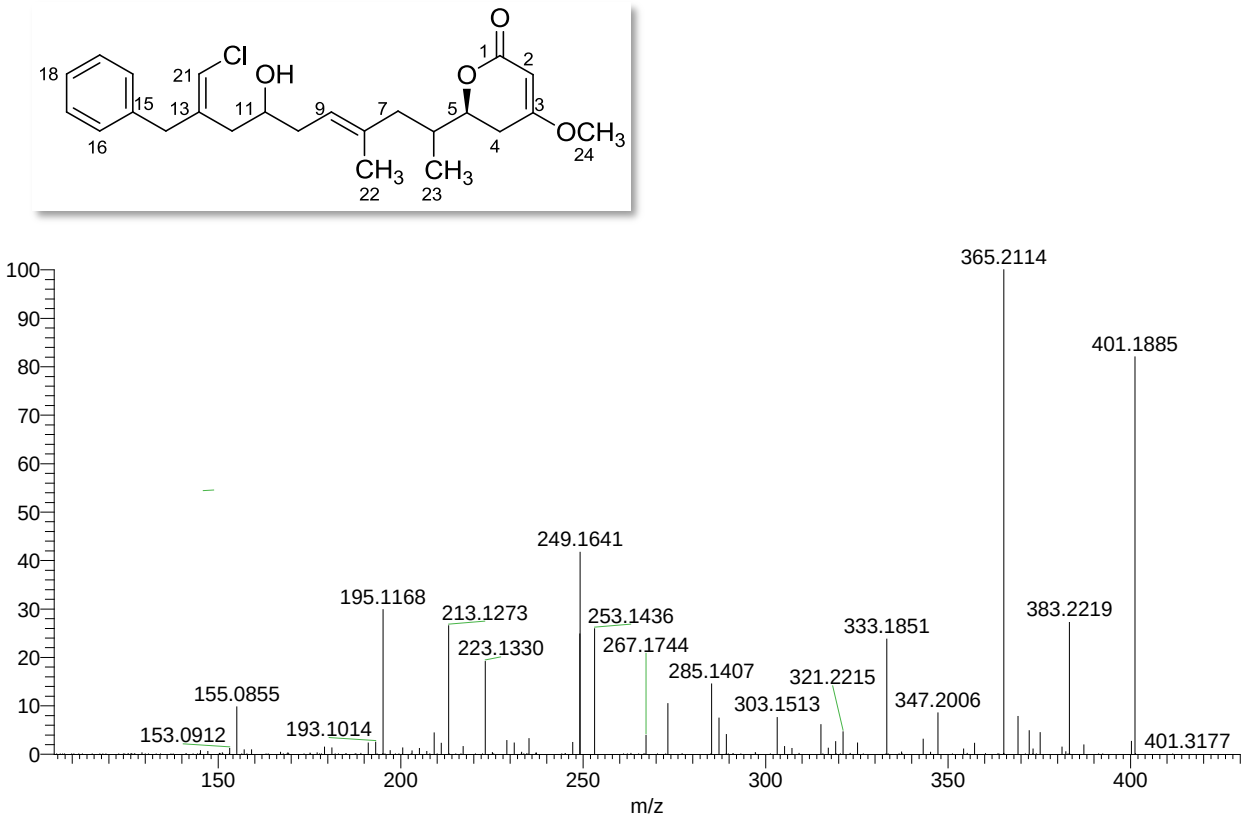


Figure S25. MS2 spectrum of smenolactone D (**4**)

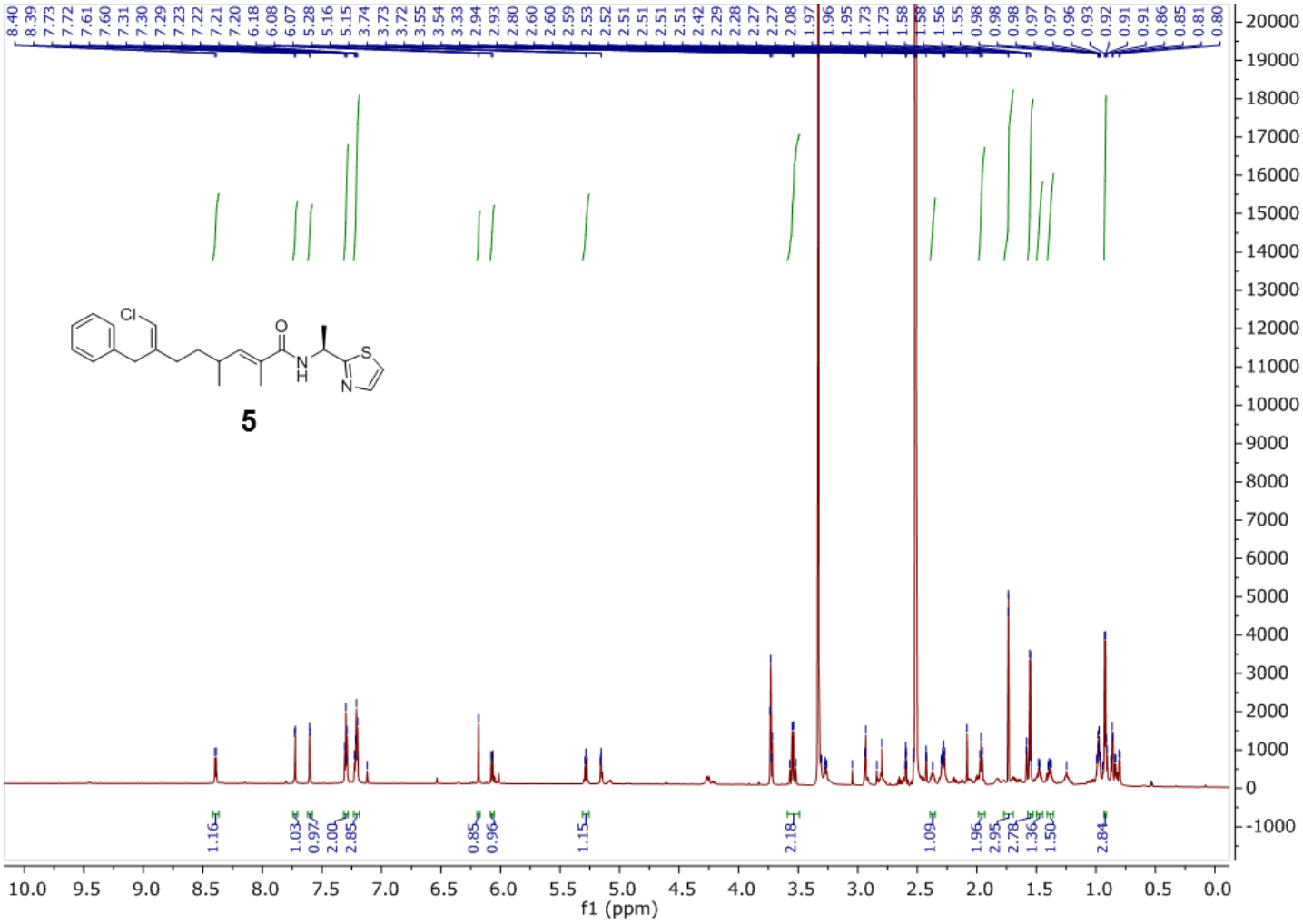


Figure S26. ^{1}H NMR spectrum of isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).

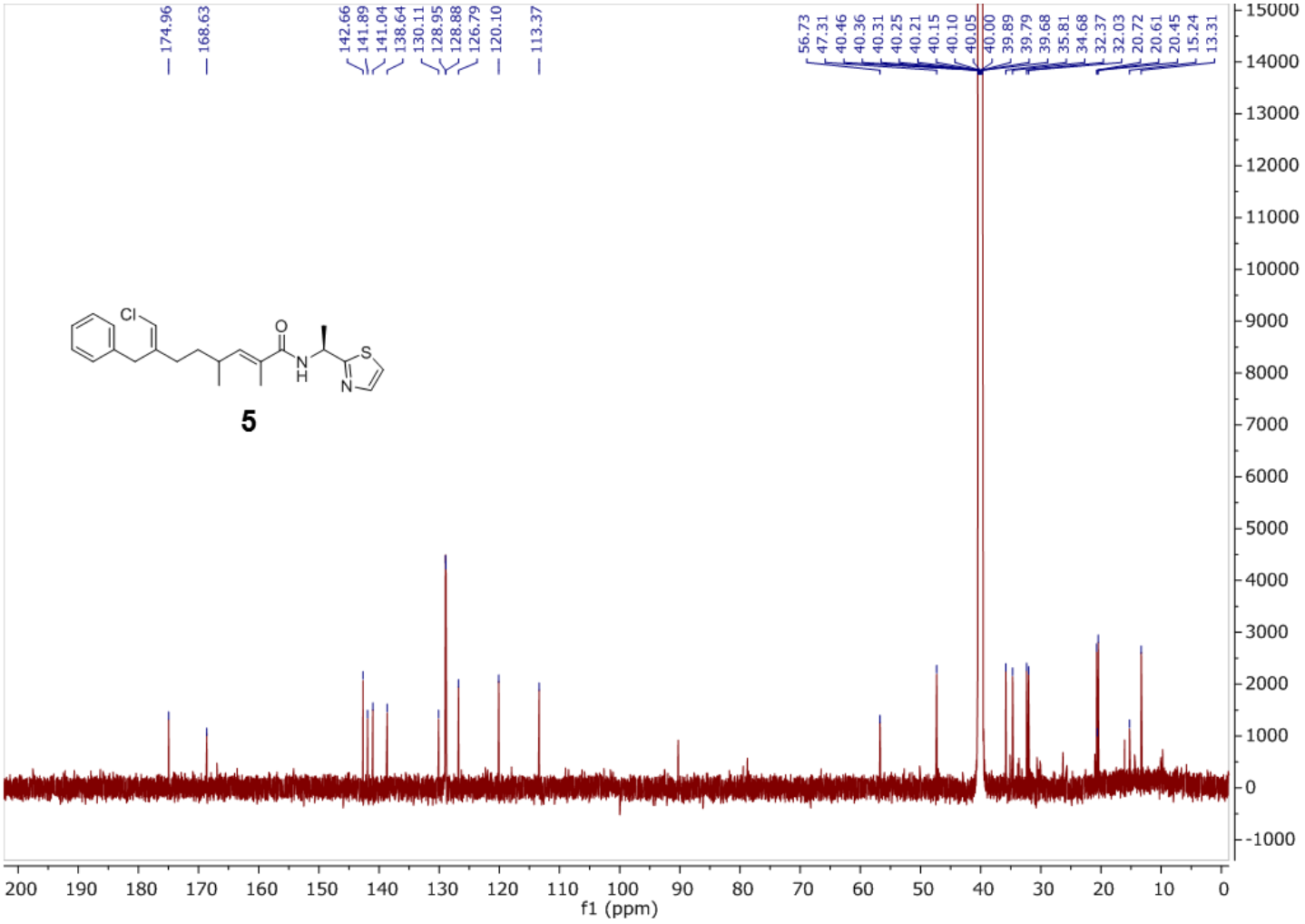


Figure S27. ^{13}C NMR spectrum of isoconulothiazole B (**5**) (200 MHz, DMSO-d_6).

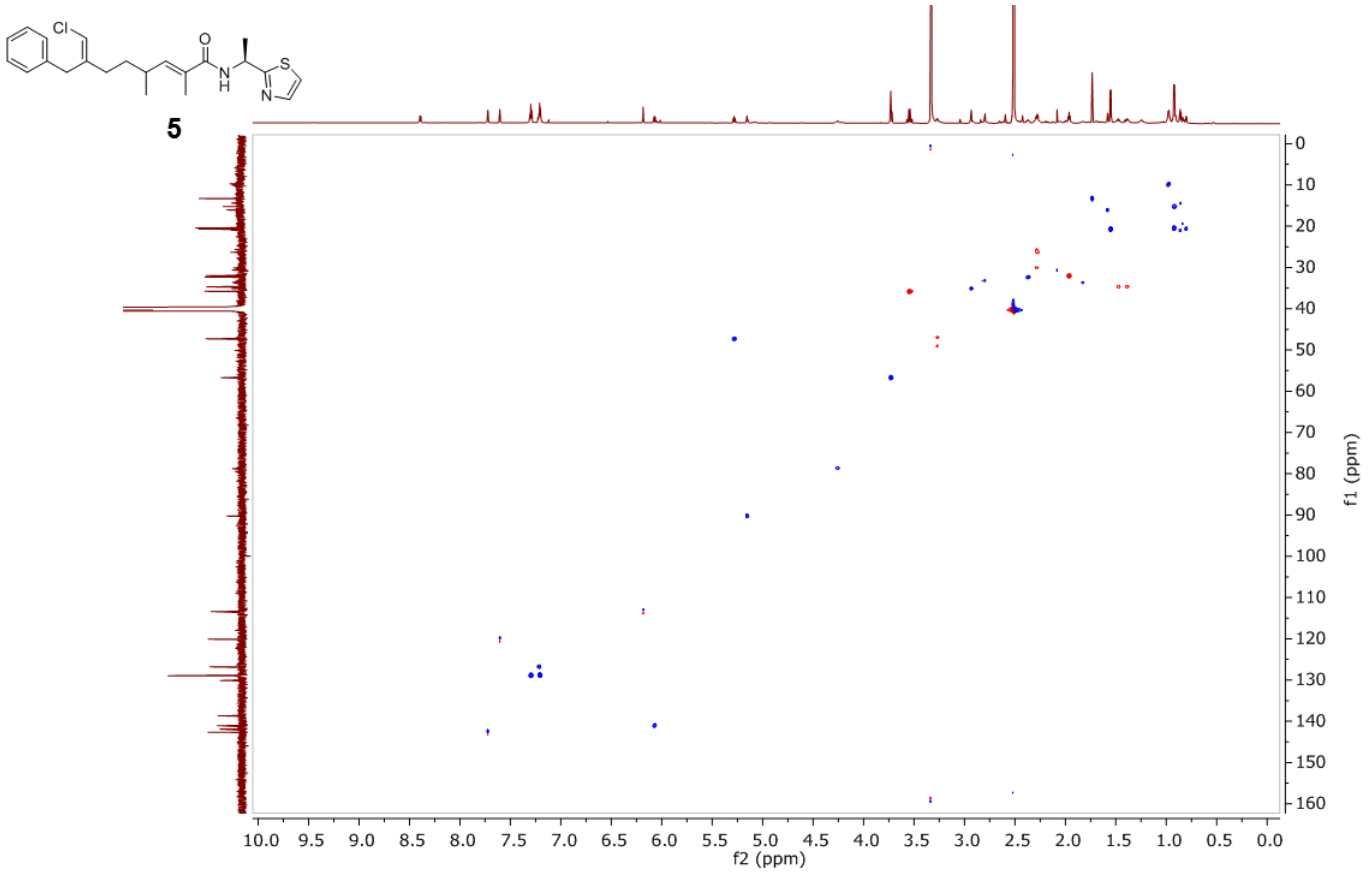


Figure S28. HSQC spectrum of isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).

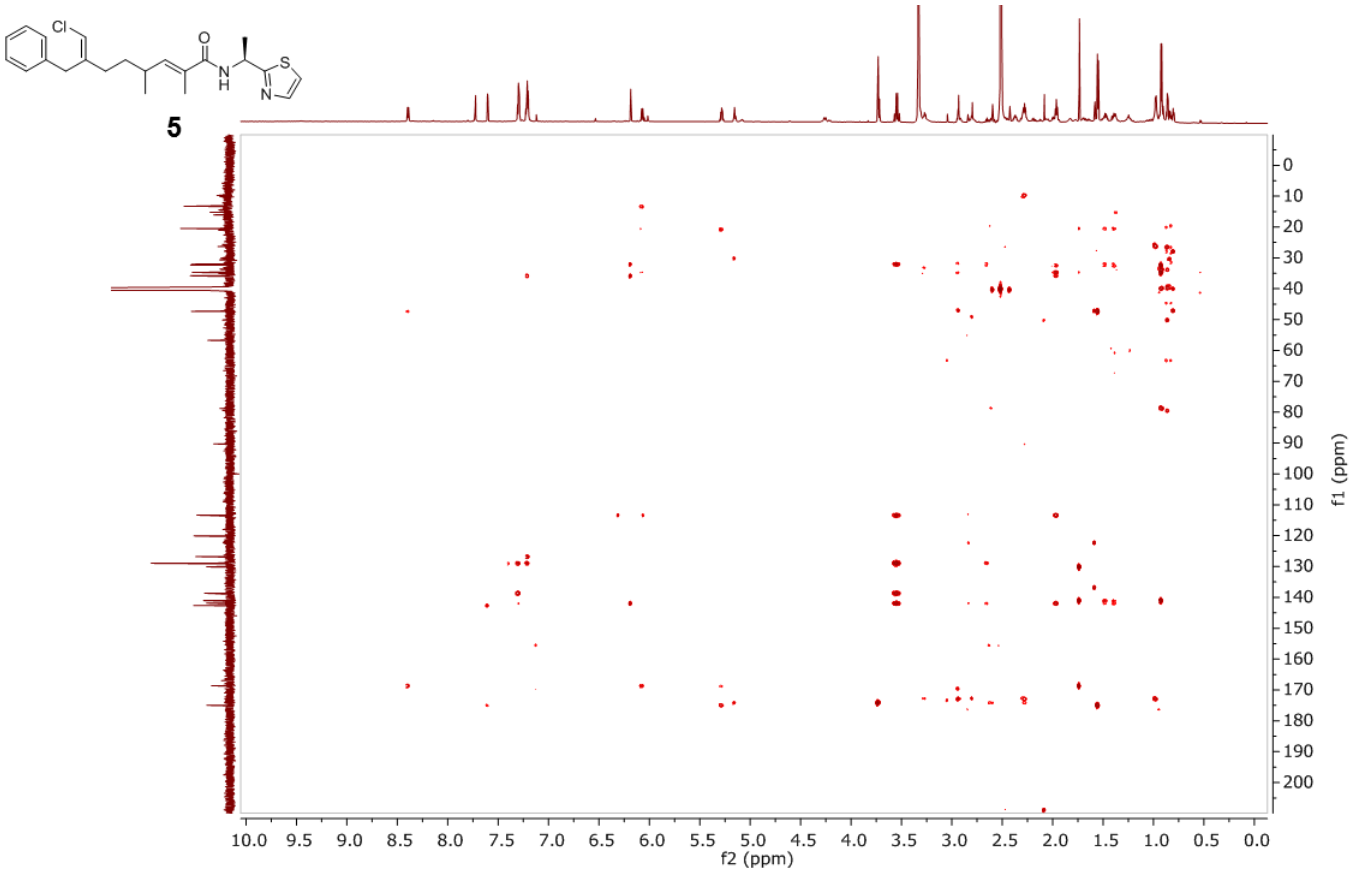


Figure S29. HMBC spectrum of isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).

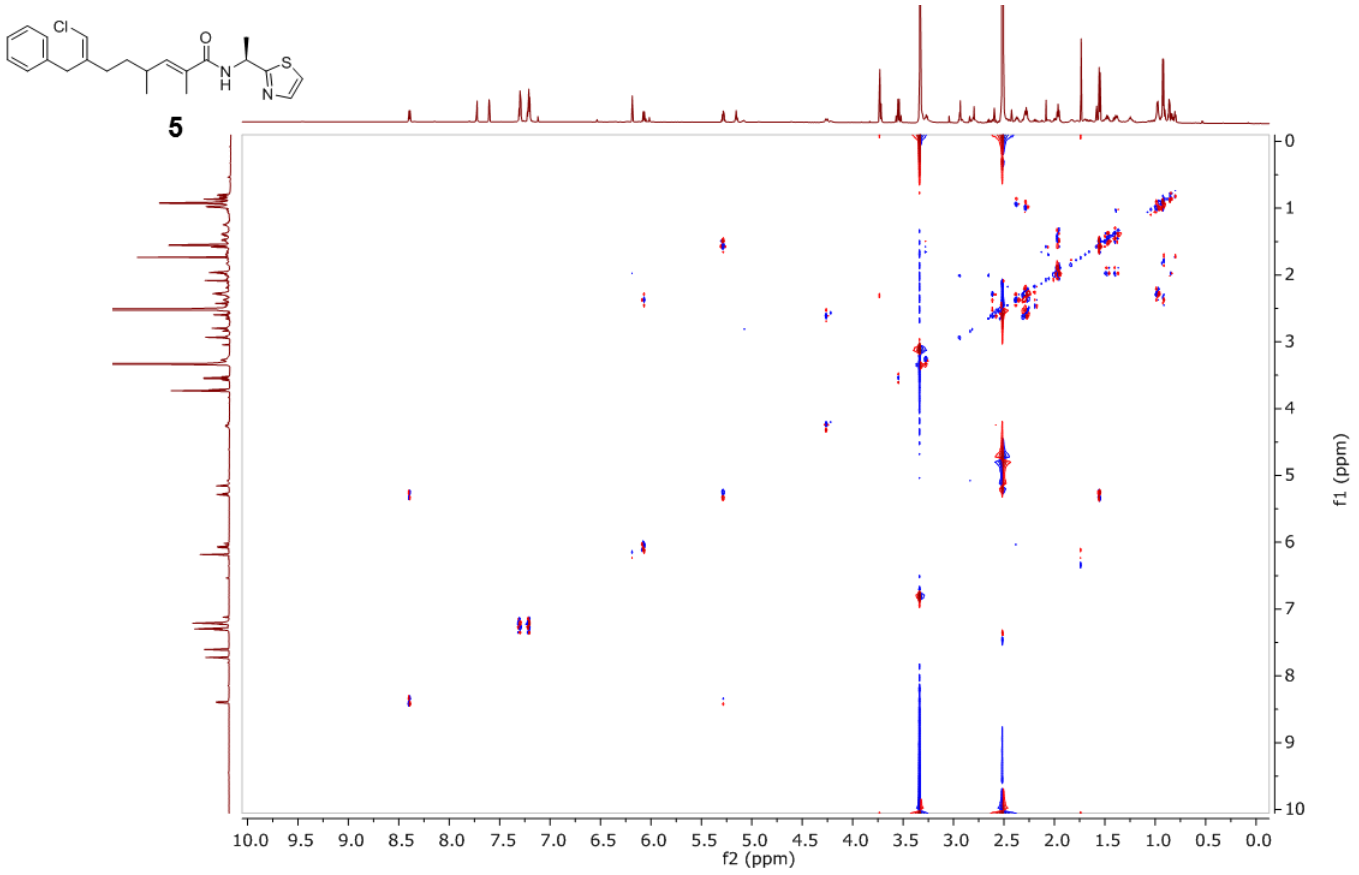


Figure S30. DQF-COSY spectrum of isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).

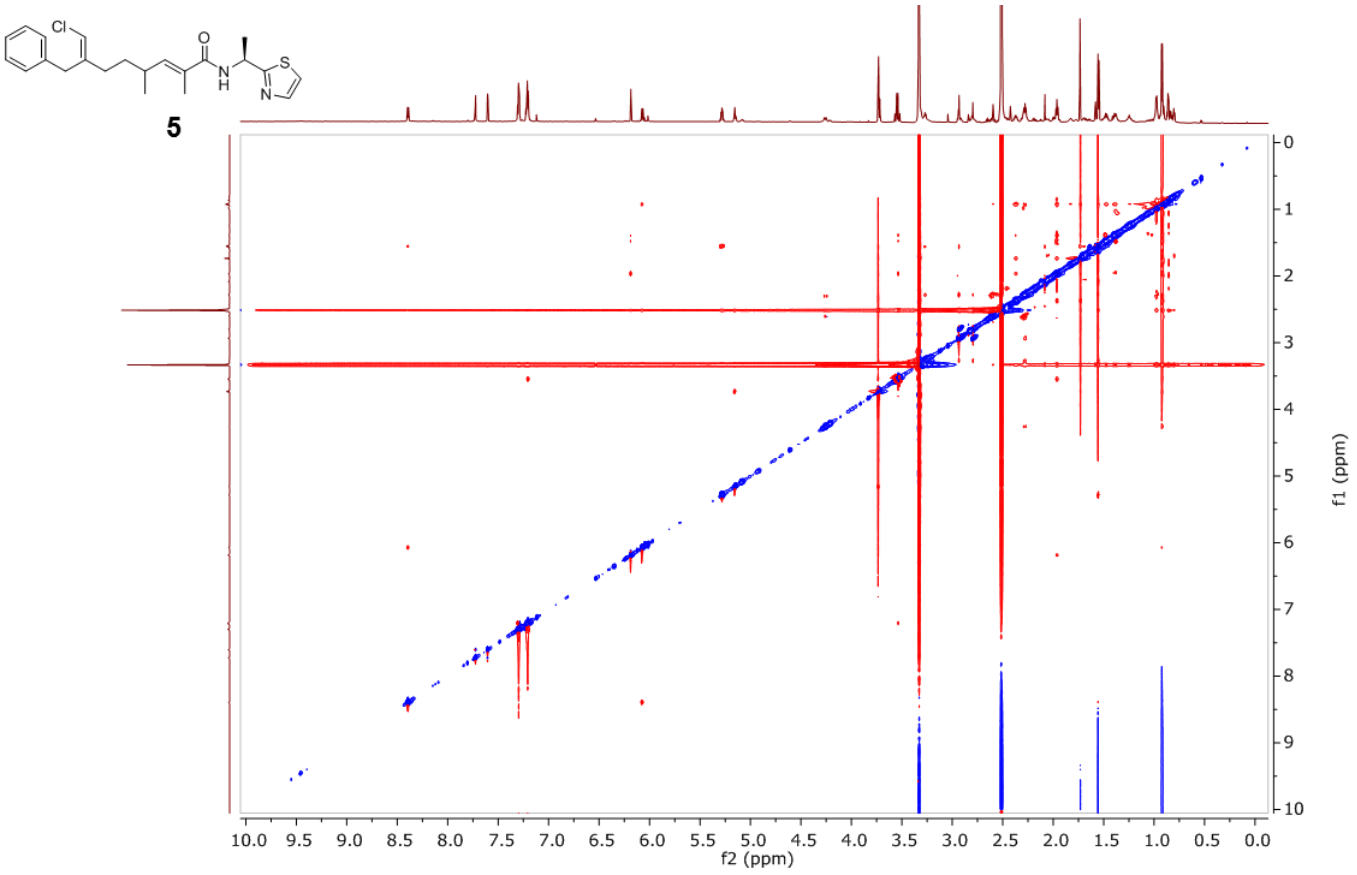
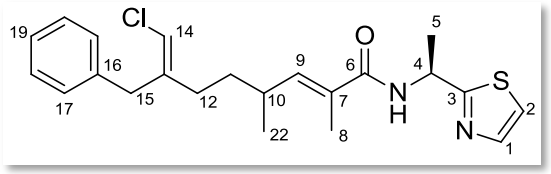


Figure S31. NOESY spectrum of isoconulothiazole B (**5**) (800 MHz, DMSO-d_6).



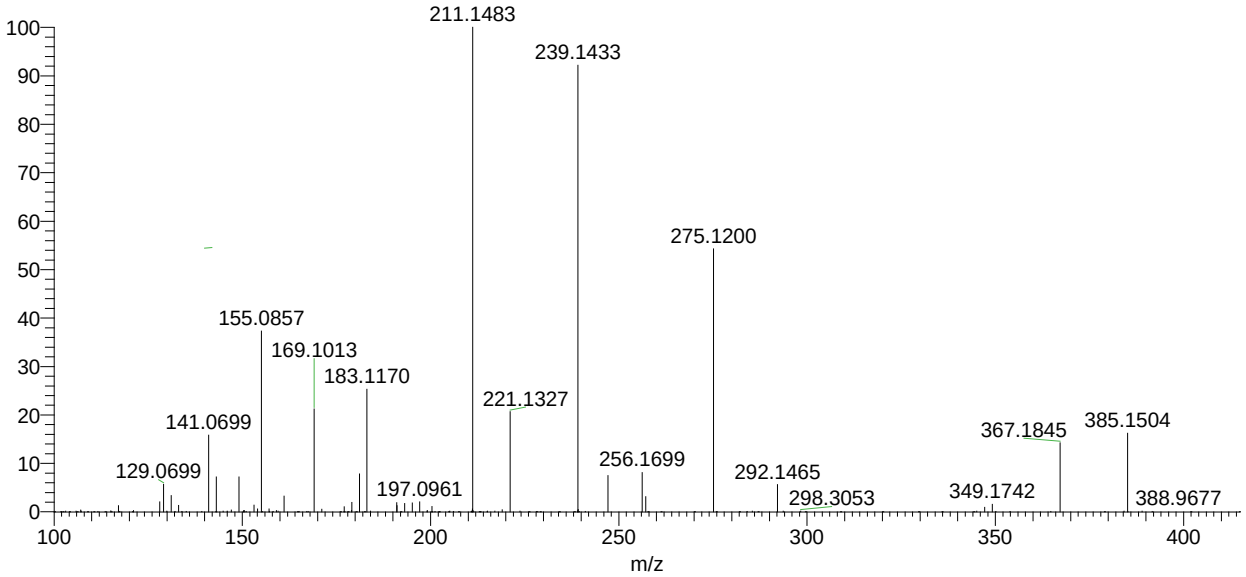


Figure S32. MS2 spectrum of isoconulothiazole B (**5**)

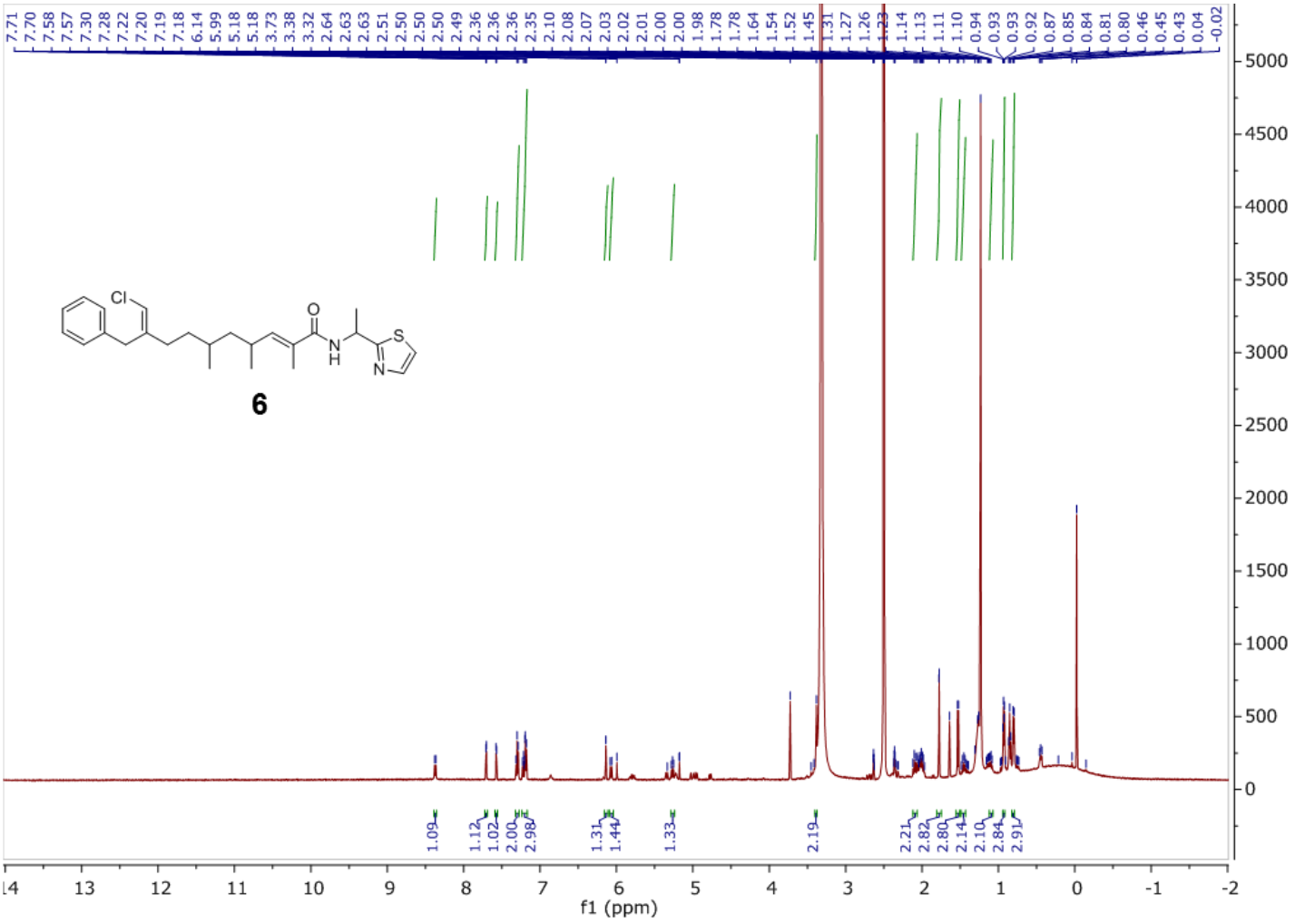


Figure S33. ^{1}H NMR spectrum of conulothiazole C (**6**) (500 MHz, DMSO-d_6).

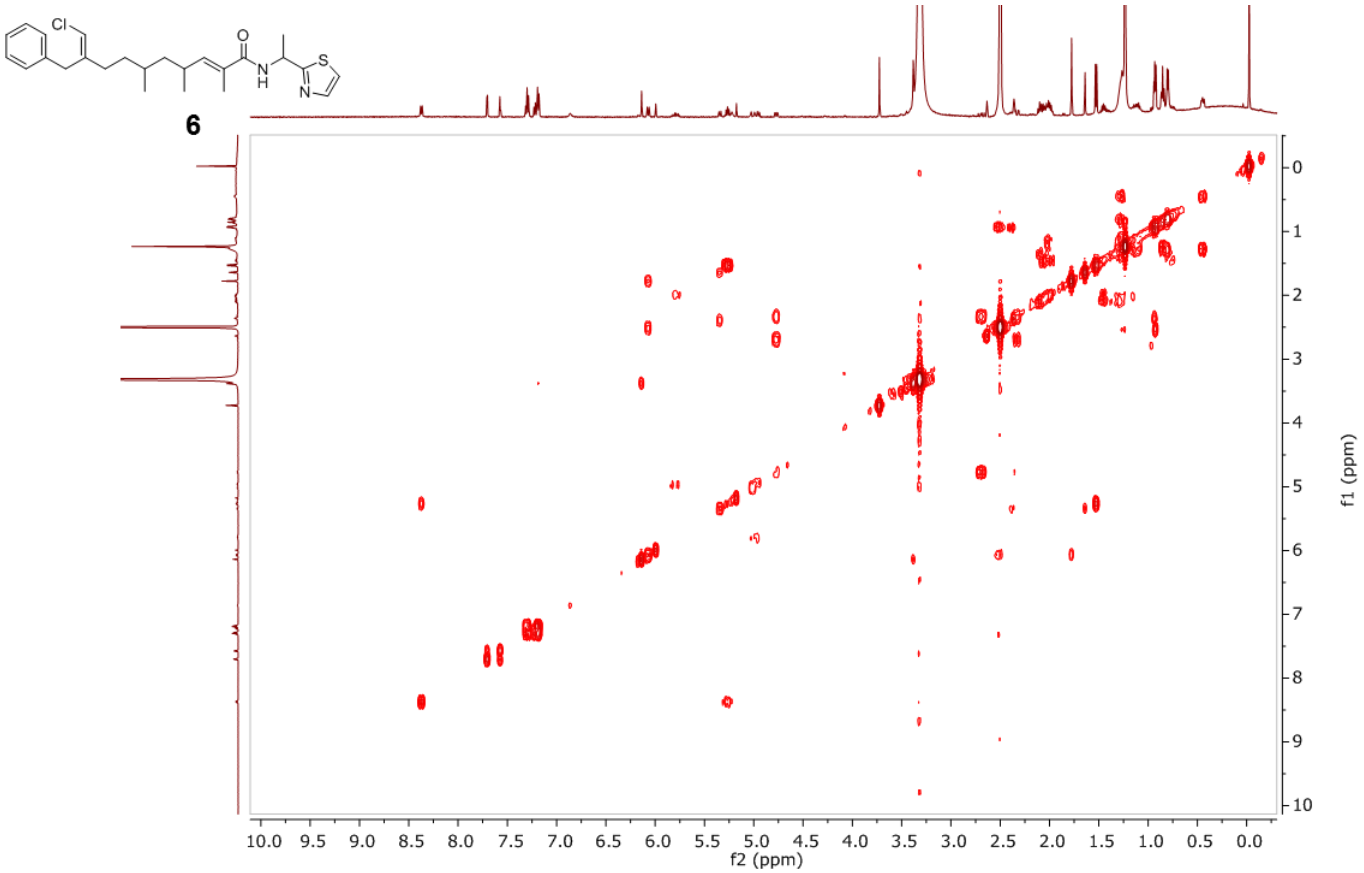


Figure S34. COSY spectrum of conulothiazole C (**6**) (500 MHz, DMSO-d_6).

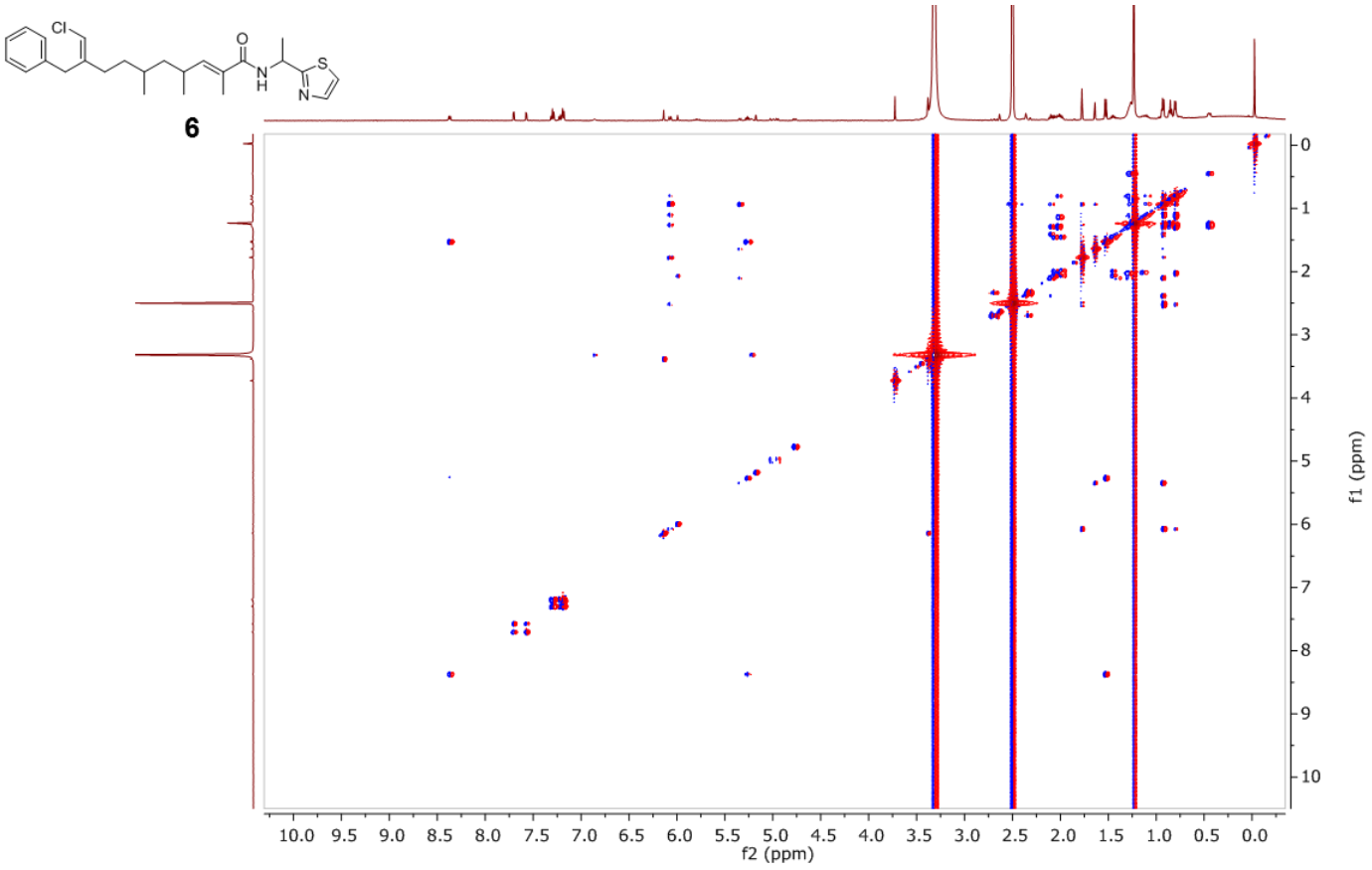


Figure S35. TOCSY spectrum of conulothiazole C (**6**) (500 MHz, DMSO-d_6).

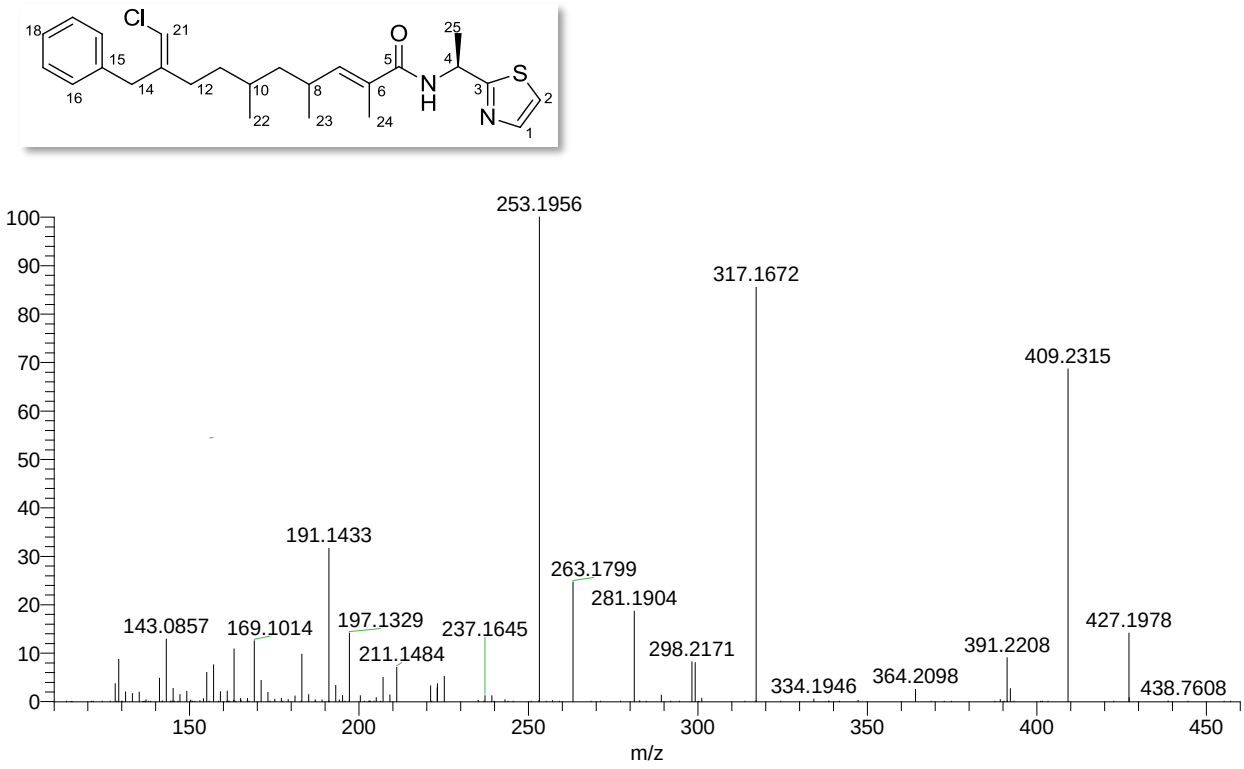


Figure S36. MS2 spectrum of conulothiazole C (**6**)

Table S7. Cartesian coordinates, internal energies, and free energies of the 12 low-energy conformers of smenolactone A (**1**) optimized at the B3LYP/6-311+G(d,p)/SMD(MeOH) level. Free energies are corrected for low vibrational frequencies according to S. Grimme, *Chem. - A Eur. J.*, 2012, **18**, 9955–9964.

Compound 1, conformer 1
***E* = -1462.12676, Δ*E* = 0.00 kcal/mol**
***G* = -1461.79419, Δ*G* = 0.00 kcal/mol, population 31.5%**

C	-0.63245	0.00160	-0.52335
C	0.23795	-0.95157	-0.16469
C	1.67355	-1.11364	-0.60457
C	2.60826	-1.23099	0.58105
C	2.99574	0.05624	1.28734
C	3.86418	0.97873	0.44411
C	3.08359	-2.38198	1.05366
Cl	2.72506	-3.96795	0.36408
C	3.44590	2.27810	0.14041
C	4.25253	3.13289	-0.61347
C	5.49257	2.69663	-1.07645
C	5.92035	1.40099	-0.77977
C	5.11191	0.55103	-0.02750
C	-2.04349	-0.09133	0.01340
C	-3.11626	-0.27116	-1.05767
O	-2.30027	1.12080	0.78153
C	-4.47763	-0.14673	-0.43536
C	-3.55775	1.32731	1.26542
C	-4.66996	0.55903	0.70960
O	-3.69274	2.18236	2.12693
O	-5.55366	-0.69294	-1.03295
C	-5.41176	-1.51105	-2.20849
C	-0.33628	1.15833	-1.44332
C	-6.01967	0.72568	1.35656
H	-0.11122	-1.72789	0.51331
H	1.75133	-2.01465	-1.21989
H	1.99238	-0.27617	-1.22774
H	2.08223	0.58971	1.56914
H	3.51908	-0.18411	2.21743
H	3.73649	-2.46313	1.91100
H	2.48295	2.62694	0.49903
H	3.91038	4.13725	-0.83757
H	6.12090	3.35819	-1.66210
H	6.88463	1.05322	-1.13384
H	5.45277	-0.45458	0.19607
H	-2.11049	-0.92948	0.71297
H	-3.01257	0.46793	-1.85993
H	-2.97687	-1.25567	-1.50757
H	-4.91819	-0.96536	-3.01401
H	-4.86744	-2.42983	-1.98139
H	-6.42826	-1.75701	-2.50649
H	0.73193	1.29079	-1.60811
H	-0.80567	1.01775	-2.42308
H	-0.73298	2.08808	-1.02778
H	-6.69220	-0.07836	1.05936
H	-5.92598	0.72346	2.44411
H	-6.48587	1.67605	1.07461

Compound 1, conformer 2
***E* = -1462.12593, Δ*E* = 0.52 kcal/mol**
***G* = -1461.79367, Δ*G* = 0.33 kcal/mol, population 18.1%**

C	-0.85240	0.44386	-0.72063
C	0.31049	0.13334	-0.13244
C	1.70392	0.39473	-0.65143
C	2.57860	1.06288	0.39038
C	3.24208	0.16943	1.42498
C	4.28275	-0.76971	0.83360
C	2.78654	2.37642	0.46096
Cl	2.09117	3.55317	-0.65495
C	4.10124	-2.15595	0.86343
C	5.06317	-3.01602	0.32974
C	6.22329	-2.49801	-0.24298
C	6.41534	-1.11533	-0.27784
C	5.45220	-0.26065	0.25451

C	-2.12986	0.02675	-0.02743
C	-2.99476	-0.94207	-0.82958
O	-2.88251	1.23945	0.27179
C	-4.31897	-1.12520	-0.14484
C	-4.13800	1.11322	0.78679
C	-4.82715	-0.17125	0.67828
O	-4.64025	2.10713	1.28823
O	-5.06004	-2.22577	-0.37573
C	-4.55516	-3.30057	-1.18874
C	-1.00361	1.15910	-2.03947
C	-6.15954	-0.30336	1.36765
H	0.26756	-0.38291	0.82435
H	2.16359	-0.56572	-0.91492
H	1.67933	0.99065	-1.56250
H	3.70672	0.79110	2.19542
H	2.47300	-0.42694	1.92670
H	3.40209	2.85479	1.20934
H	3.20235	-2.56801	1.31075
H	4.90442	-4.08824	0.36307
H	6.97221	-3.16346	-0.65736
H	7.31645	-0.70334	-0.71868
H	5.60974	0.81250	0.22091
H	-1.88682	-0.43939	0.93185
H	-3.15844	-0.58254	-1.85161
H	-2.45557	-1.88791	-0.90464
H	-3.69645	-3.77966	-0.71424
H	-5.37427	-4.01259	-1.25724
H	-4.29197	-2.95122	-2.18823
H	-1.27445	0.46377	-2.84162
H	-1.79825	1.90689	-1.97935
H	-0.08720	1.66525	-2.33957
H	-6.94975	0.21869	0.81718
H	-6.44727	-1.35059	1.45471
H	-6.11975	0.13560	2.36634
C	-0.85240	0.44386	-0.72063

Compound 1, conformer 3
***E* = -1462.12654, Δ*E* = 0.14 kcal/mol**
***G* = -1461.79363, Δ*G* = 0.35 kcal/mol, population 17.4%**

C	0.64659	-0.13193	-0.81125
C	-0.24509	-1.08100	-0.49608
C	-1.72601	-1.10599	-0.79138
C	-2.53913	-1.21972	0.48216
C	-2.81042	0.06376	1.24669
C	-3.74191	1.02134	0.51740
C	-3.00125	-2.36592	0.97884
Cl	-2.76700	-3.94410	0.22216
C	-3.31937	2.30736	0.16677
C	-4.18104	3.19233	-0.48440
C	-5.48175	2.80022	-0.79531
C	-5.91470	1.51839	-0.45002
C	-5.05110	0.63817	0.19895
C	2.07983	-0.33583	-0.37194
C	2.60343	0.72573	0.59207
O	2.90571	-0.37244	-1.57266
C	4.07916	0.53680	0.79843
C	4.25979	-0.42765	-1.42617
C	4.85140	-0.07564	-0.13678
O	4.91691	-0.73922	-2.40732
O	4.68125	1.02042	1.90167
C	3.91472	1.62711	2.95774
C	0.35019	1.13266	-1.57577
C	6.33650	-0.26953	0.02089
H	0.11514	-1.95525	0.04239
H	-2.03815	-0.21029	-1.33032
H	-1.93981	-1.96239	-1.43717
H	-3.23419	-0.17947	2.22540
H	-1.85710	0.56885	1.43290
H	-3.56518	-2.44720	1.89716
H	-2.30868	2.62166	0.40607
H	-3.83422	4.18547	-0.74787
H	-6.15291	3.48515	-1.30110
H	-6.92576	1.20498	-0.68592

H	-5.39643	-0.35657	0.46095
H	2.17550	-1.31410	0.10797
H	2.41345	1.73804	0.21862
H	2.05794	0.62182	1.53158
H	4.65143	1.97819	3.67646
H	3.33343	2.47374	2.58943
H	3.26082	0.89546	3.43624
H	0.44363	2.01768	-0.93753
H	1.06186	1.25459	-2.39669
H	-0.65379	1.13546	-1.99676
H	6.62061	-0.23793	1.07221
H	6.64427	-1.22916	-0.39868
H	6.90125	0.50839	-0.50436

Compound 1, conformer 4
***E* = -1462.12510, Δ*E* = 1.05 kcal/mol**
***G* = -1461.79291, Δ*G* = 0.81 kcal/mol, population 8.1%**

C	0.60308	0.58944	-0.32495
C	-0.15925	-0.50559	-0.41987
C	-1.57626	-0.59826	-0.93754
C	-2.48994	-1.27932	0.05937
C	-2.99033	-0.44171	1.22304
C	-3.94317	0.67081	0.80994
C	-2.85586	-2.55845	-0.00369
Cl	-2.35838	-3.67714	-1.27727
C	-5.14638	0.37488	0.15653
C	-6.03161	1.38906	-0.20361
C	-5.72712	2.72141	0.08237
C	-4.53267	3.02817	0.73165
C	-3.64875	2.00872	1.09089
C	2.02547	0.51325	0.19662
C	3.07306	0.82722	-0.87256
O	2.27192	-0.78815	0.76867
C	4.44908	0.58042	-0.32378
C	3.53574	-1.08598	1.18840
C	4.65412	-0.27813	0.70875
O	3.66633	-2.05249	1.92214
O	5.52254	1.17205	-0.88065
C	5.37127	2.13658	-1.93814
C	0.18092	1.98477	-0.71769
C	6.01539	-0.56640	1.28405
H	0.27007	-1.45057	-0.10394
H	-1.98053	0.38850	-1.17105
H	-1.57130	-1.16660	-1.87211
H	-3.48497	-1.09091	1.95148
H	-2.12763	0.00130	1.73098
H	-3.49321	-3.04483	0.72098
H	-5.39147	-0.65708	-0.07228
H	-6.95961	1.14019	-0.70664
H	-6.41520	3.51093	-0.19810
H	-4.28611	4.05943	0.95921
H	-2.72193	2.25653	1.59805
H	2.13814	1.24459	1.00802
H	2.90853	0.21028	-1.76458
H	2.95963	1.86853	-1.17602
H	4.86291	3.03348	-1.57905
H	6.38562	2.39089	-2.23639
H	4.83748	1.71099	-2.78907
H	0.50921	2.71534	0.02865
H	0.62390	2.28374	-1.67394
H	-0.89963	2.07454	-0.81751
H	6.70619	0.24794	1.06791
H	5.95361	-0.69881	2.36586
H	6.43962	-1.48738	0.86969

Compound 1, conformer 5
***E* = -1462.12486, Δ*E* = 1.20 kcal/mol**
***G* = -1461.79249, Δ*G* = 1.07 kcal/mol, population 5.2%**

C	-0.60554	0.10609	-1.15672
C	0.16856	-0.90906	-0.75715
C	1.66661	-1.04415	-0.90847
C	2.33941	-1.24547	0.43375
C	2.59548	-0.00599	1.27252

C	3.64111	0.92759	0.67930
C	2.69166	-2.43049	0.92946
Cl	2.45791	-3.96942	0.09444
C	4.94963	0.48209	0.45212
C	5.91581	1.34036	-0.06926
C	5.58875	2.66282	-0.37557
C	4.28991	3.11726	-0.15450
C	3.32515	2.25385	0.36829
C	-2.10760	0.07948	-0.94257
C	-2.59681	1.15631	0.02697
O	-2.51721	-1.22543	-0.48298
C	-4.06193	0.96698	0.29792
C	-3.82211	-1.41130	-0.12953
C	-4.65642	-0.24549	0.15045
O	-4.21328	-2.56283	-0.02703
O	-4.81179	1.99208	0.74434
C	-4.26100	3.31648	0.86216
C	-0.12286	1.35024	-1.86252
C	-6.11766	-0.48618	0.42240
H	-0.31340	-1.75258	-0.27435
H	1.87932	-1.90253	-1.55197
H	2.10122	-0.16647	-1.38944
H	1.65399	0.54143	1.38387
H	2.90604	-0.30551	2.27789
H	3.15456	-2.57222	1.89564
H	5.21356	-0.54437	0.68466
H	6.92430	0.97799	-0.23598
H	6.33981	3.33077	-0.78201
H	4.02466	4.14238	-0.38871
H	2.31667	2.61672	0.53798
H	-2.59942	0.24541	-1.91027
H	-2.03267	1.11292	0.96683
H	-2.41028	2.13509	-0.41558
H	-5.05582	3.91560	1.30014
H	-3.39190	3.32665	1.52150
H	-4.00044	3.72001	-0.11826
H	-0.18471	2.23144	-1.21526
H	0.90964	1.26132	-2.19518
H	-0.73998	1.55815	-2.74291
H	-6.27630	-0.90393	1.42248
H	-6.68120	0.44376	0.35405
H	-6.52810	-1.20068	-0.29365

Compound 1, conformer 6
***E* = -1462.12473, Δ*E* = 1.27 kcal/mol**
***G* = -1461.79215, Δ*G* = 1.28 kcal/mol, population 3.6%**

C	-0.30854	-0.79498	-0.77529
C	0.85043	-1.03492	-0.14849
C	2.17045	-1.41433	-0.77996
C	3.37357	-0.80619	-0.08710
C	3.94742	0.48258	-0.65066
C	3.01803	1.68128	-0.53849
C	3.96907	-1.35016	0.97304
Cl	3.44225	-2.85226	1.73775
C	2.47877	2.28464	-1.67831
C	1.64023	3.39590	-1.57120
C	1.33228	3.92127	-0.31776
C	1.86955	3.32958	0.82737
C	2.70312	2.21902	0.71594
C	-1.53197	-0.53152	0.07226
C	-2.62349	-1.59140	-0.05807
O	-2.05790	0.77604	-0.30086
C	-3.85967	-1.13587	0.66311
C	-3.24271	1.17732	0.23908
C	-4.11527	0.18341	0.86223
O	-3.53180	2.35995	0.14057
O	-4.77384	-2.03091	1.08446
C	-4.53074	-3.44502	0.97418
C	-0.50893	-0.80579	-2.26964
C	-5.35062	0.68561	1.56190
H	0.85809	-1.00128	0.93829
H	2.26573	-2.50591	-0.74664
H	2.18976	-1.13517	-1.83498

H	4.88900	0.70837	-0.14208
H	4.19005	0.31915	-1.70590
H	4.83345	-0.93337	1.46972
H	2.71725	1.88517	-2.65878
H	1.23021	3.84926	-2.46695
H	0.68165	4.78419	-0.23183
H	1.63874	3.73425	1.80672
H	3.11441	1.76460	1.61164
H	-1.23750	-0.46640	1.12377
H	-2.86526	-1.79263	-1.10792
H	-2.23839	-2.52003	0.36647
H	-4.34145	-3.73574	-0.06007
H	-3.69944	-3.74920	1.61319
H	-5.44623	-3.91768	1.32211
H	-0.98332	-1.73623	-2.60118
H	-1.16003	0.01617	-2.57626
H	0.43244	-0.71173	-2.81022
H	-5.11720	1.56056	2.17154
H	-6.12311	0.98751	0.84633
H	-5.77192	-0.08760	2.20347

Compound 1, conformer 7
***E* = -1462.12456, Δ*E* = 1.38 kcal/mol**
***G* = -1461.79191, Δ*G* = 1.43 kcal/mol, population 2.8%**

C	1.07380	-0.93128	-0.90890
C	0.12316	-1.11281	0.01459
C	-1.10117	-1.99236	-0.08360
C	-2.37864	-1.20211	0.12112
C	-2.84097	-0.40887	-1.09352
C	-4.04710	0.48480	-0.91182
C	-3.06536	-1.16836	1.26072
Cl	-2.60712	-2.05002	2.72194
C	-5.33465	0.01914	-1.20219
C	-6.44895	0.84117	-1.03135
C	-6.29065	2.14662	-0.56660
C	-5.01168	2.62369	-0.27686
C	-3.90103	1.79848	-0.44941
C	2.25782	-0.01957	-0.64745
C	3.58682	-0.77180	-0.56373
O	2.03755	0.73976	0.55915
C	4.67977	0.17076	-0.14820
C	3.04583	1.53438	1.02191
C	4.40728	1.30744	0.54402
O	2.75357	2.37768	1.85435
O	5.96764	-0.11839	-0.41333
C	6.32261	-1.27781	-1.18865
C	1.10592	-1.58130	-2.27122
C	5.46984	2.27595	0.99130
H	0.22157	-0.57964	0.95437
H	-1.15245	-2.49711	-1.05078
H	-1.03213	-2.77393	0.67790
H	-1.98897	0.19085	-1.43381
H	-3.03698	-1.12845	-1.89754
H	-3.96884	-0.59837	1.41305
H	-5.46591	-0.99425	-1.56814
H	-7.43820	0.46312	-1.26464
H	-7.15492	2.78799	-0.43564
H	-4.87820	3.63923	0.07929
H	-2.90942	2.17843	-0.22497
H	2.32814	0.70355	-1.47083
H	3.51487	-1.60140	0.15042
H	3.80272	-1.20576	-1.54053
H	7.40981	-1.29959	-1.18346
H	5.93813	-2.19155	-0.73342
H	5.96659	-1.18502	-2.21647
H	1.36955	-0.85158	-3.04371
H	1.85443	-2.37971	-2.31770
H	0.14636	-2.01905	-2.54166
H	5.74254	2.11595	2.03999
H	6.37097	2.16536	0.38916
H	5.11253	3.30399	0.90526

Compound 1, conformer 8

***E* = -1462.12505, Δ*E* = 1.07 kcal/mol**
***G* = -1461.79186, Δ*G* = 1.47 kcal/mol, population 2.7%**

C	-0.13622	-1.32518	-0.28400
C	0.91545	-0.55356	-0.58941
C	2.35044	-0.98220	-0.78587
C	3.33365	-0.16281	0.03285
C	4.06901	0.97158	-0.66194
C	3.16039	2.08176	-1.16656
C	3.60758	-0.40193	1.31417
Cl	2.87185	-1.70204	2.25201
C	2.91523	2.24910	-2.53296
C	2.07853	3.26918	-2.99040
C	1.47761	4.14026	-2.08356
C	1.71948	3.98578	-0.71688
C	2.55229	2.96449	-0.26466
C	-1.47821	-0.65043	-0.10976
C	-2.08557	-0.79902	1.28281
O	-2.38353	-1.20397	-1.11087
C	-3.48976	-0.26602	1.28120
C	-3.69380	-0.83107	-1.07481
C	-4.22719	-0.21962	0.14096
O	-4.37046	-1.06422	-2.06468
O	-4.06992	0.13266	2.42927
C	-3.32562	0.16933	3.66043
C	-0.10288	-2.81982	-0.09269
C	-5.64387	0.28937	0.09737
H	0.74058	0.51120	-0.72099
H	2.47803	-2.03862	-0.54804
H	2.60736	-0.86122	-1.84441
H	4.81191	1.39248	0.02096
H	4.61918	0.55129	-1.51081
H	4.31301	0.16582	1.90382
H	3.38451	1.58004	-3.24702
H	1.90024	3.38267	-4.05401
H	0.82925	4.93431	-2.43646
H	1.26052	4.66231	-0.00434
H	2.73266	2.85030	0.79947
H	-1.37796	0.41624	-0.33005
H	-2.09257	-1.84472	1.60996
H	-1.45540	-0.24750	1.98264
H	-2.91471	-0.81132	3.90464
H	-2.52948	0.91479	3.61344
H	-4.04829	0.45925	4.41958
H	0.84199	-3.25609	-0.41244
H	-0.25410	-3.09239	0.95717
H	-0.90396	-3.29382	-0.66619
H	-6.36757	-0.53177	0.14236
H	-5.84072	0.95583	0.93651
H	-5.82810	0.82974	-0.83299

Compound 1, conformer 9
***E* = -1462.12443, Δ*E* = 1.46 kcal/mol**
***G* = -1461.79185, Δ*G* = 1.47 kcal/mol, population 2.6%**

C	-0.87064	0.55253	-1.12315
C	0.24868	0.09688	-0.55012
C	1.64585	0.65476	-0.69589
C	2.28539	0.91768	0.65311
C	2.91771	-0.26375	1.36947
C	4.13351	-0.82784	0.64956
C	2.31282	2.10737	1.25103
Cl	1.62141	3.58004	0.56497
C	5.28950	-0.05273	0.49158
C	6.41106	-0.56752	-0.15553
C	6.39465	-1.86961	-0.65971
C	5.24982	-2.64998	-0.50898
C	4.12850	-2.13048	0.14105
C	-2.20780	-0.12203	-0.87826
C	-3.19406	0.76095	-0.11217
O	-2.00988	-1.36919	-0.17967
C	-4.42608	-0.02821	0.22658
C	-3.10768	-2.06743	0.23158
C	-4.39526	-1.38332	0.31651
O	-2.93959	-3.23394	0.54906

O	-5.58508	0.59961	0.50055
C	-5.70792	2.02620	0.35430
C	-0.95740	1.73294	-2.06056
C	-5.60191	-2.21396	0.66455
H	0.16447	-0.77679	0.08730
H	2.26521	-0.08028	-1.22416
H	1.65265	1.56475	-1.29313
H	3.19994	0.03575	2.38275
H	2.17055	-1.05704	1.47486
H	2.75951	2.29268	2.21747
H	5.31112	0.96101	0.87822
H	7.29843	0.04614	-0.26563
H	7.26679	-2.27052	-1.16379
H	5.22644	-3.66271	-0.89604
H	3.24213	-2.74602	0.25621
H	-2.65659	-0.36893	-1.84952
H	-2.73256	1.14771	0.80483
H	-3.44596	1.62115	-0.73309
H	-4.97396	2.55215	0.96638
H	-5.61271	2.32075	-0.69267
H	-6.70953	2.26148	0.70638
H	-1.53880	1.47519	-2.95207
H	-1.45702	2.58613	-1.58973
H	0.02326	2.07007	-2.39102
H	-6.52062	-1.67628	0.43223
H	-5.59318	-3.15374	0.10937
H	-5.62067	-2.46838	1.72987

Compound 1, conformer 10
***E* = -1462.12500, Δ*E* = 1.11 kcal/mol**
***G* = -1461.79176, Δ*G* = 1.53 kcal/mol, population 2.4%**

C	0.34880	-0.99476	-0.96770
C	-0.88017	-0.48801	-0.80203
C	-2.16414	-0.95851	-1.44301
C	-3.30096	-1.12892	-0.45032
C	-4.31140	-0.00109	-0.32024
C	-3.72385	1.30508	0.19180
C	-3.47702	-2.22201	0.29023
Cl	-2.42019	-3.63247	0.23216
C	-3.59884	2.41755	-0.64593
C	-3.06201	3.61563	-0.16993
C	-2.64458	3.71691	1.15585
C	-2.76904	2.61356	2.00291
C	-3.30274	1.41945	1.52306
C	1.49583	-0.31206	-0.25801
C	2.57114	0.24722	-1.18575
O	2.08334	-1.28330	0.65849
C	3.74561	0.71512	-0.37472
C	3.21916	-0.93879	1.32760
C	4.00959	0.19537	0.85249
O	3.53848	-1.63004	2.28268
O	4.59792	1.63126	-0.87296
C	4.34634	2.26348	-2.14101
C	0.69799	-2.18627	-1.82314
C	5.18608	0.62127	1.69069
H	-0.98884	0.37529	-0.15061
H	-2.47182	-0.21568	-2.18829
H	-2.00923	-1.89377	-1.98251
H	-4.75648	0.17393	-1.30566
H	-5.12189	-0.31764	0.34192
H	-4.28748	-2.35921	0.99177
H	-3.92796	2.35029	-1.67788
H	-2.97372	4.46763	-0.83500
H	-2.22912	4.64648	1.52832
H	-2.45141	2.68454	3.03736
H	-3.39283	0.56631	2.18784
H	1.10782	0.50640	0.35507
H	2.90382	-0.50200	-1.91293
H	2.13018	1.07013	-1.75102
H	5.21047	2.89998	-2.31638
H	4.26819	1.52709	-2.94225
H	3.44510	2.87817	-2.09975
H	1.42469	-2.82373	-1.31339

H	-0.17572	-2.79303	-2.05722
H	1.14869	-1.87741	-2.77281
H	4.92210	0.61922	2.74982
H	6.03478	-0.06053	1.56825
H	5.51714	1.62123	1.41196

Compound 1, conformer 11
***E* = -1462.12457, Δ*E* = 1.37 kcal/mol**
***G* = -1461.79174, Δ*G* = 1.54 kcal/mol, population 2.3%**

C	0.91219	-1.09688	0.51419
C	-0.19677	-0.47112	0.10487
C	-1.61548	-0.75123	0.54290
C	-2.55142	-0.90782	-0.63857
C	-3.09057	0.36090	-1.27744
C	-4.00921	1.15642	-0.36206
C	-2.91475	-2.07968	-1.15656
Cl	-2.37646	-3.64574	-0.54399
C	-3.66982	2.44846	0.05143
C	-4.52055	3.18174	0.88107
C	-5.72604	2.62932	1.30999
C	-6.07530	1.33996	0.90324
C	-5.22285	0.61134	0.07612
C	2.27903	-0.69293	-0.00434
C	3.18182	-0.10266	1.07988
O	2.13665	0.23978	-1.09578
C	4.44986	0.41155	0.46074
C	3.26232	0.80430	-1.62101
C	4.50099	0.77339	-0.84768
O	3.15791	1.34779	-2.70886
O	5.55815	0.57396	1.20748
C	5.59480	0.14800	2.58176
C	0.95796	-2.23166	1.50955
C	5.74543	1.30536	-1.50773
H	-0.08266	0.33297	-0.61421
H	-1.66807	-1.63078	1.18280
H	-1.96920	0.09570	1.14371
H	-2.24913	0.99649	-1.57190
H	-3.62415	0.10498	-2.19721
H	-3.57427	-2.19223	-2.00525
H	-2.73424	2.88738	-0.28000
H	-4.23985	4.18255	1.19027
H	-6.38862	3.19661	1.95389
H	-7.01257	0.90288	1.22975
H	-5.50178	-0.39079	-0.23287
H	2.77434	-1.58513	-0.41015
H	2.66720	0.70867	1.60948
H	3.39710	-0.87962	1.81409
H	4.80909	0.62830	3.16648
H	5.51589	-0.93839	2.65603
H	6.56721	0.46569	2.95064
H	-0.01005	-2.71814	1.62045
H	1.67958	-2.99356	1.19802
H	1.26690	-1.88448	2.50162
H	5.80939	0.95767	-2.54044
H	5.74911	2.40048	-1.53469
H	6.63616	0.98059	-0.97078

Compound 1, conformer 12
***E* = -1462.12465, Δ*E* = 1.33 kcal/mol**
***G* = -1461.79163, Δ*G* = 1.61 kcal/mol, population 2.1%**

C	0.07643	-0.91284	-1.06341
C	-1.05521	-1.23834	-0.42550
C	-2.44018	-1.37444	-1.01625
C	-3.53150	-0.79773	-0.13478
C	-4.02130	0.60936	-0.43103
C	-2.98508	1.69815	-0.19816
C	-4.10267	-1.46595	0.86614
Cl	-3.66912	-3.11474	1.32470
C	-2.48747	2.45768	-1.26112
C	-1.55481	3.47317	-1.04070
C	-1.10814	3.74378	0.25139
C	-1.60127	2.99364	1.32125
C	-2.53003	1.97996	1.09630

C	1.35102	-0.84501	-0.25350
C	2.03403	0.52022	-0.25256
O	2.25952	-1.85744	-0.78224
C	3.37772	0.41207	0.41015
C	3.52655	-1.91320	-0.28383
C	4.05213	-0.76665	0.45448
O	4.17699	-2.92066	-0.51635
O	3.97021	1.50150	0.93524
C	3.29245	2.77044	0.96534
C	0.19403	-0.61307	-2.53602
C	5.40750	-0.91585	1.09366
H	-0.99329	-1.45968	0.63724
H	-2.49431	-0.90161	-1.99764
H	-2.64528	-2.44069	-1.16736
H	-4.34605	0.64753	-1.47608
H	-4.90381	0.81776	0.18069
H	-4.88939	-1.07247	1.49365
H	-2.83444	2.25769	-2.26976
H	-1.18111	4.05191	-1.87827
H	-0.38628	4.53372	0.42578
H	-1.26359	3.20060	2.33088
H	-2.90711	1.40193	1.93389
H	1.13642	-1.12375	0.78223
H	2.15844	0.90908	-1.26932
H	1.38583	1.21802	0.28061
H	2.41904	2.73205	1.61897
H	4.01884	3.46978	1.37271
H	3.00327	3.08844	-0.03736
H	0.41981	0.44375	-2.71374
H	1.00951	-1.19300	-2.97684
H	-0.71811	-0.85249	-3.08050
H	5.49339	-1.88635	1.58589
H	6.21080	-0.85856	0.35100
H	5.57580	-0.13122	1.83064