Supporting Information

Hydroxylated Sclerosporin Derivatives from the Marine-derived Fungus *Cadophora malorum*[†]

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[†]Dedicated to the late Dr. John W. Daly of NIDDK, NIH, Bethesda, Maryland and to the late Dr. Richard E. Moore of the University of Hawaii at Manoa for their pioneering work on bioactive natural products.

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Figure S1. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **2**

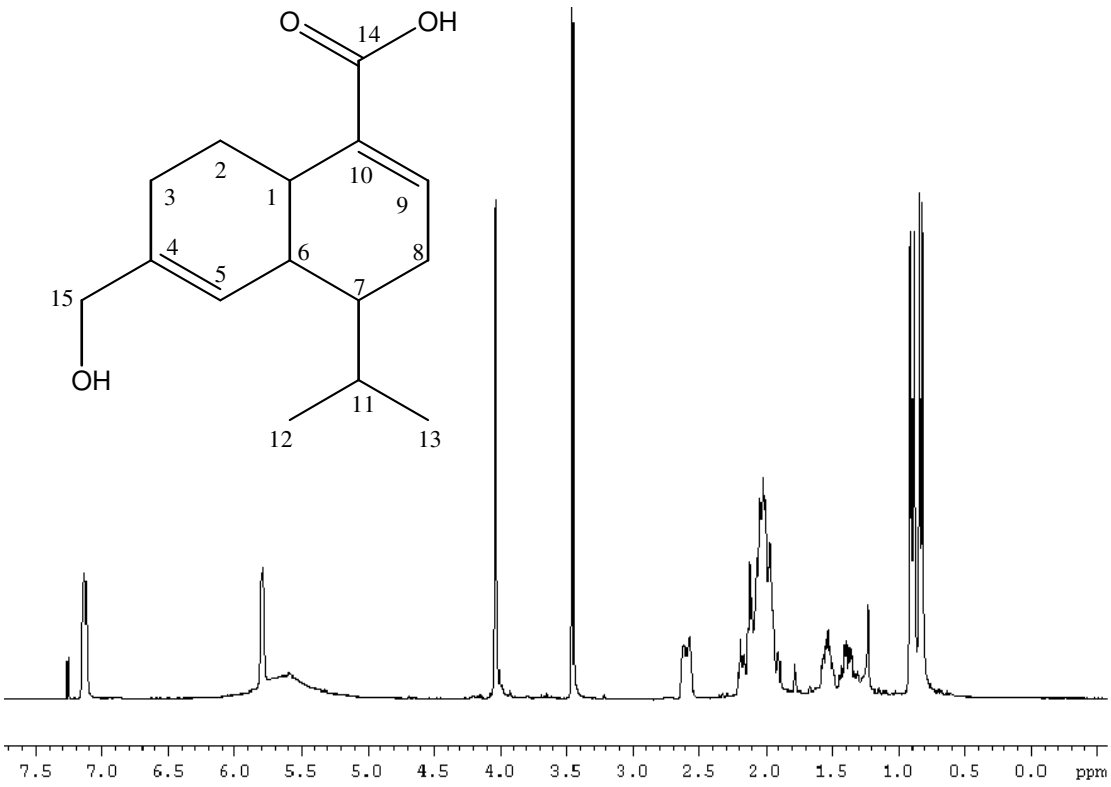


Figure S2. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **2**

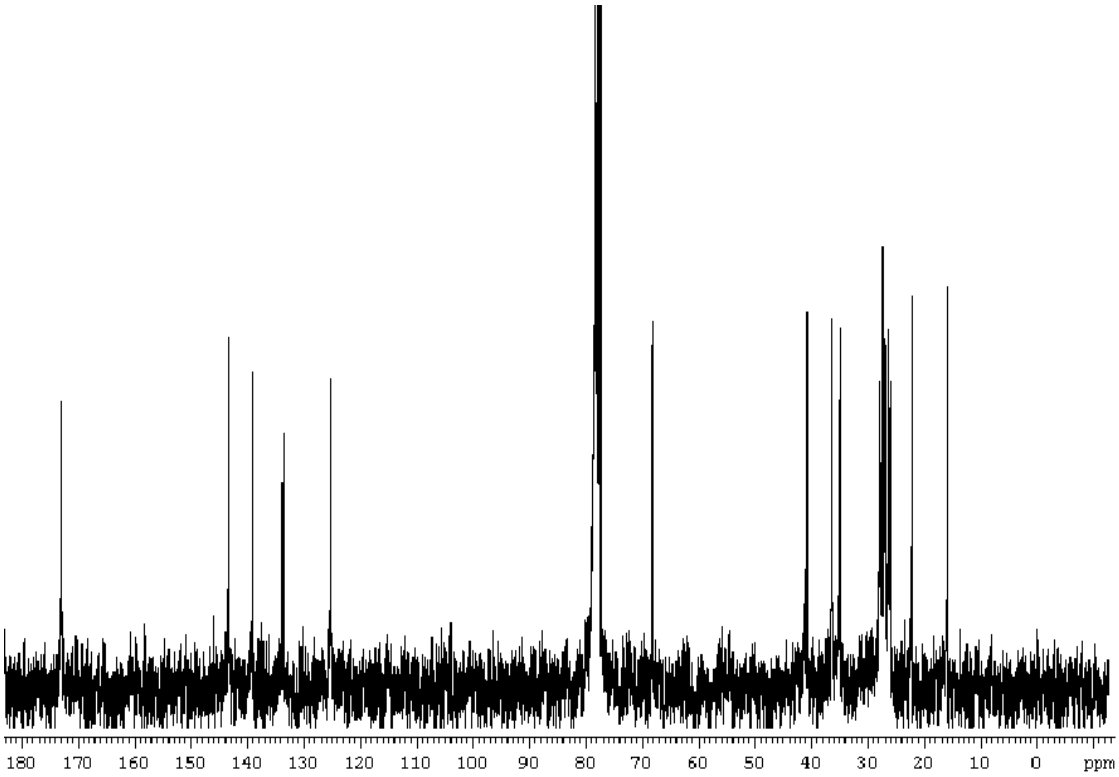


Figure S3. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3**

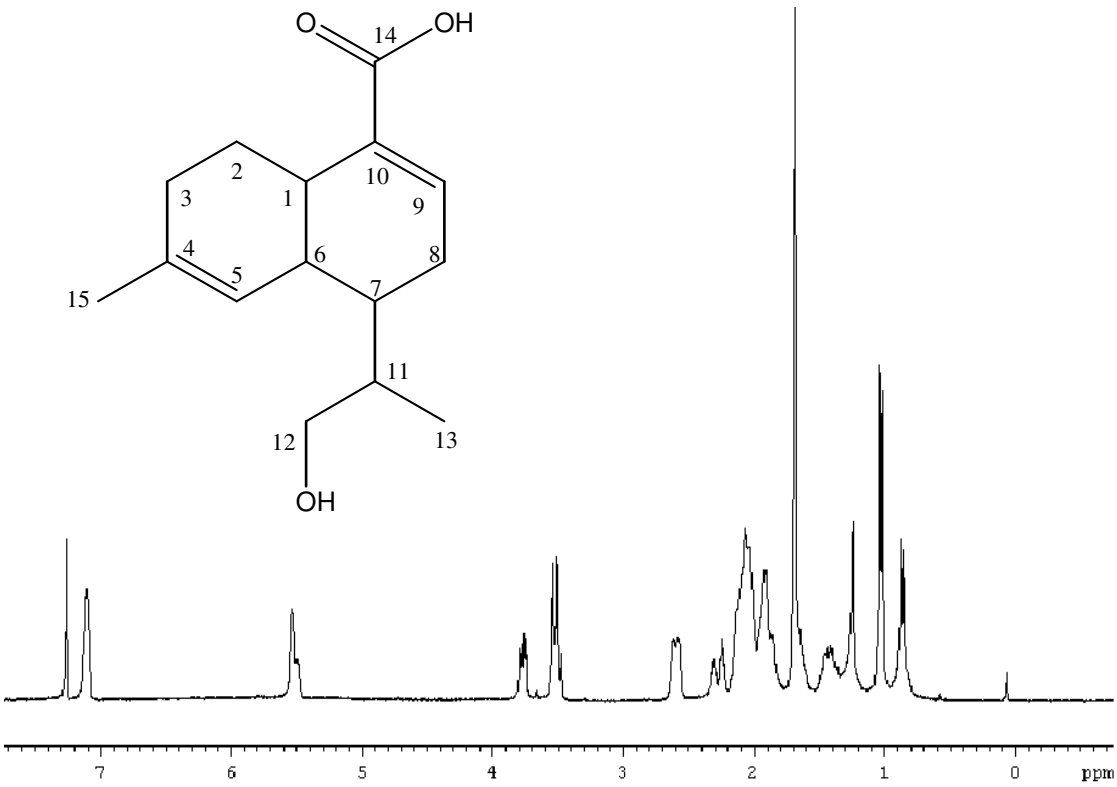


Figure S4. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **3**

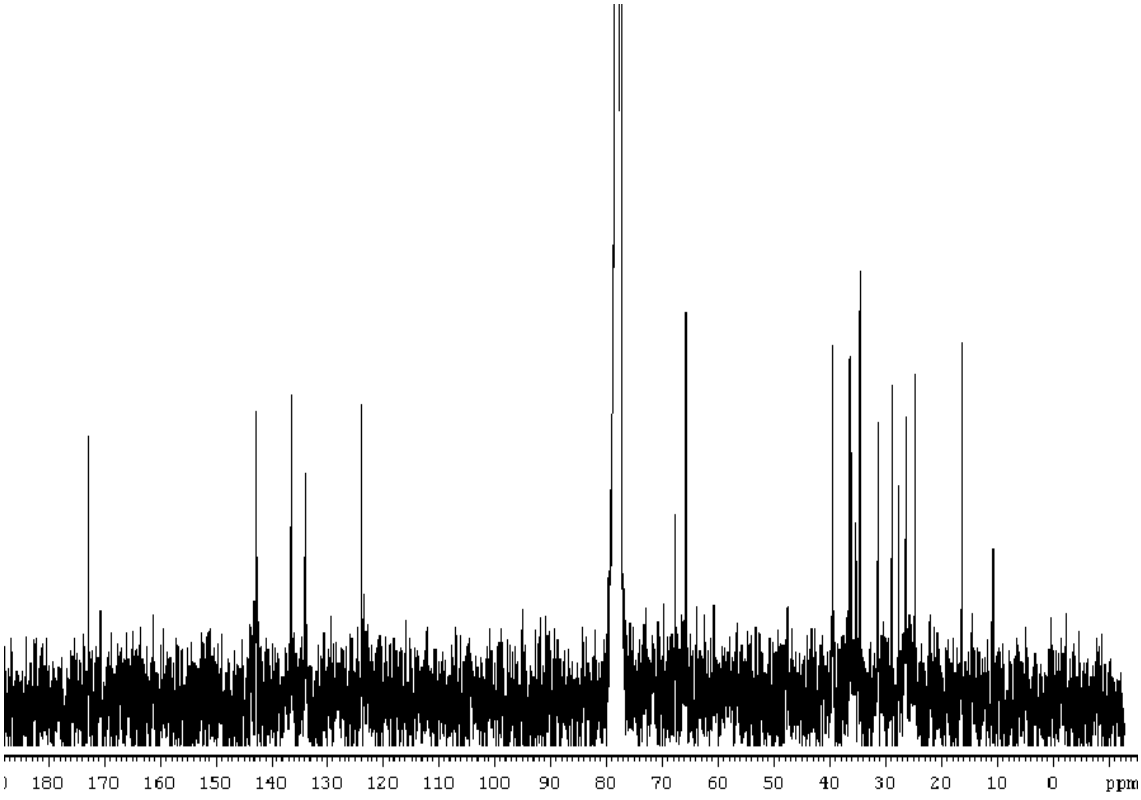


Figure S5. ^{1}H NMR spectrum (300 MHz, acetone-d_6) of compound **4**

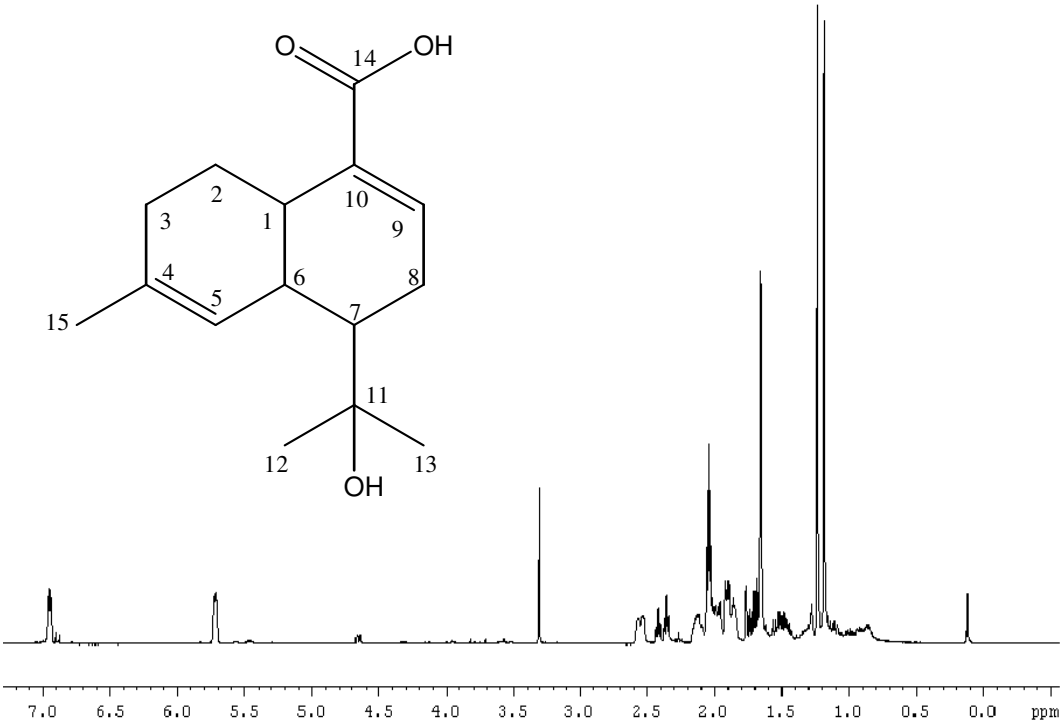


Figure S6. ^{13}C NMR spectrum (75 MHz, acetone-*d6*) of compound **4**

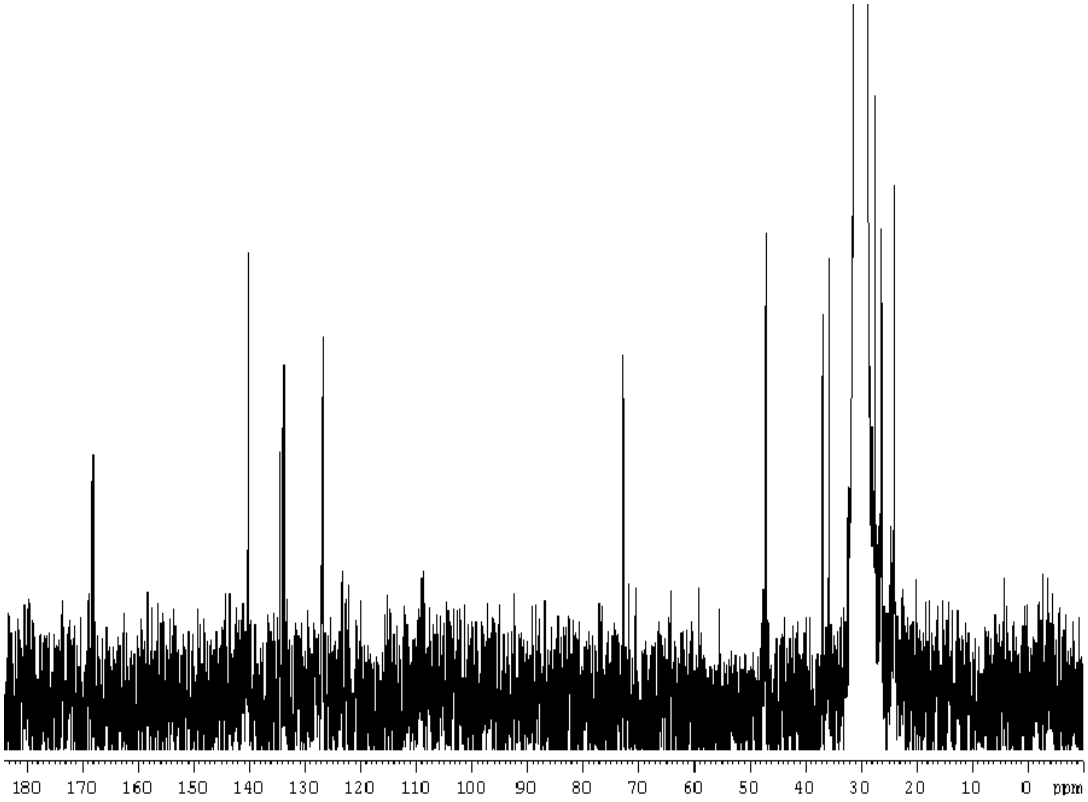


Figure S7. ^{1}H NMR spectrum (300 MHz, acetone-d_6) of compound **5**

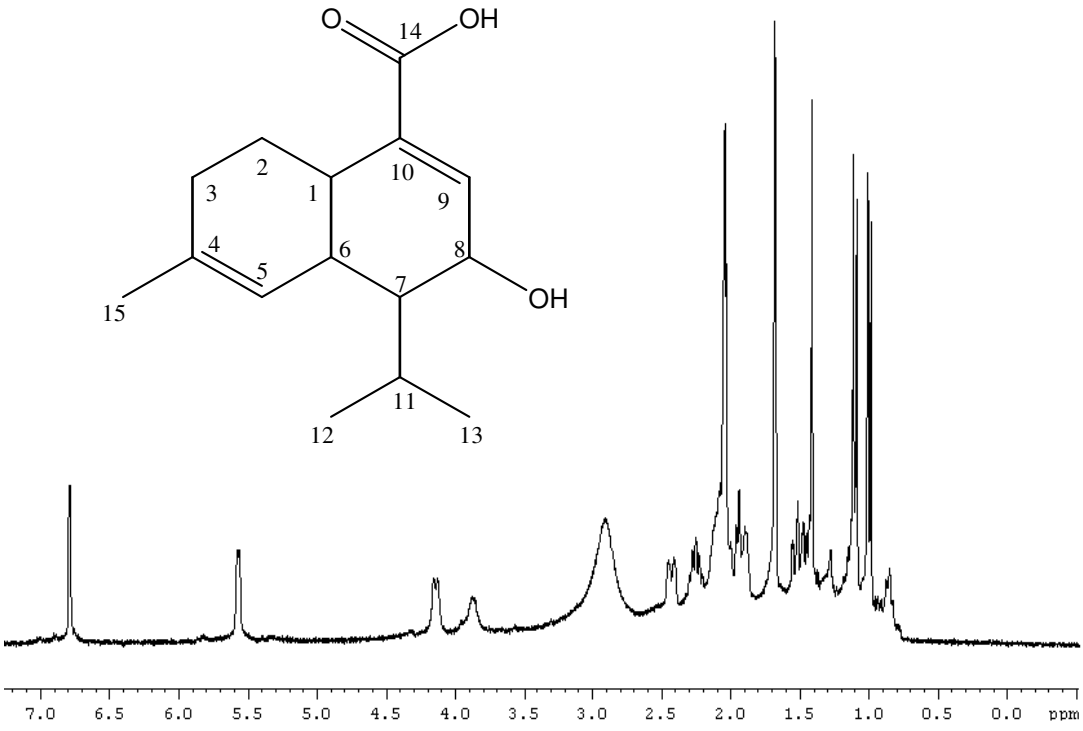


Figure S8. ^{13}C NMR spectrum (75 MHz, acetone-d_6) of compound **5**

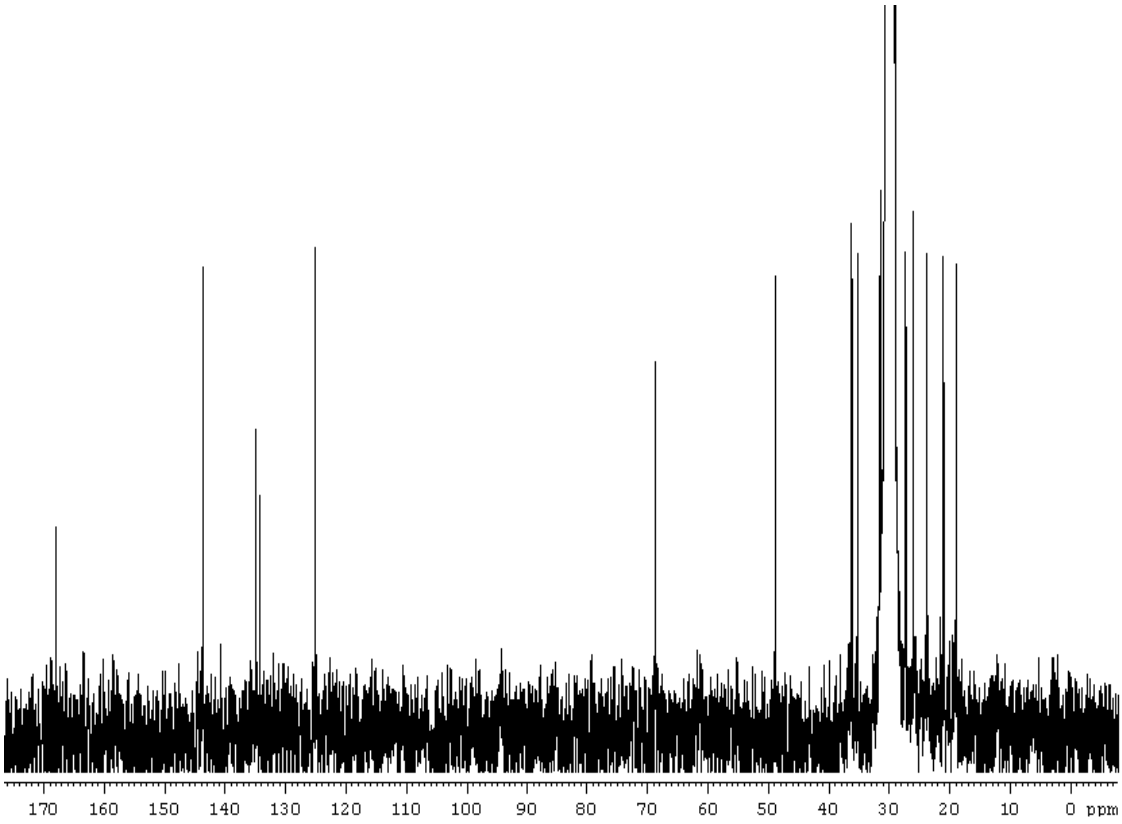


Figure S9. Infra-red spectra of compounds **1**-**5**

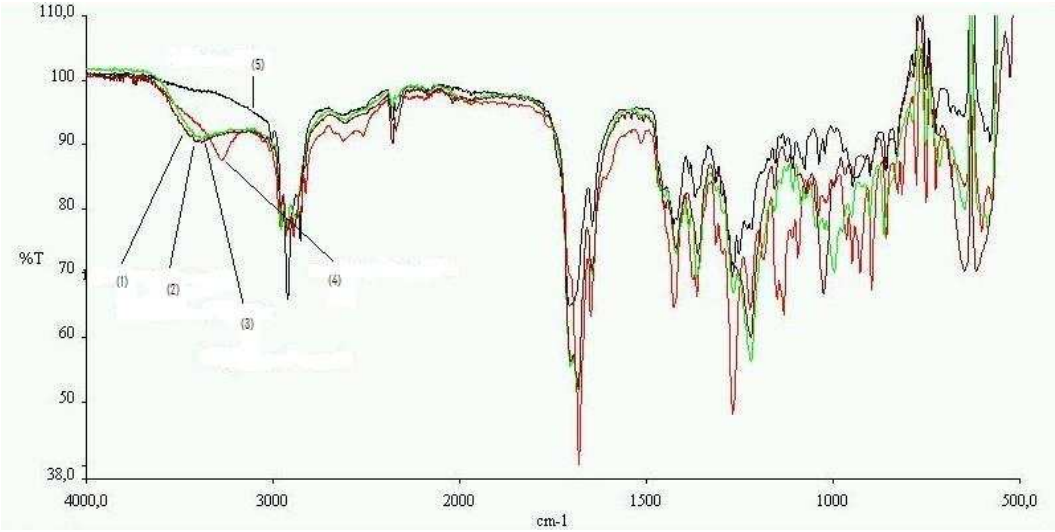


Figure S10. HREIMS for compound **2**

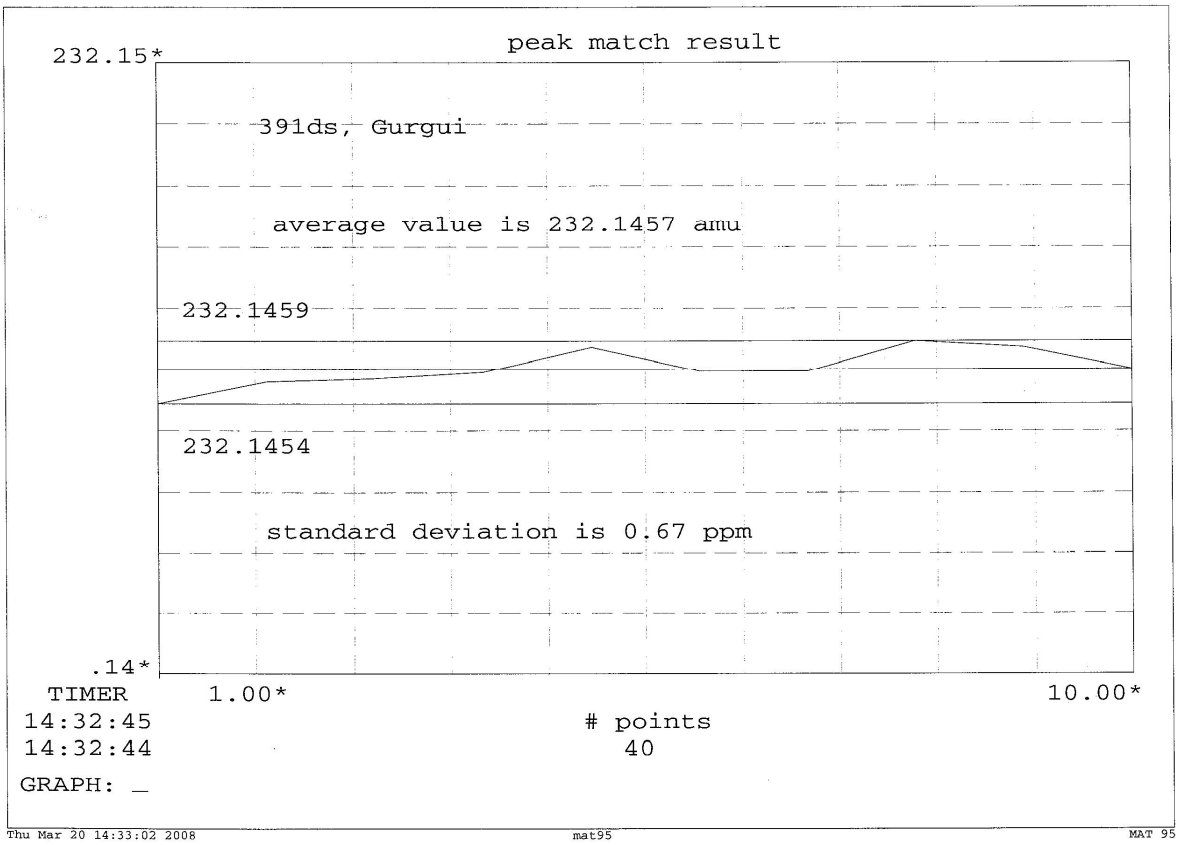


Figure S11. HREIMS for compound **3**

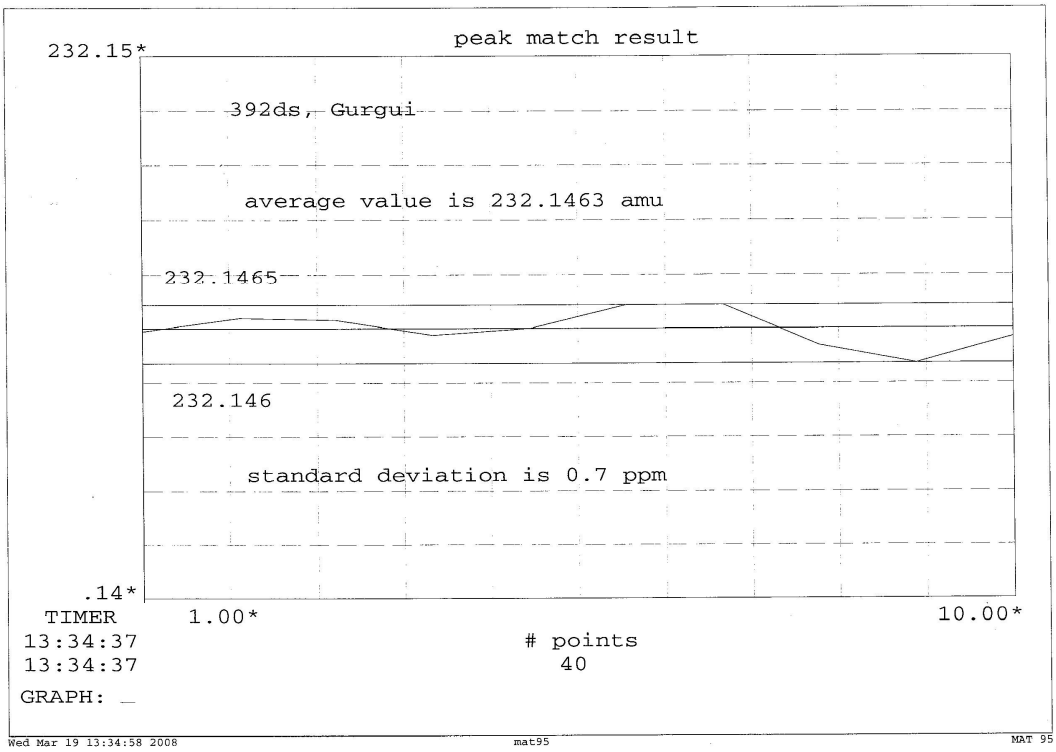


Figure S12. HREIMS for compound **4**

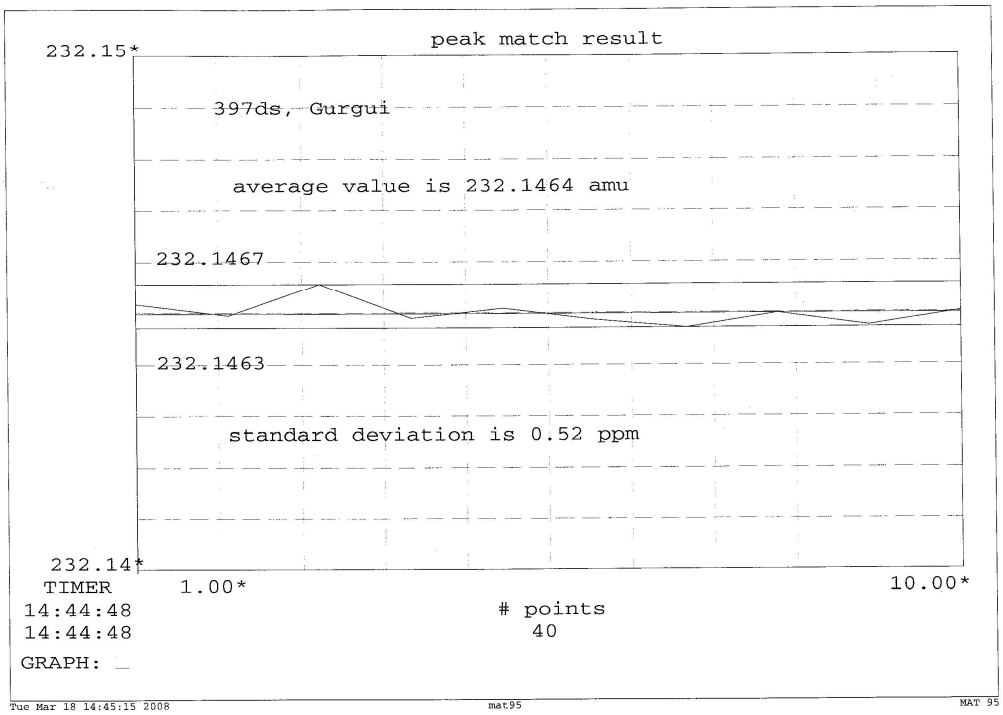


Figure S13. HREIMS for compound **5**

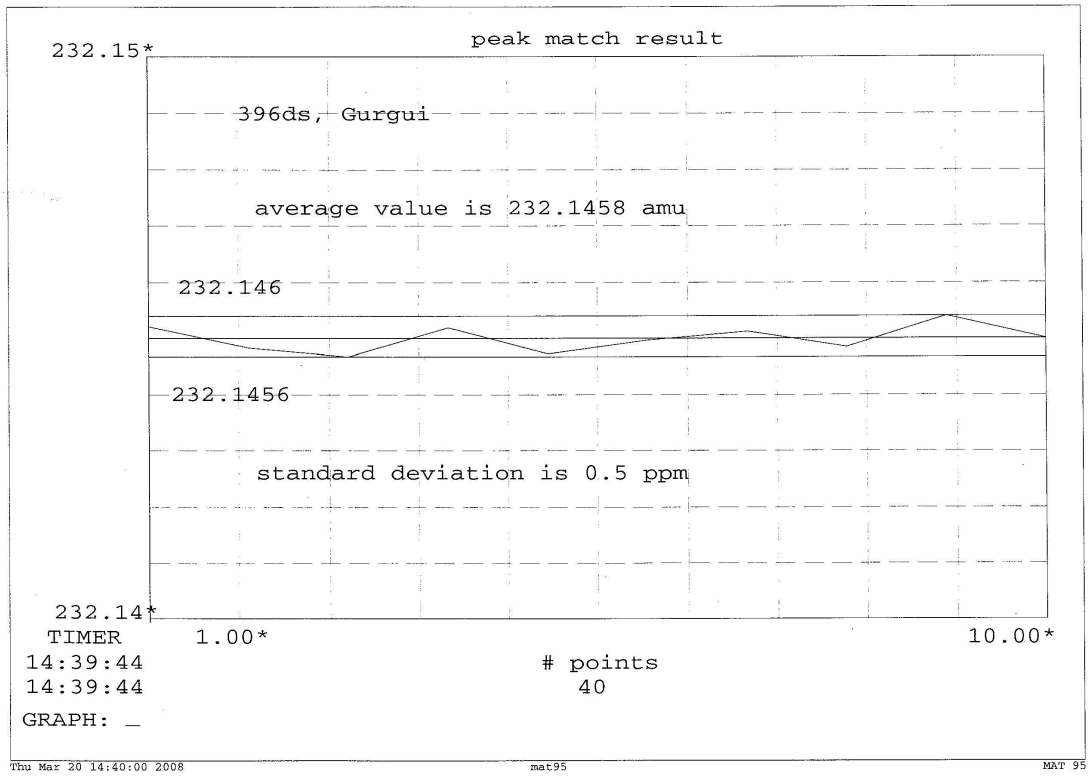


Figure S14. HREIMS for compound **1** (sclerosporin)

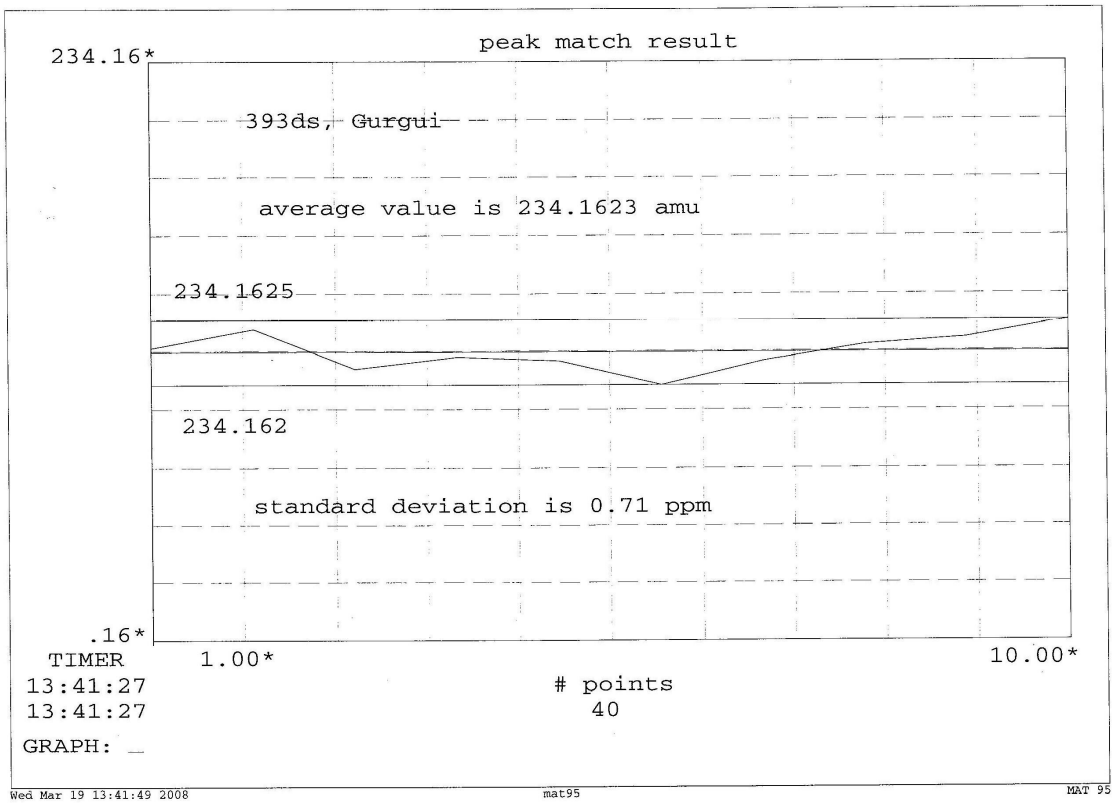
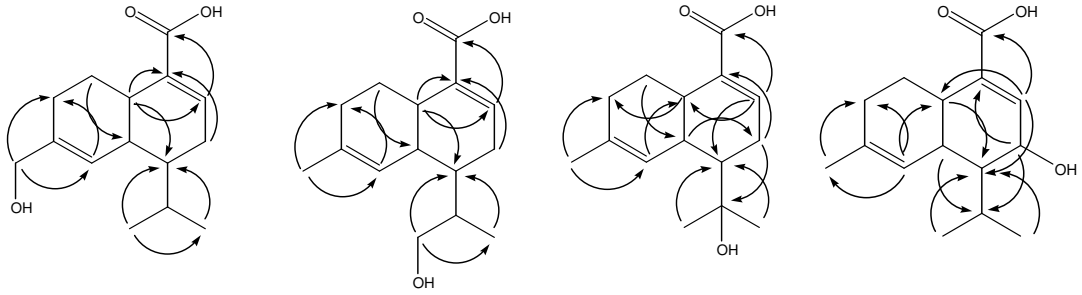
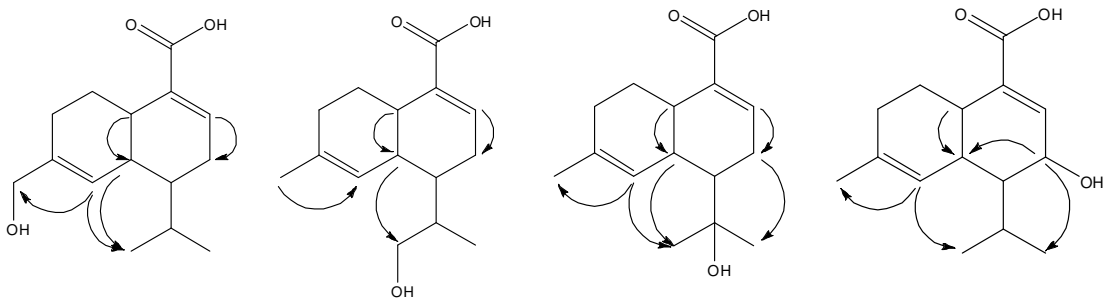


Figure S15. Key HMBC correlations for compounds **2**-**5**



(+)-15-hydroxysclerosporin (2) **(+)-12-hydroxysclerosporin (3)** **(+)-11-hydroxysclerosporin (4)** **(-)-8-hydroxysclerosporin (5)**

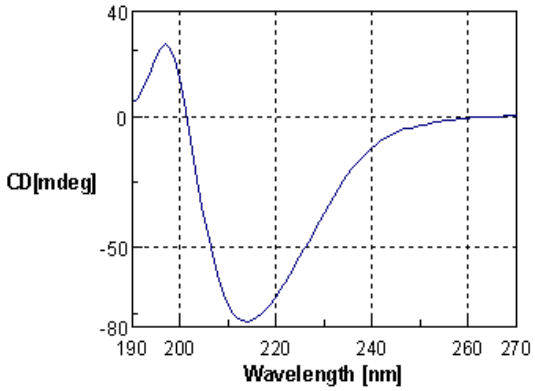
Figure S16. Key NOESY correlations for compounds **2**-**5**

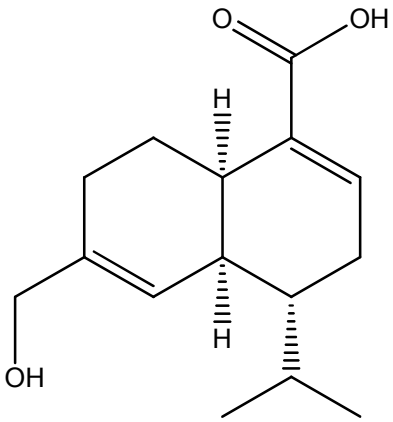


(+)-15-hydroxysclerosporin (2) **(+)-12-hydroxysclerosporin (3)** **(+)-11-hydroxysclerosporin (4)** **(-)-8-hydroxysclerosporin (5)**

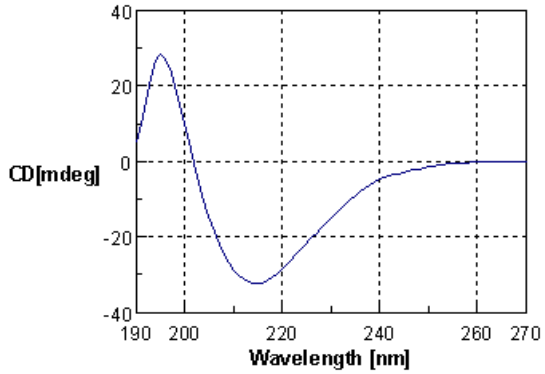
Figures S17. CD spectra for compounds **1-5;** respective absolute configuration on the right side.

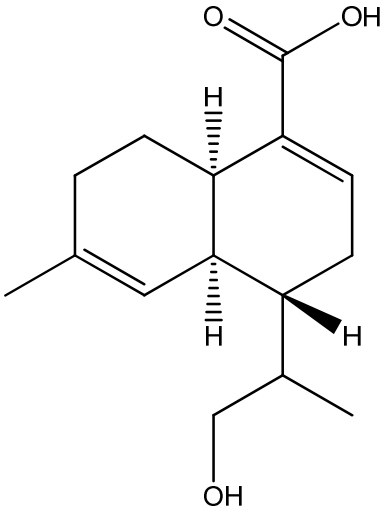
Compound **2**, (+)-15-hydroxysclerosporin



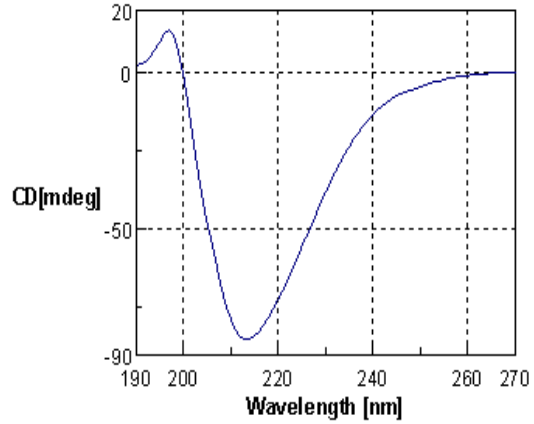


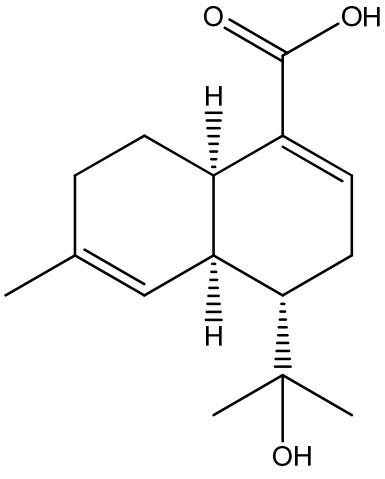
Compound **3**, (+)-12-hydroxysclerosporin



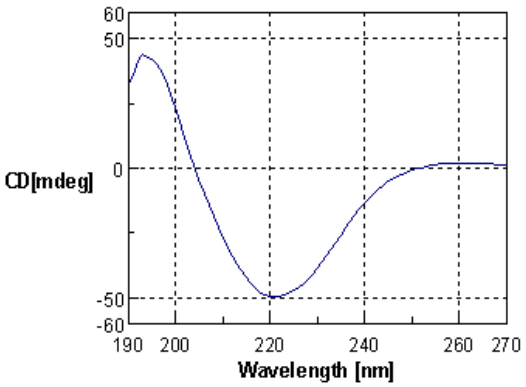


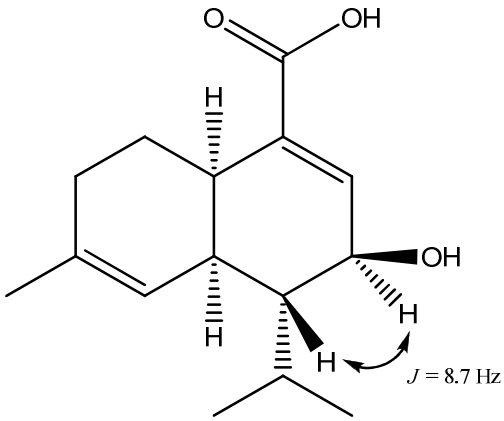
Compound **4**, (+)-11-hydroxysclerosporin



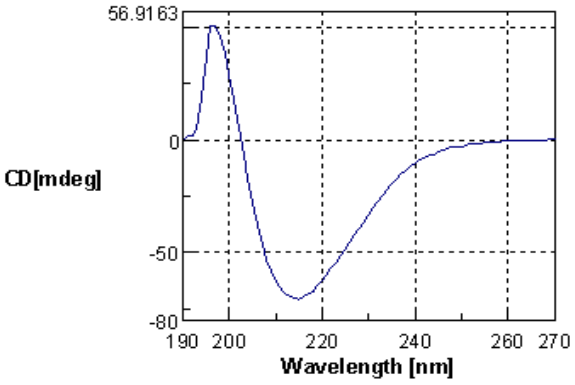


Compound **5**, (-)-8-hydroxysclerosporin





Compound **1**, (+)-sclerosporin



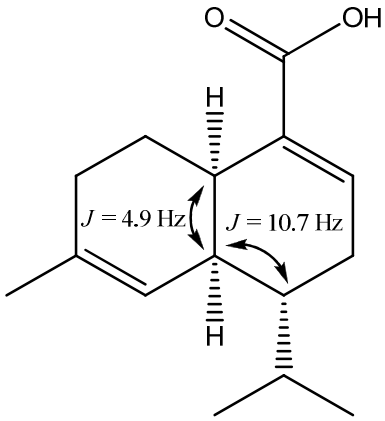


Figure S18. Isolation scheme for compounds **1- 5**.

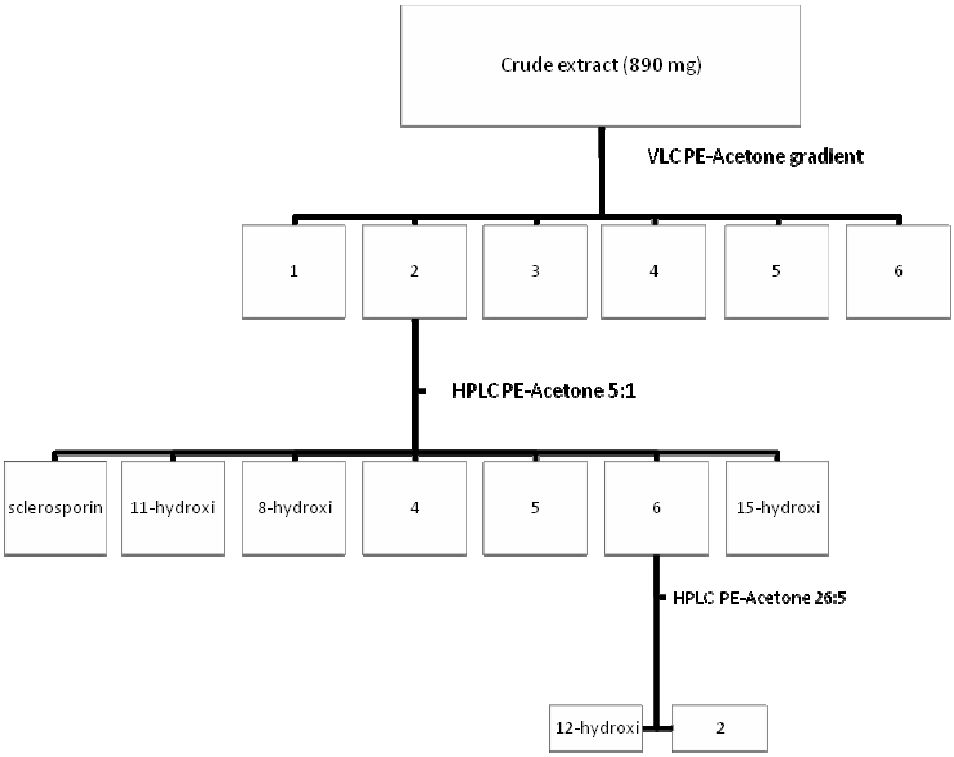


Table S19 a and b. Data of the 3T3-L1 murine adipocytes assay for compound **5** (IC_{50} values are the mean of quadruplicate determinations; blue numbers refer to the indicated concentrations (µg/mL) used of tested compounds; Arterenol was used as control for activity comparison)

A:

Sample Name	Triglyceride Accumulation (% of control)			IC_{50}
	100	20	4	(µg/mL)
Compound **5**	26	133	117	53 ± 1
	100	50	25	
(-)-Arterenol	33	64	71	69 ± 4

B:

Sample Name	Cell Number of 3T3-L1 (% of control)			IC_{50}
	100	20	4	(µg/mL)
Compound **5**	46	79	82	76
	100	50	25	
(-)-Arterenol	69	102	123	> 100

Table S20. 1D and 2D NMR Spectroscopic Data for Compound **2** [(+)-15-hydroxysclerosporin]

Position	δ_C, mult.[a, b, e]	δ_H[a, b] (*J* in Hz)	COSY[a, c]	HMBC[a, d]	NOESY[a, c]
1	34.0, CH	2.58, br d (11.4)	2a, 2b, 6	6, 7, 9, 10	6
2	25.1, CH_2	a: 1.99, m	1, 2b, 3	1, 3, 6	2b
		b: 1.37, qd (11.4, 5.4)	1, 2a, 3	1, 3, 6	2a, 7
3	26.2, CH_2	2.08, m	2a, 2b	4, 5	
4	138.3, qC				
5	124.3, CH	5.79, d (4.1)	6, 15	1, 3, 6, 15	6, 12, 15
6	35.5, CH	2.04, m	1, 5, 7	1	1, 8a, 12
7	40.0, CH	1.53, tt (10.2, 5.1)	6, 8a, 8b	6, 11, 12, 13	2b, 11
8	25.4, CH_2	a: 2.15, dt (19.8, 5.1)	7, 8b, 9	6, 7, 9, 10, 14	8b, 9
		b: 1.97, m	7, 8a, 9	6, 7, 9, 10, 14	8a, 9
9	142.6, CH	7.14, br s	8a, 8b	1, 7, 8, 10, 14	8a, 8b
10	132.9, qC				
11	26.4, CH	2.03, m	7, 12, 13	12, 13	12, 13
12	15.0, CH_3	0.83, d (6.8)	11	7, 11, 13	5, 11
13	21.3, CH_3	0.90, d (6.8)	11	7, 11, 12	11
14	172.2, qC				
15	67.3, CH_2	4.03, br s	5	3, 4, 5	5

[a]$CDCl_3$, 300/75.5 MHz. [b] Assignments are based on extensive 1D and 2D NMR experiments (HMBC, HSQC, COSY). [c] Numbers refer to proton resonances. [d] Numbers refer to carbon resonances. [e] Implied multiplicities determined by DEPT.

Table S21. 1D and 2D NMR Spectroscopic Data for Compound **3** [(+)-12-hydroxysclerosporin]

Position	δ_C, mult [a, b, e]	δ_H [a, b] (*J* in Hz)	COSY [a, c]	HMBC [a, d]	NOESY [a, c]
1	33.8, CH	2.58, br d (10.2)	2a, 2b, 6	3	6
2	25.4, CH_2	a: 1.91, m	1, 2b, 3a, 3b	1, 6	2b
		b: 1.42, qd (11.7, 5.4)	1, 2a, 3a, 3b	1,6	2a, 7
3	30.3, CH_2	a: 2.06, m	2a, 2b, 3b		3b
		b: 1.88, m	2a, 2b, 3a		2b, 3a
4	135.6, qC				
5	123.0, CH	5.52, br s	6, 15	1, 3, 6, 15	6, 12a, 12b, 15
6	35.8, CH	2.10, m	1, 5	8	1, 5
7	38.6, CH	1.65, tt (10.2, 5.1)	6, 8a, 8b	11, 12	2b, 11
8	28.0, CH_2	a: 2.27, dt (19.8, 5.1)	7, 8b	6, 7, 9, 10	8b, 9
		b: 2.02, m	7, 8a, 9	6, 7, 9, 10	8a, 9
9	142.1, CH	7.10, br s	8a, 8b	1, 7, 8, 10, 14	8a, 8b
10	133.1, qC				
11	35.3, CH	2.05, m	7, 12a, 12b, 13		7
12	64.9, CH_2	a: 3.77 (dd, 4.8, 10.6)	11, 12b	7, 11, 13	5, 6, 12b
		b: 3.52, t (10.6)	11, 12a	7, 11, 13	5, 6, 12a
13	15.4, CH_3	1.03, d (7.0)	11	7, 11, 12	11
14	172.0, qC				
15	23.9, CH_3	1.68, br s	5	3, 4, 5	5

[a] $CDCl_3$, 300/75.5 MHz. [b] Assignments are based on extensive 1D and 2D NMR experiments (HMBC, HSQC, COSY). [c] Numbers refer to proton resonances. [d] Numbers refer to carbon resonances. [e] Implied multiplicities determined by DEPT.

Table S22. 1D and 2D NMR Spectroscopic Data for Compound **4** [(+)-11-hydroxysclerosporin]

Position	δ_C, mult. [a, b, e]	δ_H [a, b] (*J* in Hz)	COSY [a, c]	HMBC [a, d]	NOESY [a, c]
1	35.6, CH	2.54, br d (10.6)	2a, 2b, 6		6
2	26.2, CH_2	a: 1.89, m	1, 2b, 3a, 3b	1, 6	2b
		b: 1.50, qd (11.7, 5.5)	1, 2a, 3a, 3b		2a, 7
3	30.8, CH_2	a: 1.98, m	2a, 2b		
		b: 1.95, m	2a, 2b		
4	133.7, qC				
5	126.6, CH	5.71, br d (5.1)	6, 15	1, 3, 6, 15	6, 12, 15
6	36.9, CH	2.11, m	1, 5	5, 7, 8	1, 5, 12
7	47.2, CH	1.68, td (10.3, 5.1)	8a, 8b	6, 11	2b, 8a, 12, 13
8	29.7, CH_2	a: 2.38, dt (19.6, 5.1)	7, 8b, 9	6, 7, 9, 10, 11	7, 8b, 9, 13
		b: 2.01, m	7, 8a, 9		8a, 9
9	140.2, CH	6.95, br t (3.9)	8a, 8b	1, 7, 8, 10, 14	8a, 8b
10	134.3, qC				
11	72.6, qC				
12	27.4, CH_3	1.23, s		7, 11, 13	5
13	28.7, CH_3	1.18, s		7, 11, 12	
14	168.0, qC				
15	23.9, CH_3	1.66, br s	5	3, 4, 5	5

[a]Acetone-d_6, 300/75.5 MHz. [b] Assignments are based on extensive 1D and 2D NMR experiments (HMBC, HSQC, COSY). [c] Numbers refer to proton resonances. [d] Numbers refer to carbon resonances. [e] Implied multiplicities determined by DEPT.

Table S23. 1D and 2D NMR Spectroscopic Data for Compound **5** [(-)-8-hydroxysclerosporin]

Position	δ_C, mult.[a, b, e]	δ_H[a, b] (*J* in Hz)	COSY[a, c]	HMBC[a, d]	NOESY[a, c]
1	35.2, CH	2.43, br d (10.6)	2a, 2b, 6	7	6
2	26.0, CH_2	a: 1.93, m	1, 2b, 3a, 3b		2b
		b: 1.45, qd (11.7, 5.4)	1, 2a, 3a, 3b		2a
3	31.5, CH_2	a: 2.08, m	2a, 2b, 3b		3b
		b: 1.93, m	2a, 2b, 3a		3a
4	134.9, qC				
5	125.1, CH	5.57, br d (4.4)	6, 15	1, 3, 6, 15	6, 11, 12, 13, 15
6	36.2, CH	2.10, m	1, 5, 7	1, 7, 11	1
7	48.8, CH	1.52, ddd (3.2, 8.7, 10.7)	6, 8, 11	1, 6, 8	12, 13
8	68.7, CH	4.13, br d (8.7)	7, 9	7, 9, 10, 11	6, 9, 11, 12, 13
9	143.7, CH	6.79, d (1.8)	8	1, 7, 10, 14	8
10	134.3, qC				
11	27.3, CH	2.25, m	7, 12, 13	7, 8	7, 8, 9, 12, 13
12	18.9, CH_3	1.00, d (7.1)	11	7, 11, 13	5, 7, 8, 11
13	21.1, CH_3	1.10, d (7.1)	11	7, 11, 12	5, 7, 8, 11
14	168.0, qC				
15	23.9, CH_3	1.68, br s	5	3, 4, 5	5

[a]Acetone-d_6, 300/75.5 MHz. [b] Assignments are based on extensive 1D and 2D NMR experiments (HMBC, HSQC, COSY). [c] Numbers refer to proton resonances. [d] Numbers refer to carbon resonances. [e] Implied multiplicities determined by DEPT.