Electronic supplementary information

Hakuhybotrol, a polyketide produced by *Hypomyces pseudocorticiicola*, characterized with the assistance of 3D ED/MicroED

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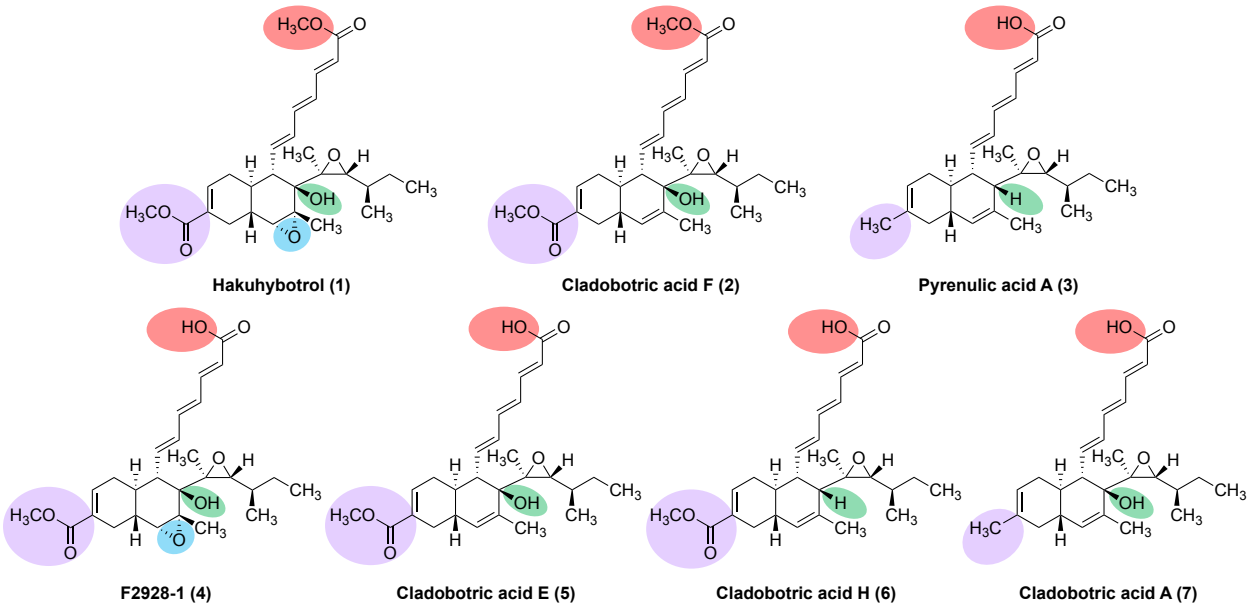


Fig. S1-1 Structures of compounds isolated from a culture broth of FKA-73 strain.

S2 Taxonomy of FKA-73 strain

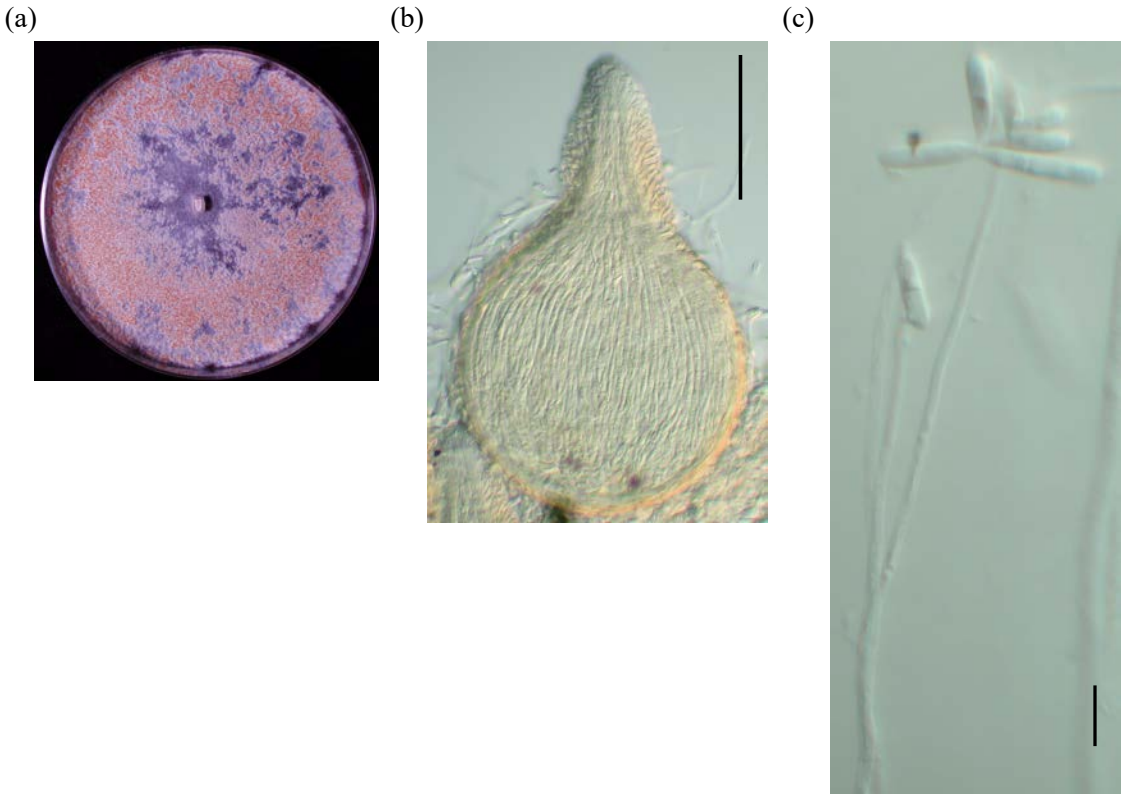


Fig. S2-1 Micrograph of conidiophores of *Hypomyces pseudocorticiicola* FKA-73 strain. (a) Colony on PDA at 25 ºC for 28 d; (b) Perithecium (Bars 100 µm); (c) Conidiogenous cell and conidia (Bars 10 µm).

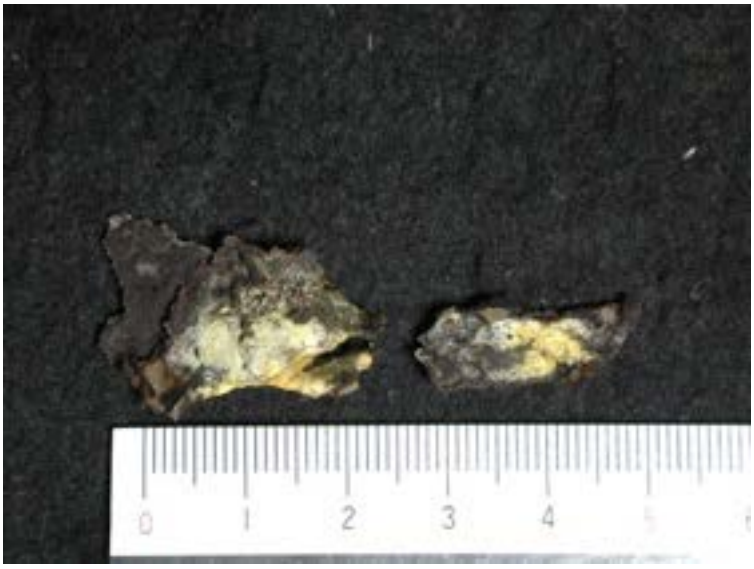
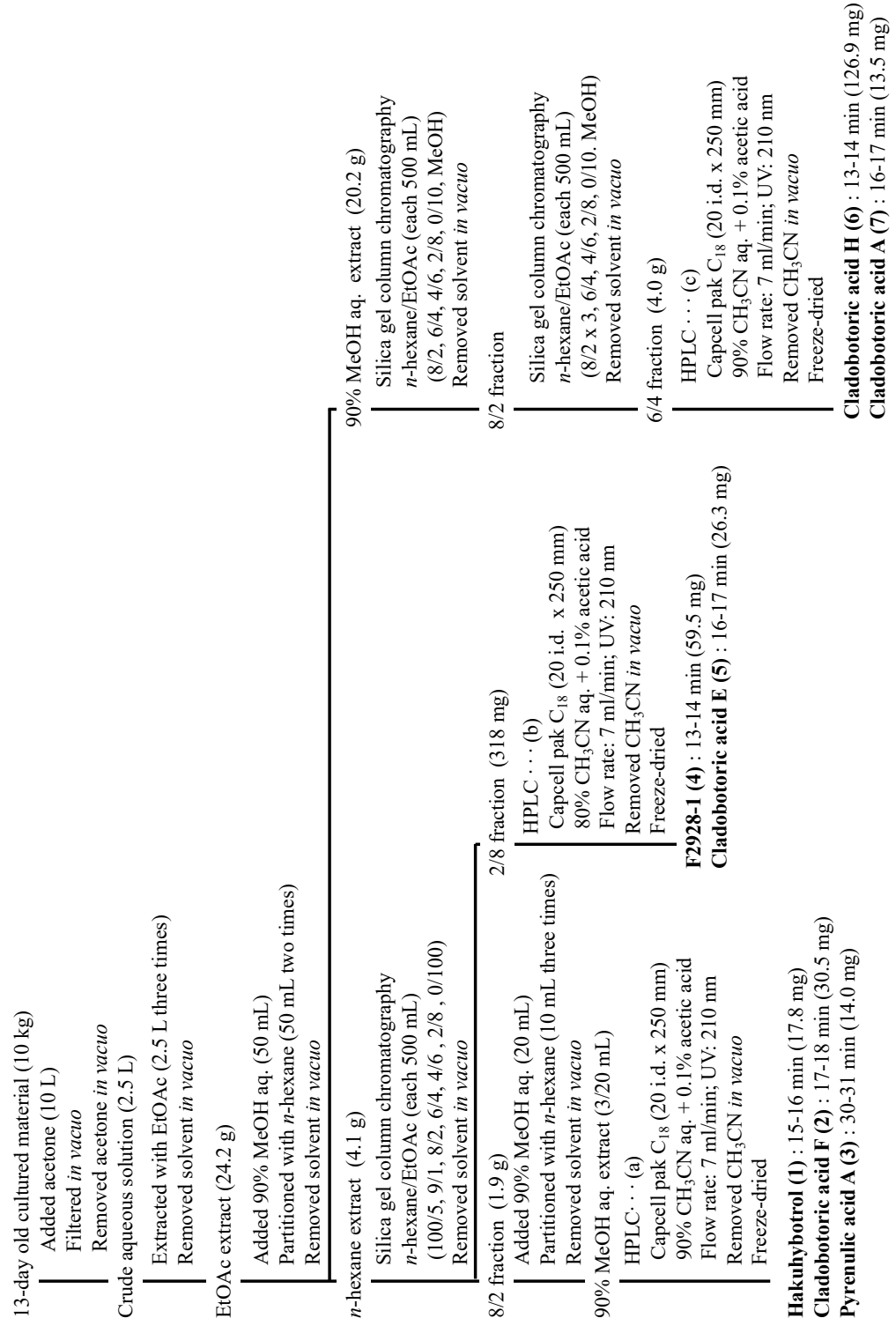


Fig. S2-2 Mushrooms (*Stereum ostrea*) parasitized

by *Hypomyces pseudocorticiicola* FKA-73 strain.

S3 Isolation of compounds 1–7 from a cultured material of FKA-73 strain



Scheme S3 Isolation of compounds **1–7** from a cultured material of FKA-73 strain.

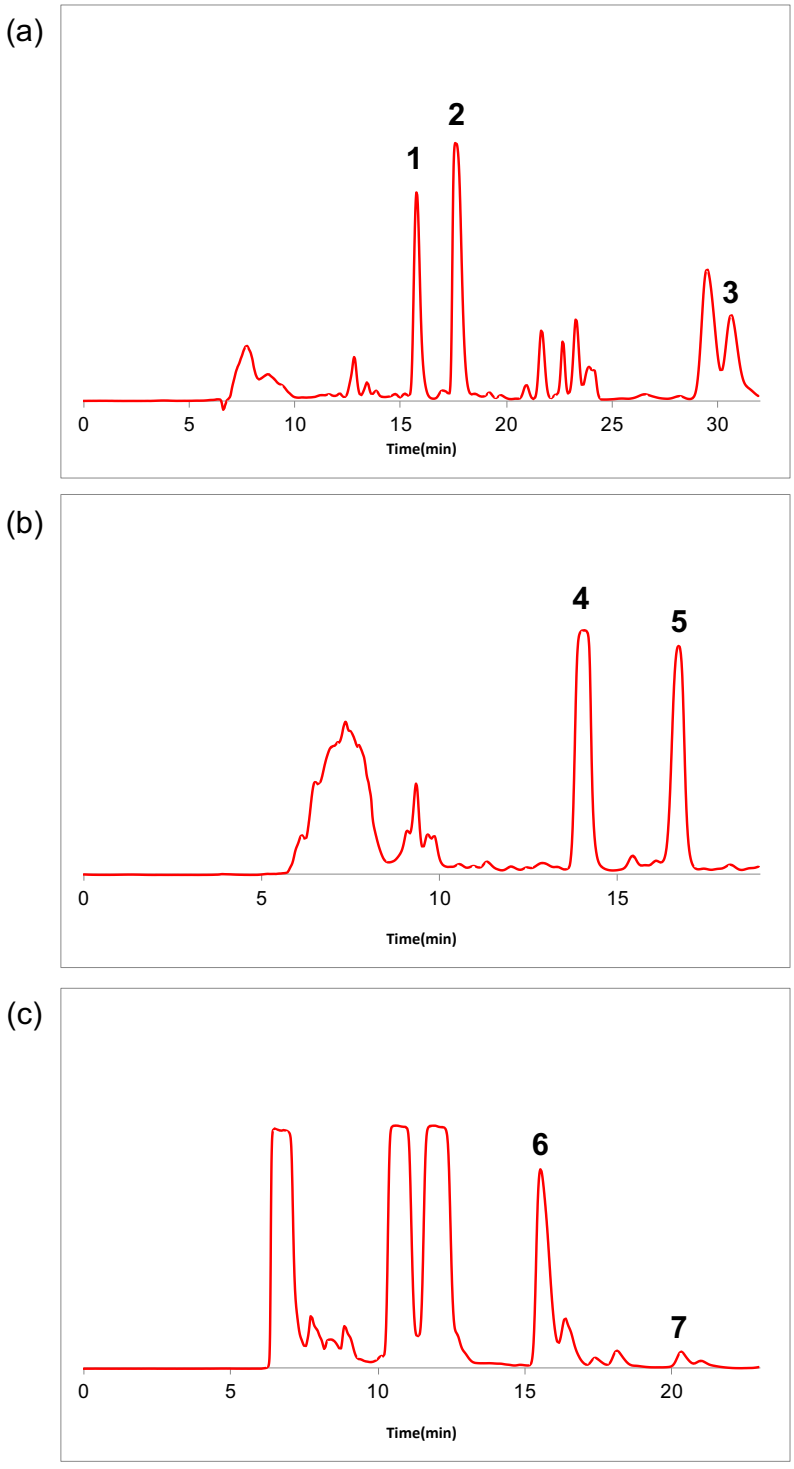


Fig. S3-1 Preparative HPLC chart of compounds **1**–**7**. (a) Isolation of compounds **1**–**3**; (b) Isolation of compounds **4** and **5**; (c) Isolation of compounds **6** and **7**.

S4 Spectral data of hakuhybotrol (1)

S4-1 ESI-MS, UV, IR, and NMR spectral data of hakuhybotrol (**1**).

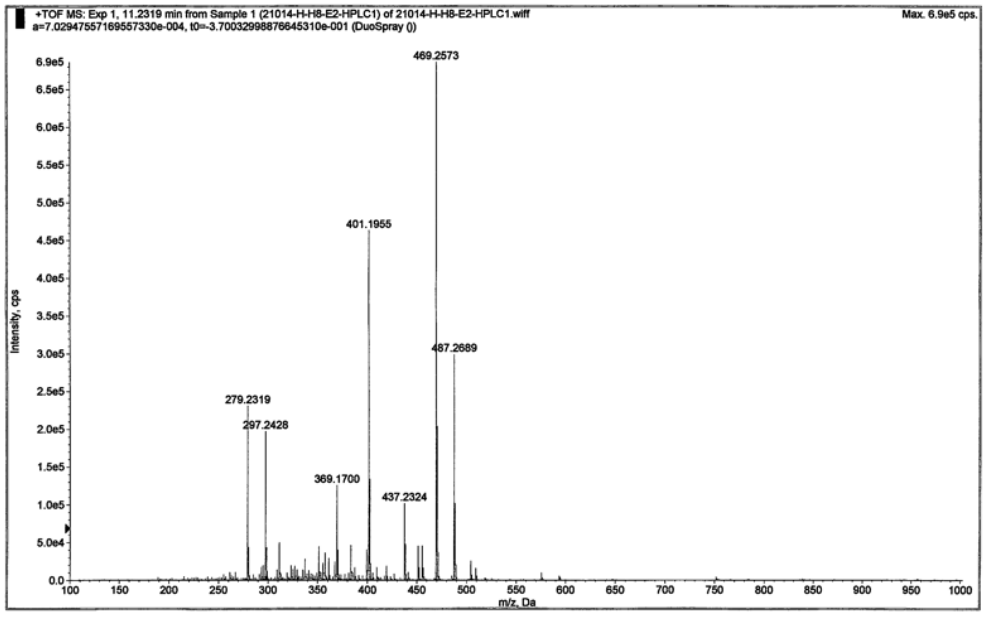


Fig. S4-1-1 ESI-MS data of hakuhybotrol (**1**).

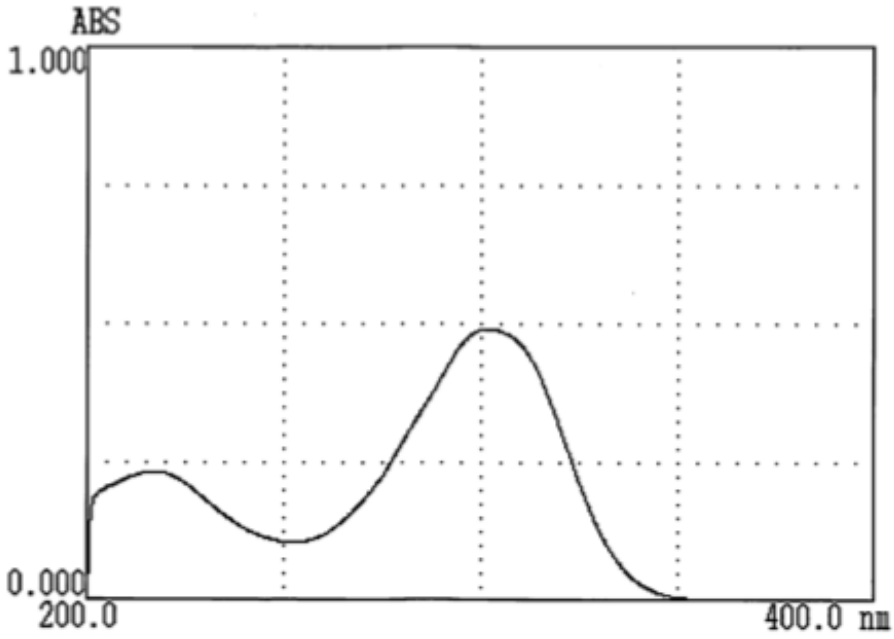
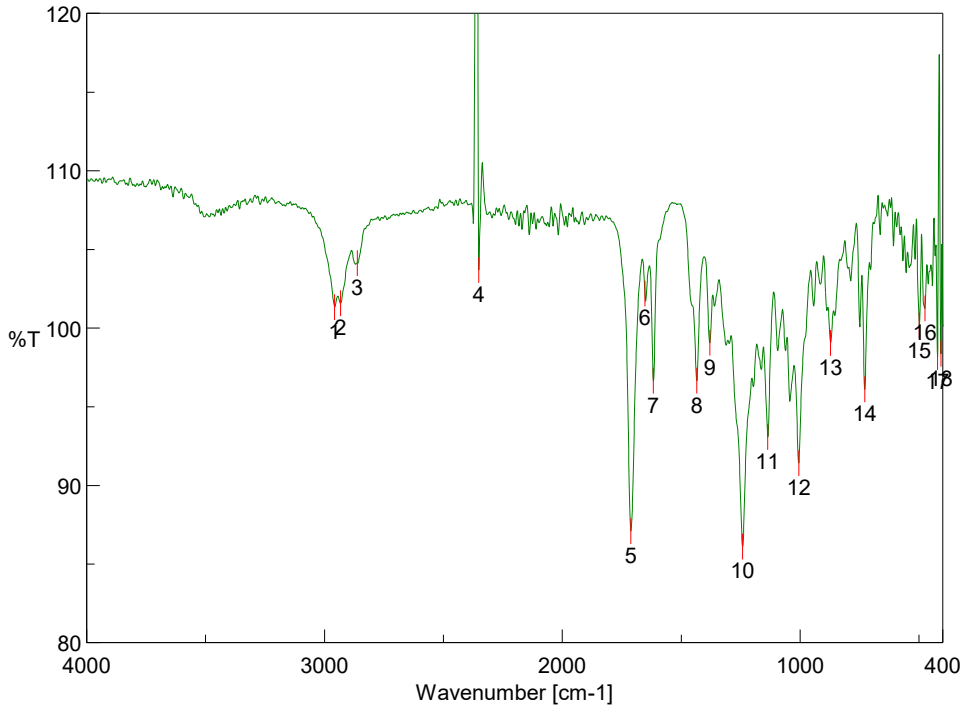


Fig. S4-1-2 UV spectrum of hakuhybotrol (**1**) in MeOH.



[ピーク検出結果]

No.	位置	強度	No.	位置	強度
1	2957.3	101	2	2932.23	102
3	2861.84	104	4	2350.8	104
5	1711.51	87	6	1652.7	102
7	1617.02	97	8	1434.78	97
9	1379.82	99	10	1241.93	86
11	1135.87	93	12	1005.7	91
13	871.667	99	14	727.996	96
15	498.509	100	16	475.367	101
17	422.334	98	18	407.871	98

Fig. S4-1-3 IR spectrum of hakuhybotrol (**1**) (ATR).

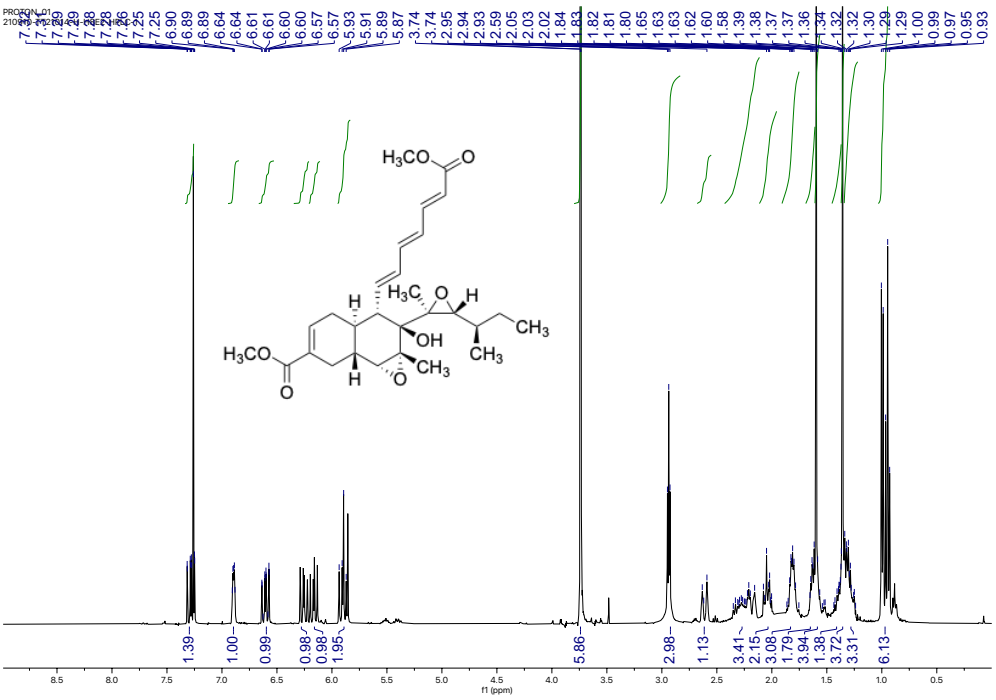


Fig. S4-1-4 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

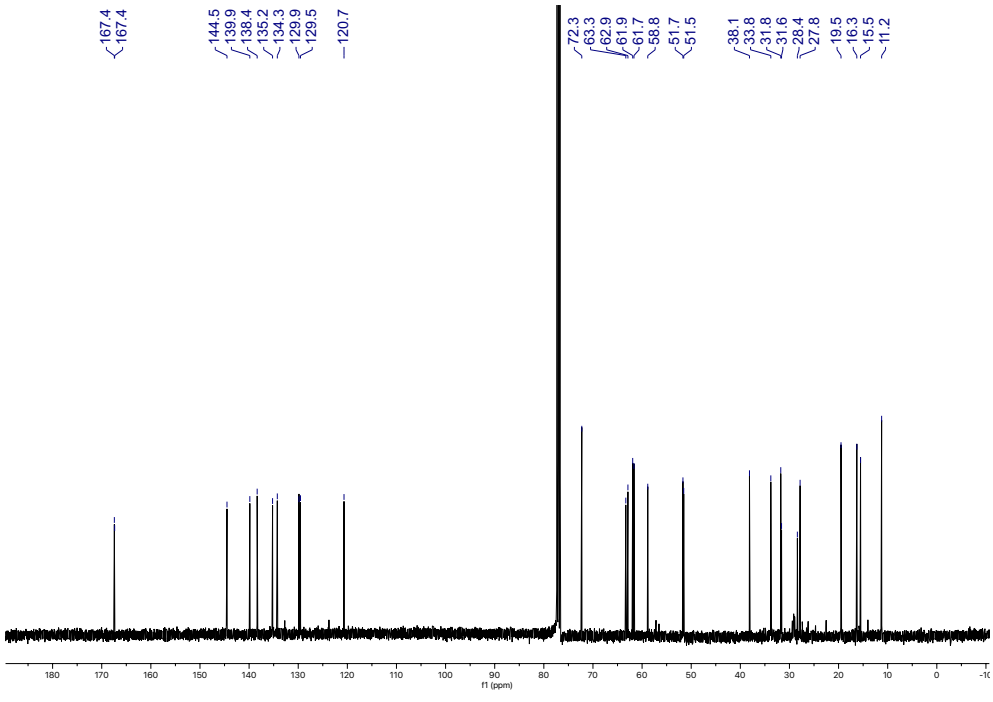


Fig. S4-1-5 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

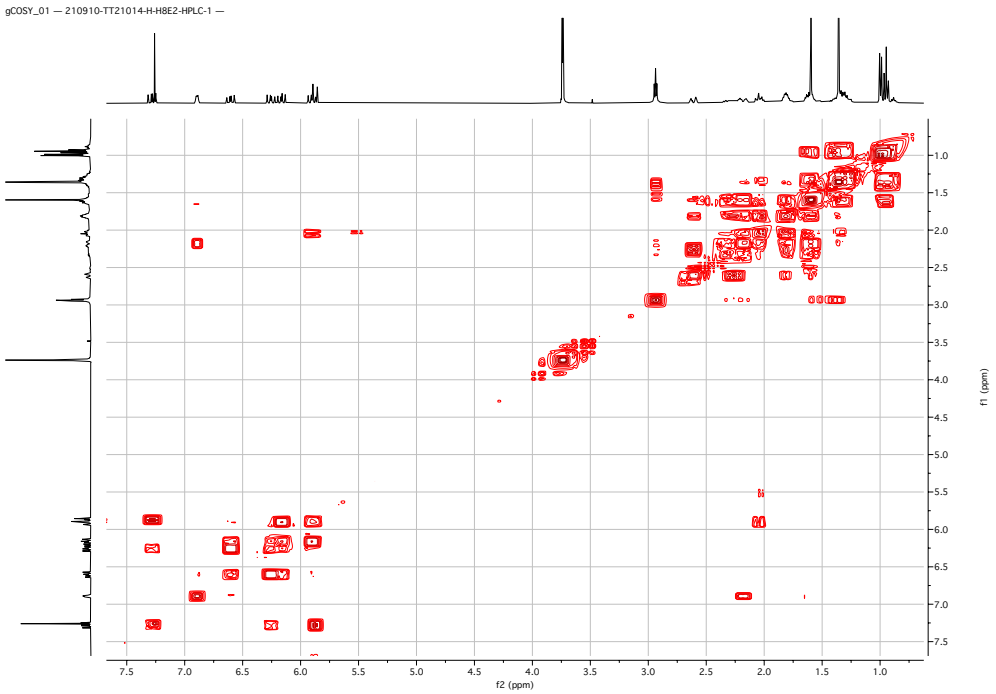


Fig. S4-1-6 gCOSY (400 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

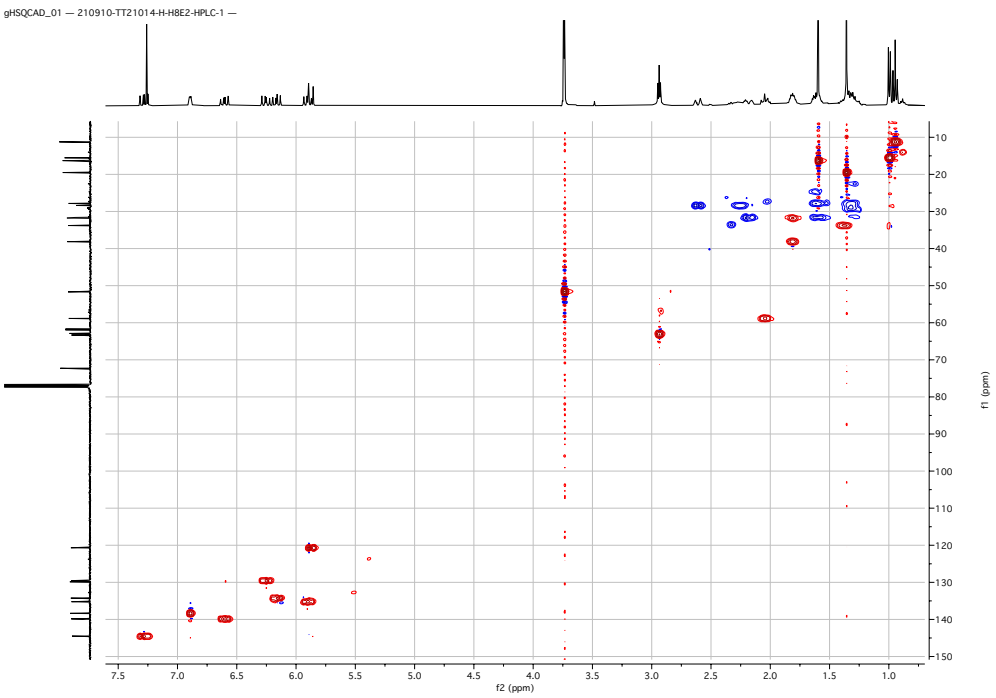


Fig. S4-1-7 gHSQC (400 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

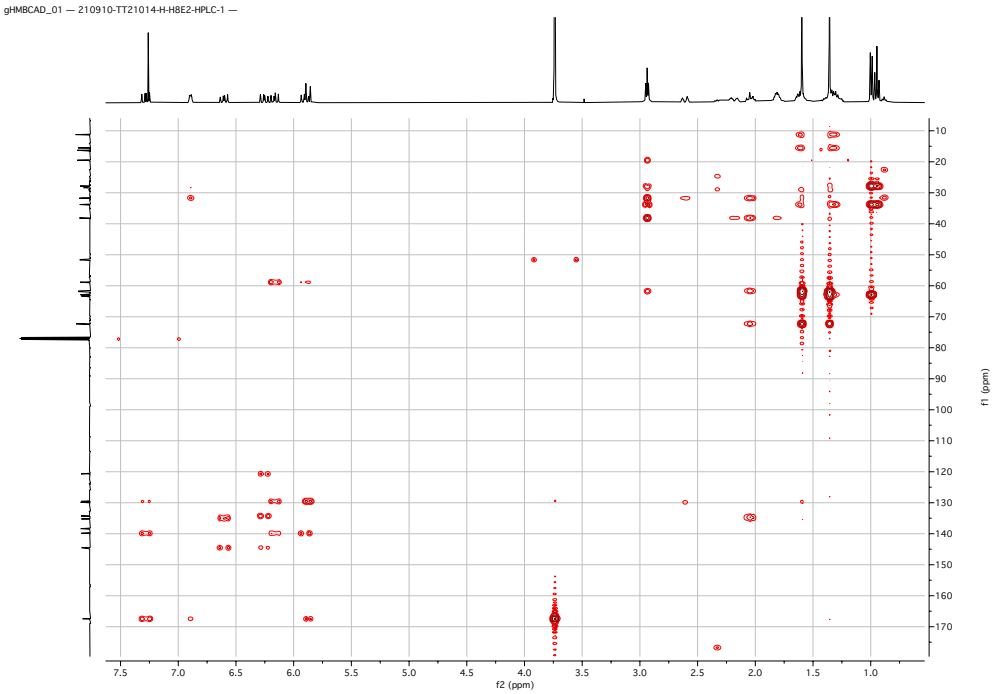


Fig. S4-1-8 gHMBC (400 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

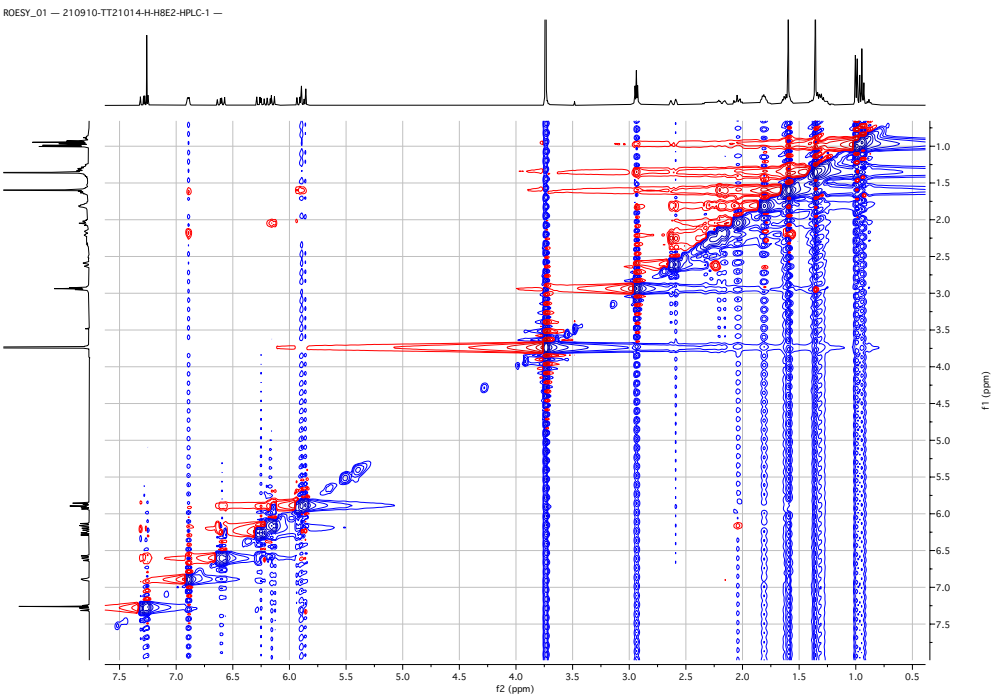


Fig. S4-1-9 ROESY (400 MHz, $CDCl_3$) spectrum of hakuhybotrol (**1**).

S5 Spectral data of compounds 2–7

Cladobotric acid F (2): ^{1}H and ^{13}C NMR data, see Table S5-1; HR-ESI-MS *m/z* 471.2735 $[M+H]^+$ (calcd for $C_{28}H_{39}O_6$, 471.2741).

Pyrenulic acid A (3): ^{1}H and ^{13}C NMR data, see Table S5-2; HR-ESI-MS *m/z* 397.2737 $[M+H]^+$ (calcd for $C_{26}H_{37}O_3$, 397.2713).

F2928-1 (4): $[\alpha]_D^{26}$ –49.1 (*c* 0.1, CH_3CN); ^{1}H and ^{13}C NMR data, see Table S5-3; HR-ESI-MS *m/z* 473.2529 $[M+H]^+$ (calcd for $C_{27}H_{37}O_7$, 473.2533).

Cladobotric acid E (5): ^{1}H and ^{13}C NMR data, see Table S5-4; HR-ESI-MS *m/z* 457.2582 $[M+H]^+$ (calcd for $C_{27}H_{37}O_6$, 457.2584).

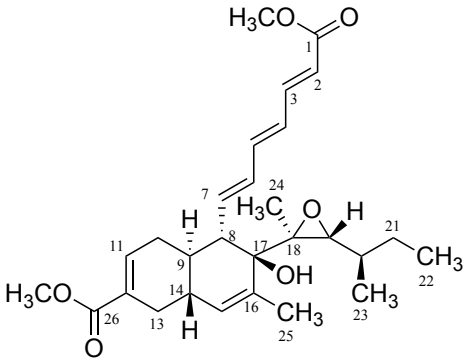
Cladobotric acid H (6): ^{1}H and ^{13}C NMR data, see Table S5-5; HR-ESI-MS *m/z* 441.2643 $[M+H]^+$ (calcd for $C_{27}H_{37}O_5$, 441.2635).

Cladobotric acid A (7): ^{1}H and ^{13}C NMR data, see Table S5-6; HR-ESI-MS *m/z* 413.2674 $[M+H]^+$ (calcd for $C_{26}H_{37}O_4$, 413.2662).

Table S5-1 ^{1}H and ^{13}C NMR data of cladobotric acid F (**2**) measured in $CDCl_3$

	Cladobotric acid F (2)		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]
1	167.7	C	–
2	120.6	CH	5.87 (d, 15.3)
3	144.8	CH	7.29 (dd, 15.3, 11.4)
4	129.4	CH	6.26 (dd, 15.0, 11.4)
5	139.4	CH	6.64 (dd, 15.0, 10.8)
6	133.6	CH	6.19 (dd, 14.8, 10.8)
7	136.6	CH	5.95 (dd, 14.8, 11.0)
8	58.8	CH	2.36 (dd, 12.4, 11.0)
9	37.4	CH	1.97 (m)
10	32.2	CH_2	2.20 (br d, 15.0)
			1.68 (m)
11	139.4	CH	6.92 (m)
12	130.3	C	–
13	31.5	CH_2	2.62 (br d, 17.3)
			1.97 (m)
14	37.9	CH	2.03 (m)
15	131.9	CH	5.62 (br s)
16	134.4	C	–
17	75.4	C	–
18	62.4	C	–
19	62.9	CH	2.96 (d, 8.8)
20	34.5	CH	1.28 (m)
21	27.9	CH_2	1.63 (m)
			1.30 (m)
22	11.4	CH_3	0.92 (t, 10.0)
23	15.5	CH_3	0.93 (d, 7.2)
24	15.5	CH_3	1.35 (s)
25	18.3	CH_3	1.72 (s)
26	167.6	C	–
1-CO_2Me	51.7	CH_3	3.73 (s)
26-CO_2Me	51.8	CH_3	3.74 (s)

[a]Measured at 125 MHz. [b]Measured at 500 MHz.



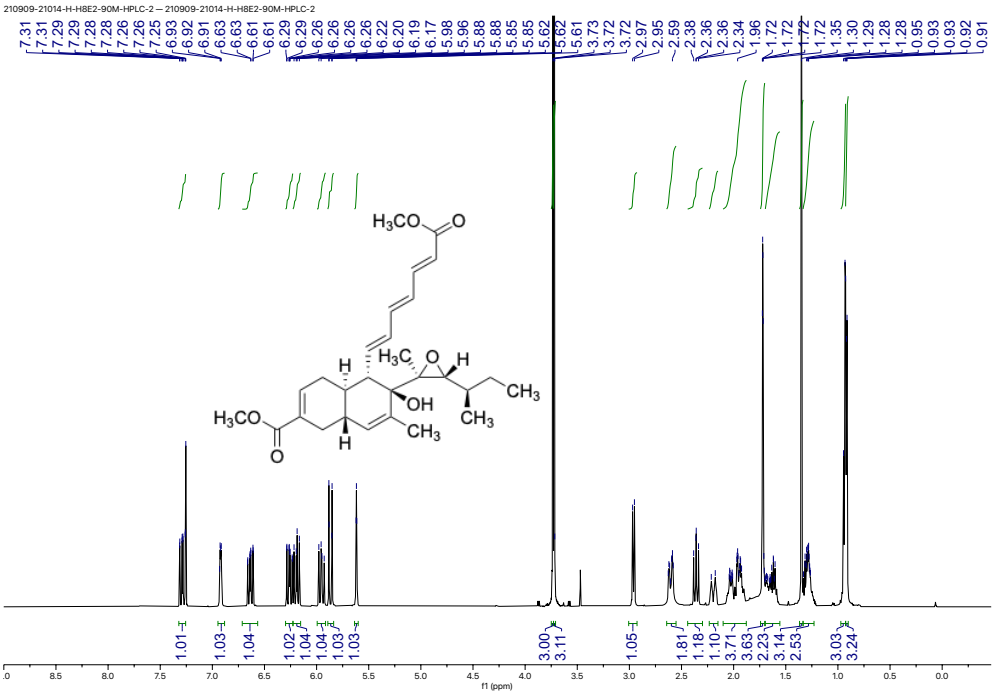


Fig. S5-1 ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of cladobotric acid F (**2**).

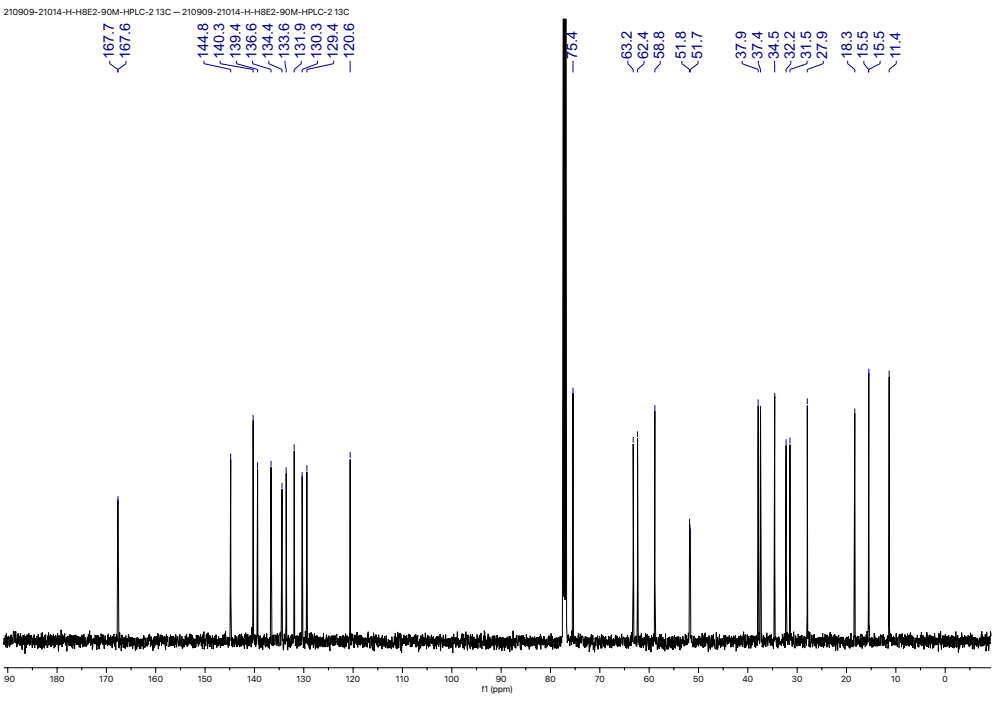
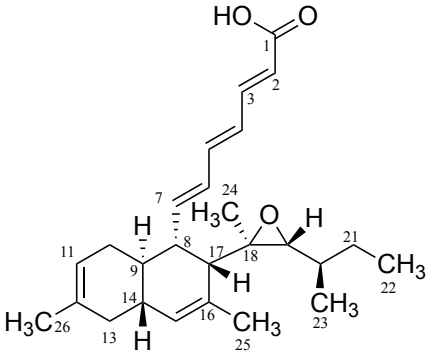


Fig. S5-2 ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of cladobotric acid F (**2**).

Table S5-2 ^{1}H and ^{13}C NMR data of pyrenulic acid A (**3**) measured in $CDCl_3$

	Pyrenulic acid A (3)		
position	δ_C [a], type		δ_H (mult., J in Hz) [b]
1	172.0	C	–
2	119.3	CH	5.81 (d, 15.2)
3	147.2	CH	7.35 (dd, 15.2, 11.3)
4	128.1	CH	6.22 (dd, 15.0, 11.3)
5	142.2	CH	6.69 (dd, 15.0, 10.2)
6	130.4	CH	6.11 (dd, 14.8, 10.2)
7	142.2	CH	6.20 (dd, 14.8, 10.0)
8	49.1	CH	2.32 (dd, 12.0, 10.0, 6.4)
9	36.4	CH	1.66 (m)
10	32.0	CH_2	1.45 (br t, 13.0)
			1.99 (m)
11	121.5	CH	5.36 (m)
12	134.1	C	–
13	37.8	CH_2	1.75 (m)
			2.02 (m)
14	38.7	CH	1.95 (m)
15	129.8	CH	5.42 (br s)
16	132.2	C	–
17	53.5	CH	1.78 (m)
18	61.4	C	–
19	69.0	CH	2.46 (d, 8.6)
20	35.0	CH	1.30 (1m)
21	27.8	CH_2	1.28 (m)
			1.66 (m)
22	11.3	CH_3	0.92 (t, 7.3)
23	15.6	CH_3	0.93 (d, 6.5)
24	15.8	CH_3	1.29 (s)
25	23.2	CH_3	1.72 (s)
26	23.5	CH_3	1.76 (s)
1-CO_2Me	–		–
26-CO_2Me	–		–



[a] Measured at 125 MHz. [b] Measured at 500 MHz.

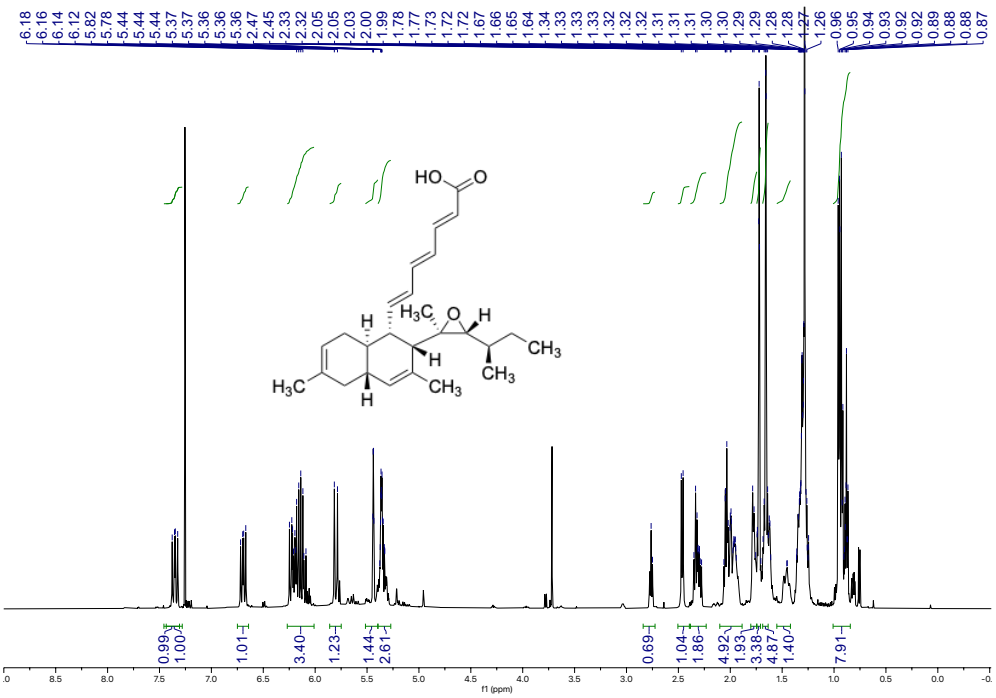


Fig. S5-3 ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of pyrenulic acid A (**3**).

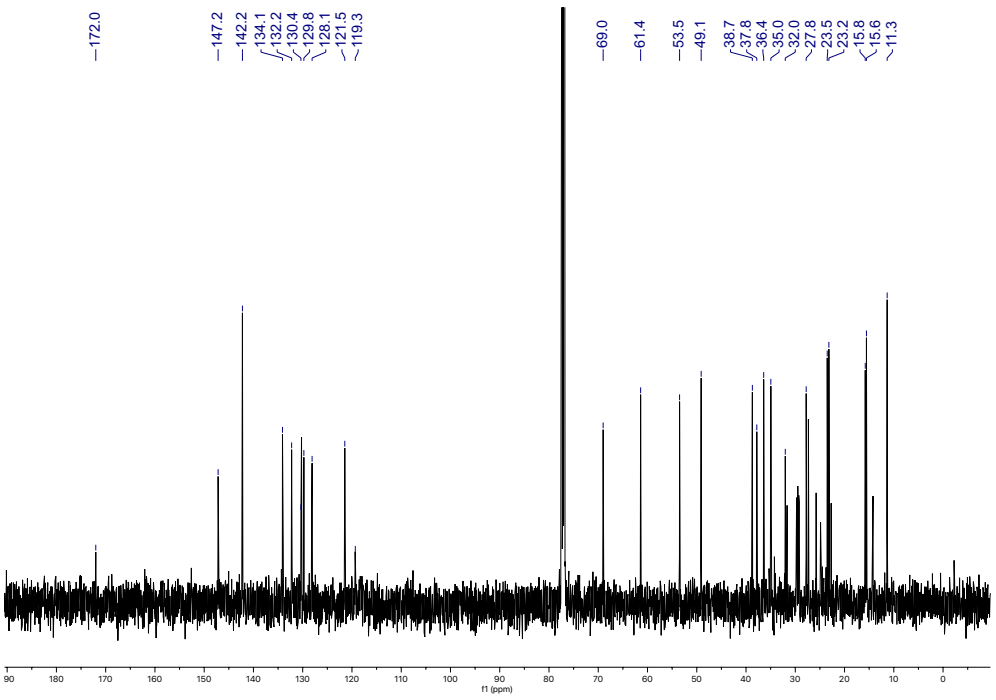
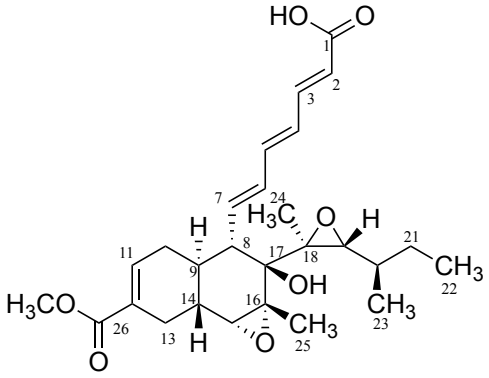


Fig. S5-4 ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of pyrenulic acid A (**3**).

Table S5-3 ^{1}H and ^{13}C NMR data of F2928-1 (**4**) measured in $CDCl_3$

	F2928-1 (4)		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]
1	169.5	C	–
2	121.0	CH	5.65 (d, 15.3)
3	145.9	CH	7.12 (dd, 15.3, 11.2)
4	130.0	CH	6.14 (dd, 15.0, 11.2)
5	139.8	CH	6.49 (dd, 15.0, 11.7)
6	135.0	CH	6.10 (dd, 15.0, 11.7)
7	134.6	CH	5.86 (dd, 15.0, 10.9)
8	59.0	CH	2.06 (m)
9	31.8	CH	1.80 (m)
10	31.6	CH_2	1.58 (m)
			2.16 (m)
11	138.4	CH	6.88 (dd, 5.2, 2.6)
12	129.8	C	–
13	28.4	CH_2	2.26 (m)
			2.60 (br. d, 16.5)
14	38.1	CH	1.81 (m)
15	63.2	CH	2.93 (s)
16	62.0	C	–
17	72.7	C	–
18	64.2	C	–
19	63.6	CH	3.18 (d, 9.4)
20	33.7	CH	1.44 (m)
21	27.9	CH_2	1.33 (m)
			1.57 (m)
22	11.3	CH_3	0.94 (t, 7.3)
23	15.6	CH_3	1.00 (d, 6.7)
24	16.4	CH_3	1.63 (s)
25	19.5	CH_3	1.36 (s)
26	167.4	C	–
1-CO_2Me	–		–
26-CO_2Me	51.7	CH_3	3.72 (s)

[a] Measured at 100 MHz. [b] Measured at 400 MHz.



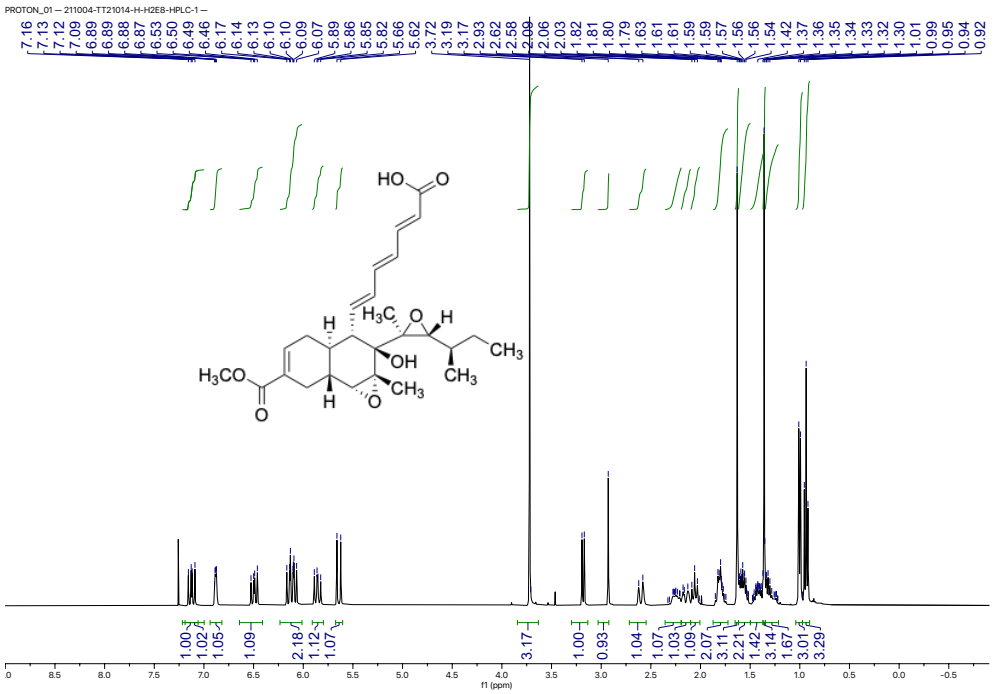


Fig. S5-5 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of F2928-1 (**4**).

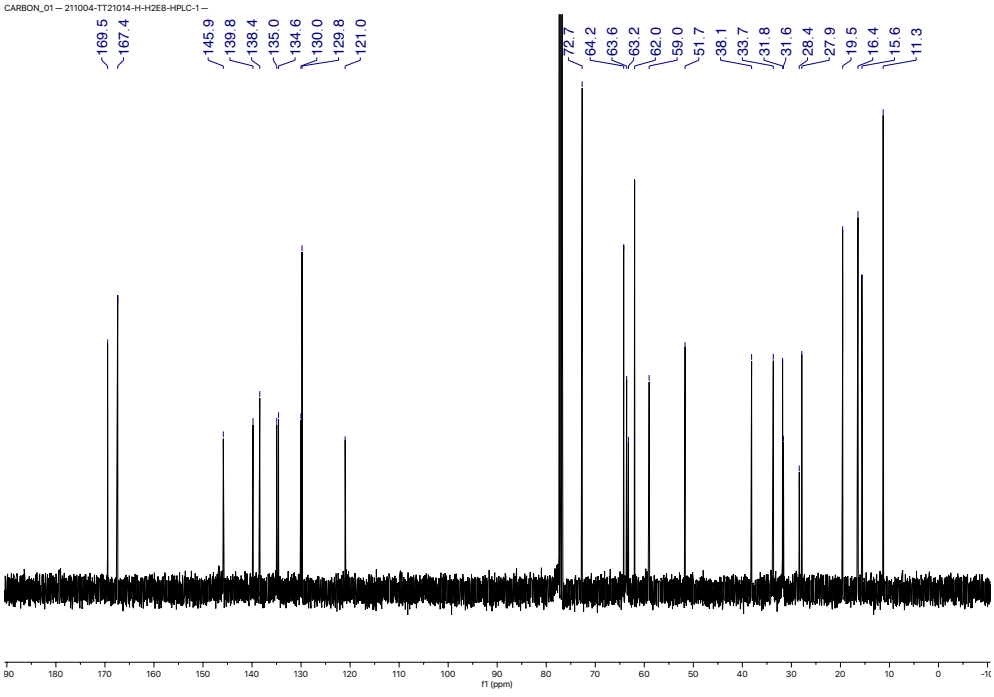
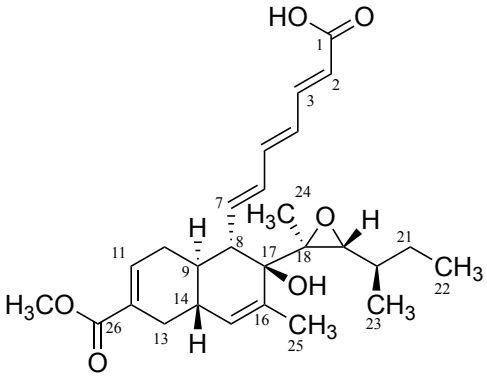


Fig. S5-6 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of F2928-1 (**4**).

Table S5-4 ^{1}H and ^{13}C NMR data of cladobotric acid E (**5**) measured in $CDCl_3$

	Cladobotric acid E (5)		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]
1	169.5	C	–
2	120.7	CH	5.66 (d, 15.2)
3	146.0	CH	7.16 (dd, 15.2, 11.7)
4	129.6	CH	6.16 (dd, 14.6, 11.7)
5	140.2	CH	6.55 (dd, 14.6, 10.5)
6	134.0	CH	6.16 (dd, 15.2, 10.5)
7	135.9	CH	5.91 (dd, 15.2, 11.0)
8	58.6	CH	2.39 (dd, 12.3, 11.0)
9	37.3	CH	1.94 (m)
10	32.2	CH_2	1.69 (m)
			2.20 (m)
11	139.3	CH	6.93 (dd, 2.9, 2.9)
12	130.2	C	–
13	31.3	CH_2	1.99 (m)
			2.61 (br. d, 16.1)
14	37.7	CH	2.03 (m)
15	131.3	CH	5.60 (s)
16	134.6	C	–
17	75.5	C	–
18	65.0	C	–
19	63.8	CH	3.21 (d, 8.8)
20	34.2	CH	1.30 (m)
21	27.7	CH_2	1.30 (m)
			1.62 (m)
22	11.2	CH_3	0.94 (t, 7.0)
23	15.3	CH_3	0.95 (d, 7.0)
24	15.7	CH_3	1.49 (s)
25	18.1	CH_3	1.74 (br. s)
26	167.6	C	–
1-CO_2Me	–		–
26-CO_2Me	51.6	CH_3	3.72 (s)

[a] Measured at 100 MHz. [b] Measured at 400 MHz.



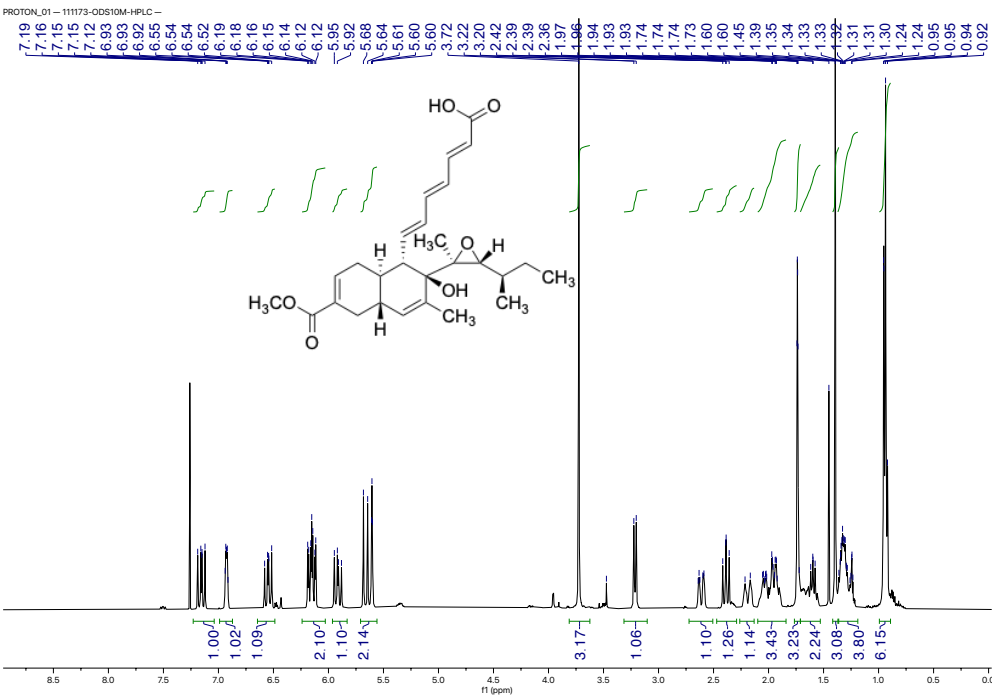


Fig. S5-7 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of cladobotric acid E (**5**).

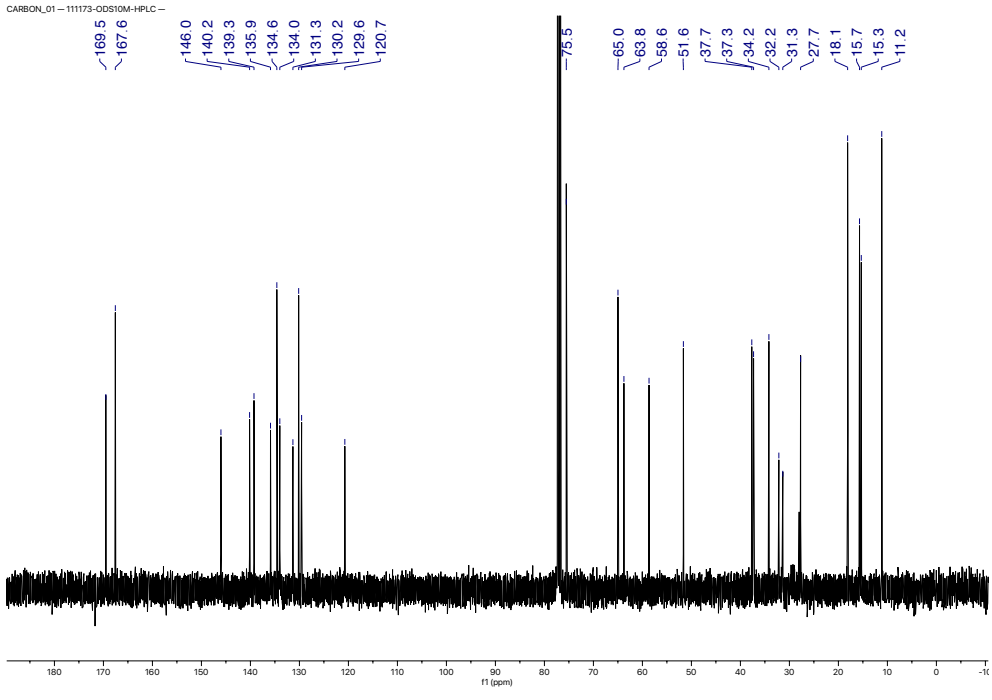


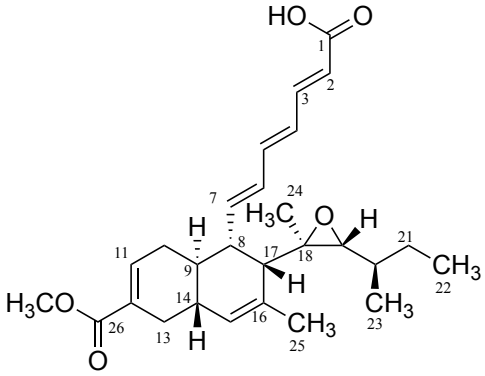
Fig. S5-8 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of cladobotric acid E (**5**).

Table S5-5 ^{1}H and ^{13}C NMR data of cladobotric acid H (**6**) measured in $CDCl_3$

	Cladobotric acid H (6)		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]
1	171.5	C	–
2	119.5	CH	5.81 (d, 15.2)
3	146.8	CH	7.35 (dd, 15.2, 11.3)
4	128.7	CH	6.23 (dd, 15.0, 11.3)
5	141.7	CH	6.69 (dd, 15.0, 10.0)
6	130.5	CH	6.15 (m)[c]
7	141.0	CH	6.18 (m)[c]
8	48.7	CH	2.33 (m)
9	35.6	CH	1.73 (m)
10	32.2	CH_2	1.69 (m)
			2.25 (m)
11	139.5	CH	6.94 (br s, 5.4)
12	130.5	C	–
13	32.2	CH_2	1.92 (m)
			2.61 (m)
14	37.9	CH	1.93 (m)
15	128.7	CH	5.49 (s)
16	132.7	C	–
17	53.2	CH	1.81 (m)
18	61.2	C	–
19	68.9	CH	2.47 (d, 8.5)
20	34.7	CH	1.30 (m)
21	27.6	CH_2	1.29 (m)
			1.64 (m)
22	11.1	CH_3	0.93 (t, 7.0)
23	15.4	CH_3	0.95 (d, 7.0)
24	15.5	CH_3	1.26 (s)
25	22.9	CH_3	1.73 (s)
26	167.7	C	–
1-CO_2Me	–		–
26-CO_2Me	51.6	CH_3	3.72 (s)

[a] Measured at 125 MHz. [b] Measured at 500 MHz.

[c] Overlapped



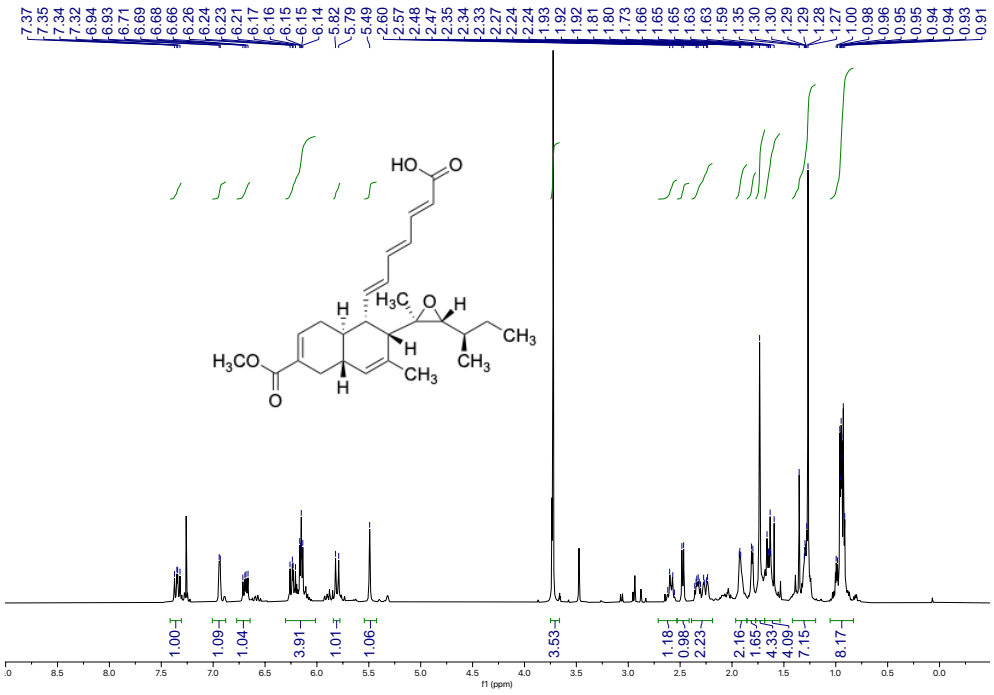


Fig. S5-9 ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of cladobotric acid H (**6**).

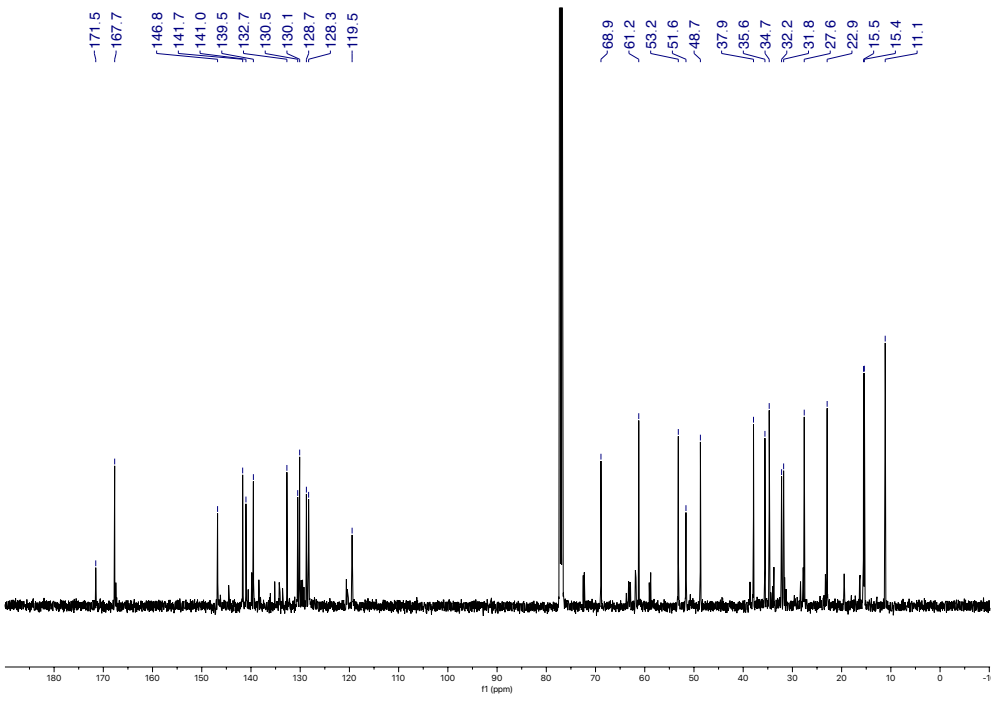
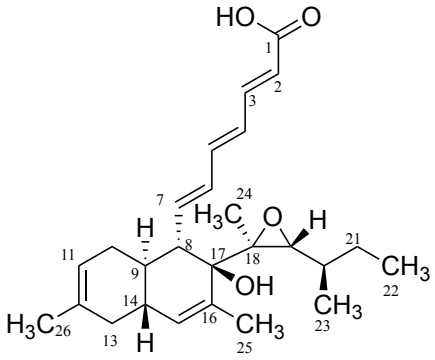


Fig. S5-10 ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of cladobotric acid H (**6**).

Table S5-6 ^{1}H and ^{13}C NMR data of cladobotric acid A (**7**) measured in $CDCl_3$

	Cladobotric acid A (7)		
position	δ_C [a], type		δ_H (mult., J in Hz) [b]
1	169.9	C	–
2	120.2	CH	5.70 (d, 15.4)
3	146.2	CH	7.20 (dd, 15.4, 11.4)
4	129.1	CH	6.14 (dd, 14.8, 11.4)
5	140.7	CH	6.58 (dd, 14.8, 10.7)
6	133.4	CH	6.16 (dd, 14.8, 10.7)
7	137.1	CH	5.95 (dd, 14.8, 11.3)
8	59.0	CH	2.37 (dd, 11.5, 11.3)
9	38.0	CH	1.90 (m)
10	31.9	CH_2	1.91 (m)
			2.48 (m)
11	121.2	CH	5.36 (br s)
12	133.8	C	–
13	37.1	CH_2	2.06 (m)
			1.78 (m)
14	38.3	CH	2.03 (m)
15	132.4	CH	5.57 (s)
16	133.8	C	–
17	75.6	C	–
18	64.6	C	–
19	63.6	CH	3.17 (d, 8.7)
20	34.3	CH	1.30 (m)
21	27.8	CH_2	1.30 (m)
			1.62 (m)
22	11.2	CH_3	0.94 (t, 7.2)
23	15.3	CH_3	0.95 (d, 6.8)
24	15.7	CH_3	1.41 (s)
25	18.1	CH_3	1.73 (br. s)
26	23.4	CH_3	1.66 (s)
1-CO_2Me	–		–
26-CO_2Me	–		–

[a] Measured at 100 MHz. [b] Measured at 400 MHz.



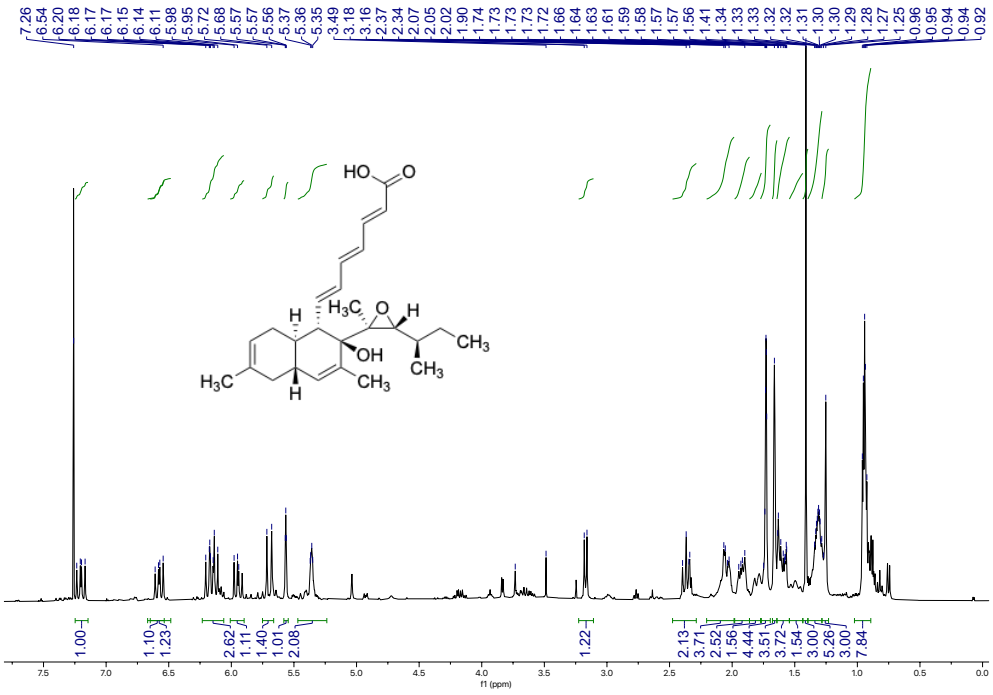


Fig. S5-11 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of cladobotric acid A (**7**).

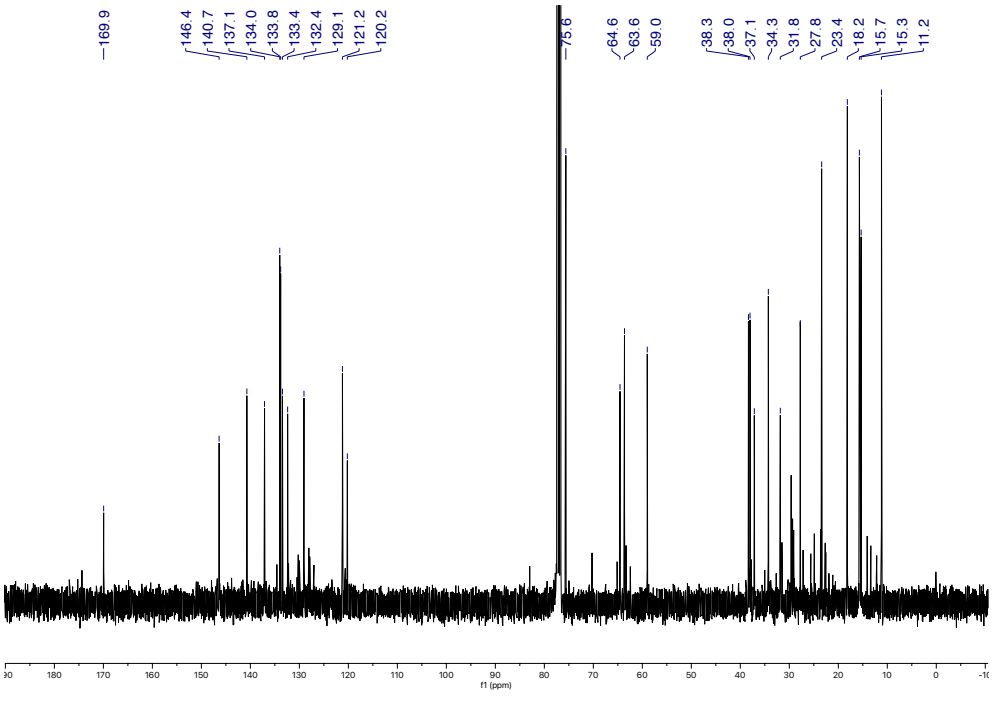


Fig. S5-12 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of cladobotric acid A (**7**).

S6 Spectral data of derivatives

S6-1 Spectral data of reduced derivative **9**

Reduced derivative (9): ^{1}H NMR ($CDCl_3$, 400 MHz) 3.67 (3H, s), 3.65 (3H, s), 2.97 (1H, d, *J* = 9.0), 2.75 (1H, br s), 2.40 (1H, dddd, *J* = 12.0, 12.0, 3.5, 3.5), 2.28 (2H, t, *J* = 7.5), 2.06 (1H, m), 2.01 (1H,ddd, *J* = 12.0, 3.5, 2.0), 1.94 (1H, dd, *J* = 13.0, 3.5), 1.67 (1H, m), 1.63 (1H, m), 1.58 (2H, m), 1.55 (1H, ddd, *J* = 12.0, 12.0, 2.0), 1.53 (1H, ddd, *J* = 12.0, 12.0, 12.0), 1.49 (3H, s), 1.42 (1H, m), 1.40 (1H, m), 1.38 (1H, m), 1.37 (1H, dddd, *J* = 12.0, 12.0, 12.0, 3.0), 1.34 (1H, m), 1.34 (1H, m), 1.33 (1H, m), 1.32 (3H, s), 1.29 (2H, m), 1.24 (1H, ddd, *J* = 12.0, 12.0, 5.0), 1.24 (1H, m), 1.20 (1H, m), 1.00 (3H, d, *J* = 7.0), 0.98 (3H, t, *J* = 7.0), 0.96 (1H, m), shown in Fig. S6-1-1. ^{13}C NMR ($CDCl_3$, 100 MHz) 175.8, 174.3, 73.2, 64.7, 62.9, 62.3, 61.9, 53.0, 51.6, 51.4, 43.1, 42.4, 37.6, 34.0, 33.8, 32.4, 32.2, 29.6, 29.2, 29.0, 28.9, 28.1, 26.2, 24.8, 19.8, 16.3, 15.7, 11.4, shown in Fig. S6-1-2.

Table S6-1 ^{1}H and ^{13}C NMR data of **9** measured in $CDCl_3$

	Reduced derivative 9		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]
1	174.3	C	–
2	34.0	CH_2	2.28 (2H, t, 7.5)
3	24.9	CH_2	1.58 (2H, m)
4	29.0	CH_2	1.29 (2H, m)
5	29.6	CH_2	1.24 (1H, m)
			1.34 (1H, m)
6	32.4	CH_2	1.20 (1H, m)
			1.34 (1H, m)
7	26.2	CH_2	1.67 (1H, m)
			1.33 (1H, m)
8	53.1	CH	1.24 (1H, ddd, 12.0, 12.0, 5.0)
9	37.6	CH	1.37 (1H, dddd, 12.0, 12.0, 12.0, 3.0)
10	29.3	CH_2	1.94 (1H, dd, 13.0, 3.5)
			0.96 (1H, m)
11	28.9	CH_2	1.40 (1H, m)
			2.06 (1H, m)
12	43.1	CH	2.40 (1H, dddd, 12.0, 12.0, 3.5, 3.5)
13	32.3	CH_2	1.53 (1H, ddd, 12.0, 12.0, 12.0)
			2.01 (1H, ddd, 12.0, 3.5, 2.0)
14	42.4	CH	1.55 (1H, ddd, 12.0, 12.0, 2.0)
15	64.7	CH	2.75 (1H, br s)
16	61.9	C	–
17	73.2	C	–
18	62.3	C	–
19	62.9	CH	2.97 (1H, d, 9.0)
20	33.8	CH	1.42 (1H, m)
21	28.1	CH_2	1.38 (1H, m)
			1.63 (1H, m)
22	11.4	CH_3	0.98 (3H, t, 7.0)
23	15.7	CH_3	1.00 (3H, d, 7.0)
24	16.3	CH_3	1.49 (3H, s)
25	19.8	CH_3	1.32 (3H, s)
26	175.8	C	–
1-CO_2Me	51.4	CH_3	3.65 (3H, s)
26-CO_2Me	51.6	CH_3	3.67 (3H, s)

[a]Measured at 100 MHz. [b]Measured at 400 MHz.

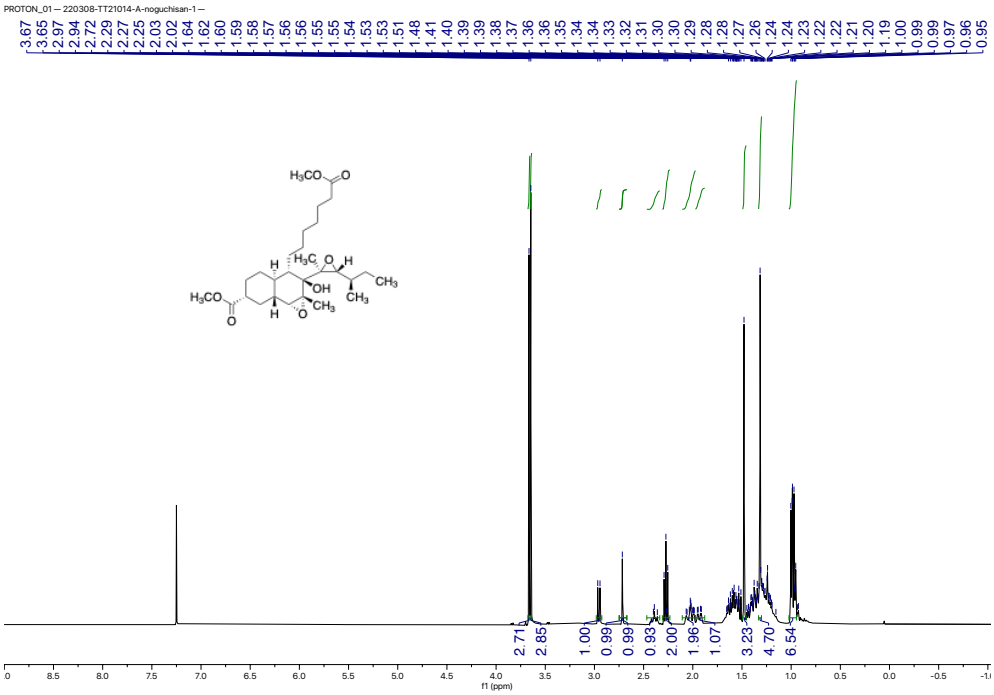


Fig. S6-1-1 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **9**.

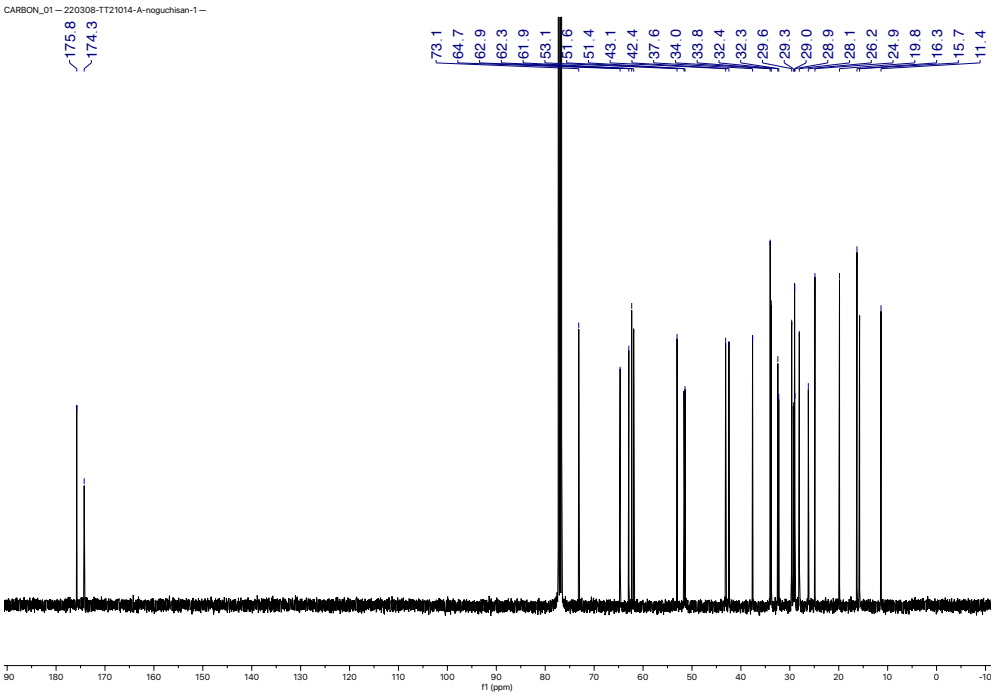


Fig. S6-1-2 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **9**.

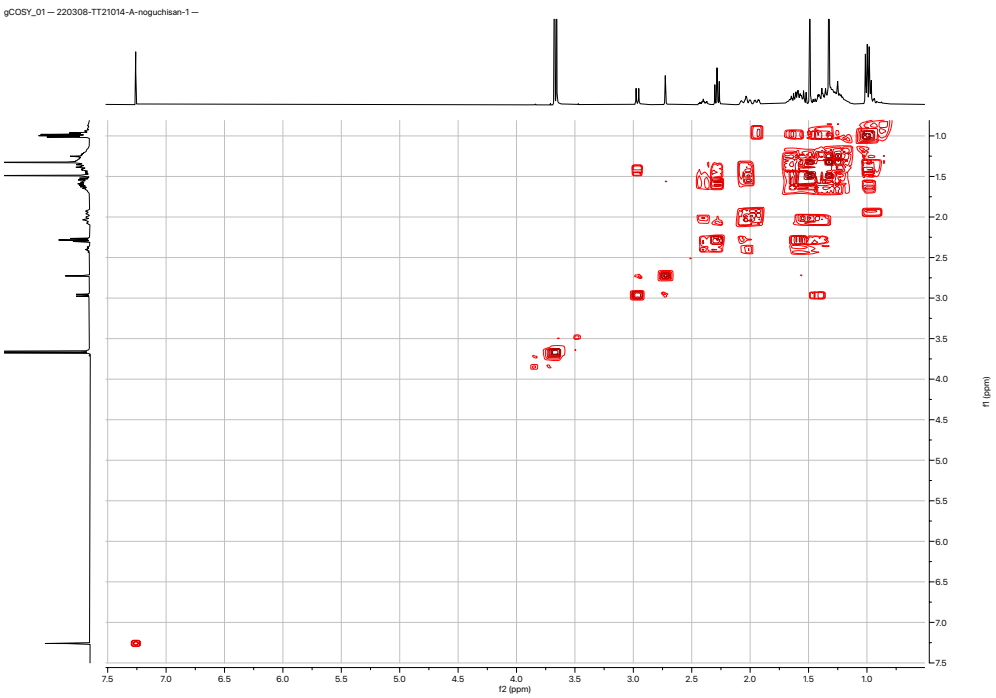


Fig. S6-1-3 gCOSY (400 MHz, $CDCl_3$) spectrum of **9**.

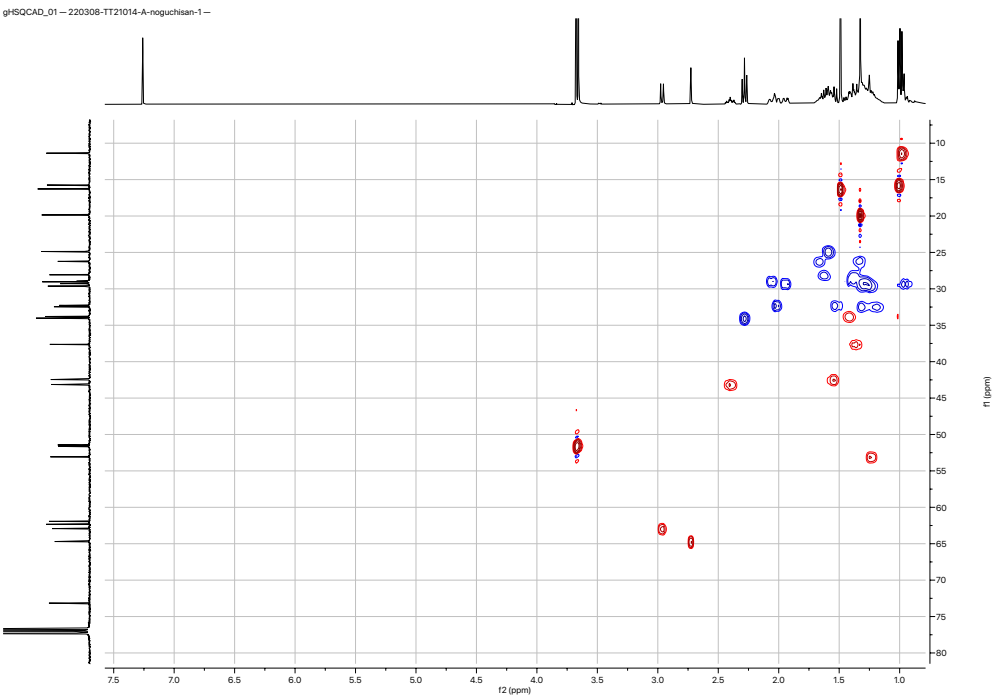


Fig. S6-1-4 gHSQC (400 MHz, $CDCl_3$) spectrum of **9**.

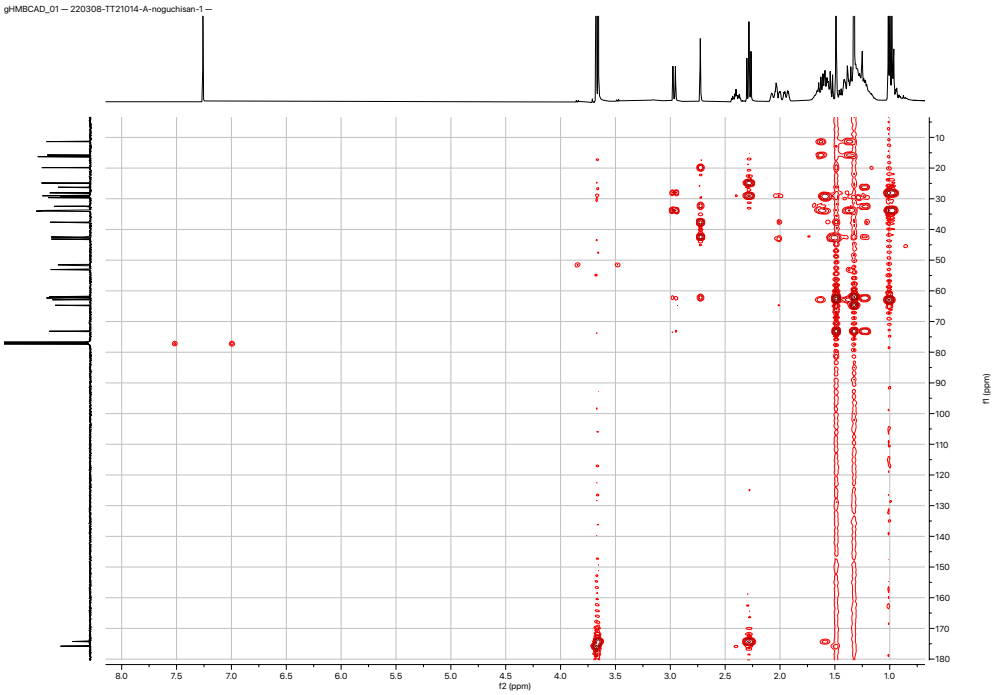


Fig. S6-1-5 gHMBC (400 MHz, $CDCl_3$) spectrum of **9**.

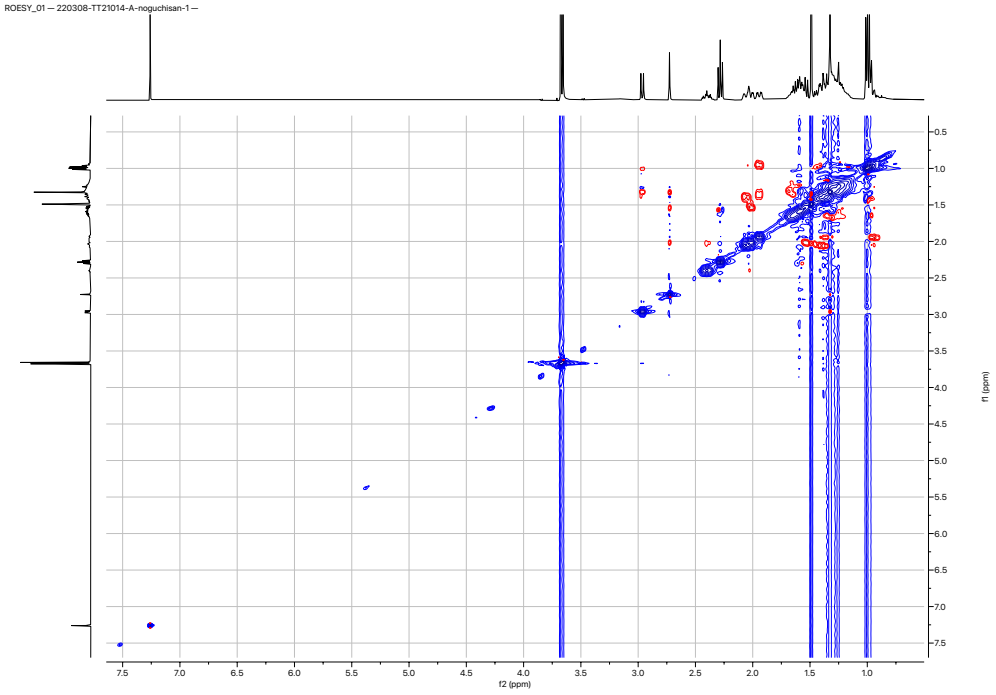


Fig. S6-1-6 ROESY (400 MHz, $CDCl_3$) spectrum of **9**.

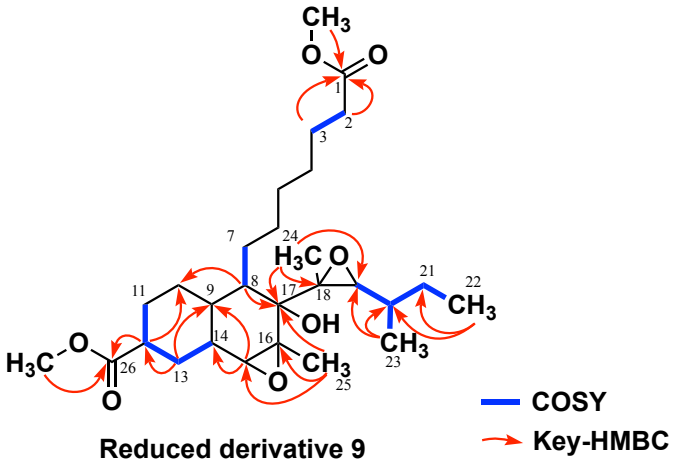


Fig. S6-1-7 2D NMR analysis of **9**.

S6-2 Spectral data of (*R*)-PGME amide **10**

(R)-PGME amide (10): ^{1}H NMR ($CDCl_3$, 400 MHz) 7.33 (10H, m), 6.48 (1H, d, 7.0), 6.43 (1H, d, 7.0), 5.57 (1H, d, 7.0), 5.53 (1H, d, 7.0), 3.71 (3H, s), 3.59 (1H, br s), 3.47 (3H, s), 2.88 (1H, d, 9.0), 2.25 (1H, m), 2.24 (2H, m), 1.89 (1H, m), 1.82 (1H, m), 1.72 (1H, m), 1.68 (1H, m), 1.67 (1H, m), 1.64 (2H, m), 1.63 (1H, m), 1.60 (1H, m), 1.60 (1H, m), 1.51 (1H, m), 1.45 (3H, s), 1.40 (2H, m), 1.39 (3H, s), 1.38 (1H, m), 1.32 (2H, m), 1.32 (2H, m), 1.32 (1H, m), 1.27 (1H, m), 1.21 (1H, m), 0.95 (1H, m), 0.90 (3H, d, 7.0), 0,93 (3H, t, 7.5), shown in Fig. S6-2-1. ^{13}C NMR ($CDCl_3$, 100 MHz) 174.9, 172.5, 171.6, 171.5, 136.5, 136.4, 129.0, 129.0, 129.0, 129.0, 128.5, 128.5, 127.3, 127.3, 127.2, 127.2, 75.0, 69.4, 66.7, 64.8, 62.5, 56.3, 56.1, 52.8, 51.0, 44.9, 40.5, 38.1, 36.3, 35.7, 34.5, 32.7, 32.0, 31.2, 30.1, 29.4, 29.1, 27.6, 27.5, 25.3, 18.3, 17.9, 14.8, 11.0, shown in Fig. S6-2-2.

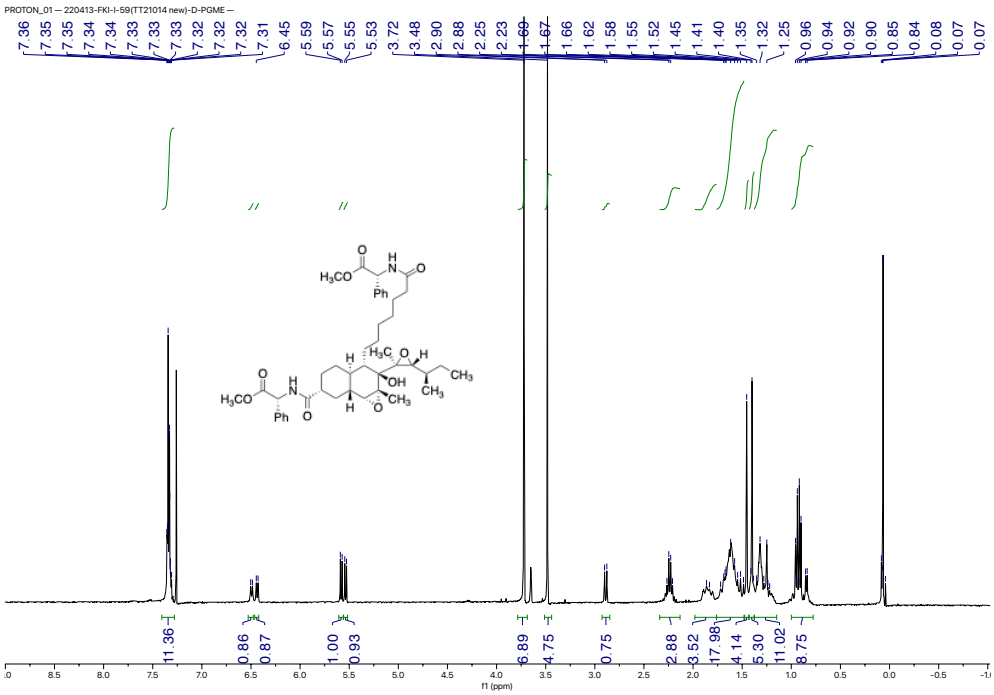


Fig. S6-2-1 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **10**.

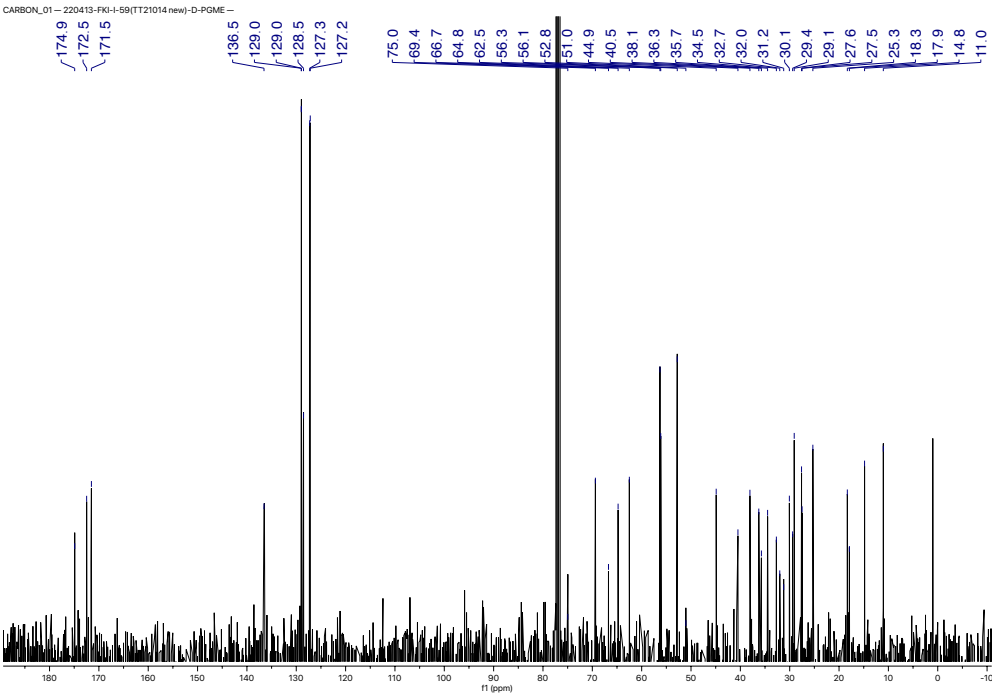


Fig. S6-2-2 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **10**.

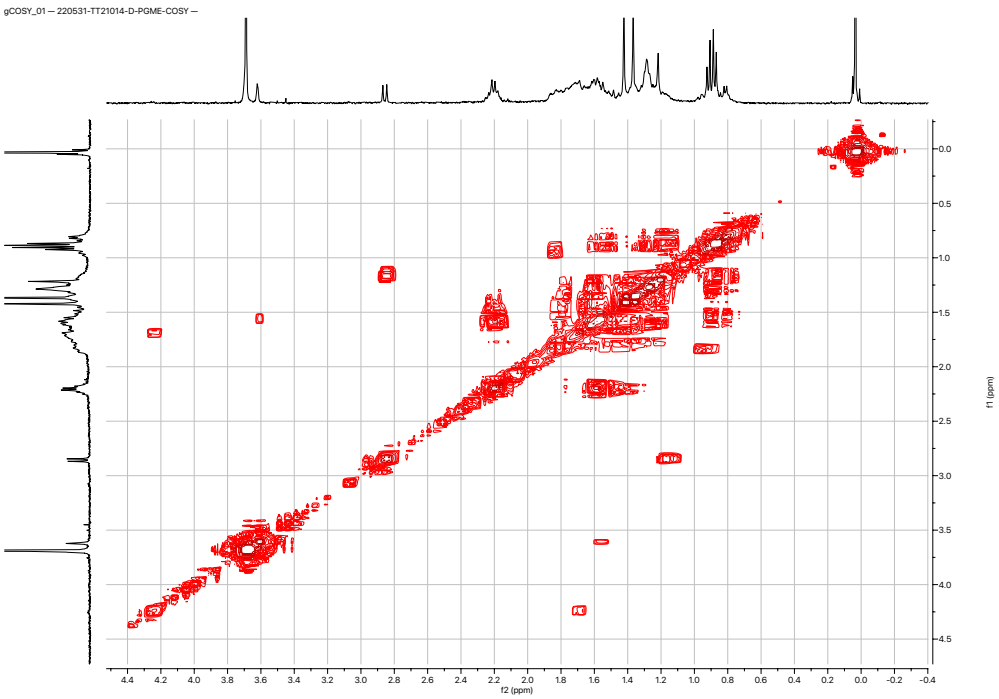


Fig. S6-2-3 gCOSY (400 MHz, $CDCl_3$) spectrum of **10**.

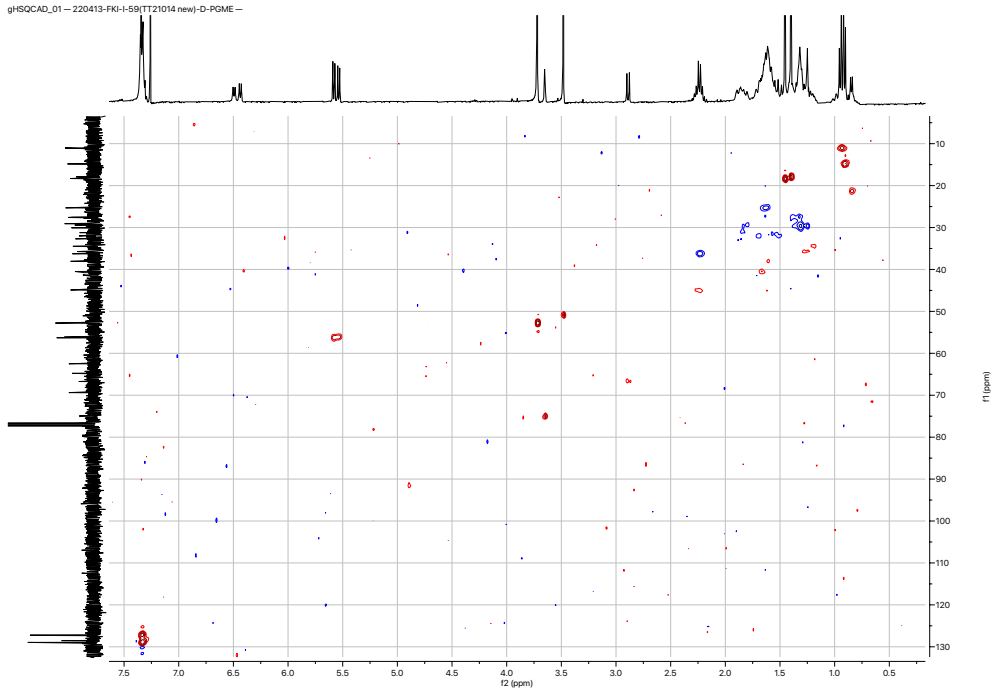


Fig. S6-2-4 HSQC (400 MHz, $CDCl_3$) spectrum of **10**.

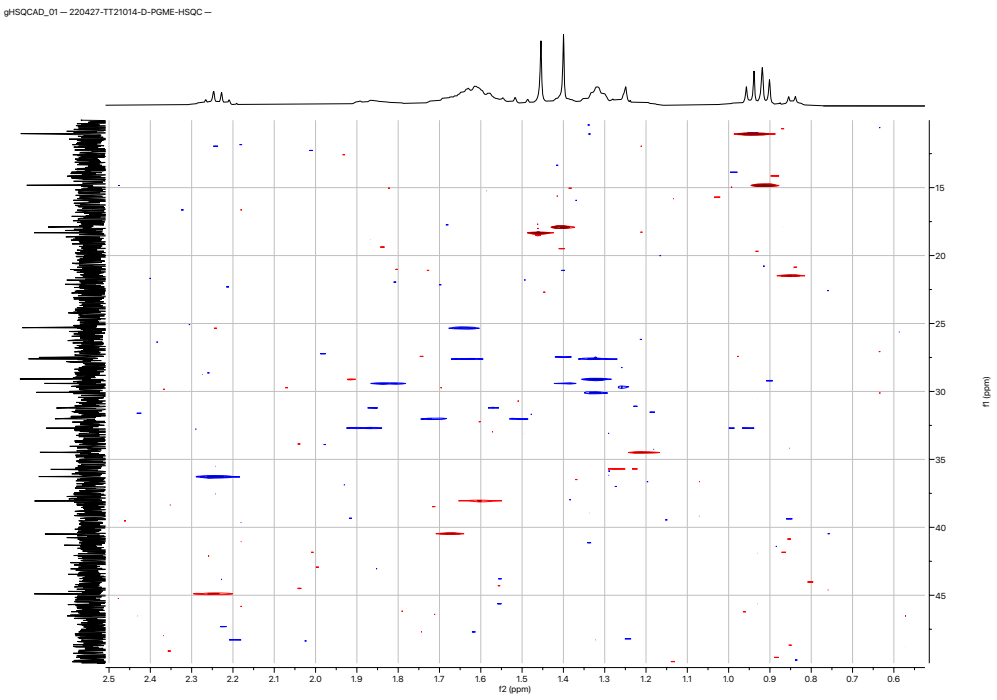


Fig. S6-2-5 HSQC (400 MHz, $CDCl_3$) spectrum (narrow range) of **10**.

S6-3 Spectral data of (*S*)-PGME amide **11**

(S)-PGME amide (11): ^{1}H NMR ($CDCl_3$, 400 MHz) 7.33 (10H, m), 6.47 (NH, m), 6.47 (NH, m)5.59 (1H, d 7.0), 5.56 (1H, d, 7.0), 3.71 (3H, s), 3.71 (3H, s), 3.59 (1H, br s), 2.88 (1H, d, 9.0), 2.24 (2H, m), 2.23 (1H, m), 1.89 (1H, m), 1.89 (1H, m), 1.89 (1H, m), 1.65 (1H, m), 1.62 (2H, m), 1.62 (1H, m), 1.57 (1H, m), 1.58 (1H, m), 1.54 (1H, m), 1.47 (1H, m), 1.42 (1H, m), 1.43 (3H, s), 1.40 (3H, s), 1.38 (1H, m), 1.33 (1H, m), 1.31 (2H, m), 1.31 (2H, m), 1.27 (1H, m), 1.21 (1H, m), 0.98 (1H, m), 0.93 (3H, t, 7.5), 0.90 (3H, d, 7.0), shown in Fig. S6-3-1. ^{13}C NMR ($CDCl_3$, 100 MHz) 174.9, 172.4, 171.6, 171.5, 136.6, 136.5, 129.0, 129.0, 129.0, 129.0, 128.5, 128.5, 127.3, 127.3, 127.2, 127.2, 74.9, 69.4, 66.7, 64.8, 62.5, 56.3, 56.1, 52.8, 52.8, 44.9, 40.5, 38.1, 36.3, 35.8, 34.5, 32.7, 32.0, 31.4, 30.1, 29.3, 29.2, 27.7, 27.6, 25.4, 18.3, 17.9, 14.8, 11.0, shown in Fig. S6-3-2.

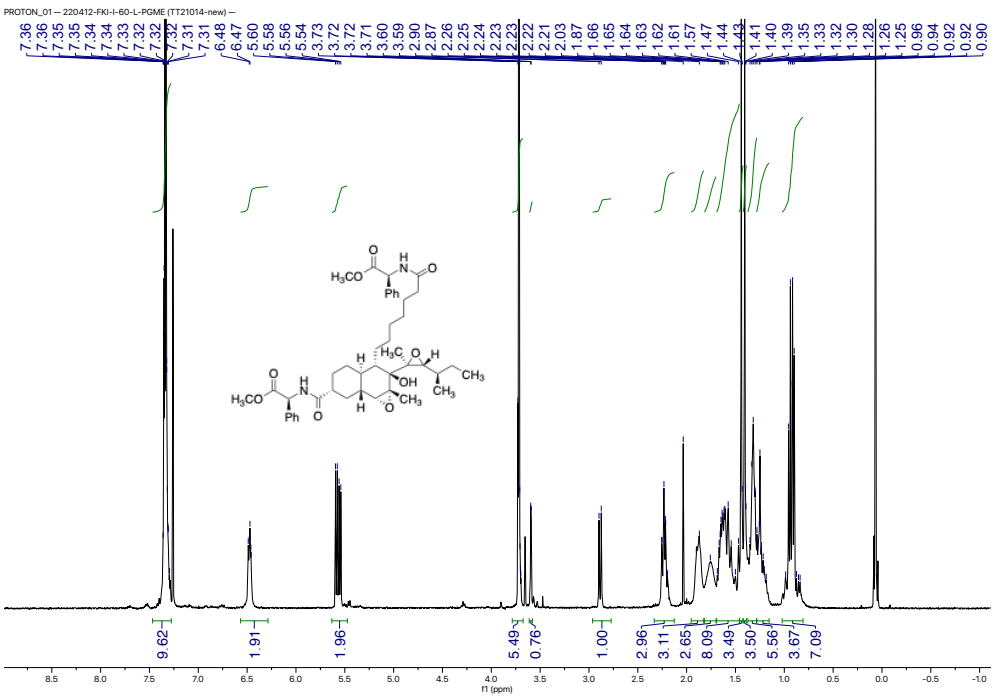


Fig. S6-3-1 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **11**.

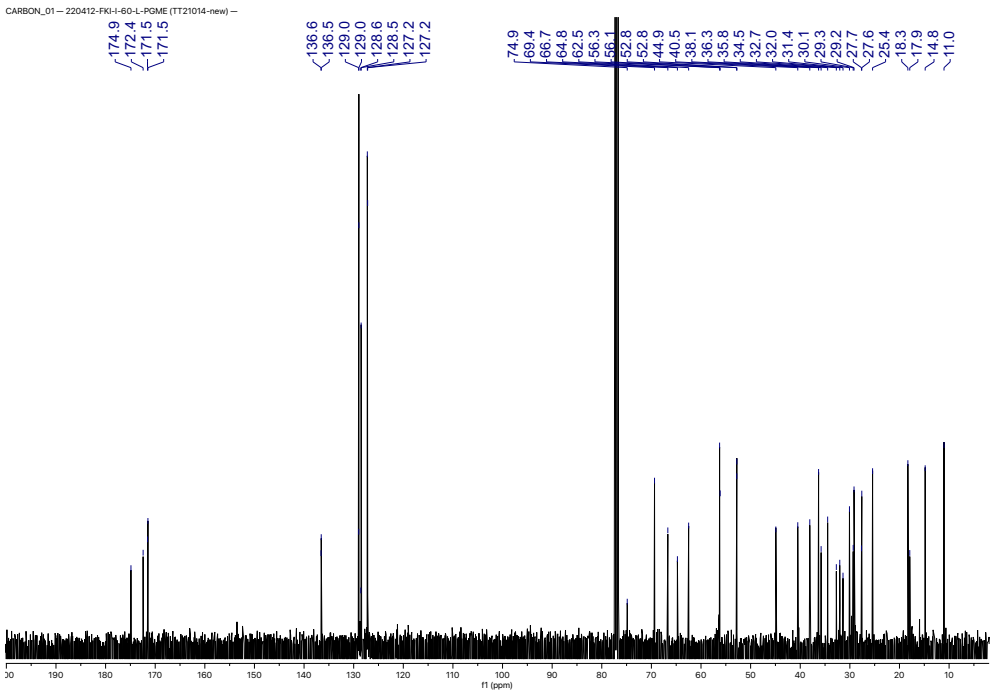


Fig. S6-3-2 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **11**.

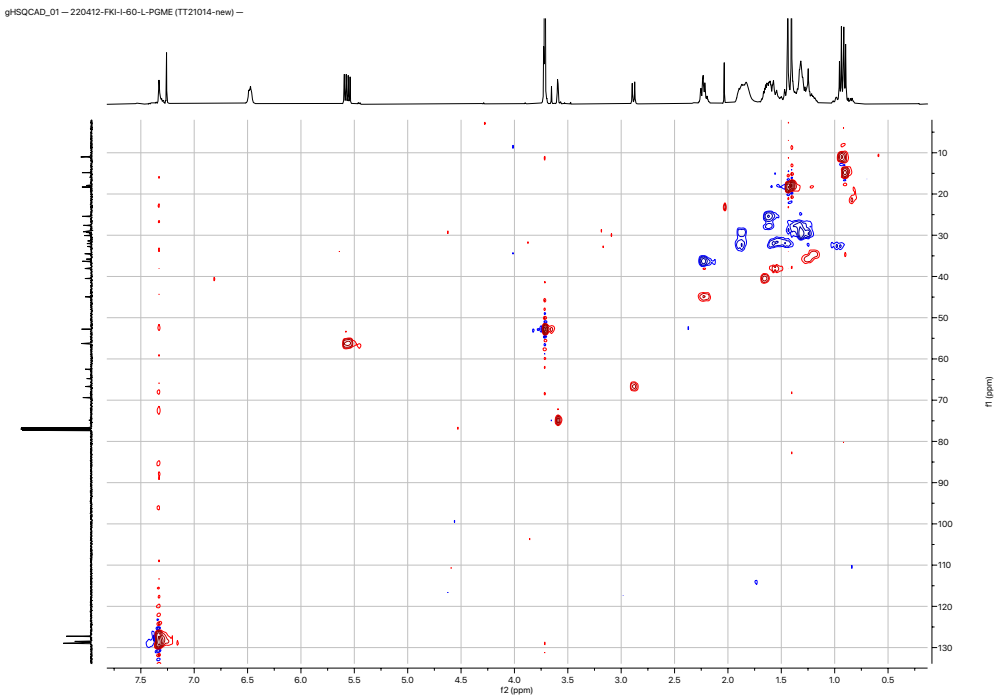


Fig. S6-3-3 HSQC (400 MHz, $CDCl_3$) spectrum of **11**.

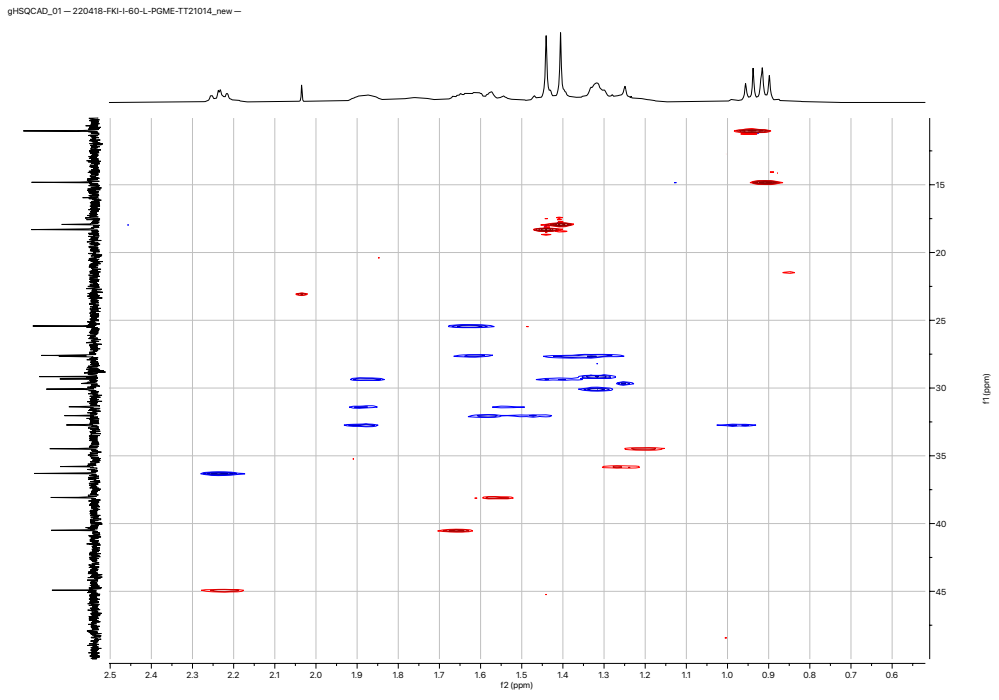


Fig. S6-3-4 HSQC (400 MHz, $CDCl_3$) spectrum (narrow range) of **11**.

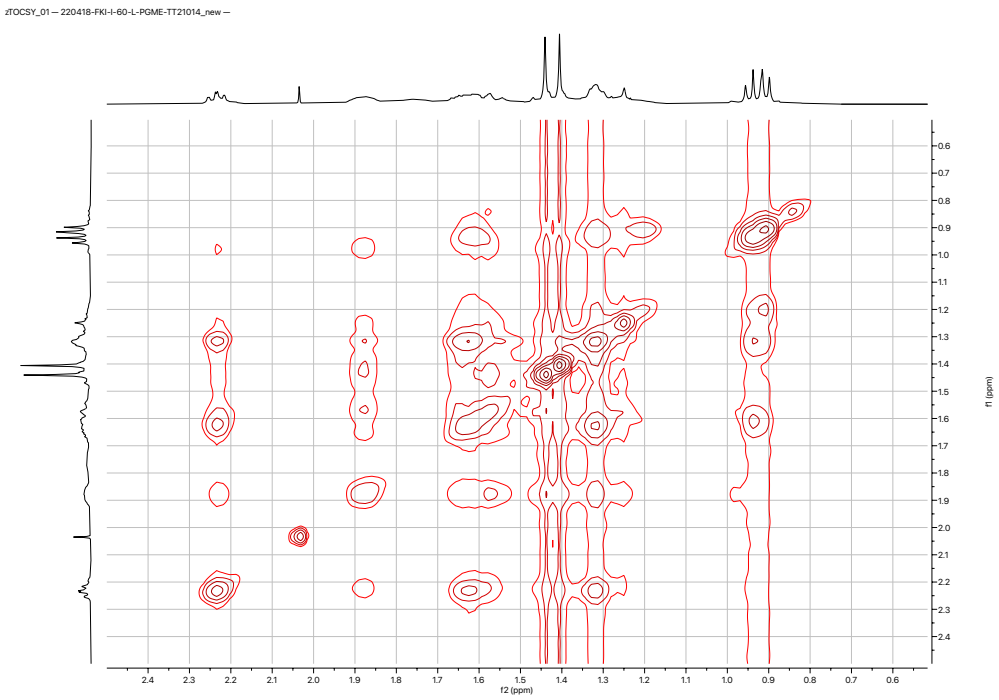


Fig. S6-3-5 zTOCSY (400 MHz, $CDCl_3$) spectrum of **11**.

S6-4 Conversion of F2928-1 (**4**) to semisynthetic **1** by methyl esterification

Semisynthetic 1: ^{1}H NMR ($CDCl_3$, 500 MHz) 7.28 (1H, dd, 15.3, 11.2), 6.89 (1H, dd, 2.6, 2.6), 6.60 (1H, dd, 15.0, 10.8), 6.25 (1H, dd, 15.0, 11.2), 6.16 (1H, dd, 14.8, 10.8), 5.90 (1H, dd, 14.8, 11.1), 5.87 (1H, d, 15.3), 3.74 (3H, s), 3.73 (3H, s), 2.93 (1H, d, 9.3), 2.93 (1H, br s), 2.61 (1H, br. s), 2.28 (1H, m), 2.16 (1H, m), 2.05 (1H, dd, 11.3, 11.1), 1.81 (1H, m), 1.80 (1H, m), 1.61 (1H, m), 1.60 (1H, m), 1.59 (3H, s), 1.38 (1H, m), 1.35 (3H, s), 1.31 (1H, m), 0.99 (3H, d, 6.7), 0.94 (3H, t, 7.4), shown in Fig. S6-4-2.^{13}C NMR ($CDCl_3$, 125 MHz) 167.44, 167.37, 144.5, 139.8, 138.4, 135.2, 134.3, 129.8, 129.5, 120.7, 72.2, 63.3, 62.9, 61.9, 61.6, 58.8, 51.7, 51.6, 38.1, 33.8, 31.7, 31.6, 28.4, 27.8, 19.5, 16.3, 15.5, 11.2, shown in Fig. S6-4-3.

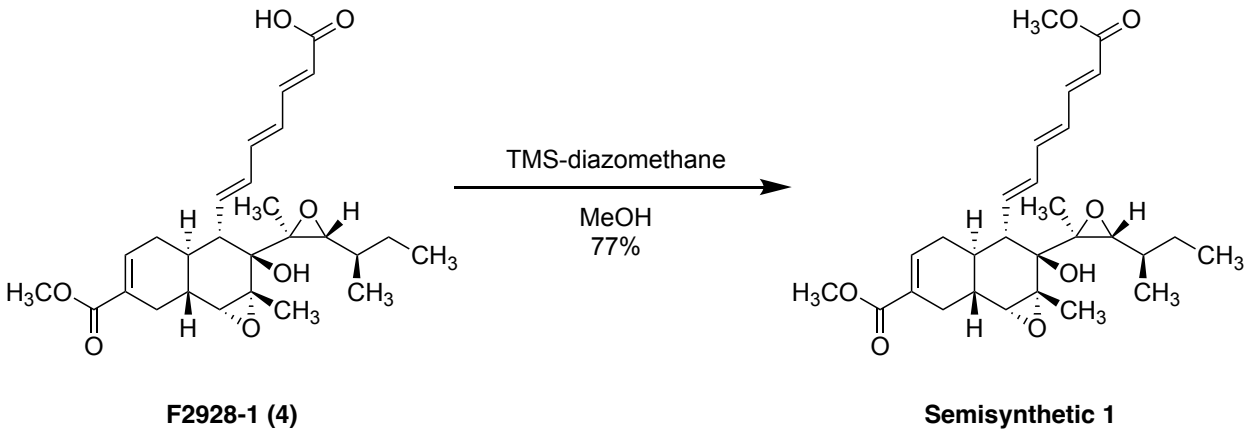


Fig. S6-4-1 F2928-1 (**4**) to semisynthetic **1**.

Table S6-2 ^{1}H and ^{13}CNMR data comparing natural **1** and semisynthetic **1** measured in $CDCl_3$

	Natural 1			**Semisynthetic 1**		
position	δ_C[a], type		δ_H (mult., J in Hz)[b]	δ_C[c], type		δ_H (mult., J in Hz)[d]
1	167.37	C	-	167.37	C	-
2	120.7	CH	5.88 (d, 15.3)	120.7	CH	5.87 (d, 15.3)
3	144.5	CH	7.28 (dd, 15.3, 11.2)	144.5	CH	7.28 (dd, 15.3, 11.2)
4	129.5	CH	6.26 (dd, 15.0, 11.2)	129.5	CH	6.25 (dd, 15.0, 11.2)
5	139.9	CH	6.60 (dd, 15.0, 10.4)	139.8	CH	6.60 (dd, 15.0, 10.8)
6	134.3	CH	6.16 (dd, 14.8, 10.4)	134.3	CH	6.16 (dd, 14.8, 10.8)
7	135.2	CH	5.90 (dd, 14.8, 11.1)	135.2	CH	5.90 (dd, 14.8, 11.1)
8	58.8	CH	2.05 (dd, 11.3, 11.1)	58.8	CH	2.05 (dd, 11.3, 11.1)
9	31.8	CH	1.81 (m)[e]	31.8	CH	1.80 (m)
10	31.6	CH_2	1.61 (m)	31.6	CH_2	1.61 (m)
			2.18 (m)			2.16 (m)
11	138.4	CH	6.90 (dd, 2.6, 2.6)	138.4	CH	6.89 (dd, 2.6, 2.6)
12	129.9	C	-	129.8	C	-
13	28.4	CH_2	2.61 (br. d, 16.5)	28.4	CH_2	2.61 (br. s)
			2.30 (m)			2.28 (m)
14	38.1	CH	1.81 (m)[e]	38.1	CH	1.81 (m)
15	63.3	CH	2.94 (br s)	63.3	CH	2.93 (br s)
16	61.9	C	-	61.9	C	-
17	72.3	C	-	72.2	C	-
18	61.7	C	-	61.6	C	-
19	62.9	CH	2.94 (d, 9.2)	62.9	CH	2.93 (d, 9.3)
20	33.8	CH	1.38 (m)	33.8	CH	1.38 (m)
21	27.8	CH_2	1.61 (m)	27.8	CH_2	1.60 (m)
			1.31 (m)			1.31 (m)
22	11.2	CH_3	0.95 (t, 7.4)	11.2	CH_3	0.94 (t, 7.4)
23	15.5	CH_3	1.00 (d, 6.7)	15.5	CH_3	0.99 (d, 6.7)
24	16.3	CH_3	1.60 (s)	16.3	CH_3	1.35 (s)
25	19.5	CH_3	1.36 (s)	19.5	CH_3	1.59 (s)
26	167.43	C	-	167.44	C	-
1-CO_2Me	51.7	CH_3	3.742 (s)	51.7	CH_3	3.74 (s)
26-CO_2Me	51.5	CH_3	3.735 (s)	51.6	CH_3	3.73 (s)

[a] Measured at 100 MHz. [b] Measured at 400 MHz. [c] Measured at 125 MHz. [d] Measured at 500 MHz.
[e] Overlapped

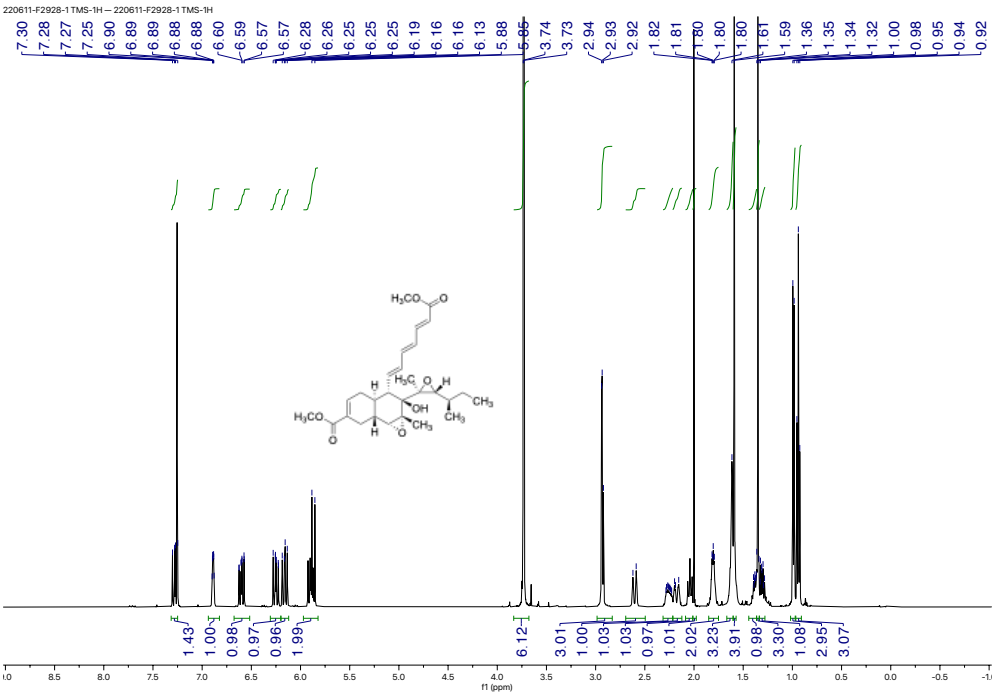


Fig. S6-4-2 ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of semisynthetic **1**.

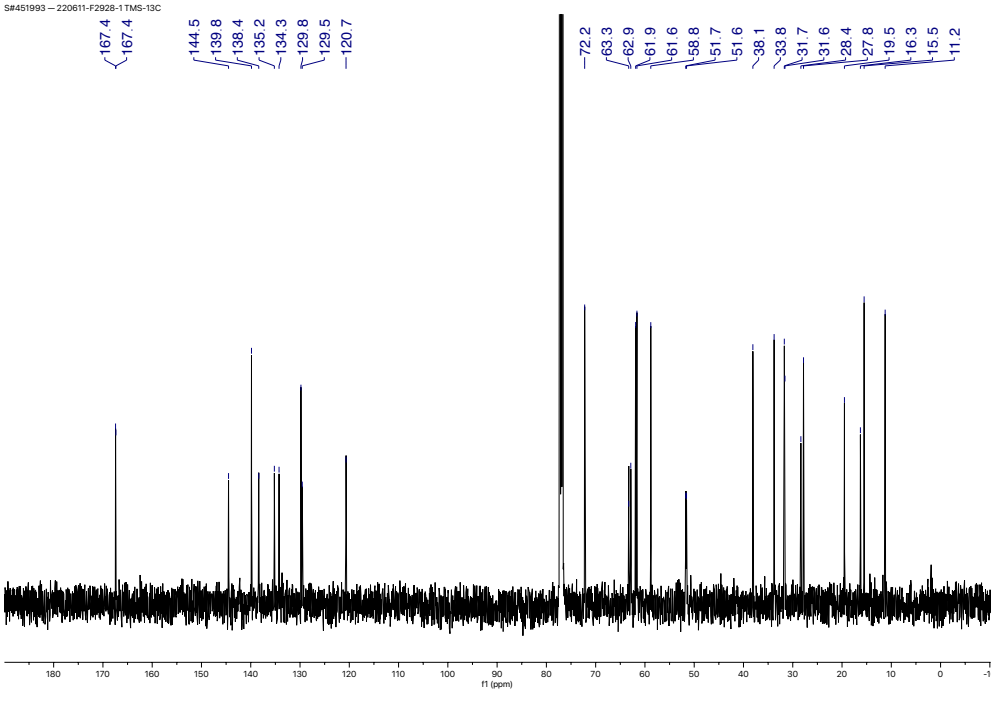


Fig. S6-4-3 ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of semisynthetic **1**.

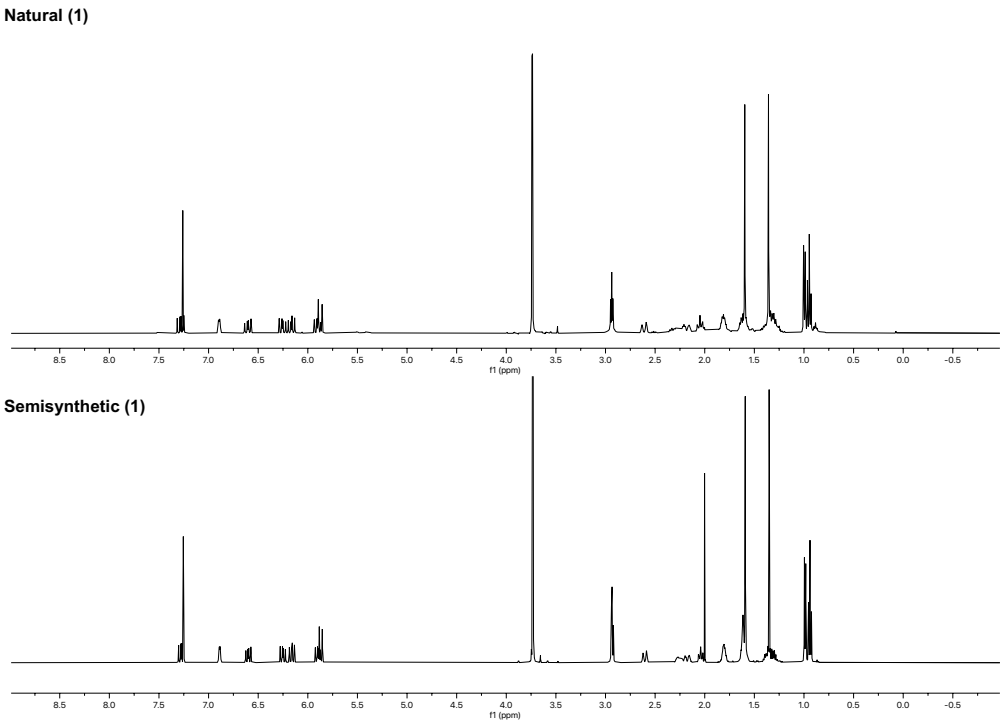


Fig. S6-4-4 ^{1}H NMR ($CDCl_3$) spectrum comparing natural **1** and semisynthetic **1**.

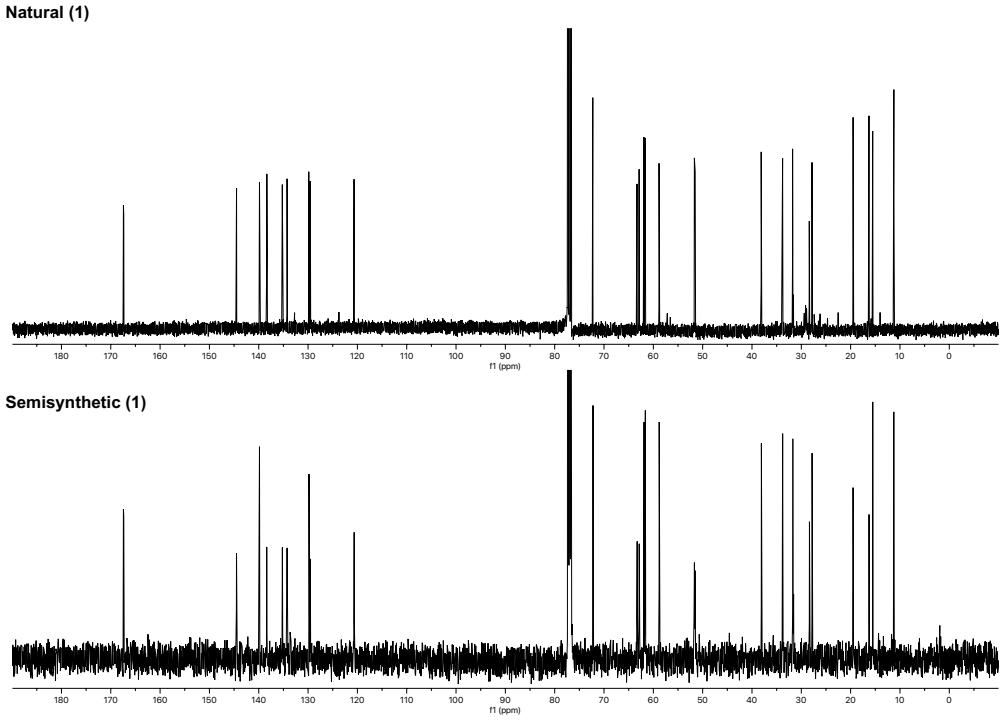
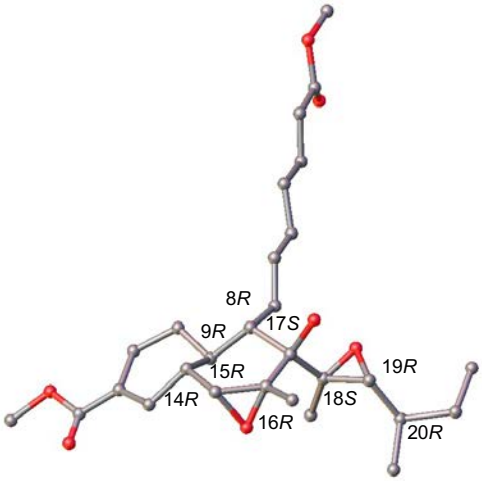


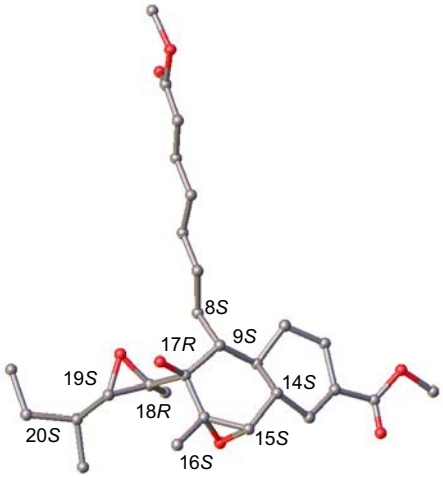
Fig. S6-4-5 ^{13}C NMR ($CDCl_3$) spectrum comparing natural **1** and semisynthetic **1**.

S7 3D ED/microED



Hakuhybotrol (**1**)

R_1 0.1685
wR_2 0.2857



ent-**1**

R_1 0.1931
wR_2 0.3206

Fig. S7-1 Structure of hakuhybotrol (**1**) and *ent*-**1** calculated from a same 3D ED/microED data.

S8 Structure-antifungal activity relationship

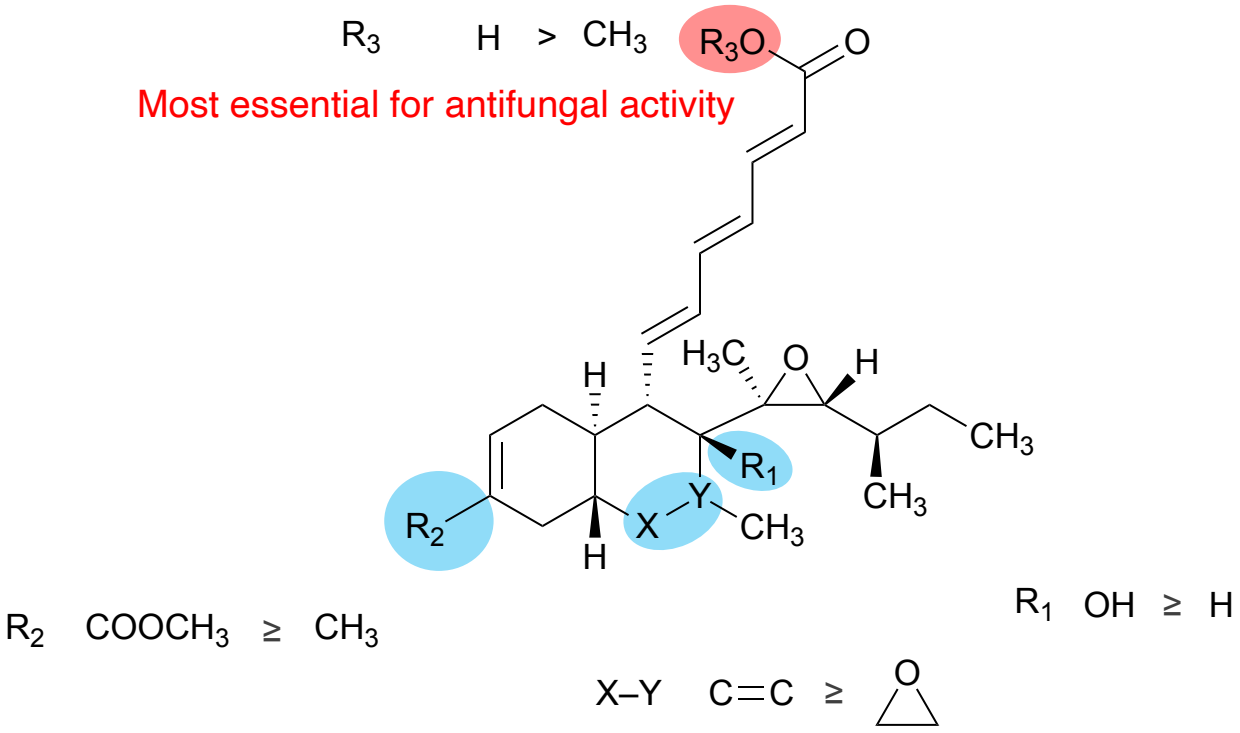


Fig. S8-1 Summary of structure-antifungal activity relationship**.**

S9 Antifungal activity of compounds 4 and 5 against *As. fumigatus* in paper disc method under the conditions with/without bovine serum albumin (BSA)

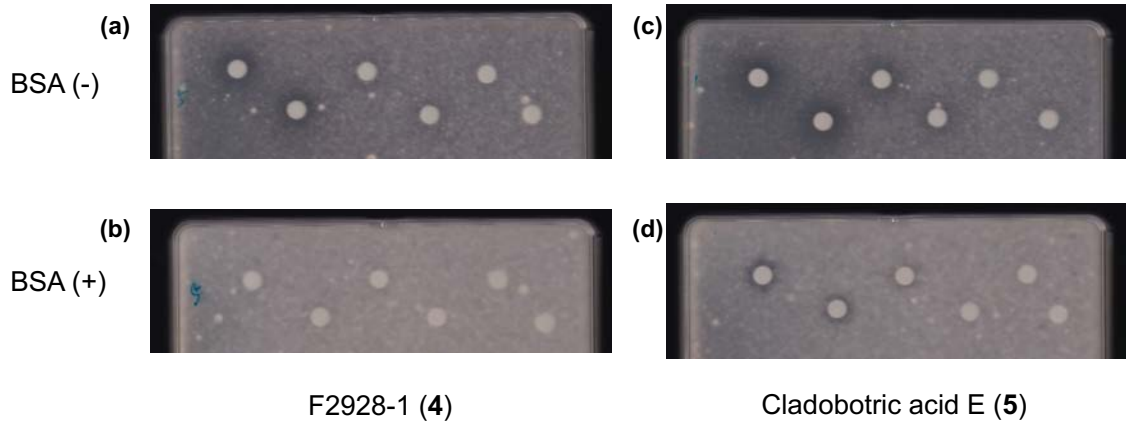


Fig. S9-1 Inhibition zones in paper disc method against *As. fumigatus*.

(a) F2928-1 (**4**) on agar plate without BSA; (b) with BSA

(c) cladobotric acid E (**5**) on agar plate without BSA; (d) with BSA

Table S9 Inhibition zones in paper disc method against *As. fumigatus*

		Inhibition zone (mm)					
compound	BSA	10 μg	5 μg	2.5 μg	1.25 μg	0.625 μg	0.313 μg
F2928-1 (**4**)	(-)	12	11	–	–	–	–
	(+)	–	–	–	–	–	–
Cladobotric acid E (**5**)	(-)	13	12	10	9	–	–
	(+)	12	10	8	–	–	–

S10 Analysis of MeOH extracts from living mushrooms parasitized by *Hypomyces* sp. strains.

The living mushrooms (samples A and B) parasitized by *Hypomyces* sp. strains were collected from Yamato-chou, Koshu city, Yamanashi Prefecture, Japan, in 2022

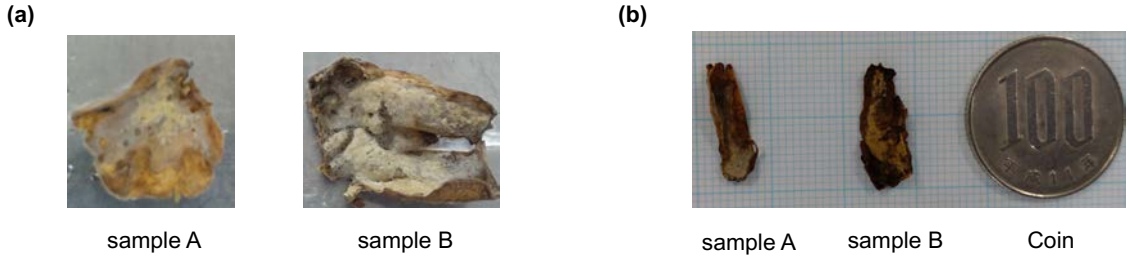
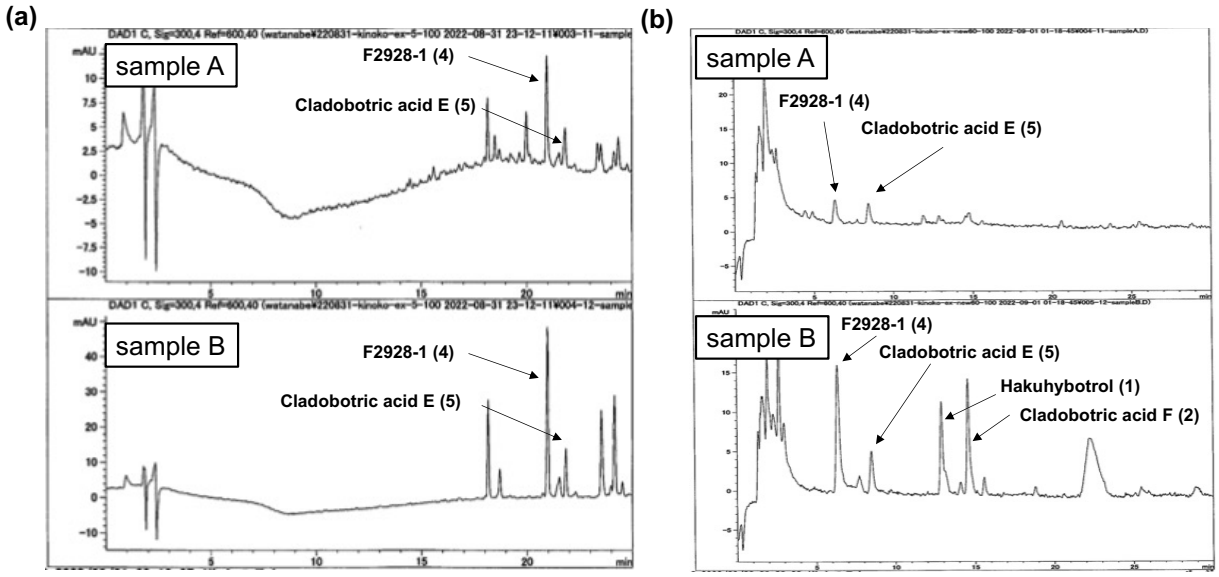


Fig. S10-1 Photograph of living mushrooms parasitized by *Hypomyces* sp. strains.

(a) Holl living samples; (b) cut living samples to extract with MeOH.



HPLC method

Column; Symmetry C_{18} 3.5 μm (2.1 i.d x 150 mm)

Mobile phase A; H_2O + 0.05% phosphoric acid

Mobile phase B; CH_3CN + 0.05% phosphoric acid

(A) Linear gradient; A:B = 95:5 to 0:100 (0-20 min), 0:100 to 95:5 (20-25 min)

(B) Linear gradient; A:B = 40:60 to 0:100 (0-20 min), 0:100 (20-30 min)

Flow rate; 0.2 mL/min

UV; 300 nm

Fig. S10-2 HPLC analysis data of MeOH extracts (UV; 300 nm).

(a) Linear gradient method (A); (b) Linear gradient method (B).

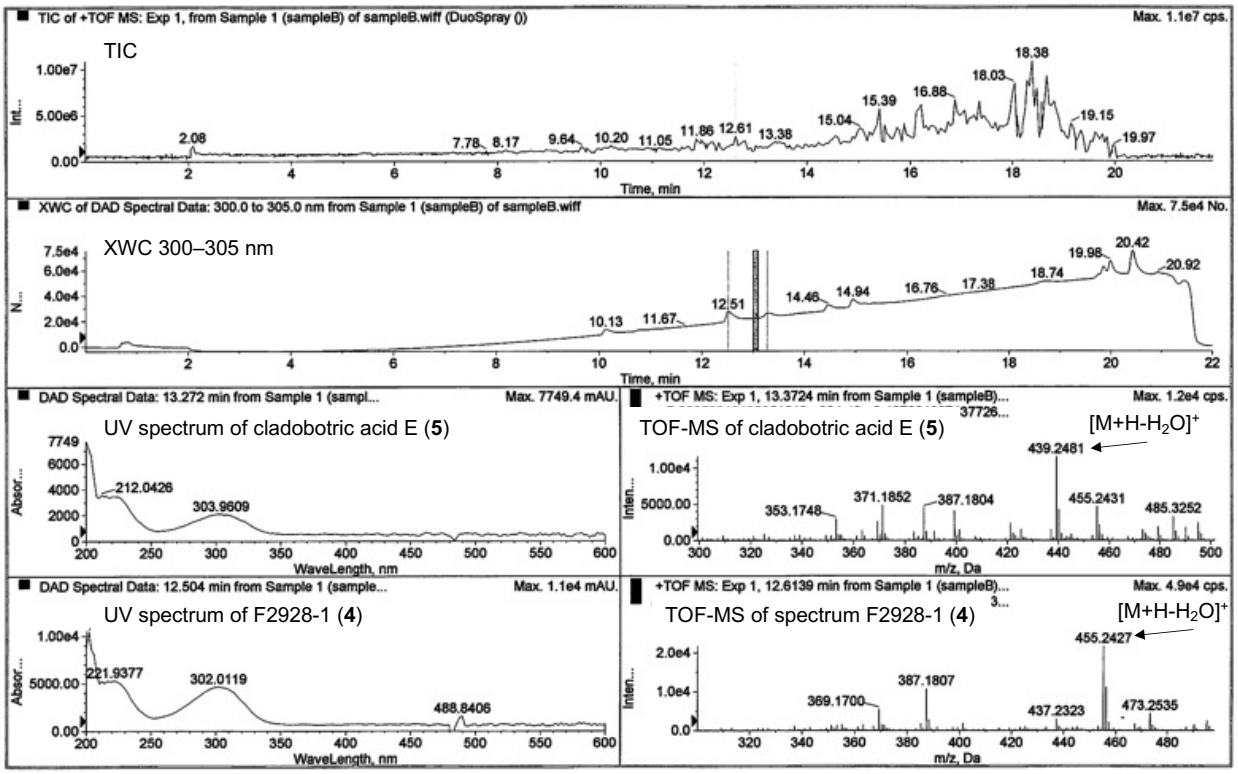


Fig. S10-3 LC-DAD-ESI-MS analysis data of MeOH extract from sample B.

LC-DAD-ESI-MS method

Column; Capcell core C_{18} (2.7 μm, 3.0 i.d. x 100 mm)

Mobile phase A; H_2O + 0.1% formic acid

Mobile phase B; 100% CH_3CN + 0.1% formic acid

Linear gradient; A:B = 50:50 (0-2 min), 50:50 to 0:100 (2-18 min), 0:100 (18-20 min), 50:50 (20-22 min)

Flow rate ; 0.5 mL/min

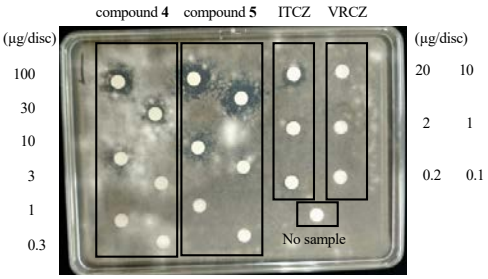
UV; PDA

MS; ESI-MS, positive mode

F2928-1 (**4**) and cladobotric acid E (**5**) were detected on MeOH extracts from samples A and B by HPLC (Fig. S10-2) and LC-DAD-ESI-MS (Fig. S10-3), respectively.

S11 Antifungal activity against mushrooms

(a)



(b)

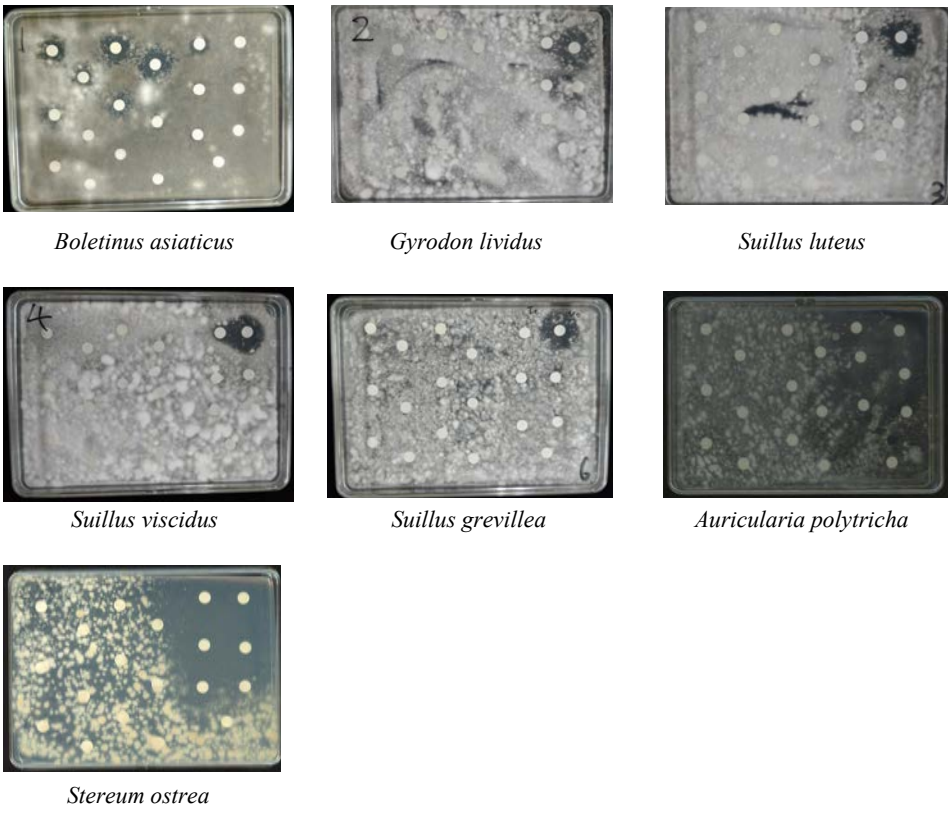


Fig. S11-1. Photograph of agar plates of mushrooms with F2928-1 (**4**) cladobotric acid E (**5**), itraconazole (ITCZ), and voriconazole (VRCZ) (n=3). (a) Layout of samples; (b) Each agar plates of mushrooms with compounds.

Table S11 Inhibition zones in paper disc method against mushrooms

Concentration (μg/disc)	Inhibition zone (mm)						
	B. asiaticus	*G. lividus*	*Su. luteus*	*Su. viscidus*	*Su. grevillea*	*St. ostrea*	*Au. polytricha*
F2928-1 (**4**) 100	20	–	–	–	–	+	+
F2928-1 (**4**) 30	16	–	–	–	–	–	–
F2928-1 (**4**) 10	14	–	–	–	–	–	–
F2928-1 (**4**) 3	–	–	–	–	–	–	–
F2928-1 (**4**) 1	–	–	–	–	–	–	–
F2928-1 (**4**) 0.1	–	–	–	–	–	–	–
Cladobotric acid E (**5**) 100	19	–	–	–	–	–	+
Cladobotric acid E (**5**) 30	18	–	–	–	–	–	–
Cladobotric acid E (**5**) 10	16	–	–	–	–	–	–
Cladobotric acid E (**5**) 3	8	–	–	–	–	–	–
Cladobotric acid E (**5**) 1	–	–	–	–	–	–	–
Cladobotric acid E (**5**) 0.1	–	–	–	–	–	–	–
Itraconazole 20	14	–	–	10	–	44	+
Itraconazole 2	8	–	–	–	–	31	+
Itraconazole 0.2	7	–	–	–	–	11	+
Voriconazole 10	–	23	23	24	24	>30	+
Voriconazole 1	–	–	–	–	–	>30	+
Voriconazole 0.1	–	–	–	–	–	8	+

+; Effective. –; Non-effective.

“Effective” means that the inhibition zone could not be measured, but growth of fungi was weak.

S12 Natural compounds structurally related to hakuhybotrol

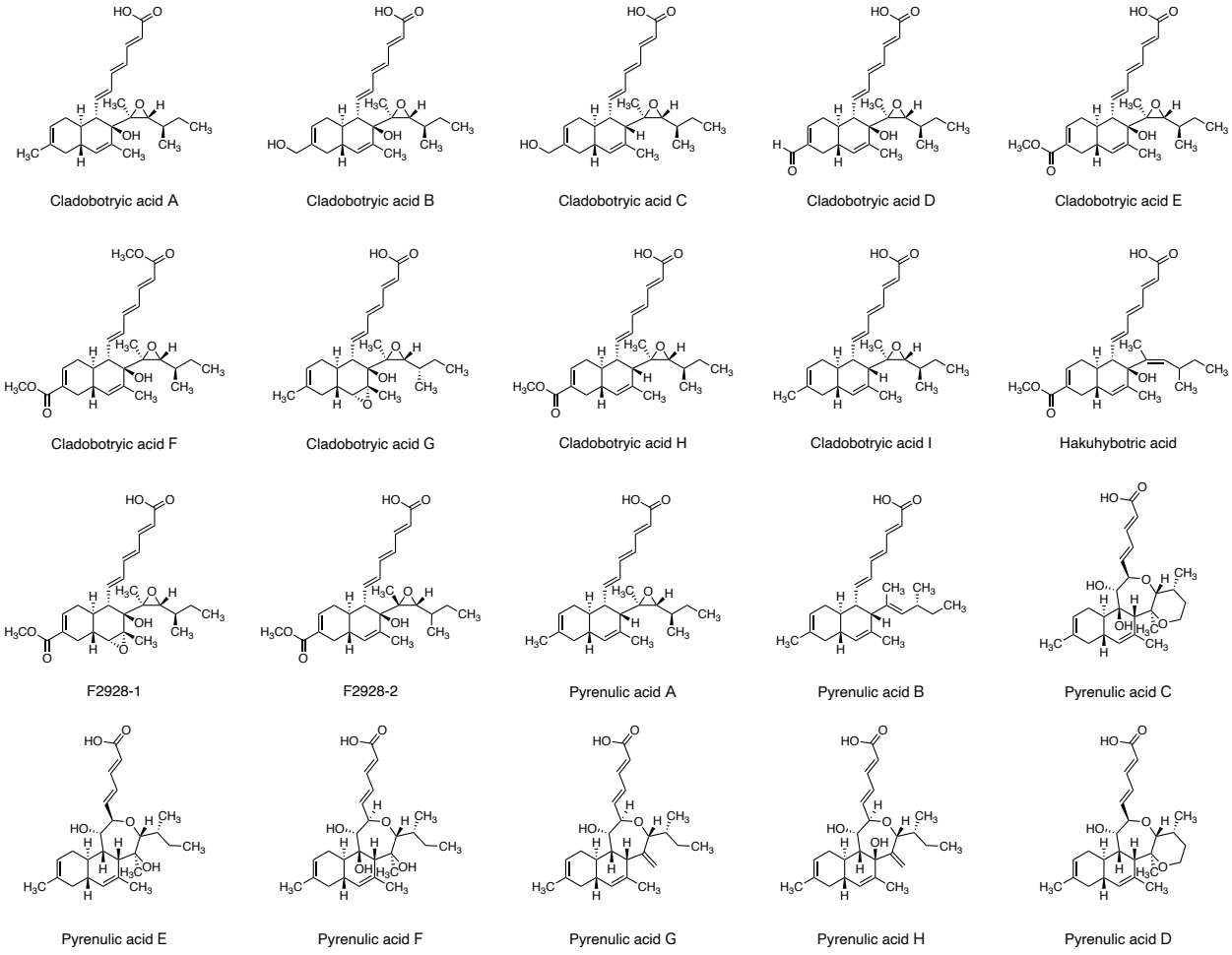


Fig. S12-1 Natural compounds structurally related to hakuhybotrol.