C_{28} Terpenoids from Lamiaceous Plant *Perovskia scrophulariifolia*: Their Structures and Anti-neuroinflammatory Activity

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Supporting Information

EXPERIMENTAL SECTION

General Experimental Procedures. Specific rotations were obtained by a JASCO P-2200 digital polarimeter. NMR spectra were measured on a Bruker AVANCE-500 spectrometer using the resonances of C_5D_5N (δ_H 8.71; δ_C 123.5) and $CDCl_3$ (δ_H 7.26; δ_C 77.0) as internal references for ^1H and ^{13}C NMR chemical shifts, respectively. IR, UV, and CD spectra were recorded on a JASCO FT/IR-6200, a Hitachi UV-3900H, and a JASCO J-1500 spectrophotometers, respectively. HRESIMS were recorded on a Waters LCT PREMIER 2695.

Extraction and Isolation. The aerial parts of *Perovskia scrophulariifolia* collected in Uzbekistan were dried and then extracted with MeOH at rt to give the extract (180 g). The extract was partitioned between EtOAc and water. The EtOAc-soluble materials were further partitioned between *n*-hexane and 90% MeOH aq. The 90% MeOH aq.-soluble materials (94 g) were subjected to Sephadex LH-20 column chromatography (MeOH/water, 6:4 to 10:0) to give eight fractions (frs. 1~8). Fr. 5 was applied to a silica gel column ($CHCl_3$/MeOH, 99:1 to 0:100) to give 17 fractions (frs. 5.1~5.17) including methyl rosmarinate (**3**, 2.8 g) as fr. 5.17. Fr. 5.14 was further separated by Sephadex LH-20 column chromatography (MeOH/water, 6:4) to afford 10 fractions (frs. 5.14.1~5.14.10). Fr. 5.14.7 was loaded on an ODS column (MeOH/water, 6:4 to 10:0), and purified by reversed-phase HPLC (COSMOSIL 5C_{18}-MS-II, 10 i.d. x 250 mm, MeCN/water, 58:42 with 0.1% TFA) to furnish perovsfolins A (**1**, 3.7 mg) and B (**2**, 2.7 mg).

*Perovsfolin A (**1**)*: colorless amorphous solid; $[\alpha]_D$ +251.1 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 249 (ε 14,500), 288 (7,000), and 335 (6,200) nm; ECD (MeOH) Δε (nm) +15.2 (369), −17.8 (296), +51.1 (220), and −24.9 (203); ^1H and ^{13}C NMR (Table S1); HRESIMS *m/z* 677.2360 $[M+Na]^+$ (calcd for $C_{38}H_{38}O_{10}Na^+$, 677.2357).

*Perovsfolin B (**2**)*: colorless amorphous solid; $[\alpha]_D$ −190.7 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 245 (ε 13,600), 289 (7,300), and 335 (6,900) nm; ECD (MeOH) Δε (nm) −13.4 (367), +13.8 (296), −43.5 (220), and +34.6 (204); ^1H and ^{13}C NMR (Table S1); HRESIMS *m/z* 677.2366 $[M+Na]^+$ (calcd for $C_{38}H_{38}O_{10}Na^+$, 677.2357).

Chemical Conversions of Perovsfolins A (1) and B (2). A mixture of perovsfolin A (**1**, 0.4 mg), CH_3I (60 μL), and K_2CO_3 (60 mg) in dry acetone (0.4 mL) was heated at 60 ºC (oil bath) in a screw-capped vial for 5 h with stirring. After removal of inorganic salts by filtration, the filtrate was concentrated under the reduced pressure. The residue was purified by silica gel column chromatography (toluene/EtOAc, 1:0 to 9:1) to give permethylperovsfolin A (**1a**, 0.4 mg). Permethylpervsfolin A (**1a**, 0.2 mg) was treated with NaOH in MeOH/acetone (2:1, 0.75 mL) at rt for 12 h with stirring. The reaction mixture was neutralized with 1M HCl and diluted by water.

The solution was extracted with EtOAc, washed successively with water and brine, dried over Na_2SO_4, and concentrated to give a residue. Purification of the residue by silica gel column chromatography (*n*-hexane/acetone, 6:4 to 0:1) gave a terpenoid (**1b**) and a C_6-C_3 (**1c**) moieties. A solution of **1c** in MeOH (0.2 mL) was treated with drops of TMS-CHN_2 (0.6 M solution in *n*-hexane), and the mixture was stirred at rt for 0.5 h. The reaction mixture was concentrated to give trimethyltanshinol (**1d**). The terpenoid moiety (**2b**) and trimethyltanshinol (**2d**) were obtained from perovsfolin B (**2**) according to the same procedure.

*Permethylperovsfolin A (**1a**)*: colorless amorphous solid; $[\alpha]_D$ +126.7 (*c* 0.02, MeOH); ^{1}H NMR (C_5D_5N, *J* in Hz) δ_H 7.45 (1H, s), 7.31 and 7.27 (each 1H, d, 8.0), 7.14 (1H, s), 7.12 (1H, d, 2.0), 7.01 (1H, dd, 8.2, 2.0), 6.95 (1H, s), 6.95 (1H, d, 8.2), 6.05 (1H, d, 3.), 5.90 (1H, dd, 9.3, 3.8), 4.48 (1H, dt, 11.1, 6.1), 3.84, 3.75, 3.71, 3.61, and 3.56 (each 3H, s), 3.43 (1H, dd, 14.3, 3.8), 3.32 (1H, dd, 11.1, 3.5), 3.25 (1H, dd, 14.3, 9.3), 3.23 (1H, m), 1.86, 1.74, 1.45, and 1.34 (each 1H, m), 1.23 x 2 (each 3H, d, 7.0), 1.15 and 1.03 (each 3H, s); HRESIMS *m/z* 733.2990 $[M+Na]^+$ (calcd for $C_{42}H_{46}O_{10}Na^+$, 733.2983).

*Terpenoid moiety (**1b**) of **1***: colorless amorphous solid; ^{1}H NMR (C_5D_5N, *J* in Hz) δ_H 7.46 (1H, s), 7.32 and 7.27 (each 1H, d, 8.0), 7.12 (1H, s), 6.99 (1H, s), 6.10 (1H, d, 3.0), 4.50 (1H, dt, 11.4, 5.7), 3.78, 3.58, and 3.55 (each 3H, s), 3.31 (1H, dd, 11.4, 3.0), 3.26 (1H, sept, 7.1), 1.83, 1.69, 1.61, and 1.40 (each 1H, m), 1.25 and 1.24 (each 3H, d, 7.1), 1.18 and 1.01 (each 3H, s); HRESIMS *m/z* 525.2265 $[M+Na]^+$ (calcd for $C_{31}H_{34}O_6Na^+$, 525.2248); UV (MeOH) λ_{max} 250 (ε 14,400), 287 (5,400), and 335 (6,200) nm; CD (MeOH) Δε +14.4 (368), –5.6 (322), –18.2 (293), –0.7 (260), –7.1 (249), +54.2 (222), –41.6 (203). UV (ε values) and CD (Δε values) data for **1b** were estimated on the basis of its UV absorption at 335 nm by comparing that of **1**, since a small amount of **1b** was obtained (< 0.1 mg).

*Trimethyltanshinol (**1d**)*: colorless amorphous solid; ^{1}H NMR ($CDCl_3$, *J* in Hz) δ_H 6.80 (1H, d, 8.5), 6.75 (1H, brs), 6.74 (1H, m), 4.43 (1H, dd, 6.6, 4.3), 3.87, 3.86, and 3.76 (each 3H, s), 3.08 (1H, dd, 14.1, 4.3), and 2.92 (1H, dd, 14.1, 6.6); HRESIMS *m/z* 263.0872 $[M+Na]^+$ (calcd for $C_{12}H_{16}O_5Na^+$, 263.0890).

*Permethylperovsfolin B (**2a**)*: colorless amorphous solid; $[\alpha]_D$ –69.2 (*c* 0.02, MeOH); ^{1}H NMR (C_5D_5N, *J* in Hz) δ_H 7.45 (1H, s), 7.30 and 7.26 (each 1H, d, 8.0), 7.14 (1H, d, 2.0), 7.12 (1H, s), 7.03 (1H, dd, 8.4, 2.0), 6.93 (1H, d, 8.4), 6.75 (1H, s), 6.31 (1H, d, 3.2), 5.82 (1H, dd, 10.0, 3.9), 4.46 (1H, dt, 11.0, 5.7), 3.80, 3.72, 3.71, 3.54, and 3.52 (each 3H, s), 3.46 (1H, dd, 14.0, 3.9), 3.31 (1H, dd, 11.0, 3.2), 3.30 (1H, dd, 14.0, 10.0), 3.23 (1H, sept, 6.9), 1.23 and 1.22 (each 3H, d, 6.9), 1.16 and 0.97 (each 3H, s); HRESIMS *m/z* 733.2977 $[M+Na]^+$ (calcd for $C_{42}H_{46}O_{10}Na^+$, 733.2983).

*Terpenoid moiety (**2b**) of **2***: colorless amorphous solid; ^{1}H NMR (C_5D_5N) data was identical to that of **1b**; HRESIMS *m/z* 525.2260 $[M+Na]^+$ (calcd for $C_{31}H_{34}O_6Na^+$, 525.2248); UV (MeOH)

λ_{max} 250 (ε 16,300), 288 (5,700), and 335 (6,900) nm; CD (MeOH) Δε –17.6 (368), +6.2 (323), +5.7 (319), +21.9 (293), +0.7 (259), +8.8 (248), –63.5 (222), and +48.2 (204). UV (ε values) and CD (Δε values) data for **2b** were estimated on the basis of its UV absorption at 335 nm by comparing that of **2**, since a small amount of **2b** was obtained (< 0.1 mg).

*Trimethyltanshinol (**2d**)*: colorless amorphous solid; ^{1}H NMR ($CDCl_3$) data was not obtained due to low sample amount; HRESIMS *m/z* 263.0894 $[M+Na]^+$ (calcd for $C_{12}H_{16}O_5Na^+$, 263.0890).

Chemical Conversion of Methyl Rosmarinate (3) to (±)-Trimethyltanshinol {(±)-3b}. Methyl rosmarinate (**3**, 690 mg) was treated with CH_3I (0.44 mL) and K_2CO_3 (1.0 g) in dry acetone (8 mL) and refluxed in an oil bath for 6 h. After filtration and evaporation, the reaction mixture was purified by silica gel column chromatography (toluene/EtOAc, 1:0 to 9:1) to give rosmarinic acid permethylate (**3a**, 680 mg). To a MeOH solution (15 mL) of **3a** (610 mg) was added K_2CO_3 (75 mg) and stirred at rt for 12 h. The reaction mixture was neutralized with 1M HCl and diluted by water. The solution was extracted with EtOAc, and the organic layer was washed successively with water and brine, dried over Na_2SO_4, and concentrated to give a residue. Purification of the residue by silica gel column chromatography (*n*-hexane/EtOAc, 7:3 to 1:1) gave trimethyltanshinol (**3b**, 156 mg). To a CH_2Cl_2 solution (8 mL) of **3b** (100 mg) were added Dess-Martin periodinane (185 mg) and $NaHCO_3$ (175 mg) and stirred at rt for 4 h. The reaction mixture was quenched with sat. $NaHCO_3$ aq. (1 mL) and sat. $Na_2S_2O_3$ aq. (1 mL). The aqueous phase was extracted with EtOAc, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give the residue. The residue was chromatographed over a silica gel column (*n*-hexane/EtOAc, 8:2) to give an oxidized product (24 mg). A mixture of the product (24 mg) and $NaBH_4$ (4.4 mg) in MeOH (1 mL) was stirred for 1 h in an ice bath (0 ^{o}C). The reaction was quenched with water and evaporated to give a residue. The residue was partitioned with EtOAc/water, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue on a silica gel column (*n*-hexane/EtOAc, 8:2 to 7:3) afforded (±)-**3b** (2.5 mg).

*Rosmarinic acid permethylate (**3a**)*: colorless amorphous solid; $[\alpha]_D$ +42.3 (*c* 1.1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, *J* in Hz) δ_H 7.65 (1H, d, 15.8), 7.09 (1H, dd, 8.4, 1.8), 7.04 (1H, d, 1.8), 6.86 (1H, d, 8.4), 6.80 (3H, m), 6.33 (1H, d, 15.8), 5.37 (1H, dd, 8.0, 4.8), 3.92, 3.91, 3.86 × 2, and 3.75 (each 3H, s), 3.19 (1H, dd, 14.3, 4.8), and 3.14 (1H, dd, 14.3, 8.0); HRESIMS *m/z* 453.1526 $[M+Na]^+$ (calcd for $C_{23}H_{26}O_8Na^+$, 453.1520).

*(+)-Trimethyltanshinol (**3b**)*: colorless amorphous solid; $[\alpha]_D$ +11.7 (*c* 0.3, CH_2Cl_2) {*lit.* $[\alpha]_D$ +10.6 (*c* 0.67, CH_2Cl_2)}[15]; ^{1}H NMR ($CDCl_3$) data was identical to that of **1d**: HRESIMS *m/z* 263.0899 $[M+Na]^+$ (calcd for $C_{12}H_{16}O_5Na^+$, 263.0890).

*(±)-Trimethyltanshinol [(±)-**3b**]*: colorless amorphous solid; ^{1}H NMR ($CDCl_3$) data was identical to that of **1d**: HRESIMS *m/z* 263.0886 $[M+Na]^+$ (calcd for $C_{12}H_{16}O_5Na^+$, 263.0890).

Chiral HPLC Analyses of Trimethyltanshinols (1d, 2d, and 3b). (+)-Trimethyltanshinol (**3b**) was subjected to HPLC with a chiral column (YMC Chiral Art Cellulose-SB, 5 mm, i.d. 4.6 x 250 mm; *n*-hexane/*i*-PrOH, 85:15; flow 1.0 mL/min; UV 254 nm; temp. 40 ºC) to give a peak at t_R 14.7 min. The chiral resolution of (±)-**3b** with the same condition gave a pair of peaks at t_R 12.1 min {(–)-**3b**} and t_R 14.7 min {(+)-**3b**} in the ratio of ca. 1:1. Similarly, the chiral HPLC analyses of **1d** and **2d** were carried out to show a single peak at t_R 14.7 min in each case.

Calculation of ECD Spectrum. A conformational search for the possible stereoisomer (**1b**, 1*R*,11*R*,7′*R*,8′*R*) of the terpenoid moiety (**1b**) of perovsfolin A (**1**) with the Molecular Mechanics gave stable conformers. Further optimization of the initial conformers (Boltzmann distributions over 1%) by DFT calculations {B3LYP/6-31G(d), in the presence of MeOH with a polarizable continuum model (PCM)} gave three stable conformers. The absence of imaginary frequencies of the stable conformers were confirmed by calculations of harmonic vibrational frequencies at the B3LYP/6-31G(d) level in the presence of MeOH with PCM. The stable conformers were subjected to TDDFT calculations {CAM-B3LYP/6-31+G(d), in the presence of MeOH with a PCM}. Conversion of the resultant rotatory strengths of the lowest 30 excited states for each conformer with half-bands (0.25 eV) by SpecDis (v1.61)[S1] gave Gaussian-type curves. Finally, the calculated ECD spectra were composed after correction based on the Boltzmann distribution, and red-shifted by 15 nm. The conformational search was run on Spartan 18 program (Wavefunction Inc. Irvine, CA.), while DFT calculations were carried out on Gaussian 09 program,[S2] respectively.

Evaluation of Biological Activity. Perovsfolins A (**1**) and B (**2**) were evaluated for their inhibitory effect of IL-1β production from LPS stimulated microglial cells and their antiproliferative activity against human cancer cell lines (A549, Hela, and MCF7) by identical procedures as described in our previous report.[11]

References

(S1) Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. SpecDis, Version 1.61, University of Wuerzburg, Germany, 2013.

(S2) Frisch, M. J. *et al*., *Gaussian 09,* Revision C.01, Gaussian, Inc., Wallingford, CT, 2010.

Scheme S1. Possible biogenetic pathway of perovsfolin A (**1**).

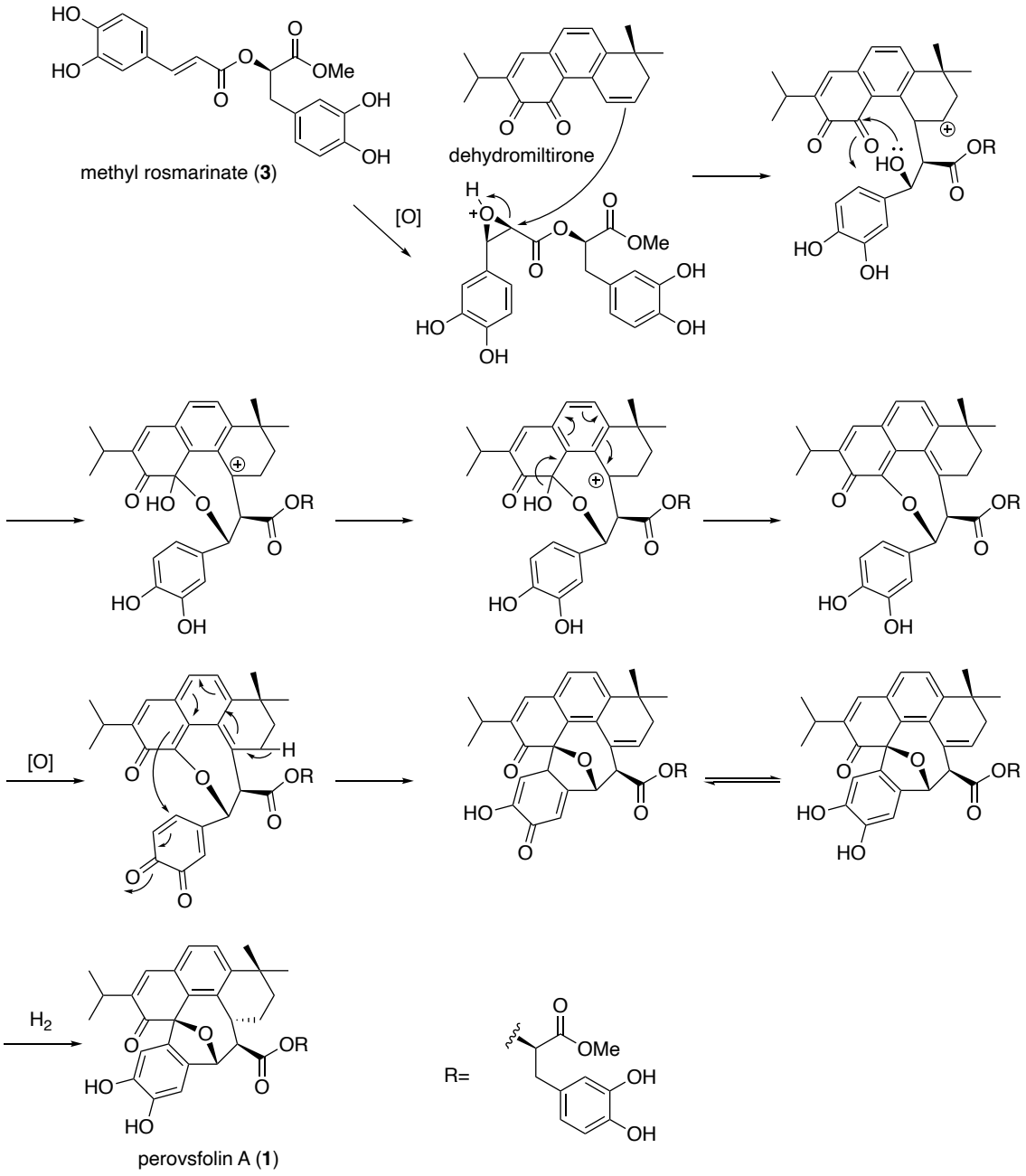


Figure S1. ECD spectra of perovsfolins A (**1**) and B (**2**).

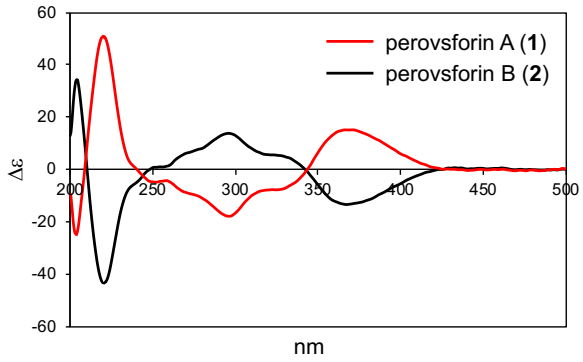


Figure S2. ^{1}H NMR spectrum of perovsfolin A (**1**) in C_5D_5N (500 MHz).

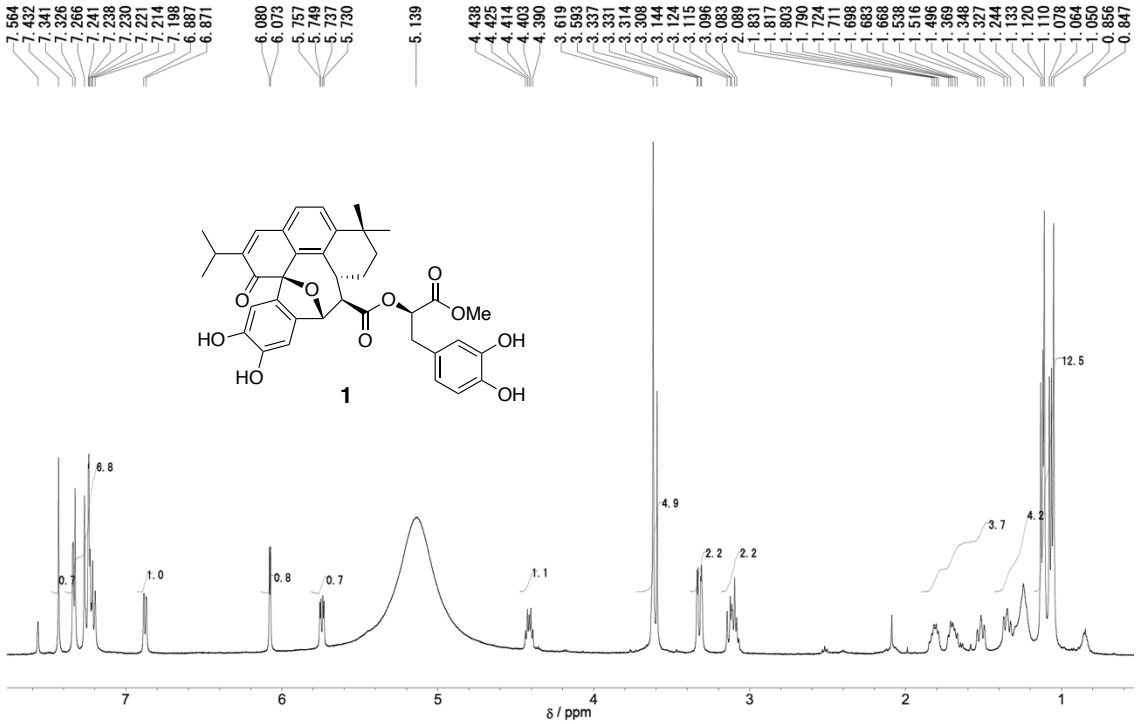


Figure S3. ^{13}C NMR spectrum of perovsfolin A (**1**) in C_5D_5N (125 MHz).

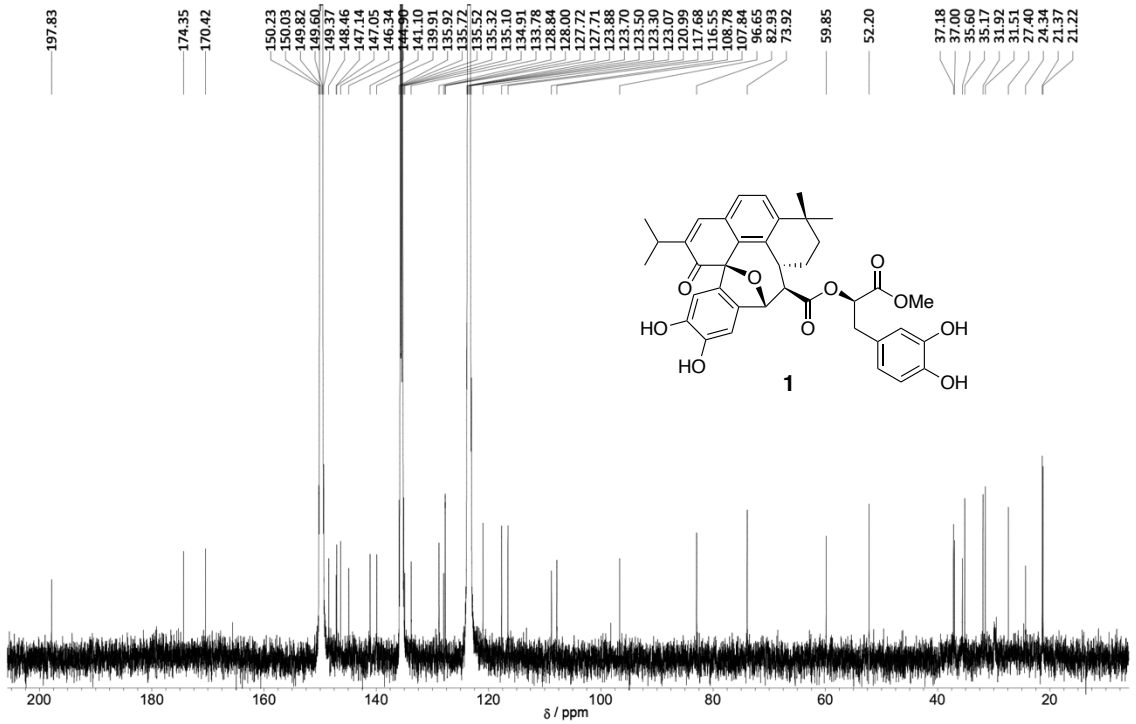


Figure S4. ^{1}H-^{1}H COSY spectrum of perovsfolin A (**1**) in C_5D_5N (500 MHz).

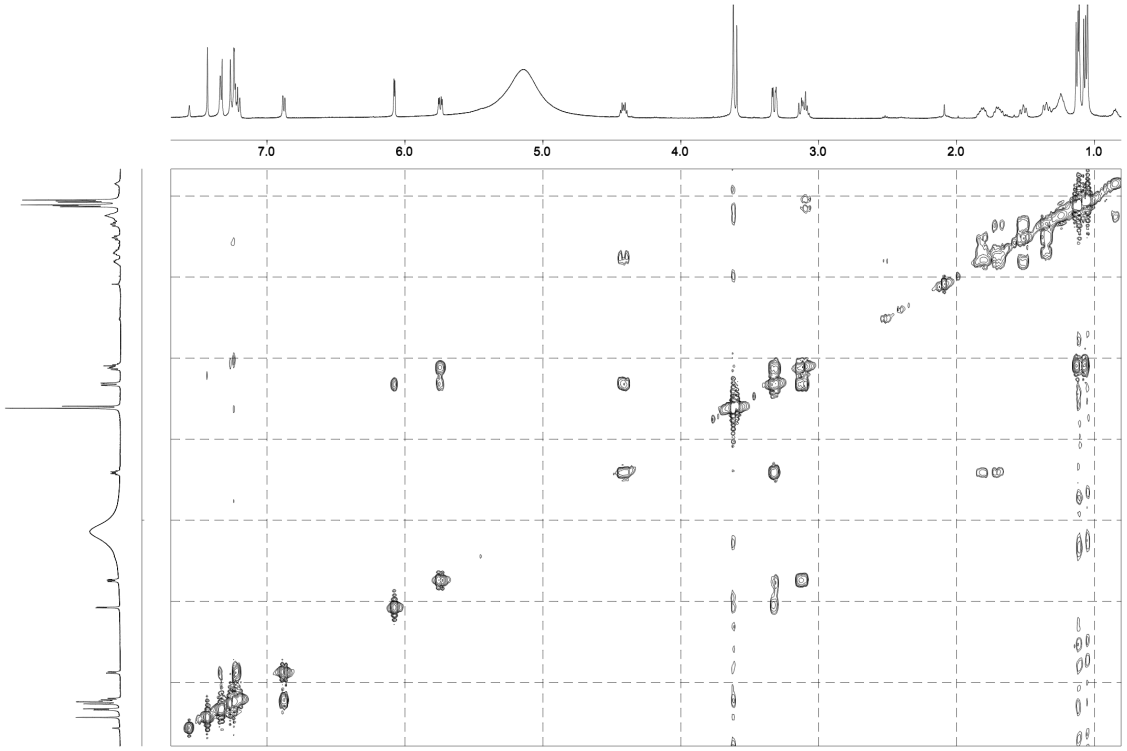


Figure S5. HSQC spectrum of perovsfolin A (**1**) in C_5D_5N (500 MHz).

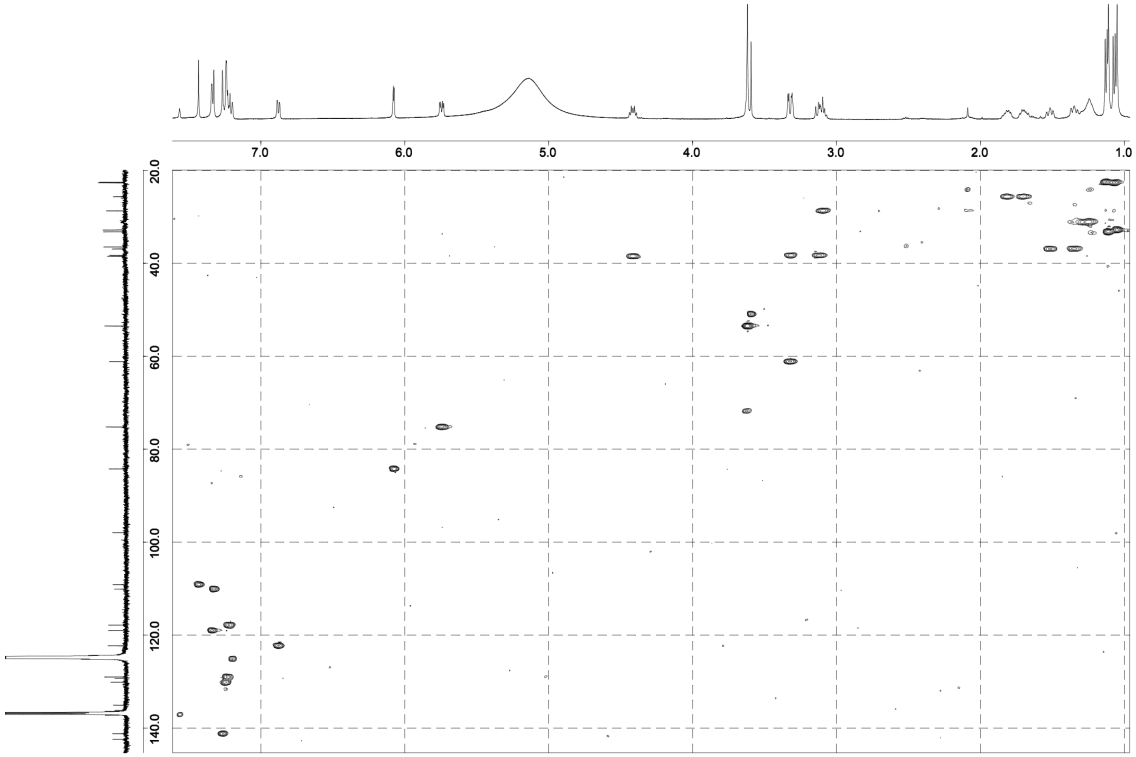


Figure S6. HMBC spectrum of perovsfolin A (**1**) in C_5D_5N (500 MHz).

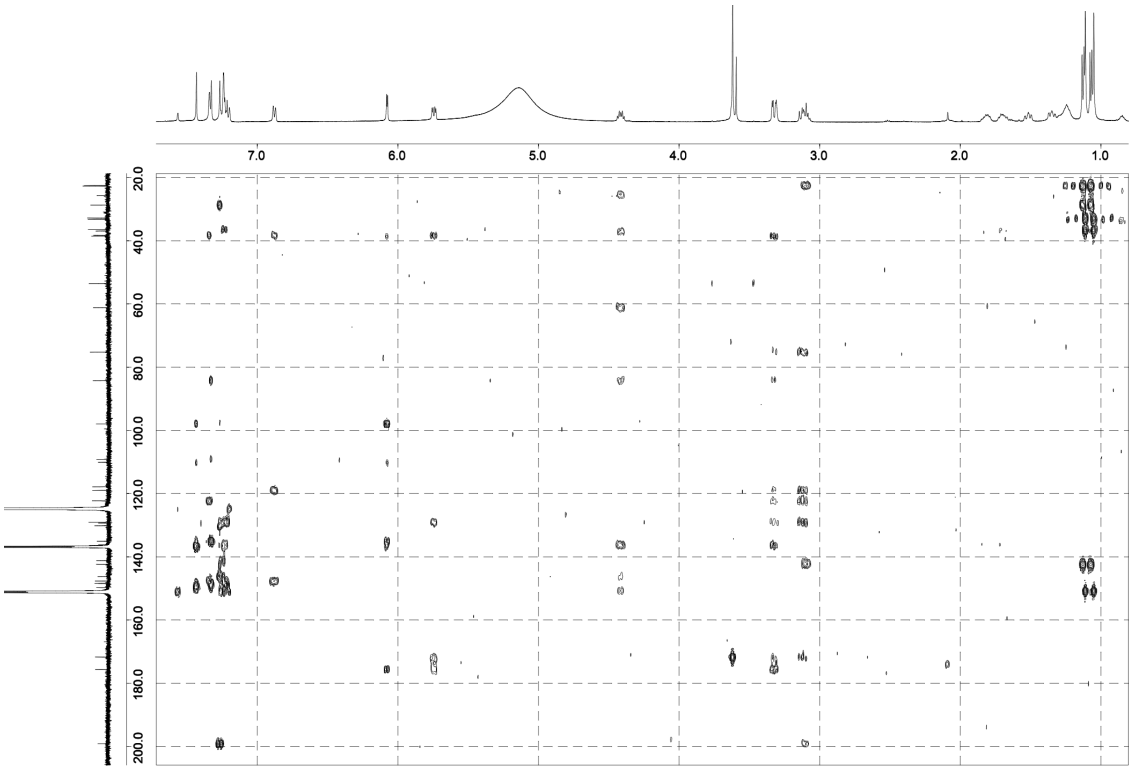


Figure S7. ROESY spectrum of perovsfolin A (**1**) in C_5D_5N (500 MHz).

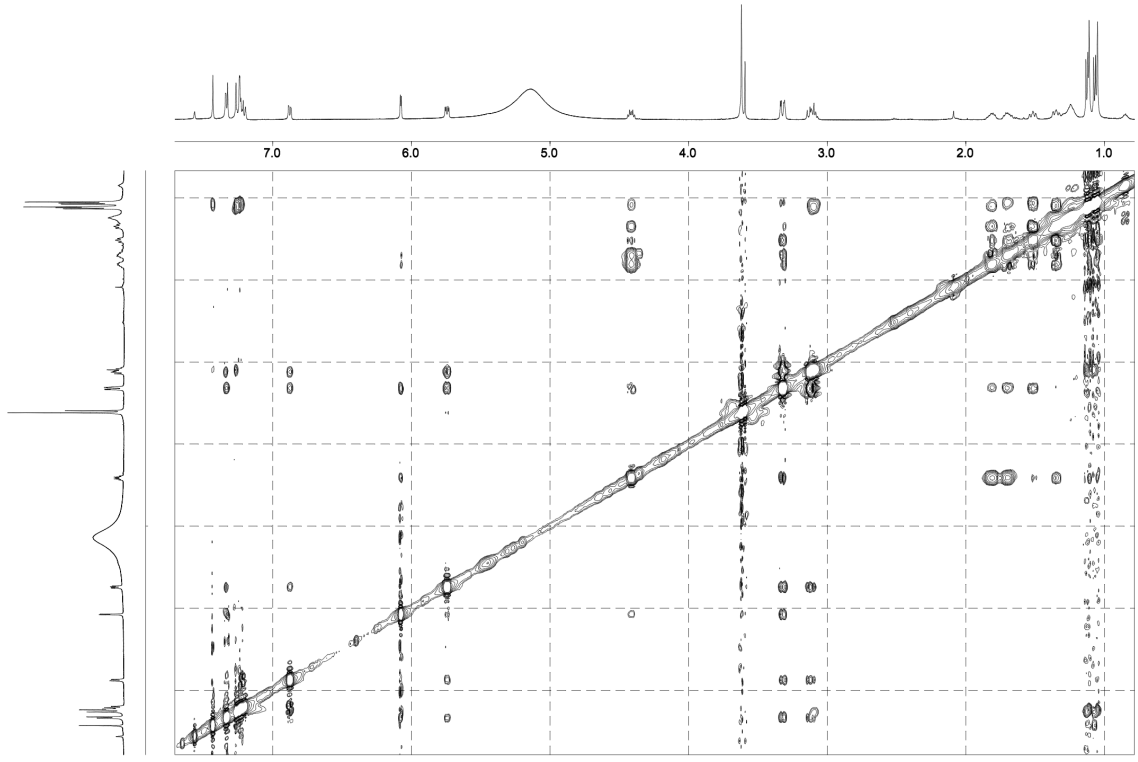


Figure S8. ^{1}H NMR spectrum of perovsfolin B (**2**) in C_5D_5N (500 MHz).

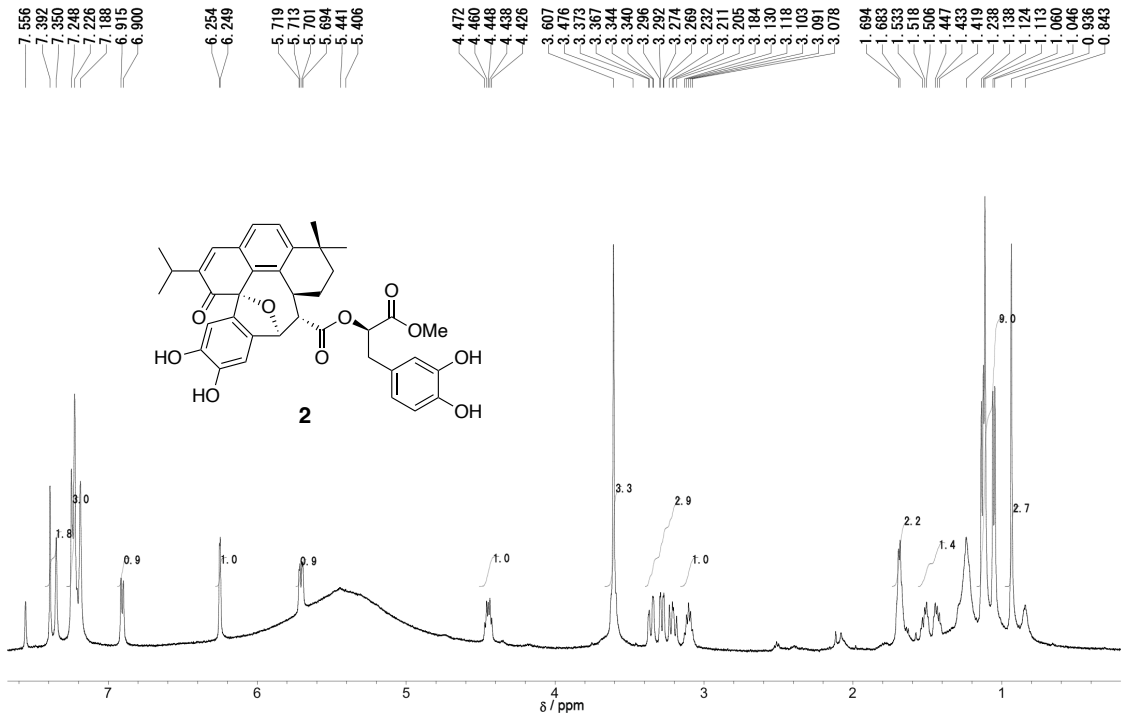


Figure S9. ^{13}C NMR spectrum of perovsfolin B (**2**) in C_5D_5N (125 MHz).

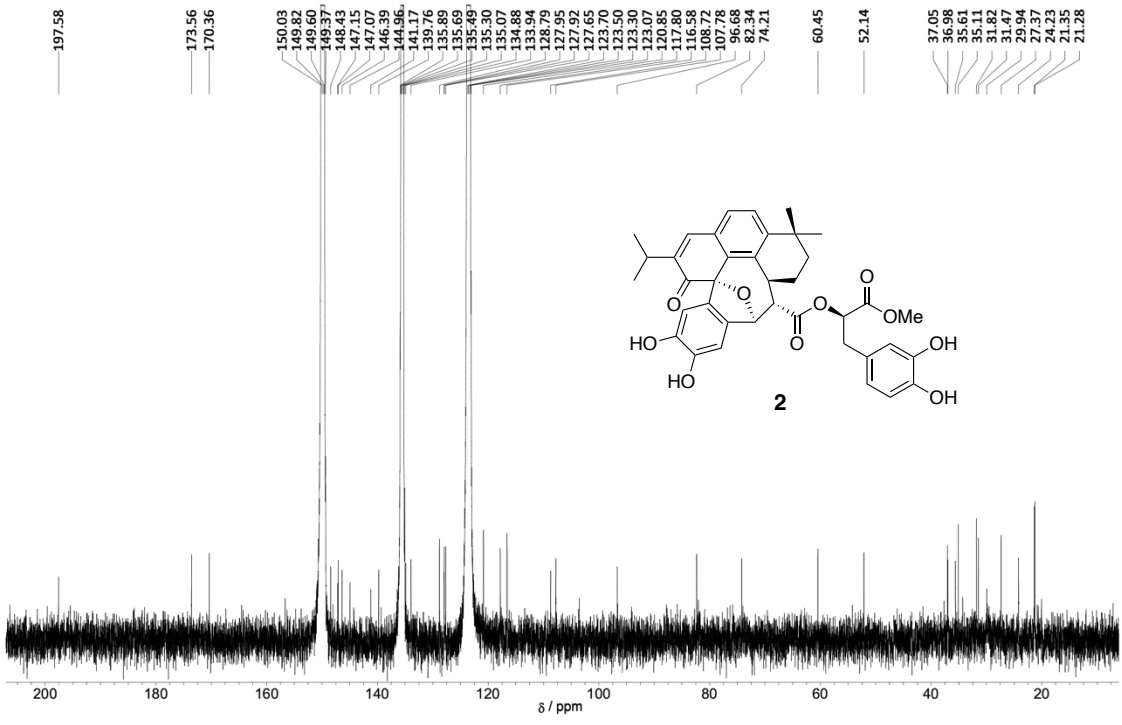


Figure S10. ^{1}H-^{1}H COSY spectrum of perovsfolin B (**2**) in C_5D_5N (500 MHz).

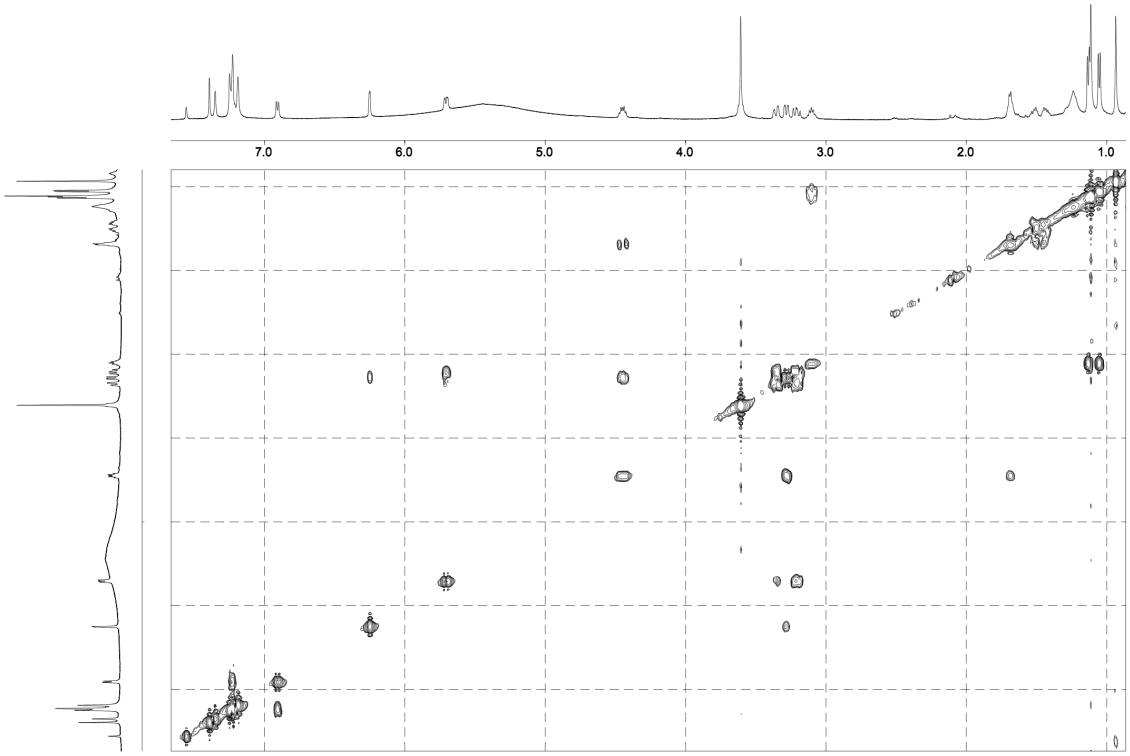


Figure S11. HSQC spectrum of perovsfolin B (**2**) in C_5D_5N (500 MHz).

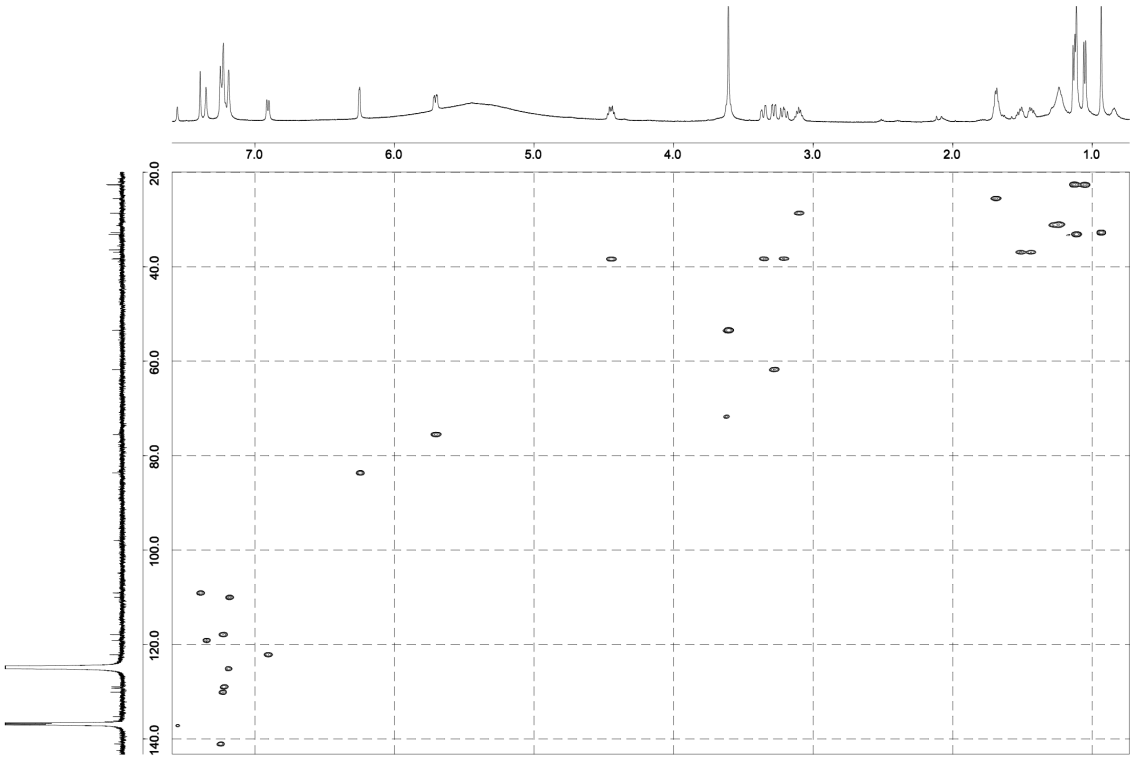


Figure S12. HMBC spectrum of perovsfolin B (**2**) in C_5D_5N (500 MHz).

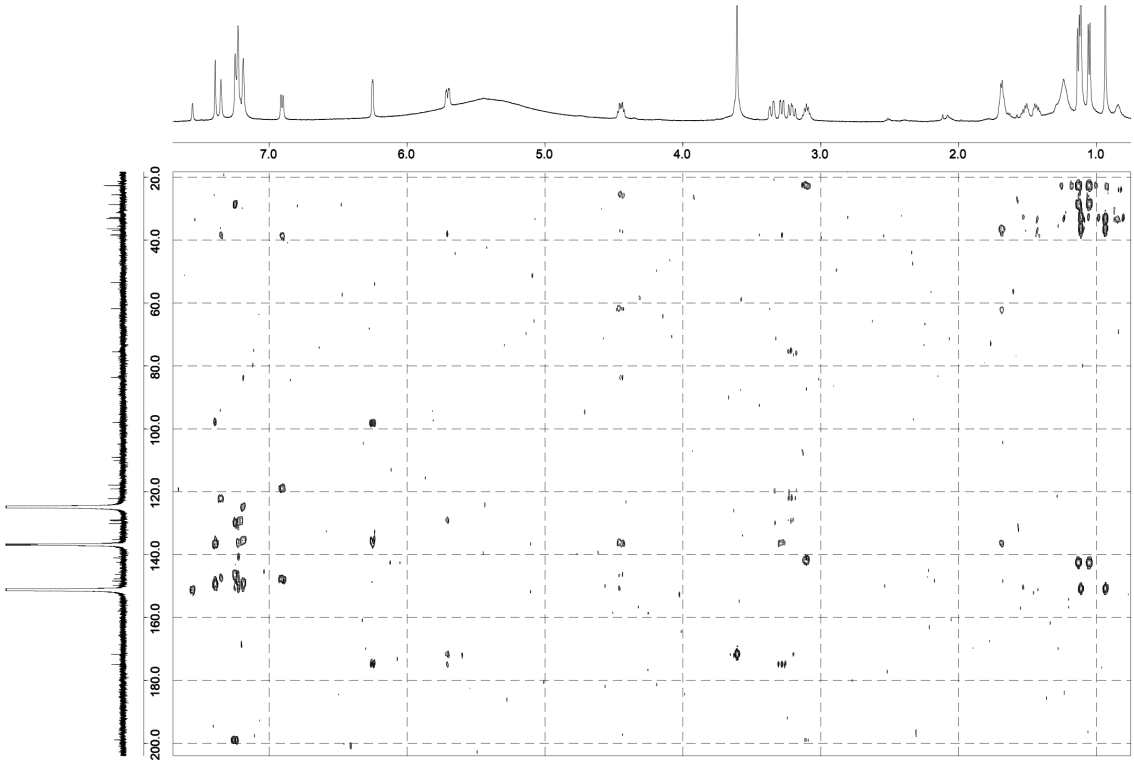


Figure S13. ROESY spectrum of perovsfolin B (**2**) in C_5D_5N (500 MHz).

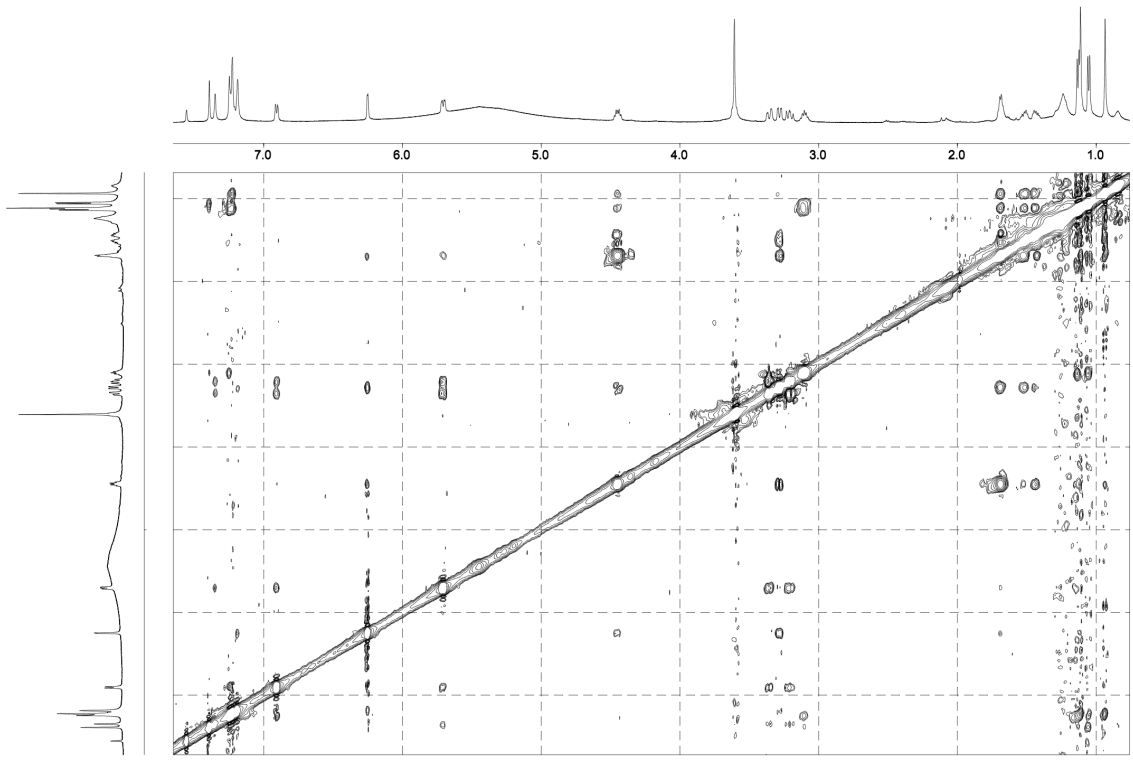


Figure S14. ^{1}H NMR spectrum of permethylperovsfolin A (**1a**) in C_5D_5N (500 MHz).

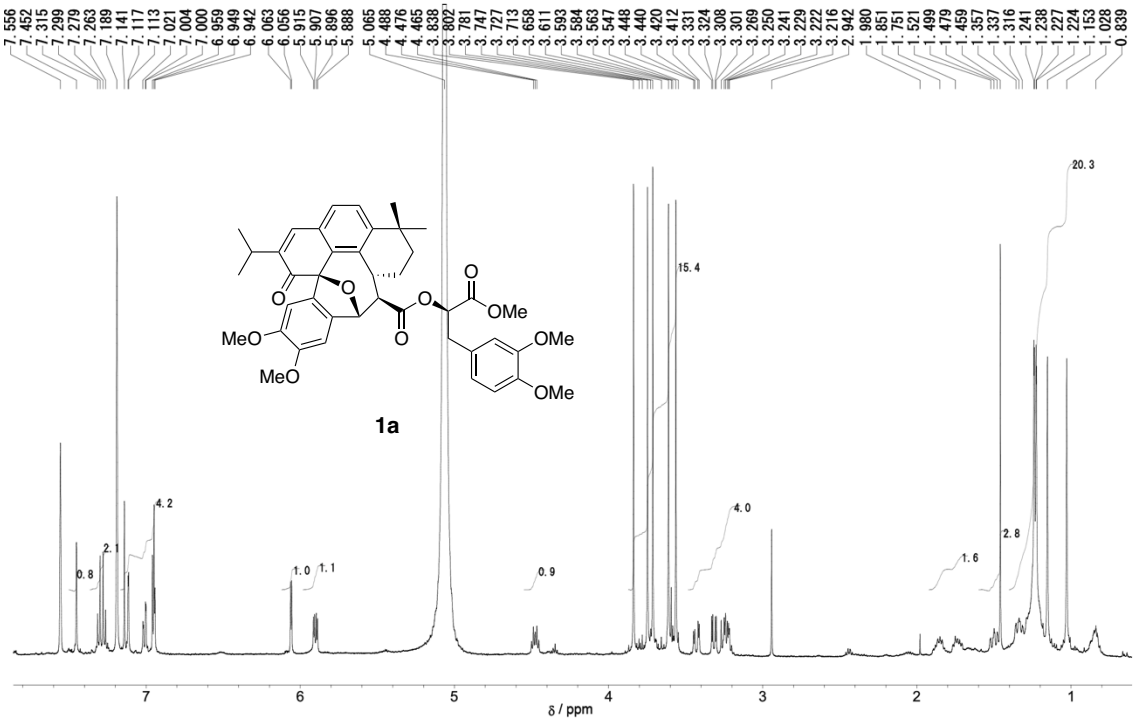


Figure S15. ^{1}H NMR spectrum of terpenoid moiety (**1b**) of **1** in C_5D_5N (500 MHz).

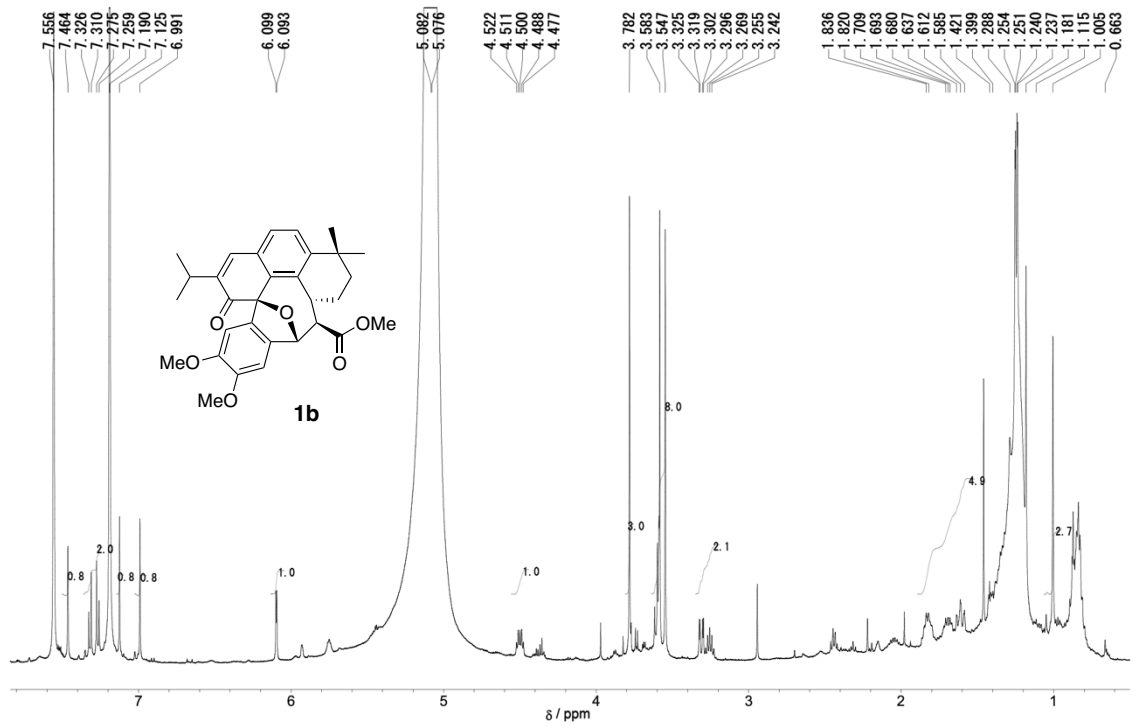


Figure S16. ^{1}H NMR spectrum of trimethyltanshinol (**1d**) in $CDCl_3$ (500 MHz).

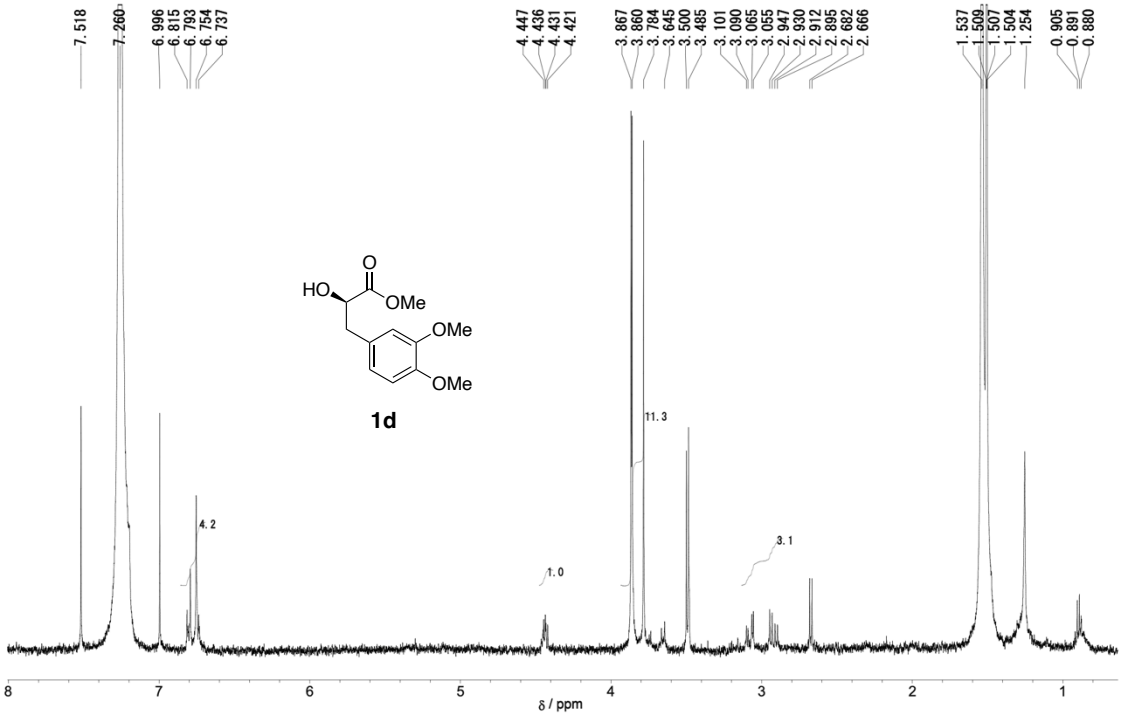


Figure S17. ^{1}H NMR spectrum of permethylperovsfolin B (**2a**) in C_5D_5N (500 MHz).

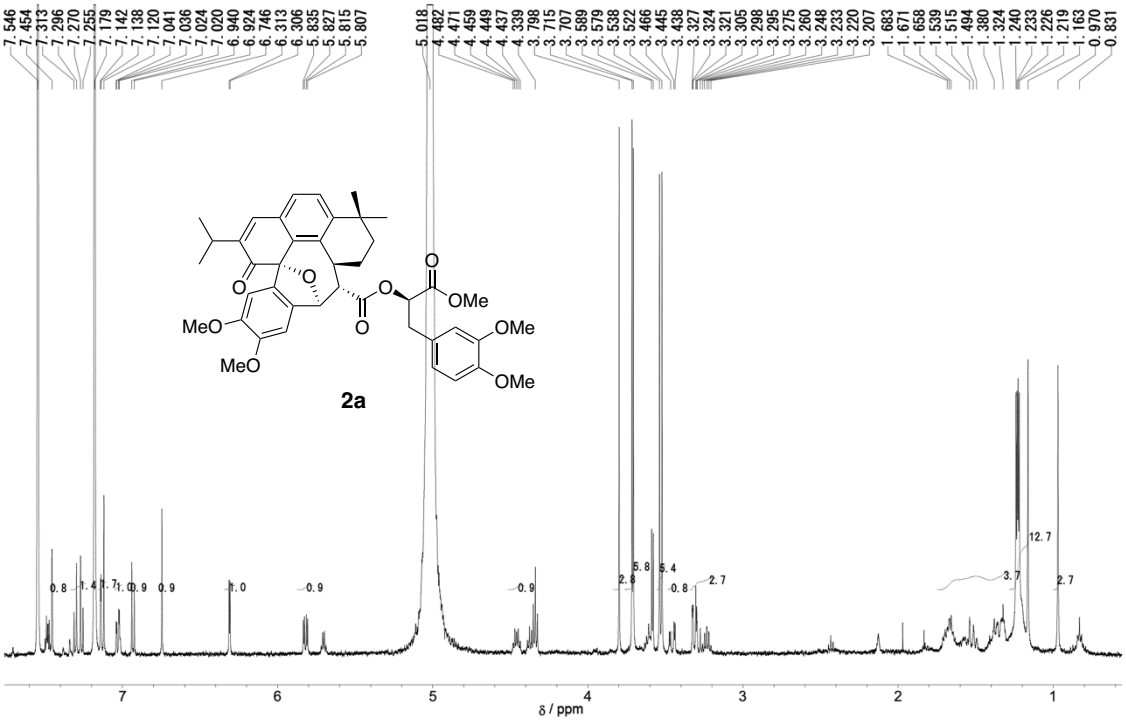


Figure S18. ^{1}H NMR spectrum of terpenoid moiety (**2b**) of **2** in C_5D_5N (500 MHz).

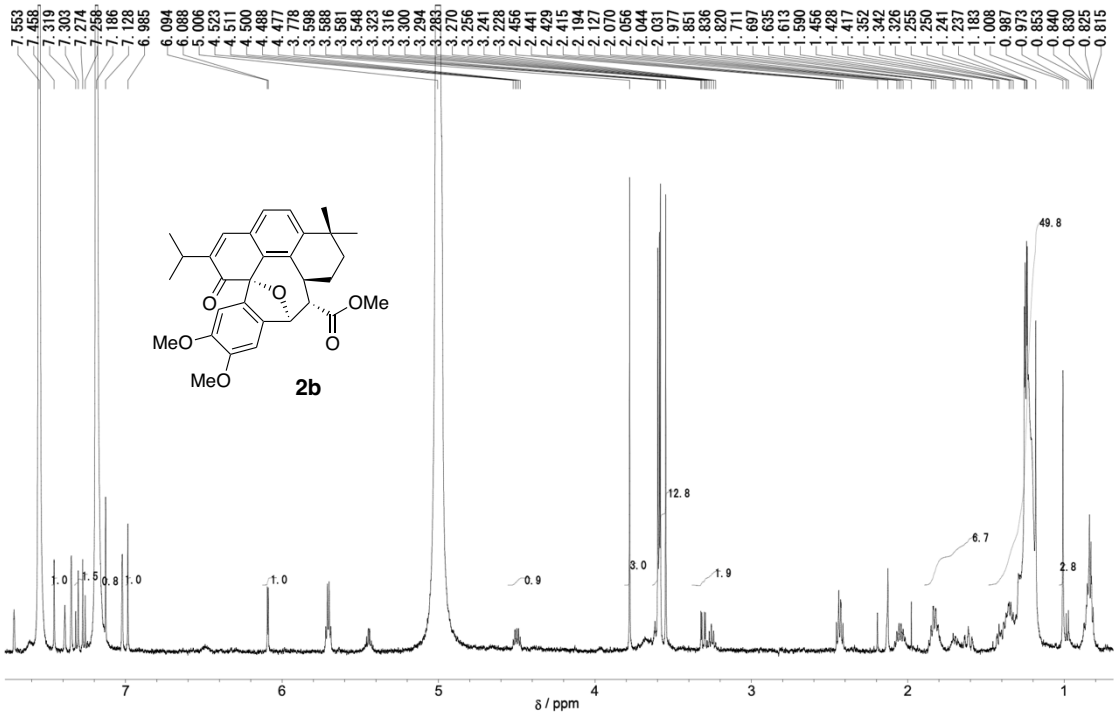


Figure S19. ^{1}H NMR spectrum of rosmarinic acid permethylate (**3a**) in $CDCl_3$ (500 MHz).

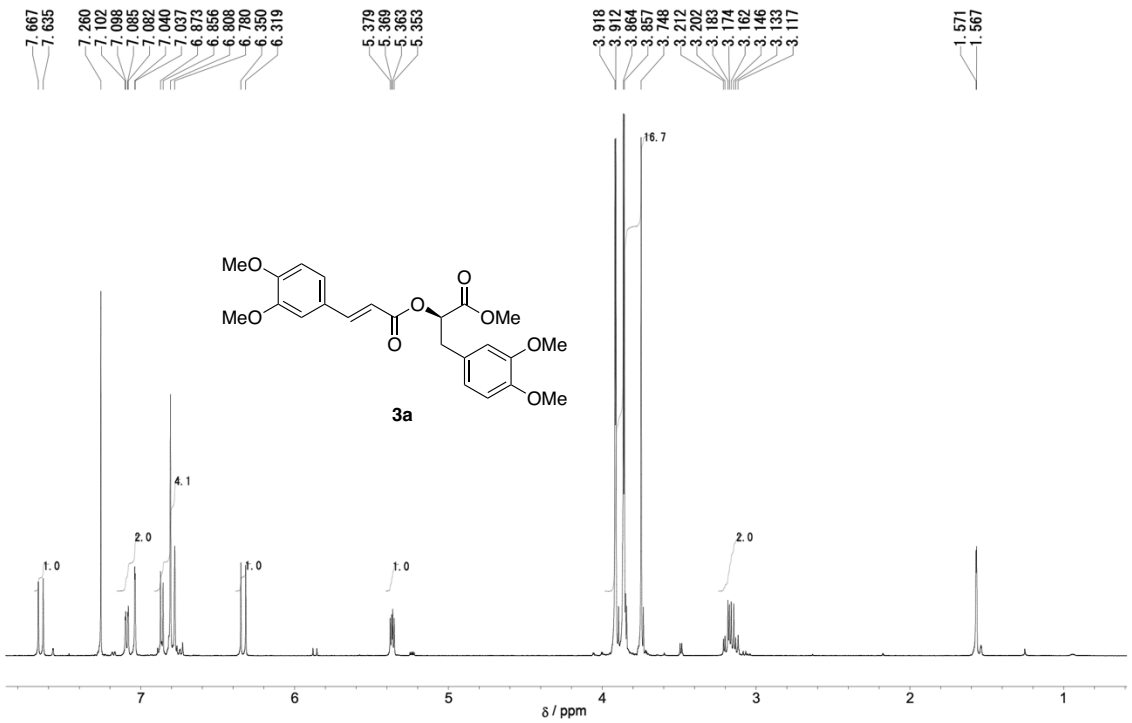


Figure S20. ^{1}H NMR spectrum of (+)-trimethyltanshinol (**3b**) in $CDCl_3$ (500 MHz).

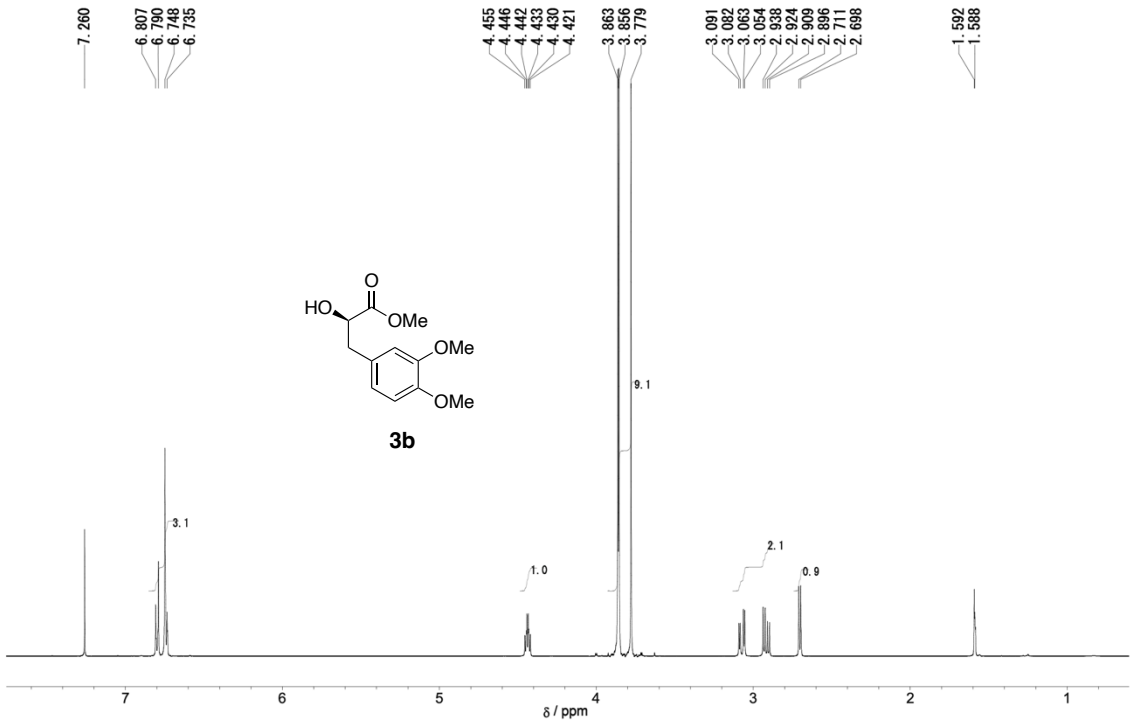


Figure S21. ^{1}H NMR spectrum of (±)-trimethyltanshinol (**3b**) in $CDCl_3$ (500 MHz).

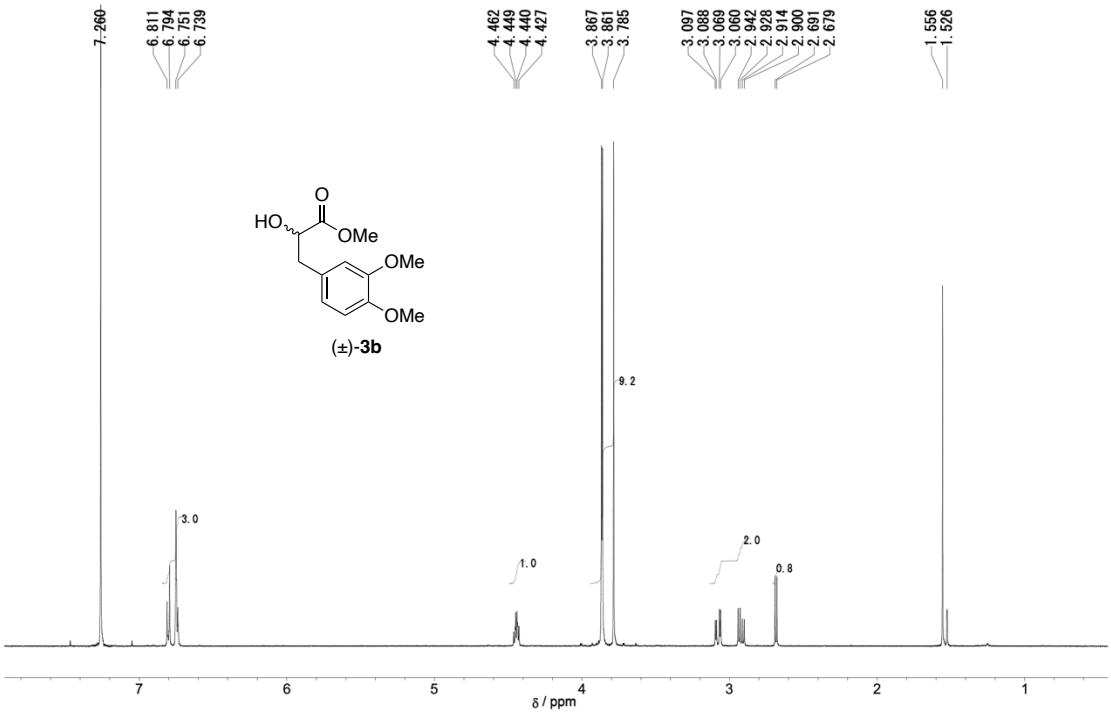
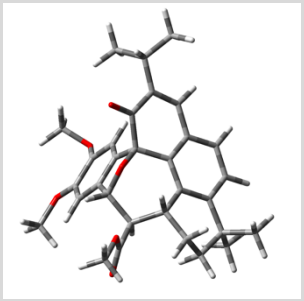


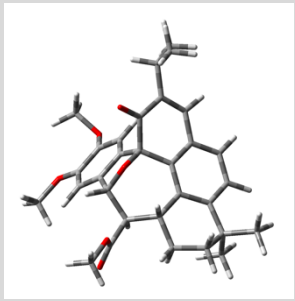
Table S1. ^{1}H and ^{13}C NMR data for perovsfolins A (**1**) and B (**2**) in C_5D_5N.

	1		**2**	
position	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)
1	37.2	4.41, dt (11.2, 6.5)	37.1	4.45, dt (10.9, 6.5)
2	24.3	1.82, m	24.2	1.68, m
		1.70, m		1.68, m
3	35.6	1.52, brt (10.8)	35.6	1.51, m
		1.35, brt (10.8)		1.44, m
4	35.2	–	35.1	–
5	149.6[a]	–	149.4	–
6	127.7	7.23 [d]	127.7	7.23 [d]
7	128.8	7.24 [d]	128.8	7.23 [d]
8	127.7	–	127.9[b]	–
9	144.9	–	145.0	–
10	134.9	–	134.9	–
11	96.7	–	96.7	–
12	197.8	–	197.6	–
13	141.1	–	141.2	–
14	139.9	7.27, s	139.8	7.25, s
15	27.4	3.10, sept (6.9)	27.4	3.10, sept (6.7)
16	21.4	1.07, d (6.9)	21.4	1.05, d (6.7)
17	21.2	1.13, d (6.9)	21.3	1.13, d (6.7)
18	31.5	1.05, s	31.5	0.94, s
19	31.9	1.11, s	31.8	1.11, s
1′	135.3[a]	–	135.1	–
2′	108.8	7.33, s	108.7	7.19, s
3′	148.5	–	148.4	–
4′	147.1	–	147.1[c]	–
5′	107.8	7.43, s	107.8	7.39, s
6′	133.8	–	134.0	–
7′	82.9	6.08, d (3.4)	82.3	6.25, d (2.4)
8′	59.9	3.32 [d]	60.5	3.28, dd (10.9, 2.4)
9′	174.4	–	173.6	–
10′	128.0	–	128.0[b]	–
11′	117.7	7.34, d (1.4)	117.8	7.35, brs
12′	147.1	–	147.2[c]	–
13′	146.3	–	146.4	–
14′	116.6	7.22, d (8.1)	116.6	7.23 [d]
15′	121.0	6.88, dd (8.1, 1.4)	120.9	6.91, brd (7.5)
16′	37.0	3.32 [d]	37.0	3.36, dd (14.0, 3.2)
		3.12, dd (14.5, 9.9)		3.21, dd (14.0, 9.5)
17′	73.9	5.74, dd (9.9, 3.7)	74.2	5.71, dd (9.5, 3.2)
18′	170.4	–	170.4	–
OMe	52.2	3.62, s	52.1	3.61, s

[a] overlapped with the signals of C_5D_5N; [b,c] signals maybe interchangeable; [d] overlapped signal

Table S2. Cartesian coordinates, total energies (E), relative energies (ΔE), and Boltzmann populations for the stable conformers of terpenoid moiety (**1b**: 1*R*,11*R*,7′*R*,8′*R*) of perovsforin A (**1**).



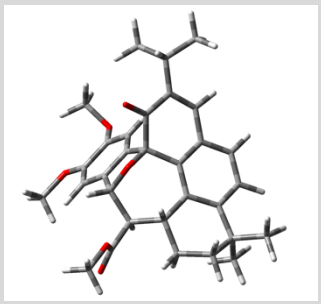


	conformer 1			**conformer 2**			
E (Hartree)	-1653.16328689			-1653.1620621			
ΔE (kcal/mol)	0			0.77			
population (%)	66.7			18.2			
	coordinates				coordinates		
symbol	X	Y	Z	symbol	X	Y	Z
C	-3.83421	-0.86921	0.273986	C	-3.879	0.085039	-0.03997
C	-4.08412	-0.71989	-1.22143	C	-4.50022	-1.23111	-0.46812
C	-3.30749	-1.78365	-2.02475	C	-3.74075	-1.86035	-1.64656
C	-1.88712	-1.97442	-1.45641	C	-2.23742	-1.92368	-1.31263
C	-1.40472	-1.31411	-0.2931	C	-1.604	-1.11173	-0.32069
C	-2.37224	-0.55541	0.639045	C	-2.43527	-0.07066	0.48163
C	-1.03229	-2.8528	-2.14827	C	-1.47635	-2.86234	-2.02904
C	0.25687	-3.11397	-1.71369	C	-0.15573	-3.13073	-1.71501
C	0.769332	-2.42546	-0.60482	C	0.457744	-2.43112	-0.67074
C	-0.04333	-1.48501	0.057689	C	-0.24165	-1.38742	-0.02432
C	2.102139	-2.74163	-0.10472	C	1.77148	-2.86494	-0.20905
C	2.659578	-2.22979	1.023624	C	2.3876	-2.42988	0.919692
C	1.882388	-1.22576	1.77391	C	1.719538	-1.36225	1.679345
C	0.692855	-0.56822	1.036006	C	0.621753	-0.56234	0.932471
C	-3.22814	-1.30985	-3.49654	C	-3.94886	-1.04079	-2.94553
C	-4.07804	-3.1282	-1.98031	C	-4.33932	-3.27135	-1.86794
C	3.998461	-2.66244	1.599725	C	3.667394	-3.02086	1.487414
C	4.491297	-4.02018	1.07999	C	3.353275	-4.09705	2.550784
C	5.072306	-1.57407	1.377057	C	4.611667	-3.58098	0.412393
O	2.185484	-0.85542	2.904694	O	2.065536	-1.02583	2.808296
C	-0.71074	1.250335	1.454084	C	-0.4802	1.43312	1.370772
O	-0.16729	0.036553	1.999772	O	-0.15352	0.141144	1.896821
C	0.360416	1.712219	0.499615	C	0.683962	1.756747	0.471769
C	1.207136	0.646109	0.231064	C	1.328838	0.570514	0.15523
C	2.255026	0.789154	-0.67802	C	2.396163	0.568051	-0.74355
C	2.450246	2.023762	-1.29649	C	2.810996	1.775684	-1.30438
C	1.586195	3.114938	-1.02216	C	2.15033	2.989044	-0.98131

(Table S2 continued)

C	0.529643	2.952839	-0.11502	C	1.072744	2.974929	-0.08491
O	-3.31933	1.27783	2.757701	O	-3.11565	2.033765	2.456572
C	-3.20011	1.704698	1.489011	C	-2.8085	2.356606	1.188233
C	-2.09119	0.980048	0.742643	C	-1.82709	1.369056	0.56763
O	-3.89545	2.58675	1.010978	O	-3.23977	3.350485	0.627107
C	-4.33181	1.911764	3.572469	C	-4.00815	2.924578	3.163975
H	-2.20067	-0.9502	1.643033	H	-2.49461	-0.45116	1.50758
O	1.855273	4.269935	-1.69124	O	2.625574	4.107461	-1.59572
O	3.455668	2.150278	-2.23032	O	3.832101	1.763198	-2.22974
C	1.01135	5.402995	-1.46546	C	1.996775	5.361523	-1.31501
C	4.62096	2.869937	-1.7868	C	5.098547	2.260492	-1.75945
H	-4.5175	-0.23492	0.848651	H	-3.89903	0.789515	-0.88091
H	-4.05356	-1.89807	0.586251	H	-4.48772	0.533439	0.752909
H	-5.15337	-0.80934	-1.45013	H	-4.50044	-1.93371	0.378057
H	-3.78178	0.284487	-1.54875	H	-5.54943	-1.07911	-0.75223
H	-1.39607	-3.36671	-3.03224	H	-1.94407	-3.43381	-2.82278
H	0.876758	-3.84109	-2.23276	H	0.391159	-3.90744	-2.24416
H	2.63934	-3.50455	-0.66389	H	2.228743	-3.66146	-0.79245
H	-2.78438	-2.06342	-4.15556	H	-3.4435	-1.52355	-3.78988
H	-4.23894	-1.09929	-3.86808	H	-5.01826	-0.97517	-3.18415
H	-2.63696	-0.39063	-3.58314	H	-3.55311	-0.02342	-2.86451
H	-5.07819	-2.99908	-2.41246	H	-5.42993	-3.18748	-1.95131
H	-3.56331	-3.90576	-2.55436	H	-3.9832	-3.74938	-2.78573
H	-4.1953	-3.49718	-0.95544	H	-4.11505	-3.93587	-1.02533
H	3.850848	-2.75152	2.683925	H	4.187307	-2.2018	2.0013
H	5.404593	-4.30899	1.612544	H	4.281395	-4.45825	3.010963
H	3.745946	-4.80934	1.234724	H	2.712123	-3.69954	3.344114
H	4.735117	-3.98615	0.010582	H	2.84366	-4.95452	2.093388
H	6.008056	-1.8589	1.873281	H	5.562139	-3.87547	0.872156
H	4.756918	-0.60662	1.781597	H	4.826476	-2.83788	-0.36449
H	5.280238	-1.44858	0.307011	H	4.196321	-4.47223	-0.07372
H	-0.8483	1.928721	2.299703	H	-0.57038	2.102364	2.229432
H	2.927481	-0.02574	-0.92652	H	2.92264	-0.33828	-1.02525
H	-0.14859	3.770681	0.101997	H	0.542863	3.887203	0.165381
H	-2.07116	1.424987	-0.25519	H	-1.66016	1.732099	-0.45028
H	-4.26136	1.427281	4.545575	H	-4.12741	2.484564	4.153343
H	-4.12915	2.981764	3.658952	H	-3.56539	3.920731	3.235743
H	-5.32002	1.75415	3.133986	H	-4.96985	2.981011	2.64865
H	1.410448	6.19543	-2.09935	H	2.540827	6.099667	-1.90512
H	-0.02347	5.186366	-1.75457	H	0.943997	5.350387	-1.61965
H	1.0474	5.717198	-0.41596	H	2.07459	5.610622	-0.2504
H	5.309927	2.880237	-2.63371	H	5.786908	2.177994	-2.60289
H	4.364192	3.895872	-1.5052	H	5.017636	3.306274	-1.44761
H	5.085976	2.35293	-0.93867	H	5.460946	1.646838	-0.92575

(Table S2 continued)



	conformer 3		
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ΔE (kcal/mol)	0.93		
population (%)	14.0		
	coordinates		
symbol	X	Y	Z
C	-3.89163	0.242563	-0.06972
C	-4.58948	-1.06467	-0.39342
C	-3.86687	-1.8357	-1.50907
C	-2.36262	-1.92997	-1.18434
C	-1.68843	-1.08968	-0.24383
C	-2.46901	0.037628	0.489633
C	-1.64522	-2.93588	-1.85264
C	-0.33546	-3.24307	-1.52884
C	0.311239	-2.51759	-0.52308
C	-0.33959	-1.41137	0.067288
C	1.604482	-2.98826	-0.03719
C	2.242048	-2.52555	1.067973
C	1.607622	-1.40351	1.781522
C	0.559216	-0.58222	0.987993
C	-4.06068	-1.1384	-2.87938
C	-4.51971	-3.23815	-1.58328
C	3.509919	-3.12218	1.656568
C	3.831341	-4.53288	1.143615
C	4.7149	-2.17944	1.44165
O	1.931721	-1.0595	2.9141
C	-0.44517	1.482036	1.32672
O	-0.1864	0.201231	1.913115
C	0.739821	1.708018	0.425245
C	1.323338	0.477321	0.163633
C	2.38478	0.380168	-0.73668
C	2.858928	1.538362	-1.35206
C	2.263422	2.797497	-1.08211
C	1.189296	2.878722	-0.18498
O	-3.06219	2.272745	2.340074
C	-2.71952	2.514182	1.062743
C	-1.78456	1.44515	0.50916

(Table S2 continued)

O	-3.08807	3.500004	0.445557
C	-3.91868	3.242353	2.985744
H	-2.56708	-0.28277	1.533285
O	2.792565	3.861148	-1.74733
O	3.872837	1.430808	-2.2792
C	2.23072	5.157415	-1.52185
C	5.164984	1.887575	-1.83835
H	-3.85309	0.873589	-0.96686
H	-4.48159	0.793471	0.670836
H	-4.63362	-1.69096	0.509718
H	-5.62714	-0.87609	-0.69717
H	-2.14198	-3.52945	-2.61212
H	0.175456	-4.06915	-2.01768
H	2.018361	-3.8388	-0.57375
H	-3.57942	-1.71447	-3.67809
H	-5.12972	-1.06097	-3.11555
H	-3.63225	-0.13117	-2.89625
H	-5.60776	-3.12263	-1.66235
H	-4.19325	-3.81796	-2.4522
H	-4.30743	-3.82358	-0.68101
H	3.342648	-3.18798	2.739823
H	4.698398	-4.93235	1.681969
H	2.992583	-5.22235	1.295849
H	4.0835	-4.53167	0.075578
H	5.601278	-2.5766	1.950943
H	4.519034	-1.17743	1.837248
H	4.949769	-2.08786	0.373846
H	-0.51222	2.192957	2.153431
H	2.860557	-0.56423	-0.97955
H	0.706645	3.827142	0.023842
H	-1.58667	1.744129	-0.52382
H	-4.06604	2.865831	3.997279
H	-3.43194	4.220147	3.005179
H	-4.87276	3.311911	2.45787
H	2.806027	5.83833	-2.1499
H	1.175891	5.186142	-1.81812
H	2.331143	5.451737	-0.47079
H	5.843706	1.728638	-2.67866
H	5.13739	2.950401	-1.57956
H	5.50116	1.299517	-0.97583
C	-3.89163	0.242563	-0.06972