

Four Guaianolides from *Sinodielsia yunnanensis*

Nian-He WANG,^a Masahiko TANIGUCHI,^b Daisuke TSUJI,^b Mitsunobu DOI,^b Hirohumi OHISHI,^b Kenji YOZA,^c and Kimiye BABA^{*,b}

^aInstitute of Botany Jiangsu Province and Academia Sinica; 210014, Nanjing, China; ^bOsaka University of Pharmaceutical Sciences; 4–20–1 Nasahara, Takatsuki, Osaka 569–1094, Japan; and ^cBruker AXS; 3–21–5 Ninomiya, Tsukuba, Ibaraki 305–0051, Japan. Received August 26, 2002; accepted October 7, 2002

Four new guaianolides, sinodielides A–D (1–4), were isolated from *Sinodielsia yunnanensis* WOLFF together with a known polyacetylene, faltarindiol, and two known coumarins, bergapten and scopoletin. Their structures were established by spectral and X-ray analyses.

Key words *Sinodielsia yunnanensis*; Umbelliferae; guaianolide; sinodielide A; sinodielide B; sinodielide C

Sinodielsia yunnanensis is a species endemic to China and classified into one genus and one species of Umbelliferae. It grows in the mountains (2000–3100 m above sea level) of Yunnan province.¹⁾ Its root is used in Chinese folk medicine as an antipyretic, analgesic, and diaphoretic agent in local areas. In the course of our studies on the components of Umbelliferous plants, we investigated the constituents of the root of this plant and isolated four new guaianolides, sinodielides A–D (1–4) together with a polyacetylene, faltarindiol, and two coumarins, bergapten and scopoletin. This paper describes the structure elucidation of compounds 1–4.

Compound **1**, colorless needles, mp 145.5–146.5 °C, $[\alpha]_D^{22} -42.3^\circ$ ($c=0.511$, CHCl₃), was assigned the molecular formula C₁₅H₂₀O₂ ($[M]^+$ m/z 232.1460) by high resolution electron impact (HR-EI)-MS. The IR spectrum of **1** showed absorption bands due to a lactone carbonyl at 1757 cm⁻¹. The ¹H-NMR spectrum of **1** (Table 1) showed the presence of an olefinic proton [δ 5.44 (1H, tq, $J=5.3$, 1.6 Hz)], two adjacent methine protons [δ 4.37 (1H, dd, $J=9.8$, 5.8 Hz), 3.56 (1H, br d, $J=9.8$ Hz)], and adjacent methine proton and methyl groups [δ 2.79 (1H, dq, $J=7.3$, 7.3 Hz), 1.19 (3H, d, $J=7.3$ Hz)], a methine proton [δ 2.56 (1H, m)], three methylene protons [δ 2.95 (2H, br s), 2.56, 2.09 (each 1H, m), 1.78, 1.54 (each 1H, m)], and two olefinic methyl groups [δ 1.83 (3H, dd, $J=1.6$, 0.9 Hz), 1.56 (3H, br s)]. On the other hand, the ¹³C-NMR spectrum (Table 2) showed the presence of a lactone carbonyl carbon (δ 179.46), three quaternary car-

bons (δ 142.00, 130.98, 127.55), five methine carbons (δ 124.15, 86.13, 50.71, 42.14, 38.55), three methylene carbons (δ 38.06, 36.39, 18.92), and three methyl carbons (δ 21.34, 16.77, 10.33). The connectivities of the above fragments were clarified by H–H correlation spectroscopy (H–H COSY) and heteronuclear multiple-bond coherence (HMBC) experiments (Fig. 1). The spectral data indicated that **1** is guaianolide.

To confirm the stereostructure of **1**, the nuclear Overhauser effect correlation spectroscopy (NOESY) experiment was performed. Cross-peaks between 5-H/8-Hb, 6-H/11-H, and 8-Ha/13-Me were observed (Fig. 2). From the above results, the relative stereostructure of **1** was established as shown in Fig. 2. This structure was also supported by the X-ray analysis of **1** (Fig. 3).

Compound **2**, colorless needles, mp 104.3–105.0 °C, $[\alpha]_D^{22} -16.1^\circ$ ($c=0.506$, CHCl₃), was assigned the molecular formula C₁₅H₁₈O₂ ($[M]^+$ m/z 230.1311) by HR-EI-MS. Comparison of the ¹H-NMR spectral data (Table 1) of **1** and **2** indicated that **2** is closely related to **1**, except for the presence of an olefinic methyl group [δ 1.83 (3H, dm, $J=1.4$ Hz)] instead of the signals due to two methine protons at the C-7 and C-11 positions and a methyl group linked to a methine proton. The ¹³C-NMR spectrum (Table 2) of **2** also resembled that of **1** except for the presence of two olefinic carbons (δ 164.00, 121.65) instead of signals two methine carbons in **1**. These spectral data suggest that **2** has a unsaturated lac-

Table 1. ¹H-NMR Data for Compounds 1–4 in CDCl₃

	1	2	3	4
2	2.95 br s	2.99 m		2.85 m 2.21 dqm (17.8, 1.8)
3	5.44 tq (5.3, 1.6)	5.59 dm (0.9)	6.23 q (1.4)	5.64 dq (1.4, 1.4)
5	3.56 br d (9.8)	2.99 m	3.14 dd (10.5, 0.9)	2.29 m
6	4.37 dd (9.8, 5.8)	4.36 dd (10.3, 1.4)	4.39 d (10.5)	4.56 dd (11.2, 1.6)
7	2.56 m			
8	1.54 m	2.14 m	2.23 m	2.29 m
	1.78 m	2.86 m	2.98 ddm (5.5, 1.8)	2.85 m
9	2.56 m	2.14 m	2.35 m	2.29 m
	2.09 m			1.50 brt (14.0)
11	2.79 dq (7.3, 7.3)			
13	1.19 d (7.3)	1.83 dm (1.4)	1.90 t (1.6)	1.83 t (1.6)
14	1.56 br s	1.77 d (1.4)	2.48 d (0.9)	1.40 d (0.7)
15	1.83 dd (1.6, 0.9)	1.95 dd (0.9, 0.7)	2.35 dm (1.4)	1.98 d (1.8)

Chemical shifts are δ values and followed by multiplicities and J values (in Hz).

* To whom correspondence should be addressed. e-mail: baba@gly.oups.ac.jp

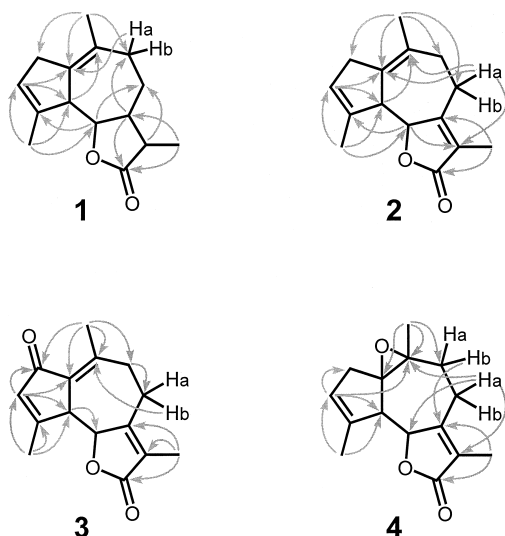


Fig. 1. The Main HMBC Correlations of 1—4

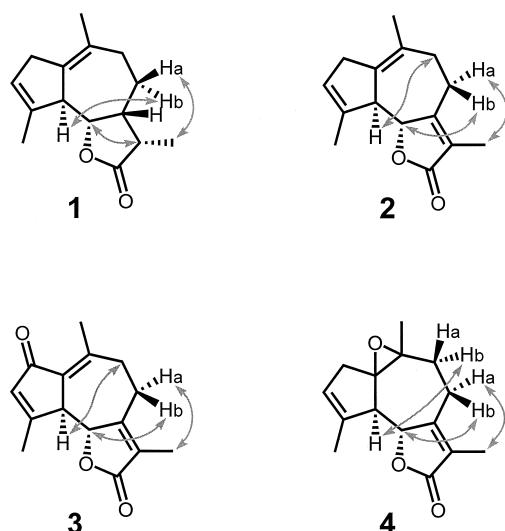


Fig. 2. NOE Correlations of 1—4

tone ring taking the place of a saturated lactone ring in **1**. This was confirmed by the analyses of the two dimensional (2D)-NMR experiments including HMBC and NOESY (Figs. 1, 2). To elucidate the relative stereostructure of **2**, X-ray analysis of **2** was performed (Fig. 4).

Compound **3**, colorless crystalline powder, mp 140.5—141.0 °C, $[\alpha]_D^{22} -20.3^\circ$ ($c=0.463$, CHCl_3), was assigned the molecular formula $\text{C}_{15}\text{H}_{16}\text{O}_3$ ($[\text{M}]^+ m/z$ 224.1102) by HR-EI-MS. The ^1H -NMR spectrum of **3** showed the presence of two adjacent methine protons [δ 4.39 (1H, d, $J=10.5$ Hz), 3.14 (1H, dd, $J=10.5$, 0.9 Hz)], two methylene protons [δ 2.98 (1H, ddm, $J=5.5$, 1.8 Hz), 2.23 (1H, m), 2.35 (2H, m)], and three olefinic methyl groups [δ 2.48 (3H, d, $J=0.9$ Hz), 2.35 (3H, dm, $J=1.4$ Hz), 1.90 (3H, dm, $J=1.6$ Hz)]. These spectral data were closely related to those of **2**, except for the lack of the signals assignable to a methylene proton at the C-2 position of **2** and the observation of the downfield-shifted methine proton at the C-3 position from δ 5.59 to δ 6.23 (1H, q, $J=1.4$ Hz). In the ^{13}C -NMR spectrum of the methylene carbon at the C-2 position, the presence of the carbonyl carbon

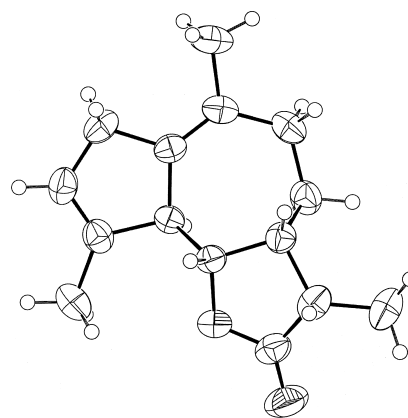


Fig. 3. ORTEP Diagram of 1

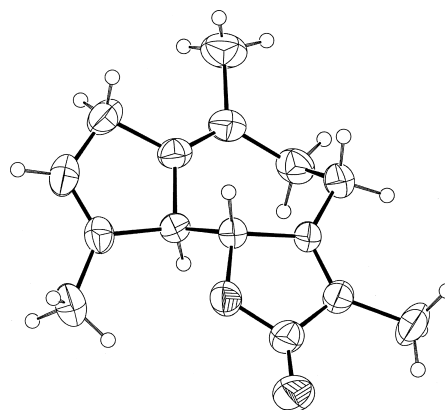


Fig. 4. ORTEP Diagram of 2

Table 2. ^{13}C -NMR Data for Compounds 1—4 in CDCl_3

	1	2	3	4
1	130.98	134.40	130.50	70.54
2	38.06	36.71	198.59	37.55
3	124.15	126.40	135.70	124.90
4	142.00	141.38	170.48	141.60
5	50.71	55.65	52.22	56.56
6	86.13	84.38	83.45	84.28
7	42.14	164.00	151.79	151.74
8	18.92	27.28	25.39	23.21
9	36.39	31.75	34.75	34.41
10	127.55	132.27	151.81	62.84
11	38.55	121.65	122.85	122.66
12	179.46	174.36	173.33	173.89
13	10.33	8.27	8.50	8.44
14	21.34	21.82	20.60	19.78
15	16.77	17.85	19.88	17.90

(δ 195.59) was observed, indicating that the methylene at C-2 was replaced by the carbonyl group in **3**. The stereostructure of **3** was estimated on the basis of the analysis of its NOESY spectrum (Fig. 2).

Compound **4**, colorless amorphous powder, $[\alpha]_D^{22} +35.4^\circ$ ($c=0.596$, CHCl_3), was assigned the molecular formula $\text{C}_{15}\text{H}_{18}\text{O}_3$ ($[\text{M}]^+ m/z$ 246.1256) by HR-EI-MS. The NMR spectra (^1H , ^{13}C , COSY, HMBC) were closely related to those of **2**, except for the presence of the signals due to two quaternary carbons linked to an oxygen atom (δ 70.54, 62.84) instead of the signal assignable to two olefinic carbons

(δ 134.40, 132.27) at C-1 and C-10 in **2**, indicating the formation of an epoxy ring between C-1 and C-2 of **4**. The stereostructure of **4** was determined from HMBC and NOESY spectral analyses (Figs. 1, 2).

Experimental

General ^1H - and ^{13}C -NMR, distortionless enhancement by polarization transfer (DEPT), heteronuclear multiple-quantum coherence (HMQC), and HMBC spectra were recorded on a Varian UNITY INOVA-500 spectrometer, operating at 500 MHz for proton and 125 MHz for carbon, with tetramethylsilane (TMS) as an internal standard. HR-EI-MS spectra were obtained using a Hitachi M-4100H (70 eV) mass spectrometer. UV and IR spectra were recorded on a Shimadzu UV-2100 and a Perkin Elmer FT-IR 1720 spectrophotometer, respectively. Optical rotatory dispersion (ORD) spectra were recorded on a JASCO J820 digital polarimeter. Column chromatography was performed using Merck Silica gel F₂₅₄ plates (0.25 mm) and Sephadex LH-20. Spots and bands were detected by UV irradiation (254 and 365 nm).

Plant Material Air-dried roots of *S. yunnaensis* (5 kg) were collected from plants grown in Lijiang, Yunnan Province, China, in September 1999. A voucher specimen is deposited in the Institute of Botany, Jiangsu Province, and Academia Sinica, Nanjing, China. The plant was identified by one of the authors (N.W.).

Extraction and Isolation The roots were chopped into small pieces and extracted with EtOH (101×5) under reflux. The combined EtOH extracts were concentrated to dryness *in vacuo*. The residue (626.4 g) was subjected to column chromatography on silica gel (4.5 kg) eluted successively with a hexane–EtOAc solvent system with increasing polarity (5 : 1→1 : 2) to afford 17 fractions (fr.) [fr. 1 (91.5 g), fr. 2 (78.4 g), fr. 3 (156.6 g), fr. 4 (7.7 g), fr. 5 (5.7 g), fr. 6 (6.5 g), fr. 7 (2.7 g), fr. 8 (3.6 g), fr. 9 (6.1 g), fr. 10 (6.5 g), fr. 11 (8.2 g), fr. 12 (12.4 g), fr. 13 (7.7 g), fr. 14 (14.3 g), fr. 15 (28.2 g), fr. 16 (54.7 g), and fr. 17 (38.9 g). Fraction 2 was rechromatographed on silica gel with hexane–EtOAc (3 : 1) followed by Sephadex LH-20 to give **1** (3.09 g), **2** (1.2 g), and falcariindiol (145 g). Fractions 6 and 7 were rechromatographed on silica gel with hexane–EtOAc (3 : 1) to afford **3** (75 mg), **4** (50 mg), and bergapten (20 mg). Fraction 11 was rechromatographed on silica gel with hexane–EtOAc (1 : 1) to afford scopoletin (15 mg).

Sinodiellide A (1): Colorless needles, mp 145.5–146.5 °C, HR-EI-MS: m/z 232.1460 [M]⁺ (Calcd for C₁₅H₂₀O₂: 232.1480). [α]_D²² –42.3° (c = 0.511, CHCl₃), IR (KBr) cm⁻¹: 1757, 1434, 1352. UV λ_{max} (MeOH) nm (log ϵ): 203.5 (3.06). ^1H - and ^{13}C -NMR data are shown in Tables 1 and 2.

Sinodiellide B (2): Colorless needles, mp 104.3–105.0 °C, HR-EI-MS: m/z 230.1311 [M]⁺ (Calcd for C₁₅H₁₈O₂: 230.1261). [α]_D²² –16.1° (c =

0.506, CHCl₃), IR (KBr) cm⁻¹: 1741, 1671, 1438. UV λ_{max} (MeOH) nm (log ϵ): 245.0 (2.68), 209.0sh (3.37). ^1H - and ^{13}C -NMR data are shown in Tables 1 and 2.

Sinodiellide C (3): Colorless crystalline powder, mp 140.5–141.0 °C, HR-EI-MS: m/z 244.1102 [M]⁺ (Calcd for C₁₅H₁₆O₃: 244.1072). [α]_D²² –20.3° (c = 0.463, CHCl₃), IR (KBr) cm⁻¹: 1747, 1685, 1439. UV λ_{max} (MeOH) nm (log ϵ): 252.0 (3.87), 239.0 (3.83), 223.0 (3.88). ^1H - and ^{13}C -NMR data are shown in Tables 1 and 2.

Sinodiellide D (4): Colorless amorphous powder, HR-EI-MS: m/z 246.1246 [M]⁺ (Calcd for C₁₅H₁₈O₃: 246.1246). [α]_D²² +35.4° (c = 0.596, CHCl₃), IR (KBr) cm⁻¹: 1757, 1673, 1446. UV λ_{max} (MeOH) nm (log ϵ): 262.0sh (2.80), 217.0 (3.88). ^1H - and ^{13}C -NMR data are shown in Tables 1 and 2.

X-Ray Analyses of 1 and 2 X-Ray diffraction data of **1** were measured on a Bruker AXS SMART APEX diffractometer. The structure was elucidated using SHELXS97 and refined SHELXL97.²⁾ Crystal data of **1**: formula = C₁₅H₂₀O₂, M_r = 232.31, orthorhombic, $P2_12_12_1$, a = 4.7838(6) Å, b = 7.8933(9) Å, c = 33.700(4) Å, V = 1272.5(3) Å³, Z = 4, D_x = 1.213 g cm⁻³, $F(000)$ = 504, $\mu(\text{MoK}\alpha)$ = 0.079 mm⁻¹. Observed reflections = 9419, R_{int} = 0.0322. Reflections used in refinement = 3164, θ_{max} = 28.3°, number of parameters = 157, R = 0.0526, wR = 0.1212, (Δ/σ)_{max} = 0.025, $\Delta\rho_{\text{max}}$ = 0.250 e Å⁻³, $\Delta\rho_{\text{min}}$ = –0.165 e Å⁻³. The absolute structure was not determined from the Flack x parameter,³⁾ because no element with relatively large abnormal dispersion factors on MoK α radiation was included in **1**.

X-Ray diffraction data of **2** were measured in a Rigaku AFC5R diffractometer. Crystal data of **2**: formula = C₁₅H₁₈O₂, M_r = 230.29, monoclinic, $P2_1$, a = 6.558(6) Å, b = 18.512(4) Å, c = 10.435(4) Å, β = 96.36(5)°, V = 1259.0(13) Å³, Z = 4, D_x = 1.215 g cm⁻³, $F(000)$ = 496, $\mu(\text{CuK}\alpha)$ = 0.625 mm⁻¹. Observed reflections = 2720, R_{int} = 0.0604. Reflections used in refinement = 2247, θ_{max} = 67.62°, Flack x parameter²⁾ = –0.26(36), number of parameters = 308, R = 0.0508, wR = 0.1444, (Δ/σ)_{max} < 0.001, $\Delta\rho_{\text{max}}$ = 0.198 e Å⁻³, $\Delta\rho_{\text{min}}$ = –0.180 e Å⁻³. The asymmetric unit of **2** included two independent molecules with similar structures, and only one molecule was drawn in Fig. 4. The absolute structure was examined by the calculation of the Flack x parameter, and the present structure was suggested as a better solution because the Flack x parameter was 0.48(36) for the reversed structure.

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