

Two New Guaianolides and a New Daucene Derivative from *Sinodielsia yunnanensis*

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Abstract

From the roots and rhizomes of *Sinodielsia yunnanensis*, three new sesquiterpenes were isolated and their structures were established as 5 α ,6 β -H-1(10),3,7(11)-guaiatrien-12,6 α -olide (**1**), 5 α ,6 β ,7 β -H-1(10),3-guaiadien-12,6 α -olide (**2**) and 5 β -hydroxy-10 α -O-angeloyl-3-oxodauc-8-ene (**3**) by means of spectroscopic analyses and single-crystal X-ray experiment (for compound **1**).

Sinodielsia yunnanensis Wolff. (Apiaceae), distributed in south-west China, has been used as a substitute of the traditional Chinese medicine *Gao-Ben* by local practitioners for antibacterial, anti-inflammatory and analgesic purposes [1]. A phytochemical study of this plant has resulted in the isolation of three new sesquiterpenes (**1–3**). In the present paper, we described the isolation, structural elucidation and identification of compounds **1–3**.

Compound **1** was deduced as C₁₅H₁₈O₂ from a combination of elementary analysis with EI-mass spectrometry ([M]⁺ *m/z* = 230), as well as ¹H-NMR, ¹³C-NMR and DEPT spectra. Its IR spectrum showed the absorption bands for an α,β -unsaturated lactone group (1670 cm⁻¹). The NMR spectra (see Materials and Methods section as well as Table 1) of **1** exhibited signals for three methyls (δ_{H} = 1.68, s; 1.74, s; 1.86, s), one olefinic proton (δ_{H} = 5.49), one oxygenated methane (δ_{C} = 86.0; δ_{H} = 4.27, d, *J* = 10.2 Hz), and a lactone carbonyl (δ_{C} = 179.1). Except for the difference caused by the additional double bond at 7(11) in **1**, the ¹H-NMR and ¹³C-NMR data of **1** were nearly superposable with those of 11 β ,13-dihydrokauniolide (**4**) [2], which suggested that both compounds have the same skeleton. Thus, **1** was determined as 5 α ,6 β -H-1(10),3,7(11)-guaiatrien-12,6-olide, which was also confirmed by X-ray single-crystal analysis (Fig. 1).

The molecular formula C₁₅H₂₀O₂ of **2**, determined by elementary analysis and EI-mass spectrometry ([M]⁺ *m/z* = 232), indicated

the presence of two extra hydrogens, when compared to **1**. The ¹H-NMR, ¹³C-NMR and DEPT spectra (see Materials and Methods as well as Table 1) of **2** were very similar to those of **1**, suggesting that **2** was a derivative of **1**. The absence of two sp² carbon signals in ¹³C-NMR spectrum and the presence of H-6 (δ = 4.31, dd, *J* = 10.0, 5.8 Hz) and Me-13 (δ = 1.12, 3H, d, *J* = 7.6 Hz) showed that the additional hydrogens were attached to C-7 and C-11, respectively. The strong NOESY correlations observed between H-6 and H-11, H-7 and H-11 suggested that H-6, H-7 and H-11 should be in the same β orientation. It is significant to find that **2** and **4** [2] have the same planar structure, but different chemical shift values of H-5, H-6, H-7 and H-11 and opposite optical rotational values [α]_D²⁵: -59.82° (c 0.56, CHCl₃); **4**: [α]_D²⁵: +14.3° (c 0.5, CHCl₃), which further validated the relative configuration of H-7 in **2**, which should be β -oriented, contrary to that in **4**. Therefore, **2** was assigned as 5 α ,6 β ,7 β ,11 β -H-1(10),3-guaiatrien-12,6-olide.

Compound **3** was determined as C₂₀H₃₄O₄ by elementary analysis and EI-mass spectrometry ([M]⁺ *m/z* = 334). The IR spectrum of **3** indicated the presence of hydroxy (3428 cm⁻¹), ester (1713 and 1157 cm⁻¹), and double bond (1647 cm⁻¹) groups. The NMR spectra (see Materials and Methods as well as Table 1) of **3** showed the signals for four methyls, one trisubstituted double bond [δ_{H} = 5.68 (1H, d, *J* = 7.7 Hz, H-9); δ_{C} = 146.1, 119.6], one angeloyloxy group [δ = 6.03 (1H, dq, *J* = 7.2, 1.4 Hz), 1.96 (3H, d, *J* = 7.2 Hz), 1.87 (1H, s)], one oxygenated quaternary carbon (δ = 82.2) and a ketone group (δ = 220.1). The ¹H-NMR and ¹³C-NMR data of **3** were similar to those of 15-hydroxyvaginatin, which suggested that **3** had the same daucane skeleton as 15-hydroxyvaginatin [3]. The signal at δ = 220.1 in the ¹³C-NMR

Table 1 ¹³C-NMR chemical shifts for **1–3**

| Carbon | $\delta(\text{C})$ (mult.) | | |
|--------|----------------------------|-----------|-----------|
| | 1 | 2 | 3 |
| 1 | 130.9 (s) | 134.2 (s) | 60.2 (s) |
| 2 | 37.9 (t) | 36.5 (t) | 37.0 (t) |
| 3 | 124.0 (d) | 126.3 (d) | 220.1 (s) |
| 4 | 141.9 (s) | 141.2 (s) | 50.8 (d) |
| 5 | 50.6 (d) | 55.5 (d) | 82.2 (s) |
| 6 | 86.0 (d) | 84.2 (d) | 38.5 (t) |
| 7 | 38.4 (d) | 163.8 (s) | 29.0 (t) |
| 8 | 18.8 (t) | 27.1 (t) | 146.1 (s) |
| 9 | 36.2 (t) | 31.6 (t) | 119.6 (d) |
| 10 | 127.4 (s) | 132.2 (s) | 75.7 (d) |
| 11 | 42.0 (d) | 121.4 (s) | 26.3 (d) |
| 12 | 179.1 (s) | 174.2 (s) | 24.5 (q) |
| 13 | 10.2 (q) | 8.0 (q) | 18.2 (q) |
| 14 | 21.2 (q) | 21.6 (q) | 21.0 (q) |
| 15 | 16.6 (q) | 17.7 (q) | 26.0 (q) |
| 1' | | | 166.1 (s) |
| 2' | | | 127.0 (s) |
| 3' | | | 138.8 (d) |
| 4' | | | 15.6 (q) |
| 5' | | | 20.6 (q) |

Measured in CDCl₃, with TMS as internal standard.

OAng: C₁-C₅.

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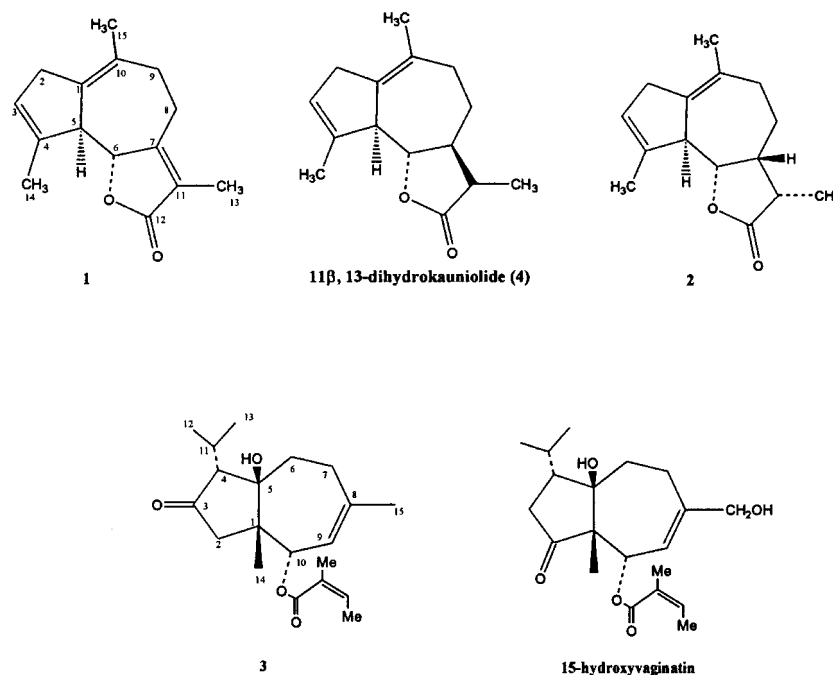
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(DEPT) spectrum and a peak at 1789 cm^{-1} in IR spectrum indicated the presence of a carbonyl group located on the 5-membered ring. In the HMBC spectrum, the methylene carbon signal ($\delta = 37.0$) correlated with Me-14, which unequivocally indicated the ketone group located at C-3. Consequently, compound **3** was determined as 5 β -hydroxy-10- α -O-angeloyl-3-oxodauc-8-ene.

Material and Methods

All melting points were obtained on a Koffler apparatus and are uncorrected. IR spectra were obtained on a Bio-Rad FTS-135 spectrometer with KBr pellets. NMR spectra were recorded on a Bruker AM-400 or DRX-500 instrument with TMS as an internal standard and CDCl_3 or $\text{C}_5\text{D}_5\text{N}$ as a solvent. $^1\text{H-NMR}$, $^1\text{H-}^1\text{H}$ COSY spectra were measured at 400.13 or 500.13 MHz; $^{13}\text{C-NMR}$ and DEPT spectra were recorded at 100.6 MHz; the HMBC spectrum was obtained at 500.13 MHz/125.8 MHz. $^{13}\text{C-NMR}$ assignments were determined by $^{13}\text{C-}^1\text{H}$ COSY and HMQC spectra. The EIMS were carried out on a VG Auto Spec-3000 spectrometer at 70 eV. The roots and rhizomes of *S. yunnanensis* were collected in the Yongsheng Natural Reserve Area, Lijiang Prefecture of the Yunnan Province, in March 1998, and identified by Professor X. H. Liao, Yunnan College of Traditional Chinese Medicine. A voucher specimen (YNTCM 980301 Liao) is deposited in the Herbarium of the Department of TCM, Yunnan College of Traditional Chinese Medicine, Kunming, Yunnan, People's Republic of China.

Air-dried and powdered roots and rhizomes of *S. yunnanensis* (5.0 kg) were extracted with EtOH (10 L \times 3) under reflux for 2.5 h each time. After evaporation of the solvent under vacuum a total of 700.0 g of crude extract was obtained. The extract was suspended in H_2O and partitioned with petroleum ether (60–90°C), EtOAc and *n*-BuOH, respectively. Evaporation of the petroleum layer yielded 498.0 g of a waxy solid, 200.0 g of which were subjected to repeated chromatography on a silica gel column

(200–300 mesh, 2.0 kg). Elution with petroleum and with a gradient of EtOAc in petroleum gave six fractions. Fraction 4 (20 g) was further purified by crystallization (petroleum ether-EtOAc, 10:1) to afford **1** (5.0 g). Fraction 5 (25 g) was chromatographed over 600 g silica gel column (200–300 mesh) with petroleum ether-EtOAc (20:1 to 5:1, each: 150 mL) to furnish frs. 5.4 (8.0 g) and frs. 5.5 (200 mg). Fraction 5.4 was further purified by crystallization from petroleum ether-EtOAc, 5:1 to afford **2** (4.0 g). After purification (2 \times) by CC over 20 g silica gel (400 mesh) with petroleum-EtOAc (5:1), fr. 5.5 afforded **3** (100 mg, R_f : 0.30).

5 α , 6 β -H-1(10),3,7(11)-Guaiaatrien-12,6-olide (1): Colorless needles from EtOAc, m.p. 91–92°C; $[\alpha]_D^{25}$: -30.09° (c 0.62, CHCl_3); IR (KBr): $\nu_{\text{max}} = 3064, 3043, 2559, 2922, 2850, 1670, 1438, 1363, 1315, 1094, 996\text{ cm}^{-1}$; EI-MS: $m/z = 230$ (78, $[\text{M}]^+$), 215 (20), 201 (16), 187 (14), 173 (16), 159 (14), 151 (25), 135 (19), 120 (100), 105 (83), 91 (46), 77 (41), 67 (28), 55 (48); Elemental analysis C: 78.44%, H: 7.96% (calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_2$); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): $\delta = 5.49$ (1H, br.s, H-3), 4.27 (1H, d, $J = 10.2\text{ Hz}$, H-6), 2.90 (2H, br.s, H-2), 2.90 (1H, br.s, H-5), 2.78 (1H, m, H-8), 2.06

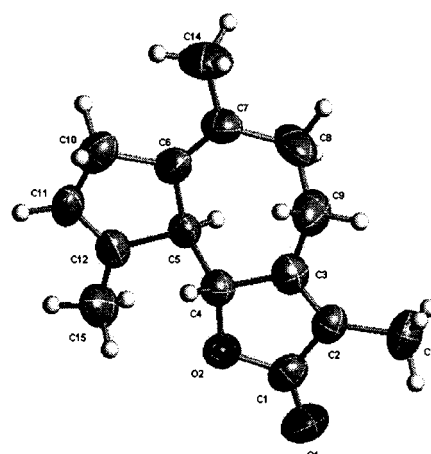


Fig. 1 ORTEP structure of **1**.

(1H, m, H-8), 2.06(2H, m, H-9), 1.86 (3H, s, Me-15), 1.74(3H, s, Me-13), 1.68(3H, s, Me-14); ^{13}C -NMR: see Table 1.

5 α ,6 β ,7 β ,11 β -H,1(10),3-Guaiadien-12,6-olide (2): White powder from EtOAc, m.p. 127–128 °C; $[\alpha]_{\text{D}}^{21}$: –59.82° (c 0.56, CHCl_3); IR (KBr): ν_{max} = 2964, 2860, 1732, 1620, 1090 cm^{-1} ; EI-MS: m/z = 232(100, $[\text{M}]^+$), 217 (36), 204 (8), 189 (15), 175 (26), 158 (93), 143 (50), 133 (55), 120 (77), 105 (70), 91 (49), 85 (24), 79 (43), 65 (25), 55 (42); Elemental analysis C: 77.65%, H: 8.71% (calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_2$); ^1H -NMR (CDCl_3 , 400 MHz): δ = 5.37 (1H, br.s, H-3), 4.31 (1H, dd, J = 10.0, 5.8 Hz, H-6), 3.49 (1H, br.d, J = 10.0 Hz, H-5), 2.89 (2H, br.s, H-2), 2.73 (1H, m, H-7), 2.50 (2H, m, H-9 α , H-11), 2.03 (1H, m, H-9 β), 1.77 (3H, s, Me-15), 1.74 (1H, ddd, J = 5.2, 5.2, 5.2 Hz, H-8 α), 1.50 (3H, s, Me-14), 1.47 (1H, m, H-8 α), 1.12 (3H, d, J = 7.6 Hz, Me-13); ^{13}C -NMR: see Table 1.

5 β -Hydroxy-10 α -O-angeloyl-3-oxodauc-8-ene (3): Colorless cubes from EtOAc, m.p. 62–63 °C; $[\alpha]_{\text{D}}^{21}$: –222.56° (c 1.22, CHCl_3); IR (KBr): ν_{max} = 3428, 2954, 2930, 2857, 1789, 1713, 1647, 1453, 1387, 1238, 1157, 996 cm^{-1} ; EI-MS: m/z = 334 (45, $[\text{M}]^+$), 316 (10), 291 (18), 251 (70), 234 (81, $[\text{M} - \text{angeloyloxy} - \text{H}]^+$), 217(41), 205 (19), 191 (64), 177 (67), 163 (38), 155 (60), 137 (90), 119 (92), 108 (59), 95 (65), 83 (100, $[\text{angeloyl}]^+$), 69 (52), 55 (90); elemental analysis C: 71.94%, H: 9.02% (calcd. for $\text{C}_{20}\text{H}_{30}\text{O}_4$); ^1H -NMR (CDCl_3 , 400 MHz): δ = 6.03 (1H, dq, J = 7.2, 1.4 Hz, H-3'), 5.68 (1H, d, J = 7.7 Hz, H-9), 5.25 (1H, d, J = 7.7 Hz, H-10), 2.39 (2H, m, H-2 and H-7), 2.26 (2H, m, H-4 and H-6), 2.10 (3H, m, H-2, H-7 and H-11), 1.96 (3H, d, J = 7.2 Hz, H-4'), 1.87 (3H, s, H-5'), 1.63 (3H, s, H-15), 1.05 (3H, d, J = 7.0 Hz, H-12), 1.05 (3H, s, H-14), 0.98 (3H, d, J = 7.0 Hz, H-13); ^{13}C -NMR: see Table 1.

X-ray crystallographic analysis of 1: Empirical formula = $\text{C}_{15}\text{H}_{18}\text{O}_2$, MW = 230.29; Orthorhombic; $P212121$; a = 6.5638(7) Å, b = 18.5331(19) Å, c = 10.4407(11) Å, V = 1262.4(2) Å³; D_{calc} = 1.212 mg/m^3 , Z = 4; T = 293 K. A colorless crystal of dimension of 0.420 × 0.203 × 0.157 mm was used for data collection on a Bruker SMART CCD area detector, equipped with a graphite monochromated Mo-K α radiation (λ = 0.71073 Å). The collected data were reduced using SAINT and empirical absorption correction was performed using SADABS. A total of 10,800 reflections were measured of which 4100 (R_{int} = 0.1146) reflections were unique. The structure was solved by a direct method and refined by full-matrix least squares against F^2 for all data using the program package SHELXTL. The crystallographic data have been deposited with the Cambridge Crystallographic Data Center as deposition No. CCDC-211801. Copies of data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (1223) 336 033; e-mail: deposit@ccdc.ac.uk].

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