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SESQUITERPENE LACTONES FROM THE PERICARP OF *ILLICIUM DUNNIANUM*

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Key Word Index—*Illicium dunnianum*; Illiciaceae; pericarp; sesquiterpene lactone; 1,4-epoxy-6-deoxypseudoanisatin; neodunnianin.

Abstract—Two new sesquiterpene lactones, 1,4-epoxy-6-deoxypseudoanisatin and neodunnianin, were isolated from the pericarp of *Illicium dunnianum*, together with a sesquiterpene, phaseic acid. Their structures were elucidated on the basis of spectroscopic and chemical data. The structure of neodunnianin was confirmed by X-ray diffraction analysis. © Elsevier Science Ltd

INTRODUCTION

The fruits of some *Illicium* plants are locally taken to dispel wind and cold, regulate the flow of qi and relieve pain in Traditional Chinese Medicine, but some are toxic. So far, the toxicity is believed to be due to sesquiterpene lactones. Anisatin, 2-oxo-6-deoxy-neoanisatin and neomajucin cause convulsion and are lethally toxic in mice [1, 2]. We have examined the chemical constituents of *Illicium* plants and some anisatin-, pseudoanisatin- and majucin-type sesquiterpene lactones were isolated [3, 4]. In the previous paper [5], we reported the structure of a novel sesquiterpene lactone, 3-benzoyl pseudoanisatin (**3**) and dunnianin (**4**), pseudomajucin (**5**), pseudoanisatin (**6**), 6-deoxypseudoanistan (**7**) isolated from *Illicium dunnianum* Tutcher. Recently two other new sesquiterpene lactones, 1,4-epoxy-6-deoxypseudoanisatin (**1**) and neodunnianin (**2**) were isolated along with a sesquiterpene, phaseic acid (**8**).

RESULTS AND DISCUSSION

1,4-Epoxy-6-deoxypseudoanisatin (**1**) had the molecular formula $C_{15}H_{20}O_5$ (EI-MS *m/z* 280[M]$^+$ and elemental analysis). Intense absorption band at ν_{max} 3567, 3544, 3379, 1735, 1718 and 1685 cm^{-1} in the IR spectrum of **1** was in accord with the presence of hydroxyl and carbonyl functions. The ^{13}C NMR signals at δ_c 173.4 and 210.2 confirmed the presence of the carbonyl groups. The ^{1}H NMR spectrum of **1** showed two tertiary methyl signals at δ_H 1.24 and 1.32, a methyl doublet at δ_H 1.07, and three sets of signals for isolated methylene groups (H_2-8, H_2-10 and H_2-14). The ^{13}C NMR data were similar to those of 6-deoxypseudoanisatin except the signal of C-1 (Table 1). Thus, the primary skeleton of **1** was deduced to resemble that of 6-deoxypseudoanisatin. However, the signal of C-1 was at δ 82.7, indicating that C-1 was connected with an oxygen atom. The ^{13}C NMR data and the number of oxygen atoms indicated that compound **1** included an ether bond and a hydroxyl group. The signal at δ_H 4.60 was changed to δ 5.35 in

Table 1. ^{13}C NMR (75 MHz) spectra data of compound **1**, **2**, **7** in CD_3COCD_3

c	1	2	7
1	82.7*	50.2	40.8
2	51.8	35.2	43.3
3	79.3	73.5	78.5
4	84.0*	97.4	83.1
5	47.7†	55.2*	47.9
6	48.7	79.6	48.8
7	210.2	109.5	209.5
8	41.7	49.2	47.1
9	51.0†	53.5*	48.1
10	38.6	39.0	35.2
11	173.4	175.9	174.2
12	8.3	19.4†	8.2
13	17.3	19.2†	17.0
14	69.5	64.0	69.5
15	24.5	71.6	13.9

*, † Assignments may be interchanged.

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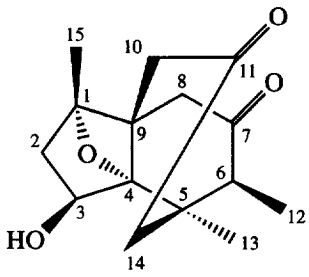

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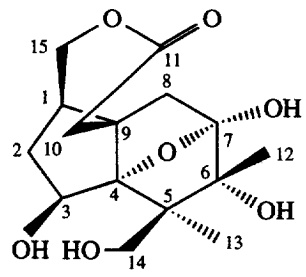

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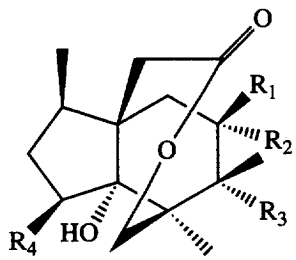
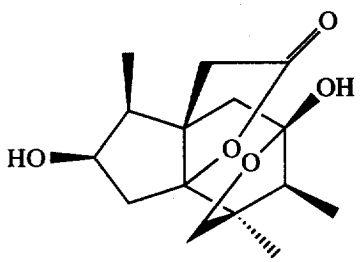


3 R1, R2 = O, R3 = OH, R4 = COBz
4 R1 = OH, R2 = H, R3 = OH, R4 = COBz
6 R1, R2 = O, R3 = OH, R4 = OH
7 R1, R2 = O, R3 = H, R4 = OH



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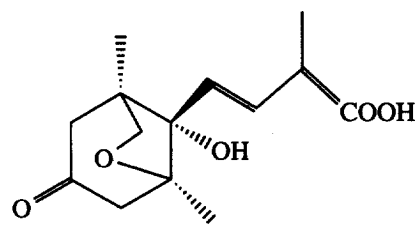

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the ^{1}H NMR spectrum after acetylation, showing that the hydroxyl-bonded carbon was a tertiary carbon, not a quaternary carbon, and the ether bond was between two quaternary carbons. Additionally, there was NOE interaction between the proton signals at δ_H 4.60 and δ 1.24. All of these findings indicated the structure of a five-membered ring as shown. The configuration of H-3, C-12 and C-15 methyl groups were deduced from NOE experiments. When irradiated at the frequency of H-15, the signal of H-10 (δ_H 2.47) was enhanced, the irradiation of H-12 produced the enhancement of δ_H 3.72 of H-14 and δ_H 1.24 of H-13 and irradiation of the H-13 caused the enhancement of the signals of H-12 and H-3. Thus, the configuration of H-3 was α-, and the C-12, C-15 methyl groups were β-oriented.

The structure assignment of neodunnianin (**2**) was mainly based on X-ray analysis. The IR, ^{1}H NMR and ^{13}C NMR data were in accord with this structure. The largest ion peak was *m/z* 278 ([M-36]$^+$) in the EI-mass spectrum; there was no molecular ion peak. According to the ^{13}C NMR spectrum, **2** included 15 carbons. The absorption band ν_{max} 1706 cm^{-1} in the IR spectrum and the ^{13}C NMR signal, δ_c 175.9 indicated the presence of a carbonyl group. The IR spectrum also displayed absorption bands attributable to hydroxyl groups (3376, 3327 and 3200 cm^{-1}).The ^{1}H NMR spectrum showed three sets of signals for iso-

Table 2. ^{1}H NMR (300 MHz) spectral data of compound **1**, **1a**, **2**, **7** in CD_3COCD_3

H	1	1a	2	7
1			2.41*dddd* (11.1, 9.6, 7.2, 1.5)	2.57–2.68*m*
2	1.97*dd* (15.5, 2.8)*	1.97*dd* (15.9, 3.3)	1.34*dd* (13.8, 1.5)	1.24–1.34*m*
	2.74*dd* (15.5, 7.9)	2.85*dd* (15.9, 8.4)	2.23 *ddd* (13.8, 3.6, 9.6)	2.38–2.48*m*
3	4.60*dd* (7.9, 2.8)	5.35*dd* (8.4, 3.3)	4.09*d* (3.6)	4.43*dd* (7.7, 3.0)
6	2.90*q* (6.9)	2.94*q* (6.6)		2.81*q* (6.8)
8	2.20*d* (16.8)	2.25*d* (17.1)	1.94*d* (12.6)	2.30*d* (16.2)
	2.96*dd* (16.8, 2.0)	2.99*dd* (17.1, 2.2)	2.06*d* (12.6)	2.52*dd* (16.2, 1.8)
10	2.47*d* (14.3)	2.52*d* (14.7)	2.65*d* (13.5)	2.31*d* (14.5)
	3.53*dd* (14.3, 2.0)	3.28*dd* (14.7, 2.2)	3.27*d* (13.5)	3.45*dd* (14.5, 1.8)
12	1.07*d* (6.9)	1.08*d* (6.9)	1.22*s*	1.07*d* (6.8)
13	1.24*s*	1.11*s*	1.26*s*	1.26*s*
14	3.72*d* (13.4)	3.71*d* (14.1)	3.50*d* (10.8)	3.74*d* (13.2)
	5.44*d* (13.4)	5.11*d* (14.1)	4.00*d* (10.8)	5.39*d* (13.2)
15	1.32*s*	1.33*s*	4.18*dd* (11.1, 11.1)	0.92*d* (7.1)
			4.23*dd* (11.1, 7.2)	
$COCH_3$		2.14*s*		

* Coupling constants (J in Hz) are given in parentheses.

lated methylene groups (H_2-8, H_2-10 and H_2-14), and two isolated methyl signals at δ_H 1.22 and 1.26 (Table 2). The connectivities H_2-15-H_1-1-H_2-2-H_1-3 was concluded by the coupling constants and ^{1}H–^{1}H two dimensional correlation spectroscopy. The ^{13}C NMR data are shown in Table 1.

EXPERIMENTAL

General. Mps, uncorr.; IR: KBr discs; MS: MM70-70H spectrometer; ^{1}H NMR and ^{13}C NMR: 400 MHz spectrometer with the solvent as reference.

Plant material. The fruits of *Illicium. dunnianum* Tutch. was collected in Guangxi, China and identified by Prof. Yang Chunshu (Beijing University of Traditional Chinese Medicine). A voucher specimen 88105 is deposited in the Herbarium of Beijing University of Traditional Chinese Medicine.

Extraction and isolation. The dried pericarp powder of *I. dunnianum* (4.0 kg) was extracted with MeOH at room temp. The extract was evapd to give a brown gum (1.03 kg) which was dissolved in H_2O and partitioned against hexane, $CHCl_3$, and EtOAc, respectively. The EtOAc soluble partion (39.5 g) was fractionated by silica gel (100–140 mesh), using a $CHCl_3$–MeOH gradient into 19 Frs. Compounds **8** (200 mg), **6** (2 g), **7** (8 g), **1** (90 mg), **2** (50 mg) were purified from Fr. 6, 7, 8, 10 and 11, respectively, by recrystallization.

Compound **1**. Slice (from Me_2CO), mp: 205–207°C; IR: ν_{max}^{KBr} cm^{-1}: 3567, 3544, 3379 (OH), 1734, 1718, 1685 (C=O); EI-MS m/z: 280[M]$^+$(7), 113 (35), 43 (100). Elemental analysis (%): C, 63.35, H, 7.25; ^{1}H and ^{13}C NMR: Tables 1 and 2.

Acetylation of compound **1**. Compound 1 (20 mg) was dissolved in a mixt. of dry pyridine (1 ml) and Ac_2O (1 ml), and the soln was left overnight at room temp., then partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ soluble part was purified by silica gel to give the monoacetate (**1a**), ^{1}H NMR: Table 2.

Compound **2**. Slice (from EtOAc–MeOH), mp: 213–215°C; IR: ν_{max}^{KBr} cm^{-1}: 3376, 3327 (OH), 1706 (C=O); EI-MS m/z: 278 [M-36]$^+$ (5), 206 (35), 43 (100). ^{1}H and ^{13}C NMR: Table 2.

X-ray analysis of compound **2**. The compound crystallized in the orthorhombic space group $P2_1$ with one molecule of composition $(C_{15}H_{22}O_7)_2 \cdot CH_3OH$ (Z=2) forming the asymmetric unit. Accurate cell constants of $a = 8.353$ Å, $b = 10.628$ Å, $c = 17.725$ Å, $\beta = 84.229°$, V = 1565.574 Å^3 were determined on a Mac Science DIP-2000 Imaging Plate Area detector with graphite monochromated MoKα radiation (0.71073 Å), using the programes DENZO and SCALEPACK to reduce data ($R_{merge} = 0.36$). After correction for Lorentz, polarization and background effects, 2083 of the 2088 unique reflections were judged observed ($|F_o| > 3\sigma(F_o)$). The structure was solved by Mac Science crystan G. Hydrogen atoms were located

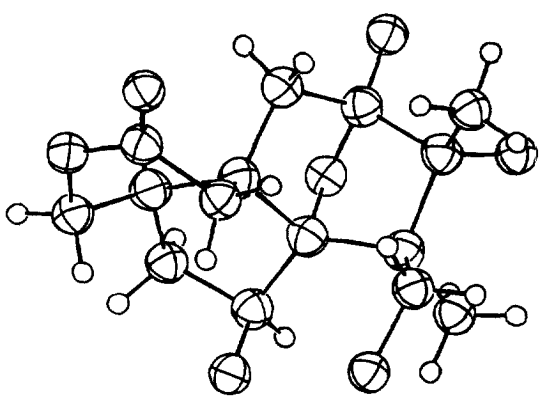

Fig. 1. ORTEP drawing of the neodunnianin.

in a difference electron density synthesis after full least-squares refinement of the non-hydrogen atoms. The final conventional crystallographic residual is $R = 0.0407$, $R_w = 0.0445$ for 2083 observed reflections (Fig. 1).

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