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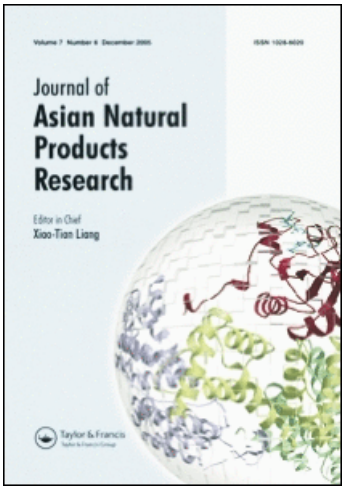

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Prenylated C_6-C_3 compounds from the fruits of *Illicium simonsii*

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Two new prenylated C_6-C_3 compounds, 4-*epi*-illicinone E-12-shikimate (**1**) and 3-hydroxyillifunone B (**2**), together with five known prenylated C_6-C_3 compounds (**3**–**7**), were isolated from the fruits of *Illicium simonsii*. Their structures were elucidated on the basis of extensive spectroscopic methods, including 1D and 2D NMR, CD spectra, and ESI-MS analysis.

Keywords: *Illicium simonsii*; prenylated C_6-C_3 compounds; 4-*epi*-illicinone E-12-shikimate; 3-hydroxyillifunone B

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1. Introduction

Prenylated C_6-C_3 compounds, also named phytoquinoids, were isolated frequently from *Illicium* plants in the previous reports [1–9]. *Illicium simonsii* belongs to the genus *Illicium* and is mainly distributed in Guizhou, Sichuan, and Yunnan Provinces of China, India, and Myanmar [10]. Since there are only a few reports concerning the chemical constituents of this plant [11,12], the fruits of *I. simonsii* were studied as part of an ongoing phytochemical investigation of the genus *Illicium*. As a result, seven prenylated C_6-C_3 compounds, including two new compounds (**1** and **2**), were isolated (Figure 1). In this paper, we report the isolation and structural elucidation of the two new compounds.

2. Results and discussion

Compound **1** was obtained as a colorless oil with the molecular formula $C_{22}H_{28}O_9$ established by positive HR-ESI-MS at *m/z* 437.1817. The IR spectrum showed absorption bands attributable to hydroxyl groups (3404 cm^{-1}), one ester carbonyl (1708 cm^{-1}), and one α,β-conjugated carbonyl (1685 cm^{-1}). The ^1H and ^{13}C NMR spectra of **1** (Table 1) revealed the presence of an allyl group [δ_H 2.96 (2H, d, $J = 6.5$ Hz, H_2-7), 5.82 (1H, m, H-8), 5.07 (1H, dd, $J = 10.5$, 1.5 Hz, H-9a), and 5.04 (1H, dd, $J = 17.5$, 1.5 Hz, H-9b); δ_C 33.7 (C-7), 135.8 (C-8), and 117.4 (C-9)], an α,β-conjugated carbonyl group [δ_H 6.63 (1H, s, H-3); δ_C 194.5 (C-1), 138.9 (C-2), and 139.0 (C-3)], two isolated methylene groups [δ_H 3.09 (1H, d, $J = 16.5$ Hz, H-6a), 2.92 (1H, d, $J = 16.5$ Hz, H-6b), 2.51 (1H, dd, $J = 14.0$, 5.0 Hz, H-10a), and 2.23 (1H, dd, $J = 14.0$, 11.0 Hz, H-10b); δ_C 46.9 (C-6) and 38.4 (C-10)], two dimethyl groups linked to a quaternary carbon [δ_H 1.47 (3H, s, H_3-13) and 1.51 (3H, s, H_3-14); δ_C 22.0 (C-13) and 22.5 (C-14)], and a methylenedioxy group [δ_H 4.92 (1H, s, H-15a) and 5.16 (1H, s, H-15b); δ_C 95.3 (C-15)]. The above NMR spectral

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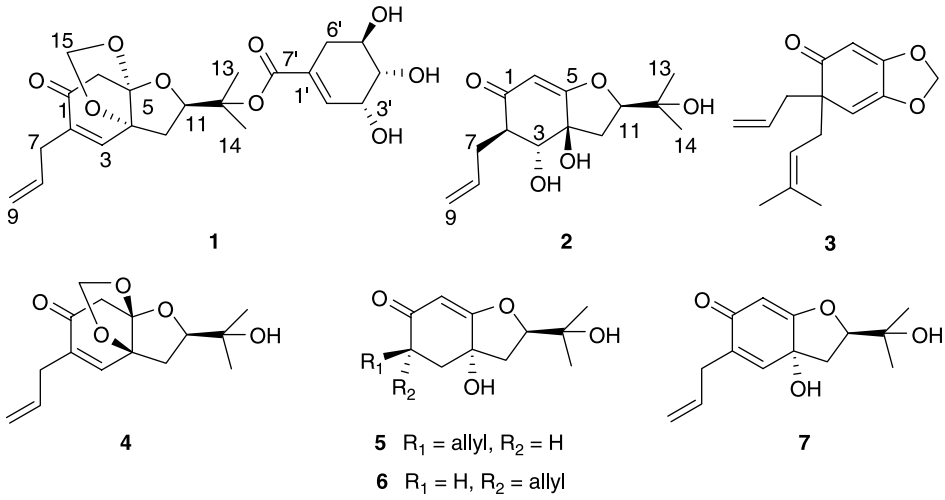

Figure 1. Structures of compounds **1**–**7**.

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data were similar to those of illicinone E [13], indicating that compound **1** possessed a structure moiety (part A), which was supported by HMBC correlations (Figure 2). In addition, the ^{1}H and ^{13}C NMR spectral data exhibited the presence of an ester carbonyl group [δ_C 166.2 (C-7′)], conjugated double bonds [δ_H 6.61 (1H, br s, H-2′); δ_C 131.0 (C-1′) and 138.4 (C-2′)], three oxygen-bearing methine groups [δ_H 4.34 (1H, t, $J = 4.0$ Hz, H-3′), 3.66 (1H, dd, $J = 7.0$, 4.0 Hz, H-4′), and 3.97 (1H, m, H-5′); δ_C 66.7 (C-3′), 72.3 (C-4′), and 68.0 (C-5′)], and a methene group [δ_H 2.07 (1H, dd, $J = 19.0$, 5.0 Hz, H-6′a) and 2.55 (1H, dd, $J = 19.0$, 5.0 Hz, H-6′b); δ_C 31.4 (C-6′)], which were determined to be a shikimic acid moiety (part B) [14]. In the ^{13}C NMR spectrum, the downfield shift of C-11 and C-12 ($\Delta\delta + 1.6$ and +11.1 ppm, respectively) of part A compared with those of illicinone E suggested that part B was attached to C-12 of part A.

The relative configuration of **1** was determined by the NOE experiment and coupling constant values. Selective irradiation of the signal H-11 caused distinct NOE enhancement of the signal H-15b (δ_H 5.16), suggesting that H-11 and methylenedioxy were on the same side. No NOEs were observed between H-3′ and H-5′, suggesting that they were on the different faces of the cyclohexene ring (Figure 2). In the ^{1}H NMR spectrum, the coupling constant ($J = 7.0$ Hz) between H-4′ and H-5′ indicated that they were in *trans*-diaxial disposition in the Haworth projection (Figure 2), which was further supported by the large coupling constant ($J = 19.0$ Hz) between H-6′a and H-6′b [15]. The negative Cotton effect at 320 nm was in agreement with 4*R*,5*S*-configuration [5]. Alkaline hydrolysis of **1** afforded (−)-shikimic acid [14]. Therefore, the structure of **1** was determined as shown in Figure 1.

Compound **2** was obtained as a colorless oil and its HR-ESI-MS exhibited an $[M+Na]^+$ ion at *m/z* 291.1209 corresponding to the pseudomolecular formula of $C_{14}H_{20}O_5Na$. The IR spectrum showed the presence of hydroxy groups (3429 cm^{-1}), an α,β-conjugated carbonyl (1657 cm^{-1}), and a double bond (1624 cm^{-1}). The ^{1}H and ^{13}C NMR spectral data of **2** indicated the presence of an allyl group [δ_H 2.32 (1H, ddd, $J = 5.0$, 7.0, 14.0 Hz, H-7a), 2.44 (1H, dd,

Table 1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectral data for compounds **1** and **2** in acetone-d_6.

	1		**2**	
No.	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		194.5		199.2
2		138.9	3.56 m	44.2
3	6.63 s	139.0	4.15 d (3.0)	72.4
4		86.0		78.5
5		111.9		180.4
6	3.09 d (16.5) 2.92 d (16.5)	46.9	5.21 s	96.4
7	2.96 d (6.5)	33.7	2.44 dd (7.5, 14.0) 2.32 ddd (5.0, 7.0, 14.0)	41.8
8	5.82 m	135.8	5.87 m	133.9
9	5.07 dd (10.5, 1.5) 5.04 dd (17.5, 1.5)	117.4	5.10 dd (10.0, 1.5) 5.04 dd (17.0, 1.5)	118.2
10	2.51 dd (14.0, 5.0) 2.23 dd (14.0, 11.0)	38.4	2.36 dd (5.0, 11.5) 2.10 dd (11.0, 11.5)	26.3
11	4.52 dd (11.0, 5.0)	85.7	4.52 dd (5.0, 11.0)	93.3
12		82.1		70.4
13	1.47 s	22.0	1.27 s	26.5
14	1.51 s	22.5	1.17 s	25.6
15	4.92 s 5.16 s	95.3		
1′		131.0		
2′	6.61 br s	138.4		
3′	4.34 br s	66.7		
4′	3.66 dd (4.0, 7.0)	72.3		
5′	3.97 m	68.0		
6′	2.07 dd (5.0, 19.0) 2.55 dd (5.0, 19.0)	31.4		
7′		166.2		

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$J = 7.5$, 14.0 Hz, H-7b), 5.87 (1H, m, H-8), 5.04 (1H, dd, $J = 10.0$, 1.5 Hz, H-9a), and 5.10 (1H, dd, $J = 17.0$, 1.5 Hz, H-9b); δ_C 41.8 (C-7), 133.9 (C-8), and 118.2 (C-9)], a dimethyl carbinol group [δ_H 1.27 (3H, s, H_3-13) and 1.17 (3H, s, H_3-14); δ_C 70.4 (C-12), 26.5 (C-13), and 25.6 (C-14)], and an α,β-conjugated carbonyl [δ_H 5.21 (1H, s, H-6); δ_C 199.2 (C-1), 180.4 (C-5), and 96.4 (C-6)]. The NMR spectral data of **2** were similar to those of illifunone B [1], except that the signal at δ_C 34.9 (C-3) in illifunone B was shifted downfield to δ_C 72.4 (C-3) in **2**, which disclosed that one proton at C-3 in illifunone B was replaced by a hydroxyl

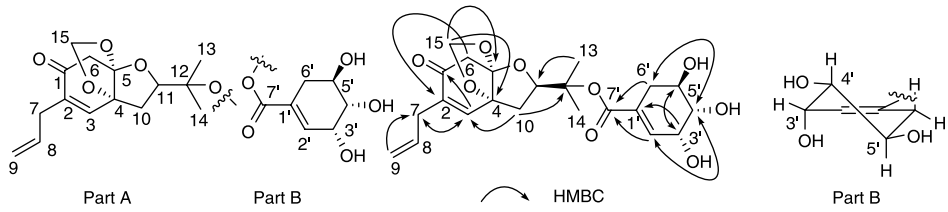

Figure 2. Structures of parts A and B, key HMBC correlations of **1**, and Haworth projection of part B.

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group in **2** in combination with their molecular formula.

The relative configuration of **2** was established by the chemical shift of H-11 and the NOE experiment (Figure 3). A *syn*-relationship between the hydroxyl group at C-4 and the dimethyl carbinol group at C-11 was elucidated from the chemical shift of H-11 (δ_H 4.52) appearing at higher field than δ_H 4.6 [7]. Moreover, an *anti*-relationship between the allyl group at C-2 and the hydroxyl group at C-3 was confirmed by the observation of NOE for H-3 upon irradiation of H-7b (δ_H 2.44). In addition, a *syn*-relationship between the allyl group at C-2 and the dimethyl carbinol group at C-11 was established for the NOEs between H-2 and H-11. The absolute configuration of C-2 was determined to be *R* on the basis of the positive Cotton effect at 310 nm [7]. Therefore, the absolute configuration for compound **2** was deduced as 2*R*, 3*R*, 4*S*, 11*R*. Thus, the structure of **2** was determined as shown in Figure 1.

The structures of the other five known prenylated C_6–C_3 compounds, 6-allyl-6-(3-methyl-2-butenyl)-3,4-methylenedioxycyclohexa-2,4-dienone (**3**) [3], illicinone E (**4**) [16], illifunone C (**5**) [1,7], illifunone D (**6**) [1,7], and 2,3-dehydroillifunone C (**7**) [7], were elucidated by comparison of their spectral data with those reported.

3. Experimental

3.1 General experimental procedures

Optical rotations were determined on a Perkin-Elmer 241 automatic digital polarimeter. A CD spectrum was obtained from a JOUAN Mark II spectropolarimeter. IR spectra were recorded on a Nicolet 5700 FT-IR spectrometer. 1D and 2D NMR spectra were recorded on a Varian INOVA-500 spectrometer with TMS as an internal standard. ESI-MS were measured on an Agilent 1100 series LC/MSD trap mass spectrometer. HR-ESI-MS spectra were recorded on an Autospec-Ultima ETOF Spec mass spectrometer. Preparative HPLC was performed on a Shimadzu LC-6AD instrument with an SPD-10A detector. Silica gel GF_{254} for TLC was obtained from Qingdao Marine Chemical Company, Qingdao, China. ODS (50 μ) and Sephadex LH-20 were purchased from Fuji Silysica Chemical Ltd (Greenville, NC, USA).

3.2 Plant material

The fruits of *I. simonsii* were collected from Yunnan Province of China, which was identified by Prof. Lin Ma of the Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medica, where a voucher specimen (No. 90204) has been deposited.

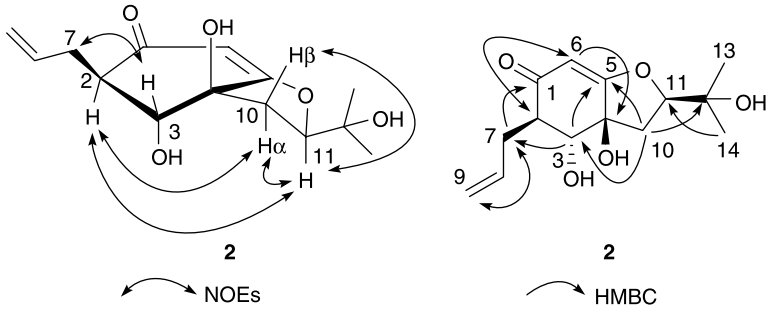

Figure 3. Key NOE and HMBC correlations of **2**.

3.3 Extraction and isolation

The dried powder of the fruits of *I. simonsii* (1.1 kg) was extracted with 95% EtOH (15 liters ×3) and concentrated *in vacuo* to give the crude extract (158 g), which was absorbed by kieselguhr, and then successively extracted with petroleum ether, $CHCl_3$, EtOAc, and MeOH. The $CHCl_3$ extract (25 g) was subjected to the ODS column eluted with MeOH–H_2O (from 65:35 to 85:15) to give five fractions (A–E). Fraction B (2.6 g) was subjected to Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) and then further purified on preparative HPLC (MeOH–H_2O, 84:16) to yield compounds **1** (13.1 mg), **2** (9.1 mg), and **7** (16.1 mg). Fraction E (3.3 g) was chromatographed on the ODS column, eluted with a gradient system of MeOH–H_2O (from 60:40 to 90:10), and further separated by preparative HPLC (MeOH–H_2O, 88:12) to afford compounds **3** (4.1 mg), **4** (9.6 mg), **5** (12.4 mg), and **6** (6.1 mg).

3.3.1 Compound *1*

Colorless oil; $[\alpha]_D^{20}$ −38.1 ($c = 0.08$, MeOH); UV (MeOH) λ_{max}: 225 nm; CD (MeOH) $\Delta\varepsilon_{200\,nm}$ 18.2, $\Delta\varepsilon_{224\,nm}$ 0, $\Delta\varepsilon_{320\,nm}$ −1.66, $\Delta\varepsilon_{325\,nm}$ 0; IR (KBr) ν_{max}: 3404, 2981, 2907, 1708, 1685, 1613, 1369, 1235, 1137, 1095, 1072 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; positive HR-ESI-MS *m/z*: 437.1817 $[M+H]^+$ (calcd for $C_{22}H_{29}O_9$, 437.1806).

3.3.2 Compound *2*

Colorless oil; $[\alpha]_D^{20}$ −68.3 ($c = 0.05$, MeOH); UV (MeOH) λ_{max}: 265 nm; CD (MeOH) $\Delta\varepsilon_{201\,nm}$ 0, $\Delta\varepsilon_{256\,nm}$ −11.8, $\Delta\varepsilon_{296\,nm}$ 0, $\Delta\varepsilon_{310\,nm}$ 1.04, $\Delta\varepsilon_{348\,nm}$ 0; IR (KBr) ν_{max}: 3429, 2988, 2911, 1657, 1624, 1389, 1376, 1190, 1079 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; positive HR-ESI-MS *m/z*: 291.1209 $[M+Na]^+$ (calcd for $C_{14}H_{20}O_5Na$, 291.1203).

3.4 Alkaline hydrolysis of *1*

Compound **1** (6.2 mg) was hydrolyzed with 0.5 M NaOH (3 ml) and MeOH (0.5 ml) for 1 h at room temperature. After adjusting the pH to 5.0 with 0.5 M HCl, the reaction mixture was extracted with EtOAc, which was separated by HPLC (CH_3CN–H_2O, 18:92) to afford (−)-shikimic acid (1.2 mg).

3.4.1 (−)-Shikimic acid

Colorless powder; $[\alpha]_D^{20}$ −138.1 ($c = 0.05$, MeOH); ^1H NMR (500 MHz, acetone-d_6): δ_H 6.71 (1H, m, H-2), 4.40 (1H, t, $J = 4.0$ Hz, H-3), 3.68 (1H, dd, $J = 7.0$, 4.0 Hz, H-4), 3.99 (1H, m, H-5), 2.68 (1H, dd, $J = 19.0$, 5.0 Hz, H-6a), 2.11 (1H, dd, $J = 19.0$, 5.0 Hz, H-6b); ^{13}C NMR (125 MHz, acetone-d_6): δ_C 138.1 (C-1), 133.7 (C-2), 71.6 (C-3), 68.1 (C-4), 67.2 (C-5), 31.3 (C-6), 170.1 (C-7).

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