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A SESQUILIGNAN FROM *ILLICIUM DUNNIANUM*

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Key Word Index—*Illicium dunnianum*; Illiciaceae; Dunn's star anise; biosynthesis; *o,p*-coupling, sesquilignan; triphenyl-neolignan.

Abstract—The aerial parts of *Illicium dunnianum* yielded a sesquilignan with a novel skeleton, thought to be produced by both *o,o*- and *o,p*-coupling of three 4-allylphenol molecules. Its structure was deduced from two-dimensional NMR spectroscopy. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Illicium dunnianum is a robust bush from Southern China which is reportedly toxic [1]. Previous phytochemical investigations [1, 2] have identified sesquiterpene lactones, neolignans and sesquilignans. The present work reports the isolation and structural determination of a sesquilignan with a novel skeleton from this species.

RESULTS AND DISCUSSION

Extraction of the aerial parts of *I. dunnianum* with dichloromethane followed by column chromatography and HPLC yielded the novel compound **1**, identified in the following manner. Accurate mass spectroscopy demonstrated the elemental composition $C_{27}H_{26}O_3$ and IR revealed the presence of hydroxyl (3315 cm^{-1} br) and carbonyl (1672 cm^{-1}) groups. ^{13}C DEPT confirmed the presence of 27 carbons with 25 directly attached protons (two CH resonances at δ 137.6 were overlapping; Table 1), consistent with the presence of a single hydroxyl group. We suspected that compound **1** was a sesquilignan (derived from three 4-allylphenol molecules) from its molecular formula ($3 \times C_9$). Inspection of the ^1H NMR spectrum seemed to confrim this hypothesis and suggested that all three of the 4-allyl groups were unmodified, since complex overlapping resonances were observed with chemical shifts and integral intensities expected for three such functionalities (δ 2.72 [1H], 2.90 [1H] and 3.32 [4H] H-7,7′,7″; 5.87–6.00 [3H] H-8,8′,8″; 5.00–5.30 [6H] H-9,9′,9″). Inspection of the ^{13}C DEPT spectra also demonstrated three sets of resonances for aliphatic methylene (δ 41.4, 39.7, 39.2; C-7,7′,7″), alkene methine (δ 132.08, 137.6; 137.6; C-8,8′,8″) and alkene methylene carbons (δ 120.1, 115.8, 115.7; C-9,9′,9″) at the chemical shifts expected for an allyl group.

Further analysis of chemical shifts showed aromatic resonances consistent with only two phenolic systems, while the presence of aliphatic resonances (δ_C 40.3 CH_2, 84.3 CH, 49.5 C; δ_H 4.88 [1H] *m*, 3.20 [1H] *dd*, J = 16.8, 3.1 Hz, 2.98 [1H] *dd*, J = 16.8, 4.1 Hz) and a carbonyl group (δ_C 199.1 C) seemed to require partial saturation in the structure of compound **1**. In fact, analysis of PFG-HSQC, PFG-HMBC and ^1H–^1H COSY spectra (Table 1) indicated that these aliphatic resonances to be part of a 4-allyl cyclohexenone ring system, which was further linked to two 4-allylphenol groups. One of the 4-allylphenol groups was linked by a single carbon–carbon bond and the other by both a carbon–carbon bond and an ether group, creating an additional 2,3-dihydrofuran ring in the structure of compound **1**. The relative stereochemistry for the dihydrofuran ring fused onto the cyclohexenone ring was determined as *cis* from NOESY spectra (Table 1, in particular correlation between H-5 and H-7 is only possible for *cis*-stereochemistry).

Isolation of compound **1** is of biosynethetic interest since because it is apparently derived from three 4-allylphenol units linked together by both *ortho*, *ortho*-coupling and *ortho*, *para*-coupling. We propose that the first *o,o*-linkage occurs by standard oxidative coupling of two molecules of chavicol (**2**) (as oxidized radicals formally located at the *ortho*-position) yielding magnolol (**3**). In support of this, compound **3** was isolated from the extract in large amounts.

The second *o,p*-linkage (Fig. 1) then arises by oxidative coupling of magnolol (as an oxidized radical formally located at the *para*-position) with a further molecule of chavicol (*ortho* radical) leading to formation of a trimer, which is unable to regain aromaticity at the central ring (an allyl substituent is present at the *para*-position) but can undergo rearomatization at the right-hand ring (by proton loss at C-2′) accompanied

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Table 1. NMR data for compound **1**

Assignment	δ ^{13}C	Mult.*	δ ^{1}H	HMBC correlation from ^{1}H to ^{13}C	^{1}H–^{1}H COSY correlation	NOESY correlation from ^{1}H to ^{1}H
1	199.1	C				
2	137.4	C				
3	150.5	CH	6.61	199.1, 137.4, 124.2, 84.3, 49.5, 41.4		7.04, 2.90
4	49.5	C				
5	84.3	CH	4.88		3.20, 2.98	3.20, 2.98, 2.72
6	40.3	CH_2	3.20	199.1, 84.3, 49.5	4.88, 2.98	4.88, 2.98
			2.98	199.1, 84.3	4.88, 3.20	4.88, 3.20
7	41.4	CH_2	2.90	150.5, 132.08, 120.1, 84.3, 49.5	5.87, 2.72	7.04, 6.61, 5.87, 2.72
			2.72	150.5, 132.08, 120.1, 84.3, 49.5	5.87, 2.90	5.30, 5.25, 4.88, 2.90
8	132.08	CH	5.87		5.30, 5.25 2.90, 2.72	5.30, 5.25, 2.90
9	120.1	CH_2	5.30, 5.25	41.4	5.87	5.87, 2.72
1′	157.1	C				
2′	133.6	C				
3′	123.1	CH	7.04	157.1, 130.6, 49.5, 39.7		6.61, 3.32
4′	130.6	C				
5′	129.7	CH	7.02	157.1, 123.1, 39.7	6.76	6.76, 3.32
6′	110.4	CH	6.76	157.1, 133.6	7.02	7.02
7′	39.7	CH_2	3.32 [2H]	137.6, 130.6, 129.7, 123.1, 115.8	5.9–6.0	7.04, 7.02, 5.9–6.0, 5.1–5.0
8′	137.6	CH	5.9–6.0		5.0–5.1, 3.32	5.0–5.1
9′	115.8[a]	CH_2	5.0–5.1 [2H]	39.7	5.9–6.0	6.0–5.9, 3.32
1″	152.3	C				
2″	124.2	C				
3″	130.2	CH	6.76	152.3, 137.4, 132.1, 39.2		3.32
4″	132.1	C				
5″	130.5	CH	7.06	152.3, 39.2	6.85	6.85, 3.32
6″	118.5	CH	6.85	152.3, 132.1, 124.2	7.06	7.06
7″	39.2	CH_2	3.32 [2H]	137.6, 132.1, 130.5, 130.2, 115.7	5.9–6.0	7.06, 6.76, 5.9–6.0, 5.0–5.1
8″	137.6	CH	5.9–6.0		5.0–5.1, 3.32	5.0–5.1
9″	115.7[a]	CH_2	5.0–5.1 [2H]	39.2	5.9–6.0	5.9–6.0, 3.32
2′-OH			7.48	152.3, 124.2, 118.5		

*Multiplicity determined from DEPT.
[a]Assignments interchangeable.

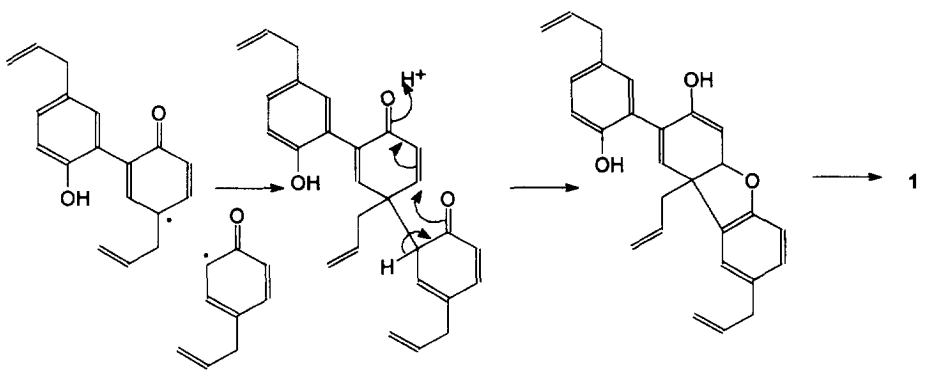

Fig. 1. Possible biosynthesis of compound **1** from compounds **2** and **3**.

by intramolecular Michael-type addition to the 5,6-double bond of the central ring, thereby introducing a second (ether) linkage between the two rings. An exact analogue of this mechanism is known from synthetic organic chemistry where Pummerer's ketone **4** is formed from treatment of *p*-cresol with potassium ferricyanide [3]. We are aware of only three other natural products incorporating the 4a,9b-dihydro-3(4H)-dibenzofuranone skeleton expected from such coupling, a bi-flavanone [4], a bi-isoflavanone [5] and the alkaloid narwedine (**5**) [6]. The biosynthesis of narwedine has been proposed to involve the same mechanism of *o,p*-coupling accompanied by Michael addition, as is described in Fig. 1. This appears to be the first report for this kind of *ortho, para*-coupling in the neolignan class of natural products [7–11].

EXPERIMENTAL

General. Chemical shifts are expressed in ppm (δ) relative to TMS as int. standard. All NMR experiments were run on a Bruker DRX 500 instrument with $CDCl_3$ as solvent. PFG-HSQC and PFG-HMBC experiments were normally recorded with 2048 data points in F_2 and 128 data points in F_1. Mass spectra were recorded in EI mode (70 eV). FTIR spectra were recorded in CCl_4. TLC plates were visualized using *p*-anisaldehyde. HPLC sepns were performed using a PREP-SIL 20 mm × 25 cm column, flow rate 8 ml min^{-1}.

Extraction and isolation. Illicium dunnianum Tutch. (1 kg) was collected in November, while fruiting from Plover Cove Country Park, New Territories, Hong Kong. The sample was ground to a fine powder under liquid N_2 and immediately extracted with CH_2Cl_2 in a Soxhlet apparatus (8 hr). The organic extract was then dried and evapd under red. pres. to yield a dark green oil (21.96 g; 2.2% w/w). Compound **1** (47.3 mg) was isolated by CC (R_f 0.24 in 22% EtOAc in hexane) followed by HPLC (R_t 19.2 min in 22% EtOAc in hexane).

A voucher specimen of *I. dunnianum* is deposited in the University of Hong Kong Herbarium (GDBROWN 96/3).

Compound **1**. Gum. MS *m/z* (rel. int.) 398.1882 $[M]^+$ $\Delta = 0.5$ mmu for $C_{27}H_{26}O_3$) (25), 357 (100), 298 (17), 200 (12). IR ν_{max} cm^{-1} 3315 (*br*), 2937, 2840, 1672, 1610. ^1H NMR δ 7.48 (1H, *s*), 7.06 (1H, *dd*, $J = 8.3$, 2.0 Hz), 7.04 (1H, *s*), 7.02 (1H, *d*, $J = 8.0$ Hz), 6.85 (1H, *d*, $J = 8.3$ Hz), 6.76 (1H, *d*, $J = 2.0$ Hz), 6.76 (1H, *d*, $J = 8.0$ Hz), 6.61 (1H, *d*, $J = 1.4$ Hz), 5.9–6.0 (2H, *m*), 5.87 (1H, *m*), 5.25–5.30 (2H, *m*), 5.00–5.10 (4H, *m*), 4.88 (1H, *m*), 3.32 (4H, *m*), 3.20 (1H, *dd*, $J = 16.8$, 3.1 Hz), 2.98 (1H, *dd*, $J = 16.8$, 4.1 Hz), 2.90 (1H, *dd*, $J = 14.2$, 6.9 Hz), 2.72 (1H, *dd*, $J = 14.2$, 8.0 Hz).

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