A New Triphenyl-Type Neolignan and a Biphenylneolignan from the Bark of *Illicium simonsii*

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A new triphenyl-type sesquineolignan, named simonsinol (1), was isolated from the bark of *Illicium simonsii* and its structure was elucidated based on the detailed analysis of its ^{1}H- and ^{13}C-NMR spectra. A new biphenylneolignan, named isomagnolone (5), was also isolated and its structure was determined by the analysis of the two dimensional (2D) NMR spectra.

Keywords *Illicium simonsii*; triphenyl-type neolignan; simonsinol; Illiciaceae; isomagnolone; biphenylneolignan

A diverse series of sesquineolignans has been isolated from the *Illicium* plants; *i.e.* macranthol (**2**) from the pericarps of *Illicium macranthum*,[1] dunnianol (**3**) and isodunnianol (**4**) from the bark of *I. dunnianum*.[2] They are regarded as characteristic constituents of *Illicium* plants.

As a part of our continuing research aimed at the discovery of toxic sesquiterpenes and other sesquineolignans, this paper describes the isolation and structural elucidation of a new triphenyl- and a biphenyl-neolignan from the bark of *Illicium simonsii* MAXIM. The plant is found in western Szechuan and northern and eastern Assam at altitudes between 1800 and 3000 m.

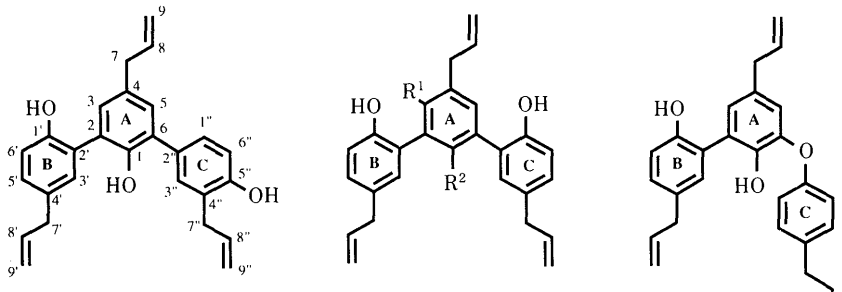
The MeOH extract (362 g) of the bark (1 kg) of *Illicium simonsii* was dissolved in water, then extracted with *n*-hexane, EtOAc and *n*-BuOH, successively. The *n*-hexane soluble fraction produced a precipitate, which was purified by recrystallization from *n*-hexane, and proved to be identical to dunnianol (**3**) (2.4 g) following comparison with an authentic sample.[1,2] Chromatography of the mother liquor from **3** on silica-gel with *n*-hexane–EtOAc afforded a new sesquineolignan as a colorless oil (13.2 mg), which we named simonsinol (**1**).

The *n*-hexane soluble part was separated and purified by means of silica-gel and medium pressure liquid chromatography (MPLC) as described in the Experimental section to give dunnianol (**3**) (1.47 g), macranthol (**2**) (288.1 mg), isodunnianol (**4**) (1.90 g), simonsinol (**1**) (82.4 mg), together with a colorless oil (5 mg), named isomagnolone (**5**), and also β-eudesmol (**7**) (6.6 mg), and α-eudesmol (**8**) (4.0 mg).

Compounds **2**, **3** and **4** were identified by direct comparison with authentic samples. The structure of compounds **7** and **8** were elucidated by comparisons of their spectral data with reported data.[3]

Simonsinol (**1**) was obtained as a colorless oil and had a molecular formula $C_{27}H_{26}O_3$, identical with macranthol and dunnianol, being determined by electron-impact mass spectrometry (EI-MS) (*m/z*: 398 [M^+]) and the number of carbon signals in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **1**. Compound **1** gave a positive reaction to iron(III) chloride. The features of the infrared (IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectra of **1** were very similar to those of **2** and **3**, suggesting a triphenyl-type neolignan structure for **1**. The signals of the methylenes of arylpropenyl moieties in the ^{1}H-NMR spectrum indicated a non-symmetrical structure like macranthol (see Table I). As shown in Table II, the carbon signals of rings A and B were very similar to those of dunnianol (**3**). On the other hand, the carbon signals of rings A and C were similar to those of honokiol. Thus, the structure of a triphenyl-type neolignan **1** was considered for simonsinol.

Simonsinol (**1**) afforded three *O*-methyl derivatives (**1'a**, **1'b** and **1'c**) on brief treatment with CH_3I and K_2CO_3 in acetone. The molecular ion peak of **1'a** in the EI-MS (*m/z*: 440) suggested a tri-*O*-methyl derivative. In support of this, **1** afforded a tri-*O*-acetyl derivative (**1''**) (*m/z*: 524) on treatment with a mixture of 4,4'-dimethylaminopyridine (DMAP), Ac_2O and pyridine. These results



simonsinol (1) macranthol (2): R¹=OH, R²=H dunnianol (3): R¹=H, R²=OH isodunnianol (4)

Fig. 1

TABLE I. ^{1}H-NMR Spectral Data of Simonsinol (**1**) (400 MHz in $CDCl_3$)

Position	
3	7.12 d (J=2.2 Hz)
5	7.10 d (J=2.2 Hz)
7	3.37 br d (J=7.0 Hz)
8	5.95 ddd (J=7.0, 10.3, 16.9 Hz)
9	5.09 dd (J=1.8, 16.9 Hz)
	5.05 dd (J=1.8, 10.3 Hz)
3′	7.26 d (J=2.2 Hz)
5′	7.12 dd (J=2.2, 8.8 Hz)
6′	6.96 d (J=8.8 Hz)
7′	3.39 d (J=6.2 Hz)
8′	6.00 ddd (J=6.2, 9.9, 16.9 Hz)
9′	5.11 dd (J=1.8, 16.9 Hz)
	5.07 dd (J=1.8, 9.9 Hz)
1″	7.26 dd (J=2.3, 8.8 Hz)
3″	7.08 d (J=2.3)
6″	6.89 d (J=8.8 Hz)
7″	3.45 d (J=7.0 Hz)
8″	6.03 ddd (J=7.0, 9.9, 16.9 Hz)
9″	5.18 dd (J=1.8, 16.9 Hz)
	5.15 dd (J=1.8, 9.9 Hz)

TABLE II. ^{13}C-NMR Data for the Aromatic Ring Moieties of Macranthol (**2**), Dunnianol (**3**), Simonsinol (**1**) (100 MHz in $CDCl_3$), with Magnolol and Honokiol

Carbon	**2**	**3**	Magnolol[a]	Honokiol[a]	**1**
1	130.0	147.7			147.4
2	124.7	125.4			128.9
3	150.9	131.3			131.2[b]
4	128.3	134.0			132.8
5	130.9				130.8
6	130.2				124.5
1′	150.8	151.4	151.0	150.5	151.7
2′	127.5	124.4	124.5	127.8	124.9
3′	130.3	131.6	131.4	129.6	130.5
4′	132.4	133.2	133.3	132.3	133.1
5′	129.0	130.0	129.8	128.8	128.7
6′	115.8	117.2	116.8	116.4	117.7
1″	151.2			128.9	129.7
2″	123.3			130.3	129.4
3″	131.3			130.2	131.3[b]
4″	133.4			126.5	126.4
5″	130.3			153.6	154.1
6″	116.8			115.7	116.4

a) Quoted from reference 4. *b*) Assignments may be interchanged.

indicated that **1** has three phenolic hydroxyl groups. As was seen in the ^{1}H-NMR spectrum of the corresponding derivative of dunnianol,[2] one of the methoxy and acetoxy signals in **1′a** and **1″** appeared at an unusually high field (δ 3.20 and 1.72, respectively), indicating that the position of the hydroxy group on ring A should be at C_1. In the case of the methoxy and acetoxy derivatives of macranthol, which has the hydroxy group at the *meta* position to the arylpropenyl group on ring A, all acetoxy proton signals appeared in the normal field and one methoxy group appeared at a higher field.

When the methoxy methyl signals at δ 3.86 and 3.77 of **1′a** were irradiated, the signals at δ 6.90 (1H, d, J=8.4 Hz) and 6.91 (1H, d, J=8.1 Hz) were both enhanced. Irradiation of the signal at δ 3.19 caused the enhancements

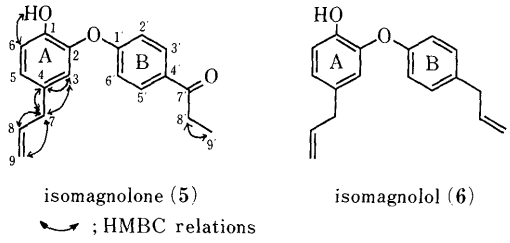


Fig. 2

TABLE III. ^{1}H-(400 MHz) and ^{13}C-(100 MHz) NMR Spectral Data of Isomagnolone (**5**) and Isomagnolol (**6**) ($CDCl_3$)

	5		**6**[a]
	δ_H	δ_C	δ_C
1		146.0 s	145.9 s
2		141.8 s	143.6 s
3	6.80 d (J=1.8 Hz)	120.3 d	119.2 d
4		133.1 s	132.6 s
5	6.94 dd (J=8.4, 1.8 Hz)	126.1 s	124.8 d
6	7.00 d (J=8.4 Hz)	116.6 d	116.2 d
7	3.29 d (J=6.6 Hz)	39.3 t	
8	5.95 ddd (J=15.8, 9.2, 6.6 Hz)	137.2 d	
9	5.03 dd (J=15.8, 1.5 Hz)	116.0 t	
	5.04 dd (J=9.2, 1.5 Hz)		
1′		161.0 s	155.4 s
2′, 6′	7.02 d (J=9.2 Hz)	116.7 d	117.9 d
3′, 5′	7.96 d (J=9.2 Hz)	130.4 d	129.9 d
4′		132.2 s	135.3 s
7′		193.5 s	
8′	2.97 q (J=7.3 Hz)	31.6 t	
9′	1.22 t (J=7.3 Hz)	8.3 q	
C_1-OH	5.27 br s		

a) Quoted from reference 5.

of the signals at δ 7.39 (1H, d, J=2.2 Hz) and 7.42 (1H, dd, J=8.4, 2.2 Hz). In addition to these results, the ^{13}C signals of rings A and B in **1** were compatible with those of dunnianol, indicating the position of the hydroxy group on ring C at 5″.

The other *O*-methyl derivatives, **1′b** and **1′c**, were proved to be dimethyl derivatives by EI-MS (*m/z*: 426) and ^{1}H-NMR spectra, respectively. In the ^{1}H-NMR spectra, **1′b** exhibited methoxy signals at δ 3.86 and 3.83. On the other hand, the two methoxy signals of **1′c** appeared at δ 3.87 and 3.28. These observations indicated that **1′b** is a 1′,5″-di-*O*-methyl derivative and **1′c** is a 1,1′- or 1,5′-di-*O*-methyl derivative. The nuclear Overhauser effect (NOE) experiments were performed on compound **1′b**. When each of the two methoxy signal was irradiated, the aromatic proton, which coupled with the *ortho* proton, was enhanced in each case. This evidence supports the assigned structure of simonsinol (**1**).

Isomagnolone (**5**) was obtained as a colorless oil. The molecular formula of **5** was determined as $C_{18}H_{18}O_3$ by EI-MS (*m/z*: 282) and the number of signals in its ^{13}C-NMR spectrum. The IR spectrum indicated the absorption of a carbonyl group (1730 cm^{-1}) along with that of an aromatic ring. In the ^{1}H-NMR spectrum of **5**, there was an ABC system due to aromatic protons at δ 7.00 (d, J=8.4 Hz), 6.94 (dd, J=8.4, 1.8 Hz), and 6.80 (d,

$J=1.8$ Hz), together with signals of a *p*-substituted aromatic ring at δ 7.96 and 7.02 (each 2H, d, $J=9.2$ Hz). In addition, the proton signals of the α-propenyl moiety and ethyl group were observed as shown in Table III. As a biphenylneolignan, with a *p*-substituted benzene ring, only a type of isomagnolol (**6**) has been characterized so far. The ^{13}C signals of isomagnolol were similar to those of **5**, except for the signals of C-1, C-1′, and C-4′, as shown in Table III. Moreover, the presence of the isolated ethyl group and a carbonyl group in the IR (1730 cm^{-1}) and ^{13}C-NMR spectra (δ 193.5) suggested the presence of a 1-propanone moiety in **5**. Protons on the *p*-substituted benzene ring (B-ring) appeared with a separation *ca.* 1 ppm, indicating that one of the substituents is ketonic. In contrast, the difference between the proton signals of the C-ring of isodunnianol (**4**), is only 0.2 ppm.[2] Figure 2 shows the observed heteronuclear multiple bond correlation (HMBC) of **5**, which supports the location of the α-propenyl group. The carbon signal at δ 116.6 was ascribed to C-6 by heteronuclear multiple quantum coherence (HMQC), corresponding to the proton signal at δ 7.00 (d, $J=8.4$ Hz). The observation of HMBC correlation between the C-6 signal and the 1-hydroxyl proton signal supported the location of 1-hydroxy group. Thus, the structure of **5** was assigned to isomagnolone.

Although β-eudesmol (**7**) and α-eudesmol (**8**) are well known sesquiterpenes, this is the first time that these compounds have been isolated from *Illicium* plants.

Experimental

^1H- and ^{13}C-NMR spectra were recorded using JEOL GX-400 spectrometers. NOE and two dimensional correlation spectroscopy (2D COSY) experiments were also performed using this equipment. Chemical shifts are expressed in δ (ppm) values with tetramethylsilane as an internal standard. EI-MS are recorded on a JEOL JMX-DX-303 spectrometer. IR spectra were recorded on a Shimadzu IR-408 spectrometer.

Extraction and Isolation The bark (1 kg) of *I. simonsii*, collected in Sichuan province, China, in the summer season of 1989, was extracted three times with methanol (6 l) to give a MeOH extract (362 g). This was suspended in water and extracted successively with *n*-hexane, EtOAc, and *n*-BuOH. The *n*-hexane extract was separated into a precipitate (3.45 g) and a soluble fraction (14.9 g) when concentrated. The former gave dunnianol (**3**) (2.4 g) by crystallization from *n*-hexane. The mother liquor from **3** afforded simonsinol (**1**) (13.2 mg) after separation by silica-gel chromatography with *n*-hexane–EtOAc (9 : 1). The *n*-hexane soluble part was chromatographed on silica-gel to give four fractions (I—IV). Repeated silica-gel column chromatography of fraction II afforded isodunnianol (**4**) (1.90 g), β-eudesmol (**7**) (6.6 mg) and α-eudesmol (**8**) (4.0 mg). Fraction III was subjected to silica-gel chromatography and then MPLC using a Kusano Si-5 column, to give simonsinol (**1**) (82.4 mg). Similar separation of fraction IV, gave dunnianol (**3**) (1.47 g), macranthol (**2**) (288.6 mg) and isomagnolone (**5**) (5 mg). Compounds **2**, **3** and **4** were identified by direct comparison with authentic samples. Compounds **7** and **8** were identified as β-eudesmol and α-eudesmol, respectively, by comparison with reference data.[3]

Simonsinol (1) A colorless oil, MS *m/z*: 398 [M^+], $C_{27}H_{26}O_3$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510, 3020, 1638, 1598, 1210.

Methylation of Simonsinol (1) A mixture of **1** (22.8 mg), K_2CO_3 (1 g), CH_3I (1.3 ml) in dry acetone (20 ml), was refluxed for 8 h. After the solution had cooled, K_2CO_3 was removed by filtration. The filtrate was concentrated to dryness under reduced pressure, and the residual oil was chromatographed on silica-gel [*n*-hexane–EtOAc (1 : 9)] to give three *O*-methylated compounds (**1′a** (12.1 mg), **1′b** (5.2 mg) and **1′c** (7.2 mg)). **1′a**: colorless oil, EI-MS *m/z*: 440 (M^+), 426 (M^+-14). ^1H-NMR ($CDCl_3$) δ: 3.20 (3H, s, OMe), 3.37 (2H, d, $J=6.6$ Hz), 3.40 (2H, d, $J=6.6$ Hz), 3.42 (2H, d, $J=6.6$ Hz), 3.78 (6H, s, OMe), 5.02 (1H, dd, $J=9.9$, 1.5 Hz), 5.05 (1H, dd, $J=17.2$, 1.8 Hz), 5.06 (1H, dd, $J=9.9$, 1.8 Hz), 5.07 (1H, dd, $J=17.6$, 1.5 Hz), 5.09 (1H, dd, $J=9.9$, 1.8 Hz), 5.12 (1H, dd, $J=17.2$, 1.8 Hz), 5.97—6.03 (3H, m), 6.90 (1H, d, $J=8.4$ Hz), 6.90 (1H, d, $J=8.1$ Hz), 6.91 (1H, d, $J=8.1$ Hz), 7.03 (1H, d, $J=2.2$ Hz), 7.12 (2H, d, $J=2.2$ Hz), 7.13 (1H, dd, $J=8.1$, 2.2 Hz), 7.39 (1H, d, $J=2.2$ Hz), 7.42 (1H, dd, $J=8.4$, 2.2 Hz). ^{13}C-NMR ($CDCl_3$) δ: 34.2 (t), 39.2 (t), 39.5 (t), 55.3 (q), 55.7 (q), 60.2 (q), 110.0 (d), 110.9 (d), 115.2 (t), 115.3 (t), 115.7 (t), 127.9 (d), 128.0 (s), 128.1 (s), 128.3 (d), 130.2 (d), 130.4 (d), 130.7 (d), 131.2 (s), 131.5 (d), 131.7 (s), 132.4 (s), 134.3 (s), 134.7 (s), 137.0 (d), 137.4 (d), 137.8 (d), 153.7 (s), 155.2 (s), 156.4 (s); **1′b**: colorless oil, EI-MS *m/z*: 426 (M^+). ^1H-NMR ($CDCl_3$) δ: 3.395 (2H, d, $J=7.0$ Hz), 3.398 (2H, d, $J=7.0$ Hz), 3.43 (2H, d, $J=7.0$ Hz), 3.83 (3H, s, OMe), 3.86 (3H, s, OMe), 5.03 (1H, dd, $J=10.3$, 1.5 Hz), 5.05 (1H, dd, $J=10.2$, 1.8 Hz), 5.06 (1H, dd, $J=10.3$, 1.5 Hz), 5.08 (1H, dd, $J=15.0$, 1.5 Hz), 5.10 (1H, dd, $J=15.0$, 1.5 Hz), 5.12 (1H, dd, $J=15.0$, 1.8 Hz), 5.90—6.10 (3H, m), 6.92 (1H, d, $J=8.4$ Hz), 7.00 (1H, d, $J=7.7$ Hz), 7.12 (1H, d, $J=2.2$ Hz), 7.18 (2H, d, $J=2.2$ Hz), 7.19 (1H, dd, $J=7.7$, 2.2 Hz), 7.36 (1H, d, $J=2.2$ Hz), 7.42 (1H, dd, $J=8.4$, 2.2 Hz). ^{13}C-NMR ($CDCl_3$) δ: 34.3 (t), 39.2 (t), 39.4 (t), 55.4 (q), 56.0 (q), 110.1 (d), 111.4 (d), 115.3 (t), 115.5 (t), 115.7 (t), 126.6 (s), 127.2 (s), 128.3 (d), 129.0 (d), 129.7 (s), 130.1 (s), 130.2 (2d), 130.7 (s), 131.0 (d), 131.9 (s), 132.5 (d), 133.3 (s), 136.9 (d), 137.4 (s), 137.7 (d), 148.7 (s), 154.2 (s), 156.4 (s); **1′c**: colorless oil, EI-MS *m/z*: 426 (M^+). ^1H-NMR ($CDCl_3$) δ: 3.28 (3H, s, OMe), 3.39 (2H, d, $J=6.6$ Hz), 3.44 (4H, d, $J=6.6$ Hz), 3.88 (3H, s, OMe), 5.04 (1H, dd, $J=9.9$, 1.8 Hz), 5.05 (1H, dd, $J=16.9$, 1.5 Hz), 5.07 (1H, dd, $J=9.9$, 1.5 Hz), 5.09 (1H, dd, $J=15.0$, 1.8 Hz), 5.10 (1H, dd, $J=9.5$, 1.5 Hz), 5.13 (1H, dd, $J=16.9$, 1.5 Hz), 5.98—6.04 (3H, m), 6.92 (1H, d, $J=8.1$ Hz), 7.00 (1H, d, $J=8.1$ Hz), 7.12 (1H, d, $J=2.2$ Hz), 7.13 (1H, dd, $J=8.1$, 2.2 Hz), 7.15 (1H, d, $J=2.2$ Hz), 7.18 (1H, d, $J=2.2$ Hz), 7.37 (1H, d, $J=2.2$ Hz), 7.41 (1H, dd, $J=8.1$, 2.2 Hz). ^{13}C-NMR ($CDCl_3$) δ: 34.3 (t), 39.4 (t), 39.7 (t), 55.5 (q), 61.2 (q), 110.2 (d), 115.5 (2t), 116.2 (t), 118.8 (d), 126.5 (s), 128.2 (d), 128.5 (s), 129.5 (d), 130.1 (s), 130.8 (d), 130.9 (d), 131.1 (d), 131.2 (d), 132.2 (s), 132.5 (s), 135.2 (s), 136.9 (d), 137.1 (d), 137.2 (s), 137.9 (d), 151.7 (s), 152.1 (s), 156.8 (s).

Permethylation of Simonsinol (1) A mixture of **1** (23.2 mg), K_2CO_3 (3.6 g), CH_3I (3 ml), in dry acetone (20 ml) was refluxed for 24 h. After a work-up as described above, an oily product (20.7 mg) was obtained, identical with **1′a** on thin-layer chromatography (TLC) and in terms of its ^1H- and ^{13}C-NMR spectra.

Acetylation of Simonsinol (1) A mixture of **1** (15.2 mg) and DMAP (2 mg) in dry pyridine (1 ml) and Ac_2O (0.5 ml) was left 2 h at room temperature, then concentrated to dryness under reduced pressure. The residue was chromatographed on silica-gel [*n*-hexane–EtOAc (1 : 9)] to give an oily acetylated compound (**1″**) (16.8 mg). EI-MS *m/z*: 524 (M^+), 482, 440, 396. ^1H-NMR ($CDCl_3$) δ: 1.72 (3H, s, OAc), 2.11 (6H, s, OAc), 3.32 (4H, d, $J=7.0$ Hz), 3.40 (2H, d, $J=6.6$ Hz), 5.06—5.14 (6H, m), 5.91—6.03 (3H, m), 7.08 (1H, d, $J=7.0$ Hz), 7.09 (1H, d, $J=6.6$ Hz), 7.09 (1H, dd, $J=6.6$, 1.8 Hz), 7.15 (1H, d, $J=1.8$ Hz), 7.19 (1H, d, $J=2.2$ Hz), 7.21 (1H, d, $J=2.2$ Hz), 7.29 (1H, dd, $J=7.0$, 2.2 Hz), 7.30 (1H, d, $J=2.2$ Hz).

Isomagnolone (5) Colorless oil, MS *m/z*: 282 [M^+], $C_{18}H_{18}O_3$. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510, 1730, 1495, 1462.

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