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A New Lignan from Leaves of *Ormosia xylocarpa*

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Abstract: A new lignan, 4,4″-dihydroxy-3,3′,5′,3″,5″,7″-pentamethoxy-7,9′;7′,9-diepoxy-4′,8″-oxy-8,8′-sesquineo-lignan-propanol (**1**), along with six known lignans (**2**-**7**) was isolated from the leaves of *Ormosia xylocarpa* (Chun ex L. Chen). The structure of compound **1** was elucidated through comprehensive 1D and 2D NMR, UV, IR, and HRMS analyses. Compounds **2~3** performed strong antioxidant activity, the median clearance concentration of DPPH, $ABST^{+}$, and ·OH were lower than 40 μM.

Keywords: *Ormosia xylocarpa*; lignans; chemical constituents; antioxidant activity.

1. Plant Source

The leaves of *Ormosia xylocarpa* (Chun ex L. Chen) were collected from the 15-year-old tree in September 2019 in Shaxian County, Fujian Province, China (117°78' N latitude, 26°40' E longitude), and were identified by one of the authors (Xiaoxing Zou). The voucher specimen (accesssion number: 20190812) was preserved in the Engineering Research Center of Natural Biological Resources Conservation & Utilization of Fujian Province, FAFU, Fuzhou, China.

2. Previous Studies

Ormosia xylocarpa is a valuable timber tree species belonging to the genus *Ormosia*, widely distributed in southern China [1]. Its huge canopy produces a lot of fallen leaves, which possess rich medicinal value and can be used for treating eye diseases in the folk [2]. The ancient method of

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decoction with its branches and leaves to prevent cardiovascular diseases indicated its potential antioxidant ability [3]. Some lignans have been isolated from *O. xylocarpa*, including xylocarpalignan, syringaresino-4′-O-*β*-D-glucoside, and zhebeir esinol [4-5]. In our research, seven lignans were isolated and identified (Figure 1), one of them was a new compound. They all showed certain antioxidant activity in the DPPH, $ABST^+$, and ·OH radical scavenging activity assays. All compounds were first found in the *Ormosia* genus.

3. Present Study

The leaves of *O. xylocarpa* (10.0 kg) were powdered and then extracted with 70% ethanol (2×20 L, 2×2 h) to give an extract (1.86 kg). The extract was extracted with EtOAc (2×45 L) to obtain the EtOAc fraction. The EtOAc fraction (407 g) was chromatographed over polyamide macroporous (60-100 mesh) with EtOH-H_2O gradient (H_2O, 3:7, 1:1, 6:4, 7:3, EtOH) as eluent to obtain 18 fractions (Fr.1~Fr.18). Fr.1 (87.3 g) was chromatographed over silica gel with CH_2Cl_2-MeOH as eluent to obtain 10 fractions (Fr.1.1~Fr.1.10). Compound **1** (3.2 mg) was isolated from Fr.1.1 (3.1 g) by HPLC (CH3CN/H2O (28: 72), 8.0 mL/min) after separating by Sephadex LH-20 with MeOH. Fr.1.3 (8.1g) was separated by PRP-512A and eluted with EtOH-water (1:9, 3:7, 1:1, 7:3, 9:1, EtOH) to give 6 subfractions (Fr.1.3.1~Fr.1.3.6). Fr.1.3.2 (640 mg) was further separated by Sephadex LH-20 with MeOH to obtain 5 subfractions (Fr.1.3.1.1~Fr.1.3.6.5). Compound **2** (5.3 mg) and **4** (3.4 mg) were separated from Fr.1.3.1.2 (168 mg) by semi-preparative HPLC (MeOH/H_2O (47: 53), 8.0 mL/min). Fr.1.3.1.3 (180 mg) was subjected to semi-preparative HPLC (CH_3CN/H_2O (28: 72), 8.0 mL/min) to obtain compound **3** (7.2 mg). Fr.1.3.3 (700 mg) was chromatographed over Sephadex LH-20 eluted with MeOH and further purified by HPLC (MeOH/H_2O (30: 70), 8.0 mL/min) to yield compound **5** (2.8 mg), **6** (3.7 mg) and **7** (3.2 mg).

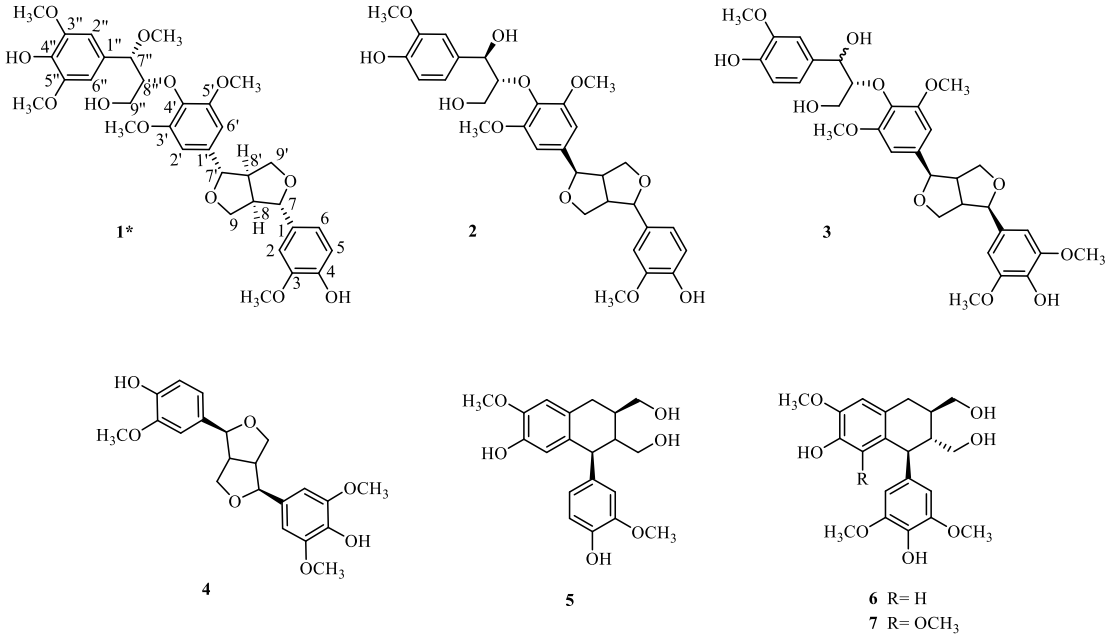

Figure 1. The structure of compounds **1-7**. * indicates new compound

Compound **1**: Yellow oil; UV (MeOH) λmax: 280, 250, 230 nm, IR (KBr) λmax 3413.0, 1611.0, 1461.4, 1224.8, 1026.4 cm^{-1}. CD (MeOH) λmax (Δε) 247 (+6.73), 278 (+9.48); HR-ESI-MS *m/z* 651.2409 $[M + Na]^+$ (calcd for $C_{33}H_{40}O_{12}Na$, 651 .2412). ^{1}H-NMR (DMSO-d_6, 400 MHz) and ^{13}C-NMR (DMSO-d_6, 100 MHz) data see Table 1.

Table 1. ^{1}H-NMR (400MHz, DMSO-d_6) and ^{13}C-NMR (100 MHz, DMSO-d_6) data of compound **1**

Position	δ_H	δ_C
1		132.2
2	6.88 (1H, d, *J* = 2.0 Hz)	115.2
3		147.7
4		146.0
5	6.72 (1H, d, *J* = 8.0 Hz)	110.4
6	6.75 (1H, dd, *J* = 8.0, 2.0 Hz)	118.7
7	4.61 (1H, d, *J* = 3.6 Hz)	85.2
8	3.05 (1H, m)	53.5
9	4.14 (2H, m)	71.3
1′		136.8
2′, 6′	6.61 (2H, d, *J* = 2.0Hz)	103.2
3′, 5′		152.6
4′		134.7
7′	4.64 (1H, d, *J* = 3.6 Hz)	85.2
8′	3.02 (1H, m)	53.8
9′	3.77 (overlapped)	71.0
1″		126.7
2″, 6″	6.54 (2H, m)	104.9
3″, 5″		147.6
4″		134.7
7″	4.39 (1H, d, *J* = 6.8 Hz)	82.6
8″	4.19 (1H, m)	84.9
9″	3.65 (1H, overlapped) 3.47 (1H, overlapped)	59.8
3-OCH_3	3.76 (3H, s)	55.6
3′, 5′-OCH_3	3.72 (6H, s)	56.0
3″, 5″-OCH_3	3.70 (6H, s)	55.9
7″-OCH_3	3.71 (3H, s)	56.6

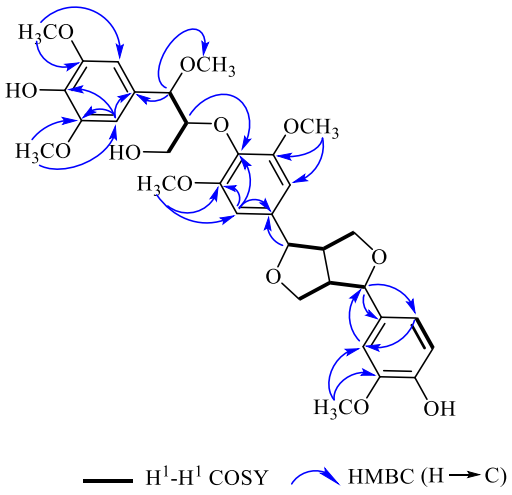

Figure 2. Key HMBC and ^{1}H-^{1}H COSY Correlations of Compound **1**

Compound **1** was isolated as a yellow oil, and its UV spectrum showed three absorption peaks at 280, 250 and 230 nm. Its molecular formula was defined as $C_{33}H_{40}O_{12}$, based on analysis of the HRESIMS (*m/z* 651.2409 $[M + Na]^+$, calcd. 651 .2412). In the IR spectrum, absorption bands at 3413 cm^{-1} (hydroxy), 1611.0 and 1461.4 cm^{-1} (aromatic ring) were observed.

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The ^{1}H NMR spectrum of **1** showed hydrogen proton signals of a benzene ring ABX system [δ_H 6.88 (1H, d, *J* =2.0 Hz), 6.75 (1H, dd, *J* =8.0, 2.0 Hz), and 6.72 (1H, d, *J* =8.0 Hz)], two sets of symmetrical aromatic hydrocarbon proton signals [δ_H 6.61 (2H, m) and 6.54 (2H, m)], four oxygenated methines [δ_H 4.64 (1H, d, *J* = 3.6 Hz), 4.61 (1H, d, *J* = 3.6 Hz), 4.39 (1H, d, *J* = 6.8 Hz), and 4.19 (1H, m)], and six methoxy groups [δ_H 3.76 (3H, s), 3.76 (6H, s), and 3.72 (9H, s)]. The ^{13}C NMR associated with the DEPT spectra of **1** classified 33 carbon resonances indicated the existence of a 3,4-distributed phenyl and two symmetric 3′,4′,5′-trisubstituted phenyl, three methylene groups, and two methines. These data manifested compound **1** as a sesquineolignan [6-7].

In the ^{1}H-^{1}H COSY spectrum, the correlations of H-7/H-8/H-9 [δ_H 4.61 (1H, d, *J* = 3.6 Hz), 3.05 (1H, m), 4.14 (2H, m)] and H-7′/H-8′/H-9′ [δ_H 4.64 (1H, d, *J* = 3.6 Hz), 3.02 (1H, m), and 3.77 (overlapped)] suggested the existence of a 7,9′;7′,9-diepoxy moiety [8]. The HMBC correlations from δ_H 3.72 (6H, s, 3′, 5′-OCH_3) to C-3′ (δ_C 152.6), C-2′ (δ_C 103.2), C-5′ (δ_C 152.6), and C-6′ (δ_C 103.2), from δ_H 3.76 (3H, s, 3-OCH_3) to C-2 (δ_C 115.2) and C-3 (δ_C 147.7) indicated the location of MeO-3, 3′, 5′. The ^{1}H-^{1}H COSY correlations of H-5/H-6 [δ_H 6.72 (1H, d, *J* = 8.0 Hz), 6.75 (1H, dd, *J* = 8.0, 1.6 Hz)], and the HMBC correlations from H-6 [δ_H 6.75 (1H, dd, *J* = 8.0, 1.6 Hz)] to C-2 (δ_C 115.2), from H-2 [δ_H 6.88 (1H, d, *J* =2.0 Hz)] to C-7 (δ_C 85.2), from H-7 [δ_H 4.61 (1H, d, *J* = 3.6 Hz)] to C-1 (δ_C 132.2) and C-6 (δ_C 118.7), from H-6′ [δ_H 6.61 (2H, dd, *J* = 2.0 Hz)] to C-1′ (δ_C 136.8), C-5′ (δ_C 152.6), and C-4′ (δ_C 134.7), from H-7′ [δ_H 4.64 (1H, d, *J* =3.6 Hz)] to C-1′ (δ_C 136.8) indicated that the compound **1** has a 4-hydroxy-3,4′,5′,-trimethoxy-7,9′;7′,9-diepoxy lignan structural unit. The ^{1}H-^{1}H COSY spectrum indicated a glycerol-type moiety at H-7″/H-8″/H-9″ [δ_H 4.39 (1H, d, *J* = 6.8 Hz), 4.19 (1H, m), 3.65 (1H, overlapped) and 3.47 (1H, overlapped)] [9]. In addition, the HMBC correlations from H-2″ [δ_H 6.54 (2H, m)] to C-1″ (δ_C 126.7), C-3″ (δ_C 147.6), and C-4″ (δ_C 134.7), from H-7″ [δ_H 4.39 (1H, d, *J* = 6.8 Hz)] to C-1″ (δ_C 126.7), from δ_H 3.70 (6H, s, 3″, 5″-OCH_3) to C-2″(δ_C 104.9), C-3″(δ_C 147.6), C-5″(δ_C 147.6), and C-6″(δ_C 104.9) indicated that the compound **1** has a 3″,5″-dimethyl-4-hydroxy-phenylpropanol structural unit. The HMBC correlations from H-7″ [δ_H 4.39 (1H, d, *J* = 6.8 Hz)] to MeO-7″ (δ_C 56.6) indicated that MeO-7″ was located at C-7″. Moreover, the HMBC spectrum confirmed the 4′-8′′-oxy linkage between the two units at H-8′′ [δ_H 4.19 (1H, m)] to C-4′ (δ_C 134.7) [10-11].

According to H-7′[δ_H 4.64 (1H, d, *J* = 3.6 Hz)] and H-7 [4.61 (1H, d, *J* = 3.6 Hz)], the coupling constant of 3.6 Hz between H-7/H-8 and H-7′/H-8′ confirmed an *erythro* relative configuration [12]. The coupling of 6.8 Hz between H-7″ and H-8″ defined a *threo* relative configuration [13]. The spectrum showed a positive cotton effect at 247 nm and 278 nm agreeing with the configuration of **1** to be 7*S*, 7′*S* ,7″*S*, 8*R*, 8′*R*, and 8″*S* [14-15]. Compound **1** was given a trivial name xylocarpalignan B, and its structure was determined and illustrated in Figure 2.

Six known lignans (**2-7**) isolated from *O. xylocarpa* were identified as hedyotol C (**2**) [16], buddlenol C (**3**) [17], (+)-medioresinol (**4**) [18], (+)-isolariciresinol (**5**) [19], 5-methoxy-(+)-isolariciresinol (**6**) [20], and (+)-lyoniresinol (**7**) [21], by comparison with the published NMR data.

Table 2. Antioxidant activity values of Compounds **1*-7**

Compounds	DPPH (EC_{50}, μM)	$ABTS^+$ (EC_{50}, μM)	·OH (EC_{50}, μM)
VC	48.79	5.03	39.10
1*	26.61	18.01	28.44
2	15.43	7.63	17.43
3	29.38	13.30	32.54
4	38.33	18.29	37.26
5	121.87	11.45	28.36
6	173.71	12.23	22.31
7	101.76	5.07	12.78

The DPPH, $ABTS^{+}$ and ·OH radical scavenging activity assays [22-24] were conducted to determine the antioxidant ability of compounds **1-7**. The results showed that compounds **2-3** and **5-7** exerted strong antioxidant activity (Table 2). Compounds **2-3** are 8.O.4′-neolignans and their antioxidant properties were related to the conformation of C-7″and C-8″ [25], and 8.O.4′-neolignans with the *threo* series possessed stronger activity. The lignans with a phenolic hydroxyl (compounds **5-7**) showed significant antioxidant activity like phenolic compounds.

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Supporting Information

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