

Lignans from *Wikstroemia hainanensis*

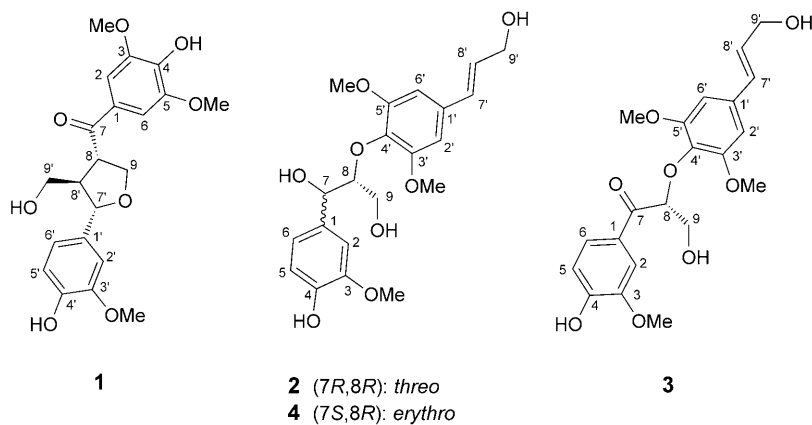
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The structures and conformations of three new lignans, wikstrone (**1**), wikstroemol (**2**), and wikstroemone (**3**) – isolated from the aerial parts of *Wikstroemia hainanensis* – were determined, together with those of twelve known compounds, including *erythro*-guaiacylglycerol- β -*O*-4'-sinapyl ether (**4**). The configuration of **4**, falsely assigned in the literature (*threo* configuration), was redetermined, and the compound was identified as *erythro*-guaiacylglycerol- β -*O*-4'-sinapyl ether.

Introduction. – The genus *Wikstroemia* belongs to the family Thymelaeaceae. Several species of this genus were shown to produce biologically active daphnane- [1] and tigliane-type [2] diterpenoids, lignans [3], biflavonoids [3b] [4], and bicoumarins [3]. *Wikstroemia hainanensis* MERR., a tiny shrub indigenous to Hainan Province, China, has not been chemically investigated previously. In the current paper, three new lignans, wikstrone (**1**), wikstroemol (**2**), and wikstroemone (**3**), along with twelve known compounds, *erythro*-guaiacylglycerol- β -*O*-4'-sinapyl ether (**4**), 4-hydroxy-*trans*-cinnamic acid, (+)-pinoresinol, (+)-medioresinol, (+)-syringaresinol, (+)-nortrachelogenin, (–)-lariciresinol, ficusesquilignan A, sitosterol, hederagenin, umbelliferone, and daphnoretin, were isolated from the aerial parts of *W. hainanensis*, and structurally identified by spectroscopic methods.



Results and Discussion. – The crude EtOH extract of the aerial parts of *W. hainanensis* was suspended in H₂O and extracted with AcOEt and BuOH. Extensive purification by column and preparative thin-layer chromatography of the AcOEt-soluble fraction afforded **1–3** and the above twelve known compounds.

Wikstrone (**1**) was obtained as a colorless amorphous powder. The M^+ signal in the HR-EI mass spectrum was observed at m/z 404.1456, consistent with a molecular formula of C₂₁H₂₄O₈. The IR spectrum showed absorptions for OH (3419), conjugated C=O (1662), and aromatic (1605, 1518, 1462 cm⁻¹) groups. The UV maxima at 230, 285, and 308 nm were indicative of the presence of a lignan skeleton based on a tetrahydrofuranoketone [5]. The presence of a conjugated ketone C=O moiety was further supported by the ¹³C-NMR resonance at δ (C) 198.4. Further analysis of 1D- and 2D-NMR (Table 1) and circular dichroism (CD) data enabled us to elucidate the structure of **1** as (4-hydroxy-3,5-dimethoxyphenyl)[(3*S*,4*R*,5*S*)-tetrahydro-5-(4-hydroxy-3-methoxyphenyl)-4-(hydroxymethyl)furan-3-yl]methanone.

In the ¹H-NMR spectrum of **1** (Table 1), a 4-substituted 3,5-dimethoxybenzoyl group (δ (H) 7.41 (*s*, 2 H); 3.90 (*s*, 6 H)) and a 1,3,4-trisubstituted benzene (δ (H) 7.04 (*d*, $J=1.2$ Hz, 1 H); 6.85 (*dd*, $J=8.1, 1.2$

Table 1. NMR Data of Compounds **1** and **3**. At 400 MHz (¹H, HMBC) or 100 MHz (¹³C) in (CD₃)₂CO (**1**) and CDCl₃ (**3**) solution; δ in ppm, J in Hz.

Position	1			3		
	δ (H)	δ (C)	HMBC (H → C)	δ (H)	δ (C)	HMBC (H → C)
H-C(1)	–	128.2	–	–	128.3	–
H-C(2)	7.41 (<i>s</i>)	107.0	1, 3, 4, 6, 7	7.67 (<i>d</i> , $J=1.9$)	113.9	1, 3, 5, 6, 7
H-C(3)	–	148.2	–	–	146.7	–
H-C(4)	–	141.7	–	–	150.6	–
H-C(5)	–	148.2	–	6.96 (<i>d</i> , $J=8.2$)	110.7	1, 3, 4
H-C(6)	7.41 (<i>s</i>)	107.0	1, 2, 4, 5, 7	7.64 (<i>dd</i> , $J=8.2, 1.9$)	124.0	4, 5, 7
H-C(7)	–	198.4	–	–	194.7	–
H-C(8)	4.13 (<i>m</i>)	49.3	7, 7', 8'	5.15 (<i>dd</i> , $J=7.4, 2.9$)	87.3	1', 7, 9
H _{α} -C(9)	4.18 (<i>m</i>)	70.7	7, 8, 7', 8'	3.95 (<i>dd</i> , $J=12.0, 7.4$)	63.6	8
H _{β} -C(9)	4.32 (<i>dd</i> , $J=13.6, 6.9$)	70.7	7, 7', 8'	3.85 (<i>dd</i> , $J=12.0, 2.9$)	63.6	8
H-C(1')	–	133.7	–	–	133.1	–
H-C(2')	7.04 (<i>d</i> , $J=1.2$)	110.8	1', 3', 6', 7'	6.61 (<i>s</i>)	103.5	1', 3', 4', 6', 7'
H-C(3')	–	148.0	–	–	152.5	–
H-C(4')	–	146.6	–	–	136.3	–
H-C(5')	6.77 (<i>d</i> , $J=8.1$)	115.0	1', 2', 3', 4'	–	152.5	–
H-C(6')	6.85 (<i>dd</i> , $J=8.1, 1.2$)	120.0	1', 2', 4', 7'	6.61 (<i>s</i>)	103.5	1', 2', 3', 4', 7'
H-C(7')	4.66 (<i>d</i> , $J=8.5$)	83.9	1', 2', 6', 8', 9'	6.55 (<i>br. d</i> , $J=15.8$)	130.7	6', 9'
H-C(8')	2.61 (<i>m</i>)	54.2	7, 8, 1', 7'	6.30 (<i>dt</i> , $J=15.8, 5.7$)	128.6	1', 9'
H _{α} -C(9')	3.67 (<i>dd</i> , $J=11.3, 4.4$)	60.2	8, 8', 9'	4.35 (<i>dd</i> , $J=5.7, 1.4$)	63.5	7', 8'
H _{β} -C(9')	3.63 (<i>dd</i> , $J=11.3, 4.9$)	60.2	8, 8', 9'	4.35 (<i>dd</i> , $J=5.7, 1.4$)	63.5	7', 8'
3-MeO	3.90 (<i>s</i>)	56.4	3	3.95 (<i>s</i>)	56.1	3
4-MeO	–	–	–	6.19 (<i>br. s</i>)	–	–
5-MeO	3.90 (<i>s</i>)	56.4	5	–	–	–
3'-MeO	3.83 (<i>s</i>)	55.9	3'	3.75 (<i>s</i>)	55.9	3'
5'-MeO	–	–	–	3.75 (<i>s</i>)	55.9	5'

Hz, 2 H); 6.77 (*d*, $J=8.1$ Hz, 1 H)) were distinguished. An aromatic MeO group ($\delta(\text{H})$ 3.83 (*s*, 3 H)), a diastereoisotopic, oxygenated CH_2 group ($\delta(\text{H})$ 3.67 (*dd*, $J=11.3, 4.4$ Hz, 1 H); 3.63 (*dd*, $J=11.3, 4.9$ Hz, 1 H)), as well as a tetrahydrofuran ring ($\delta(\text{H})$ 4.66 (*d*, $J=8.5$ Hz, 1 H); 4.32 (*dd*, $J=13.6, 6.9$ Hz, 1 H); 4.18 (*m*, 1 H); 4.13 (*m*, 1 H); 2.61(*m*, 1 H)) [5] were identified. The ^{13}C -NMR signal at $\delta(\text{C})$ 60.2 was assigned to $\text{C}(9')^1$. These observations suggested that **1** had a tetrahydrofuranoketone lignan skeleton similar to that of sesaminone [5b], (+) episesaminone [5c], and magnones A and B [5d]. A total of 16 carbon signals, including one $\text{C}=\text{O}$, ten aromatic carbons (four CH and six C_q), two MeO, two oxygenated CH_2 , and three CH (one oxygenated) were resolved in the ^{13}C -NMR (DEPT) spectrum (Table 1). EI-MS fragment ions at m/z 181 and 137 (Fig. 1), resulting from benzoyl and benzyl cleavages, further confirmed our structural assignments.

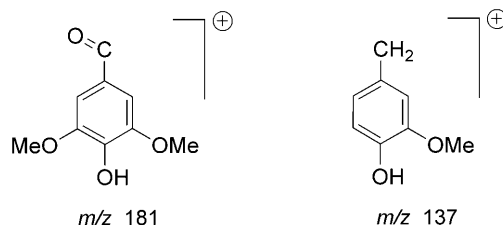


Fig. 1. Characteristic mass fragments of **1**

The structure of **1** and the complete assignment of its ^1H - and ^{13}C -NMR data were finally accomplished via an HMBC experiment (Table 1 and Fig. 2). In particular, the key correlation between the resonance at $\delta(\text{H})$ 3.83 (MeO) and $\text{C}(3')$ revealed a 3'-MeO group, the correlations of $\text{CH}_2(9)$ with $\text{C}(7)$, $\text{C}(8')$, and $\text{C}(8)$ established the tetrahydrofuran ring, and the correlations of $\text{CH}_2(9')$ with $\text{C}(7')$, $\text{C}(8')$, and $\text{C}(8)$ showed that the CH_2OH group was located at $\text{C}(8')$. Analogously, correlations of $\text{H}-\text{C}(2)$, $\text{H}-\text{C}(8)$, $\text{H}-\text{C}(8')$, and $\text{CH}_2(9)$ with $\text{C}(7)$ indicated that the 4-hydroxy-3,5-dimethoxybenzoyl group was at $\text{C}(8)$, and those of $\text{H}-\text{C}(2')$ and $\text{H}-\text{C}(6')$ with $\text{C}(7')$ revealed that the 4-hydroxy-3-methoxyphenyl group was linked to $\text{C}(7')$.

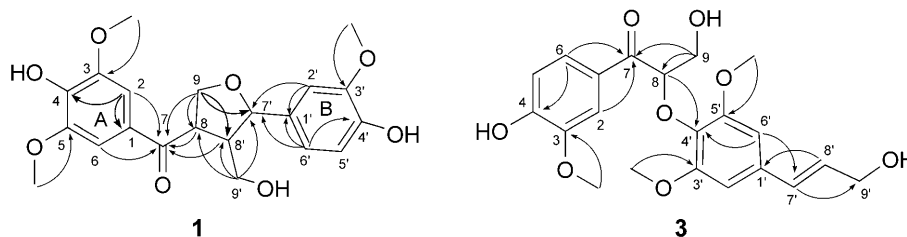


Fig. 2. Selected HMBC ($\text{H} \rightarrow \text{C}$) correlations for compounds **1** and **3**

The relative configuration of **1** was determined by analysis of ^1H -NMR data and NOESY correlations (Fig. 3, a). The chemical shift of $\text{H}-\text{C}(7')$ at *ca.* $\delta(\text{H})$ 4.7 suggested that $\text{H}-\text{C}(7')$ and $\text{H}-\text{C}(8')$ were *trans*-oriented²⁾, and this was supported by a NOESY correlation between $\text{H}-\text{C}(2')$ and $\text{H}-\text{C}(8')$. Based on NOE correlations of $\text{H}-\text{C}(8)/\text{H}-\text{C}(7')$ and $\text{H}-\text{C}(2)/\text{H}-\text{C}(6')$, we placed $\text{H}-\text{C}(8)$ and $\text{H}-\text{C}(7')$ on the same side of the tetrahydrofuran ring (*trans*-orientation of $\text{H}-\text{C}(8)$ and $\text{H}-\text{C}(8')$).

¹⁾ Arbitrary atom numbering.

²⁾ For a *cis*-form, $\delta(\text{H})$ was reported to be *ca.* 5.5 [5d].

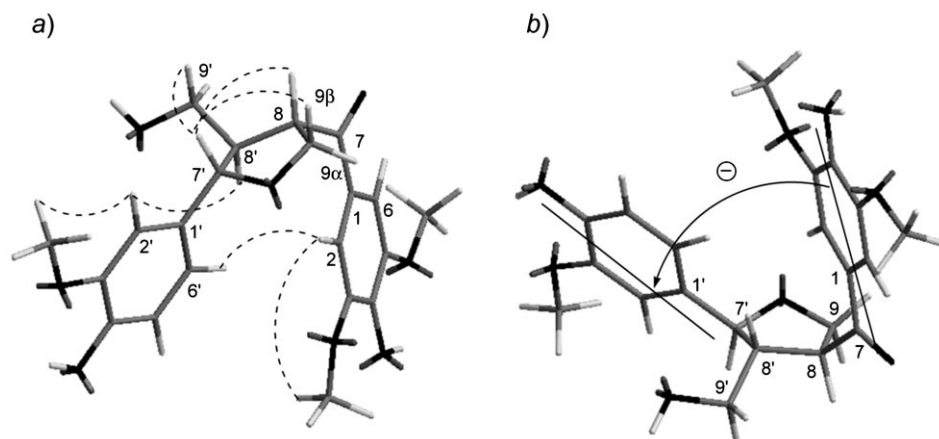


Fig. 3. a) Key NOESY correlations for compound **1**. b) Exciton coupling in **1**

The absolute configuration of **1** was established by analysis of its CD spectrum. A negative first Cotton effect caused by the exciton coupling of the benzoyl and benzene chromophores (Fig. 3,b) suggested that the compound had the (8*S*,7*S*)-configuration.

Wikstroemol (**2**) was isolated as a colorless, amorphous powder. ESI Mass spectroscopy showed signals at m/z 445.1 ($[M + K]^+$) and 429.3 ($[M + Na]^+$), which, in combination with the ^1H - and ^{13}C -NMR data (Table 2), suggested a molecular formula of $\text{C}_{21}\text{H}_{24}\text{O}_8$. The IR absorptions of **2** were indicative of the presence of OH (3427), C=C (1659), and benzene (1583, 1504, 1456 cm^{-1}) groups. The ^1H - and ^{13}C -NMR data of **2** showed high similarity with those of the known compound **4** isolated from *Brassica fruticulosa* [6], suggesting that they possibly had the same constitution. An HMBC experiment was, thus, carried out, and the proposed structure of **2** was confirmed. Conformational analysis (Fig. 4) [7] revealed that the coupling constant of 7.3 Hz between H–C(7) and H–C(8) was in accord with an *anti*- or *threo*-configuration. Furthermore, a negative Cotton effect at 234 nm indicated that the absolute configuration of **2** was (7*R*,8*R*) [8]. From these data, the structure of **2** was, therefore, established as *threo*-(1*R*,2*R*)-guaiacylglycerol- β -*O*-4'-sinapyl ether, which corresponds to (1*R*,2*R*)-1-(4-hydroxy-3-methoxyphenyl)-2-({4-[(*E*)-3-hydroxyprop-1-enyl]-2,6-dimethoxyphenyl}-oxy)propane-1,3-diol.

The above assignment was in conflict with a report of Cutillo *et al.* [6], who had assigned the *threo*-configuration to compound **4** isolated from *Brassica fruticulosa*. Since we had isolated both **2** and **4** from the current plant, we analyzed the ^1H -NMR data (Table 2) of **4** and its optical rotation ($[\alpha]_{\text{D}}^{21} = +8.5$ ($c = 0.13$, MeOH)). Our experiments unequivocally corroborated that the data of **4** isolated by us were fully identical with those reported for putative **2** [6]. The coupling constant $J(7,8)$ was 5.0 (in CD_3OD) or 3.7 Hz (in CDCl_3) for **4**, which is indicative of a *syn*- or *erythro*-configuration (Fig. 4). The absolute (7*S*,8*R*) configuration was assigned on the basis of a negative Cotton effect at 234 nm [6]. Compound **4**, thus, corresponds to *erythro*-(1*S*,2*R*)-guaiacylglycerol- β -*O*-4'-sinapyl ether. From comparison of ^{13}C -NMR data (Table 2), **4** had been isolated before [9], but not elucidated from a stereochemical point of view.

Table 2. NMR Data of Compounds **2** and **4**. δ in ppm, J in Hz.

Position	2			4			
	$\delta(\text{H})^{\text{a}}$	$\delta(\text{C})^{\text{b}}$	$\delta(\text{H})^{\text{c}}$	$\delta(\text{H})^{\text{a}}$	$\delta(\text{C})^{\text{d}}$	$\delta(\text{H})^{\text{c}}$	$\delta(\text{C})^{\text{e}}$
H–C(1)	–	133.9	–	–	134.1	–	133.3
H–C(2)	7.01 (<i>d</i> , $J=1.9$)	112.3	6.97 (<i>d</i> , $J=1.9$)	6.98 (<i>d</i> , $J=1.9$)	111.7	6.95 (<i>d</i> , $J=1.8$)	110.9
H–C(3)	–	147.7	–	–	147.2	–	147.0
H–C(4)	–	149.3	–	–	148.9	–	145.3
H–C(5)	6.75 (<i>d</i> , $J=8.2$)	116.4	6.87 (<i>d</i> , $J=7.9$)	6.75 (<i>d</i> , $J=8.1$)	116.0	6.84 (<i>d</i> , $J=8.0$)	114.7
H–C(6)	6.87 (<i>dd</i> , $J=8.2$, 1.9)	121.5	6.96 (<i>dd</i> , $J=7.9$, 1.9)	6.79 (<i>dd</i> , $J=8.1$, 1.9)	120.9	6.74 (<i>dd</i> , $J=8.0$, 1.8)	119.2
H–C(7)	4.98 (<i>d</i> , $J=7.3$)	75.1	5.03 (<i>d</i> , $J=8.9$)	4.92 (<i>d</i> , $J=5.0$)	74.3	5.00 (<i>d</i> , $J=3.7$)	72.0
H–C(8)	4.02 (<i>ddd</i> , $J=7.3$, 3.8, 3.0)	89.7	3.89 (<i>m</i>)	4.21 (<i>m</i>)	87.9	4.14 (<i>ddd</i> , $J=6.8$, 3.7, 2.8)	86.2
H _a –C(9)	3.75 (<i>dd</i> , $J=12.1$, 3.8)	62.2	3.58 (<i>dd</i> , $J=11.6$, 2.5)	3.89 (<i>dd</i> , $J=11.9$, 5.6)	61.7	3.91 (<i>dd</i> , $J=12.1$, 6.8)	59.7
H _b –C(9)	3.29 (<i>dd</i> , $J=12.1$, 3.0)		3.34 (<i>dd</i> , $J=11.6$, 3.8)	3.55 (<i>dd</i> , $J=11.9$, 3.5)		3.51 (<i>dd</i> , $J=12.1$, 2.8)	
H–C(1')	–	135.4	–	–	135.1	–	132.3
H–C(2')	6.75 (<i>s</i>)	105.3	6.65 (<i>s</i>)	6.72 (<i>s</i>)	105.2	6.64 (<i>s</i>)	103.7
H–C(3')	–	154.8	–	–	154.9	–	152.8
H–C(4')	–	137.4	–	–	136.7	–	134.9
H–C(5')	–	154.8	–	–	154.9	–	152.8
H–C(6')	6.75 (<i>s</i>)	105.3	6.65 (<i>s</i>)	6.72 (<i>s</i>)	105.2	6.64 (<i>s</i>)	103.8
H–C(7')	6.54 (<i>br. d</i> , $J=15.8$)	131.8	6.54 (<i>br. d</i> , $J=15.8$)	6.54 (<i>br. d</i> , $J=15.8$)	131.7	6.55 (<i>dt</i> , $J=15.8$, 1.3)	130.1
H–C(8')	6.32 (<i>dt</i> , $J=15.8$, 5.6)	130.5	6.31 (<i>dt</i> , $J=15.8$, 5.6)	6.31 (<i>dt</i> , $J=15.8$, 5.8)	130.1	6.31 (<i>dt</i> , $J=15.8$, 5.7)	128.5
H _a –C(9')	4.21 (<i>dd</i> , $J=5.6$, 1.5)		4.33 (<i>dd</i> , $J=5.6$, 1.3)	4.22 (<i>dd</i> , $J=5.8$, 1.3)		4.32 (<i>dd</i> , $J=5.7$, 1.3)	
H _b –C(9')	4.21 (<i>dd</i> , $J=5.6$, 1.5)	64.1	4.33 (<i>dd</i> , $J=5.6$, 1.3)	4.22 (<i>dd</i> , $J=5.8$, 1.3)	63.8	4.32 (<i>dd</i> , $J=5.7$, 1.3)	61.5
3-MeO	3.82 (<i>s</i>)	56.8	3.88 (<i>s</i>)	3.83 (<i>s</i>)	56.6	3.86 (<i>s</i>)	55.5
4-OH	–	–	5.77 (<i>br. s</i>)	–	–	–	–
3'-MeO	3.86 (<i>s</i>)	57.1	3.91 (<i>s</i>)	3.83 (<i>s</i>)	56.6	3.86 (<i>s</i>)	56.0
5'-MeO	3.86 (<i>s</i>)	57.1	3.91 (<i>s</i>)	3.83 (<i>s</i>)	56.6	3.86 (<i>s</i>)	56.0

^{a)} At 400 MHz in CD₃OD. ^{b)} At 100 MHz in CD₃OD. ^{c)} At 400 MHz in CDCl₃. ^{d)} At 125 MHz in CD₃OD. ^{e)} At 100 MHz in (D₆)DMSO

Wikstroemone (**3**) had the molecular formula C₂₁H₂₄O₈ as determined by the HR-ESI-MS (*m/z* 427.1385 (C₂₁H₂₄O₈Na⁺, calc. 427.1369)). Its IR spectrum showed absorptions for OH (3439), C=O (1672), and benzene (1587, 1506, 1464 cm⁻¹) groups. The ¹H- and ¹³C-NMR data indicated that compound **3** was likely a C(7) ketone derivative of **4**, and the HMBC spectrum further secured the proposed structure.

The ¹H-NMR data of **3** and **4** (both in CDCl₃) showed the absence of a *doublet* at ca. $\delta(\text{H})$ 5.0 for H–C(7), downfield shifted ¹H-NMR signals ($\delta(\text{H})$ 7.67 (*d*, $J=1.9$ Hz, H–C(2)); 6.96 (*d*, $J=8.2$, H–C(5)); 7.64 (*dd*, $J=8.2$, 1.9 Hz, H–C(6)), and a significant coupling pattern and chemical-shift change of H–C(8) ($\delta(\text{H})$ 5.15 (*dd*, $J=7.4$, 2.9 Hz)). The latter two differences were likely caused by the presence of

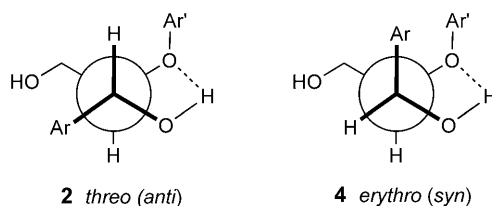


Fig. 4. Newman projections along the C(7)–C(8) bonds of compounds **2** and **4**. Dashed lines represent H-bonds.

the 7-keto group. A ^{13}C -NMR signal at $\delta(\text{C})$ 194.7 (conjugated C=O) further supported the above assumption. The observed HMBC correlations further secured the proposed structure of **3**, as depicted in Fig. 2. In consideration of the co-occurrence of compounds **2–4** in the same plant, and for biogenetic reasons, either of the two compounds **2** and **4** was supposed to be a biosynthetic precursor of **3**, and the absolute configuration of **3** was, thus, assumed to be (*8R*). From these data, wikstroemone (**3**) was designated as (2*R*)-3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-({4-[(*E*)-3-hydroxyprop-1-enyl]-2,6-dimethoxyphenyl}oxy)propan-1-one.

Among the twelve known compounds, 4-hydroxy-*trans*-cinnamic acid [10], sitosterol [11], daphnoretin [12], and umbelliferone [13] were identified from their ^1H -NMR data and by comparison with authentic samples (co-TLC); (+)-pinoresinol [14], (+)-medioresinol [15], (+)-syringaresinol [16], (+)-nortrachelogenin [17], (–)-lariciresinol [18], ficusesquilignan A [19], and hederagenin [20] were identified by comparison of their optical-rotation and ^1H - and ^{13}C -NMR data.

Financial support by the *National Natural Science Foundation* (to J.M.Y., No. 30025044) and the *Foundation from the Ministry of Science and Technology* (to J.M.Y., No. 2002CB512807) is gratefully acknowledged. We thank professor *Shi-Man Huang*, Department of Biology, Hainan University, for the collection and identification of the plant material.

Experimental Part

General. All solvents were of anal. grade (*Shanghai Chemical Plant*, Shanghai). Column chromatography (CC): silica gel (200–300 mesh), silica gel *H60*, *C18* reverse-phase (RP) silica gel (250 mesh; *Merck*), and *MCI* gel (*CHP20P*, 75–150 μm ; *Mitsubishi Chemical Industries, Ltd.*). TLC: pre-coated silica gel *GF254* plates (*Qingdao Haiyang Chemical Plant*, Qingdao). UV Spectra: *Hitachi U-2010*; λ_{max} (log ϵ) in nm. Optical rotation: *Perkin-Elmer 341* polarimeter. CD Spectra: *JASCO J-810* instrument; $\Delta\epsilon$ (λ_{max}). IR Spectra: *Perkin-Elmer 577* spectrometer. NMR Spectra: *Bruker AM-400* spectrometer; Me_4Si as internal standard; δ in ppm, J in Hz. EI-MS (70 eV): *Finnigan MAT 95* mass spectrometer; in m/z (rel. %).

Plant Material. The leaves and stems of *Wikstroemia hainanensis* MERR. were collected in September 2004 in Hainan province, P. R. China. The plant was authenticated by Prof. *Shi-Man Huang*, Department of Biology, Hainan University. A voucher specimen was deposited at the Shanghai Institute of Materia Medica (accession number WH-2004–1Y).

Extraction and Isolation. The powdered leaves and stems of *W. hainanensis* (7.5 kg) were percolated with 95% EtOH. After removal of the solvent under reduced pressure, a greenish extract (280 g) was obtained, which was suspended in H_2O (1000 ml), and extracted successively with AcOEt and BuOH. The AcOEt-soluble fraction (70 g) was fractionated by CC (SiO_2 ; petroleum ether/ Me_2CO 20:1 \rightarrow 0:1): *Fr. 1* and *Fr. 2*. *Fr. 1* (1.5 g) was separated by CC (SiO_2 ; petroleum ether/AcOEt 10:1 \rightarrow 2:1) to

give a major fraction, recrystallization of which from $\text{CHCl}_3/\text{MeOH}$ 10:1 afforded β -sitosterol (55 mg). *Fr. 2* (15 g) was subjected to CC (*MCI*-gel, $\text{MeOH}/\text{H}_2\text{O}$ 4:6 \rightarrow 9:1): *Fr. 2a* and *2b*. *Fr. 2a* (5.1 g) was further chromatographed (SiO_2 ; petroleum ether/ AcOEt 2.5:1 \rightarrow 1:3): *Fr. 2a.1–2a.7*. *Fr. 2a.1* (92 mg) was separated by CC (SiO_2 ; $\text{CHCl}_3/\text{MeOH}$ 200:1) to yield umbelliferone (4 mg) and 4-hydroxy-*trans*-cinnamic acid (5 mg). *Fr. 2a.2* (54 mg) was purified by CC (SiO_2 ; $\text{CHCl}_3/\text{MeOH}$ 200:1) to afford (+)-pinoresinol (28 mg) and (+)-nortrachelogenin (16 mg). Purification of *Fr. 2a.3* (20 mg) by prep. TLC ($\text{CHCl}_3/\text{MeOH}$ 80:1) yielded (+)-medioresinol (15 mg). Purification of *Fr. 2a.4* (927 mg) by CC (SiO_2 ; $\text{CHCl}_3/\text{MeOH}$ 200:1 \rightarrow 50:1) gave (+)-syringaresinol (33 mg) and (–)-lariciresinol (133 mg). *Fr. 2a.5* (858 mg) was first fractionated to give two fractions, *Fr. 2a.5.1* and *2a.5.2*. *Fr. 2a.5.1* (82 mg) was further purified by CC (*RP-18*; $\text{MeOH}/\text{H}_2\text{O}$ 40:60) to afford ficusesquillignan A (23 mg), and purification of *Fr. 2a.5.2* (141 mg) by CC (*RP-18*; $\text{MeOH}/\text{H}_2\text{O}$ 35:65) gave **2** (16 mg) and **4** (60 mg). *Fr. 2a.6* (121 mg) was purified by CC (SiO_2 ; $\text{CHCl}_3/\text{MeOH}$ 30:1) to afford **3** (5 mg). *Fr. 2a.7* (87 mg) was separated first on a *Sephadex LH-20* column (MeOH), and then by CC (*RP-18*; $\text{MeOH}/\text{H}_2\text{O}$ 40:60) to afford **1** (6 mg). *Fr. 2b* (0.85 g) was fractionated by CC (SiO_2 , petroleum ether/ AcOEt 2:1 \rightarrow 1:2) to afford two fractions, which were further purified by CC (SiO_2 ; $\text{CHCl}_3/\text{MeOH}$ 50:1) to provide hederagenin (12 mg) and daphnoretin (7 mg), resp.

Wikstrone (= (4-Hydroxy-3,5-dimethoxyphenyl)[(3*S*,4*R*,5*S*)-tetrahydro-5-(4-hydroxy-3-methoxyphenyl)-4-(hydroxymethyl)furan-3-yl]methanone; **1**). Colorless powder. UV (MeOH): 230 (4.22), 285 (3.95), 308 (3.96). $[\alpha]_{\text{D}}^{21} = -22$ ($c=0.09$, CHCl_3). CD (MeOH): -1.9 (320), $+0.51$ (283). IR (KBr): 3419, 2939, 1662, 1605, 1518, 1462, 1423, 1323, 1278, 1217, 1165, 1117, 1036, 864, 754, 653. ^1H - and ^{13}C -NMR: see *Table 1*. EI-MS: 404 (26, M^+), 279 (9), 239 (8), 209 (14), 205 (16), 196 (36), 181 (62), 167 (30), 149 (100), 137 (14). HR-EI-MS: 404.1456 (M^+ , $\text{C}_{21}\text{H}_{24}\text{O}_8^+$; calc. 404.1471).

Wikstroemol (= (1*R*,2*R*)-1-(4-Hydroxy-3-methoxyphenyl)-2-([4-(*E*)-3-hydroxyprop-1-enyl]-2,6-dimethoxyphenyl)oxy)propane-1,3-diol; **2**). Colorless powder. UV (MeOH): 220 (4.30), 270 (3.99). $[\alpha]_{\text{D}}^{21} = -24$ ($c=0.21$, CHCl_3). CD (MeOH): -0.86 (234). IR (KBr): 3427, 2918, 2848, 1659, 1583, 1504, 1456, 1421, 1335, 1242, 1155, 1124, 1013, 824, 1640. ^1H - and ^{13}C -NMR: see *Table 2*. ESI-MS: 445.1 (100, $\text{C}_{21}\text{H}_{26}\text{KO}_8^+$), 429.3 (62, $\text{C}_{21}\text{H}_{26}\text{NaO}_8^+$).

Wikstroemone (= (2*R*)-3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-([4-(*E*)-3-hydroxyprop-1-enyl]-2,6-dimethoxyphenyl)oxy)propan-1-one; **3**). Colorless powder. UV (MeOH): 205 (4.42), 223 (4.36), 272 (4.11), 306 (3.90). $[\alpha]_{\text{D}}^{21} = +5$ ($c=0.20$, CHCl_3). IR (KBr): 3439, 2919, 2848, 1672, 1587, 1506, 1464, 1421, 1336, 1281, 1223, 1124, 1034, 633. ^1H - and ^{13}C -NMR: see *Table 1*. ESI-MS (pos.): 443.1 (42, $[M+K]^+$), 427.2 (100, $[M+Na]^+$). ESI-MS (neg.): 403.3 (100, $[M-H]^-$). HR-ESI-MS: 427.1385 ($[M+Na]^+$, $\text{C}_{21}\text{H}_{24}\text{NaO}_8^+$; calc. 427.1369).

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Received July 30, 2005