Neolignans from the Leaves of *Casearia sylvestris* SWARTZ

by **Wei Wang**[a]), **Zulfiqar Ali**[a]), **Xing-Cong Li**[a]), and **Ikhlas A. Khan***[a])[b])

[a]) National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, University of Mississippi, MS 38677, USA (phone: 1-662-915-7821; fax: 1-662-915-7989; e-mail: ikhan@olemiss.edu)

[b]) Department of Pharmacognosy, School of Pharmacy, University of Mississippi, MS 38677, USA

Six new neolignans, casearialignans A–F (**1**–**6**, resp.) and one known lignan syringaresinol-β-D-glucoside were isolated from the leaves of *Casearia sylvestris*. Their structures were determined on the basis of 1D- and 2D-NMR, and HR-ESI-MS analyses. The relative and absolute configurations were determined by the value of the coupling constants and CD spectral analysis, respectively.

1. Introduction. – *Casearia sylvestris* SWARTZ (Flacourtiaceae) is a Brazilian and Paraguayan folk medicinal plant called as '*Guaçatonga*' or '*Chá de Bugre*', and used to treat snakebite, trauma, ulceration, obesity, and cough [1–5]. A number of clerodane diterpenes were reported from the leaves of *C. sylvestris*, some of which possess antitumoral, trypanocidal, and DNA-modifying bioactivities [6–12]. Our continued investigation of this species to look for new chemotaxonomic markers has led to the isolation of six new neolignans, casearialignans A–F (**1**–**6**, resp.; *Fig. 1*) and one known lignan glycoside syringaresinol-β-D-glucoside [13]. Here, we report the isolation and structure elucidation of the new compounds. Their structures were determined on the basis of 1D- and 2D-NMR, and HR-ESI-MS analyses. The relative and absolute configurations were determined by the value of the coupling constants and CD spectral analysis, respectively.

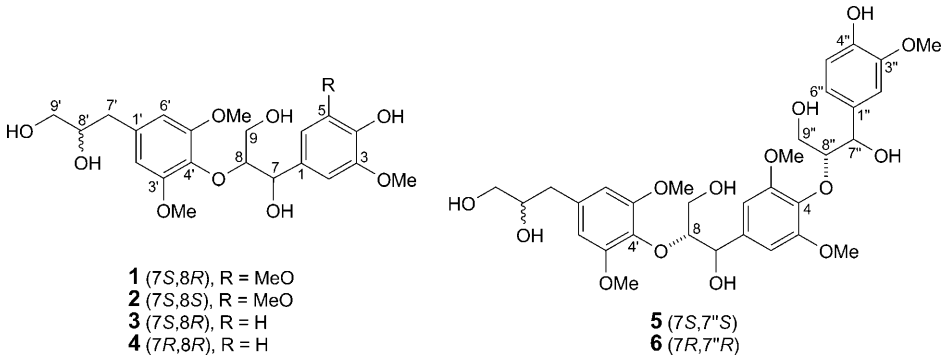

Fig. 1. *Structures of* **1**–**6**[1])

[1]) Arbitrary numbering. For systematic names, see *Exper. Part*.

2. Results and Discussion. – The AcOEt-soluble portion of the MeOH extract of the powdered leaves of *C. sylvestris* was fractionated by repeated column chromatography on silica gel. Compounds **1**–**6** and syringaresinol-β-D-glucoside were obtained from one of the above fractions by preparative reversed-phase HPLC at different retention times.

Casearialignan A (**1**) was obtained as a colorless gum with an $[\alpha]_D^{20}$ of -15.1 ($c = 0.09$, MeOH). The molecular formula of **1** was determined as $C_{22}H_{30}O_{10}$ by HR-ESI-MS (positive-ion mode, m/z 477.1739, $[M+Na]^+$ (calc. for $C_{22}H_{30}NaO_{10}^+$: 477.1737)). The ^{1}H-NMR spectrum (*Table 1*) displayed resonances for two 1,3,4,5-tetrasubstituted Ph groups at δ(H) 7.21 (*s*, H–C(2), H–C(6)[1])) and δ(H) 6.85 (*s*, H–C(2′), H–C(6′)), four MeO groups at δ(H) 3.71 (*s*, MeO–C(3), MeO–C(5)) and at δ(H) 3.76 (*s*, MeO–C(3′), MeO–C(5′)), as well as a propane-1,2,3-triol moiety (δ(H) 5.70 (*d*, $J = 4.5$, H–C(7)), 4.84 (br. *d*, $J = 3.5$, H–C(8)), 4.17 (*dd*, $J = 12.0, 3.5$, 1 H of CH_2(9)), and 4.60 (*dd*, $J = 12.0, 4.5$, 1 H of CH_2(9))), and a propane-1,2-diol moiety (δ(H) 3.04 (*dd*, $J = 14.0, 7.5$, 1 H of CH_2(7′)), 3.19 (*dd*, $J = 13.5, 4.5$, 1 H of CH_2(7′)), 4.40 (br. *s*, H–C(8′)), and 4.05 (br. *d*, $J = 5.0$, CH_2(9′))) confirmed by the ^{1}H,^{1}H-COSY correlations (*Fig. 2*) between H–C(8) and H–C(7) and CH_2(9), and between H–C(8′) and CH_2(7′) and CH_2(9′). The ^{13}C-NMR showed the corresponding resonances (*Table 2*). The presence of a 3,4,5-trisubstituted phenylglyceryl unit and a 3′,4′,5′-trisubstituted phenylpropanediol unit were confirmed by the HMBCs (*Fig. 2*) of H–C(7) to C(1), C(2), C(6), C(8), and C(9) and CH_2(7′) to C(1′), C(2′), C(6′), C(8′), and C(9′). The four MeO groups were assigned at C(3), C(5), C(3′), and C(5′), respectively, by their corresponding HMBCs (*Fig. 2*). An HMBC of H–C(8) to C(4′) established the connectivity of the two units and **1** should thus have the constitution of 4,7,9,8′,9′-pentahydroxy-3,5,3′,5′-tetramethoxy-8-*O*-4′-neolignan. The relative configuration at C(7) and C(8) was determined to be *erythro* due to a small coupling constant between H–C(7) and H–C(8) ($J(7,8) = 4.5$) [14][15]. The absolute configuration of C(7) and C(8) was identified as (7*S*,8*R*) by the CD spectroscopic evidence that an obvious negative *Cotton* effect appeared at about 246 nm in the CD spectrum (*Fig. 3*) [15]. The absolute configuration of C(8′) remains to be determined. Therefore, **1** was characterized as (−)-(7*S*,8*R*)-4,7,9,8′,9′-pentahydroxy-3,5,3′,5′-tetramethoxy-8-*O*-4′-neolignan.

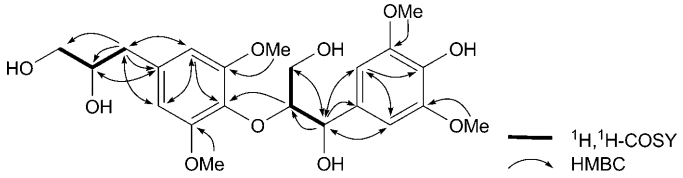

Fig. 2. *Key ^{1}H,^{1}H-COSY and HMBC correlations of* **1**

Casearialignan B (**2**) was isolated as a colorless amorphous powder with an $[\alpha]_D^{20}$ of $+2.3$ ($c = 0.08$, MeOH). The HR-ESI-MS analysis (positive-ion mode; $m/z = 477.1746$, $[M+Na]^+$ (calc. for $C_{22}H_{30}NaO_{10}^+$: 477.1737)) led to the same molecular formula $C_{22}H_{30}O_{10}$ as that of **1**. When the ^{1}H-NMR data (*Table 1*) of **2** were compared with those of **1**, the main difference was the value of $J(7,8) = 6.5$ Hz, which was larger than

Table 1. *^{1}H-NMR Data of* **1**–**6**[l]). In (D_5)pyridine; δ in ppm, J in Hz.

	1[a])	**2**[a])	**3**[b])	**4**[b])	**5**[a])	**6**[a])
H–C(2)	7.21 (*s*)	7.30 (*s*)	7.53 (*s*)	7.59 (*s*)	7.18 (*s*)	7.18 (*s*)
H–C(5)	–	–	7.27 (*d*, *J* = 8.0)	7.28 (*d*, *J* = 8.0)	–	–
H–C(6)	7.21 (*s*)	7.30 (*s*)	7.32 (*d*, *J* = 8.0)	7.48 (*d*, *J* = 8.0)	7.18 (*s*)	7.18 (*s*)
H–C(7)	5.70 (*d*, *J* = 4.5)	5.75 (*d*, *J* = 6.5)	5.72 (*d*, *J* = 4.4)	5.79 (*d*, *J* = 6.8)	5.67 (*d*, *J* = 4.5)	5.67 (*d*, *J* = 10.0)
H–C(8)	4.84 (br. *d*, *J* = 3.5)	4.58–4.61 (*m*)	4.82 (br. *d*, *J* = 3.6)	4.57–4.59 (*m*)	4.84 (br. *d*, *J* = 3.5)	4.84–4.86 (*m*)
CH_2(9)	4.17 (*dd*, *J* = 12.0, 3.5), 4.60 (*dd*, *J* = 12.0, 4.5)	3.93 (*dd*, *J* = 12.0, 3.5), 4.35–4.37 (*m*)	4.17 (br. *d*, *J* = 12.0), 4.60 (*dd*, *J* = 12.0, 4.8)	3.91 (br. *d*, *J* = 12.4), 4.34–4.37 (*m*)	4.16 (*dd*, *J* = 12.0, 3.5), 4.57 (*dd*, *J* = 12.0, 4.5)	4.17 (br. *d*, *J* = 11.5), 4.59 (*dd*, *J* = 10.5, 5.5)
H–C(2′)	6.85 (*s*)	6.83 (*s*)	6.85 (*s*)	6.85 (*s*)	6.83 (*s*)	6.82 (*s*)
H–C(6′)	6.85 (*s*)	6.83 (*s*)	6.85 (*s*)	6.85 (*s*)	6.83 (*s*)	6.82 (*s*)
CH_2(7′)	3.04 (*dd*, *J* = 14.0, 7.5), 3.19 (*dd*, *J* = 13.5, 4.5)	3.04 (*dd*, *J* = 14.0, 7.5), 3.18 (*dd*, *J* = 13.5, 4.5)	3.04 (*dd*, *J* = 14.0, 8.0), 3.20 (*dd*, *J* = 13.6, 4.8)	3.04 (*dd*, *J* = 14.0, 8.0), 3.22 (*dd*, *J* = 13.6, 4.8)	3.03 (*dd*, *J* = 14.0, 8.0), 3.18 (*dd*, *J* = 13.5, 4.5)	3.03 (*dd*, *J* = 14.0, 8.0), 3.17 (*dd*, *J* = 13.5, 4.5)
H–C(8′)	4.40 (br. *s*)	4.36–4.38 (*m*)	4.41 (br. *s*)	4.41 (br. *s*)	4.37 (br. *s*)	4.37 (br. *s*)
CH_2(9′)	4.05 (br. *d*, *J* = 5.0)	4.03 (br. *d*, *J* = 5.0)	4.06 (br. *d*, *J* = 4.8)	4.07 (br. *d*, *J* = 4.8)	4.03 (br. *d*, *J* = 5.0)	4.02 (br. *d*, *J* = 10.0)
H–C(2″)					7.52 (*s*)	7.52 (*s*)
H–C(5″)					7.24 (*d*, *J* = 8.0)	7.24 (*d*, *J* = 8.0)
H–C(6″)					7.30 (*d*, *J* = 8.0)	7.31 (*d*, *J* = 8.0)
H–C(7″)					5.68 (*d*, *J* = 4.5)	5.69 (*d*, *J* = 10.0)
H–C(8″)					4.76 (br. *d*, *J* = 3.5)	4.76–4.78 (*m*)
CH_2(9″)					4.12 (*dd*, *J* = 12.0, 3.5), 4.54 (*dd*, *J* = 12.0, 4.5)	4.12 (br. *d*, *J* = 11.5), 4.55 (*dd*, *J* = 10.5, 5.5)
MeO–C(3)	3.71 (*s*)	3.70 (*s*)	3.72 (*s*)	3.72 (*s*)	3.70 (*s*)	3.69 (*s*)
MeO–C(5)	3.71 (*s*)	3.70 (*s*)			3.70 (*s*)	3.69 (*s*)
MeO–C(3′)	3.76 (*s*)	3.75 (*s*)	3.68 (*s*)	3.70 (*s*)	3.69 (*s*)	3.68 (*s*)
MeO–C(5′)	3.76 (*s*)	3.75 (*s*)	3.68 (*s*)	3.70 (*s*)	3.69 (*s*)	3.68 (*s*)
MeO–C(3″)					3.72 (*s*)	3.71 (*s*)

[a]) Measured at 500 MHz. [b]) Measured at 400 MHz.

Table 2. *^{13}C-NMR and DEPT Data of* **1**–**6**[1]). In (D_5)pyridine; δ in ppm.

	1[a])	**2**[a])	**3**[b])	**4**[b])	**5**[a])	**6**[a])
1	133.2 (*s*)	133.2 (*s*)	135.0 (*s*)	135.1 (*s*)	135.2 (*s*)	135.2 (*s*)
2	105.3 (*d*)	105.7 (*d*)	112.2 (*d*)	112.3 (*d*)	105.1 (*d*)	105.1 (*d*)
3	149.9 (*s*)	149.2 (*s*)	149.0 (*s*)	148.7 (*s*)	153.3 (*s*)	153.3 (*s*)
4	136.4 (*s*)	136.7 (*s*)	147.8 (*s*)	147.7 (*s*)	135.7 (*s*)	135.7 (*s*)
5	149.9 (*s*)	149.2 (*s*)	116.6 (*d*)	116.4 (*d*)	153.3 (*s*)	153.3 (*s*)
6	105.3 (*d*)	105.7 (*d*)	121.0 (*d*)	121.2 (*d*)	105.1 (*d*)	105.1 (*d*)
7	73.6 (*d*)	73.7 (*d*)	74.1 (*d*)	74.1 (*d*)	73.3 (*d*)	73.3 (*d*)
8	87.6 (*d*)	89.2 (*d*)	88.4 (*d*)	89.9 (*d*)	87.6 (*d*)	87.6 (*d*)
9	61.0 (*t*)	61.4 (*t*)	61.8 (*t*)	61.9 (*t*)	61.0 (*t*)	60.9 (*t*)
1′	136.2 (*s*)	136.3 (*s*)	137.0 (*s*)	137.0 (*s*)	136.2 (*s*)	136.2 (*s*)
2′, 6′	107.5 (*d*)	107.4 (*d*)	108.3 (*d*)	107.8 (*d*)	107.5 (*d*)	107.5 (*d*)
3′, 5′	153.3 (*s*)	153.4 (*s*)	154.2 (*s*)	153.7 (*s*)	153.3 (*s*)	153.3 (*s*)
4′	134.7 (*s*)	134.8 (*s*)	135.5 (*s*)	134.9 (*s*)	134.7 (*s*)	134.7 (*s*)
7′	41.1 (*t*)	41.2 (*t*)	41.9 (*t*)	41.7 (*t*)	41.1 (*t*)	41.1 (*t*)
8′	73.7 (*d*)	73.8 (*d*)	74.5 (*d*)	74.2 (*d*)	73.6 (*d*)	73.6 (*d*)
9′	66.6 (*t*)	66.7 (*t*)	67.4 (*t*)	67.2 (*t*)	66.6 (*t*)	66.7 (*t*)
1″					133.6 (*s*)	133.6 (*s*)
2″					111.5 (*d*)	111.5 (*d*)
3″					148.5 (*s*)	148.5 (*s*)
4″					147.0 (*s*)	147.0 (*s*)
5″					115.8 (*d*)	115.8 (*d*)
6″					120.2 (*d*)	120.2 (*d*)
7″					73.4 (*d*)	73.4 (*d*)
8″					87.2 (*d*)	87.2 (*d*)
9″					60.9 (*t*)	60.9 (*t*)
MeO–C(3)	55.9 (*q*)	55.9 (*q*)	56.4 (*q*)	56.1 (*q*)	55.9 (*q*)	55.9 (*q*)
MeO–C(5)	55.9 (*q*)	55.9 (*q*)			55.9 (*q*)	55.9 (*q*)
MeO–C(3′,5′)	56.1 (*q*)	56.1 (*q*)	56.7 (*q*)	56.4 (*q*)	55.9 (*q*)	55.9 (*q*)
MeO–C(3″)					55.7 (*q*)	55.7 (*q*)

[a]) Measured at 125 MHz. [b]) Measured at 100 MHz.

that of **1** (4.5 Hz), suggesting a relative *threo* configuration for C(7) and C(8)[1]) [15]. Furthermore, in the ^{13}C-NMR data (*Table 2*) of **2**, $\Delta\delta$(C(8)/C(7)) (15.5 ppm) is larger than that of **1** (14.0 ppm), supporting a *threo*-configuration [14]. Therefore, **2** was determined to be a *threo* stereoisomer of **1**. Furthermore, the CD spectra (*Fig. 3*) showed an obvious positive *Cotton* effect at about 237 nm similar to that of (7*S*,8*S*)-*threo*-7,9,9′-trihydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-4-*O*-β-D-glucopyranoside [15], indicating that **2** had the (7*S*,8*S*)-configuration. Based on the above evidence, **2** was assigned as (+)-(7*S*,8*S*)-4,7,9,8′,9′-pentahydroxy-3,5,3′,5′-tetramethoxy-8-*O*-4′-neolignan.

Casearialignan C (**3**) was obtained as a colorless gum with an $[\alpha]_D^{20}$ of +46.6 (c = 0.13, MeOH). The HR-ESI-MS (positive-ion mode, m/z 447.1637, $[M+Na]^+$ (calc. for $C_{21}H_{28}NaO_9^+$: 447.1631)) established the molecular formula as $C_{21}H_{28}O_9$. Comparing the ^{1}H-NMR data with those of **1**, the major difference was the presence of 1,3,4-trisubstituted Ph group resonances (δ(H) 7.53 (*s*, H–C(2)[1])), 7.27 (*d*, J = 8.0, H–C(5))

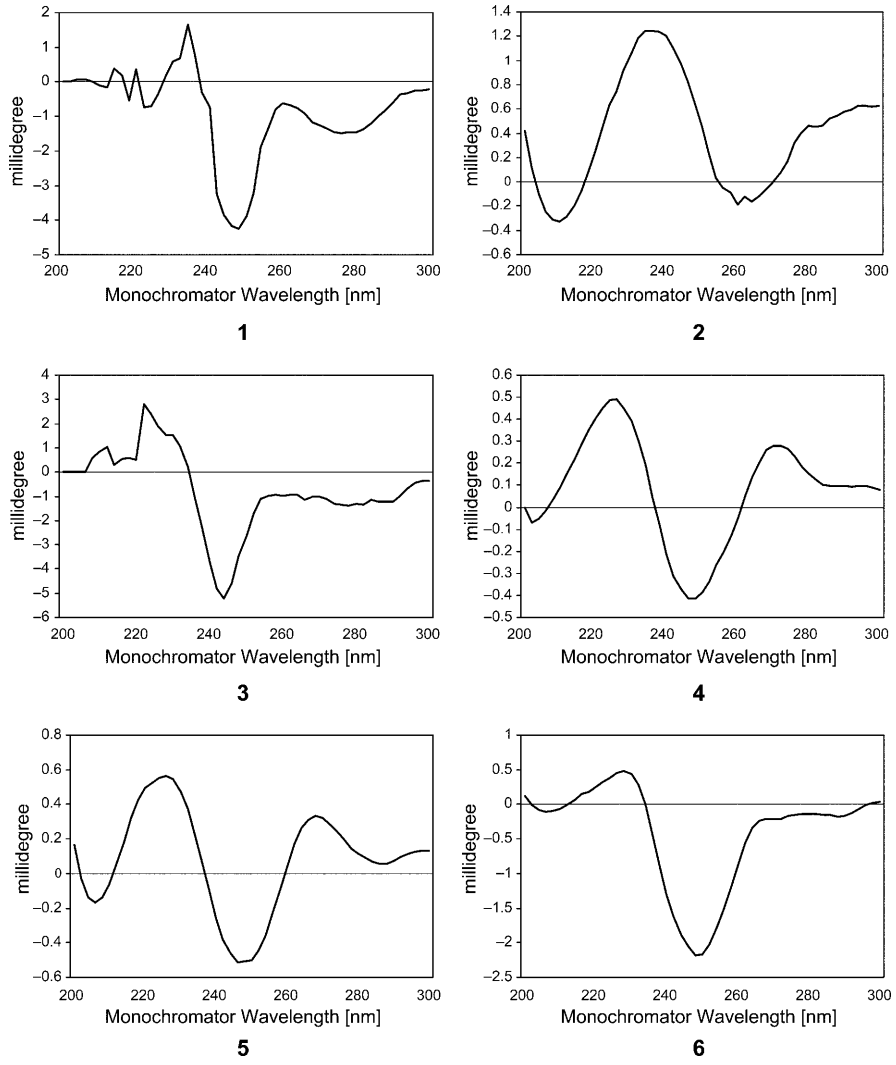

Fig. 3. *CD Spectra of* **1**–**6**

and 7.32 (*d*, $J = 8.0$, H–C(6))) instead of the former 1,3,4,5-tetrasubstituted Ph group. In a HMBC experiment of **3**, C(3) was correlated by a MeO group and H–C(2) and H–C(5) indicating the MeO group being located at C(3). The J(7,8) value of 4.4 Hz confirmed a relative *erythro* configuration, as in **1**. The absolute configuration of C(7) and C(8) was established as (7*S*,8*R*) according to the negative *Cotton* effect at 244 nm found in the CD spectrum (*Fig. 3*) [14][15]. Thus, **3** was characterized as (+)-(7*S*,8*R*)-4,7,9,8′,9′-pentahydroxy-3,3′,5′-trimethoxy-8-*O*-4′-neolignan.

Casearialignan D (**4**) was obtained as a colorless gum with an $[\alpha]_D^{20}$ of -35.6 ($c = 0.07$, MeOH). The molecular formula, $C_{21}H_{28}O_9$, was determined by positive-ion mode

HR-ESI-MS with an signal at *m/z* 447.1642 ($[M+Na]^+$; calc. for $C_{21}H_{28}NaO_9^+$: 447.1631). The NMR and MS data of **4** were similar to those of **3**, except for a larger *J*(7,8) value (6.8 Hz), suggesting **4** is a relative *threo* stereoisomer of **3** [14][15]. The (7*R*,8*R*)-configuration[1]) was determined by a negative *Cotton* effect at 246 nm in the CD spectrum (*Fig. 3*) [15]. Hence **4** was assigned as (−)-(7*R*,8*R*)-4,7,9,8′,9′-pentahydroxy-3,3′,5′-trimethoxy-8-*O*-4′-neolignan.

Casearialignan E (**5**) was obtained as a colorless gum with an $[\alpha]_D^{20}$ of +10.8 (*c* = 0.09, MeOH). The molecular formula was determined as $C_{32}H_{42}O_{14}$ by HR-ESI-MS analysis (positive-ion mode, *m/z* 673.2481, $[M+Na]^+$, calc. for $C_{32}H_{42}NaO_{14}^+$: 673.2472). The ^{1}H- and ^{13}C-NMR spectroscopic data of **5** (*Tables 1* and *2*) were found close to those of **1** except for additional resonances of a 3,4,5-trisubstituted phenylglyceryl unit which was further confirmed by ^{1}H,^{1}H-COSY, HMQC, and HMBC experiments. So **5** should be a 8-*O*-4′ type trimeric lignan[1]). The ^{1}H-NMR data showed the values of *J*(7,8) and *J*(7″,8″) as 4.5 Hz each, indicating the relative *erythro* form at C(7)−C(8) and C(7″)−C(8″). The absolute configuration was assigned as (7*S*,8*R*,7″*S*,8″*R*) on the basis of a negative *Cotton* effect at 246 nm found in the CD spectrum (*Fig. 3*). Based on the above data, the structure of **5** was elucidated as (+)-(7*S*,8*R*,7″*S*,8″*R*)-7,9,8′,9′,4″,7″,9″-heptahydroxy-3,5,3′,5′,3″-pentamethoxy-8-*O*-4′,8″-*O*-4-neolignan.

Casearialignan D (**6**), was obtained as a colorless gum with an $[\alpha]_D^{20}$ of −2.3 (*c* = 0.08, MeOH), and has the molecular formula $C_{32}H_{42}O_{14}$ as calculated from the HR-ESI-MS (positive-ion mode, *m/z* 673.2476, $[M+Na]^+$; calc. 673.2472). The ^{1}H- and ^{13}C-NMR spectra (*Tables 1* and *2*) were identical with those of **5**, the only difference were the *J*(7,8) and *J*(7″,8″) values of 10.0 Hz each, which is larger than those of **5** 4.5 Hz each, indicating that **6** possessed a relative *threo* configuration. The absolute configuration (7*R*,8*R*,7″*R*,8″*R*)[1]) of **6** was determined by the negative *Cotton* effect at 247 nm in the CD spectrum (*Fig. 3*). Therefore, **6** was a diastereoisomer of **5** and its structure was identified as (−)-(7*R*,8*R*,7″*R*,8″*R*)-7,9,8′,9′,4″,7″,9″-heptahydroxy-3,5,3′,5′,3″-pentamethoxy-8-*O*-4′,8″-*O*-4-neolignan.

Compounds **1**–**6** possessed a 3-(3,5-dimethoxyphenyl)propane-1,2-diol structural moiety. To the best of our knowledge, this is the first time to report the 8-*O*-4′ type neolignans with such a structure moiety. Therefore, this type of 8-*O*-4′ neolignans might be considered as chemotaxonomic marker of the title plant.

We are grateful to Mr. *Frank Wiggers* for NMR assistance and Dr. *Bharathi Avula* for conducting HR-ESI-MS. This work is supported by the *United States Department of Agriculture Specific Cooperative Research Agreement* Number 58-6408-6-067 and the *FDA/CFSAN* grant entitled '*Science Based Authentication of Dietary Supplements*' Number 2 U01 FD 002071-07.

Experimental Part

General. Column chromatography (CC): silica gel *H* (SiO_2; 200–300 mesh; *Merck*, D-Darmstadt). TLC: silica gel *GF254* plates; visualization under UV light and by spraying with vanillin/H_2SO_4, followed by heating. HPLC: *Waters LC II* system; *Phenomenex Gemini C18* 5 μ *ODS* column (10 × 250 mm) for semi-prep. and a mobile phase consisting of MeOH/H_2O. Optical rotation: *Rudolph Research AutoPol IV* polarimeter; in MeOH. UV Spectra: *Hewlett-Packard 8453* UV/VIS spectrometer; in MeOH soln.; λ_{max} (log ε) in nm. CD Spectra: *Olis DSM 20 CD* spectrophotometer; in MeOH. IR Spectra: *Bruker Tensor 27* FT-IR and *MIRacle ATRFT-IR* spectrometers; in cm^{-1}. NMR Spectra: *Bruker AM-500* (^{1}H 500 MHz, ^{13}C

125 MHz) spectrometer; and *American Varian Mercury plus 400* (^{1}H 400 MHz, ^{13}C 100 MHz) NMR spectrometers; in (D_5)pyridine with Me_4Si as internal standard; δ in ppm and J in Hz. HR-ESI-MS: *Agilent Series 1100 SL* mass spectrometer; in m/z.

Plant Material. The leaves of *Casearia sylvestris* SWARTZ were purchased from *Raintree Nutrition Inc* (Carson City, NV 89701, USA), and were identified by TLC and HPLC analyses with the authenticated sample offered by Dr. *Rainer W. Bussmann* (Missouri Botanical garden). Voucher specimens (#3247) were deposited with the *National Center for Natural Products Research*, *Research Institute of Pharmaceutical Sciences*, University of Mississippi, USA.

Extraction and Isolation. The dried and powdered plant material of *C. sylvestris* (3 kg) was extracted by percolation with MeOH (4 × 4 l). The pooled MeOH solns. were evaporated *in vacuo* to give a residue (342 g). The MeOH extracts were partitioned between H_2O and petroleum ether (PE), and then between H_2O and AcOEt. The AcOEt layer afforded a waxy extract residue (207 g), which was further separated into nine fractions (*Frs. 1–9*) by SiO_2 CC (2500 g, 120 × 8 cm) with gradient elution of PE/AcOEt (3:1, 1:1, 1:4, 1:10) and AcOEt/MeOH (8:1, 4:1, 1:1, 1:2, 1:5). *Fr. 6* was subjected to SiO_2 CC (80 g, 60 × 6 cm) using AcOEt to yield 13 subfractions (*Subfrs. 1–13*). *Subfr. 3* (56.3 mg) was chromatographed by prep. HPLC over a *Phenomenex Gemini C18* 5 µ *ODS* column (10 × 250 mm, flow rate 6.0 ml/min) with MeOH/H_2O (15:85) as mobile phase to yield **1** (2.8 mg), **3** (3.4 mg), **2** (2.3 mg), **4** (2.2 mg), **5** (2.8 mg) , **6** (2.6 mg), and syringaresinol-β-D-glucoside (8.2 mg) at t_R 11.2, 12.4, 17.6, 18.5, 35.1, 37.1, and 40.2 min, resp.

Casearialignan A (*=(−)-(7S,8R)-4,7,9,8′,9′-Pentahydroxy-3,5,3′,5′-tetramethoxy-8-O-4′-neolignan = 3-(4-{[(1S,2R)-1,3-Dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)propane-1,2-diol*; **1**). Colorless gum. $[\alpha]_D^{20} = -15.1$ ($c = 0.09$, MeOH). UV (MeOH): 231 (3.39), 280 (2.89). CD (MeOH): −4.22 (246). IR (KBr): 3328, 2932, 2856, 1592, 1510, 1460, 1424, 1327, 1226, 1122, 1029. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 477.1739 ($[M+Na]^+$, $C_{22}H_{30}NaO_{10}^+$; calc. 477.1737).

Casearialignan B (*=(+)-(7S,8S)-4,7,9,8′,9′-Pentahydroxy-3,5,3′,5′-tetramethoxy-8-O-4′-neolignan = 3-(4-{[(1S,2S)-1,3-Dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)propane-1,2-diol*; **2**). Colorless amorphous powder. $[\alpha]_D^{20} = +2.3$ ($c = 0.08$, MeOH). UV (MeOH): 229 (3.20), 279 (2.77). CD (MeOH): +1.68 (237). IR (KBr): 3426, 2929, 2853, 1593, 1512, 1459, 1423, 1330, 1225, 1124, 1027. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 477.1746 ($[M+Na]^+$, $C_{22}H_{30}NaO_{10}^+$; calc. 477.1737).

Casearialignan C (*=(+)-(7S,8R)-4,7,9,8′,9′-Pentahydroxy-3,3′,5′-trimethoxy-8-O-4′-neolignan = 3-(4-{[(1S,2R)-1,3-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)propane-1,2-diol*; **3**). Colorless gum. $[\alpha]_D^{20} = +46.6$ ($c = 0.13$, MeOH). UV (MeOH): 231 (3.42), 278 (3.04). CD (MeOH): −5.01 (244). IR (KBr): 3405, 2931, 2854, 1654, 1565, 1508, 1462, 1419, 1234, 1124, 1028. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 447.1637 ($[M+Na]^+$, $C_{21}H_{28}NaO_9^+$; calc. 447.1631).

Casearialignan D (*=(−)-(7R,8R)-4,7,9,8′,9′-Pentahydroxy-3,3′,5′-trimethoxy-8-O-4′-neolignan = 3-(4-{[(1R,2R)-1,3-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)-propane-1,2-diol*; **4**). Colorless gum. $[\alpha]_D^{20} = -35.6$ ($c = 0.07$, MeOH). UV (MeOH): 231 (3.37), 279 (2.98). CD (MeOH): −4.45 (246). IR (KBr): 3407, 2933, 2860, 1593, 1507, 1462, 1421, 1332, 1278, 1225, 1127, 1033. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 447.1642 ($[M+Na]^+$, $C_{21}H_{28}NaO_9^+$; calc. 447.1631).

Casearialignan E (*=(+)-(7S,8R,7″S,8″R)-7,9,8′,9′,4″,7″,9″-Heptahydroxy-3,5,3′,5′,3″-pentamethoxy-8-O-4′,8″-O-4-neolignan = 3-(4-{[(1S,2R)-1-(4-{[(1S,2R)-1,3-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)-1,3-dihydroxypropan-2-yl]oxy}-3,5-dimethoxyphenyl)propane-1,2-diol*; **5**). Colorless gum. $[\alpha]_D^{20} = +10.8$ ($c = 0.09$, MeOH). UV (MeOH): 230 (3.54), 278 (3.08). CD (MeOH): −0.51 (246). IR (KBr): 3422, 2930, 2867, 1596, 1509, 1462, 1422, 1332, 1226, 1127, 1029. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 673.2481 ($[M+Na]^+$, $C_{32}H_{42}NaO_{14}^+$; calc. 673.2472).

Casearialignan F (*=(−)-(7R,8R,7″R,8″R)-7,9,8′,9′,4″,7″,9″-Heptahydroxy-3,5,3′,5′,3″-pentamethoxy-8-O-4′,8″-O-4-neolignan = 3-(4-{[(1R,2R)-1-(4-{[(1R,2R)-1,3-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yl]oxy}-3,5-dimethoxyphenyl)-1,3-dihydroxypropan-2-yl]oxy}-3,5-dimethoxyphenyl)pro-

pane-1,2-diol; **6**). Colorless gum. $[\alpha]_D^{20} = -2.3$ ($c = 0.08$, MeOH). UV (MeOH): 231 (3.50), 279 (3.12). CD (MeOH): −2.70 (247). IR (KBr): 3413, 2928, 2849, 1592, 1505, 1461, 1421, 1329, 1234, 1127, 1027. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS (pos.): 673.2476 ($[M+Na]^+$, $C_{32}H_{42}NaO_{14}^+$; calc. 673.2472).

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