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Lignans from *Taiwania cryptomerioides*

Wang-Hong Lin, Jim-Min Fang*, Yu-Shia Cheng

Department of Chemistry, National Taiwan University, Taipei, Taiwan, 106 Republic of China

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Abstract

In addition to eleven known lignans, eight new compounds including 8-hydroxypluviatolide, 5,8-dihydroxypluviatolide, two benzofuran-type neolignans, three lignans bearing oxy substituents at the C-2 positions and a γ-piperonylmethyl-γ-butenolide were isolated from the leaves of *Taiwania cryptomerioides* Hayata. Their structures were determined by spectroscopic methods.

Keywords: Taiwania cryptomerioides; Taxodiaceae; Leaves; Lignans

1. Introduction

Taiwania cryptomerioides is an endemic evergreen species with thick linear-triangular leaves and elongated ovoid cones (Li & Keng, 1994). There are several studies on the chemical constituents of *T. cryptomerioides* (Kamil, Ilyas, Rahman, Hasaka, Okigawa et al., 1981; Kuo, Chen & Lin, 1987; Fang & Cheng, 1992; Lin, Fang & Cheng, 1995, 1996, 1997, 1998; He, Zeng, Shi, Zhao, Kozlowski et al., 1997). We recently found a number of new diterpenoids and steroids (Lin et al., 1995, 1996, 1997, 1998), including the sterols with uncommon 6–5–6–5 fused rings and the cycloadducts of diterpenoid quinones. As a continuation of this study, we herein report the isolation and structural determination of lignans **1**–**19**.

2. Results and discussion

The chloroform extract of the leaves were subjected to column chromatography and HPLC to give compounds **1**–**7**, **9**, **11**, **13** and **15**–**17**. The portion of high polarity was subjected to peracetylation, and the products were separated by HPLC to give compounds **8**, **10**, **12**, **14a**, **18** and **19**. By comparison of the physical and spectroscopic properties (mp, $[\alpha]_D$, IR, MS, ^{1}H and ^{13}C NMR spectra), the known compounds were identified as matairesinol **1** (Corrie, Green, Ritchie & Taylor, 1970; Fang, Wei & Cheng, 1985), nortrachelogenin **2** (Nishibe, Hisada & Inagaki, 1971; Khamlach, Dhal & Brown, 1989), pluviatolide **3** (Corrie et al., 1970), 7-hydroxyhinokinin **6** (Fang, Lee & Cheng, 1992), savinin **9** (Fang et al., 1992; Schrecker & Hartwell, 1954), 3,3′-dimethoxy-9,9′-epoxy-4,4′,7-trihydroxylignan **11** (Hanuman, Mishra & Sabata, 1986; Bardón, Montanaro, Catalán, Diaz & Herz, 1993), secoisolariciresinol tetraacetate **12** (Powell & Plattner, 1976; Fonseca, Campello, Barata & Rúveda, 1978), diphyllin (taiwanin H) **13** (Anjaneyulu, Ramaiah, Row, Venkateswarlu, Pelter et al., 1981; Kuo, Lin & Lin, 1985), dihydrodehydrodiconiferyl alcohol triacetate **14a** (Fang et al., 1992; Li, Iliefski, Lundquist & Wallis, 1997), 3-methoxy-3′,4,9,9′-tetrahydroxy[8-*O*-4′]neolignan **17** (Fang et al., 1992), and 1-(4-hydroxy-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2-methoxyphenoxy]propane-1,3-diol tetraacetates **18** (*erythro* isomer) and **19** (*threo* isomer) (Lundgren, Shen & Theander, 1985). The structures of new compounds were determined as follows, whereas their absolute configurations were not rigorously assigned.

Compound **4** showed a molecular ion at *m*/*z* 372.1208 consistent with the molecular formula $C_{20}H_{20}O_7$. The IR absorptions at 3458 and 1759 cm^{-1} were attributable to hydroxyl groups and the γ-lactone moiety, respectively. By comparison of the ^{1}H and ^{13}C spectra with those of pluviatolide **3** ($C_{20}H_{20}O_6$), the

* Corresponding author.

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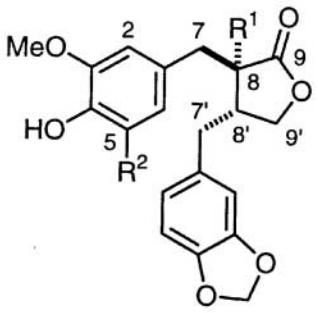
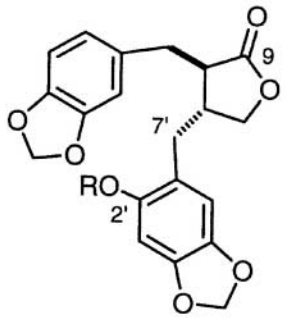
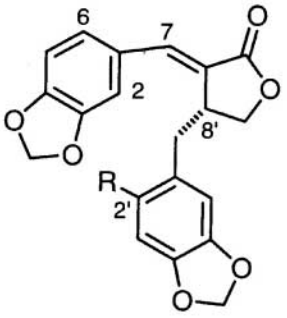


3 $R^1 = R^2 = H$
4 $R^1 = OH, R^2 = H$
5 $R^1 = R^2 = OH$



7 R = H
8 R = Glu(Ac)$_4$



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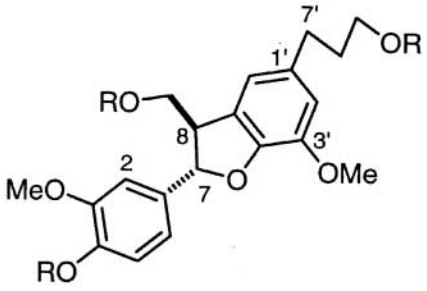
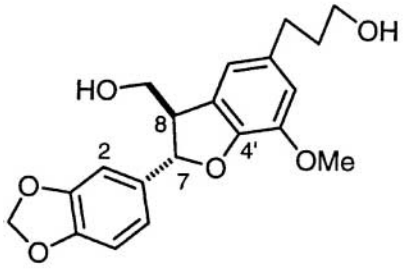
10 R = OGlu(Ac)$_4$



14 R = H
14a R = Ac



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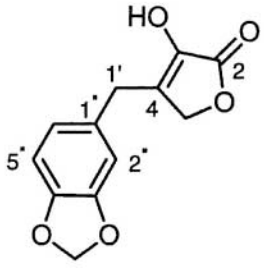

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structure of **4** was determined as 8-hydroxypluviatolide. The C-7 and C-8 of **4** occurred at lower fields of δ 41.6 and 76.5 by comparison with the corresponding carbons of **3** (at δ 34.5 and 46.5). Other carbons of **3** and **4** exhibited similar chemical shifts.

Compound **5** was readily assigned as 5,8-dihydroxypluviatolide by analyses of its mass, IR, ^{1}H and ^{13}C NMR spectra. The two aromatic protons H-2 (at δ 6.28) and H-6 (at δ 6.30) displayed as two doublets with a small coupling constant of 1.8 Hz in agreement with their *meta* orientation.

The structure of **7** was determined as 2′-hydroxyhinokinin according to its spectral properties. The exact mass measurement of molecular ion at m/z 370.1061 was in agreement with a molecular formula $C_{20}H_{18}O_7$. The IR absorptions at 3400 and 1741 cm^{-1} were attributable to the hydroxyl group and γ-lactone moieties. The ^{1}H NMR spectrum showed five aromatic protons at δ 6.34 (*s*, H-3′), 6.36 (*s*, H-6′), 6.57 (*br d*, J = 8.0 Hz, H-6), 6.60 (*br s*, H-2) and 6.66 (*d*, J = 8.0 Hz, H-5). The ^{13}C NMR spectrum showed the characteristic resonances of a lactone at δ_C 179.6 and

71.7. Two dioxymethylene carbons showed resonances at δ 101.0 and 100.9. The signals of two phenyl rings appeared in the region of δ 110–150, except that C-3′ occurred at a relatively high field of δ 98.1 presumably due to the electron-donating effect of two adjacent oxygen atoms. The signal at δ 148.4 was assigned to C-2′ as it showed correlations with H-3′ (at δ 6.34), H-6′ (at δ 6.36) and H-7′ (at δ 2.44–2.64) in the HMBC spectrum.

Compound **8** is the glucopyranoside derivative of **7**. The carbon resonances at δ 99.7, 72.3, 71.9, 70.9, 68.0 and 61.7 were typical to a moiety of glucose. The proton resonances for the glucose moiety occurred at δ 3.75 (*m*, H-5″), 4.05 (*m*, H-6″), 4.22 (*dd*, J = 12.3, 5.7 Hz, H-6″), 4.86 (*d*, J = 9.3 Hz, H-1″), 5.10 (*t*, J = 9.3 Hz, H-4″), 5.17 (*t*, J = 9.3 Hz, H-2″) and 5.23 (*t*, J = 9.3 Hz, H-3″). All the protons on the pyranoside ring should orient axially as indicated by the large coupling constants of $J_{1'',2''}$, $J_{2'',3''}$ and $J_{3'',4''}$. The NOESY spectrum showed the correlation of H-1″ with H-3″ and H-5″ consistent with this deduction. The structure of **8** was thus determined as 2′-hydroxyhinokinin 2′-*O*-(2,3,4,6-*O*-tetraacetyl)-β-glucopyranoside. This assignment was supported by the HMBC spectrum, which showed correlations of C-9 (at δ 178.5) with H-9′ (at δ 3.80 and 4.05) and H-7 (at δ 4.27), as well as correlations of C-2′ (at δ 148.9) with H-7′ (at δ 2.45) and H-1″ (at δ 4.86).

By comparison of the spectral properties of **10** with those of **8** and savinin (**9**), the structure of **10** was determined to be 2′-hydroxysavinin 2′-*O*-(2,3,4,6-*O*-tetraacetyl)-β-glucopyranoside. The exact mass of molecular ion occurred at m/z 698.1854 was in agreement with the molecular formula $C_{34}H_{34}O_{16}$. The glucose moiety showed carbon resonances at δ 101.3, 72.6, 71.9, 70.9, 67.8 and 61.5, as well as proton resonances at δ 3.70 (*m*, H-5″), 4.05 (*m*, H-6″), 4.99 (*d*, J = 9.0 Hz, H-1″), 5.18 (*t*, J = 9.0 Hz, H-4″), 5.23 (*t*, J = 9.0 Hz, H-3″) and 5.39 (*t*, J = 9.0 Hz, H-2″) similar to those of **8**. The (*E*)-configuration of the double bond between C-7 and C-8 was inferred from the correlation of H-6 (at δ 6.89) with H-7 (at δ 7.35), and the correlation of H-2 (at δ 7.08) with H-8′ (at δ 3.80) in the NOESY spectrum. The HMBC spectrum also showed the correlation of C-7′ (at δ 33.4) with H-9′ (at δ 4.05), the correlation of C-8′ (at δ 37.8) with H-7′ (at δ 7.35), as well as the correlations of C-2′ (at δ 149.6) with H-7′ (at δ 2.49 and 2.86) and H-1″ (at δ 4.99).

Compound **14a**, $[M]^+$ at m/z 486, was inferred to be the triacetate of dihydrodehydrodiconiferyl alcohol **14** from its ^1H and ^{13}C NMR spectra. Saponification of **14a** gave a product identical with **14** (Fang et al., 1992). The structure of **14a** was thus confirmed. The coupling constant of 7 Hz between H-7 and H-8 of **14a** was in agreement with their *trans* relationship (Fang et al., 1992; Li et al., 1997). The ^1H NMR spectrum of **15** was similar to that of **14**, except that **15** showed a signal at δ 5.96 (s) for the dioxymethylene group instead of the 3-methoxy group in **14**. The structure of **15**, $[M]^+$ at m/z 358, was thus determined as 9,9′-dihydroxy-3,4-methylenedioxy-3′-methoxy[7-*O*-4′, 8-5′]neolignan. Compound **15** was considered to have the *trans* configuration as it exhibited a coupling constant $J_{7,8}$ = 5.6 Hz, close to the value of 6.4 Hz in **14** (Li et al., 1997). The characteristic resonances of H-7 and H-8, showing at δ 5.55 and 3.45, were also consistent with the neolignans of *trans*-dihydrobenzofuran type (Li et al., 1997).

The molecular formula $C_{12}H_{10}O_5$ of **16** was deduced by the exact mass measurement of molecular ion at m/z 234.0528. The IR absorption at 3340 cm^{-1} was attributable to a hydroxyl group. The IR absorption at 1749 cm^{-1} and UV absorption at λ_{max} 284 nm were attributable to a moiety of α,β-unsaturated-γ-lactone. The corresponding carbon resonances occurred at δ 69.3 (C-5), 130.6 (C-3), 136.8 (C-4) and 170.9 (C-2). The presence of a piperonyl group was indicated by the proton resonances appearing at δ 5.92 (*s*, OCH_2O), 6.62 (*dd*, J = 8, 1 Hz), 6.66 (*d*, J = 1 Hz) and 6.72 (*d*, J = 8 Hz). The structure of **16** was thus determined to be 3-hydroxy-4-piperonylmethyl-5*H*-furan-2-one. The HMBC spectrum indicated the correlations of C-1′ (at δ 30.6) with H-2″ (at δ 6.66) and H-6″ (at δ 6.62), the correlation of H-1′ (at δ 3.61) with C-3 (at δ 130.6) and C-5 (at δ 69.3), as well as the correlations of H-5 (at δ 4.55) with C-2 (at δ 170.9) and C-3.

3. Experimental

3.1. General

Yanagimoto (or MP-500D) micro melting point apparatus; Jasco Dip-180 digital polarimeter, Finnigan TSQ-46c mass spectrometer; Perkin–Elmer 983G infrared spectrophotometer; Bruker AM-300 WB nuclear magnetic resonance spectrometer; ^1H NMR: 300 MHz; ^{13}C NMR: 75 MHz; Waters M-45 with Hibar Lichrosorb Si 60 column (10 μm or 7 μm, 25 cm×1 cm i.d.) were used for HPLC. Merck silica gel 60F sheets were used for TLC.

3.2. Plant material

The dried leaves (1.75 kg) of *T. cryptomerioides* were exhaustively extracted with acetone (7 l×3). The combined extracts were concd to *ca* 0.8 l, and taken up with $CHCl_3$ (0.8 l×3). The $CHCl_3$-soluble portion was concd (55 g) and subjected to silica-gel CC. The portion obtained from elution of 10–30% EtOAc in CH_2Cl_2 was further separated by HPLC with the elution of 10–40% EtOAc in hexane to give com-

pounds **1** (18 mg), **2** (17 mg), **3** (18 mg), **4** (16 mg), **5** (12 mg), **6** (18 mg), **7** (19 mg), **9** (19 mg), **11** (17 mg), **13** (8 mg), **15** (6 mg), **16** (8 mg) and **17** (9 mg). The portion of higher polarity obtained from eluent of EtOAc/CH_2Cl_2 (1:1) was subjected to peracetylation (Ac_2O, pyridine) and the products were separated by HPLC with the elution of 20–45% EtOAc in hexane to give compounds **8** (88 mg), **10** (72 mg), **12** (22 mg), **14a** (6 mg), **18** (12 mg) and **19** (11 mg).

3.3. Matairesinol (*1*)

Solid, mp 116–118°, $[\alpha]_D^{25}$ −45° ($CHCl_3$; *c* 0.9) {(lit. Fang et al., 1985) mp 117–119°, $[\alpha]_D^{25}$ −42.8° (Me_2CO)}.

3.4. Nortrachelogenin (*2*)

Gum, $[\alpha]_D^{25}$ −14° ($CHCl_3$; *c* 1.1) {(lit. Khamlach et al., 1989) $[\alpha]_D^{17}$ −16.8° (EtOH)}. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.6 (C-7′), 42.1 (C-7), 43.9 (C-8′), 55.9 (OMe×2), 70.1 (C-9′), 76.4 (C-8), 111.4 (C-2′), 112.6 (C-2), 114.3 (C-5′), 114.5 (C-5), 121.4 (C-6′), 123.1 (C-6), 126.0 (C-1), 130.2 (C-1′), 144.3 (C-4′), 145.0 (C-3), 146.5 (2 C, C-3′, C-4), 178.4 (C-9).

3.5. Pluviatolide (*3*)

Solid, mp 156–158°, $[\alpha]_D^{25}$ −29.3° ($CHCl_3$; *c* 1.6) {(lit. Corrie et al., 1970) mp 160°, $[\alpha]_D$ −35.5° ($CHCl_3$)}. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 34.5 (C-7′), 38.2 (C-7), 40.9 (C-8′), 46.5 (C-8), 55.8 (3-OMe), 71.1 (C-9′), 100.9 (OCH_2O), 108.2 (C-5′), 108.7 (C-2′), 111.5 (C-2), 114.2 (C-5), 121.5 (C-6), 122.0 (C-6′), 129.4 (C-1), 131.6 (C-1′), 144.5 (C-4), 146.2 (C-4′), 146.6 (C-3), 147.8 (C-3′), 178.6 (C-9).

3.6. 8-Hydroxypluviatolide (*4*)

$[\alpha]_D^{25}$ −32.1° ($CHCl_3$; *c* 0.6). TLC (25% EtOAc in hexane) R_f 0.15. IR ν_{max} (KBr) cm^{-1}: 3458, 1759. UV λ_{max} (MeOH) nm (ϵ): 285 (9238), 232 (17 500). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.48 (*m*, H-7′, 8′), 2.62 (*s*, OH), 2.88 (*m*, H-7′), 2.90 (*d*, *J* = 13.6 Hz, H-7), 3.06 (*d*, *J* = 13.6 Hz, H-7), 3.83 (*s*, OMe), 3.97 (2 H, *m*, H-9′), 5.63 (*s*, OH), 5.91 (*s*, OCH_2O), 6.56 (*dd*, *J* = 8.2 Hz, H-6′), 6.59 (*d*, *J* = 2 Hz, H-2′), 6.60 (*d*, *J* = 2 Hz, H-2), 6.70 (*dd*, *J* = 8, 2 Hz, H-6), 6.71 (*d*, *J* = 8 Hz, H-5′), 6.83 (*d*, *J* = 8 Hz, H-5). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 31.5 (C-7′), 41.6 (C-7), 43.5 (C-8′), 55.8 (OMe), 70.3 (C-9′), 76.5 (C-8), 100.9 (OCH_2O), 108.3 (C-5′), 109.1 (C-2′), 112.9 (C-2), 114.6 (C-5), 121.7 (C-6′), 123.0 (C-6), 126.3 (C-1), 132.3 (C-1′), 144.8 (C-4), 146.1 (C-4′), 146.6 (C-3), 147.7 (C-3′), 178.8 (C-9). EIMS (70 eV) *m*/*z* (rel. int.): 372 [M]$^+$ (15), 137 (100), 122 (9), 77 (10). HRMS for $C_{20}H_{20}O_7$ requires 372.1209; found 372.1208.

3.7. 5,8-Dihydroxypluviatolide (*5*)

$[\alpha]_D^{25}$ −37° ($CHCl_3$; *c* 0.9). TLC (40% EtOAC in hexane) R_f 0.25. IR ν_{max} (KBr) cm^{-1}: 3434, 1751. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.52 (*m*, H-7′, 8′), 2.64 (*s*, OH), 2.85 (*d*, *J* = 13.7 Hz, H-7), 2.94 (*m*, H-7′), 3.02 (*d*, *J* = 13.7 Hz, H-7), 3.80 (*s*, OMe), 3.92 (2 H, *m*, H-9′), 5.90 (*s*, OCH_2O), 5.95 (2 H, *s*, OH), 6.28 (*d*, *J* = 1.8 Hz, H-2), 6.30 (*d*, *J* = 1.8 Hz, H-6), 6.56 (*dd*, *J* = 8.0, 1.2 Hz, H-6′), 6.59 (*d*, *J* = 1.2 Hz, H-2′), 6.70 (*d*, *J* = 8.0 Hz, H-5′). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.6 (C-7′), 42.2 (C-7), 43.8 (C-8′), 56.2 (OMe), 70.1 (C-9′), 76.4 (C-8), 100.9 (OCH_2O), 105.1 (C-2), 108.4 (C-5′), 109.2(C-2′), 110.7 (C-6), 121.8 (C-6′), 125.8 (C-1), 131.8 (C-4), 132.1 (C-1′), 143.8 (C-5), 146.2 (C-4′), 147.0 (C-3), 147.8 (C-3′), 178.5 (C-9). EIMS (70 eV) *m*/*z* (rel. int.): 388 [M]$^+$ (12), 153 (100), 136 (22), 131 (1), 122 (1), 105 (1).

3.8. 7-Hydroxyhinokinin (*6*)

Solid, mp 125–126°, $[\alpha]_D^{29}$ −43° ($CHCl_3$; *c* 1.1) {(lit. Fang et al., 1992) mp 124.5–125°, $[\alpha]_D^{25}$ −43° ($CHCl_3$, *c* 2.1)}.

3.9. 2′-Hydroxyhinokinin (*7*)

Solid, mp 110–112°, $[\alpha]_D^{25}$ −20.2° ($CHCl_3$; *c* 1.6). TLC (25% EtOAC in hexane) R_f 0.18. UV λ_{max} (MeOH) nm (ϵ): 293 (10 100), 234 (11 300). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.44–2.64 (4 H, *m*, H-7′, H-8, H-8′), 2.82 (*dd*, *J* = 14.1, 5.8 Hz, H-7), 2.91 (*dd*, *J* = 14.1, 4.4 Hz, H-7), 3.90 (*t*, *J* = 7.9 Hz, H-9′), 4.10 (*t*, *J* = 7.9 Hz, H-9′), 5.83 (*s*, OCH_2O), 5.87 (*s*, OCH_2O), 6.08 (*s*, OH), 6.34 (*s*, H-3′), 6.36 (*s*, H-6′), 6.57 (*br d*, *J* = 8.0 Hz, H-6), 6.60 (*br s*, H-2), 6.66 (*d*, *J* = 8.0 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 32.5 (C-7′), 34.5 (C-7), 39.9 (C-8′), 46.6 (C-8), 71.7 (C-9′), 98.1 (C-3′), 100.9 (OCH_2O), 101.0 (OCH_2O), 108.1 (C-5), 109.7 (2 C, C-2, C-6′), 116.1 (C-1′), 122.5 (C-6), 131.4 (C-1), 141.0 (C-4′), 146.3 (C-4), 146.6 (C-5′), 147.6 (C-3), 148.4 (C-2′), 179.6 (C-9). EIMS (70 eV): *m*/*z* (rel. int.) 370 [M]$^+$ (40), 219 (45), 201 (5), 189 (8), 176 (12), 152 (100), 135 (56). HRMS for $C_{20}H_{18}O_7$ requires 370.1052; found 370.1061.

3.10. 2′-Hydroxyhinokinin 2′-O-(2,3,4,6-O-tetraacetyl)-β-glucopyranoside (*8*)

Solid, mp 172–173°, $[\alpha]_D^{23}$ −28.5° ($CHCl_3$; *c* 7.5). TLC (35% EtOAC in hexane) R_f 0.14. IR ν_{max} (KBr) cm^{-1}: 1758. UV λ_{max} (MeOH) nm (ϵ): 291 (14 900), 234 (26 600). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.96 (*s*,

Ac), 1.97 (*s*, Ac), 1.98 (*s*, Ac), 2.02 (*s*, Ac), 2.42–2.50 (4 H, *m*, H-7′, H-8, H-8′), 2.77 (2 H, *br s*, H-7), 3.70–3.80 (2 H, *m*, H-5″, H-9′), 4.05 (2 H, *m*, H-6″, H-9′), 4.22 (*dd*, $J = 12.3$, 5.7 Hz, H-6″), 4.86 (*d*, $J = 9.3$ Hz, H-1″), 5.17 (*t*, $J = 9.3$ Hz, H-2″), 5.10 (*t*, $J = 9.3$ Hz, H-4″), 5.23 (*t*, $J = 9.3$ Hz, H-3″), 5.85–5.87 (4 H, *m*, two OCH_2O), 6.38 (*s*, H-6′), 6.51 (*dd*, $J = 8.0$, 1.2 Hz, H-6), 6.54 (*s*, H-3′), 6.56 (*d*, $J = 1.2$ Hz, H-2), 6.64 (*d*, $J = 8.0$ Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.4 (2 C, Ac), 20.5 (2 C, Ac), 32.8 (C-7′), 34.4 (C-7), 39.4 (C-8′), 46.6 (C-8), 61.7 (C-6″), 68.0 (C-4″), 70.9 (C-2″), 71.0 (C-9′), 71.9 (C-5″), 72.3 (C-3″), 98.4 (C-3′), 99.7 (C-1″), 100.3 (OCH_2O), 100.7 (OCH_2O), 108.1 (C-5), 109.4 (2 C, C-2, C-6′), 120.2 (C-1′), 122.2 (C-6), 131.2 (C-1), 143.0 (C-4′), 146.1 (C-5′), 146.7 (C-4), 147.4 (C-3), 148.9 (C-2′), 169.0 (Ac), 169.2 (Ac), 169.9 (Ac), 170.3 (Ac), 178.5 (C-9). EIMS (70 eV) *m/z* (rel. int.): 700 $[M]^+$ (0.2), 331 (25), 211 (5), 164 (100), 145 (10), 127 (15), 109 (65). HRMS for $C_{34}H_{34}O_{16}$ requires 700.2003; found 700.2000.

3.11. Savinin (**9**)

Solid, mp 146–147°, $[\alpha]_D^{29}$ −25° (Me_2CO, 2.8){(lit. Schrecker & Hartwell, 1954) mp 146–147°, $[\alpha]_D^{22}$ −88° ($CHCl_3$; *c* 1.00)}.

3.12. 2′-Hydroxysavinin 2′-O-(2,3,4,6-O-tetraacetyl)-β-glucopyranoside (**10**)

Solid, mp 99–101°, $[\alpha]_D^{23}$ +7.2° ($CHCl_3$; *c* 5.8). TLC (35% EtOAC in hexane) R_f 0.12. IR ν_{max} (KBr) cm^{-1}: 1754, 1647. UV λ_{max} (MeOH) nm (ϵ): 334 (18 300), 296 (17 400), 236 (19 800). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.83 (*s*, 2 Ac), 1.99 (*s*, 2 Ac), 2.49 (*dd*, $J = 13.7$, 9.1 Hz, H-7′), 2.86 (*dd*, $J = 13.7$, 6.9 Hz, H-7′), 3.70 (*m*, H-5″), 3.80 (*m*, H-8′), 4.02–4.10 (3 H, *m*, H-6″, H-9′), 4.99 (*d*, $J = 9.0$ Hz, H-1″), 5.18 (*t*, $J = 9.0$ Hz, H-4″), 5.23 (*t*, $J = 9.0$ Hz, H-3″), 5.39 (*t*, $J = 9.0$ Hz, H-2″), 5.75 (*d*, $J = 1.2$ Hz, OCH_2O), 5.81 (*d*, $J = 1.2$ Hz, OCH_2O), 5.96 (*d*, $J = 1.2$ Hz, OCH_2O), 6.07 (*d*, $J = 1.2$ Hz, OCH_2O), 6.41 (*s*, H-6′), 6.48 (*s*, H-3′), 6.72 (*d*, $J = 7.0$ Hz, H-5), 6.89 (*dd*, $J = 7.0$, 1.0 Hz, H-6), 7.08 (*d*, $J = 1.0$ Hz, H-2), 7.35 (*s*, H-7). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.1 (Ac), 20.4 (Ac), 20.5 (Ac), 20.8 (Ac), 33.4 (C-7′), 37.8 (C-8′), 61.5 (C-6″), 67.8 (C-4″), 69.6 (C-9′), 70.9 (C-2″), 71.9 (C-5″), 72.6 (C-3″), 99.8 (C-3′), 101.3 (2 C, C-1′, OCH_2O), 101.5 (OCH_2O), 107.8 (C-2), 108.3 (C-5), 110.4 (C-6′), 121.3 (C-1′), 125.7 (C-8), 126.8 (C-6), 128.1 (C-1), 137.2 (C-7), 143.3 (C-4′), 146.9 (C-5′), 147.7 (C-3), 148.8 (C-4), 149.6 (C-2′), 169.0 (Ac), 169.3 (Ac), 169.9 (Ac), 170.2 (Ac), 172.6 (C-9). EIMS (70 eV) *m/z* (rel. int.): 698 $[M]^+$ (0.3), 368 (5), 331 (25), 169 (100), 151 (35), 127 (15), 109 (65). HRMS for $C_{34}H_{34}O_{16}$ requires 698.1846; found 698.1854.

3.13. 3,3′-Dimethoxy-9,9′-epoxy-4,4′,7-trihydroxylignan (**11**)

Solid, mp 162–164°, $[\alpha]_D^{25}$ −32° ($CHCl_3$; *c* 1.6) {(lit. Hanuman et al., 1986; Bardón et al., 1993) mp 168°, $[\alpha]_D^{22}$ −30° (Me_2CO; *c* 0.50)}.

3.14. Secoisolariciresinol tetraacetate (**12**)

Gum, $[\alpha]_D^{23}$ −7.1° ($CHCl_3$; *c* 2.1) {(lit. Powell & Plattner, 1976) $[\alpha]_D^{26}$ −7.6° ($CHCl_3$; *c* 1.0)}.

3.15. Diphyllin (**13**)

Solid, mp 286–288° {(lit. Anjaneyulu et al., 1981) mp 291°}.

3.16. Dihydrodehydrodiconiferyl alcohol triacetate (**14a**)

Gum, $[\alpha]_D^{26}$ −6° ($CHCl_3$; *c* 1.0). TLC (10% EtOAC in CH_2Cl_2) R_f 0.4. IR ν_{max} (neat) cm^{-1}: 1760, 1735, 1600, 1496. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.90 (2 H, *tt*, $J = 7$, 6.5 Hz, H-8′), 1.97 (*s*, Ac), 1.99 (*s*, Ac), 2.22 (*s*, Ac), 2.57 (2 H, *t*, $J = 7$ Hz, H-7′), 3.72 (*ddd*, $J = 8$, 7, 5 Hz, H-8), 3.74 (*s*, OMe), 3.82 (*s*, OMe), 4.02 (2 H, *t*, $J = 6.5$ Hz, H-9′), 4.22 (*dd*, $J = 11$, 8 Hz, H-9), 4.38 (*dd*, $J = 11$, 5 Hz, H-9), 5.45 (*d*, $J = 7$ Hz, H-7), 6.58 (*d*, $J = 2$ Hz, H-6′), 6.60 (*d*, $J = 2$ Hz, H-2′), 6.88 (*dd*, $J = 8.5$, 2 Hz, H-6), 6.93 (*d*, $J = 8.5$ Hz, H-5), 6.95 (*d*, $J = 2$ Hz, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.3 (Ac), 20.5 (Ac), 20.7 (Ac), 30.3 (C-8′), 31.7 (C-7′), 50.5 (C-8), 55.6 (OMe), 55.8 (OMe), 63.5 (C-9′), 65.2 (C-9), 87.4 (C-7), 109.8 (C-2), 112.5 (C-6′), 116.0 (C-2′), 118.0 (C-6), 122.6 (C-5), 126.8 (C-1′), 134.9 (C-3′), 139.3 (C-4), 139.5 (C-1), 143.9 (C-5′), 145.9 (C-4′), 151.0 (C-3), 168.7 (Ac), 170.5 (Ac), 170.9 (Ac). EIMS (70 eV) *m/z* (rel. int.): 486 $[M]^+$ (65), 426 (35), 348 (100), 369 (15), 341 (8), 324 (5), 43 (27).

3.17. 9,9′-Dihydroxy-3,4-methylenedioxy-3′-methoxy[7-O-4′, 8-5′]neolignan (**15**)

$[\alpha]_D^{25}$ −12° (MeOH; *c* 1.1). TLC (40% EtOAC in hexane) R_f 0.25. IR ν_{max} (KBr) cm^{-1}: 3374. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.78 (2 H, *m*, H-8′), 2.60 (2 H, *t*, $J = 8.0$ Hz, H-7′), 3.45 (*m*, H-8), 3.55 (2 H, *t*, $J = 8.0$ Hz, H-9′), 3.78 (*m*, H-9), 3.82 (*s*, OMe), 3.88 (*m*, H-9), 5.55 (*d*, $J = 5.8$ Hz, H-7), 5.96 (*s*, OCH_2O), 6.72 (2 H, *s*, H-2′, H-6′), 6.80 (*d*, $J = 8.4$ Hz, H-5), 6.89 (*br s*, H-2), 6.90 (*br d*, $J = 8.4$ Hz, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 32.5 (C-7′), 35.7 (C-8′), 55.2 (C-8), 56.2 (OMe), 61.6 (C-9′), 64.8 (C-9), 87.6 (C-7), 101.8 (OCH_2O), 106.7 (C-2), 108.7 (C-5), 113.7 (C-2′), 117.4 (C-6′), 119.7 (C-6), 129.3 (C-1′), 136.3 (C-5′), 137.4 (C-1), 144.7 (C-3′), 147.0 (C-4′), 147.9

(C-4), 148.6 (C-3). EIMS (70 eV) *m/z* (rel. int.): 358 $[M]^+$ (55), 340 (100), 328 (35), 310 (12), 295 (15), 281 (18), 215 (10).

3.18. 3-Hydroxy-4-piperonylmethyl-5H-furan-2-one (**16**)

Gum. TLC (25% EtOAC in hexane) R_f 0.25. IR ν_{max} (neat) cm^{-1}: 3340, 1749. UV λ_{max} (MeOH) nm (ϵ): 284 (3810), 231 (11 700). ^1H NMR ($CDCl_3$, 300 MHz): δ 3.61 (2 H, *s*), 4.55 (2 H, *s*, H-5), 5.92 (2 H, *s*, OCH_2O), 6.62 (1 H, *dd*, $J = 8.0$, 1.0 Hz), 6.66 (1 H, *d*, $J = 1.0$ Hz), 6.72 (1 H, *d*, $J = 8.0$ Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.6 (C-1′), 69.3 (C-5), 101.1 (OCH_2O), 108.5 (C-5″), 108.9 (C-2″), 121.4 (C-6″), 130.3 (C-1″), 130.6 (C-3), 136.8 (C-4), 146.6 (C-4″), 148.1 (C-3″), 170.9 (C-2). EIMS (70 eV) *m/z* (rel. int.): 234 $[M]^+$ (100), 216 (4), 189 (37), 158 (50), 135 (40), 131 (34), 122 (20). HRMS for $C_{12}H_{10}O_5$ requires 234.0528; found 234.0528.

3.19. 3-Methoxy-3′,4,9,9′-tetrahydroxy[8-O-4′]neolignan (**17**)

Gum, $[\alpha]_D^{26}$ +1.2° (MeOH, *c* 1.2) {(lit. Fang et al., 1992) $[\alpha]_D$ +0.11°}.

3.20. 1-(4-Hydroxy-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2-methoxyphenoxy]propane-1,3-diol tetraacetate (**18**) and (**19**) (Lundgren et al., 1985)

18 (*erythro* isomer): Gum. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.5 (Ac), 20.6 (Ac), 20.8 (2 Ac), 30.0 (C-2‴), 31.6 (C-1‴), 55.6 (OMe), 55.7 (OMe), 62.3 (C-3), 63.5 (C-3‴), 73.5 (C-1), 80.2 (C-2), 111.7 (C-2′), 112.5 (C-2″), 118.7 (C-5″), 119.4 (C-6′), 120.4 (C-6″), 122.4 (C-5′), 135.3 (C-1′), 136.6 (C-1″), 139.5 (C-4′), 145.1 (C-4″), 150.8 (C-3″), 150.8 (C-3′), 168.6 (Ac), 169.3 (Ac), 170.6 (Ac), 170.9 (Ac). **19** (*threo* isomer): Gum.^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.5 (Ac), 20.6 (Ac), 20.8 (Ac), 20.9 (Ac), 30.1 (C-2‴), 31.6 (C-1‴), 55.6 (OMe), 55.8 (OMe), 62.9 (C-3), 63.6 (C-3‴), 74.3 (C-1), 80.3 (C-2), 111.5 (C-2′), 112.5 (C-2″), 118.7 (C-5″), 119.4 (C-6′), 120.4 (C-6″), 122.5 (C-5′), 135.2 (C-1′), 136.3 (C-1″), 139.7 (C-4′), 145.9 (C-4″), 150.5 (C-3′), 150.9 (C-3″), 168.6 (Ac), 169.6 (Ac), 170.4 (Ac), 170.9 (Ac).

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