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Sesquineolignans and other constituents from the seeds of *Joannesia princeps*☆

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Abstract

From the methanolic extract of the seeds of the Brazilian *Joannesia princeps* 3,3′-bisdemethylpinoresinol and six new sesquineolignans were isolated besides the known neolignans americanol A, isoamericanol A and isoamericanin A which were found to be the major constituents. A method was developed to distinguish americanol- from isoamericanol-type compounds spectroscopically.

Keywords: *Joannesia princeps*; Euphorbiaceae; Sesquineolignans; (±)-3 ,3′-Bisdemethylpinoresinol; Americanol A; Isoamericanol A; Isoamericanin A; Princepin; Isoprincepin; Isoamericanols B; Isoamericanols C

1. Introduction

Joannesia princeps Vellozo (Euphorbiaceae) is a tree widespread in Brazil where it grows up to 50 m high. Its seeds are used as a purgative, mainly in veterinary practice (Mors and Rizzini, 1966). Earlier reports on the occurrence of biologically active alkaloids in the seeds (Freise, 1929) caused us to extend our phytochemical studies of the root bark of *J. princeps* (Achenbach and Benirschke, 1997) on this part of the plant also. These investigations resulted in the isolation of the known neolignans isoamericanin A (**1**), americanol A (**2**) and isoamericanol A (**3**), the hitherto unknown lignan (±) 3,3′-bisdemethylpinoresinol (**4**) and the new sesquineolignans **5**–**10** from the methanolic extract of the seeds. Alkaloids have not been found.

2. Results and discussion

A methanolic extract from defatted seeds of *J. princeps* was diluted with water and re-extracted with dichloromethane followed by ethyl acetate. The dichloromethane extract contained only one major constituent, which after chromatographic purification was identified as isoamericanin A (**1**), a prostaglandin I_2 inducer earlier isolated from *Phytolacca americana* (Hasegawa et al., 1987; Tanaka et al., 1987).

The ethyl acetate extract was separated by CC to yield the three major fractions EA-1 to EA-3, from which the least polar fraction EA-1 gave a mixture of compounds **2** and **3**. HPLC separated the two pure substances with almost identical spectroscopic properties, which resembled those reported for americanol A (**2**) and isoamericanol A (**3**) (Fukuyama et al., 1992). In agreement with earlier reports (Fukuyama et al., 1992; Antus et al., 1986) we were not able to assign the two isomeric structures undoubtfully by comparison of the available spectroscopic data. However, our further ^{1}H NMR studies demonstrated, that — when measured in CD_3OD — the spectra of **2** and **3** exhibited slight but characteristically different shifts for H-2′ and H-5′ (Table 1), which reflected the individual structures and which were found indicative for the distinction of americanol- and isoamericanol-type neolignans. Difference NOE experiments were used to assign the structures: for **2**, weak but significant long range NOE enhancements could be observed between H-2′ and H-8, and also between H-5′ and H-7. In contrast, in the same experiments with **3** NOEs were found between H-2′ and

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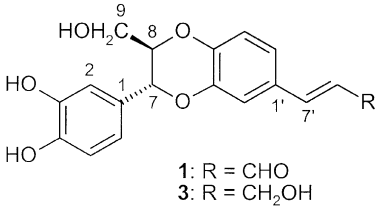
Table 1
^{1}H NMR spectral data of compounds **1**–**10** (δ in CD_3OD, *J*[Hz])

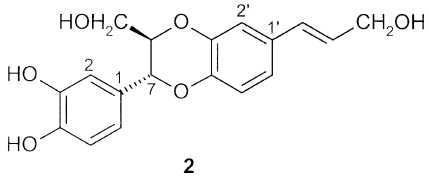
Proton	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
2	6.87 *d* 2.5	6.85 *d* 2.5	6.85 *d* 2.5	6.80 *d* 2.5	6.81 *d* 2.5	6.80 *d* 2.5	6.86 *d* 2.5	6.86 *d* 2.5	6.86 *d* 2.5	6.86 *d* 2.5
5	6.81 *d* 8.5	6.80 *d* 8.5	6.80 *d* 8.5	6.74 *d* 8.5	6.75 *d* 8.5	6.73 *d* 8.5	6.81 *d* 8.5	6.81 *d* 8.5	6.81 *d* 8.5	6.81 *d* 8.5
6	6.78 *dd* 8.5, 2.5	6.76 *dd* 8.5, 2.5	6.76 *dd* 8.5, 2.5	6.68 *dd* 8.5, 2.5	6.69 *dd* 8.5, 2.5	6.67 *dd* 8.5, 2.5	6.77 *dd* 8.5, 2.5	6.77 *dd* 8.5, 2.5	6.78 *dd* 8.5, 2.5	6.78 *dd* 8.5, 2.5
7	4.85 *d* 8	4.80 *d* 8	4.80 *d* 8	4.63 *m*	4.64 *m*	4.62 *m*	4.84 *d* 8	4.84 *d* 8	4.84 *d* 8	4.84 *d* 8
8	4.08 *ddd* 8, 4.5, 3	3.98 *ddd* 8, 5.5, 3	3.98 *ddd* 8, 5.5, 3	3.08 *m*	3.10 *m*	3.09 *m*	4.03 *ddd* 8, 5.5, 3	4.02[a] *ddd* 8, 5.5, 3	4.02[a] *ddd* 8, 5.5, 3	4.02[a] *ddd* 8, 5.5, 3
CH_2-9	3.50 *dd* 12.5, 4.5 3.71 *dd* 12.5, 3	3.48 *dd* 12.5, 5.5 3.67 *dd* 12.5, 3	3.47 *dd* 12.5, 5.5 3.66 *dd* 12.5, 3	3.80 *m* 4.20 *m*	3.82 *m* 4.20 *m*	3.81 *m* 4.20 *m*	3.49 *dd* 12.5, 5 3.69 *dd* 12.5, 3	3.49 *dd* 12.5, 5 3.69 *dd* 12.5, 3	3.49 *dd* 12.5, 5 3.69 *dd* 12.5, 3	3.49 *dd* 12.5, 5 3.68 *dd* 12.5, 3
2′	7.25 *d* 2.5	7.03 *d* 2.5	6.95 *d* 2.5	6.80 *d* 2.5	6.99 *m*	6.91 *d* 2.5	7.00 *d* 2.5	7.00 *d* 2.5	7.07 *m*	7.07 *m*
5′	7.03 *d* 8.5	6.83 *d* 8.5	6.88 *d* 8.5	6.74 *d* 8.5	6.87 *m*	6.93 *d* 8.5	7.01 *d* 8.5	7.01 *d* 8.5	6.95 *m*	6.95 *m*
6′	7.23 *dd* 8.5, 2.5	6.90 *dd* 8.5, 2.5	6.92 *dd* 8.5, 2.5	6.68 *dd* 8.5, 2.5	6.83 *m*	6.86 *dd* 8.5, 2.5	6.96 *dd* 8.5, 2.5	6.96 *dd* 8.5, 2.5	6.95 *m*	6.95 *m*
7′	7.57 *d* 16	6.50 *br d* 16	6.48 *br d* 16	4.63 *m*	4.71 *m*	4.69 *m*	4.89 *d* 8	4.90 *d* 8	4.92 *d* 8	4.91 *d* 8
8′	6.64 *dd* 16, 8	6.21 *dt* 16, 6	6.20 *dt* 16, 6	3.08*m*	3.10 *m*	3.09 *m*	4.03 *ddd* 8, 5.5, 3	4.03[a] *ddd* 8, 5.5, 3	4.03[a] *ddd* 8, 5.5, 3	4.03[a] *ddd* 8, 5.5, 3
CH_2-9′ (or H-9′)	9.58 *d* 8	4.19 *dd* 6, 1.5	4.18 *dd* 6, 1.5	3.80 *m* 4.20 *m*	3.82 *m* 4.23 *m*	3.81 *m* 4.22 *m*	3.49 *dd* 12.5, 5.5 3.70 *dd* 12.5, 3	3.49 *dd* 12.5, 5.5 3.70 *dd* 12.5, 3	3.50 *dd* 12.5, 5.5 3.71 *dd* 12.5, 3	3.50 *dd* 12.5, 5.5 3.71 *dd* 12.5, 3
2″					6.85 *m*	6.85 *d* 2.5	6.97 *d* 2.5	6.97 *d* 2.5	6.97 *d* 2.5	6.97 *d* 2.5
5″					6.80 *d* 8.5	6.81 *d* 8.5	6.89 *d* 8.5	6.89 *d* 8.5	6.90 *d* 8.5	6.90 *d* 8.5
6″					6.75 *dd* 8.5, 2.5	6.75 *dd* 8.5, 2.5	6.93 *dd* 8.5, 2.5	6.93 *dd* 8.5, 2.5	6.94 *dd* 8.5, 2.5	6.94 *dd* 8.5, 2.5
7″					4.80 *d* 8	4.80 *d* 8	6.49 *br d* 16	6.49 *br d* 16	6.50 *br d* 16	6.50 *br d* 16
8					3.99 *ddd* 8, 5, 3	3.98 *ddd* 8, 5, 3	6.20 *dt* 16, 6	6.20 *dt* 16, 6	6.21 *dt* 16, 6	6.21 *dt* 16, 6
CH_2-9″					3.48 *dd* 12.5, 5 3.68 *dd* 12.5, 3	3.47 *dd* 12.5, 5 3.66 *dd* 12.5, 3	4.18 *dd* 6, 1.5	4.18 *dd* 6, 1.5	4.19 *dd* 6, 1.5	4.19 *dd* 6, 1.5

[a] Similar values within a column might be interchanged.

H-7, and between H-5′ and H-8. HMBC spectra corroborated these assignments: using a concentrated sample and acquisition parameters optimized for small coupling constants (~3 Hz), a weak but distinct correlation between H-8 and C-3′ was observed for **2**, and a correlation between H-8 and C-4′ for **3**.



1: R = CHO
3: R = CH_2OH

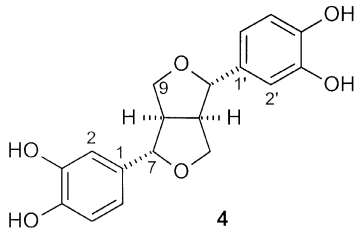


2

Based on these results the differences observed in the ^{1}H NMR spectra of americanol A (**2**) and isoamericanol A (**3**) in CD_3OD, particularly the chemical shift differences between H-2′ and H-5′, allow for an unambiguous identification of the two isomeric structures: in the spectrum of **2** a comparative large difference of 0.2 ppm is observed between the resonances of H-2′ and H-5′, whereas the respective difference in the spectrum of **3** is 0.07 ppm only.

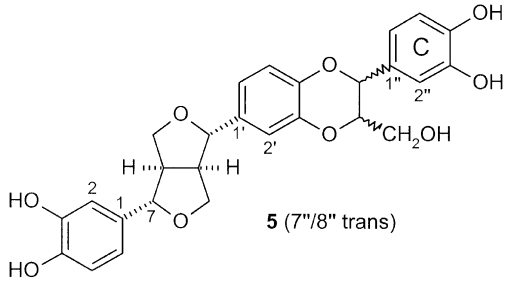
Till recently, the 1,4-benzodioxane-type neolignans **1**–**3** have been reported exclusively from seeds of *Phytolacca americana* (Hasegawa et al., 1987; Fukuyama et al., 1992). In 1998, the aldehyde **1** was also described as a constituent of *Trianthema turgidifolia* (Sarker et al., 1998). From these plants, as from *J. princeps*, compounds **1**–**3** have always been isolated as racemates. The claimed occurence of optical active americanin A, which represents the regioisomer of **1** and had earlier been reported from *Phytolacca americana* (Woo et al., 1978), was later revised (Antus et al., 1986).

Fraction EA-2 mainly contained the hitherto unknown (±) 3,3′-bisdemethylpinoresinol (**4**), whose structure was determined spectroscopically and also confirmed by the identity of its permethyl derivative with (±)-dimethylpinoresinol (Iida et al., 1982).

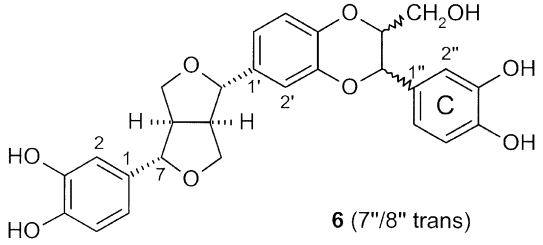


4

HPLC separation of fraction EA-3 yielded the sesquineolignans **5**–**10**. Whereas the ^{1}H and ^{13}C NMR of **5** and **6** were found related to that of **4**, the NMR of the four individual compounds **7**–**10** more resembled those of **2** and **3**. However, the spectra of **5**–**10** in comparison to **2**–**4** revealed the NMR signals of an additional condensed phenylpropane unit besides the two phenylpropanes of the basic structural moieties in **2** to **4**. DCI–MS established the corresponding molecular masses of compounds **5**–**10** in agreement with their origination from three C_6–C_3 units and also ascertained their isomeric character.



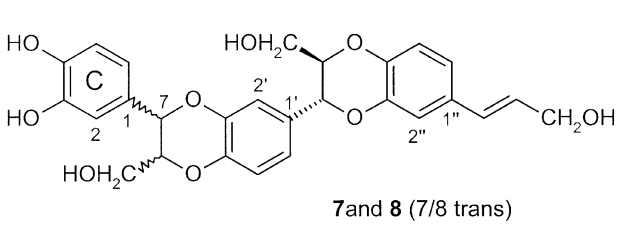
5 (7″/8″ trans)



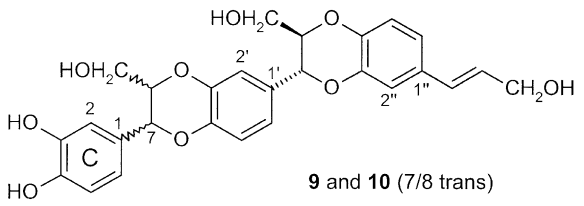
6 (7″/8″ trans)

Heteronuclear correlation spectroscopy identified compounds **5** and **6** as sesquineolignans generated by the formal condensation of 3,3′-bisdemethylpinoresinol (**4**) with an additional 3,4-dihydroxyphenyl-C_3 moiety. In the ^{1}H NMR of compound **5** (Table 1), the resonances of H-2′ and H-5′ were separated by 0.12 ppm, whereas in the spectrum of **6** a significantly smaller difference of only 0.02 ppm was measured for the doublets of H-5′ and H-2′. These results suggested an americanol-type structure for **5** with the furofuran substituent relatively close to the hydroxymethylene group and the aromatic ring C more distant, and an isoamericanol-type structure for **6** with the furofuran system closer to the aromatic ring C. The ^{13}C NMR data of **5** and **6** confirmed these structure proposals, which were finally corroborated by NOEs between H-7″ and H-5′ (for **5**) and between H-7″ and H-2′ (for **6**).

An identical relative stereochemistry of the furofuran ring systems as in **4** and the trans-configurations of the substituents at the steric centers C-7″ and C-8″ could be assigned to **5** as well as to **6** based on the complete agreement of all relevant ^{1}H and ^{13}C NMR data with those of compounds **2**–**4**. However, we were not able to establish the relative configurations between the two sets of steric centers namely between the furofuran- and the 1,4-benzodioxane-system, due to the large distance between the centers, which made NOE measurements impossible. Regarding this situation, it was of interest that some ^{13}C NMR signals in the spectra of **5** and **6**, particularly those of C-5′ and C-6′, appeared slightly 'splitted' (by about 0.02 ppm; peak intensities about 1:1), and thereby suggested the presence of a mixture of two very similar isomeric compounds, which most probably could be about the respective diastereomers of **5** and of **6** with reversed trans-stereochemistry at C-7″ and C-8″. However, all attempts to separate the supposed mixtures of furofuranylbenzodioxane-type diastereomers in **5** and **6** by HPLC were unsuccessful. On the other hand, the existence of diastereomers is strongly supported by the observation that the below described benzodioxane/benzodioxane-type sesquineolignans **7**–**10** also occur as pairs of diastereomers (**7**, **8** and **9**, **10)** which in contrast were separable chromatographically.



7and **8** (7/8 trans)



9 and **10** (7/8 trans)

The hitherto unknown furofuran/benzodioxane-type sesquineolignans were named princepin (**5**) and isoprincepin (**6**), respectively. Structurally related, partly insecticidal compounds have been reported as constituents of *Phryma leptostachya* (Taniguchi et al., 1989; Ishibashi and Taniguchi, 1998).

The almost identical spectroscopic properties (DCI-MS, ^{1}H NMR,^{13}C NMR) of the individual isomers **7**–**10** indicated very similar structures. Two dimensional NMR revealed linear condensation products from three phenylpropane units cyclically linked via two 1,4-benzodioxane systems. Applying the same methods as used above, compounds **7**–**10** were identified as diastereomeric pairs (**7**, **8** and **9**, **10**) of sesquineolignans originating from condensation of an additional caffeoyl alcohol to a basic isoamericanol A (**3**). From the diagnostic NMR shift differences of H-2′ and H-5′ (Table 1) the regio-positions of the dihydroxy-phenyl ring C and of the additional hydroxymethyl group were deduced. Analysis of the corresponding spin systems in the ^{1}H NMR established the trans-configuration of the substituents at C-7 and C-8, and also at C-7′ and C-8′.

All spectroscopic data of the individual compounds **7** and **8** as well as **9** and **10** are explained by a diastereomeric character within these pairs of regioisomers, which differ in the relative configurations between the stereochemical centers C-7/C-8 and C-7′/C-8′ only. However, as for **5** and **6**, we were not able to establish the relative configuration between the two sets of steric centers spectroscopically.

Following the nomenclature introduced by Woo et al. (1980) the new compounds were named isoamericanol B1 (**7**), isoamericanol B2 (**8**) isoamericanol Cl (**9**) and isoamericanol C2 (**10**). The structurally related sesquineolignan named americanin B—formally derived from isoamericanin A (**1**) and a further 3,4-dihydroxyphenylpropane unit—had earlier been described by Woo et al. (1980); however, the relative orientation of the 1,4-benzodioxane moieties remained uncertain.

In *J. princeps,* isoamericanol-type neolignans obviously prevail the regioisomeric americanol-type: the yield of isolated americanol A (**2**) was only about a fourth of that of isoamericanol A (**3**), and no americanol-type sesquineolignan similar to **7**–**10** was isolated. With an aldehyde group only isoamericanin A (**1**) was found.

From a biosynthetic point of view it was of interest that all isolated compounds obviously represent racemates ($\alpha_D \pm 0°$). To investigate whether the isolated compounds might have been formed artificially during work-up of the plant material by condensation of caffeoyl alcohol or a similar precursor under oxidizing conditions, two extracts were prepared from seeds of *J. princeps:* one extract in the presence of air and the other under argon. Subsequent HPLC-analysis of both extracts did not indicate any difference in the concentrations of compounds **1**–**10**. Furthermore, the proposed precursor caffeoyl alcohol could not be detected in freshly prepared extracts. We therefore regard all isolated compounds as genuine plant constituents.

3. Experimental

3.1. General

Mps uncorr. TLC was performed on precoated plates (Silica gel 60 F_{254}, Merck) using the following systems: S-1 = $CHCl_3$–MeOH (17:3); S-2 = $CHCl_3$–MeOH (4:1); detection by UV and anisaldehyde reagent (Stahl and Kaltenbach, 1961). For CC and MPLC silica gel 60 (Merck) was used; for CC also Fractogel® PVA-500 and Fractogel® TSK HW-40(S) (Merck). HPLC on Eurospher® RP-18, 7 μ (Knauer) and Nucleosil® RP-18, 7 μ (Macherey-Nagel). Unless otherwise stated [α_D at 21 °C in MeOH, IR in KBr, UV in MeOH, ^{1}H and ^{13}C NMR in CD_3OD at 360 and 90 MHz, respectively; int. standard: TMS for ^{1}H, solvent for ^{13}C NMR. EIMS at 70 eV using direct inlet; DCIMS with NH_3, unless key ions only ions $\geqslant 15\%$ and $m/z > 100$ are presented. HREIMS at resolution $M/\Delta M = 12\,000$, neg. HRFABMS (glycerol) at resolution $M/\Delta M = 8000$, the values are means of five independent measurements. The systematic names of the described compounds follow the IUPAC recommendations for the nomenclature of lignans and neolignans (Moss, 2000).

3.2. Plant material

Seeds of *Joannesia princeps* Vellozo (Euphorbiaceae) were collected in the Brazilian state of Espirito Santo in April 1995. A voucher specimen is kept at the Institute of Pharmacy and Food Chemistry, University of Erlangen under No. 95/04.

3.3. Extraction and isolation

Dried, pulverized seeds (1.19 kg) were extracted exhaustively at room temp. with petrol (410 g extract) and then with MeOH (48 g extract). The MeOH extract was suspended in H_2O–MeOH (2:1), and the suspension was successively extracted first with CH_2Cl_2 and then with EtOAc to yield 8.8 g CH_2Cl_2 fraction and 4.4 g EtOAc fraction. Repeated CC of the CH_2Cl_2 fraction on silica gel and Fractogel PVA 500 and final purifica-

Table 2
^{13}C NMR shifts of compounds **1**–**10** (δ in CD_3OD)

Carbon	1	2	3	4	5	6	7	8	9	10
1	129.2	129.6	129.6	133.9	133.9	133.9	129.4	129.4	129.5	129.4
2	115.6	115.5[a]	115.6	114.5	114.5	114.5	115.6	115.6	115.6	115.6
3	146.7	146.6	146.6	146.5	146.5	146.5	146.7	146.7	146.7	146.7
4	147.3	147.2	147.1	146.0	146.1	146.1	147.2	147.2	147.2	147.2
5	116.4	116.4	116.4	116.2	116.3[a]	116.3[a]	116.4	116.4	116.4	116.4
6	120.5	120.4	120.4	118.9	118.9	118.9	120.4	120.4	120.4	120.4
7	77.6	77.7	77.6	87.4	87.5	87.4	77.6	77.7	77.7	77.7
8	80.5	80.0	80.0	55.3	55.3[a]	55.3[a]	80.1[a]	80.1[a]	80.0	80.0[a]
9	62.0	62.1	62.1	72.6	72.6[a]	72.6[a]	62.1	62.1	62.1	62.1
1′	129.2	132.2	132.0	133.9	135.8	135.7	131.3	131.2[a]	131.3[a]	131.4
2′	118.2	115.6[a]	115.6	114.5	115.8	115.8	117.2	117.3	117.3	117.3
3′	145.8	144.9[a]	144.6	146.5	144.8[a]	145.3	145.5	145.5	145.9	145.9
4′	148.2	145.0[a]	145.3	146.0	144.9[a]	144.5	145.5	145.5	145.0[a]	145.0[a]
5′	118.6	117.9	117.9	116.2	117.9[b]	117.9[b]	118.1[a]	118.1[a]	118.1[a]	118.1[a]
6′	124.0	120.7	120.8	118.9	120.1[b]	120.2[b]	121.8	121.7	121.6	121.6
7′	155.2	131.4	131.4	87.4	87.1[b]	87.1	77.3	77.2	77.3	77.2
8′	127.9	128.2	128.1	55.3	55.4[a]	55.4[a]	80.0[a]	79.9[a]	80.0	80.1[a]
9′	196.0	63.8	63.8	72.6	72.7[a]	72.7[a]	62.1	62.0[a]	62.1	62.1
1″	–	–	–	–	129.6	129.6	132.1	132.1	132.2	132.2
2″	–	–	–	–	115.5	115.6	115.6	115.6	115.6	115.6
3″	–	–	–	–	146.7	146.7	144.6	144.6	144.5	144.6
4″	–	–	–	–	147.1	147.2	145.2	145.2	145.2[a]	145.2[a]
5″	–	–	–	–	116.4[a]	116.4[a]	118.0[a]	118.0[a]	118.0[a]	118.0[a]
6″	–	–	–	–	120.4	120.4	120.9	120.9	120.9	120.9
7″	–	–	–	–	77.6	77.6	131.3	131.3[a]	131.4	131.4
8″	–	–	–	–	80.0	80.0	128.2	128.2	128.3	128.3
9″	–	–	–	–	62.1	62.1	63.8	63.8	63.8	63.8

[a] Similar values within a colunm might be interchanged.
[b] Signals slightly 'splitted'.

tion by HPLC (Nucleosil) resulted in the isolation of isoamericanin (**1**). The EtOAc fraction was separated by repeated CC on silica gel, Fractogel PVA 500 and Fractogel TSK HW-40(S) and subsequently by HPLC on Nucleosil and Eurospher, respectively, to yield compounds **2**–**10**.

*3.4. Isoamericanin A (**1**) (= rel-(7′E)-(7α8β)-3,4,9-trihydroxy-3′,7-epoxy-8,4′-oxyneolign-7′en-9′-al)*

Crystals (40 mg). Mp 172–175 °C (from MeOH); (Tanaka et al., 1987): mp 174–176 °C (from MeOH). TLC: R_f 0.43 (S-1); anisaldehyde: green-blue. IR and UV/vis in agreement with published data (Tanaka et al., 1987). ^1H NMR: Table 1. ^{13}C NMR: Table 2. EIMS *m/z* (rel. int.): 328 [M^+] (30), 175 (17), 166 (52), 164 (67), 163 (37), 148 (38), 147 (62), 138 (31), 137 (18), 136 (30), 135 (19), 124 (18), 123 (100), 119 (18), 110 (44).

*3.5. Americanol A (**2**) (= rel-(7′E)-(7α,8β)-3,4,9,9′-tetrahydroxy-4′,7-epoxy-8,3′-oxyneolign-7′-ene)*

Crystals (58 mg). Mp 116–118 °C (from MeOH–$CHCl_3$); (Fukuyama et al., 1992): mp 125–128 °C (from EtOAc–acetone). TLC: R_f 0.44 (S-1); anisaldehyde: violet. IR, UV/vis, NMR in DMSO-d_6 and EIMS in agreement with published data (Fukuyama et al., 1992). ^1H NMR: Table 1. ^{13}C NMR: Table 2.

*3.6. Isoamericanol A (**3**) (= rel-(7′E)-(7α,8β)-3,4,9,9′-tetrahydroxy-3′,7-epoxy-8,4′-oxyneolign-7′-ene)*

Crystals (240 mg). Mp 106–108 °C (from MeOH–$CHCl_3$); (Fukuyama et al., 1992): mp 157–159 °C (from EtOAc–acetone). TLC: R_f 0.39 (S-1); anisaldehyde: violet. IR, UV/vis, NMR in DMSO-d_6 and EIMS in agreement with published data (Fukuyama et al., 1992). ^1H NMR: Table 1. ^{13}C NMR: Table 2.

*3.7. (±)-3′,3″-Bisdemethylpinoresinol (**4**) (= rel-(7α,7′α,8α,8′α)- 7,9′:7′9-diepoxylignan-3,3′,4,4′-tetraol)*

Brown crystals (90 mg). Mp 106–109 °C (from MeOH–$CHCl_3$). TLC: R_f 0.55 (S-2); anisaldehyde: red-violet. IR υ_{max} cm^{-1}: 3368 (OH). UV/vis λ_{max} nm (log ε): 208 (4.88), 224 (4.57), 282 (4.29). EIMS *m/z* (rel. int.) 330 [M^+] (16), 191 (17), 166 (15), 149 (22), 138 (29), 137 (100), 131 (16), 123 (44), 110 (28). ^1H NMR: Table 1. ^{13}C NMR: Table 2. HIREIMS *m/z* 330.11035 $[M]^+$ (calc. for $C_{18}H_{18}O_6$: 330.11034), 137.02388 (calc. for $C_7H_5O_3$: 137.02387). Conversion of **4** to (±)-dimethylpinoresinol [= (±)eudesmin].

Methylation of **4** (9 mg) with diazomethane in MeOH for 24 h at room temp. afforded dimethylpinoresinol (11 mg): mp 97–99 °C (from MeOH–$CHCl_3$). All physicochemical data are in agreement with published data (Iida et al., 1982).

*3.8. Princepin (**5**) (=rel-(7α,7′α,8α,8′α,7″α,8″β)-4′,7″:7,9′:7′,9-triepoxy-3′8″-oxy-8,8′-sesquineolignan-3,3″,4,4″,9″-pentaol and rel-(7α,7′α,8α,8′α,7″β,8″α)-4′,7″:7,9′:7′,9-triepoxy-3′8″-oxy-8,8′-sesquineolignan-3,3″,4,4″,9″-pentaol)*

Colorless amorphous solid (11 mg). TLC: R_f 0.32 (S-1); anisaldehyde: red-violet. IR υ_{max} cm^{-1}: 3412, 2926. UV/vis λ_{max} nm (log ε): 207 (4.97), 225 *sh* (4.36), 282 (4.07). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (rel. int.): 512 $[M+18]^+$ (28), 480 (18), 313 (100). HRFABMS *m/z* 493.1498 $[M-H]^-$ (calc. for $C_{27}H_{26}O_9$: 493.1498), 367.1181 (calc. for $C_{21}H_{19}O_6$: 367.1182).

*3.9. Isoprincepin (**6**) (=rel-(7α,7′α,8α,8′α,7″α,8″β)-3′,7″:7,9′:7′,9-triepoxy-4′8″-oxy-8,8′-sesquineolignan-3,3″,4,4″,9″-pentaol and rel-(7α,7′α,8α,8′α,7″β,8″α)-3′,7″:7,9′:7′,9-triepoxy-4′8″oxy-8,8′-sesquineolignan-3,3″,4,4″,9″-pentaol)*

Colorless amorphous solid (10 mg). TLC: R_f 0.32 (S-1); anisaldehyde: red-violet. IR υ_{max} cm^{-1}: 3392, 2929. UV/vis λ_{max} nm (log ε): 208 (5.01), 225 *sh* (4.44), 282 (4.15). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (rel. int.) 512 $[M+18]^+$ (31), 480 (16), 313 (100). HRFABMS *m/z* 493.1497 $[M-H]^-$ (calc. for $C_{27}H_{26}O_9$: 493.1498), 367.1184 (calc. for $C_{21}H_{19}O_6$: 367.1182).

*3.10. Isoamericanol B1 (**7**) (=rel-(7″E)-(7α,8β,7′α,8′β)-3,4,9,9′9″-pentahydroxy-3′,7:3″,7′-diepoxy-8,4′:8′,4″-bisoxysesquineolign-7″-ene)[1]*

Colorless amorphous solid (8 mg). TLC: R_f 0.32 (S-1); anisaldehyde: blue. IR υ_{max} cm^{-1}: 3400. UV/vis λ_{max} nm (log ε): 206 (4.72), 229 *sh* (4.33), 269 (4.00), 287 *sh* (3.88), 304 *sh* (3.55), 314 *sh* (3.36). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (ret. int.): 512 $[M+18]^+$ (35), 480 (27), 313 (100). HRFABMS *m/z* 493.1496 $[M-H]^+$ (calc. for $C_{27}H_{26}O_9$: 493.1498).

*3.11. Isoamericanol B2 (**8**) (=rel-(7″E)-(7α,8β,7′β,8′α)-3,4,9,9′9″-pentahydroxy-3′,7:3″,7′-diepoxy-8,4′:8′,4″-bisoxysesquineolign-7″-ene)[1]*

Colorless amorphous solid (5 mg). TLC: R_f 0.32 (S-1); anisaldehyde: blue. IR υ_{max} cm^{-1}: 3400. UV/vis λ_{max} nm (log ε): 206 (4.72), 229 *sh* (4.33), 269 (4.00), 287 *sh* (3.88), 304 *sh* (3.55), 314 *sh* (3.36). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (rel. int.): 512 $[M+18]^+$ (30), 480 (20), 313 (100). HRFABMS *m/z* 493.1499 $[M-H]^-$ (calc. for $C_{27}H_{26}O_9$: 493.1498).

*3.12. Isoamericanol C1 (**9**) (=rel-(7″E)-(7α,8β,7′α,8′β)-3,4,9,9′9″-pentahydroxy-4′,7:3″,7′-diepoxy-8,3′:8′,4″-bisoxysesquineolign-7″-ene)[1]*

Colorless amorphous solid (6 mg). TLC: R_f 0.32 (S-1); anisaldehyde: blue. IR υ_{max} cm^{-1}: 3400. UV/vis λ_{max} nm (log ε): 206 (4.72), 229 *sh* (4.33), 269 (4.00), 287 *sh* (3.88), 304 *sh* (3.55), 314 *sh* (3.36). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (rel. int.): 512 $[M+18]^+$ (32), 480 (29), 313 (100).

*3.13. Isoamericanol C2 (**10**) (=rel-(7″E)-(7α,8β,7′β,8′α)-3,4,9,9′,9″-pentahydroxy-4′,7:3″,7′-diepoxy-8,3′:8′,4″-bisoxysesquineolign-7″-ene)[1]*

Colorless amorphous solid (4 mg). TLC: R_f 0.32 (S-1); anisaldehyde: blue. IR υ_{max} cm^{-1}: 3400. UV/vis λ_{max} nm (log ε): 206 (4.72), 229 *sh* (4.33), 269 (4.00), 287 *sh* (3.88), 304 *sh* (3.55), 314 *sh* (3.36). ^1H NMR: Table 1. ^{13}C NMR: Table 2. DCIMS *m/z* (ret. int.): 512 $[M+18]^+$ (38), 480 (22), 313 (100).

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[1] The values for compounds **7** and **8**, as well as **9** and **10** might be interchanged, since the unambiguous assignment of the individual structures was not possible.

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