Pergamon

0031-9422(95)00331-2

Phytochemistry, Vol. 40, No. 3, pp. 933–938, 1995

0031-9422/95 $9.50 + 0.00

TETRAMERIC PROANTHOCYANIDINS CONTAINING A DOUBLE INTERFLAVANOID (A-TYPE) LINKAGE FROM *PAVETTA OWARIENSIS**

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(*Received* 15 *February* 1995)

Key Word Index—*Pavetta owariensis*; Rubiaceae; stem bark; proanthocyanidins; doubly linked structures; A-type linkages; tetramers; pavetannins; aesculitannin F.

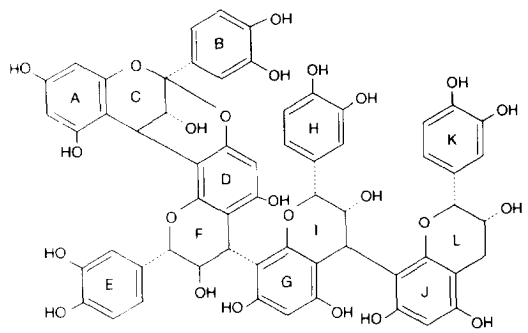
Abstract—Pavetannins C-2 to C-6, five new tetrameric proanthocyanidins containing one or two double interflavanoid (A-type) linkages have been isolated from the stem bark of *Pavetta owariensis*. Spectroscopic investigations and partial acid-catalysed degradation established their structure as epicatechin-(4$\beta \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-*ent*-catechin-(4$\beta \rightarrow$8)-epicatechin-(4$\beta \rightarrow$8)-epicatechin, epicatechin-(4$\beta \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-*ent*-epicatechin-(4$\alpha \rightarrow$8)-*ent*-epicatechin-(4$\alpha \rightarrow$8)-epicatechin, epiafzelechin-(4$\beta \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-epicatechin-(4$\beta \rightarrow$8)-epicatechin-(4$\beta \rightarrow$8)-epicatechin, epiafzelechin-(4$\beta \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-*ent*-afzelechin-(4$\alpha \rightarrow$8)-*ent*-epicatechin-(4$\alpha \rightarrow$8,2$\alpha \rightarrow O \rightarrow$7)-*ent*-catechin and epiafzelechin-(4$\beta \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-*ent*-catechin-(4$\alpha \rightarrow$8)-*ent*-epicatechin-(4$\alpha \rightarrow$8,2$\beta \rightarrow O \rightarrow$7)-*ent*-catechin, respectively. While aesculitannin F is being reported from a plant source for the second time, the remaining tetramers are new natural metabolites.

INTRODUCTION

Our chemical investigations on the acetone-soluble portion of the ethanol extract from the stem bark of *Pavetta owariensis* revealed the presence of a series of polyphenolic components. A number of proanthocyanidins containing one or two double interflavanoid (A-type) linkages have already been identified [1–4]. Herein, we report on the isolation and identification of five new tetrameric proanthocyanidins from the same source.

RESULTS AND DISCUSSION

The acetone-soluble portion, obtained from the ethanol extract of the stem bark of *P. owariensis*, was fractionated by a combination of droplet counter-current chromatography (DCCC) and Sephadex LH-20 chromatography [1] to afford, in addition to a series of A-type proanthocyanidins [1–4], five new proanthocyanidin tetramers (**1**–**5**) posessing one or two doubly linked interflavanyl linkages. Compounds **1**–**5**, responding positively to the vanillin–sulphuric acid and anisaldehyde–sulphuric acid reagents, were obtained as an amorphous powder in a yield of 0.004, 0.003, 0.0004 and 0.001% (mixture of **4** and **5**), respectively.



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In the FAB–mass spectrum of **1**, a $[M + H]^+$ ion peak at *m/z* 1153 was detected, corresponding to a tetraflavanoid structure. The ^{1}H NMR spectrum of **1** (recorded in CD_3OD) proved to be exceedingly complex, presumably due to the effects of dynamic rotational isomerism at ambient temperatures and, hence, rendering its interpretation impossible. Although the ^{13}C NMR spectrum was similarly affected by phenomena of conformational isomerism, this spectroscopic technique permitted structural conclusions to be drawn. Thus, proof for the presence of an A-type unit was available from the spin echo Fourier transform (SEFT) ^{13}C NMR spectrum, which displayed the characteristic ketal carbon at δ104.3.

*Part 5 in the series 'Proanthocyanidins from stem bark of *Pavetta owariensis*'. For Part 4, see ref. [4].

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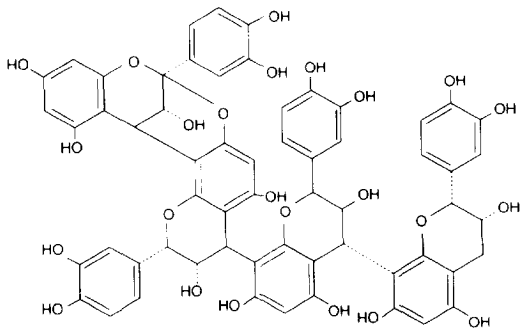

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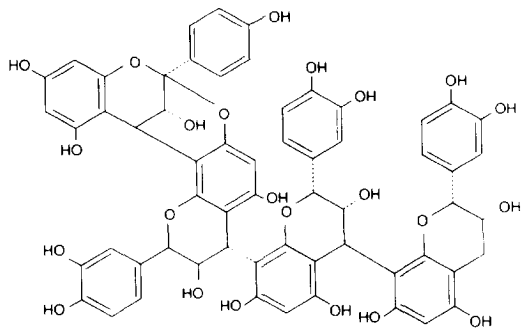

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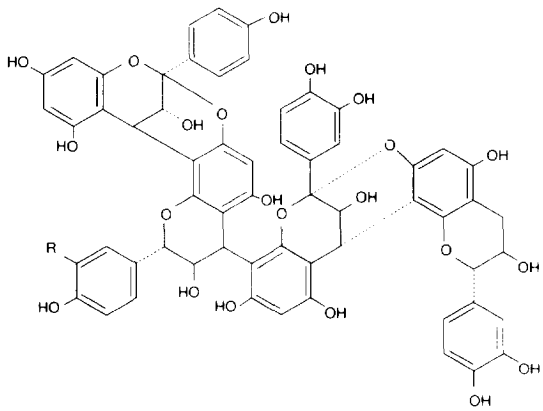

4 R = H

5 R = OH

That an A-type unit represented the upper terminal entity followed from one set of *meta*-coupled protons (A ring) in the ^{1}H NMR spectrum. The presence of four flavanyl units was indicated by the ^{13}C resonances at δ66.4 (× 2), 71.3 and 73.4, each attributable to the C-3 of a flavan framework. Furthermore, the ^{13}C NMR spectrum displayed three carbon signals at δ76.6, 78.8 (two epicatechin entities) and 83.8 (catechin unit) corresponding to C-2 of the C, F, and L heterocyclic rings. The position of heterocyclic ^{13}C resonances also indicated that epicatechin was the terminal unit [5]. The absence of signals in the heterocyclic region of the ^{1}H NMR spectrum exhibiting large coupling constants lends support to the conjecture that the catechin moiety was the upper chain terminating unit of the A-type entity in **1**. These chemical shifts were reminiscent of those reported for aesculitannin F [epicatechin-(4β,8;2β,7)-*ent*-catechin-(4β,8)-epicatechin-(4β,8)-epicatechin] (naming revised according to the graphical presentation in ref. [6], see ref. [7]). The nature of the interflavanyl linkages was concluded from the ^{13}C chemical shifts of the equivalent aromatic A-ring carbons, shown to be substituted at C-8 in each instance (Table 1). Circular dichroism measurements revealed a high-amplitude positive Cotton effect in the diagnostic wavelength region (220–240 nm), reflecting β-orientation of the 4-flavanyl substituents. From the foregoing collective evidence, **1** was identified as aesculitannin F, not previously encountered in this natural source.

The FAB–mass spectrum of **2** indicated a $[M + H]^+$ ion at *m/z* 1153, consistent with a tetraflavanoid moiety. Owing to similar phenomena in the ^{1}H NMR spectrum of **2**, which were indicative of intermittent exchange of rotational isomers, structural assessment was again effected by the analysis of ^{13}C NMR data. Attempts at corroborating the structure of **2** by degradative studies failed due to the low quantity of sample, as was the case for compound **1**. In the ^{13}C NMR spectrum of **2**, the ketal carbon signal at δ104.8 again indicated the presence of a doubly linked subunit. The chemical shifts of all the C-2 resonances of the flavanoid extender units were observed in the upfield region (*ca* 77 ppm) (Table 1), consistent with the relative 2,3-*cis* stereochemistry [5], as depicted in the formula of **2**. In addition, the C-2 chemical shift of the lower terminal unit in **2**, located at δ78.7, indicated epicatechin to be the lower terminal flavanyl unit. The chemical shifts of the C-3 signals at δ72.4, 71.3, 67.3 and 66.7 re-affirmed **2** to be a tetramer consisting only of epicatechin-like units. From related compounds, only ^{13}C resonances of aesculitannin E (**6**) [epicatechin-(4$\beta \rightarrow$ 8,2$\beta \rightarrow$ *O*-7)-epicatechin-(4$\beta \rightarrow$ 8)-epicatechin-(4$\beta \rightarrow$ 8)-epicatechin; for renaming see above] [6] were quite close to those of **2**, except for the shielding of two C-2 signals at δ76.4 [C-2(F), $\Delta\delta$ – 1.1 ppm] and δ76.7 [C-2(I), $\Delta\delta$ – 1.8 ppm] in **2** relative to **7** [epiafzelechin-(4$\beta \rightarrow$ 8,2$\beta \rightarrow$ *O*-7)-*ent*-afzelechin]. Although slight differences in chemical shifts are attributable to solvent-dependency (acetone-d_6 *vs* CD_3OD), we have observed a tendency for C-2 resonate of *ent*-epicatechin units to resonate at somewhat higher magnetic field strengths (*ca* 0.5 ppm) relative to those of epicatechin entities under the conditions employed (CD_3OD) [1]. Based on these results, compound **2**, designated as pavetannin C-2, was tentatively identified as the novel epicatechin-(4$\beta \rightarrow$ 8,2$\beta \rightarrow$ *O*-7)-*ent*-epicatechin-(4$\alpha \rightarrow$ 8)-*ent*-epicatechin-(4$\alpha \rightarrow$ 8)-epicatechin.

Compound **3** differed from **1** and **2** in that its FAB–mass spectrum indicated a $[M + H]^+$ ion at *m/z* 1137, which was 16 mu lower than that of **1** or **2**, suggesting the replacement of a pentahydroxy flavanyl unit by a tetraoxygenated moiety in the molecule. The 600 MHz

Table 1. ^{13}C NMR data for proanthocyanidins **1–5** (150 MHz, CD_3OD)

Ring	Carbon	1	2	3	4	5
C	2	104.3	104.8	103.7	103.6	103.7
	3	66.4	66.7	66.4	67.6	67.2
	4	30.9	29.1	29.8	30.4	30.3
F	2	83.8	76.4	78.6	83.9	83.8
	3	73.4	72.4	72.6	73.6	73.8
	4	37.4	38.3	38.2	30.7	31.0
I	2	76.6	76.7	78.1	103.7	103.7
	3	71.3	71.3	71.5	68.6	68.7
	4	38.4	37.7	38.2	30.0	29.7
L	2	78.2	78.7	80.2	81.5	81.9
	3	66.4	67.3	67.6	68.1	68.2
	4	28.9	28.9	29.9	29.8	29.6
A	6	98.3	98.3	98.6	98.3	98.4
	8	96.5	96.5	96.5	97.8	97.9
	4a	99.4	100.1	99.9	99.9	99.9
	5; 7; 8a	150.0–159.3	150.2–157.8	151.0–158.0	150.5–158.1	150.5–158.1
D	6	96.5	96.5	96.5	96.4	96.4
	8	108.3	108.7	108.8	108.9	108.9
	4a	99.3	99.4	100.0	100.8	100.8
	5; 7; 8a	150.0–159.3	150.2–157.8	151.0–158.0	150.5–158.1	150.5–158.1
G	6	96.5	96.5	96.5	96.4	96.4
	8	106.4	106.9	106.7	107.7	107.7
	4a	99.7	100.1	100.4	100.8	100.8
	5; 7; 8a	150.0–159.3	150.2–157.8	151.0–158.0	150.5–158.1	150.5–158.1
J	6	96.2	96.5	96.5	96.4	96.4
	8	106.6	106.9	106.7	106.7	106.7
	4a	106.7	106.7	106.6	106.1	106.1
	5; 7; 8a	150.0–159.3	150.2–157.8	151.0–158.0	150.5–158.1	150.5–158.1
B	1	131.7	131.6	131.9	131.1	131.4
	2	116.2	116.2	129.6	129.6	129.9
	3	145.9	145.8	115.4	115.5	115.4
	4	145.9	145.8	145.6	145.6	145.6
	5	115.9	115.9	115.4	115.5	115.4
	6	119.3	119.3	130.1	129.6	129.9
E	1	131.7	131.6	132.3	132.3	132.3
	2	116.7	116.5	116.1	130.1	116.3
	3	145.9	145.8	145.8	116.3	145.6
	4	145.9	145.8	145.8	145.7	145.6
	5	115.9	115.9	115.8	116.3	115.8
	6	119.9	119.8	119.6	130.1	119.8
H	1	132.3	132.2	132.3	132.3	132.3
	2	116.7	116.5	116.1	115.7	115.7
	3	146.1	146.2	146.2	146.2	146.2
	4	146.1	146.2	146.2	146.2	146.2
	5	115.9	115.9	115.4	115.4	115.3
	6	120.6	120.7	120.1	120.3	120.4
K	1	132.8	132.8	132.7	132.5	132.5
	2	116.7	116.5	116.1	115.7	115.7
	3	146.6	146.6	146.7	146.9	146.9
	4	146.6	146.6	146.7	146.9	146.9
	5	115.9	115.9	115.4	115.4	115.3
	6	121.4	121.4	121.0	121.1	121.1

^1H NMR spectrum of **3** (recorded in CD_3OD) showed an A_2B_2 system (δ7.45 and 6.83, *dd*, J = 2.0 and 8.0 Hz) in the downfield aromatic region, supporting the presence of a flavanyl entity with a 4-oxygenated B-ring element [8, 9], as already concluded from mass spectral analysis. This feature was further substantiated by the ^{13}C NMR data, which showed the unsubstituted C-2′ and C-6′ resonances for one B ring at δ129.6 and 130.1, in agreement with a proanthocyanidin containing an epiafzelechin unit [8, 10, 11]. The remaining analogous ^{13}C signals, located upfield at δ115–116, indicated the presence of three catechol B-rings in the molecule (Table 1)

Table 2. ^{1}H NMR spectral data for proanthocyanidins **3**–**5** (600 MHz, CD_3OD) (*J* in Hz)

Ring	H	3	4	5
B	2	7.45 (*dd*, *J* = 2,8)	7.48 (*dd*, *J* = 2,8)	7.47 (*dd*, *J* = 2,8)
	3	6.83 (*dd*, *J* = 2,8)	6.86 (*dd*, *J* = 2,8)	6.83 (*dd*, *J* = 2,8)
	5	6.83 (*dd*, *J* = 2,8)	6.86 (*dd*, *J* = 2,8)	6.83 (*dd*, *J* = 2,8)
	6	7.45 (*dd*, *J* = 2,8)	7.48 (*dd*, *J* = 2,8)	7.47 (*dd*, *J* = 2,8)
E	2	7.35 (*d*, *J* = 2)	7.45 (*dd*, *J* = 2,8)	7.39 (*d*, *J* = 2)
	3		6.88 (*dd*, *J* = 2,8)	
	5	6.87 (*d*, *J* = 8)	6.88 (*dd*, *J* = 2,8)	6.85 (*d*, *J* = 8)
	6	7.23 (*dd*, *J* = 2,8)	7.45 (*dd*, *J* = 2,8)	7.22 (*dd*, *J* = 2,8)
H	2	7.37 (*d*, *J* = 2)	7.38 (*d*, *J* = 2)	7.37 (*d*, *J* = 2)
	5	6.94 (*d*, *J* = 8)	6.95 (*d*, *J* = 8)	6.97 (*d*, *J* = 8)
	6	7.26 (*dd*, *J* = 2,8)	7.25 (*dd*, *J* = 2,8)	7.26 (*dd*, *J* = 2,8)
K	2	7.12 (*d*, *J* = 2)	7.31 (*d*, *J* = 2)	7.33 (*d*, *J* = 2)
	5	6.82 (*d*, *J* = 8)	6.90 (*d*, *J* = 8)	6.89 (*d*, *J* = 8)
	6	7.01 (*dd*, *J* = 2,8)	7.31 (*dd*, *J* = 2,8)	7.33 (*dd*, *J* = 2,8)

[5]. The doubly linked structure of **3** was evident from the characteristic ketal carbon resonance at δ103.7, whereas the flavan C-2 signals at δ80.2, 78.6 and 78.1, along with the C-3 signals at δ66.4, 67.6, 71.5 and 72.6, were in agreement with a tetraflavanoid containing epicatechin and epiafzelechin units. The unsubstituted carbon signals at *ca* δ96.5 for C-6 of rings D, G and J were in agreement with the C-4/C-8 nature of the interflavanoid linkages, whereas the configuration at each point of juncture was tentative. Partial cleavage of **3** with toluene-α-thiol in the presence of acetic acid yielded epicatechin and, among others, a 4-benzylthioproanthocyanidin (**3a**). The latter showed a $[M + H]^+$ ion at *m/z* 683, in accord with a thioether, derived from the upper A-type unit in **3**. Upon consideration of the above results, compound **3**, designated as pavetannin C-3, was characterized as epiafzelechin-(4β → 8,2β → *O*-7)-epicatechin-(4β → 8)-epicatechin-(4β → 8)-epicatechin.

Compounds **4** and **5** were identified by mass and NMR spectroscopy of a chromatographically homogeneous mixture. In the FAB–mass spectrum, two $[M + H]^+$ ions at *m/z* 1135 (**5**) and 1119 (**4**) were detected, which were 2 and 18 mu lower than that of **3**. This finding suggested the presence of two doubly linked flavanyl units in the case of **5** and, in addition, replacement of a pentahydroxy flavanyl entity by its tetrahydroxy analogue in the case of **4**. Notably, the ^{1}H NMR (600 MHz) spectrum of the mixture appeared less complex than anticipated, which may be attributed to the rigidity of the molecules associated with the presence of two doubly linked units in **4** and **5**. It showed A_2B_2 type aromatic spin patterns at δ7.45 and 6.88, δ7.48 and 6.86, and δ7.47 and 6.83 (*dd*, *J* = 2.0 and 8.0 Hz in each instance), respectively, confirming earlier mass spectral evidence that **4** and **5** possessed tetraoxygenated flavanyl units. This was further corroborated by the ^{1}H–^{1}H COSY spectrum of **4** and **5** recorded at 600 MHz, which showed connectivities between the following protons of the equivalent B rings: H-6 and H-5, H-6 and H-2, H-2 and H-3, H-3 and H-5. The presence of two closely structurally related compounds was evident from the SEFT ^{13}C NMR spectrum (recorded in CD_3OD). Owing to unequal intensities (relative ratio of **4** to **5**, 2:1) the signals arising from each compound could be allocated (Table 1). The proanthocyanidin nature of both of these compounds was again apparent from their ^{13}C NMR spectra, where the C-2 and C-6 resonances of *p*-hydroxyphenyl groups were present at δ129.6, 129.9 and 130.1 [8, 10, 11]. The ketal carbon signals at δ102.5, 103.1, 103.7 and 105.6 were consistent with the presence of two A-type units in each instance. The ^{13}C NMR spectrum of **4** and **5** also showed pairs of signals for C-2 (δ83.9 and 81.5 for **4**; δ83.8 and 81.9 for **5**) and C-3 (δ73.6 and δ68.1 for **4**; δ73.8 and 68.2 for **5**), showing that both proanthocyanidins consisted of one catechin-like extender unit and terminated with a flavanyl moiety of 2,3-*trans* stereochemistry [5]. Furthermore, as shown in Table 1, the heterocyclic carbon signals of the upper and lower units of **4** were close to those of **7** (C-3: δ67.7 and 68.0; C-2: δ84.1) and pavetannin A-1 [*ent*-epicatechin-(4α → 8,2α → *O* → 7)-*ent*-catechin] (**8**) (C-3: δ66.9 and 68.1; C-2: δ81.8 ppm), respectively [1, 8], but also the heterocyclic carbon signals of the lower unit of **5** resembled those of pavetannin A-1.

Treatment of the mixture with benzylthiol–acetic acid afforded a series of compounds from which two thioethers (**4a** and **5a**): $[M + H]^+$ at *m/z* 667 and 683, respectively), derived from the corresponding upper A-type subunits in **4** and **5**, were identified. In addition, an A-type proanthocyanidin (**9**) ($[M + H]^+$ at *m/z* 577) was detected among the reaction products, reflecting the lower A-type moiety in both the compounds. Acetylation of the mixture of degradation products with acetic anhydride–pyridine at room temperature, followed by column chromatography and preparative TLC on silica gel yielded the acetates, **4b** and **5b**, respectively, which assisted in identifying the structures of the parent proanthocyanidins **4** and **5**. The mode of bonding (C-4/C-8) between the two A-type units in both **4** and **5** followed tentatively from the general congruence of chemical shifts of heterocyclic F ring proton resonances {H-4: δ4.58 and

4.31 (*d*, $J = 4.0$ Hz) for **4b**, δ4.59 and 4.32 (*d*, $J = 4.0$ Hz) for **5b** compared to the analogous signals at δ4.63 and 4.30 for pavetannin B-1 acetate [epicatechin-(4$\beta \rightarrow$ 8, 2$\beta \rightarrow O \rightarrow$ 7)-epicatechin-(4$\alpha \rightarrow$ 8)-*ent*-epicatechin] [3]; duplication of signals due to rotational isomerism}. Hence, the configuration of the interflavanoid bond at C-4(F) was denoted as α.

Based on these results, compounds **4** and **5**, designated as pavetannins C-4 and C-5, were identified as epiafzelechin-(4$\beta \rightarrow$ 8,2$\beta \rightarrow O \rightarrow$ 7)-*ent*-afzelechin-(4$\alpha \rightarrow$ 8)-*ent*-epicatechin-(4$\alpha \rightarrow$ 8,2$\beta \rightarrow O \rightarrow$ 7)-*ent*-catechin and epiafzelechin-(4$\beta \rightarrow$ 8,2$\beta \rightarrow O \rightarrow$ 7)-*ent*-catechin-(4$\alpha \rightarrow$ 8)-*ent*-epicatechin-(4$\alpha \rightarrow$ 8,2$\beta \rightarrow O \rightarrow$ 7)-*ent*-catechin, respectively. The characterization of **4** and **5** not only extends the unique series of proanthocyanidins possessing two doubly linked flavanyl units in their molecules [4, 6], but also provides the first examples of analogues with tetrahydroxyflavanyl entities, e.g. epiafzelechin and *ent*-afzelechin units, within this group of metabolites.

EXPERIMENTAL

General experimental procedures have been described in earlier publications [1–4].

Isolation. Proanthocyanidin-containing frs were obtained from the Me_2CO-soluble portion of the EtOH extract from the stem bark of *P. owariensis* P. Beauv. by DCCC [1, 2]. Compounds **1**–**5** were obtained from polar and enriched frs by repetitive CC on Sephadex LH-20 with Me_2CO and EtOH.

Thiolytic degradation. Carried out as described in ref. [2].

Aesculitannin F (**1**). Amorphous solid (200 mg). FAB–MS: *m/z* 1175 $[M + Na]^+$, 1153 $[M + H]^+$. ^{1}H NMR (200 MHz, CD_3OD): δ2.77 [*br s*, H-4(L)], 3.61 (*br s*), 3.74 (*br s*), 4.06 (*br s*), 4.20 (*br s*), 4.43 (*m*), 5.65 (*br s*) (C-, F-, I- and L-ring protons; some protons of these rings, overlapped with the solvent signal), 5.93–6.30 [5H, *m*, H-6 and H-8 (rings A, E, G and J)], 6.65–7.31 [12H, *m*, H-2, H-5 and H-6 (rings B, D, H and K)]. ^{13}C NMR (50 MHz, CD_3OD), see Table 1. CD $[\Theta]_{242} + 59705$, $[\Theta]_{270} - 9185$.

Pavetannin C-2 (**2**). Brown amorphous solid (150 mg). FAB–MS: *m/z* 1175 $[M + Na]^+$, 1153 $[M + H]^+$ ^{1}H NMR (200 MHz, CD_3OD): δ2.77 [2H, *m*, H-4 (L)]; 4.02–5.60 (rings C, F, I and L)], 5.88–6.25 (A-, E-, G- and J-ring protons), 6.50–7.31 (B-, D-, H- and K-ring protons). ^{13}C NMR (50 MHz, CD_3OD): see Table 2. CD $[\Theta]_{245} + 49186$, $[\Theta]_{269} - 8439$, $[\Theta]_{295} + 3895$.

Pavetannin C-3 (**3**). Brown amorphous solid (20 mg). FAB–MS: *m/z* 1159 $[M + Na]^+$, 1137 $[M + H]^+$. ^{1}H NMR (200 MHz, CD_3OD): δ2.98 [2H, *m*, H-4(L)], 4.03–4.99 (rings, C, F, I and L; some protons of these rings overlapped with the solvent signal); 6.05–6.15 (A-, E-, G- and J-ring protons), 6.72–7.45 (B-, D-, H- and K-ring protons). ^{13}C NMR (50 MHz, CD_3OD), see Table 1. Reaction of **3** with benzylthiol gave epicatechin and an amorphous powder **3a**. FAB–MS: *m/z* 705 $[M + Na]^+$, 683 $[M + H]^+$, 559 $[M - PhCH_2SH]^+$.

Pavetannin C-4 (**4**). Brown amorphous solid (50 mg). FAB–MS: *m/z* 1157 $[M + Na]^+$, 1135 $[M + H]^+$. ^{1}H NMR (600 MHz, CD_3OD): δ3.00 [2H, *m*, H-4(L)], 4.02, 4.15, 4.22, 4.36, 4.54, 4.70, 4.75 (rings, C, F, I and L; some protons of these rings overlapped with the solvent signal); 6.04–6.13 (A, E, G and J-ring protons); B-, D-, H- and K-ring protons, see Table 2. ^{13}C NMR (150 MHz, CD_3OD), see Table 1. Reaction of the mixt. (**4** and **5**) (40 mg) with benzylthiol yielded the thioethers **4a** and **5a** along with an A-type proanthocyanidin as amorphous powders. FAB–MS (**4a**): *m/z* 689 $[M + Na]^+$, 667 $[M + H]^+$, 543 $[M - PhCH_2SH]^+$. Acetylation of the mixt. **4** and **5** yielded the amorphous compounds **4b** and **5b**. ^{1}H NMR (600 MHz, $CDCl_3$): **4b**: δ1.25–2.34 (OAc), 2.97 [C-4(L)], 4.30, 4.57, 4.65, 5.03, 5.20, 5.26, 5.30 (C-, F-, I- and L-ring protons), 6.32 [1H, *s*, H-6 (D and J)], 6.38 [2H, *s* (A and G)], 6.52 [1H, *d*, $J = 2$ Hz, H-6 (A)], 6.64 [3H, *s*, H-6(D, G, J)], 6.84 [1H, *d*, $J = 2$ Hz, H-8 (A)], 7.86 [1H, *d*, $J = 2$ Hz, H-8 (A)], 7.10–7.55 (rings B, E, H and K).

Pavetannin C-5 (**5**). Brown amorphous solid. FAB–MS. *m/z* 1141 $[M + Na]^+$, 1119 $[M + H]^+$. ^{1}H NMR (600 MHz, CD_3OD): δ [2H, *dd*, H-4(L)]9, 4.04, 4.12, 4.28, 4.36, 4.57, 4.70, 4.75 (rings C, F, I and L; some protons of these rings overlapped with the solvent signal), 6.04–6.13 (A-, E-, G- and J-ring protons); B-, D-, H- and K-ring protons, see Table 2. ^{13}C NMR (150 MHz, CD_3OD), see Table 1. Reaction of the mixt. (**4** and **5**) (40 mg) with benzylthiol yielded the thioethers **4a** and **5a** along with an A-type proanthocyanidin as amorphous powders. FAB–MS (**5a**) *m/z* 705 $[M + Na]^+$, 683 $[M + H]^+$, 559 $[M - PhCH_2SH]^+$. Acetylation of the mixt. **4** and **5** yielded the amorphous products **4b** and **5b**. ^{1}H NMR (600 MHz, $CDCl_3$) **5b**: δ1.25–2.34 (OAc), 2.86 [C-4(L)], 4.32, 4.59, 4.65, 5.03, 5.20, 5.26, 5.28 (rings C, F, I and L), 6.32 [1H, *s*, H-6 (D and J)], 6.38 [2H, *s*, H-6 (A and G)], 6.52 [1H, *d*, $J = 2$ Hz, H-6 (A)], 6.64 [3H, *s*, H-6(D,G,J)], 6.84 [1H, *d*, $J = 2$ Hz, H-8 (A)], 6.87 [1H, *d*, $J = 2$ Hz, H-8 (A)], 7.10–7.55 (B-, E-, H- and K-ring protons).

Acknowledgements—M. C. is a reserach director of the National Fund for Scientific Research (Belgium). A. B. was a recipient of a grant from the Belgian General Agency for Development and Cooperation (ABOS). This work was supported by the Flemish Government (Belgium) (grant no. 92/94-09). Dr V. Wray (GBF, Braunschweig, Germany) is kindly acknowledged for recording NMR spectra at 600 MHz, and Mrs H. Van den Heuvel (University of Antwerp, Belgium) for recording FAB–MS.

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