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OLIGOMERIC FLAVAN-3-OLS FROM MEDICINAL WILLOW BARK*

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Key Word Index—*Salix* spp.; Salicaceae; willow; flavan-3-ols; procyanidins; tannins; ^{1}H shift parameters.

Abstract—Chemical investigation of medicinal willow bark (*Salix* spp.) has led to the isolation and characterization of four dimeric (B_1, B_3, B_6, B_7) and five trimeric procyanidins. The structures of the triflavanoids were established on the basis of spectroscopic evidence. Circular dichroism combined with the application of diagnostic chemical shifts of heterocyclic and aromatic protons available from high-temperature ^{1}H NMR spectroscopy permitted the structural elucidation of the dodecamethyl ether triacetates of catechin-(4α → 8)-catechin-(4α → 8)-catechin (C_2), epicatechin-(4β → 8)-epicatechin-(4β → 8)-catechin, catechin-(4α → 8)-catechin-(4α → 6)-catechin, catechin-(4α → 8)-epicatechin-(4β → 8)-epicatechin and its (4α → 6, 4β → 8)-isomer. The last three compounds are being reported from a natural source for the first time.

INTRODUCTION

The bark of willow species (*Salix* spp.) is known to contain a complex mixture of polyphenols, including flavonoids [1–3], condensed tannins [4–7] and phenolic glycosides [8–15] such as salicin. Owing to their alleged medicinal properties, e.g. analgesic and antipyretic effects, the phenolic glycosides have been the subject of intensive recent investigation. As part of our chemical studies on tannins, medicinal willow bark was investigated to determine the precise structures of dimeric and trimeric proanthocyanidins, polyphenols which have been used for treating gastric trouble although their effects are still subject to controversy [16]. Recent studies of the bark extractives of willow revealed the presence of a novel biflavonoid, [2′,2′]-(+)-catechin-(+)taxifolin [17]. This is the first report on associated condensed tannins derived from flavan-3-ols.

RESULTS AND DISCUSSION

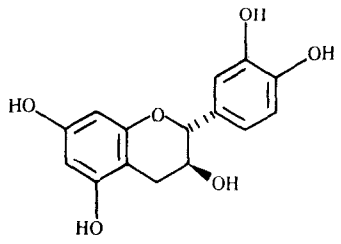
Examination of the phenolic metabolites of willow bark indicated the natural existence of simple flavanoids which apparently represent the precursors of associated condensed tannins. (+)-Catechin (**1**), accompanied by traces of (−)-epicatechin (**2**), was isolated and identified by direct chromatographic and spectroscopic comparison with an authentic sample. Chromatography of the ethyl acetate soluble portion of the methanol extract on Sephadex LH-20 using ethanol as eluant afforded four dimeric and five trimeric procyanidins, dominated by those derived from (2*R*,3*S*)-2,3-*trans*-3′,4′,5,7-tetrahydroxylated precursors [(+)-catechin **1**].

The dimeric fraction was shown to contain the (4 → 8)-linked procyanidins B_1 (**3**) and B_3 (**6**) and their (4 → 6)-isomers B_7 (**9**) and B_6 (**12**). The pairs of positional isomeric (4 → 8)- and (4 → 6)-procyanidins were identified as their octamethyl ether diacetates (**4**, **7**, **10** and **13**) in the approximate proportions 4:12:2:3, respectively, with (4 → 8)-interflavanoid bonding predominating over (4 → 6) and all-*trans* configurations over 2,3-*cis*-3,4-*trans*. The purity and relative configurations of the methyl ether acetates were assessed by ^{1}H NMR spectroscopy at increased temperatures ($CDCl_3$, 100°), thus overcoming the effects of dynamic rotational isomerism [4, 18, 19]. Their absolute configurations were determined by circular dichroism [20–22]. Allocation of the points of bonding at C-6 or C-8 of the flavan unit is based on chemical-shift differences between the residual 8-H or 6-H [23, 24] under the conditions employed. These dimers were readily identified by spectral properties (^{1}H NMR, CD) identical to those of synthetic products [24].

By contrast the full acetates, hitherto widely used for NMR spectroscopy of procyanidin oligomers, were recorded of necessity under ambient temperatures, considering the higher activation energy for 'fast' rotation about interflavanoid bonds required and limitations imposed by the boiling point of the solvent. Although these derivatives have proved to be less suitable in terms of established spectrometric parameters [24], structural assessment of the procyanidin acetates was similarly effected by comparing the ^{1}H NMR and CD data with those of their synthetic counterparts.

Examination of the triflavanoid fractions of the extracts of medicinal willow bark revealed the presence of two all-*trans* procyanidins, (**15**) and (**18**), as judged from the large coupling constants of their heterocyclic proton resonances ($J_{2,3}$ and $J_{3,4}$ 8.0–10.0 Hz) of the dodecamethyl ether triacetates (**16**) and (**19**), respectively. The stereochemistry at the point of junction of the interflavanoid bonds was supported by intense negative Cotton effects in each instance. Differentiation between the methyl ether acetates of the predominant (4α → 8, 4α → 8)-triflavanoid **16** and its (4α → 8, 4α → 6)-isomer was pos-

*Dedicated to Prof. D. G. Roux on the occasion of his 70th birthday.



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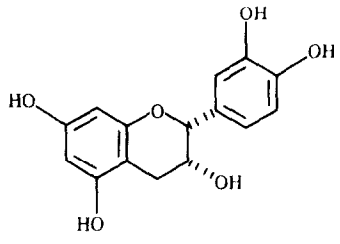

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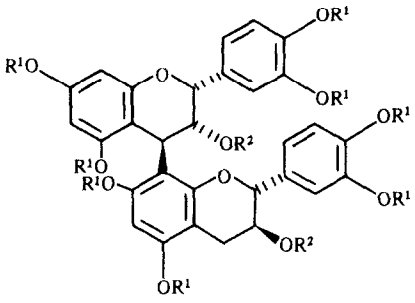

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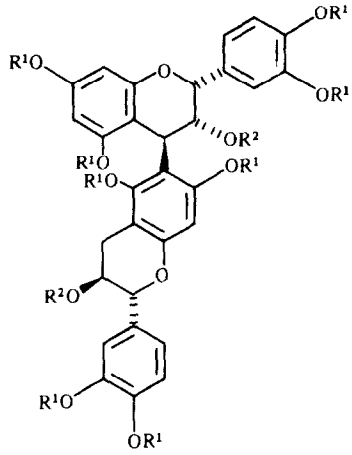

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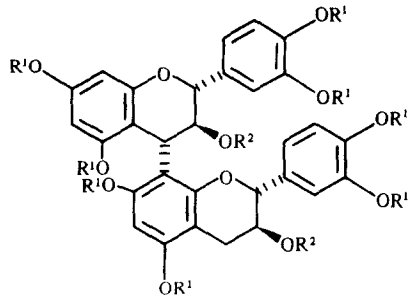

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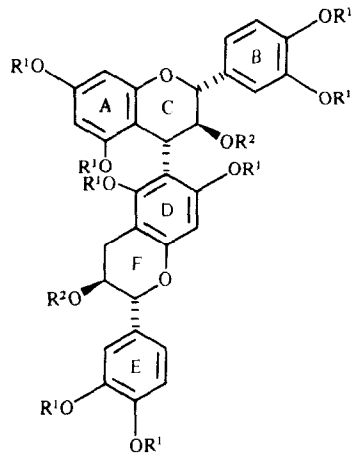
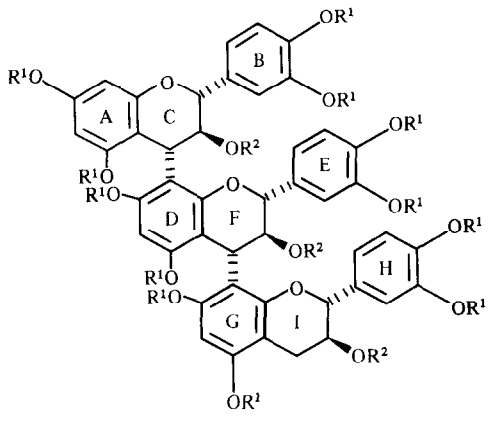


12 $R^1 = R^2 = H$
13 $R^1 = Me$, $R^2 = Ac$
14 $R^1 = R^2 = Ac$

sible by diagnostic shift parameters as follows. The upfield position of two overlapping high-field aromatic proton singlets at δ6.06 in the ^{1}H NMR spectrum of **16** defines successive (4→8)-coupling of both 'upper' catechin units [23, 24]. The (4α→8, 4α→6)-isomer **19** is differentiated from the aforementioned one by the appearance of aromatic singlets at δ6.23 [8-H(G)] and 6.07 [6-H(D)], signifying interflavanoid links to the 6- and 8-position, respectively, of different flavan units. Another significant feature is the chemical-shift difference between 2-H(I) and 3-H(I) of the 'lower' terminal (+)-catechin moiety, furnishing a parameter for determining the sequence of linkage [25]. While the chemical-shift difference ($\Delta\delta$0.23) between these heterocyclic protons of **16** correlates with that of the catechin-(4α→8)-catechin derivative **7** ($\Delta\delta$0.19), the enhanced chemical-shift difference ($\Delta\delta$ 0.33) of the isomeric triflavanoid **19** is in line with that of the (4α→6)-analogue **13** ($\Delta\delta$ 0.36). The catechin-(4α→8)-catechin-(4α→6)-catechin is reported for the first time from a plant source.



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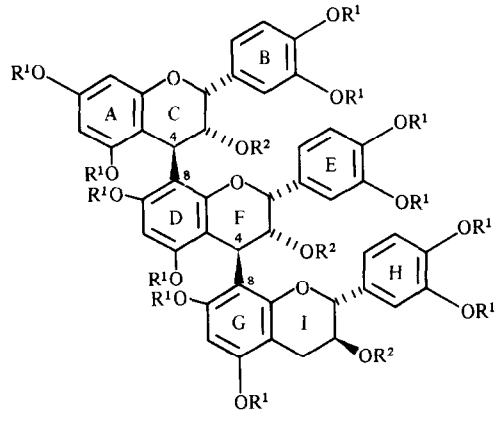

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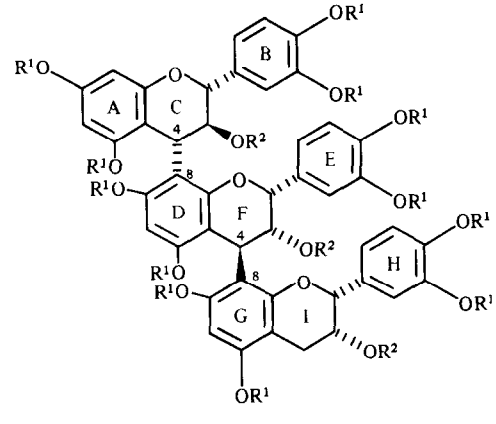

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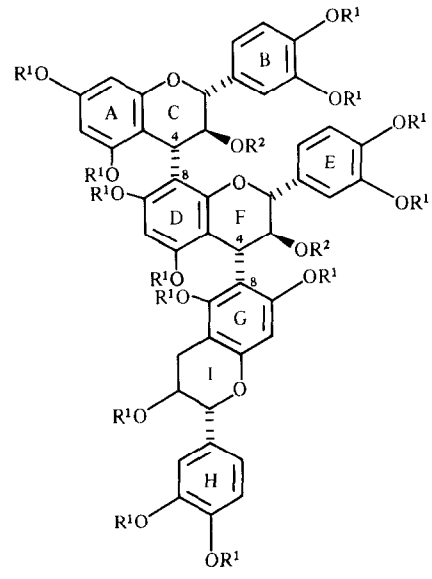
23 $R^1 = Me$, $R^2 = Ac$



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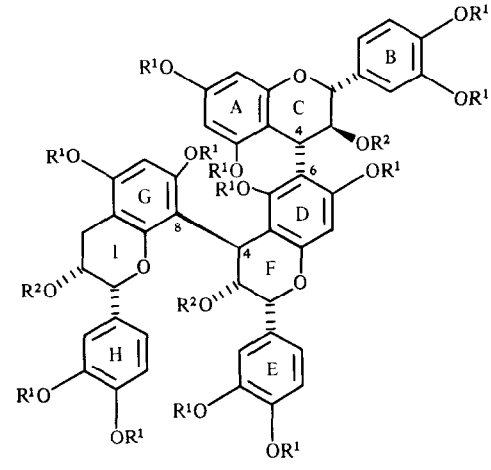
19 $R^1 = Me$, $R^2 = Ac$



24 $R^1 = R^2 = H$
25 $R^1 = Me$, $R^2 = Ac$

Although the (4α→8, 4α→8)-analogue **15** has already been reported from several plant sources [4], its recent synthesis [21] now provides unambiguous spectroscopic evidence obtained from the methyl ether acetate **16** of this procyanidin triflavanoid. The ^1H NMR spectrum of its acetate (**17**), previously tentatively characterized [26], is now unequivocally analysed by the preparation of the acetate from the synthetic product. Noteworthy is the absence of the effects of rotational isomerism in its 300 MHz ^1H NMR spectrum at ambient temperatures. Similarly, no rotamers were observed in the 300 MHz ^1H NMR spectrum of B_3 acetate **8**. Progressive tempera-

ture elevation over the range 20 to 100° showed that the acetate **8** is undergoing 'fast' rotation at room temperatures, indicating that the bulky acetoxy groups at C-5, C-3 (A-ring) and C-7 (D-ring) are very pliable, thus permitting 'fast' rotation on the NMR time scale. However, a few interesting phenomena were evident with temperature elevation under the conditions employed (80 MHz, $CDCl_3$). Some heterocyclic protons undergo slight shifts and also broadening at various temperatures. This may be related to temperature-dependent variation in spin-relaxation times (T_1). Another notable feature was a degree of broadening and then sharpening of 3-OAc resonances with temperature elevation. At higher temperatures than those indicated [$> 100°$, $(CD_3)_2SO$] the ^1H NMR spectrum remained sharp. It should be mentioned that a 20:1 ratio of rotamers for **8** was estimated in $CDCl_3$, while a 4:1 ratio of rotamers was observed in d_5-nitrobenzene (slowing down of rotation), but both at 360 MHz.* At present we cannot explain this peculiar solvent-dependent behaviour.

Complete NMR assignment was established by means of extensive spin-decoupling experiments. A notable feature is the broadened signal at δ5.20 due to the overlap of 2-H(I) and 3-H(I), thus precluding determination of the expected large coupling constants, indicative of the 2,3-*trans* orientation of the 'lower' terminal unit. Recording of the ^1H NMR spectrum of **17** in C_6D_6 showed this two-proton signal resolved into two resonances which, however, remained broadened, similar to those prominent signals which characterize spectra of 2,3-*cis* analogues.

The remaining triflavanoid procyanidins (**20**), (**22**) and (**24**) isolated from medicinal willow bark all possess flavan-3-ol units of both 2,3-*trans* and 2,3-*cis* configuration. The predominant epicatechin-(4β→8)-epicatechin-(4β→8)-catechin **20**, recently isolated from *Salix sieboldiana* [7], was characterized as the phenolic methyl ether acetate (**21**) by comparison of its spectroscopic data with those of a synthetic specimen [24].

Following extensive fractionation and enrichment procedures the catechin-(4α→8)-epicatechin-(4β→8)-epicatechin **22** and its (4α→6, 4β→8)-isomer **24** were obtained from a natural source for the first time. The similar application of shift parameters not only permitted differentiation between the derivatives **23** and **25**, but also determination of the sequence of units in these trimers of mixed stereochemistry.

Comparison of the 80 MHz ^1H NMR spectra of the methyl ether acetate **23** with that of **25** showed their close structural resemblance. Both displayed AMX systems [δ4.72, *d*, J = 10.0 Hz, 2-H(C); δ4.94, *d*, J = 9.0 Hz, 4-H(C); δ5.81, *m*, 3-H(C) for **23**; δ4.75, *d*, J = 10.0 Hz, 2-H(C); δ5.00, *d*, J = 9.0 Hz, 4-H(C), δ5.86, *m*, 3-H(C) for **25**] in the heterocyclic regions, as well as aromatic AB-patterns for their respective A-rings. Notable differences included conspicuous deshielding of one of two high-field aromatic proton singlets [δ6.37, 8-H(D); δ6.08, 6-H(G)] in the ^1H NMR spectrum of **25**, signifying interflavanoid links to the 6- and 8-position, respectively, of different flavanoid units. By contrast, the chemical shift of the two-proton singlet at δ6.09 in the ^1H NMR spectrum of **23** defined both (4→8)-modes of linkage. The heterocyclic AMX systems with their large coupling constants for both derivatives are indicative of the presence of a flavan unit with 2,3-*trans*-3,4-*trans* configuration. The broadened singlets and the small couplings of remaining resonances in the heterocyclic region defined the 2,3-*cis*-3,4-*trans* configuration of epicatechin units. That a catechin unit is the 'upper' terminal unit was deduced from the chemical shifts of the aromatic A-ring protons. The chemical shifts of 6-H(A) (δ6.03) and 8-H(A) (δ6.15) resonances of **23** are in line with either 'upper' terminal catechin units, irrespective of the type of linkage, or (4→6-)-coupled epicatechin units. The range of chemical shifts of the *meta* coupled doublets of (4→8)-linked epicatechin units tend to lie at slightly higher field strengths and fall within the range of δ5.8–6.0. On this basis the structure of **23** was unequivocally established, supported by the negative Cotton effect at low wavelengths in the CD spectrum. The remaining oligomer **25**, obtained in very low yields, proved to be the (4α→6, 4β→8)-isomer. The position of the aromatic AB system in the ^1H NMR spectrum of **25**, taken in conjunction with the high-field aromatic singlets (δ6.08 and 6.37) was consistent with a catechin-(4α→8)-epicatechin-(4β→6)-epicatechin, catechin-(4α→6)-epicatechin-(4β-→8)-epicatechin or epicatechin-(4β→6)-catechin-(4α→8)-epicatechin sequence. Differentiation between these possibilities was effected by comparison of the chemical shifts of the aromatic A-ring protons of **25** [δ6.05 (6-H) and 6.23 (8-H)] with those of the corresponding derivatives of procyanidin dimers B_4 [δ6.06, and 6.16], B_8 [δ6.06 and 6.23] and B_7 [δ6.02 and 6.27] [24] as representatives of the respective 'upper' biflavanoid units. On this basis the (4α→8, 4β→6)-sequencing was excluded. Confirmation of the structure of a catechin-(4α→6)-epicatechin-(4β→8)-epicatechin was provided by circular dichroism as evident from negative Cotton effects as opposed to similar positive effects for the remainder.

Considering the likely course of natural condensations, formation of the triflavanoids **15**, **18** and **20** may be attributed to couplings of the respective 2,3-*trans*- and 2,3-*cis*-flavan-3,4-diols with the biflavanoids **6**, **12** and **3**, respectively. Notable is the absence of epicatechin-(4β→8)-epicatechin (B_2) as potential precursor of **22** and **24**, which may be formed by nucleophilic attack of 2,3-*trans*-flavan-3,4-diol at the accessible nucleophilic centres C-6 and C-8 respectively, of the 'upper' terminal epicatechin unit of B_2. A plausible interpretation is that procyandin B_2, when available at low concentration in the presence of an excess of competitive nucleophiles is immediately and quantitatively converted into the triflavanoids **22** and **24**. A similar case is to be found in *Rhus leptodictya* Diels, where fisetinidol-(4β→8)-epicatechin has been identified, while the precursor (−)-epicatechin appeared to be absent [27].

EXPERIMENTAL

^1H NMR spectra were recorded on Bruker WP-80 FT (methyl ether acetates, 100°) and AM-300 spectrometers (acetates, 30°) in $CDCl_3$ with TMS as int. standard, unless stated otherwise. NMR tubes were firmly stoppered to avoid loss owing to pressure at temperatures above the boiling point of $CDCl_3$. CD data were obtained in MeOH. Analyses (C and H) were performed by the Department of Organic Chemistry, Westfälische Wilhelms-Universität, Münster. Prep. plates (prep. TLC) (20 × 20 cm; Kieselgel PF_{254}, 0.5 mm) were air-dried and used without prior activation.

*Foo, L. Y. and Porter, L. J. (1983) *J. Chem. Soc. Perkin Trans.* 1, 1535.

Methylations were performed with an excess of CH_2N_2 in MeOH–Et_2O during 48 hr at −15°, while acetylations were in Ac_2O–pyridine at room temperature.

Extraction and isolation of compounds. Plant material (1 kg) (Fa. Caesar & Loretz, Hilden) was exhaustively extracted with MeOH and the combined extracts (5 l) evapd *in vacuo* to 500 ml, diluted with H_2O (2 l) and defatted with hexane (5 × 500 ml). Extraction with EtOAc (15 × 500 ml) gave, on evapn of the solvent, a brown solid. A portion (15 g) of this material was chromatographed on Sephadex LH-20 (2.5 × 90 cm) using EtOH as eluant. After the emergence of phenolic material, 15 ml fractions were collected: test tubes 1–52 afforded a mixture (4.47 g) of flavonoids; tubes 53–82 (1.2 g) contained (+)-catechin (**1**), (−)-epicatechin (**2**) and [2′,2′]-(+)-catechin-(+)-taxifolin.

Dimeric procyanidins. From fractions 83–125 (1.7 g) procyanidin B_1 (**3**) and B_3 (**6**) were obtained as a brown solid. The methylated mixture (910 mg) was resolved by prep. TLC [C_6H_6–Me_2CO (4:1)] to give two bands at R_f 0.24 and 0.20. Acetylation of the R_f 0.24 fraction followed by prep. TLC: in the same solvent system afforded the octamethyl ether diacetate (R_f 0.65; 112 mg) of B_1 (**4**) as an amorphous solid, identical with a synthetic product [24] by ^{1}H NMR, CD and mass spectrometry. Acetylation and subsequent purification by prep. TLC of the band at R_f 0.20 yielded the octamethyl ether diacetate of B_3 (**7**) (282 mg), the physical data (^{1}H NMR, CD, and MS) of which were identical with those of an authentic sample [24].

Fractions 126–156 (0.72 g) containing procyanidin B_7 (**9**) and B_6 (**12**) were methylated and the mixture [R_f 0.22 (660 mg); C_6H_6–Me_2CO (4:1)], subsequently subjected to acetylation, resolved by prep. TLC into two bands at R_f 0.69 (54 mg), octamethyl ether diacetate of B_7 (**10**), and R_f 0.69 (75 mg), octamethyl ether diacetate of B_6 (**13**). These derivatives proved to be identical (^{1}H NMR, CD, and MS) to the corresponding derivatives obtained by synthesis [24].

Trimeric procyanidins. Epicatechin-(4β → 8)-epicatechin-(4β→8)-catechin (**20**). Methylation of a portion (625 mg) of the contents of tubes 156–240 (1.3 g) afforded the methyl ether of **20** [C_6H_6–Me_2CO (3:2); R_f 0.24]. Acetylation and further purification in C_6H_6–Me_2CO (3:1) gave the dodecamethyl ether triacetate (**21**) (57 mg), the physical data (^{1}H NMR, CD and MS) of which were identical with those of an authentic sample [24]. A portion (1.0 g) of the fractions 241–390 (1.5 g) were methylated and the product purified in C_6H_6–Me_2CO (3:1). The R_f 0.31 fraction was acetylated and subjected to prep. TLC in the same solvent system to give two bands, R_f 0.63 and 0.58.

Catechin-(4α→8)-epicatechin-(4β→8)-epicatechin (**22**). The former fraction, R_f 0.63 (17 mg), yielded the methyl ether acetate (**23**) as an amorphous powder from hexane. (Found: C, 65.2; H, 6.0. $C_{63}H_{68}O_{21}$ requires C, 65.2; H, 5.9%). ^{1}H NMR ($CDCl_3$, 100°): δ1.56, 1.70 and 1.89 [*s*, 3 × OAc (C, F and I)], 2.81 [*m*, CH_2(I)], 3.34–3.91 (*m*, 12 × OMe), 4.56 [*br s*, 2-H(I)], 4.72 [*d*, *J* = 10.0 Hz, 2-H(C)], 4.94 [*d*, *J* = 9.0 Hz, 4-H(C)], 5.12 [*br s*, 4-H(F)], 5.23 [*m*, 3-H(F)], 5.32 [*m*, 3-H(I)], 5.34 [*br s*, 2-H(F)], 5.81 [*m*, 3-H(C)], 6.03 [*d*, *J* = 2.2 Hz, 6-H(A)], 6.09 [*s*, 2 × 6-H(D and G)], 6.15 [*d*, *J* = 2.2 Hz, 8-H(A)], 6.56–6.94 [*m*, 9 × H(B, E and H)]. $[M]^+$ 1160 (11%); CD $[\theta]_{292}$ 0, $[\theta]_{280}$ − 3625, $[\theta]_{270}$ 0, $[\theta]_{265}$ + 1085, $[\theta]_{252}$ 0, $[\theta]_{237}$ − 26460, $[\theta]_{234}$ − 24650. $[\theta]_{232}$ − 25375, $[\theta]_{225}$ − 16675, $[\theta]_{219}$ − 32260.

Catechin-(4α→8)-catechin-(4α→8)-catechin (C_2) (**15**). The latter fraction, R_f 0.58 (130 mg), yielded the methyl ether acetate (**16**) as an amorphous powder from hexane exhibiting spectral properties (^{1}H NMR, CD and MS) identical to those previously reported [25].

C_2 *Acetate* (**17**). (Found: C, 60.1; H, 4, 7. Calc. for $C_{75}H_{68}O_{33}$: C, 60.1; H, 4, 6%) ^{1}H NMR ($CDCl_3$, 30°): δ1.60–2.35 (*m*, 15 × OAc), 2.63 [*m*, CH_2(I)], 4.10 [*d*, *J* = 9.0 Hz, 4-H(C)], 4.54 [*d*, *J* = 8.25 Hz, 4-H(F)], 4.59 [*d*, *J* = 10.0 Hz, 2-H(C)], 4.72 [*d*, *J* = 10.0 Hz, 2-H(F)], 5.20 [*br s*, 2-H and 3-H(I)], 5.46 [*dd*, Σ *J* = 18.25 Hz, 3-H(F)], 5.51 [*dd*, Σ *J* = 19.0 Hz, 3-H(C)], 6.18 [*d*, *J* = 2.2 Hz, 6-H(A)], 6.51 [*d*, *J* = 2.2 Hz, 8-H(A)], 6.59 [*s*, 6-H(D)], 6.64 [*s*, 6-H(G)], 6.45–7.35 [*m*, 9 × H(B, E and H)]. ^{1}H NMR (C_6D_6): δ1.50–2.20 (*m*, 15 × OAc), 2.35–2.75 [*m*, CH_2(I)], 4.41 [*d*, *J* = 10.2 Hz, 2-H(F)], 4.54 [*d*, *J* = 9.0 Hz, 4-H(C)], 4.78 [*d*, *J* = 8.5 Hz, 4-H(F)], 5.09 [*d*, *J* = 10.0 Hz, 2-H(C)], 5.35 [*br m*, 3-H(I)], 5.70 [*br s*, 2-H(I)], 5.91 [*dd*, *J* = 8.5 and 10.2 Hz, 3-H(F)], 6.06 [*dd*, *J* = 9.0 and 10.0 Hz, 3-H(C)], 6.46 (*d*, *J* = 2.3 Hz, 6-H(A)], 6.49 [*d*, *J* = 2.3 Hz, 8-H(A)], 6.75 − 7.70 [*m*, 9 × H(B, E and H)]. CD $[\theta]_{290}$ 0, $[\theta]_{268}$ − 45690, $[\theta]_{245}$ − 17685, $[\theta]_{232}$ − 74430, $[\theta]_{210}$ 0.

Fractions 391–470 (0.5 g) were methylated and the product purified in C_6H_6–Me_2CO (7:3). The R_f 0.18 (× 2) fraction was acetylated and subjected to prep. TLC in dichloroethane–Me_2CO (9:1; × 2) to give two bands, R_f 0.57 and 0.52.

Catechin-(4α→6)-epicatechin-(4β→8)-epicatechin (**24**). The former fraction, R_f 0.57 (5 mg), yielded the methyl ether acetate (**25**) as an amorphous powder from hexane. ^{1}H NMR ($CDCl_3$, 100°): δ1.66, 1.75 and 1.94 (*s*, 3 × OAc), 2.87 [*m*, CH_2(I)], 3.44–3.91 (*m*, 12 × OMe), 4.75 [*d*, *J* = 10.0 Hz, 2.H(C)], 5.00 [*d*, *J* = 9.0 Hz, 4-H(C)], 5.12 [*br s*, 2-H(I)], 5.25 [*m*, 3-H(I)], 5.31 [*br s*, 2-H(F)], 5.41 [*m*, 3-H(F)], 5.86 [*m*, 3-H(C)], 6.05 [*d*, *J* = 2.5 Hz, 6-H(A)], 6.08 [*s*, 6-H(D)], 6.23 [*d*, *J* = 2.5 Hz, 8-H(A)], 6.37 [*s*, 8-H(G)], 6.62–7.03 [*m*, 9 × H(B, E and H)]. CD $[\theta]_{290}$ 0, $[\theta]_{280}$ − 2900, $[\theta]_{273}$ 0, $[\theta]_{265}$ + 2175, $[\theta]_{248}$ 0, $[\theta]_{237}$ − 10150, $[\theta]_{234}$ − 725, $[\theta]_{230}$ − 50750, $[\theta]_{250}$ 0.

Catechin-(4α→8)-catechin-(4α→6)-catechin (**18**). The latter fraction, R_f 0.52 (11 mg), yielded the methyl ether acetate (**19**) as an amorphous powder from hexane (Found: C, 65.0; H, 6.0. Calc. for $C_{63}H_{68}O_{21}$: C, 65, 2; H, 5.9%) ^{1}H NMR ($CDCl_3$, 100°): δ1.64, 1.66 and 1.91 (*s*, 3 × OAc), 2.70 [*dd*, *J* = 7.5 and 16.5 Hz, 4-H_{ax}(I)], 3.05 [*dd*, *J* = 5.5 and 16.5 Hz, 4-H_{eq} (I)], 3.34–3.85 (*m*, 12 × OMe), 4.64 [*d*, *J* = 10.0 Hz, 2-H(C)], 4.75 [*br d*, *J* = 9.0 Hz, 4-H(F)], 4.80 [*d*, *J* = 10.0 Hz, 2-H(F)], 4.82 [*d*, *J* = 8.5 Hz, 4-H(C)], 4.95 [*d*, *J* = 7.5 Hz, 2-H(I)], 5.28 (*m*, Σ *J* = 19.8 Hz, 3-H(I)], 5.54 [*dd*, Σ *J* = 19.0 Hz, 3-H(F)], 5.81 [*dd*, Σ *J* = 19.0 Hz, 3-H(C)], 6.05 [*d*, *J* = 2.0 Hz, 6-H(A)], 6.07 [*s*, 6-H(D)], 6.13 [*d*, *J* = 2.5 Hz, 8-H(A)], 6.23 [*s*, 8-H(G)], 6.60–7.10 [*m*, 9 × H(B, E and H). CD $[\theta]_{290}$ 0, $[\theta]_{282}$ − 4530, $[\theta]_{268}$ 0, $[\theta]_{258}$ + 4150, $[\theta]_{252}$ 0, $[\theta]_{230}$ − 172340, $[\theta]_{223}$ − 148210, $[\theta]_{215}$ − 184670, $[\theta]_{205}$ − 60420.

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