Synthesis of Condensed Tannins. Part 6.† The Sequence of Units, Coupling Positions and Absolute Configuration of the First Linear [4,6:4,6]-Triflavanoid with Terminal 3,4-Diol Function

By **Phillip M. Viviers, Desmond A. Young, Jacobus J. Botha, Daneel Ferreira,** and **David G. Roux,*** Department of Chemistry, University of the Orange Free State, P.O. Box 339, Bloemfontein, 9300 Republic of South Africa
William E. Hull, Bruker Analytische Messtechnik GmbH, Silberstreifen, D-7512 Rheinstetten-Forchheim, West Germany

The first linear triflavanoid with a terminal 3,4-diol function, (2*R*,3*S*,4*S*:2′*R*,3′*S*,4′*R*:2″*R*,3″*S*,4″*R*)-[4,6:4,6]-bi-[(−)-fisetinidol]-(+)-mollisacacidin, is associated with a set of four diastereoisomeric biflavanoid homologues, [4,6]-(−)-fisetinidol-(+)-mollisacacidins, in the heartwood of the black wattle tree, *Acacia mearnsii*. The sequence of units in the triflavanoid and its bonding points have been determined by n.m.r. spectroscopy at 500 MHz using spin-decoupling techniques. The triflavanoid and two biflavanoids with (2*R*,3*S*,4*S*)-2,3-*trans*-3,4-*cis*-configurations in their ' upper ' units, result from the *in vitro* self-condensation of their putative precursor (2*R*,3*S*,4*R*)-flavan-3,3′,4,4′,7-pentaol[(+)-mollisacacidin], thus permitting definition of their respective absolute configurations.

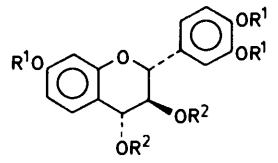
A BIOMIMETIC synthesis representative of the initial steps in condensed tannin formation has been demonstrated for the heartwood of the mopane tree (*Colophospermum mopane*).[1,2] Similar evidence of a succession of flavanoid oligomers of increasing molecular complexity exists in many other sources, notably the bark and heartwood of the black wattle tree (*Acacia mearnsii*) and in numerous species representative of this genus. The heartwood of the black wattle (and also of those species which fall under the section Uninerves, sub-section Racemosae)[3] is chemically unique in that it contains a preponderance of the flavan-3,4-diol, (+)-mollisacacidin [4] (1a), but also the absence of free (+)-catechin which serves as powerful nucleophile in initiating bi- and triflavanoid formation.[1,2] Considering this apparently atypical environment of potential tannin precursors, it is not surprising that evidence of self-condensation of the flavan-3,4-diol was previously obtained through the isolation of three biflavanoids with terminal 3,4-diol function,[5] as well as indication from mass spectrometry of a triflavanoid homologue in the same source.[6] These compounds are presently re-investigated and their relationship with four associated ' angular ' triflavanoids [2] is assessed.

The biflavanoids of this class, shown [5] to possess 2,3-*trans*-3,4-*trans*:2′,3′-*trans*-3′,4′-*trans* (2a), 2,3-*trans*-3,4-*cis*:2′,3′-*trans*-3′,4′-*trans* (4a), and 2,3-*trans*-3,4-*cis*:2′,3′-*trans*-3′,4′-*cis* (5a) relative configurations, were re-isolated and found to accompany a fourth (3a) representing the remaining 2,3-*trans*-3,4-*trans*:2′,3′-*trans*-3′,4′-*cis* (3a) configuration. This group (2a)—(5a), isolated as methyl ether triacetates in the proportions of 1 : 1.25 : 5 : 4 respectively, remains unique as regards both terminal 3,4-diol function and 4,6-linkage; two (4a) and (5a) having been isolated recently by us from *Acacia fasciculifera*.[7] Structural and stereochemical relationships of the new addition follows from analysis ($C_{42}H_{44}O_{14}$), the mass spectrum (M^+ 772), and ^{1}H n.m.r. coupling constants [$J_{2,3} = J_{3,4} = 9.1$ Hz (C-ring); $J_{2',3'}$ 10.5 Hz, $J_{3',4'}$ 3.4 Hz (F-ring)] of its hexamethyl ether triacetate (3c).

† Part 5 is reference 2.

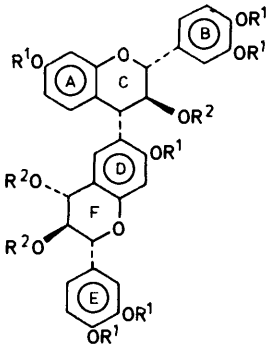
Comparison of the mass fragmentations of the methyl ether triacetates of the four diastereoisomers of the biflavanoids (2c)—(5c) under identical conditions (240 °C, appearance potential) indicates that, as in the case of the corresponding 4-arylflavan-3-ol derivatives,[8] those with 3,4-*trans*-configurations in the ' upper ' unit (2c) and (3c) are subject to more efficient loss of acetic acid than their 3,4-*cis*-counterparts [(4c) and (5c)] as judged from comparison of their respective $M^+ - 60 : M^+$ ratios (24 : 1, 20 : 1, 1.5 : 1, and 1.5 : 1). Similar comparison of the high-field heterocyclic region of their ^{1}H n.m.r. spectra shows that 4-*axial* protons [δ 4.57 (2c), 4.31 (3c)] associated with half-chair C-ring conformations and 2,3-*trans*-3,4-*trans* configurations, always lie upfield relative to 4-*axial* or -quasi-*axial* protons [δ 4.72 (4c), 4.70 (5c)] based on twisted boat conformations and 2,3-*trans*-3,4-*cis*-configurations. However, the most significant feature of these protons is the excessive line-broadening of H-4 (C) resonances associated with 3,4-*trans*-configurations [(2c) and (3c)] as compared with those connected with 3,4-*cis*-configurations [(4c) and (5c)], presumably due to the effect of differences in their dihedral angles with H-5 of both A- and D-rings on long-range benzylic couplings. This observation is of diagnostic import in stereochemical assignments of 4,6-coupled resorcinol-type flavanoid units in higher oligomers.

C.d. spectra of the trimethyl ether diacetates of (2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*trans*-flavan-3,3′,4,4′,7-pentaol (1a), and its (2*R*,3*S*,4*S*)-3,4-*cis* isomer [9] are similar to those of the corresponding derivatives of 4-arylflavan-3-ols [10] in that they exhibit high amplitude negative (4*R*) and positive (4*S*) Cotton effects contributed by chirality at C-4 (Figure 1), and thus obey the aromatic quadrant rule.[8] On this basis the c.d. spectra of the all-*trans*-biflavanoid derivative [(2c) 4*R*,4′*R*] and its 3,4-*cis*:3′,4′-*cis*-isomer [(5c) 4*S*,4′*S*] where the signs of the low wavelength Cotton-effects should reinforce each other, would

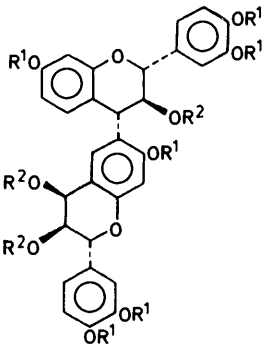


a ; $R^1 = R^2 = H$
b ; $R^1 = Me$, $R^2 = H$
c ; $R^1 = Me$, $R^2 = Ac$

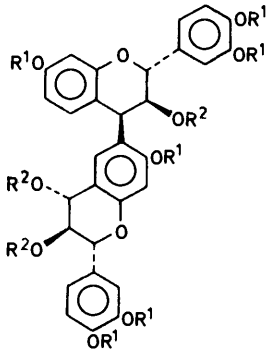
(1)



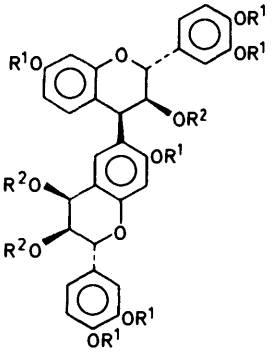
(2)



(3)



(4)



(5)

be expected to exhibit strongly negative and positive effects as observed (*cf.* Figure 1). However, for the 3,4-*trans*:3′,4′-*cis* [(3c) 4*R*,4′*S*] and 3,4-*cis*:3′,4′-*trans* [(4c) 4*S*,4′*R*] isomers, where these effects are expected to be in opposition to each other, couplets are observed with emphasis on the negative and positive Cotton-effects to low wavelength (*ca.* 230 nm) respectively. This indicates that chirality at C-4 in the ' upper ' unit (c-ring) is dominant in contributing to the overall intensity of the sign in this distinctive region.

The higher oligomer, [4,6:4,6]-2,3-*trans*-3,4-*cis*:2′,3′-*trans*-3′,4′-*trans*:2″,3″-*trans*-3″,4″-*trans*-bi-[(−)-fisetinidol]-(+)-mollisacacidin (6a) accompanies the four biflavanoids (2a)—(5a) in the heartwood of the black wattle. The compound is unique in that it represents the first rigorously proven ' linear ' triflavanoid, as well as the first oligomer of this class with a ' terminal ' 3,4-diol function. Analysis of its nonamethyl ether tetra-acetate (6c) is in agreement with the empirical formula $C_{62}H_{64}O_{20}$. Mass fragmentation, however, affords the $M^+ - 60$ ion, *m/e* 1 068 (12.1%), as fragment of highest mass due to facile loss of acetic acid presumably from the 2,3-*trans*-3,4-*trans* F-ring (see biflavanoids), followed by two further successive losses of acetic acid. ' Horizontal ' fragmentations provide fully substituted fisetinidol-mollisacacidin [*m/e* 771 (5.8%)] and fisetinidol [*m/e* 357 (3.7%)], as well as bifisetinidol [*m/e* 713 (2.5%)] and mollisacacidin [*m/e* 415 (3.4%)] segment ions, consistent with the proposed structure.

Determination of the number of functional groups; the relative stereochemistry, coupling positions, and sequence of flavanoid units, and the allocation of all aromatic and heterocyclic protons is elegantly performed by n.m.r. spectroscopy at 500 MHz. The spectrum of the derivative (6c) (*cf.* Figure 2) recorded at an elevated temperature (120 °C) in order to overcome the effects of rotational isomerism, also serves as primary criterion of

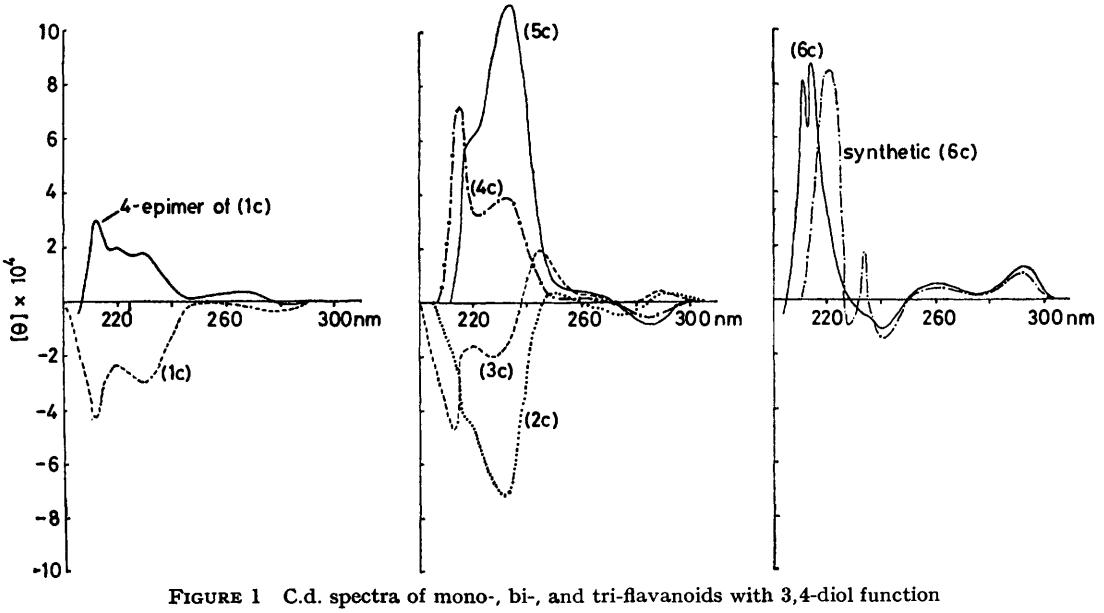
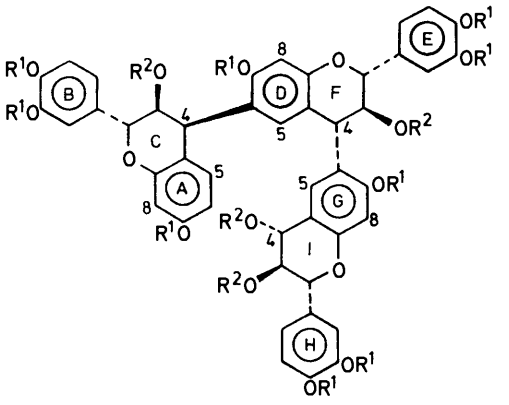


FIGURE 1 C.d. spectra of mono-, bi-, and tri-flavanoids with 3,4-diol function

purity of compounds of this class, as inferred for the angular triflavanoids.[2] Under these conditions four acetyl and nine methoxy methyl proton resonances are sharply differentiated. Four aromatic singlets and a single high-field ABC aromatic spin system correlate with [4,6:4,6] bonding between three resorcinol-type flavanoid units. Spin-decoupling of heterocyclic protons reveals three independent AMX systems of which two



(6) a; $R^1 = R^2 = H$
b; $R^1 = Me$, $R^2 = H$
c; $R^1 = Me$, $R^2 = Ac$

exhibit large ($J_{2,3} = J_{3,4} = 9.5$ Hz and $J_{2,3}$ 9.8, $J_{3,4}$ 7.5 Hz) and the remaining system smaller couplings ($J_{2,3}$ 6.5, $J_{3,4}$ 4.85 Hz) indicative of all-*trans* and 2,3-*trans*-3,4-*cis* configurations respectively, based on half-chair and twisted boat conformations as in the biflavanoid homologues.[5] Amongst these, the 2,3-*trans*-3,4-*trans* system attributable to the ' lower ' terminal unit as a 3,4-diacetate, is readily distinguished by the characteristic downfield shift of the 4-proton (I-ring, δ 6.05). The 3,4-*cis* configuration must accordingly be assigned to either the ' middle ' or ' upper ' units. Differentiation is possible by means of spin-decoupling techniques involving the 4- and line broadened 5-protons. Irradiation of H-4(I) sharpens H-5(G); decoupling of H-5(A) strongly sharpens H-4(C); while decoupling of H-5(D) sharpens H-4(F) strongly, also H-4(C), and intensifies H-5(G) in a nuclear Overhauser effect. Since the identity of the doublet H-5(A) as portion of the high-field aromatic ABC system, and also of the low-field heterocyclic doublet H-4(I) are readily established, the relationships of the heterocyclic ABX systems and the sequence of units as 2,3-*trans*-3,4-*cis*:2′,3′-*trans*-3′,4′-*trans*:2″,3″-*trans*-3″,4″-*trans* is self-evident. Such diagnosis is possible because of the first-order nature of the spectra; the applicability of spin-decoupling over small chemical shifts; and Gaussian enhancement of resonances at high magnetic field strength (*cf.* Figure 2). Spin-decoupling of aromatic 2- and 6-protons of the B- and H-rings by irradiation of the appropriate heterocyclic 2-protons (C- and I-ring systems respectively) permits assignments of all the heterocyclic and aromatic protons as indicated.

The absolute configurations of the triflavanoid (6a) as 2*R*,3*S*,4*S*:2′*R*,3′*S*,4′*R*:2″*R*,3″*S*,4″*R* * and of the biflavanoids (4a) and (5a) as 2*R*,3*S*,4*S*:2′*R*,3′*S*,4′*R* and -2′*R*,3′*S*,4′*S* respectively may be derived from the acid-induced self-condensation of natural (2*R*,3*S*,4*R*)-flavan-3,3′,4,4′,7-pentaol (1a) which gives the corresponding synthetic products in very low yield together with high molecular condensates. They are identified as the methyl ether acetates [(6c), (4c), and (5c) respectively] by ^1H n.m.r. and mass spectrometry and circular dichroism. The conditions employed for self-condensation (0.1M-HCl, 40 °C, 18 h or 0.1M-HCl, 80 °C, 5 min) of the flavan-3,4-diol are critical, since the reaction does not proceed significantly under circumstances (0.1M-HCl, 22 °C, 2 h) which permit facile condensation of the flavan-3,4-diol with its flavan-3-ol analogue, (−)-fisetinidol.[1] This difference is attributed to the deactivating inductive effect of the 4-hydroxy-group or its protonated equivalent on the reactivity of the benzenoid A-ring of the nucleophilic substrate. If this premise is correct, the more prolonged or drastic conditions required for initial ' dimerization ' of flavan-3,4-diols to biflavanoids (2a)—(5a) should subsequently result in preferential and accelerated condensations with the ' upper ' units of products (*i.e.* 4-flavanylflavan-3-ols) to form higher condensates. Such conjecture is supported by the uncontrollable nature of self-condensation of the flavan-3,4-diol which leads to high condensates rather than to oligomers of intermediate mass.

All three products [(4a), (5a), and (6a)] formed from self-condensation under optimised conditions possess 2,3-*trans*-3,4-*cis*-flavanyl ' upper ' units. The corresponding biflavanoids (4a) and (5a) also predominate in the natural extracts of the heartwoods of *Acacia fasciculifera* and *A. mearnsii*. Taken in conjunction with the formation of a *trans-cis*:*trans-trans*:*trans-trans* triflavanoid (6a), this signifies that ' upper ' units of this type are less susceptible to electrophilic attack at C-6 than their 2,3-*trans*-3,4-*trans* analogues (2a) and (3a). Enhanced steric hindrance in the former instance is implicated from an examination of molecular models.

A complete set of four ' angular ' [4,6:4,8]-bi-[(−)-fisetinidol]-(+)-catechin diastereoisomers, with a (+)-catechin unit occupying the central position in each structure,[2] accompany the aforementioned 3,4-diol-type bi- and tri-flavanoids in wattle heartwood. The natural predominance of the flavan-3,4-diol, (+)-mollisacacidin (1a), as potential electrophile, could accordingly be responsible for the complete absence of their strongly nucleophilic (+)-catechin and [4,8]-(−)-fisetinidol-(+)-catechin precursors, much as it provides the rationale for the unique presence of the products (2a)—(6a) of self-condensation of the presumed electrophile.

* The 4*S*,4′*R*,4″*R* assignment for the triflavanoid is not supported by the predominantly positive Cotton-effect at low wavelength in the c.d. spectrum of (6c) since an overweight of negative (4′*R*,4″*R*) compared with single positive (4*S*) contributions are expected [10,1,2] from these chiral centres (*cf.* Figure 1).

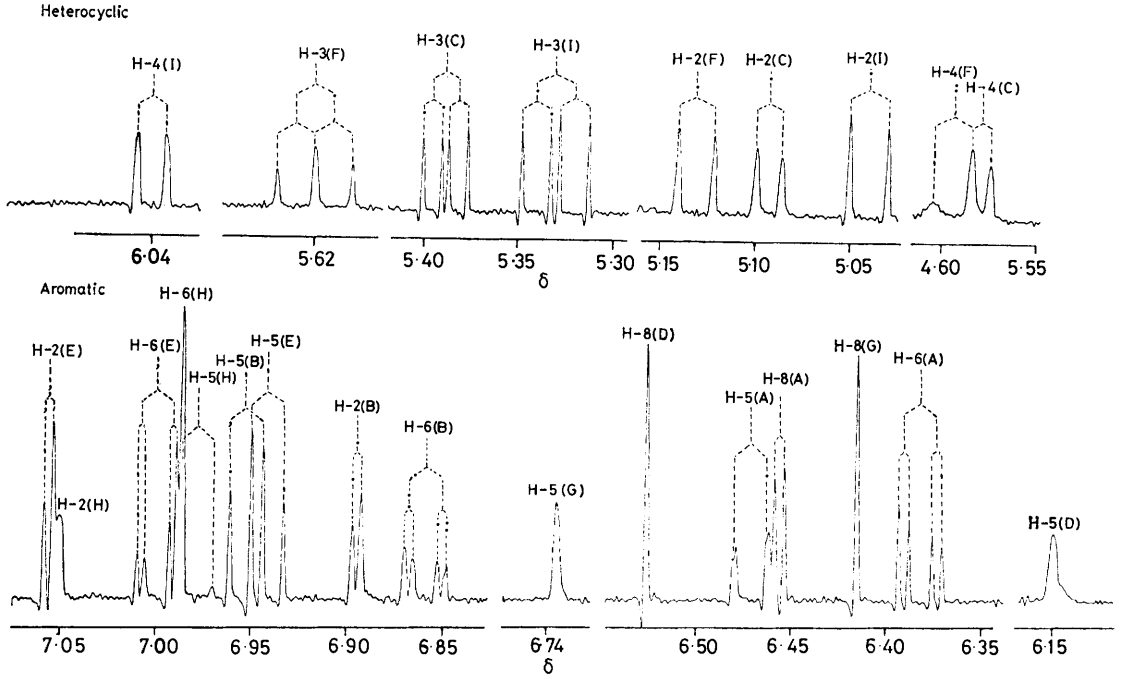


FIGURE 2 Heterocyclic and aromatic regions of the 500 MHz ^{1}H n.m.r. spectrum of the nonamethyl ether tetra-acetate (6c) of the ' linear ' triflavanoid in $(CD_3)_2SO$ at 120 °C

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded on Bruker WP-80 and WM-500 FT spectrometers in $CDCl_3$ and $(CD_3)_2SO$ with Me_4Si as internal standard. Determination of coupling constants and spin-decoupling at 500 MHz both required suitable scale expansion. Mass spectra were obtained with a Varian CH-5 instrument, and circular dichroism (c.d.) data in methanol on a Jasco J-20 spectropolarimeter. Analyses (C and H) were performed by Mr. K. I. Jones, Department of Chemistry, Imperial College of Science and Technology, London. Thin layer chromatography (t.l.c.) was done on DC-Plastikfolin, Kieselgel 60 PF_{254} (0.25 mm) and the plates sprayed with H_2SO_4–HCHO (40 : 1) after development. Preparative plates (p.l.c.) [20 × 20 cm, Kieselgel PF_{254} (1.0 mm)] were air-dried and used without prior activation. Methylations were performed with an excess of diazomethane in methanol–diethyl ether over 48 h, while acetylations were in acetic anhydride–pyridine. Evaporations were done under reduced pressure at 50 °C in a rotary evaporator.

Isolation of Metabolites from the Heartwood of Acacia mearnsii.—Drillings from freshly-cut heartwood (65 kg) was extracted in large Soxhlets with acetone. Evaporation of the solvent left a dark brown solid (832 g). This was dissolved in 80 g portions in methanol (400 ml) and each extracted (×4) with hexane (300 ml) for the removal of fats and waxes. The dewaxed extract (620 g) was chromatographed on 5 × 125 cm cellulose (' Solka Floc ', Brown Co. Berlin, New Hampshire, U.S.A.) columns (20 g per column) with water as eluant. Collection commenced when a blue band (complex of gallic acid with iron present in ' Solka Floc ') emerged. Fractions (100 ml each) 1—5 contained mainly (+)-mollisacacidin (total: 46.5—62 g), while fractions 6—25 were combined and extracted with ethyl acetate. The solution after drying (Na_2SO_4) and evaporation left a brown powder (total: 32 g).

T.l.c. separation of the latter fraction [benzene–acetone–methanol (6 : 3 : 1 by vol)] at 100 mg per plate gave three bands at R_F 0.31 (mainly biflavanoids), 0.24 (mainly triflavanoids), and 0.13 (tri- and tetra-flavanoids) in yields of 6.0, 9.8, and 5.5 g respectively.

Isolation of Biflavanoids.—Isomeric 3,3',4,4',7-*pentahydroxy*-6-(3,3',4',7-*tetrahydroxyflavan*-4-*yl*)*flavans*. Methylation of the R_F 0.31 fraction (1.1 g) with diazomethane, followed by p.l.c. [ethyl methyl ketone–toluene (3 : 2 v/v)] gave three products at R_F 0.70 (200 mg), 0.63 (150 mg), and 0.56 (82 mg).

(2R,3S,4R)-2,3-trans-3,4-trans-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-3',4',7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3',4',7-*trimethoxyflavan* (4c). Acetylation of the hexamethyl ether (4b), R_F 0.70 (52 mg) and p.l.c. separation [1,2-dichloroethane–acetone (19 : 1 v/v)] gave the triacetate as a colourless solid (15 mg), *m/e* * 772 (M^+, 66.6%), 712 ($M^+ - 60$, 100%); ^{1}H n.m.r. spectrum at 80 MHz in $CDCl_3$ was identical to that obtained before.[5]

The R_F 0.63 band consisted of a mixture of (3b) and (5b). Acetylation (81 mg) and p.l.c. separation [1,2-dichloroethane–acetone (19 : 1 v/v, ×2)] gave two products, R_F 0.46 and 0.41.

(2R,3S,4S)-2,3-trans-3,4-cis-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-3',4',7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3',4',7-*trimethoxyflavan* (5c). The triacetate, R_F 0.46, was isolated as a colourless solid (59 mg), *m/e* * 772 (M^+, 68.3%), 712 ($M^+ - 60$, 100%); ^{1}H n.m.r. spectrum at 80 MHz in $CDCl_3$ was identical to that obtained before.[5]

(2R,3S,4S)-2,3-trans-3,4-cis-6-[(2R,3S,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-3',4',7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3',4',7-*trimethoxyflavan* (3c). The triacetate, R_F 0.41, was isolated as a *colourless solid* (18.4 mg) (Found: C, 65.4; H, 6.0. $C_{42}H_{44}O_{14}$ requires C, 65.3; H, 5.7%); *m/e* * 772 (M^+, 4.9%), 712 ($M^+ - 60$, 100%); δ(80 MHz, $CDCl_3$) 7.00—6.59

* Appearance potential at 240 °C.

(m, 6 × arom. H), 6.49br [d, J 8.0 Hz, H-5 (A)], 6.36br [s, H-5(D)], 6.26 [s, H-8(D)], 6.23 [dd, J 8.0 and 2.5 Hz, H-6 (A)], 5.92 [d, $J_{3,4}$ 3.4 Hz, H-4 (F)], 5.58 [t, ΣJ_s 18.3 Hz, H-3 (C)], 5.33 [dd, ΣJ_s 13.9 Hz, H-3 (F)], 5.00 [d, $J_{2,3}$ 10.5 Hz, H-2 (F)], 4.84 [d, $J_{2,3}$ 9.1 Hz, H-2 (C)], 4.31 [d, $J_{2,3}$ 9.1 Hz, H-4 (C)], 3.77, 3.75 (× 2), 3.72, 3.66, 3.58 (s, 6 × OMe), 1.95 [s, 4-OAc (F)], 1.75 [s, 3-OAc(C)], and 1.61 [s, 3-OAc (F)].

(2R,3S,4R)-2,3-trans-3,4-trans-6-[(2R,3S,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3′,4′,7-*trimethoxyflavan* (2c). The hexamethyl ether (2b) (R_F 0.56; 82 mg) gave the triacetate [(R_F 0.55 in 1,2-dichloroethane–acetone (19 : 1 v/v)] as a colourless solid, *m/e* * 772 (M^+, 4.1%), 712 (M^+ −60, 100%); the ^{1}H n.m.r. spectrum at 80 MHz in $CDCl_3$ was identical with that obtained before.[5]

Isolation of Triflavanoids.—Methylation of the R_F 0.24 fraction (5.2 g) followed by p.l.c. separation [benzene–acetone (7 : 3 v/v)] gave three fractions at R_F 0.35 (641 mg), 0.29 (1.06 g), and 0.13 (425 mg).

Isomeric 'Angular' [4,6:4,8]-*Bi*-[(−)-*fisetinidol*]-(+)-*catechins.*—(2R,3S)-2,3-trans-3-*Acetoxy*-6,8-*bi*-[(2R,3S)-2,3-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3′,4′,5,7-*tetramethoxyflavans*. The R_F 0.35 fraction was acetylated and separated on 70 plates by p.l.c. in 1,2-dichloroethane–acetone (19 : 1 v/v, × 3) into two fractions, R_F 0.27 and 0.18.

6,8-*Bi*-[(2R,3S,4R)-2,3-trans-3,4-cis]-*isomer*. The R_F 0.27 fraction (103 mg) was isolated as a colourless solid. Its ^{1}H n.m.r. (80 MHz, $(CD_3)_2SO$, 170 °C), mass and c.d. spectra were identical with those obtained from the synthetic product.[2]

6-[(2R,3S,4S-2,3-trans-3,4-trans]-8-[(2R,3S,4R)-2,3-trans-3,4-cis]-*Isomer*. The R_F 0.18 fraction (178 mg) was isolated as a colourless solid. Spectral characteristics, as above, were identical with those obtained from the synthetic product.[2]

The methyl ether of R_F 0.29 (1.06 g) was acetylated and separated on 100 plates by p.l.c. in benzene–acetone (9 : 1 v/v, × 3) into two fractions, R_F 0.35 and 0.31.

6-[(2R,3S,4R)-2,3-trans-3,4-cis]-8-[(2R,3S,4S)-2,3-trans-3,4-trans]-*Isomer*.—The R_F 0.35 fraction (142 mg) was isolated as a colourless solid. Spectral characteristics were identical with those of the synthetic compound.[2]

6,8-*Bi*-[(2R,3S,4S)-2,3-trans-3,4-trans]-*isomer*. The R_F 0.31 fraction (160 mg) was isolated as a colourless solid. Spectral characteristics coincided with those of the synthetic product.[2]

'Linear' Tri-flavanoid with 3,4-*Diol Function.*—The methyl ether (6b) fraction, R_F 0.13 (425 mg), was acetylated and separated by p.l.c. on 50 plates in 1,2-dichloroethane–acetone (19 : 1 v/v, × 2) to give the decamethyl ether tetra-acetate (6c).

(2R,3S,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-4-[(2R,3S,4R)-2,3-trans-3,4-trans-3,4-*diacetoxy*-3′,4′,7-*trimethoxyflavan*-6-*yl*]-3′,4′,7-*trimethoxyflavan* (6c). The tetra-acetate was isolated as a *colourless solid* (147 mg) (Found: C, 65.8; H, 5.7. $C_{62}H_{64}O_{20}$ requires C, 66.0; H, 5.7%); δ(500 MHz, $(CD_3)_2SO$, 120 °C), 7.06 [d, J 2.0 Hz, H-2 (E)], 7.05br [d, H-2 (H)], 7.00 [dd, J 8.0 and 1.8 Hz, H-6 (E)], 6.99 [s, H-6 (H)], 6.98 [d, J 8.1 Hz, H-5 (H)], 6.96 [d, J 8.5 Hz, H-5 (B)], 6.94 [d, J 8.1 Hz, H-5 (E)], 6.90 [d, J 2.2 Hz, H-2′ (B)], 6.86 [dd, J 8.7 and 2.1 Hz, H-6 (B)], 6.74br [s, H-5 (G)], 6.53 [s, H-8 (D)], 6.47 [dd, J 8.5 and 1.0 Hz, H-5 (A)], 6.46 [d, J 2.5 Hz, H-8 (A)], 6.42 [s, H-8 (G)], 6.38 [dd, J 8.5 and 2.0 Hz, H-6 (A)], 6.15br [s, H-5 (D)], 6.04 [d, $J_{3,4}$ 7.5 Hz, H-4 (I)], 5.62 [t, ΣJ_s 19.0 Hz, H-3 (F)], 5.39 [dd, ΣJ_s 11.35 Hz, H-3 (C)], 5.34 [dd, ΣJ_s 17.3 Hz, H-3 (I)], 5.14 [d, $J_{2,3}$ 9.25 Hz, H-2 (F)], 5.09 [d, $J_{2,3}$ 6.5 Hz, H-2 (C)], 5.04 [d, $J_{2,3}$ 9.75 Hz, H-2 (I)], 4.59br [d, $J_{3,4}$ 9.5 Hz, H-4 (F)], 4.57 [d, $J_{3,4}$ 4.85 Hz, H-4 (C)], 3.81, 3.803, 3.80 (× 2), 3.78, 3.75, 3.72, 3.71, 3.68 (s, 9 × OMe), 1.96 [4-$COCH_3$(I)], 1.80 [s, 3-$COCH_3$(C)], 1.75 [s, 3-$COCH_3$(F)], and 1.60 [s, 3-$COCH_3$ (I)]; *m/e* 1 068 (M^+ −60, 12.1%), 1 009 (M −119, 3.7), 949 (M^+ −179, 4.0), 875 (6.6), 846 (2.7), 815 (7.3), 786 (4.1), 771 (5.8), 713 (2.5), 711 (6.6), 684 (3.4), 653 (5.3), 624 (3.8), 593 (4.5), 549 (2.9), 518 (3.6), 490 (4.1), 462 (6.1), 458 (3.4), 431 (9.2), 415 (3.4), 398 (8.4), 357 (3.7), 355 (6.0), 327 (5.3), 315 (7.3), 297 (33), 296 (7.4), 222 (17.1), 180 (73), and 151 (100).

Synthesis of Bi- and Tri-flavanoids with 3,4-*Diol Function by Self-Condensation of* (+)-*Mollisacacidin.*—(+)-Mollisacacidin, 7 × 2 g portions each dissolved in 800 ml 0.1 M-HCl, was kept at 40 °C for 18 h or at 80 °C for 5 min. Each solution was extracted with ethyl acetate and the extracts evaporated at 50 °C under reduced pressure. The combined solids (12 g) were separated by p.l.c. [benzene–acetone–methanol (6 : 3 : 1 by vol, 100 mg/plate)] giving three fractions at R_F 0.32, 0.26, and 0.14. The R_F 0.32 fraction (234 mg) represents a mixture of two biflavanoids. Diazomethane methylation and p.l.c. of their hexamethyl ethers [ethyl methyl ketone–toluene (6 : 4 v/v)] gave two products at R_F 0.70 (37.5 mg) and 0.63 (29.4 mg).

(2R,3S,4R)-2,3-trans-3,4-trans-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3′,4′,7-*trimethoxyflavan* (4c). Acetylation of the hexamethyl ether, R_F 0.70 (37.5 mg), followed by p.l.c. (× 2) in hexane–acetone–ethyl acetate (12 : 5 : 3, v/v) gave the triacetate as a colourless solid (26.8 mg). The product gave ^{1}H n.m.r., mass and c.d. spectra identical with those of the same substance derived from the heartwood of *A. mearnsii*.[5]

(2R,3S,4S)-2,3-*trans*-3,4-*cis*-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3,4-*diacetoxy*-3′,4′,7-*trimethoxyflavan* (5c). Acetylation of the hexamethyl ether, R_F 0.63 (29.4 mg), followed by p.l.c. of the product in hexane–acetone–ethyl acetate (12 : 5 : 3, v/v) gave the triacetate, R_F 0.28, as a colourless solid (24.3 mg). Spectra of the compound as above were identical with those of the same substance derived from *A. mearnsii*.[5]

(2R,3S,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-6-[(2R,3S,4S)-2,3-trans-3,4-cis-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-4-[(2R,3S,4R)-2,3-trans-3,4-trans-3,4-*diacetoxy*-3′,4′-7-*trimethoxyflavan*-6-*yl*)-3′,4′,7-*trimethoxyflavan* (6c). Methylation of the free phenolic fraction, R_F 0.26 (93 mg), with diazomethane followed by p.l.c. separation with ethyl methyl ketone–toluene (6 : 4 v/v) gave the nonamethyl ether (6b), R_F 0.45, as a *colourless solid* (21 mg). Acetylation of the methyl ether followed by p.l.c. separation (× 4) in hexane–acetone–ethyl acetate (12 : 5 : 3 by vol) gave the tetra-acetate (R_F 0.43) as a colourless solid (4.1 mg). ^{1}H N.m.r. and mass spectra were identical and the c.d. spectrum was similar (Figure 1) to that of the corresponding substance derived from the heartwood of *A. mearnsii*.

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* Appearance potential at 240 °C.

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