Synthesis of Condensed Tannins. Part 11.† Intramolecular Enantiomerism of the Constituent Units of Tannins from the Anacardiaceae: Stoicheiometric Control in Direct Synthesis: Derivation of ^{1}H Nuclear Magnetic Resonance Parameters Applicable to Higher Oligomers

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Tannins from the heartwoods of *Schinopsis* spp. (quebracho) and *Rhus* spp. (karee) represent mutual condensation products of their associated precursors (2*S*,3*R*,4*S*)(−)-leucofisetinidin, (2*R*,3*S*)-(+)-catechin and, to a minor extent, (2*R*,3*R*)-(−)epicatechin. The unique enantiomeric relationship between the electrophile and two nucleophiles at C-2 is reflected both in the biflavanoid metabolites comprising four [4,6]- and [4,8]-(+)-fisetinidol-(+)-catechins and [4,8]-(+)-fisetinidol-(−)-epicatechin, and in the extension of the former group to four 'angular' triflavanoid [4,6:4,8]-bi-[(+)-fisetinidol]-(+)catechin diastereoisomers. Stoicheiometric control of *in vitro* condensation of the precursors provide similar oligomeric mixtures with selective or specific emphasis on either bi- or tri-flavanoids respectively. ^{1}H N.m.r. coupling constants and chemical shift parameters derived from these compounds and their (−)-fisetinidol analogues are of potential diagnostic value at higher oligomeric levels.

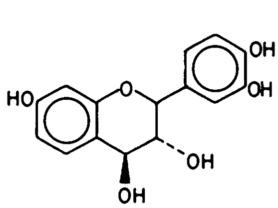
Genesis of significant concentrations of (2*S*,3*R*,4*S*)-2,3-*trans*-3,4-*trans*-3′,4′,7-trihydroxyflavan-3,4-diol [(1), (−)-leucofisetinidin, 5.7—9.5%] and of (2*R*,3*S*)-2,3-*trans*-3′,4′,5,7-tetrahydroxyflavan-3-ol [(2), (+)-catechin, 2.6—3.8%] in the peripheral heartwood of the quebracho [*Schinopsis balansae* Engl. and *S. lorentzii* (Gris.) Engl.], coupled with evidence of their decline with aging radially towards the central heartwood,[1] correlates with a progressive increase in the number-average mass of the phenolic mixture (610 ⟶ 1 203) [2] and with recognition of the predominant heartwood tannins as profisetinidins.[3,4] Limited but more direct indication of participation of both precursors in the formation of tannins of quebracho extract, one of the world's major commercial tanning materials, was obtained by our recent isolation (and synthesis) of two [4,8]-(+)-fisetinidol-(+)-catechins [(3), (2*S*,3*R*,4*R*: 2′*R*,3′*S*) and (5), (2*S*,3*R*,4*S*: 2′*R*,3′*S*)] [5] with absolute configurations at C-2 and C-3 which reflect the unique enantiomeric relationship between the parent compounds.[6,7] The range of oligomeric analogues exclusive to the Anacardiaceae by virtue of their stereochemistry is at present extended to bi- and tri-flavanoids from the heatwoods of the quebracho *S. balansae*) mountain karee (*Rhus leptodictya* Diels) and karee (*R. lancea* L.f.). Confirmatory biomimetic-type synthesis [5] furnishes either bi- or tri-flavanoids selectively through simple stoicheiometric control.

The pairs of diastereoisomeric [4,8]- and [4,6]-profisetinidins (3), (5), (7), and (9) of 2,3-*trans*-3,4-*trans* : 2′,3′-*trans* and 2,3-*trans*-3,4-*cis* : 2′,3′-*trans* relative and indicated [(3), (5), (7), and (9); Table 1)] absolute configurations were isolated from both quebracho and mountain karee heartwoods and were identified as their heptamethyl ether diacetates (4), (6), (8) and (10) in the approximate proportions 11 : 5 : 3 : 1 and 11 : 11 : 2 : 1, respectively, with [4,8]interflavanoid bonding predominating over [4,6] and 3,4-*trans* configurations generally over 3,4-*cis* for each type of linkage. In addition the mountain karee was shown by similar means to contain a low proportion of the [4,8]-2,3-*trans*-3,4-*trans* : 2′,3′-*cis*-(+)-fisetinidol-(−)-epicatechin diastereoisomer (11). Two of these [4,8]-biflavanoids, (3) and (5), were isolated from the karee (*R. lancea*) during the course of earlier work, but considering their predominance in the closely related *R. leptodictya*, we suspect that the minor [4,6] regional isomers (7) and (9) were overlooked. The purity and relative configurations of the methyl ether acetates were assessed by ^{1}H n.m.r. spectroscopy and their absolute configurations by synthesis and by circular dichroism (c.d.) (Figure 1), the sign of the intense Cotton effects at low wavelength representing the reverse of those observed for diastereoisomers of the (2*R*)-profisetinidin series (see ref. 5). Allocation of the points of bonding at C-6 or C-8 of the catechin moiety is based on chemical-shift differences between the residual 8-H or 6-H [8] (see Table 1) of the methyl ether acetates in $CDCl_3$ at 100 °C.

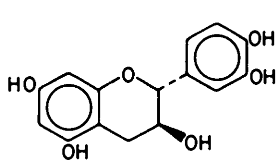
Examination of the triflavanoid fractions of the heartwood extracts of quebracho and of the mountain karee revealed the presence of all four possible 'angular' [4,6:4,8]-(2*S*)-2,3-*trans*-triflavanoid analogues (13), (15), (17), and (19) of the biflavan oids (3), (5), (7), and (9) in which (+)-catechin has served as common nucleophile. Their decamethyl ether triacetates (14), (16), (18), and (20) were obtained in the proportions 16 : 5 : 4.75 : 1 and 3 : 3.5 : 2 : 1 from the respective heartwoods, while the presence of the more prominent of the free phenols, (13), (15), and (17), in the karee (*R. lancea*) was previously established by us. The natural predominance in the triflavanoids of [4,8]-2,3-*trans*-3,4-*trans* units [(13) and (15); stereochemistry refers to C ring] over those possessing [4,8]-2,3-*trans*-3,4-*cis* units [(17),(19)] matches their relative presence amongst the biflavanoid analogues. ^{1}H N.m.r. spectra of these derivatives resemble those of the 2*R* series of 'angular' triflavanoid profisetinidin [9,10] and prorobinetinidin [11] diastereoisomers except for a number of noteworthy differences (see later). ^{1}H N.m.r. spectra of the triflavanoid derivatives provide the most satisfactory criteria of their purity, as for the biflavanoid profisetinidins. Similarly proof of absolute configuration (see Table 2) was provided by synthesis from precursors (1) and (2) of known absolute configuration, and was confirmed at C-4 by c.d. (Figure 2).[12,13]

Stoicheiometric control applied during the synthesis of both bi- and tri-flavanoids of the 2*S* series leads to the generation of the pair of [4,8]- and single [4,6]-biflavanoid profisetinidins (3), (5), and (9) in the proportions 23 : 14 : 1.5, accompanied by minimum formation of the [4,6:4,8]-tri-

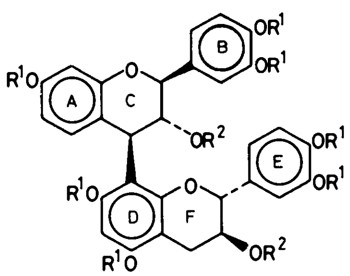
† Preceding part is D. A. Young, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2031.



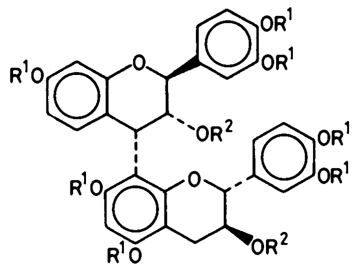
(1)



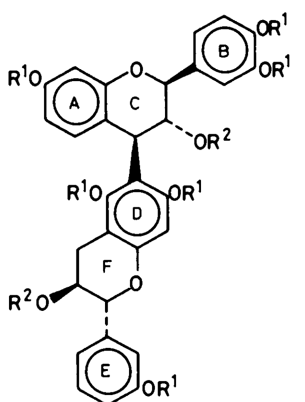
(2)



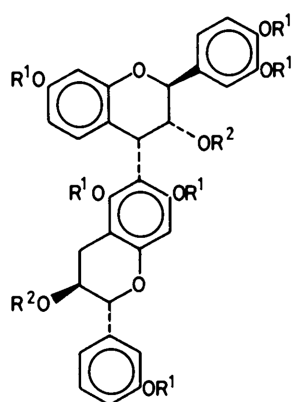
(3) R[1] = R[2] = H
(4) R[1] = Me, R[2] = Ac



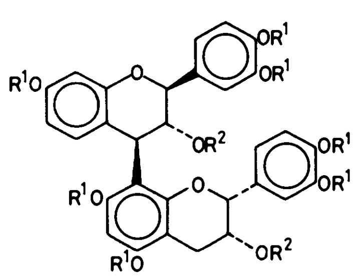
(5) R[1] = R[2] = H
(6) R[1] = Me, R[2] = Ac



(7) R[1] = R[2] = H
(8) R[1] = Me, R[2] = Ac



(9) R[1] = R[2] = H
(10) R[1] = Me, R[2] = Ac



(11) R[1] = R[2] = H
(12) R[1] = Me, R[2] = Ac

Table 1. Relative n.m.r. chemical-shift differences between heterocyclic protons ($\Delta\delta_{2\text{-H},3\text{-H}}$) [a] and absolute chemical shifts of aromatic protons ($\delta_{6\text{-H}}$, $\delta_{8\text{-H}}$) [b] of catechin moieties in biflavanoid profisetinidin heptamethyl ether diacetates

Configuration of substituents on catechins [c] Relative	Absolute	Chemical shifts $\delta_{6\text{-H}}$, $\delta_{8\text{-H}}$ [b]	$\Delta\delta_{2\text{-H},3\text{-H}}$ [a]
[4,8]-Linked to (+)-catechin		$\delta_{6\text{-H}}$	
2,3-*trans*-3,4-*trans*	2*S*,3*R*,4*R* (4)	6.20	0.55
	2*R*,3*S*,4*S*	6.14	0.14
2,3-*trans*-3,4-*cis*	2*S*,3*R*,4*S* (6)	6.22	0.17
	2*R*,3*S*,4*R*	6.13	0.61
[4,6]-Linked to (+)-catechin		$\delta_{8\text{-H}}$	
2,3-*trans*-3,4-*trans*	2*S*,3*R*,4*R* (8)	6.40	0.17
	2*R*,3*S*,4*S*	6.30	0.19
2,3-*trans*-3,4-*cis*	2*S*,3*R*,4*S* (10)	6.38	0.19
	2*R*,3*S*,4*R*	6.31	0.16
[4,8]-Linked to (−)-epicatechin		$\delta_{6\text{-H}}$	
2,3-*trans*-3,4-*trans*	2*S*,3*R*,4*R* (12)	6.15	0.56

[a] Shifts in [$^2H_6$]DMSO at 150 °C. [b] Shifts in $CDCl_3$ at 100 °C (pressure) (*cf.* ref. 8). [c] For 2*R* series see ref. 5.

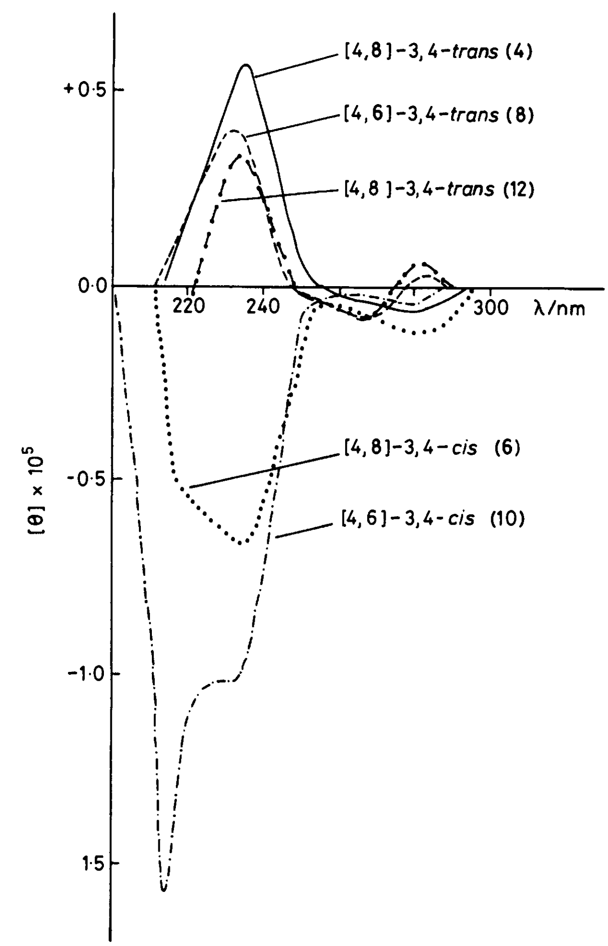
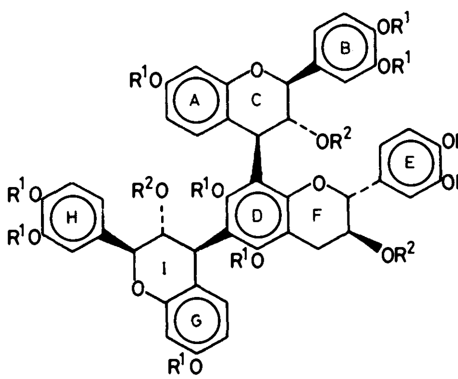
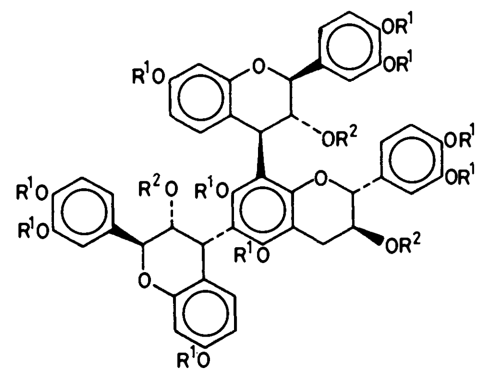


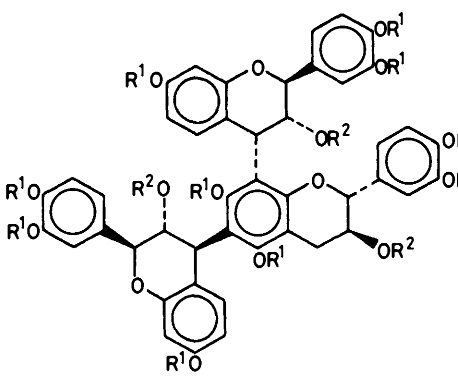
Figure 1. C.d. spectra of the heptamethyl ether diacetates of [4,8]- and [4,6]-(+)-fisetinidol-(+)-catechins, compounds (4), (6), (8), and (10), and of [4,8]-(+)-fisetinidol-(−)-epicatechin, compound (12)



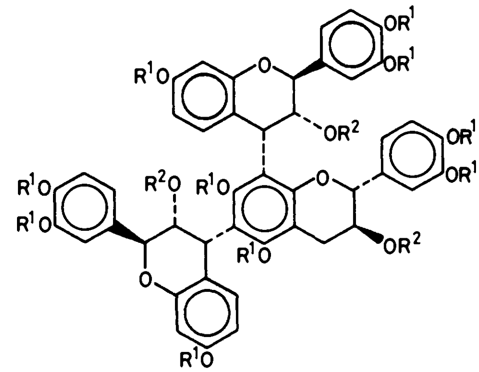
(13) $R^1 = R^2 = H$
(14) $R^1 = Me$, $R^2 = Ac$



(15) $R^1 = R^2 = H$
(16) $R^1 = Me$, $R^2 = Ac$



(17) $R^1 = R^2 = H$
(18) $R^1 = Me$, $R^2 = Ac$



(19) $R^1 = R^2 = H$
(20) $R^1 = Me$, $R^2 = Ac$

Table 2. Relative n.m.r. chemical-shift differences between heterocyclic protons ($\Delta\delta_{2\text{-H},3\text{-H}}$)[a] of (+)-catechin moieties in 'angular' [4,6:4,8]-triflavanoid profisetinidin decamethyl ether triacetates[b]

Configuration of substituents on (+)-catechin in [4,6:4,8]-sequence[c]		Chemical shifts
Relative	Absolute	$\Delta\delta_{2\text{-H},3\text{-H}}$
2,3-*trans*-3,4-*trans* :	2*S*,3*R*,4*R* : 2″*S*,3″*R*,4″*R* (14)	0.69
2″,3″-*trans*-3″,4″-*trans*	2*R*,3*S*,4*S* : 2″*R*,3″*S*,4″*S*	0.08
2,3-*trans*-3,4-*cis* :	2*S*,3*R*,4*S* : 2″*S*,3″*R*,4″*R* (16)	0.73
2″,3″-*trans*-3″,4″-*trans*	2*R*,3*S*,4*R* : 2″*R*,3″*S*,4″*S*	0.07
2,3-*trans*-3,4-*trans* :	2*S*,3*R*,4*R* : 2″*S*,3″*R*,4″*S* (18)	0.09
2″,3″-*trans*-3″,4″-*cis*	2*R*,3*S*,4*S* : 2″*R*,3″*S*,4″*R*	0.81
2,3-*trans*-3,4-*cis* :	2*S*,3*R*,4*S* : 2″*S*,3″*R*,4″*S* (20)	*a*
2″,3″-*trans*-3″,4″-*cis*	2*R*,3*S*,4*R* : 2″*R*,3″*S*,4″*R*	0.76

[a] Shift small but cannot be assessed at 80 MHz due to spectral complexity. [b] Spectra in $[^2H_6]$DMSO at 170 °C. [c] For 2*R* series see ref. 9.

flavanoid profisetinidins (15) and (17) (1 : 1) when using a 1 : 1 ratio of the reagents (−)-leucofisetinidin (1) and (+)-catechin (2). Choice of a 2 : 1 ratio of these reactants gave a mixture of the four 'angular' triflavanoids (13), (15), (17), and (19) selectively in the proportions 5.5 : 2.5 : 2 : 3.5. Although the proportions generated may vary somewhat with experimental conditions, these phenomena are readily explicable in terms of the presence on (+)-catechin of two strong nucleophilic centres at C-6 and C-8, of which the latter is sterically less hindered, and of the relatively weak nucleophilicity at C-6 of substituent (+)-fisetinidol units in all products, a factor which, under the experimental conditions, inhibits progressive condensation to oligomers beyond the triflavanoid range in profisetinidin synthesis (*cf.* ref. 14). The choice of molar ratios thus offers the advantage that specific oligomeric fractions representing the initial stages of tannin formation may be synthesised.

Four 'angular' tetraflavanoid profisetinidins, all of which exhibit complex temperature-dependent dynamic behaviour as judged by ^{1}H n.m.r. spectroscopy, accompany the 2*S* series of bi- and tri-flavanoid analogues in the heartwood of *R. lancea*. Analysis of their complex spectra, and correlation with those of three (2*R*)-tetraflavanoid isomers obtained by us from the heartwood of *Acacia mearnsii* (black wattle),[5] requires assessment of some unusual coupling constant and chemical shift phenomena. Such parameters, which may be rationalised in terms of conformational analysis under dynamic conditions by using Dreiding models, are available from two complete sets of eight each of (2*R*)- [5,9] and (2*S*)-2,3-*trans* bi- and tri-flavanoid methyl ether acetate derivatives. Assignment of the heterocyclic protons of these compounds at elevated temperatures (150 °C, 170 °C) in $[^2H_6]$DMSO * at 80 MHz were available from extensive spin-tickling experiments. This work led to a reversal of previous [9,11] allocations of resonances attributable to the pair 2-H(F) and 4-H(C) of the [4,6:4,8]-

* DMSO is dimethyl sulphoxide.

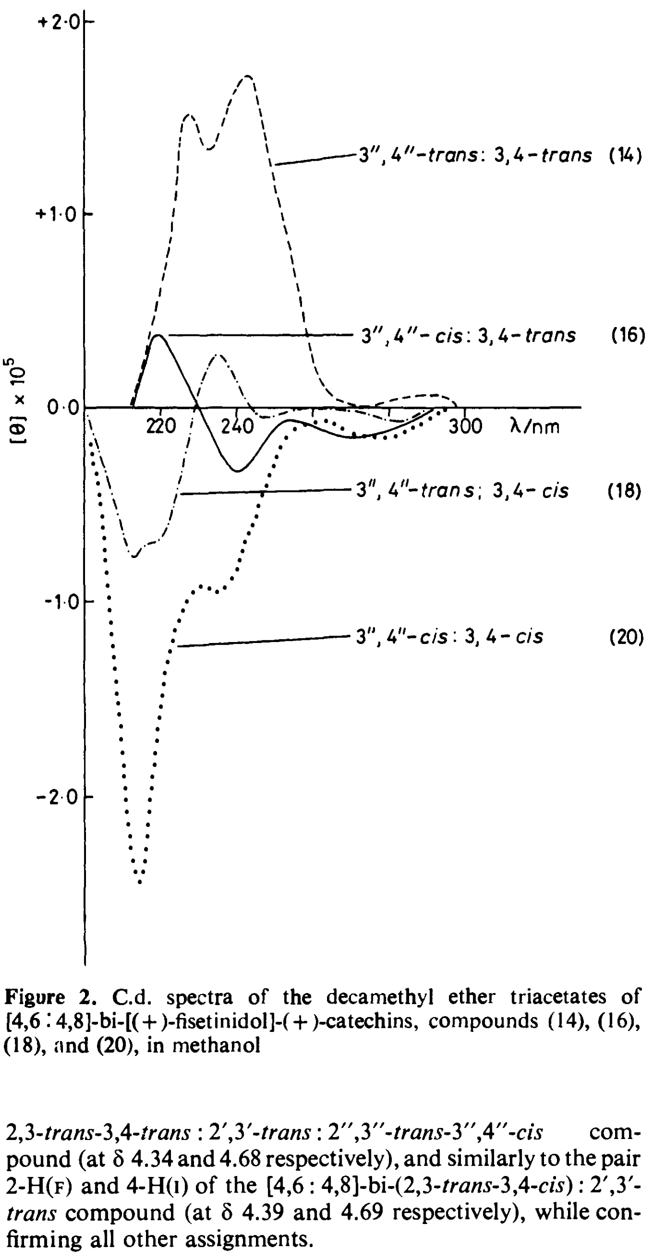


Figure 2. C.d. spectra of the decamethyl ether triacetates of [4,6 : 4,8]-bi-[(+)-fisetinidol]-(+)-catechins, compounds (14), (16), (18), and (20), in methanol

2,3-*trans*-3,4-*trans* : 2′,3′-*trans* : 2″,3″-*trans*-3″,4″-*cis* compound (at δ 4.34 and 4.68 respectively), and similarly to the pair 2-H(F) and 4-H(I) of the [4,6 : 4,8]-bi-(2,3-*trans*-3,4-*cis*) : 2′,3′-*trans* compound (at δ 4.39 and 4.69 respectively), while confirming all other assignments.

Chemical Shifts of Diagnostic Value.—Large chemical-shift differences ($\Delta\delta_{2\text{-H},3\text{-H}}$) *induced in catechin moieties by* [4,8]-(4R)-*profisetinidin substituents.* The majority of profisetinidin biflavanoid derivatives show small chemical-shift differences between resonances which are allocated to 2-H(F) and 3-H(F) of their (+)-catechin units ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.14—0.19, Table 1). However, amongst these, two representing [4,8]-(2*S*,3*R*,4*R*)-2,3-*trans*-3,4-*trans* (4) and [4,8]-(2*R*,3*S*,4*R*),2,3-*trans*-3,4-cis [5] substituents on (+)-catechin are unique in giving substantial shift differences ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.55 and 0.61 respectively). The consistency of the enhanced shifts is evidenced by comparison of spectra of the group of eight (2*R*)- [9] and (2*S*)-triflavanoids (Table 2) in which [4,8]-substituents with the same stereochemistry as above induce shifts of corresponding magnitude ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.69—0.81). The effect is contributed mainly through shielding of 2-H (F) by units of 4*R* stereochemistry which enable close if transient proximity of the anisotropic carbonyl group of their 3-acetoxy functions under dynamic conditions, assuming half-chair (for 2,3-*trans*-3,4-*trans*) and twisted boat (2,3-*trans*-3,4-*cis*) conformations of the heterocyclic ring systems. In all other instances of [4,8] {or [4,6]} substitution 3-acetoxy groups are further removed from the F-ring heterocyclic system of (+)-catechin units.

Chemical shifts ($\Delta\delta_{2\text{-H}}$ *and* $\Delta\delta_{3\text{-H}}$) *in substituent profisetinidin units as functions of their* 3,4-trans *or* 3,4-cis *stereochemistry.* The abnormally low down-field position of 3-H resonances (δ *ca.* 5.9—6.0) relative to 2-H resonances (δ *ca.* 4.9—5.0) ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.93—1.12) [5,9,11] of 2,3-*trans*-profisetinidin units whether [4,6]- or [4,8]-linked to (+)-catechin in both bi- and tri-flavanoid methyl ether acetates is associated with their 3,4-*trans* stereochemistry apart from other contributory factors postulated below. Thus, the large coupling constants of heterocyclic protons of 2,3-*trans*-3,4-*trans* substituents ($J_{2,3}$ = $J_{3,4}$ = 9.5 Hz) imply a 4-equatorial orientation, assuming a half-chair conformation, of the anisotropic aromatic D-ring (catechin moiety) is a significant contributor to this effect. By contrast, relative shielding of 3-H (δ *ca.* 5.5—5.6) and simultaneous deshielding of 2-H resonances (δ 5.2—5.4) characterise the small shift difference between them ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.18—0.30) in 2,3-*trans*-3,4-*cis*-profisetinidin units. The twisted boat conformations, assumed from both unequal and equal coupling constants ($J_{2,3}$ *ca.* 8.5, $J_{3,4}$ *ca.* 6.5 Hz, and $J_{2,3}$ = $J_{3,4}$ = 7.0—8.0 Hz), of their heterocyclic rings,[5,9,11] and hence 4-quasi-axial orientation of the aromatic D-rings, indicate not only relief from anisotropic dehielding for 3-H in these instances, but also deshielding of 2-H through 1,3-diaxial interaction with the 4-aryl substituent.

Chemical-shift differences ($\Delta\delta_{3\text{-H}}$) *in profisetinidin units in terms of their attachment to catechin or fisetinidol moieties.* Differential deshielding of 3-H resonances (Δδ *ca.* 0.30) of 2,3-*trans*-3,4-*trans*-profisetinidin units attached to either C-6 or C-8 of the phloroglucinol unit present in (+)-catechin (δ 5.9—6.0) relative to their attachment at C-6 of resorcinol units of (+)- or (−)-fisetinidols [5,9,11] [or (+)-mollisacacidin] [10,15] (δ *ca.* 5.6—5.7) is of significance in defining bonding patterns in higher oligomers. Such chemical-shift differences under dynamic conditions ([$^2H_6$]DMSO; 150—170 °C) are attributable to the enhanced deshielding effects of two oxygen functions *ortho* to the points of bonding (at both C-6 and C-8) in the former compared with a single oxygen substituent *ortho* to the 6-position in the latter instance, as expected from their weighted average proximity to 3-H over all the rotamers involved.

Differential chemical shifts of 3-*acetoxy proton resonances.* 3-Acetoxy proton resonances of substituent profisetinidin units undergoing 'rapid' rotation in bi- and 'angular' tri-flavanoid profisetinidins are invariably shielded (δ 1.59—1.70) by their weighted average proximity to the benzenoid functions of the (+)-catechin moiety, relative to resonances attributable to the 3-acetoxy function of the latter unit (δ 1.79—1.91); down-field (Δδ 0.14—0.28) resonances of the latter reflecting comparative freedom from shielding effects. The degree of shielding of acetoxy proton resonances is of potential stereochemical and structural significance.

Variation in Coupling Constants.—Profisetinidin units of 2,3-*trans*-3,4-*trans* relative configuration in oligomers may be recognised, irrespective of their absolute stereochemistry, point of linkage, or attachment to differing nucleophiles (catechin, fisetinidol) by their uniformly large ($J_{2,3}$ = $J_{3,4}$ = 9.5 Hz) coupling constants of heterocyclic protons under dynamic conditions.

'Terminal' 2,3-*trans*-3,4-*cis*-profisetinidin units which are [4,6]-linked to resorcinol-type flavanyl moieties [(−)- or (+)-fisetinidol, or (+)-mollisacidin] [5,10,15,16] are characterised by unusually small coupling constants for their heterocyclic protons ($J_{2,3}$ 6.0—7.5 and $J_{3,4}$ 4.0—5.1 Hz) attributed to twisted boat conformations. The same units when attached at

Table 3. Coupling constants of (2*R*)- and (2*S*)-profisetinidin and (2*R*)-prorobinetinidin units attached to (+)-catechin. A consistent set of parameters from the decamethyl ether triacetates of triflavanoids under dynamic conditions

Triflavanoid [4,6:4,8] 3″,4″	3,4	I-ring $J_{2'',3''}$ (Hz)	I-ring $J_{3'',4''}$ (Hz)	C-ring $J_{2,3}$ (Hz)	C-ring $J_{3,4}$ (Hz)
(2*R*)-Series of 2,3-*trans*-profisetinidins [a]					
trans	*trans*	9.5	9.5	9.5	9.5
cis	*trans*	8.5	6.5	9.5	9.5
trans	*cis*	9.5	9.5	7.5	7.5
cis	*cis*	8.5	6.5	7.3	7.3
(2*S*)-Series of 2,3-*trans*-profisetinidins					
trans	*trans* (14)	9.5	9.5	9.5	9.5
cis	*trans* (16)	8.5	6.5	9.5	9.5
trans	*cis* (18)	9.5	9.5	8.0	8.0
cis	*cis* (20)	9.0	6.3	8.0	8.0
(2*R*)-Series of 2,3-*trans*-prorobinetinidins [b]					
trans	*trans*	9.5	9.5	9.5	9.5
cis	*trans*	8.3	6.5	9.5	9.5
trans	*cis*	9.5	9.5	7.5	7.5
cis	*cis*	8.7	6.7	7.5	7.5

[a] See ref. 9. [b] See ref. 11.

either C-6 or C-8 to (+)-catechin in biflavanoids consistently reflect larger couplings (*e.g.* $J_{2,3}$ 8.5, $J_{3,4}$ 6.5 Hz), whereas in triflavanoids those couplings which are diagnostic of [4,8]-($J_{2,3} = J_{3,4} =$ *ca.* 7.5 Hz) and of [4,6]-substituents ($J_{2,3}$ *ca.* 8.5, $J_{3,4}$ *ca.* 6.5 Hz) are invariably evident (Table 3).[9,11] These are readily recognised by triplets and doublet of doublets, respectively, of down-field 3-H resonances which characterise the heterocyclic region.

The above consistent ^{1}H n.m.r. parameters are an essential adjunct to our present attempts at synthesis of 'angular' tetraflavanoid profisetinidins.

The enantiomerism at both C-2 and C-3 between (−)-leucofisetinidin (1) and (+)-catechin (2) and its persistence in the (+)-fisetinidol-(+)-catechin relationship present in biflavanoid (3), (5), (7), and (9) and angular triflavanoid (13), (15), (17), and (19) profisetinidins from similar metabolic pools in *Schinopsis* and *Rhus* species, and also the association between (−)-leucofisetinidin, (−)-epicatechin and [4,8]-(+)-fisetinidol-(−)-epicatechin in *R. leptodictya*, reaffirms the concept of tannin biogenesis based on the flavan-3,4-diol as potential electrophile and flavan-3-ols as nucleophiles.

The stereochemical differences between these participants provide significant evidence of their independent biogenetic origins, a postulate which is in agreement with conclusions drawn from labelling experiments by Haslam and his co-workers.[17] for procyanidins. Apart from previous considerations [5,9,11,12] of steric and stereochemical controls similar to those which operate *in vitro*, the course of natural condensations could also be partially subject to the stoicheiometric relationship between electrophilic and nucleophilic precursors as demonstrated.

The above are the first instances of *intra*molecular enantiomerism of the constituent units of condensed tannins, in contrast to previously established *inter*molecular enantiomerism of procyanidins between [18] or within [19] species.

Experimental

^{1}H N.m.r. spectra were recorded on a Bruker WP-80 FT spectrometer with $CDCl_3$ and $(CD)_3SO$ as solvents and Me_4Si as internal standard. Tubes were firmly stoppered to avoid loss where spectra were recorded above (100 °C) the boiling point of $CDCl_3$. All spectra were recorded at high (150 or 180 °C) temperatures in [$^2H_6$]DMSO in order to enable direct comparisons by overcoming the effects of rotational isomerism. Coupling constants under dynamic conditions (Table 3) were assessed or re-assessed using suitable scale expansions. Owing to relatively small chemical shifts between heterocyclic protons, their identity was established by extensive spin-tickling experiments. Mass spectra were obtained with a Varian CH-5 instrument and c.d. data in methanol on a Jasco J-20 spectropolarimeter. T.l.c. was performed on precoated Merck t.l.c. plastic sheets (silica gel 60 PF_{254}; 0.25 mm) and the plates were sprayed with H_2SO_4–HCHO (40 : 1 v/v) 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 at −15 °C, while acetylations were in acetic anhydride–pyridine at room temperature. Evaporations were done under reduced pressure at 50 °C in a rotary evaporator.

Comparisons of natural and synthetic products (see syntheses section) were by ^{1}H n.m.r. and mass spectrometry and by c.d.

Isolations

Isolation of Bi- and Tri-flavanoids from the Heartwood of Schinopsis balansae.—Drillings from the heartwood (740 g) of a 55 year old cultivated specimen of *S. balansae* from Port Dunford, Northern Natal were extracted with ethyl acetate over a period of 3 d with daily renewal of the solvent. Evaporation of the combined extracts (*ca.* 10 l) gave a light brown amorphous powder (223 g). A solution of the solids in methanol (500 ml) was extracted with hexane (6 × 500 ml) for complete removal of fats and waxes. The dewaxed extract (180 g) was chromatographed on cellulose columns (5 × 125 cm) using 'Solka Floc' (Brown Co., Berlin, New Hampshire, U.S.A.) (250 g) as substrate, 20 g extract per column, and water as eluant.

After the emergence of phenolic material, 100-ml fractions were collected; fractions 2—8 gave mainly (−)-leucofisetinidin (5.6 g), while fractions 9—45 were combined and extracted with ethyl acetate (7 × 400 ml) to give mainly di- and trimers (97.9 g). P.l.c. separation of the latter fraction (50 g) with benzene–acetone–methanol (6 : 3 : 1 v/v) at 85 mg per plate gave two free phenolic fractions at R_F 0.33 (3.9 g) and 0.26 (5.9 g).

Isolation of Biflavanoids.—Methylation of the phenolic fraction (R_F 0.33) (2.0 g) with diazomethane, followed by p.l.c. [benzene–acetone (4 : 1 v/v)] on 60 plates gave two products, R_F 0.39 (467 mg) and 0.29 (190 mg). Acetylation of the former (R_F 0.39) followed by p.l.c. separation (200 mg) [benzene–acetone (9 : 1 v/v), × 2)] gave two compounds at R_F 0.52 and 0.48.

(2S,3R,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-4-[(2R,3S)-2,3-trans-3-*acetoxy*-3′,4′,5,7-*tetramethoxyflavan*-6-*yl*]-3′,4′,7-*trimethoxyflavan* (10). The *heptamethyl ether diacetate*, R_F 0.52, was isolated as a solid (20 mg) (Found: C, 65.8; H, 5.8. $C_{41}H_{44}O_{13}$ requires C, 66.1; H, 6.0%); *m/z* 744 (M^+, 18.9%); δ(80 MHz; [$^2H_6$]DMSO; 150 °C) 7.12—6.44 (m, 10 × ArH), 5.49 [dd, *J* 8.0 and 6.25 Hz, 3-H(C)], 5.27 [d, *J* 8.0 Hz, 2-H(C)], 5.18 [m, 3-H(F)], 5.09 [d, *J* 7.0 Hz, 2-H(F)], 4.85 [d, *J* 6.25 Hz, 4-H(C)], 3.83, 3.79, 3.78, 3.77, 3.76, 3.58, and 3.30 (each s, OCH_3), 2.92—2.67 [m, 4-H_2(F)], 1.88 [s, 3-$COCH_3$(F)], and 1.63 [s, 3-$COCH_3$(C)]; c.d. (Figure 1).

(2S,3R,4S)-2,3-trans-3,4-cis-3-*Acetoxy*-4-[(2R,3S)-2,3-trans-

3-*acetoxy*-3′,4′,5,7-*tetramethoxyflavan*-8-*yl*]-3′,4′,7-*trimethoxyflavan* (6).[5] The diacetate, R_F 0.48, was isolated as a solid (97 mg), δ(80 MHz; [$^2H_6$]DMSO; 150 °C) 6.94—6.28 (m, 10 × ArH), 5.46 [dd, *J* 8.25 and 6.7 Hz, 3-H(C)], 5.18 [d, *J* 8.25 Hz, 2-H(C)], 5.05 [m, 3-H(F)], 4.95 [d, *J* 6.7 Hz, 4-H(C)], 4.88 [d, *J* 7.5 Hz, 2-H(F)], 3.85, 3.77, 3.76, 3.72, 3.69 (× 2), and 3.66 (each s, together 7 × OCH$_3$), 3.01—2.64 [m, 4-H$_2$-(F)], 1.85 [s, 3-COCH$_3$(F)], and 1.62 [s, 3-COCH$_3$(C)]; c.d. (Figure 1).

Acetylation of the second methyl ether, R_F 0.29 (190 mg), and p.l.c. separation [benzene–acetone (9 : 1 v/v)] gave a single diacetate, R_F 0.39.

(2S,3R,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-4-[(2R,3S)-2,3-trans-3-*acetoxy*-3′,4′,5,7-*tetramethoxyflavan*-6-*yl*]-3′,4′,7-*trimethoxyflavan* (8).[5] The diacetate, R_F 0.39, was isolated as a solid (60 mg), δ(80 MHz; [$^2H_6$]DMSO; 150 °C) 7.18—6.39 (m, 10 × ArH), 5.88 [t, *J* 9.5 and 9.5 Hz, 3-H(C)], 5.29 [m, 3-H(F)], 5.13 [d, *J* 5.75 Hz, 2-H(F)], 4.96 [d, *J* 9.5 Hz, 2-H(C)], 4.75 [d, *J* 9.5 Hz, 4-H(C)], 3.80 (× 3), 3.78, 3.75, 3.72, and 3.59 (each s, together 7 × OCH$_3$), 3.01—2.78 [m, 4-H$_2$(F)], 1.91 [s, 3-COCH$_3$(F)], and 1.55 [s, 3-COCH$_3$(C)]; c.d. (Figure 1).

Methylation of the phenolic fraction R_F 0.26 (5 g) and p.l.c. separation [benzene–acetone (7 : 3 v/v)] of the product at 50 mg per plate gave two fractions at R_F 0.42 (787 mg) and 0.34 (1.13 g). Acetylation of the methyl ether, R_F 0.42, and p.l.c. separation of the product with benzene–acetone [(93 : 7 v/v), × 2] gave a diacetate, R_F 0.29, and a triacetate, R_F 0.11.

(2S,3R,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-4-[(2R,3S)-2,3-trans-3-*acetoxy*-3′,4′,5,7-*tetramethoxyflavan*-8-*yl*]-3′,4′,7-*trimethoxyflavan* (4). The diacetate, R_F 0.29, was isolated as a solid (244 mg), δ(80 MHz; [$^2H_6$]DMSO; 150 °C) 6.99—6.24 (m, 10 × ArH), 5.81 [t, *J* 9.5 and 9.5 Hz, 3-H(C)], 5.16 [m, 3-H(F)], 4.87 [d, *J* 9.5 Hz, 2-H(C)], 4.83 [d, *J* 9.5 and 1.0 (benzylic) Hz, 4-H(C)], 4.62 [d, *J* 6.75 Hz, 2-H(F)], 3.81, 3.77 (× 2), 3.74, 3.72 (× 2), and 3.66 (each s, together 7 × OCH$_3$), 3.13—2.53 [m, 4-H$_2$(F)], 1.82 [s, 3-COCH$_3$(F)], and 1.62 [s, 3-COCH$_3$(C)]; c.d. (Figure 1).

Isolation of Triflavanoids.—(2R,3S)-2,3-trans-3-*Acetoxy*-6,8-*bis*-[(2S,3R,4S)-2,3-trans-3,4-cis-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3′,4′,5,7-*tetramethoxyflavan* (20). The *decamethyl ether triacetate*, R_F 0.11, was isolated as a solid (24 mg) (Found: C, 66.3; H, 5.8. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.9%); *m/z* 1 100 (M^+, 2.2%); δ(80 MHz; [$^2H_6$]DMSO; 170 °C) 7.11—6.34 (m, 15 × ArH), 5.61 [t, *J* 8.0 and 8.0 Hz, 3-H(C)], 5.55 [dd, *J* 9.0 and 6.25 Hz, 3-H(I)], 5.33 [d, *J* 9.0 Hz, 2-H(I)], 5.07 [m, 3-H(F)], 5.02 [d, *J* 8.0 Hz, 2-H(C)], 4.95 [d, *J* 5.0 Hz, 2-H(F)], 4.93 [d, *J* 8.0 Hz, 4-H(C)], 4.86 [d, *J* 6.25 Hz, 4-H(I)], 3.83—3.70 (m, 8 × OCH$_3$), 3.38 and 3.24 (each br s, OCH$_3$), 3.15—2.84 [m, 4-H$_2$(F)], 1.86 [s, 3-COCH$_3$-(F)], and 1.67 and 1.64 [each s, 3-COCH$_3$ (C and I)]; c.d. (Figure 2).

Reseparation of the above methylated fraction, R_F 0.34 (1.13 g), by p.l.c. [1,2-dichloroethane–acetone (8 : 2 v/v), × 2] at 14 mg per plate gave two fractions at R_F 0.45 (438 mg) and 0.32 (380 mg). Acetylation of the former, R_F 0.45, followed by p.l.c. separation [1,2-dichloroethane–acetone (9 : 1 v/v), × 2] at 5.5 mg per plate gave two products at R_F 0.53 and 0.46.

(2R,3S)-2,3-trans-3-*Acetoxy*-6-[(2S,3R,4R)-2,3-*trans*-3,4-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-8-[(2S,3R,4S)-2,3-trans-3,4-cis-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3′,4′,5,7-*tetramethoxyflavan* (18). The *decamethyl ether triacetate*, R_F 0.53, was isolated as a solid (114 mg) (Found: C, 66.3; H, 5.8%; *m/z* 1 100 (M^+, 2.2%); δ(80 MHz; [$^2H_6$]DMSO; 170 °C) 7.21—6.39 (m, 15 × ArH), 6.05 [t, *J* 9.5 and 9.5 Hz, 3-H(I)], 5.61 [t, *J* 8.0 and 8.0 Hz, 3-H(C)], 5.18 [d, *J* 8.0 Hz, 2-H(C), 5.07 [m, 3-H(F)], 5.02 [d, *J* 9.5 Hz, 2-H(I)], 5.00 [d, *J* 8.0 Hz, 2-H(F)], 4.92 [d, *J* *ca.* 8.0 Hz, 4-H(C)], 4.83 [d, *J* 9.5 Hz, 4-H(I)], 3.81 (× 2), 3.78, 3.77, 3.74 (× 2), 3.71, 3.68, 3.55, and 3.39 (each s, together 10 × OCH$_3$), 3.08—2.83 [m, 4-H$_2$(F)], 1.88 [s, 3-COCH$_3$(F)], and 1.62 [s, 2 × 3-COCH$_3$ (C and I)]; c.d. (Figure 2).

(2R,3S)-2,3-trans-3-*Acetoxy*-6-[(2S,3R,4S)-2,3-trans-3,4-cis-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-8-[(2S,3R,4R)-2,3-trans-3,4-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3′,4′,5,7-*tetramethoxyflavan* (16). The *decamethyl ether triacetate*, R_F 0.46, was isolated as a solid (123 mg) (Found: C, 66.6; H, 6.1%); *m/z* 1 100 (M^+, 1.4%); δ(80 MHz; [$^2H_6$]DMSO; 170 °C) 7.13—6.31 (m, 15 × ArH), 6.10 [t, *J* 9.5 and 9.5 Hz, 3-H(C)], 5.59 [dd, *J* 8.5 and 6.5 Hz, 3-H(I)], 5.41 [d, *J* 8.5 Hz, 2-H(I)], 5.21 [m, 3-H(F)], 4.92 [d, *J* 6.25 Hz, 2-H(F)], 4.89 [d, *J* 9.5 Hz, 2-H(C)], 4.75 [d, *J* 9.5 Hz, 4-H(C)], 4.05 [d, *J* 6.5 Hz, 4-H(I)], 3.83, 3.80, 3.79, 3.77, 3.76, 3.74, 3.71, 3.69, 3.43, and 3.34 (each s, 10 × OCH$_3$), 3.01—2.83 [m, 4-H$_2$(F)], 1.79 [s, 3-COCH$_3$(F)], and 1.65 and 1.58 [each s, 3-COCH$_3$ (C and I)]; c.d. (Figure 2).

(2R,3S)-2,3-trans-3-*Acetoxy*-6,8-*bis*-[(2S,3R,4R)-2,3-trans-3,4-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-3′,4′,5,7-*tetramethoxyflavan* (14). The methylated fraction of R_F 0.32 (380 mg) was acetylated to give the *decamethyl ether triacetate* (14) as a solid (380 mg) (Found: C, 66.3; H, 5.8%); *m/z* 1 100 (M^+, 5.2%);* δ(80 MHz; [$^2H_6$]DMSO; 170 °C) 7.25—6.28 (m, 15 × ArH), 5.98 [t, *J* 9.5 and 9.5 Hz, 3-H(C or I)], 5.95 [t, *J* 9.5 and 9.5 Hz, 3-H(I or C)], 5.16 [m, 3-H(F)], 5.02 [d, *J* 9.5 Hz, 2-H(C or I)], 4.96 [d, *J* 9.5 Hz, 2-H (I or C)], 4.82 [d, *J* 9.5 Hz, 4-H(C or I)], 4.75 [d, *J* 9.5 Hz, 4-H(I or C)], 4.48 [d, *J* 5.75 Hz, 2-H(F)], 3.83, 3.81, 3.80, 3.79, 3.74 (× 3), 3.70, and 3.67, (br), 3.34 (br) (each s, together 10 × OCH$_3$), 3.00—2.67 [m, 4-H$_2$(F)], 1.73 [s, 3-COCH$_3$(F)], 1.64, and 1.61 [each s, 3-COCH$_3$(C or I]; c.d. (Figure 2).

Mass fragmentation patterns of the decamethyl ether triacetates (14) (16), (18), and (20) are respectively as follows: *m/z* 1 100 (M^+, 5.2,* 1.4, 2.2, 2.2%), 1 040 (15.4, 16.9, 8.2, 14.9), 980 (8.7, 12.1, 8.8, 11.4), 920 (4.2, 5.7, 4.0, 4.8), 847 (3.7, 10.7, 7.8, 22), 787 (3.6, 7.9, 7.3, 16), 743 (2.2, 12.6, 10.7, 9.4), 727 (–, –, 2.8, 3.3), 683 (36.8, 28.3, 19.7, 20.4), 625 (–, 4.8, –, 7.2), 623 (5.9, –, 6.3, –), 565 (2.8, 3.5, 3.6, 5.8), 387 (2.1, 1.4, 1.3, 3.1), 357 (3.3, 3.4, 2.7, 5.8), 327 (2.0, 1.9, 1.4, 2.8), 297 (20.8, 21.6, 21.2, 28.1), 222 (5.1, 4.8, 3.6, 6.8), 180 (51, 71, 48, 81), and 151 (100, 100, 100, 100).

Isolation of Monomeric and Bi- and Tri-flavanoids from the Heartwood of Rhus leptodictya.—Drillings from the heartwood (600 g) of *Rhus leptodictya* collected in the Magaliesberg, Transvaal were extracted with methanol (4 × 2 l). The solution was reduced in volume (1 l) and treated with hexane (4 × 500 ml) for the removal of fats and waxes. Evaporation of the dewaxed extract left a brown solid (126 g) which was chromatographed on Sephadex LH-20 columns (5 × 120 cm) (10 g per column) with ethanol as eluant. Collection of the eluate in 15-ml fractions commenced after emergence of the first phenolic material. Every fifth tube was sampled by t.l.c. with ethyl acetate–water–formic acid (90 : 5 : 5 v/v) as developer. Evidence of the relative homogeneity of the fractions was obtained by two-way paper chromatography in water-saturated butan-2-ol and in 2% acetic acid.

The fractions were grouped as follows, and the components identified after methylation and acetylation by ^{1}H n.m.r., mass, and c.d. spectrometry by comparison with synthetic or authentic samples.

Fractions 38—62 (890 mg) consisted entirely of (−)-leucofisetinidin (1)[7] which was identified after methylation and p.l.c. separation [benzene–acetone (8 : 2 v/v), × 2] as its 3′,4′,7-

* Appearance potential at 320 °C.

trimethyl [m.p. 128—130 °C; R_F 0.35 (358 mg)] and 3′,4,4′,7-tetramethyl ether [R_F 0.41 (83 mg)].

Fractions 64—98 (524 mg) was dominated by (+)-catechin which after methylation, acetylation, and purification by p.l.c. [benzene–acetone (9 : 1 v/v)] gave the tetramethyl ether acetate [m.p. 95 °C; R_F 0.57 (237 mg)].

Fractions 102—248 (1.737 g). A portion (1.118 g) was methylated and the heptamethyl ether was purified by p.l.c. (R_F 0.35) with benzene–acetone (8 : 2 v/v) as developer (575 mg yield). Acetylation and further purification in benzene–acetone (9 : 1 v/v) gave the heptamethyl ether diacetate (R_F 0.31) of the [4,8]-2,3-*trans*-3,4-*cis*:2′,3′-*trans*-diastereoisomer, *i.e.* compound (6) (439 mg).

Fractions 249—284 (243 mg) were methylated, and the heptamethyl ether was purified by p.l.c. with benzene–acetone (7 : 3 v/v) as developer [(R_F 0.42 (124 mg)]. Acetylation and final purification with benzene–acetone (9 : 1 v/v) gave a heptamethyl ether diacetate, R_F 0.33.

(2S,3R,4R)-2,3-trans-3,4-trans-3-*Acetoxy*-4-[(2R,3R)-2,3-cis-3-*acetoxy*-3′,4′,5,7-*tetramethoxyflavan*-8-*yl*]-3′,4′,7-*trimethoxyflavan* (12). The *heptamethyl ether diacetate*, R_F 0.33, was isolated as a solid (45 mg) (Found: C, 66.0; H, 6.0. $C_{41}H_{44}O_{13}$ requires C, 66.1; H, 6.0%); *m/z* 744 (M^+, 4.3%); δ(80 MHz; [$^2H_6$]DMSO; 150 °C) 7.09—6.28 (m, 10 × ArH), 5.97 [t, $J_{2,3} = J_{3,4}$ = 9.5 Hz, 3-H(C)], 5.38 [m, 3-H(F)], 4.95 [d, $J_{3,4}$ 9.5 Hz, 4-H(C)], 4.92 [d, $J_{2,3}$ 9.5 Hz, 2-H(C)], 4.81 [br s, $J_{2,3}$ < 1 Hz, 2-H(F)], 3.81, 3.78, 3.77 (× 2), 3.76, 3.72, and 3.62 (each s, together 7 × OCH_3), 3.03 [dd, $J_{3,4}$ 9.2 Hz, 4-$H_{ax.}$(F)], 2.81 [dd, $J_{3,4}$ 6.0 Hz, 4-$H_{eq.}$(F)], 1.83 [s, 3-$COCH_3$-(F)], and 1.59 [s, 3-$COCH_3$(C)]; δ(80 MHz; $CDCl_3$; 100 °C) 6.15 [s, 6-H(D)]; c.d. (Figure 1).

Fractions 285—368 (2.223 g). A portion (1.005 g) was methylated and the heptamethyl ether was purified by p.l.c. with benzene–acetone (7 : 3 v/v) as developer [R_F 0.39 (388 mg)]. This product was acetylated and the diacetate, purified by p.l.c. with benzene–acetone (9 : 1 v/v) [R_F 0.32 (301 mg)], proved to be identical to the corresponding derivative of the [4,8]-2,3-*trans*-3,4-*trans*:2′,3′-*trans*-diastereoisomer, *i.e.* compound (4).

Fractions 369—470 (487 mg) were methylated and the heptamethyl ether [R_F 0.29 (95 mg)] purified by p.l.c. with benzene–acetone (8 : 2 v/v). Acetylation and similar purification [benzene–acetone (9 : 1 v/v)] gave the heptamethyl ether diacetate of the [4,6]-2,3-*trans*-3,4-*cis*:2′,3′-*trans*-diastereoisomer, *i.e.* compound (10), R_F 0.43 (66 mg).

Fractions 526—698 (1.143 g). Methylation of a portion (600 mg) and purification of the resultant decamethyl ether by p.l.c. with benzene–acetone (7 : 3 v/v) [R_F 0.38 (288 mg)], followed by acetylation and p.l.c. separation with benzene–acetone (8 : 2 v/v) by double development [R_F 0.58 (187 mg)], gave the decamethyl ether triacetate of the [4,6:4,8]-2,3-*trans*-3,4-*trans*:2′,3′-*trans*:2″,3″-*trans*-3″,4″-*cis*-profisetinidin, compound (18).

Fractions 699—832 (900 mg). A portion (600 mg) was methylated and the product was separated by p.l.c. with benzene–acetone (7 : 3 v/v) into two fractions, R_F 0.40 (146 mg) and 0.33 (246 mg). Both were acetylated; the former, after subsequent resolution by p.l.c. with benzene–acetone (8 : 2 v/v) [R_F 0.50 (64 mg)], gave the decamethyl ether triacetate of the [4,6:4,8]-2,3-*trans*-3,4-*cis*:2′,3′-*trans*-2″,3″-*trans*-3″,4″-*cis*-profisetinidin, compound (20). The latter methyl ether fraction, R_F 0.33, separated after acetylation by double development with benzene–acetone (8 : 2 v/v) gave the corresponding derivative [R_F 0.59 (159 mg)] of the [4,6:4,8]-2,3-*trans*-3,4-*cis*:2′,3′-*trans*:2″,3″-*trans*-3″,4″-*trans*-diastereoisomer, compound (16).

Fractions 833—1 060 (1.455 g). A portion (600 mg) was methylated and the methyl ethers were resolved by p.l.c. [benzene–acetone (7 : 3 v/v)] into two fractions at R_F 0.47 (195 mg) and 0.28 (190 mg). The former, after acetylation and purification with benzene–acetone (8 : 2 v/v), gave the heptamethyl ether diacetate [R_F 0.58 (55 mg)] of the [4,6]-2,3-*trans*-3,4-*trans*:2′,3′-*trans*-profisetinidin, *i.e.* compound (8). The latter methyl ether fraction, R_F 0.28, after acetylation and resolution in the same system gave the decamethyl ether triacetate [R_F 0.54 (121 mg)] of the [4,6:4,8]-2,3-*trans*-3,4-*trans*:2′,3′-*trans*:2″,3″-*trans*-3″,4″-*trans*-profisetinidin, *i.e.* compound (14).

Rhus leptodictya (mountain karee) and *Rhus lancea* (karee) are closely related species. The heartwood of the latter was shown to contain the two possible [4,8-biflavanoid profisetinidins (3) and (5), as well as three of the [4,6:4,8]-triflavanoids (13), (15), and (17), using methods similar to those applied to *S. balansae*. The minor components (7), (9), (11), and (19) in these two categories may, however, have been overlooked in *Rhus lancea*.

Syntheses

Synthesis of Biflavanoid (2S,3R)-*Profisetinidins*.—A solution of (−)-3′,4′,7-trihydroxyflavan-3,4-diol [(−)-leucofisetinidin (1)] and (+)-3,′4′,5,7-tetrahydroxyflavan-3-ol [(+)-catechin (2)] (each 870 mg, 0.003 mol) in 0.1M HCl (50 ml) was stirred at room temperature for 2 d. Extraction with ethyl acetate (4 × 300 ml) and concentration of the extract under reduced pressure gave an amorphous solid (1.56 g). Separation on Sephadex LH-20 with ethanol as eluant gave four main fractions from combinations of minor fractions (*ca.* 7 ml each) as monitored by t.l.c.: Fractions I (fractions 75—120; 311 mg), II (fractions 140—195; 457 mg), III (fractions 210—240; 49 mg), and IV (fractions 320—375; 98 mg).

[4,8]-2,3-trans-3,4-cis:2′,3′-trans-*Heptamethyl ether diacetate* (6). Methylation of the free-phenolic fraction I [(200 mg), R_F 0.26 in benzene–acetone–methanol (6 : 3 : 1 v/v)] followed by p.l.c. separation [benzene–acetone (4 : 1 v/v)] gave a single heptamethyl ether, R_F 0.32 (94 mg). Acetylation gave the diacetate (6) identical with the corresponding product derived from *S. balansae*, *R. leptodictya*, and *R. lancea*.

[4,8]-2,3-trans-3,4-trans:2′,3′-trans-*Heptamethyl ether diacetate* (4). Methylation of the free-phenolic fraction II [(300 mg), R_F 0.20 in benzene–acetone–methanol (6 : 3 : 1 v/v)] followed by p.l.c. separation [benzene–acetone (4 : 1 v/v)] gave the heptamethyl ether, R_F 0.21 (155 mg). Acetylation gave the diacetate (4) identical with samples derived from *S. balansae*, *R. leptodictya*, and *R. lancea*.

[4,6]-2,3-trans-3,4-cis:2′,3′-trans-*Heptamethyl ether diacetate* (10). Methylation of the free-phenolic fraction III [(49 mg), R_F 0.29 in benzene–acetone–methanol (6 : 3 : 1 v/v)] followed by p.l.c. separation [benzene–acetone (4 : 1 v/v)] gave the heptamethyl ether, R_F 0.34 (17 mg). Acetylation gave the diacetate (10) (18 mg) identical with samples derived from *S. balansae* and *R. leptodictya*.

Methylation of fraction IV (98 mg) followed by p.l.c. separation [benzene–acetone (7 : 3 v/v)] gave a product [R_F 0.28 (36 mg)] which comprised the decamethyl ethers of two triflavanoids. Acetylation and p.l.c. separation [1,2-dichloroethane–acetone (19 : 1 v/v), × 4] gave the corresponding triacetates at R_F 0.34 and 0.24.

[4,6:4,8]-2,3-trans-3,4-cis:2′,3′-trans:2″,3″-trans-3″,4″-trans-*Decamethyl ether triacetate* (16). The R_F 0.34 fraction (10 mg) was isolated as a solid identical with samples derived from *S. balansae*, *R. leptodictya*, and *R. lancea*.

[4,6:4,8]-2,3-trans-3,4-trans:2′,3′-trans:2″,3″-trans-3″,4″-cis-*Decamethyl ether triacetate* (18). The R_F 0.24 fraction (13 mg) was obtained as a solid identical with samples derived from *S. balansae* and *R. leptodictya*.

Synthesis of [4,8]-(+)-*fisetinidol*-(−)-*epicatechin*.—A solution of (−)-leucofisetinidin (1) (435 mg, 1.5 mmol) and (−)-epicatechin (870 mg, 3 mmol) in 0.1M HCl (120 ml) was stirred at ambient temperature under nitrogen. After 24 h the reaction was complete as monitored by t.l.c. [benzene–acetone–methanol (5 : 4 : 1 v/v)]. Extraction of the solution with ethyl acetate (5 × 100 ml) gave a phenolic product (1.34 g) which was methylated with diazomethane and subsequently separated by p.l.c. [benzene–acetone (7 : 3 v/v)] into three fractions, R_F 0.68 (395 mg), 0.47 (118 mg), and 0.41 (500 mg).

[4,8]-2,3-trans-3,4-trans:2′,3′-cis-*Heptamethyl ether diacetate* (12). The R_F 0.41 fraction was acetylated and after p.l.c. separation [benzene–acetone (8 : 2 v/v)] afforded the diacetate as a solid, R_F 0.59 (245 mg), identical with the compound derived from *R. leptodictya*.

The R_F 0.47 fraction represented the methyl ether of the [4,8]-3,4-*cis*-isomer contaminated with the above [4,8]-3,4-*trans*-diastereoisomer, while the R_F 0.68 fraction was the tetramethyl ether of (−)-epicatechin, m.p. 154 °C.

Synthesis of 'Angular' Triflavanoid (2S,3R)-*Profisetinidins*.—A solution of (−)-leucofisetinidin (1) (1.54 g, 0.006 mol) and (+)-catechin (2) (879 mg, 0.003 mol) in 0.1M HCl (75 ml) was stirred at room temperature for 5 d. Extraction with ethyl acetate (4 × 300 ml) and evaporation under reduced pressure gave an amorphous solid (2.4 g). Methylation followed by p.l.c. separation [benzene–acetone (4 : 1 v/v)] at 20 mg per plate gave two products at R_F 0.25 (129 mg) and 0.19 (546 mg).

[4,6:4,8]-2,3-trans-3,4-cis:2′,3′-trans:2″,3″-trans-3″,4″-cis-*Decamethyl ether triacetate* (20). Acetylation of the decamethyl ether [R_F 0.25 (129 mg)] followed by p.l.c. separation in 1,2-dichloroethane–acetone [(92 : 8 v/v), × 2] gave the triacetate as a solid, R_F 0.39 (39 mg), with spectral properties identical with those of the corresponding derivative derived from *S. balansae* and *R. leptodictya*.

Reseparation of the methyl ether fraction, R_F 0.19 (346 mg), in 1,2-dichloroethane–acetone [(21:4 v/v), × 2] at 12 mg per plate gave two products at R_F 0.28 (76 mg) and 0.19 (97 mg). Acetylation of the fraction of R_F 0.28 and p.l.c. separation [1,2-dichloroethane–acetone (19 : 1 v/v), × 2] gave two triacetates at R_F 0.43 and 0.37.

[4,6:4,8]-2,3-trans-3,4-cis:2′,3′-trans:2″,3″-trans-3″,4″-trans-*Decamethyl ether triacetate* (16). The R_F 0.43 fraction was isolated as a non-crystalline solid (22 mg) identical with those derived from *S. balansae*, *R. leptodictya*, and *R. lancea*.

[4,6:4,8]-2,3-trans-3,4-trans:2′,3′-trans:2″,3″-trans-3″,4″-cis-*Decamethyl ether triacetate* (18). The R_F 0.37 fraction was isolated as a non-crystalline solid (16 mg) identical with samples derived from *S. balansae* and *R. leptodictya*.

The methyl ether fraction, R_F 0.19, was acetylated and the triacetate was separated by p.l.c. [1,2-dichloroethane–acetone (94 : 6 v/v), × 2] to give a single product, R_F 0.16.

[4,6:4,8]-2,3-trans-3,4-trans:2′,3′-trans:2″,3″-trans-3″,4″-trans-*Decamethyl ether triacetate* (14). The decamethyl ether triacetate, R_F 0.16, was isolated as a solid (43 mg) with spectra identical with those of samples derived from *S. balansae*, *R. leptodictya*, and *R. lancea*.

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