Oligomeric Flavanoids. Part 4.† Base-catalysed Conversions of (−)-Fisetinidol-(+)-catechin Profisetinidins with 2,3-*trans*-3,4-*cis*-Flavan-3-ol Constituent Units

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Additional novel members of the class of natural 'phlobaphene' condensed tannins, representing the products of C-ring isomerization of 2,3-*trans*-3,4-*cis*-(−)-fisetinidol units present in (4β,6)- and (4β,8)-biflavanoid profisetinidins have been characterized. These comprise the functionalized 8,9-*trans*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromenes (**2**) and (**11**), and 8,9-*cis*-9,10-*trans* analogue (**8**), and a 6,7-*cis*-7,8-*trans*-[2,3-*f*]-regioisomer (**27**). Analogues (**8**) and (**11**) are prototypes of a unique class of phlobatannins in which the resorcinol A- and pyrocatechol B-rings are interchanged relative to their positions in the more common isomers. Their formation represents a novel rearrangement of profisetinidins with 2,3-*trans*-3,4-*cis*-flavan-3-ol units, *e.g.* (**1**) with concomitant inversion of absolute configuration at 3-C(C), under base catalysis. The proposed structures of the natural products were confirmed by synthesis *via* base-catalysed conversion of (−)-fisetinidol-(4β,8)- and (4β,6)-(+)-catechin *O*-methyl ethers (**1**) and (**14**).

In part 3 we have demonstrated a concise approach to the synthesis of naturally occurring phlobatannins in order to establish unequivocally the structures of this new group of condensed tannins. Such a methodology involved the selective protection of the 4′-hydroxy group of (+)-catechin prior to its condensation with (+)-mollisacacidin[(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*trans*-3′,4′,7-trihydroxyflavan-3,4-diol] to give the four (−)-fisetinidol-(+)-catechin 4-*O*-methyl ethers incapable of undergoing the undesired migrations and epimerizations encountered[1] during base treatment of the 4-*O*(*E*) demethyl ethers. This approach proved invaluable for differentiation of the variety of regioisomeric phlobatannins and have now enabled us to identify the remaining analogues related to the (−)-fisetinidol-(4β,6) and (4β,8)-(+)-catechins in *Guibourtia coleosperma*[2] and *Baikiaea plurijuga*.[2]

Results and Discussion

The *trans-cis* tetrahydropyrano[2,3-*h*]-, [2,3-*g*]-, and [2,3-*f*]-chromenes derived from the (−)-fisetinidol-(4α,6) and (4α,8)-(+)-catechin profisetinidins which were described in Part 3, are accompanied in the heartwoods of *G. coleosperma* and *B. plurijuga* by a novel series of the above classes of analogues possessing *cis-trans*- and *trans-trans* relative configurations of heterocyclic C-rings. These isomers most likely originated from the (−)-fisetinidol-(4β,6) and (4β,8)-(+)-catechins (**14**) and (**1**) by appropriate isomerizations of their C-rings and include the 8,9-*cis*-9,10-*trans*- and 8,9-*trans*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromenes (**8**), (**2**), and (**11**), and a regioisomeric 6,7-*cis*-7,8-*trans*-[2,3-*f*]-analogue (**27**).

Initial identification of these analogues was accomplished by analysis of ^{1}H n.m.r. data (300 MHz) of their heptamethyl ether diacetates (**3**), (**9**), (**12**), and (**28**) which revealed the familiar absence of the effects of dynamic rotational isomerism at ambient temperatures and the n.O.e. associations of 2-OMe (A) with 3-H (A) and of 4-OMe (A) with both 3- and 5-H (A) characteristic of a resorcinol moiety being 'liberated' from the heterocyclic C-ring in the parent biflavanoid.[1] These isomers could, however, not be categorized as *e.g.* [2,3-*h*] *etc.*, since both methods previously applied *i.e.* absolute chemical shifts of 'residual' D-ring proton resonances and observation of n.O.e. associations between these and methoxy(D) protons, are less reliable than for the conventional biflavanoid derivatives. Differentiation only became possible when the full complement of the phlobatannins derived from (**1**) and (**14**) were eventually synthesized (see below).

The heptamethyl ether diacetates (**3**) and (**12**) of the *trans-trans*-tetrahydropyranochromenes (**2**) and (**11**) as well as those [(**9**) and (**28**)] of the *cis-trans* analogues (**8**) and (**27**) exhibited ^{1}H n.m.r. coupling constants (Tables 1 and 3) of heterocyclic protons consistent with such configurations of their C-rings.[3] The relatively small J values for all-*trans* arrangements reflect significant contributions of A-forms towards the conformation of their C-rings.[4]

At this stage recourse to synthesis was taken to eliminate the ambiguity surrounding the structures of the natural products. Thus, treatment of the (−)-fisetinidol-(4β,8)-(+)-catechin *O*-methyl ether (**1**) (*cf.* Part 3) with 0.025M $NaHCO_3$–0.025M Na_2CO_3 buffer (pH 10) for 3 h at 50 °C under nitrogen led to complete conversion into a mixture from which four ring-isomerized products were obtained (Scheme 1). These included the 8,9-*cis*-9,10-*trans*- and 8,9-*trans*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromenes (**7**) and (**4**) [$J_{8,9}$ *ca.* 1.0, 7.0, $J_{9,10}$ 2.0, 6.0 Hz for heptamethyl ether diacetates (**6**) and (**3**) respectively] and another pair of *cis-trans*- and all-*trans* analogues (**10**) and (**13**) [$J_{8,9}$ *ca.* 1.0, 7.0, $J_{9,10}$ 2.0, 6.0 Hz for (**9**) and (**12**) respectively] (*cf.* Table 1 for their ^{1}H n.m.r. details). Prominent n.O.e. association between 8-H (C) (δ 4.90) and 6-H (A) (δ 6.73, 5.6%) in the *cis-trans* heptamethyl ether diacetate (**6**) not only confirmed this configuration and thus differentiates it from a *cis–cis* arrangement but also indicates a preferred sofa conformation (C-ring) in which the resorcinol moiety occupies a near-axial (α) orientation.

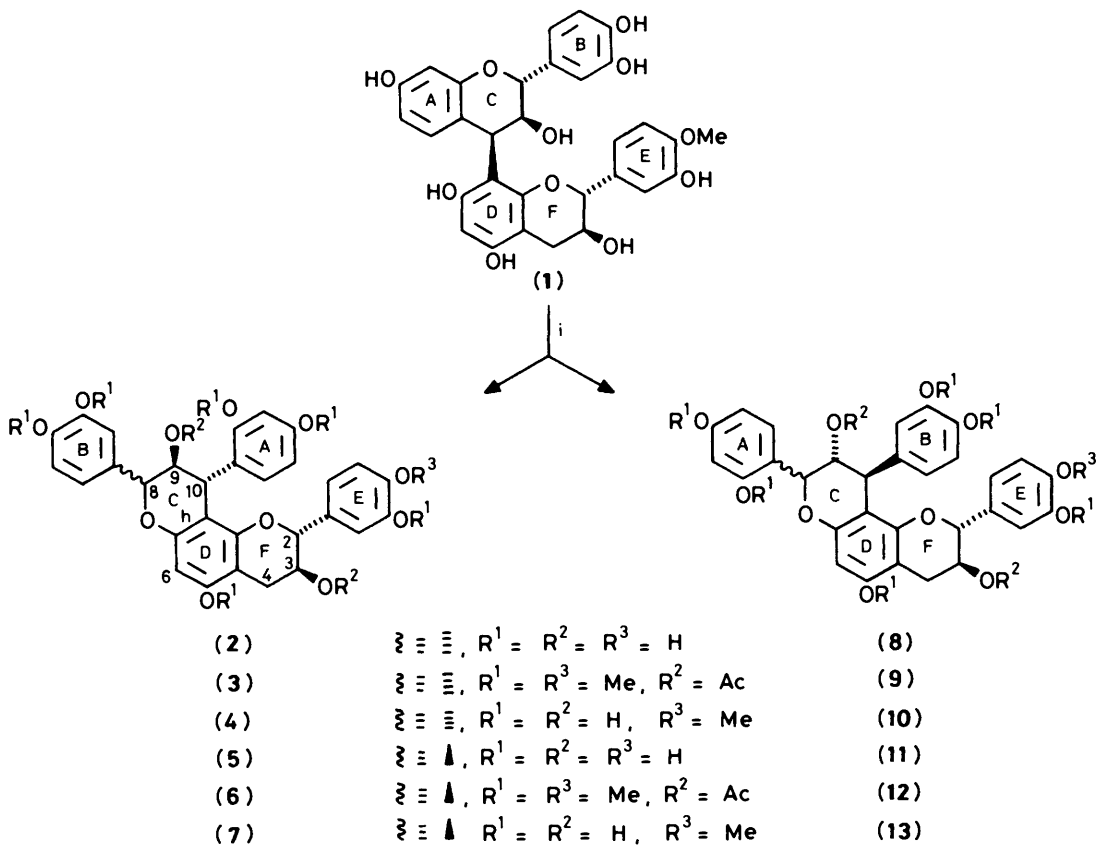
Comparison of the ^{1}H n.m.r. and c.d. data (see below) of the methyl ether acetates (**3**), (**9**), and (**12**) with those of the corresponding derivatives of the natural products proved their

† Part 3. J. P. Steynberg, J. F. W. Burger, D. A. Young, E. V. Brandt, J. A. Steenkamp, and D. Ferreira, *J. Chem. Soc., Perkin Trans. 1*, preceding paper.

Table 1. ^{1}H N.m.r. peaks (p.p.m.) of tetrahydropyrano[2,3-*h*]chromene heptamethyl ether diacetates (**3**), (**6**), (**9**), and (**12**) in $CDCl_3$ (23 °C) at 300 MHz. Splitting patterns and *J* values (Hz) are given in parentheses

Ring	Proton	(3)	(6)	(12)	(9)
A	3	6.19 (d, 2.5)	6.44 (d, 2.0)	6.19 (d, 2.5)	6.31 (d, 2.0)
	5	6.12 (dd, 2.5, 8.5)	6.41 (dd, 2.0, 8.5)	6.37 (dd, 2.5, 8.5)	6.47 (dd, 2.0, 8.5)
	6	6.46 (d, 8.5)	6.73 (d, 8.5)	7.26 (d, 8.5)	7.47 (d, 8.5)
B	2	6.76 (d, 2.0)	6.90 (d, 2.0)	} 6.40—6.45[a]	6.82 (d, 2.0)
	5	6.68 (d, 8.0)	6.76 (d, 8.5)		6.72[b] (d, 8.5)
	6	6.83 (dd, 2.0, 8.0)	6.79 (dd, 2.0, 8.5)		6.66 (dd, 2.0, 8.5)
C	8	5.03 (d, 7.0)	4.98 (br s, *ca.* 1.0)	5.36 (d, 7.0)	5.31 (d, 2.0)
	9	5.62 (dd, 6.0, 7.0)	5.38 (dd, 1.0, 2.0)	5.79 (dd, 6.0, 7.0)	5.33 (dd, 1.0, 2.0)
	10	4.47 (d, 6.0)	4.48 (d, 2.0)	4.14 (d, 6.0)	4.30 (br s, *ca.* 1.0)
D	6	6.27 (s)	6.28 (s)	6.26 (s)	6.27 (s)
E	2	6.35 (d, 2.0)	6.39 (d, 2.0)	6.57 (d, 2.0)	6.62 (d, 2.0)
	5	6.58 (d, 8.5)	6.59 (d, 8.5)	6.71 (d, 8.0)	6.75[b] (d, 8.5)
	6	6.21 (dd, 2.0, 8.5)	6.40 (dd, 2.0, 8.5)	6.54 (dd, 2.0, 8.0)	6.64 (dd, 2.0, 8.5)
F	2	4.67 (d, 8.5)	4.81 (d, 8.5)	4.47 (d, 7.0)	4.84 (d, 6.0)
	3	4.88 (m)	4.93 (m)	5.27 (m)	5.33 (m)
	$4_{ax.}$	2.58 (dd, 9.0, 17.0)	2.64 (dd, 8.0, 16.0)	2.60 (dd, 7.0, 17.0)	2.67 (dd, 6.0, 17.0)
	$4_{eq.}$	3.06 (dd, 6.0, 17.0)	3.06 (dd, 5.0, 16.0)	2.90 (dd, 6.0, 17.0)	2.84 (5.0, 17.0)
	OMe	3.49 (2-A), 3.58, 3.68 (4-A), 3.77, 3.79 (5-D), 3.80, 3.81, each s	3.54, 3.72 (2-A), 3.79 (4-A), 3.82 (5-D), 3.80, 3.83, 3.84, each s	3.59, 3.70 (2-A), 3.71, 3.72 (4-A), 3.76, 3.80 (5-D), 3.84, each s	3.50 (2-A), 3.74, 3.76 (4-A), 3.78 3.80 (5-D), 3.82, 3.84, each s
	OAc	2.32, 2.34, each s	1.89, 1.90, each s	1.83, 1.86, each s	1.88, 1.92, each s

[a] Second order. [b] Peaks may be interchanged.



Scheme. 1 Base-catalysed formation of phlobatannins from (−)-fisetinidol-(4β,8)-(+)-catechin *O*-methyl ether (**1**). *Reagents and conditions:* i, $NaHCO_3$–Na_2CO_3 (pH 10), 50 °C, 3 h, N_2

identity and thus defined these compounds as functionalized tetrahydropyrano[2,3-*h*]chromenes. The 8,9-*cis*-9,10-*trans* isomer (**5**) has, however, hitherto not been recognized in Nature.

^{1}H N.m.r. coupling constants (C-ring) for heptamethyl ether diacetates (**12**) and (**9**) ($J_{8,9}$ *ca.* 7.0, *ca.* 1.0; $J_{9,10}$ 6.0, 2.0 Hz, respectively) of the remaining 8,9-*trans*-9,10-*trans*- and 8,9-*cis*-

9,10-*trans*-tetrahyropyrano[2,3-*h*]chromenes (**11**) and (**8**) were identical with those of (**3**) and (**6**) of corresponding relative configuration. 8-H (C) (δ 5.31) furthermore exhibits prominent n.O.e. associations with 2- and 6-H of the pyrocatechol moiety in the *cis-trans* analogue (**9**) only, while 8-and 10-H (C) were correlated with, respectively, the resorcinol and pyrocatechol rings in both (**9**) and (**12**) by spin decoupling experiments using these protons as reference signals. Subject to the correct allocation of 8- and 10-H (C) resonances these features collectively indicate an interchange of the resorcinol A- and pyrocatechol B-rings in (**8**) and (**11**) relative to their positions in the 'normal' isomers (**5**) and (**2**). The chemical shifts of 8- and 10-H (C) and thus unambiguous proof for such an A-/B-ring interchange were confirmed by 2D-heteronuclear correlation of these protons with, respectively, 8- and 10-C [δ 73.3, 35.8 and δ 78.9, 29.8 for (**9**) and (**12**) respectively]. A similar strategy was also adopted to confirm the chemical shifts of 8- and 10-H (C) resonances in (**3**) and (**6**).

Notable in the spectra of the groups (**3**), (**6**), and (**12**), (**9**) is the conspicuous deshielding of 6-H (A) [Δδ −0.74 and −0.80 for (**9**) and (**12**) respectively] in the latter pair relative to its chemical shift in the *cis-trans*-and all-*trans* isomers (**6**) and (**3**). Such a feature is apparently characteristic of phlobatannins belonging to the classes (**8**) and (**11**) (see also below).

In order to establish the sequence of formation of the phlobatannins (**4**), (**7**), (**10**), and (**13**) from the (4β,8)-biflavanoid (**1**) (Scheme 1) aliquots were taken at regular intervals and fully analysed by column chromatography using Sephadex LH-20/ethanol. After 30 min the starting material is accompanied by small amounts of the ring-interchanged *cis-trans* isomer (**10**) (overlapped by starting material on t.l.c.) while after 90 min the two *cis-trans* analogues (**7**) and (**10**) (*ca.* 1:1 ratio) are present in significant proportions relative to that of the 'normal' *trans-trans* homologue (**4**). These three compounds are accompanied by low quantities of the all-*trans* isomer (**13**) with interchanged A- and B-rings after 3 h. The latter compound is also overlapped by starting material on t.l.c. which hampered conclusions regarding its formation. Owing to complications in purifying this isomer in the phenolic form, it was identified as heptamethyl ether diacetate (**12**). ^{1}H N.m.r. details for (**4**), (**7**), and (**10**) are given in Table 2 representing the first detailed analysis of phenolic oligoflavanoids at 'dimeric' level thus demonstrating the usefulness of Sephadex LH-20/Fractogel TSK HW-40(S) as effective chromatographic substrates for this class of natural products.

The above results indicated that the (−)-fisetinidol-(4β,8)-(+)-catechin (**1**) served as direct precursor to both groups of phlobatannins (**4**), (**7**), and (**10**), and (**13**). Formation of the former pair may be rationalized by stereoselective recyclization involving 7-OH (D) and both *Re* and *Si* faces in quinone-methide (**33**) (Scheme 3). In the preferred sofa conformations[4] of the *cis-trans* isomer (**7**) one of the A- or B-rings invariably approaches an axial orientation thus rendering this configuration thermodynamically less stable than the 8,9-*trans*-9,10-*trans* analogue (**4**) where both these rings may attain equatorial positions. The latter compound could then originate from the *cis-trans* isomer *via* epimerization at C-8. Treatment of the *cis-trans* compound (**7**) under conditions similar to those for its formation did, however, not give equilibration with the all-*trans* analogue (**4**) indicating their simultaneous genesis from the (4β,8)-biflavanoid (**1**). The observed stereoselectivity contrasts with stereospecific transformation of the 2,3-*trans*-3,4-*trans*-flavan-3-ol unit in (−)-fisetinidol-(4α,8)-(+)-catechin under similar conditions (*cf.* Part 3).

The novel conversion (**1**) ⟶ (**10**) + (**13**) is presumably explicable in terms of initial migration of the 'lower' flavanyl moiety to the *Re*-face at 2-C in quinone-methide (**33**) (Scheme 3). Stereoselective pyran recyclization of (**34**) *via* 7-OH (D) generates the tetrahydropyrano[2,3-*h*]chromenes (**10**) and (**13**) enantiomerically related to (**7**) and (**4**) with respect to their C-rings.

Table 2. ^{1}H N.m.r. peaks (p.p.m.) of tetrahydropyrano[2,3-*h*]chromene mono-*O*-methyl ethers (**7**), (**4**), and (**10**) in $(CD_3)_2CO$ (23 °C) at 300 MHz. Splitting patterns and *J* values (Hz) are given in parentheses

Ring	Proton	(7)	(4)	(10)
A	3	6.42 (d, 2.5)	6.37 (d, 2.5)	6.28 (d, 2.5)
	5	6.32 (dd, 2.5, 8.0)	6.32 (dd, 2.5, 8.5)	6.24 (dd, 2.5, 8.5)
	6	6.60 (d, 8.0)	6.55 (d, 8.5)	6.92 (d, 8.5)
B	2	6.93 (d, 2.0)	6.76,[b] 6.90[b]	6.56 (d, 2.0)
	5	6.73 (d, 8.0)		6.66 (d, 8.0)
	6	6.63 (dd, 2.0, 8.0)		6.44 (dd, 2.0, 8.0)
C	8	4.77 (br s, *ca.* 1.0)	4.43 (d, 9.5)	4.91 (br s, *ca.* 1.0)
	9	4.03 (dd, 1.0, 2.5)	3.90 (dd, 8.0, 9.5)	4.16 (dd, 1.0, 2.0)
	10	4.52 (d, 2.5)	4.23 (d, 8.0)	4.27 (d, 2.0)
D	6	6.14 (s)	6.10 (s)	6.10 (s)
E	2	6.60 (d, 2.0)	6.48 (d, 2.0)	6.81 (d, 2.0)
	5	6.64 (d, 8.5)	6.64 (d, 8.5)	6.79 (d. 8.0)
	6	6.29 (dd, 2.0, 8.5)	5.93 (dd, 2.0, 8.5)	6.68 (dd, 2.0, 8.0)
F	2	4.62 (d, 7.5)	4.42 (d, 8.5)	4.47 (d, 7.5)
	3	3.73 (m)	3.52 (m)	3.94 (m)
	$4_{ax.}$	*a*	*a*	2.57 (dd, 8.0, 16.0)
	$4_{eq.}$	*a*	*a*	2.90 (dd, 5.5, 16.0)
OMe		3.76 (s)	3.77 (s)	3.78 (s)

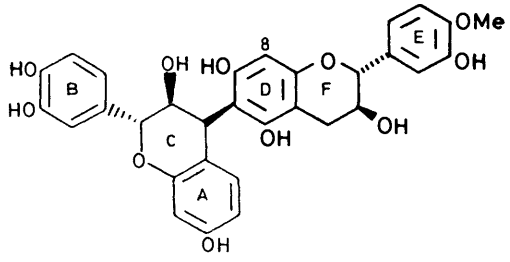
[a] Overlapped by DOH peak. [b] Second order.

The heptamethyl ether diacetates of the 'normal' analogues (**4**) and (**7**) exhibit intense negative Cotton effects in the 220—240 nm region of their c.d. spectra. These indicate a 10-C aryl substituent below the plane of the C/D-ring system[5] and thus *R*-absolute configuration at this chiral centre. When taken in conjunction with ^{1}H n.m.r. coupling constants the c.d. data define the absolute configurations as 2*R*,3*S*:8*S*,9*S*,10*R* for (**6**) and 2*R*,3*S*:8*R*,9*S*,10*R* for (**3**). The same derivatives of the ring interchanged analogues (**10**) and (**13**) showed similar c.d. characteristics to those above, thus apparently reflecting a similar 9*S*,10*R* absolute configuration for ring C. Such a contradiction results from significant contributions of A-conformers[4] (F-ring) reversing the sign of the low-wavelength Cotton effect for 8,9-*cis*-9,10-*trans*-tetrahydropyrano[2,3-*h*]-chromenes with 10β-aryl substituents. This is confirmed in a comparative study of analogues derived from the quasi-enantiomeric (+)-fisetinidol-(4α,8)-(+)-catechin* and thus enable definitions of absolute configurations as 2*R*,3*S*:8*R*,9*R*,10*S* for (**10**) and 2*R*,3*S*:8*S*,9*R*,10*S* for (**13**).

The *cis-trans* isomer (**10**), like (**7**), does not equilibrate to either of the accompanying phlobatanins (**4**), (**7**), and (**13**) thus providing additional proof for biflavanoid (**1**) being their common precursor.

Base treatment of the (−)-fisetinidol-(4β,6)-(+)-catechin *O*-methyl ether (**14**) afforded a mixture from which six ring-isomerized products (**17**), (**20**), (**23**), (**26**), (**29**), and (**32**) were obtained (Scheme 2). Since the biflavanoid (**14**) is produced in lowest yield during coupling of (+)-mollisacacidin and the 4′-*O*-methyl ether of (+)-catechin, lack of material necessitated

* J. F. W. Burger, J. P. Steynberg, D. A. Young, E. V. Brandt, and D. Ferreira, *J. Chem. Soc., Perkin Trans. 1*, 1989, in the press.



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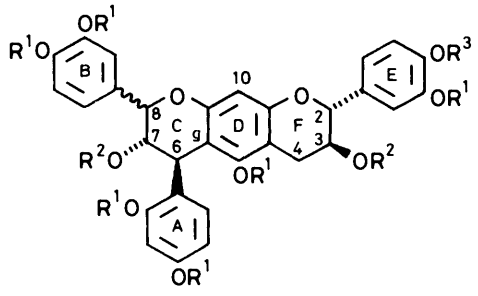
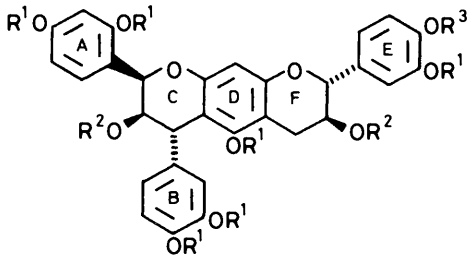
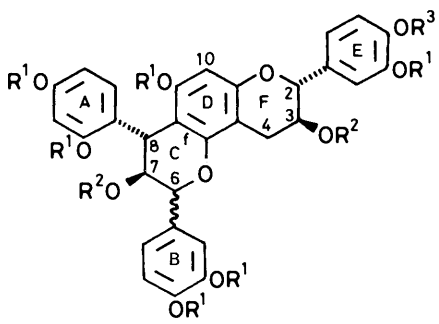


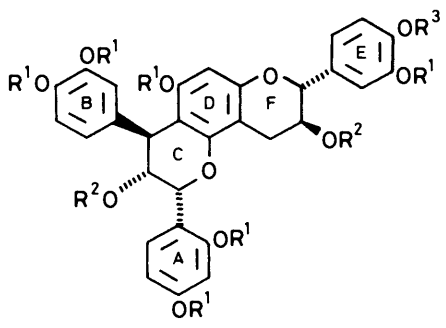
(15) ⦚ = ⦚ , $R^1 = R^2 = R^3 = H$
(16) ⦚ = ⦚ , $R^1 = R^3 = Me$, $R^2 = Ac$
(17) ⦚ = ⦚ , $R^1 = R^2 = H$, $R^3 = Me$
(18) ⦚ = ▮ , $R^1 = R^2 = R^3 = H$
(19) ⦚ = ▮ , $R^1 = R^3 = Me$, $R^2 = Ac$
(20) ⦚ = ▮ , $R^1 = R^2 = H$, $R^3 = Me$



(21) $R^1 = R^2 = R^3 = H$
(22) $R^1 = R^3 = Me$, $R^2 = Ac$
(23) $R^1 = R^2 = H$, $R^3 = Me$



(24) ⦚ = ⦚ , $R^1 = R^2 = R^3 = H$
(25) ⦚ = ⦚ , $R^1 = R^3 = Me$, $R^2 = Ac$
(26) ⦚ = ⦚ , $R^1 = R^2 = H$, $R^3 = Me$
(27) ⦚ = ▮ , $R^1 = R^2 = R^3 = H$
(28) ⦚ = ▮ , $R^1 = R^3 = Me$, $R^2 = Ac$
(29) ⦚ = ▮ , $R^1 = R^2 = H$, $R^3 = Me$



(30) $R^1 = R^2 = R^3 = H$
(31) $R^1 = R^3 = Me$, $R^2 = Ac$
(32) $R^1 = R^2 = H$, $R^3 = Me$

Scheme 2. Base-catalysed formation of phlobatannins from (−)-fisetinidol-(4β,6)-(+)-catechin *O*-methyl ether (**14**). *Reagents and conditions:* i, $NaHCO_3$–Na_2CO_3 (pH 10), 50 °C, 3 h, N_2

characterization of the above phlobatannins as their hepta-methyl ether diacetates (**16**), (**19**), (**22**), (**25**), (**28**), and (**31**) (^{1}H n.m.r. data-Tables 3 and 4). Amongst these the expected 6,7-*cis*-7,8-*trans*-tetrahydropyrano[2,3-*f*]chromene (**29**) [$J_{6,7}$ *ca.* 1.0, $J_{7,8}$ 2.0 Hz for (**28**)] and the 7,8-*cis*-6,7-*trans*[2,3-*g*] regioisomer (**17**) [$J_{7,8}$ *ca.* 1.0, $J_{6,7}$ 2.0 Hz for (**16**)], formed in equal proportions, were differentiated by the selective n.O.e. association of 10-H (D) (δ 6.18) with 9-OMe (D) (δ 3.57, 16.1%) in (**28**) but absence of association of the residual D-ring proton (δ 6.52) with methoxy hydrogens in (**16**). The typical n.O.e. effect of 8-H (C) [for (**16**)] or 6-H (D) [for (**28**)] with 6-H (A), demonstrated above for *cis-trans* configurations, were again observed for both (**16**) and (**28**). Analogous n.O.e. associations between the D-ring singlet [δ 6.15, 6.47 for (**25**) and (**19**)

Table 3. ^{1}H N.m.r. peaks (p.p.m.) of tetrahydropyrano[2,3-*g*]chromene heptamethyl ether diacetates (**16**), (**19**), and (**22**) in $CDCl_3$ (23 °C) at 300 MHz. Splitting patterns and *J* values (Hz) are given in parentheses

Ring	Proton	(16)	(19)	(22)
A	3	6.51 (d, 2.0)	6.37 (d, 2.5)	6.30 (d, 2.5)
	5	6.39 (dd, 2.0, 8.5)	6.25 (dd, 2.5, 8.5)	6.47 (dd, 2.5, 8.5)
	6	6.72 (d, 8.5)	6.67 (d, 8.5)	7.43 (d, 8.5)
B	2	*a*	6.82 (d, 2.0)[b]	6.89 (d, 2.0)
	5	6.76—6.77 and 6.83—6.87	6.73 (d, 8.5)[b]	6.78, (d, 8.5)
	6		6.88 (dd, 2.0, 8.5)[b]	6.63 (dd, 2.0, 8.5)
C	6	4.66 (d, 2.0)	4.63 (d, 7.0)	4.36 (d, 20)
	7	5.35 (dd, 1.0, 2.0)	5.56 (dd, 7.0, 8.0)	5.26 (dd, 1.0, 2.0)
	8	5.05 (br s, *ca.* 1.0)	4.92 (d, 8.0)	5.41 (br s, *ca.* 1.0)
D	10	6.52 (s)	6.47 (s)	6.54 (s)
E	2	6.93 (d, 2.0)	6.89 (d, 2.0)[b]	6.92 (d, 2.0)
	5	6.85 (d, 8.0)	6.83 (d, 8.0)[b]	6.88 (d, 8.0)
	6	6.96 (dd, 2.0, 8.0)	6.93 (dd, 2.0, 8.0)[b]	6.93 (dd, 2.0, 8.0)
F	2	4.95 (d, 8.0)	4.93 (d, 8.0)	5.08 (d, 6.5)
	3	5.30 (m)	5.26 (m)	5.37 (m)
	$4_{ax.}$	2.74 (dd, 8.0, 15.0)	2.72 (dd, 8.0, 16.0)	2.77 (dd, 6.5, 16.0)
	$4_{eq.}$	3.11 (dd, 5.5, 15.0)	2.96 (dd, 5.5, 16.0)	2.93 (dd, 5.0, 16.0)
	OMe	3.30 (5-D), 3.79 (4-A), 3.82, 3.83, 3.87 (×2), 3.89 (2-A), each s	3.25 (5-D), 3.71 (4-A), 3.80 (×2), 3.82 3.85, 3.86, each s	3.33 (5-D), 3.50 (2-A), 3.76 (4-A), 3.84, 3.85, 3.86 (×2), each s
	OAc	1.89, 1.90, each s	1.79, 1.88, each s	1.87, 1.96, each s

[a] Second order. [b] Since the 8-H (C) and 2-H (F) resonances overlap, spin systems of the B- and E-rings may be interchanged.

Table 4. ^{1}H N.m.r. peaks (p.p.m.) of tetrahydropyrano[2,3-*f*]chromene heptamethyl ether diacetates (**25**), (**28**), and (**31**) in $CDCl_3$ (23 °C) at 300 MHz. Splitting patterns and *J* values (Hz) are given in parentheses

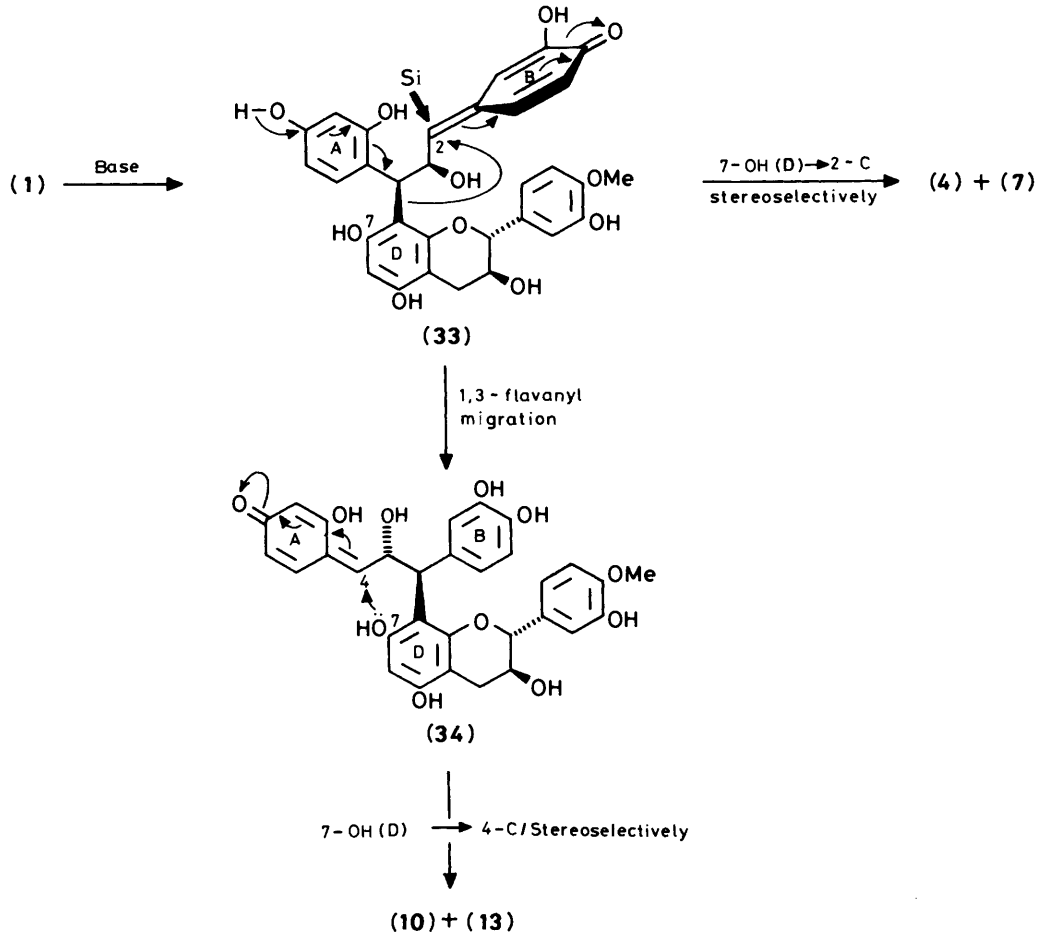
Ring	Proton	(25)	(28)	(31)
A	3	6.30 (d, 2.5)	6.50 (d, 2.5)	6.30 (d, 2.0)
	5	5.98 (dd, 2.5, 8.5)	6.34 (dd, 2.5, 8.5)	6.46 (dd, 2.0, 8.5)
	6	6.23 (d, 8.5)	6.59 (d, 8.5)	7.43 (d, 8.5)
B	2	6.63 (d, 2.0)	6.83 (d, 2.0)	6.89 (d, 2.0)
	5	6.60 (d, 8.0)	6.76 (d, 8.0)	6.78 (d, 8.0)
	6	6.69 (dd, 2.0, 8.0)	6.80 (dd, 2.0, 8.0)	6.64 (dd, 2.0, 8.0)
C	6	5.12 (d, 6.0)	4.93 (br s, *ca.* 1.0)	5.28 (br s, *ca.* 1.0)
	7	5.65 (dd, 5.0, 6.0)	5.43 (dd, 1.0, 2.0)	5.32 (dd, 1.0, 2.0)
	8	4.46 (d, 5.0)	4.51 (d, 2.0)	4.29 (d, 2.0)
D	10	6.15 (s)	6.18 (s)	6.18 (s)
E	2	6.93 (d, 2.0)	6.95 (d, 2.0)	6.95 (d, 2.0)
	5	6.85 (d, 8.0)	6.85 (d, 8.0)	6.86 (d, 8.0)
	6	6.96 (dd, 2.0, 8.0)	6.97 (dd, 2.0, 8.0)	6.99 (dd, 2.0, 8.0)
F	2	5.02 (d, 7.5)	5.00 (d, 8.0)	4.97 (d, 8.0)
	3	5.48 (m)	5.40 (m)	5.43 (m)
	$4_{ax.}$	2.80 (dd, 7.5, 16.0)	2.80 (dd, 8.0, 16.0)	2.76 (dd, 8.0, 16.0)
	$4_{eq.}$	3.13 (dd, 5.5, 16.0)	3.18 (dd, 5.5, 16.0)	3.21 (dd, 6.0, 16.0)
	OMe	3.43 (9-D), 3.67 (4-A), 3.69, 3.78, 3.80 (2-A), 3.86, 3.88, each s	3.57 (9-D), 3.79 (4-A), 3.82, 3.83, 3.87, 3.88, 3.89 (2-A), each s	3.49 (2-A), 3.59 (9-D), 3.75 (4-A), 3.85, 3.86, 3.87, 3.88, each s
	OAc	1.92, 1.93, each s	1.90, 1.92, each s	1.86, 1.92, each s

respectively] and methoxy protons of this ring also facilitated differentiation of the all-*trans* [2,3-*f*]-(**26**) [$J_{6,7}$ 6.0, $J_{7,8}$ 5.0 Hz for (**25**)] and [2,3-*g*]-(**20**) [$J_{7,8}$ 8.0, $J_{6,7}$ 7.0 Hz for (**19**)] regioisomers.

^{1}H N.m.r. data for the remaining pair of *cis-trans* tetrahydropyrano[2,3-*f*]-(**32**) [$J_{6,7}$ *ca.* 1.0, $J_{7,8}$ 2.0 Hz for (**31**)] and [2,3-*g*]-(**23**) [$J_{6,7}$ 2.0, $J_{7,8}$ *ca.* 1.0 Hz for (**22**)] chromenes, again differentiated by the appropriate n.O.e. effects, indicated the conspicuous deshielding of 6-H (A) [$\Delta\delta$ −0.84, −0.71 for (**31**) and (**22**) respectively relative to those of the *cis-trans* pair (**28**) and (**16**)] associated with analogues where interchange of the resorcinol A- and pyrocatechol B-rings had occurred (see above). Such a ring interchange was again confirmed by the relevant spin decoupling- and HETCORR experiments. The anticipated *trans-trans* regioisomers with interchanged A- and B-rings, presumably formed as minor compounds may have been overlooked due to the small quantities of available starting biflavanoid (**14**). Amongst the phlobatannins derived from the (−)-fisetinidol-(4β,6)-(+)-catechin (**14**) only the 6,7-*cis*-7,8-*trans*-tetrahydropyrano[2,3-*f*]chromene derivative (**28**) corresponds to the heptamethyl ether diacetate of the natural product from *G. coleosperma*. Despite the low concentrations of the parent biflavanoid type (**14**) in Nature the remaining phlobatannin analogues (**15**), (**18**), (**21**), (**24**), and (**30**) will, no doubt, eventually also be encountered in the sources presently being investigated. The main stream of phlobatannins derived from the (4β,6)- and (4β,8)-biflavanoids (**1**) and (**14**) is accompanied by small amounts of hitherto unidentified substances which will be dealt with elsewhere.

Negative Cotton effects in the 220—240 nm region of the c.d. spectra of the heptamethyl ether diacetates of the tetrahydropyrano[2,3-*g*]chromenes (**16**) and (**19**) are in accord with the 2*R*,3*S*:6*R*,7*S*,8*S* absolute configuration for (**16**) and 2*R*,3*S*:6*R*,7*S*,8*R* for (**19**). Positive Cotton effects in the same region for the ring-interchanged [2,3-*g*] and [2,3-*f*] regioisomers (**22**) and (**31**) similarly define their absolute configurations as 2*R*,3*S*:6*S*,7*R*,8*S* for (**22**) and 2*R*,3*S*:6*R*,7*R*,8*S* for (**31**) thus giving credence to the phenomenon of ring-interchange being associated with inversion of the absolute configuration at the equivalent of 3-C (C) of the starting biflavanoid. C.d. data in the corresponding region for the tetrahydropyrano[2,3-*f*]chromene derivatives (**25**) and (**28**) are, however, less reliable presumably due to the proximity of the 8-C aryl substituent to the plane perpendicular to the D-ring through benzylic 8-C in conformations compatible with ^{1}H n.m.r. coupling constants. The proposed 2*R*,3*S*:6*R*,7*S*,8*R* absolute configuration for (**25**) and 2*R*,3*S*:6*R*,7*S*,8*R* for (**28**) are thus based on ^{1}H n.m.r. coupling constants and assumption of a mechanism (*cf.* Scheme 3) for their formation prescribing retention of the configuration at 3-C (C) of biflavanoid (**14**).

The aforementioned results demonstrate the similarity of the behaviour of the (4β,6)-biflavanoid (**14**) under base catalysis compared with that for the (4β,8)-isomer (**1**), *i.e.* stereoselective C-ring isomerization to phlobatannins (**17**), (**20**), (**26**), and (**29**), and also its suceptibility to rearrangement to analogues (**23**) and (**32**) with interchanged A- and B-rings. The latter feature also indicates the general applicability of such a conversion in



Scheme 3. Proposed route to the formation of A-/B-ring interchanged phlobatannins (**10**) and (**13**)

profisetinidins with 2,3-*trans*-3,4-*cis*-flavan-3-ol 'upper' units. The natural occurrence of a variety of the synthetic phlobatannins presumably reflects on mechanisms in Nature similar to those proposed here for their base-catalysed formation. The necessity of a synthetic approach to define the structures of naturally occurring phlobatannins unambiguously is now firmly established.

Since the majority of the industrial applications of condensed tannins involve their dissolution/and or reactions at alkaline pH,[6,7] the results described here may have direct bearing on the increasing demand for this class of natural products.

Experimental

^{1}H N.m.r. spectra were recorded on a Bruker AM-300 spectrometer in $CDCl_3$ with Me_4Si as internal standard. Mass spectral data were obtained with a Kratos MS80 instrument and c.d. data in methanol on a Jasco J-20 spectropolarimeter. Preparative plates (p.l.c.), 20 × 20 cm, Kieselgel PF_{254} (1.0 mm) were air-dried and used without prior activation. Column chromatography was on Sephadex LH-20 and Fractogel TSK HW-40(S) in columns of various sizes and at differing flow rates (to be specified in each instance) in ethanol. Methylations were performed with an excess of diazomethane in methanol–diethyl ether at −15 °C for 48 h, while acetylations were in acetic anhydride–pyridine at ambient temperatures. Evaporations were done under reduced pressure at *ca.* 60 °C in a rotary evaporator.

Phlobatannins from Guibourtia coleosperma.—The following novel phlobatannins possessing *trans-trans-* and *cis-trans-*configurations of their C-rings were obtained from the heartwood of *G. coleosperma* and identified as heptamethyl ether diacetates (*cf.* Part 3 for experimental details): (2R, 3S:8R,9S,10R)-3,9-*diacetoxy*-2,8-*bis*(3,4-*dimethoxyphenyl*)-10-(2,4-*dimethyoxyphenyl*)-2,3-trans-8,9-trans-9,10-trans-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3-h]*chromene* (**3**) (Found: M^+, 744.2785. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 1); c.d. $[\theta]_{290}$ 0, $[\theta]_{264}$ 3.8 × 10^4, $[\theta]_{248}$ 0, $[\theta]_{230}$ −1.2 × 10^5, $[\theta]_{223}$ −2.6 × 10^5, and $[\theta]_{217}$ 0.

(2R,3S:6S,7S,8R)-3,7-*Diacetoxy*-2,6-*bis*(3,4-*dimethoxyphenyl*)-8-(2,4-*dimethoxyphenyl*)-2,3-trans-6,7-cis-7,8-trans-3,4,7,8-*tetrahydro*-2H,6H-*pyrano*[2,3-f]*chromene* (**28**) (Found: M^+, 744.2778. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 4).

Phlobatannins from Baikiaea plurijuga.—The heartwood of *B. plurijuga* afforded the following novel phlobatannins which were again identified as their heptamethyl ether diacetates (*cf.* Part 3 for experimental details).

(2R,3S:8R,9R,10S)-3,9-*Diacetoxy*-2,10-*bis*(3,4-*dimethoxyphenyl*)-8-(2,4-*dimethoxyphenyl*)-2,3-trans-8,9-cis-9,10-trans-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3-h]*chromene* (**9**) (Found: M^+, 744.2769. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 1); c.d. $[\theta]_{286}$ 0, $[\theta]_{274}$ −4.7 × 10^4, $[\theta]_{248}$ 0, $[\theta]_{239}$ 6.8 × 10^4, $[\theta]_{233}$ 0, $[\theta]_{222}$ −7.0 × 10^5, $[\theta]_{219}$ −4.6 × 10^5, $[\theta]_{216}$ −7.5 × 10^5, and $[\theta]_{206}$ 0.

(2R,3S:8S,9R,10S)-3,9-*Diacetoxy*-2,10-*bis*(3,4-*dimethoxy-*

phenyl)-8-(2,4-*dimethoxyphenyl*)-2,3-trans-8,9-trans-9,10-trans-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3-h]*chromene* (**12**) (Found: M^+, 744.2776. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 1); c.d. $[\theta]_{290}$ 0, $[\theta]_{285}$ 3.9 × 10^4, $[\theta]_{265}$ 2.2 × 10^4, $[\theta]_{240}$ 0, $[\theta]_{227}$ −3.1 × 10^5, and $[\theta]_{218}$ −7.2 × 10^4.

Base-catalysed Conversion of (−)-*Fisetinidol*-(4β,8)-(+)-*catechin*-O-*methyl Ether* (**1**).—Biflavanoid (**1**) (718 mg) (*cf.* Part 3 for its preparation) was dissolved in 200 ml of a 0.025M Na_2CO_3–0.025M $NaHCO_3$ buffer (pH 10) and the mixture stirred under nitrogen at 50 °C for 3 h. After chilling (0 °C) and acidification (0.1M HCl) the mixture was extracted with ethyl acetate (4 × 250 ml) and the solvent removed to give a light-brown powder (660 mg). This was subjected to column chromatography (3 × 85 cm column, flow rate 1.2 ml/min, 20 ml eluant/tube, first 200 ml of eluant discarded) using Sephadex LH-20/ethanol to give the following fractions: 1 [tubes 3—8 (50 mg)], 2 [12—42 (159 mg)], 3 [43—53 (88 mg)], and 4 [54—87 (318 mg)].

Fraction 1 consisted of hitherto unidentified compounds which will be dealt with elsewhere.

Methylation of fraction 2 (159 mg) followed by p.l.c. [benzene–acetone (8:2, v/v; ×2)] afforded bands at R_F 0.58 [4 mg, 3′,4′,5,7-tetra-*O*-methyl-(+)-catechin] and R_F 0.50 (45 mg). Acetylation of the latter band gave the 8,9-*cis*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromene (**9**) with interchanged A- and B-rings as a white amorphous solid (48 mg) with physical data identical with those of the corresponding derivative of the product from *B. plurijuga*.

Fraction 3 (88 mg) was methylated and the mixture resolved by p.l.c. [benzene–acetone (85:15, v/v; ×2)] to give a methyl ether band at R_F 0.29 (15 mg). Acetylation afforded the 8,9-*trans*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromene (**12**) with interchanged resorcinol A- and pyrocatechol B-rings as a white amorphous solid (16 mg). Its physical data proved to be identical to those of the corresponding derivative of the metabolite from *B. plurijuga*.

A portion (150 mg) of fraction 4 (318 mg) was methylated and the mixture (155 mg) resolved by p.l.c. [chloroform–ethyl acetate (7:3, v/v; ×2)] to give two bands at R_F 0.49 (15 mg) and R_F 0.40 (55 mg). Acetylation of the former band afforded the 8,9-*trans*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromene (**3**) as a white amorphous solid (17 mg) with physical data identical with those of the corresponding derivative of the natural product (*G. coleosperma*).

The R_F 0.40 band (55 mg) gave (2*R*,3*S*:8*S*,9*S*,10*R*)-3,9-diacetoxy-2,8-bis(3,4-dimethoxyphenyl)-10-(2,4-dimethoxyphenyl)2,3-*trans*-8,9, *cis*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromene (**6**) as a *white amorphous solid* (58 mg) (Found: M^+, 744.2771. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 1); c.d. $[\theta]_{276}$ 0, $[\theta]_{265}$ 6.0 × 10^4, $[\theta]_{245}$ 0, $[\theta]_{226}$ −4.1 × 10^5, $[\theta]_{217}$ −5.4 × 10^5, and $[\theta]_{209}$ 0.

Sequence of formation of phlobatannins (**4**), (**7**), (**10**), *and* (**13**).—The (−)-fisetinidol-(4β,8)-(+)-catechin-*O*-methyl ether (**1**) (700 mg) was dissolved in the buffer solution (180 mg) and kept at 50 °C under nitrogen. After 30 min, 60 ml of this mixture was withdrawn and worked up as above to give 214 mg of a light-brown powder. Column chromatography on Sephadex LH-20 [3 × 85 cm column, flow rate 1.2 ml/min, 20 ml eluant/tube, first 200 ml of eluant discarded] afforded three fractions: 1 [tubes 1—12 (96 mg)], 2 [13—16 (10 mg)], and 3 [17—24 (85 mg)]. Fraction 1 consisted of starting material only (^{1}H n.m.r. evidence), fraction 2 contained a mixture of starting material and 8,9-*cis*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromene (**10**), while fraction 3 afforded a pure sample of phlobatannin (**10**) with interchanged resorcinol A- and pyrocatechol B-rings [*cf.* Table 2 for ^{1}H n.m.r. data of (**10**)]. On t.l.c. [benzene–acetone–methanol (6:3:1, v/v)] (**10**) is overlapped by starting material.

After 1.5 h a further portion (60 ml) of the reaction mixture was withdrawn and analysed by column chromatography as above to give two fractions: 1 [tubes 8—20 (53 mg)] and 2 [30—60 (68 mg)]. Fraction 1 consisted of phlobatannin (**10**). Its constitution was confirmed by comparison of the physical data of its methyl ether diacetate (**9**) with those indicated above. A portion (26 mg) of fraction 2 was subjected to p.l.c. [benzene–acetone–methanol (6:3:1, v/v; ×2)] which gave two bands at R_F 0.42 (5 mg) and R_F 0.33 (12 mg). The R_F 0.42 band consisted of the 8,9-*trans*-9,10-*trans*-tetrahydropyrano[2,3-*h*]chromene (**4**) and the R_F 0.33 band of the 8,9-*cis*-9,10-*trans* isomer (**7**) (*cf.* Table 2 for their ^{1}H n.m.r. data). These structural allocations were confirmed by methylation of the remaining portion (42 mg) of fraction 2. P.l.c. [benzene–acetone (9:1, v/v)] afforded two bands at R_F 0.45 (5 mg) and R_F 0.40 (16 mg). Acetylation of the R_F 0.45 band afforded the all-*trans* heptamethyl ether diacetate (**3**) and similar treatment of the R_F 0.40 band the *cis-trans* isomer (**6**).

After 3 h the remainder (60 ml) of the reaction mixture was worked up and chromatographed on Sephadex LH-20 as above to give the following fractions: 1 [tubes 10—17 (25 mg)], 2 [18—22 (15 mg)], 3 [25—28 (6 mg)], 4 [29—32 (10 mg)], 5 [33—38 (23.6 mg)], and 6 [39—46 (13 mg)]. Fraction 1 consisted of the ring interchanged 8,9-*cis*-9,10-*trans*-phlobatannin (**10**). In fraction 2 this isomer (**10**) was accompanied by low quantities of the all-*trans*-analogue (**13**) which was identified by comparison of the ^{1}H n.m.r. data of its heptamethyl ether diacetate (**12**) with those described in the previous section. Fraction 3 consisted of a mixture of (**10**) and the *cis-trans*-isomer (**7**) which could not be further resolved at the phenolic stage.

Fraction 4 afforded a pure sample of (**7**) (^{1}H n.m.r. data in Table 2), fraction 5 a mixture of the *cis-trans*- and *trans-trans* phlobatannins (**7**) and (**4**), and fraction 6 pure sample of (**4**). These were identified by comparison of ^{1}H n.m.r. data with those described in the previous section.

Base treatment of the cis-trans *phlobatannins* (**7**) *and* (**10**). Phlobatannins (**7**) and (**10**) (20 mg each) were separately treated with base (5 ml of the buffer solution) for 3 h at 50 °C under N_2 and the reaction mixtures worked up as above. ^{1}H N.m.r. analysis indicated stability of both isomers to isomerization to the accompanying analogues (**4**) and (**13**), or of (**7**)⇌(**10**). Compound (**10**) is, however, susceptible to conversion into very small quantities of a non-mobile component on t.l.c. [benzene–acetone–methanol (6:3:1, v/v)] which is presumably related to the unidentified analogues encountered in the base treatment of biflavanoids (**1**) and (**14**) (*cf.* Discussion).

Base-catalysed conversion of (−)-*fisetinidol*-(4β,6)-(+)-*catechin*-O-*methyl ether* (**14**). Biflavanoid (**14**) (855 mg) (*cf.* Part 3 for its preparation) was treated with the buffer solution (200 ml) at 50 °C for 3 h, worked up and the mixture resolved by column chromatography as was described above for the (4β,8)-isomer (**1**). The following fractions were obtained: 1 [tubes 2—18 (266 mg)], 2 [19—54 (364 mg)], and 3 [55—75 (52 mg)].

A portion (100 mg) of fraction 1 was methylated and the mixture purified by p.l.c. [benzene–acetone (8:2, v/v; ×2)] to give a methyl ether band at R_F 0.42 (31 mg). Subsequent acetylation afforded (2*R*,3*S*:6*R*,7*R*,8*S*)-3,7-diacetoxy-2,8-bis(3,4-dimethoxyphenyl)-6-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-3,4,7,8-tetrahydro-2H,6*H*-pyrano[2,3-*f*]-chromene (**31**) as a *white amorphous solid* (35 mg) (Found: M^+, 744.2774. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 4).

Methylation of a portion (200 mg) of fraction 2 followed by p.l.c. [benzene–acetone (8:2, v/v; ×3)] gave three bands at R_F 0.50 (50 mg), 0.46 (55 mg), and 0.39 (31 mg). Acetylation of the R_F 0.50 band afforded (2*R*,3*S*:6*R*,7*S*,8*R*)-3,7-diacetoxy-2,6-

bis(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*trans*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]-chromene (**25**) as a *white amorphous solid* (53 mg) (Found: M^+, 744.2779. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 4). Acetylation of the R_F 0.46 band and subsequent p.l.c. [benzene–acetone (9:1, v/v; × 2)] gave two bands at R_F 0.56 (18 mg) and 0.49 (21 mg). The R_F 0.56 band consisted of the 6,7-*cis*-7,8-*trans*-tetrahydropyrano[2,3-*f*]chromene (**28**) with physical data identical with those of the corresponding derivative of the natural product (*G. coleosperma*). The R_F 0.49 band afforded (2*R*,3*S*:6*R*,7*S*,8*R*)-3,7-diacetoxy-2,8-bis(3,4-dimethoxyphenyl)-6-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*trans*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[2,3-*g*]chromene (**19**) as a *white amorphous solid* (Found: M^+, 744.2764. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 3); c.d. $[\theta]_{290}$ 0, $[\theta]_{280}$ -6.5×10^4, $[\theta]_{258}$ 0, $[\theta]_{242}$ 1.0×10^4, $[\theta]_{233}$ 0, $[\theta]_{216}$ -4.5×10^5, and $[\theta]_{206}$ 0. Acetylation of the R_F 0.39 band gave (2*R*,3*S*:6*S*,7*R*,8*R*)-3,7-diacetoxy-2,6-bis(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[2,3-*g*]chromene (**22**) as a *white amorphous solid* (33 mg) (Found: M^+, 744.2770. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 3); c.d. $[\theta]_{292}$ 0, $[\theta]_{283}$ -4.5×10^4, $[\theta]_{272}$ 0, $[\theta]_{241}$ 1.9×10^4, $[\theta]_{235}$ 1.3×10^4, $[\theta]_{225}$ 0, $[\theta]_{220}$ -2.4×10^5, and $[\theta]_{211}$ 0.

Fraction 3 (52 mg) was methylated and the mixture resolved by p.l.c. [benzene–acetone (8:2, v/v; × 2)] to give a methyl ether band at R_F 0.41 (36 mg). This was subsequently acetylated to afford (2*R*,3*S*:6*R*,7*S*,8*S*)-3,7-diacetoxy-2,8-bis(3,4-dimethoxyphenyl)-6-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[2,3-*g*]chromene (**16**) as a *white amorphous solid* (38 mg) (Found: M^+, 744.2778. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table 3), c.d. $[\theta]_{294}$ 0, $[\theta]_{280}$ -8.0×10^4, $[\theta]_{269}$ 0, $[\theta]_{260}$ 2.5×10^4, $[\theta]_{248}$ 1.8×10^4, $[\theta]_{237}$ 3.6×10^4, $[\theta]_{231}$ 0, $[\theta]_{226}$ -5.1×10^4, and $[\theta]_{224}$ 0.

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