Oligomeric Flavanoids. Part 3.† Structure and Synthesis of Phlobatannins Related to (−)-Fisetinidol-(4α,6)- and (4α,8)-(+)-catechin Profisetinidins

Jan P. Steynberg, Johann F. W. Burger, Desmond A. Young, Edward V. Brandt, Jacobus A. Steenkamp, and Daneel Ferreira*

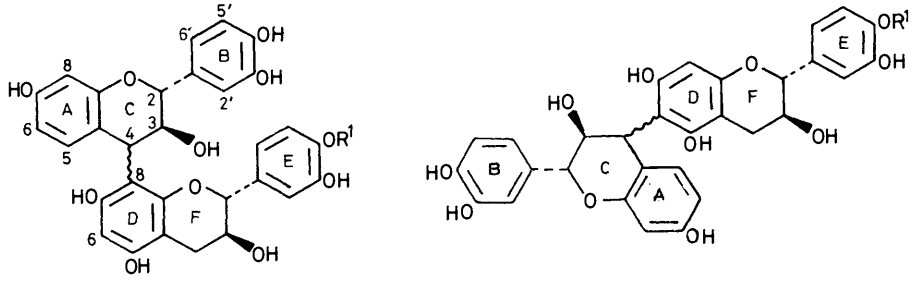
Department of Chemistry, University of the Orange Free State, P.O. Box 339, Bloemfontein, 9300 South Africa

Several members of the novel class of natural 'phlobaphene' condensed tannins, representing the products of C-ring isomerization of 2,3-*trans*-3,4-*trans*-(−)-fisetinidol units present in (4,6)- and (4,8)-biflavanoid profisetinidins, have been characterized by ^{1}H n.m.r. n.O.e. difference spectroscopy. These include the functionalized 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromenes (**9**) and (**12**), and the [2,3-*f*]- and [2,3-*g*] regioisomers (**14**) and (**19**). Since the (4α,8)-biflavanoid (**1**) is subject to extensive base-catalysed rearrangement and epimerization, the protected 4-*O*-methyl ethers (E-ring) (**2**) and (**6**) were utilized to confirm the proposed structures of phlobatannins by stereospecific C-ring isomerization of (**2**) and (**6**) under basic conditions.

The natural occurrence of the novel class of C-ring isomerized condensed tannins, termed phlobatannins, and their biomimetic synthesis *via* facile nucleophilic displacement of resorcinol A-ring by phloroglucinol D-ring functionality under mild alkaline conditions have recently been demonstrated.[1,2] These functionalized mono- and di-pyranochromenes represent products of stereospecific ring isomerization of (2*R*,3*S*)-2,3-*trans*-flavan-3-ol units present in 'conventional' (4,8)-bi- and (4,6:4,8)-triflavanoid profisetinidins. Continued investigations of two species of the Caesalpiniodeae, *Guibourtia coleosperma* (false mopane)[3] and *Baikiaea plurijuga* (Rhodesian teak)[3] have revealed more extensive structural and stereochemical diversity amongst these compounds than were previously anticipated. We thus now disclose our detailed results of relevance to those naturally occurring and synthetic phlobatannins originating from (−)-fisetinidol-(4α,6) and (4α,8)-(+)-catechin biflavanoids.

Results and Discussion

The four (−)-fisetinidol-(+)-catechins (**1**), (**3**), (**5**), and (**7**), derived from (+)-mollisacacidin [(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*cis*-3′,4′,7-trihydroxyflavan-3-ol] and (+)-catechin [(2*R*,3*S*)-2,3-*trans*-3′,4′,5,7-tetrahydroxyflavan-3-ol][4,5] are accompanied in the heartwoods of *G. coleosperma* and *B. plurijuga* by a series of functionalized tetrahydropyrano[2,3-*h*]-, [2,3-*g*]-, and [2,3-*f*]chromenes which presumably originate from the conventional dimers *via* appropriate C-ring isomerizations. Only those possessing *trans-cis* configurations of ring C, *i.e.* the [2,3-*h*]-(**9**) and (**12**) [2,3-*g*]-(**19**), and [2,3-*f*]-(**14**) isomers will be dealt with in this paper.‡ These compounds have been identified by means of the spectroscopic data of their heptamethyl ether diacetates, *e.g.* (**10**), and the structures confirmed by synthesis. Their ^{1}H n.m.r. spectra at 300 MHz are characterized by the conspicuous absence of the effects of dynamic rotational isomerism at ambient temperatures when compared to those of the corresponding derivatives of their biflavanoid precursors.[6]



(**1**) ≡ , R^1 = H (**5**)

(**2**) ≡ , R^1 = Me (**6**)

(**3**) ≡ , R^1 = H (**7**)

(**4**) ≡ , R^1 = Me (**8**)

The structure of the 8,9-*trans*-9,10-*cis*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromene (**9**) was established by application of ^{1}H nuclear Overhauser effect (n.O.e.) difference spectroscopy of its heptamethyl ether diacetate (**10**) ($J_{8,9}$ 10.0,

† Part 2, J. C. S. Malan, D. A. Young, J. A. Steenkamp, and D. Ferreira, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2567.

‡ The remaining isomers will be discussed in the following paper.

Table. ^{1}H N.m.r. peaks (p.p.m.) of the tetrahydropyranochromene heptamethyl ether diacetates (**10**), (**13**), (**15**), (**18**), and (**20**) in $CDCl_3$ (23 °C) at 300 MHz. Splitting patterns and *J* values (Hz) are given in parentheses

Ring	Proton	(**10**)	(**13**)	(**15**)	(**18**)	(**20**)
A[a]	3	6.32 (d, 2.5)	6.49 (d, 2.5)	6.46 (d, 2.5)	6.46 (d, 2.5)	6.47 (d, 2.5)
	5	6.37 (dd, 2.5, 8.5)	6.44 (dd, 2.5, 8.5)	6.42 (dd, 2.5, 8.5)	6.40 (dd, 2.5, 8.5)	6.41 (dd, 2.5, 8.5)
	6	6.82 (d, 8.5)	6.91 (d, 8.5)	6.82 (d, 8.5)	6.82 (d, 8.5)	6.81 (d, 8.5)
B[a]	2	6.89 (d, 2.0)	6.86 (d, 2.0)	6.79 (d, 2.0)	6.81 (d, 2.0)	6.89 (d, 2.0)
	5	6.79 (d, 8.5)	6.79 (d, 8.5)	6.77 (d, 8.5)	6.77 (d, 8.5)	6.78[b] (d, 8.0)
	6	6.91 (dd, 2.0, 8.5)	6.90 (dd, 2.0, 8.5)	6.86 (dd, 2.0, 8.5)	6.87 (dd, 2.0, 8.5)	6.85 (dd, 2.0, 8.0)
C	8/6	4.96 (d, 10.0)	4.96 (d, 10.0)	4.95 (d, 10.0)	4.95 (d, 10.0)	4.99 (d, 10.5)
	9/7	5.50 (dd, 6.0, 10.0)	5.51 (dd, 6.0, 10.0)	5.31 (dd, 5.5, 10.0)	5.34 (dd, 5.5, 10.0)	5.42 (dd, 6.0, 10.5)
	10/8/6	5.08 (d, 6.0)	5.04 (d, 6.0)	5.06 (d, 5.5)	5.08 (d, 5.5)	5.13 (d, 6.0)
D		6.17 (s)	6.19 (s)	6.11 (s)	6.17 (s)	6.45 (s)
E[a]	2	6.72 (d, 2.0)	6.42 (d, 2.0)	6.91 (d, 2.0)	7.04 (d, 2.0)	6.87 (d, 2.0)
	5	6.75 (d, 8.0)	6.61 (d, 8.5)	6.84 (d, 8.0)	6.84 (d, 8.5)	6.82[b] (d, 8.0)
	6	6.68 (dd, 2.0, 8.0)	6.26 (dd, 2.0, 8.5)	6.94 (dd, 2.0, 8.0)	6.95 (dd, 2.0, 8.5)	6.90 (dd, 2.0, 8.0)
F	2	4.63 (d, 7.0)	4.90 (br s, *ca.* 1.0)	4.96 (d, 8.0)	5.04 (br s, *ca.* 1.0)	5.07 (d, 6.0)
	3	5.21 (m)	5.20 (m)	5.37 (m)	5.41 (m)	5.31 (m)
	$4_{ax.}$	2.58 (dd, 7.0, 16.0)	2.88 (m)	2.69 (dd, 8.0, 16.5)	2.92 (dd, 6.5, 16.0)	2.78 (dd, 6.0, 16.5)
	$4_{eq.}$	2.89 (dd, 5.5, 16.0)		3.00 (dd, 5.5, 16.5)	3.02 (dd, 5.0, 16.0)	2.83 (dd, 5.0, 16.5)
	OMe	3.52 (2-A), 3.75 (5-D), 3.76 (4-A), 3.83 (×2), 3.84, 3.85, each s	3.58 (2-A), 3.69, 3.77 (5-D), 3.81 (4-A), 3.82, 3.83, 3.84, each s	3.54 (9-D), 3.79 (2-A), 3.80 (4-A), 3.81, 3.84, 3.87 (×2), each s	3.57 (9-D), 3.78 (2-A), 3.79 (4-A), 3.83, 3.85, 3.87, 3.88, each s	3.27 (5-D), 3.78 (4-A), 3.80 (2-A), 3.83 (×2), 3.84, 3.85, each s
	OAc	1.66, 1.86, each s	1.66, 1.68, each s	1.71, 1.90, each s	1.71, 1.95, each s	1.71, 1.95, each s

[a] Identified by spin decoupling using the adjacent benzylic proton resonance as reference signal. [b] Peaks may be interchanged.

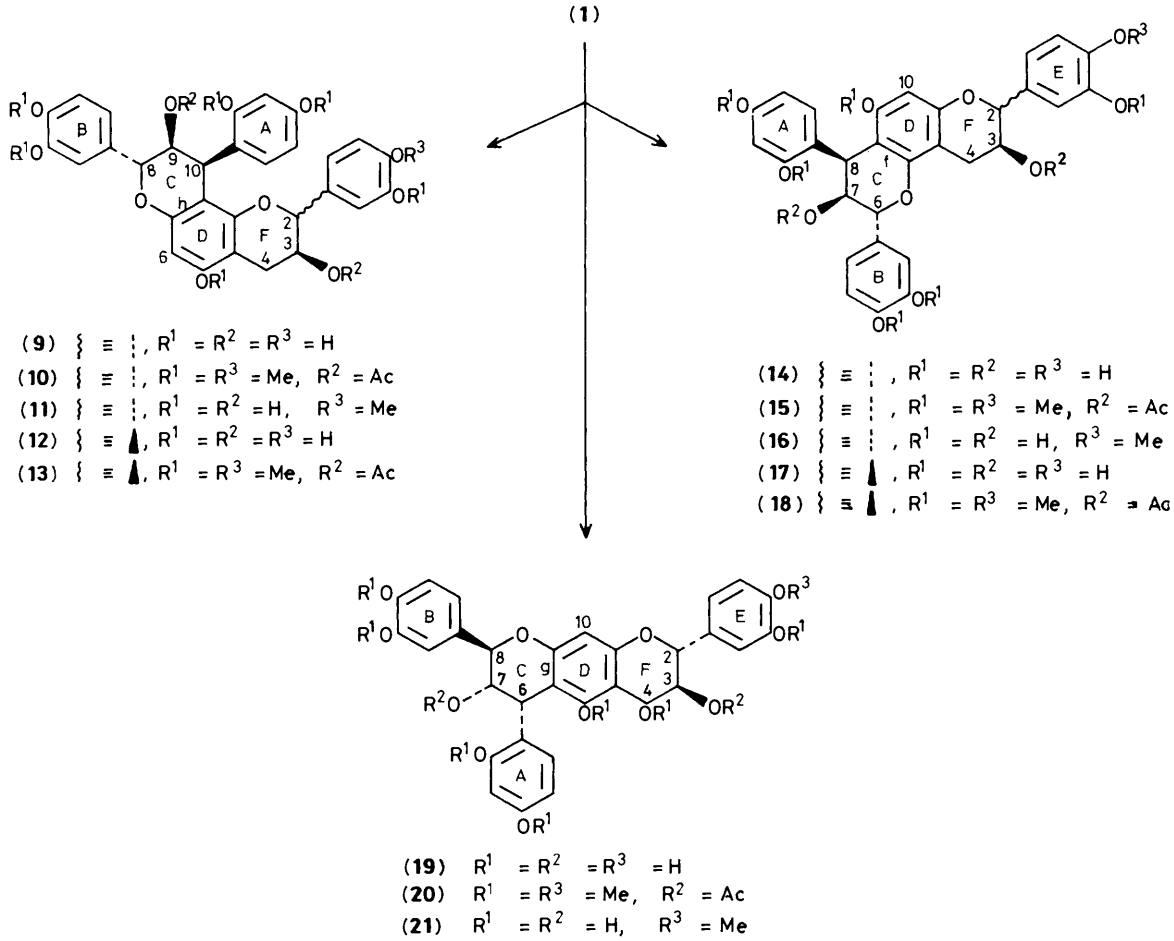
$J_{9,10}$ 6.0 Hz). Association of 2-OMe(A) with 3-H(A) (16.8%) and of 4-OMe(A) with both 3-H(A) (4.7%) and 5-H(A) (9.5%) indicated that both hydroxy groups of the resorcinol moiety are available for methylation in contrast to involvement of the equivalent of one of these in the heterocyclic C-ring of the (−)-fisetinidol-(4α,8)-(+)-catechin precursor (**1**). The heterocyclic region of the ^{1}H n.m.r. spectra (Table) indicated significant and consistent reversals of chemical shifts of benzylic C-ring protons in all four analogues, *e.g.* (**10**), in comparison to those of the corresponding 2- and 4-proton resonances (C-ring) in (4,6)- and (4,8)-biflavanoids of both 2,3-*trans*-3,4-*trans*- and 3,4-*cis* stereochemistry.[4] The chemical shift for 6-H(D) (δ 6.17) in (**10**) is in agreement with coupling at 8-C of a (+)-catechin moiety[7] ($J_{2,3}$ 7.0 Hz) and thus indicative of the tetrahydropyrano[2,3-*h*]chromene arrangement (**10**). Such an allocation was substantiated by n.O.e. associations of 10-H(C) with 2-H(E) (1.5%), 6-H(E) (2.0%), and 3-OMe(E) (0.2%) and eventually confirmed by synthesis (see below). A similar strategy was adopted in assigning the structures of the remaining isomers (**13**), (**15**), and (**20**).

Differentiation between the regioisomeric phlobatannins, *e.g.* (**10**) and (**20**), on the basis of the absolute chemical shifts of residual D-ring protons[7] and by observation of n.O.e. effects between this hydrogen and methoxy protons of ring D appear to be less useful than for conventional (4,6)- and (4,8)-biflavanoids. These difficulties prompted recourse to synthesis in order to establish unequivocally the structures of the series of novel tetrahydropyranochromenes.

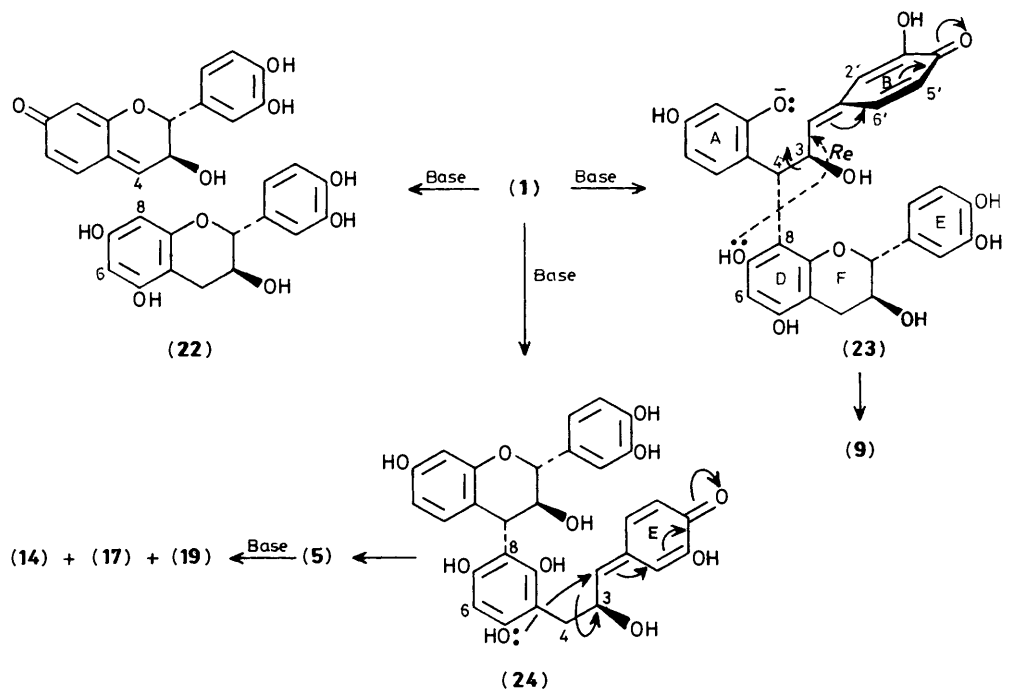
Thus, treatment of (−)-fisetinidol-(4α,8)-(+)-catechin (**1**) with 0.025M $NaHCO_3$–0.025M Na_2CO_3 buffer (pH 10)[8] for 5 h at 50 °C under nitrogen, *i.e.* conditions similar to those applied by Freudenberg[9] for epimerization at 2-C of (+)-catechin, gave a complex mixture from which five products (**9**), (**12**), (**14**), (**17**), and (**19**) were obtained (Scheme 1). The expected 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**9**) [$J_{2,3(F)}$ 7.0 Hz for (**10**)] is accompanied by its C-2(F) epimer (**12**) [$J_{2,3(F)}$ *ca.* 1.0 Hz for (**13**)]; a corresponding isomeric pair which have tentatively (see below) been assigned structures (**14**) and (**17**), their formation implying the equivalent of positional isomerization of the (−)-fisetinidol unit to 6-C of the (+)-catechin moiety followed by ring isomerization involving its 5-OH function and also epimerization at 2-C(F) [$J_{2,3(F)}$ 8.0 Hz for (**15**) and *ca.* 1.0 Hz for (**18**)] and, finally their structural isomer (**19**) indicative of the alternative mode of cyclization *via* 7-OH(D). Differentiation of the heptamethyl ether diacetates (**10**), (**13**), (**15**), (**18**), and (**20**) presented problems similar to those encountered for the natural product derivatives. The structures of the pairs (**10**) and (**13**), and (**15**) and (**18**) followed tentatively from the general congruence of chemical shifts of heterocyclic C-ring proton resonances. [(**10**) and (**13**): δ 4.96, 4.96 (8-H), 5.50, 5.51 (9-H), 5.08, 5.04 (10-H); (**15**) and (**18**): δ 4.95, 4.95 (8-H), 5.31, 5.34 (9-H), 5.06, 5.08 (10-H)]. In addition 2-H(F) is shielded (δ 4.63) in (**10**) relative to the same protons in the corresponding derivatives of (**14**) (δ 4.96) and (**17**) (δ 5.04) presumably reflecting the anisotropic effect of its A-ring.

Formation of the series of tetrahydropyranochromenes from a single biflavanoid under mild basic conditions necessitates mechanistic explanations for both C-ring isomerization and the observed migrations and epimerizations (Scheme 2). Substitution of resorcinol A-ring by phloroglucinol D-ring functionality presumably occurs *via* a B-ring quinone-methide[10] (**23**). Re-cyclization involving 7-OH(D) requires rotation about the C(3)–C(4) bond which will invariably lead from the 3,4-*trans* to the 3,4-*cis* configuration. Dreiding models indicate preference for *Re* face attack in the quinone-methide (**23**) and thus for retention of absolute configuration at 2-C(C)* for biflavanoids with 3,4-*trans* stereochemistry, *e.g.* (**1**) and (**5**). Under the prescribed conditions positional isomerization may proceed *via* an A-ring derived quinone-methide [arrangement (**22**)] as was

* 8-C(C) In phlobatannin (**9**).



Scheme 1. Base-catalysed formation of the series of phlobatannins from the (−)-fisetinidol-(4α,8)-(+)-catechin (**1**); *Reagents and conditions:* i, $NaHCO_3$–Na_2CO_3, 50 °C, 5 h, N_2

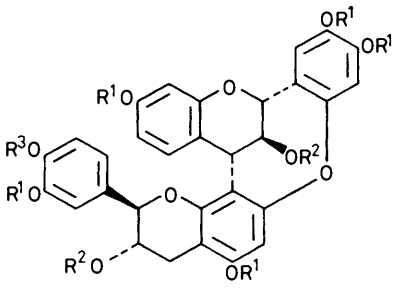


Scheme 2. Proposed route to the formation of phlobatannins and the origin of a 'migrating' flavanyl moiety

initially postulated by Whalley[10–12] in the biosynthesis of dracorubins and recently also by Hemingway[13–15] for interflavanyl condensations under alkaline conditions. Such an intermediate (**22**) would then be susceptible to 1,6-Michael addition from 6-C of the liberated (+)-catechin moiety.* Alternatively a quinone-methide (**24**) derived from the E-ring could undergo rotation about the C(3)–C(4) bond and recyclization *via* either 5-OH(D) or 7-OH(D) thus simultaneously achieving the observed regio- and configurational isomerizations. In view of the relative stability of the interflavanyl bond in profisetinidins of type (**1**) the latter mechanism presumably provides more reasonable explanation for the phenomena of migration and epimerization. The natural existence of the 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**12**) with its (+)-epicatechin flavan-3-ol unit presumably indicates operation of a similar mechanism in Nature.

The above failure† to provide unambiguous synthetic proof for the structures of the naturally occurring phlobatannins prompted us to embark on a strategy of selectively protecting the C-4(B) hydroxy group of (+)-catechin prior to its utilization in the synthesis of the series of (4,6)- and (4,8)-(−)-fisetinidol-(+)-catechin mono-*O*-methyl ethers (**2**), (**4**), (**6**), and (**8**) in order to prevent unwanted reactions associated with an E-ring quinone-methide of type (**24**). Methylation of (+)-catechin with methyl iodide (1:1 molar ratio) in anhydrous K_2CO_3–acetone afforded a 1:1 mixture of the 3′-*O*- and 4′-*O*-methyl ethers. Acid-catalysed condensation of the latter with (+)-mollisacadidin[4] and subsequent chromatography on Sephadex LH-20 and Fractogel TSK HW-40 (S)[16] afforded the four 'protected' (−)-fisetinidol-(+)-catechins (**2**), (**4**), (**6**), and (**8**). These dimers were characterized by comparison of ^{1}H n.m.r. data of their hexamethyl ether diacetates with those of the permethyl ether diacetates of the corresponding phenols[4].

Treatment of the (−)-fisetinidol-(4α,8)-(+)-catechin *O*-methyl ether (**2**) with base (pH 10) as above followed by chromatography on Sephadex LH-20 gave the 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**11**) (^{1}H n.m.r. data in Table) in 58% yield. Comparison of the physical data of its methyl ether diacetate (**10**) with those of the corresponding derivative of the product from Nature and from the 'uncontrolled' synthesis proved their identity. Phlobatannin (**11**) resulting from stereospecific ring isomerization with retention of the configuration at C-2 in (**2**), is accompanied by small amounts of a dehydro-(−)-fisetinidol-(+)-catechin (**25**) [δ 6.19, s, 6-H(B); 6.82, s, 3-H(B) for its methyl ether acetate (**26**)], representing the alternative mode of cyclization *via* C-6(B) in quinone-methide (**23**) followed by oxidative removal of hydride ion. Presence of analogue (**25**) provides indirect evidence for the proposed quinone-methide mechanism. All efforts to trap intermediate (**23**) intermolecularly with strong nucleophiles such as phenyl sulphide- and selenide ions invariably failed. Absence of products resulting from a migrating flavanyl moiety in the protected biflavanoid (**2**) thus confirms our conjecture regarding the mechanism of such a migration in the 'uncontrolled' synthesis.



(**25**) $R^1 = R^2 = H$, $R^3 = Me$
(**26**) $R^1 = R^3 = Me$, $R^2 = Ac$

Base treatment of the (−)-fisetinidol-(4α,6)-(+)-catechin *O*-methyl ether (**6**) afforded the expected products of stereospecific C-ring isomerization with retention of the absolute configuration at C-2, *i.e.* the 6,7-*trans*-7,8-*cis*-tetrahydropyrano[2,3-*f*]chromene (**16**) [$J_{6,7}$ 10.0, $J_{7,8}$ 5.5 Hz for heptamethyl ether diacetate (**15**)] and the [2,3-*g*] regioisomer (**21**) [$J_{7,8}$ 10.5, $J_{6,7}$ 6.0 Hz for (**20**)] as minor component. Significant n.O.e. associations between 10-H(D) (δ 6.11) and 9-OMe(D) (δ 3, 54, 15.2%) in the [2,3-*f*]chromene (**15**) and absence of similar associations with 5-OMe(D) (δ 3.27) in the [2,3-*g*] isomer (**20**) clearly differentiates these regioisomers. ^{1}H N.m.r. data (Table) of the heptamethyl ether diacetates (**15**) and (**20**) proved to be identical with those of the corresponding derivatives of the natural products. The notable preference for ring isomerization involving 5-OH(D) cannot be explained satisfactorily at present.

The natural and synthetic phlobatannin derivatives (**10**), (**13**), (**15**), and (**20**) all exhibit intense positive Cotton effects in the 220–240 nm region of their c.d. spectra thus corresponding to 10*S* absolute configuration for (**10**) and (**13**), 8*S* for (**15**), and 6*S* for (**20**) by application of the aromatic quadrant rule.[17] These data, when taken in conjunction with ^{1}H n.m.r. coupling constants of heterocyclic protons and known absolute configurations of the biflavanoids (**2**) and (**6**), define the absolute stereochemistry as 2*R*, 3*S*:8*R*, 9*S*, 10*S* for (**9**), 2*S*, 3*S*:8*R*, 9*S*, 10*S* for (**12**), 2*R*, 3*S*:6*R*, 7*S*, 8*S* for (**14**), and 2*R*, 3*S*:6*S*, 7*S*, 8*R* for (**19**). Our strategy of protecting the 4′-OH function of the (+)-catechin unit to prevent base-catalysed transformations associated with quinone-methides of type (**24**) and also the systematic synthesis of the full complement of phlobatannins derived from a specific group of (−)-fisetinidol-(+)-catechins, *e.g.* (**2**) and (**6**), proved to be of prime importance in establishing the structures of the naturally occurring analogues. Furthermore, we have developed an efficient method of inducing ring isomerization in biflavanoid units present in commercially-available condensed tannins, our ultimate aim being their activation for use in 'cold-set' adhesive applications through 'liberation' of reactive nucleophilic resorcinol units.

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 spectra were obtained with a Kratos MS80 instrument and c.d. data in methanol on a Jasco J-20 spectropolarimeter. T.l.c. was performed on pre-coated Merck plastic sheets (silica gel 60 PF_{254}, 0.25 mm) and the plates 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. Separations on Sephadex LH-20 and Fractogel TSK HW-40(S) were on various column 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 over 48 h at −15 °C, 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.—Heartwood drillings (6 kg) were slightly moisturized and extracted with

* According to t.l.c. evidence (+)-catechin is indeed released in the reaction mixture.

† Base treatment of the (−)-fisetinidol-(4β,8)-(+)-catechin (**3**) gave an even more complex mixture than the (4α,8)-isomer. This mixture was not further investigated.

EtOAc (3 × 3 l) at room temperature. Evaporation of the solvent afforded a light-brown powder (240 g) which was dissolved in methanol and dewaxed with hexane (3 × 300 ml). Evaporation of the methanol solution gave a brown powder (210 g). This (4 × 50 g) was partitioned between a butan-2-ol–water–hexane (4:5:1, v/v) mixture in a 20-tube, 100 ml underphase, Craig countercurrent assembly.

Following qualitative paper chromatographic analysis the fractions were combined as follows: 1 [tubes 1—8 (72.5 g)], 2 [tubes 9—14 (62.4 g)], and 3 [tubes 15—20, (60.5 g)]. Subsequent column chromatography (Sephadex LH-20) of fraction 2 in three portions of 20 g each on columns of 5 × 150 cm (24 ml eluant/tube) afforded the following fractions (first 1.5 l of eluant was discarded): 2A [tubes 8—28 (0.5 g)], 2B [55—75 (1.2 g)], 2C [83—120 (3.3 g)], 2D [138—186 (2.54 g)], 2E [187—306 (10.89 g)], 2F [307—420 (5.19 g)], 2G [421—468 (4.49 g)], and 2H [468—600 (15.3 g)]. Since the phlobatannins all exhibit a characteristic purple-red colouration on t.l.c. with the spray reagent, fractions for further investigations were selected according to this phenomenon.

Methylation of fraction 2D (2.54 g) and subsequent purification by p.l.c. [benzene–acetone (9:1, v/v, ×3)] gave five bands, $2D_1$ (R_F 0.5, 152 mg), $2D_2$ (R_F 0.42, 69 mg), $2D_3$ (R_F 0.33, 120 mg), $2D_4$ (R_F 0.23, 630 mg), and $2D_5$ (R_F 0.20, 454 mg). Fraction $2D_4$ was acetylated and the mixture resolved by p.l.c. in benzene–acetone (19:1, v/v; ×2) to give a main band at R_F 0.23 (74 mg) which was further resolved by p.l.c. in hexane–acetone–ethyl acetate (65:20:15, v/v; ×4) to give a homogenous fraction at R_F 0.44 (39 mg).

(2R,3S:8R,9S,10S)-3,9-*Diacetoxy*-2,8-*bis*(3,4-*dimethoxyphenyl*)-10-(2,4-*dimethoxyphenyl*)-2,3-trans-8,9-trans-9,10-cis-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3-h]*chromene* (**10**). The R_F 0.44 band afforded the title compound as a *white amorphous solid* (Found: C, 66.2; H, 6.1. $C_{41}H_{44}O_{13}$ requires C, 66.1; H, 5.95%); ^{1}H n.m.r. data (Table); c.d. $[\theta]_{286}$ 0, $[\theta]_{279}$ 4.1 × 10^4, $[\theta]_{273}$ 0, $[\theta]_{262}$ − 8.3 × 10^4, $[\theta]_{249}$ 0, $[\theta]_{238}$ 2.05 × 10^5, $[\theta]_{228}$ 0, $[\theta]_{214}$ − 3.5 × 10^5, and $[\theta]_{210}$ 0.

The $2D_5$ fraction consisted mainly of the heptamethyl ether of the (−)-fisetinidol-(4β,8)-(+)-catechin (**3**) by comparison of physical data of its diacetate with those of an authentic specimen.[5]

Fraction 2E from the Sephadex LH-20 column consists of phlobatannins based on (−)-epicatechin, details of which will be published elsewhere. These compounds are accompanied by the (−)-fisetinidol-(4α,8)-(+)-catechin (**1**) by chromatographic comparison with an authentic sample.[5] Fraction 2F (5.19 g) was methylated and the mixture resolved by p.l.c. (benzene–acetone (8:2, v/v; ×2) into nine bands, $2F_1$ (R_F 0.60, 130 mg), $2F_2$ (R_F 0.52, 300 mg), $2F_3$ (R_F 0.45, 286 mg), $2F_4$ (R_F 0.41, 704 mg), $2F_5$ (R_F 0.34, 886 mg), $2F_6$ (R_F 0.28, 490 mg), $2F_7$ (R_F 0.21, 474 mg), $2F_8$ (R_F 0.14, 510 mg), and $2F_9$ (R_F 0.10, 393 mg). Fraction $2F_2$ consisted mainly of the heptamethyl ether of the (−)-fisetinidol-(4β,6)-(+)-catechin (**7**) and $2F_3$ of the same derivative of the (4α,6)-isomer (**5**).

The $2F_4$ band was subjected to p.l.c. [hexane–acetone–ethyl acetate (5:3:2, v/v; ×3)] to give a main band at R_F 0.52 (267 mg) which was further purified by p.l.c. [1,2-dichloroethane–acetone (9:1 v/v)] into a fraction at R_F 0.47 (104 mg). This was finally resolved by p.l.c. [hexane–acetone–ethyl acetate (5.5:2.5:2, v/v)] to afford two bands at R_F 0.50 (41 mg) and R_F 0.46 (18 mg).

(2R,3S:8R,9S,10R)-3,9-*Diacetoxy*-2,8-*bis*(3,4-*dimethoxyphenyl*)-10-(2,4-*dimethoxyphenyl*)-2,3-trans-8,9-trans-9,10-trans-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3h]*chromene*. Acetylation of the R_F 0.50 band gave the title compound as a *white amorphous solid*, details of which will be presented in Part 4 of this series.

(2R,3S:6S,7S,8R)-3,7-*Diacetoxy*-2,8-*bis*(3,4-*dimethoxyphenyl*)-6-(2,4-*dimethoxyphenyl*)-2,3-trans-6,7-cis-7,8-trans-3,4,6,7-*tetrahydro*-2H,8H-*pyrano*[2,3-g]*chromene* (**20**). Acetylation of the R_F 0.46 fraction afforded the title compound as a *white amorphous solid* (Found: M^+, 744.2738. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table); c.d. $[\theta]_{283}$ 0, $[\theta]_{248}$ 1.86 × 10^4, $[\theta]_{233}$ 2.42 × 10^5, and $[\theta]_{220}$ 0.

The $2F_5$ band was purified by successive p.l.c. in hexane–acetone–ethyl acetate (5:3:2, v/v; ×4, R_F 0.54, 79 mg) and in 1,2-dichloroethane–acetone (8.5:1.5, v/v; ×3) to give a homogenous methyl ether band at R_F 0.43 (25 mg). Acetylation followed by p.l.c. in 1,2-dichloroethane–acetone (9:1, v/v; ×2) afforded a single band at R_F 0.63 (18 mg) which consisted of the (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*, details of which will be given in Part 4 of this series.

Phlobatannins from Baikiaea plurijuga.—Heartwood drillings (4.3 kg) were extracted with methanol (6 × 2.5 l) for 48 h at room temperature. The extract was concentrated (*ca.* 2 l), dewaxed with hexane (7 × 1 l), and the methanol evaporated to give a red-brown powder (582 g). A portion (2 × 75 g) of this was subjected to countercurrent distribution (Quickfit Steady State Model 20, 25 ml underphase, 103 tubes) in water–butan-2-ol–hexane (5:4:1, v/v). Following paper-chromatographic analysis the fractions were combined as follows: 1 [tubes 1—23 (27.9 g)], 2 [24—38 (23.7 g)], 3 [39—63 (36.1 g)], 4 [64—77 (10.3 g)], and 5 [78—103 (4.7 g)].

Subsequent column chromatography (Sephadex LH-20) of fraction 3 in two portions of 18 g each on columns of 4.5 × 120 cm (18 ml eluant/tube) afforded the following fractions (first 1 l of eluant was discarded): 3A [tubes 32—47 (448 mg)], 3B [48—84 (2.93 g)], 3C [85—94 (318 mg)], 3D [95—120 (137 mg)], 3E [121—154 (187 mg)], 3F [155—215 (1.91 g)], 3G [224—267 (3.08 g)], 3H [268—337 (2.64 g)], 3I [338—436 (2.79 g)], 3J [437—593 (3.21 g)], 3K [594—633 (2, 53 g)], 3L [634—685 (1.17 g)], 3M [686—786 (2.34 g)], 3N [787—907 (2.61 g)], 3O [908—1 062 (2.57 g)], and 3P [1 063—1 313 (1.95 g)]. Fraction 3G (3.08 g) contained metabolites exhibiting the diagnostic purple-red colouration with the spray reagent on t.l.c. and was further resolved on a Fractogel TSK HW-40(S) column (3 × 55 cm, 15 ml eluant/tube, first 500 ml of eluant discarded) to the following fractions: $3G_1$ [tubes 84—101 (497 mg)], $3G_2$ [102—121 (876 mg)], $3G_3$ [122—161 (554 mg)], $3G_4$ [162—216 (534 mg)], $3G_5$ [217—296 (147 mg)], and $3G_6$ [297—350 (33 mg)].

Fraction $3G_1$ (497 mg) was methylated and the mixture resolved by p.l.c. [benzene–ethyl acetate–acetone (7:2:1, v/v; ×2) to give a main band at R_F 0.43 (189 mg). Acetylation afforded the 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**10**) identical with the sample from *G. coleosperma*.

Methylation of fraction $3G_2$ (876 mg) and subsequent purification by p.l.c. [benzene–ethyl acetate–acetone (7:2:1, v/v; ×2)] afforded a R_F 0.46 band (126 mg) which was further resolved by p.l.c. in chloroform–ethyl acetate (17:3. v/v; ×2) to give a homogeneous band at R_F 0.36 (32 mg). Acetylation afforded (2*R*,3*S*:8*S*,9*S*,10*R*)-3,9-diacetoxy-2,10-bis(3,4-dimethoxyphenyl)-8-dimethoxyphenyl-2,3-*trans*-8,9-*cis*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*] chromene as a white amorphous solid (36 mg). Its identification will be described in Part 4 of this series.

Fraction $3G_3$ (554 mg) was methylated and the mixture subsequently resolved by successive p.l.c. separation [benzene–ethyl acetate–acetone (7:2:1, v/v; ×2, R_F 0.63, 66 mg)]; hexane–acetone–ethyl acetate (11:6:3, v/v; ×2, R_F 0.39, 14 mg).

(2S,3S:8R,9S,10S)-3,9-*Diacetoxy*-2,8-*bis*(3,4-*dimethoxyphenyl*)-10-(2,4-*dimethoxyphenyl*)-2,3-cis-8,9-trans-9,10-cis-3,4,9,10-*tetrahydro*-2H,8H-*pyrano*[2,3-h]*chromene* (**13**). Acetylation of the R_F 0.39 methyl ether band afforded the title compound as a

white amorphous solid (Found: M^+, 744.2759. $C_{41}H_{44}O_{13}$ requires M, 744.2782; ^{1}H n.m.r. data (Table), c.d. $[\theta]_{270}$ 0, $[\theta]_{264}$ − 3.1 × 10^4, $[\theta]_{248}$ 0, $[\theta]_{227}$ 5.4 × 10^4, and $[\theta]_{222}$ 4.6 × 10^5.

A portion (1.8 g) of fraction 3H was chromatographed on Fractogel TSK HW-40(S) (3 × 90 cm column, 15 ml eluant/tube, first 250 ml of eluant discarded) to give the following fractions: $3H_1$ tubes [44—63 (172 mg)], $3H_2$ [64—77 (342 mg)], and $3H_3$ [78—125 (638 mg)]. Fraction $3H_1$ (172 mg) was methylated and the mixture resolved by p.l.c. [benzene–acetone (9:1, v/v; × 3)] to give a methyl ether band at R_F 0.53 (16 mg). Acetylation afforded (2*R*,3*S*:8*R*,9*S*,10*R*)-3,9-diacetoxy-2,10-bis(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*trans*-8,9-*trans*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromene as a white amorphous solid, details of which will be presented in Part 4 of this series. Fraction $3H_3$ consisted of the (4α,8)- and (4β,8)-biflavanoids (**1**) and (**3**) by t.l.c.- and 2D-paper chromatographic comparisons with authentic samples.[5] The (4,6)-isomers (**5**) and (**7**) were similarly identified in fraction 3I from the Sephadex LH-20 fractionation.

Synthesis of Phlobatannins with trans-cis-*Configuration of their* C-*Rings*

'Uncontrolled' Synthesis.—The (−)-fisetinidol-(4α,8)-(+)-catechin (**1**) (450 mg) was dissolved in 200 ml of a 0.025M Na_2CO_3—0.025M $NaHCO_3$ buffer (pH 10) and the mixture stirred under N_2 at 50 °C for 5 h. The mixture was cooled to 0 °C, acidified with 0.1M HCl, and extracted with ethyl acetate (4 × 250 ml). Drying (Na_2SO_4) of the extract followed by evaporation of solvent afforded a light-brown powder (390 mg). A portion (300 mg) of this mixture was methylated and subsequently resolved by p.l.c. [benzene–acetone (8.5:1.5, v/v; × 2)] into five bands: 1 (R_F 0.56, 21 mg), 2 (R_F 0.49, 26 mg), 3 (R_F 0.41, 45 mg), 4 (R_F 0.27, 23 mg), and 5 (R_F 0.17, 30 mg).

Acetylation of band 1 followed by successive p.l.c. separation [benzene–acetone (9:1, v/v; × 2], R_F 0.42, 13 mg); hexane–acetone–ethyl acetate (13:4:3, v/v; × 3; R_F 0.55, 5 mg) afforded (2*S*,3*S*:6*R*,7*S*,8*S*)-3,7-diacetoxy-2,6-bis(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*cis*-6,7-*trans*-7,8-*cis*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]chromene (**18**) as a *white amorphous solid* (Found: M^+, 744.2783. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table); c.d. $[\theta]_{275}$ 0, $[\theta]_{265}$ − 4.0 × 10^4, $[\theta]_{246}$ 0, $[\theta]_{228}$ 1.9 × 10^5, $[\theta]_{225}$ 4.5 × 10^4, $[\theta]_{221}$ 1.4 × 10^5, and $[\theta]_{220}$ 0.

Band 2 (26 mg) was acetylated and purified by p.l.c. [benzene–acetone (9:1, v/v; × 2)] to give the 2,3-*cis*-8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**13**), R_F 0.45 (12 mg) as a white amorphous solid, identical (^{1}H n.m.r.-, c.d.-, and ms-data) with the natural product from *B. plurijuga*.

Acetylation of band 3 (45 mg) followed by p.l.c. [benzene–acetone (9:1, v/v; × 2)] afforded two fractions at R_F 0.54 (11 mg) and R_F 0.44 (15 mg). The R_F 0.54 fraction gave (2*R*,3*S*:6*R*,7*S*,8*S*)-3,7-diacetoxy-2,6-bis(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]chromene (**15**) as a *white amorphous solid* (Found: M^+, 744.2733. $C_{41}H_{44}O_{13}$ requires M, 744.2782); ^{1}H n.m.r. data (Table), c.d. $[\theta]_{271}$ 0, $[\theta]_{261}$ − 2.8 × 10^4, $[\theta]_{254}$ 0, $[\theta]_{233}$ 4.4 × 10^5, and $[\theta]_{214}$ 0. The R_F 0.44 fraction consisted of the *cis-trans*-tetrahydropyrano[2,3-*h*]chromene (**10**), identical (^{1}H n.m.r., c.d., and m.s. data) to the corresponding derivative of the natural product from *G. coleosperma* and *B. plurijuga*.

Acetylation of band 4 (23 mg) followed by p.l.c. [benzene–acetone (9:1, v/v; × 2)] gave the 7,8-*trans*-6,7-*cis*-tetrahydropyrano[2,3-*g*]chromene (**20**), R_F 0.53 (11 mg), identical with the corresponding derivative of the natural product from *G. coleosperma*.

Band 5 (30 mg) consisted of unchanged starting material.

'Controlled' Synthesis.—Selective methylation of (+)-*catechin.* Dry (+)-catechin (2 × 10 g portions) was dissolved in dry acetone (200 ml) containing anhydrous K_2CO_3 (23.8 g) and methyl iodide (5.88 g). The mixture was refluxed for 36 h, filtered, evaporated to dryness, and the residue subjected to column chromatography (Sephadex LH-20, 5 × 150 cm column, 24 ml eluant/tube, first 1.5 l of eluant discarded). The following fractions were gathered: 1 [tubes 5—38 (600 mg)], 2 [39—85 (8.5 g)], and 3 [85—120 (9.0 g)]. Fraction 1 consisted of di, tri-, and tetra-*O*-methyl ethers and fraction 3 of unchanged (+)-catechin. Fraction 2 contained a mixture of the 3′-*O*- and 4′-*O*-methyl ethers and was subsequently dissolved in methanol–chloroform (3:1, v/v) which led to selective crystallization of 4′-*O*-methyl-(+)-catechin as white solid (4.0 g), m.p. 228.4 °C, lit.[18] m.p. 228—230 °C (Found: M^+, 304.0941. Calc. for $C_{16}H_{16}O_6$ M^+, 304.0947).

Synthesis of 'protected' biflavanoids (**2**), (**4**), (**6**), *and* (**8**). 4′-*O*-Methyl-(+)-catechin (4.0 g) was dissolved in 0.1M HCl (500 ml) containing ethanol (20 ml) to which a solution of (+)-mollisacacidin (2 g) in 0.1M HCl (100 ml) was added slowly (*ca.* 3 h) with stirring at ambient temperature. After 12 h a further portion of (+)-mollisacacidin (1 g) in 0.1M HCl (50 ml) was added and stirring continued for 12 h. The mixture was extracted with ethyl acetate (4 × 250 ml), dried (Na_2SO_4), and evaporated to dryness. The light-brown residue (7 g) was subjected to column chromatography on a Büchi MPLC-system (5 × 150 cm column, 0.6—0.8 bar pressure, flow rate—8 ml/min, 24 ml eluant/tube, first 1.5 l of eluant discarded) using Sephadex LH-20/ethanol to give the following fractions: 1 [tubes 3—18 (1.54 g)], 2 [36—61 (1.44 g)], 3 [73—110 (1.96 g)], 4 [120—146 (250 mg)], and 5 [205—234 (708 mg)]. Fraction 1 consisted of 4′-*O*-methyl-(+)-catechin, fraction 2 of the (−)-fisetinidol-(4β,8)-(+)-catechin-*O*-methyl ether (**4**), fraction 3 of the (4α,8)-dimer (**2**), fraction 4 of the (4β,6)-biflavanoid (**8**), and fraction 5 of a mixture of the (4α,6)-analogue (**6**) and small amounts of 'trimeric' species. The latter mixture was resolved by column chromatography on Fractogel TSK HW-40(S)/ethanol under m.p.l.c. conditions (3 × 100 cm column, 2.7 bar, flow rate 3 ml/min, 24 ml eluant/tube, first 250 ml of eluant discarded) to give the (−)-fisetinidol-(4α,6)-(+)-catechin-*O*-methyl ether (**6**) [tubes 2—35 (412 mg)] and a trimeric fraction [tubes 40—73 (380 mg)] which was not further investigated. The 'protected' biflavanoids (**2**), (**4**), (**6**), and (**8**) were characterized by comparison of ^{1}H n.m.r. data of their heptamethyl ether diacetates with those of the corresponding derivatives of authentic samples.[5]

Base-catalysed conversion of (−)-*fisetinidol*-(4α,8)-(+)-*catechin*-O-*methyl ether* (**2**). The biflavanoid (**2**) (800 mg) was treated with base as was described above for (**1**) in the 'uncontrolled' synthesis, and the resulting mixture resolved by column chromatography (3 × 85 cm column, flow rate 1.2 ml/min, 20 ml eluant/tube, first 200 ml of eluant discarded) on Sephadex LH-20 to give the following fractions: 1 [tubes 11—17 (38 mg)], 2 [34—53 (280 mg)], and 3 [54—74 (325 mg)].

Fraction 1 (38 mg) was methylated and the mixture resolved by p.l.c. [benzene–acetone–methanol (70:28:2, v/v; × 2)] to give two bands at R_F 0.70 (12 mg) and R_F 0.28 (5 mg). The former consisted of 3′,4′,5,7-tetra-*O*-methyl-(+)-catechin. Acetylation of the R_F 0.28 band afforded the dehydro-(−)-fisetinidol-(+)-catechin (**26**) as *white amorphous solid* (6.4 mg) (Found: M^+, 728.2458. $C_{40}H_{40}O_{13}$ requires M, 728.2469); ^{1}H n.m.r. ($CDCl_3$, 300 MHz, 23 °C) δ 6.81 [d, *J* 2.5 Hz, 3-H(A)], 6.49 [dd, *J* 2.5, 8.5, 5-H(A)], 6.15 [d, *J* 8.5, 6-H(A)], 6.19 [s, 2-H(B)], 6.82 [s, 5-H(B)], 5.17 [dd, *J* 2.5, 3.0, 2-H(C)], 6.09 [dd, *J* 3.0, 3.0, 3-H(C)], 3.36 [dd, *J* 2.5, 3.0, 4-H(C)], 5.61 [s, 6-H(D)], 6.06 [d, *J* 2.0, 2-H(E)], 6.51 [d, *J* 8.5, 5-H(E)], 5.88 [dd, *J* 2.0, 8.5, 6-H(E)], 4.08 [d, *J* 10.0, 2-H(F)], 4.97 [m, 3-H(F)], 3.15 [dd, *J* 6.5, 17.0, 4-$H_{eq.}$(F)], 2.36 [dd, *J* 9.5, 17.0, 4-$H_{ax.}$(F)], 3.65, 3.67, 3.72,

3.73, 3.77, 3.87 (each s, 6 × OMe), 1.80, and 1.95 (each s, 2 × OAc).

A portion (100 mg) of fraction 2 was methylated and the mixture resolved by p.l.c. [benzene–acetone (8:2, v/v; × 2)] to give a single band at R_F 0.5 (38 mg). Acetylation of this material afforded the 8,9-*trans*-9,10-*cis*-tetrahydropyrano[2,3-*h*]chromene (**10**) with physical data identical with those of the corresponding derivative of the natural product.

A portion (50 mg) of fraction 3 was methylated, the mixture resolved by p.l.c. [benzene–acetone–methanol (90: 9:1, v/v], and the R_F 0.24 band (35 mg) acetylated to give the starting material (**2**).

Base-catalysed conversion of (−)-*fisetinidol*-(4α,6)-(+)-*catechin*-O-*methyl ether* (**6**). Treatment of biflavanoid (**6**) (412 mg) with base and work-up as above afforded the phlobatannin mixture as a light-brown amorphous solid (395 mg). This was resolved by column chromatography (3 × 85 cm column, flow rate 1.2 ml/min. 20 ml eluant/tube, first 200 ml of eluant discarded) on Sephadex LH-20/ethanol to the following fractions: 1 [tubes 8—29 (165 mg)], 2 [36—56 (86 mg)], and 3 [78– 99 (27 mg)]. Fraction 3 consisted of unchanged starting material.

Methylation of fraction 1 (165 mg) followed by p.l.c. [benzene–acetone–methanol (90:9:1, v/v)] afforded a methyl ether band (R_F 0.28, 100 mg) which was acetylated to give the 6,7-*trans*-7,8-*cis*-tetrahydropyrano[2,3-*f*]chromene (**15**), identical with the derivative encountered during the 'uncontrolled' synthesis.

Fraction 2 (86 mg) was methylated, the mixture resolved by p.l.c. [benzene–acetone (8:2, v/v; × 2)], and the resulting methyl ether band (R_F 0.41, 34 mg) acetylated to afford the 6,7-*cis*-7,8-*trans*-tetrahydropyrano[2,3-*g*]chromene (**20**), identical with the corresponding derivative of the natural product.

Acknowledgements

Support by the Foundation for Research Development, C.S.I.R., Pretoria, the Sentrale Navorsingsfonds of this University, and the Marketing Committee, Wattle Bark Industry of South Africa, Pietermaritzburg, is acknowledged. Mass spectral data were supplied by Dr. J. M. Steyn, Department of Pharmacology of this University.

References

1 J. A. Steenkamp, J. P. Steynberg, E. V. Brandt, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Chem. Commun.*, 1985, 1678.
2 J. P. Steynberg, D. A. Young, J. F. W. Burger, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Chem. Commun.*, 1986, 1013.
3 K. C. Palgrave in 'Trees of Southern Africa,' ed. E. J. Moll, C. Struik Publishers, Cape Town, 1983, p. 262.
4 J. J. Botha, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1235.
5 D. A. Young, A. Cronjé, A. L. Botes, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2521.
6 I. C. du Preez, A. C. Rowan, D. G. Roux, and J. Feeney, *Chem. Commun.*, 1971, 315.
7 H. K. L. Hundt and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1227.
8 Vogel's Textbook of Quantitative Inorganic Analysis, 4th edn., eds. J. Bassett, R. C. Denney, G. H. Jeffery, and J. Mendham, Longman, London, 1978, Appendix IX.
9 K. Freudenberg and L. Purrmann, *Chem. Ber.*, 1923, **56**, 1185; *Liebigs Ann. Chem.*, 1924, **437**, 274.
10 W. B. Whalley in 'The Chemistry of Flavanoid Compounds,' ed. T. A. Geissmann, Pergamon, Oxford, 1962, p. 446.
11 W. B. Whalley in 'Recent Developments in the Chemistry of Natural Phenolic Compounds,' eds. W. D. Ollis and I. O. Sutherland, Pergamon, London, 1961, p. 26.
12 G. Cardillo, L. Merlini, G. Nasini, and P. Salvadori, *J. Chem. Soc. C*, 1971, 3967.
13 R. W. Hemingway and L. Y. Foo, *J. Chem. Soc., Chem. Commun.*, 1983, 1035.
14 P. E. Laks and R. W. Hemingway, *J. Chem. Soc., Perkin Trans. 1*, 1987, 465.
15 P. E. Laks, R. W. Hemingway, and A. H. Conner, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1875.
16 G. Derdelinckx and J. Jerumanis, *J. Chromatogr.*, 1984, **285**, 231, and refs. therein.
17 J. H. van der Westhuizen, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1220.
18 G. J. Sweeny and G. A. Iacobucci, *J. Org. Chem.*, 1979, **44**, 2298.

Received 7th March 1988; *Paper* 8/00915E