Pergamon

PII: S0031-9422(96)00240-3

Phytochemistry, Vol. 43, No. 1, pp. 253–263, 1996

0031-9422/96 $15.00 + 0.00

STRUCTURE AND SYNTHESIS OF PHLOBATANNINS RELATED TO BIS-FISETINIDOL-EPICATECHIN PROFISETINIDIN TRIFLAVANOIDS*

SUSANNA L. BONNET, JAN P. STEYNBERG, BAREND C. B. BEZUIDENHOUDT, CATHARINA M. SAUNDERS and DANEEL FERREIRA†

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

(*Received in revised form* 26 *February* 1996)

Key Word Index—*Baikiaea plurijuga*; *Colophospermum mopane*; *Guibourtia coleosperma*; Leguminosae; Caesalpiniodeae; profisetinidins; phlobatannins; triflavanoids; C-ring isomerization.

Abstract—The class of natural phlobatannins originating by stereoselective pyran rearrangement of the 2,3-*trans*-3,4-*trans*- and 3,4-*cis*-flavan-3-ol moieties in the hitherto unknown bis-fisetinidol-(4,6:4,8)-epicatechin profisetinidins is extended by identification of several novel analogues. These comprise four functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromenes with an epicatechin DEF unit, as well as one based on an *ent*-catechin moiety, a fisetinidiol-(4α,10)-tetrahydropyrano[2,3-*f*]chromene and a fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromene. The structure of one of the dipyranochromes was established unequivocally by synthesis via base-catalysed pyran ring rearrangement of the bis-fisetinidol-(4α,6:4α,8)-epicatechin triflavanoid. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In contrast to the ubiquitous involvement of catechin as the chain-terminating unit in the 5-deoxy (A-ring) proanthocyanidins [1, 2], incorporation of epicatechin into these classes of condensed tannins is hitherto restricted to a limited number of dimeric proguibourtinidins and profisetinidins [1, 2]. The recent demonstration of the natural occurrence and facile biomimetic synthesis of phlobatannins representing the products of stereoselective C-ring isomerization of the 2,3-*trans*-3,4-*trans*- and 3,4-*cis*-flavan-3-ol units in fisetinidol-(4,8)-epicatechin profisetinidin biflavanoids [3], has suggested that the putative bis-fisetinidol-epicatechin triflavanoids may also participate in this mode of pyran rearrangement. Our continued investigation of the polyphenols in the heartwoods of *Baikiaea plurijuga*, *Colophospermum mopane* and *Guibourtia coleosperma* [4–7] has indeed now revealed the presence of phlobatannins, which are based on these, as yet unknown, profisetinidin triflavanoids.

RESULTS AND DISCUSSION

Besides the diverse group of phlobatannins that are derived from the bis-fisetinidol-catechin triflavanoids [5–8], the methanol extracts of the heartwoods of the aforementioned tree species contain a series of 'trimeric' compounds, which are related to the putative bis-fisetinidol-(4,6:4,8)-epicatechin triflavanoids (**1**, **2** and **3**) and the analogue (**4**) with an *ent*-catechin DEF moiety. The compounds with rearranged heterocyclic rings are the four hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromenes* (**5**, **11**, **13** and **15**) with epicatechin DEF units and the isomeric compound (**17**) with an *ent*-catechin DEF unit, as well as the fisetinidol-(4α,10)-tetrahydropyrano[2,3-*f*]chromene (**7**) and the fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromene (**9**), both with epicatechin DEF moieties. Identification of these compounds by means of 300 MHz ^{1}H NMR analysis (Tables 1 and 2) of the decamethyl ether triacetate derivatives (**6**, **8**, **10**, **12**, **14**, **16** and **18**) was performed by the protocol employed in the characterization of the catechin derived analogues that was described previously [5]. Thus, only key features will be discussed here.

The ^{1}H NMR spectrum of each of the derivatives with epicatechin-type DEF units exhibits coupling constants ($J_{2,3}$ = *ca* 1.0 Hz), which are reminiscent of a 2,3-*cis*-flavan-3-ol central moiety. Since we could not find evidence for the existence of phlobatannins which are based on an *ent*-epicatechin DEF unit during investigation of the polyphenols from the different species of the Caesalpiniodeae, it was assumed that compounds **5**, **7**, **9**, **11**, **13** and **15** all possess an epicatechin central unit. Such an assumption was ratified for the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]-

*Part 23 in the series 'Oligomeric Flavanoids'. For part 22 see ref. [7].

†Author to whom correspondence should be addressed.

*Non-systematic name/numbering to retain the heterocyclic oxygen of the DEF-unit as position 1 for all compounds.

Table 1. ^{1}H NMR peaks (ppm) of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives **6**, **12**, **14**, **16**, **18** and **26** at 300 MHz and 296 K

Ring	H	**6** ($CDCl_3$)	**12** ($CDCl_3$)	**14** (C_6D_6)	**16** ($CDCl_3$)	**18** (C_6D_6)	**26** (C_6D_6)
A	3	6.28 (*d*, 2.5)	6.28 (*d*, 2.5)	6.45 (*d*, 2.5)	6.31 (*d*, 2.5)	6.42 (*d*, 2.5)	6.31 (*d*, 2.5)
	5	6.30 (*dd*, 2.5, 8.5)	6.37 (*dd*, 2.5, 8.5)	6.37 (*dd*, 2.5, 8.5)	6.37 (*dd*, 2.5, 8.5)	6.35 (*dd*, 2.5, 8.5)	7.47 (*dd*, 2.5, 8.5)
	6	6.59 (*d*, 8.5)	6.86 (*d*, 8.5)	7.24 (*d*, 8.5)	6.91 (*d*, 8.5)	7.19 (*d*, 8.5)	7.35 (*d*, 8.5)
B	2	6.73 }	6.27 (*d*, 2.0)	7.06 (*br.s*)	6.31 (*d*, 2.0)	6.59 (*d*, 2.0)	7.05 (*d*, 2.0)
	5	6.69 } 2nd order	6.48 (*d*, 8.0)	6.54 (*d*, 8.5)	6.47 (*d*, 8.5)	6.50 (*d*, 8.5)	6.55 (*d*, 8.5)
	6	6.69 }	6.00 (*dd*, 2.0, 8.0)	7.08 (*dd*, 2.0, 8.5)	6.12 (*dd*, 2.0, 8.5)	6.43 (*dd*, 2.0, 8.5)	7.10 (*dd*, 2.0, 8.5)
C	10	4.64 (*d*, 10.0)	4.88 (*d*, 10.5)	5.61 (*br.s*)	4.95 (*d*, 10.5)	5.29 (*d*, 10.0)	5.49 (*d*, 10.0)
	11	5.32 (*dd*, 6.0, 10.0)	5.06 (*dd*, 6.0, 10.5)	6.09 (*d*, 1.5, 2.0)	5.04 (*d*, 5.5, 10.5)	5.62 (*d*, 6.0, 10.0)	6.08 (*dd*, 6.0, 10.0)
	12	5.26 (*d*, 6.0)	5.22 (*d*, 6.0)	5.33 (*d*, 2.0)	5.26 (*d*, 5.5)	5.54 (*d*, 6.0)	5.69 (*d*, 6.0)
E	2	6.88 (*d*, 2.5)	6.92 (*d*, 2.0)	6.59 (*d*, 2.0)	6.95 (*d*, 2.0)	6.64 (*d*, 2.0)	6.65 (*d*, 2.0)
	5	6.74 (*d*, 8.5)	6.74 (*d*, 8.0)	6.58 (*d*, 8.5)	6.74 (*d*, 8.5)	–	6.49 (*d*, 8.5)
	6	6.81 (*dd*, 2.5, 8.5)	6.78 (*dd*, 2.0, 8.0)	6.44 (*d*, 2.0, 8.5)	6.78 (*dd*, 2.0, 8.5)	6.56–6.49 (*m*)	6.56 (*dd*, 2.0, 8.5)
F	2	4.72 (*br.s*)	4.69 (*br.s*)	4.77 (*br.s*)	4.77 (*br.s*)	5.00 (*d*, 7.5)	5.17 (*d*, 6.0)
	3	5.45 (*m*)	5.48 (*m*)	5.54 (*m*)	5.48 (*m*)	5.33 (*m*)	5.46 (*m*)
	$4_{ax.}$	2.94 (*m*)	3.01 (*m*)	Overlapped by OMe	3.05–3.09 (*m*)	3.14 (*dd*, 7.5, 17.0)	3.05 (*dd*, 7.0, 16.0)
	$4_{eq.}$	2.94 (*m*)	3.01 (*m*)	resonances	–	3.54 (*dd*, 5.5, 17.0)	3.48 (*dd*, 5.5, 16.0)
G	3	6.35 (*d*, 2.5)	6.14 (*d*, 2.5)	6.50 (*d*, 2.5)	6.44 (*d*, 2.5)	6.46 (*d*, 2.5)	6.40 (*d*, 2.5)
	5	6.51 (*dd*, 2.5, 8.5)	6.14 (*dd*, 2.5, 8.5)	6.33 (*dd*, 2.5, 8.5)	6.48 (*dd*, 2.5, 8.5)	6.37 (*dd*, 2.5,8.5)	6.36 (*dd*, 2.5, 8.5)
	6	7.01 (*d*, 8.5)	6.48 (*d*, 8.5)	7.28 (*d*, 8.5)	6.83 (*d*, 8.5)	7.12 (*d*, 8.5)	7.23 (*d*, 8.5)
H	2	6.83 (*d*, 2.0)	6.75 (*d*, 2.0)	6.60 }	6.88 (*d*, 2.0)	7.11 (*d*, 2.0)	6.93 (*d*, 2.0)
	5	6.80 (*d*, 8.0)	6.64 (*d*, 8.5)	6.45 } 2nd order	6.76 (d, 8.5)	6.61 (*d*, 8.5)	6.48 (*d*, 8.5)
	6	6.91 (*dd*, 2.0, 8.0)	6.76 (*dd*, 2.0, 8.5)	6.45 }	6.77 (*dd*, 2.0, 8.5)	6.98 (*dd*, 2.0, 8.5)	6.76 (*dd*, 2.0, 8.5)
I	6	5.03 (*d*, 10.5)	5.12 (*d*, 6.5)	5.35 (*d*, 10.0)	5.06 (*br.s*)	5.59 (*br.s*)	5.18 (*d*, 10.0)
	7	5.44 (*dd*, 6.0, 10.5)	5.57 (*dd*, 5.5, 6.5)	5.78 (*dd*, 6.0, 10.0)	5.41 (*dd*, 1.0, 2.0)	5.97 (*dd*, 1.0, 2.0)	5.80 (*dd*, 6.0, 10.0)
	8	5.13 (*d*, 6.0)	4.58 (*d*, 5.5)	5.70 (*d*, 6.0)	4.57 (*d*, 2.0)	5.22 (*d*, 2.0)	5.76 (*d*, 6.0)
	OMe	3.42(2-A), 3.61(2-G)	3.47(2-G), 3.55(3-B),	3.20(2-G), 3.28 (2-A),	3.49(3-B), 3.61(2-A),	3.23(2-A), 3.39, 3.41	3.12(2-A), 3.14(2G),
		3.72(4-G), 3.81(4-A),	3.59(2-A), 3.71(4-G),	3.31(3-H/4-H), 3.32,	3.66(2-G), 3.74(4-A),	(2-G), 3.42(×2), 3.44	3.23(4-A), 3.31
		3.82(5-B/3-H/4-H),	3.74(4-A), 3.77 (3-H),	3.33 (×2), 3.35(3-B),	3.78(4-B), 3.82(4-G),	(4-A), 3.47(4-G), 3.48,	(4-G), 3.32, 3.34,
		3.84(4-E), 3.85(4-B)	3.79(4-B), 3.81(4-H), 3.85	3.40(4-E) and 3.52	3.83(3-H/4-H), 3.85(4-E),	3.49, 3.50, each *s*	3.36, 3.37, 3.40,
		and 3.87(3-E), each *s*	(4-E), 3.88(3-E), each *s*	(3-E), each *s*	3.88(3-*E*), each *s*		3.53, each *s*
	OAc	1.69, 1.72, 1.91, each *s*	1.65, 1.88, 1.95, each *s*	1.24, 1.40, 1.48, each *s*	1.69, 1.93, 1.94, each *s*	1.49, 1.52, 1.77, each *s*	1.47(×2), 1.51, each *s*

Table 2. ^{1}H NMR peaks (ppm) of the fisetinidol- and chromanyl-tetrahydropyranochromene derivatives **8**, **10**, **28**, **30** and **32** at 300 MHz and 296 K

Ring	H	**8** ($CDCl_3$)	**10** ($CDCl_3$)	**10** (C_6D_6)	**28** ($CDCl_3$)	**30** (acetone-d_6)	**32** ($CDCl_3$)
A	3/8	6.20 (*d*, 2.5)	6.24 (*d*, 2.5)	6.39 (*d*, 2.5)	6.35 (*d*, 2.5)	6.29 (*d*, 2.5)	6.43 (*d*, 2.5)
	5/6	6.33 (*dd*, 2.5, 8.5)	6.35 (*dd*, 2.5, 8.5)	6.74 (*dd*, 2.5, 8.5)	6.44 (*dd*, 2.5, 8.5)	6.54 (*dd*, 2.5, 8.5)	6.39 (*dd*, 2.5, 8.5)
	6/5	6.71 (*d*, 8.5)	6.90 (*d*, 8.5)	7.77 (*d*, 8.5)	6.79 (*d*, 8.5)	6.95 (*d*, 8.5)	6.74 (*d*, 8.5)
B	2	6.90 (*d*, 2.0)	6.36 (*d*, 2.0)	6.50*	6.36 (*d*, 2.0)	–	6.81 (*d*, 2.0)
	5	6.83 (*d*, 8.0)	6.55 (*d*, 8.0)	6.47*	6.54 (*d*, 8.5)	6.75–6.92*	6.79 (*d*, 8.5)
	6	6.94 (*dd*, 2.0, 8.0)	6.24 (*dd*, 2.0, 8.0)	6.47*	6.20 (*dd*, 2.0, 8.5)		6.87 (*dd*, 2.0, 8.5)
C	2/8	4.85 (*d*, 10.0)	5.09 (*d*, 4.0)	5.67 (*d*, 10.5)	4.07–5.61 (*d*, 10.0)*†	4.83 (*d*, 10.0)	4.98 (*d*, 10.5)
	3/9	6.10 (*t*, 10.0)	5.23 (*dd*, 1.5, 4.0)	5.61 (*dd*, 5.5, 10.5)	4.07–5.73* (*dd*, 6.0, 10.0)†	6.26 (*t*, 10.0)	5.34 (*dd*, 5.5, 10.5)
	4/10	4.62 (*d*, 10.0)	5.08 (*d*, 1.5)	5.87 (*d*, 5.5)	5.05–5.79* (*d*, 6.0)†	4.91 (*d*, 10.0)	5.04 (*d*, 5.5)
E	2	6.86 (*d*, 2.0)	6.93*	7.12 (*d*, 2.0)	6.39 (*d*, 2.0)	7.10 (*d*, 2.0)	not detectable
	5	6.76 (*d*, 8.5)	6.75*	6.57 (*d*, 8.0)	6.59 (*d*, 8.5)	6.96 (*d*, 8.5)	6.72 (*d*, 8.0)
	6	6.81 (*dd*, 2.0, 8.5)	6.75*	6.80 (*dd*, 2.0, 8.0)	6.28 (*dd*, 2.0, 8.5)	7.03 (*dd*, 2.0, 8.5)	6.76 (*dd*, 2.0, 8.0)
F	2	4.48 (*br.s*)	4.74 (*br.s*)	4.34 (*br.s*)	4.84 (*d*, 8.0)	5.16 (*d*, 7.0)	5.11 (*br.s*)
	3	5.31 (*m*)	5.43 (*m*)	5.51 (*m*)	5.01 (*m*)	5.31 (*m*)	5.67 (*m*)
	$4_{ax.}$	2.93 (*m*)	3.04 (*m*)	2.81 (*m*)	2.78 (*dd*, 8.0, 16.0)	2.80 (*dd*, 7.0, 16.0)	2.87–3.14 (*m*)
	$4_{eq.}$	2.93 (*m*)	3.04 (*m*)	2.81 (*m*)	3.03 (*dd*, 5.5, 16.0)	3.05 (*dd*, 5.0, 16.0)	
G	3/8	6.47 (*d*, 2.5)	6.33 (*d*, 2.5)	6.49 (*d*, 2.5)	6.35 (*d*, 2.5)	6.56 (*d*, 2.5)	6.40 (*d*, 2.5)
	5/6	6.38 (*dd*, 2.5, 8.5)	6.48 (*d*, 2.5, 8.5)	6.44 (*dd*, 2.5, 8.5)	6.49 (*dd*, 2.5, 8.5)	6.42 (*dd*, 2.5, 8.5)	6.48 (*dd*, 2.5, 8.5)
	6/5	6.79 (*d* 8.5)	6.77 (*d* 8.5)	6.96 (*d* 8.5)	6.79 (*d* 8.5)	6.97 (*d* 8.5)	6.88 (*d* 8.5)
H	2	6.83 (*d*, 2.0)	6.69 (*d*, 2.0)	7.05 (*d*, 2.0)	6.67 (*d*, 2.0)	6.45 (*d*, 2.0)	6.76 (*d*, 2.0)
	5	6.80 (*d*, 8.5)	6.74 (*d*, 8.5)	6.54 (*d*, 8.0)	6.74 (*d*, 8.0)	6.66 (d, 8.5)	6.65 (*d*, 8.5)
	6	6.89 (*dd*, 2.0, 8.5)	6.82 (*dd*, 2.0, 8.5)	7.00 (*dd*, 2.0, 8.0)	6.81 (*dd*, 2.0, 8.0)	6.19 (*dd*, 2.0, 8.5)	6.54 (*dd*, 2.0, 8.5)
I	2/6	4.99 (*d*, 10.0)	4.88 (*d*, 10.0)	4.94 (*d*, 10.0)	4.89 (*d*, 10.0)	5.11 (*d*, 5.5)	5.58 (*br.s*)
	3/7	5.46 (*dd*, 6.0, 10.5)	6.26 (*t*, 10.0)	6.75 (*t*, 10.0)	6.21 (*t*, 10.0)	4.92 (*dd*, 5.5, 10.0)	5.37 (*dd*, 1.5, 2.0)
	4/8	5.19 (*d*, 6.5)	4.71 (*d*, 10.0)	5.06 (*d*, 10.0)	4.71 (*d*, 10.0)	5.10 (*d*, 10.0)	4.16 (*d*, 2.0)
	OMe	3.55(9-D), 3.59(7-A), 3.76(4-G), 3.77(3-B), 3.79(3-E), 3.82(2-G), 3.84(3-H), 3.85(4-E), 3.86(4-B/4-H), each *s*	3.53(2-A), 3.64(3-B/3H), 3.71(4-A), 3.74(4-G), 3.78(5-D), 3.81(4-B), 3.83(4-H), 3.85(4-E), 3.88(3-E), each *s*	3.24(4-A), 3.25 (2-A), 3.29(4-B), 3.34 (3-B/4-H), 3.36(2-G, 3.41(4-E), 3.50(3-H), 3.73(3-E), 3.75(5-D), each *s*	3.46, 3.62(3-H), 3.64(3-B/3-E), 3.75, 3.78(4-A), 3.79 (4-G), 3.80(4-B), 3.82(4-E) 3.83(4-H), each *s*	3.22(5-D), 3.56, 3.62, 3.75, 3.76, 3.77, 3.78 (4-G), 3.79(7-A), 3.80, 3.85(2-G), each *s*	3.11, 3.34, 3.67(4-G), 3.75, 3.76(×2), 3.78(4-H), 3.82, 3.84, 3.85, each *s*
	OAc	1.47, 1.74, 1.93, each *s*	1.66, 1.69, 1.93, each *s*	1.39, 1.45, 1.58, each *s*	1.63, 1.70, 1.94, each *s*	1.70(×2), 1.89, each *s*	1.71, 1.75, 1.82, each *s*

*Second order.
†In C_6D_6.

chromene (**5**) by synthesis via the base-catalysed pyran ring rearrangement of the bis-fisetinidol-(4α,6:4α,8)-epicatechin triflavanoid (**1**) (see below).

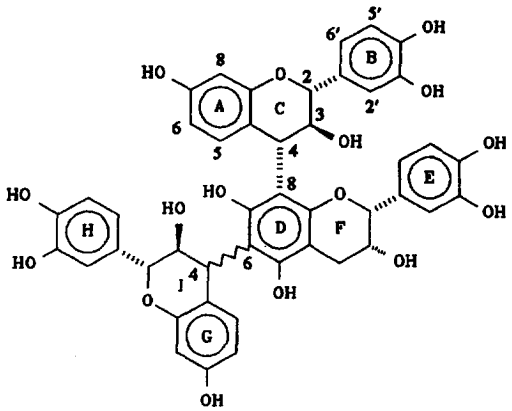
The 'trimeric' nature of all the derivatives was evident from the presence of 10 methoxyl and three acetoxy proton signals in their ^{1}H NMR spectra. NOE experiments confirmed the 'liberation' of two resorcinol moieties (A- and G-rings) and, hence, the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene constitution for analogues **6**, **12**, **14**, **16** and **18**. Coupling constants for the protons of the two heterocyclic AMX-systems corresponded with 6,7-*trans*-7,8-*cis*-10,11-*trans*-11,12-*cis* ($J_{6,7}$ = 10.5, $J_{10,11}$ = 10.0, $J_{7,8}$ = $J_{11,12}$ = 6.0 Hz for **6**), 6,7-*trans*-7,8-*trans*-10,11-*trans*-11,12-*cis* ($J_{6,7}$ = 6.5, $J_{7,8}$ = 5.5, $J_{10,11}$ = 10.5, $J_{11,12}$ = 6.0 Hz for **12**, 6,7-*trans*-7,8-*cis*-10,11-*cis*-11,12-*trans* ($J_{6,7}$ = 10.0, $J_{7,8}$ = 6.0, $J_{10,11}$ = 1.5, $J_{11,12}$ = 2.0 Hz for **14**, 6,7-*cis*-7,8-*trans*-10,11-*trans*-11,12-*cis* ($J_{6,7}$ *ca* 1.0, $J_{7,8}$ = 2.0, $J_{10,11}$ = 10.5, $J_{11,12}$ = 5.5 Hz for **16** and 6,7-*cis*-7,8-*trans*-10,11-*trans*-11,12-*cis* ($J_{6,7}$ = 1.0, $J_{7,8}$ = 2.0, $J_{10,11}$ = 10.0, $J_{11,12}$ = 6.0 Hz for **18** relative configurations for the C- and I-rings. These configurations were confirmed by the NOE association of 10-H(C) with 6-H(A) for compounds **6**, **12**, **14**, **16** and **18**, and of 6-H(I) with 6-H(G) for **6**, **14**, **16** and **18**.

The ^{1}H NMR coupling constants of the protons of the heterocyclic AMX-systems of derivatives **8** and **10** indicated, respectively, an 'intact' 2,3-*trans*-3,4-*trans* C-4 substituted fisetinidol unit [$J_{2,3(C/I)} = J_{3,4(C/I)}$ = 10.0 Hz] and a rearranged pyran ring with *trans*–*cis* relative configuration ($J_{6,7}$ = 10.5, $J_{7,8}$ = 6.0 Hz for **8**; $J_{8,9}$ = 10.5, $J_{9,10}$ = 5.5 Hz for **10** for both compounds. Such involvement of a single heterocycle in pyran ring rearrangement was additionally confirmed by the appropriate NOE experiments, indicating the 'release' of a single resorcinol moiety from a triflavanoid precursor of type **1**. The *trans*–*cis* relative configuration of the rearranged pyrans rings was again confirmed by the significant NOE association of 6-H(I) with 6-H(G) for derivative **8** and of 8-H(C) with 6-H(A) for compound **10**. A notable feature that was observed in the ^{1}H NMR spectrum of a phlobatannin for the first time is the solvent-dependence of the heterocyclic proton coupling constants of the tetrahydropyrano[2,3-*h*]chromene unit in compound **10**. In contrast to 'normal' coupling constants of these protons in benzene-d_6 (Table 2), the ^3J values are conspicuously smaller in $CDCl_3$ ($J_{8,9}$ = 4.0, $J_{9,10}$ = 1.5 Hz) indicating a conformational equilibrium for the 8,9-*trans*-9,10-*cis*-moiety, which is predominantly populated by an A-conformer [9, 10].

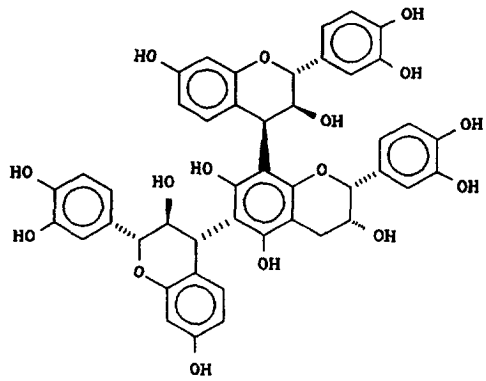
NOE association of 12-H(C) with 2-H(E) served to differentiate the C- and I-rings in compounds **6**, **12** and **16**, thus confirming the regiomerism of their ABC- and GHI-units. For compound **8**, the NOE association of 9-OMe(D) with both 4-H(C) and 8-H(I) indicated the tetrahydropyrano[2,3-*f*]chromene arrangement, hence, the NOE effect of 5-OMe(D) with both 4-H(I) and 5-H(G) affirming the tetrahydropyrano[2,3-*h*]-chromene framework for compound **10**. Owing to the *trans*-relationship between 12-H(C) and the E-ring, the key NOE association of this proton and 2-H(E), which would have permitted differentiation of the spin systems of the ABC- and GHI-units, was conspicuously absent in derivative **14**. However, since the coupling constants of the heterocyclic protons of compound **14** are identical to those of derivative **16** (cf. Table 1) in which the locations of the C- and I-rings are evident from the NOE associations of 12-H(C) with 2-H(E), 2-OMe(G) with 2- and 5-H(B) and of 3-OMe(B) with both 3- and 5-H(G), the constitution of the former compound must necessarily conform to formulation **14**.

A high-amplitude positive Cotton effect at 246.5 nm ([θ] = 3.4 × 10^4) in the circular dichroic (CD) spectrum of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivative (**6**) strongly indicates an 8β,12β-orientation of the G- and A-rings by application of the aromatic quadrant rule [11–13]. When taken in conjunction with ^{1}H NMR coupling constants and the relevant NOE observations, this strongly indicates the 2*R*,3*R*:6*R*,7*S*,8*S*:10*R*,11*S*,12*S* absolute configuration for the natural product (**5**), an allocation that was confirmed by a biomimetic synthesis (see below). However, in those instances where the substituents at the double benzylic centres are *trans*-oriented (e.g. at C-8 and C-12 in derivative) the 230–250 nm region of the CD spectra did not permit stereochemical assignment. Based on the assumption that the F-ring in derivatives **6**, **8**, **10**, **12**, **14** and **16** possesses the 2*R*,3*R* absolute stereochemistry, ^{1}H NMR coupling constants of heterocyclic constants and the key NOE associations between protons of different units [e.g. between 12-H(C) and 2-H(E) in derivative **12** we favour the 2*R*,3*R*(F):6*R*,7*S*,8*S*:2*R*,3*S*,4*S*(C) absolute configuration for **8**, 2*R*,3*R*(F) : 2*R*,3*S*,4*S*(I) : 8*R*,9*S*,10*S* for **10**, 2*R*,3*R* : 6*R*,7*S*,8*R* : 10*R*,11*S*,12*S* for **12**, 2*R*,3*R* : 6*R*,7*S*,8*S* : 10*S*,11*S*,12*R* for **14**, and 2*R*,3*R* : 6*S*,7*S*,8*R*:10*R*,11*S*,12*S* for **16**. The hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivative (**18**) with an *ent*-catechin DEF unit exhibited identical ^{1}H NMR data compared to those of the synthetic compound **20** (see below). Their CD spectra, however, indicated an enantiomeric relationship, hence defining the absolute configuration of the natural product (**17**) as 2*S*,3*R*:6*S*,7*S*,8*R*:10*R*,11*S*,12*S*.

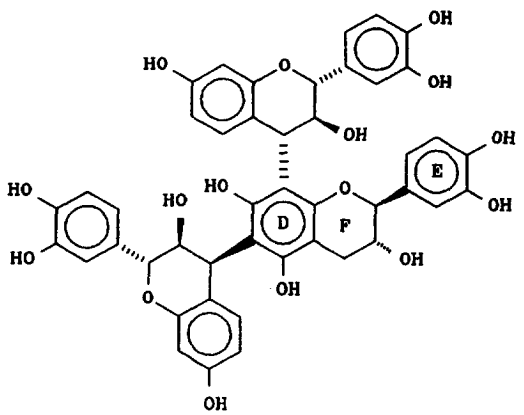
In order to establish the structures of some of the natural products with epicatechin DEF units unequivocally, the base-catalysed pyran ring rearrangement of their presumed biogenetic precursor, bis-fisetinidol-(4α,6:4α,8)-epicatechin (**1**) was investigated. Owing to the failure of the protocol of selective protection of epicatechin at 4′-OH [3] precursor **1** had to be used in 'unprotected' form and was available via the acid-catalysed condensation of fisetinidol-(4α,8)-epicatechin (**21**) [3] and fisetinidol-4α-ol (**22**) (Scheme 1). In addition to exhibiting the anticipated effects of dynamic rotational isomerism, the ^{1}H NMR spectrum of the decamethyl ether triacetate (**23**) revealed four distinctive triplets ($^3J_{3,4}$ *ca* 10.0 Hz) in the δ 6.02–6.31 region, representing the 3/3′-H(C and I) resonances and indicating the 2,3-*trans*-3,4-*trans* relative configuration for the ABC- and GHI-moieties, hence establish-



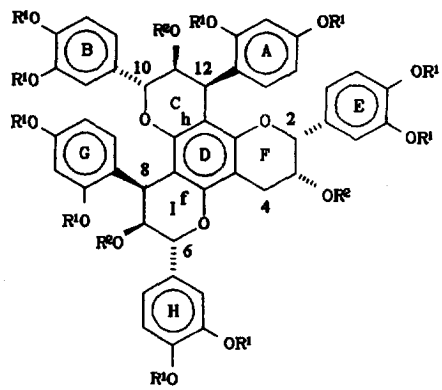
(1) $\{\equiv\}$
(2) $\{\equiv|$



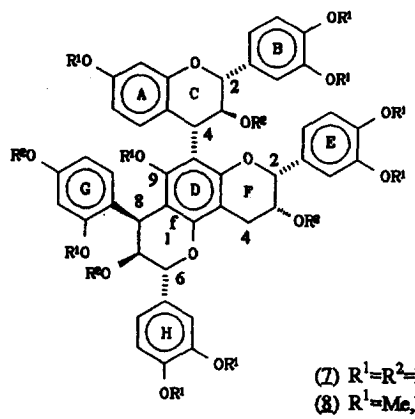
(3)



(4)



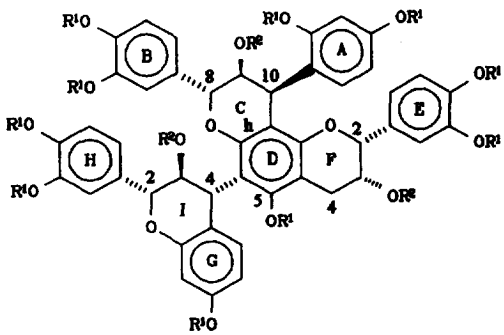
(5) $R^1=R^2=H$
(6) $R^1=Me, R^2=Ac$



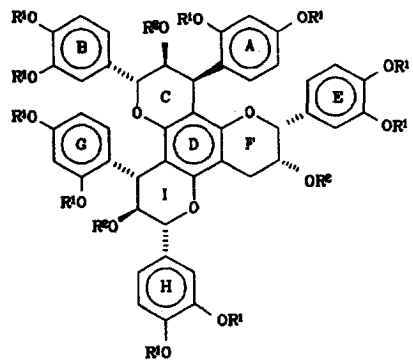
(7) $R^1=R^2=H$
(8) $R^1=Me, R^2=Ac$

ing the structure of compound **1** as the bis-fisentinidol-(4α,6:4α,8)-epicatechin. Full ^{1}H NMR details of derivative **23** and of the decamethyl ether triacetate (**24**) of the *bis*-fisetinidol-(4β,6:4α,8)-catechin (**2**) will be presented elsewhere.

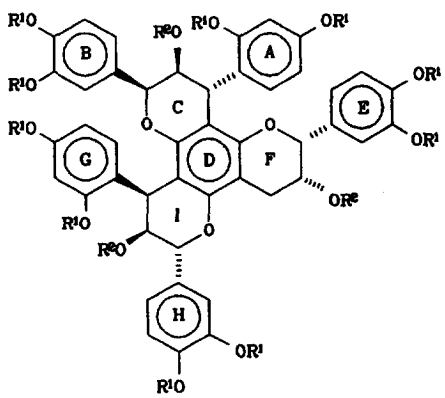
Treatment of the profisetinidin triflavanoid **1** with 0.025 M $NaHCO_3$–0.025 M Na_2CO_3 buffer (pH 10) for 5 hr at 50° under nitrogen gave complete conversion into a mixture comprising the 6,7-*trans*-7,8,-*cis*-10,11-*trans* - 11,12 - *cis* - hexahydrodipyrano[2,3 - *f*:2′,3′-*h*]chromene (**5**) and its C-2(F) epimer (**25**), the fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromene (**27**) and fisetinidol-(4α,10)-tetrahydropyrano[3,2-*g*]chromene (**29**) based on an *ent*-catechin DEF unit, and the 4-



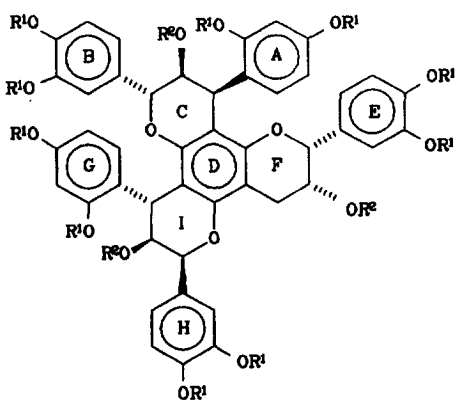
(9) $R^1=R^2=H$
(10) $R^1=Me, R^2=Ac$



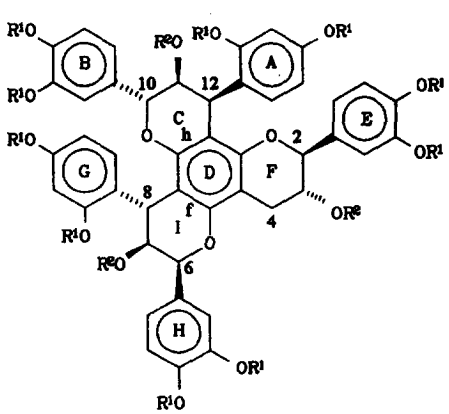
(11) $R^1=R^2=H$
(12) $R^1=Me, R^2=Ac$



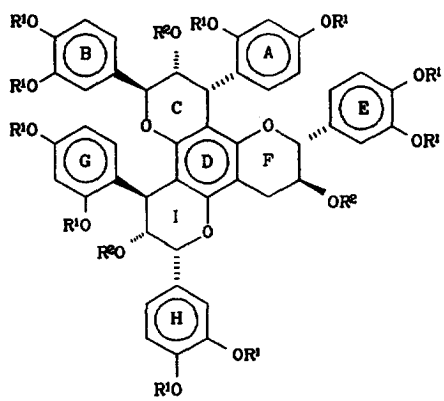
(13) $R^1=R^2=H$
(14) $R^1=Me, R^2=Ac$



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

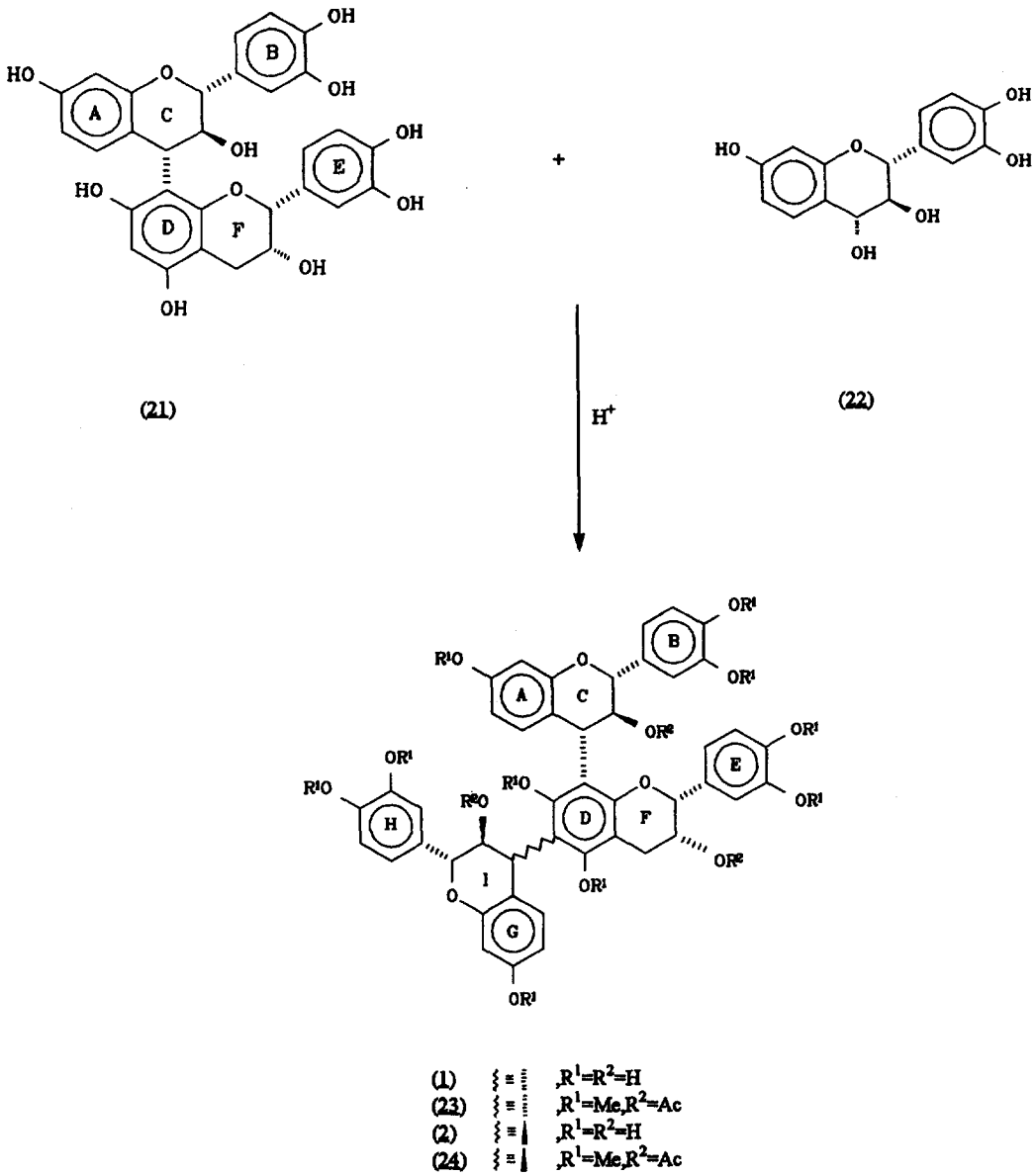


(17) $R^1=R^2=H$
(18) $R^1=Me, R^2=Ac$



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

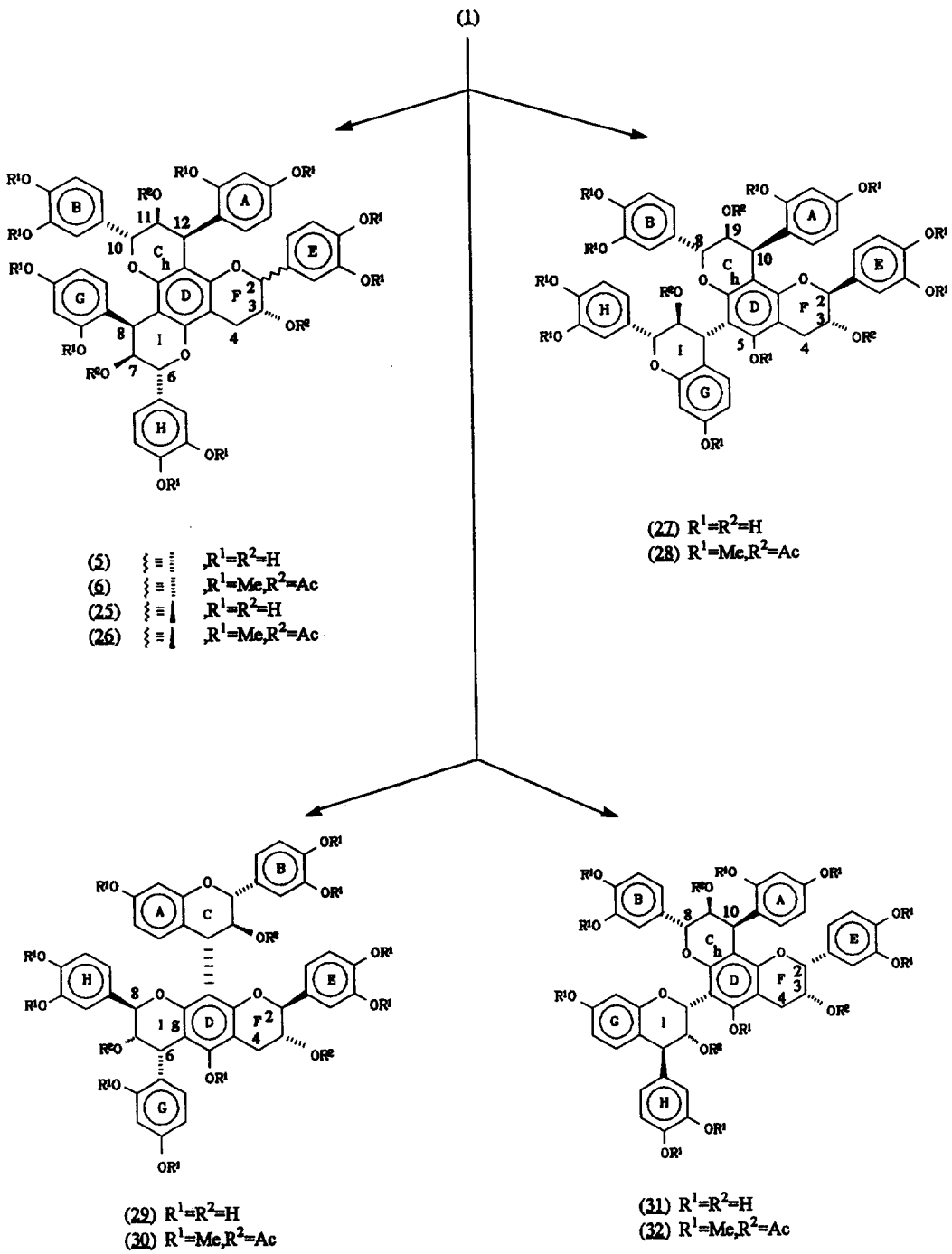
arylchroman-(2α,6)-tetrahydropyrano[2,3-*h*]chromene (**31**) (Scheme 2). Owing to difficulties in purifying the products as free phenols, and in order to facilitate comparison with possible natural counterparts, structural elucidation was performed on the decamethyl ether triacetate derivatives, e.g. **6**. Application of the ^{1}H NMR criteria for establishing the structures of this class of compounds in conjunction with the known mechanism of their genesis from the triflavanoid precursor **1** [5], confirmed the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene backbone and the 6,7-*trans*-7,8-*cis*-10,11-*trans*-11,12-*cis* relative configuration for derivatives **6** and **26**, respectively. The ^{1}H NMR and CD data for compound **6** are identical to those of the corresponding derivative of the natural product, hence proving the structure of the latter unequivocally. The transformation



Scheme 1. Acid-catalysed condensation of fisetinidol-(4α,8)-epicatechin (**21**) with fisetinidol-4α-ol (**22**).

of the 2,3-*cis* DEF unit in precursor **1** to the thermodynamically more stable 2,3-*trans*-flavan-3-ol moiety in compound **25** and indeed also in analogues **27** and **29** ($J_{2,3}$ = 8.0 and 7.0 Hz for **28** and **30**, respectively, under alkaline conditions, is well documented [14] and requires no further attention. Such facile epimerization at C-2 may suggest that the natural product (**17**) with an *ent*-catechin DEF unit also originated from a profisetinidin triflavanoid precursor with an epicatechin central moiety.

Application of the established ^{1}H NMR protocol [5] (Table 2) to derivatives **28** and **30** indicated the 'release' of a single resorcinol moiety from a heterocyclic C/I-ring in the triflavanoid precursor **1** and the presence of an unchanged fisetinidol unit ($J_{2,3}$ = $J_{3,4}$ = 10.0 Hz for both compounds), thus confirming the flavanyltetrahydropyranochromene skeleton in each instance. Coupling constants of the protons of the remaining heterocycle were reminiscent of 8,9-*trans*-9,10-*cis*-($J_{8,9}$ = 10.0, $J_{9,10}$ = 6.0 Hz) and 6,7-*cis*-7,8-*trans*-($J_{6,7}$ = 5.5, $J_{7,8}$ = 10.0 Hz) relative configurations of the tetrahydropyranochromene units for derivatives **28** and **30**, respectively. NOE association of 5-OMe(D) with 4-H(I), 5-H(G) and 4-$H_{ax.}$ and $_{eq.}$(F) confirmed the tetrahydropyrano[2,3-*h*]chromene arrangement for compound **28**. The observed NOE associations of 5-OMe(D) with 6-H(G) and 6-H(I) did not permit differentiation between the tetrahydropyrano[3,2-*g*]- and [2,3-*f*]-chromene arrangements for derivative **30**. However, comparison of the ^{1}H NMR and CD data for compound **30** with those of its enantiomer that was synthesized via base treatment of the *ent*-fisetinidol-



Scheme 2. Base-catalysed pyran rearrangement of bis-(4α,6:8)-fisetinidol-epicatechin (**1**).

(4β,6:4β,8)-catechin triflavanoid confirmed the tetrahydropyrano[3,2-*g*]chromene arrangement unequivocally. The hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivative (**20**) was similarly available by treatment of the *ent*-fisetinidol-(4α,6:4β,8)-catechin triflavanoid. Details of these transformations will be discussed elsewhere.

The ^{1}H NMR spectrum (Table 2) of the decamethyl ether triacetate (**32**) is conspicuously free of the effects of dynamic rotational isomerism at ambient temperatures and closely resembles that of related 4-arylchroman-(2α,6)-tetrahydropyrano[2,3-*h*]chromenes that were obtained during base treatment of the bis-fisetinidol-(4α,6:4β,8)-catechin triflavanoid [7]. Coupling constants of the protons of the heterocycles indicated a 2,3-*cis* relative configuration for the flavan-3-ol DEF unit ($J_{2,3}$ = *ca* 1.0 Hz), *cis–trans* configuration for the I-ring ($J_{2,3}$ = 1.5, $J_{3,4}$ = 2.0 Hz) and *trans–*

cis configuration for the C-ring ($J_{8,9} = 10.5$, $J_{9,10} = 5.5$ Hz). The remaining basic structural features were again elaborated by means of the appropriate NOE, COSY and spin-decoupling experiments, while the absolute configurations of the compounds shown in Scheme 2 could be designated trivially and are indicated at the Experimental section.

The results presented in this and the preceding three papers demonstrate a remarkable structural diversity amongst the C-ring isomerized condensed tannins and presumably indicate ubiquity in nature similar to that of their apparent precursors at the triflavanoid level. These and previous results [15, 16] clearly indicate that the phenomenon of pyran ring rearrangement with concomitant 'release' of resorcinol-type functionality and, hence, the availability of potent nucleophilic centers, especially at the triflavanoid and higher oligomeric levels, may significantly contribute towards the utility of the condensed tannins in cold-setting adhesives and leather-tanning applications.

EXPERIMENTAL

The same general experimental procedures described in ref. [5] were also employed here. Isolation of the novel compounds **5**, **7**, **9**, **11**, **13** and **17** and their identification as the corresponding decamethyl ether triacetates **6**, **8**, **10**, **12**, **14** and **18** are also fully described in ref. [5]. Thus, only the physical data of the latter six compounds will be described here.

(2R,3R:6R,7S,8S:10R,11S,12S)-3,7,11-*Triacetoxy*-2,6,10-*tris*-(3,4-*dimethoxyphenyl*)-8,12-*bis*-(2,4-*dimethoxyphenyl*)-2,3-cis-6,7-trans-7,8-cis-10,11-trans-11,12-cis-3,4,7,8,11,12-*hexahydro*-2H,6H,10H-*dipyrano*[2,3-f:2′,3′-h]*chromene* (**6**). Found $[M]^+$, 1100.4049, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 1.7×10^2, $[\theta]_{285.5}$ 2.0×10^4, $[\theta]_{279.0}$ 1.1×10^1, $[\theta]_{271.0}$ -1.7×10^4, $[\theta]_{256.0}$ -3.3×10^2, $[\theta]_{247.5}$ 2.0×10^4, $[\theta]_{240.5}$ -4.9×10^1, $[\theta]_{239.0}$ -2.9×10^3.

(2R,3R:6R,7S,8S)-3,7-*Diacetoxy*-9-*methoxy*-10-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-2,6-*bis*-(3,4-*dimethoxyphenyl*)-8-(2,4-*dimethoxyphenyl*)-2,3-cis-6,7-trans-7,8-cis-3,4,7,8-*tetrahydro*-2H,6H-*pyrano*[2,3-f]*chromene* (**8**). Found $[M]^+$, 1100.4043, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 9.5×10^1, $[\theta]_{284.0}$ 4.8×10^3, $[\theta]_{281.5}$ 4.6×10^3, $[\theta]_{262.0}$ 1.2×10^3, $[\theta]_{246.5}$ 1.3×10^4, $[\theta]_{238.0}$ 3.2×10^2.

(2R,3R:8R,9S,10S)-3,9-*Diacetoxy*-5-*methoxy*-6-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*acetoxy*-3′,4′,7-*trimethoxyflavan*-4-*yl*]-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 (**10**). Found $[M]^+$, 1100.4047, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{286.5}$ 9.7×10^3, $[\theta]_{280.5}$ -3.5×10^2, $[\theta]_{271.5}$ -8.9×10^3, $[\theta]_{256.0}$ -3.3×10^3, $[\theta]_{245.0}$ -3.8×10^4, $[\theta]_{237.5}$ -7.9×10^2.

(2R,3R:6R,7S,8R:10R,11S,12S)-3,7,11-*Triacetoxy*-2,6,10-*tris*-(3,4-*dimethoxyphenyl*)-8,12-*bis*-(2,4-*dimethoxyphenyl*)-2,3-cis-6,7-trans-7,8-trans-10,11-trans-11,12-cis-3,4,7,8,11,12-*hexahydro*-2H,6H,10H-*dipyrano*[2,3-f:2′,3′-h]*chromene* (**12**). Found $[M]^+$, 1100.4042, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 1.6×10^3, $[\theta]_{285.5}$ 2.0×10^4, $[\theta]_{275.5}$ 3.8×10^2, $[\theta]_{269.0}$ -5.3×10^3, $[\theta]_{259.5}$ 2.0×10^2, $[\theta]_{252.5}$ 6.1×10^3, $[\theta]_{247.5}$ -2.2×10^2, $[\theta]_{241.5}$ -1.1×10^4, $[\theta]_{229.5}$ -3.2×10^2.

(2R,3R:6R,7S,8S:10S,11S,12R)-3,7,11-*Triacetoxy*-2,6,10-*tris*-(3,4-*dimethoxyphenyl*)-8,12-*bis*-(2,4-*dimethoxyphenyl*)-2,3-cis-6,7-trans-7,8-cis-10,11-cis-11,12-trans-3,4,7,8,11,12-*hexahydro*-2H,6H,10H-*dipyrano*[2,3-f:2′,3′-h]*chromene* (**14**). Found $[M]^+$, 1100.4045, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 1.3×10^3, $[\theta]_{283.0}$ 1.1×10^4, $[\theta]_{259.0}$ 1.9×10^3, $[\theta]_{244.5}$ 8.3×10^3, $[\theta]_{226.0}$ -7.9×10^2.

(2S,3R:6S,7S,8R:10R,11S,12S)-3,7,11-*Triacetoxy*-2,6,10-*tris*-(3,4-*dimethoxyphenyl*)-8,12-*bis*-(2,4-*dimethoxyphenyl*)-2,3-trans-6,7-cis-7,8-trans-10,11-trans-11,12-cis-3,4,7,8,11,12-*hexahydro*-2H,6H,10H-*dipyrano*[2,3-f:2′,3′-h]*chromene* (**18**). Found: C, 66.6; H, 5.9%, $C_{61}H_{64}O_{19}$ requires C, 66.5, H, 5.8%. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 3.7×10^2, $[\theta]_{283.5}$ 8.0×10^3, $[\theta]_{261.0}$ 1.2×10^3, $[\theta]_{242.5}$ 2.1×10^4, $[\theta]_{234.5}$ 2.1×10^3.

Phlobatannin (**15**) *from* G. coleosperma. Extraction of heartwood and fractionation of the extract by a Craig counter-current procedure and gel chromatography (Sephadex LH-20, EtOH), leading to a 'purified' fr. 2F and its methylation and sepn to give a fr. $2F_5$, is described in ref. [17]. Resolution of this fr. by prep. TLC into 5 bands, $2F_5A$–$2F_5E$, is described in [8]. Fr. $2F_5E$ (185 mg) was further purified by prep. TLC in 1,2-dichloroethane–Me_2CO (17:3, ×2) to give 2 bands at R_f 0.40 (39 mg) and 0.31 (54 mg). The R_f 0.40 band was acetylated and purified by prep. TLC in C_6H_6–Me_2CO (9:1, ×3) to give (2*R*,3*R* : 6*S*,7*S*,8*R* : 10*R*,11*S*,12*S*)-3,7,11-triacetoxy-2,6,10-tris-(3,4-dimethoxyphenyl-8,12-bis(2,4-dimethoxyphenyl-2,3-*cis*-6,7-*cis*-7,8-*trans*-10,11-*trans*-11,12-*cis*-3,4,7,8,11,12-hexahydro-2*H*,6*H*,10*H*-dipyrano[2,3-*f*:2′,3′-*h*]-chromene as an amorphous solid (R_f 0.34, 17 mg). Found: C, 66.6; H, 5.8%, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.9%. ^{1}H NMR data (Table 1). Acetylation of the R_f 0.31 band (54 mg) and successive prep. TLC sepn in C_6H_6–Me_2CO (9:1, ×3; R_f 0.37, 24 mg) and 1,2-dichloroethane–Me_2CO (24:1, ×6) afforded (2*R*,3*S*:6*R*,7*S*,8*S*:10*S*,11*S*,12*R*)-3,7,11-triacetoxy-2,6,10-tris-(3,4-dimethoxyphenyl)-8,12-bis-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-10,11-*cis*-11,12-*trans*-3,4,7,8,11,12-hexahydro-2*H*,6*H*,10*H*-dipyrano-[2,3-*f*:2′,3′-*h*]chromene as an amorphous solid (R_f 0.65, 15 mg). This derivative is described in ref. [7], where it was designated compound **6**.

Triflavanoids derived from fisetinidol-(4α,8)-epicatechin (**21**). Fisetinidol-(4α,8)-epicatechin (**21**) (3.7 g) [3] and fisetinidol-4α-ol (**22**) (1.0 g) [3] were

dissolved in 0.1 M HCl (450 ml). The mixt. was stirred at room temp. for 17 hr and extracted with EtOAc (5 × 250 ml). Drying (Na_2SO_4) of the extract and removal of solvent gave a brown powder (5.1 g) which was subjected to CC (Sephadex LH-20, EtOH, 3 × 180 cm column, flow rate 0.8 ml min^{-1}, 25 ml per tube, first 1.8 l eluate removed) to give the following frs: 1 (tubes 161–240, 2.1 g), 2 (401–484, 805 mg), 3 (492–640, 945 mg) and 4 (641–705, 200 mg). Fr. 1 consisted of unchanged dimer (**21**), fr. 2 of the (4β,6:4α,8:)-trimer (**2**), fr. 3 of a mixt. of the (4α,6:4α,8)-trimer (**1**) and higher oligomers, and fr. 4 of higher oligomers. Fr. 3 was subjected to CC (Sephadex LH-20 EtOH–H_2O, 1:1, 3 × 180 cm column, flow rate 0.8 ml min^{-1}, 24 ml per tube, first 3.5 l eluate removed) to give the following frs: 3.1 (tubes 126–170, 798 mg) and 3.2 (171–213, 105 mg). Fr. 3.1 consisted of a mixt. of **1** and higher oligomers and fr. 3.2 of **1**. Fr. 3.1 was subjected to MPLC (3 × 100 cm column, 2.7 bar pressure, 3 ml min^{-1}, 24 ml eluate per tube, first 2 l eluate removed) on Fractogel TSK HW-40 (S) using EtOH to give 2 frs, 3.1.1 (tubes 333–423, 318 mg), and 3.1.2 (438–545, 155 mg). Fr. 3.1.1 consisted of **1**, giving a total of 423 mg of this compound, and fr. 3.1.2 of higher oligomers. The novel triflavanoids **1** and **2** were identified as decamethyl ether triacetates **23** and **24**, details of which will be disclosed elsewhere.

Base-catalysed conversion of bis-fisetinidol-(4α,6:4α,8)-epicatechin (**1**). Triflavanoid **1** (400 mg) was dissolved in a 0.025 M Na_2CO_3–0.025 M $NaHCO_3$ buffer soln (250 ml) (pH 10) and the mixt. stirred under N_2 for 5 hr at 55°. The mixt. was cooled to 0°, acidified with 1 M HCl and extracted with EtOAc (5 × 250 ml). The organic extracts were dried (Na_2SO_4) and evapd to afford a brown powder (409 mg) which was subjected to CC on Sephadex LH-20 (3 × 120 cm column, 0.8 ml min^{-1}, 24 ml eluate per tube, first 3.2 l eluate removed) to give two frs: 1 (tubes 81–126, 219 mg) and 2 (127–208, 113 mg).

Methylation of fr. 1 followed by prep. TLC in $CHCl_3$-hexane–Me_2CO–MeOH (60:29:10:1, ×2) gave 3 main bands: 1-A (R_f 0.58, 35 mg), 1-B (R_f 0.51, 29 mg) and 1-C (R_f 0.36, 29 mg). Acetylation of 1-A afforded (2*S*,3*R*:6*R*,7*S*,8*S*:10*R*,11*S*,12*S*)-3,7,11-triacetoxy-2,6,10-tris-(3,4-dimethoxyphenyl)-8,12-bis-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-10,11-*trans*-11,12-*cis*-3,4,7,8,11,12-hexahydro-2*H*,6*H*,10*H*-dipyrano[2,3-*f*:2′,3′-*h*]chromene (**26**) as an amorphous solid (39 mg). Found: C, 66.4; H, 5.7% $C_{61}H_{64}O_{19}$ requires, C, 66.5; H, 5.9%. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 1.1×10^2, $[\theta]_{285.5}$ 1.9×10^4, $[\theta]_{278.0}$ 5.5×10^2, $[\theta]_{270.0}$ -1.0×10^4, $[\theta]_{257.5}$ 1.3×10^2, $[\theta]_{246.5}$ 3.4×10^4, $[\theta]_{238.5}$ -2.2×10^2. Fr. 1-B was acetylated and resolved by prep. TLC in $CHCl_3$–hexane–Me_2CO (13 : 10 : 2, ×2) to give 2,3-*cis*-6,7-*trans*-7,8-*cis*-10,11-*trans*-11,12-*cis*-hexahydro-2*H*,6*H*,10*H*-dipyrano[2,3-*f*:2′,3′-*h*]chromene (**6**) as an amorphous solid (R_f 0.42, 10 mg) with physical data identical to those for the natural product (see above). Acetylation of 1-C followed by 2 consecutive purifications by prep. TLC in $CHCl_3$–hexane–Me_2CO (13 : 10 : 2, ×2, R_f 0.38) and $CHCl_3$–hexane–Me_2CO (5 : 4 : 1, ×2, R_f 0.50) afforded (2*S*,3*R*:6*S*,7*S*,8*R*)-3,7-diacetoxy-5-methoxy-10-[(2R,3S,4S)-2,3-trans-3,4-trans-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,8-bis-(3,4-dimethoxyphenyl)-6-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[3,2-*g*]chromene (**30**) as an amorphous solid (8 mg). Found $[M]^+$, 1100.4045. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 1.3×10^2, $[\theta]_{293.0}$ -1.4×10^2, $[\theta]_{281.5}$ 2.1×10^4, $[\theta]_{258.0}$ -1.6×10^2, $[\theta]_{248.0}$ -2.8×10^4, $[\theta]_{241.5}$ -5.3×10^2.

Fr. 2 was similarly methylated and resolved by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (60 : 29 : 10 : 1, ×2) to give a main band at R_f 0.31 (33 mg). This was resubjected to prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30 : 14 : 5 : 1, ×2) to give 2 main bands at R_f 0.68 (5 mg) and 0.57 (8 mg). Acetylation of the R_f 0.68 band and prep. TLC in $CHCl_3$–hexane–Me_2CO (5 : 4 : 1, ×2) afforded (2*R*,3*R*:8*R*,9*S*,10*S*)-3,9-diacetoxy-5-methoxy-6-[(2R,3R,4S)-2,3-cis-3,4-trans-3-acetoxy-4-(3,4-dimethoxyphenyl)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]-2,8-bis-(3,4-dimethoxyphenyl)-10-(2,4-dimethoxyphenyl)-2,3-*cis*-8,9-*trans*-9,10-*cis*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano-[2,3-*h*]chromene (**32**) as an amorphous solid (R_f 0.41, 3 mg). Found: $[M]^+$, 1100.4032, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ -6.4×10^2, $[\theta]_{292.0}$ -1.0×10^3, $[\theta]_{288.5}$ 1.7×10^1, $[\theta]_{282.5}$ 2.0×10^3, $[\theta]_{279.0}$ 2.3×10^3, $[\theta]_{261.0}$ 6.3×10^2, $[\theta]_{242.5}$ 2.6×10^4, $[\theta]_{231.0}$ 3.7×10^2. The R_f 0.57 fr. was acetylated to afford (2*S*,3*R*:8*R*,9*S*,10*S*)-3,9-diacetoxy-5-methoxy-6-[(2*R*,3*S*,4*S*)-2,3-*trans*-3,4,-*trans*-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,8-bis-(3,4-dimethoxyphenyl)-10-(2,4-dimethoxyphenyl)-2,3-*trans*-8,9-*trans*-9,10-*cis*-3,4,9,10-tetrahydro-2*H*,8*H*-pyrano[2,3-*h*]chromene (**28**) as an amorphous solid (9 mg). Found: $[M]^+$, 1100.4050, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 1.8×10^2, $[\theta]_{285.5}$ 1.5×10^4, $[\theta]_{275.0}$ -2.0×10^1, $[\theta]_{270.5}$ -2.9×10^3, $[\theta]_{256.5}$ -6.7×10^2, $[\theta]_{247.5}$ -6.4×10^3, $[\theta]_{241.0}$ 3.9×10^2.

Acknowledgements—Financial support by the Foundation for Research Development, Pretoria, the Sentrale Navorsingsfonds of this University and the Marketing Committee, Wattle Bark Industry of South Africa, Pietermaritzburg, is gratefully acknowledged.

REFERENCES

1. Porter, L. J. (1993) in *The Flavonoids, Advances in Research Since 1986* (Harborne, J. B., ed.), p. 23. Chapman & Hall, London.
2. Porter, L. J. (1988) in *The Flavonoids, Advances in Research Since 1980* (Harborne, J. B., ed.), p. 21. Chapman & Hall, London.
3. Steynberg, J. P., Burger, J. F. W., Cronje, A., Bonnet, S. L., Malan, J. C. S., Young, D. A. and

Ferreira, D. (1990) *Phytochemistry* **29**, 2979.
4. Palgrave, K. C. (1983) in *Trees of Southern Africa* (Moll, E. J., ed.), p. 262. C. Struik Publishers, Cape Town.
5. Bonnet, S. L., Steynberg, J. P., Bezuidenhoudt, B. C. B., Saunders, C. M. and Ferreira, D. (1996) *Phytochemistry* **43**, 215.
6. Bonnet, S. L., Steynberg, J. P., Bezuidenhoudt, B. C. B., Saunders, C. M. and Ferreira, D. (1996) *Phytochemistry* **43**, 229.
7. Bonnet, S. L., Steynberg, J. P., Bezuidenhoudt, B. C. B., Saunders, C. M. and Ferreira, D. (1996) *Phytochemistry* **43**, 241.
8. Steynberg, J. P., Steenkamp, J. A., Burger, J. F. W., Young, D. A. and Ferreira, D. (1990) *J. Chem. Soc., Perkin Trans. 1* 235.
9. Porter, L. J., Wong, R. Y., Benson, M., Chan, B. G., Viswanadhan, V. N., Gandour, R. D. and Mattice, W. L. (1986) *J. Chem. Res. (S)* 86.
10. Porter, L. J., Wong, R. Y., Benson, M., Chan, B. G., Viswanadhan, V. N., Gandour, R. D. and Mattice, W. L. (1986) *J. Chem. Res. (M)* 830.
11. De Angelis, C. G. and Wildman, W. C. (1969) *Tetrahedron* **25**, 5099.
12. Botha, J. J., Ferreira, D. and Roux, D. G. (1978) *J. Chem. Soc., Chem., Commun.* 698.
13. Botha, J. J., Ferreira, D. and Roux, D. G. (1981) *J. Chem. Soc., Perkin Trans. 1* 1213.
14. Ferreira, D., Steynberg, J. P., Burger, J. F. W. and Bezuidenhoudt, B. C. B. (1992) in *Phenolic Metabolism in Plants* (Stafford, H. A., and Ibrahim, R. K., eds.), p. 255.
15. Cronje, A., Steynberg, J. P., Brandt, E. V., Young, D. A. and Ferreira, D. (1993) *J. Chem. Soc., Perkin Trans. 1* 2467.
16. Pizzi, A., Orovan, E. and Cameron, F. A. (1988) *Holzforzung* **46**, 67.
17. Steynberg, J. P., Burger, J. F. W., Young, D. A., Brandt, E. V., Steenkamp, J. A. and Ferreira, D. (1988) *J. Chem. Soc., Perkin Trans. 1* 3323.