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STRUCTURE AND SYNTHESIS OF PHLOBATANNINS RELATED TO THE (4α,6:4β,8)-BIS-FISETINIDOL-CATECHIN PROFISETINIDIN TRIFLAVANOID*

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Key Word Index—*Baikiaea plurijuga*; *Colophospermum mopane*; Leguminosae; Caesalpiniodeae; profisetinidins; phlobatannins; triflavanoids; pyran rearrangement.

Abstract—The natural class of phlobaphene condensed tannins is complemented by two functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromenes representing the products of stereoselective pyran ring rearrangement of the 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*-flavan-3-ol moieties in the bis-fisetinidol-(4α,6:4β,8)-catechin triflavanoid. Structural eludication of these complex natural products was effected by synthesis via base-catalysed conversion of the 4-*O*(E)-methyl ether of their presumed profisetinidin triflavanoid precursor. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

The natural occurrence and biomimetic-type synthesis of a series of novel phlobatannins that originated by stereoselective C-ring isomerization of the 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*-fisetinidol units of (4α,6:4α,8)- (4β,6:4α8)- and (4β,6:4β,8)-bis-fisetinidol-catechin triflavanoids have recently been demonstrated [1–3]. Continued investigation of the polyphenols in the heartwood extracts of the southern African trees, *Baikiaea plurijuga* and *Colophospermum mopane* [2, 3], has now revealed the presence of 'trimeric-type' phlobatannins, which are related to the bis-fisetinidol-(4α,6:4β,8)-catechin triflavanoid. This necessitated an analysis of the products resulting from treatment of the latter precursor with mild base, such an approach being a prerequisite for structural elucidation of these complex natural condensed tannin analogues. The results discussed herein then conclude our tetralogy of papers dealing with phlobatannins related to the profisetinidin triflavanoids based on catechin as the chain terminating unit in the biosynthetic sequence leading to this class of natural products.

RESULTS AND DISCUSSION

The aptitude of the constituent units in oligoflavanoids for quinone-methide formation at a B-ring and the subsequent potential for epimerization and rearrangment reactions [4–6] prompted the use of the triflavanoid **1** as its 4-*O* (E-ring) methyl ether (**2**). Treatment of this derivative (**2**) with 0.025 M $NaHCO_3$–0.025 M Na_2CO_3 buffer (pH 10), for 5 hr at 50° under nitrogen, effected complete conversion into a mixture comprising 12 ring-isomerized products (Scheme 1). The compounds with rearranged pyran rings are the four functionalized hexahydrodipyrano-[2,3-*f*:2′,3′-*h*]chromenes* (**5**, **10**, **13** and **16**), the three fisetinidol - (4α,6) - tetrahydropyrano[2,3-*h*]chromenes (**19**, **22** and **25**), a fisetinidol-(4β, 10)-tetrahydropyrano[3,2-*g*]chromene (**28**), the three 4-arylchroman-(2α,6)-tetrahydropyrano[2,3-*h*]chromenes (**31**, **34** and **37**), and the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]-chromene (**7**), where methylation had occurred on the G-ring (see below). For reasons outlined previously [2], these compounds were again identified as decamethyl ether triacetates, e.g. (**6**), by the methods that have been described previously [2].

Analysis of the ^{1}H NMR data (Table 1) of the functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives (**6**, **11**, **14** and **17**) revealed the familiar absence of the effects of dynamic rotational isomerism at ambient temperatures. NOE associations of 2-OMe(A)/2-OMe(G) with 3-H(A)/3-H(G), respectively, and of 4-OMe(A)/4-OMe(G) with both 3- and 5-H(A)/3- and 5-H(G), respectively, confirmed the 'liberation' of the resorcinol-type A- and G-rings in the triflavanoid precursor (**2**) and, thus, the dipyranochromene constitution for all four compounds. The heterocyclic region of the ^{1}H NMR spectra exhibited

*Part 22 in the series 'Oligomeric Flavanoids'. For part 21 see ref. [3].

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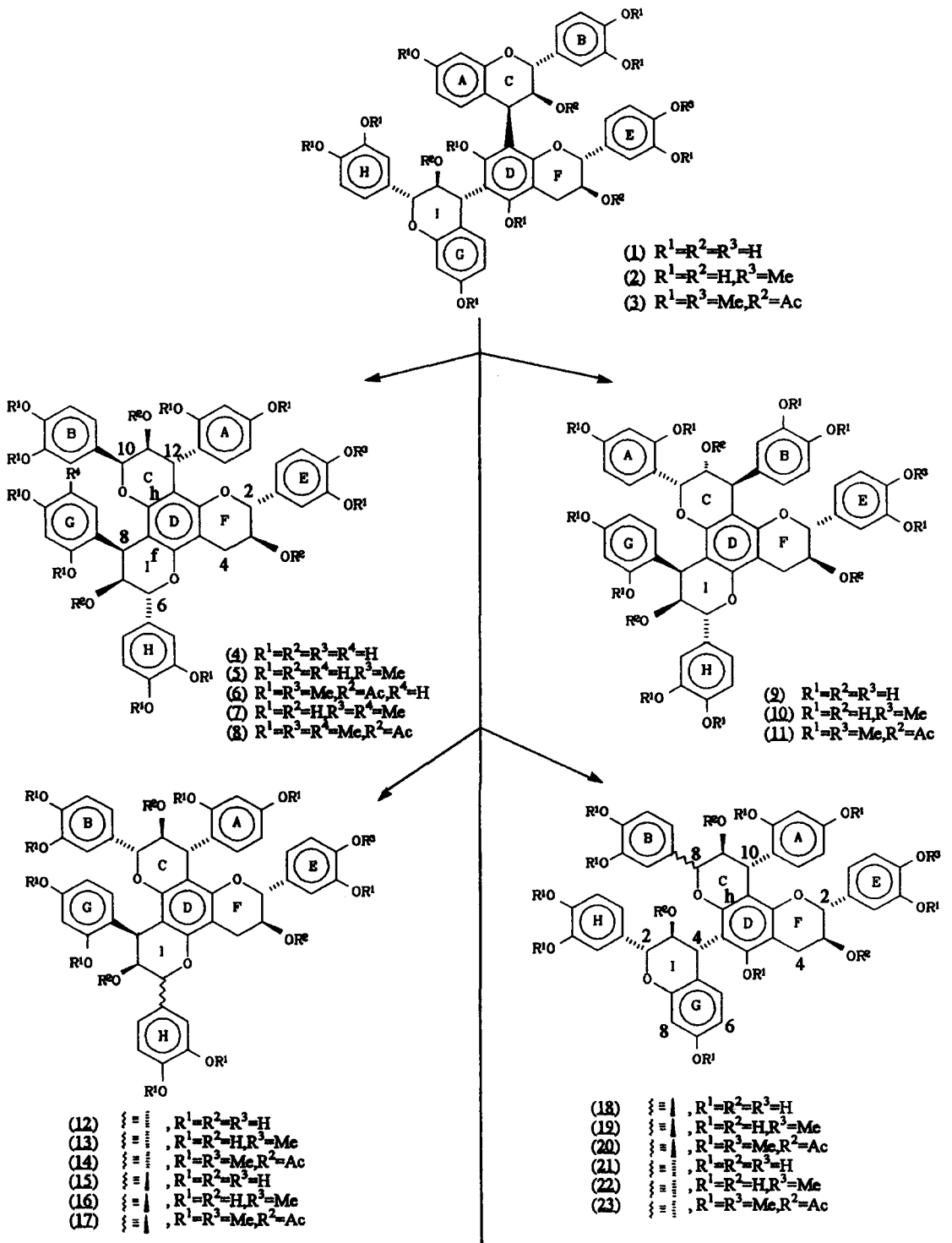
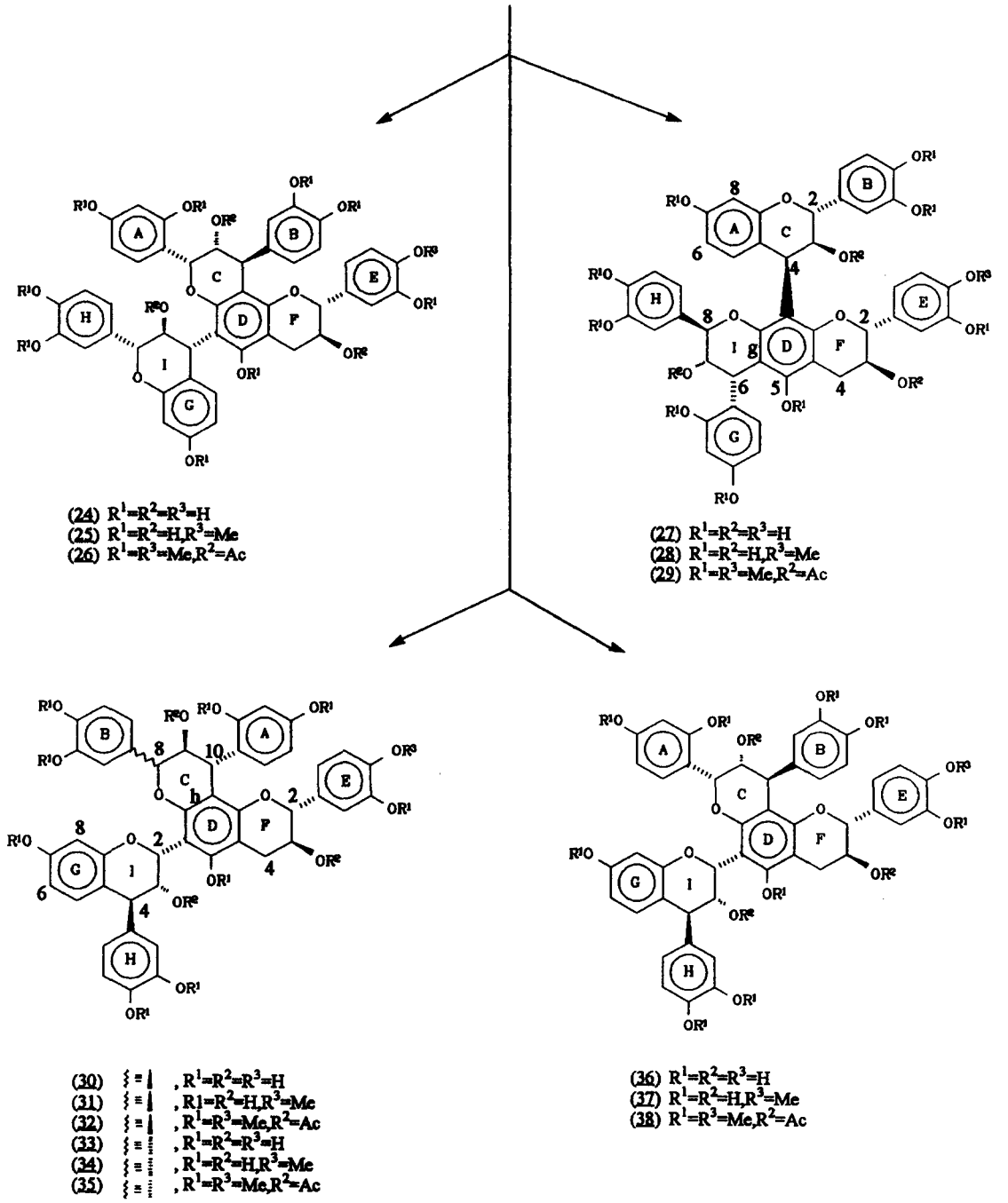
*Non-systematic name/numbering (cf. structure **4**) to retain the heterocyclic oxygen of the catechin DEF-unit as position 1 for all compounds.



Scheme 1. Base-catalysed pyran rearrangement of (4β, 8: 4α, 6)-fisetinidol – (+) – catechin (**2**).

the ABMX four-spin system of the intact F-ring protons and the two AMX three-spin systems of the protons of the C- and I-rings. For compounds **6**, **11** and **14** coupling constants ($J_{6,7}$ = 10.0 and $J_{7,8}$ = 6.0 Hz) are reminiscent of the 6,7-*trans*-7,8-*cis* relative configuration dictated by the mechanism [6] for rearrangement of the 2,3-*trans*-3,4-*trans* I-ring in precursor **2**. The I-ring configuration was confirmed by the prominent NOE association of 6-H(I) with 6-H(G) for all three compounds.

The ^{1}H NMR coupling constants of I-ring protons ($J_{6,7}$ = 1.0 and $J_{7,8}$ = 6.0 Hz) of compound **17** are



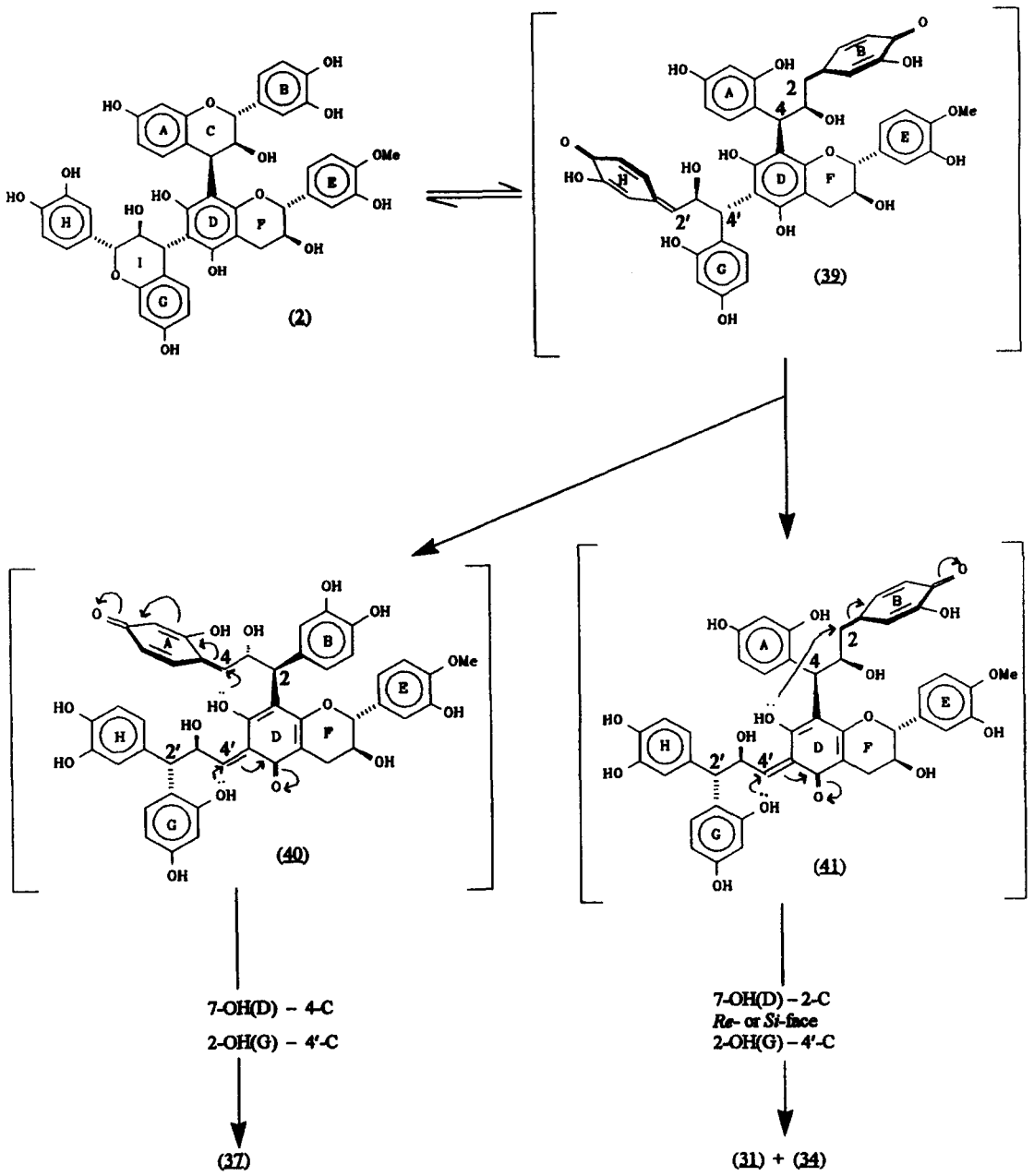
Scheme 1. *Continued.*

consistent with the 6,7-*cis*-7,8-*cis* relative configuration [7, 8] of this heterocycle. The 6,8-*cis* orientation of the H- and G-rings is confirmed by the prominent NOE association between 6- and 8-H(I). Since base treatment of dimeric profisetinidins with a C-4 substituted 2,3-*trans*-3,4-*trans*-fisetinidol moiety has hitherto effected highly stereoselective ring isomerization to yield exclusively phlobatannins with *trans–cis* stereochemistry, the above observation represents the first example where pyran rearrangement of such a fisetinidol unit affords products with both *trans–cis* and *cis–cis* relative stereochemistry. Attack of 5-OH(D) at the *Re*-(*trans–cis* products) as well as the *Si*-faces (*cis–cis* product) of C-2′ in the intermediate I-ring quinonemethide (**39**, Scheme 2) presumably results from asymmetric induction that may start operating at the higher oligomeric level. Coupling constants of the second AMX-system in the heterocyclic region of the ^{1}H NMR spectra confirmed a 10,11-*cis*-11,12-*trans* relative C-ring configuration for derivatives **6** and **11** ($J_{10,11} = 1.0$ and $J_{11,12} = 2.0$ Hz) and a 10,11-*trans*-11,12-*trans* configuration for compounds **14** and **17**

Table 1. ^{1}H NMR peaks (ppm) of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives **6**, **8**, **11**, **14** and **17** in $CDCl_3$ at 300 MHz

Ring	H	**6**	**8**	**11**	**14**	**17**
A	3	6.44 (*d*, 2.5)	6.44 (*d*, 2.0)	6.20 (*d*, 2.5)	6.20 (*br.s*)	6.19 (*d*, 2.5)
	5	6.45 (*dd*, 2.5, 8.5)	6.45 (*dd*, 2.0, 8.5)	6.38 (*dd*, 2.5, 8.5)	6.18 (*dd*, 2.5, 8.5)	6.23 (*dd*, 2.5, 8.5)
	6	6.79 (*d*, 8.5)	6.79 (*d*, 8.5)	7.43 (*d*, 8.5)	6.55 (*d*, 8.5)	6.60 (*d*, 8.5)
B	2	6.23 (*d*, 2.0)	6.20 (*d*, 2.0)	6.65 (*d*, 2.0)	6.54 (*d*, 2.00)	6.44 (*d*, 2.0)
	5	6.50 (*d*, 8.5)	6.48 (*d*, 8.5)	6.76* (*d*, 8.5)	6.58 (*d*, 8.0)	6.56 (*d*, 8.0)
	6	6.02 (*dd*, 2.0, 8.5)	6.02 (*dd*, 2.0, 8.5)	6.64 (*dd*, 2.0, 8.5)	6.39 (*dd*, 2.0, 8.0)	6.34 (*dd*, 2.0, 8.0)
C	10	4.66 (*br.s*)	4.85 (*br.s*)	4.81 (*br.s*)	4.48 (*d*, 7.5)	4.19 (*d*, 8.0)
	11	5.21 (*dd*, 1,0, 2.0)	5.19 (*dd*, 1.0, 2.0)	5.47 (*dd*, 1.0, 2.0)	5.52 (*dd*, 6.0, 7.5)	5.38 (*dd*, 6.5, 8.0)
	12	4.41 (*d*, 2.0)	4.43 (*d*, 2.0)	4.31 (*d*, 2.0)	4.44 (*d*, 6.0)	4.49 (*d*, 6.5)
E	2	6.40 (*d*, 2.0)	6.41 (*d*, 2.0)	6.67 (*d*, 2.0)	6.37 (*d*, 2.0)	6.39 (*d*, 2.0)
	5	6.62 (*d*, 8.0)	6.63 (*d*, 8.5)	6.75* (*d*, 8.5)	6.60 (*d*, 8.0)	6.61 (*d*, 8.5)
	6	6.47 (*dd*, 2.0, 8.0)	6.48 (*dd*, 2.0, 8.5)	6.68 (*dd*, 2.0, 8.5)	6.27 (*dd*, 2.0, 8.0)	6.25 (*dd*, 2.0, 8.5)
F	2	4.59 (*d*, 9.0)	4.83 (*d*, 9.0)	4.86 (*d*, 6.5)	4.71 (*d*, 9.00)	4.73 (*d*, 9.0)
	3	4.93 (*m*)	4.94 (*m*)	5.36 (*m*)	4.93 (*m*)	4.89 (*m*)
	$4_{ax.}$	2.69 (*dd*, 9.0, 16.5)	2.71 (*dd*, 9.0, 16.5)	2.73 (*dd*, 6.5, 17.0)	2.65 (*dd*, 9.0, 16.0)	2.79 (*dd*, 10.0, 16.5)
	$4_{eq.}$	3.18 (*dd*, 5.5, 16.5)	3.18 (*dd*, 6.0, 16.5)	2.90 (*dd*, 5.0, 17.0)	3.12 (*dd*, 6.0, 16.0)	3.25 (*dd*, 6.0, 16.5)
G	3	6.56 (*d*, 2.5)	6.46 (*s*)	6.28 (*d*, 2.5)	6.30 (*d*, 2.5)	6.00 (*d*, 2.5)
	5	6.52 (*dd*, 2.5, 8.5)	—	6.37 (*dd*, 2.5, 8.5)	6.44 (*dd*, 2.5, 8.5)	6.21 (*dd*, 2.5, 8.5)
	6	7.04 (*d*, 8.5)	6.86 (*s*)	6.98 (*d*, 8.5)	6.86 (*d*, 8.5)	6.65 (*d*, 8.5)
H	2	6.88 (*d*, 2.0)	6.88 (*d*, 2.0)	6.84 (*d*, 2.0)	6.85 (*d*, 2.0)	7.02 (*d*, 2.0)
	5	6.81 (*d*, 8.5)	6.81 (*d*, 8.5)	6.79 (*d*, 8.0)	6.80 (*d*, 8.5)	6.83 (*d*, 8.5)
	6	6.95 (*dd*, 2.0, 8.5)	6.95 (*dd*, 2.0, 8.5)	6.91 (*dd*, 2.0, 8.0)	6.93 (*dd*, 2.0, 8.5)	7.02 (*dd*, 2.0, 8.5)
I	6	5.03 (*d*, 10.0)	5.02 (*d*, 10.5)	5.05 (*d*, 10.0)	5.02 (*d*, 10.0)	5.13 (*br.s*)
	7	5.45 (*dd*, 6.0, 10.0)	5.45 (*dd*, 6.5, 10.5)	5.49 (*dd*, 6.0, 10.0)	5.47 (*dd*, 6.0, 10.0)	5.69 (*dd*, 1.0, 6.0)
	8	5.14 (*d*, 6.0)	5.09 (*d*, 6.5)	5.34 (*d*, 6.0)	5.15 (*d*, 6.0)	5.11 (*d*, 6.0)
	OMe	3.50(3-E), 3.55(2-G), 3.58 (3-B), 3.67(2-A), 3.77(4-B), 3.81(4-A/4-E), 3.83 (4-G), 3.84(3-H) and 3.86 (4-H), each *s*	3.50(3-E/4-G), 3.55(3-B), 3.68(2-A), 3.77(4-B), 3.81 (4-A), 3.82(4-E), 3.85(3-H), 3.86(4-H), 3.90(2-G), 2.26(5Me-G), each *s*	3.43(2-A), 3.67(2-G), 3.73 (4-A/4-G), 3.75(3-B), 3.77 (3-E), 3.82(3-H), 3.83, 3.84 and 3.85(4-H), each *s*	3.46(2-A), 3.48(2-G), 3.59 (3-E), 3.71(4-A), 3.74(3-B), 3.78(4-B/4-G), 3.82(4-E), 3.84(3-H) and 3.85(4-H), each *s*	3.42(2-G), 3.58(2-A), 3.62 (3-E), 3.64(4-G), 3.71(4-A), 3.73(3-B), 3.79(4-B), 3.83(4-E), 3.85(4-H) and 3.87(3-H), each *s*
	OAc	1.67, 1.69, 1.85, each *s*	1.67, 1.70, 1.85, each *s*	1.72, 1.85, 1.90, each *s*	1.69, 1.74, 1.82, each *s*	1.59, 1.74, 1.83, each *s*

*Assignments may be interchanged.



Scheme 2. Proposed mechanism for formation of the 6-(4-arychromen-2-yl)-tetrahydropyrano[2,3-*h*]chromenes (**31**, **34** and **37**). The quinone methides (**39–41**) are postulated and have not been isolated.

($J_{10,11} = 7.5$ and 8.0, and $J_{11,12} = 6.0$ and 6.5 Hz). These relative configurations were confirmed by the now familiar NOE associations of heterocyclic protons with a proton or the proton of an aryl substituent, showing a 1,3-diaxial relationship.

The relative positions of the C- and I-rings that may be inferred from the mechanism of pyran ring rearrangement leading to compound **5** were confirmed by the NOE association of 2-OMe(G) with 2-H(B) and of 3-OMe(B) with 3-H(G). This association also proved the 8,10-*cis* orientation of the G- and B-rings. A COSY experiment, using 10-H(C) and 12-H(C) as reference signals, correlated these protons with the resorcinol A- and pyrocatechol B-rings, respectively, which indicated an 'interchange' of these rings in derivative **11** relative to their positions in the 'normal' isomer (**6**). Such an interchange was confirmed by the NOE of 10-H(C) with both 2- and 6-H(B) and by the association of 8-H(I) with 2-OMe(A), as well as by the conspicuous deshielding of 6-H(A) relative to its chemical shift in derivative (**6**). Differentiation of the C- and I-rings in the latter compound was again facilitated by the observed NOE between 8-H(I) and 6-H(A).

Decoupling and COSY experiments, using the benzylic protons of the C-, F- and I-rings of compounds **14** and **17** as reference signals, facilitated assignment of

Table 2. ^{1}H NMR peaks (ppm) of the fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromene derivatives **20**, **23** and **26** and the fisetinidol-(4β,10)-tetrahydropyrano[3,2-*g*]chromene derivative **29** at 300 MHz

Ring	H	**20a** ($CDCl_3$)	**20b** ($CDCl_3$)	**23** (C_6D_6)	**26** ($CDCl_3$)	**29a** (C_6D_6)	**29b** (C_6D_6)
A	3/8	6.40 (*d*, 2.5)	6.46 (*d*, 2.5)	6.27 (*d*, 2.5)	6.18 (*d*, 2.5)	6.36 (*d*, 2.5)	6.26 (*d*, 2.5)
	5/6	6.40 (*dd*, 2.5, 9.0)	6.38 (*dd*, 2.5, 9.0)	6.17 (*dd*, 2.5, 8.5)	6.13 (*dd*, 2.5, 8.5)	6.48 (*dd*, 2.5, 8.5)	6.67 (*dd*, 2.5, 8.5)
	6/5	6.49 (*d*, 9.0)	6.58 (*d*, 9.0)	7.00 (*d*, 8.5)	6.07 (*d*, 8.5)	6.94 (*d*, 8.5)	7.23 (*d*, 8.5)
B	2	6.87 } 2nd order	6.89 (*d*, 2.0)	6.89 (*d*, 2.0)	6.71 (*d*, 2.0)	7.01 (*br.s*)	6.87 (*d*, 2.0)
	5	6.72 } 2nd order	6.77 (*d*, 8.5)	6.51 (*d*, 8.5)	6.73* (*d*, 8.0)	6.36 (*d*, 8.5)	6.53 (*d*, 8.5)
	6	6.72 } 2nd order	6.81 (*dd*, 2.0, 8.5)	6.84 (*dd*, 2.0, 8.5)	6.67 (*dd*, 2.0, 8.0)	7.00 (*dd*, 2.0, 8.5)	6.87 (*dd*, 2.0, 8.5)
C	8/2	4.47 (*br.s*)	4.96 (*br.s*)	5.47 (*d*, 9.0)	5.37 (*br.s*)	5.69 (*d*, 7.0)	5.62 (*d*, 9.0)
	9/3	5.24 (*dd*, 1.5, 2.0)	5.51 (*dd*, 1.5, 2.0)	5.87 (*dd*, 7.5, 9.0)	5.21 (*dd*, 1.0, 2.0)	6.26 (*dd*, 6.5, 7.0)	6.24 (*dd*, 6.0, 9.0)
	10/4	4.46 (*d*, 2.0)	5.54 (*d*, 2.0)	4.92 (*d*, 7.5)	4.21 (*d*, 2.0)	5.43 (*d*, 6.5)	5.59 (*d*, 6.0)
E	2	6.36 (*d*, 2.0)	6.33 (*d*, 2.0)	6.56 (*d*, 2.0)	6.67 (*d*, 2.0)	6.96 (*d*, 2.0)	
	5	6.61 (*d*, 8.0)	6.61 (*d*, 8.0)	6.54 (*d*, 8.0)	6.78* (*d*, 8.0)	6.57 (*d*, 8.0)	
	6	6.39 (*dd*, 2.0, 8.0)	6.43 (*dd*, 2.0, 8.0)	6.44 (*dd*, 2.0, 8.0)	6.70 (*dd*, 2.0, 8.0)	6.83 (*dd*, 2.0, 8.0)	
F	2	4.80 (*d*, 9.0)	4.73 (*d*, 9.0)	4.66 (*d*, 8.0)	4.74 (*d*, 7.0)	4.53 (*d*, 8.0)	5.35 (*d*, 5.0)
	3	4.83 (*m*)	4.93 (*m*)	5.35 (*m*)	5.34 (*m*)	5.41 (*m*)	5.55 (*m*)
	$4_{ax.}$	2.76 (*dd*, 10.0, 16.0)	2.67 (*dd*, 10.0, 16.0)	2.85 (*dd*, 8.5, 16.0)	2.81 (*dd*, 7.5, 16.0)	2.82–3.35 (*m*)	2.82–3.35 (*m*)
	$4_{eq.}$	3.33 (*dd*, 5.0, 16.0)	3.24 (*dd*, 5.5, 16.0)	Overlapped by OMe	3.10 (*dd*, 5.0, 16.0)	2.82–3.35 (*m*)	2.82–3.35 (*m*)
G	5/6	6.69 (*d*, 8.5)	6.99 (*d*, 8.5)	7.31 (*d*, 8.5)	6.86 (*d*, 8.5)	7.44 (*d*, 8.5)	6.97 (*d*, 8.5)
	6/5	6.44 (*dd*, 2.5, 8.5)	6.51 (*dd*, 2.5, 8.5)	6.83 (*dd*, 2.5, 8.5)	6.50 (*dd*, 2.5, 8.5)	6.53 (*dd*, 2.5, 8.5)	6.19 (*dd*, 2.5, 8.5)
	8/3	6.27 (*d*, 2.5)	6.57 (*d*, 2.5)	6.67 (*d*, 2.5)	6.60 (*d*, 2.5)	6.49 (*d*, 2.5)	6.43 (*d*, 2.5)
H	2	6.88 (*d*, 2.0)	7.00 (*d*, 2.5)	6.96 (*d*, 2.0)	6.64 (*d*, 2.0)	6.90 (*d*, 2.0)	7.11 (*d*, 2.0)
	5	6.87 (*d*, 8.0)	6.89 (*d*, 8.0)	6.58 (*d*, 8.5)	6.71 (*d*, 8.0)	6.48 (*d*, 8.0)	6.56 (*d*, 8.0)
	6	6.95 (*dd*, 2.0, 8.0)	7.05 (*dd*, 2.5, 8.0)	6.86 (*dd*, 2.0, 8.5)	6.83 (*dd*, 2.0, 8.0)	6.92 (*dd*, 2.0, 8.0)	7.04 (*dd*, 2.0, 8.0)
I	2/6	4.89 (*d*, 10.0)	4.84 (*d*, 10.0)	4.98 (*d*, 10.0)	4.98 (*d*, 10.0)	5.78 (*d*, 5.5)	5.61 (*d*, 5.5)
	3/7	6.30 (*t*, 10.0)	6.11 (*t*, 10.0)	6.69 (*t*, 10.0)	6.19 (*t*, 10.0)	5.92 (*dd*, 5.5, 10.0)	5.92 (*dd*, 5.5, 10.0)
	4/8	4.82 (*d*, 10.0)	5.10 (*d*, 10.0)	5.08 (*d*, 10.0)	4.77 (*d*, 10.0)	5.50 (*d*, 10.0)	4.89 (*d*, 10.0)
	OMe	3.53(3-E), 3.64(2-A), 3.65(7-G), 3.71(3-B), 3.79(4-A), 3.82(4-E), 3.83(4-B), 3.85(5-D) and 3.87(3-H/4-H), each *s*	3.07(5′-D), 3.48(3′-E), 3.71(2′-A), 3.73, 3.74, 3.76(4′-G), 3.78 (4′-A), 3.81, 3.86(4′-H) and 3.90(3′-H), each s	3.20(5-D), 3.27(3-H), 3.30(3-E), 3.34(3-B), 3.35(4-E), 3.40(4-H), 3.47(7-G), 3.49(4-A), 3.51(4-B) and 3.62(2-A), each *s*	3.41(2-A/3-H), 3.71 (4-A), 3.78(3-B), 3.77 (3-E), 3.79(4-H), 3.80 (5-D), 3.81(7-G/4-E), 3.85(4-B), each *s*	3.25(5-D), 3.27(7-A), 3.29(2-G), 3.30, 3.32, 3.33(3-H/4-G), 3.38 (4-B), 3.39(4-E) and 3.70(3-E), each *s*	3.07(5′-D), 3.23(2′-G), 3.25(4′-G), 3.27, 3.29 (7′-A), 3.34(4′-E), 3.37, 3.40, 3.47 and 3.53, each *s*
	OAc	1.72, 1.88, 1.91, each *s*	1.66, 1.84, 1.91, each *s*	1.43, 1.44, 1.55, each *s*	1.63, 1.71, 1.90, each *s*	1.55(×2), 1.86, each *s*	1.43, 1.56, 1.79, each *s*

*Assignments may be interchanged.

the spin systems and locations of the pyrocatechol and resorcinol rings. These allocations were additionally confirmed by the NOEs of 8-H(I) with 2-H(B) for derivative **14** and of 10-H(C) with 5-H(G) for derivative **17**.

The hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene (**6**) was accompanied by a compound (**8**) with a very closely related ^{1}H NMR spectrum (Table 1) differing from that of derivative **6** by the presence of a benzylic methyl group (δ 2.26) and replacement of an aromatic ABX-spin system of a resorcinol-type ring with two one-proton singlets (δ 6.46 and 6.86). This strongly indicated that C-methylation had occurred on one of the activated resorcinol-type rings on treatment of the mixture with diazomethane. Methylation at 5-C(G) was confirmed by the NOE association of the methyl protons with 6-H(G) and by the association of both 2- and 4-OMe(G) with 3-H(G). Although C-methylation of *meta*-oxygenated aromatic rings commonly occurs when methyl iodide in anhydrous acetone–K_2CO_3 is employed, such a phenomenon is now documented for diazomethane for the first time. Our recent claim concerning the natural occurrence of a fisetinidol-(4α,8)-6-methylcatechin [9] might thus be dubious.

Besides confirming the $[M]^+$ (*m/z* 1100) for the aforementioned derivatives, FAB mass spectrometry contributed very little towards the differentiation of these complex structures. The absolute configurations depicted are again based on ^{1}H NMR data and the mechanism of their formation from a precursor of known absolute configuration. Thus, the absolute stereochemistry of the derivatives **6** and **8** follows as 2*R*,3*S*:6*R*,7*S*,8*S*:10*S*,11*S*,12*R*, of **11** as 2*R*,3*S*:6*R*,7*S*,8*S*: 10*R*,11*R*,12*S*, of **14** as 2*R*,3*S*:6*R*,7*S*,8*S*:10*R*,11*S*,12*R* and of **17** as 2*R*,3*S*:6*S*,7*S*,8*S*:10*R*,11*S*,12*R*. Although little information could be extracted from the circular dichroic (CD) data for these derivatives, it could be used comparatively in conjunction with ^{1}H NMR data to facilitate the unambiguous structural elucidation of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene (**4**) from *B. plurijuga* and of the analogue (**12**) that was obtained from both *B. plurijuga* and *C. mopane*.

Involvement of a single heterocycle in the pyran rearrangment leading to the 'isomerization-intermediates', the fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromenes (**19**, **22** and **25**) and the fisetinidol-(4β,10)-tetrahydropyrano[3,2-*g*]chromene (**28**), was evident from the heterocyclic AMX system in each of the ^{1}H NMR spectra (Table 2) of the decamethyl ether triacetates which corresponded with an intact 2,3-*trans*-3,4-*trans* ($J_{2,3} = J_{3,4} = 10.0$ Hz) C-4 substituted fisetinidol moiety for **20**, **23** and **26** and with a 2,3-*trans*-3,4-*cis* unit for the two rotamers of **29** ($J_{2,3} = 7.0$

Table 3. ^{1}H NMR peaks (ppm) of the 4-arylchromenyltetrahydrophyranochromene derivatives **32**, **35** and **38** at 300 MHz

Ring	H	**32** ($CDCl_3$)	**35** (C_6D_6)	**38** ($CDCl_3$)
A	3	6.44 (*d*, 2.5)	6.19 (*d*, 2.5)	6.22 (*d*, 2.5)
	5	6.42 (*dd*, 2.5, 8.5)	6.26 (*dd*, 2.5, 8.5)	6.16 (*dd*, 2.5, 8.5)
	6	6.68 (*d*, 8.5)	6.61 (*d*, 8.5)	6.90 (*d*, 8.5)
B	2	6.87 (*d*, 2.0)	6.72 (*d*, 2.0)	6.82 (*d*, 2.0)
	5	6.63 (*d*, 8.5)	6.62 (*d*, 8.0)	6.75 (*d*, 8.0)
	6	6.73 (*dd*, 2.0, 8.5)	6.65 (*dd*, 2.0, 8.0)	6.62 (*dd*, 2.0, 8.0)
C	8	4.94 (*br.s*)	4.73 (*d*, 8.5)	5.14 (*br.s*)
	9	5.40 (*dd*, 1.5, 2.0)	5.33 (*dd*, 7.0, 8.5)	5.35 (*dd*, 1.0, 2.0)
	10	4.58 (*d*, 2.0)	4.63 (*d*, 7.0)	4.30 (*d*, 2.0)
E	2	6.39 (*d*, 2.0)	6.38 (*d*, 2.0)	6.62 (*d*, 2.0)
	5	6.56 (*d*, 8.5)	6.54 (*d*, 8.5)	6.76 (*d*, 8.5)
	6	6.29 (*dd*, 2.0, 8.5)	6.08 (*dd*, 2.0, 8.5)	6.66 (*dd*, 2.0, 8.5)
F	2	4.92 (*d*, 7.0)	4.85 (*d*, 6.5)	4.94 (*d*, 5.0)
	3	5.02 (*m*)	5.02 (*m*)	5.30 (*m*)
	4_{ax}	2.71 (*dd*, 7.0, 16.0)	2.69 (*dd*, 7.5, 16.5)	2.72 (*dd*, 5.0, 16.0)
	4_{eq}	2.85 (*dd*, 5.0, 16.0)	2.84 (*dd*, 5.0, 16.5)	2.82 (*dd*, 5.0, 16.0)
G	5	6.87 (*d*, 8.5)	6.86 (*d*, 8.5)	6.92 (*d*, 9.0)
	6	6.51 (*dd*, 2.5, 8.5)	6.47 (*dd*, 2.5, 8.5)	6.51 (*dd*, 2.5, 9.0)
	8	6.60 (*d*, 2.5)	6.33 (*d*, 2.5)	6.50 (*d*, 2.5)
H	2	6.78 (*d*, 2.0)	6.69 (*d*, 2.0)	6.59 (*d*, 2.0)
	5	6.71 (*d*, 8.0)	6.57 2nd order	6.44 (*d*, 9.0)
	6	6.65 (*dd*, 2.0, 8.0)	6.57 2nd order	6.59 (*dd*, 2.0, 9.0)
I	2	5.82 (*d*, 2.0)	5.73 (*d*, 2.0)	5.87 (*d*, 2.0)
	3	5.43 (*dd*, 2.0, 2.5)	5.42 (*dd*, 2.0, 2.5)	5.51 (*dd*, 2.0, 2.5)
	4	4.21 (*d*, 2.5)	4.14 (*d*, 2.5)	4.11 (*d*, 2.5)
	OMe	3.33(4-B), 3.59(3-E), 3.61(3-B), 3.74(2-A), 3.77(3-H), 3.78 (4-A/7-G), 3.80(4-E/4-H) and 3.81(4-B), each *s*	3.49(2-A), 3.51(5-D), 3.55(3-B), 3.65(3-E), 3.66(7-G), 3.69 (4-A), 3.72(3-H), 3.76(4-H), 3.81(4-E) and 3.83(4-B), each *s*	3.45(2-A), 3.64(3-H), 3.66 (4-H), 3.69(5-D), 3.73(7-G), 3.75 (3-E), 3.78(4-A), 3.82(3-B), 3.84(4-B) and 3.85(4-E), each *s*
	OAc	1.75, 1.88, 1.91, each *s*	1.80, 1.90, 1.95, each *s*	1.79, 1.92, 1.93, each *s*

and 9.0 Hz; $J_{3,4} = 6.5$ and 6.0 Hz). The remaining structural features were ascertained by means of the well-established and trustworthy ^{1}H NMR methods that were advanced above, as well as in the preceding two papers [2, 3]. The ^{1}H NMR spectra of both derivatives **20** and **29** displayed the typical effects of dynamic rotational isomerism. In compound **20**, 5-OMe(D) displayed an NOE association with 4-H(I) in the major rotamer and with 3′-H(I) in the minor rotamer. Thus, for the preferred conformation (**20a**), $\theta = +90°$ [10] and for the minor rotamer (**20b**), $\theta = -90°$. Similarly, the NOE association of 7-OMe(A) with 5-H(E) and of 3-OMe(E) with 8-H(A) confirmed **29a** as the major rotamer with $\theta = +90°$; thus, for rotamer **29b**, $\theta = -90°$.

A notable feature in the ^{1}H NMR spectrum of the fisetinidol-(4α,6)-tetrahydropyrano[2,3-*h*]chromene (**26**) with 'interchanged' resorcinol A- and pyrocatechol B-rings, is the absence of the now familiar deshielded 6-H(A) resonance. This indicated that such a phenomenon is less reliable at the triflavanoid level than in the case of the biflavanoid analogues, thus eliminating a useful parameter towards differentiating between compounds of type **20** and those with 'exchanged' A- and B-rings, e.g. **26**. In addition, the prominent NOE associations of 5-OMe(D) with 4-H(I), 5-H(G) and 4-H(F)$_{ax.}$ and $_{eq.}$ that were used to confirm the tetrahydropyrano[2,3-*h*]chromene arrangement in derivative **23** were conspicuously absent in compound **26**. The absence of both the NOE correlations and the deshielding of 6-H(A) may presumably be explained in terms of an attracting π-alkyl interaction [11, 12] between the aromatic G-ring and 2-OMe(A), thus anchoring the GHI-flavanyl unit in a position facing away from 5-OMe(D).

The absolute configurations of compounds **20** [2*R*,3*S*(F):2*R*,3*S*,4*S*(I):8*S*,9*S*,10*R*], **23** [2*R*,3*S*(F):2*R*,3*S*,4*S*(I):8*R*,9*S*,10*R*], **26** [2*R*,3*S*(F):2*R*,3*S*,4*S*(I):8*R*,9*R*,10*S*] and **29** [2*R*,3*S*(F):6*S*,7*S*,8*R*:2*R*,3*S*,4*R*(C)] followed from the same principles that were previously discussed.

When the differentiation of the rotamers in those flavanyl-tetrahydropyranochromenes that are prone to the effects of dynamic rotational isomers, e.g. **29** in this and the previous two papers [2, 3] is considered collectively, there is often a marked preference for the more compressed conformation [10]. Such a conformational preference for the more sterically congested form may presumably be explicable in terms of the aptitude of these molecules to minimize their effective surface area and, hence, solute–solvent interactions, as was hypothesized by Foo and Porter [13] in their consideration of procyanidin peracetate derivatives.

The ^{1}H NMR spectra (Table 3) of the remaining decamethyl ether triacetate derivatives (**32**, **35** and **38**) were conspicuously free of the effects of dynamic rotational isomerism at ambient temperatures. Coupling constants of the heterocyclic I-ring protons ($J_{2,3} = 2.0$ and $J_{3,4} = 2.5$ Hz for each compound) were in accord with the *cis–trans* relative configurations of these rings, while the coupling constants of the C-ring proton resonances ($J_{8,9} = 1.5$ and 1.0 Hz for **32** and **38**, and 8.5 Hz for **35**; $J_{9,10} = 2.0$ Hz for **32** and **38**, and 7.0 Hz for **35**) were reminiscent of *cis–trans* configurations for **32** and **38**, and of *trans–trans* configuration for **35**. These relative configurations, as well as the locations of the resorcinol A- and pyrocatechol B-rings, were confirmed by appropriate NOE, COSY and decoupling experiments using the benzylic proton resonances as reference signals.

The 'release' of only one resorcinol moiety for each derivative (**32**, **35** and **38**) was again evident from a few key NOE experiments. NOE association of 7-OMe(G) with 6- and 8-H(G), as well as the observed benzylic coupling of 4-H(I) and 5-H(G), were indicative of un unchanged resorcinol G-/I-ring system in each instance. Benzylic coupling of 4-H(I) with both 2- and 6-H(H) established the location of the pyrocatechol ring at C-4 of the I-ring for **32**, **35** and **38**. NOE association of 5-OMe(D) with 2-H(I), but absence of additional benzylic coupling of the latter proton, strongly indicated that the structures of these unique products comprised a 4-aryl-3-hydroxy-3,4-dihydro-2*H*-benzopyran nucleus that is substituted at C-2 with a functionalized tetrahydropyrano[2,3-*h*]chromene moiety in all three compounds. The chemical shifts of 2- and 4-H(I) and, thus, unequivocal proof of the positions of the pyrocatechol H-rings and the tetrahydropyranochromenyl units were confirmed by a HETCOR experiment in which these protons could be correlated with, respectively, C-2 and -4 (I-ring). Additional evidence for the proposed structures was provided by the NOEs of 5-OMe(D) with 4H$_{ax.}$ and $_{eq.}$ for each derivative and by association of 2-H(I) with 2-H(B) (for **32**) and with 6-H(A) (for **38**).

The quinone methide (**39**) (Scheme 2) presumably served as common precursor to the array of compounds given in Scheme 1. Since the transformation of intermediate **39** into the hexahydrodipyranochromens (**5**, **10**, **13** and **16**), and the fisetinidol-(4α,6- or 4β,10)-tetrahydropyranochromenes (**19**, **22**, **25**) and (**28**), will be very similar to the processes described previously [2], it need not be repeated here. Formation of the 3,4-dihydro-2*H*-benzopyranyl analogues (**31**, **34** and **37**) is explicable in terms of the initial 1,3-aryl migration of the resorcinol G-ring to the *Si*-face at C-2′ in quinone methide **39** to give quinone methide **41** or of dual 1,3-migration of the DEF-flavanyl unit to the *Re*-face at C-2 and migration of the resorcinol G-ring to the *Si*-face at C-2′ to give quinone methide **40**. Recyclization involving 7-OH(D) and both the *Si*- and *Re*-faces at C-2 in quinone methide **41** then explains the formation of the ABC moieties of **31** and **34**, while recyclization involving 7-OH(D) and the *Si*-face at C-4 in quinone methide **40** explains the generation of the ring-interchanged ABC-unit of compound **37**. Cyclization involving 2-OH(G) and the *Si*-face at C-4′ in intermediates **40** and **41** could possibly explain the formation of the unique benzopyranyl GHI structural units of **31**, **34** and **37** with inversed stereochemistry at

C-3 (I-ring) [8]. Migrations of the above nature, first postulated in quinone methides of type **39** generated from the 2,3-*trans*-3,4-*trans* constituent flavanyl unit in procyanidin B-3 [14], were explained in terms of the comparable migratory aptitude anticipated for the phloroglucinol A-ring and the flavanyl unit with a 2,4,6-trioxygenated D-ring.

Based on the known absolute configuration of the triflavanoid **2** and the mechanisms outlined in Scheme 2, the absolute configuration of **32** followed as 2*R*,3*S*(F):2*R*,3*R*,4*S*(I):8*S*,9*S*,10*R*, of **35** as 2*R*,3*S*(F):2*R*,3*R*,4*S*(I):8*R*,9*S*,10*R* and of **38** as 2*R*,3*S*(F):2*R*,3*R*,4*S*(I):8*R*,9*R*,10*S*. The $[M]^+$ (*m/z* 1100) was, as before, confirmed by FAB mass spectrometry.

Although only two of the compounds shown in Scheme 1 (**4** and **12**) have hitherto been encountered in nature, the protocol of establishing their structures via the base-catalysed transformation of their presumed triflavanoid precursor, has proved invaluable, despite the formation of a considerable number of apparently 'redundant' analogues. The physical data of these will, no doubt, play a significant role in the structural elucidation of their natural counterparts, which will probably result from our continued investigations of the above sources.

EXPERIMENTAL

The general experimental procedures that were employed previously [2] are also applicable to the present study.

Base-catalysed conversion of triflavanoid **2**. Compound **2** (800 mg) [2] was dissolved in 0.025 M Na_2CO_3–0.025 M $NaHCO_3$ buffer (pH 10) (350 ml) and mixt stirred under N_2 for 5.5 hr at 55°. The mixt. was cooled to 0°, acidified with 1 M HCl and extracted with EtOAc (5 × 300 ml). The organic extracts were dried (Na_2SO_4) and evapd to afford a brown powder (880 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 2.8 l eluate removed), to give 6 frs: 1 (tubes 45–62, 62 mg), 2 (63–70, 73 mg), 3 (71–89, 378 mg), 4 (90–110, 127 mg), 5 (111–128, 38 mg) and 6 (129–175, 73 mg).

Methylation of fr. 1 (62 mg) followed by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) afforded a main band at R_f 0.33 (17 mg). Acetylation gave (2*R*,3*S*:6*S*,7*S*,8*R*)-3,7-diacetoxy-5-methoxy-10-[(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*cis*-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,8-di-(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 (**29**) as an amorphous solid (15 mg). Found: C, 66.6; H, 5.8%. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ −1.4, $[\theta]_{287.5}$ 1.3×10^4, $[\theta]_{274.0}$ 1.9×10^2, $[\theta]_{246.0}$ 5.4×10^4, $[\theta]_{238.0}$ 4.1×10^2.

Methylation of fr. 2 (73 mg) and subsequent prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) afforded 2 bands at R_f 0.45 (29 mg) and 0.35 (8 mg). The R_f 0.45 band was acetylated to give (2*R*,3*S*:6*R*,7*S*,8*S*:10*R*,11*R*,12*S*)-3,7,11-triacetoxy-2,6,12-tris-(3,4-dimethoxyphenyl)-8,10-di-(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 (**11**) as an amorphous solid (32 mg). Found: C, 66.7; H, 5.9%. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.8%. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ -4.0×10^1, $[\theta]_{286.0}$ 7.7×10^3, $[\theta]_{281.0}$ -2.3×10^2, $[\theta]_{271.5}$ -1.3×10^4, $[\theta]_{255.5}$ -2.1×10^2, $[\theta]_{248.0}$ 7.3×10^3, $[\theta]_{241.0}$ 5.8×10^2. Similar acetylation of the R_f 0.35 band afforded (2*R*,3*S*:8*R*,9*R*,10*S*)-3,9-diacetoxy-5-methoxy-6-[(2*R*,3*R*,4*S*)-2,3-*cis*-3,4-*trans*-3-acetoxy-4-(3,4-dimethoxyphenyl)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]-2,10-di-(3,4-dimethoxyphenyl)-8-(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 (**38**) as an amorphous solid (8 mg). Found: $[M]^+$, 1100.4056. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 3). CD $[\theta]_{300.0}$ -1.1×10^3, $[\theta]_{283.0}$ -1.3×10^4, $[\theta]_{255.0}$ 2.9×10^1, $[\theta]_{243.0}$ 1.8×10^4, $[\theta]_{236.5}$ 9.3×10^2.

Fr. 3 (378 mg) was methylated and the mixt. sepd by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) to give 2 main bands at R_f 0.74 (72 mg) and 0.68 (128 mg). The R_f 0.74 fr. was purified by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×3) to give a band at R_f 0.72 (25 mg) which was acetylated and sepd by prep. TLC in hexane–Me_2CO–EtOAc (11:6:3, ×2), to afford the (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-(2,4-dimethoxy-5-methylphenyl)-12-(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*-dipyano[2,3-*f*:2′,3′-*h*]chromene (**8**) as an amorphous solid (R_f 0.40, 13 mg). Found: $[M]^+$, 1114.4211, $C_{62}H_{66}O_{19}$ requires $[M]^+$, 1114.4197. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ -9.9×10^1, $[\theta]_{290.5}$ -1.2×10^2, $[\theta]_{286.0}$ 2.0×10^3, $[\theta]_{280.5}$ -5.2×10^1, $[\theta]_{266.0}$ 1.6×10^3, $[\theta]_{247.0}$ 3.4×10^4, $[\theta]_{239.0}$ 1.8×10^3. Similar purification of the R_f 0.68 band by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×3) gave 2 bands at R_f 0.78 (18 mg) and 0.73 (58 mg). Acetylation of the R_f 0.78 band followed by prep. TLC in $CHCl_3$–hexane–Me_2CO (11:8:1, ×2) afforded (2*R*,3*S*:6*R*,7*S*,8*S*:10*R*,11*S*,12*R*)-3,7,11-triacetoxy-2,6,10-tris-(3,4-dimethoxyphenyl)-8-12-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-10,11-*trans*-11,12-*trans*-3,4,7,8,11,12-hexahydro-2*H*,6*H*,10*H*-dipyrano[2,3-*f*:2′,3′-*h*]chromene (**14**) as an amorphous solid (R_f 0.20, 14 mg). Found: C, 66.4; H, 5.7%, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.8%. ^{1}H NMR data (Table 1). CD $[\theta]_{286.0}$ 1.4×10^4, $[\theta]_{276.0}$ 3.5×10^2, $[\theta]_{270.0}$ -4.9×10^3, $[\theta]_{261.5}$ -1.3×10^2, $[\theta]_{248.5}$ 2.6×10^4, $[\theta]_{239.5}$ -1.3×10^3, $[\theta]_{236.0}$ -6.1×10^3, $[\theta]_{232.5}$ -3.4×10^2. The R_f 0.73 band was acetylated to give (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-di-(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 (**6**) as an amorphous solid (65 mg). Found: C, 66.5; H, 5.8%, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.8%. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 5.4×10^1, $[\theta]_{282.5}$ 2.9×10^3, $[\theta]_{267.5}$ 4.7×10^2, $[\theta]_{247.5}$ 2.0×10^4, $[\theta]_{236.5}$ -4.1×10^3.

Methylation of fr. 4 (127 mg) followed by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) afforded 3 bands, 4-A (R_f 0.33, 12 mg), 4-B (R_f 0.25, 20 mg) and 4-C (R_f 0.21, 23 mg). Acetylation of the 4-A fr. followed by prep. TLC hexane–Me_2CO–EtOAc (11:6:3, ×2) gave (2*R*,3*S*:8*R*,9*R*,10*S*)-3,9-*diacetoxy*-5-*methoxy*-6-[(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*cis*-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,10-di-(3,4-dimethoxyphenyl)-8-(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 (**26**) as an amorphous solid (R_f 0.25, 10 mg). Found: 1100.4057, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ -1.3×10^2, $[\theta]_{282.0}$ -1.1×10^4, $[\theta]_{257.0}$ -2.8×10^3, $[\theta]_{245.0}$ -3.9×10^4, $[\theta]_{237.5}$ -8.9×10^2. Acetylation of the 4-B band and subsequent prep. TLC in hexane–Me_2CO–EtOAc (11:6:3, ×2) similarly afforded (2*R*,3*S*:8*S*,9*S*,10*R*)-3,9-*diacetoxy*-5-*methoxy*-6-[(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*trans*-3-acetoxy-3′,4′-dimethoxyphenyl)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]-2,8-di-(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 (**32**) as an amorphous solid (R_f 0.28, 16 mg). Found: C, 66.53; H, 5.9%, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.8%. ^{1}H NMR data (Table 3). CD $[\theta]_{300.0}$ 6.0×10^2, $[\theta]_{288.0}$ -9.5×10^3, $[\theta]_{284.0}$ -3.9×10^2, $[\theta]_{273.5}$ 2.8×10^4, $[\theta]_{257.0}$ 7.7×10^3, $[\theta]_{246.0}$ 4.9×10^4, $[\theta]_{237.5}$ 1.5×10^3. Fr. 4-C was subjected to an identical procedure to afford (2*R*,3*S*:8*R*,9*S*,10*R*)-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-di-(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 (**20**) as an amorphous solid (R_f 0.18, 16 mg). Found: $[M]^+$, 1100.4046, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ -6.2×10^2, $[\theta]_{287.0}$ -1.0×10^4, $[\theta]_{282.0}$ 4.1×10^2, $[\theta]_{273.5}$ 1.7×10^4, $[\theta]_{252.5}$ 1.5×10^2, $[\theta]_{246.5}$ -1.3×10^4, $[\theta]_{241.0}$ 1.0×10^2.

Fr. 5 (38 mg) was methylated and the mixt. sepd by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) to give a band at R_f 0.39 (12 mg). Acetylation afforded (2*R*,3*S*:8*R*,9*S*,10*R*)-3,9-diacetoxy-5-methoxy-6-[(2*R*,3*R*,4*S*)-2,3-*cis*-3,4-*trans*-3-acetoxy-4-(3,4-dimethoxyphenyl)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]-2,8-di(3,4-dimethoxyphenyl)-10-(2,4-dimethoxyphenyl)-2,3-*trans*-8,9-*trans*-9,10-*trans*-3,4,9,10-tetrahydro-2*H*,8*H*-pyano-[2,3-*h*]chromene (**35**) as an amorphous solid (12 mg). Found: $[M]^+$, 1100.4049, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 3). CD $[\theta]_{300.0}$ -5.5×10^2, $[\theta]_{287.5}$ -9.7×10^3, $[\theta]_{282.5}$ -3.7×10^2, $[\theta]_{273.5}$ 1.0×10^4, $[\theta]_{259.0}$ 2.7×10^3, $[\theta]_{247.0}$ 2.3×10^4, $[\theta]_{241.0}$ 2.8×10^2, $[\theta]_{239.0}$ -5.0×10^4.

Methylation of fr. 6 (73 mg) and subsequent prep. TLC sepn in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) gave 2 main bands at R_f 0.36 (9 mg) and 0.25 (27 mg). Acetylation of the R_f 0.36 band afforded (2*R*,3*S*:6*S*,7*S*,8*S*:10*R*,11*S*,12*R*)-3,7,11-triacetoxy-2,6,10-tris-(3,4-dimethoxyphenyl)-8,12-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*cis*-10,11-*trans*-11,12-*trans*-3,4,7,8,11,12-hexahydro-2*H*,6*H*,10*H*-dipyrano[2,3-*f*:2′,3′-*h*]chromene (**17**) as an amorphous solid (9 mg). Found: $[M]^+$, 1100.4042, $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 5.3×10^2, $[\theta]_{289.0}$ 2.8×10^3, $[\theta]_{277.0}$ -5.1×10^1, $[\theta]_{267.5}$ -1.1×10^3, $[\theta]_{251.5}$ -5.0×10^3, $[\theta]_{247.5}$ 1.3×10^2, $[\theta]_{241.5}$ -4.6×10^3, $[\theta]_{238.5}$ -8.5×10^2. Acetylation of the R_f 0.25 band gave (2*R*,3*S*:8*R*,9*S*,10*R*)-3,9-diacetoxy-5-methoxy-6-[(2*R*,3*R*,4*S*)-2,3-*trans*-3,4-*trans*-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,8-di-(3,4-dimethoxyphenyl)-10-(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 (**23**) as an amorphous solid (28 mg). Found: C, 66.4; H, 5.7%, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.8%. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 7.7×10^2, $[\theta]_{292.5}$ -1.9×10^1, $[\theta]_{286.0}$ -1.1×10^4, $[\theta]_{276.5}$ -4.5×10^1, $[\theta]_{270.5}$ 2.3×10^3, $[\theta]_{259.0}$ -1.0×10^3, $[\theta]_{246.0}$ -2.8×10^4, $[\theta]_{236.5}$ -6.6×10^2.

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REFERENCES

1. Steynberg, J. P., Steenkamp, J. A., Burger, J. F. W., Young, D. A. and Ferreira, D. (1990) *J. Chem. Soc., Perkin Trans. 1* 235.
2. Bonnet, S. L., Steynberg, J. P., Bezuidenhoudt, B. C. B., Saunders, C. M. and Ferreira, D. (1996) *Phytochemistry* **43**, 215.
3. Bonnet, S. L., Steynberg, J. P., Bezudenhuodt, B. C. B., Saunders, C. M. and Ferreira, D. (1996) *Phytochemistry* **43**, 229.
4. Freudenberg, K. and Purrmann, L. (1923) *Chem. Ber.* **56**, 1185.
5. Freudenberg, K. and Purrmann, L. (1924) *Ann. Chem.* **437**, 274.
6. 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, 3331.
7. Clark-Lewis, J. W. (1968) *Aust. J. Chem.* **21**, 2059.
8. Steynberg, J. P., Burger, J. F. W., Young, D. A., Brandt, E. V. and Ferreira, D. (1989) *Heterocycles* **28**, 923.
9. Cronje, A., Steynberg, J. P., Brandt, E. V., Young,

D. A. and Ferreira, D. (1993) *J. Chem. Soc., Perkin Trans. 1* 2467.
10. Steynberg, J. P., Brandt, E. V., Ferreira, D., Helfer, C. A., Mattice, W. L., Gornik, D., and Hemingway, R. W. (1995) *Magn. Reson. Chem.* **33**, 611.
11. Nishio, M. and Hirota, M. (1989) *Tetrahedron* **45**, 7201.
12. Steynberg, J. P., Brandt, E. V. and Ferreira, D. (1991), *J. Chem. Soc., Perkin Trans. 11* 1569.
13. Foo, L. Y. and Porter, L. J. (1983) *J. Chem. Soc., Perkin Trans. 1* 1535.
14. Steynberg, J. P., Bezuidenhoudt, B. C. B., Burger, J. F. W., Young, D. A. and Ferreira, D. (1990) *J. Chem. Soc., Perkin Trans. 1* 203.