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

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

Abstract—Additional members of the class of natural phlobatannins, resulting from stereoselective C-ring isomerization of the 2,3-*trans*-3,4-*cis*-flavan-3-ol moieties in the (4β,6:4β,8)-bis-fisetinidol-catechin triflavanoid have been identified from natural sources. These comprise three functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]-chromenes and a fisetinidol-(4β,10)-tetrahydropyrano[2,3-*f*]chromene. The complex structures of these novel natural condensed tannins were confirmed by synthesis via base-catalysed pyran rearrangement of the 4-*O*(E)-methyl ether of their postulated biogenetic triflavanoid precursor. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Previously [1], we have demonstrated the natural occurrence and biomimetic-type synthesis of a series of novel phlobatannins representing the products of stereoselective C-ring isomerization of 2,3-*trans*-3,4-*cis*- and all-*trans*-fisetinidol units present in (4α,6:4α,8)- and (4β,6:4α,8)-bis-fisetinidol-catechin triflavanoids. The need to establish unequivocally the absolute configuration at the eight stereocentres of these complex natural products via synthesis has also been outlined. We now describe results applicable to the naturally occurring (*Baikiaea plurijuga* and *Colophospermum mopane*) and synthetic phlobatannins related to the (4β,6:4β,8)-bis-fisetinidol-catechin triflavanoid. The general protocol for structural elucidation using ^{1}H NMR methods is fully described elsewhere [1] and need not be repeated here.

RESULTS AND DISCUSSION

In order to avoid the unwanted epimerization and migration reactions that are associated with an intermediate E-ring quinone-methide [2], the triflavanoid precursor (**1**) was employed as 4-*O* (E-ring) methyl ether (**2**) [1]. Owing to the susceptibility of constituent flavan-3-ol units with 3,4-*cis*-stereochemistry for 1,3-migrations under basic conditions [2–4], the base-catalysed pyran rearrangement of the bis-fisetinidol-(4β,6:4β,8)-catechin (**2**) presented a special challenge. In spite of the myriad of structural possibilities of products, the reaction was nevertheless performed since it was essential to determine whether indirect asymmetric induction might influence the product distribution.

Treatment of the bis-fisetinidol-(4β,6:4β,8)-catechin mono-*O*-methyl ether (**2**) with 0.025 M $NaHCO_3$–0.025 M Na_2CO_3 buffer solution (pH 10) [5, 6] for 5 hr at 50° under nitrogen (Scheme 1) gave complete conversion into a mixture comprising 16 ring-isomerized products. The compounds with rearranged pyran rings are the nine functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromenes* (**4**, **7**, **10**, **13**, **16**, **19**, **22**, **25** and **28**), the two fisetinidol-(4β,10)-tetrahydropyrano[2,3-*f*]chromenes (**31** and **37**), the fisetinidol-(4β,6)-tetrahydropyrano-[2,3-*h*]chromene (**34**), the two fisetinidol-(4β,10)-tetrahydropyrano[3,2-*g*]chromenes (**40** and **43**) a didehydro-fisetinidol-(4β,10)-tetrahydropyrano[2,3-*f*]chromene (**47**) and the 'dimeric' tetrahydropyrano[2,3-*f*]chromene (**45**). These compounds were again identified from the physical data for their decamethyl ether triacetates, e.g. **5**, except for compounds **45** and **47**, which were characterized as heptamethyl ether diacetate (**46**) and nonamethyl ether triacetate (**49**), respectively. The derivatives not only facilitated comparison with their natural counterparts, but also provided additional structural probes for appropriate ^{1}H NMR experiments, the extra chromatographic steps offered by the process of derivatization being a prerequisite for compound purity.

The absence of the effects of dynamic rotational

*Part 21 in the series 'Oligomeric Flavanoids'. For part 20 see ref. [1].

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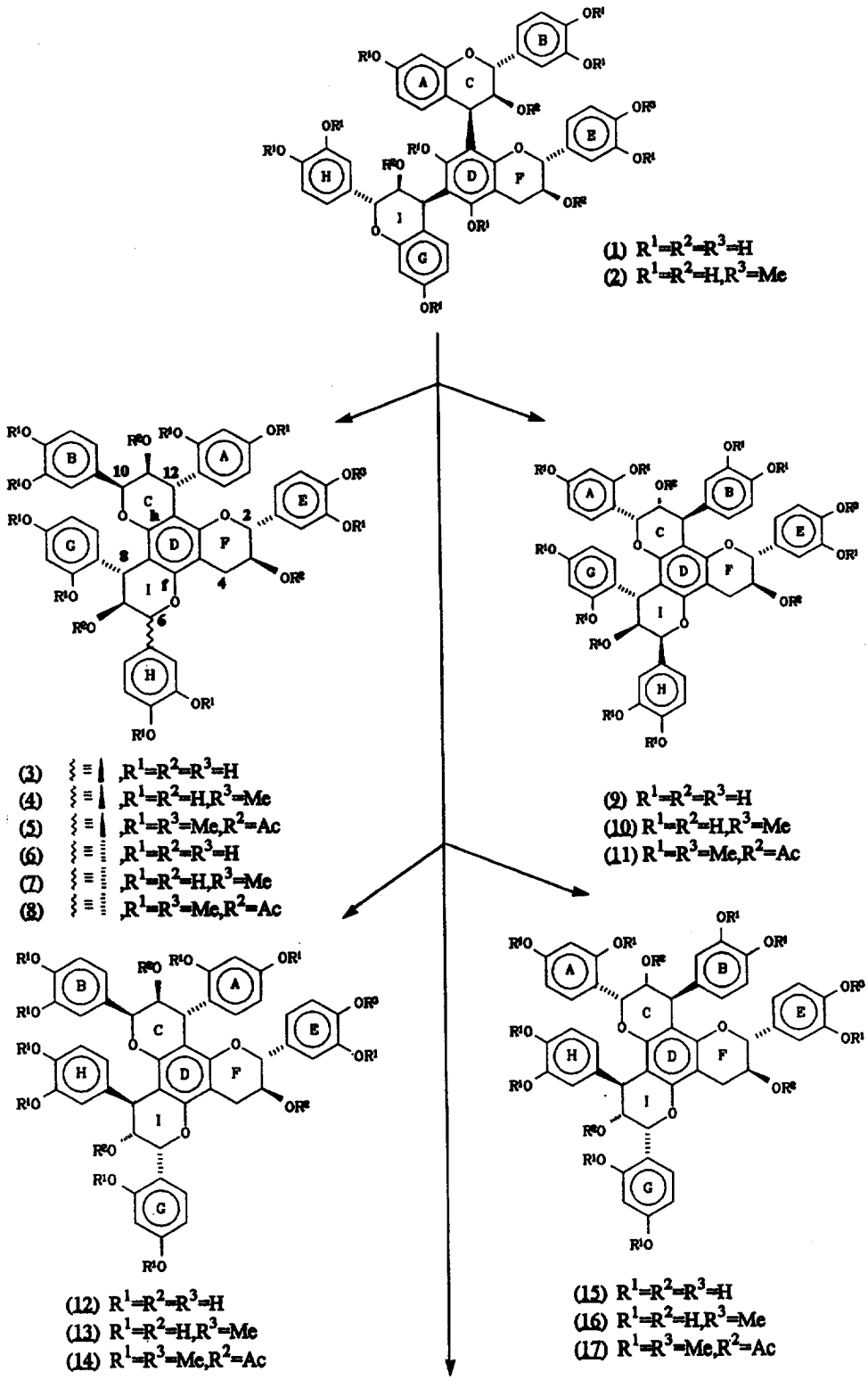
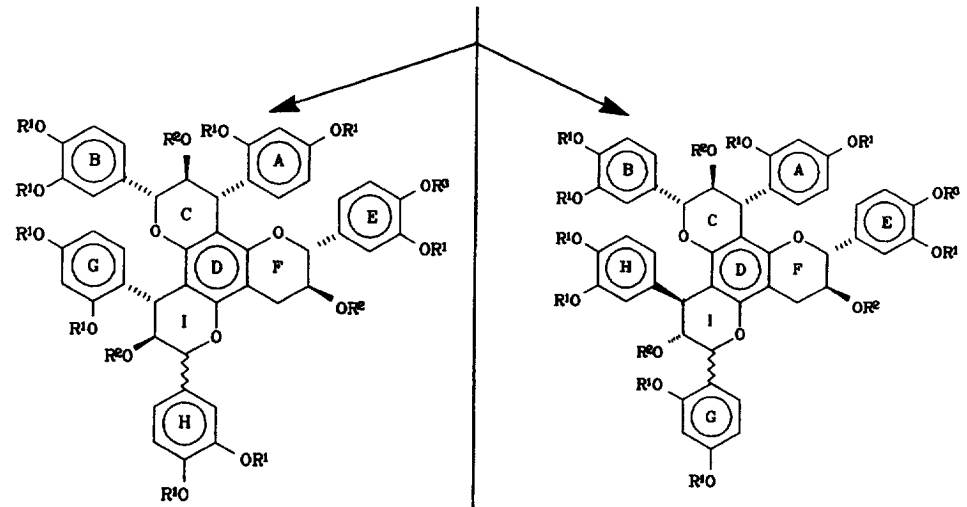
*Non-systematic name/numbering (cf. structure **3**) to retain the heterocyclic oxygen of the catechin DEF-unit as position 1 for all compounds.



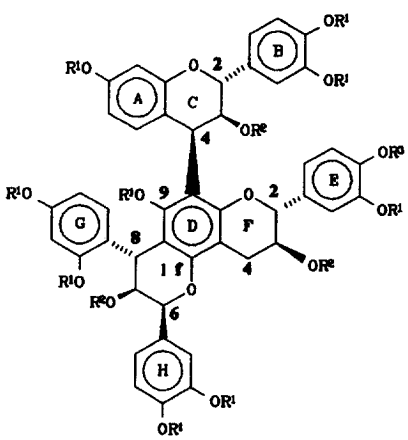
Scheme 1. Base-catalysed pyran rearrangement of the (4β,8:4β,6)-bis-(−)-fisetinidol-(+)-catechin mono-*O*-methyl ether (**2**).

isomerism at ambient temperatures in the ^{1}H NMR spectra (Tables 1 and 2) of the decamethyl ether triacetates (**5**, **8**, **11**, **14**, **17**, **20**, **23**, **26** and **29**) as well as the NOE associations of 2-OMe (A-ring)/2-OMe(G) with 3-H(A)/3H(G) and of 4-OMe(A)/4-OMe(G) with both 3-H(A)/3-H(G) and 5-H(A)/5-H(G) (cf. structure **5**), typical of resorcinol rings being 'liberated' from the heterocyclic C- and I-rings in the triflavanoid precursor (**2**), indicated unequivocally participation of both the C- and I-rings in the pyran rearrangements and, thus, a functionalized hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene constitution for each compound.

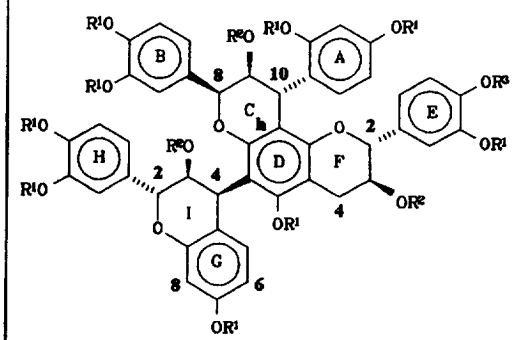


(18) ,R^1=R^2=R^3=H
(19) ,R^1=R^2=H,R^3=Me
(20) ,R^1=R^3=Me,R^2=Ac
(21) ,R^1=R^2=R^3=H
(22) ,R^1=R^2=H,R^3=Me
(23) ,R^1=R^3=Me,R^2=Ac

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



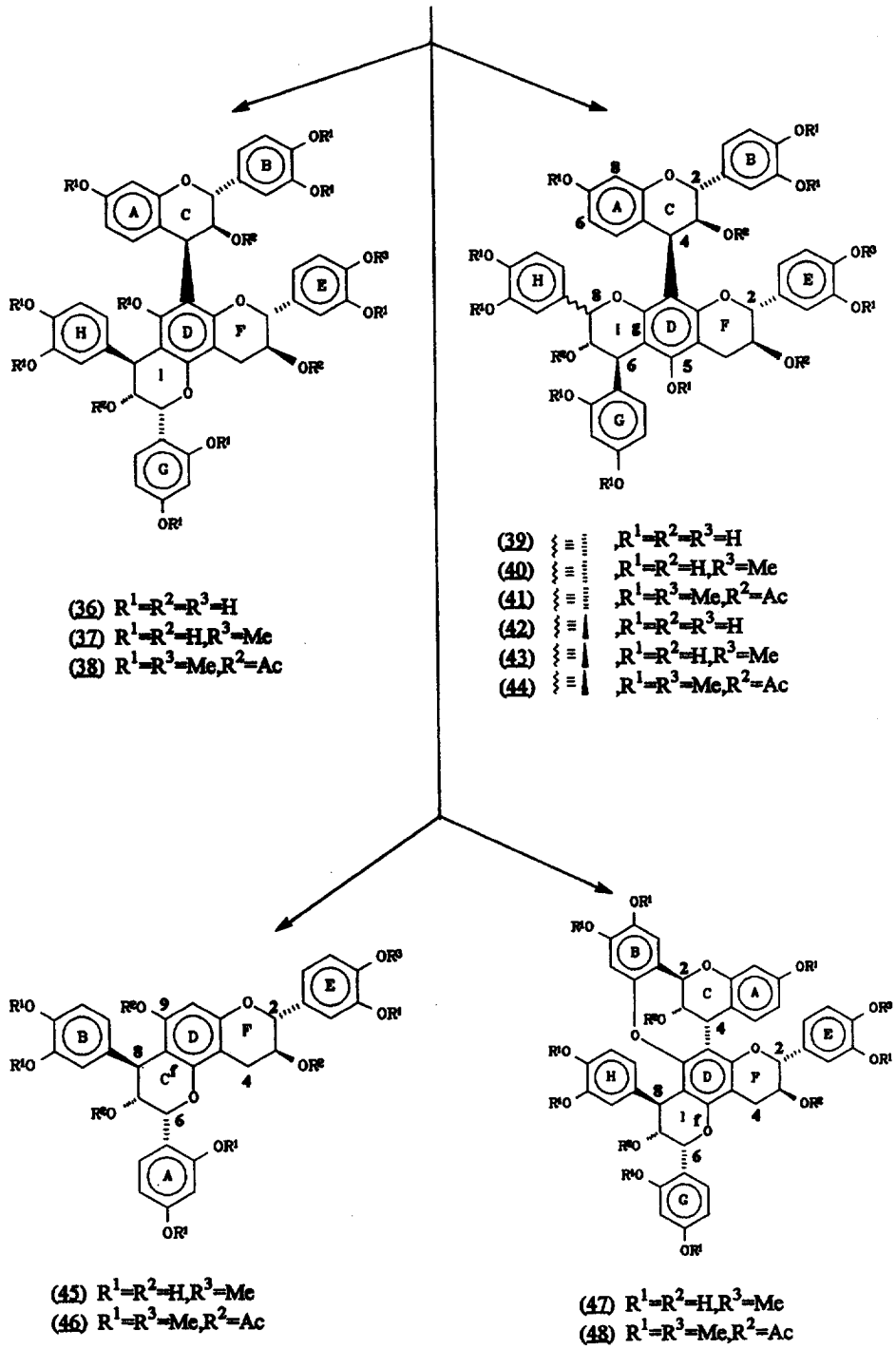
(30) R^1=R^2=R^3=H
(31) R^1=R^2=H,R^3=Me
(32) R^1=R^3=Me,R^2=Ac



(33) R^1=R^2=R^3=H
(34) R^1=R^2=H,R^3=Me
(35) R^1=R^3=Me,R^2=Ac

Scheme 1. *Continued.*

The heterocyclic region of the ^{1}H NMR spectra of derivatives **5**, **11**, **14** and **17** (Table 1) exhibited coupling constants reminiscent of 6,7-*cis*-7,8-*trans*: 10,11-*cis*-11,12-*trans* relative configurations for the C- and I-ring protons in each instance ($J_{6,7}$ = 1.0–1.5, $J_{7,8}$ = 2.0, $J_{10,11}$ = 1.0–1.5 and $J_{11,12}$ = 2.0 Hz) [2]. These relative configurations for the C-rings were corroborated by NOE association of 10-H(C) with 6-



Scheme 1. *Continued.*

H(A) for compounds **5** and **14**, and by the NOE effect of 10-H(C) with 2- and 6-H(B) for derivatives **11** and **17**. The observed NOE association of 6-H(I) with 6-H(G) in compounds **5** and **11**, and of 6-H(I) with both 2- and 6-H(H) for derivatives **14** and **17**, similarly confirmed the *cis–trans* configurations of their I-rings. NOE effects of 10-H(C) with 2- and 6-H(B) in **11** and **17**, and of 6-H(I) with 2- and 6-H(H) in **14** and **17**, in conjunction with a detailed realization of the conformational preferences of hexahydrodipyranochromenes and the demonstration that 10- and 12-H(C) (for **11** and **17**) and 6- and 8-H(I) (for **14** and **17**) could be correlated with resorcinol- and pyrocatechol-type rings, respectively, indicated an interchange of the resorcinol A- and pyrocatechol B-rings (for **11** and **17**) and the resorcinol G- and pyrocatechol H-rings (for **14** and **17**) relative to

Table 1. ^{1}H NMR peaks (ppm) of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives with *cis–trans* configuration of both C- and I-rings **5**, **11**, **14** and **17** at 300 MHz (297 K)

Ring	H	**5** ($CDCl_3$)	**11** (C_6D_6)	**14** ($CDCl_3$)	**17** ($CDCl_3$)
A	3	6.44 (d,2.5)	6.17 (*d*, 2.5)	6.45 (*br.s*)	6.21 (*d*, 2.5)
	5	6.41 (*dd*, 2.5, 8.5)	6.39 (*dd*, 2.5, 8.5)	6.47 (*dd*, 2.5, 8.5)	6.39 (*dd*, 2.5, 8.5)
	6	6.65 (*d*, 8.5)	6.48 (*d*, 8.5)	6.88 (*d*, 8.5)	7.26 (*d*, 8.5)
B	2	6.62 (*d*, 2.0)	7.15 (*d*, 2.0)	6.27 (*d*, 2.0)	6.77 (*d*, 2.0)
	5	6.63 (*d*, 8.0)	6.54 (*d*, 8.0)	6.53 (*d*, 8.5)	6.74 (*d*, 8.5)
	6	6.55 (*dd*, 2.0, 8.0)	6.94 (*dd*, 2.0, 8.0)	6.20 (*dd*, 2.0, 8.5)	6.62 (*dd*, 2.0, 8.5)
C	10	4.73 (*br.s*)	5.75 (*br.s*)	4.91 (*br.s*)	4.97 (*br.s*)
	11	5.60 (*dd*, 1.0, 2.0)	6.00 (*dd*, 1.0, 2.0)	5.28 (*dd*, 1.5, 2.0)	5.39 (2nd order)
	12	4.51 (*d*, 2.0)	4.92 (*d*, 2.0)	4.47 (*d*, 2.0)	4.32 (*d*, 2.0)
E	2	6.42 (*d*, 2.0)	6.83 (*d*, 2.0)	6.42 (*d*, 2.0)	6.67 (*d*, 2.0)
	5	6.66 (*d*, 8.0)	6.46 (*d*, 8.0)	6.63 (*d*, 8.5)	6.77 (*d*, 8.5)
	6	6.46 (*dd*, 2.0, 8.0)	6.82 (*dd*, 2.0, 8.0)	6.49 (*dd*, 2.0, 8.5)	6.72 (*dd*, 2.0, 8.5)
F	2	4.84 (*d*, 9.5)	5.01 (*d*, 7.5)	4.83 (*d*, 9.0)	4.75 (*d*, 7.5)
	3	4.96 (*m*)	5.72 (*m*)	5.00 (*m*)	5.42 (*m*)
	$4_{ax.}$	2.78 (*dd*, 9.5, 16.0)	overlapped by OMe	2.75 (*dd*, 10.0, 17.0)	2.79 (*dd*, 7.5, 17.0)
	$4_{eq.}$	3.32 (*dd*, 5.5, 16.0)	3.61 (*dd*, 6.0, 16.5)	5.35 (*dd*, 5.5, 17.0)	3.21 (*dd*, 6.0, 17.0)
G	3	6.46 (*d*, 2.5)	6.69 (*d*, 2.5)	6.33 (*d*, 2.5)	6.33 (*d*, 2.5)
	5	6.44 (*dd*, 2.5, 8.5)	6.54 (*dd*, 2.5, 8.5)	6.50 (*dd*, 2.5, 8.5)	6.49 (*dd*, 2.5, 8.5)
	6	6.87 (*d*, 8.5)	6.48 (*d*, 8.5)	7.49 (*d*, 8.5)	7.46 (*d*, 8.5)
H	2	6.91 (*d*, 2.0)	7.11 (*d*, 2.0)	7.00 } 2nd order	6.88 (*d*, 2.0)
	5	6.78 (*d*, 8.0)	6.56 (*d*, 9.0)	6.83 } 2nd order	6.70 (*d*, 8.0)
	6	6.83 (*dd*, 2.0, 8.0)	7.11 (*dd*, 2.0, 9.0)	6.83 } 2nd order	6.76 (*dd*, 2.0, 8.0)
I	6	5.01 (*br.s*)	5.56 (*br.s*)	5.29 (*br.s*)	5.39 } 2nd order
	7	5.49 (*dd*, 1.5, 2.0)	6.15 (*dd*, 1.0, 2.0)	5.43 (*dd*, 1.0, 2.0)	5.39 } 2nd order
	8	4.78 (*d*, 2.0)	5.37 (*d*, 2.0)	4.43 (*d*, 2.0)	4.47 (*d*, 2.0)
	OMe	3.53 (3-E), 3.72 (3-B), 3.74 (2-A), 3.79 (4-E/4-G/4-A), 3.81 (2-G), 3.82 (4-B), 3.83 (3-H) and 3.84 (4-H), each *s*	2.97 (2-A), 3.28 (4-A), 3.30 (4-E), 3.33 (3-B), 3.34 (4-H), 3.37 (3-H/4-B), 3.43 (4-G), 3.47 (3-E), and 3.50 (2-G), each *s*	3.34 (3-B), 3.51 (3-E), 3.53 (2-G), 3.69 (2-A), 3.75 (4-B), 3.78 (4-G), 3.81 (4-A), 3.83 (4-E), 3.86 (3-H) and 3.87 (4-H), each *s*	3.43 (2-A), 3.52 (2-G), 3.73 (4-A), 3.76 (3-E), 3.77 (3-B), 3.78 (3-H/4-G), 3.80 (4-H), 3.84 (4-B), and 3.85 (4-E), each *s*
	OAc	1.87, 1.88, 1.96, each *s*	1.45, 1.54, 1.59, each *s*	1.76, 1.89, 1.95, each *s*	1.84, 1.91, 1.95, each *s*

their positions in the 'normal' isomers, e.g. compound **5** [2]. The conspicuous deshielding of 6-H(A) in compounds **11** and **17** and of 6-H(G) in derivatives **14** and **17** (see Table 1), reminiscent of this class of phlobatannins [2–4], confirmed such an exchange of aromatic rings.

Decoupling experiments using the benzylic protons of the C-, F- and I-rings as reference signals not only permitted differentiation of the very similar AMX-spin systems of the C- and I-rings, but also facilitated identification of both the spin systems and positions of the pyrocatechol- and resorcinol-type rings. An intricate series of NOE experiments served to differentiate the ABC- and GHI-units and, hence, to establish the molecular framework of each compound unambiguously via the observed effect between 8-H(I) and 2-H(B) for **5**, of 12-H(C) with both 2-H(E) and 3-OMe(E) for **11**, of 2- and 6-H(B) with both 2- and 6-H(H) for **14** and between 6-H(A) and 8-H(I) for **17**. It should be emphasized that such NOE associations between aromatic ring and heterocyclic protons of a different pyran ring are only permitted when the relevant ring and proton occupy the same face of the molecule. The aforementioned NOE associations thus additionally provided strong probes towards confirmation of the proposed relative configuration. FAB mass spectrometry confirmed the molecular ion ($[M]^+$ *m/z* 1100) for compound **5** as well as the *m/z* 1041, 981 and 879 fragments, but provided, as before [1], limited structural information.

The absolute configurations depicted for compounds **5**, **11**, **14** and **17** are based on the known absolute configuration of the triflavanoid precursor **2**, the mechanism of both pyran rearrangement and the 1,3-diaryl migrations that led to the ring-interchanged products, e.g. **11** [1–4] and the coupling constants of the heterocyclic ring protons. Thus, compound **5** possesses 2*R*,3*S*:6*S*,7*S*,8*R*:10*S*,11*S*,12*R*-, compound **11** 2*R*,3*S*:6*S*,7*S*,8*R*:10*R*,11*R*,12*S*-, compound **14** 2*R*,3*S*:6*R*,7*R*,8*S*:10*S*,11*S*,12*R*- and compound **17** 2*R*,3*S*:6*R*,7*R*,8*S*:10*R*,11*R*,12*S*- absolute configuration. Compound **5** was identical to the same derivative of the natural product (**3**) from *C. mopane*, compound **11** identical to the derivative of the natural product (**9**) from *B. plurijuga*, and compound **14** identical to the derivative of the natural product (**12**) from both *B. plurijuga* and

Table 2. ^{1}H NMR peaks (ppm) of the hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives (**8**, **20**, **23**, **26** and **29**) at 300 MHz (297 K)

Ring	H	**8** ($CDCl_3$)	**20** ($CDCl_3$)	**23*** ($CDCl_3$)	**26** ($CDCl_3$)	**29*** ($CDCl_3$)
A	3	6.42 (*d*, 2.5)	6.18 (*d*, 2.5)	6.19 (*d*, 2.5)	6.20 (*d*, 2.5)	6.19 (*d*, 2.5)
	5	6.39 (*dd*, 2.5, 8.5)	6.21 (*dd*, 2.5, 8.5)	6.28 (*dd*, 2.5, 8.5)	6.12 (*dd*, 2.5, 8.5)	6.21 (*dd*, 2.5, 8.5)
	6	6.54 (*d*, 8.5)	6.58 (*d*, 8.5)	6.66 (*d*, 8.5)	6.49 (*d*, 8.5)	6.61 (*d*, 8.5)
B	2	6.62 (*d*, 2.0)	6.37 (*d*, 2.0)	6.33 (*d*, 2.0)	6.44 (*d*, 2.0)	6.42 (*d*, 2.0)
	5	6.63 (*d*, 8.5)	6.51 (*d*, 8.0)	6.56 (*d*, 8.0)	6.50 (*d*, 8.0)	6.55 (*d*, 8.0)
	6	6.46 (*d*, 2.0, 8.5)	6.38 (*dd*, 2.0, 8.0)	6.34 (*dd*, 2.0, 8.0)	6.35 (*dd*, 2.0, 8.0)	6.30 (*dd*, 2.0, 8.0)
C	10	4.36 (*br.s*)	4.87 (*d*, 8.0)	4.68 (*d*, 9.0)	4.78 (*d*, 7.0)	4.30 (*d*, 8.0)
	11	5.29 (*dd*, 1.5, 2.0)	5.24 (*dd*, 7.0, 8.0)	5.07 (*dd*, 8.0, 9.0)	5.68 (*dd*, 5.0, 7.0)	5.46 (*dd*, 6.0, 8.0)
	12	4.49 (*d*, 2.0)	4.48 (*d*, 7.0)	4.47 (*d*, 8.0)	4.48 (*d*, 5.0)	4.47 (*d*, 6.0)
E	2	6.43 (*d*, 2.0)	6.41 (*d*, 2.0)	6.43 (*d*, 2.0)	6.37 (*d*, 2.0)	6.38 (*d*, 2.0)
	5	6.60 (*d*, 8.0)	6.63 (*d*, 8.5)	6.62 (*d*, 8.0)	6.61 (*d*, 8.5)	6.61 (*d*, 8.5)
	6	6.39 (*dd*, 2.0, 8.0)	6.24 (*dd*, 2.0, 8.5)	6.18 (*dd*, 2.0, 8.0)	6.32 (*dd*, 2.0, 8.5)	6.26 (*dd*, 2.0, 8.5)
F	2	4.85 (*d*, 8.5)	4.74 (*d*, 9.5)	4.72 (*d*, 8.5)	4.74 (*d*, 9.0)	4.74 (*d*, 9.0)
	3	5.03 (*m*)	4.96 (*m*)	5.02 (*m*)	4.98 (*m*)	4.90 (*m*)
	4_{ax}	2.74 (*dd*, 8.5, 16.5)	2.74 (*dd*, 9.5, 16.0)	2.70 (*dd*, 9.0, 16.5)	2.71 (*dd*, 10.0, 16.0)	2.69 (*dd*, 9.0, 16.0)
	4_{eq}	3.19(*dd*,5.5,16.5)	3.28(*dd*,5.5,16.0)	3.19(*dd*,5.5,16.5)	3.30(*dd*,5.5,16.0)	3.17(*dd*,6.0,16.0)
G	3	6.03 (*d*, 2.5)	6.50 (*d*, 2.5)	6.27 (*d*, 2.5)	6.33 (*d*, 2.5)	6.27 (*d*, 2.5)
	5	6.13 (*dd*, 2.5, 8.5)	6.54 (*dd*, 2.5, 8.5)	6.21 (*dd*, 2.5, 8.5)	6.48 (*dd*, 2.5, 8.5)	6.41 (*dd*, 2.5, 8.5)
	6	6.65 (*d*, 8.5)	6.94 (*d*, 8.5)	6.59 (*d*, 8.5)	7.46 (*d*, 8.5)	7.27 (*d*, 8.5)
H	2	6.84 (*d*, 2.0)	6.88 (*d*, 2.0)	6.73 (*d*, 2.0)	6.85 (*d*, 2.0)	6.46 (*d*, 2.0)
	5	6.74 (*d*, 8.0)	6.78 (*d*, 8.0)	6.68 (*d*, 8.0)	6.79 (*d*, 8.0)	6.43 (*d*, 8.5)
	6	6.87 (*dd*, 2.0, 8.0)	6.84 (*dd*, 2.0, 8.0)	6.77 (*dd*, 2.0, 8.0)	6.69 (*dd*, 2.0, 8.0)	6.45 (*dd*, 2.0, 8.5)
I	6	5.12 (*d*, 8.0)	5.03 (*br.s*)	5.10 (*d*, 7.0)	5.35 (*br.s*)	5.38 (*d*, 8.0)
	7	5.56 (*dd*, 7.0, 8.0)	5.44 (*dd*, 1.0, 2.0)	5.60 (*dd*, 6.0, 7.0)	5.42 (*dd*, 1.0, 2.0)	5.68 (*dd*, 7.0, 8.0)
	8	4.78 (*d*, 7.0)	4.60 (*d*, 2.0)	4.54 (*d*, 6.0)	4.41 (*d*, 2.0)	4.26 (*d*, 7.0)
	OMe	3.52 (2-G), 3.57 (3-E), 3.61 (4-G), 3.70 (2-A), 3.76 (3-B), 3.79 (4-A/4-B), 3.80 (3-H), 3.82 (4-E) and 3.83 (4-H), each *s*	3.54 (2-A), 3.52 (3-B), 3.65 (3-E), 3.71 (4-A), 3.76 (4-H) 3.82, 3.83, 3.84 and 3.86 (4-G), each *s*	3.40 (2-A), 3.52 (2-G), 3.56 (3-B), 3.71 (3-E), 3.72 (4-A), 3.74 (4-G), 3.75 (3-H), 3.78 (4-B), 3.81 (4-H) and 3.84 (4-E), each *s*	3.51 (2-A), 3.53 (2-G), 3.55 (3-E), 3.64 (3.B), 3.70 (4-A), 3.75 (4-B), 3.77 (4-G), 3.82 (3-H), 3.83 (4-E) and 3.87 (4-H), each *s*	3.44 (2-A), 3.61 (3-E), 3.62 (3-H), 3.71, 3.72, 3.73, 3.74 (2-G/4-G), 3.78 (4-B) and 3.83 (4-E), each *s*
	OAc	1.82, 1.88, 1.90, each *s*	1.76, 1.87, 1.92, each *s*	1.67, 1.84, 1.85, each *s*	1.82, 1.84, 1.95, each *s*	1.71, 1.81 (×2), each *s*

*Chemical shifts of ABC- and GHI-moieties could not be differentiated.

C. mopane by comparison of their ^{1}H NMR and circular dichroic (CD) data. As before [1], the CD data were only used comparatively since the chiroptical method does not permit stereochemical assessment at this molecular level.

An identical experimental protocol was used to establish the structures of the remaining hexahydrodipyrano[2,3-*f*:2′,3′-*h*]chromene derivatives with *cis–trans* and *trans–trans* relative configurations of their rearranged pyran rings (**8**, **20** and **26**), and of those with *trans–trans* configuration of both their C- and I-rings (**23** and **29**). The assignment of all-*trans* relative configuration to appropriate heterocyclic rings in these derivatives was based on coupling constants (see Table 2) ($J_{6,7}$ = 7.0–8.0, $J_{7,8}$ = 6.0–7.0, $J_{10,11}$ = 7.0–9.0 and $J_{11,12}$ = 5.0–8.0 Hz) and was unambiguously confirmed by the NOE association of 8-H(I) with 6-H(I) (for **8**, **23** and **29**) and between 12-H(C) and 10-H(C) for compounds **20**, **23**, **26** and **29**. The relatively small *J* values observed for the protons of the pyran rings with all-*trans* configuration are attributable to significant contributions of A-forms [7–9] towards the conformational equilibrium of the respective heterocyclic rings, a phenomenon that is confirmed by the small but significant NOE association of 2-OMe(A) with 6-H(G) for derivative **23**. According to Dreiding models, such an association is only permitted when the A- and G-rings are co-facial and the A-conformers of both the C- and the I-rings are substantially populated.

The significant structural information that may be extracted from NOE associations between substituents on different pyran rings was again utilized to differentiate between the spin systems of the ABC- and GHI-units in derivatives **8**, **20** and **26** only. For compound **8**, the NOE association between 8-H(I) and 2-H(B), 4-OMe(G) and 10-H(C) and of 3-OMe(E) with both 3- and 6-H(A) not only facilitated unambiguous definition of the regiomerism of the C- and I-heterocycles, but also confirmed the 8,10-*trans* relationship between the G- and B-rings, as well as the 2,12-*cis*-orientation of the A- and E-rings. The relative orientation of the five aromatic substituents on the 'central' hexahydrodipyranochromene core was thus accessible from a few key NOE associations. Utilization of the relevant NOE, COSY and decoupling experiments again permitted differentiation of the resorcinol- and pyrocatechol-type aromatic rings, which, in conjunction with the characteristic deshielding of the 6-H resonance of resorcinol-type rings (Table 2), facilitated identification of those compounds (**26** and **29**) where ring interchange had occurred. FAB mass spectral data confirmed the molecular ion ($[M]^+$, *m/z* 1100) as well as a retro-Diels–Alder fragmentation and three successive losses of acetic acid in each instance.

Definition of the absolute configuration of the hexahydrodipyranochromene derivatives **8** (2*R*,3*S* : 6*R*,7*S*, 8*R* : 10*S*,11*S*,12*R*), **20** (2*R*,3*S* : 6*S*,7*S*,8*R* : 10*R*,11*S*,12*R*), **23** (2*R*,3*S* : 6*R*,7*S*,8*R* : 10*R*,11*S*,12*R*), **26** 2*R*,3*S* : 6*R*,7*R*,8*S* : 10*R*,11*S*,12*R*) and **29** (2*R*,3*S* : 6*S*,7*R*,8*S* : 10*R*,11*S*,12*R*) were again based on their ^{1}H NMR data, the known absolute configuration of their triflavanoid precursor (**2**) and the mechanism of their formation from **2**.

Involvement of a single heterocycle in the pyran rearrangements leading to the 'isomerization-intermediates', the fisetinidol-(4β,10)-tetrahydropyranochromenes (**31**, **37**, **40** and **43**) and the (4β,6)-regioisomer (**34**), was evident from the heterocyclic AMX-system in each of the ^{1}H NMR spectra (Tables 3 and 4) of the decamethyl ether triacetates (**32**, **35**, **38**, **41** and **44**), which corresponds to an 'intact' 2,3-*trans*-3,4-*cis* [$J_{2,3(C/I)}$ = 6.5–10.0, $J_{3,4(C/I)}$ = 6.0–7.0 Hz] C-4 substituted fisetinidol moiety. Such an intact fisetinidol unit and, hence, a fisetinidol-(4β,6 or 4β,10)-tetrahydropyranochromene-type structure was confirmed by NOE experiments, which indicated the 'release' of a single resorcinol moiety in each instance. The involvement of the remaining resorcinol unit in the A/C-ring system of, e.g. **32** was evident from the NOE association of only 7-OMe(A) with 8-H(A). Differentiation of these closely related analogues as fisetinidol-(4β,10)-tetrahydropyrano[2,3-*f*]chromenes (**32** and **38**), fisetinidol-(4β,10)-tetrahydro-pyrano[3,2-*g*]chromenes (**41** and **44**) and the fisetinidol-(4β,6)-tetrahydropyrano[2,3-*h*]chromene (**35**) was effected by the NOE association of 9-OMe(D) with 4-H(C), 8-H(I) and 5-H(A) for **32** and **38**, of 5-OMe(D) with 6-H(I) for **41** and with 6-H(I), 6-H(G) and 4-H(F)$_{ax.}$ and $_{eq.}$ for **44**, and of 5-OMe(D) with 4-H(I) and 5-H(G) for **35**.

The ^{1}H NMR spectra of the decamethyl ether triacetates (**38**, **41** and **44**) displayed the typical effects of dynamic rotational isomerism about the (4,10)-interflavanyl bond. The same techniques [1] were used to identify the different rotamers. Thus, for compound **38** the NOE association of 9-OMe(D) with 4-H(C) differentiates (**38a**) as the major rotamer with a dihedral angle [10] $\theta = +90°$, while the association of 2-H(C) with 2-H(H) characterizes **44a** as the major rotamer, $\theta = -90°$. Owing to insufficient sample quantity, the rotamers of compound **41** could not be differentiated.

In addition to the aforementioned AMX-system of the intact fisetinidol-type moiety, the heterocyclic region of the ^{1}H NMR spectra of derivatives **32**, **35**, **38**, **41** and **44** displayed an AMX-system reminiscent of the three-spin system of rearranged pyran rings with *cis–trans* ($J_{6,7}$ = 1.5 Hz for **32** and 1.0 Hz for both rotamers of **38**; $J_{7,8}$ = 2.5 Hz for **32** and 2.0 Hz for the rotamers of **38**; $J_{7,8}$ = 1.0, $J_{6,7}$ = 2.0 Hz for both rotamers of **41**; and $J_{8,9}$ = 1.0, $J_{9,10}$ = 2.0 Hz for **35**) and *trans–trans* ($J_{7,8}$ = 9.0 and 8.5, and $J_{6,7}$ = 7.0 and 7.0 Hz for the two rotamers of **44**) relative configurations. These configurations were confirmed by the NOE association in the *cis–trans* analogues of 6-H(I) with 6-H(G) for **32**, 8-H(C) with 6-H(A) for **35**, 6-H(I) with 2- and 6-H(H) for (**38**), 8-H(I) with 6-H(G) for **41**, and of 8/8′-H(I) and 6/6′-H(I) for the 6,7-*trans*-7,8-*trans* derivative (**44**). The 'interchanged' resorcinol G- and pyrocatechol H-rings in compound **38** were evident

Table 3. ^{1}H NMR peaks (ppm) of the tetrahydropyranochromene derivatives (**38**, **41** and **44**) and their rotamers (**38b**, **41b** and **44b**) in $CDCl_3$ at 300 MHz (297 K)

Ring	H	**38a**	**38b**	**41a**	**41b**	**44a**	**44b**
A	5	6.65 (*d*, 8.5)	6.98 (*d*, 8.5)	6.74 (*d*, 8.5)	6.90 (*d*, 8.5)	6.65 (*d*, 8.5)	6.75 (*d*, 8.5)
	6	6.25 (*dd*, 2.5, 8.5)	6.43 (*dd*, 2.5, 8.5)	6.28 (*dd*, 2.5, 8.5)	6.38 (*dd*, 2.5, 8.5)	6.18 (*dd*, 2.5, 8.5)	6.21 (*dd*, 2.5, 8.5)
	8	5.85 (*d*, 2.5)	6.44 (*d*, 2.5)	5.98 (*d*, 2.5)	6.52 (*d*, 2.5)	5.88(*d*,2.5)	5.99 (*d*, 2.5)
B	2	6.86 (*d*, 2.0)		6.81 (*d*, 2.0)		6.84 (*d*, 2.0)	6.79 (*d*, 2.0)
	5	6.78 (*d*, 8.0)		6.79 (*d*, 8.0)		6.57 (*d*, 8.0)	6.71 (*d*, 8.0)
	6	6.89 (*dd*, 2.0, 8.0)		6.84 (*dd*, 2.0, 8.0)		6.79 (*dd*, 2.0, 8.0)	6.61 (*dd*, 2.0, 8.0)
C	2	5.29 (*d*, 9.0)	5.18 (*d*, 10.0)	5.32 (*d*, 7.5)	5.23 (*d*, 6.5)	5.40 (*d*, 7.5)	5.30 (*d*, 7.0)
	3	5.55 (*dd*, 6.5, 9.5)	5.63 (*dd*, 6.5, 10.0)	5.86 (*dd*, 7.0, 7.5)	5.66 (*dd*, 6.0, 6.5)	5.66 (*dd*, 6.0, 7.5)	5.71 (*dd*, 6.0, 7.0)
	4	4.62 (*d*, 6.5)	5.14 (*d*, 6.5)	5.03 (*d*, 7.0)	5.18 (*d*, 6.0)	4.99 (*d*, 6.0)	4.92 (*d*, 6.0)
E	2	6.66 (*br.s*)	6.93 (*d*, 2.0)	6.68 (*br.s*)		6.81 (*d*, 2.0)	6.65 (*d*, 2.0)
	5	6.74 (*d*, 8.5)	6.87 (*d*, 8.5)	6.74 (*d*, 8.0)		6.81 (*d*, 8.0)	6.44 (*d*, 8.0)
	6	6.65 (*dd*, 2.0, 8.5)	6.98 (*dd*, 2.0, 8.5)	6.66 (*dd*, 2.0, 8.0)		6.86 (*dd*, 2.0, 8.0)	6.61 (*dd*, 2.0, 8.0)
F	2	4.22 (*d*, 9.5)	4.98 (*d*, 7.0)	4.22 (*d*, 9.0)	4.94 (*d*, 8.5)	5.00 (*d*, 7.0)	4.19 (*d*, 9.0)
	3	5.31 (*m*)	5.50 (*m*)	5.15 (*m*)	5.25 (*m*)	5.28 (*m*)	5.02 (*m*)
	$4_{ax.}$	2.73 (*dd*, 9.0, 17.0)	2.87 (*dd*, 6.5, 17.0)	2.68 (*dd*, 9.0, 16.5)	2.77 (*dd*, 8.5, 16.0)	2.80 (*dd*, 7.0, 17.0)	2.66 (*dd*, 9.0, 16.5)
	$4_{eq.}$	3.42 (*dd*, 6.5, 17.0)	3.16 (*dd*, 5.5, 17.0)	3.20 (*dd*, 5.5, 16.5)	3.14 (*dd*, 5.5, 16.0)	2.97 (*dd*, 5.0, 17.0)	3.14 (*dd*, 6.5, 16.5)
G	3	6.32 (*d*, 2.5)	6.31 (*d*, 2.5)			6.40 (*d*, 2.5)	6.38 (*d*, 2.5)
	5	6.48 (*dd*, 2.5, 8.5)	6.47 (*dd*, 2.5, 8.5)			6.37 (*dd*, 2.5, 8.5)	6.26 (*dd*, 2.5, 8.5)
	6	7.44 (*d*, 8.5)	7.40 (*d*, 8.5)			6.83 (*d*, 8.5)	6.64 (*d*, 8.5)
H	2	6.94 (*d*, 2.0)		6.93		6.51 (*d*, 2.0)	—
	5	6.84 (*d*, 8.5)		6.77 } 2nd order		6.61 (*d*, 8.0)	6.74 (*d*, 8.0)
	6	6.69 (*dd*, 2.0, 8.5)		6.77		6.47 (*dd*, 2.0, 8.0)	6.88 (*dd*, 2.0, 8.0)
I	6	5.50 (*br.s*)	5.24 (*br.s*)	4.72 (*d*, 2.0)	4.64 (*d*, 2.0)	4.58 (*d*, 7.0)	4.67 (*d*, 7.0)
	7	5.30 (*dd*, 1.0, 2.0)	5.38 (*dd*, 1.0, 2.0)	5.41 (*dd*, 1.0, 2.0)	5.31 (*dd*, 1.0, 2.0)	5.28 (*dd*, 7.0, 9.0)	5.59 (*dd*, 7.0, 7.5)
	8	4.44 (*d*, 2.0)	4.29 (*d*, 2.0)	5.07 (*br.s*)	4.91 (*br.s*)	4.02 (*d*, 9.0)	4.90 (*d*, 7.5)
	OMe	3.25 (9-D), 3.49 (7-A), 3.52 (2-G), 3.75 (3-E), 3.77 (4-G), 3.81 (3-B), 3.84 (4-B), 3.85 (4-E), 3.87 (4-H) and 3.91 (3-H), each *s*	3.71, 3.77 (4-G), 3.78, 3.83, 3.86 (3-E), 3.88 and 3.89, each *s*	3.32 (5-D), 3.52 (7-A), 3.71, 3.74, 3.76, 3.79, 3.80, 3.83 (4-H), 3.85 (4-E) and 3.86 (3-H), each *s*	3.32 (5-D), 3.66, 3.68, 3.72, 3.73, 3.78, 3.79, 3.88, 3.90 and 3.92, each *s*	3.30 (5-D), 3.45 (7-A), 3.72 (3-H), 3.74 (×3), 3.78 (3-E), 3.80 (4-H), 3.81 (4-B) and 3.87 (4-E), each *s*	3.25 (5-D), 3.48 (7-A), 3.66 (3-B), 3.72 (4-G), 3.74, 3.78 (4-E), 3.81 (3-E/2-G) and 3.84 (×2), each *s*
	OAc	1.73, 1.83, 1.84, each *s*	1.70, 1.85, 1.93, each *s*	1.76, 1.84, 1.92, each *s*	1.77, 1.85, 1.93, each *s*	1.77, 1.88, 1.91, each *s*	1.82, 1.83 (×2), each *s*

Table 4. ^{1}H NMR peaks (ppm) of the tetrahydropyranochromene derivatives (**32**, **35** and **48**) in $CDCl_3$ at 300 MHz (297 K)

Ring	H	**32**	**35**	**48**
A	5/6	6.75 (*d*, 8.5)	6.66 (*d*, 8.5)	6.34 (*d*, 10.0)
	6/5	6.27 (*dd*, 2.5, 8.5)	6.39 (*dd*, 2.5, 8.5)	6.24 (*dd*, 1.5, 10.0)
	8/3	5.74 (*d*, 2.5)	6.44 (*d*, 2.5)	5.55 (*d*, 1.5)
B	2/3	6.82 (*d*, 2.0)	6.29 (*d*, 2.0)	6.82 (*s*)
	5	6.77 (*d*, 8.0)	6.51 (*d*, 8.5)	—
	6	6.84 (*dd*, 2.0, 8.0)	6.08 (*dd*, 2.0, 8.5)	6.34 (*s*)
C	2/8	5.26 (*d*, 9.5)	4.84 (*br.s*)	5.07 (*t*, 2.5)
	3/9	5.46 (*dd*, 6.5, 9.5)	5.29 (*dd*, 1.0, 2.0)	6.06 (*dd*, 2.5, 3.5)
	4/10	4.61 (*d*, 6.5)	4.47 (*d*, 2.0)	3.74 (*dd*, 2.0, 3.5)
E	2	6.66 (*d*, 2.0)	6.36 (*d*, 2.5)	6.78 }
	5	6.72 (*d*, 8.0)	6.61 (*d*, 8.5)	6.91 } 2nd order
	6	6.62 (*dd*, 2.0, 8.0)	6.39 (*dd*, 2.5, 8.5)	6.91 }
F	2	4.21 (*d*, 9.5)	4.80 (*d*, 8.5)	4.73 (*d*, 9.0)
	3	5.27 (*m*)	4.93 (*m*)	5.12 (*m*)
	$4_{ax.}$	2.72 (*dd*, 9.5, 17.0)	2.77 (*dd*, 9.0, 16.0)	2.71 (*dd*, 10.0, 16.5)
	$4_{eq.}$	3.36 (*dd*, 6.5, 17.0)	3.20 (*dd*, 6.0, 16.0)	3.36 (*dd*, 6.0, 16.5)
G	5/6	6.63 (*d*, 8.5)	6.91 (*d*, 8.5)	7.43 (*d*, 8.5)
	6/5	6.33 (*dd*, 2.5, 8.5)	6.43 (*dd*, 2.5, 8.5)	6.47 (*dd*, 2.5, 8.5)
	8/3	6.49 (*d*, 2.5)	6.53 (*d*, 2.5)	6.31 (*d*, 2.5)
H	2	6.84 (*d*, 2.0)	6.73 }	7.01 (*d*, 2.0)
	5	6.77 (*d*, 8.0)	6.78 } 2nd order	6.73 (*d*, 8.0)
	6	6.81 (*dd*, 2.0, 8.0)	6.78 }	6.52 (*dd*, 2.0, 8.0)
I	2/6	5.06 (*br.s*)	5.23 (*d*, 6.5)	5.19 (*br.s*)
	3/7	5.38 (*dd*, 1.5, 2.5)	5.70 (*dd*, 6.5, 7.0)	5.37 (*dd*, 1.0, 2.0)
	4/8	4.63 (*d*, 2.5)	4.89 (*d*, 7.0)	4.21 (*d*, 2.0)
	OMe	3.48, 3.60, 3.72 (3-E), 3.75 (4-G), 3.81 (3-B), 3.83 (3-H), 3.84 (4-E), 3.85 (4-H/4-B) and 3.89 (2-G), each *s*	3.54 (3-E), 3.59 (5-D), 3.63 (3-B), 3.69 (2-A), 3.76 (7-G), 3.77 (4-B), 3.78 (3-H), 3.79 (4-A), 3.82 (4-E) and 3.84 (4-H), each *s*	3.50 (2-G), 3.61 (7-A), 3.71 (5-B), 3.76 (4-G), 3.86 (4-H), 3.89 (3-E), 3.90 (4-B) and 3.92 (3-H/4-H), each *s*
	OAc	1.29, 1.82, 1.94, each *s*	1.71, 1.81, 1.89, each *s*	1.85, 1.86, 1.94, each *s*

from a COSY experiment, which correlated 6/6′-H(I) with the resorcinol G/G′-ring and also from the characteristic deshielded 6/6′-H(G) resonance compared to its chemical shift in, e.g. derivative **32** (Table 3). Assignment of the absolute configurations to the substituted tetrahydropyranochromenes was based on the same considerations as above and may be formulated as 2*R*,3*S*(F):6*S*,7*S*,8*R*:2*R*,3*S*,4*R*(C) for **32**, 2*R*,3*S*(F):2*R*,3*S*,4*R*(I):8*S*,9*S*,10*R* for **35**, 2*R*,3*S*(F):6*R*,7*R*,8*S*:2*R*,3*S*,4*R*(C) for (**38**), 2*R*,3*S*(F):6*R*,7*S*,8*S*:2*R*,3*S*,4*R*(C) for **41** and 2*R*,3*S*(F):6*R*,7*S*,8*R*:2*R*,3*S*,4*R*(C) **44**.

Comparison of the ^{1}H NMR and CD data for the decamethyl ether triacetate (**32**) of the fisetinidol-(4β,10)-tetrahydropyrano[2,3-*f*]chromene (**30**) with those of the same derivative of the natural product from *B. plurijuga* proved its identity and, hence, confirmed its structure unambiguously.

The structure of the heptamethyl ether diacetate (**46**) of the tetrahydropyrano[2,3-*f*]chromene (**44**) was deduced by comparison of its physical data with those of a synthetic specimen [2]. Under the mild basic conditions effecting the pyran ring rearrangements, the more labile (4,8)-interflavanyl bond in triflavanoid (**2**) is presumably cleaved [11] to give a fisetinidol-(4β,6)-catechin biflavanoid, which then serves as precursor to the tetrahydropyrano[2,3-*f*]chromene (**46**) [2].

The presence of nine methoxyl and three acetoxy signals in conjunction with two one-proton singlets (δ 6.34 and 6.82) in the ^{1}H NMR spectrum (Table 4) of compound **48** strongly indicated a didehydro bis-fisetinidol-catechin-type structure related to the analogue that was described previously [1]. The small coupling constants of the C-ring protons ($J_{2,3} = 2.5$ and $J_{3,4} = 3.5$ Hz) are compatible with dihedral angles approaching 90°, as a result of conformational restrictions imposed on this ring by the eight-membered oxygen heterocycle. The abnormal shielding of 4-H(C) relative to the chemical shift of this proton in the permethyl ether triacetate derivative of the parent triflavanoid (**3**) is, as before [1], explicable in terms of anisotropy of proximal functionalities. Similar deshielding of 3-H(C) results from its close proximity to the oxygen of the eight-membered ring. The NOE association of 2-H(C) with the 6-H(B) singlet strongly supported the proposed 9-D → 2-B linkage. NOE experiments again indicated the 'release' of a single resorcinol unit, while the coupling constants of the second heterocyclic AMX spin system corresponded to a 6,7-*cis*-7,8-*trans* heterocyclic I-ring ($J_{6,7} = 1.0$ and

$J_{7,8}$ = 2.0 Hz). COSY experiments correlated 6- and 8-H(I) with the resorcinol G- and pyrocatechol H-rings, respectively, which in conjunction with the conspicuous deshielding of 6-H(G), confirmed compound **47** as a ring-interchanged product. Since no evidence could be found to differentiate the spin systems of the upper and lower flavanyl units, the ABC and GHI moieties cannot be firmly designated, thus leading to tentative assignment of structure.

The mechanism explaining the C-ring isomerization and the 1,3-diaryl rearrangement that lead to the 'interchange' of resorcinol- and pyrocatechol-type rings via the putative quinone methide intermediates are now well understood and documented [1] and do not deserve further attention. We found no evidence that the product distribution might have been influenced by indirect asymmetric induction and, thus, the formation of the considerable number of pyran rearranged products from a single precursor triflavanoid (**2**).

In spite of the multitude of compounds that are generated (Scheme 1), our approach nevertheless provided the only feasible method of establishing unequivocally the structure and absolute configuration of the complex natural products **3**, **9**, **12**, and **30**. The mild conditions that are required for the pyran rearrangement reactions indicate that a similar *in vivo* process might also be feasible and that the remaining compounds shown in Scheme 1 will eventually also be encountered in natural sources.

EXPERIMENTAL

The general experimental procedures described in ref. [1] were also employed during the course of the present investigation.

Base-catalysed conversion of triflavanoid **2**. Compound **2** (780 mg) [1] was dissolved in a 0.025 M Na_2CO_3–0.025 M $NaHCO_3$ buffer (350 ml) (pH 10) and the mixt. stirred under N_2 for 3 hr at 52°. 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 (850 mg) which was subjected to CC on Sephadex LH-20 (3 × 120 cm), 0.8 ml min^{-1}, 24 ml eluate per tube, first 2.5 l eluate removed) in EtOH, to give the following frs: 1 (tubes 31–47, 25 mg); 2 (48–66, 126 mg); 3 (67–76, 62 mg); 4 (77–102, 305 mg); 5 (103–129, 143 mg); 6 (130–150, 48 mg); 7 (151–193, 43 mg).

Fr. 1 (25 mg) was methylated and the mixt. resolved by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (12:5:2:1, ×2). The resulting band (R_f 0.49, 2 mg) was acetylated to give didehydrofisetinidol-(2′,9:4α,10)-tetrahydropyrano[2,3-*f*]chromene (**48**) as an amorphous solid (3 mg). Found: $[M]^+$, 1084.3722. $C_{60}H_{60}O_{10}$ requires $[M]^+$, 1084.3728. ^1H NMR data (Table 4). CD $[\theta]_{300}$ -7.1×10^3, $[\theta]_{293.5}$ -8.9×10^3, $[\theta]_{286}$ 3.9×10^1, $[\theta]_{277.5}$ 1.2×10^4, $[\theta]_{263.5}$ −7.3, $[\theta]_{246.0}$ -2.1×10^4, $[\theta]_{233.0}$ 1.6×10^3.

Fr. 2 (126 mg) was methylated and sepd by prep. TLC in $CHCl_3$-hexane–Me_2CO–MeOH (30:14:5:1, ×2) to give three main bands 2-A (R_f 0.65, 4 mg), 2-B (R_f 0.51, 34 mg) and 2-C (R_f 0.41, 18 mg). Acetylation of fr. 2-A gave (2*R*,3*S*:6*R*,7*R*,8*S*)-3,7-diacetoxy-2,8-di-(3,4-dimethoxyphenyl)-6-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]chromene (**46**) as an amorphous solid (5 mg) [2]. Acetylation of the 2-B band followed by prep. TLC in $CHCl_3$–hexane–Me_2CO (11:20:1) afforded (2*R*,3*S*:6*R*,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-*trans*-7,8-*trans*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[3,2-*g*]chromene (**44**) as an amorphous solid (R_f 0.42, 18 mg). Found: $[M]^+$, 1100.4047. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^1H NMR data (Table 3). CD $[\theta]_{300}$ 7.8×10^2, $[\theta]_{282.5}$ -1.1×10^4, $[\theta]_{268.0}$ -5.9×10^1, $[\theta]_{248.5}$ 4.1×10^4, $[\theta]_{239.5}$ -1.2×10^3. Prep. TLC sepn of fr. 2-C in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2), afforded one band (R_f 0.35, 3 mg). Acetylation gave (2*R*,3*S*:6*R*,7*S*,8*S*)-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-dimetohoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*cis*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[3,2-*g*]chromene (**41**) as an amorphous solid (4 mg). Found: $[M]^+$, 1100.4051. $C_{61}H_{64}O_{19}$ requires $[M]^+$ 1100.4041. ^1H NMR data (Table 3). CD $[\theta]_{300}$ -2.8×10^2, $[\theta]_{284.5}$ -9.7×10^3, $[\theta]_{267.0}$ 2.4×10^3, $[\theta]_{246.0}$ 3.8×10^4.

Methylation of fr. 3 (62 mg), followed by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1) afforded one main band at R_f 0.40 (16 mg). Acetylation and further purification by prep. TLC in hexane–Me_2CO–EtOAc (11:6:3, ×2) gave 2 bands at R_f 0.38 (8 mg) and 0.31 (3 mg). The R_f 0.38 band was comprised of (2*R*,3*S*:6*R*,7*R*,8*S*)-3,7-diacetoxy-9-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*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]chromene (**38**) as an amorphous solid. Found: $[M]^+$, 1100.4045. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^1H NMR data (Table 3). CD $[\theta]_{300}$ 6.2×10^1, $[\theta]_{276.5}$ 1.4×10^4, $[\theta]_{260.5}$ 6.5×10^3, $[\theta]_{246.5}$ 8.1×10^4, $[\theta]_{233.0}$ 2.1×10^3. The R_f 0.31 band afforded (2*R*,3*S*:6*R*,7*R*,8*S*:10*R*,11*R*,12*S*)-3,7,11-triacetoxy-2,8,12-tris-(3,4-dimethoxyphenyl)-6,10-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-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 (**17**) as an amorphous solid. Found: $[M]^+$, 1100.4043. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041. ^1H NMR data (Table 1). CD $[\theta]_{300}$ 2.4×10^2, $[\theta]_{289.5}$ -8.7×10^1, $[\theta]_{282.5}$ -7.0×10^3, $[\theta]_{268.0}$ -1.2×10^3, $[\theta]_{260.5}$ 1.9×10^1, $[\theta]_{245.0}$ 3.9×10^3, $[\theta]_{239.0}$ 1.8×10^2.

Fr. 4 (305 mg) was methylated and resolved by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) to give 3 main bands, 4-A (R_f 0.55, 89 mg), 4-B (R_f 0.48, 40 mg) and 4-C (R_f 0.41, 15 mg). Acetylation

of 4-A followed by prep. TLC in hexane–Me_2CO–EtOAc (11:6:3, ×4) gave 2 bands at R_f 0.54 (40 mg) and R_f 0.52 (25 mg). Further prep. TLC purification of the R_f 0.54 fr. in hexane–Me_2CO–EtOAc (11:6:3, ×3) afforded (2*R*,3*S*:6*R*,7*R*,8*S*:10*R*,11*S*,12*R*)-3,7,11-triacetoxy-2,8,10-tris-(3,4-dimethoxyphenyl)-6,12-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-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 (**26**) as an amorphous solid (R_f 0.48, 29 mg). Found: C, 66.6; H, 5.9. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 2). CD $[\theta]_{291.5}$ 6.0×10^3, $[\theta]_{271.5}$ 8.3×10^2, $[\theta]_{251.0}$ 9.4×10^3, $[\theta]_{246.0}$ -5.4×10^2, $[\theta]_{242.0}$ -9.0×10^3. Similar purification of the R_f 0.52 fr. by prep. TLC in hexane–Me_2CO–EtOAc, (11:6:3, ×2) gave (2*R*,3*S*:6*R*,7*R*,8*S*:10*S*,11*S*,12*R*)-3,7,11-triacetoxy-2,8,10-tris-(3,4-dimethoxyphenyl)-6,12-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-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 (**14**) as an amorphous solid (R_f 0.43, 17 mg). Found: C, 66.7; H, 5.7. $C_{61}H_{64}O_{19}$ requires C, 66.54; H, 5.86%. ^{1}H NMR data (Table 1). CD $[\theta]_{300}$ 1.8×10^2, $[\theta]_{294.5}$ 3.6×10^2, $[\theta]_{285.0}$ -2.3×10^3, $[\theta]_{281.0}$ 2.1×10^2, $[\theta]_{272.0}$ 6.0×10^3, $[\theta]_{252.0}$ -7.7×10^1, $[\theta]_{247.0}$ -3.3×10^3, $[\theta]_{243.0}$ 2.6×10^1. Acetylation of fr. 4-B followed by prep. TLC in $CHCl_3$–hexane–Me_2CO (53:40:7, ×3) gave (2*R*,3*S*:6*S*,7*S*,8*R*: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-*cis*-7,8-*trans*-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 (R_f 0.53, 30 mg). Found: C, 66.6; H, 5.43. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 1). CD $[\theta]_{300}$ 2.0×10^2, $[\theta]_{296.5}$ 3.7×10^2, $[\theta]_{285.5}$ -4.6×10^3, $[\theta]_{281.5}$ 1.3×10^2, $[\theta]_{272.0}$ 1.1×10^4, $[\theta]_{256.5}$ 3.4×10^3, $[\theta]_{249.0}$ -3.9×10^2, $[\theta]_{245.5}$ -9.5×10^3, $[\theta]_{240.0}$ -1.8×10^2. Band 4-C was similarly acetylated and purified by prep. TLC in $CHCl_3$–hexane–Me_2CO (5:4:1, ×3) to give (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-*cis*-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 (**35**) as an amorphous solid (R_f 0.58, 7 mg). Found: $[M]^+$, 1100.4039. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 4). CD $[\theta]_{300}$ -3.3×10^2, $[\theta]_{287.5}$ -1.3×10^4, $[\theta]_{272.0}$ 9.3×10^3, $[\theta]_{259.5}$ 4.2×10^3, $[\theta]_{246.0}$ 4.6×10^4, $[\theta]_{238.0}$ 1.4×10^2.

Fr. 5 (143 mg) was methylated and resolved by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) to give 3 main bands, 5-A (R_f 0.40, 23 mg), 5-B (R_f 0.25, 18 mg) and 5-C (R_f 0.19, 15 mg). Fr. 5-A was purified by prep. TLC in hexane–toluene–Me_2CO–MeOH (4:12:3:1, ×2), and the resulting band (R_f 0.25, 10 mg) was acethylated to give (2*R*,3*S*:6*S*,7*R*,8*S*:10*R*,11*S*,12*R*)-3,7,11-triacetoxy-2,8,10-tris-(3,4-dimethoxyphenyl)-6,12-di-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*trans*-7,8-*trans*-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 (**29**) as an amorphous solid (8 mg). Found: $[M]^+$, 1100.4053. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 3.4×10^3, $[\theta]_{288.0}$ 1.1×10^4, $[\theta]_{280.5}$ 1.4×10^4, $[\theta]_{260.5}$ 5.4×10^3, $[\theta]_{252.0}$ 9.3×10^3, $[\theta]_{248.0}$ -9.1×10^2, $[\theta]_{244.5}$ -1.3×10^4, $[\theta]_{236.0}$ 2.1×10^2. Acetylation of fr. 5-B afforded (2*R*,3*S*:6*R*,7*S*,8*R*: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-*trans*-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 (**8**) as an amorphous solid (20 mg). Found: C, 66.6; H, 5.7. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 8.2×10^2, $[\theta]_{294.0}$ 2.3×10^3, $[\theta]_{290.0}$ 1.6×10^2, $[\theta]_{287.0}$ -1.8×10^3, $[\theta]_{284.5}$ -1.0×10^2, $[\theta_{272.5}$ 1.3×10^4, $[\theta]_{260.0}$ 5.8×10^3, $[\theta]_{252.0}$ 9.1×10^3, $[\theta]_{247.5}$ -9.3×10^2, $[\theta]_{244.0}$ -1.5×10^4, $[\theta]_{243.0}$ -1.7×10^4. Similar acetylation of fr. 5-C gave (2*R*,3*S*:6*S*,7*S*,8*R*: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-*cis*-7,8-trans-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 (**5**) as an amorphous solid (16 mg). Found: C, 66.7; H, 6.0. $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 1). CD $[\theta]_{300.0}$ 1.8×10^2, $[\theta]_{291.0}$ -4.9×10^2, $[\theta]_{286.5}$ -1.8×10^3, $[\theta]_{284.5}$ -3.2×10^2, $[\theta]_{272.5}$ 2.3×10^4, $[\theta]_{249.0}$ 6.7×10^1, $[\theta]_{245.0}$ -1.0×10^4, $[\theta]_{243.0}$ -7.6×10^3, $[\theta]_{238.0}$ 1.9×10^2.

Methylation of fr. 6 (48 mg) and subsequent sepn by prep. TLC in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) gave 2 main bands at R_f 0.42 (8 mg) and 0.28 (18 mg). Acetylation of the R_f 0.42 band followed by prep. TLC in $CHCl_3$–hexane–Me_2CO (11:8:1, ×2) gave (2*R*,3*S*:6*S*,7*S*,8*R*)-3,7-diacetoxy-9-methoxy-10-[(2*R*,3*S*,4*R*)-2,3-*trans*-3,4-*cis*-3-acetoxy-3′,4′,7-trimethoxyflavan-4-yl]-2,6-di-(3,4-dimethoxyphenyl)-8-(2,4-dimethoxyphenyl)-2,3-*trans*-6,7-*cis*-7,8-*trans*-3,4,7,8-tetrahydro-2*H*,6*H*-pyrano[2,3-*f*]chromene (**32**) as an amorphous solid (R_f 0.54, 3 mg). Found: $[M]^+$, 1100.4054. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^{1}H NMR data (Table 4). CD $[\theta]_{300.0}$ -4.1×10^1, $[\theta]_{277.0}$ 7.6×10^3, $[\theta]_{259.5}$ 3.3×10^3, $[\theta]_{247.5}$ 1.5×10^4, $[\theta]_{240.0}$ 1.9×10^3. Acetylation of the R_f 0.28 band afforded (2*R*,3*S*:6*S*,7*S*,8*R*: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-*trans*-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 (**20**) as an amorphous solid (18 mg). Found: C, 66.7; H, 6.04, $C_{61}H_{64}O_{19}$ requires C, 66.5; H, 5.86%. ^{1}H NMR data (Table 2). CD $[\theta]_{300.0}$ 1.8×10^3, $[\theta]_{291.5}$ 6.3×10^3, $[\theta]_{286.5}$ 4.7×10^3, $[\theta]_{277.0}$ 1.2×10^4, $[\theta]_{256.0}$ 4.0×10^3, $[\theta]_{246.0}$ -2.7×10^4, $[\theta]_{236.5}$ -3.2×10^2.

Methylation of fr. 7 (43 mg) and subsequent prep. TLC sepn in $CHCl_3$–hexane–Me_2CO–MeOH (30:14:5:1, ×2) gave one main band at R_f 0.39

(11 mg). Acetylation followed by prep. TLC in $CHCl_3$–hexane–Me_2CO (11:8:1, ×3) afforded (2*R*,3*S*:6*R*,7*S*,8*R*: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 - *trans* - 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 (**23**) as an amorphous solid (R_f 0.35, 6 mg). Found: $[M]^+$, 1100.4043. $C_{61}H_{64}O_{19}$ requires $[M]^+$, 1100.4041). ^1H NMR data (Table 2). CD $[\theta]_{300.0}$ 2.9×10^3, $[\theta]_{292.0}$ 9.4×10^3, $[\theta]_{281.5}$ 4.6×10^3, $[\theta]_{266.0}$ -3.4×10^2, $[\theta]_{253.0}$ 9.3×10^3, $[\theta]_{244.0}$ -4.2×10^4, $[\theta]_{233.5}$ 5.2×10^2.

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