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SYNTHESIS AND CHARACTERIZATION OF PROCYANIDIN DIMERS AS THEIR PERACETATES AND OCTAMETHYL ETHER DIACETATES*

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Key Word Index—Biomimetic synthesis; procyanidins B_1–B_8; 3,4-*cis*-biflavanoid; all-[4,8]-bi-[(−)-epicatechin]-(+)-catechin; ^{1}H NMR parameters.

Abstract—Condensation of (2*R*,3*S*,4*R* or *S*)-leucocyanidin or the 5,7,3′,4′-tetramethyl ether of (2*R*,3*R*,4*S*)-leucocyanidin with flavan-3-ols yielded dimeric flavanoids which were converted to their octamethyl ether diacetates, or the deca-acetates for the 2,3-*trans*-procyanidin series. Comparison is made of the ^{1}H NMR spectra of the deca-acetate and octamethyl ether diacetate derivatives which lead to useful diagnostic shift parameters characteristic of their structures. Condensations afforded a novel biflavanoid with a 3,4-*cis*-configuration and a triflavanoid of 'mixed' stereochemistry.

INTRODUCTION

Biomimetic synthesis of procyanidins initiated by Haslam *et al.* [1, 2] was exclusively based on an indirect method represented by the reaction of 4-benzylthioflavan-3-ols and polymeric procyanidins, respectively, as source of the appropriate carbocation with flavan-3-ols. The direct biomimetic approach to condensed tannin synthesis, however, based on the premise [3] that flavan-3,4-diols as potential electrophiles, and flavan-3-ols as nucleophiles jointly initiate the prime step in condensed tannin formation which leads by further repetitive condensation to the higher oligomers was established by Roux *et al.* [4, 5]. The present work provides an expansion of the synthetic approach to procyanidins in close analogy to the recent concepts of tannin biogenesis via flavan-3,4-diols [6, 7]. The condensations were aimed at studying the stereochemical course of the reaction and also its regioselectivity on a basis similar to that adopted by Delcour *et al.* [8], but with emphasis on comparison of diagnostic shift parameters for methyl ether acetates and full acetates, and hence on the relative advantage attached to the use of either.

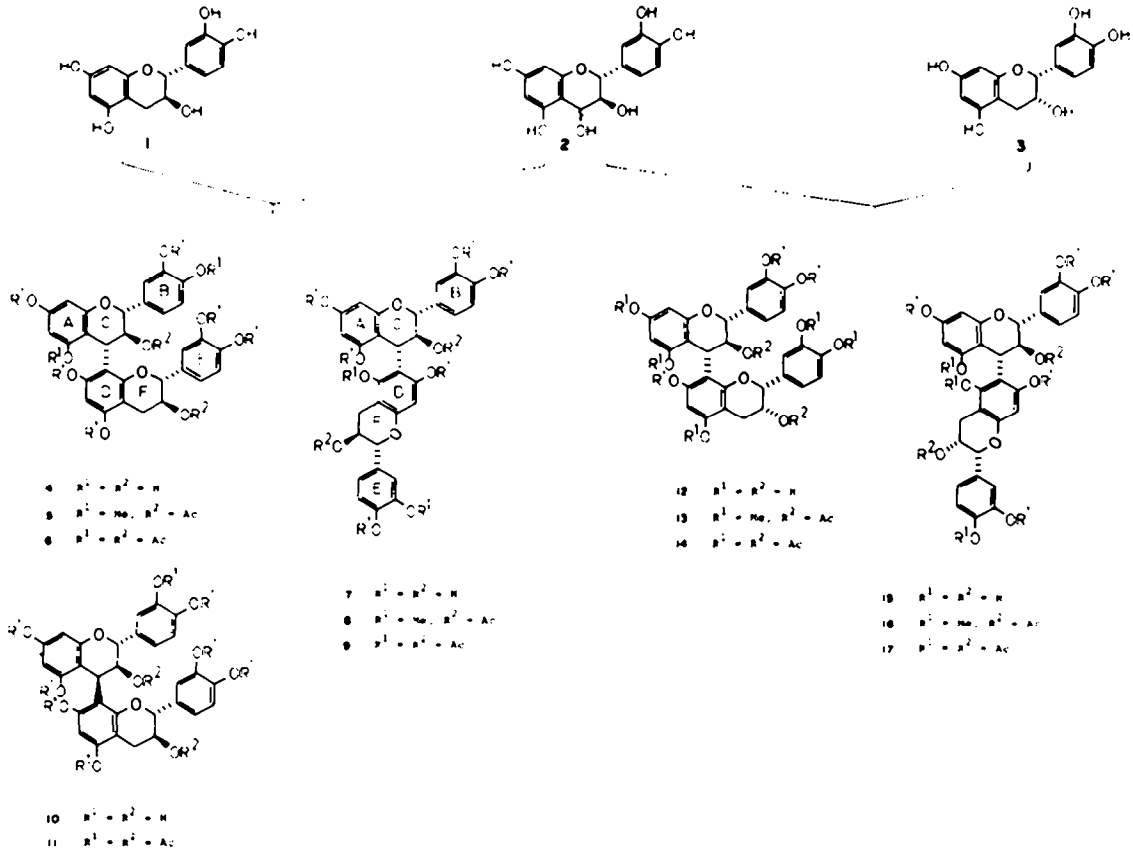
RESULTS AND DISCUSSION

Biomimetic condensations leading to biflavanoids in support of the biogenetic hypothesis involving flavan-3-ols and the 4-carbenium ion derived from flavan-3,4-diols have been demonstrated for proanthocyanidins [8–10]. Pharmacological tests requiring procyanidins in the free phenolic form prompted repetition of controlled biomimetic synthesis resulting in the range of the all-2,3-*trans*-configurated products **4**, **7** and the all-*trans*-[4,8]-linked tri- and tetraflavanoid analogues (cf. Scheme 1) as previously reported [8]. The same reaction of direct condensation of (2*R*,3*S*,4*R* or *S*)-leucocyanidin (**2**) with (+)-catechin (**1**) performed with an excess of the flavan-3,4-diol (**2**) (3:1 ratio) and under more acidic conditions (0.1 M HCl) led to the generation of a mixture of bi- and triflavanoids and higher components in the proportion of 1:1:18. The production of predominantly oligomers when compared with the above coupling (1:1:3) indicates that direct synthesis of procyanidins may be approached stoichiometrically. This is in line with the stoichiometric control applied during the synthesis of profisetinidins leading selectively to bi- and triflavanoids [11]. The formation of oligomeric procyanidins in higher proportions relative to the synthesis of analogous profisetinidins under similar conditions may be attributed to enhanced nucleophilicity of the products. An introduced second (+)-catechin unit possesses stronger nucleophilic centres and, taken in conjunction with the high reactivity of leucocyanidins, this should cause rapid condensation resulting in oligomeric products but to a limited extent controlled by the selected concentration of the flavan-3,4-diol.

Acetylation and subsequent prep. TLC separation of the biflavanoid fraction afforded the novel product (**11**) which was identified by spectroscopic techniques as the first representative of a 3,4-*cis*-procyanidin unit [12]. The formation of products with both 3,4-*trans*- and 3,4-*cis*-stereochemistry is in line with studies on reduction products of (+)-taxifolin [13] and the recent report on procyanidins possessing units of 'mixed' stereochemistry [14]. However, the significant (12%) yield of **10** under the experimental conditions supports the view that 3,4-*cis*-configurated oligomers may exist in nature.

In a modified procedure coupling of the flavan-3,4-diol (**2**) with (−)-epicatechin (**3**) again followed the expected course of regioselective and stereospecific condensation to form the predominant [4,8]-2,3-*trans*-3,4-*trans*:2,3-*cis*-(+)-catechin-(−)-epicatechin biflavanoid (**12**, procyanidin B_4) and the [4,6]-analogue (**15**, procyanidin B_8) (cf. Scheme 1). Approach by the nucleophilic (−)-epicatechin is presumably favoured from the less hindered 'lower' side of the 2,3-*trans*-4-carbenium ion. The yields of

*Dedicated to Prof. D. G. Roux, Bloemfontein, on the occasion of his 65th birthday.



Scheme 1. Condensation of the 2,3-*trans*-flavan-3,4-diol (**2**) with (+)-catechin (**1**) and (−)-epicatechin (**3**).

biflavanoids **12** and **15** (45 and 10%, respectively) reflect the lower steric hindrance at the 8-position relative to that at C-6.

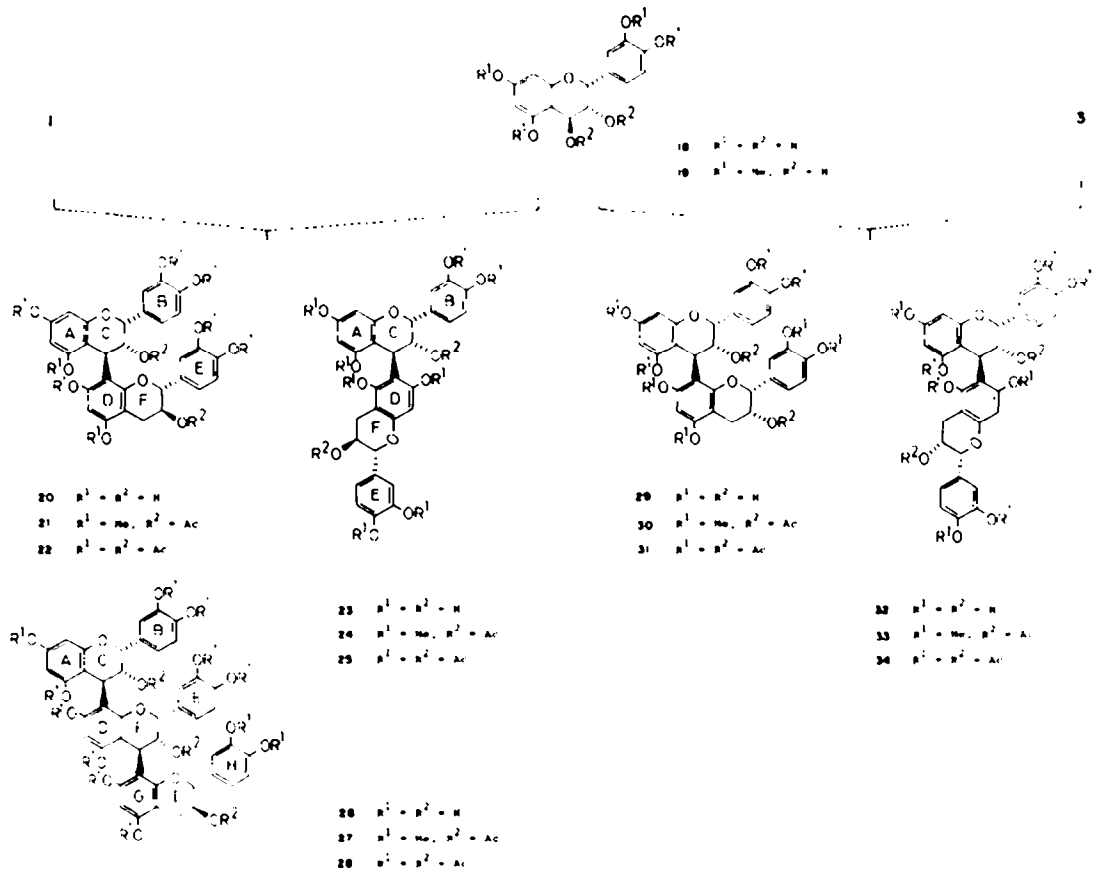
The regioselectivity in these condensations of [4,8]- and [4,6]-procyanidins (*ca* 5:1) may be due to the relative stability of the 4-carbenium ion derived from (2*R*,3*S*,4*R* or *S*)-leucocyanidin and hence its reactivity in favour of the sterically less hindered 8-position on (+)-catechin [9].

In a previous paper [9] direct access to methyl ether acetates of procyanidins B_2 and B_5 has been described. The remaining coupling of the synthetic flavan-3,4-diol tetramethyl ether (**19**) with (+)-catechin in a 1:1 molar ratio again followed the expected course of condensation to give the desired [4,8]- and [4,6]-biflavanoid octamethyl ether diacetates **21** and **24** (procyanidins B_1 and B_7, respectively) in significant yields (*ca* 15%) after methylation and subsequent acetylation (cf. Scheme 2). Similarly, lack of regioselectivity in this condensation correlated with observations for the synthesis of B_2 and B_5, thus confirming the hypothesis of the 'selectivity-reactivity relationship' [9].

The same condensation of the flavan-3,4-diol (**19**) with (+)-catechin revealed evidence of a novel triflavanoid with procyanidin units of 'mixed' stereochemistry. Analysis of the ^{1}H NMR spectrum of the dodecamethyl ether triacetate of **26** exhibited *meta*-coupled doublets (δ5.84 and 5.94) uniquely shifted upfield indicating [4,8:4,8]-interflavanoid linkages (cf. Table 3) [9]. Chemical shifts of the two high-field aromatic singlets (δ6.05 and 6.11, I- and G-rings) independently confirmed successive [4,8]-couplings of both 'upper' units [9, 15]. The relative 2,3-*cis*-3,4-*trans* stereochemistry of the biflavanoid procyanidin substituent on (+)-catechin was evident from coupling constants ($J_{2,3}$ = 1.5, 1.5, $J_{3,4}$ = 2.0, 2.2 Hz, respectively, for the C- and F-rings) in close agreement with those observed for B_2 [9]. Assignments of resonances to the three heterocyclic ring systems were possible by means of extensive spin-tickling experiments.

The sequence of the constituent units of the triflavanoid **26** followed from decoupling experiments of the methylene protons and their large coupling constants thus defining (+)-catechin as the 'terminal' unit. Another significant feature which correlated with the proposed sequencing was the chemical shift of 2-H and 3-H of the 'lower' (+)-catechin unit (I-ring) (δ5.06 and 5.25, respectively) which fell in line with those of the 'terminal' (+)-catechin moiety of the methyl ether acetate of procyanidin C_2 [8]. Furthermore, the resultant chemical shift difference ($\Delta\delta_{2\text{-H},3\text{-H}}$ 0.19, I-ring) consistent with similar effects for both the corresponding derivatives of B_3 and C_2 signified substitution in the 8-position. Similarly, the chemical shifts of 2-H and 3-H resonances of the 'upper' (−)-epicatechin unit (δ5.56 and 5.31, respectively) correlated with those similarly placed in the corresponding derivatives of both the dimer B_2 and the trimer C_1 [9]. The proposed stereochemical assignments of **26** were confirmed by circular dichroism as evident from positive Cotton effects at 222 and 231 nm [16–18].

The natural co-occurrence of the three procyanidins, i.e. the biflavanoids **20** and **23**, and the triflavanoid **26** was demonstrated by their isolation from *Pinus maritima* and by the identity of the ^{1}H NMR and CD spectra of their



Scheme 2. Condensation of the 2,3-*cis*-flavan-3,4-diol methyl ether (19) with (+)-catechin (1) and (−)-epicatechin (3).

methyl ether acetates with those of their synthetic counterparts.* Other analogies to be found in nature may be derived from phytochemical studies on natural tannin extracts of *Crataegus oxyacantha* [9], *Salix* and *Betula* species [unpublished] following the biomimetic course as illustrated in Schemes 1 and 2.

In general, structural and stereochemical differentiation of procyanidin biflavanoids was provided by chemical shifts in combination with characteristic splitting-pattern of resonances in the 'fingerprint' heterocyclic and aromatic region coupled with various chemical shift differences between the aromatic protons 6-H and 8-H (A- and D-rings), together with significant shifts of the heterocyclic protons 2-H and 3-H (C- and F-rings) [8, 9, 15, 19]. Coupling constants of the heterocyclic systems indicated the presence of 2,3-*trans* ($J_{2,3}$ = 8–10 Hz) and 2,3-*cis* ($J_{2,3}$ = 0–2 Hz) configurated flavan-3-ol units, while allocations of resonances were established by extensive spin-tickling experiments. Circular dichroism confirmed the absolute configuration (C-ring) at the point of bonding as concluded from diagnostic positive and negative Cotton effects in the low-wavelength region [4, 5, 16] (cf. Table 5). Similarly proof of absolute configuration was provided by synthesis from precursors of known absolute configuration.

The natural free-phenolic procyanidins B_1–B_8 were previously characterized by Haslam *et al.* [17] on the basis of degradative and synthetic studies coupled with spectroscopic evidence. However, complete NMR assignments were limited by the complexity of spectra of both the free phenolic forms and their acetate derivatives at ambient temperatures due to rotational isomerism [17, 18, 21]. ^{1}H NMR spectra of the acetates and methyl ethers of procyanidins were accordingly recorded at increased temperatures [2]. Methyl ether acetates have proved to be useful derivatives for ^{1}H NMR analysis at elevated temperatures (100°, $CDCl_3$) [8, 9]. Under these conditions the effects of dynamic rotational isomerism, evident from ^{1}H NMR analysis at ambient temperatures, were overcome, thus enabling spectral interpretations.

The availability of procyanidins B_1–B_8 as both methyl ether acetates and full acetates enables direct comparison of ^{1}H NMR data in order to establish those parameters which may prove useful in the analysis of oligomeric procyanidins (cf. Tables 1–4). Their significance is therefore briefly discussed.

Direct comparison of ^{1}H NMR data of both derivatives demonstrates that spectrometric parameters in terms of bonding positions, relative 3,4-stereochemistry and accordingly of absolute configurations are unequivocally established for methyl ether acetates, while lack of suitable parameters and the necessity of selecting shifts representative of major rotamers characterize the problem of ^{1}H NMR spectrometry of procyanidin acetates. This

*These results are in agreement with similar observations reported on the procyanidin composition of *Pinus taeda* [19, 20].

Table 1. Chemical shifts of procyanidin aliphatic 3-OAc functions (C- and F-rings) of methyl ether acetates in $CDCl_3$ (100°) relative to TMS

Procyanidins	C-ring δ	F-ring δ	Δδ
B_1 (21)	1.74	1.84	0.07
B_7 (24)	1.80	1.91	
B_2 (30)	1.72	1.86	0.05
B_5 (33)	1.78	1.91	
B_3 (5)	1.61	1.88	0.03
B_6 (8)	1.67	1.91	
B_4 (13)	1.68	1.80	0.08
B_8 (16)	1.66	1.88	
(+)-Catechin (1)		1.88	
(−)-Epicatechin (3)		1.91	

Table 2. Chemical shifts of procyanidin 2-H (F-ring) of methyl ether acetate and acetate derivatives in $CDCl_3$ relative to TMS

Procyanidins	Methyl ether acetates ($CDCl_3$, 100°) δ	Δδ		Peracetates ($CDCl_3$, 30°) δ	Δδ
B_1 21	4.50	0.53	22	4.37	0.98
B_7 24	5.03		25	5.35*	
B_2 30	4.60	0.51	31	4.54	0.61
B_5 33	5.11		34	5.15*	
B_3 5	4.92	0.05	6	4.94	0.10
B_6 8	4.97		9	5.04	
B_4 13	4.98	0.07	14	5.01	0.13
B_8 16	5.05		17	5.14	

*Tentative assignment due to overlapping of resonances.

difference is due to the higher activation energy for rotation about the interflavanoid bonds required by the acetates.

Thus, assessment of bonding positions is most reliably derived from absolute chemical shifts of remaining D-ring protons of 'dimeric' methyl ether acetates under specific experimental conditions ($CDCl_3$, 100°). The chemical shifts ($\Delta\delta_{6\text{-H},8\text{-H}}$ 0.13–0.20) are in line with those previously established for analogues bearing 6- and 8-substituents of flavan-3-ols [9, 15] and resorcinol-type condensed tannins [5, 22]. By contrast the margin of shift differences ($\Delta\delta_{6\text{-H},8\text{-H}}$ 0.01–0.12) of residual D-ring protons appears to be relatively small for dimeric acetates and their overlap in some instances implies that this parameter is less suitable for differentiating between the full acetates of [4,8]- and [4,6]-bonded 'dimeric' procyanidins (cf. Table 3).

Chemical shift differences [$\Delta\delta_{2\text{-H},3\text{-H}}$ (F-ring)] of (+)-catechin constituents have also proved of diagnostic value as to structure and stereochemistry of profisetinidins [11], and in distinguishing between [4,6]- and [4,8]-procyanidin biflavanoids [8]. However, this parameter is less suitable in procyanidins with substituent monomeric units of 2,3-*cis* configuration (Δδ 0.68, 0.46, 0.42 and 0.42 for **30**, **13**, **33** and **16**, respectively) (cf. Table 4). Another significant feature of all [4,6]-procyanidins is the somewhat less shielded 2-H (F-ring) [δ 4.97–5.11 (methyl ether acetates) and 5.04–5.35 (acetates)] relative to the same proton of their [4,8]-isomers [δ 4.50–4.98 (methyl ether acetates) and 4.37–5.01 (acetates)] (cf. Table 2).

The potential stereochemical and structural significance is the consistent but small deshielding of the 3-OAc (F-ring) resonance of all [4,6]-isomers (δ 1.66–1.80) relative to those of the [4,8]-procyanidins (δ 1.61–1.74), reflecting comparative freedom from shielding effects (cf. Table 1).

Although conversion of condensed tannins into methyl ether acetates requires successive chromatographic purification at each step resulting in substantial losses of

Table 3. Chemical shifts of A- and D-ring protons of methyl ether acetate and acetate derivatives of procyanidins in $CDCl_3$ relative to TMS (δ-values)

[4,8]-Procyanidins	6-H and 8-H (A-ring)	6-H (D-ring)	[4,6]-Procyanidins (counterparts)	6-H and 8-H (A-ring)	8-H (D-ring)	Rotamer	
Acetates ($CDCl_3$, 30°)							
B_1 (22)	6.00 6.31	6.67	B_7 (25)	6.62 6.74	6.76	6.66 6.77	6.64
B_2 (31)	6.00 6.25	6.65	B_5 (34)	6.60 6.73	6.61	6.47 6.61	6.79
B_3 (6)	6.48 6.50	6.62	B_6 (9)	6.64 6.64	6.63	6.46 6.49	6.60
B_4 (14)	6.52 6.58	6.63	B_8 (17)	6.71 6.72	6.75	6.49 6.50	6.75
Methyl ether acetates ($CDCl_3$, 100°)							
B_1 (21)	5.82 5.92	6.14	B_7 (24)	6.02 6.25	6.33		
B_2 (30)	5.83 5.94	6.20	B_5 (33)	6.06 6.30	6.38		
B_3 (5)	6.05 6.05	6.16	B_6 (8)	6.06 6.23	6.29		
B_4 (13)	6.06 6.16	6.12	B_8 (16)	6.06 6.23	6.32		

Table 4. Chemical shifts and coupling constants of heterocyclic protons (C- and F-rings) of methyl ether acetate and acetate derivatives of procyanidins B_1–B_8 in $CDCl_3$ relative to TMS

Acetates ($CDCl_3$, 30°)										
Ring C	**22**	**31**	**6**	**14**	**34**•	**9**		**25**•	**17**	
							rotamer			rotamer
2-H	5.45 *s*	5.57 *s*	4.76 *d*, J = 9.6	4.82 *d*, J = 9.6		4.78 *d*, J = 10.0	4,80 *d*, J = 10.0		4.88 *d*, J = 10.0	4.88 *d*, J = 10.0
3-H	5.15 *s*	5.16 *m*	5.62 *t*, ΣJ = 19.2	5.72 *t*, ΣJ = 19.2	5.15–5.43	5.68 *m*	5.68 *m*	5.14–5.40	5.72 *t*, ΣJ = 19.0	5.82 *t* ΣJ = 19.0
4-H	4.41 *d*, J = 1.5†	4.46 *d* J = 1.6	4.48 *d*, J = 9.6	4.53 *d*, J = 9.6		4.34 *d*, J = 9.0	4.44 *d*, J = 9.0		4.52 *d*, J = 9.0	4.45 *d*, J = 9.0
Ring F										
2-H	4.37 *d* J = 10.0	4.54 *s*	4.94 *d*, J = 8.0	5.01 *s*		4.86 *d*, J = 9.0	5.04 *d*, J = 9.0		5.14 *s*	5.20 *s*
3-H	5.05 *m*	5.06 *m*	5.12 *m*	5.22 *m*		5.06 *m*	5.06 *m*		5.34 *m*	5.40 *m*
Methyl ether acetates ($CDCl_3$, 100°)										
Ring C	**21**	**30**	**5**	**13**	**33**	**8**		**24**	**16**	
2-H	5.36 *s*	5.54 *s*	4.66 *d*, J = 10.0	4.73 *d*, J = 10.0	5.47 *s*	4.80 *d*, J = 9.9		5.44 *s*	4.72 *s*, J = 10.0	
3-H	5.28 *t* J = 1.5 and 2.0	5.34 *t* J = 1.7 and 2.2	5.84 *dd*, ΣJ = 18.8	5.89 *dd*, ΣJ = 19.5	5.31 *t* J = 1.5 and 2.2	5.77 *dd*, ΣJ = 18.6		5.28 *m*	5.77 *dd*, ΣJ = 18.8	
4-H	4.58 *d* J = 2.0	4.68 *d* J = 2.2	4.80 *d*, J = 8.75	4.86 *d*, J = 9.5	4.59 *d* J = 2.2	4.73 *d*, J = 8.7		4.61 *d* J = 2.2	4.70 *d*, J = 9.0	
Ring F										
2-H	4.50 *d* J = 8.25	4.60 *s*	4.92 *d*, J = 7.25	4.98 *s*	5.11 *br d*	4.97 *d*, J = 7.0		5.03 *d* J = 6.5	5.05 *s*	
3-H	5.15 *m*	5.28 *m*	5.11 *m*, ΣJ = 20.5	5.44 *m*	5.53 *m*	5.33 *m*, ΣJ = 19.5		5.30 *m*	5.47 *m*	

•Signals overlapped.
†Coupling constants in Hz.

Table 5. CD data of methyl ether acetate and acetate derivatives of procyanidins in MeOH (λ, nm)

	[θ]	λ	[θ]	λ	[θ]	λ	[θ]	λ	[θ]	λ	Sign*
Acetates											
B_1 (22)			+1850	265	+29570	228	+97030	222	0	210	+
B_2 (31)	−2310	282	−2540	272	+12700	235	+66100	211	+21710	201	+
B_3 (6)	−14850	278	−3090	252	−22270	234	−193400	208	−131510	200	−
B_4 (14)	−13490	267	−5900	245	−13490	230	−121380	214	−25290	200	−
B_5 (34)	+3560	277	+1780	258	+83760	233	0	212			+
B_6 (9)	−16630	269	−5820	245	−30770	228	−48240	215	−24950	208	−
B_7 (25)	+3900	265			+92000	228			0	204	+
B_8 (17)	−12100	278	0	248	−13000	235	−8470	230	−33260	210	−
Methyl ether acetates											
B_1 (21)	−635	268			+34260	236	+22200	222	+50750	217	+
B_2 (30)	−3280	268			+31160	237	+48860	218	0	203	+
B_3 (5)	−2780	280			−83520	236	−118320	216	−16700	205	−
B_4 (13)	−2320	280	+774	265	−89000	230			−11610	200	−
B_5 (33)	+1700	280	+8490	250	+57710	237	+37340	223	+73840	215	+
B_6 (8)	−4520	278			−35470	228	−24190	220	−51600	215	−
B_7 (24)	−1600	284			+87960	236	+41580	222	0	210	+
B_8 (16)	−3100	280			−43340	232	−34830	225	−48000	218	−

*Cotton effect between 200 and 230 nm indicating the position of the 4-flavanyl substituent relative to the plane of ring A, i.e. below (−) and above (+).

material due to side-reactions these derivatives permit simple structural and stereochemical conclusions under the conditions employed. Additionally the stereochemical purity of compounds under investigation is unequivocally demonstrated by the number of resonances due to aliphatic acetoxy functions from high temperature spectra.

The comparative ^{1}H NMR data now described should prove helpful in unambiguous structure elucidation of natural procyanidins. The identification of the triflavanoid **26** based on a combination of parameters discussed above represents an example.

EXPERIMENTAL

^{1}H NMR spectra recorded in $CDCl_3$ with TMS as int. standard. NMR tubes were firmly stoppered for recording at temps (100°) above the bp of $CDCl_3$. CD data were obtained in MeOH. Methylations were performed with an excess of CH_2N_2 over 48 hr at −15°, while acetylations were in Ac_2O–pyridine at room temp. Prep. plates (Kieselgel PF_{254}, 0.5 mm) were used for separation of derivatives in C_6H_6–Me_2CO (4:1).

General condensations and work-up procedures. Biomimetic synthesis of procyanidins B_1–B_8 were performed by the condensation of a flavan-3,4-diol with flavan-3-ol in a 1:1 molar ratio under acidic conditions (0.1 M HCl). Based on the preparation of flavan-3,4-diols of different 2,3-stereochemistry the coupling reactions may be grouped as follows:

(i) *Reaction of 2,3-trans-flavan-3,4-diol with flavan-3-ols.* Mutual couplings of 2,3-*trans*-flavan-3,4-diol (**2**) obtained by the reduction of (+)-taxifolin [8] with (+)-catechin and (−)-epicatechin gave the isomeric pairs B_3/B_6 and B_4/B_8, respectively (cf. Scheme 1).

(ii) *Reaction of 2,3-cis-flavan-3,4-diol with flavan-3-ols.* Alternative couplings of 2,3-*cis*-flavan-3,4-diol (**19**) prepared from tetramethyl ether (−)-epicatechin according to the procedure of ref. [23] with either (+)-catechin or (−)-epicatechin yielded the isomeric pairs B_1/B_7 and B_2/B_5, respectively (cf. Scheme 2).

The reaction mixture was stirred under N_2 at room temp. and then extracted with EtOAc. After evapn of solvent the product was separated on Sephadex LH-20 using EtOH as eluant. The free-phenolic procyanidins were converted into their respective Me ether acetates with prep. TLC purification at each step and their full acetates followed by prep. TLC separation. For ^{1}H NMR and CD data see Tables 1–5. Similar values for full acetates of procyanidins are reported in parts [2, 16, 17, 19, 24, 25].

All-[4,8]-*bi*-[(−)-*epicatechin*]-(+)-*catechin* (**26**). Methylation of appropriate fractions obtained by chromatography on Sephadex LH-20 and subsequent acetylation yielded the dodecamethyl ether triacetate (**27**), exhibiting the following spectral properties. ^{1}H NMR ($CDCl_3$, 100°): δ 1.66 [*s*, 3-OAc (C or F)], 1.71 [*s*, 3-OAc (F or C)], 1.90 [*s*, 3-OAc (I)], 2.94 [*m*, 2 × H (I)], 3.41–3.84 (*m*, 12OMe), 4.66 [*br s*, 4-H (F)], 4.78 [*d*, *J* = 2.0 Hz, 4-H (C)], 5.06 [*d*, *J* = 6.0 Hz, 2-H (I)], 5.09 [*br s*, 2-H (F)], 5.15 [*t*, *J* = 1.5 and 2.2 Hz, 3-H (F)], 5.25 [*m*, 3-H (I)], 5.31 [*t*, *J* = 1.5 and 2.0 Hz, 3-H (C)], 5.56 [*br s*, 2-H (C)], 5.84 [*d*, *J* = 2.0 Hz, 6-H (A)], 5.94 [*d*, *J* = 2.0 Hz, 8-H (A)], 6.05 [*s*, 6-H (D or G)], 6.11 [*s*, 6-H (G or D)], 6.59–7.00 [*m*, 9 × H (B, E and H)]. CD $[\theta]_{290}$ 0, $[\theta]_{277}$ −3295, $[\theta]_{256}$ 0, $[\theta]_{231}$ +101 060, $[\theta]_{225}$ +83 480, $[\theta]_{222}$ +107 650, $[\theta]_{206}$ 0.

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REFERENCES

1. Haslam, E. (1974) *J. Chem. Soc. Chem. Commun.* 594.
2. Fletcher, A. C., Porter, L. J., Haslam, E. and Gupta, R. K. (1977) *J. Chem. Soc. Perkin Trans.* 1, 1628.
3. Creasy, L. L. and Swain, T. (1965) *Nature* **208**, 151.

4. Botha, J. J., Ferreira, D. and Roux, D. G. (1978) *J. Chem. Soc. Chem. Commun.* 698.
5. Botha, J. J., Young, D. A., Ferreira, D. and Roux, D. G. (1981) *J. Chem. Soc. Perkin Trans.* 1, 1213.
6. Stafford, H. A. (1983) *Phytochemistry* **22**, 2643.
7. Kristiansen, K. N. (1984) *Carlsberg Res. Commun.* **49**, 503.
8. Delcour, J. A., Ferreira, D. and Roux, D. G. (1983) *J. Chem. Soc. Perkin Trans.* 1, 1711.
9. Kolodziej, H., Ferreira, D. and Roux, D. G. (1984) *J. Chem. Soc. Perkin Trans.* 1, 343.
10. Fonknechten, G., Moll, M., Cagniant, D., Kirsch, G. and Muller, J. F. (1983) *J. Inst. Brewing* **89**, 424.
11. Viviers, P. M., Kolodziej, H., Young, D. A., Ferreira, D. and Roux, D. G. (1983) *J. Chem. Soc. Perkin Trans.* 1, 2555.
12. Kolodziej, H. (1985) *Phytochemistry* **24**, 2460.
13. Porter, L. J. and Foo, L. Y. (1982) *Phytochemistry* **21**, 2947.
14. Delcour, D. A., Serneels, E. J., Ferreira, D. and Roux, D. G. (1985) *J. Chem. Soc. Perkin Trans.* 1, 669.
15. Hundt, H. K. L. and Roux, D. G. (1978) *J. Chem. Soc. Chem. Commun.* 696.
16. Barrett, M. W., Klyne, W., Scopes, P. M., Fletcher, A. C., Porter, L. J. and Haslam, E. (1979) *J. Chem. Soc. Perkin Trans.* 1, 2375.
17. Thompson, R. S., Jacques, D., Haslam, E. and Tanner, R. J. N. (1972) *J. Chem. Soc. Perkin Trans.* 1, 1387.
18. Du Preez, I. C., Rowan, A. C., Roux, D. G. and Feeney, J. (1971) *J. Chem. Soc. Chem. Commun.* 315.
19. Hemingway, R. W., Foo, L. Y. and Porter, L. J. (1982) *J. Chem. Soc. Perkin Trans.* 1, 1209.
20. Hemingway, R. W., Karchesy, J. J., McGraw, G. W. and Wielesek, R. A. (1983) *Phytochemistry* **22**, 275.
21. Weinges, K., Marx, H.-D. and Göritz, K. (1970) *Chem. Ber.* **103**, 2336.
22. Botha, J. J., Ferreira, D. and Roux, D. G. (1981) *J. Chem. Soc. Perkin Trans.* 1, 1235.
23. Betts, M. J., Brown, B. R. and Shaw, M. R. (1969) *J. Chem. Soc. C* 1178.
24. Weinges, K., Göritz, K. and Nader, F. (1968) *Liebigs Ann. Chem.* **715**, 164.
25. Rauwald, H.-W. (1982) *Planta Med.* **46**, 110.