Synthesis of Condensed Tannins. Part 2.† Synthesis by Photolytic Rearrangement, Stereochemistry, and Circular Dichroism of the First 2,3-*cis*-3,4-*cis*-4-Arylflavan-3-ols

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Photolytic rearrangements of those 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*-4-arylflavan-3-ols in which the nucleophilicity of D-ring (4-aryl group) functionality exceeds that of the A-ring, provide the first access to 2,3-*cis*-3,4-*cis*-diastereoisomers. The circular dichroism of these new isomers is at variance with the proposed general rule for assessing the absolute configuration at C-4. In terms of the aromatic quadrant rule such discrepancies correlate with deviations from the preferred C-ring conformations.

THE generation of 4-carbo-cations from flavan-3,4-diols of known absolute configuration under extremely mild acidic conditions and their regioselective aromatic substitution (where applicable) on the strongly nucleophilic rings of phloroglucinol and resorcinol,[1] flavan-3-ols,[2] and biflavonoids [3] to form 4-arylflavan-3-ols, biflavonoids, and triflavonoids, respectively, was recently demonstrated in these laboratories. Multiple high-intensity Cotton effects in the low-wavelength region of their c.d. spectra, contributed by two aryl chromophores at C-4, permit assignment of absolute configurations at this chiral centre linking 2,3-*trans*-3,4-*trans*-, 2,3-*trans*-3,4-*cis*-, and 2,3-*cis*-3,4-*trans*-isomers. Subsequently a single exception was noted amongst 4-arylflavan-3-ols, and others are now added through the first availability of certain 2,3-*cis*-3,4-*cis*-diastereoisomers by photolytic rearrangement. These broader findings accordingly call for evaluation in terms of the aromatic quadrant rule.

RESULTS AND DISCUSSION

Thus, sensitised photolysis (0.05M benzophenone) of the 2,3-*trans*-3,4-*trans*-4-(2,4,6-trihydroxyphenyl)flavan-3-ol [(1); 2*R*,3*S*,4*S*] [1,4,5] gives the 2,3-*cis*-3,4-*cis*-4-(2,4-dihydroxyphenyl)flavan-3-ol [(4); 2*S*,3*S*,4*S*] and trace quantities of the 2,3-*trans*-3,4-*cis*-4-(2,4,6-trihydroxyphenyl)flavan-3-ol [(7); 2*R*,3*S*,4*R*]. Under similar conditions the 2,3-*cis*-3,4-*trans*-4-(2,4,6-trihydroxyphenyl)flavan-3-ol [(10); 2*R*,3*R*,4*R*] affords the 2,3-*cis*-3,4-*cis*-4-(2,3,4-trihydroxyphenyl)-analogue [(13); 2*R*,3*R*,4*R*] while the 2,3-*trans*-3,4-*trans*-4-(2,4-dihydroxyphenyl)flavan-3-ol [(16); 2*R*,3*S*,4*R*] gives the 2,3-*trans*-3,4-*cis*-4-(2,4-dihydroxyphenyl)-isomer [(19); 2*R*,3*S*,4*S*]. In the absence of benzophenone the 4-arylflavan-3-ols (1), (10), and (16) are notably photo-stable even in methanol, ethyl acetate and water, presumably indicating that transfer of triplet energy is a prerequisite for the above conversions.

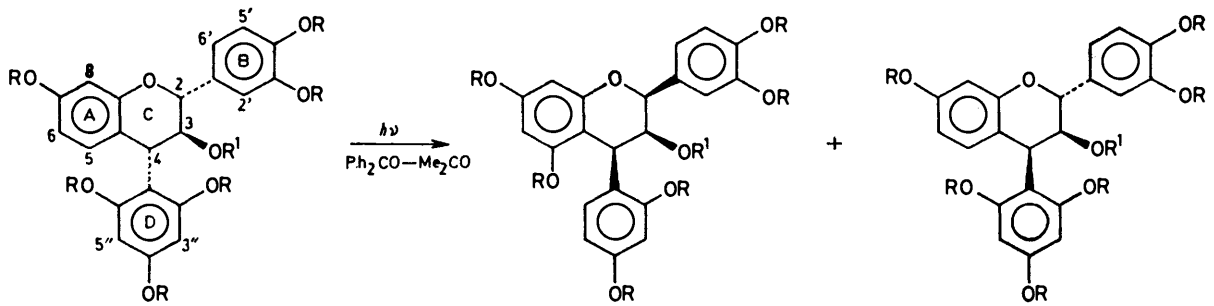
Evidence supporting the photochemical rearrangements (1) ⟶ (4) and (10) ⟶ (13), involving ring isomerization, follow from comparison of the magnetic equivalence of the high-field aromatic H-3 and H-5 resonances of the phloroglucinol D-ring of the methyl ether acetates [(3) and (12)] of the substrates (1) and (10) (*cf.* Part 1 [5]) with the non-equivalence of resonances attributable to the same protons in the spectra of the corresponding derivatives [(6) and (15)] of the products (4) and (13). Such non-equivalence persists in spectra recorded at progressively higher temperatures, and in the absence of indications of rotational isomerism over the entire range (20—100 °C). Attempts at chemical differentiation between (1) and (4) through generation of anthocyanidins in 3M HCl–propan-2-ol under pressure were inconclusive, since cyanidin and fisetinidin chlorides (3,3′,4′,5,7-pentahydroxy- and 3,3′,4′,7-tetrahydroxyflavylium chlorides, respectively) were both obtained in the ratio *ca.* 1 : 10 in each instance. This is indicative of ring isomerization under acid conditions; formation of fisetinidin chloride presumably being favoured by the relative ease of hydrolysis of the 4-phloroglucinol unit of the 4-arylflavan-3-ol (1) isomer.‡ The relative stereochemistry of all the products of photoisomerization [(4), (7), (13), and (19)] is self-evident from comparison of the coupling constants of the complete series of 4-arylflavan-3-ol derivatives with those of their flavan-3,4-diol analogues (*cf.* Table 1).

Mechanistically these novel photochemical rearrangements of phenolic units apparently require formal heterolytic cleavage of the heterocyclic ether bond [6] and simultaneous intramolecular re-cyclization *via* the zwitterion (22) involving the more strongly nucleophilic hydroxy-group of the phloroglucinol D-ring. The inversion at C-4 in the formation of both (4) and (13) is thus due to *ca.* 180° rotation about the C-3–C-4 bond; rearrangements proceed with either inversion (4) or retention (13) of configuration at C-2. Where rearrangements do not occur, as in the formation of the 2,3-*trans*-3,4-*cis*-4-(2,4,6-trihydroxyphenyl)-diastereoisomer (7), or where structural parameters permitting rearrangement, *i.e.* nucleophilicity of functional groups of the D-ring exceeding that of the A-ring in the case of the 4-(2,4-dihydroxyphenyl)-analogue (19), are not fulfilled, the parent compounds [(1) and (16) respectively] are subject to inversion at C-4 only.

Plausible rationalizations for the stereochemical

† Part 1 is ref. 5.

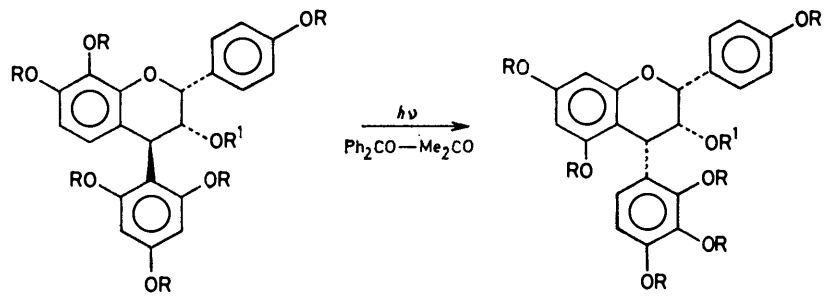
‡ This provides an interesting chemical analogy for the sensitized photoisomerizations.



(1) R = R¹ = H
(2) R = Me; R¹ = H
(3) R = Me; R¹ = Ac

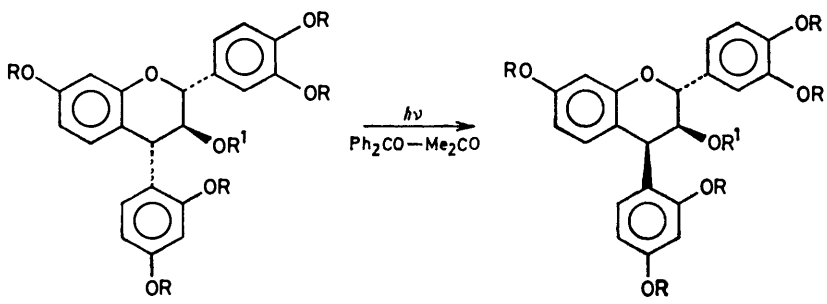
(4) R = R¹ = H
(5) R = Me; R¹ = H
(6) R = Me; R = Ac

(7) R = R¹ = H
(8) R = Me; R¹ = H
(9) R = Me; R¹ = Ac



(10) R = R¹ = H
(11) R = Me; R¹ = H
(12) R = Me; R¹ = Ac

(13) R = R¹ = H
(14) R = Me; R¹ = H
(15) R = Me; R¹ = Ac



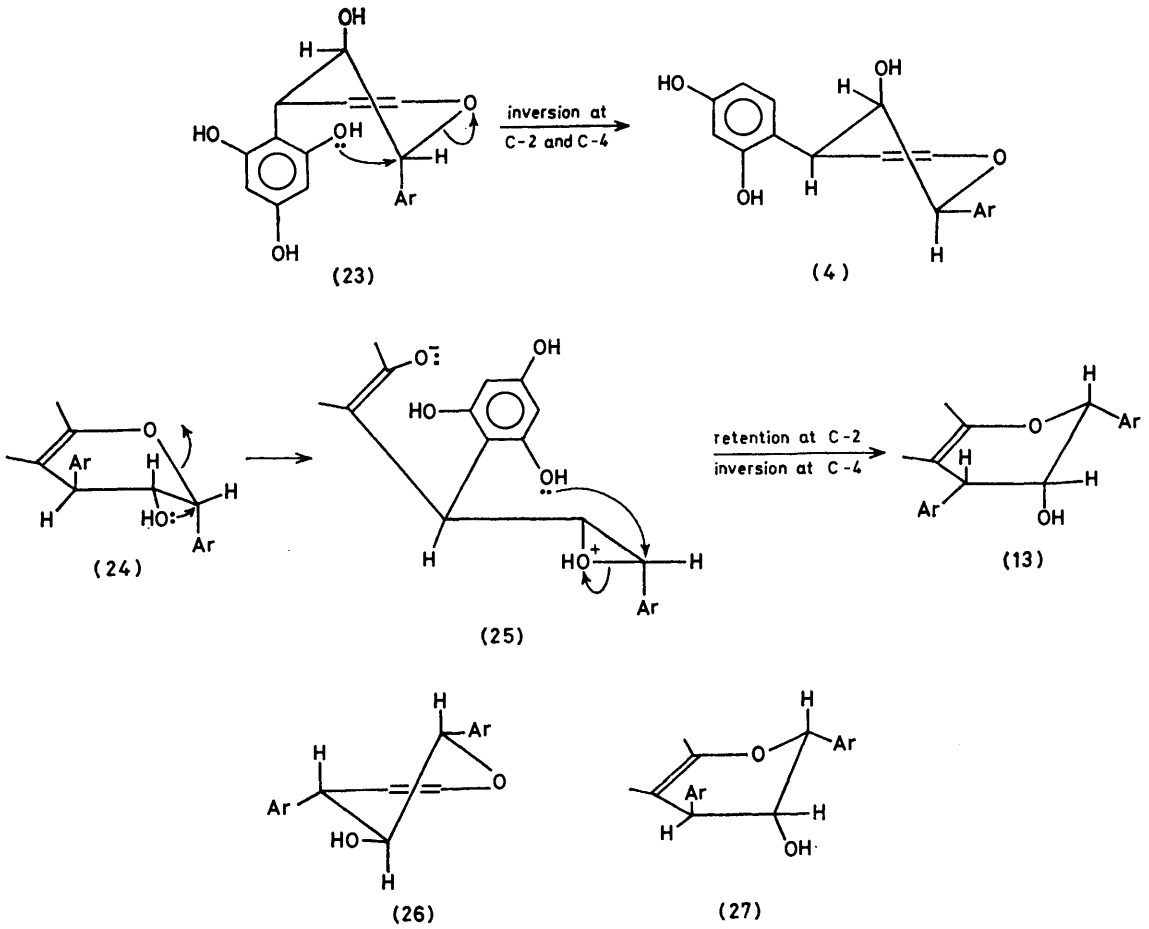
(16) R = R¹ = H
(17) R = Me; R¹ = H
(18) R = Me; R¹ = Ac

(19) R = R¹ = H
(20) R = Me; R¹ = H
(21) R = Me; R¹ = Ac

TABLE 1

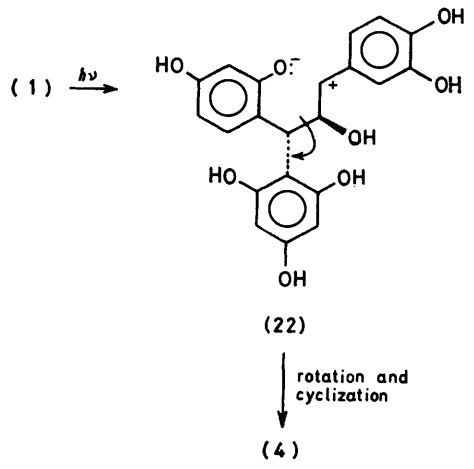
Coupling constants (Hz) of *O*-methylflavan-3,4-diols (and 3,4-diacetates) [7,9,10] and *O*-methyl-4-arylflavan-3-ols [5,11] (and 3-acetates)

	Flavan-3,4-diol		Flavan 3,4-diacetate		4-Arylflavan-3-ol		4-Arylflavan-3-acetate	
Stereochemistry	$J_{2,3}$	$J_{3,4}$	$J_{2,3}$	$J_{3,4}$	$J_{2,3}$	$J_{3,4}$	$J_{2,3}$	$J_{3,4}$
5-Deoxy-analogues								
2,3-*trans*-3,4-*trans*	9.8—10.0	7.8—8.5	8.3—10.0	6.8—7.4	9.4—10.6	7.5—9.8	10.0	9.0—9.8
2,3-*trans*-3,4-*cis*	9.5—10.2	3.5—3.8	10	3.0—3.7	8.8	5.0	8.0—9.5	5.0—6.5
2,3-*cis*-3,4-*trans*	*ca.* 1	*ca.* 3	<1	*ca.* 2.7	1.0—2.4	2.1—4.6	<1	1.9—3.8
2,3-*cis*-3,4-*cis*	*ca.* 1	3.9—4.1	<1	*ca.* 4.4				
5-Hydroxy-analogues								
2,3-*trans*-3,4-*trans*	10.1	7.1	7.4	5.2	9.0	7.5—8.3	6.5—10.0	5.5—8.5
2,3-*trans*-3,4-*cis*	10.1	4.1	11.1	3.5	10.0	5.5	10	5.8
2,3-*cis*-3,4-*trans*	0.9	2.5	1.4	2.6	1	2.3	0.9	2.3—3.0
2,3-*cis*-3,4-*cis*	1.0	4.8	1.6	5.4	0.5	3.75—4.5	1.2	4.75—4.90



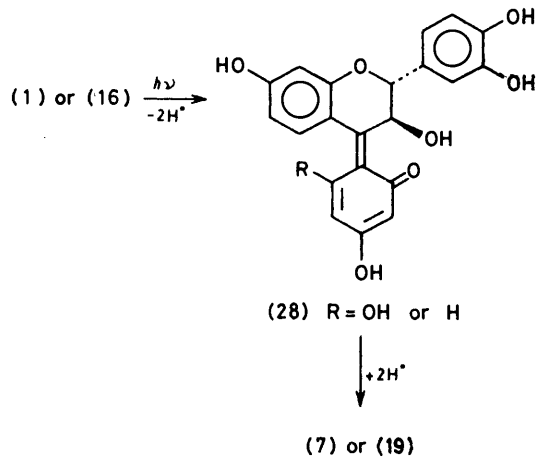
course of the observed structural rearrangements are possible by invoking the participation of the high-energy 2-*ax*,3-*ax*,4-*ax* (23) and 2-*ax*,3-*eq*,4-*ax* (24) conformations under conditions of photolysis. The close proximity of 2-OH of ring D and the C-2–O bond in conjunction with their ' *anti*-orientation ' in an inverted C-2, C-3 half-chair conformation (23) facilitates an S_N2-type cleavage of the heterocyclic ether linkage and thus inversion of configuration at C-2 in the case of the 2,3-*trans*-3,4-*trans*-analogue (1). In an inverted C-2 half-chair conformation (24), the quasi-equatorial C-3-OH of the 2,3-*cis*-3,4-*trans*-4-arylflavan-3-ol [(10), preferred conformation (27)] occupies an *anti*-configuration relative to the O–C-2 bond. Cleavage of this bond is then enhanced by anchimeric assistance of the lone pair of the 3-OH group with formation of a protonated oxiran species (25). Subsequent nucleophilic attack by the D-ring hydroxy-group gives the 4-arylflavan-3-ol (13) with retention of configuration at C-2. The high-energy conditions of photolysis presumably facilitate rearrangement predominantly from the less-favoured conformers (23) and (24).

Due to the high-energy requirements [7] for fragmentation of the C-4–aryl bond, inversion at C-4 in the case of the 2,3-*trans*-3,4-*trans*-flavan-3-ols (1) and (16) [*i.e.* (1) ⟶ (7) and (16) ⟶ (19)] is explicable in terms of hydrogen abstraction by benzophenone. Subsequent reaction of the intermediate quinone methides of type



(28) with hydrogen radicals gives the thermodynamically more stable 2,3-*trans*-3,4-*cis*-analogues (7) and (19). Proof for the 3,4-*cis*-stereochemistry of (7) was provided by acid-catalysed synthesis of its hexamethyl ether (8)

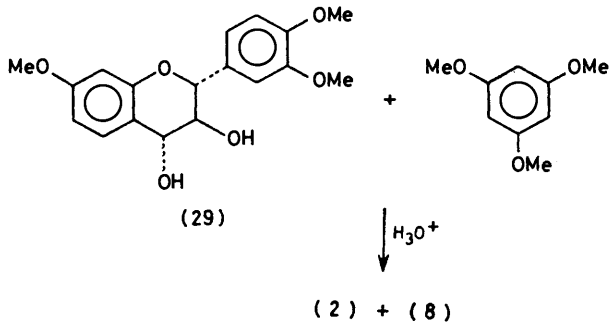
from (+)-tri-*O*-methyl-leucofisetinidin (29) and tri-*O*-methylphloroglucinol, followed by comparison of their physical data (n.m.r., mass spectra, and c.d.).



Whereas ^{1}H n.m.r. data permit accurate assignment of the relative stereochemistry of derivatives of 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*-5-deoxyflavan-3,4-diols [7,9] and 4-arylflavan-3-ols,[5] coupling constants for the corresponding 2,3-*cis*-3,4-*trans*- [8,9] and 2,3-*cis*-3,4-*cis*-4-aryl-5-deoxyflavan-3-ols and leucocyanidin 5-hydroxy-analogues [10,11] are less diagnostic (*cf.* Table 1).* Synthesis of the first 2,3-*cis*-3,4-*cis*-4-aryl-leucocyanidins (4) [$J_{2,3}$ 1.2 and $J_{3,4}$ 4.75 Hz for the methyl ether acetate (6)] and (13) [$J_{2,3}$ 1.25 and $J_{3,4}$ 4.9 Hz for the methyl ether acetate (15)] thus necessitates unambiguous differentiation between these and the 2,3-*cis*-3,4-*trans*-isomers.

Investigation of the mass spectral fragmentation patterns of a series of 4-arylflavan-3-*O*-acetates [4] reveals a marked relationship between the ease of 1,2-elimination of acetic acid and 3,4-stereochemistry (*cf.* Table 2).

Whereas 3,4-*trans*-analogues (3-OAc group *cis* to H-4) are susceptible to a facile McLafferty-type rearrangement ($M^+ - 60 : M^+$ ratio varying from 40 : 1 to 83 : 1), the loss of acetic acid is less pronounced for the 3,4-*cis*-isomers (3-OAc group *trans* to H-4; $M^+ - 60 : M^+$ ratio



varying from 2.6 : 1 to 3.3 : 1). The ratios obtained for the methyl ether acetates (6) and (15) ($M^+ - 60 : M^+$ 2.5 and 1.4 : 1, respectively) thus support 3,4-*cis*-stereochemistry, while the small coupling constants ($J_{2,3}$ 0.5—1.2 Hz) in the n.m.r. spectra define the 2,3-*cis*-configuration.† The results obtained from the 4-arylflavan-3-ols further indicate that the loss of acetic acid preferentially involves the 3-OAc group and the 4-H to give a stable 4-arylflav-3-ene fragment of type (30).

TABLE 2

$M^+ - 60 : M^+$ ratio in the mass spectra of 4-arylflavan-3-acetates

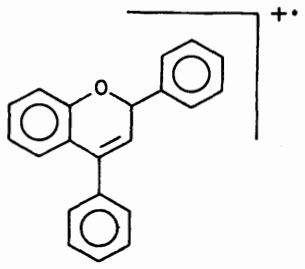
4-Arylflavan-3-acetate	Intensity M^+	Intensity $M^+ - 60$	$M^+ - 60 : M^+$
2,3-*trans*-3,4-*trans*			
(3)	1.3	100	77 : 1
(18)	1.2	100	83 : 1
3′,4′,5,7-$(OMe)_4$-4-[2,4,6-$C_6H_2(OMe)_3$] [5]	1.3	100	77 : 1
3′,4′,5,7-$(OMe)_4$-4-[2,4-$C_6H_3(OMe)_2$] [5]	1.5	100	67 : 1
2,3-*trans*-3,4-*cis*			
(9)	9	30	3.3 : 1
(21)	26	75	2.9 : 1
3′,4′,5,7-$(OMe)_4$-4-[2,4-$C_6H_3(OMe)_2$] [5]	21	55	2.6 : 1
2,3-*cis*-3,4-*trans*			
(12)	2.5	100	40 : 1
4′,7,8-$(OMe)_3$-4-[2,4-$C_6H_3(OMe)_2$]	2.5	100	40 : 1
3′,4′,5,7-$(OMe)_4$-4-[2,4-$C_6H_3(OMe)_2$] [5]	2.0	100	50 : 1
2,3-*cis*-3,4-*cis*			
(6)	8	20	2.5 : 1
(15)	11	15	1.4 : 1

Circular dichroism data have recently been applied to the problem of determining the absolute configuration at C-4 of a series of 4-arylflavan-3-ols.[1,5] These results, *i.e.* correlation of 4*R*- and 4*S*-configurations for the same C-4 substituent with positive and negative high-amplitude Cotton effects, respectively, in the low-wavelength (220—240 nm) region, have also been extended to bi- [2] and tri-flavonoids [3] and, following publication of our results, confirmed by Haslam and his collaborators [13] for various procyanidins and their

* Evident from Table 1 is the close correlation between the coupling constants of the flavan-3,4-diol and 4-arylflavan-3-ol derivatives. This indicates that substitution of the 4-hydroxy-group by an aryl group has no significant effect on c-ring conformation.

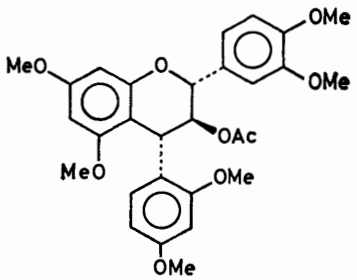
† Although a similar correlation between stereochemistry and the ratio of the intensity of M^+ and $M^+ - 60$ peaks exists for the methyl ether diacetates of flavan-3,4-diols,[12] these (3,4-*trans* : 0.4—0.7; 3,4-*cis* : 0.12—0.3) are too small to permit unequivocal assignment of 3,4-stereochemistry.

derivatives. C.d. data of the methyl ether acetates [(6) and (15)] of the novel 2,3-*cis*-3,4-*cis*-4-arylflavan-3-ols (4) and (13), as well as the 2,3-*trans*-3,4-*trans*-cyanidin analogue (31) with 'abnormal' coupling



(30)

constants ($J_{2,3}$ 6.5, $J_{3,4}$ 5.5 Hz) [positive Cotton effects for (15) and (31) and negative for (6) indicate 4*R*- and 4*S*-configurations, respectively], however, represent exceptions to the otherwise simple rule. The latter results indicate that deviations from the normal dihedral angles between substituents on the heterocyclic ring, and thus from the anticipated half-chair conformations, strongly influence the sign of the Cotton effect.



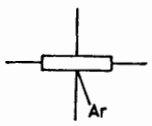
(31)

These observations are explicable in terms of the aromatic quadrant rule;[14] substituents in the upper left and lower right quadrants make positive contributions to 220—240 nm dichroism, and substituents in the upper right and lower left quadrants make a negative contribution. Since the 4-aryl substituent in 4-arylflavan-3-ols is attached directly to the chiral centre, it will obviously account for the major contribution towards the sign of the low-wavelength and high-intensity Cotton effect.

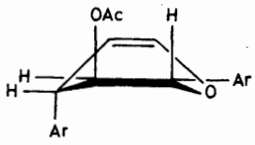
Consideration of the preferred conformations of the heterocyclic rings of 2,3-*trans*-3,4-*trans* [half-chair or sofa (26)], 2,3-*trans*-3,4-*cis* [half-chair or sofa of type (26) with 4-*ax*-Ar], and 2,3-*cis*-3,4-*trans*- [half-chair or sofa of type (27)], results in a sound correlation between the sign of the high-amplitude Cotton effect [1,5] and the quadrant in which the 4-aryl substituent is located.

For both the 'abnormal' *trans-trans*-isomer (31) and the 2,3-*cis*-3,4-*cis*-analogues (6) and (15) the predicted and experimental Cotton effects may be correlated only for boat-conformations [(32) for (31) and (15)], and (33) for (6), respectively]. The compounds requiring

2,3-*trans*-3,4-*trans* (2*R*, 3*S*)
2,3-*cis* -3,4-*cis* (2*R*, 3*R*)

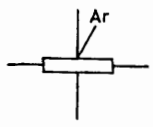


Positive Cotton effect predicted* and found

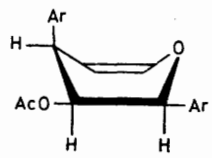


(32)

2,3-*cis*-3,4-*cis* (2*S*, 3*S*)



Negative Cotton effect predicted* and found



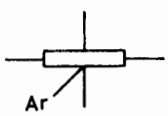
(33)

*Based on boat conformations

boat-conformations have in common a 5-methoxy-substituent; such conformations notably reduce the non-bonding interaction of the 4-aryl and 5-methoxy-groups, additional to that between 3-acetyl and both 2- and 4-aryl substituents on the heterocyclic ring.

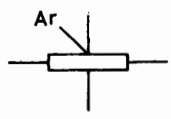
These results thus illustrate that the sign of the Cotton effect is determined primarily by the spatial orientation and thence conformation of the heterocycle of 4-arylflavan-3-ols. Since minor deviations in orientation in the vicinity of the chiral centre may largely influence the amplitude and sign of the Cotton effect, the c.d. method

2,3-*trans*-3,4-*trans* (2*R*, 3*S*)



Negative Cotton effect, predicted* and found

2,3-*trans*-3,4-*cis* (2*R*, 3*S*) and
2,3-*cis* -3,4-*trans* (2*R*, 3*R*)



Positive Cotton effect, predicted* and found

*Based on half-chair or sofa confirmations

of assessing the absolute configuration at C-4 of 4-arylflavan-3-ols and higher oligomers may provide erroneous results unless the conformations of their heterocycles are established.

Thus, only for those 4-arylflavan-3-ols with 2,3-*trans*-3,4-*trans*-, 2,3-*trans*-3,4-*cis*-, and 2,3-*cis*-3,4-*trans*-configurations where the inter-proton coupling constants of heterocyclic protons are in line with dihedral angles derived from preferred half-chair conformations, may the stereochemistry at C-4 be correlated with c.d. data, and the results translated with confidence to bi- and tri-flavonoids. However, the observed deviations from the general rule explicable in terms of 'abnormal' boat conformations may find future application at the oligomeric level provided that suitable reference compounds are available.

EXPERIMENTAL

Irradiation of compounds in acetone containing benzophenone (0.05M) in a quartz vessel was carried out in a slow current of nitrogen (*ca.* 1 ml min^{-1}) in a Rayonet photochemical reactor at 350 nm. T.l.c. was performed on DC-Plastikfolin Kieselgel 60 F_{254} (0.25 mm) and the plates sprayed with H_2SO_4–HCHO (40 : 1) after development. Colours indicated are those obtained with this reagent. Preparative plates [Kieselgel PF_{254} (1.0 mm)] were air-dried and used without prior activation. Methylations were performed with an excess of diazomethane in methanol–diethyl ether at −15 °C for 48 h, while acetylations were carried out with acetic anhydride–pyridine. M.p.s were determined with a Reichert hot-stage apparatus and are uncorrected. ^1H N.m.r. spectra were recorded on a Bruker WP-80 spectrometer for solutions in $CDCl_3$ with $SiMe_4$ as internal standard. Mass spectral data were recorded on a Varian CH-5 instrument, and c.d. data on a Jasco J-20 spectropolarimeter. Analyses (C and H) were performed by Analytische Laboratorien, Fritz-Pregl-Strasse 24, 5270 Gummbersbach 1 Elbach, Germany.

Synthesis of 4-*Arylflavan*-3-*ols*.—2,3-*trans*-3,4-*trans*-4-(2,4,6-trihydroxyphenyl)flavan-3,3′,4′,7-tetraol (1; 2*R*,3*S*,4*R*), 2,3-*cis*-3,4-*trans*-4-(2,4,6-trihydroxyphenyl)flavan-3,4′,7,8-tetraol (10; 2*R*,3*R*.4*R*), and 2.3-*trans*-3,4-*trans*- (16; 2*R*,-3*S*,4*R*) and 2,3-*trans*-3,4-*cis*-4-(2,4-dihydroxyphenyl)flavan-3,3′,4′,7-tetraol (19; 2*R*,3*S*,4*S*) and their phenolic methyl ethers [(2), (11), (17), and (20), respectively] and methyl ether acetates [(3), (12), (18), and (21), respectively] were synthesized according to the standard literature procedures.[4,5]

2,3-trans-3,4-trans- (2) *and* 2,3-trans-3,4-cis-3′,4′,7-*trimethoxy*-4-(2,4,6-*trimethoxyphenyl*)*flavan*-3-*ol* (8; 2R,3S,4S). —(+)-3′,4′,7-Tri-*O*-methylflavan-3,4-diol (29) (200 mg) and tri-*O*-methylphloroglucinol (200 mg) were stirred for 2 h at room temperature in ether (210 ml) containing concentrated sulphuric acid (0.1 ml). The mixture was washed acid-free with water (4 × 50 ml) and the solvent evaporated. P.l.c. separation [benzene–acetone (8 : 2)] of the residual solids gave two bands, R_F 0.58 (80 mg, red-brown), and 0.47 (128 mg, red-brown).

Crystallization of the former fraction from methanol afforded the 2,3-trans-3,4-cis-4-*arylflavan*-3-*ol* (8) as fine white needles, m.p. 142—143 °C; *m/e* 482 (M^+, 8.9%), 464 (3.1), 315 (16.5), 314 (10.5), 304 (17.5), 303 (100), 272 (12.9), 271 (67), 180 (12.1), 167 (55), 151 (43), and 137 (28); δ 6.97—6.41 (m, aromatic), 6.25 (dd, aromatic, *J* 8.5 and 2.0 Hz), 6.10 (s, 3″- and 5″-H), 5.22 (d, 2-H, *J* 4.75 Hz), 4.66 (d, 4-H, *J* 4.70 Hz), 4.22 (t, 3-H, *J* 4.75 and 4.70 Hz), and 3.80, 3.77, 3.72, and 3.53 (all s, 6 × OMe); c.d. (MeOH) $[\theta]_{300}$ 0, $[\theta]_{285}$ −5 380, $[\theta]_{263}$ 0, $[\theta]_{236}$ +43 145, and $[\theta]_{227}$ 0 (Found: C, 67.2; H, 6.3. $C_{27}H_{30}O_8$ requires C, 67.2; H, 6.3%).

Acetylation of the 4-arylflavan-3-ol (8) followed by crystallization from methanol gave the 2,3-*trans*-3,4-*cis*-4-*arylflavan*-3-*acetate* (21) as colourless plates, m.p. 158—159 °C; *m/e* 524 (M^+, 8.6%), 464 (30.3), 327 (6.6), 317 (28), 315 (13.4), 272 (11.7), 271 (100), 180 (11.1), 151 (34), and 137 (12.2); δ 6.97—5.59 (m, aromatic), 6.44 (d, aromatic, *J* 2.5 Hz), 6.28 (dd, aromatic, *J* 8.5 and 2.5 Hz), 6.08 and 6.02 * (2 d, 3- and 5-H, *J* 2.5 Hz), 5.46 (dd, 3-H, *J* 9.5 and 6.5 Hz), 5.16 (d, 2-H, *J* 9.5 Hz), 4.88 (d, 4-H, *J* 6.5 Hz), 3.81, 3.76, 3.72, and 3.30 (all s, 6 × OMe), and 1.66 (s, 3-OAc); c.d. (MeOH) $[\theta]_{298}$ 0, $[\theta]_{289}$ −1 786, $[\theta]_{282}$ 0, $[\theta]_{235}$ +43 345, and $[\theta]_{210}$ 0.

The R_F 0.47 fraction gave the 2,3-*trans*-3,4-*trans*-analogue (2) with physical data (n.m.r., m.s., and c.d.) identical to those previously described.[4,5]

Photolysis of 4-*Arylflavan*-3-*ols*.—2,3-cis-3,4-cis-3′,4′,5,7-*Tetramethoxy*-4-(2,4-*dimethoxyphenyl*)*flavan*-3-*ol* (5). The 4-arylflavan-3-ol (1) (200 mg) was irradiated for 2 h, the solvent evaporated, and the mixture separated by p.l.c. with benzene–acetone (9 : 1). Three bands, R_F 0.48 (30 mg, red-brown), 0.45 (5 mg, red-brown), and 0.34 (90 mg, red-brown) were obtained.

Methylation of the R_F 0.48 fraction followed by p.l.c. [benzene–acetone (19 : 1)] afforded the 2,3-*cis*-3,4-*cis*-3′,4′,5,7-*tetramethoxy*-4-(2,4-*dimethoxyphenyl*)*flavan*-3-*ol* (5; 2*S*,3*S*,4*S*) (R_F 0.32, 25 mg) as a colourless amorphous solid; *m/e* 482 (M^+, 45%), 464 (21), 330 (25), 317 (47), 315 (40), 303 (100), 286 (39), 271 (78), 180 (41), 167 (46), 151 (47), and 137 (42); δ 7.17 (d, 2′-H, *J* 2.5 Hz), 7.03 (dd, 6′-H, *J* 8.5 and 2.5 Hz), 6.78 (d, 5′-H, *J* 8.5 Hz), 6.55 (dd, 6″-H, *J* 8.5 and 0.75 Hz), 6.48 (d, 3″-H, *J* 2.5 Hz), 6.28 (dd, 5″-H, *J* 8.5 and 2.5 Hz), 6.17 and 6.06 (2 d, 6- and 8-H, *J* 2.5 Hz), 5.06 (dd, 4-H, *J* 3.75 and 0.75 Hz), 5.02 (d, 2-H, *J* 0.5 Hz), 4.11 (dd, 3-H, *J* 3.75 and 0.5 Hz), 3.89 (s, 3-OH), and 3.85, 3.81, 3.78, 3.75, 3.70, and 3.34 (all s, 6 × OMe); c.d. (MeOH) $[\theta]_{289}$ 0, $[\theta]_{281}$ −3 265, $[\theta]_{277}$ 0, $[\theta]_{266}$ +8 663, $[\theta]_{249}$ 0, $[\theta]_{232}$ −35 821, $[\theta]_{210}$ 0 (Found: C, 67.0; H, 6.1. $C_{27}H_{30}O_8$ requires C, 67.2; H, 6.3%).

Acetylation of the 3-hydroxyflavan hexamethyl ether (5) (20 mg) gave the monoacetate (6) (19 mg) as a colourless amorphous solid; *m/e* 524 (M^+, 8.1%), 464 (20), 327 (3.3), 317 (23), 315 (10.5), 271 (100), 180 (15.4), 151 (37), and 149 (16.4); δ 7.01 (s, 2′-H), 6.95 (dd, 6′-H, *J* 8.5 and 2.5 Hz), 6.75 (d, 5′-H, *J* 8.5 Hz), 6.66 (dd, 6″-H, *J* 8.5 and 0.9 Hz), 6.50 (d, 3″-H, *J* 2.5 Hz), 6.32 (dd, 5″-H, *J* 8.5 and 2.5 Hz), 6.08 and 5.93 † (2 × d, 6- + 8-H, *J* 2.5 Hz), 5.52 (dd, 3-H, *J* 4.75 and 1.2 Hz), 5.18 (d, 2-H, *J* 1.2 Hz), 5.09 (dd, 4-H, *J* 4.75 and 0.9 Hz), 3.85, 3.81, 3.73, and 3.32 (all s, 6 × OMe), and 1.64 (s, 3-OAc); c.d. (MeOH) $[\theta]_{286}$ 0, $[\theta]_{281}$ −1 855, $[\theta]_{277}$ 0, $[\theta]_{266}$ +8 187, $[\theta]_{251}$ 0, $[\theta]_{239}$ −21 393, and $[\theta]_{225}$ 0.

The R_F 0.45 fraction gave the 2,3-*trans*-3,4-*cis*-4-(2,4,6-

* Magnetic non-equivalence is due to chirality at C-4 coupled with restricted rotation as shown by the merging of these resonances after partial collapse with increasing temperature (20—100 °C).

† These resonances do not merge with increase in temperature over the range 20–100 °C.

trihydroxyphenyl)flavan-3,3′,4′,7-tetraol (7), identical to that previously described.[5]

The R_F 0.34 band consisted of unconsumed starting material (1).

2,3-cis-3,4-cis-4′,5,7-*Trimethoxy*-4-(2,3,4-*trimethoxyphenyl*)*flavan*-3-*ol* (14). The 4-arylflavan-3-ol (10) (200 mg) was irradiated for 2 h, the solvent evaporated, and the residual solids separated by means of p.l.c. [benzene–acetone (1 : 1)]. Two bands, R_F 0.43 (35 mg, red-brown) and 0.38 (85 mg, red-brown) were obtained.

Methylation of the R_F 0.43 fraction followed by p.l.c. [benzene–acetone (19 : 1)] gave the 2,3-*cis*-3,4-*cis*-4′,5,7-*trimethoxy*-4-(2,3,4-*trimethoxyphenyl*)*flavan*-3-*ol* (14; 2*R*,3*R*,4*R*) as a white amorphous solid; *m/e* 482 (M^+, 7.6%), 334 (10), 333 (44), 302 (22), 301 (100), 287 (23), 286 (14.1), 167 (47), 150 (7.5), and 121 (27); δ 7.46, and 6.83 (2 d, 2′- and 6′-H, 3′- and 5′-H, *J* 8.5 Hz), 6.30 (s, 5″- and 6″-H), 6.19 and 6.06 (2 d, 6- and 8-H, *J* 2.5 Hz), 5.09 (d, 2-H, *J* 4.5 Hz), 5.06 (d, 4-H, *J* 4 Hz), 4.11 (d, 3-H, *J* 4.5 Hz), and 3.88, 3.80, 3.76, and 3.38 (all s, 6 × OMe); c.d. (MeOH) $[\theta]_{284}$ 0, $[\theta]_{280}$ +803, $[\theta]_{276}$ 0, $[\theta]_{268}$ −4 820, $[\theta]_{252}$ 0, $[\theta]_{237}$ +24 175, $[\theta]_{220}$ 0 (Found: C, 66.9; H, 6.1. $C_{27}H_{30}O_8$ requires C, 67.2; H, 6.3%).

Acetylation of the 3-hydroxy-4-arylflavan (13) afforded the monoacetate (15) as a colourless amorphous solid; *m/e* 524 (M^+, 10.8%), 464 (14.6), 302 (23), 301 (100), 287 (48), 286 (14), 167 (10.1), 150 (7.7), and 121 (33); δ 7.36 and 6.79 (2 d, 2′- and 6′-H, 3′- and 5′-H, *J* 8.5 Hz), 6.44 (dd, 6″-H, *J* 8.5 and 0.9 Hz), 6.29 (d, 5″-H, *J* 8.5 Hz), 6.07 and 5.91 * (2 d, 6- and 8-H, *J* 2.0 Hz), 5.39 (dd, 3-H, *J* 4.9 and 1.25 Hz), 5.17 (br s, H-2), 5.09 (d, 4-H, *J* 4.90 Hz), 3.88, 3.81, 3.78, 3.74, and 3.31 (all s, 6 × OMe), and 1.60 (s, 3-OAc); c.d. (MeOH) $[\theta]_{287}$ 0, $[\theta]_{281}$ +491, $[\theta]_{278}$ 0, $[\theta]_{268}$ −3 684, $[\theta]_{252}$ 0, $[\theta]_{232}$ +23 803, and $[\theta]_{205}$ 0.

The R_F 0.38 fraction gave the starting material (10).

2,3-trans-3,4-cis-4-(2,4-*Dihydroxyphenyl*)*flavan*-3,3′,4′,7-*tetraol* (19). The 4-arylflavan-3-ol (16) (200 mg) was irradiated for 2 h, the solvent evaporated, and the residual solids separated by means of p.l.c. [benzene–acetone (1 : 1)]. Two fractions, R_F 0.43 (35 mg, red-brown) and 0.38 (85 mg, red-brown) were obtained.

The R_F 0.43 fraction consisted of the 2,3-*trans*-3,4-*cis*-4-(2,4-dihydroxyphenyl)flavan-3,3′,4′,7-tetraol (19; 2*R*,3*S*,4*S*) as a light-red amorphous solid. This was identified by means of comparison of the physical data (n.m.r., m.s., and c.d.) of (19), its phenolic methyl ether (20), and the methyl ether acetate (21) with those of an authentic specimen.[5]

The R_F 0.38 fraction gave starting material (16).

Under similar photolytic conditions the *cis-cis*- (4), *cis-cis*- (13), and *trans-cis*- (19) 4-arylflavan-3-ols are stable.

Acid Hydrolysis Products of 4-*Arylflavan*-3-*ols*.—Treatment of the 4-arylflavan-3-ol (1) and its photoisomerization product (4) with 3M HCl–propan-2-ol at 97 °C under pressure [15] gave cyanidin and fisetinidin chlorides [16] in a *ca.* 1 : 10 ratio in both instances.

* These resonances do not merge with increase in temperature over the range 20—100 °C.

We thank the South African Council for Scientific and Industrial Research, Pretoria; the Sentrale Navorsingsfonds of this University; the Wattle Bark Industry of South Africa Marketing Committee; and the Leather Industries Research Institute, Grahamstown, for financial support; and Dr. J. M. Steyn, Department of Pharmacology of this University, for mass spectra. One of us (J. H. v. d. W.) is the recipient of a post-graduate Merit Bursary by the South African C.S.I.R.

[0/455 *Received*, 25*th March*, 1980]

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