912. *Polymerisation of Flavans. Part V.* The Stereochemistry of 2,3-*trans*-Flavan-3,4-diols.*

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The *cis*- or *trans*-arrangement of the hydroxyl groups in eight 2,3-*trans*-flavan-3,4-diol racemates has been established by consideration of their isopropylidene derivatives, their rates of reaction with lead tetra-acetate, and the proton magnetic resonance spectra of their diacetates. This necessitates a revision of the existing assignment of relative stereochemistry to the two racemates of 4′-methoxy-6-methyl-2,3-*trans*-flavan-3,4-diol. The most convenient preparative method for the 2,3-*trans*-flavan-3,4-*cis*-diols makes use of the reduction of 3-hydroxy-2,3-*trans*-flavan-4-ones with a mixture of lithium aluminium hydride and aluminium chloride.

The realisation [1] of the wide occurrence and importance of flavan-3,4-diols (leucoanthocyanidins) (I) in Nature has focused attention on the stereochemistry both of the natural diols [2] and of those produced by various synthetical routes.[3] Flavan-3,4-diol (I; R = R′ = H) can exist in eight stereoisomeric forms, which afford four racemates. The work described here is limited to 2,3-*trans*-flavan-3,4-diols obtained from 3-hydroxy-2,3-*trans*-flavan-4-ones, whose relative stereochemistry at the 2,3-positions is well established.[4,3c]

Bognár and Rákosi [3b] have shown that reduction of 2,3-*trans*-3-hydroxyflavan-4-one (II; R = R′ = H) with lithium aluminium hydride, sodium borohydride, or hydrogen over palladium–charcoal leads to a flavan-3,4-diol of m. p. 145—146°. Examination of the crude products from these reductions by chromatography on thin silica films [5] has shown that they contain 3-hydroxyflavanone and its oxidation product, 3-hydroxyflavone,

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* Part IV, *J.*, 1961, 3677.

[1] *E.g.*, Bate-Smith and Swain, *Chem. and Ind.*, 1953, 377; King and Bottomley, *J.*, 1954, 1399; Keppler, *J.*, 1957, 2721.

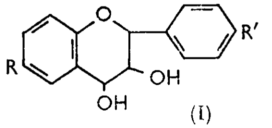
[2] *E.g.*, King and Clark-Lewis, *J.*, 1955, 3384; Weinges, *Annalen*, 1959, **627**, 229; Clark-Lewis and Roux, *J.*, 1959, 1402; Clark-Lewis and Mortimer, *J.*, 1960, 4106; Clark-Lewis and Katekar, *Proc. Chem. Soc.*, 1960, 345.

[3] *E.g.*, (*a*) Kulkarni and Joshi, *Chem. and Ind.*, 1954, 1421; *J. Indian Chem. Soc.*, 1957, **34**, 753; (*b*) Bognár and Rákosi, *Acta Chim. Acad. Sci. Hung.*, 1958, **14**, 369; (*c*) Bognár, Rákosi, Fletcher, Philbin, and Wheeler, *Tetrahedron Letters*, 1959, No. 19, 4.

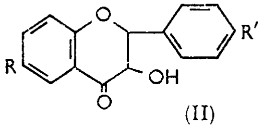
[4] Mahesh and Seshadri, *Proc. Indian Acad. Sci.*, 1955, **41**, 210.

[5] Stahl, *Arch. Pharm.*, 1959, **292**, 411.

which are easily removed by recrystallisation and chromatography on alumina to yield the pure diol of m. p. 146°. This diol yields a diacetate of m. p. 92—93·5°; Bognár and Rákosi [3b] could only obtain this diacetate as an oil. It has already been reported [6] that this diol is cleaved by lead tetra-acetate to yield a dihydrobenzofuran aldehyde which can



(I)



(II)

be converted into 2-phenylbenzofuran and that this may be regarded as a diagnostic reaction for flavan-3,4-diols.

Reduction of 3-hydroxyflavanone with a mixture of lithium aluminium hydride and aluminium chloride [7] yields another flavan-3,4-diol, of m. p. 162—163°, which has been shown to be identical with that obtained by the method of Bognár *et al.*[3c] from 3-hydroxyflavanone oxime through 4-aminoflavan-3-ol. The preparation using the mixed reagent is the more convenient. Since it is known that aluminium chloride, in these mixed reductions, is capable of causing rearrangements [8] and also that rearrangements can occur in the treatment of amines with nitrous acid,[9] this compound of m. p. 162—163° has been cleaved with lead tetra-acetate and 2-phenylbenzofuran has been isolated, which establishes the flavan-3,4-diol structure of this compound.[6]

The diol of m. p. 162—163° yields, with ethyl chloroformate, a cyclic carbonate, m. p. 134·5—135°; the diol of m. p. 146° yields a different cyclic carbonate, m. p. 129—130·5°; so, contrary to the assumption of Kulkarni and Joshi,[3a] the formation of a cyclic carbonate cannot be taken as evidence for a *cis*-diol.[10] However, the diol of m. p. 162—163° yields an isopropylidene derivative in 69% yield, whereas the diol of m. p. 146° yields 10% of the same isopropylidene derivative under identical conditions. Hydrolysis of this derivative with aqueous acid gives the diol of m. p. 162—163°. From these observations, the conclusion is drawn that the diol of m. p. 162—163° is a *cis*-diol, *i.e.*, 2,3-*trans*-flavan-3,4-*cis*-diol and that the diol of m. p. 146° is a *trans*-diol, *i.e.*, 2,3-*trans*-flavan-3,4-*trans*-diol. The conclusions of H. C. Brown [11] about the stability of five-membered rings and the observations of Angyal and Macdonald [10] on the formation of carbonates make it not unexpected that only the *cis*-diol forms an isopropylidene derivative, but that the *cis*- and *trans*-diols form distinct cyclic carbonates.

The diol of m. p. 162—163° reacts with lead tetra-acetate approximately five times as fast as does the diol of m. p. 146°. Comparison with values in the literature [12] for known *cis*- and *trans*-diols confirms the above assignment of stereochemistry.

Finally, these conclusions have been confirmed by an examination of the proton magnetic resonance spectra of the diacetates of the two diols in chloroform. The acetoxy-group in these compounds shows a sharp proton resonance peak unsplit by spin–spin coupling. Similar single peaks have been found in the proton resonance spectra of some acetylated pyranose sugars.[13] In these it has been found that peaks for axial acetoxy-groups always occur at a lower field than those for equatorial acetoxy-groups, *i.e.*, $\tau_{ax.}$ 7·97—8·13 and $\tau_{eq.}$ 8·13—8·31. On this basis, the acetoxy-group proton resonance peaks from the flavan-3,4-diol diacetates have been assigned. Since only relative values of chemical shifts for axial and equatorial acetoxy-groups are required, the diamagnetic

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[6] Bokadia, Brown, and Cummings, *J.*, 1960, 3308.

[7] Brown, *J.*, 1952, 2756; Brown and White, *J.*, 1957, 3755.

[8] Clark-Lewis, *J.*, 1960, 2433; Brown, Trown, and Woodhouse, *J.*, 1961, 2478.

[9] Henry, *Compt. rend.*, 1907, **145**, 899, 1247.

[10] Angyal and Macdonald, *J.*, 1952, 686.

[11] Brown, *J.*, 1956, 1248.

[12] Criegee, *Ber.*, 1932, **65**, 1770; 1940, **73**, 563, 571; *Sitzungsber. Ges. Naturwiss. Marburg*, 1934, **69**, 26; Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 159.

[13] Lemieux, Kullnig, and Moir, *J. Amer. Chem. Soc.*, 1958, **80**, 2237.

anisotropy effect from the aromatic rings is not thought to be important here. Further, the configurations assigned in what follows agree with those deduced from kinetic and chemical results. Now, the diol diacetates differ in the stereochemistry of the heterocyclic ring. In each of their proton magnetic resonance spectra one peak (τ 8·16) lies in the range of chemical shifts found for equatorial acetoxy-groups in pyranose sugars. Hence, in each diol diacetate, there is an equatorial acetoxy-group. The conformation at the 2-position is expected to be the same in the two compounds and hence the difference between them depends on the conformation of the second acetoxy-group. For the diacetate of the diol of m. p. 146°, the peak of the second acetoxy-group lies at a higher field (τ 8·02) than that of the second acetoxy-group of the other diacetate (τ 7·87), and hence the former is thought to be equatorial. The second acetoxy-group in the isomer is therefore axial. This leads to the same conclusions as were drawn above, *viz.*, that the diol of m. p. 162—163° is a 3,4-*cis*-diol and the diol of m. p. 146° is a 3,4-*trans*-diol.

If we assume that the 2-aryl group in each diacetate is equatorial, it follows that, since the diols are 2,3-*trans*, the 3-acetoxy-group in each diacetate is truly equatorial (τ 8·16). The occurrence of the peak for the 4-acetoxy-group at a lower field than for acetylated pyranose sugars is probably a result of the quasi-equatorial (τ 8·02) and quasi-axial (τ 7·87) nature [14] of the 4-acetoxy-groups.

The two 6-methyl-2,3-*trans*-flavan-3,4-diols (I; R = Me, R′ = H) and the two 4′-methoxy-2,3-*trans*-flavan-3,4-diols (I; R = H, R′ = OMe), prepared from the corresponding 3-hydroxyflavanones, follow the same pattern as the two unsubstituted diols, leading to assignments of stereochemistry shown in the Table.

2,3-*trans*-Flavan-3,4-diols (I) prepared from hydroxyflavanones (II).

R	R′	Reagent	M. p.	Carbonate, m. p.	Isopropylidene deriv., m. p.	$Pb(OAc)_4$, *k* at 20°	Stereochem. at pos. 3,4
H	H	1 or 2 [3c]	162—163°	134·5—135°	113—114° (69%)	0·20	*cis*
		3 [3b] or 4 [3b]	146—146·5	129—130·5	112·5—113·5 † (10%)	0·036	*trans*
Me	H	1	178—179	173—174	91·5—92·5 (58%)	0·24	*cis*
		3	118—119	159·5—161	91—92 † (10%)	0·079	*trans*
H	MeO	1	160—161	185·5—187	110—110·5 (69%)	0·29	*cis*
		3	177—177·5	190—191	—	0·039	*trans*
Me	MeO	1 or 2 [3c]	192·5—194	167—168	129—130 (70%)	0·43	*cis*
		3 [3a] or 5 [3a]	172—173	136—137·5	129—130 † (71%)	0·063	*trans*

* Reagents: 1, $LiAlH_4$–$AlCl_3$. 2, Through oxime. 3, $LiAlH_4$. 4, H_2–Pd. 5, H_2–Pt–AcOH.
† Deriv. of *cis*-diol.

The two diols obtained by Kulkarni and Joshi [3c] from 3-hydroxy-4′-methoxy-6-methylflavanone (II; R = Me, R′ = OMe) have been re-examined. Reduction of the hydroxyflavanone with lithium aluminium hydride yields the diol of m. p. 172—173° in greater amount, and reduction with the mixed reagent gives the diol of m. p. 192·5—194°. By analogy with the diols previously discussed, it can be inferred, from the methods of preparation alone, that these are the *trans*- and the *cis*-diol respectively, and this conclusion is confirmed by consideration of the cyclic derivatives of the diols and of their rates of reaction with lead tetra-acetate (see the Table). Further, the proton magnetic resonance spectra of the diol diacetates are, on this basis, analogous to those of the diacetates of the unsubstituted diols described above. The assignments are contrary to those made by Kulkarni and Joshi [3c] on the basis of the formation of a cyclic carbonate by the lower-melting diol and of conformational analysis.

EXPERIMENTAL

Light petroleum refers to the fraction of b. p. 60—80°. Alumina was Spence's grade H deactivated with acetic acid. Infrared spectra were measured for Nujol mulls on a Perkin-Elmer model 21 spectrometer.

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[14] Philbin and Wheeler, *Proc. Chem. Soc.*, 1958, 167.

2,3-trans-*Flavan*-3,4-cis-*diol*.—(i) *Preparation.* 3-Hydroxyflavanone (1·00 g.) in tetrahydrofuran (35 ml.) was added at room temperature to a solution of lithium aluminium hydride (0·30 g.) and aluminium chloride (2·10 g.) in tetrahydrofuran (40 ml.). The mixture was boiled for 1·5 hr. Decomposition with methyl formate and dilute acid and extraction with ether gave the diol, which separated from methanol as prisms (0·60 g.), melting at 162—163° with progressive sublimation and change of crystalline form to needles (Found: C, 74·6; H, 5·64. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%), $\nu_{max.}$ 3378, 3268 (OH), 798, 758, 703 cm.$^{-1}$ (aromatic). The m. p. was unchanged on admixture with a specimen prepared by the method of Bognâr *et al.*,[3c] and the infrared and ultraviolet spectra of the two specimens were identical. Chromatography in ethyl acetate–light petroleum (1 : 1 v/v) on glass plates coated with silica[5] showed the presence of one compound (brown spot after being sprayed with antimony trichloride and heated at 105° for 20 min., R_F 0·24).

(ii) *Reaction with lead tetra-acetate.* By the method previously reported[6] this diol (500 mg.) yielded benzaldehyde 2,4-dinitrophenylhydrazone (15 mg.), m. p. and mixed m. p. 237°, salicylaldehyde 2,4-dinitrophenylhydrazone (13 mg.), m. p. and mixed m. p. 252°, and the oxime (400 mg.), m. p. 170—171°, of 2-formyl-2,3-dihydro-3-hydroxy-2-phenylbenzofuran. Treatment of the oxime with hot dilute sulphuric acid gave 2-phenylbenzofuran, m. p. and mixed m. p. 120—121·5°, identical in infrared and ultraviolet spectra with authentic material.

This reaction had $k = 0{\cdot}20$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

The general method of determining such rate constants was as follows.[15] Lead tetra-acetate was recrystallised from acetic acid. Acetic acid was purified by the method of Eichelberger and LaMer.[16] Water was twice distilled from potassium permanganate in an all-glass apparatus. A thermostat bath was used whose temperature was controlled within ±0·05°. The reactions were performed in a standard 50-ml. flask. The diols used were analytically pure specimens. The diol (*ca.* $2{\cdot}5 \times 10^{-4}$ mole) was weighed into the reaction vessel, and acetic acid (37·5 ml.) containing 10 moles % of water was added. The vessel was left in the thermostat bath for several hours to attain a constant temperature. A solution (12·5 ml.) of lead tetra-acetate ($2{\cdot}5$—$3{\cdot}0 \times 10^{-2}$M) in acetic acid (containing 10 moles % of water), also kept in the thermostat bath for several hours, was added and the flask was shaken. 5-Ml. aliquot parts were withdrawn at determined times and added to *ca.* 5 ml. of stopping solution [potassium iodide (100 g.) and sodium acetate (500 g.) in water (1 l.)]. The iodine liberated was titrated against 0·005N-sodium thiosulphate (starch indicator). The original strength of the solution of lead tetra-acetate was also estimated. The rate constants were calculated in the usual way from straight-line plots of $\log_{10} a(b - x)/b(a - x)$ against time.

(iii) The *diacetate*, prepared in the usual way by using pyridine and acetic anhydride, separated from light petroleum as prisms, m. p. 97—98° (Found: C, 70·0; H, 5·4. $C_{19}H_{18}O_5$ requires C, 69·95; H, 5·5%). Hydrolysis of the diacetate (100 mg.) with a boiling mixture of 40% aqueous sodium hydroxide (1 ml.) and ethanol (4 ml.) or reduction with lithium aluminium hydride in ether gave 2,3-*trans*-flavan-3,4-*cis*-diol (60 mg.), m. p. and mixed m. p. 162—163°.

This diacetate in chloroform gave $\tau = 7{\cdot}87$ (axial OAc) and 8·16 (equatorial OAc).

In general, proton magnetic resonance spectra were recorded at 29·913 mc./sec. on a high-resolution spectrometer described previously.[17] Chemical shifts were measured relative to tetramethylsilane as an internal standard and are quoted as τ values.[18] The instrument was adjusted to repeat the recordings of each spectrum five times, and the base line was calibrated by the conventional side-band technique. The compounds were dissolved in chloroform which had been washed twice with concentrated sulphuric acid and three times with water, followed by distillation.

(iv) *Carbonate.* The diol (100 mg.) in benzene (6 ml.), ethyl chloroformate (1 ml.), and dioxan (1 ml.) was treated with triethylamine (1 ml.) and kept at room temperature overnight. Filtration, removal of the solvent, and crystallisation of the residue from light petroleum gave 2,3-trans-*flavan*-3,4-cis-*diol carbonate* (65 mg.), m. p. 134·5—135° (Found: C, 71·7; H, 4·45. $C_{16}H_{12}O_4$ requires C, 71·65; H, 4·5%), $\nu_{max.}$ 1815 and 1797 cm.$^{-1}$ (cyclic carbonate).[19] Bognâr *et al.*[3c] report m. p. 159° for a carbonate prepared by the action of carbonyl chloride on the diol.

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[15] Cordner and Pausacker, *J.*, 1953, 102.
[16] Eichelberger and LaMer, *J. Amer. Chem. Soc.*, 1933, **55**, 3633.
[17] Leane, Richards, and Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.
[18] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.
[19] Angell, *Trans. Faraday Soc.*, 1956, **52**, 1178.

(v) *Isopropylidene derivative.* The diol (100 mg.) was shaken with anhydrous copper sulphate (1·00 g.) in acetone (30 ml.) for 8 days at room temperature. Filtration, removal of the solvent, and crystallisation from methanol gave the isopropylidene derivative (80 mg.) as needles, m. p. 112·5—113·5° (Found: C, 76·6, 77·0, 76·2; H, 6·6, 6·6, 6·2. Calc. for $C_{18}H_{18}O_3$: C, 76·6; H, 6·4%), $\nu_{max.}$ 884 cm.$^{-1}$ (CMe_2O_2;[20] not present in original diol). Bognár *et al.*[3c] report m. p. 110—111°.

2,3-trans-*Flavan*-3,4-trans-*diol*.—(i) *Preparation*. The methods described by Bognár and Rákosi[3b] gave crude material, m. p. 135—141°. Chromatography on silica films in ethyl acetate–light petroleum (1 : 1 v/v) showed the presence of 3-hydroxyflavone (yellow fluorescent spot in ultraviolet light, yellow in daylight, R_F 0·55), 3-hydroxyflavanone (white fluorescent spot in ultraviolet light, R_F 0·49), and flavan-3,4-diol (brown spot with antimony trichloride, R_F 0·24). Recrystallisation from aqueous methanol gave needles, m. p. 139—142°, which contained 3-hydroxyflavanone and flavan-3,4-diol. Chromatography of this mixture (1·20 g.) on alumina (15% deactivated; 30 g.) and elution with ether (50 ml.) gave 3-hydroxyflavanone (0·086 g.) which separated from benzene as needles, m. p. and mixed m. p. 178—180°. Further elution with ether (150 ml.) gave 2,3-*trans*-flavan-3,4-*trans*-diol (0·86 g.), needles (from methanol), m. p. 146—146·5° (Found: C, 74·1; H, 5·85. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%), $\nu_{max.}$ 3260 (OH), 755, 698 cm.$^{-1}$ (aromatic), R_F 0·24 on a silica film (one spot, brown, antimony trichloride).

(ii) *Rate of reaction with lead tetra-acetate.* This reaction had k 0·036 mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(iii) The *diacetate* separated from light petroleum as prisms, m. p. 92—93·5° (Found: C, 70·1; H, 5·4. $C_{19}H_{18}O_5$ requires C, 69·95; H, 5·5%). Hydrolysis of the diacetate (100 mg.) with a boiling mixture of 40% aqueous hydroxide (1 ml.) and ethanol (4 ml.) gave 2,3-*trans*-flavan-3,4-*trans*-diol (60 mg.), m. p. and mixed m. p. 146—147°.

The diacetate in chloroform gave τ 8·02 and 8·16 (equatorial acetoxy-groups).

(iv) *Carbonate.* By the method described above for the *cis*-diol the 3,4-*trans*-diol (100 mg.) gave the *carbonate* (60 mg.) as needles, m. p. 129—130·5°, from hexane (Found: C, 71·9; H, 4·55. $C_{16}H_{12}O_4$ requires C, 71·65; H, 4·45%), $\nu_{max.}$ 1845 and 1818 cm.$^{-1}$ (cyclic carbonate). The mixed m. p. of this carbonate with that from the *cis*-diol was 100—112°.

(v) The 3,4-*trans*-diol (100 mg.) was treated with copper sulphate and acetone as described above. The product was an oil whose infrared spectrum showed the presence of 3-hydroxyflavanone. Chromatography on silica films showed the presence of four compounds with R_F 0·26, 0·54, 0·49, and 0·60 (pink spot with antimony trichloride) corresponding respectively to markers of flavan-3,4-diol, 3-hydroxyflavone, 3-hydroxyflavanone, and the isopropylidene derivative of the 3,4-*cis*-diol. Several recrystallisations of the oil from acetone–water (2 : 1 v/v) gave a solid which was chromatographed on alumina in benzene and recrystallised from methanol to yield the isopropylidene derivative of 2,3-*trans*-flavan-3,4-*cis*-diol (12 mg.) as needles, m. p. and mixed m. p. 113—114°, hydrolysed by dilute acid to the *cis*-diol.

6-*Methyl*-2,3-trans-*flavan*-3,4-cis-*diol*.—(i) 3-*Hydroxy*-6-*methyl*-2,3-trans-*flavan*-4-*one*. 2′-Hydroxy-5′-methylchalcone (3·80 g.) in fine suspension in ethanol (30 ml.) was treated with a mixture of aqueous hydrogen peroxide (30% v/v) (4·80 ml.) and 2N-sodium hydroxide (3·90 ml.) in one portion. After 4 hr. at 30° with occasional shaking, the mixture was acidified (60 ml. of 1·7% aqueous sulphuric acid), and the precipitate was separated, washed with water, and crystallised from methanol (50 ml.), to give yellow needles (0·10 g.) of 3-hydroxy-6-methylflavone, m. p. 201—202°. Auwers and Müller[21] give m. p. 196—197°. Evaporation of the mother liquor and two recrystallisations of the residue from benzene gave 3-*hydroxy*-6-*methyl*-2,3-trans-*flavan*-4-*one* as needles (1·50 g.), m. p. 147—149° (Found: C, 75·3; H, 5·7. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%), $\nu_{max.}$ (in EtOH) 216·5, 254, and 329 mμ (log ε 4·51, 3·94, and 3·52), $\nu_{max.}$ 3420 (OH) and 1692 cm.$^{-1}$ (C=O).

(ii) (a) 6-*Methyl*-2,3-trans-*flavan*-3,4-cis-*diol*. The above flavanone (1·00 g.) was reduced in the usual way with lithium aluminium hydride (0·30 g.) and aluminium chloride (2·30 g.) in tetrahydrofuran (40 ml.). Recrystallisation of the product from methanol gave the 3,4-cis-*diol* (0·75 g.) as needles, m. p. 178—179° (Found: C, 75·4; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·25%), $\nu_{max.}$ 3230, 3510 (infl.) (OH), 825, 817, 774, 753, 698, and 688 cm.$^{-1}$ (aromatic).

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[20] Ginsburg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.

[21] Auwers and Müller, *Ber.*, 1908, **41**, 4239.

Its reaction with lead tetra-acetate had $k = 0{\cdot}24$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(b) The *carbonate*, prepared in the usual way, separated from benzene–light petroleum (1 : 2 v/v) as needles, m. p. 173—174° (Found: C, 72·45; H, 5·15. $C_{17}H_{14}O_4$ requires C, 72·35; H, 5·0%), $\nu_{max.}$ 1818 and 1792 (infl.) cm.$^{-1}$ (cyclic carbonate).

(c) *Isopropylidene derivative.* The diol (80 mg.) with acetone and copper sulphate gave an oil which yielded a solid (40 mg.) on crystallisation from aqueous methanol. Recrystallisation from methanol gave the *isopropylidene derivative* as needles, m. p. 91·5—92·5° (Found: C, 76·65; H, 6·8. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%), $\nu_{max.}$ 884 cm.$^{-1}$ (CMe_2O_2). Evaporation of the mother liquors gave an oil which was chromatographed on alumina (10% deactivated; 10 g.); elution with benzene (20 ml.) gave an oil (8 mg.) which was discarded; elution with ether (30 ml.) gave the unchanged diol (20 mg.), m. p. and mixed m. p. 178—179°.

6-*Methyl*-2,3-trans-*flavan*-3,4-trans-*diol*.—(i) *Preparation.* 3-Hydroxy-6-methylflavanone (1·00 g.) on reduction with lithium aluminium hydride gave the 3,4-trans-*diol* (0·80 g.) which separated from methanol as needles, m. p. 118—119° (Found: C, 75·4; H, 5·95%), $\nu_{max.}$ 3230 (OH), 864, 822, 773, 752, and 698 cm.$^{-1}$ (aromatic).

Its reaction with lead tetra-acetate had $k = 0{\cdot}079$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The *diacetate* separated from light petroleum as prisms, m. p. 106—107° (Found: C, 70·5; H, 6·1%).

(iii) The *carbonate* separated from benzene–hexane as needles, m. p. 159·5—161° (Found: C, 72·6; H, 5·1%), $\nu_{max.}$ 1828 and 1795 cm.$^{-1}$ (cyclic carbonate).

(iv) Treatment of the diol (80 mg.) with acetone and copper sulphate gave an oil which on several recrystallisations from methanol gave the isopropylidene derivative of the 3,4-*cis*-diol (9 mg.) as needles, m. p. and mixed m. p. 91—92°.

4′-*Methoxy*-2,3-trans-*flavan*-3,4-cis-*diol*.—(i) *Preparation.* Reduction of 3-hydroxy-4′-methoxy-2,3-*trans*-flavan-4-one (1·35 g.) with lithium aluminium hydride and aluminium chloride in tetrahydrofuran yielded the 3,4-cis-*diol* (0·97 g.) as needles (from methanol), m. p. 160—161° (Found: C, 70·85; H, 6·4. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

(ii) *Reaction with lead tetra-acetate.* Treatment of the diol (500 mg.) in the usual way gave 2-*p*-methoxyphenylbenzofuran [6] (156 mg.) as plates, m. p. and mixed m. p. 150—151°, identical in infrared and ultraviolet spectra with authentic material.

This reaction had $k = 0{\cdot}29$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(iii) The *diacetate* separated from ethyl acetate–light petroleum as prisms, m. p. 100—102° (Found: C, 67·0; H, 5·5; Ac, 24·05. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6; 2Ac, 24·15%).

(iv) The *carbonate* separated from benzene–hexane (1 : 2 v/v) as needles, m. p. 185·5—187° (Found: C, 68·45; H, 4·8. $C_{17}H_{14}O_5$ requires C, 68·45; H, 4·7%), $\nu_{max.}$ 1800 and 1772 cm.$^{-1}$ (cyclic carbonate).

(v) Prepared in the usual way by treatment of the diol (100 mg.) with acetone and copper sulphate, the *isopropylidene derivative* separated from methanol as needles (79 mg.), m. p. 110—110·5° (Found: C, 72·7, 73·05; H, 6·3, 6·6. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%), $\nu_{max.}$ 878 cm.$^{-1}$ (CMe_2O_2).

4′-*Methoxy*-2,3-trans-*flavan*-3,4-trans-*diol*.—(i) *Preparation.*[6] The crude diol was obtained as needles, m. p. 172—176°. Examination on a silica film in ethyl acetate–light petroleum (1 : 1 v/v) showed the presence of 3-hydroxy-4′-methoxyflavanone (white fluorescent spot in ultraviolet light, R_F 0·43) and the 3,4-*trans*-diol (brown spot with antimony trichloride, R_F 0·20). Several recrystallisations from aqueous methanol (50% v/v) and finally one from methanol gave the diol as needles, m. p. 177—177·5° (Found: C, 70·5; H, 5·7%). Examination on a silica film showed one spot (brown, antimony trichloride) of R_F 0·20.

Its reaction with lead tetra-acetate had $k = 0{\cdot}039$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(ii) The *diacetate* separated from light petroleum as plates, m. p. 92—93° (Found: C, 67·4; H, 5·8; Ac, 24·25, 23·85%).

(iii) The *carbonate* separated from hexane as needles, m. p. 190—191° (Found: C, 68·85; H, 4·95%), $\nu_{max.}$ 1842 and 1810 cm.$^{-1}$ (cyclic carbonate).

Treatment of the diol (100 mg.) with acetone and copper sulphate in the usual way gave the unchanged diol (90 mg.), m. p. and mixed m. p. 177—178°.

4′-*Methoxy*-6-*methyl*-2,3-trans-*flavan*-3,4-cis-*diol*.—(i) *Preparation.* 3-Hydroxy-4′-methoxy-6-methyl-2,3-*trans*-flavan-4-one (1·00 g.) was reduced in the usual way with lithium aluminium hydride (0·30 g.) and aluminium chloride (2·10 g.) in tetrahydrofuran (75 ml.). Crystallisation of the product from tetrahydrofuran gave the 3,4-*cis*-diol (0·585 g.) as needles, m. p. 192·5—194° (Found: C, 71·1; H, 6·45. Calc. for $C_{17}H_{18}O_4$: C, 71·3; H, 6·3%). Kulkarni and Joshi[3a] and Bognár *et al.*[3c] record m. p. 193°. Its reaction with lead tetra-acetate had $k = 0{\cdot}43$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The diacetate separated from light petroleum as prisms, m. p. 97—98° (Found: C, 68·0; H, 6·1. Calc. for $C_{21}H_{22}O_6$: C, 68·1; H, 6·0%). Kulkarni and Joshi[3a] record m. p. 98°. This diacetate in chloroform gave $\tau = 7{\cdot}84$ (axial OAc) and 8·14 (equatorial OAc).

(iii) The *carbonate* separated from light petroleum–benzene (1 : 2 v/v) as needles, m. p. 167—168° (Found: C, 69·25; H, 4·8. $C_{18}H_{16}O_5$; requires C, 69·25; H, 5·1%), $\nu_{max.}$ 1797 cm.$^{-1}$ (cyclic carbonate).

(iv) The diol (90 mg.) with acetone and copper sulphate gave, in the usual way, a solid isopropylidene derivative (86 mg.) which separated from methanol as needles (62 mg.), m. p. 129—130° (Found: C, 73·75; H, 6·85. Calc. for $C_{20}H_{22}O_4$: C, 73·6; H, 6·75%). Bognár *et al.*[3c] give m. p. 126—127°. The mother-liquors afforded only unchanged diol (12 mg.), m. p. and mixed m. p. 191—193°.

4′-*Methoxy*-6-*methyl*-2,3-trans-*flavan*-3,4-trans-*diol*.—(i) *Preparation.* 3-Hydroxy-4′-methoxy-6-methyl-2,3-*trans*-flavan-4-one (2·30 g.) was reduced with lithium aluminium hydride (0·70 g.) in boiling ether (60 ml.). Crystallisation of the product from ether gave the 3,4-*trans*-diol (1·90 g.) as needles, m. p. 169—170°. Recrystallisation from methanol raised the m. p. to 172—173° (Found: C, 71·2; H, 6·4%). Kulkarni and Joshi[3a] give m. p. 169°.

Its reaction with lead tetra-acetate had $k = 0{\cdot}063$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The diacetate separated from light petroleum as prisms, m. p. 121—123° (Found: C, 67·9; H, 6·0%). Kulkarni and Joshi[3a] give m. p. 123°. This diacetate in chloroform gave $\tau = 7{\cdot}97$ and 8·17 (equatorial OAc).

(iii) The *carbonate* separated from light petroleum as needles, m. p. 136—137·5° (Found: C, 69·1; H, 5·1. $C_{18}H_{16}O_5$ requires C, 69·25; H, 5·1%), $\nu_{max.}$ 1826 and 1805 cm.$^{-1}$ (cyclic carbonate).

(iv) The 3,4-*trans*-diol (100 mg.) with acetone and copper sulphate gave a yellow solid (97 mg.) which on crystallisation from methanol yielded the isopropylidene derivative of the 3,4-*cis*-diol as needles (73 mg.), m. p. and mixed m. p. 129—130°. Hydrolysis of the isopropylidene derivative (15 mg.) with 2N-sulphuric acid (1 ml.) in ethanol (10 ml.) gave the 3,4-*cis*-diol (10 mg.), m. p. and mixed m. p. 191—193°.

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