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STEREOCHEMICAL STUDIES IN FLAVANOIDS

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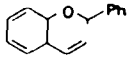
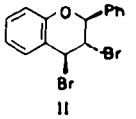
Abstract—The chemistry and stereochemistry of flav-3-ene derivatives are discussed. Three of the four possible racemates of 4-acetoxy-3-bromoflavans are described; the fourth racemate was obtained in a mixture with another isomer. Syntheses of trans-3-hydroxyflavan, the parent compound of the catechin series and of the acetate of *cis*-3-hydroxyflavan, parent compound of the epicatechin series, are outlined.

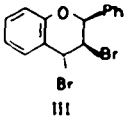
PREVIOUSLY we reported[1] that *cis*-hydroxylation of flav-3-ene by osmium tetroxide gave 2,3-*trans*-3,4-*cis*-flavan-3,4-diol. In extension of this work bromination of flav-3-ene (I) resulted in the formation of two isomeric 3,4-dibromoflavans, m.p. 118° and 103° respectively. On the basis of NMR data and of the expected *trans* addition of bromine, the former is regarded as 2,3-*trans*-3,4-*trans*-3,4-dibromoflavan (II) ($J_{3,3}$ = 9·5 c/s, $J_{3,4}$ = 7·8 c/s) and the latter, m.p. 103°, ($J_{2,3}$ = 2·0, $J_{3,4}$ = 1·2 c/s) as 2,3-*cis*-3,4-*trans*-3,4-dibromoflavan (III). The possibility that (III) is an all *trans* rotamer of (II) having the phenyl group on carbon-2 and the two bromine atoms in axial conformations, which cannot be ruled out on the basis of NMR alone, is highly unlikely since this structure would have a large 1, 3 bromine-phenyl interaction.



I



II



III

Isolation of di-axial and di-equatorial dihalides on halogenation of various cholestenes has been accounted for by the suggestion that the initially formed di-axial products rearrange to the *trans* di-equatorial isomers.[2] Neither 2,3-*cis*-3,4-*trans*-3,4-dibromoflavan (III) nor its 2,3-*trans*-3,4-*trans* isomer (II) undergo this type of rearrangement. The production of both isomers was therefore attributed to the simultaneous formation of the bromonium ions (IV and V), followed in each case by *trans* opening and attack at the electronically favoured benzylic carbon atom, leading to di-axial as well as di-equatorial products. In the present case the geometry of the bromonium ions (Dreiding models) is such as to permit facile attack of an anion at position-4 from either side of the molecule and hence electronic rather than steric

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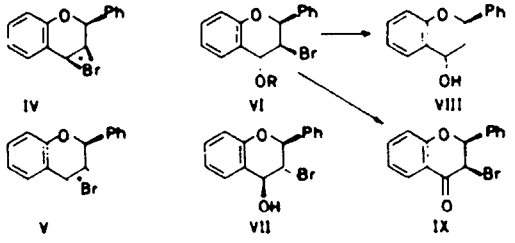
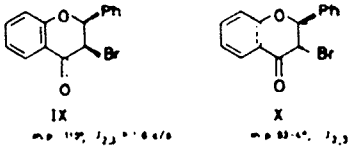
[1] K. G. Marathe, Eva M. Philbin and T. S. Wheeler, *Chem. & Ind.* 1793 (1962).
[2] G. H. Alt and D. H. R. Barton, *J. Chem. Soc.* 4284 (1954).

factors must govern the course of the reaction. In support of the above mechanism 2,3-*cis*-3,4-*trans*-3-bromoflavan-4-ol (VI; R = H) acetate, m.p. 133° ($J_{2,3}$ = 1·7 c/s, $J_{3,4}$ = 2·3 c/s) and 2,3-*trans*-3,4-*trans*-3-bromoflavan-4-ol (VII) acetate, m.p. 141° ($J_{2,3}$ = 9·2 c/s, $J_{3,4}$ = 8·3 c/s) have been obtained from the action of N-bromsuccinimide–sulphuric acid on flav-3-ene. These compounds are evidently formed by attack of hydroxide ions at position 4 of the bromonium ions (IV and V).



Treatment of 2,3-*cis*-3,4-*trans*-3,4-dibromoflavan (III) with silver acetate gave 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan (VI; R = Ac). Retention of configuration at positions −3 and −4 in this reaction suggests that it takes place via the intermediate IV with neighbouring group participation by the 3-axial bromine atom. Reduction of compound VI (R = Ac) with lithium aluminium hydride gave flavan-4α-ol (VIII).[3] Sodium borohydride treatment of this acetate followed by oxidation of the resulting bromohydrin VI (R = H) with chromium trioxide gave *cis*-3-bromoflavanone (IX), m.p. 110°.

The two 3-bromoflavanones were prepared according to the method described by Bognar *et al.*[4] and are found by a study of their NMR spectra to have the stereochemistry shown at IX and X. These assignments are in agreement with those



observed by Clark-Lewis *et al.*[5] for the 3-bromo derivatives of 6-methyl-4′-methoxy- and 6-methyl-3′,4′-dimethoxy-flavanones.

When 2,3-*trans*-3,4-*trans*-3,4-dibromoflavan (II) was treated with silver acetate a product which was shown to be 60–40% mixture of 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*- 4-acetoxy-3-bromoflavan resulted. Although it was not possible to effect a separation of these isomers, the NMR characteristics of each could be clearly detected. Since a spectrum of pure 2,3-*trans*-3,4-*trans*-4-acetoxy-3-bromoflavan was available assignment of signals to the 2,3-*trans*-3,4-*cis*-isomer ($J_{2,3}$ = 10·4, $J_{3,4}$ = 3·5 c/s) in the spectrum of the mixture was relatively simple.

The fourth racemate of 4-acetoxy-3-bromoflavan, the 2,3-*cis*-3,4-*cis*-isomer, m.p.

[3] C. P. Lillya, D. Kehoe, E. M. Philbin, M. A. Vickars and T. S. Wheeler, *Chem. & Ind.* 84 (1963); B. J. Bolger, A. Hirwe, K. G. Marathe, E. M. Philbin, M. A. Vickars and C. P. Lillya, *Tetrahedron* 22, 621 (1966).

[4] R. Bognar, M. Rakosi and Gy. Litkei, *Acta Chim. Hung.* 34, 353 (1962).

[5] J. W. Clark-Lewis, T. McL. Spotswood and L. R. Williams, *Austral. J. Chem.* 107 (1963).

125° was prepared by reduction of 2,3-*cis*-3-bromoflavanone[4] with sodium borohydride and acetylation of the product with pyridine-acetic anhydride.

For comparison purposes the NMR data for the four possible racemates of 4-acetoxy-3-bromoflavan are given in Table 1 and compare well with similar data for the flavan-3,4-diols.[6] In metal hydride reductions of flavanones, 2,3-dihydroflavonols[7] and 3-bromoflavanones[5] the hydroxyl group generated is the equatorial isomer and is *cis* to the aryl group at position-2.

TABLE 1. SPECTRAL PARAMETERS FOR 4-ACETOXY-3-BROMOFLAVANS

	Chemical shifts (τ)[a]			Coupling constants in c/s[b]	
	2H	3H	4H	$J_{2,3}$	$J_{3,4}$
2,3-*cis*-3,4-*cis*	4·63	5·4	3·6	1·5	4·5
2,3-*cis*-3,4-*trans*	4·67	5·6	3·7	1·7	2·3
2,3-*trans*-3,4-*trans*	4·65	5·37	3·5	9·2	8·3
2,3-*trans*-3,4-*cis*	4·6	5·36	3·74	10·4	3·5

[a] Tetramethylsilane was used as internal standard in deuteriochloroform solution

[b] Coupling constants are accurate to ±0·2 c/s.

Treatment of 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan (VI; R = Ac) with methanolic potassium hydroxide for 30 min furnished *trans*-flav-3-ene epoxide (XI; $J_{2,3} = 1$, $J_{3,4} = 4·6$ c/s), m.p. 106°. The bromoacetate VI (R = Ac) or the latter epoxide on prolonged treatment with methanolic potassium hydroxide gave 2,3-*trans*-3,4-*trans*-3-hydroxy-4-methoxyflavan (XII), m.p. 143°. The structure of this methoxyflavan was assigned on the basis of NMR data; the large coupling values $J_{2,3} = 9·5$ c/s, $J_{3,4} = 8·5$ c/s, are characteristic of *trans* di-axial hydrogens, and clearly indicate a *trans-trans* stereochemistry. Since attack by methoxide ion on the *trans*-flav-3-ene epoxide (XI) would give either XIII or XII depending upon whether attack was at carbon 3 or 4 it is clear from the above assignments of stereochemistry that the product must be XII.

A hydroxymethoxyflavan was also the product when 2,3-*trans*-3,4-*trans*-4-acetoxy-3-bromoflavan was similarly treated with methanolic alkali. By analogy with the results quoted above and with those obtained by other workers[8] the compound is regarded as 2,3-*cis*-3,4-*trans*-3-hydroxy-4-methoxyflavan ($J_{2,3} = 0$, $J_{3,4} = 0$, $J_{OH,3} = 6$ c/s), formed via the intermediate *cis*-flav-3-ene epoxide.

Anionic attack at position-4 also occurred when a solution of the *trans*-epoxide (XI) in diethyl ether was treated with hydrochloric acid gas. The product of this reaction was 2,3-*trans*-3,4-*cis*-4-chloro-3-hydroxyflavan (XIV; $J_{2,3} = 9·4$, $J_{3,4} = 2·8$ c/s) formed by *cis*-opening[9] of the epoxide ring.

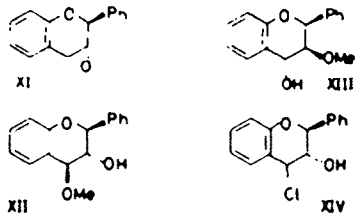
As regards the geometry of *trans*-flav-3-ene epoxide, apart from the method of preparation a further proof of the assigned stereochemistry was obtained when the epoxide was reduced with LAH. The product formed by preferential reduction at the

[4] M. A. Vickars, *Tetrahedron* **20**, 2873 (1964).

[7] R. Bognar, M. Rakosi, H. Fletcher, E. M. Philbin and T. S. Wheeler, *Tetrahedron* **19**, 391 (1963).

[6] J. W. Clark-Lewis and L. R. Wilson, *Austral. J. Chem.* **18**, 90 (1965); C. G. Joshi and A. B. Kulkarni, *J. Indian Chem. Soc.* **10**, 34 (1957).

[8] C. C. Tung and A. J. Speziale, *Chem. & Ind.* 1985 (1963); H. H. Wasserman and N. E. Aubrey, *J. Amer. Chem. Soc.* **78**, 1726 (1956).



benzylic carbon atom at position-4 was *trans*-3-hydroxyflavan, m.p. 110°, characterized as its acetate, m.p. 53° ($J_{2,3}$ = 6 c/s, $J_{3,4a} + J_{3,4e}$ = 10 c/s). The low $J_{2,3}$ = 6 c/s value was comparable with that ($J_{2,3}$ = 6·7 c/s) obtained for the 3-acetyl derivative of *O*-tetramethylcatechin.[10] Further 2,3-*trans*-3,4-*trans*-flavan-3,4-diol[11] on catalytic reduction with palladous chloride, or 2,3-*trans*-3,4-*cis*-4-chloro-3-hydroxyflavan on treatment with lithium aluminium hydride gave *trans*-3-hydroxyflavan identical with that obtained from the *trans*-epoxide XI.

The reduction of the epoxide function to an equatorial hydroxyl on position-3 is unusual as epoxides preferentially open to give di-axial products. However, recently, an analogous opening of an epoxide ring in an aromatic A ring steroid has also been attributed to the benzylic nature of the epoxidic carbon atom.[12] Similar reduction of *cis*-flav-3-ene epoxide[13] with LAH gave an oil, which on acetylation gave *cis*-3-acetoxyflavan, m.p. 110° ($J_{2,3}$ = 1·0 c/s). This reaction again showed preference for attack at the benzylic carbon of the flavan structure.

In the case of conformationally rigid *cis*-bromohydrins the action of alkali usually gives ketones rather than epoxides.[14,15] However, treatment of 2,3-*cis*-3,4-*cis*-4-acetoxy-3-bromoflavan with methanolic potassium hydroxide gave an unstable bromine free compound, m.p. 88° which decomposed on standing. It yielded flav-2-ene[1] on reduction with lithium aluminium hydride and gave flavylium chloride[16] with hydrochloric acid gas in dry ether. These reactions could best be accommodated by assigning a 4-hydroxyflav-2-ene structure to the compound which presumably resulted from di-axial dehydrobromination from the 2,3-sites. The IR spectrum showed the presence of a hydroxyl group and oxidation with active manganese dioxide[17] gave flavone[18] in good yield. Attempts to prepare a derivative of the hydroxyl function failed, probably due to its allylic nature.[15]

EXPERIMENTAL

NMR spectra: a Varian Associates A-60 spectrometer at 60 mc; Chemical shifts relative to TMS as an internal standard.

Bromination of flav-3-ene. Br (2·8 g) in CCl_4 (40 ml) was added to a cooled soln of flav-3-ene[1] (4 g) in CCl_4 (30 ml). The solvent was removed after 24 hr and fractional crystallization of the oily residue from pet. ether (b.p. 60–80°) gave 2,3-cis-3,4-trans-3,4-*dibromoflavan* (3·1 g) in cubes, m.p.

[10] J. W. Clark-Lewis, L. M. Jackman and T. M. Spotswood, *Austral. J. Chem.* 632 (1964).
[11] E. J. Corey, E. M. Philbin and T. S. Wheeler, *Tetrahedron Letters* 429 (1961).
[12] O. Wintersteiner, M. Moore and A. I. Cohen, *J. Org. Chem.* **29**, 1325 (1964).
[13] Method of preparation kindly supplied by Dr. M. A. Vickars (unpublished work).
[14] D. H. R. Barton, D. A. Lewis and J. F. McGhie, *J. Chem. Soc.* 2907 (1957).
[15] A. Hassner and T. C. Mead, *Tetrahedron* **20**, 2201 (1964).
[16] A. Lowenbein, E. Pongracz and E. A. Spiess, *Ber. Dtsch. Chim. Ges.* **54**, 1517 (1924).
[17] G. Stork and M. Tomasz, *J. Amer. Chem. Soc.* **86**, 471 (1964).
[18] W. Feuerstein and St. v. Kostanecki, *Ber. Dtsch. Chim. Ges.* **31**, 1757 (1898).

103°. (Found: C, 49·1; H, 3·4; Br, 43·2. $C_{15}H_{10}Br_2O$ requires: C, 48·9; H, 3·3; Br, 43·4%) and 2,3-trans-3,4-trans-3,4-*dibromoflavan* (0·6 g) in needles, m.p. 118°. (Found: C, 49·4; H, 3·3; Br, 42·7%. Requires: as above.) No rearrangement occurred when either dibromide was refluxed for 5 hr in CCl_4.

Action of N-*bromosuccinimide-sulphuric acid on flav*-3-*ene*. N-bromosuccinimide (0·8 g) in acetone was added slowly in two portions at 30 min intervals to a soln of flav-3-ene (0·5 g) in aqueous acetone 10 ml H_2O; 50 ml Me_2CO) and 1N H_2SO_4 (0·8 ml). After addition of the first portion, water (9 ml) was added and after the second portion additional 1N H_2SO_4 (0·35 ml) was added and the mixture was stirred for 5 hr. The soln was diluted with water and extracted with ether. The ethereal layer was washed with water and dried. Removal of the ether gave an oily residue from which a solid precipitated. The oil was soluble in pet. ether (b.p. 60–80°). Crystallization of the solid from a pet. ether–benzene mixture gave in needles 2,3-*trans*-3,4-*trans*-3-bromoflavan-4-ol (0·07 g), m.p. 195° (lit.[9] m.p. 195°). This compound was identical (m.p. and IR spectrum) with a sample prepared by reduction of *trans*-3-bromoflavanone with $NaBH_4$;[9] acetate (pyridine–Ac_2O) needles, m.p. 141°, from pet. ether. (Found: C, 58·3; H, 4·4; Br, 23·1. $C_{17}H_{15}BrO_3$ requires: C, 58·8; H, 4·3; Br, 23·1%). The acetate of the oil fraction was 2,3-cis-3,4-trans-4-*acetoxy*-3-*bromoflavan* (see below).

Bromination of flavanone. Br (16·9 g) in $CHCl_3$ (25 ml) was added to a soln of flavanone (24 g) in $CHCl_3$ (250 ml). After 24 hr the solvent was removed. Fractional crystallization of the residue from pet. ether (b.p. 60–80°) gave *cis*-3-bromoflavanone[4] (11·5 g), m.p. 110°, and *trans*-3-bromoflavanone[4] (2·5 g), m.p. 93–94°.

Action of silver acetate on 2,3-cis-3,4-trans-3,4-*dibromoflavan*. AcOAg (0·3 g) was added to a soln of 2,3-*cis*-3,4-*trans*-3,4-dibromoflavan (0·5 g) in AcOH (7 ml) and the mixture refluxed for 1 hr. Precipitated AgBr was removed and the filtrate was diluted with water. The resulting ppt crystallized from pet. ether (b.p. 60–80°) in plates of 2,3-cis-3,4-trans-4-*acetoxy*-3-*bromoflavan* (0·34 g), m.p. 133°. (Found: C. 58·4; H, 4·3; Br, 22·8. $C_{17}H_{15}BrO_3$ requires: C, 58·8; H, 4·3; Br, 23·1%.)

Lithium aluminium hydride reduction of 2,3-cis-3,4-trans-4-*acetoxy*-3-*bromoflavan*. LAH (1 g) was added to a soln of 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan (1 g) in dry ether (60 ml) and the soln refluxed for 6 hr. The ethereal layer was washed with 10% HCl, water, and dried. Removal of the ether under red. press. gave flavan-4α-ol[9] (0·25 g), m.p. 118° (identified by mixed m.p. and comparison of its IR spectrum with that of an authentic sample).

Action of sodium borohydride on 2,3-cis-3,4-trans-4-*acetoxy*-3-*bromoflavan*. $NaBH_4$ (0·23 g) was added slowly to a soln of 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan (1·36 g) in MeOH (50 ml) and the mixture allowed to stand for 24 hr. Water was added and the mixture extracted with ether. Removal of the ether gave 2,3-*cis*-3,4-*trans*-3-bromoflavan-4-ol as an oil which decomposed on distillation and which was directly oxidized to the bromoflavanone.

Oxidation of 2,3-cis-3,4-trans-3-*bromoflavan-4-ol with chromium trioxide*. 2,3-*cis*-3,4-*trans*-3-Bromoflavan-4-ol (1 g) obtained as described in the previous experiment was dissolved in AcOH (300 ml) and the soln cooled to 0–5°. A soln of CrO_3 (0·8 g) in aqueous acetone (66%; 118 ml) was added and the mixture was stirred for 5 hr and poured into ice-water. The ether extract of this mixture was washed with 5% $NaHCO_3$aq and dried. Removal of the ether and crystallization of the residue from pet. ether (b.p. 60–80°) gave *cis*-3-bromoflavanone in prisms (0·63 g). m.p. 110°. The identity of this compound was confirmed by mixed m.p. and comparison of its IR spectrum with that of an authentic sample.[4]

Action of silver acetate on 2,3-trans-3,4-trans-3,4-*dibromoflavan*. AcOAg (0·4 g) was added to a solution of 2,3-*trans*-3,4-*trans*-3,4-dibromoflavan (0·4 g) in AcOH (10 ml) and the soln was refluxed for 1 hr. AgBr which precipitated was removed and the filtrate was diluted with water. The resulting ppt was crystallized from pet. ether (b.p. 60–80°) and gave a product, m.p. 131°. NMR studies on this product showed the presence of 2,3-*trans*-3,4-*trans*-4-acetoxy-3-bromoflavan and 2,3-*trans*-3,4-*cis*-4-acetoxy-3-bromoflavan. These compounds could not be separated by fractional crystallization; furthermore, only one spot was observed on a silica gel TLC run with pet. ether (b.p. 60–80°)-benzene (50% mixture).

2,3-cis-3,4-cis-4-*Acetoxy*-3-*bromoflavan*. Pyridine (5 ml) was added to a soln of 3-bromoflavan-4-ol (0·95 g), m.p. 142°,[9] in Ac_2O (25 ml) and the mixture was allowed to stand overnight. The solid obtained on pouring the mixture into ice–HCl crystallized from pet. ether (b.p. 60–80°) in plates of 2,3-cis-3,4-cis-4-*acetoxy*-3-*bromoflavan* (0·65 g), m.p. 125°. (Found: C, 59·2; H, 4·5; Br, 22·8. $C_{17}H_{15}BrO_3$ requires: C, 58·8; H, 4·3; Br, 23·1%.)

trans-*Flav*-3-*ene epoxide*. Methanolic KOH (2·8 g in 60 ml) was added to a soln of 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan (3·2 g) in MeOH (60 ml) and the soln was allowed to stand for 1 hr. Addition of water precipitated trans-*flav*-3-*ene epoxide* (1·62 g) which crystallized from pet. ether (b.p. 60–80°) in needles, m.p. 106°. (Found: C, 80·3; H, 5·3. $C_{15}H_{12}O_3$ requires: C, 80·3; H, 5·4%.)

2,3-trans-3,4-trans-3-*Hydroxy*-4-*methoxyflavan*. Methanolic KOH (0·4 g in 25 ml) was added to a soln of *trans*-flav-3-ene epoxide (0·8 g) in MeOH (25 ml) and the mixture was refluxed for 10 min. Water was added and the soln was extracted with ether. Removal of the ether and crystallization of the residue from EtOH gave 2,3-trans-3,4-trans-3-*hydroxy*-4-*methoxyflavan* (0·3 g), m.p. 143°. (Found: C, 75·0; H, 6·2; OMe, 12·4. $C_{16}H_{16}O_3$ requires: C, 75·0; H, 6·3; OMe, 12·1%.) This compound was also the product when the experiment was repeated using 2,3-*cis*-3,4-*trans*-4-acetoxy-3-bromoflavan instead of the epoxide.

2,3-*cis*-3,4-*trans*-3-*Hydroxy*-4-*methoxyflavan*. When 2,3-*trans*-3,4-*trans*-4-acetoxy-3-bromoflavan (0·29 g) was treated with methanolic alkali as described in the previous experiment the product was 2,3-*cis*-3,4-*trans*-3-hydroxy-4-methoxyflavan (0·19 g), m.p. 103–104°. (Found: C, 75·1; H, 6·4. $C_{16}H_{16}O_3$ requires: as above.)

Action of hydrochloric acid gas on trans-flav-3-*ene epoxide*. Dry HCl gas was passed through a soln of *trans*-flav-3-ene epoxide (0·63 g) in dry ether (50 ml) and the mixture allowed to stand for 12 hr. After washing with water and 5% $NaHCO_3$aq evaporation of the dried organic solvent gave a residue which crystallized from pet. ether (b.p. 60–80°) to yield 2,3-trans-3,4-cis-4-*chloro*-3-*hydroxyflavan* (0·59 g), m.p. 96°. (Found: C, 68·7; H, 5·0; Cl, 14·0. $C_{15}H_{13}ClO_3$ requires: C, 69·1; H, 5·0; Cl, 13·6%.)

trans-3-*Hydroxyflavan*. *trans*-Flav-3-ene epoxide (0·5 g) in dry ether (25 ml) was treated with LAH (0·4 g) and the soln was refluxed for 2 hr. The ethereal soln was washed with 10% HCl, water, and dried. Removal of the ether and crystallization of the residue from pet. ether (b.p. 60–80°) gave trans-3-*hydroxyflavan* in needles (0·4 g), m.p. 110°. (Found: C, 79·8; H, 6·2. $C_{15}H_{14}O_2$ requires: C, 79·6; H, 6·2%); *acetate* (Ac_2O-pyridine) needles, m.p. 53° (pet. ether b.p. 60–80°). (Found: C, 76·2; H, 6·2. $C_{17}H_{16}O_3$ requires: C, 76·1; H, 6·0%.) Similar treatment of 2,3-*trans*-4,3-3,4-*cis*-4-chloro-3-hydroxyflavan (0·2 g) in dry ether (30 ml) with LAH (0·2 g) also gave *trans*-3-hydroxyflavan (0·06 g), m.p. and mixed m.p. 110°.

Hydrogenolysis of 2,3-*trans*-3,4-*trans-flavan*-3,4-*diol*. 2,3-*trans*-3,4-*trans*-Flavan-3,4-diol[11] (0·75 g) in MeOH (30 ml) was hydrogenated over palladous chloride (0·1 g) at 60 atm/50° for 12 hr. The catalyst was filtered off, water was added and the mixture was extracted with $CHCl_3$. Evaporation of the $CHCl_3$ gave a white residue which was partly soluble in pet. ether (b.p. 60–80°). The pet. ether solution was filtered hot and reduced in volume. 2,3-*trans*-3-Hydroxyflavan (0·044 g) crystallized from the soln in needles, m.p. 110°. (Mixed m.p. with product from reduction of *trans*-flav-3-ene epoxide gave no depression.)

Treatment of 2,3-cis-3,4-cis-4-*acetoxy*-3-*bromoflavan with methanolic alkali*. Methanolic KOH (2·5 g in 30 ml) was added to a soln of 2,3-*cis*-3,4-*cis*-4-acetoxy-3-bromoflavan (3 g) in MeOH (70 ml). After 18 hr the soln was diluted with water and the solid obtained crystallized from pet. ether (b.p. 60–80°) in needles of 4-*hydroxyflav*-2-*ene* (1·1 g), m.p. 88°. (Found: C, 80·3; H, 5·5. $C_{15}H_{12}O_2$ requires: C, 80·3; H, 5·4%.)

Lithium aluminium hydride reduction of 4-*hydroxyflavan*-2-*ene*. 4-Hydroxyflav-2-ene (0·9 g) was refluxed with LAH (1·5 g) in dry ether (30 ml) for 3 hr. The ethereal layer was washed with water, 10% HCl and dried. Removal of the ether gave an oil which crystallized from MeOH in prisms of flav-2-ene (0·4 g), m.p. and mixed m.p.[1] 52°.

Action of hydrochloric acid gas on 4-*hydroxyflav*-2-*ene*. Dry HCl gas was passed through a soln of 4-hydroxyflav-2-ene (1 g) in dry ether (40 ml). A yellow ppt formed which was collected and washed with dry ether. The yellow solid was flavylium chloride (0·8 g), m.p. 84–86°. A mixed m.p. determination and a comparison of its IR spectrum with that of an authentic sample[16] confirmed its identity.

Oxidation of 4-*hydroxyflav*-2-*ene*. MnO_2 (3 g) was added to a stirred soln of 4-hydroxyflav-2-ene (0·4 g) in dry ether (30 ml). After 24 hr the soln was filtered and the ether dried and evaporated under red. press. The residue crystallized from MeOH in needles of flavone (0·2 g) m.p. 96°. (Mixed m.p.[19] confirmation.)

cis-3-*Acetoxyflavan*. LAH (0·1 g) was added to a soln of *cis*-flav-3-ene epoxide[19] (0·1 g) in dry ether and the mixture was refluxed on a steam-bath for 3 hr. Wet ether was added followed by water and the ether layer was washed with HCl, water, and dried. Evaporation of the ether gave an oil (0·07 g).

Pyridine (1 ml) was added to a soln of the oil in Ac_2O (3 ml) and the mixture allowed to stand overnight. The ppt obtained on pouring the mixture into ice-water crystallized from pet. ether (b.p. 60–80°) in colourless plates of cis-3-*acetoxyflavan* (0·04g), m.p. 110°. (Found: C, 76·2; H, 6·0. $C_{17}H_{16}O_3$ requires: C, 76·1; H, 6·0%.)

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