Reactions of Flav-2-enes and Flav-2-en-4-ones (Flavones)

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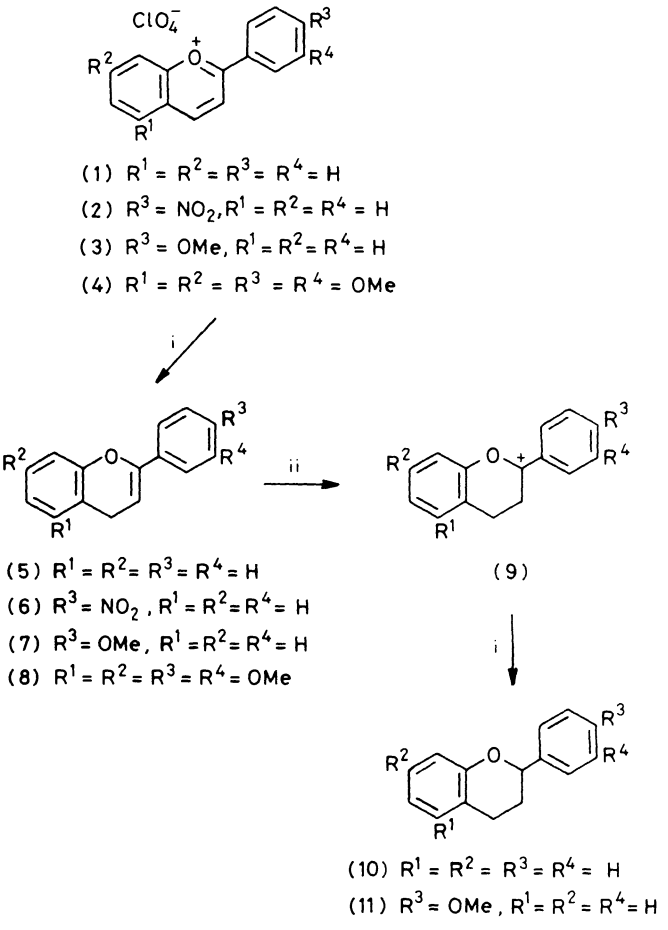
Flav-2-enes, flavones, and 3-alkyl ethers of flavonols add alcohols and carboxylic acids in the presence of *N*-bromosuccinimide to give 2-alkoxy- and 2-acyloxy-3-bromoflavans which provide routes to *cis*-3-bromoflavans by reduction and to 3,4-diols by elimination and reaction with osmium tetraoxide. The 2-acyloxyflavans react with alcohols yielding 2-alkoxyflavans. Flavonols react with *N*-bromosuccinimide and alcohols to give bromine-free hemiacetals, the known 2,3-dialkoxy-3-hydroxyflavanones.

Flav-2-enes and flav-2-en-4-ones (flavones) are readily available compounds which, in view of their expected reactivity, might be more widely exploited for the synthesis of other flavonoids. In this paper we describe some reactions of these compounds which we have used (see later papers) for the synthesis of polyflavonoids.

Flav-2-enes.—We obtained many of the flav-2-enes we required by the reduction of flavylium salts with lithium aluminium hydride [1] which is a quick and convenient method and appears to be of general applicability for the preparation of flav-2-enes unsubstituted at C-3 or C-2′. 3- and 2′-Substituted flavylium salts give considerable quantities of flav-3-enes on reduction with lithium aluminium hydride: 3,4′-dimethoxyflavylium chloride gave 40% of the 3-ene [2] and we have obtained 3-methylflav-3-ene (22%) and 3-methylflav-2-ene (53%) from 3-methylflavylium perchlorate and mixtures of the 2- and 3-enes from 2′-benzoyloxy- and 2′-methoxyflavylium salts so that the method is less useful for the preparation of 3- and 2′-substituted flav-2-enes. We have investigated the reduction of flavylium salts in acetic acid with sodium borohydride and with sodium cyanoborohydride. With sodium borohydride, flavylium perchlorate (1) gave 54% of flav-2-ene (5) containing a small proportion of a contaminant which was apparently (t.l.c.) flavan (10) (Scheme 1). With sodium cyanoborohydride, 4′-nitroflavylium perchlorate (2) gave 90% of 4′-nitroflav-2-ene (6); 4′-methoxyflavylium perchlorate (3), however, gave 79% of 4′-methoxyflavan (11) and the yield was similar (86%) with sodium borohydride in acetic acid. Analogously, 2′-methoxyflavylium perchlorate gave 62% of 2′-methoxyflavan with sodium cyanoborohydride. It seems probable that a flav-2-ene is always the initial product and that for further reduction to occur this enol ether must be protonated at C-3 [structure (9)], a reaction which can occur under these mild conditions only if the resulting positive charge is stabilised by a +M substituent suitably placed in the B-ring. In accordance with this mechanism, we have found that flav-2-ene (5), 3-bromoflav-2-ene (12), and 4-phenylflav-2-ene (13) are not reduced by sodium cyanoborohydride in acetic acid but that 4′-methoxy- (7), 3′,4′,5,7-tetramethoxy- (8), and 4′-methoxy-4-phenylflav-2-ene (14) give 60—80% yields of the corresponding flavans. 4-Phenylflav-2-ene (13) and 4′-methoxy-4-phenylflav-2-ene (14) were prepared by treating flavylium and 4′-methoxyflavylium perchlorates with phenyl magnesium bromide.[3]

3-Bromoflav-2-ene (12) was prepared by thermal decomposition of *cis*-2-acetoxy-3-bromoflavan (44) † as described below.

We have also prepared flav-2-enes by the reduction of



(1) $R^1 = R^2 = R^3 = R^4 = H$
(2) $R^3 = NO_2, R^1 = R^2 = R^4 = H$
(3) $R^3 = OMe, R^1 = R^2 = R^4 = H$
(4) $R^1 = R^2 = R^3 = R^4 = OMe$

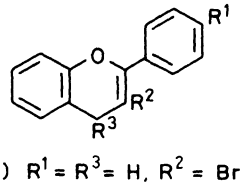
(5) $R^1 = R^2 = R^3 = R^4 = H$
(6) $R^3 = NO_2, R^1 = R^2 = R^4 = H$
(7) $R^3 = OMe, R^1 = R^2 = R^4 = H$
(8) $R^1 = R^2 = R^3 = R^4 = OMe$

(9)

(10) $R^1 = R^2 = R^3 = R^4 = H$
(11) $R^3 = OMe, R^1 = R^2 = R^4 = H$

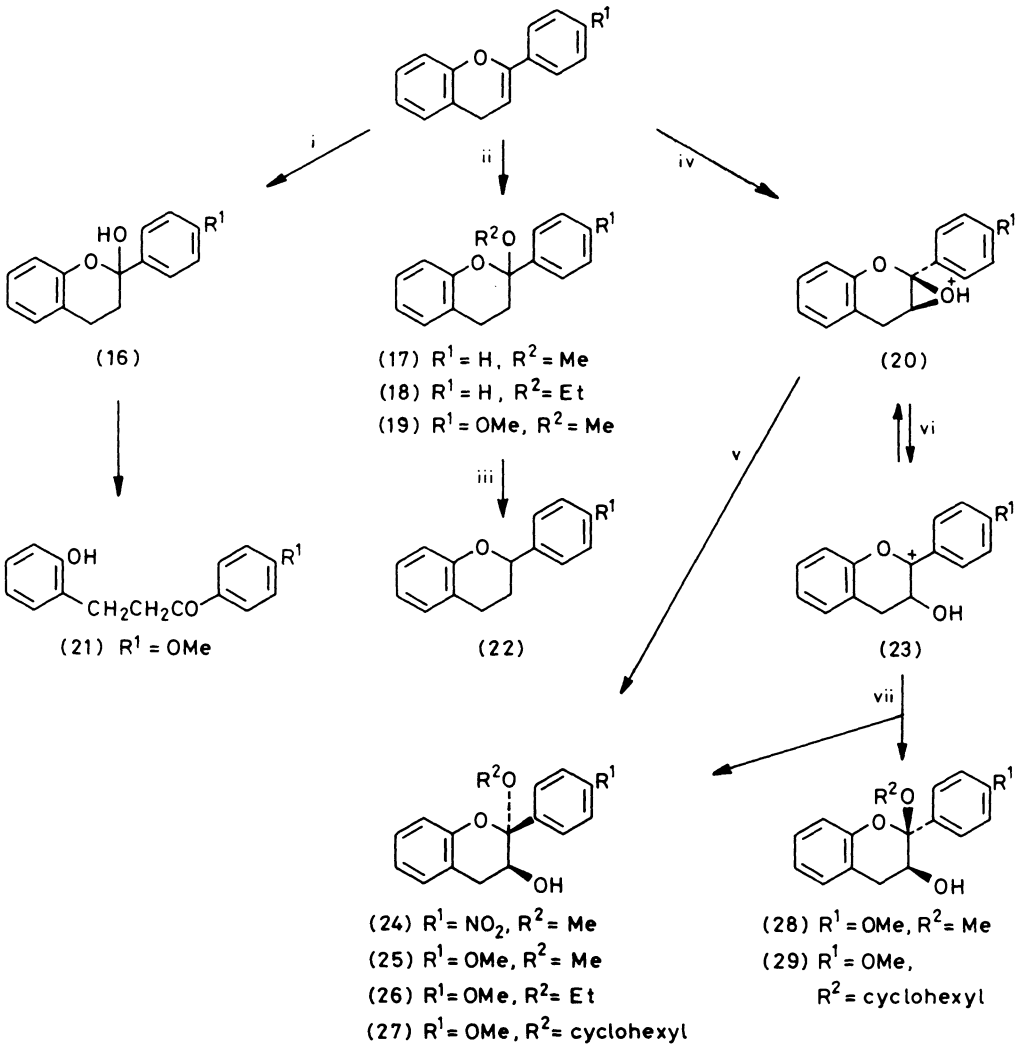
All compounds are racemic. Relative stereochemistry is indicated

Scheme 1. *Reagents:* i, $NaBH_3CN$–AcOH; ii, H^+



(12) $R^1 = R^3 = H, R^2 = Br$
(13) $R^1 = R^2 = H, R^3 = Ph$
(14) $R^1 = OMe, R^2 = H, R^3 = Ph$
(15) $R^1 = OMe, R^2 = Br, R^3 = H$

† The 2,3-stereochemistry in flavonoid compounds is defined by the relationship between the aryl group at C-2 and the substituent, other than hydrogen, at C-3.



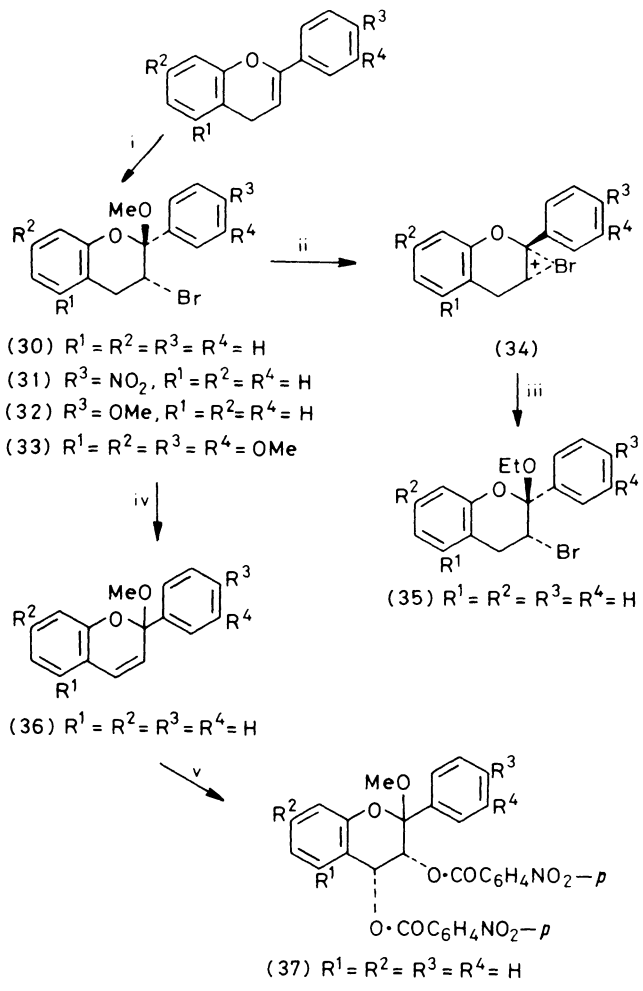
Scheme 2. *Reagents:* i, H_3O^+; ii, R^2OH–$AlCl_3$; iii, $NaBH_3CN$–HOAc; iv, $ArCO_3H$; v, R^2OH, S_N2; vi, S_N1; vii, R^2OH

flavone (56) and 4′-methoxyflavone (57) with lithium aluminium hydride and aluminium chloride,[4] a method which gives somewhat better yields than those obtained by the use of lithium aluminium hydride alone.[5]

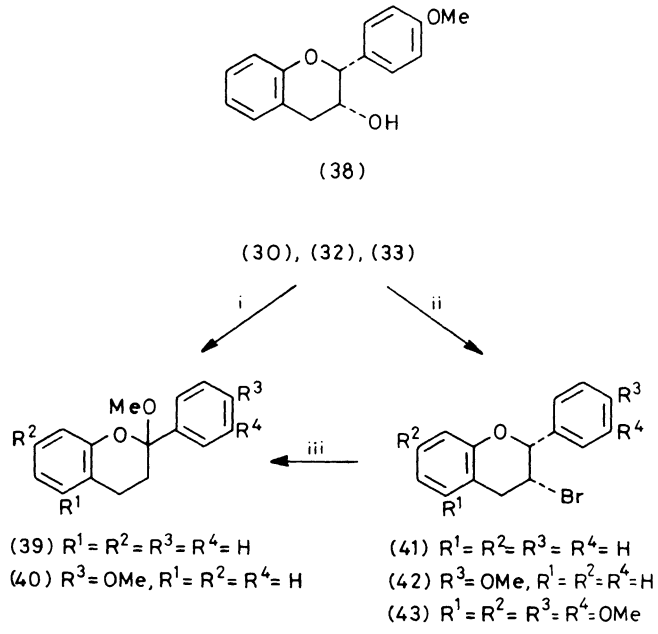
Flav-2-enes, being enol ethers, react with a variety of reagents by addition across the double bond (Scheme 2); in this lies their principal value for synthesis. Ring-opening occurs with aqueous acid [6] to yield the 2-hydroxydihydrochalcones (21), presumably *via* the 2-hydroxyflavans (16) produced by the addition of water. Like dihydropyran, flav-2-enes react with alcohols in the presence of Lewis acids, the products being the 2-alkoxyflavans (17), (18), and (19).

Treatment of flav-2-enes with perbenzoic acids and alcohols in chloroform or dichloromethane results in the addition of an alkoxy group and a hydroxy group to give good yields of 2-alkoxyflavan-3-ols, generally as mixtures of 2,3-*cis*- and 2,3-*trans*-stereoisomers [*e.g.* (25) and (28)] which are easily separated and in which the *cis*-isomer predominates. Treatment of 4′-methoxyflav-2-ene (7) with *m*-chloroperbenzoic acid in a 1 : 3 mixture of methanol and dichloromethane gave 11% of the *trans*- and 77% of the *cis*-isomer. Reaction in methanol–dichloromethane (1 : 1) gave 23% of the *trans*-, 54% of the *cis*-isomer, and 14% of 2,4′-dimethoxyflavan (19) by acid-catalysed addition of methanol to the flav-2-ene. Treatment of 4′-nitroflav-2-ene (6) with *m*-chloroperbenzoic acid in methanol–dichloromethane (1 : 1) gave an oil which was found (t.l.c. and n.m.r.) to be pure 2,3-*cis*-2-methoxy-4′-nitroflavan-3-ol (24), characterised as its crystalline toluene-*p*-sulphonate. These reactions presumably proceed through protonated 2,3-epoxides (20) which are opened by reaction with an alcohol. Attack of methanol by an S_N2 mechanism at C-2 of the protonated epoxide would give rise to a *cis*-product (*i.e.* a product with the 2-methoxy group *trans* to the 3-hydroxy group). Opening of the epoxide ring by an S_N1 mechanism would give a 2-carbonium ion (23) which might then be attacked by methanol from either side, to give rise to either a *cis*- or a *trans*-product, though the steric effect of the 3-hydroxy group might be expected to favour formation of a *cis*-product. Our results suggest the occurrence of both mechanisms, the ratio of the S_N1 to the S_N2 mechanism and hence the proportion of *trans*-product being increased by factors which stabilise a C-2 carbonium ion, namely increasing solvent polarity (*i.e.* the methanol : dichloromethane ratio) and the presence of a +M substituent at C-4′.

The bromination of flav-2-enes with *N*-bromosuccinimide in methanol gives the expected 2,3-*cis*-2-methoxy-3-bromoflavans in excellent yield (Scheme 3). It is evident that addition of bromine to the double bond of flav-2-enes occurs more rapidly than substitution into the aromatic nuclei and it is noteworthy that 3′,4′,5,7-tetramethoxyflav-2-ene (8) with a



Scheme 3. *Reagents:* i, *N*-bromosuccinimide–MeOH; ii, $AlCl_3$; iii, EtOH; iv, KOH; v, (a) OsO_4, (b) *p*-$O_2NC_6H_4COCl$



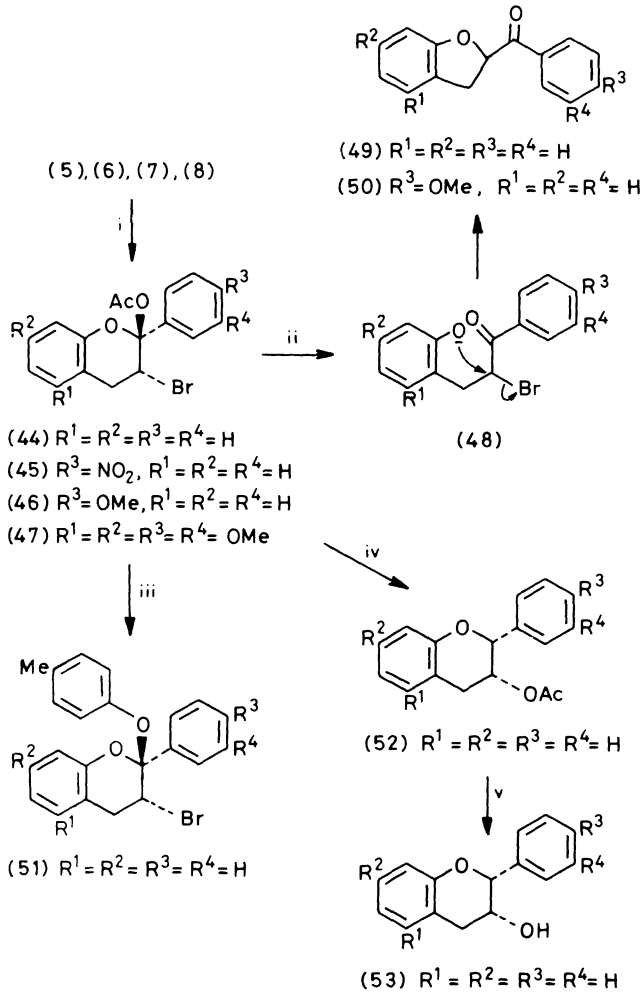
Scheme 4. *Reagents:* i, Bu^n_3SnH; ii, $LiAlH_4$–$AlCl_3$; iii, $AgNO_3$–MeOH

highly activated A ring, did not undergo aromatic bromination. Exchange of the 2-alkoxy group occurs when 2,3-*cis*-2-methoxy-3-bromoflavan (30) is treated with ethanol and a trace of aluminium chloride. In the product, 2,3-*cis*-2-ethoxy-3-bromoflavan (35), the *cis*-stereochemistry is retained which is expected if the mechanism involves a cyclic bromonium ion (34) and the control is kinetic, or if the 2,3-*cis*-isomer is thermodynamically stable with respect to the *trans*-isomer under these conditions.

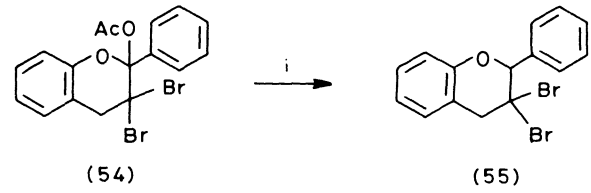
Elimination of hydrogen bromide from 2,3-*cis*-2-methoxy-3-bromoflavan (30) by means of methanolic potassium hydroxide in tetrahydrofuran gave in high yield an unstable, colourless oil whose n.m.r. spectrum was consistent with its formulation as 2-methoxyflav-3-ene (36).[7] Treatment of this compound with osmium tetraoxide gave one major product as an oil which was shown by its n.m.r. spectrum and t.l.c. examination to be a stereochemically homogeneous 3,4-*cis*-diol. A crystalline, analytically pure bis-(*p*-nitrobenzoate) (37) was obtained from this oil. It is to be expected that the diol and its diester (37) have 3,4-*cis*-stereochemistry, but it cannot be stated with certainty what the 2,3-stereochemistry is. From tentative interpretations of n.m.r. and i.r. results we favour a 2,3-*cis*-configuration but further, more conclusive evidence is desirable.

The reduction of 3-substituted 2-alkoxyflavans with a variety of reagents has provided convenient routes to some interesting 3-substituted flavans. The 2-alkoxy group is easily removed from 2-alkoxyflavans by reduction with sodium cyanoborohydride, the product being the corresponding flavan and analogously removal of the 2-methoxy group from 2,3-*cis*-2,4′-dimethoxyflavan-3-ol (25) was achieved by means of lithium aluminium hydride and aluminium chloride (70%) or better by acidic sodium cyanoborohydride (79%), the product being *cis*-4′-methoxyflavan-3-ol (38). The same product (51%) was obtained from 2,3-*trans*-2,4′-dimethoxyflavan-3-ol (28) on reduction with sodium cyanoborohydride. The formation of the same product (38) from the 2,3-*cis*- (25) and from the 2,3-*trans*- (28) compounds indicates that under the acidic conditions of the reductions, the 2-methoxy group may be removed to give a carbonium ion (23) which is attacked by the nucleophilic cyanoborohydride anion from the less hindered side giving in each case 2,3-*cis*-stereochemistry in the product (38). The reduction of 2,3-*cis*-3-bromo-2-methoxyflavan (30) with tri-n-butyltin hydride gave a good yield of 2-methoxyflavan (39) by hydrogenolysis of the bromine atom (Scheme 4). Removal of the 2-methoxy group from the compound (30) to give 2,3-*cis*-3-bromoflavan (41) was best achieved by means of lithium aluminium hydride and aluminium chloride and this reaction was successful with the methoxy substituted analogues (32) and (33). When exposed to air these 2,3-*cis*-3-bromoflavans decompose giving dark coloured products. Methanolic potassium hydroxide causes elimination of hydrogen bromide from *cis*-3-bromoflavan (41) to give a 5 : 2 ratio of flav-2-ene and flav-3-ene and the ease of this elimination prevents substitution reactions at C-3 such as those achieved with 4-bromoflavans.[8] As expected, *cis*-3-bromoflavan (41) reacted readily with magnesium and, being a β-halogenoether,[9] gave, by fission of the carbon–oxygen bond, a mixture (n.m.r.) of diarylpropenes which were characterised by hydrogenation to a diarylpropane, identified by conversion into its known 3,5-dinitrobenzoate.[10] Treatment of *cis*-3-bromoflavan (41) or *cis*-3-bromo-4′-methoxyflavan (42) with silver nitrate in methanol gave the corresponding 2-methoxyflavans (39) and (40).

Flav-2-ene (5) reacted with bromine and acetic acid to give the expected 2,3-*cis*-2-acetoxy-3-bromoflavan (44) in 68% yield (Scheme 5). On being boiled in benzene, this compound loses acetic acid, and a 65% yield of 3-bromoflav-2-ene (12)



Scheme 5. *Reagents:* i, *N*-bromosuccinimide–HOAc; ii, aq.NaOH; *iii*, *p*-cresol; iv, Bu^n_3SnH; v, MeOH–OH^-



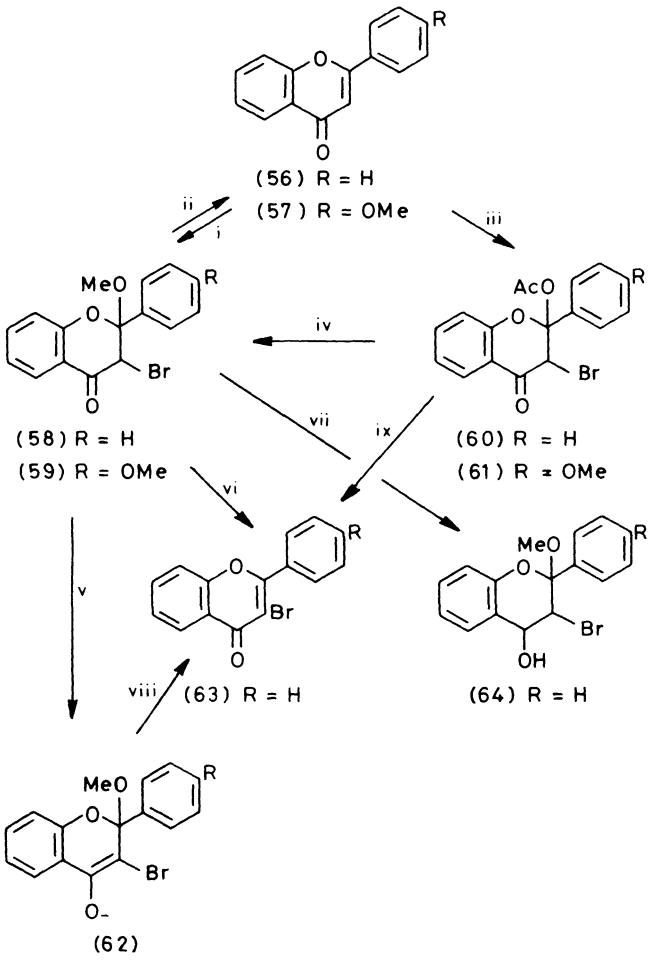
Scheme 6. *Reagents:* i, $LiAlH_4$–$AlCl_3$

is obtained. When the acetoxy compound (44) was boiled with methanol, 2,3-*cis*-3-bromo-2-methoxyflavan (30) was obtained; the retention of stereochemistry in this product indicates participation of the bromonium ion (34) in the mechanism of exchange as in the interchange of alkoxy groups discussed above. The ease of exchange is probably a result of the anchimeric assistance given by the 3-bromine atom since a 2-acetoxyflavan lacking this atom is stable to boiling methanol.[11] The reaction occurs quickly when 2,3-*cis*-2-acetoxy-3-bromoflavan (44) and cold alcohols come into contact and in the solid state the compound deteriorates within 1—2 days, despite being kept *in vacuo*. Reaction with aqueous sodium hydroxide at room temperature gives 2-benzoyl-coumaran (-2,3-dihydrobenzofuran) (49) presumably by hydrolysis followed by ring closure of the intermediate phenolate ion (48). We have used the lability of the 2-acetoxy group to synthesise a 2-aryloxyflavan, *viz.* 2,3-*cis*-3-bromo-2-*p*-tolyloxyflavan (51) by treatment of the 2-acetoxy-3-bromo compound (44) with *p*-cresol at 55 °C. Again the retention of stereochemistry is indicative of the participation of the bromonium ion (34). Reaction of flav-2-ene (5) with bromine and propionic acid gave a very hygroscopic crystalline solid, identified as 2,3-*cis*-3-bromo-2-propionyloxyflavan from its spectra, but which proved too unstable to be analysed. The compound decomposed in *ca.* 2 h when exposed to air and its reaction with methanol gave 2,3-*cis*-3-bromo-2-methoxyflavan (30). Treatment of 4′-methoxyflav-2-ene (7) with bromine and acetic acid gave a product which contained several compounds and when it was boiled with methanol it yielded 51% of 2,3-*cis*-3-bromo-2,4′-dimethoxyflavan (32), showing that it contained an appreciable quantity of the expected product, 2,3-*cis*-2-acetoxy-3-bromo-4′-methoxyflavan (46). Small amounts of 3-bromo-4′-methoxyflav-2-ene (15), 2-anisoylcoumaran (50), and 2-anisoyl-5,7-dibromocoumaran were also isolated, all of which appear to arise from transformations undergone by the reactive compound (46). The 2-ene (15) is probably formed by elimination of acetic acid, whilst the coumarans probably result from hydrolysis of compound (46) and ring-closure [as for the conversion of (44) into (49)], with some concomitant bromination of the A ring. An attempt to add bromine and an acetoxy group to 3′,4′,5,7-tetramethoxyflav-2-ene (8) resulted, not unexpectedly, in extensive aromatic bromination and none of the desired 2-acetoxy-3-bromo compound (47) was detected.

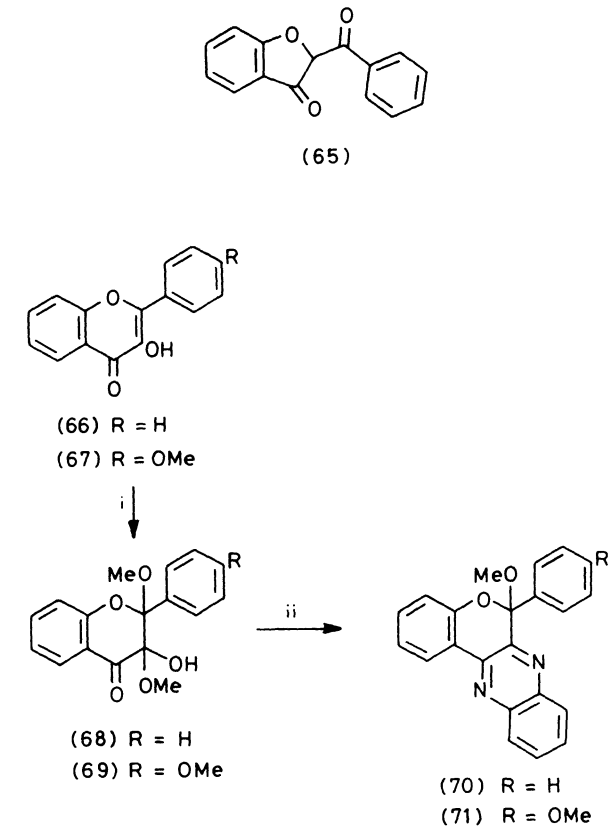
In view of the aromatic bromination caused by free bromine, especially with the more highly methoxylated flav-2-ene, we examined the use of *N*-bromosuccinimide in acetic acid which has been used to add bromine and an acetoxy group to dihydropyran [12] and which would be expected to cause less aromatic bromination than free bromine. Our expectations were fulfilled: several 2,3-*cis*-2-acetoxy-3-bromoflavans [(44), (45), and (54)] were isolated and, by reaction with methanol *in situ*, we showed that the less stable compounds, 2,3-*cis*-2-acetoxy-3-bromo-4′-methoxyflavan (46) and 2,3-*cis*-2-acetoxy-3-bromo-4′-methoxy-4-phenylflavan, were produced in good yield. Though these acetoxybromo compounds were not isolated, their preparation in good yield *in situ* proved to be of great importance for later synthetic work (see later papers).

As expected, the 2,3-*cis*-2-acetoxy-3-bromoflavans are more reactive towards reducing agents than are the analogous 2-alkoxy-3-bromoflavans. The acetoxy group was smoothly removed from 2,3-*cis*-2-acetoxy-3-bromoflavan (44) by zinc borohydride or by lithium aluminium hydride and aluminium chloride giving, respectively, 75 and 84% of 2,3-*cis*-3-bromoflavan (41). Lithium aluminium hydride alone, however, caused ring-opening and yielded 2-hydroxydihydrochalcone. An attempt to remove the bromine atom from the flavan (44) with tri-n-butyltin hydride gave 60% of 2,3-*cis*-3-acetoxyflavan (52), presumably by a mechanism involving the neighbouring acetoxy group. Hydrolysis of the acetate (52) gave 2,3-*cis*-flavan-3-ol (53). 2-Acetoxy-3,3-dibromoflavan (54) is more stable to reducing agents than is 2-acetoxy-3-bromoflavan; thus zinc borohydride had no effect upon the dibromo compound. The acetoxy group was removed with lithium aluminium hydride and aluminium chloride which gave 3,3-dibromoflavan (55) in 38% yield (Scheme 6).

Flavones.—The reaction of flavone (56) and 4′-methoxyflavone (57) with *N*-bromosuccinimide in methanol gives 2-methoxy-3-bromoflavanones, a reaction analogous to that already described for flav-2-enes (Scheme 7). It has not been possible to determine the 2,3-stereochemistry of these com-



Scheme 7. *Reagents:* i, *N*-bromosuccinimide–MeOH; ii, Li-$(Bu^tO)_3AlH$ or H_2/Pd–C or Bu^n_3SnH; iii, *N*-bromosuccinimide–HOAc; iv, hot MeOH, 5 min; v – H^+; vi, $NaBH_4$ or KOH–MeOH; vii, $LiAlH_4$ at 0 °C; viii, $-MeO^-$; ix, hot MeOH, 6 h



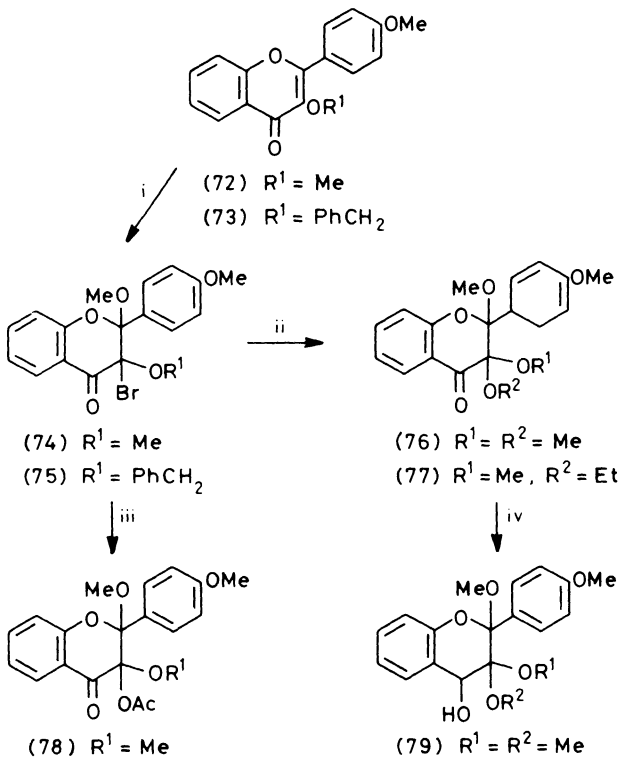
Scheme 8. *Reagents:* i, *N*-bromosuccinimide–MeOH; ii, *o*-phenylenediamine

pounds since it cannot be deduced by n.m.r. It seems likely that the 4-oxo group, which can enolise, will ensure that the thermodynamically more stable product is formed and this would probably have bromine *trans* to the aryl group. The chemistry of these 2-alkoxy-3-bromoflavanones is dominated by the extreme ease with which they lose a molecule of alcohol to give the 3-bromoflavones (63), a reaction which often occurs during their preparation and occasionally on recrystallisation, and which occurs rapidly on treatment with methanolic potassium hydroxide at room temperature. The ease of the reaction is accounted for by the formation of a resonance-stabilised enolate intermediate (62) and by the aromatic character of the heterocyclic ring of the resultant 3-bromoflavone (63). The ready occurrence of this elimination severely limits the use which can be made of 2-alkoxy-3-bromoflavanones for the synthesis of other flavonoids either by taking advantage of the reactivity of the 2-alkoxy group or of the 3-bromine atom. The reaction of the 2-alkoxy-3-bromoflavanones with reducing agents is also dominated by elimination reactions: with the 2-methoxy compound (58) sodium borohydride gives 3-bromoflavone (63) (94%) while lithium tri-t-butoxyaluminium hydride, catalytic hydrogenation, or tri-n-butyltin hydride gives flavone (56). However, brief treatment of 3-bromo-2-methoxyflavanone (58) with lithium aluminium hydride at 0 °C afforded 55% of 3-bromo-2-methoxyflavan-4-ol (64), an unstable compound of unknown stereochemistry.

In a reaction analogous to that observed with flav-2-enes, flavone (56) and 4′-methoxyflavone (57) react with *N*-bromosuccinimide in acetic acid–acetic anhydride–sodium acetate to give good yields of the 2-acetoxy-3-bromoflavanones (60) and (61) of undetermined stereochemistry. Elimination of acetic acid from these compounds occurred easily. For example, boiling a solution of 2-acetoxy-3-bromoflavanone (60) in methanol for 6 h gave 92% of 3-bromoflavone (63), and aqueous base gave the same product and a smaller amount of 2-benzoylcoumaranone (65), probably formed by the action of the base on the 3-bromoflavone (63).[13] Reduction with tri-n-butyltin hydride gave flavone (56). However, by boiling 2-acetoxy-3-bromo-4′-methoxyflavanone (61) briefly in methanol, the acetoxy group was replaced by methoxy and the product was 3-bromo-2,4′-dimethoxyflavanone (59).

Finally we turned our attention to the addition reactions of 3-hydroxyflavones (flavonols) and of their ethers. Flavonol (66) and 4′-methoxyflavonol (67) were found to react rapidly with *N*-bromosuccinimide in methanol (Scheme 8) and the products, which contained no bromine, were identified as 2,3-dimethoxy-3-hydroxyflavanones (68) and (69), first obtained by a different route by Smith *et al.*[14] The hemiacetals (68) and (69) which we obtained had spectroscopic properties as reported, but they melted over large ranges and turned into yellow liquids, probably losing methanol and forming the parent diones. On treatment with *o*-phenylenediamine they gave derivatives (70) and (71) with sharp m.p.s as described.[14]

The methyl (72) and benzyl (73) ethers of 4′-methoxyflavonol (67) were found to behave like flavones when treated with *N*-bromosuccinimide and methanol, being converted into 3-bromo-2,3-dialkoxyflavanones (Scheme 9). When 3-bromo-



Scheme 9. *Reagents:* i, *N*-bromosuccinimide–MeOH; ii, R^2OH–$AgNO_3$; iii, AgOAc–HOAc–Ac_2O; iv, $LiAlH_4$

2,3,4′-trimethoxyflavanone (74) was treated with hot methanol for many hours, solvolysis of the 3-bromine atom occurred in good yield giving 2,3,3,4′-tetramethoxyflavanone (76). Solvolysis in boiling methanol in the presence of silver nitrate was complete within 15 min. At room temperature in benzene, silver-catalysed solvolysis took 4 h; replacement of benzene with acetonitrile slowed the reaction considerably. The 3-ethoxy derivative (77) was prepared similarly in boiling ethanol with silver nitrate. 2,3,3,4′-Tetramethoxyflavanone (76) was unaffected by sodium borohydride but quickly gave a 2,3,3,4′-tetramethoxyflavan-4-ol (79) with lithium aluminium hydride. Treatment of 3-bromo-2,3,4′-trimethoxyflavanone (74) with silver acetate in acetic acid–acetic anhydride at room temperature for 24 h gave two isomers of 3-acetoxy-2,3,4′-trimethoxyflavanone (78) in the ratio 9 : 1, and the major component was obtained pure by recrystallisation.

Experimental

Measurements of n.m.r. spectra were made in $CDCl_3$ unless otherwise stated. I.r. spectra were recorded in CCl_4 unless otherwise stated. Mass spectra were recorded on a Varian MAT CH7 instrument using direct insertion. Merck silica HF_{254} was used for t.l.c. and PF_{254} for p.l.c. and M 60 silica gel for columns. Light petroleum refers to that fraction with b.p. 60—80 °C unless stated otherwise. The composition of the acetic acid–acetic anhydride used was 9 : 1 v/v. Ether refers to diethyl ether.

2′-Benzyloxy-2-hydroxychalcone.—Salicylaldehyde (20 g) and *o*-benzyloxyacetophenone (20 g) in methanol (235 ml) were stirred at 0 °C and sodium hydroxide (40 g) in water (75 ml) was added during 20 min. After being stirred for 5 days at 20 °C the mixture was added to acetic acid (250 ml) in water (250 ml) with stirring. The precipitate was washed with water and dried *in vacuo*. *2′-Benzyloxy-2-hydroxychalcone* (20 g) separated from methanol as yellow prisms, m.p. 149—150 °C (decomp.) (Found: C, 80.0; H, 5.4. $C_{22}H_{18}O_3$ requires C, 80.0; H, 5.5%); τ [$CDCl_3$–$(CD_3)_2SO$] 0.1 (1 H, br s, disappears with D_2O, OH), 2.0—3.4 (15 H, complex, aromatics), and 4.87 (2 H, s, $PhCH_2$); $\nu_{max.}$ (Nujol) 3 370 (OH), 1 645 (CO), 1 600, 1 580, and 1 570 cm^{-1}; *m/z* (145 °C) 330 (M^+, 2%), 91 (100), 239 (18), 92 (11), and 121 (11).

2-Hydroxy-2′-methoxychalcone.—Sodium hydroxide (40 g) in water (75 ml) was added during 15 min to a stirred solution of *o*-methoxyacetophenone (20 g) and salicylaldehyde (20 g) in methanol (10 ml) at 0 °C. The resulting precipitate was suspended in methanol (50 ml) and stirred for 4 days. The red solution was poured into 50% aqueous acetic acid (750 ml) and recrystallisation of the precipitate from aqueous methanol gave *2-hydroxy-2′-methoxychalcone* (22 g) as prisms, m.p. 107 °C (decomp.) (Found: C, 75.7; H, 5.7. $C_{16}H_{14}O_3$ requires C, 75.55; H, 5.55%); τ 2.0—3.3 (11 H to 10 H with D_2O, complex, 8 aromatic, 2 olefinic and 1 OH), and 6.2 (3 H, s, Me); $\nu_{max.}$ ($CHCl_3$) 3 600—2 800 (br, OH), 1 650, 1 600, 1 480, 1 460, and 1 430 cm^{-1}; *m/z* (95 °C) 254 (M^+, 38%), 135 (100), 77 (40), 237 (34), 91 (32), 108 (24), and 142 (22).

2′-Benzyloxyflavylium Perchlorate.—2′-Benzyloxy-2-hydroxychalcone (7.4 g), acetic acid (250 ml), and conc. hydrochloric acid (10 ml) were kept at 55—60 °C for 15 min. 15% Aq. perchloric acid (40 ml) was added, the mixture was heated at *ca.* 60 °C for 5 min and cold water (100 ml) was added. The deep red crystals (7.3 g) which precipitated overnight were washed well with water, and after two recrystallisations *2′-benzyloxyflavylium perchlorate* separated from acetic acid as needles, m.p. 159—160 °C (Found: C, 63.6; H, 4.25. $C_{22}H_{17}ClO_6$ requires C, 63.9; H, 4.1%).

2′-Methoxyflavylium Perchlorate.—Conc. hydrochloric acid (3.8 ml) was added to a solution of 2-hydroxy-2′-methoxychalcone (2.0 g) in acetic acid (38 ml) and the mixture was heated at *ca.* 65 °C for 15 min. Aq. perchloric acid (15.2 ml) was added and the mixture was heated at *ca.* 65 °C for a further 5 min. Cold water (38 ml) was added and the salt separated overnight. *2′-Methoxyflavylium perchlorate* separated from acetic acid as orange plates (2.3 g), m.p. 215—216 °C (Found: C, 57.15; H, 3.8; Cl, 10.75. $C_{16}H_{13}ClO_6$ requires C, 57.1; H, 3.9; Cl, 10.5%).

3′,4′,5,7-Tetramethoxyflavylium Perchlorate (4).—2-Hydroxy-3′,4,4′6-tetramethoxychalcone (9.5 g) in glacial acetic acid (200 ml) and conc. hydrochloric acid (20 ml) was kept at 55—60 °C for 10 min. 60% Aqueous perchloric acid (20 ml) in water (260 ml) was stirred in and the mixture was kept for 12 h. The red precipitate was washed with water, dried *in vacuo*, and triturated with boiling glacial acetic acid (290 ml). In the cold *3′,4′,5,7-tetramethoxyflavylium perchlorate* (4) (11.3 g) separated as a bright red powder, m.p. 255—260 °C with softening from 240 °C (Found: C, 53.6; H, 4.6; Cl, 8.2. $C_{19}H_{19}ClO_9$ requires C, 53.5; H, 4.5; Cl, 8.3%).

Reduction of 3-Methylflavylium Perchlorate with Lithium Aluminium Hydride.—3-Methylflavylium perchlorate (1.0 g) was added at 0 °C during 5 min to a stirred solution of lithium aluminium hydride (260 mg) in dry ether (25 ml) and the mixture was stirred at room temperature for 1 h when t.l.c. indicated that two products had been formed. The excess of lithium aluminium hydride was decomposed with wet ether, and the products were extracted into ether in the usual way. Removal of the solvent gave a pale yellow oil which was transferred to a column of neutral alumina (150 g) made up

in light petroleum. Elution with benzene–light petroleum mixtures of gradually increasing polarity (ultimately 1 : 1), separated the two components.

Evaporation of fractions containing the product of higher R_F gave an unstable oil (365 mg) which decomposed in air and, apparently, in deuteriochloroform (complex n.m.r. spectrum). A sample of this product, presumed to be 3-methylflav-2-ene, was converted into 3-bromo-2-methoxy-3-methylflavan (see later). Evaporation of fractions containing the product of lower R_F gave an oil (153 mg) which slowly crystallised. Recrystallisation from methanol yielded 3-*methylflav*-3-*ene* as prisms, m.p. 79.5—80.5 °C (Found: C, 86.45; H, 6.5. $C_{16}H_{14}O$ requires C, 86.45; H, 6.35%); τ 2.57—3.32 (9 H, complex, aromatics), 3.64 (1 H, s, 4-H), 4.32 (1 H, s, 2-H), and 8.32 (3 H, s, Me); $J_{2,4}$ *ca.* 1 Hz (2- and 4-H signals are broadened); *m/z* (25 °C) 222 (M^+, 39%), 207 (100), 145 (55), 208 (20), 178 (19), and 115 (19); $\nu_{max.}$ 1 487, 1 457, 1 209, and 700 cm^{-1}.

4′-*Nitroflav*-2-*ene* (6).—Sodium cyanoborohydride (100 mg) was added to a stirred suspension of 4′-nitroflavylium perchlorate (500 mg) in acetic acid–acetic anhydride (10 ml) at 15 °C. After 15 min the precipitate was separated and more was recovered from the filtrate by dilution. Recrystallisation from methanol gave the *flav*-2-*ene* (6) (324 mg) as yellow prisms, m.p. 109—110 °C (Found: C, 71.4; H, 4.5; N, 5.4. $C_{15}H_{11}NO_3$ requires C, 71.1; H, 4.4; N, 5.5%); τ 1.53—2.20 (4 H, approx. q, B-ring aromatics), 2.64—3.03 (4 H, complex, A-ring aromatics), 4.20 (1 H, t, 3-H), and 6.34 (2 H, d, 4-H); $J_{3,4}$ 4.1 Hz.

4′-*Methoxy*-4-*phenylflav*-2-*ene* (14).—The method was based on that reported for 4-phenylflav-2-ene;[3] magnesium (0.33 g), ether (7 ml), bromobenzene (1.33 ml), and 4′-methoxyflavylium perchlorate (1.0 g) gave a solid (1.23 g) which separated from methanol as platelets (700 mg) of the *flavene* (14), m.p. 118—119 °C (Found: C, 84.1; H, 5.7. $C_{22}H_{18}O_2$ requires C, 84.0; H, 5.8%); τ 2.23—3.21 (13 H, aromatics), 4.52 (1 H, d, 3-H), 5.18 (1 H, d, 4-H), and 6.19 (3 H, s, OMe); $J_{3,4}$ 4.3 Hz.

Reduction of Flavylium Perchlorate (1) *with Acidic Sodium Borohydride*.—Flavylium perchlorate (1.0 g) was stirred in acetic acid–acetic anhydride (10 ml), and sodium borohydride (0.25 g) was added during 1 h. T.l.c. showed the presence of flav-2-ene and a trace of flavan. The bulk of the solution was worked up to give a substantially solid residue which separated from methanol as impure flav-2-ene (320 mg) of melting range 36—46 °C.

Reduction of 4′-*Methoxyflavylium Perchlorate* (3) *with Acidic Sodium Cyanoborohydride*.—Sodium cyanoborohydride (220 mg) in acetic acid–acetic anhydride (5 ml) was added to a stirred suspension of 4′-methoxyflavylium perchlorate (500 mg) in acetic acid–acetic anhydride (5 ml) during 1 h. The resulting solution was worked up to give 4′-methoxyflavan (280 mg) which separated from methanol as prisms, identified by n.m.r.; m.p. and mixed m.p. 79.5—80.5 °C.

Reduction of 4′-*Methoxyflavylium Perchlorate* (3) *with Acidic Sodium Borohydride*.—Sodium borohydride (110 mg) was added during 3 h to the perchlorate (250 mg) stirred in acetic acid–acetic anhydride (5 ml). The product, 4′-methoxyflavan, separated from light petroleum as prisms (152 mg), m.p. 80.0—80.5 °C.

Reduction of 2′-*Methoxyflavylium Perchlorate with Acidic Sodium Cyanoborohydride*.—The perchlorate (250 mg) was stirred in acetic acid–acetic anhydride (5 ml) and portions of sodium cyanoborohydride were added during 3.5 h. After a further 4 h, the solution was worked up to give 2′-*methoxyflavan* (163 mg) which separated from methanol as prisms, m.p. 78.5—80 °C (Found: C, 80.1; H, 6.7. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.7%); τ 2.48—3.27 (8 H, complex, aromatics), 4.52—4.63 (1 H, q, 2-H), 6.20 (3 H, s, OMe), 6.90—7.44 (2 H, complex, 4-H), and 7.64—8.30 (2 H, complex, 3-H); *m/z* (100 °C) 240 (M^+, 100%), 119 (36), 91 (34), 121 (27), 122 (22), and 209 (21).

Flav-2-*ene* (5).—A solution of flavone (2.00 g) in tetrahydrofuran (30 ml) was dropped during 20 min into a stirred solution of aluminium chloride (4.20 g) and lithium aluminium with hydride (0.60 g) in ether (40 ml) at 0 °C. After decomposition with wet ether, an oil was isolated; on p.l.c. of this a solid (0.76 g) was obtained from the highest running streak. Recrystallisation from methanol gave pure flav-2-ene (5), m.p. and mixed m.p. 52—53 °C.

4′-*Methoxyflav*-2-*ene* (7).—4′-Methoxyflavone (3.40 g) treated as above yielded 4′-methoxyflav-2-ene (1.99 g), m.p. and mixed m.p. 123—124 °C.

Flav-2-enes are unstable compounds and are best stored at 0 °C, or, preferably, prepared immediately before use.

Treatment of Flav-2-*enes with Acidic Sodium Cyanoborohydride*.—Flav-2-ene (5), 3-bromoflav-2-ene (12), and 4-phenylflav-2-ene (13) were all recovered (m.p., mixed m.p., and n.m.r.) in high yield after treatment for 24 h with sodium cyanoborohydride in acetic acid–acetic anhydride.

Reduction of 4′-*Methoxyflav*-2-*ene* (7) *with Acidic Sodium Cyanoborohydride*.—A solution of the flavene (50 mg) in acetic acid–acetic anhydride (4 ml) was treated with sodium cyanoborohydride (20 mg) during 3 h. The only (t.l.c.) product, 4′-methoxyflavan, separated from methanol as prisms (29 mg), m.p. and mixed m.p. 79.5—80.5 °C.

Reduction of 3′,4′,5,7-*tetramethoxyflav*-2-*ene* (8) *with Acidic Sodium Cyanoborohydride*.—The flavene (58 mg) was dissolved in dichloromethane (0.5 ml), and acetic acid–acetic anhydride (2 ml) was added, followed by sodium cyanoborohydride (20 mg). After 20 min the usual procedure gave a crude product which on crystallisation from light petroleum gave 3′,4′,5,7-tetramethoxyflavan (45 mg), as prisms, m.p. 109—110 °C.

Reduction of 4′-*Methoxy*-4-*phenylflav*-2-*ene* (14) *with Acidic Sodium Cyanoborohydride*.—The flavene (50 mg) was treated with sodium cyanoborohydride under the conditions described for 4-phenylflav-2-ene. T.l.c. in ether–light petroleum (1 : 3) showed that the flavene was reduced to a very slightly slower running product in *ca.* 19 h. After isolation 2,4-cis-4′-*methoxy*-4-*phenylflavan* separated from methanol as needles (41 mg), m.p. 121.5—123 °C (Found: C, 83.3; H, 6.5. $C_{22}H_{20}O_2$ requires C, 83.5; H, 6.4%), τ 2.12—3.29 (13 H, complex, aromatics), 4.85 (1 H, q, 3-H), 5.65 (1 H, q, 4-H), 6.20 (3 H, s, OMe), and 7.43—7.95 (2 H, complex, 3-H); $J_{3,4}$ 7.1 and 10.9 Hz; $J_{2,3}$ 4.0 and 9.2 Hz.

2-*Hydroxy*-4′-*methoxy*-α,β-*dihydrochalcone* (21).—Hydrogen chloride was passed through a solution of 4′-methoxyflav-2-ene (200 mg) in ether (50 ml) for 5 min. The solution was washed with saturated aqueous sodium hydrogen carbonate and with water. Removal of solvent gave a solid which separated from light petroleum, b.p. 30—40 °C, as plates

(114 mg), m.p. 56—58 °C (Found: C, 75.5; H, 6.2. Calc. for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3%); $\nu_{max.}$ (CCl_4) 1 670 (CO) and 3 300 cm^{-1} (OH). Tasaki [23] gives m.p. 59—60 °C for 2-hydroxy-4′-methoxy-α,β-dihydrochalcone.

The 2,4-*dinitrophenylhydrazone* separated from ethanol as red needles, m.p. 200—202 °C (Found: C, 60.3; H, 4.7; N, 12.6. $C_{22}H_{20}N_4O_6$ requires C, 60.5; H, 4.6; N, 12.8%).

2-*Methoxyflavan* (17).—Flav-2-ene (88 mg) in methanol (5 ml) was treated with aluminium chloride. After 2 h ether (25 ml) was added and the mixture was washed with 2M-sodium hydroxide and water. Removal of solvent gave an oil (70 mg) which was kept at 0.5 mmHg for 20 h at 20 °C before analysis (Found: C, 79.8; H, 6.8. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.65%); τ 2.38—3.26 (9 H, aromatics), 6.93 (3 H, s, OMe), and 6.63—8.32 (4 H, complex, 3- and 4-H).

2-*Ethoxyflavan* (18).—Flav-2-ene (782 mg), ethanol (15 ml), and aluminium chloride (*ca.* 30 mg) gave, after 4 days, an oil (900 mg), b.p. 116 °C/0.35 mmHg, n_D^{25} 1.5617 (Found: C, 80.0; H, 7.05. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.10%); τ (CCl_4) 2.38—3.24 (9 H, complex, aromatics), 6.41—8.37 (33 lines distinguishable: 2 H, OCH_2CH_3, 2 H, 3-H, and 2 H, 4-H), and 9.00 (3 H, t, OCH_2CH_3).

2-Ethoxyflavan was boiled in aqueous alcoholic hydrochloric acid for 3.5 h and then treated with 2,4-dinitrophenylhydrazine. The 2,4-*dinitrophenylhydrazone* of 2-hydroxydihydrochalcone separated from ethanol as an orange solid, m.p. 200—201 °C (Found: C, 62.3; H, 4.4; N, 13.7. $C_{21}H_{18}N_4O_5$ requires C, 62.1; H, 4.5; N, 13.8%).

2,4′-*Dimethoxyflavan* (19).—4′-Methoxyflav-2-ene (1.00 g) in ether (25 ml) and methanol (15 ml) was treated with aluminium chloride (*ca.* 30 mg). After 1.5 h, 2,4′-*dimethoxyflavan* (19) (1.03 g) was obtained as an oil which was kept at 0.5 mmHg for 12 h at 20 °C before analysis (Found: C, 75.3; H, 6.8. $C_{17}H_{18}O_3$ requires C, 75.5; H, 6.7%); τ (CCl_4) 2.49—3.26 (8 H, complex, aromatics), 6.24 (3 H, s, aromatic OMe), 6.96 (3 H, s, aliphatic OMe), and 6.69—8.39 (4 H, complex, 3- and 4-H).

2,3-cis- (25) *and* 2,3-trans-2,4′-*Dimethoxyflavan*-3-*ol* (28).—(*a*) *p*-Nitroperbenzoic acid (46 mg) in dichloromethane (11 ml) was added during 30 min to a stirred solution of 4′-methoxyflav-2-ene (48 mg), in dichloromethane (3 ml) and methanol (7 ml). After 2 h more dichloromethane was added and the resulting solution was washed with saturated aqueous sodium hydrogen carbonate and water. Removal of the solvent gave an oil (65 mg) which was separated into two components by p.l.c. (1 20 × 20 cm plate; 15 elutions with 10% ether in light petroleum). The faster running component, 2,3-cis-2,4′-*dimethoxyflavan*-3-*ol* (25), was obtained as an oil (44 mg) which was kept at 0.4 mmHg for 18 h at 20 °C before analysis (Found: C, 70.9; H, 6.0. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3%); τ 2.35—3.13 (8 H, complex, aromatics), 5.94 (1 H, q, 3-H), 6.18 (3 H, s, aryl OMe), 6.94 (3 H, s, 2-OMe), 6.41—7.39 (2 H, complex, 4-H), and 8.13 (1 H, br s, OH).

The *toluene*-p-*sulphonate* separated from methanol as plates, m.p. 129.5—130.5 °C (Found: C, 65.7; H, 5.5; S, 7.3. $C_{24}H_{24}O_6S$ requires C, 65.4; H, 5.5; S, 7.3%).

The slower running component, 2,3-trans-2,4′-*dimethoxyflavan*-3-*ol* (28), separated from light petroleum as prisms (6 mg), m.p. 122—124 °C (Found: C, 71.1; H, 6.5. $C_{17}H_{18}O_4$ requires 71.3; H, 6.3%); τ 2.48—3.23 (8 H, complex, aromatics), 6.09 (1 H, q, 3-H), 6.21 (3 H, s, aryl OMe), 6.82 (3 H, s, 2-OMe), 6.90—7.30 (2 H, complex, 4-H), and 7.80 (1 H, br s, OH); $J_{3,4}$ 6.5 and 8.9 Hz.

(*b*) *m*-Chloroperbenzoic acid (190 mg) was added during 5 min to a stirred solution of 4′-methoxyflav-2-ene (238 mg) in dichloromethane (5 ml) and methanol (5 ml). More peracid (20 mg) was added after 45 min and after a total of 2.5 h the reaction mixture was worked up to give an oil which was applied to a p.l.c. plate. The fastest band afforded 2-methoxyflavan (34 mg) identified by n.m.r. The main band gave 2,3-*cis*-2,4′-dimethoxyflavan-3-ol (154 mg) and the slowest band afforded 2,3-*trans*-2,4′-dimethoxyflavan-3-ol (67 mg), m.p. 122—124 °C.

2,3-cis-2-*Ethoxy*-4′-*methoxyflavan*-3-*ol* (26).—4′-Methoxyflav-2-ene (476 mg), in chloroform (35 ml) and ethanol (75 ml) was stirred and treated dropwise with *p*-nitroperbenzoic acid (414 mg) in chloroform (115 ml). After 1.5 h the solution was washed with aqueous sodium hydrogen carbonate and water and evaporated to give 2,3-cis-2-*ethoxy*-4′-*methoxyflavan*-3-*ol* (26) (550 mg) as an oil which was kept at 0.4 mmHg and 20 °C for 24 h before analysis (Found: C, 71.85; H, 6.7. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%); τ (CCl_4) 2.47—3.31 (8 H, complex, aromatics), 6.16 (1 H, partially obscured q, 3-H), 6.26 (3 H, s, OMe), 6.47—7.53 (4 H, complex, OCH_2CH_3 and 4-H), 8.32 (1 H, br s, OH), and 9.08 (3 H, t, OCH_2CH_3).

The *toluene*-p-*sulphonate* separated from methanol as prisms, m.p. 134—137 °C (Found: C, 66.2; H, 5.9; S, 7.15. $C_{25}H_{26}O_6S$ requires C, 66.1; H, 5.8; S, 7.0%); τ (CCl_4) 2.70—3.43 (12 H, complex, aromatics), 5.26 (1 H, q, 3-H), 6.24 (3 H, s, OMe), 6.43—6.94 (4 H, complex, OCH_2CH_3 and 4-H), 7.67 (3 H, s, tosyl Me), and 9.08 (3 H, t, OCH_2CH_3).

2,3-cis-2-*Methoxy*-4′-*nitroflavan*-3-*yl Toluene*-p-*sulphonate*.—*m*-Chloroperbenzoic acid (20 mg), 4′-nitroflav-2-ene (25 mg), dichloromethane (0.5 ml), and methanol (0.5 ml) gave after 14 h 2,3-*cis*-2-methoxy-4′-nitroflavan-3-ol (33 mg) as an oil, τ 1.57—2.32 (4 H, approx. q, B-ring aromatics), 2.72—3.05 (4 H, A-ring aromatics), 5.94 (1 H, q, 3-H), 6.57 (1 H, q, 4-H), 6.92 (3 H, s, OMe), 7.28 (1 H, q, 4-H), and 8.02 (1 H, br s, OH); $J_{3,4}$ 1.8 and 4.2 Hz, $J_{4,4}$ 16.8 Hz.

Treatment of the oil with toluene-*p*-sulphonyl chloride in pyridine for 2.5 days gave 2,3-cis-2-*methoxy*-4′-*nitroflavan*-3-*yl toluene*-p-*sulphonate* which separated from methanol as prisms, m.p. 182—184 °C (Found: C, 60.8; H, 4.7; N, 3.5. $C_{23}H_{21}NO_7S$ requires C, 60.6; H, 4.6; N, 3.1%); τ 1.93—2.50 (4 H, approx. q, B-ring aromatics), 2.57—3.08 (8 H, A-ring and tosyl aromatics), 5.18 (1 H, q, 3-H), 6.47 (1 H, q, 4-H), 6.82 (1 H, q, 4-H), 7.01 (3 H, s, 2-OMe), and 7.63 (3 H, s, tosyl Me); $J_{3,4}$ 2.1 and 3.7 Hz, $J_{4,4}$ 17.7 Hz.

2,3-cis- (27) *and* 2,3-trans-2-*Cyclohexyloxy*-4′-*methoxyflavan*-3-*ol* (29).—*p*-Nitroperbenzoic acid (254 mg) in dichloromethane (15 ml) was added during 10 min to a stirred solution of 4′-methoxyflav-2-ene (238 mg) in dichloromethane (15 ml) and cyclohexanol (6 ml). After 0.5 h dichloromethane (150 ml) was added, the solution was washed with saturated aqueous sodium hydrogen carbonate and dried. After removal of the solvent, the residue was transferred to a column of neutral alumina (350 g; 7.5% deactivated) made up in benzene. Elution with benzene gave the two components as a mixture free from minor by-products. On p.l.c. the lower band gave an oil (182 mg) which was passed through a short column of neutral alumina (7.5% deactivated) with ether to give 2,3-cis-2-*cyclohexyloxy*-3-*hydroxy*-4′-*methoxyflavan* (27) as an oil which was kept at 0.5 mmHg and 25 °C for 12 h before analysis (Found: C, 74.7; H, 7.6. $C_{22}H_{26}O_4$ requires C, 74.55; H, 7.4%); τ 2.33—3.17 (8 H, complex, aromatics), 5.86 (1 H, br s, which sharpens to a q, on addition of D_2O, 3-H), 6.16 (3 H, s, ArO-Me), 6.45 (1 H, complex obscured by 2 lines of the 4-H signal, cyclohexyl proton adjacent to oxygen), 6.55 (1 H, pair of d, 4-H), 7.20 (1 H, pair of d, 4-H), and 8.20—9.20 (11 H,

envelope, cyclohexyl protons and OH); $J_{3,4}$ 2.1 and 3.7 Hz, $J_{4,4}$ 16.6 Hz; *m/z* (95 °C) 354 (M^+, 12%), 135 (100), 136 (25), 107 (20), 137 (20), and 77 (16); $\nu_{max.}$ 3 590 (OH), 2 940, 1 135, and 1 070 cm^{-1}. The *toluene*-p-*sulphonate* separated from methanol as prisms, m.p. 150—154 °C (decomp.) (Found: C, 68.2; H, 6.3; S, 6.5. $C_{29}H_{32}O_6S$ requires C, 68.5; H, 6.3; S, 6.3%); *m/z* (120 °C) 508 (M^+, 1.5%), and 135 (100).

The higher running band gave a solid (47 mg) which was recrystallised from methanol to yield 2,3-trans-2-*cyclohexyloxy*-3-*hydroxy*-4′-*methoxyflavan* (29) as needles, m.p. 159—166.5 °C (Found: C, 74.4; H, 7.5%); τ 2.48—3.20 (8 H, complex, aromatics), 6.03—6.53 (2 H, complex, 3-H plus cyclohexyl proton adjacent to oxygen), 6.20 (3 H, s, ArOCH_3), 7.00 (1 H, pair of d, 4-H), 7.30 (1 H, pair of d, 4-H), 7.61 (1 H, d, OH, disappears on addition of D_2O), and 8.15—9.05 (10 H, envelope, cyclohexyl protons); $J_{3,4}$ 5.2 and 7.8 Hz, $J_{4,4}$ 15.8 Hz, $J_{3,OH}$ 5.5 Hz; *m/z* (75 °C) 354 (M^+, 22%), 135 (100), 136 (27), 137 (12), 272 (22), and 108 (21); $\nu_{max.}$ 3 580 (OH), 2 920, 1 168, and 1 030 cm^{-1}.

2,3-cis-2′-*Benzyloxy*-3-*bromo*-2-*methoxyflavan*.—2′-Benzyloxyflavylium perchlorate (1.0 g) was added to a suspension of lithium aluminium hydride (0.5 g) in ether (20 ml) at 0 °C and the mixture was stirred for 15 min. The excess of reducing agent was decomposed with wet ether and inorganic material was dissolved by adding 2M-hydrochloric acid (100 ml). The organic products were extracted into ether, washed in the usual way and dried. Removal of the solvent gave an oil (0.62 g) which showed one spot on t.l.c. and was identified as a 2 : 1 mixture of 2′-benzyloxyflav-2-ene and 2′-benzyloxyflav-3-ene from its n.m.r. spectrum. The oil (225 mg) was dissolved in methanol (10 ml) and stirred while *N*-bromosuccinimide (200 mg) was added. After 2 h cyclohexene (1 ml) was added to destroy the excess of *N*-bromosuccinimide and the white solid which had precipitated was recrystallised from methanol to give needles (94 mg), m.p. 143.5—144.5 °C, of 2,3-cis-2′-*benzyloxy*-3-*bromo*-2-*methoxyflavan* (Found: C, 65.15; H, 5.05; Br, 18.6. $C_{23}H_{21}BrO_3$ requires C, 64.95; H, 5.0; Br, 18.8%); τ 2.0—3.2 (13 H, complex, aromatics), 4.5—4.6 (1 H, q, 3-H), 4.8 (2 H, s, $PhCH_2$), 5.9—6.2 (1 H, pair of d, 4-H), 6.8—7.1 (1 H, pair of d, 4-H), and 6.9 (3 H, s, Me), $J_{3,4}$ 2.0 and 4.6 Hz, $J_{4,4}$ 17.2 Hz.

2,3-cis-3-*Bromo*-2,2′-*dimethoxyflavan*.—2′-Methoxyflavylium perchlorate (2.0 g) was added at 0 °C to a stirred suspension of lithium aluminium hydride (1.0 g) in ether (40 ml). After 15 min wet ether was added, and work-up with 2M-hydrochloric acid and ether extraction yielded an oil (1.14 g) which after purification by p.l.c. gave an oil which was identified as a 2 : 1 mixture of 2′-methoxyflav-2-ene and 2′-methoxyflav-3-ene by n.m.r.

The oil (310 mg) in methanol (15 ml) was stirred while *N*-bromosuccinimide (300 mg) was added. After 1 h cyclohexene (1 ml) was added and crystallisation of the precipitate from methanol gave 2,3-cis-3-*bromo*-2,2′-*dimethoxyflavan* as needles (181 mg), m.p. 151—152 °C (Found: C, 58.7; H, 4.95; Br, 23.25. $C_{17}H_{17}BrO_3$ requires C, 58.45; H, 4.9; Br, 22.9%); τ 2.0—3.2 (8 H, complex, aromatics), 4.5—4.6 (1 H, q, 3-H), 5.8—6.2 (1 H, pair of d, 4-H), 6.1 (3 H, s, ArOMe), 6.7—7.0 (1 H, pair of d, 4-H), and 6.9 (3 H, s, ROMe); $J_{3,4}$ 2.0 and 4.1 Hz, $J_{4,4}$ 17.5 Hz.

2,3-cis-3-*Bromo*-2-*methoxyflavan* (30).—To a stirred solution of flav-2-ene (250 mg) in dry ether (20 ml) and methanol (10 ml) was added *N*-bromosuccinimide (236 mg) in methanol (12.5 ml) dropwise during 10 min. After 45 min, cyclohexene (0.2 ml) was added and the solvent was evaporated. A solution of the residue in ether (200 ml) was washed with water (2 × 100 ml) and dried. Removal of the solvent gave a solid which was recrystallised from methanol yielding 2,3-cis-3-*bromo*-2-*methoxyflavan* (30) as needles (334 mg), m.p. 134—135 °C (Found: C, 59.9; H, 4.7; Br, 25.0. $C_{16}H_{15}BrO_2$ requires C, 60.2; H, 4.7; Br, 25.0%); τ 2.30—3.10 (9 H, complex, aromatics), 5.52 (1 H, q, 3-H), 6.04 (1 H, pair of d, 4-H), 6.81 (*ca.* 0.5 H, d, part of 4-H), and 6.98 (*ca.* 3.5 H, s, remaining lines of 4-H, signals obscured by OMe); $J_{3,4}$ 1.8 and 4.6 Hz, $J_{4,4}$ 16.9 Hz.

2,3-*cis*-3-Bromo-2-methoxyflavan (670 mg) in tetrahydrofuran (10 ml) was boiled with potassium hydroxide (1.0 g) in methanol (10 ml) for 8 h. The solution was diluted with ether (200 ml), washed with water (3 × 150 ml), and dried. Evaporation of the solvent gave 2-methoxyflav-3-ene (36) [7] (*ca.* 500 mg) as an oil which darkened when exposed to air. Owing to the instability of the product, it was not feasible to pump out the last traces of solvent; τ (CCl_4) 2.42—3.20 (9 H, complex, aromatics), 3.41 (1 H, d, 4-H), and 4.39 (1 H, d, 3-H), 6.83 (3 H, s, OCH_3); $J_{3,4}$ 10.0 Hz. The flav-3-ene may be safely stored in solution in ether for a few days, preferably over a small quantity of solid sodium hydrogen carbonate.

To a stirred solution of 2-methoxyflav-3-ene (300 mg) in ether (30 ml) containing dry pyridine (1.0 ml) was added a solution of osmium tetraoxide (320 mg) in ether (32 ml) during 5 min. The mixture was stirred for 5 h, the solvent was evaporated, and the residue stirred with sodium sulphite (6 g) in water (50 ml) and ethanol (10 ml) overnight; the mixture was then boiled under reflux for 1.25 h. The black colloidal suspension was filtered through a pad of Celite, which was washed several times with hot chloroform. The two-phase filtrate was shaken, the organic layer separated, and the aqueous layer again extracted with chloroform. The combined organic extracts were dried, evaporated, and a solution of the residue in ether washed twice with 2M-hydrochloric acid to remove pyridine. The solution was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated yielding an oil (189 mg). Purification by p.l.c. gave a product believed to be 2,3-*cis*-3,4-*cis*-2-methoxyflavan-3,4-diol as an oil from which traces of solvent were removed under high vacuum. τ 2.28—3.02 (9 H, complex, aromatics), 4.89 (1 H, br s, resolved into d on addition of D_2O, 4-H), 6.00 (1 H, br d, sharpens on addition of D_2O, 3-H), 6.96 (3 H, s, OMe), 7.40 (1 H, br s, disappears on addition of D_2O, 4-OH), and 7.99 (1 H, br s, disappears on addition of D_2O, 3-OH), $J_{3,4}$ 4.1 Hz; *m/z* (35 °C) 272 (M^+, 5.5%), 150 (100), 77 (22), 79 (21), 135 (13), and 105 (13); $\nu_{max.}$ 3 615 (OH), 3 575 (OH), 1 118, 1 060, and 1 050 cm^{-1}.

Treatment of 2,3-*cis*-3,4-*cis*-2-methoxyflavan-3,4-diol with *p*-nitrobenzoyl chloride in pyridine at 100 °C for 30 min gave the 2-*methoxy*-3,4-*bis*(p-*nitrobenzoyloxy*)*flavan* (37) as needles, m.p. 170.5—172 °C when heated slowly from 50 °C (Found: C, 63.1; H, 4.1; N, 5.0. $C_{30}H_{22}N_2O_{10}$ requires C, 63.2; H, 3.9; N, 4.9%).

2,3-cis-3-*Bromo*-2-*methoxy*-4′-*nitroflavan* (31).—*N*-Bromosuccinimide (90 mg) was stirred with 4′-nitroflav-2-ene (100 mg) in dichloromethane (2 ml) and methanol (2 ml) until it dissolved. After 30 min, ether (30 ml) was added and the solution was worked up to give a crude product (146 mg) which separated from methanol as pale yellow needles of 2,3-cis-3-*bromo*-2-*methoxy*-4′-*nitroflavan* (31) (133 mg), m.p. 158.5—160 °C with sublimation (Found: C, 52.6; H, 4.0; N, 21.7. $C_{16}H_{14}BrNO_4$ requires C, 52.8; H, 3.9; N, 22.0%); τ 1.60—2.30 (4 H, approx. q, B-ring), 2.70—3.08 (4 H, complex, A-ring), 5.52 (1 H, q, 3-H), 6.01 (1 H, q, 4-H), 6.96 (3 H, s, OMe), and 6.88 (1 H, q, 4-H); $J_{3,4}$ 1.7 and 4.5 Hz, $J_{4,4}$ 16.9 Hz.

2,3-cis-3-*Bromo*-2,4′-*dimethoxyflavan* (32).—4′-Methoxyflav-2-ene (500 mg), *N*-bromosuccinimide (400 mg), and methanol (15 ml) were stirred together for 15 min. Cyclohexene (0.2 ml) was added to the mixture which was heated to dissolve the solid material and then left to cool. 2,3-cis-3-*Bromo*-2,4′-*dimethoxyflavan* (32) (590 mg) separated as prisms, m.p. 117—118 °C (Found: C, 58.55; H, 4.8; Br, 23.2. $C_{17}H_{17}BrO_3$ requires C, 58.5; H, 4.9; Br, 22.9%); τ 2.40—3.10 (8 H, complex, aromatics), 5.50 (1 H, q, 3-H), 6.02 (4-H, 3 lines visible, 4th is obscured), 6.14 (*ca.* 3.25H, s, ArOMe and one line of 4-H), 6.89 (4-H; 1 d visible at τ 6.80, remaining d obscured), and 6.94 (*ca.* 3.5H, s, OMe plus two lines of 4-H); $J_{3,4}$ 1.8 and 4.6 Hz, $J_{4,4}$ 16.9 Hz.

3,3-*Dibromo*-2-*methoxyflavan*.—*N*-Bromosuccinimide (70 mg) was added to a stirred solution of 3-bromoflav-2-ene (107 mg; see below) in methanol (3 ml). Cyclohexene (2 drops) was added after 15 min. The crude product (160 mg) separated from methanol to give 3,3-dibromo-2-methoxyflavan (106 mg) as prisms, m.p. 149—149.5 °C (Found: C, 48.4; H, 3.6; Br, 39.9, $C_{16}H_{14}BrO_2$ requires C, 48.3; H, 3.5; Br, 40.2%); τ 2.00—3.03 (9 H, aromatics), 5.42 and 6.17 (2 × 1 H, 2 × d, 4-H), and 6.80 (3 H, s, OMe); $J_{4,4}$ 17.0 Hz.

2,3-cis-3,4-trans-3-*Bromo*-2-*methoxy*-4-*phenylflavan*.—*N*-Bromosuccinimide (75 mg) was added to 4-phenylflav-2-ene (100 mg) in dichloromethane (1 ml) and methanol (2 ml). Cyclohexene (2 drops) was added after 15 min. The dichloromethane was evaporated, the solution was allowed to cool, and the prisms (110 mg) of 2,3-cis-3,4-trans-3-*bromo*-2-*methoxy*-4-*phenylflavan* which separated had m.p. 103—104 °C, partially resolidifying and remelting at 121—122 °C (Found: C, 67.1; H, 5.1; Br, 20.4. $C_{22}H_{19}BrO_2$ requires C, 66.9; H, 4.8; Br, 20.2%); τ 2.35—3.03 (14 H, aromatics), 5.18—5.33 (2 H, complex, C-ring), and 7.12 (3 H, s, OMe).

2,3-cis-3,4-trans-3-*Bromo*-2,4′-*dimethoxy*-4-*phenylflavan*.—This was prepared as above from *N*-bromosuccinimide (70 mg), 4′-methoxy-4-phenylflav-2-ene (100 mg), dichloromethane (1 ml), and methanol (2 ml). The resulting 2,3-cis-3,4-trans-3-*bromo*-2,4′-*dimethoxy*-4-*phenylflavan* (107 mg) was recrystallised from methanol to give prisms, m.p. 109—111 °C (Found: C, 65.3; H, 5.1; Br, 19.0. $C_{23}H_{21}BrO_3$ requires C, 65.0; H, 5.0; Br, 18.8%); τ 2.34—3.15 (13 H, complex, aromatics), 5.25 (2 H, br s, C-ring), 6.18 (3 H, s, 4′-OMe), and 7.09 (3 H, s, 2-OMe).

2,3-cis-3-*Bromo*-2,3′,4′,5,7-*pentamethoxyflavan* (33).—To a stirred solution of 3′,4′,5,7-tetramethoxyflav-2-ene (250 mg) in dry ether (25 ml) and methanol (12.5 ml) was added *N*-bromosuccinimide (149 mg) in methanol (15 ml) during 5 min. After 1.5 h, cyclohexene (0.3 ml) was added, and the reaction mixture was worked up as above. 2,3-cis-3-*Bromo*-2,3′,4′,5,7-*pentamethoxyflavan* (33) separated from methanol as prisms (186 mg), m.p. 131—132.5 °C (decomp.), which gradually turned pink in air (Found: C, 55.0; H, 5.4; Br, 17.9. $C_{20}H_{23}BrO_6$ requires C, 54.7; H, 5.3; Br, 18.2%); τ 2.77—3.17 (3 H, complex, aromatic B-ring), 3.72 and 3.83 (each 1 H, each d, *J* 2.2 Hz, *m*-coupled aromatic A-ring), 5.53 (1 H, q, 3-H), 6.08—6.23 [12 H, 4 s (two superimposed), ArOMe], 6.50 (1 H, pair of d, 4-H), 6.85 (4 H, 1 d visible at τ 6.76: remaining d obscured), and 6.97 (*ca.* 3.5 H, s, alkyl OMe and remaining lines of 4-H); $J_{3,4}$ 1.9 and 4.7 Hz, $J_{4,4}$ 17.2 Hz.

2,3-cis-3-*Bromo*-2-*ethoxyflavan* (35).—(*a*) *From flav*-2-*ene* (5). To a stirred solution of flav-2-ene (262 mg) in dry ether (20 ml) and ethanol (10 ml) was added *N*-bromosuccinimide (258 mg) in dioxane (10 ml) and ethanol (10 ml) dropwise during 2 min. After 20 min, cyclohexene (0.25 ml) was added, and the reaction mixture was worked up as above. 2,3-cis-3-*Bromo*-2-*ethoxyflavan* (35) separated from methanol as prisms (321 mg), m.p. 100—101 °C (Found: C, 61.45; H, 5.1; Br, 23.75. $C_{17}H_{17}BrO_2$ requires C, 61.3; H, 5.1; Br, 24.0%); τ 2.24—3.08 (9 H, complex, aromatics), 5.49 (1 H, q, 3-H), 5.96 (1 H, pair of d, 4-H), 6.88 (1 H, pair of d, 4-H), 6.48—6.88 (2 H, complex, OCH_2CH_3), and 9.06 (3 H, t, OCH_2CH_3); $J_{3,4}$ 1.8 and 4.6 Hz, $J_{4,4}$ 16.9 Hz.

(*b*) *From* 2,3-cis-3-*bromo*-2-*methoxyflavan* (30). To a solution of 2,3-*cis*-3-bromo-2-methoxyflavan (36 mg) in dry benzene (1 ml) and ethanol (1 ml) was added anhydrous aluminium chloride (*ca.* 10 mg) and the mixture was boiled for 1 h. Ether (100 ml) was added, the solution was washed with saturated aqueous sodium hydrogen carbonate and dried. Evaporation of the solvent and recrystallisation gave 2,3-*cis* 3-bromo-2-ethoxyflavan (35) as needles (21 mg), m.p. and mixed m.p. 99.5—100.5 °C, n.m.r. identical with that of material obtained from flav-2-ene by method (*a*).

(2RS,3RS)-3-*Bromo*-2-*methoxy*-3-*methylflavan*.—A sample (*ca.* 120 mg) of the unstable oil presumed to be 3-methylflav-2-ene (see above) was dissolved in ether (10 ml) and methanol (5 ml). To the stirred solution was added *N*-bromosuccinimide (116 mg) in methanol (7.5 ml) dropwise during 5 min. After 25 min, cyclohexene (0.3 ml) was added, and the mixture was worked up as before. The crude product was purified on a column of neutral alumina (150 g) made up in light petroleum, and eluted with light petroleum mixed with increasing amounts (ultimately 15%) of benzene. Fractions containing the major product gave an oil (104 mg) which separated from methanol to give (2RS,3RS)-3-*bromo*-2-*methoxy*-3-*methylflavan* as needles (41 mg), m.p. 79—80.5 °C (Found: C, 61.2; H, 5.0; Br, 24.3. $C_{17}H_{17}BrO_2$ requires C, 61.3; H, 5.1; Br, 24.0%); τ 2.23—3.08 (9 H, complex, aromatics), 6.26 and 6.83 (each 1 H, each d, 4-H), 6.89 (3 H, s, OMe), and 8.15 (3 H, s, Me); $J_{4,4}$ 17.1 Hz.

Reduction of 2-*Alkoxyflavans with Sodium Cyanoborohydride*.—Sodium cyanoborohydride (13 mg) was added to acetic acid–acetic anhydride (0.5 ml) containing 2-methoxyflavan (50 mg) or 2,4′-dimethoxyflavan (57 mg) and the n.m.r. spectra in the region τ 5—6 were determined periodically. The quartet resulting from the C-2 proton of flavan or of 4′-methoxyflavan grew to its constant maximum intensity in 1—2 h and no other products were detected by n.m.r. or by t.l.c.

cis-4′-*Methoxyflavan*-3-*ol* (38).—(*a*) 2,3-*cis*-2,4′-Dimethoxyflavan-3-ol (25) (200 mg) in ether (5 ml) was added to aluminium chloride (1.0 g) and lithium aluminium hydride (100 mg) in ether (5 ml) at 0 °C. After 45 min the product was isolated and purified by p.l.c. to give cis-4′-*methoxyflavan*-3-*ol* (38) (132 mg) which separated from methanol as prisms, m.p. 131—132 °C (Found: C, 74.9; H, 6.2. $C_{16}H_{16}O_3$ requires C, 75.00; H, 6.30%); τ 2.50—3.18 (8 H, complex, aromatics), 4.98 (1 H, s, 2-H), 5.69—5.85 (1 H, complex, 3-H), 6.18 (3 H, s, OMe), 6.56—7.14 (2 H, complex, 4-H), and 8.23 (1 H, s, OH, disappears on addition of D_2O).

(*b*) 2,3-*cis*-2,4′-Dimethoxyflavan-3-ol (25) (120 mg) in acetic acid–acetic anhydride (1 ml) was treated with sodium cyanoborohydride (39 mg) in 3 portions during 41 h. *cis*-4′-Methoxyflavan-3-ol (96 mg), m.p. and mixed m.p. 131—132 °C, was obtained.

(*c*) 2,3-*trans*-2,4′-Dimethoxyflavan-3-ol (28) (24 mg), reduced similarly with sodium cyanoborohydride, gave *cis*-4′-methoxyflavan-3-ol (11 mg), m.p. and mixed m.p. 131—132 °C.

Reduction of 3-*Bromo*-2-*methoxyflavan* (30) *with Tri-n-butyltin Hydride*.—A solution of tri-n-butyltin hydride (280 mg) and 3-bromo-2-methoxyflavan (150 mg) in benzene (1 ml) was maintained at 75 °C for 1 h. Ether was added and the mixture was washed with aq. sodium hydroxide, dilute hydrochloric acid, and saturated sodium hydrogen carbonate, then dried and evaporated to give an oil which was applied to a p.l.c. plate. After 1 elution with 10% ether–light petroleum the main band was removed to yield 2-methoxyflavan (68 mg), identified by spectral comparisons with authentic material.

cis-3-*Bromoflavan* (41).—3-Bromo-2-methoxyflavan (100 mg) in ether (5 ml) was added to aluminium chloride (450 mg) and lithium aluminium hydride (35 mg) in ether (5 ml) at 0 °C and stirred for 12 h. The usual isolation procedure gave cis-3-*bromoflavan* (41) which separated from light petroleum as prisms (25 mg), m.p. *ca.* 110—120 °C (Found: C, 62.4; H, 4.6; Br, 27.5. $C_{15}H_{13}BrO$ requires C, 62.3; H, 4.5; Br, 27.6%); τ 2.45—3.20 (9 H, complex, aromatics), 4.90 (1 H, br s, 2-H), 5.35 (1 H, complex, 3-H), 6.18 (1 H, q, 4-H), and 6.71 (1 H, q, 4-H); $J_{3,4}$ 4.9 and 2.2 Hz, $J_{4,4}$ 17.6 Hz.

cis-3-*Bromo*-4′-*methoxyflavan* (42).—3-Bromo-2,4-dimethoxyflavan (100 mg), aluminium chloride (450 mg), and lithium aluminium hydride (35 mg) in ether (10 ml) at 0 °C after being stirred for 45 min gave cis-3-*bromo*-4′-*methoxyflavan* (42) (84 mg) which separated from methanol as needles, m.p. 113.5—114.5 °C (Found: C, 59.9; H, 5.0; Br, 24.8. $C_{16}H_{15}BrO_2$ requires C, 60.2; H, 4.7; Br, 25.0%); τ 2.53—3.22 (8 H, complex, aromatics), 4.97 (1 H, br s, 2-H), 5.41 (1 H, complex, 3-H), 6.20 (3 H, s, OMe), 6.22 (1 H, q, partly obscured by OMe, 4-H), and 6.73 (1 H, q, 4-H); $J_{2,3}$ *ca.* 1.3 Hz, $J_{3,4}$ 4.4 and 2.5 Hz, $J_{4,4}$ 17.1 Hz.

cis-3-*Bromo*-3′,4′,5,7-*tetramethoxyflavan* (43).—3-Bromo-2,3′,4′,5,7-pentamethoxyflavan (125 mg), aluminium chloride (450 mg), and lithium aluminium hydride (35 mg) were boiled in tetrahydrofuran (7.5 ml) for 40 min to give 3-*bromo*-3′,4′,-5,7-*tetramethoxyflavan* (43) (81 mg) which on recrystallisation from methanol and then from ethyl acetate–light petroleum had m.p. 156—157 °C (decomp.) (Found: C, 56.0; H, 5.1; Br, 19.8. $C_{19}H_{21}BrO_5$ requires C, 55.7; H, 5.2; Br, 19.5%); τ 2.91—3.23 (3 H, B-ring aromatics), 3.77—3.93 (2 H, A-ring aromatics), 5.07 (1 H, br s, 2-H), 5.40 (1 H, complex, 3-H), 6.10, 6.13, 6.21, and 6.22 (4 × 3 H, 4 s, 4 × OMe), and 6.60—7.60 (2 H, br d, 4-H); $J_{2,3}$ *ca.* 1.0 Hz, $J_{3,4}$ *ca.* 3.3 and 2.2 Hz.

Dehydrobromination of cis-3-*Bromoflavan* (41).—*cis*-3-Bromoflavan (60 mg) and potassium hydroxide (300 mg) in methanol (9 ml) gave, after 2 h at room temperature, a solid (39 mg) which was shown by n.m.r. and t.l.c. to be a 5 : 2 mixture of flav-2-ene and flav-3-ene. Recrystallisation gave a pure sample of flav-2-ene, identified by spectra and mixed m.p.

Reaction of cis-3-*Bromoflavan* (41) *with Magnesium*.—*cis*-3-Bromoflavan (433 mg) and magnesium (45 mg) in tetrahydrofuran (5 ml) were boiled for 90 min after reaction had been induced by the addition of a crystal of iodine. The usual method of isolation gave an oil (305 mg), shown by n.m.r. to be a mixture of 1,3-diarylpropenes. Hydrogenation of a sample (86 mg) in ethanol over 10% Pd–C for 10 h at room temperature and 1 atm gave 2-(3-phenylpropyl)phenol as an oil (Greenwood and Nierenstein [15] give m.p. 21.5 °C) which was converted into its 3,5-dinitrobenzoate (228 mg,) m.p. 142—143 °C (Mitsui and Kiseki [10] report m.p. 142—143 °C).

Reaction of cis-3-*Bromoflavan* (41) *with Methanol and Silver Nitrate*.—*cis*-3-Bromoflavan (100 mg) and powdered silver nitrate (100 mg) in dry methanol (3 ml) were stirred and boiled for 10 h. Isolation and p.l.c. (2 elutions with ether) gave pure 2-methoxyflavan, identified by comparison with a sample obtained as above.

Reaction of cis-3-*Bromo*-4′-*methoxyflavan* (42) *with Methanol and Silver Nitrate*.—In a reaction similar to that above, *cis*-3-bromo-4′-methoxyflavan (100 mg) gave, after p.l.c. (plate eluted once with benzene; the main band gave a mixture which was applied to another plate and eluted with 10% ether–light petroleum), 2,4′-dimethoxyflavan (52 mg), identified by comparison with authentic material (see above).

2,3-cis-2-*Acetoxy*-3-*bromoflavan* (44).—(*a*) A solution of bromine (0.66 ml) in acetic acid–acetic anhydride (31 ml) was added dropwise during 25 min at 10—15 °C to a stirred solution of flav-2-ene (2.54 g) in acetic acid–acetic anhydride (47 ml) containing anhydrous sodium acetate (3.13 g).

A precipitate soon formed and, after the reaction mixture had been stirred for a further 6 h and allowed to stand at 0 °C overnight, the crude product was collected, washed with ether, and obtained as a powder (2.87 g), m.p. 117.5—118.5 °C. Recrystallisation from ether gave 2,3-cis-2-*acetoxy*-3-*bromoflavan* (44) as needles, m.p. 119—120 °C (Found: C, 58.9; H, 4.5; Br, 23.2. $C_{17}H_{15}BrO_3$ requires C, 58.8; H, 4.4; Br, 23.0%); τ 2.28—3.05 (9 H, complex, aromatics), 5.29 (1 H, q, 3-H), 6.05 (1 H, pair of d, 4-H), 6.79 (1 H, pair of d, 4-H), and 8.10 (3 H, s, OAc); $J_{3,4}$ 1.9 and 4.6 Hz, $J_{4,4}$ 17.4 Hz; *m/z* (70 °C) 348/346 (M^+, 3.5%), 207 (100), 105 (95), 225 (80), 267 (62), and 208 (45); $\nu_{max.}$ 1 777 and 1 745 (C=O), 955, and 1 202 cm^{-1}.

' Recrystallisation ' of a sample of crude 2,3-*cis*-2-acetoxy-3-bromoflavan (73 mg) from methanol gave 2,3-*cis*-3-bromo-2-methoxyflavan as needles (38 mg), m.p. and mixed m.p. 133—135 °C, n.m.r., i.r., and mass spectra identical with those of 2,3-*cis*-3-bromo-2-methoxyflavan previously obtained.

(*b*) To a solution of flav-2-ene (208 mg) in acetic acid–acetic anhydride (3 ml) was immediately added *N*-bromosuccinimide (196 mg) in acetic acid–acetic anhydride (3.5 ml) during 1 min, and the solution was stirred for 20 min. Cyclohexene (0.2 ml) was added, and the mixture was cooled to 10—15 °C when a solid separated. After 3.25 h, the product was collected, washed with ether, and dried *in vacuo*. 2,3-*cis*-2-Acetoxy-3-bromoflavan (44) was obtained as a powder (232 mg), m.p. 119.5—120.5 °C, with R_F and i.r. spectrum identical with those of the product obtained by method (*a*).

2,3-*cis*-2-Acetoxy-3-bromoflavan (44) is unstable and turns yellow within 36 h, even when stored *in vacuo*. The crude material prepared by either method was dried for a few hours and then used without purification in subsequent experiments.

3-*Bromoflav*-2-*ene* (12).—2-Acetoxy-3-bromoflavan (500 mg) in benzene (5 ml) was boiled for 8.5 h. The solvent was removed and crystallisation of the residue from ethanol gave 3-*bromoflav*-2-*ene* (12) (268 mg), as needles, m.p. 69—70 °C (Found: 62.8; H, 3.8; Br, 28.2. $C_{15}H_{11}BrO$ requires C, 62.7; H, 3.9; Br, 27.9%); τ 2.27—3.17 (9 H, aromatics) and 6.09 (2 H, s, 4-H).

2-*Benzoyl*-2,3-*dihydrobenzofuran* (49).—A two-phase mixture of 2,3-*cis*-2-acetoxy-3-bromoflavan (328 mg) in dioxane (10 ml), and 2M-aq. sodium hydroxide (10 ml) was vigorously stirred for 2.75 h. Ether (200 ml) was added and the organic layer was washed with water (6 × 100 ml) and dried. Evaporation of the solvent gave a solid (164 mg) which crystallised from methanol yielding 2-*benzoyl*-2,3-*dihydrobenzofuran* (116

mg) as plates, m.p. 96.5—98 °C (Found: C, 80.3; H, 5.4. $C_{15}H_{12}O_2$ requires C, 80.3; H, 5.4%); τ 1.94—3.23 (9 H, complex, aromatics), 4.11 (1 H, q, 2-H), and 6.46 (2 H, br d, 3-H); $\Sigma J_{2,3}$ 18.0 Hz; *m/z* (250 °C) 224 (M^+, 35%), 91 (100), 105 (82), 119 (78), 77 (60), and 118 (46); $\nu_{max.}$ 1 695 (C=O), 1 481, 1 465, and 1 219 cm^{-1}.

cis-3-*Bromoflavan* (41).—(*a*) 2-Acetoxy-3-bromoflavan (80 mg) in benzene (2.5 ml) was added to a cooled (ice–sodium chloride) and stirred mixture of lithium aluminium hydride (28 mg) and aluminium chloride (360 mg) in ether (5 ml). After 10 min the mixture was worked up to give *cis*-3-bromoflavan (41) (56 mg) which separated from light petroleum as prisms, m.p. *ca.* 110—120 °C, identical with that previously described.

(*b*) Ethereal zinc borohydride (2 ml) was added to 2-acetoxy-3-bromoflavan (210 mg) in benzene (8 ml). After 30 min a solid (180 mg) was isolated. Recrystallisation from methanol gave *cis*-3-bromoflavan (41) (127 mg), m.p. *ca.* 105—114 °C, identical with that prepared above.

cis-*Flavan*-3-*ol* (53).—A solution of 2-acetoxy-3-bromoflavan (130 mg), tri-n-butyltin hydride (230 mg) and α,α′-azobisisobutyronitrile (6 mg) in benzene (2 ml) was boiled for 8 h. The benzene was removed to leave an oil which slowly deposited crystals. Recrystallisation from methanol gave *cis*-3-acetoxyflavan (55 mg), m.p. 108—109 °C (lit.,[16] 110 °C).

The acetoxyflavan (20 mg) was dissolved in methanol (1 ml) containing potassium hydroxide (25 mg), and left overnight. The product was isolated and recrystallised from light petroleum to give cis-*flavan*-3-*ol* (53), m.p. 81—82 °C (Found: C, 79.6; H, 6.3. $C_{15}H_{14}O_2$ requires C, 79.6; H, 6.2%); τ 2.36—3.13 (9 H, aromatics), 4.93 (1 H, br s, $w_{\frac{1}{2}}$ 3.7 Hz; 2-H), 5.58—5.86 (1 H, complex, modified by D_2O, 3-H), 6.70 (1 H, q, 4-H), 7.11 (1 H, q, 4-H), and 8.21 (1 H, d, OH); $J_{4,4}$ *ca.* 17.3 Hz, $J_{3,4}$ 2.3 and 4.0 Hz, $J_{3,OH}$ 6 Hz.

2,3-cis-3-*Bromo*-2-p-*tolyloxyflavan* (51).—2,3-*cis*-2-Acetoxy-3-bromoflavan (200 mg) and *p*-cresol (200 mg) were heated at 50—55 °C in benzene (11 ml) for 15 h. The solution was evaporated, and the residue eluted from a column of neutral alumina (140 g) with benzene–light petroleum (3 : 1). Evaporation of fractions containing the major product, and recrystallisation of the residue from methanol, afforded 2,3-cis-3-*bromo*-2-p-*tolyloxyflavan* (51) as prisms (177 mg), m.p. 123—125 °C (Found: C, 67.0; H, 5.0; Br, 19.85. $C_{22}H_{19}BrO_2$ requires C, 66.8; H, 4.8; Br, 20.2%); τ 2.24—3.39 (13 H, complex, aromatics), 5.21 (1 H, q, 3-H), 5.79 (1 H, pair of d, 4-H), 6.74 (1 H, pair of d, 4-H), and 7.87 (3 H, s, ArMe); $J_{3,4}$ 1.7 and 4.6 Hz, $J_{4,4}$ 17.4 Hz; $\nu_{max.}$ 1 230, 1 209, 960, and 1 113 cm^{-1}.

The solid was unstable, and decomposed to a yellow liquid smelling of *p*-cresol within a few days.

Reaction of Flav-2-*ene* (5) *with Bromine and Propionic Acid.*—A solution of bromine (805 mg) in propionic acid–propionic anhydride (9 : 1, 12 ml) was added dropwise at 2—5 °C to flav-2-ene (1.0 g) in propionic acid–propionic anhydride (18.5 ml) containing anhydrous sodium propionate (1.26 g). After 12 h at 0 °C, the reaction mixture was filtered from inorganic material, the filtrate was evaporated to dryness under reduced pressure, and ether (200 ml) was added to the residue. The solution was washed with saturated sodium hydrogen carbonate (2 × 200 ml), and dried. Removal of the solvent gave crude 2,3-*cis*-3-bromo-2-propionyloxyflavan as a solid (1.68 g) with a sharp smell; τ 2.25—2.98 (9 H, complex, aromatics), 5.28 (1 H, q, 3-H), 6.04 (1 H, pair of d, 4-H), 6.78 (1 H, pair of d, 4-H), 7.84 (2 H, q, *J* 8 Hz, $OCOCH_2CH_3$), and 9.08 (3 H, t, $OCOCH_2CH_3$); $J_{3,4}$ 1.9 and 4.5 Hz, $J_{4,4}$ 17.5 Hz; $\nu_{max.}$ 1 778 and 1 750 (C=O), 1 135 and 940 cm^{-1}. Recrystallisation from ether–light petroleum (b.p. 40—60 °C) gave hygroscopic needles (670 mg) which absorbed moisture from the air so rapidly that a m.p. could not be taken and analysis was not possible. A sample allowed to decompose gave, after 1.75 h, a yellow oil, the i.r. spectrum of which contained bands at 1 683 and 1 699 (C=O), and 3 420 (br, phenolic OH), but only a very weak absorption at 1 778 cm^{-1}.

'Recrystallisation' of the crude 2,3-*cis*-3-bromo-2-propionyloxyflavan from methanol gave 2,3-*cis*-3-bromo-2-methoxyflavan as needles, m.p. and mixed m.p. with an authentic sample 133—134.5 °C.

2,3-cis-2-*Acetoxy*-3-*bromo*-2′-*methoxyflavan*.—A mixture of 2′-methoxyflav-2-ene and 2′-methoxyflav-3-ene (550 mg) (see above) was dissolved in acetic acid–acetic anhydride (10 ml) and *N*-bromosuccinimide (600 mg) was added. After 1 h cyclohexene (1 ml) was added. 2,3-cis-2-*Acetoxy*-3-*bromo*-2′-*methoxyflavan* separated as plates (375 mg) which were washed with ether and then had m.p. 122—124 °C (Found: C, 57.85; H, 4.75. $C_{17}H_{18}BrO_4$ requires C, 57.4; H, 4.5%) τ 2.0—3.2 (8 H, complex, aromatics), 4.8 (1 H, q, 3-H), 5.9—6.2 (1 H, pair of d, 4-H), 6.15 (3 H, s, ArOMe), 6.7—7.0 (1 H, pair of d, 4-H), and 8.1 (3 H, s, OAc); $J_{3,4}$ 1.8 and 4.0 Hz, $J_{4,4}$ 15.5 Hz.

cis-3-*Bromo*-2′-*methoxyflavan*.—Ethereal zinc borohydride (2 ml) was added to a stirred solution of 2-acetoxy-3-bromo-2′-methoxyflavan (200 mg) in ether. After 1 h the mixture was worked up with 2M-hydrochloric acid and isolation by ether extraction gave cis-3-*bromo*-2′-*methoxyflavan* which separated from methanol as prisms (120 mg), m.p. 111—114 °C (Found: C, 60.65; H, 4.6; Br, 24.7. $C_{16}H_{15}BrO_2$ requires C, 60.3; H, 4.55; Br, 25.1%); τ 2.1—3.8 (8 H, complex, aromatics), 4.8 (1 H, s, 2-H), 5.0—5.2 (1 H, complex, 3-H), 6.0—6.3 (1 H, pair of d, 4-H), 6.1 (3 H, s, ArOMe), and 6.6—6.8 (1 H, pair of d, 4-H); $J_{3,4}$ 1.8 and 5.1 Hz, $J_{4,4}$ 17.7 Hz.

Reaction of 4′-*Methoxyflav*-2-*ene* (7) *with Bromine and Acetic Acid.*—A solution of bromine (1.13 g) in acetic acid–acetic anhydride (20 ml) was added dropwise at *ca.* 10 °C during 40 min to a stirred suspension of 4′-methoxyflav-2-ene (1.60 g) in acetic acid–acetic anhydride (30 ml) containing anhydrous sodium acetate (2.0 g). All the solid dissolved, and the bromine solution was only added until the colour was no longer discharged. The mixture was stirred at room temperature for 1 h, at *ca.* 7 °C for 2.5 h, and finally kept at 0 °C overnight. The solvent was removed under reduced pressure, and ether (200 ml) added to the residue. The solution was washed with water (150 ml), 2M-sodium hydrogen carbonate solution (2 × 150 ml), and dried. Removal of the solvent gave an orange gum which failed to crystallise; $\nu_{max.}$ 1 690, 1 788, and 3 400 cm^{-1}.

The crude product was dissolved in benzene (30 ml) and methanol (30 ml), and boiled for 5 h when t.l.c. indicated that 4 main components were present. After evaporation of the solvent, the residue was transferred to a column of neutral alumina (300 g) made up in light petroleum. Elution with benzene–light petroleum mixtures of gradually increasing polarity, and finally with ethyl acetate–benzene (1 : 99), separated the products.

Early fractions yielded needles (78 mg) of 3-*bromo*-4′-*methoxyflav*-2-*ene* which on recrystallisation from methanol had m.p. 78—80 °C (decomp.) (Found: C, 61.0; H, 4.3; Br, 24.8. $C_{16}H_{13}BrO_2$ requires C, 60.6; H, 4.1; Br, 25.2%); τ 2.31—3.10 (8 H, complex, aromatics), 6.05 (2 H, s, 4-H), and 6.17 (3 H, s, ArOMe); *m/z* (25 °C) 318/316 (M^+, 43%),

237 (100), 194 (33), 165 (30), 135 (27), and 238 (20); $\nu_{max.}$ 1 665 (C=C), 1 453, 1 168, and 1 025 cm^{-1}. The compound is air-sensitive and turns red within a few hours.

The second compound eluted from the column was obtained as a pale yellow solid (1.21 g) which crystallised from methanol yielding 2,3-*cis*-3-bromo-2,4′-dimethoxyflavan as needles (1.01 g), m.p. 116.5—118.5 °C whose n.m.r. spectrum was identical with that of material previously prepared.

Evaporation of fractions containing the next component gave a gum (99 mg) which was recrystallised from methanol yielding 2-*anisoyl*-5,7-*dibromo*-2,3-*dihydrobenzofuran* as needles (70 mg), m.p. 110.5—113.5 °C (Found: C, 46.7; H, 2.7; Br, 39.1. $C_{16}H_{12}Br_2O_3$ requires C, 46.6; H, 2.9; Br, 38.8%); τ 1.94 (2 H, d, B-ring aromatics adjacent to the carbonyl group, *J* 9 Hz), 2.56 (1 H, br s, *m*-coupled A-ring proton), 3.01 (2 H, d, *J* 9 Hz, B-ring aromatics adjacent to OMe), 4.05 (1 H, q, 2-H), 6.11 (3 H, s, ArOMe), and 6.18—6.61 (2 H, complex, 3-H); $\Sigma J_{2,3}$ 17.5 Hz; *m*/*z* (60 °C) 414/410 (M^+, 2.5%), 412 (M^+, 4.5), 135 (100), 77 (12), 136 (9), 92 (9), and 89 (5.5); $\nu_{max.}$ 1 689 (CO), 1 455, 1 175, and 1 180 cm^{-1}.

Evaporation of fractions containing the component of lowest R_F gave a gum (105 mg) which slowly crystallised. Recrystallisation from methanol gave 2-*anisoyl*-2,3-*dihydrobenzofuran* as blades (79 mg), m.p. 110.5—112 °C (Found: C, 75.65; H, 5.7. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.55%); τ 1.96 (2 H, d, *J* 9 Hz, A-ring aromatics adjacent to C=O), 2.75—3.40 (6 H, complex, aromatics), 4.12 (1 H, q, 2-H), 6.11 (3 H, s, ArOMe), and 6.40—6.51 (2 H, complex, 3-H); $\Sigma J_{2,3}$ 17.5 Hz; *m*/*z* (40 °C) 254 (M^+, 14%), 135 (100), 108 (20), 91 (20), 77 (18), and 92 (13); $\nu_{max.}$ 1 688 (CO), 1 605, 1 477, and 1 165 cm^{-1}.

2,3-cis-2-*Acetoxy*-3-*bromo*-4′-*nitroflavan* (45).—*N*-Bromosuccinimide (45 mg) was dissolved in acetic acid–acetic anhydride (1 ml) containing 4′-nitroflav-2-ene (50 mg). After 15 min cyclohexene (1 drop) was added, and crystallisation was induced by scratching the flask. The *acetoxybromoflavan* (45) separated as pale yellow prisms (71 mg), m.p. 141—144 °C (decomp.) (Found: C, 52.3; H, 3.6; Br, 20.2; N, 3.5. $C_{17}H_{14}BrNO_5$ requires C, 52.0; H, 3.6; Br, 20.4; N, 3.6%); τ 1.62—2.23 (4 H, approx. d, B-ring) 2.58—3.06 (4 H, complex, A-ring), 5.36 (1 H, q, 3-H), 6.02 (1 H, q, 4-H), 6.75 (1 H, q, 4-H), and 8.06 (3 H, s, OAc); $J_{3,4}$ 1.9 and 4.6 Hz, $J_{4,4}$ 17.5 Hz.

2,3-cis-3,4-trans-2-*Acetoxy*-3-*bromo*-4-*phenylflavan*.—*N*-Bromosuccinimide (45 mg) was dissolved in acetic acid–acetic anhydride (1 ml) containing 4-phenylflav-2-ene (50 mg). After 15 min cyclohexene (1 drop) was added and the solution was left to deposit prisms of 2,3-cis-3,4-trans-2-*acetoxy*-3-*bromo*-4-*phenylflavan* (42 mg) which separated from light petroleum as prisms, m.p. 108—109 °C (decomp.) (Found: C, 65.5; H, 4.5; Br, 18.8. $C_{23}H_{19}BrO_3$ requires C, 65.3; H, 4.5; Br, 18.9%); τ 2.35—2.97 (14 H, aromatics), 4.95 (1 H, d, 3-H), 5.15 (1 H, d, 4-H), and 8.54 (3 H, s, OAc); $J_{3,4}$ 2.4 Hz.

2-*Acetoxy*-3,3-*dibromoflavan* (54).—3-Bromoflav-2-ene (200 mg) in acetic acid–acetic anhydride (4 ml) was treated with *N*-bromosuccinimide (150 mg). After 5 h the solution was worked up to give 2-*acetoxy*-3,3-*dibromoflavan* (54) which separated from ether as prisms (207 mg), m.p. 124—125 °C. A sample recrystallised from methanol had m.p. 122—122.5 °C (Found: C, 48.2; H, 3.4; Br, 37.9. $C_{17}H_{14}B_2rO_3$ requires C, 47.9; H, 3.3; Br, 37.5%); τ 2.12—3.10 (9 H, aromatics), 5.47 and 6.13 (2 × 1 H, 2 d, 4-H), and 8.02 (3 H, s, OAc); $J_{4,4}$ 16.7 Hz.

Preparation of 2,3-cis-2-*Acetoxy*-3-*bromo*-4′-*methoxyflavan* (46) in situ, *and Its Reaction with Methanol*.—Acetic acid–acetic anhydride (10 ml) was added to a solution of 4′-methoxyflav-2-ene (238 mg) in dioxane (10 ml), and *N*-bromosuccinimide (196 mg) in dioxane (10 ml) and acetic acid–acetic anhydride (10 ml) was added with stirring. After 30 min cyclohexene (0.3 ml) was added and t.l.c. indicated that no 4′-methoxyflav-2-ene remained but a product was detected. Dry methanol (20 ml) was added and after the reaction mixture had been heated for 11 h at 70 °C, the solvent was removed under reduced pressure, and ether was added to the residue. The solution was washed well with saturated sodium hydrogen carbonate and dried. Evaporation of the solvent gave a residue which was recrystallised from methanol yielding 2,3-*cis*-3-bromo-2,4′-dimethoxyflavan as needles (268 mg), m.p. 117.5—119.5 °C, with an n.m.r. spectrum identical with that of authentic material obtained previously.

Preparation of 2,3-cis-3,4-trans-2-*Acetoxy*-3-*bromo*-4′-*methoxy*-4-*phenylflavan* in situ *and Its Reaction with Methanol*.—*N*-Bromosuccinimide (45 mg) was dissolved in acetic acid–acetic anhydride (1 ml) containing 4′-methoxy-4-phenylflav-2-ene (50 mg). After 15 min, cyclohexene (1 drop) and then methanol (0.5 ml) were added. After 12 h isolation and recrystallisation as above gave 2,3-*cis*-3,4-*trans*-3-bromo-2,4′-dimethoxy-4-phenylflavan (36 mg), m.p. and mixed m.p. 109—111 °C.

3,3-*Dibromoflavan* (55).—2-Acetoxy-3,3-dibromoflavan (118 mg) in ether (2.5 ml) was added to aluminium chloride (500 mg) and lithium aluminium hydride (40 mg) in ether (5 ml) at 0 °C. The mixture was stirred and the temperature was allowed to rise to 20 °C. After 35 min isolation in the usual way gave an oil, which on crystallation from methanol yielded 3,3-*dibromoflavan* (55) (31 mg) as prisms, m.p. 122.5—124 °C (Found: C, 49.2; H, 3.3; Br, 42.9. $C_{15}H_{12}Br_2O$ requires C, 48.9; H, 3.3; Br, 43.4%); τ 2.19—3.16 (9 H, aromatics), 4.93 (1 H, s, 2-H), and 5.71 and 6.04 (2 × 1 H, 2 d, 4-H); $J_{4,4}$ 18.2 Hz.

3-*Benzyloxy*-4′-*methoxyflavone* (73).—4′-Methoxyflavonol (1.0 g), benzyl chloride (0.9 ml), potassium carbonate (2.0 g), potassium iodide (0.5 g), and dioxane (50 ml) were heated under reflux for 12 h, then poured into water. The resulting 3-*benzyloxy*-4′-*methoxyflavone* (73) separated from light petroleum as yellow needles (1.08 g), m.p. 102.5—103.5 °C (Found: C, 77.3; H, 5.2. $C_{23}H_{18}O_4$ requires C, 77.1; H, 5.1%); τ 1.70—3.31 (13 H, complex, aromatics), 4.91 (2 H, s, OCH_2-Ph), and 6.15 (3 H, s, OMe). The solid reddens superficially in air.

3-*Bromo*-2-*methoxyflavan*-4-*one* (58).—Flavone (1.0 g) and *N*-bromosuccinimide (1.0 g) were stirred in methanol (30 ml) until a homogeneous solution resulted. Cyclohexene (0.8 ml) was added after 2 h. After a further 1 h, needles of 3-*bromo*-2-*methoxyflavan*-4-*one* (58) (980 mg) were collected, and the liquor afforded a further crop of needles (360 mg after work-up and recrystallisation from methanol), m.p. *ca.* 136.5—138 °C, with much prior distillation (Found: C, 57.5; H, 4.0; Br, 23.7. $C_{16}H_{13}BrO_3$ requires C, 57.7; H, 3.9; Br, 24.0%); τ 1.97—2.99 (9 H, aromatics), 5.60 (1 H, s, 3-H), and 6.98 (3 H, s, OMe).

Treatment of the bromomethoxyflavanone (58) (100 mg) with potassium hydroxide (20 mg) in methanol (10 ml) for 40 min gave, after dilution with ether and the usual isolation procedure, 3-bromoflavone which separated from light petroleum as needles (88 mg), m.p. 125—126 °C. Bognár *et al.*[17] record m.p. 125—126 °C.

With sodium borohydride (20 mg) in methanol (10 ml), the

bromomethoxyflavanone (58) (100 mg) gave, after 4 h, 3-bromoflavone which separated from methanol as needles (78 mg), m.p. and mixed m.p. 125—126 °C.

Reduction of 3-*Bromo*-2-*methoxyflavan*-4-*one* (58) *to Flavone*.—(*a*) Portions of lithium tri-t-butoxyaluminium hydride (100, 50, 50, and 50 mg) were dissolved in a solution of the bromomethoxyflavanone (58) (100 mg) in tetrahydrofuran (5 ml) at intervals of 0, 2, 13, and 20 h respectively. T.l.c. after 40 h showed the presence of starting material, 3-bromoflavone, and a slower running component. This was isolated by p.l.c. (1 small plate; 1 elution with 1 : 1 ether–light petroleum) after work-up, and identified as flavone (41 mg) by n.m.r., m.p., and mixed m.p.

(*b*) The bromomethoxyflavanone (300 mg) was dissolved in ethanol (20 ml) and stirred under hydrogen with 10% Pd–C for 1 h to give a pale yellow solution containing a small quantity of crystals. Filtration and washing through with acetone gave a solution which was evaporated to give a yellow solid. Extraction with boiling light petroleum gave flavone (32 mg). The residue separated from acetone as colourless needles of flavone hydrobromide, melting at *ca.* 93—94 °C, resolidifying and remelting at *ca.* 104—105 °C. The n.m.r. spectrum [in $(CD_3)_2SO$–$CDCl_3$] was identical with that of flavone. A portion of the solid was taken up in ether and washed with water. Removal of the ether afforded flavone.

(*c*) A solution of the bromomethoxyflavanone (100 mg) and tri-n-butyltin hydride (325 mg) in benzene (1 ml) was boiled for 30 min. Removal of the solvent left an oil which was taken up in ether and stirred with powdered calcium chloride for 30 min.[18] The solid was collected, washed with ether, and partitioned between water and ether. The ether layer afforded flavone (63 mg).

3-*Bromo*-2-*methoxyflavan*-4-*ol* (64).—3-Bromo-2-methoxyflavanone (100 mg) in ether (4 ml) was added to a cooled (ice–sodium chloride) and stirred solution of lithium aluminium hydride (20 mg) in ether (5 ml). After 5 min at 0 °C, the mixture was worked up to give an oil which on t.l.c. showed at least 7 components. Recrystallisation from light petroleum gave needles of 3-*bromo*-2-*methoxyflavan*-4-*ol* (64) (56 mg) which rapidly turned pink. Their melting range depended on the rate of heating, being *ca.* 145—147 °C or 147—150 °C (Found: C, 57.6; H, 4.4; Br, 23.5. $C_{16}H_{15}BrO_3$ requires C, 57.3; H, 4.5; Br, 23.8%); τ 2.30—3.12 (9 H, aromatics), 4.68 (1 H, q altered to d by D_2O, 4-H), 5.35 (1 H, d, 3-H), 6.95 (3 H, s, OMe), and 7.82 (1 H, d, OH); $J_{4,OH}$ 12.3 Hz, $J_{3,4}$ 4.7 Hz.

3-*Bromo*-2,4′-*dimethoxyflavan*-4-*one* (59).—*N*-Bromosuccinimide (900 mg) was dissolved in a solution of 4′-methoxyflavone (1.0 g) in methanol (20 ml) and dichloromethane (10 ml). After 30 min the solution was worked up to give a solid. Recrystallisation from methanol gave 3-*bromo*-2,4′-*dimethoxyflavan*-4-*one* (59) (1.22 g), m.p. 148—150 °C (Found: C, 56.3; H, 4.3; Br, 22.2. $C_{17}H_{15}BrO_4$ requires C, 56.2; H, 4.2; Br, 22.0%); τ 1.92—3.07 (8 H, aromatics), 5.60 (1 H, s, 3-H), 6.13 (3 H, s, ArOMe), and 6.97 (3 H, s, 2-OMe).

Treatment of this compound (200 mg) with potassium hydroxide (100 mg) in 1 : 1 dioxane–methanol (4 ml) for 5 min gave 3-bromo-4′-methoxyflav-4-one which separated from methanol as prisms (130 mg), m.p. 144.5—146 °C. Pendse and Limaye [19] reported m.p. 140 °C. 3-Bromo-2,4′-dimethoxyflavanone (100 mg) was dissolved in ethanol (15 ml) and shaken under hydrogen with 10% Pd–C (10 mg) for 2 h to give a pale yellow solution with a blue fluorescence. Removal of catalyst and solvent left 4′-methoxyflavone hydrobromide as a yellow solid (94 mg) which melted at *ca.* 100—103 °C, resolidified as needles, and remelted at 152—155 °C. 'Recrystallisation' from methanol gave 4′-methoxyflavone (47 mg) of m.p. and mixed m.p. 157.5—158 °C.

3-*Bromo*-2-*ethoxyflavan*-4-*one*.—Flavone (200 mg), *N*-bromosuccinimide (200 mg), and ethanol (2 ml) were stirred until homogeneous. After 3 h the solution was worked up to give a solid. Recrystallisation from methanol gave 3-*bromo*-2-*ethoxyflavan*-4-*one* as prisms (250 mg), m.p. 120.5—122 °C (Found: C, 59.0; H, 4.5; Br, 22.9. $C_{17}H_{15}BrO_3$ requires C, 58.8; H, 4.4; Br, 23.0%); τ 1.87—2.99 (9 H, aromatics), 5.57 (1 H, s, 3-H), 6.69 (2 H, q, OCH_2CH_3), and 9.12 (3 H, t, OCH_2CH_3); J_{Et} 7.0 Hz.

3-*Bromo*-2-*isopropoxyflavan*-4-*one*.—Propan-2-ol (0.5 ml) and *N*-bromosuccinimide (375 mg) were added during 1 h to a solution of flavone (100 mg) in dioxane (2 ml). After a further 2 h the solution was worked up to give a lachrymatory oil (185 mg) which was applied to 2 p.l.c. plates. These were eluted with ether–light petroleum (1 : 1). The main (fastest) band yielded 3-*bromo*-2-*isopropoxyflavanone* (105 mg) which separated from methanol as prisms, m.p. 93.5—94.5 C (Found: C, 59.6; H, 4.8; Br, 22.4. $C_{18}H_{17}BrO_3$ requires C, 59.9; H, 4.8; Br, 22.1%); τ 1.89—3.05 (9 H, aromatics), 5.52 (1 H, s, 3-H), 6.17 (1 H, septet, $OCHMe_2$), and 9.15 and 9.30 (2 × 3 H, 2 d, $OCHMe_2$); J_{Pr^i} 6.2 Hz.

The middle and slowest p.l.c. bands yielded 9 and 18 mg of products shown by t.l.c. to be 3-bromoflavone and flavone respectively.

3-*Bromo*-2-*t-butyloxyflavan*-4-*one*.—Flavone (100 mg) and *N*-bromosuccinimide (100 mg) were dissolved in dichloromethane (2 ml) and t-butyl alcohol (0.5 ml). After 13 days, t.l.c. showed a dominant product and minor amounts of flavone and 3-bromoflavone. A small quantity of crystals had separated; these were water-soluble and n.m.r. showed them to be succinimide. The reaction solution was diluted with ether and washed with aqueous sodium hydrogen carbonate *etc.* An oil (173 mg) was recovered; this was separated by p.l.c. (2 small plates; 1 elution with ether–light petroleum, 1 : 1) into flavone (8 mg; slowest band), 3-bromoflavone (8 mg), and 3-*bromo*-2-*t-butyloxyflavanone* (86 mg, fastest band) which separated from methanol as prisms, m.p. 117.5—119 °C (Found: C, 60.7; H, 5.1; Br, 21.3. $C_{19}H_{19}BrO_3$ requires C, 60.8; H, 5.1; Br, 21.3%); τ 2.00—3.13 (9 H, aromatics), 5.73 (1 H, s, 3-H), and 9.0 (9 H, s, Bu^t).

2-*Acetoxy*-3-*bromoflavan*-4-*one* (60).—(*a*) A solution of *N*-bromosuccinimide (190 mg) in acetic acid–acetic anhydride (3 ml) was added to a solution of flavone (200 mg) in acetic acid–acetic anhydride (1 ml). After 4 days, large prisms of the product (240 mg) were collected. A further crop (72 mg) separated from acetone–light petroleum after work-up, m.p. 148—150 °C; Obara and Onodera [20] reported m.p. 151—152 °C; τ 1.99—2.96 (9 H, aromatics), 5.49 (1 H, s, 3-H), 8.16 (3 H, s, OAc).

(*b*) Flavone (100 mg) and *N*-bromosuccinimide (100 mg) were stirred in a saturated solution of sodium acetate in acetic acid–acetic anhydride (2 ml) until a homogeneous solution was obtained. After 1 h, some crystals had separated and t.l.c. showed that no flavone remained. Cyclohexene (2 drops) was added, and the mixture was left overnight. The crystals (99 mg) were collected and identified as acetoxybromoflavanone (60) by m.p. (148—150 °C) and n.m.r.

2-Acetoxy-3-bromoflavan-4-one (60) (100 mg) and tri-n-butyltin hydride (350 mg) were boiled in benzene (1 ml) for 4 h. Removal of the solvent left an oil which on p.l.c. (1 large plate; 1 elution with ethyl acetate–light petroleum, 1 : 3) gave

a solid; this gave crystals (40 mg) identified as flavone on recrystallisation from light petroleum.

3-*Bromoflavone* (63).—(*a*) A solution of 2-acetoxy-3-bromoflavanone (100 mg) in methanol (10 ml) was boiled for 6 h. T.l.c. showed complete conversion into 3-bromoflavone, confirmed by n.m.r. and m.p. (125—126 °C) after isolation and recrystallisation of the product (77 mg) from light petroleum.

(*b*) Aqueous sodium hydroxide (5 ml) was added to a solution of 2-acetoxy-3-bromoflavanone (200 mg) in dioxane (5 ml), and the 2-phase mixture was stirred for 75 min and then partitioned between water and ether. The organic phase was washed with sodium hydroxide until colourless. The yellow washings were combined with the aqueous phase and acidified. Extraction with ether gave a solution which was washed with water and then dried. Removal of the ether yielded a yellow solid (59 mg) which gave a positive reaction with ferric chloride and was identified as 2-benzoylbenzofuran-3(2*H*)-one. Recrystallisation from light petroleum gave needles, m.p. and mixed m.p. 81—82 °C. Geissman and Arman [21] give m.p. 79—80 °C and Bryant and Haslam [22] give 82—83 °C.

The organic phase afforded 3-bromoflavone (80 mg), m.p. 125—126 °C.

A subsequent experiment with a reaction time of 30 min yielded 3-bromoflavone (62%) and 2-benzoylbenzofuran-3(2*H*)-one (14%).

2-*Acetoxy*-3-*bromo*-4′-*methoxyflavan*-4-*one* (61).—*N*-Bromosuccinimide (90 mg) was dissolved in a solution of 4′-methoxyflavone (100 mg) in acetic acid–acetic anhydride saturated with sodium acetate (4 ml). After 30 min the solution was worked up to give an oil which solidfied and separated from ether as prisms of 2-*acetoxy*-3-*bromo*-4′-*methoxyflavanone* (61) (83 mg), m.p. 109—111 °C (Found: C, 55.3; H, 3.8; Br, 20.7. $C_{18}H_{15}BrO_5$ requires C, 55.2; H, 3.9; Br, 20.4%); τ 1.80—3.09 (8 H, aromatics), 5.41 (1 H, s, 3-H), 6.15 (3 H, s, OMe), 8.15 (3 H, s, OAc).

'Recrystallisation' of the acetoxybromo compound from methanol gave 3-bromo-2,4′-dimethoxyflavanone, identified by n.m.r. and m.p. and mixed m.p.

3-*Hydroxy*-2,3-*dimethoxyflavan*-4-*one* (68).—Flavonol (500 mg) and *N*-bromosuccinimide (425 mg) were stirred in methanol (10 ml) until they dissolved (1 min). Within 5 min crystals began to be deposited. Cyclohexene (5 drops) was added after 15 min and after 12 h the crystals (276 mg) were collected. The filtrate was worked up to give a further crop of prisms (from methanol) (178 mg). Both crops were identified as 3-hydroxy-2,3-dimethoxyflavan-4-one (68). The prisms melted and decomposed over a range, *ca.* 90—112 °C (Found: C, 67.7; H, 5.5. Calc. for $C_{17}H_{16}O_5$: C, 68.0; H, 5.4%); τ 1.97—2.99 (9 H, aromatics), 5.30 (1 H, s, OH), and 6.93 and 7.02 (2 × 3 H, 2 s, 2 × OMe). Smith *et al.*[14] reported m.p. 151—152 °C.

The hemiacetal (125 mg) and *o*-phenylenediamine (recrystallised; 45 mg), magnesium sulphate (2 g), and chloroform (25 ml) were boiled for 20 h. Work-up gave a buff solid which separated from methanol as needles (81 mg), m.p. 165—166 °C (Found: C, 77.3; H, 4.9; N, 8.3. Calc. for $C_{22}H_{16}N_2O_2$: C, 77.6; H, 4.7; N, 8.2%). Smith *et al.*[14] reported m.p. 169—170 °C for the quinoxaline from the hemiacetal.

3-*Hydroxy*-2,3,4′-*trimethoxyflavan*-4-*one* (69).—4′-Methoxyflavonol (1.0 g) was stirred in methanol (2 ml) and dioxane (20 ml). Addition of *N*-bromosuccinimide (900 mg) gave a homogeneous solution. After 15 min cyclohexene (0.6 ml) was added, and the solution was worked up to give a solid which separated from methanol as prisms of 3-hydroxy-2,3,4′-trimethoxyflavanone (69) (950 mg). On being heated, the crystals gradually became yellow and liquified over a wide range. Smith *et al.*[14] reported m.p. 162—164 °C; τ 2.06—3.15 (8 H, aromatics), 5.35 (1 H, s, OH), 6.17 (3 H, s, ArOMe), and 6.97 and 7.02 (2 × 3 H, 2 s, 2- and 3-OMe).

The hemiacetal was converted as above into the quinoxaline which had m.p. 166.5—168 °C. Smith *et al.*[14] reported m.p. 166—167 °C; τ 1.45—3.15 (12 H, aromatics), 6.17 (3 H, s, 4′-OMe), and 6.66 (3 H, s, 2-OMe); *m/z* (125 °C) 339 (100%), 370 (M^+ 14), 308 (12), 263 (12), 295 (9), and 154 (7).

3-*Bromo*-2,3,4′-*trimethoxyflavan*-4-*one* (74).—Methanolic solutions of *N*-bromosuccinimide (400 mg, 8 ml) and 3,4′-dimethoxyflavone (560 mg, 16 ml) were mixed. Within seconds, crystallisation started. Cyclohexene (8 drops) was added after 15 min and the mixture was left overnight. The product was collected and identified as plates of 3-*bromo*-2,3,4′-*trimethoxyflavanone* (74) (750 mg), m.p. 162—171 °C (decomp.). Portions were recrystallised from methanol giving plates, m.p. 164—174 °C, and from benzene as prisms, m.p. 156—170 °C (Found: C, 55.0; H, 4.4; Br, 20.6. $C_{18}H_{17}BrO_5$ requires C, 55.0; H, 4.4; Br, 20.3%); τ 1.96—3.08 (8 H, aromatics), 6.11 and 6.12 (2 × 3 H, 2 s, 3- and 4′-OMe), and 6.91 (3 H, s, 2-OMe).

3-*Bromo*-2-*ethoxy*-3,4′-*dimethoxyflavan*-4-*one*.—3,4′-Dimethoxyflavone (100 mg) and *N*-bromosuccinimide (70 mg) were stirred in ethanol (5.5 ml) until they dissolved. Cyclohexene (2 drops) was added after 1 h. The solution was stored at 0 °C overnight, and then the prisms which had separated were collected and identified as 3-*bromo*-2-*ethoxy*-3,4′-*dimethoxyflavanone* (90 mg), m.p. 124—126 °C (Found: C, 55.9; H, 4.5; Br, 19.8. $C_{19}H_{19}BrO_5$ requires C, 56.0; H, 4.7; Br, 19.6%); τ 1.97—3.10 (8 H, aromatics), 6.12 (6 H, s, 3- and 4′-OMe), 6.66 (2 H, 12 lines, OCH_2CH_3), and 9.11 (3 H, t, OCH_2CH_3).

3-*Benzyloxy*-3-*bromo*-2,4′-*dimethoxyflavan*-4-*one* (75).—3-Benzyloxy-4′-methoxyflavone (100 mg) and *N*-bromosuccinimide (60 mg) were stirred in methanol (3 ml) until both had dissolved (5 min). After 45 min, cyclohexene (3 drops) was added. The solution was left overnight, then the prisms (102 mg) which had separated were shown by n.m.r. to be 3-*benzyloxy*-3-*bromo*-2,4′-*dimethoxyflavanone* (75) containing methanol of crystallisation (½ mol). The prisms of methanolate melted at *ca.* 80—85 °C, resolidified, and remelted at 92—94 °C.

Recrystallisation from ethanol gave prisms containing ethanol (½ mol); these melted at 72—76 °C, resolidified, and remelted at 93—94 °C.

Recrystallisation from light petroleum gave solvent-free prisms of m.p. 105—111 °C (Found: C, 61.5; H, 4.7; Br, 17.0. $C_{24}H_{21}BrO_5$ requires C, 61.4; H, 4.5; Br, 17.0%); τ 1.93—3.13 (13 H, aromatics), 4.35 and 5.01 (2 × 1 H, 2 d, OCH_2Ph), 6.14 (3 H, s, 4′-OMe), and 6.92 (3 H, s, 2-OMe), J_{PhCH_2} 12.3 Hz.

2,3,3,4′-*Tetramethoxyflavan*-4-*one* (76).—(*a*) A solution of 3-bromo-2,3,4′-trimethoxyflavanone (49 mg) in methanol (10 ml) was boiled for 16 h. Removal of the solvent left a solid which separated from methanol as plates of 2,3,3,4′-tetramethoxyflavanone (76) (31 mg), m.p. 146.5—149 °C. Recrystallisation from light petroleum gave plates, m.p. 148—149 °C (Found: C, 66.0; H, 5.9. $C_{19}H_{20}O_6$ requires C, 66.3; H, 5.8%); τ 1.99—3.10 (8 H, aromatics), 6.14 (3 H, s, ArOMe), 6.60, 6.88, 6.91 (3 × 3 H, 3 s, 3 × aliphatic OMe).

(*b*) The bromoflavanone (50 mg) and silver nitrate (34 mg)

were stirred and boiled in methanol (8 ml). T.l.c. after 15 min showed complete reaction to have occurred.

(*c*) The bromoflavanone (50 mg) and silver nitrate (25 mg) were stirred in benzene (2 ml) containing methanol (0.1 ml). T.l.c. showed that the reaction was complete after 4 h, and almost complete after 2.5 h.

(*d*) The bromoflavanone (50 mg) and silver nitrate (25 mg) were stirred in acetonitrile (2 ml) containing methanol (0.1 ml). T.l.c. after 4 h showed partial reaction.

3-*Ethoxy*-2,3,4′-*trimethoxyflavan*-4-*one* (77).—3-Bromo-2,3,4′-trimethoxyflavanone (100 mg) and silver nitrate (70 mg) were stirred and boiled in ethanol (10 ml) for 10 min. T.l.c. in 20% ether–light petroleum showed complete conversion into a single product had occurred. Work-up (including washing an ethereal solution with aqueous ammonia) gave an oil which on recrystallisation from light petroleum gave needles of 3-*ethoxy*-2,3,4′-*trimethoxyflavanone* (77) (71 mg), m.p. 97—98.5 °C (Found: C, 66.9; H, 6.1. $C_{20}H_{22}O_6$ requires C, 67.0; H, 6.2%); τ 1.97—3.20 (8 H, aromatics), 6.19 (3 H, s, ArOMe), 6.00—6.52 (2 H, complex, OCH_2CH_3), 6.92 and 6.97 (2 × 3 H, 2 s, 2 × OMe), and 8.78 (3 H, t, OCH_2CH_3).

2,3,3,4′-*Tetramethoxyflavan*-4-*ol* (79).—A solution of 2,3,3,4′-tetramethoxyflavanone (200 mg) in ether (15 ml) was added to a solution of lithium aluminium hydride (50 mg) in ether (5 ml) at 0 °C. T.l.c. after 15 min indicated the absence of starting material. Work-up gave an oil which solidified and separated from light petroleum as nodules of 2,3,3,4′-*tetramethoxyflavan*-4-*ol* (161 mg), m.p. 101—103 °C (Found: C, 65.8; H, 6.4. $C_{19}H_{22}O_6$ requires C, 65.9; H, 6.4%); τ 2.20—3.21 (8 H, aromatics), 4.85 (1 H, d altered to s by D_2O, 4-H), 6.20 (3 H, s, ArOMe), 6.42, 7.11, 7.20 (3 × 3 H, 3 s, 3 × OMe), and 7.41 (1 H, d, OH); $J_{4,OH}$ 11.9 Hz.

3-*Acetoxy*-2,3,4′-*trimethoxyflavan*-4-*ones* (78).—3-Bromo-2,3,4′-trimethoxyflavanone (100 mg), silver acetate (70 mg), and acetic acid–acetic anhydride (5 ml) saturated with sodium acetate were mixed and kept at room temperature for 24 h. Dilution with ether, washing successively with brine, water, saturated aqueous sodium hydrogen carbonate, and water, and evaporation of the ether gave a mixture (93 mg) of the two stereoisomers of 3-*acetoxy*-2,3,4′-*trimethoxyflavanone* (78) in the ratio (by n.m.r.) of 9 : 1. Recrystallisation from methanol gave the major isomer (73 mg), as prisms, m.p. 164—165.5 °C (Found: C, 64.3; H, 5.3. $C_{20}H_{20}O_7$ requires C, 64.5; H, 5.4%); τ 1.93—3.17 (8 H, aromatics), 6.15 (3 H, s, ArOMe), 6.71 and 6.95 (2 × 3 H, 2 s, 2 × OMe), and 7.85 (3 H, s, OAc).

The n.m.r. spectrum of the minor isomer, obtained from the spectra of mixtures, is as follows: τ *ca.* 1.93—3.17 (8 H, aromatics), 6.39 (3 H, s, ArOMe), 6.71 and 6.95 (2 × 3 H, 2 s, 2 × OMe), and 8.10 (3 H, s, OAc).

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