Synthesis of Biflavonoids in which the Flavan Units are linked through Oxygen from C-2 to C-3 or C-4

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Flav-2-enes [*e.g.* (**1**)] have been utilised *via* 2,3-*cis*-2-acetoxy-3-bromoflavans for the synthesis of C-2–*O*–C-3- and C-2–*O*–C-4-linked biflavonoids. For example, 2,3-*cis*-2-acetoxy-3-bromoflavans [*e.g.* (**19**)] react with (±)-tetra-*O*-methylcatechin (**18**) to give 2,3-*cis*-3-bromo-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavans (**21**) and (**23**) which have been converted into 3,4-*cis*-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan-3,4-diols (**24**) and (**25**). The reaction between the 2-acetoxy-3-bromoflavans (**4**) and (**5**) and 2,4-*cis*-flavan-4-ols (**2**) and (**3**) yields 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavans (**6**)—(**11**) which similarly are convertible into biflavonoid 3,4-*cis*-diols [*e.g.* (**12**) and (**13**)]. Flavan-3,4-*trans*-diols [*e.g.* (**30**)] react with 2-acetoxy-3-bromoflavans [*e.g.* (**4**)] to give 2,3-*cis*-3-bromo-2-(2,3-*trans*-3,4-*trans*-4-hydroxyflavan-3-yloxy)-(**31**) and (**33**) and 2,3-*cis*-3-bromo-2-(2,3-*trans*-3,4-*trans*-3-hydroxyflavan-4-yloxy)flavans (**35**) and (**37**), and flavan-3,4-*cis*-diols [*e.g.* (**42**)] give the corresponding 2,3-*cis*-(2,3-*trans*-3,4-*cis*)-compounds (**43**)—(**46**). The structures and stereochemistries of the biflavonoids have been established by analysis of n.m.r. spectra and by chemical transformations.

Our discovery[1] that flav-2-enes, *e.g.* (**1**), can be converted in good yield into 2-acyloxy-3-bromoflavans, *e.g.* (**4**), has opened the way to a general synthesis of biflavonoids in which a flavan skeleton is linked through oxygen from C-2 to C-3 or to C-4 of another flavan, *e.g.* (**20**) and (**22**) or (**6**) and (**9**). Essentially these syntheses have been achieved by the interaction of flav-2-enes with flavan-3-ols, *e.g.* (**18**) or with flavan-4-ols, *e.g.* (**2**). Naturally occurring biflavonoids linked through oxygen at C-2 are rare and no general methods for their synthesis exist.[2] However, from time to time, such structures have been advanced[3,4] and some subsequently disproved[5] for various natural products.

2,3-*cis*-2-Acetoxy-3-bromoflavan (**4**)†, which can easily be prepared from flav-2-ene (**1**),[1] reacted with 2,4-*cis*-flavan-4-ol (**2**) in benzene to give, in 90% yield, a 1:1 mixture of two diastereoisomeric C-2–O–C-4-linked biflavonoids (**6**) and (**9**) (Scheme 1) as expected from the known[1] reaction of 2-acetoxy-3-bromoflavans, *e.g.* (**4**), with alcohols. The two isomers were separated on preparative t.l.c. plates and gave rise to very weak molecular ions of the expected mass and analysed satisfactorily for the dimeric structures (**6**) and (**9**). Their n.m.r. spectra were consistent with these structures, but although the spectra differed appreciably (see Experimental section), it was not possible to assign the relative stereochemistry of the two flavan units. However, it is clear that both isomers have 2,3-*cis*-stereochemistry (between the 2-phenyl and 3-bromine substituents) ($J_{3,4}$ 6.0—6.5 Hz) in the lower (as drawn), bromine-containing flavan unit. For one of the diastereoisomers, (**6**) or (**9**), it was possible from the appearance of the 3-H n.m.r. resonance in the upper flavan unit to calculate $J_{2,3}$ (*ca.* 2.2 and 11.8 Hz) and $J_{3,4}$ (*ca.* 6.3 and 10.1 Hz). These values are only consistent with 2,4-*cis* relative stereochemistry. Since the 2,4-stereochemistry of the flavan ring is unlikely to change under the reaction conditions employed, we believe that both isomers have 2,4-*cis*-stereochemistry in the upper flavan unit and 2,3-*cis*-stereochemistry (between phenyl and bromo groups) in the lower flavan unit as in the starting materials (**2**) and (**4**).

The two isomers (47%) can be prepared more directly but less conveniently by the reaction between flav-2-ene (**1**), a large excess of 2,4-*cis*-flavan-4-ol (**2**), and *N*-bromosuccinimide (NBS), as expected from the known[1] addition of alcohols and bromine to flav-2-enes. The preparation of 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) from flav-2-ene (**1**) and its reaction, without isolation, with 2,4-*cis*-flavan-4-ol (**2**) gave a 74% yield of the mixture of the two diastereoisomers (**6**) and (**9**), a procedure which is tantamount to a synthesis of the biflavonoids directly from flav-2-ene (**1**).

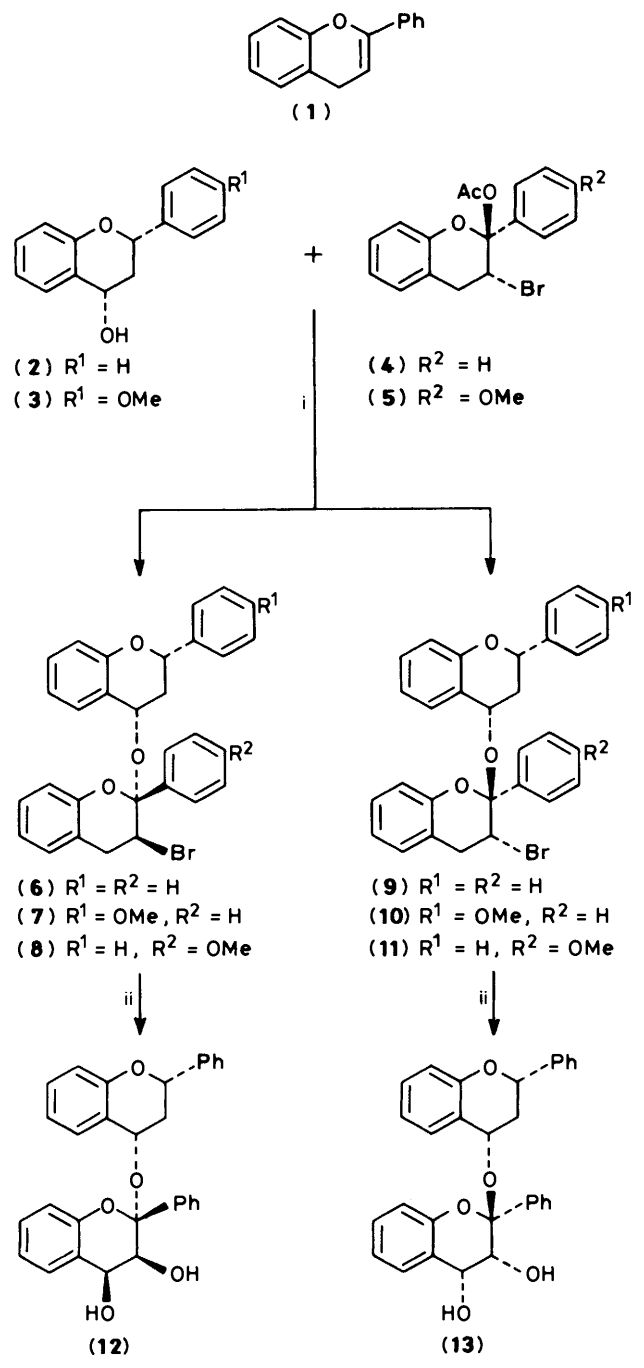
Each of the biflavonoids (**6**) or (**9**) underwent elimination of hydrogen bromide with methanolic potassium hydroxide to yield a respective unstable flav-3-ene which was immediately treated with osmium tetraoxide. The resulting osmate esters were hydrolysed to give *ca.* 80% yields of the dimeric 3,4-*cis*-diols (**12**) and (**13**). By an analogous argument to that used for a monomeric 2-alkoxyflavan-3,4-diol synthesized by this route[1] it seems likely that both these biflavonoids have 2,3-*cis*-(between Ph and OH)-3,4-*cis*-stereochemistry in the lower flavan unit as shown, but this assignment of 2,3-*cis*-stereochemistry cannot be regarded as established beyond all doubt.

2,3-*cis*-2-Acetoxy-3-bromo-4′-methoxyflavan (**5**), which has not been isolated,[1] reacted *in situ* with 2,4-*cis*-flavan-4-ol (**2**) to give in *ca.* 50% yield the two expected biflavonoids (**8**) and (**11**); and 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) reacted with 2,4-*cis*-4′-methoxyflavan-4-ol (**3**) to give two more biflavonoids (85%), (**7**) and (**10**).

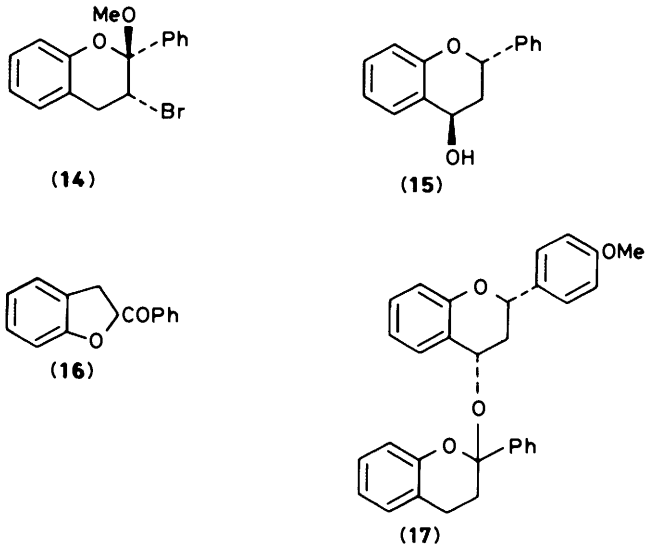
The biflavonoids are readily cleaved by acidic reagents. For example, one of the biflavonoids of structure (**7**) or (**10**) is converted into 2,4-*cis*-4′-methoxyflavan-4-ol (**3**) (68%) and 2,3-*cis*-3-bromo-2-methoxyflavan (**14**) (72%) by methanol and toluene-*p*-sulphonic acid at room temperature. Hot aqueous hydrochloric acid converts one of the biflavonoids of structure (**6**) or (**9**) into 2,4-*trans*-flavan-4-ol (**15**) (51%) and flav-3-ene (36%), both presumably formed by the action of hot acid on the original product, 2,4-*cis*-flavan-4-ol (**2**).[6] From the bromoflavan unit, 2-benzoylcoumaran (2-benzoyl-2,3-dihydrobenzofuran) (**16**) (57%) was obtained as expected on acid hydrolysis.[1] By analogy with the reaction previously reported,[1] the bromine atom was efficiently removed from one of the biflavonoids of structure (**7**) or (**10**) by tri-n-butyltin hydride, yielding (71%) one diastereoisomer of 2-(2,4-*cis*-4′-methoxyflavan-4-yloxy)-flavan (**17**).

Biflavonoids containing a C-2–O–C-3 link, *e.g.* (**20**) and (**22**), result from the reaction of 2,3-*cis*-2-acetoxy-3-bromoflavans,

† 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 1. *Reagents:* i, hot benzene; ii, (*a*) KOH–MeOH, (*b*) OsO_4, (*c*) Na_2SO_3, aq. EtOH. All compounds are racemic. Relative stereochemistry is indicated.

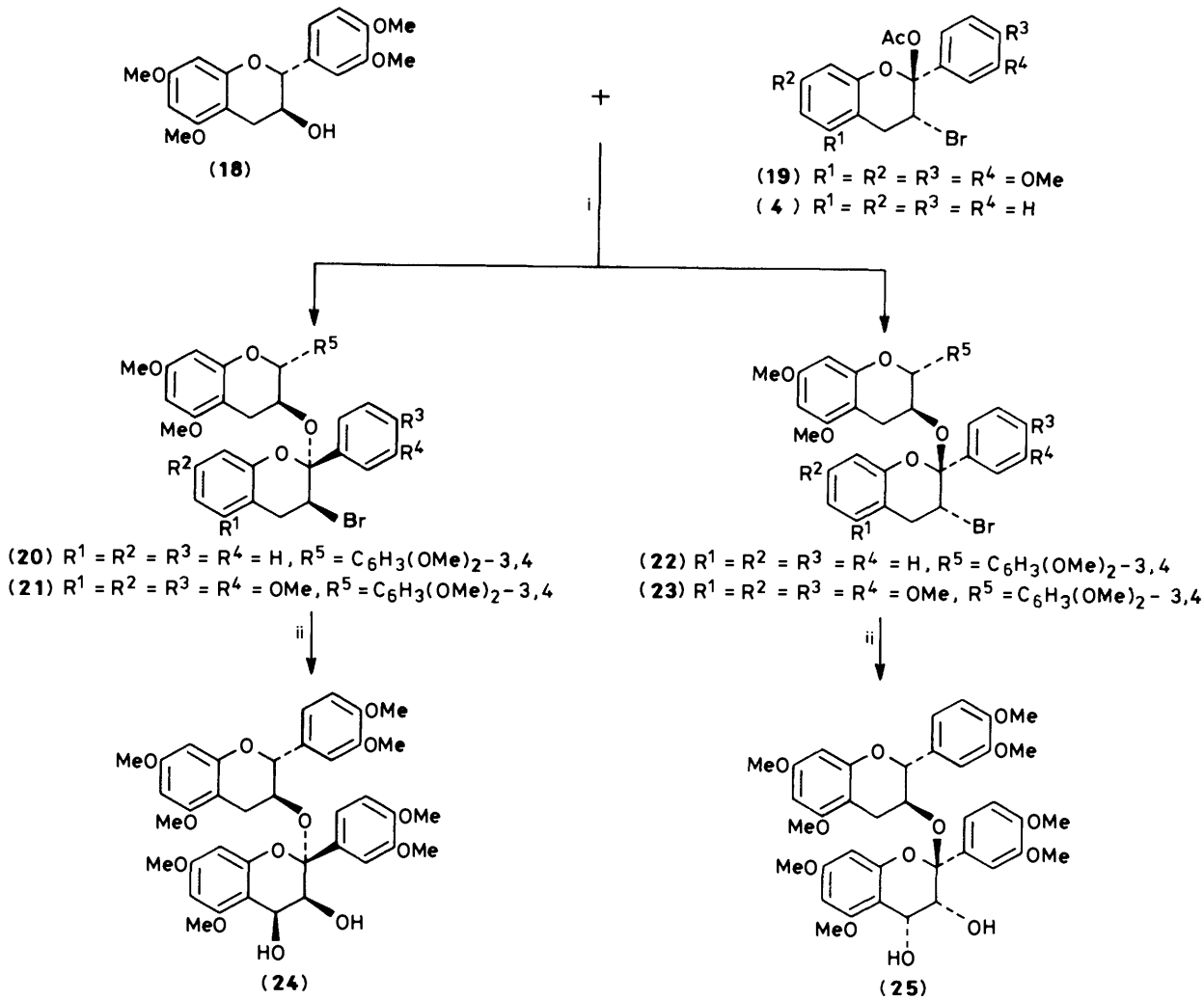


e.g. (**4**), with (±)-tetra-*O*-methylcatechin (**18**) (Scheme 2). 2,3-*cis*-2-Acetoxy-3-bromoflavan (**4**) reacted to give a 95% yield of the diastereoisomeric biflavonoids (**20**) and (**22**). 2,3-*cis*-2-Acetoxy-3-bromo-3′,4′,5,7-tetramethoxyflavan (**19**) reacted *in situ* with (±)-tetra-*O*-methylcatechin (**18**) to yield a mixture of two isomeric biflavonoids (**21**) and (**23**) which were separated on preparative t.l.c. plates with difficulty.

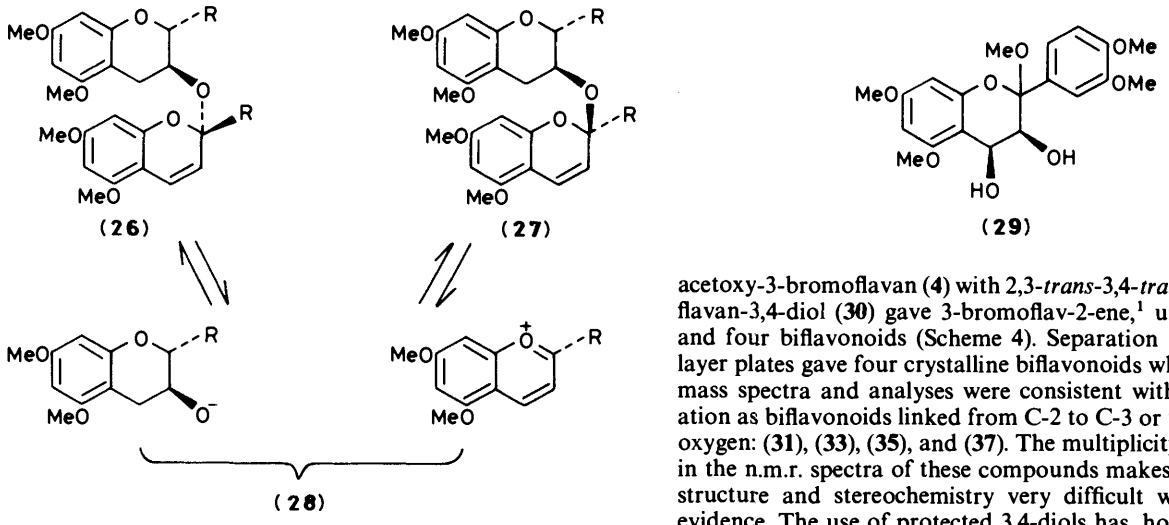
This difficulty caused us first to use the mixture of diastereoisomers (**21**) and (**23**) for our investigation of the dehydrobromination to flav-3-enes (**26**) and (**27**), which proved to be a slow reaction. The best procedure found was to use potassium hydroxide in hot dioxane and to hydroxylate the flav-3-enes immediately with osmium tetraoxide which gave a 66.5% yield of a 1:1 mixture of the expected stereoisomeric 3,4-*cis*-diols (**24**) and (**25**). Surprisingly, when either of the two isomers (**21**) or (**23**) was treated in the same way as the mixture, an identical 1:1 mixture of the stereoisomeric, 3,4-*cis*-diols (**24**) and (**25**) was obtained. A plausible explanation of this behaviour is that the diastereoisomeric flav-3-enes (**26**) and (**27**) can undergo dissociation into a common ion pair (**28**), the driving force being the formation of a stabilised flavylium cation (Scheme 3). Recombination of the ions can give either diastereoisomer (**26**) or (**27**) and thus each biflavonoid is epimerised at the 2-position. In confirmation of this dissociation we found that the ions could be trapped by methanol. When the flav-3-enes (**26**) and (**27**) were generated by treatment of the diastereoisomeric 3-bromoflavans (**21**) and (**23**) with methanolic potassium hydroxide in tetrahydrofuran (THF) until the reaction had reached completion and the products were hydroxylated with osmium tetraoxide, (±)-tetra-*O*-methylcatechin (**18**) was obtained from the anion and a 2,3′,4′,5,7-pentamethoxyflavan-3,4-*cis*-diol (**29**) (probably 2,3-*cis* between Ar and OH) was obtained from the cation by hydroxylation of the assumed initial 2,3′,4′,5,7-pentamethoxyflav-3-ene. The possibility that the diastereoisomeric 3-bromobiflavonoids (**21**) and (**23**) dissociated and were solvolysed before elimination of hydrogen bromide seems unlikely because a mixture of the biflavonoids was unchanged in boiling ethanol and dioxane in the absence of acid.

The two dimeric 3,4-*cis*-diols (**24**) and (**25**), which have the structure proposed [3] for the octamethyl ether of a procyanidin isolated from barley, had different retention times when examined by analytical h.p.l.c. (high-pressure liquid chromatography) on a reversed-phase column and were separated preparatively by reversed-phase partition t.l.c. Both were obtained as analytically pure solids whose n.m.r. spectra each contained half of the signals associated with the original 1:1 mixture. From the dissimilar values of the 2*,3*-coupling* constants and from the chemical shifts of the 4*-protons in each diol, it was possible to decide which diol and which starting 3-bromobiflavonoid had the same stereochemistry.

* Hydrogen atoms designated with an asterisk, *e.g.* 2*-H, *etc.*, refer to those in the 'upper,' alcohol-derived flavan unit as written in the reaction schemes.

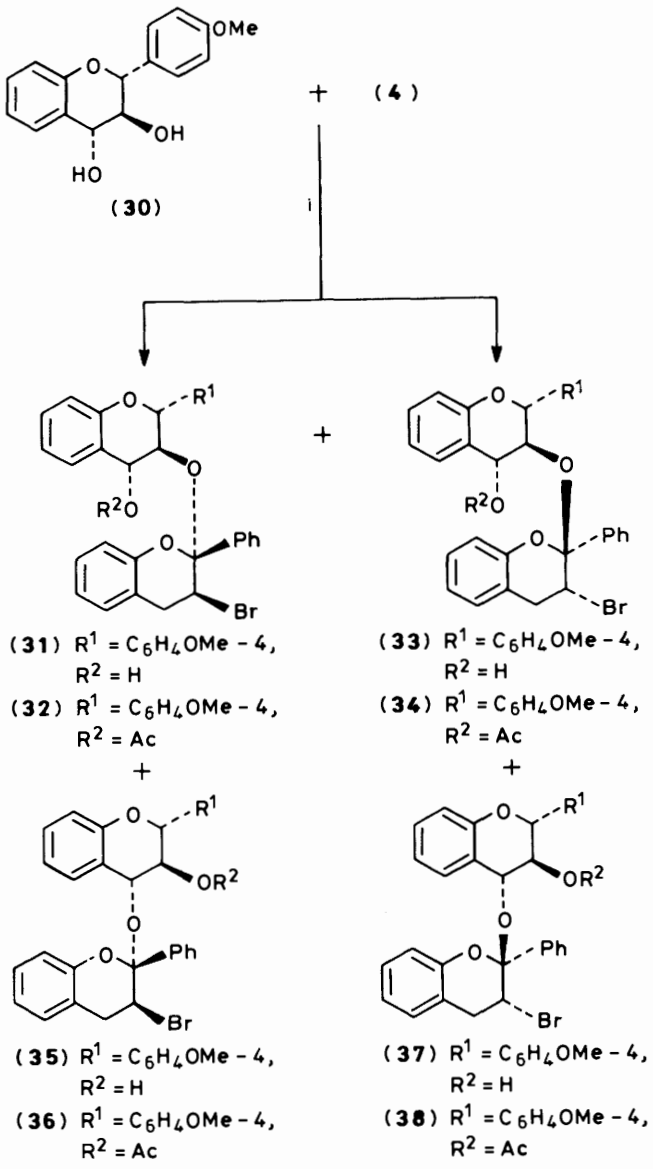


Scheme 2. *Reagents:* i, hot benzene; ii (*a*) KOH–dioxane, (*b*) OsO_4, (*c*) Na_2SO_3, aq. EtOH

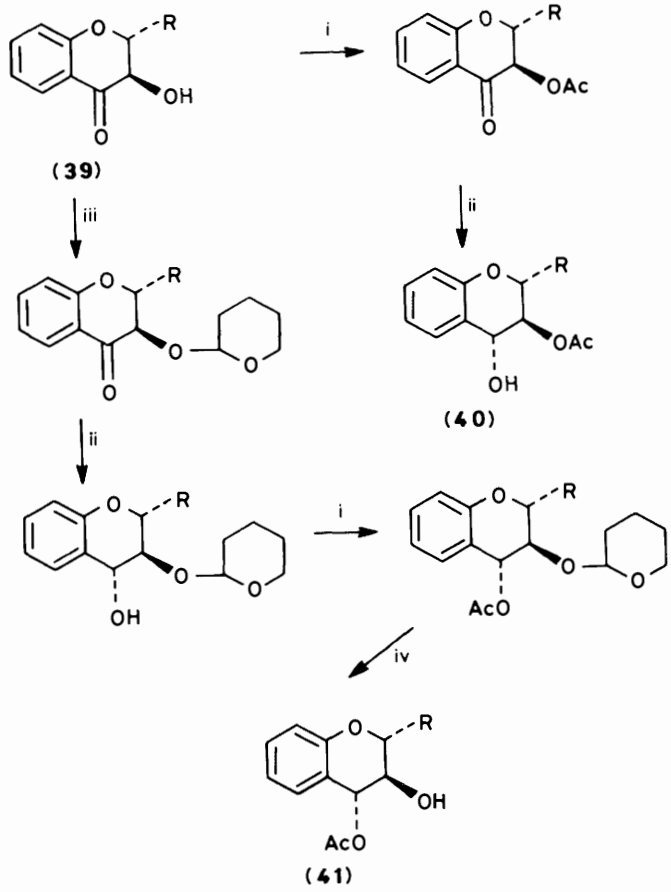


Scheme 3. R = 3,4-Dimethoxyphenyl

From the 4′-methoxyflavan-3,4-diols, 3,4-*cis* (**42**) and 3,4-*trans* (**30**), we have synthesized C-2–O–C-3-linked biflavonoids containing a 4-hydroxy group and C-2–O–C-4-linked compounds with a 3-hydroxy group. The reaction of 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) with 2,3-*trans*-3,4-*trans*-4′-methoxyflavan-3,4-diol (**30**) gave 3-bromoflav-2-ene,[1] unchanged diol, and four biflavonoids (Scheme 4). Separation on preparative layer plates gave four crystalline biflavonoids whose n.m.r. and mass spectra and analyses were consistent with their formulation as biflavonoids linked from C-2 to C-3 or to C-4 through oxygen: (**31**), (**33**), (**35**), and (**37**). The multiplicity of the signals in the n.m.r. spectra of these compounds makes assignment of structure and stereochemistry very difficult without further evidence. The use of protected 3,4-diols has, however, enabled the structures with a C-2–O–C-3 link, (**31**) and (**33**), and those with a C-2–O–C-4 link, (**35**) and (**37**), to be assigned. 2,3-*trans*-3,4-*trans*-3-Acetoxy-4′-methoxyflavan-4-ol (**40**) and the isomeric 4-acetoxy-4′-methoxyflavan-3-ol (**41**) were synthesized by the routes shown (Scheme 5) from 2,3-*trans*-3-hydroxy-4′-methoxyflavan-4-one (**39**). The 3-acetoxyflavan-4-ol (**40**)



Scheme 4. *Conditions:* i, hot benzene



Scheme 5. *Reagents:* i, Ac_2O–pyridine; ii, H_2/Pd–C; iii, dihydropyran–H^+; iv, H_3O^+. R = C_6H_4OMe-4

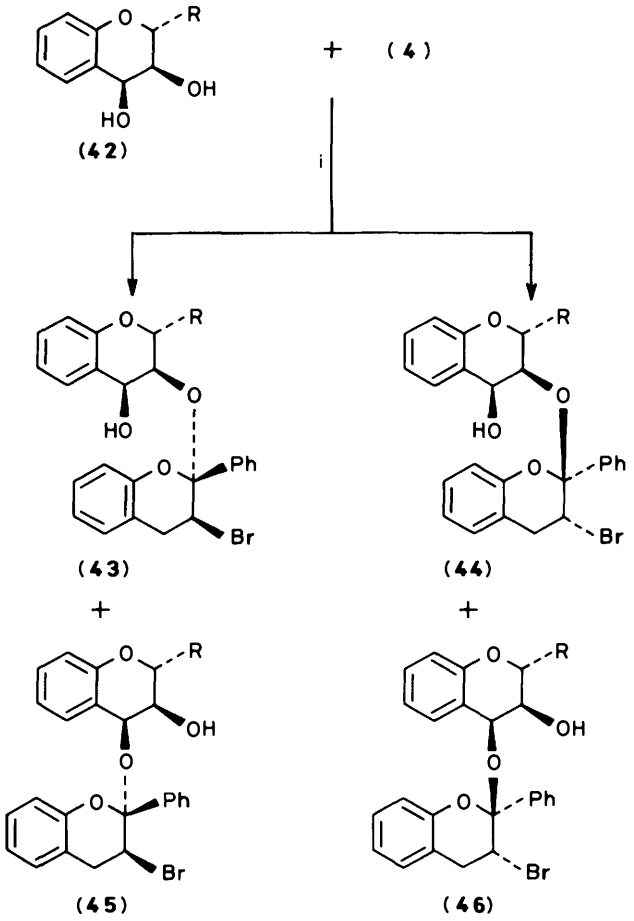
reacted with 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) to give two 3-acetoxybiflavonoids, (**36**) and (**38**). The 4-acetoxyflavan-3-ol (**41**) gave two 4-acetoxybiflavonoids, (**32**) and (**34**). Each of the biflavonoids (**31**), (**33**), (**35**), and (**37**) obtained from 2,3-*trans*-3,4-*trans*-4′-methoxyflavan-3,4-diol (**30**) was acetylated and each of the four products was found to be identical with a different one of the biflavonoid acetates synthesized from the acetoxyflavanols (**40**) and (**41**), thus identifying the pair with a C-2–O–C-4 link [(**35**) and (**37**)] and the pair [(**31**) and (**33**)] with a C-2–O–C-3 link.

2,3-*trans*-3,4-*cis*-4′-Methoxyflavan-3,4-diol (**42**) reacted with 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) to give 3-bromoflav-2-ene, unchanged diol, and four crystalline compounds, separated on an alumina column and shown by n.m.r. spectroscopy and analysis to be biflavonoids linked through oxygen from C-2 to C-3 and from C-2 to C-4 (Scheme 6). Complete assignment of the stereochemistry in each compound could not be made. However, from the effects of D_2O addition on the multiplicity of the 3*-H and the 4*-H signals in the n.m.r. spectra of the four biflavonoids (designated A, B, C, and D; see Experimental section), it was deduced which of them (B and D) have linkages to C-3 of the diol moiety, (**43**) and (**44**), and which (A and C) are 4-linked, (**45**) and (**46**).

Experimental

Measurements of n.m.r. spectra were made in $CDCl_3$ on a Perkin-Elmer R14 spectrometer. Coupling constants are quoted in Hz. I.r. spectra were recorded in CCl_4 unless otherwise stated, on a Perkin-Elmer 257 spectrophotometer. Mass spectra were recorded on a Varian MAT CH7 or an AE1 MS9 instrument with direct insertion. Merck silica HF_{254} was used for t.l.c. and PF_{254} for p.l.c. and M60 silica gel or Camag neutral alumina deactivated by shaking with 5% of its weight of water for columns. Unbaked glass plates coated with silanised Kieselgel PF_{254} or ordinary HF_{254} silica plates which had been impregnated with paraffin by immersion in a 10% solution of heavy paraffin in light petroleum, b.p. 40—60 °C, for 2 min were used for reversed-phase t.l.c. Paraffin-impregnated layers were used for reversed-phase preparative layer chromatography (p.l.c.). For analytical h.p.l.c. a Perkin-Elmer Model 1240 instrument equipped with a Corasil C-18 column (supplied by Waters Associates) was used. Light petroleum refers to that fraction with b.p. 60—80 °C unless otherwise stated. Ether refers to diethyl ether.

2,3-cis-3-*Bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)*flavans* (**6**) *and* (**9**).—(a) A solution of 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) (1.50 g) and 2,4-*cis*-flavan-4-ol (**2**) (1.47 g) in benzene (75 ml) was refluxed under nitrogen for 12 h. The solution was



Scheme 6. *Conditions:* i, hot benzene. R = C_6H_4OMe-4

evaporated to *ca.* 10 ml, and some of the excess of 2,4-*cis*-flavan-4-ol (371 mg) was removed by filtration. The filtrate was evaporated, and the residue was transferred to a column of alumina (300 g) made up in benzene–light petroleum (1:9), and eluted with light petroleum containing progressively more benzene (ultimately 50%). Evaporation of fractions containing the minor component yielded 3-bromoflav-2-ene[1] (87 mg).

Evaporation of fractions containing the major product yielded a solid (1.99 g), a sample (610 mg) of which was applied to three 100 cm p.l.c. plates and eluted 20 times with 1% ether–light petroleum (b.p. 40—60 °C). Work-up of the band of higher R_F yielded a solid (289 mg) which separated from methanol to yield one diastereoisomer of 2,3-cis-3-*bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)*flavan* as plates (270 mg), m.p. 167—169 °C (Found: C, 70.3; H, 4.95; Br, 15.3. $C_{30}H_{25}BrO_3$ requires C, 70.2; H, 4.9; Br, 15.6%); τ 2.14—3.31 (18 H, m, ArH), 5.07—5.27 (3 H, m, superimposed 2*-, 3-, and 4*-H), 6.14 (1 H, 2 d, 4-H), 6.94 (1 H, pair of incompletely resolved doublets, 4-H), 7.49 (1 H, 2 q, 3*-H), and 8.22 (1 H, 2 q, 3*-H); $J_{3,4}$ 1.8 and 4.3, $J_{4,4}$ 17.1; *m/z* (120 °C) 514/512 (M^+, 0.1%), 209 (100), 210 (17), 207 (14), 208 (13), and 91 (11).

Work-up of the band of lower R_F gave a solid which separated from methanol to yield the other diastereoisomer of 2,3-cis-3-*bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)*flavan* as needles (209 mg), m.p. 170—170.5 °C (decomp.) (Found: C, 70.5; H, 5.0; Br, 15.8%); τ 2.20—2.59 (18 H, m, ArH), 4.76 (1 H, q, 4*-H), 5.15—5.30 (2 H, m, superimposed 2*- and 3-H), 6.00 (1 H, 2 d, 4-H), 6.79 (1 H, pair of incompletely resolved doublets, 4-H), 8.21 (1 H, 2 q, 3*-H), and 8.56 (1 H, 2 q, 3*-H); $J_{3,4}$ 2.0 and 4.5, $J_{4,4}$ 17.2; *m/z* (110 °C) 514/512 (M^+, 0.2%), 209 (100), 210 (17), 207 (16), 208 (13), and 91 (7).

(b) A suspension of 2,4-*cis*-flavan-4-ol (**2**) (1.10 g) in dioxane (5 ml) was stirred for 15 h in the presence of a few pellets of molecular sieve (type 4A) before solid flav-2-ene (50 mg) was added, followed after 5 min by a solution of NBS (47 mg) in dioxane (1 ml). After 10 min more NBS (23.5 mg) in dioxane (0.5 ml) was added, followed after 4 h by cyclohexene (0.1 ml). Chloroform (200 ml) was added, and the solution was washed with water (4 × 150 ml) and dried ($MgSO_4$). Evaporation gave a solid which was triturated with ether (20 ml). Undissolved material (excess of 2,4-*cis*-flavan-4-ol) was collected, the filtrate was evaporated, and the process was repeated, this time triturating the solid with benzene. After evaporation of the filtrate, the residue was transferred to a column of alumina (170 g) made up in benzene. Elution with benzene gave a mixture of reaction products from which was isolated by p.l.c. a mixture (58 mg; 1:1) of diastereoisomers of 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavan identified by t.l.c. comparison with the products of the preceding reaction and by its n.m.r. spectrum which was identical with that of the mixture of diastereoisomers obtained above.

(c) To a stirred solution of flav-2-ene (208 mg) in dioxane (2 ml) and acetic acid–acetic anhydride (9:1; 2 ml) was added a solution of NBS (196 mg) in dioxane (2 ml) and acetic acid–acetic anhydride (2 ml) during 1 min. After 15 min, cyclohexene (0.2 ml) was added, followed by powdered 2,4-*cis*-flavan-4-ol (455 mg) and the solution was heated at 70—80 °C for 20 h. Ether (200 ml) was added, and the solution was washed in turn with saturated aqueous sodium hydrogen carbonate (3 × 150 ml) and water (1 × 150 ml), and dried ($MgSO_4$). Removal of the solvent gave a solid which was transferred as a suspension in benzene to a column of alumina (170 g) made up in benzene–light petroleum (1:4). Elution with benzene–light petroleum mixtures of gradually increasing polarity gave fractions containing the major product free from 2,4-*cis*-flavan-4-ol. Further purification on a column of alumina (50 g) made up in light petroleum and eluted with benzene–light petroleum (95:5) gave a mixture of diastereoisomers of 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy) flavan (381 mg) which exhibited identical t.l.c. behaviour with that of the mixture of diastereoisomers obtained above and had the same n.m.r. spectrum.

The faster running diastereoisomer of 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavan, m.p. 167—169 °C (200 mg) was dissolved in dioxane (10 ml) and the solution was boiled with dil. hydrochloric acid (1 ml) for 40 min. Isolation with ether gave a mixture which was applied to a column of silica (30 g) in light petroleum and eluted with 4% ether–light petroleum to give an oil (29 mg) identified (n.m.r.) as flav-3-ene. Elution with 32% ether–light petroleum gave 2,4-*trans*-flavan-4-ol (45 mg), m.p. and mixed m.p. 117—118 °C. Fractions eluted between these two products gave mixtures which were subjected to p.l.c.: 14 elutions with 5% ether–light petroleum gave a near-continuum of bands; the region of highest R_F afforded 2-benzoylcoumaran (**16**) (50 mg) which separated from methanol as plates, m.p. and mixed m.p. 96—97 °C.[1]

2,3-cis*-3,4-cis-2-(2,4-cis-*Flavan*-4-*yloxy*)*flavan*-3,4-*diols* (**12**) *and* (**13**).—(a) *First diastereoisomer.* A solution of the faster running diastereoisomer of 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavan, m.p. 167—169 °C (625 mg) in THF (15 ml) was boiled with 10% methanolic potassium hydroxide (15 ml) for 5.25 h. Ether (200 ml) was added and the solution was washed with water (3 × 150 ml) and dried ($MgSO_4$). Evaporation of the solvent gave the 3-ene as a solid which began to discolour when exposed to air.

* This stereochemical assignment must be regarded as tentative.

To a stirred solution of the 3-ene in THF (45 ml) containing dry pyridine (3 ml) was added a solution of osmium tetraoxide (500 mg) in ether (50 ml). After 12 h the solvent was evaporated and the residue was stirred with sodium sulphite (9 g) in water (75 ml) and ethanol (15 ml) for 5 h and the mixture was boiled for 1.5 h. The black colloidal suspension was filtered through a pad of Celite which was washed several times with hot chloroform. The organic layer was separated from the two-phase filtrate and the aqueous layer was again extracted with chloroform. The combined organic extracts were dried ($MgSO_4$), evaporated, and a solution of the residue in ether was washed in turn with 2M-hydrochloric acid (twice) and then with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to give a solid. Recrystallisation from methanol gave one diastereoisomer of 2,3-cis-3,4-cis-2-(2,4-cis-*flavan*-4-*yloxy*)*flavan*-3,4-*diol* as needles (470 mg), m.p. 108.5—110.5 °C, which resolidified and then melted again at 207—207.5 °C (Found, on material dried *in vacuo* at room temperature: C, 74.0; H, 5.7. Found, on material dried at 60 °C *in vacuo* for 18 h: C, 74.2, 74.4; H, 5.6, 5.5. $C_{30}H_{26}O_5 \cdot CH_3OH$ requires C, 74.7; H, 6.1%); τ 2.08—3.26 (18 H, m, ArH), 4.85—5.18 (3 H, br m, sharpens on addition of D_2O giving a doublet at τ 4.92, 4-H, plus 6 lines, superimposed 2*- and 4*-H), 5.67 (1 H, br t, collapses to a doublet when D_2O is added, 3-H), 6.59 (*ca.* 0.7 H, s, CH_3OH of crystallisation), 7.37—7.58 (2 H, br m, collapses into 2 q on addition of D_2O, 4-OH and 3*-H), 7.99—8.33 (2 H, br m, collapses into 2 q on addition of D_2O, 3-OH and 3*-H), and 8.43 (small br s, disappears on addition of D_2O, CH_3OH of crystallisation); $J_{3,4}$ 4.1, $J_{3,OH}$ *ca.* 5. Methanol of crystallisation was removed by heating the material at 115—135 °C *in vacuo* for 6 h, when the diol melted and slowly resolidified to give a solid, m.p. 206.5—208 °C (Found: C, 76.9; H, 5.55. $C_{30}H_{26}O_5$ requires C, 77.2; H, 5.6%); *m/z* (225 °C, MS9) M^+ not observed; 209 (100%), 207 (27), 104 (25), 210 (24), 208 (24), and 426 (23); $\nu_{max.}$ (Nujol) 3 520 ws and 3 300br (OH), 1 238, 1 051, and 1 030 cm^{-1}.

(b) *Second diastereoisomer.* The slower running diastereoisomer of 2,3-cis-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavan, m.p. 170—170.5 °C (210 mg) was dissolved in THF (10 ml) and the solution was boiled with 10% methanolic potassium hydroxide (10 ml) for 5 h; the 3-ene was extracted into ether as above. To a stirred solution of the 3-ene in THF (10 ml) containing dry pyridine (1 ml) was added a solution of osmium tetraoxide (155 mg) in ether (15.5 ml). After 11 h, the osmate ester was hydrolysed with sodium sulphite (6 g) in water (50 ml) and ethanol (10 ml) as above. Since the diol was sparingly soluble in ether, pyridine was extracted directly from the chloroform solution with 2M-hydrochloric acid. Evaporation gave a solid which separated from methanol to yield a second diastereoisomer of 2,3-cis-3,4-cis-2-(2,4-cis-*flavan*-4-*yloxy*)-*flavan*-3,4-*diol* as needles (97 mg), m.p. 93—95 °C, which slowly resolidified and melted again at 166.5—168 °C (Found, on material dried *in vacuo* at room temperature: C, 73.7; H, 5.9. $C_{30}H_{26}O_5 \cdot 1.5\ CH_3OH$ requires C, 73.6; H, 6.3%); τ 2.15—3.45 (18 H, m, ArH), 4.68—4.87 (2 H, br m, sharpens on addition of D_2O, superimposed 4- and 4*-H), 5.21 (1 H, q, 2*-H), 5.70 (1 H, t, collapses into a doublet when D_2O is added, 3-H), 6.58 (*ca.* 2.5 H, s, CH_3OH of crystallisation), 7.37 (1 H, d, disappears on addition of D_2O, 4-OH), 7.97 (1 H, d, disappears when D_2O is added, 3-OH), 8.14 (1 H, 2 q 3*-H), 8.48 (1 H, 2 q, 3*-H), and 8.95 (small br s, disappears on addition of D_2O, CH_3OH of crystallisation); $J_{3,4}$ 4.1, $J_{3,OH}$ 5.0, $J_{4,OH}$ 10.8. Material which had been heated at 115—130 °C *in vacuo* for 6 h had m.p. 165.5—167.5 °C (Found: C, 77.2; H, 5.6. $C_{30}H_{26}O_5$ requires C, 77.2; H, 5.6%); *m/z* (205 °C, MS9) 466 (M^+, just detectable at high gain), 209 (100%), 104 (70), 222 (67), 207 (65), and 208 (62); $\nu_{max.}$ (Nujol) 3 540 w, 3 505sh, and 3 380br (OH), 1 232, 1 010br, and 760 cm^{-1}.

2,3-cis-3-*Bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)-4′-*methoxyflavans* (**8**) *and* (**11**).—To a stirred solution of 4′-methoxyflav-2-ene (238 mg) in dioxane (3 ml) and acetic acid–acetic anhydride (9:1; 3 ml) was added a solution of NBS (196 mg) in dioxane (2 ml) and acetic acid–acetic anhydride (2 ml) during 1 min. After 15 min, dry cyclohexene (0.2 ml) was added, followed after a further 5 min by powdered 2,4-*cis*-flavan-4-ol (**2**) (455 mg). The solution was heated at *ca.* 70 °C for 9 h and worked up as described above for the diastereoisomers of 2,3-*cis*-3-bromo-2-(2,4-*cis*-flavan-4-yloxy)flavan. The products were purified on a column of alumina (160 g, 6.5% deactivated) made up in benzene–light petroleum (1:4). Elution with benzene–light petroleum (3:7) gave fractions which on evaporation yielded 3-bromo-4′-methoxyflav-2-ene (15 mg) as needles, m.p. 78—80.5 °C. The n.m.r. spectrum was identical with that of an authentic specimen.[1] Elution with benzene–light petroleum (65:35) gave five fractions (35 ml each), the first two of which were combined and evaporated. Recrystallisation of the residue from methanol gave one diastereoisomer of 2,3-cis-3-*bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)-4′-*methoxyflavan* as prisms (131 mg), m.p. 141.5—143.5 °C (Found: C, 68.3; H, 4.9; Br, 14.5. $C_{31}H_{27}BrO_4$ requires C, 68.5; H, 5.0; Br, 14.7%); τ 2.23—3.30 (17 H, m, ArH), 5.03—5.29 (3 H, m, superimposed 2*-, 3-, and 4*-H), 6.03—6.25 (4 H, s at τ 6.18, OCH_3 partially obscuring 2 d for 4-H), 6.94 (1 H, incompletely resolved pair of doublets, 4-H), 7.50 (1 H, 2 q, 3*-H), and 8.23 (1 H, 2 q, 3*-H); $J_{3,4}$ 1.8 and 4.3, $J_{4,4}$ 17.2; *m/z* (100 °C); M^+ not observed, 318/316 (40), 237 (100), 194 (45), 165 (47), 121 (52), and 104 (95).

Evaporation of the remaining 3 column fractions and recrystallisation of the residue from methanol gave the second diastereoisomer of 2,3-cis-3-*bromo*-2-(2,4-cis-*flavan*-4-*yloxy*)-4′-*methoxyflavan* as needles (78 mg), m.p. 143—145 °C (Found: C, 68.65; H, 4.95; Br, 14.9%); τ 2.38—3.55 (17 H, m, ArH), 4.83 (1 H, q, 4*-H), 5.18—5.38 (2 H, m, superimposed 2*-and 3-H), 5.96—6.24 (4 H, s at τ 6.23, OCH_3 partly obscuring 2 d, 4-H), 6.86 (1 H, 2 d, 4-H), 8.20 (1 H, 2 q, 3*-H), and 8.50 (1 H, 2 q, 3*-H); $J_{3,4}$ 1.8 and 4.1, $J_{4,4}$ 17.2; *m/z* (120 °C) M^+ not observed, 318/316 (16), 104 (100%), 209 (43), 121 (42), 237 (41), 122 (32), and 77 (30).

2,3-cis-3-*Bromo*-2-(2,4-cis-4′-*methoxyflavan*-4-*yloxy*)-*flavans* (**7**) *and* (**10**).—(*a*) A solution of 2-acetoxy-3-bromoflavan (1.1 g) and 2,4-*cis*-4′-methoxyflavan-4-ol (**3**) (1.2 g) in benzene (60 ml) was boiled for 6 h. The volume was reduced to 10 ml, and the flavanol which separated was collected. The filtrate was chromatographed on a column of silica (200 g) which was made up in 5% ether–light petroleum. Elution gave firstly 3-bromoflav-2-ene (50 mg) and subsequently (with 20% ether–light petroleum) mixed diastereoisomers of the flavan-yloxyflavan (1.5 g).

A portion (585 mg) of the diastereoisomeric mixture was separated by p.l.c. (three 100 × 20 cm plates; 15 elutions with 2% ether–light petroleum) to give a slower running isomer of 2,3-cis-3-*bromo*-2-(2,4-cis-4′-*methoxyflavan*-4-*yloxy*)*flavan* (161 mg) which separated from dichloromethane–methanol as needles, m.p. 165—168 °C (Found: C, 68.2; H, 5.1; Br 14.9%); τ 2.13—3.54 (17 H, m, ArH), 4.75 (1 H, q, 4*-H), 5.17—5.38 (2 H, m, 2*- and 3-H), 5.95 (1 H, q, 4-H), 6.24 (3 H, s, OCH_3), 6.77 (1 H, q, 4-H), 8.20 (1 H, octet, 3*-H), and 8.61 (1 H, octet, 3*-H); $J_{4,4}$ 16.7, $J_{3,4}$ 4.7 and *ca.* 1.

The faster running diastereoisomer of 2,3-cis-3-*bromo*-2-(2,4-cis-4′-*methoxyflavan*-4-*yloxy*)*flavan* (165 mg) separated from dichloromethane–methanol as flakes, m.p. 161—163 °C (Found: C, 68.2; H, 4.7; Br, 15.0%); τ 2.06—2.33 (17 H, m, ArH), 5.01—5.29 (3 H, m, 2*-H, 3-, and 4*-H), 6.05 (1 H, q, 4-H), 6.20 (3 H, s, OCH_3), 6.88 (1 H, q, 4-H), 7.46 (1 H, octet, 3*-H), and 8.17 (1 H, octet, 3*-H); $J_{4,4}$ 17.1, $J_{3,4}$ 4.6 and 1.1.

(b) Trifluoroacetic acid (1 drop) was added to a solution of 2-

acetoxy-3-bromoflavan (110 mg) and 2,4-*cis*-4'-methoxyflavan-4-ol (**3**) (120 mg) in dichloromethane (5 ml). After 40 min the solution was diluted with ether and washed with aqueous sodium hydrogen carbonate. The mixture of diastereoisomers (152 mg) was isolated by p.l.c. (one 100 × 20 cm plate eluted with 25% ether–light petroleum, and its identity was confirmed by n.m.r. spectroscopy and t.l.c.

Methanolysis. The slower running diastereoisomer, m.p. 165—168 °C, (53 mg) and toluene-*p*-sulphonic acid monohydrate (5 mg) were dissolved in methanol (1 ml) and THF (2 ml). More methanol (2 ml) was added after 14 h. After 2.5 days, p.l.c. (one 20 × 20 cm plate eluted with 1:1 ether–light petroleum) afforded 2,4-*cis*-4'-methoxyflavan-4-ol (17 mg), m.p. and mixed m.p. 148.5—149.5 °C, and 2,3-*cis*-3-bromo-2-methoxyflavan (**14**) (22 mg), m.p. and mixed m.p. 134—135 °C.[1]

2-(2,4-cis-4'-*Methoxyflavan*-4-*yloxy*)*flavan* (**17**).—A solution of the faster running diastereoisomer of 2,3-*cis*-3-bromo-2-(2,4-*cis*-4'-methoxyflavan-4-yloxy)flavan, m.p. 161—163 °C, (90 mg) and tri-n-butyltin hydride (310 mg) in benzene (1 ml) was boiled for 2 h. Removal of the solvent and recrystallisation from methanol gave 2-(2,4-cis-4'-*methoxyflavan*-4-*yloxy*)*flavan* (**17**) as prisms (55 mg), m.p. 143—144 °C (Found: C, 79.9; H, 6.1. $C_{31}H_{28}O_4$ requires C, 80.2; H, 6.1%); τ 2.02—3.31 (17 H, m, ArH), 4.93—5.21 (2 H, m, 2*- and 4*-H), 6.20 (3 H, s, OCH_3), 6.62—7.01 (1 H, m, 4-H), 7.23—7.57 (3 H, m, 4-H and 3*-H), and 7.84—8.34 (2 H, m, 3-H_2).

2,3-cis-3-*Bromo*-2-(2,3-trans-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavans* (**20**) *and* (**22**).—2,3-*cis*-2-Acetoxy-3-bromoflavan (**4**) (600 mg) and (±)-tetra-*O*-methylcatechin (**18**) (895 mg) were boiled in benzene (30 ml) for 12 h under nitrogen. The solvent was evaporated, and the residue was transferred to a column of alumina (300 g) made up in benzene. Elution with benzene containing progressively more ethyl acetate (ultimately 5%) gave fractions containing the major product. Evaporation of the solvent gave a mixture of two components (t.l.c.) (1.03 g), some (130 mg) of which was transferred to two 20 × 20 cm p.l.c. plates and eluted 19 times with 20% ether–light petroleum (b.p. 40—60 °C), once with 1% ethyl acetate–benzene, and once again with 20% ether–light petroleum, (b.p. 40—60 °C).

Work-up of the band of higher R_F gave one diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan* as an amorphous solid (58 mg) which was purified by elution from a column of alumina (50 g) with 1:1 ether–light petroleum (b.p. 40—60 °C) (Found, for material dried at 55 °C/0.3 mmHg for 6 h: C, 64.9; H, 5.45; Br, 13.15. $C_{34}H_{33}BrO_7$ requires C, 64.5; H, 5.25; Br, 12.6%); τ 2.61—3.46 (12 H, m, ArH), 3.97 (2 H, 2 d, *J ca.* 2, substituted aromatic A ring), 5.34 (1 H, d, 2*-H), 5.57 (1 H, q, 3-H), 6.00—6.37 (14 H, 4 s at τ 6.08, 6.25, 6.29, and 6.37, 4 OCH_3 obscuring 3*-H and 4-H), 6.92 (1 H, 2 d, 4-H), 7.18 (1 H, 2 d, 4*-H), and 7.81 (1 H, 2 d, 4*-H); $J_{3,4}$ 1.8 and 4.3, $J_{4,4}$ 17.8, $J_{2*,3*}$ 7.4, $J_{3*,4*}$ 5.4 and 7.6, $J_{4*,4*}$ 16.8; *m/z* (200 °C, MS9) M^+ not observed, 346 (4%), 288/286 (89), 287/285 (65), 208 (33), 207 (100), 178 (50), and 149 (60).

Work-up of the band of lower R_F gave a residue which was recrystallised from methanol to yield the second diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan* as prisms (36 mg), m.p. 178—178.5 °C (decomp.). When the product was dried at 50 °C for 36 h *in vacuo*, material with m.p. 161—165 °C (decomp.) was obtained (Found: C, 64.2; H, 5.2; Br, 12.5%); τ 2.24—4.00 (14 H, m, ArH), 5.31 (1 H, d, 2*-H), 5.46 (1 H, q, 3-H), 5.75 (1 H, q, 3*-H), 6.20—6.52 (13 H, 4 s at τ 6.20, 6.30, 6.33, and 6.36, 4 OCH_3 partially obscuring 4-H), 7.10 (1 H, 2 d, 4-H), and 7.86 (2 H, 8 lines, 4*-H_2); $J_{3,4}$ 1.8 and 4.1, $J_{4,4}$ 17.1, $J_{2*,3*}$ 5.2; *m/z* (100 °C) M^+ not observed, 207 (100%), 288/286 (38.5), 167 (57.5), and 178 (36.5).

2,3-cis-3-*Bromo*-3',4',5,7-*tetramethoxy*-2-(2,3-trans-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavans* (**21**) *and* (**23**).—To a stirred solution of 3',4',5,7-tetramethoxyflav-2-ene (1.52 g) in dioxane (14 ml) was added acetic acid–acetic anhydride (9:1; 14 ml) followed by a solution of NBS (908 mg) in dioxane (9.5 ml) and acetic acid–acetic anhydride (9.5 ml). After 15 min, cyclohexene (0.5 ml) was added, followed after 5 min by dry, powdered (±)-3',4',5,7-tetra-*O*-methylcatechin (**18**) (3.20 g). The solution was heated at *ca.* 70 °C for 9 h. Ether (250 ml) was added, and the solution was washed in turn with water (2 × 150 ml) and saturated aqueous sodium hydrogen carbonate (3 × 150 ml) and was then dried ($MgSO_4$). Removal of the solvent gave an oil which consisted (t.l.c.) of a major product and at least four other components, in addition to unchanged (±)-tetra-*O*-methylcatechin. The oil was transferred to a column of Camag alkaline alumina (350 g, 7.5% deactivated with water) made up in benzene, and eluted with benzene mixed with progressively more ethyl acetate (ultimately 6%). Fractions containing a mixture of the major product and one of the higher running components were concentrated, and further purified on a column of Camag alkaline alumina (350 g, 5% deactivated with water) made up in 3:7 ether–light petroleum (b.p. 40—60 °C). The column was eluted with ether–light petroleum mixtures of gradually increasing polarity, and finally with pure ether, giving the major product and a slower running minor product. The major product, obtained as an amorphous powder (1.47 g), was shown by t.l.c. to consist of two components and analysis by h.p.l.c. produced two distinct peaks with well separated retention times. A sample (260 mg) was applied to two 100 × 20 cm p.l.c. plates and eluted with (*x*%) acetone–light petroleum: 18 times with 15%, 12 times with 17.5%, 7 times with 20%, and 4 times with 25% during 3 days before the bands were stripped. The band of high R_F gave a solid which was further purified by elution from a column of Camag alkaline alumina (50 g) with ether. Evaporation of fractions containing the major product yielded one diastereoisomer of 2,3-cis-3-*bromo*-3',4'5,7-*tetramethoxy*-2-(2,3-cis-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan* as a powder (90 mg), m.p. 87—103 °C (Found: C, 60.7; H, 5.8; Br 10.3. $C_{38}H_{41}BrO_{11}$ requires C, 60.6; H, 5.5; Br, 10.6%); τ 3.09—4.05 (10 H, m, ArH), 5.38 (1 H, d, 2*-H), 5.59 (1 H, q, 3-H), 6.02—6.64 (26 H, m, 6 separate, and 2 superimposed, singlets, 8 OCH_3 plus 3*- and 4-H), 6.84 (1 H, pair of incompletely resolved doublets, 4-H), 7.10 (1 H, 2 d, 4*-H), and 7.78 (1 H, 2 d, 4*-H); $J_{3,4}$ 1.7 and 4.2, $J_{4,4}$ 17.4, $J_{2*,3*}$ 7.3, $J_{3*,4*}$ 5.4 and 7.6, $J_{4*,4*}$ 16.7; *m/z* (200 °C, MS9) M^+ not observed, 167 (100%), 327 (85), 346 (60), 151 (46), 296 (40), 165 (40), and 408/406 (35).

Work-up of the band of lower R_F gave a solid which was further purified by elution from a column of Camag alkaline alumina (50 g) with ether to give the second diastereoisomer of 2,3-cis-3-*bromo*-3',4'5,7-*tetramethoxy*-2-(2,3-trans-3',4',5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan* (108 mg) as a powder, m.p. 100—110 °C (Found: C, 60.45; H, 6.0; Br, 9.95%); τ 2.68—4.04 (10 H, m, ArH), 5.32 (1 H, d, 2*-H), 5.44 (1 H, q, 3-H), 5.73 (1 H, m, 3*-H), 6.07—6.35 (24 H, 6 separate, and 2 superimposed, singlets, 8 OCH_3), 6.67 (weak) and 6.85 (together 1 H, each d, 4-H), 6.91 and 7.09 (weak) (together, 1 H, each d, 4-H), and 7.68 and 7.96 (together 2 H, 2 d, 4*-H); $J_{3,4}$ 1.9 and 4.3, $J_{4,4}$ 17.2, $J_{2*,3*}$ 5.2; *m/z* (200 °C, MS9) M^+ not observed, 167 (100%), 327 (81), 165 (50), 151 (50), 296 (43), 346 (37), and 408/406 (28).

The slower running minor product, obtained from the second column (see above), was isolated as a solid (366 mg), m.p. 120—127 °C (decomp.) (Found: C, 55.3; H, 5.1; Br, 18.65. $C_{38}H_{40}Br_2O_{11}$ requires C, 54.8; H, 4.8; Br, 19.2%); τ 2.60—4.02 (*ca.* 18 H, m, ArH), 5.13—5.80 (*ca.* 6 H, poorly resolved multiplets), 6.05—6.32 (*ca.* 48 H, many superimposed singlets, 16 ArOCH_3), and 6.41—8.17 (*ca.* 10 H, m); *m/z* (230 °C, MS9)

M^+ not observed, 167 (100%), 180 (50), 247/245 (10), 346 (9), 407/405 (5), 327 (5), 486 (4), and 488/484 (2). The isolation of this material, presumably a mixture of diastereoisomeric biflavanoids, indicates that NBS causes some aromatic bromination of the tetramethoxyflavene.

When a mixture of diastereoisomers (*ca.* 1:1) of 2,3-*cis*-3-bromo-3′,4′,5,7-tetramethoxy-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan (32 mg) was boiled in dioxane (1.5 ml) and ethanol (1.5 ml) in the presence of powdered sodium hydrogen carbonate, no reaction was detected by t.l.c. after 3 h.

2,3′,4′,5,7-*Pentamethoxyflavan*-3,4-cis-*diol* (**29**).—A mixture (*ca.* 1:1) of diastereoisomers of 2,3-*cis*-3-bromo-3′,4′,5,7-tetramethoxy-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan (250 mg) was boiled in THF (10 ml) with 10% methanolic potassium hydroxide (10 ml) for 60 h and the products were extracted into ether in the usual way. Removal of the solvent gave an oil which was dissolved in THF (10 ml) containing pyridine (1 ml) and to the stirred solution was added a solution of osmium tetraoxide (130 mg) in ether (13 ml). After 14 h, the reaction mixture was worked up in a similar manner to that described above for 3,4-diols (**12**) and (**13**). Evaporation of the ether gave an oil which was found (t.l.c.) to consist of two components which were separated by p.l.c. (two 20 × 20 cm plates eluted four times with 20% acetone–light petroleum). Work-up of the band of high R_F gave a solid (76 mg) which was recrystallised from methanol to yield (±)-tetra-*O*-methylcatechin (**18**) as needles, m.p. and mixed m.p. 138—140 °C.

The band of lower R_F gave a product which was recrystallised from methanol to yield 2,3′,4′,5,7-*pentamethoxyflavan*-3,4-cis-*diol* (**29**) (56 mg) as prisms, m.p. 148.5—150 °C (Found: C, 61.2; H, 6.2. $C_{20}H_{24}O_8$ requires C, 61.2; H, 6.2%); τ 2.72—3.14 (3 H, m, B-ring ArH), 3.74 and 3.84 (each 1 H, d, *J ca.* 2, A-ring ArH), 4.76 (1 H, br d, sharpens on addition of D_2O, 4-H), 5.77 (1 H, br s, disappears on addition of D_2O, 4-OH), 5.86 (1 H, br d, sharpens on addition of D_2O, 3-H), 6.08, 6.10, 6.12, and 6.20 (together 12 H, 4 s, 4 ArOCH_3), 6.98 (3 H, s, OCH_3), and 7.07 (1 H, br s, disappears on addition of D_2O, 3-OH); $J_{3,4}$ 4.6; *m/z* (120 °C) 392 (M^+, 2%), 210 (100), 183 (27), 211 (13), 181 (10), and 165 (9).

2,3-cis*-3,4-cis-3′,4′,5,7-*Tetramethoxy*-2-(2,3-trans-3′,4′,5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan*-3,4-*diols* (**24**) *and* (**25**).—(*a*) To a mixture (*ca.* 1:1) of diastereoisomers of 2,3-*cis*-3-bromo-3′,4′,5,7-tetramethoxy-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan (200 mg) in freshly distilled dioxane (10 ml) at 85—90 °C was quickly added powdered potassium hydroxide (a large excess). The suspension was stirred for 3 h at 85—90 °C before ether was added, and the solution was washed with water and dried ($MgSO_4$). Removal of the solvent gave an oil which was immediately dissolved in THF (8 ml) and pyridine (0.8 ml). To the stirred solution was added a solution of osmium tetraoxide (110 mg) in ether (11 ml) and a brown solid rapidly separated. After 13 h the osmate esters were treated with sodium sulphite (6 g) in water (50 ml) and ethanol (10 ml) in the usual way. The product was purified by p.l.c.: two 20 × 20 cm plates eluted twice with 45% acetone–light petroleum and once with 50% acetone–light petroleum. Work-up yielded a 1:1 mixture of diastereoisomers of 2,3-*cis**-3,4-*cis*-3′,4′,5,7-tetramethoxy-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan-3,4-diol as a solid (125.5 mg).

(*b*) A similar reaction sequence with the faster running diastereoisomer of 2,3-*cis*-3-bromo-3′,4′,5,7-tetramethoxy-2-(2,3-*trans*-3′,4′,5,7-tetramethoxyflavan-3-yloxy)flavan, m.p. 87—103 °C, (200 mg) gave a 1:1 mixture of diastereoisomers of the 3,4-diol (104 mg), identical in n.m.r. spectrum and in behaviour on reversed-phase t.l.c. plates with that from (*a*) above.

(*c*) The same diastereoisomeric mixture of diols (78 mg) was obtained in the same way from the slower running diastereoisomer (142 mg) of m.p. 100—110 °C.

A sample (80 mg) of the mixture of diastereoisomeric 3,4-diols was applied to two paraffin-impregnated p.l.c. plates which were eluted 21 times with 55% methanol–water during 1 week. The two bands were stripped, and each compound was separately purified further by p.l.c. [a 20 × 20 cm conventional plate for each diastereoisomer, eluted twice with light petroleum (b.p. 40—60 °C) and then twice with 45% acetone–light petroleum].

The band with the higher R_F on a paraffin-impregnated plate yielded one diastereoisomer of 2,3-cis*-3,4-cis-3′,4′,5,7-*tetramethoxy*-2-(2,3-trans-3′,4′,5,7-*tetramethoxyflavan*-3-*yloxy*)-*flavan*-3,4-*diol* as a solid (27 mg), m.p. 105—108 °C (Found, on material dried *in vacuo* at 50 °C for 2 d: C, 64.6; H, 6.1. $C_{38}H_{42}O_{13}$ requires C, 64.6; H, 6.0%); τ 2.60—4.03 (10 H, m, ArH), 5.09 (1 H, d, 4-H), 5.35 (1 H, d, 2*-H), 5.80 (3 H, m, reduced to 2 H on addition of D_2O, 3*-H, 3-H, and 4-OH), 6.09—6.36 (24 H, 8 s, 8 ArOCH_3), 7.25 (1 H, very br s, disappears on addition of D_2O, 3-OH), and 7.78 (2 H, 8 lines, 4*-H_2); $J_{3,4}$ 4.5, $J_{2*,3*}$ 6.0; *m/z* (200 °C, MS9) M^+ not observed, 167 (100%), 165 (30), 346 (23), 180 (21), 316 (15), and 182 (12.5); $\nu_{max.}$ 3 560br (OH), 1 625, 1 150, 1 122, and 1 038 cm^{-1}.

The band with the lower R_F on a paraffin-impregnated plate yielded the other diastereoisomer of 2,3-cis*-3,4-cis-3′,4′,5,7-*tetramethoxy*-2-(2,3-trans-3′,4′,5,7-*tetramethoxyflavan*-3-*yloxy*)*flavan*-3,4-*diol* as a solid (29.5 mg), m.p. 109—112 °C (Found, on material dried *in vacuo* at 50 °C for 2 d: C, 64.4; H, 6.3%); τ 3.05—4.04 (10 H, m, ArH), 4.78 (1 H, d, 4-H), 5.38 (1 H, d, 2*-H), *ca.* 5.80 (2 H, br s, diminishes on addition of D_2O, 3*-H and 4-OH), 5.93 (1 H, d, 3-H), 6.10—6.33 (24 H, 5 distinct, and 3 superimposed singlets, 8 ArOCH_3), 7.00—7.25 (2 H, q at τ 7.12, 4*-H, superimposed on a broad s which disappears on addition of D_2O, 3-OH), and 7.84 (1 H, q, 4*-H); $J_{3,4}$ 4.6, $J_{2*,3*}$ 7.9; *m/z* (210 °C, MS9) M^+ not observed, 167 (100%), 346 (34), 180 (33), 165 (30), 151 (25), and 316 (17); $\nu_{max.}$ 3 560br (OH), 1 622, 1 202, 1 150, and 1 120 cm^{-1}.

2,3-cis-3-*Bromo*-2-(2,3-trans-3,4-trans-4-*hydroxy*-4′-*methoxyflavan*-3-*yloxy*)*flavans* (**31**) *and* (**33**) *and* 2,3-cis-3-*Bromo*-2-(2,3-trans-3,4-trans-3-*hydroxy*-4′-*methoxyflavan*-4-*yloxy*)-*flavans* (**35**) *and* (**37**).—A solution of 2,3-*trans*-3,4-*trans*-4′-methoxyflavan-3,4-diol (**30**) (1.07 g) and 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) (880 mg) in benzene (30 ml) was boiled for 9 h. The volume was reduced to *ca.* 8 ml, and the flavandiol which separated (570 mg) was collected. The mother liquor was applied to a column of alumina (100 g) in light petroleum. Elution with light petroleum containing an increasing proportion of ether gave the following products in order of elution. (i) 3-Bromoflav-2-ene (60 mg); (ii) probably mixed isomers of 2,3-*trans*-3,4-*trans*-3,4-bis-(3-bromoflavan-2-yloxy)-4′-methoxyflavan (295 mg) having a complex n.m.r. spectrum including signals at τ 2.25—3.90 (ArH), 4.27 and 4.45 (both small doublets), and large signals at τ 5.44, 5.57, 5.76, 6.09, 6.13, 6.21 (s, ArOCH_3), 6.36, 6.89, and 7.25; (iii) one diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-trans-4-*hydroxy*-4′-*methoxyflavan*-3-*yloxy*)*flavan* which separated from methanol as prisms (395 mg), m.p. 158—160 °C (Found: C, 66.3; H, 4.9; Br, 14.6. $C_{31}H_{27}BrO_5$ requires C, 66.6; H, 4.9; Br, 14.3%); τ 2.57—3.32 (17 H, m, ArH), 5.25 (1 H, d, 2*-H), 5.54 (1 H, d, becomes shoulder with D_2O, 4*-H), 5.69 (1 H, q, 3-H), 6.05 (1 H, q, 4-H), 5.9—6.3 (1 H, partly obscured, OH), 6.12 (3 H, s, OCH_3), 6.2 (1

* This stereochemical assignment must be regarded as tentative.

H, partly obscured, 3*-H), and 6.87 (1 H, q, 4-H); $J_{2*,3*}$ 8.9, $J_{3*,4*}$ 6.4, $J_{3,4}$ 1.7 and 4.1, $J_{4,4}$ 17.1.

Acetylation with 1:1 pyridine–acetic anhydride overnight gave the acetate, m.p. 169—172 °C (slow heating, some decomp.) or 175—178 °C (normal rate of heating), with an identical n.m.r. spectrum with a 4-acetate recorded below; (iv) One diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-trans-3-*hydroxy*-4′-*methoxyflavan*-4-*yloxy*)*flavan* which separated from methanol as prisms (263 mg), m.p. 138—140.5 °C (Found: C, 66.3; H, 5.0; Br, 14.4%); τ 2.15—3.30 (17 H, m, ArH), 5.12—5.45 (3 H, obscured, 2*-, 4*-, and 3-H), 6.06—6.37 (1 H, obscured, 3*-H), 6.1—6.4 (1 H, obscured, OH), 6.20 (1 H, q, 4-H), 6.20 (3 H, s, OCH_3), and 6.93 (1 H, q, 4-H); $J_{3,4}$ 1.9 and *ca.* 5.1, $J_{4,4}$ 17.6. Acetylation gave the acetate, m.p. 148—152 °C, identical (n.m.r. spectrum) with a 3-acetate below; (v) The second diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-trans-4-*hydroxy*-4′-*methoxyflavan*-3-*yloxy*)*flavan* which separated from light petroleum as prisms (82 mg), m.p. 150—156 °C (Found: C, 66.8; H, 4.9; Br, 14.4%); τ 2.12—3.38 (17 H, m, ArH), 5.06 (1 H, d, 2*-H), 5.40—5.59 (2 H, m, 3* and 3-H), 5.69 (1 H, distorted q, becomes d with D_2O, 4*-H), 6.26 (3 H, s, OCH_3), 6.50 (1 H, q, 4-H), 7.08 (1 H, d, 4-H), and 8.98 (1 H, d, OH); $J_{2*,3*}$ 4.2, $J_{3*,4*}$ 3.9, $J_{3,4}$ *ca.* 1.7 and 4.3, $J_{4,4}$ 17.0. The acetate had m.p. 166—167 °C (very slow heating) and 172—174 °C (normal rate of heating) and an identical n.m.r. spectrum with that of a 4-acetate below; (vi) The second diastereoisomer of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-trans-3-*hydroxy*-4′-*methoxyflavan*-4-*yloxy*)*flavan* which separated from methanol as prisms, m.p. 132—134.5 °C and, after resolidification, 145—147 °C (decomp.) (Found: C, 66.4; H, 4.8; Br, 13.9%); τ 2.27—3.40 (17 H, m, ArH), 5.06—5.23 (2 H, m, 2*-and 4*-H), 5.60 (1 H, q, 3-H), *ca.* 6.19 (1 H, obscured, 3*-H), 6.19 (3 H, s, OCH_3), 6.39 (1 H, q, 4-H), 7.00 (1 H, q, 4-H), and 8.20 (1 H, br s, OH); $J_{3,4}$ 2.0 and 4.3, $J_{4,4}$ 17.2. The acetate had m.p. 158—158.5 °C and an identical n.m.r. spectrum with that of a 3-acetate below.

2,3-trans-3-*Acetoxy*-4′-*methoxyflavanone*.—2,3-*trans*-3-Hydroxy-4′-methoxyflavan-4-one (1 g) was dissolved in acetic anhydride (5 ml) and pyridine (5 ml). Work-up after 24 h and recrystallisation from light petroleum gave 2,3-trans-3-*acetoxy*-4′-*methoxyflavanone* as prisms (0.9 g), m.p. 95—97.5 °C (Found: C, 69.1; H, 5.2. $C_{18}H_{16}O_5$ requires C, 69.2; H, 5.2%); τ 2.00—3.13 (8 H, m, ArH), 4.18 (1 H, d, 2-H), 4.65 (1 H, d, 3-H), 6.18 (3 H, s, OCH_3), and 8.00 (3 H, s, OAc); $J_{2,3}$ 12.3.

2,3-trans-3,4-trans-3-*Acetoxy*-4′-*methoxyflavan*-4-*ol* (**40**).—A solution of 2,3-*trans*-3-acetoxy-4′-methoxyflavanone (2 g) in ethyl acetate (45 ml) and ethanol (45 ml) was shaken overnight under hydrogen with 10% Pd–C (100 mg). A solid product was recovered; it separated from methanol to give 2,3-trans-3,4-trans-3-*acetoxy*-4′-*methoxyflavan*-4-*ol* (**40**) as needles (1.58 g), m.p. 159—160 °C (Found: C, 68.75; H. 5.8. $C_{18}H_{18}O_5$ requires C, 68.8; H. 5.8%); τ 2.40—3.20 (8 H, m, ArH), 4.68 (1 H, q, 3-H), 5.05 (1 H, d, 2-H), 5.06 (1 H, q, converted into d by D_2O, 4-H), 6.20 (3 H, s, OCH_3), 7.52 (1 H, d, OH), and 8.11 (3 H, s, OAc); $J_{2,3}$ 9.4 $J_{3,4}$ 7.7, $J_{4,OH}$ 7.9.

A portion (10 mg) was hydrolysed in methanol (5 ml) containing potassium hydroxide (70 mg) overnight. The product was identified as 2,3-trans-3,4-trans-4′-methoxyflavan-3,4-diol (**30**) by n.m.r. spectral comparison and mixed m.p. (176.5—178 °C) with an authentic sample.

2,3-trans-3,4-trans-4-*Acetoxy*-4′-*methoxyflavan*-3-*ol* (**41**).—2,3-*trans*-3-Hydroxy-4′-methoxyflavan-4-one (250 mg) was stirred in benzene (5 ml) containing dihydropyran (0.25 ml) and toluene-*p*-sulphonic acid (5 mg). After 8 h a further portion (0.1 ml) of dihydropyran was added. Work-up after a further 2 h gave an oil (540 mg) which separated from light petroleum as a solid presumed to be the tetrahydropyranyl derivative of the hydroxyflavanone contaminated with an excess of dihydropyran. This product (385 mg) was dissolved in ethanol (30 ml) and the solution was shaken under hydrogen for 3 h with 10% Pd–C (30 mg). Removal of catalyst and solvent left a solid, presumed to be mixed diastereoisomers of 2,3-*trans*-3,4-*trans*-4′-methoxy-3-(tetrahydropyran-2-yloxy)flavan-4-ol. A portion (50 mg) was hydrolysed (1 drop of dil. hydrochloric acid in 5 ml of methanol for 1 h) to 2,3-*trans*-3,4-*trans*-4′-methoxyflavan-3,4-diol (**30**) (29 mg), identified by mixed m.p. The tetrahydropyranyl derivative (200 mg) was acetylated (1 ml each of acetic anhydride and pyridine for 10 h) to give a crude acetate (213 mg) which was taken up in methanol (20 ml) and treated with dil. hydrochloric acid (4 drops). Work-up after 15 min and recrystallisation from light petroleum gave 2,3-trans-3,4-trans-4-*acetoxy*-4′-*methoxyflavan*-3-*ol* (**41**) (145 mg) as prisms, m.p. 119.5—121 °C (Found: C, 68.8; H, 5.7. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.8%); τ 2.47—3.29 (8 H, m, ArH), 3.83 (1 H, d, 4-H), 5.13 (1 H, d, 2-H), 5.18 (1 H, octet converted by D_2O into q, 3-H), 6.20 (3 H, s, OCH_3), 7.36 (1 H, d, OH), and 7.84 (3 H, s, OAc); $J_{2,3}$ 9.7, $J_{3,4}$ 7.7, $J_{3,OH}$ 3.4.

2,3-cis-2-(2,3-trans-3,4-trans-4-*Acetoxy*-4′-*methoxyflavan*-3-*yloxy*)-3-*bromoflavans* (**32**) *and* (**34**).—A solution of 2,3-*trans*-3,4-*trans*-4-Acetoxy-4′-methoxyflavan-3-ol (**41**) (370 mg) and 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) (350 mg) in benzene (10 ml) was boiled for 7 h. The resulting mixture of products was applied to a column of silica (100 g) in light petroleum. Elution with an increasing proportion of ether in light petroleum gave impure 3-bromoflav-2-ene (110 mg), unchanged 4-acetoxy-4′-methoxyflavan-3-ol, and a mixture which was applied to a 100 × 20 cm p.l.c. plate which was eluted four times with ether–light petroleum (1:9). Two closely spaced bands of low R_F were removed. The slower one afforded one diastereoisomer of 2,3-cis-2-(2,3-trans-3,4-trans-4-*acetoxy*-4′-*methoxyflavan*-3-*yloxy*)-3-*bromoflavan* which separated from methanol as prisms (82 mg), m.p. 166-167 °C (slow heating), 172—174 °C (normal rate of heating) (Found: C, 66.1; H, 4.7; Br, 12.9. $C_{33}H_{29}BrO_6$ requires C, 65.9; H, 4.9; Br, 13.3%); τ 2.16—3.38 (17 H, m, ArH), 4.75 (1 H, br s, 3*-H), 5.01 (1 H, br s, 4*-H), 5.37—5.52 (2 H, m, 2*- and 3-H), 6.31 (3 H, s, OCH_3), 6.97 (2 H, dq, 4-H_2), and 8.78 (3 H, s, OAc); $J_{3,4}$ 1.2 and 4.3, $J_{4,4}$ 17.5.

The faster band gave the other diastereoisomer of the 4-*acetoxybiflavonoid* which separated from methanol as prisms (139 mg), m.p. 169—172 °C (slow heating), 175—178 °C (normal rate of heating) (Found: C, 66.2; H, 4.7; Br, 13.0%); τ 2.12—3.56 (17 H, m, ArH), 4.70 (1 H, br d, 4*-H), 4.84 (1 H, br s, 2*-H), 5.39 (1 H, br d, 3-H), 5.56 (1 H, t/q, 3*-H), 6.27 (3 H, s, OCH_3), 6.49 (1 H, q, 4-H), 7.05 (1 H, q, 4-H), and 8.65 (3 H, s, OAc); $J_{3*,4*}$ *ca.* 3.4, $J_{3,4}$ 1.8 and 4.4, $J_{4,4}$ 17.2.

2,3-cis-2-(2,3-trans-3,4-trans-3-*Acetoxy*-4′-*methoxyflavan*-4-*yloxy*)-3-*bromoflavans* (**36**) *and* (**38**).—A solution of *trans*-*trans*-3-acetoxy-4′-methoxyflavan-4-ol (**40**) (250 mg) and 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) (200 mg) in benzene (10 ml) was boiled for 5.5 h. The resulting mixture of products was applied to two 100 × 20 cm p.l.c. plates. Two closely spaced bands were removed together and afforded an oil which was applied to three 20 × 20 cm plates and eluted 8 times with ether–light petroleum (1:10). The slower band yielded one diastereoisomer of 2,3-cis-2-(2,3-trans-3,4-trans-3-*acetoxy*-4′-*methoxyflavan*-4-*yloxy*)-3-*bromoflavan* which separated from methanol as prisms (46 mg), m.p. 157.5—158.5 °C (Found: C, 66.2; H, 4.8; Br, 13.6. $C_{33}H_{29}BrO_6$ requires C, 65.9; H. 4.9; Br, 13.3%); τ 2.20—3.90 (17 H, m, ArH), 4.83 (1 H, br s, 2*-H), 4.92 (1 H, t, 3*-H), 5.28 (1 H, br s, 4*-H), 5.61 (1 H, q, 3-H), 6.20 (3 H, s, OCH_3), 7.40 (1 H, q, 4-H), 7.73 (1 H, q, 4-H), and 8.06 (3 H, s, OAc); $J_{3,4}$ 2.2 and 4.0, $J_{4,4}$ 17.0

The faster band gave the other 3-*acetoxybiflavanoid stereoisomer* which separated from methanol as prisms (69 mg), m.p. 148—152 °C (Found: C, 66.1; H, 4.6; Br, 13.4%); τ 2.53—3.66 (17 H, m, ArH), 4.67 (1 H, br s, 2*-H), 5.08 (1 H, t, 3*-H), 5.38 (1 H, br s/q, 4*-H), 5.99 (1 H, q, 3-H), 6.18 (3 H, s, OCH_3), 6.86 (1 H, q, 4-H), 7.28 (1 H, q, 4-H), and 8.20 (3 H, s, OAc); $J_{2*,4*}$ *ca.* 1.2, $J_{3*,4*}$ *ca.* 3.0, $J_{3,4}$ 1.9 and 4.2, $J_{4,4}$ 17.0.

2,3-cis-3-*Bromo*-2-(2,3-trans-3,4-cis-4-*hydroxy*-4′-*methoxyflavan*-3-*yloxy*)- (**43**) *and* (**44**) *and* 2,3-cis-3-*Bromo*-2-(2,3-trans-3,4-cis-3-*hydroxy*-4′-*methoxyflavan*-4-*yloxy*)-*flavans* (**45**) *and* (**46**).—2,3-*trans*-3,4-*cis*-4′-Methoxyflavan-3,4-diol (**42**) (1.4 g) and 2,3-*cis*-2-acetoxy-3-bromoflavan (**4**) (1.18 g) were boiled in benzene (100 ml) for 9 h. The solution was then reduced in volume and the precipitated diol was collected by filtration. The filtrate was evaporated and the residue taken up in light petroleum and applied to a column of alumina (200 g). Elution with light petroleum containing an increasing proportion of ether gave 3-bromoflav-2-ene and four isomeric biflavonoids in the following order of elution.

One diastereoisomer (A) of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-cis-3-*hydroxy*-4′-*methoxyflavan*-4-*yloxy*)*flavan* which separated from methanol as prisms (240 mg), m.p. 152—155 °C (decomp.) (Found: C, 66.4; H, 5.1; Br, 14.1. $C_{31}H_{27}BrO_4$ requires C, 66.6; H, 4.9; Br, 14.3%); τ 2.07—3.75 (17 H, m, ArH), 5.25 (1 H, d, 2*-H), 5.56 (1 H, q, 3-H), 5.65 (1 H, d, 4*-H), 5.88 (1 H, dd, 4-H), 6.21 (1 H, q, 3*-H), 6.24 (3 H, s, OCH_3), 7.16 (1 H, dd, 4-H), and 8.54 (1 H, s, OH); $J_{2*,3*}$ 3.0, $J_{3*,4*}$ 2.3 $J_{3,4}$ 1.9 and 4.0, $J_{4,4}$ 16.6; one diastereoisomer (B) of 2,3-cis-3-*bromo*-2-(2,3-trans-3,4-cis-4-*hydroxy*-4′-*methoxyflavan*-3-*yloxy*)*flavan* which separated from methanol as prisms (130 mg), m.p. 159—160.5 °C (decomp.) (Found: C, 66.3; H, 5.0, Br, 14.1%); τ 2.52—3.33 (17 H, m, ArH), 4.98 (1 H, d, 2*-H), 5.26 (1 H, q [d with D_2O], 4*-H), 5.62 (1 H, q, 3-H), 5.95 (1 H, dd, 4-H), 6.11 (3 H, s, OCH_3), 6.22 (1 H, q, 3*-H), 6.81 (1 H, dd, 4-H), and 8.38 (1 H, d, OH); $J_{2*,3*}$ 9.6, $J_{3*,4*}$ 3.1, $J_{3,4}$ 2.0 and 4.4, $J_{4,4}$ 17.4; the second diastereoisomer (C) of the above 2-(3-*hydroxyflavan*-4-*yloxy*)-*flavan* as prisms (210 mg) from light petroleum, m.p. 138.5—140.5 °C (Found: C, 66.6; H, 4.8; Br, 14.0%); τ 2.31—3.39 (17 H, m, ArH), 4.93 (1 H, d, 2*-H), 5.18 (1 H, q, 3-H), 5.35 (1 H, d, 4*-H), 5.92 (1 H, dd, 4-H), 5.96 (1 H, octet [q with D_2O], 3*-H), 6.24 (3 H, s, OCH_3), 6.77 (1 H, dd, 4-H), and 8.22 (1 H, d, OH); $J_{2*,3*}$ 6.9, $J_{3*,4*}$ 2.7, $J_{3,4}$ 1.7 and 4.7, $J_{4,4}$ 17.6; the second diastereoisomer (D) of the above 2-(4-*hydroxyflavan*-3-*yloxy*)-*flavan* as prisms (435 mg) from aqueous methanol, m.p. 154—156 °C (Found: C, 66.4: H, 5.0; Br, 14.3%); τ 2.13—3.56 (17 H, m, ArH), 4.93 (1 H, d, 2*-H), 5.37 (1 H, q, 3-H), 5.66 (1 H, q, 3*-H), 6.21 (1 H, q [d with D_2O], 4*-H), 6.26 (3 H, s, OCH_3), 6.93 (1 H, dd, 4-H), 7.26 (1 H, dd, 4-H), and 8.00 (1 H, br s, OH); $J_{2*,3*}$ 8.7, $J_{3*,4*}$ 3.0, $J_{3,4}$ 1.9 and 4.0, $J_{4,4}$ 16.8.

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