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THE CONFIGURATION OF FLAVAN-4-OLS

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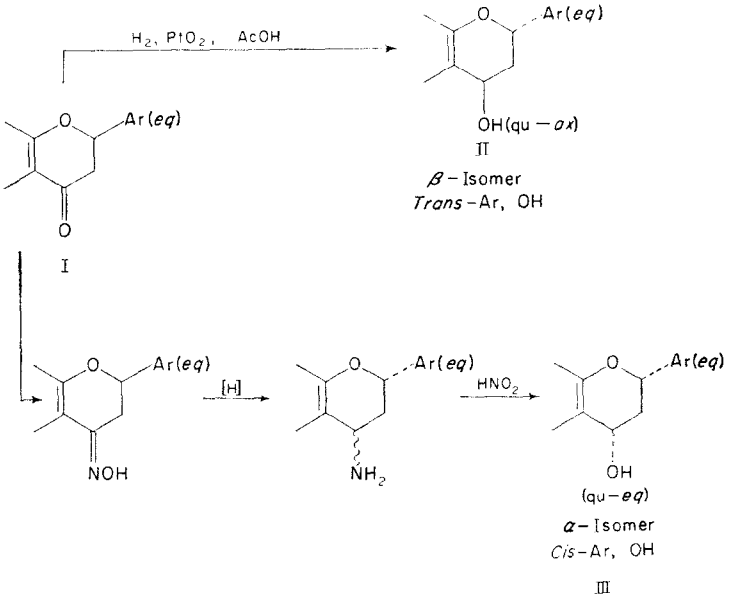
Abstract—Flavan-4-ones have been found to yield the corresponding probably equatorial 4-hydroxy compounds by oximation, reduction to the amine and deamination. Configurations have been tentatively assigned to some flavan-4-ols on the basis of this reaction and of results of catalytic hydrogenation (PtO_2, AcOH).

This paper relates to the provisional assignment of conformations and configurations to some geometrically isomeric pairs of flavan-4-ols (II, III) obtained from the corresponding flavan-4-ones (I) by two reactions which appear to be sterospecific for the compounds examined. The first, hydrogenation in acetic acid with a platinum catalyst, has been shown by Hückel *et al.*[1] to be possibly the most stereospecific of the ketone to alcohol reduction processes: the axial-type alcohol (II) is, normally, the main product. The second approach which is recent[2] involves the reduction of a 4-oximinoflavan to the amine which is then converted by nitrous acid into the 4-hydroxyflavan (III). The process yields a compound stereoisomeric with that from the first method; the product is, therefore, considered to be the equatorial-type alcohol. This isomer is also formed by reduction of the ketone by aluminium amalgam in ethanol[3] but the yield is poor.

Since in flavans the 2-phenyl group is usually assumed to be equatorial, the reduction product (II) will be *trans*-2-Ph(*eq*)-4-OH(quasi-*ax*), and the other alcohol (III), *cis*-2-Ph(*eq*)-4-OH(quasi-*eq*). The quasi-nature of the 4-substituents is discussed below.

Table 1 summarizes the results with the reactions mentioned in it; references to other work are given in the footnotes to the table. The conformations deduced for flavan-4-ol and 4′-methoxy-6-methylflavan-4-ol are in agreement with those assigned by Mitsui and Kasahara[4] whose results were not available when the first draft of this paper was prepared. They[4b] examined the NMR spectra of flavan-4α- and -4β-ol, but based their assignments on a mechanism for catalytic hydrogenation proposed by Mitsui and Imaizumi.[5] The reactions used by the Japanese authors (Raney-nickel hydrogenation under neutral conditions; Meerwein-Ponndorf) for the reduction of flavanones 1 and 4 (Table 1) are not generally accepted as stereospecific.[1,6]

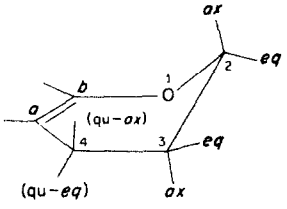
[1] W. Hückel, M. Maier, E. Jordan and W. Seeger, *Liebigs Ann.* **616**, 46 (1958).
[2] R. Bognár, M. Rákosi, H. Fletcher, Eva M. Philbin and T. S. Wheeler, *Tetrahedron Letters* No. 19, 4 (1959).
[3] K. Freudenberg and L. Orthner, *Ber. Dtsch. Chem. Ges.* **55**, 1748 (1922).
[4] S. Mitsui and A. Kasahara, [a] *J. Chem. Soc. Japan* **79**, 1328 (1958); *Chem. Abstr.* **55**, 523 (1961); [b] *J. Chem. Soc. Japan* **81**, 1583 (1960).
[5] S. Mitsui and S. Imaizumi, *J. Chem. Soc. Japan* **77**, 1516 (1956); *Chem. Abstr.* **53**, 5180 (1959).
[6] See footnote *e* to Table 1, and citations by N. F. Janes and J. W. W. Morgan, *J. Chem. Soc.* 2560 (1960); also V. R. Shah and A. B. Kulkarni, *J. Sci. Ind. Res., India* **17B**, 420 (1958); K. D. Hardy and R. J. Wicker, *J. Amer. Chem. Soc.* **80**, 640 (1958).



Conformation of β-isomers (II)

The conclusion that the isomer (*β*) obtained by catalytic hydrogenation (platinum-acetic acid) has the 4-hydroxyl group in the quasi-axial position is not at variance with Philbin and Wheeler's[7] "sofa" conformation (IV) for the chroman ring; their view is supported by ultra-violet absorption data obtained by Hart and Wagner.[8]

The molecule (IV) may be visualized as sited on the catalyst at atoms 1, 3, 4, *a*, *b*, so that the triangle formed by atoms 1, 2, 3, points away from the surface; the catalyst



is thus on the equatorial side of carbon-4. If the reduction of the carbonyl double bond is assumed to be effected by previous non-catalytic attachment of a solvent proton to the 4-oxygen atom[9] followed by deposition of a hydrogen anion by the catalyst on the 4-carbon atom, the C(4)-OH bond will be released into the quasi-axial conformation at an early stage of the reduction process, and the C(4)-H bond subsequently developed will be formed in what corresponds to the equatorial position. Similar spatial considerations were applied by Mitsui and Kasahara[4] to the catalytic reduction of flavanone in neutral solution.

[7] E. M. Philbin and T. S. Wheeler, *Proc. Chem. Soc.* 167 (1958).
[8] H. Hart and C. R. Wagner, *Proc. Chem. Soc.* 248 (1958).
[9] J. H. Brewster, *J. Amer. Chem. Soc.* 76, 6361 (1954).

TABLE 1. ISOMERIC FLAVAN-4-OLS (II, III) PREPARED STEREOSPECIFICALLY FROM THE CORRESPONDING FLAVAN-4-ONES (I)

No.	Ketone	Melting points of isomeric alcohols obtained (underlined m.p. indicates new compound)		
		cis-2-Ph(*eq*)-4-OH(quasi-*eq*) α-compound (III)[a]		*trans*-2-Ph(*eq*)-4-OH(quasi-*ax*) β-compound (II)[a]
		Al,Hg reduction method	Oxime-amine[b] process	H_2,PtO_2,AcOH
1	Flavanone	118°	118°	148°
2	6-Chloro-flavanone	117–119°[b]	117–119°	(114–115°)[c]
3	4′-Methoxy-flavanone	130–132°[b]	132–134°	150–151°[b,d]
4	4′-Methoxy-6-methyl-flavanone	127–128°[e]	No useful result	138°[e]

[a] P. Karrer, Y. Yen and I. Reichstein, *Helv. Chim. Acta* **13,** 1308 (1930) designated as α the flavan-4-ol previously prepared by reduction of flavanone by aluminium amalgam in aqueous ethanol (Freudenberg and Orthner[3]), and as β the second isomer (new) which, together with flavan-4α-ol they isolated using ammoniacal titanous chloride. This nomenclature is here by analogy extended to other flavan-4-ols (see Table 1).

Citations for the reduction of flavanone to flavan-4-ol are given by the authors mentioned.[2,4] (see also K. Freudenberg and J. M. Alonso de Lama, *Liebigs Ann.* **612,** 78 (1958)). Generally the 4β-ol is formed by catalytic hydrogenation under a variety of conditions and by the use of metallic hydrides and of sodium in ethanol. However, a mixture of diol isomers was obtained from 4′-methoxy-6-methyldihydroflavonol using lithium aluminum hydride (see footnote *e*). Further sodium borohydride yielded isomeric flavandiols when applied to 5,7,3′,4′-tetramethoxydihydroflavonol (A. R. Ganguly and T. R. Seshadri, *Tetrahedron* **6,** 21 (1959)). Diborane (see Experimental) produced usually the β-isomer, but a mixture with dihydroflavonol; results so far available indicate that dihydroflavonols are more likely than flavanones to yield α,β-mixtures.

Effective for the production of the α-isomer are dissolving magnesium (T. A. Geissman and R. O. Clinton, *J. Amer. Chem. Soc.* **68,** 700 (1946)) and aluminium (see Table 1), and lead tetra-acetate applied to the flavan.

[b] Present work.

[c] No useful result was obtained using H_2, PtO_2, AcOH. The isomer m.p. 114–115°, was prepared by Karrer *et al.* (see footnote *a*) employing ammoniacal titanous chloride. As it differs from the product (m.p. 117–119°) of the oxime method, it is the β-compound (OH-quasi-*ax*).

[d] Brown *et al.*[10] (see Experimental section) showed that the compound, m.p. 144–145° obtained by Karrer *et al.* using ammoniacal titanous chloride (see footnote *a*) was a mixture, and synthesized a purer product (m.p. 152–153°) by application of lithium aluminium hydride.

[e] These results were obtained by C. G. Joshi and A. B. Kulkarni, *J. Sci. Ind. Res., India* **16B,** 307 (1957); *J. Indian Chem. Soc.* **34,** 753 (1957); M. D. Kashikar and A. B. Kulkarni, *J. Sci. Ind. Res., India* **18B,** 418 (1959); *Curr. Sci.* **30,** 127 (1961) who investigated the reduction of 4′-methoxy-6-methylflavanone and the corresponding dihydroflavonol by hydrogenation (PtO_2, AcOH; Raney Ni, ethanol); ammoniacal titanous chloride; metal hydrides; and aluminium amalgam. All but the last reagent gave the β-compound.

Conformation of α-isomers (III)

If the product (β) of reduction by hydrogen–platinum in acetic acid has a quasi-axial hydroxyl group, the oxime–amine method may be taken as a stereospecific process for the production of the quasi-equatorial alcohol (α) from the flavan-4-ones shown in Table 1. Brown *et al.*[10] found that the action of lead tetra-acetate on flavan and 4′-methoxyflavan gave the corresponding 4α-acetoxy compounds. Attack by this reagent is presumably along the less hindered quasi-equatorial route.

[10] M. M. Bokadia, B. R. Brown and W. Cummings, *J. Chem. Soc.* 3308 (1960). See also footnote *d* to Table 1.

Conformation of amines from oximes

For the flavanones shown in Table 1, only one amine was obtained from an oxime regardless of the reduction method employed. The conformation of the amino-group cannot be deduced from the course of the deamination reaction[11] as quasi-positioned bonds are involved. Non-catalytic agents (e.g. metal hydrides) would be expected to yield the quasi-equatorial amine if bulky complex formation with the oximino-group occurs.[12] Quasi-equatorial placement of the complex would remove it from steric interference by an axial hydrogen atom on C-2 (see IV). Catalytic reduction of the oxime in either acid or neutral solution may involve the mechanism postulated by Brewster[9] for formation of an equatorial alcohol by catalytic hydrogenation of a ketone in neutral solution.

Shoppee *et al.*[11] found that hydrogenation of the oxime of 5α-cholestan-1-one by a variety of reagents (Na, EtOH; $LiAlH_4$ in ether; H_2, PtO_2, AcOH) gave the same 1-amino-5α-cholestane with the amino-group probably β and equatorial. On the other hand, the deamination reaction indicated axial amine for it yielded the axial 1α-alcohol and related alkenes—hence the conformation of the amino-group remains uncertain.[11]

Extended catalytic reduction of 4-oximinoflavan effected decyclization with production of 1-amino-1-*o*-hydroxyphenyl-3-phenylpropane. The structure of this amine was confirmed by its preparation from *o*-hydroxy-β-phenylpropiophenone oxime. Many examples of such reductive decyclization have been observed.[4b,13]

Further work to confirm the configurations here provisionally assigned is in hand.

EXPERIMENTAL

Flavan-4β-ol

(a) *Reduction by diborane.* Diborane, obtained by addition during 1 hr of boron trifluoride etherate (2·8 g) in diglyme (5·0 ml) to sodium borohydride (0·5 g) in diglyme (12·5 ml), was passed into flavanone (2·2 g) in tetrahydrofuran in an atmosphere of nitrogen. After 12 hr ethanol was added until effervescence ceased, and the solvents were removed under red press. The residue separated from methanol in needles (1·8 g), the m.p. (148°) of which was not depressed by admixture with an authentic specimen prepared by catalytic hydrogenation (Pd/C, EtOH)[13a] of flavanone. Reduction of flavone by diborane also yielded flavan-4β-ol.

(b) *Catalytic reduction.* Flavanone (1·0 g) in acetic acid solution was hydrogenated (1 mole H) at room temp and press in presence of PtO_2 (about 4 hr). Removal of the catalyst and solvent (red press) afforded 0·8 g of flavan-4β-ol (mixed m.p. confirmation).

Flavan-4α-ol through 4-aminoflavan

4-Oximinoflavan. This oxime (Found: C, 75·3; H, 5·4; N, 5·9. $C_{15}H_{13}NO_2$ requires: C, 75·3; H, 5·5; N, 5·9%) which was prepared from flavanone, hydroxylamine hydrochloride and sodium hydroxide, sodium acetate or pyridine[14] separated from aqueous ethanol in needles, m.p. 170–171° (λ_{max} EtOH, 256, 306, 316, mμ; log ε 4·00, 3·75, 3·66).

4-Aminoflavan and salts

(a) *Catalytic reduction.* The oxime in acetic acid solution was hydrogenated (2 moles H) at room temp and press in presence of (i) Pd/C (8 hr) or (ii) PtO_2 (2½ hr). Removal of the catalyst and solvent (red press) gave *4-aminoflavan acetate* as a syrup which separated from ethanol in needles, m.p.

[11] D. H. R. Barton, *J. Chem. Soc.* 1027 (1953); D. H. R. Barton and R. C. Cookson, *Quart. Rev.* **10,** 71 (1956); C. W. Shoppee, S. K. Roy and B. S. Goodrich, *J. Chem. Soc.* 1585 (1961) and references there cited.

[12] D. M. S. Wheeler and J. W. Huffman, *Experientia* **16,** 516 (1960).

[13] R. Mozingo and H. Adkins, *J. Amer. Chem. Soc.* **60,** 669 (1938); *a* R. Bognár and M. Rákosi, *Acta Chim. Acad. Sci. Hungary* **13,** 217 (1957); *Magyar Kémiai Folyóirat* **64,** 111 (1958).

[14] K. C. Gulati and J. N. Ray, *Curr. Sci.* **5,** 75 (1936).

162–163°. (Found: C, 71·0; H, 6·8; N, 5·0; AcOH, 20·5. $C_{15}H_{15}NO.CH_3COOH$ requires: C, 71·6; H, 6·7; N, 4·9; AcOH, 21·0%). The *hydrochloride* (Found: C, 68·9; H, 6·1; N, 5·4; Cl, 13·6. $C_{15}H_{15}NO.HCl$ requires: C, 68·8; H, 6·1; N, 5·4; Cl, 13·6%) was obtained when the syrup or the pure acetate was crystallized from 5% hydrochloric acid; it separated from ethanol in needles, m.p. 268–270°. The yield of hydrochloride was 70% with Pd/C and 40% with PtO_2; the figures for acetate were 40% and 20% respectively. *4-Aminoflavan*, m.p. 112° from aqueous methanol. (Found: C, 80·1; H, 6·8; N, 6·0. $C_{15}H_{15}NO$ requires: C, 80·0; H, 6·7; N, 6·2%) separated as an oil which formed needles when a 5% aqueous solution of the hydrochloride was neutralized by aqueous sodium hydroxide. The crystals (yield 50%) of the amine acquired a yellow colour on storage (λ EtOH, 276, 284 mμ; log ε 3·3, 3·3).

(b) *Use of lithium aluminium hydride.* A mixture of 4-oximinoflavan (1 g), tetrahydrofuran (30 ml), lithium aluminium hydride (1·0 g) and ether (300 ml) was refluxed for 10 hr. 4-Aminoflavan hydrochloride (mixed m.p. confirmation) separated on the controlled addition of hydrochloric acid. The yield of crystallized material was 0·6 g.

(c) *Use of aluminium amalgam.* A solution of 4-oximinoflavan (2·0 g) in aqueous ethanol (80%; 200 ml) was refluxed with aluminium amalgam (18 g) for 4 hr. The solid was collected and the solvent removed under red press. Trituration of the residual oil with dil hydrochloric acid afforded 4-aminoflavan hydrochloride (mixed m.p.). The yield of product crystallized from methyl alcohol was 1·2 g.

4-Acetamidoflavan

(a) A mixture of 4-oximinoflavan (1·0 g), acetic acid (90 ml) and zinc dust (8 g) was refluxed for 24 hr. The *amide* obtained on removal of the residual zinc and the solvent (red press) separated from methanol in needles (0·5 g), m.p. 204–206° (Found: C, 76·8; H, 6·6; N, 5·1. $C_{17}H_{17}NO_2$ requires: C, 76·4; H, 6·4; N, 5·2%). This compound (mixed m.p.) was also obtained by the action of pyridine and acetic anhydride on 4-aminoflavan hydrochloride.

(b) A hot solution of 4-oximinoflavan (1·0 g) in butanol (20 ml) was treated with sodium metal and refluxed for 1 hr and, after addition of water (1 ml) for a further 4½ hr. The cooled solution was washed with water and dried, and the solvent removed (red press). The residual oil on acetylation (pyridine–acetic anhydride) in the cold yielded 4-acetamidoflavan (mixed m.p. confirmation).

Flavan-4α-ol

(a) A solution of the amine hydrochloride (1·5 g) in aqueous acetic acid (50%; 80 ml) was added at room temp during 45 min to a stirred solution of sodium nitrite (4 g; 10 ml H_2O) which had been treated with acetic acid (20 ml). The mixture was stirred for 30 min, heated at 50° for 40 min. cooled and neutralized by powdered sodium hydrogen carbonate (ca. 90 g); water was added to promote solution of the carbonate. The mixture was kept overnight at 0°. The precipitated flavan-4α-ol (Found: C, 79·7; H, 6·2; Calc. for $C_{15}H_{14}O$: C, 79·6; H, 6·2%) separated from light petroleum (b.p. 60–80°) in needles, (0·5 g), m.p. and mixed m.p. 116–117°. Freudenberg and Orthner[3] give m.p. 119°. The syrup obtained by evaporation of the mother liquor when recrystallized from that solvent gave in addition to needles (flavan-4α-ol), prisms (0·2 g) m.p. 85–87°, which were manually separated. The m.p. of the prisms was not depressed by addition of an authentic sample of 4α-acetoxyflavan.[3]

(b) A solution of 4-aminoflavan acetate (0·5 g) in acetic acid (2 ml) was treated with 2% hydrochloric acid (200 ml). Aqueous sodium nitrite (2%; 25 ml) was added dropwise with stirring to the mixture at 0·5° and after 1 hr the solution was heated in 30 min to 100° and cooled. Flavan-4α-ol separated in needles, m.p. and mixed m.p., 118°. The crystals exhibited a brownish-violet colouration when moistened with sulphuric acid.

Flavan-4α-ol (authentic sample) was prepared (yield 12%) from flavanone by reduction by aluminium amalgam as described by Freudenberg and Orthner.[3]

1-Amino-1-o-hydroxyphenyl-3-phenylpropane hydrochloride

When hydrogenation (Pd/C, AcOH) of 4-oximinoflavan was continued until 3 moles of hydrogen had been absorbed (16 hr), the syrup obtained on removal of the catalyst and the solvent separated from 5% hydrochloric acid in micro-crystals, m.p. 203–206° (yield 70%). This m.p. was not depressed by addition of an authentic sample of *1-amino-1-o-hydroxyphenyl-3-phenylpropane hydrochloride*

prepared as described below (Found: C, 68·7; H, 6·5; N, 5·4; Cl, 13·5. $C_{15}H_{17}NO.HCl$ requires: C, 68·3; H, 6·8; N, 5·3; Cl, 13·5%).

o-Hydroxy-β-phenylpropiophenone oxime. This was prepared from the parent ketone,[13a] hydroxylamine hydrochloride and sodium hydroxide in aqueous ethanol. The product separated from aqueous ethanol in micro-crystals, m.p. 117–118° (Found: C, 74·7; H, 5·9; N, 5·7. $C_{15}H_{15}NO_2$ requires: C, 74·7; H, 6·3; N, 5·8%). This oxime when hydrogenated (Pd/C, AcOH) for 13 hr absorbed 2 moles hydrogen and gave the above (mixed m.p.) aminopropane hydrochloride (yield of crystallized product, 50%).

No useful result was obtained when the aminopropane was treated with aqueous sodium nitrite under the conditions described for 4-aminoflavan (method *a*).

6-Chloroflavan-4β-ol

Use of diborane. Reduction of 6-chloroflavanone by diborane (see under flavanone) yielded 6-chloroflavan-4β-ol, m.p. 114–115°. Karrer *et al.*[15] give m.p. 114–115°. Acetylation (pyridine–acetic anhydride) afforded *4β-acetoxy-6-chloroflavan*, m.p. 115–118° as needles from methanol. (Found: C, 67·1; H, 5·0; Cl, 11·8. $C_{17}H_{15}ClO_3$ requires: C, 67·4; H, 5·0; Cl, 11·7%). Addition of the 4α-isomer depressed the m.p. by more than 10°. The flavan-4β-ol (mixed m.p. confirmation with the Karrer (Table 1) product) was recovered when the 4β-acetoxy compound was refluxed with 5% ethanolic potassium hydroxide for 30 min. The mixture was diluted with water and the precipitate crystallized from methanol.

Use of sodium borohydride. A mixture of 6-chloroflavanone (1·0 g) in ethanol and sodium borohydride (0·3 g) was kept overnight. Acetic acid (trace) was added and the volume of the solvent reduced. The precipitate separated from methanol in needles, m.p. 114–116°. The m.p. of the acetate of this product was depressed by addition of 4α-acetoxy-6-chloroflavan. No depression was observed when 4β-acetoxy-6-chloroflavan was employed.

Catalytic hydrogenation (PtO_2, AcOH, 1 mole H) of the flavanone yielded 6-chloro-4β-hydroxyflavan (mixed m.p. authentication).

6-Chloroflavan-4α-ol

6-Chloro-4-oximinoflavan (Found: C, 65·3; H, 4·2; Cl, 13·2; N, 5·2. $C_{15}H_{12}ClNO_2$ requires: C, 65·8; H, 4·4; Cl, 13·0; N, 5·1%) crystallized from methanol in needles, m.p. 185–186°. Reduction by lithium aluminium hydride (see under 4-aminoflavan) yielded *4-amino-6-chloroflavan hydrochloride*, m.p. 272–274° as needles from aqueous methanol. (Found: C, 61·3; H, 5·0; Cl, 23·9; N, 5·0. $C_{15}H_{14}ClNO.HCl$ requires: C, 60·8; H, 5·1; Cl, 23·9; N, 4·7%). *4-Acetamido-6-chloroflavan* (from the amine hydrochloride and pyridine–acetic anhydride) formed needles, m.p. 243–244° from methanol. (Found: C, 67·6; H, 5·4; Cl, 12·3; N, 5·2. $C_{17}H_{16}ClNO_2$ requires: C, 67·7; H, 5·3; Cl, 11·8; N, 4·6%). The amide (mixed m.p. authentication) was also prepared by reducing the oxime with aluminium amalgam in aqueous ethanol and acetylating the product. Treatment of 4-amino-6-chloroflavan hydrochloride with nitrous acid (see above under flavan-4α-ol) afforded *6-chloroflavan-4α-ol*, m.p. 117–119° from benzene–light petroleum. (Found: C, 69·6; H, 4·8; Cl, 13·3. $C_{15}H_{13}ClO_2$ requires: C, 69·1; H, 5·0; Cl, 13·6%).

4α-Acetoxy-6-chloroflavan (pyridine–acetic anhydride) separated from methanol in prisms, m.p. 118–119° (Found: C, 67·3; H, 4·7; Cl, 11·8. $C_{17}H_{15}ClO_3$ requires: C, 67·4; H, 5·0; Cl, 11·7%).

Reduction of 6-chloroflavanone by aluminium amalgam. A mixture of aluminium amalgam (from 3 g aluminium foil), 6-chloroflavanone (1·0 g) and aqueous ethanol (80%; 100 ml) was refluxed for 6 hr and the catalyst collected and solvent removed under red press. The residue separated from methanol as needles, m.p. 117–119°. The acetate of the product did not depress the m.p. of an authentic sample of 4α-acetoxy-6-chloroflavan.

4′-Methoxyflavan-4β-ol

Catalytic hydrogenation of the flavanone (PtO_2, AcOH, 1 mole H) yielded 4-methoxyflavan-4β-ol (70%) which separated from methanol in needles, m.p. 150–151°. *4β-Acetoxy-4′-methoxyflavan* separated from methanol in prisms, m.p. 126–127° (Found: C, 72·8; H, 6·3; OMe, 10·1;. $C_{18}H_{18}O_4$ requires: C, 72·5; H, 6·1; OMe, 10·4%).

The β-isomer, m.p. 150–151° was also obtained when reduction of the flavanone was effected by

[15] Footnote *a*, Table 1.

lithium aluminium hydride. Diborane, sodium borohydride and ammoniacal titanous chloride yielded a product, m.p. 146–148° which showed an intermediate m.p. with the higher-melting compound, and gave the same (mixed m.p.) acetate.[10]

4′-Methoxyflavan-4α-ol

4′-Methoxy-4-oximinoflavan crystallized from methanol in needles, m.p. 170–172° (Found: C, 71·1; H, 5·6; N, 5·1; OMe, 12·0. $C_{16}H_{15}NO_3$ requires: C, 71·4; H, 5·6; N, 5·2; OMe, 11·5%). Reduction by lithium aluminium hydride produced *4-amino-4′-methoxyflavan hydrochloride*, m.p. 260–263° as microcrystals from aqueous methanol. (Found: C, 65·5; H, 6·1; Cl, 12·5; N, 4·7; OMe, 11·0. $C_{16}H_{17}NO_2.HCl$ requires: C, 65·8; H, 6·2; Cl, 12·2; N, 4·8; OMe, 10·6%).

4-Acetamido-4′-methoxyflavan (pyridine–acetic anhydride) crystallized from methanol in needles, m.p. 230–232° (Found: C, 72·7; H, 6·4; N, 5·1; OMe, 10·7. $C_{18}H_{19}NO_3$ requires: C, 72·7; H, 6·4; N, 4·7; OMe, 10·4%).

Reduction of 4′-methoxy-4-oximinoflavan by catalytic hydrogenation (PtO_2, AcOH, 2 moles H) or by application of aluminium amalgam in aqueous ethanol, followed by acetylation of the product, yielded the above acetamido-compound (mixed m.p. confirmation).

4′-Methoxyflavan-4α-ol. Treatment of 4-amino-4′-methoxyflavan hydrochloride with nitrous acid (see preparation of flavan-4α-ol), afforded 4′-methoxyflavan-4α-ol, m.p. 132–134° as needles from benzene–light petroleum. Brown *et al.*[10] give m.p. 131–132° (Found: C, 75·0; H, 6·1; OMe, 12·6. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·3; OMe, 12·1%). This compound was also prepared by refluxing a mixture of 4′-methoxyflavanone (1·0 g), ethanol (80 ml); water (20 ml) and aluminium amalgam (from 3 g aluminium) for 6 hr. The residue obtained by removal of the catalyst and solvent, was dissolved in benzene and chromatographed on alumina. The benzene–light petroleum eluate yielded the 4α-ol compound (0·1 g), m.p. and mixed m.p. with the nitrous acid product, 130–132°.

Acetylation by acetic anhydride and pyridine gave 4α-acetoxy-4′-methoxyflavan, which separated from methanol in needles, m.p. 87–88°. Brown *et al.*[10] give m.p. 71° (Found: C, 72·7; H, 5·8; OMe, 10·9. Calc. for $C_{18}H_{18}O_4$: C, 72·5; H, 6·1; OMe, 10·4%).