

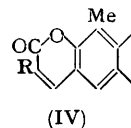
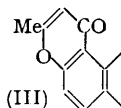
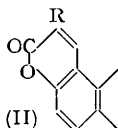
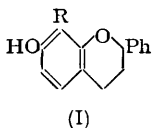
The Pigments of "Dragon's Blood" Resin. Part V. Some Flavans.*

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The method developed in Part III (*J.*, 1950, 3117) has been extended to the synthesis of flavans and their derivatives from a series of polyhydroxyphenols. From some a number of α - and γ -pyronoflavans have been prepared.

IN reviewing possible routes for the synthesis of dracorubin-type compounds we were attracted by the idea of employing a residue of type (I), containing the flavan system already formed, rather than to attempt the construction of this unit on to a flavylum compound, more especially because of the experimental limitations encountered in the synthesis of the flavan system (Part III, *J.*, 1950, 3117). As a preliminary to exploring this route to the dracorubin system the general procedure developed in Part III (*loc. cit.*) has been extended to the synthesis of a series of flavans from resorcinol, orcinol, quinol, hydroxyquinol, phloroglucinol, and pyrogallol. Further, from some of the formyl- and keto-derivatives it has been possible to obtain, *e.g.*, α - and γ -pyronoflavans, types (II), (III), and (IV).



In these studies there emerged several experimental features of general interest which may be noted. (a) Most parent flavans are extremely difficult to crystallise and several of the hydroxy-compounds are readily susceptible to aerial oxidation. (b) The flavan oxygen system is sensitive to acidic reagents above room temperature and attempts to demethylate *O*-methylflavans by the standard methods are uniformly unsuccessful. Further, whilst, *e.g.*, 8-formyl-7-hydroxyflavan (I; R = CHO) readily reacted with acetophenone in ethereal hydrogen chloride, the resulting flavylum salt was resinous and could not be purified. (c) With chromic anhydride *O*-methylflavans furnish low yields of the corresponding flavanones, thus providing a method of detecting the flavan system.

EXPERIMENTAL

7-Hydroxyflavan (I; R = H).—A solution of 7-hydroxyflavanone (Ellison, *J.*, 1927, 1722) (1 g.) in acetic acid (40 ml.), containing concentrated hydrochloric acid (5 ml.), was reduced with zinc amalgam (from 10 g. of zinc dust) at room temperature and 24 hr. later the solution was decanted and diluted with water. Purification of the resulting precipitate from light petroleum (b. p. 60–80°), containing a small amount of methanol, yielded *7-hydroxyflavan* (0.7 g.) in prisms, m. p. 71°, readily soluble in 2*N*-aqueous sodium hydroxide and having a negative ferric reaction (Found: C, 79.6; H, 6.3. C₁₆H₁₄O₂ requires C, 79.6; H, 6.2%).

7-Hydroxy-8-methylflavan (I; R = Me).—(a) Prepared by Gattermann's method from 7-hydroxyflavan (1 g.), hydrogen cyanide (5 ml.), and zinc chloride (0.5 g.) in ethereal hydrogen

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chloride (100 ml.), 8-formyl-7-hydroxyflavan (ca. 0.5 g.) separated from benzene and then methanol in rectangular plates, m. p. 111°, readily soluble in the usual organic solvents, except light petroleum (b. p. 60—80°), and having an intense red-brown ferric reaction in alcohol (Found: C, 75.4; H, 5.9. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.6%); the 2:4-dinitrophenylhydrazone formed deep red prisms, m. p. 300° (decomp.), from a large volume of ethyl acetate (Found: N, 12.6. $C_{22}H_{18}O_8N_4$ requires N, 12.9%). Reduction of this aldehyde (1 g.) during 24 hr. by the modified Clemmensen technique furnished a good yield of 7-hydroxy-8-methylflavan which separated from light petroleum (b. p. 60—80°) in prisms (yield, 75%), m. p. 130°, having a negative ferric reaction in alcohol (Found: C, 79.7; H, 6.8. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.7%).

(b) A solution of 3-methylresacetophenone (10 g.), benzaldehyde (10 g.), and potassium hydroxide (20 g.) in a mixture of methanol (50 ml.) and water (20 ml.) was heated under reflux for 4 hr. After dilution with water followed by removal of the excess of benzaldehyde with ether, acidification with concentrated hydrochloric acid gave a yellow viscous liquid which on trituration with ether deposited crude flavanone (3 g.); a further quantity (1.5 g.) was obtained from an acetic acid solution of the residue left on evaporation of the ethereal mother-liquor. 7-Hydroxy-8-methylflavanone formed prisms, m. p. 219°, from alcohol, moderately soluble in alcohol, acetic acid, and acetone, and sparingly soluble in ether, benzene, and light petroleum (b. p. 60—80°) (Found: C, 75.6; H, 5.5. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.6%). Reduction of this flavanone by the modified Clemmensen technique furnished 7-hydroxy-8-methylflavan (yield, ca. 80%), m. p. and mixed m. p. 130°.

α -Pyrono(6':5'-7:8)flavan (II; R = H).—The condensation of 8-formyl-7-hydroxyflavan (0.5 g.) and ethyl malonate (0.5 g.) with piperidine (5 drops) at 0° during 24 hr. gave 3'-ethoxycarbonyl- α -pyrono(6':5'-7:8)flavan (II; R = CO_2Et) which separated from alcohol in plates (0.5 g.), m. p. 120° (Found: C, 72.0; H, 5.4. $C_{21}H_{18}O_5$ requires C, 72.0; H, 5.2%). An alcoholic solution of this coumarin exhibits a blue fluorescence. Simultaneous hydrolysis and decarboxylation of this coumarin (2 g.) with 20% alcoholic potassium hydroxide (40 ml.) on the steam-bath for 2 hr. furnished α -pyrono(6':5'-7:8)flavan which separated from ethyl acetate-light petroleum (b. p. 60—80°) and then methanol in prisms (1.5 g.), m. p. 153°, insoluble in cold 2N-sodium hydrogen carbonate and -sodium hydroxide (Found: C, 72.7; H, 5.4; H_2O , 6.4. $C_{18}H_{14}O_3, H_2O$ requires C, 73.0; H, 5.4; H_2O , 6.1%).

3'-Acetyl- α -pyrono(6':5'-7:8)flavan (II; R = Ac).—Prepared by the condensation of 8-formyl-7-hydroxyflavan (1 g.) and ethyl acetoacetate (0.8 g.) with piperidine (5 drops) during 24 hr., 3'-acetyl- α -pyrono(6':5'-7:8)flavan separated from light petroleum (b. p. 60—80°) or methanol in needles or plates (1.2 g.), m. p. 180° (Found: C, 75.3; H, 5.4. $C_{20}H_{16}O_4$ requires C, 75.0; H, 5.0%).

Furano(2':3'-7:8)flavan.—The interaction of 8-formyl-7-hydroxyflavan (1.25 g.), ethyl bromoacetate (0.9 g.), and potassium carbonate (10 g.) in boiling acetone (50 ml.) gave 7-ethoxycarbonylmethoxy-8-formylflavan, forming needles (1 g.), m. p. 119°, from alcohol (Found: C, 70.4; H, 5.8. $C_{20}H_{20}O_5$ requires C, 70.6; H, 5.9%); the 2:4-dinitrophenylhydrazone separated from ethyl acetate in orange prisms, m. p. 202° (Found: N, 10.9. $C_{26}H_{24}O_8N_4$ requires 10.8%). Simultaneous cyclisation, hydrolysis, and decarboxylation of this ester (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 30 min. gave furano(2':3'-7:8)flavan which crystallised from light petroleum and sublimed at 190°/0.01 mm., forming needles (50 mg.), m. p. 182° (Found: C, 81.4; H, 5.5. $C_{17}H_{14}O_2$ requires C, 81.6; H, 5.6%).

7-Hydroxyflavan-8-carboxylic Acid (I; R = CO_2H) and its Derivatives.—Prepared by the pyridine method, 7-acetoxy-8-formylflavan separated from methanol or ethyl acetate in needles, m. p. 104°, with a negative ferric reaction (Found: C, 72.8; H, 5.5. $C_{18}H_{16}O_4$ requires C, 73.0; H, 5.4%); the 2:4-dinitrophenylhydrazone formed scarlet needles, m. p. 223°, from ethyl acetate (Found: C, 60.5; H, 4.4; N, 11.8. $C_{24}H_{20}O_7N_4$ requires C, 60.5; H, 4.2; N, 11.8%). This acetoxy-aldehyde (2 g.), in acetone (20 ml.), was oxidised with potassium permanganate (3 g.) in water (80 ml.) added during 1 hr. Next day the mixture was clarified with sulphur dioxide, the acetone evaporated, and the solid crystallised from methanol, giving 7-acetoxyflavan-8-carboxylic acid in prisms (1.4 g.), m. p. 183°, with a negative ferric reaction (Found: C, 69.3; H, 5.4. $C_{18}H_{16}O_5$ requires C, 69.2; H, 5.2%). Deacetylation of this product (1.4 g.) with warm 2N-aqueous sodium hydroxide (20 ml.) gave a quantitative yield of 7-hydroxyflavan-8-carboxylic acid, forming plates, m. p. 190°, from methanol, with an intense brownish-blue ferric reaction (Found: C, 71.1; H, 5.5. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%). Prepared with ethereal diazomethane, the methyl ester separated from methanol in plates, m. p. 148°, with an

intense brown ferric reaction (Found: C, 71.9; H, 5.8. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.7%). Methylated by the methyl iodide-potassium carbonate method, this ester gave a quantitative yield of 7-methoxy-8-methoxycarbonylflavan, forming plates, m. p. 107°, from methanol, with a negative ferric reaction [Found: C, 72.6; H, 6.0; OMe, 21.0. $C_{16}H_{15}O_2(OMe)_2$ requires C, 72.5; H, 6.1; OMe, 20.8%].

6-Formyl-7-hydroxy-8-methylflavan.—Prepared from 7-hydroxy-8-methylflavan (1 g.) by Gattermann's method, this flavan separated from methanol in prisms (0.5 g.), m. p. 121°, with an intense violet-brown ferric reaction (Found: C, 75.9; H, 6.4. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%); the 2:4-dinitrophenylhydrazone formed scarlet plates, m. p. 277°, from ethyl acetate (Found: N, 12.5. $C_{23}H_{20}O_6N_4$ requires N, 12.5%). By the ethyl malonate-piperidine method this aldehyde (0.5 g.) furnished 3'-ethoxycarbonyl-8-methyl- α -pyrono(5':6'-6:7)flavan (IV; R = CO₂Et), forming plates (0.6 g.), m. p. 174°, from light petroleum (b. p. 60–80°) (Found: C, 72.5; H, 5.3. $C_{22}H_{20}O_5$ requires C, 72.5; H, 5.5%). An alcoholic solution of this has a violet fluorescence.

Hydrolysis of the ethoxycarbonylcoumarin (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 1 hr. gave 8-methyl- α -pyrono(5':6'-6:7)flavan (IV; R = H) in plates (0.5 g.), m. p. 167°, from light petroleum (b. p. 80–100°) or methanol, insoluble in cold 2N-sodium hydroxide (Found: C, 73.0; H, 5.5. $C_{19}H_{16}O_3 \cdot H_2O$ requires C, 73.5; H, 5.9%).

8-Acetyl-7-hydroxyflavan (I; R = Ac).—Prepared from 7-hydroxyflavan in moderate yield by the Hoesch method, 8-acetyl-7-hydroxyflavan formed prisms, m. p. 143°, from methanol, with an intense brown ferric reaction (Found: C, 75.8; H, 5.8. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%); the 2:4-dinitrophenylhydrazone separated from much ethyl acetate in red plates, m. p. 242° (Found: N, 12.2. $C_{23}H_{20}O_6N_4$ requires N, 12.5%). This flavan (1.5 g.) was heated on the steam-bath with ethyl acetate (10 ml.) and powdered sodium (1.4 g.) for 1 hr. and on isolation the resulting mixed diketone and chromone were boiled with alcohol (10 ml.), containing concentrated hydrochloric acid (6 drops), for 10 min., giving 2'-methyl- γ -pyrono(6':5'-7:8)flavan which separated from light petroleum (b. p. 80–100°) and then from methanol in prisms (0.5 g.), m. p. 158°, insoluble in 2N-sodium hydroxide and having a negative ferric reaction (Found: C, 78.3; H, 5.8. $C_{19}H_{16}O_3$ requires C, 78.1; H, 5.5%).

8-Ethyl-7-hydroxyflavanone.—Prepared from 3-ethyl resacetophenone (Limaye and Limaye, *Rasayanam*, 1937, 1, 109; *Chem. Abs.*, 1938, 32, 2095) (5 g.) and benzaldehyde (5 g.), in the usual manner, 8-ethyl-7-hydroxyflavanone formed prisms (2 g.), m. p. 294°, from ethyl acetate (Found: C, 75.9; H, 6.1. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%).

6-Ethyl-7-hydroxyflavan.—Prepared from 5-ethylresacetophenone (Weiss and Kratz, *Monatsh.*, 1929, 51, 386) (10 g.) and benzaldehyde (10 g.), 6-ethyl-7-hydroxyflavanone separated in plates (6.2 g.), m. p. 243°, from methanol (Found: C, 76.0; H, 6.0%). Reduction of this gave a high yield of 6-ethyl-7-hydroxyflavan, forming prisms, m. p. 118°, from aqueous methanol (Found: C, 80.3; H, 7.3. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1%).

7-Hydroxy-6-methylflavan.—From 5-methylresacetophenone (Yanagita, *Ber.*, 1938, 71, 2270) (11 g.) and benzaldehyde (10 g.), 7-hydroxy-6-methylflavanone separated from acetic acid in plates (6.2 g.), m. p. 234–236° (Found: C, 75.8; H, 5.7. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.6%). Reduction of this gave 7-hydroxy-6-methylflavan, in prisms, m. p. 119°, from methanol (Found: C, 75.9; H, 6.5. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.7%); mixed with isomeric 7-hydroxy-8-methylflavan, this had m. p. ca. 80°. Application of the Gattermann aldehyde synthesis to this flavan (1.0 g.) furnished 8-formyl-7-hydroxy-6-methylflavan, yellow needles (0.4 g.), m. p. 120° (from methanol), with an olive-green ferric reaction in alcohol (Found: C, 76.0; H, 5.6. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%); the 2:4-dinitrophenylhydrazone separated from ethyl acetate in orange needles, m. p. 265° (Found: N, 12.2. $C_{23}H_{20}O_6N_4$ requires N, 12.5%). Prepared from this aldehyde (0.3 g.) and ethyl malonate in the usual way, 3'-ethoxycarbonyl-6-methyl- α -pyrono(6':5'-7:8)flavan separated from alcohol in yellow needles (0.25 g.), m. p. 160° (Found: C, 72.4; H, 5.7. $C_{22}H_{20}O_5$ requires C, 72.5; H, 5.5%).

7-Methoxyflavan.—Reduction of 7-methoxyflavanone (Kostanecki and Stoppani, *Ber.*, 1904, 37, 1180) (5 g.) furnished 7-methoxyflavan as a colourless liquid (3.5 g.), b. p. 130°/0.001 mm. (Found: C, 80.4; H, 6.7. $C_{16}H_{16}O_2$ requires C, 80.0; H, 6.7%). Demethylation of this compound with aluminium chloride or hydriodic acid, under a variety of conditions, yielded only intractable products.

Oxidation of 7-methoxyflavan (0.5 g.), dissolved in acetic acid (30 ml.) [by the addition of a solution of chromic oxide (0.5 g.) in acetic acid (10 ml.)], on the steam-bath during 30 min. furnished a viscous oil from which warm light petroleum (b. p. 80–100°) extracted 7-methoxyflavanone (50 mg.), identical with an authentic specimen (*loc. cit.*).

5-Hydroxyflavan.—The reduction of 5-hydroxyflavanone (1 g.) (Narasimhachari and Seshadri, *Proc. Indian Acad. Sci.*, 1948, **27**, A, 223) by the usual method gave 5-hydroxyflavan, plates (0.8 g.), m. p. 160°, from light petroleum (b. p. 80—100°) containing a trace of methanol (Found : C, 79.6; H, 6.0. $C_{15}H_{14}O_2$ requires C, 79.6; H, 6.2%). Similarly, 5-methoxyflavanone (*idem*, *ibid.*) (1.0 g.) yielded 5-methoxyflavan, plates (0.75 g.), m. p. 60°, from ethanol (Found : C, 79.8; H, 6.8. $C_{16}H_{16}O_3$ requires C, 80.0; H, 6.7%). Oxidation of this flavan (0.5 g.) with chromic oxide (as for the 7-methoxy-analogue) regenerated 5-methoxyflavanone (50 mg.).

7-Hydroxy-5-methylflavan.—A mixture of oracetophenone (10 g.), benzaldehyde (7.5 g.), methanol (60 ml.), water (20 ml.), and potassium hydroxide (20 g.) was boiled during 3½ hr., diluted with water, extracted with ether, and acidified with hydrochloric acid. The solid (14 g.) was triturated with cold benzene and then crystallised from ethyl acetate, giving 7-hydroxy-5-methylflavanone in plates (11.5 g.), m. p. 212° (Found : C, 75.4; H, 5.5. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.6%). Reduction of this furnished 7-hydroxy-5-methylflavan, needles, m. p. 82—85° (from methanol), which in moist air readily oxidised to a sticky resin and so was utilised immediately for the subsequent operations.

Prepared from this flavan by Gattermann's method, 8-formyl-7-hydroxy-5-methylflavan separated from light petroleum (b. p. 80—100°) or methanol in prisms, m. p. 127°, with an intense red-brown ferric reaction in alcohol (yield, 50%) (Found : C, 76.0; H, 6.0. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%); the 2 : 4-dinitrophenylhydrazone formed scarlet needles, m. p. 276—278° (decomp.), from ethyl acetate (Found : N, 12.5. $C_{23}H_{20}O_6N_4$ requires N, 12.5%). Reduction of the aldehyde (1 g.) gave 7-hydroxy-5 : 8-dimethylflavan in needles (0.7 g.), m. p. 117°, from light petroleum (b. p. 60—80°) which became brown during 24 hr. (Found : C, 80.4; H, 7.1. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1%). Prepared from this aldehyde (1 g.) and ethyl malonate (0.7 g.) in the usual manner, 3'-ethoxycarbonyl-5-methyl- α -pyrono(6' : 5'-7 : 8)flavan separated from light petroleum (b. p. 80—100°) in plates (1.2 g.), m. p. 144° (Found : C, 72.8; H, 5.8. $C_{22}H_{20}O_5$ requires C, 72.5; H, 5.5%). Similarly, the aldehyde (0.5 g.) and ethyl acetoacetate (0.3 g.) furnished 3'-acetyl-5-methyl- α -pyrono(6' : 5'-7 : 8)flavan, pale yellow plates (0.7 g.), m. p. 103° [from light petroleum (b. p. 80—100°)] (Found : C, 75.1; H, 5.1. $C_{21}H_{18}O_4$ requires C, 75.4; H, 5.4%).

Derivatives of 5-Hydroxy-7-methoxyflavan.—Prepared by the interaction of 5-hydroxy-7-methoxyflavan (Part III, *loc. cit.*) (1 g.), hydrogen cyanide (5 ml.), and zinc chloride (0.5 g.), in ethereal hydrogen chloride, the semi-solid aldimine complex was hydrolysed with warm water, and the product repeatedly extracted with light petroleum (b. p. 80—100°). Crystallised from methanol, the residue gave 6-formyl-5-hydroxy-7-methoxyflavan in pale yellow needles (0.15 g.), m. p. 99°, with an intense red-brown ferric reaction (Found : C, 71.6; H, 5.8; OMe, 10.6. $C_{16}H_{13}O_3 \cdot OMe$ requires C, 71.8; H, 5.7; OMe, 10.9%). The light petroleum extract contained 8-formyl-5-hydroxy-7-methoxyflavan, forming plates (0.4 g.), m. p. 211°, from methanol, with a negative ferric reaction (Found : C, 71.6; H, 5.8; OMe, 10.9. $C_{16}H_{13}O_3 \cdot OMe$ requires C, 71.8; H, 5.7; OMe, 10.9%). The 2 : 4-dinitrophenylhydrazone separated from ethanol in red plates, m. p. 214° (Found : N, 11.8. $C_{23}H_{20}O_7N_4$ requires N, 12.1%).

Obtained from 5-hydroxy-7-methoxyflavan (1 g.), by the Hoesch method, 8-acetyl-5-hydroxy-7-methoxyflavan separated from methanol in prisms (0.4 g.), m. p. 152°, with a negative ferric reaction (Found : C, 72.3; H, 6.3. $C_{18}H_{18}O_4$ requires C, 72.5; H, 6.1%). The 2 : 4-dinitrophenylhydrazone crystallised from ethanol in red prisms, m. p. 154° (decomp.) (Found : N, 12.0. $C_{24}H_{22}O_7N_4$ requires N, 11.7%).

8-Formyl-7-hydroxy-5-methoxyflavan.—The reduction of 7-benzyloxy-5-hydroxyflavanone (Part III, *loc. cit.*) (1 g.) furnished 7-benzyloxy-5-hydroxyflavan, prisms (0.7 g.), m. p. 139°, from methanol (Found : C, 79.4; H, 6.1. $C_{22}H_{20}O_3$ requires C, 79.5; H, 6.1%).

Similarly, 7-benzyloxy-5-methoxyflavanone (Part III, *loc. cit.*) gave 7-benzyloxy-5-methoxyflavan, prisms, m. p. 71° (from ether) (Found : C, 80.1; H, 6.3. $C_{23}H_{22}O_3$ requires C, 79.7; H, 6.4%). By the Gattermann aldehyde synthesis this flavan (1 g.) yielded 7-benzyloxy-8-formyl-5-methoxyflavan (0.6 g.), plates, m. p. 200° (from methanol), with a negative ferric reaction (Found : C, 76.9; H, 5.9. $C_{24}H_{22}O_4$ requires C, 77.0; H, 5.9%); the 2 : 4-dinitrophenylhydrazone separated from ethyl acetate in red prisms, m. p. 249—250° (Found : N, 10.2. $C_{30}H_{26}O_7N_4$ requires N, 10.1%). Debzylation of this compound with hydrogen and a palladium-charcoal catalyst furnished 8-formyl-7-hydroxy-5-methoxyflavan, m. p. and mixed m. p. 128° (Part III, *loc. cit.*).

Prepared from 8-formyl-7-hydroxy-5-methoxyflavan (1 g.) and ethyl malonate (0.7 g.) with piperidine (5 drops), 3'-ethoxycarbonyl-5-methoxy- α -pyrono(6' : 5'-7 : 8)flavan separated from

alcohol in colourless plates (1.1 g.), m. p. 192°, an alcoholic solution of which exhibits a violet fluorescence (Found: C, 69.1; H, 5.1. $C_{22}H_{20}O_6$ requires C, 69.5; H, 5.3%). Hydrolysis and simultaneous decarboxylation of this ester (1 g.) with boiling 10% alcoholic potassium hydroxide (20 ml.) for 1 hr. gave 5-methoxy- α -pyrono(6': 5'-7: 8)flavan, plates (0.8 g.), m. p. 263°, from dioxan, insoluble in cold 2*N*-aqueous sodium hydroxide (Found: C, 69.6; H, 5.7; H_2O , 5.6. $C_{19}H_{16}O_4 \cdot H_2O$ requires C, 69.9; H, 5.6; H_2O , 5.5%).

Condensation of 8-formyl-7-hydroxy-5-methoxyflavan (0.5 g.) and ethyl acetoacetate (0.35 g.) by the piperidine method furnished 3'-acetyl-5-methoxy- α -pyrono(6': 5'-7: 8)flavan, yellow prisms (0.5 g.), m. p. 210° (from alcohol) (Found: C, 72.4; H, 4.8; OMe, 8.9. $C_{20}H_{15}O_4 \cdot OMe$ requires C, 72.0; H, 5.2; OMe, 8.9%).

6-Formyl-7-hydroxy-5-methoxy-8-methylflavan.—Prepared from 7-hydroxy-5-methoxy-8-methylflavan (Part III, *loc. cit.*) (1 g.) by the Gattermann method, the aldehyde separated from methanol in prisms (0.3 g.), m. p. 146°, with an intense red-brown ferric reaction (Found: C, 72.4; H, 6.2; OMe, 10.3. $C_{17}H_{15}O_3 \cdot OMe$ requires C, 72.5; H, 6.1; OMe, 10.4%); the 2: 4-dinitrophenylhydrazone crystallised from ethyl acetate-ethanol in deep red prisms, m. p. 239° (Found: N, 11.5. $C_{24}H_{22}O_7 \cdot N_4$ requires N, 11.7%). By the standard methods this aldehyde (0.5 g.) gave 3'-ethoxycarbonyl-5-methoxy-8-methyl- α -pyrono(5': 6'-6: 7)flavan, forming plates (0.45 g.), m. p. 144°, from methanol (Found: C, 70.4; H, 5.7. $C_{23}H_{22}O_6$ requires C, 70.0; H, 5.6%), and 7-hydroxy-5-methoxyflavan (1 g.) gave 8-acetyl-7-hydroxy-5-methoxyflavan (0.5 g.), prisms, m. p. 148° (from alcohol), with an intense violet-brown ferric reaction (Found: C, 72.2; H, 6.2. $C_{18}H_{18}O_4$ requires C, 72.5; H, 6.1%). Heated with ethyl acetate (10 ml.) and sodium (1.5 g.) on the steam-bath for 1 hr., this ketone (1.5 g.) furnished 5-methoxy-2'-methyl- γ -pyrono(6': 5'-7: 8)flavan, yellow prisms (1.5 g.), m. p. 215°, from light petroleum (b. p. 80–100°) (Found: C, 74.1; H, 5.9. $C_{20}H_{18}O_4$ requires C, 74.5; H, 5.6%), which on condensation with piperonaldehyde under standard conditions gave 5-methoxy-3'': 4''-methylenedioxy-styryl- γ -pyrono(6': 5'-7: 8)flavan, forming orange prisms, m. p. 222°, from light petroleum (b. p. 80–100°) (Found: C, 74.3; H, 5.0. $C_{28}H_{22}O_6$ requires C, 74.0; H, 4.9%).

Boiled for 3½ hr., a mixture of 8-acetyl-7-hydroxy-5-methoxyflavan (1.5 g.), benzaldehyde (0.75 g.), potassium hydroxide (4 g.), methanol (10 ml.), and water gave 8-cinnamoyl-7-hydroxy-5-methoxyflavan which separated from light petroleum (b. p. 80–100°) in yellow prisms (1 g.), m. p. 204°, with an intense red-brown ferric reaction (Found: C, 77.6; H, 5.6; OMe, 8.0. $C_{24}H_{21}O_3 \cdot OMe$ requires C, 77.3; H, 6.2; OMe, 8.0%).

5: 7-Dimethoxyflavan.—Obtained from 5: 7-dimethoxyflavanone (Shinoda and Sato, *J. Pharm. Soc., Japan*, 1928, 48, 111), 5: 7-dimethoxyflavan separated from methanol in prisms, m. p. 137° (Found: C, 75.2; H, 6.8. $C_{17}H_{18}O_3$ requires C, 75.5; H, 6.7%). On being heated under reflux for 1 hr. with aluminium chloride (2 g.) and benzene (20 ml.), the flavan (1 g.) gave 5-hydroxy-7-methoxyflavan (0.6 g.), m. p. and mixed m. p. 204°. Attempts to demethylate the dimethoxyflavan with hot hydriodic acid were unsuccessful.

Oxidation of 5: 7-dimethoxyflavan with chromic oxide furnished a low yield of 5: 7-dimethoxyflavanone, m. p. and mixed m. p. 144–145°.

6-Hydroxyflavan.—6-Hydroxyflavanone [from 2: 5-dihydroxyacetophenone (10 g.) and benzaldehyde (7.5 g.)] separated from methanol in prisms (7.2 g.), m. p. 220° (Found: C, 75.4; H, 5.3. $C_{15}H_{12}O_3$ requires C, 75.0; H, 5.0%), and on reduction by the standard method gave 6-hydroxyflavan, forming prisms (75%), m. p. 119°, from methanol (Found: C, 79.9; H, 6.1. $C_{15}H_{14}O_2$ requires C, 79.6; H, 6.2). By the Gattermann method this gave a low yield of 8-formyl-6-hydroxyflavan, plates, m. p. 102° (from methanol), with a negative ferric reaction (Found: C, 75.7; H, 5.7. $C_{16}H_{14}O_3$ requires C, 75.6; H, 5.6%).

6-Hydroxy-7-methoxyflavan.—Condensation of 2: 5-dihydroxy-4-methoxyacetophenone (10 g.) with benzaldehyde (5 ml.) in the usual manner gave a mixture which on fractional crystallisation from alcohol furnished the sparingly soluble chalkone in orange needles (*ca.* 2 g.), m. p. 177°, with an intense green-brown ferric reaction (Found: C, 71.3; H, 5.2; OMe, 11.7. $C_{15}H_{11}O_3 \cdot OMe$ requires C, 71.1; H, 5.2; OMe, 11.5%), and the more easily soluble flavanone (6.2 g.) in plates, m. p. 173°, with a negative ferric reaction (Found: C, 71.2; H, 5.4; OMe, 11.6%). This flavanone (1 g.) was readily reduced to 6-hydroxy-7-methoxyflavan, prisms (0.8 g.), m. p. 112° (from dilute methanol) (Found: C, 74.7; H, 6.5; OMe, 12.1. $C_{15}H_{13}O_2 \cdot OMe$ requires C, 75.0; H, 6.3; OMe, 12.1%).

7: 8-Dimethoxyflavan.—By the methyl iodide-potassium carbonate method 7: 8-dihydroxyflavanone (Geissmann and Clinton, *J. Amer. Chem. Soc.*, 1946, 68, 697) gave 7: 8-dimethoxyflavanone, forming prisms, m. p. 120°, from light petroleum (b. p. 60–80°) [Found: C, 71.5; H, 5.4; OMe, 21.6. $C_{15}H_{10}O_2(OMe)_2$ requires C, 71.8; H, 5.7; OMe, 21.8%], which on reduction

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yielded 7 : 8-dimethoxyflavan, prisms (*ca.* 70%), m. p. 100° (from methanol) [Found : C, 75.1; H, 6.7; OMe, 23.9. $C_{15}H_{12}O(OMe)_2$ requires C, 75.5; H, 6.7; OMe, 23.0%].

Reduction of 7 : 8-dihydroxyflavanone yielded the flavan as colourless needles, which rapidly darkened and could not be purified.

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