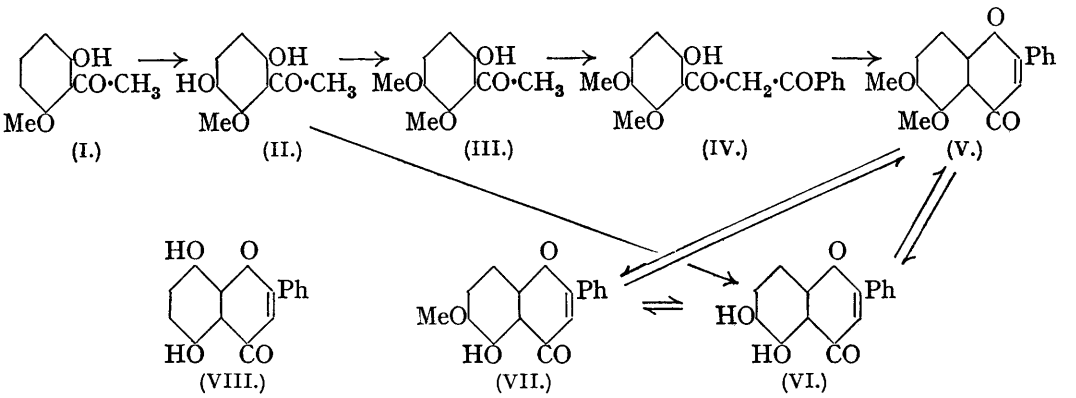
204. *The Synthesis of* 5 : 6-*Dihydroxyflavone and the Structure of Primetin.*

By Wilson Baker.

An unambiguous synthesis of 5 : 6-*dimethoxyflavone* has been achieved *via* the stages (I) to (V). Demethylation of this dimethoxy-derivative gave a dihydroxyflavone, which, because it regenerated 5 : 6-dimethoxyflavone on methylation and for other reasons, must be regarded as 5 : 6-dihydroxyflavone (VI) and not the possible alternative 5 : 8-dihydroxyflavone (VIII). This substance and its derivatives differ from primetin and corresponding derived compounds, and a revision of the structure of primetin, hitherto regarded as 5 : 6-dihydroxyflavone is therefore necessary. A review of the available evidence and the definite exclusion of the 7 : 8-dihydroxy-structure leads to the conclusion that primetin is 5 : 8-dihydroxyflavone (VIII).

Primetin, $C_{15}H_{10}O_4$, isolated from the leaves of *Primula modesta* (Hattori and Nagai, *J. Chem. Soc. Japan*, 1930, **51**, 162; *Acta Phytochim.*, 1930, **5**, 1) exhibits the properties of a dihydroxyflavone. It yields benzoic acid as the only recognisable product by hydrolytic fission, and gives a green ferric chloride reaction. One of the hydroxyl groups resists methylation by diazomethane or methyl iodide and is therefore assumed to occupy position 5. Since, moreover, its absorption spectrum closely resembles that of 6-hydroxyflavone, it has been assumed to be 5 : 6-dihydroxyflavone (VI), and several attempts have been made to prepare this compound (Sugasawa, J., 1933, 1621; *J. Pharm. Soc. Japan*, 1936, **56**, 105; Baker, J., 1934, 1953; see also Mahal and Venkataraman, *Current Sci.*, 1938, **6**, 450). Its synthesis is now recorded, but it differs widely from primetin. In the light of present work it is clear that Sugasawa succeeded in preparing two derivatives of 5 : 6-dihydroxyflavone and even a crude specimen of 5 : 6-dihydroxyflavone itself, but he erroneously believed that his products were derived from 5 : 8-dihydroxyflavone (VIII).



2 : 6-Dihydroxyacetophenone was converted into 2-hydroxy-6-methoxyacetophenone (I), and thence by oxidation with potassium persulphate in alkaline solution into 2 : 5-*dihydroxy*-6-*methoxyacetophenone* (II) (for applications of this method of preparing quinol derivatives, see Baker and Savage, J., 1938, 1602). The position of the second hydroxyl group in (II) is proved by the fact that, like 2 : 5-dihydroxyacetophenone, it gives no precipitate with lead acetate in 50% alcoholic solution, a behaviour which distinguishes it from the only alternative, a 2 : 3-dihydroxyacetophenone; the latter gives an immediate precipitate of a bright yellow lead derivative under these conditions. Methylation of (II) gave 2 : 3 : 6-*trimethoxyacetophenone*. Partial methylation of 2 : 5-dihydroxy-6-methoxyacetophenone (II) gave the bright yellow, volatile ketone 2-*hydroxy*-5 : 6-*dimethoxyacetophenone* (III). The colour of this substance, which is retained after conversion into the colourless *benzoyl* derivative and regeneration by hydrolysis, is noteworthy; it recalls the yellow colour of *m*-xylorcylaldehyde (Robertson and Robinson, J., 1927, 2197). The

O-benzoyl derivative of (III) underwent a smooth conversion into 2-*hydroxy*-5 : 6-*dimethoxydibenzoylmethane* (IV) under the influence of sodamide in toluene, and ring-closure of (IV) to 5 : 6-*dimethoxyflavone* (V), about whose constitution there can be no ambiguity, was effected by heating with acetic acid and sodium acetate.

Demethylation of 5 : 6-dimethoxyflavone (V) by means of either hydrobromic acid in acetic acid or aluminium chloride in nitrobenzene gave a dihydroxyflavone which is regarded as 5 : 6-*dihydroxyflavone* (VI). Demethylation of (V) might conceivably give rise to 5 : 8-dihydroxyflavone (VIII) owing to opening of the pyrone ring and closure in the alternative direction; such an alteration of orientation during demethylation of flavone derivatives with hydriodic acid has been recorded by Shah, Mehta, and Wheeler (J., 1938, 1555; see also *Ann. Reports*, 1931, **28**, 149), but the alteration of orientation did not occur with aluminium chloride in nitrobenzene. Moreover, complete methylation of the supposed 5 : 6-dihydroxyflavone regenerates 5 : 6-dimethoxyflavone, and the double ring-change that would be involved if the dihydroxyflavone were the 5 : 8-dihydroxy-derivative is most improbable. Further reasons for believing that the dihydroxyflavone is correctly represented as 5 : 6-dihydroxyflavone (VI) are: (1) it gives a green colour with alcoholic ferric chloride which does not fade; (2) it gives an orange precipitate with lead acetate in alcoholic solution; (3) it is not oxidised to a quinone by means of either silver oxide or *p*-benzoquinone in alcoholic solution (cf. gossypetin, 5 : 7 : 8 : 3′ : 4′-pentahydroxyflavonol, which yields gossypetone with the latter reagent; Perkin, J., 1913, **103**, 657); (4) the sodium salt is extremely sparingly soluble in water; the 5-hydroxyl group in flavones does not generally yield a sodium salt in aqueous solution, and hence 5 : 6-dihydroxyflavone might be expected to behave towards aqueous alkalis like 6-hydroxyflavone, which yields an extremely sparingly soluble sodium salt in contrast with both 7- and 8-hydroxyflavone which dissolve easily in alkalis; (5) the orientation of the hydroxyl groups is analogous to that occurring in the synthesis of the tetrahydroxybenzene derivative quercetagetin (Baker, Nodzu, and Robinson, J., 1929, 76), where a similar alternative exists.

The foregoing facts establish beyond possibility of doubt that the demethylation of (V) yields 5 : 6-dihydroxyflavone (VI). The diacetyl derivative, which regenerates the same dihydroxyflavone on hydrolysis, must be 5 : 6-*diacetoxyflavone*, and the weakly phenolic monomethyl ether, prepared by partial demethylation of (V) with aluminium chloride in ether, and which regenerates (V) on methylation, must be 5-*hydroxy*-6-*methoxyflavone* (VII), and its acetyl derivative must be 5-*acetoxy*-6-*methoxyflavone*. 5 : 6-Dihydroxyflavone (VI) was also formed by heating 2 : 5-dihydroxy-6-methoxyacetophenone (II) with benzoic anhydride and sodium benzoate, followed by alkaline hydrolysis, demethylation having occurred during the process. Other cases are known where demethylation occurs during the production of flavones by the " fusion method " (see *Ann. Reports*, 1931, **28**, 149).

Reference must here be made to the work of Sugasawa (*loc. cit.*). This author hydrolysed the benzyl ether of (III) with hydrochloric acid in acetic acid and benzoylated the crude product, obtaining a hydroxymethoxyflavone, which, because it and its acetyl derivative differed from primetin monomethyl ether and its acetyl derivative, was assumed to be 5-hydroxy-8-methoxyflavone (monomethyl ether of VIII). These products are, however, identical with compound (VII) and its acetyl derivative described in this paper, and the demethylation observed by Sugasawa probably occurred during the benzoylation and not, as he suggested, during the debenzylation. Sugasawa further demethylated the hydroxymethoxyflavone to a product (not obtained pure or analysed) which was not identical with primetin and was therefore assumed to be 5 : 8-dihydroxyflavone (VIII). This product is, however, clearly identical with 5 : 6-dihydroxyflavone.

The non-identity of the 5 : 6-dihydroxyflavone and primetin necessitates a revision of the structure of the latter, unless the extremely unlikely assumption is made that primetin and its three derivatives described by Hattori and Nagai are all dimorphous. The close similarity in properties between primetin and 5 : 6-dihydroxyflavone (see Table below) might seem to render this view just possible, were it not for the fact that they differ in their behaviour towards aqueous sodium hydroxide, and their monomethyl ethers show differing ferric chloride reactions.

It may be assumed with some certainty that primetin is a dihydroxyflavone as distinct from a hydroxyflavonol. Both 6- and 7-hydroxyflavonol are known substances and may be excluded, and the remaining alternatives, 5- and 8-hydroxyflavonols, would yield resorcinol and catechol respectively on alkaline hydrolysis, and both these products should have been easily recognisable. The inability to isolate a definite phenol strongly indicates that primetin is a derivative of either hydroxyquinol or pyrogallol, and the latter alternative is ruled out by other considerations (see below). The following Table gives the chief properties of primetin, 5 : 6-, 6 : 7-, and 7 : 8-dihydroxyflavones and of their corresponding derivatives (primetin is known to differ from 5 : 7-dihydroxyflavone, chrysin, which is not included in the Table). The unknown dihydroxyflavones fulfilling the above condition are the 6 : 8- and 5 : 8-dihydroxy-derivatives.

	Description.	M. p.	Aqueous NaOH.	Alcoholic $FeCl_3$.	Conc. H_2SO_4.
Primetin	Ochre-yellow prisms [1]	230—231°	Red solution	Green	Yellow solution, no fluorescence.
,, diacetate	Needles	189	—	—	—
,, monomethyl ether	Sulphur-yellow needles	210—211	Insoluble	Brown-violet	—
Primetin monomethyl ether acetate	Needles	175—176	—	—	—
5 : 6-Dihydroxyflavone	Honey-yellow needles	189—190	Crystals coloured dark red. Insoluble	Olive-green	Yellow solution, no fluorescence.
5 : 6-Dihydroxyflavone diacetate	Thin, flaky prisms	164	—	—	—
5 : 6-Dihydroxyflavone 6-monomethyl ether	Yellow needles or thin plates	129	Insoluble	Intense bluish-green	—
5 : 6-Dihydroxyflavone 6-monomethyl ether acetate	Flat prisms	149	—	—	—
6 : 7-Dihydroxyflavone [2]	Cream-coloured needles	254	Bright yellow solution	Intense green	Colourless solution, no fluorescence.
6 : 7-Dihydroxyflavone diacetate	Needles	201	—	—	—
7 : 8-Dihydroxyflavone [3]	Yellow, rhombic prisms [1]	243 [4]	Bright orange-red solution	Intense olive-green	Yellow solution, no fluorescence.[5]
7 : 8-Dihydroxyflavone diacetate	Needles	198 [6]	—	—	—
7 : 8-Dihydroxyflavone 7-monomethyl ether	Pale, honey-yellow prisms	227	Bright yellow solution	Pale apple-green	—
7 : 8-Dihydroxyflavone 7-monomethyl ether acetate	Yellow needles	227	—	—	—

[1] From methyl alcohol; see experimental section.

[2] Reigrodski and Tambor, *Ber.*, 1910, **43**, 1966; Hattori, *Acta Phytochim.*, 1932, **6**, 131; Chadha and Venkataraman, J., 1933, 1073.

[3] Woker, Kostanecki, and Tambor, *Ber.*, 1903, **36**, 4242; Venkataraman, J., 1929, 2222; Baker, J., 1933, 1387; Seka and Prosche, *Monatsh.*, 1936, **69**, 284.

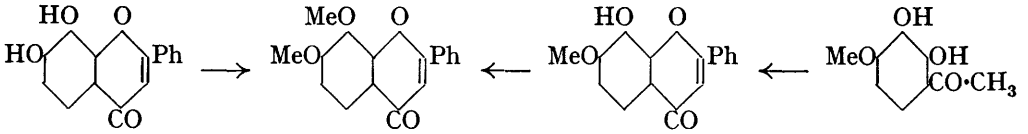
[4] Rapid heating; the m. p. varies according to the rate of heating.

[5] Venkataraman reports a green fluorescence, but this is not apparent in daylight.

[6] Baker. Other recorded m. p.'s are 193° and 194°.

It is clear that primetin can be neither 5 : 6- nor 6 : 7-dihydroxyflavone, but it shows a remarkable resemblance to 7 : 8-dihydroxyflavone (IX). It has been found, however, that 7 : 8-dihydroxyflavone does not yield a monomethyl but a dimethyl ether under the conditions of formation of primetin monomethyl ether, and that the most likely monomethylation product of 7 : 8-dihydroxyflavone, namely 8-*hydroxy*-7-*methoxyflavone* (XI), which was prepared synthetically, differs widely from primetin monomethyl ether. If the formation of the feebly phenolic primetin monomethyl ether is to be interpreted as meaning that it possesses a hydroxyl group in position 5, then primetin can only be 5 : 8-dihydroxyflavone (VIII). Although a green ferric chloride reaction is usually indicative of vicinal hydroxyl groups, it is probable that 5 : 8-dihydroxyflavone would give such a reaction,

since 2 : 5-dihydroxy-6-methoxyacetophenone (II) gives a fairly stable deep olive-green colour with alcoholic ferric chloride.



(IX.) (XII.) (XI.) (X.)

In the author's opinion primetin is, therefore, to be regarded as 5 : 8-dihydroxyflavone (VIII), and the synthesis of this compound is in progress. It seems probable that another 5 : 8-dihydroxyflavone occurs in Nature. This was isolated from the leaves of *Ginkgo biloba*, L., by Furukawa (*Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1932, **19**, 27, 39; 1933, **21**, 278) and is believed to be 5 : 8-dihydroxy-4'-methoxyflavone. It shows a close resemblance to primetin.

The 8-hydroxy-7-methoxyflavone (XI) was prepared from 2 : 3-dihydroxy-4-methoxyacetophenone (X) by fusion with benzoic anhydride and sodium benzoate, followed by alkaline hydrolysis, and purified *via* its *acetyl* derivative. Methylation of (XI) by means of methyl sulphate and alkali gave 7 : 8-dimethoxyflavone (XII), identical with that prepared by the methylation of 7 : 8-dihydroxyflavone with either methyl sulphate or diazomethane.

Experimental.

2-Hydroxy-6-methoxyacetophenone (I).—This compound was isolated by Limaye and Gangal (*Rasayanam*, **1936**, **1**, 65) as a by-product in about 20% yield in the preparation of the dimethyl ether of 2 : 6-dihydroxyacetophenone. It is conveniently prepared as follows. 2 : 6-Dihydroxyacetophenone (Baker, *loc. cit.*) (30·4 g.), benzene (300 c.c.), anhydrous potassium carbonate (60 g.), and methyl sulphate (26·4 g.; 1·05 mols.) were refluxed for 12 hours, water (500 c.c.) added to the hot mixture, and the whole filtered. The benzene layer was shaken with a solution of sodium hydroxide (20 g.) in water (200 c.c.); the aqueous solution on acidification deposited the desired methyl ether (23·5 g.). After crystallisation from methyl alcohol it formed almost colourless, fine prisms, m. p. 60° (Found: C, 65·1; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·0%).

2 : 5-Dihydroxy-6-methoxyacetophenone (II).—To a stirred solution of 2-hydroxy-6-methoxyacetophenone (25 g.) in water (300 c.c.) containing sodium hydroxide (30 g.) was added dropwise during 4 hours a solution of potassium persulphate (40·5 g.; 1 mol.) in water (800 c.c.), the temperature being maintained at 15—20°. After 24 hours the solution was acidified to Congo-red by the addition of concentrated hydrochloric acid, and the liquid filtered from the precipitate of unchanged 2-hydroxy-6-methoxyacetophenone (4 g.) and heated for 1 hour on the steam-bath with the addition of concentrated hydrochloric acid (200 c.c.). The hot liquid was treated with charcoal, filtered, and cooled; after several hours the brownish-yellow 2 : 5-*dihydroxy-6-methoxyacetophenone* was collected, washed and dried (5 g.), and a further quantity (4 g.) was obtained by extracting the mother-liquor twice with ether, distilling and crystallising from water (charcoal). For analysis the compound was crystallised from light petroleum (b. p. 60—80°) and then from water; it formed long, yellow prisms, m. p. 90° (Found: C, 59·3; H, 5·2. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5%). Addition of ferric chloride to its alcoholic solution gives a deep olive-green coloration, which turns brownish in ¼ hour; the solution in sodium hydroxide is at first bright yellow, turning brownish, and that in concentrated sulphuric acid is orange-yellow.

2 : 3 : 6-Trimethoxyacetophenone.—Methylation of the preceding compound (II) with a large excess of methyl sulphate and aqueous potassium hydroxide in coal gas gave 2 : 3 : 6-*trimethoxyacetophenone*, which, after twice crystallising from light petroleum (b. p. 40—60°), formed silky needles, m. p. 41·5° (Found: C, 63·1; H, 6·9. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

2 : 5-Dibenzoyloxy-6-methoxyacetophenone.—Compound (II) (2·0 g.), pyridine (3 c.c.), and benzoyl chloride (3·1 g.; 2 mols.) were heated on the steam-bath for ¼ hour and shaken with dilute hydrochloric acid, and the resulting solid *dibenzoyl* derivative (4·3 g.) was crystallised twice from alcohol. It formed prismatic needles, m. p. 151—152° (Found: C, 70·8; H, 4·6. $C_{23}H_{18}O_6$ requires C, 70·8; H, 4·6%).

5 : 6-Dihydroxyflavone (VI.)—A mixture of 2 : 5-dihydroxy-6-methoxyacetophenone (II) (2 g.), benzoic anhydride (30 g.), and sodium benzoate (4 g.) was stirred at 190—200° for 4 hours,

a further quantity of sodium benzoate (1 g.) added, and heating and stirring continued for 10 hours. The product was hydrolysed by heating on the water-bath for 20 minutes with alcohol (80 c.c.), water (16 c.c.), and a solution of potassium hydroxide (25 g.) in water (25 c.c.), most of the alcohol being allowed to distil away, and the solution obtained on dilution with water (200 c.c.) was saturated with carbon dioxide. The precipitated phenolic material (1·5 g.) was crystallised from 50% acetic acid (charcoal) and then from alcohol, being obtained in honey-yellow, prismatic needles (0·4 g.), m. p. 189—190° (Found: C, 70·9; H, 4·1; OMe, 0·0. $C_{15}H_{10}O_4$ requires C, 70·9; H, 3·9%) (Sugasawa described the substance as "grains" from alcohol, m. p. 189—190°; it was not characterised). **5 : 6-*Dihydroxyflavone*** becomes converted into a dark red sodium salt on the addition of aqueous sodium hydroxide, but does not dissolve appreciably even on heating. With alcoholic ferric chloride it develops an intense olive-green colour. The solution in concentrated sulphuric acid is yellow and exhibits no fluorescence. Addition of a solution of lead acetate to its alcoholic solution gives an orange, gelatinous precipitate. The *diacetyl* derivative, prepared by boiling with acetic anhydride and sodium acetate for 2 hours and then shaking with water, separates from alcohol in thin, flaky prisms, frequently exhibiting lateral growths, m. p. 164° (Found: C, 67·4; H, 4·2. $C_{19}H_{14}O_6$ requires C, 67·4; H, 4·1%).

2-*Hydroxy*-5 : 6-*dimethoxyacetophenone* (III).—Compound (II) (1·8 g.), benzene (20 c.c.), anhydrous potassium carbonate (5 g.), and methyl sulphate (1·3 g.) were boiled for 8 hours; water and dilute hydrochloric acid were then added, and the mixture steam-distilled. The steam-distillate yielded to ether **2-*hydroxy*-5 : 6-*dimethoxyacetophenone*** (1·3 g.) as a bright yellow oil, b. p. 162—163°/22 mm. (Found: C, 61·3; H, 6·2. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%). Its alcoholic or dilute alcoholic solution gives an intense greenish-blue ferric chloride reaction; it dissolves in aqueous sodium hydroxide with a yellow colour, and in concentrated sulphuric acid with a bright orange colour. Sugasawa obtained this compound in the crude state as a brown, viscous oil.

2-*Benzoyloxy*-5 : 6-*dimethoxyacetophenone*.—2-Hydroxy-5 : 6-dimethoxyacetophenone (III) (1·18 g.) in pyridine (4 c.c.) was heated on the water-bath for ½ hour with benzoyl chloride (0·85 g.; 1 mol.) and the solid obtained by shaking the product with dilute hydrochloric acid was crystallised from alcohol, from which it separated in colourless, thick, rhombic plates or prisms (1·3 g.), m. p. 87° (Found: C, 68·3; H, 5·6. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

2-*Hydroxy*-5 : 6-*dimethoxydibenzoylmethane* (IV).—The preceding benzoyl compound (1 g.) was added to sodamide (2 g.) finely powdered under toluene (20 c.c.) and the mixture, which rapidly became yellow, was heated on the water-bath for 5 hours with occasional shaking. The solid was collected, washed well with benzene, dried, stirred slowly into water and ice (unchanged sodamide!), and the resulting solution saturated with carbon dioxide. The orange-yellow precipitate was collected, washed, dried (yield 0·75 g.), and crystallised from light petroleum (b. p. 60—80°). **2-*Hydroxy*-5 : 6-*dimethoxydibenzoylmethane*** forms bright orange-yellow, flaky crystals, m. p. 87° (Found: C, 67·8; H, 5·6. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). The alcoholic solution gives a reddish-brown colour with ferric chloride, and it dissolves in aqueous sodium hydroxide with a pure yellow colour. The crystals are coloured red on the addition of concentrated sulphuric acid and rapidly dissolve to a yellow solution with conversion into 5 : 6-dimethoxyflavone.

5 : 6-*Dimethoxyflavone* (V).—(a) Compound (IV) (0·75 g.), acetic acid (10 c.c.), and anhydrous sodium acetate (1 g.) were heated on the water-bath for 4 hours, water added, and the solid (0·64 g.) collected, washed, and crystallised from alcohol. **5 : 6-*Dimethoxyflavone*** separated in colourless, thin, four-sided plates, m. p. 196° (Found: C, 72·4; H, 5·1. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%). It is insoluble in boiling aqueous sodium hydroxide, and gives no coloration with ferric chloride in alcoholic solution. Its solution in concentrated sulphuric acid is yellow.

(b) 5 : 6-Dihydroxyflavone, dissolved in acetone, was refluxed for 6 hours with a large excess of methyl sulphate and anhydrous potassium carbonate. The solid obtained on dilution with much water was collected and crystallised from alcohol; it formed plates, m. p. and mixed m. p. 196°. Yield, almost quantitative.

(c) 5-Hydroxy-6-methoxyflavone (VII) (below), when treated as under (b), gave **5 : 6-**dimethoxyflavone, m. p. and mixed m. p. 196°.

Demethylation of **5 : 6-*Dimethoxyflavone*** (V).—(a) *Production of* **5 : 6-*dihydroxyflavone*** (VI). **5 : 6-**Dimethoxyflavone (V) (0·5 g.) was refluxed for 8 hours with acetic acid (2·5 c.c.) and hydrobromic acid (*d* 1·5; 2·5 c.c.), water added, and the precipitated solid collected, washed, dried (0·38 g.), and crystallised from 50% acetic acid (30 c.c.) (charcoal). Yellow needles separated, m. p. 189—190° either alone or in admixture with the specimen of **5 : 6-**dihydroxyflavone previously described. The diacetyl derivative had m. p. and mixed m. p. 164°.

Demethylation to the same compound was also effected by means of a solution of aluminium chloride in nitrobenzene at 100° for 4 hours.

(b) *Production of 5-hydroxy-6-methoxyflavone* (VII). 5 : 6-Dimethoxyflavone (2 g.) was dissolved in a solution of anhydrous aluminium chloride (20 g.) in dry ether (80 c.c.), and the mixture refluxed on the steam-bath for 18 hours. Water was added and the orange precipitate, which appeared to be an aluminium complex, was collected and decomposed by boiling for several minutes with acetic acid (50 c.c.) containing concentrated hydrochloric acid (20 c.c.). The yellow solid (1·7 g.) obtained by dilution with water was crystallised from dilute and then absolute alcohol; it appeared to be dimorphous and separated in long, amber-yellow, prismatic needles or in centimetre-long, thin, flat prisms, m. p. 128—129° (Found : C, 71·5; H, 4·5. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). It gives an intense bluish-green coloration with alcoholic ferric chloride. It is unchanged on addition of cold dilute sodium hydroxide solution, but the crystals become covered with an almost insoluble orange sodium salt on boiling. The acetyl derivative, prepared by the action of acetic anhydride and anhydrous sodium acetate at 100° for 4 hours, separated from alcohol in flat, colourless prisms, m. p. 149°. Sugasawa describes these compounds as " bright yellow leaflets, or long, hairy needles, m. p. 129—130°," and " very pale-yellow prisms, m. p. 146—147°," respectively. Compound (VII) was also prepared by the partial methylation of 5 : 6-dihydroxyflavone by shaking with a hot, dilute alcoholic solution of potassium hydroxide and a large excess of methyl sulphate, collecting the orange alkali salt of (VII) which separated and decomposing it with hydrochloric acid.

7 : 8-*Dihydroxyflavone* (IX).—A specimen was prepared according to the directions of Baker (J., 1933, 1387). The substance is dimorphous; from ethyl alcohol it separates in labile, faintly greyish-yellow, prismatic needles (cf. descriptions given by Venkataraman, and by Woker, Kostanecki, and Tambor, *locc. cit.*), which, on standing in the mother-liquor at room temperature, are slowly (4—5 days) converted into the yellow, flattened, rhombic prisms of the stable form. The change takes place rapidly (1 minute) when the labile form is covered with cold methyl alcohol. Neither form appears to contain solvent of crystallisation. 7 : 8-Dihydroxyflavone dissolves in aqueous sodium carbonate with a yellow colour, and in aqueous sodium hydroxide with an orange-red colour. The red solution fades to yellow on considerable dilution. Woker, Kostanecki, and Tambor state that it dissolves in alkalis with a yellow colour, whilst Venkataraman states that the solution in aqueous sodium hydroxide is orange-yellow. Its methyl-alcoholic solution when treated with excess of ethereal diazomethane, or methyl sulphate and alkali, gave directly the dimethyl ether, m. p. 150°; no monomethyl ether was isolated.

2 : 3-*Dihydroxy-4-methoxyacetophenone* (X).—Pyrogallol 1-monomethyl ether (10 g.) in acetic acid (80 c.c.) and coarsely crushed, anhydrous zinc chloride (100 g.) were boiled for 10 minutes, some of the acetic acid being allowed to escape, and then poured into water (350 c.c.). After some hours the solid was collected, washed, and dried (yield, 8 g.) (cf. Baker, Jukes, and Subrahmanyam, J., 1934, 1683).

8-*Hydroxy-7-methoxyflavone* (XI).—The preceding compound (5 g.), benzoic anhydride (50 g.), and sodium benzoate (5 g.) were stirred and heated in an oil-bath at 180—185° for 2 hours, a further quantity of sodium benzoate (2·5 g.) added, and heating continued for 6 hours. The product was now boiled with alcohol (200 c.c.), a solution of potassium hydroxide (35 g.) in water (100 c.c.) added, and the mixture boiled on the water-bath for ½ hour, diluted with much water, and saturated with carbon dioxide. The dark product was collected, washed with water and then cold methyl alcohol (yield, 2 g.), and acetylated by boiling for 3 hours with acetic anhydride (15 c.c.) containing a few drops of pyridine. The yellow, crystalline *acetyl* derivative which separated on cooling was collected, washed with cold acetic anhydride and then alcohol, and crystallised from alcohol, in which it was very sparingly soluble. It separated in long, yellow, prismatic needles (0·8 g.), m. p. 227° (Found : C, 69·7; H, 4·4. $C_{18}H_{14}O_5$ requires C, 69·7; H, 4·5%). Hydrolysis (of 0·5 g.) was effected by heating on the water-bath for 10 minutes with alcohol (10 c.c.), potassium hydroxide (1 g.), and water (5 c.c.), diluting and acidifying. 8-*Hydroxy-7-methoxyflavone* separated from slightly diluted alcohol in pale honey-yellow prisms, which, owing to twinning, frequently formed bunches resembling sheaves of corn. It had m. p. 227° (mixed m. p. with the acetyl derivative, 190—210°) (Found : C, 71·6; H, 4·6. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). It dissolves in dilute sodium hydroxide solution with a bright yellow colour, and it gives a pale apple-green ferric chloride reaction in alcoholic solution. Treatment with methyl sulphate and alkali in dilute alcoholic solution readily gave 7 : 8-dimethoxyflavone, m. p. and mixed m. p. 150°.

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