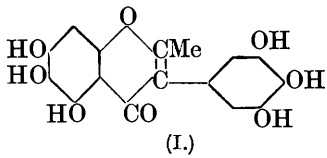
XXII.—*Synthetical Experiments in the* iso*Flavone Group. Part IV. A Synthesis of 2-Methylirigenol.*

By WILSON BAKER and ROBERT ROBINSON.

IRIGENOL, obtained by the demethylation of irigenin (de Laire and Tiemann, *Ber.*, 1893, **26**, 2010), has recently been proved to be 5 : 6 : 7 : 3′ : 4′ : 5′-hexahydroxy*iso*flavone (Baker, J., 1928, 1022). The synthesis of *2-methylirigenol* (I) is now described and a comparison of this substance with irigenol itself fully substantiates the correctness of the previous work. This paper is, therefore, Part IV

of the series *Synthetical Experiments in the* iso*Flavone Group* and also Part II of *The Constitution of Irigenin and Iridin.*

The synthesis was carried out by methods which have been used to prepare other 2-substituted *iso*flavones (Baker and Robinson, Part I, J., 1925, **127**, 1981; Part II, 1926, 2713; Part III, 1928, 3115), the starting materials being 4 : 5-dimethoxyresorcinol (II) and 3 : 4 : 5-*trimethoxyphenylacetonitrile* (III).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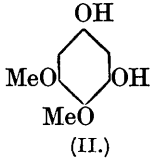
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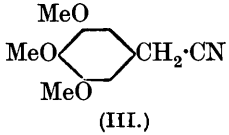
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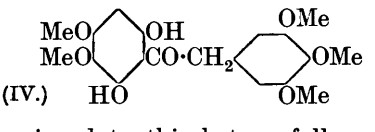
4 : 5-Dimethoxyresorcinol (II) has recently been obtained by hydrolysis of irigenin 5 : 3′- and 7 : 3′-dimethyl ethers (Baker, *loc. cit.*), and has been synthesised by Chapman, Perkin, and Robinson (J., 1927, 3015) from 4 : 6-dinitroguaiacol through 3 : 5(4 : 6)-dinitroveratrole and 3 : 5(4 : 6)-diaminoveratrole. The tedious processes involved in the preparation of (II) have been somewhat simplified by the observation that 4 : 6-dinitroguaiacol can be obtained in excellent yield by the direct nitration of guaiacol in ethereal solution with nitrous fumes. The nitrile (III) was prepared from 3 : 4 : 5-trimethoxybenzaldehyde, which was itself obtained by the reduction of the corresponding acid chloride in boiling xylene solution with hydrogen in the presence of palladinised barium sulphate, an application of Rosenmund's method (*Ber.*, 1918, **51**, 585, 591). Condensation of the aldehyde with hippuric acid, followed by alkaline hydrolysis of the azlactone, gave 3 : 4 : 5-trimethoxyphenylpyruvic acid, the oxime of which when heated with acetic anhydride gave (III).

Condensation of (II) and (III) under the conditions of the Hoesch synthesis gave as the only product 2 : 6-*dihydroxy*-3 : 4-*dimethoxyphenyl* 3 : 4 : 5-*trimethoxybenzyl ketone* (IV). The constitution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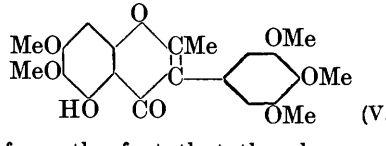
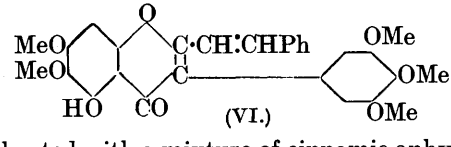

(V.)

assigned to this ketone follows from the fact that the chromone produced by boiling it with a mixture of acetic anhydride and sodium acetate and then hydrolysing the acetoxy-group has the properties of a 5- and not a 7-hydroxy-derivative. Its phenolic function is very weak and its behaviour with ferric chloride leaves no doubt that the free hydroxyl group occupies position 5. This

reactivity of 4 : 5-dimethoxyresorcinol in position 2 has already been observed in the preparation of 2 : 6-dihydroxy-ω : 3 : 4-trimethoxyacetophenone by its condensation with methoxyacetonitrile (Baker, Nodzu, and Robinson, this vol., p. 74). The direction of ring closure was established by methylating the free hydroxyl group by vigorous treatment with methyl sulphate and decomposing the product with alkali; antiarol (3 : 4 : 5-trimethoxyphenol) and 3 : 4 : 5-trimethoxyphenylacetic acid were then obtained. The methylated chromone was therefore 5 : 6 : 7 : 3′ : 4′ : 5′-*hexamethoxy*-2-*methyl*isoflavone (2-*methylirigenin trimethyl ether*), and the deacetylated product of the ring closure was 5-*hydroxy*-6 : 7 : 3′ : 4′ : 5′-*pentamethoxy*-2-*methyl*isoflavone (2-*methylirigenin* 7 : 3′-*dimethyl ether*) (V). It appears to be a general rule that when a derivative of 1 : 2 : 3 : 5-tetrahydroxybenzene undergoes ring closure, it is the hydroxyl group in position 5 which is concerned. For instance, Bargellini (*Gazzetta*, 1919, **49**, 47), by heating 2 : 3 : 4 : 6-tetramethoxyphenyl phenacyl ketone with hydriodic acid, obtained 5 : 6 : 7-trihydroxyflavone or, by heating for a short time only, 5 : 6 : 7-trimethoxyflavone, and in a similar manner (*ibid.*, 1915, **45**, 69) 2 : 3 : 4 : 6-tetramethoxyphenyl *p*-methoxyphenacyl ketone gave only 5 : 6 : 7 : 4′-tetrahydroxyflavone (scutellarein). Again, Chapman, Perkin, and Robinson (*loc. cit.*) showed that iretol yielded pyrylium salts having hydroxyl groups in positions 5, 6, and 7, and finally 2 : 6-dihydroxy-ω : 3 : 4-trimethoxyacetophenone, when heated with veratric anhydride and sodium veratrate, gave quercetagetin pentamethyl ether (Baker, Nodzu, and Robinson, *loc. cit.*).

Demethylation of (V) gave 5 : 6 : 7 : 3′ : 4′ : 5′-*hexahydroxy*-2-*methyl*isoflavone (2-*methylirigenol*) (I). In its appearance, reactions with alkali, ferric chloride, etc., it is indistinguishable from irigenol and, as a dye, the colours produced on wool mordanted with aluminium, tin, chromium, and iron are identical with those given by irigenol. (The dyeing properties of 2-methylgenistein—not previously recorded—are identical with those of genistein itself.)

With the object of synthesising irigenin trimethyl ether by the methods previously used (Parts I, II, and III), the ketone (IV) was



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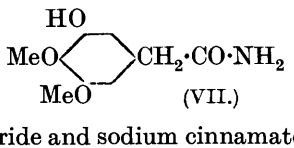

(VII.)

heated with a mixture of cinnamic anhydride and sodium cinnamate, giving 5-*hydroxy*-6 : 7 : 3′ : 4′ : 5′-*pentamethoxy*-2-*styryl*isoflavone (VI).

The methyl ether of this compound could not be successfully oxidised in pyridine solution with potassium permanganate to a substituted *iso*flavone-2-carboxylic acid, but the labour involved in its preparation prevented the experiment from being carried out on as large a scale as was desirable.

Iridamide (3-*hydroxy*-4 : 5-*dimethoxyphenylacetamide*) (VII) was prepared by the action of aqueous ammonia upon methyl iridate. Attempts to bring about direct dehydration to the nitrile were unsuccessful.

The Reactivity of Some Phenolic Ethers.

The persistent reactivity of 4 : 5-dimethoxyresorcinol in position 2 has led to the investigation of the reactive centres of other phenolic ethers under parallel conditions.

Resorcinol monomethyl ether was found by Gattermann (*Annalen*, 1907, **357**, 346) to give only 4-hydroxy-2-methoxybenzaldehyde, and Hoesch (*Ber.*, 1915, **48**, 1122) found that by the action of acetonitrile it gave about equal quantities of the two isomeric ketones pæonol and *iso*pæonol. It has now been found that the Hoesch synthesis with phenylacetonitrile gives approximately 3 parts of 2-hydroxy-4-methoxyphenyl benzyl ketone to 1 part of 4-*hydroxy*-2-*methoxyphenyl benzyl ketone*, the orientation of the first being established by ring closure with sodium acetate and acetic anhydride to 7-methoxy-2-methyl*iso*flavone. It has usually been found that this closure could not be effected with derivatives of pæonol (Crabtree and Robinson, J., 1918, **113**, 864; Baker and Robinson, J., 1925, **127**, 1430), but it appears that the reaction takes place if a large excess of the reagents is used and sufficient time is allowed (compare Nagai, *Ber.*, 1892, **25**, 1284; Kostanecki and Rózycki, *Ber.*, 1901, **34**, 102).

Phloroglucinol monomethyl ether yields an aldehyde by Gattermann's reaction (Herzig and Wenzel, *Monatsh.*, 1903, **24**, 857) shown by Pratt and Robinson (J., 1924, **125**, 188) to be 2 : 4-dihydroxy-6-methoxybenzaldehyde. The Hoesch reaction with *n*-butyronitrile (Karrer, *Helv. Chim. Acta*, 1919, **2**, 466) gives a mixture of 2 : 4-dihydroxy-6-methoxyphenyl *n*-propyl ketone and 2 : 6-dihydroxy-4-methoxyphenyl *n*-propyl ketone, and benzonitrile (*idem*, *ibid.*, p. 486) gives only 2 : 4-dihydroxy-6-methoxybenzophenone (*iso*cotoin).

Orcinol monomethyl ether was found by Gattermann (*loc. cit.*) to give only 4-hydroxy-2-methoxy-6-methylbenzaldehyde, this orientation being confirmed by Hirst (J., 1927, 2490), and Hoesch (*loc. cit.*) prepared from it by the action of acetonitrile a mixture of the 2-methyl ether of orcacetophenone and a slightly smaller

amount of the corresponding 4-methyl ether. The Hoesch reaction with phenylacetonitrile (this paper) gives chiefly 4-*hydroxy*-2-*methoxy*-6-*methylphenyl benzyl ketone* and about one-sixth the amount of 2-*hydroxy*-4-*methoxy*-6-*methylphenyl benzyl ketone*. The orientation of the last substance was established by conversion into 7-*methoxy*-2 : 5-*dimethyl*iso*flavone*.

EXPERIMENTAL.

4 : 6-*Dinitroguaiacol*.—A mixture of concentrated hydrochloric acid (425 c.c.) and water (425 c.c.) was gradually added during several hours to a solution of sodium nitrite (250 g.) n water (1 l.) underlying one of guaiacol (50 g.) in ether (750 c.c.) (compare dinitration of *iso*creosol; Graesser-Thomas, Gulland, and Robinson, J., 1926, 1973). After 12 hours, the ether was removed in a current of air, leaving dinitroguaiacol, m. p. 119—121·5° (47 g.).

3 : 5(4 : 6)-*Dinitroveratrole*.—Methyl sulphate (150 g., redistilled) was added to a constantly stirred mixture of 4 : 6-dinitroguaiacol (50 g.), potassium carbonate (75 g.), and xylene (25 c.c.) heated for 2 hours at 130°. Water (500 c.c.) was added, the xylene distilled off, and the hot solution rendered alkaline by sodium hydroxide and cooled while being shaken (yield, 55 g.; m. p. 99—100°).

3 : 5(4 : 6)-*Diaminoveratrole and* 4 : 5-*Dimethoxyresorcinol* (II) (see Chapman, Perkin, and Robinson, *loc. cit.*).—3 : 5-*Diaminoveratrole* crystallises from alcohol in colourless, approximately octahedral crystals, m. p. 106° (Found: C, 57·1; H, 7·3; N, 16·8. $C_8H_{12}O_2N_2$ requires C, 57·1; H, 7·2; N, 16·7%). It is readily soluble in water; the solution darkens on keeping and gives a reddish-brown coloration with nitrous acid. The dimethoxyresorcinol is best obtained, after the hydrolysis, by extraction with chloroform and is then crystallised directly from a little water (charcoal), large prisms of the monohydrate, m. p. 74°, separating. By heating to 100° it melts and then solidifies to the anhydrous substance, m. p. 115°. Yield from 30 g. of dinitroveratrole, about 5 g. The unhydrolysed diamine may be recovered by concentration and hydrolysed as before.

3 : 4 : 5-*Trimethoxybenzaldehyde*.—This substance was first prepared by Stephen's method (J., 1925, **127**, 1874), but the process is tedious and not suitable for the preparation of the aldehyde in quantity, the yields being only about 10—20% from the nitrile.

3 : 4 : 5-Trimethoxybenzoyl chloride (25 g.) in dry xylene (100 c.c.) was reduced at the boiling point in the presence of palladinised barium sulphate (5 g.; *Ber.*, 1919, **52**, 409) by a slow stream of pure hydrogen for 6 hours (see Rosenmund, *loc. cit.*). Evolution of hydrogen chloride ceased in about 5 hours. The filtered liquor

was shaken with saturated sodium bisulphite solution (45 c.c.) and the solid bisulphite compound was filtered off, washed with ether, and decomposed with hydrochloric acid, yielding the pure aldehyde, m. p. 74—75° (10—11 g.).

3 : 4 : 5-*Trimethoxyphenylpyruvic Acid.*—The condensation of the foregoing aldehyde with hippuric acid, the hydrolysis to the substituted pyruvic acid, and the preparation of its oxime have been described by Mauthner (*Ber.*, 1908, **41**, 3662), who, however, worked with very small quantities. Since, moreover, difficulty was experienced with the initial condensation and the subsequent steps proved to be unnecessarily tedious, the simpler methods used in this investigation are recorded.

3 : 4 : 5-Trimethoxybenzaldehyde (15 g.), hippuric acid (22·5 g.), and anhydrous sodium acetate (7·5 g.) were finely ground and heated in a boiling water-bath with acetic anhydride (40 c.c.) for 6 minutes while being constantly stirred; the bright yellow, crystalline precipitate at first produced just dissolved. Alcohol (10 c.c.) was added to the cooled mixture and the azlactone was collected and washed with alcohol and with hot water (average yield, 17 g.). The azlactone (30 g.) was boiled with a solution of sodium hydroxide (15 g.) in water (90 c.c.) for 1 hour, water (100 c.c.) was added, the solution saturated with sulphur dioxide (compare Haworth, Perkin, and Rankine, J., 1924, **125**, 1693), and after a few hours the benzoic acid was filtered off. The filtrate was heated on the water-bath with excess of hydrochloric acid for 1 hour; 3 : 4 : 5-trimethoxyphenylpyruvic acid (16—17 g.) was then deposited. The quinoxaline derivative (Mauthner, *loc. cit.*), prepared by condensation with *o*-phenylenediamine, crystallised from alcohol in tiny needles, m. p. 196—197°, containing $\frac{1}{2}$EtOH (Found in material dried at 100°: N, 8·0. Found in material dried at 130°: N, 8·5. Calc. for $C_{18}H_{18}O_4N_2,\frac{1}{2}$EtOH: N, 8·0%. Calc. for $C_{18}H_{18}O_4N_2$: N, 8·6%).

3 : 4 : 5-*Trimethoxyphenylacetonitrile* (III).—3 : 4 : 5-Trimethoxyphenylpyruvic acid (10 g.) and hydroxylamine hydrochloride (8 g.) dissolved in aqueous sodium hydroxide (100 c.c.; 8%) were warmed at 50° for a few minutes. After 12 hours, addition of hydrochloric acid threw down the oxime as an oil which rapidly crystallised (10 g.). The dry oxime (10 g.) was heated with acetic anhydride (5 c.c.) on the steam-bath and when the vigorous reaction had abated (2—3 minutes) water (50 c.c.) was added and the mixture shaken. The product rapidly crystallised and was collected and washed with dilute sodium bicarbonate solution. 3 : 4 : 5-*Trimethoxyphenylacetonitrile* crystallises from benzene–ligroin or from carbon tetrachloride in irregular fern-like crystals, m. p. 77° (Found :

C, 63·6; H, 6·1; N, 6·8. $C_{11}H_{13}O_3N$ requires C, 63·7; H, 6·3; N, 6·8%). The corresponding 3 : 4 : 5-*trimethoxyphenylacetamide* was prepared by dissolving the nitrile (5 g.) in 95% sulphuric acid (25 c.c.) and after 24 hours pouring the solution on crushed ice and extracting the amide with chloroform. The extracts were shaken with a little saturated sodium bicarbonate solution and yielded a solid residue which crystallised from benzene in prismatic needles, m. p. 121° (Found : N, 6·2. $C_{11}H_{15}O_4N$ requires N, 6·2%).

2 : 6-*Dihydroxy*-3 : 4-*dimethoxyphenyl* 3 : 4 : 5-*Trimethoxybenzyl Ketone* (IV).—A solution of 3 : 4 : 5-trimethoxyphenylacetonitrile (2·1 g.) and anhydrous 4 : 5-dimethoxyresorcinol (1·8 g.) in dry ether (60 c.c.) was saturated with hydrogen chloride at 0° in presence of anhydrous zinc chloride (0·5 g.). After 12 hours, the ketimine was completely precipitated by the addition of dry ether (100 c.c.), washed with ether, and hydrolysed by boiling for ½ hour with dilute hydrochloric acid (50 c.c.). The ketone (2 g.) crystallised from methyl alcohol (charcoal) in tiny colourless prisms, m. p. 162° (Found : C, 60·1; H, 6·0. $C_{19}H_{22}O_8$ requires C, 60·3; H, 5·9%). No isomeric ketone could be detected in the mother-liquors. 2 : 6-*Dihydroxy*-3 : 4-*dimethoxyphenyl* 3 : 4 : 5-*trimethoxybenzyl ketone* gives pale yellow solutions in dilute alkalis and in concentrated sulphuric acid, and its alcoholic solution develops a dull greenish-violet colour with a trace of ferric chloride, changing to dull greyish-olive with excess.

5-*Hydroxy*-6 : 7 : 3′ : 4′ : 5′-*pentamethoxy*-2-*methyl*isoflavone (2-*Methylirigenin* 7 : 3′-*Dimethyl Ether*) (V).—The ketone (IV) (1·5 g.), anhydrous sodium acetate (1·5 g.), and acetic anhydride (10 c.c.) were heated at 180° for 6 hours. The homogeneous *acetyl* derivative, isolated by shaking the product with dilute hydrochloric acid, crystallised from alcohol in small colourless prisms, m. p. 232—233° (Found : C, 62·0; H, 5·6. $C_{23}H_{24}O_9$ requires C, 62·1; H, 5·5%). The parent substance was obtained by heating the acetyl derivative in alcohol for a few minutes with a little concentrated potassium hydroxide solution. Addition of water threw down tiny crystals which subsequently separated from alcohol in very pale yellow, silky needles, m. p. 179—180° (Found : C, 62·4; H, 5·6. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·5%). This substance (V) is quite insoluble in aqueous alkalis, but dissolves readily in alcoholic potassium hydroxide to a bright yellow solution. Its alcoholic solution gives an intense, dull violet colour with a trace of ferric chloride, changing to deep olive-green with excess. In these ways its behaviour resembles that of the corresponding irigenin 7 : 3′-dimethyl ether.

5 : 6 : 7 : 3′ : 4′ : 5′-*Hexamethoxy*-2-*methyl*isoflavone (2-*Methyliri*-

genin Trimethyl Ether).—The compound (V) was treated in boiling methyl-alcoholic solution with a large excess of methyl sulphate and methyl-alcoholic potassium hydroxide. Addition of water caused the precipitation of crystals, which were suspended in a little methyl alcohol and, after addition of a few drops of alkali to dissolve a trace of unmethylated substance, were collected and crystallised from methyl alcohol, giving small, colourless, lustrous prisms, m. p. 166° (Found: C, 63·3; H, 5·8. $C_{22}H_{24}O_8$ requires C, 63·4; H, 5·8%). Decomposition with concentrated alkali at 180° and isolation of the products as described in the case of irigenin trimethyl ether (Baker, *loc. cit.*) gave antiarol, m. p. 147°, and 3 : 4 : 5-trimethoxyphenylacetic acid, m. p. 120°.

5 : 6 : 7 : 3′ : 4′ : 5′-*Hexahydroxy*-2-*methyl*iso*flavone* (2-*Methyliri-genol*) (I).—Demethylation of (V) was effected by heating with 10 times its weight of hydriodic acid (*d* 1·7) at 130° for 1 hour. The product, isolated by the addition of water, crystallised from 50% acetic acid in tiny, glistening, yellow prisms, m. p. 325° (decomp., rapid heating) (Found: C, 53·3; H, 4·3; H_2O, 7·2. $C_{16}H_{12}O_8,1\frac{1}{2}H_2O$ requires C, 53·5; H, 4·2; H_2O, 7·5%). 2-*Methyl-irigenol* in its appearance and in its behaviour with alkali, ferric chloride, and sodium amalgam in alcoholic solution is indistinguishable from irigenol, but is rather more soluble in the usual organic solvents. Methylation with methyl sulphate in an atmosphere of hydrogen gave its hexamethyl ether, m. p. 166°, identical with the methyl ether of 5-hydroxy-6 : 7 : 3′ : 4′ : 5′-pentamethoxy-2-methyl-*iso*flavone.

5-*Hydroxy*-6 : 7 : 3′ : 4′ : 5′-*pentamethoxy*-2-*styryl*iso*flavone* (VI).—The cinnamoylation of the ketone (IV) was effected as described in Part II (*loc. cit.*) for the preparation of 5 : 7-dihydroxy-4′-methoxy-2-styryl*iso*flavone. After hydrolysis of the product with alcoholic potassium hydroxide and dilution, the substance was precipitated with carbon dioxide and successively crystallised from alcohol, acetic acid, and ethyl acetate, being obtained in tiny bright yellow needles, m. p. 270° (Found: C, 68·3; H, 5·6. $C_{28}H_{26}O_8$ requires C, 68·5; H, 5·4%). It is insoluble in aqueous alkalis and very sparingly soluble in alcohol; the solution, however, develops a brownish-green coloration with ferric chloride. The *methyl* ether was obtained by shaking an acetone solution with methyl sulphate and aqueous potassium hydroxide (compare methylation of 5-hydroxy-7 : 4′-dimethoxy-2-styryl*iso*flavone; Baker and Robinson, Part III, *loc. cit.*). The pale yellow product was suspended in methyl alcohol containing a little potassium hydroxide, collected, and crystallised repeatedly from methyl alcohol, being ultimately obtained in very pale yellow, hair-like needles, m. p. 214—215°.

It exhibits no colour with ferric chloride, and gives no alkali salt in acetone or other solvents.

Iridamide (VII).—The alkaline hydrolysis of irigenin (20 g.) gave pure iridic acid (5 g.) by the following modification of the method of de Laire and Tiemann (*loc. cit.*). To the acidified product, an equal volume of water and a little charcoal were added, and the solution was filtered, made alkaline by sodium hydroxide, saturated with carbon dioxide, extracted with ether, and again acidified. The iridic acid now obtained by extraction with ether crystallised from a little water in colourless prisms, m. p. 118°. The acid was converted into the methyl ester (5 g.; de Laire and Tiemann), which was dissolved in concentrated aqueous ammonia (*d* 0·880) and left in a closed vessel for 24 hours. The solution was evaporated, the dark sticky residue dissolved in warm alcohol, much ether added, and a dark flocculent precipitate removed by filtration. The filtrate yielded an oil which rapidly crystallised. This was dissolved in acetone, and benzene added to the hot solution, which was then treated with charcoal and filtered, and the acetone distilled off. On seeding, large, many-faced prisms slowly separated, which were again crystallised from a small quantity of water (charcoal), being thus obtained colourless and of m. p. 113° (Found: N, 6·7. $C_{10}H_{13}O_4N$ requires N, 6·6%). *Iridamide* is sparingly soluble in benzene and ether and easily soluble in alcohol and acetone. In aqueous solution it gives a weak green coloration with ferric chloride and is exceedingly readily hydrolysed to iridic acid.

Condensation of Phenylacetonitrile with Resorcinol Monomethyl Ether.—A solution of the nitrile (15 g.) and resorcinol monomethyl ether (15 g.) in ether (150 c.c.) was saturated with hydrogen chloride at 0° in presence of anhydrous zinc chloride (2·5 g.). After 48 hours, water was added and the excess of phenylacetonitrile removed in steam. The mixed ketones were dissolved in ether and shaken twice with excess of 1% aqueous sodium hydroxide. The ethereal layer yielded a residue (6·7 g.) of almost pure 2-hydroxy-4-methoxyphenyl benzyl ketone, m. p. 90° (see Tambor, *Ber.*, 1910, **43**, 1884). This compound is insoluble in cold dilute alkaline solutions, and its alcoholic solution becomes red on the addition of ferric chloride. The constitution assigned to this substance by Tambor (*loc. cit.*) was confirmed by heating it for 18 hours at 180° with a large excess of acetic anhydride and about 5 times its weight of sodium acetate; it then yielded 7-methoxy-2-methyl*iso*flavone, m. p. 135·5°, identical with that prepared by the methylation of 7-hydroxy-2-methyl*iso*flavone (Part I, *loc. cit.*).

The 1% sodium hydroxide washings were acidified and extracted

with ether, and the extract was dried and distilled, yielding resorcinol monomethyl ether, b. p. 152°/20 mm., and a fraction, b. p. 260—265°/13 mm., which rapidly solidified and then crystallised from ether–ligroin in colourless granular crystals (2·1 g.), m. p. 113° (Found: C, 74·4; H, 5·8. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). *4-Hydroxy-2-methoxyphenyl benzyl ketone* possesses normal phenolic properties and gives a brownish-violet ferric chloride reaction. The acetyl derivative crystallises from alcohol in diamond-shaped rhombohedra, m. p. 68°.

Condensation of Phenylacetonitrile with Orcinol Monomethyl Ether.—A solution of orcinol monomethyl ether (20 g.) and phenylacetonitrile (20 g.) in dry ether (100 c.c.) was saturated with hydrogen chloride at 0° in presence of anhydrous zinc chloride (5 g.). After 24 hours, water at 0° was added and the resulting aqueous solution of the mixed ketimines was hydrolysed on the steam-bath. Ether–benzene extracted a solid, from which the ketones were separated by fractional crystallisation from ether–ligroin. Thin, colourless, diamond-shaped plates first separated, followed by clusters of colourless needles. The two substances were sorted out and each was separately crystallised from ether–ligroin.

The plate form (2·6 g.) has m. p. 93° (Found: C, 74·9; H, 6·2. $C_{16}H_{16}O_3$ requires C, 74·9; H, 6·3%) and is *4-hydroxy-2-methoxy-6-methylphenyl benzyl ketone*. It is exceedingly soluble in ether, alcohol, methyl alcohol, benzene, and acetone. Its alcoholic solution gives with ferric chloride a very pale yellow colour. The acetyl derivative crystallises from alcohol in thin rhombic plates, m. p. 88°.

The needles (0·4 g.) have m. p. 110° (Found: C, 75·1; H, 6·3. $C_{16}H_{16}O_3$ requires C, 74·9; H, 6·3%) and consist of *2-hydroxy-4-methoxy-6-methylphenyl benzyl ketone*. It is much less soluble in ether than its isomeride, and gives a strong purplish-brown ferric chloride reaction. By heating at 180° for 12 hours with an equal weight of sodium acetate and excess of acetic anhydride, isolation of the product, and acetylation as before, a substance was obtained which crystallised from methyl alcohol in colourless needles, m. p. 165° (Found: C, 77·2; H, 5·9. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·8%). This substance contains no acetoxy-group, dissolves in concentrated sulphuric acid to a colourless solution exhibiting a blue fluorescence, and is therefore *7-methoxy-2 : 5-dimethylisoflavone*.

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