675. *The Isomerisation of* iso*Flavones.*

By W. B. Whalley.

Conditions are detailed for the demethylation of 5 : 7 : 2′-trimethoxy*iso*flavone (I; R = Me) (Whalley, *J. Amer. Chem. Soc.*, 1953, **75**, 1059) to 5 : 7 : 2′-trihydroxy*iso*flavone (I; R = H). The removal, by the same methods, of the methoxyl groups from 5 : 7 : 2′- or 5 : 7 : 4′-trimethoxy-8-methyl*iso*flavone gave a mixture of the corresponding trihydroxy-8- and -6-methyl*iso*flavones (Whalley, *Chem. and Ind.*, 1953, 277).

Difficulties in demethylation of 5 : 7 : 2′-trimethoxy- (I; R = Me) and 5 : 7 : 2′-trimethoxy-8-methyl-*iso*flavone (II; R = Me) have been previously described (Whalley, *J. Amer. Chem. Soc.*, 1953, **75**, 1059). An improved technique is now reported, and cyclisation of several deoxybenzoins to the corresponding 2-hydroxy*iso*flavanones (Whalley, *loc. cit.*) is described.

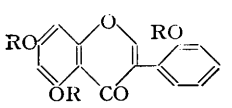
Attempts to demethylate 5 : 7 : 2′-trimethoxy*iso*flavone (I; R = Me) by hydriodic acid which had been purified by *distillation* over red phosphorus in the usual manner gave a resin from which only a trace of 5 : 7 : 2′-trihydroxy*iso*flavone (I; R = H) was obtained. Use of hydriodic acid which had been refluxed with red phosphorus until colourless and then filtered, or, better, which had " phosphorous acids " added (*e.g.*, as a stabiliser, as in the product marketed by Merck & Co., Rahway, N.J.) gave a superior result. Even so the yield was poor, and better results were obtained by using aluminium chloride, though its quality is important. When this work was almost complete the synthesis, by a different method, of 5 : 7 : 2′-trihydroxy*iso*flavone was described by Baker, Harborne, and Ollis (*Chem. and Ind.*, 1952, 1058)

Demethylation of 5 : 7 : 2′-trimethoxy-8-methyl*iso*flavone (II; R = Me) with stabilised hydriodic acid or aluminium chloride furnished (in moderate yield) 5 : 7 : 2′-trihydroxy-8-methyl- (II; R = H) and 5 : 7 : 2′-trihydroxy-6-methyl-*iso*flavone (III; R = R′ = H) (Whalley, *Chem. and Ind.*, 1953, 277), best separated after methylation. 5 : 7 : 2′-Trimethoxy-6-methyl*iso*flavone (III; R = R′ = Me) was synthesised by the conversion of 5 : 7 : 2′-trihydroxy*iso*flavone (I; R = H) into 5-hydroxy-7 : 2′-dimethoxy-6-methyl*iso*flavone (III; R = Me, R′ = H) by means of methyl iodide in methanol containing sodium

methoxide (Baker and Robinson, *J.*, 1926, 2713; Whalley, *loc. cit.*), followed by full methylation with methyl sulphate and potassium carbonate.

The possibility that the methyl ether of the second demethylation product of (II; R = Me) was (V; R = Me), formed by way of the intermediate (IV) (cf. Whalley, *loc. cit.*) and yet equatable with the methylation product of 5 : 7 : 2′-trihydroxy*iso*flavone (I; R = H) because of a similar rearrangement occurring during the methylation of (I; R = H), was excluded as follows. Alkaline degradation of (III; R = R′ = Me) gave 2-hydroxy-4 : 6 : 2′-trimethoxy-5-methyldeoxybenzoin (VII), converted by ethylation into 2-ethoxy-4 : 6 : 2′-trimethoxy-5-methyldeoxybenzoin (VI; R = Me), which was identical with a specimen prepared by the methylation of 2-ethoxy-4 : 6-dihydroxy-2′-methoxy-5-methyldeoxybenzoin (VI; R = H), obtained by the Hoesch condensation of 4-ethoxy-2 : 6-dihydroxytoluene and 2-methoxybenzyl cyanide.

Alkaline degradation of the unknown 3-aroylcoumarone type (V) might be expected to proceed similarly to that of the isomeric *iso*flavone (III; R = R′ = Me) to give, however,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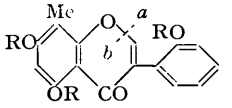
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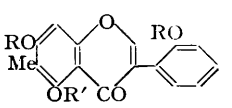
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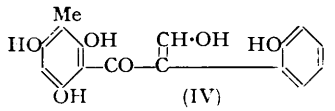
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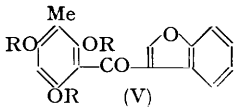
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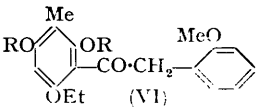
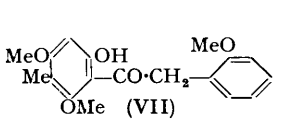

(VI)

instead of the ketone (VII), 2′-hydroxy-2 : 4 : 6-trimethoxy-3-methyldeoxybenzoin (VIII; R = Me, R′ = H) which would be converted by ethylation into 2′-ethoxy-2 : 4 : 6-trimethoxy-3-methyldeoxybenzoin (VIII; R = Me, R′ = Et). Condensation of 2-ethoxybenzyl cyanide with *C*-methylphloroglucinol furnished the ketone (VIII; R = H, R′ = Et) which was converted by methylation into the deoxybenzoin (VIII; R = Me, R′ = Et) isomeric, but not identical, with (VI; R = Me).

Similarly, demethylation of 5 : 7 : 4′-trimethoxy-8-methyl*iso*flavone (IX; R = R′ = Me) (Whalley, *loc. cit.*) with hydriodic acid during a prolonged period gave 5 : 7 : 4′-trihydroxy-8-methyl*iso*flavone together with small quantities of 5 : 7 : 4′-trihydroxy-6-methyl*iso*flavone (X; R = R′ = H), which was converted by methylation into 5 : 7 : 4′-trimethoxy-6-methyl*iso*flavone (X; R = R′ = Me), identical with a specimen prepared by the methylation of 5-hydroxy-7 : 4′-dimethoxy-6-methyl*iso*flavone (X; R′ = H, R = Me) (Baker and Robinson, *loc. cit.*; Whalley, *loc. cit.*). Partial methylation of 5 : 7 : 4′-trihydroxy-8-methyl*iso*flavone (IX; R = R′ = H) gave its 7 : 4′-dimethyl ether.

The postulate (Whalley, *loc. cit.*) that the *iso*flavone system may open across *a*—*b* in (II) during demethylation is thus confirmed, at least for certain cases, and this supports the suggestion that the difficulties in demethylation of 2′-methoxy*iso*flavones may be due to this scission with the subsequent formation, by way of the intermediates of type (IV), of the acid-sensitive 3-aroylcoumarones of type (V).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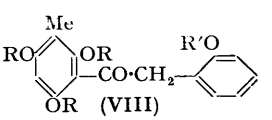
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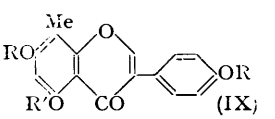
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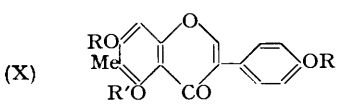
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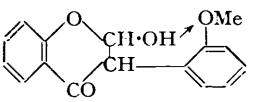
(XI)

Those flavones which undergo demethylation by hydriodic acid with concomitant rearrangement can be demethylated without structural changes by aluminium chloride (cf., *e.g.*, Narasimhachari, Row, and Seshadri, *Proc. Indian Acad. Sci.*, 1952, **35**, *A*, 46) and

it is worthy of note that the isomerisation of 5 : 7 : 2′-trimethoxy-8-methyl*iso*flavone occurs with both of these reagents.*

This isomerisation in the *iso*flavone series has been independently observed by Professor W. Baker, F.R.S., and his colleagues (personal communications and *Chem. and Ind.*, 1953, 277).

We previously suggested that the stability of a number of 2-hydroxy*iso*flavanones might be ascribed, at least in part, to the stabilisation of the system by hydrogen bonding as in (XI). The preparation of further 2-hydroxy-2′-methoxy*iso*flavanones of type (XI) is described in the Experimental section; their formulation as 2-hydroxy*iso*flavanones rather than as *iso*flavones containing a molecule of water of crystallisation rests upon the arguments previously advanced (Whalley, *loc. cit.*) and is substantiated by a comparison of the ultra-violet absorption spectra. Our repeated attempts to obtain *iso*flavanones from deoxybenzoins lacking the 2′-methoxyl group have provided only ill-defined products, but Professor W. Baker (personal communication) informs us that he has obtained 2-hydroxy-*iso*flavanones from deoxybenzoins which do not possess 2′-methoxyl groups, and hence whilst the presence of the 2′-group might well enhance the stability of 2-hydroxy*iso*-flavanones it is apparently not necessary for the production of this system.

The 2′-methoxy*iso*flavones described in this paper are resinified very readily by hydriodic acid, even on use of the modified technique now detailed; in particular 7 : 2′-dimethoxy*iso*flavone is extremely sensitive.

Experimental

5 : 7 : 2′-*Trihydroxy*iso*flavone* (I; R = H).—(*a*) A solution of 5 : 7 : 2′-trimethoxy*iso*flavone (Whalley, *loc. cit.*) (2·5 g.) in benzene (50 ml.) containing powdered aluminium chloride (6 g.) was heated on the steam-bath during 5 hr. The cooled mixture was decomposed by ice and excess of 2N-hydrochloric acid, and the sticky precipitate collected, dried, and extracted with hot benzene. The insoluble residue (0·5 g.) separated from aqueous methanol in colourless needles, m. p. 224°, unchanged on sublimation and having a violet ferric reaction in alcohol. Two subsequent recyclisations of the partially demethylated *iso*flavones contained in the benzene extracts furnished a further 0·5 g. of 5 : 7 : 2′-trihydroxy*iso*flavone (Found: C, 66·9; H, 3·7. Calc. for $C_{15}H_{10}O_5$: C, 66·7; H, 3·7%).

(*b*) 5 : 7 : 2′-Trimethoxy*iso*flavone (1·5 g.) in hydriodic acid (*d* 1·7; 50 ml.) containing a little "phosphorous acids" was refluxed during 45 min. (demethylation was incomplete if shorter times were employed), then cooled, and the sticky solid collected, washed, dried, and sublimed, giving 5 : 7 : 2′-trihydroxy*iso*flavone (0·1 g.), m. p. 224°, identical with the product from (*a*) and converted quantitatively by methyl sulphate and anhydrous potassium carbonate in boiling acetone into 5 : 7 : 2′-trimethoxy*iso*flavone.

Demethylation of 5 : 7 : 2′-*Trimethoxy*-8-*methyl*iso*flavone.*—(*a*) 5 : 7 : 2′-Trimethoxy-8-methyl-*iso*flavone (Whalley, *loc. cit.*) (2 g.) in hydriodic acid (*d* 1·7; 100 ml.) containing "phosphorous acids" was refluxed for 45 min. (needed for complete demethylation). After isolation the semi-crystalline mass was purified from aqueous methanol, to give a very difficultly separable mixture of 5 : 7 : 2′-trihydroxy-8-methyl- and of 5 : 7 : 2′-trihydroxy-6-methyl-*iso*flavone, in very pale buff-coloured needles, m. p. 200—245° (Found: C, 67·8; H, 4·7. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·3%). Methylation of this mixture by methyl sulphate–potassium carbonate–acetone during 50 hr. furnished a crystalline product, purified from methanol, gave 5 : 7 : 2′-*trimethoxy*-6-*methyl*iso*flavone* (0·2 g.), needles, m. p. 220°, having a negative ferric reaction in alcohol, dissolving in concentrated sulphuric acid to a pale yellow solution, unchanged on warming, and subliming at 200°/0·1 mm. without change in m. p. [Found: C, 69·9; H, 5·7; OMe, 28·2. $C_{16}H_9O_2(OMe)_3$ requires C, 69·9; H, 5·6; OMe, 28·5%]. This was identical with a synthetic specimen. Concentration of the methanolic mother-liquors furnished a second product, which after purification from ethyl acetate gave 5 : 7 : 2′-trimethoxy-8-methyl*iso*flavone (0·2 g.), m. p. and mixed m. p. 180°.

(*b*) Demethylation of 5 : 7 : 2′-trimethoxy-8-methyl*iso*flavone (1 g.) in benzene (25 ml.)

* [*Note added*, 16.7.53.] Since the preparation of this paper Donnelly, Philbin, and Wheeler (*Chem. and Ind.*, 1953, 567) have suggested that, as no rearrangement has yet been observed during demethylation of 5 : 8-dimethoxyflavones by aluminium chloride, the production of some 5 : 7 : 2′-trihydroxy-6-methyl*iso*flavone from 5 : 7 : 2′-trimethoxy-8-methyl*iso*flavone by this reagent might be ascribed to the direct migration of the methyl residue rather than to ring opening followed by ring closure in an alternative position.

containing powdered aluminium chloride (3 g.) on the steam-bath during 2½ hr. furnished a product (0·8 g.) which, after purification from aqueous methanol and subsequent complete methylation, was separated into 5 : 7 : 2′-trimethoxy-8- (0·3 g.) and 5 : 7 : 2′-trimethoxy-6-methyl*iso*flavone (0·3 g.).

5 : 7 : 2′-*Trimethoxy*-6-*methyl*iso*flavone* (III; R = R′ = Me).—5 : 7 : 2′-Trihydroxy*iso*flavone (1·5 g.) in methanol (50 ml.) containing dissolved sodium (2 g.) and methyl iodide (10 ml.) was refluxed for 15 hr. Purification of the product from methanol gave 5-*hydroxy*-7 : 2′-*dimethoxy*-6-*methyl*iso*flavone* (0·5 g.) in very pale yellow prisms, m. p. 155°, exhibiting an intense green ferric reaction in alcohol and moderately soluble in alcohol and methanol [Found: C, 69·6; H, 5·7; OMe, 18·9. $C_{16}H_{10}O_3(OMe)_2$ requires C, 69·2; H, 5·1; OMe, 19·8%].

Further methylation during 60 hr. by methyl sulphate–potassium carbonate–acetone gave a quantitative yield of 5 : 7 : 2′-trimethoxy-6-methyl*iso*flavone, m. p. 220° (Found: C, 70·4; H, 5·7; OMe, 27·5%).

The last-mentioned *iso*flavone (0·7 g.) in methanol (15 ml.) and water (10 ml.) containing sodium hydroxide (2 g.) was refluxed for 1½ hr.; acidification of the cooled hydrolysate furnished 2-*hydroxy*-4 : 6 : 2′-*trimethoxy*-5-*methyldeoxybenzoin* (0·5 g.), prisms (from methanol), m. p. 134°, having an intense olive-green ferric reaction in alcohol (Found: C, 68·6; H, 6·5. $C_{18}H_{20}O_5$ requires C, 68·3; H, 6·4%). With ethyl iodide and potassium carbonate in boiling acetone during 6 hr. this gave quantitatively 2-*ethoxy*-4 : 6 : 2′-*trimethoxy*-5-*methyldeoxybenzoin*, plates (from methanol), m. p. 89°, having a negative ferric reaction in alcohol and identical with a synthetic specimen (Found: C, 69·9; H, 6·7. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%).

2-*Ethoxy*-4 : 6 : 2′-*trimethoxy*-5-*methyldeoxybenzoin* (VI; R = Me).—A solution of 4-ethoxy-2 : 6-dihydroxytoluene (Herzig and Eisenstein, *Monatsh.*, 1902, **23**, 565) (2 g.) and *o*-methoxybenzyl cyanide (2 g.) in ether (75 ml.) containing zinc chloride (2 g.) was saturated at 0° with hydrogen chloride. 24 Hr. later the semicrystalline ketimine salt was separated and hydrolysed with water (50 ml.) on the steam-bath during 1 hr. Purification of the crystalline ketone from methanol gave 2-*ethoxy*-4 : 6-*dihydroxy*-2′-*methoxy*-5-*methyldeoxybenzoin* (1·2 g.) in needles, m. p. 185°, having an intense red-violet ferric reaction in alcohol (Found: C, 68·7; H, 6·3. $C_{18}H_{20}O_5$ requires C, 68·4; H, 6·4%).

Methylation by methyl sulphate, etc., furnished quantitatively 2-ethoxy-4 : 6 : 2′-trimethoxy-5-methyldeoxybenzoin, plates (from methanol), m. p. 89°, having a negative ferric reaction in alcohol.

2′-*Ethoxy*-2 : 4 : 6-*trimethoxy*-3-*methyldeoxybenzoin* (VIII; R = Me, R′ = Et).—Prepared from *o*-ethoxybenzaldehyde (47 g.) (Perkin, *Annalen*, 1868, **145**, 306) in the usual manner the *azlactone* (60 g.) separated from ethanol in bright yellow needles, m. p. 182° (Found: N, 4·7. $C_{18}H_{15}O_3N$ requires N, 4·7%). After hydrolysis of this (60 g.) the crude *o*-ethoxyphenylpyruvic acid was converted into the *oxime* (15 g.) which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in needles, m. p. 164—165° (Found: N, 6·1. $C_{11}H_{13}O_4N$ requires N, 6·3%). Dehydration of this oxime (16 g.) with acetic anhydride furnished *o-ethoxybenzyl cyanide* (5·4 g.) as almost colourless prisms [from light petroleum (b. p. 40—60°)], m. p. 42° (Found: N, 7·9. $C_{10}H_{11}ON$ requires N, 8·7%).

The Hoesch reaction of *C*-methylphloroglucinol (5 g.) and *o*-ethoxybenzyl cyanide (5 g.) furnished 2′-*ethoxy*-2 : 4 : 6-*trihydroxy*-3-*methyldeoxybenzoin* (1 g.), needles (from benzene–methanol), m. p. 174°, having an intense violet ferric reaction in alcohol (Found: C, 68·0; H, 6·0. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%), giving with methyl sulphate, etc., the *trimethyl ether* (VIII; R = Me, R′ = Et), tablets (from aqueous methanol), m. p. 88°, having a negative ferric reaction in alcohol (Found: C, 69·8; H, 7·2. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%). The mixed m. p. with the isomeric 2-ethoxy-4 : 6 : 2′-trimethoxy-5-methyldeoxybenzoin was *ca.* 70°.

Demethylation of 5 : 7 : 4′-*Trimethoxy*-8-*methyl*iso*flavone* (IX; R = R′ = Me).—A solution of 5 : 7 : 4′-trimethoxy-8-methyl*iso*flavone (4·5 g.) in hydriodic acid (*d* 1·7; 75 ml.) was refluxed during 12 hr., then diluted with water, and the crystalline precipitate purified from aqueous methanol to furnish 5 : 7 : 4′-trihydroxy-8-methyl*iso*flavone (3·5 g.), m. p. 252° (Whalley, *loc. cit.*). On evaporation the methanolic mother-liquors deposited crystals, m. p. *ca.* 200° (0·5 g.), which, after repeated crystallisation, had m. p. 274°, undepressed on admixture with authentic 5 : 7 : 4′-trihydroxy-6-methyl*iso*flavone. Methylation of this product during 24 hr. by the methyl sulphate method gave 5 : 7 : 4′-trimethoxy-6-methyl*iso*flavone (0·2 g.) as prisms (from methanol), m. p. 169°, identical with a specimen prepared by the methylation during 50 hr. of 5-hydroxy-7 : 4′-dimethoxy-6-methyl*iso*flavone (Whalley; Baker and Robinson, *locc. cit.*) (Found: C, 69·8; H, 5·4; OMe, 28·2%).

5-*Hydroxy*-7 : 4′-*dimethoxy*-8-*methyl*iso*flavone* (IX; R = Me, R′ = H).—Methylation of 5 : 7 : 4′-trihydroxy-8-methyl*iso*flavone (Whalley, *loc. cit.*) during 2 hr. by methyl sulphate, etc., gave quantitatively 5-*hydroxy*-7 : 4′-*dimethoxy*-8-*methyl*iso*flavone* which separated from a large volume of methanol in needles, m. p. 167°, having an intense green ferric reaction in alcohol [Found: C, 69·5; H, 5·3; OMe, 19·8. $C_{16}H_{10}O_3(OMe)_2$ requires C, 69·2; H, 5·2; OMe, 19·3%].

7 : 2′-*Dimethoxy*iso*flavone*.—Prepared by a Hoesch reaction from resorcinol (6 g.) and *o*-methoxybenzyl cyanide (5 g.), 2 : 4-*dihydroxy*-2′-*methoxydeoxybenzoin* (2 g.) separated from aqueous methanol or benzene in prisms, m. p. 164°, very soluble in methanol and ethanol and having an intense red-brown ferric reaction in alcohol (Found: C, 70·2; H, 5·7. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%).

Methylation by methyl iodide and potassium carbonate in boiling acetone during 1½ hr. gave quantitatively 2-*hydroxy*-4 : 2′-*dimethoxydeoxybenzoin*, prisms (from methanol), m. p. 94°, having an intense red-brown ferric reaction in alcohol (Found: C, 69·9; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

Cyclisation of this ketone (2 g.) in methyl formate solution (25 ml.) containing sodium dust (1 g.), during 24 hr. at 0°, decomposition by iced water, and crystallisation from ethyl acetate–hexane gave 2-*hydroxy*-7 : 2′-*dimethoxy*iso*flavanone* (1·5 g.) as prisms, m. p. 134°, very easily soluble in ethanol, insoluble in cold 2N-sodium hydroxide, and having a negative ferric reaction in alcohol (Found: C, 68·1; H, 5·5. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

The foregoing compound (1·2 g.) was refluxed with acetic acid (5 ml.) during 30 min. Dilution with water gave quantitatively 7 : 2′-*dimethoxy*iso*flavone*, needles (from aqueous methanol), m. p. 109° (Found: C, 72·4; H, 5·2. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%). In boiling hydriodic acid (*d* 1·7; 50 ml.), containing "phosphorous acid" (20 min.) this (1·0 g.) gave only an intractable red gum.

5 : 7 : 2′ : 4′-*Tetramethoxy*iso*flavone*.—2-Hydroxy-4 : 6 : 2′ : 4′-tetramethoxydeoxybenzoin (King and Neill, *J.*, 1952, 4752) (3 g.) in ethyl formate (40 ml.) containing sodium (3 g.) furnished, in the usual manner, 2-*hydroxy*-5 : 7 : 2′ : 4′-*tetramethoxy*iso*flavanone* (2 g.) as needles (from ethyl acetate) m. p. 178° (decomp.) (Found: C, 63·2; H, 5·8. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%), insoluble in cold 2N-sodium hydroxide, very sparingly soluble in methanol and ethanol, and having a negative ferric reaction in alcohol.

Boiling acetic acid converted it quantitatively into 5 : 7 : 2′ : 4′-tetramethoxy*iso*flavone, m. p. 204° (Found: C, 66·7; H, 5·7. Calc. for $C_{19}H_{18}O_6$: C, 66·7; H, 5·3%) (King and Neill, *loc. cit.*, record m. p. 203—204°). Demethylation of this *iso*flavone, even under the most favourable conditions, with hydriodic acid furnished a resin from which only traces of crystalline material could be isolated.

5 : 7 : 2′ : 3′-*Tetramethoxy*-8-*methyl*iso*flavone*.—Prepared from a solution of *C*-methylphloroglucinol (5 g.) and 2 : 3-dimethoxybenzyl cyanide (5 g.) in ether (150 ml.) containing zinc chloride (4 g.) 2 : 4 : 6-*trihydroxy*-2′ : 3′-*dimethoxy*-3-*methyldeoxybenzoin* (4·2 g.) separated from aqueous methanol in almost colourless prisms, m. p. 201°, having an intense violet ferric reaction in alcohol (Found: C, 64·1; H, 5·9. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%).

Methylation of this (2 g.) by methyl sulphate, etc., furnished 2-*hydroxy*-4 : 6 : 2′ : 3′-*tetramethoxy*-3-*methyldeoxybenzoin* (1·5 g.) in prisms, m. p. 160° (from ethyl acetate), exhibiting a red-brown ferric reaction in alcohol (Found: C, 66·2; H, 6·4. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%).

Cyclisation in the usual way furnished 2-*hydroxy*-5 : 7 : 2′ : 3′-*tetramethoxy*-8-*methyl*iso*flavanone* (1·5 g. from 2 g.) as tablets, m. p. 178° (decomp.), from methanol or needles, m. p. 178° (decomp.), from ethyl acetate (Found: C, 64·2; H, 6·2. $C_{20}H_{22}O_7$ requires C, 64·2; H, 5·9%). It was moderately soluble in methanol, ethanol, and ethyl acetate but insoluble in cold 2N-sodium hydroxide and had a negative ferric reaction in alcohol.

The foregoing *iso*flavanone was converted rapidly and quantitatively into 5 : 7 : 2′ : 3′-*tetramethoxy*-8-*methyl*iso*flavone* in boiling acetic acid and separated from aqueous acetone or aqueous alcohol in needles, m. p. 141°, readily soluble in methanol, ethanol, and ethyl acetate and having a negative ferric reaction in alcohol (Found: C, 67·5; H, 5·3. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·7%).

5 : 7 : 2′ : 3′-*Tetramethoxy*iso*flavone*.—Prepared from phloroglucinol (6 g.) and 2′ : 3′-dimethoxybenzyl cyanide (6 g.) in the usual manner, 2 : 4 : 6-*trihydroxy*-2′ : 3′-*dimethoxydeoxybenzoin* (4·5 g.) separated from aqueous methanol in almost colourless plates, m. p. 193°, having an intense violet ferric reaction in alcohol (Found: C, 63·3; H, 5·6. $C_{16}H_{16}O_6$ requires C, 63·2; H, 5·3%). Methylation by methyl sulphate, etc., furnished 2-*hydroxy*-4 : 6 : 2′ : 3′-

tetramethoxydeoxybenzoin (4 g. from 4 g.) as prisms, m. p. 132° (from methanol–acetone), having an intense violet ferric reaction in alcohol (Found : C, 64·7; H, 6·1. $C_{18}H_{20}O_6$ requires C, 65·1; H, 6·1%).

Cyclisation with ethyl formate in the usual way gave 2-*hydroxy*-5 : 7 : 2′ : 3′-*tetramethoxy*iso*flavanone* (2 g. from 4 g.) as prisms, m. p. 191—192° (decomp.) (from ethanol), insoluble in 2N-sodium hydroxide, sparingly soluble in methanol and ethanol, having a negative ferric reaction in alcohol, and decomposing on sublimation at 0·001 mm. (Found : C, 63·4; H, 5·9. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%).

Prepared from the foregoing *iso*flavanone in refluxing acetic acid, 5 : 7 : 2′ : 3′-*tetramethoxy*iso*flavone* separated from aqueous acetic acid in prisms, m. p. 178° [Found : C, 66·7; H, 5·5; OMe, 36·5. $C_{15}H_6O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·3%].

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