The Chemistry of Extractives from Hardwoods. Part XX. Distemonanthin, a New Type of Flavone Pigment from* Distemonanthus benthamianus.

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Distemonanthin, $C_{17}H_{10}O_9$, a new type of flavonoid pigment, has been found in the wood of *Distemonanthus benthamianus.* It contains one methoxyl and four hydroxyl groups, and the formation on prolonged methylation of an ester $C_{15}H_3O_2(OMe)_6{\cdot}CO_2Me$ gave evidence also of the presence of a lactone ring.

Alkali degradation of the fully methylated derivative yielded hemipinic acid and 2-hydroxy-ω : 4 : 5 : 6-tetramethoxyacetophenone, while similar treatment of the corresponding ethyl compound $C_{15}H_3O_2(OMe)(OEt)_5{\cdot}CO_2Et$ produced 3 : 4-diethoxyphthalic acid and ω : 4 : 6-triethoxy-2-hydroxy-5-methoxyacetophenone, the latter being already known as a decomposition product of patuletin (Row and Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 140). Distemonanthin is therefore 7 : 8 : 5′ : 7′-tetrahydroxy-6′-methoxychromono(3′ : 2′-3 : 4)*iso*coumarin.

7′-Hydroxy- and 5′ : 7′-dihydroxy-chromono(3′ : 2′-3 : 4)*iso*coumarin and 2 : 3 : 5-trimethoxyphenol have been synthesised.

Of the new colouring matters isolated from ayan, the yellow wood of *Distemonanthus benthamianus*, those so far described (see Part V, *J.*, 1952, 92, and Part XIX *) are ayanin (3 : 7 : 4′-tri-*O*-methylquercetin), oxyayanin-A (6′-hydroxyayanin), and oxyayanin-B (6-hydroxyayanin). The fourth, a bright yellow very sparingly soluble compound, $C_{17}H_{10}O_9$, which has been named distemonanthin, is of particular interest in containing the formerly unknown chromono(3′ : 2′-3 : 4)*iso*coumarin nucleus. The following account of the new pigment describes the determination of its constitution (I; R = H) and the synthesis of simple derivatives of this novel ring-system.

The relation of distemonanthin to the flavone series was evident from its general properties, including the colour of its solutions in alkali and in aqueous-alcoholic hydrochloric acid treated with magnesium. The hydroxylic nature of four of its oxygen atoms followed from the formation of tetra-acetyl and tetrabenzoyl derivatives; a fifth was present as a methoxyl group (Zeisel). These groups and the pyrone ring account for all but two of the oxygen atoms.

Significant data were derived from methylation studies, primarily with methyl sulphate–potassium carbonate in acetone, for a tetramethyl ether which was first obtained was gradually replaced by a hexamethyl derivative. Moreover, in the formation of hexa-*O*-methyldistemonanthin an additional oxygen atom was introduced, a result consistent with the conversion of a lactone grouping $\overbrace{\mathrm{CO{-}O}}^{\mathrm{X}}$ into the corresponding *O*-methyl methyl ester $\overbrace{\mathrm{CO{\cdot}OMe\quad MeO}}^{\mathrm{X}}$. In agreement, it was later shown that mild alkaline hydrolysis of the hexamethyl derivative eliminated a methyl group, producing a carboxylic acid.

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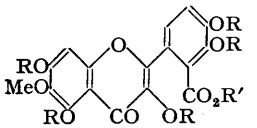
* Part XIX, preceding paper.

The latter, which was also obtained from the tetramethyl ether by methylation in aqueous solution, was reconverted into hexa-*O*-methyldistemonanthin with diazomethane.

When alkylated with methyl iodide–potassium carbonate in acetone, distemonanthin yielded a high proportion of very sparingly soluble dimethyl ether, the remaining product consisting of hexa-*O*-methyldistemonanthin. With methyl sulphate in aqueous alkali, however, an acidic trimethyl ether was formed, indicating fission of the lactone ring and methylation of the liberated phenolic hydroxyl group. These properties of distemonanthin and of its compounds appeared to be most readily explained on the assumption that the lactone system spans the 2′ : 3-positions, the stability of those derivatives containing the free carboxyl group—which if located at position 3 would constitute a β-keto-acid—requiring the assignment of this substituent to the 2′-carbon atom. Distemonanthin is thus constituted as a 2′-carboxyflavonol anhydride.

Further information bearing on the structure of the compound was obtained by alkali degradation. However, the lactone-containing compounds, *i.e.*, distemonanthin and tetra-*O*-methyldistemonanthin, exhibited remarkable stability towards alkali, 80% of the tetramethyl ether, for example, being recovered after 8 hours' refluxing with 20% aqueous potassium hydroxide. Hexa-*O*-methyldistemonanthin, on the other hand, which was first fused with alkali at 250° and gave a small quantity of protocatechuic acid isolated as methyl ester, was readily hydrolysed with 20% aqueous-alcoholic potassium hydroxide, affording hemipinic acid (VI; R = Me) and a monohydric phenol $C_{12}H_{16}O_6$ which was identified by comparison with a synthetic sample as 2-hydroxy-ω : 4 : 5 : 6-tetramethoxyacetophenone (V; R = Me) (Row and Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 23). Methylation of the hydroxy-ketone gave the previously unknown ω : 2 : 4 : 5 : 6-pentamethoxyacetophenone.



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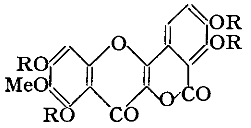
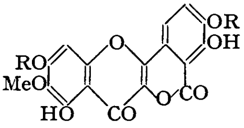


(I) Distemonanthin (R = H)



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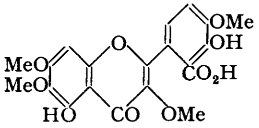

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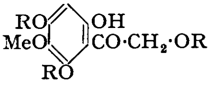

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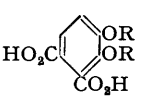

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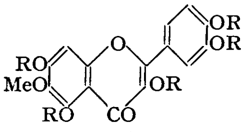
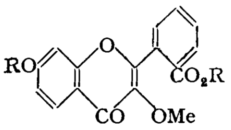


(VII)

From these results it is evident that hexa-*O*-methyldistemonanthin is the hexamethoxyflavone-2′-carboxylic ester shown as (II; R = R′ = Me), and consequently the tetramethyl ether is the corresponding lactone (I; R = Me). The formation of a dimethyl ether under less vigorous conditions of alkylation may be attributed to the restrictive influence on the phenolic substituents at the 5- and the 3′-position (flavone numbering) of chelation with the adjacent carbonyl groups, whence it may be concluded that the constitution of this product is (III; R = Me). Consequently, the acidic trimethyl ether has structure (IV) since it is presumably again these two hydroxyl groups which resist methylation.

Prolonged treatment of distemonanthin with ethyl sulphate–potassium carbonate in refluxing acetone gave a mixture of the hexaethyl derivatives (present in solution) and the sparingly soluble diethyl and tetraethyl ethers, of which the last two were isolated from the undissolved solid and separated by crystallisation from acetic acid. Degradation of the hexaethyl compound with 20% aqueous-alcoholic potassium hydroxide resulted in the formation of a diethoxyphthalic acid and a phenolic ketone $C_{15}H_{22}O_6$. The formation of hemipinic acid (VI; R = Me) in the hydrolysis of the corresponding methyl compound (II; R = R′ = Me) enabled the new phthalic acid to be identified as (VI; R = Et). The phenolic ketone was already known as a degradation product of penta-*O*-ethylpatuletin, prepared by Row and Seshadri (*Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 140) from patuletin, a pigment found in the French marigold, *Tagetes patula*, and its identity was confirmed by direct comparison with the product (V; R = Et) obtained from a specimen of patuletin kindly provided by Professor Seshadri. Having in this way established the orientation of the methoxyl group it was obvious that the total structure of distemonanthin is expressed by the formula (I; R = H). The relation between distemonanthin and patuletin evident in these formulæ was then experimentally demonstrated by mild hydrolysis of the hexaethyl compound (II; R = R′ = Et) to the corresponding acid (II; R = Et, R′ = H) which, when decarboxylated in boiling quinoline containing copper, yielded a product identical with penta-*O*-ethylpatuletin (VII; R = Et).

A synthesis of 7′-hydroxychromono(3′ : 2′-3 : 4)*iso*coumarin (IX; R = H) was carried out from ω-methoxyresacetophenone, which first was acylated in pyridine with excess of 2-methoxycarbonylbenzoyl chloride. When heated with pyridine and potassium carbonate to effect the Baker–Venkataraman rearrangement, the resulting diacyl derivative gave 7-hydroxy-3-methoxyflavone-2′-carboxylic acid (VIII; R = H), further characterised in the form of the methyl 7-methoxy-carboxylic ester (VIII; R = Me). The chromono-*iso*coumarin (IX; R = H) was formed by heating the 7-hydroxy-acid (VIII; R = H) with aqueous hydrogen iodide in acetic acid. Similarly, 5′ : 7′-dihydroxychromono-(3′ : 2′-3 : 4)*iso*coumarin was synthesised from ω-methoxyphloracetophenone.



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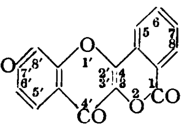

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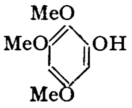

(X)

2 : 3 : 5-Trimethoxyphenol (X), a possible requirement at one stage of the investigation, was synthesised from pyrogallol 1-methyl ether *via* the following new intermediates : 2 : 3-dibenzyloxyanisole, 2-benzyloxy-6-methoxy-1 : 4-benzoquinone, 2-benzyloxy-6-methoxyquinol, and 3-benzyloxy-1 : 2 : 5-trimethoxybenzene. 2 : 3-Dibenzyloxy-5-nitroanisole was obtained as a by-product from the preparation of the quinone.

EXPERIMENTAL

Light petroleum used had b. p. 60—80°.

Distemonanthin (I; R = H).—Isolated as described in Part XIX and crystallised from pyridine–methanol, *distemonanthin* was obtained in bright yellow needles, m. p. (*in vacuo*) 351° (decomp.) (Found, in a sample dried at 110° *in vacuo* : C, 57·0, 56·9; H, 2·8, 3·0; OMe, 8·5. $C_{17}H_{10}O_8$ requires C, 57·0; H, 2·8; 1OMe, 8·7%); light absorption in EtOH : max. at 217, 240, 268, 312, 374, and 390 mμ; log ε 4·49, 4·40, 4·24, 3·94, 4·34, and 4·33. Distemonanthin is very sparingly soluble in most common solvents but dissolves more readily in dioxan and freely in pyridine or 2-ethoxyethanol. Its solutions in aqueous sodium carbonate or hydroxide are dark orange; in concentrated mineral acids it forms yellow solutions, and in alcohol its ferric reaction is brownish-green.

When treated with acetic anhydride–pyridine at 100° for 2 hr. distemonanthin gave a *tetra-acetate* which crystallised from ethyl acetate as colourless plates, m. p. 225—227° after slight sintering [Found, in a sample dried at 110° *in vacuo* : C, 56·7; H, 3·6; OMe, 5·4; Ac, 35·4%; *M* (Rast), 504. $C_{25}H_{18}O_{13}$ requires C, 57·0; H, 3·4; 1OMe, 5·9; 4Ac, 32·7%; *M*, 526]. The *tetrabenzoate*, prepared with benzoyl chloride–pyridine at 100° for 2 hr., was obtained as an oil which solidified in contact with ethanol and formed colourless needles, m. p. 239—240°, from ethyl acetate (Found, in a specimen dried at 110° *in vacuo* : C, 70·1; H, 3·9; OMe, 4·4. $C_{45}H_{26}O_{13}$ requires C, 69·8; H, 3·4; 1OMe, 4·0%).

Tetra-O-methyldistemonanthin (I; R = Me) *and Methyl* 3 : 5 : 6 : 7 : 3′ : 4′-*Hexamethoxyflavone-2′-carboxylate* (II; R = R′ = Me).—A mixture of distemonanthin (1 g.), methyl sulphate (3 c.c.), and potassium carbonate (6 g.) in acetone (200 c.c.) was refluxed for 24 hr. The insoluble material was then isolated and treated with hydrochloric acid; the residue of *tetra-O-methyldistemonanthin* crystallised from acetic acid in colourless plates (0·4 g., 35%),

m. p. 272° [Found, in a specimen died at 110° *in vacuo*: C, 60·5; H, 4·5; OMe, 34·9. $C_{16}H_8O_4(OMe)_5$ requires C, 60·9; H, 4·4; OMe, 37·5%].

Evaporation of the acetone solution and washings yielded a gum which was triturated with aqueous ammonia. The residue (0·5 g., 39%) when repeatedly crystallised from benzene–light petroleum gave *methyl* 3 : 5 : 6 : 7 : 3′ : *4′-hexamethoxyflavone-2′-carboxylate* as prisms, m. p. 151—152° [Found, in a specimen dried at 110° *in vacuo*: C, 59·6; H, 5·5; OMe, 44·7. $C_{16}H_8O_3(OMe)_7$ requires C, 60·0; H, 5·3; OMe, 47·2%]. Continued treatment of the tetramethyl derivative yielded the hexamethoxyflavone ester (66%) which also was the sole product (74%) from the prolonged methylation (90 hr.) of distemonanthin.

3 : 5 : 6 : 7 : 3′ : *4′-Hexamethoxyflavone-2′-carboxylic Acid* (II; R = Me, R′ = H).—(i) A solution of the hexamethoxyflavone methyl ester (II; R = R′ = Me) (0·5 g.) in water (2 c.c.) and ethanol (20 c.c.) containing potassium hydroxide (1 g.) was refluxed for 1 hr. and then concentrated. Acidification yielded a precipitate from which the *hexamethoxyflavonecarboxylic acid* (0·34 g., 70%) was obtained *via* aqueous sodium hydrogen carbonate and crystallisation from ethanol as prisms, m. p. 229—231° (effervescence) [Found, in a specimen dried at 110° *in vacuo*: C, 59·0; H, 4·6; OMe, 40·4. $C_{16}H_4O_4(OMe)_6$ requires C, 59·2; H, 5·0; OMe, 41·7%].

(ii) Tetra-*O*-methyldistemonanthin (0·2 g.) was dissolved by heating in 2N-sodium hydroxide (10 c.c.), and the solution shaken at room temperature for 1½ hr. with methyl sulphate (1 c.c.). After further warming the solution was acidified and the precipitated product purified *via* sodium hydrogen carbonate and crystallisation as above. The resulting acid had m. p. 229—231° (effervescence) (Found: C, 59·2; H, 4·8%). The material insoluble in the carbonate solution gave tetra-*O*-methyldistemonanthin when crystallised from acetic acid.

A solution of the acid (0·1 g.) in methanol (5 c.c.) was treated with ethereal diazomethane. The product isolated by evaporation was dissolved in benzene and washed with aqueous sodium hydrogen carbonate; addition of light petroleum to the dried benzene solution gave methyl 3 : 5 : 6 : 7 : 3′ : 4′-hexamethoxyflavone-2′-carboxylate, m. p. and mixed m. p. 151—152°.

Dimethyldistemonanthin (III; R = Me).—The insoluble material obtained from distemonanthin (0·5 g.), potassium carbonate (2 g.), methyl iodide (5 c.c.), and boiling acetone (100 c.c.) for 14 hr. afforded, when treated with hydrochloric acid, a yellow solid (0·38 g., 70%) consisting of *di-*O*-methyldistemonanthin*. It crystallised from acetic acid or pyridine–methanol as pale yellow needles, m. p. 332—334° [Found, in a specimen dried at 130° *in vacuo*: C, 59·4; H, 3·6; OMe, 23·6. $C_{16}H_5O_6(OMe)_3$ requires C, 59·1; H, 3·7; OMe, 24·1%]. This derivative is very sparingly soluble in organic solvents (thus precluding the ferric colour test); with aqueous alkalis deep orange, difficultly soluble salts are formed. Acetylation with acetic anhydride–pyridine gave the *diacetate*, colourless plates (from chloroform–ethyl acetate), m. p. 271—272° (decomp.) (Found: C, 59·0; H, 4·2. $C_{23}H_{18}O_{11}$ requires C, 58·7; H, 3·9%).

From the acetone solution used in the methylation hexamethoxyflavone methyl ester (0·1 g., 15·5%), m. p. 151—152°, was isolated.

5 : *3′-Dihydroxy*-3 : 6 : 7 : *4′-tetramethoxyflavone-2′-carboxylic Acid* (IV).—A solution of distemonanthin (0·5 g.) in 2N-sodium hydroxide (10 c.c.) was shaken with methyl sulphate (1 c.c.) at room temperature for 3 hr., and after warming on a steam-bath it was acidified. The gummy precipitate was dissolved in chloroform, and the light yellow solid extracted therefrom with aqueous sodium hydrogen carbonate was crystallised from benzene–light petroleum, whereby 5 : *3′-dihydroxy*-3 : 6 : 7′ : *4′-tetramethoxyflavone-2′-carboxylic acid* was obtained as pale yellow needles, m. p. 219—220° [Found: C, 57·5; H, 4·5; OMe, 28·9. $C_{16}H_6O_6(OMe)_4$ requires C, 57·4; H, 4·3; OMe, 29·7%].

Alkali Degradation of Methyl 3 : 5 : 6 : 7 : 3′ : *4′-Hexamethoxyflavone-2′-carboxylate*.—(i) A mixture of the flavone ester (II; R = R′ = Me) (0·5 g.), potassium hydroxide (5 g.), and water (2 c.c.) was heated for 10 min. in a nickel crucible at 250°, and the melt dissolved in water, acidified, and extracted with ether (3 × 25 c.c.). The product was fractionated by shaking the ethereal solution first with aqueous sodium hydrogen carbonate and then with 2N-sodium hydroxide. The fractions recovered by acidification and ether-extraction were tarry, but the more acidic portion when treated with ethereal diazomethane yielded a product which after distillation [b. p. 180—200° (bath-temp.)/1·5 mm.] crystallised from benzene in needles and had m. p. 134—135° alone or mixed with methyl protocatechuate (Found: C, 57·5; H, 4·9. Calc. for $C_8H_8O_4$: C, 57·1; H, 4·8%).

(ii) A mixture of the ester (II; R = R′ = Me) (2 g.), potassium hydroxide (10 g.), water (10 c.c.), and ethanol (40 c.c.) was refluxed for 8 hr. and the product derived by evaporation was dissolved in water (25 c.c.) and fractionated by saturation of the solution with carbon dioxide. The precipitated solid (0·9 g.) and a further small quantity (0·05 g.) obtained by ether-extraction consisted of 2-hydroxy-ω : 4 : 5 : 6-tetramethoxyacetophenone (V; R = Me); the remaining solution was acidified, traces of solid were removed by filtration, and hemipinic acid (VI; R = Me) (0·7 g.) was isolated from the filtrate by ether-extraction (4 × 25 c.c.).

Repeated crystallisation from light petroleum (b. p. 40—60°) afforded the phenol (V; R = Me) as needles, m. p. 71—72° alone or mixed with 2-hydroxy-ω : 4 : 5 : 6-tetramethoxyacetophenone prepared by the method of Row and Seshadri (*loc. cit.*, p. 23) who, however, record m. p. 77—78° [Found: C, 56·2; H, 6·3; OMe, 46·6%; *M* (Rast), 231. Calc. for $C_{12}H_{16}O_6$: C, 56·4; H, 6·3; 4OMe, 48·5%; *M*, 256]. Both specimens exhibited a brown colour with alcoholic ferric chloride, and when refluxed for 18 hr. with methyl sulphate–potassium carbonate in acetone yielded the identical product, isolated by evaporating the filtered acetone solution, and consisting of ω : 2 : 4 : 5 : 6-*pentamethoxyacetophenone*, which crystallised from light petroleum in prisms, m. p. and mixed m. p. 89—90° (Found: C, 57·8; H, 6·5. $C_{13}H_{18}O_6$ requires C, 57·8; H, 6·7%).

After decolorisation by crystallisation from methanol–benzene, the acid fraction gave hemipinic acid as elongated prisms, m. p. 178—179° (effervescence), from ethyl acetate, being less soluble therein than in the usual solvent, water (Perkin, *J.*, 1916, **109**, 922, records m. p. 180° (effervescence) (Found: C, 52·8; H, 4·7; OMe, 26·6. Calc. for $C_{10}H_{10}O_6$: C, 53·1; H, 4·5; 2OMe, 27·4%). The anhydride, needles from benzene, had m. p. 166—167°; Soffer *et al.* (*J. Amer. Chem. Soc.*, 1950, **72**, 3707) give m. p. 166—167° (Found: C, 58·0; H, 4·1. Calc. for $C_{10}H_8O_5$: C, 57·7; H, 3·9%); the N-ethylimide had m. p. 91—92° (recorded values range from 90° to 96—98°) (Found: C, 61·6; H, 5·7; N, 5·8. Calc. for $C_{12}H_{13}O_4N$: C, 61·3; H, 5·6; N, 6·0%).

Ethylation of Distemonanthin.—A mixture of distemonanthin (7·5 g.), ethyl sulphate (25 g.), and potassium carbonate (40 g.) in acetone (500 c.c.) was heated under reflux for 140 hr., and the principal product isolated by evaporation of the filtered solution and trituration of the residue with aqueous sodium hydroxide. The residue (6·0 g., 53%) of *ethyl* 3 : 5 : 7 : 3′ : 4′-*pentaethoxy*-6-*methoxyflavone*-2′-*carboxylate* (II; R = R′ = Et) crystallised from benzene–light petroleum as colourless prisms, m. p. 111—112° (Found: C, 64·1; H, 6·7. $C_{29}H_{36}O_{10}$ requires C, 64·0; H, 6·7%).

The solid collected from the reaction mixture was treated with dilute hydrochloric acid, and the residue (2·8 g.) was heated with boiling acetic acid (100 c.c.) for 5 min. The undissolved portion (1·1 g., 13%) consisting of *di*-O-*ethyldistemonanthin* (III; R = Et) crystallised from pyridine in small yellow needles, m. p. 327—328° (decomp.) (Found, in a specimen dried at 110° *in vacuo*: C, 60·9; H, 4·7. $C_{21}H_{18}O_9$ requires C, 60·9; H, 4·4%). *Tetra*-O-*ethyldistemonanthin* (0·35 g., 3·6%) separated from the acetic acid filtrate after it had been concentrated to 25 c.c. (charcoal), and when recrystallised from acetic acid formed colourless plates, m. p. 246—247° (Found, in a specimen dried at 110° *in vacuo*: C, 63·9; H, 5·3. $C_{25}H_{26}O_9$ requires C, 63·8; H, 5·6%).

3 : 5 : 7 : 3′ : 4′-*Pentaethoxy*-6-*methoxyflavone*-2′-*carboxylic Acid.*—Hydrolysis of ethyl 3 : 5 : 7 : 3′ : 4′-pentaethoxy-6-methoxyflavone-2′-carboxylate (0·75 g.) with 5% alcoholic potassium hydroxide as for the corresponding ester (II; R = R′ = Me) yielded the *acid* (II; R = Et, R′ = H) (0·5 g., 70%) which crystallised from aqueous methanol in colourless plates, m. p. 156—157° (Found, in a specimen dried at 100° *in vacuo*: C, 63·0; H, 6·5. $C_{27}H_{32}O_{10}$ requires C, 62·8; H, 6·3%).

3 : 5 : 7 : 3′ : 4′-*Pentaethoxy*-6-*methoxyflavone* (*Penta*-O-*ethylpatuletin*).—A mixture of the acid (II; R = Et, R′ = H) (0·5 g.) and copper powder (0·1 g.) was heated in quinoline (5 c.c.) under reflux for 15 min. The product was isolated after the addition of ether (100 c.c.) by washing the filtered solution with 2N-hydrochloric acid (5 × 50 c.c.), and then evaporating the dried liquid. The crystalline residue separated from ethanol in colourless prisms (0·27 g., 59%), m. p. 126—127°, undepressed by penta-*O*-ethylpatuletin (Found, in a specimen dried *in vacuo* at 100°: C, 66·0; H, 6·7. Calc. for $C_{26}H_{32}O_8$: C, 66·1; H, 6·8%).

Alkali Degradation of Ethyl 3 : 5 : 7 : 3′ : 4′-*Pentaethoxy*-6-*methoxyflavone*-2′-*carboxylate.*—The ester (II; R = R′ = Et) (2 g.) was hydrolysed with 20% alcoholic potassium hydroxide under the conditions used for the related methylated product (II; R = R′ = Me), and after removal of the solvent alcohol the phenolic component (0·86 g.) was precipitated with carbon dioxide. It crystallised from aqueous methanol in elongated prisms, m. p. 88—89° alone and mixed with 2-hydroxy-ω : 4 : 6-triethoxy-5-methoxyacetophenone (V; R = Et) obtained from patuletin, and the similarity of their brown ferric reactions in alcoholic solution was also observed (Found: C, 60·0; H, 7·3. Calc. for $C_{15}H_{22}O_6$: C, 60·4; H, 7·4%).

Acidification of the residual sodium hydrogen carbonate solution precipitated a solid (0·67 g.)

of which a further quantity (0·3 g.) was procured by ether-extraction of the filtrate. When crystallised from methanol–benzene it afforded elongated prisms, m. p. 192—193°, consisting of 3 : 4-*diethoxyphthalic acid* (VI; R = Et) (Found, in a specimen dried at 110° *in vacuo*: C, 56·5; H, 5·7%; equiv., 126. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·6%; equiv., 127).

2 : 4-*Di*-(o-*methoxycarbonylbenzoyl*)-ω-*methoxyresacetophenone*.—2-Methoxycarbonylbenzoyl chloride (5 g., 2·3 mols.) (Meyer, *Monatsh.*, 1901, **22**, 578) was slowly added to a cooled solution of ω-methoxyresacetophenone (2 g., 1 mol.) in pyridine (8 c.c.). After 15 hr. at room temperature the mixture was treated with 2N-hydrochloric acid (50 c.c.), and the oily product dissolved in ether (200 c.c.). The liquid was successively washed with 2N-acid (4 × 50 c.c.) and 2N-sodium carbonate, and then dried (Na_2SO_4) and evaporated. The residue crystallised from ethyl acetate–light petroleum, to give 2 : 4-*di*-(o-*methoxycarbonylbenzoyl*)-ω-*methoxyresacetophenone* (4·2 g., 76%) as prisms, m. p. 79—80° (Found: C, 64·4; H, 4·7. $C_{27}H_{22}O_{10}$ requires C, 64·0; H, 4·4%).

7-*Hydroxy*-3-*methoxyflavone*-2′-*carboxylic Acid* (VIII; R = H).—2 : 4-Di-(*o*-methoxycarbonylbenzoyl)-ω-methoxyresacetophenone (1·2 g.) was heated under reflux with pyridine (10 c.c.) and anhydrous potassium carbonate (2 g.) for 1 hr. The pyridine was then decanted and the residue treated with dilute hydrochloric acid to give a solid (0·6 g., 81%) which on crystallisation from aqueous ethanol (charcoal) yielded 7-*hydroxy*-3-*methoxyflavone*-2′-*carboxylic acid* as colourless prisms, m. p. 265—266° (Found, in a specimen dried at 110° *in vacuo*: C, 65·3; H, 4·0; OMe, 10·8. $C_{16}H_9O_5$·OMe requires C, 65·4; H, 3·9; OMe, 9·9%). The compound dissolves in aqueous sodium hydrogen carbonate to a yellow solution. It is insoluble in hydrochloric acid but in concentrated sulphuric acid it gives a yellow solution with a weak green fluorescence. With magnesium–hydrochloric acid an alcoholic solution of the flavone became yellow; sodium amalgam reduction and acidification produced no colour change.

Methyl 3 : 7-*Dimethoxyflavone*-2′-*carboxylate* (VIII; R = Me).—The flavone (VIII; R = H) (0·7 g.) was refluxed in acetone (25 c.c.) with methyl sulphate (1 c.c.) and potassium carbonate (2 g.) for 18 hr. Evaporation of the filtered solution and trituration of the residue with aqueous ammonia gave *methyl* 3 : 7-*dimethoxyflavone*-2′-*carboxylate* which crystallised from benzene–light petroleum in colourless prisms, m. p. 133—134° (Found, in a specimen dried at 100° *in vacuo*: C, 66·8; H, 4·5. $C_{19}H_{16}O_6$ requires C, 67·1; H, 4·7%).

7′-*Hydroxychromono* (3′ : 2′-3 : 4)iso*coumarin* (IX; R = H).—7-Hydroxy-3-methoxyflavone-2′-carboxylic acid (0·4 g.) was heated with acetic acid (5 c.c.) and hydriodic acid (10 c.c.; *d* 1·7) at 140° (oil-bath) for 2½ hr. Water was then added and the liquid decolorised with sulphur dioxide. The precipitated *hydroxychromono*iso*coumarin* (IX; R = H) (0·3 g., 90%) crystallised from pyridine in colourless rods, m. p. >350° (Found, in a specimen dried at 110° *in vacuo*: C, 68·4; H, 3·0. $C_{16}H_8O_5$ requires C, 68·6; H, 2·9%); light absorption in EtOH: max. at 210, 230, 278, 336, and 392 mμ; log ε 4·50, 4·42, 3·91, 4·27, and 3·37. The chromono*iso*coumarin is very sparingly soluble in organic solvents and dissolves in aqueous sodium hydroxide and in sodium carbonate to a yellow solution; reduction colour (Mg–HCl), yellow-brown, (Na–amalgam, acid), nil. Reaction with pyridine–acetic anhydride gave the *acetate* (IX; R = COMe), colourless needles (from pyridine), m. p. 272—274° (Found, in a specimen dried at 110° *in vacuo*: C, 67·2; H, 3·1. $C_{18}H_{10}O_6$ requires C, 67·1; H, 3·1%). The *methyl ether* was prepared by refluxing (IX; R = H) in acetone with methyl sulphate–potassium carbonate for 18 hr. and was obtained from the acetone solution. It crystallised from pyridine–methanol in needles, m. p. 277—278° (Found, in a specimen dried at 110° *in vacuo*: C, 69·2; H, 3·6. $C_{17}H_{10}O_5$ requires C, 69·4; H, 3·4%).

5 : 7-*Dihydroxy*-3-*methoxyflavone*-2′-*carboxylic Acid*.—ω-Methoxyphloracetophenone (3 g., 1 mol.) was treated in pyridine (10 c.c.) with 2-methoxycarbonylbenzoyl chloride (10 g., 3·3 mols.), and the product worked up as for the analogous ω-methoxyresacetophenone; after being washed in ethyl acetate solution (150 c.c.), the product was isolated as a pale yellow uncrystallisable gum (8·6 g., 83%). The presumed ω-methoxy-2 : 4 : 6-tri-(*o*-methoxycarbonylbenzoyl)phloracetophenone (8·6 g.), anhydrous potassium carbonate (15 g.), and pyridine (50 c.c.) were refluxed for 1 hr., and the residual solid was treated with acid. By solution in aqueous sodium carbonate and reprecipitation the product was obtained as a buff powder (3 g.) which by wasteful crystallisation from methanol and then from ethyl acetate afforded 5 : 7-*dihydroxy*-3-*methoxyflavone*-2′-*carboxylic acid* as bright yellow prisms, m. p. 264—265° (Found, in a specimen dried at 110° *in vacuo*: C, 62·1; H, 4·2. $C_{17}H_{12}O_7$ requires C, 62·2; H, 3·7%). In alcohol it gave a green-brown ferric reaction; reduction colour (Mg–HCl), orange. Its solution in concentrated sulphuric acid was yellow with a very slight green fluorescence.

5′ : 7′-*Dihydroxychromono*(3′ : 2′-3 : 4)iso*coumarin*.—The dihydroxymethoxyflavonecarboxylic acid (0·4 g.) of m. p. 262—263° was refluxed with acetic acid (5 c.c.) and hydriodic acid (10 c.c.; *d* 1·7) for 2 hr. and the crystalline product (0·3 g., 83%) collected from the cooled mixture. After being washed with water containing sulphur dioxide it was crystallised from pyridine–methanol; the *dihydroxychromono*iso*coumarin* formed yellow elongated prisms, m. p. >350°, darkening slightly at 330° (Found, in a specimen dried at 110° *in vacuo* : C, 64·6; H, 2·9. $C_{16}H_8O_6$ requires C, 64·9; H, 2·7%); light absorption: max. at 215, 270, 298, 330, and 358 mμ; log ε, 4·52, 4·32, 3·98, 4·02, and 3·97. Alcoholic solutions gave with ferric chloride a brown-green and with magnesium and hydrochloric acid a pink colour, and with sodium amalgam–acid, nil. With pyridine–acetic anhydride the chromono*iso*coumarin gave a *diacetate*, colourless rods, m. p. 252—253° (decomp.), from pyridine–ethyl acetate (Found, in a specimen dried at 110° *in vacuo* : C, 62·9; H, 3·6. $C_{20}H_{12}O_8$ requires C, 63·2; H, 3·2%).

2 : 3-*Dibenzyloxyanisole*.—Pyrogallol 1-monomethyl ether (50 g., 1 mol.) (*Org. Synth.*, 1946, **26**, 90), potassium carbonate (160 g., 3·25 mols.), and acetone were refluxed for 28 hr. under coal gas during the gradual addition of benzyl chloride (135 g., 3 mols), and then for a further 14 hr. The mixture was cooled, treated with water (700 c.c.), and extracted with ether (4 × 200 c.c.). The ethereal solution was washed with 2N-sodium hydroxide (2 × 200 c.c.) and evaporated, and excess of benzyl chloride removed in steam. Distillation of the residue gave 2 : 3-*dibenzyloxyanisole* as a colourless oil (88·5 g., 77·5%), b. p. 210—212°/3 mm. (Found : C, 78·2; H, 6·2. $C_{21}H_{20}O_3$ requires C, 78·7; H, 6·3%).

2 : 3-*Dibenzyloxy*-5-*nitroanisole*.—A solution of 2 : 3-dibenzyloxyanisole (40 g.) in acetic acid (200 c.c.) was treated with nitric acid (25 c.c.; *d* 1·2), and 4 hours later a further similar quantity of acid was added. The pale yellow solid, consisting of 2 : 3-*dibenzyloxy*-5-*nitroanisole* (4·4 g., 9·6%), which separated overnight, crystallised from alcohol in colourless needles, m. p. 94—95° (Found : C, 69·0; H, 5·5. $C_{21}H_{19}O_5N$ requires C, 69·0; H, 5·2%).

2-*Benzyloxy*-6-*methoxy*-1 : 4-*benzoquinone*.—The acetic acid filtrate from the foregoing experiment was diluted with water and then neutralised with solid sodium carbonate. The spongy orange mass was collected and triturated with ether, whereupon the residue crystallised, and then separated from ethanol in yellow prisms (13·3 g., 44%), m. p. 142—143°, consisting of 2-*benzyloxy*-6-*methoxy*-1 : 4-*benzoquinone* (Found : C, 68·7; H, 4·7; OMe, 12·9. $C_{11}H_{12}O_4$ requires C, 68·8; H, 5·0; OMe, 12·7%). The quinone dissolved in aqueous sodium hydroxide to a red-purple solution changed by the addition of zinc powder to yellow.

2-*Benzyloxy*-6-*methoxyquinol*.—A mixture of 2-benzyloxy-6-methoxy-1 : 4-benzoquinone (10 g.) and zinc dust (25 g.) in gently boiling alcohol was stirred with the addition during 2 hr. of sulphuric acid (20 c.c. of 25%). The hot solution was then filtered and the colourless 2-*benzyloxy*-6-*methoxyquinol* (7 g., 70%) precipitated with sulphurous acid. It crystallised from benzene in glistening plates, m. p. 156—157° (decomp.) (Found : C, 67·7; H, 5·2; OMe, 13·8. $C_{13}H_{11}O_3$·OMe requires C, 68·3; H, 5·7; OMe, 12·6%).

3-*Benzyloxy*-1 : 2 : 5-*trimethoxybenzene*.—The above quinol (3·5 g., 1 mol.) was refluxed in acetone (100 c.c.) with methyl sulphate (4 g., 2·2 mols.) and potassium carbonate (5 g.) for 21 hr. under coal gas. The material isolated by evaporation of the filtered solution was dissolved in ether and washed with alkali. Distillation of the dried product gave 3-*benzyloxy*-1 : 2 : 5-*trimethoxybenzene* as a colourless oil (3·2 g., 82%), b. p. 190—200° (air-bath temp.)/1 mm. [Found : C, 69·9; H, 6·4. $C_{13}H_9O(OMe)_3$ requires C, 70·1; H, 6·6%].

2 : 3 : 5-*Trimethoxyphenol*.—A solution of the benzyloxytrimethoxybenzene (1 g.) in alcohol was hydrogenated at room temperature and pressure with palladised charcoal (0·1 g.) as catalyst. The brown oil obtained by evaporation was dissolved in ether and shaken with 2N-sodium hydroxide. Acidification of the alkaline layer liberated an oil which distilled at 90—100° (air-bath temp.)/1 mm. and solidified, the product (0·5 g., 74%) crystallising from light petroleum (b. p. 40—60°) in colourless prisms consisting of 2 : 3 : 5-*trimethoxyphenol*, m. p. 53—54° [Found : C, 58·4; H, 6·4; OMe, 50·8. $C_6H_3O(OMe)_3$ requires C, 58·7; H, 6·6; OMe, 50·5%].

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