The Chemistry of Extractives from Hardwoods. Part XIX. The Structures of Further New Flavones occurring in Ayan* (Distemonanthus benthamianus).

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The heartwood of *Distemonanthus benthamianus*, from which ayanin (5 : 3′-dihydroxy-3 : 7 : 4′-trimethoxyflavone) was recently isolated (Part V, *J.*, 1952, 92), also contains 5 : 3′ : 5′-trihydroxy-3 : 7 : 4′-trimethoxyflavone (oxyayanin-A). Its relation to ayanin was established by synthesis of trimethyloxyayanin-A, the orientation of the unmethylated substituents in the new colouring matter being deduced from the nature of the alkali-hydrolysis products of its triethyl ether.

An isomeric flavone (oxyayanin-B) obtained from one specimen of the wood has been identified by alkali degradation of its triethyl derivative as 5 : 6 : 3′-trihydroxy-3 : 7 : 4′-trimethoxyflavone (3 : 7 : 4′-trimethylquercetagetin).

A PRELIMINARY examination of the deep yellow extracts from ayan, the wood of a W. African tree *Distemonanthus benthamianus*, has shown that they contain 5 : 3′-dihydroxy-3 : 7 : 4′-trimethoxyflavone, ayanin (I), a new trimethyl ether of quercetin (Part V, *J.*, 1952, 92). Renewed investigation of the material obtained from several batches of the wood by extraction with ether and then with acetone has resulted in the complete identification of three further constituents. The less soluble part of the two extracts corresponding to the fraction formerly described as (A) (*J.*, 1952, 94) consists of distemonanthin, a new type of flavone pigment which is the subject of the following communication.

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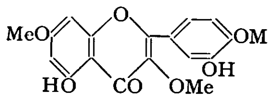
* Part XVIII, *J.*, 1954, 3995.

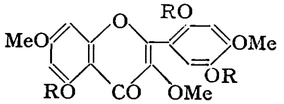
The remaining two compounds are isomers of molecular formula $C_{18}H_{16}O_8$, and since they bear a close resemblance to ayanin, differing from it merely in the location of an additional hydroxyl group, they were respectively termed oxyayanin-A and oxyayanin-B.

Oxyayanin-A (II; R = H) is present in the more soluble portion of the ether extract; the quantity isolated varied with the wood sample from 0·08 to 0·15%. It is found mixed with ayanin (yield of mixture 0·19—0·35%) from which it cannot readily be separated by crystallisation, and the impure compound was used in some of the initial experiments. Later it was observed that incomplete neutralisation of an aqueous sodium hydroxide solution of the mixed phenols caused preferential precipitation of ayanin. Alternatively, refluxing the mixture with 20% aqueous potassium hydroxide favoured the disintegration of ayanin, and pure oxyayanin-A was recovered from the product by recrystallisation.

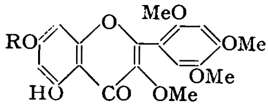
Oxyayanin-A contains three methoxyl groups (Zeisel) and yields a triacetate; indications of its flavonoid character were obtained by the usual colour reactions. A chelated hydroxyl group (position 5) was disclosed by the formation with diazomethane of a dimethyl ether (III; R = Me) exhibiting a pronounced ferric reaction, and of a trimethyl ether (II; R = Me) by prolonged treatment with methyl sulphate and potassium carbonate. The action of boiling alcoholic potassium hydroxide on oxyayanin-A trimethyl ether accomplished its hydrolysis into 2-hydroxy-ω : 4 : 6-trimethoxyacetophenone (IV; R = Me) and asarylic acid (2 : 4 : 5-trimethoxybenzoic acid) (V; R = Me); a small quantity of asarylic acid was also obtained by oxidation of the trimethyl ether with potassium permanganate. Thus the constitution of oxyayanin-A trimethyl ether is established as 3 : 5 : 7 : 2′ : 4′ : 5′-hexamethoxyflavone (II; R = Me) and that of oxyayanin-A as the trimethyl ether of a new hexahydroxyflavone. The structure of the ether (II; R = Me) was confirmed by its synthesis using the Allan–Robinson method, from ω-methoxyphloracetophenone and asarylic anhydride–sodium asarylate; a previous attempt by Watson (*J.*, 1914, **105**, 338; see also Perkin and Watson, *ibid.*, 1915, **107**, 198) to prepare it from pentamethylquercetin, *via* the 6′-nitro-derivative, was unsuccessful. The condensation product, which after alkali treatment consisted of (III; R = H), afforded either oxyayanin-A dimethyl ether (III; R = Me) or the trimethyl ether (II; R = Me) when methylated with methyl sulphate–potassium carbonate under the appropriate conditions.



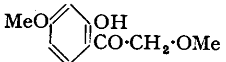
(I) Ayanin



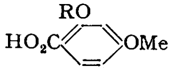
(II) Oxyayanin-A (R = H)



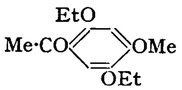
(III)



(IV)



(V)

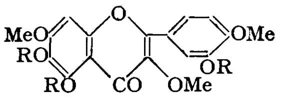


(VI)

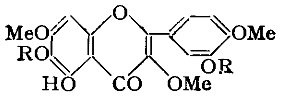
The disposition of the hydroxyl groups in oxyananin-A was determined in the usual way, *i.e.*, by ethylation followed by hydrolysis with alcoholic alkali. Both degradation products were new, but from the evidence already acquired were known to be derivatives of ω-hydroxyphloracetophenone and of 2 : 4 : 5-trihydroxybenzoic acid respectively. The presence in the parent compound of a 5-hydroxyl group thus enables the ketonic compound to be defined as 2-ethoxy-6-hydroxy-ω : 4-dimethoxyacetophenone (IV; R = Et). The accompanying product, a diethoxymethoxybenzoic acid, was identified by synthesis as (V; R = Et), the presence in ayanin of a methoxyl group at the 4′-position determining the choice of this as the most likely of the three possible stuctures. The preparation of the ether (V; R = Et) began with alkylation of methoxyquinol, by ethyl sulphate and potassium carbonate in acetone, to 2 : 5-diethoxyanisole which was converted by a Friedel–Crafts reaction into 2 : 5-diethoxy-4-methoxyacetophenone (VI). The desired acid (V; R = Et) was thereafter obtained by oxidation, first with potassium permanganate and then with alkaline hydrogen peroxide, identity of the specimens of natural and synthetic origin being confirmed by means also of their methyl and *p*-bromophenacyl esters. The constitution of oxyayanin-A as 5 : 2′ : 5′-trihydroxy-3 : 7 : 4′-trimethoxyflavone (6′-hydroxyayanin) (II; R = H) is thus rigidly established.

Of the six batches of ayan used in this investigation, one was remarkable for the large amount (>6%) of its ether extract and for its failure to yield distemonanthin. From a methanol solution of his extract, after the mixture of ayanin and oxyayanin-A had been removed, the isomeric oxyayanin-B (yield 0·67% of the wood) gradually separated. Its recognition as a position isomer of oxyayanin-A followed from a determination of the methoxyl content and from the preparation of derivatives, *e.g.*, a triacetate. Certain colour reactions were suggestive of a possible relation to quercetagetin (3 : 5 : 6 : 7 : 3′ : 4′-hexahydroxyflavone), and this was substantiated when the complete methylation of oxyayanin-B (with methyl sulphate–potassium carbonate) afforded quercetagetin hexamethyl ether (VII; R = Me). By the action of diazomethane, on the other hand, the pentamethyl ether (VIII; R = Me) of quercetagetin was obtained, thereby showing that the 5-substituent of oxyayanin-B was unmethylated. The chloro-pentamminocobaltic chloride test for *ortho*- or *para*-dihydroxy-groups (Sashina, Asano, and Ueno, *Bull. Chem. Soc. Japan*, 1942, **17**, 104) was positive for oxyayanin-B, denoting the existence of phenolic groups at the 5 : 6-, 6 : 7- (hence 5 : 6 : 7-), or 3′ : 4′-positions. From the absence of the 3100-Å absorption band characteristic of the flavanol-hydroxyl group the substituent at position 3 was assumed to be methylated (Skarzynski, *Biochem. Z.*, 1939, **301**, 150).

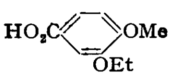
The action of ethyl sulphate–potassium carbonate on oxyayanin-B yielded a mixture of di- and tri-ethyl ethers, and the situation of the remaining methoxyl groups was disclosed by the appearance of 3-ethoxy-4-methoxybenzoic acid (IX) among the alcoholic-alkali degradation products of both ethyl derivatives. From these results it was possible to assign a complete structure, namely, (VII; R = H), to oxyayanin-B; consequently its di- and tri-ethyl ethers are respectively (VIII; R = Et) and (VII; R = Et). The ketonic product obtained with the acid (IX), from the decomposition of oxyayanin-B triethyl ether, had not previously been described, but with the acceptance of (VII; R = H) as the constitution of the parent flavone it becomes identifiable as 2 : 3-diethoxy-6-hydroxy-ω : 4-dimethoxyacetophenone (X).



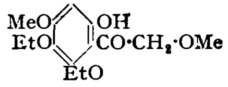
(VII) Oxyayanin-B (R = H)



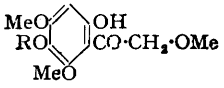
(VIII)



(IX)



(X)



(XI)

Oxyayanin-B diethyl ether (VIII; R = Et) yields a monomethyl ether hydrolysed with boiling alcoholic alkali to the acid (IX) and a new ketone which is presumably (XI; R = Et). The latter stucture was proved by preparation of the ketone from 2 : 5-dihydroxy-ω : 4 : 6-trimethoxyacetophenone (XI; R = H) (Row and Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 23), the monoethyl derivative obtained from the latter by using a limited amount of ethyl iodide–potassium carbonate being identical with the degradation product designated (XI; R = Et). The structures of the flavone mixed ethers are thus substantiated and oxyayanin-B fully identified as the 6-hydroxy-derivative of ayanin.

Experimental

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

Isolation of the Extractable Contituents of Ayan.—In view of the small quantity of material obtained by means of light petroleum (see *J.*, 1952, 94), this preliminary treatment was omitted and the finely ground wood was extracted in batches of 3·8 kg. with boiling ether for 18 hr.

The yellow solid (55—101 g.) which had then separated was collected and heated under reflux with methanol (400—800 c.c.); the solid remaining undissolved was identical with the substance described in Part V (*J.*, 1952, 94) as (A) and consisted of crude distemonanthin (4·9—6·9 g., 0·13—0·18%). The methanol solution was concentrated to 50% of its original volume and set aside at room temperature for 2 weeks. The crystalline deposit (0·19—0·35%) consisted of a mixture (M) of ayanin and oxyayanin-A which after repeated crystallisation formed deep yellow prisms, m. p. 215—217° (Found, in a sample dried at 100° *in vacuo* : C, 61·2; H, 4·7; OMe, 24·8%).

The ether-exhausted wood was then extracted with boiling acetone for 18 hr. and a yellowish-brown friable solid (212—255 g.) isolated by evaporating the acetone solution. When this was dissolved in 1 : 1 (v/v) pyridine–methanol (2 c.c./g.) and kept at 0°, the crystalline material slowly deposited during 7 weeks consisted of distemonanthin (0·41—0·52%).

The mixture M, with acetic anhydride–pyridine, yielded, after several crystallisations from ethyl acetate–light petroleum, ayanin diacetate as plates (*J.*, 1952, 94), m. p. and mixed m. p. 176—177° (Found, in a sample dried at 110° *in vacuo* : C, 61·9; H, 4·8; OMe, 22·1; OAc, 20·7. Calc. for $C_{22}H_{20}O_9$: C, 61·7; H, 4·7; OMe, 21·7; OAc, 20·1%). Methylation, on the other hand, with methyl sulphate–potassium carbonate in acetone for 18 hr., and repeated crystallisation of the product from methanol gave 3 : 5 : 7 : 2′ : 4′ : 5′-*hexamethoxyflavone* (*tri-O-methyloxyayanin-A*) (II; R = Me), m. p. 195—196°, after slight sintering at 186° [Found, in a sample dried at 110° *in vacuo* : C, 62·5; H, 5·5; OMe, 45·3%; *M* (Rast) 409. $C_{15}H_4O_2(OMe)_6$ requires C, 62·7; H, 5·5; OMe, 46·3%), *M*, 402].

Ayanin (I) *and Oxyayanin-A* (II; R = H).—(i) The mixture M (0·4 g.) was dissolved in 2N-sodium hydroxide and incompletely precipitated by a limited quantity of carbon dioxide. Repeated crystallisation of the product from methanol gave ayanin (0·1 g.) as yellow plates m. p. and mixed m. p. 172—173°. Saturation with carbon dioxide thereafter gave only a limited amount of difficulty crystallisable material.

(ii) A solution of M (4 g.) in 20% aqueous potassium hydroxide (50 c.c.) was heated under reflux for 4 hr., then diluted with water (100 c.c.) and saturated with carbon dioxide. Repeated crystallisation of the precipitated solid from acetic acid afforded 5 : 2′ : 5′-*trihydroxy*-3 : 7 : 4′-*trimethoxyflavone* (*oxyayanin-A*) as yellow needles (1·1 g.), m. p. 229—230° [Found, in a sample dried at 110° *in vacuo* : C, 60·3; H, 4·5; OMe, 23·9. $C_{15}H_7O_5(OMe)_3$ requires C, 60·0; H, 4·5; OMe, 25·8%]; light absorption in EtOH : max. at 2580 (log ε 4·06), 3020 (log ε 3·74), and 3490 Å (log ε 3·49).

Oxyayanin-A dissolves in aqueous sodium hydroxide and carbonate, but not in sodium hydrogen carbonate, to orange solutions, and forms a bright yellow solution in concentrated hydrochloric acid. Its ferric reaction is brownish-green. With magnesium and hydrochloric acid, or with sodium amalgam followed by acid, its alcoholic solution was coloured red. Warming with alkali gave a dark brown solution restored to orange-yellow by the addition of zinc dust.

With pyridine–acetic anhydride oxyayanin-A formed 5 : 2′ : 5′-*triacetoxy*-3 : 7 : 4′-*trimethoxyflavone* which crystallised from methanol in colourless prisms, m. p. 183—184° (Found, in a sample dried at 110° *in vacuo* : C, 59·2; H, 4·4; OMe, 18·7; OAc, 26·5. $C_{42}H_{22}O_{11}$ requires C, 59·3; H, 4·6; OMe, 19·1; OAc, 26·6%).

5-*Hydroxy*-3 : 7 : 2′ : 4′ : 5′-*pentamethoxyflavone* (III; R = Me).—A solution of oxyayanin-A (0·15 g.) in methanol (30 c.c.) mixed with excess of ethereal diazomethane was kept at 0° for 2 days. Evaporation and crystallisation of the residue from methanol gave a small amount of tri-*O*-methyloxyayanin-A, m. p. and mixed m. p. 193—194°. The combined methanol filtrates were evaporated to *ca.* 2 c.c. and mixed with ether (50 c.c.), the solution then being extracted with 2N-sodium hydroxide (3 × 25 c.c.). 5-*Hydroxy*-3 : 7 : 2′ : 4′ : 5′-*pentamethoxyflavone* was obtained from the aqueous solutions by acidification and extraction with ether; it separated from methanol in pale yellow elongated prisms, m. p. 149—150° [Found, in a sample dried at 100° *in vacuo* : C, 61·6; H, 4·8; OMe, 41·0. $C_{15}H_5O_8(OMe)_5$ requires C, 61·9; H, 5·2; OMe, 40·0%]. An alcoholic solution became brownish-green with ferric chloride.

Alkali Degradation of Trimethyloxyayanin-A.—The incompletely purified hexamethoxyflavone (II; R = Me) (2 g.) was heated under reflux for 8 hr. with potassium hydroxide (10 g.) in water (10 c.c.) and ethanol (40 c.c.). The crystalline solid deposited from the cold mixture was collected and dissolved in water (10 c.c.), and its solution saturated with carbon dioxide. The colourless precipitate (0·64 g.), when crystallised from alcohol, afforded 2-hydroxy-ω : 4 : 6-trimethoxyacetophenone (IV; R = Me) in prisms, m. p. 103—104° alone or mixed with a sample prepared by Row and Seshadri's method (*loc. cit.*) [Found : C, 58·3; H, 6·5; OMe, 40·2%;

M (Rast), 218. Calc. for $C_6H_5O_2(OMe)_3$: C, 58·4; H, 6·2; OMe, 41·2%; *M*, 226]. The ferric reaction in alcohol was wine-red. The ketoxime crystallised in needles, m. p. and mixed m. p. 147—148·5° (decomp.) (Found : C, 55·1; H, 6·6; N, 5·9. Calc. for $C_{11}H_{15}O_5N$: C, 54·8; H, 6·3; N, 5·8%).

The residual hydrogen carbonate solution was washed with ether and acidified, and thereby afforded a colourless solid (0·27 g.). Crystallised from benzene–light petroleum it afforded asarylic acid (V; R = Me) as needles, m. p. and mixed m. p. 143—144° [Found, in a sample dried at 100° *in vacuo* : C, 56·6; H, 5·8; OMe, 43·5%; equiv., 217. Calc. for $C_7H_3O_2(OMe)_3$: C, 56·6; H, 5·7; OMe, 43·9%; equiv., 212]. A solution of the acid in methanol with ethereal diazomethane yielded the methyl ester, crystallising from methanol in blades, m. p. and mixed m. p. 92—94° (Found : C, 58·7; H, 5·8. Calc. for $C_{11}H_{14}O_5$: C, 58·4; H, 6·2%).

The alcoholic alkaline filtrate from the degradation was evaporated, the residue was dissolved in water, and the mixed products were partitioned as above with ether–sodium hydrogen carbonate. The phenolic component consisted of a small amount of 2-hydroxy-ω : 4 : 6-trimethoxyacetophenone, prisms (from alcohol), m. p. and mixed m. p. 101—102·5°, and the hydrogen carbonate-soluble portion was veratric acid, m. p., after crystallisation from benzene–light petroleum, and mixed m. p. 179—180°.

Oxidation of Trimethyloxyayanin-A.—The hexamethoxyflavone (II; R = Me) (0·5 g.) and powdered potassium permanganate (2 g.) were heated in refluxing acetone (100 c.c.) for 8 hr. The solvent was then largely evaporated, water (50 c.c.) was added, and the mixture saturated with sulphur dioxide. The solution was extracted with ether (3 × 50 c.c.) and the products therein were separated by shaking with aqueous sodium hydrogen carbonate. The acidic portion, isolated from the carbonate solution by acidification and ether-extraction, was esterified in methanol with diazomethane. The product, a pale yellow oil, b. p. 140—150° (bath-temp.)/1 mm., crystallised from light petroleum in blades, m. p. 90—92° alone or mixed with methyl asarylate. The non-acidic material then obtained from the carbonate-washed ether extract consisted only of unoxidised hexamethoxyflavone (II; R = Me).

Asarylic Anhydride.—Asarylic acid was prepared in improved yield (4·95 g., 49%) by the oxidation of 2 : 4 : 5-trimethoxyacetophenone (10 g.) with potassium permanganate (22·5 g., 3 mols.) in water (120 c.c.), and then with hydrogen peroxide, without isolation of the intermediate glyoxylic acid (cf. Smith and Haller, *J. Amer. Chem. Soc.*, 1934, **56**, 238), the product crystallising from the acidified mixture after cooling. The acid chloride (Haraszti, *Chem. Abstr.*, 1931, **25**, 5154) from 13·4 g. acid was suspended in ether (100 c.c.) and gradually treated with pyridine (20 g.); several hours later the mixture was treated with ice and water, and the sparingly-soluble anhydride collected, washed, and dried over phosphoric oxide, having m. p. without crystallisation 140—142° (yield 8·5 g., 66%) [Found : C, 59·4; H, 5·2; OMe, 47·2. Calc. for $C_{14}H_4O_3(OMe)_6$: C, 59·1; H, 5·5; OMe, 45·8%].

5 : 7-*Dihydroxy*-3 : 2′ : 4′ : 5′-*tetramethoxyflavone* (III; R = H).—A mixture of ω-methoxyphloracetophenone (1·1 g., 1 mol.), asarylic anhydride (4·5 g., 2·3 mols.), and potassium asarylate (1·8 g., 1·5 mols.) was heated at 180°/13 mm. for 4 hr. The product was refluxed for 30 min. with potassium hydroxide (2·5 g.) in water (3 c.c.) and alcohol (30 c.c.). The deposit of potassium asarylate was removed from the cold liquid, and the filtrate and alcohol washings were evaporated, the residue being dissolved in water and saturated with carbon dioxide. 5 : 7-*Dihydroxy*-3 : 2′ : 4′ : 5′-*tetramethoxyflavone* (1·9 g., 91%) was thus liberated, and by repeated crystallisation from pyridine–methanol was obtained as pale yellow plates, m. p. 264—265° [Found, in a sample dried at 110° *in vacuo* : C, 60·6; H, 4·8; OMe, 33·3. $C_{15}H_6O_4(OMe)_4$ requires C, 61·0; H, 4·9; OMe, 33·2%].

5-*Hydroxy*-3 : 7 : 2′ : 4′ : 5′-*pentamethoxyflavone* (III; R = Me).—Treatment of the flavone (III; R = H) (0·5 g., 1 mol.) with methyl sulphate (0·185 g., 1·1 mols.) and potassium carbonate (1 g.) in acetone (50 c.c.) under reflux for 4 hr. gave as the acetone-soluble product, 5-*hydroxy*-3 : 7 : 2′ : 4′ : 5′-*pentamethoxyflavone* which crystallised from methanol in pale yellow elongated prisms, m. p. 149—150° [Found, in a sample dried at 100° *in vacuo* : C, 61·9; H, 5·1; OMe, 40·9. $C_{15}H_5O_3(OMe)_5$ requires C, 61·9; H, 5·2; OMe, 40·0%]. Its solution in alcohol was coloured brownish-green with ferric chloride.

3 : 5 : 7 : 2′ : 4′ : 5′-*Hexamethoxyflavone* (*Tri*-O-*methyloxyayanin-A*) (II; R = Me).—5 : 7-Dihydroxy-3 : 2′ : 4′ : 5′-tetramethoxyflavone (2 g., 1 mol.) was heated under reflux for 16 hr. with methyl sulphate (1·6 g., 2·4 mols.) and potassium carbonate (5 g.) in acetone (100 c.c.). From the filtered solution the *hexamethoxy-flavone* (II; R = Me) was obtained as prisms which crystallised from methanol and had m. p. 195—196° (slight sintering at 186°) alone or mixed with tri-*O*-methyloxyayanin-A [Found : C, 60·8; H, 5·6; OMe, 43·9; loss at 140° *in vacuo*,

6·9. $C_{15}H_4O_2(OMe)_6$,MeOH requires C, 60·8; H, 6·0; OMe, 42·9; loss, 7·4%. Found, in the dried sample: C, 62·9; H, 5·4; OMe, 44·9%].

Triethyloxyayanin-A (II; R = Et).—The acetone-soluble product obtained by refluxing oxyayanin-A (1 g., 1 mol.), ethyl sulphate (1·7 g., 4 mols.), and potassium carbonate (5 g.) in acetone (100 c.c.) for 48 hr. consisted of *tri-O-ethyloxyayanin-A* (0·9 g.) which crystallised from benzene–light petroleum in prisms, m. p. 78—79° (Found, in a sample dried at 80° *in vacuo*: C, 65·0; H, 6·5. $C_{24}H_{28}O_8$ requires C, 64·9; H, 6·4%).

Alkali Degradation of Triethyloxyayanin-A.—By refluxing the triethyl derivative (II; R = Et) (0·75 g.) for 8 hr. with alcohol (20 c.c.) containing potassium hydroxide (4 g.) a solid was obtained as in the corresponding experiment with the trimethyl ether. The portion precipitated from its aqueous solution with carbon dioxide consisted of *2-ethoxy-6-hydroxy-ω : 4-dimethoxyacetophenone* (IV; R = Et) (0·23 g.) which crystallised from light petroleum in long rectangular plates, m. p. 109—110°, exhibiting in alcohol a red-brown ferric reaction (Found: C, 60·0; H, 6·5. $C_{12}H_{16}O_5$ requires C, 60·0; H, 6·7%). The product remaining in the hydrogen carbonate solution was *2 : 5-diethoxy-4-methoxybenzoic acid* (V; R = Et); it formed glistening hexagonal plates, m. p. 155—156°, from ethanol (Found, in a sample dried at 100° *in vacuo*: C, 60·1; H, 7·0. $C_{12}H_{16}O_5$ requires C, 60·0; H, 6·7%). A methanolic solution of the acid with diazomethane afforded the *methyl ester*, plates (from light petroleum), m. p. 93—95° (Found: C, 61·4; H, 7·4. $C_{13}H_{18}O_5$ requires C, 61·4; H, 7·1%). The *p-bromophenacyl ester*, fluffy needles from aqueous ethanol, had m. p. 115—116° (Found: C, 53·6; H, 5·0; Br, 18·5. $C_{20}H_{21}O_6Br,\frac{1}{2}H_2O$ requires C, 53·8; H, 5·0; Br, 17·9%).

2 : 5-*Diethoxyanisole.*—Methoxyquinol (35 g., 1 mol.), ethyl sulphate (85 g., 2·2 mols.), and potassium carbonate (85 g.) were refluxed in acetone (400 c.c.) for 24 hr. The liquid isolated from the acetone solution was taken up in ether, washed with 2N-sodium hydroxide and water, dried, and distilled. The fraction, b. p. 148—152°/17 mm., solidified to a colourless solid (27 g. 55%), m. p. 43—45°. Recrystallised from light petroleum (b. p. 40—60°), the *diethoxyanisole* formed leaflets, m. p. 44—45° (Found: C, 67·5; H, 8·0. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

2 : 5-*Diethoxy-4-methoxyacetophenone* (VI).—A solution of 2 : 5-diethoxyanisole (24 g.) and acetyl chloride (10·5 g.) in carbon disulphide (40 c.c.) was cooled in ice-salt and treated gradually with aluminium chloride (22 g.). The product obtained after 46 hr. at 0° by treatment with ice–dilute hydrochloric acid was crystallised from aqueous ethanol and thus afforded the *ketone* (VI) as silky needles (20·9 g., 72%), m. p. 103—104°, raised by recrystallisation to 104—104·5° (Found, in a sample dried at 80° *in vacuo*: C, 65·3; H, 7·8. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%).

2 : 5-*Diethoxy-4-methoxybenzoic Acid* (V; R = Et).—The ketone (VI) (20 g.), mixed with water (200 c.c.) and heated on a steam-bath, was gradually treated with potassium permanganate (30 g.) during 2 hr. The insoluble matter was suspended in water and saturated with sulphur dioxide, and the solution filtered from unchanged ketone (13·8 g.). The filtrate was concentrated and acidified, whereby a pale yellow solid (3 g.), presumably the phenylglyoxylic acid, was precipitated. This was dissolved in 10% aqueous potassium hydroxide (15 c.c.) at 60° and treated with 30% hydrogen peroxide (6 c.c.). Finally, after boiling, the liquid was cooled and acidified, *2 : 5-diethoxy-4-methoxybenzoic acid* (V; R = Et) (2·5 g., yield on ketone oxidised, 12·4%) being obtained; it had m. p. and mixed m. p. with the acid derived from (II; R = Et), 155—156° (Found, in a dried sample: C, 59·7; H, 6·7%). The *methyl ester*, plates from light petroleum, had m. p. and mixed m. p. 94—95° (Found: C, 61·3; H, 7·0%), and the *p-bromophenacyl ester*, fluffy needles from aqueous ethanol, had m. p. and mixed m. p. 115—116° (Found: C, 53·9; H, 5·0; Br, 18·0; loss at 100° *in vacuo*, 2·0. $C_{20}H_{21}O_6Br,\frac{1}{2}H_2O$ requires loss, 2·0%. Found, in dried sample: C, 55·0; H, 5·0. $C_{20}H_{21}O_6Br$ requires C, 54·9; H, 4·8%).

Oxyayanin-B (VII; R = H).—A specimen of ayan (3·5 kg.) from which were obtained an abnormally high quantity of ether-soluble material (212 g.) and an acetone extract of 305 g., failed to yield distemonanthin when these products were digested with boiling methanol. In the case of the ether extract, both the undissolved yellow solid and that deposited from the methanolic solution during 18 days at room temperature consisted of mixtures of ayanin and oxyayanin-A, but further material which had appeared after several weeks consisted of crude *oxyayin-B* (31·4 g., 0·9%). When recrystallised from acetic acid it formed pale yellow needles (23·5 g.), m. p. 208—209° [Found, in a sample dried at 110° *in vacuo*: C, 60·0; H, 4·7; OMe, 23·8. $C_{15}H_7O_5(OMe)_3$ requires C, 60·0; H, 4·5; OMe, 25·8%]; light absorption in EtOH: max. at 2150 (log ε 4·54), 2410 (log ε 4·22), 2560 (log ε 4·25), 2820 (log ε 4·28), and 3480 Å. (log ε 4·36).

Oxyayanin-B dissolves in concentrated hydrochloric acid and in sulphuric acid to yellow solutions. In alcohol with magnesium–hydrochloric acid a crimson colour appears; the lack of colour change after alkaline reduction is attributed to precipitation by the solvent of the sodium salt. The flavone gives a green solution with aqueous sodium carbonate which becomes orange readily when heated. The deep yellow solution in sodium hydroxide becomes dark brown when shaken in air, and yellow again upon the addition of zinc dust. Quercetagetin is reported (Perkin, *J.*, 1913, **103**, 209) to be green in alkali, turning to brown. Moreover, oxyayanin-B dissolved in alcohol yields a green flocculent precipitate with sodium amalgam (Bargellini test, *Gazzetta*, 1919, **49**, 47; cf. Marini-Bettolo and Ballio, *ibid.*, 1946, **76**, 410). Its ferric reaction in alcohol is brown-green. A solution of the flavone in alcohol was coloured dark brown by chloropentamminocobaltic chloride.

Triacetyloxyayanin-B, prepared with acetic anhydride–pyridine, crystallised from ethyl acetate as colourless plates, m. p. 214—216° (Found, in a specimen dried at 100° *in vacuo*: C, 58·9; H, 4·7. $C_{24}H_{22}O_{11}$ requires C, 59·3; H, 4·6%).

3 : 5 : 6 : 7 : 3′ : 4′-*Hexamethoxyflavone* (*Tri*-O-*methyloxyayanin-B*) (VII; R = Me).—A mixture of oxyayanin-B (0·5 g.), methyl sulphate (0·75 g.), potassium carbonate (2·5 g.), and acetone (75 c.c.), when refluxed for 18 hr., filtered, and then evaporated to dryness, yielded a gum which solidified on trituration with aqueous ammonia. Crystallisation of the residue from benzene–light petroleum gave elongated prisms, m. p. 141—142°, alone or mixed with (α)-hexa-*O*-methylquercetagetin (Found, in a sample dried at 100° *in vacuo*: C, 62·3; H, 5·6. Calc. for $C_{21}H_{22}O_8$: C, 62·7; H, 5·5%).

5-*Hydroxy*-3 : 6 : 7 : 3′ : 4′-*pentamethoxyflavone* (*Di*-O-*methyloxyayanin-B*) (VIII; R = Me).—The solid which separated from a solution containing oxyayanin-B (0·5 g.), methanol (30 c.c.) and diazomethane in ether (30 c.c.) after 18 hr. at 0° was identical with 3 : 6 : 7 : 3′ : 4′-penta-*O*-methylquercetagetin, long pale yellow silky needles, m. p. and mixed m. p. 158—159° (Found, in a sample dried at 100° *in vacuo*: C, 62·0; H, 5·4. Calc. for $C_{20}H_{20}O_8$: C, 61·9; H, 5·2%).

Ethylation of Oxyayanin-B.—The flavone (2·5 g.), ethyl sulphate (5 g.), potassium carbonate (10 g.), and acetone (120 c.c.) were refluxed for 18 hr., and the insoluble material containing the red alkali salt of the flavone diethyl ether collected and treated with dilute hydrochloric acid. The residue (1·4 g., 48%) was then crystallised from methanol, thus affording *di*-O-*ethyloxyayanin-B* (VIII; R = Et) as yellow elongated prisms, m. p. 142—143°, exhibiting a brown-green ferric reaction (Found, in a sample dried at 100° *in vacuo*: C, 63·4; H, 5·8. $C_{22}H_{24}O_8$ requires C, 63·5; H, 5·8%). Prolonged methylation of (VIII; R = Et) (1 g.) with methyl sulphate–potassium carbonate resulted in *di*-O-*ethyl*-O-*methyloxyayanin-B* (0·95 g.), prisms (from benzene–light petroleum), m. p. 130° (Found, in a sample dried at 100° *in vacuo*: C, 64·0; H, 6·3. $C_{23}H_{26}O_8$ requires C, 64·2; H, 6·1%).

The filtered acetone solution and washings were evaporated, and when stirred with aqueous alkali gave *tri*-O-*ethyloxyayanin-B* (VII; R = Et) as a colourless solid (0·9 g., 27%). It crystallised from benzene–light petroleum in glistening plates, m. p. 124—125° (Found, in a sample dried at 80° *in vacuo*: C, 64·8; H, 6·5. $C_{24}H_{28}O_8$ requires C, 64·9; H, 6·4%).

Alkali Degradation of Triethyloxyayanin-B.—The products obtained by refluxing for 7 hr. the flavone (VII; R = Et) (1 g.) with a solution of potassium hydroxide (2 g.) in water (2 c.c.) and alcohol (10 c.c.) were separated, after evaporation under reduced pressure and addition of water (25 c.c.), by saturating the resulting solution with carbon dioxide. The crystalline precipitate (0·46 g.) was collected and residual traces were removed from the filtrate with ether. Crystallisation of the substance from light petroleum yielded glistening flat prisms, m. p. 79—80°, giving a brown ferric reaction and consisting of 2 : 3-*diethoxy*-6-*hydroxy*-ω : 4-*dimethoxyacetophenone* (X) (Found: C, 59·5; H, 7·15. $C_{14}H_{20}O_6$ requires C, 59·1; H, 7·1%).

The component remaining in the sodium hydrogen carbonate solution was 3-ethoxy-4-methoxybenzoic acid (IX) which crystallised from aqueous methanol in glistening elongated plates, m. p. and mixed m. p. 163—164° (Found, in a sample dried at 100° *in vacuo*: C, 61·4; H, 6·2%; equiv., 200. Calc. for $C_{10}H_{12}O_4$: C, 61·2; H, 6·2%; equiv., 196).

Alkali Degradation of Di-O-*ethyl*-O-*methyloxyayanin-B.*—Under conditions similar to those used for (VII; R = Et), this ether (0·5 g.) afforded (*a*) 5-*ethoxy*-2-*hydroxy*-ω : 4 : 6-*trimethoxyacetophenone* (XI; R = Et) (0·23 g.), elongated prisms from light petroleum, m. p. 78—79° (Found: C, 58·2; H, 6·9. $C_{13}H_{18}O_6$ requires C, 57·8; H, 6·7%), and (*b*) 3-ethoxy-4-methoxybenzoic acid (0·22 g.), m. p. and mixed m. p. 163—164°.

5-*Ethoxy*-2-*hydroxy*-ω : 4 : 6-*trimethoxyacetophenone* (XI; R = Et).—By refluxing for 18 hr. the dihydroxydimethoxyacetophenone (XI; R = H) (Row and Seshadri, *loc. cit.*) (0·5 g., 1 mol.) with ethyl iodide (0·36 g., 1·1 mols.) and potassium carbonate (1 g.) in acetone (30 c.c.), and isolating the portion soluble in 2N-sodium hydroxide, the 5-*ethyl ether* (XI; R = Et) was obtained. It crystallised from light petroleum (charcoal) in elongated prisms, m. p. and mixed m. p. with the specimen derived from diethylmethyloxyayanin-B 78—79°; both samples exhibited in alcohol solution the identical brown colour with ferric chloride (Found: C, 57·9; H, 6·7%).

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