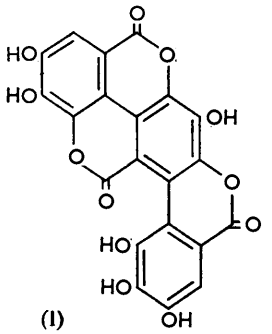
813. *Flavogallol.*

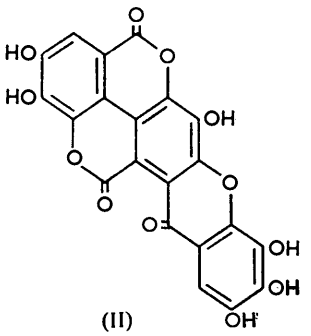
By J. GRIMSHAW and R. D. HAWORTH.

Structure (I), considered but rejected by earlier workers, is now proposed for flavogallol. The properties of the compound are satisfactorily accounted for on the basis of this structure (I) which has been confirmed by rational synthesis.

DURING experiments on the oxidation of hydroxybenzoic acids, Bleuler and A. G. Perkin [1] isolated flavogallol from the products of the action of arsenic acid on gallic acid in sulphuric acid solution, and made an extensive study of its reactions. Flavogallol is a hexahydric phenol of molecular formula, $C_{21}H_8O_{12}$, characterised as the hexa-acetate, the hexabenzoate, and, in the present work, the hexamethyl ether. Bleuler and Perkin concluded that flavogallol contained two lactone groups, and as ellagic acid is a by-product of its formation they suggested that flavogallol possessed structure (I) or (II). In their view, structure (II) accorded better with its properties but until now no further evidence has been brought forward to support either formulation.

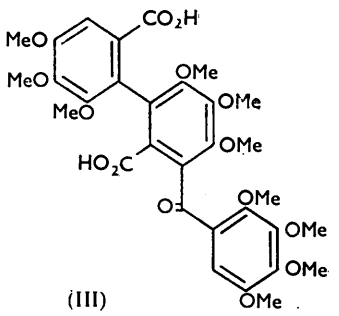


(I)

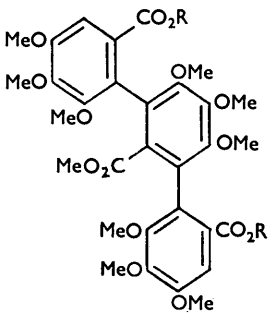


(II)

Evidence for the presence of two lactone rings was obtained by exhaustive treatment of flavogallol with methyl sulphate and an excess of aqueous alkali. This afforded two isomeric acids, $C_{19}H_2O(OMe)_{10}(CO_2H)_2$, further characterised as their dimethyl esters. The acids were not readily interconverted but on demethylation both gave flavogallol, identified as its hexa-acetate. Bleuler and Perkin considered that structure (I) would give a tribasic acid containing nine methoxyl groups and therefore concluded that this evidence



(III)



(IV)

supported structure (II), from which a dibasic acid (III) containing ten methoxyl groups would be expected if the reaction conditions may be assumed to be sufficiently vigorous to rupture the phenolic ether link. Their objection to formula (I) is however invalid, for the

[1] Bleuler and Perkin, *J.*, 1916, **109**, 529.

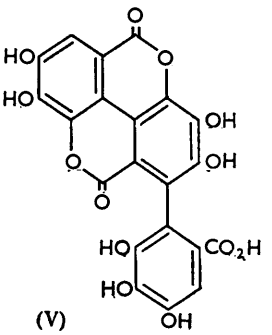
product here would be expected to be the dibasic acid (IV; R = H) because of the difficulty of hydrolysis of 2 : 6-disubstituted benzoic esters. The difficulty of hydrolysis and re-esterification of such benzoic esters is well known, and later two cases closely analogous to (IV) will be cited. Derivatives of the acid (IV) can exist in *meso*- and racemic forms, owing to restricted rotation about the diphenyl links, thus explaining the isomerisation encountered.

One of the lactone rings in flavogallol is extremely unstable and may be opened under conditions which do not affect coumarin itself. Bleuler and Perkin termed the resulting parent compound, $C_{20}H_2O_4(OH)_7 \cdot CO_2H$, flavogallonic acid, and its decarboxylation product flavogallone. Flavogallonic acid was re-lactonised only on dissolution in sulphuric acid or on acetylation, when it furnished hexa-*O*-acetylflavogallol. Acetylation of flavogallonic esters gave the corresponding esters of hepta-*O*-acetylflavogallonic acid and we have now prepared methyl hepta-*O*-methylflavogallonate. An explanation of this instability is not readily apparent from structure (II). However, the steric crowding of structure (I) will result in the non-planar arrangement of one lactone ring which in consequence will be weakened, and give rise to structure (V) for flavogallonic acid containing an unstrained arrangement of lactone rings.

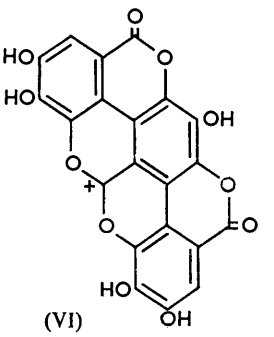
Besides giving a series of alkali-metal salts, flavogallol also behaved as an anhydro-base, yielding the orange, crystalline anhydro-hydrogen sulphate on treatment with sulphuric acid in acetic acid, according to the equation :

$$C_{21}H_8O_{12} + H_2SO_4 \longrightarrow C_{21}H_7O_{11} \cdot HSO_4 + H_2O$$

Ellagic acid does not behave in an analogous manner and consequently Bleuler and Perkin considered that this reaction could not be accommodated on structure (I). In their view it could only be accounted for on the xanthone structure (II); they overlooked the fact, however, that xanthone salts are formed without the elimination of a molecule of water demanded to satisfy the analytical data on flavogallol anhydro-hydrogen sulphate. Structure (I) may, however, function as an anhydro-base, affording the cation (VI) which is completely planar and therefore stabilised as a resonance hybrid to which a number of canonical forms may be regarded as contributing [only one is shown in (VI)].



(V)



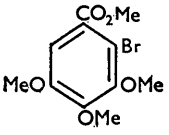
(VI)

Evidently more information was required in order to settle the constitution of flavogallol. For this re-investigation considerable difficulty was experienced in repeating the original preparation of flavogallol. Here Bleuler and Perkin's paper is incoherent—possibly part of the text is missing—and we record in the Experimental section a method for preparing the compound from gallic acid. Whilst carrying out structural investigations on valoneic acid dilactone, isolated from *Valonea* tannin, Schmidt and Komarek [2] prepared a xanthone to which they assigned structure (II), stating that it appeared not to be identical with flavogallol. Direct comparison of hexa-*O*-methylvaloneaxanthone and hexa-*O*-methylflavogallol has confirmed this; the two compounds differ in m. p., mixed m. p., and infrared absorption spectrum. Both compounds show a band at 1745 cm.$^{-1}$

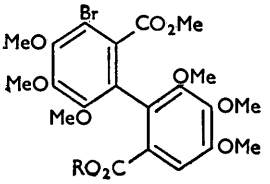
[2] Schmidt and Komarek, *Annalen*, 1955, **591**, 156.

(lactone-carbonyl) but only the valoneaxanthone has a band at 1664 cm.$^{-1}$ (benzophenone-type carbonyl). In addition, it has been shown that the hexamethyl ether of flavogallol may be oxidised to 3 : 4 : 5-trimethoxyphthalic acid; this observation cannot be accommodated on structure (II) but is quite in accord with structure (I) for flavogallol. As we have shown, structure (I) accounts for the properties of flavogallol and its correctness has now been demonstrated by rational synthesis.

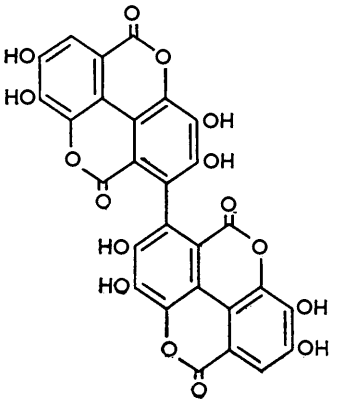
An obvious route to the ester (IV; R = Me), intermediate in a synthesis of flavogallol, is by the Ullmann reaction between the esters (VII) and (VIII; R = Me). In preliminary experiments, the action of copper powder on the gallic acid derivative (VII) alone was examined. This route to the corresponding hexamethoxydiphenic ester does not appear to have been previously recorded and the product is usually prepared from ellagic acid.[3] The new route is very convenient, for it avoids working with the very insoluble ellagic acid and its tetramethyl ether. Successive bromination of the hexamethoxydiphenic ester furnished its mono- (VIII; R = Me) and di-bromo-derivative (X). The mixture of di-



(VII)



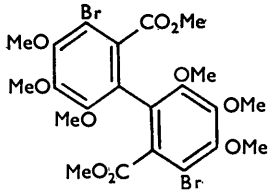
(VIII)



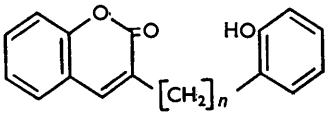
(IX)

and ter-phenyls resulting from the Ullmann reaction between the bicyclic ester (VIII; R = Me) and an excess of the monocyclic ester (VII) was separated by distillation. Saponification of the oily terphenyl fraction gave an acidic mixture from which no crystalline material other than a trace of the hexamethoxydiphenic acid could be isolated. However, demethylation of the remainder afforded flavogallol which did not give the Griessmayer test for ellagic acid and was identified as its hexa-acetate, hexabenzoate, and hexamethyl ether, thus establishing structure (I) for the phenol.

For completeness the Ullmann product from the bromodiphenyl (VIII) alone was examined. On demethylation it afforded " dehydrodiellagic acid " (IX), where the

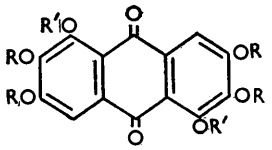


(X)



(XI): n = 1

(XII): n = 0

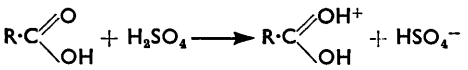


(XIII)

arrangement of lactone rings is probably as shown since any other grouping would introduce strain due to steric crowding and so be less stable. This phenol gave the Griessmayer reaction and was further distinguished from flavogallol by its great insolubility and the properties of its octa-acetate and octamethyl ether.

[3] Herzig and Pollak, *Monatsh.*, 1908, **29**, 263; Schmidt and Demmler, *Annalen*, 1952, **576**, 85.

The compound (VIII; R = Me) possesses a 2 : 6-disubstituted benzoic ester group and, as expected, the major product of alkaline hydrolysis was the half-ester (VIII; R = H). Under the usual conditions of alkaline hydrolysis about half of the dibromo-ester (X) was recovered unchanged. These two examples are analogous to the difficultly hydrolysable ester group present in the degradation product (IV; R = H or Me). Unfortunately no simple analogue of the cation (VI) has been found which affords a crystalline salt under the conditions tried. Salts could not be prepared from the simpler coumarin analogues (XI) and (XII). Analogy may be drawn, however, between the cation (VI) and the protonation of carboxylic acids in sulphuric acid solution which has been investigated by cryoscopy [4] and proceeds according to the equation :



In the early stages of this work it was thought that rufigallol might be a possible contaminant of flavogallol. Rufigallol (XIII; R = R′ = H) is the product of the action of sulphuric acid alone on gallic acid.[5] Its structure was advanced by Klobukowski [6] in 1877 and since this date little further work has appeared. In order to confirm the early observation the compound was re-prepared. Purified *via* the hexa-acetate, rufigallol formed scarlet needles which with diazomethane furnished the tetramethyl ether (XIII; R = Me, R′ = H).

Experimental

M. p.s are corrected.

Isolation of Flavogallol.—Arsenic pentoxide (33 g.) was dissolved in water (85 ml.), 98% sulphuric acid (270 ml.) added, and the mixture stirred and heated in an oil-bath at 120°. After the addition of gallic acid hydrate (30 g.) during about ½ hr., the mixture was kept at 110—120° for 6 hr., then cooled and poured on crushed ice. The resulting precipitate was washed by decantation, centrifuged, and dried, first on a steam-bath in a current of air and finally at 130°/15 mm. A dark brown powder (24 g.) resulted which was heated with acetic anhydride (80 ml.) and pyridine (1 ml.) (vigorous initial reaction) for 3 hr., then allowed to cool overnight. The precipitate was collected, digested with hot acetic anhydride (600 ml.), cooled, and filtered. Evaporation of the filtrate to *ca.* 60 ml. caused the separation of hexa-*O*-acetylflavogallol (2—3 g.) which was filtered off when cold, and recrystallised from acetic anhydride as colourless needles, m. p. 290—292° (decomp.) (lit.,[1] m. p. 278—280°) (Found : C, 56·0, 56·1; H, 3·2, 3·2. Calc. for $C_{33}H_{20}O_{18}$: C, 56·25; H, 2·9%).

For hydrolysis, the hexa-acetate (1·0 g.) was dissolved in 98% sulphuric acid (10 ml.), kept at 55° for 3 hr., cooled and poured on crushed ice. Flavogallol was precipitated and was collected at the centifruge, washed repeatedly with water till free from acid, then dried in a desiccator, giving a greenish powder. Traces of sulphuric acid afforded an orange product. Crude flavogallol was dissolved in a minimum of hot dimethylformamide, and the solution rapidly cooled and diluted with an equal volume of water, the phenol slowly separating as greenish-yellow needles. When air-dried, flavogallol forms a trihydrate * (Found : C, 49·6, 50·1; H, 3·0, 3·1; H_2O, 10·5; N, 0. Calc. for $C_{21}H_8O_{12},3H_2O$: C, 49·8; H, 2·8; H_2O, 10·7%), completely dehydrated after 3 hr. at 130°/0·01 mm. and affording a *dihydrate* over phosphoric oxide at 18°/0·1 mm. (2 hr.) (Found : C, 51·8; H, 2·8. $C_{21}H_8O_{12},2H_2O$ requires C, 51·6; H, 2·5%). The anhydrous phenol was very hygroscopic; it rapidly increased in weight and after 1 hr. in air formed the dihydrate (Found : H_2O, 6·9. $C_{21}H_8O_{12},2H_2O$ requires H_2O, 7·4%) which very slowly re-formed the trihydrate.

Flavogallol was insoluble in all solvents except pyridine and dimethylformamide. With 2N-sodium hydroxide it gave an orange solution (distinction from ellagic acid) and with sulphuric acid a magenta-red solution from which acetic acid precipitated the orange anhydro-sulphate.

* Bleuler and Perkin's analyses fit a trihydrate; their calculated values for a tetrahydrate are in error.

[4] Gillespie and Leisten, *Quart. Rev.*, 1954, **8**, 52.
[5] Robiquet, *Annalen*, 1836, **19**, 204; Löwe, *J. prakt. Chem.*, 1869, **107**, 298.
[6] Klobukowski, *Ber.*, 1877, **10**, 885.

In dimethylformamide it gave an indigo-blue ferric test. In the Griessmayer reaction [7] it afforded a purple solution decolorised on addition of water (distinction from ellagic acid).

The hexabenzoate, prepared with benzoic anhydride and a trace of pyridine, and precipitated with benzene, separated from nitrobenzene as canary-yellow prisms, m. p. 326—328° (lit.,[1] m. p. 326—328°) (Found : C, 70·05; H, 3·1. Calc. for $C_{63}H_{32}O_{18}$: C, 70·25; H, 3·0%).

Hexa-O-methylflavogallol.—Methylation of flavogallol with ethereal diazomethane furnished the *hexamethyl ether* which crystallised from dimethylformamide as yellow needles, m. p. 328—330° (Found : C, 60·2; H, 4·1. $C_{27}H_{20}O_{12}$ requires C, 60·45; H, 3·8%), depressed by hexa-*O*-methylvalonea xanthone.[2] Hexa-*O*-methylflavogallol in a potassium bromfde disc showed infrared bands at 1744, 1598, 1584, 1505, 1490, 1462, 1421, 1400, 1351, 1334, 1320, 1242, 1199, 1169, 1156, 1120, 1093, 1040, 1020, 990, 966, 955, 927, 904(s), 860(s), 790, 782, 772, 760(s), 752, and 743 cm.$^{-1}$. Hexa-*O*-methylvalonea xanthone as a similar disc had absorption bands at 1744, 1664, 1602, 1560(w), 1511(w), 1459, 1430, 1408, 1358, 1324, 1291, 1257, 1229, 1204, 1161, 1150, 1129, 1106, 1042, 1027, 993, 968, 938, 889(s), 750(s), and 740(s) cm.$^{-1}$.

A portion of the hexamethyl ether was treated with equivalent amounts of methyl sulphate and alkali according to the procedure of Schmidt and Komarek [2] for hexa-*O*-methylvalonea xanthone. The gummy ester product, on trituration with methanol, left a small amount of an insoluble residue which crystallised from chloroform–methanol as colourless needles, m. p. 275—277° [Found : OMe, 50·2. $C_{21}H_{12}O_4(OMe)_{10}$ requires OMe, 49·4%], probably a *monolactonic dimethyl ester*. Evaporation of the filtrate followed by dilution with water precipitated one form of the ester (IV; R = Me), crystallising from aqueous methanol as needles, m. p. 128—129° (lit.,[1] m. p. 128—130°) (Found : C, 58·8; H, 5·9; OMe, 53·9. Calc. for $C_{32}H_{38}O_{15}$: C, 58·8; H, 5·6; 12OMe, 55·2%).

Methyl Hepta-O-methylflavogallonate.—Flavogallol was digested with 2% methanolic sulphuric acid (100 parts) for 2 hr., forming a colourless solution. Evaporation of the solvent and addition of water precipitated methyl flavogallonate. This ester re-formed flavogallol, identified as the hexamethyl ether, on dissolution in 98% sulphuric acid followed by precipitation with ice. With excess of ethereal diazomethane *methyl hepta-O-methylflavogallonate* was formed and crystallised from methanol as colourless needles, m. p. 242—244° (Found : C, 59·0; H, 4·8; OMe, 41·0. $C_{29}H_{26}O_{13}$ requires C, 58·8; H, 4·4; 8OMe, 42·6%).

Oxidation of Hexa-O-methylflavogallol.—Hexa-*O*-methylflavogallol (1·25 g.) was dissolved in a solution of potassium hydroxide (1·5 g.) in water (30 ml.), and the mixture cooled to room temperature. Finely powdered potassium permanganate (6·8 g.) was slowly added with occasional cooling; the rapid uptake ceased abruptly. The mixture was then diluted with water and filtered and the manganese dioxide washed with hot 2N-potassium hydroxide. The filtrates were combined, acidified with dilute sulphuric acid, and extracted with ether for 9 hr. Evaporation of the dried (Na_2SO_4) ethereal extract left a brown solid (0·19 g.) which sublimed at 160°(bath)/0·15 mm. as pale yellow needles (0·10 g.). This sublimate crystallised from ether as colourless silky needles, m. p. 143—144°, undepressed on admixture with 3 : 4 : 5-trimethoxyphthalic anhydride.[8] The anil [8] crystallised from 50% ethanol as needles, m. p. and mixed m. p. 144—145° (Found : N, 4·7. Calc. for $C_{17}H_{15}O_5N$: N, 4·5%).

Methyl 2-Bromo-3 : 4 : 5-trimethoxybenzoate.—Bromination of methyl 3 : 4 : 5-trimethoxybenzoate in carbon tetrachloride (after Hamburg [9a]) afforded material containing some 10—15% of unbrominated ester difficult to remove by distillation. Re-esterification of the pure acid, m. p. 150—151°, afforded the bromo-ester as a mobile oil, b. p. 119—120°/0·03 mm. (Found : C, 43·4; H, 4·4; Br, 26·1. Calc. for $C_{11}H_{13}O_5Br$: C, 43·3; H, 4·25; Br, 26·25%), which did not solidify. In the literature it is described as an oil,[9a] a solid [9b] of m. p. 90°, and a solid [9c] of m. p. 33°.

Dimethyl 2 : 3 : 4 : 2′ : 3′ : 4′-Hexamethoxy-6 : 6′-diphenate.—Crude methyl 2-bromo-3 : 4 : 5-trimethoxybenzoate (25 g.) was heated at 210—220° and copper bronze (15 g.) gradually stirred in. After 2 hr. the mixture was cooled, extracted with chloroform, and filtered. The filtrate was washed with water and sodium hydrogen carbonate solution and dried (Na_2SO_4) and the solvent removed. Distillation of the residue afforded (*a*) methyl 3 : 4 : 5-trimethoxybenzoate, b. p. 114—118°/0·1 mm. (2·75 g.), and (*b*) the dimethyl hexamethoxydiphenate, b. p. 192—195°/0·1 mm., which solidified and crystallised from aqueous methanol as stout needles (11 g.), m. p. 110—111°. Hydrolysis of a sample furnished the diphenic acid, needles (from aqueous

[7] Griessmayer, *Annalen*, 1871, **160**, 51.
[8] Bargellini and Molina, *Atti R. Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1912, **21**, II, 146.
[9] (*a*) Hamburg, *Monatsh.*, 1898, **19**, 596; (*b*) Bogert and Plant, *J. Amer. Chem. Soc.*, 1915, **37**, 2726; (*c*) Feist and Dschu, *Festschrift für A. Tschirch* (*Leipzig*), 1926, 29; *Chem. Zentr.*, 1927, II, 58.

ethanol), m. p. 242—243° undepressed by material of m. p. 239—240° prepared from ellagic acid.[3] It formed mixed crystals with tri-*O*-methylgallic acid, making their separation tedious.

Dimethyl 5-Bromo-2 : 3 : 4 : 2′ : 3′ : 4′-hexamethoxy-6 : 6′-diphenate (VIII; R = Me).—The above diphenic ester (10 g.) and iodine (0·05 g.) were dissolved in carbon tetrachloride (30 ml.); then bromine (3·6 g.) in carbon tetrachloride (30 ml.) was slowly added at room temperature. After 30 min., the mixture was washed successively with sodium sulphite solution, sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Distillation afforded the crude monobnomo-derivative, b. p. 218—220°/0·05 mm. (10 g.). Hydrolysis of the ester with 2N-methanolic potassium hydroxide for 1 hr. afforded the *hydrogen bromo-ester* (VIII; R = H), crystallising from 30% ethanol as stout needles, m. p. 190—191° (Found : C, 49·2; H, 4·6; Br, 15·1. $C_{21}H_{23}O_{10}Br$ requires C, 48·9; H, 4·45; Br, 15·5%); rapid cooling of solutions afforded an unstable dimorph as fine needles, m. p. 150—151°. Re-esterification of the pure acid afforded the pure *monobromo-ester* (VIII; R = Me), b. p. 219—220°/0·04 mm., a colourless glass (Found : C, 49·6; H, 4·9; Br, 14·8. $C_{22}H_{25}O_{10}Br$ requires C, 49·9; H, 4·7; Br, 15·1%). After some time it solidified and separated from dilute methanol as stout needles, m. p. 74—75°.

Dimethyl 5 : 5′-Dibromo-2 : 3 : 4 : 2′ : 3′ : 4′-hexamethoxy-6 : 6′-diphenate (X).—Treatment of the diphenic ester with 3 times the above quantity of bromine afforded the *dibromo-ester* (X), which separated from methanol as needles, m. p. 126—127° (Found : C, 43·45; H, 4·0; Br, 26·4. $C_{22}H_{24}O_{10}Br_2$ requires C, 43·4; H, 3·95; Br, 26·3%). After this ester (0·150 g.) had been refluxed with an excess of 10% methanolic potassium hydroxide for 90 min., 0·083 g. (55%) was recovered unchanged and a gummy acid fraction (0·056 g.; 37%) was formed.

" *Dehydrodiellagic Acid* " (IX).—Pure dimethyl 5-bromo-2 : 3 : 4 : 2′ : 3′ : 4′-hexamethoxy-6 : 6′-diphenate (2 g.) and copper bronze (2 g.) were heated at 220° for 1½ hr. with stirring; then the mixture was cooled and triturated with chloroform. Filtration and evaporation of the filtrate left a gum which was demethylated by 4 hours' refluxing with hydriodic acid (15 ml.; *d* 1·7) and acetic anhydride (5 ml.). The phenol was precipitated as an almost colourless powder (1·0 g.) which was collected and washed with dilute sulphurous acid and water. " Dehydrodiellagic acid " was almost insoluble in hot dimethylformamide and no satisfactory solvent was found. It gave the Griessmayer test and an orange solution in 2N-sodium hydroxide.

The overnight action of excess of ethereal diazomethane furnished the *octamethyl ether* which was washed with cold 2N-potassium hydroxide. It was almost insoluble in hot dimethylformamide, acetic anhydride, anisole, and acetophenone but crystallised from benzyl cyanide as pale cream-coloured needles, m. p. >365° (Found : C, 60·5; H, 3·85. $C_{36}H_{26}O_{16}$ requires C, 60·5; H, 3·75%).

Acetylation by 4 hours' refluxing with acetic anhydride and a little pyridine gave the sparingly soluble *octa-acetate* which separated from a large bulk of nitrobenzene, containing acetic anhydride, as colourless needles, m. p. 318—320° (Found : C, 57·3; H, 3·4. $C_{44}H_{26}O_{24}$ requires C, 56·8; H, 2·8%).

Synthesis of Flavogallol.—Copper bronze (6 g.) was added to a mixture of methyl 2-bromo-3 : 4 : 5-trimethoxybenzoate (10 g.) and dimethyl 5-bromo-2 : 3 : 4 : 2′ : 3′ : 4′-hexamethoxy-6 : 6′-diphenate (4 g.) at 220—230° (metal-bath) for 2 hr. After cooling, the mixture was triturated with chloroform and filtered and the filtrate washed successively with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Distillation afforded fractions : (*a*) b. p. 118—120°/0·1 mm. (1·4 g.), m. p. 81—82° (from aqueous methanol) undepressed by methyl tri-*O*-methylgallate; (*b*) b. p. 185—190°/0·03 mm. (4·1 g.), m. p. 109—110° (from aqueous methanol), undepressed by dimethyl hexamethoxydiphenate; and (*c*) b. p. 225—240°/0·015 mm. (1·8 g.), a viscous oil, hydrolysed by 2 hours' refluxing with potassium hydroxide (2 g.) in methanol (30 ml.). The resulting acid, isolated with ether, was a gum (halogen test negative) which afforded successive crops of crude hexamethoxydiphenic acid (0·23 g. in all) on slow evaporation of its aqueous-ethanolic solution. When the m. p. of these crystals had fallen to 215—225° no further crystalline material would separate. The filtrate was evaporated to dryness and the residue (1·4 g.) demethylated by 4 hours' refluxing with hydriodic acid (15 ml.; *d* 1·7) and acetic anhydride (5 ml.). An orange precipitate was rapidly formed. Dilution with water and centrifuging afforded a yellow powder which was washed with dilute sulphurous acid and water and dried in a desiccator (yield, 0·72 g.).

This phenol (0·72 g.) was refluxed with acetic anhydride (10 ml.) and pyridine (3 drops) for 3 hr., filtered hot, cooled, and poured into water (10 ml.). The precipitated *acetate* (0·55 g.) was collected and crystallised from acetic anhydride as colourless needles, m. p. 278—280° (decomp.)

undepressed by hexa-*O*-acetylflavogallol, m. p. 290—292° (Found : C, 55·8; H, 3·0%). This acetate was converted successively into flavogallol (negative Griessmayer test) and its *hexamethyl ether* which separated from dimethylformamide as yellow needles, m. p. 329—330° (Found : C, 60·3; H, 4·1%) undepressed by authentic hexa-*O*-methylflavogallol and showing an identical infrared adsorption spectrum.

The *hexabenzoate* had m. p. and mixed m. p. 326—328° (Found : C, 70·4; H, 3·6%).

3-2′-*Methoxybenzylcoumarin*.—β-*o*-Methoxyphenylpropionic acid (10 g.) and potassium hydrogen carbonate (5·27 g.) were dissolved in methanol, the solution evaporated to dryness, and the residue heated at 120° for 3 hr. The resulting potassium salt was heated with salicylaldehyde (7 g.) and acetic anhydride (15 ml.) at 170—180° for 18 hr. When cold, the mixture was stirred with water and extracted with ether. Washing the ether layer with potassium hydrogen carbonate solution removed a brownish acid (7·2 g.), purified *via* the methyl ester and identified as β-*o*-methoxyphenylpropionic acid. Evaporation of the ether then left a neutral fraction (8·8 g.) which was distilled giving fractions : (*a*) b. p. 140—150°/11 mm. (4·1 g.), crystallising from *cyclo*hexane as needles, m. p. 68—69° undepressed by coumarin; and (*b*) b. p. 160—165°/0·01 mm. (3·2 g.), which crystallised from light petroleum (b. p. 60—80°) as colourless needles (2 g.) of 3-2′-*methoxybenzylcoumarin*, m. p. 95—96° (Found : C, 76·5; H, 5·4; OMe, 12·0. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3; OMe, 11·7%).

3-*o*-*Hydroxybenzylcoumarin* (XI).—The methyl ether (2 g.) was refluxed with hydriodic acid (5 ml.; *d* 1·7) and acetic anhydride (5 ml.) for 3 hr. Dilution with water precipitated the *phenol* which crystallised from 50% ethanol as colourless needles (1·7 g.), m. p. 154—155° (Found : C, 76·1; H, 5·0. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·75%). Acetic anhydride and sodium acetate furnished the *phenylacetate*, crystallising in prisms (from *cyclo*hexane), m. p. 127—128° (Found : C, 73·5; H, 4·9. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8%).

3-*o*-*Methoxyphenylcoumarin*.—*o*-Methoxyphenylacetic acid (10 g.) and potassium hydrogen carbonate (6·02 g.) were caused to react in methanol as before. The potassium salt, salicylaldehyde (7·4 g.), and acetic anhydride (15 ml.) were heated at 170—180° for 6 hr. On cooling, the mixture was stirred with water, taken up in chloroform, washed with potassium hydrogen carbonate solution, and dried (Na_2SO_4). Evaporation of the solvent left an oil which crystallised from acetic acid as needles (8·3 g.) of 3-*o*-*methoxyphenylcoumarin*, m. p. 139—140°. An analytical specimen separated from a large volume of ethanol as stout needles, m. p. 140—141° (Found : C, 76·1; H, 5·1. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·75%). Acidification of the carbonate extract precipitated a solid (1·5 g.), crystallising from 50% ethanol as colourless needles, m. p. 155—156°, probably the corresponding O-*acetylcoumaric acid* (Found : C, 69·7; H, 5·4. $C_{18}H_{16}O_5$ requires C, 69·3; H, 5·1%).

3-*o*-*Hydroxyphenylcoumarin* (XII).—Demethylation of the methyl ether as in the previous case afforded this *phenol* which separated from aqueous dioxan as colourless needles, m. p. 208—209° (Found : C, 75·0; H, 4·4. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%). The *phenylacetate* crystallised from 75% ethanol as colourless plates, m. p. 137—138° (Found : C, 72·3; H, 4·3. $C_{17}H_{12}O_4$ requires C, 71·8; H, 4·2%). Methylation of the phenol with diazomethane refurnished the methyl ether, m. p. and mixed m. p. 140—141°.

Neither 3-*o*-hydroxybenzylcoumarin nor 3-*o*-hydroxyphenylcoumarin reacted with hydrogen chloride or hydrogen bromide in benzene, acetic acid, ether, or dioxan with or without the addition of ferric chloride. Sulphuric acid reacted, to form water-soluble products from which the original coumarins could not be recovered.

Rufigallol (XIII; R = R′ = H).—Anhydrous gallic acid (10 g.) was dissolved in 98% sulphuric acid (30 ml.) and heated on a water-bath for 2 hr., cooled, and poured into water. The resulting orange precipitate (2·1 g.) was centrifuged, dried, and acetylated by refluxing with acetic anhydride (25 ml.) and sulphuric acid (3 drops) for 2 hr. On cooling, the hexa-acetate, separated as yellow plates (1·6 g.) and, recrystallised from acetic anhydride, had m. p. 268—270° (decomp., in sealed evacuated tube; no m. p. previously recorded) (Found : C, 56·4; H, 4·0; Ac, 45·4. Calc. for $C_{26}H_{20}O_{14}$: C, 56·2; H, 3·6; 6Ac, 46·4%). For hydrolysis, the acetate (1 g.) was dissolved in boiling pyridine (20 ml.), and acetic acid (25 ml.) was added; a deep purple solution resulted. When concentrated hydrochloric acid (20 ml.) was added down the condenser, the mixture became orange and deposited rufigallol as a scarlet powder (0·6 g.) which was collected when cold. Good analytical figures were not obtained. Rufigallol was kept overnight with excess of ethereal diazomethane, the solvent evaporated, and the residue crystallised from ethyl acetate as orange-yellow needles of the tetramethyl ether (XIII; R = Me, R′ = H), m. p. 251—252° (Found : C, 59·8; H, 4·8; OMe, 32·7. Calc. for $C_{18}H_{16}O_8$: C, 60·0; H, 4·5; OMe, 34·5%). Occasionally an unstable modification separated, having m. p.

239—240° (resolidifies and remelts at 251—252°). Klobukowski [6] records m. p. 235—237° for this substance.

Our thanks are offered to the Department of Scientific and Industrial Research and to Imperial Chemical Industries Limited for grants.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, May* 31*st*, 1956.]