207. *Purpurogallin. Part I.*

By Robert D. Haworth, Barry P. Moore, and Peter L. Pauson.

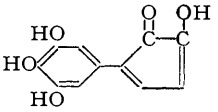
The reduction of purpurogallin and its tri- and tetra-methyl ethers has been examined. Oxidation of tetramethyl tetrahydropurpurogallin with alkaline hydrogen peroxide has yielded a dibasic acid identical with γ-(3 : 4 : 5-trimethoxy-2-carboxyphenyl)butyric acid (X) which has been synthesised; the isomeric γ-(2 : 3 : 4-trimethoxy-6-carboxyphenyl)butyric acid (IX) has also been synthesised. The identification of (X) establishes structure (VI; R = Me) for tetramethyl tetrahydropurpurogallin and supports the benz*cyclo*heptatrienolone structure (III) for purpurogallin.

Further evidence supporting structure (III) is obtained from the atmospheric oxidation of alkaline solutions of purpurogallin which results in the rupture of the benzenoid ring and the formation of the acid (XV; R = H). This acid (XV; R = H) and its decarboxylation product, 2-hydroxy-6-methyl*cyclo*heptatrienone (XVI) closely resemble stipitatic acid in properties.

The mechanism of the conversion of pyrogallol into purpurogallin is discussed.

Purpurogallin, $C_{11}H_8O_5$, which is obtained by oxidation of pyrogallol in a variety of ways, has been the subject of numerous investigations which are adequately summarised in the important contribution of Willstätter and Heiss (*Annalen*, 1923, **433**, 17). As a result of an ingenious theoretical treatment, these authors advanced structure (I) for purpurogallin, and this structure appears to have been widely accepted. The evidence discussed by the proposers is, however, not by any means conclusive, and recently several chemists in this country have shown an interest in the problem and considered alternative structures. During the course of lectures given to the Chemical Societies at Imperial College and Bangor in 1943, one of us suggested the

quinonoid formula (II), and similar ideas had occurred to Professor Wilson Baker (private communication, December 3rd, 1945). Professor J. W. Cook also informs us (private



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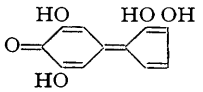

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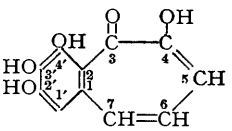
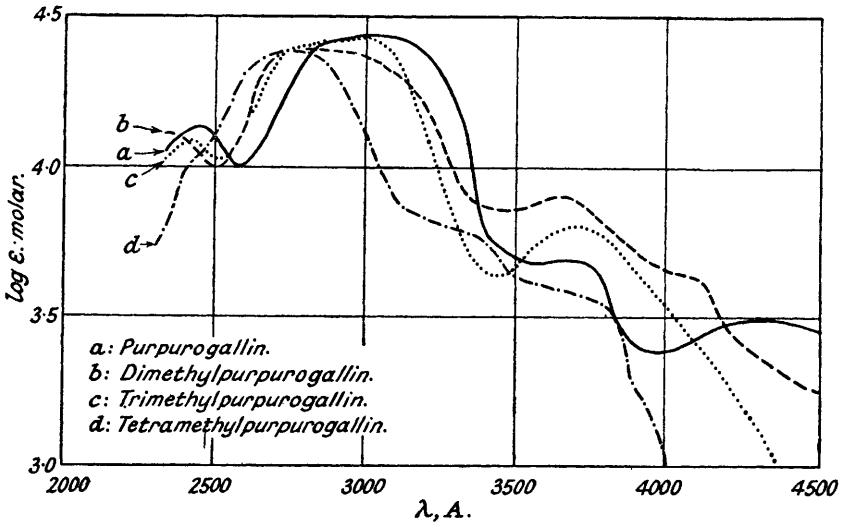


(III.)

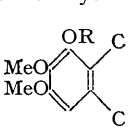
communication, June 17th, 1947) that Dr. J. D. Loudon had considered the benz*cyclo*hepta-trienolone structure (III) and that some preliminary reduction experiments were carried out in 1945 by Dr. Loudon and Mr. J. Robertson. Recently, Barltrop and Nicholson have submitted a paper on purpurogallin for publication, and Dr. J. A. Barltrop has informed us (private communication, May 24th, 1947) that they have established the structure (IV; R = Me) in tetramethylpurpurogallin, and suggested that the trimethyl ether contains the phenolic structure (IV; R = H) and, in addition, they have adduced theoretical reasons in favour of structure (III) for purpurogallin.



In order to obtain further experimental evidence bearing on the problem, an investigation involving reduction, methylation, and oxidation of purpurogallin was planned, and the synthesis of some of these derivatives was commenced in 1943. Certain aspects of this work are at present incomplete, but in view of the work of Barltrop and Nicholson it is desirable that some of our results, which provide very strong experimental evidence in favour of structure (III), should be described and interpreted in terms of this structure.

Catalytic hydrogenation of purpurogallin yielded the yellow *tetrahydropurpurogallin*, but, as the reduction was very slow and the results erratic, this approach was soon abandoned in favour of experiments in which methylation preceded reduction. When purpurogallin was methylated in dioxan solution with excess of diazomethane, the yellow trimethyl purpurogallin (V; R = H), prepared by earlier investigators, was obtained. Methylation with a limited amount of diazomethane gave an orange *dimethyl purpurogallin* which was converted into the trimethyl ether (V; R = H) by further methylation. The colourless alkali-insoluble tetramethyl purpurogallin (V; R = Me) was prepared by the action of methyl sulphate on a solution of the trimethyl ether (V; R = H) in concentrated sodium hydroxide. The reduction in colour and the use of concentrated alkali during the methylation suggested, at one time, that structural modification may be associated with the introduction of the fourth methyl ether group, but a comparison of the absorption spectra of purpurogallin and its di-, tri-, and tetra-methyl ethers (see Fig.) indicates that profound structural change is very unlikely. In addition it was found that tetramethyl purpurogallin (V; R = Me) was quantitatively converted into the trimethyl ether by warming for a few minutes with 2N-hydrochloric acid. This ready hydrolysis

and the absence of ketonic properties in purpurogallin and its di-, tri-, and tetra-methyl ethers is noteworthy.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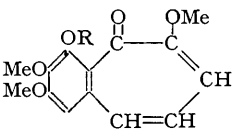
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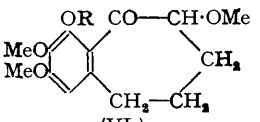
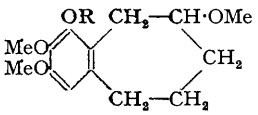
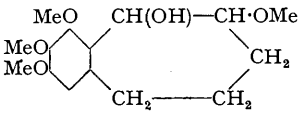
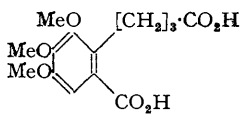

(VI.)

Attempts to oxidise tri- and tetra-methyl purpurogallin under a variety of conditions failed to yield recognisable products, and reduction processes were investigated. Trimethyl purpurogallin is readily reduced to colourless phenolic ketones by the action of amalgamated zinc and acids, and it is hoped to describe these products when the constitutions have been elucidated more fully. Trimethyl purpurogallin is not easily hydrogenated in the presence of palladium catalysts, but was readily reduced with Adams's platinum catalyst. The product was always a mixture the nature of which was very dependent on the activity of the catalyst and the nature of the solvent employed. Hydrogenation in acetic acid with freshly prepared catalyst gave an oil which was resolved by Girard-T into *trimethyl tetrahydropurpurogallin* (VI; R = H), giving a 3 : 5-*dinitrobenzoate* and a 2 : 4-*dinitrophenylhydrazone*, and *trimethyl hexahydrodeoxypurpurogallin* (VII; R = H) which had no ketonic properties but gave a *methyl ether* (VII; R = Me). With the same catalyst but with ethanol as solvent the proportion of ketonic phenol (VI; R = H) was increased, and the same result was achieved by the use of a less active catalyst in acetic acid. With a less active catalyst in ethanol reduction was very slow, and the product, a ketonic *phenol* (A), $C_{14}H_{18}O_5$, which gave a 3 : 5-*dinitrobenzoate*, resembled the isomeric ketonic phenol (VI; R = H) very closely except that the 2 : 4-dinitrophenylhydrazone was

(VII.) 


(VIII.)

amorphous. The relationship between the two isomers is not understood, but the production of these phenolic reduction products indicates the presence of one phenolic group in the benzene nucleus of trimethyl purpurogallin or alternatively suggests a quinonoid structure such as (II) for purpurogallin. Methylation of trimethyl tetrahydropurpurogallin (VI; R = H) afforded *tetramethyl tetrahydropurpurogallin* (VI; R = Me) as an oil giving a 3 : 4-*dinitrophenylhydrazone*, and the same tetramethyl ether was obtained together with *tetramethyl hexahydropurpurogallin* (VIII) by reducing tetramethyl purpurogallin with Adams's catalyst in ethanol. Tetramethyl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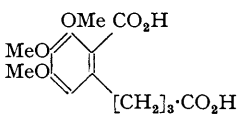
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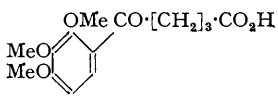
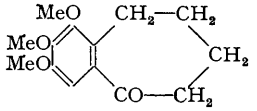

(XI.)

tetrahydropurpurogallin (VI; R = Me) was readily oxidised by alkaline hydrogen peroxide to a dibasic acid which did not give a cyclic anhydride or imide. The properties suggested a γ-(*o*-carboxyphenyl)butyric acid structure, and, after some experiments involving the Wieland method of degrading carboxylic acids had failed to give useful information, the synthesis of the acids (IX) and (X) was undertaken and led to the exclusion of (IX) and the establishment of structure (X) for the dibasic acid.

Condensation of glutaric anhydride with pyrogallol trimethyl ether in the presence of aluminium chloride yielded a mixture of γ-(2 : 3 : 4-*trimethoxybenzoyl*)*butyric acid* (XI) and a γ-(*hydroxydimethoxybenzoyl*)*butyric acid*. Clemmensen reduction of (XI) or the demethylated product in toluene solution yielded a δ-(*hydroxydimethoxyphenyl*)*valeric acid* which was methylated to give δ-(2 : 3 : 4-*trimethoxyphenyl*)*valeric acid*. Cyclisation with phosphoric oxide in benzene afforded 1′ : 2′ : 3′-*trimethoxybenzocyclohepten*-3-*one* (XII) as an oil giving a crystalline 2 : 4-*dinitrophenylhydrazone*. The cyclic ketone (XII) was oxidised first with selenium dioxide to the α-diketone which was not isolated, the crude diketone being converted by means of alkaline hydrogen peroxide into γ-(2 : 3 : 4-*trimethoxy*-6-*carboxyphenyl*)*butyric acid* (IX). For the synthesis of the isomeric acid (X), ethyl γ-(3 : 4 : 5-trimethoxybenzoyl)acetate and ethyl β-iodopropionate were condensed and the resulting oil was hydrolysed by 20% sulphuric acid to

γ-(3 : 4 : 5-*trimethoxybenzoyl*)*butyric acid* (XIII). The acid (XIII) was reduced by Minlon's modification (*J. Amer. Chem. Soc.*, 1946, **68**, 2487) of the Wolff–Kishner method to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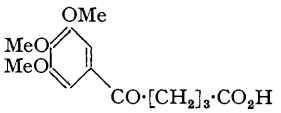
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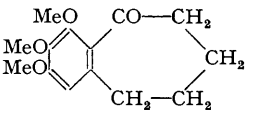
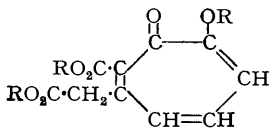

(XIV.)

δ-(3 : 4 : 5-*trimethoxyphenyl*)*valeric acid*, which was cyclised by phosphoric oxide in benzene to 2′ : 3′ : 4′-*trimethoxybenz*cyclo*hepten*-3-*one* (XIV). Successive oxidations with selenium dioxide and hydrogen peroxide proceeded smoothly to give the required γ-(3 : 4 : 5-*trimethoxy*-2-*carboxyphenyl*)*butyric acid* (X), which had m. p. 146—147° and was identical with the dibasic acid, m. p. 146—147°, obtained by oxidising tetramethyl tetrahydropurpurogallin as described above.

The elucidation of the structure of the dibasic acid proves that tetramethyl tetrahydropurpurogallin has the 4 : 2′ : 3′ : 4′-tetramethoxybenz*cyclo*hepten-3-one structure (VI; R = Me) and definitely excludes phenyl*cyclo*pentadiene structures such as (I) and (II), and naphthalene formulae such as that advocated by Dean and Nierenstein (*Ber.*, 1913, **46**, 3868).

In addition, important evidence supporting the presence of the *cyclo*heptatrienolone ring in purpurogallin has been obtained by examining the action of air on an alkaline solution of the pigment. Much humic acid was produced, but continuous ether extraction led to the isolation of 5% yields of a tribasic acid, $C_{10}H_8O_6$, probably 4-*hydroxy*-3-*keto*-2-*carboxy*cyclo*heptatrienyl*-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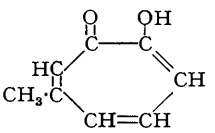
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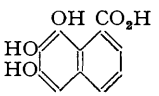
(XVII.)

acetic acid (XV; R = H), which was very soluble in water, gave a yellow sodium salt and a red ferric test, did not react with 2 : 4-dinitrophenylhydrazine, and with diazomethane yielded the neutral *trimethyl* derivative (XV; R = Me). When heated above the melting point, (XV; R = H) was converted into 2-*hydroxy*-6-*methyl*cyclo*heptatrienone* (XVI) which dissolved in sodium hydrogen carbonate solution, gave a green ferric test, but did not react with 2 : 4-dinitrophenylhydrazine. Catalytic reduction of (XVI) resulted in the absorption of 3·5 mols. of hydrogen and the formation of a neutral oil which gave an amorphous 2 : 4-dinitrophenylhydrazone. These substances are being further investigated, but their properties closely resemble those recorded by Birkenshaw, Chambers, and Raistrick (*Biochem. J.*, 1942, **36**, 242) for stipitatic acid, for which Dewar (*Nature*, 1945, **155**, 50) has suggested a *cyclo*heptatrienolone structure, and the rupture and removal of the phenolic ring is interesting in connection with the biogenetic suggestions advanced previously (Tilden lecture, *J.*, 1942, 456) by one of us.*

The conversion of pyrogallol into the benzotropolone (Dewar, *loc. cit.*) system (III) can be readily accommodated by a slight modification of the suggestions of Willstätter and Heiss (*loc. cit.*). These authors assume the production of 3 : 4 : 5 : 2′ : 3′ : 4′-hexahydroxydiphenyl followed by oxidation and benzilic rearrangement to (I) by (*a*) union of carbon atoms in positions 1′ and 3′, (*b*) the rupture of the bond between carbon atoms 1′ and 2′, and (*c*) elimination of carbon dioxide. The benzotropolone structure (III) may be derived similarly by retaining the changes (*b*) and (*c*) but postulating union of carbon atom 3′ with carbon atom 2 instead of with carbon atom 1′; such a modification is reasonable in view of the conjugation of positions 2 and 1′.

Experiments on the mechanism of this reaction have been initiated, and it is hoped to publish shortly the results of synthetical experiments which aim at the synthesis of purpurogallone (XVII). This structure (XVII), suggested by Perkin (*J.*, 1903, **83**, 192; 1912, **101**, 803), is readily derived by further benzilic acid change from the benzotropolone structure (III).

* *Added July 2nd*, 1948.—The isolation of three isomeric *iso*propyl*cyclo*heptatrienolones from Western red cedar (Erdtman and Gripenberg, *Nature*, 1948, **161**, 719) is interesting; these probably arise from the corresponding pyrogallols by oxidation to purpurogallin analogues and subsequent fission of the benzene nucleus.

Experimental.

Purpurogallin, obtained in 60% yields from pyrogallol by oxidation with potassium iodate as described by Evans and Dehn (*J. Amer. Chem. Soc.*, 1939, **52**, 3647), was purified either by sublimation in a vacuum * (4 mm.), or by crystallisation from a mixture of equal parts of phenol and glacial acetic acid. It was isolated as red prisms or plates, m. p. 276° (decomp.) (Found: C, 60·0; H, 3·8. Calc. for $C_{11}H_8O_5$: C, 60·0; H, 3·6%), which did not react with ketonic reagents; it was readily reduced by zinc and dilute hydrochloric acid to colourless ill-defined amorphous products.

Tetrahydropurpurogallin. Finely powdered purpurogallin (1 g.) was suspended in acetic acid (50 c.c.) and hydrogenated over Adams's catalyst (20 mg.) until hydrogen absorption ceased (24 hours; approximately 2·8 mols. of hydrogen were absorbed). Evaporation yielded *tetrahydropurpurogallin* which separated from acetic acid in yellow laminæ, m. p. 232—233° (decomp.) (Found: C, 58·9; H, 5·4. $C_{11}H_{12}O_5$ requires C, 59·0; H, 5·4%), which dissolved in aqueous alkali to a stable yellow solution.

Dimethyl Purpurogallin.—Purpurogallin (5 g.) in dioxan (200 c.c.) was treated with an ethereal solution of diazomethane prepared (by distillation) from *N*-nitrosomethylurethane (13·5 c.c.). After 12 hours the mixture was evaporated, finally in a vacuum, and the residue crystallised from ethanol. *Dimethylpurpurogallin* separated in orange needles (4 g.), m. p. 156° (Found: C, 62·7; H, 5·1; OMe, 24·5. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·8; OMe, 25·0%), which dissolved in aqueous alkali to a stable yellow-orange solution. A Zerewitinoff determination in anisole solution indicated two active hydrogen atoms per molecule.

Trimethyl Purpurogallin (V; R = H).—Purpurogallin (16 g.) in dioxan (40 c.c.) was treated with diazomethane (20% excess) in ether (1200 c.c.). After 1 hour, ligroin (400 c.c.) was added; the trimethyl ether which gradually separated was collected after 48 hours and crystallised from ethanol. Yellow needles (15 g.), m. p. 176°, were obtained and a further small crop (1 g.) was obtained from the mother liquors. A Zerewitinoff determination showed the presence of one active hydrogen atom per molecule. The 3 : 5-*dinitrobenzoate*, prepared in pyridine, crystallised from acetic acid in yellow plates, which decomposed to a dark red liquid at 260° (Found: C, 55·1; H, 3·4; N, 6·5; OMe, 20·2. $C_{21}H_{16}O_{10}N_2$ requires C, 55·3; H, 3·5; N, 6·1; OMe, 20·4%).

Tetramethyl Purpurogallin (V; R = Me).—Methyl sulphate (3 c.c.) was added with shaking to a suspension of finely powdered trimethyl purpurogallin (1 g.) in 65% potassium hydroxide (15 c.c.). The mixture was warmed to initiate the vigorous reaction which then proceeded to completion without further attention. The cooled mixture was diluted with water and acidified. The *tetramethyl ether*, which separated as an oil, rapidly solidified, and crystallised from *cyclo*hexane in colourless plates, m. p. 94°, which did not react with ketonic reagents. A Zerewitinoff determination showed the absence of active hydrogen. The tetramethyl ether (0·1 g.) and 2N-hydrochloric acid (5 c.c.) were warmed on a water-bath until the colourless solution assumed a deep orange colour (5 minutes); on dilution with water, trimethylpurpurogallin, m. p. 173—175° (80 mg.), separated.

Catalytic Reduction of Trimethyl Purpurogallin.—(*a*) Trimethyl purpurogallin (4 g.) was suspended in acetic acid (100 c.c.) and hydrogenated at 15° and ordinary pressure in the presence of freshly prepared Adams's catalyst (10 mg.). After 2·5 hours, when 950 c.c. of hydrogen had been absorbed, the product was distilled to give an oil (2·7 g.), b. p. 160—170°/0·03 mm. This oil was dissolved in ethanol (20 c.c.) and acetic acid (2 c.c.), warmed for 1 hour with Girard's reagent-T (1 g.), diluted with water, and freed from non-ketonic material by extraction with ether. Removal of the ether yielded 4′-*hydroxy*-4 : 2′ : 3′-*trimethoxybenz*cyclo*heptene* (*trimethyl hexahydrodeoxypurpurogallin*) (VII; R = H), which separated from *cyclo*hexane in pale cream prisms, m. p. 82° (Found: C, 66·8; H, 7·6. $C_{14}H_{20}O_4$ requires C, 66·7; H, 7·9%). Methylation with methyl sulphate and alkali yielded 4 : 2′ : 3′ : 4′-*tetramethoxybenz*cyclo*heptene* (VII; R = Me), which crystallised from aqueous methanol in colourless prisms, m. p. 75—76° (Found: C, 67·7; H, 8·2; OMe, 46·1. $C_{15}H_{22}O_4$ requires C, 67·8; H, 8·3; OMe, 46·6%). The aqueous liquor from the above ether extraction was heated for 1 hour with concentrated hydrochloric acid (10 c.c.); ether then removed 4′-*hydroxy*-4 : 2′ : 3′-*trimethoxybenz*cyclo*hepten*-3-*one* (*trimethyl tetrahydropurpurogallin*) (VI; R = H), which separated from *cyclo*hexane in colourless prisms (0·3 g.), m. p. 86—87° (Found: C, 63·5; H, 6·8. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8%), and gave a 3 : 5-*dinitrobenzoate* as yellow prisms, m. p. 161—162° (Found: C, 54·5; H, 4·5; N, 6·4. $C_{21}H_{20}O_{10}N_2$ requires C, 54·8; H, 4·4; N, 6·1%), from ethanol, and a 2 : 4-*dinitrophenylhydrazone*, crystallising from ethanol in deep yellow prisms, m. p. 204° (Found: C, 54·0; H, 5·0; N, 13·0. $C_{20}H_{22}O_8N_4$ requires C, 53·8; H, 4·9; N, 12·6%). This ketonic phenol (VI; R = H) was converted by methyl sulphate and sodium hydroxide into 4 : 2′ : 3′ : 4′-*tetramethoxybenz*cyclo*hepten*-3-*one* (*tetramethyl tetrahydropurpurogallin* (VI; R = Me), an oil, b. p. 140—145°/0·5 mm. (Found: C, 64·6; H, 7·2; OMe, 44·0. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·1; OMe, 44·3%), giving a 2 : 4-*dinitrophenylhydrazone* which crystallised from ethanol in yellow needles, m. p. 176° (Found: C, 54·6; H, 5·4; N, 12·5. $C_{21}H_{24}O_8N_4$ requires C, 54·8; H, 5·2; N, 12·2%).

(*b*) Trimethyl purpurogallin (8·6 g.) suspended in ethanol (250 c.c.) was reduced in presence of freshly prepared Adams's catalyst (0·1 g.). After 48 hours, when 2200 c.c. of hydrogen had been consumed, the product was isolated by distillation as an oil (5·5 g.), b. p. 170—180°/0·4 mm., from which (VI; R = H) (3·3 g.), m. p. 84°, rapidly separated. The residual oil was separated by Girard-T reagent into the ketonic phenol (VI; R = H) (0·6 g.) and (VII; R = H) (1·3 g.), m. p. 82°, as described in (*a*).

(*c*) Trimethyl purpurogallin (1 g.) was suspended together with Adams's catalyst (10 mg., prepared 2 months previously) in ethanol (60 c.c.). After 48 hours, when 240 c.c. of hydrogen had been absorbed, the ketonic phenol (A) was isolated as an oil, b. p. 145—150°/0·01 mm., which rapidly solidified and crystallised from *cyclo*hexane in cream-coloured prisms, m. p. 87° (Found: C, 63·4; H, 6·9; OMe, 34·5. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8; OMe, 35·0%). A Zerewitinoff determination showed the presence of one active hydrogen atom per molecule. The ketonic phenol (A) gave a 3 : 5-*dinitrobenzoate*

* Professor W. Baker kindly drew our attention to this method of purification, which had been used by Miss J. D. Hayward.

which crystallised from ethanol in yellow plates, m. p. 168° (Found: C, 54·9; H, 4·5; N, 6·5. $C_{21}H_{20}O_{10}N_2$ requires C, 54·8; H, 4·4; N, 6·1%), and an amorphous 2 : 4-dinitrophenylhydrazone.

Catalytic Reduction of Tetramethyl Purpurogallin.—Tetramethyl purpurogallin (0·4 g.) was reduced in ethanol (20 c.c.) in presence of freshly prepared Adams's catalyst (10 mg.). After 10 hours, when 100 c.c. of hydrogen had been absorbed, the product was distilled, and the oil, b. p. 120—130°/0·005 mm. (0·25 g.), deposited 4 : 2′ : 3′ : 4′-*tetramethoxybenz*cyclo*hepten*-3-*ol* (*tetramethyl hexahydropurpurogallin*) (VIII) on trituration with ether; crystallisation from acetone–ligroin gave colourless prisms, m. p. 142—143° (Found: C, 63·6; H, 8·0. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·8%), which yielded a crystalline 3 : 5-*dinitrobenzoate*, m. p. > 250°. The mother liquors from the carbinol yielded on evaporation tetramethyl tetrahydropurpurogallin (VI; R = Me) which was identified as the 2 : 4-dinitrophenylhydrazone, m. p. 176°, described on page 1049.

Oxidation of Tetramethyl Tetrahydropurpurogallin (VI; R = Me).—The ketonic ether (VI; R = Me) (1·8 g.) was dissolved in ethanol (30 c.c.), mixed with a solution of sodium hydroxide (3 g.) in water (9 c.c.), and heated on the water-bath for 1 hour with hydrogen peroxide (25 c.c. of 20 vol.). The mixture was cooled, neutral impurities were removed in ether, and, after acidification, γ-(3 : 4 : 5-*trimethoxy*-2-*carboxyphenyl*)*butyric acid* (X) was isolated with ether and crystallised from acetone–ligroin; colourless prisms (1·6 g.), m. p. 146—147° (Found: C, 56·0; H, 6·0; equiv., 150. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·0%; equiv., 149), were obtained. The *dimethyl* ester (4·2 g.) of (X), prepared by the use of ethereal diazomethane as an oil, b. p. 170—180°/0·4 mm., was dissolved in ether (10 c.c.) and added to a solution of methylmagnesium iodide, prepared from magnesium (2·9 g.), methyl iodide (8·5 c.c.) and ether (80 c.c.). After 1 hours' refluxing, the resulting carbinol was isolated and heated with potassium hydrogen sulphate (10 g.) and potassium sulphate (0·5 g.) at 180° for ½ hour. The product, isolated with ether, was separated by distillation into approximately equal quantities of two fractions, b. p. 150—155°/0·4 mm. and b. p. 165—170°/0·4 mm. respectively, which rapidly decolourised bromine in chloroform solution. The fraction, b. p. 165—170°/0·4 mm. (1 g.) was ozonised at − 78° in ethyl acetate (30 c.c.) for ½ hour; a crystalline *aldehyde* separated and crystallised from acetone–ligroin in colourless prisms, m. p. 111° (Found: C, 58·1; H, 6·1. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0%), which reduced Tollens's reagent and gave a 2 : 4-*dinitrophenylhydrazone* which crystallised from ethyl acetate in orange prisms, m. p. 196° (Found: C, 51·2; H, 4·6. $C_{19}H_{20}O_9N_4$ requires C, 50·9; H, 4·5%). This aldehyde has not been identified, and ozonisation of the fraction, b. p. 150—155°/0·4 mm., did not yield recognisable products.

Synthesis of γ-(3 : 4 : 5-*Trimethoxy*-2-*carboxyphenyl*)*butyric Acid* (X).—γ-(3 : 4 : 5-*Trimethoxybenzoyl*)-*butyric acid* (XIII). Ethyl β-iodopropionate (4·2 g.) was added with constant swirling to an ice-cold solution of the sodio-derivative prepared from ethyl 3 : 4 : 5-trimethoxybenzoylacetate (4·2 g.) (Perkin and Weizmann, *J.*, 1906, **89**, 1655), sodium (0·5 g.), and ethanol (40 c.c.). After 1 hour at 0° and 12 hours at 15°, the mixture was diluted with water, and the product, isolated with ether, was refluxed for 48 hours with 20% sulphuric acid (40 c.c.). Ice cooling deposited a crude acid which was taken up in dilute sodium hydroxide solution, neutral impurities were removed in ether, and the recovered *acid* (XIII) (4·2 g.) crystallised from benzene–ligroin in colourless plates, m. p. 120—121° (Found: C, 59·7; H, 6·1. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%). The *methyl* and the *ethyl* ester crystallised from ligroin in stout prisms, m. p. 60—61° (Found: C, 60·7; H, 7·0. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·8%) and m. p. 68° (Found: C, 62·3; H, 7·0. $C_{16}H_{22}O_6$ requires C, 61·9; H, 7·1%) respectively.

δ-(3 : 4 : 5-*Trimethoxyphenyl*)*valeric acid.* The keto-acid (XIII) (3 g.) was refluxed for 2·5 hours with trimethylene glycol (20 c.c.), powdered potassium hydroxide (2·4 g.), and 90% hydrazine hydrate (2·4 c.c.). The condenser was removed and the boiling continued until the temperature of the liquid reached 195°. The condenser was then replaced and the refluxing continued for a further 2·5 hours. As some demethylation took place during the reduction, the mixture was cooled, diluted with sodium hydroxide solution, and treated at 60° with 3 successive portions (5 c.c. each) of methyl sulphate at intervals of 10 minutes. After 1 hours' heating on the water-bath, acidification and ether extraction gave an oil which was distilled under reduced pressure; δ-(3 : 4 : 5-*trimethoxyphenyl*)*valeric acid*, b. p. 210—220°/0·5 mm., crystallised from *cyclo*hexane in colourless plates, m. p. 70° (Found: C, 62·9; H, 7·5. $C_{14}H_{20}O_5$ requires C, 62·7; H, 7·5%), which were unaffected by 50% sulphuric acid.

2′ : 3′ : 4′-*Trimethoxybenz*cyclo*hepten*-3-*one* (XIV). Phosphoric oxide (8 g.) was added in small portions to a boiling solution of the above valeric acid (1 g.) in benzene (15 c.c.). After 2·5 hours the mixture was cooled, and the dark phosphorus-containing complex was decomposed with ice, rendered alkaline, extracted with ether, and dried. Removal of the ether yielded the *ketone* (XIV), which separated from *cyclo*hexane in colourless rhombs (0·6 g.), m. p. 102° (Found: C, 67·4; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). The 2 : 4-*dinitriphenylhydrazone* crystallised from ethyl acetate in orange elongated prisms, m. p. 176—177°.

γ-(3 : 4 : 5-*Trimethoxy*-2-*carboxyphenyl*)*butyric acid* (X). 2′ : 3′ : 4′-Trimethoxybenz*cyclo*hepten-3-one (XIV) (1 g.) was refluxed with selenium dioxide (0·6 g.; 25% excess) in dioxan (15 c.c.) for 6 hours. Selenium was collected from the cooled solution and the filtrate was warmed on the water-bath with sodium hydroxide (15 c.c. of 2N), hydrogen peroxide (10 c.c. of 20 vol.), and ethanol (15 c.c.). When evolution of oxygen ceased, more peroxide (10 c.c.) was added and the process repeated. The solution was cooled and a small amount of ketone (XIV) recovered by extraction with ether; the aqueous layer was acidified, and the acid (X), isolated with ether, was purified by solution in sodium hydrogen carbonate, recovery with ether, and crystallisation from acetone–ligroin. γ-(3 : 4 : 5-*Trimethoxy*-2-*carboxyphenyl*)-*butyric acid* was obtained in colourless prisms (0·25 g.), m. p. 146—147° (Found: C, 56·2; H, 5·9; equiv., 151. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·0%; equiv., 149).

Synthesis of γ-(2 : 3 : 4-*Trimethoxy*-6-*carboxyphenyl*)*butyric Acid* (IX).—γ-(2 : 3 : 4-*Trimethoxybenzoyl*)*butyric acid* (XI). Trimethyl pyrogallol (2 g.) and glutaric anhydride (2 g.) were added to a solution of aluminium chloride (5 g.) in nitrobenzene (20 c.c.) and the mixture left for 48 hours. The resultant viscous liquid was decomposed with ice and hydrochloric acid, steam distilled to remove nitrobenzene, and extracted with ether. Evaporation to a small bulk yielded a small amount of a γ-(*hydroxydimethoxybenzoyl*)*butyric acid*, which crystallised from aqueous alcohol and then from

benzene–ligroin, giving colourless needles, m. p. 174° (Found : C, 58·5; H, 6·5. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0%). The remaining oil, which solidified after 48 hours, was crystallised from *cyclo*hexane; colourless elongated prisms of γ-(2 : 3 : 4-*trimethoxybenzoyl*)*butyric acid*, m. p. 73—75° (Found : C, 60·0; H, 6·2. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%), were obtained.

δ-(2 : 3 : 4-*Trimethoxyphenyl*)*valeric acid*. The crude mixture of trimethoxybenzoylbutyric acid and the corresponding dimethyl ether was dissolved in toluene and reduced by Clemmensen's method for 18 hours. On concentration of the toluene layer a δ-(*hydroxydimethoxyphenyl*)*valeric acid* separated; it crystallised in stout prisms from benzene (charcoal), and in plates from water, m. p. 108—109° (Found : C, 61·3; H, 7·1. $C_{13}H_{18}O_5$ requires C, 61·4; H, 7·1%). This and the remaining oil were dissolved in excess of aqueous sodium hydroxide and methylated with methyl sulphate. The ether extract of the acidified solution yielded δ-(2 : 3 : 4-*trimethoxyphenyl*)*valeric acid*, b. p. 200—210°/0·15 mm., which crystallised from ligroin in prisms, m. p. 66—67° (Found : C, 62·6; H, 7·4. $C_{14}H_{20}O_5$ requires C, 62·7; H, 7·5%).

1′ : 2′ : 3′-*Trimethoxybenz*cyclo*hepten*-3-*one* (XII). Phosphoric oxide (10 g.) was added to a solution of δ-(2 : 3 : 4-trimethoxyphenyl)valeric acid (1 g.) in benzene (20 c.c.), and, after refluxing for 3 hours, the dark complex was decomposed with ice, rendered alkaline, and extracted with ether. The extract was washed with sodium hydroxide solution, dried, and distilled, yielding 1′ : 2′ : 3′-*trimethoxybenz*-cyclo*hepten*-3-*one* (0·5 g.), b. p. 170°/0·3 mm. (Found : C, 67·0; H, 7·6. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). The 2 : 4-*dinitrophenylhydrazone* crystallised from aqueous acetic acid in orange-red plates, m. p. 179° (Found : C, 56·0; H, 5·3. $C_{20}H_{22}O_7N_4$ requires C, 55·8; H, 5·1%).

γ-(2 : 3 : 4-*Trimethoxy*-6-*carboxyphenyl*)*butyric acid* (IX). 1′ : 2′ : 3′-Trimethoxybenz*cyclo*hepten-3-one (0·65 g.) was oxidised as described for the isomeric ketone (XIV) with selenium dioxide (0·4 g.) and then with hydrogen peroxide (15 c.c. of 20 vol. added in 2 portions). The resulting acidic oil was methylated with diazomethane in ethereal solution, and the dimethyl ester was distilled at 0·1 mm., and hydrolysed with aqueous sodium hydroxide; γ-(2 : 3 : 4-*trimethoxy*-6-*carboxyphenyl*)*butyric acid* crystallised from water in needles, m. p. 132° (Found : C, 56·4; H, 6·0. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·0%).

4-*Hydroxy*-3-*keto*-2-*carboxy*cyclo*heptatrienylacetic Acid* (XV; R = H).—A steady stream of carbon dioxide-free air was drawn through a solution of purpurogallin (2 g.) in 5% potassium hydroxide (150 c.c.) for 20 hours. The solution was acidified with dilute sulphuric acid, the precipitated humic acid was collected, and the filtrate was extracted continuously with ether for 20 hours. The extract was decanted from tar, clarified with charcoal, dried, and evaporated. The residual amber oil gradually deposited a crystalline solid (0·11 g.) which was freed from oily impurities with a little ether and recrystallised from ligroin containing a small amount of acetone; colourless prisms, m. p. 182° (decomp.) (Found : C, 53·7; H, 3·6; equiv., 76. $C_{10}H_8O_6$ requires C, 53·6; H, 3·6%; equiv., 75), were obtained which dissolved in aqueous sodium hydrogen carbonate giving a bright yellow solution and gave a deep red ferric test. The *methyl* 3-*keto*-2-*carbomethoxy*-4-*methoxy*cyclo*heptatrienylacetate* (XV; R = Me), prepared by the action of diazomethane in ether–acetone solution, crystallised from benzene in colourless needles, m. p. 110° (Found : C, 58·9; H, 5·6. $C_{13}H_{14}O_6$ requires C, 58·7; H, 5·3%).

2-*Hydroxy*-6-*methyl*cyclo*heptatrienone* (XVI), prepared by decarboxylation of the acid (XV; R = H) by heating at the melting point, was purified by sublimation; colourless prisms, m. p. 77° (Found : C, 70·2; H, 6·2; equiv., 136. $C_8H_8O_2$ requires C, 70·5; H, 5·9%; equiv., 136), which dissolved with effervescence in aqueous sodium hydrogen carbonate and gave a green ferric test, were obtained.

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