359. *Gallotannins. Part II.* Some Esters and Depsides of Gallic Acid.*

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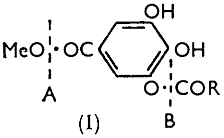
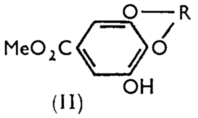
During attempts to distinguish between depside and ester linkages it has been discovered that *o*-hydroxydepsides such as (I) and (III) undergo methanolysis with 90% methanol at pH 5—6, giving in the case of (III) a mixture of methyl protocatechuate and methyl benzoate. The mechanism of the reaction which has applications in gallotannin chemistry is briefly discussed.

A suggestion that *m*-digallic acid was produced as an artefact during the hydrolysis of the gallotannin has been disproved by studies of the hydrolysis of model compounds including digalloyloxyethane, tri-*O*-galloylglycerol, and cyclohexane-*cis*- and -*trans*-1,2-diol digallate.

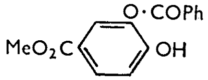
The presence in the gallotannin of *m*-digalloyl and possibly polygalloyl groups has been postulated by previous writers including Fischer,[1] Freudenberg,[2] Karrer,[3] and others. In Part I of this series (preceding paper) the fractionation of the enzyme tannase to give a specific galloyl esterase was described and it was hoped that further fractionation would provide an enzyme with specific reactivity at the depside linkage, *e.g.*, " A " in formula (I), but without effect on the ester aliphatic linkage, *e.g.*, " B " in formula (I). Evidence that two such enzymes exist in tannase was put forward by Toth and Barsony.[4] Such a depsidase would have valuable application in gallotannin chemistry and in order that the fractionation of tannase could be tested model compounds of type (I) have been synthesised.



(I)



(II)



(III)

The preparation of depsides of this type (I) containing methyl gallate residues presented difficulties. Fischer and Freudenberg[5] used the cyclic carbonate (II; R = $>$CO) and after condensing tri-*O*-methoxycarbonylgalloyl chloride, prepared *m*-digallic acid by hydrolysis of the protecting groups with dilute sodium hydroxide. In a later method[6] methyl 3-*O*-benzoylgallate (I; R = Ph) was prepared by reaction of 3,5-di-*O*-acetylgallic acid and benzoyl chloride, followed by methylation to give the methyl ester of the protected *p*-depside. This was converted into the *m*-depside by alkaline hydrolysis of the acetyl groups and simultaneous rearrangement of the benzoyl group. The latter method has, however, proved unreliable in some cases[7] and we have prepared methyl 3-*O*-benzoylgallate (I; R = Ph) by a modification of the method of Seshadri *et al.*,[8] which uses the preferential acylation at a *meta*- rather than *para*-hydroxyl group relative to a carboxyl group. Methylation of the diester (I; R = Ph) gave methyl 3-benzoyloxy-4,5-dimethoxybenzoate (V); and methyl 3-*O*-benzoylprotocatechuate (III) was prepared

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* Part I, preceding paper.

[1] Fischer, *Ber.*, 1919, **52**, 809.

[2] Freudenberg, " Naturliche Gerbstoffe," Verlag Chemie, Berlin, 1920, p. 101.

[3] Karrer, Salomon, and Payer, *Helv. Chim. Acta*, 1923, **6**, 17.

[4] Toth and Barsony, *Enzymologia*, 1943—1945, **11**, 19.

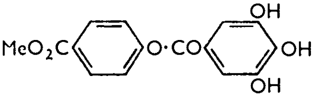
[5] Fischer and Freudenberg, *Ber.*, 1913, **46**, 1116.

[6] Fischer, Bergmann, and Lipschitz, *Ber.*, 1918, **51**, 45.

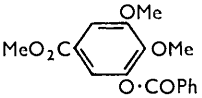
[7] Cavallito and Buck, *J. Amer. Chem. Soc.*, 1943, **65**, 2141.

[8] Seshadri, Aghoramurtny, and Venkatasubramanian, *Tetrahedron*, 1957, **1**, 310.

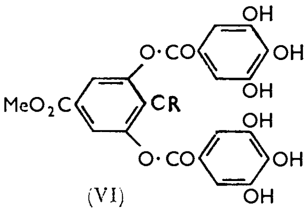
similarly by benzoylation of methyl protocatechuate. For the preparation of other depsides a new method was developed, the potentialities of which have, since the completion of this work, been hinted at by Jurd.[9] Methyl gallate was converted into methyl 3,4-diphenylmethylenedioxy-5-hydroxybenzoate (II; R = $>CPh_2$) as described by Robinson, Bradley, and Schwarzenbach;[10] then condensation with tri-*O*-benzylgalloyl chloride[11] followed by hydrogenolysis of the protecting groups from the resultant depside gave methyl *m*-digallate (I; R = 3,4,5-trihydroxyphenyl). A similar method was used to prepare methyl 3-*p*-hydroxybenzoylgallate (I; R = *p*-$HO\cdot C_6H_4$). Methyl *p*-galloyloxybenzoate (IV) was prepared by condensation of methyl *p*-hydroxybenzoate and tri-*O*-benzylgalloyl chloride and subsequent removal of the protecting groups by hydrogenolysis. Methyl tri-*O*-galloylgallate (VI; R = 3,4,5-trihydroxybenzoyl) and methyl 3,5-di-*O*-galloylgallate (VI; R = H) were prepared by condensation of tri-*O*-benzylgalloyl chloride with methyl gallate and methyl 4-*O*-benzylgallate respectively, followed by hydrogenation to remove protecting groups.



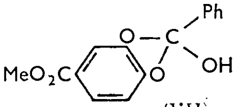
(IV)



(V)



(VI)



(VII)

The possibility that tannase contained esterases specific for both the aliphatic ester and the depside linkages, as " B " and " A " respectively in structure (I), was investigated by partial denaturation of the enzyme. The incubation at pH 3 and pH 7 considerably reduced its activity towards methyl gallate, but a smaller decrease was observed with methyl *m*-digallate (I; R = 3,4,5-trihydroxyphenyl), and a possible explanation of this would be the greater stability at these pH values of a depsidase than of the normal esterases. Generally, however, the low solubility in aqueous buffer created difficulties in testing the depsides as tannin substrates, but surprising results were obtained by carrying out the reaction in aqueous methanol. When methyl *m*-digallate (I; R = 3,4,5-trihydroxyphenyl) was treated with tannase in 30% methanolic buffer at pH 5—6, methanolysis occurred with the formation of methyl gallate and small amounts of gallic acid. It was shown that rupture of the depside linkage occurred independently of the tannase, and methanolysis of methyl *m*-digallate proceeded smoothly with 90% methanol at 37° at pH 5—6. No methanolysis took place at or below pH 3, and at pH 6 spontaneous hydrolysis occurred. Preliminary experiments indicated that the reaction took place more readily in methanol than ethanol, and in s- or t-butyl alcohol there was no alcoholysis. Examination of other depsides showed that (I; R = Ph or *p*-$HO\cdot C_6H_4$), (III), and (VI; R = H) underwent methanolysis under similar conditions, the first two giving methyl gallate and methyl benzoate or methyl *p*-hydroxybenzoate respectively, (III) yielding a mixture of methyl protocatechuate and methyl benzoate, and (VI; R = H) giving methyl gallate alone. As the depsides (IV), (V), the *O*-benzoate of (II; R = $>CPh_2$), and methyl trigalloylgallate (VI; R = 3,4,5-trihydroxybenzoyl), and esters such as tri-*O*-galloylglycerol, 1-*O*-galloyl- and β-penta-*O*-galloyl-glucose were stable to the conditions of methanolysis, it was concluded that the reaction requires the presence of an *o*-hydroxydepside grouping, and it is tentatively suggested that the mechanism of the reaction depends on the formation of a cyclic intermediate of the type (VII), which by

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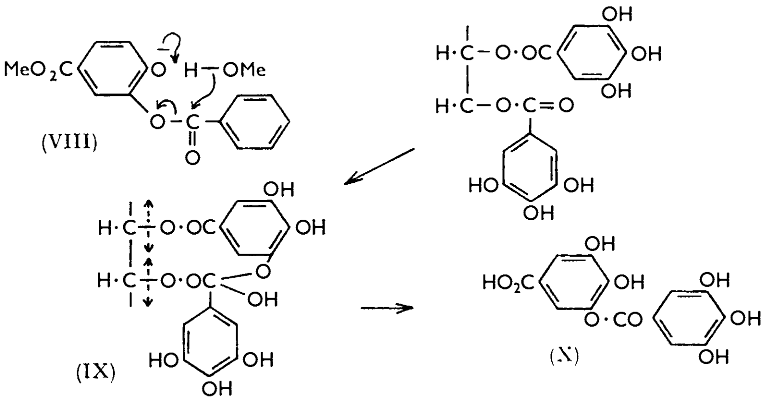
[9] Jurd, *J. Amer. Chem. Soc.*, 1959, **82**, 4606.
[10] Robinson, Bradley, and Schwarzenbach, *J.*, 1930, 812.
[11] Clinton and Geissmann, *J. Amer. Chem. Soc.*, 1943, **65**, 85.

analogy with carbinol-amines, such as cotarnine, might be expected to be methylated easily. Alternative mechanisms, such as (VIII), based on the initial ionisation of the hydroxyl group *para* to the methoxycarbonyl group, followed by attack of the methanol, are not so favoured in view of the inability to methanolyse phenyl salicylate. Mechanisms based on activating effects from the methoxylcarbonyl group are unlikely, since mono-*O*-benzoylcatechol was readily methanolysed to methyl benzoate and catechol. The mechanism of the reaction is being investigated more fully, but the methanolysis has obvious applications to gallotannin chemistry, since it brings about the decomposition of depsides of type (I) in a manner for which we had hoped to find an enzyme catalyst. Some of the preliminary results of the reaction with gallotannins are described in Part III of this series.

The presence of *m*-digallic acid (X) in the structure of Chinese gallotannin is based on (*a*) the isolation of 3,4-di-*O*-methylgallic acid and 3,4,5-tri-*O*-methylgallic acid from alkaline hydrolysis of the methylated tannins,[12] (*b*) the detection of *m*-digallic acid (X) (and possibly a trigallic acid) by paper chromatography of the acid and alkaline hydrolysis of gallotannin,[13] and (*c*) the isolation of methyl penta-*O*-methyl-*m*-digallate by methylation of the gallotannin with diazomethane in methanol.[14] It seemed feasible that the *m*-digallic acid might be produced as an artefact during the hydrolysis of the tannin, after intermediate formation of the cyclic derivative (IX) from suitably disposed galloyl groups. Alternatively such structures might exist permanently within the tannin itself. Hydrolysis could then proceed in two ways to give either gallic or *m*-digallic acid and the reaction would be analogous in many ways to that of methanolysis already described.



(VIII)

(IX)

(X)

In order to test this supposition, digalloyloxyethane, tri-*O*-galloylglycerol, and cyclohexane-*cis*- and -*trans*-1,2-diol digallate were prepared by condensing tri-*O*-benzylgalloyl chloride and the appropriate alcohol and then removing the benzyl groups by hydrogenation. Two-dimensional paper chromatography was eminently suited for the detection of intermediate products of the acid and alkaline hydrolysis of these galloyl esters. For example, in the case of tri-*O*-galloylglycerol, after hydrolysis with acids for half an hour, six phenolic substances were then detected; these may be attributed to unchanged tri-*O*-galloyl-, the two isomeric 1,2- and 2,3-di-*O*-galloyl-, the two isomeric 1- and 2-mono-*O*-galloyl-glycerols, and free gallic acid. Similar but less complex patterns were found with other galloylated glycols and all point to the multiplicity of products to be expected from a gallotannin. In all cases, however, acid or alkaline hydrolysis of these galloyl esters gave gallic acid and the corresponding alcohol, no trace of *m*-digallic acid was observed on the paper

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[12] Herzig, *Ber.*, 1905, **38**, 989; *Monatsh.*, 1909, **30**, 543.

[13] White, "The Chemistry of the Vegetable Tannins, Society of Leather Trades' Chemists, Croydon, 1956, p. 13.

[14] Herzig, *Ber.*, 1923, **56**, 221.

chromatogram, and there are no grounds for believing that *m*-digallic acid arises as an artefact from gallotannin hydrolysis. The original proposal that di-, tri-, and poly-galloyl chains are present in the tannin structure is thus more consistent with the known facts.

EXPERIMENTAL

Methyl 3-O-*Benzoylgallate* (I; R = Ph).—To a solution of methyl gallate (1·8 g.) in ether (100 c.c.) containing pyridine (2·0 c.c.), benzoyl chloride (1·4 g.) was added. An oil separated and after 6 hr. the ether was decanted, the oil was taken up in ethyl acetate (50 c.c.), and the combined solutions were washed with 2N-hydrochloric acid (50 c.c.), water, sodium hydrogen carbonate solution, and finally water, and dried (Na_2SO_4). Removal of the solvent gave an oil which crystallised on trituration with warm benzene (20 c.c.). Residual methyl gallate was removed in boiling water and crystallisation from ether–light petroleum (b. p. 40—60°) yielded methyl 3-*O*-benzoylgallate (1·1 g.) as prisms, m. p. 172—174° (Fischer, Bergmann, and Lipschitz [6] give m. p. 173—175°) (Found: C, 62·3; H, 4·4. Calc. for $C_{15}H_{12}O_6$: C, 62·5; H, 4·2%). The infrared spectrum, determined on a potassium bromide disc, showed bands at 1718 and 1682 cm.$^{-1}$.

Methyl 3-*Benzoyloxy*-4,5-*dimethoxybenzoate* (V).—An excess of ethereal diazomethane was added to methyl 3-*O*-benzoylgallate (9·0 g.) in ethyl acetate (50 c.c.). After 12 hr. the solution was filtered through a small column of alumina (20 g.) and evaporated; the resultant oil separated from ethyl acetate–light petroleum (b. p. 60—80°) as plates (7·5 g.), m. p. 90° (Fischer, Bergmann, and Lipschitz [6] give m. p. 91—92°).

Methyl p-*Benzyloxybenzoate*.—A solution of methyl *p*-hydroxybenzoate (28 g.) in acetophenone (50 c.c.) and potassium carbonate (28·4 g.) were heated to 150° and benzyl chloride was added with stirring during 1 hr. After a further 7 hours' heating the solvent was removed in steam, and the product collected and crystallised from benzene–light petroleum (b. p. 40—60°); *methyl* p-*benzyloxybenzoate* (31 g.) separated as needles, m. p. 90° (Found: C, 74·2; H, 5·8. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%).

p-*Benzyloxybenzyl Chloride*.—Methyl *p*-benzyloxybenzoate (30·0 g.) was refluxed for 2 hr. in ethanol (100 c.c.) and 10% aqueous sodium hydroxide (800 c.c.). *p*-Benzyloxybenzoic acid (21·0 g.), liberated by acidification, crystallised from ethanol in needles, m. p. 186° (Cavallito and Buck [7] give m. p. 188°). The *chloride* prepared by refluxing the acid (21·0 g.) for 1 hr. with thionyl chloride (25 c.c.) separated from benzene–light petroleum (b. p. 40—60°) in prisms (19·0 g.), m. p. 102° (Found: C, 68·2; H, 4·6. $C_{14}H_{11}ClO_2$ requires C, 68·2; H, 4·4%).

Methyl 3-p-*Benzyloxybenzoyl*-4,5-*diphenylmethylenedioxybenzoate*.—*p*-Benzyloxybenzoyl chloride (2·75 g.) and methyl 3,4-diphenylmethylenedioxy-5-hydroxybenzoate (II; R = $>CPh_2$) (3·5 g.) were dissolved in chloroform (100 c.c.) containing pyridine (4·0 c.c.). After 48 hr. the solution was washed successively with dilute hydrochloric acid, sodium hydroxide, and water, dried, and evaporated under reduced pressure. The product separated from benzene–light petroleum (b. p. 40—60°) in prisms (4·5 g.), m. p. 168° (Found: C, 75·3; H, 4·8. $C_{35}H_{26}O_7$ repuires C, 75·1; H, 4·7%).

Methyl 3-*Benzoyl*-4,5-*diphenylmethylenedioxybenzoate*.—Prepared as above, this *ester* crystallised from methanol in plates, m. p. 113—114° (Found: C, 74·1; H, 4·7. $C_{28}H_{20}O_6$ requires C, 74·3; H, 4·4%).

Methyl 3-O-p-*Hydroxybenzoylgallate*.—A solution of methyl 3-*p*-benzyloxybenzoyl-4,5-diphenylmethylenedioxybenzoate (4·99 g.) in tetrahydrofuran (50 c.c.) was reduced in the presence of 10% palladium–charcoal (0·5 g.) until hydrogen uptake (624 c.c.) was complete, then evaporated under reduced pressure and the product was extracted with benzene to remove diphenylmethane. *Methyl* 3-O-p-*hydroxybenzoylgallate* (1·80 g.) crystallised from ethyl acetate–benzene in prisms, m. p. 210° (Found: C, 59·3; H, 4·4. $C_{15}H_{12}O_7$ requires C, 59·2; H, 4·0%), $\nu_{max.}$ (KBr disc) 1728 and 1709 cm.$^{-1}$.

Methyl 4,5-*Diphenylmethylenedioxy*-3-(*tri*-O-*benzylgalloyloxy*)*benzoate*.—Tri-*O*-benzylgalloyl chloride (9·0 g.) and methyl 4,5-diphenylmethylenedioxy-3-hydroxybenzoate (6·83 g.) were dissolved in chloroform (100 c.c.) containing pyridine (8·0 c.c.). After 24 hr. the solution was washed with 2N-hydrochloric acid and water, and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residual oil was taken up in benzene–ethyl acetate (3 : 1; 50 c.c.) and filtered through a column of alumina (100 g.), and washing continued with the same solvent.

Removal of the solvent from the eluate gave an oily *ester* which crystallised from ethyl acetate–ethanol in slender needles (8·0 g.), m. p. 102—104° (Found: C, 76·8; H, 5·3. $C_{49}H_{38}O_9$ requires C, 76·4; H, 4·9%).

Methyl m-*Digallate* (I; R = 3,4,5-trihydroxyphenyl).—Methyl 4,5-diphenylmethylenedioxy-3-(tri-*O*-benzylgalloyloxy)benzoate (2·5 g.) was reduced in ethyl acetate (25 c.c.) in presence of 10% palladium–charcoal (0·289 g.). *Methyl* m-*digallate,* crystallised from acetone–benzene and then from ethyl acetate–light petroleum (b. p. 40—60°), was obtained as small prisms (1·07 g.), m. p. 230—232° (Found: C, 53·4; H, 3·6. Calc. for $C_{15}H_{12}O_9$: C, 53·6; H, 3·6%). (Fischer, Bergmann, and Lipschitz[6] give m. p. 175° for a monohydrate.) Methyl *m*-digallate (in a KBr disc) showed infrared peaks at 1710 and 1699 cm.$^{-1}$.

Methyl 3-O-*Benzoylprotocatechuate* (III).—After 12 hr. a mixture of benzoyl chloride (7·5 g.) and methyl protocatechuate (8·4 g.) in ether (50 c.c.) containing pyridine (2 c.c.) was diluted with ethyl acetate (50 c.c.), washed with 2N-hydrochloric acid (75 c.c.) and water, and dried (Na_2SO_4). After removal of the solvents the resultant gum was extracted with boiling water, and the residue separated from benzene–light petroleum (b. p. 60—80°) in prisms (10·0 g.), m. p. 152—153° (Found: C, 65·9; H, 4·3. Calc. for $C_{15}H_{12}O_5$: C, 66·1; H, 4·4%). Fischer, Bergmann, and Lipschitz[6] give m. p. 153—155°.

*Methyl Tri-*O*-benzylgalloyloxybenzoate.*—Tri-*O*-benzylgalloyl chloride (4·6 g.) in chloroform (50 c.c.) was added to a solution of methyl *p*-hydroxybenzoate (1·5 g.) in chloroform (50 c.c.) containing pyridine (8·0 c.c.). After 12 hr. and dilution with ethyl acetate (200 c.c.) the solution was washed with dilute hydrochloric acid (3 × 100 c.c.) and water, and dried (Na_2SO_4). The solution was filtered through a small column of alumina and evaporation of the filtrate gave the *diester* which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in colourless needles (4·8 g.), m. p. 127—128° (Found: C, 75·3; H, 5·4. $C_{36}H_{30}O_7$ requires C, 75·3; H, 5·3%).

Methyl p-*Galloyloxybenzoate* (IV).—Methyl *p*-tri-*O*-benzylgalloyloxybenzoate (1·8 g.) was reduced in ethyl acetate (50 c.c.) in presence of 10% palladium–charcoal (0·5 g.); the *product* separated from ethyl acetate in colourless needles (0·7 g.), m. p. 207—208° (Found: C, 58·9; H, 4·2. $C_{15}H_{12}O_7$ requires C, 59·2; H, 3·9%), $\nu_{max.}$ (in KBr) 1713 and 1682 cm.$^{-1}$.

*Methyl Tris(tri-*O*-benzylgalloyl)gallate.*—Methyl gallate (0·46 g.) and tri-*O*-benzylgalloyl chloride (4·6 g.) were dissolved in chloroform (30 c.c.) containing pyridine (3·0 c.c.) and kept for 4 days, then further chloroform (30 c.c.) was added and the solution washed with 2N-hydrochloric acid and water, and dried ($MgSO_4$). Removal of the solvent gave an oil which was dissolved in benzene (50 c.c.) and chloroform (50 c.c.) and filtered through alumina (65 g.). Evaporation of the solvents from the eluate gave an oily *product* which crystallised from ether–light petroleum (b. p. 40—60°) in fine needles (2·8 g.), m. p. 107° (Found: C, 76·3; H, 5·4. $C_{92}H_{74}O_{17}$ requires C, 76·2; H, 5·1%), $\nu_{max.}$ (in KBr) 1740 cm.$^{-1}$.

*Methyl Tri-*O*-galloylgallate* (VI; R = 3,4,5-trihydroxybenzoyl).—Methyl tris(tri-*O*-benzylgalloyl)gallate (0·5 g.) was reduced in the presence of 10% palladium–charcoal (0·06 g.) in ethyl acetate (12 c.c.). The *product* crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in small plates (0·17 g.), m. p. 208—212° (decomp.) (Found: C, 54·2; H, 3·4. $C_{29}H_{20}O_{17}$ requires C, 54·5; H, 3·0%), $\nu_{max.}$ (in KBr) 1726 cm.$^{-1}$. Hydrolysis with 10% hydrochloric acid for 5 hr. gave gallic acid.

Methyl 4-O-*Benzyl*-3,5-*di*-O-(*tri*-O-*benzylgalloyl*)*gallate.*—Methyl 4-*O*-benzylgallate (0·82 g.) and tri-*O*-benzylgalloyl chloride (4·13 g.) were dissolved in chloroform (50 c.c.) and pyridine (2·4 c.c.) and kept for 3 days. After dilution with chloroform (50 c.c.) the solution was washed with 2N-hydrochloric acid and water, dried ($MgSO_4$), and evaporated to 25 c.c. Benzene (25 c.c.) was added and the solution filtered through neutralised alumina (30 g.). Removal of the solvents gave an *ester* which crystallised in fine needles (from ethyl acetate), m. p. 152° (Found: C, 75·8; H, 5·5. $C_{71}H_{58}O_{13}$ requires C, 76·2; H, 5·2%).

Methyl 3,5-*Di*-O-*galloylgallate* (VI; R = H).—Methyl 4-*O*-benzyl-3,5-di-*O*-(tri-*O*-benzylgalloyl)gallate (10·7 g.) was hydrogenated in ethyl acetate (50 c.c.) with 10% palladium–charcoal (0·1 g.) as catalyst. When the uptake of hydrogen had ceased, the catalyst was removed and the solvent evaporated; the residual *hydroxy-ester* separated from ethyl acetate–benzene in crystals, m. p. 195—200° (decomp.) (Found: C, 53·8; H, 3·3. $C_{22}H_{16}O_{13}$ requires C, 54·1; H, 3·3%).

Methanolysis of Substrates.—A 0·5% solution (0·5 c.c.) of the substrate in a mixture of 0·1N-sodium acetate buffer pH 5 (7 parts) and methanol (3 parts) was incubated at 37° for 12 hr.

and then chromatographed in two dimensions on Whatman No. 1 chromatography paper with the solvent systems 6% aqueous acetic acid and butan-2-ol–acetic acid–water (14 : 1 : 5). The position of the *o*-dihydric phenols was located with a ferric chloride–potassium ferricyanide [15] spray, and the products were identified with standard marker substances. Neutral esters were identified as described below in the case of methyl benzoate.

Methanolysis of Methyl 3-O-*Benzoylprotocatechuate* (III).—Methyl 3-*O*-benzoylprotocatechuate (0·9 g.) was dissolved in methanol (10 c.c.) containing 0·5N-sodium acetate buffer (1·0 c.c.; pH 6·0) and incubated at 37° for 24 hr. The solvents were removed on a rotary evaporator at 30°, the residue was dissolved in ether (40 c.c.), and phenolic material was removed in 2N-sodium hydroxide (20 c.c.). Evaporation of the ethereal solution at 40° gave an oil with a strong ester odour which was distilled (bath-temp. 205°), to give a colourless oil (0·06 g.). 10% Ethanolic sodium hydroxide (5 c.c.) was added to the oil, and the solution was refluxed for 1 hr., cooled, and acidified with concentrated hydrochloric acid. The crystals which separated had m. p. 120°, alone and on admixture with benzoic acid. Benzoic acid was also identified by paper chromatography on Whatman No. 1 chromatography paper in the system butan-1-ol saturated with aqueous ammonia; [16] the acids were revealed with a spray of B.D.H. universal indicator adjusted to pH 9·0.

Bistri-O-*benzylgalloyloxyethane.*—Ethyleneglycol (1·01 g.) and tri-*O*-benzylgalloyl chloride (18·0 g.) were dissolved in chloroform (65 c.c.) containing quinoline (8·2 g.), and the solution heated at 60° for 10 days with the exclusion of moisture. The mixture was diluted with chloroform (200 c.c.) and washed successively with 2N-hydrochloric acid (2 × 75 c.c.), water, sodium hydrogen carbonate solution, and finally water. After drying of the chloroform solution ($CaCl_2$) the solvent was removed and the residue crystallised several times from aqueous acetone. *Bistri*-O-*benzylgalloyloxyethane* (11 g.) crystallised in small needles, m. p. 141° (Found: C, 76·7; H, 5·6. $C_{58}H_{50}O_{10}$ requires C, 76·8; H, 5·5%).

Digalloyloxyethane.—A solution of bistri-*O*-benzylgalloyloxyethane (2·0 g.) in tetrahydrofuran (100 c.c.) was reduced in presence of 10% palladium–charcoal (0·133 g.) until uptake of hydrogen (260 c.c.) was complete. The product crystallised from water–acetone (2 : 3) in slender needles which did not melt below 260° (Found: C, 52·1; H, 4·4. Calc. for $C_{16}H_{14}O_{10}$: C, 52·4; H, 3·9%). Fischer and Bergmann [17] give no m. p. below 289°.

Tri-O-*galloylglycerol.*—Tri-*O*-galloylglycerol was prepared by Schmidt and Blank's method.[18]

Cyclohexane-cis-1,2-*diol Bistri*-O-*benzylgallate.*—Cyclohexane-*cis*-1,2-diol [19] (0·7 g.) and tri-*O*-benzylgalloyl chloride (11·0 g.) in chloroform (60 c.c.) containing quinoline (5 g.) were heated at 60° for 20 days. The product, isolated as described above for bistri-*O*-benzylgalloyloxyethane, was dissolved in benzene (75 c.c.) and filtered through a column of activated alumina (200 g.). The column was washed with benzene (150 c.c.) and removal of the benzene from the eluate gave an oily *ester* which separated from acetone in needles (3·4 g.), m. p. 129° (Found: C, 77·6; H, 6·1. $C_{62}H_{56}O_{10}$ requires C, 77·5; H, 5·9%).

Cyclohexane-cis-1,2-*diol Digallate.*—The above gallate (1·3 g.) was hydrogenated in tetrahydrofuran (150 c.c.) with 10% palladium–charcoal (0·11 g.). Removal of the solvent and crystallisation of the product from aqueous acetone gave *cyclohexane*-cis-1,2-*diol digallate* in small rhombs (0·5 g.), m. p. 222° (Found: C, 56·8; H, 4·8. $C_{20}H_{20}O_{10}$ requires C, 57·1; H, 4·8%).

Cyclohexane-trans-1,2-*diol Bistri*-O-*benzylgallate.*—Cyclohexane-*trans*-1,2-diol [20] (1·2 g.) and tri-*O*-benzylgalloyl chloride (10·0 g.) in chloroform (50 c.c.) containing quinoline (5 g.) were heated for 10 days at 60°. The *product*, isolated as described above for the *cis*-isomer, crystallised from acetone in slender needles (8·2 g.), m. p. 111° (Found: C, 77·3; H, 6·0%).

Cyclohexane-trans-1,2-*diol Digallate.*—The above *trans*-ester (1·5 g.), reduced as described above for the *cis*-isomer, gave a *product* that crystallised from aqueous acetone in irregular prisms (0·48 g.), m. p. 150° (Found: C, 56·7; H, 4·9%).

Hydrolysis of Gallates.—(a) *By alkali.* The gallate (0·09 g.) was added to 25% potassium hydroxide solution (1 c.c.), through which a brisk stream of oxygen-free nitrogen was passed.

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[15] Kirby, Knowles, and White, *J. Soc. Leather Trades' Chemists*, 1953, **37**, 283.

[16] Fewster and Hall, *Nature*, 1951, **168**, 78.

[17] Fischer and Bergmann, *Ber.*, 1918, **51**, 1760.

[18] Schmidt and Blank, *Ber.*, 1956, **89**, 287.

[19] Clark and Owen, *J.*, 1949, 365.

[20] Adkins and Roebuck, *J. Amer. Chem. Soc.*, 1950, **72**, 3639.

The temperature was kept at 0°, and after 1, 3, 6, 12, and 24 hr. samples (0·2 c.c.) were withdrawn, neutralised with glacial acetic acid (0·12 c.c.), and passed down a column (3 × 1 cm.) of Dowex " 50 " to remove potassium ions, and the hydrolysate was collected in water (5 c.c.). After concentration to 0·5 c.c. at 30° in a rotary evaporator the sample was analysed by paper chromatography as outlined on p. 1841.

(b) *By acid.* The gallate (0·004 g.) was heated at 100° for 2 hr. with 10% hydrochloric acid (0·1 c.c.) and sampled after 0·5, 1, 1·5, and 2 hr. The sample was spotted directly on to Whatman No. 1 chromatography paper and chromatographed as described on p. 1841.

The gallates and their hydrolysis products had the following R_F values in (*a*) 6% aqueous acetic acid and (*b*) s-butyl alcohol–acetic acid–water (14 : 1 : 5) respectively. Di-*O*-galloyloxyethane (0·06, 0·45); ethylene glycol monogallate (0·52, 0·59); tri-*O*-galloylglycerol (0·06, 0·54); 1,2-di-*O*-galloylglycerol (0·13, 0·41); 1,3-di-*O*-galloylglycerol (0·23, 0·47); 1-*O*-galloylglycerol (0·64, 0·51); 2-*O*-galloylglycerol (0·56, 0·46); cyclohexane-*cis*-1,2-diol digallate (0·29, 0·79); cyclohexane-*cis*-1,2-diol monogallate (0·63, 0·74); cyclohexane-*trans*-1,2-diol digallate (0·36, 0·82); cyclohexane-*trans*-1,2-diol monogallate (0·59, 0·85); methyl tri-*O*-galloylgallate (VI; R = 3,4,5-trihydroxybenzoyl) (0·36, 0·70); gallic acid (0·52, 0·63); *m*-digallic acid (X) (0·25, 0·73).

The designation of the products of hydrolysis of tri-*O*-galloylglycerol was deduced from the rates of hydrolysis of the various compounds and from the knowledge that esters of primary alcohols undergo more rapid hydrolysis than those of secondary alcohols.

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