2. The effect of structure on the reactivity of the hydroxyl-hydrogen atoms in these alcohols is discussed.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF BRISTOL]

GALLOTANNIN. XIII. THE IDENTITY OF DIGALLIC ACID FROM GALLOTANNIN WITH SYNTHETIC META-DIGALLIC ACID

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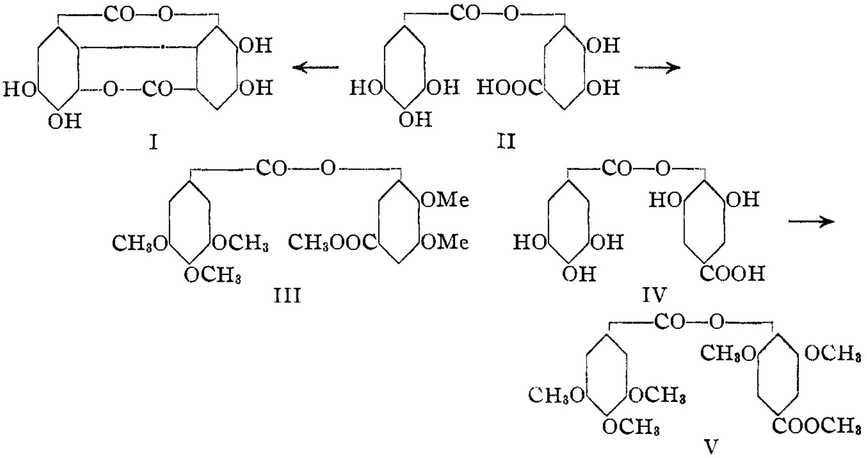
Fischer and Freudenberg[1] have come to the conclusion that there is a fundamental difference between their synthetic *m*-digallic acid (m. p., 271°) and the *m*-digallic acid (m. p., 268–270°) found by Nierenstein[2] in gallotannin. Whereas the latter yields ellagic acid (I) on oxidation,[3] no such oxidation product is obtained from synthetic *m*-digallic acid.[4] The same difference has previously been observed by Nierenstein[3] in the case of the synthetic digallic acid (m. p., 275–280°) prepared by Fischer[5] and it was therefore assumed by Nierenstein that the naturally occurring product is *m*-digallic acid (II), since it yields ellagic acid (I) on oxidation, and that Fischer's synthetic product is probably *p*-digallic acid (IV), which can obviously not be oxidized to ellagic acid (I).



This view was favored at first by Fischer and Freudenberg[6] but it was

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[1] Fischer and Freudenberg, *Ber.*, **46**, 1128 (1913).

[2] Nierenstein, *Ber.*, **43**, 628 (1910).

[3] Ref. 2, p. 630.

[4] Ref. 1, p. 1123.

[5] Fischer, *Ber.*, **41**, 2890 (1908).

[6] (a) Fischer and Freudenberg, *Ann.*, **384**, 225 (1911). Compare also (b) Fischer and Pfeffer, *Ann.*, **389**, 198 (1912).

later somewhat discounted[7] by the fact that on repeated crystallization Fischer's digallic acid (m. p., 275–280°), prepared by him in 1908, gives a product that melts at 275°. This latter product they regarded as being identical with their digallic acid (m. p., 271°), to which they assigned Formula II, since with diazomethane methyl pentamethyl-*m*-digallate (III), which they found to melt at 128–129°, is obtained from it. This latter product had previously been synthesized by Mauthner[8] who has also found that it melts at 128–129°.

In view of the well-established fact that over 60% of the gallotannin molecule is oxidized to ellagic acid, which has been shown by Nierenstein, Spiers and Geake[9] to be derived from the *m*-digallic acid nuclei present in gallotannin, the observation of Fischer and Freudenberg that their synthetic *m*-digallic acid (II) does not yield ellagic acid (I) on oxidation, and that there is therefore a fundamental difference between the *m*-digallic acid from gallotannin (Nierenstein) and the synthetic *m*-digallic acid (Fischer) obviously requires confirmation. It was with this object in view that the present investigation was undertaken, with the result that the absolute identity of these two substances was conclusively established, as may be judged from the following results:

1. Diazomethane converts the *m*-digallic acid (II) from gallotannin, into methyl pentamethyl-*m*-digallate (III), which melts correctly at 127–128°. This melting point is not depressed on admixture with synthetic methyl pentamethyl-*m*-digallate kindly sent us by Professor Mauthner.
2. The melting point of *m*-digallic acid from gallotannin is not depressed on admixture with synthetic *m*-digallic acid, which we have prepared according to Fischer and Freudenberg,[10] and Fischer, Bergmann and Lipschitz,[11] respectively. All three preparations yield the same methyl pentamethyl-*m*-digallate, which melts correctly at 127–128°. Mixtures of the various preparations of methyl pentamethyl-*m*-digallate show no depression; neither is any depression observed on admixture with synthetic methyl pentamethyl-*m*-digallate sent us by Professor Mauthner.
3. *m*-Digallic acid, prepared either from gallotannin or according to the two synthetic methods of Fischer and his collaborators, yields ellagic acid on oxidation. The three different specimens of ellagic acid thus obtained give the Griessmayer test for ellagic acid[12] and yield on acetylation tetra-acetyl-ellagic acid, which melts correctly[12] at 343–346°.

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[7] Ref. 1, p. 1117.

[8] Mauthner, *J. prakt. Chem.*, [2] **85**, 319 (1912).

[9] Nierenstein, Spiers and Geake, *J. Chem. Soc.*, **119**, 275 (1921). Compare also Herzig and Von Broneck, *Monatsh.*, **29**, 248 (1908); Sisley, *Bull. soc. chim.*, [4] **5**, 727 (1909); Trunkel, *Arch. Pharm.*, **248**, 202 (1911).

[10] Ref. 1, p. 1116.

[11] Fischer, Bergmann and Lipschitz, *Ber.*, **51**, 61 (1918).

[12] Perkin and Nierenstein, *J. Chem. Soc.*, **87**, 1416 (1905).

4. Different melting points are given for penta-acetyl-*m*-digallic acid, namely, 211–214° by Nierenstein, 191–192° by Fischer and Freudenberg and 204–205° by Fischer, Bergmann and Lipschitz. We find that penta-acetyl-*m*-digallic acid, from naturally derived *m*-digallic acid or synthetic *m*-digallic acid, prepared by either of the above-mentioned methods of Fischer and his collaborators, melts at 208–209°. Any one of these three preparations does not depress the melting point of any other individual specimen. All give with diazomethane the identical methyl penta-acetyl-*m*-digallate (m. p., 167–168°), previously described by Fischer, Bergmann and Lipschitz.[13] Mixed melting points of any two specimens of this methyl ester show no depression.

During the course of these investigations we were struck by the low yields of 37 to 65% which have been recorded by Fischer and his collaborators for synthetic *m*-digallic acid.[14] Our experiments have confirmed these low yields, as we have obtained the following results: one synthesis by Fischer and Freudenberg's method gave 41%, whereas three syntheses by the method of Fischer, Bergmann and Lipschitz gave 43%, 51% and 64%, respectively. This suggested to us the possibility that the different syntheses lead not only to *m*-digallic acid (II) but also to *p*-digallic acid (IV), which we have found to be actually the case.

The simultaneous production of *meta*- and *para*-digallic acid is in agreement with the observation made by Fischer, Bergmann and Lipschitz[15] that penta-acetyl-*p*-digallic acid yields *m*-digallic acid on removal of the acetyl groups. It does not, however, agree with their assumption that penta-acetyl-*m*-digallic acid only yields *m*-digallic acid under the same conditions:

Penta-acetyl-*m*-digallic acid ⟶ *m*-Digallic acid ⟵ Penta-acetyl-*p*-digallic acid

Our results on the other hand show that penta-acetyl-*m*-digallic acid and penta-acetyl-*p*-digallic acid lead to the simultaneous production of both *meta*- and *para*-digallic acid:

$$\begin{tikzcd}
 & \text{m-Digallic acid} & \\
\text{Penta-acetyl-m-digallic acid} \arrow[ur] \arrow[dr] & & \text{Penta-acetyl-p-digallic acid} \arrow[ul] \arrow[dl] \\
 & \text{p-Digallic acid} &
\end{tikzcd}$$

This is again in agreement with the suggestion made by Fischer, Bergmann and Lipschitz that on hydrolysis penta-acetyl-*p*-digallic acid first loses one acetyl group, with the result that the ring compound "A" is intermediately produced. Our results show that this also applies to penta-acetyl-*m*-digallic acid. This ring compound according to Fischer undergoes scission at "a" when *m*-digallic acid is formed on further hydroly-

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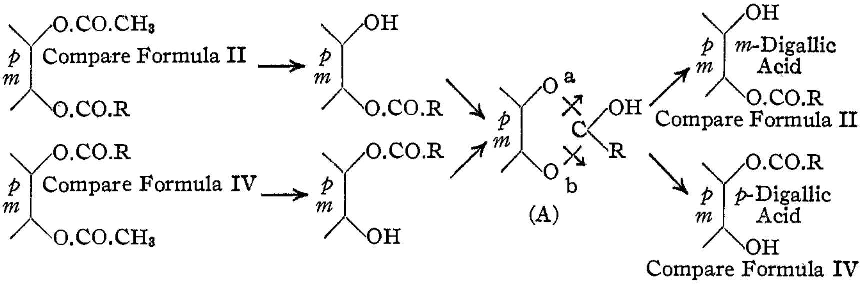
[13] Ref. 11, p. 63.

[14] Ref. 6 a, Ref. 10, Ref. 11, p. 45. See also Bergmann and Dangschat, *Ber.* **52**, 371 (1919). Pacsu, *Ber.*, **56**, 407 (1923).

[15] Ref. 11, p. 47.

sis. From our results it is evident that scission also takes place at "b," which leads to the formation of *p*-digallic acid.



The simultaneous production of the two digallic acids explains the low yields that have been obtained for *m*-digallic acid which is far less soluble in water than *p*-digallic acid with the result that the latter has been overlooked by previous workers. It seems also to explain why Nierenstein and subsequently Fischer and Freudenberg have failed to obtain ellagic acid when oxidizing synthetic *m*-digallic acid, since it is quite possible that they have used *p*-digallic acid and not *m*-digallic acid for their experiments. *p*-Digallic acid (m. p., 290–291°) resembles *m*-digallic acid (m. p., 271°) in its general appearance, and the high melting point (275–280°) found by Fischer and Freudenberg[6a] for Fischer's digallic acid, synthesized by him in 1908, seems to suggest that it contained large proportions of *p*-digallic acid admixed with *m*-digallic acid.

Experimental Part

The following melting points have been obtained by us for *m*-digallic acid, prepared according to the method of Nierenstein,[3] from authentic Aleppo gallotannin and Chinese gallotannin. We give our results as compared with those observed by Nierenstein and also with those obtained by Fischer for synthetic *m*-digallic acid.

	°C.	Nierenstein °C.	Fischer °C.
m-Digallic acid	271	268–270	271
Penta-acetyl-*m*-digallic acid	208–209	211–214	191–192; 204–205
Methyl penta-acetyl-*m*-digallate	168–169	.....	167–168
Methyl pentamethyl-*m*-digallate	127–128	.....	128–129
Penta-benzoyl-*m*-digallic acid	191	187–189	.....

p-Digallic Acid (IV) from Synthetic Penta-acetyl-*m*-digallic Acid. Penta-acetyl-*p*-digallic Acid and Penta-acetyl-*m*-digallic Acid from Gallotannin

Fifty g. of the acetyl derivative is hydrolyzed with ammonium hydroxide as described by Fischer, Bergmann and Lipschitz.[11] The filtrate obtained after separation of the *m*-digallic acid, yields on concentration in an atmosphere of hydrogen to about one-third of its volume and on standing on ice practically pure *p*-digallic acid. The latter is purified by dissolving 5 g. of the acid in 80 cc. of water, and allowing the mixture to stand on ice for some time, whereupon 3 to 4 g. of the product separates. *p*-Digallic acid crystallizes from water in small needles that contain from 2.5 to 3% of water. It melts at 290–291° with decomposition and evolution of carbon dioxide, and is easily soluble in hot water, alcohol, acetone and to some extent in ethyl acetate. Ferric chloride produces a black-blue coloration when added to the aqueous and alcoholic solutions. The acid is precipitated by gelatin and quinine acetate.

Anal. Subs. (dried at 130° in a vacuum over P_2O_5), 0.1065, 0.1528: CO_2, 0.2039, 0.2932; H_2O, 0.0298; 0.0422 g. Calcd. for $C_{14}H_{10}O_9$: C, 52.2; H, 3.1. Found: C, 52.2, 52.3; H, 3.1, 3.1.

Penta-acetyl-*p*-digallic Acid, prepared by digesting *p*-digallic acid with acetic anhydride, crystallizes from acetic acid in small needles; m. p., 198–199°. This melting point is a little lower than that found by Fischer, Bergmann and Lipschitz who give its melting point as 202–203°.

Anal. Subs. (dried at 100° in a vacuum over P_2O_5), 0.1496: CO_2, 0.2963; H_2O, 0.0490. Calcd. for $C_{24}H_{20}O_{14}$: C, 54.0; H, 3.8. Found: C, 54.0; H, 3.7.

Methyl Penta-acetyl-*p*-digallate is prepared by the action of diazomethane on an alcoholic solution of the penta-acetyl-*p*-digallic acid; it crystallizes from methyl alcohol in small needles, m. p. 192–193°, as found by Fischer, Bergmann and Lipschitz.

Anal. Subs. (dried at 100° in a vacuum over P_2O_5), 0.1580: CO_2, 0.3173; H_2O, 0.0582. Calcd. for $C_{25}H_{22}O_{14}$: C, 55.0; H, 4.1. Found: C, 54.8; H, 4.2.

Methyl Pentamethyl-*p*-digallate (V).—Two g. of *p*-digallic acid is methylated with an excess of diazomethane. The ester crystallizes from alcohol in small plates, m. p., 169–170°, as found by Mauthner.[16] This melting point is not depressed on admixture with authentic methyl pentamethyl-*p*-digallate, kindly sent us by Professor Mauthner.

Anal. Subs. (dried at 100° and 30 mm. over P_2O_5), 0.1607: CO_2, 0.3470; H_2O, 0.0779 g. Calcd. for $C_{20}H_{22}O_9$: C, 59.1; H, 5.4. Found: C, 58.9; H, 5.5.

In conclusion we wish to thank Professor F. Mauthner for his specimens and the University of Bristol Colston Research Committee for a grant which has covered the expenses of this research.

Summary

1. The identity of Nierenstein's digallic acid from gallotannin with Fischer's synthetic *m*-digallic acid has been established.
2. It is shown that Fischer's syntheses of *m*-digallic acid lead also to the production of *p*-digallic acid. It is therefore suggested that the previous observations of Nierenstein and also of Fischer and Freudenberg that synthetic *m*-digallic acid does not yield ellagic acid on oxidation are probably due to the fact that not *meta*- but *para*-digallic acid has been used by them for their experiments.
3. *p*-Digallic acid and some of its derivatives are described.

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[16] Mauthner, *J. prakt. Chem.*, [2] **84**, 142 (1911).