

# THE NATURAL TANNINS

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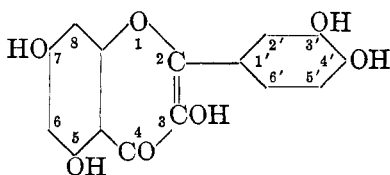
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## I. INTRODUCTION, PHYSIOLOGICAL SIGNIFICANCE, EXTRACTION, PROPERTIES

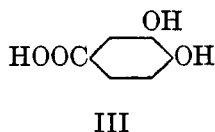
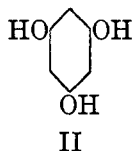
The name "tannin" covers a large range of naturally occurring compounds that are not necessarily structurally related and are widely distributed throughout the vegetable kingdom. The wood, bark, leaves, and roots of nearly all plants supply specimens, and they are particularly abundant in certain pathological growths such as oak galls, where the content may be as high as 80 per cent.

The physiological significance even of the normal members, as distinct from those occurring as a result of pathological processes, is not clear, although some relationships have been pointed out. A. G. Perkin (39) noted that the fission products given by tannins were, in some cases, the same as those given by the accompanying coloring matter; thus, quercetin (5,7,3',4'-tetrahydroxyflavonol (I))



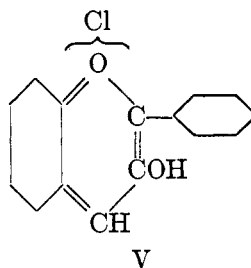
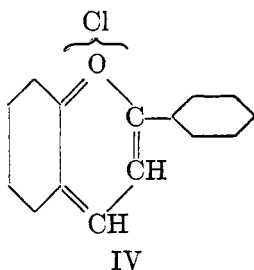
I

occurs in gambier and in acacia catechu associated with catechu tannin, and both quercetin and catechu tannin give, as fission products, phloroglucinol and protocatechuic acid (II and III).

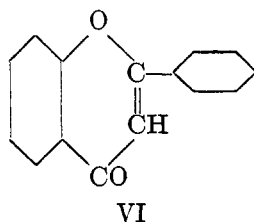


Other examples may be quoted: fisetin (7,3',4'-trihydroxyflavonol) occurs in quebracho Colorado and gives, by decomposition, resorcinol and protocatechuic acid; quebracho tannin gives the same pair of fission products. Sicilian sumach contains myricetin (5,7,3',4',5'-pentahydroxyflavonol) in the form of a glucoside,—myricitrin. On alkali fusion phloroglucinol and gallic acid result; the tannin also present gives the same decomposition products.

Similar results have been recorded by various botanists. Pick (52) found in some cases that as anthocyanin developed the tannin disappeared; anthocyanins are glucosides of anthocyanidins and these have the essential structures IV or V.



Much earlier Wiesner (63) noted, but did not make any appreciation of, the presence, side by side, of tannins and flavones: the essential flavone structure is shown in formula VI.



Other workers have noted like phenomena (36).

Attempts have been made to identify tannins as protective toxic materials inhibiting the growth of fungi (24), as fungi nutrients after enzymatic conversion by tannase to gallic acid (26), although this could only apply to gallotannin (which has been hydrolyzed by tannase), and, because of the seasonal variation in the quantity present, as reserve materials (25). The results described cannot, however, be accepted without qualification, as the tests often applied by botanists to identify tannins, such as the frequently occurring iron-greening property, are none too satisfactory; many plant products other than tannins give such a color with iron salts. It seems likely, nevertheless, that there may be some relationship between many tannins and the accompanying coloring matter of the benzopyran type. This expected relationship is the more interesting since it has now been established that many tannins are built on the benzopyran model.

Photosynthesis appears to play some part in the natural production of tannins, as they are more abundant in light than in etiolated shoots and, of the former, sun shoots have a higher content than shade shoots (30).

Tannins are amorphous, often hygroscopic, more or less soluble in water, and, in many cases, decompose somewhat in air and light, particularly if kept in a damp condition. When the difficulties of purifying crystalline plant products are appreciated, it will be realized how much greater these are where the usual criteria of purity are absent and where drastic methods of purification result in more or less extensive decomposition. All have the property in common of precipitating proteins from aqueous solution and this, although the exact nature of the change that occurs is not known, is generally supposed to form the basis of leather manufacture, the tannin converting the protein of the hide into a tough insoluble material that resists putrefaction. All tannins are polyhydroxylic phenols and, hence, have an astringent taste, are easily oxidized, and give colors or precipitates with various metallic salts.

Because of their technical importance and unusual nature the tannins attracted much attention until the past twenty years. However, more recently the subject has fallen somewhat into discredit, partly owing to the absence of constructive synthetic work but largely because of the prevalence of earlier theoretical speculations based on analytical results obtained from tannins of doubtful, obscure, or indefinite botanical origin. Other factors contributed to confusion, and a few of these need mentioning. Among them is the failure to recognize the existence of a large number of different tannins, to appreciate the difference between other members and gallotannin, the tannin present in oak galls, and the consequent careless application of the name "tannic acid" to any tanning material, to gallotannin itself, and, specifically, to digallic acid. The failure to specify tannins properly led to the publication of apparently contradictory results:

thus, oak tannin was confused with gallotannin till Eckert (6) realized the difference between them. More recently, it has been stated by Etti (7) that oak tannin is insoluble in water and gives a green color with ferric salts, whilst Löwe (27) and Böttinger (3) agree that the tannin is soluble in water and gives a blue color with ferric salts. These anomalous results are explained by the fact that oak wood tannin and oak bark tannin are different and give, respectively, blue and green colors with ferric salts. The insoluble oak tannin of Etti was probably the insoluble material—phlobaphene—produced by heating the tannin with acid. Again, commercial tanning extracts have often been used as sources of tannins, and technical extraction often involves the use of alkaline sulfites, bisulfites, sulfides, or even hydroxides. Whilst these reagents may not have affected seriously empirical tanning properties, their use may have caused extensive structural alterations and so rendered such extracts useless as sources of pure tannins.

For laboratory examination the tannin should be freshly extracted from its native source by the use of inert solvents; several have been employed for this purpose. Pelouze (37) used a mixture of alcohol, ether, and water, and even yet this is an important technical method of extracting gallotannin. The use of acetone was introduced by Trimble (60). This solvent has the advantage of not removing free sugar along with tannin; however, it extracts considerable amounts of insoluble coloring matters, resins, and waxes, and these must be separated afterwards. The following procedure is quite adequate for laboratory use where quantitative extraction of the bark or other material is not necessary. The dried and crushed material is extracted with cold water on the counter current principle and the extract treated with sufficient salt, whereupon the tannin precipitates as an amorphous solid. It is collected, dried in a vacuum, and the tannin separated by extraction, in a Soxhlet apparatus, with acetone. The acetone is removed on the water bath till the extract becomes very viscous; it is now transferred to a vacuum, when the tannin rapidly puffs up and dries. By washing the dried and ground material so obtained with ether a moderately homogeneous product results. For quantitative measurements the tannin must be dried in a vacuum pistol, using a suitable drying agent, at 100–120°C. for twenty-four hours or more, as traces of solvents are retained with great obstinacy. Too much emphasis cannot be laid on the necessity for adequate drying; the high analytical values recorded for hydrogen, and reports as to the presence of traces (0.5 to 5 per cent) of methoxyl in various tannins can only be attributed to the examination of insufficiently dried specimens that still contained some quantity of the solvent employed in extraction. Thus, Manning and Nierenstein (28) separated natural hemlock tannin in a somewhat arbitrary

fashion into seven fractions, and found that these had methoxyl contents varying from 0.80 to 3.56 per cent. In the procedure described resins, waxes, and insoluble materials are not removed from the bark, or other material extracted, by water; precipitation with common salt separates readily soluble impurities such as free sugar; extraction with acetone frees the tannin from inorganic materials; and washing with ether, in which tannins are insoluble, removes simple organic impurities. Tannins isolated in the manner described are light in color (fawn-pink), are readily and completely soluble in water, alcohols, ethyl acetate, and acetone, and insoluble in ether, hydrocarbons, or chloroform. Further purification through salt formation or other means is usually unnecessary and may even be harmful. It must be noted, however, that, since this and other methods of isolation and purification are largely empirical, individual tannins probably contain relatively large amounts of foreign material and a broad view must be taken of analytical results.

## II. CLASSIFICATION OF THE NATURAL TANNINS

The most satisfactory classification of tannins is that advocated by Perkin and Everest (41) by which the tannins are divided into three groups.

- I. Tannins related to depsides.
- II. Tannins related to diphenyldimethylolid.
- III. Phlobaphene-producing tannins: phlobatannins.

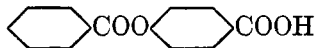
The group to which a particular member belongs is determined by boiling the tannin with dilute mineral acids, when the members of groups I and II hydrolyze giving crystalline fission products, gallic acid and glucose, and ellagic acid and glucose, respectively, whilst those of group III are completely converted into dark (red or brown) colored amorphous, insoluble phlobaphenes. Freudenberg (15) prefers to include the members of the first two groups in a single class as "hydrolyzable tannins." However, the Perkin and Everest classification is to be preferred, as the tannins related to depsides are quite different structurally from those related to diphenyldimethylolid, in spite of the fact that both hydrolyze with dilute acids. Older classifications based on the colors produced by the tannins with ferric salts are meaningless, as such colors depend on the orientation of the free phenolic hydroxyl groups present and have no other structural significance. It seems that the members of group I are more particularly abundant in pathological growths; those of group II occur chiefly in certain nuts and pods; whilst group III includes the tannins present in wood, bark, leaves, and roots. So that the members of groups II and III are of physiological origin. Nevertheless, a classification into pathological and physiological tannins, which has been suggested, would be misleading as

the chief, and probably only, member of the first group is widely distributed in small quantities and may not always be of pathological origin. In view of the fact that most tannins belong to the phlobatannin class and the existence of only one member each of groups I and II has been established with certainty, it may eventually be unnecessary to consider classification at all and sufficient to regard tannins that do not produce phlobaphenes as exceptional members that happen to have the tanning property.

Various qualitative reactions in aqueous solution differentiate between phlobatannins and the others, the more important being the effects on phlobatannins of (1) dilute mineral acids to give phlobaphenes, (2) bromine water, giving an immediate heavy yellow-orange precipitate, (3) formaldehyde and dilute hydrochloric acid, to give immediate precipitation of a condensation product on warming, (4) potassium dichromate, giving an immediate brown or red-brown precipitate, (5) nitrous acid, giving an immediate brown or red-brown precipitate, and (6) lead acetate to give a light colored precipitate readily soluble in acetic acid. In order to identify definitely a given product as a tannin it is necessary to carry out a tanning test or some modified form of tanning test such as the goldbeaters' skin test recommended by Nierenstein (32).

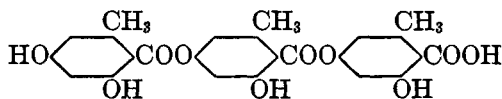
### III. TANNINS RELATED TO DEPSIDES

The depsides are crystalline substances occurring in small quantities in different varieties of lichens (53). They are acidic in character and derived from *p*-benzoyloxybenzoic acid (VII).

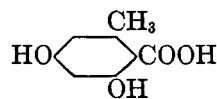


VII

Ortho or meta coupling is exceptional. Didepsides contain two, tridepsides three, and tetradepsides four benzene nuclei, respectively. Most natural members are didepsides, and the different members have various hydroxyl patterns. Only one natural tridepside—gyrophoric acid—and no higher member is known, but synthetic polydepsides may be obtained without much difficulty (5, 9). Gyrophoric acid (VIII) is *p, p'*-triorsellinic acid (orsellinic acid (IX)) and its constitution has been established through the work of Hesse (21), E. Fischer (12), Y. Asahina (1, 2), and A. Robertson (4).

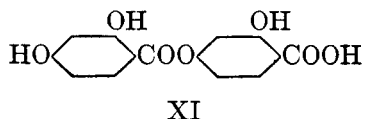
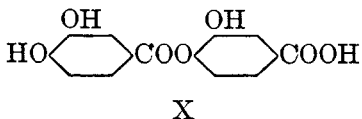


VIII



IX

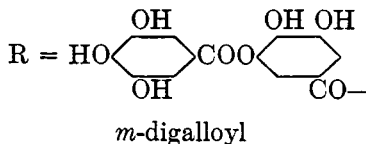
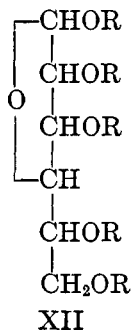
E. Fischer noted that certain depsides prepared by him, such as diprotocatechuic acid (X) and di- $\beta$ -resorcylic acid (XI), had tanning properties.



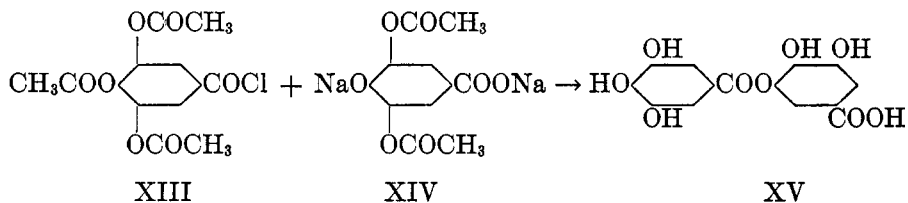
Only one natural tannin has been definitely linked to the depsides. Gallotannin (42) occurs chiefly in the galls produced by the puncture of insects on the leaves and buds of certain species of oak and sumach, but small amounts are often associated with other tannins. Aleppo and Chinese galls are the chief commercial sources of gallotannin.

By hydrolysis with dilute mineral acids glucose and gallic acid result and, by other methods of decomposition, pyrogallol; the pyrogallol presumably is formed by decarboxylation of gallic acid. Because of the accessibility of its crystalline fission products, gallotannin attracted much attention from the earlier chemists but, owing to the empirical methods of purification necessarily employed, much difficulty was experienced in determining the relative amounts of glucose and gallic acid resulting from hydrolysis. Indeed, gallotannin was reported to contain quantities of glucose varying from upwards of 20 per cent to none at all, the purer specimens containing less sugar. It seems certain, however, from the work of E. Fischer (9), Strecker (59), and others (42), that unaltered gallotannin is a glucoside and that, by acid hydrolysis, it gives nearly one molecule of glucose and ten molecules of gallic acid. E. Fischer therefore concluded that probably gallotannin was glucose fully esterified with five molecules of digallic acid, this being the most feasible way of accounting for the relative amounts of the fission products.

It having been shown that the digalloyl residues in gallotannin had the unusual (for depsides) meta coupling, in support of his view E. Fischer synthesized penta-*m*-digalloyl- $\alpha$ -glucose (10) and penta-*m*-digalloyl- $\beta$ -glucose (11).



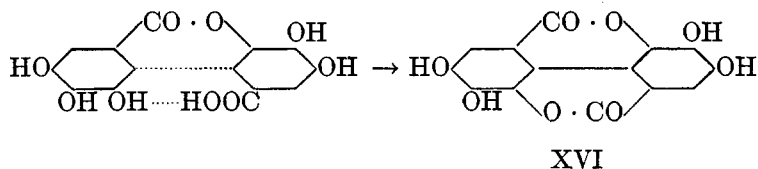
The synthesis of this unusual compound was carried out in the following way. Assuming that the digallic acid residues in gallotannin had the usual para coupling, triacetylgalloyl chloride (XIII) was condensed with disodium 3,5-diacetyl gallate (XIV). The resulting mixture of acetylated depside and acid anhydride having been separated with bicarbonate it was found, after deacetylation, that *m*-digallic acid (XV) had resulted.



The mechanism of this acyl migration is not clear, but from the point of view of the research its occurrence was advantageous rather than otherwise, since the depside obtained had the required meta configuration. Pentaacetyl-*m*-digalloyl chloride was condensed with glucose, by means of quinoline in solution in dry chloroform, to give the desired compound (XII) after deacetylation.

Penta-*m*-digalloylglucose compared very closely with natural gallotannin both qualitatively and quantitatively although, since both are amorphous, comparison of molecular weights was not satisfactory.

The value for combined sugar in specimens of natural gallotannin seldom reaches the figure required for penta-*m*-digalloylglucose, but, since the tannin is always associated with some free glucose, digallic acid, gallic acid, and ellagic acid (XVI), it is reasonable to accept E. Fischer's structure for unaltered gallotannin and to regard the other substances named as decomposition products. The occurrence of ellagic acid (XVI) need cause no confusion, since it may readily be obtained by treatment of gallotannin with alkali, resulting by oxidation of the *m*-digallic acid as shown below:—



It is to be expected then that small quantities of ellagic acid should accompany natural gallotannin. The earlier anomalous results with regard to the sugar content of the tannin are explained by the fact that gallotannin hydrolyzes readily, and repeated processes of purification cause more and more hydrolysis with the final production chiefly of digallic acid.



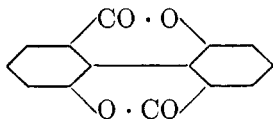
Taking the broad view then, it is probable that unaltered gallotannin is penta-*m*-digalloylglucose, but that commonly the natural tannin is a mixture of this compound with various decomposition products. It seems certain that it owes its tanning properties to the presence of the digalloyl residues in its structure and that the sugar plays no essential part since digallic acid, like the other depsides already mentioned, has tanning properties.

It must be pointed out, however, that Nierenstein (34) takes almost unqualified exception to Fischer's views and considers that gallotannin is a polydigalloyl-leucodigallic acid anhydride that may or may not be associated with glucose in the form of a glucoside.

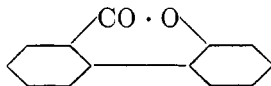
Various other hydrolyzable plant products have been recorded under the name "tannin." Some of these are crystalline. Some precipitate gelatin from aqueous solution; others do not. It should be noted that many non-tannins produce an insoluble precipitate with proteins, so that this property in itself is not sufficient to indicate the presence of a tannin. Two of these members appear to be structurally similar to gallotannin. Acer-tannin (49) occurs in the leaves of the Korean maple; it is crystalline and is accompanied by a much larger proportion of an amorphous variety. The crystalline product is stated to give, by acid hydrolysis, a molecule of aceritol and two molecules of gallic acid and is presumed to be digalloylaceritol. Hamameli tannin is also crystalline and gives an undetermined amount of gallic acid and an unidentified hexose as fission products (18). Since neither of these products appears to have been rigidly examined for tanning properties, their crystalline nature and apparently simple structure make it unlikely that they are really tannins. Their inclusion here is merely a matter of convenience and to avoid unnecessary multiplication of what may well be entirely speculative classes.

#### IV. TANNINS RELATED TO DIPHENYLDIMETHYLOLID

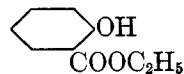
The parent substance of ellagic acid, the essential constituent of ellagitannin, is diphenyldimethylolid (XVII).



XVII



XVIII



XIX

Diphenyldimethylolid has not yet been prepared, but diphenylmethylohd (XVIII) is well known and may readily be obtained by the method of Richter (52) through the action of phosphorus oxychloride on ethyl salicylate (XIX).

Ellagitannin, the only member of this group that has positively been identified, occurs chiefly in myrobalans, divi-divi, algarobilla, and valonia. Myrobalans are nuts of the *Terminalia Chebula* (China and the East Indies); divi-divi are the dried seed pods of *Caesalpinia coriaria* (West Indies, Central America); algarobilla are the pods of *Caesalpinia brevifolia* (Chile); valonia are acorn cups of certain oaks (Southern Europe).

The constitution of ellagitannin is not definite; it gives ellagic acid and glucose by acid hydrolysis and is therefore probably a glucoside of ellagic acid. However, Nierenstein (31) considers that some specimens of ellagitannin are mono- or poly-galloyl derivatives of ellagic acid and contain no sugar.

Ellagitannin or extracts containing ellagic acid are valuable constituents of tanning liquors, since ellagic acid produces the "bloom" on leather so desired by tanners. For this reason chestnut and oak extracts are highly prized, the phlobatannins chiefly present being accompanied by suitably large amounts of ellagic acid or of some component that produces ellagic acid readily. The chestnut extract referred to is that of the wood of the true chestnut, *Castanea vesca*: it is not to be confused with the horse chestnut, *Aesculus hippocastanum*, which yields a tannin of little practical value.

Ellagic acid and a number of its congeners have been prepared by the oxidation of simple phenolic acids with potassium persulfate (40), but the exact constitution of ellagitannin itself still awaits elucidation.

#### V. PHLOBAPHENE-PRODUCING TANNINS: PHLOBATANNINS

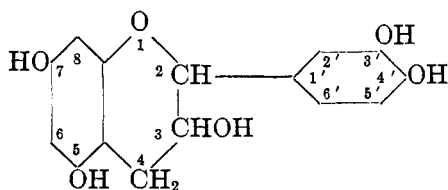
All those tannins, with the few doubtful exceptions already noted (acer-tannin, hamameli tannin), occurring as the result of normal physiological processes in the wood, bark, leaves, and roots of plants are phlobatannins. Because of their numerical preponderance and the ready accessibility of some or several members in all parts of the world, the phlobatannin group includes the most important tanning materials. Indeed, it is not at all certain, as has already been noted, that all classification of tannins is not somewhat artificial, phlobatannins representing the true tannin class, the others being exceptional members that happen to have tanning properties.

By treatment with boiling dilute mineral acids phlobatannins do not give recognizable hydrolytic products, but are slowly and completely converted into red or brown amorphous, insoluble materials that have been named *phlobaphenes* ("anhydride" or "tanners red"). In some cases, after acid treatment, traces of simple phenolic acids, protocatechuic or gallic acids, and of sugars are found. However, since many phlobatannins do not give them at all and the quantities are always very small, the occasional occurrence of phenolic acids in small amounts can be dismissed as due to some trivial decomposition, and of sugar to the presence of some

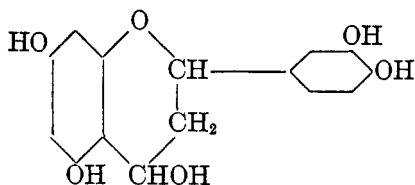
foreign glucoside. Owing to the empirical methods of purification necessarily adopted, the presence of traces of impurity is only to be expected. It must be noted too, that small amounts of gallotannin and ellagitannin are so frequently found associated with various phlobatannins that traces of gallic acid may often be detected even if the phlobatannin present contains no pyrogallol nucleus.

E. Fischer's convincing comparison of penta-*m*-digalloylglucose with natural gallotannin, and the fact that ellagitannin, although structurally different, is also probably a glucoside containing the —CO·O— group, have led to the erroneous supposition (43) that phlobatannins, too, are glucosides and related to depsides. This view is purely traditional and very misleading. It was not subscribed to at all by E. Fischer himself who, when abandoning the subject after his successful work on gallotannin, stated: "Aber die übrigen Bestandteil des natürlichen Tannin die nicht krystallisieren bleiben auch dann noch in ihrer chemischen Individualität unbekannt." There is no experimental evidence whatsoever for such a view; phlobatannins, as might have been supposed from their frequent occurrence side by side, are constituted in an entirely different manner and are related not to depsides or sugars, but to the normal plant pigments of the benzopyran type, flavones, flavonols, and anthocyanins. Their nearest analogues are the flavans, and therefore it is necessary to introduce here some account of catechin, as the solitary known natural member of the flavan group.

Catechin ( $C_{15}H_{14}O_6$ ) is a difficultly crystalline material that occurs in small quantities chiefly in certain varieties of "catechu" or "cutch." The botanical origin of commercial cutches is often obscure, but the best source of catechin is gambier catechu or terra japonica which is extracted from the leaves and twigs of *Uncaria gambier* (Malacca, Penang, Singapore). Catechin was first isolated by Nees van Esenbeck (61), and has been examined from time to time by various workers (46). By fusion with alkali it gives phloroglucinol, protocathechuic acid, and, probably, acetic acid; whilst catechin tetramethyl ether gives, by oxidation with permanganate, veratric acid and phloroglucinol dimethyl ether. A. G. Perkin (38) therefore considered that catechin was 3(or 4),5,7,3',4'-pentahydroxyflavan (XX or XXI),

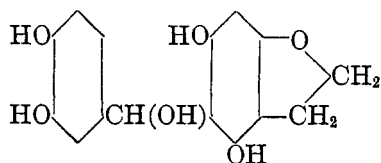


XX



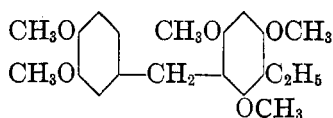
XXI

a reduction product of quercetin (see I), of which some quantity is present with catechin in gambier catechu. Von Kostanecki and Lampe (62), however, found that catechin gave only a monobromide readily and therefore abandoned Perkin's formula (which, it might be supposed, would brominate equally readily in positions 6 and 8) in favor of a constitution of the chroman type (XXII).



XXII

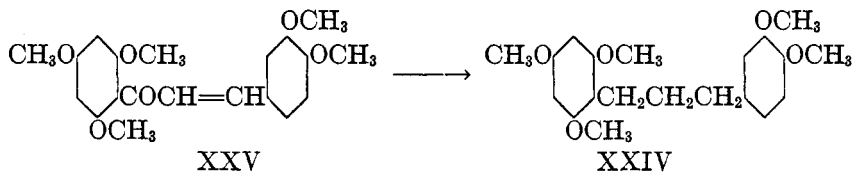
The same workers also claimed to have obtained pentamethoxyethyl-diphenylmethane (XXIII) by reduction of catechin and methylation of the resulting oil.



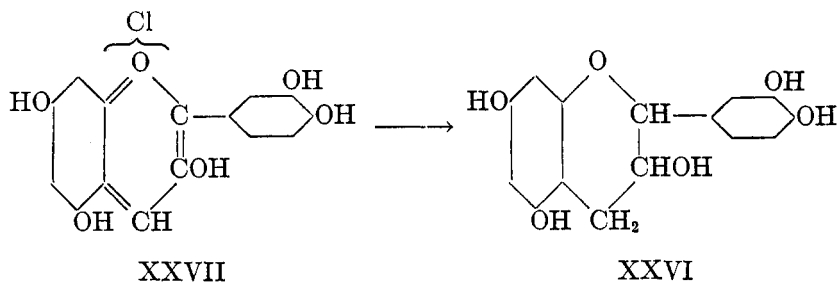
XXIII

However, Ryan and Walsh (58) could not identify the product obtained by von Kostanecki with synthetic pentamethoxyethyl-diphenylmethane prepared by them in an unambiguous way.

Finally the constitution of catechin was established by K. Freudenberg in the following way. Reduction of catechin tetramethyl ether and methylation of the product gave a compound identical with that (XXIV) obtained by reducing 2,4,6,3',4'-pentamethoxychalcone (XXV) with hydrogen and platinum.

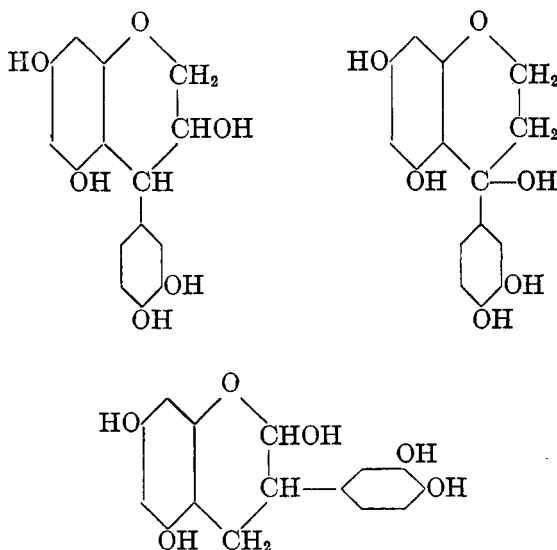


The production of a derivative of diphenylpropane points to the Perkin formula for catechin, and this was ultimately shown to be correct by Freudenberg's synthesis (19) of catechin (XXVI) from cyanidin chloride (XXVII) of known constitution.



Furthermore, similar reductions of both cyanidin chloride pentamethyl-ether (see XXVII) and of quercetin pentamethyl ether (see I) gave catechin pentamethyl ether (see XXVI). It is, then, very fully established that catechin is 3,5,7,3',4'-pentahydroxyflavan.

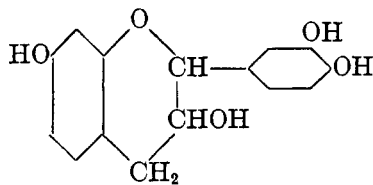
Freudenberg (16) has extended his work to a comprehensive stereochemical examination of catechin and has identified the six possible stereoisomers. Nierenstein (33) disagrees with Freudenberg's view and considers that some of the alleged stereoisomeric catechins are really structural isomers, the singly bound phenyl group occupying the 3- or 4-position instead of the 2-position. He submits three structurally isomeric formulas for catechin:



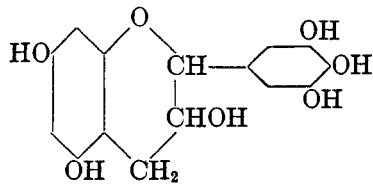
and claims to have recognized eight of the fifteen stereoisomers possible according to this scheme. However, the Perkin formula as advocated by Freudenberg is to be preferred, because of the more constructive nature of Freudenberg's work and because of its resemblance to the well authenticated formulas of the plant pigments.

Catechin-containing cutches and many others in which no catechin is present are used for tanning, since a phlobatannin, catechu tannin, is also present; more often they are associated with an oxidizing agent in an approximate tanning processes known as "barking," for waterproofing lines and cords. Barking processes are quite empirical, and it is not clear whether some change analogous to the tanning of hides occurs, or whether there is merely involved the deposition throughout the material of a relatively large amount of insoluble matter protecting the fibers from disintegration by water.

Catechin is not itself a tannin, but it resembles phlobatannins in some respects. It is crystalline, is converted, by boiling with dilute mineral acids, to an insoluble phlobaphene-like material, gives a colorless precipitate with lead acetate and a green color with ferric salts, but does not precipitate gelatin. Its fission products, phloroglucinol and protocatechuic acid, correspond to those given by catechu tannin and by many other phlobatannins (47). Freudenberg has therefore expressed the view that each phlobatannin is a polymer of that 3-hydroxypolyhydroxyflavan that gives fission products corresponding to those given by the tannin. If this attractive view is accepted and it is assumed that the relation between catechin and catechu tannin, which occur together, is a usual one, then it is to be expected that each phlobatannin should have accompanying it a corresponding 3-hydroxypolyhydroxyflavan. Unfortunately catechin is the only member of its class that has been identified as a natural product. Several synthetic congeners have been prepared by Freudenberg (17), namely, 3,7,3',4'-tetrahydroxyflavan and 3,5,7,3',4',5'-hexahydroxyflavan (XXVIII and XXIX).



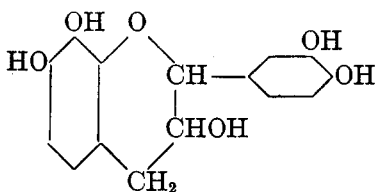
XXVIII



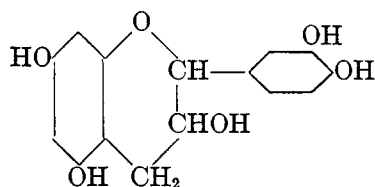
XXIX

From consideration of the various results recorded it seems certain that phlobatannins must be built on the catechin model; this has been established by A. Russell through the synthesis of a number of compounds of unambiguous structure that are qualitatively indistinguishable from typical natural phlobatannins. Where individual quantitative comparison has been possible there is also a close correspondence of values, but it is clear that the properties of the different members of the phlobatannin group are too alike to make comparison of synthetic products with individuals really convincing. Moreover, the difficulty of preparing amorphous compounds for exact quantitative comparison is too well appreciated to need emphasis.

A careful analytical examination of two typical members of the phlobatannin group, hemlock and mimosa tannins, newly extracted from hemlock and mimosa barks, respectively, was made and the fission products with fused alkali determined. It is somewhat desirable, but not necessarily essential, to examine freshly isolated tannins, since the exact behavior of a tannin depends to some extent on its previous history. Hemlock tannin, from the bark of the Canadian hemlock, gave as fission products pyrogallol, protocatechuic acid, and pyrocatechol (by decarboxylation of protocatechuic acid). Mimosa tannin, from South African mimosa or wattle bark, gave phloroglucinol, protocatechuic acid, and pyrocatechol. By acid treatment each was converted to a phlobaphene, and hemlock tannin gave a trace of glucose. Values of 60 to 62 per cent for carbon and of 4.5 to 4.9 per cent for hydrogen are, taken with the fission products, in agreement with the two corresponding pentahydroxyflavans (XXX and XXXI).



XXX



XXXI

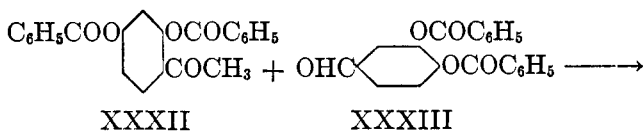
Purification of the tannins through their lead salts did not alter appreciably the values quoted except that, in the case of hemlock, the glucose was no longer detectable.

At this stage reference made to the results recorded (44) for numerous other phlobatannins showed that in every case are obtained, as fission products, a polyhydroxyphenol (phloroglucinol, resorcinol, or pyrogallol)

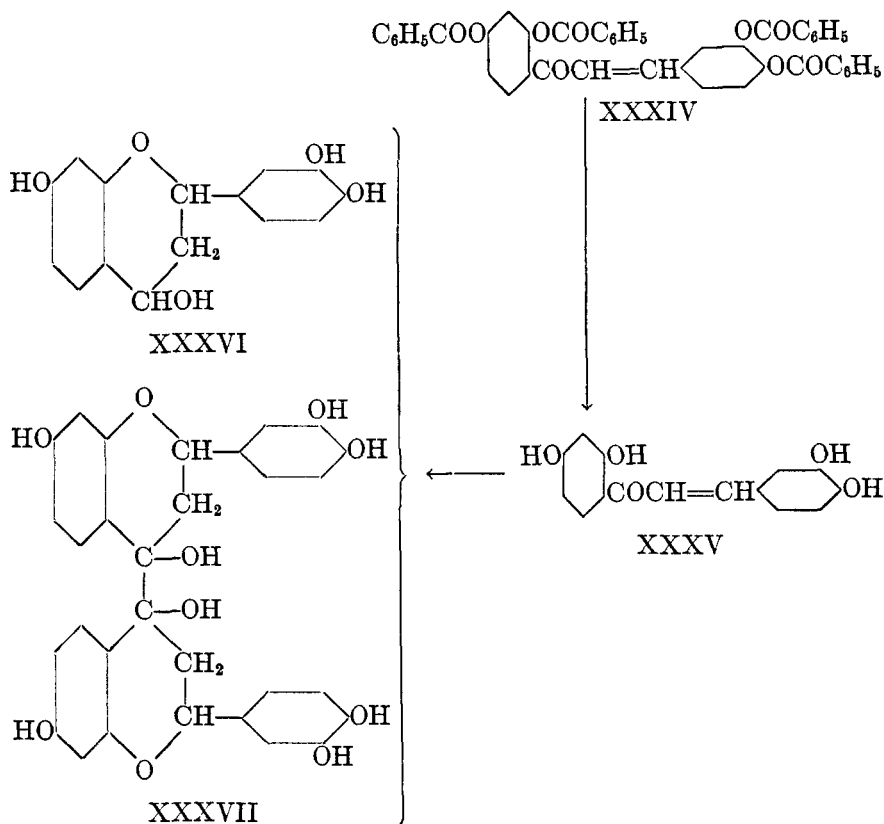
and a phenolic acid (protocatechuic or gallic acid). Amongst the decomposition products there may appear the phenol resulting by decarboxylation of the phenolic acid (pyrocatechol from protocatechuic acid, pyrogallol from gallic acid). Again, where the botanical origin is not definite, as in the case of quebracho tannin, or where wood and bark tannin of the same tree have not been separately identified, doubt may arise owing to the presence of two distinct phlobatannins. Allowance must also be made for the presence of traces of gallotannin and of ellagitannin in some cases. However, these various factors being considered, the recorded results may be interpreted in the manner stated.

The failure positively to identify phlobatannins as derivatives of 3-hydroxypolyhydroxyflavans led A. Russell (54) to suppose that in the phlobatannin structure the pyranoid hydroxyl might be in the 4-position instead of the 3-position, and experiments carried out to investigate this possibility led to the solution of the problem. Were this a normal synthetic problem dealing with crystalline compounds, trial experiments using methyl ethers and comparison of synthetic compounds with methylated natural products would be of value as a preliminary to the synthesis of similar polyhydroxy compounds. Since, however, comparison of natural with synthetic substances must be qualitative, tannins only being recognizable by their qualitative properties which depend largely, or even entirely, on the presence of free phenolic hydroxyl groups, and methylated natural tannins being amorphous and very poorly characterized, no comparison with synthetic methyl ethers could be of value. Therefore the synthesis of polyhydroxy compounds having the required flavan structure with the pyranoid hydroxyl in the 4-position was proceeded with.

Resacetophenone dibenzoate (XXXII) condensed with protocatechualdehyde dibenzoate (XXXIII) by means of anhydrous hydrogen chloride in solution in dry ethyl acetate to give 2,4,3',4'-tetrabenzoyloxychalcone (XXXIV), which, by debenzoylation in an atmosphere of nitrogen, gave the corresponding 2,4,3',4'-tetrahydroxychalcone (XXV). This, by reduction with zinc dust and dilute alcoholic acid, gave a pink amorphous compound that, by its mode of formation, must be either 4,7,3',4'-tetrahydroxyflavan (XXXVI) or the corresponding bis compound (XXXVII), —bis(7,3',4'-trihydroxy)flavpinacol.







The choice of phenol pattern was made partly for the sake of simplicity, difficulties of manipulation increasing greatly with increased numbers of phenol groups, and partly because quebracho tannin is probably hydroxylated on this pattern. Moreover, the intermediate 2,4,3',4'-tetrahydroxychalcone is a known natural product (butein), and the synthetic compound had properties identical with those given for natural butein (48).

The amorphous reduction product of 2,4,3',4'-tetrahydroxychalcone was qualitatively indistinguishable from typical natural phlobatannins as is shown in the table of reactions (table 1), and it may therefore be inferred that, whatever its structural make-up may be, phlobatannins are constituted in the same way.

The 0.5 per cent aqueous solutions used for the tests were each light yellow in color. In the later work, when the term "qualitatively indistinguishable" is used, the product referred to repeats with complete fidelity this list of tests. Of course the colors produced with the various salt-

forming reagents are not always the same, since these depend on the phenolic hydroxyl pattern.

TABLE 1

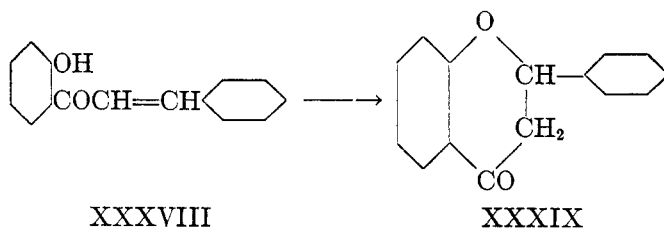
*Qualitative comparison of the reduction product of 2,4,3',4'-tetrahydroxychalcone with typical natural phlobatannins*

REAGENT	REDUCTION PRODUCT OF 2, 4, 3', 4'-TETRAHY- DROXYCHALCONE	HEMLOCK TANNIN	MIMOSA TANNIN
Alcoholic FeCl <sub>3</sub> . . . . .	Dark green color	Dark green color	Dark blue-violet color
Aqueous FeCl <sub>3</sub> . . . . .	Dark green color; dark blue precipitate	Dark green color; dark precipitate	Dark blue-violet color; dark precipitate
Gelatin . . . . .	Dirty white precipitate	Dirty white precipitate	Dirty white precipitate
Lead acetate . . . . .	Light colored precipitate soluble in acetic acid	Light colored precipitate soluble in acetic acid	Light colored precipitate soluble in acetic acid
Boiling dilute HCl (phlobaphene reaction) . . . . .	Solution reddens slowly and red precipitate separates	Solution reddens slowly and red precipitate separates	Solution reddens slowly and red precipitate separates
Bromine water . . . . .	Immediate heavy orange precipitate	Immediate heavy yellow precipitate	Immediate heavy orange precipitate
Calcium hydroxide . . . . .	Green color; faint green precipitate	Pink color; faint pink precipitate	Violet color; violet precipitate
Sodium sulfite . . . . .	Pink color	Pink color	Pink color
HCHO + HCl . . . . .	Precipitate on warming	Precipitate on warming	Precipitate on warming
Nitrous acid . . . . .	Immediate brown precipitate	Immediate brown precipitate	Immediate brown precipitate
Copper sulfate . . . . .	Faint green color	Faint green color	Faint green color
Copper sulfate + aqueous NH <sub>3</sub> . . . . .	Heavy dark precipitate	Heavy dark precipitate	Heavy dark precipitate
Aqueous ammonia . . . . .	Solution darkens slowly	Solution darkens slowly	Solution darkens slowly
Potassium dichromate . . . . .	Brown precipitate	Brown precipitate	Brown precipitate
K <sub>3</sub> Fe(CN) <sub>6</sub> + aqueous NH <sub>3</sub> . . . . .	Orange red color	Orange red color	Orange red color
Hide powder . . . . .	Absorbed quantitatively	Absorbed quantitatively	Absorbed quantitatively
Shaving of sheepskin . . . . .	Tanned	Tanned	Tanned

TABLE 1—*Concluded*

SOLVENT	REDUCTION PRODUCT OF 2, 4, 3', 4'-TETRAHY- DROXYCHALCONE	HEMLOCK TANNIN	MIMOSA TANNIN
	SOLUBILITIES		
Water.....	Soluble: concen- trated solutions red, dilute solu- tions yellow	Soluble: concen- trated solutions red, dilute solu- tions yellow	Soluble: concen- trated solutions red, dilute solu- tions yellow
C <sub>2</sub> H <sub>5</sub> OH, CH <sub>3</sub> OH, CH <sub>3</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> , (CH <sub>3</sub> ) <sub>2</sub> CO.....	Readily soluble	Readily soluble	Readily soluble
(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O, C <sub>6</sub> H <sub>6</sub> etc., ligroin, CHCl <sub>3</sub> , etc.....	Insoluble	Insoluble	Insoluble
Sodium hydroxide..	Readily soluble; dark solution bleached by acid	Readily soluble; dark solution bleached by acid	Readily soluble; dark solution bleached by acid

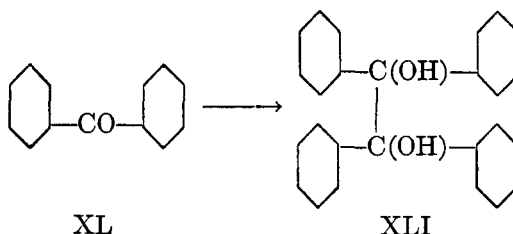
The exact constitution of the amorphous reduction product of 2,4,3',4'-tetrahydroxychalcone was finally established in a somewhat roundabout fashion. A series of similar reduction experiments with a number of other 2-hydroxychalcones was carried out, and in every case an exactly similar amorphous product resulted; the reaction is therefore a general one for 2-hydroxychalcones. In those cases where the hydroxyl group in the 2-position in the chalcone was the only free one, the reaction products were totally insoluble even in warm normal alkali; hence, during the change, at least the pyran ring must have closed. Moreover, the experimental conditions favor and were designed to favor ring closure. If, under the mild conditions used, ring closure without reduction had occurred, the products would have been flavanones (XXVIII  $\rightarrow$  XXXIX), which are colorless, or nearly so, and readily crystalline.



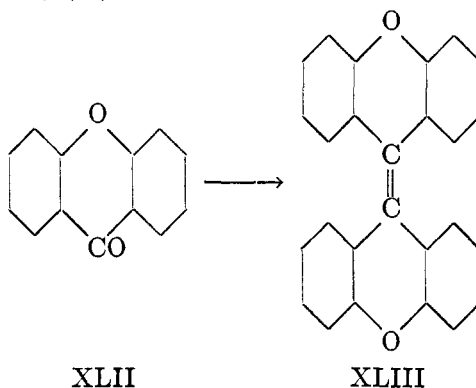
The products are not flavanones; therefore simultaneous ring closure and reduction must have occurred with the formation of flavans or flavpinacols. That is, the amorphous reduction product of 2,4,3',4'-tetrahydroxy

chalcone must be either XXXVI or XXXVII. Analytical values will not distinguish between these two, and molecular weight determinations are not practicable for amorphous compounds, but the flavpinacol structure was finally shown to be correct.

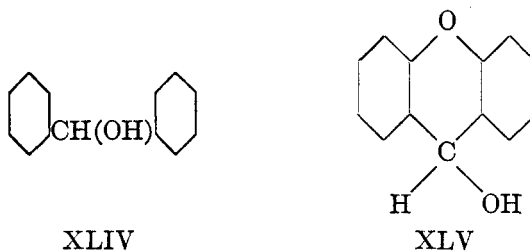
The flavan structure is unlikely, since the known 3-hydroxyflavans and all similarly constituted compounds of the benzopyran type are crystalline. Moreover, ketones commonly reduce to compounds of the bis type with zinc dust and acids; it is well known that benzophenone (XL) reduces to benzpinacol (XLI) in this way:



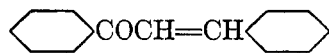
and, under more vigorous conditions, xanthone (XLII) gives dioxyxanthylene (XLIII) (20).



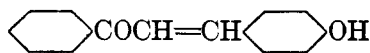
Whereas, by reduction with zinc dust and alkali, the same two ketones give, respectively, benzhydrol (XLIV) and xanthydrol (XLV) (29).



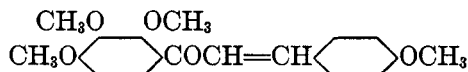
To find if the reaction went in a similar fashion using phenyl styryl ketones (chalcones), a series of chalcones was prepared of which the members had no free phenol group in the 2-position; the members selected were chalcone (XLVI), 4'-hydroxychalcone (XLVII), and 2,3,4,4'-tetramethoxychalcone (XLVIII).



XLVI



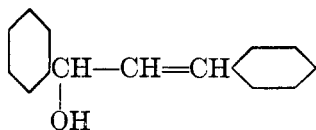
XLVII



XLVIII

By treatment with zinc dust and dilute alcoholic acids each of these gave a high-melting crystalline reduction product; that from chalcone itself, being readily obtained, was subjected to a somewhat extended examination.

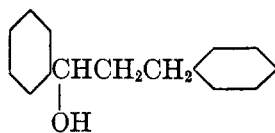
Chalcone ( $C_{15}H_{12}O_6$ , m.p. 56–57°C.) forms light yellow needles. Its reduction product forms colorless needles, m.p. 197°C., and has the empirical formula  $C_{15}H_{13}O$ . The simple (unimolecular) reduction products of chalcone are diphenylallyl alcohol (XLIX), m.p. 56°C. (35), hydrochalcone (L), m.p. 72°C. (22, 50), and hydrochacol (LI), b.p. 330°C. (22, 50).



XLIX



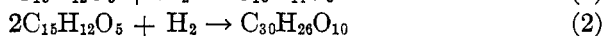
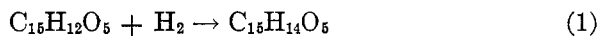
L



LI

By comparison with these it was concluded that the product under examination was bimolecular, and this was confirmed by determinations of molecular weight. The similarly obtained reduction products of 4'-hydroxychalcone and 2,3,4,4'-tetramethoxychalcone must be bimolecular too. Since, like the other ketones mentioned, simple chalcones are thus shown to polymerize on reduction, it is in the highest degree probable that in the case of 2-hydroxychalcones the reaction follows the same course and that the reduction products of these are likewise of the bis type.

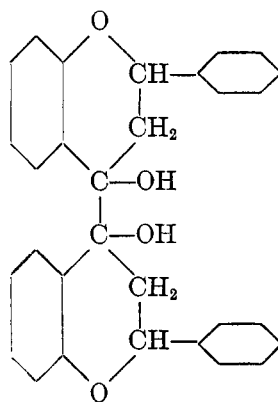
Finally, direct evidence of polymerization was obtained. Comparison of the two courses the reaction may have taken shows that for the production of the flavan one molecule of chalcone absorbs two equivalents of hydrogen (equation 1), whilst for the flavpinacol only one molecule of hydrogen for each molecule of chalcone is needed (equation 2).



Reduction of various 2-hydroxychalcones in a closed system, each experiment controlled by a blank, and measurement of the volume of hydrogen absorbed during reduction showed that the amount of hydrogen taken up corresponded to the amount required for the production of flavpinacols (55). The examples given in table 2 illustrate the order of correspondence obtained.

Therefore it may finally be concluded, retaining the standard nomenclature, that the reduction product of 2,4,3',4'-tetrahydroxychalcone is bis(7,3',4'-trihydroxy)flavpinacol, and, since this compound is qualitatively indistinguishable from typical natural members, that natural phlobatannins are built on the same model.

Phlobatannins are, then, phenolic hydroxy derivatives of flavpinacol (LII):



LII

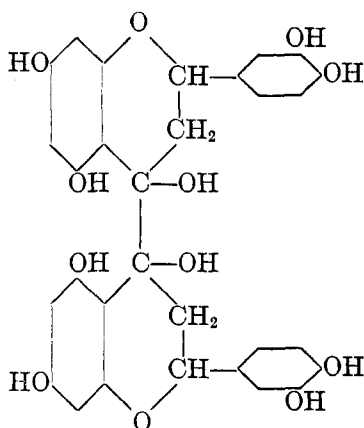
The phenolic hydroxyl pattern of individual members is indicated by the fission products given with alkali. Thus quebracho tannin gives resorcinol and protocatechuic acid, indicating that it is hydroxylated on the pattern of the flavpinacol just described—bis(7,3',4'-trihydroxy)flavpinacol. The alternative phenol pattern that would produce resorcinol

on decomposition, required for bis(5,3',4'-trihydroxy)flavpinacol, is improbable on general considerations of other plant products.

TABLE 2  
*Hydrogen absorbed by 2-hydroxychalcones during reduction*

CHALCONE	WEIGHT	HYDROGEN ABSORBED	HYDROGEN REQUIRED	
			Flavan	Flavpinacol
	<i>grams</i>	<i>cc.</i>	<i>cc.</i>	<i>cc.</i>
2-Hydroxy-3,4-dimethoxy.....	0.2009	7.3	16.0	8.0
2-Hydroxy-3,4,4'-trimethoxy.....	0.2396	9.2	17.2	8.6
2,4,4'-Trihydroxy.....	0.2074	7.8	18.1	9.1
2,4,3',4'-Tetrahydroxy.....	0.1548	5.3	12.8	6.4
2,4,6,3',4'-Pentahydroxy.....	0.3040	9.7	22.4	11.2

Some twenty phlobatannins give as fission products phloroglucinol and protocatechuic acid. These must be essentially hydroxylated on the pattern of bis(5,7,3',4'-tetrahydroxy)flavpinacol (LIII).

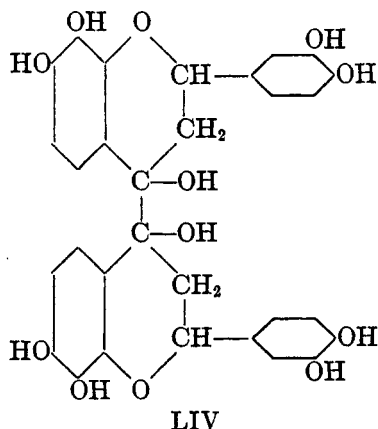


LIII

Assuming that the number of individuals is as great as this, individual differences are probably accounted for by partial alkylation of the phenol groups and the presence of various nuclear substituents, such as carboxyl, formyl, methyl etc., that would disappear during alkali fusion. This flavpinacol was obtained by the same general route as before described from phloroacetophenone tribenzoate and protocatechualdehyde dibenzoate, and it also is qualitatively indistinguishable from typical natural phlobatannins (55).

Hemlock tannin gives pyrogallol and protocatechuic acid as fission products. Extracts of hemlock are not so extensively used as they might be for tanning, since the leather produced has the deep red color of the solutions. The fission products indicate that the tannin is hydroxylated on the pattern of bis(7,8,3',4'-tetrahydroxy)flavpinacol (LIV). Since no other phlobatannin appears to give pyrogallol as its phenolic component, the natural tannin may even be identical with the flavpinacol, and quantitative comparison was therefore made between the two. The departure of hemlock tannin from the usual phloroglucinol or resorcinol pattern may well account for the unusually high color of its solutions; amongst natural products of the benzopyran type and in the case of polyhydroxychalcones, multiplication of phenolic groups ortho to each other produces a deepening of color. The absorption spectra measurements that will be described presently show that phlobatannins have no absorption in the visible, so that their colored solutions are due to the presence of traces of highly colored decomposition products; nevertheless, the explanation offered still holds good.

The synthesis of bis(7,8,3',4'-tetrahydroxy)flavpinacol (LIV) has been carried out by Russell and Todd (56) from gallacetophenone tribenzoate (2,3,4-tribenzoyloxyacetophenone) and protocatechualdehyde dibenzoate by the same route as before described; the synthetic product reproduces exactly the qualitative properties of natural hemlock tannin. Because of the unusual (for natural products) phenolic hydroxyl pattern indicated for hemlock tannin by its fission products, these were repeatedly examined for phloroglucinol and resorcinol, but neither could be detected. Should, in spite of this, another phenolic residue be found eventually amongst the decomposition products of hemlock tannin, the results just described would at least indicate that flavpinacols hydroxylated on the 7,8,3',4' pattern are phlobatannins.

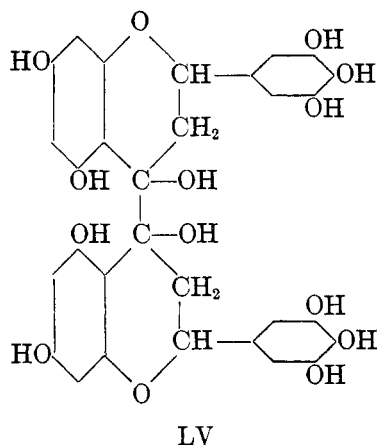




A quantitative comparison was also very close, as is illustrated by the values in the following list: Bis(7,8,3',4'-tetrahydroxy)flavpinacol: found C, 62.0; H, 4.55.  $C_{30}H_{26}O_{12}$  requires: C, 62.2, H, 4.5 per cent. Crude hemlock tannin: found, C, 61.7, 62.7; H, 4.9, 4.5 per cent. Purified hemlock tannin: found, C, 62.0; H, 4.4 per cent. Lead (hemlock) tannate: found, Pb, 27.3, 28.2.  $C_{30}H_{24}O_{12}Pb$  requires: Pb, 27.6 per cent. Methylated hemlock tannin (methyl sulfate and alkali): found, C, 66.5; H, 6.15;  $OCH_3$ , 31.8, 32.6.  $C_{30}H_{18}O_4(OCH_3)_8$  requires: C, 66.1; H, 6.1;  $OCH_3$ , 36.0 per cent.

Having obtained a sufficient number of synthetic polyhydroxyflavpinacols, the next step was a comparison of their absorption spectra with those of natural phlobatannins, and here the results obtained (57) verified the previous conclusions. The spectra of the parent polyhydroxychalcones of the polyhydroxyflavpinacols, and of the natural tannins are compared. The chalcone spectrum consists of a pair of moderately sharp bands in the ultra-violet with heads at about  $\lambda$  2690 and  $\lambda$  2890, together with a broad "color" band partly in the visible region with its head at about  $\lambda$  3900 (accounting for the complementary yellow-red color of the chalcones.) On reduction of the chalcone, corresponding to the destruction of the chromophoric character of the molecule, the "color" band disappears with little alteration in the rest of the spectrum. The flavpinacol spectrum consists of a pair of bands in the ultra-violet with heads at  $\lambda$  2700 and  $\lambda$  2870 corresponding exactly to the spectra of natural hemlock and mimosa tannins where the band heads measure at  $\lambda$  2700 and  $\lambda$  2860. The various flavpinacol spectra differ no more from each other than from the tannin spectra or than the tannin spectra do from each other. In the same paper (57) incidental measurements are included of the absorption spectra of gallotannin and of ellagic acid; these differ completely both from each other and from the phlobatannin spectrum.

A brief summary may be included of results further obtained by A. Russell and his collaborators. A number of phlobatannins (tea, pistachia, maletto, oak wood) give blue-black colors with ferric salts and, as fission products, phloroglucinol and gallic acid (or pyrogallol by decarboxylation). According to the views now under examination these must be hydroxylated essentially on the pattern of bis(5,7,3',4',5'-pentahydroxy)flavpinacol (LV). Prepared by the usual route this flavpinacol gives a blue-black color with ferric salts and has all the reactions of phlobatannins (compared with tea tannin).



There have now been obtained flavpinacols hydroxylated essentially on all the patterns indicated by the fission products determined or recorded for natural phlobatannins and the research has been extended to a comprehensive synthetic examination of flavpinacols having various other phenol patterns, with a view to determining what orientations of phenolic hydroxyl groups are essential to phlobatannin properties. Some of these may eventually find representatives amongst natural phlobatannins.

It has been found that all flavpinacols hydroxylated in the 3', 4'-positions are phlobatannins, whatever the phenol pattern of the rest of the molecule. In addition to the three members already described the following three have the necessary properties (the parent hydroxy ketone and aldehyde are included for each member): bis(6, 3', 4'-trihydroxy)flavpinacol, quinacetophenone, and protocatechualdehyde; bis(5, 3', 4'-trihydroxy)flavpinacol, 2, 6-dihydroxyacetophenone, and protocatechualdehyde; bis(3', 4'-dihydroxy)flavpinacol, *o*-hydroxyacetophenone, and protocatechualdehyde.

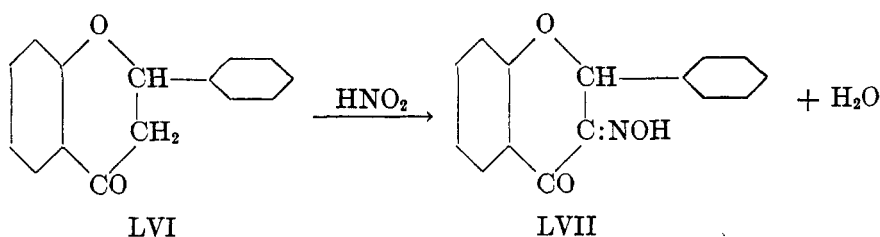
Qualitatively indistinguishable from phlobatannins are also: bis(5, 7, 2', 3', 4'-pentahydroxy)flavpinacol, phloroacetophenone, and 2, 3, 4-trihydroxybenzaldehyde (pyrogallaldehyde); bis(5, 7, 2', 4', 6'-pentahydroxy)flavpinacol, phloroacetophenone, and 2, 4, 6-trihydroxybenzaldehyde (phloroglucinaldehyde); bis(5, 7, 2', 4'-tetrahydroxy)flavpinacol, phloroacetophenone, and 2, 4-dihydroxybenzaldehyde (resorcyaldehyde); bis(5, 7, 2'-4'-tetrahydroxy-6'-methyl)flavpinacol, phloroacetophenone, and 2, 4-dihydroxy-6-methylbenzaldehyde (orcealdehyde).

In spite of the encouraging nature of the results just described, until more detailed examination, in the light of present information, has been made of them, it would be idle to indulge in much speculation as to the meaning of the various reactions of the phlobatannins. Of course many

are due simply to salt formation and can be dismissed at once; of the remainder little need be said.

The formation of phlobaphenes may involve some change analogous to the pinacol-pinacolone rearrangement, and to this view is lent support by the observation that each phlobaphene appears to consist of two components of similar composition but differing greatly in solubility; one part (5 to 10 per cent of the whole) being readily soluble in alcohol and the other insoluble. Furthermore, conversion of tannin to phlobaphene seems to be accompanied by the loss of a single molecule of water.

The precipitate given with nitrous acid may be an isonitroso compound formed in an exactly analogous manner to the well-known isonitrosoflavanones (LVI  $\rightarrow$  LVII).

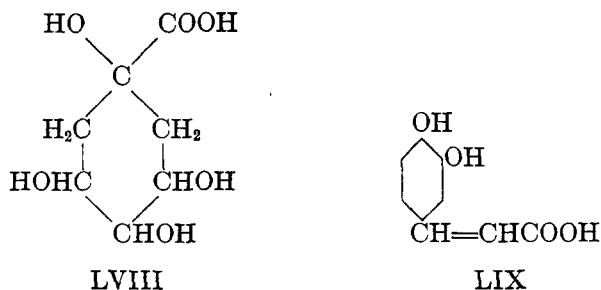


The bromotannins obtained by the action of bromine water contain upwards of 40 per cent of halogen and are likely to be just polybromophenols, their formation having little structural significance, although this offers no explanation as to why gallotannin, also essentially a polyhydroxyphenol, does not readily give a similar compound.

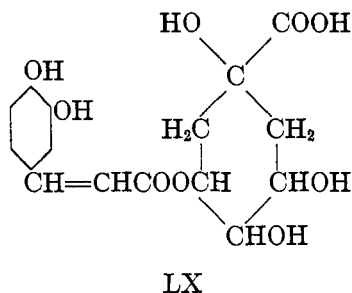
The very characteristic formaldehyde reaction appears to be due to the formation of a condensation compound.

#### VI. CAFFETANNINS

The various caffetannins extracted from different coffee berries and recorded in the literature (45) as tannins do not precipitate proteins and therefore certainly should not properly be identified with this group of natural products at all. By hydrolysis result quinic acid (LVIII), caffeic acid (LIX), and a residue of unknown composition.



The constitution of quinic acid has been established by H. O. L. Fischer and his collaborators (13). Caffetannins are usually associated in nature with chlorogenic acid, for which the constitution (LX) has been established synthetically also by H. O. L. Fischer (14).



It is likely then that caffetannins are closely related to or even identical with chlorogenic acid.

#### VII. SUMMARY AND CONCLUSION

1. The methods of classification applied to that group of natural products of which the members have tanning properties are probably somewhat artificial since, with a few well-defined exceptions, all are phlobatannins. It is likely, too, that many natural products have tanning properties, although they have never been used as tannins and never recognized as such owing to the greater abundance and more ready accessibility of other materials. Thus, many, probably all, depsides that have more than an optimum number of free phenol groups, and, probably, many polyhydroxy-chalcones and polyhydroxyphenols of the benzopyran type have tanning properties.

2. Gallotannin occurs chiefly in oak galls, as a result of pathological processes, but small amounts are frequently associated with phlobatannins. It is likely, from the work of E. Fischer and his collaborators, that unaltered gallotannin is penta-*m*-digalloylglucose, but commonly the tannin is a mixture of this compound with various decomposition products. That it owes its tanning properties to the presence of the digalloyl residues present in its structure, the sugar playing no essential part, appears certain, since many depsides, including digallic acid itself, have tanning properties. Gallotannin is the only member of its class that has been properly authenticated, although acer-tannin and hamameli tannin may have somewhat analogous structures.

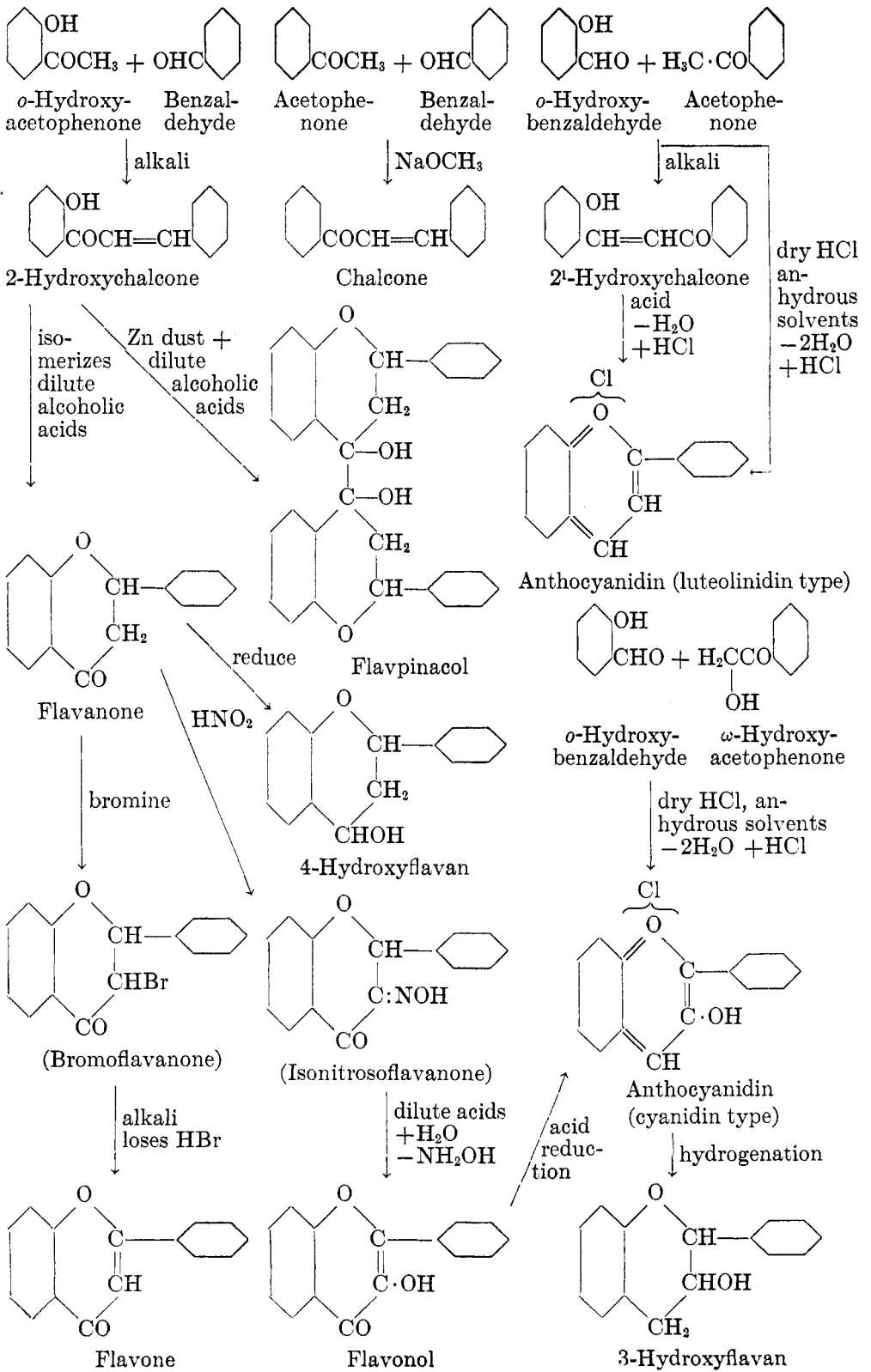
3. The constitution of ellagitannin is obscure but, from its fission products, glucose and ellagic acid, it is probably a glucoside of ellagic acid. Ellagic acid is a valuable constituent of tanning liquors, producing the much desired "bloom" on leather. The value of certain extracts, such as chestnut and oak, is much enhanced by the fact that the phlobatannins chiefly present are accompanied by suitably large amounts of free or combined ellagic acid.

4. Most of the natural tannins, and apparently all those occurring as normal products of physiological life in the wood, bark, and leaves of almost all plants, are phlobatannins. They are not related to depsides, as are gallotannin and ellagitannin, but are polyhydroxyflavpinacols derived from the corresponding 4-hydroxyflavans and are related to the usual plant pigments of the benzopyran type. Flavpinacols hydroxylated on the essential phenol patterns of the natural phlobatannins have been prepared by A. Russell and his collaborators by reduction of 2-hydroxypolyhydroxy-chalcones having suitably oriented phenolic hydroxyl groups. Qualitatively, quantitatively (where comparison has been practicable), and by exact absorption spectra measurements, the synthetic polyhydroxyflavpinacols are indistinguishable from typical natural phlobatannins.

5. The various caffetannins recorded in the literature do not possess tanning properties. They appear to be closely related to chlorogenic acid, although it cannot be said whether one or several members exist.

#### VIII. GRAPHIC SUMMARY OF THE RELATIONS BETWEEN THE VARIOUS PLANT COLORING MATTERS OF THE BENZOPYRAN TYPE

In view of the connection now established between phlobatannins and the common plant pigments, it would seem of interest to summarize graphically the interrelations between the members. The changes shown have all been carried out *in vitro* and it is probable that such, or similar, transformations *in vivo* form part of the regular plant economy.



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