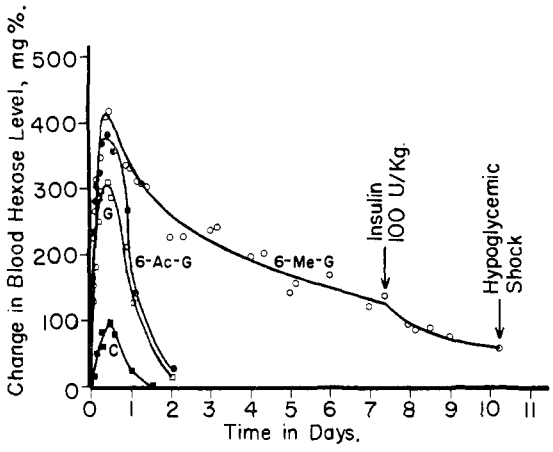


Fig. 1.—Change in blood reducing sugar levels in the alligator following (O, 6-Me-G) injection of 6-O-methylglucose; (●, 6-Ac-G) injection of monoacetylglucose; (□, G) injection of glucose; (■, C) handling comparable to that given the injected animals.

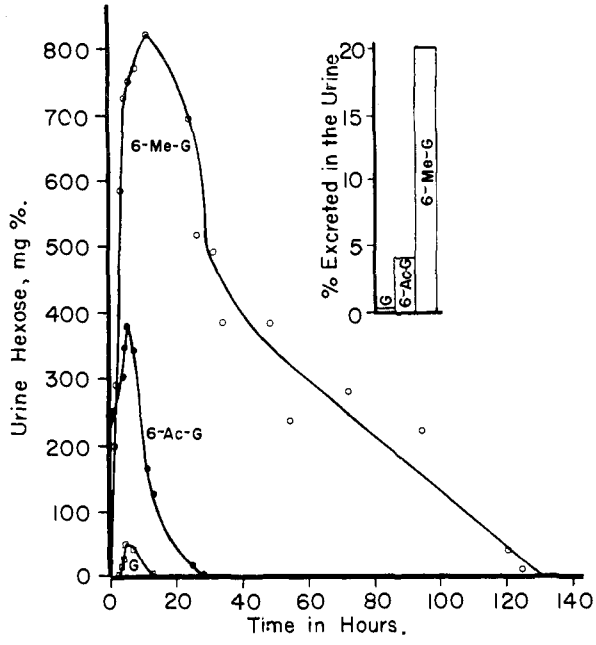


Fig. 2.—Urine reducing sugar levels in the alligator following injection of (O, 6-Me-G) 6-O-methylglucose; (●, 6-Ac-G) monoacetylglucose, (□, G) glucose.

the acetate is correctly represented by 6-O-acetylglucose. Secondly, methylglucose which bears a substituent of much greater chemical stability was metabolized at a much slower rate.

The observations on the animal receiving methylglucose present some interesting aspects in addition to the slow rate of disappearance of this substance from the blood and urine. It is noted that in this animal the blood sugar remained elevated long after reducing sugar ceased appearing in the urine. That this blood sugar was not entirely glucose was shown by that portion of the curve (Fig. 1) following the injection of a large amount of insulin, administered seven days after the injection of methylglucose. Insulin reduced the blood sugar level by an amount roughly equivalent to the normal glucose level in this animal, and hypoglycemic shock occurred three days later at a time when the total reducing sugar level in the blood was approximately 50 mg. % (calculated as glucose). Since hypoglycemic shock does not occur in the alligator until the blood glucose level is below 10 mg. %, it is concluded that the reducing sugar present in the blood in the later stages of the experiment was not principally glucose.

The non-glucose reducing sugar present in the blood from the 5th to the 8th day in an amount exceeding an estimated 100 mg. % was not being excreted in the urine. Further work will be required to show whether or not the circulating reducing sugar was largely 6-methylglucose.

NEW ORLEANS 12, LOUISIANA

[CONTRIBUTION FROM THE FRUIT AND VEGETABLE CHEMISTRY LABORATORY, WESTERN UTILIZATION RESEARCH AND DEVELOPMENT DIVISION, AGRICULTURAL RESEARCH SERVICE, UNITED STATES DEPARTMENT OF AGRICULTURE]

Plant Polyphenols. II. The Benzylation of Ellagic Acid[1]

BY LEONARD JURD

RECEIVED MAY 27, 1957

In strongly alkaline aqueous solution ellagic acid reacts with benzyl chloride to form the red quinoidal pigment, ellagorubin. Traces of pyridine or triethylamine inhibit the formation of ellagorubin and give both a colorless and a golden-yellow compound. The colorless compound has been identified as the hitherto unknown 5,5′-di-C-benzyl-tetra-O-benzyl-ellagic acid. The yellow pigment has a structure intermediate between that of ellagorubin and the colorless compound. One of its two rings is quinoidal as in ellagorubin while the other is aromatic as in the colorless compound.

The ellagitannins of the walnut pellicle produce a red pigment when treated briefly with alcoholic mineral acids.[2] The color reactions of this pigment in Robinson's tests[3] indicate that it is almost certainly not an anthocyanidin although a leuco-anthocyanin giving rise to cyanidin with acids has been reported in the walnut seed coat.[4] Since ellagic acid and gallic acid are the only phenols which have been isolated by the complete acid or alkaline hydrolysis of the walnut tannins, it seems most likely that the pigment is derived from one or both of these compounds.

The constitution of ellagic acid (I) has been

(1) Financial support for this work was provided by the Diamond Walnut Growers, Inc.

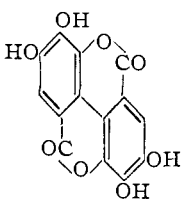
(2) L. Jurd, THIS JOURNAL, **78**, 3445 (1956).

(3) G. M. Robinson and R. Robinson, *Biochem. J.*, **25**, 1687 (1931); **26**, 1647 (1932).

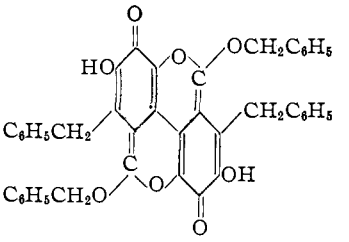
(4) E. C. Bate-Smith, *ibid.*, **58**, 122 (1954).

known since the early work of Perkin, Graebe and others,[5] but it was only recently that Schmidt and his co-workers[6] demonstrated the ability of this compound to react under some conditions in a highly colored tautomeric quinoidal form. The possibility that the conversion of ellagic acid into a quinoidal form is involved in the development of color and in some of the reactions of the commercially important ellagitannins prompted this extension of Schmidt's work on the alkylation of ellagic acid under alkaline conditions.

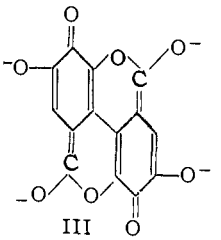
In strongly alkaline, aqueous solution Schmidt reported that ellagic acid reacted with benzyl chloride to form a red pigment, ellagorubin. The quinoidal structure II proposed for ellagorubin suggested that in alkaline solution ellagic acid reacts as the anion of a tautomeric form III. It was found in the present investigation, however, that under conditions similar to those employed by Schmidt the benzylation of ellagic acid gave a



I



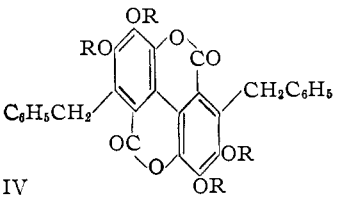
II



III

colorless, crystalline product, m.p. 235–236°, in addition to ellagorubin. Variable results were obtained. In some experiments both ellagorubin and the colorless compound were formed, while in others only the colorless compound was produced. Furthermore, in addition to these two major products, a small quantity of a crystalline, golden yellow compound, m.p. 176–177°, also was isolated. The ellagic acid used in these experiments had been purified by crystallization from pyridine and digestion with alcohol.[7] The variability of the benzylation reaction was traced to the presence in the ellagic acid of a small amount of pyridine of crystallization which remained after treatment with alcohol. When the benzylation reaction was repeated with ellagic acid freed of pyridine by digestion with mineral acid, ellagorubin was consistently formed as the chief product of the reaction. Addition of a small quantity of either pyridine or triethylamine to the reaction mixture, however, resulted in the exclusive formation of the colorless compound. It is possible, therefore, that in the latter case the active benzylating agent is an N-benzyl compound. Although ellagic acid reacted with N-benzyl-pyridinium chloride in aqueous sodium hydroxide, a crystalline product was not isolated.

The colorless product, $C_{56}H_{42}O_8$, did not react with ferric chloride, cold aqueous alkali, or acetic anhydride and sodium acetate. Thus it does not contain a free hydroxyl group. Unlike ellagorubin, the ultraviolet absorption spectrum of the colorless compound closely resembles that of ellagic acid, indicating that it is a derivative of the lactone form I of ellagic acid (Fig. 1). On catalytic hydrogenation the colorless product absorbed four molecular equivalents of hydrogen. Four benzyl groups were thereby removed to give a phenol, $C_{28}H_{18}O_8$. The properties of this phenol and its tetramethyl ether and tetraacetate proved that it was identical with the 5,5′-di-C-benzylellagic acid (IV, R = H) produced on catalytic hydrogenation of ellagorubin. The colorless product was debenzylated by long treatment with acetic anhydride and sulfuric acid to give 5,5′-di-C-benzylellagic acid tetraacetate. From these data it was apparent that the colorless product was the hitherto unknown 5,5′-di-C-benzyl-tetra-O-benzyl-ellagic acid (IV, R = $C_6H_5CH_2$–). This structure for the colorless product was confirmed by its preparation from 5,5′-di-C-benzylellagic acid by reaction with benzyl chloride and potassium carbonate in acetone solution.



IV

Analysis of the yellow compound established its molecular formula as $C_{56}H_{42}O_8$. This indicates that it is isomeric with the colorless compound and contains six benzyl groups. It did not give a ferric reaction, dissolve in aqueous alkalies nor react with acetic anhydride and sodium acetate, thereby confirming the absence of free hydroxyl groups. The ultraviolet absorption spectrum of the yellow compound (Fig. 1) did not show the intense peak at 255 mμ characteristic of ellagic acid and 5,5′-di-C-benzylellagic acid (Fig. 2). The latter compound, however, was formed on catalytic hydrogenation of the yellow compound. One of the benzyl groups in the yellow compound is labile and is more readily replaced than any of the benzyl groups in 5,5′-di-C-benzyl-tetra-O-benzyl-ellagic acid (IV, R = $C_6H_5CH_2$–). Thus treated with cold acetic anhydride and sulfuric acid the yellow compound immediately loses one benzyl group and forms a colorless monoacetate (V, R = $C_6H_5CH_2$–). On catalytic hydrogenation of this acetate the three remaining O-benzyl groups were removed to give the monoacetate (V, R = H) of 5,5′-di-C-benzylellagic acid. This behavior closely resembles that of ellagorubin under identical conditions. Treated with cold acetic anhydride and sulfuric acid, ellagorubin readily lost its two labile

(5) F. M. Dean, "Progress in the Chemistry of Organic Natural Products," Vol. IX, Springer-Verlag, Vienna, 1949, p. 283.

(6) O. T. Schmidt, H. Voigt and K. Bernauer, *Chem. Ber.*, **88**, 91 (1955).

(7) A. G. Perkin and M. Nierenstein, *J. Chem. Soc., Trans. sec.*, **87**, 1412 (1905).

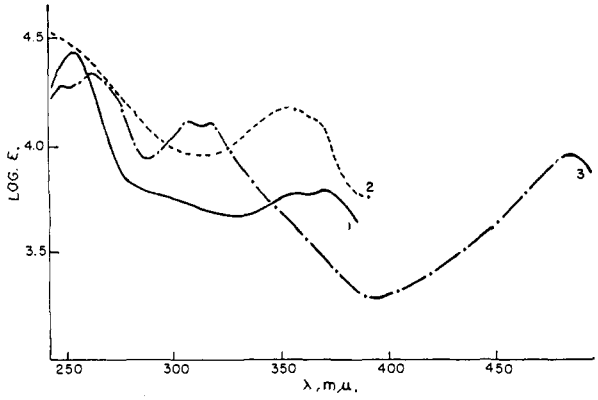
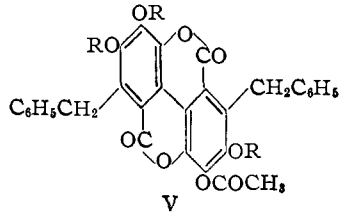
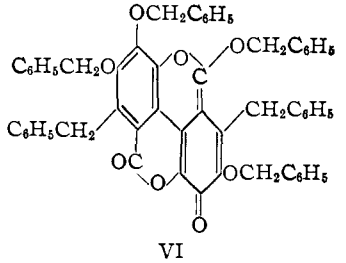


Fig. 1.—Ultraviolet absorption spectra in absolute ethanol of (1) the colorless benzylation product, (2) the yellow benzylation product and (3) ellagorubin.

O-benzyl groups and formed 5,5′-di-C-benzylellagic acid tetraacetate. These reactions indicate that the yellow compound has a structure intermediate between that of ellagorubin and the colorless compound. One of the two rings is aromatic as in the colorless compound, while the other is quinoidal as in ellagorubin. On the basis of Schmidt's structure for ellagorubin (II), structure VI may be assigned to the yellow compound. It also follows that the acetate formed by the action of acetic anhydride and sulfuric acid on the yellow compound has the orientation shown in V.



V



VI

The possibility of obtaining an acyl derivative corresponding to the benzyl derivative of the enol form of ellagic acid was also investigated. Ellagic acid, treated in cold aqueous alkali with benzoyl chloride, gave a tetrabenzoate identical with the product of benzoylation in pyridine solution. The benzoate was colorless indicating that it was derived from the lactone form of ellagic acid.

Experimental

Ellagic Acid.—Ellagic acid, prepared by the sodium persulfate oxidation of gallic acid or by the acid hydrolysis of the crude tannin extracted from the walnut pellicle,[2] was recrystallized from pyridine and digested with warm methanol as described by Perkin.[7] It was obtained in yellow-green needles which still contained some pyridine of crystallization.

Pyridine was removed completely from a sample of ellagic acid (10 g.) by digesting it with 10% aqueous sulfuric acid (100 ml.). The ellagic acid was collected, washed thoroughly with hot water, methanol and acetone and air-dried at 100°.

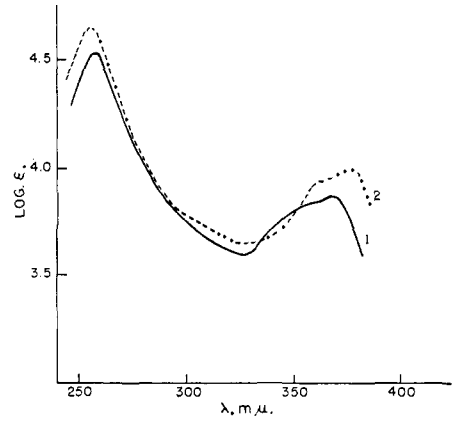


Fig. 2.—Ultraviolet absorption spectra in absolute ethanol of (1) ellagic acid, (2) 5,5′-di-C-benzyl-ellagic acid (from the hydrogenation of ellagorubin, the colorless benzylation product, and the yellow benzylation product).

Benzylation of Pyridine-free Ellagic Acid.—A mixture of acid-treated, pyridine-free ellagic acid (3.0 g.), aqueous 5% sodium hydroxide (20 ml.) and benzyl chloride (8.0 ml.) was immersed in a water-bath maintained at 70°. Twenty per cent. aqueous sodium hydroxide (10.0 ml.) was then added dropwise with mechanical stirring during 1 hour. Stirring was continued for an additional 0.5 hour. Fifty per cent. aqueous potassium hydroxide (5.0 ml.) was then added and stirring was continued for 1 hour. After cooling at 0° for 2 hours the aqueous layer was decanted from the oily black product which had separated from the reaction mixture. The black product was washed successively with water (40 ml.), methanol (2 × 30 ml.) and ether (2 × 30 ml.). The residual gum was then warmed with acetone (100 ml.) and the brown acetone solution[8] was filtered from the deep blue undissolved solid. The blue solid was suspended in water (300 ml.) containing a few drops of concentrated ammonia, heated to boiling and filtered. Treatment of the undissolved solid once more with boiling water (200 ml.) gave a colorless insoluble crystalline solid (0.1–0.2 g.). Recrystallization from dioxane–methanol caused the solid to separate in colorless needles, m.p. 235–236°. The deep blue aqueous filtrates were combined and acidified with hydrochloric acid. The orange-red precipitate was collected and recrystallized from acetone. Ellagorubin thereby separated in orange-red prisms, m.p. 219–220° (1.2–1.4 g.).

Benzylation of Ellagic Acid in the Presence of Pyridine or Triethylamine.—Ellagic acid (3.0 g.) was benzylated as described above except that pyridine (1.0 ml.) or triethylamine (1.0 ml.) was added with the benzyl chloride (8.0 ml.) at the beginning of the reaction. The aqueous layer was decanted from the cooled reaction mixture leaving a red-brown gum. This was washed with water, methanol and ether and warmed with acetone (100 ml.). On filtering the brown acetone solution a colorless crystalline residue remained (1.3–1.8 g.). This solid did not contain a trace of the deep blue color characteristic of the salts of ellagorubin. Recrystallization from dioxane–methanol caused the solid to separate in colorless needles, m.p. 235–236°, undepressed on admixture with the colorless product described above.

Benzylation of Ellagic Acid Containing Pyridine of Crystallization. Isolation of a Yellow Compound.—Before the influence of traces of pyridine in promoting the formation of the colorless compound, m.p. 235–236°, was recognized a number of benzylations were carried out with the ellagic acid containing pyridine of crystallization which remained after digestion with methanol. Variable amounts of ellagorubin and the colorless compound were formed in all of these experiments. A third compound also was isolated from the warm acetone washings of the dark reaction product. The acetone filtrates were allowed to evaporate slowly.

(8) The blue sodium and potassium salts of ellagorubin did not dissolve in acetone as reported.

The residual gum was digested with boiling methanol and filtered. An insoluble yellow crystalline solid (about 1 g. from 12 g. of ellagic acid) was thereby obtained. This product was recrystallized from methanol–acetone. It separated in rectangular, golden yellow rods, m.p. 176–177°.

Identity of the Red Benzylation Product with Ellagorubin.—(a) The red benzylation product, m.p. 219–220°, gave an intense blue-violet coloration with alcoholic ferric chloride. For ellagorubin Schmidt, *et al.*,[6] report m.p. 220–224°.

(b) **Acetylation.**—The red product was acetylated by boiling with acetic anhydride for 3 minutes. The acetyl derivative, crystallized successively from dilute acetic acid and from methanol–acetone separated in golden yellow rectangular plates, m.p. 195° (lit.[6] for ellagorubin diacetate, m.p. 192–193°).

Anal. Calcd. for $C_{46}H_{34}O_{10}$: C, 74.0; H, 4.59. Found: C, 73.9; H, 4.69.

(c) **Methylation.**—Methylation of the pigment by the action of excess of ethereal diazomethane gave an orange methyl ether which separated in rhombs, m.p. 241°, from chloroform–hexane (lit.[6] for ellagorubin dimethyl ether, m.p. 237°).

Anal. Calcd. for $C_{44}H_{34}O_8$: C, 76.5; H, 4.96; 2MeO, 8.99. Found: C, 76.1; H, 5.01; MeO, 8.78.

(d) **Catalytic Hydrogenation.**—On catalytic hydrogenation with 30% palladium charcoal at room temperature and pressure, the red pigment (0.01 g.) absorbed two molecular equivalents of hydrogen. The catalyst was filtered off and the filtrate was evaporated. The product, recrystallized from methanol–acetone, separated in pale yellow needles, m.p. 324–325° (lit.[6] for 5,5′-di-C-benzylellagic acid, dark at 250°). This compound gave a blue coloration with methanolic ferric chloride and in ethanol its spectrum was closely similar to that of ellagic acid (Fig. 2). The acetate, prepared by the action of acetic anhydride and pyridine on the phenol for 20 hours at room temperature, crystallized from dioxane–methanol in colorless needles, m.p. 306–308° (lit.[6] for 5,5′-di-C-benzylellagic acid tetraacetate. pale yellow prisms, m.p. 333°). Analyses of this phenol and several of its derivatives, described in the following section, established its identity with 5,5′-di-C-benzylellagic acid even though there is a discrepancy in the melting point reported for this compound.

Constitution of the Colorless Benzylation Product, m.p. 235–236°.—(a) The colorless benzylation product, m.p. 235–236°, did not give a color with methanolic ferric chloride and was insoluble in aqueous alkalies. The ultraviolet spectrum of this compound is closely similar to that of ellagic acid and of ellagic acid tetramethyl ether (Fig. 1).

Anal. Calcd. for $C_{56}H_{42}O_8$: C, 79.8; H, 5.03. Found: C, 79.7; H, 5.06.

(b) **Catalytic Hydrogenation.**—The colorless benzylation product (0.2062 g.) was dissolved in hot tetrahydrofuran (50 ml.). The solution was cooled rapidly, 30% palladium charcoal catalyst (0.1 g.) was added and the mixture was hydrogenated at 26° and atmospheric pressure; 25.1 ml. of hydrogen was absorbed. Theoretical amount of hydrogen required for the removal of four benzyl groups is 24.03 ml. The filtered solution was evaporated and the product recrystallized from methanol–acetone. It separated in pale yellow needles, m.p. 324–325° dec., undepressed on admixture with the 5,5′-di-C-benzylellagic acid produced by the hydrogenation of ellagorubin. The product gave an intense blue color with methanolic ferric chloride and deeply yellow solutions in aqueous alkalies.

Anal. Calcd. for $C_{28}H_{18}O_8$: C, 69.7; H, 3.76. Found: C, 69.5; H, 3.76.

The acetate of the hydrogenation product was prepared by heating it with acetic anhydride and sodium acetate for 30 minutes on the steam-bath. When crystallized from dioxane containing a little methanol, the acetate separated in colorless needles. m.p. 306–308° (with acetate, m.p. 306–308°, of hydrogenation product of ellagorubin, mixed m.p. 306–308°).

Anal. Calcd. for $C_{36}H_{26}O_{12}$: C, 66.4; H, 4.03; $4CH_3CO$, 26.47. Found: C, 66.1; H, 4.24; CH_3CO, 26.6.

The methyl ether of the hydrogenation product was prepared by adding excess of ethereal diazomethane to a suspension of the product in methanol–acetone. After standing 4 hours the colorless needles were collected and recrystallized from benzene–hexane. Colorless, felted needles, m.p. 245°, were obtained (lit.[6] for 5,5′-di-C-benzylellagic acid tetramethyl ether, m.p. 246°). The methyl ether did not give a color with ferric chloride and was not soluble in alkalies.

Anal. Calcd. for $C_{32}H_{26}O_8$: C, 71.3; H, 4.87; 4MeO, 23.05. Found: C, 71.5; H, 4.94; MeO, 22.6.

5,5′-Di-C-benzylellagic acid tetrabenzoate was prepared by adding benzoyl chloride (0.3 ml.) to a solution of the hydrogenation product (70 mg.) in warm pyridine (1.0 ml.). After standing overnight the solution was diluted with water. The gummy precipitate was collected and heated for a short time with methanol. The undissolved crystalline benzoate was recrystallized successively from benzene–hexane and dioxane–methanol for analysis. It was obtained in glistening colorless rectangular prisms, m.p. 306–306.5°.

Anal. Calcd. for $C_{56}H_{34}O_{12}$: C, 74.8; H, 3.82. Found: C, 74.7; H, 4.02.

(c) **Reaction with Acetic Anhydride and Sulfuric Acid.**—Concentrated sulfuric acid (1.0 ml.) was added to a suspension of the colorless benzylation product (0.54 g.) in acetic anhydride (20 ml.). The mixture was heated to the boiling point and maintained at this temperature for 2 minutes. The benzyl ether thereby dissolved. The solution was allowed to stand at room temperature for 30 hours. Water was added and the colorless solid product was collected and recrystallized from acetone–methanol. It separated in colorless needles, m.p. 304–306°, undepressed on admixture with the acetate, m.p. 306–308°, of the phenol formed on catalytic hydrogenation (0.19 g.).

Reactions of the Yellow Benzylation Product, m.p. 176–177°.—(a) The golden yellow benzylation product, obtained as rods, m.p. 176–177°, did not give a coloration with methanolic ferric chloride and did not dissolve in dilute aqueous alkali.

Anal. Calcd. for $C_{56}H_{42}O_8$: C, 79.8; H, 5.03. Found: C, 79.5; H, 5.10.

(b) **Catalytic Hydrogenation.**—A solution of the yellow compound (0.1793 g.) in cold tetrahydrofuran (10 ml.) was hydrogenated at 24° and atmospheric pressure in the presence of 30% palladium charcoal catalyst (0.1 g.); 21.4 ml. of hydrogen was absorbed. Theoretical amount of hydrogen required for the removal of four benzyl groups is 21.2 ml. The catalyst was removed and the filtrate was evaporated to a crystalline residue. Recrystallized from methanol–acetone the hydrogenation product was obtained in lemon yellow needles, m.p. 323–324° dec., undepressed on admixture with 5,5′-di-C-benzylellagic acid (from the hydrogenation of the colorless benzylation product).

Anal. Calcd. for $C_{28}H_{18}O_8$: C, 69.7; H, 3.76. Found: C, 69.7; H, 3.85.

The acetate of this hydrogenation product, prepared by heating with acetic anhydride and sodium acetate, crystallized from dioxane–methanol in colorless needles. m.p. 307–308°, undepressed on admixture with 5,5′-di-C-benzylellagic acid tetraacetate.

Anal. Calcd. for $C_{36}H_{26}O_{12}$: C, 66.4; H, 4.03. Found: C, 66.3; H, 4.17.

(c) **Acetylation.**—The yellow compound, heated with acetic anhydride and sodium acetate, was recovered unchanged, m.p. and mixed m.p. 176–177°.

The yellow compound (0.067 g.) was dissolved in warm acetic anhydride (2 ml.). The solution was cooled in an ice-bath and one drop of concentrated sulfuric acid was added. The solution immediately became colorless and colorless crystals began to separate. After standing for 5 minutes, water was added and the crystalline solid was collected. The product was recrystallized from acetone–methanol, being obtained in colorless felted needles, m.p. 225–226°.

Anal. Calcd. for $C_{51}H_{38}O_9$: C, 77.0; H, 4.82; CH_3CO, 5.42. Found: C, 76.9; H, 4.92; CH_3CO, 5.67.

The crude acetate was hydrogenated in tetrahydrofuran with 30% palladium charcoal. Removal of the catalyst and evaporation of the filtrate gave a crystalline residue which was recrystallized from methanol–acetone. It separated in slightly yellow needles, m.p. 319–320° dec. It gave an intense blue ferric reaction and dissolved at once in dilute alkali to give a deeply yellow solution.

Anal. Calcd. for $C_{30}H_{20}O_9$: C, 68.7; H, 3.85. Found: C, 68.8; H, 3.99.

Action of Acetic Anhydride and Sulfuric Acid on Ellagorubin.—Two drops of concentrated sulfuric acid were added to a solution of ellagorubin (0.1 g.) in acetic anhydride (3.0 ml.) cooled in an ice-bath. Colorless crystals began to separate at once. After ten minutes, excess of water was added and the crystals were collected and recrystallized from dioxane–methanol. Colorless needles, m.p. 307–308°, undepressed on admixture with 5,5′-di-C-benzylellagic acid tetraacetate, were obtained.

The Benzylation of 5,5′-Di-C-benzylellagic Acid.—A mixture of 5,5′-di-C-benzylellagic acid (50 mg.), benzyl chloride (1.0 ml.), potassium iodide (0.1 g.), anhydrous potassium carbonate (3.0 g.) and dry acetone (25 ml.) was heated under reflux for 6 hours. The filtered solution was diluted with an equal volume of methanol and concentrated until crystallization began (yield 12 mg.). The solid from the reaction flask was suspended in water to dissolve the potassium carbonate and the undissolved colorless crystalline solid was collected (53 mg.) and combined with the product from the acetone filtrate. Recrystallization from dioxane–methanol caused the colorless benzylation product to separate in needles, m.p. and mixed m.p. 235–236°.

Benzoylation of Ellagic Acid. (a) In Pyridine.—Ellagic acid (0.2 g.) was dissolved in hot pyridine (6.0 ml.). Benzoyl chloride (1.0 ml.) was added and the hot solution was allowed to cool and stand for 20 hours. The red solution was then poured into excess of water. The gummy precipitated benzoate was washed with ether and filtered, leaving the benzoate as a white crystalline solid. On recrystallization from dioxane–methanol ellagic acid tetrabenzoate separated in colorless thick rods, m.p. 329–330°.

Anal. Calcd. for $C_{42}H_{22}O_{12}$: C, 70.2; H, 3.09. Found: C, 69.9; H, 3.20.

(b) **In Aqueous Sodium Hydroxide.**—Ellagic acid (0.2 g.) was dissolved in 20 ml. of 5% aqueous sodium hydroxide by heating to the boiling point for about 10 seconds. The solution was cooled quickly in an ice-bath and benzoyl chloride (1.0 ml.) was added with shaking. After 5 minutes a further 10 ml. of 10% sodium hydroxide and 1.0 ml. of benzoyl chloride were added with shaking. The solid benzoate was collected, washed free of excess benzoyl chloride with hot methanol (20 ml.) and recrystallized from dioxane–methanol. Ellagic acid tetrabenzoate separated in colorless rods, m.p. 329°.

Acknowledgments.—The author wishes to thank L. Rolle for his helpful assistance in the preparation of ellagic acid and L. M. White for performing the elementary analyses.

PASADENA, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KANSAS]

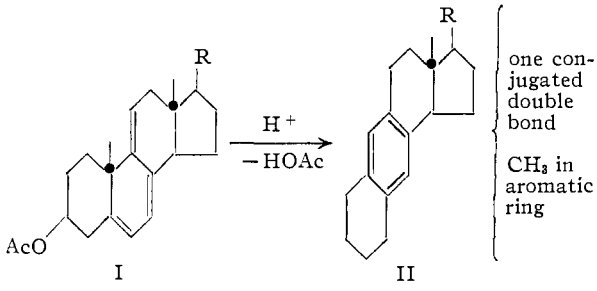
A Contribution to the Anthrasteroid Problem. The Location of the Aromatic C-Methyl Group and the Position of the Conjugated Double Bond

BY ALBERT W. BURGSTAHLER

RECEIVED JULY 3, 1957

As a proof of structure, an oxidative opening of the unsaturated ring followed by a reverse Michael reaction of the resulting keto-aldehyde has been employed to convert the anthrasteroid rearrangement product IIb derived from 5,7,9(11)-cholestatrien-3β-ol acetate (Ib) to 4-keto-3,9-dimethyl-*s*-octahydroanthracene (VII) which has been degraded further to 3,9-dimethylanthracene (IX).

The typical conversion, by acid catalysis, of a steroid containing the nuclear triene system of dehydroergosterol acetate (Ia) to an unsaturated derivative of *s*-octahydroanthracene (IIa) has been investigated extensively in recent years, especially by Nes and Mosettig and their co-workers, and has been designated by them as the "anthrasteroid rearrangement."[1] Numerous lines of evidence have



Ia, R = ergosterol side-chain
Ib, R = cholesterol side-chain
IIa, R = ergosterol side-chain
IIb, R = cholesterol side-chain

been accumulated, largely by the skillful experiments of these authors, to establish and to verify the anthrasteroid structure (II) as the correct formula of the rearrangement products derived from such steroidal trienes. Thus, the ultraviolet absorption spectrum of IIa reveals the presence of a highly alkylated benzene ring conjugated to an olefinic bond,[1a,c] and further evidence, including precise ultraviolet spectral comparisons of the corresponding double bond-reduced product with *s*-octahydroanthracene and *s*-octahydrophenanthrene,[1b] an oxidative degradation to 1-methyl-2,3,5,6-tetracarboxybenzene[1b] and dehydrogenation to hydrocarbon derivatives of anthracene,[1b,d,e] has served to demonstrate the general structure II for the rearrangement products, without, however, distinguishing between the two possible locations of the aromatic C-methyl group or determining the position of the conjugated double bond.

In consideration of the probable mechanism for the rearrangement, as outlined at the end of this discussion, it appeared to the present author that formula II could be reasonably expanded to III, and, as a means to establish these further details indicated by structure III, it was proposed to submit a typical rearrangement product to the degradation sequence indicated below. For this purpose, in order to avoid possible complications arising from unsaturation present in the side-chain in the ergosterol series (IIa), it was decided to employ the rearrangement product (IIb) derived from 5,7,9(11)-cholestatrien-3β-ol acetate (Ib) in the degradation scheme.

(1) (a) W. R. Nes and E. Mosettig, THIS JOURNAL, **75**, 2787 (1953); (b) **76**, 3182, 3186 (1954); (c) W. R. Nes, *ibid.*, **78**, 193 (1956); (d) W. R. Nes, R. B. Kostic and E. Mosettig, *ibid.*, **78**, 436 (1956); (e) *cf.* K. Tsuda and R. Hayatsu, *ibid.*, **77**, 3089 (1955).