

dm.). When mixed with the corresponding derivative from alfalfa seed oil, the melting point was not depressed.

Anal. Calcd. for $C_{27}H_{52}O_2$: C, 83.72; H, 10.25. Found: C, 83.73; H, 9.96.

β -Amyrin *p*-Nitrobenzoate.—A small sample of the β -amyrin from alfalfa leaves was converted to the *p*-nitrobenzoate in a manner similar to that previously described. The product when crystallized twice from ethanol gave a m. p. of 257–258°. This product gave no depression in m. p. when mixed with the previously described *p*-nitrobenzoate.

Summary

1. β -Amyrin has been isolated from the unsaponifiable fraction of alfalfa seed oil (Hardigan).
2. It has also been isolated from alfalfa leaf meal oil.
3. β -Amyrin from these sources has been characterized by its acetate, benzoate and *p*-nitrobenzoate.

EVANSTON, ILLINOIS
EAST LANSING, MICHIGAN

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[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

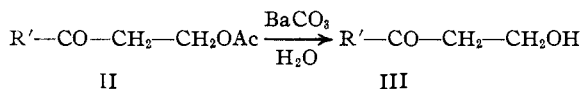
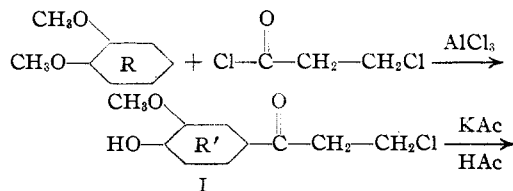
Studies on Lignin and Related Compounds. LXIV. Synthesis and Properties of 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone¹

BY KENNETH A. WEST² AND HAROLD HIBBERT

The relationship between certain oxygenated propyl phenol derivatives and lignin and their possible role as plant respiratory catalysts have been discussed recently by Hibbert.³

In a previous paper¹ the synthesis of 3-hydroxy-1-(3,4-dimethoxyphenyl)-1-propanone⁵ was described and the possibility of the existence in wood of a lignin progenitor of the type $R-CO-CH_2-CH_2OH$ discussed. It was considered³ possible that its derivative ($R-CHOH-CH-CH_2OH$) may play the same role in the plant respiratory system as is performed by citric (or isocitric) acid in the animal system (Krebs). The present communication deals with the synthesis of the unmethylated derivative, 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III), and a study of its properties, in particular its behavior toward common lignin extractants.

The synthesis was carried out according to the following series of reactions



The synthesis of the chloride (I) is dependent upon simultaneous condensation and demethylation reactions similar to those recorded in the literature in the syntheses of 4-hydroxy-3-methoxy- α -chloroacetophenone⁶ and 2-bromo-1-(4-hydroxy-3-methoxyphenyl)-1-propanone⁷ obtained by the condensation of veratrole with α -bromoacetyl bromide and α -bromopropionyl bromide, respectively. Each of these reactions takes place at room temperature in the presence of two equivalents of aluminum chloride whereas under the same conditions veratrole and β -chloropropionyl chloride condense to give a 75% yield of 3-chloro-1-(3,4-dimethoxyphenyl)-1-propanone, no appreciable demethylation occurring. 3-Chloro-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (I) was finally synthesized by heating a mixture of veratrole and β -chloropropionyl chloride in the presence of *four* equivalents of aluminum chloride at 50° for four hours followed by twenty minutes at 100°; yield after two recrystallizations, 60%. Each product in this series of reactions was methylated with diazomethane and the methylated derivative compared with the corresponding member of the veratryl series.⁴

It was necessary to show that demethylation had taken place in the position *para* and not *meta* to the propyl side chain. This was done by ethylating the acetate (II) with diethyl sulfate and alkali and then subjecting the ethyl ether to per-

(1) From a thesis submitted to the Graduate Faculty of McGill University by Kenneth A. West in partial fulfillment of the requirements for the degree of Doctor of Philosophy, May, 1942.

(2) Holder of a National Research Council of Canada Studentship, 1941–1942.

(3) Hibbert, *Ann. Rev. Biochem.*, **11**, 183 (1942).

(4) West, Hawkins and Hibbert, *THIS JOURNAL*, **63**, 3035 (1941).

(5) The question of correct nomenclature for the numerous new derivatives arising from these researches has occasioned the senior author (H. H.) much concern. After consultation with Dr. Austin Patterson it seems advisable, in the future, to follow closely the Geneva system to promote clarity and avoid confusion.

(6) Pratt and Robinson, *J. Chem. Soc.*, **123**, 245 (1923).

(7) Cramer and Hibbert, *THIS JOURNAL*, **61**, 2204 (1939).

manganate oxidation. The oxidation product was shown to be ethyl vanillic acid by a mixed melting point determination with an authentic sample, thus proving the structure of the nucleus to be 4-hydroxy-3-methoxyphenyl with the side chain in the 1-position (Formulas I, II, III).

A smooth conversion of the chloride (I) into the crystalline acetate (II) was effected by use of a mixture of potassium acetate and glacial acetic acid. The acetate was converted into crystalline 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III) by refluxing the former with aqueous barium carbonate.

3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone was found to be very soluble in ethanol, readily in water and only slightly in ether and in benzene. It crystallized from the latter in the form of fine needles, m. p. 109–110°.

The primary hydroxyl group in the side chain was readily etherified in high yield (80%) by treatment with ethanolic hydrogen chloride but it did not react with diazomethane. The action of the former reagent, as used under conditions of a standard wood ethanolsis,⁸ gave a high yield (80%) of 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (IV) together with an amorphous lignin-like product (15%).

The 3-ethyl ether (IV) exists in two interconvertible forms, one modification (A) melting at 35–37° and the other (B) at 71–73°. (A) may be converted into (B) by recrystallization from ether and (B) may be converted into (A) either by drying at room temperature under reduced pressure or by heating on the steam-bath at ordinary pressure. The low melting modification was shown by analysis to be the true 3-ethyl ether whereas the other form apparently contained solvent of crystallization.

Treatment of III with sulfuric acid under the conditions employed in the Klason lignin determination⁹ gave about a 50% conversion into an amorphous product, the carbon, hydrogen and methoxyl analyses of which were in good agreement with the values obtained by Klason¹⁰ for the product resulting from treatment of spruce wood with 72% sulfuric acid. Refluxing with dilute sulfuric acid (5%) and with dilute alkali (1%) also resulted in the formation of similar amorphous lignin-like products.

(8) Patterson, West, Lovell, Hawkins and Hibbert, *THIS JOURNAL*, **63**, 2065 (1941).

(9) Ritter, Seborg and Mitchell, *Ind. Eng. Chem., Anal. Ed.*, **4**, 202 (1932).

(10) See Fuchs, "Chemie des Lignins," J. Springer, Berlin, 1926.

Experimental

I. Synthesis of 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III)

Preparation of 3-Chloro-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (I).—Aluminum chloride (18.0 g.) was added to a mixture of veratrole (15.0 g.) and carbon disulfide (40 cc.) in a three-necked flask equipped with a stirrer, dropping funnel and condenser. The reaction vessel was immersed in a water-bath (20°) and β -chloropropionyl chloride (15.0 g.) added slowly through the dropping funnel to the continuously-stirred reaction mixture. Three more portions of aluminum chloride (18.0 g. each) were then added at five-minute intervals and the mixture heated at 50° for four hours. The solvent was finally removed and the residue heated on the steam-bath for twenty minutes, then allowed to cool and the aluminum chloride complex decomposed by stirring the reaction product with ice and concentrated hydrochloric acid for six hours. The resulting dark-colored product was filtered, washed thoroughly with dilute hydrochloric acid and then with water, dried as thoroughly as possible by suction filtration, and finally crystallized from methanol after decolorizing the solution with charcoal. On concentrating and cooling the solution the crude chloro derivative (I) crystallized out. It was recrystallized from ether, the ether filtrate concentrated, cooled and a second crop of crystals removed by filtration. The total yield of (I) (m. p. 96–98°) was 15.0 g. (60%). A small amount of this substance was purified for analysis by repeated recrystallizations from ether and from methanol (m. p. 101–102°). *Anal.* Calcd. for $C_{10}H_{11}O_3Cl$: C, 56.0; H, 5.13; OCH_3 , 14.4. Found: C, 56.0; H, 5.30; OCH_3 , 14.4.

Preparation of 3-Acetoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (II).—A mixture of 3-chloro-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (19.0 g.), freshly-fused potassium acetate (50 g.) and glacial acetic acid (140 cc.) was heated on the steam-bath for twelve hours with continuous stirring. The reaction mixture was cooled, poured into 500 cc. of ice-water and the mixture stirred for two hours and then allowed to stand at 4° for forty-eight hours. The crystalline product (II) which separated was filtered and dried; m. p. 76–78°; yield, 14.0 g. (67%).

On repeated recrystallization from a chloroform-petroleum ether (b. p. 30–50°) mixture the melting point was raised to 80–81°. *Anal.* Calcd. for $C_{12}H_{14}O_5$: C, 60.5; H, 5.98; OCH_3 , 13.0. Found: C, 60.5; H, 6.14; OCH_3 , 13.1.

Hydrolysis of 3-Acetoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (II).—The product (II) (14.0 g.) was refluxed for ten hours with a suspension of freshly precipitated barium carbonate (16.0 g.) in water (500 cc.). The mixture was cooled, acidified with hydrochloric acid to dissolve the barium carbonate, filtered, and the filtrate continuously extracted with benzene. On concentrating and cooling the benzene solution, 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone separated as a white crystalline product; m. p. 107–109°; yield, 6.3 g. (55%). After several recrystallizations from benzene the melting point was increased to 109–110°. *Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.2; H, 6.12; OCH_3 , 15.8. Found: C, 61.4; H, 6.38; OCH_3 , 15.7.

Methylation with diazomethane gave 3-hydroxy-1-(3,4-

dimethoxyphenyl)-1-propanone, identified by a mixed melting point determination with an authentic sample.

II. Proof of the Structure of 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III)

Diazomethane Methylation of 3-Chloro-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (I).—The substance assumed to have structure I (0.45 g.) was dissolved in dry ether (10 cc.) and mixed with an ethereal solution containing two equivalents of diazomethane. After standing for four hours at 0° the solution was concentrated to 2-3 cc. and cooled. A crystalline product separated out, and was filtered and dried; yield, 0.39 g. (82%). It was shown to be 3-chloro-1-(3,4-dimethoxyphenyl)-1-propanone by a mixed melting point determination with an authentic sample (m. p. 113-114°).

Ethylation and Oxidation of 3-Acetoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (II).—Diethyl sulfate (7.0 g.) was added to a solution of II (2.0 g.) in 1.5% aqueous sodium hydroxide solution (20 cc.) and the mixture refluxed for ninety minutes. The alkali insoluble portion was extracted with chloroform, the solution filtered and the solvent removed from the filtrate leaving a light-colored oil. An aliquot (0.250 g.) of this material was suspended in 2% aqueous sodium hydroxide (50 cc.) and aqueous potassium permanganate (1.125 g. in 25 cc. of H₂O) added slowly to the well-stirred reaction mixture at 100° over a period of two hours. The precipitated manganese dioxide was removed, the filtrate acidified and the crystalline product (m. p. 189-191°) which separated on cooling recrystallized from dioxane (m. p. 193-194°); yield, 15%. A mixed melting point with an authentic sample of ethyl vanillic acid showed no depression.

Diazomethane Methylation of 3-Acetoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (II).—This material (II) (0.300 g.) was methylated with an ethereal solution containing two equivalents of diazomethane. An 80% yield of 3-acetoxy-1-(3,4-dimethoxyphenyl)-1-propanone was obtained, its identity being proven by a mixed melting point determination with an authentic sample.

III. Properties of 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III)

Action of Ethanolic Hydrogen Chloride.—3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III) (2.0 g.) was refluxed with 2% ethanolic hydrogen chloride (100 cc.) for forty-eight hours in an atmosphere of carbon dioxide. The reaction mixture was neutralized with sodium ethoxide, concentrated to 10 cc., filtered to remove sodium chloride and the filtrate dropped, with vigorous stirring, into 30-50° petroleum ether (200 cc.). The amorphous precipitate was removed by centrifuging and dried; wt., 0.30 g. (15%) (OCH₃, 19.0).

The petroleum ether-ethanol solution was taken to dryness, leaving a light-colored oil which crystallized (m. p. 35-37°) on sustained cooling and scratching; yield, 1.80 g. (80%). It was shown by methylation (see below) to be 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-pro-

panone (IV). Recrystallization of the crude crystalline material from ether gave a product (m. p. 72-74°) which reverted to the original product (m. p. 35-37°) on drying at 65° (20 mm.). *Anal.* Calcd. for 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (IV) (C₁₂H₁₆O₄): C, 64.3; H, 7.14; alkoxy calcd. as methoxyl, 27.7. Found: C, 64.5; H, 7.54; alkoxy calcd. as methoxyl, 27.6.

The product (IV) prepared above (0.275 g.) was methylated with an ethereal solution containing two equivalents of diazomethane. Crystalline 3-ethoxy-1-(3,4-dimethoxyphenyl)-1-propanone (0.25 g.) (86%) was obtained and identified by a mixed melting point determination.

Action of Concentrated Sulfuric Acid (72%).—3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III) (0.50 g.) was treated at room temperature for two hours with 72% sulfuric acid (4 cc.). The mixture was then diluted to 150 cc. with distilled water and refluxed for four hours. The pink-colored amorphous precipitate which separated was filtered, washed and dried; yield, 0.22 g. (44%). *Anal.* Found: C, 66.2; H, 6.0; OCH₃, 16.0. Found for Klason lignin⁹: C, 66.67; H, 5.49; OCH₃, 14.47.

Action of Dilute Sulfuric Acid (5%).—3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III) (0.100 g.) was refluxed for twenty-four hours with 5% sulfuric acid solution (10 cc.). The mixture was cooled and the amorphous precipitate filtered, washed and dried; yield, 0.02 g. (20%).

Action of Sodium Hydroxide (1%).—Similar treatment of III with an aqueous sodium hydroxide solution (1%) (10 cc.) gave, after cooling and acidification, a dark colored amorphous precipitate; yield after washing and drying, 0.040 g. (40%).

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Summary

1. 3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone has been synthesized and its properties studied.

2. Under the conditions customarily employed for the extraction of lignin from wood by ethanolysis, this product is converted into 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone in high yield (80%).

3. The action of acids and alkalis on 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone brings about a partial conversion into amorphous lignin-like products. The product obtained by the action of concentrated sulfuric acid has the same empirical composition as a typical Klason lignin from spruce wood.