Summary

1. The β-cellobioside of acetovanillone and the β-*d*-glucoside of α-hydroxypropioveratrone have been prepared.

2. The rates of hydrolysis of a series of one aliphatic and several phenolic glycosides have been determined under a variety of conditions. These results, viewed in light of the knowledge of lignin extraction, indicate that a phenolic glycosidic linkage is a plausible type for the lignin-carbohydrate complex in wood (if such exists).

MONTREAL, CANADA RECEIVED JULY 9, 1941

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

Studies on Lignin and Related Compounds. LV. Synthesis and Properties of β-Hydroxypropioveratrone

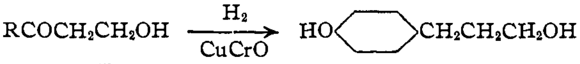
BY KENNETH A. WEST, W. LINCOLN HAWKINS AND HAROLD HIBBERT

As a result of recent studies on the structure of lignin[1] it is now apparent that the fundamental lignin building units consist of an aromatic phenol nucleus with a substituted propyl side chain. Such building units, when isolated by ethanolysis and other reactions from soft woods, contain only the guaiacyl nucleus, while from hard woods a mixture of guaiacyl and syringyl components usually results. Ethanolysis of various woods has led to the isolation of α-ethoxypropiovanillone[2] and α-ethoxypropiosyringone[3] from the alkali-soluble fraction of the total ethanolysis "distillable oils."[4] It is very probable these derivatives are formed during the ethanolysis reaction from α-hydroxypropiovanillone and α-hydroxypropiosyringone, respectively, and such conversions have now been accomplished, under the usual conditions of ethanolysis.[5] From the bisulfite-soluble fraction of the ethanolysis "distillable oils," vanilloyl[6] and syringoyl methyl ketones[7] have recently been isolated, as such. Up to the present time only these four C_6–C_3 units have been identified among the ethanolysis products, and in each of them the side chain is terminated by a methyl group.

In the light of the recent theory of Hibbert[1] that lignin is a composite mixture of both low- and high-molecular weight polymers derived from a series of plant respiratory catalysts, the existence has been postulated by him of a further series of C_6–C_3 units, analogous to the Szent-Györgyi C_4 system[8] functioning in animal respiratory processes. This includes, among others, the type compound, $RCOCH_2CH_2OH$, where R may be guaiacyl or syringyl.

Hydrogenation of both isolated lignins and wood has given rise to a series of products closely related to those obtained by ethanolysis. As a result of hydrogenolysis, however, many of the functional groups, particularly those of the propyl side chain, are removed.[9] Thus 4-*n*-propylcyclohexanediol-1,2, 4-*n*-propylcyclohexanol, and 3-(4-hydroxycyclohexyl)-propanol-1 (I) have been obtained by the hydrogenation of methanol lignin (aspen)[10] and ethanol lignin (maple)[11] and the latter two compounds by the hydrogenation of maple wood.[12]

Isolation of I from the hydrogenation products of both lignin and wood suggests the presence in the latter of a "lignin building unit" such as β-hydroxypropiovanillone (II) in which the side chain terminates in a primary hydroxyl group.



II I

(R = Guaiacyl)

At the present time, however, no lignin building unit having this type of side chain has been obtained by ethanolysis or other reactions. This failure may be due to its absence in older wood, to the manner in which it is united in the lignin complex, or to the fact that it may, under conditions of ethanolysis, undergo rearrangement, yielding eventually α-ethoxypropiovanillone. Such

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[1] For a comprehensive review, see Hibbert, "Status of the Lignin Problem," *Paper Trade J.*, **113**, No. 4, 35 (1941).

[2] Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939).

[3] Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

[4] Patterson, West, Lovell, Hawkins and Hibbert, *ibid.*, **63**, 2065 (1941).

[5] West, Hawkins and Hibbert, *ibid.*, **63**, 3038 (1941).

[6] Brickman, Hawkins and Hibbert, THIS JOURNAL, **62**, 2149 (1940).

[7] Kulka, Hawkins and Hibbert, *ibid.*, **63**, 2371 (1941).

[8] For review see *Ber.*, **72**, 53 (1939).

[9] Cooke, McCarthy and Hibbert, THIS JOURNAL, **63**, 3052 (1941).

[10] Harris, D'Ianni and Adkins, THIS JOURNAL, **60**, 1467 (1938).

[11] Cooke, McCarthy and Hibbert, *ibid.*, **63**, 3056 (1941).

[12] Godard, McCarthy and Hibbert, *ibid.*, **63**, 3061 (1941).

a rearrangement has been postulated by Hibbert[1]

$$\text{II} \xrightarrow{-H_2O} \underset{\text{Guaiacyl vinyl ketone (III)}}{RCOCH{=}CH_2} \xrightarrow{+EtOH} \underset{\alpha\text{-Ethoxypropiovanillone}}{RCOCHOEtCH_3}$$

Synthesis of β-hydroxypropioveratrone was therefore undertaken in order to study its properties, in particular its behavior under conditions of ethanolysis, with a view to facilitating its identification and possible isolation in a series of researches now in progress on the chemical structure of plant tissues at various stages of growth.

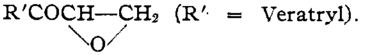
Discussion

Synthesis of β-hydroxypropioveratrone was first attempted by conversion of β-chloro- to β-acetoxypropioveratrone, followed by deacetylation. Acetylation was accomplished by treatment with glacial acetic acid and potassium acetate, but several attempts to deacetylate the β-acetoxypropioveratrone were unsuccessful, anomalous but interesting results being obtained. For example, methanolic and ethanolic potassium hydroxides, in contrast to the normal deacetylation brought about with α-acetoxypropiovanillone[13] and α-acetoxypropiosyringone,[14] convert the β-acetoxy derivative to β-methoxypropioveratrone and the β-ethoxy analog, respectively, an almost quantitative yield being obtained in the former case. If etherification proceeds through the free hydroxyl derivative as an intermediate, the results indicate an unusually reactive hydroxyl group. β-Hydroxypropioveratrone, with the same reagents and under similar conditions, gave the methyl ether, but the yields were much lower, indicating that the reaction may not proceed through the above simple mechanism.

An alternate explanation involving the primary formation of guaiacyl vinyl ketone (III) as the intermediate is also possible. This latter could then undergo 1,4 addition of ethanol to yield β-ethoxypropiovanillone (II).

$$\underset{\beta\text{-Acetoxypropiovanillone}}{RCOCH_2CH_2OAc} \longrightarrow \text{III} \xrightarrow[KOH]{EtOH} RCOH{=}CHCH_2OEt \longrightarrow \text{II}$$

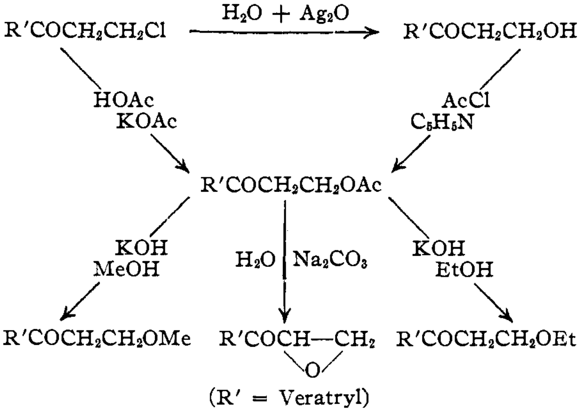
Synthesis of the vinyl ketone is now in progress with a view to studying this mechanism and the general properties of this and similar unsaturated ketones.

In an attempted deacetylation of β-acetoxypropioveratrone with sodium carbonate in aqueous dioxane a crystalline product was obtained which corresponded in analytical and chemical behavior to the ethylene oxide derivative,  $R'COCH{-}CH_2$ (R' = Veratryl). This product could not be reacetylated under normal conditions to yield the original acetate.

The various reactions of β-hydroxypropioveratrone and its derivatives are summarized in Chart I.

CHART I

REACTIONS OF β-HYDROXYPROPIOVERATRONE AND ITS DERIVATIVES



Synthesis of β-hydroxypropioveratrone was finally accomplished by treatment of the corresponding chloro derivative with boiling water in presence of silver oxide, and its structure confirmed by conversion to the acetate, identical with β-acetoxypropioveratrone prepared from the β-chloro derivative.

The action of ethanolic hydrogen chloride on β-hydroxypropioveratrone, under the usual conditions employed in ethanolysis of wood, gave 96% conversion to β-ethoxypropioveratrone. Its identity was established by comparison with the product obtained by the action of ethanolic potassium hydroxide on β-acetoxypropioveratrone and also with an authentic sample of β-ethoxypropioveratrone, previously synthesized in these laboratories[2] by action of sodium iodide on β-chloropropioveratrone in ethanol solution. Complete conversion of β-hydroxypropioveratrone to the corresponding β-ethyl ether under ethanolysis conditions is of considerable importance for the study of lignin, since, if this type of derivative were present as a free lignin building unit in wood, it would be unlikely to undergo polymerization or rearrangement and should be isolable as its ethyl ether. Since no such derivative has been found,

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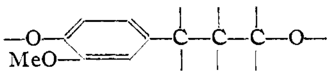
(13) Cramer and Hibbert, THIS JOURNAL, **61**, 2204 (1939).

(14) Hunter and Hibbert, *ibid.*, **61**, 2190 (1939).

as yet, in the products from the ethanolysis reaction, it is possible that the 3-(4-hydroxycyclohexyl)-propanol-1, obtained on hydrogenation of lignin, arises from hydrogenolysis of a polymer (IV) in which the terminal hydroxyl is combined in an ether linkage.



(IV)

This type of union may also exist in the "irreversible polymer" type of lignin, discussed by Hibbert in a recent communication,[15] a complex which is stable to the conditions of ethanolysis.

The tendency of β-hydroxypropioveratrone to undergo polymerization under conditions employed in the isolation of lignin is indicated by its almost complete conversion to an amorphous, lignin-like product when subjected to the usual Klason lignin determination.

Work on the synthesis of β-hydroxypropiovanillone is in progress.

Experimental

(I) Synthesis of β-Hydroxypropioveratrone.—β-Chloropropioveratrone (2.5 g.), prepared by Freudenberg's method,[16] and silver oxide (1.5 g.) were refluxed for ten hours with distilled water (300 cc.). The reaction mixture was cooled, filtered and continuously extracted with ether for ten hours. After drying over sodium sulfate, the ether extract was concentrated, yielding a white crystalline product; yield, 1.19 g. (50%). The crude β-hydroxypropioveratrone was recrystallized alternately from ether and from 30–50° petroleum ether; m. p. 83–84°.

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.66; OCH_3, 29.5. Found: C, 62.5; H, 6.82; OCH_3, 29.3.

β-Hydroxypropioveratrone was converted into its methyl ether by methanolic potassium hydroxide (4%) on standing for five minutes at room temperature; yield, 20%; m. p., 70–71°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.3; H, 7.14; OCH_3, 41.5. Found: C, 64.5; H, 7.14; OCH_3, 41.5.

(II) Action of Alcoholic Hydrogen Chloride on β-Hydroxypropioveratrone

(A) Ethanolic Hydrogen Chloride.—β-Hydroxypropioveratrone (0.50 g.) was refluxed under carbon dioxide for forty-eight hours with 2% ethanolic hydrogen chloride (25 cc.). The reaction mixture was neutralized with sodium ethoxide, concentrated to 10 cc., filtered from sodium chloride and precipitated with vigorous stirring into 30–50° petroleum ether (100 cc.). The small amount of amorphous precipitate was removed by centrifugation, and the solution taken to dryness, leaving an oil which crystallized on standing; yield, 0.50 g., (96%). Recrystallization from 30–50° petroleum ether gave pure β-ethoxypropioveratrone; m. p. 50–51° (a mixed melting point with an authentic sample showed no depression).

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.5; H, 7.60. Found: C, 65.3; H, 7.69.

(B) Methanolic Hydrogen Chloride.—Under analogous conditions, β-hydroxypropioveratrone gave with 2% methanolic hydrogen chloride the β-methyl ether; yield, 75%. Repeated recrystallization from 30–50° petroleum ether gave pure β-methoxypropioveratrone; m. p. 70–71° (mixed melting point with the corresponding product from (I) gave no depression).

(III) Action of Sulfuric Acid on β-Hydroxypropioveratrone.—β-Hydroxypropioveratrone (0.50 g.) was allowed to stand at room temperature with 72% sulfuric acid (4 cc.) after which time the solution was diluted to 150 cc. with distilled water and refluxed for four hours. The aqueous solution was decanted from the amorphous precipitate and the latter taken up in ether. The ether solution was dried over sodium sulfate and the ether removed leaving a glassy, resinous material which, when ground, was an amorphous lignin-like powder; yield, 0.38 g. (75%).

(IV) Synthesis of β-Acetoxypropioveratrone.—β-Acetoxypropioveratrone was synthesized by two independent methods.

Method A.—β-Chloropropioveratrone (5.3 g.), freshly fused potassium acetate (12.7 g.) and glacial acetic acid (30 cc.) were heated on a steam-bath for twelve hours. The reaction mixture was cooled and poured into a mixture of ice and water (500 g.). The crystalline product, which separated out at this point, was filtered and washed thoroughly with water; yield, 4.0 g. (70%). Repeated recrystallizations from ether and then from methanol gave the pure acetate, m. p. 100–101°.

Anal. Calcd. for $C_{13}H_{16}O_5$: C, 61.9; H, 6.35; OCH_3, 24.6. Found: C, 61.7; H, 6.37; OCH_3, 24.4.

Method B.—A 1.5 *N* solution (2.5 cc.) of acetyl chloride in toluene was mixed in the cold with dry pyridine (0.4 cc.). This mixture was immersed in an ice-water-bath and β-hydroxypropioveratrone (0.100 g.), dissolved in benzene, added. The reaction mixture was then heated to 65° for twenty minutes, cooled and the benzene layer separated. This benzene solution was washed with water, dried over sodium sulfate, and the benzene removed, leaving a crystalline residue; yield, 1.08 g. (90%). Recrystallization from methanol yielded the pure acetate; m. p. 100–101° (a mixed melting point with the product from Method A showed no depression).

(V) Reactions of β-Acetoxypropioveratrone

(A) Action of Methanolic Potassium Hydroxide.—β-acetoxypropioveratrone (1.2 g.) was dissolved in methanol (60 cc.) containing potassium hydroxide (2 g.). After standing at room temperature for five minutes, the reaction mixture was neutralized with dilute acetic acid and the methanol removed under reduced pressure. The crystalline residue was washed thoroughly with water; yield, 0.9 g. (90% theor.). Recrystallization from 30–50° petroleum ether gave the pure methyl ether; m. p. 70–71° (no mixed melting point depression).

(B) Action of Ethanolic Potassium Hydroxide.—Substitution of ethanol for methanol as solvent in the above ex-

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[15] Hibbert, This Journal, **61**, 725 (1939).

[16] Freudenberg and Kentscher, *Ann.*, **440**, 36 (1924).

periment gave the corresponding ethyl ether; yield 10%; m. p. 50–51° (no mixed melting point depression).

(C) Action of Sodium Carbonate in Dioxane–Water Solution.—β-Acetoxypropioveratrone (1.2 g.) was dissolved in aqueous dioxane (1:1) (100 cc.) containing sodium carbonate (2 g.). After standing at room temperature for fourteen hours, the mixture was neutralized with dilute acetic acid and then extracted with benzene. On evaporation of the benzene a crystalline residue resulted; yield, 0.60 g. (60%). Alternate recrystallizations from ether and then from methanol gave a pure, crystalline product which corresponded in its analyses to the ethylene oxide (V); m. p. 93–94°.

Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.4; H, 5.77; OCH_3, 29.8; mol. wt., 208. Found: C, 62.9; H, 5.80; OCH_3, 29.7; mol. wt., 225 (Rast).

This product formed a crystalline 2,4-dinitrophenylhydrazone; m. p. 182–183°.

Anal. Calcd. for $C_{17}H_{16}O_7N_4$: C, 52.2; H, 4.12; OCH_3, 15.9. Found: C, 52.1; H, 4.56; OCH_3, 15.7.

Acknowledgment.—The authors wish to thank the Canada Pulp and Paper Association for their kind financial assistance rendered in the form of a scholarship granted to one of them (K. A. W.).

Summary

1. β-Hydroxypropioveratrone has been synthesized and its properties studied, especially under conditions of ethanolysis.

2. Under the conditions customarily employed in wood ethanolysis, this product undergoes quantitative conversion into β-ethoxypropioveratrone.

3. Its acetyl derivative, β-acetoxypropioveratrone, is converted to β-alkyl ethers by the action of cold alcoholic potassium hydroxide.

4. The bearing of these results on the structure of lignin is discussed.

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

Studies on Lignin and Related Compounds. LVI. Stability of Lignin Building Units and Ethanol Lignin Fractions toward Ethanolic Hydrogen Chloride

BY KENNETH A. WEST, W. LINCOLN HAWKINS AND HAROLD HIBBERT

Two types of product have been obtained by the ethanolysis of spruce and maple woods. The first group includes monomeric propyl phenol "lignin building units"[1]; two of these monomers, α-hydroxypropiovanillone and -syringone, have been assumed to undergo etherification during ethanolysis with formation of the ethoxy derivative actually isolated from the reaction product. The second group consists of various amorphous lignin fractions separable by solvent fractionation methods.[2]

A study of these fractions has shown their pronounced tendency to polymerize under the influence of heat[3] but no evidence of depolymerization in these cases was reported. A previous attempt using an acetylated oak lignin fraction[4] gave a 36% yield of oils on ethanolysis. In order to determine the relationship existing between the amorphous lignin fractions[2] and the monomeric C_6–C_3 compounds, samples of each of the lignin fractions were subjected to ethanolysis conditions. The present paper is concerned with the results of this investigation.

The prolonged action of 2% ethanolic hydrogen chloride on the C_6–C_3 building units isolated by ethanolysis of various woods under the same conditions as used in all previous ethanolyses has been investigated in order to determine the stability of these products as well as their tendencies toward polymerization. The modified technique for separating the lignin "distillable oils," described in a recent communication,[2] has been followed in the isolation of the various products.

The fact that vanilloyl and syringoyl methyl ketones obtained from the bisulfite-soluble fraction of the ethanolysis oils are readily synthesized by mild oxidation from α-hydroxypropiovanillone and its syringyl analog, respectively, suggests the possibility that these diketones may have been formed in this manner during ethanolysis (in spite of efforts to maintain an oxygen-free atmosphere). However, both α-hydroxypropiovanillone and α-hydroxypropiosyringone were found to be readily convertible into their corresponding α-ethoxyethers without any evidence of oxidation to diketones. Thus the latter are primary prod-

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[1] For a comprehensive review, see Hibbert, "Status of the Lignin Problem," *Paper Trade J.*, **113**, no. 4, 35 (1941).

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

[3] Lovell and Hibbert, unpublished results.

[4] Peniston, McCarthy and Hibbert, THIS JOURNAL, **61**, 530 (1939).