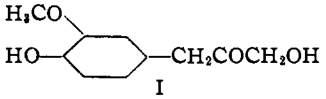
[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. LXXXV. Synthesis and Properties of Dimers Related to Lignin[1]

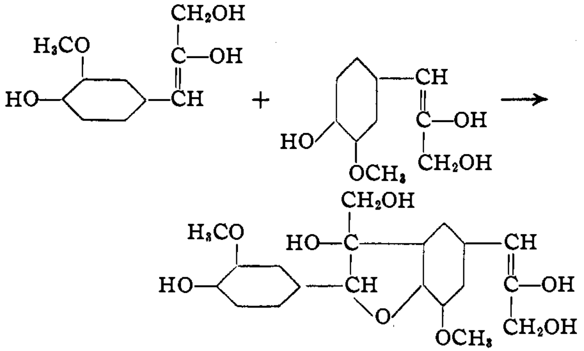
BY SAMUEL B. BAKER,[2] TAYLOR H. EVANS[3] AND HAROLD HIBBERT[4]

A considerable number of previous investigations[5-9] carried out in these laboratories have given clear experimental support to Hibbert's assumption that protolignin consists of a mixture of different substances derived from relatively simple propylphenol units. Although considerable uncertainty still exists regarding the nature of the C_3 side chain and the mode of its linkage in the complex protolignin structure, several experimental facts have been established. The aromatic portion of spruce protolignin is always the guaiacyl (4-hydroxy-3-methoxyphenyl) nucleus,[10] the side chain is an oxygenated radical[7,8,9] without terminal methyl groups[11] and it contains primary hydroxyl groups.[5,6]

According to Hibbert,[12] the experimental results seem to indicate that a large portion of native lignin consists of a polymer or polymers of the dehydrodiisoeugenol type, in which the isoeugenol unit is replaced by β-oxyconiferyl alcohol (I). Dimerization of the enol modification of (I) to yield dehydrodi-(β-oxyconiferyl)-alcohol (II) is highly probable since this has been shown by Erdtman[13] and by Haworth[14] to be typical of the dimeric plant resins or lignins.

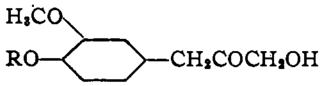


I



II

Inasmuch as the ethanolysis reaction indicates that some of the native lignin is present in a much less complex form (water-soluble) than the remainder (water-insoluble fractions),[15] it has been suggested that the ethanolysis products result from the decomposition of the less complex form. Hibbert suggests three general types of relatively simple units that could yield the ethanolysis products. These are assumed to be the glycosides (III), (IV), (V), the hemiketals (VI), (VII) and the ether (VIII).



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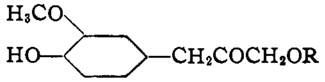
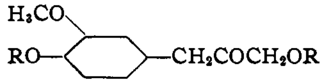
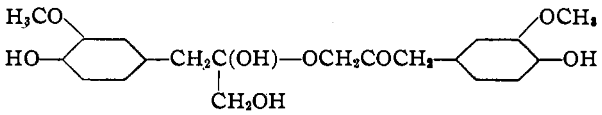


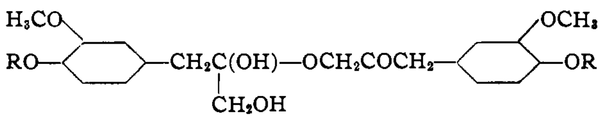
IV



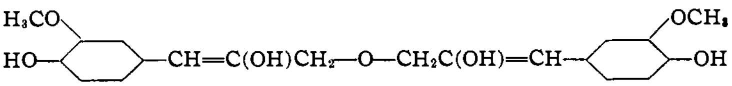
V



VI



VII



VIII

(R is carbohydrate unit)

These (III, IV, V, VI, VII, VIII) could yield β-oxyconiferyl alcohol (I) on ethanolysis and the latter could undergo dismutation and rearrangement[12] to yield the ethyl ethers of (IX) and (XII) and also (X) and (XI), actually obtained by ethanolysis of spruce wood.

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(1) This paper represents part of a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by Samuel B. Baker, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, October, 1943.

(2) Present address: Montreal General Hospital, Montreal, Que.

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(4) Late E. B. Eddy Professor of Chemistry, McGill University.

(5) Godard, McCarthy and Hibbert, THIS JOURNAL, **63**, 3061 (1941).

(6) Cooke, McCarthy and Hibbert, *ibid.*, **63**, 3056 (1941).

(7) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

(8) Brickman, Hawkins and Hibbert, *ibid.*, **62**, 2149 (1940).

(9) Kulka, Hawkins and Hibbert, *ibid.*, **63**, 2371 (1941).

(10) Creighton, Gibbs and Hibbert, *ibid.*, **66**, 32 (1944).

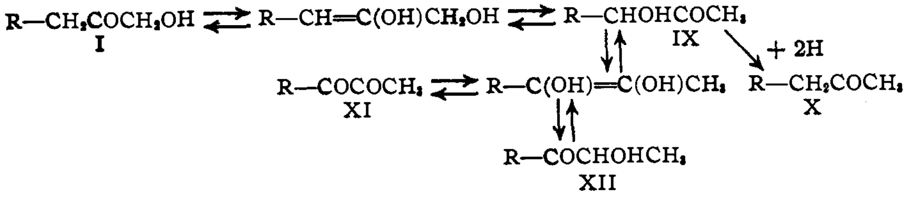
(11) MacGregor, Evans and Hibbert, *ibid.*, **66**, 41 (1944).

(12) Hibbert, *Biochem. Rev.*, **11**, 183 (1942).

(13) Erdtman, *Svensk Papperstidn.*, **44**, 243 (1941); translation in *Pulp and Paper Magazine of Canada*, Feb. (1942).

(14) Haworth, *Nature*, **147**, 255 (1941).

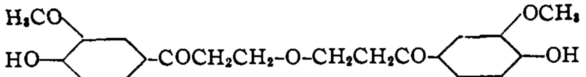
(15) Kulka, Fisher, Baker and Hibbert, THIS JOURNAL, **66**, 39 (1944).



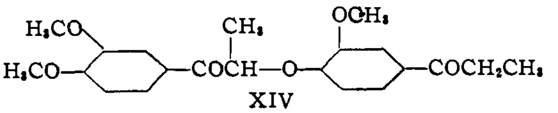
(R is 4-hydroxy-3-methoxyphenyl)

Experimental support for this mechanism recently has been obtained.[16]

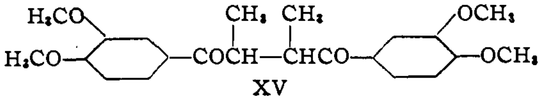
It was desirable to synthesize compounds of structures similar to (II) and (VIII) in order to test the validity of Hibbert's[11] suggestions regarding the probable structures of the simple and more complex portions of spruce protolignin. Three dimeric compounds have been synthesized, 2,2'-divanilloyl diethyl ether (XIII), 1-veratroyl-1-(2-methoxy-4-(propanone-1)-phenoxy)-ethane (XIV), and 2,3-diveratroylbutane (XV). The first (XIII) was synthesized by the iodine de-



XIII



XIV



XV

hydration[17] of 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone. The second (XIV) was prepared by a Williamson reaction between the sodium phenolate of 1-(4-hydroxy-3-methoxyphenyl)-1-propanone and 2-bromo-1-(3,4-dimethoxyphenyl)-1-propanone. The third (XV) was prepared by means of an acetoacetic ester synthesis.

The first dimer (XIII) is characterized by the presence of a dialkyl ether linkage between the two propylphenol units, each of which has a carbonyl group in the γ-position to the ether linkage and adjacent to the ring. The second dimer (XIV) differs from the first (XIII) in that it contains (a) an alkaryl ether linkage and (b) the carbonyl group in the β-position to the ether linkage and adjacent to the ring. The third dimer (XV) is characterized by (a) a carbon–carbon linkage between carbon atoms β- to the ring and (b) carbonyl groups adjacent to the rings.

Each of these dimers (XIII), (XIV), (XV) was heated with 2% ethanolic hydrogen chloride. The first (XIII) yielded about 15% of an amorphous lignin-like product, the balance about 80% being recovered unchanged. Chain fission probably did occur to a small extent and the fission products underwent immediate polymerization. The second (XIV) was unaffected by this treatment; no monomolecular fission products were isolable. The third (XV) treated similarly, with 2% ethanolic hydrogen chloride, gave a high yield (80%) of an amorphous lignin-like product with no indication of chain fission to stable monomolecular units. Hydrogenation[18] of this carbon–carbon linked dimer (XV) did not result in cleavage into monomolecular products. Therefore it may be that polymerization of (XV) during ethanolysis occurred not due to primary cleavage into reactive monomolecular units but due to the inherent reactivity of the 1,4-diketonic grouping.

Experimental

Synthesis of 2,2'-Divanilloyl Diethyl Ether (XIII)

3-Bromo-1-(4-hydroxy-3-methoxyphenyl)-1-propanone. Powdered anhydrous aluminum chloride (10 g.) was suspended in anhydrous carbon disulfide (40 cc.) in a three-necked round-bottomed flask equipped with a mercury-sealed stirrer, a reflux condenser with drying tube and a dropping funnel. The reaction flask was cooled by immersion in ice-water and β-bromopropionyl chloride (13.0 g.) added rapidly to the well-stirred suspension. Veratrole (10.0 g.) was added gradually during one hour with vigorous stirring, then two more 10-g. portions of aluminum chloride were added, the second portion fifteen minutes after the first. The reaction mixture was heated at 50° for one hour, allowed to stand overnight at room temperature and the carbon disulfide decanted. The Perrier complex was decomposed in a mixture of ice and concentrated hydrochloric acid. The product was filtered, washed on the filter with 10% hydrochloric acid and finally with water. The crude, dried product was dissolved in ether and decolorizing charcoal added. The suspension was heated under reflux for one hour, filtered and petroleum ether (30–50°) added until a permanent turbidity was formed. A crystalline product separated from the cooled solution and was recrystallized from ether–petroleum ether yielding 11.1 g. (60%), m. p. 103–104°.

Anal. Calcd. for $C_{10}H_{11}O_3Br$: OCH_3, 11.9; Br, 30.9. Found: OCH_3, 11.8; Br, 30.7.

The product was further characterized by conversion into the known[19] 3-acetoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone.

3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone.—Aqueous sodium hydroxide (1%, 100 cc.) was added to 3-bromo-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (2 g.) in a round-bottomed flask. The reaction mixture was heated at 50° for four hours, cooled and then acidified with dilute hydrochloric acid. The acidified solution was extracted with eight portions of chloroform (60 cc.) and the combined chloroform solutions were dried over anhydrous sodium sulfate. The solvent was removed and the resulting product twice recrystallized from hot benzene (30 cc.) yielding 1.32 g. (88%), m. p. 109–110°. A mixed melting point determination with an authentic sample of 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone showed no depression.

2,2'-Divanilloyl Diethyl Ether (XIII).—3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (3.0 g.) was dissolved in hot anhydrous benzene (25 cc.) in a small Claisen flask fitted with a reflux condenser. A crystal of

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[16] Fisher, Kulka and Hibbert, This Journal, 66, 598 (1944).

[17] Hibbert, *ibid.*, 37, 1748 (1915).

[18] Baker and Hibbert, *ibid.*, 70, 63 (1948).

[19] K. E. West and Hibbert, *ibid.*, 65, 1170 (1943).

re-sublimed iodine (0.05 g.) was added and the solution was refluxed for one hour on the steam-bath. The benzene was removed by distillation at atmospheric pressure. The resulting product, a viscous oil, was dissolved in hot methanol (5 cc.) and on cooling, crystals separated rapidly. The crude product was recrystallized from anhydrous methanol yield 1.0 g. (36%), m. p. 153–154°.

Anal. Calcd. for $C_{20}H_{22}O_7$: C, 64.17; H, 5.88; OCH_3, 16.6; mol. wt., 374. Found: C, 64.2; H, 5.9; OCH_3, 16.6; Rast mol. wt., 380.

The bis-2,4-dinitrophenylhydrazone was prepared by the usual method.

Anal. Calcd. for $C_{32}H_{30}O_{13}N_8$: C, 52.31; H, 4.08; OCH_3, 8.4. Found: C, 52.4; H, 4.1; OCH_3, 8.4.

Diazomethane Methylation of XIII.—2,2′-Divanilloyl diethyl ether (0.16 g.) was dissolved in benzene and a solution of diazomethane in benzene was added. The solvent was removed after twenty-four hours and the unmethylated portion was removed by washing with 2% alkali. The remaining portion was dissolved in hot ethanol. Crystals separated rapidly when the solution was cooled yielding 0.15 g. (89%), m. p. 139–140°.

Anal. Calcd. for $C_{22}H_{26}O_7$: C, 65.69; H, 6.47; OCH_3, 30.8; mol. wt., 402. Found: C, 65.6; H, 6.6; OCH_3, 30.6; Rast mol. wt., 395.

Oxidation of 2,2′-Diveratroyl Diethyl Ether.—The methylated ether (0.13 g.) was suspended in 3% aqueous sodium hydroxide (50 cc.) in a small three-necked flask fitted with a reflux condenser, stirrer, and a dropping funnel. Aqueous potassium permanganate (9%, 25 cc.) was added dropwise to the hot (100°) stirred alkaline suspension during one hour. The precipitated manganese dioxide was removed by filtration and the clear filtrate acidified with dilute hydrochloric acid. A crystalline substance separated and was recrystallized from methanol-water (3:1) yielding 0.09 g. (77%), m. p. 180–181°. A mixed melting point determination with an authentic sample of veratric acid showed no depression.

Synthesis of 1-Veratroyl-1-[2-methoxy-4-(propanone-1)-phenoxy]-ethane (XIV)

2-Methoxyphenyl Propionate.—A solution of guaiacol (25 g.), pyridine (20 g.) and propionyl chloride (19 g.) was heated on the steam-bath during one hour. The reaction mixture was cooled and then poured into 2% aqueous hydrochloric acid. The aqueous solution was extracted with two portions (50 cc.) of ether and the combined solutions dried over anhydrous sodium sulfate. The solvent was removed and the resulting oil distilled from a Claisen flask at 140–143° (20 mm.) yielding 34.5 g. (95%).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.67; H, 6.67; OCH_3, 17.2. Found: C, 66.6; H, 6.9; OCH_3, 17.0.

1-(4-Hydroxy-3-methoxyphenyl)-1-propanone.—Powdered anhydrous aluminum chloride (30 g.) was dissolved in anhydrous nitrobenzene (75 cc.) at 100°. The solution was cooled and added to a three-necked round-bottomed flask, equipped with a mercury-sealed stirrer, a reflux condenser with drying tube, and a thermometer. Stirring was started and 2-methoxyphenyl propionate (20 g.) was added rapidly. The reaction mixture was heated at 60° for one hour, then allowed to stand overnight at room temperature. The mixture was filtered with the exclusion of air and moisture and the Perrier complex washed well with a mixture of benzene and ligroin (2:1). The complex was decomposed in ice–hydrochloric acid and the oily layer extracted with chloroform. The chloroform solution was refluxed for one hour with activated charcoal and after filtration the solvent was removed under reduced pressure. The oily product crystallized and it was recrystallized from ether–petroleum ether (30–50°) yielding 13 g. (65%), m. p. 62–63°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.67; H, 6.67; OCH_3, 17.2. Found: C, 66.6; H, 6.9; OCH_3, 17.2.

1-Veratroyl-1-[2-methoxy-4-(propanone-1)-phenoxy]-ethane.[20]—The sodium phenolate, prepared from sodium (2.0 g.) and 1-(4-hydroxy-3-methoxyphenyl)-1-propanone (14.7 g.) was dissolved in anhydrous ethanol (300 cc.) in a round-bottomed flask. 2-Bromo-1-(3,4-dimethoxyphenyl)-1-propanone[21] (22.3 g.) was added and the solution heated under reflux for four hours. The hot solution was poured into cold water and the microcrystalline precipitate removed by filtration. The crude product was recrystallized twice from methanol yielding 23.8 g. (78%), m. p. 148–149°.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.74; H, 6.45; OCH_3, 25.0; mol. wt., 372. Found: C, 67.7; H, 6.5; OCH_3, 24.9; Rast mol. wt., 387.

The bis-2,4-dinitrophenylhydrazone was prepared by the usual method.

Anal. Calcd. for $C_{33}H_{32}O_{12}N_8$: C, 54.09; H, 4.37; OCH_3, 12.7; mol. wt., 732. Found: C, 54.0; H, 4.4; OCH_3, 12.6; Rast mol. wt., 724.

Synthesis of 2,3-Diveratroylbutane (XV)

Ethyl Veratrate.—The ester was prepared by refluxing during four hours veratric acid (80 g.), anhydrous ethanol (500 cc.) and sulfuric acid (15 cc.). The product was isolated in the usual manner yielding 82 g. (89%) which after one recrystallization from ether–petroleum ether (30–50°) melted sharply at 43.5–44.5°.

Anal. Calcd. for $C_{11}H_{14}O_4$: OCH_3, 44.3. Found: OCH_3, 43.9.

Ethyl Veratroylacetate.—Ethyl veratrate (50 g.) was added to a three-necked flask equipped with a reflux condenser, a dropping funnel and a glycerol-sealed stirrer. Granulated sodium (4 g.) was added, the stirrer started and the mixture heated at 80°. A pasty mass was obtained to which ethyl acetate (15 g.) was added dropwise, and the temperature raised to 90°. An additional quantity of sodium (4 g.) and ethyl acetate (15 g.) was added to the reaction mixture. This addition of sodium and ethyl acetate was continued until a total of 20 g. of sodium and 75 g. of ethyl acetate had been added. Stirring and heating were continued for sixteen hours. The mixture was cooled, added with stirring to ice–hydrochloric acid, and the acidic solution extracted with three portions of ether (250 cc.). The combined ethereal solutions were dried over anhydrous sodium sulfate and the solvent removed. The resulting oil was distilled under reduced pressure. The first fraction, boiling up to 120° (0.01 mm.), consisting mainly of ethyl acetoacetate and ethyl veratrate was discarded. The required product distilled as a viscous oil at 150–160° (0.01 mm.) yielding 24.1 g. (40%).

Anal. Calcd. for $C_{13}H_{16}O_5$: OCH_3, 36.9. Found: OCH_3, 37.3.

Methyl Ethyl Veratroylacetate.—Ethyl veratroylacetate (24 g.) was dissolved in anhydrous benzene (150 cc.) in a three-necked round-bottomed flask equipped with a reflux condenser, dropping funnel, and a glycerol-sealed stirrer. Granulated sodium (2.2 g.) was added in small portions during four hours and the mixture heated with stirring during twelve hours. Methyl iodide (15 g.), dissolved in anhydrous benzene (200 cc.), was added dropwise to the cooled mixture. Stirring was continued until the reaction mixture became transparent. The mixture was heated on the steam-bath during one hour, then cooled and added in a fine stream to cold water (500 cc.). The benzene layer was decanted and the aqueous solution extracted with ether (100 cc.). The combined benzene and ether solutions were dried over anhydrous sodium sulfate and the solvent removed under reduced pressure. The resulting oil was distilled and the fraction boiling at 155–167° (0.01 mm.) collected yielding 25 g. (98%).

Anal. Calcd. for $C_{14}H_{18}O_5$: OCH_3, 34.9. Found: OCH_3, 34.3.

bis-(Methyl Ethyl Veratroylacetate).—Methyl ethyl veratroylacetate (25 g.) was dissolved in anhydrous benzene (300 cc.) in a three-necked flask equipped with a dropping funnel, a glycerol-sealed stirrer and a reflux con-

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[20] Kratzl, *Ber.*, **77B**, 717 (1944).

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

denser with a drying tube. The solution was heated on a steam-bath and granulated sodium (2.2 g.) added in small portions during two hours, with vigorous stirring. The reaction mixture became very viscous and another portion of benzene (300 cc.) was added. Iodine (13 g.) dissolved in anhydrous benzene (250 cc.), was added dropwise to the hot, well-stirred mixture during four hours. Stirring was continued for one hour longer and the solution added in a fine stream to water (one liter). The benzene layer was decanted, washed with 5% aqueous sodium thiosulfate (100 cc.) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the resulting oil distilled at 210–216° (0.01 mm.), yielding 23.3 g. (93%).

Anal. Calcd. for $C_{28}H_{34}O_{10}$: OCH_3, 35.1. Found: OCH_3, 34.6.

2,3-Diveratroylbutane (XV).—bis-(Methyl ethyl veratroylacetate) (23 g.) was dissolved in anhydrous ethanol (375 cc.) containing sodium hydroxide (8.5 g.) and the mixture allowed to stand at room temperature during twenty-four hours with occasional stirring. The reaction mixture was cooled and concentrated hydrochloric acid added dropwise until the evolution of carbon dioxide ceased. The mixture was immediately added to cold water (450 cc.), the solution filtered, the oily product dissolved in chloroform–ethanol (1:2, 200 cc.) and charcoal added. The mixture was heated under reflux on the steam-bath during two hours and filtered while hot. The solvent was removed under reduced pressure and the tan-colored crystalline substance which separated was twice recrystallized from hot methanol yielding 8.4 g. (48%), m. p. 189–190°.

Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.39; H, 6.76; OCH_3, 32.1; mol. wt., 386. Found: C, 68.3; H, 6.9; OCH_3, 31.9; Rast mol. wt., 395.

The bis-2,4-dinitrophenylhydrazone was prepared by the usual method.

Anal. Calcd. for $C_{34}H_{34}O_{12}N_8$: OCH_3, 16.6. Found: OCH_3, 16.6.

Action of 2% Ethanolic Hydrogen Chloride on XIII.—2,2′-Divanilloyl diethyl ether (1.00 g.) was heated under reflux with 2% ethanolic hydrogen chloride (50 cc.) for forty-eight hours in an atmosphere of carbon dioxide. A small amount (0.15 g.) of an amorphous lignin-like substance which separated was removed by filtration. The filtrate was neutralized with sodium ethylate and the precipitated sodium chloride removed by filtration. The solvent was removed under reduced pressure and the product recrystallized from methanol yielding 0.75 g., m. p. 153–154°. A mixed melting point determination with an authentic sample of XIII showed no depression.

Action of 2% Ethanolic Hydrogen Chloride on XIV.—The effect of 2% ethanolic hydrogen chloride on this dimer (XIV) (1.00 g.) was determined as above. The starting material was recovered unchanged in a yield of 0.91 g.

Action of 2% Ethanolic Hydrogen Chloride on XV.—In this reaction 1.00 g. of dimer (XV) was used and the amorphous product weighed 0.79 g.

Acknowledgment.—The authors gratefully acknowledge the kind financial assistance of the Canadian Pulp and Paper Association and the Spruce Falls Power and Paper Company.

Summary

1. Several propylphenol monomolecular compounds related to lignin progenitors were prepared. Some of these were new compounds, while others were prepared by new and better methods.

2. The synthesis of three dimers from these propylphenol units has been carried out.

3. Ethanolysis of the three dimers did not yield the customary monomolecular fission products, obtained by the ethanolysis of wood. This indicates that these synthetic dimers differ from those materials forming the readily hydrolyzable portion of native lignin.

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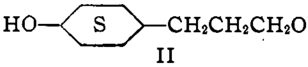
[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

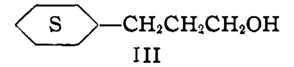
Studies on Lignin and Related Compounds. LXXXVI. Hydrogenation of Dimers Related to Lignin[1]

BY SAMUEL B. BAKER[2] AND HAROLD HIBBERT[3]

Complete liquefaction of spruce wood has been achieved by means of high-pressure catalytic hydrogenation.[4] The protolignin is converted in part to 4-*n*-propylcyclohexanol (I), 3-(4-hydroxycyclohexyl)-1-propanol (II) and 3-cyclohexyl-1-propanol (III) in yields of 9.9, 5.8 and 12.6%, respectively (based on the Klason lignin content of the wood).[4,5,6] These isolated products (I, II, III) serve to establish the propylphenol units in lignin. Further investigations[7,8] have shown that a relatively high proportion of the cyclohexylpropane units contains oxygen atoms attached to the terminal carbon atoms in the side chains.



I



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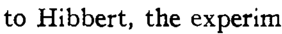

III

According to Hibbert, the experimental results seem to indicate that a large portion of native lig-

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[1] This paper represents part of a thesis submitted to the Faculty of Graduate Studies and Research, McGill University, by Samuel B Baker, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Oct., 1943.

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[4] Godard, McCarthy and Hibbert, THIS JOURNAL, **63**, 3061 (1941).

[5] Bower, Cooke and Hibbert, *ibid.*, **65**, 1192 (1943).

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

[7] Harris, D'Ianni and Adkins, *ibid.*, **60**, 1467 (1938).

[8] Harris and Adkins, *Paper Trade J.*, **107**, No. 20, 38 (1938).