benzene. The benzene layer was washed with water several times. The residue obtained by evaporation of the benzene was boiled with 500 cc. of petroleum ether (b. p. 60–110°) and filtered. On cooling, the unreacted aminoquinoline was obtained as yellow crystals. More of this starting amine was obtained on concentrating the petroleum ether solution. The product was distilled at 0.01 mm. The excess 1-diethylamino-4-pentanol was much lower boiling than the desired alkylated amine which was distilled at a bath temperature of 230–250°. The distillate was dissolved in 80 cc. of petroleum ether and more of the unalkylated amine separated after cooling at 4° for twenty-four hours. The petroleum ether again was evaporated and the resulting viscous material distilled at 0.01 mm. The first few drops of the distillate were discarded because they contained most of the starting amine still present. Finally 1.8 g. of product was obtained as a red viscous oil which still contained a small amount of unalkylated amine.

Anal. Calcd. for $C_{24}H_{29}N_3O$: C, 76.67; H, 7.78. Found: C, 77.14; H, 7.63.

The presence of potassium iodide did not improve the yield of alkylated amine.

Deamination of 5-Aminobenzofuro[3,2-f]quinoline (XIII).—The amine (0.2 g.) was dissolved in 35 cc. of hot concentrated hydrochloric acid and the resulting solution cooled to 0°. The suspension thus obtained was diazotized rapidly with 0.088 g. of sodium nitrite in 5 cc. of water. After five minutes at 0–3°, the diazonium solution was filtered quickly and to the clear filtrate 35 cc. of ice-cold 50% aqueous hypophosphorous acid was added. The reaction mixture was allowed to stand in the refrigerator for twelve hours, followed by an additional twelve hours at room temperature. The solution was made alkaline with aqueous sodium hydroxide and the precipitate which formed was filtered, washed with a little water and dried. After two "short path" distillations at a pressure of 2 mm. and a bath temperature of 100–120°, 0.090 g. of needles which melted at 81–82° was obtained. The product was recrystallized from petroleum ether (b. p. 35–60°); very pale yellow needles, m. p. 82–83.5° (cor.). The melt solidified and remelted at the same value. The product is insoluble in Claisen potash solution and gives a negative ferric chloride test and a negative Beilstein test for halogens.

Anal. Calcd. for $C_{15}H_9NO$: C, 82.17; H, 4.14; N, 6.39. Found: C, 82.13; H, 4.42; N, 6.41.

Summary

1. Benzofuro[3,2-g]quinoline was nitrated to a single mononitro derivative. By reduction the corresponding amino compound was synthesized and converted into 3-diethylaminopropylamino and 3-(4-morpholinyl)-propylamino derivatives. Neither showed antimalarial activity.

2. Benzofuro[2,3-f]quinoline yielded two difficultly separated mononitro derivatives. The corresponding amines and, through them, the corresponding bromo compounds were synthesized.

3. 5-Nitrobenzofuro[2,3-f]quinoline was synthesized from 2-nitro-3-aminodibenzofuran. It was then reduced, and the morpholinylpropyl derivative prepared. This latter compound had no antimalarial activity.

4. 3-Benzenesulfonamido-2-nitrodibenzofuran was reduced to the corresponding amine which, in turn, was converted by means of a Skraup synthesis to the benzenesulfonamidobenzofuroquinoline. This last compound was hydrolyzed to the aminobenzofuroquinoline and attempts made to substitute the amino group with appropriate alkyl radicals.

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

Studies on Lignin and Related Compounds. LXXIV. Relation of Wood Ethanolysis Products to the Hibbert Series of Plant Respiratory Catalysts. Allylic and Dismutation Rearrangements of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone and 1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone

BY ARTHUR M. EASTHAM,[1] H. E. FISHER,[1] MARSHALL KULKA AND HAROLD HIBBERT

In previous communications[2,3] on the origin and function of lignin in the plant, a comparison was drawn between the Szent-Györgyi animal cell system of hydrogen-transporting respiratory catalysts[4] and a suggested analogous system composed of assumed lignin progenitors capable of functioning in a similar manner in the plant cell (Scheme 1).

SCHEME 1

	Szent–Györgyi System (Animal)		Hibbert System (Plant)
A.	$COOH—CH_2—CO—COOH$	A'.	$R—CH_2—CO—CH_2OH$
	↑↓		↑↓
B.	$COOH—CH_2—CHOH—COOH$	B'.	$R—CH_2—CHOH—CH_2OH$
	↑↓		↑↓
C.	$COOH—CH{=}CH—COOH$	C'.	$R—CH{=}CH—CH_2OH$
	↑↓		↑↓
D.	$COOH—CH_2—CH_2—COOH$	D'.	$R—CH_2—CH_2—CH_2OH$

(R = 4-hydroxy-3-methoxyphenyl)

The third member of the Hibbert system, coniferyl alcohol (C') (corresponding to fumaric acid in the animal system), is known to be present in practically all plants in the early stages of growth.[5] The non-appearance of this and the other three members among the lignin fission products isolated in the ethanolysis of wood is assumed to be due to their very labile character, resulting in their ready conver-

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[1] Holder of a National Research Council of Canada Studentship 1941–1942.

[2] Hibbert, *Paper Trade J.*, **113**, No. 4, 35 (1941).

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

[4] Szent-Györgyi, *Ber.*, **72A**, 53 (1939).

[5] Czapek, "Biochemie der Pflanzen," Vol. III, G. Fischer, Jena, 1921, p. 464.

sion, under the influence of the extraction medium, into stabilized end-products.

It was suggested[3] that possibly only the first and second members (A' and B') actually are present (probably as dimers) in native lignin, in view of the pronounced oxidizing character of the postmortal plant cell environment. Moreover, it was predicted that the first member of the series, namely, 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, should exist in equilibrium with its enol form, oxyconiferyl alcohol, and that the latter should readily undergo an allylic rearrangement to give a more stable benzoin type. There existed the further probability that this benzoin would form an equilibrium mixture with its ene-diol and dismutation isomers.

$$\mathrm{R{-}CH_2{-}CO{-}CH_2OH\ (A') \rightleftarrows}$$
$$\mathrm{R{-}CH{=}C(OH){-}CH_2OH \rightleftarrows}$$
$$\mathrm{R{-}CHOH{-}C(OH){=}CH_2 \rightleftarrows}$$
$$\mathrm{R{-}CHOH{-}CO{-}CH_3 \rightleftarrows}$$
$$\mathrm{R{-}C(OH){=}C(OH){-}CH_3 \rightleftarrows R{-}CO{-}CHOH{-}CH_3}$$

In preceding communications[6] the isolation of the isomeric benzoin dismutation forms as their ethyl ethers from the ethanolysis products of spruce wood is described, and in the present paper experimental proof is given of the above theoretical conceptions.

It is a well-known fact that aromatic and aliphatic substituted allyl halides, such as cinnamyl chloride[7] and crotyl chloride[8] readily undergo rearrangement when the halide is replaced by hydroxyl, ethoxyl or acetate groups. Thus, when cinnamyl chloride is treated with aqueous or alcoholic alkali, or potassium acetate in glacial acetic acid, equilibrium mixtures of cinnamyl and phenylvinylcarbinyl alcohols, -ethyl ethers and -acetates are formed. The treatment of either crotyl chloride or methylvinylcarbinyl chloride with potassium or silver acetate gives a mixture of crotyl- and methylvinylcarbinyl acetates, the extent of rearrangement being determined by the type of solvent used.[8]

This communication deals with (i) the synthesis of the four new products 1-bromo-, 1-hydroxy- and 1-acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II), and 3-acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series I), and (ii) the rearrangements (see below) occurring when the halogen atoms in 1-bromo-1-(3,4-dimethoxyphenyl)-2-propanone (Series II, $X = Br$) and 3-chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I, $X = Cl$) are replaced by hydroxyl, ethoxyl and acetate groups.

$$\mathrm{R'{-}CH_2{-}CO{-}CH_2X} \underset{\text{rearr.}}{\overset{\text{allylic}}{\rightleftarrows}}$$

SERIES I

$$\mathrm{R'{-}CHX{-}CO{-}CH_3} \underset{\text{rearr.}}{\overset{\text{dismutation}}{\rightleftarrows}}$$

SERIES II

$$\mathrm{R'{-}CO{-}CHX{-}CH_3}$$

SERIES III

(R' = 3,4-dimethoxyphenyl- and X = —Br or —Cl, —OH, —O—CO—CH_3 or —OC_2H_5)

Synthesis of Members of the Series I, II and III.—In order to study the rearrangement reactions involved in the conversion of the halides of Series I, II and III to the corresponding alcohols, acetates and ethyl ethers, it was necessary to have available twelve pure reference compounds, namely: **Series II:** 1-bromo-1-R''; 1-hydroxy-1-R''; 1-acetoxy-1-R''; 1-ethoxy-1-R''.[9] **Series I:** 3-chloro-1-R''[10]; 3-hydroxy-1-R''; 3-acetoxy-1-R''; 3-ethoxy-1-R''.[9] **Series III:** 2-bromo-1-R'''[6c]; 2-hydroxy-1-R'''[6b,6c]; 2-acetoxy-1-R'''[6b,6c]; 2-ethoxy-1-R'''.[6b,6d]

(R'' = (3,4-dimethoxyphenyl)-2-propanone; R''' = (3,4-dimethoxyphenyl)-1-propanone)

Synthesis of Members of Series II.—The derivatives of Series II (X = Br, —OH, —O—CO—CH_3 and —OC_2H_5) were synthesized from 1-(3,4-dimethoxyphenyl)-2-propanone by the following type reactions[11]

$$\mathrm{R'{-}CHO + NO_2{-}CH_2{-}CH_3 \longrightarrow}$$
$$\mathrm{R'{-}CH{=}C(NO_2){-}CH_3 \longrightarrow}$$
$$\mathrm{R'{-}CH_2{-}C({=}NOH){-}CH_3 \longrightarrow}$$
$$\mathrm{R'{-}CH_2{-}CO{-}CH_3 \xrightarrow{Br_2} R'{-}CHBr{-}CO{-}CH_3 \xrightarrow[aq.]{KOAc}}$$
$$\mathrm{R'{-}CHOH{-}CO{-}CH_3}$$

$$\text{Also } \mathrm{R'{-}CH_2{-}CO{-}CH_3 \xrightarrow{Pb(OAc)_4}}$$
$$\mathrm{R'{-}CHOAc{-}CO{-}CH_3}$$

(R' = 3,4 dimethoxyphenyl-)

In an attempt to synthesize 3-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) from the corresponding halide (Series I) rearrangement reactions resulted, no normal product being formed, the latter evidently undergoing rapid transformation into a mixture of members of Series II and III (Scheme 2)

Synthesis of Members of Series I.—3-Acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) was synthesized from homoveratric acid[12] by treatment of the acid chloride with diazomethane and interaction of the resulting diazomethyl ketone with acetic acid as applied by Wolfrom.[13]

$$\mathrm{R'{-}CH_2{-}COOH \xrightarrow{SOCl_2} R'{-}CH_2{-}COCl \xrightarrow{CHN_2}}$$

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(6) (a) E. West, MacInnes and Hibbert, THIS JOURNAL, **65**, 1187 (1943); (b) Cramer, Hunter and Hibbert, *ibid.*, **61**, 509 (1939); (c) Cramer and Hibbert, *ibid.*, **61**, 2204 (1939); (d) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

(7) Meisenheimer and Link, *Ann.*, **479**, 211 (1930).

(8) Roberts, Young and Winstein, THIS JOURNAL, **64**, 2157 (1942).

(9) Kulka and Hibbert, *ibid.*, **65**, 1185 (1943).

(10) Haworth and Atkinson, *J. Chem. Soc.*, 797 (1938).

(11) Kulka and Hibbert, THIS JOURNAL, **65**, 1180 (1943).

(12) (a) Hahn, Stiehl and Schultz, *Ber.*, **72**, 1291 (1939); (b) Hahn and Schultz, *ibid.*, **72**, 1302 (1939).

(13) Wolfrom, Waisbrot and Brown, THIS JOURNAL, **64**, 2329 (1942).

$$R'{-}CH_2{-}CO{-}CHN_2 \xrightarrow{HOAc} R'{-}CH_2{-}CO{-}CH_2{-}O{-}CO{-}CH_3$$

The method of Hahn, Stiehl and Schultz[12a] for the preparation of homoveratric acid was slightly modified, in that α-chlorohomoveratric amide was converted to homoveratric amide by use of hydriodic acid in glacial acetic acid instead of by catalytic hydrogenation.

Members of Series III.—These have been synthesized previously.[6b,d] The physical constants of the three series of reference compounds (I, II and III) are summarized in Table I. The fourth isomeric series (R'—CO—CH$_2$—CH$_2$—X)[14] is included for comparative purposes.

TABLE I

PHYSICAL CONSTANTS OF REFERENCE COMPOUNDS

Compound	M. p. °C., if solid or $n^{25}D$ if liquid Bromide	Alcohol	Acetate	Ethyl ether
1-Substituted-1-R''	87–88	77–78	1.5260	1.5160
3-Substituted-1-R''	44–45	....	55–56	1.5215
2-Substituted-1-R'''	88–89	1.5590	65–66	81–82
3-Substituted-1-R'''	107–108	83–84	100–101	50–51

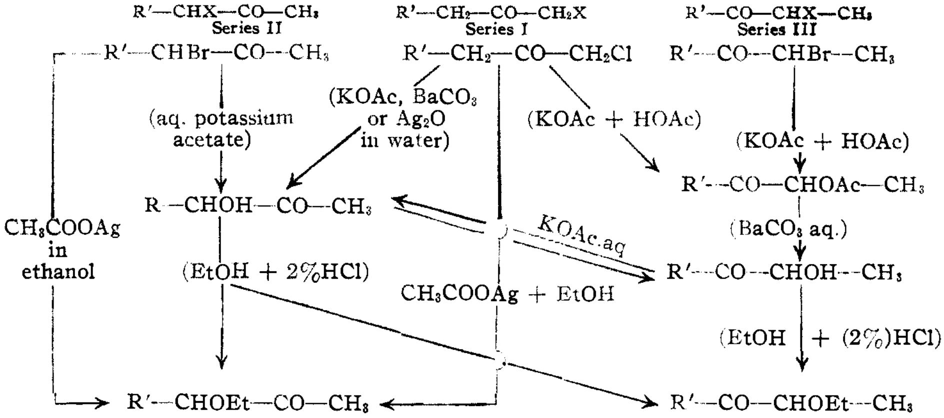
R'' = (3,4-dimethoxyphenyl)-2-propanone; R''' = (3,4-dimethoxyphenyl)-1-propanone.

Since the three bromides of Series I, II and III were prepared by standard methods and also were found to be different from each other, it was assumed that the formulas assigned them according to the method of preparation were correct and that no rearrangements had taken place. The structures of the alcohols, acetates and ethyl ethers were arrived at in a similar manner. Further proof of structure in certain cases was obtained from absorption spectra studies.[15]

Replacement Reactions.—The attempted replacement of halogen in the halides, R'—CHBr—CO—CH$_3$ (Series II) and R'—CH$_2$—CO—CH$_2$Cl (Series I), by hydroxyl, acetate or ethoxyl groups resulted in some cases in a complete, in other cases a partial, rearrangement whereby a mixture of the normal and abnormal products was obtained. These replacement reactions are summarized in Scheme 2.

SCHEME 2

REPLACEMENT REACTIONS



(R' = 3,4-dimethoxyphenyl)

Treatment of the bromide (Series II) with silver acetate in ethanol gave the normal ethyl ether, namely, 1-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone in yield of 88%; no ethyl ethers of I or III could be detected. On the other hand, treatment of the 1-hydroxyketone (II) with 2% hydrogen chloride in ethanol yielded a mixture of the dismutation rearrangement products, namely, 2-ethoxy-1-(3,4-dimethoxyphenyl)-1-propanone (III) (60%) and the normal 1-ethyl ether (II) (30%). The replacement of bromine by the hydroxyl group on treatment of II (X = Br) with aqueous potassium acetate yielded the normal 1-hydroxyketone (II), some unchanged bromide and a small amount of the 2-hydroxyketone (III) formed as the result of a dismutation rearrangement.

Members of Series III showed, as far as could be ascertained, no tendency to rearrangement[6b,d] and also the 1-hydroxyketone (II) was found to be quite stable toward dilute acid. On the other hand, members of I proved to be very reactive and underwent rearrangements frequently. Thus treatment of the chloroketone (I) with aqueous potassium acetate, barium carbonate or silver oxide gave the 1-hydroxyketone (II) in 70% yield (as the result of an allylic rearrangement), and a small amount of the diketone, 1-(3,4-dimethoxyphenyl)-1,2-propanedione. Treatment of the chloroketone (I) with silver acetate in ethanol yielded the 1-ethyl ether (II) in approximately 60% yield together with a high alkoxyl-containing compound not further investigated. Refluxing the same chloroketone (I) with potassium acetate in glacial acetic acid also yielded a mixture of substances one of which was identified as the acetate (III).

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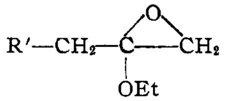
(14) (a) K. A. West and Hibbert, THIS JOURNAL, **63**, 3035 (1941); (b) Baker, Evans and Hibbert, unpublished results.

(15) Patterson and Hibbert, *ibid.*, **65**, 1862 (1943).

In other attempts to prepare the normal 3-ethyl ether of I, the 3-chloroketone (I) was treated with sodium ethylate and also with potassium hydroxide in ethanol solution. In both cases the reaction product was a carbonyl-free ethyl ether believed to have the structure[16]



$$\mathrm{R'{-}CH_2{-}\underset{OEt}{C}\overset{O}{\frown}CH_2}$$

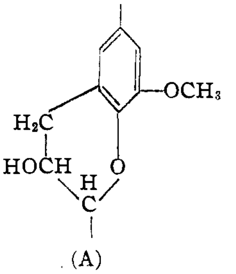
The remarkable ease with which members of Series I rearrange to give types II and III possesses marked significance for the structure of lignin. In the former type (I) there are no terminal methyl groups, in contrast to the presence of these in each of the latter (II and III). Moreover, members of Series III, when subjected to ethanolysis conditions, do not readily undergo rearrangement, while under similar treatment members of Series II are partially converted to type III.

It follows that if native lignin contains structures of the type Series I these might very well rearrange during ethanolysis to give products containing —CH$_3$ groups and belonging to Series II and III.

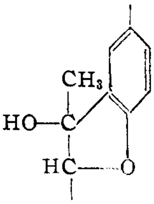
Previous work on the hydrogenation of lignin and of wood under high pressure[17] has demonstrated the presence in native lignin of large amounts of products containing terminal —CH$_2$OH or —CH$_2$—O—CH$_2$— groupings. In a following communication[18] it is shown by a chromic acid oxidation technique that native lignin contains no terminal methyl groups as postulated by Freudenberg, so that the present experimental evidence permits of the conclusion that the ethanolysis products from wood, R—CHOH—COCH$_3$[7]; R—CO—CHOH—CH$_3$ and R—CO—COCH$_3$ (R = 4-hydroxy-3-methoxyphenyl- or 4-hydroxy-3,5-dimethoxyphenyl-), represent stabilized end products derived from a more reactive lignin progenitor[3b], namely, the keto form of oxyconiferyl alcohol. The present experimental observation that hydrolysis with aqueous barium carbonate or potassium acetate of the chloroketone R—CH$_2$—CO—CH$_2$Cl (Series I) yields a small amount of the diketone, R—CO—COCH$_3$, in addition to the main product R—CHOH—COCH$_3$, is of marked significance in this connection.

The present experimental results bring into contrast the marked divergence of theoretical views on the structure of lignin advocated by Freudenberg and by Hibbert.

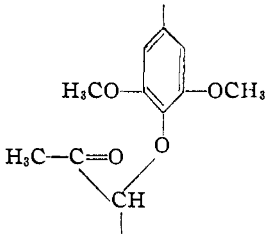
According to the former investigator[19] native spruce lignin consists of the polymeric forms of propylphenol units (A) and (B) essentially derived by condensation reactions from the two building stones R—CHOH—CHOH—CH$_2$OH and R—CHOH—CO—CH$_3$ (R = 4-hydroxy-3-methoxyphenyl).



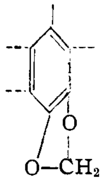
(A)



(B)



(C)



(D)

Freudenberg considers that five out of eight units in spruce lignin belong to types (A) and (B), two units contain methylenedioxy groups, type (D), and one is of the pyrogallol type (C).

Hibbert has pointed out repeatedly[20,21] the complete lack of experimental evidence supporting Freudenberg's claim of the presence of the piperonyl type (D) (based on the amount of formaldehyde formed on hydrolysis of an "extracted" lignin[18]) and has suggested "that the formaldehyde (1–4%) is formed from an aromatic side-chain, possibly one existing as part of a complex present in lignin condensation polymers and similar to cinnamyl alcohol." [21]

Freudenberg has now accepted this explanation[22] in his very recent abandonment of type (D) as part of the native lignin aggregate. His type (B) is characterized by the presence of terminal methyl groups while type (A) could give rise to a minor amount of free primary alcohol groups. No adequate experimental evidence is available indicating the presence in spruce lignin of his type (C)—syringyl component—in other than minute quantity. Up to the present Freudenberg has not been successful in isolating any propylphenol lignin units.

Hibbert regards native lignin as a mixture of polymers derived by condensation reactions from a different type of propylphenol building unit, oxyconiferyl alcohol ($\beta\gamma$-dioxyisoeugenol) the keto form of which is R—CH$_2$—CO—CH$_2$OH.

Polymer formation is assumed to occur by one or more of three mechanisms (E), (F), (G).

The syringyl lignin building unit R'—CH$_2$—COCH$_2$OH (R' = 4-hydroxy-3,5-dimethoxyphenyl) is assumed by Hibbert to be present in

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[16] Aston and Greenburg, THIS JOURNAL, **62**, 2590 (1940).

[17] Ref. 3b, pp. 186–187.

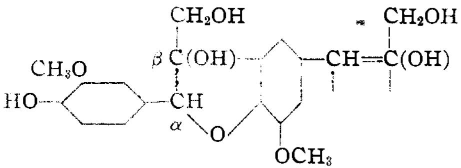
[18] MacGregor, Evans and Hibbert, THIS JOURNAL, **66**, 41 (1944).

[19] Freudenberg, *Ann. Rev. Biochem.*, **8**, 81-112 (1939).

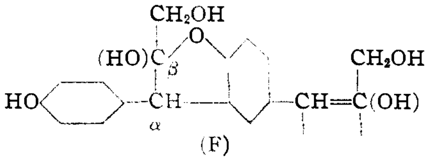
[20] Hunter, Wright and Hibbert, *Ber.*, **71**, 734 (1938).

[21] Hunter and Hibbert, THIS JOURNAL, **61**, 2196 (1939).

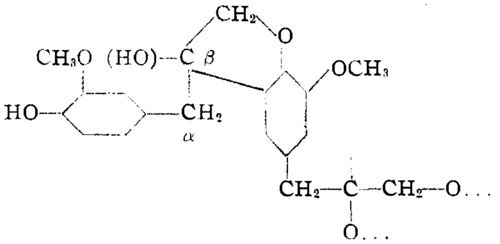
[22] Freudenberg, *Ber.*, **76**, 305 (1943).



(E)



(F)



(G)

the native lignin of all angiosperms and is probably present as the initial monomeric buildingstone since the blocking by methoxyl groups of both positions ortho to the phenol group would prevent polymerization proceeding in the manner indicated above.

(E) and (F) represent condensation polymers of dehydro-di-(dioxyisoeugenol), while (G) is related to the furan series. Available experimental evidence does not permit of a distinction between the three types but it is evident that they differ markedly in structure from those proposed by Freudenberg, and in particular are distinguished by the absence of methyl groups.

Removal of water from the positions (α) and (β) would yield an unsaturated type, capable of forming cross linkages, and such may form part of the native lignin aggregate.

These structural theories of Freudenberg and of Hibbert are still highly speculative in character. The source of the small quantity of monomolecular ethanolysis products obtained in the case of spruce, and of the much larger amount in the case of maple, is still unknown. That they are derived from oxyconiferyl and oxysyringyl alcohols now seems reasonably certain, but the actual form in which the latter are present in native lignin, whether as mono- or diglucosides, phenol ethers, ketals involving the carbonyl and phenol groups, or as readily reversible dimers of the truxillic acid type is, as yet, quite unknown. It would seem somewhat unlikely they are formed from polymers of the type depicted above.

Experimental

1-(3,4-Dimethoxyphenyl)-2-nitro-1-propene.—This was synthesized by the condensation of veratric aldehyde with nitroethane.[23]

1-(3,4-Dimethoxyphenyl)-2-propanone.—1-(3,4-Dimethoxyphenyl)-2-nitro-1-propene was reduced to the oxime by treatment with a mixture of iron dust, ferric chloride and hydrochloric acid and the oxime hydrolyzed to the ketone[11]; yield, 70%; b. p. 118° (0.2 mm.); n^{25}_{D}, 1.5330. *Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.0; H, 7.2; OCH_3, 32.0. Found: C, 67.8; H, 7.1; OCH_3, 32.0.

1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone (Series II).—To a solution of 1-(3,4-dimethoxyphenyl)-2-propanone (10.14 g.) and benzoyl peroxide (0.1 g.) in chloroform (100 cc.), contained in a three-necked flask fitted with a dropping funnel, mercury-sealed stirrer and drying tube, bromine (9.6 g.) was added through the dropping funnel over a period of ninety minutes. The temperature of the reaction mixture was kept below 10° by means of an ice-bath. At the conclusion of the addition, the reaction mixture was allowed to attain room temperature and then stirred for two hours. The chloroform solution was washed, successively, twice with cold water, twice with cold 1% bicarbonate solution and finally with water, then decolorized with charcoal and dried over sodium sulfate. Removal of the solvent under reduced pressure yielded a dark oily product, convertible to a white crystalline solid from a mixture of ether and petroleum ether (b. p. 30–50°), m. p. 87–88°; yield 8.5 g. (58%). *Anal.* Calcd. for $C_{11}H_{13}O_3Br$: C, 48.4; H, 4.8; OCH_3, 22.7; Br, 29.3. Found: C, 48.5; H, 4.9; OCH_3, 22.7; Br, 29.5.

Semicarbazone of 1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone.—Fine white crystals from water, m. p., 201.5–202.5°. *Anal.* Calcd. for $C_{12}H_{16}O_3N_3Br$: C, 43.6; H, 4.9; OCH_3, 18.8. Found: C, 43.8; H, 5.0; OCH_3, 18.7.

1 - Hydroxy - 1 - (3,4 - dimethoxyphenyl) - 2 - propanone (Series II).—1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone (2.0 g.) was dissolved in 5% potassium acetate (200 cc.) and the solution heated on the steam-bath for four hours. The reaction mixture was extracted with chloroform, the extract dried over sodium sulfate and the solvent removed. The residual oil distilled at 135–145° bath temperature (0.1 mm.); yield of light-yellow distillate which soon solidified, 1.27 g.; recrystallized from a mixture of ether and petroleum ether as white plates, m. p. 76–77°; yield, 0.84 g. (55%). *Anal.* Calcd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.7; OCH_3, 29.6. Found: C, 63.0, H, 6.8; OCH_3, 29.5.

Semicarbazone of 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone.—White crystals from water, m. p. 155–156°. *Anal.* Calcd. for $C_{12}H_{17}O_4N_3$: C, 53.9; H, 6.4; OCH_3, 23.2. Found: C, 53.8; H, 6.4; OCH_3, 23.0.

Action of Aqueous Potassium Acetate on 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II).—The hydroxyketone (0.5 g.) was heated twelve hours (100°) with 5% aqueous potassium acetate (50 cc.) in an atmosphere of carbon dioxide. The reaction mixture was extracted with chloroform and the solvent removed, leaving a yellow oil which distilled at 125–135° bath temperature (0.02 mm.). The distillate quickly solidified and was recrystallized from ether-petroleum ether (b. p. 30–50°). 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (0.205 g.) (45%) was recovered, m. p. 76–77°. On evaporation of the mother liquors, a yellow oil (0.230 g., 50%) n^{25}_{D} 1.5610 was obtained. The semicarbazone of this oil when mixed with that of 2-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone showed no depression in melting point.

Synthesis of 1-Acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II)

(a) **Acetylation of 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone.**—The hydroxyketone was acetylated with acetyl chloride and pyridine,[24] yield, 1.6 g. (89%); n^{25}_{D} 1.5260. Fractional distillation showed that this acetate was a pure homogeneous product. *Anal.* Calcd. for $C_{13}H_{16}O_5$: C, 61.9; H, 6.4; OCH_3, 24.6. Found: C, 62.0; H, 6.3; OCH_3, 24.6.

2,4-Dinitrophenylhydrazone of 1-Acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone.—Orange crystals from ethanol, m. p. 149–150°. *Anal.* Calcd. for $C_{19}H_{20}O_8N_4$: C,

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(23) Kauffmann, *Ber.*, **52**, 1431 (1919).

(24) Smith and Bryant, This Journal, **57**, 61 (1935).

52.8; H, 4.7; OCH_3, 14.4. Found: C, 52.5; H, 4.8; OCH_3, 14.5.

(b) **Treatment of 1-(3,4-Dimethoxyphenyl)-2-propanone with Lead Tetraacetate.**—1-(3,4-Dimethoxyphenyl)-2-propanone (2.3 g.) was dissolved in glacial acetic acid (80 cc.) and freshly prepared lead tetraacetate (7 g.)[25] added. The mixture was heated for eight hours at 88° in a two-necked flask equipped with a mercury-sealed stirrer and a condenser. The solution was decanted into water (400 cc.) and the aqueous solution extracted with ether. The ether extract was washed with 5% sodium bicarbonate, then with water, and dried over sodium sulfate. Removal of the solvent left a dark-colored oil which distilled at 160–190° bath temperature (0.1 mm.); yield 2.2 g. (74%); $n^{25}\text{D}$ 1.5290. On fractional distillation (0.2 mm.) the greater part of this material distilled over as pure 1-acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone. Its 2,4-dinitrophenylhydrazone when mixed with that prepared from the pure synthetic product (previous experiment) showed no depression in melting point.

Homoveratric Acid.—α-Chloro-homoveratric amide[12a] (6.0 g.) was dissolved in glacial acetic acid (20 cc.) and constant-boiling hydriodic acid (8 cc.) added. After standing for fifteen hours at room temperature the reddish-purple crystalline precipitate (22 g.) was filtered, dried *in vacuo* and added to a well-stirred, saturated solution of sodium bisulfite. Addition of ammonium hydroxide to the bisulfite solution precipitated the homoveratric amide (4.2 g., 82%) m. p. 141–144°. The amide was then hydrolyzed to homoveratric acid.[12a]

3-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone (Series I).—Homoveratric acid was converted to the acid chloride, the latter treated with diazomethane and the resulting diazomethyl ketone allowed to react with hydrogen bromide in ether. The method used was identical with that employed for the preparation of 3-chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I),[10] X = Cl. Yield of the bromide 80%; recrystallized from a mixture of ether and petroleum ether, m. p. 44–45°. *Anal.* Calcd. for $C_{11}H_{13}O_3Br$: OCH_3 22.7. Found: OCH_3, 22.5.

3-Acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series I).—Homoveratric acid (1.4 g.) was treated with pure thionyl chloride (2.0 cc.) for fifteen minutes at room temperature and then at 70° for an additional thirty minutes. The excess thionyl chloride was removed under reduced pressure and the residual product freed from last traces by two additions and removals of benzene. The light orange-colored oil was dissolved in ether and the solution added gradually to a cold solution of diazomethane in ether (prepared from 4 g. of nitrosomethyl urea). After standing at 0° for three hours, the ether was distilled off and the residual diazomethyl ketone refluxed with glacial acetic acid (20 cc.) for fifteen minutes. The acetic acid was removed under reduced pressure and the residue distilled at 165–190° (bath temperature) (0.1 mm.); yield of light-yellow oil, which solidified with difficulty, 1.44 g. (85%); white needle-like crystals from a mixture of ether and petroleum ether, m. p. 55–56°. *Anal.* Calcd. for $C_{13}H_{16}O_5$: C, 61.9; H, 6.4; OCH_3, 24.6. Found: C, 62.0; H, 6.4; OCH_3, 24.8.

Semicarbazone of **3-Acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone.**—White crystals from water and from ethanol–petroleum ether, m. p. 128–129°. *Anal.* Calcd. for $C_{14}H_{19}O_5N_3$: C, 54.4; H, 6.3; OCH_3, 20.1. Found: C, 54.4; H, 6.3; OCH_3, 20.2.

Synthesis of 1-(3,4-Dimethoxyphenyl)-1,2-propanedione.—To a hot solution of copper sulfate (1.45 g.) dissolved in pyridine (2.4 cc.) and water (1.2 cc.), was added 1-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II, X = –OH) (0.50 g.) and the resulting solution heated on the steam-bath for two hours. The reaction mixture was poured with stirring into 3 *N* hydrochloric acid (14 cc.) and the acid solution extracted with ether. Removal of the ether yielded a yellow solid (0.30 g.); recrystallized from a mixture of ether and petroleum ether, m. p. 69–70°. *Anal.* Calcd. for $C_{11}H_{12}O_4$: OCH_3, 29.8. Found: OCH_3, 29.7°. Oxidation of 2-hydroxy-1-(3,4-dimethoxyphenyl)-1-propanone (Series III), in a similar manner, yielded the same diketone.

Semicarbazone of 2-Hydroxy-1-(3,4-dimethoxyphenyl)-1-propanone.—A solution of 2-hydroxy-1-(3,4-dimethoxyphenyl)-1-propanone[6a] (0.1 g.), semicarbazide hydrochloride (0.1 g.) and potassium acetate (0.2 g.) in water (5 cc.) was heated at 70° for two hours and then allowed to stand at room temperature for one week; white crystals from water, m. p. 154–155°. *Anal.* Calcd. for $C_{12}H_{17}O_4N_2$: C, 53.9; H 6.4; OCH_3, 23.2. Found: C, 53.8; H, 6.5; OCH_3, 23.1.

Reaction of 1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone (Series II) with Silver Acetate and Ethanol.—1-Bromo-1-(3,4-dimethoxyphenyl)-2-propanone (2.0 g.) was dissolved in ethanol (150 cc.) and silver acetate (2.0 g.) added. The suspension was refluxed for twelve hours in an atmosphere of carbon dioxide. The silver bromide was filtered, the filtrate taken to dryness under reduced pressure and the residue distilled at 140–150° bath temperature (0.1 mm.); yield, 1.53 g. (88%). The 2,4-dinitrophenylhydrazone of this product, m. p. 141–142°, when mixed with the 2,4-dinitrophenylhydrazone of 1-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone[8] showed no depression, but when mixed with that of 2-ethoxy-1-(3,4-dimethoxyphenyl)-1-propanone showed a marked depression.

Reaction of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) with Silver Acetate and Ethanol.—3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone was treated with silver acetate and ethanol in a similar manner. The resulting product was fractionally distilled (0.2 mm.) yielding 1-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II, X = $-OC_2H_5$) (approx. 60%) and a high alkoxyl-containing compound (alkoxyl, 43.5%) which was not investigated further.

Behavior of 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II) toward 2% Ethanolic Hydrogen Chloride.—1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (1.5 g.) was dissolved in a 2% solution of hydrogen chloride in ethanol (150 cc.) and the mixture refluxed for forty-eight hours under an atmosphere of carbon dioxide. The reaction product was neutralized with solid sodium bicarbonate, filtered and the filtrate taken to dryness under reduced pressure. The residual oil was dissolved in ether and the ether solution extracted with 10% sodium bisulfite. The ether solution was then dried and the solvent removed. The residue distilled at 120–130° bath temperature (0.05 mm.); yield of pale-yellow distillate, which soon solidified, 1.406 g. The product was treated with a small amount of warm petroleum ether, and the insoluble material (0.792 g.) filtered off and washed; recrystallized from dilute ethanol, m. p. 81–82°; no depression in melting point when mixed with an authentic sample of 2-ethoxy-1-(3,4-dimethoxyphenyl)-1-propanone (Series III).

The combined petroleum ether filtrate and washings were taken to dryness and the residual oil (0.561 g.) converted to the 2,4-dinitrophenylhydrazone; recrystallized from ethanol, m. p. 141–142°; no depression in melting point when mixed with the 2,4-dinitrophenylhydrazone of 1-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II).

The bisulfite extract from the original ether solution was neutralized, the sulfur dioxide removed, and the resulting solution extracted with ether. Removal of the ether left a small amount of bisulfite-soluble material (0.04 g.) which was not investigated.

Reaction of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) with Aqueous Potassium Acetate, Barium Carbonate and Silver Oxide.—The chloroketone (3.3 g.) was refluxed with 5% aqueous potassium acetate (250 cc.) for five hours and the solution then extracted with chloroform. The extract was dried over sodium sulfate and the solvent removed. The residue was recrystallized from ether, yielding white crystalline material (1.5 g.), m. p., 76–77°; no depression in melting point when mixed with an authentic sample of 1-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II, X = –OH). The filtrates from the recrystallizations were taken to dry-

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[25] Dimroth and Schweizer, *Ber.*, **56**, 1375 (1923).

ness and the residue (A) fractionally distilled in the Cooke-Bower fractionating column[26] at 0.1 mm. pressure. About 20% (0.35 g.) of the starting material (A) was obtained as a yellow crystalline solid and after recrystallization from ether melted at 68–69°. A mixed melting point determination, with 1-(3,4-dimethoxyphenyl)-1,2-propanedione showed no depression. The remainder of the material was not identified.

Reaction of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) with a Mixture of Potassium Acetate and Glacial Acetic Acid.—The chloroketone (8.0 g.) was dissolved in glacial acetic acid (35 cc.), freshly-fused potassium acetate (21 g.) added, and the resulting solution heated for eight hours at 90–100°. The reaction mixture was diluted with water (300 cc.), neutralized with sodium carbonate, and extracted with chloroform. The extract was dried, the solvent removed and the residue fractionally distilled under reduced pressure. Each of the fractions obtained was semicrystalline. The crystalline material (40%) was separated on a porous plate and recrystallized from a mixture of ether and petroleum ether, m. p. 65–66°; no depression when mixed with an authentic sample of 2-acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series III).

Reaction of 1-Hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (Series II) with 5% Sulfuric Acid.—The hydroxyketone (0.4 g.) was heated at 70–80° with 5% sulfuric acid (100 cc.) for three and one-half hours and the solution extracted with chloroform. The chloroform extract was dried and the solvent removed. The residue was recrystallized from ether yielding the pure unchanged 1-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (0.35 g.).

Reaction of 2-Hydroxy-1-(3,4-dimethoxyphenyl)-1-propanone (Series III) with Aqueous Potassium Acetate.—The hydroxyketone (0.5 g.) was refluxed for four hours with 5% aqueous potassium acetate (75 cc.). From the solution the starting material was recovered as the semicarbazone (m. p. 153–155°) in 40% yield. No 1-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone could be detected.

Reaction of 3-Chloro-1-(3,4-dimethoxyphenyl)-2-propanone (Series I) with Methanolic and Ethanolic Alkali.—The chloroketone (2.5 g.) was dissolved in methanol (15 cc.) and a solution of sodium (0.32 g.) in methanol (16 cc.) added dropwise at room temperature. The alkaline solution was acidified very slightly with hydrochloric acid, and then neutralized by addition of solid sodium bicarbonate, filtered and the filtrate taken to dryness under reduced pressure. The residue (1.75 g.) was recrystallized from petroleum ether (b. p. 30–50°) and then from aqueous ethanol; m. p. 40–41°. *Anal.* Calcd. for $(CH_3O)_2$—C_6H_3—$C_3H_4O(OCH_3)$: C, 64.3; **H**, 7.1; OCH_3, 41.5; mol. wt., 224. Found: C, 64.2; H, 7.0; OCH_3, 41.7; mol. wt. (Rast), 234.

Treatment of the same chloroketone with *methanolic* potassium hydroxide yielded the same compound in 80% yield.

The substitution of *ethanol* for *methanol* and sodium *ethylate* for sodium *methylate* in this experiment yielded the corresponding ethyl ether; b. p. 104° (0.04 mm.); $n^{25}D$ 1.5150; alkoxyl, calcd. for $(CH_3O)_2$—C_6H_3—$C_3H_4O(OC_2H_5)$, 39.1. Found, 39.2.

Treatment of these reaction products with semicarbazide or acidified 2,4-dinitrophenylhydrazine yielded no carbonyl derivatives.

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Summary

1. Four new substances, namely, 1-bromo-, 1-hydroxy-, 1-acetoxy- and 3-acetoxy-1-(3,4-dimethoxyphenyl)-2-propanone have been synthesized.

2. The allylic and dismutation rearrangement reactions attendant upon the conversion of the two halides, 1-bromo-1-(3,4-dimethoxyphenyl)-2-propanone and 3-chloro-1-(3,4-dimethoxyphenyl)-2-propanone to the corresponding alcohols, acetates and ethyl ethers have been studied under a variety of conditions.

3. The ease with which these rearrangements occur provides valuable confirmation of the theory of Hibbert that the ethanolysis products from wood are in reality stabilized end-products formed from more reactive lignin progenitors of the type represented by oxyconiferyl alcohol (β,γ-dioxyisoeugenol) or its keto isomer, and provides strong support for his views on the structure of native lignin.

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[26] Bower and Cooke, *Ind. Eng. Chem., Anal. Ed.*, **15**, 290 (1943).

[Contribution from the Division of Industrial and Cellulose Chemistry, McGill University]

Studies on Lignin and Related Compounds. LXXV. Alkaline Nitrobenzene Oxidation of Plant Materials and Application to Taxonomic Classification[1]

By R. H. J. Creighton, R. Darnley Gibbs and Harold Hibbert

The two types of classification recognized by botanists for higher plants are (1) an *artificial* classification, or "key," compiled merely for the purpose of identification and based on any *obvious* characteristic, such as flower or leaf morphology, convenience being the sole criterion; (2) a *natural* one in which all available criteria should be employed[2] to indicate true relationships between species, genera, etc. In general, flower morphology is the most suitable basis for classification, but many other criteria (*e. g.*, morphology of other parts, cytology, comparative anatomy and chemistry) have been employed occasionally for its support.

Chemical methods have been employed in clarifying the relationships of many closely related species. Thus, Manske[3] has pointed

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[2] Gilmour, *Nature*, **139**, 1040 (1937).

[3] Manske, *Can. Chem. Process Inds.*, **23**, 199 (1939).