STUDIES ON LIGNIN BUILDING UNITS.

by

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TABLE OF CONTENTS

CLAIM TO ORIGINAL RESEARCH

A. The syntheses of β-hydroxypropiovanillone (A) and β-hydroxypropioveratrone (B) have been carried out and their behaviour towards chemical reagents studied.

B. Conversion of (A) and (B) into amorphous lignin-like products by acid and by alkali has been effected.

C. Exceptional reactivity of the terminal carbinol group of the side chains of (A) and (B) has been demonstrated.

D. A detailed study has been made of the stabilities of α-hydroxypropiovanillone, α-acetoxypropiovanillone, vanilloyl methyl ketone, their syringyl analogs, and various mixtures of these compounds, towards ethanolic hydrogen chloride under conditions of the standard "ethanolysis" procedure.

E. Depolymerization of various amorphous maple ethanol lignin fractions into simpler units has been effected by ethanolic hydrogen chloride.

I.

GENERAL INTRODUCTION

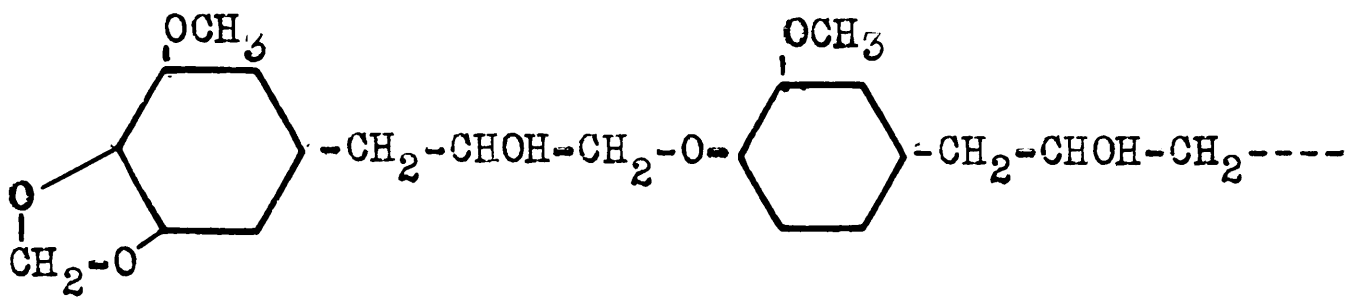
Part A. Historical Review

Recent reviews on the structure of lignin by von Wacek (1), Freudenberg (2), Erdtman (3) and Hibbert (4) have emphasized the essentially aromatic character of lignin and its relationship to coniferyl types.

During the period 1897 (5) to 1936 (6), Klason's original "coniferyl-oxyconiferyl alcohol hypothesis," in which polymers of coniferyl alcohol, coniferyl aldehyde, guaiacol aldol, etc. were included, underwent various modifications. This theory, which may be regarded as constituting the first phase of lignin research, was based (i) on the universal occurrence of coniferyl alcohol in young plant tissue (7), (ii) on data derived from the ethanolysis of the spruce lignin sulfonic acids and from solvent-extracted material (spruce wood) presumably containing both polyermized coniferyl and oxyconiferyl alcohol, and (iii) on the occurrence of products such as catechol, guaiacol and protocatechuic acid among the products in the lignin alkali-fusion reaction mixture (8).

In the second phase of lignin research (1926-1932) emphasis was laid on new methods for the isolation of lignin from wood and on identification of functional groups (methoxyl, hydroxyl, carbonyl, aromatic nucleus) in the extracted lignins. In this connection, methods were employed involving the use of concentrated acids such as sulfuric acid (9), hydrochloric acid (10), and mixtures of hydrochloric and phosphoric acids (11), as well as much milder procedures such as alcoholysis (4) by the use of alcohols, glycols, glycerol and glycerol chlorhydrin.

Freudenberg's earlier theory of the structure of lignin (12) was based essentially on the isolation of small amounts of catechol, protocatechuic acid and formaldehyde from spruce hydrochloric acid lignin, and on analyses of this lignin. These results indicated (a) aromatic character and absence of free phenol groups; (b) attachment of the methoxyl groups to aromatic nuclei; and (c) presence of aliphatic hydroxyl groups in side chains attached to the benzene nucleus. Freudenberg's modification of Klason's view of lignin as a propylphenol derivative differed only in the type of side chain envisaged and in the assumption that the building units were joined through ether linkages to give a "linear type" condensation polymer (12, page 154).

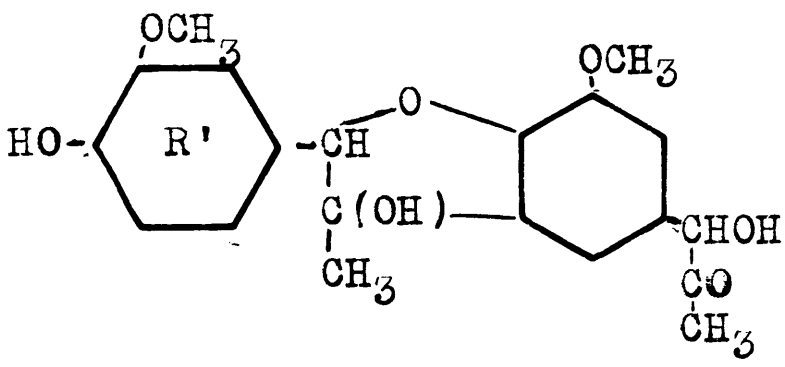


I.

Such a polymer, however, should readily undergo degradation by hydrolytic action into simple molecular units, and, this not being the case, Freudenberg found it difficult to postulate transformation into "secondary lignins" (12, page 135). The presence of the dioxymethylene group was based on the liberation of a small amount of formaldehyde (up to 1.2 per cent) (13, 14, 15). The side chains visualized by Freudenberg were R-CHOH-CHOH-CH_2OH, R-CH_2-CHOH-CHO, R-CHOH-CH_2-CHO and R-CHOH-CO-CH_3 (12, p.135). According to his definition these compounds are "biochemically identical" (12, p.137); this expression, however, has, scientifically, no biochemical significance and can only be assumed to imply they are in equilibrium with each other, at least <u>in vivo</u>.

In later investigations, in which cuproxam lignin was subjected to alkali degradation followed by methylation and permanganate oxidation, veratric, isohemipinic and dehydro-diveratric acids were isolated in yields of 10-14, 2-4 and 3 per cent, respectively (16, 17, 18).

On the basis of these newer spruce lignin studies, Freudenberg has abandoned the ether-type linkage of assumed propylphenol units and now considers the union to be of a carbon-to-carbon type involving oxygen-ring formation between side chains and aromatic nuclei (2, p.95) (II).



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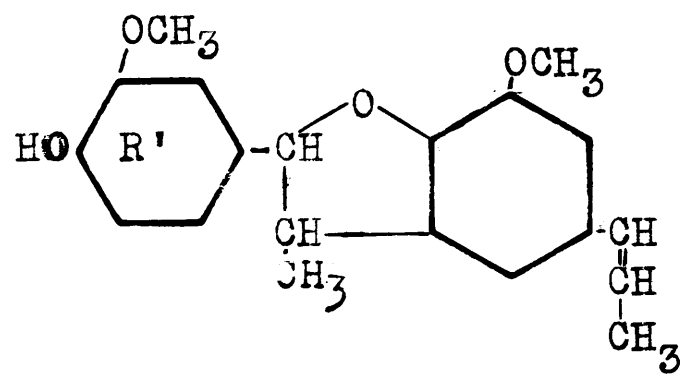


III.

(from two moles of R'-CHOH-$COCH_3$)

It can be seen that this structure (II) is similar to the dimer resin-type polymer (e.g. dehydrodiisoeugenol, (III) suggested by Erdtman (19).

One of the chief objections to this new Freudenberg conception has been the assumed presence of the dioxymethylene group either on terminal (12, p.134) or (in his later theory) centrally disposed (2, p. 95, 109) aromatic nuclei to the extent of 25 per cent of the spruce lignin structure. This theory has been seriously criticised (4), especially from the point of view of the non-isolation of piperonyl units. Furthermore the inclusion of such nuclei as centrally-located

units in a dehydrodiisoeugenol type of polymer implies a new and unusual form of condensation. It is also of importance to note that such a condensation polymer (II) could not be formed with syringyl derivatives where the five position (ortho to the phenol group) is blocked by a methoxyl group.

The recent developments (constituting the third phase) which have led to a clearer understanding of the structure and origin of protolignin are those connected with studies on (i) alkaline oxidation of lignin, wood, and lignin sulfonic acids; (ii) high-pressure hydrogenation of wood and lignin; and (iii) early experiments on the alcoholysis of wood. The results of these studies have provided experimental support for (i) the above-mentioned theoretical conception of lignin originally proposed by Klason and extended by Freudenberg and (ii) the modern theory of plant respiratory catalysts as lignin progenitors developed by Hibbert (4).

1. Alkaline Oxidation of Lignin and Lignin Derivatives

The action of alkali on lignin sulfonic acids has been investigated extensively following earlier observations (4, p.37) regarding the presence of vanillin, at least in small quantities, in the reaction mixture. With spruce lignin sulfonic acid a yield of 6-7 per cent of vanillin (20)

and a smaller amount of acetovanillone (21) and guaiacol (22) are obtained, while, with oak lignin sulfonic acid, in addition to these there are present syringaldehyde (23), acetosyringone (24), and 1,3-dimethoxypyrogallol (25). The addition of an oxidizing agent, such as meta-nitrobenzene sulfonic acid, in small quantity, to the alkaline spruce lignin sulfonic acid mixture gave a lower yield of aldehyde (25). More recently Freudenberg and co-workers have developed an alkali-nitrobenzene oxidation technique by which yields of 20-25 per cent of vanillin from spruce wood and spruce lignin sulfonic acid are obtained (26).

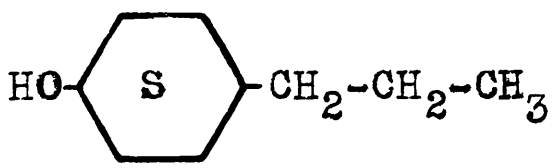
Although yields of 25 per cent vanillin appear to be the maximum obtainable from soft woods, an extension of this method to maple and aspen woods gave yields of 46 and 48 per cent respectively of mixtures of vanillin and syringaldehyde (27). If it be assumed that these aldehydes are derived from propylphenol units similar to those obtained by the ethanolysis of maple wood these yields indicate that approximately 58-62 per cent of the protolignin in angiosperms is aromatic in nature, and, thus, the validity of Klason's assumption that lignin has a fundamentally aromatic structure is established.

Lautsch and Piazolo (28) oxidized a brominated spruce lignin with alkali and nitrobenzene and obtained 6-bromovanillin

(8 per cent yield), a product which cannot be prepared directly from vanillin. This result is assumed to prove that the units in lignin are united with each other by etherification at the 4-position. Attempts to increase the yield of aromatic lignin oxidation products by substituting certain metallic oxides (29) for the nitrobenzene were unsuccessful.

2. Hydrogenation of Wood and Lignin

The preliminary work concerned with the high-pressure hydrogenation of lignin has been reviewed (3, 4). Complete liquefaction of the wood is effected by application of this technique to spruce and maple woods (30), the protolignin being converted, in part, to 4-n-propylcyclohexanol (IV) and 3-(4-hydroxycyclohexyl)propanol-1 (V) in yields of 19.5 and 5.8 per cent respectively (based on the Klason lignin content of wood).



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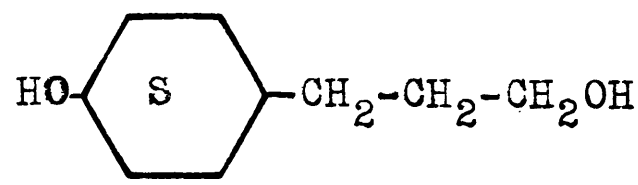


V.

Using the carbon content of these isolated units and of the "methoxyl-free protolignin" in the wood as a basis for calculation, the combined yield of propylcyclohexane derivatives represents a recovery of 36 per cent (30).

Examination of the yields of hydrogenation products from various amorphous fractions of a maple lignin isolated by ethanolysis (31) indicates that, for a given series of such fractions, increasing solubility and increasing susceptibility to depolymerization into simple, monomolecular propylphenol units by ethanolysis are paralleled by an increasing yield of the water-insoluble propylcyclohexanol hydrogenation products. This observation is thought to indicate the prevalence of -C-O-C- bonds between the propylphenol "lignin building-units" in those lignin fractions which are readily-soluble and are easily cleaved by ethanolysis and hydrogenolysis and, conversely, an increasing incidence of -C-C-C- bonds in lignin fractions having these characteristics to a lesser extent.

Hatihama et al. (32) hydrogenated hydrochloric acid lignin in the presence of several less active catalysts, particularly nickel, and obtained a 50 per cent yield of ether-soluble aromatic oils containing pyrocatechin and n-propylguaiacol. Similar results have been reported by Freudenberg and co-workers (33) who, following earlier work by Bobrov and Kolotova (34), extended the investigations to sulfite liquor. More recently, Freudenberg and Adam (35) have developed a procedure which consists of the simultaneous dry distillation and catalytic hydrogenation of isolated lignins on the surface of which various metallic catalysts

had been precipitated. In this manner ether-soluble, tarry fractions (20-50 per cent yield) containing among other products, phenols and phenolic ethers were obtained.

In addition to establishing the foregoing evidence for the presence of the propylphenol unit in lignin, hydrogenation studies have shown that a relatively large proportion of the propylcyclohexane derivatives obtained from wood (30) and certain lignins (31, 36, 37) contain oxygen atoms attached to the terminal carbon atom in the propyl side chain. This result provides the only experimental proof of the presence of oxygen in that position in protolignin.

A further contribution of the hydrogenating technique to lignin chemistry has been the classification of lignins according to their relative complexities (based on the yield and nature of hydrogenation resins). The results of Adkins and co-workers (37, 38) have shown that sulfuric acid, soda and alkali lignins are more complex than either protolignin (30) or alcoholysis lignins (31, 36).

3. Alcoholysis of Wood

The fourth phase in the elucidation of lignin structure may be regarded as that associated with the more recent contributions of Hibbert and co-workers on the action of ethanolic hydrogen chloride on various plant materials.

The belief that proto- and extracted lignins exist only as highly polyermized, complex substances led investigators to conclude that the amorphous water-insoluble product obtained by customary extraction methods was the only form in which lignin could be isolated. Precipitation into water from concentrated alcohol, acetic acid, or other solutions has been almost an invariable step in the isolation or purification of lignin.

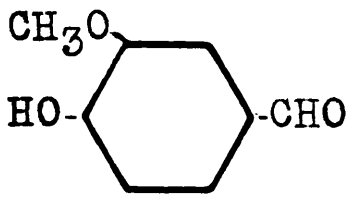
Prior to the recent developments of the ethanolysis lignin extraction process by Hibbert and co-workers, the aqueous precipitating liquors had been examined on only two occasions, namely, by Friedrich and Brüda (39) (methanolysis of beech) and by Brauns and Hibbert (40) (methanolysis of spruce). The former investigators isolated a small amount of lignin which apparently had been suspended in the water as a sol, and only minute traces of methoxyl-containing material were found in true solution in the concentrated aqueous liquors. Brauns and Hibbert also found only a small quantity of methoxyl-containing material in their work.

When it was observed, however, that the sum of the weights of the amorphous water-insoluble, lignin and of the Klason lignin remaining in the alcoholysis wood residue was almost always considerably less than the weight of the Klason lignin in the untreated wood, Hibbert became interested

in the cause of this discrepancy. The explanation of this was found when Cramer, Hunter and Hibbert (41) showed that the loss in weight was due (in the case of the ethanolysis of spruce and maple woods) to the water-solubility of a large proportion (12% of the Klason lignin, spruce; 30%, maple) of the methoxyl-containing materials.

As a result of this important observation an extensive series of investigations was started immediately in these laboratories to determine (a) the structure of the components of the water-soluble fraction; (b) the factors involved in their isolation, especially those relating to their actual presence as such in the wood or their appearance as stabilized end-products derived from more complex polymers and/or more reactive simple units; (c) the significance of the simple units in relation to the structure of the amorphous, water-insoluble ethanol lignin; and (d) the significance of the simple units in relation to photosynthesis, plant respiration and the formation of protolignin.

To date, approximately one-third (10% of Klason lignin content) of the water-soluble oils from maple wood has been shown to be composed of vanillin (VI) (42), syringaldehyde (VII) (42), α-ethoxypropiovanillone (VIII) (41a) and its syringyl homologue (IX) (41b), and vanilloyl methyl ketone (X) (43a) and its syringyl homologue (XI) (43b).



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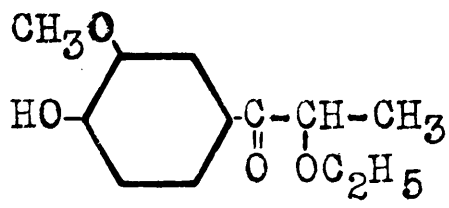
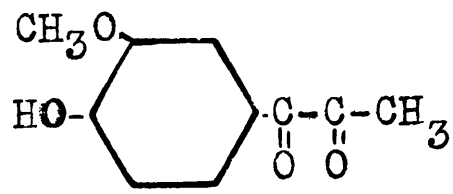
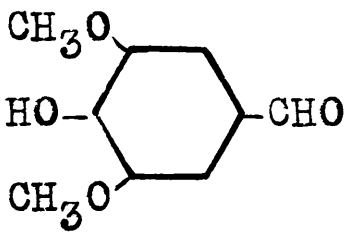


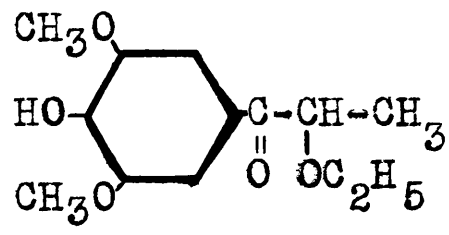
VIII.



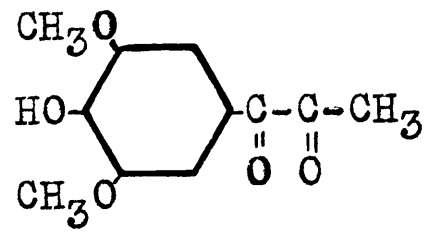
X.



VII.



IX.

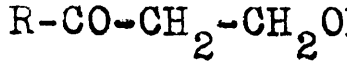


XI.

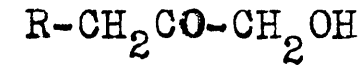
An actual relationship between these monomeric units and extracted lignins has been established by Peniston, McCarthy and Hibbert (44). These investigators refluxed an acetylated oak lignin with anhydrous ethanolic hydrogen chloride (2%) for 15 hours. The crude, water-soluble oils thus obtained (36% of the acetyl-free lignin content of the starting material) were separated into four fractions whose characteristics were very similar to those obtained by the action of ethanolic hydrogen chloride on maple wood.

As a direct result of the isolation and identification of the propyl phenol derivatives and of 3-(4-hydroxycyclohexyl)-propanol-1(V) (by means of hydrogenation) interest has been centered on the potential significance of related compounds such as β-hydroxypropiovanillone (XII), 1-guaiacyl-3 hydroxy-

propanone-2 (XIII) and their corresponding syringyl derivatives.



XII.



XIII.

4. Miscellaneous Experiments

The effect of variables in the Klason lignin determination has been carefully studied by Freudenberg and Ploetz (45, 46). The results indicate that this determination is, to a large extent, an arbitrary one and of particular significance is the fact that reaction conditions applicable to the production of the lowest yield of lignin of highest methoxyl content in the case of soft woods are not necessarily applicable to hardwoods. The use of hydrogen fluoride as a solvent for lignin has been suggested by Wiechert (47, 48). Preliminary investigations indicate that its use in a standardized method for the determination of lignin would eliminate many of the objections to the established sulfuric acid procedure, although the requisite expensive equipment (platinum or silver) renders its general acceptance doubtful. The difficulties encountered in applying the Klason procedure to plant products (grains, vegetables, etc.) have been emphasized recently (49); in particular with respect to

(i) the apparent condensation of lignin with protein material and (ii) the higher values found when the plant material is pre-dried at a relatively high temperature (100°C.).

Benson and co-workers (50, 51), in an attempt to establish a lignin research program of industrial significance, have commenced a study of desulfonated (with sodium hydroxide) calcium lignin sulfonate. Their recent results (52) indicate that nitrated desulfonated lignin closely resembles nitrated butanol lignin.

Butanol lignin, obtained by treating wood with butanol-water and butanol-water-alkali at 160°C., has been studied extensively by Bailey (53). He concludes (54) from comparative butanolysis studies of aspen and jack pine that a portion of the lignin in softwoods (but not in hardwoods) is chemically bound to cellulose. The presence of glucosidic linkages involving phenolic hydroxyl groups of the lignin is rendered doubtful by the results of investigations (55) on model substances (glucosides of the ethanolysis lignin units).

The necessity for careful classification of lignin sources is re-emphasized in results obtained by Ritter (56) on the lignin content of various cross-sectional regions of birch trees. For example, the lignin content in a twenty-nine year old white birch was found to drop from 37.4 per cent at the center to 19.5 per cent at the periphery.

The similarity in the behavior of coumarin and of acetic acid lignin towards diazomethane has led Wright (57) to suggest that lignins contain a coumarin-type of lactone linkage. von Wacek and Nittner (58) subjected beechwood tars to ozonolysis and from analyses of the reaction products concluded that substituted coumarones were present in the tars. The presence of two pyran rings in each "lignin building unit" (60) is indicated in absorption spectra studies (59) on spruce native lignin (60), spruce native lignin derivatives, lignins isolated from spruce wood by compounds containing hydroxyl and mercaptyl groups, and related compounds.

5. Biochemical Aspects of Protolignin Formation

(a) Mechanism of Plant Synthesis of Propylphenol Derivatives

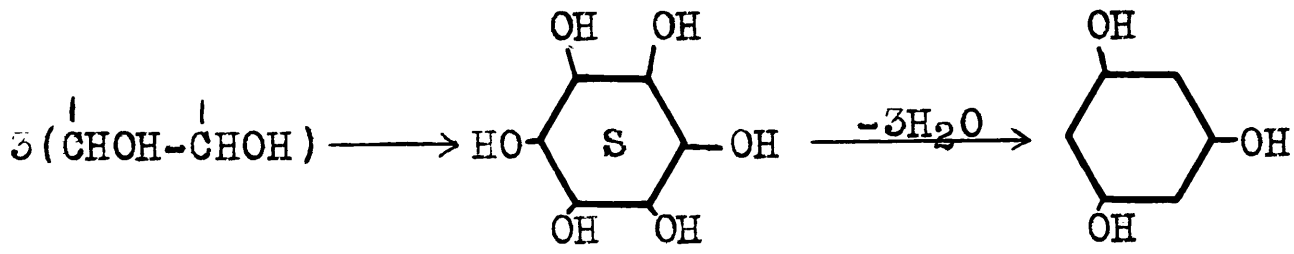
Synthesis of Simple Phenols - Various theories concerning the synthesis of phenolic compounds in plants have been based on assumed transformation of hexoses (61, 62), while a more recent theory (4) considers the phenolic substances as being formed from intermediate photosynthetic and/or plant respiratory products.

(i) Free Radical Theory (63) - Specific types are assumed to be present in the active stages of plant

growth (formic acid(XIV), glycollic aldehyde (XV), and acetaldehyde (XVI)) in equilibrium with the corresponding enol-radicals:

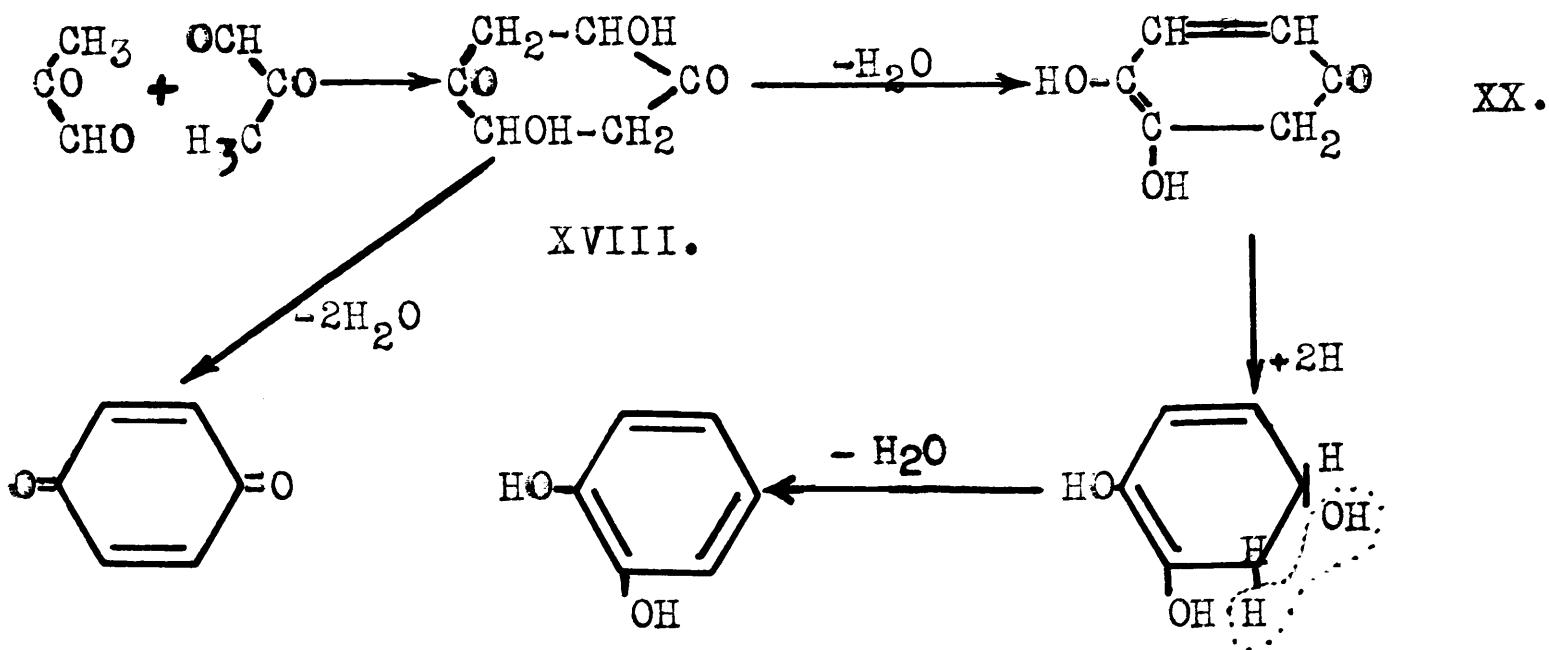
$HCOOH \rightleftharpoons {}^{\cdot}C(OH)_2$ XIV. $\quad CH_2OH.CHO \rightleftharpoons {}^{\cdot}CHOH.{}^{\cdot}CHOH$ XV. $\quad CH_3.CHO \rightleftharpoons {}^{\cdot}CH_2.CHOH$- XVI.

Union of the free radicals may give rise to hydroaromatic derivatives which, by loss of water, could yield phenols; for example, phloroglucinol (XVII) from (XV):



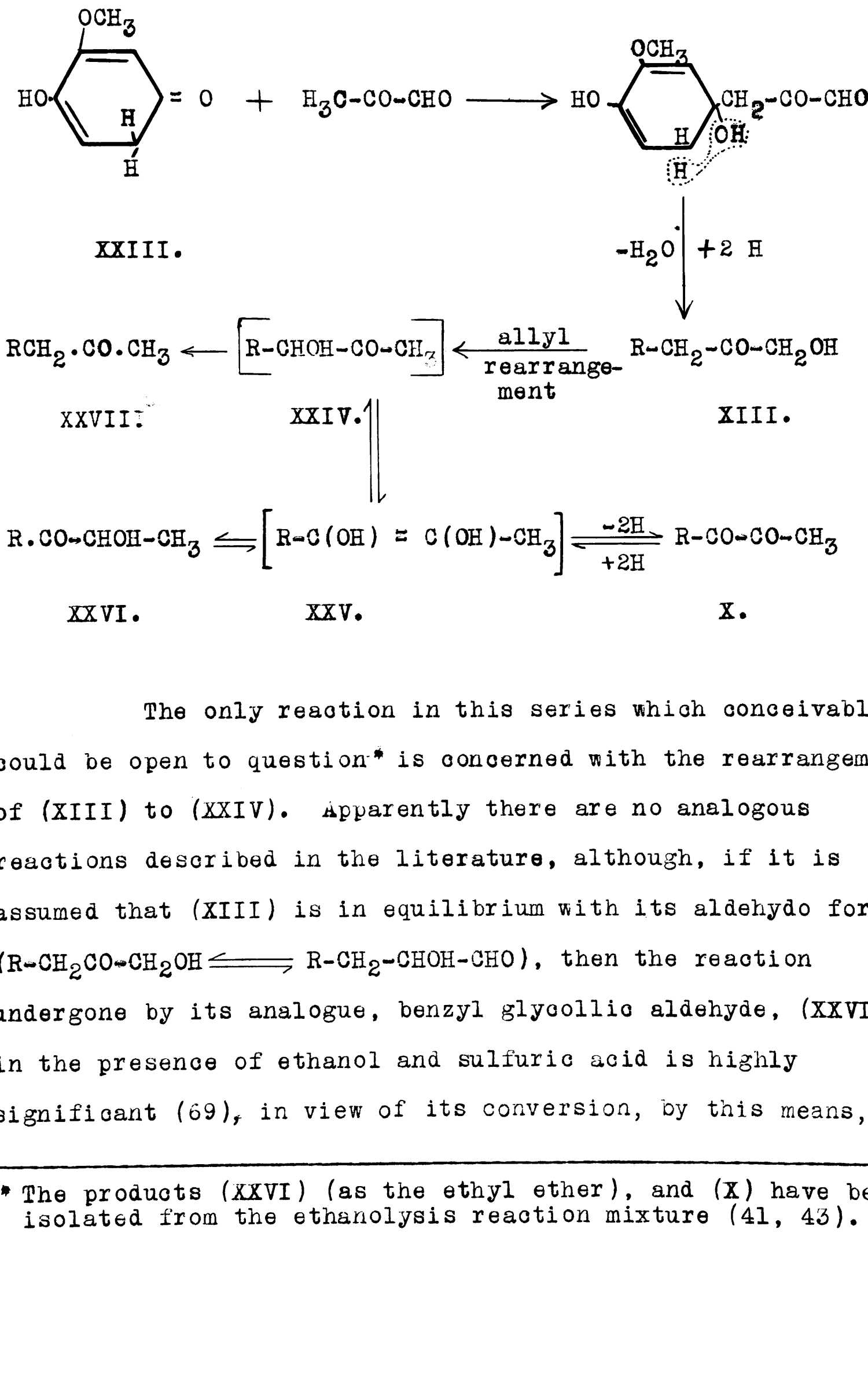
XV. Inositol XVII. (Phloroglucinol)

(ii) Methyl Glyoxal Theory of Phenol Formation (64) - Methyl glyoxal, which is a well-recognized intermediate in animal cell respiratory processes (65, p.244), presumably occupies a somewhat analogous position in plant carbohydrate metabolism (p. 264, 66) and has actually been isolated from a number of higher plants (67). Hibbert suggests the possibility of two molecules of methyl glyoxal polymerizing to yield a cyclic dihydroxydiketone (XVIII) capable of undergoing the indicated reactions to give quinone (XIX) and 1,2-dihydroxy-4-ketocyclohexadiene (XX).



This ketohexadiene, (XX), on reduction could give rise to a hydroxy enediol, (XXI), which would yield catechol (XXII) upon the loss of a mole of water. Pyrogallol (the precursor of the syringyl nucleus) could be formed by enzymatic oxidation of catechol (XXII) just as the latter is formed from phenol (68).

Synthesis of Propylphenol Derivatives - Condensation of the "methoxylated" ketocyclohexadiene, (XXIII), with a third mole of methyl glyoxal, followed by the loss of a mole of water and reduction would yield (XIII). An intramolecular change involving an allyl shift in (XIII) would give the primary dismutation isomer, (XXIV), (not yet isolated) which could then yield the ene-diol (XXV), this in turn giving the benzoin (XXVI). The benzoin derivative (XXIV) on reduction could yield the desoxybenzoin (XXVII). Moreover the ene-diol, (XXV) is a dihydro derivative of the 1,2-diketone (X).



The only reaction in this series which conceivably could be open to question* is concerned with the rearrangement of (XIII) to (XXIV). Apparently there are no analogous reactions described in the literature, although, if it is assumed that (XIII) is in equilibrium with its aldehydo form ($R\text{-}CH_2CO\text{-}CH_2OH \rightleftharpoons R\text{-}CH_2\text{-}CHOH\text{-}CHO$), then the reaction undergone by its analogue, benzyl glycollic aldehyde, (XXVIII), in the presence of ethanol and sulfuric acid is highly significant (69), in view of its conversion, by this means, into

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* The products (XXVI) (as the ethyl ether), and (X) have been isolated from the ethanolysis reaction mixture (41, 43).

a mixture of phenyl acetyl carbinol and benzoyl acetone.

$$2C_6H_5\text{-}CH_2\text{-}CHOH\text{-}CHO \longrightarrow C_6H_5\text{-}CHOH\text{-}CO\text{-}CH_3 \cdot + \; C_6H_5\text{-}CO\text{-}CO\text{-}CH_3$$

XXVIII. LXXV (a).

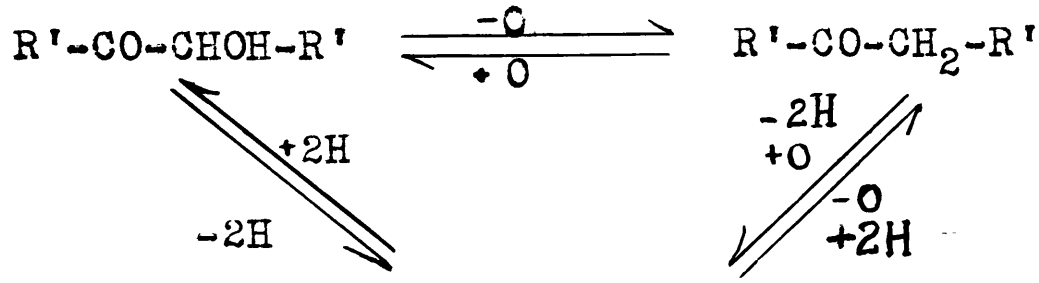
Furthermore, since it has been shown experimentally (70) that the veratryl derivative of (XIII) is converted into the ethyl ether of (XXVI) by ethanolic hydrogen chloride, the postulation of (XXIV) and (XXV) as intermediates would appear to be justified.

There is ample support in the literature for the postulated equilibrium (XXIV)$\rightleftharpoons$(XXVI). The simplest, and best known examples of such dismutation reactions, in the case of 1,2-hydroxy ketones and aldehydes, are to be found in the field of carbohydrate chemistry, as for example, the well-known Lobry de Bruyn equilibrium transformation of glucose $\rightleftharpoons$ mannose $\rightleftharpoons$ fructose, and of glyceric aldehyde $\rightleftharpoons$ dihydroxy-acetone, etc. (71). A detailed review of this type of dismutation transformation is given in part B of this introduction (page 39).

One of the most interesting properties of the α-hydroxy ketones (R'CO-CHOH-R", R' is phenyl or substituted phenyl; R" is either aromatic or aliphatic), considered in relationship to the above equilibrium (XIII)$\rightleftharpoons$(XXIV) is their behaviour toward alcoholic solutions of hydrogen chloride. Although the hydroxyl and carbonyl groups are attached to adjacent carbon atoms, the former possess many

of the properties of a carboxylic hydroxyl group. Thus E. Fischer (72) showed that benzoin may be etherified by the same process used for ordinary acid etherification, i.e., treatment with ethanol and hydrogen chloride.

The interrelationship of benzoins ((XXIV) and (XXVI)), desoxybenzoins (XXVII) and benzils (diketones) (X) has been well established. Numerous experimental confirmations of the following cycle of reactions are available:



R' - CO - CO - R'

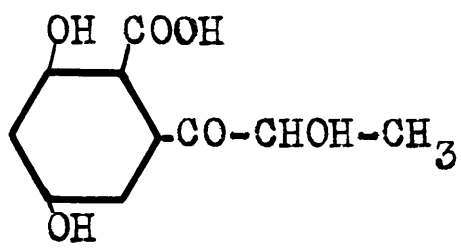
where R' is aromatic or aliphatic.

In addition to a marked susceptibility to oxidation, benzoins are characterized by their tendency to undergo intramolecular oxidation-reduction reactions as shown by Kohler (73). Thus in the presence of alkali, 1,3-diphenyl-2-hydroxypropanone-1, (XXIX), yields both a reduction product (XXX), and an oxidation product, (XXXI).

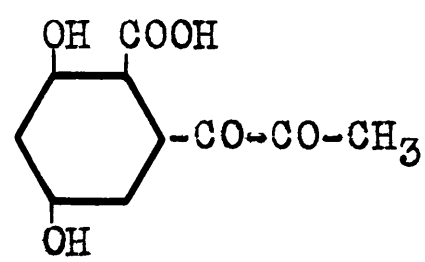
$$2\ \phi\text{-}CH_2\text{-}CHOH\text{-}CO\text{-}\phi \longrightarrow \phi\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}\phi + \phi\text{-}CH_2\text{-}CO\text{-}CO\text{-}\phi$$

XXIX. XXX. XXXI.

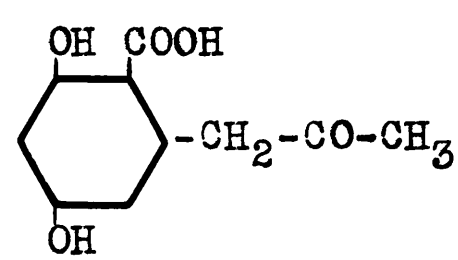
Experimental support for the view that the ethanolysis derivatives, obtained by Hibbert and co-workers (4),,.are true synthetic plant products is provided in the recent researches of Oxford and Raistrick (74) on the action of Penicillium brevi-compactum on glucose in acid medium (pH 4-5) whereby the derivatives (XXXII), (XXXIII) and (XXXIV), are formed.



XXXII.



XXXIII.



XXXIV.

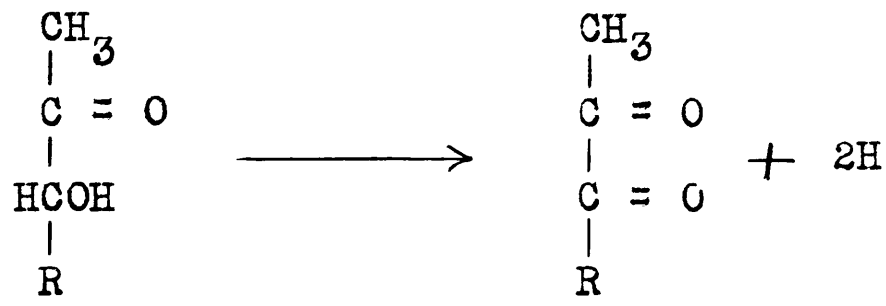
These products were not subjected to the action of chemical reagents and were isolated by simple evaporation, under reduced pressure, of their aqueous solutions.

The parallelism between these carboxylic acids and the products isolated by ethanolysis is remarkable. Moreover it seems probable that the acids were synthesized from phloroglucinol (1,3,5-trihydroxybenzene) by a process of plant synthesis similar to that outlined above for the formation of the corresponding guaiacyl derivatives from the keto form of 1,4-dihydroxy-3-methoxybenzene (XXIII).

The introduction of the carboxyl group (XXXII) (XXXIII) (XXXIV) is not remarkable in the light of the ease

with which carboxylation of phenols (resorcinol (75), phloroglucinol (76)) occurs on heating with aqueous bicarbonate at quite low temperatures (50-100°C.).

These investigators (74) also studied the order of production of the above mentioned C_6C_3 acids in a glucose-tartaric acid mixture. The hydroxy ketone (XXXII) was produced in increasing amounts until all of the glucose had been consumed; at this point the quantity of (XXXII) decreased to zero and the concentration of the diketone increased. Apparently after complete consumption of the glucose, the following reaction occurred and the mold was then able to obtain additional energy:



The desoxybenzoin (74) was never present in large amounts.

The significance of the above observation lies in the fact that the complete conversion of the α-hydroxy ketone to the diketone occurred after all of the glucose had been consumed. Prior to this time both compounds were present in approximately equal amounts suggesting that an equilibrium existed during the respiration stage. Cessation of respiration resulted in the accumulation of the diketone; thus indicating the system

$$R\text{-}CHOH\text{-}CO\text{-}CH_3 \underset{+2H}{\overset{-2H}{\rightleftharpoons}} R\text{-}CO\text{-}CO\text{-}CH_3$$

played a positive role in the respiration process. Although their results do not prove necessarily that C_6C_3 units can act as hydrogen transportation catalysts as proposed by Hibbert, it does show that this equilibrium may exist in plant systems.

6. Possible Significance of Lignin Progenitors in Plant Oxidase Systems[x]

Hibbert has pointed out (4) the striking similarity between the structure of the lignin ethanolysis units and the ene-diol plant oxidase systems of Szent-Györgyi (77). Thus α-hydroxypropiovanillone (isolated as the ethyl ether) is a benzoin, and should be capable of undergoing the ene-diol dismutation changes (page 18) shown by other similar benzoins (78). These ene-diols may function as reductants of ene-diol-1,2-diketone systems, the oxidants being the isolated ethanolysis products, vanilloyl and syringoyl methyl ketones, (X, XI). The similarity of such systems to those investigated by Szent-Györgyi (79, 80, 81), namely catechol (XXII), dioxymaleic acid (XXXV), and ascorbic acid (XXXVI) is apparent.

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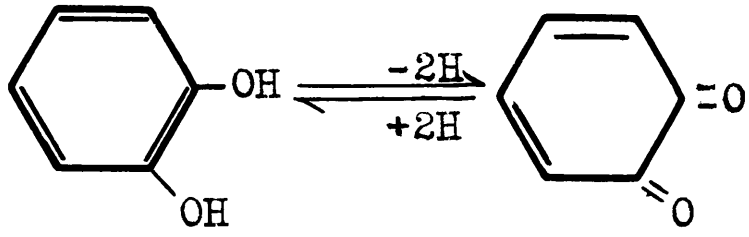
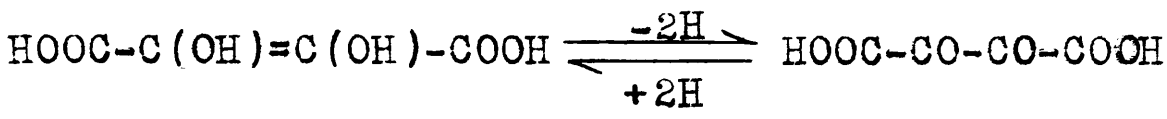
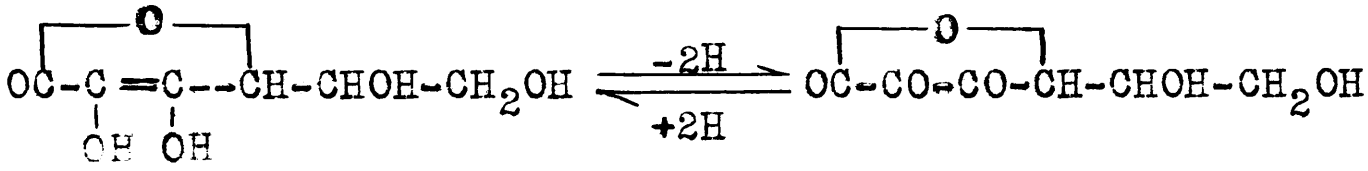
[x] For a recent comprehensive review on plant oxidase systems see Boswell and Whiting (86).



XXII.



XXXV.



XXXVI.

There would also seem to be a close relationship between the C_4 aliphatic dicarboxylic acid system of animal cell respiratory catalysts (77) and a possible aromatic C_6C_3 system related to lignin progenitors. In the latter system one carboxyl group is replaced by guaiacyl or syringyl, the other by the carbinol group.

Szent-Györgyi C_4 System (animal)	Hibbert C_6C_3 System (plant)
(R' = -COOH)	(R = guaiacyl or syringyl)
(A) $R'.CH_2.CO.R'$	(A') $R.CH_2.CO.CH_2OH$
$-2H \uparrow\downarrow +2H$	$-2H \uparrow\downarrow +2H$
(B) $R'.CH_2.CHOH.R'$	(B') $R.CH_2.CHOH.CH_2OH$
$\downarrow -H_2O$	$\downarrow -H_2O$
(C) $R'.CH{=}CH.R'$	(C') $R.CH{=}CH.CH_2OH$
$-2H \uparrow\downarrow +2H$	$-2H \uparrow\downarrow +2H$
(D) $R'.CH_2{-}CH_2.R'$	(D') $R.CH_2.CH_2.CH_2OH$

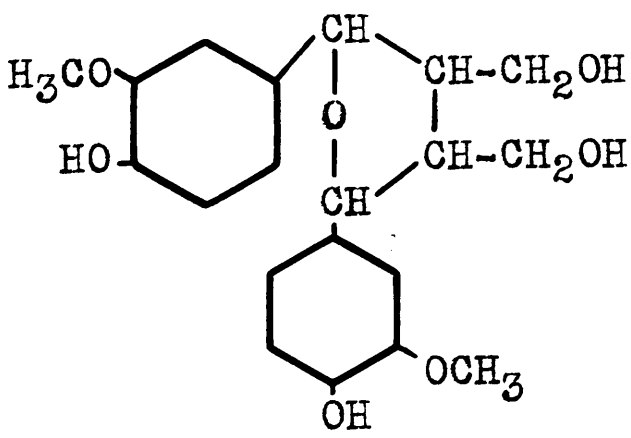
The first member (A') of the plant system, corresponding to oxalacetic acid (A), is the keto alcohol presumably obtained as a primary condensation product from three moles of methyl glyoxal (page 18). Coniferyl alcohol, C', would be the analog of fumaric acid, C. The passage from this system to the ene-diol-1,2-diketone system can take place by an allylic rearrangement of the oxyconiferyl or oxysyringyl alcohol isomer: (A') $R.CH_2.CO.CH_2OH \rightleftharpoons R.CH{=}C(OH).CH_2OH \rightleftharpoons R.CHOH.C(OH){=}CH_2 \rightleftharpoons R.CHOH.COCH_3$ (page 18). The isomeric form of A', $R.COCH_2.CH_2OH$, may possibly function similarly to A' in the suggested C_6C_3 system, while the interconvertible reduction products from these ((B'') $R.CHOH.CH_2.CH_2OH$ and (B') $R.CH_2.CHOH.CH_2OH$) would provide analogs of citric and isocitric acids which are components of the Krebs animal cell oxidation system (82).

Experimental support for the assumption that a primary hydroxyl group is present in lignin progenitors is to be found in the experiments on hydrogenation of wood showing the presence in protolignin of large amounts of primary carbinol ($-CH_2OH$) or of methylene ether ($-CH_2.O.CH_2-$) linkages.

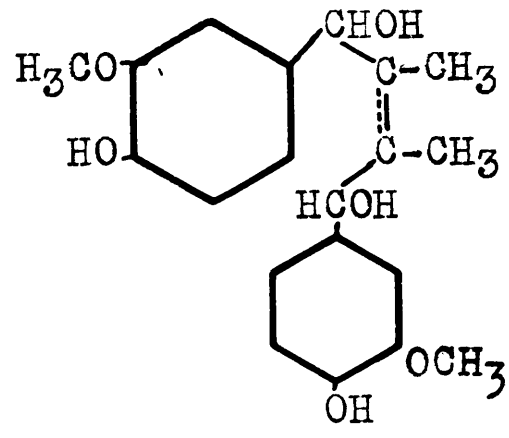
7. Formation of Protolignin from Propylphenol Units

Freudenberg's earlier speculations (2) regarding the polymerization mechanism (page 2) for spruce lignin building

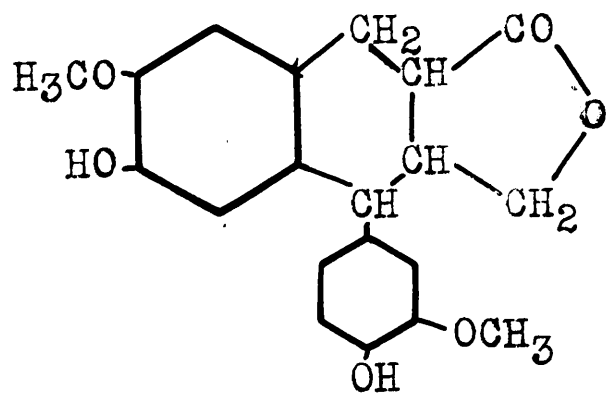
units have recently aroused greater interest in view of (i) Erdtman's interesting researches in the field of plant resins; (ii) results of lignin and wood hydrogenation at high pressures; and (iii) isolation of $C_6.C_1$, $C_6.C_2$ and, especially, $C_6.C_3$ units in increased yields (4). In the absence of such experimental results Freudenberg's speculations hitherto have lacked real significance. Erdtman, in his recent review (3), points out that the structure of a wide variety of plant resins (olivil (XXXVII), laricіresinol (XXXVIII), conidendrin (XXXIX), and others) conforms to a general dimer type, the monomer being a propylphenol derivative closely related to coniferyl alcohol and the dimer formation apparently always involving the β-carbon atom.



Olivil
(XXXVII).



Laricіresinol
(XXXVIII).



Conidendrin
(XXXIX).

Erdtman has stressed repeatedly (3) the analogy between isoeugenol and coniferyl alcohol, and the probable existence of a close relationship between lignin and dehydrodiisoeugenol (III) (page 4). Haworth (83) however, believes the absence of free phenolic groups suggests an important difference in the mechanism of the hypothetical polymerizations of propylphenol units to plant resins and to lignin.

8. Possible Relationships of Ethanolysis Products to Proto-lignin

(a) Structure of Lignin Progenitors

Since the ethanolysis products (α-hydroxypropiovanillone and α-hydroxypropiosyringone (as their ethyl ethers) (XXVI), vanilloyl- and syringoylmethyl ketones (X)) may only represent stabilized end products originating from dimeric types similar to dehydrodiisoeugenol, Erdtman concludes that these monomers are not necessarily the true lignin building units. That such may well be the case has been recognized by Hibbert, and, accordingly, investigations concerning the synthesis and properties of isomeric forms of the diketones and hydroxyketones are in progress.

A comparison of the side chains (enolic forms of certain propylphenol derivatives (XXVI), (XXVII), and (XIII) now known to be directly related to the lignin complex, with

the side chains of isoeugenol (XL) and coniferyl alcohol (XLI) shows a close relationship; R.C(OH)=C(OH).CH_3 (XXV); R.CH=C(OH).CH_3 (XXVII); R.CH=C(OH).CH_2OH (XIII); R'.CH=CH.CH_3 (XL); R.CH=CH.CH_2OH (XLI) (R' = guaiacyl).

The universal occurrence of coniferyl alcohol (XLI) in the early period of plant growth, and its later absence, may point to its conversion into the oxyconiferyl type (XIII) during the postmortal stage.

The question arises as to which of these units ((XXVI) (XIII),(XLI)) represent the primary form or forms from which lignin is derived. The 1,2-diketones (X) apparently do not exist as such in the wood; while oxyconiferyl alcohol (XIII), in view of its extraordinary reactivity and the indicated presence of terminal -CH_2OH groups in protolignin (page 7) is probably present along with its isomeric forms, the guaiacyl and syringyl ene-diol systems (XXIV), (XXV), (XXVI) (page 18)

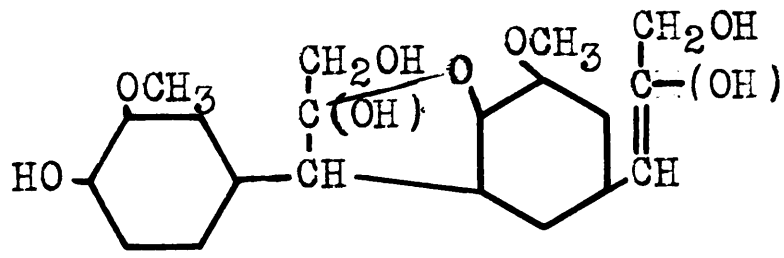
At the moment a rational view of lignin structure would seem to indicate that protolignin is present in the plant in large measure as a series of polymers of the dehydro-diisoeugenol type (III), derived, for example, from monomeric oxyconiferyl alcohol (although oxyconiferyl alcohol was presumably first isolated from spruce by Klason (84) it was characterized merely by empirical analysis). During, or prior to, extraction by ethanolysis these highly reactive products

probably undergo partial transformation to the stabilized ethanolysis units.

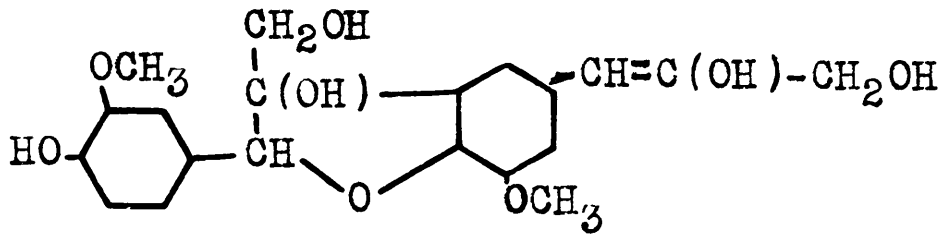
(b) Nature of Polymer Formation

The tendency for the lignin progenitors (the assumed hydrogen transportation respiratory catalysts) to undergo polymerization is apparently due to (i) the presence of a phenolic hydroxyl group in the para position with respect to a three-carbon side chain; (ii) the presence, in the three-carbon side chain, of a propenyl group conjugated with an aromatic ring; (iii) the pronounced reactivity of the hydrogen atom in the phenol group and of that attached to the nuclear carbon atom in the position ortho to the phenol hydroxyl group; (iv) the reactivity of the terminal carbinol grouping; (v) the tendency of the side chain to undergo an intramolecular rearrangement; and (vi) the labile character of the methylene group in 1-guaiacyl-3-hydroxypropanone-2 (the keto form of oxyconiferyl alcohol) situated, as it is, between a phenyl and a carbonyl group.

Application of the principle of dehydrodiisoeugenol polymerization (3) to oxyconiferyl alcohol (XIII) would yield a dimer (XLII) or (XLIII).

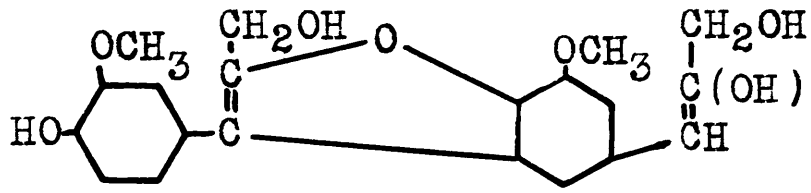


XLII.

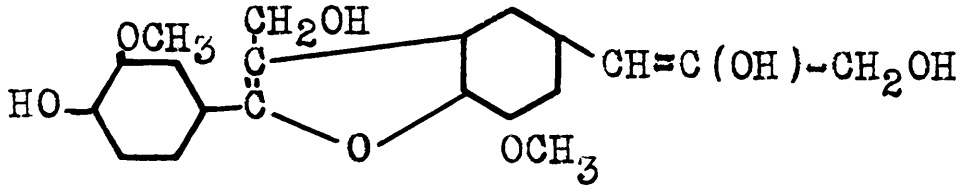


XLIII.

which could then react further to give a trimer, tetramer, etc. Through loss of water, benzofuran polymers (XLIV) and (XLV)

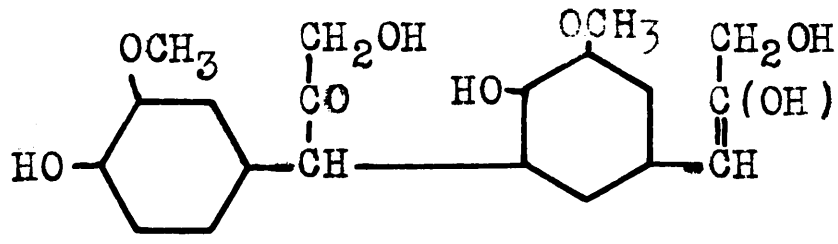


XLIV.

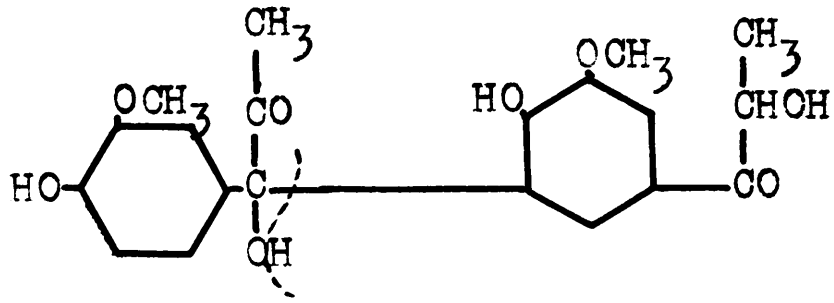


XLV.

could be formed, whereas ring opening of (XLII) could give (XLVI) from which (XLVII) could be obtained by a double allyl shift. The latter could split, as indicated (dotted line), to give one mole of the diketone (X) and the ketoalcohol (XXVI)

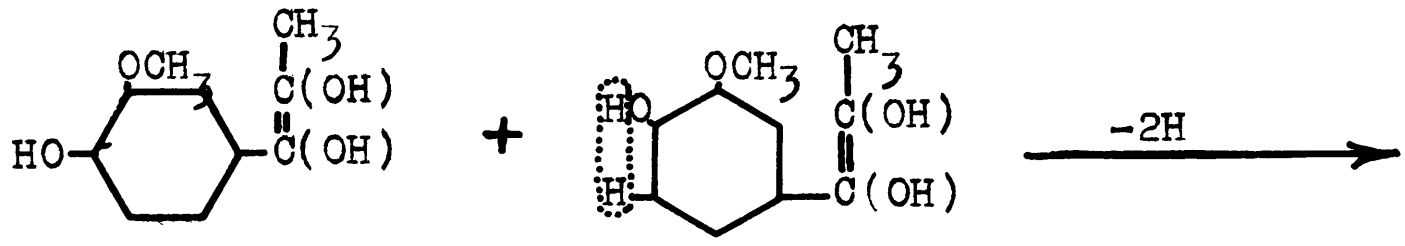


XLVI.

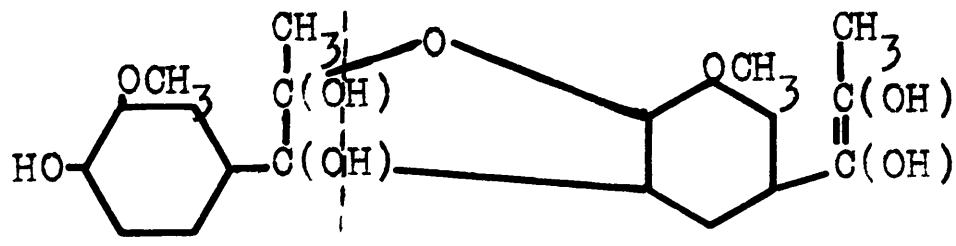


XLVII

Similarly, two moles of α-hydroxypropiovanillone (XXVI) (enol form) upon enzymatic oxidation could yield a dimer (XLVIII) which could also split to yield (XXVI) and (X).



XXVI (two moles)

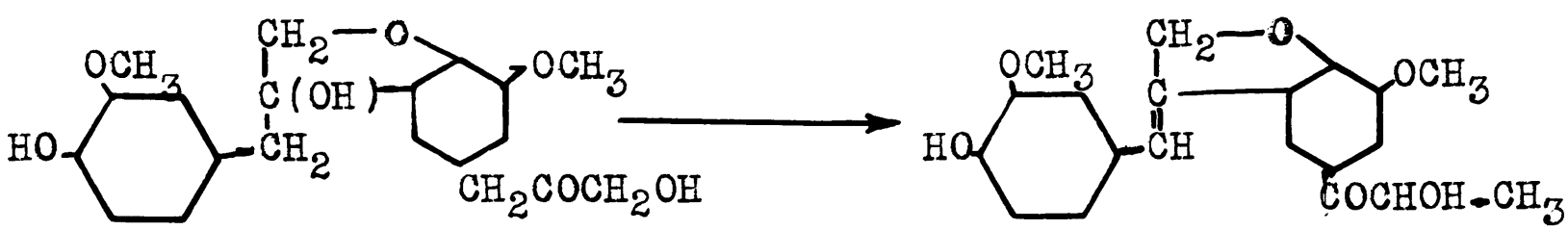


XLVIII

Such fission reactions would only be possible with the "reversible type polymer" in contradistinction to the benzofuran "irreversible type".

It is not justifiable to assume that the dehydrodiisoeugenol type of lignin polymer is the only one capable of providing a satisfactory explanation of the known experimental facts. For example, a polymer (XLIX) derived from two moles

of (XIII) would presumably undergo preferential dehydration to give (L) rather than a benzofuran derivative.



XLIX. L.

This system ((XLIX) and (L)) would account for such well-known properties of spruce lignin as (i) absence of phenolic hydroxyl groups; (ii) presence of tertiary, secondary and primary hydroxyl groups; (iii) formation of labile and stable sulfonic acids; (iv) formation of vanillin on oxidation, and (v) presence of terminal methyl groups, but it would not explain the formation of the 1,2-diketones.

It is apparent that the syringyl analogs, due to the blocking of the two positions ortho to the phenol group could not function in this manner except as end groupings.

Inasmuch as coniferyl, oxyconiferyl, syringyl and oxysyringyl alcohols may be regarded as substituted cinnamyl alcohols and in view of the ease with which cinnamyl derivatives, in presence of dilute acids, not only undergo the allyl shift but also form dicinnamyl ethers (85) in high yield, it is possible that the syringyl units may exist as

ethers in the woody tissue, thus accounting for their much readier extraction by ethanolysis and other methods.

Finally, the ene-diol forms of the propylphenol units under discussion (page 28) may be regarded as derivatives of styrene, and therefore possibly capable of undergoing a typical linear styrene-type of polymerization. Other types of condensation polymers such as those involving condensation reactions between ketone and end methyl or active methylene groups appear less probable. The solution of this problem must evidently await much further experimentation.

In any event the type of lignin polymerization in the case of gymnosperms appears to be much more complex than in the case of angiosperms, the reversible type being present in the latter to a much greater extent (4). Recent work has shown that both the ether-soluble and -insoluble maple ethanol lignins undergo degradation (depolymerization) on further treatment with ethanol-hydrochloric acid to give the 1,2-diketone (X) and the keto alcohol monomers (XXVI) a result in harmony with the above theoretical speculations.

It seems probable that in the case of both the lower and higher forms of plant life monomolecular 1,4-propylphenols are synthesized in order that they may function as hydrogen transportation respiratory catalysts. With the lower forms these, or their more stable end products, or both, are

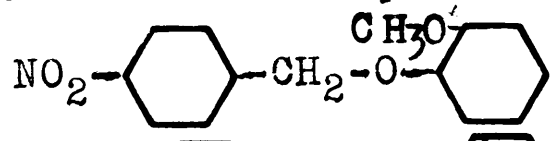
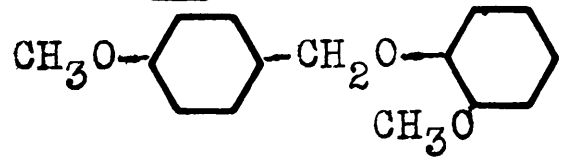
isolable, as such, from the slightly acid medium; with the higher forms the catalysts presumably function in a similar manner but due to the strongly oxidizing, postmortal environment readily undergo dehydrogenation-condensation-polymerization reactions to yield protolignin.

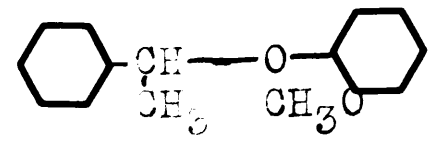
The reactions of lignin with mercaptans, particularly with thioglycolic acid, have been investigated over a period of years by Holmberg (87) and are of particular importance in any appraisal of the various suggested polymerization mechanisms. The mercaptans, R-SH, are thio-substituted derivatives of alcohols, and, in the presence of acids, react in the same manner (namely through the (SH) group) with the lignin in the wood. This is emphasized by the fact that treatment of ethanol lignin with thioglycolic acid results in the replacement of the ethoxyl groups by the $-S-CH_2-COOH$ radicals (88).

Holmberg's experiments dealing with the reactions of model substances (presumably related to lignin) with thioglycolic acid (87), as well as the related experiments carried out by Freudenberg (89), by Hägglund (90) and by Richtzenhain (91) were all designed to throw light upon the question of the actual groupings present in proto- and isolated lignins.

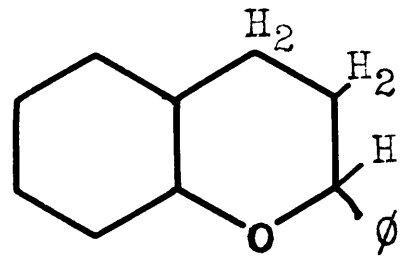
Hellström and Lauritzson found (92) that, while tertiary butyl alcohol reacts with thioglycolic acid, the

secondary and normal butyl and propyl alcohols do not (92). The structures typified in phenyl substituted alcohols and their ethers are more closely related to those suggested for lignin polymers and these were found to react with thioglycolic acid in varying manner. Thus, while addition of thioglycolic acid, through the medium of the hydroxyl group, takes place with or without cleavage, with benzyl alcohol $C_6H_5CH_2OH$ (LI) (93); phenyl dimethyl carbinol, $C_6H_5C(CH_3)_2OH$ (LII) (93); benzyhydrol $(C_6H_5)_2CHOH$ (LIII) (93); cinnamyl alcohol $C_6H_5CH = CHCH_2OH$ (93); diphenylglycolic acid $(C_6H_5)_2C(OH)CO_2H$ (LIV) (93); styrene $C_6H_5CH = CH_2$ (93); benzyl ethyl ether $C_6H_5CH_2OC_2H_5$ (LV) (88); α-phenyl diethyl ether $C_6H_5CH(CH_3)\text{-}OC_2H_5$ (LVI) (88); triphenyl methyl ethyl ether $(C_6H_5)_3COC_2H_5$ (LVII) (88) diphenyl methyl ethyl ether $(C_6H_5)_2CHOC_2H_5$ (LVIII) (88); it does not take place with 3-phenylpropanol-1 $C_6H_5\text{-}CH_2\text{-}CH_2\text{-}CH_2OH$ (93), phenyl glycolic acid $C_6H_5\text{-}CH(OH)COOH$ (93) and β-phenylethyl alcohol $C_6H_5\text{-}CH_2\text{-}CH_2OH$ (88).

Richtzenhain (91) investigated the behaviour of a series of guaiacyl ethers with bisulfites, aqueous sulfur dioxide and thioglycolic acid. He found that with the last-named, a reaction did not take place with either p-nitrobenzyl guaiacyl ether  or p-methoxybenzyl guaiacyl ether  when heated on the

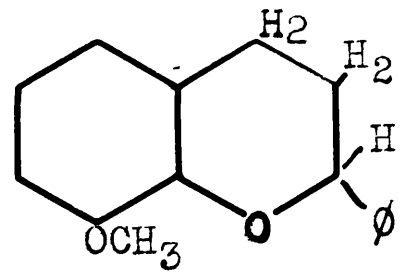
water-bath for several hours in the presence of 2N hydrogen chloride. On the other hand cleavage to the extent of 22% occurred with α-methylbenzyl guaiacyl ether  under the same conditions.

His most significant experiments (91) from the point of view of relationship to lignin structure were those dealing with the behaviour of heterocyclic compounds having structures similar to those proposed for lignin polymers. He found that while flavan,

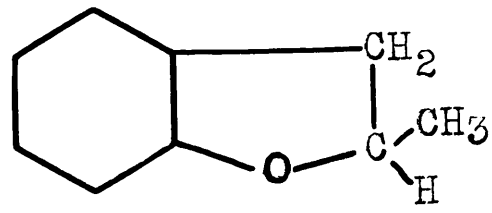
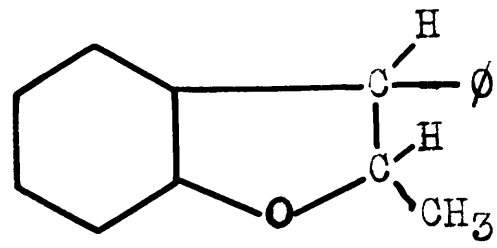
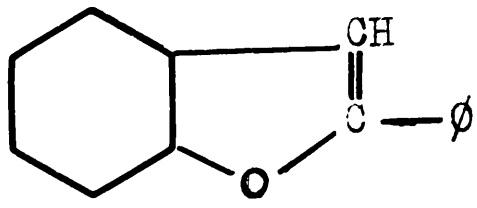


LIX. ;

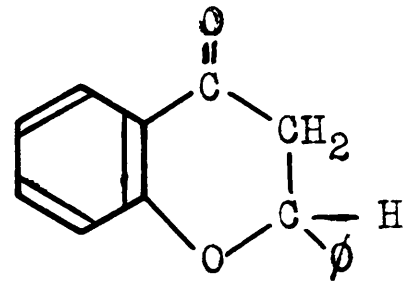
9-methoxyflavan,



LX. ;

2-methylcoumarane,  (LXI); 2-methyl-3-phenylcoumarane,  (LXII); and 2-phenyl-coumarone  (LXIII), did not react with

thioglycolic acid, the introduction of a carbonyl group, as typified in flavanone



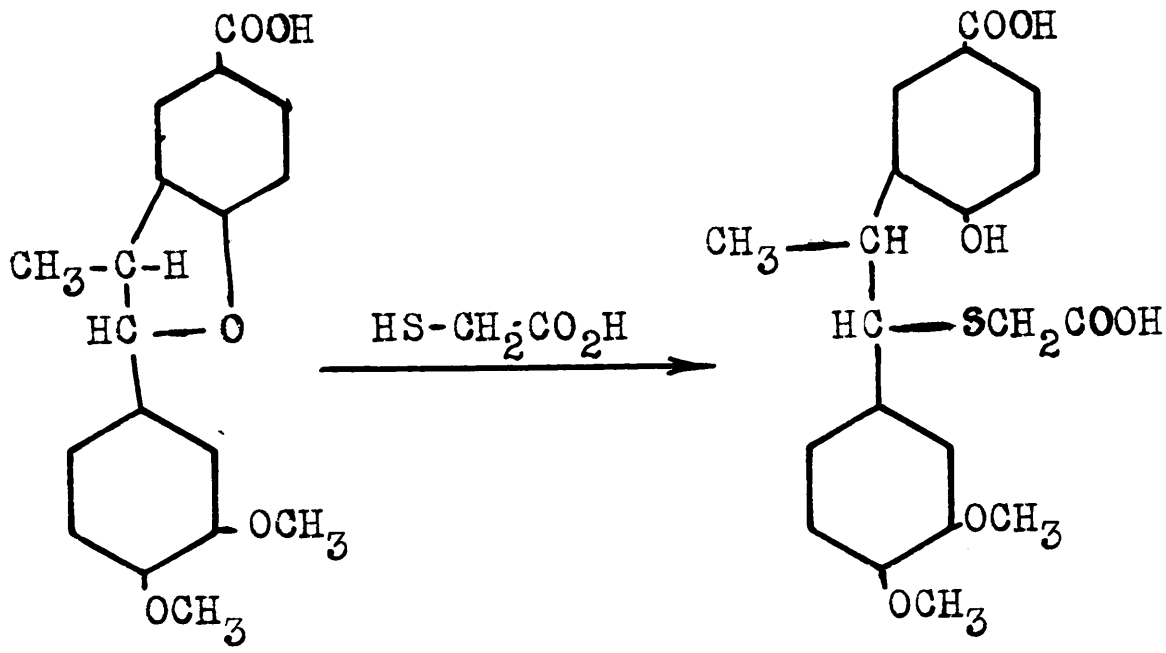
LXIV

sufficed to bring about a reaction to the extent of 38% (91).

In view of the foregoing, it is possible to draw a few general conclusions regarding the acceptability of the various structures proposed for lignin polymers. It would seem that reactivity towards thioglycolic acid is a property common to both benzyl and substituted benzyl alcohols (LI to LVIII). Examination of the various proposed lignin formulae II, XLVIII, and XLIX shows the presence in each of a substituted benzyl alcohol, thus implying possible reactability towards thioglycolic acid.

On the other hand, since heterocyclic ethers, typified by flavans (LIXandLX), and coumaranes (LXI, LXII, LXIII), do not undergo cleavage with thioglycolic acid, the reactivity shown by lignin polymers would indicate the necessity for postulating the presence of a carbonyl group in any lignin structure assumed to contain an ether of this type. It is evident that this is not the case with the proposed structures (XLII, XLIII, XLIV, XLV, XLVIII, XLIX, L). Freudenberg (89) claims to have proven that the acid (LXV)

undergoes ring fission, even in the absence of a carbonyl group under the influence of thioglycolic acid, as shown:



LXV. LXVI.

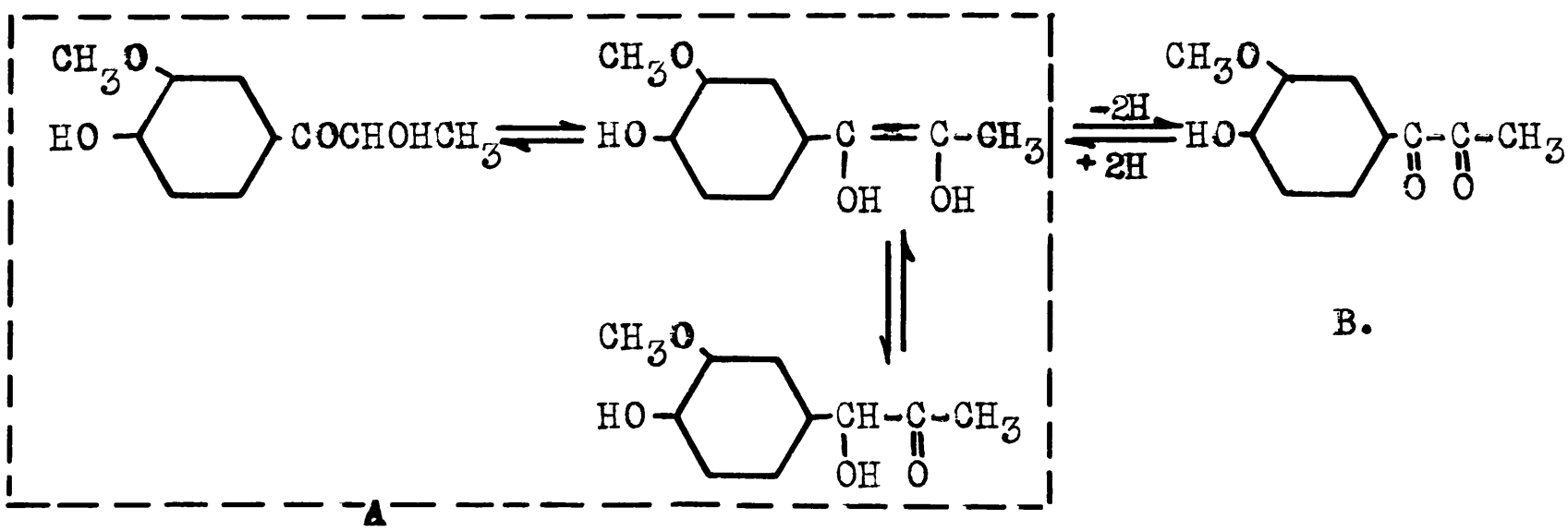
However due to the uncertainty connected with the structure of both the acid (LXV) and its degradation product (89, 91) (LXVI), little value can at present be attached to conclusions drawn from this work.

Before definite structural conclusions can be drawn from the behaviour of lignin polymers toward thioglycolic acid a much wider variety of model compounds of known structure will have to be studied.

PART B

DISMUTATION TRANSFORMATIONS OF HYDROXY KETONES AND RELATED COMPOUNDS

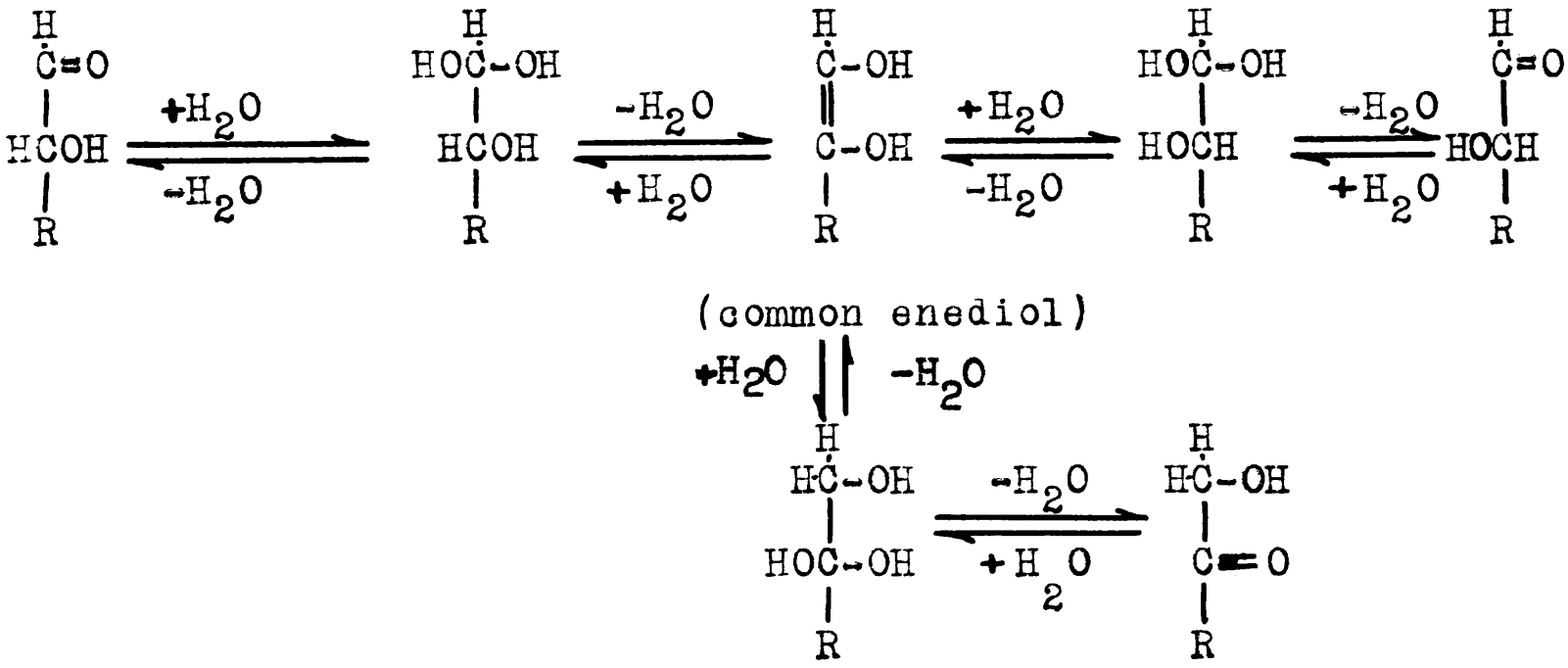
In Part A (pp. 27-29) the evidence for the possibility of lignin building units of the types (a) $RCOCHOHCH_3$; (b) $RCHOHCOCH_3$; (c) $RCOCH_2CH_2OH$; (d) RCH_2COCH_2OH; and (e) $RCOCOCH_3$ has been discussed. One of the most important properties of these types of compounds, especially in view of the recent theories of Hibbert (4) on the mechanism of lignin formation, is their marked tendency to undergo intramolecular dismutation transformations, such as typified below.



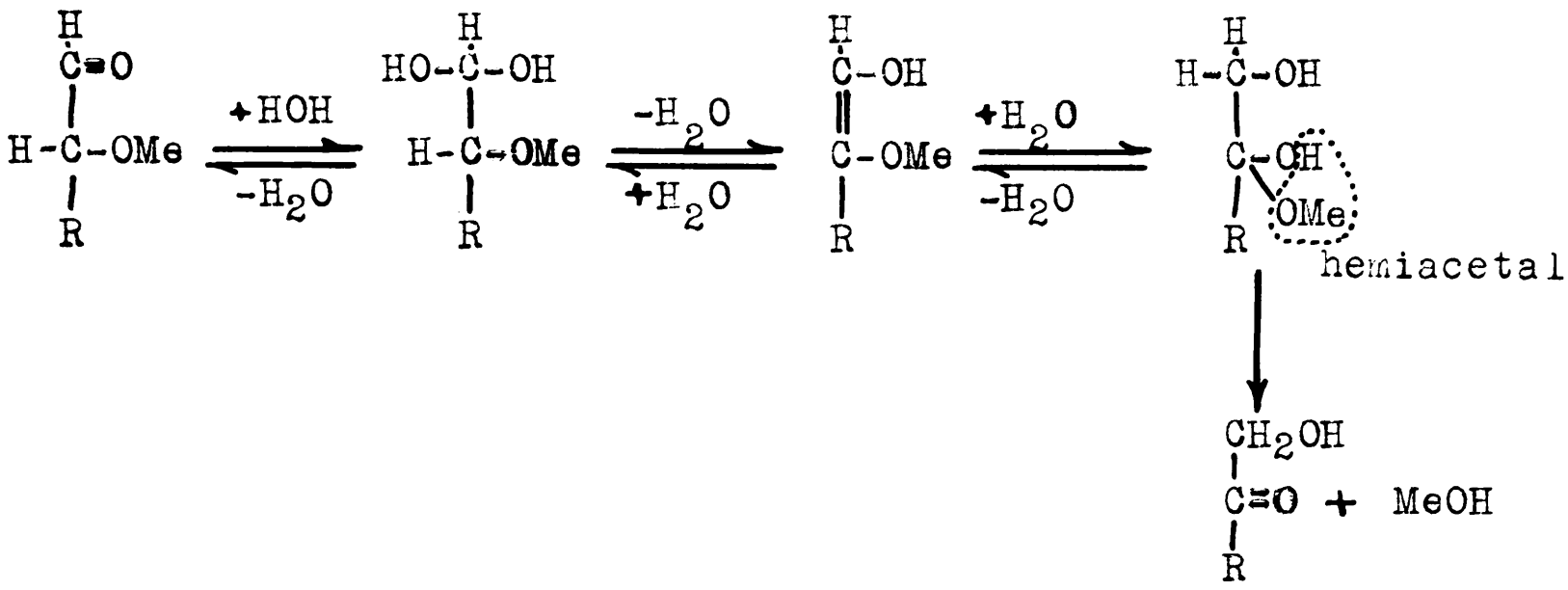
It can be seen that two different types are involved in such cycles; (I) the dismutation system **A** and (2) the oxidation-reduction system **A**-B.

With respect to (A) perhaps the best examples of such intramolecular dismutation rearrangements are those known to occur in the field of carbohydrate chemistry. The well known

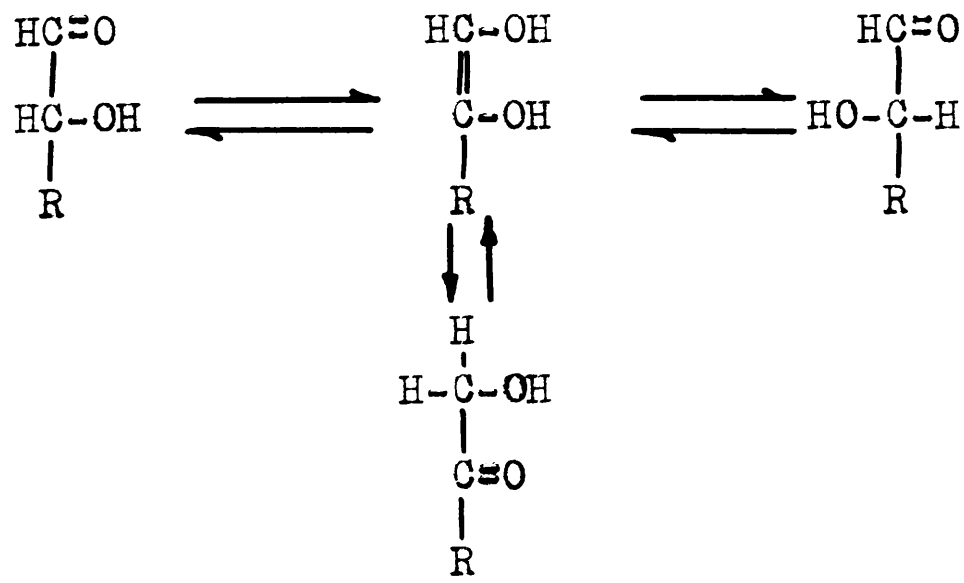
Lobry de Bruyn transformations, already mentioned, embracing the equilibrium system glucose, mannose and fructose (94) and that of glyceric aldehyde and dihydroxy acetone (96, 97, 95), both occurring in weakly alkaline solution, are only two of a very large number of similar examples. Nef (98) explained this phenomenon on the basis of selective hydration and dehydration of the sugars involved and postulated a common enediol intermediate:



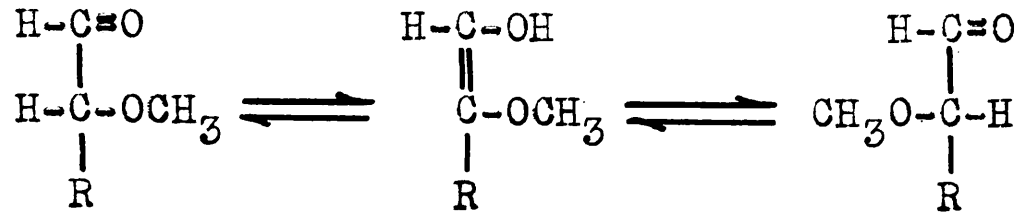
Lewis and co-workers (99), however, showed that such a mechanism was not tenable - at least in the case of the methylated sugars. Thus, for example, on the basis of Nef's hypothesis, tetramethyl glucose should be converted by alkali not only into tetramethylmannose but also into methylated fructose by the loss of methanol from the intermediate hemiacetal.



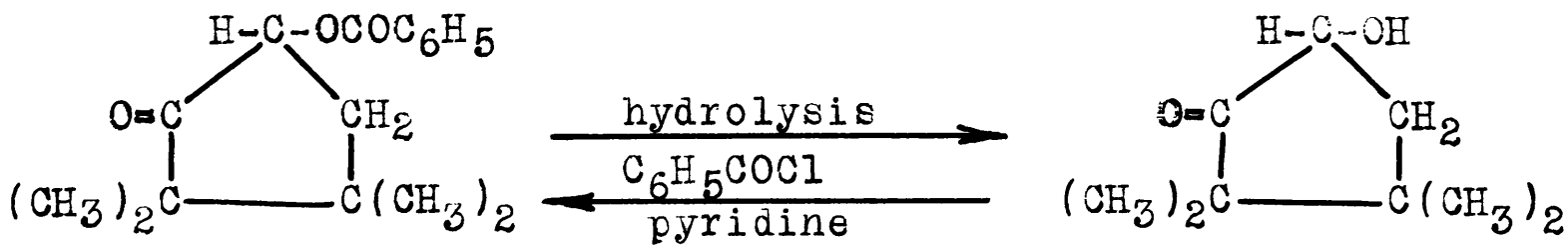
Wolfram and Lewis (99(b)) showed, however, that no tetra methyl fructose was formed by the action of dilute alkali on tetramethyl glucose. To explain this result, as well as those obtained from alkaline oxidation studies of methylated sugars, Gustus and Lewis (99(a)) postulated a simple keto-enol shift to the intermediate enediol. Thus in the case of the unsubstituted sugars the labile hydrogen could migrate in the following manner:



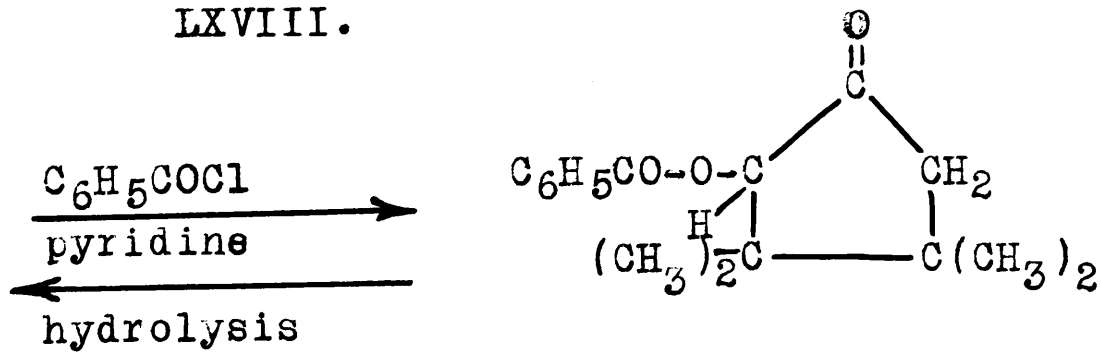
whereas in the case of the methylated sugars, the methyl group of the methoxyl presumably could not shift in this way and the changes would be limited to the following:



Such dismutations are also encountered with many other types of compounds as observed, for example, by Shoppee (100) in the case of highly substituted cyclic hydroxy ketones. Thus 2,2, 3,3-tetra methyl- 5-hydroxy cyclopentanone (LXVII) on treatment with benzoyl chloride and pyridine, gave two distinct benzoyl derivatives (LXVIII) and LXIX), each possessing different physical properties. However, on hydrolysis both benzoates yielded the same original starting material.



LXVIII. LXVII.



LXIX.

Favorskii(101) working with a series of 1,2 aliphatic hydroxy ketones found that intramolecular rearrangements of the hydroxyl and carbonyl groups took place very readily with formation of the products shown below:

$CH_3-CH_2-CHOH-CO-CH_2-CH_2-CH_3 \longrightarrow CH_3-CH_2CO-CHOH-CH_2-CH_2-CH_3$

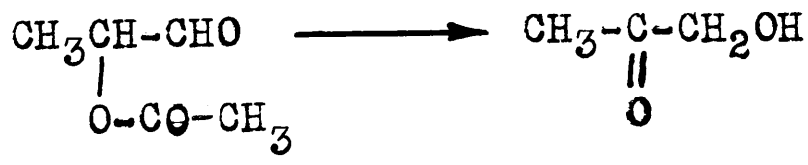
$CH_3-CHOH-CO-CH_2-CH_3 \longrightarrow CH_3-CO-CHOH-CH_2-CH_3$

$CH_3-CHOH-CO-C(CH_3)_3 \longrightarrow CH_3-CO-CHOH-C(CH_3)_3$

These rearrangements occurred on heating an alcoholic solution of the keto alcohol with a few drops of concentrated sulfuric acid in a sealed tube at 120-130°.

Favorskii concluded from these studies that the carbonyl group has a tendency to shift towards the end of the chain, forming, wherever possible, an acetyl linkage.

This tendency to form an acetyl grouping is shown also by other substances. Thus acid hydrolysis of lactic aldehyde acetate (LXX) at 100° gives acetol (LXXI) and not the corresponding aldehyde (102)



LXX. LXXI.

Similarly, attempts to prepare mandelic aldehyde (LXXII) by hydrolysis of either the acetate (102) or the acetal (103) yielded invariably the isomeric benzoyl carbinol (LXXIII). Evans (103) has summarized the behaviour of these aldehydes as follows:

(a) Lactic aldehyde and mandelic aldehyde in the presence of water, at 100°, rearrange to acetol and benzoyl carbinol, respectively;

(b) Lactic aldehyde does not undergo this rearrangement at ordinary temperature;

(c) Mandelic aldehyde, the aromatic analogue of lactic aldehyde, not only undergoes this rearrangement to benzoyl carbinol at ordinary temperature in the presence of water and dilute sulfuric acid, but this transformation also takes place at 0°;

(d) Mandelic aldehyde undergoes rearrangement to benzoyl carbinol not only in the presence of water and of dilute ethyl alcohol at ordinary temperature and at 0° but also with the water vapour of the atmosphere at room temperature.

$C_6H_5CHOHCHO$ $C_6H_5COCH_2OH$

LXXII. LXXIII.

Similarly, when benzyl glycolic aldehyde (LXXIV) is heated to 130-135° in a sealed tube for six to seven hours

with a 14% ethanolic sulfuric acid solution, a mixture of phenyl acetyl carbinol (LXXV(a)) and a diketone are obtained (69).

$$C_6H_5CH_2CHOHCHO \xrightarrow[H_2SO_4]{EtOH} C_6H_5CHOHCOCH_3 + C_6H_5COCOCH_3$$

LXXIV. LXXV(a).

Of especial interest in the field of lignin chemistry is the marked ease of rearrangement of compounds of the type $C_6H_5COCHOHR$ where R may be either aliphatic or aromatic. The nature of the group R as well as that of the substituents in the benzene ring have a marked influence on the tendency towards intramolecular dismutation changes. While a thorough study of the effect of these substituent groups has not been made as yet, sufficient work has been done to indicate a few basic principles, and these are of considerable importance in view of the close relationship of some of the postulated lignin units, e.g. α-hydroxypropiovanillone.

Thus Henze (104) effected the isomerization of benzoyl acetonyl carbinol (LXXVI) into its dismutation isomer mandelyl acetone (LXXVII) by treatment with a cold alcoholic solution of sodium ethoxide.

$$C_6H_5COCHOHCH_2COCH_3 \xrightarrow[Alc.]{NaOEt} C_6H_5CHOHCOCH_2COCH_3$$

LXXVI. LXXVII.

Considerable work has been done on rearrangements of the two isomeric ketols, phenyl acetyl carbinol (LXXV(a)) and benzoyl methyl carbinol (LXXV(b))

$C_6H_5CHOHCOCH_3$ $C_6H_5COCHOHCH_3$

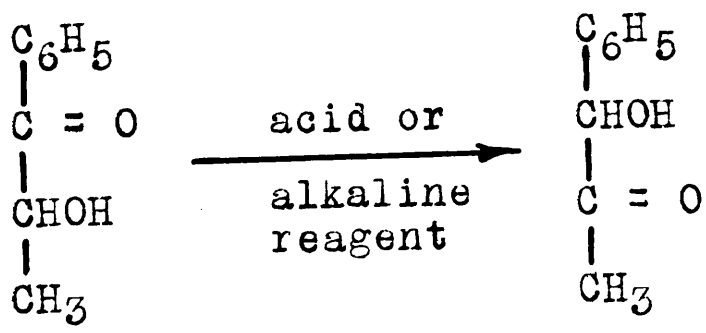
LXXV(a). LXXV(b).

Favorskii (105) predicted that the isomer which contained the acetyl grouping (LXXV(a)) would be the stable form. He (101) confirmed this view experimentally by heating an alcoholic solution of (LXXV(b)) with a few drops of concentrated sulfuric acid in a sealed tube at 120-130° whereby the isomer (LXXV(a)) was obtained. This isomerization has since been confirmed by Temnikova and co-workers (106, 107) and by v.Auwers and co-workers (108, 109) under a variety of conditions discussed below.

Temnikova and Favorskii (106) showed that each of the ketols (LXXV(a)) and (LXXV(b)) was stable in the absence of catalysts (acids, bases, yeast), but that on treatment with semicarbazide, phenyl isocyanate, the Grignard reagent and benzoyl chloride they behaved as tautomeric mixtures. v.Auwers and co-workers found that the conversion of methyl benzoyl carbinol into phenyl acetyl carbinol could be effected either by refluxing with aqueous barium carbonate for 20 hours (108), by the action of dilute sodium ethoxide at 0° for 24 hours

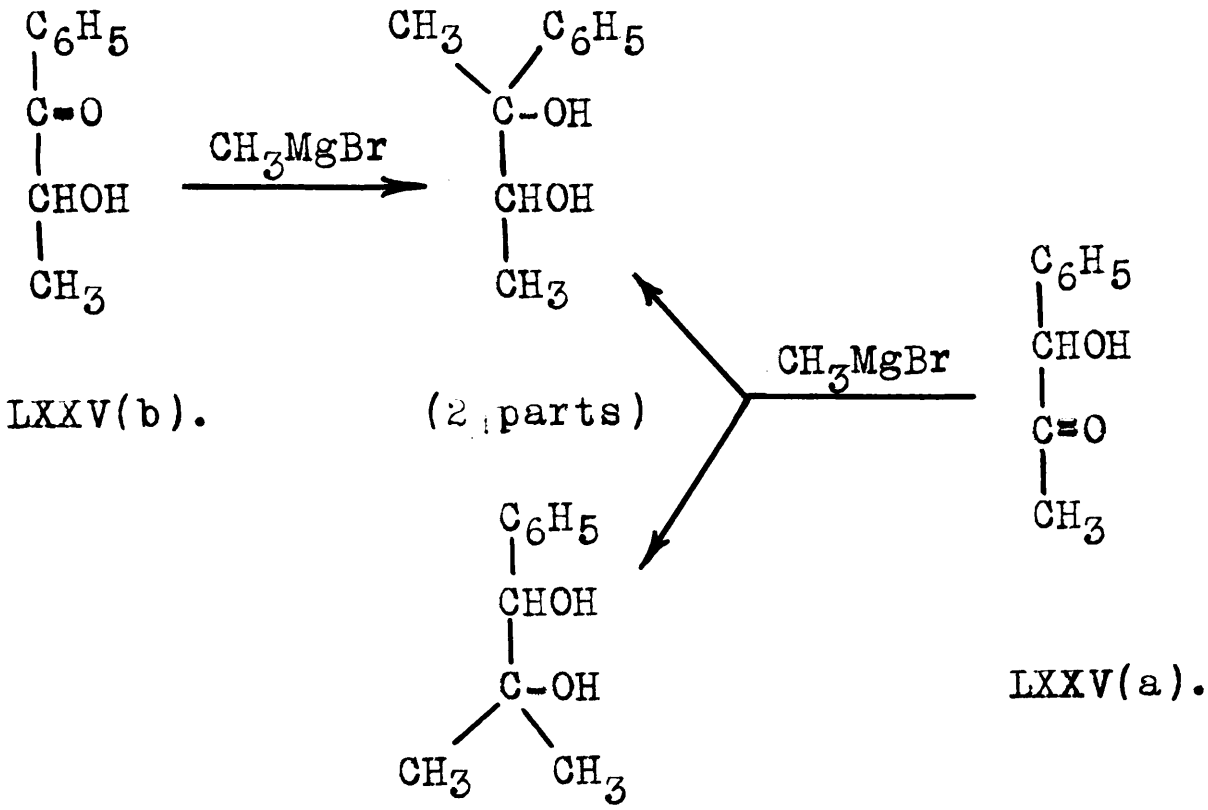
(108) or by heating with 2% methanolic hydrogen chloride (109). Unfortunately many of the early workers prepared their ketols by the action of barium carbonate on the bromo derivative, so that the assumed homogeneous starting material was, in reality a mixture of isomers. For this reason, much of the early work is both controversial and unreliable. For example, v. Auwers and Jordan (110) had found much earlier (1924) that the product resulting from the action of aqueous barium carbonate on α-acetoxypropiophenone ($C_6H_5COCH(OCOCH_3)CH_3$) and regarded by them as a pure material (LXXV(b)) was unchanged on warming with dilute alkali or acid. However, in the light of more recent work, it is apparent that their starting material was in reality an equilibrium mixture of (LXXV(a)) and (LXXV(b)). Temnikova (107) reinvestigated the problem of the inter-relationship existing between these two ketols (LXXV(a) - (b)), with special attention to (a) the preparation of a <u>pure</u> ketol, (b) the conditions for mutual interconversion of the ketols, and (c) the dismutation changes occurring during the preparation of their derivatives. These transformations were summarized by her as follows:

(a)



LXXV(b). LXXV(a).

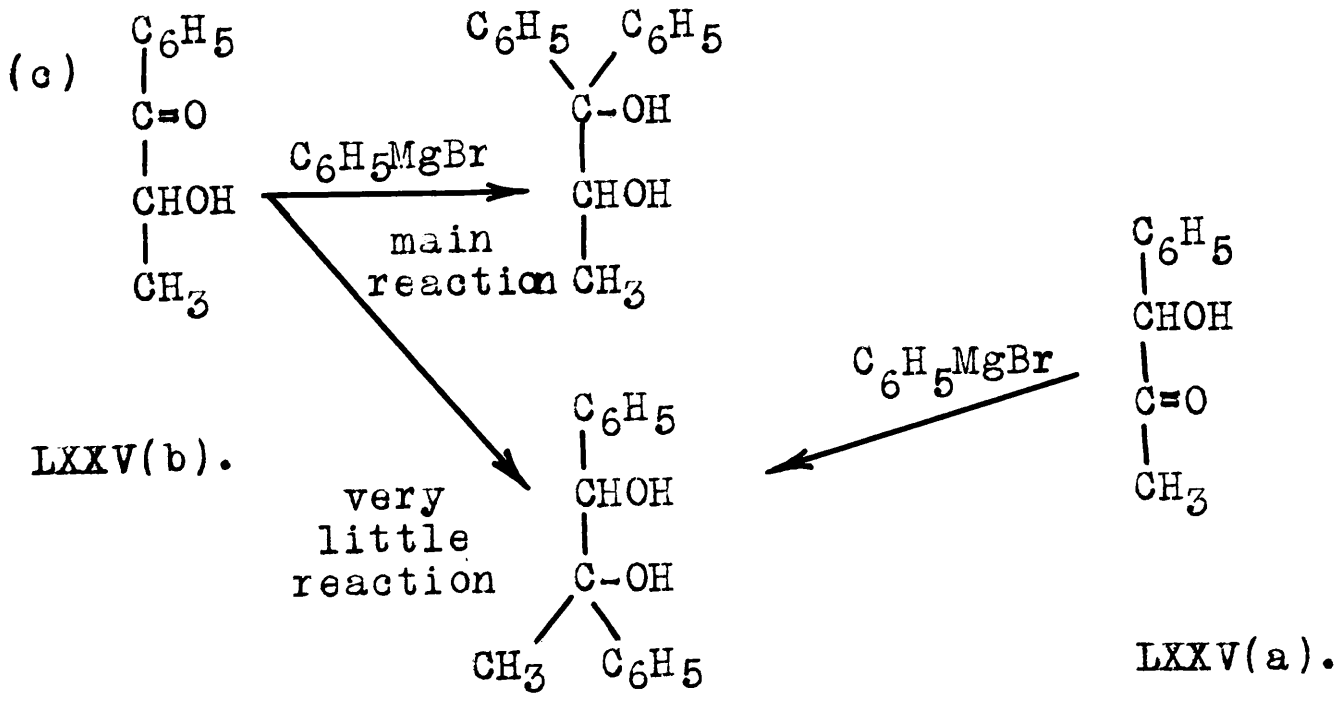
(b)



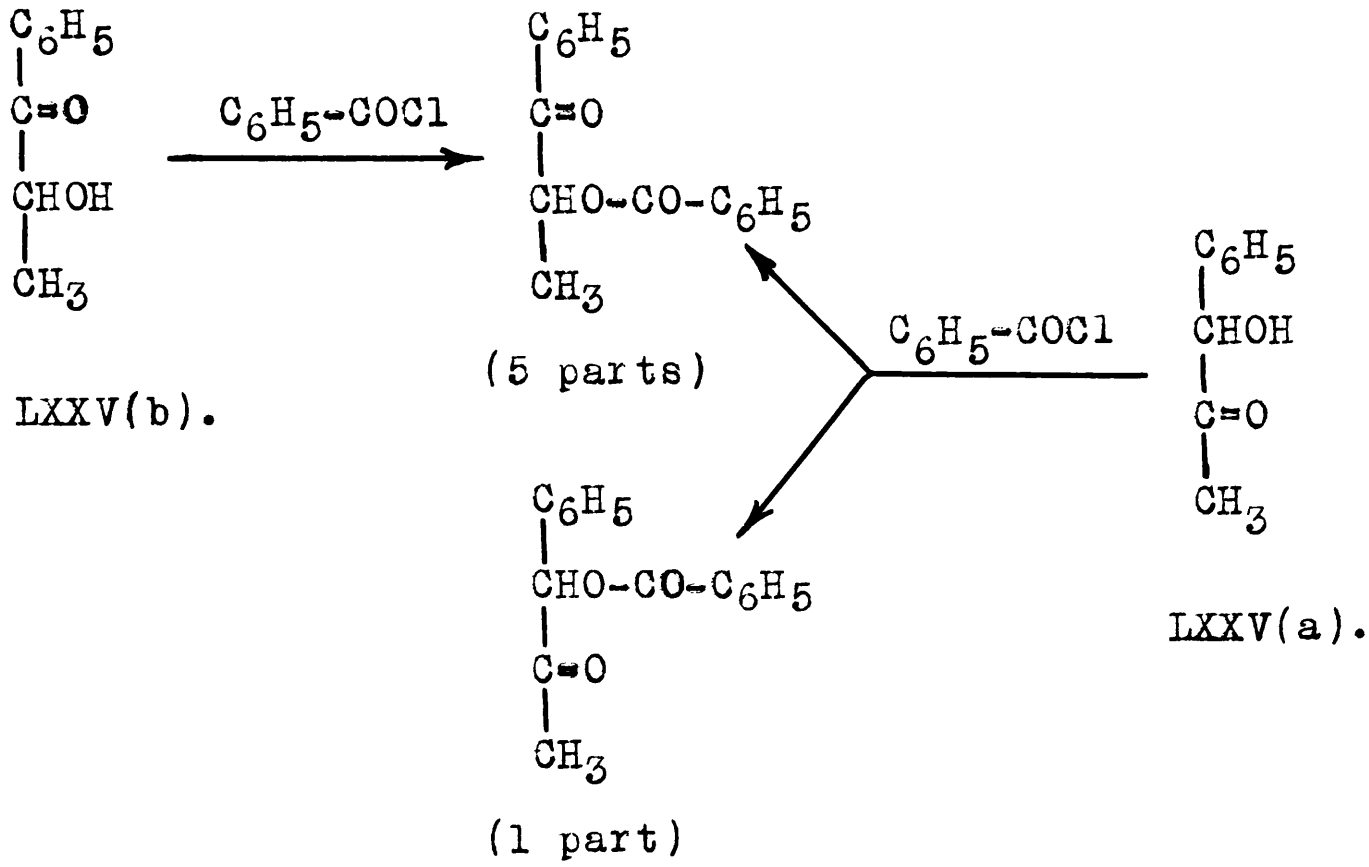
LXXV(b). (2 parts) LXXV(a).

(3 parts)

(c)



LXXV(b). LXXV(a).



The figures in brackets indicate the approximate quantitative ratio between the isolated products of the reaction.

The main conclusions to be drawn from this author's studies are:

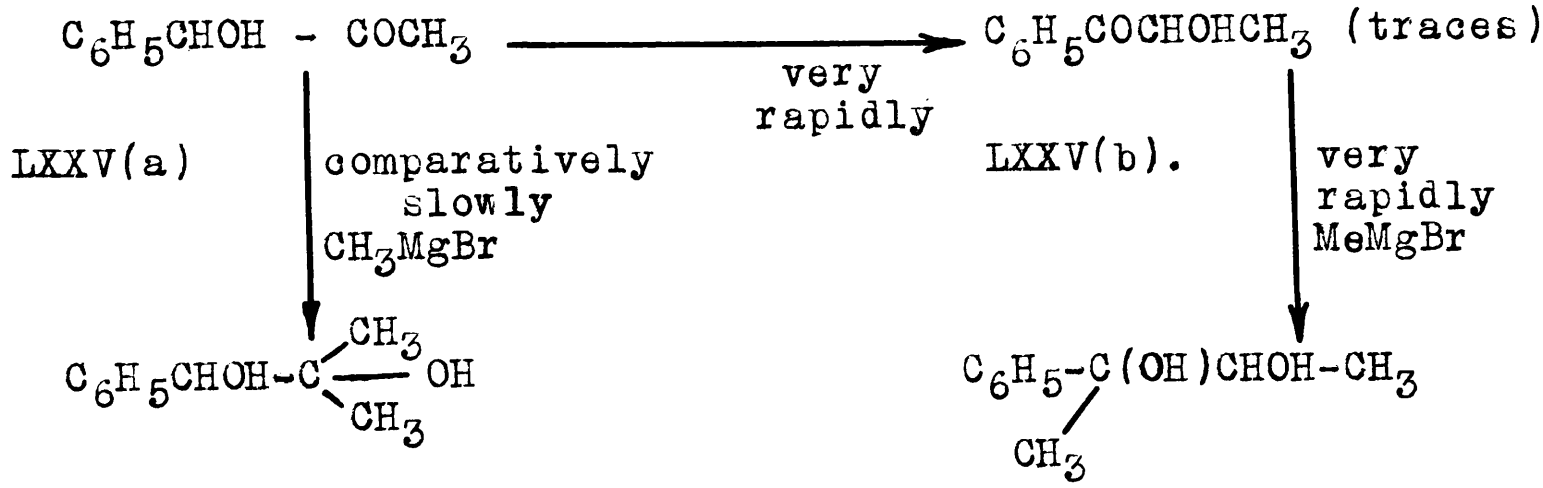
1. Benzoyl methyl carbinol (LXXV(b)) is readily converted into its stable isomer, phenyl acetyl carbinol (LXXV(a)) by the action of either acid or alkali.

2. The reverse isomerization has not been effected.

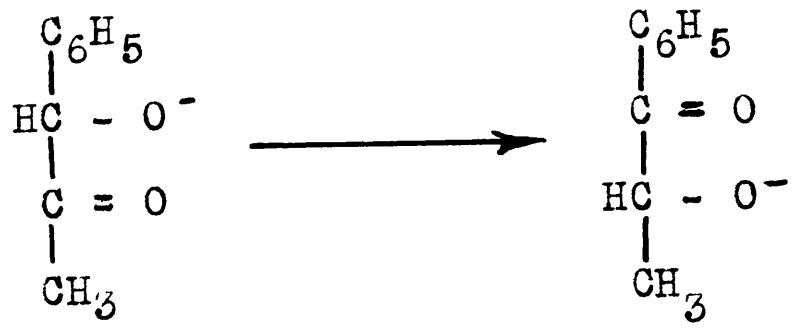
3. The stable isomer (LXXV(a)) may be converted into <u>derivatives</u> of the unstable isomer (LXXV(b)).

In view of these facts Temnikova believes no true dynamic equilibrium exists between the two ketols, but rather,

that the isomerization takes place under the influence of the reagent. Considering the effect of CH_3MgBr on the stable ketol (LXXV(a)) from which a mixture of glycols is obtained, Temnikova endeavoured to show that the existence of an equilibrium is unlikely as this would necessarily entail a very much more rapid addition of the Grignard to (LXXV(b)) than to (LXXV(a)) a fact which does not appear likely.



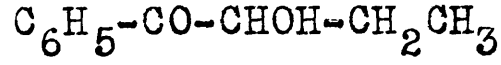
Instead, she believes that an intermediate fragment is formed during the reaction and that this is capable of rearrangement. In the case of addition of the Grignard reagent, first a proton is lost and then the remaining fragment rearranges.



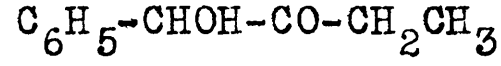
The entering radical may then add directly to either the rearranged or unrearranged fragment.

Temnikova (107) also draws attention to the fact that the reaction is greatly influenced by the nature of the incoming radical. When the radical in the Grignard reagent is the same as that on the carbonyl group, derivatives of both isomers are obtained, whereas when the two radicals are different there seems to be no tendency towards rearrangement.

Recently she (111, 112) has extended this work to a study of the two isomeric ketols, ethyl benzoyl carbinol (LXXVIII(a)) and phenyl propionyl carbinol (LXXVIII(b)).

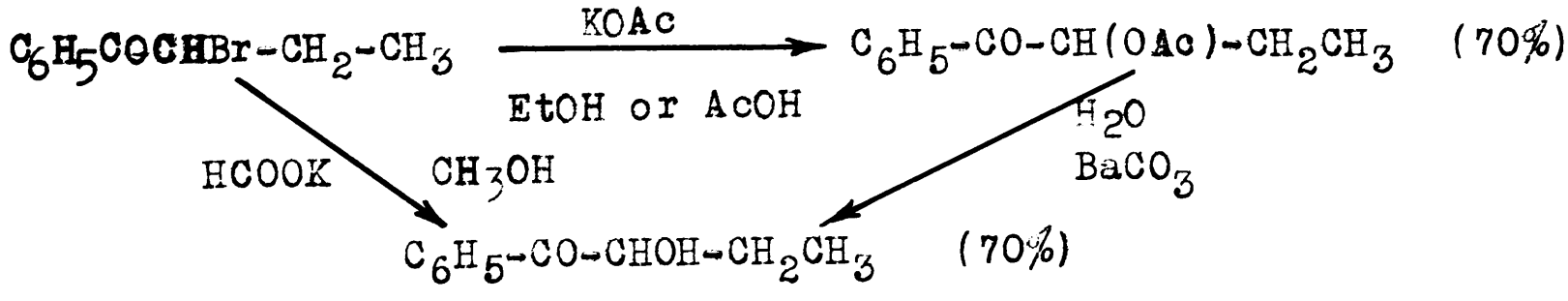


LXXVIII(a).



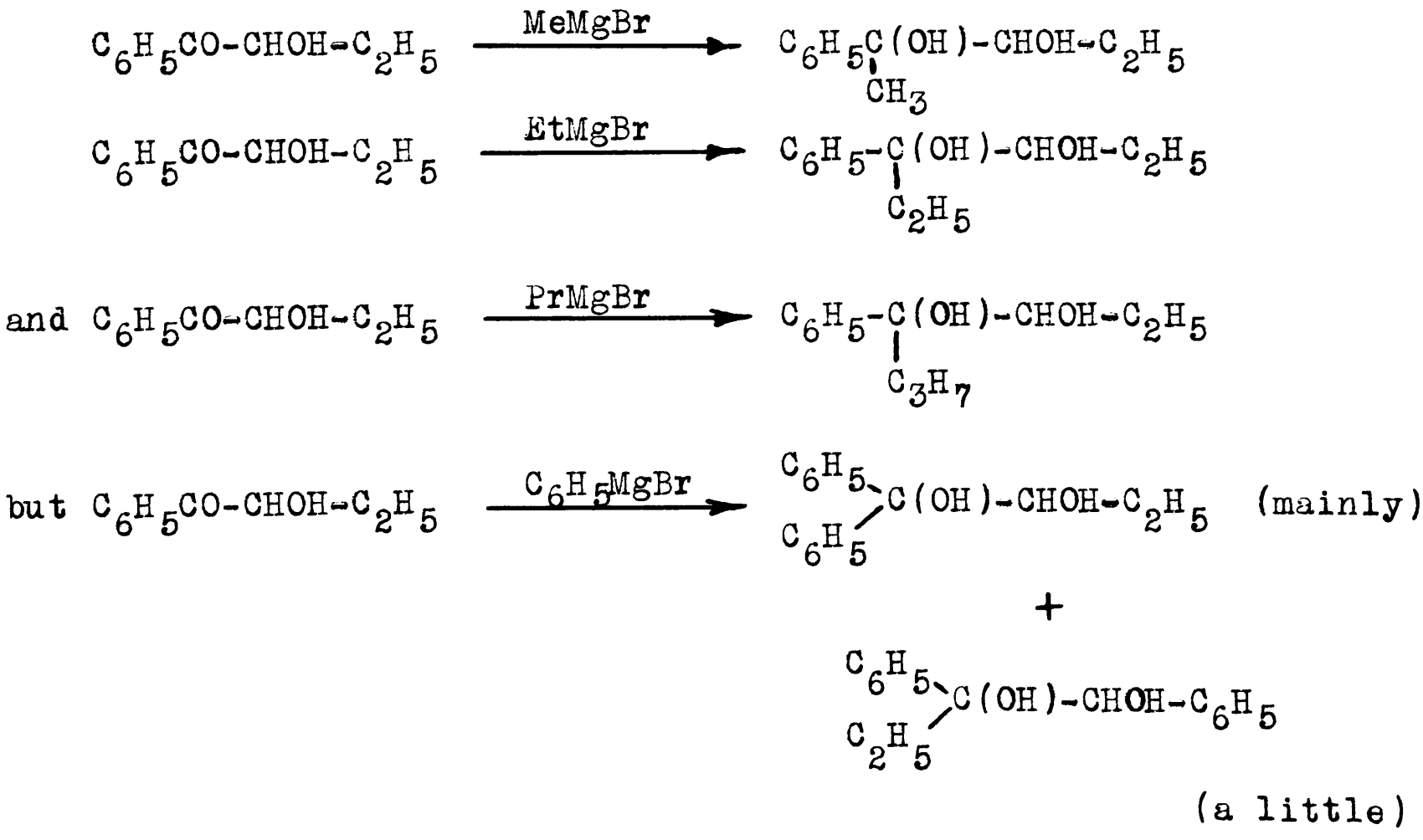
LXXVIII(b).

(LXXVIII(a)) was prepared either directly from the corresponding bromo derivative by treatment with potassium formate in methanol or by the action of aqueous barium carbonate on the corresponding acetate (111).

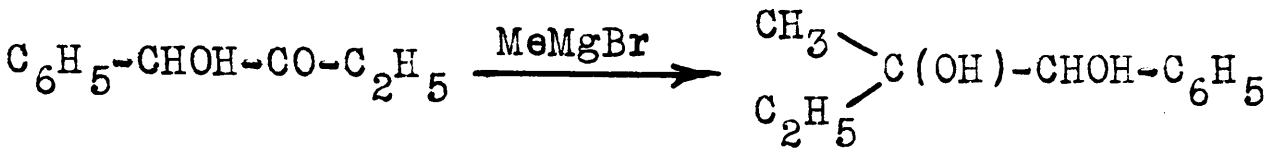


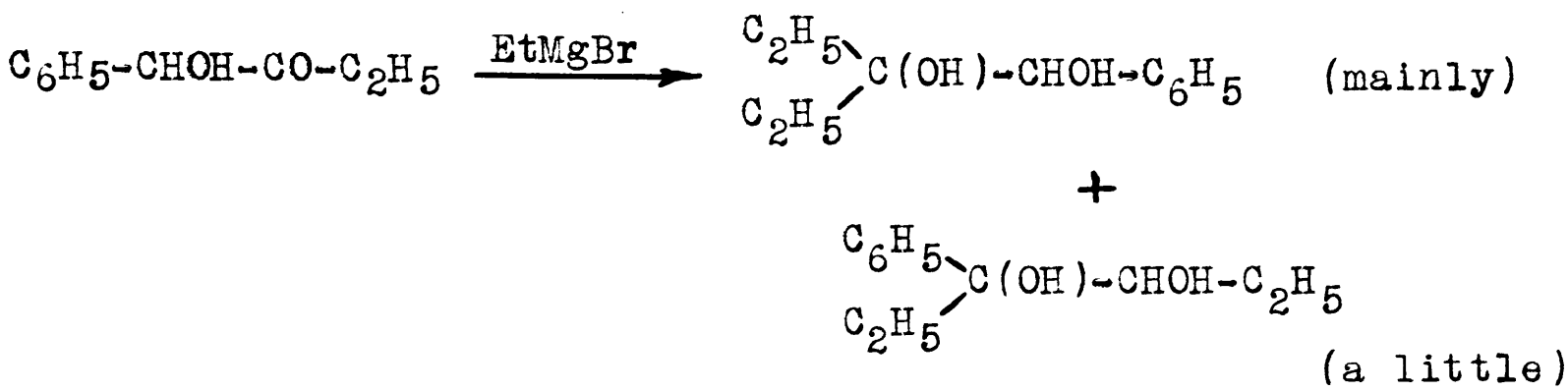
When (LXXVIII(b)) is heated in a sealed tube with a little sulfuric acid in ethanol an equilibrium mixture containing 60-65% (LXXVIII(a)) and 40-35% (LXXVIII(b)) is obtained. The same equilibrium mixture is obtained when either (LXXVIII(a) or (b)) is allowed to stand at room temperature with a little ethanolic potassium hydroxide.

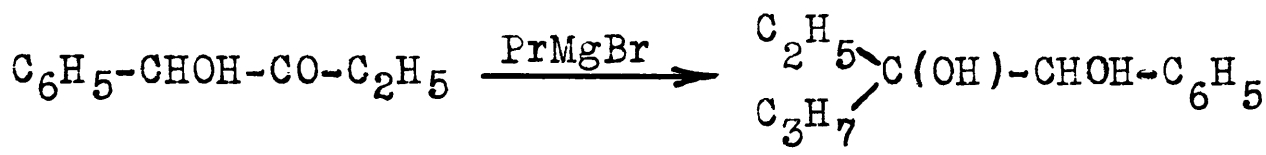
As with the methyl homologue, Temnikova (112) found that only the normal glycol is formed by the action of the Grignard reagent on either isomer except when the radical in the Grignard reagent is the same as that attached to the carbonyl group in the keto alcohol. In this case a mixture of glycols is obtained from both isomers.



Similarly,



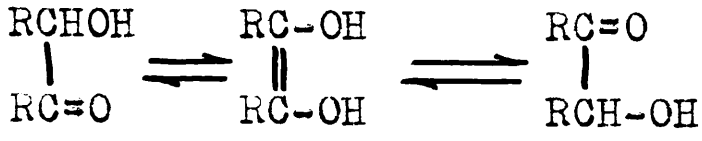




Urion and Baum (113) also have studied the isomeric ketols (LXXVIII(a) and (b)). They found that (LXXVIII(a)) was readily converted into (LXXVIII(b)) and could only be distilled without dismutation at a pressure less than 2-3 mm. whereas (LXXVIII(b) was heat stable. The dismutation was shown to be markedly catalyzed by the presence of hydroxyl ions. However, in contrast with the work of Temnikova, Urion and Baum found no evidence for the inverse isomerization and concluded that this could only be effected by preparing derivatives of the alcoholic hydroxyl group.

Dismutations similar to those discussed above also have been observed with benzoin type compounds. Thus McKenzie and co-workers (114) assumed benzoin transformations represent

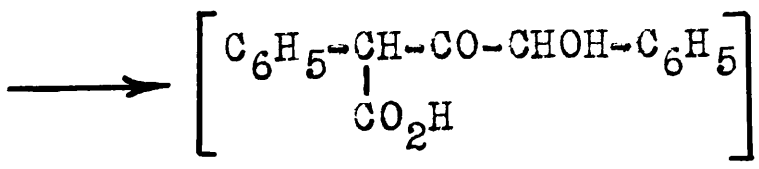
equilibrium reactions proceeding through the ene-diol stage.



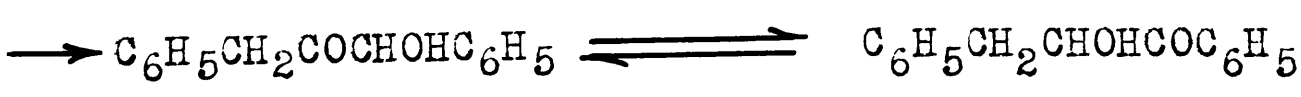
Kohler and co-workers (115) studied rearrangements of diphenyl propane derivatives which they regarded as equilibrium reactions, although in no case was this demonstrated experimentally.

Kohler and Kimball (115a) found that the β-lactone (LXXIX(a)) of α-phenyl-β-hydroxy-β-benzoyl propionic acid (LXXIX), on shaking for an hour with 5% aqueous sodium hydroxide, lost carbon dioxide with formation of a mixture of the isomeric hydroxy ketones (LXXXI) and (LXXXII) and of other products.

LXXIX(a). LXXIX.



LXXX.



LXXXI. LXXXII.

They believed that (LXXXI) was the primary reaction product and that this was converted secondarily to its isomer (LXXXII). Accordingly, they considered there must have been a previous shift from (LXXIX) to (LXXX). Treatment of the lactone (LXXIX(a)) with a solution containing 20 cc. of methanol and 10 cc. of 40% hydrobromic acid for 24 hours gave the ester corresponding to the original acid, but none of the isomeric ester was detected.

In order to study this mechanism further, Kohler and Leers (115(b)) investigated α-phenyl-β-hydroxy-β-anisoyl propionic acid (LXXXIII) in which one of the phenyl groups is "tagged" by a methoxyl group. The behaviour of this compound as outlined below confirmed their previous views.

$$C_6H_5\text{-}\underset{\displaystyle CO_2H}{\underset{|}{CH}}\text{-}CHOH\text{-}CO\text{-}C_6H_4\text{-}OCH_{3p} \longrightarrow \left[C_6H_5\text{-}\underset{\displaystyle CO_2H}{\underset{|}{CH}}\text{-}CO\text{-}CHOH\text{-}C_6H_4\text{-}OCH_{3p}\right]$$

LXXXIII.

$$\longrightarrow C_6H_5CH_2\text{-}CO\text{-}CHOH\text{-}C_6H_4\text{-}OCH_{3p} \longrightarrow C_6H_5\text{-}CH_2\text{-}CHOH\text{-}CO\text{-}C_6H_4\text{-}OCH_3$$

LXXXIV. LXXXV.

At ordinary temperatures, in the presence of cold dilute alkali, (LXXXIV) is the only product of the reaction, but the latter, on heating with dilute alkali, passes completely into a low melting isomeric ketone (LXXXV). Kohler et al. believed that these isomeric hydroxy ketones were in

equilibrium, but they cite no experimental evidence and were unable to demonstrate the reverse shift $-CH_2-CHOH-CO- \longrightarrow -CH_2-CO-CHOH-$.

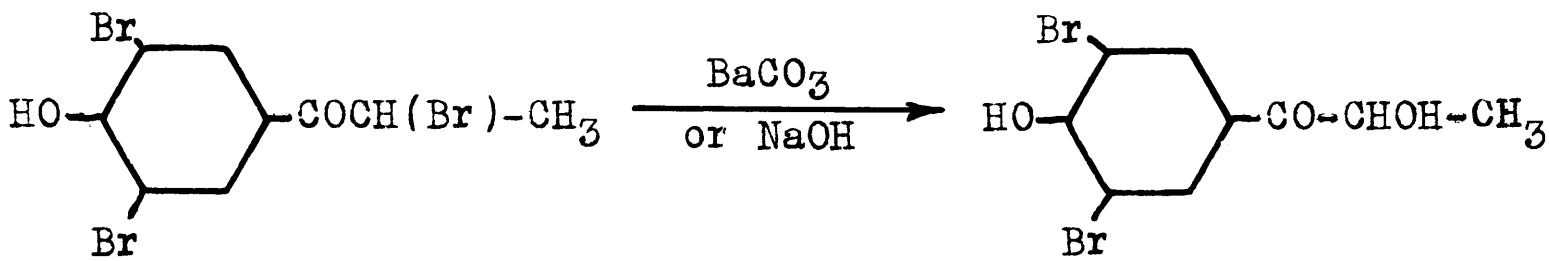
Stevens (78), however, working with the para-chlor analogue of (LXXXIV) succeeded in doing so and provided definite experimental evidence for this equilibrium.

$$C_6H_5-CH_2-CHOH-CO-C_6H_4-Cl_p \rightleftharpoons C_6H_5-CH_2-CO-CHOH-C_6H_4-Cl_p$$

Starting with either isomer he was able to show that under the influence of aqueous alcoholic sodium carbonate both isomers were present in the reaction mixture. He concluded that probably all such 1:2 ketols represent, in solution, equilibrium mixtures of dismutation isomers, and that the failure to observe this in some cases may be due either to the position of equilibrium being almost entirely to one side or the other or to the peculiar properties of one of the two isomers in question rendering the isolation difficult.

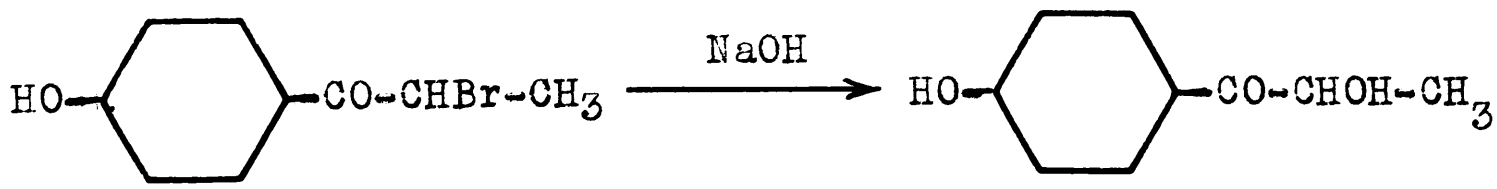
The position of the equilibrium, as well as the stability of isomeric ketols, is markedly affected by the presence of substituents in the benzene ring. Thus Auwers and co-workers (116) have shown that, whereas in the parent ketols phenyl acetyl carbinol (LXXV(a)) and benzoyl methyl carbinol (LXXV(b)) (page 46) (LXXV(a)) is the stable form, this stability is reversed by introducing substituents in the benzene

ring. They found that 3,5-dibromo-4-hydroxyphenyl bromoethyl ketone (LXXXVI) did not undergo rearrangement when subjected to treatment with aqueous barium carbonate or sodium hydroxide but yielded (LXXXVII) exclusively.

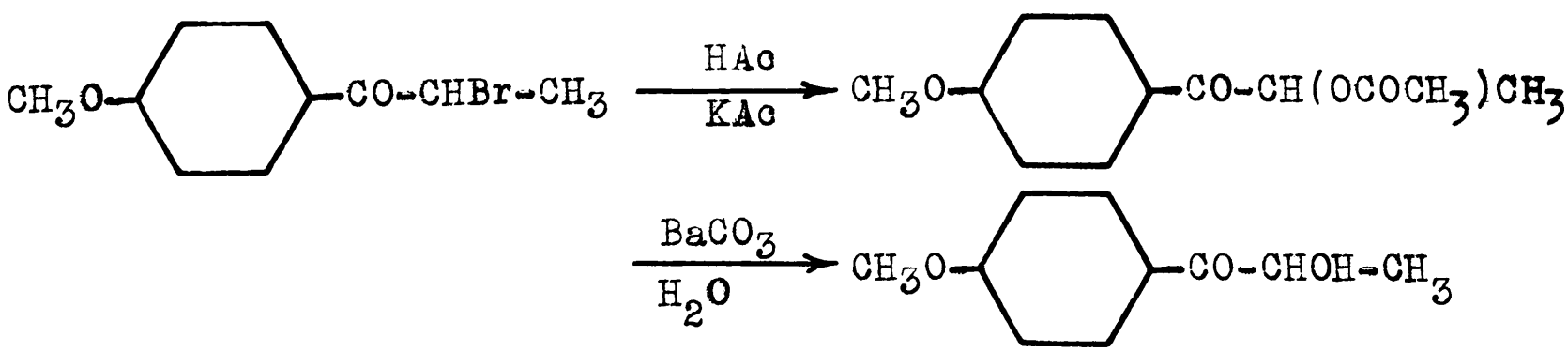


LXXXVI. LXXXVII.

v. Auwers and Noll (117) extended these investigations to a study of methyl (p-hydroxybenzoyl) carbinol (LXXXVIII) and its methyl ether (LXXXIX). In both cases it was found that the presence of the substituent conferred stability on the unstable parent ketol (LXXV(b)).



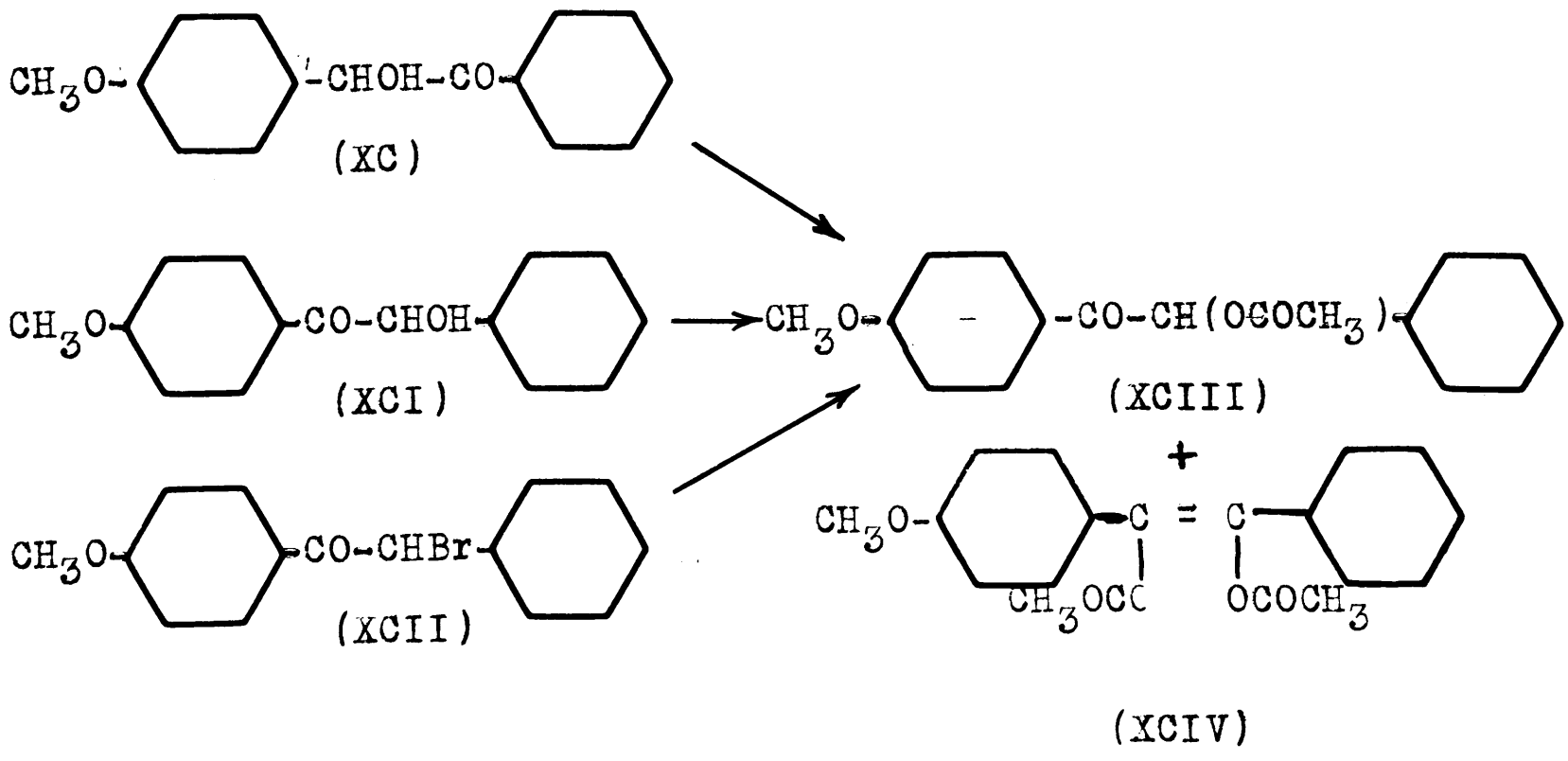
LXXXVIII.



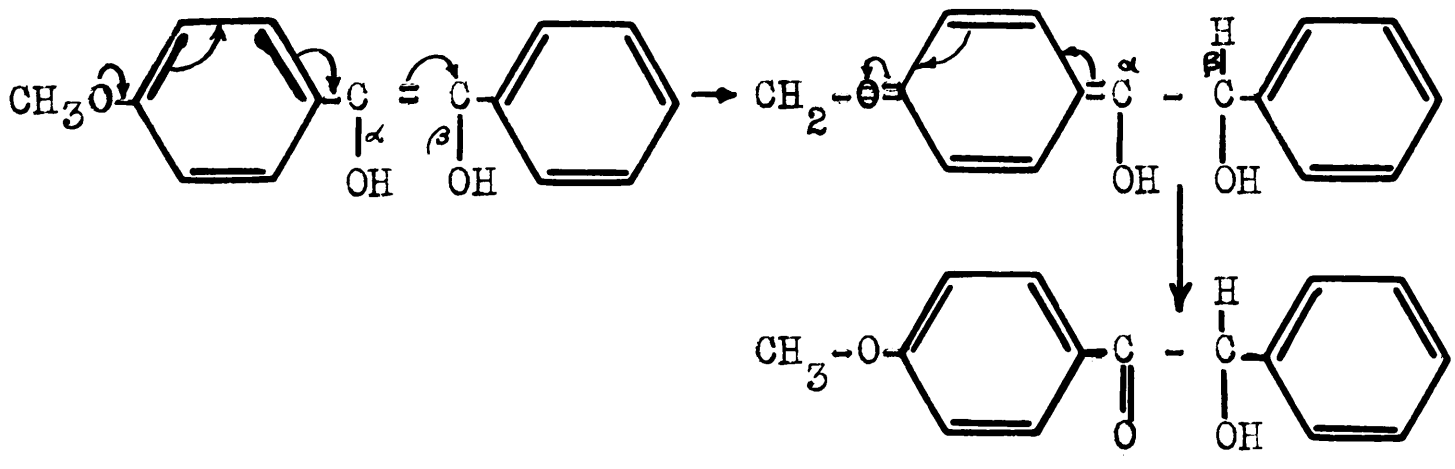
LXXXIX.

This inversion of stability by the presence of a para methoxyl group is also evident in the work of Kohler and co-workers (115). Thus, while C_6H_5-CHOH-CO-CH_2-C_6H_5 (LXXXI) appears to be the stable form of the unsubstituted benzoin (115(a)), in the case of the para methoxyl substituted compounds the stable form is C_6H_5-CH_2-CHOH-CO-C_6H_4-OCH_{3p} (LXXXV) (115 (b)).

Barnes and Tulane (118) have studied this same effect. They acetylated para methoxyphenyl benzoin (XC), its isomer (XCI) and the bromo derivative, anisoyl phenyl bromomethane (XCII) and in each case obtained a mixture of the monoacetate (XCIII) and the diacetate (XCIV).



When an alcoholic solution of the diacetate was treated with acid, benzanisoin (XCI) separated out. The authors believe that the diacetate on acid hydrolysis is converted into the unstable enediol which then passes into the more stable high melting benzanisoin. They believe also that the directing influence of the methoxyl group is manifest in the intermediate enediol and explain this effect in the following manner. The methoxyl group has a strong tendency towards electron release thereby giving rise to an electronic strain in the aromatic nucleus. The <u>para</u> carbon will be negatively charged and the two intermediate carbon atoms (alpha and beta) charged positively and negatively, respectively. A proton is therefore added at the beta carbon followed by the ejection of a proton from the alpha hydroxyl, the stable benzanisoin resulting.



Of interest to plant chemists is the observation that dismutation reactions may also be brought about by the action of fermenting yeast.

v. Auwers and Mauss (119) demonstrated the conversion of benzoyl methyl carbinol (LXXV(b)) into phenyl acetyl carbinol (LXXV(a)) under the influence of yeast carboligase.

The same dismutation was effected by Favorskii (101) in an extension of Neuberg's (120) synthesis of phenyl acetyl carbinol (LXXV(a)). Neuberg had found that this compound was synthesized by adding benzaldehyde to a solution of glucose undergoing a vigorous yeast fermentation. Favorskii believed that (LXXV(a)) was not the primary reaction product, but that it was formed from its dismutation isomer (LXXV(b)). He accordingly introduced the latter into a vigorously fermenting yeast solution and succeeded in isolating a considerable quantity of phenyl acetyl carbinol (LXXV(a)).

Summary

The principal generalizations to be drawn from this review of work on dismutations of compounds of the type $R_1COCHOHR_2$ are as follows:

1. Hydroxy carbonyl compounds, either aliphatic, aromatic or both, readily undergo intramolecular dismutation reactions in the presence of either dilute acid or alkali and in some cases with fermenting yeast.

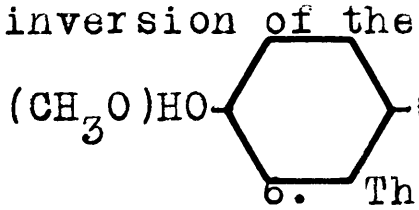
2. In aliphatic chains containing the 1:2 ketol grouping there appears to be a pronounced tendency for the

carbonyl group to move towards the end of the chain with the accompanying formation, wherever possible, of an acetyl grouping.

3. When R_1 is phenyl and R_2 is methyl, the isomer $C_6H_5CHOHCOCH_3$ (LXXV(a)) is the more stable form in the presence of either acids or alkalis.

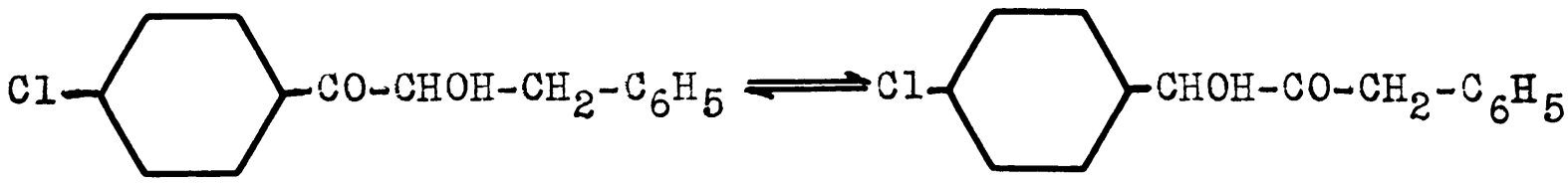
4. The isomerization of C_6H_5-CHOH-$COCH_3$ (LXXV(a)) to C_6H_5-CO-CHOH-CH_3 (LXXV(b)) has not yet been effected; however, derivatives of the unstable isomer may be formed from the stable isomer (LXXV(a)).

5. The presence of a hydroxyl or methoxyl group in the benzene ring <u>para</u> to the side chain results in an inversion of the stability of the two dismutation isomers,



being the stable form.

6. The presence of an equilibrium has been shown in the case of

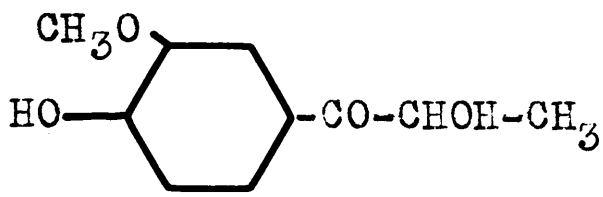


7. It is possible that with all 1,2-hydroxy ketones an equilibrium exists in the presence of acid or alkali.

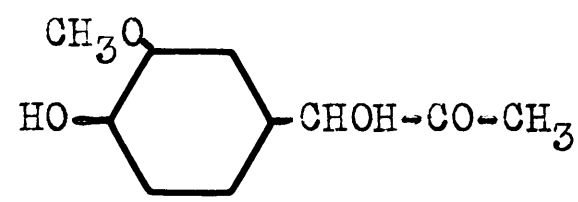
In view of the foregoing discussion, the difficulties encountered in the isolation and synthesis of lignin building units of the oxygenated phenyl propane type are not surprising.

Treatment of such monomers with ethanolic hydrogen chloride during the isolation procedure almost certainly brings about dismutation reactions, so that a mixture of products in the ethanolysis oils is to be expected in which the preponderance of any one unit will depend, to a marked extent, on the dismutation equilibria involved.

Thus with the isomeric ketols (XCV) and (XCVI)

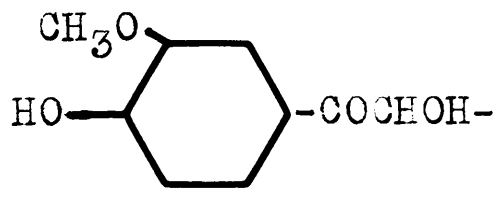


(XCV)



(XCVI)

the presence of the methoxyl group in the <u>meta</u> position should exert no electronic effect upon the side chain and the <u>para</u> hydroxyl should therefore be the determining factor resulting in the stabilization of the form



This is in accord with the observation that the main product from the alkali soluble ethanolysis oils is α-ethoxy propiovanillone (41a). However this is not necessarily the <u>primary product</u> of the ethanolysis reactions, it may represent merely the final stabilized form of a less stable parent constituent. The probable presence of other isomeric compounds can also be predicted on this basis.

Finally such dismutation changes may explain the presence of the large amounts of amorphous material found among the ethanolysis products of wood in spite of the relatively slight tendency of α-hydroxypropiovanillone to polymerize under these conditions. It is possible that one or other naturally occurring or intermediate isomeric form may undergo conversion to an amorphous material much more readily than does α-hydroxypropiovanillone.

II.

DISCUSSION OF EXPERIMENTAL RESULTS

A. Introductory Remarks

The primary object of this research was to study the synthesis and properties of β-hydroxy propiovanillone and its relationship to the structure of protolignin. The latter, according to Hibbert (4), is an aggregate of substances representing stabilized end products of a highly reactive group of plant respiratory catalysts whose assumed function is the facilitation of hydrogen transfer in the metabolism of plant carbohydrates, in order to provide the requisite energy for plant growth. To fulfill such a function the catalysts in question, of the general C_6C_3 type R-C-C-C- (R = guaiacyl or syringyl), must necessarily be highly reactive and therefore capable of undergoing remarkably ready transformation with change of pH and other cell environmental factors. From this point of view the methods in common use for the extraction of lignin from plant material are much too drastic, the one involving acid alcoholysis, as used in these laboratories, probably representing the mildest existing method. However, even under these conditions it has now been shown that depolymerization and concurrent condensation-polymerization

reactions take place, so that the products isolated certainly cannot be regarded as unchanged "protolignin".

The difficulties inherent in the older (and some of the modern) methods of investigation relating to lignin structure, are to be closely associated with the lack of recognition of these facts and the still evident assumption that the amorphous lignins isolated by various processes represent actual protolignin entities, modified only to the extent of polymerization-condensation reactions with formation of a more or less uniform lignin aggregate. A marked departure from this point of view is to be found in Hibbert's recent theories based on the assumption that protolignin actually represents a series of stabilized end products possibly (at least in the case of hardwood) dimeric in type, and derived from highly reactive plant respiratory catalysts. The isolation in high yield (about 12% calculated on the Klason lignin) of water-soluble monomolecular maple wood ethanolysis products, together with the conversion of maple "protolignin" into a mixture of syringaldehyde and vanillin on oxidation (in yield of about 48%), has established definitely its aromatic character.

Inasmuch as, at the time that this research was commenced, not more than about 5-8% of lignin present in the ethanolysis reaction mixture had been identified, it appeared probable that other assumed respiratory catalysts

of the types $RCOCH_2CH_2OH$ and RCH_2COCH_2OH might be present in the ethanolysis reaction mixture, their isolation being rendered difficult on account of lack of knowledge of their properties, hence the necessity for their synthesis and chemical examination.

B. Stability of Lignin Building Units and Ethanol Lignin Fractions towards Ethanolic Hydrogen Chloride

Two types of products have been obtained in the ethanolysis of spruce and maple woods. The first group includes the monomeric propylphenol "lignin building units", α-hydroxypropiovanillone and -syringone (isolated as their ethyl ethers) and the 1:2 diketones, namely vanilloyl and syringoyl methyl ketones. The second group consists of various amorphous ethanolysis lignin fractions separable by solvent fractionation methods. One of these, developed by the writer in conjunction with Hawkins, Lovell and Patterson (121), is based on varying solubility in the solvents water, ethanol, petroleum ether, ethyl ether, acetone, benzene and pyridine. The method is outlined in the flow sheets (Fig. 1 (a) and (b)).

It can be seen that the total amount of material extractable from maple wood meal (by ethanol hydrogen chloride) is separable into three distinct types of lignin referred to

Figure 1 (a)

Ethanolysis of Maple Wood Meal

Separation of the Ethanol Lignin into Solvent Groups

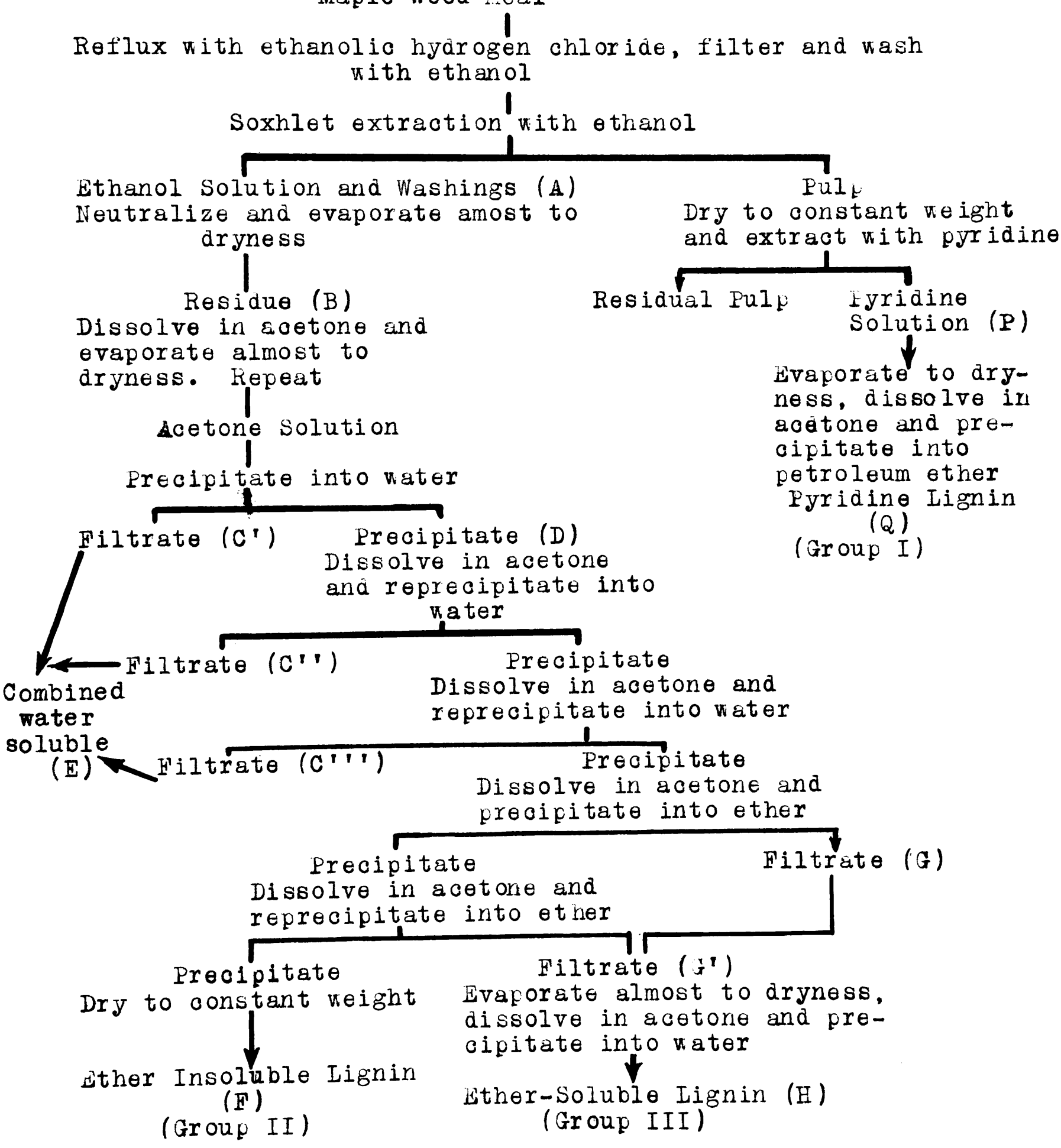
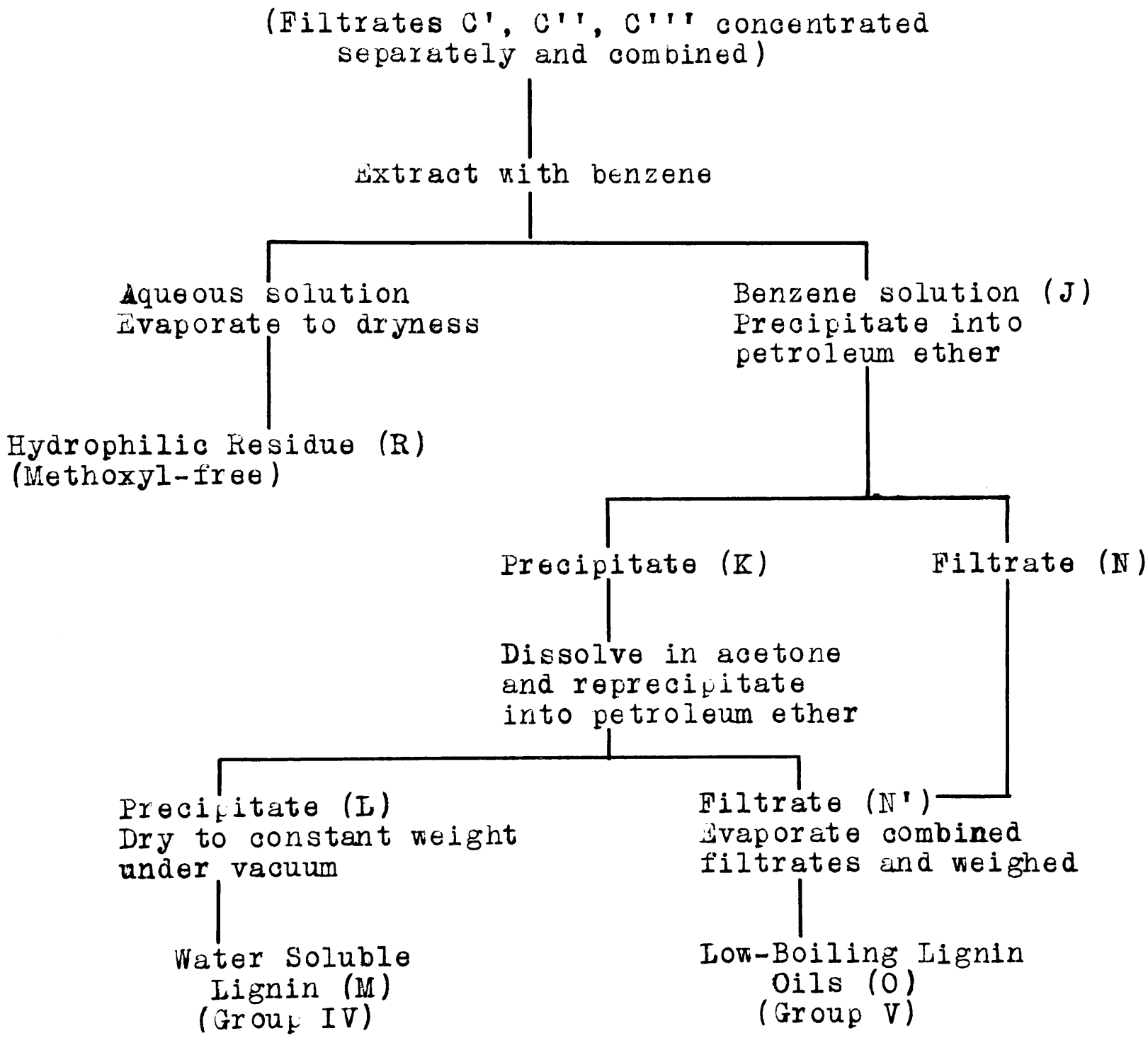


Figure 1 (b)

Combined Concentrates (E)



in the flow sheet as (a) "water soluble", (b) "ether soluble" and (c) "ether insoluble" (characterized by an increase in the degree of polymerization as shown by viscosity measurements) and also the additional fractions namely (d) "petroleum ether soluble, readily distillable oils", and (e) a "hydrophilic part ". The last named is a hygroscopic material not extractable from its aqueous solution by benzene and showing on isolation a zero lignin content by the usual Klason lignin determination. In addition, a further lignin-like product was obtained from the residual wood meal after ethanolysis, by continuous extraction with pyridine. The Klason lignin content of the wood meal was reduced in this manner by an amount corresponding to that of the lignin-like product isolated.

The weight of low-boiling oils obtained by this procedure is in good agreement with those obtained by earlier methods of isolation (122)

The technique of the separation of lignin into distinct solubility groups involves essentially the precipitation of suitably concentrated lignin solutions into an excess of a second organic solvent which has the property of being a non-solvent for a part, or parts, of the total dissolved lignins, the conditions being so arranged as to bring about the desired precipitations. A ratio of 1:20 of solvent to

non-solvent was found very satisfactory and under these conditions the precipitated product settles out in a flocculent, powdery form whereas with a smaller ratio of non-solvent the material separates as an oily mass. Under these conditions the solubility factor due to the presence of solvent is very low.

Of particular practical importance has been the application of this procedure to the separation of monomeric lignin building units from the more complex material. Thus when a mixture of high- and low-boiling material was dissolved in a solvent such as acetone, or chloroform, and precipitated into petroleum ether, an almost complete separation into distillable and non-distillable oils was obtained.

In order to determine the relationship existing between the amorphous lignin fractions and the monomeric C_6-C_3 compounds, the monomers as well as samples of the lignin fractions were subjected to a re-treatment with ethanolic hydrogen chloride under the standard conditions of ethanolysis, the object being to study the relative amounts of monomer and polymer present after the ethanolysis rather than to determine the actual identity and characteristics of the products. However, in most cases the monomeric oils were identified by the preparation of crystalline derivatives.

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 analogue, respectively, suggested that these diketones might possibly have been formed 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-ethoxy ethers without any evidence of oxidation to diketones. In view of the previous work it seems highly probable these are actually formed during ethanolysis by degradation of a polymeric or more likely a dimeric type of product, the building unit of which is one or other of Hibbert's assumed plant respiratory catalysts (page 24).

α-Hydroxypropiovanillone (XCV) and vanilloyl methyl ketone (X) in various concentrations were then subjected to treatment with 2% ethanolic hydrogen chloride. Both derivatives were found to be relatively stable in dilute solution but their stability decreased sharply at higher concentrations, a result apparently, of condensation-polymerization reactions. The tendency towards polymerization is least at a concentration of 0.2% of either (XCV) or (X), that is under conditions similar to those existing in the customary ethanolysis extraction (122)

While α- hydroxy propiovanillone was converted, under such conditions, into α-ethoxy propiovanillone (identified as α- ethoxy propioveratrone) vanilloyl methyl ketone was recovered unchanged, and similar results were obtained with the corresponding syringyl derivatives. With both series, the diketones have been found to be more stable towards such treatment than the α-hydroxy derivatives. In general, the monomolecular syringyl derivatives under discussion appear to show a somewhat greater tendency towards polymerization-condensation reactions than their guaiacyl analogues.

The presence of the diketone (vanilloyl or syringyl methyl ketone) did not increase the tendency of α- hydroxy propiovanillone or -syringone to undergo polymerization. Thus with a mixture of α- hydroxy propiosyringone and syringoyl methyl ketone, the diketone component was recovered unchanged, in almost quantitative yield, indicating no tendency towards interaction or interconversion during the ethanolysis of maple wood.

In the guaiacyl series, α- acetoxy propiovanillone was found to be considerably more stable than the corresponding α-hydroxy derivative under ethanolysis conditions, which is in agreement with an earlier observation that reconversion into monomers proceeds readily in the case of an acetylated

lignin (44). With the corresponding syringyl derivatives, α-acetoxy- and α-hydroxypropiosyringone, the reverse is true, and at the present time, no explanation for this anomaly can be offered. Both acetoxy derivatives are converted to the corresponding ethyl ethers under ethanolysis conditions. These results are summarized in Table I (page 102).

This work was extended to include three lignin fractions obtained in the standard ethanolysis of maple wood (121), namely a water-soluble-(Fig. I (E)), an ether-soluble - (Fig. I (H)), and an ether-insoluble maple lignin (Fig. I (F)). A retreatment of each under standard ethanolysis conditions (ethanol-hydrogen chloride (2%) for 48 hours) indicated a correlation between degree of polymerization and reconversion to monomeric (petroleum ether-acetone soluble) products, the less highly polymerized fractions undergoing reconversion to a greater extent. These results are summarized in Table II (page 103).

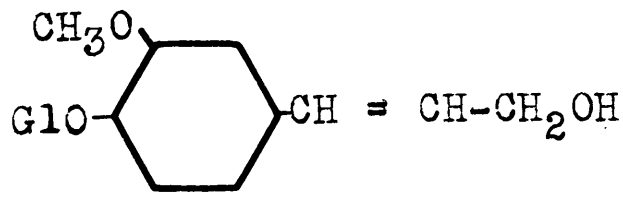
It would seem from these results that in addition to degradation of monomolecular derivatives there takes place, concurrently, formation of complex polymerization-condensation products either from monomers or more probably from dimers or other low molecular weight products present initially.

C. Synthesis and Properties of β-Hydroxy Propioveratrone and β-Hydroxy Propiovanillone

From the review given in the historical introduction (pp. 1-38), it is apparent that the fundamental lignin building units consist of an aromatic phenol nucleus with a substituted propyl side chain.

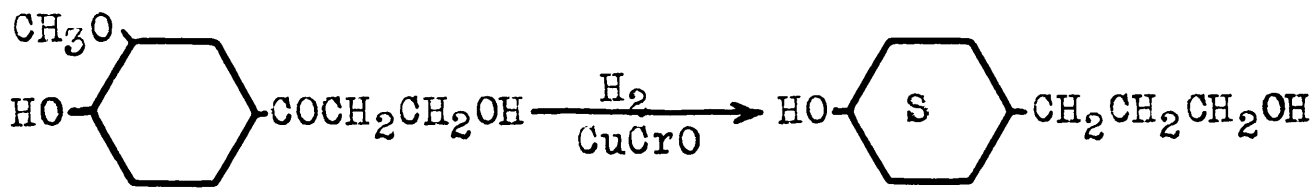
Ethanolysis of various woods has led to the isolation from the reaction mixture of α-ethoxy propiovanillone (VIII) and-syringone (IX) and of vanilloyl-(X) and syringoyl (XI) methyl ketones. Up to the present time, these four are the only C_6C_3 units which have been positively identified among the ethanolysis products, and in each the side chain is characterized by the presence of a terminal methyl group.

However, there are various indications of the presence in lignin of building units in which the side chain terminates in a primary hydroxyl group. The possible role of a compound of the type $RCOCH_2CH_2OH$ (R = guaiacyl or syringyl) as a plant respiratory catalyst has been discussed (pp. 29-32). Furthermore, coniferyl alcohol, which also contains a terminal carbinol group, is known to be present in the form of its glucoside, coniferin (XCVII) in practically all young plants (7).



XCVII.

Further evidence for the presence of this type of terminal group is to be found in recent hydrogenation studies on wood and extracted lignins (56), one of the hydrogenation products being 3-(4-hydroxycyclohexyl)-propanol-1.X Its presence suggests the possibility of its derivation by demethoxylation and reduction of a lignin building unit such as β-hydroxypropiovanillone (XII),



XII.

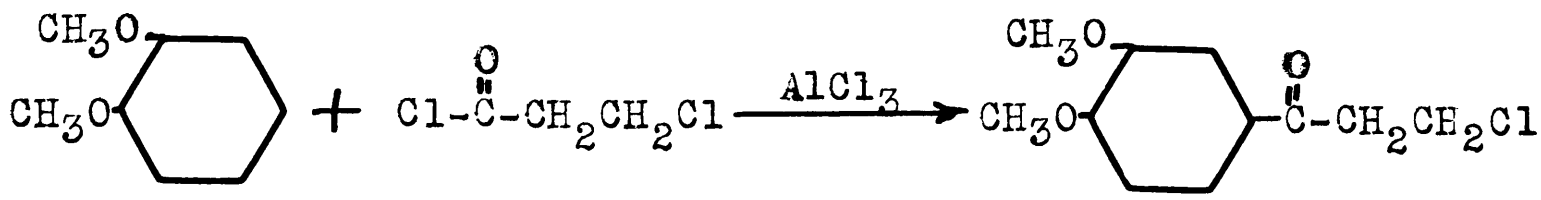
since this type of change takes place (123) with related model substances such as α-hydroxypropiovanillone and α-ethoxypropiovanillone. However, up to the present time, no lignin building unit having this type of side chain (XII) has been isolated from wood or extracted lignins by ethanolysis or other reactions. Nevertheless, it may be present in one or other of the fractions isolable from the ethanolysis "distillable oils" still under investigation. On the other hand, failure to isolate it by present methods of lignin extraction may be due to the manner in which it is united in the lignin complex or possibly to its absence in older woods. Another less likely possibility, in view of the results of the author's investigations, is that a rearrangement may occur

during the ethanolysis treatment so that the terminal carbinol-containing constituent undergoes transformation into α-ethoxy-propiovanillone.

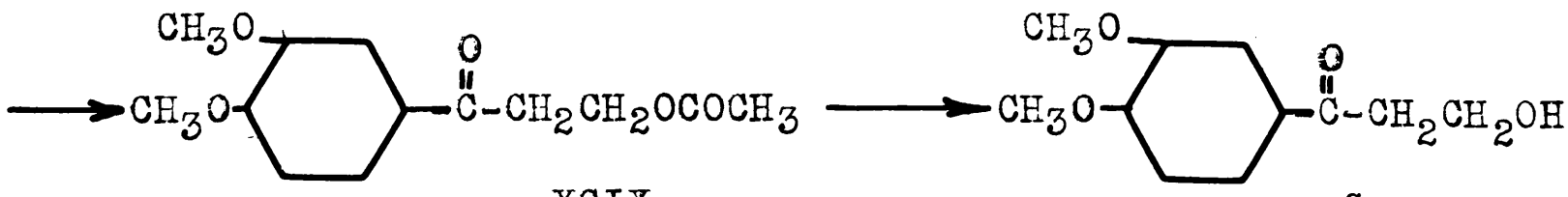
The synthesis of β-hydroxypropioveratrone and β-hydroxypropiovanillone were therefore undertaken in order to study their properties and possible interconversion to other lignin building units. Their behaviour under conditions of ethanolysis has also been studied with a view to facilitating their identification and possible isolation from wood.

1. Synthesis of β-Hydroxypropioveratrone (C)

The synthesis of β-hydroxypropioveratrone was first attempted by the following series of reactions:



XCVIII.



XCIX. C.

The β-chloropropioveratrone (XCVIII) was prepared by a slight modification of the method of Freudenberg (124) consisting of

a Friedel-Crafts condensation of veratrol and β-chloro propionylchloride. It was found that an increase in the amount of aluminum chloride in this condensation gave an improved yield of β-chloro propioveratrone. Thus, whereas one molar equivalent of aluminum chloride gave yields of around 60% (124), with two mols this has been increased to around 75%.

Acetylation of the chloro compound was first carried out by treatment with acetic anhydride and freshly-fused sodium acetate. The product obtained from this reaction mixture by the usual manipulations had a rubber-like texture. However it was found possible to extract from it with a hot 30°-50° petroleum ether a small amount (approximately 20%) of the crystalline acetate. By carrying out this acetylation with freshly-fused potassium acetate and glacial acetic acid a much improved yield (70%) of the acetate was obtained.

Various attempts to deacetylate β-acetoxy propioveratrone were unsuccessful although a series of somewhat anomalous and interesting results were obtained.

The Zemplén method of deacetylation as applied successfully by Fisher, Hawkins and Hibbert (55) to similar compounds, was first attempted but the acetoxy derivative was recovered unchanged.

The next attempt involved the use of methanolic potassium hydroxide as applied to the deacetylation of α-acetoxy propiovanillone (41 (a)) and α-acetoxy propio-

syringone (41 (b)). By varying the conditions of this treatment it was finally found possible to obtain a crystalline compound, in almost quantitative yield, by merely allowing the acetate to stand for five minutes at room temperature with a 4% solution of methanolic-potassium hydroxide. However attempts to re-acetylate this product were unsuccessful, indicating absence of hydroxyl groups. Furthermore, cryscopic molecular weight determinations gave a value of 225 showing that the molecule was monomeric and obviating the possibility of an ether linkage between two molecules through the primary hydroxyl groups. Also the methoxyl value of the compound was 41.5% in contrast to the theoretical value for β-hydroxypropioveratrone of 29.5%. This latter value, the carbon and hydrogen values and the properties of the product, indicated that etherification had taken place by reaction with the methanol with formation of the β-methyl ether. This was confirmed by preparing the β-ethyl ether in an analogous manner using ethanol as solvent and comparing it with a sample of β-ethoxypropioveratrone (CII) prepared according to the method previously outlined by Cramer, Hunter and Hibbert (41 (a)).

If this etherification takes place through the free hydroxyl derivative as an intermediate, the results indicate an unusually reactive hydroxyl group. An alternative explanation, involving the primary formation of veratryl vinyl ketone (CI) as an intermediate is also possible. The latter could then

undergo 1,4 addition of ethanol to yield β-ethoxy propioveratrone (CII).

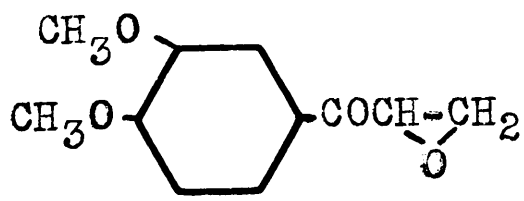
$$RCOCH_2CH_2OCOCH_3 \longrightarrow RCOCH{=}CH_2$$

CI.

$$\xrightarrow[KOH]{EtOH} RC(OH){=}CHCH_2OC_2H_5 \longrightarrow RCOCH_2CH_2OC_2H_5$$

(R = veratryl) CII.

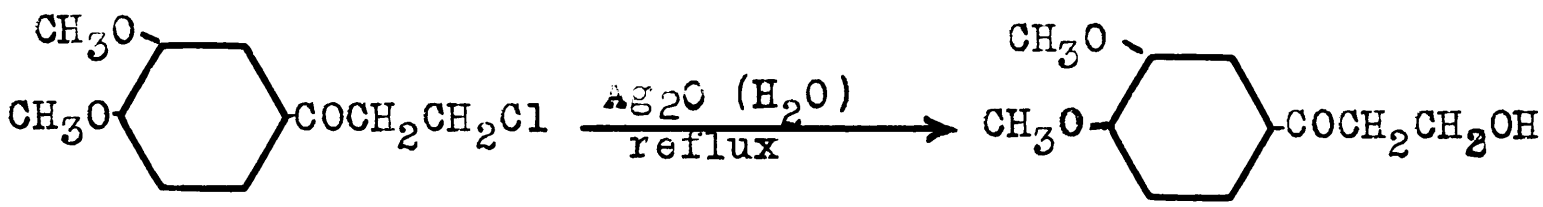
In an attempted deacetylation of β-acetoxy propioveratrone with sodium carbonate in aqueous dioxane a crystalline compound was obtained which did not agree either in analysis or chemical behaviour with the expected β-hydroxy derivative. This new substance could not be reacetylated under normal conditions to yield the original acetate. Its molecular weight (Rast) was 225 showing that the product was monomolecular. The carbon and methoxyl values (C, 62.9; OMe, 29.7) were very similar to those for β-hydroxy propioveratrone (C, 62.8; OMe, 29.3), although the hydrogen was somewhat low. These facts suggest the possibility of an ethylene oxide structure of the type (CIII),



CIII. (C, 65.4; H, 5.77; OCH_3, 29.8)

although no simple mechanism for this type of reaction can be given. The presence of a free carbonyl group was shown by the ready formation of a 2,4-dinitrophenylhydrazone. It was not further investigated.

β-Hydroxy propioveratrone was finally synthesized by refluxing β-chloro propioveratrone with water in the presence of silver oxide.



XCVIII. C.

Its structure was confirmed by reconversion into the acetate by means of acetyl chloride and pyridine.

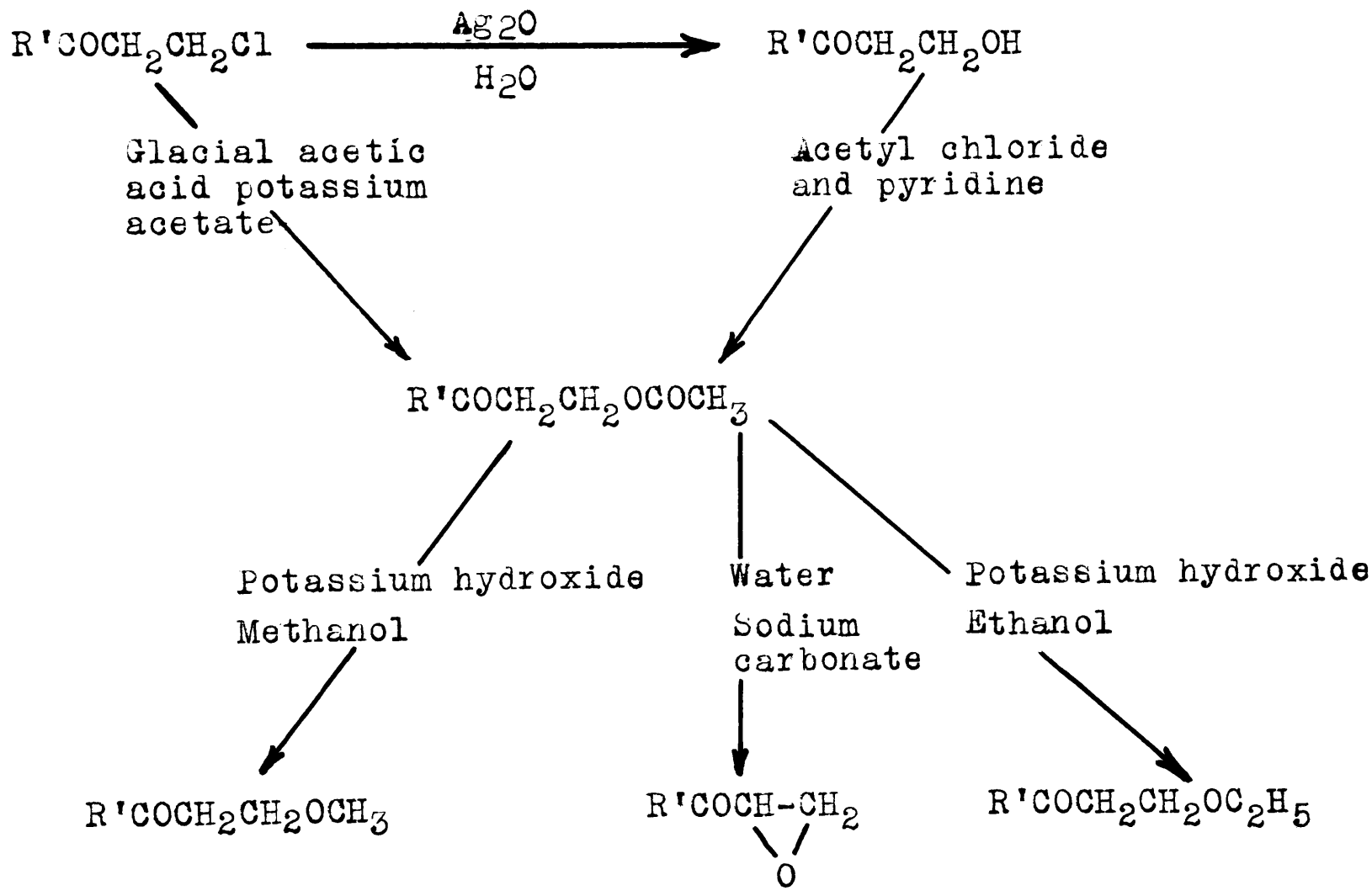
These experimental results are summarized in Chart I.

2. Properties of β-Hydroxy Propioveratrone

The action of ethanolic hydrogen chloride on β-hydroxy propioveratrone, under the usual conditions employed in the ethanolysis of wood, gave an almost quantitative conversion into β-ethoxy propioveratrone while the corresponding treatment with 2% methanolic hydrogen chloride yielded the β methyl ether (75%) although in this case considerable quantities of high-boiling materials were formed. This latter phenomenon is in accord with previous work on wood

Chart I

Reactions of β-Hydroxy Propioveratrone and its Derivatives



R' = Veratryl.

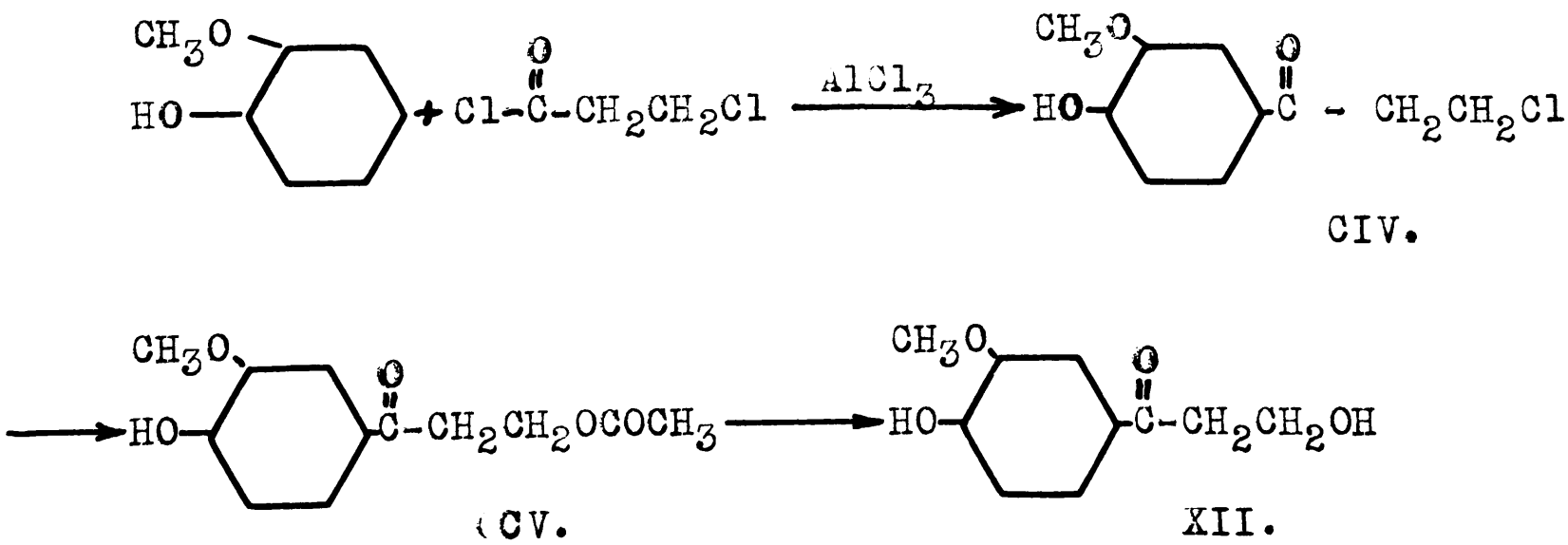
methanolysis (40) in which it was found that methanolic hydrogen chloride gives rise to less distillable oils and more amorphous lignins than does ethanolic hydrogen chloride.

The importance of using mild extraction methods for the isolation of monomeric lignin building units is apparent from the results obtained when β-hydroxy propioveratrone was treated with sulfuric acid under the conditions of the usual Klason lignin determination. An almost complete conversion to an amorphous lignin-like material was obtained in contrast to the negligible amounts formed by "ethanolysis".

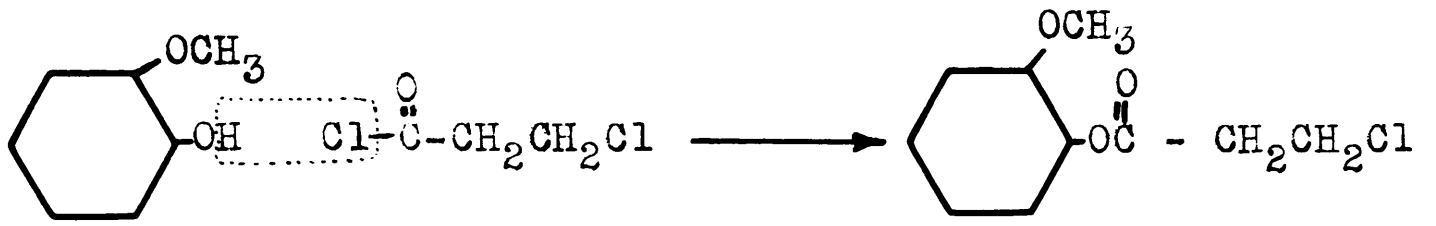
3. Synthesis of β-Hydroxy Propiovanillone

Attempts to prepare β-hydroxy propiovanillone by the syntheses (1, 2 and 3) outlined below were unsuccessful. However, after considerable experimentation the synthesis was accomplished as indicated in Method (4).

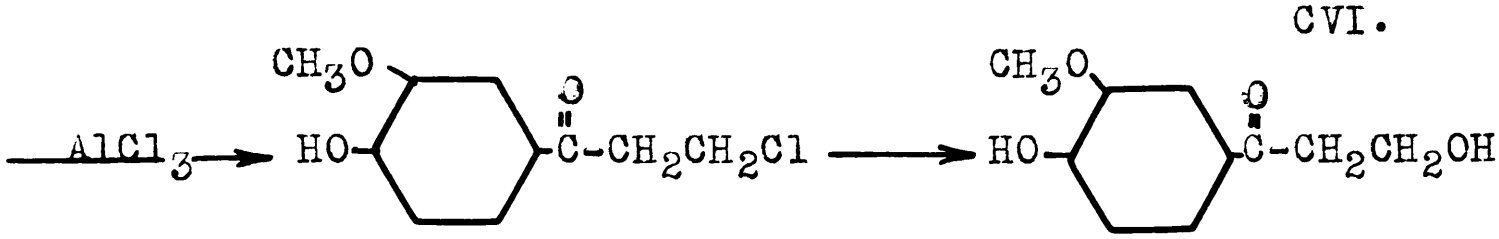
Method 1.



Method 2.

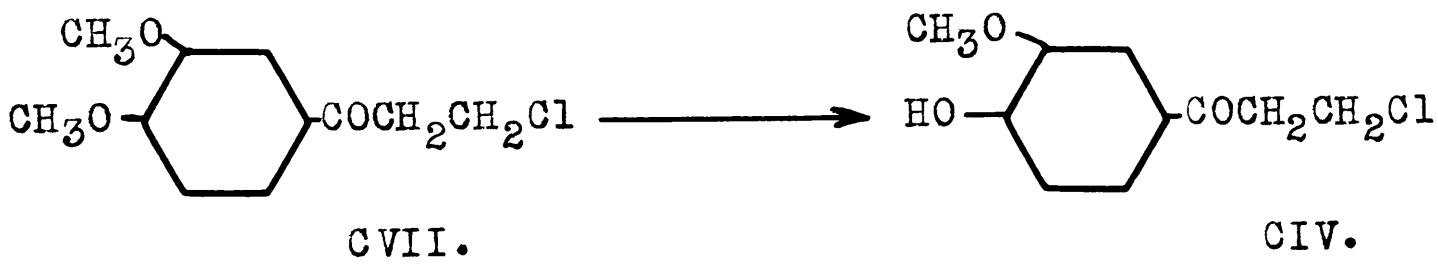


CVI.

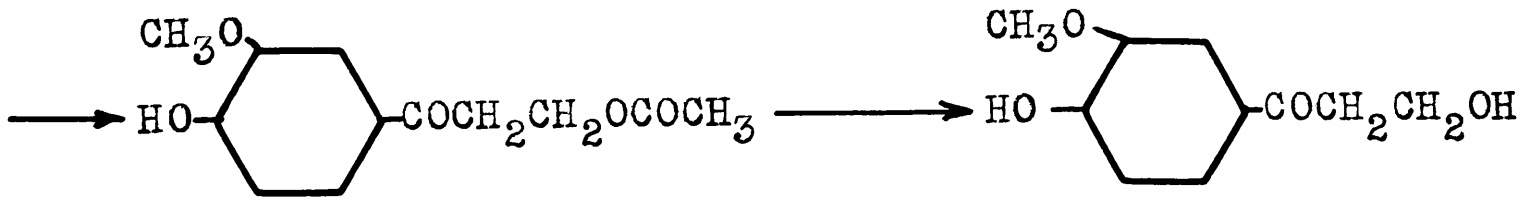


XII.

Method 3.

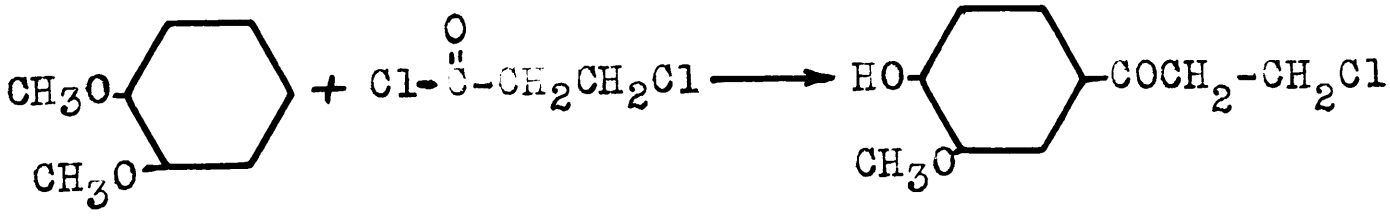


CVII. CIV.

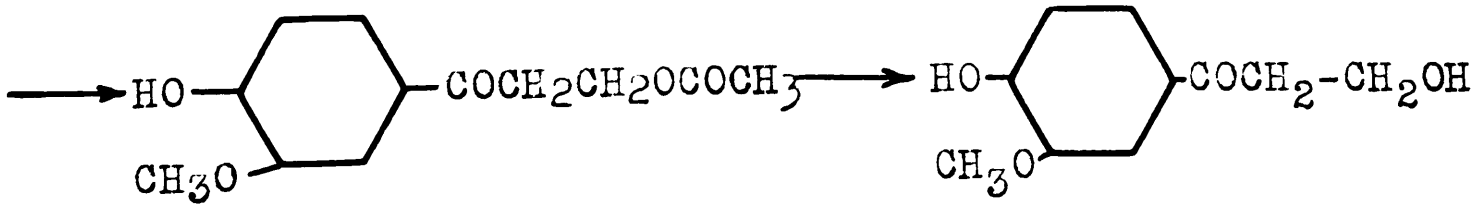


CV. XII.

Method 4.



CIV.



CV. XII.

Method 1. It was not found possible to condense β-chloro propionylchloride with guaiacol in a similar manner to that using veratrol.

Method 2. The attempted Fries rearrangement was abandoned due to inability to synthesize the intermediate ester (CVI).

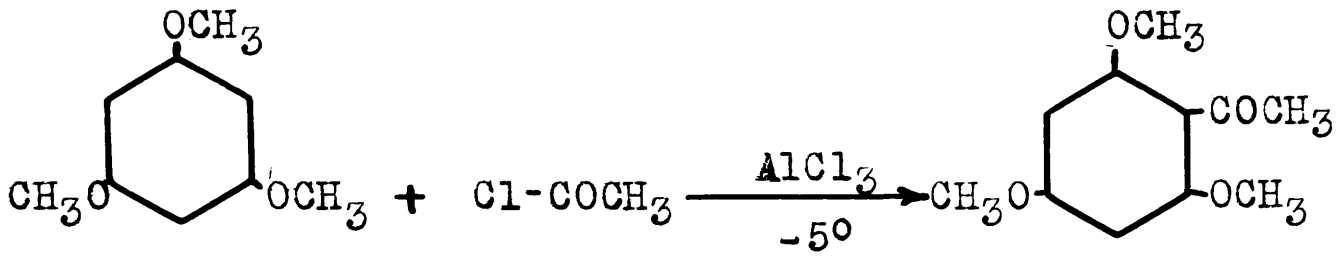
Method 3. This was not fully investigated as a successful synthesis (Method 4) was developed in the meantime. In an attempt to demethylate (CVII) by heating to 45°-47° for twelve hours in the presence of concentrated sulfuric acid (41(b)) the starting material was recovered unchanged. Use of hydriodic acid (Sp. G. 1.70^{15}) at room temperature was also unsuccessful.

A careful review of the literature was made on the use of aluminum chloride as a demethylating agent and the following interesting data compiled in this connection:

The demethylating action of aluminum chloride has long been observed in Friedel-Crafts reactions, and in those involving phenolic ethers prolonged heating is avoided in order to prevent same.

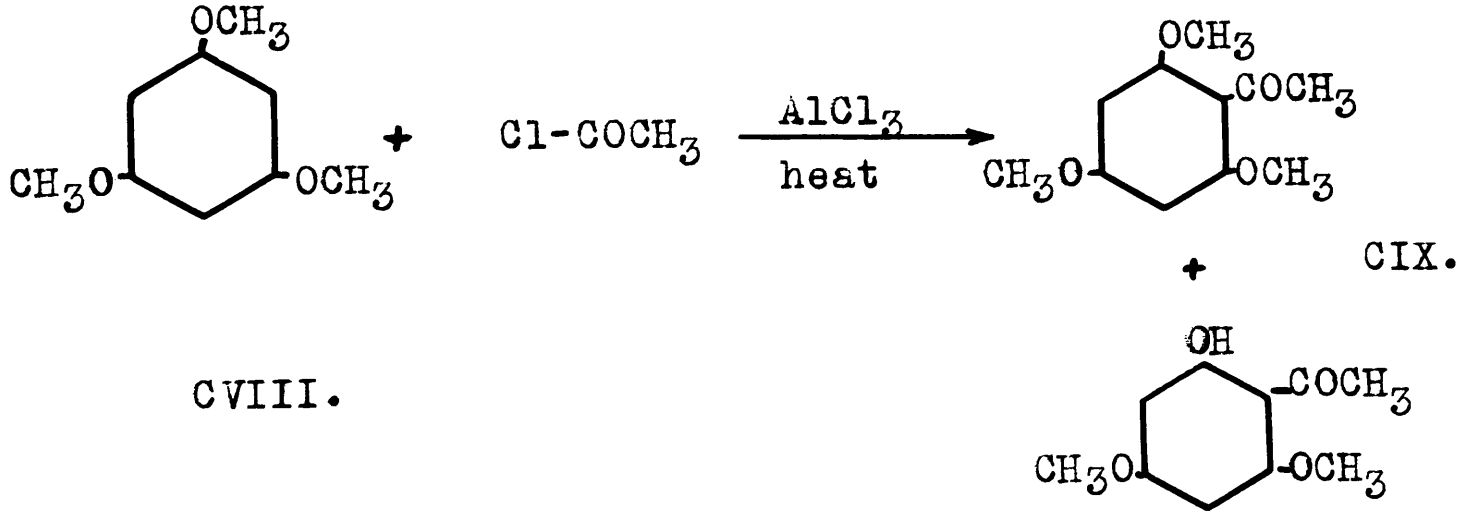
This ether cleavage is well illustrated in the condensation of phloroglucinol trimethyl ether (CVIII) with acetyl chloride in the presence of aluminum chloride. When this reaction is carried out at a low temperature in the

absence of solvent, 2,4,6-trimethoxy acetophenone (CIX) is obtained (126)



CVIII. CIX.

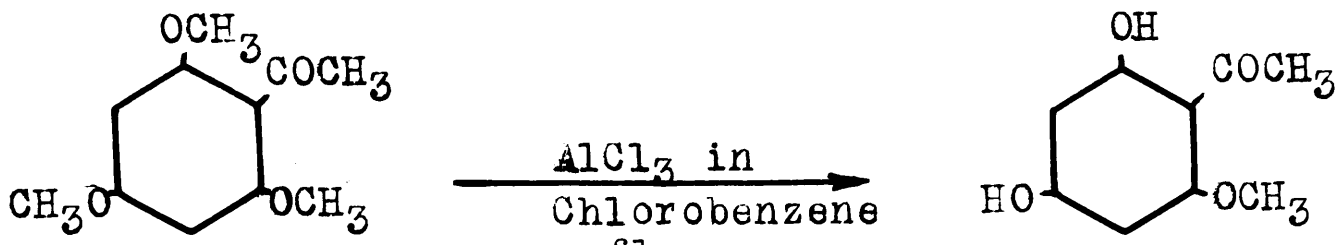
At a temperature of 50° in the presence of petroleum ether, a mixture of the trimethyl ether (CIX) and the dimethyl ether 2-hydroxy-4,6-dimethoxy acetophenone (CX) is obtained (127).



CVIII. CIX.

CX.

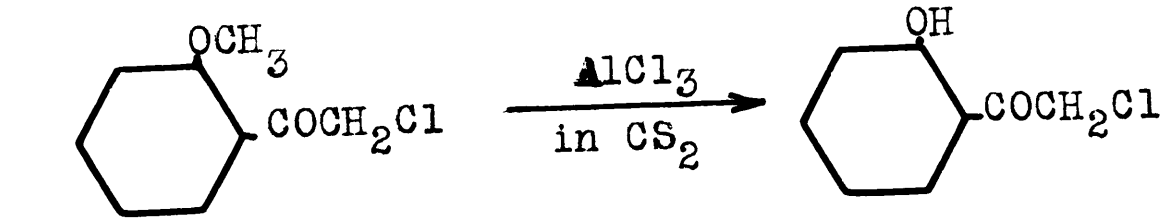
By heating (CVIII) with acetyl chloride and aluminum chloride to 110° for thirty minutes Kostanecki and Tambor (128) also obtained the dimethyl ether (CX). Finally, the monomethyl ether (CXI) was obtained (126) by refluxing the trimethyl ether (CIX) in chlorobenzene with aluminum chloride for one hour.



CIX. CXI.

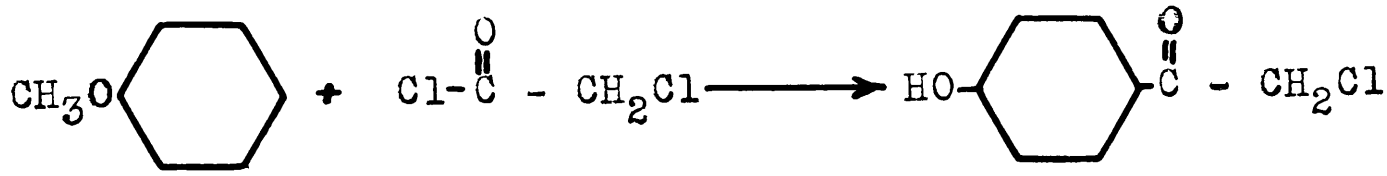
These studies indicate a marked difference in the ease of removal of methyl groups dependent on their position with respect to the acetyl group, the ortho methyl group being most labile.

This cleavage action during Friedel-Crafts reactions was also noted by Tutin (129) in the preparation of o-methoxy chloroacetophenone (CXII) by the condensation of chloroacetyl chloride and anisole. He found it was important to avoid an excess of aluminum chloride and the application of heat due to the marked ease of elimination of the methyl group. He also found (129), that if the methylated product (CXII) was dissolved in carbon disulfide, refluxed for two hours with one molar equivalent of aluminum chloride then heated to 100° for ten minutes in the absence of solvent, the methyl group was removed.

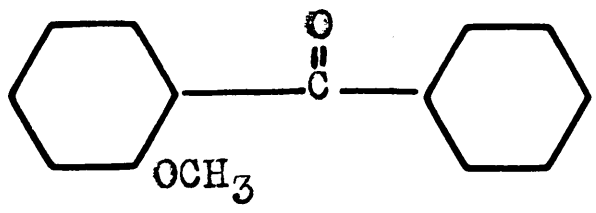


CXII.

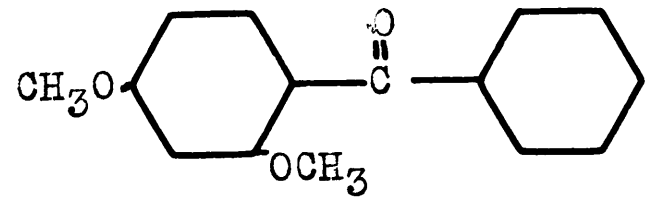
On the other hand, removal of the methyl group from the para isomer of (CXII) is apparently much more difficult. Robertson and Robinson (150) accomplished this during the condensation of anisole and chloroacetyl chloride by heating the mixture with one mol. of aluminum chloride on the steam bath for four hours.



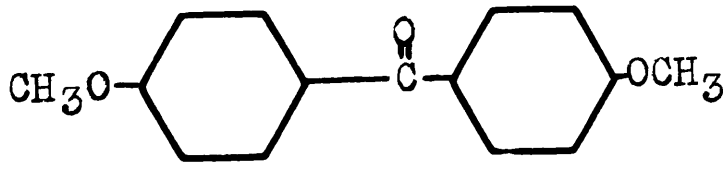
Pfeiffer and Loewe (151) found that aluminum bromide (one mol.) in boiling benzene was a very effective demethylating agent. Thus in the cases(CXIII), (CXIV), (CXV), (CXVI) and (CXVII) demethylation occurred almost quantitatively and (CXVIII) was demethylated to the extent of 72%.



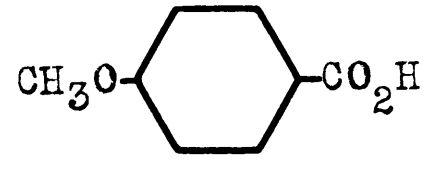
CXIII.



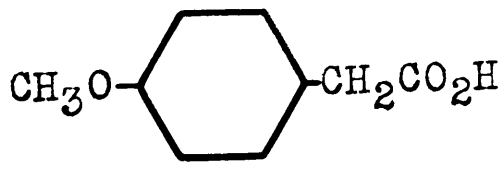
CXIV.



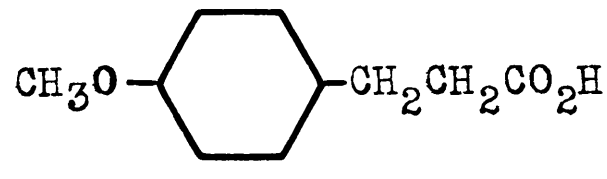
CXV.



CXVI.

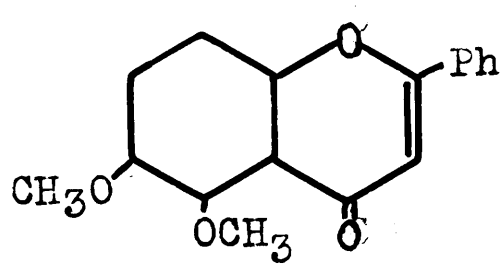


CXVII.

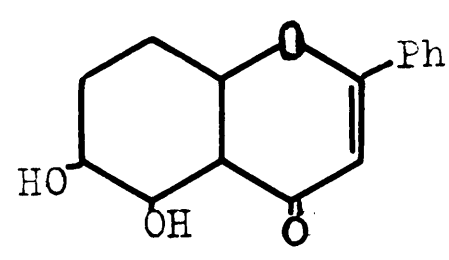


CXVIII.

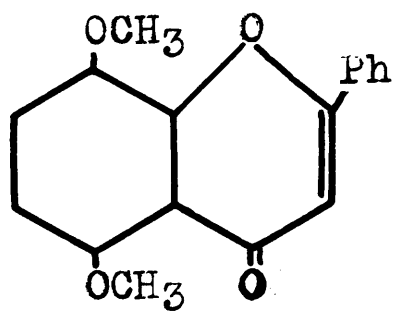
Baker and co-workers (132) have made very extensive use of aluminum chloride as a demethylating agent in the synthesis of a variety of naturally occurring flavones and their derivatives, as, for example, 5,6-dihydroxy flavone (CXIX) (132 (a)) and 5-hydroxy-8-methoxy flavone (CXX) (132 (b)) from 5,6-dimethoxy flavone (CXXI) and 5,8-dimethoxy flavone (CXXII) respectively.



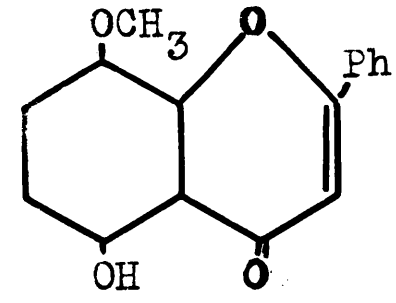
CXXI.



CXIX.



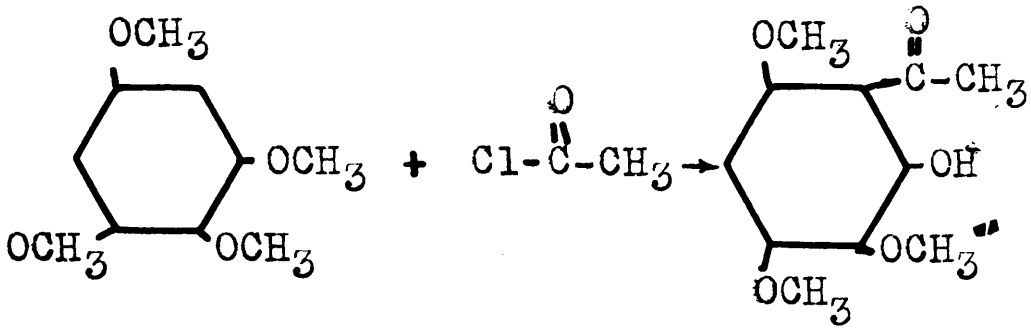
CXXII.



CXX.

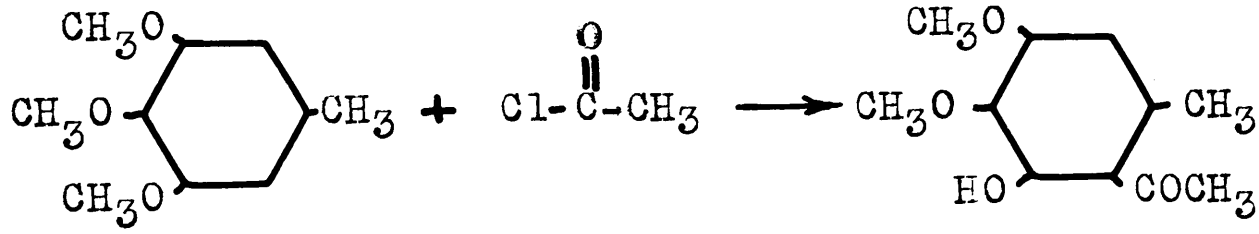
More recently, these workers have made use of a simultaneous condensation and preferential demethylation reaction. Baker (132 (c)) found that 1,2,3,5-trimethoxy benzene (CXXIII) condensed with acetyl chloride in the presence of an ethereal solution of aluminum chloride to

give the partially demethylated product 2-hydroxy-3,4,6-trimethoxy acetophenone (CXXIV).



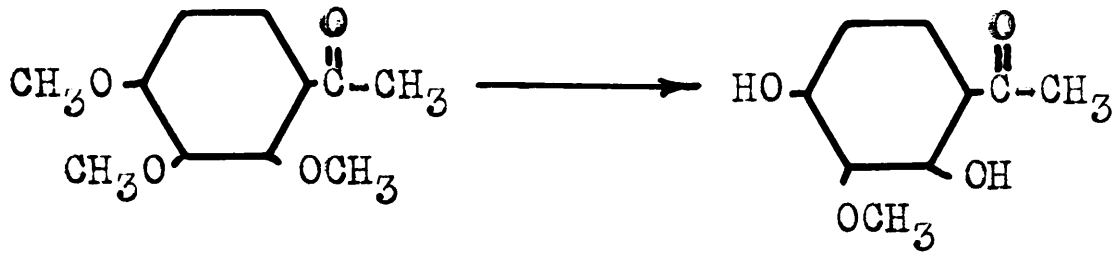
CXXIII. CXXIV.

Similarly (132 (d)) with 1,2,3-trimethoxy-5-methyl benzene (CXXV), the mono hydroxy ketone 1,2-dimethoxy-3-hydroxy-4-acetyl-5-methyl benzene (CXXVI) was formed.



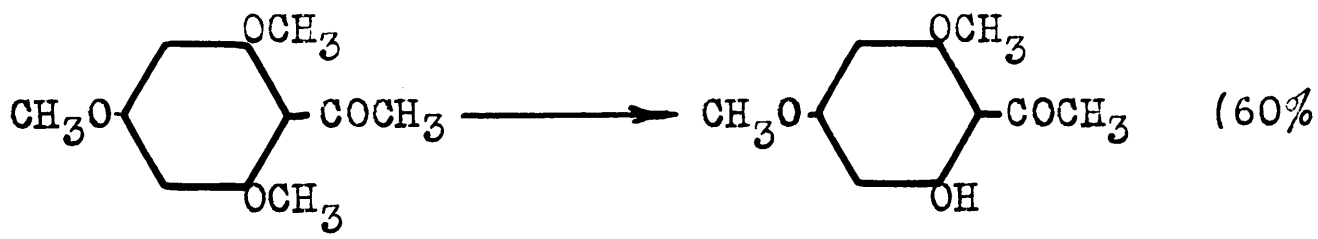
CXXV. CXXVI.

Baker concluded that demethylation of ortho-methoxy ketones by ethereal aluminum chloride involves activation by a carbonyl group in either the ortho or para position. Demethylation in the para position takes place less readily than in the ortho, however it occurred when 2,3,4-trimethoxy acetophenone (CXXVII) was subjected to prolonged action of aluminum chloride in boiling ether solution (132 (c)).



CXXVII.

Hutchins and Wheeler (133) also observed a preferential ease of removal of the ortho methyl group in 2,4,6-trimethoxy acetophenone (CXXVIII).

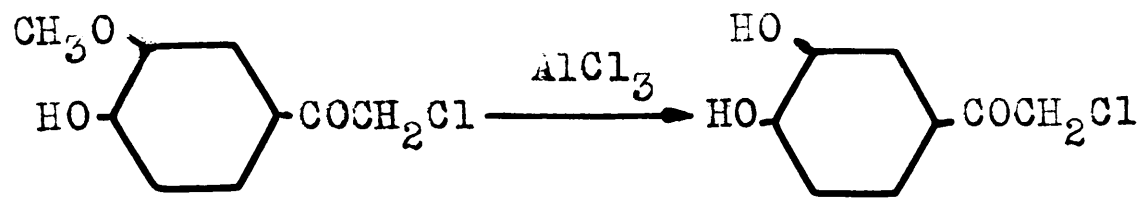


CXXVIII.

Of especial interest to workers in these laboratories is the stability of the methyl group in veratrol during a Friedel-Crafts reaction. Stephen and Weizmann (134) prepared chloraceto-veratrone by condensing chloracetyl chloride with veratrol and aluminum chloride in (a) carbon disulfide, (b) petroleum ether (80-90°) and (c) nitro benzene. While in (a) and (b) a mixture of methylated and unmethylated products was obtained, in (c) an 80% yield of the fully demethylated product was obtained after eight hours' heating at 40°.

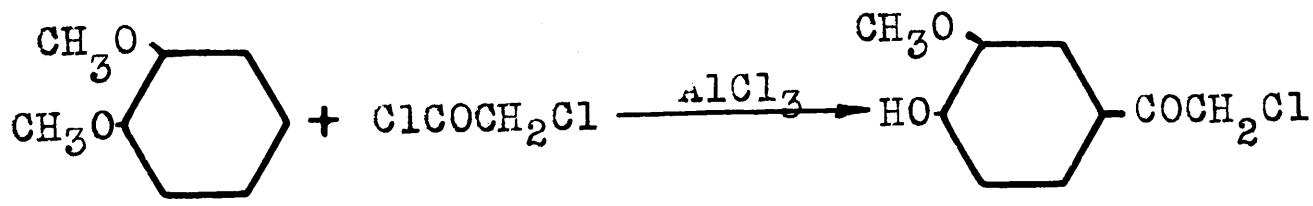
Krannichfeldt (135) found that quite drastic conditions were required to remove the methyl group from the guaiacyl nucleus in chloroacetovanillone (CXXIX), this

necessitating heating at 100° with four mols. of aluminum chloride for eight hours.



CXXIX.

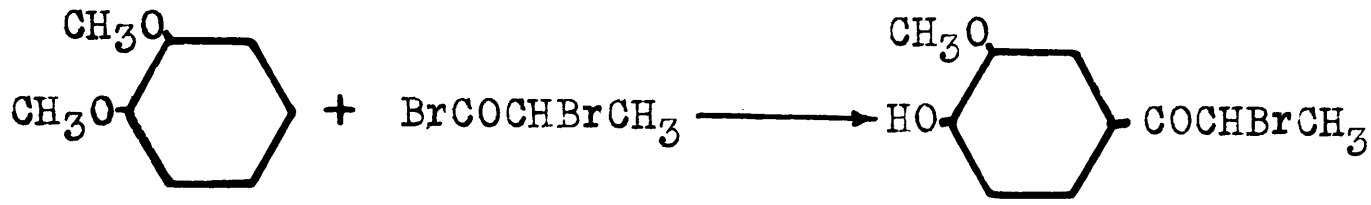
These differences in ease of removal of methyl groups, dependent upon their position in the aromatic nucleus, suggested the possibility of bringing about a preferential demethylation of the methyl groups in the veratryl nucleus with formation of the guaiacyl grouping. Such a reaction had, in fact, already been achieved by Pratt and Robinson (136) in the preparation of chloroacetovanillone (CXXIX) in the condensation of veratrol with chloroacetylchloride.



CXXIX. (60%)

The reaction was carried out at room temperature in the presence of two mols. of aluminum chloride (136).

Cramer and Hibbert (137) used this method in the preparation of α-bromo-propiovanillone from veratrol and α-bromo-propionyl bromide.



(35%)

This simultaneous condensation and demethylation also occurred at room temperature in the presence of two mols. of aluminum chloride (137).

On the basis of these latter two experiments, the synthesis of β-chloropropiovanillone was accomplished as shown graphically in Method 4 (page 83).

The synthesis of the chloro-compound (CIV) (page 82) was accomplished by a simultaneous demethylation-condensation reaction although a higher temperature was necessary than in the analogous syntheses of chloroacetovanillone and α-bromopropiovanillone. In each of the latter two experiments the reaction was brought about at room temperature in the presence of two mols. of aluminum chloride but under these conditions veratrol and β-chloropropionyl chloride condense to give a 75% yield of β-chloropropioveratrone, no appreciable demethylation occurring.

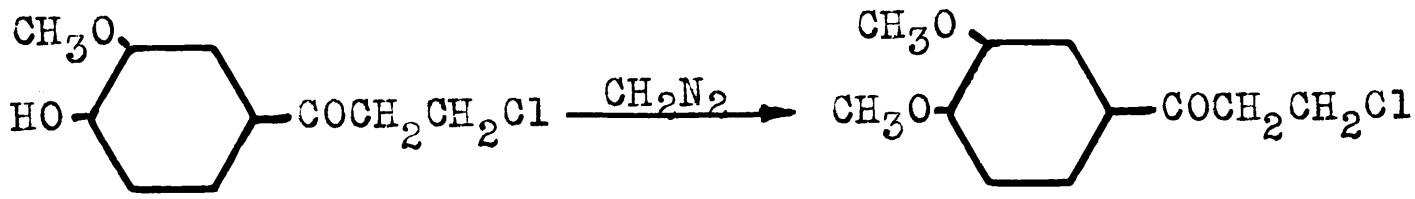
(a) Synthesis of β-Chloropropiovanillone

This was finally synthesized by heating veratrol and β-chloropropionyl chloride in the presence of four mols. of aluminum chloride to 50° for four hours, followed by

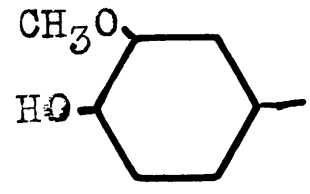
twenty minutes on the steam bath. After two recrystallizations, a 60% yield of the demethylated product was obtained.

(b) Determination of Structure

Compounds (CIV), (CV) and (XII) (page 83) were methylated with diazomethane and the resulting products compared with the corresponding members of the veratryl series, for example,



It was necessary to show that the demethylation took place in the position *para* and not *meta* to the propyl side chain. This was done by ethylating the chloride with diethyl sulfate and alkali followed by permanganate oxidation. The oxidation product was shown to be ethyl vanillic acid by a mixed melting point determination with an authentic sample thereby confirming the structure of the nucleus as



(c) Conversion of the Chloride to the Hydroxy Derivative

The chloride (XXXI) was readily converted into the crystalline acetate (CV) on treatment with potassium acetate and glacial acetic acid, and the acetate in turn, into the crystalline β-hydroxypropiovanillone (XII) on

refluxing with aqueous barium carbonate. Although the conditions of deacetylation were varied over a wide range it was impossible to obtain a higher yield than approximately 60% of the β-hydroxypropiovanillone. This is presumably due to two factors (1) the effect of alkali on β-hydroxy-propiovanillone as discussed below, and (2) the ease of oxidation of the guaiacyl nucleus in alkaline solution.

4. Properties of β-Hydroxypropiovanillone

β-Hydroxypropiovanillone, as was to be expected from the point of view of its suggested function as a plant respiratory catalyst (page 24) was found to be a very reactive substance.

The primary hydroxyl group in the side chain is readily etherified with ethanolic hydrogen chloride but does not react with diazomethane. The action of the former reagent, under conditions of the standard wood ethanolysis, gave a high yield (80%) of β-ethoxypropiovanillone together with an amorphous lignin-like product (15%). The β-ethyl ether exists in two 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) into (A) either by drying at room temperature or heating on the steam bath at ordinary pressures. The low-melting modification is the

true β-ethyl ether as shown by analysis whereas the other form apparently contains solvent of crystallization.

Treatment of β-hydroxy propiovanillone with sulfuric acid under the conditions employed in the Klason lignin determination gave about a 50% yield of an amorphous lignin-like product. Carbon, hydrogen and methoxyl analyses are in good agreement with the values obtained by Klason (142) for a lignin obtained by treatment of spruce wood with 72% sulfuric acid. Treatment with dilute sulfuric acid (5%) and with dilute alkali (1% NaOH) also resulted in the formation of similar "lignins".

An attempt was made to prepare guaiacyl vinyl ketone (CXXX) by dehydration of β-hydroxy propiovanillone, by heating the latter with a trace of iodine following the method of Hibbert (138).

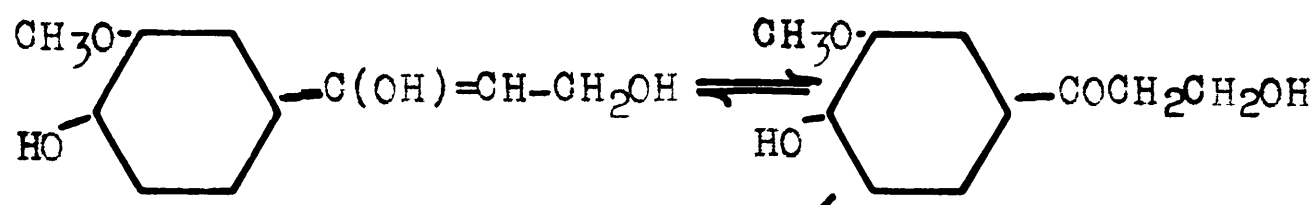
$$RCOCH_2CH_2OH \longrightarrow RCOCH = CH_2$$

CXXX.

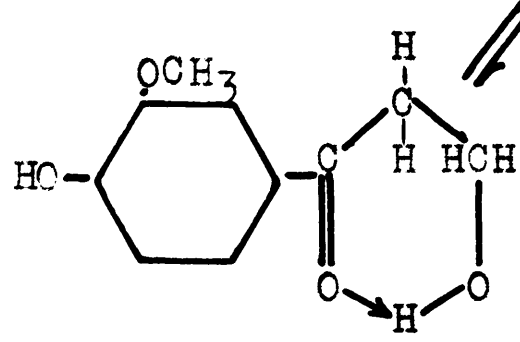
A crystalline product (20%) was extracted from the reaction mixture but methoxyl analysis indicated that this was not the desired product (CXXX). (Methoxyl analysis: Calc'd for (CXXX), 17.5; found, 16.7). The methoxyl content indicates that one molecule of water may have split off between two molecules of (XII) giving rise to an ether of the type $RCOCH_2CH_2$-O-CH_2-CH_2OC-R (CXXIII) (OMe: 16.6%). However, time did not permit of

further investigation of the structure of this compound.

In the light of these experimental findings it is of interest to examine the structure of β-hydroxypropiovanillone more closely, especially with respect to certain of its stereochemical properties and possible enol-configuration (CXXXI).



CXXXI. XII.



CXXXII.

The indicated presence of unsaturation as well as of an active hydrogen and hydroxyl group as seen in (CXXXI), (XII) and (CXXXII) suggests the following reaction tendencies;

(1) Intramolecular dehydration to give the vinyl derivative (CXXX).

(2) Intermolecular dehydration to produce the dimeric ether (CXXXIII). Such a reaction is typical of unsaturated alcohols of the cinnamyl alcohol type (85) (the enolic form (CXXXI) of β-hydroxypropiovanillone is both an oxyconiferyl alcohol and a substituted cinnamyl alcohol).

(3) β-Hydroxypropiovanillone should undergo

polymerization-condensation reactions, especially in the presence of alkalis. The tendency of a carbonyl group attached to an aromatic nucleus to undergo aldol formation (followed by spontaneous loss of water) with an alkyl radical containing an active hydrogen such as $H_2C(COOEt)_2$; $C_6H_5CH_2CN$; CH_3COCH_3; $C_6H_5COCH_3$; $C_6H_5COCH_2CH_3$ etc., is well known as for example in the case of benzaldehyde and acetophenone

$$C_6H_5CHO + CH_3COC_6H_5 \rightleftharpoons C_6H_5CHOHCH_2COC_6H_5$$

$$\Big\downarrow -H_2O$$

$$C_6H_5CH = CHCOC_6H_5$$

β-hydroxy propiovanillone might therefore be expected to undergo a similar condensation with itself to give a bimolecular condensation product of the type

$$2R.CO.CH_2.CH_2OH \longrightarrow R.C(CH_2-CH_2OH) = C(CH_2OH)-COR$$

This dimer could then react with further molecules to give a trimer, tetramer, etc.,

$$R-C(CH_2-CH_2OH)=C(CH_2OH)-C(R)=C(CH_2OH)-CO-R$$

each characterized by an increasing number of conjugated linkages. Ample opportunity would thus be afforded for the formation of a more complex, cross-linked type of polymer

characterized by a diminishing number of unsaturated linkages. A polymer of this general type may well be that represented by "alkali lignin" .

(4) From the point of view of the possible enolic character of β-hydroxy propiovanillone, its existence as oxy-coniferyl alcohol (CXXXI) would imply a relationship to allyl alcohol H-CH=CH-CH_2OH and hence the possibility of an allyl shift under the influence of suitable reagents.

$$RC(OH)=CH-CH_2OH \rightleftharpoons RC(OH)_2-CH=CH_2 \underset{+H_2O}{\overset{-H_2O}{\rightleftharpoons}} R-CO-CH=CH_2$$

CXXX.

The resulting vinyl ketone (CXXX) is also a conjugated derivative and might be expected to undergo polymerization into more complex products.

Conclusions

While a complete examination of the properties of β-hydroxy propiovanillone was not carried out, the author's experimental results are in general harmony with the foregoing speculations. Thus,as a 1-3-hydroxy ketone, in which the carbonyl group is attached directly to the benzene nucleus, β-hydroxy propiovanillone contains abnormally active hydrogen atoms and a very reactive hydroxyl group as shown
(1) in the remarkable ease of etherification of its acetoxy derivative by alcohols in the presence of alkali to give the

β-ethers R-CO-$CH_2CH_2OR_1$ (R_1 = methyl or ethyl) (page 81); (2) by its very marked ease of alkylation on refluxing with alcohols in the presence of hydrogen chloride (2%) (page 80); and (3) by its conversion, in high yield, into amorphous lignin-like products in the presence of acids and alkalis (page 82).

III.

EXPERIMENTAL

A. Ethanolysis of Lignin Building Units

The ethanolysis of α-hydroxypropiovanillone is given in detail as an example of the procedure used throughout this work. In certain cases, where large amounts of the particular lignin building units were not available, stability determinations were carried out using only 0.15 g. of material. Such small scale runs, however, gave results comparable to those obtained when larger quantities were employed.

α-Hydroxypropiovanillone (1.00 g.) was refluxed with 2% ethanolic hydrogen chloride in an atmosphere of carbon dioxide for forty-eight hours in an all-glass apparatus. The reaction mixture was cooled, neutralized with sodium ethoxide, the solvent removed under reduced pressure and the residue taken up in chloroform (5 cc.). The chloroform solution was filtered to remove inorganic salts and the amorphous lignin-like product precipitated by pouring the filtrate, in a fine stream, into 30-50° petroleum ether (5 cc.). It was removed by centrifugence and the supernatant liquor taken to dryness. The residual reddish oil was dissolved in chloroform and again precipitated into 30-50° petroleum ether. A small amount of amorphous precipitate was removed as above

and combined with that obtained previously; yield, 4%, based on weight of starting material.

On removal of the solvent from the petroleum ether-chloroform solution left after the second precipitation, a golden-colored oil remained which on methylation with diazomethane gave a white, crystalline product; m.p. 81-82°; mixed melting point with authentic α-ethoxypropioveratrone showed no depression; recovery 90%, based on α-hydroxypropiovanillone.

A modified procedure in which the neutralized reaction mixture was concentrated, filtered, and then precipitated directly into 30-50° petroleum ether gave values, both for the percentage of low boiling oils and of amorphous product, agreeing closely with the first procedure.

The results obtained with the various lignin building units are given in Table I, page 102.

TABLE I.

REACTION OF LIGNIN BUILDING UNITS AND THEIR DERIVATIVES WITH 2% ETHANOLIC HYDROGEN CHLORIDE.

	Lignin building unit	Concn., %	Percentage yield of Polymer	Monomer	Monomer identified as
(1)	α-Hydroxypropiovanillone	0.2	4	90	α-Ethoxypropioveratrone
		.6	13	83	α-Ethoxypropioveratrone
		1.0	20,18[a]	71,76[a]	α-Ethoxypropioveratrone
		4.0	33	60	α-Ethoxypropioveratrone
(2)	Vanilloyl methyl ketone	0.2	4	91	Vanilloyl methyl ketone
		.6	9	88	Vanilloyl methyl ketone
		1.0	13	83	Vanilloyl methyl ketone
		4.0	30	65	Vanilloyl methyl ketone
(3)	α-Acetoxypropiovanillone	4.0	20	74	----------
(4)	Mixture of (1) and (2)	0.2(1),0.1(2)	4	90	----------
(5)	α-Hydroxypropiosyringone	1.0	43	55[a]	p-Nitrobenzoate of α-ethoxypropiosyringone
(6)	Syringoyl methyl ketone	1.0	26	73[a]	Syringoyl methyl ketone
(7)	α-Acetoxypropiosyringone	1.0	76	20[a]	p-Nitrobenzoate of α-ethoxypropiosyringone
(8)	Mixture of (5) and (6)	0.5 (5,6)	20	80[a]	Syringoyl methyl ketone

[a] These values were obtained by the modified procedure described in the experimental section.

B. Ethanolysis of Maple Ethanol Lignin Fractions

Each of the maple ethanol lignin fractions was treated as follows.* The water-soluble fraction (1.00 g.) was refluxed with 2% ethanolic hydrogen chloride (200 cc.) in an atmosphere of carbon dioxide for forty-eight hours in an all-glass apparatus. The reaction mixture was cooled, neutralized with sodium ethoxide and the solvent removed under reduced pressure in an inert atmosphere at a temperature below 25°. The residual amorphous product was dissolved in chloroform (10 cc.) and the inorganic salts removed. Precipitation of the filtrate into 30-50° petroleum ether yielded an amorphous lignin. This was removed by centrifugation and reprecipitated from acetone into petroleum ether; yield, 0.720 g. or 72% recovery.

The petroleum ether-chloroform liquors from both precipitations were combined and the solvents removed leaving a reddish oil; yield, 0.304 g. or approximately 30% conversion to petroleum ether-soluble oils, (Table II).

Table II

Reaction of Maple Ethanol Lignin Fractions with 2% Ethanolic Hydrogen Chloride

Fraction of maple ethanol lignin	Conc., %	Percentage yield of amorphous lignin	Percentage yield of low boiling oils	Viscosity of lignin fraction before treatment	Viscosity of lignin fraction after treatment
I Water soluble	0.5	72	30	389	538
II Ether-soluble	.5	75	22	469	541
III Ether-insoluble	.5	87	12	600	...

C. Synthesis of β-Hydroxypropioveratrone

1. Preparation of β-Chloropropioveratrone (modification of Freudenberg's method (124))

Veratrol (6.0 g.) was added to a suspension of aluminum chloride (5.0 g.) in carbon disulfide (40 cc.) in a three-necked flask equipped with a stirrer, a dropping funnel and a condenser. β-chloropropionyl chloride (5.0 g.) was added slowly while the reaction mixture was stirred vigorously at room temperature. When this addition was completed a further 5.0 g. of aluminum chloride was added, the reaction mixture heated to 40° for one hour and allowed to stand overnight at room temperature. The carbon disulfide was decanted off and the reaction product decomposed by pouring on to a mixture of chipped ice (500 g.) and concentrated hydrochloric acid (40 cc.). The mixture was stirred vigorously for three hours and filtered. The resulting white crystalline product was washed several times with 5% sodium carbonate solution and finally with water. The dried product melted at 109-111°. Yield = 6.7 g. (75%). On recrystallization from ethanol this product melted at 113-114° in agreement with Freudenberg's value (124).

2. Preparation of β-Acetoxypropioveratrone

Method I - Action of Sodium Acetate and Acetic Anhydride on β-Chloropropioveratrone

A mixture of β-chloropropioveratrone (5.0 g.), anhydrous sodium acetate (10.0 g.) and acetic anhydride (35 cc.) was heated on a steam bath for four hours, cooled, poured into a mixture of ice and water (500 g.) and stirred vigorously for three hours. After standing overnight the aqueous solution was neutralized with sodium carbonate and the precipitate which had separated removed by filtration. After washing with water and drying, the crude product (5.4 g.) was extracted with hot methanol leaving an insoluble rubber-like residue. The acetoxy derivative crystallized from the methanol solution on cooling as a colorless crystalline product, m.p. 99-100°. Yield = 15%.

Methoxyl Analysis

Calc'd. for $C_{15}H_{16}O_5$: 24.6%. Found 24.4%.

Method 2 - Action of Potassium Acetate and Glacial Acetic Acid on β-Chloropropioveratrone

A mixture of β-chloropropioveratrone (5.5 g.), freshly fused potassium acetate (12.7 g.) and glacial acetic acid (50 cc.) was heated on a steam bath for twelve hours, cooled, and poured into a mixture of ice and water (500 g.).

A heavy white crystalline material separated out almost immediately. Recrystallization from methanol gave 4.0 g. (70%) of β-acetoxypropioveratrone. m.p. 99-100°.

A small portion of this product was recrystallized repeatedly from ether and from methanol to give a pure sample for analysis, m.p. 100-101°.

Analysis

Calc'd. 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.

A mixed melting point of this product and the product obtained by method I showed no depression.

3. Attempted Deacetylation of β-Acetoxypropioveratrone

Method 1 - Zemplén Method

(a) β-Acetoxypropioveratrone (0.6 g.) was dissolved in a solution of sodium methylate (formed by solution of two milligrams of sodium in absolute methanol (15 cc.)) and the reaction mixture refluxed for seven minutes. On cooling, a white crystalline product separated and this was shown to be unchanged starting material by a mixed melting point determination.

(b) The procedure was repeated and the time of heating extended to fifteen minutes. Again the original product was recovered unchanged.

Method 2 - 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 solvent removed under reduced pressure. The crystalline residue was thoroughly washed with water, filtered and dried. Yield, 1.08 g. (90%), m.p. 68-70°. Recrystallization from 30-50° petroleum ether gave pure β-methoxypropioveratrone. m.p. 70-71°.

Analysis

Calc'd. 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.

Method 3 - Action of Ethanolic Potassium Hydroxide

Substitution of ethanol for methanol as solvent in the above experiment gave the corresponding β-ethyl ether; m.p. 50-51°. A mixed melting point with an authentic sample of β-ethoxypropioveratrone prepared by the action of sodium iodide and ethanol on β-chloropropioveratrone (41 (a)) showed no depression.

Analysis.

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

Method 4 - Action of Sodium Carbonate in Aqueous Dioxane Solution

β-Acetoxypropioveratrone (1.2 g.) was dissolved in aqueous dioxane (1:1) (100 cc.) containing sodium carbonate (2.0 g.). After standing at room temperature for fourteen hours, the mixture was neutralized with dilute acetic acid then extracted with benzene. On evaporation of the solvent a crystalline residue was left which on recrystallization from ether melted at 88-90°. Yield 0.60 g. (60%). Alternate recrystallizations from ether and from methanol gave a pure, crystalline product which corresponded in its analyses to the suggested ethylene oxide structure (CIII) (page 79) m.p. 93-94°.

Analysis.

Calc'd. 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. 182-185°.

Analysis.

Calc'd. 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.

4. Conversion of β-Chloropropioveratrone into β-Hydroxypropioveratrone by Refluxing with Aqueous Silver Oxide.

β-Chloropropioveratrone (2.5 g.) and silver oxide (1.5 g.) were refluxed for ten hours with distilled water (300 cc.). The reaction mixture was cooled, filtered and continously extracted with ether for ten hours. After drying over sodium sulfate, the ether extract was concentrated, giving a white crystalline product. Yield 1.19 g. (50%). M.p. 78-80°. By repeated recrystallizations from ether and 30-50° petroleum ether pure β-hydroxypropioveratrone m.p. 83-84° was obtained.

Analysis.

Calc'd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.66; OMe, 29.5.

Found: C, 62.5; H, 6.82; OMe, 29.3.

D. Properties of β-Hydroxypropioveratrone

1. Action of Ethanolic Hydrogen Chloride

β-Hydroxypropioveratrone (0.50 g.) was refluxed with 2% ethanolic hydrogen chloride (25 cc.) for forty-eight hours under an atmosphere of carbon dioxide. 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 very small amount of amorphous precipitate was removed by centrifugence, and the solution taken to dryness, leaving an oil which crystallized on standing. Recrystallization from 30-50° petroleum ether gave β-ethoxypropioveratrone as shown by a mixed melting point determination with an authentic sample. M.p. 47-49°. Yield = 0.50 g. (96%). On recrystallization from 30-50° petroleum ether this product melted at 50-51°.

2. Action of Methanolic Hydrogen Chloride

β-Hydroxypropioveratrone (0.50 g.) was refluxed with 2% methanolic hydrogen chloride (25 cc.) for forty-eight hours under an atmosphere of carbon dioxide. The reaction mixture was neutralized with sodium ethoxide, the methanol removed at reduced pressure, and the residue extracted with hot petroleum ether. From this solution, on cooling, a crystalline product

(m.p. 67-69°) was obtained. Yield 75%. Repeated recrystallizations from 30-50° petroleum ether gave pure β-methoxypropioveratrone. M.p. 70-71° (mixed melting point with the corresponding product from (III. C-3 Method 2) showed no depression).

3. Action of Methanolic Potassium Hydroxide

β-Hydroxypropioveratrone (1.0 g.) was mixed with 4% methanolic potassium hydroxide (65 cc.) and the mixture allowed to stand at room temperature for thirty-minutes. It was neutralized with dilute acetic acid, the methanol removed at reduced pressure, and the solid residue shaken with a mixture of benzene and water to dissolve the product and inorganic salt, respectively. The benzene layer was separated, thoroughly washed, then dried and the solvent removed. The residual oil was extracted with hot petroleum ether (30-50°) leaving a large amount of insoluble residue. On cooling the petroleum ether extract a crystalline product separated. Yield = 0.100 g. (10%) m.p. 67-69°. A mixed melting point determination with the β-methyl ether (from III C-3 Method 2) showed no depression.

4. Action of Concentrated Sulfuric Acid

β-Hydroxypropioveratrone (0.50 g.) was treated for two hours 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%).

E. Synthesis of β-Hydroxypropiovanillone

1. Attempted Preparation by Condensation of Guaiacol and β-Chloropropionyl Chloride using Aluminum Chloride

A Friedel-Crafts condensation of guaiacol with β-chloropropionylchloride under conditions similar to those used in the condensation of veratrol with β-chloropropionyl chloride (III C-1 page 104) was unsuccessful. The light-colored residual oil (b.p. 40-45°/0.100 mm.) could not be crystallized and gave no carbonyl reaction indicating that condensation had not occurred.

2. Attempted Preparation of Guaiacol β-Chloropropionate ($C_6H_4(OCH_3)(OCOCH_2CH_2Cl)$)

(a) Action of Heat on a Mixture of Guaiacol and β-Chloropropionyl Chloride

Guaiacol (11.0 g.) and β-chloropropionyl chloride (10.0 g.) were heated on the steam bath for five hours, then allowed to stand overnight at room temperature. The reaction mixture was dissolved in ether (50 cc.), washed well with 1% sodium hydroxide and with water, dried over sodium sulfate and the ether removed, leaving a light-colored oil (12.2g.). This was

distilled at 50-100°/0.020-0.100 mm. Attempts to fractionate the distilled product by use of a Widmer column were unsuccessful, the product again distilling over the range 55-90°/0.010-0.020 mm. Also, its methoxyl content (12.1%) indicated that this was not the desired product (OCH_3, 14.4% calc'd.).

(b) Attempted Condensation of Guaiacol with β-Chloropropionyl Chloride in the Presence of Pyridine

β-Chloropropionyl chloride (5 g.) was added to a mixture of guaiacol (7.0 g.) and pyridine (7 cc.) and allowed to stand overnight at room temperature. It was poured into a mixture of ice (500 g.) and concentrated hydrochloric acid (50 cc.), the aqueous solution extracted with benzene and the benzene extract washed well with a 5% sodium carbonate solution and with water. Removal of the solvent left a light colored oil (5.0 g.) which on distillation (100-105°/30 mm.) yielded a very mobile water-white liquid. Its methoxyl content (20.6%) indicated it was not the desired product.

(c) Condensation of the Sodium Salt of Guaiacol with β-Chloropropionyl Chloride

β-Chloropropionyl chloride (2.6 g.) was added dropwise to a suspension of the sodium salt of guaiacol (5.0 g.) in toluene (20 cc.). When the addition had been completed, water was added and the aqueous and toluene layers

separated. The toluene extract was washed well with 2% sodium hydroxide then with water, the toluene removed and the residual oil (2.2 g.) distilled at 70-85°/0.100-0.150 mm. The methoxyl content (12.6%) of the distillate again indicated that it was not the desired product.

5. Attempted Demethylation of β-Chloropropioveratrone

(a) Use of Concentrated Sulfuric Acid

β-Chloropropioveratrone (1.0 g.) was heated for sixteen hours at 50-55° with concentrated sulfuric acid (5 cc.). The reaction mixture was cooled and poured on to ice (100 g.). A bluish-grey crystalline precipitate separated which on recrystallization was found to be unchanged starting material.

(b) Use of Hydriodic Acid

β-Chloropropioveratrone (1.5 g.) was treated for twelve hours at room temperature with hydriodic acid (Sp.G. 1.7^{15}) (15 cc.). The reaction mixture was then poured on to a mixture of ice and water and the precipitate filtered off. This was shown to be unchanged starting material by melting-point and mixed-melting point determination.

4. Preparation of β-Chloropropiovanillone by Condensation of Veratrol with β-Chloropropionyl Chloride by use of Aluminum Chloride

Aluminum chloride (18.0 g.) was added to a mixture of veratrol (15.0 g.) and carbon disulfide (40 cc.) in a three-necked flask equipped with a stirrer, dropping funnel and condenser. The reaction mixture was surrounded by cold water and β-chloropropionyl chloride (15.0 g.) then added slowly through the dropping funnel while the reaction mixture was stirred continually. When this addition was completed, three more portions of aluminum chloride (18.0 g. each) were added at five minute intervals. The mixture was heated at 50° for four hours, the solvent removed and the residue heated on the steam bath for twenty minutes. After cooling, the complex was decomposed by stirring for six hours with ice and concentrated hydrochloric acid, with formation of a dark colored product. This was filtered, washed well with dilute hydrochloric acid and then with water. The crude product was dried as thoroughly as possible by suction filtration, then crystallized from methanol after first decolorizing with charcoal. It was recrystallized from ether and the ether filtrate concentrated, cooled and the second crop of crystals again removed by filtration. The combined yield of β-chloropropiovanillone (m.p. 96-98°) was 15.0 g. (60%).

A small amount was repurified for analysis by repeated recrystallizations from ether and from methanol (m.p. 101-102°).

Analysis.

Calc'd. for $C_{10}H_{11}O_3Cl$: C, 56.0; H, 5.13; OMe, 14.4.
Found: C, 56.0; H, 5.30; OMe, 14.4.

(a) Proof of the Presence of the Guaiacyl Nucleus

(1) Diazomethane Methylation

The assumed β-chloropropiovanillone (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 around 2-3 cc, cooled, and the crystalline product separating out, filtered and dried. Yield = 0.39 g. (82%). It was shown to be β-chloropropioveratrone by a mixed melting point determination with the product from (III C-1, page 104).

(2) Ethylation and Oxidation

Diethyl sulfate (7.0 g.) was added to a solution of β-chloropropiovanillone (2.0 g.) in 1.5% aqueous sodium hydroxide solution (20 cc.) and the mixture refluxed for ninety minutes. The alkali insoluble portion was dissolved in

chloroform and the solvent removed leaving a light colored oil.

An aliquot (0.250 g.) of this was suspended in 2% aqueous sodium hydroxide (50 cc.) and aqueous potassium permanganate (1.125 g. in 25 cc. H_2O) added slowly to the well stirred reaction mixture at 100° during about two hours. The precipitated manganese dioxide was removed and the filtrate acidified and cooled. A crystalline product separated (m.p. 189-191°) and this was recrystallized from dioxane (m.p. 193-194°). A mixed melting point with an authentic sample of ethyl vanillic acid showed no depression.

5. Conversion of β-Chloropropionyl Chloride into β-Acetoxypropiovanillone

A mixture of β-chloropropiovanillone (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 continual stirring. The reaction mixture was cooled and poured into 500 cc. of ice-water, stirred for two hours and allowed to stand in the cold room for forty-eight hours. The crystalline β-acetoxypropiovanillone which separated was filtered and dried. M.p. 76-78°; yield 14.0 g. (67%).

On repeated recrystallization from chloroform-petroleum ether (30-50°) the melting point was raised to 80-81°.

Analysis.

Calc'd. for $C_{12}H_{14}O_8$: C, 60.5; H, 5.98; OCH_3, 13.0.
Found: C, 60.5; H, 6.14; OCH_3, 13.1.

(a) Methylation with Diazomethane

β-Acetoxypropiovanillone (0.300 g.) was methylated with an ethereal solution containing two equivalents of diazomethane. An 80% yield of β-acetoxypropioveratrone was obtained, its identity being proven by a mixed melting point determination with the product synthesized above (III C-2 page 105).

6. Hydrolysis of β-Acetoxypropiovanillone to β-Hydroxypropiovanillone

The acetate (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 then continuously extracted with benzene. On concentrating and cooling the benzene solution, β-hydroxypropiovanillone separated as a white crystalline product. M.p. 107-109°. Yield = 6.3 g. (55%).

After repeated recrystallizations from benzene the product melted at 109-110°.

Analysis

Calc'd. for $C_{10}H_{12}O_4$: C, 61.2; H, 6.12; OCH_3, 15.8. Found: C, 61.4; H, 6.08; OCH_3, 15.7.

Methylation with diazomethane gave β-hydroxypropioveratrone identified by a mixed melting point determination with the previous product (III C-4, page 109).

F. Properties of β-Hydroxypropiovanillone

1. Action of Ethanolic Hydrogen Chloride

β-Hydroxypropiovanillone (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 from sodium chloride and precipitated with vigorous stirring into 30-50° petroleum ether (200 cc.). The amorphous precipitate was removed by centrifugence and dried. Wt. = 0.30 g. (15%) (% OMe, 19.0).

The petroleum ether-ethanol solution was taken to dryness leaving a light colored oil which crystallized (m.p. 35-37°) on sustained scratching. Yield = 1.80 g. (80%). It was shown by methylation (see below) to be β-ethoxypropiovanillone. Recrystallization of this product from ether gave a product (m.p. 72-74°) which reverted to the

original product (m.p. 55-57°) on drying at 65°/20 mm.

Analysis

Calc'd. for β-ethoxypropiovanillone ($C_{12}H_{16}O_4$): C, 64.3; H, 7.14; Alkoxyl calc'd as methoxyl, 27.7.

Found: C, 64.5; H, 7.54; Alkoxyl calc'd as methoxyl, 27.6.

(a) Methylation with Diazomethane

The β-ethoxypropiovanillone (0.275 g,) prepared above was methylated with an ethereal solution containing two equivalents of diazomethane. Crystalline β-ethoxypropioveratrone (0.25 g.)(86%) was obtained and identified by a mixed melting point determination.

2. Action of Acids

(a) Concentrated Sulfuric Acid (72%)

β-Hydroxypropiovanillone (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%).

Analysis

Found : C, 66.2; H, 6.0; OMe, 16.0. Found for "Klason Lignin" C, 66.67; H, 5.49; OMe, 14.47 (142).

(b) Dilute Sulfuric Acid (5%)

β-Hydroxypropiovanillone (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 %).

3. Action of Sodium Hydroxide (1%)

β-Hydroxypropiovanillone (0.100 g.) was refluxed for twenty-four hours with an aqueous sodium hydroxide solution (1%) (10 cc.). The mixture was cooled and acidified and the dark colored amorphous precipitate filtered, washed and dried. Yield = 0.040 g. (40%).

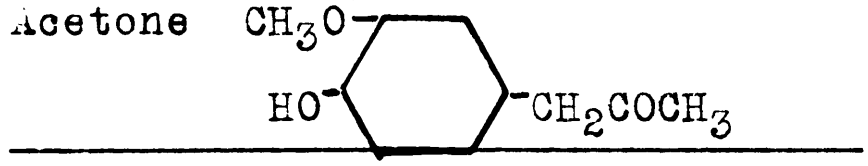
4. Action of Iodine

β-Hydroxypropiovanillone (0.500 g.) was heated at 110° for twenty minutes in the presence of a trace of iodine (0.015 g.). The reaction mixture was extracted with hot benzene leaving a dark insoluble residue. On removing the benzene solution a light colored oil (0.56 g.) was obtained which could not be caused to crystallize. It did not adsorb bromine from a chloroform solution indicating the absence of unsaturation. On solution in hot methanol and cooling, a crystalline product (A) (0.11 g.) and an oil (B) separated out. It was not found possible to induce crystallization of

the latter. Both products (A) and (B) were tested for unsaturation with a chloroform solution of bromine and gave negative results. Repeated recrystallization of (A) from methanol gave an apparently pure product melting at 153-155° and containing methoxyl (16.7%). This latter value pointed to the structure of the substance as a di-ether formed from two molecules of β-hydroxypropiovanillone by loss of one molecule of water (CXXIII).

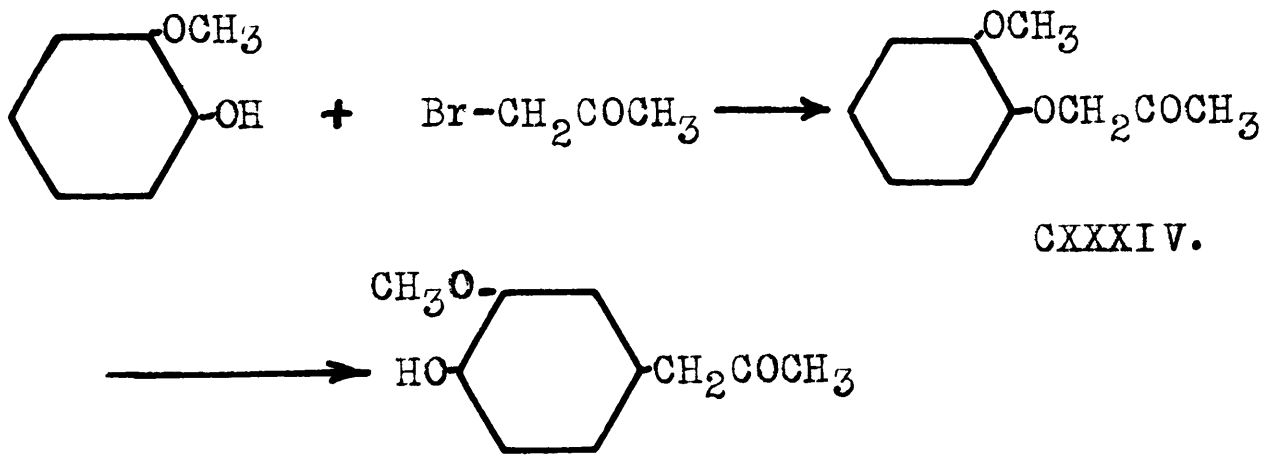
G. Miscellaneous Experiments

1. Attempted Preparation of Guaiacol Acetone

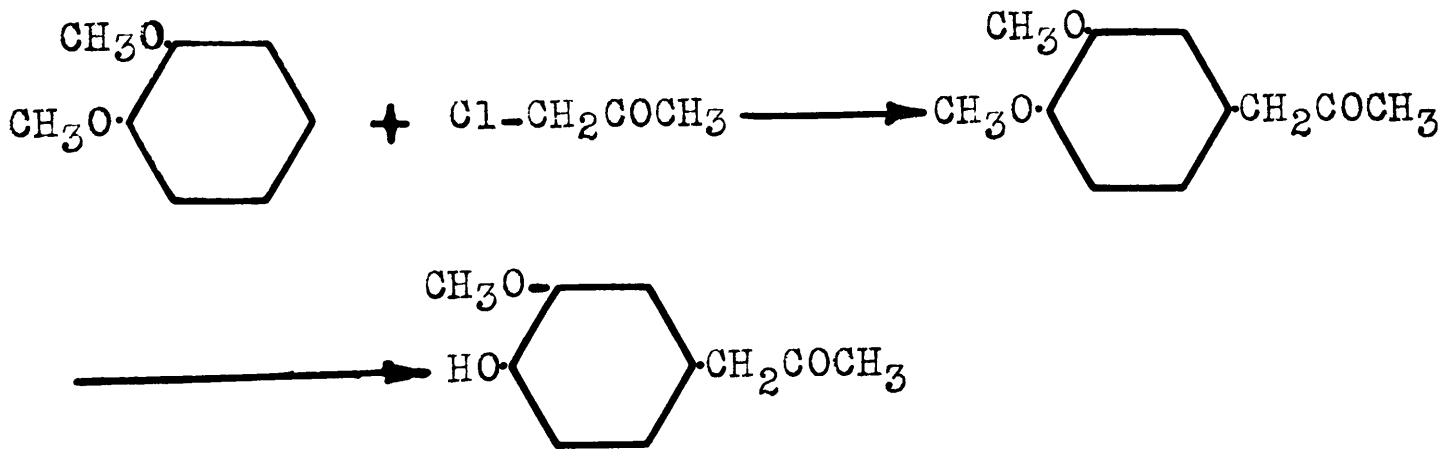


The preparation of guaiacol acetone was attempted by methods indicated in the following reactions:

Method I

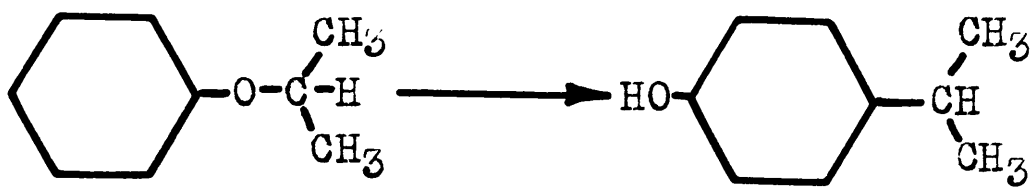


Method II



Method I is based on the possibility of a rearrangement of the intermediate ether, guaiacyl acetonyl ether (CXXXIV) similar to that occurring in the rearrangement of

isopropyl phenyl ether (CXXXV) (139).

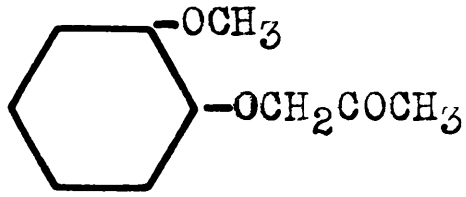


CXXXV.

Unfortunately, only a negative result was obtained.

Method II represents a Friedel-Crafts condensation similar to that carried out with benzene and monochloro acetone (140). A negative result was obtained in this case also.

(a) Preparation of Guaiacyl Acetonyl Ether



(1) To a solution of sodium ethylate prepared from ethanol (17 cc.) and sodium (1.15 g.), guaiacol (7.2 g.) was added and the mixture refluxed for a few minutes, then cooled and monobromoacetone (7.0 g.), (prepared by the method of Levene (141)) added through a dropping funnel, taking care that the temperature did not rise above 25°. After standing at room temperature for forty-five minutes, the solution was freed from sodium bromide and the ethanol removed under reduced pressure. The resulting oily residue was dissolved

in ether, washed well with sodium hydroxide (10%) then with water, dried, and the solvent removed. The alkali---insoluble product which remained was only partially distillable (78-82°/0.100 mm.). Yield = 1.5 g. (15%)

Methoxyl Analysis:

Calc'd. for $C_{10}H_{11}O_3$: 17.2%; Found: 17.0%.

(2) A mixture of guaiacol (6.2 g.), acetone (8 cc.), sodium carbonate (5.5 g.) and monobromoacetone (6.8 g.) was refluxed for ten hours. The sodium bromide was filtered off and the acetone removed. The residual oil was processed as in previous experiment. Yield of distilled product (75-82°/0.050-0.100 mm.) = 1.6 g. (20%) (OMe, 16.8 g.).

(b) Attempted Rearrangement of Guaiacyl Acetonyl Ether

(1) The ether was heated to 50° for one hour in the presence of aluminum chloride (2.8 g.) and the mixture then allowed to stand at room temperature for twenty-four hours. By the usual processes an ether soluble oil was obtained, insoluble in 20% bisulfite solution indicating that the desired rearrangement had not occurred.

(c) Attempted Condensation of Veratrol and Monochloroacetone

(1) $AlCl_3$ (13.8 g.) was added to a solution of veratrol (13.8 g.) in carbon disulfide in a three-necked flask equipped with a stirrer, a dropping funnel and a condenser. Monochloroacetone (9.2 g.) was added slowly while the reaction mixture was stirred vigorously at room temperature. The reaction mixture was allowed to stand overnight and the reaction product then worked up as described in (III C-1) The isolated oil was insoluble in 20% bisulfite solution indicating that no condensation had taken place.

(2) The above experiment was repeated, this time by heating the reaction mixture at 55° (bath temp.) for five hours. Also in this case no appreciable bisulfite soluble product was obtained.

SUMMARY

A. The syntheses of β-hydroxypropiovanillone (A) and β-hydroxypropioveratrone (B) have been carried out and their behaviour towards chemical reagents studied.

B. Conversion of (A) and (B) into amorphous lignin-like products by acid and by alkali has been effected.

C. Exceptional reactivity of the terminal carbinol group of the side chains of (A) and (B) has been demonstrated.

D. A detailed study has been made of the stabilities of α-hydroxypropiovanillone, α-acetoxypropiovanillone, vanilloyl methyl ketone, their syringyl analogs, and various mixtures of these compounds, towards ethanolic hydrogen chloride under conditions of the standard "ethanolysis" procedure.

E. Depolymerization of various amorphous maple ethanol lignin fractions into simpler units has been effected by ethanolic hydrogen chloride.

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