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Doctor's Dissertation

A Study of the Reaction Products Formed
Upon the Alkaline Peroxide Oxidation of
Lignin-Related Model Compounds

R. Heath Reeves

June, 1964

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A STUDY OF THE REACTION PRODUCTS FORMED UPON THE ALKALINE
PEROXIDE OXIDATION OF LIGNIN-RELATED MODEL COMPOUNDS

A thesis submitted by

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SUMMARY

Several lignin-related model compounds were treated with alkaline hydrogen peroxide to study the effect of the side-chain structure upon the oxidation of substituted phenylpropane derivatives. The isolation and characterization of intermediate and final reaction products provided information which suggested the mechanisms by which the model compounds reacted.

A large part of coniferous lignin consists of 4-hydroxy-3-methoxyphenylpropane units, the phenolic hydroxyl groups of which are partially etherified. Since the etherified phenols are more representative of the monomer units after incorporation into the lignin system, 3,4-dimethoxyphenylpropane derivatives were included in this study. The model compounds studied were primarily "non-condensed" phenylpropane derivatives, that is, they were not condensed with other monomer units at the position ortho to the phenolic hydroxyl group.

α,β -Unsaturated aldehydes ($\text{Ar}-\text{CH}=\text{CH}-\text{CHO}$) were cleaved at the double bond giving the corresponding benzaldehydes. For example, 3,4-dimethoxycinnamaldehyde gave veratraldehyde and veratric acid in 83 and 16% yield, respectively. Cinnamaldehyde, in a similar oxidation, gave only benzaldehyde and benzoic acid.

α -Ketones ($\text{Ar}-\text{CO}-\text{CH}_2-\text{CH}_3$) were found to react according to the requirements of the Dakin reaction, that is, the α -ketones that were examined were reactive only when a free hydroxyl group was present in the position para to the side chain. 4'-Hydroxy-3'-methoxypropiophenone, 4'-hydroxy-3'-methoxyacetophenone, and 2,4'-dihydroxy-3'-methoxypropiophenone were readily oxidized and gave methoxyhydroquinone in 80, 67, and 88% yield, respectively. On the other hand, 3',4'-dimethoxypropiophenone and 3-hydroxy-3',4'-dimethoxypropiophenone were not attacked by the alkaline hydrogen peroxide.

β -Ketones ($\text{Ar}-\text{CH}_2-\text{CO}-\text{CH}_3$) reacted with alkaline hydrogen peroxide presumably through the enol tautomer with the subsequent cleavage of the double bond that was formed. (4-Hydroxy-3-methoxyphenyl)-2-propanone was oxidized to vanillic acid in 57% yield, whereas (3,4-dimethoxyphenyl)-2-propanone gave veratraldehyde and veratric acid in 8.3 and 59.7% yield, respectively.

The α -ketocarboxylic acid, (3,4-dimethoxyphenyl)-pyruvic acid, was decarboxylated by alkaline hydrogen peroxide to give (3,4-dimethoxyphenyl)-acetic acid in 80% yield.

In addition to 3',4'-dimethoxypropiophenone and 3-hydroxy-3',4'-dimethoxypropiophenone, the following compounds were not oxidized by alkaline hydrogen peroxide under the conditions employed in this study: 3,4-dimethoxycinnamic acid, 4-hydroxy-3-methoxycinnamic acid, 3,4-dimethoxypropenylbenzene, 4-hydroxy-3-methoxypropenylbenzene, dehydrodiisoeugenol, and α - and β -conidendrin.

On the basis of these results, it appears that the lignin-peroxide reaction in the bleaching of groundwood pulps may be initiated through the carbonyl group and may also involve keto-enol tautomerism. Depending upon the particular structure under consideration, this work has demonstrated that the alkaline peroxide oxidation of phenylpropane side chains involved the carbonyl functional group which can react both in conjunction with, and independent of, phenolic hydroxyl groups.

The results of the several reactions are discussed in relation to the use of alkaline hydrogen peroxide in the bleaching of mechanical pulps and, whenever possible, the course of the reaction has been described.

INTRODUCTION

In 1944, Lee (1) described the first commercial application of alkaline peroxide bleaching in the pulp and paper industry in a groundwood bleaching process at the Norfolk mill of the St. Regis Paper Co. Continued research and development brought out technical and economic advantages from the use of alkaline peroxide so that in 1960 over one-fourth of the pulp bleached in the United States (excluding newsprint) used the process either alone or in conjunction with other bleaching agents (2).

The importance of the peroxide bleaching process in the United States pulp and paper industry is shown in Table I (2). (The figures for groundwood do not include newsprint.)

TABLE I

PULP BLEACHED WITH PEROXIDE IN THE UNITED STATES

| Pulp | Total Bleached, M tons/yr. | Peroxide Bleached, M tons/yr. | Bleached with Peroxide, % |
|------------|-------------------------------|----------------------------------|------------------------------|
| Groundwood | 860 | 650 | 76 |
| Kraft | 4000 | 740 | 18 |
| Sulfite | 1850 | 240 | 13 |
| Cold soda | <u>150</u> | <u>150</u> | 100 |
| Total | 6860 | 1780 | |

When applied to mechanical pulps, the alkaline peroxide bleaching process is capable of virtually eliminating the serious disadvantage of poor color while maintaining a yield of 98-100%. The alkaline peroxide process was developed originally for improving the brightness of unbleached groundwood. It has been

considered, experimentally at least, in connection with the bleaching of all types of wood pulps.

As is frequently the case, theory has fallen behind practice and very little is known about the mechanism of bleaching with peroxides. When considering the action of alkaline peroxide solutions on mechanical pulps, which results in increased pulp brightness, it is important to know which constituents in the pulp are changed upon application of and reaction with the peroxide.

Groundwood is a complex substance with regard to its chemical composition. In groundwood production, the pulp collected in the grinding process represents almost the entire solid substance of the wood delivered to the grinder. Whether, or to what extent, a chemical change has occurred as a result of the grinding action has not been established.

The light-yellow or brownish color of wood is due to certain unspecified pigments present in very low concentration. Lignin, as it is in wood, is presumably colorless (3). In pulp preparation, either mechanical or chemical, lignin may become colored by what is referred to as lignin condensation reactions. However, condensed lignin is not always highly colored (4). More detailed knowledge concerning the chemical nature of the substances causing the color in pulps is desirable.

It has been suggested that the action of peroxide on mechanical pulps is a selective oxidation and hydrolysis of some of the organic coloring matter naturally present in the wood (5). Another point of view is that peroxides bleach mechanical pulp almost wholly by their action on the total lignin in the pulp (6). Jones (7) suggested that the peroxide attacks lignin primarily through

a portion of the carbonyl groups (and possibly the phenolic hydroxyl groups) in the lignin structure. The studies made with Brauns isolated native lignin indicated that there are two or more fractions of lignin which have essentially the same elementary composition and methoxyl content, but which show differences in their chemical reactivity toward alkaline peroxide solutions (7). The efficiency of the peroxide bleaching action was attributed to a relatively high specificity on the part of the peroxide for the more highly colored fractions. It still remains to be shown, however, whether the highly colored fractions of the Brauns isolated native lignin are truly related to lignin or whether they would better be described as contaminating materials.

Lignin frequently has been considered as the primary source of color in wood and wood pulps (5-7). Lignin has been defined by Brauns (8) "as that incrusting material of the plant which is built up mainly, if not entirely, of phenylpropane building stones; it carries the major part of the methoxyl content of the wood; it is unhydrolyzable by acids, readily oxidizable, soluble in hot alkali and bisulfite, and readily condenses with phenols and thio compounds."

No method has yet been developed which will give high yields of lignin under conditions which do not alter the structure of the material. Methods using strong acids or bases promote changes in the lignin yielding materials best described as "lignin derivatives" or lignin preparations.

In the present investigation, lignin-related model compounds having a phenylpropane structure were used to study the reaction with alkaline hydrogen peroxide. This choice avoided the use of lignin preparations, such as Klason lignin, Brauns native lignin, etc., which cannot be characterized structurally. A better understanding of the reaction mechanisms and of the changes effected by the oxidizing agent can be expected from the use of simple homogeneous starting materials.

Aside from indirectly studying reactions which may take place in the peroxide bleaching of groundwood, this study is directed toward extending the present state of knowledge concerning the relationship between the structure of the side chains in lignin-related model compounds and their susceptibility to oxidation by alkaline hydrogen peroxide.

The problem then involved the selection and synthesis of model compounds which contained the desired functional groups and side-chain configurations. The model compounds were treated with alkaline hydrogen peroxide and the reaction products were isolated and identified. Special attention has been directed toward those compounds which were oxidized and, whenever possible, the course of the reaction has been described.

BACKGROUND INFORMATION

OXIDATION STUDIES

In many studies, oxidation has been used to help determine the structure of organic compounds, being of most value when the oxidation does not alter the essential structure of the starting material. Oxidation of the lignin polymer has resulted predominantly in monomeric degradation products. The general failure to recover oligomeric degradation products has impeded efforts to elucidate the linkages involved in the lignin polymer.

Various lignin preparations have been oxidized with peroxide in neutral, acid, and alkaline solutions under more drastic conditions than are normally encountered in pulp bleaching. In many cases, complete degradation took place with the formation of simple compounds such as formic, acetic, oxalic, and malonic acids which no longer retained the benzene nucleus. Other studies involved the use of milled wood which made it difficult to determine whether the reaction products originated from the lignin or from the carbohydrate portion of the wood (9, 10).

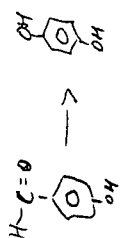
Friedrich and Diwald (11) subjected "primary" spruce lignin to oxidation in a weakly alkaline solution with 3% hydrogen peroxide. These workers obtained a light yellow amorphous oxidation product which failed to give the lignin color reactions.

Richtzenhain (12) oxidized vanillin with hydrogen peroxide for 10 hours at 60°C. and obtained glycolic, malonic, succinic, tartronic, and malic acids. Wacek and Kratzl (13-15) investigated the high pressure and temperature, alkaline nitrobenzene oxidation of variously substituted aliphatic side chains of lignin

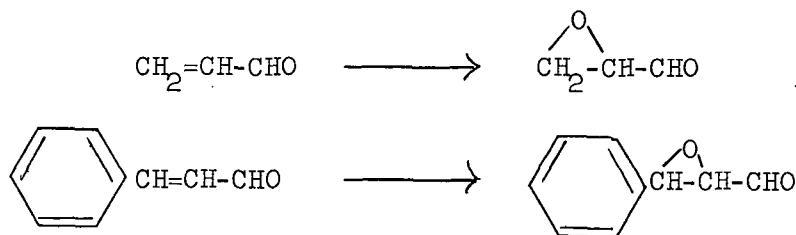
model compounds. These workers found that when a double bond is conjugated with a carbonyl group, oxidation occurred readily. A free phenolic hydroxyl group in the position para to the side chain favored the oxidation of the side chain. The extent to which such oxidations occurred depended upon the side-chain structure. These workers also reported that etherification of the p-hydroxyl group annulled its influence upon the oxidizability of the side chain.

REACTIONS WITH ALKALINE HYDROGEN PEROXIDE

In 1909, Dakin (16) described a "new and somewhat remarkable reaction by which polyhydric phenols result from the oxidation, under certain conditions, of hydroxy derivatives of benzaldehyde and acetophenone." He found that the reaction took place in the proportions of one mole of the carbonyl compound, one mole of alkali, and one mole of hydrogen peroxide. Thus, p-hydroxybenzaldehyde could be converted smoothly and quantitatively to p-dihydroxybenzene (hydroquinone) at room temperature using concentrations of less than 3% hydrogen peroxide. By studying the behavior of several derivatives of benzaldehyde and acetophenone, Dakin found that only those derivatives containing ortho- or para-hydroxyl groups yielded dihydroxybenzenes upon oxidation with alkaline hydrogen peroxide. A note of further interest on this reaction is that no significant amount of the related benzoic acid was formed along with the polyhydric phenols.



α,β -Unsaturated ketones react readily with alkaline hydrogen peroxide solutions and the primary products isolated have been epoxides (17). Payne (18) successfully synthesized the epoxy aldehyde, glycidaldehyde, by reacting equimolar amounts of acrolein and hydrogen peroxide in an alkaline solution held at pH 8.0-8.5. A similar oxidation of cinnamaldehyde resulted in a 24% yield of β -phenylglycidaldehyde (19).



α,β -Unsaturated carbonyl compounds are generally oxidized to esters by peracids (20).

Weitz and Scheffer (17) reported that α,β -unsaturated carboxylic acids, such as cinnamic, fumaric, and maleic acid, were not oxidized by alkaline hydrogen peroxide. Fumaric and maleic acids were epoxidized, however, using hydrogen peroxide and sodium acid tungstate as a catalyst (21). α,β -Unsaturated acids have also reacted with peracids to form the corresponding hydroxy acids (22).

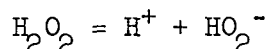
Compounds containing an isolated double bond can be converted to the epoxide form through the action of peracids (23). Alkaline hydrogen peroxide, on the other hand, does not attack isolated double bonds (24).

Weitz and Scheffer (17) found that α -diketones reacted readily with alkaline hydrogen peroxide and are split quantitatively with the formation of two moles of acid. Benzil and substituted benzil compounds were cleaved to the corresponding benzoic acids (25).

Alkaline hydrogen peroxide oxidizes α -ketocarboxylic acids and their esters to acids of one less carbon atom (17). Aliphatic and aromatic aldehydes react directly with alkaline hydrogen peroxide to form unstable peroxides as primary products. Carboxylic acids are almost always the final products of the oxidations (26).

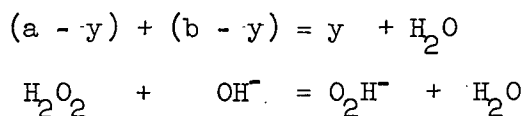
ALKALINE HYDROGEN PEROXIDE SOLUTIONS

Hydrogen peroxide dissociates according to the reaction:



The results of Evans and Uri (27) are taken to establish the equilibrium constant, $K_a = 2.24 \times 10^{-12}$, for this reaction at 25°C. The second dissociation constant is about 10^{-25} (28) and would have a negligible effect on the ion composition of the solution. The formation of the hydroperoxide anion, HO_2^- , is promoted by neutralizing the hydrogen ion with alkali. Bunton and Minkoff (29) showed that for concentrations of hydrogen peroxide greater than that of the initial hydroxide ion, the hydroperoxide ion concentration is reasonably constant and slightly below the concentration of the hydroxide ion. When the concentration of hydrogen peroxide is less than that of the hydroxide ion, the hydroperoxide anion concentration decreases linearly with the decreasing hydrogen peroxide concentration.

If a represents the total concentration of hydrogen peroxide and hydroperoxide anion, b the initial concentration of hydroxyl ion, and y the concentration of hydroperoxide anion (each in moles per liter), the concentrations of the various species are given by:



With known values of the first dissociation constant of hydrogen peroxide and the ionization constant of water, $K_w = 1.005 \times 10^{-14}$ (International Critical Tables), the following equation may be written in terms of the concentrations

of the various components:

$$y/[(a-y)(b-y)] = K_a/K_w$$

The ratio K_a/K_w is constant for a given temperature. At 25°C. (the reaction temperature used in the present study), the value is 213. For 0.5M mixtures of hydrogen peroxide and sodium hydroxide, calculation shows that 84% of the hydrogen peroxide is present as the hydroperoxide anion. The solution, in this case, would have a pH value of ca. 12.5.

The extensive ionization of hydrogen peroxide to hydroperoxide anion in alkaline solutions has been correlated with the experimental observations that the hydroperoxide anion is a strong oxidizing agent (29).

The reactions of hydrogen peroxide in alkaline media are considered to result from the nucleophilic attack of the hydroperoxide anion which displaces an existing group or a pair of electrons, i.e., substitution or addition occurs at a carbon atom (30). In many systems, the peroxidic intermediate is not stable and decomposes by a rapid oxidation-reduction reaction with the breaking of the peroxide linkage, -O-O-. In most cases kinetic proof of the assumed mechanisms is not available.

Hydrogen peroxide in alkaline solutions is susceptible to decomposition, especially in the presence of heavy metal contaminants. Martin (31) found that 20 to 30% of the peroxide added to a pulp is "lost" through decomposition and, presumably, serves no useful purpose in terms of the desired bleaching action. In the laboratory, this undesirable decomposition may be diminished by the use of properly cleaned glassware and by avoiding contamination by such extraneous matter as heavy metal salts.

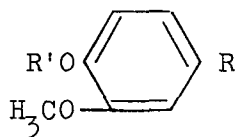
STRUCTURAL ELEMENTS OF LIGNIN

It is generally accepted that most, if not all, of the coniferous lignin is built up of guaiacylpropane monomers. An examination of the particular structures of the aromatic nucleus and the side chain soon becomes involved in the linkages between monomers, that is, the occurrence of dimeric structures. No attempt will be made to prove or disprove the presence of certain constituent groups as this subject has been extensively treated in the literature (32, 33). Recent reviews concerning the reactive groups and structural elements of lignin have also been presented by Gierer (34) and Adler (35).

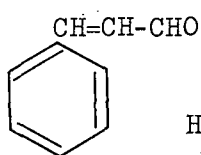
The value of a model compound study depends, in a large part, upon the resemblance of the model substance to the material it is to represent. Thus, the proper choice of model compounds for lignin requires prior knowledge of the structure of lignin as far as it is known. Since a large part of coniferous lignin consists of guaiacylpropane groups, the hydroxyl groups of which are partially etherified, the following compounds were selected for this study: 4'-hydroxy-3'-methoxyacetophenone (I), 3,4-dimethoxycinnamic acid (II), 4-hydroxy-3-methoxycinnamic acid (III), (3,4-dimethoxyphenyl)-2-propanone (IV), (4-hydroxy-3-methoxyphenyl)-2-propanone (V), 3',4'-dimethoxypropiophenone (VI), 4'-hydroxy-3'-methoxypropiophenone (VII), 3-hydroxy-3',4'-dimethoxypropiophenone (VIII), 3,4-dimethoxycinnamaldehyde (IX), 3,4-dimethoxypropenylbenzene (X), 4-hydroxy-3-methoxypropenylbenzene (XI), 2,4'-dihydroxy-3'-methoxypropiophenone (XII), (3,4-dimethoxyphenyl)-pyruvic acid (XIII), cinnamaldehyde (XIV), 4-(2,3-dihydro-7-methoxy-3-methyl-5-propenylbenzofuranyl)-guaiacol (dehydrodiisoeugenol, XV), α - and β -conidendrin (XVI).

All of the above compounds, except perhaps XIII, have been used at one time or another to study reactions that are attributed to lignin.

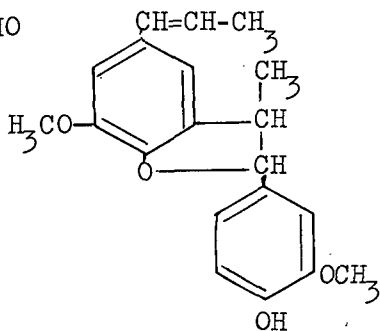
The model compounds used in this study, except V, IX, and XIV, were colorless as were all the oxidation products.



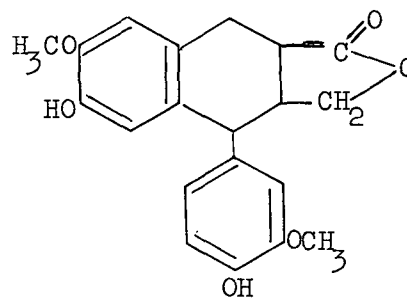
| R | R' |
|--|------------------|
| I -CO-CH ₃ | -H |
| II -CH=CH-COOH | -CH ₃ |
| III -CH=CH-COOH | -H |
| IV -CH ₂ -CO-CH ₃ | -CH ₃ |
| V -CH ₂ -CO-CH ₃ | -H |
| VI -CO-CH ₂ -CH ₃ | -CH ₃ |
| VII -CO-CH ₂ -CH ₃ | -H |
| VIII -CO-CH ₂ -CH ₂ OH | -CH ₃ |
| IX -CH=CH-CHO | -CH ₃ |
| X -CH=CH-CH ₃ | -CH ₃ |
| XI -CH=CH-CH ₃ | -H |
| XII -CO-CH(OH)-CH ₃ | -H |
| XIII -CH ₂ -CO-COOH | -CH ₃ |



XIV



XV



XVI

EXPERIMENTAL

SYNTHESES

Many of the model compounds used in this study were obtained from Dr. I. A. Pearl at The Institute of Paper Chemistry. These materials were purified as required before use in the subsequent oxidations. The remaining compounds were prepared according to procedures given in the literature. All melting points reported in this work were taken on a Thomas-Hoover Melting Point Apparatus and are uncorrected.

3,4-DIMETHOXYCINNAMIC ACID (II)

This material was prepared by the condensation of veratraldehyde with malonic acid in the presence of piperidine with pyridine as the solvent according to the procedure outlined by Pearl and Beyer (36). The product melting at 185.5-187°C. was obtained in 54% yield.

4-HYDROXY-3-METHOXYCINNAMIC ACID (III)

The above procedure was used to prepare this material from vanillin and malonic acid (36). The product melting at 173-184.5°C. was obtained in 63% yield.

(3,4-DIMETHOXYPHENYL)-2-PROPANONE (IV)

1-(3,4-Dimethoxyphenyl)-2-nitro-1-propene was prepared by treating veratraldehyde successively with nitroethane, methylamine hydrochloride, and sodium carbonate with 95% ethanol as the solvent. This material was then reduced with iron powder, hydrated ferric chloride, and hydrochloric acid to the oxime, which was then hydrolyzed to (3,4-dimethoxyphenyl)-2-propanone (37). The crude product

was distilled twice in a semimicro spinning band distillation column* to give 26 g. of (3,4-dimethoxyphenyl)-2-propanone boiling at 110°C. at 0.4 mm. pressure. Pearl and Beyer (37) reported this material boiling at 135°C. at 0.8 mm. pressure. The semicarbazone of (3,4-dimethoxyphenyl)-2-propanone was obtained from 25% ethanol and melted at 175-177°C. Muller and co-workers (38) reported a melting point of 176-177°C. for the semicarbazone of this model compound which was obtained from the chromic acid oxidation of diisohomogenol.

3',4'-DIMETHOXYPROPIOPHENONE (VI)

This material was prepared by treating veratrole with propionyl chloride in the presence of anhydrous aluminum chloride according to the procedure of Adams and co-workers (39). The product was obtained in 85% yield and melted at 58.5-60°C.

3-HYDROXY-3',4'-DIMETHOXYPROPIOPHENONE (VIII)

3-Chloro-3',4'-dimethoxypropiophenone (40) and freshly prepared silver oxide in water were heated under reflux for 10 hours and gave 3-hydroxy-3',4'-dimethoxypropiophenone according to the procedure of Hibbert and co-workers (41). This product was obtained in 37% yield and melted at 83-84°C.

3,4-DIMETHOXYCINNAMALDEHYDE (IX)

This compound was prepared by the condensation of veratraldehyde with acetaldehyde in the presence of dilute potassium hydroxide according to the procedure of Feuerstein (42). The product was obtained as bright yellow crystals weighing 3 g. and melting at 82-83°C.

*Nester and Faust Mfg. Corp., Newark, Delaware.

(3,4-DIMETHOXYPHENYL)-PYRUVIC ACID (XIII)

Veratrylidenehippuric anhydride, prepared from veratraldehyde, hippuric acid, acetic anhydride, and sodium acetate, was heated with 10% sodium hydroxide to give (3,4-dimethoxyphenyl)-pyruvic acid according to the procedure of Kropp and Decker (43). The product weighing 13 g. was obtained as long colorless plates from acetic acid and melted at 185-187°C. with decomposition.

METHOXYHYDROQUINONE

Methoxyhydroquinone was obtained by the oxidation of the sodium salt of vanillin with hydrogen peroxide according to the method of Dakin (16). The Dakin procedure was modified to the extent that the aqueous solution was saturated with ammonium sulfate prior to extracting with ether. The product was obtained as colorless crystals which melted at 82-83°C.

When the melt was permitted to crystallize, the material then melted at 88-89°C. Dimroth and co-workers (44) reported a melting point of 88-88.5°C. for methoxyhydroquinone. Drake and co-workers (45) obtained methoxyhydroquinone which melted at 80-82°C., but, after two recrystallizations from benzene, the melting point was raised to 90-91°C.

A portion of the material prepared above was recrystallized from chloroform. These crystals were then carefully mixed with the crystals obtained from the benzene solution initially and the mixture exhibited two melting points: 80-81.5 and 88.5-89.5°C. The crystals of the higher melting dimorphic form could be seen clearly in the melt of the lower melting form. It appears that both forms may be obtained from benzene solutions (45).

(A similar oxidation of veratraldehyde resulted in the formation of veratric acid, m.p. 179-181°C. This material was identified by its infrared spectrum.)

GENERAL OXIDATION PROCEDURE

In general, these experiments were conducted by treating a mixture of the model compound and an equivalent amount of one normal sodium hydroxide with 1.25 equivalents of dilute hydrogen peroxide (ca. 1M) which was added in one portion. The reactions were conducted at 25°C. for a period of one hour. Sufficient sodium bisulfite was added to react with any residual hydrogen peroxide. The reaction mixture was made acid to litmus by adding one normal sulfuric acid. In some cases, a precipitate formed at this point and was recovered by filtration.

The combined washings and filtrate were extracted exhaustively with ether (occasionally, other solvents were used). This extract was dried over sodium sulfate and concentrated under reduced pressure to a small volume. These concentrated solutions were then used to separate and identify the reaction products.

Often, preliminary reactions were run so that several methods could be tried to tentatively identify the reaction products. In this manner, the recovery and identification of the reaction products was facilitated.

QUANTITATIVE GAS CHROMATOGRAPHY (46)

The reaction mixtures were investigated initially by means of gas chromatography using an Aerograph Model A-90-S* gas chromatograph with a thermal conductivity detector.

*Wilkins Instrument and Research Inc., Walnut Creek, California.

conductivity detector unit. Quantitative results were obtained by the techniques of internal normalization and internal standardization.

In the internal normalization technique, the area of all the peaks present on the recorder trace is summed to give a total area which is normalized to 100%. This method assumes that the sample does not contain significant amounts of non-volatile materials or substances which have very long retention times.

In the internal standard technique, a known amount of a suitable material is added to the original sample, and the peak areas are referred to the peak area of the internal standard. This procedure must be calibrated by an analysis of a known mixture.

The physical measurement of the peak area was the limiting factor in the accuracy of the results. Two methods were used to measure the peak areas. The first method involved cutting out the peaks from the chromatographic trace and weighing the paper. The second method used to determine peak areas took advantage of a recorder equipped with an automatic integrator. The area enclosed by the chromatographic peak was given by a secondary pipping pen.

TABLE II

ANALYSIS OF 2-PHENYLETHANOL-(3,4-DIMETHOXYPHENYL)-
2-PROPANE MIXTURES

| | Mixture 1 | | Mixture 2 | |
|-----------------|-----------|--------|-----------|--------|
| | A | B | A' | B' |
| Weight, g. | 0.2394 | 0.2381 | 0.0650 | 0.1247 |
| Mol. wt. | 122.16 | 194.22 | 122.16 | 194.22 |
| Millimoles | 1.96 | 1.23 | 0.532 | 0.642 |
| Mole, % | 61.4 | 38.6 | 45.4 | 54.6 |
| Area, mg. | 55.6 | 35.4 | 25.5 | 32.5 |
| Area, % | 60.9 | 39.1 | 44.0 | 56.0 |
| Mole % - area % | +0.5 | -0.5 | +1.4 | -1.4 |

Table II shows the results obtained from two mixtures of 2-phenylethanol (A and A') and (3,4-dimethoxyphenyl)-2-propanone (B and B'). The areas were determined by weighing the paper cut from the recorder trace. These results are indicative of the accuracy obtainable by these techniques.

When using gas chromatography to analyze the reaction mixtures, conditions were arranged to facilitate the recovery and identification of the aromatic portion of the model compounds. Under these conditions, any highly volatile or very low molecular weight material would not be separated from the solvent front. Unless otherwise specified, the carrier gas flow rate used was 100 ml./min.

OXIDATION OF MODEL COMPOUNDS

4'-HYDROXY-3'-METHOXYACETOPHENONE (I)

The following analysis of the ether extract from the reaction mixture was obtained by gas chromatography on a DEGS* column at 190°C. and a gas flow rate of 75 ml./min.

1. Solvent, retention time (RT, in min.) 0.0.
2. 4'-Hydroxy-3'-methoxyacetophenone, RT 16.9; ca. 33%.
3. Methoxyhydroquinone, RT 37.4; ca. 67%.

The percentages are based on the starting material and were determined by the internal normalization technique. Sample collectors were connected to the gas chromatograph when the peak for the desired component appeared on the chromatographic trace.

*See footnote next page.

The material in the first collector was analyzed further by gas chromatography on a Hyprose* column at 150°C. and a Carbowax 20M* column at 100°C. Comparison of the retention times on the two columns with known materials tentatively identified the side-chain fragment as being acetic acid.

The material in the second collector crystallized readily. The crystals melted sharply at 113°C. and gave an infrared spectrum (KBr pellet) identical with the spectrum of known 4'-hydroxy-3'-methoxyacetophenone.

Methoxyhydroquinone was obtained from the third collector. This material was recrystallized from benzene and the following data were obtained:

| | Melting Point, °C. |
|-------------------------------------|--------------------|
| Methoxyhydroquinone (this reaction) | 79-80 |
| Methoxyhydroquinone (known) | 82-83 |
| Mixture | 79-80 |

The infrared spectrum (KBr pellet) for methoxyhydroquinone obtained in this reaction was compared with the spectrum of the known material prepared by the Dakin oxidation of vanillin (16). The two spectra were identical except for a very weak carbonyl band in the spectrum of the methoxyhydroquinone obtained from the oxidation of 4'-hydroxy-3'-methoxyacetophenone. The spectrum of authentic methoxyhydroquinone is shown in Fig. 1. The spectrum for this material has not been published in the literature.

*Columns obtained from Wilkens Instrument and Research, Inc. The solid support, in each case, is 60/80 acid-washed Chromosorb 'W'.

DEGS-20% Diethyleneglycol succinate

Hyprose-20% octakis-Hydroxypropylsucrose

Carbowax 20M-20% Polyethyleneglycol polymer

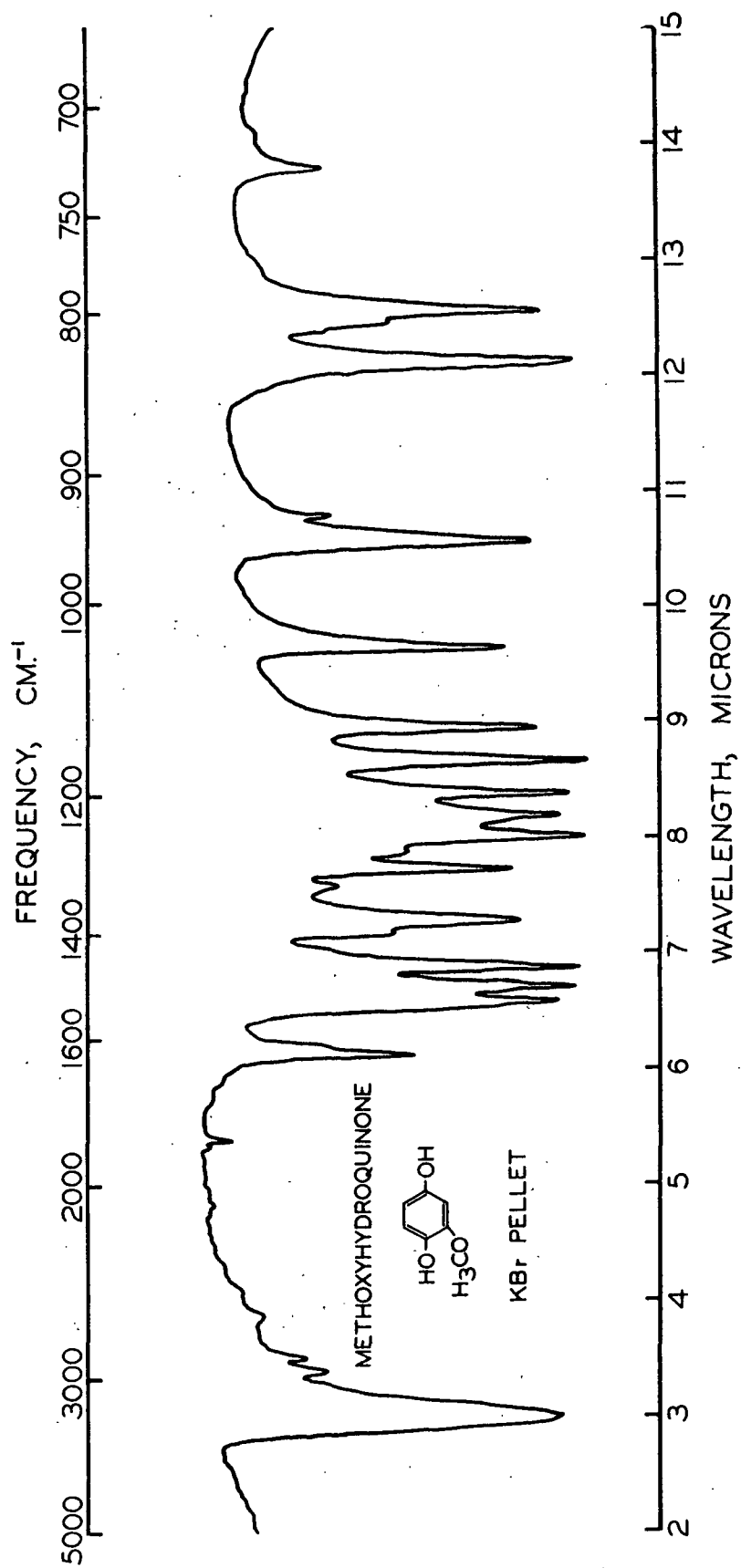
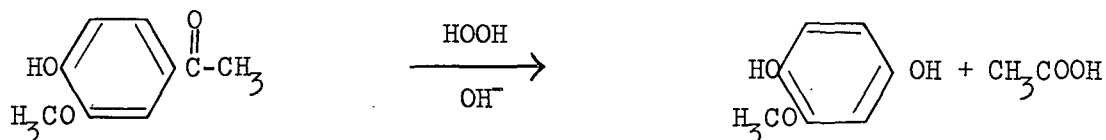


Figure 1. Infrared Spectrum for Authentic Methoxyhydroquinone

The over-all reaction is represented as:



In fact, neither vanillin nor vanillic acid could be detected by gas and paper chromatography. This is an example of the Dakin reaction and the corresponding benzoic acid, in this case vanillic acid, is not to be expected as a reaction product.

3,4-DIMETHOXYCINNAMIC ACID (II)

The attempted oxidation of 10 mmol. of 3,4-dimethoxycinnamic acid resulted in the recovery of 95% of the starting material. After recrystallization from ethanol, the recovered precipitate melted at 186-187°C. A mixture melting point with known 3,4-dimethoxycinnamic acid showed no depression.

4-HYDROXY-3-METHOXYCINNAMIC ACID (III)

The attempted oxidation of 10 mmol. of 4-hydroxy-3-methoxycinnamic acid resulted in the recovery of almost 95% of the starting material. The recovered solid melted at 171-172°C. Recrystallization from 1:1 ethanol-water raised the melting point to 173-174°C. There was no depression in the mixture melting point with the starting material.

(3,4-DIMETHOXYPHENYL)-2-PROPANONE (IV)

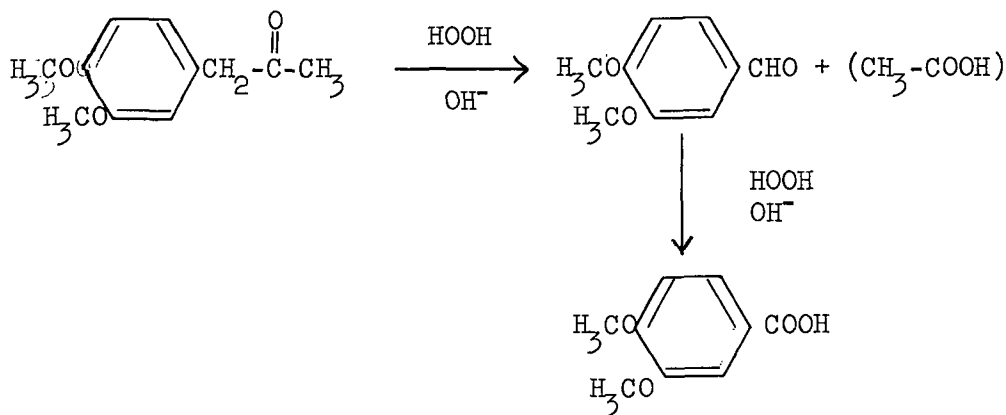
The ether extract from the oxidation of 1.2 mmol. of (3,4-dimethoxyphenyl)-2-propanone was extracted with saturated sodium bicarbonate solution. The ether solution was analyzed by gas chromatography on a DEGS column at a temperature of

175°C. with the following results:

1. Solvent peak, RT 0.0.
2. Minor constituent, (unidentified), RT 2.95; ca. 1.5%.
3. Veratraldehyde, RT 7.10; ca. 8.3%.
4. (3,4-Dimethoxyphenyl)-2-propanone, RT 9.0; ca. 24%.

The percentages are based on the starting material and were determined using 2-phenylethanol as an internal standard. The materials represented by the third and fourth chromatographic peaks were collected from the gas chromatograph and were identified by comparing their infrared spectra with the spectra for the authentic compounds.

Veratric acid was obtained in 60% yield from the bicarbonate fraction. Colorless needles were collected that melted sharply at 180-181.5°C. and a mixed melting point with authentic veratric acid was undepressed. The mother liquor, from which the crystals of veratric acid were obtained, was checked by paper chromatography for (3,4-dimethoxyphenyl)-acetic acid. As none of this latter compound could be detected, it appears that the cleavage of the ketone is specific. The over-all reaction is:



This reaction was repeated substituting a saturated sodium carbonate solution for the one normal sodium hydroxide originally used (pH 10.2 vs. 12.2). Under these conditions, an analysis of the ether extract by gas chromatography showed that 26% of the starting material remained at the end of the reaction. The other products were not investigated at the lower pH.

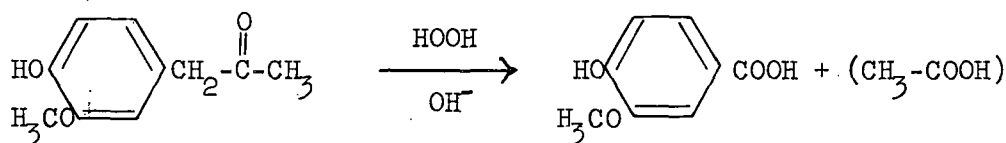
(4-HYDROXY-3-METHOXYPHENYL)-2-PROPANONE (V)

The ether extract from the oxidation of 1.23 mmol. of (4-hydroxy-3-methoxyphenyl)-2-propanone was investigated by gas chromatography on a DEGS column at 200°C. with the following results:

1. Solvent peak, RT 0.0.
2. (4-Hydroxy-3-methoxyphenyl)-2-propanone, RT 7.7; ca. 30%.

The percentage of unreacted starting material was determined using 2-phenylethanol as an internal standard. (At increased sensitivities, no other peaks were noted.)

The ether extract was then washed with a saturated sodium bicarbonate solution. The bicarbonate fraction yielded 57% of the theoretical amount of vanillic acid which melted at 202-203°C. Recrystallization from benzene raised the melting point to 205-207°C. There was no depression in the mixture melting point with authentic vanillic acid. The over-all reaction may be represented by:



This reaction was also repeated, similar to the preceding model compound, at pH 10.2. In this case, only 13.5% of the starting material remained at the end of the reaction period. These results indicate an increased rate at the

lower pH; however, since these were not in any way controlled rate studies, the results are to be considered tentative.

3',4'-DIMETHOXYPROPIOPHENONE (VI)

A preliminary, small-scale reaction showed that this material was not oxidized under the normal experimental conditions. The reaction was conducted, therefore, at 100°C. and this resulted in the recovery of 97.6% of the starting material. 3',4'-Dimethoxypropiophenone was recovered, melting point 58-59.5°C., which gave no depression in mixture melting point with the starting material.

Another reaction was run at 100°C., only in this case 0.03 mmol. of ferrous sulfate was added as a catalyst. The reaction was accompanied by a very rapid decomposition of the hydrogen peroxide and an extra 1.25 equivalents of peroxide were added. Again, about 98% of the starting material was recovered unchanged from the ether extract. These crystals melted at 58.5-60°C. and a mixed melting point with authentic material was not depressed.

4'-HYDROXY-3'-METHOXYPROPIOPHENONE (VII)

The ether extract from the oxidation of 1.0 mmol. of 4'-hydroxy-3'-methoxypropiophenone was analyzed by gas chromatography on a DEGS column at 200°C. with the following results:

1. Solvent peak, RT 0.0.
2. 4'-Hydroxy-3'-methoxypropiophenone, RT 10.8; ca. 20%.
3. Methoxyhydroquinone, RT 20.8; ca. 80%.

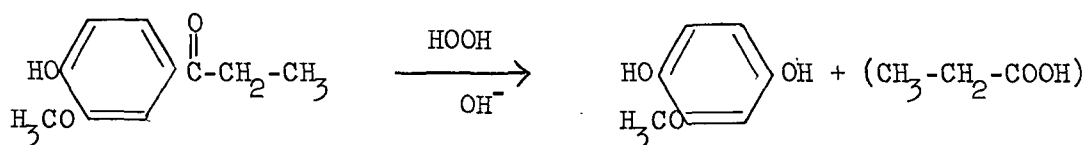
The percentages are based on the starting material and were determined by the internal normalization technique. Sample collectors were connected to the gas chromatograph when the peak for the desired material appeared on the chromatographic trace.

The material in the first collector was analyzed further by gas chromatography on a Hyprose column at 150°C. and a Carbowax 20M column at 100°C. Comparison of the retention times on the two columns with known materials tentatively identified the side-chain fragment as being propionic acid.

The material obtained from the second collector crystallized readily and melted at 57-59°C. A mixture melting point with the starting material was not depressed.

The material from the third collector was recrystallized twice from benzene and melted at 82-83°C. When allowed to crystallize in the melting point tube, the crystals remelted at 88-89°C. A mixed melting point with known methoxyhydroquinone showed no depression and confirmed the identification of this fraction.

The over-all reaction is:



Vanillin and vanillic acid were not detected by paper and gas chromatography.

3-HYDROXY-3',4'-DIMETHOXYPROPIOPHENONE (VIII)

Acidification of the reaction mixture from the attempted oxidation of 1.0 mmol. of this model compound resulted in the recovery of 83.1% of the starting material. These crystals melted at 82-83.5°C. and did not depress the melting point when mixed with the starting material.

The ether extract was analyzed by gas chromatography on a DEGS column at 175°C. Using veratraldehyde, RT 2.8, as an internal standard, this analysis

showed that 11.4% of the starting material, RT 5.5, was present in the ether extract. Thus, a total of 94.5% of the 3-hydroxy-3',4'-dimethoxypropiophenone was found to be unchanged at the end of the reaction period.

3,4-DIMETHOXYCINNAMALDEHYDE (IX)

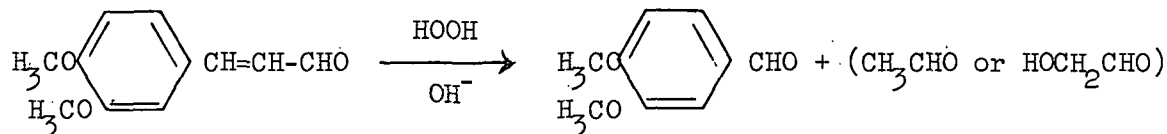
The primary product from the oxidation of 3,4-dimethoxycinnamaldehyde was veratraldehyde, ca. 83%. This material was collected from the gas chromatograph and identified by its infrared spectrum. No other peaks were noted on the chromatographic trace. Known 3,4-dimethoxycinnamaldehyde would produce a peak at 13.8 min. on the DEGS column at 200°C., whereas the product, veratraldehyde, had a retention time of only 2.8 min.

Prior to the ether extraction, veratric acid was obtained from the acidified reaction mixture by filtration. Crystals which melted at 178-180°C. were obtained in 16% yield. These crystals gave an infrared spectrum which was identical with the spectrum for known veratric acid.

Paper chromatography showed that traces of 3,4-dimethoxycinnamic acid, in addition to veratraldehyde and veratric acid, were present in the ether extract.

The uniform cleavage of the double bond suggested that a reverse aldol condensation might be taking place in the alkaline medium. However, treatment of 1.0 mmol. of 3,4-dimethoxycinnamaldehyde with an equivalent amount of one normal sodium hydroxide for 2 hours at 25°C. resulted in the recovery of about 93% unchanged starting material. The recovered crystals melted at 82-83°C. and gave no depression in mixture melting point with the starting material.

The over-all reaction appears to be:



Both reaction products may be oxidized further to veratric and either or both acetic and glycolic acid. Several attempts were made to identify the side-chain fragment; however, glycolaldehyde and glycolic acid could not be detected in the ether extract by paper chromatography.

Approximately 5 mmol. of 3,4-dimethoxycinnamaldehyde were oxidized according to the previously outlined scheme. The reaction mixture in this case was investigated using the Craig-Post countercurrent distribution apparatus. The upper and lower phases of a n-butanol and water mixture were used in the Craig machine. After 46 transfers were completed, each tube was monitored by means of paper chromatography using methyl ethyl ketone-acetone-formic acid-water (40:2:1:6 parts by volume) as the developer (47).

The orienting chromatograms indicated that either or both glyoxal and glyoxalic acid were present in the first four tubes. Attempts to make a 2,4-dinitrophenylhydrazone were not successful as pure crystals were not obtained. Chromatography of the 2,4-dinitrophenylhydrazone mixture on a dimethylformamide-impregnated sheet of Whatman No. 1 paper using cyclohexane-carbon tetrachloride-dimethylformamide (20:4:1 parts by volume) as the developer showed at least two spots. A similar separation was attempted by using the same solvent system with a dimethylformamide-impregnated sheet of Whatman No. 17 paper. Two predominant bands were eluted from the chromatogram and collected. Upon removal of the solvent from the faster moving band, a bright yellow amorphous solid was obtained.

An infrared spectrum of this material could not be identified, although it appeared to be a relatively simple compound. ($\nu_{\text{C-H}}$ 2945 mw, 2855 w; $\nu_{\text{C=O}}$ 1730 w, 1690 vs; ν_{CH_3} 1390 m; $\nu_{\text{C-O}}$ 1087 m; cm.^{-1} in CCl_4 .)

After removing the eluting solvent from the second band, crystals which melted at 306-311°C. with sintering at about 200°C. were obtained. An infrared spectrum (KBr pellet) of these crystals was identical with the spectrum of known glyoxal-bis-2,4-dinitrophenylhydrazone (48) except for small carbonyl and hydroxyl bands which indicated the presence of impurities. The melting point for glyoxal-bis-2,4-dinitrophenylhydrazone has been reported to be 328°C. (49).

3,4-DIMETHOXYPROPENYLBENZENE (X)

The ether extract from the attempted oxidation of this model compound was analyzed by gas chromatography on a DEGS column at 160°C. Using 2-phenylethanol as an internal standard, 96.5% of the starting material was found to be unchanged. This material was identified by its infrared spectrum (film between sodium chloride windows).

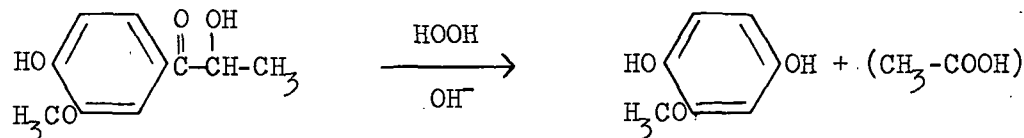
4-HYDROXY-3-METHOXYPROPENYLBENZENE (XI)

The ether extract from the attempted oxidation of 1.2 mmol. of this model compound was analyzed by gas chromatography on a DEGS column at 160°C. Using 2-phenylethanol as an internal standard, 93.5% of the starting material was found in the ether extract. The infrared spectrum (film between sodium chloride windows) of the recovered material was identical with the spectrum of known 4-hydroxy-3-methoxypropenylbenzene.

2,4'-DIHYDROXY-3'-METHOXYPROPIOPHENONE (XII)

The oxidation of this model compound resulted in the collection of 87.5% of the theoretical amount of methoxyhydroquinone. The ether extract was investigated by gas chromatography on a DEGS column at 200°C. A single large peak was noted on the recorder trace at 21 min. The material represented by this peak was collected in a U-tube cooled by dry ice and acetone. Crystals which melted at 82.5-83°C. and remelted at 88-89°C. were obtained from the collector. This material exhibited dimorphic properties characteristic of methoxyhydroquinone prepared by known methods. Paper chromatography of the ether extract indicated the presence of methoxyhydroquinone and small amounts of the starting material, whereas vanillin and vanillic acid could not be detected.

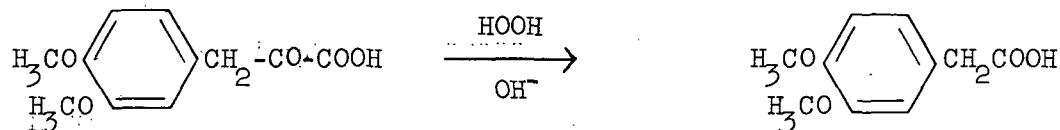
The over-all reaction may be represented as:



(3,4-DIMETHOXYPHENYL)-PYRUVIC ACID (XIII)

The oxidation of this model compound resulted in the collection of 80% of the theoretical amount of (3,4-dimethoxyphenyl)-acetic acid. The crystalline material obtained from the benzene extract melted sharply at 97-98°C. and a mixed melting point with authentic material was not depressed. The infrared spectrum (KBr pellet) of the reaction product was identical with the spectrum of known (3,4-dimethoxyphenyl)-acetic acid.

The over-all reaction is:



CINNAMALDEHYDE (XIV)

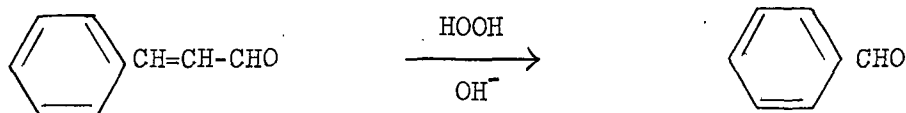
The ether extract from the oxidation of cinnamaldehyde was analyzed by gas chromatography on a Carbowax 20M column at 150°C. with the following results:

1. Solvent peak, RT 0.0.
2. Benzaldehyde, RT 2.4; ca. 60%.
3. Cinnamaldehyde, RT 19.5; ca. 40%.

The percentages above are based on the two volatile components and were determined by internal normalization. Sample collectors, cooled by dry ice and acetone, were connected to the gas chromatograph when the peak for the desired material appeared on the recorder trace. Benzaldehyde and cinnamaldehyde were identified by comparing their spectra with the spectra (liquid films between sodium chloride windows) of the authentic materials.

Prior to the ether extraction, crystals of benzoic acid were recovered from the acidified reaction mixture. These iridescent prisms melted at 121-123°C. There was no depression in the mixture melting point with authentic benzoic acid.

The over-all reaction, similar to 3,4-dimethoxycinnamaldehyde, is:



DEHYDRODIISOEUGENOL (XV)

The attempted oxidation of 5 mmol. of this model compound resulted in the recovery of 99% of the starting material. The collected product melted at 128-131°C. After recrystallization from ethanol, the melting point was raised to 132-133°C. and a mixed melting point with the starting material gave no depression.

α - AND β -CONIDENDRIN (XVI)

α - and β -Conidendrin were both stable under the reaction conditions employed in this study. In both cases, almost a quantitative recovery of the starting material was obtained.

The precipitate recovered from the attempted oxidation of α -conidendrin melted at 255-256.5°C. A mixture melting point with the starting material was not depressed.

The precipitate from the attempted oxidation of β -conidendrin melted at 211-212°C. and gave no depression in the mixture melting point with the starting material.

DISCUSSION OF THE RESULTS

RING-CONJUGATED DOUBLE BONDS

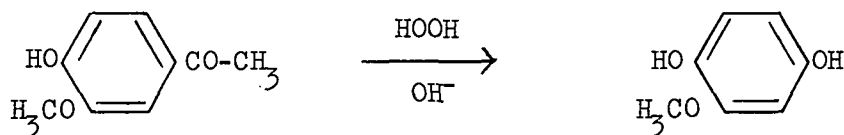
Alkaline hydrogen peroxide does not attack isolated double bonds in contrast to peracid treatment which results in the formation of epoxy (oxirane) compounds (24). In the present study, 4-hydroxy-3-methoxypropenylbenzene and 3,4-dimethoxypropenylbenzene were recovered unchanged from the reaction mixture in over 90% yield. Thus, the ring-conjugated double bond is not attacked by alkaline hydrogen peroxide.

Weitz and Scheffer (17) reported that α,β -unsaturated carboxylic acids, such as cinnamic acid, were not attacked by alkaline hydrogen peroxide. Taylor (50), on the other hand, stated that α,β -unsaturated ketones and acids were not epoxidized by peracids, but that alkaline hydrogen peroxide has been found to effect this reaction. In the present study, the attempted oxidation of 4-hydroxy-3-methoxycinnamic acid and 3,4-dimethoxycinnamic acid resulted, in both cases, in the recovery of 95% of the starting material. Thus, under the relatively mild conditions employed in this study, the α,β -unsaturated acids were not oxidized.

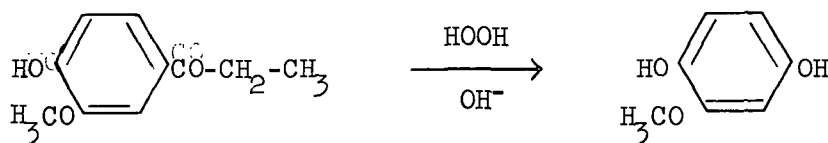
α -KETO GROUPS

In the Dakin reaction (16) p-hydroxyacetophenone and p-hydroxypropiophenone were both converted (with some difficulty) to hydroquinone, whereas vanillin gave a quantitative yield of methoxyhydroquinone under similar treatment with alkaline hydrogen peroxide. In the present study, compounds related to lignin were shown to behave according to the conditions set down by Dakin (16). For example, the α -keto compounds with a hydroxyl group para to the side chain were

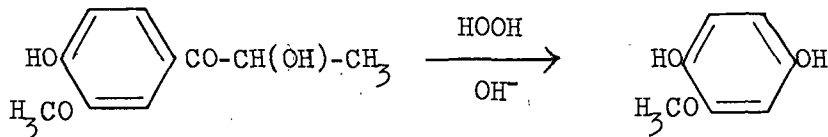
oxidized to the corresponding hydroquinone. In the oxidation of 4'-hydroxy-3'-methoxyacetophenone, 67% of the starting material reacted to give methoxyhydroquinone.



Similarly, 4'-hydroxy-3'-methoxypropiophenone, when oxidized with alkaline hydrogen peroxide gave 80% of the theoretical amount of methoxyhydroquinone.



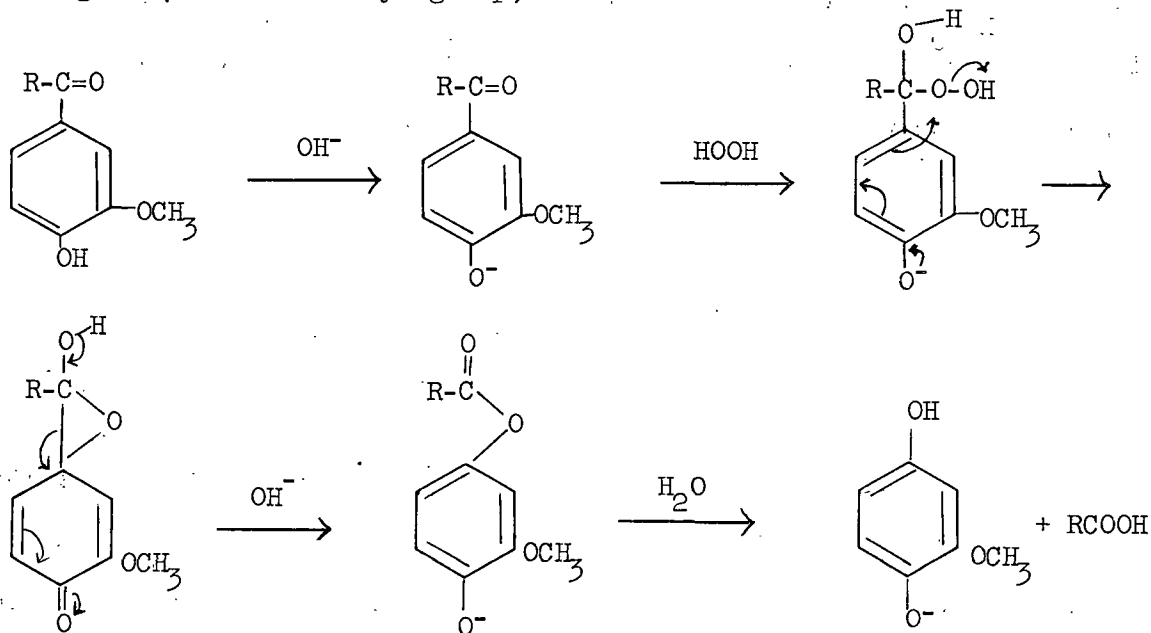
2,4'-Dihydroxy-3'-methoxypropiophenone gave 87% of the theoretical amount of methoxyhydroquinone upon oxidation with alkaline hydrogen peroxide. This reaction appeared to be facilitated by the alcohol group on the adjacent carbon atom.



In all cases where methoxyhydroquinone was formed, no vanillin or vanillic acid could be detected by either paper or gas chromatography.

The attempted oxidation of 3',4'-dimethoxypropiophenone resulted in the recovery of 98% of the starting material unchanged after one hour at 100°C. Likewise, 3-hydroxy-3',4'-dimethoxypropiophenone did not react under the conditions employed in this study, and 98% of this material was recovered unchanged.

The following mechanism is proposed for the oxidation of the α -keto compounds related to lignin (R = -H or alkyl group):



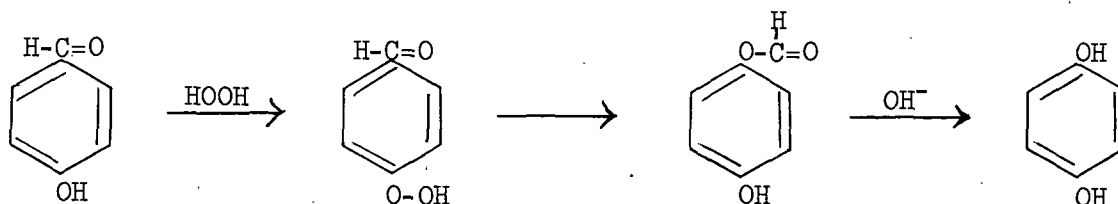
In the suggested mechanism, the ionized phenolic hydroxyl group provides the driving force for the formation of the proposed quinoid intermediate. This mechanism also suggests the formation of a cyclic ether. Restoration of the more stable benzene ring would then provide the necessary driving force for the breakdown of the quinoid intermediate with the subsequent formation of an ester.

[Attempts were made to detect long-lived peroxidic intermediates by means of polarography*. A portion of the reaction mixture (20 μL) was injected into the polarographic cell which contained 20 ml. of 1:1 ethanol-water with 0.3M lithium chloride as the supporting electrolyte. Peroxide intermediates were not detected by this technique.]

The intense maroon color of the reaction mixture, which was found to be characteristic of all the reactions in which methoxyhydroquinone was formed, may be due in part to the quinoid intermediate suggested in the above mechanism.

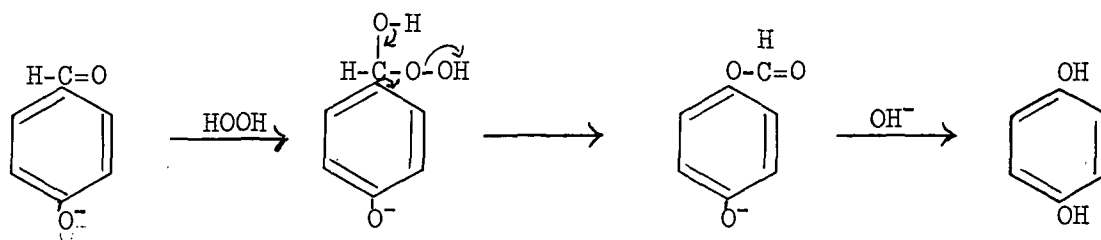
*A Sargent Model XII polarograph was used in conjunction with a recording potentiometer.

Wacek and Eppinger (51) considered this reaction and suggested that the peroxide initially attacks the p-hydroxyl group forming a "theoretical peroxide." This is followed by a double rearrangement to the ester which is readily hydrolyzed to hydroquinone.



In the above mechanism, both the phenolic hydroxyl group and hydrogen peroxide are electronegative moieties. It is not probable that these electronegative centers would react to form the so-called "theoretical peroxide" suggested by Wacek and Eppinger (51).

Bunton (52) suggests still another, yet similar mechanism, as follows:



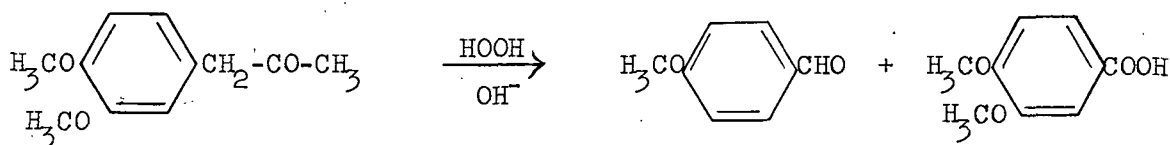
This latter mechanism is in accord with the results of tracer experiments using oxygen-18. This mechanism does not involve the free phenolic hydroxyl group. Yet, it is well known that only those derivatives of benzaldehyde having a free ortho or para-hydroxyl group react in this manner. It is not unreasonable then to assume that the phenolic hydroxyl group should be involved in the reaction mechanism.

All three mechanisms propose the formation of an ester although the first mechanism above also suggests the formation of a cyclic ether as an intermediate.

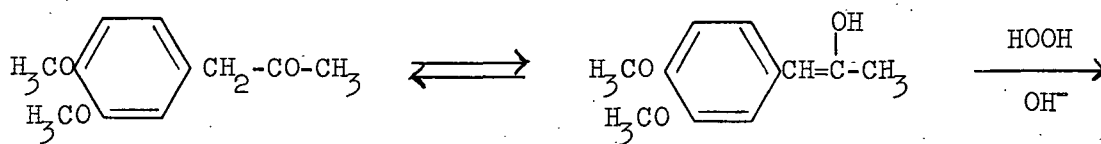
Wacek and Bezard (53) assumed that the mechanism of the Dakin reaction was similar to the peracetic acid oxidation of salicylaldehyde. Consequently, they showed that in the absence of water, the monoformate of catechol could be obtained in high yields. They further showed that the reaction occurs in two ways: (1) the aldehyde group migrates to the initially free hydroxyl group, and (2) an oxygen atom is introduced between the aldehyde group and the aromatic nucleus.

β -KETO GROUPS

The alkaline peroxide oxidation of (3,4-dimethoxyphenyl)-2-propanone resulted in the formation of 8% veratraldehyde and 60% veratric acid.

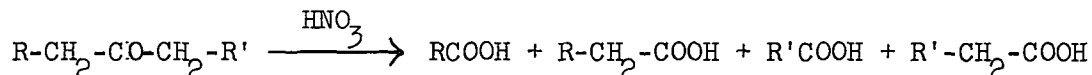


It is suggested that this material reacted through the addition of the hydroperoxide anion to the double bond formed upon enolization.



The oxidation of ketones requires the breaking of carbon-carbon bonds, and hence takes place under rather severe conditions. The reaction is seldom of value in synthesis as many ketones can be cleaved on either side of the carbonyl

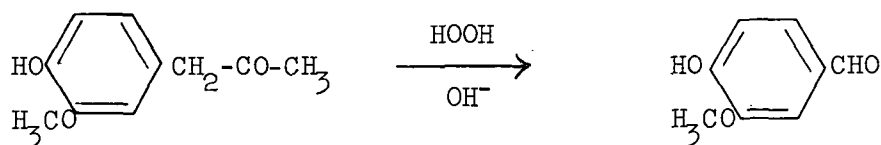
group to yield a mixture of acids (54). For example:



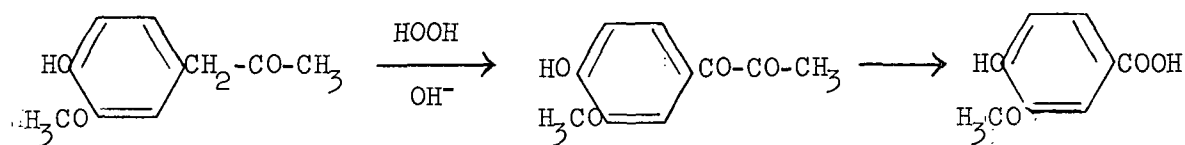
Thus, the specific oxidation of (3,4-dimethoxyphenyl)-2-propanone is attributed to the reaction with the enol form. It is assumed that the proton involved in the tautomeric change originates in the methylene rather than the methyl group. Thus, the enol is stabilized by conjugation of the double bond with the benzene ring. Bredereck and Gompper (55) provided experimental evidence for this position of the double bond. These workers obtained 1-bromo-1-phenyl-2-propanone in 70% yield from the reaction of 1-phenyl-2-propanone with bromine water. Evidence is available to show that the rate-controlling step in the bromination of ketones is the transformation of the ketone into its enol form or enolate anion, which is then brominated almost instantaneously.

The fact that enol formation might be a contributing factor in the oxidation of β -ketones has been shown by Gero (56). He has shown that the enol content of propiophenone is 0.01% and the enol content of 1-phenyl-2-propanone is 2.9%. Since most simple ketones have enol concentrations of 0.1 to 0.001%, the relatively high enol content of 1-phenyl-2-propanone (and its derivatives), ca. 3%, has been considered as an important factor in the oxidation of the β -ketones.

Veratraldehyde was obtained in a significant quantity from the oxidation of (3,4-dimethoxyphenyl)-2-propanone and it was expected that vanillin would be formed as an intermediate in a similar oxidation of (4-hydroxy-3-methoxyphenyl)-2-propanone. That is,

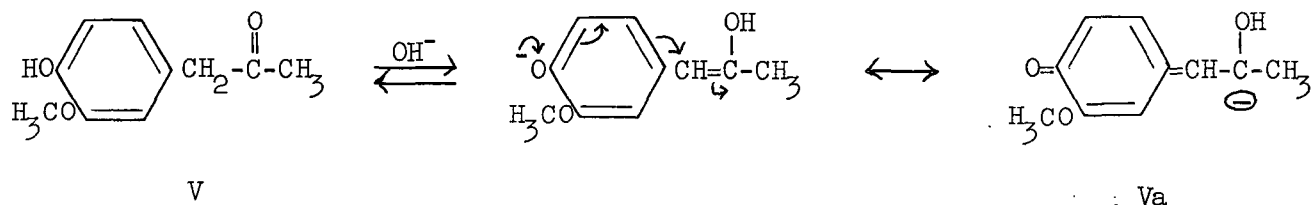


If this was indeed the case, then methoxyhydroquinone, from the oxidation of vanillin, would be one of the reaction products. However, this was not the case, and the only reaction product isolated from the reaction mixture was vanillic acid in 57% yield. Because vanillic acid is not formed when vanillin is oxidized to methoxyhydroquinone by alkaline hydrogen peroxide, vanillin cannot be considered as an intermediate in this reaction. A mechanism consistent with these results would involve the formation of an α -diketone as an intermediate. This intermediate would then be oxidized further to give a mixture of two acids (17, 25).



The unexpected behavior of (4-hydroxy-3-methoxyphenyl)-2-propanone upon treatment with alkaline hydrogen peroxide may be attributed to the free phenolic hydroxyl group. The data, however, were not sufficient to show how the phenolic hydroxyl group might affect the reaction.

In an alkaline medium, the phenolic hydroxyl group would be ionized. The phenolate anion may then be stabilized by resonance as shown in Va:



The increased electron-density on the side chain due to the resonance stabilization of the phenolate anion, Va, may reduce the rate of the reaction, particularly if the hydroperoxide anion is the attacking species.

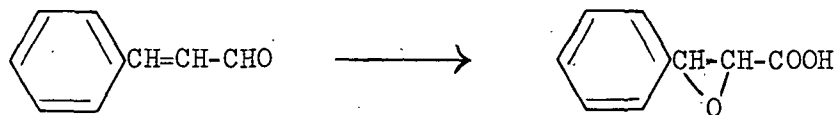
The initial oxidation of (4-hydroxy-3-methoxyphenyl)-2-propanone was conducted in a hydrogen peroxide solution made basic with sodium hydroxide. (A similar solution, without the model compound, exhibited a pH of 12.2.) In this reaction, 30% of the starting material was unchanged at the end of one hour. When a saturated sodium carbonate solution was used in place of one normal sodium hydroxide (initial pH 10.2), only 13.5% of the starting material was unoxidized at the end of the one-hour reaction period.

A similar treatment of (3,4-dimethoxyphenyl)-2-propanone showed that 24 and 26% (pH 12.2 and 10.2, respectively) was unchanged at the end of the one-hour reaction time.

α,β -UNSATURATED ALDEHYDE GROUPS

The following quotation is from Wallace's review on the organic reactions of hydrogen peroxide (24):

Alkaline hydrogen peroxide is effective in the epoxidation of α,β -unsaturated carbonyl compounds and nitriles. Nitrile and aldehyde functions in such molecules may be oxidized further, however, to amides and acids, respectively, during epoxidation. Cinnamaldehyde, for example, is converted to the glycidic acid derivative.



The work referred to in the above quotation is that of Weitz and Scheffer in 1921 (17). These workers, in their oxidation procedures used 1.2 to 2.4

equivalents of hydrogen peroxide, 0.5 to 2.4 equivalents of sodium hydroxide, and 1.0 equivalent of the α,β -unsaturated carbonyl compound. However, no experimental conditions were given for α,β -unsaturated aldehydes. A translation of a portion of their article follows:

α,β -Unsaturated ketones react very easily with alkaline hydrogen peroxide and the primary products, where they have been isolated, have been found to be 'oxides' having the composition of the original ketone plus one oxygen atom... These new oxides are monomolecular and liberate iodine from cold potassium iodide only slowly or not at all, hence they are not peroxides and can be only ethylene oxides; some in fact are identical with the products obtained by the condensation of benzaldehydes with bromoacetone...

Cinnamaldehyde, (which in air is oxidized less quickly than benzaldehyde), on the other hand, reacts so vigorously that the methanol solution (1:10) soon begins to boil. The product obtained in this case is not unreactive, as with the ketones, but is acidic; apparently both the ethylene group and the aldehyde group are attacked...

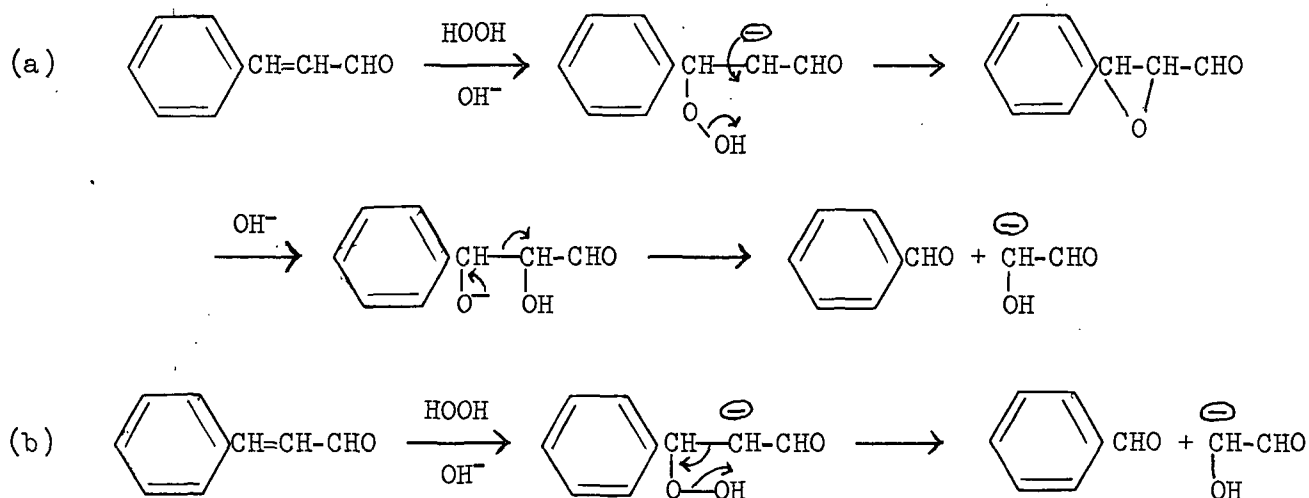
These workers did not isolate and identify an epoxy aldehyde or acid from their reaction of cinnamaldehyde with alkaline hydrogen peroxide. Such a result, however, might be inferred if their article is not read critically and carefully.

Payne (57) has stated that the epoxidation of α,β -unsaturated ketones by alkaline hydrogen peroxide is a well-known reaction; however, the similar reaction with simple α,β -unsaturated aldehydes has not been confirmed experimentally. In studying this reaction further, Payne successfully synthesized the epoxide of acrolein (18) and cinnamaldehyde (19). His procedure involved the dropwise addition of both hydrogen peroxide and the unsaturated aldehyde to an aqueous solution held at pH 8.0-8.5 by the addition of dilute alkali as required. He could not obtain these compounds when the reactants were added in one portion to the reaction vessel which is in accord with the results of

this study. Thus, the quotation in Wallace's review (24) appears to be in error. The epoxidation of simple α,β -unsaturated aldehydes by alkaline hydrogen peroxide is not a general reaction, but rather this reaction takes place only under carefully controlled conditions.

In the present investigation, the oxidation of 3,4-dimethoxycinnamaldehyde resulted in the formation of veratraldehyde and veratric acid. A similar treatment of cinnamaldehyde yielded benzaldehyde and benzoic acid as reaction products. In neither case, could the glycidic acid derivatives be detected.

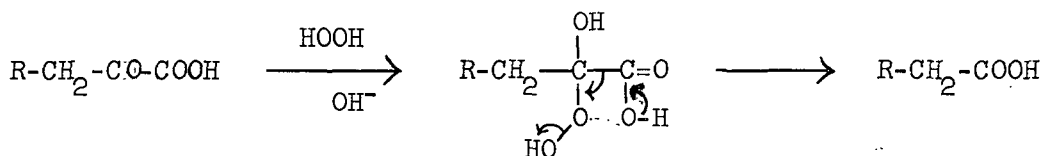
The formation of benzaldehyde, or its derivatives, is explained on the basis of the formation of an intermediate peroxide which rearranges to an unstable epoxide (a) or decomposes according to the mechanism shown in (b).



If the epoxyaldehyde is formed, as in the first mechanism above, it is believed that its decomposition would be relatively slow since similar materials have been isolated from alkaline solutions in high yield. Firm support for these or other mechanisms might be obtained by the isolation and identification of the side-chain fragment. Since this has not been done, the above mechanisms are suggested on the basis of the identified aromatic portion of the model compounds.

REACTIONS WITH OTHER GROUPS

(3,4-Dimethoxyphenyl)-pyruvic acid was decarbonylated by alkaline hydrogen peroxide solution giving (3,4-dimethoxyphenyl)-acetic acid in 80% yield. Bunton (58) reports that the reaction path for the decarbonylation of a keto-acid is:



The mechanism of this reaction has also been studied by using tracer techniques with oxygen-18 (58).

Dehydrodiisoeugenol was recovered unchanged from the oxidation mixture which indicates that this oxidizing system is not effective in the oxidative-hydrolytic cleavage of the phenylcoumaran linkage. α - and β -Conidendrin were also resistant to attack by alkaline hydrogen peroxide.

SUMMARY AND CONCLUSIONS

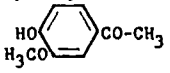
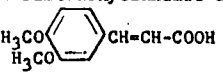
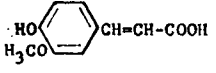
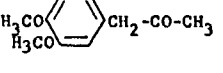
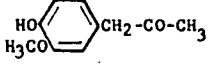
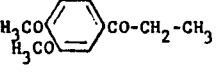
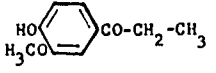
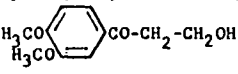
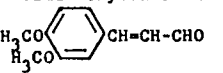
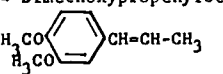
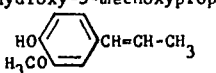
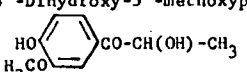
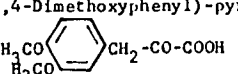
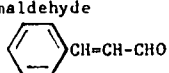
The peroxide bleaching of groundwood has been favorably accepted by the pulp and paper industry as it has the advantage of producing a relatively large increase in brightness without materially decreasing the yield or adversely affecting the pulp quality. Thus, alkaline hydrogen peroxide appears to be able to differentiate, in part at least, between the colored material and the natural lignin in pulps. Jones (7) showed that the elementary composition of the total lignin is not appreciably affected by the bleaching action of alkaline hydrogen peroxide. The present investigation has demonstrated how specific functional groups on lignin-related model compounds were changed upon application of and reaction with alkaline hydrogen peroxide.

Model compounds containing several types of functional groups were treated with alkaline hydrogen peroxide. The reaction products isolated and identified are listed in Table III. (The percentages are based on the starting material.)

Olefinic groups of the type represented by the propenylbenzene and cinnamic acid derivatives did not react with alkaline hydrogen peroxide. This result indicates that double bonds of this nature do not play an essential role in the response of lignin preparations to alkaline peroxide bleaching.

α,β -Unsaturated aldehydes reacted readily with alkaline hydrogen peroxide, and the isolated reaction products showed that cleavage occurred at the double bond. The two compounds with this side chain which were studied were both light yellow in color. The reaction products from these oxidations were colorless. According to Adler (35), who worked with Björkman lignin or milled wood lignin

TABLE III
MODEL COMPOUNDS AND THEIR REACTION PRODUCTS

| Model Compounds | Products |
|--|---|
| I 4'-Hydroxy-3'-methoxyacetophenone  | Methoxyhydroquinone (67%) |
| II 3,4-Dimethoxycinnamic acid  | No reaction |
| III 4-Hydroxy-3-methoxycinnamic acid  | No reaction |
| IV (3,4-Dimethoxyphenyl)-2-propanone  | Veratraldehyde (8.3%) Veratric acid (60%) |
| V (4-Hydroxy-3-methoxyphenyl)-2-propanone  | Vanillic acid (57%) |
| VI 3',4'-Dimethoxypropiophenone  | No reaction |
| VII 4'-Hydroxy-3'-methoxypropiophenone  | Methoxyhydroquinone (80%) |
| VIII 3-Hydroxy-3',4'-dimethoxypropiophenone  | No reaction |
| IX 3,4-Dimethoxycinnamaldehyde  | Veratraldehyde (ca. 83%) Veratric acid (16%) |
| X 3,4-Dimethoxypropenylbenzene  | No reaction |
| XI 4-Hydroxy-3-methoxypropenylbenzene  | No reaction |
| XII 2,4'-Dihydroxy-3'-methoxypropiophenone  | Methoxyhydroquinone (88%) |
| XIII (3,4-Dimethoxyphenyl)-pyruvic acid  | (3,4-Dimethoxyphenyl)-acetic acid (80%) |
| XIV Cinnamaldehyde  | Benzaldehyde (ca. 60%) |
| XV Dehydrodiisoeugenol | No reaction |
| XVI α- and β-Conidendrin | No reaction |

(MWL)* from spruce, the α,β -unsaturated aldehyde groups are present in about 3% of the lignin monomers and may thus be oxidized to colorless degradation products upon treatment with alkaline hydrogen peroxide.

The α -keto compounds, i.e., the derivatives of propiophenone, that were studied were oxidized by alkaline hydrogen peroxide only when a free phenolic hydroxyl group was para to the side chain. The β -keto isomers, both guaiacyl and veratryl, were oxidized readily by alkaline hydrogen peroxide. These compounds reacted presumably through the enol tautomer. On the basis of his studies with MWL, Adler (35) reported that the β -keto grouping is present in 10% of the lignin monomers. This functional group might also contribute to the color of lignin preparations if a free hydroxyl group is present para to the side chain.

The phenylcoumaran linkage is not attacked by alkaline hydrogen peroxide as shown by the stability of dehydrodiisoeugenol. According to Adler's studies with MWL this grouping would be present in 16% of the lignin polymer. The lignan conidendrin was not oxidized under the conditions employed in this study. The stability of these groups might help to explain why alkaline hydrogen peroxide is effective as a bleaching agent without causing delignification.

On the basis of Adler's analytical work with MWL (35), the structural elements in lignin which reacted with subsequent cleavage of the side chain represent about 14% of the monomer units in the lignin polymer. Oxidation of

*Both Björkman's milled wood lignin (MWL) and the lignin in groundwood have become "accessible" at the expense of considerable mechanical energy. Thus, a close relationship may exist between the lignin in groundwood and MWL, as any changes in the natural lignin due to the grinding action in the mechanical defibering of the whole wood, are expected to be similar. The same close relationship is not expected to hold for chemical pulps where lignin degradation results from a reaction with the components of the cooking liquor.

all these functional groups would result in extensive degradation and loss of the lignin in mechanical pulps. It is not expected, however, that the potentially oxidizable elements present in the lignin system would be available to react with the alkaline hydrogen peroxide with the same ease as the corresponding structures examined in the model compounds. In the polymeric lignin, these elements are probably less accessible to the oxidizing agent and would thus react less readily. The reactions of the various side-chain structures and functional groups examined in the low molecular weight model compounds are indicative of the reactions which occur in the more complex lignin system.

Wacek and Kratzl (13-15) were also concerned with the oxidation of variously substituted aliphatic side chains of lignin model compounds. These workers treated the model substances with alkaline nitrobenzene for 3 hours at a temperature of 160°C. On the basis of their results, Wacek and Kratzl reported that the presence of a phenolic hydroxyl group in the position para to the side chain favored the oxidation of the side chain. The extent of the oxidation was dependent upon the side-chain structure, but even a saturated aliphatic side chain, such as in 1-(4-hydroxy-3-methoxyphenyl)-propane, was oxidized to a limited extent. In the etherified phenols, the oxidation of the side chain was restricted to specific structures.

In the present study, the presence of a carbonyl group on the side chain favored the subsequent oxidation. The oxidation, in some instances, was dependent upon the presence of a free hydroxyl group in the position para to the side chain. Wacek and Kratzl obtained vanillin in high yields from the oxidation of 4-hydroxy-3-methoxypropenylbenzene (13) and 4-hydroxy-3-methoxycinnamic acid (15), whereas in the present study these compounds were not attacked by alkaline hydrogen peroxide.

Jones (7) indicated that only a portion of the carbonyl groups (and possibly the phenolic hydroxyl groups) were involved in the lignin-peroxide reaction. He was unable, however, to show whether these two groups react in conjunction with, or independent of, one another.

In the present investigation, the only compounds to react were those having a carbonyl group on the aliphatic side chain. Since those compounds which do not have carbonyl groups were not oxidized, the initial point of attack is probably due to this oxygen-containing functional group. The oxidative cleavage of the carbon-carbon bond by alkaline hydrogen peroxide appears to depend upon the polarizability of the bond under the influence of a carbonyl group.

The presence of the carbonyl group appeared to be a necessary, but not a sufficient, prerequisite for the oxidation of the phenylpropane side chain. For example, the derivatives of propiophenone all have the carbonyl function, but in the present study only those derivatives with a free phenolic hydroxyl group in the position para to the side chain were oxidized by the alkaline hydrogen peroxide. In these compounds, the carbonyl group reacted in conjunction with the phenolic hydroxyl group. A similar reaction might be expected to occur with "condensed" phenolic units, where the hydroxyl group is in the position ortho to a side chain.

It is not possible to interpret all of the reactions of lignin in the peroxide bleaching of mechanical pulps on the basis of a few model compounds. However, the results of the alkaline peroxide oxidation do point out some structural requirements for the reaction. The experimental results have shown that the α -keto compounds react only when a free phenolic hydroxyl group is present in the position para to the side chain. Furthermore, the β -keto groups

and the α,β -unsaturated aldehydes were shown to be degraded readily by alkaline peroxide solutions independently of the phenolic hydroxyl group.

It is suggested that only a small portion of the lignin in mechanical pulps and lignin preparations is responsible for the color. This modified lignin may be present in two tautomeric forms due to the presence of ionizable enolic groups in which the color is dependent upon the quantity of the colored tautomer. After reaction with the alkaline peroxide solution, the colored material has been changed further yielding colorless products.

The isolation and identification of intermediate and final reaction products has provided information which supports the above hypothesis and the suggestion made earlier by Jones (7). That is, the lignin-peroxide reaction appears to be initiated through the carbonyl group and may also involve keto-enol tautomerism. Depending upon the particular structure under discussion, this work demonstrated that the oxidation of the phenylpropane side chain of lignin model compounds involved the carbonyl functional group which could react both in conjunction with, and independent of, phenolic hydroxyl groups.

SUGGESTIONS FOR FUTURE WORK

1. Most of the materials used in this study were colorless as were the reaction products. Logically, then, the next step would involve a study of initially colored materials. For the most part, these would be in the class of extractives or extraneous materials, many of which are highly colored and may be present in high-yield pulps.
2. The oxidation of α,β -unsaturated aldehydes should be studied in more detail so that the mechanism of this reaction will be clarified in the literature.
3. A kinetic or Hammett study of the oxidation of derivatives of propiophenone, phenyl-2-propanone, and benzalacetone would provide further information on the importance of enolization and the effect of aromatic substitution in the peroxide oxidation.

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LITERATURE CITED

1. Lee, J. A., Chem. Met. Eng. 51, no. 8:106-8(1944).
2. Fennell, F. L., Smedberg, G. E., and Stalter, N. J., Tappi 43:903-9(1960).
3. Giertz, H. W., Tappi 44:1-4(1961).
4. Erdtman, H., Svensk Papperstid. 43:255-63(1940).
5. Stobo, W. E., and Russell, J. K., Pulp Paper Mag. Can. 48, no. 3:224-32 (1947).
6. Van den Akker, J. A., Lewis, H. F., Jones, G. W., and Buchanan, M. A., Pulp Paper Mag. Can. 50, no. 4:87-92(1949).
7. Jones, G. W. The effect of sodium peroxide bleaching on the components of eastern spruce groundwood. Doctor's Dissertation. Appleton, Wis., The Institute of Paper Chemistry, 1948. 134 p.
8. Brauns, F. E. The chemistry of lignin. p. 15. New York, Academic Press, 1952.
9. Brauns, F. E. Ref. 8, p. 538-49.
10. Brauns, F. E., and Brauns, D. A. The chemistry of lignin. Suppl. vol. p. 507. New York, Academic Press, 1960.
11. Friedrich, A., and Diwald, J., Monatsh. 46:31-46(1925); C.A. 20:1598.
12. Richtzenhain, H., Ber. 75:269-90(1942).
13. Wacek, A. v., and Kratzl, K., Cellulosechem. 20:108-11(1942).
14. Wacek, A. v., and Kratzl, K., Ber. 76:891-5(1943).
15. Wacek, A. v., and Kratzl, K., Ber. 77:516-19(1944).
16. Dakin, H. D., Am. Chem. J. 42:477-98(1909).
17. Weitz, E., and Scheffer, A., Ber. 54B:2327-44(1921).
18. Payne, G. B., J. Am. Chem. Soc. 81:4901-4(1959).
19. Payne, G. B., J. Org. Chem. 26:250-2(1961).
20. English, J., and Gregory, J. D., J. Am. Chem. Soc. 69:2120-2(1947).
21. Payne, G. B., and Williams, P. H., J. Org. Chem. 24:54-5(1959).
22. Boeseken, J., and Jacobs, J., Rec. trav. chim. 55:786-90(1936).

23. Swern, D., Chem. Revs. 45:1-68(1949).
24. Wallace, J. G. Hydrogen peroxide in organic chemistry. p. 32. Wilmington, Del., E. I. du Pont de Nemours and Co., 1960.
25. Barnes, R. P., and Lewis, R. E., J. Am. Chem. Soc. 58:947-8(1936).
26. Wallace, J. G. Ref. 24, p. 44.
27. Evans, M. G., and Uri, N., Trans. Faraday Soc. 45:224-30(1949).
28. Latimer, W. M. The oxidation states of the elements and their potentials in aqueous solutions. p. 40. New York, Prentice Hall, 1938.
29. Bunton, C. A., and Minkoff, G. J., J. Chem. Soc. 1949:665-70.
30. Wallace, J. G. Ref. 24, p. 31.
31. Martin, D. M. The bleaching of eastern spruce groundwood with alkaline peroxide. Doctor's Dissertation. Appleton, Wis., The Institute of Paper Chemistry, 1951. 223 p.
32. Brauns, F. E. Ref. 8, p. 236-69.
33. Brauns, F. E., and Brauns, D. A. Ref. 10, p. 227-70.
34. Gierer, J., Svensk Papperstid. 61:648-55(1959).
35. Adler, E., Papier 15:604-9(1961).
36. Pearl, I. A., and Beyer, D. L., J. Org. Chem. 16:216-20(1951).
37. Pearl, I. A., and Beyer, D. L., J. Org. Chem. 16:221-4(1951).
38. Muller, A., Lempert-Sréter, M., and Karczag-Wilhelms, A., J. Org. Chem. 19:1533-47(1954).
39. Adams, R., Geissman, T. A., Baker, B. R., and Teeter, H. M., J. Am. Chem. Soc. 63:528-34(1941).
40. Freudenberg, K., and Fikentscher, H., Ann. 440:36-8(1924).
41. West, K. A., Hawkins, W. L., and Hibbert, H., J. Am. Chem. Soc. 63:3035-8 (1941).
42. Feuerstein, K., J. prakt. Chem. 143:174-8(1935).
43. Kropp, K., and Decker, H., Ber. 42:1184-92(1909).
44. Dimroth, O., Eber, H., and Wehr, K., Ann. 446:132-47(1926).
45. Drake, N. L., Harris, H. C., and Jaeger, C. B., Jr., J. Am. Chem. Soc. 70:168-70(1948).

46. Pecsok, R. L. Principles and practice of gas chromatography. p. 142-50. New York, Wiley, 1959.
47. Reio, L., J. Chromatog. 4:458-76(1960).
48. Ross, H. A., Anal. Chem. 25:1297(1953).
49. Shriner, R. L., Fuson, R. C., and Curtin, D. Y. The systematic identification of organic compounds. 4th ed. p. 283. New York, Wiley, 1956.
50. Taylor, H. V., Ind. Chemist 29:9-15(1953).
51. Wacek, A. v., and Eppinger, H. O., Ber. 73:644-51(1940).
52. Bunton, C. A. In Edward's Peroxide reaction mechanisms. p. 15. New York, Interscience Publishers, 1962.
53. Wacek, A. v., and Bezard, A. v., Ber. 74B:845-57(1941).
54. Fieser, L. F., and Fieser, M. Advanced organic chemistry. p. 425. New York, Reinhold, 1961.
55. Bredereck, H., and Gompper, R., Chem. Ber. 87:700-7(1954).
56. Gero, A., J. Org. Chem. 19:1960-70(1954).
57. Payne, G. B., J. Am. Chem. Soc. 80:6461(1958).
58. Bunton, C. A. Ref. 52, p. 16.