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LIGNIN MODEL COMPOUNDS

II. PREPARATION AND PROPERTIES OF 1-HYDROXY-1-(4-HYDROXY-3-METHOXYPHENYL)-2-PROPANONE*

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ABSTRACT

Modern concepts of lignin structure suggest that the ketol 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, VI, should be detectable in the hydrolysis products of lignin and wood. A reference sample of VI, previously unavailable, has now been prepared by catalytic hydrogenation of the diketone 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione, II. Both fermentative and catalytic hydrogenation of II gave mixtures of, according to paper chromatography, mainly 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone, V; the desired ketol, VI; small amounts of vanillic acid; and traces of guaiacyl acetone and an unknown phenolic compound. The ketol VI was isolated from the catalytic hydrogenation products by solvent fractionation and was identified by absorption spectra, derivatives, and comparison with the other two possible isomeric ketols. Dilute alkali converted VI to the isomeric ketol V. Both ethanolysis and acidolysis of VI gave the same monomeric products as lignin.

Since the discovery by Hibbert and co-workers (1) that the four guaiacylpropane derivatives I–IV were produced by refluxing extractive-free coniferous wood with ethanol containing a small percentage of hydrogen chloride, extensive studies have been conducted on related monomers and dimers as model compounds for lignin reactions. In this way significant new knowledge of lignin structure and behavior has been acquired.

$R\text{—}CO\text{—}CH(OC_2H_5)\text{—}CH_3$ I

$R\text{—}CO\text{—}CO\text{—}CH_3$ II

$R\text{—}CH(OC_2H_5)\text{—}CO\text{—}CH_3$ III

$R\text{—}CH_2\text{—}CO\text{—}CH_3$ IV

$R\text{—}CO\text{—}CHOH\text{—}CH_3$ V

$R\text{—}CHOH\text{—}CO\text{—}CH_3$ VI

$R\text{—}CH_2\text{—}CO\text{—}CH_2OH$ VII

R = 4-hydroxy-3-methoxyphenyl

In seeking an explanation for the formation from lignin of the "ethanolysis" products, the synthesis and study of the three isomeric α-ketols V, VI, and VII were undertaken by the Hibbert group. The synthesis of V, 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone, and VII, 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, was accomplished (2, 3) but repeated attempts failed to provide VI, 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, and therefore it was necessary to perform ethanolysis and other reactions on its diacetate (4). Wacek and Horak (5) also attempted to prepare VI but found, as had Mitchell (6), that even very mild deacetylation techniques applied to the diacetate of VI invariably resulted in rearrangement to the more stable V. These findings were in accord with the results obtained with related alkylaryl α-ketols by Auwers and Noll (7) and Temnikova (8). Thus methylbenzoyl carbinol (V, R = phenyl) rearranged with a variety of reagents to phenylacetyl carbinol (VI, R = phenyl) whereas

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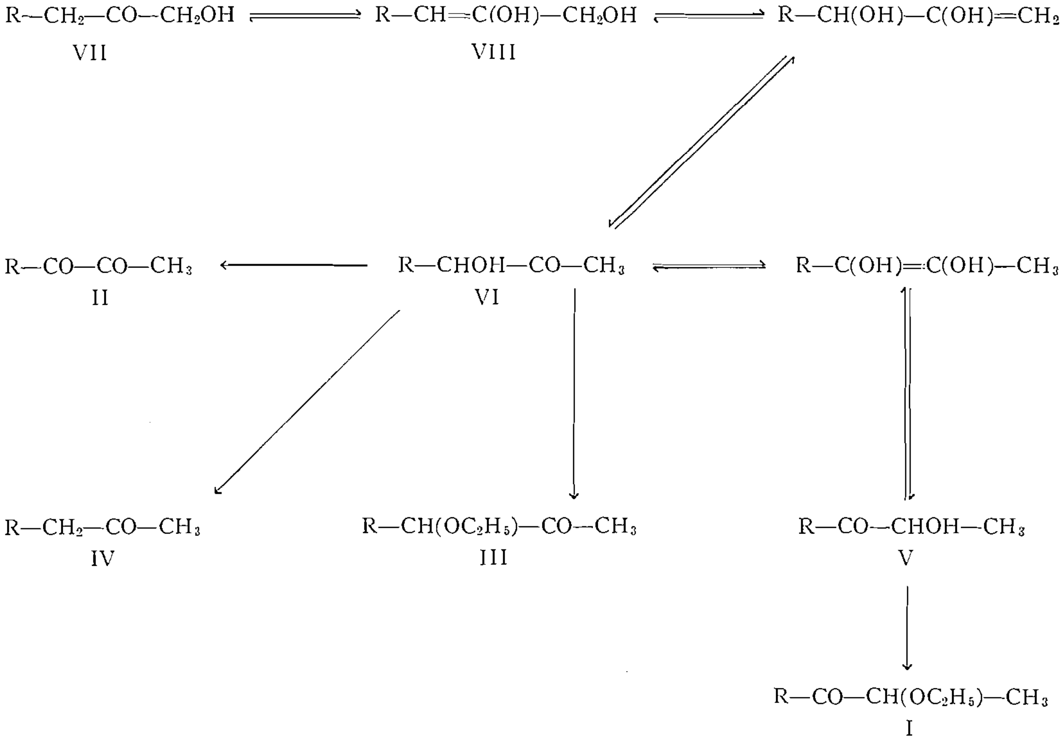
substitution of a methoxyl or hydroxyl group into the para position of the benzene ring stabilized the methylbenzoyl carbinol and completely reversed the order of stability. In the guaiacylpropane series, therefore, the para hydroxyl group stabilizes the 2-hydroxy derivative V and accounts for the difficulties experienced in attempts to prepare the 1-hydroxy derivative VI.

In a previous paper (9) strong experimental support was provided for Hibbert's proposal that the ethanolysis products, I–IV, are derived from lignin via a more reactive β-hydroxyconiferyl alcohol unit, VIII, by a series of rearrangements:



R = 4-hydroxy-3-methoxyphenyl

The relatively small amount of the ethyl ether, III, of the ketol VI compared to that of I of the ketol V obtained in lignin ethanolysis is consistent with the above scheme and the apparent relative stability of the ketols.

The same explanation applies to the formation of the lignin ethanolysis products by ethanolysis of guaiacylglycerol and its β-guaiacyl and β-coniferyl ethers, substances which have been found to be excellent model compounds for the study of characteristic lignin reactions (10). A primary α–β dehydration would yield an enol ether which would hydrolyze to β-hydroxyconiferyl alcohol, VIII. According to this scheme small amounts of the intermediate 1-hydroxy ketone VI should occur in the hydrolysis and acidolysis products of lignin and lignin model compounds. Goldschmid (11) suspected that an unknown substance detected among the products of aqueous hydrolysis of extractive-free western hemlock woodmeal was the 1-hydroxy derivative VI but this awaits confirmation. Adler *et al.* (12) showed that refluxing guaiacylglycerol-β-guaiacyl ether and two isolated lignins with dioxane–water containing 0.2 *N* hydrogen chloride ("acidolysis") gave a mixture

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of products containing the 2-hydroxy ketone V, the diketone II, and guaiacyl acetone, IV. Other guaiacylpropane derivatives, if present, were not identified. The purpose of the present work was to prepare a sample of the 1-hydroxy compound VI for reference purposes in lignin hydrolytic studies and to permit a study of its properties in relation to lignin and related propylphenols.

In seeking methods that would avoid the chance of acid- and base-catalyzed rearrangements in the final stages, the possibility of preparing VI by treating vanillin with fermenting sugar solutions was investigated. Neuberg and Hirsh (13) had found that addition of benzaldehyde to sugar solutions yielded some phenylacetyl carbinol as well as benzyl alcohol. Application of this technique to vanillin showed that as well as the main product, vanillyl alcohol, minor amounts of vanillic acid, and two unknown compounds were produced. Paper chromatographic examination showed that neither of these was the known 2-hydroxy derivative V. While it was considered possible that some of the desired 1-hydroxy compound VI was present, this technique as a method of preparation was abandoned because of the obvious difficulties in purification. Subsequently, reports of the similar work of Higuchi *et al.* (14) came to hand. These workers also found that vanillyl alcohol, vanillic acid, and small amounts of the diketone II were formed from vanillin in fermenting sugar solution. Another minor product detected by paper chromatography (15) was believed to be the 1-hydroxy derivative VI but no confirmation has been published.

The hydrogenation of the diketone II as a means of preparing a sample of VI was investigated. This approach would eliminate contamination of the products with reduction products of vanillin. Both phytochemical and catalytic reduction methods were examined.

Addition of the yellow diketone to fermenting sucrose solution resulted in rapid decolorization. Descending paper chromatography in two solvent systems showed the presence of six phenolic substances: the ketol V (the main component), vanillic acid, unchanged diketone (trace), guaiacyl acetone, IV (trace), and two unknown compounds. One of these ($R_f = 0.89$ in butanol–ethanol–ammonia–water, 40:10:1:49 v/v) gave a pink color with diazotized sulphanilic acid (DSA) and was present in traces. The other ($R_f = 0.76$), present in substantial quantities, gave an orange color with DSA.

When the diketone II was treated in ethanol with 1 mole of hydrogen at room temperature and pressure over a palladium – barium sulphate catalyst prepared according to Kuhn (16), a very similar mixture of phenolic products was obtained according to paper chromatography. In this case the mixture was not contaminated with yeast and sugar fermentation products and it crystallized on standing. Recrystallization from benzene gave the pure 2-hydroxy derivative V. Attempts to isolate the other products by chromatography on celite and cellulose columns were unsuccessful. However, extraction of an ether solution of the mixture with aqueous bisulphite solution gave a bisulphite-soluble fraction containing the substance $R_f = 0.76$, believed to be the desired 1-hydroxy derivative, VI, contaminated with unreacted diketone, II. Distribution of this fraction between benzene and water gave a good separation, the diketone being retained in the benzene layer.

The product isolated from the aqueous layer as a colorless oil gave a strongly positive test for *p*-hydroxybenzyl alcohols with quinone monochloroimide (17) and exhibited only one spot on paper chromatograms using several solvent systems. It slowly crystallized and after recrystallization from ether – petroleum ether had a melting point of 53–54° C. The ultraviolet and infrared absorption spectra were consistent with a 1-aryl-2-propanone structure. Proof that it was the expected 1-hydroxy derivative, VI, was

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provided by preparing the diacetate, which, obtained in high yield, was identical with an authentic sample of the diacetate of VI synthesized by the method of Mitchell and Hibbert (4).

It was of interest to determine the relative proportion of the two α-ketols V and VI produced by catalytic hydrogenation of the diketone. By quantitative paper chromatography (18), the mixture was found to consist of 73% 2-hydroxy derivative, V; 13% 1-hydroxy derivative, VI; 14% unchanged diketone; 2.6% vanillic acid; and a trace of guaiacyl acetone, IV, and an unknown ($R_f = 0.89$).

No systematic investigation of the effect different solvents or catalysts might have on the hydrogenation of the diketone was undertaken. However, after this paper was presented, the results of Adler and Marton (19) on the hydrogenation of a series of lignin model compounds became available. Using 93% acetic acid as solvent and a palladium chloride - barium sulphate catalyst, unwashed after prehydrogenation, they found that carbonyl groups conjugated to the guaiacyl ring, as in the ketol V and the diketone II, were reduced rapidly, whereas those in the position β to the ring, as in IV, were practically unaffected. Thus rapid addition of 2 moles of hydrogen to the diketone was reported to yield guaiacyl acetone, IV, via hydrogenation and then hydrogenolysis, the β-carbonyl not being reduced. This report prompted us to hydrogenate the diketone with Kuhn's catalyst (16) in 95% acetic acid instead of ethanol. After addition of 1 mole of hydrogen, the products were approximately the same as when ethanol was used as solvent, the main product being, as before, the 2-hydroxy derivative V. The indicated marked effect of the catalyst on the course of the reaction is now being investigated.

Ethanolysis of 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, VI, gave the same propylphenol products, I–IV, as lignin, in accord with the prior work on the diacetate (4).

Treatment of VI with dilute alkali at 95° C rapidly brought about complete conversion to the 2-hydroxy derivative V, a result predictable from the findings of Mitchell (6) and of Wacek and Horak (5).

Acidolysis of VI in dioxane–water according to the method of Adler *et al.* (12) gave a mixture consisting of mainly the 2-hydroxy derivative V and the diketone II with traces of vanillic acid, vanillin, and an unknown phenol. Both V and II were obtained by Adler *et al.* by the acidolysis products of wood and isolated lignin. After 4 hours of acidolysis, roughly 10% of the ketol VI was unchanged. This measure of stability indicates that there is a good possibility of detecting the occurrence of the ketol VI in the acidolysis and hydrolysis products of lignins and wood.

The preparation of 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, VI, completes the syntheses of the three possible α-ketols in the guaiacylpropane series and provides reference samples for use in lignin degradation studies. Its behavior in ethanolysis and acidolysis reactions confirms conclusions based on prior studies with derivatives and isomers.

EXPERIMENTAL

Solvent systems for paper chromatographic examinations were butanol–ethanol–ammonia–water (40:10:1:49 v/v) (BEAW) and tetrahydrofuran - petroleum ether (65–110°) - water (3:7:5 v/v) (THF). In the case of the latter system R_f's depended to a marked extent on the care exercised in equilibrating the paper with the solvent and therefore are not quoted.

Preparation of Diketone 1-(4-Hydroxy-3-methoxyphenyl)-1,2-propanedione, II

Two methods were used: 2-hydroxy-1(4-hydroxy-3-methoxyphenyl)-1-propanone was prepared from guaiacol and oxidized with copper sulphate by the method of Brickman *et al.* (20), or propiovanillone (22)

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was converted with isobutyl nitrite by the method of Fodor *et al.* (21) to the α-oximino ketone, which was hydrolyzed to the diketone with 2% HCl at reflux or with 12 *N* H_2SO_4 at room temperature. The yellow diketone was extracted with benzene and recrystallized from petroleum ether, m.p. 62–63° C.

Preparation of 1-Hydroxy-1(4-hydroxy-3-methoxyphenyl)-2-propanone, VI

Kuhn's catalyst (16) (0.5 g) was added to 95% ethanol (50 ml), the flask evacuated, and the contents equilibrated with H_2 (13.7 ml) by mechanical shaking at slight pressure. The diketone (3 g = 0.0155 mole) was added, the flask again evacuated, and H_2 (348 ml = 0.0155 mole) added with mechanical shaking over 21 minutes. The catalyst was filtered and washed with ethanol, the filtrate and washings being evaporated under reduced pressure to yield a yellow oil (3 g). This oil gave a positive color test for *p*-hydroxybenzyl alcohols with quinone monochloroimide (17), and descending paper chromatographic examination showed the presence of six substances giving positive color reactions with DSA. The use of reference samples established the presence of vanillic acid (orange, R_f 0.22 BEAW); 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone, V (tan, R_f 0.54); diketone II (tan, R_f 0.60); guaiacyl acetone, IV (red, R_f 0.89); and two unknowns (strong orange, R_f 0.76; and weak red, R_f 0.89). The unknown with the same R_f on paper as guaiacyl acetone using BEAW was readily separated from it with the other solvent (THF).

The unknown with the orange color reaction, which also gave a positive 2,4-dinitrophenylhydrazone test, was isolated by the following fractionation, each step being monitored by paper chromatography. A diethyl ether solution (100 ml) was extracted with 15% sodium bisulphite solution (4×20 ml), then was back-extracted with diethyl ether (4×25 ml) to ensure removal of the 2-hydroxy derivative V and vanillic acid from the bisulphite-soluble compounds. The bisulphite solution was acidified to pH 3 with 6 *N* H_2SO_4, stripped of SO_2 using partial vacuum and a nitrogen bubbler, and then extracted with chloroform (5×25 ml). After drying, the chloroform was evaporated to leave a yellow oil which in benzene solution (50 ml) was extracted with water (5×25 ml). The water after back extraction with benzene (2×25 ml) was extracted with chloroform (7×25 ml). Drying and removal of the chloroform left a colorless oil (280 mg; 9% yield) which slowly crystallized. This material showed only one spot (orange, R_f 0.76 BEAW) on a papergram. Recrystallization from ether – petroleum ether gave colorless crystals, melting point 53–54° C. The infrared absorption spectrum, $\nu_{\mathrm{KBr}}^{\mathrm{max}}$ in cm^{-1} 3450, 3325, 2950, 2860, 1700 (unconjugated carbonyl), 1610, 1516, 1470, 1433, 1355, 1270, 1150, 1125, 1080, 1030, 866, 814, 735, was consistent with structure VI being very similar to that of the isomeric α-ketol VII (9). The ultraviolet absorption spectrum in ethanol (max. 282 mμ; min. 261 mμ; shoulder 234 mμ) was also consistent with this formulation. The semicarbazone, m.p. 170.5–172° C from hot water, differed from those of authentic specimens of the two α-ketols V and VII, m.p. 147–148 and 194–196° C respectively, prepared by identical procedures. The diacetate prepared in high yield (80%) by a 5-minute reflux in acetic anhydride – pyridine was identical by mixed melting point, 95.5–96° C, and infrared spectra with an authentic sample of 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone synthesized by the method of Mitchell and Hibbert (4).

If the oily hydrogenation product from the diketone was seeded with the 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone, V, partial crystallization occurred. Trituration with cold benzene followed by recrystallization from benzene gave colorless crystals, m.p. 110–111° C, identical with authentic V.

The presence of vanillic acid in the diketone hydrogenation product was proved by extraction of the ether solutions with cold 5% sodium bicarbonate solution. Acidification gave crystalline material identical with an authentic sample of vanillic acid.

Quantitative Estimation of Diketone Hydrogenation Products

A quantitative paper chromatographic method (18) with BEAW as developing solvent and Folin–Ciocalteu reagent for phenols was used, the spots being detected with ultraviolet light. Optical densities were measured at 750 mμ on a Beckman DK-2.

Ethanolysis of 1-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone

A sample (20 mg) was refluxed with ethanol – 3% HCl (1.5 ml) for 24 hours in a carbon dioxide atmosphere. After cooling, the mixture was added to water (10 ml) and filtered. The filtrate was extracted with ether, the extract dried, and solvent removed. Paper chromatographic examination of the residue in comparison with synthetic mixtures of authentic specimens using BEAW, 20% aqueous KCl, and isopropanol–ammonia–water (8:1:1 v/v) as solvents showed the presence of the ethanolysis products I–IV.

Alkaline Rearrangement of 1-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone

A sample (36 mg) was dissolved in 1% NaOH (15 ml), forming a yellow-colored solution which turned orange on warming under a nitrogen atmosphere on a steam bath (95° C) for ½ hour. Acidification and extraction with chloroform yielded, after removal of the solvent, a yellowish oil (30 mg) which slowly crystallized. It was shown to be the isomeric 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone by infrared absorption spectrum and chromatographic comparison with an authentic sample in BEAW and 20% aqueous KCl.

Acidolysis of 1-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone

The ketol VI (10 mg) was refluxed in dioxane-water (9:1) (15 ml) containing 0.2 *N* hydrogen chloride by weight for 4 hours (12). The mixture was neutralized with sodium bicarbonate, evaporated to remove

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most of the dioxane, diluted with water (10 ml), and extracted with chloroform (3×20 ml). Removal of the chloroform yielded a yellow oil (9 mg). Paper chromatography with BEAW solvent, THF solvent, and 20% aqueous KCl using DSA and ultraviolet light for detection showed, besides unchanged starting material (roughly 10%), the 2-hydroxy isomer V and the diketone II with traces of vanillin, vanillic acid, and an unknown phenol.

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