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Studies on Lignin and Related Products. IX.[1] Cupric Oxide Oxidation of Lignin Model Substances[2,3]

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Reaction of vanillin, 5-propenylvanillin and 5-allylvanillin with cupric oxide and alkali under conditions of lignosulfonate oxidations yielded only monoguaiacyl compounds. Reaction of the bis-vanillyl compounds, vanillil, vanilloin, desoxyvanilloin, hydrovanilloin and bivanillyl under the same conditions yielded vanillil, vanillovanillone, vanillin, vanillic acid, dehydrodivanillin and others. Thus, the occurrence of many of the compounds in lignosulfonate–cupric oxide reaction mixtures can be accounted for on the basis of a bis-vanillyl structure for a portion of the lignin molecule.

The recent isolations of vanillil and vanillovanillone (4,4′-dihydroxy-3,3′-dimethoxybenzophenone) from cupric oxide and alkali–lignosulfonate oxidation mixtures[4] led to a study of the mechanism of the formation of these materials under the conditions of the oxidation reaction. The possible secondary condensation of vanillin first formed by the oxidation and decarboxylation of guaiacyl units with carbon linkages in the 5-position was investigated along with the possible presence of a linkage between the α-carbon atoms of two C_6–C_3 units in at least a part of the complex lignin structure, as noted earlier.[4] The present paper presents a study of the oxidation with cupric oxide and alkali at 170° of vanillin, 5-allylvanillin, 5-propenylvanillin and the bimolecular vanillyl compounds, vanillil, vanilloin, desoxyvanilloin, hydrovanilloin and bivanillyl under conditions used previously for the oxidation of lignosulfonates.[4,5]

Oxidation of vanillin and analysis of the products by paper chromatography indicated that vanillic acid was the only product of the reaction. Similar reaction of 5-allylvanillin yielded 5-propenylvanillin, 5-formylvanillin, 5-carboxyvanillin, 5-formylvanillic acid, 5-carboxyvanillic acid, vanillin and vanillic acid. The same products were obtained from the analogous oxidation of *cis*-5-propenylvanillin. Oxidation of *trans*-5-propenylvanillin gave all of these compounds except 5-formylvanillin. In no case was even a trace of a bivanillyl derivative noted.

Therefore, it is apparent that guaiacyl units with carbon linkages in the 5-position as represented by 5-allylvanillin and 5-propenylvanillin can account for the occurrence of the 5-formyl- and 5-carboxyguaiacyl compounds isolated in lignosulfonate oxidation, but it is improbable that such structures (or unsubstituted guaiacyl units) can account for the bivanillyl derivatives such as vanillil, vanillovanillone and 4,4′-dihydroxy-3,3′-dimethoxystilbene[6] which have been isolated from lignosulfonate oxidation mixtures.

Oxidation of vanillil, separation of the reaction products by fractional solubility and analysis of the fractions by means of paper chromatography resulted in the recovery of 81% vanillil along with yields of 11% vanillic acid and 7% vanillovanillone. Increase in reaction time yielded more vanillovanillone at the expense of vanillil. The high recoveries in these experiments indicated that in one case vanillil is cleaved to give two molecules of vanillic acid and in the other case, is rearranged by alkali to give an intermediate vanillilic acid which is decarboxylated and oxidized by the alkaline cupric hydrate reaction mixture to yield vanillovanillone.

Similar reaction of vanilloin gave vanillil, vanillic acid and vanillovanillone in yields of 69, 15 and 16%, respectively. Thus, it appears that vanillil in the nascent form, produced upon oxidation of vanilloin with alkaline cupric oxide, is more susceptible to benzilic acid rearrangement than is preformed vanillil. Apparently, this is also true for the oxidation to vanillic acid. The stability of vanillin in this reaction makes remote the possibility of cleavage of vanilloin before oxidation and subsequent oxidation of the produced vanillin.

Analogous oxidation of hydrovanilloin gave vanillin (70%) and vanillic acid (28%) as the chief products along with small amounts of vanillil (1%) and dehydrodivanillin (1%). It is interesting to note the high yield of vanillic acid in this case in contrast to the same reaction at atmospheric pressure[7] in which no vanillic acid was obtained. It is evident that the "enediol," 3,3′-dimethoxy-α,α′,-4,4′-tetrahydroxystilbene, formed by oxidation of hydrovanilloin must split to form two molecules of vanillin which is oxidized directly to vanillic acid in its nascent state. Dehydrodivanillin was also noted earlier in the oxidation of hydrovanilloin with cupric sulfate and pyridine.[7]

Desoxyvanilloin upon similar oxidation, yielded 17% vanillil and 8% vanillic acid. The chief product (54%) in this reaction was a carbonyl compound having the same ultimate analysis as desoxyvanilloin, but a molecular weight of a dimer. The dimer appears to be the aldol condensation product of desoxyvanilloin, 3-hydroxy-1,2,3,4-tetra-(4-hydroxy-3-methoxyphenyl)-butan-1-one (I). In addition to the aldol, there was obtained in 16% yield a new compound having carbonyl function and an ultimate analysis corresponding with the aldol, I, less one mole of water. In all probability, the compound is the unsaturated ketone, 1,2,3,4-tetra-(4-hydroxy-3-methoxyphenyl)-3-butene-1-one (II). Ultraviolet absorption spectra for I and

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[1] For paper VIII of this series, see *Anal. Chem.*, **24**, 1366 (1952).

[2] Presented before the Division of Cellulose Chemistry at the 124th Meeting of the American Chemical Society, Chicago, Illinois, September 6 to 11, 1953.

[3] A portion of this paper represents results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

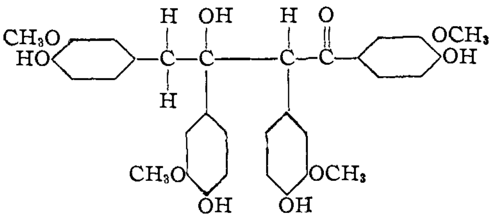
[4] I. A. Pearl and E. E. Dickey, THIS JOURNAL, **74**, 614 (1952).

[5] I. A. Pearl and D. L. Beyer, *Tappi*, **33**, 544 (1950).

[6] H. Richtzenhain and C. von Hofe, *Ber.*, **72B**, 1890 (1939).

[7] I. A. Pearl, THIS JOURNAL, **74**, 4260 (1952).

II are shown in Fig. 1. In this experiment the alkali appears to have played a more important role than did the cupric oxide.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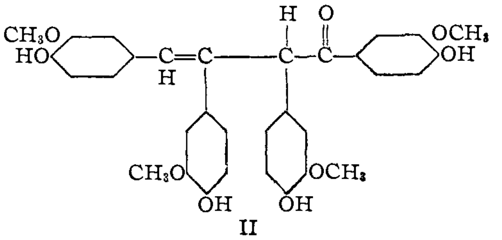
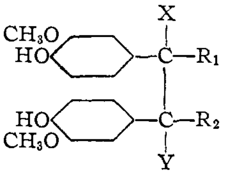

II

Oxidation of bivanillyl under the same conditions yielded a complex reaction mixture from which vanillin, vanillic acid and vanillil were isolated in yields of 32, 14 and 28%, respectively.

Except for the desoxyvanilloin experiment, the bis-vanillyl compounds lower in oxidation level than vanillin yielded vanillin as the main product of alkaline cupric oxide oxidation along with vanillic acid and vanillil as other important products. The other bis-vanillyl compounds yielded vanillic acid, vanillil and vanillovanillone, but no vanillin. It is apparent from these experiments that the occurrence of many of the compounds in alkaline lignosulfonate–cupric oxide reaction mixtures can be accounted for on the basis of a bis-vanillyl structure (formula III) for a portion of the lignin complex. Oxidations of compounds of formula III in which R_1 and R_2 are alkyl groups and X and Y are either hydrogen, hydroxyl, or absent entirely are in progress and will be reported at a later date.


III

Experimental

All melting points are uncorrected.

Starting Materials.—The 5-substituted vanillins and bis-vanillyl compounds employed in this study are products whose syntheses have been described earlier.[7–9]

General Oxidation Procedure for Monoguaiacyl Compounds. The Oxidation of Vanillin.—A mixture of 72 g. of vanillin, 160 g. of sodium hydroxide, 446 g. of cupric hydroxide and 2400 cc. of water was stirred and heated in a one-gallon stainless steel autoclave at 170° for 3 hours as described earlier.[5] The reaction mixture was filtered, and the residue was washed thoroughly with hot water. The filtrate and washings were diluted to 3000 cc. An aliquot ($^1/_8$) was acidified first with sulfur dioxide, then with carbon dioxide, and finally with sulfuric acid, and extracted with ether after each acidification as described previously.[10]

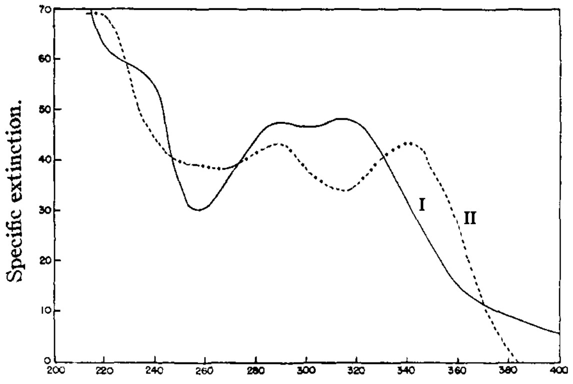


Fig. 1.—Ultraviolet absorption curves.

All ether extracts were dried and distilled, and the residues dissolved in acetone and spotted on Whatman No. 1 filter paper in triplicate. The papers were developed in a descending system with butanol saturated with 2% aqueous ammonia, and the chromatograms sprayed separately with bis-diazotized benzidine,[11] 5% ferric chloride solution and a saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid. Vanillin spots appeared at R_f 0.48 and vanillic acid at R_f 0.10. No other products were indicated on the paper chromatograms.

The other monoguaiacyl compounds were oxidized and analyzed in the same manner. R_f values for this developer and colors produced with the ferric chloride spray reagent for the products of oxidation were: 5-carboxyvanillic acid, 0.01, deep purple; 5-formylvanillic acid, 0.02, brownish black; vanillic acid, 0.10, yellow; 5-carboxyvanillin, 0.22, violet; 5-formylvanillin, 0.31, light blue; vanillin, 0.48, light bluish violet; and 5-propenylvanillin, 0.79, light bluish green. In all cases, positive identification of spots was made by elution of the unsprayed spot with a solution containing 60 volumes of 95% ethanol, 30 volumes of water and 10 volumes of concentrated ammonium hydroxide by a modified Dent[12] procedure. The ethanol was evaporated, and the remaining aqueous solution was acidified with dilute sulfuric acid and extracted with ether. The product recovered from the ether was recrystallized and compared with the authentic sample[8] by mixed melting point. Both 5-propenylvanillins have the same R_f value, but only the *trans*-isomer was isolated from the reaction mixtures.

General Oxidation Procedure for Bis-vanillyl Compounds.—All such oxidations were made in an identical manner. A mixture of 26 g. of the bis-vanillyl compound, 80 g. of sodium hydroxide, 223 g. of copper hydrate and 1250 g. of water was stirred and heated as described above at 170° for 2 hours. The combined filtrate and washings were diluted to 2000 cc. One-fourth aliquots were taken for evaluation.

Vanillil Oxidation.—The aliquot was saturated with sulfur dioxide gas, and the precipitate was filtered and washed with water. The sulfur dioxide saturated solution was extracted with ether, and the ether was dried and distilled to yield the bisulfite-insoluble extract. The aqueous solution was acidified with sulfuric acid, boiled to remove sulfur dioxide, cooled and extracted with ether. The ether was dried and distilled to yield the acid-insoluble extract.

The original precipitate (5.3 g.) was covered with benzene, allowed to stand 16 hours at 20° and filtered. Both residue and filtrate were chromatographed as before on paper, and the spots were located by means of the ferric chloride–potassium ferricyanide spray reagent of Barton, Evans and Gardner.[13] The benzene residue gave only one spot at R_f 0.19, and the benzene solution gave a spot at R_f 0.49. The R_f 0.19 residue was recrystallized from acetic acid to give yellow crystals of vanillil which did not depress a mixed melting point with the starting material. The benzene solution was evaporated to dryness and recrystallized

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[8] I. A. Pearl and D. L. Beyer, THIS JOURNAL, **74**, 4263 (1952).

[9] I. A. Pearl, *ibid.*, **74**, 4593 (1952).

[10] I. A. Pearl, *ibid.*, **71**, 2196 (1949).

[11] J. E. Koch and W. Krieg, *Chem. Z.*, **62**, 140 (1938).

[12] C. E. Dent and C. Rimington, *Biochem. J.*, **41**, 240 (1947).

[13] G. M. Barton, R. S. Evans and J. A. F. Gardner, *Nature*, **170**, 249 (1952).

from benzene to give colorless crystals of vanillovanillone melting at 154–155° and which did not depress the melting point of a mixture with authentic synthetic vanillovanillone.[14]

The bisulfite-insoluble extract was leached similarly with benzene to give a residue and filtrate which were chromatographed to give spots at R_f 0.10 and 0.49, respectively. The residue was recrystallized from water to yield white needles of vanillic acid melting at 209–210°. The benzene solution was evaporated to dryness, and the residue recrystallized from benzene to give crystals of vanillovanillone melting at 154–155°.

Total yields obtained were: recovered vanillil, 81%; vanillovanillone, 7%; and vanillic acid, 11%. The acid-insoluble extract amounted to 0.6%.

A similar reaction mixture maintained at 170° for 7.5 hours yielded vanillil, vanillovanillone and vanillic acid in yields of 74, 15 and 11%, respectively.

Vanilloin Oxidation.—This reaction mixture was treated in an identical manner to yield 69% vanillil, 16% vanillovanillone and 15% vanillic acid.

Hydrovanilloin Oxidation.—The aliquot, upon saturation with sulfur dioxide, yielded 1% of vanillil as a precipitate. The filtrate was extracted with ether to yield 28% vanillic acid. The residual bisulfite solution was acidified with sulfuric acid, freed of sulfur dioxide by boiling and extracted with ether. Paper chromatography of the evaporated extract indicated vanillin and small amounts of vanillic acid and dehydrodivanillin (R_f 0.01). The evaporated extract was extracted completely with boiling petroleum ether (b.p. 65–110°) to yield colorless needles of vanillin melting at 80–81°. The residue was extracted with saturated sodium bicarbonate solution and then dissolved in acetone. The entire acetone solution was spotted on several sheets of Whatman No. 1 filter paper and chromatographed as before. Bands were obtained at R_f 0.01 (dehydrodivanillin) and R_f 0.10 (vanillic acid). The bands were cut, and the strips containing the R_f 0.01 bands were eluted by the modified Dent procedure described above. The eluted material was recrystallized from glacial acetic acid to yield crystals of dehydrodivanillin melting at 315–317° which did not depress a mixed melting point with an authentic sample.[7] The yields of vanillin and dehydrodivanillin were 70 and 1%, respectively.

Desoxyvanilloin Oxidation.—The aliquot was saturated with sulfur dioxide, and the precipitate was filtered and washed. The aqueous filtrate was extracted with ether. Paper chromatography indicated that the ether extract and the original precipitate were identical and gave heavy spots at R_f's 0.10, 0.19, 0.48 (bright yellow fluorescence) and 0.88 (bright blue fluorescence). The products were combined and allowed to stand with acetone for 16 hours. The acetone-insoluble portion was recrystallized from boiling acetone to give colorless crystals of I melting at 270–271° and having an R_f of 0.48.

Anal. Calcd. for $C_{32}H_{32}O_{10}$: C, 66.66; H, 5.59; mol. wt., 577. Found: C, 66.56; H, 5.59; mol. wt., 558.

The original acetone filtrate was evaporated, and the residue (3.51 g.) was dissolved in 50 cc. of butanol–2% aqueous ammonia and mixed with 12 cc. of cellulose powder.[15] This slurry was chromatographed on a column (70 mm. in diameter and 650 mm. in length) of cellulose powder prewet with butanol–2% aqueous ammonia. The chromatogram was developed with 5 liters of butanol–2% aqueous ammonia to give four visible bands which were collected in the effluent as a flowing chromatogram. Band A was blue and had a strong blue fluorescence in ultraviolet light. Band B was red, band C was a multicolored band, and band D was yellow. Paper chromatograms indicated only a compound of R_f 0.88 in bands A and B, I with R_f 0.48 in band C, and vanillil with R_f 0.19 in band D. Bands A and B were combined and distilled to remove most of the butanol, and the butanol was finally displaced with water. The crystals were filtered and recrystallized twice from benzene in the presence of decolorizing carbon to yield colorless crystals of II melting at 250–251° and having an R_f of 0.88.

Anal. Calcd. for $C_{32}H_{30}O_9$: C, 68.81; H, 5.41. Found: C, 68.76; H, 5.15.

Similar treatment of band C gave more I melting at 270–271°.

Band D, on evaporation and recrystallization from acetic acid yielded vanillil as yellow needles melting at 230–231°.

The cellulose column was eluted with 50% acetone, and the eluate was evaporated to dryness. Paper chromatography indicated vanillic acid and dehydrodivanillin. The entire product was chromatographed as before on a smaller cellulose column. The effluent was collected until a test sample no longer showed a test for vanillic acid by paper chromatography. The total effluent was evaporated to dryness, and the residue recrystallized from water to yield vanillic acid crystals.

The column was eluted with 50% acetone and the eluate was evaporated to dryness. The residue was recrystallized to give dehydrodivanillin.

The yields in the oxidation of desoxyvanilloin were: I, 54%; II, 16%; vanillil, 17%; vanillic acid, 8%; and dehydrodivanillin, 3%.

Bivanillyl Oxidation.—The aliquot was saturated with sulfur dioxide, and the precipitate was filtered, washed with water and dried. Leaching with cold acetone left a residue of almost pure vanillil. The acetone solution was evaporated and chromatographed on cellulose powder to give bands of vanillil, vanillic acid and several unidentified materials.

The original sulfur dioxide saturated solution was extracted with ether, and the ether extract was evaporated and chromatographed on cellulose powder to give more vanillil, vanillic acid and an unidentified material melting at 218–219° (fluffy yellow needles from water).

Cellulose column chromatography of the acidified sulfur dioxide saturated solution after ether extraction yielded vanillin.

The yields in the oxidation of bivanillyl were: vanillil, 28%; vanillic acid, 14%; vanillin, 32%; and 218–219° compound, 2%.

Ultraviolet Absorption Spectra.—Ultraviolet absorption spectra were determined in 95% ethanol with a Beckman model DU spectrophotometer. Concentrations were approximately 0.02 g. per liter.

Acknowledgment.—The authors wish to thank Mr. Harold Willemsen for the analyses and spectra reported in this paper.

APPLETON, WISCONSIN

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[14] I. A. Pearl, THIS JOURNAL, in press.

[15] Whatman Ashless Powder for Chromatography···Standard Grade.