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

Studies on Lignin and Related Compounds. LXXX. The Ethanolysis of 1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone and its Relation to Lignin Structure[1]

BY LEONARD MITCHELL[2] AND HAROLD HIBBERT

In recent communications of this series[3,4] ample experimental evidence has been provided in confirmation of the theory[3,5] that the water-soluble spruce lignin ethanolysis products 2-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (I)[6] and 1-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II)[7] obtained by the action of ethanol containing 2% hydrogen chloride represent stabilized end-products originating from an oxyconiferyl alcohol type of lignin building unit present in the spruce native lignin. Experimental evidence supporting this theory and also proving that the two remaining propyl phenol ethanolysis units, namely, the diketone, 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (III)[8,9] and the desoxybenzoin, 1-(4-hydroxy-3-methoxyphenyl)-2-propanone (IV)[10] belong in the same category is provided in the present communication.

The authors find that ethanolysis of 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (V) under the identical conditions used in the ethanolysis of wood[7] gives a mixture containing I, II, III and IV in yields of 54.6, 16.7, 7.3 and 1.3%, respectively, together with a petroleum–ether (b. p. 30–50°) insoluble polymer (10%). Inasmuch as the acetyl groups are readily removed under the experimental conditions, the four products may be regarded as formed from the corresponding free dihydroxy derivative, namely, 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (VI). This latter, however, in the form of its phenolic methyl ether, is readily obtained[4] under the same experimental conditions from the phenolic methyl ether of β-oxyconiferyl alcohol, (3-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone) as the result of an allylic shift

$$\mathrm{RCH_2COCH_2OH} \rightleftarrows \mathrm{RCH{=}C(OH)CH_2OH} \rightleftarrows$$

$$\mathrm{RCHOHC(OH){=}CH_2} \rightleftarrows \mathrm{RCHOHCOCH_3}$$

$$(\mathrm{R} = \text{veratryl})$$

so that all four ethanolysis products may be envisaged as originating from β-oxyconiferyl alcohol (β,γ-dioxyisoeugenol). As stated previously,[3] it is probable the four products originate from a simple lignin building unit rather than from a higher lignin polymer. The value of the present discovery is much enhanced by the isolation for the first time in any synthetic ethanolysis mixture of the 1,2-diketone (III) and the desoxybenzoin (IV). Their relation to spruce lignin and the probable mechanism for the formation of all four products are both illustrated in the chart.

The results are thus in startling agreement with the earlier suggestion of Erdtman,[11] and accepted by the senior author (H. H.),[5] that the ethanolysis derivatives from spruce wood are stabilized end-products from a more reactive lignin progenitor, postulated by Hibbert as β-oxyconiferyl alcohol.

Experimental

The starting material for this investigation, 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone was prepared from 1-bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone[12] by the action of silver acetate in aqueous dioxane solution at room temperature. The conditions of ethanolysis and the procedure for isolation of the ethanolysis products were identical with those used previously in connection with the isolation of the ethanolysis products from wood.[7]

Synthesis of 1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone.—1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone[12] (15 g.) was dissolved in aqueous dioxane (1:1) (180 cc.), freshly-precipitated silver acetate (13 g.) added, and the mixture stirred at room temperature for thirty-six hours. The silver bromide was removed by filtration, the liquor extracted thoroughly with chloroform, and the solvent removed under reduced pressure (15 mm.) leaving a very light yellow oil which solidified on standing. The crude crystalline product (13.5 g.) was recrystallized from dilute methanol; yield 11.0 g. (80%); m. p. 95–96°. By repeated recrystallization from dilute methanol, or ether-petroleum ether (b. p. 30–50°), the melting point was raised to 97–98°. *Anal.* Calcd. for $C_{14}H_{16}O_6$: C, 60.0; H, 5.85; OCH_3, 11.05. Found: C, 60.2; H, 5.58; OCH_3, 10.95.

Ethanolysis of 1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone.—1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (11.0 g.) was refluxed with 2% ethanolic hydrogen chloride (500 cc.) for forty-eight hours in an atmosphere of carbon dioxide. The reaction mixture was neutralized with the calculated amount of sodium bicarbonate, concentrated to 50 cc., filtered free of sodium chloride and the filtrate poured in a fine stream, and with vigorous stirring, into petroleum ether (b. p. 30–50°) (1000 cc.). The precipitated dark tarry oil (probably a condensation polymer) was allowed to settle overnight and then separated by decantation. Removal of solvent from it, *in vacuo*, left a dark brittle resin (0.87 g.).

Concentration of the petroleum ether–ethanol solution, followed by removal of the last traces of solvent under reduced pressure, left an orange-red oil (8.1 g.). This was dissolved in benzene (100 cc.), extracted with five 15-cc. portions of aqueous sodium bisulfite (20%) and the bisulfite extract back-extracted with three 15-cc. portions of benzene which were then combined with the main benzene solution. This treatment resulted in a rough separation of the ethanolysis oil into a bisulfite-soluble (A) and a so-called "phenol" fraction[7] (B).

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[1] Extract from the thesis work of Leonard Mitchell to be presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy, McGill University.

[2] Holder of a National Research Council of Canada Studentship, 1942–1943.

[3] Eastham, Fisher, Kulka and Hibbert, THIS JOURNAL, **66**, 26 (1944).

[4] Fisher, Kulka and Hibbert, *ibid.*, **66**, 598 (1944).

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

[6] Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939).

[7] West, MacInnes and Hibbert, *ibid.*, **65**, 1187 (1943).

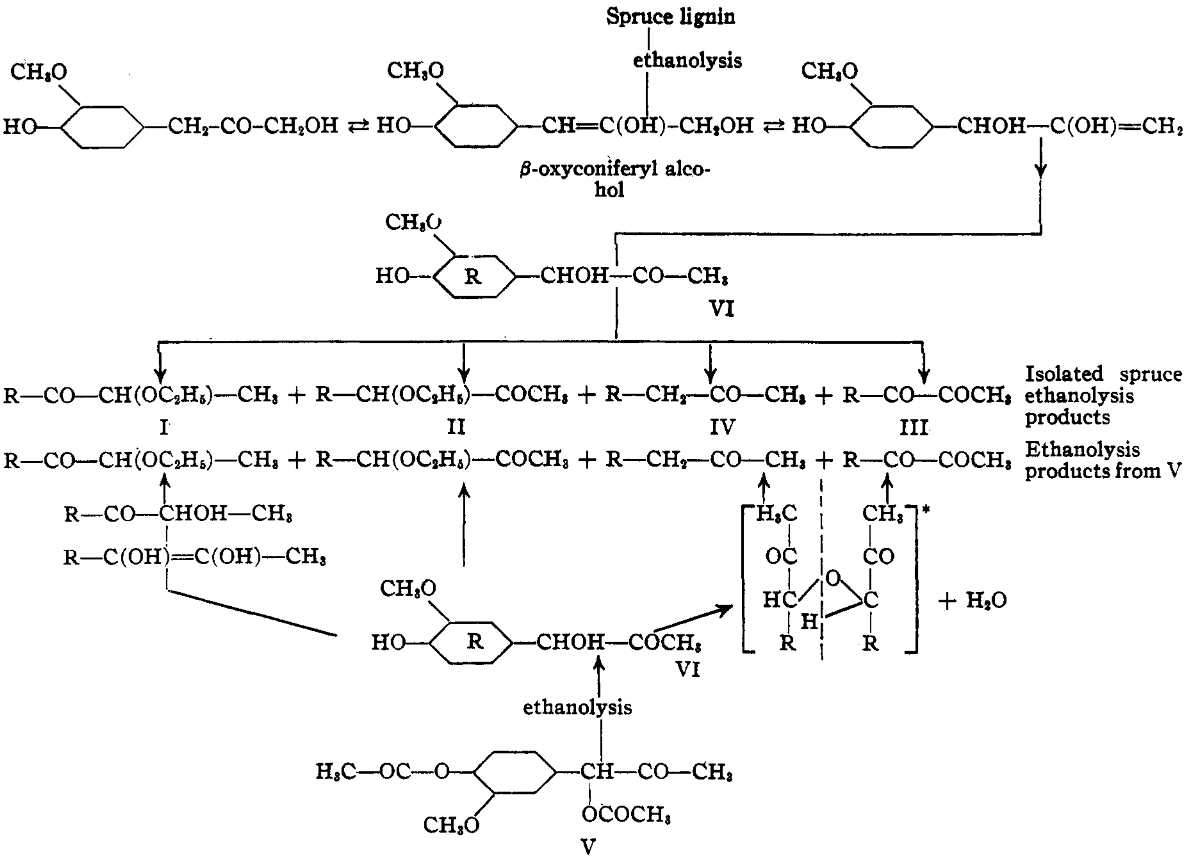
[8] Brickman, Hawkins and Hibbert, *ibid.*, **62**, 986 (1940).

[9] Kulka, Hawkins and Hibbert, *ibid.*, **63**, 2371 (1941).

[10] Kulka and Hibbert, *ibid.*, **65**, 1180 (1943).

[11] Erdtman, *Svensk Papperstidn.*, **44**, 243 (1941).

[12] Mitchell, Evans and Hibbert, THIS JOURNAL, **66**, 604 (1944).



* This reaction may actually proceed *via* an intermediary, unstable six-membered ring, as indicated in the following communication, this Series, Pt. LXXXI.

Investigation of the Bisulfite-soluble Fraction (A).—The bisulfite solution (A) was acidified (congo red) with dilute sulfuric acid, the sulfur dioxide expelled (using a carbon dioxide bubbler under reduced pressure) and then extracted with eight 15-cc. portions of benzene. The united benzene extracts were dried with sodium sulfate and the solvent removed under reduced pressure. Distillation of the residual oil between 140–160° (bath temperature) (0.10 mm.) yielded a clear yellow oil (0.90 g.) from which the diketone, 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione, and the desoxybenzoin, 1-(4-hydroxy-3-methoxyphenyl)-2-propanone, were isolated as follows:

(a) **Isolation of 1-(4-Hydroxy-3-methoxyphenyl)-1,2-propanedione.**—The above oil (0.90 g.), nickel chloride (5 cc. of 5% solution), hydroxylamine sulfate (0.75 g.) and sodium acetate (5.0 g.) were dissolved in water (200 cc.) and treated in the manner described previously[9] for the quantitative isolation of the nickel glyoxime salt of the diketone; yield of the latter (0.66 g.), equivalent to 0.60 g. diketone.

Distillation of the crude diketone obtained on hydrolysis[9] of the nickel glyoxime salt gave an oil (0.39 g.) which solidified on standing. After recrystallization from dilute ethanol the product melted at 69–70° and showed no melting point depression when mixed with an authentic sample of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione.

(b) **Isolation of 1-(4-Hydroxy-3-methoxyphenyl)-2-propanone.**—The aqueous filtrate left after separation of the insoluble nickel glyoxime salt was extracted continuously with benzene for twenty-four hours. Evaporation of the solvent and hydrolysis[10] of the residual oxime yielded an orange-yellow oil (0.12 g.). The crude semicarbazone (0.10 g.) of this melted at 155–156° and, after recrystallization from ethanol, at 156–158°; no depression when mixed with an authentic sample of the semicarbazone of 1-(4-hydroxy-3-methoxyphenyl)-2-propanone.

Investigation of the "Phenol" Fraction.—The original benzene solution (B) left after extraction with bisulfite and containing the "phenol" fraction mentioned previously was dried and evaporated to dryness under reduced pressure leaving a yellow oil (8.0 g.) which was dissolved in anhydrous ether (200 cc.).

(a) **Isolation of 2-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone.**—Dry ammonia gas was passed through the ether solution in the manner described for the separation of this component of the spruce wood ethanolysis "phenol" fraction.[7] The yellow ammonium salt (C) was filtered, washed with anhydrous ether and dried; weight, 5.1 g., equivalent to 4.9 g. of 2-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone.

Preparation of the Methyl Ether.—The ammonium salt (C) (5.1 g.), dissolved in sodium hydroxide (30 cc. of 5% solution), was methylated at room temperature in an atmosphere of nitrogen by the slow simultaneous addition, over a period of one-half hour, of dimethyl sulfate (15 cc.) and strong sodium hydroxide (15 cc. of 30% solution) the reaction mixture being stirred throughout, and then for a further period of two hours. The oily mixture was extracted thoroughly with benzene and the benzene solution back-extracted with dilute sodium hydroxide (5% solution). Removal of the benzene left a brownish oil which on distillation yielded an oil boiling constantly at 150–155° (bath temp.) (0.05 mm.), yield, 4.5 g. The oil solidified immediately and completely in the receiver; m. p. 80–81°. Recrystallization from dilute ethanol raised the m. p. to 82–83°; no depression when mixed with an authentic sample of 2-ethoxy-1-(3,4-dimethoxyphenyl)-1-propanone.

(b) **Isolation of 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone.**—The ethereal solution remaining after separation of the insoluble ammonium salt (C) of 2-

ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone was evaporated to dryness and the residual light brown oil (1.8 g.) then distilled *in vacuo* (b. p. 150–170° (bath temperature) (0.25 mm.)) yielding relatively pure 1-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (1.5 g.). This crude distillate solidified partially after inoculation with a trace of pure crystalline product (m. p. 62–63°). The partially crystalline material was recrystallized, although with difficulty and in poor yield, from dilute ethanol (m. p. 61–62°). It showed no depression in melting point when mixed with a pure sample.

The semicarbazone was prepared from a portion of the crude semi-solid oil (0.20 g.); yield 0.125 g. (60%). Recrystallized from ethanol–ethyl acetate (1:1) this derivative melted at 171.5–172.5° (yield, 0.110 g.) and gave no depression when mixed with a sample of the semicarbazone of the pure compound.

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Summary

1. The synthesis of 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone has been effected. When subjected to the same treatment as employed in the ethanolysis of spruce wood, the reaction mixture was found to contain the same four ethanolysis products as isolated from the wood, namely, 2-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (54.6%), 1-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (16.7%), 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (7.3%), 1-(4-hydroxy-3-methoxyphenyl)-2-propanone (1.3%).

2. Since the acetyl groups in 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone are readily removed in the ethanolysis treatment, the results provide clear proof of the ease with which the corresponding 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone is convertible to the same stabilized ethanolysis end-products.

3. The remarkable ease with which the phenolic methyl ether of β-oxyconiferyl alcohol passes over into the phenolic methyl ether of 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone; the known absence of terminal methyl groups in spruce native lignin, and the newly discovered behavior of 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone on ethanolysis form a composite picture indicating clearly a common parent progenitor, namely, the lignin building unit, β-oxyconiferyl alcohol (β,γ-dioxyisoeugenol), or its keto form, as the source of all of the water-soluble, spruce lignin propyl phenol ethanolysis products.

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Studies on Lignin and Related Compounds. LXXXI. Properties of 1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone and Relation to Lignin Structure[1]

BY LEONARD MITCHELL,[2] T. H. EVANS AND HAROLD HIBBERT

In the preceding communication[3] it was shown experimentally that 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (I), on ethanolysis under the identical conditions used for the extraction of spruce lignin from wood, gave a reaction product containing each of the four propyl phenol units found in the spruce wood ethanolysis mixture.

In the present paper additional confirmatory evidence for the β-oxyconiferyl alcohol theory of lignin structure is provided in the action of aqueous silver sulfate on 1-bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (II). In aqueous solution at room temperature interaction takes place readily with precipitation of the theoretical quantity of silver bromide. The aqueous solution on analysis was shown to contain a distillable mixture (60% of original material) of 1-(4-acetoxy-3-methoxyphenyl)-1,2-propanedione (III) and 1-(4-acetoxy-3-methoxyphenyl)-2-propanone (IV) together with a non-distillable product (35%), presumably a polymer of 1-hydroxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (V). The amounts of III and IV present in the distillable mixture were found to be 44 and 27%, respectively, equivalent to 24 and 16% when calculated on the original bromo derivative (II). The low value for IV is to be regarded as a minimum due to the extensive losses involved in its isolation.

The formation of the theoretical quantity of silver bromide in this reaction indicates (1) absence of any secondary type of oxidation change; and (2) formation of 1-hydroxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (V) as the primary product of the reaction. Inasmuch as the veratryl analog[4] of V is stable to even *hot* dilute sulfuric acid, it is very improbable the formation of III and IV proceeds directly (intramolecularly) through V.

It is possible a bimolecular reaction takes place between the bromo product (II) and the hydroxy derivative (V) to give silver bromide, sulfuric

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(4) Eastham, Fisher, Kulka and Hibbert, *ibid.*, **66**, 26 (1944).