

crude product was washed with small portions of an ether-petroleum ether (b. p. 30–50°) mixture (1:1) until almost colorless. The product (0.28 g.) then melted at 101–102°, this value being raised, following one recrystallization from benzene, to 108–109° and gave no depression in melting point when mixed with a pure sample of 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (IX). The ether-petroleum ether washings were evaporated and the presence of the diketone in the residual yellow oil shown by precipitation of its nickel glyoxime salt; yield of the latter, 0.075 g., equivalent to 0.058 g. diketone (VIII). No attempt was made to isolate the desoxybenzoin from the reaction mixture.

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Summary

1. The synthesis of 1-bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone has been carried out.
2. Aqueous silver sulfate reacts with this product at room temperature (*that is, under ap-*

proximate biological conditions) to give a mixture containing 1-(4-acetoxy-3-methoxyphenyl)-1,2-propanedione and 1-(4-acetoxy-3-methoxyphenyl)-2-propanone in a combined yield of 60% based on the starting material. The amounts of these two components present in the mixture were 44 and 27%, respectively, equivalent to 24 and 16% based on the starting material. A possible mechanism for their formation is suggested.

3. Hydrolysis of 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone with aqueous barium carbonate yielded 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone as the main product together with small quantities of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione.

4. The formation of these two products (the 1,2-diketone and desoxybenzoin), as indicated, supplies additional evidence in support of Hibbert's β -oxyconiferyl alcohol theory of spruce native lignin structure.

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

Studies on Lignin and Related Compounds. LXXXII. Synthesis and Properties of 1,3-Diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone and 1-Acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone and their Relation to Lignin Structure¹

BY J. A. F. GARDNER² AND HAROLD HIBBERT

In the two preceding communications^{3,4} experimental evidence was presented showing the remarkable ease of formation of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (I) from 1-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II) under very mild conditions. The latter product (as its phenolic methyl ether) is, in turn, readily formed⁵ under the influence of mild reagents from 3-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone (III) (the keto form of methylated β -oxyconiferyl alcohol) through an allylic shift. The presence of the diketone (I) in the ethanolysis mixture from spruce wood is thus satisfactorily accounted for by Hibbert's theory of lignin structure^{5,6,7} which assumes the presence, in the spruce native lignin complex, of a building unit of the β -oxyconiferyl alcohol (β - γ -dioxyisoeugenol) type.

Consideration of this new type of allyl transformation, involving a *mono*-hydroxylated allyl alcohol indicated the possibility of a similar type

(1) Extract from thesis work of J. A. F. Gardner to be presented to the Graduate Faculty of McGill University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Holder of a National Research Council of Canada Studentship for the Session 1942–1943.

(3) Mitchell and Hibbert, *THIS JOURNAL*, **66**, 602 (1944).

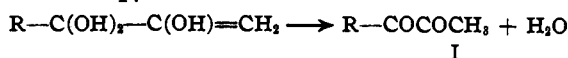
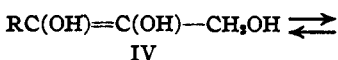
(4) Mitchell, Evans and Hibbert, *ibid.*, **66**, 604 (1944).

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

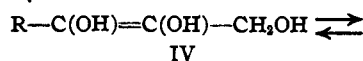
(6) Hibbert, *Paper Trade J.*, **118**, No. 4, 35 (1941).

(7) Hibbert, *Ann. Rev. Biochem.*, **11**, 183 (1942).

of reaction occurring with the analogous *dihydroxy* derivative, R—C(OH)=C(OH)—CH₂OH (IV) (R = 4-hydroxy-3-methoxyphenyl) since in this case the final product should also be the above diketone (I).



The product IV is the ene-diol intermediate of a dismutation system

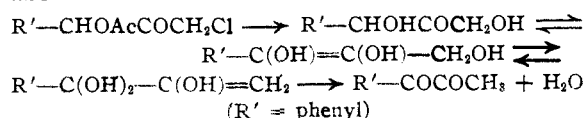


and, by analogy, either V or VI (or their halides) might be expected to undergo an allyl shift in the presence of suitable mild chemical reagents.

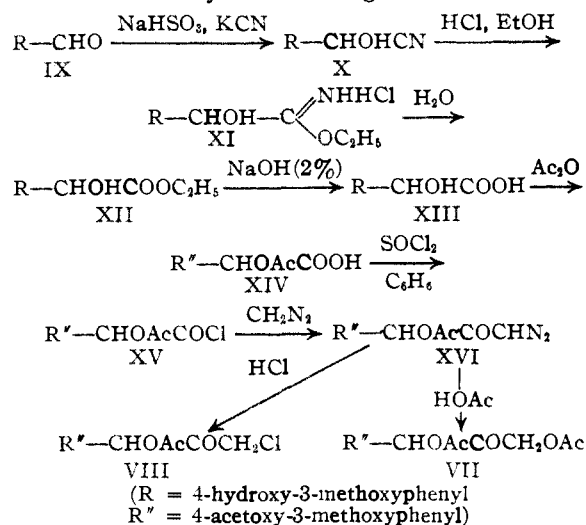
Formation of a diketone has been observed by Bradley and Eaton⁸ in the case of 1-acetoxy-1-phenyl-3-chloro-2-propanone, mild hydrolysis of the latter yielding 1-phenyl-1,2-propanedione. These authors made no comment concerning the mechanism of its formation. Based on the above

(8) Bradley and Eaton, *J. Chem. Soc.*, 1913 (1937).

theory, however, it could have been formed as the result of an allyl shift similar to that postulated above



In view of the experimental difficulties attendant upon the synthesis of V, the preparation of the triacetate of VI, 1,3-diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII), and of the corresponding chloride, 1-acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VIII) was carried out by the following series of reactions



The substituted mandelic ester (XII) has been prepared previously from vanillin through the cyanohydrin (X) and imino ether hydrochloride (XI) in 16% yield by Schwartz and McCarthy.⁹ By utilizing the method of Hahn, Stiehl and Schulz,¹⁰ for preparation of the cyanohydrin and carrying out the reactions at lower temperatures the yield was increased to 24%.

The 4-hydroxy-3-methoxymandelic acid (XIII), which readily resinified on heating or on exposure to air, was acetylated to prevent reaction of thionyl chloride with the phenolic and secondary hydroxyls. The resulting diacetate, 4-acetoxy-3-methoxy-acetylmandelic acid (XIV), crystallized readily from aqueous solution as a monohydrate, readily dehydrated at room temperature *in vacuo*. Considerable difficulty was experienced in obtaining a good yield of the acid chloride (XV) but this was accomplished by using a solution of thionyl chloride in benzene and employing a much shorter period of reflux than in the case of mandelic acid.¹¹

While the diazoketone (XVI) did not react with cold glacial acetic, at reflux temperature it yielded the desired triacetate (VII).

(9) Schwartz and McCarthy, *Can. J. Research*, **19B**, 150 (1941).

(10) Hahn, Stiehl and Schulz, *Ber.*, **72B**, 1296 (1939).

(11) Thayer, "Organic Syntheses," **4**, 1 (1925).

As anticipated, this triacetate, on ethanolysis, gave the 1,2-diketone (I) together with an amorphous resinous product, in yields of 8 and 66%, respectively. No work has been carried out on the nature of this resin. Hydrolysis of VII with dilute sulfuric acid (2%) gave a 9% yield of I. A much larger amount (75%) of the diketone was obtained on mild hydrolysis of the monochlor derivative (VIII) with acidified sodium acetate solution, little or no resinification taking place.

The 1,2-diketone (I) was determined by precipitation as the nickel glyoxime salt and identified by hydrolysis of this and preparation of the quinoxaline and semicarbazone^{12,13} of the hydrolyzed product.

The formation of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (I), from the intermediary dihydroxy ketone (VI), raises the question as to whether the latter product (VI) or its dismutation isomer (V), might not also be present, to a limited extent, as one of the building-stones of the spruce native lignin complex. If the dismutation reactions shown in the chart are capable of taking place under the conditions of spruce wood ethanolysis, then either V or VI could serve as the source of origin of a portion of the 1,2-diketone (I) but neither could account for the presence in the ethanolysis mixture of the remaining ethanolysis products, R-CH(OC₂H₅)-CO-CH₃, R-CO-CH(OC₂H₅)-CH₃ and R-CH₂-CO-CH₃ (R = 4-hydroxy-3-methoxyphenyl). It is significant, however, that spruce ethanolysis products contain only small amounts (3-5%) of monomolecular units and very large amounts of amorphous ethanol lignins. Conceivably VI could be synthesized in the plant by condensation of guaiacol with hydroxypyruvic aldehyde. No direct experimental evidence, however, regarding its presence in spruce native lignin has been obtained, as yet.

Experimental

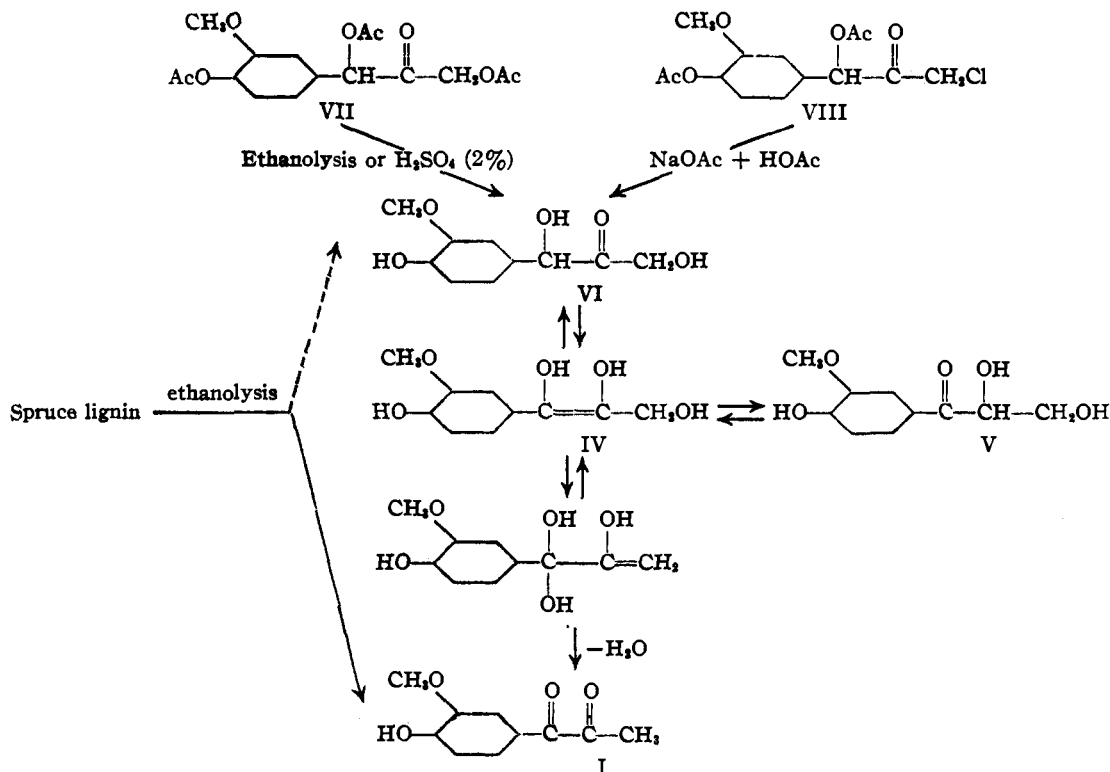
Synthesis of 1-Acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VIII)

Preparation of Ethyl 4-Hydroxy-3-methoxymandelate (XII).—An ethereal solution (200 cc.) of vanillin cyanohydrin, prepared from vanillin (50 g.) by the method of Hahn, Stiehl and Schulz,¹⁰ was dried for twelve hours at -10° over sodium sulfate and drierite and then filtered. Absolute ethanol (20 cc.) was added and dry hydrogen chloride (10 g.) bubbled in at -10°. After forty-eight hours at this temperature the crude imino ether hydrochloride was hydrolyzed by the procedure of Schwartz and McCarthy.⁹ The crude ester (21 g.) on distillation (140-160° (0.4 mm.)) gave a light yellow oil (17.8 g.) which crystallized to a white solid; m. p. 75-77°; yield, 24%. One recrystallization from benzene-petroleum ether (b. p. 30-50°) gave colorless crystals, m. p. 77°. *Anal.* Calcd. for C₁₁H₁₄O₅: OR, 27.4. Found: OR, 27.3.

4-Hydroxy-3-methoxymandelic Acid (XIII).—The ester (XII) (17 g.) was refluxed one hour with sodium hydroxide (600 cc., 2%) under a nitrogen atmosphere, the mixture then extracted with benzene (2 × 50 cc.), acidified with hydrochloric acid, saturated with sodium chloride and continuously extracted with ether. Drying of the ethereal extract

(12) Kufka, Hawkins and Hibbert, *This Journal*, **63**, 2371 (1941).

(13) Brickman, Hawkins and Hibbert, *ibid.*, **62**, 2149 (1940).



over sodium sulfate and removal of the solvent left a light yellow oil (15.2 g.) which crystallized after washing with a small quantity of benzene. Recrystallization from an acetone-petroleum ether (b. p. 30–50°) mixture gave colorless crystals, m. p. 129–131°; yield, 12.2 g. (80%). Repeated recrystallization from ether-benzene raised the melting point to 133°. The product was very soluble in water and acetone, moderately soluble in ether, and almost insoluble in benzene. *Anal.* Calcd. for $C_{17}H_{16}O_7$: C, 54.5; H, 5.05; OCH_3 , 15.6. Found: C, 54.7; H, 5.15; OCH_3 , 15.4.

4-Acetoxy-3-methoxyacetylmandelic Acid (XIV).—Pure 4-hydroxy-3-methoxyacetylmandelic acid (XIII) (m. p. 133°) (3.6 g.) was dissolved in a mixture of pyridine (27 cc.) and acetic anhydride (22 cc.), refluxed for twenty-five minutes, and the excess pyridine and acetic anhydride removed under reduced pressure. The residual oil was dissolved in hot water, and the solution decolorized with charcoal and filtered. Crystals of the monohydrate (m. p. 112–113°) separated on cooling. On addition of 6 *N* hydrochloric acid (3 cc.) a further quantity was obtained. The combined products were dehydrated by standing for forty-eight hours in a vacuum desiccator; m. p. 142°; yield, 4.15 g. (81%). Recrystallization from benzene did not raise the melting point. *Anal.* Calcd. for $C_{13}H_{14}O_7 \cdot H_2O$: C, 55.3; H, 5.0; OCH_3 , 11.0; neut. equiv., 282. Found: C, 55.5; H, 4.9; OCH_3 , 10.9; neut. equiv., 281.

4-Acetoxy-3-methoxyacetylmandelyl Chloride (XV).—The above diacetate (XIV, 0.8 g.) was dissolved in a mixture of anhydrous benzene (8 cc.) and carefully purified thionyl chloride (3.2 cc.) and then refluxed one and three-quarters hours. The excess thionyl chloride was distilled off (reduced pressure) and the last traces removed by successive addition and distillation (reduced pressure) of two portions (5 cc.) of anhydrous benzene. The residual light yellow oil solidified completely on cooling and was recrystallized from an anhydrous benzene-petroleum ether (b. p. 30–50°) mixture; m. p. 71–72°; yield, 0.804 g. (94%). On repeated recrystallization from petroleum ether (b. p. 30–50°) the m. p. was raised to 72°. *Anal.*

Calcd. for $C_{17}H_{15}O_6Cl$: OCH_3 , 10.3; Cl, 11.8. Found: OCH_3 , 10.2; Cl, 11.8.

1-Acetoxy-3-diazo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (XVI).—Crude acid chloride (XV) prepared from the acid (XIV) (1.07 g.) was dissolved in benzene (5 cc.) and poured in a fine stream into a well-stirred dry ethereal solution of diazomethane (from 4 g. of nitroso-methylurea) cooled previously to 0° and the mixture allowed to stand at this temperature for twelve hours. The ether solution was decanted from the first crop of crystals, filtered, and evaporated in a stream of dry air. Scratching caused the light yellow residual oil to crystallize. The two crops of crystals were washed with cold ether and combined; yield, 0.96 g. (88%). Recrystallization from benzene gave light yellow crystals, m. p. 129–130°. *Anal.* Calcd. for $C_{14}H_{14}O_6N_2$: C, 55.0; H, 4.61; OCH_3 , 10.10. Found: C, 55.2; H, 4.58; OCH_3 , 10.05.

1-Acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone.—The diazoketone (XVI) (0.38 g.) dissolved in anhydrous benzene (10 cc.), was treated with anhydrous ethereal hydrogen chloride (1.6 cc., 0.89 *N*) and the mixture allowed to stand at 0° for three hours. It was washed with 1% sodium bicarbonate solution, then with water, dried over sodium sulfate and the solvent removed. Colorless crystals, m. p. 109–110°; yield, 0.316 g. (81%). Recrystallization from ether or ether-benzene raised the melting point to 110–111°. *Anal.* Calcd. for $C_{17}H_{15}O_6Cl$: C, 53.4; H, 4.81; OCH_3 , 9.85; Cl, 11.3. Found: C, 53.09; H, 4.94; OCH_3 , 9.80; Cl, 11.2.

Hydrolysis of 1-Acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VIII) and Isolation of the Diketone (I)

Action of Acidified Sodium Acetate Solution.—The above chloro derivative (VIII) (0.31 g.) was suspended in an aqueous solution of sodium acetate (0.4 g. in 50 cc.) and acetic acid (0.5 cc.) and the mixture refluxed for six hours under an atmosphere of carbon dioxide. The deep yellow colored solution was filtered, sodium acetate (0.4 g.), hydroxylamine sulfate (0.2 g.) and 5% nickel chloride solu-

tion (1 cc.) added and the mixture refluxed gently under a carbon dioxide atmosphere for twenty-four hours. The precipitated nickel salt was separated, more hydroxylamine sulfate (0.05 g.) and nickel chloride (0.5 cc., 5%) added to the filtrate and the refluxing continued until precipitation was complete. The combined precipitated salts were washed with cold water and dried at 100°; yield, 0.171 g. (equivalent to 0.142 g. of diketone on the basis of the customary 90% precipitation or 75% calculated on the chloroketone).

The nickel salt (0.171 g.) was hydrolyzed with 12 N sulfuric acid (70 cc.) at room temperature¹³ and gave a yellow oil (0.119 g.) which crystallized on standing. The quinoxaline of the product was prepared and recrystallized from ethanol-water; m. p. 161-162°. It showed no melting point depression when mixed with an authentic sample of the quinoxaline of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (I). The semicarbazone, m. p. 213°, was prepared and also showed no mixed melting point depression with the corresponding derivative of I.

Synthesis of 1,3-Diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII)

1 - Acetoxy - 3 - diazo - 1 - (4 - acetoxy - 3 - methoxyphenyl)-2-propanone (XVI) (2.89 g.) was dissolved in glacial acetic acid (60 cc.), acetic anhydride (1.5 cc.) added, and the solution refluxed until nitrogen evolution had ceased (thirty minutes). The excess acetic acid was removed (reduced pressure) and the residual oil dissolved in benzene (75 cc.). The resulting solution was extracted successively with aqueous sodium bicarbonate (5%) and sodium bisulfite (20%), then washed with water, dried over sodium sulfate, treated with charcoal and filtered. Evaporation of the solvent (reduced pressure) left a yellow viscous oil (2.85 g., OCH₃ 8.9) which underwent marked decomposition on vacuum distillation. Purification of the product was achieved by solution in acetone (95 cc.) and addition of this in a fine stream to vigorously-stirred petroleum ether (b. p. 30-50°, 950 cc.). The solvent was removed (the last traces under reduced pressure, two hours at 65-70° (0.025 mm.)), leaving a homogeneous light yellow oil (*n*_D²⁰ 1.5028); yield, 2.46 g. (77%). *Anal.* Calcd. for C₁₆H₁₈O₆: C, 56.8; H, 5.34; OCH₃, 9.17. Found: C, 56.9; H, 5.48; OCH₃, 9.13.

Hydrolysis of 1,3-Diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII)

Action of Ethanolic Hydrogen Chloride.—1,3-Diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII) (1.35 g.) was refluxed with 2% ethanolic hydrogen chloride (130 cc.) for thirty-six hours in an atmosphere of carbon dioxide. The reaction mixture was neutralized with freshly precipitated calcium carbonate, filtered, and evaporated to dryness (reduced pressure) in a stream of carbon dioxide. The residual reddish-brown tar was extracted thoroughly with hot benzene (50 cc.) and then washed with hot water (to remove calcium acetate), leaving an amorphous black powder (0.56 g., 66%). The benzene solution was extracted with sodium bisulfite solution (20%, 50 cc.), the extract acidified with sulfuric acid and sulfur dioxide removed in a stream of carbon dioxide (reduced pressure). The acid solution was extracted with benzene (30 cc.), the benzene extract dried, and the solvent re-

moved leaving a yellow oil (0.086 g.) which crystallized on cooling. This product, in aqueous solution, gave the nickel glyoxime salt of the diketone (I); yield, 0.073 g. (equivalent to an 8% yield of diketone). The quinoxaline of the free diketone, obtained by hydrolysis of the nickel salt, melted at 161-162° and showed no mixed melting point depression with an authentic sample of the quinoxaline of I.

Action of Dilute Sulfuric Acid (2%).—1,3-Diacetoxy-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII) (0.47 g.) was suspended in 2% sulfuric acid (100 cc.) and the mixture refluxed for two hours, cooled, filtered and extracted with benzene (50 cc.). The bisulfite soluble extract of the benzene solution yielded the same diketone as above, identified in similar manner; yield of nickel glyoxime salt, 0.027 g., equivalent to 8.6% yield of the diketone.

Action of Strong Sulfuric Acid (72%).—1,3-Diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII) (0.66 g.) when subjected to the customary treatment employed in a Klason lignin determination gave an amorphous, dark-colored, lignin-like product in high yield (0.28 g., equivalent to 68% based on the deacetylated product). *Anal.* Found C, 61.1; H, 5.32; OCH₃, 14.8.

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Summary

1. The triacetate, 1,3-diacetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VII) and the chloroketone, 1-acetoxy-3-chloro-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VIII) have been synthesized.

2. Under the influence of mild hydrolytic agents, both the triacetate and chloro derivative are converted into 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (I) (found in the ethanolysis products of spruce wood) in yields of 8 and 75%, respectively.

3. It is concluded that the 1,2-diketone is formed as the result of an allyl shift in a dismutation ene-diol product arising from the hydrolysis intermediate, 1,3-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone. The allyl shift is thus indicated as taking place with a dihydroxy substituted allyl alcohol.

4. Attention is drawn to the possibility that a dihydroxy ketone of the type R—CO—CHOH—CH₂OH or R—CHOH—CO—CH₂OH (R = 4-hydroxy-3-methoxyphenyl) may function to a limited extent as a lignin progenitor.

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