

on a steam-bath, with a mixture of 20% hydrochloric acid containing a few cc. of concentrated nitric acid, until the supernatant solution no longer contained iron. The charcoal was filtered off, washed with water and dried at 100° under reduced pressure (15 mm.) for eight hours. This purified charcoal was activated by heating (luminous flame of a Bunsen burner) in an evacuated test-tube (20 mm.) for fifteen minutes. The activated charcoal (3.0 g.) was suspended in a mixture of palladium chloride (0.5 g.) in concentrated hydrochloric acid (0.5 cc.) and water (25 cc.), and cooled to 5°. While the suspension was stirred vigorously, 40% formaldehyde (10 cc.) was added, followed by a drop-by-drop addition of a 50% solution of potassium hydroxide (10 cc.), the temperature being kept below 5°. The temperature of the mixture was raised slowly to 60° and maintained there for a few hours. The catalyst was filtered off, washed successively with water, dilute acetic acid, and hot water until the filtrate gave no test for chloride, then dried under reduced pressure.

The palladiumized carbon (0.5 g.) was suspended in a solution of 2-nitro-1-(4-hydroxy-3-methoxyphenyl)-1-propene (XIV) (2.0 g.) in pyridine (25 cc.) and the suspension shaken in an atmosphere of pure hydrogen at 60–65° until 2 moles of hydrogen had been absorbed (eight hours). The catalyst was filtered off and washed with pyridine. The solvent was removed from the combined filtrate and washings under reduced pressure (20 mm.) and the residual oxime hydrolyzed as described above. The ketone (0.94 g.) (56%) was obtained by extraction of the acid solution.

Raney nickel was also employed as a catalyst for the

reduction of the nitroalkenes under similar conditions at room temperature, but only low yields (15–25%) of the ketones were obtained.

Acknowledgment.—The authors wish to thank Canadian Industries Limited for kind financial assistance, in the form of a fellowship to one of them (M. K.).

Summary

1. Two additional products, 1-(4-hydroxy-3,5-dimethoxyphenyl)-2-propanone and 1-(4-hydroxy-3-methoxyphenyl)-2-propanone have been isolated from the water-soluble lignin ethanolysis fraction of maple wood.

2. The similarity of their side-chains and those of previously-isolated lignin entities with those present in the phenol carboxylic acids obtained by the action of molds on glucose as sole organic substrate (Raistrick and Oxford) is pointed out.

3. The specific variation noted in the nature of the side chain of the latter products when the mold functions with a shortage of metabolite provides indirect evidence in support of Hibbert's views on the biological significance of lignin in plant metabolism.

MONTREAL, CANADA

RECEIVED FEBRUARY 23, 1943

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

Studies on Lignin and Related Compounds. LXVIII. Synthesis and Properties of 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, 3-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone and Their Methyl Ethers

BY MARSHALL KULKA AND HAROLD HIBBERT

Two isomeric ethyl ethers have been found in the water-soluble ethanolysis products of spruce wood, namely, 2-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (I)¹ and 1-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II).² A third isomer, 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (III)³ has been synthesized but not as yet isolated from the ethanolysis products of spruce or other woods. A fourth isomer of this series, 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (IV) representing the ethyl ether of the first member of the Hibbert system⁴ of plant respiratory catalysts has been neither synthesized nor isolated from the ethanolysis products.

(1) (a) Cramer and Hibbert, *THIS JOURNAL*, **61**, 2204 (1939); (b) Cramer, Hunter and Hibbert, *ibid.*, **61**, 509 (1939).

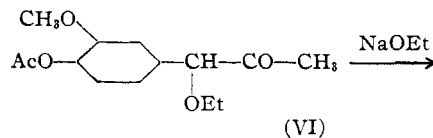
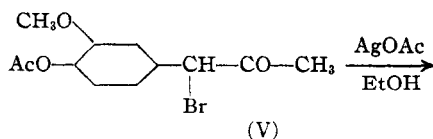
(2) E. West, MacInnes and Hibbert, *ibid.*, **65**, 1187 (1943).

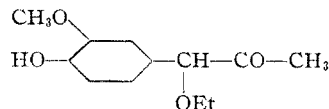
(3) (a) K. A. West and Hibbert, *ibid.*, **65**, 1170 (1943); (b) K. A. West, Hawkins and Hibbert, *ibid.*, **63**, 3035 (1941).

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

The purpose of this investigation was to synthesize the isomeric ethyl ethers ($R-CH(O-C_2H_5)COCH_3$) (II) and $R-CH_2COCH_2(OC_2H_5)$ (IV) and to compare their properties with those of $R-COCH(OC_2H_5)CH_3$ (I), and $R-COCH_2CH_2(OC_2H_5)$ (III) ($R = 4\text{-hydroxy-3-methoxyphenyl}$).

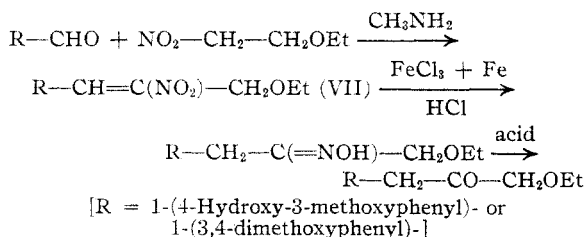
The isomer II was synthesized by the following procedure





The initial product (V) was prepared from 1-(4-acetoxy-3-methoxyphenyl)-2-propanone⁵ by direct bromination.⁶

The second ethyl ether (IV) and its methylated product were synthesized by a method similar to that used for the preparation of 1-(4-hydroxy-3-methoxyphenyl)-2-propanone.⁵ Vanillin and veratric aldehyde, respectively, were condensed with 1-nitro-2-ethoxyethane, the resulting nitroalkenes reduced to the oxime and the latter hydrolyzed.



1-Nitro-2-ethoxyethane was prepared from 1-hydroxy-2-ethoxyethane by treatment of the latter with phosphorus tribromide⁷ and the bromide then converted into the nitro derivative by the action of silver nitrite.⁸

The properties of the four isomeric ethyl ethers and of their corresponding methylated products are summarized in Table I.

TABLE I

Ethyl ether	M. p., °C. (if solid) or refr. index <i>n</i> _D ²⁰ (if liquid)	Melting point, °C. 2,4-Di- nitrophenyl semicarbazone hydrazone
R-CO-CH(OEt)-CH ₃ (I)	1.545	
R-CH(OEt)-CO-CH ₃ (II)	62-63	173.5-174.5
R-CO-CH ₂ -CH ₂ OEt (III)	35-37	
R-CH ₂ -CO-CH ₂ OEt (IV)	1.533	144-144.5
R'-CO-CH(OEt)-CH ₃ (I')	81-82	140-142 ^a
R'-CH(OEt)-CO-CH ₃ (II')	1.516	141-142 ^a
R'-CO-CH ₂ -CH ₂ OEt (III')	50-51	
R'-CH ₂ -CO-CH ₂ OEt (IV')	1.522	114-116

(R' is the fully methylated product)

^a A depression in melting point of a mixture of the 2,4-dinitrophenylhydrazones of (I') and (II') showed that the two compounds were not identical.

Experimental

Synthesis of 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II) and 1-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (II')

Preparation of 1-Ethoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VI).—1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (V)⁵ (2.5 g.) was dissolved in ethanol (100 cc.), silver acetate (2.2 g.) added, and the mixture refluxed for ten hours. The silver bromide was removed, washed with ethanol and the combined filtrate and washings taken to dryness at reduced pressure. The residual oil was fractionally distilled at 0.1 mm. in the Bower-Cooke fractionating column⁹ in order to remove a small amount of unchanged material; yield of pure product, 1.3 g. (60%); *n*_D²⁰ 1.5060. *Anal.* Calcd. for C₁₄H₁₅O₅: C, 63.2; H, 6.8; alkoxy (calcd. as methoxy), 23.3. Found: C, 63.2; H, 6.8; alkoxy, 23.3.

Synthesis of 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II).—1-Ethoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (VI) (0.57 g.) was dissolved in ethanol (12 cc.) and a solution of sodium (0.06 g.) in ethanol (10 cc.) added. The mixture was allowed to stand at room temperature for three hours, then neutralized with acetic acid and the solution evaporated to dryness under reduced pressure. The oily residue distilled at 150-170° (bath temperature) (0.07 mm. pressure); yield, 0.43 g. (80%). The distillate solidified slowly on scratching; recrystallized from ether-petroleum ether and from water, m. p., 62-63°. *Anal.* Calcd. for C₁₃H₁₅O₄: C, 64.3; H, 7.1; alkoxy, 27.7. Found: C, 64.2; H, 7.1; alkoxy, 27.5.

Semicarbazone of 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (II).—White crystals from dilute ethanol and from ethanol-petroleum ether; m. p. 173.5-174.5°. *Anal.* Calcd. for C₁₃H₁₅O₄N₂: C, 55.5; H, 6.8; alkoxy, 22.1. Found: C, 55.5; H, 6.9; alkoxy, 22.1.

Preparation of 1-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (II').—1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone was methylated with diazomethane. *Anal.* Calcd. for C₁₅H₁₇O₄: C, 65.5; H, 7.6; alkoxy, 39.1. Found: C, 65.4; H, 7.9; alkoxy, 39.0.

2,4-Dinitrophenylhydrazone of 1-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone.—Orange needle-like crystals; recrystallized from ethanol, m. p. 141-142°. *Anal.* Calcd. for C₁₉H₂₂O₇N₄: C, 54.5; H, 5.3; alkoxy, 22.3. Found: C, 54.4; H, 5.4; alkoxy, 22.3.

Synthesis of 3-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (IV) and 3-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (IV')

Preparation of 3-Ethoxy-2-nitro-1-(4-hydroxy-3-methoxyphenyl)-1-propene (VII).—Vanillin (6.5 g.) was dissolved in a mixture of ethanol (2 cc.) and 1-nitro-2-ethoxyethane (5.0 g.), and methylamine hydrochloride (0.2 g.) and sodium carbonate (0.16 g.) then added to the solution. The reaction mixture was allowed to stand at room temperature in the dark for fourteen days, ether added and the ether solution extracted successively with 10% sulfuric acid, 20% sodium bisulfite and water. The ether solution was dried, the solvent removed and the dark residual oil dissolved in hot dilute ethanol. On cooling, yellow needle-like crystals (3.2 g.) (30%) separated; recrystallized from dilute ethanol, m. p., 78-79°. *Anal.* Calcd. for C₁₂H₁₅O₅N: C, 57.0; H, 5.9; alkoxy, 24.5. Found: C, 57.1; H, 6.1; alkoxy, 24.6.

3-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (IV).—3-Ethoxy-2-nitro-1-(4-hydroxy-3-methoxyphenyl)-1-propene (VII) (2.5 g.) was dissolved in a hot

(5) Kulka and Hibbert, *THIS JOURNAL*, **65**, 1180 (1943).

(6) Mitchell, Evans and Hibbert, details will be published in a later communication.

(7) Hurd and Fowler, *THIS JOURNAL*, **61**, 251 (1939).

(8) Reynolds and Adkins, *ibid.*, **61**, 279 (1929).

(9) Bower and Cooke, *Ind. Eng. Chem., Anal. Ed.*, **15**, 290 (1943).

solution of ethanol (25 cc.) and water (60 cc.), and to the solution iron powder (5.0 g.), ferric chloride (0.2 g.) and concentrated hydrochloric acid (2.5 cc.) then added. The reaction mixture was refluxed for five hours, concentrated to about 50 cc. at atmospheric pressure, filtered, the iron oxide washed with water and ether, and the combined filtrate and washings extracted with ether. The ether solution was extracted eight times with 8-cc. portions of sodium bisulfite solution (20%), the bisulfite solution acidified, sulfur dioxide removed by bubbling in carbon dioxide under reduced pressure and the resulting solution extracted with ether. The ether extract was dried and the solvent removed, yielding 1.4 g. of a yellow oil. The ether solution, containing a small amount of the bisulfite-insoluble oxime was evaporated to dryness, the residue hydrolyzed by treatment with 7 *N* sulfuric acid (25 cc.) for twenty-four hours at room temperature, and the acid solution extracted with ether yielding an additional 0.1 g. of the ketone (IV); total yield, 1.5 g. (68%). The yellow oil was distilled at 0.15 mm. pressure and 165–180° bath temperature; n_D^{25} 1.5330. *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.3; H, 7.1; alkoxy, 27.7. Found: C, 64.1; H, 7.4; alkoxy, 27.4.

Semicarbazone of 3-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone (IV).—White crystals from water or ethanol–petroleum ether, m. p. 144–144.5°. *Anal.* Calcd. for $C_{13}H_{19}O_4N_3$: C, 55.5; H, 6.8; alkoxy, 22.1. Found: C, 55.3; H, 6.8; alkoxy, 22.2.

3-Ethoxy-2-nitro-1-(3,4-dimethoxyphenyl)-1-propene (VII').—Veratric aldehyde was condensed with 1-nitro-2-ethoxyethane in the same manner as was vanillin; yield of the yellow needle-like crystals, 25%; recrystallized from dilute ethanol and then from ethyl acetate–petroleum ether; m. p. 90–91°. *Anal.* Calcd. for $C_{13}H_{17}O_5N$: C, 58.4; H, 6.4; alkoxy, 34.9. Found: C, 58.3; H, 6.5; alkoxy, 34.7.

3-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone (IV').—3-Ethoxy-2-nitro-1-(3,4-dimethoxyphenyl)-1-propene

(VII') was reduced with iron powder, ferric chloride and hydrochloric acid in the same manner as was 3-ethoxy-2-nitro-1-(4-hydroxy-3-methoxyphenyl)-1-propene; yield of the ketone (IV'), 67%. Fractional distillation at 0.1 mm. pressure gave a pure homogeneous reduction product, n_D^{25} 1.5215. *Anal.* Calcd. for $C_{13}H_{18}O_4$: C, 65.5; H, 7.6; alkoxy, 39.1. Found: C, 65.4; H, 8.0; alkoxy, 39.0.

2,4-Dinitrophenylhydrazone of 3-Ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone.—Orange needle-like crystals from ethanol and from ethanol–petroleum ether; m. p., 114–116°. *Anal.* Calcd. for $C_{19}H_{22}O_7N_4$: C, 54.5; H, 5.3; alkoxy, 22.3. Found: C, 54.7; H, 5.4; alkoxy, 22.4.

Acknowledgment.—The writers wish to acknowledge their indebtedness to Dr. L. M. Cooke for his assistance in preliminary work on this investigation. They also express their appreciation to the Canadian Industries Limited for the award of a Fellowship to one of them (M. K.).

Summary

The four products, 1-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone, 1-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone, 3-ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone and 3-ethoxy-1-(3,4-dimethoxyphenyl)-2-propanone required as reference products in connection with studies on lignin structure have been synthesized and their properties compared with those of their known isomers previously isolated from wood ethanolysis products.

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

Studies on Lignin and Related Compounds. LXIX. Isolation of 1-(4-Hydroxy-3-methoxyphenyl)-2-propanone and 1-Ethoxy-1-(4-hydroxy-3-methoxyphenyl)-2-propanone from the Ethanolysis Products of Spruce Wood¹

BY EINAR WEST, A. S. MACINNES AND HAROLD HIBBERT

In a previous communication² an account was given of the isolation of 1-(4-hydroxy-3-methoxyphenyl)-2-propanone and 1-(4-hydroxy-3,5-dimethoxyphenyl)-2-propanone from the ethanolysis products of maple wood. Since other ethanolysis³ and oxidation⁴ studies on a variety of woods had established the presence of 4-hydroxy-3-

methoxyphenyl derivatives in gymnosperms and both the 4-hydroxy-3-methoxyphenyl and 4-hydroxy-3,5-dimethoxyphenyl types in angiosperms, it seemed probable that the application of a modification of the procedure already outlined for maple wood² should also lead to the isolation of 1-(4-hydroxy-3-methoxyphenyl)-2-propanone among the ethanolysis products from spruce wood.

This substance has now been isolated (0.02% of the initial Klason lignin) from the water-soluble ethanolysis products and identified as its thio-

(1) From a thesis submitted to the Graduate Faculty of McGill University by Einar West in partial fulfillment of the requirements for the degree of Doctor of Philosophy, October, 1942.

(2) Kulka and Hibbert, *THIS JOURNAL*, **65**, 1180 (1943).

(3) MacInnes, West, McCarthy and Hibbert, *ibid.*, **62**, 2803 (1940).

(4) Creighton, McCarthy and Hibbert, *ibid.*, **63**, 3049 (1941).