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.

Acknowledgment.—The authors wish to thank the National Research Council of Canada for the award of a Studentship and the Canadian Pulp and Paper Association for financial assistance to one of them (L. M.).

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.

MONTREAL, QUEBEC, CANADA
RECEIVED DECEMBER 10, 1943

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

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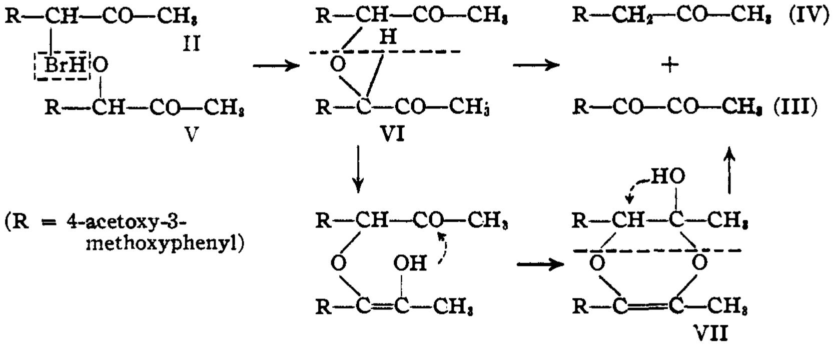
(1) Extract from the thesis work of Leonard Mitchell to be presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy, McGill University.

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

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

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

acid and an unstable ether (VI) which then decomposes into III and IV.



(R = 4-acetoxy-3-methoxyphenyl)

It is also conceivable that VI, by an intramolecular rearrangement could yield an unstable six-membered ring VII also capable, on decomposition, of giving III and IV in the manner indicated.

The fact that these changes take place under such mild conditions, *at room temperature*, may have considerable biological significance. The reaction is, in many ways, analogous to that found by Kohler[5] in the behavior of a series of aromatic α-bromoketones toward alkalies, whereby, in addition to the hydroxy substitution products, 1,2-diketones and desoxybenzoins were obtained.

In the present investigation it was found that small amounts of the 1,2-diketone, 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (VIII), are obtained both when the bromo derivative (II) is refluxed with 5% aqueous potassium acetate and when 1-acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (I)[3] is refluxed with an aqueous suspension of barium carbonate. In both cases the principal product of hydrolysis is 2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone (IX).

It has been shown previously[4] that a considerable amount of diketone, 1-(3,4-dimethoxyphenyl)-1,2-propanedione is obtained by the action of 5% aqueous potassium acetate on 3-chloro-1-(3,4-dimethoxyphenyl)-2-propanone, in addition to the main product, 1-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone, the latter being formed as the result of an allyl shift similar to that found more recently[6] with 3-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone.

These results, Chart I, considered in conjunction with those of the present research, Chart II, would seem to provide definite proof of the following interrelated mechanisms and in turn supply

$$\begin{array}{l} RCH_2COCH_2OH \rightleftharpoons RCH{=}C(OH)CH_2OH \rightleftharpoons RCHOHC(OH){=}CH_2 \rightleftharpoons \\ \quad RCHOHCOCH_3 \rightleftharpoons RC(OH){=}C(OH)CH_3 \rightleftharpoons RCOCHOHCH_3 \\ \quad \downarrow \\ \quad RCOCOCH_3 + RCH_2COCH_3 \\ \qquad\qquad (R = \text{4-hydroxy-3-methoxyphenyl}) \end{array}$$

further substantial confirmation of the views of Hibbert that spruce native lignin is derived from building-units of the β-oxyconiferyl alcohol (β,γ-dioxyisoeugenol) type.

Experimental

The synthesis of 1-bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (II) was accomplished by a preliminary acetylation of the phenolic hydroxyl in 1-(4-hydroxy-3-methoxyphenyl)-2-propanone[7] and subsequent bromination in the presence of a trace of benzoyl peroxide.[8] The procedure for isolation of the free hydroxy hydrolysis products, 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (VIII) and 1-(4-hydroxy-3-methoxyphenyl)-2-propanone (X) was similar to that employed for the components of the bisulfite soluble fraction from the ethanolysis of wood.[7]

Synthesis of 1-(4-Acetoxy-3-methoxyphenyl)-2-propanone.—1-(4-Hydroxy-3-methoxyphenyl)-2-propanone[7] (20 g.) was dissolved in aqueous sodium hydroxide (65 cc. of 10% solution) and the solution cooled by the addition of cracked ice. Acetic anhydride (15 cc.) was added rapidly and the mixture shaken for five to ten minutes, sufficient ice being present to maintain the temperature at 0–10°. The heavy oil was separated and the aqueous layer extracted thoroughly with ether. The ether extracts were combined with the oil and the entire solution back-extracted once with dilute sodium hydroxide (1% solution), the ethereal solution washed with water and dried over sodium sulfate. Removal of solvent and vacuum distillation of the crude product at 150–160° (bath temperature) (0.075 mm.) yielded an almost colorless oil which crystallized rapidly; yield, 22.0 g. (98%). This distilled product was sufficiently pure for the succeeding step in the synthesis. When recrystallized from dilute ethanol it melted at 47–48°. *Anal.* Calcd. for $C_{12}H_{14}O_4$: C, 64.8; H, 6.30; OCH_3, 14.0. Found: C, 64.5; H, 6.35; OCH_3, 13.9. The semicarbazone, recrystallized from dilute ethanol, melted at 168–169°. *Anal.* Calcd.: OCH_3, 11.1. Found: OCH_3, 11.1.

Synthesis of 1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (II).—To a solution of 1-(4-acetoxy-3-methoxyphenyl)-2-propanone (15 g.) and benzoyl peroxide (0.15 g.) in anhydrous chloroform (100 cc.) contained in a three-necked flask, fitted with a dropping funnel, a thermometer and a stirrer was added a solution of bromine (12.5 g.) in chloroform (50 cc.) over a period of one hour. During the addition the solution was stirred vigorously and the temperature kept below 10° by means of an ice-bath. At the conclusion of the addition the stirring was continued for an additional one and one-half hours at room temperature. The solution was washed twice with water, once with 1% sodium bicarbonate and, finally, twice again with water. Remaining traces of water were removed by passage through a dry filter paper and the solution evaporated almost to dryness at room temperature under reduced pressure (15 mm.). Addition of ether to the residue precipitated a crude yellowish product which was filtered on a sintered glass funnel and washed with ether until most of the color had been removed. The crude product, only slightly soluble in ether, was dissolved in a large volume of the pure dry solvent, boiled with charcoal, filtered and the solution concentrated to a volume of 50 cc. On cooling, the almost pure compound (12.5 g.), m. p. 98–99°, separated out. From the mother liquors and washings an additional amount (2.5 g.), m. p. 98–99°, was obtained; total yield, 15.0 g. (73%). On recrystallization, alternately from ether and ether–petroleum ether

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(5) Kohler, *Am. Chem. J.*, **41**, 417 (1908).

(6) Fisher, Kulka and Hibbert, This Journal, **66**, 598 (1944).

(7) Kulka and Hibbert, *ibid.*, **65**, 1180 (1943).

(8) Kharasch, White and Mayo, *J. Org. Chem.*, **2**, 33 (1938).

CHART I[4,6]

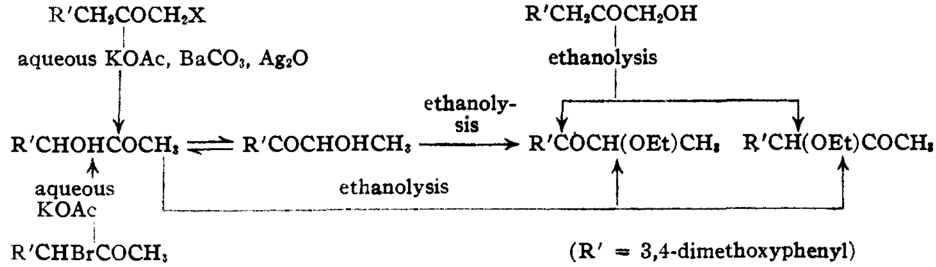
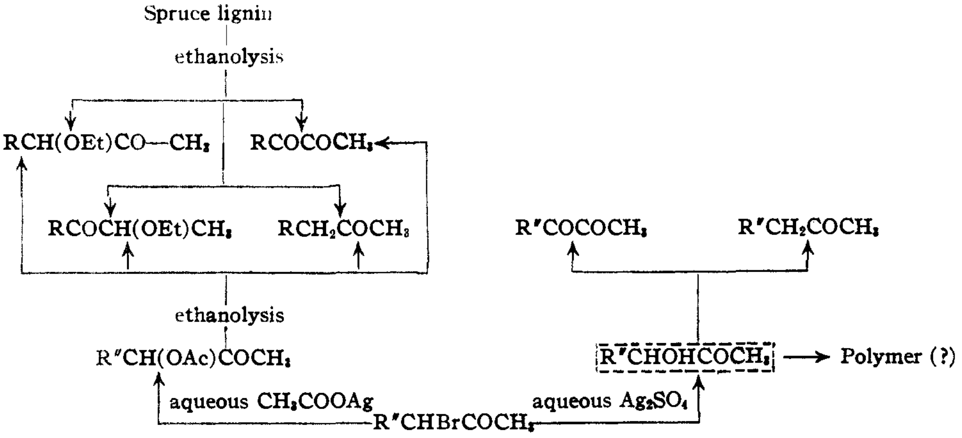


CHART II



R′ = 4-acetoxy-3-methoxyphenyl
R = 4-hydroxy-3-methoxyphenyl

(b. p. 30–50°) the melting point was raised to 100–101°. *Anal.* Calcd.: OCH_3, 10.3; Br, 26.5. Found: OCH_3, 10.2; Br, 26.5. The semicarbazone, recrystallized from dilute methanol, melted at 180–181°. *Anal.* Calcd.: OCH_3, 8.65. Found: OCH_3, 8.5.

Action of Aqueous Silver Sulfate on 1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (II).—1-Bromo-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (3.5 g.) was dissolved in a mixture of dioxane (100 cc.) and water (50 cc.). Freshly precipitated silver sulfate (3.0 g.) and barium carbonate (3.0 g.) were added and the mixture stirred at room temperature in an atmosphere of nitrogen for five days. The insoluble salts were filtered off and the filtrate concentrated at room temperature (using a carbon dioxide bubbler under reduced pressure) to a volume of 25 cc. This solution was extracted thoroughly with chloroform, and the extract dried over sodium sulfate, filtered and the solvent removed under reduced pressure leaving a crude yellowish-orange oil (3.0 g.) which could not be crystallized. Vacuum distillation of this product at 150–180° (bath temperature) (0.10 mm.) yielded a mobile orange-colored distillate (A), 1.5 g. (60%) and a non-distillable residue (B), 0.90 g. (35%). The low methoxyl value of the distillate (A), 13.2%, as compared with that of 15.8% for IX and 17.2% for X indicated that the phenolic acetate group was still intact. The highly colored residue (B) was dissolved in chloroform (5 cc.) and poured in a fine stream into petroleum ether (b. p. 30–50°) (100 cc.), the dark-colored precipitated tar separated by decantation and dried *in vacuo* leaving a brittle resinous material (0.75 g.), probably a condensation polymer of the intermediate 1-hydroxy derivative.

(a) **Isolation of 1-(4-Hydroxy-3-methoxyphenyl)-1,2-propanedione (VIII) from (A).**—The oil (A) (1.5 g.), nickel chloride (15 cc. of 5% solution), hydroxylamine sulfate (1.0 g.) and sodium acetate (8 g.) were dissolved in water (400 cc.) and the nickel glyoxime salt (C) isolated and hydrolyzed as described previously[9]; yield of nickel salt (C), 0.82 g., equivalent to 0.66 g. diketone present in (A) (44%).

Distillation of the crude diketone obtained from the hydrolysis of the nickel glyoxime salt (C) yielded a yellow distillate which solidified rapidly on standing. Recrystallized once from dilute ethanol the product melted at 69–70° and gave no depression in melting point when mixed with an authentic sample of 1-(4-hydroxy-3-methoxyphenyl)-1,2-propanedione (VIII).

(b) **Isolation of 1-(4-Hydroxy-3-methoxyphenyl)-2-propanone (X) from (A).**—The aqueous solution remaining after separation of the nickel glyoxime salt (C) was concentrated to about 250 cc. and extracted continuously with benzene for thirty-six hours. The benzene extract was dried and the solvent removed under reduced pressure, leaving the crude oxime of the desoxybenzoin. After removal of the last traces of solvent this crystallized partially as a yellow solid, yield 0.63 g. Distillation of the crude product remaining after hydrolysis of the oxime yielded a mobile yellow oil analyzing correctly for 1-(4-hydroxy-3-methoxyphenyl)-2-propanone (X); yield, 0.33 g., equivalent to 0.40 g. (27%) of 1-(4-acetoxy-3-methoxyphenyl)-2-propanone (IV) in the oil (A). *Anal.* Calcd.: OCH_3, 17.2. Found: OCH_3, 17.1. The semicarbazone of this distilled product, after one recrystallization from ethanol, melted at 157–158° and showed no depression when mixed with the pure semicarbazone of (X). *Anal.* Calcd.: OCH_3, 13.1. Found: OCH_3, 13.1.

Hydrolysis of 1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone (I) with Barium Carbonate.—1-Acetoxy-1-(4-acetoxy-3-methoxyphenyl)-2-propanone[3] (I) (1.0 g.) was refluxed in an atmosphere of nitrogen for ten hours with a suspension of barium carbonate (2.0 g.) in distilled water (50 cc.). The mixture was cooled, the excess barium carbonate removed and the orange-colored filtrate extracted thoroughly with chloroform. Removal of solvent and vacuum distillation of the residue at 150–180° (bath temperature) (0.075 mm.) gave a clear yellow oil which solidified on standing; yield, 0.50 g. (74%). The

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(9) Kulka, Hawkins and Hibbert, THIS JOURNAL, 63, 2371 (1941).

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.

Acknowledgment.—The authors wish to thank the National Research Council of Canada for the award of a Studentship and the Canadian Pulp and Paper Association for financial aid to one of them (L. M.).

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 approximate 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 Structure[1]

BY J. A. F. GARDNER[2] 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 formed[5] 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 of reaction occurring with the analogous *dihydroxy* derivative, R—C(OH)=C(OH)—CH$_2$OH (IV) (R = 4-hydroxy-3-methoxyphenyl) since in this case the final product should also be the above diketone (I).

$$\underset{\text{IV}}{\text{RC(OH)=C(OH)—CH}_2\text{OH}} \rightleftharpoons$$

$$\text{R—C(OH)}_2\text{—C(OH)=CH}_2 \longrightarrow \underset{\text{I}}{\text{R—COCOCH}_3} + \text{H}_2\text{O}$$

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

$$\underset{\text{V}}{\text{R—COCHOHCH}_2\text{OH}} \leftrightarrows$$

$$\underset{\text{IV}}{\text{R—C(OH)=C(OH)—CH}_2\text{OH}} \rightleftharpoons$$

$$\underset{\text{VI}}{\text{R—CHOHCOCH}_2\text{OH}}$$

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 Eaton[8] 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

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[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.*, 113, No. 4, 35 (1941).

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

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