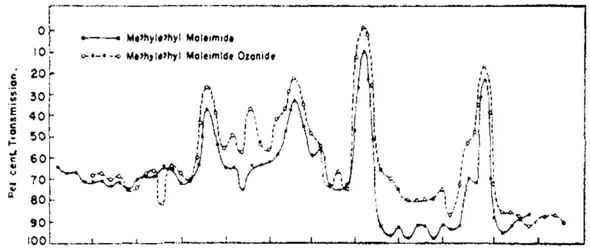

Fig. 2.—Infrared absorption spectra of methylethylmaleimide and methylethylmaleimide ozonide.

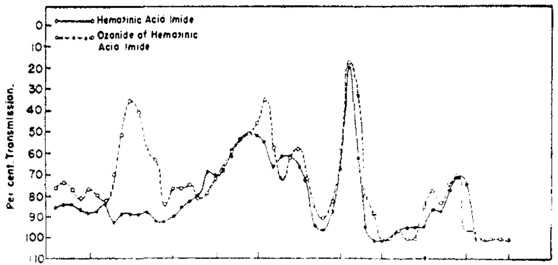

Fig. 3.—Infrared absorption spectra of hematinic acid imide and the ozonide of hematinic acid imide.

imide –CO and of the –CO of the carboxyl group of hematinic acid imide may be identified with the absorption band at 5.8 μ. It is also likely that the –C–O– groups of the ozonide make a contribution to the spectral band at this frequency.[14] The absorption band exhibited by methylethylmaleic acid imide and its ozonide at 7.3–7.5 μ is probably due to deformation vibrations of the $-CH_3$ group.[15] Hematinic acid imide has a comparable absorption band between 7.2–7.4 μ whereas in the case of the corresponding ozonide there is a shift of this band to the region of 6.8–7.2 μ. Both ozonides possess an absorption band in the region between 7.7–8.5 μ. It appears likely that the –C–O– grouping of the ozonide contributed to this vibrational frequency as has been observed for ozonides in solution.[14] At 9.3–9.6 μ an intense absorption band is observed with methylethylmaleic acid imide and its ozonide although hematinic acid imide and its ozonide fail to show such a band. It seems probable, particularly in view of the absence of this band in hematinic acid imide and its ozonide, that the $-CH_2CH_3$ grouping contributes to this absorption.[16] It should, furthermore, be noted that a striking difference exists between hematinic acid imide ozonide and its parent compound, inasmuch as the former compound exhibits a strong absorption band between 10.7–11.2 μ. Although the nature of the structural configuration responsible for this band has not been established, it is possible that the association of H with the –O–O-grouping might lead to a structure closely related to the O–O–H grouping to which Shreve, *et al.*,[17] have assigned the absorption band at approximately 12 μ. Hydrogen bonding involving the H atom of the carboxyl group and the ozonide configuration could only occur in the case of hematinic acid imide ozonide, thus explaining the absence of a band in the 12 μ region for methylethylmaleic acid imide ozonide.

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(14) E. Briner, *et al.*, *Helv. Chim. Acta*, **35**, 340, 345, 353 (1952).

(15) H. W. Thompson, *J. Chem. Soc.*, 238 (1948).

(16) K. F. Luft, *Angew. Chem.*, **19B**, 2 (1947).

(17) O. D. Shreve, M. R. Heether, H. B. Knight and D. Swern, *Anal. Chem.*, **23**, 277 (1951).

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[Contribution from Havemeyer and Chandler Laboratories, Columbia University]

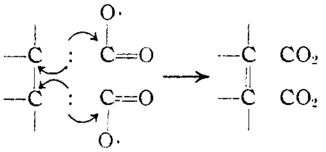
The Oxidative Bisdecarboxylation of α,β-Dicarboxylic Acids[1]

By W. von E. Doering,[2] Milton Farber and Adnan Sayigh

Received March 18, 1952

Lead dioxide has been discovered to oxidize α,β-dicarboxylic acids and their anhydrides to carbon dioxide and the corresponding α,β-olefin. Although the yields are only about 25% of theoretical, the new reaction offers degradative and synthetic possibilities.

The search for a reagent which would remove two adjacent carboxyl groups in a single operation was initiated when many of our schemes projected for the synthesis of 1-substituted bicyclic compounds seemed unfeasible for lack of such a reaction. That a diamagnetic or paramagnetic diradical of the structure I should decompose to two molecules of carbon dioxide and the olefin was the basic working hypothesis. In the electrolysis of succinic acid and fumaric acid to carbon dioxide and ethylene and acetylene, respectively,[3,4] and in the decomposition of succinyl and fumaryl peroxides to the same respective olefins[5] one has examples of the desired reaction and support for the hypothesis. When applied to substituted succinic acids the electrolysis has so far been quite unsatisfactory. Extension of the peroxide decomposition to hexahydrophthaloyl peroxide was successful in that cyclohexene in variable yield was obtained but the peroxide, which was prepared according to Vanino and Thiele,[6] was extremely unstable and could not be purified.



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Investigation of tetravalent lead compounds as reagents to effect the desired reaction was prompted by their use in the cleavages of glycols and α-hydroxy acids, two reactions which resemble the projected reaction rather closely. The lead tetraacetate cleavage of glycols is not only structurally similar but has been shown to proceed through a

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[1] Taken in part from a dissertation submitted by Milton Farber in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

[2] Department of Chemistry, Yale University, New Haven, Connecticut.

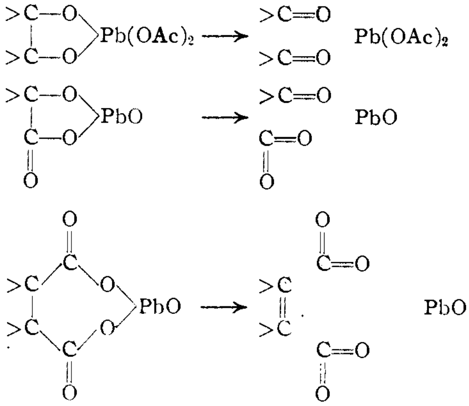
[3] A. Kekule, *Ann.*, **131**, 79 (1864).

[4] See also J. Peterson, *Z. physik. Chem.*, **33**, 698 (1900); F. Fichter and A. Petrovitch, *Helv. Chim. Acta*, **24**, 549 (1941).

[5] F. Fichter and A. Fritsch, *ibid.*, **6**, 329 (1923).

[6] L. Vanino and E. Thiele, *Ber.*, **29**, 1724 (1896).

cyclic intermediate,[7] while the oxidation of α-hydroxy acids with lead dioxide[8] or with lead tetraacetate[9] is probably comparable as well although the mechanism is not elucidated. The clear, formal similarity of the three reactions is indicated in the scheme below. Although these decompositions can be formulated to suggest either diradical or ionic intermediates such detailed specification, amounting to no more than appropriate allocation of electrons, has no significance, neither in these cases nor in the intramolecular decomposition of cyclic intermediates in general (no-mechanism reactions).



Heating molten succinic acid at 200° with lead dioxide leads to extensive decomposition and the formation of ethylene in only very small amount. In a high-boiling diluting solvent the reaction proceeds more satisfactorily but may present difficulties in separating the olefinic product from the large volume of solvent. In boiling decalin *cis*-hexahydrophthalic acid is oxidatively bisdecarboxylated to cyclohexene in 21% of the theoretical amount (35% based on starting material not recovered). In a similar way *cis*-4,5-dimethylhexahydrophthalate gives 4,5-dimethylcyclohexene (35%), the structure being assigned on the basis of oxidation to β,β'-dimethyladipic acid. With bicyclo[2,2,1]heptane-2,3-dicarboxylic acid, the difficulty of isolating product becomes insurmountable on the scale employed so that the presence of bicycloheptene is inferred from the isolation of cyclopentane 1,3-dicarboxylic acid obtained by oxidation of the crude product.

A more convenient procedure avoids the use of solvent by grinding a mixture of the anhydride with lead dioxide in a ball mill to a fine powder which is then heated carefully either alone or diluted with powdered glass. By this method bicyclo[2,2,2]octane-2,3-dicarboxylic anhydride affords bicyclo[2,2,2]octene in about 20% of the theoretical amount. Two other examples 1-acetoxy- and 1-carbomethoxy- bicyclo[2,2,2]octane-2,3-dicarboxylic anhydrides studied in connection with another problem, give the corresponding 1-acetoxy- and 1-carbomethoxy-bicyclo[2,2,2]octene in about the same yield.[10]

Experimental[11]

Hexahydrophthaloyl Peroxide and its Decomposition.—A mixture of 5 g. of *cis*-hexahydrophthalic acid in 50 ml. of ether to which 13 g. of phosphorus pentachloride had been added with stirring was refluxed for 1/2 hr. After removal of the ether and phosphorus oxychloride at 25 mm., the diacid chloride of *cis*-hexahydrophthalic acid was distilled in 72% of the theoretical yield; b.p. 118–123° at 4 mm.

Addition of 0.5 g. of the acid chloride to 2 g. of aniline at 0° produced the dianilide, m.p. 234–234.5°; reported m.p. 234°.[12]

A solution of 3.8 g. of the diacid chloride in 20 ml. of toluene was added dropwise to a stirred, ice-cooled solution of 1.8 g. of sodium peroxide in 20 ml. of water, the resulting reaction mixture being stirred for 1/2 hr. Removal of the aqueous layer and addition of methanol to the toluene layer precipitated the crude, gummy peroxide which on washing thrice with methanol solidified (1.8 g.). Being unstable and exploding when warmed, the peroxide was used at once and was not dried.

On gentle warming the decomposition of 1.8 g. of the peroxide in 10 ml. of xylene proceeded smoothly with the evolution of carbon dioxide. Distillation yielded 0.5 g. of impure cyclohexene, b.p. 60–95°, identified by oxidation to adipic acid.

When 10.7 g. (0.051 mole) of the acid chloride was converted to the peroxide in xylene which was then decomposed without isolation, 0.025 mole of carbon dioxide was obtained corresponding to 25% of theory, while 0.45 g. of cyclohexene was isolated (44% of theory based on carbon dioxide evolved).

Bisdecarboxylation of α,β-Dicarboxylic Acids with Lead Dioxide. (a) Succinic Acid.—In a 250-ml. 3-necked flask with stirrer, Gooch addition tube and gas exit tube leading to a gas absorber filled with bromide, 25 g. of succinic acid was heated at 200° and treated with excess lead dioxide in small portions until no more gas was evolved. The contents of the gas absorber were then washed with 20% sodium hydroxide solution leaving a small amount of water-insoluble material which was dried with anhydrous calcium chloride and distilled to give 0.6 g. of ethylene bromide, b.p. 132° (micro); m.p. 9.5–10.5°; n^{22}D 1.5362; reported b.p. 131.6°, m.p. 10°, n^{22}D 1.5379.

(b) ***cis*-Hexahydrophthalic Acid.**—A mixture of 17.2 g. (0.1 mole) of *cis*-hexahydrophthalic acid, m.p. 189–191°, 100 ml. of decalin (b.p. 189–194°; purified by extraction with concentrated sulfuric acid and distillation) and 48 g. (0.2 mole) of lead dioxide in a 200-ml. flask fitted with a Vigreux column and a receiver cooled in Dry Ice was refluxed for 2 hr. The contents of the receiver was separated from water, dried with calcium chloride and distilled to give 1.6 g. of material, b.p. 70–75° and 0.3 g., b.p. 75–90°. On reheating the reaction mixture, 2 g. of liquid was obtained from which 0.1 g. of material, b.p. 75–80°, was separated. By redistillation a total of 1.7 g. (21% of theory based on acid introduced) of cyclohexene, b.p. 83.7° (micro), n^{28}D 1.4432, was obtained which afforded adipic acid; m.p. 149–150°, on oxidation with potassium permanganate and a nitrosochloride, m.p. 146–147° with dec., for which Baeyer[13] reports m.p. 152–153° with dec.

By distilling the decalin, boiling the residue with 150 ml. of 3 *N* sodium hydroxide, filtering, acidifying with 6 *N* sulfuric acid, filtering and concentrating the aqueous solution to 50 ml., there was obtained crude recovered acid which was recrystallized to give 7.0 g. (41% of the starting amount) of *cis*-hexahydrophthalic acid. Based on the amount of acid consumed, the yield of cyclohexene was 35% of the theoretical amount.

(**c**) ***cis*-4,5-Dimethylhexahydrophthalic Acid.**—Catalytic hydrogenation of *cis*-4,5-dimethyl-Δ^4-tetrahydrophthalic acid[14] in glacial acetic acid with platinum oxide afforded *cis*-**4,5-dimethylhexahydrophthalic acid**, m.p. 167–170° on crystallization from water and m.p. 172–173° after two recrystallizations.

Anal. Calcd. for $C_{16}H_{10}O_4$: C, 60.0; H, 8.1; neut.

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[7] R. Criegee, L. Kraft and B. Bank, *Ann.*, **507**, 159 (1933).

[8] J. Houben, "Die Methoden der Organischen Chemie," 3rd Ed., Vol. 2, G. Thieme, Leipzig, Germany, 1925, p. 147.

[9] H. Oeda, *Bull. Chem. Soc. Japan*, **9**, 8 (1934).

[10] The experimental details will be published later.

[11] All m.ps. and b.ps. are corrected. Microanalyses are by Miss Lois May, Columbia University and Schwarzkopf Microanalytical Laboratory, Middle Village, Long Island, N. Y.

[12] R. Stoermer and H. J. Steinbeck, *Ber.*, **65**, 413 (1932).

[13] A. Baeyer, *Ann.*, **278**, 88 (1894).

[14] E. H. Farmer and F. L. Warren, *J. Chem. Soc.*, 897 (1929).

equiv., 100.1. Found: C, 59.9; H, 8.1; neut. equiv., 100.8.

Using the same procedure as in (a), 20 g. (0.1 mole) of *cis*-4,5-dimethylhexahydrophthalic acid and 24 g. (0.1 mole) of lead dioxide in 100 ml. of decalin afforded 1.71 g. (16%) of *cis*-4,5-dimethylcyclohexene; b.p. 127.8° (micro); $n^{25}\text{D}$ 1.4467.

Anal. Calcd. for C_8H_{14}: C, 87.2; H, 12.8. Found: C, 87.2; H, 13.0.

Oxidation with alkaline potassium permanganate yielded β,β'-dimethyladipic acid, m.p. 132–133, where m.p. 133° is reported for the higher melting isomer.[15]

(d) **Bicyclo[2,2,1]heptane-2,3-dicarboxylic Acid.**—Proceeding in the same manner and with the same molar quantities as above, this acid lost carbon dioxide and gave a mixture of product and decalin which could not be separated. A crude fraction (100 mg., b.p. 85–115°), was oxidized with potassium permanganate and gave 35 mg. of *cis*-cyclopentane-1,3-dicarboxylic acid, m.p. 120–120.5°. The reported m.p. is 120–121°.[16]

Bisdecarboxylation of Bicyclo[2,2,2]octane-2,3-dicarboxylic Anhydride with Powdered Lead Dioxide.—A mixture of 2.0 g. of the anhydride, 10 g. of lead dioxide and 40 g. of powdered Pyrex was ground thoroughly in a mortar and placed in a 250-ml. flask with side-arm connected to a 100-ml. flask leading successively to an empty trap, one cooled in ice and containing 5% bromine in carbon tetrachloride and a third containing aqueous barium hydroxide. On heating slowly to 250°, a solid sublimed and barium carbonate precipitated. When sublimation ceased, the contents were cooled and extracted with *n*-pentane. Concentration of the *n*-pentane with a Vigreux column gave material which was sublimed at room temperature (0.2 g.). After crystallization from methanol and sublimation, the bicyclo[2,2,2]-octene melted at 141–144°; reported m.p. 143–144°.[17]

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[15] F. Foltis and H. Wagner, *Ann.*, **433**, 103 (1923).

[16] S. F. Birch, W. J. Oldham and E. A. Johnson, *J. Chem. Soc.*, 818 (1947).

[17] R. Seka and O. Tramposch, *Ber.*, **75**, 1379 (1942).

NEW YORK 27, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF OKLAHOMA]

The Isolation and Identification of Quercetin and Isoquercitrin from Grapes (*Vitis vinifera*)[1]

BY BYRON L. WILLIAMS AND SIMON H. WENDER

RECEIVED MARCH 6, 1952

Grapes, *Vitis vinifera*, have been previously reported to possess a relatively high "vitamin P" activity, which is generally attributed to the flavonoid compounds present. This paper is the first to report the isolation and identification in pure form from grapes of quercetin (3,3',4',5,7-pentahydroxyflavone) and of isoquercitrin (quercetin-3-glucoside). The three types of grapes individually studied were Thompson white seedless, tokay and emperor. All three belong to *Vitis vinifera*.

Introduction

Scarborough[2] has reported that a concentrate from grapes, *Vitis vinifera*, possesses a relatively high "vitamin P" activity. This so-called "vitamin P" activity is generally attributed to the flavonoids present.[3] To date, to our knowledge, isoquercitrin has not been reported as having been isolated and identified from grapes or grape concentrates. The present paper reports the isolation in pure form and identification of quercetin (3,3',4',5,7-pentahydroxyflavone) and isoquercitrin (quercetin-3-glucoside) from grapes, *Vitis vinifera*.

For the isolation of the flavonoid compounds, the method reported involves hot water extraction, ion exchange chromatography, concentration and drying *in vacuo*, extraction with hot anhydrous acetone, adsorption chromatography, and recrystallization from water. Use is made of paper partition chromatography, acetylation, hydrolysis, ultraviolet absorption spectra, and mixed melting points in the identification procedure.

The three types of grapes studied, individually, each in 50-lb. batches, were Thompson white seedless, tokay and emperor. All belong to *Vitis vinifera*.

Experimental

In a typical experiment, 50 lb. of one of the three types of grapes studied, were processed, with stems removed, through a wet grinder,[4] and extracted in an aluminum pot with 20 gal. of distilled water at boiling temperature. The extract was filtered, the residue discarded, and the filtrate allowed to cool to room temperature. The cooled extract was then passed over ion exchange columns at the rate of 1 gal./hr. for each column. Four columns were used with 5 gal. of extract being passed over each. Each column consisted of a glass tube 6 × 100 cm. drawn to an outlet at one end. The resin bed was composed of Amberlite IRC-50(H), (Rohm and Haas, Philadelphia, Pa.). The columns containing the material adsorbed[5] from the extract were each washed with 5 gal. of distilled water to get rid of the sugar. The effluent and washings were discarded. The adsorbed material, containing the flavonoids present, was then eluted from the columns with 500 ml. of 95% ethanol for each of the four columns. This eluate was then taken to dryness *in vacuo* using a resin pot immersed in a hot water-bath. The pulverized residue was then extracted with five 100-ml. portions of hot, anhydrous acetone. These acetone extracts, after cooling to room temperature, were passed through a chromatographic column, 20 × 220 mm., containing a bed of magnesol (Food Machinery and Chemical Corp., Westvaco Chemical Division, New York) 10 mm. deep. This passage removed a considerable amount of dark, nonflavonoid material which remained adsorbed on the column. The effluent from the column was then chromatographed in a column, 20 × 220 mm., but with a fresh magnesol bed made 100 mm. deep. Material in the extract was adsorbed on the magnesol, giving a band about 5 mm. deep and yellow in visible light. The chromatogram was developed with

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[1] This research was supported in part by the Office of Naval Research (Project NR-059-226).

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[3] H. Scarborough and A. L. Bacharach, "Vitamins and Hormones," Vol. VII, Academic Press, Inc., New York, N. Y., 1949, pp. 1 55.

[4] L. S. Ciereszko, T. B. Gage and S. H. Wender, *Anal. Chem.*, **24**, 767 (1952).

[5] T. B. Gage, Q. L. Morris, W. E. Detty and S. H. Wender, *Science*, **113**, 522 (1951).