which induce optimal enzymic activity are even more dependent upon each other than has previously been realized and that none of them should be regarded as fixed if any of the others is changed.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

CATALYTIC OXIDATIONS IN AQUEOUS SOLUTIONS

I. THE OXIDATION OF FURFURAL

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Introduction

The present investigations are part of the applications of catalysts such as osmium tetroxide, vanadium pentoxide, etc., to the oxidation of organic compounds by means of chlorates.

In previous communications[2] it has been shown that small quantities of osmium tetroxide can induce the oxidation of relatively large quantities of organic substances by means of chlorates. The use of vanadium pentoxide with chlorates has been heretofore limited only to a very few special cases[3] in which vanadium salts were used rather than the oxide in the presence of strong acids. The present paper describes several experiments in which vanadium pentoxide has been successfully used in neutral as well as in dilute acid solutions to induce the oxidation of furfural and pyromucic acid by means of chlorates.

Furfural has been oxidized with dil. potassium permanganate solution to pyromucic acid by Volhard,[4] with bromine water at the temperature of the water-bath to mucobromic acid by Simonis,[5] with hydrogen peroxide in the presence of ferrous salts to δ-hydroxyfurfural by Cross, Bevan and Heiberg,[6] and with Caro's acid to succinic acid by Cross, Bevan and Briggs.[7]

In the Experimental Part, it will be shown that with a mixture of sodium chlorate and small quantities of osmium tetroxide in dilute acid solution, furfural yields principally mesotartaric acid, while fumaric acid is the chief product formed when the reaction is carried out in neutral solution with osmium tetroxide replaced by vanadium pentoxide. Similar results

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[1] National Research Fellow in Chemistry.

[2] (a) Milas and Terry, THIS JOURNAL, **47**, 1414 (1925). (b) Terry and Milas, *ibid.*, **48**, 2647 (1926).

[3] Guyard, *Bull. soc. chim.*, [2] **25**, 58 (1876); *Chem. News*, **33**, 70 (1876). Willstätter and Dorogi, *Ber.*, **42**, 4128 (1909).

[4] Volhard, *Ann.*, **261**, 379 (1891).

[5] Simonis, *Ber.*, **32**, 2084 (1899).

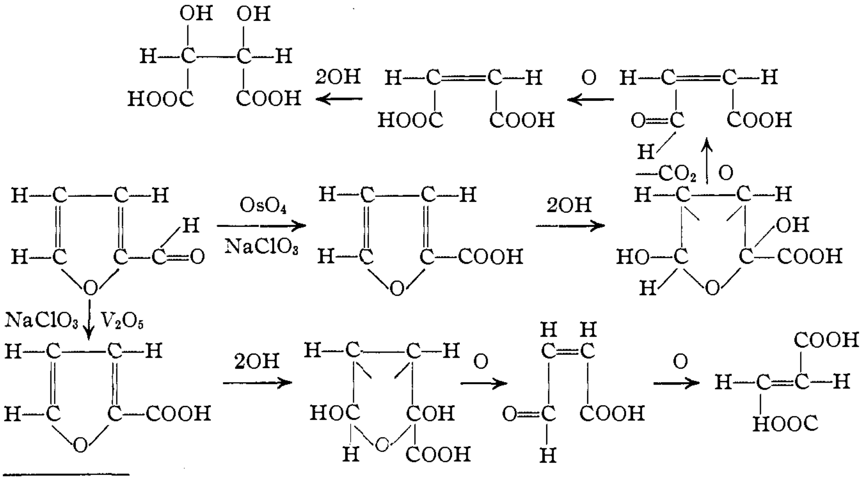
[6] Cross, Bevan and Heiberg, *J. Chem. Soc.*, **75**, 747 (1899).

[7] Cross, Bevan and Briggs, *Ber.*, **33**, 3132 (1900).

but lower yields of the principal products were obtained when pyromucic acid was used instead of furfural.

These results are not at all surprising but quite in accordance with the classical researches of Hill and his co-workers on the structure of the furane ring. Hill and Sanger[8] have shown that pyromucic acid is slowly oxidized with bromine water first to fumaryl aldehyde, then at low temperatures to maleic acid or, at higher temperatures, to fumaric acid. More striking results were obtained by Hill and Hartshorn[9] who found that α,δ-dibromofurane, prepared from δ-bromopyromucic acid, oxidizes to give, in the cold, maleic acid and at higher temperatures fumaric acid, hydrogen bromide being given off in both cases. Obviously hydroxylation of the conjugated system of the furane ring occurred first on the α,δ-carbon atoms followed by splitting of hydrogen bromide and subsequent hydrolysis of the maleic anhydride. At higher temperatures hydrolysis of maleic anhydride and transmutation of maleic acid to fumaric acid may occur simultaneously.

A similar mechanism may be adopted to explain the catalytic oxidation of furfural. Although no pyromucic acid was isolated, furfural must first be oxidized to this acid. In the reactions studied, there are two distinct stages of each reaction, a violent followed by a mild reaction. This is particularly true in the oxidation of furfural with vanadium pentoxide and sodium chlorate in which the temperature rises during the violent reaction from 70 to 105°. Furthermore, carbon dioxide is evolved in greater quantities during the violent stage. In addition to the temperature effect in this last case, considerable quantities of chlorine dioxide are formed, which are responsible for the transmutation of maleic acid as



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[8] Hill and Sanger, *Proc. Am. Acad.*, **21**, 144 (1885–6).

[9] Hill and Hartshorn, *Ber.*, **18**, 448 (1885).

soon as it is formed. This view has been substantiated by actual experiments in which maleic acid was transmuted, in aqueous solution, to the extent of 10% in eight hours at 70 to 75° by the mixture of vanadic oxide and sodium chlorate. The mechanism of the principal reactions, therefore, might be best expressed as shown on the preceding page.

This mechanism seems, to the author, the most probable, although other mechanisms are possible. So far, attempts to isolate the dihydroxypyromucic acid failed, due perhaps to its extreme instability. However, maleic acid aldehyde has been actually isolated as the intermediate product of the reaction. Several investigators have already shown that when pyromucic acid is carefully oxidized in water or alkaline solution with bromine,[10] or with oxygen[11] in presence of light, maleic acid aldehyde is formed.

Experimental Part

Oxidation of Furfural with Sodium Chlorate and Vanadium Pentoxide

Materials Used.—Two grades of furfural were used, the C. P. grade and the technical grade, both furnished by the Eastman Kodak Company. The sodium chlorate used was the U. S. P. grade furnished by Merck.

Preparation of the Catalyst.—Twenty g. of C. P. ammonium metavanadate was suspended in 200 cc. of water and to this was added slowly 30 cc. of concd. hydrochloric acid (d., 1.90). The reddish-brown semicolloidal precipitate was washed several times with water by decantation and finally suspended in 300 cc. of water and allowed to stand at room temperature for three days. This treatment made the precipitate almost granular and easy to filter. The precipitate was then collected on filter paper by means of the pump, washed several times to free it from hydrochloric acid and dried for 12 hours at 120°. To free it completely from occluded hydrochloric acid, it was finely powdered and dried again at 120° for 12 hours longer; yield of the dried oxide, 11 g. The catalyst thus prepared is very active for all purposes of oxidations with chlorates.

The Reaction.—Preliminary experiments showed that sodium chlorate in aqueous solution without the aid of the catalyst does not oxidize furfural even if the solution is made acid or heated to the boiling point of water. However, vanadium pentoxide in the absence of chlorate oxidizes furfural and shows the following changes of color:[12] V_2O_5 (yellow) $\longrightarrow$ V_2O_4 (blue) $\longrightarrow$ V_2O_3 (green). These color changes are instantly reversed when a small crystal of chlorate is added to the solution and reappear when

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[10] (a) Schmelz and Beilstein, *Ann. Suppl.*, **3**, 279 (1865). (b) Limpricht, *Ann.*, **165**, 285 (1873). (c) Hill and Allen, *Am. Chem. J.*, **19**, 650 (1897). (d) Fecht, *Ber.*, **38**, 1272 (1905).

[11] Ciamician and Silber, *Ber.*, **46**, 1563 (1913).

[12] T. F. Rutter [*Dissertation*, Leipzig, **1904**] has shown that salts of vanadium tetroxide are blue and those of vanadium trioxide are green.

the chlorate is completely reduced to the chloride. Ordinarily, when chlorate is present in excess, vanadium pentoxide does not undergo the above color changes and the reaction appears to take place entirely on its surface. As the acidity of the solution rises, due to the organic acids produced as a result of the oxidation, vanadium pentoxide goes slowly into solution and is held there, perhaps in the colloidal state. One therefore may easily conceive that vanadium pentoxide acts as an "oxygen carrier" in inducing the oxidation of organic compounds by means of chlorates.

The general procedure as finally adopted was as follows.

Forty-six g. of sodium chlorate, 0.2 g. of vanadium pentoxide and 100 cc. of water were placed in a 500cc. Erlenmeyer flask which was connected to a condenser and a dropping funnel with a two-hole rubber stopper. The mixture was heated to 70–75° by supporting the flask 10 cm. above a hot electric plate. This arrangement was very satisfactory in keeping the temperature constant to within 3°. Twenty g. of furfural was then slowly dropped into the solution at the rate of about 0.5 g. per minute, and allowed to undergo the violent reaction. During this reaction the temperature of the solution rises to 105° and a rapid evolution of carbon dioxide takes place. If the addition of furfural is too rapid the reaction becomes too violent and almost uncontrollable; if it is too slow the fumaric acid formed is further oxidized to oxalic acid and thence to carbon dioxide and water. The violent reaction lasts from 50 to 75 minutes. At the end of a definite number of hours, the reaction was stopped, the flask disconnected, stoppered and allowed to stand at room temperature overnight. The fumaric acid which separated was collected on the filter paper, washed once with cold water, dried and weighed. This acid is fairly pure; m. p., 282–284° in a sealed tube. After one recrystallization from hot water, the melting point rose to 285–287° and remained unaltered on further recrystallizations.

Anal. Subs., 0.2881: CO_2, 0.4342; H_2O, 0.0910. Calcd. for $C_4H_4O_4$: C, 41.37; H, 3.44. Found: C, 41.11; H, 3.51.

Titration with sodium hydroxide. Subs., 0.2606, 0.1957; required 43.54, 32.50 cc. of 0.1037 *N* NaOH (phenolphthalein). Calcd. for $C_4H_4O_4$: 43.33, 32.52 cc.

The last two experiments of Table I show the influence of a 2% solution of sulfuric acid on the speed of the reaction as well as on the yield of fumaric acid. The reaction, however, is much too violent to be of practical use.

TABLE I

VARIATION OF YIELD OF FUMARIC ACID WITH TIME OF HEATING

Expt.	1	2	3	4	5[a]	6[b]	7[a,b]
Time of heating, hrs.	22	16	12.5	7	8	4.5	3
Fumaric acid, yield, %	51.7	70.3	77.8	64.1	66.2	72.4	70.0

[a] Technical furfural was used in these experiments.

[b] The water used was replaced with 2% sulfuric acid.

It will be seen from Table I that the maximum yield of fumaric acid, assuming that all furfural is oxidized to this acid, was obtained when the reaction mixture was heated for 12.5 hours.

Treatment of the Filtrate.—The filtrate of Expt. 4 shown in Table I was boiled with an excess of barium carbonate for two hours, cooled, and then filtered by means of the pump. The filtrate was treated with two volumes of 95% alcohol; a white, semigranular precipitate formed. This was collected on the filter paper and dried at room temperature; yield, 9.3 g. Since this salt was more soluble in hot than in cold water, it was recrystallized twice from this solvent and dried in a vacuum desiccator over concd. sulfuric acid for several days.

Anal. Subs., 0.2873, 0.2132, 0.2812; $BaSO_4$, 0.2211, 0.1664, 0.2195. Calcd. for $C_5H_2O_5Ba.H_2O$: Ba, 46.2. Found: 45.32, 45.94, 45.95.

Determination of water. Subs., 0.4504, heated at 150–160° to constant weight; H_2O, 0.0241. Calcd. for $C_5H_2O_5Ba.H_2O$: H_2O, 6.05. Found: 5.36.

Combustion of the barium salt. Here the assumption is made that all barium is converted to barium carbonate and the percentage of carbon is calculated accordingly. Subs., 0.2745, CO_2, 0.1939; H_2O, 0.0365. Calcd. for $C_5H_2O_5Ba.H_2O$: C, 20.16; H, 1.36. Found: C, 19.57; H, 1.48.

The empirical formula of this acid, therefore, is $C_5H_4O_5$. Work is now in progress to determine its structure.

Isolation of Maleic Acid Aldehyde.—An experiment was then performed in the usual way except that it was stopped at the end of the violent reaction. The reaction mixture was cooled in ice and the solid which separated was dried and weighed; yield of fumaric acid, 6 g. The filtrate was shaken with 500 cc. of ether and the ether extract dried for several days over anhydrous sodium sulfate. When the ether was distilled the residue consisted of a mixture of a thick, brownish oil of a very penetrating odor and a whitish solid which proved to be fumaric acid. The oil is very unstable and decomposes when heated with water on the water-bath, to give fumaric acid. The ether extraction, however, is not efficient and the original aqueous solution was found to contain large quantities of maleic acid aldehyde, which gives a rich orange-reddish color in water when heated on the water-bath with a few drops of an alcoholic solution of phloroglucinol. The phenylhydrazone derivative of this aldehyde was then prepared as follows. The original aqueous solution was neutralized with sodium carbonate (litmus), cooled in ice and phenylhydrazine added in excess. A yellowish-brown precipitate was formed which became deep yellow upon the addition of dil. acetic acid. The precipitate was quickly removed from the solution mixture, dried and weighed; yield, 11 g. When recrystallized twice from hot benzene, it yielded crystals (needles under the microscope); m. p., with decomposition, 157.5–158°. Fecht[10d] describes the same substance having a melting point of 158–159°.

Anal. Subs., 0.1297, 0.2295; N_2, 16.5 cc. (18°, 759 mm.), 28.6 cc. (18°, 759.5 mm.) (over 50% KOH).

Calcd. for $C_{10}H_{10}O_2N_2$: N, 14.74. Found: 15.04, 14.71.

Oxidation of Pyromucic Acid with Sodium Chlorate and Vanadium Pentoxide

Pyromucic acid was prepared according to Wilson.[13] It was purified by recrystallization from a hot mixture of two parts of carbon tetrachloride and one part of chloroform, and melted at 132–133°.

Five g. of pyromucic acid, 9 g. of sodium chlorate, 0.08 g. of vanadium pentoxide and 25 cc. of water were brought together in a 250cc. Erlenmeyer flask which was connected to a reflux condenser. The mixture was heated at 70–75° for eight hours, then cooled and the solid, 3.5 g., separated and dried. Since this appeared to be a mixture of unoxidized pyromucic and fumaric acids, it was treated with a small volume of ether,

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[13] Wilson, "Organic Syntheses," John Wiley's Sons and Co., **6**, 44, (1926).

which extracted the former. The residual solid was recrystallized twice from hot water; m. p., 284 to 286° in a sealed tube; yield, 1 g. The presence of small quantities of oxalic acid was detected in the original mixture by the calcium oxalate test, but no attempt was made to isolate any other acid.

Oxidation of Furfural with Sodium Chlorate and Osmium Tetroxide

The catalyst was prepared according to Milas and Terry.[2a] Preliminary experiments showed that osmium tetroxide, without the presence of chlorates, oxidizes furfural and forms a dark film of one of its lower oxides which adheres to the furfural and is not readily reoxidized by the addition of a solution of sodium chlorate. An experiment run continuously for a week at 50° in a thermostat failed to show an appreciable diminution of volume of the furfural layer. However, when the water used was replaced with an equivalent volume of a solution of 0.1 N hydrochloric acid furfural was oxidized, at first rapidly, then slowly to mesotartaric and oxalic acids. The following procedure was finally adopted.

Fifty-five g. of sodium chlorate, 10 cc. of a 0.98% solution of osmium tetroxide, 260 cc. of water and 30 cc. of about a 1 N solution of hydrochloric acid were brought together in a 500cc. Erlenmeyer flask connected to a reflux condenser and a dropping funnel. The mixture was brought to 50° in a thermostat, then 20 g. of pure furfural was dropped into it at the rate of about 5 cc. for every 30 minutes. The solution was heated until the odor of furfural had almost completely disappeared. This took 110 hours. At the end of this period of time, the solution was cooled and shaken with 200 cc. of benzene to extract the catalyst. The water layer contained tartaric and oxalic acids and was neutralized with dil. ammonium hydroxide (litmus), brought to boiling, then treated with a 10% solution of calcium chloride and allowed to stand overnight. The precipitate, which had separated was collected, dried and weighed; yield, 28.3 g. This was extracted with a 20% solution of sodium hydroxide, the extract neutralized with hydrochloric acid (litmus) and allowed to stand overnight. The calcium mesotartrate was then collected, dried and weighed; yield, 24.5 g. or 48.7% of mesotartaric acid.

Anal. Subs., 0.4603, 0.4456. CaO, 0.1087, 0.1048. Calcd. for $C_4H_4O_6Ca.3H_2O$: Ca, 16.53. Found: 16.87, 16.79.

Determination of water. Subs., 0.5889. H_2O, 0.1301. Calcd. for $C_4H_4O_6Ca.$-$3H_2O$: H_2O, 22.30. Found: 22.09.

Titration of the free acid with sodium hydroxide. Subs., 0.3306, 0.3353; required 38.25, 38.76 cc. of 0.1037 N NaOH (phenolphthalein). Calcd. for $C_4H_6O_6.H_2O$: 37.95, 38.49 cc.

The residual salt from the sodium hydroxide extraction was reprecipitated once, dried and analyzed.

Anal. Subs., 0.5929. CaO, 0.2275. Calcd. for $C_2O_4Ca.H_2O$: Ca, 47.41. Found: 47.42.

Oxidation of Pyromucic Acid with Sodium Chlorate and Osmium Tetroxide

Five g. of pyromucic acid, 5 g. of sodium chlorate, 2 cc. of osmium tetroxide solution, and 25 cc. of water were brought together in a 250cc. Erlenmeyer flask fitted with a reflux condenser. The mixture was heated at 50° in a thermostat for 60 hours. The experiment yielded 4 g. of calcium mesotartrate and 0.5 g. of calcium oxalate.

In conclusion, I wish to express my sincere thanks to Professors H. S. Taylor and L. W. Jones for their invaluable suggestions in this research.

Summary

1. Vanadium pentoxide induces the oxidation of furfural and pyromucic acid with chlorates to give fumaric acid as the principal product.
2. Osmium tetroxide also induces the oxidation of furfural and pyromucic acid with chlorates to give mesotartaric acid as the principal product and oxalic acid as the by-product.
3. The mechanism of the reaction has been worked out and maleic acid aldehyde has been isolated as the intermediate product.
4. An acid having the empirical formula $C_5H_4O_6$ has also been isolated.

PRINCETON, NEW JERSEY

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, NO. 548]

RESEARCHES ON SELENIUM ORGANIC COMPOUNDS.
VII. THE SYNTHESIS OF 2-PHENYL-, 2-FURYL- AND 2-THIENYL-BENZOSELENAZOLES, OF 2-PHENYL-BENZOSELENAZOLE-4'-ARSONIC ACID AND OF OTHER BENZOSELENAZOLES[1]

BY MARSTON TAYLOR BOGERT AND ARTHUR STULL[2]

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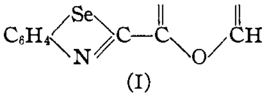
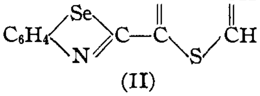
Nitro-, amino- and hydroxy-phenyl-benzoselenazoles have been synthesized by methods entirely analogous to those developed in these Laboratories for the corresponding benzothiazoles, by condensing the zinc *o*-aminoselenophenolate with the appropriate aldehyde or acid halide. As was expected, these compounds proved rather more difficult to prepare and less stable than their sulfur analogs.

Perhaps the most remarkable result of these syntheses is the persistence of the "Rosenkoerper" odor of 2-phenyl-benzothiazole even when the thiazole sulfur is replaced by selenium and the phenyl by a furyl or thienyl group. The odor of the dry compounds at ordinary temperature is faint, but when heated or in solution is of pronounced geranium or tea-rose type.

Further, these furyl (I) and thienyl (II) derivatives present new and interesting combinations of dissimilar heterocyclic systems, which offer



(I)



(II)

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[1] That portion of this paper which deals with the arsonic acid was presented at the Washington Meeting of the National Academy of Sciences, April 26, 1926. The other syntheses were reported to the Division of Organic Chemistry of the American Chemical Society, at the Philadelphia Meeting, September 8, 1926.

[2] Research Assistant, Columbia University, for the academic year 1925–1926.