secondary and tertiary alcohols, inositol, threonine and tartaric acid could not be quantitatively determined by this method.

2. On the basis of experimental data, a generalization is offered for the variation in reactivity of aliphatic hydroxy compounds toward hydriodic acid. The presence of adjacent negative groups increases the reactivity of a hydroxyl while an adjacent methyl group decreases its reactivity.

3. The analytical data give some indication of structural relationships of the functional groups in a compound.

4. It is suggested that the analytical method described might be useful in the determination of any group readily reacted upon by hydriodic acid.

CORVALLIS, OREGON RECEIVED JUNE 8, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Kinetics of the Periodate Oxidation of 1,2-Glycols

BY CHARLES C. PRICE AND HARRY KROLL

The cleavage by periodic acid oxidation of the carbon to carbon bond in compounds in which the two carbon atoms each bear an oxygen atom either as a hydroxyl or carbonyl group was first observed by Malaprade.[1]

$$\mathrm{RCHOHCHOHR} + \mathrm{HIO_4} \longrightarrow 2\mathrm{RCHO} + \mathrm{H_2O} + \mathrm{HIO_3}$$

$$\mathrm{RCHOHCOR} + \mathrm{HIO_4} \longrightarrow \mathrm{RCHO} + \mathrm{RCOOH} + \mathrm{H_2O} + \mathrm{HIO_3}$$

The original investigator, as well as Fleury and Lange,[2] were concerned chiefly with the analytical applications of the reaction. Fleury, Hérissey and Joly[3] made use of the reaction in studying the problem of the ring structure of the sugars, an application which was extensively and successfully investigated by Karrer and Pfaehler and by Jackson and Hudson.[4]

Although Malaprade made the observation that the reaction was much more rapid in acid than in neutral or basic solution, no measurements of the kinetics of the reaction have been made. The purpose of the present investigation was to study the kinetics under various conditions with the object of elucidating the mechanism of this oxidative cleavage in the particular case of 1,2-glycols.

Ethylene glycol and 2,3-butylene glycol consumed the theoretical amount of periodate almost instantaneously in acid solution. Pinacol, however, was found to oxidize at a conveniently measurable rate and was therefore the material used for the kinetic investigation.

Experimental

Standard aqueous solutions of periodic acid or sodium periodate and pinacol were mixed at 25.0° after adjusting the *p*H with 0.5 *N* solutions of sulfuric acid or sodium hydroxide. The course of the reaction was followed by withdrawing samples which were added to acidified potassium iodide solution, the liberated iodine then being titrated with sodium thiosulfate to the disappearance of the iodine color.

The hydrogen ion concentration of the reaction mixture was determined with a Beckmann *p*H meter. It did not vary appreciably during the course of the oxidation.

The Kinetics of the Reaction at Constant *p*H.—The dependence of the rate of the oxidation on the concentrations of the periodate and pinacol was first determined by measurements at a particular hydrogen ion concentration. The reaction was found to follow simple second order kinetics, the rate being directly proportional to the glycol and periodate concentrations as is illustrated by the results of these experiments summarized in Table I. The average deviation for the constants in any of the experiments was less than 5%.

TABLE I

THE RATE CONSTANTS FOR EXPERIMENTS WITH VARIOUS PINACOL AND PERIODATE CONCENTRATIONS AT A CONSTANT *p*H

*p*H, 5.5–5.6; temp., 25.0°

[Periodate][a]	[Pinacol][a]	k[b]
0.00550	0.02327	0.205
.00611	.03116	.207
.00916	.01871	.199
.01221	.01558	.202
.01221	.03513	.197
.01486	.02180	.197
.01960	.05270	.196

[a] Concentrations in moles per liter. [b] $dx/dt = k \times$ [Periodate][Pinacol]; the [Periodate] being the total periodate as determined by titration.

The Effect of Changing *p*H.—It was found that the value of k for the simple second order reaction varied greatly with the *p*H of the reaction mixture. Since this

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(1) Malaprade, *Bull. soc. chim.*, **43**, 683 (1928); *Compt. rend.*, **186**, 382 (1928).

(2) Fleury and Lange, *J. pharm. chim.*, **17**, 196, 313, 409 (1933).

(3) Fleury, Hérissey and Joly, *ibid.*, **20**, 149 (1934).

(4) Karrer and Pfaehler, *Helv. Chim. Acta*, **17**, 766 (1934); Jackson and Hudson, THIS JOURNAL, **59**, 994 (1937).

latter factor remained constant during any one particular experiment, however, the rate constants for each experiment readily were determined. The variation of these constants with the *p*H of the reaction mixture is illustrated in Fig. 1.

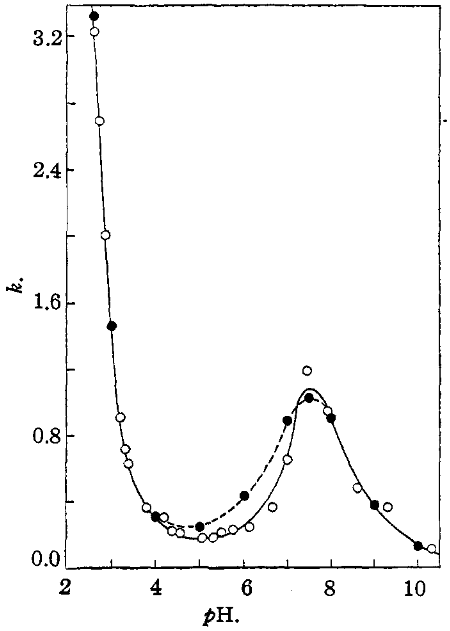

Fig. 1.—The second order rate constants plotted against the *p*H: ○, experimental values; ●, calculated values.

Comparison of Pinacol and Ethylene Glycol.—It has been reported[5] that pinacol and other highly substituted glycols react more readily with lead tetraacetate than those substituted to a lesser degree such as ethylene or 2,3-butylene glycols. This order of reactivity, however, holds for periodate oxidation only in alkaline solution. In acid the relative rates are reversed, since ethylene glycol and 2,3-butylene glycol react much more rapidly than pinacol. The results of experiments demonstrating this fact are summarized in Table II.

TABLE II

COMPARISON OF THE RATE OF OXIDATION OF ETHYLENE GLYCOL AND PINACOL IN ACID AND BASE

	*p*H 4		*p*H 9	
Time, min.	% ethylene glycol oxidized	% pinacol oxidized	% cthylene glycol oxidized	% pinacol oxidized
2	95	20	..	...
5	99	32	26	33
10	100	58	..	...
30	...	86	34	65
240	...	100	51	100

Discussion of Results

It was found that the variation of the simple second order rate constant, *k*, with the *p*H could be accounted for by assuming an uncatalyzed, an acid catalyzed and a base catalyzed reaction between the pinacol and a monovalent periodate ion. The acid reaction was directly proportional to the hydrogen ion concentration while the base reaction was proportional to the square root of the hydroxyl ion concentration.

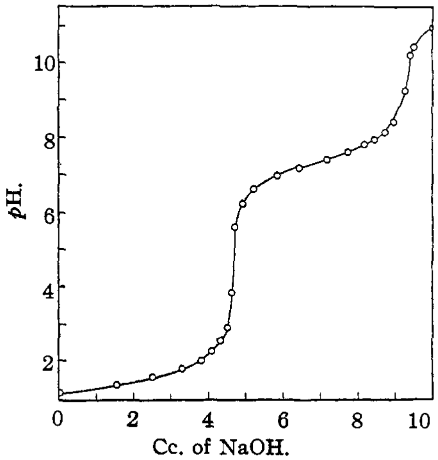

Fig. 2.—The titration of periodic acid (0.1 *N*) with sodium hydroxide (1.0 *N*).

The simple second order rate constant *k*, as calculated from the equation

$$dx/dt = k(A - x)(B - x)$$

where *A* is the total initial periodate concentration, *B* the initial pinacol concentration and *x* the amount of pinacol oxidized (equivalent to the decrease in the periodate titer), is thus a function of the *p*H of the solution which may be expressed as

$$k = k_0 + k_1[\mathrm{H}^+] + k_2[\mathrm{OH}^-]^{1/2}$$

By substituting the experimentally determined values for *k* at the various values for the *p*H and solving the resultant simultaneous equations, these constants were found to be $k_0 = 0.14$, $k_1 = 1.3 \times 10^3$ and $k_2 = 3.0 \times 10^3$.

The simple rate equation above also must be corrected for the fact that the rate is dependent on the monovalent periodate ion rather than the total periodate concentration. The ratio of these two concentrations as a function of the hydrogen ion concentration may be calculated from the dissociation constants of periodic acid as a mono- and dibasic acid.[6]

$$\mathrm{H_5IO_6} \underset{}{\overset{K_1}{\rightleftarrows}} \mathrm{H^+} + \mathrm{H_4IO_6^-} \overset{K_2}{\rightleftarrows} \mathrm{H^+} + \mathrm{H_3IO_6^{=}}$$

From these equilibria two independent equations

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[5] Criegee, Kraft and Rank, *Ann.*, **507**, 159 (1933).

[6] From the titration curve of periodic acid with sodium hydroxide (Fig. 2) the values for these two constants were determined as $K_1 = 0.11$ and $K_2 = 2.5 \times 10^{-8}$.

for the concentration of the monovalent ion may be derived.

$$[H_4IO_6^-] = K_1[H_5IO_6]/[H^+] \qquad (1)$$
$$[H_4IO_6^-] = [H^+][H_3IO_6^=]/K_2 \qquad (2)$$

Expressing the total periodate concentration as A, that of the monovalent ion as x, and that of the divalent ion as y these equations become

$$x = K_1(A - x - y)/[H^+] \qquad (1')$$
$$x = \frac{[H^+]y}{K_2} \text{ or } y = \frac{K_2x}{[H^+]} \qquad (2')$$

Substitution of (2′) in (1′) leads finally to equation (3) for the ratio of monovalent ion to total periodate as a function of hydrogen ion concentration.

$$x = \frac{K_1\left(A - x - \frac{K_2x}{[H^+]}\right)}{[H^+]}$$
$$[H^+]^2\frac{x}{A} = K_1[H^+] - K_1[H^+]\frac{x}{A} - K_1K_2\frac{x}{A}$$
$$\frac{x}{A} = \frac{K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2} \qquad (3)$$

Multiplication of the original rate equation by this factor leads to an equation for k as follows

$$k = \frac{(k_0 + k_1[H^+] + k_2[OH^-]^{1/2})K_1[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2} \qquad (4)$$

Values for k calculated from this expression, using the constants as noted, have been included in Fig. 1 for comparison with those determined experimentally.

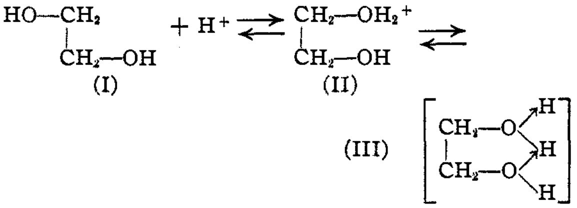
No simple and completely plausible explanation for the dependence of the rate on the square root of the hydroxyl ion concentration seems apparent although it may be accounted for on the basis of some such equilibrium as

$$\underset{\text{metaperiodate ion}}{2IO_4^- + OH^-} \rightleftharpoons \underset{\text{dimesoperiodate ion}}{HI_2O_9^=}$$

If now the rate of the reaction were dependent on the square root of such a dimesoperiodate ion value, the kinetics of the reaction would indeed agree with those observed.

The direct dependence of the rate on the hydrogen ion concentration is capable of two simple interpretations: (1) that the rate is dependent not on the periodate ion but on the undissociated periodic acid concentration, the effect of the hydrogen ion being to repress the ionization of the latter; or (2) that the reaction is a hydrogen ion catalyzed reaction between the glycol and periodate ion. The second concept is in better agreement with other observations on the reaction but the first cannot be rigorously excluded.

The reversal of the relative rates of oxidation of ethylene glycol and pinacol on shifting from an acidic to a basic reaction medium, as well as the fact that the order of glycol reactivity toward oxidation in acidic periodate is the reverse of the order with lead tetraacetate, may be due to the effect of hydrogen ion on the relative position of the two hydroxyl groups. In non-aqueous solvents (as for the lead tetraacetate oxidation) or in basic aqueous solution, the glycol probably exists largely as the free molecular species in which the negative character of the two hydroxyl groups may favor a configuration with these two groups on opposite sides of the molecule. On the addition of acid, however, the oxygen of an hydroxyl group may associate with a proton, resulting in a change in the configuration.



It is reasonable to suppose that there is at least considerably more glycol present as (II) or (III) in acid than in base and that (I) should, as an average, tend more toward a *trans* configuration for the hydroxyl groups while in (II) they would tend to be *cis*. Furthermore, the separate or combined effect of dipole moment, electrical charge and hydrogen bonding on promoting or inhibiting the *cis* configuration should be more pronounced the smaller the molecule, *i. e.*, ethylene glycol should tend to be more *trans* in base and *cis* in acid than pinacol in corresponding solutions. On the basis of these premises the experimental facts lead to the conclusion that the *cis* configuration is that more readily oxidized by periodate, a fact which has been experimentally established for lead tetraacetate.[5] Experiments to test the validity of this conclusion by comparison of glycols of known *cis* and *trans* configuration are under way. An alternative interpretation of the experimental facts, however, may be made simply on the basis of the relative base strength of the various glycols. If the acid-catalyzed reaction depends solely on the formation of the complex ion (II), regardless of configuration, then the oxidation of the glycol with the greater base strength (which must be ethylene glycol) would be more effectively catalyzed by acid.

The further experimental work may lead to a decision between these alternatives, although actual measurements of base strength may be required.

Summary

The oxidation of pinacol with aqueous solutions of sodium periodate has been found to obey simple bimolecular reaction kinetics. The variation of the rate with the *p*H of the reaction mixture may be interpreted accurately on the basis of reaction between pinacol and the monovalent periodate ion catalyzed by both acid and base.

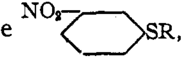
The reversal of the relative rates of oxidation of pinacol and ethylene glycol on shifting from an acidic to a basic reaction medium may be interpreted either on the basis of the configuration of the hydroxyl groups or on the relative base strengths of the two glycols.

URBANA, ILLINOIS RECEIVED AUGUST 13, 1938

[CONTRIBUTION FROM THE GRADUATE SCHOOL OF DUQUESNE UNIVERSITY]

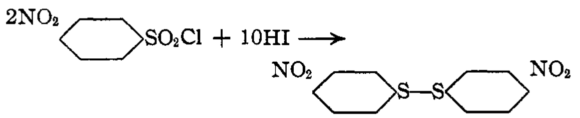
Some Unsymmetrical Aryl Sulfides[1]

BY NOEL E. FOSS,[2] JOHN J. STEHLE, HOWARD M. SHUSETT AND DAVID HADBURG

Zincke and Lenhart[3] and Foss, Dunning and Jenkins[4] have prepared a number of unsymmetrical aryl sulfides of the general type , where R may be various phenolic groups, and NO_2 may be in either the ortho or para position. The present investigation is concerned with the preparation of *m*-nitrophenyl sulfur phenols, , where R may be *p*-hydroxyphenyl, resorcyl, or *β*-hydroxynaphthyl.

The new nitro derivatives were chemically characterized by the preparation of their acetates and bromine substitution products. Two of the series were further identified by the synthesis of their benzyl and benzoyl derivatives, as well as by the reduction of the nitro compounds to the amino compounds.

The general scheme consists in preparing *m,m'*-dinitrodiphenyl disulfide by the following reaction



m-Nitrophenylsulfur chloride was prepared by allowing chlorine to react on the *m,m'*-dinitrodiphenyl disulfide by the method of Zincke and Lenhart[3] and subsequently condensed with the respective phenols. The reactions with phenol are represented by the scheme

$$NO_2C_6H_4SSC_6H_4NO_2 \xrightarrow{Cl_2} 2NO_2C_6H_4SCl$$

$$NO_2C_6H_4SCl + C_6H_5OH \longrightarrow NO_2C_6H_4SC_6H_4OH \xrightarrow{H_2} NH_2C_6H_4SC_6H_4OH$$

Experimental

m,m'-Dinitrodiphenyl disulfide was prepared by a modification of the method of Ekbom.[5] Two moles of the *m*-nitrobenzenesulfonyl chloride were reduced directly by the addition of the calculated amount of 45% hydriodic acid (ten moles). The reaction proceeded smoothly as evidenced by the precipitation of iodine crystals. After refluxing for several hours on the water-bath, the mixture was cooled and sodium bisulfite added until the iodine had been entirely reduced. The crude crystalline material was washed with water and recrystallized from hot acetone. Yellow crystals melting at 81–82° were obtained. The yield of pure product was about 80%.

Condensation of *m*-Nitrophenylsulfur Chloride with Phenols.—*m*-Nitrophenylsulfur chloride was prepared from *m,m'*-dinitrodiphenyl disulfide and condensed with the respective phenol according to the method described by Foss, Dunning and Jenkins.[4] In the case of the resorcinol derivative, 1,3-dihydroxy-2,6-*bis*-(3-nitrophenylthio)-benzene is formed principally unless the resorcinol is kept in excess during the reaction. The crude condensation products were recrystallized from sodium hydroxide and hydrochloric acid. The mononitro derivative also could be recrystallized from hot alcohol. These yellow compounds were insoluble in water, fairly soluble in hot alcohol, and very soluble in acetone and ether.

Acetylation.—The hydroxynitrosulfides and hydroxyaminosulfide were acetylated in the regular manner by refluxing with acetic anhydride and anhydrous sodium acetate. The pale yellow acetyl derivatives were very insoluble in cold water and slightly soluble in hot water,

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[1] Taken in part from theses presented by J. J. Stehle, H. M. Shusett, and D. Hadburg in partial fulfilment of the requirements for the degree of Master of Science in the Graduate School of Duquesne University.

[2] Present address: Burroughs Wellcome & Co. (U. S. A.), Inc., Tuckahoe, New York.

[3] Zincke and Lenhart, *Ann.*, **400**, 1 (1924).

[4] Foss, Dunning and Jenkins, THIS JOURNAL, **56**, 1978 (1934).

[5] Ekbom, *Ber.*, **24**, 335 (1891).