[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY, MIAMI UNIVERSITY]

The Periodate–Glycol Reaction. I. A Quantitative Study of Certain Chemical Equilibria and their Effects upon the Rate of Reaction

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Although the reaction of ethylene glycol with potassium periodate is kinetically of second order in very dilute solutions, the calculated rate constant markedly decreases with increasing concentrations of either potassium periodate or ethylene glycol. Three reaction mechanisms quantitatively explain the observed data. These are: (1) the formation of an intermediate equilibrium complex; (2) the formation of an inactive equilibrium complex; or (3) simultaneous reaction of the periodate ion with the glycol and decomposition of the complex to form the final products. Exact rate equations have been developed and the rate constants calculated for each of the above assumptions. Partial hydration of the monovalent periodate ion affects its reactivity and the rate constant values were corrected for this variation. The rate constants and the energies, free energies and entropies of activation for both the inactive complex and the intermediate complex mechanisms and the instability constants and the heats, free energies and entropies of decomposition of the complex have been determined.

The reaction of ethylene glycol and a periodate salt to form formaldehyde and an iodate salt is excellent for a mechanism study. It is quantitative, it proceeds at a measurable rate, and the amount of periodate may be readily determined. The reactions of periodates are quite specific to adjacent dihydroxy, diketo or diamino compounds.

Little is known of the nature of the reaction. Price and co-workers[2,3] in a study of the effects of the variation of *p*H upon the reaction rate showed that in the neutral and basic range the reaction rate decreased with increasing *p*H. It has been further shown[4] that the variation in reaction rate with *p*H is dependent upon the available concentration of monovalent periodate ion, and this in turn is dependent upon the hydrogen ion concentration of the reacting solution in accordance with the equation

$$H_5IO_6 \rightleftarrows H_4IO_6^- + H^+ \rightleftarrows H_3IO_6^- + 2H^+$$

A plot of the rate constants *versus* *p*H shows a broad maximum between *p*H 2.5 and 6.0, and in this range there is little change in rate with *p*H. Further work showed that low concentrations of salt have little effect upon the rate. The reaction therefore appears to be an ion-dipole type involving the monovalent periodate ion and the glycol molecule.

A cyclic ester intermediate has been proposed as the mechanism for this reaction by Criegee.[5] Price enlarged upon the proposal by suggesting an initial rearward approach of the periodate ion to the glycol molecule. Heidt, *et al.*,[6] correlated ionic radii and oxidation potentials for the periodate–glycol and lead tetraacetate–glycol reactions and predicted correctly the similar reactivity of sodium bismuthate and silver(III) ion toward glycols. Duke[7] has studied the variation of the reaction rate with varying high glycol concentrations. His results have been well correlated by assuming an intermediate coördination complex whose formation must precede that of the final products. It is this type of complex, according to Duke, which is responsible for specific oxidations.

The purpose of this work has been twofold: (1) to develop precise methods for the determination of the rate constants of this reaction and (2) to make a detailed study of the variation of reaction rate with varying glycol concentrations.

Experimental

Apparatus and Technique.—Precision methods have been developed so that the reaction rate constants may be determined with reproducibilities varying between ±0.2 and ±1.0%.

The most satisfactory method of analysis of periodate salts for these rate studies was the reaction of the periodate with potassium iodide in acid solution and titration of the liberated iodine with standard thiosulfate. Due to uncertainties in connection with the rate of removal of the periodate the neutral KI–As_2O_3 method was less reliable.

Since both the periodate and iodate are reduced to iodide, the accuracy of the determination of the amount of periodate reduced to iodate is less than the over-all accuracy of the titration by a factor of four. It was therefore necessary to extend the accuracy of the iodine–thiosulfate titration to its limit in order to achieve a final high accuracy.

A weight buret containing 0.02 *M* sodium thiosulfate was used for all titrations. Creeping of the solution was prevented by applying a coating of anti-wetting agent[8] both inside and outside the buret. The weight of standard solution was determined to the nearest milligram.

The precision pipet shown in Fig. 1 delivered 9.820 ml. at 25°. Before using the pipet it was first cleaned with a sulfuric acid–dichromate mixture, washed ten times with doubly distilled water, and dried by suction. The thermostated solution was drawn into the pipet to the top calibration mark D and then was released by opening the stopcock to the atmosphere. When the solution reached the mark at E, the stopcock was reversed to slow the rate of drainage, and then the flow was stopped exactly at the lower calibration mark F. The pipet was supported by a movable trapeze.

The reaction flask at A was designed so that separate solutions could be brought to temperature without premature mixing. Since aqueous solutions tend to creep when the container is very clean, the flask was coated with the Silicone preparation.[8] After applying the coating the flask was cleaned with dichromate cleaning solution and rinsed ten times with redistilled water. The grease was not attacked by periodic acid and had no discernible effect upon the rate of reaction. The flask was supported in the constant temperature bath by the buoyancy of the water holding it against the wire holder shown at B.

Since the half life of these reactions varied between 10 and 800 seconds, the accurate measurement of the time of

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(2) C. C. Price and H. Kroll, THIS JOURNAL, **60**, 2726 (1938).

(3) C. C. Price and M. Knell, *ibid.*, **64**, 552 (1942).

(4) B. Soldano, Ph.D. thesis, 1949, University of Wisconsin; *cf.*, Taylor and Soldano, Abstracts of the American Chemical Society meeting, Atlantic City, N. J., September 1949. Publication of this work has been delayed in order to interpret the data more accurately in the light of this paper.

(5) R. Criegee, *Sitzber. Ges. Beförder. ges. Naturw. Marburg*, **69**, 25 (1934).

(6) L. J. Heidt, E. K. Gladding and C. B. Purvis, *Paper Trade J.*, **121**, No. 9, 35 (1945).

(7) F. R. Duke, THIS JOURNAL, **69**, 3054 (1947).

(8) One gram of regular Silicone stopcock grease was dissolved in 50 ml. of petroleum ether (40–60°) and filtered. The coating was applied by rinsing the flask with this solution and thoroughly drying.

TABLE I

VARIATION OF THE RATE OF REACTION AND ACTIVATION ENERGY OF 0.0025 *M* KIO_4 WITH VARYING CONCENTRATIONS OF GLYCOL

KIO_4 moles/l.	Glycol moles/l.	k(0.00°) moles^{-1} l. sec.$^{-1}$	k(15.09°) moles^{-1} l. sec.$^{-1}$	k(25.04°) mole^{-1} l. sec.$^{-1}$	$E_{act.}$ 0–15° kcal./mole	$E_{act.}$ (0–25°) kcal./mole	$E_{act.}$ 15–25° kcal./mole
0.00250	0.00250	0.482	1.52	2.50	11.90	10.60	8.55
.00500	.00250	.404	1.41		12.95		
.00250	.00500	.401	1.40	2.40	12.95	11.55	9.25
.00250	.01250	.238		2.21		14.40	
.00250	.0250	.143	0.873	1.90	18.75	16.70	13.35
.00250	.0500	.0795	0.574	1.50	20.50	18.95	16.50
.00250	.0750	.0545		1.24		20.20	
.00250	.1000	.0415	0.346	1.08	21.95	21.10	19.55
.00250	.1250	.0337		0.92		21.35	
.00250	.200	.0213					

starting and stopping the reaction was most important. The reaction starting apparatus was made up of a wire flask holder bound between the halves of a split mop handle H. A centrifugal action mercury switch J on the handle controlled the starting of a "Time It" timer L. When it was desired to start a given reaction, the flask was slipped into the wire holder K. Rapid forward and backward rotation of the wire holder mixed the solutions and started the timer simultaneously. Each filling of the flask allows but one analysis.

The timing of the stopping of the reaction was achieved by rapidly emptying the contents of the flared end pipet P into flask A and simultaneously stopping the timer. This was done by applying air pressure to the mouthpiece N and pressing the lever above M. The pipet was coated with Silicone grease[8] so that 1 ml. of 0.5 *M* H_3PO_4, 1 ml. of 1 *M* KI and 15–20 ml. of water could be taken into the pipet and held without mixing. This procedure was necessary since upon mixing air saturated solutions of 1 *M* KI and 0.5 *M* H_3PO_4 oxidation is noticeable within a few minutes.

The temperature of the water-bath was held constant to the nearest 0.005°. It was measured with a Beckmann thermometer previously calibrated with a platinum resistance thermometer. The calibration was good to the nearest 0.02° or better.

Purification of Reagents.—Tap distilled water, previously allowed to settle to remove traces of oil, was redistilled first from dilute basic permanganate and then from dilute sulfuric acid. The glycol was Eastman Kodak Co. white label distilled twice under vacuum with the first and final portions being rejected. Potassium periodate was recrystallized four or more times from redistilled water before use.

The solutions of both the periodate and glycol were made up by weighing specific amounts of the purified substances. The *p*H of all experiments was in the range of 5 where an appreciable change in *p*H had a negligible effect upon the rate. In acid solutions the *p*H is very constant during the course of the reaction.[4] Since potassium periodate solutions decompose slowly in the presence of light, the solutions were prepared fresh every few days and were kept in a humidity closet in black painted Pyrex flasks.

Interpretation of Data

Although at any given concentration of periodate and glycol the rate data followed the second-order rate equation quite closely, the rate constants were not invariant. The trend of these values to increase as the reaction proceeded was noticeable at low temperatures and equal concentrations of periodate and glycol. Much more striking was the effect of increasing the glycol to periodate ratio. The rate constants decreased markedly as the glycol concentration was increased (Table I). An increase in activation energy paralleled the decrease in reaction rate constant.

In attempting to explain these phenomena many possibilities were considered. The only quantitative explanation was that of an equilibrium complex as proposed by Duke.[7] There are three postulated mechanisms,[9] involving a complex, which *quantitatively* explain these data.

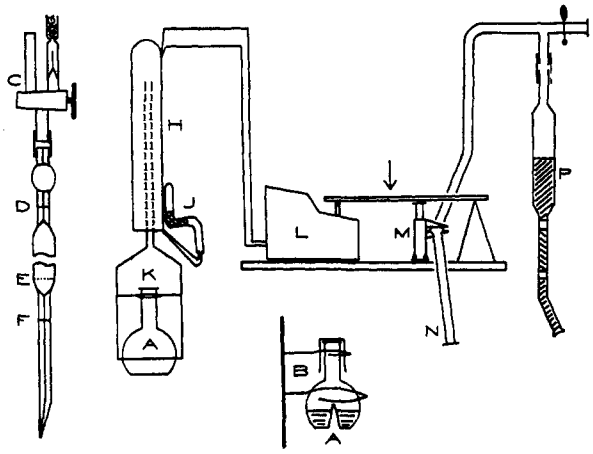


Fig. 1.—Apparatus for determination of reaction rates: A, two views of the reaction flask made from a 125-ml. Florence flask; B, flask cover and wire holder; C, three way stopcock with one capillary side arm protected by a glass wool filter; D and F, precision pipet showing calibration marks on 1.5 mm. capillary tubing; H, handle; J, centrifugal action mercury switch; K, heavy wire flask holder; L, "Time It" timer; M, pinchclamp which may be opened simultaneously with the stopping of the timer; N, mouthpiece for applying air pressure; P, silicone coated pipet containing the reaction stopping solutions.

1. Assume the formation of an inactive complex which is in equilibrium with the reactive periodate and glycol. The inactive complex is represented by Q and the remaining active periodate and glycol concentrations by *P* and *G*.

$$Q \text{ (inactive)} \rightleftharpoons P + G \qquad (1)$$

$$K = PG/Q \text{ or } KQ = PG \qquad (2)$$

(9) Two other mechanisms involving a complex were eliminated by the data of Table I. For one possibility there was postulated the presence of a trace of catalyst which forms an inactive equilibrium complex with the glycol. This concept may be used to explain all the data of Table I except those taken in the presence of excess periodate. In order to explain the latter quantitatively it must be assumed that both the periodate and the glycol inhibit the catalyst exactly to the same extent. This is very unlikely. For the other possibility it was proposed that one molecule of periodate and one of glycol combine with a molecule of a catalyst to form either an inactive or an intermediate complex. Since the data were very reproducible even with different batches of purified glycol and periodate, this would seem to preclude the possibility of a trace catalyst.

Since the rate of reaction is assumed to be proportional to the concentrations of P and G, then

$$dx/dt = k'PG = k'KQ \quad (3)$$

The values of P, G and Q are not known but may be evaluated by substituting the equalities $P = b - x - Q$ and $G = a - x - Q$ in equation (2); $a - x$ and $b - x$ represent the over-all glycol and periodate concentrations at any time t. After solving for Q by the use of the quadratic equation and eliminating a physically unreal solution the rate expression becomes

$$\frac{dx}{dt} = \frac{k'K}{2}\left[K + a + b - 2x - \sqrt{(K + a - b)^2 + 4K(b - x)}\right] \quad (4)$$

After integration

$$k' = \frac{2.303}{tK}\log\frac{1 + \frac{2b}{K + a - b} - \sqrt{1 + \frac{4Kb}{(K + a - b)^2}}}{1 + \frac{2(b - x)}{K + a - b} - \sqrt{1 + \frac{4K(b - x)}{(K + a - b)^2}}} \quad (5)$$

$$+ \frac{2.303}{t(a - b)}\log\frac{\left[\frac{a - b - K}{a - b + K} + \sqrt{1 + \frac{4K(b - x)}{(K + a - b)^2}}\right]\left[\sqrt{1 + \frac{4Kb}{(K + a - b)^2}} - 1\right]}{\left[\frac{a - b - K}{a - b + K} + \sqrt{1 + \frac{4Kb}{(K + a - b)^2}}\right]\left[\sqrt{1 + \frac{4K\ (b - x)}{(K + a - b)^2}} - 1\right]}$$

For the special case when the concentrations of the reactants are equal the rate expression is somewhat simpler. Let $P = G$ and $a = b$ then

$$\frac{dx}{dt} = k'K[a - x + K/2 - \sqrt{K(a - x) + K^2/4}] \quad (6)$$

Upon integration

$$k' = \frac{2}{tK}\left[2.303\log\frac{\sqrt{1 + (4a/K)} - 1}{\sqrt{1 + \frac{4(a - x)}{K}} - 1} + \frac{1}{\sqrt{1 + \frac{4(a - x)}{K}} - 1} - \frac{1}{\sqrt{1 + \frac{4a}{K}} - 1}\right] \quad (7)$$

2. Assume an active and intermediate complex which is in equilibrium with the inactive periodate and glycol. This was the proposal of Duke.[7] The derivation postulating the inactive complex may with but a slight modification be applied to this mechanism and the one to follow.

$$P + G(\text{inactive}) \rightleftharpoons Q(\text{active}) \longrightarrow \text{Products} \quad (8)$$

then

$$dx/dt = k''Q \quad (9)$$

But with equation (3)

$$k'' = Kk' \quad (10)$$

3. Assume that both mechanisms 1 and 2 take place simultaneously. Let m be the fraction of the reaction taking place by reaction of P with G and n the fraction resulting from the decomposition of Q. Then

$$dx/dt = mk'PG + nk''Q = (mk'K + nk'')Q \quad (11)$$

where $m + n = 1$.

If either mechanism 1 or 2 is correct, only the rate constants calculated for the real mechanism have meaning. For the combination mechanism both sets of rate constants are real, but additional variables, m and n, have been introduced. For any of these possibilities the equilibrium constants calculated for the complex should be valid.

Expressions (5), (7), (10) and (11) were derived without approximation. If certain approximations are made, a simpler but less satisfactory expression is obtained. From equation (2), *et seq.*, $KQ = (a - x - Q)(b - x) - Q(a - x - Q)$. Since a is large and Q is small, $Q(a - b/2)$ may be substituted for $Q(a - x - Q)$ and $a - x$ for $a - x - Q$.

$$\frac{dx}{dt} = \frac{k'K}{K + a - b/2}(a - x)(b - x) \quad (12)$$

$$k = \frac{k'K}{K + a - b/2} \simeq \frac{k'K}{K + a} \quad (13)$$

Duke and Bremer[10] have derived the approximate expression in terms of the first-order equation and the intermediate complex postulation.

The determination of K and either k' or k'' from the exact equation is very tedious and time consuming since these constants can be evaluated only by approximation methods. Equation (13) was used to determine the first approximate values of K and k'.

Values of k', k'' and K from the exact equations are recorded in Table II. The constancy of these values is an excellent indication of the correctness of the original postulations. At these dilute concentrations there appears to be no tendency for any other than a 1:1 complex between the periodate and the glycol.

TABLE II

VALUES FOR THE TRUE REACTION RATE CONSTANTS ASSUMING THE FORMATION OF AN INACTIVE COMPLEX (k') AND AN INTERMEDIATE COMPLEX (k'')

	0.00°, K = 0.0053		15.09°, K = 0.0250		25.04°, K = 0.066	
Glycol[a] mole/l.	k' mole^{-1} l. sec.$^{-1}$	k'' sec.$^{-1}$	k' mole^{-1} l. sec.$^{-1}$	k'' sec.$^{-1}$	k' mole^{-1} l. sec.$^{-1}$	k'' sec.$^{-1}$
0.00250	0.814[b]	0.00431	1.747[b]	0.0437	2.65[b]	0.175
.00500	.824	.00437	1.748	.0437	2.64	.174
.01250	.820	.00435			2.66	.176
.0250	.813	.00431	1.747	.0437	2.64	.174
.0500	.824	.00437	1.718	.0430	2.64	.174
.0750	.825	.00437			2.65	.175
.1000	.819	.00434	1.728	.0432	2.67	.176
.1250	.826	.00438			2.66	.176
.200	.831	.00440				

[a] The KIO_4 for all experiments was 0.00250 M. The solutions for all experiments were made up at 25°. At 15 and 0° correction for change in volume is included in the calculations of the rate constants. [b] These columns represent a total of about 27 experiments at 0°, 21 at 15°, and 26 at 25°.

The k' value at any given temperature may be assumed to be the value of the second-order rate constant extrapolated to infinite dilution. On the other hand the k'' value is the second-order rate constant extrapolated to infinite glycol or periodate concentration. This trend is readily observable in Table I. A similar observation can be made in regard to the activation energies.

In Table III there are listed the activation energies calculated by assuming either the inactive complex or the intermediate complex.

(10) F. R. Duke and R. F. Bremer, *Iowa State Coll. J. Sci.*, **25**, 527 (1951).

TABLE III

HEAT OF FORMATION OF THE COMPLEX AND ACTIVATION ENERGIES CALCULATED FROM TABLE II

	Inactive complex		Intermediate complex		The complex	
T., °C.	k', l. mole^{-1} sec.$^{-1}$	$E_{act.}$, kcal./ mole	k'', sec.$^{-1}$	$E_{act.}$, kcal./ mole	$K_{instab.}$, mole/l.	$\Delta H_{decomp.}$, kcal./mole
0.00	0.820	7.8[a]	0.00435	23.9[a]	0.0053	16.1[a]
15.09	1.74	7.6[b]	.0435	23.9[b]	.0250	16.3[b]
25.04	2.65	7.2[c]	.175	23.9[c]	.066	16.7[c]

[a] Calcd. from 0 to 15°, av. dev. ± 0.1 kcal. [b] Calcd. from 0 to 25°, av. dev. ± 0.07 kcal. [c] Calcd. from 15 to 25°, av. dev. ± 0.17 kcal.

reactive form. A similar reasoning can of course be applied upon assuming either of the other possibilities. The data of Crouthamel, *et al.*, can be used to correct the values of the rate constants of Table III by using the equation

$$k'_{cor.} = k' \frac{K_D + 1}{K_D} \qquad (16)$$

where K_D is the instability constant for the hydration equilibrium. These corrected values along with other constants calculated from them are listed in Table IV. It should be noted that the $E_{act.}$ values of Table III have been replaced with

TABLE IV

SUMMARY OF VARIOUS CONSTANTS

	Inactive complex				Intermediate complex				The complex			
T., °C.	k', l. mole^{-1} sec.$^{-1}$	$\Delta H_{act.}$, kcal./ mole	$\Delta F_{act.}$, kcal./ mole	$\Delta S_{act.}$, cal. deg.$^{-1}$ mole^{-1}	k'', sec.$^{-1}$	$\Delta H_{act.}$, kcal./ mole	$\Delta F_{act.}$, kcal./ mole	$\Delta S_{act.}$, cal. deg.$^{-1}$ mole^{-1}	$K_{instab.}$, mole/l.	$\Delta H_{decomp.}$, kcal./ mole	$\Delta F_{decomp.}$, kcal./ mole	$\Delta S_{decomp.}$, cal. deg.$^{-1}$ mole^{-1}
0.00	0.928[a,b]	6.4[c]	15.99	−35	0.00435[b]	23.3[c]	18.90	16.1	0.00468[a,b]	16.9[c]	2.91	51
15.09	1.82[a,b]	6.4[d]	16.51	−35	.0435[b]	23.3[d]	18.65	16.1	.0239[a,b]	16.9[d]	2.14	51
25.04	2.72[a,b]	6.3[e]	16.87	−36	.175[b]	23.3[e]	18.49	16.1	.0644[a,b]	17.0[e]	1.62	52

[a] The K_D values used to calculate these values from the rate constants of Table IV are: at 0°, K_D = 7.6; at 15°, K_D = 21.7; at 25°, K_D = 40. [b] Av. dev. ± 0.5%. [c] Av. dev. ± 0.1 kcal.; calcd. from 0 to 15°. [d] Av. dev. ± 0.07 kcal.; calcd. from 0 to 25°. [e] Av. dev. ± 0.17 kcal.; calcd. from 15 to 25°.

The variation of activation energy with glycol concentration and with temperature (Table I) can be correlated mathematically. The values of 7.2–7.8 and 23.9 kcal. (Table III) represent the limiting energies; intermediate values are obtained by adding to the smaller values (or subtracting from the larger value) a fraction of the heat of decomposition of the complex (16.1–16.7 kcal.). A rigorous derivation of the change of activation energy with glycol concentration gives a very complicated function. A relatively simple relationship is obtained upon using the approximate equation (13) and assuming an inactive complex.

$$E - E_0 = \frac{2.3R}{1/T_2 - 1/T_1} \log \frac{(K_1 + a_0 - b/2)(K_2 + a - b/2)}{(K_2 + a_0 - b/2)(K_1 + a - b/2)} \qquad (14)$$

If E_0 is the lower limiting activation energy, then $a_0 - b/2$ may be set equal to 0. The observed activation energy also varies with temperature since there is a variation in concentration of Q resulting from the alteration of K. Equation (14) used with two sets of temperatures will predict this variation.

In Table III it is seen that the heat of decomposition of the complex and the activation energy from k' are not constant with temperature. This lack of constancy is indicative of another equilibrium. Crouthamel, Hayes and Martin[11] using spectrophotometric techniques have shown that the hydrated periodate ion is in equilibrium with an ion of lesser hydration[12] as follows

$$2H_2O + IO_4^- \rightleftarrows H_4IO_6^- \quad \Delta H = -10.9 \text{ kcal.} \qquad (15)$$

Either the hydrated ion, the unhydrated ion or both together must be the reactive species. For the following discussion it is assumed that IO_4^- is the slight alteration by $\Delta H_{act.}$ values. The previously varying values are now constant within experimental error. Thus the postulation of the effect of the hydration equilibria upon the rate is given firm support.

The lack of constancy of the activation energies for the inactive complex mechanism (Table III) and the constancy of these values for the intermediate complex mechanism result from the method of calculation of these values. Since in the first case the K and k' values are directly dependent upon the erroneous periodate values, both the energy of activation and the heat of formation of the complex are in error. In the second case the k'' value is the product of K and k'. The error in k' balances the error in K so that the observed k'' and its activation energy values are correct.

Discussion of Mechanism

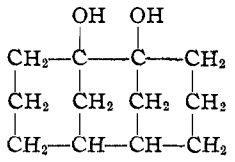
Although it is not possible from the data in this paper to describe completely the mechanism of the reaction under consideration, certain possibilities will be considered.

The glycol molecule is not a simple one so there are at least two routes through which the periodate ion may attack it. There may be either a forward attack upon the hydroxyls or a rearward attack upon the carbons to form an intermediate. Both possibilities have been proposed. A frontal attack upon the carbons is another less likely possibility. For the following discussion the two types of frontal attack are indistinguishable and will therefore be considered together. Using the concept of the inactive complex it is possible that the complex may be formed by a forward attack and the products by a rearward attack or *vice versa*.

The synthesis of *cis*- and/or *trans*-tricyclo[5,3,-1,1^{2,6}]dodecane-1,2-diol from 3,3′-dihydroxybiphenyl is being attempted. Since the adjacent hydroxyls are both on bridgehead carbons, there is no possibility of a rearward approach to the mole-

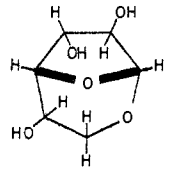
(11) C. E. Crouthamel, A. M. Hayes and D. S. Martin, THIS JOURNAL, **73**, 82 (1951).

(12) The data of Crouthamel, *et al.*, do not eliminate from consideration these equilibria: $H_2O + IO_4^- \rightleftarrows H_2IO_5^-$ and $H_2O + H_2IO_5^- \rightleftarrows H_4IO_6^-$. However to avoid complication only the IO_4^- and $H_4IO_6^-$ ions will be considered.

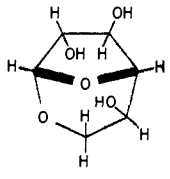


cule. By determining if this compound can react to form (1) the products and no complex, (2) the complex and no products, (3) both the complex and products, or (4) neither the complex nor products, a choice of the above possible routes of reaction can then be made. Further if conditions (1) or (2) were demonstrated, this would be an excellent proof of the inactive complex mechanism since it is obvious that both the complex and the products could not be formed through the same contact point of the glycol molecule. Condition (4) would strongly support the intermediate complex postulation, but condition (3) could be interpreted by either the intermediate complex or the combination mechanism.

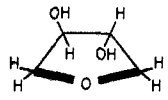
A favoring of the rearward approach mechanism comes from an interpretation of the work of Dimler, *et al.*,[13,14] and Klosterman and Smith.[15] Dimler, *et al.*, have prepared β-1,6-anhydro-D-glucofuranose (I) and α-1,6-anhydro-D-galactofuranose (II) and have shown that these compounds do not react with periodic acid or sodium periodate. Klosterman and Smith have shown that L-threitan (III) and erythritan (IV) do react with these reagents.



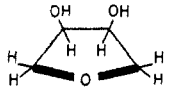
I



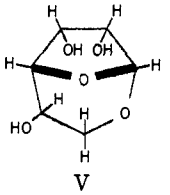
II



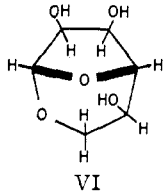
III



IV



V



VI

These apparently anomalous observations can be very reasonably explained upon assuming a rearward approach mechanism. There are two conditions which undoubtedly contribute to the inactivity of I and II. First, since the bridge structure makes the furanose ring more rigid than normal, the glycol carbons of this ring should resist attack by any reactant which might alter their relative positions in space. This has been discussed by Dimler, *et al.* The second is the effect of the ring oxygens. The data of Klosterman and Smith show that III and probably IV react more slowly with periodates than ethylene glycol. But, *cis*- and *trans*-1,2-cyclohexanediol *both* react more rapidly than glycol.[3] Although the latter compounds are not directly comparable to the former due to the different size of rings, it is at least indicated that the ring oxygens inhibit the reactivity of III and IV. Since these are saturated molecules, the primary effect of the ring oxygen should be a field effect to repel the negative periodate ion. This could cause a noticeable change in rate only if the periodate ion makes a rearward attack upon the glycol carbons. Further, for I and II Fisher–Hirschfelder models could not be made with all rings closed. In the actual molecule there must be an appreciable puckering of the furanose ring. The puckering must result in a protrusion of the ring oxygen and this can only magnify the protection of the glycol carbons by this oxygen. The effectiveness of the protection may be enhanced by hydration. The purely steric effect of the ring puckering cannot be sufficient to halt a rearward attack of the periodate ion. Pinacol appears to be more hindered than I or II, but it does react slowly.[3]

It has been proposed that the variation of reactivity of various glycols with periodates is due to the variation of the extent of separation of the hydroxyls; that is, the greater the separation the less the reactivity. For example, this explanation has been used with *cis*- and *trans*-cyclohexanediol.[3] However in I and II the puckering of the rings does not push the hydroxyls farther apart than in III. The only effect is to restrict to some degree the range of movement of these groups. The inactivity of I and II is therefore not explained by the hydroxyl separation theory.

If the above generalizations are correct, it is possible to make certain predictions. (1) α-1,6-Anhydro-D-mannofuranose (V), suggested by Dimler, *et al.*, should react with periodates since a rearward approach to the glycol carbons can be made. (2) β-1,6-Anhydro-D-talofuranose (VI) with the adjacent *cis*-hydroxyls on the other side of the ring and the 5-hydroxyl facing the glycol carbons should react very slowly or not at all with periodates. (3) The activation energies for the reactions of III and IV should be greater and the rates less than for the corresponding *cis*- and *trans*-cyclopentanediols. (4) If the inactive complex proposal is correct, I and II although not decomposed by periodates should form coördination complexes with the periodate ion.

And finally, it should be noted that a not insignificant contribution of this paper is to demonstrate the need for greater accuracy in determining rates of reactions. With data of higher experimental error conclusions as were drawn in this paper would have little significance.

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