492. *Periodate Oxidation. Part III.* The Mechanism of Oxidation of Cyclic Glycols.*

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The kinetics of the periodate oxidation of methyl 4 : 6-*O*-ethylidene-α-D-glucoside and the -α-D-mannoside have been studied in aqueous solution at several values of pH and temperature. The reaction appears to proceed through an intermediate cyclic complex, the formation of which is rate-determining.

IN a study of the periodate oxidation of ethylene glycol, Duke[1] found the equation $k' = A[\mathrm{G}]/(1+B[\mathrm{G}])$ to be obeyed, where k' is the first-order rate constant with respect to periodate, [G] is the concentration of glycol, and A and B are constants. This was explained in terms of a rapid reversible formation from glycol and periodate of an intermediate complex which slowly decomposed:

$$(\mathrm{CH_2{\cdot}OH})_2 + \text{periodate} \overset{K}{\rightleftharpoons} \text{intermediate} \xrightarrow[\text{slow}]{k} \text{products}$$

This requires $1/k' = (1/kK[\mathrm{G}]) + 1/k$, where k is the first-order rate constant for the decomposition of the intermediate, and K is the equilibrium constant for its formation.

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* Part II, preceding paper.

[1] Duke, *J. Amer. Chem. Soc.*, 1947, **69**, 3054.

From a plot of $1/k'$ against $1/[G]$, k and K were calculated. We have extended this type of analysis to methyl 4 : 6-*O*-ethylidene-α-D-glucoside and the -α-D-mannoside. The results suggest that the reactions of these compounds with periodate follow a different course from the oxidation of acyclic glycols.[1-8] With a large excess of methyl 4 : 6-*O*-ethylidene-α-D-glucoside at pH 4·06 and 25°, the reaction was of first-order with respect to periodate, and the reciprocal plot of $1/k'$ against $1/[G]_\infty$ was a straight line passing through the origin ($[G]_\infty$ is the concentration of glucoside at the end of the reaction). For the same compound at pH 4·06 and 0°, the first-order graphs showed a small non-linear reduction in periodate concentration at the beginning of the reaction, followed by a straight-line relation. From the first-order rate constants calculated from the slopes of the linear sections of the graphs, the plot of $1/k'$ against $1/[G]_\infty$ was again a straight line through the origin (Fig. 1). The oxidations of methyl 4 : 6-*O*-ethylidene-α-D-mannoside at pH 4·06 and 25° and 0° were similar, with the initial non-linear parts of the graphs more pronounced at 0°. At both temperatures the reciprocal plots were straight lines passing through the origin. For the same compound at pH 6·93 or 10·10 and 0°, initially-curved first-order rate curves were found, and the reciprocal plots were straight lines making very small intercepts on the $1/k'$ axis (Fig. 2). Using Duke's method of analysis, we calculated values for k of 7×10^{-7} and 9×10^{-7} sec.$^{-1}$, and for K of 8 and 5 l. mole^{-1}, for pH 6·93 and 10·10, respectively. These values can only be approximate, because of the small intercept involved. If a mechanism:

FIG. 1. *Plots of* $1/k'$ *against* $1/[G]_\infty$ *for methyl* 4 : 6-O-*ethylidene-α-*D-*glucoside at* pH 4·06. *Temp.*: ○, 0°. □, 25°.

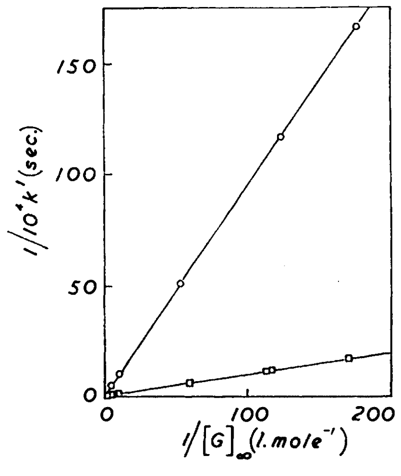
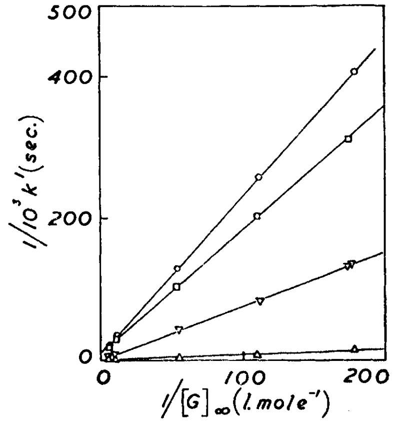


FIG. 2. *Plots of* $1/k'$ *against* $1/[G]_\infty$ *for methyl* 4 : 6-O-*ethylidene-α-*D-*mannoside.*



○, pH 10·10; 0°. ▽, pH 4·06; 0°.
□, pH 6·93; 0°. △, pH 4·06; 25°.

$$\text{periodate} + \text{glycol} \longrightarrow \text{intermediate} \longrightarrow \text{products}$$

is to account for the oxidation of the two methyl 4 : 6-*O*-ethylidene-α-D-glycosides discussed here, then the rate-determining step cannot be the decomposition of the intermediate, as for ethylene glycol. The best explanation of the observed kinetics would seem to be that the formation of the intermediate has become rate-determining or, less likely, the rates of formation and decomposition are of the same order. Confirmation of these theories is

[2] Duke and Bulgrin, *J. Amer. Chem. Soc.*, 1954, **76**, 3803.
[3] Taylor, *ibid.*, 1953, **75**, 3912.
[4] Buist and Bunton, *J.*, 1954, 1406.
[5] Buist, Bunton, and Miles, *J.*, 1957, 4567.
[6] *Idem*, *J.*, 1957, 4575.
[7] Buist and Bunton, *J.*, 1957, 4580.
[8] Zuman, Sicher, Krupička, and Svoboda, *Coll. Czech. Chem. Comm.*, 1958, **23**, 1237.

difficult. Ultraviolet spectrophotometric measurements were made of the optical densities of solutions of periodate in the presence of glycols, but, because many of the reactions studied were complete only after several hours or days, considerable reduction of the optical density occurred owing to decomposition of periodate in ultraviolet light. Whilst this method is suitable for the quantitative study of fast periodate oxidations,[6] it is unreliable for the determination of the rate constants of these slower reactions. It was also difficult to interpret the change of pH occurring when the reactions were carried out in unbuffered solutions, since methyl 4 : 6-*O*-ethylidene-α-D-glucoside and -α-D-mannoside are not neutral but produce considerable pH change when added to aqueous solutions in the absence of periodate. If reactions of this type do occur *via* the formation of an intermediate, it is extremely likely that the intermediate would have an optical rotation different from that of either the reactant or the products. Jones [9] followed the oxidation of methyl 4 : 6-*O*-*iso*propylidene-α-D-glucoside polarimetrically and found a reduction in specific rotation for 65 minutes, followed by a slow increase to a constant value in 20 hours, corresponding to a reduction of one mole of periodate per mole of glucoside. This can be explained in terms of the formation of an intermediate, followed by its decay to the products, but an equally effective explanation would be that the product mutarotated. Similar results have now been found by following the oxidation of methyl 4 : 6-*O*-benzylidene-α-D-guloside polarimetrically.

Very little work has been reported on the mechanism of periodate oxidation of other cyclic glycols. Results, very similar to those found for methyl 4 : 6-*O*-ethylidene-α-D-glucoside, have been reported by Bulgrin [10,11] for *cis*- and *trans*-*cyclo*pentane-1 : 2-diol and some methyl homologues. In a study of the oxidation of cellulose by periodate, Nevell [12] found that the rate of consumption of periodate was relatively high at first, but then diminished and became almost constant; this effect was much greater at 0° than at 20°. Nevell suggested that the initial fast reaction might be identified with the formation of an intermediate complex, which then broke down into the oxidation products more slowly than it was formed. However, this oxidation is a heterogeneous reaction, and irrelevant to consideration of the present homogeneous reactions.

EXPERIMENTAL

Materials.—Sodium metaperiodate, $NaIO_4$, used in solutions of pH $\leqslant 7$, was the B.D.H. "Analytical Reagent," recrystallised from hot water. The salt, $K_4I_2O_9,9H_2O$, used for reactions above pH 7, was prepared by recrystallising potassium metaperiodate from hot concentrated aqueous potassium hydroxide, and then from water.

Methyl 4 : 6-*O*-ethylidene-α-D-glucoside, prepared from methyl α-D-glucopyranoside and 1 : 1-dimethoxyethane,[13] had m. p. 76—77°, $[\alpha]_D^{19}$ +111·3° (*c* 1·176 in water). Methyl 4 : 6-*O*-ethylidene-α-D-mannoside was prepared from methyl α-D-mannopyranoside and paraldehyde.[14,15] After four recrystallisations from carbon tetrachloride, the compound had m. p. 116·5—117·5°, $[\alpha]_D^{19}$ +76·5° (*c* 1·418 in chloroform).

All experiments were carried out in aqueous buffer solutions of low ionic strength. The solutions used were sodium acetate and acetic acid with ionic strength 0·036 for pH 4·06, potassium dihydrogen phosphate and sodium hydroxide with ionic strength 0·05 for pH 6·93, and ammonium acetate and ammonia with ionic strength 0·02 for pH 10·10. Solutions more acid than pH 4 were not used, because they usually caused hydrolysis of groups attached to the sugars. The pH of each buffer solution was measured with a Cambridge pH meter, which was standardised against potassium hydrogen phthalate (0·05M), pH 4·01 at 0°, and sodium tetraborate (0·01M), pH 9·46 at 0°.

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[9] Jones, *Canad. J. Chem.*, 1956, **34**, 840.
[10] Bulgrin, *J. Phys. Chem.*, 1957, **61**, 702.
[11] Bulgrin and Dahlgren, *J. Amer. Chem. Soc.*, 1958, **80**, 3883.
[12] Nevell, *Shirley Inst. Mem.*, 1957, **30**, 35.
[13] Honeyman and Stening, *J.*, 1957, 3316.
[14] Honeyman and Morgan, *J.*, 1954, 744.
[15] Aspinall and Zweifel, *J.*, 1957, 2271.

Kinetic Measurements.—Various known amounts of each glycol, sufficient to give solutions ranging from approximately 0·5M to 0·005M, were used with the appropriate buffer and enough periodate to give an approximately 0·001M-solution. A solution prepared in exactly the same manner, containing all the reagents but omitting the compound to be oxidised, served as blank. At suitable times, samples of the reaction solution and the blank were withdrawn and analysed for periodate by Müller and Friedberger's method.[16] The samples were pipetted into saturated aqueous sodium hydrogen carbonate (*ca.* 10 ml.) containing potassium iodide (*ca.* 1 g.). The mixture was left for about 15 min. in the dark before the free iodine was titrated with standard sodium arsenite solution (0·00125—0·01N), sodium starch glycollate indicator (2 ml. of 1% solution) being used. All reactions were carried out in the dark.[17]

A typical example shows the first-order rate constants, *k'*, for methyl 4 : 6-*O*-ethylidene-α-D-glucoside at pH 4·06, ionic strength 0·036, temperature 0°, and initial concentration of periodate, $[\text{Periodate}]_0$, 0·0009085M.

$[G]_\infty$ (mole l.$^{-1}$)	0·1951	0·09718	0·01868	0·008146	0·005663
$1/[G]_\infty$ (l. mole^{-1})	5·125	10·29	53·53	122·8	176·6
$10^6k'$ (sec.$^{-1}$)	22·05	9·867	1·955	0·8527	0·5971
$1/10^4k'$ (sec.)	4·535	10·13	51·15	117·3	167·5

In this case the plot of $1/k'$ against $1/[G]_\infty$ is a straight line through the origin.

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[16] Müller and Friedberger, *Ber.*, 1902, **35**, 2652.

[17] Head, *Nature*, 1950, **165**, 236.