149. *The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part V.** cycloHexane-1 : 2-diols.*

By G. J. Buist, C. A. Bunton, and J. H. Miles.

The kinetic form of the periodate oxidation of *cis*- and *trans-cyclo*hexane-1 : 2-diol shows that an intermediate complex is formed. The equilibrium constant is greater for the *trans*-isomer, but the rate constant of breakdown of the *cis*-complex is much the larger. The values of equilibrium and rate constants are compared with those of the butane-2 : 3-diols.
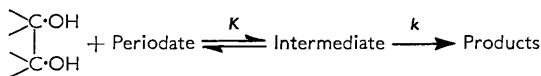
THE first kinetic study of the periodate oxidation of the *cyclo*hexane-1 : 2-diols showed that, at 25°, and with pH <8 in water, the rate decreased with increasing pH. The rate of oxidation of the *cis*-diol was *ca.* 30 times that of the *trans*-diol, and it was suggested that this was because the hydroxyl groups of the *cis*- but not the *trans*-diol were in convenient positions for formation of a cyclic intermediate with the periodic acid.[1]

Our aim was to relate the periodate oxidations of the *cyclo*hexane-1 : 2-diols to those of other 1 : 2-diols, and to obtain evidence for formation of intermediate complexes between diols and periodate. We found that, as for other diols, addition of either diol to an aqueous solution of periodate, at 0°, gave an immediate decrease in pH. This suggests that intermediates are formed rapidly, and decompose slowly to the reaction products, and that they are stronger acids than periodic acid.[2]

Kinetics.—The methods were those used in earlier work.[2] With diol in large excess over periodate a plot of the reciprocal of k' (the first-order rate constant with respect to periodate) against the reciprocal of the diol concentration [G] was a straight line, with a positive intercept. This is the kinetic form observed first for the oxidation of ethanediol,[3] and subsequently for the oxidations of a number of 1 : 2-diols.[4,5] It is usually expressed as:

$$1/k' = 1/kK[\text{G}] + 1/k \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k and K are constants in the reaction sequence:

$$\begin{array}{c} >\!\text{C·OH} \\ | \\ >\!\text{C·OH} \end{array} + \text{Periodate} \underset{}{\overset{K}{\rightleftharpoons}} \text{Intermediate} \xrightarrow{k} \text{Products}$$

(Periodate represents the totality of periodic acid and its ions.)

Observation of this kinetic form (eqn. 1) does not, of itself, prove that the reactants and intermediate complex are in equilibrium, nor does it necessarily give true values of k and K [although the value of k so determined is approximately correct (Part IV)]. As a test for equilibrium we compared the slopes of the " reciprocal plots " (eqn. 1) with the reciprocals of the limiting second-order constants, k_s. If the reactant concentrations are reduced sufficiently the concentration of the intermediate complex tends to zero and the kinetic order to second. In the limit when both [G] and [Periodate] → 0, $k_s = kK$ if the system is in equilibrium.[5] Then the equilibrium constant $K = k_f/k_b$ (k_f and k_b are the rate constants for the reversible reaction between diol and periodate to form the intermediate complex [6]). Reactants and the intermediate are in equilibrium when the rate of decomposition back to reactants is much greater than its rate of decomposition to products, *i.e.*, when $k_b \gg k$.

Our kinetic results are summarised in the Experimental section, where we list values of

* Part IV, *J.*, 1957, 4580.

[1] Price and Knell, *J. Amer. Chem. Soc.*, 1942, **64**, 552.
[2] Buist and Bunton, *J.*, 1954, 1406.
[3] Duke, *J. Amer. Chem. Soc.*, 1947, **69**, 3054.
[4] Duke and Bulgrin, *ibid.*, 1954, **76**, 3903.
[5] Buist, Bunton, and Miles, *J.*, 1957, 4567.
[6] *Idem, ibid.*, 1957, 4574.

" *k* " and " *K*," the apparent rate and equilibrium constants respectively, as determined from the " reciprocal plots." From comparisons between the values of k_s and " kK " we conclude that the reactants and the intermediate complex of the *cis*-diol are in equilibrium at pH > 7. This test could not be applied to the *trans*-diol, because the equilibrium constant is too high in alkaline solution (cf. Part IV). However, we assume that, as for other diols, reactants and intermediate complex are in equilibrium in alkaline solution.

From these rate and equilibrium constants we can calculate the rate constant k_1 for breakdown of the single negatively charged intermediate complex (cf. ref. 2). The value of the equilibrium constant K at pH 9 is that of the equilibrium constant K'' between the periodate dianion, $H_3IO_6^{2-}$, the diol, and the dinegatively charged intermediate complex. This is because the dissociation constants are such that both periodate and intermediate exist largely as dianions in solutions of pH 9.[2,5]

Discussion.—The chair form of *cyclo*hexane is energetically preferred to the boat form.[7] The *cis*-diol in the chair form can have its hydroxyl groups in the axial-equatorial conformations, but the *trans*-diol can have these groups in either the axial-axial or the equatorial-equatorial conformation. The *trans*-diol exists preferentially in the equatorial-equatorial conformation both in water[8] and in non-hydroxylic solvents;[9] the energy barrier for interconversion is probably not large (cf. the interconversion of the conformations of *trans*-1 : 2-dichloro*cyclo*hexane[10]). The calculated inter-oxygen distance is *ca.* 2·86 Å for both the *cis*-diol and the *trans*-diol in the equatorial-equatorial conformation.[11] It is close to the value of 2·73 Å for the distance[12] between adjacent oxygen atoms in the ion $H_3IO_6^{2-}$. Thus the hydroxyl-oxygen atoms of both the *cis*- and the *trans*-*cyclo*hexanediol
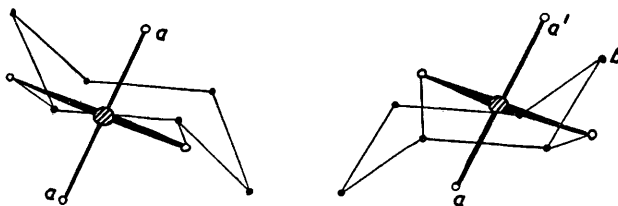

Left: *Intermediate complex of the* trans-diol *(equatorial-equatorial conformation)*; *bonds joining oxygen atoms " a " to iodine are in the plane of the paper.*
Right: *Intermediate complex of the* cis-diol; *bonds joining oxygen atoms " a," " a' " to iodine are out of the plane of the paper, " a' " being away from the observor.*
In both models, two of the oxygen atoms joined to iodine are omitted.   ⊘ *Iodine.*   ○ *Oxygen.*   ● *Carbon.*

should be able to co-ordinate with the octahedral iodine atom to form a strain-free puckered ring[5] with only slight changes in their original interatomic distances. The situation is therefore different from that for the formation of cyclic ketals,[11] where the ring formed will be nearly planar, as it probably will be for borate complexes. In these cases ring formation occurs most readily with the *cis*-diol.

The arguments do not necessarily apply to the formation of neutral or mononegatively charged periodate complexes. These may exist in a dehydrated form with a penta-co-ordinated iodine atom,[2] *e.g.*, (A). Such a dehydrated complex could have a structure more akin to that of a borate complex. There is slight experimental evidence for this because the apparent value of K in acid solution is greater for the *cis*- than for the *trans*-diol, in contrast to their relative values at higher pH. However, we must also consider steric repulsions between atoms in the octahedral intermediate complexes. Suggested structures of the dinegatively
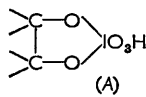
[7] Hassell, *Quart. Rev.*, 1953, **7**, 221.
[8] Whiffen, *Chem. and Ind.*, 1956, 964.
[9] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[10] Tulinskie, Giacomo, and Smyth, *ibid.*, 1953, **75**, 3552.
[11] Angyal and Macdonald, *J.*, 1952, 686.
[12] Helmholtz, *J. Amer. Chem. Soc.*, 1937, **59**, 2036.

charged forms of the intermediate complex are shown in the Figure (this representation is similar to that used earlier for the structures of intermediate complexes from periodate and open-chain diols[5]). There are no large internal repulsions in the dinegatively charged intermediate complex from the *trans-cyclo*hexanediol, but there is interference between one of the oxygen atoms attached to the iodine atom and one of the carbon atoms (marked *b*), or the hydrogen atoms attached to it, in the dinegatively charged intermediate complex of the *cis*-diol. Distortion of the *cyclo*hexane ring into a flattened half-chair structure would reduce this interference, but it would introduce further strains in both the *cyclo*hexane and the periodate ring of the complex, and the actual geometry of the complex will depend upon the relative importance of these internal strains.

We can now compare the structures of the intermediate complexes of the *cyclo*hexane-1 : 2-diols with those of the butane-2 : 3-diols.[5] The intermediate complex of the *meso*-butane-2 : 3-diol has one methyl group in a " hindered " position, with interference between this group and one of the oxygen atoms of the periodate. The structure of this complex is therefore similar to that of the *cis-cyclo*hexane-1 : 2-diol, and the equilibrium constant K'' for formation of the dinegatively charged complex is very similar for both these diols (Table 1). Thus the favourable orientation of the hydroxyl groups of *cis-cyclo*hexane-1 : 2-diol, which should facilitate complex formation, is outweighed by internal repulsions in the complex. These repulsions may be less severe for the complex of the open-chain *meso*-butane-2 : 3-diol than for the more rigid fused-ring system of the complex from *cis-cyclo*hexane-1 : 2-diol.

TABLE 1. *Rate and equilibrium constants.*

Diol	$10^4 k_1$ (sec.$^{-1}$)	K'' (mole^{-1} l.)	$10^2 K'_1$ (mole l.$^{-1}$)	$10^7 K'_2$ (mole l.$^{-1}$)
*cis-cyclo*Hexane	3300	400	0·83	0·48
trans- ,,	165	1000	3·11	0·85
(−)-Butane-2 : 3-	308	8000	3·4	0·42
meso- ,,	182	373	2·6	0·50

The structure of the dinegatively charged intermediate complex of *trans-cyclo*hexane-1 : 2-diol is similar to that of (−)-butane-2 : 3-diol, and there is no large interference between the atoms of the *cyclo*hexane ring and the oxygen atoms of the periodate (see Figure). The equilibrium constant K'' is less for *trans-cyclo*hexane-1 : 2-diol than for (−)-butane-2 : 3-diol. This may be due to disruption of some intramolecular hydrogen-bonding[9] during complex formation, or to the distortion of the *cyclo*hexane ring which must occur when the distance between the hydroxyl-oxygen atoms is reduced (by *ca.* 0·1 Å) in forming the octahedral complex. (The latter effect will be much smaller than for formation of a cyclic ketal where, because of formation of a nearly planar ring, the reduction of the inter-hydroxyl distance will be *ca.* 0·5 Å.[11])

Thus we have the situation that, in this particular case, the equilibrium constant for complex formation at high pH is greater for the *trans-* than for the *cis*-diol (Table 1). This comes about because of the arrangement of oxygen atoms around the octahedral iodine atom in the dinegatively charged intermediate complex. It may not occur in the neutral or mononegatively charged intermediate complexes, because these may exist in dehydrated forms with only five oxygen atoms around the iodine atom. We are not able to test this point, because meaningful equilibrium constants can be determined only for the dinegatively charged complexes. However, the " apparent " equilibrium constants (from the " reciprocal plots ") in acid solution are greater for the *cis-cyclo*hexane-1 : 2-diol, a reversal of the situation in alkaline solution (see Experimental section). Because the neutral and the mononegatively charged complexes may exist in either hydrated or de-hydrated forms comparisons between their equilibrium constants might be misleading, even if we could measure them.

There is no evidence, from this work, that the greater stability of the *trans-* than

of the *cis*-complex (relative to the reactants) will extend to more rigid ring systems, or to co-ordinating agents other than periodate.

We have calculated ionisation constants for the complexes. They are given with those for the intermediate complexes of the butane-2 : 3-diols [5] in Table 1. The values, except for that of the first ionisation constant K'_1, of the complex of *cis-cyclo*hexane-1 : 2-diol, are little affected by changes in structure or configuration.

The rate of breakdown, to products, of the mononegatively charged complex of *cis-cyclo*hexane-1 : 2-diol is ~20 times that for the *trans*-complex. This factor is much larger than that between the complexes of the butane-2 : 3-diols.[5]

TABLE 2. *Second-order rate constants for oxidation of the* cyclo*hexane-1 : 2-diols at* 0°; [reactants] *ca.* 10^{-3}M.

pH	0·98	4·30	7·30	8·80	9·86
cis-	0·42	2·8	6·9	1·1 *	0·98 *
trans-	0·033	0·58	0·41	0·007 *	—

* These values are kK from the slopes of the " reciprocal plots."

The high reactivity of the mononegatively charged complex of the *cis*-diol may be caused by internal steric strains, which are released by breakdown, but it is possible that the proportion of the mononegatively charged intermediate which exists as a reactive dehydrated form [2] may be greater for the *cis*- than for the *trans*-diol.

These results show that the faster oxidation of the *cis*- than of the *trans*-diol is due, not to ease of intermediate-complex formation, but to the rapid breakdown of this complex. The rate of reactions with glycol-splitting reagents is sometimes used for determination of configuration. However, it is often difficult to interpret the kinetic effects of structural changes for multi-stage reactions, and this is particularly so for periodate oxidations because here the rate has a complicated dependence upon equilibrium and rate constants. The generalisation that a *threo*-isomer is more reactive towards periodate than an *erythro*-isomer seems to be well-founded experimentally [13,4,5] and is supported by what we know of the detailed mechanism, but the generalisation that a *cis-cyclo*hexanediol is more reactive than the *trans*-diol is much less reliable as a structural test. Exceptions to it are well known,[14] and it is therefore desirable to consider the details of the reaction mechanism, and the non-bonding interactions which may occur in any intermediate complexes of the reaction wherever such a test is applied.

EXPERIMENTAL

Materials.—The diols were prepared from *cyclo*hexene which had been purified by treatment with sodium hydrogen sulphite and fractionated under nitrogen; it had b. p. 82°, n_D^{25} 1·444.

The *trans*-diol was prepared *via* the chlorohydrin and recrystallised from ethyl acetate; it had m. p. 101—103°.[15]

The *cis*-diol was prepared by oxidation of *cyclo*hexene with *tert.*-butyl hydroperoxide, catalysed by osmium tetroxide. It was recrystallised from ethyl acetate and had m. p. 97—99°.[16]

Kinetics.—Addition of one drop of a 6M-solution of the *trans*-diol in water to 0·1M-periodate at pH 7·07 gave an immediate fall in pH of 0·32 unit. A similar experiment with the *cis*-diol gave a pH change from 9·03 to 8·92.

Runs, at 0°, were followed with diol in excess, or with reagents in comparable, low concentrations. The iodometric methods were those described earlier.[2]

Because it may be of interest to compare the rates of oxidation in regions for which we did not observe formation of an intermediate complex in equilibrium with reactants, we report rate constants for all the kinetic runs.

[13] Zuman, Sicher, Krupicka, and Svoboda, *Nature*, 1956, **178**, 1407.
[14] Levesley, Waters, and Wright, *J.*, 1956, 840; Criegee, Hoger, Huber, Kruch, Marktscheffel, and Schellenberger, *Annalen*, 1956, **599**, 81.
[15] Coleman and Johnson, *Org. Synth.*, Coll. Vol. I, p. 151.
[16] Milas and Sussman, *J. Amer. Chem. Soc.*, 1937, **59**, 2347.

Rate constants have the units of sec.$^{-1}$ for first-order and sec.$^{-1}$ mole^{-1} l. for second-order reactions. Concentrations are those at the beginning of a run. The value of k at pH 4 was taken as k_1 (cf. ref. 2), and K'_1 and K'_2 (the first and second ionisation constants of the intermediate complex) were calculated by the use of equations (11a) and (10b) of ref. 2. The value of the equilibrium constant K in alkaline solution is taken as K''. The values of k give reliable values of the rate constant for breakdown of the complex even when the system is not in equilibrium (cf. Part IV).

cis-*Diol*. Results were:

pH 0·98, ionic strength 0·130 mole l.$^{-1}$.

10^2[diol] (M)	0·980	1·265	1·83	2·04	3·49	9·10
$10^3k'$	7·68	11·5	13·6	16·0	17·9	33·2

The reciprocal plot gives $10^2k = 3·3$, and $K = 40$ mole^{-1} l. The limiting second-order rate constant $k_s = 0·42$ (from runs with 10^3[diol] $= 2·64$M, and 10^3[periodate] $= 0·731$M, having $k_2 = 0·423$, and 10^4[diol] $= 1·56$M, and 10^3[periodate] $= 0·700$M, having $k_2 = 0·417$). The value of k_s does not agree with that of kK (from the reciprocal plot), so equilibrium conditions do not hold.

pH 4·30, ionic strength 0·021 mole l.$^{-1}$.

10^2[dioll] (M)	0·850	1·15	1·30	1·56	2·53	3·53
$10^2k'$	3·95	5·37	5·18	6·72	8·86	13·0

$k = 0·33$, and $K = 15$ mole^{-1} l.

$k_s \approx 2·8$ (from runs with 10^3[diol] $= 1·60$M, and 10^3[periodate] $= 0·64$M, having $k_2 = 3·2$, and 10^3[diol] $= 1·26$M, and 10^3[periodate] $= 0·62$M, having $k_2 = 2·4$). Equilibrium conditions do not hold.

pH 7·30, ionic strength 0·123 mole l.$^{-1}$.

10^2[diol] (M)	0·850	1·12	1·37	2·15	3·34	8·44
$10^2k'$	4·09	4·95	5·76	6·99	7·53	8·49

$k = 0·11$ and $K = 72$ mole^{-1} l.

$k_s \approx 7$ (from runs with 10^3[diol] $= 2·61$M, and 10^3[periodate] $= 0·648$M, having $k_2 = 6·22$, and 10^3[diol] $= 1·03$M, and 10^3[periodate] $= 0·678$M, having $k_2 = 7·67$). The value of k_s agrees with the value of 8·0 for kK, and we conclude that reactants and complex are in equilibrium. We assume, by analogy with oxidation of other diols, that equilibrium will be maintained at higher pH.

pH 8·80, ionic strength 0·100 mole l.$^{-1}$.

10^2[diol] (M)	0·730	0·972	1·817	3·04	9·38
$10^3k'$	2·00	2·19	2·36	2·36	2·71

From calculation by the method of least squares we estimate $10^3k = 2·7$, and $K = 410$ mole^{-1} l.

pH 9·86, ionic strength 0·120 mole l.$^{-1}$.

10^2[diol] (M)	1·11	1·74	2·51	9·31
$10^4k'$	2·37	2·56	2·68	2·92

$10^4k = 3·0$, and $K \sim 330$ mole^{-1} l.

trans-*Diol*. Results were:

pH 0·98, ionic strength 0·130 mole l.$^{-1}$.

10^2[diol] (M)	0·637	1·161	3·11	7·78
$10^3k'$	0·474	0·769	1·60	2·66

$10^3k = 4·76$, and $K = 16·8$ mole^{-1} l.

$k_s = 3·3$ (from runs with 10^3[diol] $= 1·94$M, and 10^3[periodate] $= 1·07$M, having $10^2k_2 = 3·22$, and 10^3[diol] $= 2·02$M, and 10^3[periodate] $= 0·679$M, having $10^2k_2 = 3·46$). Equilibrium conditions do not hold.

pH 4·30, ionic strength 0·021 mole l.$^{-1}$.

10^2[diol] (M)	1·03	1·32	1·85	2·39	3·33	9·07	9·48
$10^2k'$	0·745	0·909	1·04	1·07	1·18	1·46	1·41

$10^2k = 1·65$, and $K = 83$ mole^{-1} l.

$k_s = 0.58$ (from runs with with $10^3[\text{diol}] = 1.44\text{M}$, and $10^3[\text{periodate}] = 0.739\text{M}$, having $k_2 = 0.59$, and $10^3[\text{diol}] = 2.11\text{M}$, and $10^3[\text{periodate}] = 0.736\text{M}$, having $k_2 = 0.56$). Equilibrium conditions do not hold.

pH 7·30, ionic strength 0·124 mole l.$^{-1}$.

$10^2[\text{diol}]$ (M)	0·947	1·16	1·70	3·88	9·43
$10^3 k'$	2·56	2·71	2·76	2·88	3·03

$$10^3 k = 3.06, \quad K \approx 580 \text{ mole}^{-1} \text{ l.}$$

Because of the high value of the equilibrium constant we could not reach sufficiently low reactant concentrations for observation of a limiting second-order rate constant, k_s.

pH 8·80, ionic strength 0·100 mole l.$^{-1}$.

$10^2[\text{diol}]$ (M)	0·554	1·01	1·57	9·96
$10^5 k'$	6·40	6·44	6·86	7·06

$$10^5 k = 7.2, \quad K \approx 1000 \text{ mole}^{-1} \text{ l.}$$

We assume that this value of K gives a reliable value for K'', because we know from observations on the open-chain diols [3,6] that reactants and intermediate complex are in equilibrium at pH 9.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
    UNIVERSITY COLLEGE, GOWER STREET, LONDON, W.C.1.   [*Received, September 4th, 1958.*]