420. *Some Isotope Effects in Oxidations of Cyclohexanol.*

By J. S. LITTLER.

The kinetics of oxidation of cyclohexanol and 1-deuteriocyclohexanol by mercury(II), thallium(III), manganese(III), and manganese(VII) in acid solution have been studied. Comparative measurements have also been made with deuterium oxide as solvent.

THE rates of oxidation of secondary alcohols by vanadium(V),[1] chromium(VI),[2] cerium(IV),[3] and bromine[4] are reduced when the CH·OH group is replaced by CD·OH; the rate of oxidation by bromine, but not by vanadium or chromium, is also reduced when the OH group is replaced by OD by using deuterium oxide as solvent. Recent work[5] on the oxidation of cyclohexanone has shown that mercury(II) and thallium(III) perchlorates are powerful two-electron oxidants, and that manganese(III) sulphate is a powerful one-electron

---

[1] Littler and Waters, *J.*, 1959, 4046.
[2] Westheimer und Nicolaides, *J. Amer. Chem. Soc.*, 1949, **71**, 25.
[3] Littler, *J.*, 1959, 4135.
[4] Swain, Wiles, and Bader, *J. Amer. Chem. Soc.*, 1961, **83**, 1945.
[5] Littler, *J.*, 1962, 827.

oxidant.[6] It seemed interesting to investigate whether or not oxidations of cyclohexanol by these oxidants and by manganese(VII) proceed by mechanisms similar to those previously postulated, by making measurements of the CH/CD and OH/OD isotope effects.

RESULTS

The rate of oxidation of cyclohexanol by thallium(III) was of the first order in thallium(III) for the first 30% of the reaction. At the acidities used, the reduction of the thallium solutions by water was relatively unimportant, but at 3·2M-[H$^+$] this reaction prevented measurements being made. Table 1 shows the isotope effects and that the reaction was of the first order in cyclohexanol; it was retarded by an increase in the salt concentration and accelerated by an increase of acidity.

TABLE 1.

Oxidation by 0·005M-thallic perchlorate at 49·3° ± 0·1°.

[Alcohol] (M)	Solvent	[H_3O^+] (M)	[Salt] (M)	$10^4k'$ (sec.$^{-1}$) †	$10^4k'$/[Alcohol] (l. mole^{-1} sec.$^{-1}$)	
0·173	H_2O	0·276	0·30	0·59	3·44	Mean 3·1
0·327	H_2O	0·276	0·30	0·95	2·9	
0·327	H_2O	0·276	0·30	1·0	3·05	
0·256 *	H_2O	0·276	0·30	0·136	0·53	Mean 0·56
0·256 *	H_2O	0·276	0·30	0·15	0·59	
0·256	D_2O	0·276	0·30	1·35	5·3	
0·256	D_2O	0·276	0·30	1·30	5·1	
0·310	H_2O	0·276	0·622	0·63	2·0	
0·310	H_2O	0·598	0·622	0·98	3·16	
0·0	H_2O	3·2	3·2	*ca.* 2·1	—	
0·310	H_2O	3·2	3·2	*ca.* 2·1	—	

* With 1-deuteriocyclohexanol. $k_H/k_D = 5{\cdot}5$; $k_{D_2O}/k_{H_2O} = 1{\cdot}7$.

† The rate of reduction of Tl^{+3} by water, accounting for $k' = \sim 0{\cdot}02 \times 10^{-4}$ sec.$^{-1}$, has not been subtracted from these values.

TABLE 2.

Oxidation by mercuric perchlorate at 49·9°.

(*a*) Order in oxidant and effect of salt and acid. [Cyclohexanol] = 0·173M.

[Hg^{+2}] (M)	[H_3O^+] (M)	[Salt] (M)	$10^4k'$ (sec.$^{-1}$)
0·05	2·3	2·5	3·58
0·02	0·92	0·96	2·75
0·01	0·46	0·48	2·27
0·005	0·23	0·24	2·17
0·005	0·23	0·56	2·31
0·005	0·55	0·56	2·26
0·005	3·8	3·8	1·65

(*b*) Order in alcohol. [Hg^{+2}] = 0·01M; [H_3O^+] = 0·46M; [Salt] = 0·48M.

[Alcohol] (M)	$10^{-4}k'$ (sec.$^{-1}$)	$10^4k'$/[Alcohol] (l. mole^{-1} sec.$^{-1}$)
0·069	0·825	12·0
0·1034	1·62	15·6
0·173	2·27	13·1
0·31	3·8	12·3
	Mean	13·1
0·224 *	0·714	3·19
0·223 *	0·81	3·48
	Mean	3·33

(*c*) Solvent isotope effect. [Hg^{+2}] = 0·005M; [H_3O^+] = 0·23M; [Salt] = 0·24M.

[Alcohol] (M)	Sol- vent	$10^4k'$ (sec.$^{-1}$)	$10^4k'$/[Alcohol] (l. mole^{-1} sec.$^{-1}$)
0·173	H_2O	2·13	12·3
0·228	H_2O	2·74	12·0
0·331	H_2O	4·09	12·4
0·256	D_2O	4·8	18·8
0·256	D_2O	4·79	18·7
0·240	D_2O	4·36	18·2

Mean value of $k'_{D_2O}/k'_{H_2O} = 1{\cdot}5$.

* With 1-deuteriocyclohexanol. $k'_H/k'_D = 3{\cdot}9$.

The rate of oxidation of cyclohexanol by mercury(II) was of the first order in mercury(II) for the first 30—50% of the reaction. Oxidation by the mercury(I) formed was negligible under the conditions used. Table 2 shows the isotope effects and that the reaction was of the first order with respect to oxidant and to alcohol. The reaction was not significantly affected by changes in acid or salt concentration.

The oxidation of cyclohexanol by manganese(III) sulphate was of the first order in manganese(III) for at least 50% of the reaction. Table 3 shows the isotope effect and that the

---

[6] Littler, *J.*, 1962, 832.

reaction was independent of acid concentration; the variation of the rate with the concentration of cyclohexanol indicates that an alcohol–manganese(III) complex was formed.

The rate of oxidation of cyclohexanol by potassium permanganate, in the presence of sufficient hydrogen sulphate to prevent the precipitation of manganese dioxide in the early stages of the reaction, was of the first order in manganese(VII) for 50% of the reaction, or until the formation of a precipitate if this occurred earlier. Table 4 shows the isotope effects and an acid-dependence of the form $k = a + b[H^+]$.

TABLE 3.

Oxidation by manganic sulphate.

[Alcohol]	$[H_3O^+]$	$[HSO_4^-]$	$10^4k'$ (sec.$^{-1}$)		[Alcohol]	$[H_3O^+]$	$[HSO_4^-]$	$10^4k'$ (sec.$^{-1}$)	
(M)	(M)	(M)	obs.	calc.	(M)	(M)	(M)	obs.	calc.
0·069	2·52	4·71	4·8	—	0·1325	4·77	4·79	6·48	6·6
0·069	3·88	4·76	4·9	—	0·199	4·77	4·79	7·95	7·86
0·069	4·77	4·79	4·6	4·7	0·118 *	4·77	4·79	4·0	3·92
0·0345	4·77	4·79	3·02	2·96	0·0785 *	4·77	4·79	3·12	3·16

* With 1-deuteriocyclohexanol.

Calc. values are obtained from the equation:

$$-d/dt[\mathrm{Mn^{III}}] = kK[\mathrm{Mn^{III}}][\mathrm{Alcohol}]/\{1 + K[\mathrm{Alcohol}]\} = k'[\mathrm{Mn^{III}}]$$

where K = stability constant of an alcohol–manganese(III) complex, of value 1·03; k = rate constant for the redox decomposition of the complex, of value 1·18 × 10^{-4} sec.$^{-1}$; $k_H/k_D = 1·6$.

TABLE 4.

Oxidation by 9·05 × 10^{-4}M-potassium permanganate.

(*a*) Dependence on concentration of acid; [Alcohol] = 0·0345M; temp. 24·9°.

$[H_2SO_4]$	$[NaHSO_4]$	$[H_3O^+]$	$10^{-4}k'$ (sec.$^{-1}$)	
(M)	(M)	(M)	obs.	calc.
1·125	0·0	1·125	21·8	21·5
0·9	0·217	0·924	18·6	18·2
0·679	0·434	0·70	14·5	14·7
0·45	0·651	0·494	11·2	11·4
0·225	0·868	0·2945	8·7	8·2
0·0	1·085	0·1363	5·66	5·67
0·225	0·0	0·225	6·0	7·1

Calc. values are obtained from the equation $k' = 3·5 + 16·0[H^+]$ (10^{-4} sec.$^{-1}$).

Values of $[H_3O^+]$ are calculated on the assumption that the hydrolysis constant of the hydrogen sulphate ion is 2·0 × 10^{-2}.

(*b*) Dependence on concentration of alcohol; $[NaHSO_4]$ = 1·08M; no additional acid; temp. 27·5°.

[Alcohol] (M)	$10^4k'$ (sec.$^{-1}$)	$10^4k'$/[Alcohol] (l. mole^{-1} sec.$^{-1}$)
0·0173	4·42	256
0·0345	8·1	235
0·0518	12·6	243
0·069	19·8	287
	Mean	254
0·052 *	4·08	78·4
0·052 *	4·15	79·8
	Mean	79·1

* With 1-deuteriocyclohexanol. k'_H/k'_D = 3·2.

(*c*) Isotope effect at high acidity; $[H_2SO_4]$ = 1·125M; no additional salt; temp. 27·5°.

[Alcohol] (M)	$10^4k'$ (sec.$^{-1}$)	$10^4k'$/[Alcohol] (mole^{-1} sec.$^{-1}$)
0·0173	11·7	676
0·0173	12·15	703
0·0262 *	7·2	275
0·0262 *	7·7	294

$$k'_H/k'_D = 2·42.$$

* With 1-deuteriocyclohexanol.

These values are consistent with k_H'/k'_D = 2·23 for the acid-catalysed reaction, and about 4·4 for the acid-independent reaction.

(*d*) Solvent effect; $[H_2SO_4]$ = 0·45M; no other salt added; temp. 10·3°.

[Alcohol] (M)	Solvent	$10^{-4}k'$ (sec.$^{-1}$)	$10^{-4}k'$/[Alcohol] (l. mole^{-1} sec.$^{-1}$)
0·311	H_2O	18·6	59·8
0·243	D_2O	25·1	104

$$k'_{D_2O}/k'_{H_2O} = 1·74.$$

The solvent isotope effect is consistent with a value of k'_{D_2O}/k'_{H_2O} for the acid-catalysed reaction of 2·37, if the acid-independent reaction rate is independent of the solvent and the relative rates of the reactions are the same as at 25°.

DISCUSSION

The kinetics of the oxidation of cyclohexanol by thallium(III) and mercury(II) indicate that the transition states for the reactions contain one molecule of cyclohexanol and one of oxidant. The acid-dependence of the oxidation by thallium can be explained by the partial hydrolysis: $Tl^{3+}aq + H_2O \overset{K}{\rightleftharpoons} TlOH^{2+} + H_3O^+$, where Tl^{3+} is the only important oxidant, and K is of the order of 0·14 at 50° and 0·6M-salt concentration ($K = 0{\cdot}073$ at 25° and 3M-salt concentration [7]). The rate of oxidation by Hg^{2+} is approximately three times that by Tl^{3+}. In both reactions the primary isotope effect indicates that the C–H(C–D) bond of the alcohol is stretched in the transition state, and the absence of retardation when deuterium oxide is used as solvent indicates that the O–H bond is not stretched or broken in the transition state.

The large solvent isotope effects in both these reactions are most unusual, for in reactions where there is no acid-catalysis a small retardation is usually observed in deuterium oxide.[8] In the oxidation by Tl^{3+} this isotope effect might be due to the expected change of the hydrolysis constant of Tl^{3+} resulting from the change of solvent (this explanation cannot be applied to the oxidation by Hg^{2+} which is hydrolysed to a negligible extent at the acidities used [9]). However, it has been shown that the hydrolysis constant of Tl^{3+} is identical in water and in deuterium oxide.[10] This is surprising as uncharged acids of this strength are weaker in deuterium oxide than in water by a factor of ~2·5.[11] It appears that this generalisation cannot be extended to acids of the type $M^{3+}aq$, as it also fails with the iron $Fe^{3+}aq$.[12]

The ferric–ferrous electron exchange also has an abnormally large solvent isotope effect ($k_{H_2O}/k_{D_2O} = 2$) and this effect has been explained by the greater stability of highly charged cations in water than in deuterium oxide.[13] Both the abnormal hydrolysis constant of Tl^{3+} in deuterium oxide, and the solvent isotope effects in the present reactions, can be explained similarly, as they involve dispersal of a large positive charge, a process that will be favoured in deuterium oxide.

Previous studies of the oxidations of secondary alcohols by two-electron oxidants have led to the postulation of the following mechanisms: (1) A direct hydride transfer to the oxidant.[14] (2) A base-catalysed elimination within an ester or complex.[15] (3) An intramolecular elimination within an ester or complex.[16] (4) A bimolecular reaction involving a cyclic transition state with both proton and hydride transfer.[17,18] (5) An acyclic hydride transfer of the O–H hydrogen atom to the oxidant.[4] Of these, the last has never been proved to occur and appears inherently improbable. Mechanisms (3) and (4) are also unlikely for the present reactions; both Tl^{3+} and Hg^{2+} are small ions which tend to form linear complexes L–M–L, so that a cyclic transition state is sterically improbable. It is also unlikely that any water molecules co-ordinated to these ions could act as proton or hydride ion acceptors in a cyclic transition state. Mechanism (4) would also be expected to be retarded by the replacement of OH by OD.[19] The present reactions show no such isotope effect.

The isotope effects in oxidation by bromine [$k(CH)/k(CD) = 2{\cdot}9$; $k(OH)/k(OD) = 1{\cdot}5$ at 50°] have been interpreted as evidence that the reaction proceeds by mechanism (1) (with rate-determining loss of the proton to the solvent).[4] If this is so, by a process of

---

[7] Gilks and Waind, *Discuss. Faraday Soc.*, 1960, **29**, 102.

[8] Wiberg, *Chem. Rev.*, 1955, **55**, 713.

[9] Anderegg, Schwarzenbach, Padmoyo, and Borg, *Helv. Chim. Acta*, 1958, **41**, 988; Sillén, *Quart. Rev.*, 1959, **13**, 146.

[10] Rogers and Waind, *Trans. Faraday Soc.*, 1961, **57**, 1360.

[11] Rule and La Mer, *J. Amer. Chem. Soc.*, 1938, **60**, 1974; Bell, " The Proton in Chemistry," Cornell Univ. Press, New York, 1959.

[12] Hudis and Dodson, *J. Amer. Chem. Soc.*, 1956, **78**, 911.

[13] Sutin, Rowley, and Dodson, *J. Phys. Chem.*, 1961, **65**, 1248; Bigeleisen, *J. Chem. Phys.*, 1960, **32**, 1583.

[14] Bartlett and McCollum, *J. Amer. Chem. Soc.*, 1956, **78**, 1441.

[15] Westheimer, *Chem. Rev.*, 1949, **45**, 419.

[16] Kwart and Francis, *J. Amer. Chem. Soc.*, 1959, **81**, 2116.

[17] Barker, Overend, and Rees, *Chem. and Ind.*, 1961, 558.

[18] Roček, *Coll. Czech. Chem. Comm.*, 1960, **25**, 1052.

[19] Brownell, Leo, Chang, and Westheimer, *J. Amer. Chem. Soc.*, 1960, **82**, 406.

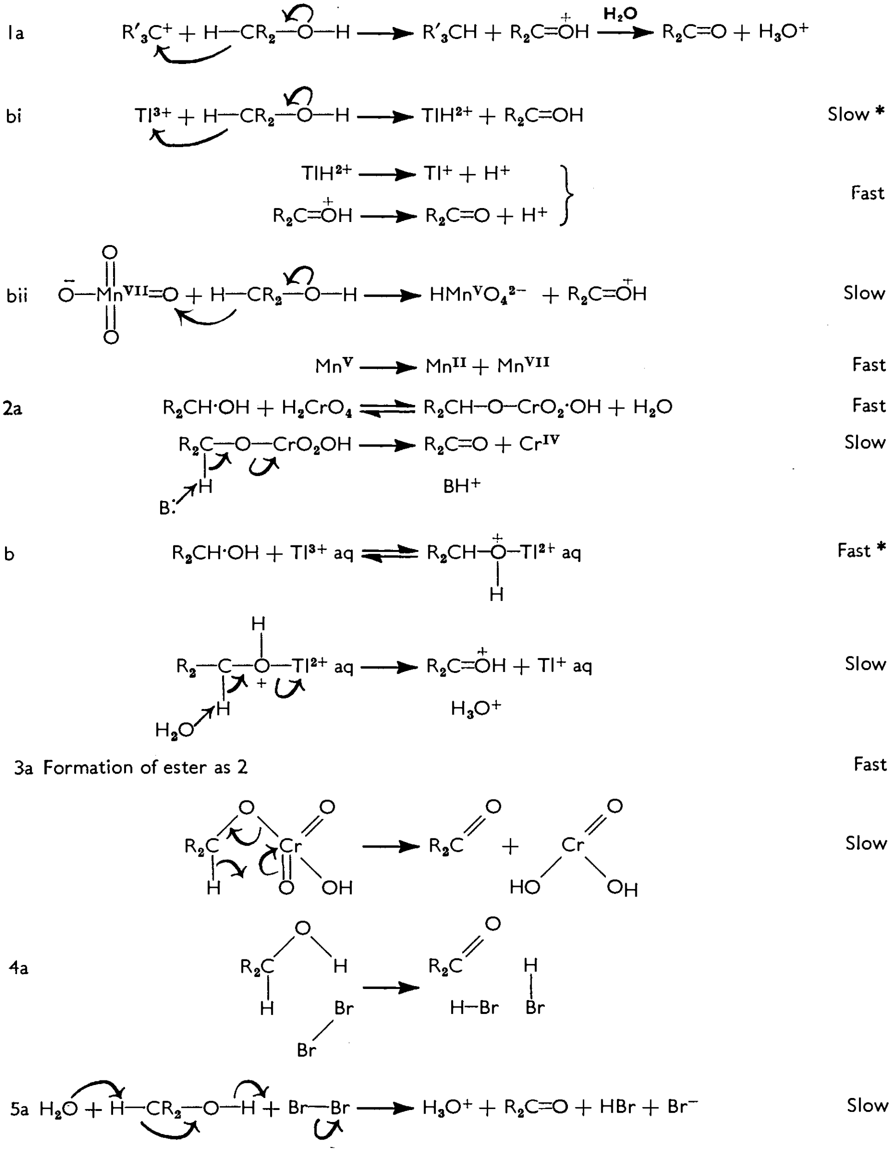
elimination, the present reactions must proceed by mechanism (2). An alternative interpretation is that oxidation by bromine proceeds by mechanism (4)[17] and that in mechanism (1) the loss of the proton is not rate-determining. This means that mechanism (1) is also consistent with the present results. This mechanism is closely

MECHANISMS DISCUSSED.

(a) Previously proposed mechanism. The quoted oxidant is not necessarily the only one for which it has been suggested.

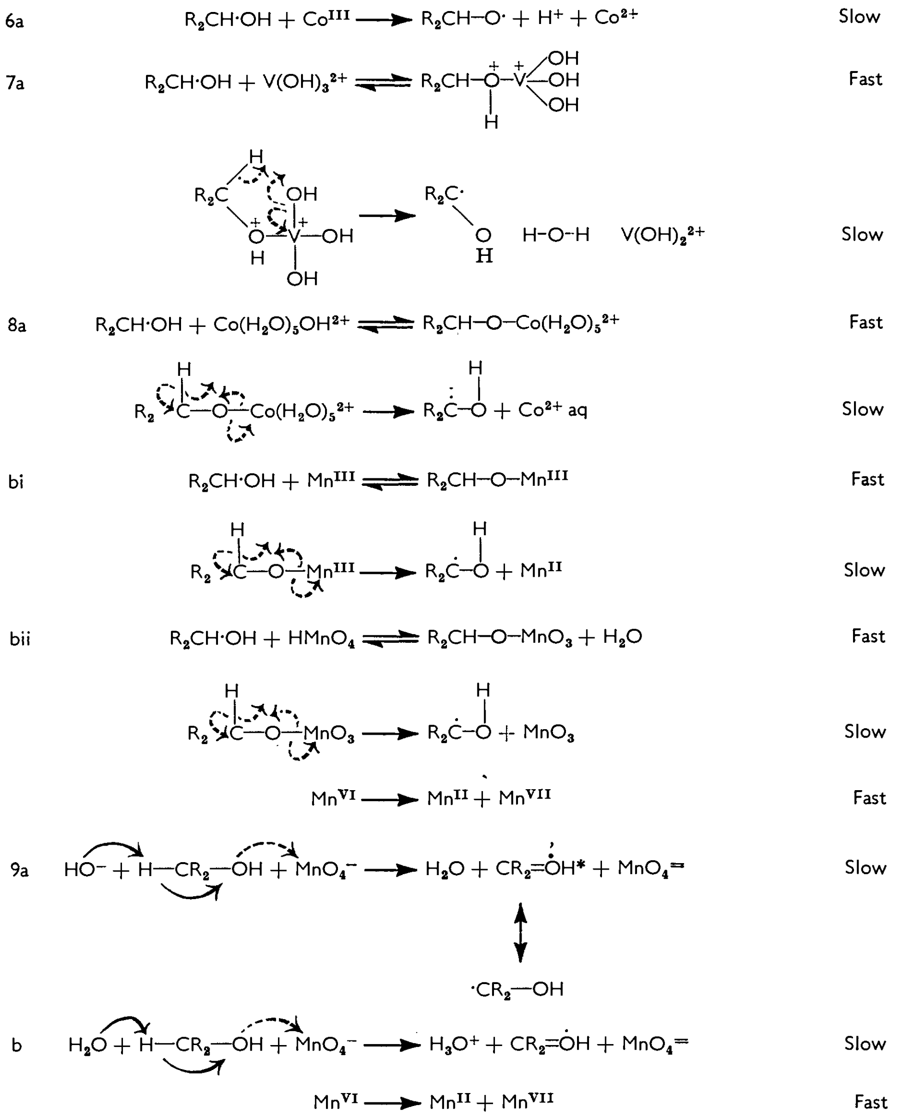
(b) Mechanism as applied to the present systems.

Two-electron processes.



* The mechanism of oxidation by Hg^{2+} is identical with that by Tl^{3+} except that the subsequent fast step is $HgH^+ + Hg^{2+} \longrightarrow Hg_2^{2+} + H^+$, or $Hg + Hg^{2+} \longrightarrow Hg_2^{2+}$.

One-electron processes.



In all cases the radical liberated will reduce a further molecule of oxidant.

* Written this way in order to emphasise the formation of the π-bond by base-catalysed elimination, leaving the odd electron in the π^*-orbital.

analogous to that proposed for the reactions of Hg^{2+} and other ions with dissolved hydrogen.[20]

The kinetics of the oxidation of cyclohexanol by manganic sulphate show that a complex is formed which contains one molecule of alcohol and one of a manganese(III) species, and that the transition state of the oxidation has the same composition. The value of the primary isotope effect ($k_H/k_D = 1{\cdot}6$) is unusually small;[21] similar values were

---

[20] Harrod and Halpern, *J. Phys. Chem.*, 1961, **65**, 563.

[21] Westheimer, *Chem. Rev.*, 1961, **61**, 265.

observed for oxidation by cerium(IV) sulphate ($k_H/k_D = 1{\cdot}9$) [3] and cobalt(III) ($k_H/k_D = 1{\cdot}6$, corrected to 50° *),[23] so it is probable that these one-electron oxidants react by similar mechanisms. Mechanisms which have been proposed previously involve (6) hydrogen-atom abstraction from the OH group,[22] (7) an intramolecular removal of a hydrogen atom,[1] (8) shift of a hydrogen atom,[23] and (9) base-catalysed electron abstraction.[24] Mechanisms (7) and (9) result in a large CH(CD) isotope effect, while mechanism (6) should give $k_H/k_D = 1$. Mechanism (8) is, however, consistent with the oxidation of cyclohexanol by manganese(III) and cerium(IV) sulphate.

The kinetics of the oxidation of cyclohexanol by magnanese(VII), which can be either a one-electron or a two-electron oxidant, are consistent with attack on the alcohol by both MnO_4^- and $HMnO_4$. The acid-catalysed reaction shows a solvent isotope effect consistent with the protonation of MnO_4^- in a pre-equilibrium step.[11] The value of the CH(CD) primary isotope effect ($k_H/k_D = 2{\cdot}1$, corrected to 50° *), and the absence of a primary OH(OD) isotope effect are consistent only with mechanism (8). The solvent isotope effect could not be determined accurately for the acid-independent portion of this reaction; the larger CH(CD) isotope effect excludes mechanism (8), and, since preliminary complex formation between cyclohexanol and the permanganate ion is unlikely, mechanism (1) fits the facts best. Mechanism (9) would also accommodate the observations on this reaction.

It can be seen that the close similarity between the one-electron oxidants studied, which was previously noted in their action on cyclohexanone, persists in their reactions with cyclohexanol. The similarities in the reactions of Hg^{2+}, Tl^{3+}, and MnO_4^- with cyclohexanone [6] also persist in their reactions with cyclohexanol, though they no longer behave in the same manner as bromine. It has been possible to assign all of the present reactions to one or other of the mechanisms of oxidation previously suggested.

EXPERIMENTAL

The solutions were prepared and the reactions were followed as described previously.[1,5,6]

Product Studies.—(1) 60% Perchloric acid (20 ml.), cyclohexanol (10 g., 1 mol.), and mercuric oxide (43·3 g., 2 mol) were made up with water to 100 ml. and were kept at 50 for 20 hr. with occasional shaking. A white precipitate developed after 1 hr., but at the end of the reaction no white precipitate or mercuric oxide remained, and a considerable quantity of mercury had been deposited. The mixture was filtered and the brown filtrate was neutralised with sodium hydrogen carbonate and extracted three times with ether. The aqueous layer was then acidified with dilute hydrochloric acid and extracted with ether. After the ethereal solutions had been dried ($MgSO_4$) and evaporated, the former gave a red neutral liquid (4·5 g.) and the latter a tarry acid (1 g). As by no means all the material had been recovered, the aqueous residues were subjected to continuous ether-extraction; a further 2·3 g. of tar was recovered.

The neutral fraction reacted with 2,4-dinitrophenylhydrazine, giving cyclohexanone dinitrophenylhydrazone, m. p. and mixed m. p. 158° (from ethanol). This fraction also contained at least 0·16 g. of cyclohexane-1,2-dione, determined by gravimetric assay of the nickel dioxime complex; [5] this would be expected to arise from further oxidation of the cyclohexanone formed in the initial stages of the reaction.[5]

(2) As the conditions of the above reaction are rather different from those at which the kinetics were studied, the following mixtures were made up: (*a*) 0·24N-manganic sulphate (15 ml.), 10 ml. concentrated sulphuric acid (10 ml.), and 0·35M-aqueous cyclohexanol (30 ml.) solution. (*b*) Mercuric oxide (0·8 g.) dissolved in 9M-perchloric acid (2 ml.), and the above cyclohexanol solution (30 ml.). (*c*) 0·1M-Thallic perchlorate (20 ml.), cyclohexanol solution (30 ml.), and water (300 ml.). (*d*) 0·1N-Potassium permanganate (35 ml.), 9M-sulphuric acid (5 ml.), and cyclohexanol solution (30 ml.). (*e*) 0·1N-Ceric sulphate (35 ml.), concentrated

---

* Corrected values of isotope effects at 50° are calculated with the assumption that the isotope effects are entirely due to differences in activation energy.

[22] Bawn and White, *J.*, 1959, 343.
[23] Hoare and Waters, *J.*, 1962, 965.
[24] Stewart and Linden, *Discuss. Faraday Soc.*, 1960, **29**, 211.

sulphuric acid (5 ml.), and cyclohexanol solution (30 ml.). In all cases there is an excess (*ca.* four-fold) of cyclohexanol in order to reduce the tendency for the initial products to be removed rapidly by further oxidation. The mixtures were placed in a thermostat-bath at 50° until the reaction was complete (*a*, 25 min.; *d*, 2 min.; *e*, 3 hr.) or until it was considered that the reaction was complete (*b* and *c*, 1·5 hr.), and then cooled. The excess of acid was neutralised if necessary, and the mixtures were each extracted three times with ether (total 60—80 ml.). Samples (10 ml.) of the ethereal solutions were warmed with 0·25M-2,4 dinitrophenylhydrazine (2 ml.), and the crystals formed on cooling were separated and dried. Only the product from reaction (*d*) was substantially pure cyclohexanone 2,4-dinitrophenylhydrazone (crude m. p. 154°, mixed m. p. 156°). The other derivatives all melted below 150° even after recrystallisation from aqueous ethanol. However, all the samples, when chromatographed on paper with 5% of diethyl ether in cyclohexane as solvent,[25] gave R_F values between 0·85 and 0·90, identical with that for the cyclohexanone derivative. The materials from reactions (*b*) and (*c*) contained a considerable amount of phenylhydrazones of lower R_F.

Ethereal solutions of the products were also analysed by gas chromatography at 60° with 5% of stearic acid in polyethoxyethanol as stationary phase. The chromatograms of all samples except (*c*) showed a well-defined peak with the retention time given by authentic cyclohexanone.

I thank Mr. R. P. Bell, F.R.S., for discussions of the solvent isotope effects.

THE DYSON PERRINS LABORATORY, SOUTH PARKS ROAD,
OXFORD.

[*Received, August* 11*th*, 1961.]

---

[25] Rice, Kellner, and Kichner, *Analyt. Chem.*, 1951, **23**, 194.