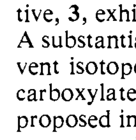
A Bell-Shaped pH–Rate Profile for an Oxidation. The Reaction of Permanganate with Hydroxycyclohexanecarboxylic Acids[1]

Ross Stewart* and J. Anthony MacPhee

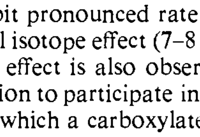
Contribution from the Department of Chemistry,
University of British Columbia, Vancouver 8, Canada. *Received October 19, 1970*

Abstract: The effect of a neighboring carboxyl group on the oxidation of a number of cyclohexanols by aqueous permanganate has been examined. *cis*-2-Hydroxycyclohexanecarboxylic acid (**1**) and its *cis*-5-*tert*-butyl derivative, **3**, exhibit pronounced rate accelerations at intermediate pH values, producing bell-shaped pH–rate profiles. A substantial isotope effect (7–8 : 1) is observed when the alcoholic carbon of **1** is substituted by deuterium. A solvent isotope effect is also observed. Compounds **1** and **3** exist predominantly in conformations that allow the carboxylate ion to participate in the removal of the hydrogen from the alcoholic carbon atom. A mechanism is proposed in which a carboxylate–permanganate adduct, C^-, is formed between the neutral hydroxy acid and permanganate ion. Dissociation of C^- gives C^{2-} which decomposes to products. Rate equations have been derived, based on the steady-state approximation, which give satisfactory agreement with experiment.

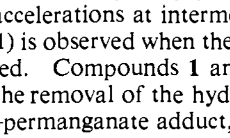
The permanganate oxidation of alcohols is known to be catalyzed by strong acids and bases.[2] Activation by strong acids is due in many cases to protonation of the permanganate ion and in others to carbonium ion formation, whereas activation by strong bases is due to the formation of alkoxide ion. The precise form in which the hydrogen atom in an alkoxide ion, RCH_2O^-, is abstracted by permanganate ion has been a matter of speculation.[2d,e,3] In order to learn more about the activation of alcohols by bases we decided to investigate the general effect of basic groups at neighboring positions in the alcohol molecule. We chose for this purpose a set of 2-hydroxycyclohexanecarboxylic acids (**1–5**). These compounds exist in the carboxylate form above about pH 5 and their various conformational arrangements provide the possibility of varying the position of the carboxylate group (the base) with respect to both hydrogen atoms that must be removed in the conversion of alcohol to ketone.



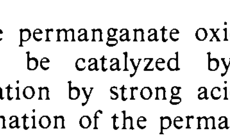
1



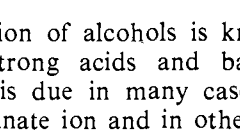
2



3



4



5

The principal conformational forms for *cis*- and *trans*-2-hydroxycyclohexanecarboxylic acid are **1** and **2**, respectively. Substitution of a *tert*-butyl group at the 5 position gives rise to four different compounds whose conformations are virtually fixed, owing to the *tert*-butyl group's high steric requirement. Three of these compounds (**3–5**) have been studied in the present work, which reveals a most unusual catalytic effect of neighboring carboxyl on the permanganate oxidation of alcohols.

Experimental Section

***cis*- and *trans*-2-Hydroxycyclohexanecarboxylic Acids (1 and 2).** Both isomers were prepared by the catalytic hydrogenation of ethyl 2-oxocyclohexanecarboxylate,[4] using a procedure similar to that given by Pascual, Sistare, and Regas.[5] The cis isomer had a mp of 81–82° (lit.[5] 82°) and the trans isomer 110–111° (lit.[5] 110°). When sodium borohydride was used for the reduction *trans*-2-deuterio-*cis*-2-hydroxycyclohexanecarboxylic acid was obtained after hydrolysis with base. After purification by recrystallization of the sodium salt the acid was found to melt at 80–81°.

Ethyl 5-*tert*-butyl-2-oxocyclohexanecarboxylate (6) was prepared by the condensation of ethyl oxalate with 4-*tert*-butylcyclohexanone followed by thermal decarbonylation by a procedure similar to that employed by Snider, Brooks, and Shapiro:[4] yield 52%; bp 90–92° (0.5 Torr); n^{20} 1.4805. *Anal.* Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.12; H, 10.00.

***cis*-5-*tert*-Butyl-*cis*-2-hydroxycyclohexanecarboxylic Acid (3).** Catalytic hydrogenation of **6** over Adams' catalyst and subsequent basic hydrolysis produced **3**, mp 149–150° (lit.[6] 149–149.5°).

***cis*-5-*tert*-Butyl-*trans*-2-hydroxycyclohexanecarboxylic Acid (4).** Sodium borohydride reduction of **6** followed by fractional crystallization of the sodium salt and work-up with acid gives **4**, mp 144–145° (lit.[6] 145–146°). Although the melting points of **3** and **4** are close there are distinct differences in their infrared and nmr spectra.

***trans*-5-*tert*-Butyl-*cis*-2-hydroxycyclohexanecarboxylic Acid (5).** This compound was isolated from a mixture of isomeric acids obtained by the reduction of **6** with sodium borohydride. Fraction crystallization of the sodium salt and work-up with acid gave **5**, mp 133–134° (lit.[6] 133–135°).

5-*tert*-Butyl-2-oxocyclohexanecarboxylic acid was prepared by the method of Sicher, *et al.*[6]

Rate Studies. Except for the runs in deuterium oxide the reaction was followed titrimetrically, as previously described.[2a,c] Phosphate buffers were used to control the pH. (Adding either droplets of concentrated sulfuric acid or particles of solid sodium hydroxide to a solution of KH_2PO_4 produces a series of buffers whose ionic strength does not vary greatly.) Because the composition of the buffer alters considerably in the pH range studied and because the second ionization constant of *o*-phosphoric acid is near the pH_{max}

---

[1] Taken in part from the Ph.D. Thesis of J. Anthony MacPhee, University of British Columbia, 1969.

[2] (a) R. Stewart, *J. Amer. Chem. Soc.*, **79**, 3057 (1957); (b) R. Stewart and R. Van der Linden, *Discuss. Faraday Soc.*, **29**, 211 (1960); (c) F. Banoo and R. Stewart, *Can. J. Chem.*, **47**, 3199 (1969); (d) R. Stewart, "Oxidation Mechanisms, Applications to Organic Chemistry," W. A. Benjamin, New York, N. Y., 1964, pp 63–70; (e) R. Stewart in "Oxidation in Organic Chemistry," Part A, K. B. Wiberg, Ed., Academic Press, New York, N. Y., 1965.

[3] J. L. Kurz, *J. Amer. Chem. Soc.*, **86**, 2229 (1964).

[4] H. R. Snyder, L. A. Brooks, and S. H. Shapiro, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 531.

[5] J. Pascual, J. Sistare, and J. Regas, *J. Chem. Soc.*, 1943 (1949).

[6] J. Sicher, F. Sipos, and M. Tichy, *Collect. Czech. Chem. Commun.*, **26**, 847 (1961).

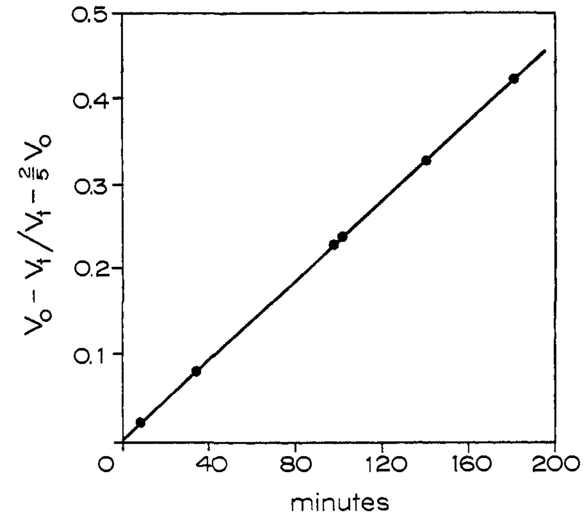


Figure 1. Second-order rate plot for the oxidation of **1** by permanganate: (**1**) = 2.48 × 10^{-3} *M*, [MnO_4^-] = 1.65 × 10^{-3} *M*, *T* = 25°, pH 6.20, ionic strength = 0.43, *k* = 0.944 l. mol^{-1} min^{-1}.

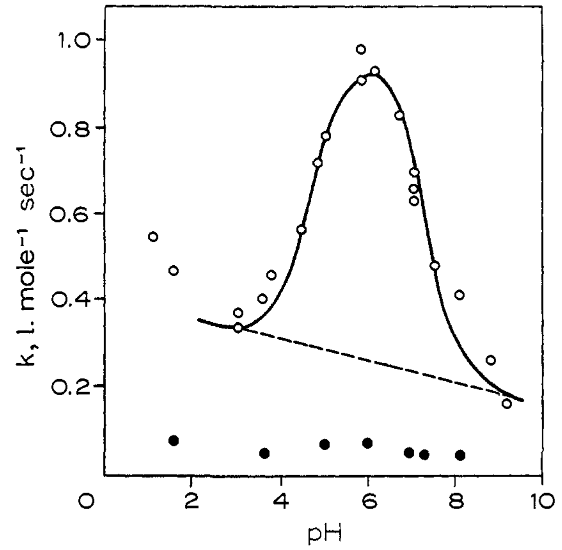


Figure 2. The pH-rate profiles for the oxidation of **1** (○) and **2** (●) by permanganate. The dashed line represents the contribution of the "normal" reaction path to the oxidation of **1**.

value (pK_2 = 7.12) it was necessary to determine the effect of varying the buffer concentration on the rate. At pH 5.88 the second-order rate constant for the oxidation of compound **1** was found to remain substantially constant over a fivefold change in buffer concentration. Thus, effects due to the buffer (*e.g.*, general base catalysis) are not important.

The rate studies in deuterium oxide were conducted in 99.7% D_2O using mixtures of K_2DPO_4 and D_2SO_4 as buffer. The pD measurements were made according to the directions of Gary, Bates, and Robinson[7] and the rates measured spectrophotometrically as previously described.[2a,c]

Conformational Assignments. The principal conformations of *cis*- and *trans*-2-hydroxycyclohexanecarboxylic acids are generally believed to be those shown in **1** and **2**, and this is confirmed by their nmr spectra. The spectrum of **1** contains an upfield axial proton and a downfield equatorial proton. The spectrum of the 2-deuterio compound of similar melting point clearly shows that the equatorial proton is the one attached directly to the carbon bearing the hydroxyl group because of the disappearance of the absorption of this proton and the corresponding loss of coupling in the resonance of the axial proton.

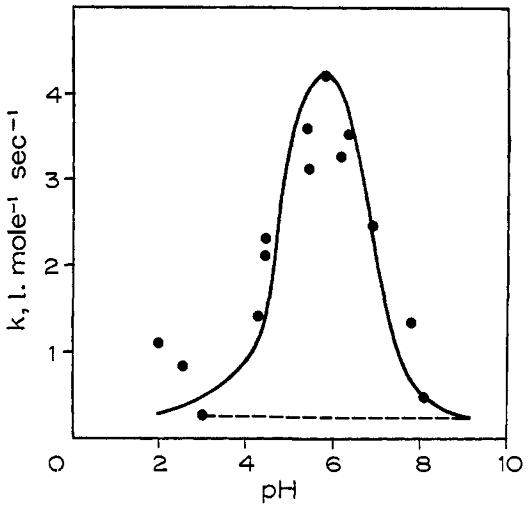


Figure 3. The pH-rate profile for the oxidation of **3** by permanganate. The dashed line represented the contribution of the "normal" reaction path.

The trans isomer can be taken to be **2**. On the basis of p*K* measurements in solvents other than water previous authors[8] have concluded that this isomer might exist in a diaxial conformation in solvents of lower dielectric constant than water. In water, however, this is not the case and the nmr spectrum bears this out. Only one ring proton is observable, separated from the remaining protons. This proton (presumably one adjacent to the hydroxyl or carboxyl group) has a broad resonance composed of two large couplings and one smaller coupling. This proton must then be axial and the molecule has the conformation **2**.

The three 5-*tert*-butyl-2-hydroxycyclohexanecarboxylic acids used in this work were studied by Sicher[6] and assigned the conformations **3**, **4**, and **5** on the basis of chemical reactivity studies. The arrangements of functional groups in **1** and **3** are identical and we would expect these compounds to have similar nmr spectra. This is indeed the case.

Results

To provide a basis for comparison the kinetics of the oxidation of the unsubstituted compound cyclohexanol with permanganate was examined. The results were unremarkable. As with other alcohols studied earlier a slow reaction occurs in the neutral region which speeds up when the pH is raised or lowered. The reaction was clearly second order and produced only cyclohexanone as product.[9]

The carboxy-substituted cyclohexanols gave a similar kinetic dependency on the alcohol and permanganate concentrations. In these cases the initial product is a β-keto acid which will be subject to decarboxylation. A product study of the permanganate oxidation of **3** indeed revealed that the keto acid is the initial product, which then undergoes slower decarboxylation. This was accomplished by extracting the aqueous reaction mixtures at various times with ether and comparing the ultraviolet spectra of the extracts with those of solutions of 5-*tert*-butyl-2-oxocyclohexanecarboxylic acid in ether saturated with water (λ_{max} 254 nm, ε 5570).

Enolization of the product ketones subjects them to further attack and it was observed that in basic solution, particularly, the second-order rate plots began to show curvature after the reaction had proceeded part way to completion. In neutral solution it was possi-

---

(7) R. Gary, R. G. Bates, and R. A. Robinson, *J. Phys. Chem.*, **68**, 3806 (1964).

(8) M. Kilpatrick and J. G. Morse, *J. Amer. Chem. Soc.*, **75**, 1846 (1953).

(9) J. S. Littler, *J. Chem. Soc.*, 2190 (1962).

ble to observe good second-order kinetics up to about 50% reaction (Figure 1).

The pH–rate profiles for the cis and trans isomers, **1** and **2**, shown in Figure 2, reveal a curious effect. The cis compound, which is oxidized much faster than the trans isomer, exhibits a marked bell-shaped rate profile. (The trans isomer shows a similar effect but it is very much less pronounced.)

The oxidation of the cis compound, **1**, was studied in deuterium oxide solution and the effect of deuterium substitution at C-2 also examined. The rate at the maximum, near pH 6, is lower in D_2O than in H_2O by approximately one-third and this is probably due to a solvent isotope effect on the values of K_a and K. *trans*-2-Deuterio-*cis*-2-hydroxycyclohexanecarboxylic acid exhibited a pH curve similar to that of its prototype except that the rate was considerably less. The isotope effect, k_H/k_D, is in the region 7–8, exact comparison being difficult to make because of the large effect that small pH changes have on the rate. There is no doubt, however, that the hydrogen attached to the alcoholic carbon atom is removed in the rate-controlling step, just as with the simple alcohols studied earlier.

Although **1** and **2** are the predominant forms for *cis*- and *trans*-2-hydroxycyclohexanecarboxylic acid, this does not ensure their being the forms that undergo reaction with permanganate. There seems little doubt that this is so, however, since the bell-shaped effect observed with **1** becomes *more pronounced* with **3**, the compound which exists almost completely in this conformation (Figure 3). The relatively slow rate and flattish curve observed with **2** are also observed with **4**. Compound **5**, which would correspond to a minor conformational form of **1**, was examined only cursorily. Its rate is midway between those of **3** and **4** and it does not appear to show any pronounced bell-shaped effect.

Discussion

The bell-shaped pH–rate profiles observed in this work, although they are very seldom met in oxidation reactions, are rather common in certain areas of mechanistic investigation.[10] Most of these involve multiple protonic equilibria and it is highly likely that in the present work the ionization of the carboxyl group is involved in an important way.

Abbreviating the substrate as HA, we can write the following sequence

$$\mathrm{HA} \xrightleftharpoons{K_a} \mathrm{H^+ + A^-}$$

$$\mathrm{HA + MnO_4^-} \xrightleftharpoons[k_2]{k_1} \mathrm{C^-}$$

$$\mathrm{C^-} \xrightleftharpoons{K} \mathrm{C^{2-} + H^+}$$

$$\mathrm{C^{2-}} \xrightarrow{k_3} \text{products}$$

According to this scheme the neutral hydroxy acid, HA, reacts with permanganate to form an intermediate; this intermediate dissociates, and the resulting dianion decomposes to products. For the moment the identity of the intermediate will be left open and we will pursue the kinetic consequences of the reaction scheme.

The overall rate is given by

$$\text{rate} = k_3[\mathrm{C^{2-}}]$$

Assuming the equilibria involving protons to be rapid we make use of the steady-state assumption regarding $[\mathrm{C^{2-}}]$ and $[\mathrm{C^-}]$ to obtain

$$-\frac{d[(\mathrm{C^-}] + [\mathrm{C^{2-}}]}{dt} = k_3[\mathrm{C^{2-}}] + k_2[\mathrm{C^-}] - k_1[\mathrm{HA}][\mathrm{MnO_4^-}] = 0$$

Because $[\mathrm{C^-}] = [\mathrm{C^{2-}}][\mathrm{H^+}]/K$ we have

$$[\mathrm{C^{2-}}] = \frac{k_1[\mathrm{HA}][\mathrm{MnO_4^-}]}{k_3 + k_2[\mathrm{H^+}]/K}$$

Thus, the rate is given by

$$\text{rate} = \frac{k_1k_3[\mathrm{HA}][\mathrm{MnO_4^-}]}{k_3 + k_2[\mathrm{H^+}]/K}$$

If we now express the rate in terms of the permanganate concentration and the total substrate concentration ($[\mathrm{HA}]_t = [\mathrm{HA}] + [\mathrm{A^-}]$), we get

$$\text{rate} = \frac{k_1k_2[\mathrm{HA}]_t[\mathrm{MnO_4^-}]}{(k_3 + k_2[\mathrm{H^+}])(1 + K_a/[\mathrm{H^+}])}$$

$$k_{\mathrm{obsd}} = \frac{k_1k_3}{(k_3 + k_2[\mathrm{H^+}]/K)(1 + K_a/[\mathrm{H^+}])} \tag{1}$$

Equation 1 has the form to produce a bell-shaped pH–rate profile. The pH corresponding to the maximum rate can be obtained by differentiating k_{obsd} with respect to $[\mathrm{H^+}]$ and is

$$\mathrm{pH_{max}} = \frac{1}{2}\log\,(k_2/k_3KK_a) \tag{2}$$

Equation 1 may be rearranged to give

$$\frac{1}{k_{\mathrm{obsd}}} = \frac{1}{k_1}\left[1 + \frac{k_2K_a}{k_3K}\right] + \frac{1}{k_1}\left[\frac{K_a}{[\mathrm{H^+}]} + \frac{k_2[\mathrm{H^+}]}{k_3K}\right] = \frac{1}{k_1}(1 + C) + \frac{1}{k_1}(A + B) \tag{3}$$

with $C = k_2K_a/k_3K$, $A = K_a/[\mathrm{H^+}]$, and $B = k_2[\mathrm{H^+}]/k_3K$. A plot of $1/k_{\mathrm{obsd}}$ against $A + B$ should then give a straight line of slope $1/k_1$ and intercept $(1 + C)/k_1$. Thus we can obtain k_1 and the term k_3K/k_2 from the values of k_{obsd}.

This kinetic analysis was applied to the experimental rate data for *cis*-2-hydroxycyclohexanecarboxylic acid. A word about the computational procedure is in order before the actual results are given. A separation of the contribution of the "normal" oxidation (that occurring without the participation of the neighbor carboxyl group and exemplified by the reaction of cyclohexanol) must be made in order to analyze numerically the actual bell-shaped reaction. Several attempts were made but the one represented in Figure 2 seemed the simplest and best solution. The area below the dotted line represents "normal" behavior and that

---

[10] (a) B. Zerner and M. L. Bender, *J. Amer. Chem. Soc.*, **83**, 2267 (1961); (b) K. J. Laidler, "Chemical Kinetics of Enzyme Action," Oxford University Press, Cambridge, 1958; (c) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959; (d) R. K. Chaturvedi, A. E. MacMahon, and G. L. Schmir, *J. Amer. Chem. Soc.*, **89**, 6984 (1967); (e) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, Chapter 10; (f) for examples involving oxidation see J. M. Pink and R. Stewart, *Can. J. Chem.*, **49**, 649 (1971), and N. C. Deno and N. H. Potter, *J. Amer. Chem. Soc.*, **89**, 3555 (1967).

Table I. Reaction Parameters Calculated from Equations 1-3

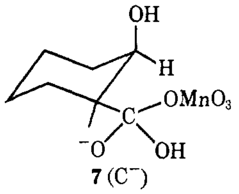
Compd	Solvent	pH_{max}	pK_a	k_1, l. mol^{-1} min^{-1}	C	k_3K/k_2	Correlation coeff
1	H_2O	6.020	4.70	315 ± 24	429.86	4.61×10^{-8}	0.984
1	D_2O	6.378	4.96	288 ± 5	689.89	1.59×10^{-8}	0.995
3	H_2O	5.964	4.85	559 ± 27	166.06	8.42×10^{-8}	0.991

above the line "bell-shaped" behavior. The most critical item involved in the calculation is the determination of the value of pH_{max}. This number can of course be estimated from the experimental results but a sufficiently precise value cannot be obtained in this way. The procedure followed was to estimate a value and see how closely the plot of $1/k_{obsd}$ against $(A + B)$ approached a straight line. The criterion used for this was the correlation coefficient of the line. It appeared that the correlation coefficient went through a maximum as the pH was varied over a certain interval. The pH corresponding to this maximum correlation could be determined to any desired degree of accuracy. The values estimated from the bell-shaped plots by inspection were in all cases consistent with the values of pH_{max} calculated this way.

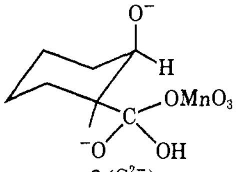
Once the appropriate pH_{max} is determined the next step is to adjust K_a such that k_1 determined from the slope is consistent with that determined from the intercept. This can be done to any desired degree of accuracy as well, the limiting feature being the standard error in k_1. A change in K_a is found not to produce any change in the correlation coefficient or pH_{max}. Consequently, K_a and pH_{max} can be adjusted quite independently, with pH_{max} being determined first, of course. These calculations were carried out using a computer least-squares program. The result of the calculations for compounds **1** in H_2O and in D_2O and **3** in H_2O are given in Table I. The theoretical curves generated by this treatment are shown as solid lines in Figures 2 and 3.

Nature of the Intermediate. Despite the strong kinetic evidence[11] favoring a reactive intermediate we have been unable to detect such a species directly. The visible spectrum of permanganate does not change as a result of addition of any of the substrates associated with bell-shaped pH-rate profiles other than to diminish with time. The nmr spectrum of **1** was recorded in deuterium oxide at pD 6 and 2. The two spectra were virtually identical except for a slight shift toward higher field of the spectrum at pD 6 relative to that at pD 2.

It is clear from the disparity between the pH-rate profiles for cyclohexanol and **1** that the carboxyl group is implicated mechanistically. This consideration and the behavior shown by the three isomers bearing a *tert*-butyl substituent specifies more precisely the role that conformation plays in the reaction. With this in mind a more exact mechanistic picture can be provided in terms of the general scheme put forward earlier. We believe that the first step is the formation in low concentration of the species C^- from the neutral alcohol and permanganate ion. The intermediate C^- may be represented by structure **7**, in which the permanganate ion has intruded into the carboxyl group. A complex similar to this in which permanganate ion adds to a carboxyl has been considered in the case of formate oxidation. It can be seen that the "permanganate ion" in **7** is favorably placed with regard to the hydrogen which is removed during the rate-controlling step of the oxidation. The following step indicated in the reaction scheme is the dissociation of C^- to give C^{2-}. The scheme also requires that C^{2-} be considerably more reactive than C^-. There are in C^- only two protons at all likely to be removed in a dissociation step. One of these is attached to an oxygen atom which has a negative charge very close by; the other is part of the alcoholic OH. If this latter proton is removed, C^{2-} would then be **8**. In **8**, the hydrogen to be removed in the rate-controlling step is activated toward oxidation by being part of an alkoxide ion, the rate-enhancing influence of alcohol ionization being well known.[2]

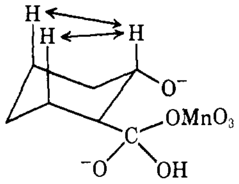


7 (C^-)



8 (C^{2-})

In terms of the intermediate structures presented, the role of conformation in the reaction becomes explicable. For **2** the intermediate equivalent to C^{2-} would be



The removal of the appropriate hydrogen atom in the transition state would involve surmounting steric interactions of the kind indicated in the above figure. Compound **2** does show a very slight maximum around pH 6. This behavior may be due to a minute contamination with compound **1** or it may be real. In any case it indicates that an intermediate of type C^{2-} is less likely to proceed to products with **2** than the analogous intermediates of compounds **1** and **3**.

Activation Parameters. Enthalpies and entropies of activation for *cis*-2-hydroxycyclohexanecarboxylic acid at three pH values (2.00, 5.88, 10.38) are given in Table II together with the values determined by Barter and Littler for cyclohexanol at pH 4.6.[12]

---

[11] Some apt remarks concerning kinetic evidence for mechanism appear in ref 10e, p 555.

[12] R. M. Barter and J. S. Littler, *J. Chem. Soc. B*, 205 (1967).

Table II. Activation Parameters

Compd	pH	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
1	2.00	11.5	−29.7
1	5.88	15.9	−13.9
1	10.38	16.1	−16.4
Cyclohexanol[a]	4.6	14.0	−23.3

[a] See ref 12.

The activation parameters at pH 5.88 (the peak of the bell-shaped curve) are significantly different from those at pH 2.00. The rate acceleration is caused by a more favorable entropy term which more than overcomes the effect of a less favorable enthalpy term. It is difficult to interpret the precise significance of these changes; they do, however, confirm our conclusion that distinctly different mechanisms are operative in the two regions.

Acknowledgment. The financial support of the National Research Council of Canada is gratefully acknowledged.

The Oxidation of Alcohols by Fenton's Reagent. The Effect of Copper Ion[1]

Cheves Walling* and Shin'ichi Kato[2]

Contribution from the Department of Chemistry,
University of Utah, Salt Lake City, Utah 84112. *Received November 3, 1970*

Abstract: The oxidation of alcohols in Fe^{2+}–H_2O_2 systems has been reexamined and a new kinetic analysis developed. Relative reactivities of methyl, ethyl, isopropyl, and *tert*-butyl alcohols are in good agreement with those from radiolysis experiments. The analysis and product studies indicate attack on both α- and β-hydrogens of ethyl and isopropyl alcohols. The β-hydroxyalkyl radicals are not oxidized by Fe^{3+}, but dimerize, terminating kinetic chains. They are, however, oxidized by Cu^{2+} to yield glycols with chain propagation. Thus the oxidation of *tert*-butyl alcohol is converted to a long-chain process by Cu^{2+}. We suggest that, in these systems, radical oxidation by Fe^{3+} is an electron-transfer process, but, with Cu^{2+}, involves either ligand transfer or an organocopper intermediate. The Fe^{3+} oxidation is evidently reversible in some cases, since solvolysis of ethyl trifluoromethanesulfonate in the presence of Fe^{2+} yields significant amounts of Fe^{3+} and butane.

Merz and Waters,[3] in a classic series of papers in the 1940's, undertook a kinetic analysis of the oxidation of a variety of organic substrates by Fenton's reagent (ferrous ion–hydrogen peroxide). Their study was intended to measure the relative reactivities of the different substrates toward hydroxyl radicals, and they also concluded that most substrates fell into two distinct classes: compounds such as primary and secondary alcohols and ethers which oxidized by a chain process, and a variety of other compounds in which chains were not involved. In addition, a few materials such as acetone and acetic acid were not oxidized by the reagent, but apparently inhibited the oxidation of other substrates.

Merz and Waters' findings were confirmed and their kinetic scheme modified by Kolthoff and Medalia[4] and a similar analysis of the initiation of vinyl polymerization carried out by Baxendale and colleagues.[5] Although the similar system titanous ion–hydrogen peroxide has been extensively used as a means of generating radicals for esr study, and a variety of ferrous ion-hydroperoxide systems have been examined, Fenton's reagent itself has received little subsequent quantitative study. Rather, the reactions of hydroxyl radicals have become a province of radiation chemistry and radiation biology. Here rates of hydroxyl radical reactions have either been studied by competitive techniques, or measured directly by pulse radiolysis. Results for a large number of substrates have recently been summarized by Anbar and Neta.[6]

We have been interested in comparing the properties of hydroxyl radicals with those of alkoxy radicals, and also in the role of metal ions in radical processes, and Fenton's reagent offers obvious experimental economies over the complexities of radiation chemistry. This paper describes a preliminary reinvestigation of the Fenton's reagent oxidation of alcohols, shows it to be more complex than previously recognized, and discloses a profound effect of added copper ion on the course of the reaction.

Kinetic Scheme. The present accepted scheme for the Fenton's reagent chain is the sequence

$$Fe^{2+} + H_2O_2 \xrightarrow{k_1} Fe^{3+} + OH^- + HO\cdot \quad (1)$$

$$Fe^{2+} + HO\cdot \xrightarrow{k_2} Fe^{3+} + HO^- \quad (2)$$

$$HO\cdot + RH \xrightarrow{k_3} H_2O + R\cdot \quad (3)$$

$$R\cdot + Fe^{3+} \xrightarrow{k_4} R^+ + Fe^{2+} \quad (4)$$

---

(1) Support of this work by a grant from the Petroleum Research Fund of the American Chemical Society is gratefully acknowledged.

(2) Visiting Professor from Kyoto Technical University, Kyoto, Japan.

(3) J. H. Merz and W. A. Waters, *Discuss. Faraday Soc.*, **2**, 179 (1947); *J. Chem. Soc.*, S 15 (1949).

(4) I. M. Kolthoff and A. I. Medalia, *J. Amer. Chem. Soc.*, **71**, 3777, 3784 (1949).

(5) J. H. Baxendale, M. G. Evans, and G. S. Park, *Trans. Faraday Soc.*, **42**, 155 (1946), and subsequent papers. For a more detailed discussion of early work, *cf.* C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, pp 565–572.

(6) M. Anbar and P. Neta, *Int. J. Appl. Radiat. Isotop.*, **18**, 493 (1967).