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.

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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

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

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

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

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

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(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).

where (1) and (2) are chain initiation and termination and (3) and (4) the chain propagation steps. Reaction 4 is rapidly followed by reaction of the carbonium ion with solvent, or it could be a kinetically equivalent ligand transfer without carbonium ion formation.

The most likely side reactions are

$$HO\cdot + H_2O_2 \xrightarrow{k_5} H_2O + HO_2\cdot \qquad (5)$$

$$2R\cdot \xrightarrow{k_6} R{-}R \qquad (6)$$

Since $k_5 = 10^7\ M\ \text{sec}^{-1}$ while $k_3 > 10^8$, (5) can be made unimportant by maintaining a high [RH]:[H_2O_2] ratio, and (6) can be suppressed by maintaining as low a radical concentration as feasible in the system.

Considering only reactions 1–4

$$-d[Fe^{2+}]/dt = k_1[Fe^{2+}][H_2O_2] + k_2[Fe^{2+}][HO\cdot] - k_4[Fe^{3+}][R\cdot] \qquad (7)$$

$$-d[H_2O_2]/dt = k_1[Fe^{2+}][H_2O_2] \qquad (8)$$

$$-d[RH]/dt = k_3[RH][\cdot OH] \qquad (9)$$

or, eliminating radical concentrations by the usual steady-state assumption for HO· and R· and taking the ratio of (8)/(7)

$$2d[H_2O_2]/d[Fe^{2+}] = 1 + k_3[RH]/k_2[Fe^{2+}] \qquad (10)$$

We see that [H_2O_2] does not appear in the right side of (10), and the experimental technique for employing (10) should be to add a deficiency of hydrogen peroxide to a ferrous ion–substrate solution (preferably slowly to minimize possible interference by reactions 5 and 6) and determine the amount of iron oxidized after complete reaction. If only small amounts of ferrous ion and substrate are consumed

$$2\Delta[H_2O_2]/\Delta[Fe^{2+}] = 1 + k_3[RH]/k_2[Fe^{2+}] \qquad (11)$$

The ratio $2\Delta[H_2O_2]/\Delta[Fe^{2+}]$ is the kinetic chain length of the reaction in terms of H_2O_2 consumed, and a plot of this chain length *vs.* [RH]/[Fe^{2+}] for a series of experiments should be linear with an intercept of unity and slope k_3/k_2.[7]

We shall shortly be concerned with more complex systems involving several radicals. The above treatment can be generalized to a system of three substrates so that (3) is replaced by

$$\begin{aligned} R_1H + HO\cdot &\xrightarrow{k_{31}} R_1\cdot + H_2O \\ R_2H + HO\cdot &\xrightarrow{k_{32}} R_2\cdot + H_2O \qquad (12) \\ R_3H + HO\cdot &\xrightarrow{k_{33}} R_3\cdot + H_2O \end{aligned}$$

We assume that $R_1\cdot$ undergoes the chain propagation step (4), but that $R_2\cdot$ is not oxidized by ferric ion but dimerizes *via* (6). Further, $R_3\cdot$ is not oxidized, but is capable of oxidizing ferrous ion[8]

$$R_3\cdot + Fe^{2+} \longrightarrow Fe^{3+} + R_3^- \xrightarrow{H_2O} R_3H \qquad (13)$$

Solution of this system of equations[9] in the same manner as above yields

$$\frac{\Delta[Fe^{2+}]}{2\Delta[H_2O_2]} = \frac{2k_2[Fe^{2+}] + k_{32}[RH_2] + 2k_{33}[R_3H]}{2k_2[Fe^{2+}] + 2k_{31}[R_1H] + 2k_{32}[R_2H] + 2k_{33}[R_3H]} \qquad (14)$$

This expression gives the reciprocal of the kinetic chain length, and can be considerably simplified for the case where RH's simply represent different sorts of reactive hydrogens on the same molecule RH

$$\frac{\Delta[Fe^{2+}]}{2\Delta[H_2O_2]} = \frac{2k_2[Fe^{2+}] + (k_{32} + 2k_{33})[RH]}{2k_2[Fe^{2+}] + (2k_{31} + 2k_{32} + 2k_{33})[RH]} \qquad (15)$$

If we make the substitutions $[Fe^{2+}]/2[RH] = r$, $\Delta[Fe^{2+}]/2\Delta[H_2O_2] = R$, $k_2/(k_{31} + k_{32} + k_{33}) = a$, and $(k_{32} + 2k_{33})/(2k_{31} + 2k_{32} + 2k_{33}) = b$, (15) may be rearranged to give

$$R = a(2r - 2rR) + b \qquad (16)$$

A plot of R *vs.* $(2r - 2rR)$ should be linear with slope a and intercept b. Equation 16 provides the key to our subsequent analysis, and, in the case that $k_{32} = k_{33} = 0$, reduces to (11).

Isopropyl Alcohol. The oxidation of isopropyl alcohol was selected for initial study. Experiments were carried out as described above on systems containing approximately 0.1 N $HClO_4$, 0.02 M ferrous perchlorate, and 0.01–0.5 M alcohol, adding enough hydrogen peroxide to oxidize a relatively small portion (usually 5–20%) of the ferrous ion and alcohol. Preliminary experiments showed that the results were independent of the rate of hydrogen peroxide addition or the initial presence of added ferric ion. Previous work has shown that the reaction is insensitive to pH in this acid range or to ionic strength, but is sensitive to oxygen.[4] We have confirmed this last finding, and all experiments reported below were carried out under nitrogen, using solutions from which dissolved oxygen had been flushed by bubbling with nitrogen before use. The oxidation is also retarded somewhat by acetone, the expected product. However, since an amount of acetone equal to the alcohol present only reduces the chain length by 25%, and the effect is roughly linear in acetone concentration, the retardation is negligible at the low extents of oxidation we have employed.

Typical results, plotted according to eq 11, appear in Figure 1. We see that, while the reaction obeys (11) at small alcohol:iron ratios, at higher ratios the kinetic chain length approaches a limiting value of about 13. Evidently the reaction is more complicated than the simple chain previously considered. In Figure 2 the same data are plotted according to (16). The entire plot is now linear, suggesting that isopropyl alcohol undergoes several reactions with hydroxyl radicals, some of which yield chain propagating species and some of which do not. A rather obvious interpretation is that we are seeing attack on both α- and β-hydrogens, the former yielding α-hydroxyalkyl radicals oxidized by

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(7) Merz and Waters' original treatment substituted $R\cdot + H_2O_2 \rightarrow ROH + \cdot OH$ for (4). Although the reasons for preferring (4) are well founded and further substantiated here, it is interesting that their treatment also yields (11).

(8) Reaction 13 appears of minor importance in alcohol oxidations, but was proposed by Merz and Waters to explain the inhibiting effect of acetone and acetic acid. It is found that it is important in other systems which will be discussed in later papers.

(9) It might be argued that cross-couplings of radicals are ignored in this treatment. However, if (4) and (13) are rapid, they consume most of $R_1\cdot$ and $R_3\cdot$; $R_2\cdot$'s build up and have the greatest probability of bimolecular coupling.

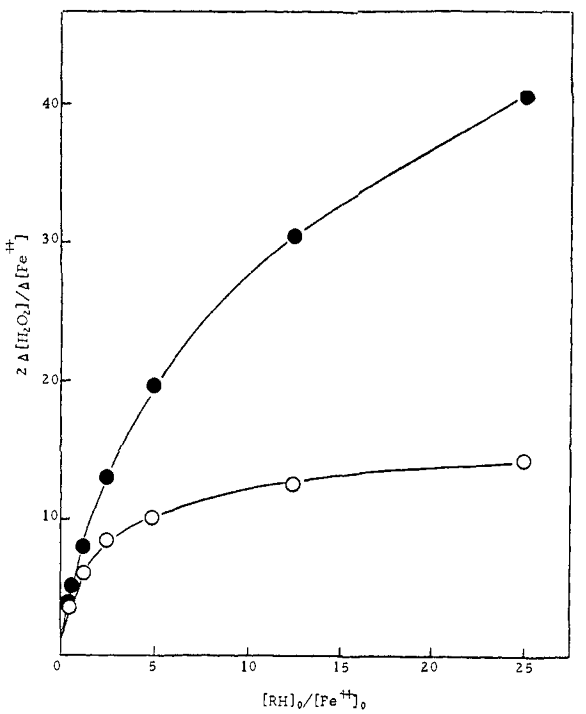

Figure 1. Oxidation of isopropyl alcohol: 0.02 M Fe^{2+}, pH 0.82, 30°; ○, without Cu; ●, 0.040 M Cu^{2+}.

ferric ion, and the latter simple alkyl radicals which are not, but instead dimerize.

We have tested this hypothesis in several ways. Recent work, notably by Kochi,[10] has shown that cupric ion is an effective oxidant for simple alkyl radicals. Accordingly, in our systems it should in effect convert k_{32} (or perhaps k_{33}) to an additional k_{31} *via* the sequence

$$R\cdot + Cu^{2+} \longrightarrow Cu^{+} + \text{products}$$

$$Cu^{+} + Fe^{3+} \rightleftharpoons Cu^{2+} + Fe^{2+}$$

In Figure 1 we see that cupric ion indeed increases the kinetic chain length at high alcohol:iron ratios. Figure 2 gives more quantitative results. Cupric ion does not change the slope of the plot, indicating no effect upon the ratio $k_2/\Sigma k_3$, but reduces the intercept from 0.075 to 0.02, indicating that 98% of the radicals from the alcohol are now propagating the chain. We have examined the effect of varying concentrations of cupric ion on the reaction and find that chain lengths go through a rather flat maximum at about 0.04 M, decreasing slightly again at much higher concentrations. In short, some nonpropagating reaction is never entirely eliminated, and this question is discussed further when product compositions are considered.

Deuterium substitution in isopropyl alcohol leads to large kinetic isotope effects, shown in Figure 3, which are also consistent with our hypothesis. Substitution of β-hydrogens by deuterium has little effect on the slope of the plots (*cf.* Figure 2) since most of the reaction goes through α-attack, but, in the absence of Cu^{2+}, reduces the intercept by a factor of 5. On the other hand, α-substitution increases the slope (since the α-position is now less reactive) and increases the intercept for the same reason. Quantitative analysis of these results in terms of k_H/k_D ratios is given in the Discussion.

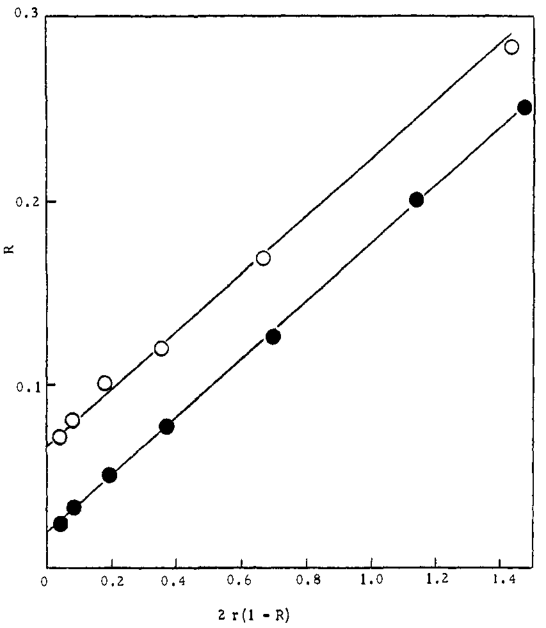

Figure 2. Oxidation of isopropyl alcohol. Plot of eq 16.

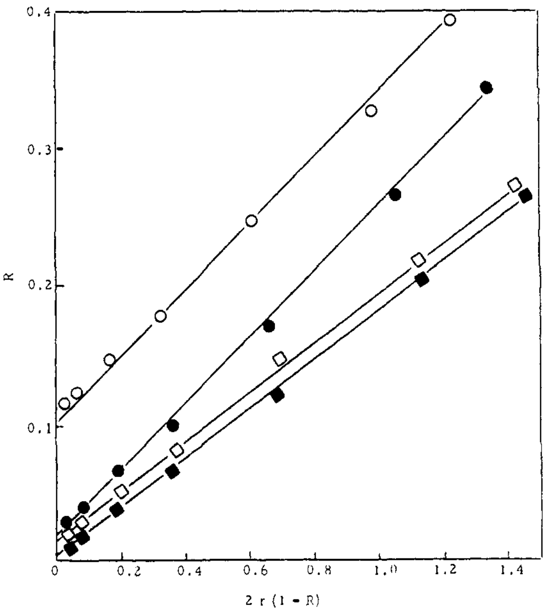

Figure 3. Kinetic isotope effects in oxidation of isopropyl alcohol: ○, α-d alcohol; ●, α-d alcohol + Cu^{2+}; □, β-d_6 alcohol; ■, β-d_6 alcohol plus Cu^{2+} (same conditions as Figure 1).

The final demonstration of the validity of our picture comes from a semiquantitative analysis of products (using somewhat higher concentrations of reactants and analysis by flame-ionization gas–liquid chromatography (glc)), Table I. As expected, the major product in all cases is acetone, but reaction in the absence of Cu^{2+} also shows 2,5-hexanediol, the expected product of coupling of radicals for β-attack. In the presence of Cu^{2+}, coupled products almost vanish and are replaced by 1,2-dihydroxypropane. In no case could coupling products involving the 2-hydroxy-2-propyl radical (2,3-dimethyl-2,3-butanediol and 2-methyl-2,4-pentanediol)

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(10) (a) J. K. Kochi, *Tetrahedron*, **18**, 482 (1962); (b) H. F. DeLaMare, J. K. Kochi, and F. F. Rust, *J. Amer. Chem. Soc.*, **85**, 1437 (1963), and subsequent papers. The second paper cited clearly shows the difference in oxidizing properties of ferric and cupric ion and also presents qualitative data on products similar to those in Tables I and II.

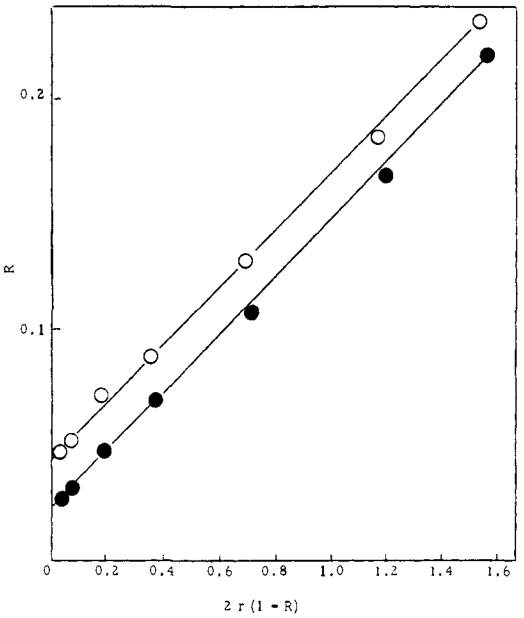

Figure 4. Oxidation of ethyl alcohol: ○, without Cu^{2+}; ●, Cu^{2+} added (same conditions as Figure 1).

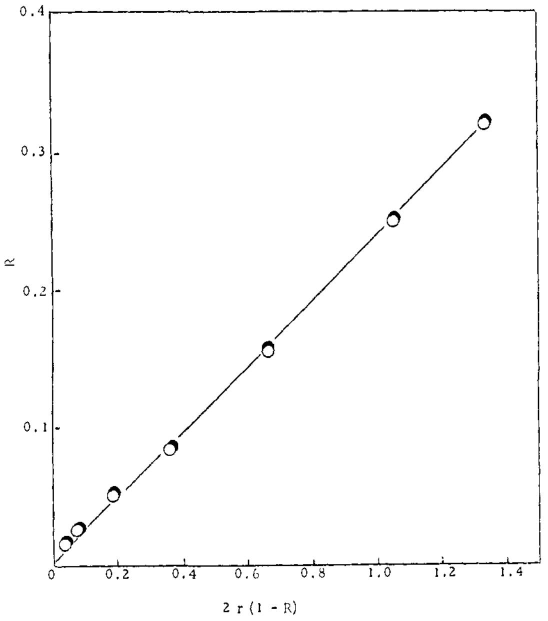

Figure 5. Oxidation of methyl alcohol: ○, without Cu^{2+}; ●, Cu^{2+} added (same conditions as Figure 1).

be detected. The failure of copper to eliminate entirely dimer formation may well account for the nonzero intercept of Figure 2.

Table I. Products of Fenton's Reagent Oxidation of Isopropyl Alcohol[a]

Product[b]	% yield Fe	% yield Fe–Cu
Acetone	93	84
1,2-Propanediol		11.2
2,5-Hexanediol	4.4	0.7

[a] Conditions: 1.25 M alcohol; 0.25 M H_2O_2; 0.1 M Fe^{2+}; 0 or 0.4 M Cu^{2+}; 30°. [b] Absent: 2,3-dimethyl-2,3-butanediol, 2-methyl-2,4-pentanediol.

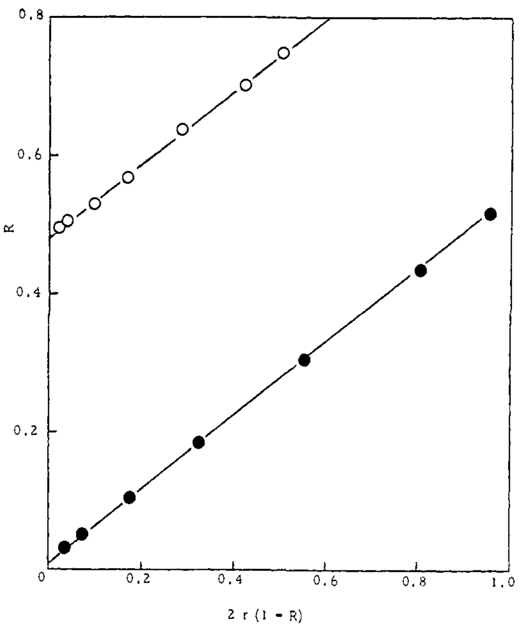

Figure 6. Oxidation of *tert*-butyl alcohol: ○, without Cu^{2+}; ●, Cu^{2+} added (same conditions as Figure 1).

Other Alcohols. The oxidation of several other alcohols was examined more briefly. Ethyl alcohol, Figure 4, resembles isopropyl alcohol in that it shows evidence of both α- and β-attack by HO·, Cu^{2+} reducing the intercept of the plot without changing the slope. Methyl alcohol, which can yield only α-hydroxy radicals, oxidizes *via* long chains and shows an almost zero intercept and no sensitivity to added copper, Figure 5. On the other hand, *tert*-butyl alcohol can yield only β-hydroxy radicals which are not oxidized by ferric iron. In the absence of copper it gives almost the predicted intercept of 0.5. With copper, chains become long, and the intercept is greatly reduced without change of slope, Figure 6. Products of oxidation are given in Table II.

Table II. Products of Fenton's Reagent Oxidation of Other Alcohols[a]

Alcohol		% yield Fe	% yield Fe–Cu
Methyl	HCHO	81	80
	HCOOH	<0.5	<0.5
Ethyl[b]	CH_3CHO	72	63
	CH_3COOH	20	22
	$HOCH_2CH_2OH$		1.8
	$(HOCH_2CH_2)_2$	1.1	.13
tert-Butyl[c]	CH_3COCH_3	<0.1	<0.1
	$(CH_3)_2COHCH_2OH$		86.2
	$[(CH_3)_2COHCH_2]_2$	84.4	1.6

[a] Conditions: same as Table I except with *tert*-butyl alcohol, 0.05 M H_2O_2. [b] Absent: $CH_3CH(OC_2H_5)_2$. [c] Absent: $CH_3COC_2H_5$, $(CH_3)_2CHCHO$, isobutylene oxide.

Ethyl and *tert*-butyl alcohol show dimerization of β-hydroxy radicals which is again almost, but not completely, eliminated by cupric ion. With ethyl alcohol at the relatively high conversions employed there is also considerable further oxidation of intermediate acetaldehyde.

Competitive Oxidations. Our general equation (14) can obviously be expanded to include systems containing several alcohols, each of which reacts in more than one manner, and should permit prediction of oxidation chain lengths in mixed systems from slopes and intercepts of plots of eq 16 for individual alcohols. Thus, qualitatively, addition of *tert*-butyl alcohol to a methanol–Fe^{2+}–H_2O_2 system should shorten chain lengths by diverting the reaction to the production of non-chain-propagating β-hydroxy radicals. However, in the same system plus Cu^{2+}, *tert*-butyl alcohol should increase chain lengths. Quantitative data appear in Figure 7. With iron alone results agree almost exactly with the calculated curve. In the presence of Cu^{2+} the inhibition is eliminated, although chain lengths do not increase as rapidly as predicted.

Discussion

Our results may first be compared with other data in the literature on hydroxyl radical reactions with alcohols, obtained either by competitive methods or directly by pulse radiolysis. Table III lists such a comparison with Merz and Waters' early data,[3] Anbar and Neta's summary of radiolysis results,[6] and a single set of radiolysis experiments run under comparable conditions *vs.* *p*-nitrosodimethylaniline.[11] Since other workers measured simply the sum of all hydroxyl radical reactions, the proper comparison is with the reciprocal of the slopes of our plots, $\Sigma k_3/k_2$. We see that, while our ratios are approximately twice those of other investigators (possibly in part because of uncertainty in k_2 which we have taken as 3.2×10^8), relative reactivities of different alcohols are in substantial agreement, supporting the conclusion that hydroxyl radicals are indeed the reactive intermediates in the Fe^{2+}–H_2O_2 system, a matter which has been questioned[12,13] and will be discussed further shortly.

Table III. Relative Reactivities of Alcohols with Hydroxyl Radicals[a]

Alcohol	$\Sigma k_3/k_2$	M & W[b]	A & N[c]	AM & N[d]
Methyl	4.30 (1)	2.3 (1)	1.22–2.04	1.91 (1)
Ethyl	7.00 (1.63)	3.8 (1.65)	2.25–3.75	3.4 (1.78)
Isopropyl	6.65 (1.55)	3.0 (1.3)	3.44–12.2	3.75 (1.99)
tert-Butyl	1.90 (0.44)	0.65 (0.28)	0.78–1.3	0.88 (0.46)

[a] Radiolysis results calculated assuming $k_2 = 3.2 \times 10^8$ l./mol sec. [b] Merz and Waters.[3] [c] Range of values from Anbar and Neta.[6] [d] Anbar, Meyerstein, and Neta, radiolysis experiments *vs.* *p*-nitrosodimethylaniline.

Our analysis also permits calculating relative rates of attack on α- and β-hydrogens. Here we have assumed that k_{33} is negligible with alcohols so that k_{31} may be taken as k_α and k_{32} as k_β. Accordingly our intercepts measure $k_\beta/2(k_\alpha + k_\beta)$ and slopes $k_2/(k_\alpha + k_\beta)$. The small residual intercepts observed in the presence of copper we ascribe either to our failure to eliminate all coupling reactions, or to small incursions of other processes, *e.g.*, (5). Results are given in Table IV, on both a total molecule and per hydrogen basis.

Although ethyl alcohol shows the highest overall reactivity we see that reactivity per α-hydrogen increases smoothly in the order primary < secondary < tertiary. Similarly, while *tert*-butyl alcohol shows the greatest overall β-hydrogen reactivity, reactivities per β-hydrogen are rather similar for all alcohols. Kinetic isotope effects are also in a plausible range. For isopropyl-β-d_6 alcohol, k_H/k_D for the β-position is 4.22 and there is also a small secondary effect at the α-position, $k_H/k_D = 1.05$. For the α-*d* alcohol the primary isotope effect is smaller, $k_H/k_D = 1.68$, perhaps because the reaction is so fast ($k > 10^9$) that it is partially diffusion controlled.

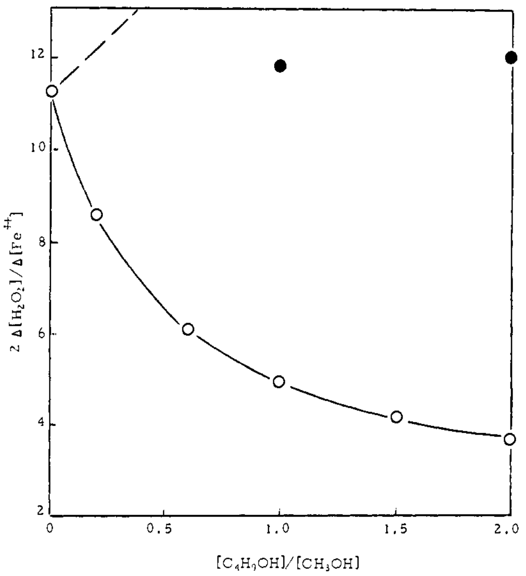

Figure 7. Oxidation of methyl alcohol–*tert*-butyl alcohol mixtures: 0.02 *M* Fe^{2+}, 0.05 *M* CH_3OH, pH 0.82: ○, without Cu^{2+}; ●, 0.04 *M* Cu^{2+}. Lines are calculated from eq 15.

Table IV. Relative Reactivities of α- and β-Hydrogens of Alcohols

Alcohol	Per molecule		Per H	
	k_α/k_2	k_β/k_2	k_α/k_2	k_β/k_2
Methyl	4.30		1.43	
Ethyl	7.32	0.69	3.66	0.23
Isopropyl	5.73	0.92	5.73	0.15
Isopropyl-α-*d*	3.42	0.91	3.42	0.15
Isopropyl-β-d_6	5.43	0.22	5.43	0.036
tert-Butyl		1.90		0.21

Since significant amounts of reaction occur at all C–H bonds of the alcohols we have investigated, it is evident that the hydroxyl radical is quite unselective in its reactions, a result consistent with the high strength (120 kcal/mol) of the HO–H bond formed and also with the fact that most of the many rate constants tabulated by Anbar and Neta lie between 10^8 and 5×10^9. It also implies that simple measurements of overall relative rate constants are not of themselves very informative, particularly for complex molecules. We are currently extending our analysis to other types of substrate in order to dissect the matter further, and defer a detailed discussion of structure–reactivity relationships.

We believe our results also account for an initially puzzling report by Shiga.[13] He has investigated the esr spectra of the radicals produced in the Fenton's reagent oxidation of alcohols (using EDTA complexed iron in neutral solution). Although methyl alcohol and eth-

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(11) M. Anbar, D. Meyerstein, and P. Neta, *J. Chem. Soc. B*, 742 (1966).
(12) A. E. Cahill and H. Taube, *J. Amer. Chem. Soc.*, **74**, 2312 (1952).
(13) T. Shiga, *J. Phys. Chem.*, **69**, 3805 (1965).

ylene glycol gave expected spectra, alcohols with β- and γ-hydrogens showed only spectra of β- and γ-hydroxyl radicals, leading him to suggest some species other than hydroxyl radicals were involved. Our results indicate that, even if β- or γ-attack is only a minor side reaction, the failure of the resulting radicals to be oxidized by ferric ion should lead to their building up in the system until they swamp out any other spectra, leading to the result observed. If correct, this interpretation again indicates the hazard of interpreting reaction mechanisms by esr measurements alone without supporting kinetic or product data.

Finally, our results suggest some conclusions as to the nature of the oxidation of radicals by simple hydrated ferric and cupric ions. Most of the previous data on cupric ions come from Kochi's work under quite different conditions, using acetate complexes in acetic acid or acetonitrile. Here his most illuminating study[14] has been done on β-arylethyl radicals and indicates two paths for the oxidation: electron transfer to yield β-arylethyl acetates involving a carbonium-ion type intermediate since electron supplying substituents facilitate the process and deuterium labeling shows extensive rearrangement, and a quite separate β-elimination which occurs without rearrangement. The second most pertinent group of studies has been on the inhibition of vinyl polymerization.[15] Here cupric ion is more effective than ferric; when $CuCl_2$ or $FeCl_2$ is employed, the reaction is apparently a ligand transfer and little affected by electron supplying or withdrawing groups on the radical; when the ion is uncomplexed, selectivity is higher as we find here.

Our results with simple hydrated cupric ion differ from Kochi's in that the oxidation products of β-hydroxyalkyl radicals are solely glycols. There is no evidence for β-elimination which would yield an enol (with isopropyl alcohol, copper leads to no increase in the yield of acetone), or any carbonium ion type rearrangement (with *tert*-butyl alcohol neither 2-butanone nor isobutylene oxide could be detected). Thus, the reaction could be interpreted as a simple ligand transfer

$$R\cdot + Cu^{2+}(H_2O)_n \longrightarrow ROH + Cu^{+}(H_2O)_{n-1} + H^+ \qquad (17)$$

which could well be a lower energy path than the two-step sequence

$$R\cdot + Cu^{2+} \longrightarrow R^+ + Cu^+ \qquad (18a)$$

$$R^+ + H_2O \longrightarrow ROH + H^+ \qquad (18b)$$

since the latter leads to the same products and (18b) is highly exothermic.

The puzzling question is why (17) occurs more readily than the corresponding reaction

$$R\cdot + Fe^{3+}(H_2O)_n \longrightarrow ROH + Fe^{2+}(H_2O)_{n-1} + H^+ \qquad (19)$$

which has a greater driving force since ferric ion is the stronger oxidizing agent. Because ferric ion does oxidize α-hydroxy radicals which yield relatively stable carboniums ions, we suggest that its oxidations here are essentially electron transfer processes analogous to (18) but that copper has an alternative path available. This is not implausible, since the square planar coordination of copper is quite different from the octahedral coordination of iron. The path could be simple ligand transfer (17) or conceivably could involve an organocopper intermediate,[16] *e.g.*

$$R\cdot + Cu^{2+}(H_2O)_n \longrightarrow RCu^{2+}(H_2O)_n \qquad (20a)$$

$$RCu^{2+}(H_2O)_n \longrightarrow ROH + Cu^{+}(H_2O)_{n-1} + H^+ \qquad (20b)$$

Regardless of the details of the cupric ion oxidation, if ferric ion is forced to oxidize *via* electron transfer, the limiting factor may be the position of the equilibrium

$$R\cdot + Fe^{3+} \rightleftharpoons R^+ + Fe^{2+} \qquad (21)$$

Little is known about radical–carbonium ion redox potentials in aqueous solution, but, to examine the possibility of (21) proceeding to the left, we have solvolyzed ethyl trifluoromethanesulfonate (triflate) in concentrated ferrous perchlorate solution in the absence of air. The triflate anion is such a good leaving group that the reaction could have some appreciable carbonium ion character.[17] Ferric ion (7–8%) is produced during the solvolysis, and butane (4%) can be detected among the products, while no butane can be detected in the absence of ion. Further, the solvolysis in the presence of ferrous ion induces the polymerization of acrylonitrile. Although these results are fragmentary they do suggest that simple redox potentials may be the factor limiting radical oxidation by hydrated ferric ion under our conditions. Indeed, we find evidence that radicals with strong electron withdrawing groups are *reduced* by ferrous ion.[18]

Experimental Section

Materials. Stock solutions of reagents were prepared from analytical grade ferrous and cupric perchlorate, perchloric acid, and 30% H_2O_2 redistilled under reduced pressure. Spectrograde methyl, ethyl, and isopropyl alcohols were used without further purification, but reagent grade *tert*-butyl alcohol was found to contain impurities leading to erratic results, and was redistilled through a fractionating column over $LiAlH_4$. α-Deuterioisopropyl alcohol was prepared by reducing acetone with $LiAlD_4$, the hexadeuterio alcohol by reducing CD_3COCD_3 with $LiAlH_4$ (isotopic purity of both alcohols, 99.5%). Determination of Fe^{2+}, Cu^{2+}, and H_2O_2 were by dichromate reduction, iodimetry, and ceric ammonium sulfate reduction, respectively.[19] Ethyl triflate was prepared from CF_3SO_3Ag and ethyl iodide.[20]

Competitive Kinetics. Reactions were carried out in a 100-cm^3 jacketed vessel thermostated at 30° and magnetically stirred through which a slow stream of nitrogen could be bubbled. Solutions of all components except H_2O_2 were made up to give a final volume of 50 cm^3 at pH 0.82 (~0.1 *N* acid) and bubbled with N_2 for 30 min. The H_2O_2, containing 0.1 *N* acid, was added dropwise from a buret with a reservoir which could also be bubbled with nitrogen. Addition was usually adjusted to 1.25 mmol/(l.min). Reaction of the H_2O_2 was complete within 10 min of completion of addition, and unreacted Fe^{2+} was determined by titration of an aliquot. Results were calculated from H_2O_2 added and Fe^{2+} consumed. Ratios of rate constants are all from least squares fits to the linear plots shown.

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[14] J. K. Kochi, A. Bemis, and C. L. Jenkins, *J. Amer. Chem. Soc.*, 90, 4616 (1968).

[15] C. H. Bamford, A. D. Jenkins, and R. Johnston, *Proc. Roy. Soc., Ser. A*, **239**, 214 (1952); W. I. Bengough and T. O'Neill, *Trans. Faraday Soc.*, **64**, 1014, 2415 (1968); W. I. Bengough and B. S. Jamieson, *Polym. Prepr.*, 11, 706 (1970).

[16] Such an intermediate has been proposed by Kochi[14] to account for his β eliminations, but it should be noted that it requires a species which is formally Cu(III) and has little precedent in organometallic chemistry.

[17] A. Streitwieser, Jr., C. L. Wilkins, and E. Kiehlmann [*J. Amer. Chem. Soc.*, **90**, 1598 (1968)] have concluded that solvolyses of ethyl triflate in 80–100% ethanol and formic and acetic acid have little carbonium ion character. However, water is a much better ionizing solvent, and, even if our results arise from an attack on undissociated triflate by ferrous ion, they are still pertinent.

[18] Unpublished work by Mr. G. El-Taliawi.

[19] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd ed, MacMillan Co., New York, N. Y., 1952, pp 579, 585, 581, respectively.

[20] T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.*, 173 (1956).

Product analyses were carried out on experiments run similarly but at higher concentrations of reagents. After reaction, solutions were neutralized with NaOH, metal hydroxides separated by centrifuging, and aliquots analyzed by flame ionization glc after addition of internal standards (dioxane, 1,4-butanediol, and 2,5-hexanediol). Most separations were done on 6 ft × $^1/_8$ in. 10% Carbowax 20M or Polapak Q columns, and products were identified by retention time on two columns.

Ethyl Triflate Hydrolyses. A solution of 10 mmol of ethyl triflate in 10 ml of CH_2Cl_2 was added dropwise with stirring to 40 ml of 0.5 *N* $Fe(ClO_4)_2$–0.25 *N* $HClO_4$ solution. The system was bubbled with nitrogen and the effluent passed through a trap at $-78°$. Titration showed the formation of 0.44 mmol of Fe^{3+} and 5.88 mmol of acid ($\Delta Fe^{3+}/\Delta H^+ = 7.48\%$). Analysis of the trap content by glc showed traces of butane. In a second experiment, undiluted ethyl triflate was used, and 1 ml of *n*-hexane was placed in the trap to give more quantitative trapping of butane: yields, Fe^{3+}, 8.35%; C_4H_{10}, 3.9%. A blank experiment without Fe^{2+} gave no butane, and a similar hydrolysis in the presence of 1.5 *M* acrylonitrile gave a small precipitate of polymer.

Nuclear Magnetic Resonance Studies of Metal Porphyrins. I. Kinetics of Ligand Exchange and of Transitions between High- and Low-Spin States in the System Hemin–Pyridine–Water[1a]

H. Asman Degani and D. Fiat*[1b]

Contribution from the Isotope Department, The Weizmann Institute of Science, Rehovot, Israel, and the Chemistry Division, Argonne National Laboratory, Argonne, Illinois 60439. *Received June 27, 1970*

Abstract: Nuclear magnetic resonance studies of hemin in pyridine–water solutions yielded information on the structure of the complex formed. The proton magnetic resonance spectra of the coordinated pyridine molecules have been observed, and it was found that one water molecule and one pyridine molecule are coordinated to the hemin in solutions containing 5–20% by weight of water in pyridine. The temperature dependence of the relaxation times and chemical shifts of the hemin protons revealed transitions between high- and low-spin states of the ferric ion of the heme moiety. The concurrent phenomena of ligand exchange and transitions between high- and low-spin states required extension of the former theoretical treatment of exchange between two magnetic environments to this particular case of exchange between three magnetic environments. The kinetic and thermodynamic parameters for the ligand exchange rates were calculated from the transverse relaxation times of the water and pyridine protons and their temperature dependence. The kinetic and thermodynamic parameters for the transitions between the high- and low-spin states were calculated from the relaxation times of the ring hemin protons in the temperature region from -60 to $+60°$. The hyperfine coupling constant of the α protons of pyridine bound to hemin was directly determined for the low-spin species and calculated for the high-spin complex. The pseudocontact contribution to the hyperfine coupling constant of the heme protons was calculated from geometrical considerations, thereby allowing the determination of the isotropic part of the hyperfine coupling constant. The spin densities at the π orbitals of the peripheral carbon atoms have been calculated from the isotropic shifts. The correlation time for the nuclear relaxation of the methyl protons in the state of low spin was calculated from the experimental data and found to be governed by the electron relaxation time.

A number of important biological functions of the heme proteins and other derivatives of the metal porphyrins result from their ability to exchange ligands coordinated to the metal ions in the axial positions. Other functions originate in the ability of these compounds to participate in oxidation–reduction reactions. These phenomena are particularly amenable to magnetic resonance studies. Such studies may yield information regarding the kinetic and thermodynamic parameters for the exchange reaction between the coordinated and noncoordinated ligands and regarding the structure of the complexes. Water molecules are among the most important ligands that may bind reversibly to the iron in the ferric and ferrous porphyrin complexes. The particular importance that may be ascribed to the studies of water exchange in these particular systems is due to the role that water plays in the process of binding oxygen to hemoglobin.

The relaxation effects of some heme proteins on the water protons have been investigated previously by Davidson and Gold[2a] and by Kon and Davidson.[2b] The relaxation times of the water protons in the systems iron(III)–water, heme, hemin, hemoglobin, myoglobin, and methmyoglobin have been measured at room temperature, and from the experimental results the distance of the iron atoms from the protein surface has been calculated.[3,4] However, these

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(1) (a) Based on the thesis submitted by Hadassa Asman Degani to the Feinberg Graduate School, The Weizmann Institute of Science, Rehovoth, Israel, in partial fulfillment of the requirements toward the M.Sc. Degree, Mar 1969. Preliminary reports were presented at the Eleventh (H. A. Degani and D. Fiat, *Proc. Int. Conf. Coord. Chem., 1968*, 11, 474 (1968)) and Twelfth (H. A. Degani and D. Fiat, *ibid., 1969*, 12, 121 (1969)) International Conferences on Coordination Chemistry and at the Second International Symposium on Nuclear Magnetic Resonance (D. Fiat, H. A. Degani, J. Reuben, and A. M. Chmelnick, *Cienc. Cult.* (*Sao Paulo*), 20, 536 (1968)). (b) Argonne National Laboratory; address correspondence to this author at: the Weizmann Institute of Science, Rehovot, Israel.

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