

National Science Foundation Grant No. GP-31199 is gratefully acknowledged. Samples of the substituted benzidines were prepared by A. K. Carpenter and the

N-tert-butylaniline was synthesized by P. Berkenkotter. Special thanks are due to Dr. R. N. Adams and Dr. D. E. Smith for their support and encouragement.

Oxidation and Fragmentation of Some Phenyl-Substituted Alcohols and Ethers by Peroxydisulfate and Fenton's Reagent¹

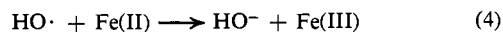
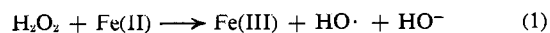
Maurice E. Snook and Gordon A. Hamilton*

Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. Received July 24, 1973

Abstract: The mechanisms of the reactions of the hydroxyl radical (generated from Fenton's reagent) and the sulfate radical anion (generated thermally from $S_2O_8^{2-}$), with various phenyl-substituted alcohols have been examined in some detail. The reaction of 1-phenylalkanols ($PhCHOHR$) with $XO\cdot$ ($X = H$ or SO_3^-) at pH 1.8 yields some $PhCOR$, but benzaldehyde is the major product when R is isopropyl or *tert*-butyl and a minor product when R is ethyl. The total yield of carbonyl products is 70–100%. From competition experiments it was determined that all the 1-phenylalkanols are 5–6 times more reactive than 2-propanol toward $HO\cdot$, and $PhCHOHCH_3$ is 22 times more reactive than 2-propanol toward $SO_4^{\cdot-}$. Para-substituted 1-phenylethanol show relative reactivities toward $HO\cdot$ increasing in the sequence: $CN < Br < H < C_2H_5$. The tertiary alcohol, $PhC(CH_3)_2OH$, is more reactive toward $XO\cdot$ than 2-propanol and is converted in good yield to $PhCOCH_3$, but *tert*-butyl alcohol is relatively unreactive and gives only a small amount of acetone. Ethers of 1-phenylalkanols are also more reactive toward $XO\cdot$ than 2-propanol and yield both fragmentation and ketone products. Secondary and tertiary alcohols of structure $Ph(CH_2)_nC(OH)(CH_3)R$ show high reactivity toward $XO\cdot$ and give fragmentation products when $n = 0-2$ and $R = H$ or CH_3 ; when $n = 3$ and $R = CH_3$, however, the alcohol has a reactivity similar to *tert*-butyl alcohol. 1-Deuterio-1-phenylalkanols show the same relative reactivities toward $HO\cdot$ as their hydrogen analogs but $PhCDOHCH(CH_3)_2$ gives a higher ratio of benzaldehyde (completely $PhCDO$) to ketone than does $PhCHOHCH(CH_3)_2$. Product studies indicate that the fragmentations occur by cleavage of alkyl radicals. The electrophilic radicals ($XO\cdot$) generated by several different methods, in the presence or absence of transition metals, give essentially the same reaction characteristics. The presence of $Fe(III)$, $Cu(II)$, $Hg(II)$, or complexing agents does not affect the yields, relative reactivities, or product ratios obtained with Fenton's reagent at pH 1.8, but increasing the pH to 4.6 does; the pH effects were shown to be largely due to the phenyl-substituted alcohol acting as a catalyst for the conversion of $Fe(II)$ to $Fe(III)$ at higher pH's. The characteristics of the reaction of thermally generated $SO_4^{\cdot-}$ are unchanged from pH 1.5 to 11. The results are interpreted in terms of a mechanism involving a resonance stabilized cation radical as an intermediate in the reactions of these reactive phenyl-substituted alcohols and ethers with $XO\cdot$; the results require that the cation radical be stabilized by delocalization over the aromatic ring and oxygen functions.

Our interest in the mechanisms of biological oxidation-reduction reactions and related model systems²⁻⁴ has led us to reexamine some aspects of the oxidation of alcohols and ethers by peroxydisulfate ($S_2O_8^{2-}$) and Fenton's reagent ($Fe(II)$ and H_2O_2). Since the original report⁵ by Fenton in 1876, numerous papers concerned with the mechanism of alcohol oxidation by Fenton's reagent⁶⁻¹³ and other hydroxyl

radical systems¹⁰⁻¹⁶ have appeared. Through the efforts of these and other workers, the mechanism of oxidation of aliphatic alcohols by Fenton's reagent has been fairly well established to be that shown in eq 1-4.



Related investigations of aliphatic alcohol oxidations by $S_2O_8^{2-}$, in the presence^{6a,17} or absence¹⁸ of transition

(1) Taken in part from the Ph.D. Thesis of M. E. Snook, The Pennsylvania State University, 1971, and presented in part at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971, Abstracts, No. ORGN-135.

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(3) G. A. Hamilton, *Progr. Bioorg. Chem.*, **1**, 83 (1971).

(4) G. A. Hamilton in "Molecular Mechanisms of Oxygen Activation," O. Hayaishi, Ed., Academic Press, New York, N. Y., 1973, p 405.

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(11) (a) T. Shiga, *J. Phys. Chem.*, **69**, 3805 (1965); (b) T. Shiga, A. Boukhors, and P. Douzow in "Recent Developments of Magnetic Resonance in Biological Systems," S. Fujiwara and L. H. Piette, Ed., Hirokawa Publishing Co., Tokyo, 1968, p 146.

(12) W. A. Armstrong, *Can. J. Chem.*, **47**, 3737 (1969).

(13) G. Czapski, A. Samuni, and D. Meisel, *J. Phys. Chem.*, **75**, 3271 (1971).

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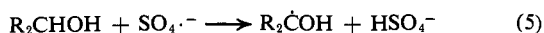
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(17) (a) R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc. B*, 1087 (1970); (b) R. O. C. Norman and P. M. Storey, *ibid.*, 1099 (1970).

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metal ions, indicate that the initial reaction of the alcohol is with the sulfate anion-radical (eq 5) in a step



very analogous to that of eq 2.

The present work is mainly concerned with the mechanistic details of the reaction of electrophilic radicals ($HO\cdot$ and $SO_4^{\cdot -}$) with alcohols. By the extensive use of internal (one alcohol giving two or more products) and external (two alcohols present) competition experiments it has been possible to gain further information concerning these reactions. The results presented here are consistent with α -hydrogen atom abstraction (eq 2 and 5) occurring with aliphatic alcohols but this is not the major initial reaction when an aromatic ring is in a suitable position. In such cases, the evidence indicates that the electrophilic radical abstracts an electron to give a resonance stabilized cation radical intermediate.

Results and Discussion

Some General Characteristics of the Oxidation and Fragmentation of Phenylalkanols by Fenton's Reagent. In some early experiments designed to determine the relative reactivity toward Fenton's reagent of a series of 1-phenylalkanols (PhCHOHR) with differing steric requirements, it was observed (Table I)¹⁹ that a major

Table I. Yields of Products from the Competitive Oxidation of PhCHOHMe and PhCHOHR by Fenton's Reagent

Reaction conditions ^a	R	% yield of observed products ^b			Moles of PhCHO/ moles of PhCOR (C/K)
		PhCOMe	PhCHO	PhCOR	
pH 1.8	Me	61	<0.001		<0.001
	Et	47	8.9	37	0.24
	<i>i</i> -Pr	46	32	6.5	4.9
	<i>t</i> -Bu ^c	37	28	4	7.0
pH 4.6	Et	12	1.3	12	0.11
	<i>i</i> -Pr	11	5.3	6.7	0.79
	<i>t</i> -Bu ^c	6.6	4.9	3.3	1.5

^a Unless otherwise noted, the reactions were run at room temperature and initiated by adding H_2O_2 . Initial concentrations of reactants: $[H_2O_2] = [FeSO_4] = 3 \times 10^{-3} M$; $[PhCHOHMe] = [PhCHOHR] = 0.011-0.013 M$. The reaction mixtures at pH 1.8 contained $HClO_4$ and those at pH 4.6 were buffered with 0.01 M acetate. ^b Based on the initial H_2O_2 concentration. ^c $[PhCHOHMe] = [PhCHOH-t-Bu] = 0.008 M$ initially.

product of the oxidation is benzaldehyde when R is ethyl, isopropyl, or *tert*-butyl. Previously, Mosher and coworkers,²⁰ while investigating the cleavage of phenyl-*tert*-butylcarbinol (PhCHOH-*t*-Bu) by chromic acid, briefly reported a similar observation using Fenton's reagent but did not follow it up. The results with Fenton's reagent were only used to point out that cleavage could proceed by a radical pathway. As will be shown presently, the large amount of cleavage observed is inconsistent with the reaction shown in eq 2 being the major reaction of $HO\cdot$ with the 1-phenylalkanols.

(19) For ease in visualization of structural variations, the following group of abbreviations are frequently used in the tables and text: Me, CH_3 ; Et, C_2H_5 ; *i*-Pr, $CH(CH_3)_2$; *t*-Bu, $C(CH_3)_3$; Ph, C_6H_5 (or C_6H_4 for disubstituted aromatic compounds).

(20) W. A. Mosher, W. H. Clement, and R. L. Hillard, *Advan. Chem. Ser.*, No. 51, 81 (1965).

A notable feature of the results shown in Table I is the high total yield (usually greater than 70%) of products obtained under acid (pH 1.8) conditions. Thus, under these conditions the cleavage to give benzaldehyde is not a minor pathway reaction. At higher pH (4.6), both the total yield and the relative amount of benzaldehyde formed decrease; the reasons for this will be discussed later. Although the molar ratio (C/K) of cleavage product (PhCHO) to ketone product (PhCOR) changes dramatically as R is varied (last column, Table I), the relative reactivities at pH 1.8 of the various 1-phenylalkanols are similar (Tables I and II). This suggests that the initial reaction of the hydroxyl radical with each of the 1-phenylalkanols is the same. Presumably some intermediate is formed which can either react to give cleavage or ketone products depending on the structure of the alcohol. As shown in Table II, all of the unsubstituted 1-phenylalkanols are considerably more reactive (5-6 times) toward Fenton's reagent than aliphatic secondary alcohols. Thus, in the former case the intermediate must have some special stability.

The formation of benzaldehyde suggests that the presence of an α hydrogen in the reactant alcohol is not necessary. Indeed it was found that the tertiary alcohol, 2-phenyl-2-propanol (cumyl alcohol), is smoothly oxidized by Fenton's reagent at pH 1.8 to acetophenone in good yield. As shown in Table II, cumyl alcohol is about half as reactive as the secondary 1-phenylalkanols but is still considerably more reactive than secondary aliphatic alcohols. A further proof that the α hydrogen of the secondary 1-phenylalkanols is not removed during the formation of benzaldehyde was obtained when PhCDOH-*i*-Pr was oxidized in H_2O solution, the benzaldehyde isolated and subjected to pmr analysis. The isolated benzaldehyde was found to be greater than 98% monodeuterated. These two results prove that eq 2 does not represent the major pathway for the reaction of $HO\cdot$ with these 1-phenylalkanols at pH 1.8.

A search for other cleavage products in the oxidation of PhCHOH-*i*-Pr by Fenton's reagent revealed the presence of 2,3-dimethylbutane (Table III). Furthermore, when the reaction is carried out in the presence of $FeCl_3$,²¹ a high yield of isopropyl chloride is obtained. These results indicate that, during the oxidation of PhCHOH-*i*-Pr by Fenton's reagent, the isopropyl radical is formed, presumably in the cleavage which leads to the benzaldehyde product. Similar radical cleavage products from two other alcohols studied in this research are also shown in Table III.

It is well known that alkyl radicals and carbonyl compounds can be formed by the fragmentation of alkoxy radicals.²³ However, the formation of alkoxy radicals from the 1-phenylalkanols upon reaction with $HO\cdot$ is unexpected on thermodynamic grounds because the oxygen-hydrogen bond energy is considerably greater than the carbon-hydrogen bond energy,²⁴

(21) J. K. Kochi (*Rec. Chem. Progr.*, 27, 207 (1966)) has shown that alkyl radicals react rapidly with various transition metal salts, frequently by an atom transfer mechanism. We have observed that $FeCl_3$ is a particularly effective alkyl radical trap in both aqueous (this work) and nonaqueous systems.²²

(22) T. M. Hellman and G. A. Hamilton, *J. Amer. Chem. Soc.*, in press.

(23) C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, 85, 1593 (1963), and references therein.

(24) S. W. Benson, *J. Chem. Educ.*, 502 (1965).

Table II. Relative Reactivities of Various Compounds (All Relative to 2-Propanol as Standard) toward the Fenton and Peroxydisulfate Systems^a

Organic compound oxidized	Products analyzed ^b	Reaction code ^c	Relative reactivity toward	
			Fenton's reagent ^d	S ₂ O ₈ ²⁻ system ^e
Secondary Aliphatic Alcohols				
2-Propanol	2-Propanone		(1.0)	(1.0)
3-Pentanol	3-Pentanone	C'	1.1	1.3
Cycloheptanol	Cycloheptanone	P ^g	0.91	2.4
Secondary 1-Phenylalkanols (Ring unsubstituted)				
PhCHOHMe	PhCOMe	C', ^h	5.8	22
PhCHOHEt	PhCHO (20), PhCOEt (80)	PH	5.5	
PhCHOH- <i>i</i> -Pr	PhCHO (84), PhCO- <i>i</i> -Pr (16)	PH	5.0	
PhCHOH- <i>t</i> -Bu	PhCHO (88), PhCO- <i>t</i> -Bu (12)	PH	5.2	
Secondary 1-Phenylalkanols (Ring substituted)				
<i>p</i> -EtPhCHOHMe	<i>p</i> -EtPhCOMe	PH	6.7	26
<i>p</i> -BrPhCHOHMe	<i>p</i> -BrPhCOMe	PH	3.2	
<i>p</i> -NPhCHOHMe	<i>p</i> -NPhCOMe	E ^g	1.3	
<i>p</i> -EtOPhCHOHMe	<i>p</i> -EtOPhCOMe	E ^g	1.4 ⁱ	
<i>p</i> -MeOPhCHOH- <i>t</i> -Bu	<i>p</i> -MeOPhCHO (83), <i>p</i> -MeOPhCO- <i>t</i> -Bu (17)	D	4.0 ⁱ	
Other Secondary Phenylalkanols				
PhCH ₂ CHOHMe	CH ₃ CHO (>90)[>90], PhCH ₂ COMe (trace)[trace]	PH	11	42
PhCH ₂ CH ₂ CHOHMe	CH ₃ CHO (50)[66], PhCH ₂ CH ₂ COMe (50)[34]	PH	9	25
α -Tetralol	α -Tetralone	PP'	3.7	
Deuterated Secondary Alcohols				
Cycloheptanol (D-1)	Cycloheptanone	PH'	0.70	1.5
PhCDOHMe	PhCOMe	B	5.9	
PhCDOH- <i>i</i> -Pr	PhCDO (89), PhCO- <i>i</i> -Pr (11)	PH	4.5	
Ethers				
PhCH ₂ OMe	PhCHO	PH	5.5	18
PhCH(OMe)- <i>i</i> -Pr	PhCHO (34)[78], PhCO ₂ Me (19)[<0.1], PhCO- <i>i</i> -Pr (47)[22]	PH	3.9	14
Tertiary Alcohols				
PhC(Me) ₂ OH	PhCOMe	C'	2.4	8.4
PhCH ₂ C(Me) ₂ OH	MeCOMe	C	9.0	
PhCH ₂ CH ₂ C(Me) ₂ OH	MeCOMe (>99), PhCH ₂ CH ₂ COMe (<1)	C'	3.1	
PhCH ₂ CH ₂ CH ₂ C(Me) ₂ OH	MeCOMe	PE ^g	<0.02	
(Me) ₃ COH	MeCOMe	PE ^g	0.01	0.05
Aromatic Hydrocarbon				
Benzene	Phenol (55), biphenyl (45)	P	2.0	

^a The relative reactivities were calculated from results obtained in a series of competition reactions involving in each case equimolar amounts of two different organic compounds, one being that listed in the first column, and the other, that indicated by the code in the third column. In all cases (except the benzene reaction) the relative reactivities were determined on the basis of quantitative carbonyl product analysis. Unless otherwise noted, the total yield of observed carbonyl products in any individual competition reaction was greater than 70% (based on the initial H₂O₂ or S₂O₈²⁻ concentrations). ^b Where two or more carbonyl products are formed the relative yields of each obtained with Fenton's reagent are given in parentheses, and the relative yields obtained with the peroxydisulfate system are given in brackets. ^c Competing reactants: PH = PhCHOHMe; C = cycloheptanol; P = 2-propanol; B = *p*-BrPhCHOHMe; PE = 3-pentanol; D = PhCHOH-*t*-Bu; E = *p*-EtPhCHOHMe; PP = PhCHOHEt; ^d Reaction conditions: room temperature, pH 1.7-1.8 (HClO₄), the total alcohol (or alcohol plus ether) concentration (usually 0.02 M or greater) was always in five- to tenfold excess of the FeSO₄ and H₂O₂ concentrations (both usually 3 × 10⁻³ M); in some cases the solubility of one of the reactants was too low and thus all the concentrations were diminished proportionately; reactions initiated by adding H₂O₂. ^e Reaction conditions: 75° for 2 hr, pH 1.8 (HClO₄), alcohol concentrations as noted in footnote *d*, [K₂S₂O₈] = 3 × 10⁻³ M or lower for the same reasons as noted in footnote *d*. ^f Total yield of observed products, 45-62%. ^g Total yield of observed products, 14-33%. ^h Similar but slightly lower numbers are obtained when PhCHOHMe and 2-propanol are the competing reactants; the competition with cycloheptanol has been repeated many times and is considered to be the more accurate. ⁱ For the reasons given in the text these numbers are not accurate measures of the relative reactivities of these compounds toward the electrophilic radicals.

especially that of the α -carbon-hydrogen of the secondary 1-phenylalkanols. In any event, by studying the oxidation of some ethers of the 1-phenylalkanols, alkoxy radicals were shown experimentally not to be necessary intermediates in either the oxidation or fragmentation reactions. Thus, benzylmethyl ether and PhCH(OCH₃)-*i*-Pr are readily oxidized by Fenton's reagent and their reactivities are similar to the 1-phenylalkanols (Table II). Furthermore, PhCH(OCH₃)-*i*-Pr gives considerable amounts of cleavage products (PhCHO and PhCO₂Me). The similarities in the ether and alcohol oxidations strongly imply that alkoxy radicals are not obligatory intermediates in

either reaction; no reasonable mechanism is available for the formation of alkoxy radicals from the ether.

In Table IV are summarized the results of some experiments designed to determine what conditions affect the ratio (C/K) of fragmentation to oxidation (ketone formation) with one specific alcohol. The overall yield and C/K ratio remain remarkably constant for a considerable variation in conditions. Several of the additives (Fe(III), Cu(II), and Hg(II)) are known to efficiently trap radicals^{7,8,25} (see, for example, eq 3) and others (Cl⁻ and CH₃COOH) form relatively strong

(25) W. A. Waters, "Mechanism of Oxidation of Organic Compounds," Wiley, New York, N. Y., 1964, p 37.

Table III. Carbonyl and Noncarbonyl Cleavage Products Obtained from the Oxidation of Various Phenyl Alcohols by Fenton's Reagent

Reactant ^a	Carbonyl cleavage product ^b	Major noncarbonyl cleavage products	
		In the absence of added FeCl ₃ ^c	In the presence of 0.1 M FeCl ₃ ^c
PhCHOH- <i>i</i> -Pr	PhCHO (67)	(Me) ₂ CHCH- <i>i</i> -PrOH (16) <i>i</i> -PrOH (33)	<i>i</i> -PrCl (39)
PhCH ₂ C(Me) ₂ OH	MeCOMe (100)	PhCH ₂ CH ₂ Ph (64)	PhCH ₂ Cl (48)
PhCH ₂ CH ₂ CHOHMe	MeCHO (46)		PhCH ₂ CH ₂ Cl (65)

^a Reaction conditions: room temperature, pH 1.8, initial concentrations: [FeSO₄] = [H₂O₂] = 3 × 10⁻³ M, [alcohol] = 0.011–0.013 M; reaction initiated by adding H₂O₂. ^b Yields in parentheses based on initial H₂O₂ concentration; yield given for the reaction in the absence of FeCl₃. ^c Yields in parentheses based on initial H₂O₂ concentration and calculated assuming 1 mol of monomeric product requires 1 mol of H₂O₂ and 1 mol of dimeric product requires 2 mol of H₂O₂.

Table IV. Effect of Reaction Conditions on the Products Formed on Oxidation of PhCHOH-*i*-Pr by Fenton's Reagent

Alteration of standard conditions ^a	% yield of obsd products ^b		C/K ^c
	PhCHO	PhCO- <i>i</i> -Pr	
No alteration	67	13	5.1
[FeSO ₄] = 1.5 × 10 ⁻³ M	60	12	5.0
[H ₂ O ₂] = 6 × 10 ⁻³ M	71	14	5.1
FeSO ₄ added last	72	12	6.0
1.5 × 10 ⁻² M Fe(ClO ₄) ₃ present	64	12	5.3
0.1 M CuSO ₄ present	70	12	5.8
0.1 M Hg(NO ₃) ₂ present	92	16	5.8
0.1 M NaCl present	70	14	5.0
0.1 M CH ₃ COOH present	61	12	5.1
pH 4.6 ^d	8.3	8.1	1.0
pH 4.6, ^d EDTA ^e	1.5	5.2	0.3

^a Standard conditions: alcohol, 0.011 M; [H₂O₂] = [FeSO₄] = 3 × 10⁻³ M; pH 1.7–1.8 (HClO₄); reactions initiated by adding H₂O₂. ^b Based on initial H₂O₂ concentration. ^c Mol of PhCHO/mol of PhCO-*i*-Pr. ^d 0.01 M acetate buffer. ^e Ethylenediaminetetraacetic acid (EDTA) present at 6 × 10⁻³ M.

complexes, especially with Fe(III). Since these alterations do not affect C/K, it can be concluded that, if the reaction of eq 3 is involved in the formation of ketone product, that step must follow the step which is product determining. The results also indicate that the fragmentation and ketone products cannot arise from a precursor radical known to be trapped by the above metal ions. As mentioned earlier, pH does affect the yield and C/K ratio and this will be considered later.

Effects of Variations in the Alcohol Structure. The presence of a benzene ring in the alcohol is necessary in order to get the high reactivity and fragmentations discussed above. This is most readily illustrated by comparing the reactions of cumyl alcohol and *tert*-butyl alcohol (Table II). Whereas the former is oxidized readily to acetophenone, *tert*-butyl alcohol yields only a barely detectable amount of acetone;²⁶ its relative reactivity determined by ketone product analysis is

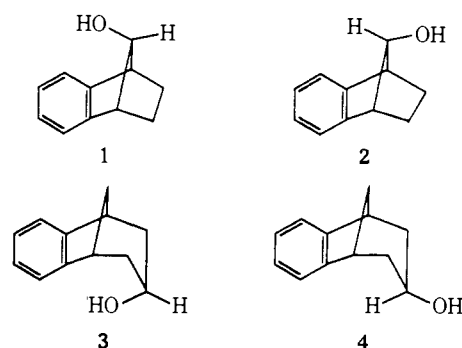
(26) This is consistent with earlier results²⁷ that Fenton's reagents converts *tert*-butyl alcohol in reasonable yield to 2,5-dimethyl-2,5-hexanediol.

(27) D. D. Coffman, E. L. Jenner, and R. D. Lipscomb, *J. Amer. Chem. Soc.*, **80**, 2864 (1958).

less than 1% that of cumyl alcohol. It is thus clear that the benzene ring is somehow involved in allowing an intermediate to form which cannot be formed in its absence.

Although the presence of a phenyl group in the molecule is required in order to obtain the above reaction characteristics, the phenyl group does not have to be attached to the same carbon as the OH group. Thus secondary and tertiary acyclic alcohols with one and two CH₂ groups separating the aromatic ring and C–OH groups also show high reactivity and fragmentation reactions (Table II). In fact the molecules with one CH₂ separating the two groups show the highest reactivity of any studied. When three CH₂ groups separate the phenyl and C–OH groups, however, the alcohol behaves as a typical aliphatic alcohol (Table II).

Some efforts were made to obtain information concerning the conformational relationship between the phenyl ring and alcohol groups required for the special reactivity. This was done by attempting to determine the relative reactivities of the cyclic alcohols, α - and β -tetralol, and the bicyclic alcohols, 1–4. Because of the



difficulties involved in predicting and analyzing for the various carbonyl products which might be formed, these relative reactivities were determined by analyzing for alcohol disappearance. Determined in this way it was found that α - and β -tetralol gave reactivities very similar to their open chain analogs (PhCHOHET and PhCH₂CHOHCH₃, respectively). A complication in the experiments with 1–4 is their extremely low solubility in water. Nevertheless, it can be qualitatively stated that 1 and 2 have nearly equal reactivity but 3 is 3–4 times more reactive than 4.

Generality of the Reaction. Systems Other than Fenton's Reagent. As indicated by the results summarized in Table V, Fenton's reagent is not unique in showing high reactivity toward, and giving fragmentation products from, phenylalkanols. The Fe(II) can be replaced by Ti(III), and even eliminated altogether (photolysis of H₂O₂), and similar reaction characteristics are observed. It is difficult to obtain quantitative data in the photolysis experiments because the carbonyl products are unstable under the reaction conditions. However, a time study of product formation indicated that benzaldehyde is formed in considerable excess over the ketone when PhCHOH-*i*-Pr is the reactant. Furthermore, acetophenone is a product when cumyl alcohol is reacted with H₂O₂ under photolysis conditions.

The results in Table V show that even the hydroxyl radical is not required; similar characteristics are ob-

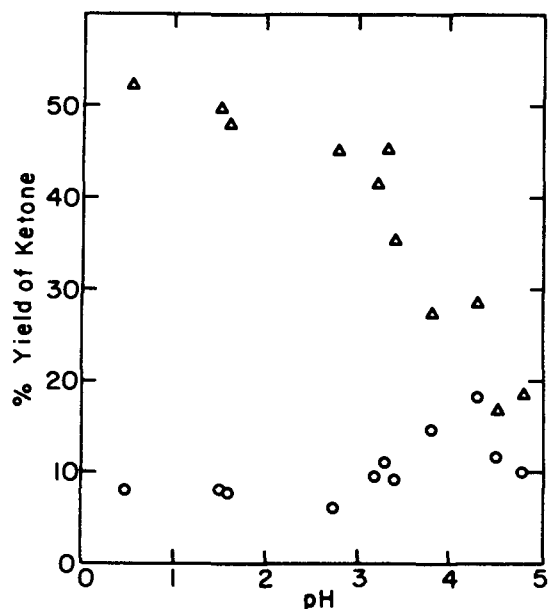


Figure 1. Effects of pH on the yields of ketones formed from the competitive oxidation of 1-phenylethanol and cycloheptanol by Fenton's reagent: (Δ) acetophenone yield; (○) cycloheptanone yield (yields based on initial amount of H_2O_2). Reaction conditions were similar to those in footnote *d*, Table II, except that acetate buffers were used at the higher pH's.

Table V. Characteristics of the Reactions of Hydroxyl and Sulfate Anion Radicals Generated by Various Methods

Radical reactant and generation method	Reactivity of PhCHOHMe relative to cycloheptanol ^a	C/K from PhCHOH- <i>i</i> -Pr ^b
$H_2O_2 + Fe(II) \rightarrow \cdot OH^c$	6.4	5.1
$H_2O_2 + Ti(III) \rightarrow \cdot OH^d$	4-5	10.6
$H_2O_2 + h\nu \rightarrow \cdot OH^e$		>4
$S_2O_8^{2-} + \text{heat} \rightarrow SO_4^{\cdot - f}$	9.1	4.0
$S_2O_8^{2-} + Fe(II) \rightarrow SO_4^{\cdot - g}$	7.8	
$S_2O_8^{2-} + Ti(III) \rightarrow SO_4^{\cdot - h}$	11	

^a Obtained from competition experiments; relative reactivity = mol of PhCOCH₃/mol of cycloheptanone produced. ^b Mol of PhCHO/mol of PhCOCH(CH₃)₂ produced in experiments where PhCHOH-*i*-Pr is the only organic reactant. ^c Reaction conditions as given in Table II. ^d Same reaction conditions as in footnote *c* except Ti(III) present at $5.3 \times 10^{-3} M$ instead of Fe(II). ^e See Experimental Section for details. ^f Reaction conditions as given in Table II, footnote *e*. ^g Same as *c* except $K_2S_2O_8$ at $3 \times 10^{-3} M$ used instead of H_2O_2 . ^h Same as *g* except $Ti_2(SO_4)_3$ at $2.4 \times 10^{-3} M$ used instead of Fe(II).

served upon reaction of the alcohols with the sulfate anion radical, generated thermally (in the absence of transition metal ions) or by metal ion reactions with peroxydisulfate. A survey of many different types of radicals was not performed but one suspects from mechanism considerations (see below) that only strongly electrophilic radicals would be effective reagents. The reaction of thermally generated (at 75°) $SO_4^{\cdot -}$ with the phenylalkanols and ethers occurs cleanly in high yield. Thus, the relative reactivities of several of these compounds toward $SO_4^{\cdot -}$, as well as the product distributions obtained, are given in Table II for comparison with those observed with Fenton's reagent. It can be seen that $SO_4^{\cdot -}$ is even more selective toward the phenylalkanols (relative to secondary aliphatic alcohols) than is $HO\cdot$.

pH Effects. Three very definite changes in the characteristics of the alcohol oxidations by Fenton's reagent occur when the pH is increased from 1.8 to 4.6. They are: (1) the total yield of carbonyl products obtained from 1-phenylalkanols decreases (Tables I and IV), (2) the ratio (C/K) of fragmentation to ketone products decreases (Tables I and IV), (3) the reactivity (as determined from carbonyl product analysis in competition reactions) of the 1-phenylalkanols relative to secondary aliphatic alcohols drops considerably (Figure 1). The results in Figure 1 indicate that this relative reactivity decrease to almost 1.0 at pH 4.6 is mainly due to the decrease in yield of product formed from the 1-phenylalkanol; the yield of ketone obtained from the aliphatic alcohol does not change as markedly.

None of the above effects is observed with the thermally generated $SO_4^{\cdot -}$ system. From competition experiments with this system it was found that the reactivity of the 1-phenylalkanols relative to secondary aliphatic alcohols remains the same at pH 4.6 as it is at pH 1.8. Also, the results summarized in Table VI

Table VI. Effects of pH on the Yields and Ratios of Products Obtained from the Oxidation of PhCHOHR with Peroxydisulfate

R	pH ^a	% yield of obsd products ^b		C/K ^c
		PhCHO	PhCOR	
Et	1.6	23	94	0.24
	4.2	24	82	0.29
	4.6	22	69	0.32
	6.3	19	82	0.23
	8.9	19	81	0.23
	10.9	19	73	0.26
	12.7	7	40	0.18
<i>i</i> -Pr	1.7	78	18	4.3
	4.6	81	21	3.9
	6.9	82	25	3.3
	8.7	78	20	3.9

^a Reaction conditions: thermostated at 75° for 2 hr; initial concentrations: $[K_2S_2O_8] = 3 \times 10^{-3} M$, $[PhCHOHR] = 0.011-0.013 M$; pH's reported were measured at the end of the reaction; buffers used: pH 1.6-1.7, 0.035 *M* HClO₄; pH 4.2, 0.01 *M* acetate; pH 4.6, 0.05 *M* (R = Et) and 0.10 *M* (R = *i*-Pr) acetate; pH 6.3, 0.01 *M* phosphate; pH 6.9, 0.05 *M* phosphate; pH 8.7-8.9, 0.01 *M* borate; pH 10.9, 0.01 *M* phosphate; pH 12.7, 0.01 *M* NaOH; in the few cases tested, the buffer concentration had no significant effect on the results. ^b Based on the initial $K_2S_2O_8$ concentration. ^c C/K is the molar ratio of aldehyde to ketone products.

indicate that the total yield and C/K ratio remain constant from pH 1.5 to 11; only above pH 12 does the yield begin to decrease and that is probably due to instability of the carbonyl products under these conditions. Thus, the changes in the reaction characteristics observed with Fenton's reagent as the pH is increased must be caused by some component of that particular system.

In further experiments designed to determine the reason for the pH effects on the Fenton system, the material balance for the reaction under various conditions was investigated, *i.e.*, attempts were made to account for all the H_2O_2 initially added. The results are summarized in Table VII. Except for the oxidation of cycloheptanol at low pH, essentially all the H_2O_2 which reacts gives rise to either carbonyl products from the alcohols or Fe(III) from Fe(II). At low pH

Table VII. Determination of the Material Balance in the Oxidation of Various Alcohols by Fenton's Reagent^a

Alcohol (initial amount, moles $\times 10^5$)	pH ^b	Mol of H ₂ O ₂ remaining $\times 10^5$ (X)	Mol of Fe(III) produced $\times 10^5$ (Y)	Mol of alcohol loss $\times 10^5$	Mol of ketone produced $\times 10^5$ (Z)	% H ₂ O ₂ accounted for ^c
None	1.8	8.4	13.5			101
Cycloheptanol (25.0)	1.8	0	9.3	11.2	1.5	41
Cycloheptanol (130)	1.8	0	10.0	16 ^d	2.3	48
2-Propanol (25.0)	2.5	0	6.4	14.3	10.7	92
2-Propanol (130)	1.8	0	3.3	18 ^d	15.3	113
PhCHOHMe (20.0)	1.8	0	5.4	10.5	9.2	79
PhCHOH- <i>i</i> -Pr (55.0)	1.8	0	3.9		11.7 ^e	91
<i>p</i> -MeOPhCHOHMe (25.0)	1.8	5.6	15.0	1.2	0.84	93
None	4.6	9.2	14.1			108
Cycloheptanol (130)	4.6	3.2	15.0		2.7	89
2-Propanol (25.0)	4.6	1.9	15.0	6.7	5.2	97
2-Propanol (25.0) ^f	4.6	0	15.6	7.2	5.7	90
PhCHOH- <i>i</i> -Pr (55.0)	4.6	2.8	15.0		2.2 ^e	83

^a Initial conditions: [H₂O₂] = [FeSO₄] = 15 $\times 10^{-5}$ mol per reaction (total volume, 50 ml); reaction initiated by adding H₂O₂. ^b pH 1.8, 0.035 M HClO₄; pH 2.5, 0.01 M H₂SO₄; pH 4.6, 0.01 M acetate. ^c Calculated from (X + 0.5Y + Z)(100)/15. ^d Inaccurate because obtained by taking the difference between two large numbers. ^e Mol of PhCHO + mol of ketone. ^f [FeSO₄] = 30 $\times 10^{-5}$ mol.

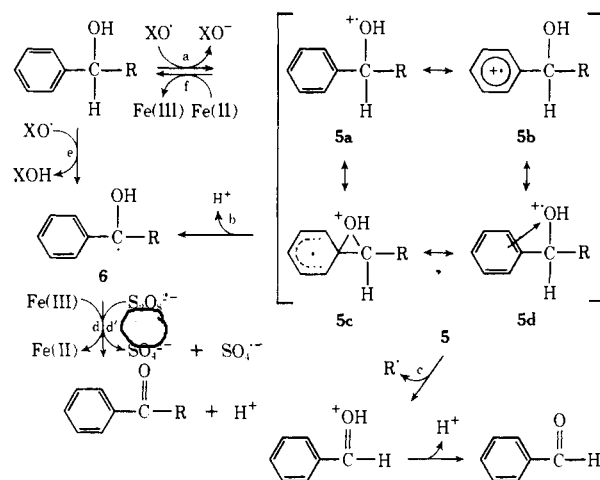
cycloheptanol obviously gives rise to other products which were not characterized.²⁸ This is shown not only by the low per cent of H₂O₂ accounted for (last column) but also by the large difference between the amount of alcohol which reacts and the amount of cycloheptanone formed. Presumably the secondary hydrogens on cycloheptanol can be abstracted and these radicals lead to other products. For the other alcohols studied the carbonyl products are the major oxidation products; usually the amount of alcohol which reacts is only slightly greater than the amount of ketone formed.

The simple oxidation of Fe(II) to Fe(III) (stoichiometry: H₂O₂ + 2Fe(II) \rightarrow 2Fe(III) + 2OH⁻) is always a competing reaction in oxidations by Fenton's reagent, and to the extent that it occurs the yield of oxidized organic products will be decreased. It can be seen from Table VII that at low pH (1.8–2.5) the amount of oxidation of Fe(II) to Fe(III) is usually fairly low (the one exception, when *p*-MeOPhCHOHMe is the reactant, will be considered later). However, at pH 4.6 the oxidation of Fe(II) to Fe(III) becomes a major reaction, so much so that some H₂O₂ usually remains at the end of the reaction if the Fe(II) is present initially at the same concentration as the H₂O₂. Thus, the yields at pH 4.6 quoted in Tables I and IV are artificially low because they were calculated assuming that the H₂O₂ completely reacted. Probably one of the reasons for the high conversion of Fe(II) to Fe(III) at pH 4.6 is that the Fe(III) comes out of solution; an orange-brown precipitate is observed under such conditions. This would prevent the reaction of eq 3 from occurring, a reaction which causes regeneration of some Fe(II) from Fe(III) in the usual Fenton oxidation. The above probably accounts for the somewhat lower yield of acetone from 2-propanol at pH 4.6 relative to pH 1.8. However, the drop in yield of carbonyl products from PhCHOH-*i*-Pr is considerably greater, and some other effect must be involved (see next section).

Mechanism. Essentially all of the present data on the reaction of electrophilic radicals (XO[•], where X = H or SO₃⁻) with the reactive phenylalkanol and

ethers can be readily rationalized in terms of the mechanism shown in Scheme I (illustrated for a secondary 1-

Scheme I



phenylalkanol but related structures and steps would apply for the other organic reactants). In considering this mechanism the discussion will focus initially on evidence for the various steps; the detailed structure of the postulated intermediate (5) will be considered in the next section.

There can be little doubt that some intermediate other than 6 is involved in the major portion of the reaction of these reactive phenylalkanol and ethers with XO[•]. The fact that the relative reactivity of PhCHOHR is independent of R, while the ratio of aldehyde to ketone products changes dramatically (Tables I and II) indicates that the steps which determine whether aldehyde or ketone will be formed occur subsequent to an irreversible reaction with XO[•]. Thus, the intermediate presumably retains most of the elements of the original reactant alcohol, and either step a or a closely related step is indicated. Strong evidence for the same conclusion is the observation (Table II) that the tertiary alcohol, PhC(Me)₂OH, which must split off a methyl radical to give acetophenone, has only a slightly lower reactivity than PhCHOHMe which gives none of the product where a methyl radical is cleaved. The results summarized in Table IV, showing that the presence of various metal

(28) This fact does not invalidate the relative reactivities listed in Table II because the conditions for those experiments were always the same, and the relative reactivities quoted are for reaction of the alcohol to give carbonyl products.

ions and complexing agents does not affect the aldehyde to ketone ratio formed from a particular alcohol, imply that the product-determining steps occur before any further interaction of an intermediate radical with the oxidized metal ions. Steps b and c are consistent with that. The observation that alkyl radicals are apparently formed during the cleavage reactions (Table III) is additional evidence for a step like c. Furthermore, the ratio (C/K) of fragmentation to ketone products formed from PhCHOHR (Table I) increases as expected for a competition between steps b and c when R is varied from methyl to *tert*-butyl (order of alkyl radical stability: tertiary > secondary > primary > CH₃). The solvent water is presumably the base which accepts the proton in step b because pH and buffer concentration have no effect on C/K when the less complex thermal SO₄^{·-} system is used as oxidant (Table VI). The present work gives no information concerning steps d (in the Fenton reaction) and d' (in the thermal SO₄^{·-} system) but these have been well authenticated by the results of other workers.^{6-8,18}

The isotope effects observed when deuterium is substituted for hydrogen in the α position of some secondary alcohols (Table II) are additional evidence for steps a, b, and c as written in Scheme I. From the relative reactivities one can calculate that cycloheptanol shows a small but definite isotope effect ($k_H/k_D = 1.3$ for the Fenton reaction and 1.6 for the SO₄^{·-} reaction), about the magnitude expected for hydrogen atom abstraction (equivalent to step e, Scheme I) by the reactive XO[·] species. On the other hand, k_H/k_D as calculated from the relative reactivities of the 1-phenylalkanols is within experimental error equal to 1.0. This is expected for step a because the C-H bond is not broken in that step. There is, however, an isotope effect on the ratio of aldehyde to ketone products formed from phenylisopropyl carbinol; C/K for PhCHOH-*i*-Pr = 5.3 and for PhCDOH-*i*-Pr = 8.1. This implies that in the *competing steps* which lead eventually to aldehyde and ketone the α -carbon-hydrogen bond is broken in the step leading to ketone (k_H/k_D ca. 1.5) and not in that leading to aldehyde. Steps b and c are consistent with that.

Step f is apparently the main reason for the pH effects observed with Fenton's reagent. The large decrease in yield of carbonyl products from the 1-phenylalkanols as the pH is raised from 1.8 to 4.6 (Tables I and IV) is largely due to the simple oxidation of Fe(II) to Fe(III) by the H₂O₂ (Table VII). A combination of the reactions in eq 1 and steps a and f would lead to that result. For most of the alcohols studied, f apparently occurs to a negligible extent at the low pH (1.8). Presumably the reason it occurs more rapidly at higher pH is because an ionized or buffer-complexed form of the aquo Fe(II) is a better electron donor than aquo Fe(II) itself. This is not unexpected.

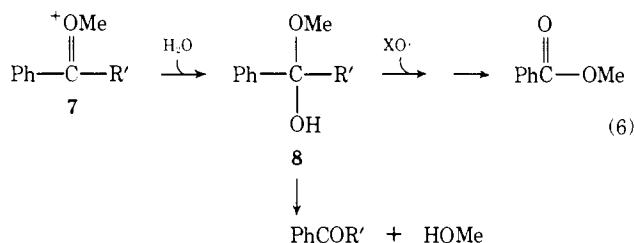
For one group of alcohols, the 4'-alkoxy-1-phenylalkanols, step f apparently competes with b and c even at pH 1.8. This is evident from the following results. Based on the initial H₂O₂ concentration, the yield of carbonyl products from the oxidation of the above alcohols by Fenton's reagent at pH 1.8 is always low (frequently less than 20%), but this is not due to other reactions of the alcohol; the results in Table VII indicate that the amount of alcohol reacted corresponds

closely to the amount of ketone formed. Rather, the main reaction is the simple oxidation of Fe(II) to Fe(III). The total yield of carbonyl products is low even when the alkoxy-substituted alcohols are oxidized in competition with another alcohol which usually gives a high yield of product. For example, in a typical competition experiment at pH 1.8 (Fenton's reagent) containing equimolar amounts of *p*-EtPhCHOHMe and *p*-EtOPhCHOHMe the yields of the ketones formed were 24 and 6.3% (based on initial H₂O₂ concentration), respectively. Such results indicate that the alkoxy-substituted alcohol is not just not reacting with XO[·], but rather is acting as a catalyst for the conversion of Fe(II) to Fe(III) as a combination of the reactions in eq 1 and steps a and f would predict. The fact that the yield of *p*-EtPhCOMe in the above competition experiment is considerably less than 50% indicates that *p*-EtOPhCHOHMe is actually more reactive in the step a reaction than is *p*-EtPhCHOHMe.

The reason that f is more important with the alkoxy-substituted aryl alcohols is presumably because 5 is now more stable and the bimolecular reaction f can compete with the essentially unimolecular reactions b (which also involves solvent) and c. Because step f does occur the relative reactivities for the 4'-alkoxy-1-phenylalkanols listed in Table II are not true measures of their reactivity with XO[·]. However, as measured by carbonyl product yields, the difference in the reactivity of *p*-EtOPhCHOHMe (1.4) and *p*-MeOPhCHOH-*t*-Bu (4.0) is further evidence for the correctness of the above arguments. In the former case only step b competes with f whereas in the latter the more rapid step c also competes, and thus effectively raises the calculated relative reactivity.

All of the present results are consistent with a step equivalent to e being the initial step in the reaction of XO[·] with secondary aliphatic alcohols. Since the α hydrogen of the 1-phenylalkanols should be at least as easily removed in a similar reaction (relative reactivity thus ca. 1.0), one suspects that step e should contribute somewhat in the oxidation of the 1-phenylalkanols (total relative reactivity only 5-6 toward Fenton's reagent). Several lines of evidence indicate that step e does occur to the extent of about 10-20% of the total reaction with Fenton's reagent. Some of this evidence is: (1) the aldehyde to ketone ratio (C/K) decreases markedly at higher pH (Tables I and IV); this would not be expected if e did not occur, but is easily understandable if f drains off most of 5 (the only path which can give aldehyde product) while step e occurs to the same extent as at lower pH; (2) the C/K ratio (Table I) for PhCHOH-*t*-Bu is not as large as expected considering those found for PhCHOEt and PhCHOH-*i*-Pr, and knowing the relative stabilities of alkyl radicals;²³ most of the PhCO-*t*-Bu is probably formed through step e, and step a in this case probably leads essentially completely to aldehyde (ratio of step e to step a thus 1 to 7); (3) the relative reactivity of cumyl alcohol (which cannot react by the pH-independent step e) drops to 0.2 at pH 4.6 whereas that for secondary 1-phenylalkanols (which can react by step e) drops to only about 1.0. Since the relative reactivities listed in Table II are based on total carbonyl product yields, they should be measures of the sum of the reactivity of the given alcohol by both steps a and e.

Oxidation of the ether, $\text{PhCH}(\text{OMe})\text{-}i\text{-Pr}$, by $\text{XO}\cdot$ gives methyl benzoate (in the Fenton system), benzaldehyde, and $\text{PhCO}\text{-}i\text{-Pr}$ (Table II). These are entirely consistent with the mechanism of Scheme I. In the ether reactions steps c and d (or d') would give **7** ($\text{R}' = \text{H}$ and $i\text{-Pr}$, respectively) which would be expected to add water rapidly to give **8** (eq 6). Such



hemiacetals (or hemiketals) dissociate to the alcohol and aldehyde (or ketone) fairly rapidly, and this is apparently what happens in the thermal $\text{SO}_4\cdot^-$ system where the reaction occurs over a considerable length of time. However, in the Fenton reaction, where a large number of radicals are generated in a very short time, **8** would probably not have time to dissociate completely before some of it is further oxidized (presumably by the mechanism of Scheme I) to the methyl benzoate.

Structure of the Reaction Intermediate. Any structure for the intermediate **5** must be consistent with the following observations and conclusions among others: (1) the same or a very similar intermediate is formed from the reaction of the alcohol with either $\text{HO}\cdot$ or $\text{SO}_4\cdot^-$,²⁹ (2) the intermediate must be capable of undergoing the competing reactions b, c, and f or closely related reactions, and (3) the intermediate must show some interaction between the oxygen function and the aromatic ring. One is forced to this latter conclusion by the observations that the reactive phenyl alcohols and ethers show higher reactivity toward $\text{XO}\cdot$ than do aliphatic alcohols or the benzene ring (Table II), or the sum of the two. Since $\text{HO}\cdot$ is known to react with 2-propanol and benzene with second-order rate constants of $1.1\text{--}1.7 \times 10^9$ and $3.0\text{--}4.7 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$, respectively,^{31,32} the relative reactivities of the phenylalcohols is all the more remarkable because the diffusion limit is being approached.

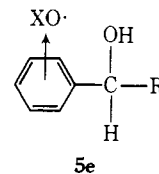
The structure of intermediate **5** which best fits all the data is the resonance stabilized cation radical illustrated by structures **5a**–**5d** in Scheme I. The data would also be consistent with the intermediate being an ion pair of XO^- with the structures illustrated in Scheme I. The small differences in the C/K ratios for the $\text{HO}\cdot$ and $\text{SO}_4\cdot^-$ reactions (Tables I, II, and VI) are some evidence for this. If the intermediate were an ion pair, then a structure such as **5e** would also contribute to the stability of the intermediate. The chlorine atom, which is another electrophilic radical, is known to form related complexes with aromatic rings.³³

(29) Under alkaline conditions ($\text{pH} > 8.5$) $\text{SO}_4\cdot^-$ apparently reacts with OH^- to give $\text{HO}\cdot$, but this does not occur³⁰ over the entire pH range investigated, so $\text{SO}_4\cdot^-$ itself must be able to react with the alcohol to give **5**. This is also evident from the fact that the relative reactivities of the various alcohols (Table II) toward $\text{SO}_4\cdot^-$ is different from that toward $\text{HO}\cdot$.

(30) L. Dogliotti and E. Hayon, *J. Phys. Chem.*, **71**, 2511 (1967).

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

(32) The results in Table II are thus in good agreement with the relative reactivity of these two compounds calculated from the reported rate constants.



It seems reasonable that **5a** and **5b** would both contribute to the stability of an intermediate cation radical because alcohols and aromatic compounds have not too dissimilar ionization potentials in the gas phase,³⁴ and a polar solvent might bring them even closer together. In order for structures like **5a** and **5b** to be in resonance the orbitals on the ring and on oxygen must overlap sufficiently so that electron transfers are more rapid than molecular vibrations. Structures **5c** (illustrating σ -orbital overlap) and **5d** (illustrating π -orbital overlap) indicate how this might occur; these are analogous to structures frequently used to illustrate homoallylic or homobenzylic resonance. If the intermediate were an ion pair, the XO part could aid in transfer of the electron from the ring to the oxygen function and vice versa (for example, by structure **5e**). For all the reactive acyclic phenyl alcohols with different numbers of methylenes between the ring and oxygen groups (Table II), five- and six-membered ring structures related to **5c** are possible, and thus resonance electron transfer seems reasonable. However, the entropy loss on cyclization eventually would become too great and $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{C}(\text{Me})_2\text{OH}$ reacts as a typical aliphatic tertiary alcohol. The data obtained using the benzocyclic systems are not too accurate but the results with **3** and **4** are in the direction expected from the above considerations. One might have expected **1** to show greater reactivity than **2** but the similar reactivity observed may be because the overlap between the oxygen and ring in **1** is small (structures related to **5c** and **5d** would require very strained four-membered rings).

The effects of substituents on the aromatic ring (Table II) are in the direction expected for an intermediate with structure **5a**–**5d**. Thus, the order of increasing reactivity for para-substituted compounds ($\text{CN} < \text{Br} < \text{H} < \text{Et}$) is the order of increasing ability to stabilize a positive charge. As discussed previously, *p*-alkoxy compounds are even more reactive but this is not reflected in the carbonyl product yields.

All of the reactions b, c, and f seem reasonable for an intermediate with the proposed structure. Reaction f (like a) is a simple electron transfer; many similar reactions are known to occur very rapidly. The ease of β -scission by alkoxy radicals suggests that a cation radical such as **5** could do the same (reaction c). Also the loss of a proton (reaction b) from positively charged intermediates in polar solvents frequently occurs very readily.

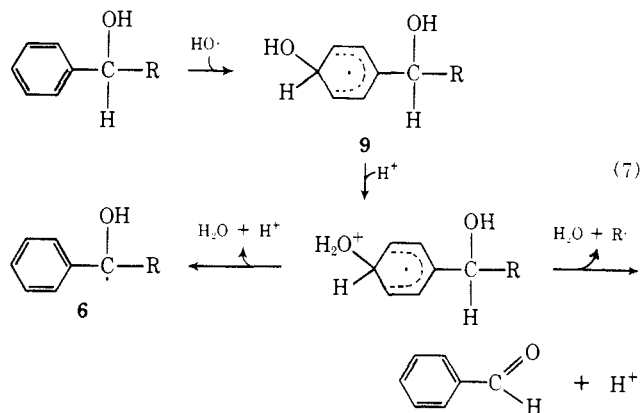
Norman and coworkers^{10b,17,35} have observed and investigated some decarboxylations of phenyl-substituted acids, and the fragmentation of 2-phenylethanol, caused by $\text{HO}\cdot$ and $\text{SO}_4\cdot^-$. They propose, largely on the basis of electron paramagnetic resonance (epr) observations, that $\text{HO}\cdot$ attacks the aromatic ring to give a σ adduct which decomposes on acid catalysis

(33) G. A. Russell, *J. Amer. Chem. Soc.*, **80**, 4987 (1958).

(34) J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, and F. H. Field, *Nat. Stand. Ref. Data Ser., Nat. Bur. Stand.*, **No. 26** (1969).

(35) R. O. C. Norman, *Chem. Soc., Spec. Publ.*, **No. 24**, 117 (1970).

to give the observed cleavage products. Their mechanism adapted to the presently studied 1-phenylalkanoles would be as shown in eq 7. For the reactions



with $\text{SO}_4^{\cdot-}$ they suggest that the mechanism may be the same (but without the acid catalysis) or possibly that the $\text{SO}_4^{\cdot-}$ abstracts an electron from the aromatic ring prior to, or synchronous with, the fragmentation.¹⁷ It is unlikely that the mechanism of eq 7 is involved in the presently studied reactions for the following reasons among others: (1) the formation of **9** is the slow step in aromatic substitutions performed by $\text{HO}\cdot$, and aromatic substitutions of benzene (Table II) and alkylbenzenes³¹ occur more slowly than the present oxidations and fragmentations by $\text{HO}\cdot$; thus it is a kinetically incompetent intermediate for the present reactions; (2) σ adducts like **9** react rapidly with Fe(III) , Cu(II) , etc. to give phenols^{36,37} yet the presence of these ions has no effect on the yield of oxidation and fragmentation products (Table IV); (3) it is not expected that Fe(II) would react with **9** in a rapid reaction to regenerate the alcohol (shown by the stoichiometry studies of Table VII) because a σ bond would have to be broken in the process; (4) the similarities of the $\text{SO}_4^{\cdot-}$ and $\text{HO}\cdot$ reactions indicate a common mechanism and one would not expect an intermediate like **9** to form from $\text{SO}_4^{\cdot-}$; (5) the pH effects and stoichiometry studies are readily explainable by the mechanism of Scheme I whereas that of eq 7 predicts that **9** should give a phenol and dimer at higher pH's rather than simply oxidation of Fe(II) and Fe(III) ; some phenol and dimer may be formed from the phenylalkanoles but their concentrations must be small and not vary much with pH (the results in Table VII indicate that phenylalkanol loss is only slightly greater than carbonyl product formed at all pH's).

Thus, the mechanism of Scheme I is strongly favored over that of eq 7 for all the reactions of $\text{HO}\cdot$ and $\text{SO}_4^{\cdot-}$ studied here. It is felt that the same mechanism may hold for the decarboxylations and fragmentations observed by Norman, *et al.*^{10,17,35} These workers based much of their mechanistic conclusions on the observation by electron paramagnetic resonance (epr) of hydroxycyclohexadienyl radicals (similar to **9**) in some of their systems. However, by epr one will observe the most stable radical in a system, and this may be involved in a side reaction rather than on the main pathway. Until the observed radicals are shown by

(36) J. R. Lindsay Smith and R. O. C. Norman, *J. Chem. Soc.*, 2897 (1963).

(37) C. R. E. Jefcoate, J. R. Lindsay Smith, and R. O. C. Norman, *J. Chem. Soc. B*, 1013 (1969).

kinetic, stoichiometric, or other means to lead to the main product of the reaction, epr results are not good evidence for a particular mechanism.

Possible Biological Significance. It has not escaped our attention that the resonance stabilization observed in **5** may be involved in various enzymic reactions. Thus, an intermediate oxycation radical, nitrogen cation radical, etc. could be stabilized if it were in proximity to enzymic aromatic residues such as the side chain of phenylalanine, tyrosine, or tryptophan. Specific enzymic reactions in which this may be involved will be discussed in subsequent publications.

Experimental Section

Materials. Unless otherwise noted, all compounds were obtained commercially and were shown by gas chromatography to be free of interfering impurities. The following alcohols (the numbers in parentheses refer respectively to the boiling point at the given pressure in mm) were prepared by NaBH_4 or NaBD_4 reduction of the corresponding ketones:³⁸ *p*-BrPhCHOHCH₃ (93, 0.35); *p*-NCPhCHOHCH₃ (133, 0.75); *p*-CH₃OPhCHOHCH₃ (83, 0.52); *p*-CH₃CH₂OPhCHOHCH₃ (88, 0.15); *p*-CH₃CH₂PhCHOHCH₃ (81.5, 0.5), PhCHOHCH(CH₃)₂ (97.5, 5.0); PhCH₂CHOHCH₃ (65–66, 1.0); PhCH₂CH₂CHOHCH₃ (85, 0.5); α -tetralol (94, 0.24); β -tetralol (91, 0.70); PhCDOHCH₃ (42–47, 0.08); PhCDOHCH(CH₃)₂ (60, 0.55); cycloheptanol (D-1) (47.5, 0.65). All gave satisfactory proton magnetic resonance (pmr) spectra (less than 3% of each of the deuterated alcohols had hydrogen in the α position), and all were shown to be free of ketone by gas chromatography.

2-Methyl-5-phenyl-2-pentanol was prepared from 4-phenylbutanoic acid as follows: 30 g (0.138 mol) of 4-phenylbutanoic acid was converted to the methyl ester with SOCl_2 and methanol.³⁹ At 84° (0.65 mm), 28 g of methyl 4-phenylbutanoate, representing a 91% yield, was isolated: pmr (CCl_4) δ 7.12 (s, 5, ring H), 3.60 (s, 3, OCH₃), 2.2 (m, 6, (CH₂)₃). Twenty-four grams of the ester was treated with 2 equiv of methyl Grignard by the method of Fieser and Fieser;⁴⁰ 20 g of 2-methyl-5-phenyl-2-pentanol was isolated by distillation at 81–86° (0.25 mm) [lit.⁴¹ 120° (7 mm)]; pmr (CCl_4) δ 7.10 (s, 5, ring H), 2.8 (s, 1, OH), 2.5 (m, 2, PhCH₂), 1.6 (m, 4, PhCH₂CH₂CH₂), 1.10 (s, 6, C(CH₃)₂OH).

1-Methoxy-2-methyl-1-phenylpropane (α -isopropylbenzyl methyl ether) was prepared from 2-methyl-1-phenyl-1-propanol; 9 g (0.06 mol) of 2-methyl-1-phenyl-1-propanol was dissolved in 90 ml of *N,N*-dimethylformamide (dried over molecular sieve). After the addition of 10.1 g (0.09 mol) of potassium *tert*-butoxide, 14.5 ml (0.15 mol) of dimethyl sulfate was slowly added while keeping the temperature between 20 and 30° with an ice bath. The mixture was stirred for 30 min and then poured into 200 ml of water. After mixing, the water was removed and the organic layer washed with 100 ml of 10% NaHCO_3 and 3 \times 100-ml portions of H_2O . The organic liquid was taken up in ether and dried over anhydrous Na_2SO_4 . The ether was evaporated and the crude product distilled. Five grams of 1-methoxy-2-methyl-1-phenylpropane was isolated by distillation at 49° (1.25 mm): pmr (CCl_4) δ 7.22 (s, 5, ring H), 3.70 (d, 1, $J = 6.5$ Hz, PhCH), 3.14 (s, 3, CH₃O), 1.8 (m, 1, CH(CH₃)₂), 0.85 (two doublets, 6, $J = 6.5$ and 6.5 Hz, CH(CH₃)₂).

Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{O}$: C, 80.44; H, 9.82; O, 9.74. Found: C, 80.21; H, 9.82; O, 9.76.

2,2-Dimethyl-1-(4'-methoxyphenyl)-1-propanol (*p*-CH₃OPhCH(OH)-*t*-Bu) was prepared from anisaldehyde and *tert*-butyllithium; 24 ml (0.0528 mol) of a solution of *tert*-butyllithium in pentane (2.2 M) was placed in a 1-l. dry-nitrogen-purged three-necked flask. A solution containing 4 g (0.03 mol) of anisaldehyde dissolved in 100 ml of dry pentane and 20 ml of dry tetrahydrofuran was slowly added to the stirred, ice-cooled *tert*-butyllithium. After addition was complete, the reaction mixture was refluxed for 2 hr and then cooled with ice. Following the addition of 75 ml of 95% ethanol

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to destroy the excess *tert*-butyllithium the mixture was poured into 200 ml of H₂O, and the solution was extracted with 3 × 100-ml portions of ether. The ether layer was dried over anhydrous Na₂SO₄, filtered, and evaporated with a rotary evaporator. Distillation at 106° (0.35 mm) [lit.⁴² 132° (5 mm)] of the crude product afforded 3.1 g (55% yield) of *p*-CH₃OPhCHOH-*t*-Bu: pmr (CDCl₃) δ 7.0 (m, 4, ring H), 4.30 (s, 1, PhCH), 3.77 (s, 3, CH₃O), 2.12 (s, 1, OH), 0.88 (s, 9, C(CH₃)₃).

endo- and exo-6,7-Benzobicyclo[3.2.1]octen-3-ol. A mixture of the two epimers was prepared by the NaBH₄ reduction of the corresponding ketone.³⁸ The ketone was prepared by hydrolysis of its oxime by levulinic acid.⁴³ Gas chromatography of the alcohol mixture with a 10 ft × 1/8 in. o.d., 20% Carbowax 20M on Gas Chrom Z column at 172° gave two peaks, retention times 6.1 and 12.3 min. No ketone was detected. The latter peak had an identical retention time with a known sample of the exo alcohol and it was assumed the peak with the shorter retention time was the endo alcohol. Samples of the exo alcohol, ketone, and its oxime were kindly supplied by Professor Peter T. Lansbury of The State University of New York at Buffalo.

syn- and anti-5,6-Benzobicyclo[2.2.1]hepten-7-ol. A mixture of the two epimers was prepared by reducing the corresponding ketone with diisoamylborane.⁴⁴ Gas chromatography with a 6 ft × 1/8 in. o.d., 20% Carbowax 20M on the Gas Chrom Z column at 200° gave two peaks, retention times 5.0 and 8.4 min. No ketone was detected. Although no authentic sample of the two epimeric alcohols was available, an analogy was drawn with the gas chromatographic behavior of *endo*- and *exo*-6,7-benzobicyclo[3.2.1]octen-3-ol (see above), in that the peak with the shorter retention time was assumed to be the syn alcohol and the peak with the longer retention time the anti alcohol. A sample of 5,6-benzobicyclo[2.2.1]hepten-7-one was kindly supplied by Dr. Hiroshi Tanida of the Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-Ku, Osaka, Japan.

Product Analyses. A. Organic. Analytical gas chromatographic analyses were carried out using a Perkin-Elmer 800 gas chromatograph equipped with flame ionization detectors. Nitrogen was used as the carrier gas. The instrument was operated in the dual column mode coupled to a Honeywell Elektronik #194 recorder. All product separations were made with various lengths (4–20 ft) 1/8-in. o.d. copper columns containing 20% Carbowax 20M Gas Chrom Z.

Products, except PhCDO (see below), were usually identified by their retention times. With several very low boiling compounds (*i.e.*, 2,3-dimethylbutane, 2-propanone, 2-propanol, and 2-chloropropane), their identity was established by adding a small amount directly to the reaction mixture and noticing the corresponding increase in peak height. Quantitation was done by the use of an internal standard. Known weights of products approximating quantities expected in reactions were used to calibrate the method. Standards indicated that the errors in the analyses are less than 5%.

The benzaldehyde formed in the reaction of PhCDOHCH(CH₃)₂ with Fenton's reagent was recovered by preparative gas chromatography. An Aerograph A-90-P3 gas chromatograph utilizing a 20 ft × 0.25 in. column containing 60–80 Chromosorb W coated with 17% poly(propylene glycol) was used. Collection of the peak corresponding to PhCDO was made in U-shaped glass tubes immersed in Dry Ice-acetone. The neat liquid was placed in a pmr micro cell and the spectrum measured.

B. Inorganic. The thiocyanate colorimetric method (with H₂SO₄ in place of HNO₃) was used to determine the Fe(III) concentration at the end of the Fenton reaction when H₂O₂ remained.⁴⁵ Standard iron solutions were used to calibrate the method. H₂O₂ remaining in the reaction mixture was detected qualitatively by the yellow color produced by 1 drop added to 2 ml of a solution containing Ti(SO₄)₂ (5 × 10⁻³ M) in 3 N H₂SO₄.

The Ce(IV) titration method of Kolthoff and Medalia^{7a} was used

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to determine the Fe(II) concentration present in the reaction mixtures when no H₂O₂ remained. The entire reaction mixture (usually 50 ml) was titrated. Aliphatic alcohols present during Ce(III) titration have been shown not to interfere with the method^{7a} and the same was assumed for the 1-phenyl alcohols.

H₂O₂ remaining in the reaction mixtures was determined quantitatively by the Ti(IV)-H₂O₂ colorimetric method of Erlenmeyer, *et al.*⁴⁶ Standard H₂O₂ solutions were used to calibrate the method.

Reaction Conditions. A. Fenton System. All solutions were purged with nitrogen and reactions were run at room temperature under a nitrogen blanket. In a typical competition experiment, 50 ml of a solution containing the FeSO₄, equimolar amounts of the two reactants, and HClO₄ (for reactions at low pH) or acetate buffer (for reactions above pH 3.5) was prepared. To this vigorously stirred solution was added over a few minutes a small aliquot containing the H₂O₂. In several experiments the FeSO₄ was added last but did not affect the results. After the solution was stirred for 5 min, an internal standard was added; the entire mixture was extracted with benzene, and the benzene layer was analyzed by gas chromatography. In cases where 2-propanone was a product, the reaction mixture was injected directly into the gas chromatograph. Blanks without H₂O₂ were treated in the same way to ensure that no carbonyl products were formed other than by the Fenton reaction. In some experiments in which the amount of oxidation cleavage *vs.* ketone formation was determined, the procedure was essentially the same except only one organic compound was present. In the competition experiment involving benzene the phenol was analyzed as previously described.⁴⁷

B. Peroxydisulfate System. Reaction solutions were prepared as in the Fenton system except K₂S₂O₈ was present and the solutions were thermostated at 75° for 2 hr. An internal standard was then added and the reactions analyzed as in the Fenton system. Blanks without K₂S₂O₈ were treated in the same way.

C. Photolysis Experiments. PhCHOH-*i*-Pr [2.06 g (0.013 mol)] was dissolved in 1 l. of 0.035 M HClO₄. Into an Ace #6523 photochemical reaction vessel fitted with a quartz immersion well was placed 250 ml of the solution. H₂O₂ was added to give a final concentration of 3 × 10⁻² M. The solution was photolyzed with a 450-W Hanovia high-pressure quartz mercury lamp utilizing a quartz filter. At periodic intervals, 50 ml was removed, an internal standard added, and the solution extracted with 5 ml of benzene. The benzene extract was then analyzed by gas chromatography. Blanks without H₂O₂ were treated in the same way; in such blanks no aldehyde or ketone was observed.

Relative Reactivities. Most of the relative reactivities (Table II) were determined by carbonyl product analyses. Thus, these are essentially reactivities of the (D) H-C-OH part of each compound being converted to a carbonyl, and all other reactions of the compound are ignored. Since the organic reactants were always in excess (only 10–15% converted) in these experiments, their relative reactivities were calculated directly from the molar ratios of carbonyl products formed.

The relative reactivities determined from alcohol disappearance were calculated from $k_A/k_B = [\ln(A_x/A_0)]/[\ln(B_x/B_0)]$, where k_A/k_B is the rate of disappearance of reactant A relative to that of reactant B, A_x and B_x are the number of moles of reactants A and B remaining after x mol of H₂O₂ have reacted, and A_0 and B_0 are the number of moles of A and B initially present. These reactivities are essentially reactivities of the whole molecule to give every possible product.

General. All quantitative results reported in the tables and figure are the average obtained from two or more duplicate experiments.

Acknowledgment. The authors would like to thank Drs. Peter T. Lansbury and Hiroshi Tanida for supplying precursors of the bicyclic alcohols, and the National Science Foundation and the National Institute of Arthritis, Metabolic and Digestive Diseases for supporting this work.

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