d, 1, J = 12.13, 6′-H), 4.128–4.082 (m, 1, 5-H), 3.847 (dd, 1, J = 9.93 and 9.93, 4-H), 3.456 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 166.1 and 165.2 (3 C=O's), 132–128 (aromatic-C's), 97.0 (C-1), 73.9 (C-3), 71.6 (C-2), 69.8 and 69.5 (C-4/C-5), 63.7 (C-6), 55.3 (OMe).

Methyl 2-*O*-methyl-3,4,6-tris(*O*-(*p*-bromobenzoyl))-α-D-glucopyranoside (33): CI-MS 757 $(M)^+$, 725 $(M - HOMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.891–7.465 (m, 12, aromatic-H's), 5.867 (dd, 1, J = 9.93 and 9.93, 3-H), 5.464 (dd, 1, J = 9.93 and 9.93, 4-H), 5.039 (d, 1, J = 3.68, 1-H), 4.553 (dd, 1, J = 12.14 and 2.94, 6-H), 4.427 (dd, 1, J = 12.14 and 5.15, 6′-H), 4.343–4.269 (m, 1, 5-H), 3.635 (dd, 1, J = 9.93 and 3.68, 2-H), 3.540 (s, 3, OMe), 3.453 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.4, 165.0, and 164.3 (3 C=O's), 132–128 (aromatic-C's), 97.2 (C-1), 79.5 (C-2), 72.5 (C-3), 70.2 (C-4), 67.4 (C-5), 63.3 (C-6), 59.2 (2-OMe), 55.6 (1-OMe).

Methyl 2-*O*-acetyl-3,4,6-tris(*O*-(*p*-bromobenzoyl))-α-D-glucopyranoside (34): CI-MS 754 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.954–7.455 (m, 12, aromatic-H's), 5.933 (dd, 1, J = 9.93 and 9.93, 3-H), 5.535 (dd, 1, J = 9.93 and 9.93, 4-H), 5.178 (dd, 1, J = 9.93 and 3.68, 2-H), 5.051 (d, 1, J = 3.68, 1-H), 4.565 (dd, 1, J = 12.13 and 3.31, 6-H), 4.435 (dd, 1, J = 12.13 and 4.78, 6′-H), 3.335 (m, 1, 5-H), 3.505 (s, 3, OMe), 2.010 (s, 3, OAc); ^{13}C NMR ($CDCl_3$), 170.1 (OAc, C=O), 165.3, 164.9, and 164.6 (OBz, C=O's), 132–128 (aromatic-C's), 97.1 (C-1), 70.8 (C-2,3), 70.0 (C-4), 67.4 (C-5), 63.1 (C-6), 55.6 (OMe), 20.5 (OAc).

Methyl 3-*O*-acetyl-2,4,6-tris(*O*-(*p*-bromobenzoyl))-α-D-galactopyranoside (35): CI-MS 786 $(M + 1)^+$, 755 $([M - OMe] + 1)^+$.

Methyl 2,3,6-tris(*O*-(*p*-bromobenzoyl))-α-D-galactopyranoside (36): CI-MS 712 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.922–7.522 (m, 12, aromatic-H's), 5.230–5.179 (m, 2, 2-H, 3-H), 4.691 (d, 1, J = 1.47, 1-H), 4.516 (br d, 1, J = 12.13, 6-H), 4.327 (br d, 1, J = 12.13, 6′-H), 3.838–3.815 (m, 2, 4-H, 5-H), 3.396 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.8, 165.3, and 165.1 (3 C=O's), 132–128 (aromatic-C's), 97.4 (C-1), 71.1 (C-3), 69.0 (C-2), 68.1 (C-4), 67.8 (C-5), 63.7 (C-6), 55.5 (OMe).

Methyl 2,3,6-tris(*O*-(*p*-bromobenzoyl))-β-D-galactopyranoside (37): CI-MS 712 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.967–7.372 (m, 12, aromatic-H's), 5.716 (dd, 1, J = 10.30 and 7.72, 2-H), 5.320 (dd, 1, J = 10.30 and 2.94, 3-H), 4.676 (d, 1, J = 7.72, 1-H), 4.736–4.575 (m, 2, 6-H's), 4.323 (br d, 1, J = 2.94, 4-H), 4.063 (m, 1, 5-H), 3.544 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.8, 165.1, and 164.7 (3 C=O's), 132–128 (aromatic-C's), 102.1 (C-1), 74.3 (C-3), 72.3 (C-5), 69.8 (C-2), 67.4 (C-4), 62.9 (C-6), 56.9 (OMe).

Methyl 2,3,4,6-tetrakis(*O*-(*p*-bromobenzoyl))-β-D-glucopyranoside (38): CI-MS 955 $(M + 29)^+$, 927 $(M + 1)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 8.002–7.432 (m, 16, aromatic-H's), 5.827 (dd, 1, J = 9.56 and 9.56, 3-H), 5.629 (dd, 1, J = 9.56 and 9.56, 4-H), 5.471 (dd, 1, J = 9.56 and 7.72, 2-H), 4.748 (d, 1, J = 7.72, 1-H), 4.643 (dd, 1, J = 12.13 and 2.94, 6-H), 4.427 (dd, 1, J = 12.13 and 4.47, 6′-H), 4.285–4.198 (m, 1, 5-H), 3.526 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.4 and 164.3 (4 C=O's), 132–128 (aromatic-C's), 101.9 (C-1), 73.2 (C-3), 71.9 (C-2,5), 70.0 (C-4), 63.2 (C-6), 57.0 (OMe).

Methyl 2,3,4,6-tetrakis(*O*-(*p*-bromobenzoyl))-α-D-glucopyranoside (39): CI-MS 927 $(M + 1)^+$, 895 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 8.002–7.438 (m, 16, aromatic-H's), 6.105 (dd, 1, J = 9.93 and 9.93, 3-H), 5.621 (dd, 1, J = 9.93 and 9.93, 4-H), 5.280 (dd, 1, J = 9.93 and 3.68, 2-H), 5.215 (d, 1, J = 3.68, 1-H), 4.606 (dd, 1, J = 11.77 and 2.57, 6-H), 4.382 (dd, 1, J = 11.77 and 4.36, 6′-H), 4.340 (m, 1, 5-H), 3.498 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.2, 164.9, and 164.4 (4 C=O's), 132–127 (aromatic-C's), 96.9 (C-1), 71.8 (C-3), 70.6 (C-2), 69.7 (C-4), 67.3 (C-5), 63.0 (C-6), 55.6 (OMe).

Methyl 2,3,4,6-tetrakis(*O*-(*p*-bromobenzoyl))-β-D-galactopyranoside (40): CI-MS 895 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.960–7.368 (m, 16, aromatic-H's), 5.942 (br d, 1, J = 3.31, 4-H), 5.716 (dd, 1, J = 10.30 and 7.72, 2-H), 5.563 (dd, 1, J = 10.30 and 3.31, 3-H), 4.746 (d, 1, J = 7.72, 1-H), 4.691 (dd, 1, J = 10.30 and 6.25, 6-H), 4.445–4.293 (m, 2, 5-H, 6′-H), 3.603 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.6, 165.3, and 165.0 (4 C=O's), 132–128 (aromatic-C's), 102.4 (C-1), 72.0 (C-3), 71.2 (C-5), 70.0 (C-2), 68.4 (C-4), 62.1 (C-6), 57.2 (OMe).

Methyl 2,3,4,6-tetrakis(*O*-(*p*-bromobenzoyl))-α-D-galactopyranoside (41): CI-MS 927 $(M + 1)^+$, 895 $(M - OMe)^+$; ^{1}H NMR ($CDCl_3$, 250 MHz) 7.957–7.363 (m, 16, aromatic-H's), 6.015 (br s, 1, 4-H), 5.989 (dd, 1, J = 10.29 and 3.31, 3-H), 5.667 (dd, 1, J = 10.29 and 3.31, 2-H), 5.325 (d, 1, J = 3.31, 1-H), 4.642–4.228 (m, 3, 5-H, 6-H's), 3.502 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.1, 164.8 and 164.6 (4 C=O's), 132–128 (aromatic-C's), 97.5 (C-1), 69.4 and 69.2 (C-3/C-2), 68.5 (C-4), 66.6 (C-5), 62.4 (C-6), 55.6 (OMe).

Methyl 2,3,4,6-tetrakis(*O*-(*p*-bromobenzoyl))-α-D-mannopyranoside (42): CI-MS 927 $(M + 1)^+$, 895 $(M - OMe)^+$; ^{1}H NNR ($CDCl_3$, 250 MHz) 7.950–7.407 (m, 16, aromatic-H's), 5.993 (dd, 1, J = 9.93 and 9.93, 4-H), 5.865 (dd, 1, J = 9.93 and 2.94, 3-H), 5.671 (dd, 1, J = 2.94 and 1.84, 2-H), 4.983 (d, 1, J = 1.84, 1-H), 4.762 (dd, 1, J = 12.14 and 2.57, 6-H), 4.512–4.219 (m, 2, 5-H, 6′-H), 3.546 (s, 3, OMe); ^{13}C NMR ($CDCl_3$) 165.2, 164.7, and 164.5 (4 C=O's), 132–127 (aromatic-C's), 98.5 (C-1), 70.4 and 70.1 (C-3/C-2), 68.5 (C-5), 67.2 (C-4), 62.9 (C-6), 55.6 (OMe).

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Registry No. 1, 80326-06-3; **2**, 80326-07-4; **3**, 80326-08-5; **4**, 80326-09-6; **5**, 80326-10-9; **6**, 80326-11-0; **7**, 80326-12-1; **8**, 80326-13-2; **9**, 80326-14-3; **10**, 80326-15-4; **11**, 80326-16-5; **12**, 80339-88-4; **13**, 80326-17-6; **14**, 80326-18-7; **15**, 80326-19-8; **16**, 80326-20-1; **17**, 80326-21-2; **18**, 80326-22-3; **19**, 80326-23-4; **20**, 80326-24-5; **21**, 80326-25-6; **22**, 80326-26-7; **23**, 80326-27-8; **24**, 80339-89-5; **25**, 80326-28-9; **26**, 80326-29-0; **27**, 80326-30-3; **28**, 78950-12-6; **29**, 78950-13-7; **30**, 78966-81-1; **31**, 78950-14-8; **32**, 78950-15-9; **33**, 78966-82-2; **34**, 78950-16-0; **35**, 78950-17-1; **36**, 78950-18-2; **37**, 78950-19-3; **38**, 78950-20-6; **39**, 78950-21-7; **40**, 78950-22-8; **41**, 78950-23-9; **42**, 78950-24-0; I, 18031-51-1; II, 50694-98-9; III, 50694-97-8; IV, 4201-66-5; **a**, 4064-06-6; **b**, 35526-05-7; **c**, 23392-30-5; **d**, 28542-03-2; **e**, 80326-31-4; **f**, 53685-11-3; **g**, 53008-63-2; methyl α-D-glucopyranoside, 97-30-3; methylsulfinyl anion, 80326-32-5; *p*-bromobenzoyl chloride, 586-75-4; D-galactose, 59-23-4; methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside, 604-70-6.

Oxidation of Mandelic Acid by Fenton's Reagent[1]

Cheves Walling* and Kalyani Amarnath

Contribution from the Department of Chemistry, University of Utah, Salt Lake City, Utah 84112. *Received August 14, 1981*

Abstract: Mandelic acid forms a stable 1:1 complex with Fe^{2+} at pH 1–3. Its oxidation by H_2O_2 and $S_2O_8^{2-}$ has been investigated in the hope of detecting intramolecular oxidation–reduction of any intermediate Fe^{IV} species, rather than the usual hydroxyl radical process. Products are benzaldehyde and hydroxymandelic acids, consistent with either, but added hydroxyl radical traps—acetone or crotonic acid—are able to intercept only about half of the reaction. However, they reduce yields of benzaldehyde but not hydroxymandelic acids, and it is concluded that the balance of the reaction involves cage reactions of newly formed hydroxyl radicals rather than a high-valence iron species.

Reactions between oxygen or peroxides and organic substrates catalyzed by transition-metal ions are of great importance in both technology and biochemistry. A critical question in understanding their mechanisms is the nature of the "primary oxidant" which

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Table I. Products of Mandelic Acid Oxidations

conditions[a]		yield,[c] %				
pH	oxidant	C_6H_5CHO	C_6H_5COOH	phenols[d] (O:M:P)	other[e]	total
<1	H_2O_2(D)	63.6	2.3			65.9
1.2	H_2O_2(D)	55.6	3.4	1.6 (56:31:13)	2.9	63.5
1.9	H_2O_2(D)	39.4	11.4	7.0 (43:36:21)		57.8
2.7	H_2O_2(D)	20.5	9.3	13.5 (54:22:24)		43.3
2.7	$S_2O_8^{=}$(I)	65.4	5.4		1.6	72.4
2.5	H_2O_2(I)[b]	16.8	10.2	12.6 (37:34:29)	3.4	43
2.5	$S_2O_8^{=}$(I)[b]	66.5	9.2		3.0	72.7

[a] 0.12 M MA, MA/Fe^{2+}/oxidant, 5:1:1, unless indicated; D, direct addition, I, inverse. [b] 0.04 M MA, MA/Fe^{2+}/oxidant, 4:2:1, + $6Fe^{3+}$. [c] Based on oxidant used. [d] Hydroxymandelic acids. [e] Hydroxybenzaldehydes and hydroxybenzoic acids.

first attacks the substrate. In our own work on the reactions of hydrogen peroxide and peroxydisulfate with iron and copper ions (Fenton's reagent), all evidence points to simple oxygen radicals, HO· or SO_4^{-}·, as the primary oxidants.[2,3] On the other hand, biochemical oxidations involving iron-containing enzymes are generally considered to involve higher valence iron or iron–oxygen complexes as primary oxidants,[4] and some model systems also show behavior which seems best interpreted the same way.[5]

A scheme which might combine these divergent views for iron-peroxide reactions is to assume that the initial Fe^{II}–H_2O_2 reaction is a 2-electron process to yield $Fe^{IV}OH$ which in turn decomposes to Fe^{III} + HO·. In simple acid aquoiron systems we

$$Fe^{II} + H_2O_2 \rightarrow Fe^{IV}OH \rightleftharpoons Fe^{III} + \cdot OH \qquad (1)$$

would assume that the intermediate ferryl radical $Fe^{IV}OH$ decomposes so rapidly and the resulting equilibrium with HO· is so unfavorable that only HO· radical reactions can be detected. On the other hand, with suitable ligands around the iron, e.g., the porphyrin rings in metalloenzymes, the Fe^{IV} state might be stabilized sufficiently to become the primary oxidant. It seemed to us that one way of detecting such an Fe^{IV} species in model systems would be to investigate the reaction of H_2O_2 with Fe^{II} complexed with an easily oxidized ligand, which might undergo fast oxidation by intramolecular electron transfer by any intermediate Fe^{IV} species before it could decompose. We here report such a study using mandelic acid as the ligand, together with some brief data on other substrates.

Results and Discussion

Iron(II)–Mandelic Acid Complex. Although a few mandelic acid complexes including that with Fe^{III} have been examined,[6] we have found no report on the Fe^{II}–mandelic acid system. When solutions of mandelic acid (MA) and Fe^{2+} (as perchlorate or sulfate) are mixed, the pH decreases and an absorbance develops with a maximum at 340 nm. At constant total [MA] + [Fe^{2+}] the absorbance is a maximum at [MA] = [Fe^{2+}], and 1:1 mixtures obey Beer's law. These results taken together indicate a 1:1 complex which is almost entirely associated under our conditions of measurement. If the pH is raised the absorbance increases (Figure 1). Analysis of the curve is consistent with an acidic complex, ϵ_{340} 3, pK_a 2.2, which ionizes to give a more strongly absorbing species, ϵ_{340} 13.3. Since our interest was in solution

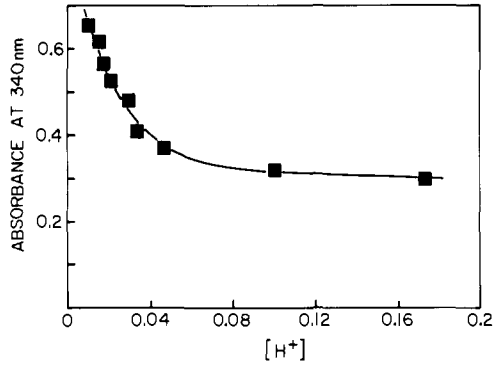
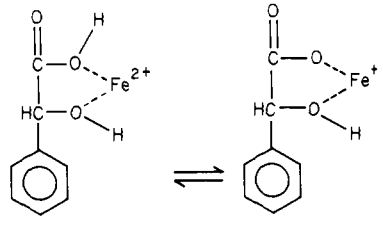


Figure 1. Variation of absorbance with hydrogen ion concentration; [Fe^{2+}] = [HMa] = 0.1 M at 25 °C.

chemistry, no attempt was made to isolate the complexes, but our results are consistent with the structures:



(2)

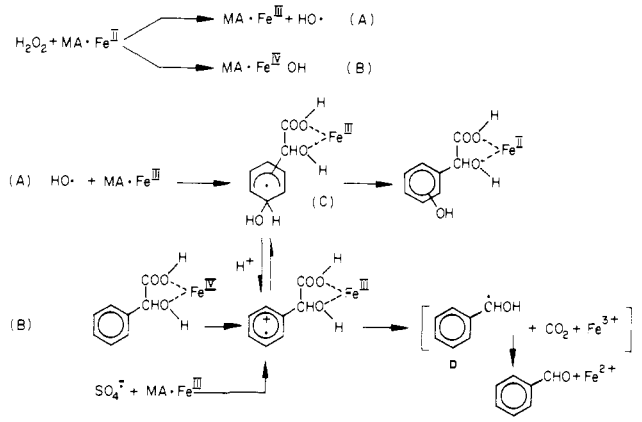
Potentiometric titration of the 1:1 complex with KOH was also in agreement with the spectroscopic measurements. One equivalent of base was taken up below pH 4, but then the pH rises steeply, and a second proton is not lost until pH >7, at which point precipitation is noticeable.

Oxidations. Only limited data exist on the oxidation of mandelic acid by Fenton's reagent related systems. Shinra[7] has reported that peroxydisulfate–Cu^{2+} or –Ag^{+} systems yield benzyl alcohol, benzaldehyde, and benzoic acid and suggests phenylglyoxalic acid as an intermediate. Norman and Pritchett[8] have examined the ESR spectra of intermediates in the oxidation by H_2O_2–Ti^{3+}, detecting both hydroxycyclohexadienyl and α-hydroxybenzyl radicals. In our own experiments, oxidations were carried out either by slow addition of H_2O_2 to Fe^{2+}–mandelic acid solutions containing an excess of mandelic acid to insure that all Fe species were complexed (direct addition) or by addition of Fe^{2+} to H_2O_2–mandelic acid (inverse addition) essentially as in our previous work involving uncomplexed iron.[3,9,10] Results, including some experiments using $S_2O_8^{2-}$ in place of H_2O_2 are listed in Table I.

In all experiments the major product is benzaldehyde, plus varyng amounts of benzoic acid, presumably arising from its

(1) Taken from the Ph.D. thesis of Kalyani Amarnath, University of Utah, 1981.
(2) Walling, C. *Acc. Chem. Res.* **1975**, *8*, 125.
(3) Walling, C.; Camaioni, D. M.; Kim, S. S. *J. Am. Chem. Soc.* **1978**, *100*, 4814.
(4) See, for example: Lowe, J. N.; Ingraham, L. L. "An Introduction to Biochemical Reaction Mechanisms"; Prentice-Hall: Englewood Cliffs, NJ, 1974; p 113.
(5) (a) Groves, J. T.; Vander Puy, M. *J. Am. Chem. Soc.* **1976**, *98*, 5290–5297. (b) Groves, J. T.; Nemo, T. E.; Meyers, R. S. *Ibid.* **1979**, *101*, 1032–1033. (c) Tabushi, I.; Koga, N. *Ibid.* **1979**, *101*, 6456–6458. These are only a few of numerous examples.
(6) (a) Bardwaj, S. D.; Bakore, G. V. *J. Ind. Chem. Soc.* **1961**, *38*, 967. (b) Gilman, A. D.; McAuley, A. *J. Chem. Soc. A* **1969**, 2345.
(7) Shinra, K.; Sakurai, K.; Ishibashi, T. Sci. Rep., *Coll. Gen Educ., Osaka Univ.* **1963**, *12*, 19–21, 125–129.
(8) Norman, R. O. C.; Pritchett, R. J. *J. Chem. Soc. B* **1967**, 926.
(9) Walling, C.; Kato, S. *J. Am. Chem. Soc.* **1971**, *93*, 4275–4281.
(10) Walling, C.; Johnson, R. A. *J. Am. Chem. Soc.* **1975**, *97*, 363–367.

Scheme I



further oxidation. However, we also observe significant ring hydroxylation, particularly in less acid solution. These results closely parallel those previously reported for phenylacetic acid.[3,10] They are inconsistent with phenylglyoxalic acid as an intermediate[7] and can be accounted for by the same hydroxyl radical scheme which, in the case of uncomplexed Fe, is strongly supported by a variety of evidence.[2] However, as is often the case in this sort of problem, the products could also be consistent with an Fe^{IV} intermediate, and the interrelation between the two formulations is shown in Scheme I. In the hydroxyl radical path A, hydroxyl radical addition leads initially to a hydroxycyclohexadienyl radical (C) which is either further oxidized to phenols or undergoes acid-catalyzed loss of water to give the radical-cation D which can fragment to yield, eventually, benzaldehyde. In the Fe^{IV} path B, we suggest a series of 1-electron steps, leading to the same radical cation D, so formation of phenolic products would involve its hydration to the hydroxycyclohexadienyl radical C. Sterically, there seems to be no way for the Fe^{IV} species to directly hydroxylate its own ring, except possibly in the ortho position, and the isomer distribution of phenols which we observe is similar to those found previously with phenylacetic acid.[10] In Scheme I it will be noted that peroxydisulfate oxidations involving the $SO_4^{\cdot-}$ radical also initially produce the radical cation D[3] and should yield the same products, a point which will become important in later discussion.

Stoichiometric Experiments. If free hydroxyl radicals are involved in this system, it should be possible to demonstrate them by trapping them with other reactive substrates, and a convenient way of examining this is by determining reaction stoichiometry. In Scheme I, it will be noted that, in both paths A and B, Fe^{II} is regenerated so that many moles of H_2O_2 are consumed per mole of Fe^{II} oxidized. On the other hand, a number of easily reduced substrates, e.g., acetone or α,β-unsaturated acids, are known in which the intermediate radicals produced by hydroxyl radical attack are not oxidized by Fe^{III} but rather are reduced by an additional equivalent of Fe^{II}.[2,11] We have previously shown how examination of the stoichiometry of oxidation of mixtures of such substrates with methanol, which undergoes the same sort of chain oxidation as proposed for MA, can be used to determine relative rates of oxidation.[11]

Here we will assume the possibility that MA may be oxidized by two paths: via "free" hydroxyl radicals (path A) or via an "untrappable" intermediate which goes to products too rapidly to be intercepted by the added substrate. This could, of course, be the Fe^{IV} species (B), but, since hydroxyl radicals, if formed, are initially produced in the immediate vicinity of MA·Fe^{III} and react with aromatic rings with k's $> 10^9$ l/mol·s,[12] it could also

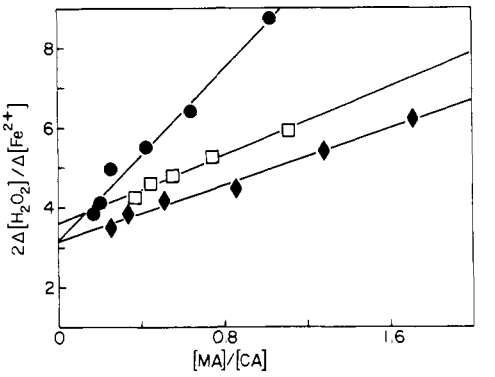


Figure 2. Plots of eq 7 for MA with crotonic acid (CA); the ratio $[MA]/[Fe^{2+}]/[H_2O_2]$, is 10:2:1 (pH 1, □), 4:2:1 (pH 1, ●), and 4:2:1 (pH 2, ♦).

Table II. Results of Stoichiometric Experiments

$MA/Fe^{2+}/H_2O_2$[a]	pH	substrate,[b] (concn, M)	f	$k_4 \times 10^{-9}$
4:2:1	2	A (0.027-.24)	0.46	.9
4:2:1	1	A (0.027-.16)	0.49	1.4
10:2:1	1	A (0.067-.34)	0.75	.9
4:2:1	2	CA (0.027-.18)	0.53	6.4
10:2:1	1	CA (0.09-.27)	0.61	2.2
4:2:1	2	B (0.108-.74)	0	3.5
4:2:1	1	B (1.06-3.18)	0.09	1.9
10:2:1	1	B (0.31-2.65)	0.37	1.4

[a] 0.02 Fe^{2+} in all runs. [b] A, acetone; CA, crotonic acid; B, *tert*-butyl alcohol.

represent some amount of "cage" reaction between MA·Fe^{III} and HO·.[13] The reactions postulated in our system are

$$H_2O_2 + Fe^{II}\cdot MA \xrightarrow{k_3} X \rightarrow \text{products} + Fe^{II} \quad (3)$$

$$H_2O_2 + Fe^{II}\cdot MA \xrightarrow{k_4} Fe^{III}\cdot MA + HO\cdot \quad (4)$$

$$HO\cdot + MA \xrightarrow{k_5} R\cdot \xrightarrow{Fe^{III}} \text{products} + Fe^{II} \quad (5)$$

$$HO\cdot + S \xrightarrow{k_6} S\cdot \xrightarrow{Fe^{II}} \text{products} + Fe^{III} \quad (6)$$

where X represents the "untrappable" intermediate, MA total mandelic acid, and S the added substrate. This set of equations predicts a stoichiometry (relative amounts of H_2O_2 and Fe^{II} consumed)

$$\frac{2\Delta H_2O_2}{\Delta Fe^{II}} = \frac{1}{1-f}\left(1 + \frac{k_5[MA]}{k_6[S]}\right) \quad (7)$$

where $f = k_3/(k_3 + k_4)$, the fraction of MA oxidation going through the intermediate X. In order to minimize the additional path for Fe^{II} oxidation

$$HO\cdot + Fe^{II} \rightarrow HO^- + Fe^{III} \quad (8)$$

experiments using acetone and crotonic acid as added substrate were carried out by inverse addition (Fe^{II} added to MA-H_2O_2) and plots of (7) are shown in Figures 2 and 3.[14]

The data give reasonable linear plots and intercepts larger than unity indicating a significant value of f, but both slopes and intercepts show some dependence on pH and the amount of uncomplexed MA present. This is not predicted by eq 7, and we suggest that it may indicate that all forms of MA—uncomplexed and complexed with Fe^{II} and Fe^{III}—do not, in fact, have equal reactivities with HO· as assumed. We have also run stoichiometric

(11) Walling, C.; El-Taliawi, G. M. *J. Am. Chem. Soc.* **1973**, *95*, 844–847.
(12) For a recent summary of rate constants for hydroxyl radical reactions, see: Frahataziz; Ross, A. B. "Selected Specific Rates of Reactions of Transients From Water in Aqueous Solution, III."; U.S. Government Printing Office: Washington, DC, 1977; NSRDS-NBS 59.

(13) We have previously concluded that there is evidence for such cage reactions between HO· and Fe–ligand complexes in the Fe^{III}–EDTA–H_2O_2 system. See: Walling, C.; Partch, R. E.; Weil, T. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 1, 140–142.
(14) Participation of reaction 8 would displace points downward in the plots. This is observed if H_2O_2 is added to a MA–Fe^{II} system.

Table III. Effect of Added Substrates on Products of Mandelic Acid Oxidations

pH	additive (concn, M)	yield,[a] % C_6H_5CHO	C_6H_5COOH	phenols (O:M:P)	other	total
2	none	38.9	7.5	4.4 (50:32:18)	0.7	51.5
2	A (0.24)	13.2	1.8	7.5 (81:9:10)	5.3	27.9
2	CA (0.18)	8.3	6.7	4.0 (72:15:13)		19.
2	B (0.74)	21.5	2.1	4.0 (45:27:28)	9.7	37.3
1	none	46.4	4.1	0.2 (50:50:0)	0.5	51.2
1	A (0.16)	24.4	4.5		1.4	30.3
1	CA (0.27)	11.2	6.6	0.7 (86:14:0)		18.5

[a] Based on H_2O_2 added. All runs inverse addition, MA, 0.04 M; Fe^{2+}, 0.02 M; H_2O_2, 0.01 M. Other abbreviations as in Table I.

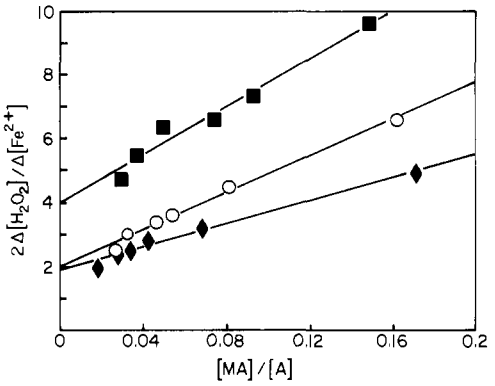


Figure 3. Plots of eq 7 for MA with acetone (A); symbols as described in Figure 2.

experiments using *tert*-butyl alcohol as an added substrate. Here intermediate radicals, S·, are not reduced, but dimerize,[9] so (6) is replaced by

$$HO\cdot + S \xrightarrow{k_6} S\cdot \xrightarrow{S\cdot} \text{products} \qquad (9)$$

and (7) becomes

$$\frac{\Delta H_2O_2}{\Delta Fe^{II}} = \frac{1}{1-f}\left(1 + \frac{k_5[MA]}{k_6[S]}\right) \qquad (10)$$

Values of f and k_4 for all sets of experiments are summarized in Table II, taking k_6's for acetone,[11] crotonic acid,[11] and *tert*-butyl alcohol[9] as 9.3×10^7,[11] 2.55×10^9,[11] and 5.25×10^8, respectively. Although k_4 has not been measured independently, our average value, 2.3×10^9, in the range of values for HO· attack on similar aromatic rings.[12] Further, the reasonable agreement between sets of data for different substrates, despite a 25-fold range in k_6's indicates that our treatment is valid. The most important feature of Table II is the significant value of f in the presence of acetone and crotonic acid.[15] While much of the reaction appears to involve free hydroxyl radicals, a significant portion, the order of 50%, appears to involve an "untrappable" oxidant, although stoichiometric experimnets by themselves tell us nothing about its nature.

We have also carried out similar sets of stoichiometric experiments on some other oxidizable ligands which might be expected to form stable iron complexes. Using acetone as the added substrate, phenylglycine, phenylalanine, and phenyllactic acids give intercepts of 1.5, 1.2, and 1.3, respectively. Since these results indicated that the bulk of the reaction goes through the usual hydroxyl radical chain, they were not investigated further, but the technique provides a simple way for screening potential systems for interesting behavior.

Product Compositions in the Presence of Added Substrates. In the hope of defining the "untrappable" oxidant indicated by our stoichiometric experiments, we have examined the products of MA oxidation in the presence of large enough amounts of substrate to eliminate most of the free hydroxyl radical oxidation. Results are shown in Table III, together with comparable experiments in the absence of added substrate run under identical conditions. As expected, the added substrates reduce the amount of MA oxidation in all cases, and crotonic acid, which is the most reactive, is the most effective.[16] The striking result is that the reduction is almost exclusively in yields of benzaldehyde and benzoic acid and that at low acidity (pH 2) the yields of ring hydroxylated products are, if anything, increased (at pH 1 yields of ring hydroxylated products are too low for significant comparison). This would be an expected result for an HO· cage reaction, since, referring back to Scheme I, the hydroxycyclohexadienyl radical C produced would be already complexed with Fe^{III} which would be available for its immediate intramolecular oxidation.[17] On the other hand, if Scheme I is correct, both Fe^{IV} and SO_4^{-}· from peroxydisulfate oxidations convert MA to its radical cation (D), and should thus lead to the same products. However, "X" gives largely hydroxymandelic acids, while, from Table I, these products are not found in peroxydisulfate reactions. We conclude that the portion of mandelic acid oxidation not intercepted by hydroxyl radical traps represents a cage reaction of newly formed hydroxyl radicals and not the intervention of a transient Fe^{IV} species. While this result is disappointing in terms of reconciling HO· and Fe^{IV} paths in this sort of oxidation, we believe it again points up the utility of simple stoichiometry and product studies in sorting out what is going on the these systems.

Finally we should comment on the relation of this work to a preliminary study by Siegel and Lanphear on the oxidation of benzoylformic (phenylglyoxalic) acid by the H_2O_2–Fe system.[18] These investigators concluded that oxidation involves an Fe^{IV} species and ruled out a HO· radical chain because the oxidation (followed spectrophotometrically by disappearance of substrate) was strongly retarded by EDTA and other species which complex Fe. We do not find this argument convincing. First, they applied none of the tests described here. Second, and more important, although they started with Fe^{II}, it is oxidized in a matter of seconds to Fe^{III} at the H_2O_2 levels used, and their kinetics (from the rate constants reported) were evidently studied over a much longer time scale. Thus they were studying the Fe^{III}–H_2O_2 system. We have shown that this is also a complex hydroxyl radical process,[13,19] and it is well-known that the rate-determining initial Fe^{III}–H_2O_2 reaction (regardless of subsequent mechanism) is strongly retarded, particularly at low pH, by species which complex Fe^{III}. Thus, the Fe^{III}, EDTA–H_2O_2 reaction is only observable in alkaline solution.[13] In short, the observation of retardation is simply consistent with the known properties of Fe^{III}–H_2O_2 systems and is not diagnostic of detailed further mechanism.

Experimental Section

Materials. Reagents and reference materials were commercial materials purified as necessary. Mandelic acid and $K_2S_2O_8$ were recrys-

(15) The smaller values of f in *tert*-butyl alcohol systems is puzzling, and we suspect that our analysis is not suitable for this system; see ref 16.

(16) Again, *tert*-butyl alcohol behaves abnormally, since, even at high concentration, it is relatively ineffective in reducing MA oxidation. Whether it also coordinates with iron and thus alters the reaction scheme is unknown, but it is clearly not a good actor in this system.

(17) Interestingly, Table III shows some difference in the isomer distribution of phenolic products in the presence and absence of radical traps. We have no obvious explanation, but it may represent a difference in the regiospecificity of HO· addition to MA·Fe^{III} and other forms of MA or some peculiarity of the cage process.

(18) Siegel, D.; Lanphear, J. *J. Am. Chem. Soc.* **1979**, *101*, 2221–2222.
(19) Walling, C.; Goosen, A. *J. Am. Chem. Soc.* **1973**, *95*, 2987–2991.

tallized from water and crotonic acid from petroleum ether. Hydrogen peroxide was distilled under vacuum to remove any stabilizer and titrated with Ce^{4+}. Stock solutions of Fe^{2+} were determined by titration with $K_2Cr_2O_7$.

Complex formation was studied spectrophotometrically at 200–500 nm by using a Beckman 24 or Cary 1115 instrument at room temperature. Samples were prepared by mixing stock solutions and adjusting pH. Solutions were shown to be free of Fe^{3+} (which forms a more strongly absorbing complex) and used fresh or stored under N_2 to prevent oxidation. Spectra starting with ferrous perchlorate or sulfate or with ferrous ammonium sulfate were indistinguishable. The analysis of the plot in Figure 1 was made by assuming a simple ionization $Fe^{II}{\cdot}MA^{2+} \rightleftharpoons Fe^{II}MA^{+} + H^{+}$.

Reactions were carried out by slowly adding ferrous perchlorate solution (or H_2O_2) over a few minutes to stirred solutions containing the other reaction components under N_2 at room temperature, essentially as in previous papers.[3,9-11] In stoichiometric experiments, $\Delta H_2O_2/\Delta Fe^{II}$ was taken as the ratio of H_2O_2 added to Fe^{II} consumed, determined by measuring remaining Fe^{II} as its phenanthroline complex. Products were determined by gas chromatography after extraction with ether. Benzaldehyde was determined immediately and the other products first silylated with bis(trimethylsilyl)trifluoroacetamide. Products were identified by retention time, and GC–MS and all procedures were essentially those given previously.[9-11] Most separations used a 6-ft 10% OV-17 on Chromosorb W column at 160 °C with biphenyl as internal standard.

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Registry No. Mandelic acid, 90-64-2; H_2O_2, 7722-84-1; $S_2O_8^{2-}$, 15092-81-6; Fe, 7439-89-6.

Stereospecific Alkyl Group Effects on Amine Lone-Pair Ionization Potentials: Photoelectron Spectra of Alkylpiperidines

Melvin D. Rozeboom and K. N. Houk*[1]

Contribution from the Departments of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803, and The University of Pittsburgh, Pittsburgh, Pennsylvania 15260.
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Abstract: Photoelectron spectra and ab initio STO-3G calculations on methylpiperidines indicate that axial 2-methyl substituents lower the amine lone-pair ionization potential (IP) by ~0.26 eV, while equatorial 2-methyl and 3- and 4-methyl substituents lower the lone pair IP by ≤0.1 eV. This establishes the mechanism of stabilization of the amine radical cation as hyperconjugative electron release, which is larger for CC bonds than for CH bonds.

The mechanism by which alkyl groups stabilize charged species is a subject of continuing interest. Because alkyl groups stabilize both cations and anions in the gas phase, a polarizability (charge, induced dipole) mechanism has gained increasing credence.[2] On the other hand, ionization potential lowering by alkyl substituents was initially attributed to inductive effects.[3] However, we have shown that the relationship between the ionization potential of a group and the lowering in ionization potential caused by alkylation is precisely that expected for hyperconjugative electron release by alkyl groups.[4] The photoelectron spectroscopic investigation of various methyl- and polymethylpiperidines reported here shows that the influence of methyl groups on amine lone-pair ionization potentials has a pronounced dependence on the stereochemical relationship between the amine lone pair and the methyl group. This dependence is only compatible with a hyperconjugative mechanism of electron release. Calculations on proton affinities indicate that alkyl groups stabilize ammonium cations in a different fashion.

Results

Photoelectron spectra of piperidine, *N*-methylpiperidine, and various ring-methylated derivatives have been measured. Figure 1 shows several representative spectra,[5] and Table I lists the amine lone-pair ionization potentials (IPs) for the piperidines studied

Table I. Ionization Potentials of Methylated Piperidines

piperidine substituent	IP_{vert},[a] eV	ΔIP_{vert},[b] eV	IP_{ad},[c] eV
	NH		
none	8.70 (8.69,[d] 8.66,[e] 8.64[f])	≡0	8.20
2-Me(eq)	8.63 (8.58[d])	−0.07	8.04
3-Me(eq)	8.63 (8.66[d])	−0.07	8.03
4-Me(eq)	8.61 (8.66[d])	−0.09	8.06
3,3-Me_2(eq, ax)	8.60	−0.10	8.05
cis-2,6-Me_2(eq, eq)	8.53	−0.17	7.93
2,2,6,6-Me_4(eq, ax, eq, ax)	8.04[g]	−0.66	7.59
	NMe		
none	8.37 (8.39,[d] 8.29[f,h])	≡0	7.80
2-Me(eq)	8.23	−0.14	7.63
3-Me(eq)	8.35	−0.02	7.76
4-Me(eq)	8.33	−0.04	7.79
4,4-Me_2(eq, ax)	8.29	−0.08	7.77
cis-3,5-Me_2(eq, eq)	8.23	−0.14	7.63
trans-3,5-Me_2(eq, ax)	8.26	−0.11	7.66
cis-2,6-Me_2(eq, eq)	8.22	−0.33	7.77
2,2,6,6-Me_4(eq, ax, eq, ax)	7.68	−0.69	7.23

[a] ±0.05 eV; previously reported values in parentheses. [b] Change in IP relative to the parent species (NH or NMe). [c] Taken as the onset of first ionization band. [d] Reference 7. [e] Reference 8. [f] Reference 9. [g] Reference 10. [h] Reference 2a.

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