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Fenton's Reagent. VI. Rearrangements During Glycol Oxidations[1]

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Abstract: The acid-catalyzed rearrangement $R\dot{C}OHCHOHR \rightarrow RCO\dot{C}HR$ proposed by Norman[2] on the basis of ESR measurements has been confirmed during the oxidation of ethylene glycol and 2,3-butanediol both by studies of reaction stoichiometry and product isolation. Results are consistent with a rapid collapse of the radical to a radical cation which competes with its oxidation by Fe^{3+}. Similar processes are confirmed with glycol derivatives, ethylene chlorohydrin and glycol monophosphate, and the scope and significance of the reaction are discussed.

In 1966, two groups[2,3] reported that, in acid solution, hydroxyl radical attack on ethylene glycol yields a product with an ESR spectrum consistent with structure **2**, rather than the expected **1**.

$$\underset{\mathbf{1}}{HO\underset{\bullet}{C}HCH_2OH} \qquad \underset{\mathbf{2}}{O{=}CH\underset{\bullet}{C}H_2}$$

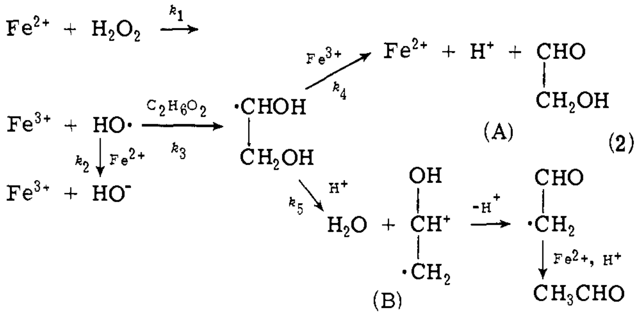
Norman's group examined the reaction further and proposed that the result is the consequence of an acid-catalyzed loss of –OH from **1**, to yield a radical cation which on proton loss yields **2** (the two steps perhaps being concerted).

$$HO\underset{\bullet}{C}HCH_2OH \xrightarrow{H^+} HO\underset{+}{C}H{-}\underset{\bullet}{C}H_2 \longrightarrow O{=}CH\underset{\bullet}{C}H_2 \qquad (1)$$

They showed that the process was quite general for glycols, and that similar loss of Cl^- occurred from chlorohydrins. Subsequently, they demonstrated that the same sort of reaction occurs when similar radicals are produced by HO· addition to enol derivatives.[4] Since their conclusions were based solely on ESR spectra of transient intermediates, we have reexamined these processes by studies of the stoichiometry of Fenton's reagent reaction in such systems and by product isolation. In general, our results confirm and extend their model.

Stoichiometry of Fenton's Reagent Oxidation of Glycols

Combining Norman's proposed reactions with our own data on hydroxyl radical reactions with a variety of substrates,[5] we would anticipate reaction scheme 2 (using ethylene glycol as a model). If H_2O_2 is added to a Fe^{2+}-substrate system, to the extent that reaction follows path B, the stoichiometry (moles of H_2O_2 consumed/mole of Fe^{2+} oxidized) would be the same as if no glycol were present; i.e., the ratio $2\Delta H_2O_2/\Delta Fe^{2+}$ will be 1.[6] However, path A regenerates Fe^{2+}, and this path predicts that the ratio will increase linearly with the ratio [substrate]/[Fe^{2+}]. Actual ratios should depend upon the concentrations of acid and Fe^{3+} and the resulting relative importance of the two paths.



Results with ethylene glycol are shown in Figure 1 and nicely confirm the model. In 0.05 *M* $HClO_4$ and only the small amount of Fe^{3+} formed in the oxidation, chain lengths are only slightly larger than unity. Addition of 0.16 *M* Fe^{3+}, however, gives long chains at high [substrate]/[Fe^{2+}] ratios, but these again are drastically reduced in 0.5 *M* acid. Results with 2,3-butanediol, Figure 2, are similar but less pronounced. (The small drop in chain length at high substrate/Fe^{3+} ratios is probably an experimental artifact due to poor titration end points at high glycol concentrations.) Plainly the collapse to radical cation has an enormous effect on the oxidation chain length; the dashed lines in Figures 1 and 2 show the predicted stoichiometry if only

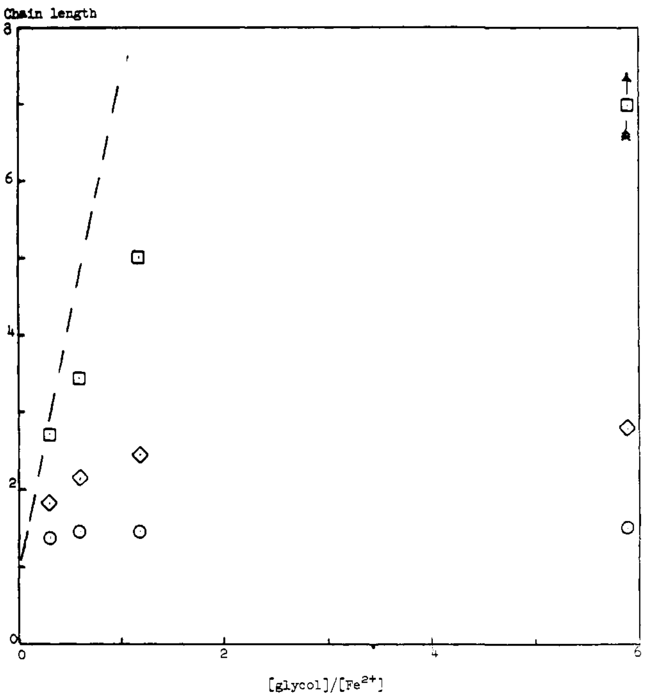


Figure 1. Stoichiometry of ethylene glycol oxidation: (circles) [H$^+$], 0.05 *M*, no [Fe^{3+}]; (squares) [H$^+$], 0.05 *M*, [Fe^{3+}], 0.16 *M*; (diamonds) [H$^+$], 0.5 *M*, [Fe^{3+}], 0.16 *M*.

path A was followed, using values of k_3/k_2 determined as described below.

The data in Figures 1 and 2 can in principle be analyzed quantitatively to yield the relative contributions of paths A and B and, in principle, the ratios k_3/k_2.[7] Results are summarized in Table I.

This treatment does not give very reliable values of k_3/k_2, particularly when the change in stoichiometry is small. A better technique is to examine the retardation by glycols of the chain oxidation of methanol under conditions when glycol oxidation predominantly follows path B.[8] Under these conditions

$$\frac{\Delta[\mathrm{Fe}^{2+}]}{2\Delta[\mathrm{H_2O_2}] - \Delta[\mathrm{Fe}^{2+}]} = \frac{k_2}{k_{3(\mathrm{MeOH})}}\frac{[\mathrm{Fe}^{2+}]}{[\mathrm{MeOH}]} + \frac{k_{3(\mathrm{glycol})}[\mathrm{glycol}]}{k_{3(\mathrm{MeOH})}[\mathrm{MeOH}]} \quad (3)$$

Plots of (3) for both glycols are shown in Figure 3 and, taking $k_3(\mathrm{MeOH})/k_2 = 4.03$[5] gives for ethylene glycol $k_3/k_2 = 4.89$ (which might be corrected to 6.11 since under these conditions only about 80% of its oxidation is going via B)[9] and for butanediol $k_3/k_2 = 8.08$. If we take $k_2 = 3 \times 10^8$, an average value from radiation-chemistry results,[10] these ratios yield $k_3 = 1.8 \times 10^9$ for glycol and $k_3 = 2.4 \times 10^9$ for butanediol. Corresponding values from radiation chemistry are 2×10^9 and 1.35×10^9,[10] a quite satisfactory agreement, in view of the uncertainties in radiation results.

Product Studies

Semiquantitative product studies by GLC analysis provide direct qualitative confirmation for reaction scheme 2. Results with butanediol are shown in Table II. At low acid and high Fe^{3+}, the product is primarily acetoin from path A. At high acid without added Fe^{3+}, it is 2-butanone via path B. The drop in yield of 2-butanone in the inverse addition experiment (slow addition of Fe^{2+} to H$_2$O$_2$-substrate) where [Fe^{2+}] is very low presumably represents loss of intermediate radicals through dimerization rather than reduction.

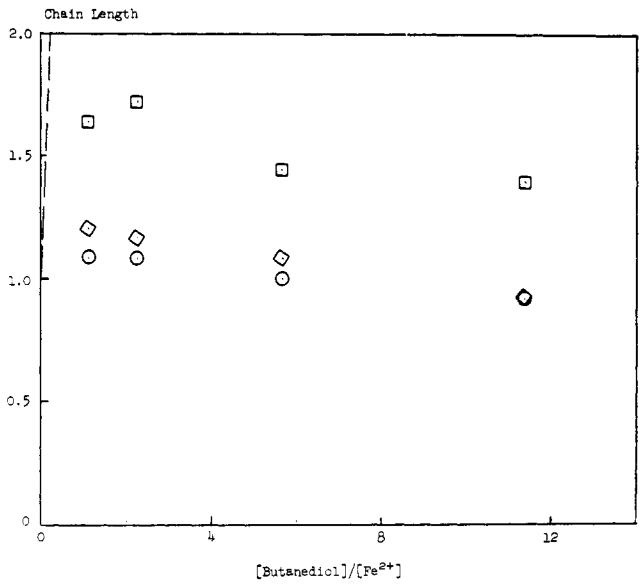


Figure 2. Stoichiometry of 2,3-butanediol oxidation. Conditions and symbols the same as in Figure 1.

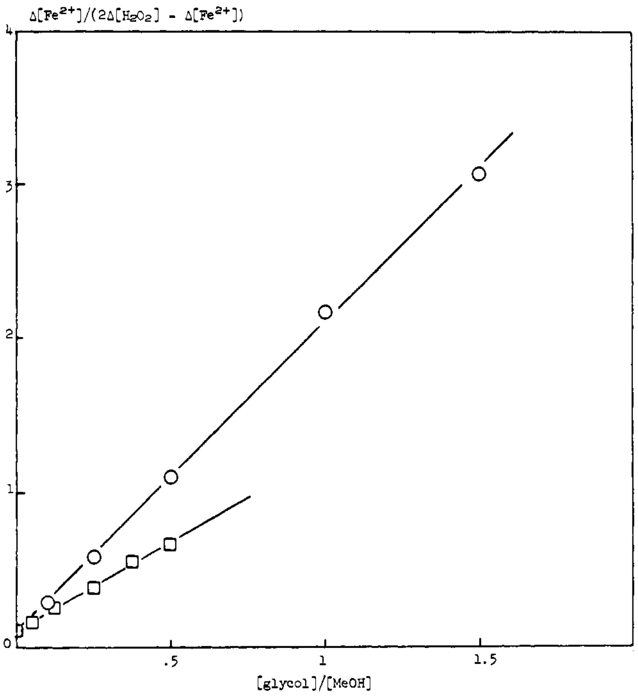


Figure 3. Plots of eq 3: (squares) ethylene glycol (slope 1.14); (circles) 2,3-butanediol (slope 2.01).

Table I. Reaction Paths in Glycol Oxidations

Substrate	[H$^+$]	[Fe^{3+}]	% path B	k_3/k_2
Ethylene glycol	0.05	0	66	(13)
	0.05	0.16	4–12	6.4
	0.5	0.16	34	7.5
Butanediol	0.05	0	90–100	
	0.05	0.16	60–70	
	0,5	0.16	77–83	

Acetaldehyde was also obtained (28%) in an ethylene glycol oxidation in 0.5 *M* acid without added Fe^{3+}. With no acid and 0.16 *M* Fe^{3+}, none could be detected.[11]

Discussion

Our results show that Norman's reaction scheme, based on ESR data, is consistent both with the products of glycol

Table II. Products of Oxidation of 2,3-Butanediol

$[Fe^{2+}]$	$[Fe^{3+}]$	$[HClO_4]$	% yield 2-Butanone	% yield Acetoin
0.04	0	0	36	30
0.04	0.16	0	19	67
0.04	0	0.2	50	0
0.06	0	0.1	38	7
0.06[a]	0	0.1	18	7

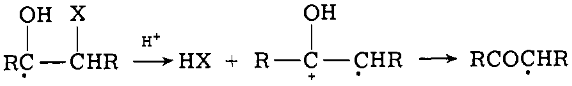
[a] Inverse addition, see text.

Table III. Stoichiometry of Oxidation of Glycol Derivatives

$[H^+]$	$[Fe^{3+}]$	Chain length $HOCH_2$-CH_2OH	Chain length $HOCH_2$-CH_2Cl	Chain length $HOCH_2$-$CH_2OPO_3^{2-}$
0.05	0	1.47	1.20	1.26
0.05	0.16	5.00	1.25	3.33
0.50	0.16	2.46	1.23	2.16

oxidation by the Fe^{2+}-H_2O_2 system and with reaction stoichiometry, and that proper analysis of the data indicates a high rate of hydroxyl radical attack consistent with other data. They also demonstrate conclusively that oxidized and rearranged products, e.g., acetoin and 2-butanone from butanediol, arise from a common intermediate radical, and we can make a rough estimate of its life. We have estimated the rate constant for reaction of the $\cdot CH_2OH$ radical with Fe^{3+} as $\geq 4 \times 10^8$ l./mol sec. If we assume a similar value for the radical from butanediol, its pseudo-first-order reaction rate in 0.16 *M* Fe^{3+} solution would be 6.4×10^7. However, from Table I, in 0.5 *M* acid, it is disappearing twice as fast by collapse to its radical cation, corresponding to a rate constant of 1.28×10^8, or an average life of 7.8×10^{-9} sec. If the collapse is first order in $[H^+]$, in 0.05 *M* acid, its life should be 7.8×10^{-8} sec, a result consistent with the change in partitioning between paths A and B in Table I. With the same assumptions, under similar conditions, the life of the radical from butanediol is about one-eighth as long.

Norman has shown that radicals from chlorohydrins undergo a similar collapse and has proposed a general process where -X is any one of a variety of good leaving groups.



$$\mathrm{R}\underset{\bullet}{\overset{\mathrm{OH}}{\mathrm{C}}}-\overset{\mathrm{X}}{\mathrm{C}}\mathrm{HR} \xrightarrow{\mathrm{H}^+} \mathrm{HX} + \mathrm{R}-\underset{+}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\bullet}{\mathrm{C}}\mathrm{HR} \longrightarrow \mathrm{RCO}\underset{\bullet}{\mathrm{C}}\mathrm{HR} \quad (4)$$

We have briefly looked at the stoichiometry of oxidation of some glycol derivatives, Table III, with results that confirm such a path and indicate that chloride and phosphate are better leaving groups than -OH. To us, these eliminations may be most profitably thought of as very rapid solvolyses of radicals, analogous to the solvolysis on nonradical species like tertiary halides and alcohols, and represent a new and potentially important branch of radical chemistry.[12] Although Norman implies that all require acid catalysis, it is hard to see why this should be the case for leaving groups which do not require protonation in ordinary solvolyses. For the chlorohydrin in Table III, acidity has no significant effect, although the chain lengths are too short for the experiment to be conclusive (with phosphate at these pH's, acid sensitivity might be expected since both mono- and diprotonated species must be present, and the second should be a better leaving group).

The scope of such processes remains to be determined, but it seems likely that the requirements are a strongly solvating medium (here, water), a good leaving group (as defined in conventional solvolyses), and the presence of strong electron-supplying groups in the radical to stabilize the resulting radical cation. Norman's results indicate this last to be the case, as does our finding of more rapid elimination in the butanediol reaction compared with ethylene glycol, and also our previous failure to detect any such process (as evidenced by liberation of Cl^-) in the oxidation of 2,2,2-trichloroethanol.[5] Of course, as we have shown here, the possibility of detecting such a process will depend upon the lifetime of the initial radical and the rates of competing reactions by which it is consumed.

Finally, we note that the reaction provides another interesting example of a coupled process in which the energy of a redox reaction is used to bring about a transformation (here a pinacol-type rearrangement) in which no net oxidation or reduction is observed.

Experimental Section

Stoichiometric experiments were carried out as in our previous papers[5] by adding H_2O_2 to Fe^{2+}-substrate systems under N_2 and determining the Fe^{2+} oxidized.

Glycol monophosphate was prepared by reacting ethylene oxide with 0.6 *M* disodium phosphate solution for 2.5 hr at 30°. It was used without further purification, and may have contained some ethylene glycol. Accordingly the results may be of only qualitative significance.

Products were determined by GLC analysis using known reference compounds and internal standards.

References and Notes

(1) Support of this work by a grant from the National Science Foundation is gratefully acknowledged.

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(5) C. Walling, G. M. El Taliawi, and R. A. Johnson, *J. Am. Chem. Soc.*, **96**, 133 (1974), and references cited therein.

(6) This ratio is also the kinetic chain length of the oxidation, and the two terms will be used interchangeably here.

(7) The rather complex equations have been presented previously.[5] In general, the equations may be put in rectified form and rate constant ratios calculated from slopes and intercepts.

(8) The situation is kinetically analogous to the retardation of methanol oxidation by acetone; cf. C. Walling and G. M. El Taliawi, *J. Am. Chem. Soc.*, **95**, 844 (1973).

(9) From Table I, 66% of the reaction goes via path B in 0.05 *M* acid, and we assume path B to be twice as fast in 0.1 *M* acid (see below).

(10) L. M. Dorfman and G. E. Adams, "Reactivity of the Hydroxyl Radical in Aqueous Solutions", Report No. NSRDS-NBS-46, U.S. Government Printing Office, Washington, D.C., 1973.

(11) Qualitative detection of acetaldehyde has been reported previously in Fenton's reagent oxidation of glycol, but without explanation; cf. "Organic Peroxides", Vol. 2, D. Swern, Ed., Wiley-Interscience, New York, N.Y., 1971, p 293.

(12) An entirely similar collapse of hydroxycyclohexadienyl radicals to aromatic radical cations is an important feature of hydroxyl radical reactions with aromatics which we have discussed elsewhere: C. Walling and R. A. Johnson, *J. Am. Chem. Soc.*, **97**, 363 (1975).