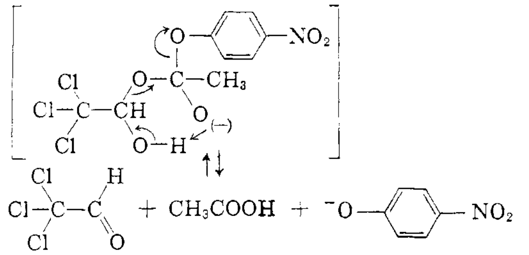
(7)

In this case, a water molecule would again function by hydrating the chloral produced. The question regarding participation of water in the over-all reaction is similar to the situation encountered in hydrolytic reactions catalyzed by various hydrolases. For the latter, evidence in most instances is lacking in regard to the participation of water in the hydrolytic reaction. In one case, however, the myosin-catalyzed hydrolysis of adenosine triphosphate, a specific myosin–water interaction has been demonstrated[7] for the hydrolysis, thus implying a specific site on the protein for participation of water in the hydrolysis.

Of further interest is the fact that a carbonyl group has been considered[8] as the active site of certain proteases, albeit without any structural evidence. Our work would seem to indicate that a protein carbonyl group of sufficient polarity to be strongly hydrated would be capable of reaction, at least, with esters provided, of course, the ester is a "high-energy" one such as *p*-nitrophenyl acetate or can be activated by another group or grouping of the protein. The latter qualification is necessary since chloral hydrate like imidazole does not react with "low energy" esters such as ethyl acetate or ethyl hippurate.[9] In this connection, the typical protease, chymotrypsin, reacts in a non-specific sense with such "high-energy" acyl derivatives as acid anhydrides and *p*-nitrophenyl acetate, but in a specific sense with "low-energy" acyl derivatives, esters and amides, of tyrosine and phenylalanine.[10]

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[7] D. E. Koshland, Jr., and E. B. Herr, Jr., *J. Biol. Chem.*, **228**, 1021 (1957).

[8] J. S. Fruton and S. Simonds, "General Biochemistry," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 616.

[9] O. Gawron and F. Draus, unpublished work.

[10] G. H. Dixon and H. Neurath, *J. Biol. Chem.*, **225**, 1049 (1957).

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[Contribution from the Department of Chemistry, Saint Joseph College]

Oxidation of Alcohols Catalyzed by Zinc Oxide and Light

By M. Clare Markham, M. Consilia Hannan, Rose M. Paternostro and Carole B. Rose

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The oxidation of glycerol, benzyl alcohol and the first seven aliphatic alcohols, including several isomeric alcohols, has been studied at room temperature using zinc oxide irradiated at 366 mμ as a photocatalyst. None of the alcohols studied absorbs light of this wave length. The accumulation of peroxides in these systems varies with the type of alcohol, the chain length and the concentration. For each alcohol there is an optimum concentration. The general pattern is consistent with other types of oxidation, primary alcohols being oxidized most rapidly and giving highest yields of peroxides. In several cases it has been possible to identify the aldehydes and ketones formed as products. There is evidence for the presence of organic peroxides in intermediate stages.

Introduction

An earlier publication from this Laboratory[1] described the factors influencing the oxidation of phenols catalyzed by zinc oxide and light. These studies indicated the formation of concentrations of hydrogen peroxide several times higher than the initial concentration of phenol. At the same time the accumulation of hydrogen peroxide up to a certain point and then the gradual decrease in peroxide concentration down to a small but constant limiting value, indicated a high degree of oxidation of the organic substances. Phenolic concentrations of 0.001 *M* or less were found to yield optimum initial rates of formation of peroxide. In solutions of higher concentration there are apparently competing reactions among the free radicals found in the oxidation process, and leading in many cases to intermediate formation of dark-colored condensation products.

In concentrations as low as 0.001 *M* the aliphatic alcohols seemed to be much less effective in forming hydrogen peroxide in similar photocatalytic systems. Therefore it was of interest to see whether alcohols would be more rapidly oxidized at higher concentration, and to discover the nature and fate of the oxidation products. The oxidations of methyl alcohol and of glycerol were subjected to analysis in considerable detail.

Experimental

The apparatus and method of procedure in exposing the suspensions of zinc oxide in aqueous solutions of alcohols to ultraviolet light were described previously.[2] The Hanovia high pressure mercury arc lamp was used with a Pyrex jacket to retain all radiation below 320 mμ. The only effective radiation was thus 366 mμ which zinc oxide absorbs strongly, and which the alcohols studied do not absorb at all. Reactions were carried out in Pyrex test-tubes, surrounded by a Pyrex jacket through which water was circulated at constant temperature. Except for a few experiments at 10 and 30°, all reactions were carried out at 20°, which seems to be the optimum temperature for formation of hydrogen peroxide. Stirring was effected and oxygen supplied for the oxidation reactions by entraining air. A few experiments with pure oxygen sufficed to show that the rate of supplying oxygen is not the limiting factor in these oxidations.

A Patwin research model polarograph was used to investigate the oxidation products of glycerol and methyl alcohol. A Beckman DU spectrophotometer was used to compare the

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[1] M. C. Markham, M. Consilia Hannan and S. W. Evans, This Journal, **76**, 820 (1954).

[2] M. C. Markham and K. J. Laidler, *J. Phys. Chem.*, **57**, 363 (1953).

absorption spectra of filtrates of the irradiated suspensions with standard solutions of hydrogen peroxide and aldehydes.

Additional analyses for aldehydes were made with Schiff reagent, and for ketones with salicylaldehyde reagent.

Tests for peroxides were made by allowing aliquot portions of the irradiated suspensions to react with iodide ion in 1.0 *N* H_2SO_4 and titrating the liberated iodine with standard solutions of thiosulfate. In some cases the peroxide concentration was also estimated colorimetrically with $Ti(SO_4)_2$ reagent, and in a few special cases by polarographic analysis. The amounts of peroxide determined by the three methods were not always equal. In some cases the blue color of the starch indicator kept returning to the titrated solutions, indicating slow reaction of certain organic peroxides with iodide ion. For this reason blanks were run on all titrations, and the titrations continued regularly for an hour or more until there was no further difference between the blank and the test solution. The amounts of peroxide so measured were higher than the amounts estimated polarographically or colorimetrically with $Ti(SO_4)_2$ reagent, notably in the case of some of the higher aliphatic alcohols. Apparently some of the organic peroxides and hydroperoxides react only slowly with iodide ion, and some do not give the characteristic yellow color with $Ti(SO_4)_2$ even in 6 *M* H_2SO_4. According to the suggestion of Satterfield,[3] the $Ti(SO_4)_2$ tests were allowed to stand for several hours to ensure that no further color would develop. Pure samples of all the possible intermediate organic peroxides or hydroperoxides are not available for comparison, since many of these compounds are so unstable that they cannot be isolated in a pure state. We have worked with samples of cumene, thymol and menthane hydroperoxides, and have found that dilute aqueous solutions of the first react very slowly with $Ti(SO_4)_2$ reagent, whereas the other two react within a few minutes; all react rapidly with iodide ion. Hydrogen peroxide itself in dilute solutions reacts slowly with iodide ion unless a drop of saturated ammonium molybdate is added as a catalyst. Molybdate was used to catalyze the reactions in all the analyses reported in this paper.

Results

Oxidation of Glycerol.—Figure 1 shows the variation in relative rates of accumulation of peroxides with glycerol solutions of various concentrations. Plotted on the same figure for purposes of comparison are the same data for resorcinol and for methyl and ethyl alcohols at 20°. Peroxide concentrations were measured after 0.5 hour in each case. At the optimum concentrations for both glycerol and methyl alcohol, the entire peroxide concentration seems to be hydrogen peroxide, or at least organic peroxides which react instantaneously with iodide ion. In the case of 1.0 *M* glycerol the reaction with iodide ion continues for several minutes, and the amount of peroxide estimated colorimetrically with $Ti(SO_4)_2$ is in agreement with the total peroxide content measured by titration, and by the polarograph. Absorbance measurements show the probable presence of glyceraldehyde and/or dihydroxyacetone in the absorption spectrum of the irradiated solution at 1.0 *M* concentration. The presence of organic peroxides is indicated by general absorption in the region of 200 to 270 mμ where hydrogen peroxide solutions of concentrations equivalent to that found in these irradiated suspensions have only slight absorption.

Polarographic analysis shows definite rises in the regions of 0.8 to 1.20 v. for H_2O_2, and 1.55 to 1.85 v. for glyceraldehyde and dihydroxyacetone in neutral solution. The rise is suppressed in solutions of *p*H 3 because of the hydration of the aldehyde.

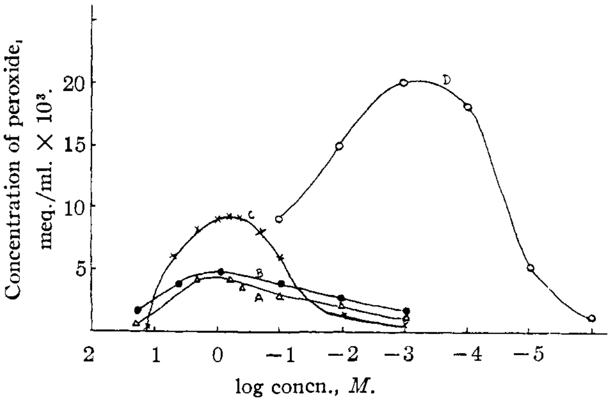

Fig. 1.—Amounts of peroxide in solutions of varying concentration of alcohols, irradiated with ZnO, 30 minutes, 366 mμ, 20°: A, ethyl alcohol (△); B, methyl alcohol (●); C, glycerol (×); D, resorcinol (○).

Suspensions of ZnO in water have a *p*H of about 7.0. On irradiation with dilute aqueous solutions of organic substances the *p*H drops only slightly to about 6.0 to 6.5, and glyceraldehyde and/or dihydroxyacetone are still evident in the filtrate. As in the case of pure glyceraldehyde and dihydroxyacetone this rise at 1.55–1.85 can be obliterated by acidifying the irradiated solution.

Oxidation of Methyl Alcohol.—Preliminary tests showed that methyl alcohol is also oxidized rapidly to hydrogen peroxide and formaldehyde on irradiation at 366 mμ in aqueous suspensions of ZnO. The optimum concentration is approximately 1.0 *M* as in the case of glycerol, and extends over a rather broad range of concentrations around 1.0 *M*. Figure 2 shows the relative rates of appearance and disappearance of formaldehyde in these systems. Note that formaldehyde is initially formed in equal concentration with the hydrogen peroxide, but that it accumulates to a limited concentration and then slowly disappears. As the formaldehyde disappears the peroxide also begins to drop off. Analyses carried out on 0.01 *M* CH_3OH over a period of 30 hr. show that a limiting concentration of about 0.008 *M* peroxide is reached and maintained for about ten hours before finally dropping off.

Polarographic analyses gave no indication of organic hydroperoxides. Work of Stern and Polak[4] demonstrated the electroreduction of methyl hydroperoxide in the region of 0.2–0.3 v. in 0.1 *N* LiCl. Polarograms indicate only hydrogen peroxide and formaldehyde in the irradiated suspensions of methyl aclohol. Formaldehyde can be reduced quantitatively only in an alkaline solution. Standard curves for H_2O_2 in 0.1 *N* LiCl and for HCHO in 0.1 *N* LiOH both gave linear plots of current *vs.* concentration. Analyses showed that formaldehyde and hydrogen peroxide are formed initially in equal concentrations. Studies of Satterfield[3] indicate that hydroperoxides of the type $H_2C(OH)(OOH)$ might be more stable in solution at lower temperatures.

Figure 3 includes the rate of oxidation of HCHO for comparison with the alcohols. Except for benzyl alcohol, formaldehyde is oxidized more

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[3] C. N. Satterfield and L. C. Case, *Ind. Eng. Chem.*, **46**, 998 (1954); C. N. Satterfield and A. H. Bonnell, *Anal. Chem.*, **27**, 1174 (1954).

[4] V. Stern and S. Polak, *Acta Physicochim. U.R.S.S.*, **11**, 1 (1939).

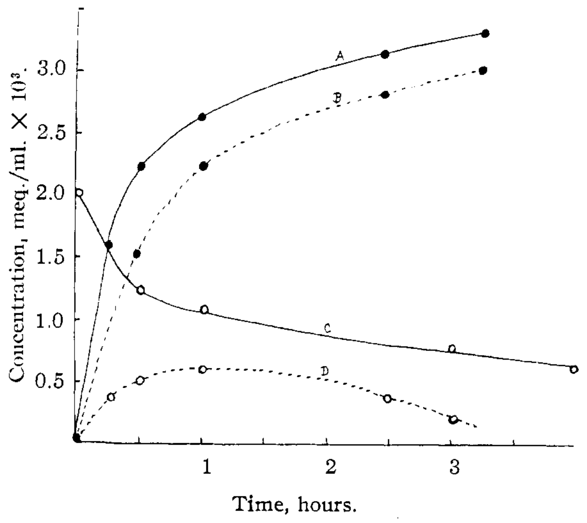

Fig. 2.—Rate of formation of peroxide in: A, 10^{-3} *M* HCHO (●–); B, 10^{-3} *M* CH_3OH (●---). Rate of disappearance of: C, HCHO in 10^{-3} *M* HCHO (O–); and D, appearance of HCHO(O---) in B; ZnO, 366 mμ, 20°.

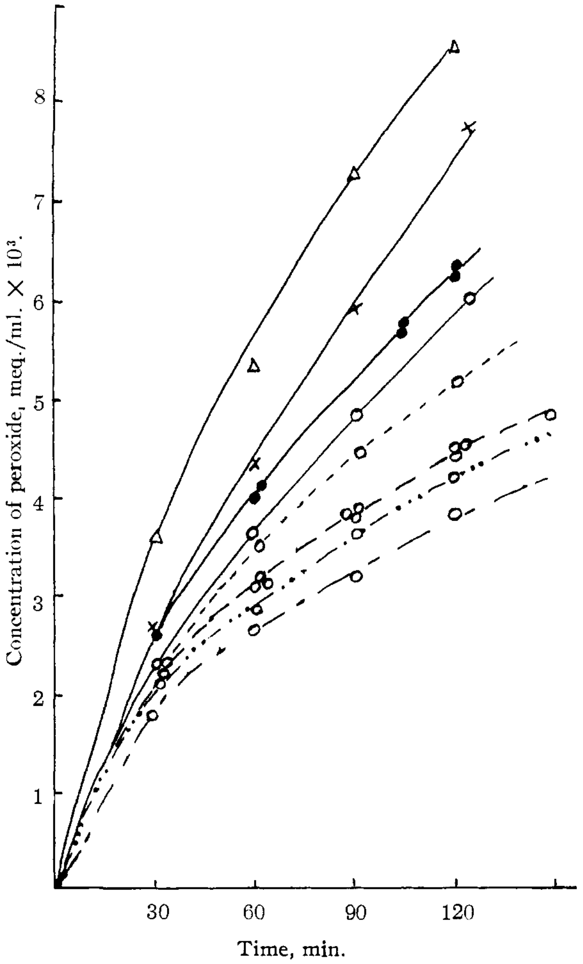

Fig. 3.—Comparative rates of oxidation of primary alcohols, 0.01 *M*, ZnO, 366 mμ: Δ–, benzyl; ×–, formaldehyde; ●–, heptyl and hexyl (*n*); O–, methyl; O– – –, ethyl, *n*-amyl, isobutyl; O— — —, *n*-propyl; O—···—, *n*-butyl; O------, isoamyl.

rapidly in these systems than any of the purely aliphatic alcohols. Tests show that CO_2 is the final oxidation product.

Comparison of Rates of Photo-catalytic Oxidation of Various Alcohols at Equimolar Concentration.—Figure 3 shows the relative rates of oxidation of several primary alcohols, all at concentration of 0.01 *M*. Note that methyl alcohol has a high rate of oxidation, ethyl somewhat lower, then propyl; but the higher alcohols, beginning with butyl alcohol, show an increase in oxidation rate. Benzyl alcohol is oxidized most rapidly of all. Isobutyl alcohol oxidizes somewhat faster than *n*-butyl, and isoamyl alcohol faster than *n*-amyl alcohol. Figure 4 shows the comparative rates of oxidation of primary, secondary and tertiary alcohols.

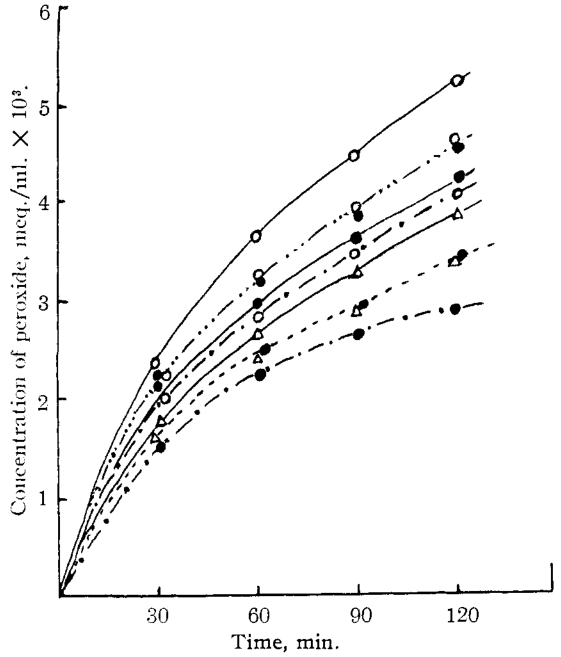

Fig. 4.—Comparative rates of oxidation of isomeric alcohols, ZnO, 366 mμ: Δ—, *n*-propyl; Δ·—, isopropyl; ●—, *n*-butyl; ●---, *sec*-butyl; ●—·—, *t*-butyl; O—, isoamyl; O—·—, diethylcarbinol, *t*-amyl; O—···—, isobutyl; O—···—, *n*-amyl.

In the initial stages of the oxidation, irradiated suspensions of isopropyl alcohol and diethylcarbinol give very definite tests for ketones with salicylaldehyde reagent. Even *t*-butyl alcohol gives slight tests for HCHO and acetone indicating cleavage of C–C bonds. The odor of benzaldehyde is easily recognizable in the irradiated suspensions of benzyl alcohol.

The table shows the results of testing aliquot portions of some of these irradiated suspensions by titration of liberated I_2 by $S_2O_3^{=}$ and by color with $Ti(SO_4)_2$ reagent.

	Meq. of peroxide by titration of liberated I_2 by $S_2O_3^{=}$ (× 10^3)	Meq. peroxide determined colorimetrically with $Ti(SO_4)_2$ (× 10^3)
0.01 *M* CH_3OH	6.2	6.0
1.00 *M* $C_3H_5(OH)_3$	9.5	9.0
0.01 *M* $C_6H_5CH_2OH$	8.6	7.6
0.01 *M* $C_6H_{13}OH$	6.3	2.2
0.01 *M* $C_7H_{15}OH$	5.5	2.9

Discussion

This study of the oxidation of alcohols confirms several significant features of the photocatalytic oxidation of organic compounds on ZnO in light which is absorbed only by zinc oxide.

If the initial reaction is the transfer of an electron from zinc to O_2 adsorbed on the surface, the resulting $\cdot O_2^-$ is a radical ion, and evidently requires water or a highly polar solvent for the efficiency of the electron transfer process. The reaction does occur to some small extent in absolute methyl alcohol, but not at all in pure glycerol; *cf.* Fig. 1.

Organic additives undergo oxidation either by electron transfer to the photopositive zinc oxide surface (after loss of a photo-excited electron by the crystal to O_2) or by hydrogen abstraction by the peroxide radical ion to form $HO_2\cdot^-$. In the case of the phenols the phenolate ion adsorbed on the zinc oxide surface can transfer an electron directly to the crystal and then undergo immediate destructive oxidation by the peroxide radical ion or by molecular oxygen. This interpretation would explain the unique ability of the phenols to promote rapid accumulation of hydrogen peroxide at very low phenolic concentrations; *cf.* ref. 1.

In the case of the aliphatic alcohols the rate of oxidation is evidently related to the case of abstraction of hydrogen atoms: primary alcohols, in general, are more easily oxidized than the isomeric secondary or tertiary alcohols. Since these alcohols are probably not initially adsorbed on the ZnO in an ionic form, it is not surprising that higher concentrations are required for rates of peroxide formation equivalent to that of the phenols. The fact that tertiary alcohols are oxidized appreciably is a further indication of the non-specific character of the initial oxidation step (*cf.* ref. 2.)

Primary alcohols would be expected to form radicals of the type $R\dot{C}(H)(OH)$. These radicals can easily lose a second hydrogen atom to form an aldehyde, or react with molecular oxygen to form a peroxide radical, $RC(H)(OH)O_2\cdot$. Subsequent reaction of this radical with a molecule of the original alcohol may lead to hydroxyalkyl hydroperoxides and their derivatives, thus initiating chain reactions. Hydroxyalkyl hydroperoxides dissociate in water in dilute solutions to form aldehydes and hydrogen peroxide; the dissociation is catalyzed by dilute acids and bases, and so would be highly probable under the conditions used for testing for peroxides.[5] Differences in rates of propagation of peroxide chains and differences in rates of hydrolysis of intermediate oxidation products are probably responsible for the variation in rates of peroxide formation in the isomeric alcohols tested. Figures 2 and 3 show that formaldehyde itself is rapidly oxidized in this system; therefore it is not likely that aldehydes will be the final products.

In the case of the higher aliphatic alcohols there are evidently fairly stable organic peroxides present in the irradiated suspensions. They react only slowly with the iodide ion; oxidation products of hexyl and heptyl alcohols continue to release iodine over the course of one or two hours. Tests for peroxide with $Ti(SO_4)_2$ give only about half the peroxide values obtained with iodide. The rest of the peroxide, not reacted with $Ti(SO_4)_2$, must be tied up in fairly stable addition products of the type $RCH(OH)(OOH)$, or possibly as bis-hydroxyalkyl peroxides. Recent work of Mosher, *et al.*, indicates an increasing stability toward thermal decomposition on the part of the higher hydroxyalkyl peroxides. It is possible that they are more stable toward hydrolysis and photochemical decomposition also.

There must be some explanation of the increase in initial rate of oxidation of these higher aliphatic alcohols. It seems likely that their effect on the surface tension of water makes for better contact between oxygen, water and alcohol on the surface of the ZnO. The foaming of 0.01 *M* solutions of hexyl, heptyl and benzyl alcohols on shaking with air and water is quite noticeable, and it is also noticeable that zinc oxide seems to be held in more homogeneous suspension with the higher aliphatic alcohols than it is in the case of the phenols and the lower alcohols.

Acknowledgment.—This work was made possible in part by a grant from Sigma-Xi-Resa Research Fund.

(5) A. V. Tobolsky and R. B. Mesrobian, "Organic Peroxides," Interscience Publishers, Inc., New York, N. Y., 1954, pp. 44, 45.

(6) C. F. Wurster, L. J. Durham and H. S. Mosher, THIS JOURNAL, **80**, 327 (1958).

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CHICAGO]

The Entropies of Activation in the Nitration of Ethyl Benzoate[1]

BY WM. J. LE NOBLE[2] AND G. W. WHELAND

RECEIVED APRIL 15, 1958

The nitration of ethyl benzoate by nitric acid in acetic acid as the solvent, and with sulfuric acid as a catalyst, was studied over a range of 100°. The isomer distribution was determined by means of the isotope dilution method. The results show that the three simultaneous substitution reactions have nearly the same entropy of activation, so that the differences between the three rates of formation can be almost entirely ascribed to the differences in activation energy.

The isomer distributions in the disubstitutions of benzene have been the subject of many investigations and a semi-quantitative understanding of the problem has been reached. In the theoretical treatments, the most significant factor affecting this distribution is commonly presumed to be the differences between the potential energies of the

(1) Based on the dissertation submitted by W. le Noble in partial fulfillment of the requirements for the Ph.D. degree.

(2) N.S.F. Fellow, 1955–1957.