[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Kinetic Evidence for Reaction of Chloralate Ion with *p*-Nitrophenyl Acetate in Aqueous Solution

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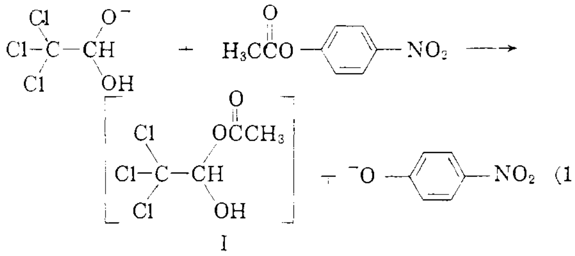
A reaction between chloral hydrate and *p*-nitrophenyl acetate liberating *p*-nitrophenol has been investigated kinetically. The reaction is first order in both chloral hydrate and *p*-nitrophenyl acetate and *p*H studies indicate the chloralate ion to be the reactive form of chloral hydrate. It is suggested the reaction is a displacement of *p*-nitrophenylate ion from *p*-nitrophenylacetate by chloralate ion with subsequent hydrolysis of chloral monoacetate.

Introduction

While the acidic character of chloral hydrate has been known for some time, little attention has been given to the nucleophilic character of its conjugate base, the chloralate anion. In investigating the nucleophilic behavior of chloralate ion, chloral hydrate and *p*-nitrophenyl acetate were allowed to react in aqueous solutions of suitable *p*H. A rapid liberation of *p*-nitrophenol occurs and the course of the reaction may be followed by spectrophotometric determination of liberated *p*-nitrophenol. Investigation of the kinetics of the reaction in this manner indicated the reaction to be first order with respect to both *p*-nitrophenyl acetate and chloral hydrate and *p*H dependence of the kinetics indicated the chloralate ion to be the reactive species. The reaction is initially, then, a displacement of *p*-nitrophenolate ion from *p*-nitrophenyl acetate and is another example of the reaction of bases with *p*-nitrophenyl acetate.[1]



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Experimental

Kinetic Procedure.—The kinetic experiments reported herein were conducted at 30° and over the narrow *p*H range, 6.5–8.0, in order to minimize chloral hydrate destruction[2] and blank hydrolysis rates, both of which increase with increasing *p*H. Phosphate buffers, 0.2 μ, were utilized for *p*H control.

Reactions were allowed to proceed in 1 cm. cuvettes in the cell compartment of a Beckman DU spectrophotometer, temperature control being attained by circulating water from a constant temperature bath. Appearance of *p*-nitrophenol was followed by periodic measurement of optical density at a wave length suitable for determination of *p*-nitrophenol at the particular reaction *p*H employed. Optical density readings were converted to concentrations with the aid of calibration curves, the curves being determined for each reaction *p*H by substituting *p*-nitrophenol for *p*-nitrophenyl acetate in reaction mixtures. Wave lengths employed were 400 mμ at *p*H 7.97, 7.76, 7.16 and 325 mμ at *p*H 6.59. At the latter wave length, the contribution of *p*-nitrophenyl acetate, in the concentration employed in reaction mixtures, to the optical density was negligible.

Reaction mixtures were made up as follows: After temperature equilibration of all solutions, 5.0 ml. of buffer solution and 1.0 ml. of chloral hydrate solution were mixed and 4.0 ml. of fresh, aqueous, *p*-nitrophenyl acetate solution (usually 1.66×10^{-3} *M*) was then added. After mixing, solution was transferred rapidly to the cuvette for rate determination.

Results

Figure 1 presents first-order plots for the reaction at *p*H 7.97 in the presence of varying concentrations of chloral hydrate. First-order kinetics were obeyed at all concentrations of chloral hydrate and similar plots were obtained at other *p*H values. The first-order behavior of *p*-nitrophenyl acetate also was demonstrated (Fig. 2) by linear dependence of initial rates on initial *p*-nitrophenyl acetate concentration. The large excesses of chloral hydrate employed, particularly at lower *p*H, were needed to provide adequate chloralate ion concentration, pK_A being 9.66 (determined by potentiometric titration, 9.70 from kinetic data[2]).

Investigation of the influence of chloral hydrate concentration on initial rates at constant *p*-nitrophenyl acetate concentration yielded the results shown in Fig. 3. The k'-values plotted were obtained from the relationship, $k' = k_c - k_b$, where k_c and k_b are first-order rate constants for reactions run in the presence and absence of chloral hydrate, respectively. The linear dependence of k'-values on initial chloral hydrate concentration indicates a first-order participation of chloral hydrate in the reaction.

Over the *p*H range investigated, k'-values, obtained as indicated above, varied inversely with hydrogen ion concentration (Fig. 4). The overall rate equation for the initial reaction may be then represented by

$$v = \frac{kK_A[\text{PNPA}]\,[\text{chloral hydrate}]}{[\text{H}^+]} \qquad (2)$$

where k is the second-order rate constant for the displacement reaction, K_A is the dissociation constant for chloral hydrate and [PNPA] is *p*-nitrophenyl acetate concentration.

Since $v_0 = k'[\text{PNPA}]$, where v_0 represents initial rate, equation 2 may be written as

$$k' = \frac{kK_A[\text{chloral hydrate}]_0}{[\text{H}^+]} \qquad (3)$$

and the data of Fig. 4 represent plots of equation 3 for the several initial chloral hydrate concentrations employed. From the slopes of these lines, k was calculated to be 51 ± 2 l. × mole^{-1} × min.$^{-1}$.

Discussion

It is of interest to compare the effectiveness of chloralate ion as a nucleophile with other nucleophilic reagents. For the same reaction as studied herein and at the same temperature but with phos-

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[1] T. C. Bruice and R. Lapinski, THIS JOURNAL, **80**, 2265 (1958).

[2] C. Gustafsson and M. Johanson, *Acta Chem. Scand.*, **2**, 42 (1948).

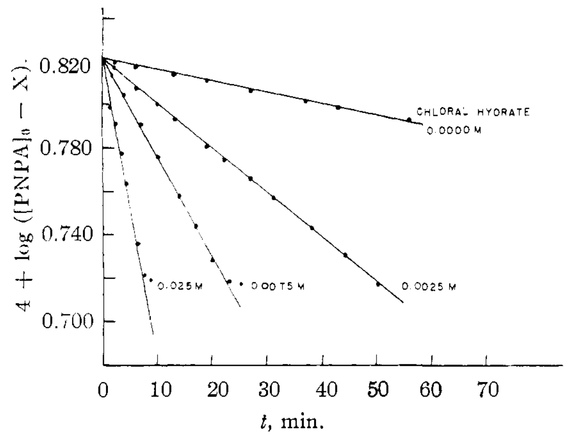
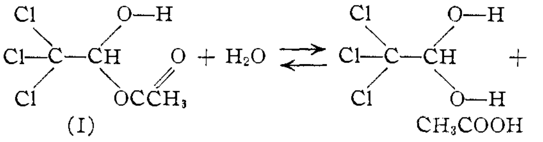


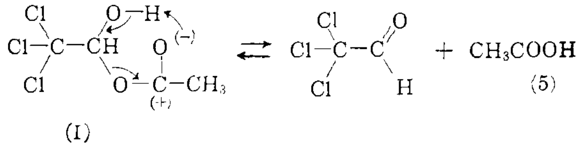
Fig. 1.—First-order plots of p-nitrophenyl acetate hydrolysis at pH 7.97 and 30° in the presence of indicated concentrations of chloral hydrate; initial concentration of p-nitrophenyl acetate, 6.64×10^{-4} M.

phate buffers of different ionic strength and in the presence of ethanol, second-order displacement constants for phenoxide ion,[1] aniline[1] and imidazole[3] were found to be 19, 0.023 and 22 l. × mole^{-1} × min.$^{-1}$, respectively. While these results were obtained under different experimental conditions and are not strictly comparable to our value for chlorate ion, they do indicate the chloralate ion to be a more potent nucleophile. Since ethoxide and methoxide are more nucleophilic than phenoxide and aniline in reaction with 1-chloro-2,4-dinitrobenzene,[4] it would seem that the chloralate ion is similar to an alkoxide ion in behavior as well as in structure. In this connection, it might also be mentioned that chloral hydrate and acetyl chloride react rapidly with evolution of hydrogen chloride.[5]

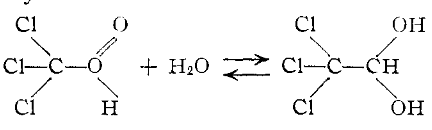
While the fate of the acetate moiety of p-nitrophenyl acetate has not been investigated, it would seem likely that intermediate I can react further and that two modes of hydrolysis are possible,


(4)

and



followed by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In reaction 4 a water molecule would participate directly while in reaction 6 it would only serve to hydrate the chloral produced by reaction 5.

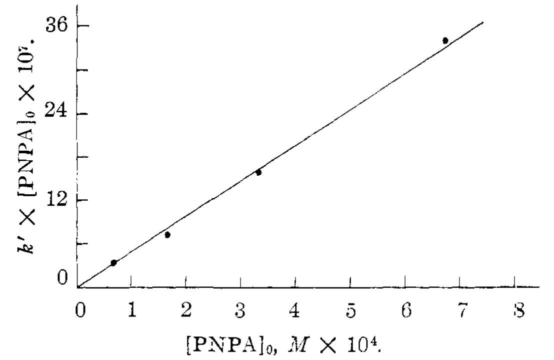

Fig. 2.—Effect of initial p-nitrophenyl acetate concentration on initial hydrolysis rates at pH 7.97, 30°, and a chloral hydrate concentration of 0.005 M; k'-values were obtained by subtracting first-order constants for blank rates from the corresponding constants for the catalyzed rates.

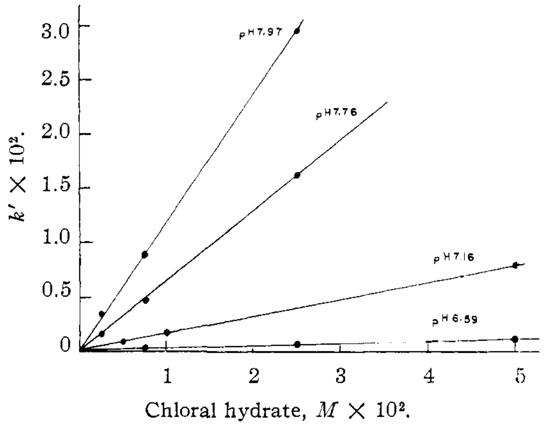

Fig. 3.—Effect of chloral hydrate concentration on k' values; initial concentration of p-nitrophenyl acetate, 6.64×10^{-4} M; pH's as indicated, 30°.

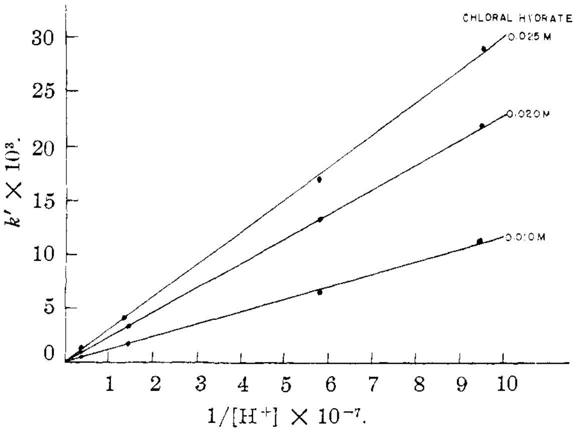

Fig. 4.—Effect of pH on k'-values at several chloral hydrate concentrations; initial concentration of p-nitrophenyl acetate, 6.64×10^{-4} M; 30°.

Since the equilibrium constant for reaction 6 is quite large[6] it is conceivable reaction 6 provides the driving force for reaction 5. It is also possible that a completely concerted decomposition of p-nitrophenyl acetate by chloral hydrate occurs

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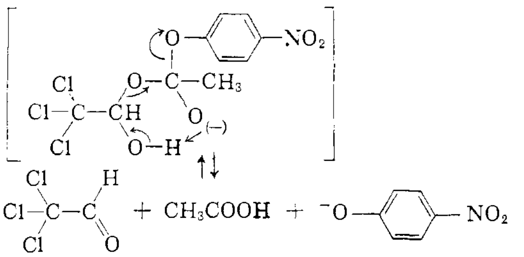
(3) T. C. Bruice and G. L. Schmir, THIS JOURNAL, **79**, 1663 (1957).

(4) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 340 (1951).

(5) V. Meyer and L. Dulk, *Ann.*, **171**, 65 (1874).

(6) P. Fedorlin, *Compt. rend.*, **235**, 44 (1952).


(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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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).