(9) D. Stigter, *J. Phys. Chem.*, **78**, 2480 (1974).
(10) H. F. Eicke, *J. Colloid Interface Sci.*, **52**, 65 (1975).
(11) I. J. Lin, J. P. Friend, and Y. Zimmels, *J. Colloid Interface Sci.*, **45**, 378 (1973).
(12) J. N. Israelachvili, D. J. Mitchell, and B. Ninham, *J. Chem. Soc., Faraday Trans. 2*, **72**, 1525 (1976).
(13) H. C. Evans, *J. Chem. Soc.*, 579 (1956).
(14) I. J. Lin and P. Somosundran, *J. Colloid Interface Sci.*, **37**, 731 (1971).
(15) E. J. Lien, *J. Med. Chem.*, **19**, 849 (1976).
(16) F. Takiwa and E. Ohki *J. Colloid Interface Sci.*, **24**, 219 (1967).
(17) B. W. Barry, J. C. Morison, and G. F. J. Russell, *J. Colloid Interface Sci.*, **33**, 554 (1970).
(18) J. W. Larsen and L. J. Magid, *J. Am. Chem. Soc.*, **96**, 5774 (1974).
(19) Unpublished results. The data we used in Evans' equation[13] were the following: the slope (S_1) of the specific conductance vs. the concentration (below the cmc) of I was 0.1; the slope (S_2) of the specific conductance vs. the various concentrations (above the cmc) of I was 0.0340; the ion conductance of Br^- (λ at 37 °C) at an infinite dilution was 97.3; and the aggregation number (N) used was 50. Only a very small difference in the calculated value of the charge density was obtained when the values of $N = 30$ and 100 were employed.
(20) For general references, see (a) E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, **8**, 271 (1970); (b) "Catalysis in Micellar and Macromolecular Systems", Academic Press, New York, N.Y., 1973; (c) E. H. Cordes and C. Gitler, *Prog. Bioorg. Chem.*, 21 (1973); (d) E. H. Cordes, "Reaction Kinetics in Micelles", Plenum Press, New York, N.Y., 1973; (e) E. H. Cordes and R. D. Dunlop, *Acc. Chem. Res.*, **2**, 329 (1969).
(21) D. G. Oakenfull and D. E. Fenwick, *Aust. J. Chem.*, **27**, 2149 (1974).
(22) (a) C. N. Sukenik and R. G. Bergman, *J. Am. Chem. Soc.*, **98**, 6613 (1976); (b) R. A. Moss, C. J. Tolkowski, D. W. Roger, and C. E. Powell, *ibid.*, **95**, 5215 (1973); (c) L. J. Magid and J. W. Larsen, *J. Org. Chem.*, **39**, 3142 (1974).
(23) R. A. Moss and W. L. Sunshine, *J. Org. Chem.*, **39**, 1083 (1974).
(24) C. A. Bunton and M. J. Minch, *J. Phys. Chem.*, **78**, 1490 (1974).
(25) M. T. A. Beheme and E. H. Cordes, *J. Am. Chem. Soc.*, **87**, 260 (1965).
(26) D. G. Herries, W. Bishoph, and F. M. Richards, *J. Phys. Chem.*, **68**, 1842 (1964).
(27) F. Reiss-Husson and V. Luzzati, *J. Phys. Chem.*, **71**, 957 (1967).
(28) Calculated by the following equations: $V = (27.4 + 26.9n)$ Å^3 and $l = (1.5 + 1.265n)$ Å, where V, l, and n are the volume of a hydrocarbon chain, the extended length of a hydrocarbon chain, and the number of carbon atoms per chain, respectively.
(29) C. Tanford, *J. Phys. Chem.*, **78**, 2469 (1974).
(30) F. Tokiwa and K. Ohki, *J. Phys. Chem.*, **70**, 3437 (1966).
(31) J. J. Cristensen, R. M. Izatt, and L. D. Hansen, *J. Am. Chem. Soc.*, **89**, 213 (1967).
(32) P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960).
(33) S. L. Walter and T. C. Bruice, *J. Am. Chem. Soc.*, **93**, 2269 (1971).
(34) D. K. Bohme, E. L. Ruff, and L. B. Young, *J. Am. Chem. Soc.*, **93**, 4608 (1971).
(35) J. I. Kurtz and J. M. Farrar, *J. Am. Chem. Soc.*, **91**, 6057 (1969).
(36) (a) J. H. Fendler, E. J. Fendler, G. A. Infante, P. Su. Shih, and L. K. Patterson, *J. Am. Chem. Soc.*, **97**, 89 (1975); (b) J. W. Larsen and L. J. Magid, *J. Phys. Chem.*, **78**, 834 (1974).

Kinetics and Mechanisms for the Acid-Catalyzed Oxidative Decarboxylation of Benzoylformic Acid

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The pH–rate profile for hydrogen peroxide promoted oxidative decarboxylation of benzoylformic acid to benzoic acid and carbon dioxide has been determined from H_0 −9 to pH +8. In aqueous solutions more acidic than pH 2, a combination of acid- and water-catalyzed reaction mechanisms accounts for the observed data. Similar kinetic results are obtained from perchloric, nitric, and sulfuric acid solutions. Saturation kinetics are observed for the reversible addition of hydrogen peroxide to the α-keto carbonyl group with a pH-dependent K_d value of 0.25 M at H_0 −2; the pH-independent value for K_d is 2.0 M. The pK_a of the proposed protonated (monocation) tetrahedral intermediate is −1.3. A linear free-energy relationship correlates the observed rate constant and the pK_a of the leaving group produced by oxygen–oxygen bond cleavage for hydrogen peroxide, *tert*-butyl hydroperoxide, and peracetic acid promoted reactions.

The study of enzymatic oxidations in which molecular oxygen is used to convert olefinic, aromatic, or aliphatic substrates into the corresponding hydroxylated derivatives has lead to current interest in the class of enzymes known as mixed function oxidases.[2] These metalloenzymes, which effect a wide variety of biochemical oxidations, require, in addition to the substrate of interest, a stoichiometric equivalent of a coreductant. One class of mixed function oxidases, responsible for several of the biosynthetic aliphatic hydroxylations, utilizes 2-ketoglutaric acid as the cofactor for reactivity.[3] Inasmuch as the chemical role of the 2-ketoglutarate is not well understood, we have initiated an investigation of the mechanisms for the hydrogen peroxide promoted oxidative decarboxylation of the 2-keto acid, benzoylformic acid (1), in aqueous

$$\underset{\mathbf{1}}{\mathrm{PhC(=O){-}C(=O)OH}} + H_2O_2 \xrightarrow{H^+} \underset{\mathbf{3}}{\mathrm{PhC(=O)OH}} + CO_2 + H_2O$$

media.[4a,b] Results from this partial model study may likely provide insight into the chemistry of the enzyme-catalyzed process. Although basic hydrogen peroxide is a well-known and synthetically useful reagent for the decarboxylation of 2-keto acids,[4c] we herein report the finding of an acid-catalyzed reaction which is as kinetically facile as the base-promoted oxidation. Furthermore, on the basis of kinetic data we propose mechanisms which account for our observations over a wide pH range.

Results

Over 30 min at ambient temperatures a 7.5 M aqueous perchloric acid solution (H_0 −4) containing 0.16 M benzoylformic acid (**1**) and 2 M hydrogen peroxide evolves carbon dioxide and produces benzoic acid (**3**) as the only isolatable organic product in yields greater than 90%. The reaction rates of dilute solutions (5×10^{-3} M) of **1** may be conveniently followed at 32.0 °C by monitoring the time-dependent change in the ultraviolet absorption spectrum. The oxidative decarboxylation exhibits good first-order kinetics with respect to **1** through greater than 90% completion. If hydrogen peroxide is omitted from the reaction mixture, no significant loss of starting material occurs over several hours. However, after several days in the acidic medium benzoylformic acid (**1**) does undergo decarbonylation to produce benzoic acid (**3**) at rates comparable to those previously reported for this reaction.[6]

As illustrated in Figure 1, the rate constant exhibits three major variations with pH. First, between pH (H_0) −5 and +3, a bell-shaped pH–rate profile is produced with a maximum

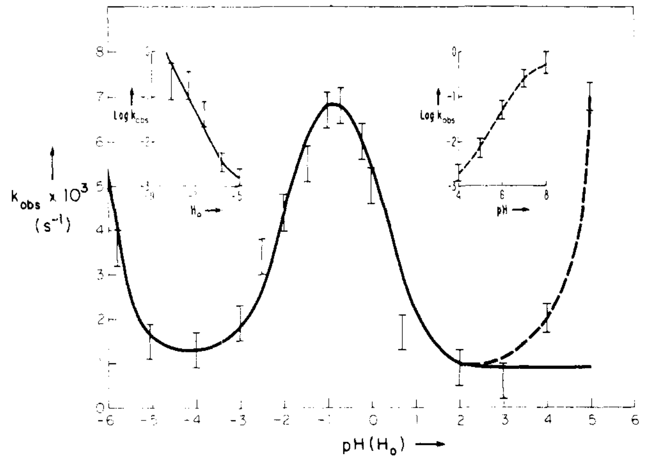
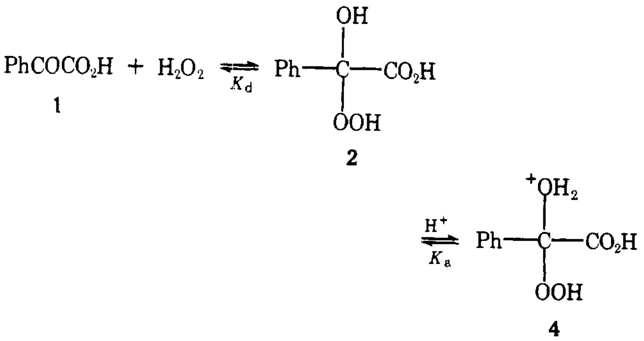


Figure 1. pH (H_0)–rate profile for oxidative decarboxylation of **1**. The solid curves are calculated using eq 1; the broken curves are used only to connect observed data points.

rate constant of 0.7×10^{-2} s^{-1} at H_0 −1.0 (0.5 M hydrogen peroxide). Second, at pH's above 3 (base catalysis), and third, at H_0's below −5 (acid catalysis), the rate constant significantly increases, such that at pH 8 and H_0 −8 the observed values (0.1 M hydrogen peroxide) are 6.3×10^{-2} and 22×10^{-2} s^{-1}, respectively. Analogous results are obtained between pH 3 and H_0 −1.5 if perchloric acid is replaced by nitric or sulfuric acids. Only slight quantitative differences in rates and curve shapes, which may be attributed to solvation and activity coefficient changes, are observed for the three structurally very different mineral acids over this acidic region. Thus, with nitric acid solutions the bell-shaped curve is characterized by a maximum rate constant of 1.9×10^{-2} s^{-1} at H_0 −1.2, whereas with sulfuric acid a maximum rate constant of 2.5×10^{-2} s^{-1} is attained at H_0 −1.1. Between H_0 −5 and −1.5, sulfuric acid uniquely exhibits a plateau rather than a bell-shaped curve for the pH–rate profile. This observation is discussed in terms of bifunctional catalysis in the following sections.

The H_0 acidity function is used throughout this study. An attempt to account for activity coefficient and solvation differences between our substrates and the acidity standards (weak amine bases) appears unnecessary in view of the consistent kinetic results obtained from the several structurally different mineral acids.[7] Perhaps the largest deviation between calculated and observed rate constants (probably due to H_0 measurements) can be seen in Figure 1 between pH (H_0) 0 and 1, where the pH and H_0 scales intersect.

As determined from the variation of the kinetics with pH, the apparent equilibrium constant for addition of hydrogen peroxide to the 2-keto carbonyl group in **1** exhibits significant



$$K_d^{apparent} = K_d/(1 + [H^+]/K_a)$$

pH dependence.[8] At pH (H_0) 0.5 ($HClO_4$) the reaction is first order in hydrogen peroxide over the concentration range studied (0–1.5 M). However, at H_0 −2 ($HClO_4$) saturation

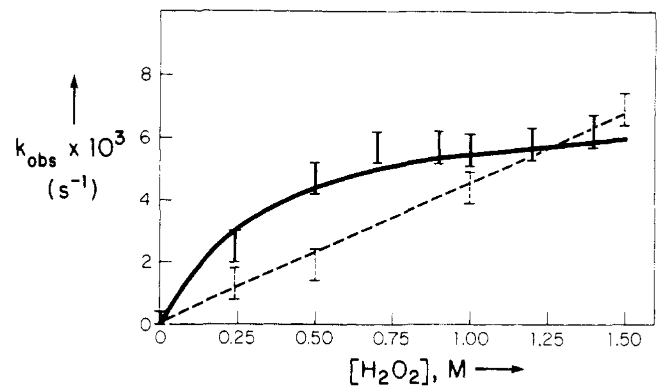


Figure 2. Observed pseudo-first-order rate constant for conversion of **1** into **3** graphed against hydrogen peroxide concentration. The solid curve is calculated using eq 1 to fit data collected at H_0 −2.0 (solid bars); the broken line connects data collected at pH ±0.5 (broken bars).

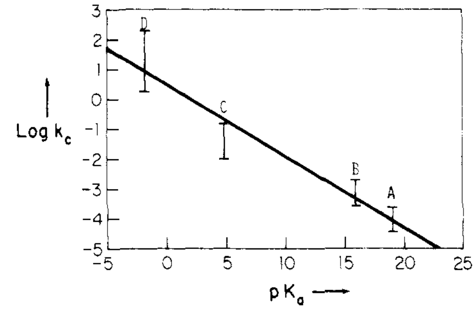


Figure 3. Logarithm of the observed pseudo-first-order rate constant for conversion of **1** into **3** (corrected as noted in text for statistical and pH effects) graphed against pK_a of the leaving group: (A) *tert*-butyl alcohol, (B) water, (C) acetic acid, and (D) hydronium ion.

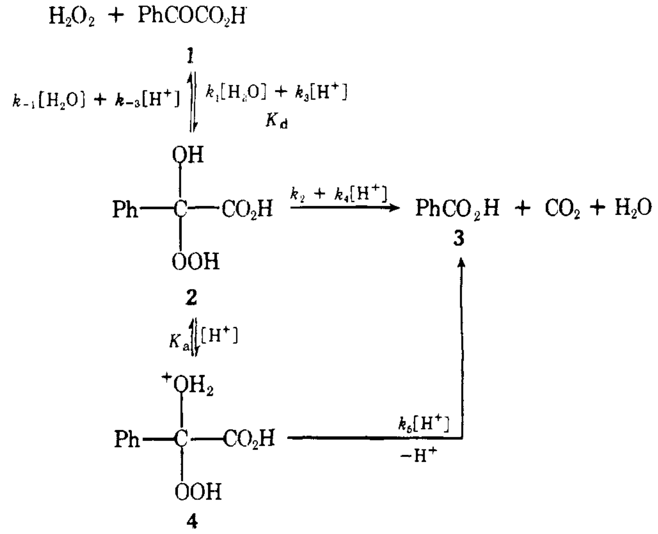
kinetics are observed, such that the rate constant rises to a plateau as the peroxide concentration increases. These data are shown in Figure 2. The apparent dissociation constant of the tetrahedral adduct at H_0 −2 is 0.25 M, a value that stands in contrast to that for the kinetically determined pH-independent dissociation constant (K_d) of 2.0 M. The basis and significance of this variation are considered in the following section.

The curve shape for the pH–rate profile (Figure 1) remains qualitatively unaltered if hydrogen peroxide is replaced by either *tert*-butyl hydroperoxide or peroxyacetic acid. However, as shown in Figure 3, a linear free-energy relationship correlates the quantitative increase in the observed rate constants with a decrease in the pK_a of the leaving groups. Thus, for the oxidants *tert*-butyl hydroperoxide, hydrogen peroxide, and peroxyacetic acid the respective rate constants at pH 2 (0.5 M oxidant) are 1.0×10^{-4}, 1.6×10^{-3}, and 4.0×10^{-2} s^{-1}. The corresponding leaving groups are *tert*-butyl alcohol, water, and acetic acid, which exhibit pK_a's of 19, 15.8, and 4.8, respectively.

Discussion

The mechanisms we propose for the oxidative decarboxylation of benzoylformic acid (**1**) in acidic media are illustrated in Scheme I. In acid, reversible addition of hydrogen peroxide to the ketone group in **1** occurs via both a water-catalyzed process (k_1 and k_{-1}) and an acid-catalyzed process (k_3 and k_{-3}) to give a tetrahedral intermediate **2**. Equilibrium protonation of **2** (K_a) produces a monocationic intermediate, **4.** Decarboxylation to product, **3,** may proceed through an acid-catalyzed path from either **2** or **4** (k_4 and k_5, respectively) or through an uncatalyzed (or an intramolecular acid-cata-

Scheme I



lyzed) path from **2** (k_2). As illustrated in Scheme III, an alternative and kinetically equivalent pathway for conversion of **2** to **3** is possible by expanding the acid-catalyzed process determined by k_4 into a process that involves prior equilibrium protonation of **2** to form a monocation (such as **5**) capable of undergoing direct decarboxylation.

In base, ionization of both **1** and hydrogen peroxide introduces additional pathways to **3**, which will not be discussed, as there is already ample literature documentation of these mechanisms.[4a,b,5] The oxidative decarboxylation of α-keto carboxylic acids with basic hydrogen peroxide is a well-established and synthetically useful reaction.[4c]

The observed first-order rate constant (k_{obsd}) for the mechanism depicted in Scheme I is given by eq 1, which is derived assuming a Bodenstein (steady-state) approximation and pH dependence for the concentration of intermediates **2** and **4**:

$$k_{obsd} = \frac{Q^{-1}[H_2O_2](k_1[H_2O] + k_3[H^+])(k_2 + k_4[H^+] + K_a^{-1}k_5[H^+]^2)}{1 + Q^{-1}[H_2O_2](1 + K_a^{-1}[H^+])(k_1[H_2O] + k_3[H^+])} \quad (1)$$

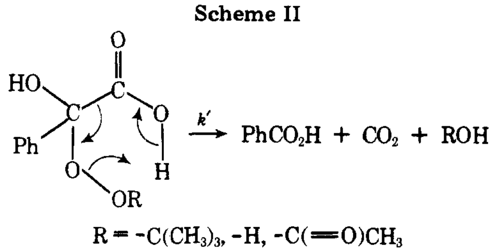
where

$$Q = [H^+](k_4 + k_{-3} + K_a^{-1}k_5[H^+]) + k_{-1}[H_2O] + k_2 \quad (2)$$

The rate and equilibrium constants needed in eq 1 to calculate the solid line shown in Figure 1 are listed in Table I. It is important to note that at any given pH (H_0), only one or two of the various constants determine (dominate) the magnitude of k_{obsd}. Thus, rather precise values of the component rate and equilibrium constants are needed in order for the calculated curve to give a good fit to the observed data over a wide pH (H_0) range.

In moderately basic solutions and in acid down to an H_0 of -2, peroxide addition to the carbonyl is slow. Thus, above pH 4 base-catalyzed (as opposed to acid- or water-catalyzed)

Scheme II



Scheme III

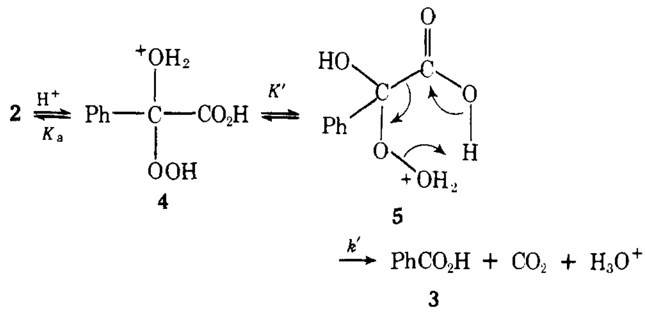


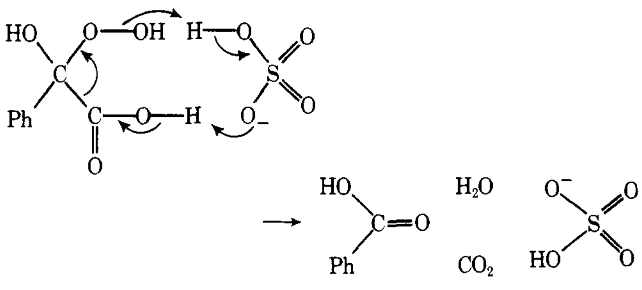
Table I. Rate and Equilibrium Constants for Oxidative Decarboxylation of 1 at 32 °C

rate constants	equilibrium constants
$k_1{}^{a,b} = 3.6 \times 10^{-5}\ M^{-2}\ s^{-1}$	
$k_{-1}{}^{a,b} = 7.1 \times 10^{-5}\ M^{-1}\ s^{-1}$	$K_d = 2.0\ M^{a,c}$
$k_3{}^{a} = 4.0 \times 10^{-2}\ M^{-2}\ s^{-1}$	
$k_{-3}{}^{a} = 8.0 \times 10^{-2}\ M^{-1}\ s^{-1}$	
$k_2 = 3.8 \times 10^{-2}\ s^{-1}$	
$k_4 = 6.0 \times 10^{-5}\ M^{-1}\ s^{-1}$	$K_a = 20\ M\ (pK_a = -1.3)$
$k_5 = 4.0 \times 10^{-9}\ M^{-1}\ s^{-1}$	

[a] Ratio of $k_{-1}/k_1 = k_{-3}/k_3 = K_d$. [b] If not water-catalyzed: $k_1 \times 55.5\ M = 2.0 \times 10^{-3}\ M^{-1}\ s^{-1}$; $k_{-1} \times 55.5\ M = 4.0 \times 10^{-3}\ s^{-1}$. [c] If statistically corrected by a factor of 2 for double-ended peroxide nucleophile, K_d is 4.0 M. Estimated error ±15%.

paths provide the most efficient routes to intermediates, which undergo decarboxylation. In the pH range 1 to 4, k_{obsd} is dominated by k_1, the water-catalyzed path for hydrogen peroxide addition to **1**. From pH 1 down to H_0 -2, the acid-catalyzed pathway through k_3 provides the predominant route to intermediates **2** and **4**. Below H_0 -2, decarboxylation is rate limiting. Thus, between H_0 -2 and -5 a relatively pH-independent reaction occurs through **2** to product via k_4. In more concentrated acid (H_0 below -5), the acid-catalyzed decarboxylation of intermediate **4** via k_5 dominates the value of k_{obsd}. This latter process involves a dicationic transition state that is attainable only in concentrated acid.

If k_4 were larger, the pH–rate profile would more resemble a plateau than a bell. Indeed, in moderately concentrated sulfuric acid, between H_0 -1.5 and -5, the pH–rate profile for



the decarboxylation of **1** more resembles a plateau than a bell-shaped curve. We interpret this result in terms of rate enhancement (increased k_4 values) due to bifunctional catalysis. In accord with this suggestion, if methanesulfonic acid, which unlike sulfuric acid cannot provide bifunctional catalysis, is used, a bell-shaped pH–rate profile essentially identical with that for perchloric and nitric acids is observed. The alternative possibility that sulfuric acid mixtures with hydrogen peroxide produce peroxysulfuric acid (Caro's acid) as the active oxidant for **1** was eliminated. Separately prepared solutions of Caro's acid[9] were kinetically less effective oxidants than simple hydrogen peroxide solutions in sulfuric acid. Moreover, this type of bifunctional interaction, unique to sulfuric acid, has been previously suggested to account for other reactions in concentrated acid solutions.[10]

The proposed mechanism requires a titration (governed by K_d) of starting keto acid **1** into intermediates **2** and **4**. Consistent with this, we have observed non-first-order kinetic dependence on hydrogen peroxide at H_0 −2. The saturation kinetics shown in Figure 2 reveal an apparent K_d value of 0.25 M. The solid line is calculated from eq 1 using the parameters in Table I and the experimentally determined hydrogen peroxide concentration. The excellent agreement between calculated and observed results lends support to the proposed mechanism. At low pH's (H_0), where the relative proportion of **4** is large due to protonation of **2**, the apparent dissociation constant should be smaller than the intrinsic pH-independent K_d. Indeed, this is the case; the value of the intrinsic K_d listed in Table I is approximately an order of magnitude larger (2.0 M) than the apparent K_d (0.25 M) at H_0 −2. Moreover, in less acidic solutions, pH (H_0) +0.5, no deviation from first-order dependence on hydrogen peroxide (between 0 and 1.5 M, concentrations below the intrinsic K_d value) is observed, as illustrated in Figure 2 by the broken line. Since at the higher pH formation of **4** is not significant, saturation kinetics should be observed only at very large hydrogen peroxide concentrations where **1** would be largely titrated into **2**.

A final issue concerning the proposed mechanism focuses on the chemistry of the decarboxylation step. As outlined in Schemes II and III, oxygen–oxygen bond cleavage occurs synchronously with the elimination of carbon dioxide through k'. Hence, we expect that the most facile reactions would involve good leaving groups with weak oxygen–oxygen bonds. Although few cases are available to provide precedent for a quantitative linear free-energy correlation between reaction rates and leaving group abilities, there is ample conjecture in the literature for such an expectation.[11] In Figure 3 the observed rate constant increases as the pK_a of the leaving group decreases. The small value for the slope (−0.2) of this Brønsted plot is consistent with the synchronous mechanisms shown in Schemes II and III in which there is only a negligible change in the charge during the decarboxylation.[11,13,14] A data point is included on this graph for H_3O^+ as the leaving group. As shown in Scheme III, the rate constant, k', is attenuated by two additional equilibria over that for the corresponding reaction if water is the leaving group (R = H in Scheme II). We have corrected the observed rate constant at H_0 −4 by (1) a factor of 4 to account for increased formation of **2**, due to the pH dependence of K_d (constant hydrogen peroxide concentration, 0.50 M), (2) a factor of 10^5 to account for the relative proportion of **5** among the monocationic species, which are mostly present as **4**, and (3) a statistical factor of 2. The error limits associated with the several corrections are dominated by limits in the estimate that the pK_a of **5** (−6.3) is 5 units less than that for **4** (−1.3). The value −6.3 is in accord with previous estimates.[12] The linear relation shown in Figure 3 (correlation coefficient, 0.98) is not, however, attributable solely to a leaving group effect on the observed rate constant since the rate for tetrahedral adduct formation is partially rate limiting. Thus, both leaving group effects and nucleophilicity apparently correlate with pK_a for this reaction. Recent work on the addition of peroxides to 2-ketols suggests that for nucleophilicity this is the case.[13]

The formation of a tetrahedral intermediate in nucleophilic addition–elimination processes is lore for carbonyl reaction mechanisms.[14] The equilibria and kinetics of addition of several "α" nucleophiles, including hydrogen peroxide, hydroxylamine, and hydrazine, to various carbonyl groups have been investigated.[15] Thus, in acidic media, reversible addition of hydrogen peroxide to carbonyls proceeds through both water- and acid-catalyzed paths analogous to those proposed in Scheme I (k_1, k_{-1}, k_3, and k_{-3}).[12,16] The water- and acid-catalyzed decarboxylation steps (k_2, k_4, and k_5) also have precedent as they involve carbon–carbon bond cleavage related to that known to occur in Baeyer–Villiger reactions, which require acidic peroxide oxidants.[16]

Bell-shaped pH–rate profiles are often observed for the nucleophilic addition–elimination reactions of carbonyls, and are usually explained by (1) a change in the rate-limiting step and (2) "off-path" equilibrium protonation of the nucleophile.[14] For example, hydroxylamine addition to acetone, leading to the oxime, exhibits a bell-shaped pH–rate profile. Above the pK_a for hydroxylamine acid-catalyzed dehydration of the tetrahedral adduct is slow, whereas below the pK_a addition to the carbonyl is rate limiting due to the "off-path" removal of the amine nucleophile through protonation. In this study, we propose that protonation of intermediate **2**, which produces **4**, leads to a change in the rate-limiting step from hydrogen peroxide addition to **1** to slow elimination of CO_2 and H_2O from **4**.[17] Thus, pH dependence of the concentration of an intermediate, rather than a nucleophile, determines the kinetics of the oxidative decarboxylation of benzoylformic acid in acidic media.

In support of the proposed mechanistic scheme, the rate and equilibrium constants in Table I are comparable in magnitude to literature values for analogous reactions.[18] Thus, we have found that the statistically corrected equilibrium constant (K_d) for dissociation of hydrogen peroxide from the tetrahedral adduct, **2**, is 4 M and is in good agreement with the values 2 and 11 M reported for dissociation of hydrogen peroxide from the corresponding *p*-chloro- and *p*-methoxybenzaldehyde adducts.[12,15] Relative to the aldehyde hydrogen, the steric and inductive effects of the carboxyl group in **1** and **2** may tend to cancel.[19] The dipole destabilization inherent in the α-dicarbonyl group of **1** could be compensated for by steric destabilization inherent in an expansion of the sp^2 hybridized carbonyl of **1** to the sp^3 hybridized carbon in **2**. K_d values are also known for hydrogen peroxide adducts of formaldehyde (3×10^{-5} M),[12,20] acetaldehyde (4×10^{-2} M),[12,21] and pyridine-4-carboxaldehyde (5×10^{-2} M)[12] and are smaller than that for **2**. The net influence of substituent effects on K_d is difficult to estimate for these aliphatic and heterocyclic species, which are likely poorer models for **1** and **2** than the benzaldehydes.

The kinetics for loss of hydrogen peroxide from the tetrahedral adduct formed from various aldehydes have been reported to proceed via separate acid-, base-, and water-catalyzed pathways. As a model for the conversion of **2** into **1**, the *p*-chlorobenzaldehyde adduct breaks down with rate constants 1.5×10^{-5} and 0.98 $M^{-1}\,s^{-1}$ for water- and acid-catalyzed reactions, respectively.[12] These values are in agreement with our values (k_{-1} and k_{-3}) listed in Table I, and thus support our interpretations of a steady-state kinetic analysis in which adduct formation is partially rate limiting for the overall oxidative decarboxylation. The pH-dependent kinetics of the Baeyer–Villiger reaction of benzaldehydes with peroxybenzoic acids have also revealed that tetrahedral adduct formation, through acid- and water-catalyzed paths, is partially rate limiting.[16] In this case the analogy to our reaction is extended, in that subsequent loss of CO_2 from the intermediate adduct in the Baeyer–Villiger reaction required both acid- and water-catalyzed routes, similar to the processes governed by k_2, k_4, and k_5 in Scheme I for loss of CO_2 from **2** and **4**.

Finally, our kinetic analysis requires a pK_a of −1.3 for the protonated hydroxy group in **4**, a value in accord with that (on the order of −2) reported for simple aliphatic alcohols.[22] The problems associated with estimating the several mutually compensating inductive, solvation, and intramolecular hydrogen bonding effects of polar groups on the pK_a of **4** relative to that for unfunctionalized alcohols preclude further scrutiny of this dissociation constant.

Experimental Section

General. Melting points were uncorrected as determined with a calibrated Thomas-Hoover melting apparatus. UV data were collected from a Coleman/Perkin-Elmer 124 spectrophotometer, thermostated at 32.0 °C with a Haake Model FE thermoregulator. All pH measurements (±0.02 units) were made with a London/Radiometer Type 26 pH meter equipped with a Type GK 2320C combination electrode, standardized with calibrated pH 2, 4, and 7 aqueous buffers. Acidic solutions below pH 1 were prepared according to literature procedures;[24] above pH (H_0)0 ionic strength was maintained at 1.0 with sodium perchlorate. Silica gel thin-layer chromatographs were eluted with ethyl acetate or 1-propanol.

Materials. Reagent grade inorganic salts, mineral acids, and benzoic and benzoylformic acids were commercially available and used without further purification. Commercial hydrogen peroxide (30%), peracetic acid (40%), and *tert*-butyl hydroperoxide (90%) were diluted in aqueous solutions and assayed by iodometric titration prior to use.[23] Glass-distilled water was used in all experiments.

Kinetic Measurements. An aliquot (50 μL) of peroxide reagent in an aqueous solution of known pH (H_0) was added to a thermally equilibrated (32.0 °C) 1.0-mL solution of benzoylformic acid at the same pH (H_0) in a semimicro quartz cell to give an initial substrate concentration of 4.8×10^{-3} M and a peroxide concentration of at least 0.1 M. Reaction rates were measured spectrophotometrically by following the absorbance change at 350 nm for 5–10 half-lives. Linear least-squares regression analysis of ln $(A_\infty - A_t/A_\infty - A_0)$ vs. time (s) rendered slopes equated to the observed first-order rate constants with correlation coefficients of 0.999 or greater. Error limits for reproducibility of k_{obsd} values were within 5%.

Rate constants, calculated from eq 1 through iterative approximations, were compared to observed values over the entire pH range studied to determine the best-fit values shown in Table I. Error limits are estimated at ±10% for these rate and equilibrium constants.

Product Analysis. A solution of 1.21 g (8.1 mmol) of benzoylformic acid in 50 mL of 7.5 M perchloric acid, containing 2 M hydrogen peroxide, was stirred for 30 min at ambient temperature. Within 2 min the benzoic acid product began to precipitate from the reaction mixture. Ether extracts of the aqueous solution were dried with magnesium sulfate and evaporated at reduced pressure to give 0.92 g (7.5 mmol) of benzoic acid (93% yield), identified by melting point (121–122 °C) and thin-layer chromatography.

For kinetic experiments, the ultraviolet spectrum of a synthetic benzoic acid product mixture was observed to be identical with that of actual reaction mixtures.

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Registry No.—**1**, 611-73-4; **3**, 65-85-0; hydrogen peroxide, 7722-84-1.

References and Notes

(1) (a) Dupont Young Faculty Fellow, to whom correspondence schould be addressed. (b) The University of Minnesota Institute of Technology Corporate Fellow, 1977–1978.
(2) "Molecular Mechanisms of Oxygen Activation", O. Hayaishi, Ed., Academic Press, New York, N.Y., 1974.
(3) M. J. Barnes and E. Koicek, *Vitam. Horm. (N.Y.)*, **30**, 1 (1972); G. J. Cardinale and S. Udenfriend, *Adv. Enzymol. Relat. Areas Mol. Biol.*, **41**, 245 (1975), and references cited therein.
(4) (a) C. A. Bunton, *Peroxide React. Mech., Pap. Conf., 1960*, 16 (1962). (b) G. A. Hamilton, *Prog. Bioorg. Chem.*, **1**, 83 (1971), has studied this reaction between pH 0 and 14. (c) H. O. House in "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972.
(5) To the extent that the conjugate base of **1** is responsible for production of **2** in acidic solutions, k_1 and k_{-1} would represent rate constants for water-catalyzed addition of hydrogen peroxide to the carboxylate anion rather than **1** as shown in Scheme I.
(6) M. Liler in "Reaction Mechanisms in Sulfuric Acid", Academic Press, New York, N.Y., 1971, pp 254–259; see also C. H. Rochester in "Acidity Functions", Academic Press, New York, N.Y., 1970.
(7) J. T. Edward and S. C. Wong, *J. Am. Chem. Soc.*, **99**, 4229 (1977), and references therein.
(8) Possible error in K_d measurements, due to unaccounted hydration of the carbonyl in **1**, is likely to be small since the equilibrium constants for tetrahedral adduct formation with water are usually orders of magnitude less than those for hydrogen peroxide.[6,9]
(9) W. D. Langley, "Organic Syntheses", Collect. Vol. 3, Wiley, New York, N.Y., 1955, p 334.
(10) See ref 6, "Reaction Mechanisms in Sulfuric Acid", p 63.
(11) E. M. Kosower in "Physical Organic Chemistry", Wiley, New York, N.Y., 1968, p 81.
(12) E. G. Sander and W. P. Jencks, *J. Am. Chem. Soc.*, **90**, 4377 (1968).
(13) Y. Ogata, Y. Sawaki, and M. Shiroyama, *J. Org. Chem.*, **42** 4061 (1977).
(14) W. P. Jencks in "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, N.Y., 1969; M. L. Bender in "Mechanisms of Homogeneous Catalysis from Protons to Proteins", Wiley-Interscience, New York, N.Y., 1971.
(15) E. G. Sander and W. P. Jencks, *J. Am. Chem. Soc.*, **90**, 6154 (1968).
(16) Y. Ogata and Y. Sawaki, *J. Am. Chem. Soc.*, **94**, 4189 (1972).
(17) An alternative and kinetically indistinguishable mechanism would involve slow decarboxylation of a monocation, such as **5**, shown in Scheme III.
(18) Although the data being compared were collected at several slightly different temperatures, all near ambient, the perturbation introduced by this variation is minor and the conclusions should remain unaltered.
(19) R. P. Bell, *Adv. Phys. Org. Chem.*, **4**, 1 (1966).
(20) B. L. Dunicz, D. D. Perrin, and D. W. G. Style, *Trans. Faraday Soc.*, **47**, 1210 (1951).
(21) C. N. Satterfield and L. C. Case, *Ind. Eng. Chem.*, **46**, 998 (1954).
(22) D. G. Lee and R. Cameron, *J. Am. Chem. Soc.*, **93**, 4724 (1971), and references therein.
(23) D. Swern, J. T. Scanlan, and G. B. Dickel, "Organic Syntheses", Collect. Vol. 4, Wiley, New York, N.Y., 1963, p 317.
(24) M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).