0.72 g (65%) of (−)-9-(1-naphthylphenylmethylsilyl)phenanthrene, mp 205–206.5°, from ethyl acetate, $[\alpha]^{22}\mathrm{D}$ −35.4° (*c* 1.5, C_6H_6).

Anal. Calcd for $C_{31}H_{24}Si$: C, 87.68; H, 5.70. Found: C, 87.40; H, 5.74.

Photoisomerization of α-(1-Naphthylphenylmethylsilyl)-*cis*-stilbene. When 1.0 g of the title compound (nmr at δ 0.67 ppm) was photolyzed in cyclohexane as described above, except in an atmosphere of dry, oxygen-free nitrogen, examination of the product at the end of 7 and 20 hr revealed the presence of two singlets at 0.43 and 0.67 ppm with the intensity ratio 48:52. These peaks were ascribed to α-(1-naphthylphenylmethylsilyl)-*trans*- and *cis*-stilbenes, respectively. No peak at 1.2 ppm, associated with the silylphenanthrene was observed.

Reaction of Triphenylgermane with Diphenylacetylene. A mixture of 0.4 g (0.00013 mol) of triphenylgermane and 0.24 g (0.00013 mol) of diphenylacetylene was heated to 130° for 24 hr in the presence of a trace of a 10% platinum on charcoal catalyst. The resultant oily wax was dissolved in carbon tetrachloride and the solution filtered. After removing the solvent under reduced pressure, the thick oil was dissolved in the minimum of boiling methanol. On cooling to room temperature a total of 0.31 g (48%) of α-triphenylgermyl-*cis*-stilbene precipitated which after recrystallization from methanol melted at 113–114°; uv$_{\max}$ (CCl_4): 264 mμ (ϵ 15,600).

Anal. Calcd for $C_{32}H_{26}Ge$: C, 79.54; H, 5.43. Found: C, 79.16; H, 5.36.

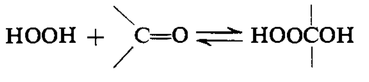
General Acid and Base Catalysis of the Reversible Addition of Hydrogen Peroxide to Aldehydes[1]

Eugene G. Sander[2] and William P. Jencks

Contribution No. 580 from the Graduate Department of Biochemistry, Brandeis University, Waltham, Massachusetts 02154. *Received January 29, 1968*

Abstract: The rates of general acid and base catalyzed breakdown of the hemiacetals formed by the addition of hydrogen peroxide to *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde have been measured spectrophotometrically, and the rates of the addition reactions have been calculated from the equilibrium constants. The general base catalyzed breakdown of the *p*-chlorobenzaldehyde adduct exhibits a β value of 0.66. It is suggested that this reaction actually involves general acid catalysis of the breakdown of the conjugate base of the adduct, possibly through a "one-encounter" mechanism. A positive deviation of the hydroxide ion catalyzed reaction suggests that this represents specific base catalysis, *i.e.*, uncatalyzed expulsion and attack of the hydroperoxide anion. The general acid catalyzed reaction exhibits an α value equal or close to 1.0 and is detectable because of a negative deviation of the proton-catalyzed reaction. It is suggested that this reaction involves proton transfer by the general acid to and from the carbonyl oxygen atom, possibly through a cyclic mechanism in catalysis by carboxylic acids. The higher affinity of hydrogen peroxide than of water for the carbonyl group appears as a slower rate of decomposition of the hydrogen peroxide adduct. The high nucleophilic reactivity of free hydrogen peroxide is apparent in the similarity of its rate of nucleophilic attack to that of water, in spite of its much smaller basicity.

The reversible addition of water to the carbonyl group has been examined in detail,[3] but much less information is available regarding the analogous addition and loss of the more acidic and less basic hydrogen peroxide molecule (eq 1). It is known that the affinity of hydro-



$$\mathrm{HOOH} + {>}\mathrm{C{=}O} \rightleftharpoons \mathrm{HOO}\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{OH} \qquad (1)$$

gen peroxide for the carbonyl group is much greater than that of water, and the addition of hydrogen peroxide to formaldehyde and acetaldehyde occurs through pH-independent and hydrogen ion catalyzed pathways.[4–6] The experiments reported here were carried out in order to obtain a more complete understanding of the mechanism of catalysis of this reaction.

Experimental Section

Materials. Reagent grade inorganic salts were used without further purification. Glass-distilled water was used in all experiments. Organic acids and bases were either recrystallized or redistilled before use. 1,1-Cyclobutanedicarboxylic acid was a gift from Dr. Gustav Lienhard. *p*-Chlorobenzaldehyde was twice recrystallized from ethanol–water. *p*-Methoxybenzaldehyde was redistilled under reduced pressure and stored at 4°. Solutions containing the *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal were freshly prepared just prior to use by adding sufficient *p*-chlorobenzaldehyde and hydrogen peroxide to make the final concentrations in the stock solution approximately 2×10^{-2} *M* and 5.1 *M*, respectively, in 20% ethanol. Sufficient ethylenediaminetetraacetic acid was added to this stock solution to give a concentration in the final reaction mixtures of 1×10^{-4} *M*. The same rate constants were obtained with solutions which had stood for 24 hr at room temperature as with fresh solutions. A similar procedure was followed to prepare *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetal except that 0.1 ml of 0.11 *M* *p*-methoxybenzaldehyde in ethanol was added to 0.9 ml of 30% hydrogen peroxide to give final concentrations of 1×10^{-2} *M* *p*-methoxybenzaldehyde and 8.0 *M* hydrogen peroxide; these solutions were prepared just prior to each kinetic run. Dimethyl phosphate was purified as the barium salt[7] and twice recrystallized from 85% ethanol–water. Just prior to use the barium salt was dissolved in a solution containing an equivalent amount of standardized sulfuric acid, and barium sulfate was removed by centrifugation and filtration.

---

[1] We are grateful to the National Science Foundation (Grant GB-1648) and to the National Institute of Child Health and Human Development of the National Institutes of Health (Grant HD-01247) for financial support.

[2] Supported by a Public Health Service Postdoctoral Fellowship (1-F2-CA-22 941-01).

[3] R. P. Bell, *Advan. Phys. Org. Chem.*, 4, 1 (1966).

[4] P. L. Kooijman and W. L. Ghijsen, *Rec. Trav. Chim.*, **66**, 205 (1947).

[5] B. L. Dunicz, D. D. Perrin, and D. W. G. Style, *Trans. Faraday Soc.*, 47, 1210 (1951).

[6] C. N. Satterfield and L. C. Case, *Ind. Eng. Chem.*, **46**, 998 (1954).

[7] P. C. Haake and F. H. Westheimer, *J. Am. Chem. Soc.*, **83**, 1102 (1961).

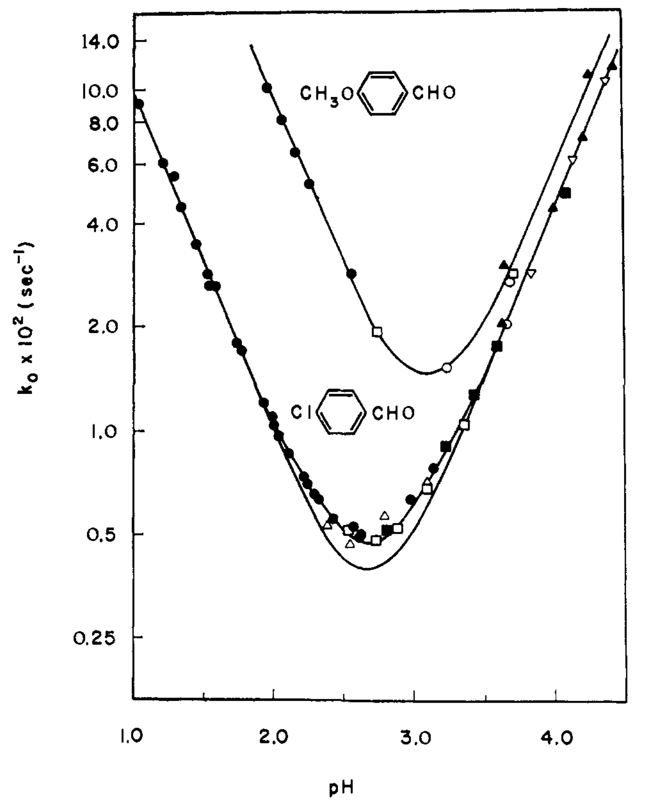


Figure 1. The dependence on pH of the rates of dissociation of the hemiacetals of hydrogen peroxide and *p*-chlorobenzaldehyde or *p*-methoxybenzaldehyde at 25° and ionic strength 1.0 *M*. Values of k_0, except in the case of hydrochloric acid, were obtained from the intercepts of plots of k_{obsd} against buffer concentration. Buffers used were: ●, hydrochloric acid; ○, potassium formate; ▲, potassium acetate; △, potassium cyanoacetate; ■, potassium methoxyacetate; □, potassium chloroacetate; ▽, potassium propionate.

Kinetic Measurements. The rates of dissociation of *p*-chloro- or *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetal were followed by measuring the increase in the carbonyl absorbance at either 270 or 285 mμ after dilution of hemiacetal solutions approximately 150-fold into buffer solutions. The reaction mixtures containing all components except the hemiacetal were prepared in cuvettes and equilibrated at 25°. The ionic strength was maintained at 1.0 *M* by the addition of potassium chloride unless noted otherwise. The reactions were initiated by the addition of 0.02 ml of the hemiacetal solutions using a small plastic spatula ("Plumpers," Calbiochem) to give rapid mixing of the solution in the thermostated cell compartment of the spectrophotometer. A Gilford Model 2000 recording spectrophotometer with a chart speed of up to 12 in./min was used for all kinetic determinations. In general, a minimum of 2–3 sec was required before absorbance recordings could be obtained using this system. The half-life of each reaction was read directly from the spectrophotometer recordings and was found to be the same for several different intervals of each recording. First-order rate constants were calculated from the equation $k_{obsd} = 0.693/t_{1/2}$. The observed rate constants obtained in this manner were generally reproducible to within ±5%.

Measurements of pH were made with a glass electrode and a Radiometer PHM-4b pH meter which was standardized at pH 4.0 with Fisher standard buffers or at pH 1.10 with 0.1 *M* hydrochloric acid.[8] Hydrogen ion concentrations were calculated from the relation $C_{H^+} = 1.11$ antilog (−pH) which was found empirically to hold under the conditions of the experiments between 0.004 and 0.07 *M* hydrogen ion. Hydroxide ion concentrations were calculated from the pH, $K_w = 10^{-14}$, and an activity coefficient for hydroxide ion[9] of 0.67. To correct for the variation of pH with the concentration of buffers containing a large fraction of the acid species, the value of k_{obsd} was corrected by 2–3, 6–20, and 11% in buffers containing 96 and 92% formic acid, 90% chloroacetic acid, and 70% malonic acid, respectively, using values of k_0 obtained from the pH–rate profile.

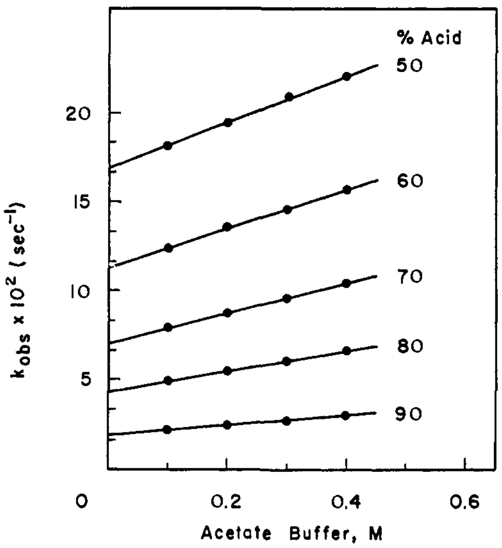


Figure 2. The rates of *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal dissociation in potassium acetate buffers at 25°, ionic strength 1.0 *M*.

With phosphoric acid, arsenic acid, dimethylphosphoric acid, dichloroacetic acid, and glycine hydrochloride buffers the hydrogen ion concentration usually represented a significant fraction of the acid component of the buffer, and the pH of each buffer solution was adjusted to a constant value by the addition of a measured amount of hydrochloric acid. The pH was redetermined at the end of each experiment and was found to vary by less than 0.02 pH units from the adjusted pH value. The final concentration of the acidic component of each buffer was calculated from the relationship

$$[HA] = [HA]_{added} - [1.11 \text{ antilog}(-pH) - [HCl]_{added}]$$

The values of pK_a' for the general acids and bases at ionic strength 1.0 *M* and 25° were determined from the pH values of the reaction mixtures and the concentrations of acidic and anionic buffer components, after correction for ionization of the acid.

Product Analyses. The products and completeness of the dissociation of *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal into *p*-chlorobenzaldehyde and hydrogen peroxide were determined by diluting a solution containing 1.0 *M* hydrogen peroxide and 1.72×10^{-3} *M* *p*-chlorobenzaldehyde 30-fold into 0.1 *M* formate buffer, pH 3.19. The absorbance at 270 mμ after complete reaction was equal to 96% of the sum of the absorbancies obtained when 1.0 *M* hydrogen peroxide and 1.72×10^{-3} *M* *p*-chlorobenzaldehyde were separately diluted in the same manner and the difference spectrum of the diluted hemiacetal solution, using the diluted 1.0 *M* hydrogen peroxide solution as a blank, was the same as that of the diluted 1.72×10^{-3} *M* *p*-chlorobenzaldehyde solution using the formate buffer as a blank. Similar results were obtained with *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetal.

Equilibrium Constants. The observed equilibrium constant for the addition of hydrogen peroxide to *p*-methoxybenzaldehyde was found to be approximately 0.18 M^{-1}, using methods described elsewhere.[10] The corresponding value for *p*-chlorobenzaldehyde[10] is 0.88 M^{-1}.

Results

The decomposition of the hydrogen peroxide addition compounds of *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde was found to follow strict first-order kinetics in each run. No indications were observed of the deviations from the expected reaction order that

---

(8) V. Gold, "pH Measurements," John Wiley and Sons, Inc., New York, N. Y., 1956, p 119.

(9) J. F. Kirsch and W. P. Jencks, *J. Am. Chem. Soc.*, **86**, 833 (1964).

(10) E. G. Sander and W. P. Jencks, *J. Am. Chem. Soc.*, in press.

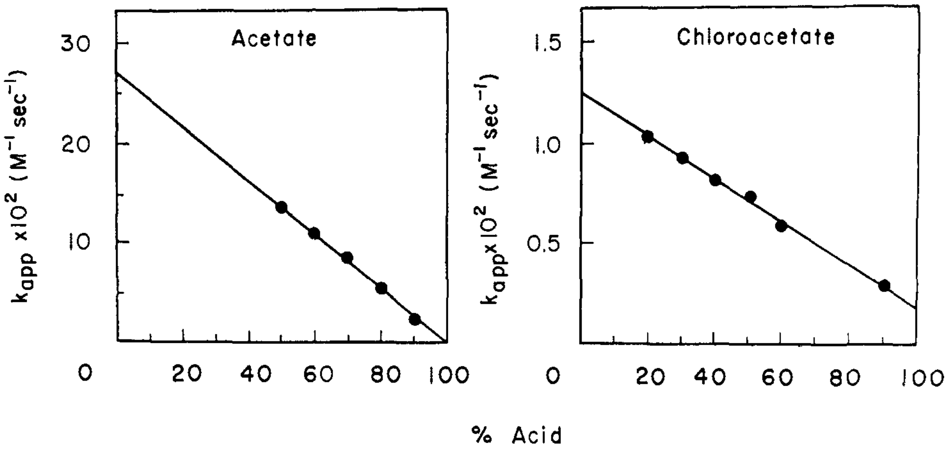


Figure 3. The apparent second-order rate constants for catalysis by potassium acetate and potassium chloroacetate buffers as a function of the percentage of the acidic component of the buffer.

were reported by Satterfield and Case for reactions of aliphatic aldehydes and were attributed to polymerization in the much more concentrated aldehyde solutions examined by these workers.[6] That the reaction involves the decomposition of an adduct containing a single molecule of hydrogen peroxide (eq 1) is shown by the rapid rates of base- and acid-catalyzed breakdown and by equilibrium measurements for formation of the adduct.[10]

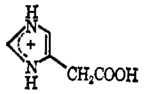
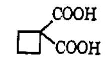
Catalysis by Hydrogen and Hydroxide Ion. The pH dependencies of the observed first-order rate constants in the absence of general acids and bases (k_0) for the dissociation of *p*-chloro- and *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetals are shown in Figure 1. Values of k_0 were obtained from reaction mixtures which contained only hydrochloric acid or from the intercepts of plots of k_{obsd} against total buffer concentration (Figure 2). The pH–rate profiles show that the reactions are both acid- and base-catalyzed and give second-order rate constants based on hydrogen and hydroxide ion activities of k_{H^+} = 0.98 and 8.9 M^{-1} sec^{-1} for k_{H^+} and 4.25 × 10^8 and 6.00 × 10^8 M^{-1} sec^{-1} for k_{OH^-} for *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde, respectively. The solid lines passing through the *p*-methoxybenzaldehyde data and the lower line for *p*-chlorobenzaldehyde in Figure 1 were calculated from these rate constants. The increase in observed rate over that calculated for the sum of the acid- and base-catalyzed reactions at the pH–rate minimum for the *p*-chlorobenzaldehyde reaction indicates that there is a "water" reaction for this compound with a second-order rate constant of 1.5 × 10^{-5} M^{-1} sec^{-1}. The rate of the acid-catalyzed decomposition of the *p*-methoxybenzaldehyde adduct is too large to permit measurement of the rate of the water reaction. The lines which pass through the experimental points in Figure 1 were calculated from these rate constants, and the first three terms of eq 2 and provide a satisfactory fit to the data over the pH range examined.

$$k_0 = k_{H^+}a_{H^+} + k_{OH^-}a_{OH^-} + 55.5k_{H_2O} + k_2[B] + k_3[HA] \quad (2)$$

Catalysis by General Acids and Bases. The effectiveness of general acids and bases as catalysts for the dissociation of *p*-chloro- and *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetals was measured by obtaining values of k_{obsd} in increasing concentrations of buffers of several different buffer ratios. Figure 2 shows the results of a typical experiment with acetate buffers. The slopes of the lines in Figure 2 represent the apparent second-order rate constants (k_{app}) for buffer catalysis. The second-order rate constants for catalysis by the acidic and basic components of the buffer (k_3 and k_2, respectively) were obtained from the intercepts of plots of k_{app} against the percentage of acid in the buffer. Figure 3 shows such plots and indicates that both acetate and chloroacetate anions act as general base catalysts while only chloroacetic acid acts as a (relatively weak) general acid catalyst. The experimental conditions and the values of k_{app} for each of the buffers examined are summarized in Table I. The second-order catalytic constants obtained for general acid and base catalysis of the dissociation of *p*-chloro- and *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetals are summarized in Tables II and III, respectively. In Table II, the values of k_3 for chloroacetic acid and malonic acid are reported with large error terms. At the pH at which these general acids are effective the catalytic contribution of hydrogen ion represents a large fraction of k_{obsd}, and the accurate determination of k_3 for these weak general acids becomes difficult. A similar situation was encountered in the case of general acid catalysis by glycine hydrochloride. The small increase in the observed rate with increasing concentration of 90% glycine hydrochloride buffer allows k_3 to be reported only as a limit.

Catalysis by dichloroacetic acid at a series of different buffer ratios is shown as a function of acid concentration in Figure 4. The dashed lines have been drawn through points which have been corrected for the decrease in dichloroacetic acid concentration caused by acid ionization, as described in the Experimental Section. The slopes of these lines are the same at different buffer ratios, which shows that only the acidic component of the buffer is active as a catalyst. The absence of detectable catalysis by dichloroacetate ion makes possible a more accurate determination of the catalytic constant for this acid than was possible for chloroacetic and malonic acids. Similar results, obtained at constant pH, were observed for catalysis of *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal dissociation by dimethylphosphoric acid and for catalysis of *p*-me-

Table I. Values of k_{app} for the Buffer-Catalyzed Dissociation of *p*-Chlorobenzyaldehyde–Hydrogen Peroxide Hemiacetal at 25° and Ionic Strength 1.0 M^{a}

Acid	% acid^{b}	Concn range,^{c} M	$k_{app} \times 10^{2}$ ^{d} M^{-1} sec^{-1}	Acid	% acid^{b}	Concn range,^{c} M	$k_{app} \times 10^{2}$ ^{d} M^{-1} sec^{-1}
HCOOH	94	0.1–0.6	0.40^{e,f}	H_3PO_4^{i}	57	0–0.6	2.72^{e}
	92	0.1–0.4	0.64^{d}		47	0–0.6	2.56
	74	0.1–0.4	1.83		38	0–0.6	2.37
	63	0.1–0.4	2.27		29	0–0.6	1.96
	57	0.1–0.4	2.82		15	0–0.6	1.79
	52	0.1–0.4	2.94		5	0–0.6	1.77^{j}
	50	0.1–0.6	3.09		0^{k}	0–0.6	1.92^{j}
	47	0.1–0.6	3.07	H_3AsO_4^{i}	47	0–0.4	2.54
	42	0.1–0.6	3.45		30	0–0.4	2.46
	(75)	(0.1–0.4)	(2.3)^{a}		19	0–0.4	2.61
	(50)	(0.1–0.4)	(4.7)^{a}	$HOP(=O)(OCH_3)_2$^{i}	18	0–0.6	22^{l}
CH_3COOH	90	0.1–0.4	2.36		0	0–0.6	0^{m}
	80	0.1–0.4	5.28	$CH_2(COOH)_2$	70	0.1–0.5	0.66^{e,n}
	70	0.1–0.4	8.22		50	0.1–0.5	1.00
	60	0.1–0.4	10.80		30	0.1–0.5	1.33
	50	0.1–0.4	13.50	$\overset{+}{N}H_3CH_2COOH$^{i}	85	0–0.6	0.33^{e}
	(90)	(0.1–0.4)	(3.1)^{a}		50	0–0.6	0.76
	(70)	(0.1–0.4)	(9.6)^{a}		30	0–0.6	1.03
CH_3CH_2COOH	90	0.1–0.4	3.32		10	0–0.6	1.28
	80	0.1–0.4	6.81	$CNCH_2COOH$	60	0.1–0.4	1.03
	70	0.1–0.4	10.79		50	0.1–0.4	0.75
	60	0.1–0.4	14.28		40	0.1–0.4	0.66
$ClCH_2COOH$	90	0.1–0.6	0.25^{e,g}		30	0.1–0.4	0.42
	60	0.1–0.4	0.59		20	0.1–0.4	0.37
	50	0.1–0.4	0.73	$Cl_2CHCOOH$^{i}	12	0–0.72	6.7^{o}
	40	0.1–0.4	0.81		20	0–0.71	7.2^{o}
	30	0.1–0.4	0.92		28	0–0.72	7.2^{o}
	20	0.1–0.4	1.03		(12)	(0–0.72)	(40)^{a,o}
	(90)	(0.1–0.4)	(2.9)^{a,e,h}		100	0–0.3	0
	(50)	(0.1–0.4)	(2.3)^{a}		75	0.1–0.6	1.74
	(10)	(0.1–0.4)	(1.8)^{a}		55	0.1–0.6	3.32
CH_3OCH_2COOH	80	0.1–0.4	0.86		50	0.05–0.30	3.49
	60	0.1–0.4	1.59				
	50	0.1–0.4	2.06		50	0.1–0.3	2.04
	40	0.1–0.4	2.41		10	0.1–0.3	4.55
	20	0.1–0.4	3.24	$NH_2C(=O)NHNH_3^{+}$^{p}	90	0.1–0.4	0.83
					50	0.1–0.4	3.4

[a] Values in parentheses are for the dissociation of *p*-methoxybenzaldehyde–hydrogen peroxide hemiacetal. [b] After correction for ionization of the acid component of the buffer (see text). [c] Concentration of total buffer. [d] Obtained from the slopes of plots of k_{obsd} against total buffer concentration unless noted otherwise. [e] Approximate value. [f] Observed $k_{app} = 0.67 \times 10^{-2}\ M^{-1}$ sec^{-1}; the value reported is after correction of the k_{obsd} values for changes in k_0 caused by variations in pH with buffer concentration. [g] Observed $k_{app} = 0.83 \times 10^{-2}\ M^{-1}$ sec^{-1}; the value reported is after correction of the k_{obsd} values for changes in k_0 caused by variation in pH with buffer concentration. [h] Observed $k_{app} = 0.19\ M^{-1}$ sec^{-1}; the value reported is after correction of the k_{obsd} values for changes in k_0 caused by variations in pH with buffer concentration. [i] The reaction mixtures in each series were brought to constant pH by the addition of hydrochloric acid if necessary. [j] The increase in k_{app} at 0 and 5% H_3PO_4 is attributed to catalysis by phosphate dianion. Estimates of the concentration of phosphate dianion and of the value of k_2 for this species from the Brønsted plot allowed corrections of k_{app} at these percentages of acid. The corrected values of k_{app} are $1.5 \times 10^{-2}\ M^{-1}$ sec^{-1} at 0 and at 5% H_3PO_4. [k] 0.05 M formate buffer, pH 3.64, was used as an external buffer. [l] k_3, obtained from a plot of k_{obsd} against acid concentration (see text). [m] 0.05 M formate buffer, pH 3.24, was used as an external buffer. See Figure 6. [n] Observed $k_{app} = 0.88 \times 10^{-2}\ M^{-1}$ sec^{-1}; the value reported is after correction of the k_{obsd} values for changes in k_0 caused by variations in pH with buffer concentration. [o] k_3, obtained from plots of k_{obsd} against acid concentration (see Figure 4). [p] Determined using the scavenger method of R. P. Bell and P. G. Evans, *Proc. Roy. Soc.* (London), **A291**, 297 (1966).

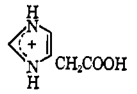
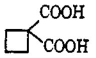
thoxybenzaldehyde–hydrogen peroxide hemiacetal dissociation by dichloroacetic acid.

Plots of k_{app} against fraction H_3PO_4 for phosphate catalysis showed higher values for catalysis by 0 and 5% H_3PO_4 buffers than predicted by the catalytic constants observed in more acidic buffers (Table I). This increase is attributed to general base catalysis by the phosphate dianion. A value of k_2 of 30 M^{-1} sec^{-1} was estimated for phosphate dianion from the Brønsted relationship obtained with other base catalysts, and this catalytic constant was found to account for the observed increase in k_{app} in these buffers.

Since relatively high concentrations of buffer were required to determine the catalytic constants for several of the weaker general acids, it is important to determine the effects of salt and organic solvents on k_{H^+} and k_{OH^-} which, in the case of the weaker general acids, represents the major fraction of k_{obsd}. The results are summarized in Table IV. The values of k_{obsd} and k_{H^+} show no significant change with increasing concentrations of potassium chloride, dioxane, or acetonitrile. This suggests that the small rate increases obtained with the weaker general acids are not caused by a solvent effect on k_{H^+}. These results also justify the validity of measuring the catalytic constants for the stronger general acids in solutions adjusted to constant pH.

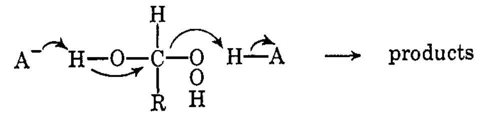
The rate of the hydroxide ion catalyzed reaction is increased with increasing potassium chloride and decreased with increasing dioxane and acetonitrile concentrations. These effects are undoubtedly caused, in large part, by changes in the concentration of the reactive anionic species in the presence of added salts and solvents.

Table II. Catalytic Constants for the General Acid–Base Catalyzed Dissociation of *p*-Chlorobenzaldehyde–Hydrogen Peroxide Hemiacetal at 25° and Ionic Strength 1.0 *M*

Acid	p^a	q	$pK_a{}^b$	k_2,[c] M^{-1} sec^{-1}	k_3,[d] M^{-1} sec^{-1}
HCOOH	1	2	3.62	0.061	$\leqslant$0.00083[e]
CH_3COOH	1	2	4.61	0.270	...
CH_3CH_2COOH	1	2	4.78	0.360	...
$ClCH_2COOH$	1	2	2.73	0.013	0.0017 ± 0.0010
CH_3OCH_2COOH	1	2	3.43	0.040	...
H_3PO_4	3	2	1.72	0.015	0.037[f]
H_3AsO_4	3	2	1.90	0.026	0.023[f]
$HOP(=O)(OCH_3)_2$	1	2	0.75	$\leqslant$0.0027[g]	0.22[f]
$CH_2(COOH)_2$	2	2	2.63	0.018	0.0017 ± 0.0010
$NH_3{}^+CH_2COOH$	1	2	2.50	0.014	$\leqslant$0.0017[e,f]
$CNCH_2COOH$	1	2	2.38	...	0.016
$Cl_2CHCOOH$	1	2	1.26	...	0.07[f]
	1	2	3.20	0.072	...
	2	2	3.00	0.042	...
$NH_2C(=O)NHNH_3{}^+$	3	1	3.88	0.070	...
H_2O	2	1	15.74	2.85×10^8[h]	1.5×10^{-5}[i]
H_3O^+	3	1	−1.74	1.5×10^{-5}[j]	0.89[j]

[a] Reference 5. [b] Apparent pK_a values were determined at ionic strength 1.0 *M* and 25° from either the pH of half-neutralized solutions or the degree of neutralization and the pH. Corrections for the ionization of the acid portion of the buffer ranging from 2 to 33% were made when the hydrogen ion concentration represented a significant fraction of the acidic portion of the buffer. [c] Second-order rate constants for general base catalysis by the conjugate base of the indicated acid. [d] Second-order rate constants for general acid catalysis. [e] Extrapolation of k_{app} to 100% HA gave the indicated small intercept, but this intercept could, within experimental error, be equal to zero. [f] Hydrochloric acid was added to bring all solutions to constant pH. Corrections ranging from 2 to 5%, 2 to 7%, 25 to 33%, 12 to 15%, and 4 to 9% of the concentration of acid added to each reaction mixture were made to account for the ionization of the acidic portion of buffers containing phosphoric acid, arsenic acid, dimethylphosphoric acid, dichloroacetic acid, and glycine hydrochloride, respectively. [g] No catalysis was observed (see Figure 6). [h] For hydroxide ion concentration, based on $K_w = 1 \times 10^{-14}$, the measured pH and an activity coefficient of 0.67 for hydroxide ion.[9] [i] K_{H_2O} (eq 2). [j] Based on the concentration of hydrogen ion.

Possible Concerted General Acid–Base Catalysis. In reactions which are catalyzed by both general acids and general bases, the possibility exists that in a given buffer a molecule of general base and a molecule of general acid could act in a concerted fashion (eq 3).



(3)

Such concerted catalysis would be manifested experimentally by a third-order term in the rate law, which would cause an upward deviation from linearity in plots of k_{obsd} against buffer concentration and would be most significant at high buffer concentrations. Figure 5 shows the dependence of k_{obsd} on the total concentration of formate, glycine, and chloroacetate buffers. There is no upward deviation suggestive of a third-order term for concerted catalysis with increasing buffer concentration, up to as high as 2.0 *M* in the case of 50% neutralized buffers of chloroacetic acid, a catalyst which has clearly demonstrable catalytic constants for both the acidic and basic species.

Figure 6 shows the effects of potassium dihydrogen phosphate and potassium dimethyl phosphate at constant pH using 0.05 *M* formate as an external buffer. The observed general base catalysis by dihydrogen phosphate anion is unexpected, because cyanoacetate anion, which has a pK_a approximately 0.7 units higher than dihydrogen phosphate anion, shows no observable general base catalysis. This catalysis is of interest because dihydrogen phosphate anion has sites available to both abstract and donate a proton simultaneously (eq 4). Dimethyl phosphate monoanion, which is

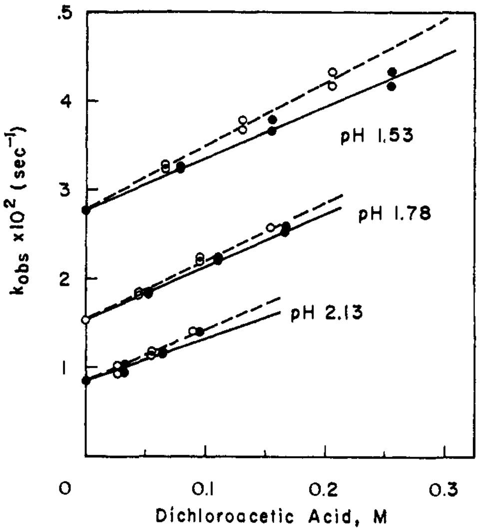
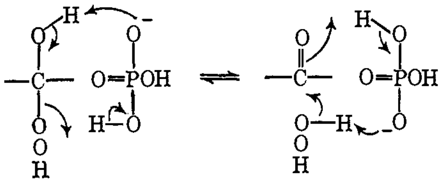


Figure 4. Dependence of the observed rate constants for *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal dissociation on dichloroacetic acid concentration at 25°, ionic strength 1 *M*, and constant pH. Buffers at pH 1.53, 1.78, and 2.13 were prepared to contain 33, 23.5, and 13.5% acid, respectively. The open circles show the data plotted against the concentration of dichloroacetic acid after correction for ionization of the acidic component of each buffer.



(4)

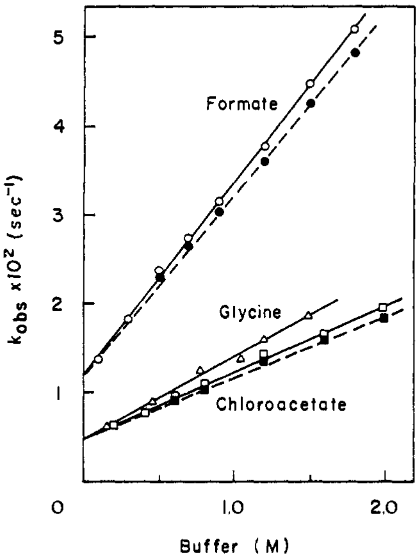


Figure 5. The linear relationship between the observed rate constants for *p*-chlorobenzaldehyde-hydrogen peroxide hemiacetal dissociation and buffer concentrations up to 2.0 *M* total buffer. Buffers used were: 35% formic acid, ionic strength 2.0 *M*, ○, 30% glycine hydrochloride, ionic strength 2.25 *M*, △, and 50% chloroacetic acid, ionic strength 1.0 *M*, □. The solid symbols and dashed lines show the rate constants corrected for small differences in pH. In the case of glycine hydrochloride no corrections were required.

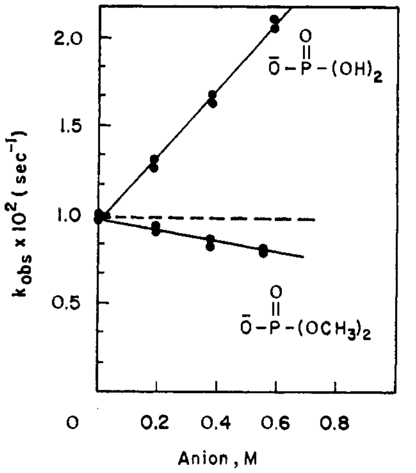


Figure 6. The effect of increasing potassium dihydrogen phosphate and potassium dimethyl phosphate concentrations on the observed rate constants for *p*-chlorobenzaldehyde-hydrogen peroxide hemiacetal dissociation at 25° and ionic strength 1.0 *M*. Hydrochloric acid was added to maintain constant pH and 0.05 *M* potassium formate, pH 3.24, was used as an external buffer. The dashed line shows the potassium dimethyl phosphate data corrected for solvent-dependent rate depression, using dioxane as a solvent model (Table IV).

incapable of concerted acid-base catalysis, causes a *decrease* in the rate of the reaction. This decrease may represent a nonspecific solvent effect, since a similar rate decrease is observed with dioxane. The rate constant for dimethyl phosphate anion in Table II and Figure 7 is a limiting value, based on the assumption that a 6% rate increase at the highest concentration examined could not have been detected experimentally.

Discussion

General Base Catalysis. The rate constants for the general base catalyzed reactions follow a Brønsted plot with a slope, β, of 0.66 for carboxylate ions (Figure 7). Other types of catalysts do not show large deviations from this line, except for the hydroxide ion reaction which is 100 times faster than predicted from the Brønsted relationship. This suggests that the hydroxide ion reaction represents a direct attack and expulsion of the hydroperoxide anion (eq 5) rather than hydroxide ion catalysis of a reaction of hydrogen peroxide.

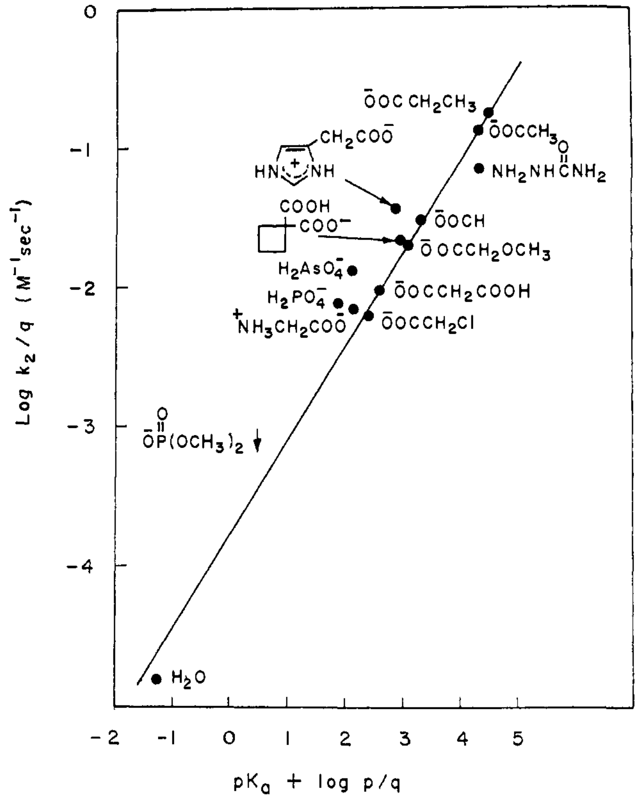
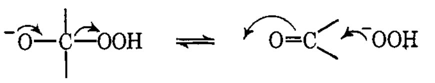


Figure 7. The relationship between the second-order rate constants for the general base catalyzed dissociation of *p*-chlorobenzaldehyde-hydrogen peroxide hemiacetal and the pK_a of the general base, corrected for statistical effects.



(5)

The simplest mechanisms for the reaction pathways which appear kinetically as general base catalysis are

Table III. Catalytic Constants for the General Acid-Base Catalyzed Dissociation of *p*-Methoxybenzaldehyde-Hydrogen Peroxide Hemiacetal at 25° and Ionic Strength 1.0 *M*

Acid	k_2,[a] M^{-1} sec^{-1}	k_3,[b] M^{-1} sec^{-1}
HCOOH	0.093	...
CH_3COOH	0.33	...
$ClCH_2COOH$	0.015	0.031[c]
$Cl_2CHCOOH$	...	0.40[d]
H_3O^+	...	8.0[e]
H_2O	4.0 × 10^8 [f]	...

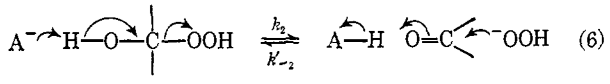
[a] Second-order rate constants for general base catalysis by the conjugate base of the indicated catalyst. [b] Second-order rate constants for general acid catalysis. [c] Corrections ranging from 23 to 35% were applied to k_{obsd} to account for pH variation in the buffers containing 90% chloroacetic acid. [d] Hydrochloric acid was added to bring all solutions to constant pH. An 11-12% correction of the concentration of dichloroacetic acid was made to account for ionization of the acid. [e] Based on the concentration of hydrogen ion. [f] k_{H_2O} (eq 2).

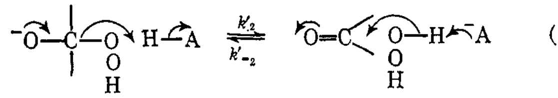
Table IV. The Effect of Ionic Strength and Organic Solvents on the Hydrogen and Hydroxide Ion Catalyzed Dissociation of *p*-Chlorobenzaldehyde–Hydrogen Peroxide Hemiacetal at 25°

Solvent[a]	pH	$k_{obsd} \times 10^2$ sec^{-1}	k_3,[b] M^{-1} sec^{-1}	k_{H^+},[c] M^{-1} sec^{-1}
0.044 M HCl	1.50	3.18	0.72	1.00
0.044 M HCl + 0.4 M KCl	1.50	3.58	0.82	1.12
0.037 M HCl + 0.96 M KCl	1.50	3.50	0.95	1.09
0.030 M HCl + 1.92 M KCl	1.50	3.02	1.00	0.95
0.03 M HCl + 0.97 M KCl	1.61	2.58		
+ 0.24 M dioxane	1.61	2.58		
+ 0.48 M dioxane	1.61	2.60		
+ 0.72 M dioxane	1.61	2.65		
+ 0.24 M acetonitrile	1.61	2.68		
+ 0.48 M acetonitrile	1.61	2.62	k_{OH^-},[d]	
+ 0.72 M acetonitrile	1.61	2.62	M^{-1} sec^{-1}	
0.05 M formate buffer	3.21	0.72	4.1×10^8	
+ 0.4 M KCl	3.21	0.85	4.8×10^8	
+ 1.0 M KCl	3.21	0.88	5.0×10^8	
+ 2.0 M KCl	3.21	0.92	5.3×10^8	
0.05 M formate buffer	3.24	1.00		
+ 1.0 M dioxane	3.24	0.58		
+ 2.0 M dioxane	3.24	0.37		
+ 2.8 M dioxane	3.24	0.25		
+ 1.0 M acetonitrile	3.24	0.77		
+ 2.8 M acetonitrile	3.24	0.48		

[a] Hydrochloric acid was added to bring all solutions to constant pH if necessary. [b] Second-order rate constants for hydrogen ion catalysis, based on the molar concentration of hydrochloride acid. [c] Based on a_{H^+}. [d] Based on a_{OH^-}, which was obtained from the apparent pH and $K_w = 10^{-14}$. A correction of 8–9% was applied to account for catalysis by formate anion.

shown in eq 6 and 7. According to the mechanism of eq 6 the base increases the driving force for the expulsion


(6)


(7)

of hydroperoxide anion by partially removing a proton from the addition compound, and, in the reverse direction, the conjugate acid of the catalyst adds a proton to the carbonyl group to assist the attack of hydroperoxide anion. According to the mechanism of eq 7 the conjugate acid of the catalyst donates a proton to increase the leaving ability of the hydroperoxide group from the anion of the adduct and, in the reverse direction, the base removes a proton from the attacking hydrogen peroxide molecule to increase its nucleophilic reactivity. Since general acid catalysis of the addition to carbonyl compounds of other strongly basic nucleophiles, such as cyanide, thiol, and bisulfite anions is not observed; *i.e.*, the value of α is zero for strongly basic nucleophiles,[11,12] the mechanism of eq 6 is unlikely, and that of eq 7 is preferred. Indeed, it has just been pointed out that the hydrogen peroxide anion itself adds to the carbonyl group without catalysis. According to the mechanism of eq 6, the hydroxide ion catalyzed reaction must represent general base catalysis by hydroxide ion of the decomposition of the adduct and, in the opposite direction, catalysis by water of the attack of hydroperoxide ion, so that the rate constant for the hydroxide ion reaction should fit on the same Brønsted plot that is followed by other bases. The positive deviation of the rate constant for the hydroxide ion reaction is therefore difficult to explain according to the mechanism of eq 6, but there is no reason why the uncatalyzed addition of hydroperoxide anion (eq 5) and the general base catalyzed addition of free hydrogen peroxide (eq 7) should not proceed concurrently, by independent mechanisms.

The anions which are formed as intermediates in the mechanisms of eq 6 and 7 do not differ greatly in stability. The very similar rate constants for the base catalyzed breakdown of the *p*-methoxybenzaldehyde adduct are consistent with either mechanism. Hydrogen peroxide is a very weak base and it is not unreasonable that its attack should be aided by partial removal of a proton with a β value of 0.66. The thiol group, which is also weakly basic, ordinarily adds to the carbonyl group with only specific base catalysis, which might be regarded as equivalent to a β value of approximately 1.0.[12,13] The values of β for the attack of the more basic water molecule on carbonyl compounds are in the range of 0.4–0.5.[14]

The rate constants for these two mechanisms are interrelated according to eq 8–10, in which K_{HA}, K_{add},

$$k_2' = k_2\frac{K_{HA}}{K_{add}} \tag{8}$$

$$k_{-2} = k_2\frac{K_{HA}K_{eq}}{K_{HOOH}} \tag{9}$$

$$k_{-2}' = k_2'\frac{K_{add}K_{eq}}{K_{HA}} \tag{10}$$

and K_{HOOH} are the dissociation constants of the conjugate acid of the catalyst, the hydroxyl group of the addition compound, and hydrogen peroxide,[15] respectively, and K_{eq} is the equilibrium constant for formation of the adduct. The experimental rate constant for general base catalyzed breakdown of the adduct (k_2, Tables II and III) is identical with the k_2 of eq 6 if this mechanism is correct and is equal to $k_2'K_{add}/K_{HA}$ if the mechanism of eq 7 is correct. The value of K_{add} is estimated to be 2.7×10^{-11} from the pK of formaldehyde hydrate,[16] the differences between the pK's of methylamine and benzylamine and of ethylamine and ethanolamine and the ρ value of 1.1 for the ionization of substituted trifluoroacetophenone hydrates.[17] The largest value of k_{-2} is 5.9×10^8 M^{-2} sec^{-1}, for the water-catalyzed reaction (*i.e.*, the proton-catalyzed addition of hydroperoxide ion in the reverse direction) and the largest value of k_2' is 3.1×10^7 M^{-1} sec^{-1} for the water-catalyzed reaction (*i.e.*, the proton-catalyzed breakdown of the anion of the addition compound). These values are large, but are not sufficiently large to exclude either mechanism.

---

(11) W. P. Jencks, *Progr. Phys. Org. Chem.*, **2**, 63 (1964).

(12) G. E. Lienhard and W. P. Jencks, *J. Am. Chem. Soc.*, **88**, 3982 (1966).

(13) R. Barnett and W. P. Jencks, *ibid.*, **89**, 5963 (1967). The apparent general base catalysis for the attack of thiophenols and thioacetic acid actually represents the kinetically equivalent general acid catalysis of the attack of the weakly basic thiol anion.

(14) R. P. Bell and P. G. Evans, *Proc. Roy. Soc.* (London), **A291**, 297 (1966).

(15) A. J. Everett and G. J. Minkoff, *Trans. Faraday Soc.*, **49**, 410 (1962).

(16) R. P. Bell and D. P. Onwood, *ibid.*, **58**, 1557 (1953).

(17) R. Stewart and R. Van der Linden, *Can. J. Chem.*, **38**, 399 (1960).

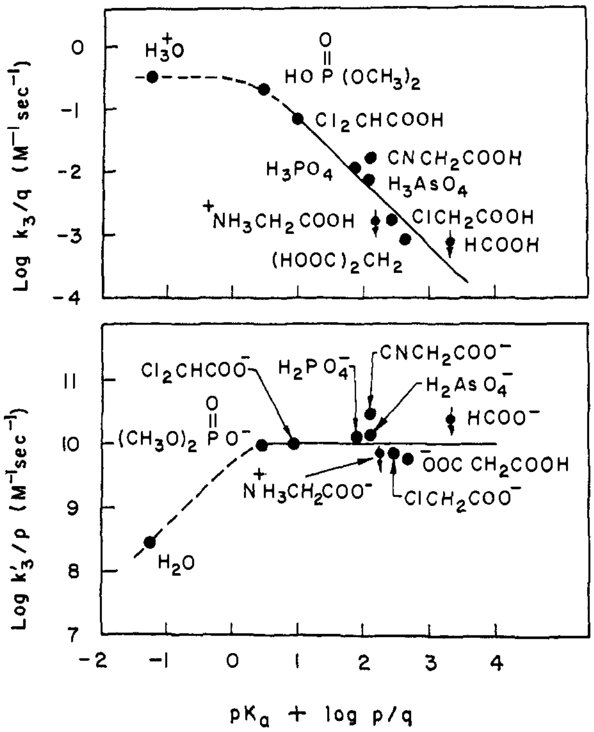
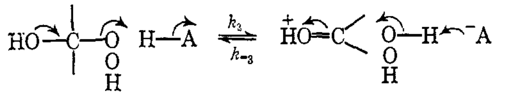


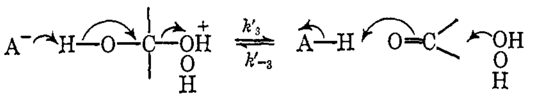
Figure 8. The relationship between the second-order rate constants for the general acid catalyzed dissociation of *p*-chlorobenzaldehyde–hydrogen peroxide hemiacetal and the pK_a of the general acid. The lower figure shows a kinetically equivalent general base catalyzed mechanism, preceded by a fast protonation of the hemiacetal. The values of k_3' were calculated using eq 13 (see text). The arrows represent estimated upper limits for rate constants.

Possible modifications of these mechanisms are a "one-encounter" mechanism in which both of the proton transfers of eq 6 and 7 are mediated by a single molecule of catalyst, but the reaction still proceeds in a stepwise manner with one or the other step rate determining, and a concerted mechanism in which the transfers of both protons are mediated by the catalyst at the same time.[3,12,18] There is no evidence which requires a one-encounter mechanism, although such a mechanism is an attractive possibility in view of the large rate constants required for the unmodified mechanisms of eq 6 and 7. There is no indication of concerted acid–base catalysis by separate catalyst molecules, which would appear as an upward deviation in plots of rate against buffer concentration, up to very high catalyst concentrations (Figure 5). Phosphate monoanion is a much more effective catalyst than dimethyl phosphate monoanion (Figure 6) and phosphate and arsenate monoanions and imidazoleacetic acid zwitterion show small positive deviations from the Brønsted plot which are suggestive of a small amount of bifunctional acid–base catalysis by these compounds. However, the greater catalytic effectiveness of phosphate monoanion than of its dimethyl ester may be explained, in large part, by its greater basicity and the fact that the positive deviations of these compounds from the Brønsted plot correspond to only about a twofold rate acceleration suggests that, as in the hydration of aldehydes, any contribution of concerted, bifunctional catalysis to the general base catalyzed hydroperoxide reaction is small.[14,19] The factors which determine the importance of bifunctional catalysis for reactions of this kind are still not understood.

General Acid Catalysis. The simplest mechanisms for the reaction pathways which appear kinetically as general acid catalysis are shown in eq 11 and 12. According to the mechanism of eq 11 the acid donates a proton to aid the expulsion of hydroperoxide and, in the reverse direction, the conjugate base of the acid removes a proton from a hydrogen peroxide molecule which is attacking the conjugate acid of the carbonyl compound. According to the mechanism of eq 12, the conjugate base of the catalyst removes a proton from the hydroxyl group of the protonated adduct to aid the expulsion of hydrogen peroxide and, in the reverse direction, the catalyzing acid donates a proton to the carbonyl group to facilitate the attack of free hydrogen peroxide. A mechanism of the type of eq 12 is preferred, but not directly proved, by analogy with the preferred mechanism for the addition of other weakly basic nucleophiles to the carbonyl group.[11,12,20] The rate constants for the two mechanisms are interrelated by eq 13–15, in which K_{CO} and K_{addH^+} are the acid dissociation constants for the conjugate acids of the aldehyde[21a] and the addition compound, respectively. The experimental rate constant for the general acid catalyzed breakdown of the adduct (k_3, Tables II and III) is identical to k_3 of eq 11 if this mechanism is correct and is equal to k_3'/K_{addH^+} if the mechanism of eq 12 is correct. The values of k_{-3} are close to 10^7 M^{-2} sec^{-1} for all catalysts except the proton, for which $k_{-3} = 2.9 \times 10^5$ M^{-2} sec^{-1}.



(11)



(12)

$$k_3' = k_3\frac{K_{addH^+}}{K_{HA}} \quad (13)$$

$$k_{-3} = k_3\frac{K_{CO}K_{eq}}{K_{HA}} \quad (14)$$

$$k_{-3}' = k_3K_{eq} \quad (15)$$

The experimental data require a Brønsted slope, α, for catalysis by carboxylic acids equal or very close to 1.0 (Figure 8, top). General acid catalysis is ordinarily not detectable with a Brønsted slope of 1.0 because any such catalysis should be small compared to catalysis by the proton; catalysis is detectable in this reaction because the proton exhibits a negative deviation from the Brønsted plot.[21b] There is a moderate scatter of the points, and the rate constants for catalysis by some acids can be given only as limits, but it does not appear possible to fit the data with a slope appreciably less than 1.0. The line is most firmly established by the rate

---

[18] M. Eigen, *Discussions Faraday Soc.*, 39, 7 (1965).

[19] Y. Pocker and J. E. Meany, *J. Phys. Chem.*, 71, 3113 (1967).

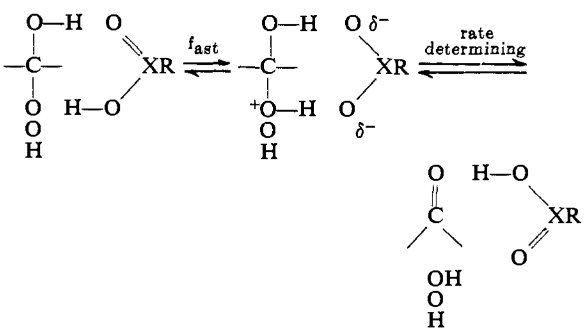
[20] L. do Amaral, W. A. Sandstrom, and E. H. Cordes, *J. Am. Chem. Soc.*, 88, 2225 (1966); C. G. Swain and J. C. Worosz, *Tetrahedron Letters*, 3199 (1965).

[21] (a) K. Yates and R. Stewart, *Can. J. Chem.*, 37, 664 (1959). (b) Brønsted slopes of 1.09 and 0.89 have been reported by A. V. Willi (*Trans. Faraday Soc.*, 55, 433 (1959)) for the general acid catalyzed decarboxylation of 4-aminosalicylate ion by pyridinium and anilinium ions, respectively.

constant for catalysis by dichloroacetic acid, which is certainly not significantly smaller than shown, and that for chloroacetic acid which, while not of high precision, is certainly not significantly larger than indicated. A large value of the Brønsted slope is expected for catalysis of the addition of the weakly basic hydrogen peroxide molecule, in view of the increasing values of α for catalysis of the attack of progressively less basic nucleophiles according to the mechanism of eq 12.[11,12,20]

If the rate of a reaction is limited only by the rate of diffusion-controlled proton transfer, it will exhibit a value of α (or β) of 0 or 1.0, depending upon whether the proton donor is a stronger or weaker acid, respectively, compared to the proton acceptor.[22] Such a diffusion-controlled proton transfer provides a possible explanation for the α value of 1.0 for the hydroperoxide reaction. The rate constants k_3' for the mechanism of eq 12 would be close to the diffusion-controlled limit of about 10^{10} M^{-1} sec^{-1} for all catalysts except water if the pK of the conjugate acid of the hydrogen peroxide adduct were -10.2; the rate constants calculated on the basis of this assumption are shown in the lower part of Figure 8 and show no dependence on the pK of the catalyst, except for the negative deviation of the point for water. The rate constants in this direction represent general base catalysis of the breakdown of the conjugate acid of the substrate and are, accordingly, plotted as a function of the basicity of the catalyzing base to give a β of zero. A pK of -10.2 for the conjugate acid of this adduct is possible, but not proved; the pK of the conjugate acid of hydrogen peroxide itself has been estimated to be between 3 and more than 6 pK units less than that of water of -1.7, which is in the range expected from the acid-strengthening effect of the hydroxyl group in other molecules. An additional decrease of 2 to 3 pK units is expected by analogy with the decrease in the pK of water and amines upon incorporation into carbonyl addition compounds.[15,16,23,24]

However, the fact that the rate constants for acid-catalyzed decomposition of the *p*-methoxybenzaldehyde adduct are 6 to 18 times faster than those for the *p*-chlorobenzaldehyde adduct means that a diffusion-controlled mechanism of this kind cannot be correct in its simplest form. The basicity of the *p*-methoxybenzaldehyde adduct is expected to be only some twofold greater than that of the *p*-chlorobenzaldehyde adduct, based on ρ values of 0.7 to 1.1 for the dissociation constants of structurally related compounds.[17,25] This difference is insufficient to account for the observed rate difference if diffusion-controlled proton transfer alone were occurring in the rate-determining step and requires that there be some carbon–oxygen bond cleavage in the transition state. A modified, cyclic mechanism, somewhat similar to those proposed for catalysis of carbonyl hydration,[8,18] provides a possible alternative (eq 16). Complete, or almost complete proton transfer in the transition state is required by the α value of 1.0. According to this mechanism, complete proton transfer occurs from the catalyzing acid to the hydroperoxide group and is followed by cleavage of the carbon–oxygen bond and proton transfer to the conjugate base of the catalyst in a concerted process. Although this second step must be at least partly rate determining, it must occur very rapidly to account for the observed rates. There is precedent for the rapid breakdown of adducts of this kind in the base-catalyzed breakdown of hemithioacetals formed from acetaldehyde and weakly basic thiols, in which carbon–sulfur bond cleavage can occur faster than a diffusion-controlled proton transfer step.[13] The large value of α in the hydrogen peroxide reaction requires that there be little proton transfer to the catalyst in the transition state of the second step (*i.e.*, β is zero for this step). According to this mechanism the negative deviation of the rate constant for the solvated proton could be accounted for by the fact that this is the only catalyst examined which does not contain a basic moiety which could abstract a proton very shortly after the proton-donation step. A complementary mechanism in which the assignment of the proton transfer and concerted steps is reversed is also possible, but seems less likely on chemical grounds, by analogy with the mechanisms of other general acid catalyzed carbonyl addition reactions.[11,12,20]



(16)

The large amount of proton transfer in the transition state required by the α value of 1.0 means that proton donation provides the principal driving force for catalysis of the reaction and is difficult to reconcile with a fully concerted mechanism in which both proton donation and removal are occurring in the transition state; the special catalytic effectiveness of bifunctional catalysts might better be ascribed to a stabilization of the transition state by hydrogen bonding or to a facilitation of the other step so that it does not become rate determining. In all of the mechanisms discussed, it is possible that one or more bridging water molecules are involved in the proton transfer steps.

It is frequently difficult to make a meaningful distinction between general acid or base catalysis by hydrogen or hydroxide ions and specific acid or base catalysis, especially if α or β = 1.0 or 0. These experiments illustrate two ways in which such a distinction may become experimentally significant. First, general acid catalysis (for example) may be experimentally demonstrable if the rate constant for the solvated proton falls below the Brønsted line; this means that true general acid catalysis can occur even if α = 1.0 and that it is different from specific acid catalysis. Second, specific base catalysis (for example) may occur concurrently with general base catalysis of the same reaction and appear as a positive deviation from the Brønsted line. This suggests that the specific base catalyzed reaction occurs by a different mechanism from the general base

---

(22) M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, 3, 1 (1964).

(23) J. O. Edwards in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, p 85; A. G. Mitchell and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, 52, 824 (1956).

(24) R. G. Kallen and W. P. Jencks, *J. Biol. Chem.*, 241, 5864 (1966).

(25) R. W. Taft, Jr., and I. C. Lewis, *J. Am. Chem. Soc.*, 80, 2436 (1958).

Table V. Comparisons of Approximate Rate and Equilibrium Constants for the Addition of Water and Hydrogen Peroxide to Formaldehyde and Acetaldehyde

	Formaldehyde		Acetaldehyde	
	H_2O[a]	H_2O_2[b]	H_2O[a]	H_2O_2[c]
		Addition		
k_{-3H^+}, M^{-2} sec^{-1}	110	154	10.2	3
k_{-3H_2O}, M^{-2} sec^{-1} [d]	3.8×10^{-3}	5×10^{-2}	1.2×10^{-6}	2×10^{-4}
		Dissociation		
k_{3H^+}, M^{-1} sec^{-1}	2.7	2.2×10^{-3}	390	6×10^{-2}
k_{3H_2O}, M^{-1} sec^{-1} [d]	9.2×10^{-5}	7.2×10^{-7}	4.6×10^{-5}	4×10^{-6}
K_{eq}, M^{-1} [e]	41	7×10^{4}	0.026[f]	48

[a] Reference 14. [b] Reference 5. [c] Estimated from the data of ref 6, assuming first-order kinetics with respect to acetaldehyde. [d] Expressed as a second- or third-order rate constant for the water-catalyzed dissociation or association, respectively. [e] For adduct formation, based on the convention that pure water is 55.5 *M*. [f] Reference 3.

catalyzed reaction, a distinction that may be useful in distinguishing between the kinetically equivalent mechanisms for general base catalysis.

Rates and Equilibria. The rate and equilibrium constants for the reactions of water and hydrogen peroxide with *p*-chlorobenzaldehyde cannot be compared because of the absence of a detectable amount of addition of water to this aldehyde, but a rough comparison may be made for the analogous reactions with formaldehyde and acetaldehyde, based on data in the literature and assuming that the addition of hydrogen peroxide to these aldehydes is first order with respect to the aldehydes, neglecting any polymerization which may affect the kinetics at higher aldehyde concentrations.[5,6,14] As shown in Table V, the more favorable equilibrium constant for the addition of hydrogen peroxide compared to water is manifested in the slower rate of decomposition of the hydrogen peroxide adduct. The especially slow rate of breakdown of the hydrogen peroxide adducts by the acid-catalyzed pathway is presumably a consequence of the low basicity of the peroxide group. The acid-catalyzed and water-catalyzed additions of hydrogen peroxide occur at a similar or faster rate compared to the corresponding additions of water. The rapid rates of addition of hydrogen peroxide, in spite of a basicity 10^3–10^7-fold less than that of water, means that the unusually high nucleophilic reactivity of hydrogen peroxide is manifested in the neutral compound, as well as in the anion. Intramolecular hydrogen bonding to the carbonyl group from the hydroxyl group of hydrogen peroxide is almost certainly not involved in this high reactivity, because the reactivity is evident in the proton-catalyzed addition reaction. Hydrogen peroxide also has a reactivity equal to or greater than that of water toward activated acyl compounds.[26] A similar high reactivity toward the carbonyl group is exhibited by uncharged thiols, as well as by the thiol anion.[12]

It is of interest that the rate constant for the acid-catalyzed attack of hydrogen peroxide on *p*-methoxybenzaldehyde of 1.44 M^{-2} sec^{-1} is *larger* than the value of 0.86 M^{-2} sec^{-1} for the corresponding reaction with *p*-chlorobenzaldehyde. This is the reverse of the order of substituent effects usually seen for carbonyl addition reactions—the acid-catalyzed attack of semicarbazide ($\alpha = 0.25$) on *p*-methoxybenzaldehyde occurs at 0.38 times the rate with *p*-chlorobenzaldehyde[27]—and reflects the great importance of proton donation to the carbonyl group ($\alpha = 1.0$) for the attack of the weakly basic hydrogen peroxide molecule.

(26) C. A. Bunton, ref 23, p 11.

(27) E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, 84, 4319 (1962).