Peroxy Acid Oxidations: A Kinetic and Mechanistic Study of Oxidative Decarboxylation of α-Keto Acids by Peroxomonophosphoric Acid

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The kinetics of oxidative decarboxylation of pyruvic acid and benzoylformic acid by peroxomonophosphoric acid (PMPA) in aqueous medium have been investigated. The reaction follows second order–first order each in PMPA and substrate concentration at constant pH. The reactivity of different peroxo species in the oxidation has been determined. Activation energy and thermodynamic parameters have been computed. A plausible mechanism consistent with the observed results is proposed.

Keywords ; Oxidative decaboxylation, α-Keto acids, Peroxomonophosphoric acid.

Introduction

α-Ketoacids are readily decarboxylated by several metallic and non-metallic oxidising agents[1] such as ceric sulphate, potassium permanganate, lead tetra acetate, peroxyphthalic acid and hydrogen peroxide. The oxidative decarboxylation of a-ketoacids using basic hydrogen peroxide is a synthetically useful reaction[2] and has been reported[3] to be catalysed by Fe^{2+}. Siegel and Lanphear[4] have undertaken a detailed kinetic study on the acid-catalysed oxidative decarboxylation of benzoylformic acid using H_2O_2 in aqueous medium. The bell-shaped pH rate profile in the above reaction was shown to remain unaltered even on replacing H_2O_2 by either *t*-butyl hydroperoxide or peroxyacetic acid.[4] In the reactions of peroxomonophosphoric acid with pyruvic acid and benzoylformic acid, currently reported here, however, the pH-rate profile is observed to be profoundly different. Even the two representative ketoacids studied showed significant difference.

The salient kinetic features of the reaction are described.

Results and Discussion

The oxidation rates at various initial PMPA concentration at fixed [ketoacid] have been measured and the data are summarised in Table 1. Plots of log $[PMPA]_t$ *vs* time are linear up to at least 80% completion of the reaction, and also the constancy of the k_1' values for different initial concentration of PMPA indicates a first-order dependence on [PMPA].

The oxidation also exhibits a first-order dependence on [ketoacid] as seen from the constancy of the second-order rate constants for varying initial ketoacid concentrations (Table 1). The plots of log k_1' versus log [substrate] are linear ($r = 0.99$ for both the ketoacids) with unit slopes which further indicate that the reactions are first-order with respect to [ketoacid].

A change in the ionic strength (μ) of the medium using $NaClO_4$ had marginal effect on the oxidation rate. Addition of acrylamide does not influence the reaction rate (Table 1).

The effect of temperature on oxidation rate has been studied at 25°, 30° and 35 °C (Table 1) for pyruvic acid reaction, and the activation parameters, Ea, $\Delta H^{\#}$, $\Delta S^{\#}$ were computed to be 75 kJ mol^{-1}, 72 kJ mol^{-1} and -21 $JK^{-1} mol^{-1}$ respectively from the linear Arrhenius plots of log k_2' *vs* T^{-1} ($r = 0.992$).

Homolytic cleavage of the peroxide bond requires[5] an energy of activation of $\simeq 138$ kJ mol^{-1}. The energy of activation $\simeq 75$ kJ mol^{-1}, computed in the present case, clearly rules out the radical pathway for the peroxide bond cleavage. Further, (a) bimolecular kinetics (b) negative entropy of activation and (c) insensitivity of rate to radical trapping agents show that the reactions involve polar

Table 1. Second Order Rate Constants for the Oxidation of Pyruvic Acid and Benzoylformic Acid by Peroxomonophosphoric Acid Temp=35 °C, Aqueous Medium, $[H^+]$=0.5 mol L^{-1}, μ=1.0 mol L^{-1}

Substrate (S)	10^2 [S] mol L^{-1}	10^4 [PMPA] mol L^{-1}	10^4 k_1' sec^{-1}	10^3 k_2' L · mol^{-1} sec^{-1}
Pyruvic acid	2.02	3.00	3.30	16.3^a
	2.03	5.34	3.09	15.2
	2.00	10.2	3.10	15.5
	2.02	18.5	2.87	14.2
	0.51	5.23	0.63	12.4
	5.04	5.27	6.80	13.5
	10.2	4.80	15.6	15.3
	2.00	4.80	4.13	20.5^b
	2.00	4.80	2.54	12.6^c
	2.00	5.30	1.20	6.00^d
	2.00	5.30	2.16	10.8^e
Benzoyl-formic acid	1.04	5.20	1.07	10.3
	2.02	8.10	1.98	9.80
	3.04	5.00	2.95	9.57
	5.10	5.30	5.03	9.87

[a] μ = 0.6 mol L^{-1}. [b] μ = 1.2 mol L^{-1}. [c] [Acrylamide] = 5 ×10^{-3} mol L^{-1}. [d] 25 °C. [e] 30 °C.

Table 2. Oxidation of Pyruvic acid and Benzoylformic acid by PMPA: Effect of pH[a,b]

Substrate	pH	$10^2\ k_2'$ $L \cdot mol^{-1} sec^{-1}$	$10^2\ k_2'{}_{Calcd}$ $L \cdot mol^{-1} sec^{-1}$
Pyruvic acid	-0.30[c]	1.82	2.10
	0	1.57	3.20
	0.30	1.52	5.10
	0.60	8.00	8.10
	1.00	14.1	14.0
	1.40	18.3	20.0
	1.75	23.5	22.4
	2.50	21.9	18.0
	3.80	21.5	6.30
	4.30	22.9	8.56
	5.70	36.7	21.1
Benzoylformic acid	0.30	9.80	–
	2.10	10.5	–
	4.14	10.6	–
	6.03	9.10	–
	6.81	7.10	7.10
	7.24	11.0	11.0
	7.85	34.0	29.0
	8.15	53.0	53.0
	8.75	170	200
	9.25	430	620

[a]Aqueous, $\mu = 1.0$ mol L^{-1}, 35 °C. [b]pH ≤ 1.0, $[H^+]$ measured titrimetrically. [c]$\mu = 2.0$ mol L^{-1}

mechanisms.[6]

The oxidation of pyruvic acid by PMPA has been studied in the pH range ≃ 0-5.7, and that of benzoylformic acid in the range 0-9.25. The rate data are summarised in Table 2, and the plots of log k_2' *vs* pH are shown in Figures 1 and 2. The reactions were immeasurably fast at pH values higher than the reported ranges. In the case of pyruvic acid oxidation the pH-rate plot was found to be sigmoid, indicating the involvement of different PMPA and substrate species in the reaction. In the oxidation of benzoylformic acid, however, the results were different; the rate of oxidation was totally insensitive to the variation of pH in the range 0-6.8, and then increased linearly with pH (≃ 6.8-9.25).

Rate Law and Mechanism. In aqueous solution PMPA exists[7] as H_3PO_5, $H_2PO_5^-$, HPO_5^{2-} and PO_5^{3-} at different pH.

$$H_3PO_5 \overset{K_1}{\rightleftharpoons} H_2PO_5^- + H^+ \tag{1}$$

$$H_2PO_5^- \overset{K_2}{\rightleftharpoons} HPO_5^{2-} + H^+ \tag{2}$$

$$HPO_5^{2-} \overset{K_3}{\rightleftharpoons} PO_5^{3-} + H^+ \tag{3}$$

The dissociation constants K_1, K_2, and K_3 are 8.0×10^{-2}, 4.2×10^{-6} and 1.6×10^{-13} mol dm^{-3} respectively[7] at 298 K and $\mu = 0.2$ mol dm^{-3}.

The pK_a of pyruvic acid[8] is 2.49.

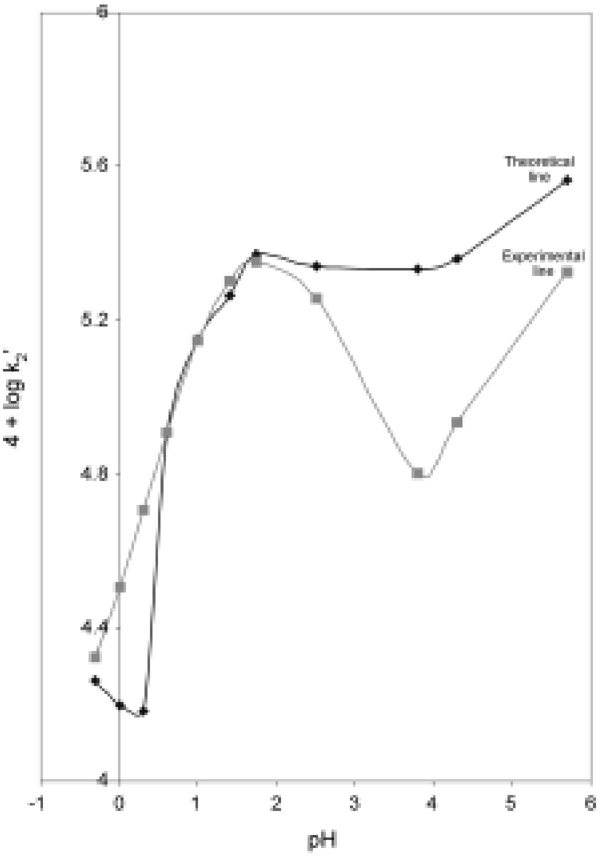


Figure 1. Plot of log k_2' *vs* pH (Pyruvic acid.)

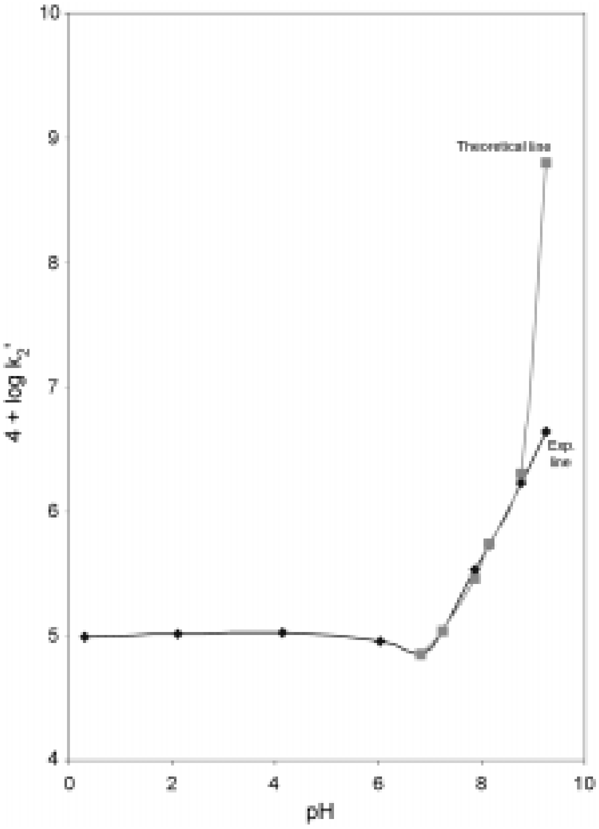
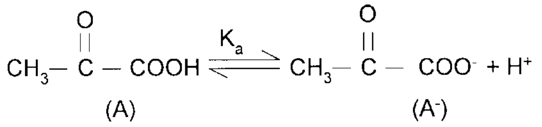


Figure 2. Plot of log k_2' *vs* pH (Benzoylformic acid).



$$\underset{(A)}{CH_3-\overset{O}{\overset{||}{C}}-COOH} \underset{}{\overset{K_a}{\rightleftharpoons}} \underset{(A^-)}{CH_3-\overset{O}{\overset{||}{C}}-COO^-} + H^+ \tag{4}$$

The steps of oxidation for pyruvic acid in the pH range 0-5.7 can be represented as

$$H_3PO_5 + A \xrightarrow{k_2} \text{Products} \tag{5}$$

$$H_3PO_5 + A^- \xrightarrow{k_3} \text{Products} \tag{6}$$

$$H_2PO_5^- + A \xrightarrow{k_1} \text{Products} \tag{7}$$

$$H_2PO_5^- + A^- \xrightarrow{k_4} \text{Products} \tag{8}$$

$$HPO_5^{2-} + A \xrightarrow{k_5} \text{Products} \tag{9}$$

$$HPO_5^{2-} + A^- \xrightarrow{k_5} \text{Products} \tag{10}$$

The rate law is expressed by Eq. (11)

$$\begin{aligned} \text{Rate} &= -\frac{d[\text{PMPA}]_t}{dt} \\ &= k_1\,[H_3PO_5][A] + k_2\,[H_3PO_5][A^-] \\ &\quad + k_3\,[H_2PO_5^-][A] + k_4\,[H_2PO_5^-][A^-] + k_5\,[HPO_5^{2-}][A] \\ &\quad + k_6\,[HPO_5^{2-}][A^-] \end{aligned} \tag{11}$$

Where $[\text{PMPA}]_t$ represents the total analytical concentration of PMPA, and is expressed as

$$[\text{PMPA}]_t = [H_3PO_5] + [H_2PO_5^-] + [HPO_5^{2-}] \tag{12}$$

The total analytical concentration of pyruvic acid, $[A]_t$, is given as

$$[A]_t = [A] + [A^-] \tag{13}$$

From Eqs. (1)-(3), and Eq. (12),

$$[H_3PO_5] = \frac{[\text{PMPA}]_t[H^+]^2}{[H^+]^2 + K_1[H^+] + K_1K_2} \tag{14}$$

$$[H_2PO_5^-] = \frac{K_1[\text{PMPA}]_t[H^+]}{[H^+]^2 + K_1[H^+] + K_1K_2} \tag{15}$$

$$[H_2PO_5^{2-}] = \frac{K_1K_2[\text{PMPA}]_t}{[H^+]^2 + K_1[H^+] + K_1K_2} \tag{16}$$

From the Eqs. (4) and (13) we have,

$$[A] = \frac{[A]_t[H^+]}{K_a + [H^+]} \tag{17}$$

and

$$[A^-] = \frac{K_a[A]_t}{K_a + [H^+]} \tag{18}$$

Using Eqs. (14)-(18) in Eq. (11) we get,

$$k_2' = \frac{k_1[H^+]^3 + k_2K_a[H^+]^2 + k_3K_1[H^+]^2 + k_4K_1K_a[H^+] + k_5K_1K_2[H^+] + k_6K_1K_2K_a}{([H^+]^2 + K_1[H^+] + K_1K_2)(K_a + [H^+])} \tag{19}$$

A least-squares analysis of the above expression resulted in the average values of the resolved parameters for the pyruvic acid reaction, k_1–k_6, which are tabulated in Table 3. These values were used to obtain $k_2'_{(\text{calcd.})}$ (Table 2). It is seen that the calculated and observed values showed agreement.

In the pH range 6.8-9.25, assuming the total benzoylformic acid (p*K*a=1.39)[9] to exist in the form of its anion, the steps for oxidation may be written as,

$$HPO_5^{2-} + OH^- \overset{K_4}{\rightleftharpoons} PO_5^{3-} + H_2O \tag{20}$$

$$HPO_5^{2-} + C_6H_5COCOO^- \xrightarrow{k_7} \text{Products} \tag{21}$$

$$PO_5^{3-} + C_6H_5COCOO^- \xrightarrow{k_8} \text{Products} \tag{22}$$

which lead to the rate law, Eq. (23)

$$\begin{aligned} \text{Rate} &= -\frac{d[\text{PMPA}]_t}{dt} \\ &= k_7\,[HPO_5^{2-}][C_6H_5COCOO^-] \\ &\quad + k_8\,[PO_5^{3-}][C_6H_5COCOO^-] \end{aligned} \tag{23}$$

$$= \left\{\frac{k_7K_h + k_8[OH^-]}{K_h + [OH^-]}\right\}[\text{PMPA}]_t\,[C_6H_5COCOO^-] \tag{24}$$

$$\text{where } [\text{PMPA}]_t = [HPO_5^{2-}] + [PO_5^{3-}] \tag{25}$$

$$\text{and } K_h = [H_2O]\,/\,K_4 \tag{26}$$

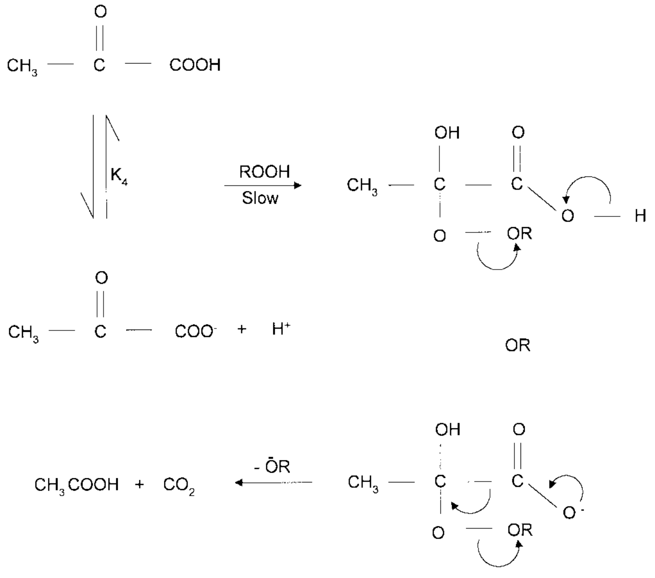
Eq. (24) can be rearranged to give Eq. (27)

$$k_2' = \left\{\frac{k_7K_h + k_8[OH^-]}{K_h + [OH^-]}\right\} \tag{27}$$

which has been used to calculate the rate constant $k_2'_{(\text{calcd.})}$ in Table 2. The K_h value for PMPA species was determined using the relationship $K_h = K_w/K_3$, where K_w is the ionic product of water and K_3 is the dissociation constant of HPO_5^{2-}. The average values of k_7 and k_8, as obtained by least-squares analysis of the data according to Eq. (27) are collected in Table 3. These values have been used to calculate $k_2'_{(\text{calcd.})}$. in Table 2.

Table 3. Average Values of the Computed Rate Constants for the Oxidation of Pyruvic Acid and Benzoylformic Acid by PMPA at 35 °C

Oxidant	Computed Rate Constant/L · mol^{-1} sec^{-1}		
	A ($CH_3COCOOH$)	A$^-$ (CH_3COCOO^-)	($C_6H_5COCOO^-$)
H_3PO_5	(k_1=) 0.0095	(k_2 =) 0.002	–
$H_2PO_5^-$	(k_3=) 0.31	(k_4 =) 0.003	–
HPO_5^{2-}	(k_5=) 48	(k_6 =) 0.280	(k_7 =) 0.005
PO_5^{3-}	–	–	(k_8 =) 4.5 × 10^3



Scheme 1

From an examination of the resolved rate constants (Table 3) corresponding to the individual reactivity of different PMPA species in pyruvic acid oxidation, it can be seen that the reactivity is more or less higher with the more nucleophilic PMPA species, thus suggesting the nucleophilic behaviour of PMPA in the oxidation. The nucleophilic behaviour of PMPA is quite in consonance with the earlier observations made in peroxide reactions.[10] The lower reactivity of pyruvic acid anion as compared to the neutral form might be due to reduced electrophilicity of the carbonyl-carbon in the anion.[11] The oxidation of pyruvic acid in the explored range of pH thus involves a rate-determining nucleophilic attack of the peroxo species on the carbonyl-carbon of the keto acid species. This is most probably followed by oxygen-oxygen bond fission in a rapid step leading to decarboxylation (Scheme 1).

The magnitude of relative reactivity of HPO_5^{2-} and PO_5^{3-} in benzoylformic acid oxidation in the pH range 6.8-9.25, also indicates this substrate to suffer nucleophilic attack by PMPA. Seigel and Lanphear,[4] in their study of oxidative decarboxylation of benzoylformic acid by hydrogen peroxide, have shown that at pH > 4, the nucleophilic attack of the peroxide is rate-determining. At low pH, however, a rate-determinating oxygen-oxygen bond cleavage was reported.

In the pH range 0-6.8, the pH rate profile for PMPA oxidation of benzoylformic acid seems to be different, when compared with the oxidations involving other peracids such as H_2O_2, peracetic acid and t-butylhydroperoxide.[4] The rate of oxidation remains totally insensitive to the variation of pH in the range 0-6.8 although there are three discernible PMPA species (*viz.* H_3PO_5, $H_2PO_5^-$ and HPO_5^{2-}) with varying degrees of concentration and nucleophilic reactivity. This observation can only mean that the observed rate of PMPA disappearance most probably corresponds to a rate-determining (*i.e.* irreversible) oxygen-oxygen bond cleavage in the pH range 0-7.

Experimental Section

PMPA solutions were prepared by acid hydrolysis of $K_4P_2O_8$. All other chemicals used were of AnalaR grade except pyruvic acid which was prepared by standard method reported.[12] Sodium perchlorate, prepared *in situ* by neutralising perchloric acid with carbonate-free sodium hydroxide, was used for adjusting ionic strength of the medium. All the solutions were prepared in doubly distilled water, the second distillation being from $KMnO_4$. Acidity of the solutions was maintained by adding calculated amounts of $HClO_4$ or standard buffers such as acetic acid-sodium acetate, sodium hydroxide-potassium hydrogen phthalate, KH_2PO_4-K_2HPO_4, Na_2CO_3-$NaHCO_3$. Measurements of pH were made on a Systronics digital pH meter 335.

Reactions were followed by measuring the rate of disappearance of PMPA which was estimated by iodometry at pH 4-5 with a drop of ammonium molybdate solution.[13] The observed second order rate constant (k_2' obs) was calculated by dividing pseudo-first-order rate constant (k_1') with respect to peroxy acid disappearance by the substrate concentration. The rate constants were reproducible to within ± 5%. The self decomposition of PMPA was found to be either nil or negligibly small under the experimental conditions. The temperature was constant to within ± 0.1 °C. Computations were done with a DCM micro system 1121.

Product Study. To a solution of PMPA (0.033 M) in water (50 mL) benzoylformic acid (3×10^{-3} mol) was added at pH $\simeq 8.0$. The mixture solution was allowed to stand over night at 35 °C, acidified with dil $HClO_4$, and then extracted with diethyl ether. The crude product was recrystallised from aqueous-ethanol and dried. The M.P. and M.M.P. of the compound corresponded to that of benzoic acid (M.P. 122 °C).

In the oxidation of pyruvic acid the product acetic acid was identified by colour reaction with a solution of sodium nitroprusside containing morpholine.[14]

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