Reactivity of Peroxomonophosphoric Acid in the Oxidation of Benzaldehydes and Dimethyl Sulfoxide in Aqueous Ethanol[1)]

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Oxidation of benzaldehydes and dimethyl sulfoxide with peroxomonophosphoric acid (PMPA) has been studied in 40% aqueous EtOH in order to examine the reactivity of undissociated and dissociated PMPA in comparison with that of peroxycarboxylic acid. The reactivity for DMSO was in the order $RCO_3^- > H_3PO_5 > H_2PO_5^- > RCO_3H > HPO_5^{2-}$. As in the peroxycarboxylic acid oxidation, PMPA oxidation of substituted benzaldehydes afforded phenols by aryl migration and benzoic acids by hydride migration. The product ratio changed with substituents and pH; salicylaldehyde (*o*-HO) gave only catechol by aryl migration, while *p*-chloro- and unsubstituted benzaldehydes afforded benzoic acids predominantly. The oxidation of aldehydes bearing *p*-MeO and *p*-Me was a borderline case and the migratory ratio of Ar~/H~ was higher at lower pH, *i.e.*, the order being $H_3PO_5 > H_2PO_5^- > HPO_5^{2-}$. The substituent effect in the apparent k_{obsd} values was very small (*i.e.*, $\rho \approx 0$), but the effect for aryl migration ($k_{\mathrm{Ar}\sim}$) estimated from product selectivity gave $\rho = -2.88$ (σ). The rate for hydride migration ($k_{\mathrm{H}\sim}$) resulted in $\rho = 1.7$ and 2.0 (σ). Reactivity of PMPA in each dissociated form was compared with that of RCO_3H.

Peroxomonophosphoric acid (PMPA) has been known for a long time,[2)] but its reactivity has not been clarified. Its decomposition[3)] and reactions with bromide[4)] and iodide ions[5)] were studied kinetically. Reports have been given on PMPA oxidation of organic substances, including the hydroxylation of aromatic rings,[6)] the Baeyer-Villiger(B-V) reaction of acetophenones,[7)] the epoxidation of *trans*-stilbene,[8)] and the oxidation of tertiary amines.[9)]

PMPA is a tribasic acid having three dissociated forms.[10)] We were interested in the reactivity of each form of PMPA as well as in their possibility as an oxidant with bifunctional catalysis since phosphoric acid is known as such a catalyst.[11)] The reaction of PMPA is also of interest from a biochemical standpoint, since PMPA might be produced by perhydrolysis of pyrophosphoric acids[12)] with oxygen species such as H_2O_2 or $O_2^{\overline{\cdot}}$.[13)] When we had almost completed our experiment a kinetic study on the PMPA oxidation of benzaldehydes was reported,[14)] the conclusion of which differing from ours.

Results and Discussion

Peroxomonophosphoric acid (PMPA) dissociates into three forms, affording $pK_1 = 1.1$, $pK_2 = 5.2$, and $pK_3 = 12.7$ in water.[10)] Oxidation of dimethyl sulfoxide

$$H_3PO_5 \overset{K_1}{\rightleftharpoons} H_2PO_5^- + H^+ \quad (1)$$

$$H_2PO_5^- \overset{K_2}{\rightleftharpoons} HPO_5^{2-} + H^+ \quad (2)$$

$$HPO_5^{2-} \overset{K_3}{\rightleftharpoons} PO_5^{3-} + H^+ \quad (3)$$

(DMSO) and benzaldehydes with PMPA was carried out in the presence of 0.4 mM EDTA in 40% aqueous ethanol at 25 °C. The decrease of PMPA was monitored by iodometric titration in 5% AcOH; its spontaneous decompositition was very slow in the absence of added substrates. Products were determined by GLC directly or after methylation with dimethyl sulfate for phenols or with diazomethane for carboxylic acids.

Oxidation of DMSO. Dimethyl sulfoxide was easily oxidized to sulfone in over 90% yield based on PMPA consumed. The oxidation follows the second-order rate equation (Eq. 4). The pH-rate profile

$$v = k_{\mathrm{obsd}}[\mathrm{PMPA}][\mathrm{Substrate}] \quad (4)$$

is shown in Fig. 1. The resulting second-order rate constant are 210, 45, and 1.2 $M^{-1}\,s^{-1}$ for H_3PO_5, $H_2PO_5^-$, and HPO_5^{2-}, respectively. The kinetically determined pK_1 and pK_2 values for PMPA in 40% EtOH are 1.6 and 4.6, respectively, close to the reported pK_a values 1.1 and 5.2, respectively, in water.[10)] The difference of *ca.* 0.5 might be partly due to the solvent effect on pK_a of PMPA.

The Baeyer-Villiger Oxidation of Benzaldehydes. Products. Products from the B-V oxidation of benzaldehydes with PMPA vary with substituents and pH (Table 1). Salicylaldehyde with strong electron-releasing *o*-HO afforded only catechol by aryl migration. The relatively low yields (*i.e.*, 65—75%) of catechol can be ascribed to further oxidation by PMPA. The other aldehydes resulted in the simultaneous formation of phenols by aryl migration and benzoic acids by hydride migration.

$$\mathrm{ArCHO} \xrightarrow{\mathrm{PMPA}} \begin{cases} \xrightarrow{\mathrm{Ar}\sim} \mathrm{ArOCHO} \xrightarrow{H_2O} \mathrm{ArOH} & (5a) \\ \xrightarrow{\mathrm{H}\sim} \mathrm{ArCO_2H} & (5b) \end{cases}$$

We see from Table 1 that the aryl migration is facilitated by an increase in electron-releasing power of ring substituents and by a decrease of pH. Higher pH and electron-attracting groups favor the hydride

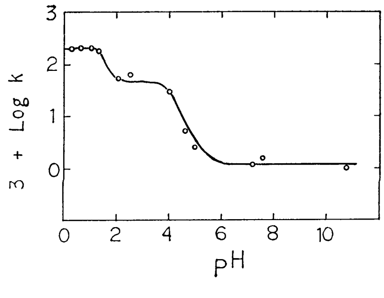


Fig. 1. The pH-rate profile for the PMPA oxidation of DMSO in 40% aqueous EtOH at 25 °C.

TABLE 1. PRODUCTS (%) FROM THE B-V REACTION OF SUBSTITUTED BENZALDEHYDES BY PMPA[a)]

Substituent	pH 1.3		pH 4.0		pH 7.3		pH 10	
	$ArCO_2H$	ArOH	$ArCO_2H$	ArOH	$ArCO_2H$	ArOH	$ArCO_2H$	ArOH
o-HO	0	65	0	72	0	75	0	73
p-MeO	0	74	2	78	7	45	23	21
p-Me	22	63	42	8	45	4	49	1
H	75	14	83	0	98	0	81	0
p-Cl	61	3	85	0	72	0.4	72	1

a) Reaction with 0.04 M each of H_3PO_5 and ArCHO in 40% EtOH at 25 °C. % Yields are based on the aldehyde consumed and determined by GLC after methylation with dimethyl sulfate for phenols or with diazomethane for carboxylic acids.

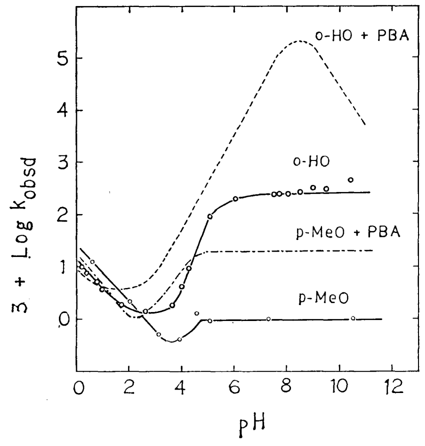
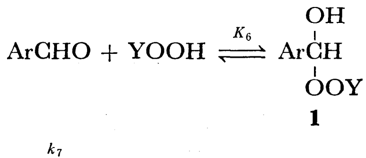


Fig. 2. pH-rate profiles for the PMPA oxidation of substituted benzaldehydes in 40% EtOH at 25.0 °C. The dotted lines are plots for perbenzoic acid (PBA) oxidation from Ref. 15. The solid line for *o*-HO is calculated according to the rate data in Table 3.

migration leading to carboxylic acids. The trend is similar to that of the B-V oxidation with perbenzoic acid (PBA).[15)]

Mechanism. In case of the PBA oxidation of salicylaldehyde the rate-determining step is the addition of PBA to C=O.[15)] Since the pK_a values of the aldehydes and PBA are 8.45 and 8.5, respectively, in 40% EtOH,[15)] the pH-rate profile gives a bell-shaped curve (dotted line, Fig. 2). The oxidation with PMPA afforded a similar profile (Fig. 2); the observed slopes of *ca.* −0.5 at pH<2 suggest an acid-catalysis, while horizontal lines at pH 5—10 indicate no catalysis by H^+ or HO^-. If the addition of PMPA to C=O were rate-limiting, the rate should slow down at pH above 9 on the basis of the dissociation of salicylaldehyde, which was not the case. This is in contrast to the PBA case, suggesting that the addition to C=O is not rate-determining. The rate is determined by the migration step (Eq. 7). Here, YOOH



$$\mathrm{ArCHO} + \mathrm{YOOH} \overset{K_6}{\rightleftharpoons} \mathrm{Ar}\overset{\overset{\displaystyle\mathrm{OH}}{|}}{\underset{\underset{\displaystyle\mathrm{OOY}}{|}}{\mathrm{C}}}\mathrm{H} \quad (6)$$

1

$$\mathbf{1} \xrightarrow{k_7} \text{Products} + \mathrm{YOH} \quad (7)$$

is H_3PO_5, $H_2PO_5^-$, or HPO_5^{2-}. In the neutral region, the most prevalent species is $H_2PO_5^-$, so that the departing group YOH from **1** is $H_2PO_4^-$ (pK_a=7.2), which is significantly less potent as a departing group than benzoic acid (pK_a=4.2) in the PBA oxidation. The rate of rearrangement of **1** (*i.e.*, k_7) is then substantially lowered, leading to the establishment of preequilibrium 6 for the PMPA case.

The PMPA oxidation of *p*-anisaldehyde (*p*-MeO) is substantially slower than that of salicylaldehyde at pH>3, but slightly faster at pH<2 (Fig. 2). The rates for the other aldehydes are similar to that of anisaldehyde, the k_{obsd} values not varying with substituent, *i.e.*, $\rho \approx 0$ (Table 2-A). It can be assumed that the ρ value for K_6 is close to the ρ value of 1.6

TABLE 2. SUBSTITUENT EFFECT ON THE B-V REACTION OF BENZALDEHYDES WITH PMPA IN 40% EtOH AT 25.0 °C[a)]

Substituent	$10^3 k/M^{-1} s^{-1}$			
	pH 1.3	pH 4	pH 7.3	pH 10
A) Observed second-order rate constant (k_{obsd})[b)]				
p-MeO	13.9 (2.1)[c)]	0.43 (9)[c)]	1.08 (13)[c)]	0.93 (13)[c)]
p-Me	8.6	0.35	0.49	0.98
H	8.0	0.39	0.45	1.17
p-Cl	10.1 (4.4)[c)]	0.98 (14)[c)]	1.22 (18)[c)]	0.97 (220)[c)]
B) Rates for aryl migration ($k_{Ar\sim}$)[d)]				
p-MeO	10.3	0.33	0.49	0.19
p-Me	5.4	0.028	0.020	0.014
H	1.2	0	≈0	≈0
p-Cl	0.27	0	0.004	0.01
ρ (*vs.* σ)	−2.88	[e)]	[e)]	[e)]
C) Rates for hydride migration ($k_{H\sim}$)[d)]				
p-MeO	0	0.010	0.075	0.22
p-Me	1.9	0.15	0.22	0.48
H	5.9	0.33	0.44	0.95
p-Cl	6.2	0.83	0.87	0.70
ρ (*vs.* σ)	[e)]	1.74	*ca.* 2.0	[e)]

a) Reaction with 0.01—0.05 M each of benzaldehyde and PMPA. b) Observed rate constant determined iodometrically. c) For comparison, the k_{obsd} values for PBA (Ref. 17) are shown in parentheses. d) Rate constants for aryl or hydride migration obtained by dividing k_{obsd} values by product selectivities in Table 1. e) Numbers of data were too small, the correlation being poor.

TABLE 3. COMPARISON OF THE REACTIVITIES OF PMPA AND PEROXYCARBOXYLIC ACID TOWARD VARIOUS SUBSTRATES

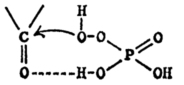
Oxidant YOOH	pK_a of YOH[b]	Second-order rate constant, $10^3\,k/\mathrm{M^{-1}\,s^{-1}}$[a]					
		I^-[c]	Br^-[d]	Stilbene[e]	DMSO	o-HOC_6H_4CHO	PhCOMe[f]
Mechanism[g]		one	one	one	one	two	two
Solvent		H_2O	H_2O	dioxane	40% EtOH	40% EtOH	MeCN
H_3PO_5	2.1	2×10^6	8×10^3	0.11	210	≈ 1[h]	2.9
$H_2PO_5^-$	7.2	6×10^4	32		45	≈ 1	
HPO_5^{2-}	12.7	4×10^2			1.2	230	
$PhCO_3H$	4.2	3×10^6	3×10^2	0.20[i]	26	5	0.015[i]
$PhCO_3^-$					(330)[j]	1×10^6	

a) Rate constant at 25 °C. b) The pK_a of parent acid in water. c) Ref. 5. d) J. O. Edwards, "Peroxide Reaction Mechanism," Interscience, New York (1962), p. 73. e) Ref. 8. f) Ref. 7. g) One: one-step electrophilic oxidation. Two: two-step reaction involving an addition and a rearrangement step. h) Rate constant for the acid catalysis at pH<1 is $k_H=9\times10^{-3}\ \mathrm{M^{-2}\,s^{-1}}$, obtained from a rate equation: $v=k_H[HClO_4][\text{aldehyde}]\times[\text{PMPA}]$. i) Peracetic acid. j) Nucleophilic oxidation of sulfoxide *via* two-step reaction.

(σ) for the H_2O_2 addition (Y=H, Eq. 6).[15] The apparent zero value of ρ for k_{obsd} might be due to the cancellation, since $k_{obsd}=k_7K_6$, between a positive ρ value for K_6 and a negative ρ value for k_7. Negative ρ values for aryl and hydride migration are well known.[15–17] Such a cancellation is often observed in reactions involving carbonyl addition.[18]

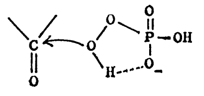
A mechanism was postulated for the PMPA oxidation of benzaldehydes, which involves a rate-determining attack of PMPA on benzaldehyde hydrates, $ArCH(OH)_2$.[14] However, the scheme is questionable. (i) No reaction is known in which the nucleophilic attack on tetrahedral carbons such as aldehyde hydrate is much faster than that on free aldehyde ArCHO. (ii) Benzaldehydes exist essentially as free aldehydes ArCHO under these conditions of aqueous EtOH; an exception is p-nitrobenzaldehyde, where 20% of the aldehyde exists as its hydrated form.[19] Likewise, the addition equilibrium of HO^- instead of H_2O shifts to the free ArCHO rather than to the adduct $ArCH(OH)O^-$ at pH<14.[20] Thus the C=O addition scheme is favorable, since both concentration and reactivity of the free aldehydes are much higher than those of the hydrates.

Polybasic acids such as phosphoric acid are sometimes effective as a bifunctional catalyst.[11] We intended to examine such a possibility in the addition to C=O, *e.g.*, an intermolecular acid-catalysis (**2a**) or an intramolecular base-catalysis (**2b**). However,



2a

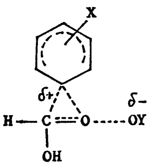
or



2b

the addition to C=O was not rate-determining even in the case of salicylaldehyde with the most facile migratory aptitude; no such catalysis could be examined.

Aryl and Hydride Migration. Although the k_{obsd} values in Table 2-A are little affected by substituents (*i.e.*, $\rho\approx0$), interesting results for the relative migratory aptitudes were obtained by multiplying the k_{obsd} values by products selectivities in Table 1. The aryl migration ($k_{Ar\sim}$) at pH 1.3 affords $\rho=-2.88$ (σ) (Table 2-B). Similar results ($\rho=-2.55$ *vs.* σ) are known for the PMPA oxidation of acetophenones.[7] These correlations are in contrast to the σ^+ correlation for the B-V reaction with PBA.[15,16] The difference might be due to the fact that in the rearrangement of **1** at pH<2 the departing phosphoric acid (pK_a= 2.1) is a much stronger acid than benzoic acid (pK_a= 4.2). The loosening of O–O bond in the PMPA oxidation is relatively weak, and hence the developing cationic charge (δ^+) in **3** is much lower than in the PBA case. The interpretation seems to be in line with the observed high rate ratios of p-MeO/p-Me for the reaction at pH 4 (*i.e.*, $H_2PO_5^-$) and pH 7 or 10 (*i.e.*, HPO_5^{2-}), suggesting a σ^+ correlation. Since $H_2PO_4^-$ (pK_a=7.2) and HPO_4^{2-} (pK_a=12.7) are much less potent departing groups as compared with H_3PO_4, the cationic charge in **3** increases leading to the σ^+ correlation at pH>4. High rate ratios of p-MeO/p-Me correspond to a σ^+ correlation, small ratios giving rise to σ correlation.



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On the other hand, Hammett's equation for the hydride shift gives $\rho=1.74$ (pH 4) and 2.0 (pH 7.3) with σ correlation (Table 2-C). The same reaction with PMPA in the presence of 0.2 M NaOH gives a ρ value 1.27 (σ) in water.[14] These ρ values are close to 1.6 (σ) for the addition equilibrium of H_2O_2 (Eq. 6).[15] Since $k_{obsd}=k_7K_6$, the net ρ value for the hydride shift (*i.e.*, k_7) might be close to zero. Similar ρ values of 1.1—1.8 were obtained at pH 1—12 in the PBA oxidation of benzaldehydes affording hydride shift,[17] which is rather insensitive to acid and base catalysis.[15] The same might be the case for the PMPA oxidation.

Comparison with Peroxycarboxylic Acid. The reactivity of PMPA was compared with that of peroxycarboxylic acids (Table 3). In one-step electrophilic oxidation, relative reactivities of PMPA and RCO_3H change with substrate. For example, the relative reactivity in the oxidation of bromide ion differs from the corresponding order for iodide ion. The rate order for olefin epoxidation is $RCO_3H \gtrsim H_3PO_5$,[8] that for the oxidation of DMSO, $H_3PO_5 > H_2PO_5^- > RCO_3H > HPO_5^{2-}$. The DMSO oxidation with RCO_3^- is of a different mechanism and excluded from the comparison; the alkaline reaction involves two steps, a nucleophilic addition to sulfoxide and its decomposition to sulfone and carboxylate ion,[21] just as the B-V reaction.

The relative reactivity for the B-V reaction also changes with substrates and pH (Fig. 2, Table 2-A, and Table 3). The rate order for the B-V reaction of benzaldehydes at pH 3—10 is $RCO_3H > PMPA$, but changes to the order $PMPA > RCO_3H$ at the lower pH. This is due to the higher sensitivity of PMPA to acid-catalysis as compared with that of RCO_3H.

Experimental

GLC analysis was performed with a Yanagimoto 550F gas chromatograph using a column of PEG 20 M on Chromosorb (1 m).

Materials. Peroxomonophosphoric acid (PMPA) was prepared from P_2O_5 and 90% H_2O_2.[9] Commercial benzaldehydes were used.

Typical Procedure. The reaction with 0.04 M each of PMPA and benzaldehyde was carried out in 40 vol% EtOH at 25.0 °C. EDTA (0.4 mM) was added to minimize a metallic ion-catalyzed decomposition of PMPA. The pH of solution was maintained with perchloric acid ($pH < 1$), 0.5 M acetate (pH 2.5—4.4), 0.5 M phosphate (pH 3.7—6.1), and 0.5 M carbonate buffers (pH 7.5—10). The pH values were determined with a glass electrode before and after the reaction. The decrease of PMPA was monitored by iodometric titration in 5% aqueous AcOH. The spontaneous decomposition of PMPA was very slow in the absence of substrate added. Reproducibility of the oxidation kinetics was ascertained to be adequate (*i.e.*, within ±5%).

Reaction products were determined by means of GLC directly or after methylation with diazomethane using biphenyl or propiophenone as an internal standard. Catechol was determined after methylation with dimethyl sulfate.

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