The Kinetics of the Phosphate-catalyzed Epoxidation of Styrenes with a Mixture of Nitrile and Hydrogen Peroxide*

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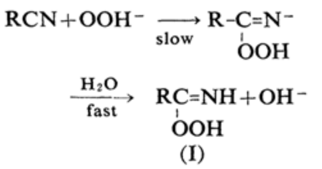
The reaction of benzonitrile with alkaline hydrogen peroxide has been found to proceed by way of peroxycarboimidic acid (I) :[1]



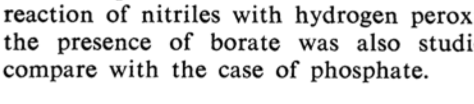
$$RCN+OOH^- \xrightarrow[slow]{} R\text{-}\underset{\displaystyle OOH}{C}{=}N^- \xrightarrow[fast]{H_2O} R\underset{\displaystyle OOH}{C}{=}NH+OH^- \qquad (1)$$

(I)

$$(I)+H_2O_2 \xrightarrow[fast]{} RCONH_2+O_2+H_2O \qquad (2)$$

Peroxycarboimidic acid can oxidize such other substrates as olefins,[2] and it is a favorable oxidant which acts under milder and alkaline conditions and avoids the Baeyer-Villiger reaction,[3] although the oxidation must be done under the controlled pH value (ca. 8).

The present authors have discovered that an aqueous methanolic mixture of nitriles and hydrogen peroxide can oxidize styrene in the presence of alkaline phosphate, giving a high yield (above 95%) of epoxide according to this stoichiometric equation[4]:



$$RCN+H_2O_2+C_6H_5CH{=}CH_2 \xrightarrow{HPO_4{}^{2-}} RCONH_2+C_6H_5\underbrace{CH\text{-}CH_2}_{O} \qquad (3)$$

The present paper summarizes the kinetic data which treats the effect of basicity of the reaction media and of substituent effects in benzonitrile and styrene. A probable mechanism is postulated from these data. The reaction of nitriles with hydrogen peroxide in the presence of borate was also studied to compare with the case of phosphate.

Experimental

Materials.—Commercial benzonitrile, acetonitrile and styrene were purified by fractional distillations, b. p. 190°C, 83°C and 58°C (35 mmHg), respectively. Substituted benzonitriles were synthesized from the corresponding anilines :[5] *p*-tolunitrile, b. p. 107—110°C (23 mmHg) ; *p*-anisnitrile was recrystallized from ethanol, m. p. 60°C ; *p*-chloro- and *p*-nitrobenzonitrile were purified by recrystallization from ethanol, m. p. 93°C and 140°C, respectively. Substituted styrenes were prepared by the dehydration of phenylmethylcarbinols[6] obtained from the corresponding acetophenones[7] : *p*-chlorostyrene, b. p. 54—55°C (3 mmHg) ; *p*-methylstyrene, b. p. 43—44 (5 mmHg) ; *m*-nitrostyrene, b. p. 100—103°C (5 mmHg).

Hydrogen peroxide, phosphate and other inorganic reagents were all of guaranteed grade. Commercial methanol was used without further purification, since no appreciable difference in the rates was found between purified methanol and the commercial one.

The Analytical Method.—Hydrogen peroxide was analyzed iodometrically, 10 ml. of a reaction mixture was added to 30 ml. of ca. 0.1 N aqueous sulfuric acid containing 0.2—0.3 g. of potassium iodide, and the mixture was titrated with 0.1 N aqueous sodium thiosulfate immediately after the addition of three drops of a 1% sodium molybdate solution, thus avoiding the reaction of iodine with styrene. Neither nitriles nor styrenes interfered with the analysis.

The concentration of styrene oxide produced was determined by adding a 10 ml. aliquot to aqueous saturated sodium chloride (40 ml.) in a separatory funnel, extracting it with three 10 ml. portions of chloroform. The organic layer was washed three times with water and dried with anhydrous sodium sulfate. Then the oxirane oxygen content was determined by the pyridinium chloride-chloroform method.[8] This method gave 90.0±1.0% of the recovery of styrene oxide and was not interfered with the presence of nitriles and styrene. The estimation of styrene oxide was corrected by the above value.

A Typical Procedure for Rate Measurement.—A 75% (v/v) methanolic solution containing nitrile and styrene of a known concentration was buffered by the addition of potassium dihydrogen phosphate-sodium hydroxide and then thermostated in a brown flask. The epoxidation was started by adding a thermostated solution of hydrogen peroxide of the desired concentration. Aliquots were taken out at appropriate intervals, and the remaining

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* Contribution No. 62.

[1] K. B. Wiberg, *J. Am. Chem. Soc.*, 75, 3961 (1953).

[2] G. B. Payne, P. H. Deming and P. H. Williams, *J. Org. Chem.*, 26, 659 (1961).

[3] G. B. Payne, *Tetrahedron*, 18, 763 (1962).

[4] Y. Ogata and Y. Sawaki, ibid., 20, 2063 (1964).

[5] H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, 514 (1948).

[6] C. G. Overberger and J. H. Saunders, ibid., Coll. Vol. II, 204 (1948).

[7] Y. Ishii and Y. Inamoto, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), 63, 765 (1960).

[8] J. L. Jungnickel, E. D. Peters, A. Polgár and F. T. Weiss, "Organic Analysis," Vol. I, Interscience Publisher, New York, N. Y. (1953), p. 136.

hydrogen peroxide was estimated as has been described above. The oxirane content was also determined, if it was necessary. Most reactions were carried out to 40—50% conversion, and the constancy of rate constants was confirmed up to 80% conversion.

The decomposition of hydrogen peroxide itself was not appreciable, and its consumption in the presence of nitrile alone was so small that it was negligible in the calculation of the rate constants.

TABLE I. A TYPICAL THIRD-ORDER RATE CONSTANT FOR THE PHOSPHATE-CATALYZED EPOXIDATION IN 75% METHANOL AT 40°C

Initial concn., $[C_6H_5CN]=[H_2O_2]=0.100$ M ; $[C_6H_5CH{=}CH_2]=0.200$ M ;

Buffer, KH_2PO_4-NaOH (4 : 5), pH=11.35

Time min.	Conversion of H_2O_2, %	$k_4\times10^3$ $l^2\,mol^{-2}\,sec^{-1}$
45	15.2	3.54
130	33.2	3.54
180	41.1	3.51
240	47.3	3.65
330	54.2	3.60
420	60.0	3.69
540	65.2	3.61

Results

Rate Law.—The rate of the epoxidation of styrene with nitrile and alkaline hydrogen peroxide catalyzed by phosphate in 75% methanol were determined by estimating the disappearence of hydrogen peroxide. The results of a typical kinetic run shown in Table I clearly indicate that the reaction is of third-order:

$$v=k_4[RCN][H_2O_2][C_6H_5CH{=}CH_2] \qquad (4)$$

These third-order kinetics are satisfactory with various initial concentrations of reactants or phosphate (Table II-A). The slight decrease in the rate with increasing concentration of styrene may be attributed to the decrease in the polarity of the reaction mixture, as will be described below.

The Effect of pH.—The effect of pH on the rate was examined by changing the composition of the phosphate buffer (Table II-B). The rate of epoxidation increased only a little with the increasing pH except at pH values below 10, which is rather surprising if it is remembered that log *k* linearly increased with the pH value in the reaction of benzonitrile with hydrogen peroxide.¹⁾ Although a small amount of hydrogen peroxide was consumed in the absence of styrene, the yields of styrene oxide based on the peroxide consumed were essentially the same (93—96%) in each pH examined.

The Effect of the Polarity of Solvent.—The rate of epoxidation was affected by the composition of the solvent (Table II-C). The higher water content in the reaction mixture tended to increase the rate. Compare methanolic solvents with 15% and 35% water. Hence, the slight decrease of rate with increasing initial concentration of styrene may be attributed to the decrease in the polarity of the reaction mixture. The addition of toluene also resulted in the same decrease in the rate.

Substituent Effect.—Substituent effects are shown in Table III-A and Fig. 1. The introduction of electron-attracting groups in benzonitrile increases the rate, the Hammett's ρ-value being 0.57, while substituents in styrene exhibit the reverse effect, giving a ρ-value of -0.51. These results suggest an electrophilic attack of the peroxycarboimidic acid intermediate.

For purposes of comparison, the reaction of substituted benzonitrile with alkaline hydrogen peroxide was also studied in the presence of borate (Table III-B and Fig. 1); the resulting ρ-value of 1.14 in 75% methanol is somewhat smaller than that obtained in 50% acetone.⁹⁾ This ρ-value is about two times greater than that in the phosphate-catalyzed epoxidation of

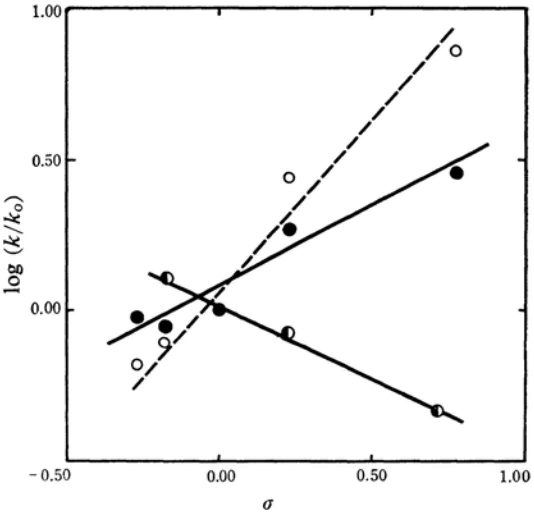

Fig. 1. Plots of logarithm of rate constants for the epoxidation of styrenes with benzonitriles and hydrogen peroxide in phosphate buffer at 40°C versus σ (Hammett and Jaffé) :

—●— Epoxidation of styrene with substituted benzonitriles

—◐— Epoxidation of substituted styrenes with benzonitrile

---○--- Reaction of substituted benzonitriles with hydrogen peroxide in borate buffer

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9) K. B. Wiberg, *J. Am. Chem. Soc.*, **77**, 2519 (1955).

TABLE II. PHOSPHATE-CATALYZED EPOXIDATION OF STYRENE WITH A MIXTURE OF NITRILE AND ALKALINE HYDROGEN PEROXIDE IN 75% (v/v) METHANOL BUFFERED WITH KH_2PO_4-NaOH AT 40°C

A) Effect of the initial concentration of reactants. Buffer solution: 0.2 M KH_2PO_4 - 0.2 N NaOH (4 : 5), pH = 11.35

[RCN] M	$[H_2O_2]$ M	$[C_6H_5CH{=}CH_2]$ M	Buffer soln.[a] ml.	$k_4 \times 10^3$ $M^{-2}\,sec^{-1}$
Benzonitrile				
0.100	0.100	0.100	15	4.01
0.100	0.150	0.100	15	4.00
0.200	0.100	0.100	15	4.13
0.100	0.100	0.200	15	3.59
0.100	0.100	0.300	15	3.25
0.100	0.100	0.100	10	3.90
0.100	0.100	0.100	20	4.15
Acetonitrile				
0.100	0.100	0.100	15	1.21
0.200	0.100	0.100	15	1.15
0.300	0.150	0.150	15	0.94
0.150	0.150	0.150	15	0.98

B) Effect of pH. Initial concn.; $[C_6H_5CN] = [H_2O_2] = [C_6H_5CH{=}CH_2] = 0.100$ M, [buffer soln.] = 15 ml.[a]

Buffer No.	0.2 M KH_2PO_4 - 0.2 N NaOH	pH (glass electrode)	at $t = 5$ hr. Conversion %	at $t = 5$ hr. Consumption of H_2O_2 without styrene %	$k_4 \times 10^3$ $M^{-2}\,sec^{-1}$
1	4 : 3	9.34	23.6	0.10	1.88
2	4 : 4	10.40	32.6	0.35	3.40
3	4 : 5	11.35	37.4	0.70	4.01
4	4 : 6	11.80	38.9	1.34	4.17
5	4 : 8	12.00	40.7	2.90	4.48

C) Effect of the solvent composition. Initial concentration is same as that in buffer 3 in B.

Solvent, vol. %			Added toluene M	$k_4 \times 10^3$ $M^{-2}\,sec^{-1}$
Methanol	Ethanol	Water		
75	0	25	0	4.01
75	0	25	0.1	3.78
75	0	25	0.2	3.61
55	20	25	0	3.48
45	30	25	0	3.40
85	0	15	0	2.65
65	0	35	0	6.00

a) Volume per 200 ml. of reaction solution.

styrene with a mixture of substituted benzonitriles and alkaline hydrogen peroxide. The energies and entropies of activation also substantially differ between these two reactions, 1 and 3.

Discussion

The reaction of nitrile with alkaline hydrogen peroxide[10] ($RCN + 2H_2O_2 \rightarrow RCONH_2 + O_2 + H_2O$, Radziszewski's reaction) is suppressed by the presence of phosphate, yielding styrene oxide almost quantitatively on addition of styrene.[4] Our results may be summarized as follows: (1) The phosphate-catalyzed epoxidation of styrene with nitrile and alkaline hydrogen peroxide follows third-order kinetics, being first-order in each reactant. (2) The rate of epoxidation is essentially constant at various pH's, while the rate increases with the increasing polarity of the reaction mixture. (3) Electron-attracting substituents on the

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[10] B. Radziszewski, *Ber.*, **17**, 1389 (1884).

TABLE III. SUBSTITUENT EFFECTS IN BENZONITRILES AND STYRENES IN 75% METHANOLIC BUFFERS

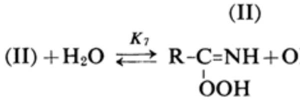
Substituent		Temp., °C			E_a, kcal. mol^{-1}	ΔS (40°C) e. u.
Benzonitrile	Styrene	30.0	40.0	50.0		
A) Third-order rate constant (M^{-2} sec^{-1}) for the epoxidation in phosphate buffer (pH=11.35)[a]						
p-CH_3O	H	2.49	3.78	5.72	8.1	−44
p-CH_3	H	2.37	3.47	4.51	6.3	−46
H	H	3.24	4.01	4.97	4.1	−56
p-Cl	H	5.16	7.33	9.60	6.0	−49
p-NO_2	H	—	11.3	—	—	—
H	p-CH_3	4.10	5.28	6.84	5.0	−53
H	p-Cl	2.55	3.34	4.23	4.9	−54
H	m-NO_2	1.26	1.83	2.60	7.5	−48
CH_3CN[b]	H	0.60	0.94	1.39	8.2	−46
B) Second-order rate constants (M^{-1} sec^{-1}) for the reaction of benzonitriles with hydrogen peroxide in borate buffer (pH=9.02)[c]						
p-CH_3O	none	—	1.28	—	—	—
p-CH_3	none	—	1.52	—	—	—
H	none	0.763	1.95	4.61	17.5	−19.8
p-Cl	none	—	5.45	—	—	—
p-NO_2	none	—	14.2	—	—	—
CH_3CN[b]	none	—	—	0.264	—	—

a) $v=k_4\,[RCN][H_2O_2][C_6H_5CH{=}CH_2]$; initial concn. : $[RCN]=[H_2O_2]=[C_6H_5CH{=}CH_2]=0.100$ M
b) Acetonitrile instead of benzonitrile
c) $v=k[RCN][H_2O_2]$; initial concn. : $[RCN]=[H_2O_2]=0.100$ M

benzonitrile accelerate the rate of epoxidation to give a Hammett's ρ-value of 0.57, while the Radziszewski's reaction results in the ρ-value of 1.14. (4) Electron-releasing groups in the styrene accelerate the rate, exhibiting a negative ρ-value of -0.51. (5) The energy of activation is low and the entropy of activation is highly negative, while with the Radziszewski's reaction the former is higher and the latter is less negative.

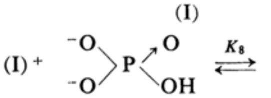
Reaction Scheme.—The kinetic data show that nitrile, hydrogen peroxide and styrene are involved in the transition state, while the phosphate catalysis suggests that the oxidizing intermediate stabilized by phosphate dianion is effective for an electrophilic attack on olefin. These results agree with the following mechanism:

$$H_2O_2+OH^- \overset{K_5}{\rightleftarrows} HO_2^-+H_2O \qquad (5)$$



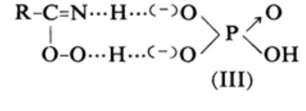
$$RCN+HO_2^- \overset{K_6}{\rightleftarrows} R\text{-}\underset{\underset{OOH}{|}}{C}{=}N^- \qquad (6)$$

(II)



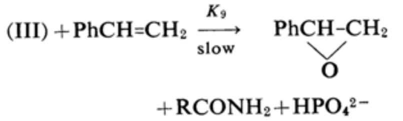
$$(II)+H_2O \overset{K_7}{\rightleftarrows} R\text{-}\underset{\underset{OOH}{|}}{C}{=}NH+OH^- \qquad (7)$$

(I)



(8)

(III)



$$(III)+PhCH{=}CH_2 \xrightarrow[\text{slow}]{K_9} PhCH\text{-}CH_2\ (\text{O}) +RCONH_2+HPO_4^{2-} \qquad (9)$$

Assuming that the concentrations of I and II are both very low and that equilibrium 8 is mobile and very favorable to the right side, the concentration of III may be expressed as:

$$\begin{aligned}[III] &\cong \frac{K_7[II][H_2O]}{[OH^-]}\\ &\cong \frac{K_6K_7[H_2O][RCN]_s[HO_2^-]}{[OH^-]}\\ &\cong K_5K_6K_7[RCN]_s[H_2O_2]_s\end{aligned}$$

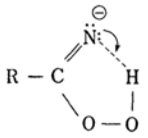
Here, k and K are the rate and equilibrium constants of the subscripted steps, respectively, and $[\ \ ]_s$ represents its stoichiometric concentration. Hence, the rate equation is:

$$\begin{aligned}v &= k_9[III][PhCH{=}CH_2]\\ &= k_9K_5K_6K_7[RCN]_s[H_2O_2]_s[PhCH{=}CH_2]_s\end{aligned} \qquad (10)$$

Rate Eq. 10 is consistent with the observed third-order kinetics and also with the independence of the rate on the hydroxide ion concentration (pH).

The mechanism assumes that II is not so active as to epoxidize styrene and that I is rapidly stabilized by phosphate to prohibit the reaction with hydrogen peroxide.

Active Epoxidizing Species.—Phosphoric acid should exist exclusively in the form of dianion, HPO_4^{2-}, in these pH's in view of the dissociation constant. The interaction of the dianion with the intermediate anion II is less probable because of the electrostatic repulsion. While the intermediate I may easily form with the nucleophilic phosphate dianion, the intermediate III is so deactivated as to fail to oxidize hydrogen peroxide. The epoxidizing species is thought to be stabilized by the electron-releasing interaction of the phosphate dianion.



(II′)

The intermediate anion, II, presumably has a chelate structure II′, resembling that of peroxyacid,[11-13] where the electrophilicity of the oxygen atom is increased by internal hydrogen bonding. However, the electophilicity of peroxide oxygen should be greatly decreased with the anion II′ by the presence of a negative charge. Although the intramolecular activation of II′ by hydrogen bonding may actually exist, this effect would not surpass the electron-releasing power of the imide anion, since hydrogen bonding may contribute much less than does the inductive effect.

When boric acid was added to the phosphate buffer, the Radziszewski's reaction[10] occurred in spite of the presence of an exess of phosphate and the rate increased with increasing amount of the added acid, although the pH's of the reaction mixture decreased.[4] This promotion of the Radziszewski's reaction by boric acid is probably due to the ability of the acid to combine with the unshared electron pair of the nitrogen atom, decreasing the electron density on the peroxide oxygen atom.

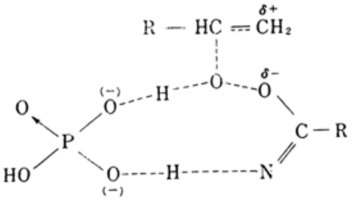
Substituent Effects.—The substituent effects on both benzonitrile and styrene imply an electrophilic attack of III on the doubly-bound carbon atoms. The same effects have been observed with the peroxybenzoic acid epoxidaion of olefins.[14] The Hammett's ρ-value for the epoxidation with substituted benzonitriles is about one-half of that for the Radziszewski's reaction, indicating a lower sensitivity to the polar effect. This lower value of ρ can be well understood by considering the effect on equilibrium 7 reverse to that on equilibrium 6, thus leading to the decrease in total ρ-value.

The Hammett's plot for epoxidation with substituted benzonitriles in Fig. 1 shows a little departure from linearity especially for the *p*-methoxy group, while the plot for the Radziszewski's reaction is more satisfactory. The deviation of the former plot may be attributed to the overestimation of the resonance effect, since II should be less resonance-stabilized than the benzoate anion; hence, the above deviation is conceivable.

As for the epoxidation of substituted styrenes, the Hammett's plot is much more satisfactory, but it has a slight deviation as to *p*-substituents. According to the correction for σ-value using the γ parameter,[15] $\sigma=\sigma+\gamma\times\Delta_{\sigma R}$, the value for ρ(meta) is calculated to be -0.48 from the rates for unsubstituted and *m*-nitrostyrene and the γ's are 0.62 for *p*-methyl- and 0.59 for *p*-chlorostyrene. The γ-value of 0.61 (average) is similar to 0.48 for the perbenzoic acid epoxidation of styrenes,[7] suggesting a similar resonance effect in the transition state.

The Approach of the Reagent to Substrate.—The rate of epoxidation increased in solvents with higher dielectric constants, which seems to mean that an increase of polarity may increase the degree of dissociation of III, resulting in the regeneration of the stronger oxidant (I). This was confirmed by the fact that the reaction rate of benzonitrile with hydrogen peroxide alone increased with the increasing water content of methanol.[4]

Considering the above discussion, the transition state may be expressed as IV:



(IV)

As is to be expected, IV, a highly-crowded transition state, would require a highly negative entropy of activation, reflecting the hindered motion of each reactant. Thus, the present reaction is considered to be slowed down by the highly negative entropy of activation in spite of the low energy of activation. The less negative entropy of activation for the Radziszewski's reaction can be well explained by the less crowded transition state containing

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[11] B. M. Lynch and K. H. Pausacker, *J. Chem. Soc.*, **1955**, 1525.

[12] T. W. Findley, D. Swern and J. T. Scanlan, *J. Am. Chem. Soc.*, **67**, 412 (1945).

[13] G. J. Minkoff, *Proc. Roy. Soc.*, **A224**, 176 (1954).

[14] D. Swern, *Chem. Revs.*, **45**, 1 (1949); "Organic Reactions," Vol. 7, John Wiley & Sons, New York, N. Y. (1953), p. 378.

[15] Y. Yukawa and Y. Tsuno, This Bulletin, **32**, 971 (1959).

only two species, e. g., nitrile and hydroperoxide ion.

Summary

The phosphate-catalyzed epoxidation of styrenes with a mixture of nitriles and alkaline hydrogen peroxide have been studied kinetically in 75% methanol. The reactions satisfy third-order kinetics, being first-order in nitrile, hydrogen peroxide and styrene. The rate is essentially constant at various pH's, while it increases with the increasing polarity of the reaction medium. The energy of activation is low (6—8 kcal. mol^{-1}), and the entropy of activation is highly negative (-50 e. u.). The effect of substituent in benzonitrile is to give a Hammett's ρ-value of 0.57, while that in styrene resulted in a negative ρ-value of -0.51. It is probable that the peroxycarbimidic acid (I), produced by mobile equilibria from nitrile and hydroperoxide ion, is stabilized by an intermolecular hydrogen bonding with the phosphate dianion, and that this species contributes mostly to the epoxidation of styrene in the following, rate-determining step.

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