Mechanism of the Reaction of Nitriles with Alkaline Hydrogen Peroxide. Reactivity of Peroxycarboximidic Acid and Application to Superoxide Ion Reaction[1]

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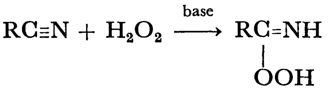
Formation of peroxycarboximidic acid (**1**) is not rate-determining in the reaction of nitrile with alkaline hydrogen peroxide to form amide and oxygen; the yield of amide based on H_2O_2 varies from 20 to 60%. When dimethyl sulfoxide (DMSO), a reactive substrate, is added, the rate is independent of [DMSO] and governed in turn by a rate-determining addition of HOO^- to nitrile. This reaction gives a reliable α-value of k_{HOO^-}/k_{HO^-}, which is 10000 for benzonitrile. A facile conversion of nitrile to amide may be achieved by the reaction in the presence of DMSO, unaccompanied by side reactions such as the epoxyamide formation from α,β-unsaturated nitrile. Kinetics and product analysis suggest that a predominant reaction is not a non-radical oxidation of H_2O_2 with **1** but a radical decomposition of H_2O_2 which is induced by the homolysis of anion of **1** (**1A**). No singlet oxygen could be trapped chemically. The reaction of superoxide ion, $O_2^{\overline{\cdot}}$, with acetonitrile is shown to be analogous to that of HOO^-; the decomposition of $O_2^{\overline{\cdot}}$ is fast in the presence of MeCN and DMSO in benzene, affording acetamide and dimethyl sulfone.

The reaction of nitrile with alkaline hydrogen peroxide is well documented[2,3] and the intermediate peroxycarboximidic acid (**1**) has been utilized as a convenient epoxidizing agent.[4,5] Because the reaction can be run under weakly basic conditions, the oxidant is useful for the epoxidation of olefins leading to acid-sensitive epoxides[4] or olefinic ketones susceptible to the Baeyer-Villiger reaction,[6] and also applicable to imines.[7] The reactivity of **1** is interesting in connection with these oxidations and with chemiluminescence from nitriles.[8,9]



$$RC{\equiv}N + H_2O_2 \xrightarrow{\text{base}} \underset{\displaystyle OOH}{RC}{=}NH \qquad (1)$$

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The reaction has also been studied kinetically in relation to an α-effect of HOO^- nucleophile,[2,10,11] where a rate-determining step was assumed to be the addition of HOO^- to nitrile. By contrast, our previous study on the epoxidation of olefins with a mixture of nitrile and alkaline H_2O_2 showed that the epoxidation with **1** is rate-determining.[3] Here, we wish to report our mechanistic study on the formation and reaction of **1**, revealing that the formation of **1** becomes rate-determining in the presence of DMSO and that the oxidation of H_2O_2 with **1** is not important, no singlet oxygen being generated. The reaction of superoxide ion, $O_2^{\overline{\cdot}}$, with nitrile is also shown to be analogous to the case of HOO^-.

Results and Discussion

Stoichiometry. The stoichiometry for the reaction of nitrile with alkaline hydrogen peroxide was sometimes written as[2]

$$RCN + 2\,H_2O_2 \xrightarrow{HO^-} RCONH_2 + O_2 + H_2O. \qquad (2)$$

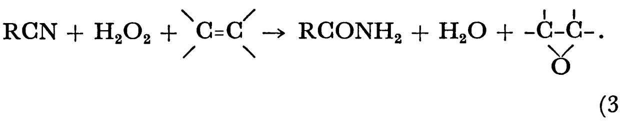
Table 1. Rates and product from the reaction of nitriles and alkaline hydrogen peroxide[a)]

RCN	Solvent % MeOH	Base	% HOO^- [b)]	Additive[c)]	Rate/$M^{-1}\,s^{-1}$ [d)]		Yield/%[e)]	
					$10^2\,k_{obsd}$	$10^2\,k_{HOO^-}$	$RCONH_2$	Me_2SO_2
PhCN	75%	5 mM Na_3PO_4	10%		0.0031	(0.031)[d)]	58	—
	75%	0.1 M NaOH	11%	f)	0.92	(8.4)	30	f)
	50%	0.01 M NaOH	23%		0.73	(3.2)	33	—
	50%	0.1 M NaOH	75%		8.6	(11.5)	25	g)
	75%	5 mM Na_3PO_4	10%	DMSO[h)]	1.52[h)]	15.2	88	86
	50%	0.01 M NaOH	23%	DMSO	2.40	10.4	64	65
	50%	0.1 M NaOH	75%	DMSO	9.0	12.0	35	24
$PhCH_2CN$	75%	5 mM Na_3PO_4	10%		0.125	(1.25)	58	—
	50%	0.01 M NaOH	23%		1.15	(5.0)	43	i)
	75%	5 mM Na_3PO_4	10%	DMSO	0.603	6.03	100	100
	50%	0.01 M NaOH	23%	DMSO	1.10	4.8	96	84

a) Reaction with 0.1 M RCN and 0.017 M H_2O_2 at 25 °C. b) % Dissociation of H_2O_2 into HOO^- as determined by UV absorbance at 280 nm (±3%). c) 0.1 M of DMSO. d) The rates were determined by iodometric titration of the remaining H_2O_2. The k_{HOO^-} value was calculated according to Eq. 5; the values in parentheses are shown to exemplify no constancy of the k_{HOO^-} value in the absence of DMSO. e) Yields were determinined by GLC and based on H_2O_2 consumed. f) When 0.04 M cumene was added, 3—6% of 2-phenyl-2-propanol was obtained. g) Oxygen was evolved in 60% yield. h) The k_{obsd} value was practically same (*i.e.*, 1.46 and 1.55) with 0.05 and 0.5 M DMSO. i) Benzaldehyde (1%) and benzyl alcohol (8%) were also detected by GLC.

However, the reaction is not so simple; the yields of amides based on H_2O_2 consumed vary in the range of 20—60% depending on the conditions and substrates (Table 1). A lower yield of amide was obtained at higher pH, perhaps suggesting a radical decomposition of H_2O_2 as discussed later.

On the other hand, the reaction in the presence of olefins was shown to have a simple stoichiometry affording a nearly quantitative yield of amide and epoxide by an ionic mechanism:[3)]



$$RCN + H_2O_2 + \text{>C=C<} \rightarrow RCONH_2 + H_2O + \text{-C(-O-)C-}. \qquad (3)$$

The same is true for the oxidation of dimethyl sulfoxide (DMSO) to sulfone in phosphate buffer, which shows the stoichiometry of reactant, $RCN:H_2O_2:\text{substrate}=1:1:1$. The yields of amide and sulfone decrease at high alkanity, again suggesting an intervention of a radical decomposition of H_2O_2. The oxidation of sulfoxide to sulfone with alkaline H_2O_2 alone is ineffective in these protic solvents as reported previously.[12)]

Kinetics. The reaction of nitrile with alkaline hydrogen peroxide has mostly been explained by a rate-determining addition of HOO^- to nitrile, the intermediary perimidic acid (**1**) being a potent oxidant capable of oxidizing H_2O_2 itself rapidly.[2,10,11)] This explanation, however, contrasts with our previous observation[3)] that the epoxidation of olefins with nitrile and alkaline H_2O_2 obeyed third-order kinetics:

$$v = k_4[RCN][H_2O][C=C]. \qquad (4)$$

Here, k_4 value was practically independent of $[HO^-]$ or $[HOO^-]$ at pH 10—12 in 75% MeOH; moreover, the consumption of H_2O_2 in the absence of olefin was very small (*i.e.*, mostly<2%). These results suggest that the rate-determining step is not the formation of **1** but the epoxidation with it.

To clarify this discrepancy, we reinvestigated the reaction of nitrile with alkaline H_2O_2 kinetically by following H_2O_2 iodometrically. As shown in Table 1, the reaction of nitrile with H_2O_2 changes with the kind and concentration of base; the resulting k_{HOO^-} value, calculated according to a rate equation 5, is far from constant.

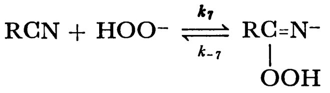
$$v = k_{obsd}[RCN][H_2O_2] = k_{HOO^-}[RCN][HOO^-] \qquad (5)$$

No constancy of k_{HOO^-} value indicates that the addition of HOO^- to nitrile is not rate-limiting in the reaction of nitrile and alkaline H_2O_2 alone.

When DMSO is added to the reaction mixture, the reaction is significantly accelerated under weakly alkaline conditions, the maximum being over one hundred times. In contrast to the case of olefin epoxidation (Eq. 4), the oxidation of DMSO to sulfone is independent of substrate concentration (see footnote h in Table 1) but dependent on $[HO^-]$ or $[HOO^-]$. Similar results were obtained for the case of acetonitrile, the $10^3 k_{obsd}$ value being constant at $1.21 \pm 0.07\ M^{-1}\ s^{-1}$ with varying concentration of DMSO from 0.05 to 0.7 M MeCN in 75% MeOH containing 5 mM Na_3PO_4. The constancy of the k_{HOO^-} value in the presence of DMSO (Table 1) seems to be adequate in view of the accuracy in estimating $[HOO^-]$. Thus, the rate expression in the presence of DMSO is Eq. 5 where no term of [DMSO] is involved.

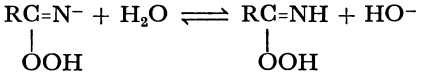
All of the above results may be well understood by the following scheme.

$$H_2O_2 + HO^- \rightleftharpoons HOO^- + H_2O \qquad (6)$$



$$RCN + HOO^- \underset{k_{-7}}{\overset{k_7}{\rightleftharpoons}} RC(OOH){=}N^- \qquad (7)$$

1A



$$RC(OOH){=}N^- + H_2O \rightleftharpoons RC(OOH){=}NH + HO^- \qquad (8)$$

1A **1**

$$\mathbf{1} + \text{Reductant} \xrightarrow{k_9} RCONH_2 + \text{Product} \qquad (9)$$

Here, k_7 equals k_{HOO^-} in Eq. 5. For olefin epoxidation, step 9 is rate-determining and preequilibrium reactions 6—8 are attained; the three equilibria could be simply written as Eq. 10, leading to the observed rate equation (Eq. 4) independent of pH. The magnitude of the

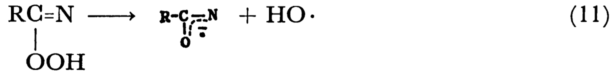
$$RCN + H_2O \underset{K_{10}}{\overset{\text{base}}{\rightleftharpoons}} \mathbf{1} \qquad (10)$$

equilibrium constant (*i.e.*, K_{10}) is probably very small since no new peak could be observed in UV spectra and no peroxy acid, a hydrolyzed product of **1**, was detected after acidification of the equilibrated mixture. Such a case is rather common in carbonyl addition reactions, *e.g.*, the Baeyer-Villiger reaction or ester hydrolysis.

The oxidation step 9 is fast for the case of DMSO, a much more reactive substrate than olefins,[13a)] and hence the rate is governed by the addition step of HOO^- to C≡N (step 7), thus being independent of [DMSO] as is observed. The apparent large solvent effect in k_{obsd} is due to the change in $[HOO^-]$ owing to the change in K_6 value. The constancy in k_{HOO^-} values was observed only for the DMSO oxidation, indicating the rate-determining addition of HOO^- to C≡N.

As for the reaction of nitrile with H_2O_2 alone, previous kinetics[2,10)] were carried out at pH<10 and explained by assuming a rate-limiting addition of HOO^- to C≡N. This assumption is not substantiated by the fact that the k_{HOO^-} values are not constant and the reaction in the presence of olefin or sulfoxide is much faster under these weakly alkaline conditions. Thus, the preequilibrium 10 must be attained in the absence of added substrate. Then there might be a case where the oxidation of H_2O_2 with **1** occurs and determine the overall rate, requiring a rate expression: $v=k[RCN][H_2O_2]^2$ which was obtained by substituting $[H_2O_2]$ for [C=C] in Eq. 4. However, this case is not probable in view of the fact that the observed order in $[H_2O_2]$ is not second-order.[2,3,10)] We ascertained this again; for example, the reaction of 0.05 M benzonitrile with 0.01 and 0.03 M H_2O_2 afforded $10^5 k_{obsd}$ value of 0.36 and $0.34\ M^{-1}\ s^{-1}$, respectively, in the presence of 5 mM Na_2HPO_4 in 50% MeOH ($1\ M = 1\ mol\ dm^{-3}$).

At high alkanity, *e.g.*, 0.1 M NaOH, the consumption of H_2O_2 becomes independent of the presence of DMSO and the yields of amide and/or sulfone are low (*i.e.*, 20—30% based on H_2O_2 consumed). Moreover, the effect of EDTA is rather small at these higher alkaline concentrations. These facts suggest a radical decomposition of H_2O_2 induced by the homolysis of peroxyimidate ion **1A**.[13b)]



$$\underset{\substack{|\\ \text{OOH}}}{\text{RC=N}} \longrightarrow \underset{\text{O}}{\text{R-C=N}} + \text{HO}\cdot \qquad (11)$$

1A

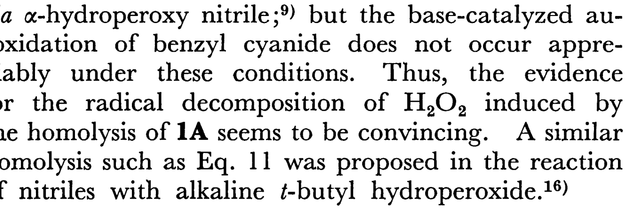
$$\text{R'O}\cdot + H_2O_2 \longrightarrow \text{R'OH} + \text{HOO}\cdot \text{ (or } H^+ + O_2^{\bar{\cdot}}) \qquad (12a)$$

$$\text{HOO}\cdot + O_2^{\bar{\cdot}} \longrightarrow \text{HOO}^- + O_2 \qquad (12b)$$

$$\text{R'O}\cdot + O_2^{\bar{\cdot}} \longrightarrow \text{R'O}^- + O_2 \qquad (12c)$$

Here, R'O· is **2** or HO·. It is well known that the base-catalyzed decomposition of hydrogen peroxide is complex and sensitive to contaminating metal ions.[14a)] Although many steps are involved in the radical decomposition of H_2O_2,[14b—d)] a major step to produce oxygen is probably the reaction 12b or 12c; the pK_a value of HOO· being 4.85 in water.[14e)]

Four lines of evidence were obtained for the intervention of radical decomposition of H_2O_2. First, the yield of amide or sulfone was sometimes as low as 20—30% on the basis of H_2O_2 consumed. Second, 2-phenyl-2-propanol (3—6%) was obtained when cumene was added (footnote f in Table 1), suggesting an initiation of radical autoxidation of added cumene. Third, the oxidation of 1,2-dimethylcyclohexene yielded, in addition to epoxide, products from its autoxidation as discussed later (Table 4). The fourth line of evidence for the homolysis of **1A** is the formation of benzyl alcohol and benzaldehyde from benzyl cyanide (footnote i in Table 1) (Eq. 13).

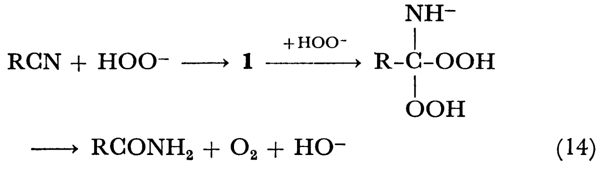


$$\text{PhCH}_2\text{CN} \xrightarrow{\text{HOO}^-} \underset{\substack{|\\ \text{OOH}}}{\text{PhCH}_2\text{C=N}^-} \xrightarrow{-\text{HO}\cdot} \underset{\substack{|\\ \text{O}\cdot\\ \mathbf{3}}}{\text{PhCH}_2\text{C=N}^-}$$

$$\xrightarrow{-\text{OCN}^-} \text{PhCH}_2\cdot \xrightarrow{O_2} \longrightarrow \text{PhCH}_2\text{OH} + \text{PhCHO} \qquad (13)$$

Facile β-scission of benzyl radical is known.[15)] Formation of benzaldehyde might be explained by a scheme *via* α-hydroperoxy nitrile;[9)] but the base-catalyzed autoxidation of benzyl cyanide does not occur appreciably under these conditions. Thus, the evidence for the radical decomposition of H_2O_2 induced by the homolysis of **1A** seems to be convincing. A similar homolysis such as Eq. 11 was proposed in the reaction of nitriles with alkaline *t*-butyl hydroperoxide.[16)]

On the basis of ^{18}O-tracer study yielding 81% of unscrambled oxygen, the reaction of **1** with HOO^- was proposed as a predominant pathway.[10a)]



$$\text{RCN} + \text{HOO}^- \longrightarrow \mathbf{1} \xrightarrow{+\text{HOO}^-} \underset{\substack{|\\ \text{OOH}}}{\overset{\substack{\text{NH}^-\\ |}}{\text{R-C-OOH}}}$$

$$\longrightarrow \text{RCONH}_2 + O_2 + \text{HO}^- \qquad (14)$$

But this pathway can not be predominant since our kinetic data show that the formation of **1** is not rate-determining and, moreover, the overall rate is not governed by the reaction of **1** with HOO^- as discussed above. One possible route to the observed unscrambled oxygen, which was conducted at pH 10 in water, is a homolytic one such as Eqs. 12a—c. This seems to be not unreasonable in view of the fact that the reported k_{HOO^-} value of *ca.* $2\times10^{-2}\,M^{-1}\,s^{-1}$ (for *p*-cyanobenzoate in water)[10a)] is much higher than the present value of $3\times10^{-4}\,M^{-1}\,s^{-1}$ in phosphate buffer (entry 1 in Table 1). The large value of the former seems to reflect an intervention of radical decomposition of H_2O_2 to yield oxygen. Since the base-catalyzed decomposition of H_2O_2 is complex[14)] and peroxyl radicals yield scrambled oxygen,[17)] it is not easy to clarify or explain the ^{18}O-tracer study (*i.e.*, 81% unscrambled and hence 19% scrambled).

α-Effect. The rate of addition of HOO^- to nitrile could be determined in the presence of DMSO (Table 2). The k_{HOO^-} value changes with nitriles, ranging from 10^{-3} to 3. Aliphatic nitriles are about ten times less reactive than aromatic ones. The substituent effect on benzonitrile affords a ρ-value of 1.54 (σ, $r=0.991$), suggesting a nucleophilic attack of HOO^- on C≡N.

Much attention has been concentrated on the origin of α-effect.[11)] Although several explanations have been noted,[18)] it seems to be that there is no single factor govering the α-effect. A typical example of α-effect is the addition of HOO^- to C≡N. The original value (k_{HOO^-}/k_{HO^-}) of 2×10^4 to 7×10^4 for benzonitriles[2)] was often cited, but later it was corrected to be 900—1200.[10)] As discussed above, a rate-determining step under these conditions is not the attack of HOO^- to C≡N but the decomposition of **1**. The obscurity may be overcome by the addition of DMSO; the results listed in Table 3 show that the α-effect is certainly large, the value of k_{HOO^-}/k_{HO^-} being in the range of 3×10^3 to 10^4.

Reactivity of Peroxyimidic Acid. Peroxyimidic acid (**1**) is a convenient epoxidizing agent.[4—6,19)] The electrophilic character of **1** was shown for substituted styrenes ($\rho=-0.48$),[3)] although the substituent effect was somewhat smaller compared to the epoxidation with peroxy acid ($\rho=-1.30$).[20)] The epoxidation of aliphatic olefins with **1** was also shown to be less selective and possesses a greater steric demand than the case of RCO_3H.[21)] Stereochemistry is retained in the present epoxidation as is the case with RCO_3H; that is, GLC analysis demonstrates that *trans*- and *cis*-β-methylstyrenes give the corresponding *trans*- and *cis*-epoxides, respectively, in the reaction with MeCN, H_2O_2, and Na_3PO_4 in 75% MeOH.

Intramolecular epoxidation was shown to occur effectively for α,β-unsaturated nitriles.[22)] However, this epoxy amide formation is not so facile; for example, cinnamonitrile gave the amide: epoxy amide ratio of 90:10 (see Table 2). Similarly, a relatively low yield of epoxy amide was also obtained (*i.e.*, **5**:**6**=4:1) from β,γ-unsaturated nitrile (**4**) (Eq. 15).

The addition of DMSO to the system dramatically accelerated the conversion of nitriles to amides un-

TABLE 2. SUBSTITUENT AND DMSO EFFECT ON THE REACTION OF NITRILES WITH ALKALINE HYDROGEN PEROXIDE IN 75% MeOH

Nitriles	Additive	Rate constants/$M^{-1} s^{-1}$ a)		Product yields$^{b)}$	
		$10^2 k_{obsd}$	$10^2 k_{HOO^-}$	Amide	Epoxy amide
A) Benzonitriles$^{c)}$					
C_6H_5CN	DMSO	1.52	15.2	84	
p-MeOPhCN	DMSO	0.969	9.69	d)	
p-MePhCN	DMSO	1.11	11.1	93	
m-MePhCN	DMSO	1.31	13.1	d)	
o-MePhCN	DMSO	0.056	0.56	83	
o-MePhCN		(<0.0001)		5	
p-ClPhCN	DMSO	e)	46.5	d)	
p-O_2NPhCN	DMSO	e)	324	d)	
B) Other nitriles					
MeCN	DMSO	0.121	1.21	d)	
i-PrCN	DMSO	0.119	1.19	d)	
$PhCH_2CN$	DMSO	0.703	7.03	92	
trans-PhCH=CHCN	DMSO	1.01	10.1	100	0
trans-PhCH=CHCN		(0.017)		55$^{f)}$	7$^{f)}$
4	DMSO	0.102	1.02	76$^{g)}$	0
4		(0.025)		16$^{f)}$	4$^{f)}$

a) Reaction with 0.1 M RCN, 0.015 M H_2O_2, 0.05 M DMSO, and 0.01 M Na_3PO_4 at 25 °C. See footnotes in Table 1. The value in parentheses is from the reaction without DMSO. b) % Yields isolated, if not noted otherwise, from the reaction with 10 mmol RCN, 15 mmol H_2O_2, 12 mmol DMSO, and 0.2 mmol NaOH in 25 ml of 80% MeOH at 50 °C for 1 h. See experimental section. c) Ph = C_6H_4. d) Not determined. e) Reaction with 0.011 M RCN and H_2O_2. f) % Yield determined by NMR. g) NMR yield is 95%.

TABLE 3. α-EFFECT ON THE ADDITION OF NITRILES$^{a)}$

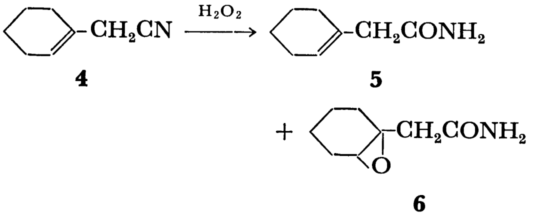
Nitrile	Nucleophile	Solvent	$k/M^{-1} s^{-1}$	k_{HOO^-}/k_{HO^-}
PhCN	HOO^-	25% Dioxane	2.02×10^{-1}	1.02×10^{4}
	HO^-	25% Dioxane	1.97×10^{-5}	
MeCN	HOO^-	25% Dioxane	2.53×10^{-2}	4.0×10^{3}
	HO^-	25% Dioxane	0.63×10^{-5}	
MeCN	HOO^-	Water	1.40×10^{-2}	3.0×10^{3}
	HO^-	Water	0.47×10^{-5}	

a) Reaction at 25 °C with hydrogen peroxide: 0.1 M RCN, 0.02 M H_2O_2, 0.1 M DMSO, and 0.1 M Na_2CO_3; the k_{HOO^-} values were calculated accoding to Eq. 5 (20.1% dissociation of H_2O_2 into HOO^- by UV). The alkaline hydrolysis: 0.1—0.4 M NaOH, 1—2.5 M MeCN or 0.1 M PhCN.

TABLE 4. OXIDATION OF 1,2-DIMETHYLCYCLOHEXENE (**7**) WITH NITRILE AND ALKALINE HYDROGEN PEROXIDE

Condition$^{a)}$	Solvent	Yields$^{b)}$			
		8	**9**	**10**	**11**
Singlet oxygen (O_2/RB/hν)	MeOH	2	1	85	12
Autoxidn. (O_2/AIBN/60 °C)$^{c)}$	MeCN	34	22	14	30
PhCN-H_2O_2 (0.02 M NaOH)	90% MeOH	59	21	8	11
PhCN-H_2O_2 (0.02 M NaOH)$^{d)}$	90% MeOH	47	28	10	16
PhCN-H_2O_2 (5 mM Na_3PO_4)$^{e)}$	85% MeOH	60	21	7	12

a) Reaction time of 30—60 min at room temperature if not noted otherwise. Reaction with 0.1 M olefin and, for the nitrile-H_2O_2 reaction, 0.2 M each of PhCN and H_2O_2. b) Product distribution (%) determined by GLC after the reduction with $NaBH_4$. c) Reaction time 4 h. d) In the presence of 1 mM EDTA. e) Reaction time 24 h.



(15)

contaminated with epoxy amide (Table 2). The accelerating effect was large especially for the case of hindered nitriles such as *o*-tolunitrile or cinnamonitrile (*i.e.*, *ca.* thousand-fold increase in rate). The reaction at 50 °C for 1 h gave a high yield of pure amide even with 1 mmol scale, which may be useful as a convenient identification of nitriles. In any case, it is apparent that the intramolecular epoxidation in the peroxyimidic acid intermediate is not so fast and the acid may be completely reduced by DMSO affording pure olefinic amide.

On the basis of approximate stoichiometry of RCN: H_2O_2 = 1 : 2, peroxyimidic acid **1** was noted as a potent oxidant capable of oxidizing H_2O_2 to O_2.[2] In analogy to the oxidation with RCO_3H,[8,23] hydrogen peroxide may be oxidized by **1** to oxygen (Eq. 16). However, the kinetics at lower pH (*e.g.*, pH<12 in 75% MeOH)

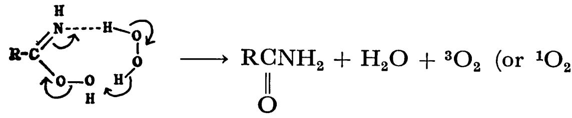


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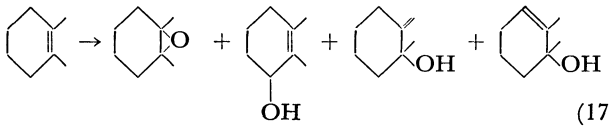
TABLE 5. REACTION OF SUPEROXIDE ION IN BENZENE[a]

Reagent	Decomposed KO_2/%[b]	Products/%[c]		
		$MeCONH_2$	Me_2SO_2	Others
KO_2	<5	—	—	
KO_2-MeCN	44	1.9	—	
KO_2-MeCN-DMSO	60	16	40	
KO_2-DMSO	18	—	3	
KO_2-DMSO-H_2O[d]	62	—	4	
KO_2-MeCN-Olefin[e]	80	1.3	—	None[f]
KO_2-MeCN-**7**	78	1.5	—	Yes[g]
KO_2-**7**	<10	—	—	Yes[h]

a) Reaction with 0.5 mmol KO_2 (suspension) and 0.1 mmol 18-crown-6 in benzene (4 ml) at 25 °C for 2 h. Acetonitrile was added in a large excess as a co-solvent, *i.e.*, 25 vol% in benzene. DMSO was 0.3 M and olefins were of 0.1 M concentration. b) Approximate value of decomposed KO_2 by titration. c) Yields were determined by GLC and based on the charged KO_2. d) Water (0.25 mmol) was added. e) α-Methylstyrene. f) Epoxide or acetophenone was not detected. g) Yields of **8**, **9**, **10**, and **11** were 1.4, 0.3, 0.3, and 2.4%, respectively. h) Yields of **8**, **9**, **10**, and **11** were 0.7, 0.1, 0.2, and 1.0%, respectively.

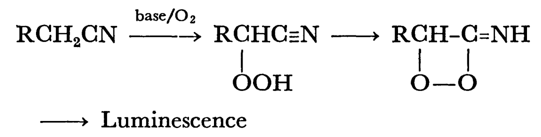
is not in accordance with this scheme; if the reaction 16 were operative as a major rate-determining pathway, the overall rate should be second-order in $[H_2O_2]$ and the yield of amide based on H_2O_2 should not exceed 50% (in the absence of DMSO or olefin), both of which were not the case. At high alkalinity, **1** should shift to **1A**[13b] which easily decomposes homolytically inducing radical decomposition of H_2O_2. This leads to the lower yield of amide or sulfone as is observed. Thus, it may be concluded that the oxidation of H_2O_2 by **1** or **1A** like Eq. 16 is not operating as a predominant reaction.

In order to examine a possible formation of singlet oxygen even as a minor reaction, 1,2-dimethylcyclohexene (**7**), a useful $^1O_2$ trapper,[24a] was oxidized with nitrile and alkaline H_2O_2. The results in Table 4 shows that the product distributions are different from singlet oxygen reaction, but are similar to that of the radical autoxidation. A relatively high yield of epoxide was obtained by the radical autoxidation of **7** as observed for other tetrasubstituted aliphatic olefins.[25] The oxidation of α,β,β-trimethylstyrene, which is also a $^1O_2$ trapper[24a] but resistant to radical autoxidation at 60 °C, gave a high yield of epoxide (95% yield) together with minor products, where allyl alcohols produced by the $^1O_2$ reaction could not be detected by GLC (*i.e.*, within 1%, if any). Thus, singlet oxygen is not formed in the RCN–H_2O_2 reaction. This results are in contrast to the reported efficient formation of $^1O_2$ from H_2O_2 and cyanates ROCN under anhydrous neutral conditions.[24b]


(17)

7 **8** **9** **10** **11**

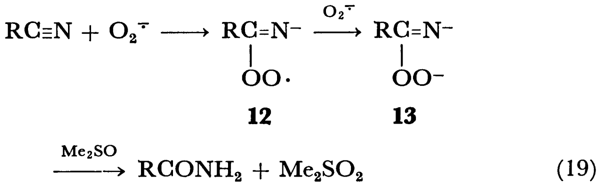
Finally, a comment should be added on the reported chemiluminescence from nitriles and H_2O_2.[8a] Contrary to the report that the luminescence is visible, blue or red, we could not see or detect it as described below. We tested acetonitrile, isobutyronitrile, benzonitrile, benzyl cyanide, and acrylonitrile under the conditions of 0.01—0.1 M each of nitrile, H_2O_2, and KOH in MeOH or EtOH. The addition of dibromo- or diphenylanthracene was of no effect. Our results show that the quantum yield of the reported luminescence is much less than 10^{-9}, if any. To our knowledge, the reported chemiluminescence might be *via* α-hydroperoxy nitrile formed by the base-catalyzed autoxidation of nitriles.[9] The reported luminescence intensity of $CH_2{=}CHCN > PhCH_2CN \gg PhCN$ may be understood on the basis of Eq. 18, where an α-proton is necessary for the base-catalyzed autoxidation. Although the authors[8a] suggested singlet oxygen formation by reaction 16, this is not in accordance with the fact that singlet oxygen could not be trapped chemically.


$$RCH_2CN \xrightarrow{base/O_2} \underset{\displaystyle OOH}{RCHC{\equiv}N} \longrightarrow \underset{\displaystyle O{-}O}{RCH{-}C{=}NH} \longrightarrow \text{Luminescence} \qquad (18)$$

Reaction of Superoxide Ion with Nitrile. Much interest has been concentrated on the reactivity of superoxide ion.[26] Acetonitrile is sometimes used as an aprotic solvent,[27] but it is noted that the reactivity of $O_2^{\cdot-}$ in MeCN is different from that in other solvents,[16b,28] typically the lifetime of $O_2^{\cdot-}$ is ten times shorter in the nitrile.[28a]

As shown in Table 5, superoxide ion $O_2^{\cdot-}$ reacts with acetonitrile just as hydroperoxide ion HOO^- does. All the experiments were carried out in the presence of 18-crown-6 in benzene to dissolve some fraction of KO_2. Suspended potassium superoxide was stable in benzene but decomposed in acetonitrile–benzene. Interestingly, considerable yields of acetamide were obtained by the reaction of KO_2–MeCN–DMSO. Since it is known that sulfoxides are oxidized to sulfones by alkyl hydroperoxide ion in aprotic solvents,[29] the sulfone might be produced by the reaction of HOO^- produced by the disproportionation of $O_2^{\cdot-}$. However, the yield of sulfone was much lower when water was added as a proton source to produce

HOO^-. These facts suggest the following scheme.



$$RC\equiv N + O_2^{\cdot -} \longrightarrow \underset{\substack{| \\ OO\cdot}}{RC=N^-} \xrightarrow{O_2^{\cdot -}} \underset{\substack{| \\ OO^-}}{RC=N^-} \xrightarrow{Me_2SO} RCONH_2 + Me_2SO_2 \qquad (19)$$

12 **13**

The reduction of radical **12** with $O_2^{\cdot -}$ to form **13** and O_2 is similar to a known process.[26c,30] Since α-methylstyrene was not epoxidized by KO_2–MeCN (Table 5), the intermediary oxidant for the sulfoxide is probably **13** as a nucleophilic oxidant. It is known that sulfoxides are efficiently oxidized by nucleophilic oxidants.[12,29] In the absence of DMSO, **13** decomposes homolytically just as the case of RCN–HOO^- reaction at high alkalinity (*cf.* Eq. 11). The product distribution from **7** seems to be in this line, suggesting a radical autoxidation (Table 5). Thus, it may be concluded that the chemistry is essentially same for the reaction of nitrile with $O_2^{\cdot -}$ or with HOO^-.

Experimental

Melting points were measured by a Yanagimoto micro melting point apparatus and are corrected. ^1H NMR spectra were recorded with a Hitachi R-24B spectrometer. GLC analyses were performed with a Yanagimoto G180 gas chromatograph using two different columns: PEG 20 M, 10% on Chromosorb W; Silicone OV-17, 5% on Shimalite W. Chemiluminescence was monitored by a Hitachi MPF-2A fluorescence spectrophotometer.

Materials. Methanol and water were purified by redistillations. Substituted benzonitriles were described in our previous paper.[3] *trans*-Cinnamonitrile,[31] bp 124—125 °C/8 Torr (lit,[32] bp 137 °C/16 Torr), and 1-cyclohexenylacetonitrile (**4**),[33] bp 105—107 °C/21 Torr (lit,[33] 110—112 °C/25 Torr), were obtained by the literature method. 2-Methyl-3-phenyl-2-butene, bp 91—92 °C/25 Torr (lit,[34] 191—192 °C), was prepared by dehydration[35] of 2-methyl-3-phenyl-2-butanol in 40% yield. 1,2-Dimethylcyclohexene (**7**) was obtained by dehydration of 1,2-dimethylcyclohexanol (50% sulfuric acid, 100 °C, 1 h) and fractionated three times with a 30 cm Vigreux column, bp 135—136 °C (lit,[36] bp 136.2 °C). Purification *via* dibromide formation[37] was unsatisfactory. 18-Crown-6 was synthesized from triethylene glycol[38] and KO_2 from xanthone-catalyzed autoxidation of potassium in THF.[39]

Rates and Products Determination. Rates were followed iodometrically and a typical procedure was noted in the previous paper.[3] The decomposition of alkaline H_2O_2 alone was negligibly small. The reaction of nitrile with alkaline H_2O_2 was not affected by the addition of 10^{-4} M EDTA, which indicates that there was no contamination by metallic ions.

The hydrolysis rate of benzonitrile was determined by following the decrease of the nitrile by GLC analysis. The reaction of acetonitrile was followed by titrating the produced acetic acid after flashing out ammonia by passing N_2 gas for 5 min. The results are shown in Table 3.

Products were determined by GLC and/or NMR, directly or after extraction with CH_2Cl_2, in comparison to an authentic sample. Authentic samples of epoxides or epoxy amide were obtained by RCO_3H or alkaline H_2O_2 oxidation.

Facile Conversion of Nitriles to Amides. *o*-Tolunitrile (1.17 g, 10 mmol) and DMSO (0.85 ml, 12 mmol) were dissolved in MeOH (20 ml), followed by addition of 11% H_2O_2 (4.85 ml, 15 mmol) and 0.2 M NaOH (1 ml, 0.2 mmol). The reaction mixture was stirred at 50 °C for 1 h, and about half of the solvent MeOH was distilled off (*ca.* 15 min). Standing at room temperature (*ca.* 30 min) afforded pure crystals of *o*-toluamide in 83% yield, mp 142—142.5 °C (lit,[40] 141—141.5 °C).

According to this convenient procedure (total working time; 2 h) the following amides were isolated in pure form (see Table 2 for the yields): *p*-toluamide, mp 161—162 °C; phenylacetamide, mp 159—160.5 °C; benzamide, mp 129—130 °C; cyclohexenylacetamide, mp 153—154 °C; *trans*-cinnamamide, mp 148.5—149.5 °C; diphenylacetamide, mp 172—174 °C. The latter two amides were isolated without evaporation of methanol. An alternative procedure for the isolation is the addition of water (20 ml), which gave a slightly lower yield of amide. The reaction in the absence of DMSO was very slow and incomplete.

Oxidation of 1,2-Dimethylcyclohexene (7). The reaction was started by adding 1 M NaOH (0.1 ml) to the mixture of 1 mmol each of **7**, benzonitrile, and H_2O_2 in 90% MeOH (5 ml). After 1 or 19 h, 0.1 g of $NaBH_4$ was added and analyzed by GLC.

For comparison, azobisisobutyronitrile (AIBN)-initiated autoxidation of the olefin was performed under O_2 in MeCN at 60 °C for 4 h; the reaction mixture was reduced by $NaBH_4$ and MeOH, and analyzed by GLC. The results are shown in Table 4.

Reaction of KO_2 with Acetonitrile. In a dry 20 ml flask were placed benzene (2 ml), MeCN (1 ml), 0.1 M 18-crown-6 (1 ml), and DMSO (0.085 ml). The reaction was started by addition of powdered KO_2 (0.5 mmol) and stirred for 2 h at 25 °C. Products were analyzed by GLC (PEG 20 M) directly or after the reduction with $NaBH_4$ and MeOH. The remaining KO_2 was determined iodometrically after pouring the reaction mixture into AcOH–MeOH–H_2O (1:1:2). Since oxygen was evolved in each run, the recovered KO_2 is mostly unchanged. The results are listed in Table 5.

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