Me or Et). A solution of 0.05 M NaOH in 50% (v/v) aqueous dioxane (300 ml) was added at once to a solution of the phosphetanium salt (0.5 mmol) in dioxane (2 ml) at 25°. After stirring for 30 sec, the mixture was immediately extracted with dichloromethane (300 ml). Drying the extracts with magnesium sulfate and concentrating afforded a crude mixture of the possible phosphetane oxide products. The crude sample was analyzed directly by ^{1}H nmr without purification. Table VII indicates the regions utilized in determining the product ratios.

The products resulting from the hydrolyses of **2a–f** were obtained by reacting a known mixture of **1** and **2** determined by ^{1}H nmr (see Table VI) and then correcting for the products which would have arisen from **1** as determined above.

All hydrolyses were repeated five times, and the product percentages indicated in Tables I and II are the average of these determinations (standard deviation *ca.* ±2%). In all cases, the products accounted for greater than 90% of theoretical, indicating very little if any further hydrolysis to the phosphinic acid.

Acknowledgment. We would like to thank Research Corporation for the generous support of this research.

Peracid Oxidation of Imines. Kinetics of Oxazirane Formation from Benzylidene-*tert*-butylamines and Perbenzoic Acid

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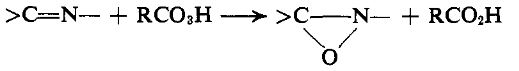
Abstract: The reaction of perbenzoic acid (PBA) with benzylidene-*tert*-butylamines to afford oxaziranes has been studied kinetically in order to decide whether the mechanism is either one step (epoxidation type) or two step (the Baeyer–Villiger type). Although the rates are summarized as $v = k_{\mathrm{obsd}}[\mathrm{C{=}N}][\mathrm{PBA}]$, the reaction exhibits complex kinetics because of two adverse effects, acceleration by carboxylic acids and protic solvents and retardation by basic solvents including ethers and alcohols. Thus, various alcohols can catalyze the oxidation with similar effectiveness as carboxylic acids, while the reaction is retarded on addition of excess of some alcohols. The substituent effect on the imines changes with reaction conditions; the effect becomes very small in the presence of ethanol. These data for the oxazirane formation show behaviors different from the PBA oxidation of amines and olefins, which has a one-step mechanism. It may be concluded that the oxazirane formation has a two-step mechanism similar to the Baeyer–Villiger reaction, where the addition to C=N is rate determining under most conditions. Significant amounts of nitrones were also formed with imines bearing electron-donating substituents.

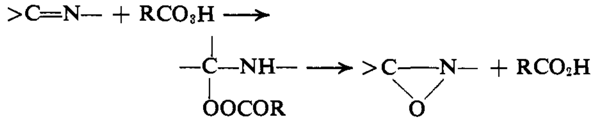
The following two mechanisms have been developed for the formation of oxaziranes by the peracid oxidation of imines.[1–5]

One-step mechanism



(1)

Two-step mechanism



(2)

Originally, Emmons[1] regarded the one-step mechanism more probable than the two-step one without any convincing evidence, while Schmitz, *et al.*,[3] preferred the latter (eq 2). Recently, Madan and Clapp[4] chose the former (eq 1) in view of the kinetic data especially from negative ρ values for substituted imines and significant acid catalysis.

We felt, however, that the two-step mechanism (eq 2) cannot be ruled out in view of the facts that imines are susceptible to nucleophilic attacks,[6,7] that the peracid oxidation of N-benzoylimines affords the Baeyer–Villiger-type rearranged products, *i.e.*, phenols,[8] and that a reaction of an aliphatic imine with hydrogen peroxide gave an adduct, which is converted to an oxazirane on gentle heating.[9] Moreover, Madan and Clapp's kinetic results for the imine oxidation[4] are fairly similar to those for the Baeyer–Villiger reaction of aromatic carbonyl compounds with perbenzoic acid (PBA).[10]

On the other hand, if the one-step mechanism is operative, it is of interest to study which electrons of C=$\ddot{\mathrm{N}}$ attack the peroxidic oxygen, C=$\ddot{\mathrm{N}}$ π-bonding electrons (oxazirane formation), or N lone-pair electrons (nitrone formation). This problem is also concerned with asym-

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(1) W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 5739 (1957).

(2) W. D. Emmons, *Chem. Heterocycl. Compounds*, **19** 630 (1964).

(3) E. Schmitz, R. Ohme, and D. Murawski, *Chem. Ber.*, **98**, 2516 (1965).

(4) V. Madan and L. B. Clapp, *J. Amer. Chem. Soc.*, **91**, 6078 (1969); **92**, 4902 (1970).

(5) The peracid oxidation of imines is an important way for synthesis of oxaziranes: L. A. Paquette, "Principles of Modern Heterocyclic Chemistry," W. A. Benjamin, New York, N. Y., 1968, p 63; ref 1; W. Krim, *Chem. Ber.*, **91**, 1057 (1958); R. G. Pews, *J. Org. Chem.*, **32**, 1628 (1967).

(6) R. W. Layer, *Chem. Rev.*, **63**, 489 (1963).

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

(8) A. Padwa, *J. Amer. Chem. Soc.*, **87**, 4365 (1965).

(9) E. Höft and A. Rieche, *Angew. Chem.*, **77**, 548 (1965).

(10) Y. Ogata and Y. Sawaki, *J. Amer. Chem. Soc.*, **94**, 4189 (1972); *J. Org. Chem.*, **37**, 2953 (1972).

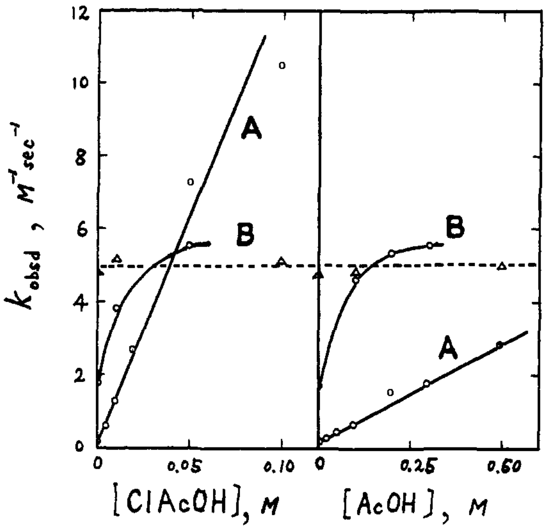

Figure 1. Acid catalysis for the PBA oxidation of I at 20°; [PBA] = 2.0 mM, [C=N] = 0.1 mM; A, in benzene; B, in 10% EtOH–90% benzene. For comparison, the rate of PBA oxidation of *p*-ClDMA in benzene is shown as a dotted line.

metric synthesis of oxaziridines with optically active peracids.[11]

The present report summarizes the kinetic data for the oxazirane formation from the PBA oxidation of benzylidene-*tert*-butylamines, which seem to favor the two-step mechanism.

Results

The oxidation rates of imines (C=N) with perbenzoic acid (PBA) were obtained by monitoring the decrease or the increase of absorbance at 310–330 nm; the second-order rate constants (k_{obsd}) were calculated by eq 3. We chose, as Madan and Clapp[4] did, *p*-nitrobenzylidene-*tert*-butylamine (I) as a substrate, which affords a quantitative amount of the corresponding oxazirane. For comparison, the rate for PBA oxidation of *p*-chloro-*N*,*N*-dimethylaniline (*p*-ClDMA) as a typical nitrogen nucleophile was determined.

$$v = k_{obsd}[\mathrm{C{=}N}][\mathrm{PBA}] \qquad (3)$$

Effect of Acids. The PBA oxidation of the imine I was accelerated by the presence of carboxylic acids (Table IA) and PBA in benzene. Plots of k_{obsd} *vs.* [acid] are linear in benzene, but nonlinear in 10% EtOH–90% benzene (Figure 1). In contrast, the oxidation rate of *p*-ClDMA is not affected by addition of these acids.

Effect of Solvents. The rate of PBA oxidation of *p*-ClDMA in benzene was reduced to *ca.* 0.25 by addition of oxygenated solvents such as dioxane and alcohols; no significant difference in rates was observed between aprotic and protic solvents.

On the other hand, the PBA oxidation of imine I is strongly accelerated by addition of alcohols but slowed down by dioxane (Table IB); the order is primary ROH > secondary ROH > tertiary ROH ≫ benzene ≫ dioxane. The reaction in the presence of 10% EtOH in benzene shows the retardation by basic solvents such as dimethylformamide (DMF), dioxane, and acetonitrile. The solvent polarity seems to have little effect, since the rate is not increased by increasing the amount of acetonitrile.

These features are apparent in Figure 2, where the dependence of solvent per cent on the oxidation rate is shown. The oxidation of *p*-ClDMA is reduced similarly by the addition of dioxane or ethanol. In contrast, the oxidation of the imine is accelerated on addition of alcohols to benzene, and plots of k_{obsd} *vs.* [ROH] are linear up to ~2% ROH. The further addition of MeOH or EtOH seems to make k_{obsd} approach a limiting value, while the addition of *i*-PrOH or *t*-BuOH reduces the rate significantly, resulting in a maximum rate at ~4 vol % ROH (Figure 2). These

Table I. Second-Order Rate Constant, k_{obsd}, for the PBA Oxdidation of *p*-$O_2NC_6H_4CH{=}N$-*t*-Bu (I) and *p*-$ClC_6H_4NMe_2$ (*p*-ClDMA) in Benzene at 20.0 ± 0.5°

Reaction conditions[a]	k_{obsd}, M^{-1} sec^{-1} I[b]	 *p*-ClDMA[c]
A. Effect of Added Acid		
None	~0.115	4.76
0.01 *M* AcOH	0.219	
0.10 *M* AcOH	0.622	4.76
0.50 *M* AcOH	2.83	4.97
1.0 *M* AcOH		4.44
0.001 *M* ClAcOH	0.159	
0.010 *M* ClAcOH	1.27	5.15
0.050 *M* ClAcOH	7.23	5.15
0.10 *M* ClAcOH	10.4	5.15
B. Effect of Solvent		
100% benzene	~0.115	4.76
20% MeOH	5.68	1.04
20% EtOH	1.86	1.38
20% *n*-PrOH	1.61	1.44
20% *n*-BuOH	1.53	1.39
20% *i*-BuOH	1.33	1.21
20% *i*-PrOH	0.575	0.962
20% *sec*-BuOH	0.405	1.09
20% *t*-BuOH	0.250	1.04
20% MeCN	0.283	2.99
20% dioxane	~0.001	1.33
40% dioxane	0.040[d]	0.756
100% benzene	0.405[d]	4.76
10% EtOH	1.65	
10% EtOH–20% MeCN	0.653	
10% EtOH–40% MeCN	0.594	
10% EtOH–40% dioxane	0.172	
10% EtOH–40% DMF	0.037	
10% EtOH–AcOH (0.1 *M*)	4.64	
10% EtOH–ClAcOH (0.01 *M*)	3.76	

[a] Reaction in benzene if not noted otherwise. Solvent % shows vol % in benzene. AcOH is acetic acid and ClAcOH is monochloroacetic acid. [b] Initial concentrations: [PBA] = 0.0020 *M*, [C=N] = 0.0001 *M*. [c] Initial concentrations: [PBA] = 0.0020 *M*, [amine] = 0.00025 *M*. [d] [PBA] = 0.020 *M*.

Table II. Solvent Deuterium Effect for the PBA Oxidation of I in Benzene at 20.0 ± 0.5° [a]

Vol % in benzene	k_{EtOH}, M^{-1} sec^{-1}	k_{EtOD}, M^{-1} sec^{-1}	k_H/k_D[b]
0.2% EtOH	0.221	0.205	1.078[c]
0.5% EtOH	0.408	0.358	1.139
1.0% EtOH	0.950	0.883	1.075
2.0% EtOH	1.541	1.450	1.063
5.0% EtOH	1.652	1.650	1.001
10% EtOH	1.861	1.840	1.011

[a] Initial concentrations: [PBA] = 0.0020 *M*, [C=N] = 0.0001 *M*. [b] Probable error ±3%. [c] Probable error ±5%.

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(11) (a) D. R. Boyd, *Tetrahedron Lett.*, 4561 (1968); (b) F. Montanari, I. Moretti, and G. Torre, *Chem. Commun.*, 1694 (1968); (c) *ibid.*, 1068 (1969); (d) D. R. Boyd, W. B. Jennings, and R. Spratt, *ibid.*, 745 (1970).

Table III. Substituent Effect for the PBA Oxidation of Substituted Benzylidene-*tert*-butylamines at 20.0 ± 0.5°

Solvent, vol % in benzene	Nitrone, %[a]				k_{obsd},[b] M^{-1} sec^{-1}			
	p-MeO	H	*p*-Cl	*p*-NO$_2$	*p*-MeO	H	*p*-Cl	*p*-NO$_2$
A. Reaction with $[PBA]_0 = [C{=}N]_0 = 0.0020\ M$								
100% benzene	18.0	3.2	3.4	0.0	1.29	1.63	1.25	0.74
50% *t*-BuOH	1.8	0.33	1.1	0.0	0.396	1.93	1.09	0.48
0.5% EtOH	7.2	1.5	1.4	0.0	3.75	1.56	6.19	2.64
20% EtOH	2.1	0.2	0.1	0.0	15.5	6.00	6.95	6.45
50% EtOH	0.85	0.1	0.03	0.0	8.76	12.9	14.1	7.10
B. Reaction with $[PBA]_0 = 0.0020\ M$ and $[C{=}N]_0 = 0.0002\ M$								
100% benzene	20.1	4.3	4.3	0.0	0.563	0.16	0.21	0.10
20% dioxane	21.6	5.8	5.3	0.0	0.115	0.023	0.046	
50% *t*-BuOH	1.80				1.55			0.136
20% EtOH	1.95	0.2	0.2	0.0	4.41			1.65
50% EtOH	1.55	0.1	0.1	0.0	3.75	1.67	1.87	2.43

[a] % selectivity for nitrone formation. The sum of the yields of nitrone and oxazirane is quantitative (100 ± 5% yield). [b] Second-order rate constant determined from the absorbance at 300–400 nm. The absorbance for *p*-MeO increased due to the formation of a considerable amount of nitrone.

show that alcohols have two adverse effects, *i.e.*, accelerating and retarding.

The solvent deuterium effect was observed for the oxidation in the presence of <2% EtOH (or EtOD) (k_H/k_D = 1.06–1.14), while no deuterium effect was appreciable in the presence of >5% EtOH (Table II).

Substituent Effects. In Table III are listed the selectivity for the formation of nitrones and the rates for the substituted benzylidene-*tert*-butylamines. Although the main reaction is the oxazirane formation, certain amounts of nitrones are also formed. The nitrone selectivity changes with substituents in the order of *p*-MeO (up to 20%) ≫ H > *p*-Cl ≫ *p*-NO$_2$ and varies with solvents in the order of dioxane > benzene ≫ *t*-BuOH > EtOH.

The oxazirane formation, however, is the main reaction under most conditions, and k_{obsd} is reasonably regarded to show the rate for the formation of oxaziranes. The substituent effect for k_{obsd} changes remarkably with changing the reaction conditions, *e.g.*, the solvent and the initial concentration. Roughly speaking, the reaction exhibits negative ρ values in benzene, dioxane, and *t*-BuOH as reported previously,[4] while the reaction in the presence of EtOH shows ρ of ~0. This complex effect of substituents seems to reflect multiple factors influencing the oxidation rate.

Discussion

Besides the kinetic data by Madan and Clapp,[4] the following features for the peracid oxidation of imines were observed. First, alcohols exhibit two adverse effects of acceleration and retardation of different extents with changing the structure of alcohols. Second, the substituent effect for imines changes with reaction conditions; especially the effect becomes very small in the presence of ethanol. Third, the solvent deuterium effect for EtOD is apparent in benzene containing a small amount (<2%) of ethanol, but not in the presence of >5% ethanol. Fourth, a certain amount of nitrones is formed, which becomes pronounced for the imines with electron-releasing substituents. These results are discussed below in comparison with the kinetic features of peracid oxidation of other nucleophiles such as amines and olefins.

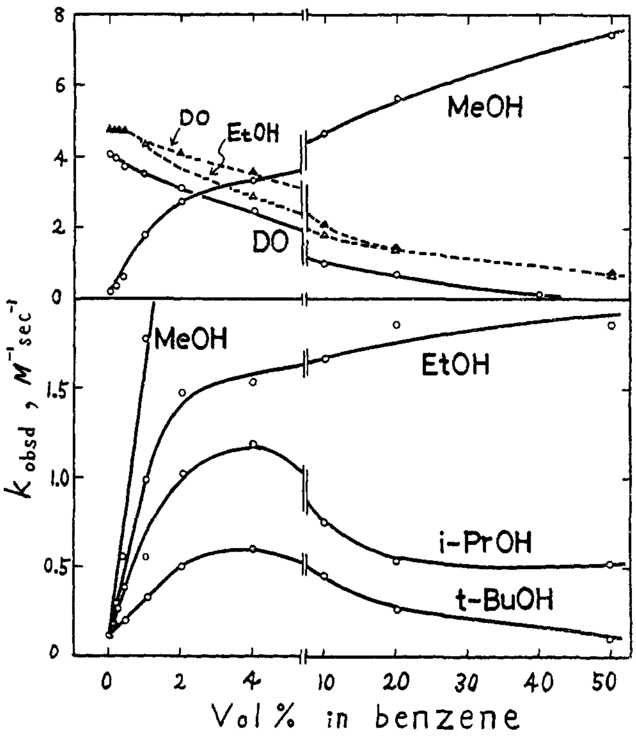
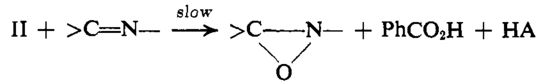


Figure 2. Effect of ROH for the PBA oxidation of I in benzene at 20°; [PBA] = 2.0 m*M*, [C=N] = 0.1 m*M*; [PBA] = 20.0 m*M* for the reaction in the presence of dioxane. For comparison, the rates for the PBA oxidation of *p*-ClDMA are shown as dotted lines.

Reaction Mechanism. Madan and Clapp postulated that the reaction is a nucleophilic attack of C=N on peracid–HA dimer (II) in view of the observed acid catalysis and substituent effect of ρ −1.75 and −0.98 on imines (mechanism A).[4] However, this scheme

$$PhCO_3H + HA \rightleftarrows \underset{\text{II}}{\text{dimer}} \qquad (4)$$



$$\text{II} + >C{=}N- \xrightarrow{\text{slow}} >\underset{\diagdown\ O\ \diagup}{C{-}N}- + PhCO_2H + HA \qquad (5)$$

mechanism A

cannot explain our additional observations. The following considerations (i–vii) suggest that the reaction goes by way of mechanism B.

(i) Acid catalysis by acetic acid is unappreciable for the PBA oxidation of olefins[12] and nitrogen bases such

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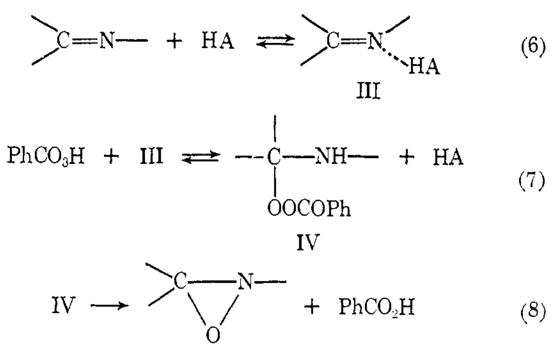
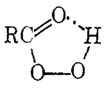
[12] Y. Sawaki and Y. Ogata, unpublished results.

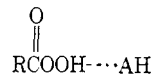


mechanism B

as azobenzene[12] and *p*-ClDMA (Figure 1). It is generally accepted that internally hydrogen-bound peracid (V) is more susceptible to an attack by nucleophiles.[13] This chelation is fairly strong, and there is no evidence for the formation of peracid dimer.[14a] It is natural that this chelation is not destroyed by weaker bases such as acetic acid,[14b] resulting in no effect of acids for the peracid (one step) oxidation of olefins and amines.[12] Therefore, it is abnormal to explain the strong acceleration by acids, according to mechanism A, with the formation of PBA–HA dimer (eq 4) as a special case only for the imine oxidation.[14c]



V



$\mathrm{RC(=O)OOH\cdots AH}$

VI

A more reasonable explanation is that the acid catalysis is due to the hydrogen bonding at the imine nitrogen, a much stronger base (mechanism B). Acid-catalyzed addition of nucleophiles to C=N is well known,[6,7] like the addition to C=O.

(ii) The effect of solvents suggests also mechanism B as discussed in the following. Peracid oxidations of olefins,[12,15] sulfides,[15a] and amines[12] show an invariant solvent effect of the order: benzene ≫ dioxane ~ alcohols. Retardation by alcohols as well as ethers is responsible for the formation of hydrogen-bonding dimer VI.

Mechanism A cannot explain the observed acceleration by various alcohols for the PBA oxidation of imines (Table IB and Figure 2), since the same dimer formation of peracid (VI) is known only to retard the reactions of peracid with many nucleophiles as mentioned above.[16a] On the other hand, the acceleration by alcohols may be explained by mechanism B, where the addition of PBA to C=N is effectively catalyzed by hydrogen bonding between C=N and protic solvents (III, eq 6). The presence of excess alcohol should cause the formation of VI, resulting in lowering the nucleophilicity of PBA as will be discussed in the next section. The retardation by basic solvents such as acetonitrile, dioxane, and DMF seems to be due to two factors, *i.e.*, the formation of VI and the decrease of acidity of the media to decrease the concentration of III, both retarding the acid-catalyzed addition of PBA to C=N.

(iii) Substituent effect for the PBA oxidation of *N*,*N*-dimethylaniline (DMA) is practically invariant with solvents, *i.e.*, ρ -2.40 in benzene and -2.14 in ethanol.[12] In contrast, the substituent effect for the oxidation of imines changes with reaction conditions (Table III).

This discrepancy cannot be understood by the interaction between PBA and HA according to mechanism A. Mechanism B can explain the apparently complex effect of substituents by assuming an interaction between C=N and HA (eq 6). That is, the hydrogen-bonding equilibrium (eq 6) is an important factor to determine the overall rate at low concentration of HA as in benzene and dioxane, affording negative ρ values. In the presence of an adequate amount of HA (*e.g.*, EtOH), the equilibrium (eq 6) should shift to the right[16b] and hence [III] is nearly constant with changing substituents. A compensation to lead to $\rho \sim 0$ may be operating between the strength of hydrogen bonding in III ($\rho < 0$) and the susceptibility of III to the nucleophilic attack of PBA ($\rho > 0$).[18a]

(iv) Two reported reactions of imines, *N*-benzoylimines[8] and an aliphatic imine,[9] have been clearly shown to go by way of the two-step (Baeyer–Villiger type) mechanism. These can be explained only by mechanism B.

(v) The assumption of mobile equilibrium for addition of peracid to C=N (eq 7) does not to explain the observed catalysis by carboxylic acids and alcohols because these catalyses are not observed for electrophilic reactions of peracid as noted in i and ii. This leads to an assumption of rate-determining addition of PBA to C=N (eq 7 in mechanism B) in most cases, which is also supported by the other consideration.[18b]

(vi) The change of the solvent deuterium effect from $k_H/k_D = 1.06$–1.14 ($<2\%$ EtOH) to 1.00 ($>5\%$ EtOH) seems to reflect the similar intervention of the preliminary equilibrium to form III (eq 6) as mentioned in item iii. That is, *ca.* 10% isotope effect may be observed when [III] is important, while there is no effect after the equilibrium shift to the right, *i.e.*, $[\mathrm{III}] \simeq [\mathrm{C{=}N}]_0$.

So far, the reaction of nucleophiles with peracid and peracid-d_1 was reported to exhibit the isotope effect of $k_H/k_D = 1.1$–1.3,[19] and a nucleophilic addition of PBA

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[13] (a) A. G. Davies, "Organic Peroxides," Butterworths, London, 1961, p 137; (b) R. Curci and J. O. Edwards, "Organic Peroxides," Vol. I, D. Swern, Ed., Wiley, New York, N. Y., 1970, p 236.

[14] (a) D. Swern, ref 13b, p 435; (b) W. V. F. Brooks and C. M. Haas, *J. Phys. Chem.*, 71, 650 (1967). (c) The results by Madan and Clapp[4] indicate that the plots of k_{obsd} *vs.* [HA] approach a limiting value in the presence of ~0.1 *M* *m*-ClPBA or *m*-ClBA. According to mechanism A, this should be explained by nearly complete formation of dimer (eq 4), which has been disproved by ir study.[14a]

[15] (a) R. Curci, R. A. DiPrete, J. O. Edwards, and G. Modena, *J. Org. Chem.*, 35, 740 (1970); (b) R. Kavčič and B. Plesničar, *ibid.*, 35, 2033 (1970).

[16] (a) An alternative explanation according to mechanism A is based on entropy factors of solvents. However, this must explain the two adverse effects on one reaction (eq 5) with the sole species (II), which is quite unnatural. Moreover, the solvent effect of PBA oxidation of *p*-ClDMA (Table IB) shows that the reactivity of VI for the one-step oxidation is independent of the structure, *i.e.*, the steric factor of AH (dioxane and alcohols). (b) Imines, >C=NR, are strong bases whose pK_a's are less than those of the parent amines, $\mathrm{RNH_2}$, only by 2–3 pK_a units. For example, the pK_a of the conjugate acid of benzylidene-*tert*-butylamine is 6.70 in water.[17]

[17] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, **85**, 2843 (1963).

[18] (a) This compensation is often observed for nucleophilic additions to C=O and C=N.[7] (b) The PBA oxidation of DMA (pK_a = 4.85) exhibits $k_{\text{obsd}} = 15\ M^{-1}\ \text{sec}^{-1}$ and ρ -2.40 (σ) in benzene at 25°.[12] These values lead to $k_{\text{calcd}} = 10^{13}$–$11^{15}\ M^{-1}\ \text{sec}^{-1}$ for the substituted DMA's with pK_a of 9–10. In fact, the rate for the PBA oxidation of triethylamine (pK_a = 10.9) was too fast to measure ($k_{\text{obsd}} > 10^3\ M^{-1}\ \text{sec}^{-1}$). Hence the nucleophilic internal substitution (SNi) reaction of IV (eq 8) should be very fast, since the assumed pK_a of the conjugate acid of IV is probably *ca.* 9–10; *i.e.*, the rate-determining step is eq 7.

[19] (a) The deuterium isotope effect (k_H/k_D) is 1.15 for *p*-nitroaniline in water: K. M. Ibne-Rasa and J. O. Edwards, *J. Amer. Chem. Soc.*, **84**, 763 (1962). (b) k_H/k_D = 1.33 for diphenyldiazo-

itself to C=O has also the same magnitude of the effect.[20a] The isotope effect for the imine oxidation is complicated by the formation of several kinds of hydrogen bondings, *e.g.*, III, V, and VI, and the addition reaction (eq 7); hence it is inadequate to derive an explicit conclusion only from this apparent isotope effect.

(vii) Optically active oxaziranes have been obtained by the reaction of imines with optically active peracids[11] as well as an asymmetric epoxidation.[21a] Asymmetric epoxides, however, were also produced by the tungstate-catalyzed epoxidation of α,β-unsaturated esters with alkaline hydrogen peroxide which involves a SNi reaction of the Michael-type adducts.[21] This shows that the SNi reaction such as eq 8 may also lead to an asymmetric reaction.[22] Thus, the selection of mechanism A or B is difficult on the basis of the formation of asymmetric oxaziranes. However, the stereochemistry of the oxazirane formation suggested a suspicion on mechanism A.[11d]

In conclusion, the available data can be reasonably explained only by mechanism B, but not by mechanism A. The slow step is the addition of PBA to C=N in most cases and the rate equation is simply written as[23]

$$v = k_{HA}[HA][C{=}N][PBA] \qquad (9)$$

Here, HA is ROH, AcOH, PBA, and so on. The apparent complexities of the kinetic data are derived from two kinds of interaction of HA: the rate-accelerating interaction of C=N with HA (as acid) and the rate-reducing action of HA as base.

Addition of PBA to C=N. Additions of various nucleophiles to C=N are facile reactions[6] and very susceptible to acid catalysis.[7] Most mechanistic studies are done in aqueous media and the mechanism in organic solvents is obscure.[24]

The catalytic constants, k_{HA}, for the acid-catalyzed addition of PBA to imine I (eq 9) are summarized in Table IV. The observed order is *t*-BuOH < *i*-PrOH < EtOH < AcOH < MeOH < PBA < ClAcOH, which is not the order of acidity (*e.g.*, ROH ≪ PBA < AcOH). The observed acid catalysis is of a general acid type, since a linear relationship was obtained for the plots of k_{obsd} *vs.* [HA] and the k_{HA} values are dependent on neither acidity of HA nor polarity of the media. In fact, the uv spectra of I show no indication for the conversion to its conjugate acid under these oxidation conditions,[25] although the basicity of I is fairly high (pK_a = 5.4 in water).[17]

Table IV. Summary of the Catalytic Constant, k_{HA}, for the PBA Oxidation of I in Benzene at 20.0 ± 0.5°

HA	Concn range, *M*	pK_a	k_{HA},[a] M^{-2} sec^{-1}
$ClCH_2CO_2H$	0–0.1	2.87	126
CH_3CO_2H	0–0.5	4.76	5.5
MeOH	0–0.3	16[b]	6.3
EtOH	0–0.2	18[b]	5.0
i-PrOH	0–0.2	18[b]	3.4
t-BuOH	0–0.2	19[b]	1.8
PBA	0.002–0.04	8.1	~35

[a] Catalytic constants, k_{HA}, were obtained from the plot of k_{obsd} *vs.* [HA]; *i.e.*, $k_{obsd} = k_0 + k_{HA}[HA]$, and k_0(M^{-1} sec^{-1}) is the intercept and close to zero. [b] The values in benzene: D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, p 4.

The similar catalytic constants have been obtained by Madan and Clapp for substituted benzoic acids to afford ρ 0.13 in dioxane and ρ 0.22 in *tert*-butyl alcohol. These results together with the data in Table IV suggest that the Brønsted relationship might be satisfied for a similar type of HA, *e.g.*, RCO_2H or ROH in spite of low α values, but that the present addition (eq 7) exerts a leveling effect on acidity and is governed equally by other factors, *e.g.*, steric retardation.

In the preceding section (item ii), we assumed that the nucleophilicity of PBA may be higher in V than in VI. So far, the enhancement by chelation (V) has been emphasized only for the electrophilic reaction of peracid. But the same acceleration may be possible for the nucleophilic attack of peracid. Such a case has been observed for the addition of PBA to C=O, the solvent effect being in the order: dioxane < MeCN < benzene.[20b] The similar effect of solvents is also observed for the PBA oxidation of ketones and aldehydes.[10,12] Hence, the retardation by some alcohols for the imine oxidation is due to the decreased nucleophilicity of PBA by forming intermolecular hydrogen bonding (VI).

A shift of a rate-determining step from the addition to migration step has been demonstrated for the Baeyer–Villiger reaction.[10] A similar shift for the present oxidation of imine seems to be shown in the plots of k_{obsd} *vs.* [HA] (Figure 1). That is, the observed curvature in the presence of 20% EtOH reflects the change of a slow step from the addition (eq 7) to the SNi reaction of the adduct (eq 8). Madan and Clapp[4] noted the similar data; the order in HA changed from first order to zero order at 0–0.1 *M* *m*-ClPBA or *m*-chlorobenzoic acid. Although they interpreted the shift by the interaction of HA with peracid (mechanism A), an alternative explanation (mechanism B) by the change of a rate-determining step is more appropriate as discussed above. In fact, a rate-determining SNi reaction of the C=N adduct is shown in the PBA oxidation of cyclic

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methane in benzene: R. Curci, F. Di Furia, and F. Marcuzzi, *J. Org. Chem.*, 36, 3774 (1971). (c) k_H/k_D = 1.09 for styrene and cyclohexene in benzene.[12]

(20) (a) The deuterium isotope effect (k_H/k_D) is 1.10 for the C=O addition of PBA to 2,4-dinitrophenyl acetate in benzene–DMF. (b) The solvent effect for the same reaction[20a] exhibits that the nucleophilicity of PBA is in the order of V > VI. This is explicable by the steric hindrance of AH for the nucleophilic attack of VI to C=O as is the case for other additions to C=O. The order of V > VI for the electrophilicity of PBA is well known and probably due to two kinds of accelerating factors, electronic and steric. Accordingly, a good electrophile can be a good nucleophile for the case of peracid. The enhancement of nucleophilicity of PBA by a basic solvent B according to an equilibrium, $PBA + B \rightleftarrows PBA^- + BH^+$, seems to be unlikely in these organic solvents, since basic solvents have only a retarding effect and an increase of solvent polarity by adding acetonitrile has no effect on the rate; *i.e.*, PBA^- is not an effective nucleophile in organic solvents because of its low concentration.

(21) (a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, N. J., 1971, p 258; (b) H. Igarashi and H. Midorikawa, *Bull. Chem. Soc. Jap.*, 40, 2624 (1967).

(22) This possibility is natural, since the most favored configuration of the C=N adduct (IV) should exist as a result of interaction of the acyl component from peracid with three substituents from imine.

(23) Autocatalysis was not observed, since most kinetic runs were carried out in the presence of excess HA in comparison to C=N and since PBA itself is an efficient catalyst (Table IV).

(24) The addition of HCN to benzylideneanilines in methanol: Y. Ogata and A. Kawasaki, *J. Chem. Soc. B*, 325 (1971).

(25) Generally, solvent effects are large on going from water to organic solvents. For example, the pK_a (*i.e.*, basicity) of the conjugate acid of aniline decreases from 4.6 in water to −0.1 in ethanol, while the pK_a of acetic acid increases from 4.2 in water to 7.2 in ethanol: H. Jaffé, *Chem. Rev.*, 53, 191 (1953).

imines.[26] These kinetic aspects resemble those of the Baeyer–Villiger oxidation which shows likewise the change of the order in HA together with the complexities of the apparent ρ values.[10] The most distinct difference between the C═N and the C═O additions lies in the relative susceptibilities to acid catalysis, reflecting the large difference in basicity between C═N and C═O ($\Delta pK_a \sim 12$–14).

Nitrone Formation. Nitrones are formed directly by the reaction of C═N with PBA, since the produced oxaziranes and nitrones are stable under the reaction conditions. The nitrone formation is favored by the electron-donating substituents in the imines and by aprotic solvents, the order being dioxane > benzene ≫ *t*-BuOH > EtOH. This solvent effect seems to show that the selectivity for the nitrone increases, when the addition of PBA to C═N is slowed down.

The approximate rate constants for the nitrone formation (k_{obsd} × nitrone selectivity) exhibit a large substituent effect, suggesting a negative ρ value. The effect of solvents on the rate is in the order: benzene ≫ dioxane ∼ alcohols. These kinetics resemble those for the peracid oxidation of olefins, amines, and sulfides, suggesting the similar mechanism. The details of this problem will be discussed in our next paper.[26]

Experimental Section

All melting and boiling points were not corrected. Uv spectra were measured by a Model 124 Hitachi spectrophotometer using 1.0-cm quartz cells. Nmr spectra were measured at room temperature with a JNM-C60-HL (Japan Electron Optics).

Materials. PBA was synthesized as previously noted.[10] Solvents were purified by fractional distillations. Substituted benzylidene-*tert*-butylamines were obtained from benzaldehydes and *tert*-butylamine.[17] Their substituents and boiling points (or melting points) are as follows: *p*-MeO, 141–143° (18 mm) [lit.[17] 110–113° (2.1 mm)]; H, 117–119° (36 mm) [lit.[17] 63–64° (1.0 mm)]; *p*-NO_2, mp 76.5–78.1° (lit.[17] 72–75°). Ethanol-d_1 was obtained by adding D_2O to dry EtONa in ether and distilled repeatedly.

Rates and Products Determinations. The rates of PBA oxidation of the imine were determined directly in an optical cell by following the decrease or increase of the absorbance at 300–340 nm. Usually excess PBA was used, and k_{obsd} was calculated by dividing the resulting pseudo-first-order rate constant by [PBA] according to eq 3.

The yield of oxazirane was determined by the following iodometry. The reaction mixture was added to EtOH (5 ml)–AcOH (5 ml)–dimethyl sulfoxide (2 ml) and allowed to stand for *ca.* 5 min to consume the remaining peracid. Then, aqueous KI (2 ml) and, after standing a few minutes, water (50 ml) were added, and the liberated iodine was titrated by aqueous $Na_2S_2O_3$.

The nitrones were determined by uv spectrophotometry; X in $XC_6H_4CH{=}N(O)$-*t*-Bu, λ_{max} (ϵ) in ethanol: *p*-MeO, 305 (20,400); H, 295 (16,700)[1]; *p*-Cl, 298 (22,650);[27] *p*-NO_2, 362 (15,800).[1]

α-(p-Methoxyphenyl)-N-*tert*-butylnitrone. To obtain pure oxazirane or nitrone, peracetic acid was used in place of PBA, since PBA was not appropriate because of the contamination of a trace of benzoic acid. Thus, *p*-methoxybenzylidene-*tert*-butylamine (2.0 g, 10.4 mmol) and peracetic acid (10.4 mmol) were allowed to react in toluene (40 ml)–EtOH (10 ml) at room temperature for 1 hr. After being washed twice with water and aqueous $NaHCO_3$ and dried over Na_2SO_4, the toluene solution of oxazirane was heated at 110° for 4 hr. The solvent was evaporated under reduced pressure. The resulting light yellow liquid was crystallized from ether–petroleum ether at −20° to afford 1.45 g (67%) of the titled nitrone, mp 96.2–97.3°; uv 305 nm (ϵ 20,400) in EtOH, 308 (19,400) in benzene; nmr (60 MHz, CCl_4 *vs.* TMS) δ 8.15 (2 H, d, J = 8.4 Hz, *o*-H), 7.29 (1 H, s, CH=N(O)), 6.79 (2 H, d, J = 8.4 Hz, *m*-H), 3.78 (3 H, s, CH_3O), 1.52 (9 H, s, *t*-Bu).

Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.5; H, 8.29; N, 6.76. Found: C, 67.0; H. 8.24; N, 7.0.

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[26] Y. Ogata and Y. Sawaki, *J. Amer. Chem. Soc.*, **95**, 4692 (1973).

[27] The data of Me in place of *t*-Bu: T. Kubota, M. Yamakawa, and Y. Mori, *Bull. Chem. Soc. Jap.*, **36**, 1552 (1963).

Peracid Oxidation of Imines. Kinetics and Mechanism of Competitive Formation of Nitrones and Oxaziranes from Cyclic and Acyclic Imines

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Abstract: The reaction of 3,4-dihydroisoquinoline (IIa) and 3,4-dihydro-1-methylisoquinoline (IIb) with perbenzoic acid (PBA) has been shown to give nitrones as well as reported oxaziranes, their selectivities changing with reaction conditions. The direct formation of nitrones is apparent irrespective of the imine structure, acyclic or cyclic. Generally, the oxazirane formation is predominant in the presence of alcohols or carboxylic acids, while the yield of nitrones increased in aprotic media. The kinetic study suggests that the oxazirane formation proceeds *via* a two-step mechanism similar to the Baeyer–Villiger reaction, and that a rate-determining step for PBA oxidation of the cyclic imines is generally a SNi reaction of the C═N adduct, contrary to the case of acyclic imines. On the other hand, the nitrone formation is a nucleophilic attack of N lone-pair electrons of C═N on peracid oxygen. The rate constants of nitrone formation in benzene at 25° are 0.52 M^{-1} sec^{-1} for IIa and 2.0 M^{-1} sec^{-1} for IIb, which are considerably smaller in comparison to that of an amine with the same pK_a value.

Although facile additions of various nucleophiles to C═N are well known,[1,2] reported nucleophilic reactions of C═N itself are rather limited to acyl and alkyl halides,[1] where a reaction site is the N lone-pair electrons of imine. One exception is the reaction of C═N with peracids to form oxaziranes; Emmons[3] postulated

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[1] R. W. Layer, *Chem. Rev.*, **63**, 489 (1963).

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

[3] (a) W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 5739 (1957); (b) W. D. Emmons, *Chem. Heterocycl. Compounds*, **19**, 630 (1964).