

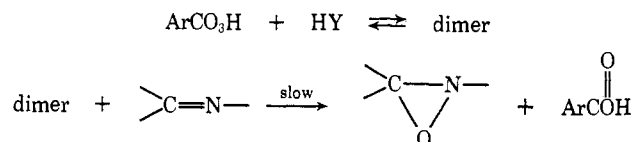
Mechanism of Oxidation of Schiff Bases to Oxaziranes by Peroxy Acids. II. In Aprotic Solvents¹

Vershal Madan and Leallyn B. Clapp

Contribution from the Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island 02912. Received January 26, 1970

Abstract: The oxidation of *N-p*-nitrobenzal-*t*-butylamine (II) with *m*-chloroperoxybenzoic acid in the aprotic solvents methylene chloride and dioxane gave a kinetic law suggesting a nucleophilic attack by the Schiff base on a peroxy acid dimer. We suggest a five-membered ring for the dimer in the transition state.

The mechanism for the oxidation of Schiff bases ($>C=N-$) with peroxybenzoic acids in *t*-butyl alcohol was proposed as follows,² where HY denotes a



solvent, benzoic acid (product), or another molecule of peroxy acid. Due to the complex kinetic behavior and to detect whether a dimer of peroxy acid is an attacking species in the oxidation, the kinetics of oxidation in aprotic solvents was studied.

The system chosen was the oxidation of *N-p*-nitrobenzal-*t*-butylamine (II) with *m*-chloroperoxybenzoic acid (MCPBA) in methylene chloride and dioxane. On a preparative scale the oxazirane IV was isolated from methylene chloride in 95% yield and from dioxane in 92% yield.

Experimental Section

Materials. Spectral grade methylene chloride was used directly. Dioxane was purified by the method of Hess and Frahm.³ Other materials were obtained and purified as described previously.²

Kinetic Technique and Product Analysis

The rates of oxidation of the Schiff base in aprotic solvents were measured² by the rate of disappearance of Schiff base as determined by spectrophotometry at 325–358 μ , depending on concentration. The uv spectra were compared with those of solutions (10^{-5} *M*) of authentic samples of the oxazirane in dioxane or methylene chloride to determine that the oxidation was quantitative.

Pseudo-first-order rate constants were calculated by the integrated form of the differential equation

$$dx/dt = k_{\text{obsd}}(a - x) \quad (1)$$

where *a* denotes the initial concentration of Schiff base, II, *x* is the amount of oxazirane formed at time "*t*," and $k_{\text{obsd}} = k[\text{MCPBA}]^n$. Difference in absorbancy ($A_t - A_\infty$) at time "*t*" was taken as a measure of the unreacted amount of II at that time. The plots of $\ln(A_t - A_\infty)$ vs. time were linear to over three half-lives. The k_{obsd} values were calculated from the slope of the lines.

(1) Supported in part by Public Health Service Grant No. CA-07521 and Atomic Energy Commission Grant No. AT(30-1) 1983.

(2) V. Madan and L. B. Clapp, *J. Amer. Chem. Soc.*, **91**, 6078 (1969).

(3) K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).

Second-order rate constants were calculated by the integrated form of the differential rate equation

$$dx/dt = k_2(a - x)(b - x) \quad (2)$$

where all notations have their usual meanings. The values of *x* at time "*t*" were calculated by the help of eq 3 at time "*t*" where ϵ_R and ϵ_P are extinction coefficients for Schiff base (II) and oxazirane (IV), respectively.

$$A_t = \epsilon_R(a - x) + \epsilon_P x \quad (3)$$

Results

Kinetic Law. The linearity of the pseudo-first-order plots indicates that the reaction is first order with respect to II. The dependence of the pseudo-first-order rate constants on the initial concentrations of the reactants was also studied for the oxidation of II. The pseudo-first-order rate constant was found to be independent of the initial concentrations of II, when varied by a factor of two (Table I), but it varied linearly at

Table I. Pseudo-First-Order Rate Constant for the Oxidation of II with MCPBA^a

MCPBA, mol/l. $\times 10^3$	[Schiff base, II], mol/l. $\times 10^4$	$k_{\text{obsd}} \times 10^4$, sec ⁻¹
89.00	10.00	267
80.00	10.00	236
70.00	10.00	208
60.00	10.00	165
50.00	10.00	127
43.75	10.00	111
37.50	10.00	91.8
31.25	10.00	73.8
25.00	10.00	55.1
20.00	10.00	39.5
17.55	10.00	32.1
15.00	10.00	27.2
12.50	10.00	21.2
10.00	10.00	16.0
10.00	8.00	15.8
10.00	6.00	16.0
10.00	5.00	15.5
8.75	5.00	12.3
7.50	5.00	9.97
6.25	5.00	8.17
5.00	5.00	4.83
4.38	3.12	3.99
3.75	3.12	3.22
3.25	3.12	2.84
2.50	2.50	1.74
1.25	12.50	0.572

^a In dioxane at $25.0 \pm 0.2^\circ$.

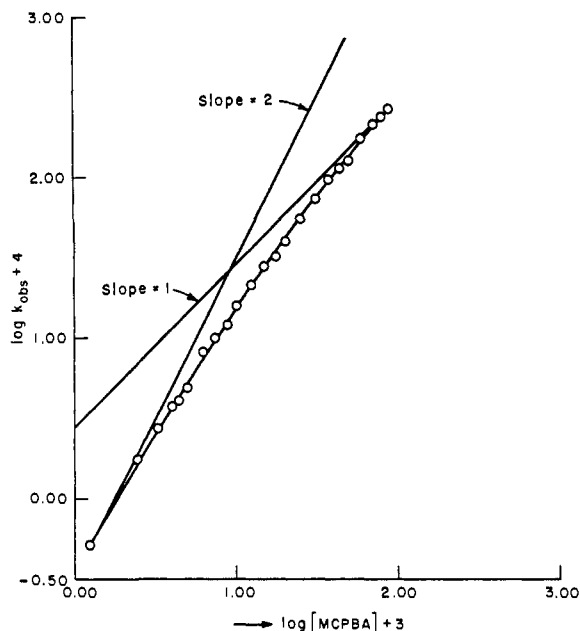


Figure 1. Order with respect to *m*-chloroperoxybenzoic acid for the oxidation of *N*-*p*-nitrobenzal-*t*-butylamine with peroxy acid in dioxane at $25.0 \pm 0.2^\circ$.

high initial concentration and with the square at low initial concentration of *m*-chloroperoxybenzoic acid (Table I and Figure 1), in contrast to the behavior in protic solvents.²

In a kinetic run in dioxane, the initial concentrations of II and the MCPBA were $5.00 \times 10^{-3} M$ in each reactant. A nonlinear $1/(a-x)$ vs. time plot was observed. In another kinetic run in dioxane with large excess of MCBA, the initial concentrations of II, MCPBA, and *m*-chlorobenzoic acid (MCBA) were $5.00 \times 10^{-3} M$, $5.00 \times 10^{-3} M$, and $1.00 \times 10^{-1} M$, respectively. A plot of $1/(a-x)$ vs. time was linear to over 80% reaction. The second-order rate constant calculated from the slope of this plot was equal to $66.6 \times 10^{-2} \text{ l. mol}^{-1} \text{ sec}^{-1}$ (Table II) which agrees well

Table II. Values of $K''k_3''/[\text{SH}]^n$ for the Oxidation of II with MCPBA^b

[MCPBA], M $\times 10^2$	[II], M $\times 10^3$	[MCBA], M $\times 10^1$	$K''k_3''/[\text{SH}] \times 10^1$, l. mol ⁻¹ sec ⁻¹
8.90	1.00		3.00
8.00	1.00		2.95
7.00	1.00		2.97
0.50	0.50	0.90	6.30
0.50	0.50	1.00	6.30
0.50	5.00	1.00	6.66
0.40	4.00	1.00	6.68
0.25	2.50	1.00	6.57

^a [SH], the concentration of monomer MCPBA or MCBA.

^b In dioxane at $25.0 \pm 0.2^\circ$.

with the value ($63.0 \times 10^{-2} \text{ l. mol}^{-1} \text{ sec}^{-1}$) calculated from the pseudo-first-order rate constant (Table II). It was thus demonstrated that the oxidation obeys the second-order kinetic law in the presence of a large excess of MCBA.

The effect of added *m*-chlorobenzoic acid on the rate of oxidation in dioxane was measured under pseudo-

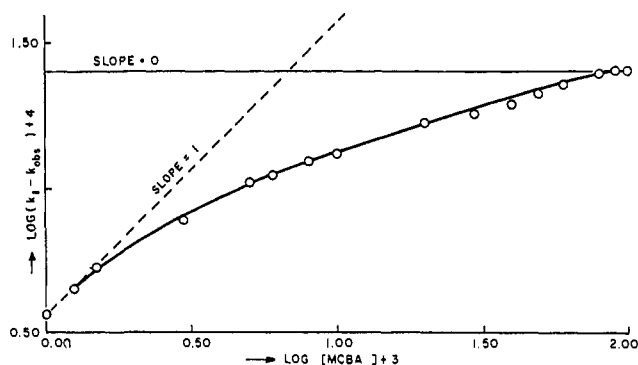
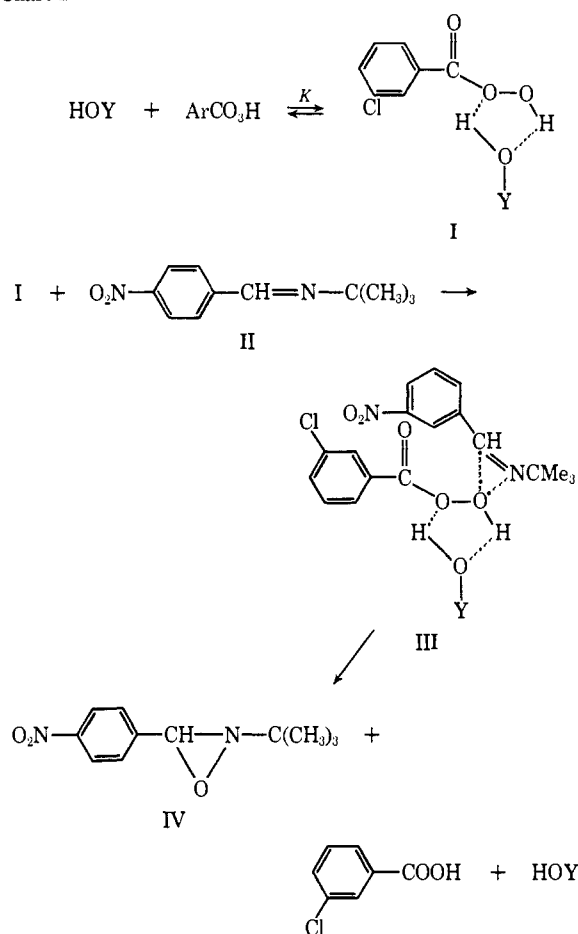


Figure 2. Order with respect to *m*-chlorobenzoic acid for the oxidation of *N*-*p*-nitrobenzal-*t*-butylamine with *m*-chloroperoxybenzoic acid in dioxane at $25.0 \pm 0.2^\circ$.

first-order conditions, using MCPBA in excess over II. The rate of oxidation increased appreciably at first but then leveled out. The order of the reaction with re-

Chart I



spect to *m*-chlorobenzoic acid was determined by plotting $\log(k_1 - k_{\text{obsd}})$ against $\log[\text{MCBA}]^4$ (Figure 2 and Table III). The oxidation rate was found to vary linearly at low initial concentration and to be independent of concentration at high initial concentration of

(4) The rate of oxidation is given by $k_1 = k_{\text{MCBA}}[\text{MCBA}]^n + k_{\text{MCPBA}}[\text{MCPBA}]^m$. Let $k_{\text{obsd}} = k_{\text{MCPBA}}[\text{MCPBA}]^m$. Then $k_1 = k_{\text{MCBA}}[\text{MCBA}]^n + k_{\text{obsd}}$ and $k_1 - k_{\text{obsd}} = k_{\text{MCBA}}[\text{MCBA}]^n$; $\log(k_1 - k_{\text{obsd}}) = \log k_{\text{MCBA}} + n \log[\text{MCBA}]$.

Table III. Kinetic Data for the Oxidation of II^a with MCPBA^{b,c}

[MCBA], <i>M</i> × 10 ³	<i>k</i> ₁ × 10 ⁴ , sec ⁻¹	(<i>k</i> ₁ - <i>k</i> _{obsd}) × 10 ⁴ , sec ⁻¹
100.00	31.3	26.47
90.00	31.3	26.47
80.00	29.7	24.87
60.00	27.6	22.77
50.00	26.1	21.27
40.00	24.2	19.37
30.00	22.9	18.07
20.00	21.7	16.87
10.00	18.0	13.17
8.00	17.3	12.47
6.00	16.0	11.17
5.00	15.5	10.67
3.00	12.5	7.67
1.50	10.2	5.37
1.25	9.40	4.57
1.00	8.55	3.72
0.00	4.83	0.00

^a [II], 5.00 × 10⁻⁴ *M*. ^b [MCPBA], 5.00 × 10⁻³ *M*. ^c In the presence of added MCBA in dioxane at 25.0 ± 0.2°.

MCBA. Therefore the overall observed rate law appears to be

$$\frac{-d[\text{II}]}{dt} = Kk_3 \frac{[\text{II}]_0[\text{MCPBA}]_0^2}{1 + K[\text{MCPBA}]_0} + K'k_3' \frac{[\text{II}]_0[\text{MCPBA}]_0[\text{MCBA}]_0}{1 + K'[\text{MCPBA}]_0} \quad (4)$$

p*K*_a Effect. Substituted benzoic acids have a small effect on the rate of oxidation of Schiff base II into oxazirane IV (Table IV). A linear relation between

Table IV. Kinetic Data for the Oxidation of II^a with MCPBA^b in the Presence of Substituted Benzoic Acids^c

Substituted benzoic acids, <i>X</i>	<i>k</i> ₁ × 10 ³ , sec ⁻¹
<i>m</i> -Cl	6.48
H	5.74
<i>p</i> - <i>t</i> -Bu	5.47
<i>p</i> -OCH ₃	5.33

^a [II], 5.00 × 10⁻⁴ *M*. ^b [MCPBA], 5.00 × 10⁻³ *M*. ^c [BH], substituted benzoic acid, 1.00 × 10⁻² *M*; in dioxane at 25.0 ± 0.2°.

log *k*₁ vs. Hammett σ values was observed, which displays a small, positive ρ value (0.13). The catalytic activity of MCPBA (p*K*_a = 7.5 in H₂O) is approximately equal to that of the substituted benzoic acid² (Table V).

Table V. Pseudo-First-Order Rate Constants for the Oxidation of II with MCPBA Acid at Various Concentrations of Peroxy Acid^a

[MCPBA], <i>M</i> × 10 ²	[SB], <i>M</i> × 10 ⁴	<i>k</i> _{obsd} , sec ⁻¹ × 10 ³
5.00	5.00	5.01
7.00	5.00	8.47
8.00	5.00	11.5
9.00	5.00	12.1
10.0	5.00	15.1
5.00 ^b	2.50	5.46
5.00 ^b	3.50	5.23
5.00 ^b	4.50	5.45
5.00 ^b	5.00	5.45

^a In methylene chloride at 25.0 ± 0.2°. ^b An impure acid was used, 89.5 ± 1.0%.

Thus the overall rate law may be approximated as

$$\frac{-d[\text{II}]}{dt} = K''k_3'' \frac{[\text{II}]_0[\text{MCPBA}]_0[\text{MCPBA} + \text{MCBA}]}{1 + K''[\text{MCPBA} + \text{MCBA}]_0} \quad (5)$$

where MCBA may also be substituted by other benzoic acids. Equation 5 can be converted into a differential rate equation of the form (eq 6)

$$dx/dt = k_4(a - x)(b - x) \quad (6)$$

where

$$k_4 = K''k_3''(b + c)/[1 + K''(b + c)] \quad (7)$$

and *a*, *b*, and *c* are the initial concentrations of II, MCPBA, and MCBA. Equation 6 explains the (1) failure to observe an autocatalytic behavior under pseudo-first-order conditions and (2) linear plots even when MCBA is not present in excess over Schiff base.

Effect of Radical Trap. The rate of oxidation of II (2.50 × 10⁻⁴ *M*) with MCPBA (3.00 × 10⁻³ *M*) in dioxane was measured in the presence of diethyl fumarate, an efficient radical trap.⁵ No effect on the rate of oxidation was observed.

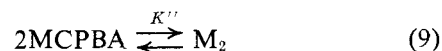
In Methylene Chloride. Similar kinetic behavior was observed in the oxidation of II by MCPBA in methylene chloride. The kinetic order was 1.5 with respect to MCPBA at intermediate concentration (Table V) and first order with respect to II (Table V). Acid catalysis was observed and the reaction was shown not to involve a free radical by adding diethyl fumarate.

Discussion

Essentially the same mechanism proposed in aprotic solvents² can be applied here but the kinetics are complicated by a monomer-dimer equilibrium of the peroxyacid. Spectral evidence⁶ is available to suggest that a hydroperoxide forms a dimer as a six-membered ring in aprotic solvents but more recently⁷ a five-membered ring has been suggested as a possibility for the hydrogen-bonded species in protic solvents as well. Kinetic data in the present work suggested that the five-membered ring (I) may be a more appropriate structure (in concentrated solution) in *m*-chloroperoxybenzoic acid oxidations in aprotic solvents where HOY is another molecule of MCPBA or MCBA. The catalytic oxidation of the C=N bond with MCPBA in aprotic solvents is complicated to some extent by the peroxy acid monomer-dimer equilibrium. This may be seen in the rate law (eq 5). At high initial concentration of MCPBA and absence of MCBA the rate law would reduce to eq 8 as was found. In the absence of

$$\frac{-d(\text{II})}{dt} = k_3''[\text{II}]_0[\text{MCPBA}]_0 \quad (8)$$

MCBA if we assume a monomer-dimer equilibrium is involved (eq 9), then the following relationship will hold,



(5) C. G. Swain, W. H. Stockmayer, and J. T. Clark, *J. Amer. Chem. Soc.*, **72**, 5426 (1950).

(6) C. Walling and L. Heaton, *ibid.*, **87**, 48 (1965).

(7) M. A. P. Dankleff, R. Curci, J. O. Edwards, and H.-Y. Pyun, *ibid.*, **90**, 3209 (1968), and other references cited here.

where [MCPBA], [M], and [M₂] are the concentrations of MCPBA, monomer, and dimer, respectively. If at

$$[\text{MCPBA}]_0 = [\text{M}] + [\text{M}_2] \quad (10)$$

high initial concentrations of MCPBA the dimeric form predominates then

$$[\text{MCPBA}]_0 \cong [\text{M}_2] = K''[\text{M}]^2$$

and eq 8 becomes eq 11

$$\frac{-d[\text{II}]}{dt} = K''k_3''[\text{II}][\text{M}]^2 \quad (11)$$

In a large excess of MCBA and low concentration of MCPBA eq 5 can be converted to eq 12.

$$\frac{-d[\text{II}]}{dt} = K''k_3''[\text{II}][\text{M}][\text{MCBA}] \quad (12)$$

The value of $K''k_3M$ calculated from eq 11 ($3.00 \times 10^{-1} \text{ l. mol}^{-1} \text{ sec}^{-1}$, Table II) and the value of $K''k_3'' \cdot [\text{MCBA}]_0$ from eq 12 ($6.30 \times 10^{-1} \text{ l. mol}^{-1} \text{ sec}^{-1}$, Table II) should be very nearly the same because pK_a has very little effect on the rate of oxidation, *i.e.*, catalytic activity of peroxy acids is nearly the same as that of the product benzoic acids formed in the oxidation.² But the experimental value of $K''k_3''[\text{M}]$ is less by a factor of two. We account for the experimental result by the following assumption. The effective concentration of the electrophile (peroxy acid) is reduced to one-half by dimer formation (M₂) before much benzoic acid is formed while the concentration of electrophile is unaffected when the dimer consists of peroxy acid-benzoic acid. Furthermore, the structure of the peroxy acid-peroxy acid dimer is a five-membered ring (I) where HOY is the second molecule of peroxy acid. If the dimer were a six-membered ring, there would be two peroxy oxygens susceptible to nucleophilic attack. Hence, this factor should annul the effect of dimer formation, but this was not found to be the case experimentally. Therefore, to account for the fact that $K''k_3''[\text{MCBA}]$ is twice $K''k_3''[\text{M}]$, the five-membered ring is suggested.

The argument leads to an observed reaction order of two at low concentration and one at high concentration with respect to MCPBA and one to zero order with respect to MCBA. The overall observed rate law is compatible with the mechanism⁸ pictured in Chart I. Experimental evidence that the rate of oxidation is twice as fast in the presence of a large excess of MCBA than in a large excess of MCPBA indicates that the dimer of the peroxy acid is an attacking species.

As in the similar reaction in *t*-butyl alcohol, the addition of a stronger acid as compared to *t*-butyl alcohol should catalyze the oxidation by performing the function of HOY more efficiently. It has been observed² that MCBA (a much stronger acid than *t*-butyl alcohol) increases the rate of oxidation. The rate of increase due

(8) K. J. Laidler, Ed., "Chemical Kinetics," McGraw-Hill, New York, N. Y., 1950, pp 278-279.

to added MCBA is much more prominent in dioxane than in *t*-butyl alcohol, which can be explained by solvent acidity. The observed rate law in *t*-butyl alcohol has three terms.² Absence of the first term in the rate law

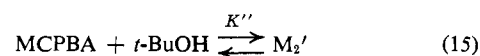
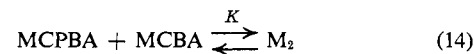
$$-d[\text{II}]/dt = k_0[\text{II}][\text{MCPBA}] + k_{\text{MCPBA}}[\text{II}][\text{MCPBA}]^2 + k_{\text{MCBA}}[\text{II}][\text{MCPBA}][\text{MCBA}]$$

in aprotic solvents indicates that *t*-butyl alcohol is involved in the oxidation as HOY (I). These observations rule out the mechanism similar to the peroxy acid cleavage of ketone.⁹ Therefore the oxidation of Schiff bases with peroxy acids should be considered as a nucleophilic attack of Schiff base on a peroxy acid dimer. Although the dimer appears to facilitate a necessary proton transfer in the transition state III there appears to be no sound explanation of why the dimer does this better than an internally hydrogen bonded peroxy acid monomer would (also a five-membered ring). Indeed, both intramolecular and intermolecular hydrogen bonding with solvent in a peroxy acid oxidation have just been suggested.¹⁰

The greater value of ρ for the substituted benzoic acids in *t*-butyl alcohol² (+0.22) than in dioxane (+0.13) is due to the simplicity of the rate law in *t*-butyl alcohol rather than to the ionizing power of the solvent. (This fact might lead to the suggestion that protonation of Schiff base is involved in the mechanism.) The rate law in *t*-butyl alcohol can be written in terms of equilibrium constants (eq 13), where K and

$$-d[\text{II}]/dt = k_0K[\text{II}][\text{MCPBA}] + kK''[\text{II}][\text{MCBA}][\text{MCPBA} + \text{MCBA}] \quad (13)$$

K'' are equilibrium constants for eq 14 and 15, respectively.



Equation 13 can be converted into a differential equation of the form

$$dx/dt = k_4(a - x)(b - x) \quad (16)$$

where the notations have the usual meanings. Then

$$k_4 = k_0K + kK''(c + b) \quad (17)$$

Equations 7 and 17 reflect the rate constants in dioxane and in *t*-butyl alcohol, respectively. Change in equilibrium constants would be reflected in the rate constants. Change will be more prominent in (17) than in (7) (*i.e.*, the rate constant in *t*-BuOH will be affected more than in dioxane) because eq 7 includes equilibrium constants in both numerator and denominator. Therefore, one would expect a greater value of ρ in *t*-butyl alcohol than in dioxane.

(9) M. F. Hawthorne and W. D. Emmons, *J. Amer. Chem. Soc.*, **80**, 6398 (1958).

(10) R. Curci, R. A. DiPrete, J. O. Edwards, and G. Modena, *J. Org. Chem.*, **35**, 740 (1970).