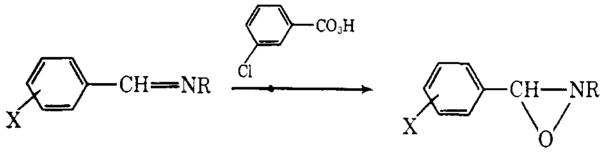
Mechanism of Oxidation of Schiff Bases to Oxaziranes by Peroxy Acids in Various Solvents[1]

Vershal Madan and Leallyn B. Clapp[2]

Contribution from the Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island 02912. *Received January 27, 1969*

Abstract: Hammett ρ values for peroxybenzoic acid oxidation of two series of Schiff bases, *para*-substituted N-benzal-*t*-butylamines and N-*p*-nitrobenzal-substituted benzylamines, were found to be -1.75 and -0.98, respectively. The ρ value for substituted peroxybenzoic acids as oxidizing agent was $+0.78$ and for substituted benzoic acids as catalyst was $+0.22$. The small solvent kinetic isotope effect, activation parameters in one case, along with the ρ values, suggested a concerted mechanism pictured as a nucleophilic displacement of the C=N bond of the Schiff base on the peroxy oxygen.

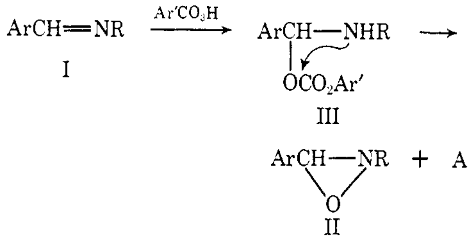
Peroxy acids oxidize Schiff bases I to oxaziranes II[3] in a reaction with external resemblance to the oxidation of alkenes to epoxides.[4] Peroxy acids also oxidize ketones to esters,[5] the Baeyer–Villiger reaction. It is well established that oxygen in the peroxy acid acts as an electrophile[6] in the oxidation of C=C and as a nucleophile in the Baeyer–Villiger oxidation of C=O.[7] Since nitrogen has an electronegativity (3.0) between carbon (2.5) and oxygen (3.5), it was not at all obvious how the peroxy acid might act toward the C=N bonding in Schiff bases. Emmons[3] had suggested the analogy to the oxidation of ketones at the time he reported the synthesis of oxaziranes. Bailey[8] described the ozonization of Schiff bases as a nucleophilic attack of ozone on the C=N bond. Edwards[9] predicted that the oxidation of C=N with peroxy acids would be nucleophilic displacement on oxygen through a cyclic transition state. Emmons[10] also mentioned the cyclic transition state or an alternative "addition of the peroxy acid to the Schiff base (I to give III) followed by internal nucleophilic displacement of the basic nitrogen atom on the peroxide bond" (to give II, Scheme I).



I II

a, X = H; R = t-C_4H_9
b, X = p-Cl; R = t-C_4H_9
c, X = p-OCH_3; R = t-C_4H_9
d, X = p-CH_3; R = t-C_4H_9
e, X = p-NO_2; R = t-C_4H_9
f, X = p-NO_2; R = n-C_4H_9
g, X = p-NO_2; R = n-C_3H_7
h, X = p-NO_2; R = i-C_3H_7
i, X = p-NO_2; R = C_2H_5
j, X = p-NO_2; R = CH_3
k, X = p-NO_2; R = $C_6H_5CH_2$
l, X = p-NO_2; R = p-$ClC_6H_4CH_2$
m, X = p-NO_2; R = m-$ClC_6H_4CH_2$
n, X = p-NO_2; R = p-$CH_3C_6H_4CH_2$
o, X = p-NO_2; R = p-$CH_3OC_6H_4CH_2$

Scheme I



A kinetic study of the oxidation of various Schiff bases Ia–o to oxaziranes IIa–o in *t*-butyl alcohol and other solvents was undertaken to determine a probable mechanism (see Tables I–X). As others have found *m*-chloroperoxybenzoic acid[11] is a convenient choice to oxidize Schiff bases to oxaziranes in high yields. The properties and analyses of the Schiff bases and oxaziranes are given in Tables XI and XII.

Experimental Section

Materials. Spectral Grade methylene chloride was used directly. Ethylene chloride, chloroform, and carbon tetrachloride were purified by methods described by Vogel.[12] *t*-Butyl alcohol was dried and distilled from calcium hydride. *m*-Chloroperoxybenzoic acid was obtained from the FMC Corp. and was further purified (98 ± 1%) by the method described in their brochure.

Schiff bases (Table XI) were prepared by the method of Bigelow and Eatough.[13] Oxaziranes (Table XII) were synthesized by the method of Emmons[3] with *m*-chloroperoxybenzoic acid. Peroxybenzoic acid[14] (mp 42–43°; lit.[15] mp 40–41°) and *p*-chloroperoxybenzoic acid[12] were synthesized by methods described in the reference given.

Kinetic Technique and Product Analysis. The rates of oxidation of Schiff bases with peroxy acids in *t*-butyl alcohol and other solvents were followed by the disappearance of Schiff base as determined by uv absorption at 325 to 359 mμ depending on concentration of Schiff base. In *t*-butyl alcohol, Beer's law was followed by all compounds except for a slight deviation at high concentrations (5×10^{-3} *M*) of N-*p*-nitrobenzal-*m*-chlorobenzylamine, compound Im.

---

(1) Supported in part by Public Health Service Grant CA-07521 and Atomic Energy Commission Grant AT(30-1)1983.

(2) To whom correspondence should be addressed.

(3) W. D. Emmons, *J. Am. Chem. Soc.*, **78**, 6208 (1956); **79**, 5739, 6522 (1957).

(4) D. Swern, *Chem. Rev.*, **45**, 1 (1949).

(5) Y. K. Syrkin and I. I. Moiseev, *Russ. Chem. Rev.*, **29**, 193 (1960).

(6) L. A. Paquette, "Principles of Modern Heterocyclic Chemistry," W. A. Benjamin, Inc., New York, N. Y., 1968, p 2.

(7) C. A. Bunton in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, p 11 ff.

(8) A. H. Riebel, R. E. Erickson, C. J. Abshire, and P. S. Bailey, *J. Am. Chem. Soc.*, **82**, 1801 (1960); P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958).

(9) J. O. Edwards in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, p 67 ff.

(10) W. D. Emmons in "The Chemistry of Heterocyclic Compounds," Vol. 19, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1964, p 630.

(11) N. N. Schwartz and J. H. Blumbergs, *J. Org. Chem.*, **29**, 1976 (1964).

(12) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., Ltd., London, 1956, p 163 ff.

(13) L. A. Bigelow and H. Eatough, "Organic Syntheses," Coll. Vol. I, 2nd ed, H. Gilman and A. H. Blatt, Ed., John Wiley & Sons, Inc., New York, N. Y., 1941, p 80.

(14) A. Kergomard and J. Bigou, *Bull. Soc. Chim. France*, 486 (1956).

(15) R. Curci, A. Giovine, and G. Modena, *Tetrahedron*, **22**, 1235 (1966).

In a few experiments (2.50×10^{-4} *M* Schiff base) 1 ml of the reaction mixture at "infinite time" was diluted with solvent to 250 ml and the uv spectrum was compared with an authentic sample of a solution of the oxazirane expected. The results showed that the oxidation was quantitative within experimental error.

Pseudo-first-order spectrophotometric rate constants for the oxidation of Schiff bases with peroxy acids (large excess) were calculated from the integrated form of the differential equation (i),

$$dx/dt = k_{\mathrm{obsd}}(a - x) \tag{i}$$

where a is initial concentration of the Schiff base, x is the amount of oxazirane formed at time "t," and k_{obsd} is the pseudo-first-order rate constant. The difference in absorbancy ($A_t - A_\alpha$) at time "t" was taken as a measure of the unreacted amount of the Schiff base at that time.[16] Plots of log ($A_t - A_\alpha$) *vs.* time were linear to over three half-lives within experimental error. The values of k_{obsd} as calculated from the slope of these lines are given in Tables I and III.

Table I. Pseudo-First-Order Rate Constants for the Oxidation of Ie with MCPBA at 25.5 ± 0.2° in *t*-Butyl Alcohol

[MCPBA], mole/l.	[Ie], mole/l.	k_{obsd},^{a} sec^{-1}
3.00×10^{-2}	2.50×10^{-4}	2.17×10^{-2}
2.62×10^{-2}	2.50×10^{-4}	1.70×10^{-2}
2.25×10^{-2}	2.50×10^{-4}	1.35×10^{-2}
1.87×10^{-2}	2.50×10^{-4}	9.89×10^{-3}
1.50×10^{-2}	2.50×10^{-4}	6.80×10^{-3}
1.12×10^{-2}	2.50×10^{-4}	4.47×10^{-3}
1.00×10^{-2}	2.50×10^{-4}	4.10×10^{-3}
8.75×10^{-3}	2.50×10^{-4}	3.04×10^{-3}
7.50×10^{-3}	2.50×10^{-4}	2.34×10^{-3}
6.25×10^{-3}	2.50×10^{-4}	1.86×10^{-3}
5.00×10^{-3}	2.50×10^{-4}	1.35×10^{-3}
5.00×10^{-3}	3.00×10^{-4}	1.32×10^{-3}
5.00×10^{-3}	4.00×10^{-4}	1.43×10^{-3}
5.00×10^{-3}	5.00×10^{-4}	1.30×10^{-3}
3.75×10^{-3}	2.50×10^{-4}	9.97×10^{-4}
3.33×10^{-3}	2.50×10^{-4}	9.12×10^{-4}
2.50×10^{-3}	2.50×10^{-4}	5.99×10^{-4}
2.00×10^{-3}	2.00×10^{-3}	4.76×10^{-4}

^{a} $k_{\mathrm{obsd}} = [k_0 + k(a + c)]a$; see eq v.

Second-order rate constants were calculated by the integrated form of the differential equation (ii), where a and b are initial concentrations of Schiff base and peroxy acid, respectively, x is the amount of oxazirane formed at time "t," and k_2 is the second-order rate constant. The values of x at different times were calculated by the help of eq iii, where A_t is the absorption at time "t" and ϵ_{R}

$$dx/dt = k_2(a - x)(b - x) \tag{ii}$$

$$A_t = \epsilon_{\mathrm{R}}(a - x) + \epsilon_{\mathrm{p}}x \tag{iii}$$

and ϵ_{p} are extinction coefficients of the reactant (Schiff base) and product (oxazirane), respectively (at the wavelength the reaction was followed). The plots of $1/(a - x)$ or $a(b - x)/b(a - x)$ *vs.* time were linear beyond two half-lives in every case (Tables II, IV, V, VII, and VIII).

Results

Kinetic Law. The linearity of the pseudo-first-order plot for the oxidation of N-*p*-nitrobenzal-*t*-butylamine (Ie) with *m*-chloroperoxybenzoic acid (MCPBA) indicates that the reaction is first order with respect to Ie. The pseudo-first-order rate constant was found to be independent of the initial concentration of Ie, when varied by a factor of 2 (Table I), but varied linearly at low initial concentration and with the square at high initial concentration of MCPBA (Table I and Figure 1).

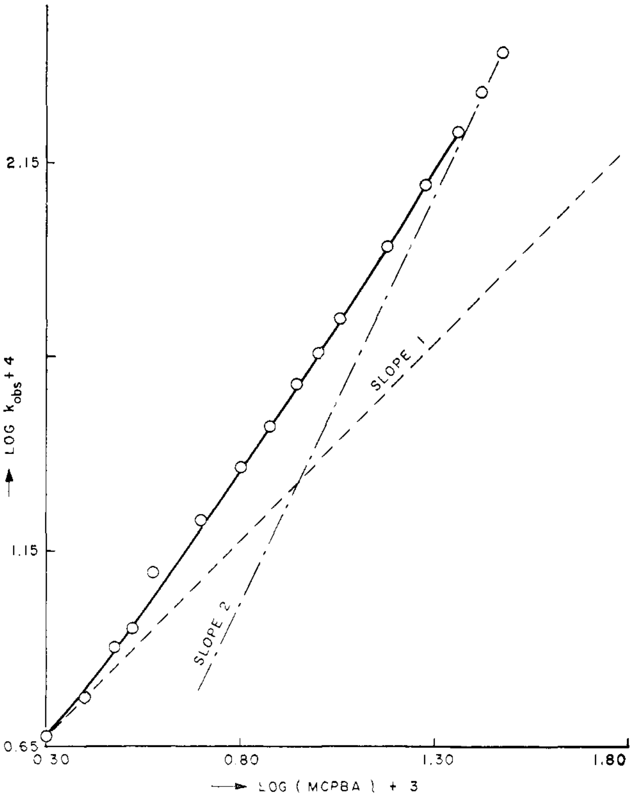


Figure 1. Order with respect to *m*-chloroperoxybenzoic acid for the oxidation of N-*p*-nitrobenzal-*t*-butylamine by *m*-chloroperoxybenzoic acid in *t*-butyl alcohol at 25.5 ± 0.2°.

Table II lists the second-order coefficients (because the rate constant is concentration dependent) for the oxidation of Ie with MCPBA. The second-order rate coefficient calculated from the pseudo-first-order rate constant (24.0×10^{-2} mole^{-1} sec^{-1}) with initial concentrations of Ie (2.50×10^{-4} *M*) and MCPBA (2.50×10^{-3} *M*) agrees well with the value (25.6×10^{-2} mole^{-1} sec^{-1}) given in Table II. It was thus demonstrated that the oxidation followed second-order kinetics at low concentrations of MCPBA.

Table II. Second-Order Rate Constants for the Oxidation of Ie with MCPBA in the Presence and Absence of Added MCBA at 25.5 ± 0.2° in *t*-Butyl Alcohol

[Ie] = [MCPBA], mole/l.	[MCBA], mole/l.	k_0 or k_2, l. mole^{-1} sec^{-1}
1.00×10^{-3}	2.00×10^{-2}	1.15^a
1.00×10^{-3}	1.20×10^{-2}	$6.83 \times 10^{-1\,a}$
1.00×10^{-3}	1.00×10^{-2}	$5.67 \times 10^{-1\,a}$
2.00×10^{-3}		$2.23 \times 10^{-1\,b}$
2.50×10^{-3}		$2.56 \times 10^{-1\,b}$
3.33×10^{-3}		$2.74 \times 10^{-1\,b}$

^{a} Corresponds to $k_2 = [k_0 + k(a + c)]$; eq v. ^{b} Corresponds to k_0; eq v.

Effect of *m*-Chlorobenzoic Acid (MCBA). The effect of added *m*-chlorobenzoic acid (MCBA) on the rate of oxidation of Ie was measured under pseudo-first-order conditions (excess MCPBA). The results (Table III) indicate that all kinetic runs in the presence of MCBA satisfy a pseudo-first-order equation even when the MCBA concentration is comparable to that of Ie. This fact is rationalized below. The order of the

---

(16) K. B. Wiberg, "Physical Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1964, p 312 ff.

Table III. Pseudo-First-Order Rate Constants for the Oxidation of Ie[a] with MCPBA[b] in the Presence of MCBA at 25.5 ± 0.2° in *t*-Butyl Alcohol

[MCBA], *M*	k_1[c], sec^{-1}
0.00	7.97×10^{-4}
2.00×10^{-3}	1.20×10^{-3}
4.00×10^{-3}	1.48×10^{-3}
6.00×10^{-3}	1.66×10^{-3}
1.00×10^{-2}	2.51×10^{-3}
4.00×10^{-2}	6.79×10^{-3}
8.00×10^{-2}	1.15×10^{-2}
1.20×10^{-1}	1.60×10^{-2}
1.60×10^{-1}	1.89×10^{-2}
2.00×10^{-1}	2.20×10^{-2}

[a] [Ie] = 2.50×10^{-4} *M*. [b] [MCPBA] = 3.00×10^{-3} *M*. [c] $k_1 = [k_0 + k(a + c)]a$; eq v.

reaction with respect to MCBA was determined by plotting log $[k_1 - k_{\mathrm{obsd}}]$ against log [MCBA].[17] The oxidation rate was found to vary linearly with the initial concentration of added MCBA.

The slope of the curve (Figure 1) shows that at low initial concentrations of MCPBA, the oxidation approaches first-order (slope = 1) dependence on MCPBA and second-order dependence (slope = 2) at high initial concentration, and the curve has a finite intercept. Since the reaction is first order each in MCBA and Ie, the observed rate law appears to be

$$\frac{-\mathrm{d[Ie]}}{\mathrm{d}t} = k_0[\mathrm{Ie}][\mathrm{MCPBA}] + k_{\mathrm{MCPBA}}[\mathrm{Ie}][\mathrm{MCPBA}]^2 + k_{\mathrm{MCBA}}[\mathrm{Ie}][\mathrm{MCPBA}][\mathrm{MCBA}]$$

pK_a Effect. To rationalize the observation that the rate plots are linear even though the reaction was catalyzed by the product, MCBA, the effect of substituted benzoic acids (a pK_a effect) on the oxidation of Ie with MCPBA was determined for four acids (Table IV). This reaction series displays a ρ value of +0.22 suggesting that pK_a has little effect on the rate of oxidation. Since pK_a for MCPBA (7.5 in water) is near that of the benzoic acids the catalytic effect of the oxidizing acid is nearly equal to that of the substituted benzoic acids, BH. Taking this fact into account, the over-all rate law reduces to

Table IV. Second-Order Rate Constants for the Oxidation of Ie[a] with MCPBA[b] in the Presence of Substituted Benzoic Acids[c] at 25.5 ± 0.2° in *t*-Butyl Alcohol

Substituent	k_2,[d] l. mole^{-1} sec^{-1}
m-Cl	11.5×10^{-1}
H	9.71×10^{-1}
p-*t*-Butyl	8.35×10^{-1}
p-OCH$_3$	8.22×10^{-1}

[a] [Ie], 1.00×10^{-3} *M*. [b] [MCPBA], 1.00×10^{-3} *M*. [c] Concentration of substituted benzoic acid = 2.00×10^{-2} *M*. [d] $k_2 = [k_0 + k(a + c)]$; eq v.

$$\frac{-\mathrm{d[Ie]}}{\mathrm{d}t} = k_0[\mathrm{Ie}][\mathrm{MCPBA}] + k[\mathrm{Ie}][\mathrm{MCPBA}][\mathrm{MCPBA + BH}] \quad \text{(iv)}$$

which is of the form

$$\frac{\mathrm{d}x}{\mathrm{d}t} = (a - x)(b - x)[k_0 + k(a + c)] \quad \text{(v)}$$

Electronic Effects. Linear correlation of log k with Hammett σ values was observed for the oxidation of Schiff bases with peroxy acids. The data for the N-*para*-substituted benzal-*t*-butylamines, N-*p*-nitrobenzal-substituted benzylamines, and substituted peroxybenzoic acids in *t*-butyl alcohol at 25.5 ± 0.2° are presented in Tables V, VI, and VII, respectively. The Hammett plots for N-*para*-substituted benzal-*t*-butylamines and N-*p*-nitrobenzal-substituted benzylamines exhibited a negative slope with ρ values of −1.75 and −0.98, respectively. Therefore, the reaction is facili-

Table V. Second-Order Rate Constants for the Oxidation of N-*para*-Substituted Benzal-*t*-butylamines[a] with MCPBA[b] at 25.5 ± 0.2° in *t*-Butyl Alcohol

Substituent	k_0,[c] l. mole^{-1} sec^{-1}
p-NO$_2$	2.23×10^{-1}
p-Cl	23.6×10^{-1}
H	46.5×10^{-1}
p-CH$_3$	83.1×10^{-1}
p-OCH$_3$	156×10^{-1}

[a] Schiff base concentration, 2.00×10^{-3} *M*. [b] [MCPBA], 2.00×10^{-3} *M*. [c] The term $[k(a + c)]$ is nearly zero at low concentration of MCBA; see eq v.

Table VI. Kinetic Data for the Oxidation of N-*p*-Nitrobenzal-Substituted Benzylamines[a] with MCPBA[b] at 25.5 ± 0.2° in *t*-Butyl Alcohol

Substituent	k_{obsd}, sec^{-1}
m-Cl	1.54×10^{-3}
p-Cl	1.87×10^{-3}
H	3.38×10^{-3}
p-CH$_3$	4.58×10^{-3}
p-OCH$_3$	6.09×10^{-3}

[a] Schiff base concentration = 1.50×10^{-3} *M*. [b] [MCPBA], 2.00×10^{-2} *M*.

Table VII. Second-Order Rate Constants for the Oxidation of Ie[a] with Substituted Peroxybenzoic Acids[b] at 25.5 ± 0.2° in *t*-Butyl Alcohol

Substituent	k, l. mole^{-1} sec^{-1}
m-Cl	2.23×10^{-1}
H	1.07×10^{-1}
p-Cl	1.59×10^{-1}

[a] [Ie], 2.00×10^{-3} *M*. [b] Substituted peroxybenzoic acid concentration = 2.00×10^{-3} *M*.

Table VIII. Second-Order Rate Constants for the Oxidation of N-*p*-Nitrobenzalalkylamines[a] with MCPBA[b] at 25.5 ± 0.2° in *t*-Butyl Alcohol

Substituent	k_0, l. mole^{-1} sec^{-1}
Methyl	4.39×10^{-1}
Ethyl	3.61×10^{-1}
n-Propyl	2.22×10^{-1}
n-Butyl	2.56×10^{-1}
Isopropyl	1.32×10^{-1}
t-Butyl	2.23×10^{-1}

[a] Schiff base concentration, 2.00×10^{-3} *M*. [b] [MCPBA], 2.00×10^{-3} *M*.

---

(17) The over-all rate of oxidation is given by $k_1 = k_{\mathrm{Ie}}[\mathrm{MCPBA}]^n \cdot [\mathrm{Ie}]^{n'} + k_{\mathrm{MCPBA}}[\mathrm{MCPBA}]^2 + k_0[\mathrm{MCPBA}]$. Let $k_{\mathrm{obsd}} = k_{\mathrm{MCPBA}} \cdot [\mathrm{MCPBA}]^2 + k_0[\mathrm{MCPBA}]$. $k_1 - k_{\mathrm{obsd}} = k_{\mathrm{Ie}}[\mathrm{MCPBA}]^n[\mathrm{Ie}]^{n'}$ or log $(k_1 - k_{\mathrm{obsd}}) = \log C + n' \log [\mathrm{Ie}]$.

Table IX. Rates of Oxidation of Ie[a] with MCPBA[b] at Different Temperatures in *t*-Butyl Alcohol

Temp, °C	k_0, l. mole^{-1} sec^{-1}
25.5 ± 0.1	2.23×10^{-1}
29.9 ± 0.1	2.35×10^{-1}
34.9 ± 0.1	2.80×10^{-1}
40.0 ± 0.1	3.12×10^{-1}
44.9 ± 0.1	3.62×10^{-1}

[a] [Ie] = 3.125×10^{-3} *M*. [b] [MCPBA] = 2.000×10^{-3} *M*.

Table X. Kinetic Data for the Oxidation of Ie[a] with MCPBA in Different Solvents at 25.0 ± 0.2°

Solvent	[MCPBA], *M*	k_{obsd}, sec^{-1}
CCl_4	5.00×10^{-3}	3.36×10^{-3}
$CHCl_3$	5.00×10^{-3}	4.31×10^{-3}
CH_2Cl_2	5.00×10^{-3}	5.01×10^{-3}
$ClCH_2CH_2Cl$	5.00×10^{-3}	5.44×10^{-3}
Dioxane	5.00×10^{-3}	4.83×10^{-4}
t-BuOH	5.00×10^{-3}	1.35×10^{-3} [b]
t-BuOH	1.00×10^{-2}	4.10×10^{-3} [b]
t-BuOD	1.00×10^{-2}	3.70×10^{-3} [b]

[a] [Ie], 5.00×10^{4} *M*. [b] Measurements were carried out at 25.5 ± 0.2°.

Table XI. Properties and Analyses of Schiff Bases

Compd I[a]	Mp, °C	Yield, %	Chemical shift, CH=N, cps	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
f	*b*	90	499	64.08	6.79	13.59	62.67	6.57	12.52
g	53.5[c]	91	499	62.50	6.25	14.58	63.11	6.28	14.29
h	54.7	92	499						
i	78.5	86	498	60.67	5.61	15.73	60.96	5.18	15.56
j	107	91	497	58.53	4.83	17.07	58.43	4.82	16.90
k	56[d]	90	502	70.00	5.00	11.66	70.00	5.03	11.95
l	92.5	96	504	61.20	4.01	10.20	60.76	4.10	9.95
m	70	97	505	61.20	4.01	10.20	60.95	4.16	10.45
n	87.5	93	498	70.87	5.51	11.02	71.05	5.33	11.59
o	71	97	497	66.66	5.18	10.37	66.66	4.86	9.91

[a] Compounds Ia, e, h, i, ref 3; Ib–d, E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **85**, 2843 (1963). Yields, Ia–e 75–95%; chemical shift, Ia–e, 485–494 cps. All nmr spectra in CCl_4 (10–15%). Chemical shift relative to tetramethylsilane. [b] Sublimed as liquid on a Dry Ice trap. [c] Analytical samples Ig–j sublimed. [d] Analytical samples Ik–o recrystallized.

tated by the electron-releasing groups on both substituents of the Schiff bases. The Hammett plot for substituted peroxybenzoic acids displays a positive slope with a ρ value of 0.78. Therefore, the reaction is accelerated by electron-withdrawing groups on the peroxy acid.

No linear correlation of log k with Taft[18] σ^* values was observed for oxidation of the reaction series, N-*p*-nitrobenzalalkylamines (Table VIII).

Activation Parameters. Arrhenius activation parameters were determined for the oxidation of Ie with MCPBA by the usual plot of log k *vs.* $1/T$ (Table IX) for a temperature range of 25–45°. The energy and entropy of activation were found to be 5.0 kcal/mole and −47 eu, respectively.

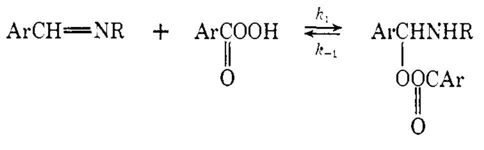
Medium Effect. The rates of oxidation of Ie with MCPBA in different solvents are given in Table X. The rate of oxidation of Ie with *m*-chloroperoxybenzoic acid-d_1 in *t*-BuOD was found to be slightly slower than that in *t*-BuOH (k_H/k_D = 1.10).

Discussion

Several mechanisms can be eliminated on the basis of these kinetic results. In preliminary experiments a free-radical type of mechanism was discarded for the following reasons: diethyl fumarate, a free-radical trap,[19] did not change the rate of oxidation of Schiff bases; evolution of carbon dioxide was not observed; the rate was insensitive to uv light; and there was no induction period in the oxidation; solvent effects are shown in Table X.

A reaction mechanism similar to that proposed by Emmons[10] which resembles the mechanism for the peroxy acid cleavage of ketones[20] is the nucleophilic attack of the peroxy acid on the Schiff base, eq 1, followed by internal nucleophilic displacement of the basic nitrogen on the peroxide bond within III to give the oxazirane II (eq 2). The proposed mechanism will be considered in light of the rate law obtained and other observations.

a. The formation of an intermediate III may occur in a fast equilibrium (eq 1) followed by a bimolecular decomposition of III (in the presence of solvent or a benzoic acid molecule BH) into the products. Equation 2 represents the rate-limiting step. It may further be assumed that the equilibrium (eq 1) largely favors the formation of the intermediate III. The situation, then,



$$ArCH{=}NR + ArC(=O)OOH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArCH(NHR)OOC(=O)Ar \qquad (1)$$

III

$$III + BH \xrightarrow{k_2} II \qquad (2)$$

requires that the reaction be zero order in the reactant which is present in excess, with the rate constant being k_2.[21] The observed kinetics show that the above assumption is not applicable to the system under investigation. Furthermore, a mechanism requiring the rapid conversion of Schiff base into a *stable* intermediate is

---

(18) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley & Sons, Inc., New York, N. Y., 1962, Chapter 13.

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

(20) M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *ibid.*, **80**, 6393 (1958); M. F. Hawthorne and W. D. Emmons, *ibid.*, **80**, 6398 (1958).

(21) L. G. Cannell, *ibid.*, **79**, 2927 (1957).

Table XII. Properties and Analyses of Oxaziranes

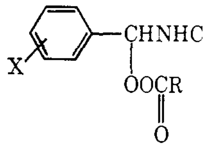
Compd II	Bp (mm) or mp, °C	Yield, %	Chemical shift -CH—N- \ / C cps[c]	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
b	68	97[b]	269	62.41	6.62	6.62	62.35	6.65	6.94
c	*a*	95[b]	269	69.56	8.21	6.76	68.74	7.84	6.31
d	*a*	96[b]	268	75.39	8.90	7.33	75.41	9.01	7.53
f	*a*		268			12.61			12.57
g	*a*		268	57.69	5.77	13.46	58.00	5.42	13.86
j	82.5	97[b]	269	53.33	4.44	15.55	54.49	4.23	15.37
k	101.8	92.5	286	65.62	4.69	10.94	65.71	4.83	10.66
l	85.5	88	281	57.83	3.78	9.64	59.17	3.90	9.13
m	97.7	90	326	57.83	3.78	9.64	58.94	3.66	9.52
n	65.5	80	286	66.66	5.18	10.37	66.20	4.83	10.28
o	98.5	81	285	62.94	4.89	9.79	63.32	4.92	9.80

[a] Liquid, purified by chromatography on silica gel. [b] Yield estimated from nmr spectrum. [c] Relative to tetramethylsilane. Nmr spectra taken in CCl_4, 10–15% solution except IIk–o in $CDCl_3$.

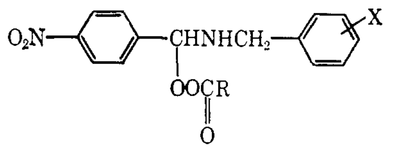
untenable because the observed rate is the rate of disappearance of Schiff base.

b. If intermediate III is formed in a reversible step with $k_{-1} > k_1$, the concentration of III will be small at time "*t*" relative to concentration of reactants. In such a case the rate constant will be the product Kk_2, where K is the equilibrium constant for eq 1. But K will require a moderate positive ρ value while eq 2 requires a moderate negative ρ value. The net effect of *para* substitution in compound I should give a ρ value that is small and perhaps negative. The observed ρ value of -1.75 is too large in absolute value to be consistent. In a comparable case, the ρ value for peroxy acid cleavage in *para*-substituted acetophenones is -1.10 in ethylene chloride.[20] Since this last reaction includes a phenyl migration in the decomposition of the Criegee intermediate, the ρ value should be more negative than would be expected in the decomposition of intermediate III.

Moreover, the observed ρ value of -0.98 for the Schiff bases of *p*-nitrobenzaldehydes and benzylamines (Table VI) is not a large enough negative number for substitution in the benzyl ring. Examination of III in two series (IIIa and IIIb) suggests that if k_2 has a greater effect than K, then ρ values might be equal in IIIa and IIIb because the nucleophilic nitrogen involved is one carbon removed from the substituted phenyl ring in each series.

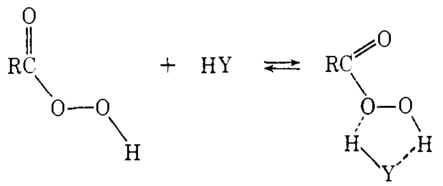


IIIa



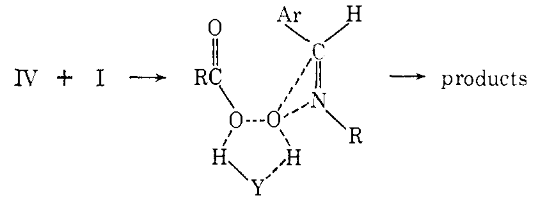
IIIb

The above mechanism was rejected in favor of the following proposal: π electrons of the C=N perform a nucleophilic attack on the sterically less hindered hydroxylic oxygen (eq 4) in a manner analogous to that suggested for epoxidation of olefins. The peroxy acid undergoes a synchronous hydrogen exchange process (eq 3) with HY, where HY is the solvent, benzoic acid (a product), or another molecule of peroxy acid. The molecule HY (if solvent) must be a protic solvent, capable of proton exchange. The transition state is composed of the peroxy acid, the Schiff base, and a molecule of HY. The direction and magnitude of the substituent effects ($\rho = -1.75$, Table V, and $\rho = -0.98$, Table VI), the activation parameters ($E_a = 5.0$ kcal mole and $\Delta S^* = -47$ cal mole deg), the slight effect of added acid, solvent effects (Table X), and the small isotope effect ($k_H/k_D = 1.10$) are all consistent with such a mechanism. The observed ρ values, including the peroxybenzoic acid series (Table VII, $\rho = 0.78$), fall in line with those in other work where a nucleophilic displacement on the sterically less hindered hydroxylic oxygen of the peroxy acid has been proposed. Furthermore, the transition state (V) for this mechanism requires a smaller negative ρ value (-0.98, Table VI) for formation of Vb than for Va (Table V, $\rho = -1.75$), which was found.



(3)

IV



(4)

V

The higher reactivity of the C=N compared to C=C is not due to the greater basicity of the Schiff base since the N atom is not the nucleophilic center in the present theory. Rather, we think it is due to a "pseudo α effect." Edwards and Pearson[22] have pointed out that besides polarizability and basicity, an added "α effect"

---

[22] J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).

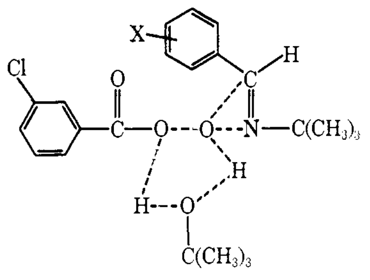
has been observed in compounds in which the nucleophilic site is directly linked to another electronegative atom (HOOH and H_2NOH examples). Electrostatic repulsions between the electron pairs of the nucleophilic site and adjacent atom increases the ground-state energy of the substrate, hence lowers the activation energy. Electrostatic repulsions are minimized in the transition state because one electron pair is engaged in forming the incipient new bond. In the present case, the low activation energy may be attributed to a "pseudo α effect" (the electron pair on nitrogen adjacent to the nucleophilic double bond, C=N).

A highly negative entropy of activation may be attributed to additional restrictions on the transition state (Va and b) imposed by the intramolecular hydrogen bonding.

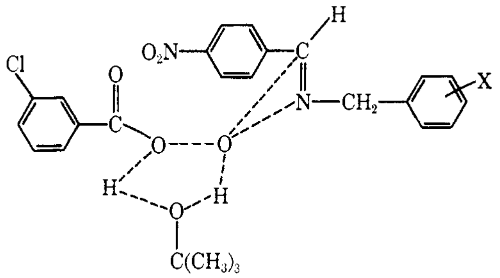
A solvent isotope effect of $k_H/k_D = 1.15$ for the oxidation of *p*-nitroaniline with peroxyacetic acid has been reported by Edwards and Ibne-Rasa.[23] The solvent isotope effect of $k_H/k_D = 1.10$ for the oxidation of Schiff bases with MCPBA is only slightly smaller ($\sim$5%). This small difference may be a specific steric requirement to solvation of the bulky MCPBA compared to peroxyacetic acid rather than to a difference in bond breaking in the O–O bonds in two cases.

In the case of oxidation of C=C with peroxy acids it has been observed that electronic effects cannot be interpreted clearly in aromatic olefins.[24] Similarly in using aromatic Schiff bases we have not found a linear relationship between log k against Taft σ^* values. Lack of a linear relationship may be due to the considerable steric effect in the transition state.

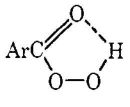
The rate of oxidation increases linearly with the increase in dielectric constant of the aprotic nonbasic solvents, indicating that the transition state is slightly more polar than the reactants. The lower values of rate constants in a protic solvent or in a solvent capable of hydrogen bonding (dioxane and *t*-butyl alcohol) are consistent with a peroxy acid structure VI. This ring is presumably present in aprotic solvents, but configurations such as VII stabilize the ground state in protic solvents, which in turn adds to the energy of activation.



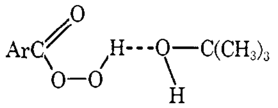
Va



Vb



VI



VII

---

[23] K. M. Ibne-Rasa and J. O. Edwards, *J. Am. Chem. Soc.*, **84**, 763 (1962).

[24] D. Swern, *ibid.*, **69**, 1692 (1947).

Mechanism of the Transformation of Cyclopenin to Viridicatin[1]

Herman W. Smith and Henry Rapoport

Contribution from the Department of Chemistry, University of California, Berkeley, California.
Received June 2, 1969

Abstract: The transformation of cyclopenin to viridicatin, which had previously been shown to occur in acid, has now been found to take place thermally and in alkali as well. Similar changes occur for isocyclopenin and methylcyclopenin, but the latter fails to rearrange in alkali. A mechanism for this decarboxylation–rearrangement, involving a tricyclic diene intermediate, is proposed based on these observations and the fact that methylisocyanate is an accompanying product in the thermal reaction. Ring-opened derivatives fail to give this reaction, demonstrating that the intact benzodiazepinedione ring is a structural requirement. The epoxide is not necessary, since a derived bromohydrin rearranges; also, the corresponding glycol gives viridicatin but requires more drastic conditions. A dihydro analog, 3-mesyloxybenzyl-4-methyl-1H-3,4-dihydro-1,4-benzodiazepine-2,5-dione, is transformed to the corresponding rearranged but not decarboxylated carbamoyldihydrocarbostyril. The same type of tricyclic diene intermediate resulting from benzylic carbon attack at the carbonyl-bearing aromatic site accommodates this observation.

Cyclopenin and cyclopenol, metabolites of *Penicillium cyclopium* and *P. viridicatum*, react in dilute acid solution with loss of optical activity and concomitant appearance, respectively, of viridicatin and viridicatol,

---

[1] Supported in part by the U. S. Army Research Office, Durham, N. C.