The Kinetic Study on the Reaction of Oxaziridine with Tri-*n*-Butylphosphine

Seizo TAMAGAKI, Keishi SAKAKI, and Shigeru OAE

Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sugimoto-cho, Sumiyoshiku, Osaka

(Received March 24, 1972)

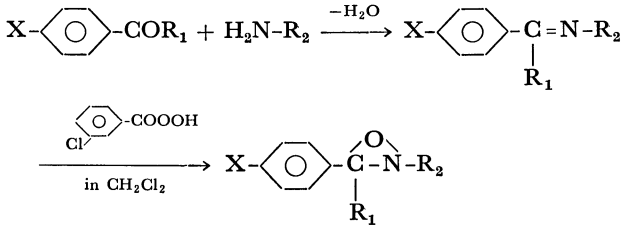
The mechanism of deoxygenation reaction of oxaziridine with trivalent phosphine was kinetically examined by changing substituents, solvents, and temperatures. The reaction proceeds through an attack of phosphine on oxgen in a concerted manner rather than on nitrogen or carbon, eventually producing the corresponding imine and phosphine oxide. The mechanism of the title reaction was compared with those of similar deoxygenations of epoxide and thioepoxide.

Oxaziridines are three-membered ring compounds bearing an active oxygen like organic peroxides and can be assayed iodometrically with potassium iodide in acetic acid. Generally, oxaziridine ring is cleavaged slowly by treatment with strong acids, but fairly stable to weakly basic reagents. The stability of the heterocycle varies sharply with the nature and number of substituents.[1] However, the reactions of oxaziridines with various nucleophiles have not been extensively explored.[2]

The present paper describes a detailed kinetic study on the reaction of oxaziridine with tervalent phosphorous compound in order to clarify the mechanism of the reaction in comparison with those of the epoxides and thioepoxides.[3]

Experimental

Materials. *Oxaziridines*: Oxaziridines were prepared by per-acid oxidation of Shiff's bases according to the method described previously.[4] The physical properties of Schiff's bases and oxaziridines are listed in Table 1 together with the NMR spectral data in Table 2.



Tri-n-butylphosphine: Commercial phosphine was purified by repeated distillation, bp 128—130°/27 mmHg (lit, 149.5°/50 mmHg).

Solvent: Commercial acetonitrile and special analytical grade *n*-hexane were dried over phosphorous pentoxide and distilled just before use.

Product Analysis. The reaction of 2-alkyl-3-aryloxaziridines with triphenylphosphine or tri-*n*-butylphosphine at room temperature quantitatively afforded the corresponding imines and the phosphine oxides. The product analysis was readily performed by measuring the NMR signals of the methyne protons of both oxaziridines and imines.

Kinetics. A typical procedure is as follows: 2-*t*-butyl-3-(*p*-chlorophenyl)oxaziridine (74.03 mg, 3.5×10^{-4} mol) was dissolved in 50 m*l* acetonitrile. Tri-*n*-butylphosphine (141.4 mg, 7×10^{-4} mol) was also dissolved in 50 m*l* of the same solvent. Five m*l* of each solution was mixed in a reaction vessel which was kept at 50.0°C in a thermostat. Accordingly, the concentrations of the oxaziridine and the phosphine at the initial reaction stage were 3.5×10^{-3} mol/*l* and 7×10^{-3} mol/*l*, respectively. Every ten minute an aliquot (1 m*l*) was withdrawn and poured into 50 m*l* of acetonitrile in order to stop the reaction. The rate was followed by measuring the concentration of the imine produced by means of UV spectrometer. The second-order rate constants were calculated by the integral form (2) of the differential equation (1), where a and b signify the initial concentrations of the oxaziridine and the phosphine, respectively,

$$dx/dt = k_2(a-x)(b-x) \quad (1)$$

$$1/(b-a)\ln(b-x)a/(a-x)b = k_2t \quad (2)$$

while, x is the amount of the imine formed at the given time (t) from the start and k_2 is the second-order rate constant. A typical run is shown in Fig. 2.

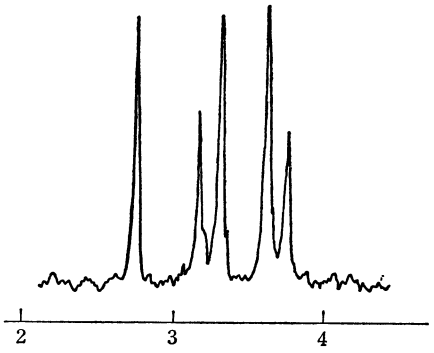


Fig. 1. NMR spectrum of reaction product of *p*-chlorophenyl-*t*-butyl-oxaziridine with phosphine.

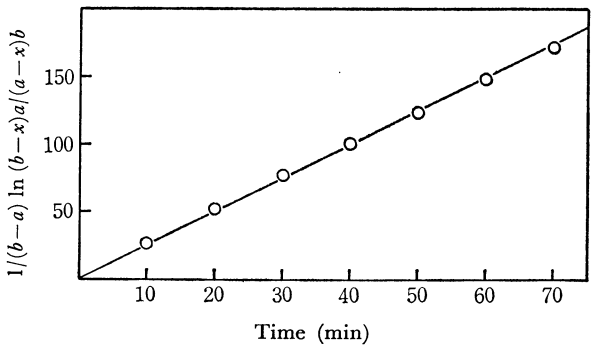


Fig. 2. Deoxygenation of 2-*t*-butyl-3-(*p*-chlorophenyl)oxaziridine with tri-*n*-butylphosphine in acetonitrile at 50°C.

1) W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 5739 (1957). E. Schmitz and D. Murawski, *Chem. Ber.*, **98**, 2525 (1965).

2) D. St. C. Black and K. G. Watson, *Angew. Chem.*, **83**, 355 (1971).

3) L. Horner and E. Jurgens, *Chem. Ber.*, **90**, 2184 (1957).

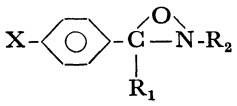
4) W. D. Emmons, *J. Amer. Chem. Soc.*, **78**, 6208 (1956); *ibid.*, **79**, 5739 (1957). R. G. Pews, *J. Org. Chem.*, **32**, 1629 (1967).

Table 1. Physical properties of oxaziridines and Schiff's bases

R_1	R_2	X	Mp or bp	Mp or bp
H	*t*-Bu	NO_2	63—63.5°C (lit, 65—66°C)	74—74.5°C (lit, 73—75°C)
H	*n*-Pr	NO_2	a)	50.5—51.5°C (lit, 53.5°C)
CH_3	*n*-Pr	NO_2	a)	b)
H	*t*-Bu	Cl	62—64°C	33—35°C
H	*t*-Bu	H	27—28°C (lit, 61—63°C/0.3 mmHg)	89—91°C/11 mmHg
H	*t*-Bu	CH_3	65—70°C	97°C/5 mmHg

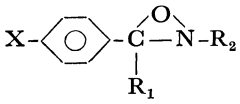
a) Purified by tlc and used without further purification.
b) Used for subsequent oxidation without any purification.

Table 2. Spectral data of some oxaziridines



R_1	R_2	X	NMR (τ) in $CDCl_3$
H	*t*-Bu	NO_2	1.95 q ; 5.12 s ; 8.75 s ;
H	*n*-Pr	NO_2	2.06 q ; 5.37 s ; 7.10 m; 8.20 m; 8.91 t
CH_3	*n*-Pr	NO_2	1.96 q ; 7.65 t ; 8.11 s ; 8.36 m; 9.01 t
H	*t*-Bu	Cl	2.52 s ; 5.25 s ; 8.75 s ;
H	*t*-Bu	H	2.53 s ; 5.28 s ; 8.80 s ;
H	*t*-Bu	H	2.73 q ; 5.35 s ; 7.65 s ; 8.82 s

Table 3. Second-order rate constants for deoxygenation reaction at 50.1°C in various solvents



R_1	R_2	X	k_2, *l*/mol·sec in *n*-hexane	k_2, *l*/mol·sec in CH_3CN	k_2, *l*/mol·sec in EtOH
H	*t*-Bu	NO_2	1.087×10^{-1}	1.46×10^{-1}	
H	*n*-Pr	NO_2	1.61×10^{-1}		
CH_3	*n*-Pr	NO_2	4.44×10^{-2}		
H	*t*-Bu	Cl	3.55×10^{-2}	4.28×10^{-2}	6.81×10^{-2}
H	*t*-Bu	H	1.69×10^{-2}	1.61×10^{-2}	
H	*t*-Bu	CH_3	1.07×10^{-2}	1.44×10^{-2}	

Results and Discussion

The second-order rate constants obtained in the deoxygenation reaction of a few substituted oxaziridines with tri-*n*-butylphosphine are given in Table 3 and the activation parameters are represented in Table 4.

A straight Hammett line was obtained by plotting log k values against sigma values as shown in Fig. 3 and a rho values of +1.12 in acetonitrile and +1.06 in *n*-hexane were obtained. Accordingly, the reactivity increases with an electron-withdrawing *para*-substituent in phenyl ring. This observation, together with the lack of reactivity of the poorly nucleophilic tri-

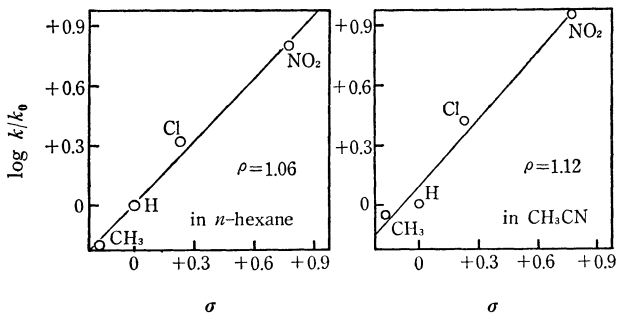
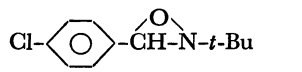


Fig. 3. Correlation of second-order rate constants with Hammett sigma values.

Table 4. Second-order rate constant for deoxygenation of 2-*tert*-butyl-3-(*p*-chlorophenyl)oxaziridine with tri-*n*-butylphosphine at various temperature



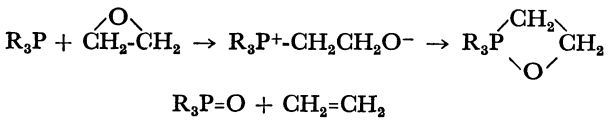
React. temp.	k_2 in CH_3CN, l/mol·sec	React. temp.	k_2 in *n*-hexane, l/mol·sec
40.3°C	2.28×10^{-2}	39.9°C	1.82×10^{-2}
50.1°C	4.28×10^{-2}	50.1°C	3.55×10^{-2}
59.0°C	7.27×10^{-2}	55.2°C	4.22×10^{-2}
		59.9°C	5.76×10^{-2}
E_a=12.1 kcal/mol		E_a=11.7 kcal/mol	
$\Delta S^{\neq}$=−29.2 e. u.		$\Delta S^{\neq}$=−33.4 e. u.	

phenylphosphite in the deoxygenation, suggests that the reaction involves the nucleophilic attack of the trivalent phosphine on the oxaziridine ring.

In general, from these data we may conclude that the rate of reaction is not much affected by the change in the dielectric constants of the reaction media. Even in ethanol which is known to act as protonating solvent, the rate increase was only less than two fold as compared with that in acetonitrile, although the values of k_2 are not very accurate due to the decomposition of phosphine itself in ethanol.

In the reaction of the oxaziridine with a trivalent phosphorous compound which is usually a softer nucleophile and a good deoxygenating or desulfurizing reagent, the deoxygenation reaction takes place instantaneously even at room temperature in benzene, *n*-hexane, and actonitrile.

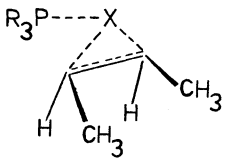
It has been well known that epoxides were also readily deoxygenated by trivalent phosphines to afford the corresponding phosphine oxides and olefins.[5] The mechanism of this reaction has been investigated extensively and is known to involve the nucleophilic attack of the phosphine on the carbon of the epoxide to form the betaine as an intermediate, as shown below.



$$R_3P=O + CH_2=CH_2$$

However, this mechanism can explain only one side of the reaction. Other stereochemical studies indicate that the reaction is better explained by the scheme involving the direct attack of the phosphine on the oxygen atom of the epoxide.[5]

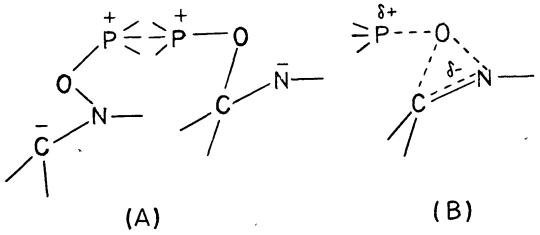
As for analogous reaction of episulfide, Neureiter *et al.*[6a] and Denney[6b] have concluded that both the direct attack of the phosphine on the sulfur atom and the subsequent desulfurization are completely stereospecific.[6]



X = O or S

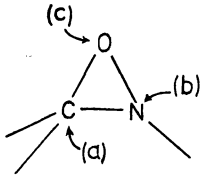
The results in Table 3 indicate that in the deoxygenation reaction of oxaziridines the effect of the change of the solvent from nonpolar to polar solvent on rate of the reaction is found insignificant like in the desulfurization reaction of the thioepoxide.[6] This fact is in a marked contrast to the results by Bartlett in the desulfurization reaction of elemental sulfur with trialkyl phosphine in which the increase in polarity of solvent resulted in a sharp increase in reaction rate by over several hundred fold.[7]

Therefore, based on these observations and considerations we may conclude that the structure of the transition state for the deoxygenation is assumed not to be like (A) which has a large charge separation, but like that (B) which is essentially non-polar. This is essentially a concerted process and dose not require any appreciable charge separation in the transition state.



(A) (B)

However, it should be open to question whether the phosphine exclusively attacks the oxygen atom rather than the carbon or nitrogen atom, because there are three possible attacking sites by a nucleophile in the oxaziridine ring at the initial step of the reaction, *i.e.*, either carbon (a) or nitrogen (b) or oxygen atom (c).



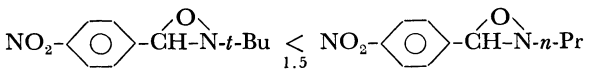
The following observation may be taken as evidence to confirm the attacking on oxygen. Substitution of *t*-butyl group on the nitrogen atom by the less sterically hindered *n*-propyl group results in the rate-increase of only 1.5. In a normal nucleophilic substitution reaction the difference in steric effects by changing the group from *n*-propyl to *tert*-butyl may be estimated as at least over ten.[8] Thus the attacking site can not be the nitrogen atom.

5) G. Witting and W. Haag, *Ber. Deut. Chem. Ges.*, **88**, 1654 (1955). C. B. Soctt, *J. Org. Chem.*, **22**, 1118 (1957).

6) a) M. J. Boskin and D. B. Denney, *Chem. Ind.* (London), **1959**, 330. b) N. P. Neureiter and F. G. Bordwell, *J. Amer. Chem. Soc.* **81**, 578 (1959). D. B. Denney and M. J. Boskin, *ibid.*, **82**, 4736 (1960).

7) P. D. Bartlett and G. Megnerian, *ibid.*, **78**, 3710 (1956).

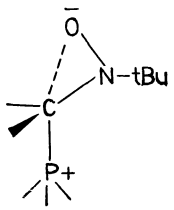
8) M. S. Newman, "Steric Effects in Organic Chemistry" John Wiley & Sons (1955), p. 205.



As for another alternative possibility involving the nucleophilic attack of the phosphine on the carbon atom, Pearson reported that in methanol various nucleophiles reacted with methyl iodide in the following decreasing rate-order:

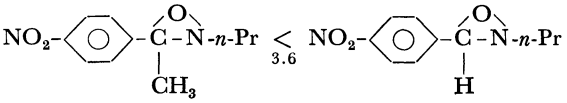
$$PhS^- > (n\text{-}Bu)_3P > Ph_3P > CN^- > P(OCH_3)_3$$
$$(17) \quad (1) \quad (2\times10^{-2}) \quad (1\times10^{-2}) \quad (3\times10^{-4})$$

where the numbers denote the relative rates.[9] Accordingly, if the initial nucleophilic attack would take place at the carbon atom, the reactivities of the nucleophiles in this reaction would fall in the same order as that found with methyl iodide. Contrary to the expectation, in the reaction of oxaziridine, PhS^-, I^-, and CN^- did not react at all even in dimethylformamide in which nucleophiles are known to be markedly activated. Meanwhile, triphenyl- and tri-*n*-butylphosphines can readily reduce the oxaziridine ring to the imine in a good yield. This cannot be account for by assuming the attack of the phosphine on the carbon atom. Moreover, the possibility of the carbon attack could not be compatible with the very small solvent dependency on the rate, because the carbon attack by phosphine must require a charge-separated structure for the transition state (C) due to C–O bond fission as shown below:



(C)

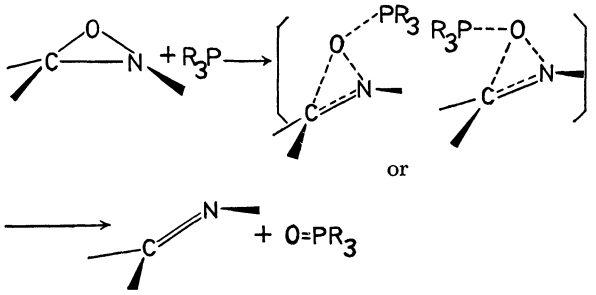
As Table 3 indicates, further striking negative evidences against nucleophilic carbon attack may be the very small influence on the rate produced by the replacement of methyne hydrogen attacked to the carbon by methyl group (D).



(D)

In usual S_N2 reaction retardation in rate caused by the change of steric crowdness from hydrogen to methyl groups has been reported to be larger than 10^2.[8] The lack of difference is markedly contrast to what one normally expects when hydrogen is replaced by methyl group in the S_N2 reaction on the carbon atom.

Such a small decrease in rate may better be explained in terms of the electron-donating nature of methyl group rather than the steric origin, since Fig. 3 indicates that the electron-donating substituents in the three-membered ring decrease the rate quite significantly. Consequently in view of these considerations, the posibility of either carbon or nitrogen attack by the trivalent phosphine seems unlikely. The remaining posibility, which is in harmony with the experimental results, is the rate-determining nucleophilic attack of the phosphine on the oxygen atom of the oxaziridine. Thus, we may conclude that deoxygenation reaction proceeds through nonpolar transition state, with subsequent synchronous deoxygenation.



The large negative entropies of the reaction in both *n*-hexane and acetonitrile can be also rationalized in terms of such a rigid and highly oriented transition state. The priority for attack on oxygen would be attributed to the large driving force of forming a strong P=O and a C=N double bond.

9) R. G. Pearson, H. Sobel, and J. Songstad, *J. Amer. Chem. Soc.*, **90**, 319 (1968).