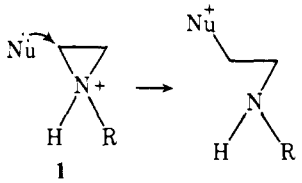
Fragmentation Reaction of Ylide. 7.[1] Reaction of Oxaziridines with Nucleophilic Reagents

Yoshiteru Hata* and Masamichi Watanabe

Contribution from the Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553 Japan. *Received January 30, 1979*

Abstract: The reaction of oxaziridines with nucleophilic reagents was studied to obtain clues toward understanding their biological properties. 2-Methyl-3-phenyloxaziridine and triethylamine gave hexamethylenetetramine as the main product. Oxaziridine also gave trimethylhydrazine or azomethane in good yield on reaction with dimethylamine or methylamine, respectively. In the reaction with 1-methyl-2-*p*-chlorophenylaziridine, the oxaziridine showed a double fragmentation reaction forming azomethane, *p*-chlorostyrene, and benzaldehyde. 2-Methyl-3-phenyloxaziridine also reacted with triphenylphosphine to give triphenylphosphinemethylimine and with thiophenol to give *N*-methylbenzenesulfenamide in a vigorous reaction even at −20 °C. The reactions were discussed as S_N2 fragmentation reactions of the three-membered ring of oxaziridines.

Studies of the reactions of aziridines with electrophilic or nucleophilic reagents are very important for understanding the biological properties of the aziridine derivative.[2] In particular, the reactions of aziridine or aziridinium salt **1** with



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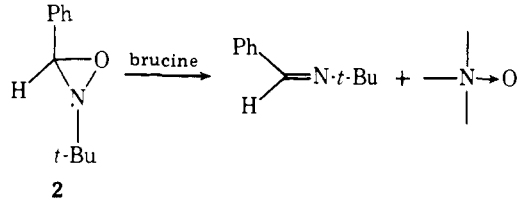
nucleophilic reagents are generally known as alkylation reactions and have been studied extensively as they are considered an essential metabolic pathway for the carcinogenic activity of aziridines.[3]

Recently, we studied the biological properties of oxaziridines and found strong cytotoxic activity in their derivatives. Oxaziridine has a ring system similar to that of aziridine except for a stronger electronegative oxygen atom and much weaker basicity of the nitrogen's lone pair.[4,5] This time we studied the reaction of oxaziridines with nucleophilic reagents to obtain clues toward understanding their biological properties.

For the reactions between nucleophilic reagent and oxaziridine, we found only few reports in literature. Phenylhydrazine formation from 3-methyl-3-ethyloxaziridine and aniline was found by the excellent work of Schmitz and his coworkers to be a characteristic property of *N*-alkyl free oxaziridines.[6] For *N*-alkylated oxaziridines, brucine or triphenylphosphine was used to abstract an oxygen atom from the oxaziridine ring.[5,7] However, a bulky substituent group bound



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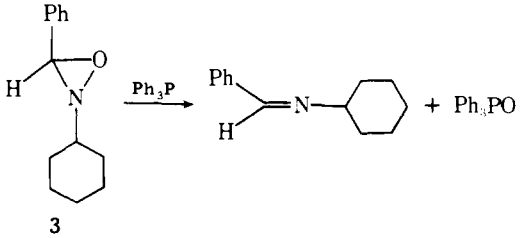

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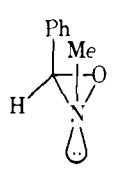
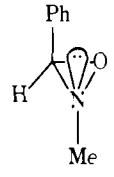
to the nitrogen atom probably masked the essential reaction property of oxaziridine and a smaller substituent compound should be used in such a study. Here we wish to report the reactions of oxaziridine, which has a methyl group on its nitrogen atom, with nucleophilic reagents having nitrogen, phosphorus, and sulfur atoms.

In our experiments, mainly *cis*- and *trans*-2-methyl-3-phenyloxaziridines (*cis*-**4** or *trans*-**4**) were used. The com-



cis-**4**



trans-**4**

pounds were stable thermally in a chloroform solution, and each isomer was not converted into the other variety by heating at 100 °C for several hours. The compounds also did not react with water, alcohol, carboxylic acids, and carbonyl compounds at room temperature. Our reactions were carried out in a sealed tube by using chloroform or benzene as solvent.

Reactions with Amines. In chloroform solution, *cis*-**4** disappeared rapidly upon addition of triethylamine at room temperature and was converted into benzaldehyde and a white precipitate. The yield of benzaldehyde was almost quantitative. When the reaction mixture was allowed to stand for a few days at room temperature, the white precipitate gradually disappeared accompanied by a decrease in the benzaldehyde formed in the initial stage of the reaction and hexamethylenetetramine was formed in the solution. The yield of hexamethylenetetramine was 32.6% at 17 h after the start of the reaction, 42.8% at 41 h and 64.6% at 4 days. Triethylamine was the only catalyst for the decomposition of *cis*-**4** and it was not consumed. The white precipitate did not yield clear elemental analysis data, but was considered to be a condensate of methylnitrene or methylenimine **8** as their NMR spectra showed a single peak at δ 4.8. The condensate **5** probably reacted slowly with benzaldehyde to form formaldehyde followed by conversion into hexamethylenetetramine by the reaction with methylenimine.[8] Thus, the reaction should proceed as shown here.

$$\textit{cis}\text{-}\mathbf{4} \xrightarrow{Et_3N} PhCHO + \underset{\mathbf{5}}{(CH_2{=}NH)_x}$$

$$PhCHO + (CH_2{=}NH)_x \rightarrow PhCH{=}NH + CH_2O$$

$$(CH_2{=}NH)_x + CH_2O \rightarrow \text{hexamethylenetetramine}$$

$$\text{or } (CH_2{=}NH)_x \rightarrow \text{hexamethylenetetramine} + NH_3$$

We thought the transition state **6** and the formation of ylide **7** probably occurred in the reaction; they will be discussed later

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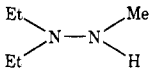
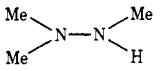
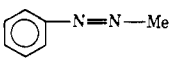
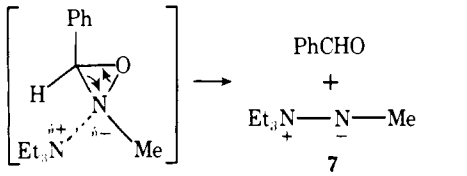
Table I. Products of the Reaction between 2-Methyl-3-phenyloxaziridine and Amines or Triphenylphosphine in Chloroform[a]

reagent	oxaziridine isomer	main product	yield, %
Et_3N	cis	hexamethylenetetramine	64.6
	trans		78
Et_2NH	cis		good[b]
	trans[c]		good
Me_2NH	cis		71.6
	trans		85.3
$MeNH_2$	cis	Me-–N=N—Me	72 (cis, 20.6;[d] trans, 51)
	trans		50 (cis, 13; trans, 37)
	trans		26[e]
			from *cis*-4 / from *trans*-4
Ph_3P	cis	Ph_3P=N—Me[f]	>84 / >58.1
	trans	PhCH=N—Me	/ >39.1

[a] Nucleophilic reagents were used in excess. [b] Accurate yield could not be obtained due to susceptibility to atmospheric oxygen. [c] 2-Methyl-3-*p*-nitrophenyloxaziridine was used. [d] Product yield was determined 50 min or 3 days after the reaction had been started at room temperature for *cis*-**4** or *trans*-**4**, respectively. Dimethylhydrazine, the initial product, was converted into azomethane by oxidation with another molecule of oxaziridine or atmospheric oxygen. *cis*-Azomethane was unstable and had diminished yields due to longer reaction times. [e] Only *trans*-methaneazobenzene was detected. The cis isomer is unstable according to literature: Ege, S. N.; Sharp, R. R. *J. Chem. Soc. B* **1971**, 2014. [f] The value is the yield of **17**. The yield of triphenylphosphinemethylimine was estimated from the formation of **17**.

in detail. *trans*-**4** also reacted with triethylamine at a slower rate than *cis*-**4** and gave hexamethylenetetramine in 70% yield



6

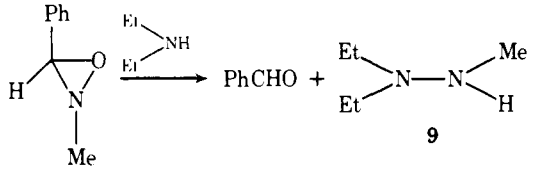
7

8

at 17 h after the start of the reaction, 76.2% at 41 h, and 78% at 4 days. In this case, the methylenimine condensate **5** did not form, probably because the slower rate of the formation of methylenimine from oxaziridine matched the reaction rate of benzaldehyde.

The reaction of secondary amines with oxaziridine, as expected from its basicity, proceeded at a much faster rate than that of triethylamine accompanying consumption of the secondary amine.

Upon addition of diethylamine, *cis*-**4** disappeared after a few hours at room temperature, and benzaldehyde and diethylmethylhydrazine **9** were formed. However, the hydrazine **9** was very sensitive to atmospheric oxygen and was converted into **10**, thus making difficult accurate determination of the yield of **9**.



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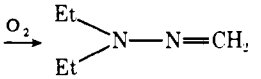

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As trimethylhydrazine was a little more stable to oxidation than **9**, we tried the reaction of oxaziridine with dimethylamine to determine the yield of hydrazine. The reaction of dimethylamine with *trans*-**4** was completed 20 min after both components had been mixed at room temperature and the yield of trimethylhydrazine was 85.3%. The compound *cis*-**4** gave 71.6% of hydrazine in a much faster reaction than with *trans*-**4**.

Excess methylamine also reacted very easily with the oxaziridine, and *trans*-**4** gave 13% and 37% of cis and trans isomers of azomethane **13**, respectively, and a quantitative amount of *N*-(benzylidene)methylamine **12** in the calculation based on the amount of *trans*-**4**. Thus we supposed that dimethylhydrazine formed in the initial stage of the reaction was converted into azomethane by oxidation with another molecule of oxaziridine or by contact with oxygen in the atmosphere. In another experiment using an authentic sample of dimethylhydrazine and *trans*-**4**, the reaction occurred immediately after mixing of both components and they were converted into azomethane and **12**, respectively. We interpreted the reaction of oxaziridine as proceeding as shown below with considerable yields of azomethane and *N*-(benzylidene)methylamine.

$$\textit{trans}\text{-}\mathbf{4} + CH_3NH_2 \rightarrow PhCHO + \underset{\mathbf{11}}{CH_3NHNHCH_3}$$

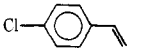
$$\textit{trans}\text{-}\mathbf{4} + \mathbf{11} \rightarrow \underset{\mathbf{12}}{PhCH{=}NCH_3} + \underset{\mathbf{13}}{CH_3{-}N{=}N{-}CH_3} + H_2O$$

$$PhCHO + CH_3NH_2 \rightarrow \underset{\mathbf{12}}{PhCH{=}N{-}CH_3} + H_2O$$

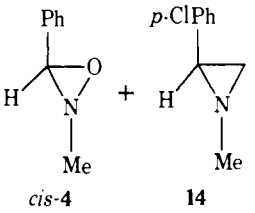
The products obtained in the reaction between oxaziridines and amines are shown in Table I.

One of the most interesting experiments with the reaction of oxaziridines with amine is the use of 1-alkylaziridine as tertiary amine. Previously, we proposed that the aziridinium ylides formed by the reaction with carbene and aziridines decomposed immediately after transformation into olefin and

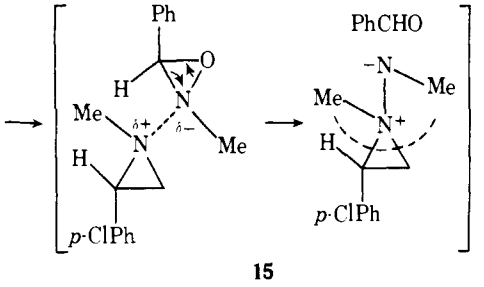
Table II. Reaction of *cis*-2-Methyl-3-phenyloxaziridine (*cis*-**4**) and 1-Methyl-2-*p*-chlorophenylaziridine (**14**) in Chloroform at 80 °C

reaction time	recovered material, %		products, %		
	cis-**4**	**14**	PhCHO	azomethane	
30 min	53.8	86	24.9	14.2	13.6
1 h	22.3	~85	77	17.9	~14

imine derivative.[9] If the reaction between oxaziridine and aziridine proceeds according to a mechanism similar to that shown in transition state **6**, which involves nucleophilic attack by the lone pair of aziridine nitrogens on electron-deficient nitrogen of oxaziridine, we can expect double fragmentation of both three-membered rings in the transition state as shown in **15**.



cis-**4** **14**



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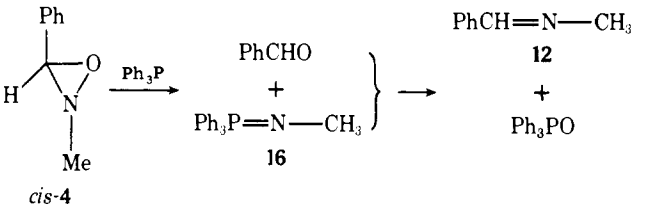
In practice, 1-methyl-2-*p*-chlorophenylaziridine (**14**) did not react with *cis*-**4** at room temperature. However, upon heating a solution of both components in chloroform at 95 °C, the reaction occurred slowly, and the amounts of *cis*-**4** and **14** decreased gradually accompanied by an increase of benzaldehyde, azomethane, and *p*-chlorostyrene as expected. Product yield and the amounts of remaining starting materials when the reaction was interrupted at 30 min and 1 h are shown in Table II.

Obviously, in the reaction between *cis*-**4** and **14**, double fragmentation occurred especially in the initial stage of the reaction, although it was followed by a side reaction with the degradation of *cis*-**4**. However, *trans*-**4** showed a much slower reaction with aziridine **14** and, when excess aziridine was used, similar products resulted.

Reaction with Triphenylphosphine. The attempted reaction between oxaziridine and triphenylphosphine was one of the most interesting for the elucidation of the chemical properties of oxaziridine. Oxygen abstraction reported by Horner and Jürgens for compound **3** seems to be the most reasonable reaction, considering the strong oxygen affinity of phosphorus atom.[7]

In practice, however, we found that the reaction of triphenylphosphine with *cis*-**4** proceeded in a manner similar to the reaction with amines.

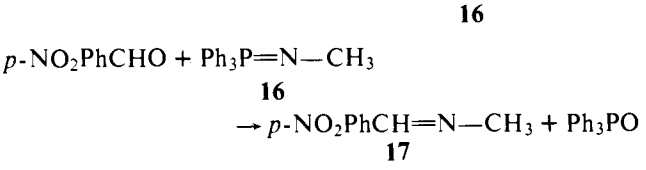
Mixing equimolar amounts of *cis*-**4** and triphenylphosphine in chloroform at 0 °C immediately caused the reaction with the accompanying color change from blue-violet to orange, which occurred within a few seconds. The NMR spectra observed immediately after mixing both components clearly showed the formation of triphenylphosphonium ylide **16** and benzaldehyde. The reaction was quantitative. However, when the mixture was allowed to stand a few minutes, ylide **16** and benzaldehyde disappeared gradually, and *N*-(benzylidene)-methylamine (**12**) and triphenyl phosphinoxide appeared in



cis-**4**

the NMR spectra or VPC. Triphenylphosphonium ylide **16** was confirmed by comparison with an authentic sample prepared according to literature,[10] but the determination of its yield was very difficult due to the fast reaction with benzaldehyde. Here, we used *p*-nitrobenzaldehyde to estimate the yield of ylide **16** as it was more reactive than benzaldehyde.[12]

Before starting the reaction, we checked the inertness of *p*-nitrobenzaldehyde and *cis*-**4** in chloroform solution and added triphenylphosphine at 0 °C. The yield of *N*-(*p*-nitrobenzylidene)methylamine (**17**) was 84% and we found a very small amount of *N*-(benzylidene)methylamine (**12**) and 92.7% of benzaldehyde as accompanying products.



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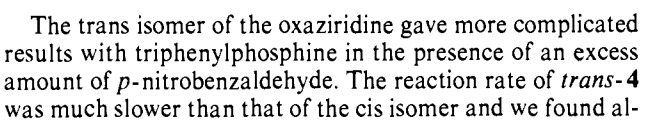


16 **17**

The trans isomer of the oxaziridine gave more complicated results with triphenylphosphine in the presence of an excess amount of *p*-nitrobenzaldehyde. The reaction rate of *trans*-**4** was much slower than that of the cis isomer and we found almost equimolar amounts of **12** and *N*-(*p*-nitrobenzylidene)-methylamine (**17**) in the solution after the reaction. This suggested that the reaction of *trans*-oxaziridine proceeded concurrently in two ways, one of which was by oxygen abstraction as shown in the reaction between epoxide[11] and triphenylphosphine and the other was by fragmentation due to nitrogen attack as indicated in the reaction with amines. The reaction at 0 °C took about 15 min for *trans*-**4** but only a few seconds for *cis*-**4**. *trans*-**4** showed large steric hindrance in the S_N2 reaction on the nitrogen atom of oxaziridine.

Reaction with Sulfide. Thiophenol reacted with oxaziridines in a manner similar to amines or triphenylphosphine, but more vigorously.

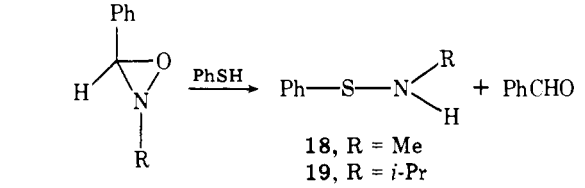
In tetrachloromethane solution at −20 °C, *cis*-**4** vanished completely only 10 min after addition of excess thiophenol and we found almost quantitative yields of *N*-methylbenzenesulfenamide (**18**) and benzaldehyde.

The trans isomer had a much slower reaction rate than *cis*-**4** and the yield of **18** reached the maximum value of 38% at 30 min after of the addition of thiophenol. Compound **18** which formed was consumed by the reaction with benzaldehyde and thiophenol added as reagents.

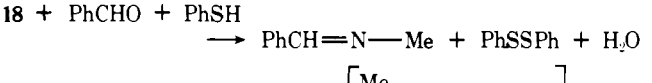
Table III. Products from 3-Phenyloxaziridines and Sulfide in $CHCl_3$ or CCl_4

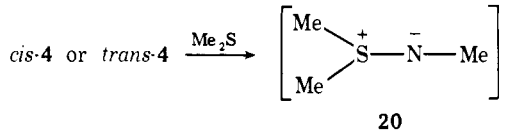
reagent	R[c]	conformation of oxaziridine	react. temp and time	main products	yield
PhSH	Me	cis	−20 °C, 10 min	PhS—N(Me)H	quant.
		trans	−20 °C, 30 min		max at 38.2% (60% of starting material recovered)
	i-Pr	cis	RT, 5 min	PhS—N(*i*-Pr)H	97.4%
		trans	RT, 10 min		max at 44.8% (50% of starting material recovered)
Me—S—Me	Me	cis	RT, 1 h	Me—N=N—Me	71.9%[a] (cis, 52.6%; trans, 19.3%)
		trans	RT, 3.5 h		29.4%[b] (cis, 19.8%; trans, 9.6%)

[a] *cis*-Azomethane was unstable and the yield was diminished by longer reaction times. [b] 22.5% of the starting material was recovered. [c] Substituent group on the 2 position of 3-phenyloxaziridine.



18, R = Me
19, R = *i*-Pr





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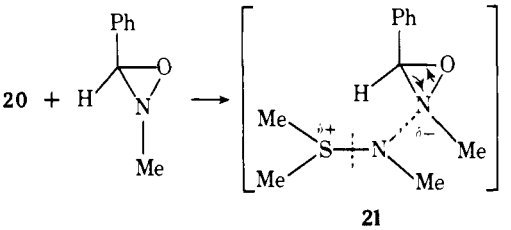

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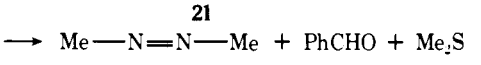
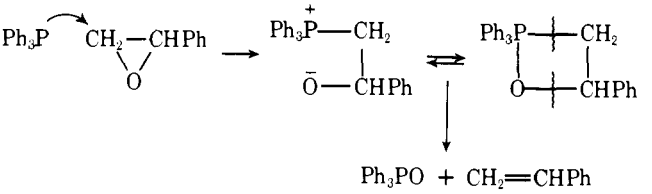


cis, trans

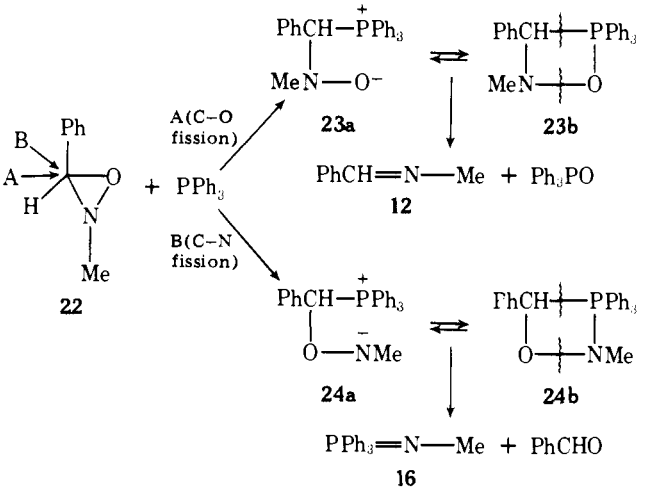
As shown in Table III, the 2-isopropyloxaziridine reacted similarly with thiophenol. With the trans isomer, the maximum yield of *N*-isopropylbenzenesulfenamide (**19**) was 44.8% at 10 min after the start of the reaction at room temperature. On the other hand, we obtained azomethane as the sole product of the reaction of oxaziridine *cis*-**4** or *trans*-**4** and dimethyl sulfide. Although dimethylsulfinemethylimine (**20**) was expected in the initial stage of the reaction, it probably reacted immediately with another molecule of oxaziridine due to its strong nucleophilicity and formed azomethane via fragmentation of the transition intermediate as shown in formula **21**. In practice, the reaction required a higher temperature than that with thiophenol, and the azomethane formed was a mixture of cis and trans isomers. The total yield of azomethane was 71.9% or 29.4% calculated from the amount of *cis*-**4** or *trans*-**4** used, respectively.

Discussion

Triphenylphosphine is capable of opening an epoxide ring. The resultant four-membered ring or betaine proposed as an intermediate is directly analogous to that formed in the Wittig reaction derived from benzaldehyde and collapses to form phosphine oxide and an olefin.[11] Attack of nucleophilic reagents on the carbon atom adjacent to oxygen in the three-membered ring seems to be the most plausible reaction course for oxaziridines. The oxygen abstraction from **3**, described in the introductory section of this report, or from the oxaziridines by triphenylphosphine probably proceeds via a mechanism very



similar to that proposed above. Thus the reaction sequence could be represented as proceeding through **23a** and **23b**. However, the formation of triphenylphosphonium ylide **16**, hydrazines **9**, **11**, and **12**, azo compound **13**, or sulfenamides **18**, **19**, and **20** could not be clearly interpreted as resulting through the intermediates **23a** and **23b**.



22

23a **23b**

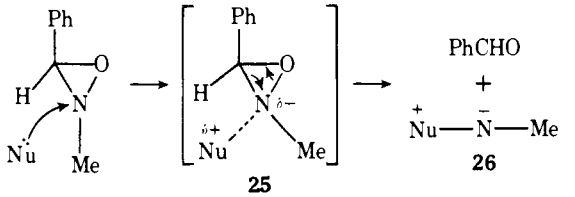
24a **24b**

16

If B attack (C–N fission) by triphenylphosphine on oxaziridine **22** occurs exclusively, only **24a** can give triphenylphosphine ylide **16**. However, the reasonable assumption that the reactions of oxaziridine with amines, triphenylphosphine, and sulfide have similar reaction pathways, formation of the nitrogen analogue of **24b** is impossible due to the small outer electron shell of nitrogen.

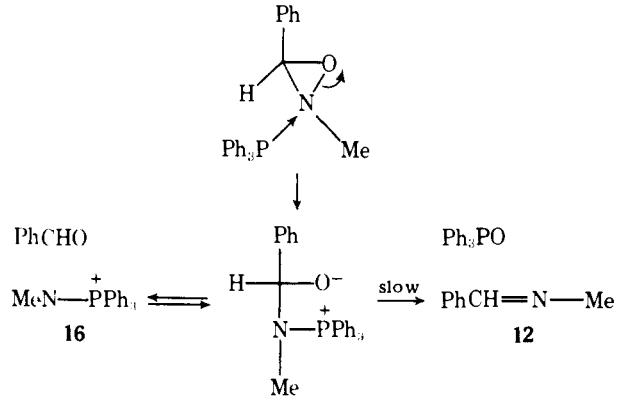
Actually, attack of nucleophilic reagents on a nitrogen atom of organic compounds is not impossible if the nitrogen atom has a strong electronegative group in an adjacent position. For example, the S_N2 substitution reaction of nitrosyl compounds[13] of several nucleophilic reactions has been studied extensively and a nucleophilic reaction toward trivalent nitrogen was also reported recently by Krueger et al.[14] The reaction of oxaziridines reported here can be understood as an S_N2 attack by a nucleophilic reagent on the nitrogen atom of oxaziridine followed by bond cleavage of N–O and C–N as shown in **25**.

After concerted cleavage of both bonds of the three-membered ring, all of our product should be formed via the formation of ylide **26**. The observed yield of triphenylphosphonium ylide **16** was also understandable from the reversibility between betaine and the stable ylide which was shown in the



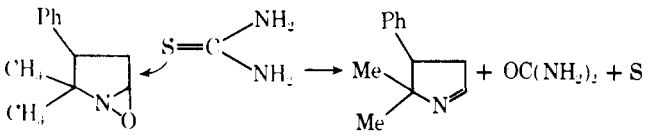
25 **26**

elegant study of Speziale and Bissing.[12] In practice, ylide **16** was stable under atmosphere at room temperature and reacted only slowly with benzaldehyde.

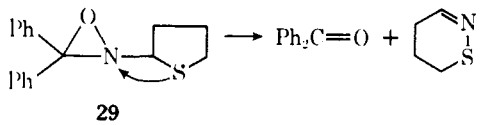


16 **27** **12**

The ability of sulfur to participate in the displacement reaction involving three-membered rings of oxaziridines has been well discussed in literature. Intermolecular reaction of sulfur nucleophiles with oxaziridines **28** has been suggested to proceed by attack at a ring carbon[15] and an intramolecular reaction as shown in **29** was proposed for the attack of the ring nitrogen



28



29

atom.[16] The results indicate that the reaction course of oxaziridines with nucleophiles is affected delicately by the steric hindrance of the substituent groups on carbon or nitrogen of the three-membered ring. In our study using sulfide reagents, we observed only the reaction occurring by the attack at the ring nitrogen. However, in the reaction of triphenylphosphine on *trans*-oxaziridine, we found the formation of almost equimolar amounts of both products **12** and **17**, resulting from oxygen abstraction due to carbon attack and from the fragmentation due to nitrogen attack, respectively. The formation of **12** suggested that the steric hindrance of substituents on *trans*-oxaziridine strongly forced the A attack to form **23a** or **23b**.

Generally, cis isomers tended to be much more reactive than trans isomers, although the kinetic study remains to be done. Obviously, the difference of reactivities between isomers should be attributed to the steric effect of the two substituents at the 2 and 3 positions of the oxaziridine ring.

Conclusion

Our experiments showed that the attack of nucleophilic reagents on the oxaziridine ring occurred at the nitrogen atom predominantly (N–O and C–N bond fission in a concerted process). The reaction of amines and sulfide proceeded exclusively on the nitrogen atom by a concerted S_N2 type reaction. However, this rule does not hold for the reaction of *trans*-**4** with triphenylphosphine. The steric effect of the substituent group and the lone pair of ring nitrogen atom probably affected these reactions.

Imine >C=N- formation by the reaction of amine with carbonyl derivatives followed by oxidation to form oxaziridine is a very plausible process even in vivo.[17] Under very mild conditions, the reaction of oxaziridines with amines or the SH group occurs at a very fast rate, and many chances develop for hydrazine or sulfenamide formation on the surface of protein or nucleic acid. Recently, we observed that oxaziridines strongly inhibit the activity of papain and considered this an example of the reaction between the SH group of papain and oxaziridines. As we showed in the first section of this report, oxaziridines also had stronger cytotoxic activity than aziridines having the same substituent groups. We hope the biological properties of oxaziridine will be completely elucidated in the near future.[18]

Experimental Section

cis- and *trans*-2-methyl-3-phenyloxaziridine (*cis*-**4** and *trans*-**4**),[19] *cis,trans*-2-methyl-3-*p*-nitrophenyloxaziridine,[19] 1,1-diethyl-2-methylhydrazine (**9**),[20,21] trimethylhydrazine,[21] *cis,trans*-azomethane (**13**),[22] methaneazobenzene,[23,24] triphenylphosphinemethylimine (**16**),[10] *N*-methyl-, and *N*-isopropylbenzenesulfenamide (**18** and **19**)[25] were prepared according to methods described in literature.

1-Methyl-2-*p*-chlorophenylaziridine (**14**) was prepared according to a method described in literature[26] by using *p*-chlorostyrene as starting material, bp 70–80.5 °C (3 mm): NMR ($CDCl_3$) δ 7.1 (d, 4), 2.45 (s, 3), 2.19 (q, 1), 1.7 (q, 2). Anal. Calcd for $C_9H_{10}NCl$: C, 64.49; H, 6.01; N, 8.36. Found: C, 64.54; H, 6.07; N, 8.37.

cis- and *trans*-2-isopropyl-3-phenyloxaziridine were prepared according to literature[27] and separated by column chromatography. Cis isomer: bp 35 °C (0.1 mm); NMR ($CDCl_3$) δ 7.46 (s, 5), 5.26 (s, 1), 2.35 (m, 1), 1.22 (d, 3), 0.72 (d, 3). Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.36; H, 8.00; N, 8.56. Trans isomer: bp 52–53 °C (1 mm); NMR ($CDCl_3$) δ 7.40 (s, 5), 4.50 (s, 1), 2.40 (m, 1), 1.30 (d, 3), 1.15 (d, 3). Anal. Found: C, 73.43; H, 7.95; N, 8.29.

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Triethylamine. *cis*- or *trans*-oxaziridine (*cis*-**4** or *trans*-**4**, 0.2 mmol) was dissolved in 0.5 mL of deuteriochloroform and then $C_{19}H_{40}$ hydrocarbon was added as an internal reference for VPC. At room temperature, excess triethylamine was added. The reaction occurred immediately and the disappearance of oxaziridine was observed by NMR. For *cis*-**4**, the reaction solution became cloudy with the deposition of white crystals which disappeared after a few hours accompanied by a decrease of the benzaldehyde formed in the initial stage of the reaction. After this, the formation of hexamethylenetetramine was observed by VPC. Its yield was 64.6% from *cis*-**4** or 78.0% from *trans*-**4** at 4 days after the reaction had been started.

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Dimethylamine. *cis*- or *trans*-oxaziridine (*cis*-**4**, or *trans*-**4**, 0.2 mmol) was dissolved in 0.5 mL of deuteriochloroform and then tetrachloroethane was added as an internal reference for NMR. At room temperature, excess dimethylamine was added. The reaction occurred immediately and was completed in about 20 min. The yield of trimethylhydrazine was 71.6% from *cis*-oxaziridine or 85.3% from *trans*-oxaziridine. The reaction of oxaziridine with diethylamine was also carried out by the same procedure and the product, diethylmethylhydrazine, was detected by VPC or NMR. Diethylmethylhydrazine was very susceptible to oxygen in the atmosphere and was converted easily into compound **10**.

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Methylamine. *cis*- or *trans*-oxaziridine (*cis*-**4** or *trans*-**4**, 0.2 mmol) was dissolved in 0.5 mL of deuteriochloroform at room temperature then dibenzyl ether for *cis*-**4** or tetrachloroethane for *trans*-**4** was added as an internal reference for NMR. At 50 min after the addition of excess methylamine, *cis*-**4** vanished and the yield of *trans*-azomethane was 51.4% and that of *cis*-azomethane 20.6%. The total yield calculated on the basis of *cis*-**4** used was 72%. For *trans*-**4**, the reaction was completed after 3 days and 37% yield of *trans*-azo-

methane and 13% yield of *cis*-azomethane were detected. Under the reaction conditions, *cis*-azomethane was unstable and gradually decomposed into an unidentified product.

Reaction of *trans*-2-Methyl-3-phenyloxaziridine (*trans*-4) with Aniline. *trans*-Oxaziridine (*trans*-**4**, 8 mmol) was dissolved in 3 mL of deuteriochloroform and 1 g of aniline was added. The mixture was heated at 100 °C for 4 h, and then $C_{10}H_{22}$ hydrocarbon was added as an internal reference for VPC into part of the reaction solution. A 26% yield of *trans*-methaneazobenzene was observed.

Reaction of *cis*-2-Methyl-3-phenyloxaziridine (*cis*-4) with 1-Methyl-2-*p*-chlorophenyl Aziridine (14). *cis*-Oxaziridine (*cis*-**4**, 0.3 mmol) and an appropriate amount of tetrachloroethane as an internal reference were dissolved in 0.5 mL of deuteriochloroform, and then 0.31 mmol of aziridine **14** was added. The reaction solution was heated at 95 °C and the change in the NMR spectrum at 15 min and 30 min was examined to determine the yield of benzaldehyde, *p*-chlorostyrene, and azomethane and the amount of recovered starting material. The result is given in Table II. The products were confirmed by VPC, NMR, and GC–MS by comparison with authentic samples.

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Triphenylphosphine. *cis*- or *trans*-Oxaziridine (*cis*-**4** or *trans*-**4**, 0.2 mmol) and *p*-nitrobenzaldehyde (0.4 mmol) were dissolved in 0.5 mL of deuteriochloroform, and then tetrachloroethane was added as an internal reference for NMR. The solution was cooled at 0 °C and 0.2 mmol of triphenylphosphine was added. For *cis*-**4**, the solution colored blue-violet by addition of triphenylphosphine changes to orange after 5 min. At this point, NMR indicated the formation of triphenylphosphinemethylimine **16** by its spectrum with peaks at δ 7.5 (m, 15) and 2.95 (d, 3).

Ten minutes of reaction at room temperature gave 84% of *N*-(*p*-nitrobenzylidene)methylamine (**17**) and a very small amount of *N*-(benzylidene)methylamine **12**.

trans-Oxaziridine (*trans*-**4**) required 15 min at 0 °C and gave 58.1% of *N*-(*p*-nitrobenzylidene)methylamine (**17**) and 39.1% of *N*-(benzylidene)methylamine (**12**).

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Thiophenol. *cis*- or *trans*-oxaziridine (*cis*-**4** or *trans*-**4**, 2 mmol) was dissolved in 6 mL of tetrachloromethane with $C_{11}H_{24}$ hydrocarbon added as an internal reference for VPC. The solution was cooled at −20 °C and exactly 1 equimolar amount of thiophenol was added.

For *cis*-**4**, the reaction was completed in 10 min and the product, *N*-methylbenzenesulfeneamide (**18**), formed quantitatively. For *trans*-**4**, the yield of **18** was 38.2% with 50% of recovered starting material after 30 min of reaction. The reaction of *cis*- or *trans*-2-isopropyl-3-phenyloxaziridine with thiophenol was carried out at room temperature by using $C_{14}H_{30}$ hydrocarbon as an internal reference. The yield of *N*-isopropylbenzenesulfeneamide (**19**) was 97.4% from *cis*-oxaziridine or 44.8% from *trans*-oxaziridine. In the latter case, 50% of the starting material was recovered after 10 min of the reaction.

Reaction of *cis*- or *trans*-2-Methyl-3-phenyloxaziridine (*cis*-4 or *trans*-4) with Dimethyl Sulfide. *cis*- or *trans*-oxaziridine (*cis*-**4** or *trans*-**4**, 0.25 mmol) and an appropriate amount of dibenzyl ether as an internal reference for NMR were dissolved in 0.5 mL of deuteriochloroform. At room temperature, excess dimethyl sulfide[28] was added. For *cis*-oxaziridine, 1 h was required for the reaction, and we observed 52.6% yield of *cis*-azomethane and 19.3% yield of *trans*-azomethane in the reaction solution. For *trans*-oxaziridine, after 3.5 h at room temperature, we observed 19.8% of *cis*-azomethane, 9.6% of *trans*-azomethane, and 22.5% of recovered starting material.

In both cases, azomethane initially formed was mainly the cis isomer which was unstable under the reaction conditions. Confirmation of *cis*- and *trans*-azomethane was done by VPC, NMR, and GC–MS by comparison with authentic samples.

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