Admixture of the IV obtained in the reaction of Ia with *p*-nitrobenzoic acid and of the authentic sample showed no melting point depression. The nmr and the infrared spectra were also identical.

Reaction of Ia with 2,6- or 2,4-dinitrophenol was accomplished in the same way as the reaction of Ia with trifluoroacetic acid. The yield of *threo*-1-(1′-methyl-2′-*o*,*o*′-dinitrophenoxypropyl)-3-phenylurea (VI) was 65%, mp 166–168°, after recrystallization from chloroform and *n*-hexane; ir (Nujol mull) 3320 (NH) and 1650 cm^{-1} (C=O); nmr (CF_3COOH) τ 8.55 (doublet, CH_3, J = 6.0 cps), 8.74 (doublet, CH_3, J = 6.0 cps), 5.80 (complex multiplet, CH), 5.53 (complex multiplet, CH), 2.53 (multiplet, aromatic protons) and 1.90 (doublet, aromatic protons, J = 8.0 cps).

Anal. Calcd for $C_{17}H_{18}N_4O_6$: C, 54.54; H, 4.85; N, 14.97. Found: C, 54.87; H, 5.01; N, 14.79.

threo-1-(1′-Methyl-2′-*o*,*p*-dinitrophenoxypropyl)-3-phenylurea (VII) was obtained in 58% yield, mp 185–187°, after recrystallization from chloroform and *n*-hexane; ir (Nujol mull) 3370 (NH) and 1690 cm^{-1} (C=O); nmr (CF_3COOH) τ 8.60 (doublet, CH_3, J = 6.0 cps), 8.49 (doublet, CH_3, J = 6.0 cps), 5.68 (complex multiplet, CH), and 5.18 (complex multiplet, CH).

Anal. Calcd for $C_{17}H_{18}N_4O_6$: C, 54.54; H, 4.85; N, 14.97. Found: C, 54.80; H, 5.05; N, 14.77.

Acknowledgment. We are indebted to Professor Mitsuhiko Hida and Dr. Toyotoshi Ueda of the University of Tokyo and Dr. Kiyoshi Shimizu, Nitto Boseki Co., Ltd., for helpful discussions.

Acid-Catalyzed Isomerization of 1-Acyl- and 1-Thioacylaziridines. II.[1] The Orientation of Ring Opening

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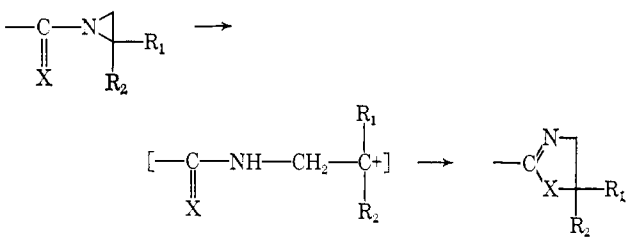
Abstract: The isomerization of 1-(N-phenylcarbamyl)- (IIIa) and 1-(N-phenylthiocarbamyl)-2-methylaziridines (IIIb) with acids was investigated. In the isomerization of IIIa, 2-anilino-5-methyl-2-oxazoline (IVa) was obtained as the major product along with the isomeric 2-anilino-4-methyl-2-oxazoline (Va). IIIb gave a mixture of almost equal amounts of 2-anilino-5-methyl-2-thiazoline (IVb) and 2-anilino-4-methyl-2-thiazoline (Vb). The orientation of the ring opening of IIIa or IIIb seems to be nearly independent of acids and solvents. Investigation using optically active IIIa and IIIb suggests that IVa is formed by an SN2 mechanism with protonic acids and by a front-side attack mechanism when boron trifluoride etherate is used, and IVb would either be an SN2 or SN1 mechanism depending upon the acid and solvent used. These results clearly indicate that the mechanism of ring opening is not determined by the orientation. Such an SN2 mechanism is considered to be a "modified" SN2 in which substituents exhibit an SN1-like effect. An interpretation in which the difference in the orientation of the ring opening between IIIa and IIIb on the assumption that the site of the protonation would be different from IIIa to IIIb was also considered.

In the ring opening of unsymmetrically substituted three-membered heterocyclic compounds, cleavage between the heteroatom and the less substituted carbon atom has often been termed "normal" cleavage and that between the heteroatom and the more substituted carbon atom termed "abnormal" cleavage. There are some discussions[3] concerning the relationship between orientation and the mechanism of ring opening of unsymmetrically substituted aziridines with acids, but no stereochemical study has been done on the relationship. As for kinetic studies, Clapp and coworkers[4] investigated the ring-opening reaction of 2-ethyl- and 2,2-dimethylaziridine with several acids and concluded from the kinetic parameters and the structure of the reaction products obtained that the "abnormal" cleavages proceed by an SN1 mechanism and the "normal" cleavages by an SN2 mechanism. The mechanism of the acid-catalyzed isomerization of 1-acyl- or 1-thioacylaziridines to oxazolines or thiazolines, respectively, has also been considered relative to the orientation of the ring opening. Heine, *et al.*,[5] found that 1-aroyl-2,2-dimethyl- or 1-aroyl-2-phenylaziridine was isomerized in cold sulfuric acid to give 2-aryl-5,5-dimethyl- or 2-aryl-5-phenyl-2-oxazoline, respectively. Deutsch and Fanta[6] reported that the isomerization of 1-(N-phenylthiocarbamyl)-2,2-dimethylaziridine with hot dilute hydrochloric acid gave 2-anilino-5,5-dimethyl-2-thiazoline. These isomerization reactions were considered to proceed *via* carbonium ion formation from the orientation of the ring cleavage, *i.e.*, "abnormal" cleavage.



X = O: R_1 = Me; R_2 = Me or R_1 = H; R_2 = Ph

X = S: R_1 = Me; R_2 = Me

(1) Paper I: T. Nishiguchi, H. Tochio, A. Nabeya, and Y. Iwakura, *J. Am. Chem. Soc.*, **91**, 5835 (1969).

(2) Nippon Rayon Co. Ltd., Ohyodo-ku, Ohsaka, Japan.

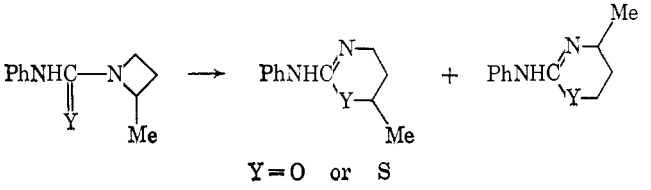
(3) See for a review: P. E. Fanta, "Heterocyclic Compounds with Three- and Four-Membered Rings," Part I, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1964, pp 524–575.

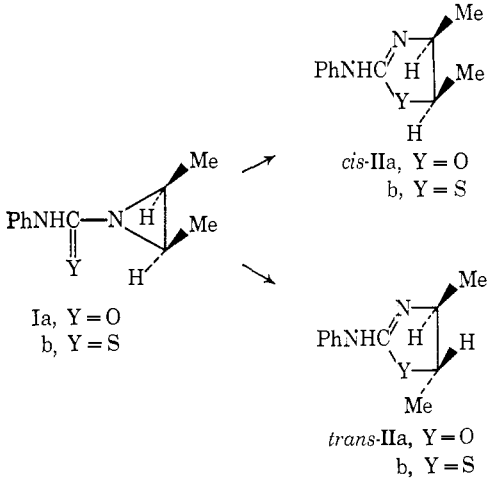
(4) (a) V. B. Schatz and L. B. Clapp, *J. Am. Chem. Soc.*, 77, 5113 (1955); (b) D. H. Powers, Jr., V. B. Schatz, and L. B. Clapp, *ibid.*, 78, 907 (1956); (c) J. E. Earley, C. E. O'Rourke, L. B. Clapp, J. O. Edwards, and B. C. Lawes, *ibid.*, 80, 3458 (1958).

(5) (a) H. W. Heine, M. E. Fetter, and E. M. Nicholson, *ibid.*, **81**, 2202 (1959); (b) H. W. Heine and M. S. Kaplan, *J. Org. Chem.*, **32**, 3069 (1967).

(6) A. S. Deutsch and P. E. Fanta, *ibid.*, **21**, 892 (1956).

In the course of the study of the ring-opening reaction of the azetidine[7] and aziridine derivatives,[1,8] we have found that in the isomerization of 1-(N-phenylcarbamyl)-2-methylazetidine with picric or *p*-toluenesulfonic acid in refluxing toluene, the "abnormal" cleavage predominates, while in the case of the corresponding sulfur compound, 1-(N-phenylthiocarbamyl)-2-methylazetidine, the "normal" cleavage is slightly favored.[7a] The result was explained in the following way—assuming that in both cases the carbonyl oxygen or the thiocarbonyl sulfur would attack the ring carbon directly because of the poor nucleophilic reactivity of the conjugate base of the acids used. The attack by the sulfur would assume more SN2 character than that by the oxygen owing to the greater nucleophilicity of the former, thus resulting in the more "normal" cleavage, while the isomerization of the oxygen compound might proceed by an SN1-like mechanism. However, the result of a stereochemical investigation of *cis*-1-(N-phenylcarbamyl)- (Ia) and *cis*-1-(N-phenylthiocarbamyl)-2,3-dimethylaziridines (Ib) seems to disprove the above explanation.[1] In the isomerization of Ia with a protonic acid, the acid adds to the three-membered ring and then the carbonyl oxygen attacks the β-carbon to form the five-membered ring resulting in complete retention of configuration (double inversion). With boron trifluoride or boron trifluoride etherate, Ia isomerized with complete retention of configuration presumably by front-side attack mechanism (SNi mechanism). In the case of Ib, complete retention of configuration caused by double inversion (SN2 mechanism), was observed with sulfonic acids or when N,N-dimethylformamide (DMF) was used as the solvent. With sterically hindered phenols, Ib gave a mixture of the *cis*- and *trans*-thiazolines showing that the reaction proceeds by a carbonium ion formation (SN1 mechanism). Ib also gave the *cis*-thiazoline *via* the polyisothiourea type polymer.[9]





In this paper, the isomerization of (*S*)-1-(N-phenylcarbamyl)- ((*S*)-IIIa) and (*S*)-1-(N-phenylthiocarbamyl)-2-methylaziridine ((*S*)-IIIb) with acids is described and the correlation between orientation and the mechanism of the ring opening is discussed.

Results

1-(N-Phenylcarbamyl)- (IIIa) or 1-(N-phenylthiocarbamyl)-2-methylaziridine (IIIb) was prepared from 2-methylaziridine and phenyl isocyanate or phenyl isothiocyanate, respectively. (*S*)-2-Methylaziridine was prepared from (*S*)-alaninol according to the reported procedure.[10] The isomerization reaction of IIIa or IIIb was carried out in the same way as in the case of Ia or Ib reported previously.[1] IIIa gave a mixture of 2-anilino-5-methyl-2-oxazoline (IVa) and 2-anilino-4-methyl-2-oxazoline (Va) in the reaction. Similarly, IIIb gave a mixture of the corresponding thiazoline derivatives, IVb and Vb. The ratio of IV and V in the product mixture was determined by nmr analysis, since both in the case of oxazolines and thiazolines, the methyl, methylene, and methine hydrogens in IV and V were well separated (Table I).

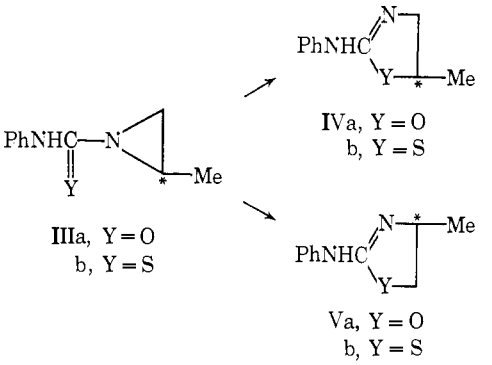


Table I. Chemical Shifts of IV and V[a]

Compd	Methyl hydrogens	Methylene hydrogens[b]	Methine hydrogens[b]
IVa	8.65, 8.57	6.80–5.96	5.50–4.93
Va	8.83, 8.74	6.30–5.50	
IVb	8.67, 8.57	6.90–5.90	
Vb	8.88, 8.78	7.38–6.65	6.30–5.86

[a] The nmr spectra were taken in chloroform solution with tetramethylsilane as the internal standard at 60 MHz. Resonance locations are given as τ values. [b] Complex multiplets.

In the isomerization of (*S*)-III, if the "normal" cleavage takes place to give V, the configuration of the asymmetric carbon should be retained. On the other hand, when IV is formed by "abnormal" cleavage, several possibilities as to the fate of the asymmetric carbon exist. The configuration of the asymmetric carbon of IV in the product mixture was estimated by the ratio IV:V and the specific rotation values of the mixture, and of optically pure (*S*)-IV and (*S*)-V (see footnotes of Table II). Optically pure samples of

(7) (a) Y. Iwakura, A. Nabeya, T. Nishiguchi, and K. Ohkawa, *J. Org. Chem.*, 31, 3352 (1966); (b) Y. Iwakura, A. Nabeya, T. Nishiguchi, and Y. Ichikawa, *ibid.*, 30, 3410 (1965).

(8) Y. Iwakura, A. Nabeya, and T. Nishiguchi, *ibid.*, 32, 2362 (1967).

(9) Y. Iwakura, A. Nabeya, and T. Nishiguchi, *J. Polymer Sci., A-1*, 6, 2591 (1968).

(10) Y. Minoura, M. Takebayashi, and C. C. Price, *J. Am. Chem. Soc.*, 81, 4689 (1959).

Table II. Acid-Catalyzed Isomerization of (*S*)-IIIa and (*S*)-IIIb in Benzene

Compd	Acid	pK_a of Acid	Total yield, %	Distribution, % IV	(*S*)-V	[α]D,[a] deg	Distribution of IV,[b] (*S*)-IV	(*R*)-IV	Isomerization of I,[1] % *cis*-II	*trans*-II
(*S*)-IIIa	*p*-Toluenesulfonic	1.0	91	85	15	+10	99	1	100	0
(*S*)-IIIa	2,4,6-Trinitrobenzene-sulfonic[c]		52	89	11	+10	96	4	100	0
(*S*)-IIIa	Picric	0.48	63	92	8	+10	95	5	100	0
(*S*)-IIIa	Boron trifluoride etherate		29	88	12	+10	97	3	100	0
(*S*)-IIIb	*p*-Toluenesulfonic		84	50	50	−21	98	2	100	0
(*S*)-IIIb	2,4,6-Trinitrobenzene-sulfonic[c]		31	50	50	−21	98	2	100	0
(*S*)-IIIb	Picric		68	37	63	−3	48	52	50	50
(*S*)-IIIb	2,6-Dinitrophenol	5.2	21	43	57	−1	44	56	50	50
IIIb	2,4-Dinitrophenol	4.0	20	36	64				74	26
(*S*)-IIIb	Trifluoroacetic	0.23	79	45	55	−14	81	19	75	25
(*S*)-IIIb	Trichloroacetic	0.64	58	35	65	−13	85	15	77	23

[a] Specific rotation values of the product mixture measured in dioxane at 20°. [b] Calculated from the formula: $[\alpha]_D = (1/100)\{[1 - (2X/100)]P[\alpha]^{(S)\text{-IV}} + Q[\alpha]^{(S)\text{-V}}\}$ where X is the percentage of (*R*)-IV in IV, P or Q is that of IV or V in the reaction product, and $[\alpha]^{(S)\text{-IV}}$ or $[\alpha]^{(S)\text{-V}}$ is the specific rotation value of (*S*)-IV or (*S*)-V, respectively. The error is presumed to be within several per cent. [c] Since the acid was insoluble in benzene, the reaction was carried out in THF.

Table III. Acid-Catalyzed Isomerization of IIIa in Various Solvents

Acid	Solvent	Total yield, %	Distribution, % IVa	Va	Isomerization of Ia,[1] % *cis*-IIa	*trans*-IIa
p-Toluenesulfonic	Nitromethane	81	89	11	100	0
	DME[a]	67	88	12	100	0
	THF[b]	81	87	13	100	0
	DMF	73	85	15	100	0
Picric	Nitromethane	82	90	10	100	0
	DME[a]	58	85	15	100	0
	THF[b]	73	93	7	100	0
	DMF	73	86	14	100	0
Boron trifluoride etherate	Nitromethane	50	89	11	100	0
	DME[a]	63	88	12	100	0
	THF[b]	45	92	8	100	0
	DMF	30	89	11	100	0

[a] 1,2-Dimethoxyethane. [b] Tetrahydrofuran.

Table IV. Acid-Catalyzed Isomerization of IIIb in Various Solvents

Acid	Solvent	Total yield, %	Distribution, % IVb	Vb	Isomerization of Ib,[1] % *cis*-IIb	*trans*-IIb
p-Toluenesulfonic	Nitromethane	58	51	49	100	0
	DME[a]	70	49	51	100	0
	THF[b]	75	50	50	100	0
	DMF	82	70	30	100	0
Picric	Nitromethane	42	52	48	50	50
	DME[a]	50	55	45	89	11
	THF[b]	75	60	40	100	0
	DMF	82	80	20	100	0
Trifluoroacetic	Nitromethane	42	42	58	76	24
	DME[a]	50	41	59	83	17
	THF[b]	63	42	58	81	19
	DMF	58	61	39	100	0

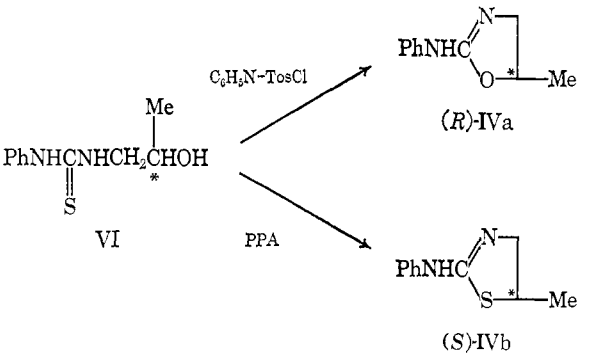
[a] 1,2-Dimethoxyethane. [b] Tetrahydrofuran.

(*S*)-Va and (*S*)-Vb were prepared from (*S*)-alaninol,[10] and the specific rotations of (*S*)-Va and (*S*)-Vb were found to be $[\alpha]^{20}D$ −6.6° (0.609 g/10 ml in dioxane) and −6.0° (0.619 g/10 ml in dioxane), respectively. An optically pure sample of (*R*)-IVa was obtained by cyclization of (*R*)-1-(2′-hydroxypropyl)-3-phenylthiourea (VI)[11] with *p*-toluenesulfonyl chloride in pyridine;[12] the specific rotation value was $[\alpha]^{20}D$ −13.2° (0.136 g/10 ml in dioxane). On the other hand, the cyclization of VI in polyphosphoric acid gave an optically pure sample of (*S*)-IVb[13] whose specific rotation was $[\alpha]^{20}D$ −37.3° (0.383 g/10 ml in dioxane). From the stereochemical point of view, the isomerization of III to IV corresponds to that of I to II. The isomerization of (*S*)-IIIa and (*S*)-IIIb with acids was carried out in benzene and the results are summarized in Table II along with results obtained in the isomerization of I to II. Results obtained by the

(11) Optically active (*R*)-1-amino-2-propanol was prepared by the procedure of P. A. Levene and A. Walti, *J. Biol. Chem.*, **68**, 415 (1926).

(12) K. Kurita and Y. Iwakura, unpublished result.

(13) The complete inversion of configuration in the cyclization in polyphosphoric acid was proved in the previous paper.[1]



isomerization of IIIa and IIIb with acids in several solvents are shown in Table III and Table IV.

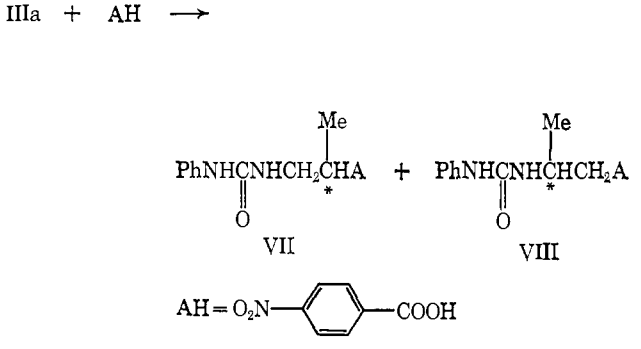
IIIb gave only polymeric substances by reaction with boron trifluoride etherate in benzene, even when the solution of IIIb in benzene was added to the solution of boron trifluoride etherate in benzene very slowly to maintain the concentration of IIIb very low. Table V

Table V. Isomerization of IIIb Catalyzed with Trifluoroacetic Acid in Benzene

Reaction time	Total yield, %	Distribution, % IVb	Vb
5 min	36	35	65
1 hr	47	40	60
10 hr	57	41	59

shows the change in the ratio of IVb and Vb *vs.* the reaction time in the reaction of IIIb with trifluoroacetic acid in benzene.

The reaction of IIIa with *p*-nitrobenzoic acid in benzene gave a mixture of the two ring-opened addition products arising from the "abnormal" cleavage (VII) and the "normal" cleavage (VIII) in 59% total yield. An authentic sample of VII was prepared from 1-(2′-hydroxypropyl)-3-phenylurea and *p*-nitrobenzoyl chloride. Similarly, VIII was prepared from 1-(1′-methyl-2′-hydroxyethyl)-3-phenylurea and *p*-nitrobenzoyl chloride. Analysis of the nmr spectrum of the reaction mixture of IIIa with *p*-nitrobenzoic acid mentioned



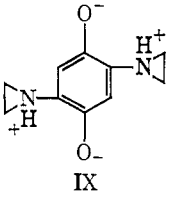
above revealed that the ratio VII:VIII in the mixture was 78:22.

Discussion

In the isomerization of III, IV is formed by the "abnormal" and V by the "normal" cleavage. It is noteworthy that first, the orientation of the ring opening is quite different in the isomerization of IIIa and IIIb; in the isomerization of IIIa, IVa is the major (about 80–90%) product, while in the case of IIIb, about the same amount of IVb and Vb is obtained. Second, except for the isomerization of IIIb in DMF, the ratio of IV and V is not greatly changed when the acid or the solvent is changed.

In the preceding paper,[1] we discussed the mechanism of the isomerization of Ia and Ib under several conditions, and the results are briefly summarized in the introductory section of this paper. It would be quite reasonable to assume that the same mechanism would prevail in the isomerization of III to IV, since as seen in Table II, the stereochemistry of the isomerization of I to II and of III to IV showed good correspondence under the same reaction conditions. In spite of the varieties of mechanism, the orientation of the ring opening remained almost unchanged in IIIa and IIIb. Moreover, in the reaction of IIIa with *p*-nitrobenzoic acid, where a mixture of the ring-opened addition products was isolated, the orientation was also nearly the same as in the isomerization of IIIa (78% "abnormal"). In the reaction of IIIb with trifluoroacetic acid, where the isomerization is considered to have partially proceeded *via* isothiourea type polymers as discussed previously, the orientation remained unchanged as the reaction time was extended (Table V). This means that the orientation of the ring opening to give the isothiourea-type polymer (addition of another molecule of IIIb) is also the same.

Two suggestions may be advauced to explain the difference in orientation of the ring opening in IIIa and IIIb. One is based upon the assumption that the position of complex formation between the acids and the aziridine derivatives is different in IIIa and IIIb. In urea or thiourea derivatives, protonation is considered to occur at the oxygen or the sulfur atom.[14] However, no decisive evidence has been advanced as to the protonation site in 1-acyl- or 1-thioacylaziridines. In some 1-substituted aziridines, the nitrogen atom is more basic than in the corresponding N-substituted strain-free secondary amines because of the difficulty of the resonance between the aziridinyl nitrogen and the 1-substituents,[15] *i.e.*, 2,5-di(1′-aziridino)-1,4-hydroquinone forms an intramolecular salt (IX) while the corresponding piperidine derivative which is of aromatic



IX

amine character does not.[15h] From these facts, it would not be unreasonable to assume that in IIIa, the protonation takes place at the nitrogen atom while in IIIb, it does at the sulfur atom. On such an

(14) (a) T. Birchall and R. J. Gillespie, *Can. J. Chem.*, **41**, 2642 (1963); (b) A. R. Katritzky and A. Y. Jones, *Chem. Ind.* (London), 722 (1961).

(15) (a) F. A. L. Anet and J. M. Osyany, *J. Am. Chem. Soc.*, **89**, 352 (1967); (b) F. A. L. Anet, R. D. Trepka, and J. D. Cram, *ibid.*, **89**, 357 (1967); (c) C. P. Nash and G. E. Maciel, *J. Phys. Chem.*, **68**, 832 (1964); (d) A. T. Botlini and C. P. Nash, *J. Am. Chem. Soc.*, **84**, 734 (1962); (e) V. F. Bystrova, O. A. Yuzhakova, and R. G. Kostyanovskii, *Dokl. Akad. Nauk SSSR*, **147**, 843 (1962); (f) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **83**, 2016 (1961); (g) H. C. Brown and A. Tsukamoto, *ibid.*, **83**, 4549 (1961); (h) A. Marxer, *Helv. Chim. Acta*, **38**, 1473 (1955).

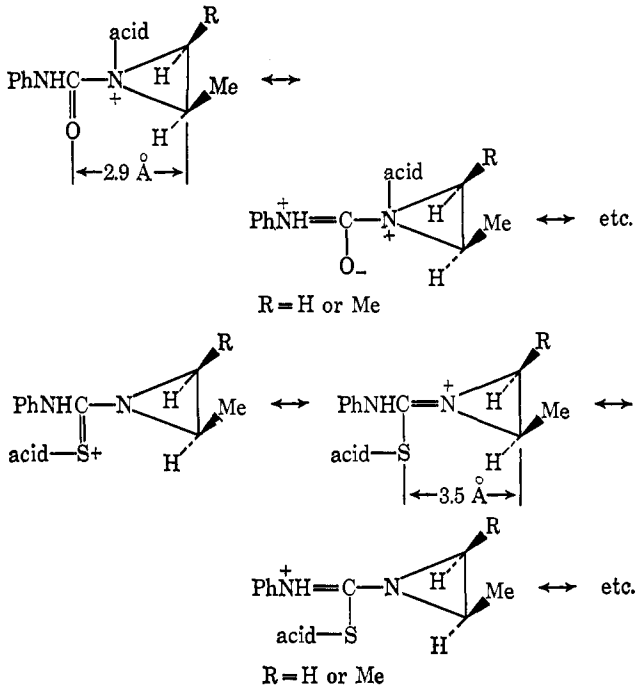


Figure 1. Resonance and dimension[18] of the complexes using the assumption that an acid adds to the ring nitrogen atom of Ia or IIIa, and to the sulfur atom of Ib or IIIb.[19]

assumption, the plus charge is localized only on the ring nitrogen atom in IIIa, while in IIIb, it is delocalized over three atoms as shown in Figure 1.

By such a delocalization the "normal" ring opening would be more favored in IIIb than in IIIa, for in the ring-opening reaction of the three-membered heterocycles, generally, "normal" cleavage predominates under neutral or basic conditions, while in an acidic medium, "abnormal" cleavage is more likely to occur.[3,16]

Another explanation is based upon the assumption that, although complex formation of an acid takes place at the corresponding position of IIIa and IIIb, the orientation of the ring opening is subject to the polar effects of urea and thiourea linkage. To examine the validity of such an assumption, we have measured the dissociation constants of several benzoic acids having $C_2H_5NHCONH-$ or $C_2H_5NHCSNH-$ groups at the *meta* and *para* positions, and obtained Hammett σ constants: $\sigma_m = 0.04$, $\sigma_p = -0.26$ (for $C_2H_5NHCONH-$), and $\sigma_m = 0.30$, $\sigma_p = 0.06$ (for $C_2H_5NHCSNH-$).[17] From the result it is difficult to explain the orientation of the ring opening in IIIa and IIIb where more "abnormal" cleavage takes place in IIIa having less electron-withdrawing urea linkage. Further, the σ values suggest that the electron density of the ring nitrogen may be higher in IIIa and that the driving force for N-protonation should be stronger in IIIa than in IIIb.

In the preceding paper,[1] the different behavior of Ia and Ib toward boron trifluoride etherate was mentioned: Ia isomerized to *cis*-IIa by front-side attack mechanism, while Ib gave only polymeric substances. On the first assumption mentioned above, it is not difficult to

(16) (a) P. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959); (b) M. Sander, *ibid.*, **66**, 297 (1966).

(17) T. Nishiguchi and Y. Iwakura, unpublished result.

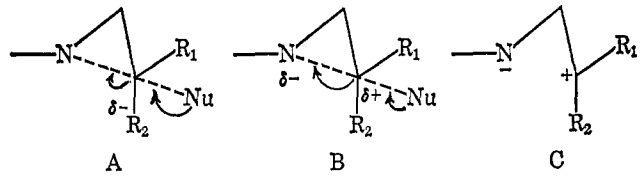


Figure 2. Inferred transition states of ring-opening reactions of aziridines: A, SN2; B, "modified" or "borderline" SN2; C, SN1 mechanism.

imagine from ball-and-stick models[18] that in Ia, which is complexed with acid at the nitrogen, the structure would be more favorable for the front-side attack to occur than in Ib where the complex formation with acids is taking place at the sulfur atom as shown in Figure 1.[19]

In ring-opening reaction of oxiranes several examples are known where the reactions are thought to proceed *via* SN2 mechanism by the reaction conditions or stereochemistry, and show SN1 type substituent effect (the orientation of the ring opening).[16a] Parker and Isaacs classified these types of reactions as "modified" or "borderline" SN2.[16a] Also the reaction of 2-methylthiirane with dimethylamine was reported,[16b] where the "abnormal" addition product predominates. In aziridines, there has been no reaction reported which is considered to be of the "modified" SN2 mechanism. The fact that IIIa opened the ring in an "abnormal" fashion with complete inversion at the asymmetric carbon atom would be well explained by the "modified" SN2 mechanism in which bond breaking is more important than bond making in the transition state, so that the alkyl substituent tends to increase the reaction rate (see Figure 2). Such a conception would also explain the fact that in each IIIa or IIIb, the orientation of ring opening was not greatly changed by the change in the nucleophile or change in the mechanism determined by stereochemistry. The fact that the ratio of IV to V hardly changed in most solvents suggests that the transition state of the "abnormal" and the "normal" ring cleavage of III would have nearly equal polarity. However, in the isomerization of IIIb in DMF as shown in Table IV, where the "abnormal" was more favored than the "normal" as compared with the reactions in other solvents, the transition state of the "abnormal" ring opening might be more polar than that of the "normal."

Nevertheless, the question of why the yield of Vb is comparable to that of IVb in the isomerization of IIIb where racemization took place, remains unanswered.

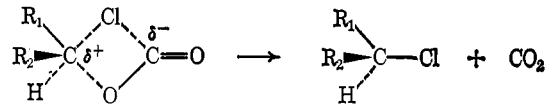
The thermal decomposition of chloroformates in the gas phase is considered to proceed by a nucleophilic substitution involving a front-side attack (SNi mechanism).[20] In this case, the substituents exhibited an

(18) The ball-and-stick model was constructed on the assumption that the ring nitrogen where an acid has added is in sp^3 hybridization, while the one to which an acid has not added has hybridization between sp^2 and sp^3.

(19) It is assumed that the site of complex formation is the same for proton and boron trifluoride by the fact that the orientation of the ring opening of IIIa catalyzed with proton and boron trifluoride showed no clear-cut difference, and by the study that both proton and boron trichloride add to oxygen in amides unless steric hindrance is not strong; see W. Gerrard, M. F. Lappert, H. Pyszora, and J. M. Wallis, *J. Chem. Soc.*, 2144 (1960).

(20) (a) E. S. Lewis and W. C. Herndon, *J. Am. Chem. Soc.*, **83**, 1955 (1961); (b) E. S. Lewis, W. C. Herndon, and D. C. Duffey, *ibid.*, **83**, 1959 (1961); (c) E. S. Lewis and W. C. Herndon, *ibid.*, **83**, 1961 (1961).

SNi type effect: the relative reaction rate was 1 (R_1 = R_2 = H), 22 (R_1 = H, R_2 = Me), 220 (R_1 = R_2 = Me),



and 640 (R_1 = Me, R_2 = Et).[21] The fact that the isomerization of IIIa with boron trifluoride etherate gave IVa predominantly (about 90%) would suggest that the transition state of such an isomerization (presumably to be front-side attack) would not be greatly different from that of "modified" SN2.

Experimental Section[22]

(*S*)-1-(N-Phenylcarbamyl)-2-methylaziridine ((*S*)-IIIa). (*S*)-2-Methylaziridine was prepared from (*S*)-alaninol according to the method of Price, *et al.*,[10] bp 64–65° (lit.[10] 66–67°), $[\alpha]^{20}D$ −12.6° (0.800 g/10 ml in ethanol) (lit.[10] $[\alpha]^{25}D$ −12.8°).

(*S*)-IIIa was prepared from equimolar (*S*)-2-methylaziridine and phenyl isocyanate in ether and found to be liquid. However, its hydrate could be recrystallized from ethanol and water, and showed various melting points.

Anal. Found: C, 68.29; H, 7.44; N, 14.83.

The hydrate was dehydrated in reduced pressure at *ca.* 60° to give (*S*)-IIIa; ir (Nujol mull) 3350 (NH) and 1669 cm^{-1} (C=O); $[\alpha]^{20}D$ +73.1° (0.345 g/10 ml in dioxane); nmr ($CHCl_3$) τ 8.76 (doublet, CH_3, J = 5.0 cps), 8.11 (doublet, CH_2, J = 5.0 cps), 7.55 (complex multiplet, CH).

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.86; N, 15.90. Found: C, 68.29; H, 6.81; N, 15.88.

1-(N-Phenylcarbamyl)-2-methylaziridine (IIIa) was synthesized in a similar manner, mp 65–66°.

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.86; N, 15.90. Found: C, 68.07; H, 6.87; N, 15.98.

(*S*)-1-(N-Phenylthiocarbamyl)-2-methylaziridine ((*S*)-IIIb) was prepared from equimolar (*S*)-2-methylaziridine and phenyl isothiocyanate in ether below 0°, and purified by dry freezing in benzene, mp 40–42°; ir (Nujol mull) 3190 cm^{-1} (NH); $[\alpha]^{20}D$ +14.6° (0.195 g/10 ml in dioxane).

Anal. Calcd for $C_{10}H_{12}N_2S$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.66; H, 6.21; N, 14.49.

1-(N-Phenylthiocarbamyl)-2-methylaziridine was obtained in a similar way, mp 75.5–76°.

Anal. Calcd for $C_{19}H_{12}N_2S$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.47; H, 6.38; N, 14.35.

(*R*)-2-Anilino-5-methyl-2-oxazoline ((*R*)-IVa). (*R*)-1-Amino-2-propanol was obtained by the method of Levene and Walti.[11] The reaction between the amino alcohol and phenyl isothiocyanate gave (*R*)-1-(2′-hydroxypropyl)-3-phenylthiourea (VI), mp 93–94°; ir (Nujol mull) 3200 (OH, broad and weak) and 3160 cm^{-1} (NH).

The cyclization reaction of VI with *p*-toluenesulfonyl chloride and pyridine by the method of Kurita and Iwakura[12] gave (*R*)-IVa, mp 104–105°; ir (KBr pellet) 3220 (NH, broad and weak) and 1677 cm^{-1} (C=N); $[\alpha]^{20}D$ −13.2° (0.136 g/10 ml in dioxane).

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.86; N, 15.90. Found: C, 68.20; H, 6.97; N, 16.02.

(*S*)-2-Anilino-5-methyl-2-thiazoline ((*S*)-IVb), (*S*)-2-Anilino-4-methyl-2-oxazoline ((*S*)-Va), and (*S*)-2-Anilino-4-methyl-2-thiazoline ((*S*)-Vb). (*S*)-IVb, (*S*)-Va, or (*S*)-Vb was prepared by the cyclization reaction of VI, (*S*)-1-(1′-methyl-2′-hydroxyethyl)-3-phenylurea or (*S*)-1-(1′-methyl-2′-hydroxyethyl)-3-phenylthiourea in polyphosphoric acid, respectively, in a manner similar to the preparation of *cis*-2-anilino-4,5-dimethyl-2-oxazoline (*cis*-IIa).[1] The physical properties of the optically active oxazolines and thiazolines were shown below.

(*S*)-IVb: mp 94–95°; ir (KBr pellet) 3060 (NH, broad and weak) and 1630 cm^{-1} (C=N); $[\alpha]^{20}D$ −37.3° (0.383 g/10 ml in dioxane).

Anal. Calcd for $C_{10}H_{12}N_2S$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.75; H, 6.33; N, 14.62.

(*S*)-Va: mp 91–92°; ir (KBr pellet) 3060 (NH, broad and weak) and 1690 cm^{-1} (C=N); $[\alpha]^{20}D$ −6.6° (0.609 g/10 ml in dioxane).

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.86; N, 15.90. Found: C, 68.22; H, 6.87; N, 15.87.

(*S*)-Vb: mp 101–102°; ir (KBr pellet) 3100 (NH, broad and weak) and 1630 cm^{-1} (C=N); $[\alpha]^{20}D$ −6.0° (0.619 g/10 ml in dioxane).

Anal. Calcd for $C_{10}H_{12}N_2S$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.60; H, 6.32; N, 14.45.

Melting points and elemental analyses of the racemic oxazolines and thiazolines are summarized as: IVa, mp 131–132° (lit.[23] 141 and 132°).

(*Anal.* Calcd for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.86; N, 15.90. Found: C, 68.30; H, 6.95; N, 16.21); IVb, mp 114–115° (lit.[24] 117°) (*Anal.* Calcd for $C_{10}H_{12}N_2S$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.30; H, 6.33; N, 14.40); Va, mp 103–104° (lit.[23a] 110°); Vb, mp 93–94° (lit.[25] 91°).

Isomerization of IIIa and IIIb with Acids. These reactions were carried out in the same way as in the isomerization reactions of *cis*-1-(N-phenylcarbamyl)- (Ia) and *cis*-1-(N-phenylthiocarbamyl)-2,3-dimethylaziridine (Ib) with acids.[1]

Yield of IVb and Vb *vs.* Reaction Time in the Isomerization of IIIb with Trifluoroacetic Acid. A solution of IIIb (5.8 g) in 30 ml of benzene was added to a solution of trifluoroacetic acid (3.5 g) in 30 ml of benzene over a period of 5 min with refluxing and stirring. Each sample (20 ml) was pipetted from the refluxing reaction mixture at the time of 5 min, 1 hr, and 10 hr after the addition. The samples were treated in the similar manner as in the isomerization of IIIb with acids.

Reaction of IIIa with *p*-nitrobenzoic acid was performed similarly to the reaction of Ia with *p*-nitrobenzoic acid. A mixture of the reaction products was isolated in 59% yield and melted at 139–145°. From the nmr spectrum of the product mixture, the ratio of VII to VIII was evaluated as 78 to 22.

Anal. Calcd for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.24. Found: C, 59.47; H, 5.01; N, 12.40.

An authentic sample of 1-(2′-*p*-nitrobenzoyloxypropyl)-3-phenylurea (VII) was prepared by the condensation reaction of 1-(2′-hydroxypropyl)-3-phenylurea and *p*-nitrobenzoyl chloride in THF in the presence of triethylamine as acid acceptor.

VII was obtained in 31% yield and recrystallized repeatedly from THF, mp 145–147°; ir (Nujol mull) 3300 (NH) and 1275 cm^{-1} (C=O); nmr (CF_3COOH) τ 8.50 (doublet, CH_3, J = 6.0 cps), 6.24 (doublet, CH_2, J = 6.0 cps), 4.50 (quintet, CH, J = 6.0 cps).

Anal. Calcd for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.24. Found: C, 59.13; H, 5.14; N, 12.16.

An authentic sample of 1-(1′-methyl-2′-*p*-nitrobenzoyloxyethyl)-3-phenylurea (VIII) was synthesized from 1-(1′-methyl-2-hydroxyethyl)-3-phenylurea and *p*-nitrobenzoyl chloride in 40% yield and recrystallized from THF. It melted at 195–196°; ir (Nujol mull) 3300 (NH) and 1725 cm^{-1} (C=O); nmr (CF_3COOH) τ 8.55 (doublet, CH_3, J = 6.0 cps) and 5.44 (broad singlet, CH_2 and CH).

Anal. Calcd for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.24. Found: C, 59.53; H, 5.16; N, 12.12.

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(21) It is difficult to decide whether these SNi type reactions proceed *via* a highly polar transition state or a tight ion pair by kinetic or polar effect study. In the previous paper,[1] we suggested that a polar transition state and a tight ion pair are continuous and essentially the same in these SNi type reactions.

(22) Melting points and boiling points are uncorrected. Nmr spectra were measured in specified solvents with tetramethylsilane as the internal standard at 60 MHz.

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