was collected by filtration to give 200 mg (41%) of the crude product. Recrystallization from methanol gave colorless needles of **9**, mp 165—167°. IR ν_{max} cm^{-1}: 2220 (CN). NMR ($CDCl_3$) δ: 3.34 and 3.42 (each 3H, each s, each NCH_3), 4.53 (3H, s, OCH_3). *Anal.* Calcd. for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.53. Found: C, 49.32; H, 4.65; N, 21.55.

b) A mixture of 500 mg (2.5 mmol) of **4** and 140 mg (2.6 mmol) of sodium methoxide in 10 ml of methanol was refluxed for 30 min. After cooling, the resulting precipitate was collected by filtration to give the crude product of **9** (86% yield) which was identical with the product prepared by the procedure (a).

5-Carbamoyl-1,3-dimethylorotic Acid (10)——A suspension of 480 mg (2.5 mmol) of **1** in 4 ml of conc. sulfuric acid was heated at 60—70° for 1 hr. After cooling, the mixture was poured into 50 ml of water and allowed to stand for a week. The resulting precipitate was collected by filtration to give 330 mg (58%) of the crude product. Recrystallization from methanol to give colorless prisms of **10**, mp 164—166°. NMR (DMSO-d_6) δ: 3.20 and 3.43 (each 3H, each s, each NCH_3), 7.49 and 8.18 (each 1H, each bs, $CONH_2$), 8.50 (1H, s, OH). *Anal.* Calcd. for $C_8H_9N_3O_5$: C, 42.29; H, 3.99; N, 18.50. Found: C, 42.00; H, 4.05; N. 18.23.

1,3-Dimethyluracil-5-carboxamide (11)——A suspension of 200 mg (0.9 mmol) of **10** in diphenyl ether (2 ml) was refluxed for 10 min. After cooling, the mixture was diluted with ether and the resulting precipitate was collected by filtration to give 100 mg (61%) of the crude product. Recrystallization from water gave colorless needles of **11**, mp 219—220° (lit.[11] mp 216—218°), which was identical with an authentic sample.[11]

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The Roles of Hetero Atoms in Solvolytic Reactions V[1] Transannular β-S-Participation in Solvolysis of S-Containing Heterocycles

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The p-nitrobenzoates of 2-methyltetrahydro-2-thiophenemethanol and 3-methyltetrahydro-3-thiopyranol have been synthesized. The rates of solvolysis of the esters in 80% aqueous acetone have been determined titrimetrically. The β-methyl substitution of the primary ester has caused the rate to increase by a factor of 28 and its rate is 3.9 times faster than that of the tertiary ester. Both esters yield the corresponding alcohols in similar ratio, so that it is concluded to intervene the same intermediary episulfonium ion.

Keywords——S-containing 5- and 6-membered heterocycles; solvolysis; neighboring group participation by divalent sulfur; rate enhancement; episulfonium ion

Neighboring group participation of the sulfur atom in solvolytic reactions, which is usually observed as unexpectedly large effect,[3] provides valuable information to mechanistic studies.[1,4] An episulfonium ion intervening in the chemical conversion of penam to cephem[5] gives us much interests in the direction of its ring-opening. In connection with this skeletal

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[1] Part IV in this series: J. Ohishi, K. Tsuneoka, S. Ikegami, and S. Akaboshi, *J. Org. Chem.*, in press.

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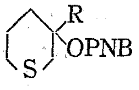
[3] For reviews, see *a*) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N.Y., 1962, pp. 16—18, 108—110; *b*) K.-D. Gundermann, *Angew. Chem.*, 75, 1194 (1963); *c*) B. Capon, *Quart. Revs.*, **18**, 45 (1964).

[4] S. Ikegami, T. Asai, K. Tsuneoka, S. Matsumura, and S. Akaboshi, *Tetrahedron*, **30**, 2087 (1974).

[5] For reviews, see *a*) R.D.G. Cooper and D.O. Spry, "Cephalosporins and Penicillins," ed. by E.H. Flynn, Academic Press, New York, N.Y., 1972, pp. 183—254; *b*) T. Kamiya, *J. Soc. Org. Synth. Chem. Japan*, 33, 24 (1975).

rearrangement, this paper deals with the evaluation of the amount of β-S-participation of the systems (**1**,**2**) and the direction of ring-opening of an intermediary bicyclic episulfonium ion (**3**).



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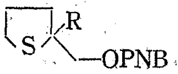

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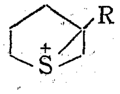
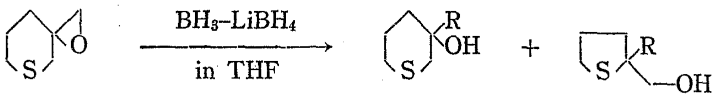


3

a: R=H
b: R=CH_3

Result and Discussion

As is shown in Chart 1, the alcohol (**6b**), which is difficultly accessible by other means, was prepared in excellent yield by the reduction of the epoxide (**4**) with the combined reagent consisted of borane-lithium borohydride (1.2:1).[6] This reduction took place in 80% ring-contraction, resulting a mixture of **5b** and **6b** in a ratio of 1:4. The isomeric alcohol (**5b**) was obtained by treatment of the corresponding ketone with methylmagnesium iodide. Both alcohols (**5b**, **6b**) were converted to *p*-nitrobenzoates (**1b**,**2b**) in the usual manner.



4 **5b**: R=CH_3 **6b**: R=CH_3

Chart 1

TABLE I. Solvolysis rates of S-Containing Heterocycles in 80% Aqueous Acetone at 50°[a]

Compound	Pseudo-first-order rate constant $k\times10^6$ sec^{-1}	1/2	CH_3/H
1a[b]	0.0166		
2a[b]	0.152	9.2	
1b[b]	1.09		66
2b[c]	4.21	3.9	28

a) All rate constants are extrapolated from rate data at higher temperatures.
b) Ref. 4.
c) Rate constants observed and physical parameters calculated using Eyring's equation are as follows: $k_1=6.17\times10^{-4}$ sec^{-1} (100°), $k_1=6.10\times10^{-5}$ sec^{-1} (75°), $\Delta H^{\ddagger}=23.2$ kcal/mol, and $\Delta S^{\ddagger}=-11.5$ e.u.

TABLE II. Summary of Solvolysis Products[a]

Ester	Yield (%)	Product ratio			
		5a (R=H)	6a (R=H)	5b	6b
1a[b]	94	81.9	18.1		
2a[b]	92	82.0	18.0		
1b	95.5			98.6	1.4
2b	~100			97.8	2.2

a) Yield and product ratios were determined by GLPC analysis.
b) Ref. 4.

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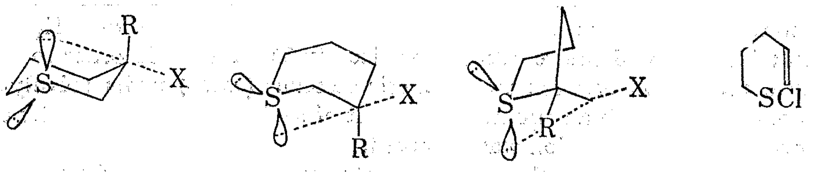
6) S. Ikegami, J. Ohishi, and S. Akaboshi, *Chem. Pharm. Bull.* (Tokyo), 23, 2701 (1975).

The solvolysis of the ester (**2b**) was carried out in 80% aqueous acetone and its rate is shown in Table I with the pertinent rates of the related esters.

The esters (**1b**, **2b**) yielded the two kinds of the corresponding alcohols (**5b**, **6b**) as solvolysis products in ratios of 98.6 : 1.4 and 97.8 : 2.2 respectively, where **5b** was a major isomer. These results are shown in Table II in relation of those of the related systems. The fact that the ratios of solvolysis products of both systems are almost the same shows that the same intermediate (**3**) must be involved.

It is of interest that a β-methyl substituent in **2** caused the rate to increase by a factor of 28, in spite of the rate-enhancing effect of 66 in **1** which is a direct substituent effect. The effect of a β-methyl substituent to affect rates of solvolysis is usually small and often observed as a rate-retarding effect,[7] although the effect varies with a change in solvent. The enhanced rate observed in **2**, therefore, is resulted from more stable transition state (**8**) than that of the 6-membered ring case (**7**).[8] The faster rates in the methyl substituents are attributed to forcing down in free energy of the intermediary episulfonium ion (**3b**) and to higher energy levels of the esters (**1b**, **2b**) than those of **1a** and **2a** in the ground state.



7A **7B** **8** **9**

Chart 2

Another interest is focussed on the structure of an intermediate ion (episulfonium ion) which is well-known to be involved in sulfenyl halide additions to olefins[9]. Major products from solvolysis of the two sets of the esters (**1a**, **2a** and **1b**, **2b**) were the 6-membered ring compounds (**5a** and **5b**). These are minor products formed initially from the intramolecular additions of sulfenyl chlorides.[10] However, thermal equilibration of the β-chloro-sulfides (**1** and **2**, OPNB=Cl) results in ratios similar to those obtained from solvolysis. Although it is still questionable whether or not an episulfonium ion involving in solvolytic reactions, sulfenyl halide additions, and equilibrating reactions of β-halo-sulfides is the same, the results of product ratios resulted from these reactions is expected to provide certain information in considering the structure of an episulfonium ion.

Experimental

Melting points are corrected. Proton nuclear magnetic resonance (PMR) spectra were obtained in $CDCl_3$ on a Varian HA-100 spectrometer (100 MHz) and chemical shifts are indicated as ppm from tetramethylsilane (TMS), internal standard. Coupling constants (J) are shown in Hz and coupling patterns are given by using the following abbreviations: AB=AB pattern, s=singlet, d=doublet. Gas liquid partition chromatographic (GLPC) analyses were carried out by a Varian gas chromatograph Model 1440 (single column, FID) using a glass column packed with 10% by weight of polydiethylene glycol adipate supported on acid-washed 80—100 mesh Chromosorb W (column; 2.4 m × 4 mm, flow rate of N_2: 30 ml/min).

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7) S. Winstein and H. Marshall, *J. Am. Chem. Soc.*, 74, 1120 (1952).

8) It is generally considered that the chair and boat forms (**7A**, **7B**) exist as an equilibrating mixture and the reaction proceeds *via* more stable transition state attributable to either form. The transition state of the boat form (**7B**) is assumed to be more stable from kinetic and steric evidences in reactions of the dithiane system (study to be published) and the 2-thia-6-norbornyl system (S. Ikegami, J. Ohishi, and Y. Shimizu, *Heterocycles*, 6, 387 (1977) and Ref. 1). Probably, a chair form may be involved in solvolysis, but the contribution of a boat form could be much important in this system.

9) For review, see W. Mueller, *Angew. Chem. Int. Ed. Engl.*, **8**, 482 (1969).

10) S. Ikegami, J. Ohishi, and Y. Shimizu, *Tetrahedron Lett.*, **1975**, 3923.

2-Methyltetrahydro-2-thiophenemethanol *p*-Nitrobenzoate (2b)——To a solution prepared freshly by mixing 12 ml (14.4 mmol) of 1.2 M BH_3-THF solution with a solution of 259 mg (12 mmol) of $LiBH_4$ suspended in 10 ml of anhydrous THF, was added a solution of 1.5 g (11.5 mmol) of the epoxide (4) dissolved in 3 ml of anhydrous THF under ice-cooling. After allowing overnight at 0°, excess hydride and complex were destroyed carefully by adding a mixture of 2 N H_2SO_4 (7.2 ml) and THF (8 ml). Filtration and evaporation gave an oil, which was dissolved in ether and the ether solution was washed with H_2O three times, dried over $MgSO_4$ and then evaporated to afford 1.50 g (98.7% yield) of a colorless oil. Analyses by GLPC and PMR revealed that the products were satisfactorily pure and consisted of a mixture of **5b**: **6b**=1: 4.

A solution of **6b** (80% purity, 1.50 g, 11.5 mmol) dissolved in 15 ml of anhydrous pyridine was reacted with *p*-nitrobenzoyl chloride (2.56 g, 13.8 mmol) under ice-cooling. After the usual work-up, a solid was obtained (2.3 g, 71% yield). Recrystallization from ether gave pale yellow needles of mp 65.5—66.0°. PMR spectrum: 4.43 (1H, d, $J=11$ (AB), 2-$C\underline{H}$H-O), 4.34 (1H, d, $J=11$ (AB), 2-$CH\underline{H}$-O), 1.55 (3H, s, 2-CH_3). *Anal.* Calcd. for $C_{13}H_{15}NO_4S$: C, 55.50, H; 5.37, N; 4.98, S; 11.29. Found: C; 55.38, H; 5.58, N; 4.85, S; 11.29.

Kinetic Measurements——The kinetic procedures of **2b** measured in 80% aqueous acetone were similar to those used for the related compounds previously described.[4] Rate constants and physical parameters were calculated by using computer (TOSBAC 3400) programmed with least-squares and Eyring's equation.

Analysis of Solvolysis Product——Solvolytic procedures were similar to those used for rate measurements. After reacting in a sealed ampoule immersed into a temperature-controlled bath (100°) for more than 10 half-lives, an equimolar amount of tetrahydro-3-thiopyranol as an internal standard for GLPC analysis was added to the reaction mixture and the resultant solution was dried over K_2CO_3. GLPC analysis (column temperature; 130°) showed the results summarized in Table II. In order to observe the absence of an acid-catalyzed equilibration between two isomeric alcohols (**5b**,**6b**) under solvolytic condition used, **5b** and **6b** were allowed to react with an equimolar amount of *p*-nitrobenzoic acid under the same condition. As a result, no appreciable interconversion was observed.

For the structural confirmation of solvolysis products by PMR analysis, the reaction mixtures of **1b** and **2b** solvolyzed under the same procedure were independently evaporated and extracted with ether. The extracts were washed with a saturated $NaHCO_3$ solution 3 times, dried over $MgSO_4$ and evaporated to give oils, whose PMR spectra revealed to be consistent with those of authentic samples and with the results of the product ratios which were obtained by GLPC analysis.

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