A Mechanistic Study of the Acetolyses of 3-Chloropropene Sulfide and 2-Chloroethyl Methyl Sulfide

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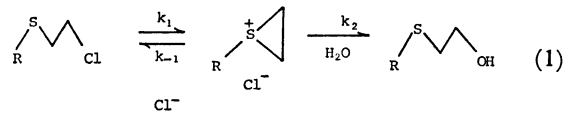
Forming a marked contrast to hydrolysis, the first-order rate constant in the acetolyses of 3-chloropropene sulfide (I) and 2-chloroethyl methyl sulfide (II) has been observed to be seriously decreased; this may be ascribed to the return to the starting material of the sulfonium intermediate (III′ or IV) by the chloride ion liberated in the course of the reaction. The reaction has substantially obeyed first-order kinetics, giving exclusively and quantitatively skeletally-rearranged 3-acetoxy-thietane (the first-order rate constant; $k_1=2.1\times10^{-5}$ s^{-1}, at 55.0 °C) and 2-acetoxyethyl methyl sulfide ($k_1=4.8\times10^{-4}$ s^{-1}, at 55.0 °C) from I and II respectively.

On the hydrolyses of 2-chloroethyl alkyl (or aryl) sulfides, the kinetics (of the profound acceleration due to sulfur participation) and mechanism (S_N1) involving the rate-determining formation of the episulfonium ion (III), followed by the facile destruction of III to alcohol, as is expressed in Eq. 1, have been well established.[1]

Making a marked contrast to the mechanistic and/or kinetic simplicities in hydrolysis, in acetolysis some complex observations have been reported.[2]



(1)

(III)

$k_2[\mathrm{III}][H_2O]>k_{-1}[\mathrm{III}][Cl^-]>k_1[RSCH_2CH_2Cl]$
R=alkyl, aryl, *etc.*

For example, one report has stated that the rate of decrease of 3-chloropropene sulfide in acetic acid follows the apparent first-order kinetics to give many kinds of unidentified products containing C–Cl bonds.[4]

Another report says that the acetolysis of 3-chloropropene sulfide gives 3-acetoxythietane only in a 33% yield.[5] Along with these intricate observations, the conspicuous mechanistic change in the acetolysis of 2-*endo*-chloro-7-thiabicyclo[2.2.1]heptane[6] (the rate-determining acetoxy ion attack on the sulfonium intermediate, S_N2) constrained us to investigate the mechanism and kinetics of the acetolysis of 3-chloroethyl alkyl sulfide, taking 3-chloropropene sulfide (I) and 2-chloroethyl methyl sulfide (II) as typical models.

Results

The acetolyses of 3-chloropropene sulfide (I) and 2-chloroethyl methyl sulfide (II) were performed in anhydrous acetic acid buffered with varying amounts of sodium acetate ([I], [II]=0.05 M, [NaOAc]=0.0, 0.065, 0.25, and 1.00 M). The rate of solvolysis was followed by means of the Volhard method for the liberated chloride ion. In several runs, the rate was also followed by means of vpc, where the amount of the acetate produced was in accord with the results of the titrimetric determination. The reuults for I and II are plotted in Figs. 1 and 2 respectively.

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The apparent first-order rate constants of I and II drifted downward, especially in the runs with low concentrations of sodium acetate. The same result was obtained for the acetolysis of II in the one-tenth concentrations involving with II and sodium acetate

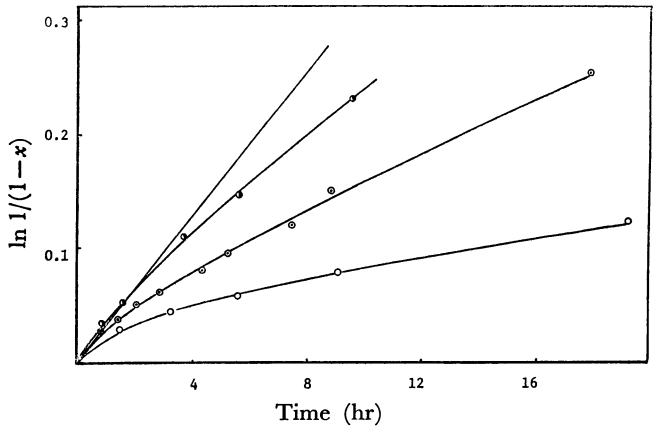


Fig. 1. Acetolysis of thiaepichlorohydrin (I) at 55.0 °C.
◑: [I]=0.05 M, [NaOAc]=1.00 M
⊙: [I]=0.05 M, [NaOAc]=0.25 M
○: [I]=0.05 M, [NaOAc]=0.065 M
Straight line was that obtained by means of numerical treatment.

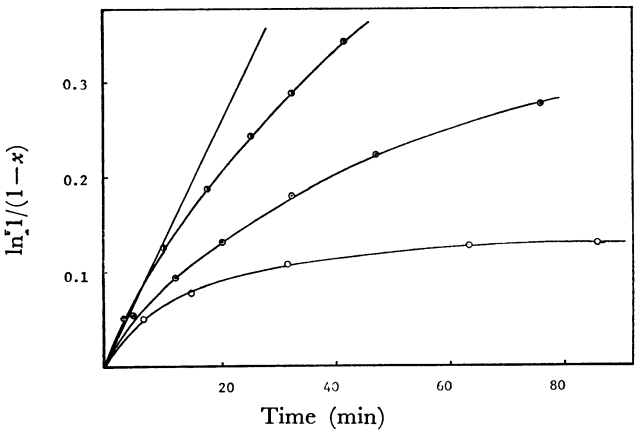


Fig. 2. Acetolysis of 2-chloroethyl methyl sulfide (II) at 55.0 °C.
◑: [II]=0.05 M, [NaOAc]=1.00 M
⊙: [II]=0.05 M, [NaOAc]=0.25 M
○: [II]=0.05 M, [NaOAc]=0.65 M
Straight line was that obtained by means of numerical treatment.

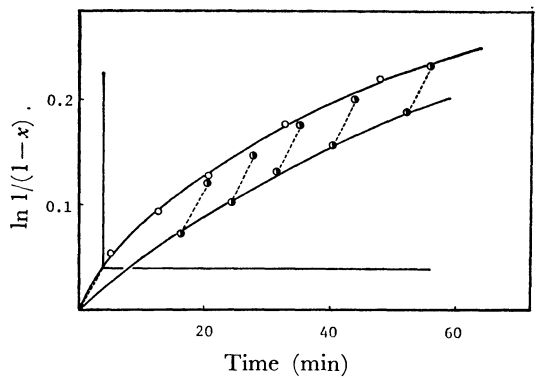


Fig. 3. Acetolysis of 2-Chloroethyl methyl sulfide (II) in the presence of added chloride ion at 55.0 °C.
○: [II[=0.05 M, [NaOAc]=0.25 M
◑: [II]=0.05 M, [NaOAc]=0.25 M, [NaCl]=0.0041 M
The plots, obtained in the presence of added chloride ion, were slided by 8.1% reaction.

([II]=0.005 M, [NaOAc]=0.0065 M).

In the absence of sodium acetate, no appreciable amount of acetate was produced or of the chloride ion was liberated within 5 hr for I and within 64 min for II at 55.0 °C, indicating that no reaction proceeded under those conditions.

The marked retardation of the reaction was observed in the presence of initially-added sodium chloride (8.1% to substrate; 0.0041 M). However, the time-conversion curve obtained in the presence of an added chloride ion could be just superimposed on the curve (at 8.1% conversion) obtained under the corresponding conditions where the chloride ion was not added (see Fig. 3).

On the basis of the vpc, NMR, and IR spectra of the reaction mixture of I, the exclusive and quantitative formation of skeletally-rearranged 3-acetoxythietane was observed, but the recovered sulfur chloride was not contaminated with the skeletally-rearranged 3-chlorothietane. From 2-chloroethyl methyl sulfide, 2-acetoxyethyl methyl sulfide was obtained in a quantitative yield (see Experimental section).

Discussion

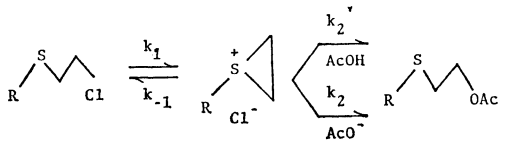
Our observation that no appreciable amount of liberated chloride ions was detected in the absence of sodium acetate is quite in accord with the observation reported by Morita and Oae[4] that, in the absence of a base, the acetolysis (at 105 °C) of 3-chloropropene sulfide (I) gave mainly many kinds of unidentified products containing C–Cl bonds, along with small amounts of acetates (3-acetoxypropene sulfide and 3-acetoxythietane).

An examination of Fig. 2 will make it clear that, under the conditions of ([KOAc]/[II]=1.45, on a steam bath for 20 hr) which Adams *et al.*[5] employed to obtain 33% of 3-acetoxythietane, the reaction practically ceases at around a 30~40% reaction.

The result in the run of a high dilution ([II]=0.005 M, [NaOAc]=0.0065 M) indicates that the direct displacement reaction by the acetoxy ion (S_N2) is not operative.

Figures 1 and 2 indicate that, in the initial period of reaction, the reaction proceeds at practically the same rate, with a small but appreciable amount of the salt effect of sodium acetate. This seems to indicate that the reaction proceeds *via* the rate-determining formation of the carbonium ion (delocalized by sulfur, S_N1 mechanism) and that the retardation is due to the liberated chloride ion (Eq. (2)). This explanation is supported by the quantitative retardation caused by the added chloride ion (Fig. 3) and can be reconciled with the fact of no reaction in the absence of a base (Eq. (2)).

The validity of this explanation is also reflected by the numerical treatment of the data (see the section on the numerical treatment of the rate data), by which the first-order rate constants, together with the ratios of the competition factors of the chloride ion to the acetoxy ion (k Cl^-/k OAc^-, given in parentheses) were determined to be 4.8×10^{-4} s^{-1} (*ca.* 30) for II and 2.1×10^{-5} s^{-1} (*ca.* 30)[7] for I.



(2)

(III')

$k_{-1}[III'][Cl^-]>k_2[III'][AcO^-]>k_1[RSCH_2CH_2Cl]$

$k_{-1}[III'][Cl^-]>k_2'[III][AcOH]$

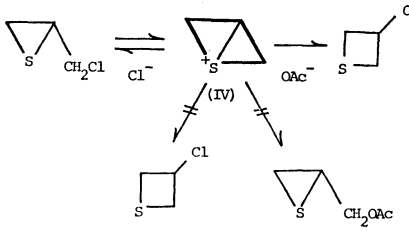
The apparent difference between the behavior in water and in acetic acid may partly be explained in terms of the differences in nucleophilicities of these solvents. Using the ratio of nucleophilicities[10] among acetic acid, water, and the chloride ion, the following relation may be drawn:

$$v_{H_2O} : v_{Cl^-} = 1 : 0.016 \text{ for hydrolysis} \quad (3)$$

$$v_{Cl^-} : v_{AcOH} = 1 : 0.0013 \text{ for acetolysis} \quad (4)$$

Thus, in a less nucleophilic solvent, as in acetic acid, the reaction seems to be governed exclusively by the chloride ion liberated, thus returning the sulfonium ion to the starting chlorosulfide (See Eqs. (2) and (4)).

The exclusive formation of the skeletally-rearranged 3-acetoxythietane and the absence of 3-acetoxypropene sulfide or 3-chlorothietane[12] in the reaction mixture (at 10% and 66% reactions), as monitored by means of vpc and NMR spectra, indicate that the acetoxy ion and the chloride ion reacted regioselectively with 1-thiabicyclo[1.1.0]butonium ion (IV) to produce 3-acetoxythietane and 3-chloropropene sulfide respectively. (See Eq. (5))



(5)

The rate of I is about seventy times the published

combined acetolysis-rearrangement constant for cyclopropylmethyl chloride.[15] This is typical of enhanced rate data supporting delocalization as the driving force for ionization. In view of the observed product, sulfur participation to form IV would seem to be a reasonable explanation for the reactivity of I. The moderately diminished reactivity of I compared with that of II may be due to the remarkable strain in the intermediate, IV, and/or to the expected poorer electron donation of episulfide.[16]

Numerical Treatment of Rate Data[17]

The most plausible reaction pathway for the acetolysis of II is illustrated in Eq. (6).

$$\underset{\text{II}}{CH_3SCH_2CH_2Cl} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\text{V}}{CH_3\overset{+}{S}<\overset{Cl^-}{\underset{OAc^-}{CH_2CH_2}}} \xrightarrow{k_2} CH_3SCH_2CH_2OAc \qquad (6)$$

where $k_{-1}[Cl^-][V]$ and $k_2[OAc^-][V]$ are assumed to be much larger than $k_1[II]$. The rate of the disappearance of the substrate can, then, be written as:

$$-\frac{d[R\text{-}Cl]}{dt} = \frac{k_1k_2[R\text{-}Cl][OAc^-]}{k_{-1}[Cl^-]+k_2[OAc^-]} \qquad (7)$$

The substitution of 1-x for R–Cl, x for Cl^-, $a-x$ for OAc^-, and x for ROAc gives:

$$-\frac{d(1-x)}{dt} = \frac{k_1k_2(1-x)(a-x)}{k_{-1}x+k_2(a-x)} \qquad (8)$$

where x: conversion expressed in terms of the fraction.
a: molar ratio of the sodium acetate to the substrate.

Integration gives:

$$k_1t = \ln\frac{1}{1-x} + \frac{k_{-1}}{k_2(a-1)}\left(\ln\frac{1}{1-x} - a\ln\frac{a}{a-x}\right) \qquad (9)$$

The k_{-1}/k_2 term is the ratio of the competition factors of the chloride ion to the acetoxy ion. Figure 4 shows the results calculated according to Eq. (9), with the value of k_{-1}/k_2 varying from 0 to 90, in which a systematic change could be observed; when the value of k_{-1}/k_2 was overestimated, an upward derivation of the calculated k_1 with the time was observed. An underestimation of the k_{-1}/k_2 value results in downward deviations of k_1. The first-order rate constant, k_1, and the ratio of the competition factors of the chloride ion to the acetoxy ion in the acetolysis of II at 55.0 °C were determined from Fig. 4 to be $(4.8\pm0.7)\times10^{-4}$ s^{-1} and *ca.* 30 respectively. Similarly, k_1 and k_{-1}/k_2 for the acetolysis of I at 55.0 °C were determined to be $(2.1\pm0.30)\times10^{-5}$ s^{-1} and *ca.* 30 respectively (see Fig. 5).

Effect of Added Chloride Ions. The rate constant, k_1, in the presence of added chloride ions was similarly expressed as:

$$k_1t = \ln\frac{1}{1-x} + \frac{k_{-1}}{k_2(a-1)}\left\{(\alpha+1)\ln\frac{1}{1-x} + (\alpha+a)\ln\frac{a}{a-x}\right\} \qquad (10)$$

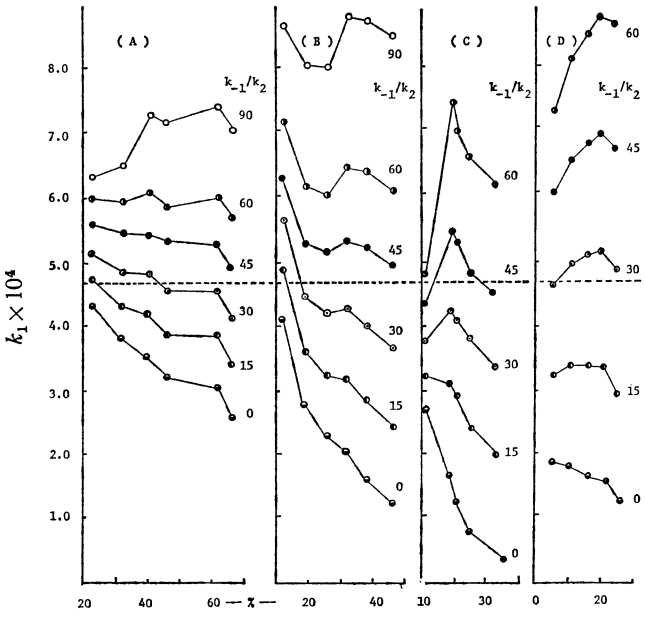


Fig. 4. Acetolysis of 2-chloroethyl methyl sulfide at 55.0 °C; The plots obtained from Eqs. (9) and (10), varying the value of k_{-1}/k_2 from 0 to 90.
(A): [NaOAc]=1.00 M, (B): [NaOAc]=0.25 M, (C): [NaOAc]=0.065 M, (D): [NaOAc]=0.25 M, [NaCl]=0.004 M.

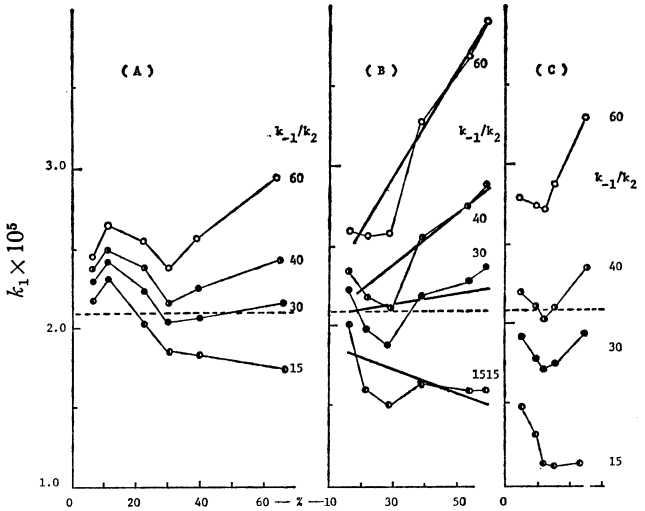


Fig. 5. Acetolysis of thiaepichlorohydrin at 55.0 °C; The plots obtained from Eqs. (9) and (10), varying the value of k_{-1}/k_2 from 0 to 60.
(A), [NaOAc]=1.00 M, (B): [NaOAc]=0.25 M, (C): [NaOAc]=0.065 M.

where α is the molar ratio of the added sodium chloride to the substrate. The k_1 value calculated on the basis of Eq. (10) is plotted in Fig. 4.

Experimental

All the boiling points are uncorrected. The NMR spectra were recorded with a Varian T 60 spectrometer, while chemical shifts were reported in δ values relative to the TMS internal standard. The infrared spectra were measured with a Hitachi Model EPI-G3 grating spectrophotometer, and

the mass spectra were recorded with a Hitachi Model RMU 6C mass spectrometer.

The acetic acid was used after distillation from a mixture containing 5% of acetic anhydride (118.0—118.3 °C). The sodium acetate was used without further purification after drying by means of Abderhalden at the toluene reflux temperature.

2-Chloroethyl Methyl Sulfide (II). Into a solution of 20.0 g of β-hydroxyethyl methyl sulfide in 100 ml of benzene we vigorously stirred dry hydrogen chloride at room temperature for 3 hr. The reaction mixture was diluted with 100 ml of pentane, and the excess hydrogen chloride was neutralized with sodium bicarbonate. After washing with saturated sodium chloride, the organic layer was dried over magnesium sulfate. After the distillation of the solvent through a 10-cm Vigreux column, II was distilled twice under reduced pressure (66.5—67.2 °C/70 mmHg, 87.0—87.8 °C/138 mmHg), 22.0 g of II was thus obtained (the yield was 82%). $\delta_{CCl_4}^{TMS}$ 3.56 (2H, triplet, J=9Hz), 2.70 (2H, triplet, J=9 Hz) and 2.08 (3H, singlet). ν_{max}^{neat} 1220 (s), 705 (s) and 680 cm^{-1} (s).

3-Chloropropene Sulfide (I). I was prepared according to the method of Culvenor.[18] Thus, into a solution of 92 g (1.0 mol) of epichlorohydrin in 300 ml of methanol, chilled with ice, 84 g (1.1 mol) of thiourea was gradually dropped as a crystalline over a period of 1 hr: the reaction mixture was then stirred at 0~5 °C for an additional 2 hr and then at room temperature for an additional 2 hr.

The reaction mixture was subsequently poured onto 2 l of ice-water and extracted with two 300-ml portions of ether. The combined ether extracts were washed twice with saturated sodium chloride and dried over calcium chloride. After the distillation of the ether through a 10-cm Vigreux column, the residue was distilled twice under reduced pressure (77.0 °C/93 mmHg, 81.0 °C/112 mmHg). Sixty grams of I were thus obtained (the yield was 55%). 3-Chloropropene sulfide should be stored in refrigerator to prevent decomposition. At room temperature, I decomposes at a moderate speed to give an amorphous white solid. $\delta_{CDCl_3}^{TMS}$ 3.9 (1H, multiplet), 3.2 (2H, multiplet), 2.6 (1H, multiplet and 2.25 (1H, multiplet). ν_{max}^{neat}, 1260 (s), 1040 (s) and 705 cm^{-1} (s).

3-Acetoxythietane. A reaction mixture consisting of 500 ml of acetic acid, 62 g (0.75 mol) of sodium acetate, and 10 g (0.093 mol) of I was heated at about 60 °C for 5 day.

The reaction mixture was then poured into 3 l of water and extracted with two 250-ml portions of petroleum ether; the combined petroleum ether extracts were washed with saturated sodium bicarbonate until the evolution of carbon dioxide had ceased and then washed with saturated sodium chloride. After the evaporation of the solvent, 3-acetoxythietane was distilled under reduced pressure (83.5 °C/23 mmHg) (the yield was 82%). $\delta_{CCl_4}^{TMS}$ 5.56 (1H, quintet, J=8 Hz), 3.46 (2H, triplet, J=8 Hz), 3.26 (2H, triplet, J=8 Hz) and 2.00 (3H, singlet). ν_{max}^{neat} 1740 (s), 1370 (m), 1240 (s), 1040 (s) and 905 cm^{-1} (w). *m/e* 132 (P^+), 89, 72 and 43.

β-Acetoxyethyl Methyl Sulfide. A mixture consisting of 50 ml of acetic acid, 2 g of II, and 10 g of sodium acetate was heated at 60 °C for 8 hr. The reaction mixture was then poured into 300 ml of water and extracted with two 50-ml portions of petroleum ether. The combined extracts were neutralized with sodium bicarbonate, washed with saturated sodium chloride, and then dried over calcium chloride. After the evaporation of the solvent, the β-acetoxyethyl methyl sulfide was distilled under reduced pressure (125 °C/133 mmHg). (Yield, *ca.* 90%). $\delta_{CCl_4}^{TMS}$ 4.20 (2H, triplet, J= 7 Hz). 2.65 (2H, triplet, J=7 Hz), 2.08 (3H, singlet) and 2.00 (3H, singlet). ν_{max}^{neat}; 1755 (s), 1396 (m), 1240 (s) and 1040 cm^{-1} (m), *m/e*; 74 (100), 61 (75), 43 (90).

Procedure for Titration. In a 25-ml measuring flask, 1.25 mmol of the substrate was dissolved with acetic acid containing some sodium acetate, heated to 55.00±0.05 °C beforehand, up to 25 ml; this flask was immersed immediately into a bath maintained constant at 55.00±0.05 °C. At desired intervals of time, 3-ml samples were measured out and dropped into a separatory funnel containing 15 ml of distilled water and 10 ml of carbon tetrachloride. After vigorous shaking, the aqueous portion was washed once more with 10 ml of carbon tetrachloride and then transferred into a flask quantitatively. (The separatory funnel was washed off with 2 ml of distilled water). To a combined aqueous layer, we then added 2.00 ml of 0.100 M of silver nitrate, two drops of fuming nitric acid, and a few drops of a saturated ferric ammonium sulfate solution, after which this solution was back-titrated with 0.116 M ammonium thiocyanate (Volhard method).

References and Notes

1) (a) G. M. Bennett and W. A. Berry, *J. Chem. Soc.* **1927**, 1626. (b) A. G. Ogston, E. R. Holiday, J. St. L. Philpot, and L. A. Stocken, *Trans. Faraday Soc.*, **44**, 45 (1948). (c) P. D. Bartlett and C. G. Swain, *J. Amer. Chem. Soc.*, **71**, 1406 (1949). (d) H. L. Goering and K. L. Howe, *ibid.*, **79**, 6542 (1957). (e) S. J. Cristol and R. P. Arganbright, *ibid.*, **79**, 3441 (1957).

2) For the acetolyses of γ- and δ-halosubstituted sulfides, normal first-order kinetics have been reported.[3]

3) (a) M. Hojo, T. Ichi, Y. Tamaru, and Z. Yoshida, *J. Amer. Chem. Soc.*, **71**, 5170 (1969). (b) L. A. Paquette, G. V. Meehan, and L. D. Wise, *ibid.*, **91**, 3231 (1969).

4) H. Morita and S. Oae, *Tetrahedron Lett.*, **1969**, 1347.

5) E. P. Adams, K. N. Agod, F. P. Doyle, D. O. Halland, W. H. Hunter, J. H. C. Nayler, and A. Queen, *J. Org. Chem*, **25**, 2665 (1960).

6) The rate of the acetolysis of 2-*endo*-chloro-7-thiabicyclo-[2.2.1]heptane was proportional to the concentration of the substrate and that of sodium acetate (S_N2 mechanism), and the product (2-*endo*-acetoxy-7-thiabicyclo[2.2.1]heptane) of the retention of the configuration was obtained exclusively and quantitatively. These results will be reported soon.

7) This value seems to be too large compared with the value (K_{Cl^-}/K_{OAc^-}=*ca.* 2) obtained in the hydrolysis of bis-β-chloroethyl sulfide,[1b,c,8] but the competition factors were found to be sensitive to substrates, the dielectric constants of solvents, and many other factors.[9]

8) E. J. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York and London (1963), p. 231.

9) (a) C. G. Swain, C. B. Scott, and H. L. Lohman, *J. Amer. Chem. Soc.*, **75**, 136 (1953). (b) D. Golomb, *J. Chem. Soc.*, **1959**, 1327, 1334. (c) D. Kovacevic, Z. Majerski, S. Borcic, and D. E. Sunko, *Tetrahedron*, **28**, 2469 (1972).

10) The ratio of nucleophilicities among acetic acid, water, and the chloride ion is $1 : 2.5\times10^2 : 2.5\times10^5$, obtained by Swain and Scott and Winstein and Marshall[11] for the solvolysis of methyl bromide. For Eq. 3, $[Cl^-]$=0.00089 M, the concentration of the substrate for the hydrolysis of 2-chloroethyl 2'-hydroxyethyl sulfide, was used (Ref. 1c). For Eq. (4), $[Cl^-]$=0.05 M was adopted.

11) (a) C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, **75**, 141 (1953). (b) S. Winstein and H. Marshall, *ibid.*, **74**, 1120 (1952).

12) 3-Chlorothietane is estimated to be less reactive than

3-chloropropene sulfide on the basis of the formolyses data of 3-chlorothietane (3.7×10^{-4} s^{-1}) and 2-chloroethyl ethyl sulfide[13] (1.21×10^{-2} s^{-1}). A similar result has been reported for nitrogen analogues; that is, in the acetolysis, 1-chloromethylaziridine reacts much faster than 3-chloroazetidine.[14]

13) H. Morita and S. Oae, 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, Abstract III, 1071 (1971).

14) (a) V. R. Gaertner, *Tetrahedron Lett.*, **1968**, 5919. see also, (b) J. A. Deyrup and C. L. Moyer, *ibid.*, 6179 (1968). (c) V. R. Gaertner, *J. Org. Chem.*, **35**, 3952 (1970). (d) R. H. Higgins, F. M. Behlen, D. F. Eggli, J. H. Kreymborg, and N. H. Cromwell, *ibid.*, **37**, 524 (1972).

15) J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.*, **73**, 2509 (1951).

16) S. Searles, M. Tamres, and E. R. Lippincott, *ibid.*, **75**, 2775 (1953); R. E. Davis, *J. Org. Chem.*, **23**, 1380 (1958).

17) The salt effect of sodium acetate was negligibly small compared with the mass law effect of the chloride ion and was neglected for the sake of simplification.

18) C. C. J. Culvenor, *J. Chem. Soc.*, **1946**, 1050.