Effect of Ring Size on the Mass Spectral Fragmentation of Cyclic Sulfoxides

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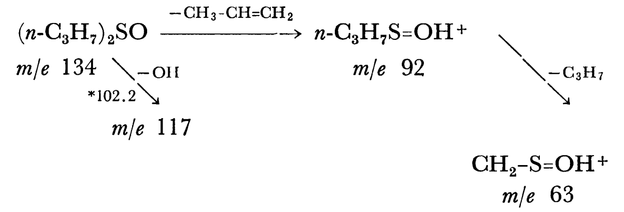
Mass spectra of six cyclic sulfoxides were determined in order to study the effects of ring size on the rate of OH-elimination from molecular ions. The ratios of the rates for the OH loss, $[M^+-OH]/[M^+]$, are: trimethylene sulfoxide: 0.23 /tetramethylene sulfoxide: 0.06 /pentamethylene sulfoxide: 0.24 /hexamethylene sulfoxide: 1.21 /9-thiamonoxybicyclo[3.3.1]nonane: 3.14 /7-thiamonoxybicyclo[2.2.1]heptane: 0.02. These findings were explained in terms of the difference in the closest approaching distance between the sulfinyl oxygen and the β- or γ-hydrogen atoms. Geometry of the ionized molecular ions appears to be an important factor in determining these ratios. The loss of HSO was also disucssed.

Although the electron impact fragmentations of open chain alkyl sulfoxides have been scrutinized in detail[1] and their common features can be illustrated as shown below by di-*n*-butyl sulfoxide as an example, no spectrometric study on cyclic sulfoxides has been made in connection with the effect of ring size on their fragmentation.



$$\begin{array}{ccccc} (n\text{-}C_3H_7)_2SO & \xrightarrow{-CH_3\text{-}CH=CH_2} & n\text{-}C_3H_7S{=}OH^+ & \searrow^{-C_3H_7} & \\ m/e\ 134 & \searrow^{-OH}_{*102.2} & m/e\ 92 & & CH_2\text{-}S{=}OH^+ \\ & m/e\ 117 & & & m/e\ 63 \end{array}$$

It has been well known that the ejection of simple molecules such as H_2O or HCl from the molecular ion of cyclohexyl alcohol or chloride produced by electron impact does not necessarily take place by way of 1,2-elimination but displays a different behavior from that of the thermal process[2] where usually the elimination occurs exclusively *via* 1,2-elimination process resulting in the concomitant formation of a double bond. While, in the mass spectral fragmentation the extent of the ejection of small molecule or radical has been known to depend on the geometry or structure of molecules. For example, in a series of studies on rigid steroid ketone, Djerassi found that the Mclafferty rearrangement proceeds only if the interatomic distance between the carbonyl oxygen and γ-hydrogen is less than 1.8 Å.[3]

Very recently, Green and his coworkers[4] studies the electron impact induced elimination reactions involving the loss of small molecules, by employing specifically deuterium-labeled cyclohexyl or cycloheptyl chlorides and concluded that the ground-state interatomic distance may be extrapolated to the ionized state and thereby used to predict the position from which the hydrogen arised.

In this work, we have also re-examined the afore-mentioned Green's posturate in alicyclic sulfoxides from which the OH group is expelled and found that the hydrogen abstraction markedly depends upon the ring-size. For further information concerning the position of hydrogen to be removed, not only the monocyclic but also bicyclic sulfoxides were synthesized and subjected for the study.

Experimental

Synthesis of Alicyclic Sulfoxides. The cyclic sulfoxides were synthesized by the usual methods described in the literatures[5-7] and the sulfides were oxidized to the corresponding sulfoxides with sodium metaperiodate, usually

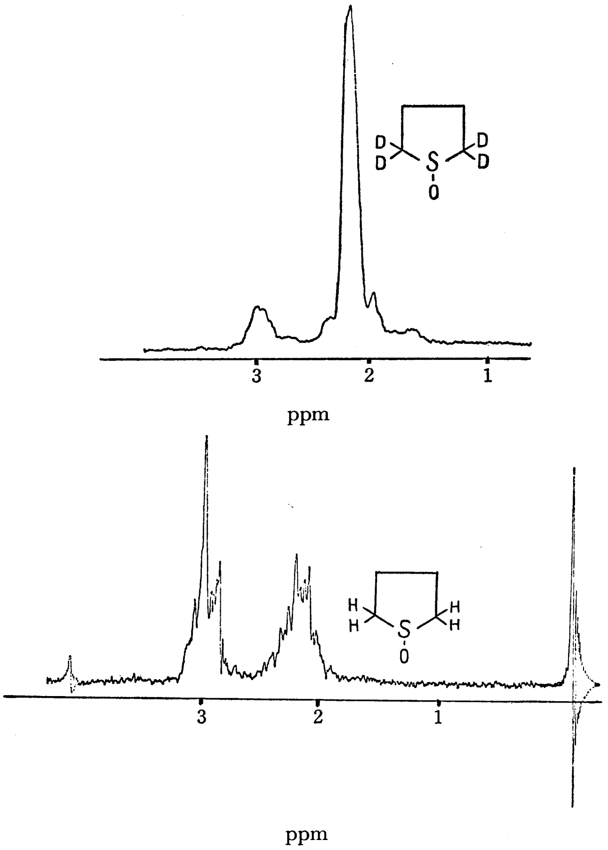


Fig. 1. NMR spectra of Tetramethylene sulfoxide and its deuterated sulfoxide in D_2O.

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[1] H. Budzikiewicz, C. Djerassi, and D. H. Williams "Mass Spectrometry of Organic Compounds," Holden-Day Inc. (1967), p. 553. J. H. Bowie, D. H. Williams, S. O. Lawesson, J. Madsen, G. Schroll, *Tetrahedron*, **22**, 3515 (1966), R. G. Gillis, and J. L. Occolowitz, *Tetrahedron Lett.*, 1887 (1966). I. D. Entwisle, R. A. W. Johnstone, and B. J. Millard, *J. Chem. Soc.*, C, **1967**, 302.

[2] B. Stephenson and O. Banjok, *J. Chem. Soc.*, *B*, **1968**, 805.

[3] C. Djerassi *et al.*, "Mass Spectrometry of Organic Compounds", Holden-Day Inc. (1967), p. 157.

[4] M. M. Green, R. J. Cook, J. M. Schwak, and R. B. Roy, *J. Amer. Chem. Soc.*, **92**, 3076 (1970).

[5] D. S. Tarbell and C. Weaver, *ibid.*, **63**, 2939 (1941).

[6] E. V. Whitehead, R. D. Dean, and F. A. Fidle, *ibid.*, **73**, 3632 (1951).

[7] G. G. Bennett and A. L. Hoak, *J. Chem. Soc.*, **1927**, 2496.

in ethanol except the oxidation of four-membered cyclic trimethylene sulfide where methanol was found to be the best solvent. The boiling (melting) points are: trimethylene sulfoxide: 91°/14 mmHg; tetramethylene: 113—114°/14 mmHg; pentamethylene: 124—125°/14 mmHg; hexamethylene: 144—145°/14 mmHg; 7-thiamonoxybicyclo[2.2.1]heptane: 205—208°C; 9-thiamonoxybicyclo[3.3.1]-nonane: 140°C/15 mmHg (sublimation temp).

Deuterium Labeling. The deuteration of the α-position to the sulfinyl group was accomplished by heating the corresponding ordinary sulfoxide of 500 mg with deuterium oxide of 5 g dissolving small pieces of sodium metal in a sealed tube at around 100°C for 2 or 3 days. After heating, the solvent was distilled off and the residue was extracted repeatedly with chloroform. The chloroform layer was concentrated and distilled off under reduced nitrogen atmosphere. The typical NMR spectrum of five-membered cyclic sulfoxide is shown in Fig. 1.

Measurement. Hitachi RMU-6E single focus mass spectrometer set at normal (80 eV) ionizing voltages and emission current of 110 mA was used to record the spectra. Samples were introduced into the ionizing chamber through a glass inlet system (141-B) prepared for heating around 200°C.

Results and Discussion

The main decomposition paths are illustrated in Figs. 2—7 and Schemes 1—2, and the main features of the mass spectra of these compounds are summerized as follows: (1) in every case, the molecular ion gives relatively higher peak height. (2) Surprisingly, in contrast to methyl phenyl sulfoxide and pyridine *N*-oxide both bearing similar semipolar linkages, no measurable deoxygenation appears to take place with

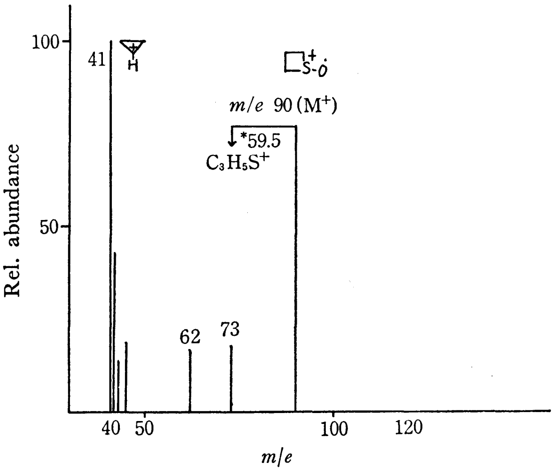


Fig. 2. Mass spectrum of trimethylene sulfoxide.

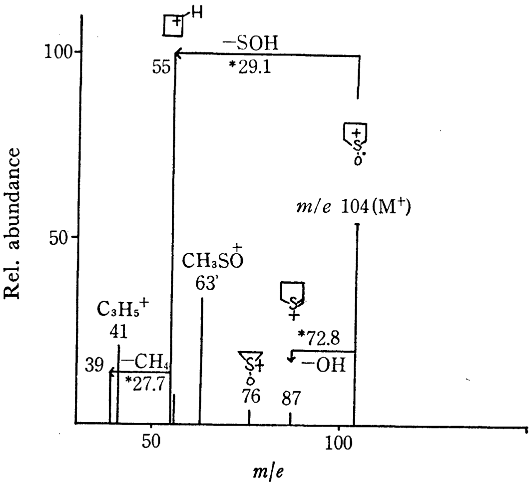


Fig. 3. Mass spectrum of tetramethylene sulfoxide.

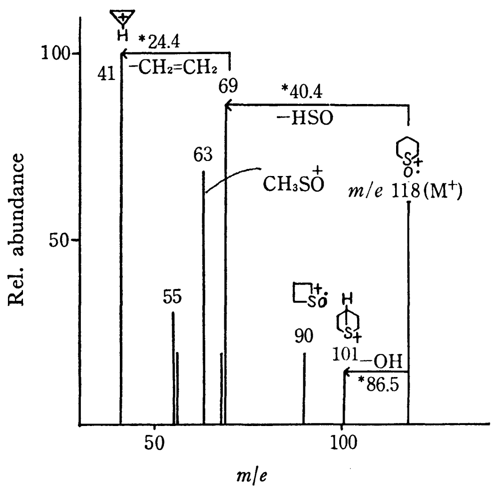


Fig. 4. Mass spectrum of pentamethylene sulfoxide.

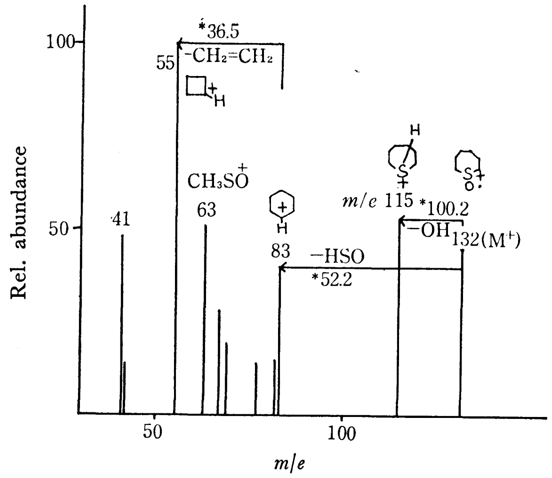


Fig. 5. Mass spectrum of hexamethylene sulfoxide.

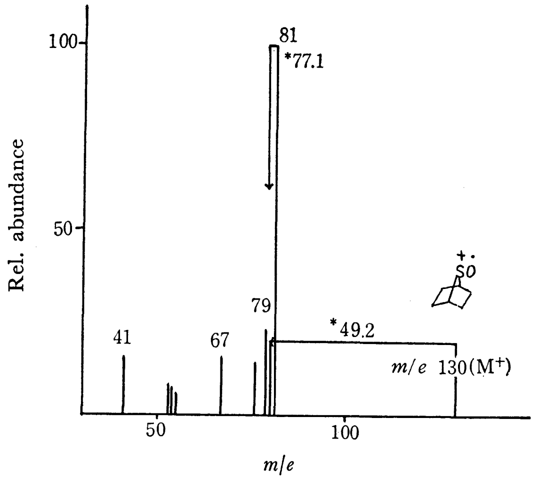


Fig. 6. Mass spectrum of 7-Thiamonoxybicyclo[2.2.1]-heptane at 80 eV.

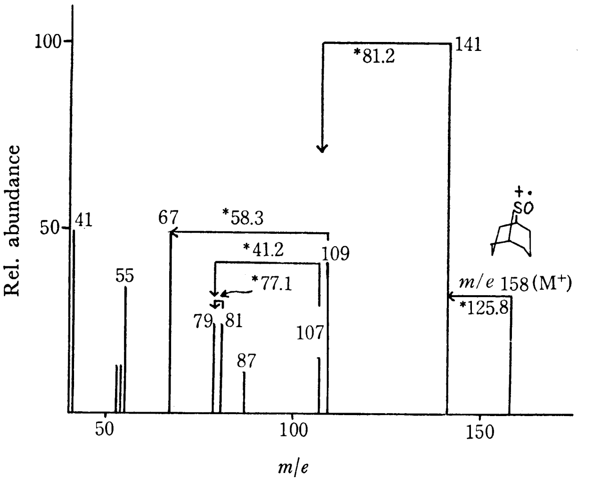
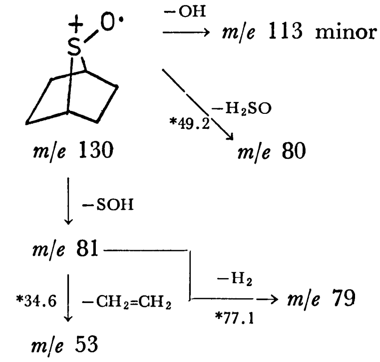


Fig. 7. Mass spectrum of 9-Thiamonoxybicyclo[3.3.1.] nonane at 80 eV.

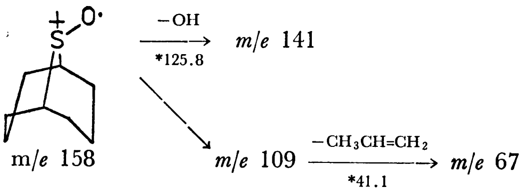
alicyclic sulfoxides at such high electron ionizing voltage as 80 eV. (3) Instead, the loss of OH and/or SOH takes place with all these sulfoxides although the extent of elimination for these simple molecules depends upon the nature of the sulfoxides. This will be discussed later in detail in connection with the effect of ring size on the dehydroxylation.

The bicyclic sulfoxides such as 7-thiamonoxybicyclo[2.2.1]heptane and 9-thiamonoxybicyclo[3.3.1]nonane exhibit quite special and interesting behavior along the successive fragmentations.

The decomposition patterns for these compounds are shown as in Schemes 1 and 2, depicted below:



Scheme 1.



Scheme 2.

From inspection of these spectra, as for the OH loss the appearance of the metastable peaks seems to indicate that the elimination of OH radical proceeds by way of the noticeably similar mechanism for all the compounds investigated except the [2.2.1]bicyclic sulfoxide in which the OH loss is relatively a minor route. While, the elimination of HSO appears to give the corresponding metastable peaks only in the case of the monocyclic compounds with an exception of trimethylene sulfoxide. With the bicyclic derivatives the corresponding metastable peaks are

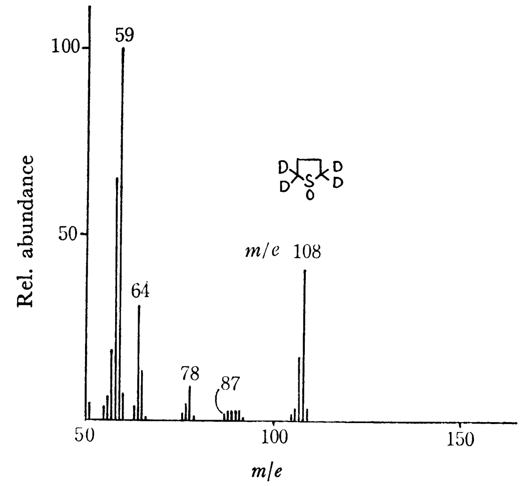


Fig. 8. Mass spectrum of tetramethylene sulfoxide-d_4 at 80 eV.

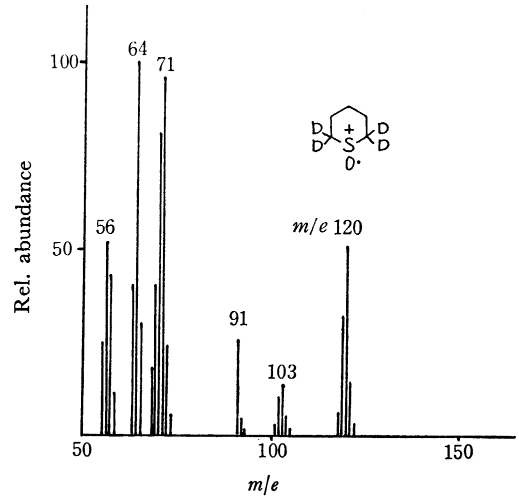


Fig. 9. Mass spectrum of pentamethylene sulfoxide-d_4 at 80 eV.

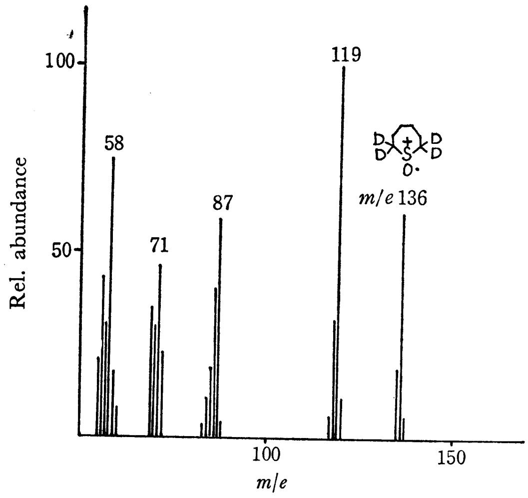
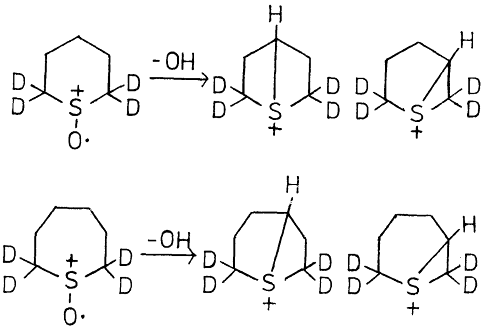


Fig. 10. Mass spectrum of Hexamethylene sulfoxide-d_4 at 80 eV.

not detected at all. At present it is not clear what factors introduce such phenomena.

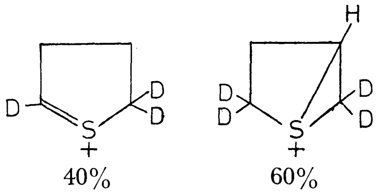
In order to dislose the origin of hydrogen abstracted in the elimination processes, a few sulfoxides deuterated were subjected to the electron impact analyses and the mass spectra of deuterated sulfoxides are shown in Figs. 8—10.

The deuterium labeling experiments confirm that the six- and seven-membered ring analogs undergo OH elimination reaction predominantly from the site other than the α-positions to the sulfinyl groups (Scheme 3).



Scheme 3.

Whereas, the behavior of the five-membered ring compound is much different. Abstraction of deuterium or hydrogen from α- and β-positions occurs concomitantly at the ratio of 40 to 60, respectively, resulting in the formation of such ion as:



As the deuterium labeling experiments indicate, with all the five-, six-, and seven-membered cyclic sulfoxides, elimination of HSO radical does occur predominantly by abstracting the hydrogen rather than the deuterium. These facts are just consistent with expectation that the OH elimination takes place without destruction of sulfoxide ring, while as for the HSO elimination ring openings prerequisite to ejection of HSO. The deuterium contents in various peaks were calculated and listed in Table 1.

Table 1. Deuterium contents in various peaks

Sulfoxide	Peak	Deuterium content,[a] %	Relative Deuterium content, %
Tetramethylene	M^+	87.8	100
	M^+-OH	52.4	59.7
	M^+-HSO	82.5	94.0
Pentamethylene	M^+	42.2	100
	M^+-OH	43.5	100
	M^+-HSO	31.7	75.1[b]
Hexamethylene	M^+	94.7	100
	M^+-OH	91.8	96.9
	M^+-HSO	83.5	88.2

a) Values after corrected for isotope peaks due to ^{13}C and ^{35}S.

b) This low value may be due to uncorrectness for the neighboring peak not attributed to HSO elimination.

Effect of Ring-Size on the Rate of Elimination. When the relative intensity ratios of peak heights of $[M^+ -OH]$ ions to the peak heights of the parent ions, *i.e.*, $[M^+ -OH]/[M^+]$, are plotted against the ring-size as shown in Fig. 11, we can get an upward concave curvature with the value of the five-membered ring sulfoxide being at minimum. The ratio ranges from a low figure of 0.06 for the five-membered sulfoxide to a high one of 1.21 for the seven-membered analog.

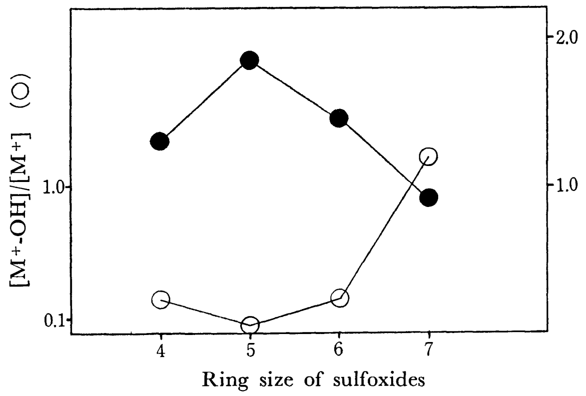
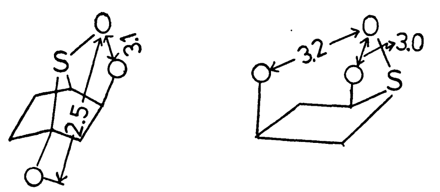


Fig. 11. Plot of intensity of OH- or SOH- eliminated fragment against ring size.

While, the plot of $[M^+ -HSO]$ intensities against those of molecular peaks, $[M^+ -HSO]/[M^+]$, is entirely different in shape from those of the above mentioned, as shown in Fig. 11 where no regularity can be seen in the plot of the $[M^+ -OH]$. Besides, the ratio of the maximum to the minimum values does not exceed only a little more than 2. Different features can be observed in the case of the bicyclic compounds. Even with the [3.3.1] bicyclic sulfoxide, the $[M^+-HSO]/[M^+]$ ratio increased up to 1.31, which is not much different from that of the monocyclic analogs. While, the ratio, $[M^+-OH]/[M^+]$, increased to as much as 3.14. On the other hand, the [2.2.1] bicyclic sulfoxide underwent much more facile HSO elimination, giving rise to the ratio of 8.70. However, $[M^+-OH]/[M^+]$ ratio was found to be negligibly small, *i.e.*, 0.03.

These observations imply that the HSO elimination does not depend so sharply upon the change of the ring size, but the ease of the expulsion of the OH group is markedly dependent on the number of methylene group. The latter finding can be readily rationalized on the basis of the strained structures. Since the five-membered and the [2.2.1] bicyclic sulfoxides are very strained and have only small degrees of freedom, the sulfoxide oxygen atom of these compounds can not easily get close enough to the β-hydrogen for elimination. In fact, on the basis of the molecular models, the closest distance between the center of the oxygen and that of each hydrogen atoms exceeds 3.0



Å with all these ring systems. This explanation may be supported further by the following observation that in the spectra for both compounds taken at 20 eV (Fig. 12) the number of ions attributed to the OH loss is far less than that of the ions arised from loss of oxygen. Namely, the sulfinyl oxygen that cannot find hydrogen atom in close vicinity has to cleave off itself (Scheme 4).

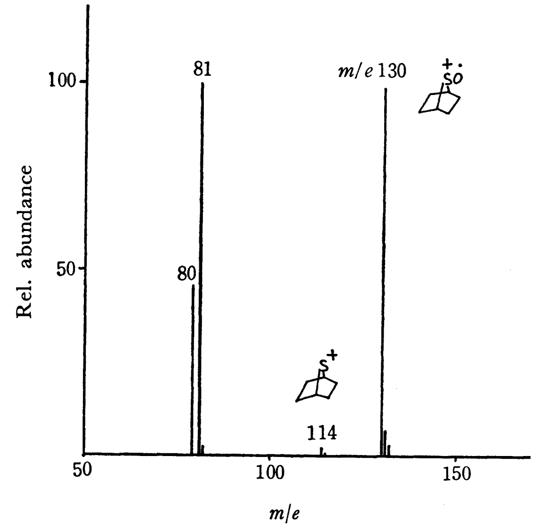
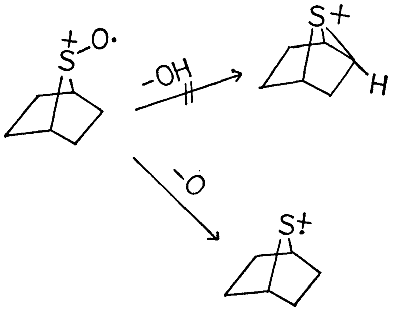


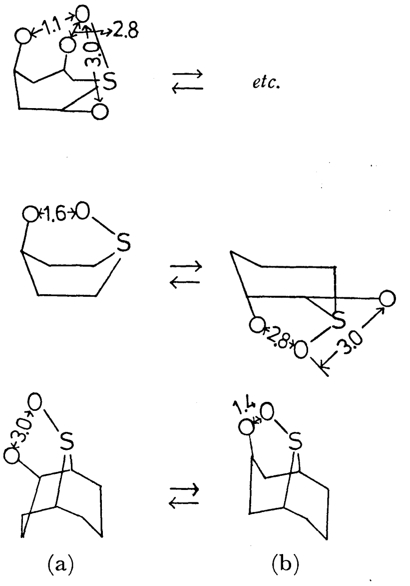
Fig. 12. Mass spectrum of 7-thiamonoxybicyclo[2.2.1]-heptane at 20 eV.



Scheme 4.

As for the more flexible six- and seven-membered cyclic sulfoxides, relative intensities of the dehydroxylated mass peaks against these of the parent ions are considerably higher than those of the strained sulfoxide and loss of OH for the seven-membered analog is more evident than for the six-membered system. All these observations seem to suggest strongly that not only the distances between hydrogen and oxygen in ground state geometry as Green and his coworkers have advocated but also the molecular motions are important for determining the extent of the OH elimination.

This is in keeping with our recent finding in the Ei reactions undergoing via five-membered cyclic transition state.[9] The distances between oxygen and hydrogen for some of possible conformations for the individual compounds studied are shown below:



In the first place, the distance between the sulfinyl oxygen and the nearest hydrogen atom in the molecule appears to determine the ease of the loss of OH. In the second place, the factor controlling the OH elimination seems to depend on the statistical stability of the molecular geometry which must satisfy the first condition for the OH elimination.

This latter condition is explicitly exemplified by the comparison of the mass pattern of the seven-membered sulfoxide with that of [3.3.1] bicyclic sulfoxide. The shortest distances between the two atoms calculated from the geometries for these two sulfoxides are 1.0 Å and 1.4 Å, respectively. On the contrary the $[M^+\text{-}OH]/[M^+]$ratios increased from 1.18 for the seven membered ring system to 3.12 for the [3.3.1] bicyclic sulfoxide. This is apparently apprehended by the assumption of the geometrical mobility toward the favorable conformation for eliminations under

TABLE 2. DISTANCE BETWEEN OXYGEN AND NEAREST HYDROGEN ATOM IN VARIOUS SULFOXIDES AND RATIO OF $[M^+-OH]/[M^+]$ OR $[M^+-HSO]/]M^+]$

Sulfoxide	Å	$[M^+\text{-}OH]/[M^+]$		$[M^+\text{-}HSO]/[M^+]$	
4	3.0	0.23		1.30	
5	3.0	0.06	(0.02)	1.85	(0.33)
6	1.6	0.24	(0.15)	1.45	(0.47)
7	1.1	1.21	(0.74)	0.91	(0.20)
221	3.1	0.03[a)]	(0.01)	8.70*	(1.01)
331	1.4	3.14	(0.90)	1.31*	(0.10)

a) Indicates the absence of metastable peak
Parentheses indicate the numerals measured at 20 eV.

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8) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

[9] K. Tsujihara, N. Furukawa, and S. Oae, *Tetrahedron Lett.*, 2663 (1970).

such a higher temperature as around 200°C in the inlet chamber room. Although the [3.3.1] bicyclic sulfoxide have been said to exist in the conformation (a) in which both six-membered rings are in the chair forms at around the room temperature,[10] at a higher temperature the steric repulsion between two hydrogens on the 3- and 7- positions would force the molecule to assume the conformations of one chair and one boat six-membered rings (b).

Such a conformation, considered to be favorable for the elimination of OH-group, would not be statistically stable in the case of the seven-membered system, because the 7-membered ring is very flexible.

Meanwhile, the behavior of the HSO elimination was found to differ from that of OH elimination. The fact that the OH loss does not depend on the change of the ring-size, *i.e.*, nor even on whether the sulfoxides are mono or bicyclic sulfoxides, may not be accounted for without the hypothesis that the molecular ions of the sulfoxides undergo OH-elimination, keeping the original skeleton, while the HSO loss does not take place without the destruction of the initial structure of the sulfoxide molecules. The C–S bond rupture at the initial step would lead molecular ions to convert to the corresponding open-chain structures.

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[10] G. A. Russell and R. G. Konlee, *J. Amer. Chem. Soc.*, **91**, 4468 (1969).