Ring Opening and Closure and Oxygen Isotope Exchange of Cyclic Sulfinate Esters[1]

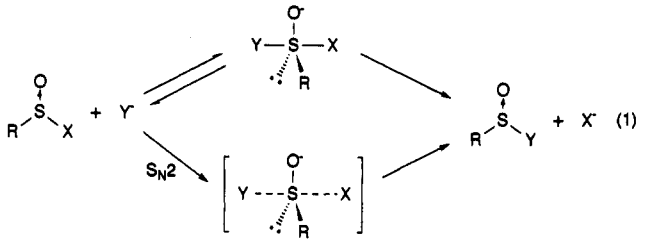
Tadashi Okuyama,*,† Hitomichi Takano,† Kazunobu Ohnishi,† and Shigeru Nagase‡

Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan, and Department of Chemistry, Faculty of Education, Yokohama National University, Hodogaya-ku, Yokohama 240, Japan

Received July 12, 1993•

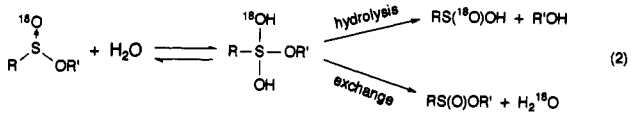
Alkaline ring opening and the reverse ring closure in an aqueous acid solution of cyclic sulfinate esters (sultines), 3*H*-2,1-benzoxathiole 1-oxide (**1a**) and 3,4-dihydro-2,1-benzoxathiin 1-oxide (**1b**), have kinetically been studied at 25 °C. The sultine **1a** is more reactive than **1b** in both the opening and closure reactions. However, acid-catalyzed oxygen isotope exchange of the ^{18}O-labeled sultine **1a** was found to be slower than that of the labeled **1b**. The contrasting reactivities of the five- and six-membered sultines in alkaline and acid solutions as well as the reaction mechanisms are considered on the basis of the ab initio molecular orbital calculations.

Nucleophilic substitution of sulfinic acid derivatives may proceed stepwise through a trigonal-bipyramidal (hypervalent) intermediate or concertedly in an S_N2 manner (eq 1). Most of such reactions occur with predominant inversion at the chiral sulfur, and a mechanism involving a hypervalent intermediate has been suggested,[2] though the S_N2-like mechanism cannot be excluded.



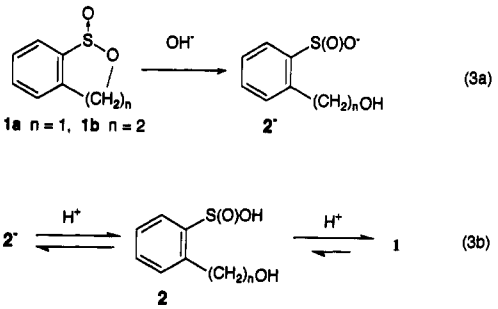
(1)

Hydrolysis of a sulfinate ester (eq 2) is formally similar to that of a carboxylate ester. Tetrahedral intermediates for the carboxylate hydrolysis were demonstrated by showing that the oxygen isotope exchange can be observed during the reaction.[3] A possible ^{18}O exchange occurring during sulfinate hydrolysis was considered to be evidence for the presence of the trigonal-bipyramidal intermediate (eq 2).[2d,4,5] However, previous efforts to detect such an isotope exchange in alkaline hydrolysis of sulfinate esters were unsuccessful.[4]



(2)

We have examined reactions of cyclic sulfinates (sultines), **1a** and **1b**, in acidic solution as well as in alkaline solution. In alkaline aqueous solution, the sultine **1** undergoes ring opening to give the hydroxy sulfinate ion **2**$^-$, while **1** seems to be stable in acid and the hydroxy sulfinic acid **2** cyclizes to **1** in strong acid (eq 3).



(3a)

(3b)

The ^{18}O-labeled sultine undergoes isotope exchange at the sulfinyl oxygen in acid. The γ- (five-membered ring) and δ-sultines (six-membered ring), **1a** and **1b**, showed contrasting reactivities in the oxygen exchange (**1b** > **1a**) in acid and the ring opening (**1a** > **1b**) in alkaline solution. Reasons for these relative reactivities, as well as the reaction mechanisms, are discussed from the theoretical viewpoints.

Results

3*H*-2,1-Benzoxathiole 1-oxide (**1a**) was prepared by oxidative cyclization of *o*-(hydroxymethyl)benzenethiol[6] while 3,4-dihydro-2,1-benzoxathiin 1-oxide (**1b**) was obtained by an $AlCl_3$-promoted cyclization of 2-phenylethyl chlorosulfite.[7]

When **1** is dissolved in alkaline solution, the UV spectrum of **1** smoothly changes to that of the hydroxy sulfinate ion **2**$^-$ with isosbestic points at 236 and 242 nm for **1a** and at 232 and 250 nm for **1b** (Figure S1, supplementary material). In acidic solutions, UV spectra of **1** are stable. The spectrum of **2**$^-$ changes on acidification in accord with acid ionization of pK_a of 1.2 and 1.4 for **2a** and **2b**, respectively (Figure S2). In prolonged time, the spectrum of **2** gradually changes to that of **1** in stronger acid (Figure S3). Acid-catalyzed cyclization must occur in the aqueous solution.

† Osaka University.
‡ Yokohama National University.
• Abstract published in *Advance ACS Abstracts*, December 15, 1993.

(1) Preliminary results were in part reported in Okuyama, T.; Takano, H.; Ohnishi, K.; Fueno, T. *Chem. Lett.* **1992**, 2055.
(2) (a) Mikolajczyk, M.; Drabowicz, J. *Top. Stereochem.* **1982**, *13*, 333. (b) Mikolajczyk, M. *Phosphorus Sulfur* **1986**, *27*, 31. (c) Mikolajczyk, M. In *Perspectives in the Organic Chemistry of Sulfur*; Zwanenburg, B., Klunder, A. J. H., Ed.; Elsevier: Amsterdam, 1987; pp 23-40. (d) Okuyama, T. In *The Chemistry of Sulphinic Acids, Esters and Their Derivatives*; Patai, S., Ed.; Wiley: Chichester, 1990; pp 623-637.
(3) Bender, M. L. *J. Am. Chem. Soc.* **1951**, *71*, 1626.
(4) Najam, A. A.; Tillett, J. G. *J. Chem. Soc., Perkin Trans. 2* **1975**, 858.
(5) Kice, J. L.; Waters, C. A. *J. Am. Chem. Soc.* **1972**, *94*, 590.
(6) King, J. F.; Rathore, R. *Tetrahedron Lett.* **1989**, *30*, 2763.
(7) Okuyama, T.; Senda, K.; Takano, H.; Ohnishi, K.; Fueno, T. *Heteroatom Chem.* **1993**, *4*, 223.

0022-3263/94/1959-0472$04.50/0

Table 1. Rate Constants for Ring Opening and Closure and ^{18}O Exchange of the Cyclic Sulfinate Esters at 25 °C

reaction	1a[a]	1b[a]	relative rate 1a/1b
ring opening[b] ($k_{OH}/M^{-1}\,s^{-1}$)	79.5[c]	0.516[d]	150
ring closure ($10^4k_{clos}/s^{-1}$)			
in $HClO_4$	0.897 (1.857 M)[e]	0.560 (1.818 M)[b]	1.6[f]
in HCl	6.07 (1.857 M)[e]	3.77 (1.818 M)[b]	1.5[f]
in HBr	23.9 (1.857 M)[e]	17.0 (1.818 M)[b]	1.3[f]
^{18}O exchange[g] ($10^6k_{ex}/s^{-1}$)			
in $HClO_4$	0.308 (1.951 M)	1.57 (1.951 M)	1/5.1
in $HClO_4$		5.61 (4.672 M)	
in HCl	3.28 (1.951 M)	17.9 (1.951 M)	1/5.5
in DCl		31.6 (1.841 M)	
in HBr	8.90 (1.951 M)	53.1 (1.951 M)	1/6.0

[a] Values in parentheses are concentrations of the acid. [b] Reaction solutions contained about 1 vol % of CH_3CN. [c] At the ionic strength of 0.10 M maintained with $NaClO_4$. A standard deviation calculated from $7k_0$ in the pH range 9.15–11.70 is 6.7. [d] At ionic strengths <0.01 M. A standard deviation calculated from $7k_{obsd}$ obtained at [NaOH] = 0.001–0.01 M is 0.025. [e] Reaction solutions contained about 5 vol % of CH_3CN. [f] Appropriate corrections for the acid concentration were made. [g] Reaction solutions contained about 2.4 vol % of CH_3CN.

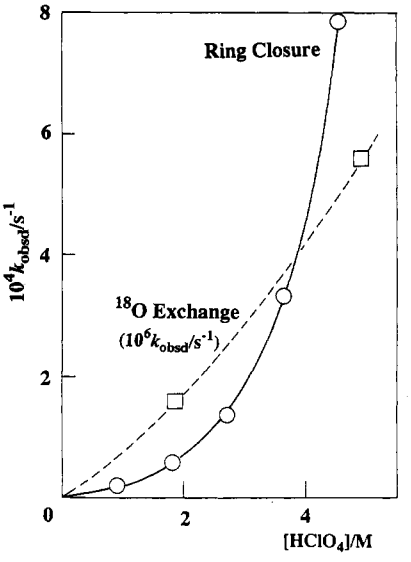


Figure 1. Observed rate constants for the ring closure of **2b** (○) and the ^{18}O exchange of **1b**-^{18}O (□) in $HClO_4$ at 25 °C.

Reaction of **1** in alkaline solution was followed spectrophotometrically at 25 °C. Time-dependent absorbance change obeyed the pseduo-first-order kinetic law and the observed rate constants k_{obsd} in dilute NaOH are proportional to [OH^-]. Reactions of **1a** were also carried out in borate and carbonate buffer solutions at the ionic strength of 0.10 M maintained with $NaClO_4$. The k_{obsd} are dependent on buffer concentrations, and the extrapolated rate constants k_0 to zero buffer concentration conform with the k_{obsd} in NaOH, being roughly proportional to [OH^-]. Buffer effects were not examined in detail. These rate constants are summarized in Tables S1 and S2 (supplementary material) and the second-order rate constants k_{OH} are given in Table 1. The γ-sultine **1a** is 150 times as reactive as the δ-sultine **1b**.

Ring-closure reaction of **2** in strong acid was monitored by decreasing absorption at 240 nm. The observed pseudo-first-order rate constants strongly increase with acid concentration as shown in Figure 1. (The k_{obsd} are summarized in Table S3.) Rates are greater in HCl and HBr solutions. At the constant acid concentration of mixed acid $HClO_4$–HCl (or HBr), the k_{obsd} increases with [HCl (or HBr)] as shown in Figure 2 (Table S4). The slope for HBr is 4.9 times greater than that for HCl at [H^+] = 1.818 M. The k_{obsd} obtained in about 2 M acids are given in Table 1.

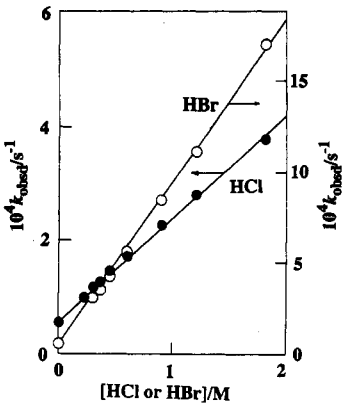


Figure 2. Rate constants for the ring closure of **2b** in mixed acids, $HClO_4$–HCl (or HBr), measured at 25 °C and at the total acid concentration of 1.818 M. ●, HCl (the left ordinate); ○, HBr (the right ordinate).

The labeled sulfines were obtained in a quantitative yield by ring opening of **1** in an ^{18}O-enriched alkaline solution followed by recyclization in acid.[7] It was confirmed by the lack of the ^{18}O isotope shift of the ^{13}C NMR of the 3-C that the ^{18}O was incorporated solely at the exocyclic sulfinyl position.[7] The contents of ^{18}O were determined by mass spectra: The substrates **1**-^{18}O obtained contained 30–40% excess ^{18}O of the natural abundance.

We first examined possible loss of ^{18}O of **1**-^{18}O during alkaline ring opening (hydrolysis). The unreacted substrate was recovered by extraction after 2–3 half-lives of the ring-opening reaction. Analysis of ^{18}O contents of the recovered substrates showed no detectable loss of the label. The ^{18}O contents are constant within experimental errors as the data are given in Tables S5 and S6 (supplementary material). No isotope exchange was detected during alkaline ring opening of **1**.

The sultine **1** does not undergo any apparent reaction in acid, but the labeled substrate **1**-^{18}O slowly loses its label in strong acid (Tables S5 and S6). The decrease in the ^{18}O content follows pseudo-first-order kinetics (Figure S4) to give rate constants listed in Table 1. The isotope exchange is faster in halogen acids: HBr > HCl > $HClO_4$. The exchange is still faster in a deuterium solvent than in a protium solvent: k_{DCl}/k_{HCl} = 2.0.

Discussion

Reactivity of Sultines. During alkaline ring opening of both **1a** and **1b**, no ^{18}O exchange was observed as was the case with the simple sultines.[4] In the previous work[4] the normal substrates were treated with alkaline $H_2{}^{18}O$ while the labeled substrates were more carefully examined in the present studies where 1% of exchange can be detected.[8] The intermediacy of the hypervalent species is not proved by these results but cannot be disproved either.[5]

(8) Our recent results show that the labeled methyl benzenesulfinate loses about 1% of the ^{18}O label during three half-lives of acid-catalyzed hydrolysis. Okuyama, T.; Nagase, S. Unpublished.

Relative reactivities of the five- and six-membered ring compounds are interesting. The five-membered ring **1a** is 150 times more reactive than the six-membered **1b** toward hydroxide ion in the ring-opening reaction. Similar results are observed with alkaline ring opening of simple sultines[4] as well as the cyclic sulfonates.[9] Higher reactivity of the five-membered ring derivative was also observed for some nucleophilic reactions of cyclic sulfoxides.[10] These relative reactivities are contrasting to those observed for lactones where the six-membered δ-lactone is 40 times more reactive than γ-lactone.[11] These contrasting reactivities may be accommodated with ring strains caused differently owing to longer bond distances involving sulfur (see below).

The difference in the rate of ring closure in acid is small but the formation of **1a** is still faster than that of **1b**. By contrast, relative rates of the ^{18}O exchange are opposite, **1a**/**1b** being 1:5–6. These opposite reactivities in ring opening–closure and ^{18}O exchange were considered at first to show that the isotope exchange occurred without ring opening but that it occurred within a hypervalent intermediate.[1] However, this consideration seems to be wrong as will be discussed below.

Both ring closure and oxygen exchange occur more rapidly in hydrobromic and hydrochloric acids than in perchloric acid. Halide ions must be nucleophilic catalysts of these acid-catalyzed reactions. A similar nucleophilic catalysis was observed for acid hydrolysis of sulfenate esters[12] as well as acid-catalyzed racemization[13,14] and oxygen isotope exchange[15,16] of sulfinyl derivatives. The relative nucleophilic reactivity of Br^- to Cl^- observed for the present reaction is compatible with that (Br^-/Cl^- = 5.4) determined for the acid-catalyzed cleavage of a sulfinyl sulfone.[17] The halide-catalyzed reactions must proceed with intermediate formation of sulfinyl halides.

Isotope Exchange via Ring Opening. If the ^{18}O exchange occurs through the acid-catalyzed ring opening (with k_{open}) and ring closure (with k_{clos}) as shown in Scheme 1, the rate constants for the exchange, k_{ex}, can be expressed by eq 4 since $k_{open} \ll k_{clos}$ judging from the equilibrium.

$$k_{ex} = k_{open}/2 \tag{4}$$

So, the equilibrium constant K_c for ring closure (eq 5) is represented by eq 6. From the kinetic data in about 2 M

$$2 \overset{K_c}{\rightleftharpoons} 1 + H_2O \tag{5}$$

$$K_c = k_{clos}/2k_{ex} \tag{6}$$

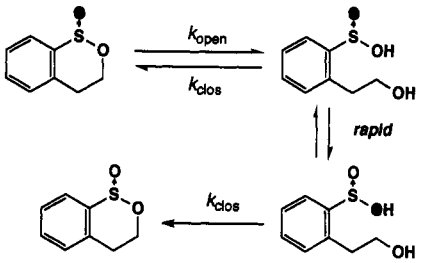
$HClO_4$, the equilibrium constants K_c are calculated to be 153 and 19.7 for **1a** and **1b**, respectively. Although the equilibrium concentration of **2a** may be too small to evaluate K_c for **1a** by some other method, about 5% of **2b**

Table 2. Equilibrium Constants for the Ring Closure 2b ⇌ 1b in Acid Solutions at 25 °C

acid	[acid]/M	K_c (UV)[a]	[acid]/M	K_c (calcd)[b]
$HClO_4$	0.857	14		
$HClO_4$	1.714	18, 20	1.95	19.7
$HClO_4$	1.714[c]	53		
$HClO_4$	2.571	37		
$HClO_4$	3.429	66, 52		
$HClO_4$	4.286	100, 118	4.67	70.3
HCl	1.714	16, 14	1.95	12.1
HCl	4.269	23, 17		
HBr			1.95	18.4

[a] Evaluated from UV spectra. [b] Calculated from kinetic data. [c] With added $NaClO_4$ of 2.571 M.

Scheme 1



in equilibrium with **1b** could be determined, e.g., spectrophotometrically. In accord with this expectation, the UV spectrum of **1a** did not show any detectable change in 2 M $HClO_4$ on standing and the spectrum obtained after prolonged time from $\mathbf{2a}^-$ in the same acid agreed very well with that of **1a**. By contrast, the spectrum of **1b** changed slightly, if examined carefully, and agreed with that obtained from $\mathbf{2b}^-$ at equilibrium (as shown in Figure S5). The equilibrium contants K_c for formation of **1b** were evaluated from the UV spectra and are listed in Table 2. Unexpectedly, K_c increases markedly with increasing [$HClO_4$]. This change in K_c was also confirmed by kinetic evaluation at [$HClO_4$] = 4.67 M; the calculated value of K_c = 70 is compatible with the UV value of 100 that contains large errors (probably ±50%). These agreements show that *the ^{18}O exchange takes place through ring opening and closure and the rate-determining step for the exchange should be acid-catalyzed ring opening.* Now, there arises a question why **1a** is more reactive in alkaline solution than **1b** while **1b** is more reactive in acid. This question will theoretically be considered below.

Variation in K_c with [$HClO_4$] needs further examinations. Effects of acid concentration of K_c are mild in HCl and the K_c is smaller in HCl than in $HClO_4$ at the same acidity. At the constant acidity of $HClO_4$ (1.714 M), the added $NaClO_4$ considerably increased the K_c. These results suggest that perchlorate ion (but not acidity) affects the magnitude of K_c. Similar effects of perchlorate salt were previously noted for lactonization and ascribed to the salt effects on the activity of lactone.[18] Increasing [ClO_4^-] results in decrease in the activity (salting in) of lactone. Similar salt effects must also be operating on the activity of sultine to affect the equilibrium. Such effects are also apparent in the reaction rates as illustrated in Figure 1: Effects of [$HClO_4$] on the rate of the ^{18}O exchange (ring opening) of **1b** are milder than those on the rate of ring closure of **2b**. The former reaction is retarded by

(9) Kaiser, E. T.; Kudo, K.; Zaborsky, O. R. *J. Am. Chem. Soc.* **1967**, *89*, 1393.
(10) Tamagaki, s.; Mizuno, M.; Yoshida, H.; Hirota, H.; Oae, S. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2456. Oae, S. *Organic Sulfur Chemistry*; CRC Press: Boca Raton, FL, 1991; pp. 149–155.
(11) Huisgen, R.; Ott, H. *Tetrahedron* **1959**, *6*, 253.
(12) Okuyama, T.; Nakamura, T.; Fueno, T. *J. Am. Chem. Soc.* **1990**, *112*, 9345. Okuyama, T.; Fueno, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2672.
(13) Landini, D.; Montanari, F.; Modena, G.; Scorrano, G. *J. Am. Chem. Soc.* **1970**, *92*, 7168.
(14) Scorrano, G. *Acc. Chem. Res.* **1973**, *6*, 132.
(15) Ookuni, I.; Fry, A. *J. Org. Chem.* **1971**, *36*, 4097.
(16) Okuyama, T.; Fueno, T. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3111.
(17) Kice, J. L.; Guaraldi, G. *J. Am. Chem. Soc.* **1968**, *90*, 4076.
(18) Long, F. A.; McDevit, W. F.; Dunkle, F. B. *J. Phys. Chem.* **1951**, *55*, 813.

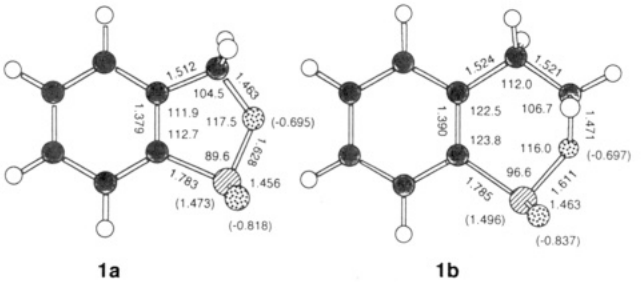


Figure 3. Optimized structures of **1a** and **1b** calculated at the HF/3-21G(*) level. H, open circles; C, closed circles; O, dotted circles; S, hatched circles. Internal bond angles (degrees) and bond lengths (Å) are given. Values in parentheses are the charge densities obtained by the MP2 calculations.

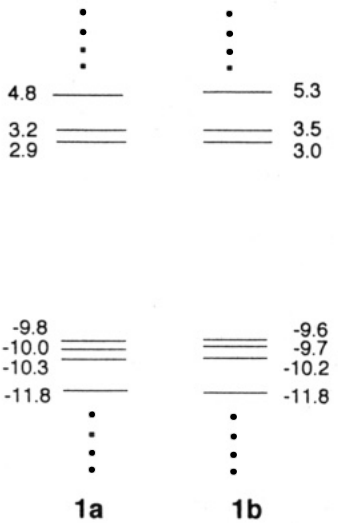


Figure 4. The HOMO–LUMO levels (eV) calculated at the HF/3-21G(*) level.

ClO_4^- through the decreasing activity of **1b** while such effects are smaller (if any) on the reverse reaction of the acid **2b**.

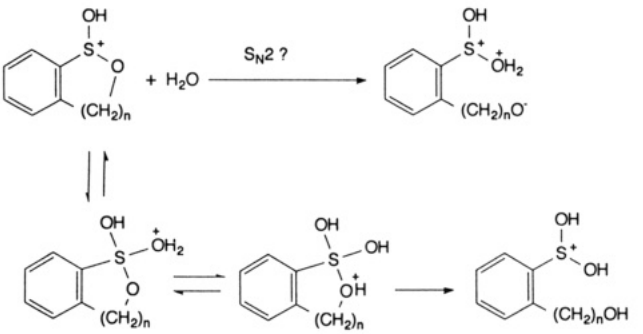
Theoretical Considerations

The molecular orbital calculations were carried out to understand the reaction mechanisms and reactivities of the sultines. Geometries were fully optimized at the Hartree–Fock (HF) level with the 3-21G(*) basis set.[19] In order to obtain improved energies, single point calculations were also performed on the basis of the second-order Møller–Plesset perturbation (MP2) theory.[20]

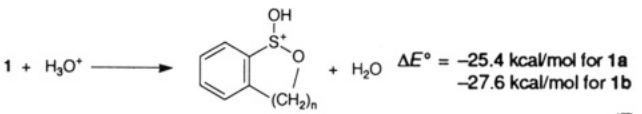
Reactivity of Sultines. Structures of the sultines **1a** and **1b** are shown in Figure 3: **1a** is essentially planar while **1b** is considerably puckered. The internal bond angles at the benzo carbons of the five- and six-membered rings may be worth noting; those of **1a** are considerably reduced to ca. 112° from the bond angle of the normal sp^2 carbon, while those of **1b** are close to 120°.

Charge distributions on the heteroatoms (based on the natural population analyses[21]) are also given in Figure 3, showing little difference between **1a** and **1b**. The HOMO–LUMO levels are illustrated in Figure 4. The LUMO's of **1a** are lower than those of **1b**. The first two LUMO's are mostly populated at the aromatic carbons and the third LUMO is localized at the sulfinyl group. The relative nucleophilic reactivity at the sulfur atom may be mainly governed by this third LUMO: that of **1a** is 0.5 eV lower than that of **1b**.

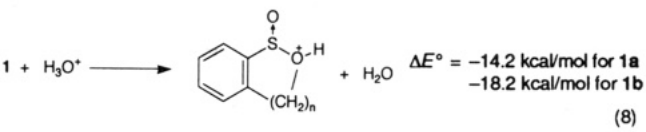
Scheme 2



Reactivity in Acid. The opposite relative reactivities of **1a** and **1b** in acid (**1b** > **1a**) were deduced from the kinetic results for acid-catalyzed oxygen exchange. The protonation of **1** is important in the acid-catalyzed reaction, and energies of protonation of **1** were examined. Energy changes for the proton transfers to the sulfinyl oxygen (eq 7) and to the alkoxyl oxygen (eq 8) are as shown below.



(7)



(8)

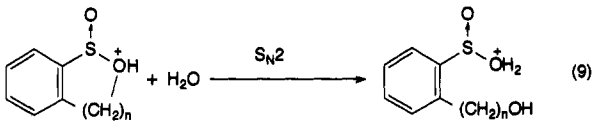
Both modes of protonation occur more readily with **1b** than with **1a**; i.e., **1b** is more basic than **1a**. This would be one of the reasons for the higher reactivity of **1b** in the acid-catalyzed reaction.

Reaction Mechanism. The acid-catalyzed oxygen exchange of **1** is concluded to occur via the ring opening as a rate-determining step. This reaction should be a nucleophilic reaction of the protonated substrate (or of the neutral substrate with general acidic participation of the acid). If the reaction proceeds through the protonation at the sulfinyl oxygen (eq 7), the addition intermediate of trigonal-bipyramid must be enforced. If it were not involved, the poorly leaving alkoxide group must have been expelled by a weakly nucleophilic water molecule in the S_N2-like reaction at the sulfur (Scheme 2), which would be highly unlikely.

Possible trigonal-bipyramidal intermediates for **1a** and **1b** were examined. In the optimized structures, the sultine ring is always placed in the apical–equatorial directions (the equatorial–equatorial form was impossible), and the apical hypervalent bonds are very much deformed: the bond angles are 145.0° and 166.2° for **1a**-OH and **1b**-OH, respectively. Although this pathway through the addition intermediate cannot be excluded, an alternative pathway through the protonation at the alkoxyl oxygen must also be considered. In this protonated substrate, the S–O bond

(19) Pietro, W. J.; Francl, M. M.; Hehre, W. J.; DeFrees, D. J.; Pople, J. A.; Binkley, J. S. *J. Am. Chem. Soc.* **1982**, *104*, 5039.
(20) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quantum Chem.* **1976**, *10*, 1.
(21) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Phys. Chem.* **1985**, *83*, 735. Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

is very much extended: 1.885 and 1.946 Å for $1aH^+$ and $1bH^+$, respectively. The nucleophilic attack of water at the sulfur would readily lead to cleavage of the weak S–O bond. That is, the S_N2-like mechanism (eq 9)through the



(9)

alkoxyl protonation may be possible. Although the alkoxyl protonation occurs less readily, the ensuing reaction must take place essentially without any barrier. In these mechanisms, proton transfers could be of general-acid type: the bond cleavage might proceed simultaneously on proton transfer.

Experimental Section

UV spectra were recorded on a Shimadzu UV 2200 and kinetic measurements were carried out by a Shimadzu UV 160 spectrophotometer. Mass spectra were recorded on a spectrometer JMS DX303.

Materials. 3*H*-2,1-Benzoxathiole 1-oxide (**1a**) was prepared from *o*-(hydroxymethyl)benzenethiol[6] and 3,4-dihydro-2,1-benzoxathiin 1-oxide (**1b**) was obtained by an $AlCl_3$-promoted cyclization of 2-phenylethyl chlorosulfite.[7] The recrystallized **1b** contained a small amount of the isomeric sulfone, 3*H*-2,1-benzoxathiole 1,1-dioxide, and kinetic samples were purified by preparative HPLC.

The labeled substrates **1**-^{18}O were obtained as described elsewhere.[7] The % ^{18}O excess of the natural abundance of the substrate used were **1a**-^{18}O, 33.5 and 41.5%; **1b**-^{18}O, 31.6 and 29.8%, as determined by MS.

Water used for preparation of alkaline solutions were freed from carbon dioxide by boiling it under argon. Aqueous NaOH solutions were freshly prepared from a sodium methoxide solution obtained by dissolving sodium metal in methanol but contained less than 1% of methanol. The concentrations were determined by titration with a standard HCl.

Ring Opening. Reactions of **1a** in alkaline solutions were carried out in borate and carbonate buffer solutions as well as in aqueous NaOH at the ionic strength of 0.10 M maintained with added $NaClO_4$ while reactions of **1b** were undertaken in aqueous NaOH without any added salt (at ionic strength less than 0.01 M). Reaction was started by adding a 30-μL sample of the stock solution of **1** in acetonitrile (ca. 0.05 M) from a microsyringe to 3.0 mL of an alkaline solution in a quartz cuvette equilibrated at 25.0 ± 0.1 °C in a cell compartment of the spectrophotometer. The spectra were recorded at appropriate time intervals or the absorbance at 245 nm was fed to a personal computer, NEC PC-9800, for data processing. The data were analyzed by the pseudo-first-order kinetics program.

Ring Closure. The stock solution of 2^- was obtained by dissolving the acetonitrile solution of **1** in 0.01 M NaOH. Reaction was carried out in the same way as the ring-opening reaction by introducing 0.10 mL of the alkaline stock solution with a pipette into 3.0 mL of an acid solution. Reaction was monitored by the decreasing absorbance at 240 nm.

Acid Dissociation. A sample of the alkaline stock solution of 2^- (0.10 mL) was added to 3.0 mL of an acid solution and the spectrum was recorded immediately after mixing. The acid concentrations of final solutions were calculated, and $-\log[H^+]$ was used for pH.

Equilibrium Studies. To attain accurately the same concentrations of **1** and **2** in acid solution, a pair of the reaction solutions were started with the same stock solution of **1** in acetonitrile. The solution of 2^- was prepared by putting 2.0 mL of the stock solution of **1** in a 20-mL volumetric flask and filling it with 0.01 M NaOH while the second stock solution of **1** was obtained in the same way from 2.0 mL of the first stock solution by dilution with water and 1 mL of methanol (for solubilization) to 20.0 mL. Each sample (0.10 mL) of the solutions of **1** and 2^- was added with a pipette to 3.0 mL of acid and the spectrum was recorded immediately after mixing and after appropriate reaction time at 25 °C. From the absorbance readings at 10 different wavelengths of 235–265 nm, the equilibrium constants K_c were calculated.

^{18}O Isotope Exchange. To 10 mL of acid in a flask maintained at 25 °C was added 0.25 mL of an acetonitrile stock solution containing about 5 mg of the labeled substrate **1**-^{18}O. At appropriate time intervals, a 2-mL sample was withdrawn with a pipette. The substrate **1** was immediately extracted with CH_2Cl_2 and analyzed by mass spectrometry.

Calculations. All the theoretical calculations were carried out using the GAUSSIAN 92 program[22] on an IBM RS6000 workstation.

Acknowledgment. The authors thank Kazuo Fukuda for recording mass spectra and Professor Takayuki Fueno for invaluable advice. This work was supported by a Grant-in-Aid for Scientific Research on Priority Area (03233217) from the Ministry of Education, Science and Culture.

Supplementary Material Available: Tables of rate constants and data of ^{18}O isotope analysis and Figures (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(22) Frisch, M.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. GAUSSIAN 92, Gaussian, Inc., Pittsburgh, PA.