

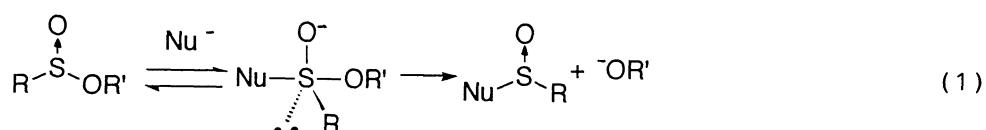
Rates of Oxygen Isotope Exchange and Ring Opening  
of Cyclic Sulfinate Esters

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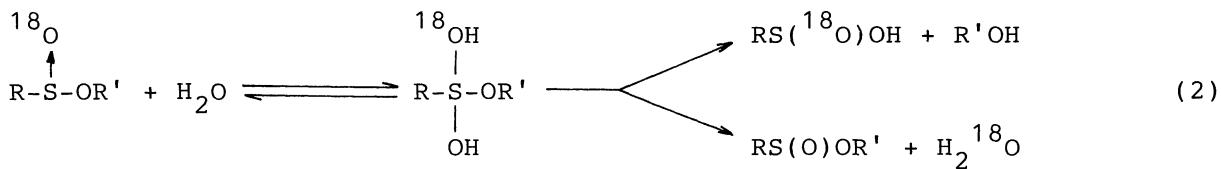
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Acid-catalyzed oxygen isotope exchange of the 6-membered cyclic sulfinate is faster than the 5-membered analog while the opposite reactivities were observed both in ring opening and closure reactions.

Nucleophilic substitution of sulfinic acid derivatives may proceed stepwise through a hypervalent intermediate or concertedly in an  $S_N^2$  manner. Most of such reactions occur with predominant inversion at the chiral sulfur and a mechanism involving a hypervalent sulfurane intermediate has been suggested,<sup>1)</sup> though the  $S_N^2$ -like mechanism cannot be excluded.

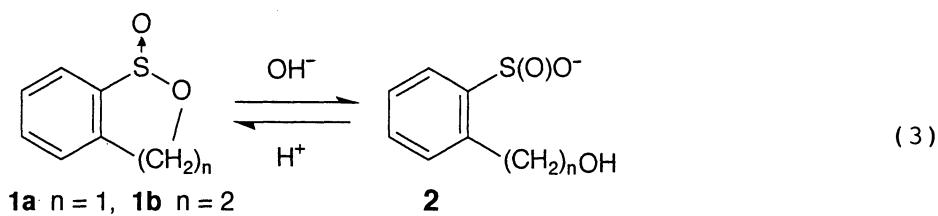


Hydrolysis of sulfinate ester is formally similar to that of carboxylate ester (Eq. 2) and a possible  $^{18}\text{O}$  exchange during hydrolysis was considered to be evidence for the presence of an intermediate.<sup>1d, 2, 3)</sup> However, previous efforts to detect such an isotope exchange in alkaline



hydrolysis of sulfinate esters were unsuccessful.<sup>2)</sup>

We have examined reaction of <sup>18</sup>O-labeled cyclic sulfinites (sultines), 1a and 1b, in acidic solution as well as in alkaline solution. In alkaline aqueous solution, sultine undergoes ring opening to give the hydroxy sulfinate ion (2), while the hydroxy sulfinic acid cyclizes to the sultine in strong acid (Eq. 3). In acidic solution, the sulfinic oxygen undergoes



isotope exchange. The 5- and 6-membered sultines, 1a and 1b, showed contrasting reactivities in the oxygen exchange and the ring opening reactions. The oxygen exchange must take place without ring opening and possible mechanisms for these reactions will be considered.

3H-2,1-Benzoxathiole 1-oxide (1a) was prepared according to King<sup>4)</sup> while 3,4-dihydro-2,1-benzoxathiin 1-oxide (1b)<sup>5)</sup> was obtained by an  $\text{AlCl}_3$ -promoted cyclization of 2-phenylethyl chlorosulfite.

Rates for alkaline ring opening of 1 were measured spectrophotometrically and found to be proportional to  $[\text{OH}^-]$ . The second order rate constants are given in Table 1, which indicate 1a is 150 times as reactive as 1b. In acidic solutions, UV spectra of 1 are stable. When an alkaline solution of 2 obtained from ring opening of 1 was acidified by addition of strong acid, the immediate

spectrum observed was different from that of sulfinate ion 2 and gradually changed to a final spectrum which is identical with that of 1. The hydroxy sulfinic acid

Table 1. Rate Constants for Ring Opening and Closure and <sup>18</sup>O Exchange at 25 °C

Reaction	<u>1a</u>	<u>1b</u>	<u>1a/1b</u> <sup>a)</sup>
Opening ( $k_{\text{OH}}/\text{mol}^{-1} \text{dm}^{-3} \text{s}^{-1}$ )	80	0.53	150
Closure ( $k_{\text{obsd}}/\text{s}^{-1}$ ) <sup>b)</sup>	8.97	5.60	1.6
Exchange ( $10^7 k_{\text{obsd}}/\text{s}^{-1}$ ) <sup>b)</sup>	3.08	15.7	1/51

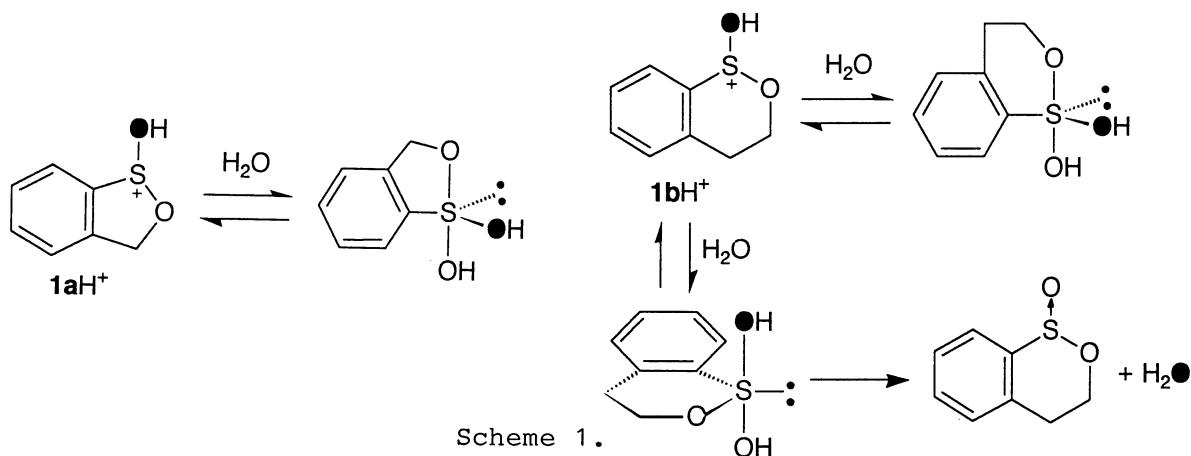
a) Relative rate. b) In 2 M  $\text{HClO}_4$ .

formed by neutralization must undergo acid-catalyzed cyclization, and this reaction was kinetically followed by decreasing absorption at 240 nm. The rate constants obtained in 2 M  $\text{HClO}_4$  are given in Table 1.

The labeled sultines were obtained in a quantitative yield by ring opening of 1 in an  $^{18}\text{O}$ -enriched alkaline solution followed by recyclization in acid. It was confirmed by the lack of the  $^{18}\text{O}$  isotope shift of the  $^{13}\text{C}$  NMR of the 3-C that the  $^{18}\text{O}$  was incorporated solely at the exocyclic sulfinyl position. The contents of  $^{18}\text{O}$  were determined by mass spectra: 41.5 (1a) and 31.6% (1b) excess of the natural abundance. To  $10\text{ cm}^3$  of 2 M  $\text{HClO}_4$  maintained at  $25^\circ\text{C}$  in a flask was added  $0.2\text{ cm}^3$  of an acetonitrile stock solution containing about 5 mg of the labeled sample of 1. At appropriate time intervals, a  $2\text{-cm}^3$  sample was withdrawn with a pipet. The substrate 1 was immediately extracted with  $\text{CH}_2\text{Cl}_2$  and analyzed. The decrease in the  $^{18}\text{O}$  content follows first-order kinetics to give rate constants listed in Table 1.

The 6-membered sultine 1b undergoes oxygen exchange 51 times more rapidly than the 5-membered analog 1a, although the former is less reactive than the latter in both ring opening and closure. The oxygen exchange is in principle possible via a successive ring opening and closure. However, the contrasting reactivities of the 5- and 6-membered cycles observed in the exchange and ring opening reactions strongly suggest that the oxygen exchange of the sultine occurs without ring opening. The reaction of 1 in acid should occur with the protonated form  $\text{1H}^+$  and possible reaction paths are depicted in Scheme 1 with sulfuranes as reaction intermediates. The  $^{18}\text{OH}$  group of  $\text{1bH}^+$  can occupy one of the apical positions upon nucleophilic attack to lead to the  $^{18}\text{O}$  exchange. By contrast, the 5-membered ring hardly occupies the diequatorial position because of the ring strain<sup>6)</sup> and the  $^{18}\text{OH}$  group of  $\text{1aH}^+$  has to occupy the equatorial position upon the apical attack of the nucleophile. With this configuration, 1a cannot undergo  $^{18}\text{O}$  exchange. Intermediacy of the sulfurane is quite possible but pseudorotation seems hardly to occur. In this situation, the stereo-

chemical arrangement of the reactive sulfurane (both attacking and leaving groups occupying the apical positions) is similar to that of an  $S_N2$ -like transition state, but an  $S_N2$ -like mechanism that requires the direct expulsion of hydroxide ion by weakly nucleophilic water is unlikely.



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