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Derivatives of Cyclic Disulfides. II.[1] Alkaline Hydrolysis of 1,2-Dithiaacenaphthene *S*-Oxide

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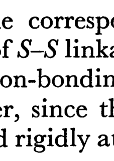
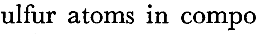
The alkaline hydrolysis of 1,2-Dithiaacenaphthene *S*-oxide has been investigated kinetically, its reactivity being compared with that of its open-chain analog, phenyl benzenethiolsulfinate. The rate was found to be of first order with respect to both hydroxide and the ester. 1,2-Dithiaacenaphthene *S*-oxide was found to be hydrolyzed 10^3 times more slowly than the open-chain analog in an alkaline medium. The reduced reactivity was interpreted on the basis of structural rigidity.

Aromatic five-membered cyclic sulfates and sulfonates are known to be hydrolyzed in alkaline solution 10^6—10^7 times faster than the corresponding open-chain esters,[2] and the main driving force for the remarkable rate enhancement in the hydrolytic reactivities of these five-membered cyclic esters has been believed to be due to the ring strain. The small values of the internal ring angle around the sulfur atom reflect the strain present in these five-membered rings. The hydrolysis of these esters is considered to proceed *via* an intermediate or transition complex which has a structure of approximately trigonal-bipyramid, in which the ring angle around the sulfur atom is close to 90° and the five-membered ring spans apical and equatorial positions. Since the ring angle around the sulfur in the five-membered cyclic esters is close to 90° even in the ground state, the compound can readily assume trigonal-bipyramidal geometry. However, in contrast to the alkaline hydrolysis of five-membered cyclic esters, that of an analogous five-membered cyclic compound containing sulfur-linkage has not been explored despite its inherent importance in biological systems.[3] Thus, we have synthesized 1,2-dithiaacenaphthene *S*-oxide (I) as a model compound, and subjected it to alkaline hydrolysis and compared its reactivity with that of phenyl benzenethiolsulfinate (II).



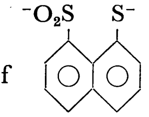
(I)

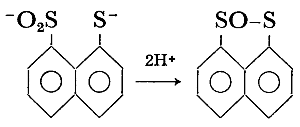


(II)

Although both sulfur atoms are confined rigidly at two peri-positions of naphthalene ring, 1,2-dithiaacenaphthene *S*-oxide is considered to be less strained than the corresponding oxygen-analogs, for the bond length of *S*–*S* linkage is considered to be nearly the same as the non-bonding distance between two peri-positions. However, since the two sulfur atoms in compound (I) are fixed rigidly at peri-positions of naphthalene nucleus, the kinetic behavior of this compound may not be similar to that of the five-membered sulfates or sulfonates.

Results and Discussion

Upon alkaline hydrolysis of I, the product could be separated into two parts; one soluble in ordinary organic solvents such as ether or chloroform, the other insoluble in common organic solvents but very soluble in water. 1,2-Dithiaacenaphthene, *i.e.*, reduced product, was obtained from the organic layer (37%). The latter water-soluble salts were neutralized with hydrochloric acid to afford 1,2-dithiaacenaphthene *S*, *S*-dioxide (8%) and 1,2-dithiaacenaphthene *S*-oxide (23%). A careful analysis of the UV spectra of an alkaline aqueous ethanol solution of 1,2-dithiaacenaphthene *S*-oxide indicates that the characteristic band due to the initial 1,2-dithiaacenaphthene *S*-oxide (247 nm) disappears, and a new band (265 nm) appears as the reaction proceeds. On completion of hydrolysis, the 265 nm band also begins to disappear at a relatively slower rate. The UV spectra and the product analysis suggest that the first stage of the reaction is the formation of a sodium salt of  because the attacking site for hydroxide ion in the initial step seems to be the sulfinyl sulfur. The starting material was regenerated in a considerable amount only after neutralization.



(III) (I)

There are two possible attacking sites for hydroxide in the initial step of the reaction, *i.e.*, the sulfinyl sulfur and the divalent sulfenyl sulfur. According to the HSAB principle,[4] the attack on the sulfinyl sulfur is more favorable than that on the sulfenyl sulfur, since hydroxide ion is a hard base. It is known that in alkaline hydrolysis of aryl arenethiolsulfinate, no hy-

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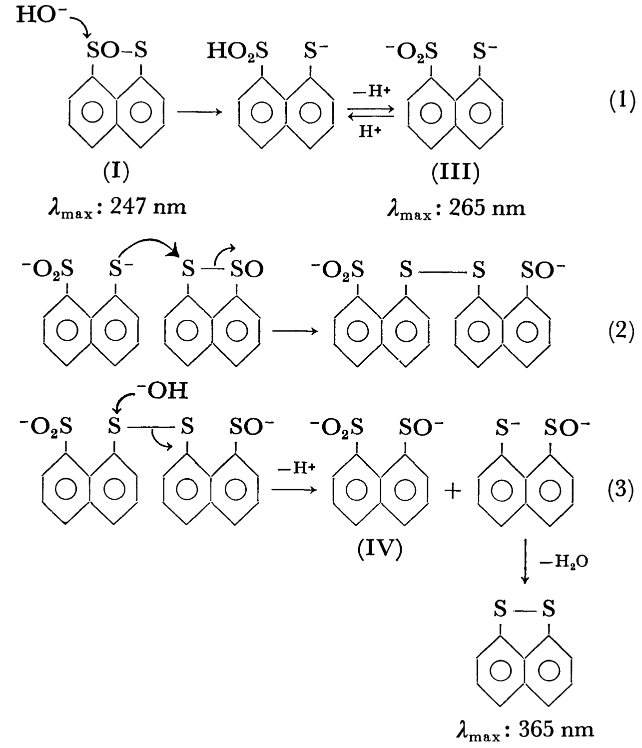
[1] Derivatives of Cyclic Disulfides I., S. Tamagaki, and S. Oae, This Bulletin, **45**, 960 (1972).

[2] E. T. Kaiser, *Accounts Chem. Res.*, **3**, 145 (1970); P. A. Pristow, J. G. Tillett, and D. W. Wiggins, *J. Chem. Soc., B*, **1968**, 1360; J. G. Tillett and D. W. Wiggins, *J. Org. Chem.*, **35**, 1359 (1970); F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968).

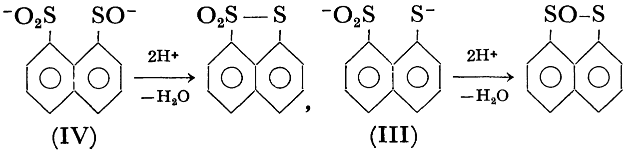
[3] N. Kharasch and C. Y. Meyers, "Organic Sulfur Compound," Vol. 2, Pergamon Press (1966), p. 336.

[4] J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962); R. G. Pearson, *ibid.*, **85**, 3533 (1963); *Science*, **151**, 172 (1966).

droxide ion attacks the sulfenyl sulfur in accordance with the HSAB principle.[5] We suggest that the most probable mechanism for this reaction is as follows.



After neutralization



In order to clarify the structural effect on the rate of hydrolysis, we carried out kinetic measurements in a weakly alkaline 60% ethanol–water solvent, keeping the concentration of the ester around 10^{-5} M. Measurements were carried out by observing spectrometrically the disappearance of the chracteristic UV absorption band of 247 nm due to 1,2-dithiaacenaphthene *S*-oxide. The first-order dependence of rate on the initial concentration of the ester was observed. The rate constants are listed in Table 1. The first-order dependence of k_{obs} on the hydroxide ion concentration is also shown in Table 2. The fact that the initial rate was found to be exactly proportional to the initial concentration of both the ester and hydroxide ion indicates that in the first step of the reaction the rate depends only on the concentration of both hydroxide ion and the ester and that the attack of hydroxide ion on sulfinyl sulfur occurs exclusively. We can thus conclude that no subsequent reaction takes place at all in the initial step of the reaction. The initial rate method was found to be approriate for kinetic measurements of the alkaline hydrolysis of 1,2-dithiaacenaphthene *S*-oxide. The second-order constants were easily calculated from the values of k_{obs} by dividing them by the initial concentration of hydroxide ion (Table 3). A kinetic experiment on the alkaline hydrolysis of phenyl benzenethiolsulfinate was also carried out in a pH-controlled buffer solution because the reaction was found to be very fast. The buffer chosen was potassium phosphate monobasic (KH_2PO_4)–sodium phosphate dibasic (Na_2HPO_4) system. The alkaline hydrolysis of 1,2-dithiaacenaphthene *S*-oxide was carried out in a medium of the same ionic strength as in the case of phenyl benzenethiolsulfinate.

TABLE 1. RATE CONSTANTS FOR ALKALINE HYDROLYSIS; DEPENDENCY OF RATE ON ESTER CONCENTRATION[a]

[Ester] $\times 10^5$, M	$-d[OD]/dt \times 10^5$	k_{OH}-$[OH^-] \times 10^5$, sec^{-1}
2.9	1.9	2.6
4.2	2.5	2.4
5.7	4.0	2.7
8.3	5.8	2.7

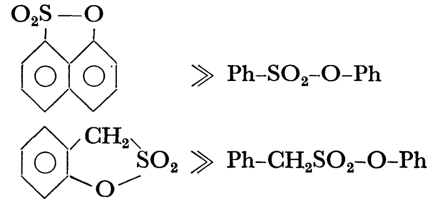
a) At 20 °C in 60% EtOH–H_2O $[OH^-]=2.3\times10^{-4}$M

TABLE 2. RATE CONSTANTS FOR ALKALINE HYDROLYSIS; DEPENDENCY OF RATE ON OH^- CONCENTRATION[a]

$[OH^-] \times 10^4$, M	$k_{obsd} \times 10^5$, sec^{-1}	k_{OH^-}, M^{-1} sec^{-1}
1.9	2.4	1.3
1.7	2.3	1.3
0.90	1.1	1.2

a) At 20 °C in 60% EtOH–H_2O $[E]=2.4\times10^{-5}$M

In the alkaline hydrolysis of aromatic sulfonates and sulfates, the rates of the five-membered cyclic esters were reported to be 10^6—10^7 times faster than those of the corresponding open-chain analogs.[6]



However, five-membered cyclic thiolsulfinate (I) was found to be hydrolyzed 1.5×10^3 times more slowly than the corresponding acylic ester.

The activation energy for the five-membered thiolsulfinate is markedly low, *i.e.*, $\Delta H^{\neq}=8.8$ kcal mol^{-1}, while the activation entropy is more negative, *i.e.*, $\Delta S^{\neq}=-32$ e.u., than that of phenyl benzenethiolsulfinate. These activation parameters suggest that the markedly small rate of the cyclic thiolsulfinate is mainly caused by the entropy term of free energy of activation. Thus, the surprisingly reduced reactivity of five-membered thiolsulfinate ester as compared with the case of sulfate ester can be rationalized on the basis of the following special nature of 1,2-dithiaacenaphthene skeleton; in 1,2-dithiaacenaphthene *S*-oxide two sulfur atoms are bound rigidly to fit just at the two peri-positions of naphthalene nucleus, *i.e.*, the bond length of *S–S* linkage being 2.1 Å according to the atomic radii

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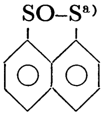
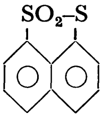
[5] S. Oae, Y. Yoshikawa, and W. Tagaki, This Bulletin, **42**, 2899 (1969).

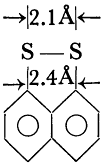
[6] O. R. Zaborsky and E. T. Kaiser, *J. Amer. Chem. Soc.*, **88**, 3084 (1966); E. T. Kaiser and O. R. Zaborsky, *ibid.*, **89**, 1393 (1967).

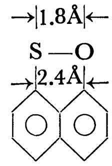
Table 3. Alkaline hydrolysis of thiolsulfinate or thiolsulfonate

	k_{OH^-}, $M^{-1}sec^{-1}$	Rel. rate	$\Delta H^{\neq}$ kcal mol^{-1}	$\Delta S^{\neq}$ e.u. (30°C)
Ph-SO-S-Ph[a]	$2.4\times10^3\pm0.2$	1.5×10^3	11.5	−11
SO-S[a] 	1.6 ± 0.3	1	8.8	−32
Ph-SO$_2$-S-Ph[b]	2.4 ± 0.2	1.5	10	−13
SO$_2$-S 	no reaction			

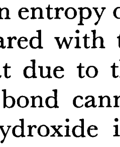
a) In 60% (v/v) EtOH-H_2O at 30°C, μ=0.2.
b) In 60% (v/v) EtOH-H_2O at 45°C.
c) 20, 25, 30, 35°C.

given by Pauling, close to the distance between two peri-positions (2.4 Å). It is evident that the five-membered ring is much less strained than the oxygen analog which is highly strained because of the shorter bond length of S–O linkage (1.8 Å). Therefore the

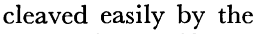




C–S–S angle is supposed to be very close to 90°. This seems to be adequate for the formation of a trigonal bipyramidal transition complex or intermediate of sp^{3}d configuration in which the ring angle around the sulfur atom is close to 90° and the five-membered ring spans apical and equatorial positions to accomodate the incoming nucleophile, *i.e.*, OH$^-$ ion, giving rise to a lower value of activation enthalpy. The large negative activation entropy of the 1,2-dithiaacenaphthene *S*-oxide as compared with that for the open-chain analog indicates that due to the confinement at the peri-positions the S–S bond cannot be cleaved easily by the attack of the hydroxide ion on the sulfinyl sulfur unless its C–S bond is bent off the normal bond angle of a peri-substituent. A similar rate-retardation should be found in the alkaline hydrolysis of the five-membered cyclic 1,2-dithiaacenaphthene *S,S*-dioxide as compared to that of the open-chain benzenethiolsulfonate. The open-chain thiolsulfonate was hydrolyzed overwhelmingly faster than that of the thiosulfonate bearing the naphthalene ring (Table 3).



no reaction



very fast

Experimental

Materials. 1,2-Dithiaacenaphthene was prepared according to the method of Zweig and Hoffmann.[7] 1,2-Dithiaacenaphthene *S*-oxide was obtained by the oxidation of 1,2-dithiaacenaphthene with sodium metaperiodate in dioxane–water or by selective deoxygenation of thiolsulfonate with trimethyl phosphite. The procedure is as follows. 1,2-Dithiaacenaphthene 3.1 g (16.1 mmol) was dissolved in 90 ml of dioxane into which a solution of 6.8 g (30.5 mmol) of sodium metaperiodate in 60 ml of water was added. The resulting solution was kept at room temperature for 12 hr, and then extracted with benzene. The solvent was evaporated and the residue was recrystallized from *n*-hexane–benzene to afford yellow needles, mp 82.5—83.5°C. Another procedure is as follows. Upon refluxing the mixture of 1,2-dithiaacenaphthene *S,S*-dioxide 220 mg (1.0 mmol) and trimethyl phosphite 310 mg (2.5 mmol) in 100 ml of benzene for 3 hr, a nearly quantitative amount of 1,2-dithiaacenaphthene *S*-oxide and a trace of 1,2-dithiaacenaphthene were obtained. The reaction mixture was evaporated and the residue was separated by column chromatography. The compound showed an IR stretching band at 1080 cm^{-1} characteristic of the S–O group. UV: max 247 nm (ε: 25700 in 60% EtOH–H_2O) Mass spectrum showed the conversion from *m/e* 206 to *m/e* 178. Found: C, 58.20; H, 2.98%. Calcd for $C_{10}H_6OS_2$: C, 58.27; H, 2.88%. Kinetics: A solution of 1 ml of 1,2-dithiaacenaphthene *S*-oxide (1.2×10^{-3}M) in absolute ethanol was added to a mixture of 29 ml of ethanol and 20 ml of 4.0×10^{-4}M KOH water solution, the latter mixture being kept in a constant temperature bath prior to addition of the ester. An aliquot of the reaction mixture was withdrawn to a UV cell and its optical density near 247 nm was recorded with a Hitachi EPS-3T recording spectrophotometer. Since the reaction was expected to be complicated as illustrated in equations (1)—(3), only the initial rate was used for calculation of the rate constant. The initial slope obtained graphically was found to be proportional to the initial rate of the reaction:

$$
\begin{aligned}
-\mathrm{d}[\mathrm{ester}]/\mathrm{d}t &= -\mathrm{d}(\mathrm{O.D})/\mathrm{d}t \times 1/\varepsilon \\
&= k_{\mathrm{obs}}[\mathrm{E_0}] = k_{\mathrm{OH}}[\mathrm{OH^-}][\mathrm{E_0}]
\end{aligned}
$$

The plot of the rates against the initial concentration of the ester gave a straight line. (Table 2)

Product. 1,2-Dithiaacenaphthene *S*-oxide (1.84 g, 8.9 mmol) and KOH (0.76 g, 14 mmol) were dissolved in methanol. After being left at room temperature for 12 hr, the solution was evaporated and the residue was extracted with ether and chloroform. Concentration of the extract afforded 1,2-dithiaacenaphthene (583 mg, 37%). The inorganic layer which did not dissolve either in ether or chloroform was neutralized with hydrochloric acid and then extracted with ether and chloroform. After the solvent was removed the residue was separated by column chromatography into 1,2-dithiaacenaphthene *S*-oxide (425 mg, 23%) and 1,2-dithiaacenaphthene *S,S*-dioxide (108 mg, 6%).

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[7] A. Zweig and A. H. Hoffmann, *J. Org. Chem.*, **30**, 3997 (1967).