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Concurrent Oxygen Exchange and Racemization Reactions of Diaryl Sulfoxides in Concentrated Sulfuric Acid[1]

Shigeru OAE and Norio KUNIEDA

Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku Osaka

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When diaryl sulfoxides are dissolved in concentrated sulfuric acid at 0°C, characteristic bluish colored solutions are obtained, from which the starting sulfoxides can be recovered quantitatively upon quenching with a large amount of water. When ^{18}O-labeled and optically active sulfoxides are used, one observes the concurrent oxygen exchange and racemization reactions of the sulfoxides. The kinetic behaviors of these reactions have been studied in detail using various substituted diaryl sulfoxides. The rate of the oxygen exchange was found to be identical to that of the racemization while the rates of the racemization were nicely correlated with the Hammett acidity functions (H_0) (Slope$=1.07$). Meanwhile the polar effect of subsituents on the rates of both oxygen exchange and racemization was found to be very small. From these results possible mechanisms for these reactions have been discussed.

The sulfur-oxygen linkage in sulfoxides is known to be considerably weaker than that of sulfones and there are number of reactions which involve the facile cleavage of the sulfur-oxygen bond of sulfoxides.[2] In the meantime, sulfoxides, being of pyramidal structure, have been resolved to pairs of optical isomers when the two substituents on the sulfur atom are different. An interesting reaction,

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[1] Paper XX on Sulfoxides.

[2] For details see Chapter 4 of "Sulfur Bonding," by C. C. Price and S. Oae, Ronald Press., N. Y. (1962).

in these connection, is the concurrent oxygen exchange and racemization reactions of sulfoxides, which have attracted considerable attentions at various laboratories in recent years.[3] Previously, we have reported that sulfoxides undergo an oxygen exchange reaction in concentrated sulfuric acid and the concurrent racemization also takes place when (+)-*p*-aminophenyl *p'*-tolyl sulfoxide is used.[4] Based on a few observations such as the complete lack of oxygen exchange in sulfones, aromatic *N*-oxides and phosphine oxide, rough kinetics and stereochemical data, *etc.*, the mechanism involving the nucleophilic attack of sulfoxide on sulfuric acid was tentatively suggested as a working hypo thesis, however, more careful kinetic studied were critically needed in order to elucidate a plausible mechanism for the reaction.

We now have compiled substantial amounts of kinetic data on the concurrent oxygen exchange and recemization reactions of diaryl sulfoxides and hence would like to report our further observations and comments concerning the nature of the reactions.

Results and Discussion

Sulfoxides used for this kinetic study are ^{18}O-labeled diaryl sulfoxides and optically active aryl-*p*-tolyl sulfoxides, and all of the sulfoxides were nicely recovered almost quantitatively and in no case the formation of the respective sulfones or sulfides was noticed.

At first careful kinetic experiments were conducted on the rates of both oxygen exchange and racemization reactions using (+)-*p*-tolyl phenyl sulfoxide in 95.5% sulfuric acid. The results, shown in Table 1, clearly reveal that the rate of the oxygen exchange is identical to that of the racemization ($k_{ex}/k_{rac}=0.97$), suggesting that the reaction proceeds through a SN_1 like S–O bond cleavage at the rate-determining step.[5] The energy and entropy of activation of this reaction are found to be 27.4 kcal/mol and +21.5 e. u., respectively. The positive value of the entropy of activation also favors the rate determining SN_1 like cleavage of S-O bond of the sulfoxide. Since our preliminary investigation has shown that the reaction is very fast in sulfuric acid of a high concentration and almost nil in a sulfuric acid of less than 85% concentration at a low temperature,[6] the rates of racemization were carefully measured in sulfuric acids of various concentrations. The results are shown in Table 2 and Fig. 1.

TABLE 1. RATE CONSTANTS OF ^{18}O-EXCHANGE AND RACEMIZATION OF *p*-TOLYL PHENYL SULFOXIDE[a] IN 95.5% SULFURIC ACID

Run No.	sec^{-1}
1	$k_{\text{exchange}}=3.22\pm0.15\times10^{-4}$ [b]
2	$k_{\text{racemization}}=3.32\pm0.20\times10^{-4}$ [b]
3	$=1.21\pm0.04\times10^{-4}$ [c]
4	$=7.25\pm0.27\times10^{-4}$ [d]

a) Sulfoxide=0.1 mol/*l*
b) at 5°C c) at 0°C d) at 10°C

TABLE 2. RATE CONSTANTS OF RACEMIZATION OF (+)-*p*-TOLYL PHENYL SULFOXIDE[a] IN SULFURIC ACID OF VARIOUS CONCENTRATIONS AT 5°C

Run No.	H_2SO_4 (%)	$k_{rac}\times10^4$, sec^{-1}	$\log k_{rac}+H_0$ [b]
5	91.8	1.16 ± 0.10	−12.45
6	93.3	1.68 ± 0.10	−12.42
7	94.4	2.58 ± 0.06	−12.38
8	95.5	3.32 ± 0.20	−12.40
9	96.3	4.48 ± 0.28	−12.38

a) Sulfoxide=0.1 mol/*l*.
b) The H_0 values of these were used the values given by Paul and Long; Ref. 7.

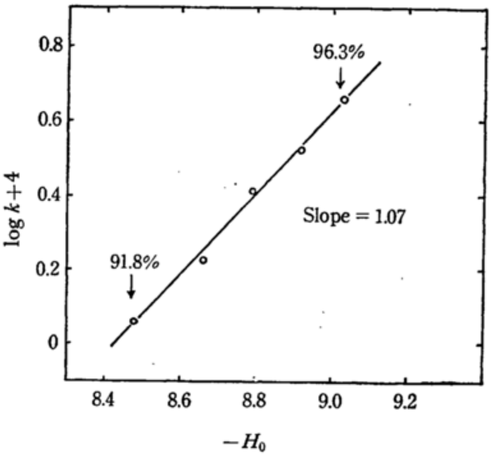

Fig. 1. The rate constants of racemization of (+)-*p*-tolyl phenyl sulfoxide protted against H_0.

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[3] a) The hydrogen chloride-catalyzed racemization; K. Mislow, T. Simmons, J. T. Mellilo and A. L. Ternay, *J. Am. Chem. Soc.*, **86**, 1452 (1964). b) The oxygen exchange and racemization reactions in dinitrogen tetroxide; S. Oae, N. Kunieda and W. Tagaki, *Chem. & Ind.*, **1965**, 1790. c) The oxygen exchange and racemization reactions in acetic anhydride; S. Oae and M. Kise, *Tetrahedron Letters*, **1967** **(No. 15)**, 1409.

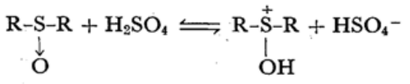
[4] S. Oae, T. Kitao, Y. Kitaoka and S. Kawamura, This Bulletin, **38**, 546 (1965).

[5] D. Samuel and B. L. Silver, "Oxygen Isotope Exchange Reactions of Organic Compounds," in "Advances in Physical Organic Chemistry," Vol. 3, ed. by V. Gold, Academic Press, London and N. Y. (1965), p. 129.

[6] It will be discussed later in this paper.

[7] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

As shown in Table 2 and Fig. 1, the rates are nicely correlated with the Hammett acidity functions (H_0) (Slope=1.07).[8] This means that the protonated species are involved in the transition state of the reaction, indicating that the reaction follows the A-I type mechanism of the Zucker-Hammett's hypothesis.[9] Meanwhile it have been shown by Gillespie and Passerini[10] and us[11] through the cryoscopic measurement and the ^{18}O-tracer experiment that sulfoxides ionize in concentrated sulfuric acid in the following manner (Eq. (1)).



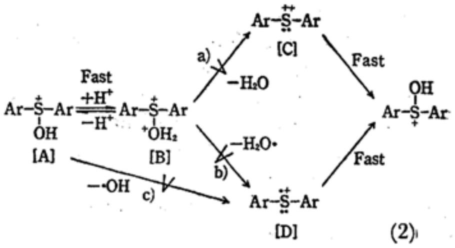
$$\mathrm{R{-}}\underset{\substack{\downarrow\\ \mathrm{O}}}{\mathrm{S}}\mathrm{{-}R} + \mathrm{H_2SO_4} \rightleftharpoons \mathrm{R{-}}\overset{+}{\underset{\substack{|\\ \mathrm{OH}}}{\mathrm{S}}}\mathrm{{-}R} + \mathrm{HSO_4^-} \qquad (1)$$

[A]

(Cryoscopic i-facter=2)

Therefore, the hydroxysulfonium ion [A] formed by the protonation of the sulfoxides in sulfuric acid in the preequilibrated ground state will probably pick up another proton from sulfuric acid before reaching the transition state of the reaction where the partial cleavage of the S–O bond will take place, as in the reduction of dimethyl sulfoxide with hydroiodic acid.[12]

There are a few ways conceivable for the cleavage of the S–O bond that fit in these observations, as shown by Eq. (2).



(2)

Path a is the heterolysis of the S–O bond involving the rate-determining formation of the doubly positive charged "sulfidonium ion" [C] intermediate. By the ^{18}O-tracer experiment and the freezing-point measurement the formation of the diaryl sulfidonium ion was excluded, but this *path a* is still attractive if one assumes that the formation of the sulfidonium ion [C] is the slow rate-determining step and that the sulfidonium ion [C] hydrolyzes to give the protonated sulfoxide [A] or [B] in the subsequent fast step.

Path b and *c* is the homolysis to form the cation radical intermediate [D]. The several ESR studies of the sulfur-containing aromatic compounds have been done. Schmidt[13] has reported that the concentrated sulfuric acid solutions of some aryl sulfoxides are paramagnetic. Especially well-studied are the sulfuric acid solutions of thianthrene oxide and phenoxathin oxide, *etc.*[14] We could

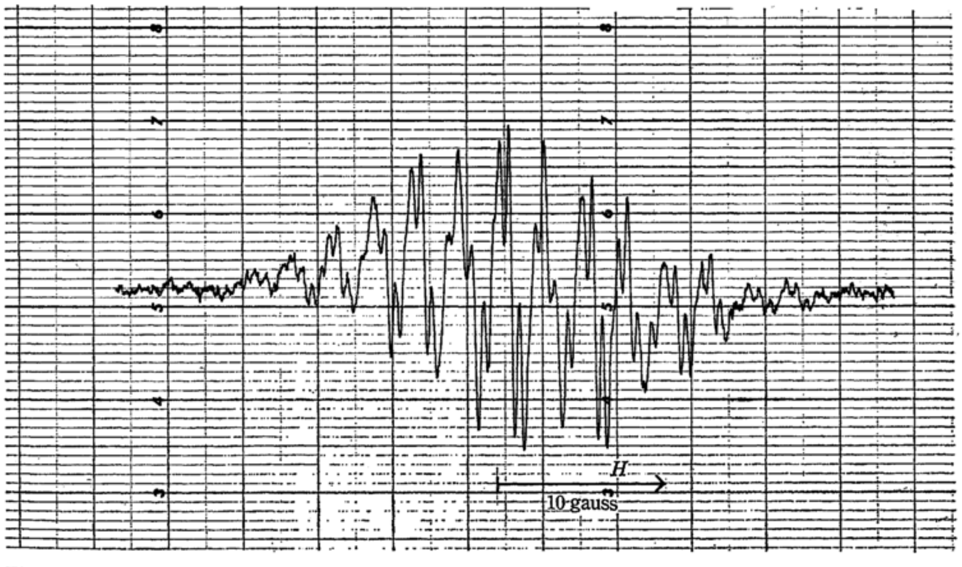


Fig. 2. The ESR spectrum of a 0.2 M solution of p,p'-ditolyl sulfoxide in 96.3% sulfuric acid.

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[8] When the H_0 values of Jorgenson and Hartter were used the slope of this correlation was 0.89; M. J. Jorgenson and D. R. Hartter, *J. Am. Chem. Soc.*, **85**, 878 (1963).

[9] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 935 (1957).

[10] R. J. Gillespie and R. C. Passerini, *J. Chem. Soc.*, **1956**, 3850.

[11] S. Oae, T. Kitao and Y. Kitaoka, This Bulletin, **38**, 543 (1965).

[12] J. H. Krueger, *Inorg. Chem.*, **5**, 132 (1966).

[13] U. Schmidt, K. Kabitze and K. Markau, *Angew. Chem.*, **72**, 708 (1960); U. Schmidt, *ibid.*, **76**, 629 (1964).

[14] H. J. Shine and L. Piette, *J. Am. Chem. Soc.*, **84**, 4798 (1962) and their successive papers.

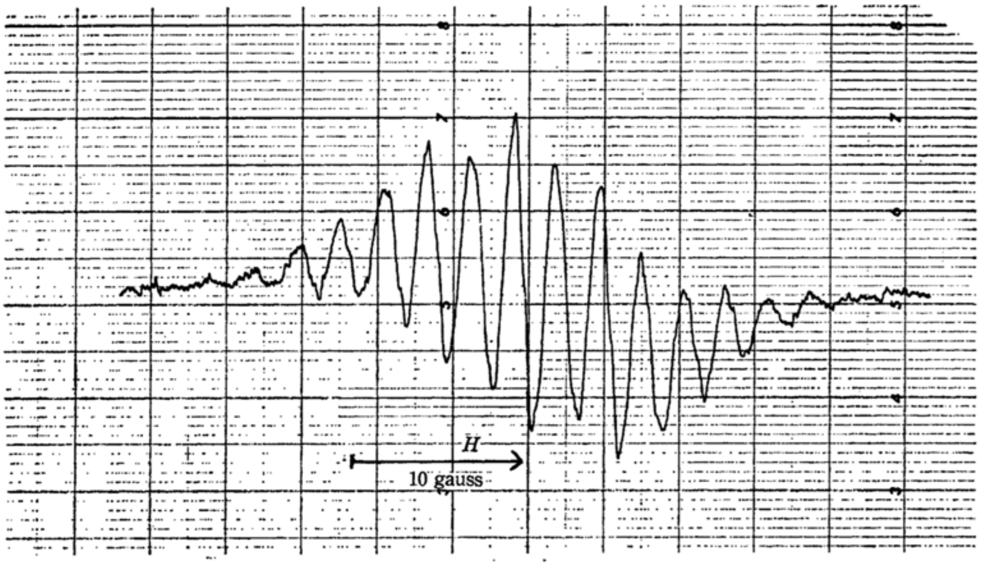

Fig. 3. The overmodulated ESR spectrum of a 0.4 M solution of *p,p'*-ditolyl sulfoxide in 96.3% sulfuric acid.

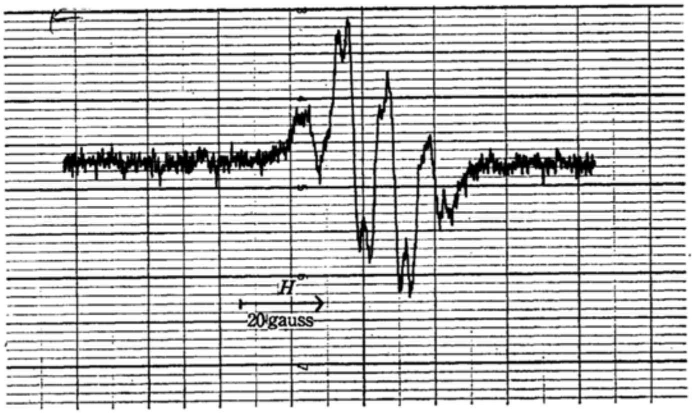

Fig. 4. The ESR spectrum of a 0.1 M solution of *p*-tolyl phenyl sulfoxide in 96.3% sulfuric acid.

detect no noticeable ESR signal from the solution of diphenyl sulfoxide in our previous work.[4] Recently, Shine and co-workers[15] have also reported that no noticeable ESR signal was found from the solution of diphenyl sulfoxide, but noticeable ESR signals were found from 96% sulfuric acid solutions of *p, p'*-substituted diphenyl sulfoxides when *p, p'*-substituents are good electron donating groups such as $-OCH_3$, $-CH_3$ and $-OH$, and ascribed it to the existence of the positive ion radicals.

We have also repeated the ESR measurements of *p*-tolyl phenyl, *p, p'*-ditolyl and *p, m'*-ditolyl sulfoxides in 96.3% sulfuric acid, and found that the same ESR signal with 15 major lines from the blue solution of *p, p'*-ditolyl sulfoxide as that of Shine. The 15 lines ESR spectra of the solution which are shown in Fig. 2 and Fig. 3 decay in a relatively short time, indicating the short life of this cation radical. The solutions of *p*-tolyl phenyl and *p, m'*-ditolyl sulfoxides gave very weak ESR signals which have no satisfactory hyperfine structure and *g* values of these were 2.0082 and 2.0080, respectively (Fig. 4 and Fig. 5). The one day old solution of *p*-tolyl phenyl sulfoxide gave a simple singlet ESR signal, but we do not know the origin of this signal. However, these ESR results suggest that the path involving the homolytic cleavage to form a incipient cation radical intermediate [D] is a likely possibility.

If the reaction follows the *path a*, the rate would

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[15] H. J. Shine, M. Rahman, H. Seeger and G.-S. Wu, *J. Org. Chem.*, **32**, 1901 (1967).

[16] E. L. Eliel, "Substitution at Saturated Carbon Atoms" in "Steric Effects in Organic Chemistry," ed. by M. S. Newman, John Wiley and Sons, N. Y. (1965), p. 88.

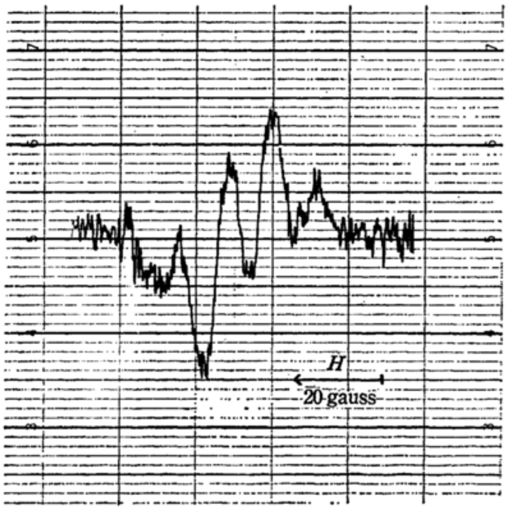
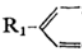


Fig. 5. The ESR spectrum of 0.15 M solution of p, m'-ditolyl sulfoxide in 96.3% sulfuric acid.

be markedly effected by polar substituents like the SN_1 type reactions of benzhydryl compounds,16) on the other hand, the effect of polar substituents would be very small when the reaction proceeds through the path of homolytic cleavage. The rates of both oxygen exchange and racemization of several substituted diaryl sulfoxides were measured and the results are tabulated in Table 3.

TABLE 3. RATE CONSTANTS OF ^{18}O-EXCHANGE AND RACEMIZATION OF R_1--SO-R_2

Run No.	Sulfoxide a) R_1	R_2	(sec^{-1}) $k_{ex}\times10^4$	$k_{rac}\times10^4$
10	H	p-CH_3-C_6H_4	3.22 ± 0.25	3.32 ± 0.20
11	H	p-Cl-C_6H_4	1.52 ± 0.03	
12	H	C_6H_5	1.11 ± 0.03	
13	CH_3	p-Cl-C_6H_4		2.77 ± 0.33
14	CH_3	m-CH_3-C_6H_4		2.53 ± 0.32
15	CH_3	C_6H_5		2.38 ± 0.10
16	CH_3	p-NH_2-C_6H_4		1.62 ± 0.10
17	CH_3	Mesityl		0.268 ± 0.013
18	CH_3	o-Cl-C_6H_4		0.236 ± 0.013

a) Sulfoxide=0.1 mol/l
Run No. 10—12; in 95.5% sulfuric acid at 5°C.
Run No. 13—18; in 96.7% sulfuric acid at 0°C.

Inspection of the kinetic data reveals clearly that the polar effect of substituents on the rates of both oxygen exchange and racemization is very small in comparison with that of the typical SN_1 type reactions. For example, the substitution of p-methyl group accelerates the rate of oxygen exchange by only less than two fold while the electron-withdrowing p-chloro group also gave a small acceleration. These tendencies are shown equally in the racemization reactions. These rather small polar effects seem to favor the homolytic cleavage for the reaction.

The rates of racemization of p-tolyl o-chlorophenyl sulfoxide and p-tolyl mesityl sulfoxide were found to be about ten fold slower than that of p-tolyl phenyl sulfoxide. The marked rate retardation by ortho substituents is perhaps due to the steric hindrance of protonation to form the corresponding diprotonated intermediates.

Reaction with Dilute Sulfuric Acid at Higher Temperature. Although our earlier paper reported that the oxygen exchange was almost nil in a sulfuric acid of less than 85% concentration at around 0°C, we have found that diaryl sulfoxides racemize readily in a sulfuric acid of less than 85% concentration when the reaction was carried out at a considerably higher temperature. For example, p-tolyl phenyl sulfoxide was found to be racemized in 82% sulfuric acid at 40—50°C. Both the energy ($\Delta E=21.6$ kcal/mol) and entropy ($\Delta S=-7.5$ eu) of activation of this reaction were quite different from those of the lower temperature reaction. Apparently, the mechanism of this reaction is different from that at the lower temperature and similar to those in polychloroacetic acid17) and phosphoric acid18) in which the reaction is presumed to depend on pK_a of the medium used and not on the Hammett acidity function. Detailed discussion on these reactions will be the subject in our forthcoming paper of this series.

Experimental

Materials. *^{18}O-Labeled Diaryl Sulfoxides* were prepared by the oxidation of the corresponding sulfides with bromine complex of pyridine and ^{18}O-enriched water (1.63 atom% ^{18}O) in acetic acid by the same procedure as described in our previous paper.19) Diphenyl sulfoxide; mp 71°C, 0.85_2 atom%. Phenyl-p-tolyl sulfoxide; mp 71—71.2°C, 0.72_0 atom%. Phenyl p-Cl-phenyl sulfoxide; mp 45—46°C, 0.95_2 atom%.

Optically Active Aryl p-Tolyl Sulfoxides were prepared from (−)menthyl (−)-p-toluenesulfinate according to the method developed by Andersen.20) p-CH_3-C_6H_4-SO-R; (R, mp, $[\alpha]_D$(c); $l=1$ in absolute ethanol). Phenyl, 91.5, +27.2°(3.65). p-Cl-phenyl, 80—80.5, +25.9°(2.85). o-Cl-phenyl, 89—89.5, −120.7°(1.43). m-Tolyl, 63.5—64, +25.1°(3.10). p-NH_2-phenyl, 150.5−151, +105.3°(2.21). Mesityl, 107—107.5, −265.0°(2.00).

Kinetic Procedure of the Oxygen Exchange and Racemization Reactions of Diaryl Sulfoxides. In order to compare the rate constants of all the sulfoxides, both oxygen exchange and reacemization reactions were carried out under identical conditions.

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17) S. Oae, M. Yokoyama and M. Kise, unpublished work.
18) S. Oae and N. Kunieda, unpublished work.
19) S. Oae, Y. Onishi, S. Kozuka and W. Tagaki, This Bulletin, **39**, 364 (1966).
20) K. K. Andersen, *Tetrahedron Letters*, **1962 (No. 3)**, 93.

An ^{18}O-labeled or an optically active sulfoxide was dissolved in a sulfuric acid, in such a way as to maintain the concentration of the sulfoxide just about 0.1 mol/*l*, at a preset temperature (0±0.06, 5±0.08 or 10±0.08°C). An aliquot portion (5.0 m*l*) of the solution was taken up from time to time for 5—7 times and was quenched with ice water. The precipitate formed was extracted with carbon tetrachloride, and the carbon tetrachloride solution was washed with water, 10% aqueous solution of sodium carbonate and water, respectively, and dried over anhydrous sodium sulfate. Finally, carbon tetrachloride was distilled *in vacuo* and then the sulfoxide recovered was subjected to the ^{18}O-analysis or the optically active measurement. The mass-spectrometric analysis was carried out with the carbon dioxide gas and the atom% ^{18}O was calculated from the mass peak heights 44 and 46 according to the following equation.

$$\text{Atom\% }^{18}\text{O} = \frac{\text{Peak 46/Peak 44}}{2 + \text{Peak 46/Peak 44}}$$

The rate constants of the oxygen exchange and racemization were calculated from the following equations. For oxygen exchange; $\log \alpha_0-\alpha/\alpha_t-\alpha=kt/2.303$, where α_0 and α_t are the atom% ^{18}O at times 0 and *t*, respectively, and α is the atom% ^{18}O of natural CO_2, and for racemization; $\log \beta_0/\beta=kt/2.303$, where β_0 and β are the rotatory powers at times 0 and *t*, respectively.

Typical Runs of Kinetics.

Polarimetric Run.

No. 2. *p*-Tolyl phenyl sulfoxide; Sulfoxide=0.1 M in 95.5% H_2SO_4 at 5°C.

Time (min)	0	5.2	10.2	15.3	25.2	30.2
$[\alpha]_D$	21.04°	18.80°	17.00°	15.50°	13.83°	12.10°

$k_1=3.32\pm0.20\times10^{-4}\ \text{sec}^{-1}$

No. 18. *o*-Chlorophenyl *p*-tolyl sulfoxide; Sulfoxide=0.1 M in 96.7% H_2SO_4 at 0°C.

Time (min)	0	10.3	40.2	60.4	80.2	110.3
$[\alpha]_D$	−113.6°	−111.9°	−107.2°	−103.4°	−102.1°	−96.5°

$k_1=2.36\pm0.13\times10^{-5}\ \text{sec}^{-1}$

Exchange Run

No. 1. *p*-Tolyl phenyl sulfoxide; Sulfoxide=0.1 M in 95.5% H_2SO_4 at 5°C.

Time (min)	0	5.2	10.4	15.3	20.2	25.2	35.2
α_t (atom%)	0.65_4	0.61_0	0.57_1	0.52_7	0.51_5	0.50_6	0.46_3

$k_1=3.22\pm0.25\times10^{-4}\ \text{sec}^{-1}$

No. 12. Diphenyl sulfoxide; Sulfoxide=0.1 M in 95.5% HS_2O_4 at 5°C.

Time (min)	0	10.2	20.2	30.2	50.3
α_t (atom%)	0.84_3	0.80_8	0.76_1	0.74_8	0.65_7

$k_1=1.11\pm0.03\times10^{-4}\ \text{sec}^{-1}$

($\alpha=0.20_7$ atom%)

ESR Spectra. The ESR spectra of 96.3% sulfuric acid solutions of the sulfoxides were measured with JES-3BSX type spectrometer of Japan Electron Optics Lab. using a capillary sample cell of aqueous type (0.75 mmϕ) with 100 Kc field modulations at room temperature.