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Kinetic Studies of Oxygen Exchange and Racemization Reactions of Diaryl Sulfoxides in Sulfuric Acid of Various Concentrations[1]

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When ^{18}O-labeled and optically active sulfoxides are dissolved in a concentrated sulfuric acid, one observes the concurrent oxygen exchange and racemization reactions of the sulfoxides, and these reactions were found to proceed through the S_N1-like path (S. Oae *et al.*, Bull. Chem. Soc. Japan, **38**, 546 (1965); **41**, 696 (1968)). We have found that the concurrent oxygen exchangeand racemization reactions also take place even in less concentrated sulfuric acid at somewhat higher temperature, *i. e.* 70% sulfuric acid at 30°C, and proceed through a different mechanistic route, very likely an S_N2-like path. Kinetic investigation on these reactions in sulfuric acid of various concentrations (66.5—96.3%) suggests there is a gradual change of mechanism of the reaction, *i. e.* from S_N2 type in 66.5% to S_N1 type in 96.3% with the increase of the concentration of sulfuric acid.

Sulfoxides, being of stable pyramidal structure, can be resolved to a pair of optically active enantiomers when two substituents on the sulfur atom are different.[2] Meanwhile, a convenient method of synthesizing optically active sulfoxides has recently been developed.[3] Therefore one can now study the stereochemistry of reactions of the sulfoxides very readily using these optically active compounds.[4] The concurrent oxygen exchange and racemization reaction of sulfoxides are particularly useful for the stereochemical studies on nucleophilic reaction on the trivalent sulfur atom, because one can readily prepare both ^{18}O-labeled and optically active

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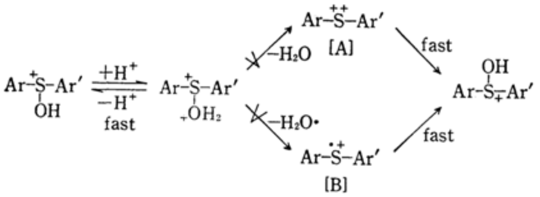
[1] Paper XXVI on Sulfoxides.

[2] K. Mislow, "Introduction to Stereochemistry," W. A. Benjamin, Inc., New York, N. Y. (1965), p. 88.

[3] K. K. Andersen, *Tetrahedron Letters*, **1962**, 93; H. Phillips, *J. Chem. Soc.*, **1925**, 2552.

[4] Summarized in; K. Mislow, *Record of Chemical Progress*, **28**, 217 (1967), and our previous paper (Ref. 5b).

sulfoxides while the analysis of ^{18}O-content in sulfoxides is also quite facile. We have reported previously[5] that the rate of the oxygen exchange of ^{18}O-labeled, optically active *p*-tolyl phenyl sulfoxide was identical to that of the racemization in 95.5% sulfuric acid and the rates of the racemization were nicely correlated with $-H_0$ (slope=1.1) in the range of concentration from 96.3% to 91.8% of sulfuric acid. In the meantime, the polar effect of *p*-substituent on phenyl ring on the rates of both oxygen exchange and racemization in 95.5% or 96.2% sulfuric acid was found to be very small, while a noticeable ESR signal was detected with 96% sulfuric acid solution of a *p,p'*-disubstituted diphenyl sulfoxide.[6] From these observations we have postulated the following S_N1-like mechanism for these reactions, and favored the homolytic cleavage of the S–O bond, the route involving [B].



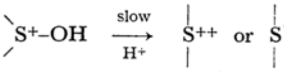
Previously, a preliminary experiment on the oxygen exchange and racemization reactions of diaryl sulfoxides was conducted in a sulfuric acid of less than 85% concentration at around 0°C[5b] and found to proceed very little. Meanwhile, we have found that these sulfoxides undergo concurrent oxygen exchange and racemization reactions with much weaker acids such as acetic, perchloroacetic acids when heated at much higher temperatures.[7] Accordingly, it was thought that the oxygen exchange reaction should take place even in dilute sulfuric acid at somewhat higher temperatures. In fact, we have found that diaryl sulfoxides undergo oxygen exchange and racemization reactions readily in a sulfuric acid of even less than 85% concentration when the reaction was carried out at considerably higher temperatures (30—50°C). We now have compiled substantial amounts of kinetic data on these reactions of diaryl sulfoxides in sulfuric acid of various concentrations (66.5—96.3%) and hence would like to report detailed accounts of the kinetic results and their implications to the mechanistic interpretations on these reactions.

Results and Discussion

At first, careful kinetic experiments were conducted on the rates of both oxygen exchange and racemization reactions of *p*-tolyl phenyl sulfoxide (0.935 atom%-^{18}O, $[\alpha]_D^{25}$ +27.8° in 96% ethanol) in sulfuric acid of various concentrations ranging between 66.5% and 96.3% at several temperatures between 0 and 60°C. The results are shown in Table 1. The sulfoxide was found to be racemized even in 66.5% sulfuric acid at a higher tempparature. The mechanistic interpretation of these results will be discussed in the light of first the values of k_{ex}/k_{rac} and activation parameters, the correlation with H_0 (Zucker-Hammett hypothesis), and then the Bunnett's *w*-values.

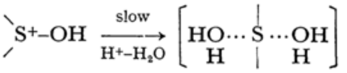
Variation of k_{ex}/k_{rac} Values and Activation Parameters. The concurrent oxygen exchange and racemization reaction of sulfoxides in acid media may proceed through the following two extreme mechanistic routes as shown below.

1) S_N1-like route.



$$>S^{+}\text{–OH} \xrightarrow[H^{+}]{\text{slow}} -\overset{|}{\underset{|}{S}}{}^{++} \text{ or } \overset{|}{\underset{|}{S}}{}^{\dot{+}}$$

2) S_N2-like route.



$$>S^{+}\text{–OH} \xrightarrow[H^{+}-H_2O]{\text{slow}} \left[\underset{H}{HO}\cdots\overset{|}{\underset{|}{S}}\cdots\underset{H}{OH}\right]$$

When the reaction proceeds through the S_N1-like route, each oxygen exchange will cause racemization, and the ratio k_{ex}/k_{rac} becomes unity. Whereas if it passes through the S_N2-like route each oxygen exchange will result in the inversion of configuration at the central sulfur atom and hence the ratio k_{ex}/k_{rac} becomes 0.5. The change of mechanistic routes will be reflected directly on the activation parameters (E_a, $\Delta S^{\neq}$) of these reactions. Therefore these parameters were estimated and the k_{ex}/k_{rac} values and activation parameters thus obtained in several concentrations are listed in Table 2.

As shown in our previous paper,[5] the k_{ex}/k_{rac} and $\Delta S^{\neq}$ values observed in a concentrated sulfuric acid (95.5% or 95.9%) were 1 and 11.5 *e. u.* respectively, suggesting that the reaction proceeds through a route involving the S_N1-like S–O bond cleavage at the rate determining step. However, in about 75% sulfuric acid, the k_{ex}/k_{rac} and $\Delta S^{\neq}$ values, are 0.5 and −18 *e. u.* respectively, indicating that the reaction proceeds through a different mechanistic route, *i. e.* very likely an S_N2-like process, from that in concentrated sulfuric acid. For example, the $\Delta S^{\neq}$ value of the racemization reaction of (+)-*p*-tolyl phenyl sulfoxide with acetic anhydride which show the typical S_N2-like mechanism is −28.6 *e. u.*[8] One finds in Table 2, that both

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[5] a) S. Oae, T. Kitao, Y. Kitaoka and S. Kawamura, This Bulletin, **38**, 546 (1965). b) S. Oae and N. Kunieda, *ibid.*, **41**, 696 (1968).

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

[7] S. Oae, M. Yokoyama and M. Kise, This Bulletin, **41**, 1221 (1968).

[8] S. Oae and M. Kise, *Tetrahedron Letters*, **1967**, 1409.

TABLE 1. RATE CONSTANTS OF ^{18}O-EXCHANGE AND RACEMIZATION OF (+)-*p*-TOLYL PHENYL SULFOXIDE-^{18}O[a)] IN SULFURIC ACID OF VARIOUS CONCENTRATIONS

H_2SO_4 %	Temp. (°C)	10^4 k_{rac} (sec^{-1})	10^4 k_{ex}
96.3	5	4.48 ±0.28	
95.9	5	4.20 ±0.10	4.07 ±0.25
95.5	0	1.93 ±0.15	
	5	3.32 ±0.20	3.22 ±0.15
	10	7.25 ±0.27	
94.9	5	3.08 ±0.12	
94.4	5	2.58 ±0.06	
93.3	5	1.68 ±0.10	
91.8	5	1.26 ±0.09	
91.0	5	0.891±0.050[b)]	0.705±0.012
90.8	5	0.600±0.091	
	10	1.36 ±0.03	
	15	2.22 ±0.18	
89.8	5	0.602±0.015	
	30	6.98 ±0.10	
86.9	30	2.91 ±0.07	1.89 ±0.23
85.6	15	0.458±0.020	
	25	1.35 ±0.09	
	30	2.06 ±0.08	
83.4	30	1.39 ±0.05	0.900±0.020
80.5	30	0.880±0.015	0.458±0.025
78.9	30	0.690±0.015	
75.4	30	0.419±0.011	
	40	1.17 ±0.05	0.549±0.013
	50	2.88 ±0.07	1.46 ±0.09
	60	6.95 ±0.25	3.40 ±0.15
72.5	30	0.328±0.020	
71.1	30	0.301±0.001	
66.5	30	0.198±0.005	

a) $[\alpha]_D^{25}$ +27.8° in 96% ethanol, 0.935 atom%-^{18}O. Concn. of sulfoxide; 0.1 mol/*l*.
b) Calcd from E_a.

TABLE 2. ACTIVATION PARAMETERS AND k_{ex}/k_{rac} VALUES OF (+)-*p*-TOLYL PHENYL SULFOXIDE-^{18}O

H_2SO_4 (%)	E_a (kcal)	$\Delta S^{\ddagger}$ (e.u.)	k_{ex}/k_{rac}
95.9	—	—	0.97
95.5	24.0±3.0	+11.5	0.97
91.0	—	—	0.75
90.8	18.5±2.7	−10.8	—
86.9	—	—	0.65
85.6	17.5±1.3	−17.5	—
83.5	—	—	0.64
80.5	—	—	0.52
75.4	18.6±0.3	−18.9	0.47[a)] 0.51[b)] 0.49[c)]

a) at 40°C. b) at 50°C. c) at 60°C.

k_{ex}/k_{rac} and $\Delta S^{\ddagger}$ values change with the change of the concentration of sulfuric acid. The gradual increase of both k_{ex}/k_{rac} and $\Delta S^{\ddagger}$ values with the increase of the acid suggests that there is a gradual shift in the mechanism of the reaction from S_N2-like in about 75% sulfuric acid to S_N1-like in about 95% acid.

The Correlation with H_0-Values. The rates of many acid-catalyzed reactions are dependent on the concentrations of acid. However, the role of acid and solvent, usually water, varies depending on the reaction conditions and reactants. The Zucker-Hammett hypothesis[9)] has been most widely used to gain an insight into the mechanisms of these acid-catalyzed reactions. They classified mechanisms of many acid-catalyzed reactions into the following two classes, the one (*i. e.* A-1 type) is a group of reactions which give linear plots of log *k* against $-H_0$, and belongs to a family of S_N1-like processes, and the other (*i. e.* A-2 type) is the group which give linear plots of log *k* against log-[HX], belonging to a family of S_N2-like reactions. A diagram correlating the logarithms of the rates of both oxygen exchange (log k_{ex}) and racemization (log k_{rac}) of *p*-tolyl phenyl sulfoxide against the $-H_0$ values of sulfuric acids of various concentrations ranging from 66.5% to 96.3% are shown in Fig. 1. In concentrated sulfuric acid (86.9% to 96.3%), both log k_{ex} and log k_{rac} values are in a

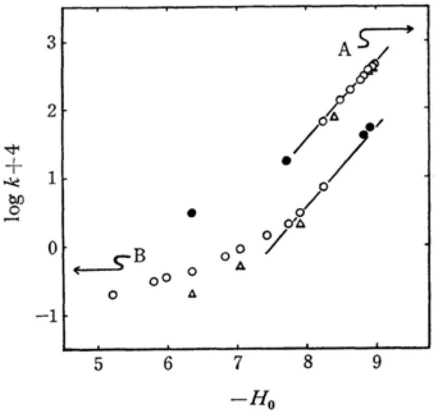


Fig. 1. The rate constants of ^{18}O-exchange and racemization of *p*-tolyl phenyl sulfoxide plotted against H_0.

○: k_{rac} (observed). ●: k_{rac} (calcd from E_a).
△: k_{ex}(observed).
A: at 5°C (the slope is 1.14, r=0.999).
B: at 30°C.

[9)] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 935 (1957); L. Zucker and L. P. Hammett, *J. Am. Chem. Soc.*, **61**, 2791 (1939).

linear relationship with $-H_0$ functions[10] both at 5°C and 30°C, with the slope=1.14, r (correlation coefficient)=0.999 at 5°C. This means that a protonated species is involved in the transition state of the reaction and the reaction is of the A-1 type mechanism. However, as the concentration of sulfuric acid decreases from 86.9%, the plots of $\log k_{ex}$ and $\log k_{rac}$ starts to deviate markedly from the linear slope, suggesting that the reaction is gradually shifted from A-1 type to other with the decrease of the concentration of sulfuric acid. Although we could not find any good relationship of $\log k$ values with those of log[HX], the mechanism of the reaction in less concentrated sulfuric acids is definitely different from that with concentrated sulfuric acid as mentioned in the preceding discussion of both k_{ex}/k_{rac} and $\Delta S^{\neq}$ values.

The Correlation with Bunnett's *w*-Values. The *w*-value is an empirical function presented by Bunnett[11] and is defined by the following equation.

$$(\log k + H_0) = w \log a_{H_2O} + C$$

This parameter, w, is associated with characteristic mode of involvement of water at the rate-determining step of a reaction and according to the magnitude of the w-value many acid-catalyzed reaction can be divided into three groups. In the first group of reactions in which w is between -2.5 to 0, water does not participate in the transition state. In the second group, in which w is between $+1.2$ and $+3.3$, water acts as a nucleophile, while in the last where $w > +3.3$, water acts as a proton transfer agent. The actual diagram plotted with $(\log k + H_0)$ against $\log a_{H_2O}$ are shown in Fig. 2. Apparently, there is a gradual shift of mechanism with the change of the concentration of sulfuric acid. In fact, the w-value in the range of concentration from 75.4 to 66.5% sulfuric acid is $+1.28$ (r=0.998) which corresponds to the second group of reactions that belong to S_N2-like mechanism whereas in a sulfuric acid of above 86.9% concentration the w-value is -0.06 (r=0.990) which is in the range of S_N1-like mechanism.

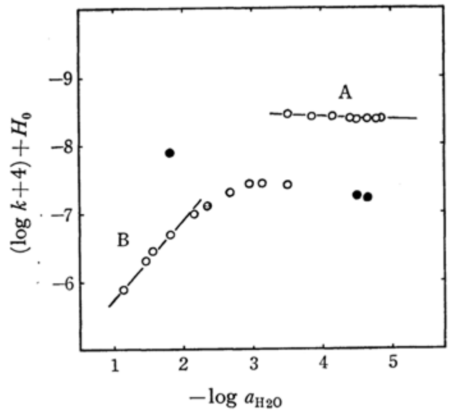
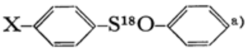


Fig. 2. Racemization of (+)-*p*-tolyl phenyl sulfoxide in sulfuric acid; plots of $(\log k_{rac}+H_0)$ against $\log a_{H_2O}$.
○: k_{rac} (observed). ●: k_{rac} (calcd from E_a).
A: at 50°C (the slope, w, is -0.06, r=0.980).
B: at 30°C (w is $+1.28$, r=0.998).

Mechanistic Change from S_N1 to S_N2 Type Pathways. The k_{ex}/k_{rac} values, the activation paramaters, the correlation with Hammett's H_0 functions and that with Bunnett's w-values show that the concurrent oxygen exchange and racemization reaction of *p*-tolyl phenyl sulfoxide in the less concentrated sulfuric acids proceed through an S_N2-like pathway which is quite different from an S_N1-like route through which the oxygen exchange and racemization reactions in a cancentrated sulfuric acid proceeds. As described in the previous section the shift of the mechanism of the reaction from

TABLE 3. KINETICS OF OXYGEN EXCHANGE OF  [a] IN 75.4% SULFURIC ACID

X	$10^4 k_{ex}$ (sec^{-1}) 40°C	50°C	60°C	E_a (kcal/mol)	$\Delta H^{\neq}$ (kcal/mol)	$\Delta S^{\neq}$ (e.u.)
CH_3O[b]	3.60 ±0.05	11.1 ±0.10	—	22.7	22.1	−3.84
CH_3[c]	0.549±0.013	1.45±0.09	3.40±0.15	18.9	18.4	−19.3
H[d]	0.728±0.015	1.85±0.02	3.85±0.20	17.4	16.8	−23.5
Cl[e]	0.820±0.010	1.98±0.05	4.12±0.13	16.7	16.6	−25.8
NO_2[f]	1.03 ±0.01	2.43±0.07	—	17.3	16.7	−23.6

a) Concn. of sulfoxides: 1.0 mol/*l*　b) 0.685 atom %-^{18}O
c) 0.935 atom%-^{18}O　d) 0.955 atom %-^{18}O
e) 1.23 atom%-^{18}O　f) 0.996 atom %-^{18}O

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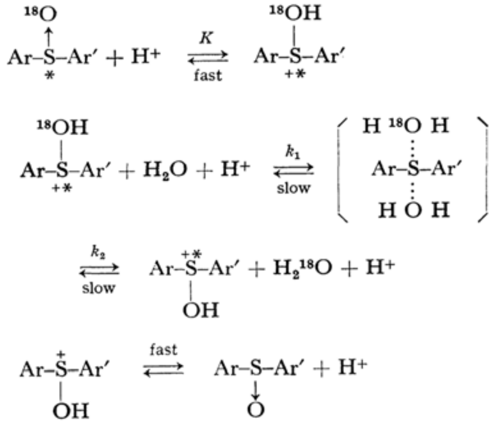
[10] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957). When the H_0 values of Jorgenson and Hartter were used, the slope of this correlation was smaller slightly than 1; J. Jorgenson and D. R. Hartter, *J. Am. Chem. Soc.*, **85**, 878 (1963).

[11] J. F. Bunnett, *J. Am. Chem. Soc.*, **82**, 499 (1960); **83**, 4956 (1961); **83**, 4968 (1961); **83** 4973 (1961); **83**, 4978 (1961).

S_N2-like in less concentrated sulfuric acid to S_N1-like in concentrated acid is apparently gradual. This shift of mechanism is caused by the change of the character of sulfuric acid solution, namely, the proton-donating ability of the solution diminishes steadily as acid concentration decreases while the activity of water increases. If the S_N1-like cleavage of S–O bond of the sulfoxide takes place through the diprotonated species ($R_2S^+{-}^+OH_2$) in rate-determining step as we have suggested,[5b] the formation of this diprotonated species will be decreased as the acid concentration decreases.

Polar Effect in a Less Concentrated Sulfuric Acid. The overall scheme of the oxygen exchange reaction of diaryl sulfoxides in a less concentrated sulfuric acid may be formulated as shown below:



In order to comfirm the S_N2 like mechanism for this reaction, we have extended the oxygen exchange reaction on a few p-substituted diphenyl sulfoxides in 75.4% sulfuric acid, and the results are shown in Table 3. Except for the p-methoxyl compound, there is no difinite trend in the effect of these substituents and the rate varies very little (For σ^+-$\log k_{ex}$; $\rho=0.185$, $r=0.980$) like in case of S_N2 reaction of substituted alkyl halides, while the large negative $\Delta S^{\neq}$ values also suggests a S_N2-like mechanism for this reaction. The small positive value of ρ may be attributed to the fact that the polar effects on the two constants K and k in the equation for the observed rate, $k_{obs} \propto k_1 K$, are canceled out considerably, since K is increased by a electron-accepting substituent while k is decreased by the same substitutent. The equilibrium constant (K) of the initial step of protonation is considered to be very large, since the pK_a values of diaryl sulfoxides are very small,[12] *i. e.* p-tolyl phenyl sulfoxide (−4.40) and diphenyl sulfoxide (−4.97), while H_0 function of 75.4% sulfuric acid is −6.35 and even that of 66.5% sulfuric acid is −5.20. Since the pK_a values are presumed to be the H_0 values of the half protonation of the sulfoxides, the sulfoxides are considered to be protonated nearly completely. Therefore, the second step of nucleophilic subsitution of the protonated sulfoxide by water (k_1) become the slow rate-determining step of the reaction. Only in the case of the p-methoxyl compound a small acceleration of rate observed, and both entropy and enthalpy of activation are off the trend of those of the other substituted sulfoxides. The mechanism of the reaction of this compound is probably different from that of the others, and similar to that of p-tolyl phenyl sulfoxide in a concentrated sulfuric acid, proceeding through an A-1 type route.

Experimental

Materials. *^{18}O-Labeled p-Substituted 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.[13] p-X–C_6H_4–$S^{18}O$–C_6H_5; (X, mp (°C) (lit),[14] atom%-^{18}O). H, 70—71 (71), 0.955. CH_3, 71—71.2 (71—72), 0.935. CH_3O, 60 (55—57), 0.685. Cl, 45—46 (45—46), 1.23. NO_2, 107 (106—107), 0.996 (from 3.50 atom%-^{18}O-water).

Optically Active p-Tolyl Phenyl Sulfoxide was prepared from (−)-menthyl (−)-p-toluenesulfinate according to the method developed by Andersen.[3] mp 91.5—92°C, $[\alpha]^{25}_{D}=+27.8°$ in 96% ethanol (l=0.5, c=1.63) (lit[15]; mp 92—93°C, $[\alpha]_D=+27.0°$ in 95% ethanol).

Kinetic Procedure. The rates of the oxygen exchange and racemization were measured by the same procedures as described in our previous paper[5] using Yanagimoto OR-10 type polarimeter and Hitachi-RMU-6E type mass-spectrometer.

Sulfuric Acid. Concentrations of sulfuric acid-water media were determined by titration with a standard alkali solution. The H_0 values used here is from the tables of Paul and Long,[10] and the activity of water ($\log a_{H_2O}$) of a sulfuric acid solution was tabulated by Deno and Taft.[16]

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12) S. Oae, K. Sakai and N. Kunieda, This Bulletin, in press (1969).

13) S. Oae, Y. Ohnishi, S. Kozuka and W. Tagaki, This Bulletin, **39**, 364 (1966).

14) G. Modena, *Gazz. Chem. Ital.*, **89**, 834 (1959).

15) K. Mislow, M. M. Green, P. Laur, J. Melillo, T. Simmons and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **87**, 1958 (1965).

16) N. C. Deno and R. W. Taft, Jr., *ibid.*, **76**, 244 (1954).