

## Oxygen Exchange and Racemization Reactions of Sulfoxides in Acetic and Chloroacetic Acid<sup>1)</sup>

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(Received November 22, 1967)

Oxygen exchange reaction of sulfoxides has been performed mainly in mineral acids such as sulfuric acid, aqueous hydrochloric and hydrobromic acids. We have found that concurrent oxygen exchange and racemization reactions take place also in carboxylic acids such as acetic, mono- and poly-chloroacetic acids. The pseudo first order reaction rates of both oxygen exchange and racemization reactions of *p*-tolyl phenyl sulfoxide have been determined using both optically active and <sup>18</sup>O-labeled *p*-tolyl phenyl sulfoxides in these acids. This reaction is found to be mainly dependent on the strengths of the acids; namely, the reaction velocity is faster in an acid of smaller *pK<sub>a</sub>* value. Together with the fact that *k*(rac.)/*k*(exch.) is unity and the substituent effect is small, the reaction is suggested to proceed through an unimolecular type S—O bond cleavage, probably involving radical cation intermediate (II).

Sulfoxide, unlike sulfones, have been known to undergo concurrent oxygen exchange and racemizations in various acidic media, such as in concentrated sulfuric acid,<sup>2,3)</sup> hydrochloric acid in aqueous dioxane,<sup>4)</sup> hydrobromic acid in acetic acid,<sup>5)</sup> dinitrogen tetroxide,<sup>6)</sup> diluted nitric acid<sup>7)</sup> and acetic anhydride.<sup>8)</sup> In the course of our further extension of these concurrent oxygen exchange and racemization reactions of sulfoxides, we have recently found that sulfoxides undergo concurrent oxygen exchange and racemization reactions even in weak organic acids, such as acetic, monochloro-, dichloro- and trichloroacetic acids.

This paper will describe the detailed account of our kinetic and stereochemical investigations of various sulfoxides and their implications for the interpretation of the mechanism of the reaction.

### Results and Discussion

#### Oxygen Exchange Reactions of Dimethyl-, Dibenzyl- and Diphenyl Sulfoxides. At the ini-

tial stage of this study, oxygen exchange reactions of sulfoxide were carried out in aqueous acetic acid. Namely, when <sup>18</sup>O-labeled diphenyl-, dibenzyl-, di-(*n*-butyl-) and dimethyl sulfoxides were treated separately in boiling 5:1 (w/w) glacial acetic acid-water mixture for three hours, a noticeable <sup>18</sup>O-exchange (13%) was observed only with dimethyl sulfoxide. However, under a prolonged heating at a somewhat higher temperature, the other sulfoxides were also found to undergo the oxygen exchange reaction. The Table 1 illustrates the amounts of oxygen-exchange of diphenyl-, dibenzyl- and dimethyl

TABLE 1. OXYGEN EXCHANGE REACTION OF <sup>18</sup>O-LABELED SULFOXIDES IN AQUEOUS ACETIC OR ACETIC ACIDS AT 130°C, FOR 24 HR

Sulfoxide	<sup>18</sup> O-concentration of starting sulfoxide (atom %)	<sup>18</sup> O-concentration of recovered sulfoxide (atom %)	
		in excess aq. acetic acid	in excess acetic acid
PhCH <sub>2</sub> -S-CH <sub>2</sub> -Ph <sup>18</sup> O	0.77	0.59	0.59
Ph-S-Ph <sup>18</sup> O	0.62	0.60	0.56
CH <sub>3</sub> -S-CH <sub>3</sub> <sup>18</sup> O	1.67	0.24	—

1) Paper XXII on Sulfoxide, Paper XXI; S. Oae, and N. Kunieda, This Bulletin, **41**, 1025 (1968).

2) a) S. Oae, T. Kitao and Y. Kitaoka, *Chem. & Ind.*, **1961**, 291. b) S. Oae, T. Kitao and Y. Kitaoka, This Bulletin, **38**, 543 (1965). c) S. Oae, T. Kitao, S. Kawamura and Y. Kitaoka, *ibid.*, **38**, 546 (1965). d) S. Oae and N. Kunieda, *ibid.*, **41**, 696 (1968).

3) H. J. Shine and D. R. Tompson, *Tetrahedron Letters*, **1966**, 1591.

4) K. Mislow, T. Simmons, J. T. Mellello and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964).

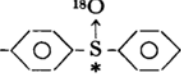
5) W. Tagaki, K. Kikukawa, N. Kunieda and S. Oae, This Bulletin, **39**, 614 (1966).

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7) N. Kunieda and K. Sakai, Unpublished work from these laboratories.

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

TABLE 2. KINETIC DATA ON OXYGEN EXCHANGE AND RACEMIZATION REACTION IN ACETIC, MONOCHLORO-, DICHLORO- AND TRICHLOROACETIC ACIDS AT 120°C

R in R- 	Acid used	$k(\text{rac.}) \times 10^5$ (sec <sup>-1</sup> )	$k(\text{exch.}) \times 10^5$ (sec <sup>-1</sup> )
CH <sub>3</sub>	CH <sub>3</sub> COOH	0.0129 ± 0.0006	
	ClCH <sub>2</sub> COOH	0.153 ± 0.007	
	Cl <sub>2</sub> CHCOOH	0.790 ± 0.023	
	Cl <sub>3</sub> CCOOH	2.39 ± 0.23	2.41 ± 0.28
	Cl <sub>2</sub> CHCOOH*	0.750 ± 0.041	
Cl	Cl <sub>3</sub> CCOOH		1.47 ± 0.12
H	Cl <sub>3</sub> CCOOH		2.17 ± 0.12

\* LiClO<sub>4</sub>, 0.001 mol, was added in 30 ml of dioxane containing 0.25 mol of dichloroacetic acid.

sulfoxides after heating each sample in both glacial and aqueous acetic acids for 24 hr at 130°C. Dimethyl sulfoxide was quite reactive as was expected, however, decomposed under the prolonged heating with glacial acetic acid. Apparently it underwent the Punmerer type rearrangement forming methyl mercaptomethyl acetate, which upon quenching with water hydrolyzed spontaneously to give acetic acid, methylmercaptan and formaldehyde. In fact, we isolated methylmercaptan by converting it to mercuric methylmercaptide.

The other sulfoxides could be nicely recovered even after a prolonged heating with glacial acetic acids. The order of the reactivities of the three sulfoxides, *i.e.*, dimethyl > dibenzyl > diphenyl, follows apparently that of the basicities of the sulfoxides,<sup>9)</sup> suggesting that the reaction may be acid-catalyzed.

**Oxygen Exchange and Racemization Reactions of *p*-Substituted Diphenyl Sulfoxides.** In order to shed further light on the nature of the oxygen exchange reaction and also to examine the possible concurrent racemization, both optically active and <sup>18</sup>O-labeled *p*-tolyl phenyl sulfoxides were prepared and subjected to the oxygen exchange and racemization reactions in four different acids of varying acid strength, namely, acetic, monochloro-, dichloro- and trichloroacetic acids. Pseudo first order rate constants of oxygen exchange and racemization reactions along with the activation parameters of these reactions were obtained from the usual kinetic determinations. In addition, the rates of the oxygen exchange reactions, of *p*-chlorophenyl phenyl and diphenyl sulfoxides were determined in trichloroacetic

acid under the same condition, in order to compare the effects of polar substituents. The results were summarized in Tables 2 and 3. When the  $\log k(s)$  were plotted against the  $pK_a(S)$  of these acids, a straight line, though rough, can be drawn as shown in Fig. 1, clearly depicting that the oxygen exchange reaction is dependent on the Brönsted acidity, as was expected; namely smaller the  $pK_a$  of acid used, faster was the reaction rate. This observation is well accord with our earlier assumption that dimethyl sulfoxide, being most basic is extremely reactive while the least basic diphenyl sulfoxide is the least reactive as was shown in Table 1. The nearly identical rates of both racemization and oxygen exchange suggest that the reaction proceed through a rate-determining unimolecular S-O bond cleavage process. This is quite different from the similar oxygen exchange reaction with acetic anhydride in which the rate of racemization of *p*-tolyl phenyl sulfoxide was twice of that of the oxygen exchange, while the rate of racemization with acetic anhydride is estimated to be about 770 times faster than that with glacial acetic acid at 120°C. Therefore S<sub>N</sub>2 type mechanism, suggested for the similar oxygen exchange reactions with acetic anhydride can not be applied for the reactions in carboxylic acids. One notices in Table 3, however, that the entropies of activation for these reactions were of large negative values. This would imply that the protonated sulfoxide was considerably solvated by carboxylic acid in the transition state.

There are two different mechanisms that can fit in these observations; the one is the heterolysis of the S-O bond that involves the rate determining formation of the doubly charged "sulfonium ion" intermediate (I) and the other is the homolysis to form radical cation intermediate (II).

The first process, involving the double-positive charged intermediate (I) would be highly energy consuming and is expected to be strongly accelerated by an electron-releasing substituent while retarded remarkable by the substitution of an electron-withdrawing group, when the geometry of the activated complex is similar to that of the carbonium ion forming

TABLE 3. ACTIVATION PARAMETER FOR RACEMIZATION REACTION OF *p*-TOLYL PHENYL SULFOXIDE (120–140°C)

Acid	$E_a$ (kcal/mol)	$\Delta S^\ddagger$ (eu) 120°C
CH <sub>2</sub> ClCOOH	24.4	-23.4
CHCl <sub>2</sub> COOH	19.6	-32.8
CCl <sub>3</sub> COOH	18.6	-32.9

9) K. K. Anderson, W. H. Edmonds, J. B. Biasotti and R. A. Strecker, *J. Org. Chem.*, **31**, 2859 (1966).

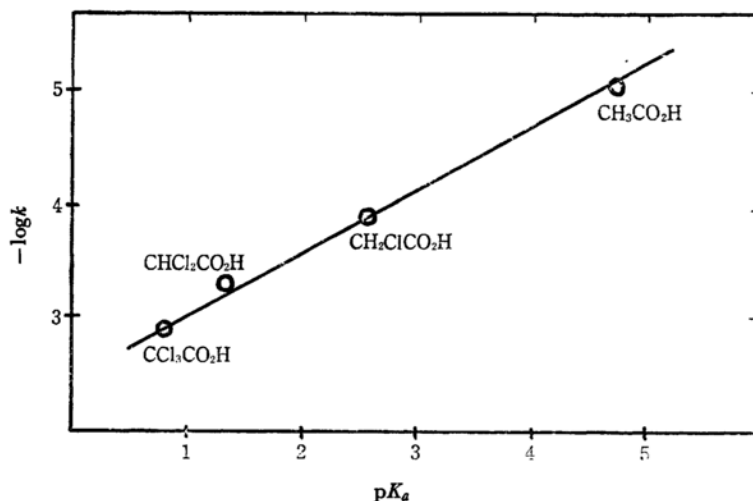
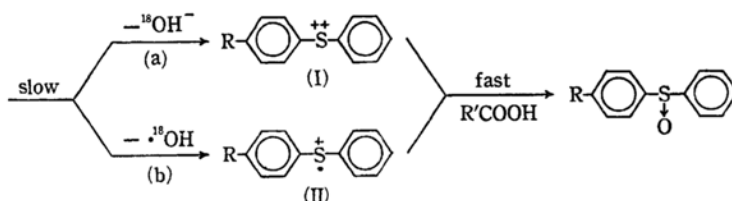
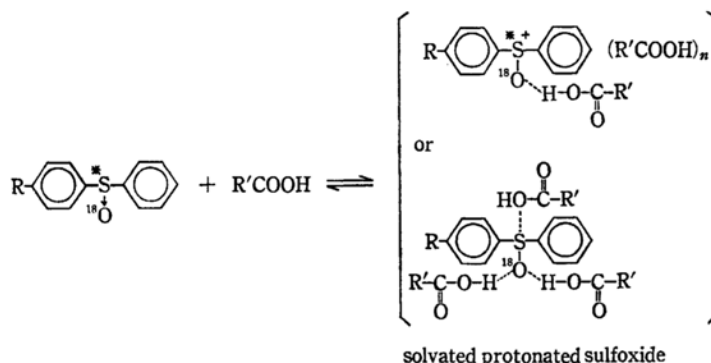


Fig. 1. The relation between the  $pK_a$ (s) of acids and the rates of racemization of optically active *p*-tolyl phenyl sulfoxide.



reaction ( $S_N1$ ). The effect of the substituents would be similar to those observed in the solvolytic reaction of substituted benzhydryl compounds and correlated with the  $\sigma^+$  values rather than the  $\sigma$  values. If, however, the hydroxy group of the sulfoxide would cleave without perturbing the original geometry of the molecular arrangement, the vacant *p*-orbitals of the leaving bond would overlap much less effectively with those  $\pi$ -molecular orbitals of the two aromatic ring due to the angular arrangement of the bonds around the sulfur atom and hence the effect of *p*-substituent would be rather small. Unfortunately very scant

kinetic data or well-defined  $S_N1$  (or  $A-1$ ) type reaction on sulfur atom are available for comparison, especially the one forming any intermediate that bears double positive charges. However, this process, being unassisted by resonance, would be very highly energy-consuming and unlikely. The second path would be less energy consuming and not be effected markedly by the polar nature of the substituent, since there is not net charge variation before and after the reaction. The small effect of the substituents in this reaction ( $\rho = -0.47$ ) and the rather facile nature of the reaction seem to suggest that the reaction follows

the homolytic cleavage process (b) of the protonated sulfoxide, as in other oxygen exchange and racemization reactions in mineral acids.

### Experimental

**Materials.** *Optically Active p-Tolyl Phenyl Sulfoxide.* This sulfoxide was prepared by the method of Anderson<sup>10</sup> in which (–)menthyl (–)*p*-toluenesulfinate was reacted with phenylmagnesium bromide in ether. (Mp 91–93°C,  $[\alpha]_D = +26.9$  in EtOH)

<sup>18</sup>O-Labeled *p-Tolyl Phenyl Sulfoxide.* The corresponding sulfide was oxidized with bromine in the presence of pyridine in acetic acid-H<sub>2</sub><sup>18</sup>O, according to our usual procedure.<sup>11</sup> (Mp 69.8–71°C <sup>18</sup>O-content 1.09 atom %)

*Dioxane*, obtained commercially, was purified according to the usual method, finally dried with sodium and distilled (bp 101.5°C).

*Acetic Acid*, obtained commercially was treated with chromic anhydride and after refluxing for several hours, it was distilled (bp 117.5–118°C).

*Monochloroacetic Acid, Dichloroacetic Acid and Trichloroacetic Acid.* These acids, obtained commercially, were distilled under reduced pressure in a dry atmosphere.

10) K. K. Anderson, *Tetrahedron Letters*, **No. 3**, 93 (1962).

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

Contact with a moisture was intercepted very carefully.

**Reaction of Dimethyl Sulfoxide with Acetic Acid.** The mixture consisting of 1 g of dimethyl sulfoxide and 5 g of glacial acetic acid was refluxed under nitrogen stream, which was bubbled into methanol solution of mercuric chloride. White crystalline material was precipitated slowly. After the reaction, white crystalline material was collected by filtration and identified from the melting point and infrared spectrum by comparing with that of the authentic sample of dimethyl sulfide-HgCl<sub>2</sub> complex.

**Kinetic Procedure.** Oxygen exchange and racemization reaction was carried out at 120±0.03°C in sealed tubes while the molar ratio of sulfoxide to an acid was kept at 1 : 50. Namely, the mixture of sulfoxide (1/200 mol), acid (1/4 mol) and 30 ml of dioxane was divided in several sealed tubes and reacted. From time to time a sealed tube was drawn out from the paraffin bath and the content was poured into an excess water then neutralized with sodium hydroxide solution. The sulfoxide, separated out was extracted with carbon tetrachloride and dried with anhydrous magnesium sulfate. Carbon tetrachloride was distilled off and the resulting sulfoxide was recovered. The recovered sulfoxide was dried thoroughly and subjected to the measurement of both specific rotation and <sup>18</sup>O-analysis. The specific rotation was measured in ethanol at *c*: 3.00. While <sup>18</sup>O-analysis of the sulfoxide-oxygen was done as usual according to the modified Rittenberg-Porticorbo method.