Hydrogen Chloride Catalyzed Oxygen-18 Exchange between Para-Substituted Phenyl Methyl Sulfoxides and Water[1]

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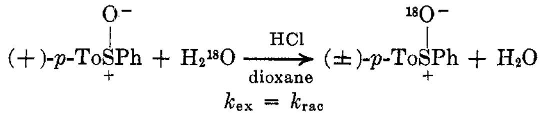
Para-substituted phenyl methyl sulfoxides-^{18}O undergo oxygen-18 exchange with water in aqueous dioxane solutions of most mineral acids (reduction of the sulfoxides to sulfides takes place with hydrobromic and hydroiodic acids), but hydrochloric acid is a more effective catalyst by at least a factor of ten than other mineral acids at the same concentration. A much slower base-catalyzed exchange has also been detected. For the hydrogen chloride catalyzed exchange, the relative rates for *p*-methoxy-, *p*-methyl-, unsubstituted, *p*-chloro-, and *p*-nitrophenyl methyl sulfoxides are 2.18, 1.61, 1.00, 0.52, and 0.21, respectively. A Hammett plot of log k/k_0 *vs.* σ is linear with $\rho = 1.046$. Coupled with the work of others, these results indicate that there are at least four mechanisms for oxygen-18 exchange between sulfoxides and water.

In the past few years Oae and coworkers have carried on an extensive and intensive investigation of the oxygen-18 exchange between sulfoxides and water,[2] other acidic[3] and basic reagents,[4] and other sulfoxides;[5] and many features of the varied mechanisms of these reactions have been worked out. In the initial[6] oxygen-18 study of sulfoxides, exchange with the oxygen atoms of sulfuric acid was demonstrated, but there was no incorporation of oxygen-18 into diphenyl sulfoxide when a solution of it in 97% sulfuric acid was diluted with water-^{18}O. Following other reports that sulfoxides did not undergo oxygen-18 exchange reactions in acidic[7,8] or basic[8] solution (under mild conditions), Mislow, Simmons, Melillo, and Ternay showed[9] that such an exchange does take place quite readily with *p*-tolyl phenyl sulfoxide in an aqueous dioxane solution of hydrogen chloride. Furthermore, the rate of oxygen-18 exchange was found to be equal to the rate of racemization of (+)-*p*-tolyl phenyl sulfoxide, indicating the presence of a symmetrical intermediate in the reaction. Since that time Oae and coworkers have shown that sulfoxides undergo acid-catalyzed oxygen exchange reactions with water in solutions of phosphoric acid,[10] various chloroacetic acids,[11] hydrobromic acid in aqueous acetic acid,[12] and sulfuric acid at various concentrations.[2,13,14] These exchange studies have frequently involved comparative measurements of the rates of racemization of optically active sulfoxides under the same conditions.[2,3,10,11,13,14] The effects of various para substituents on the rates of oxygen-18 exchange[2,3,10,11,13] or racemization[10,13] of para-substituted phenyl sulfoxides were also determined in several cases. Some of the findings of these research efforts are summarized in Table I.



$$(+)\text{-}p\text{-To}\overset{\text{O}^-}{\underset{+}{\text{S}}}\text{Ph} + \text{H}_2{}^{18}\text{O} \xrightarrow[\text{dioxane}]{\text{HCl}} (\pm)\text{-}p\text{-To}\overset{^{18}\text{O}^-}{\underset{+}{\text{S}}}\text{Ph} + \text{H}_2\text{O}$$

$$k_{\text{ex}} = k_{\text{rac}}$$

On the assumption that there is an intimate relationship between the exchange and racemization reactions, examination of the data in Table I reveals that there are at least two distinct mechanistic patterns for acid-catalyzed exchange of oxygen-18 between sulfoxides and water, one where $k_{\text{ex}}/k_{\text{rac}} \cong 1$, and another where $k_{\text{ex}}/k_{\text{rac}} \cong 0.5$. In addition, special, frequently closely related mechanisms are indicated for oxygen-18 exchange between sulfoxides and N_2O_4,[3b] carboxylic acids,[11] acetic anhydride,[3a] other sulfoxides,[5] potassium *tert*-butoxide,[4] and the oxygens of sulfuric acid.[6,14] The data in Table I reveal no clear pattern of substituent effects, the most noteworthy feature perhaps being the relative insensitivity of these reactions to substituents.

In investigating the substituent effect on the hydrogen chloride catalyzed oxygen-18 exchange between para-substituted phenyl methyl sulfoxides and water in dioxane solution, the special role of hydrochloric acid immediately became apparent, as shown in Table II. Except for hydrobromic and hydriodic acids, which reduced *p*-methoxyphenyl methyl sulfoxide to *p*-methoxyphenyl methyl sulfide, all mineral acids investigated catalyzed the oxygen-18 exchange, but hydrochloric acid was more effective[15] than any other acid by at least a factor of 10. Under conditions (50°, 24 hr) where 0.12 *N* HCl resulted in 40.5% exchange, there was no detectable exchange in 0.12 *N* $HClO_4$. At higher concentrations, however, perchloric acid shows a normal increasing fraction of exchange with increasing acid concentration. Clearly, at least two different exchange mechanisms are required by these results, one faster reaction specifically catalyzed by HCl, and another slower reaction catalyzed by other mineral acids. Since the $k_{\text{ex}}/k_{\text{rac}}$ data of Table I require at least two sulfuric acid catalyzed exchange mechanisms in the absence of chloride ion, at least three different mechanisms must be involved in acid-catalyzed exchange of oxygen-18 between sulfoxides and water.

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[1] Supported by Atomic Energy Commission Contract AT-(40-1)-3234; presented at the Southwest-Southeast Regional Meeting of the American Chemical Society, New Orleans, La., Dec 2–4, 1970; taken from the doctoral dissertation of I. O., St. Paul's University, Tokyo, Japan, 1971.

[2] For leading references see N. Kunieda and S. Oae, *Bull. Chem. Soc. Jap.*, **42**, 1324 (1969), and other papers of this research group cited below.

[3] (a) S. Oae and M. Kise, *ibid.*, **43**, 1416, 1421 (1970); (b) N. Kunieda, K. Sakai, and S. Oae, *ibid.*, **42**, 1090 (1969), and references cited therein.

[4] S. Oae, M. Kise, N. Furukawa, and Y. H. Khim, *Tetrahedron Lett.*, 1415 (1967).

[5] S. Oae, M. Yokoyama, M. Kse, and N. Furukawa, *ibid.*, 4131 (1968).

[6] S. Oae, T. Kitao, and Y. Kitaoka, *Chem. Ind. (London)*, 291 (1961).

[7] N. J. Leonard and C. R. Johnson, *J. Amer. Chem. Soc.*, **84**, 3701 (1962).

[8] D. Samuel and M. Weiss-Broday, in "Advances in Physical Organic Chemistry,' Vol. 3, V. Gold, Ed., Academic Press, New York, N. Y., 1965, p 180.

[9] K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *J. Amer. Chem. Soc.*, **86**, 1452 (1964); see also K. Mislow, *Rec. Chem. Progr.*, **28**, 217 (1967).

[10] N. Kunieda and S. Oae, *Bull. Chem. Soc. Jap.*, **41**, 1025 (1968).

[11] S. Oae, M. Yokoyama, and M. Kise, *ibid.*, **41**, 1221 (1968).

[12] W. Tagaki, K. Kikukawa, and N. Kunieda, and S. Oae, *ibid.*, **39**, 614 (1966).

[13] S. Oae and N. Kunieda, *ibid.*, **41**, 696 (1968).

[14] S. Oae, T. Kitao, Y. Kitaoka, and S. Kawamura, *ibid.*, **38**, 546 (1965).

[15] Whether there are actual differences in the catalytic effects of the other mineral acids was not investigated further.

TABLE I

COMPARISON OF SULFOXIDE OXYGEN-18 EXCHANGE AND RACEMIZATION RATES, AND THE EFFECTS OF SUBSTITUENTS ON THOSE RATES

Compounds used	Reaction medium	k_{ex}/k_{rac}	Substituents and relative rates	Ref
p-XC_6H_4SOPh	Concd HCl, dioxane	1^a		9
p-XC_6H_4SO-*p*-Tol	85% H_3PO_4	0.98^b	k_{ex}: H, 1.0; Cl, 0.6	10
		1.02^c	k_{rac}: H, 1.0; Cl, 0.6	
p-XC_6H_4SOPh	CCl_3COOH	1.01^a	k_{ex}: Me, 1.1; H, 1.0; Cl, 0.7	11
p-XC_6H_4SOPh	N_2O_4 in CCl_4	0.98^a	k_{ex}: MeO, 7.4; Me, 1.9; H, 1.0; Cl, 0.4	3b
p-XC_6H_4SO-*p*-Tol	96.7% H_2SO_4		k_{rac}: NH_2, 0.7; H, 1.0; Cl, 1.1	13
p-XC_6H_4SOPh	95.5% H_2SO_4	0.97^a	k_{ex}: Me, 3.0; H, 1.0; Cl, 1.4	13
p-XC_6H_4SOPh	91% H_2SO_4	0.75^a		2
	86.9% H_2SO_4	0.65^a		
	83.4% H_2SO_4	0.64^a		
	80.5% H_2SO_4	0.52^a		
	75.4% H_2SO_4	0.49^a	k_{ex}: MeO, 6.0; Me, 0.8; H, 1.0; Cl, 1.1; NO_2, 1.3	
p-XC_6H_4SOPh	Ac_2O	0.50^a	k_{ex}: Me, 1.1; H, 1.0; Cl, 0.8	3a
p-$XC_6H_4SOCH_2Ph$	Ac_2O	0.36^a	k_{ex}: MeO, 0.9; Me, 0.9; H, 1.0; Cl, 0.8; NO_2, 1.1	3a

[a] X = Me. [b] X = H. [c] X = Cl.

TABLE II

PRELIMINARY EXPERIMENTS ON THE CATALYTIC EFFECTS OF VARIOUS ACIDS ON THE OXYGEN-18 EXCHANGE BETWEEN *p*-METHOXYPHENYL METHYL SULFOXIDE-^{18}O AND WATER IN DIOXANE SOLUTION[a]

Catalyst	Catalyst concn, *N*	Temp, °C	% exchange after 24 hr
$HClO_4$	0.12	75	6.0
HNO_3	0.12	75	3.0
H_2SO_4	0.12	75	3.0
H_3PO_4	0.12	75	1.5
HF	0.12	75	9.9
HCl	0.12	75	95.5
HBr	0.12	75	Reduction[b]
HI	0.12	75	Reduction[b]
HCl	0.12	50	40.5
$HClO_4$	0.12	50	0.0
HCl	0.36	50	88.8
$HClO_4$	0.35	50	4.5
$HClO_4$	0.59	50	10.5
$HClO_4$	0.82	50	20.3
$HClO_4$	1.18	50	45.8

[a] 88% dioxane, 12% aqueous acid, by volume, [RSOR′] = 0.195 *M*. [b] The sulfoxide was reduced to *p*-methoxyphenyl methyl sulfide.

More quantitative data on the effects of various concentrations of hydrochloric acid and various other reagents on the rate of exchange are given in Table III.

TABLE III

RATE CONSTANTS FOR THE OXYGEN-18 EXCHANGE BETWEEN *p*-METHOXYPHENYL METHYL SULFOXIDE-^{18}O AND WATER IN DIOXANE SOLUTION[a] AS A FUNCTION OF CONCENTRATION OF HCl AND OTHER REAGENTS

Catalyst and concn	Temp, °C	$k_{ex} \times 10^4$, sec^{-1}
0.12 *N* HCl	75	2.42
0.24 *N* HCl	75	7.13
0.36 *N* HCl	75	21.8
0.48 *N* HCl	75	38.6
0.12 *N* HCl + 0.12 *N* NH_4ClO_4	50	0.046
0.12 *N* HCl + 0.12 *N* NH_4Cl	50	0.059
0.12 *N* HCl + 0.12 *N* $HClO_4$	50	0.184
0.05 *N* NaOH	125	0.006

[a] 88% dioxane, 12% aqueous solution, by volume, [RSOR′] = 0.195 *M*.

There is a clear, greater than first-order dependence of the exchange rate on hydrochloric acid concentration. Addition of 0.12 *N* ammonium chloride to 0.12 *N* hydrochloric acid gives more effective catalysis than addition of 0.12 *N* ammonium perchlorate, demonstrating again the specific catalytic effect of chloride ion. However, substitution of 0.12 *N* perchloric acid for the 0.12 *N* ammonium chloride results in much faster reaction, a fact which is probably best interpreted in terms of a mechanism involving higher order catalytic dependence on hydrogen ion than on chloride ion (see below). In the absence of activity coefficient or acidity function data for these aqueous dioxane solutions, and since the experimental limitations of the exchange procedure precluded the use of either very dilute solutions or large excesses of catalyst relative to sulfoxide, no attempt was made to put the hydrogen ion and chloride ion catalytic effects on a more quantitative basis. However, in closely related work, Landini, Montanari, Modena, and Scorrano reported[16] that the racemization of (+)-*p*-tolyl methyl sulfoxide in aqueous perchloric acid was near first order with respect to added chloride or bromide ion over a wide range of acidities, and that the slopes of the linear log k_{rac} *vs.* H_0 plots at constant halide ion concentration had slopes of near unity at high acidities and near two at low acidities, Allenmark and Hagberg reported[17] a similar first-order dependence of the rate of racemization of the same compound on halide ion concentration in aqueous acetic acid. Kunieda and Oae also reported that plots of $-H_0$ *vs.* log k_{rac}[2,13] or log k_{ex}[2] for (+)-*p*-tolyl phenyl sulfoxide-^{18}O in aqueous sulfuric acid were linear with slopes near unity at high acidities, but no halide ion catalysis was involved in those cases.

Our data on the catalytic effects of hydrogen ion and chloride ion on the rate of oxygen-18 exchange between *p*-methoxyphenyl methyl sulfoxide-^{18}O and water, coupled with the related work of Landini and coworkers and

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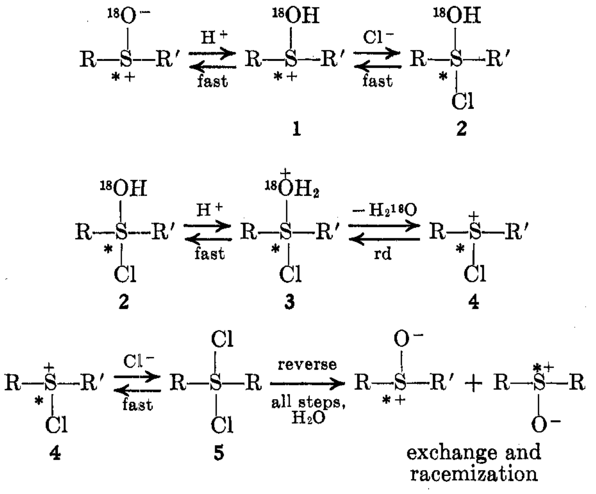
(16) D. Landini, F. Montanari, G. Modena, and G. Scorrano, *Chem. Commun.*, 86 (1968); in a very recent report [*J. Amer. Chem. Soc.*, **92**, 7168 (1970)] these authors have given more details of this research, utilizing other acidity function data, but the basic conclusions regarding orders of reaction remain unchanged.

(17) S. Allenmark and C. Hagberg, *Acta Chem. Scand.*, **22**, 1461, 1694 (1968).

Allenmark and Hagberg on the racemization of sulfoxides, seems to be best interpreted in terms of the mechansim of Scheme I (* indicates asymmetric

SCHEME I



sulfur). Sulfoxides react with concentrated sulfuric acid to yield their conjugate acids,[18] **1**, rather than dications, R–$^{+}$S^{+}–R′, as shown by oxygen-18 exchange experiments[6,18,19] and by freezing point depression measurements.[6,19–21] Suggestion that the conversion of **3** to **4** is rate determining is consistent with higher order H$^+$ than Cl$^-$ dependence of the exchange rate as observed in this research and as noted by Landini and coworkers[16] for the racemization reaction. These workers point out that at very high acidities where the sulfoxide is essentially all converted to its conjugate acid, a plot of log k_{rac} *vs.* $-H_0$ would be expected to have a slope of about unity as observed.[16] Since **5** is a symmetrical intermediate which inevitably leads to *exchange and racemization*, k_{ex} should equal k_{rac} as observed.[9] Finally, the reversible formation of dibromo and dichloro compounds from the corresponding sulfoxides by treatment with hydrobromic and hydrochloric acids is well known.[22]

Additional significant support for this mechanism is provided by the data on the effects of substituents on the oxygen-18 exchange rate as presented in Table IV. Clearly, electron-donating substituents accelerate the exchange reaction, while electron-withdrawing substituents slow it down. A Hammett plot of log k/k_0 *vs.* σ is linear with $\rho = -1.046$. A negative ρ would certainly be expected for the first step of the above mechanism, and the basicity measurements of Landini, Modena, Scorrano, and Taddei[23] on a series of para-substituted phenyl methyl sulfoxides ($\rho = -0.85$) are in accord with this view. Similarly, for para-substituted diphenyl sulfoxides[24] and para-substituted acetophenones,[25] plots of σ^+ *vs.* pK_{BH^+} are linear with ρ values of -2.00 and -2.17. For the equilibrium constants for the conversion of **1** to **2**, on the other hand, a positive ρ would be expected; perhaps a very small negative ρ would be expected for the conversion of **2** to **3**; and a relatively large negative ρ would be expected for the rate-determining conversion of **3** to **4**. The net result of this combination of substituent effects should almost certainly be a negative ρ, as observed.

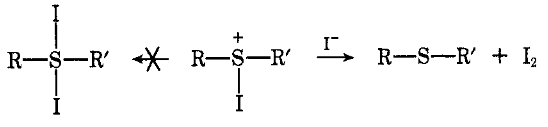
TABLE IV

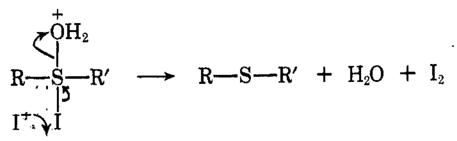
RATE CONSTANTS FOR THE HYDROCHLORIC ACID CATALYZED OXYGEN-18 EXCHANGE OF PARA-SUBSTITUTED PHENYL METHYL SULFOXIDES-^{18}O AND WATER IN AQUEOUS DIOXANE[a] AT 75°

Para substituent	Registry no.	$k_{\text{ex}} \times 10^4$, sec^{-1}	Relative k_{ex}
CH_3O	3517-99-5	2.87	2.18
CH_3	934-72-5	2.12	1.61
H	1193-82-4	1.32	1.00
Cl	934-73-6	0.685	0.52
NO_2	940-12-5	0.275	0.21

[a] 88% dioxane, 12% aqueous acid, by volume; [RSOR′] = 0.19 *M;* [HCl] = 0.14 *M.*

The validity of these arguments is further supported by consideration of substituent effects and likely mechanisms for related reactions, selected data for which are summarized in Table V. It is seen that the substituent effect data for the reduction of sulfoxides to sulfides by hydriodic acid[26,27] follow almost exactly the same pattern as that observed in this research. An attractive possibility for the mechanism of the reduction reaction (which was also observed with HBr and HI in aqueous dioxane in the present research) is the rate-determining formation of R–$^{+}$SI–R′ (corresponding to **4**) by a sequence of steps corresponding exactly to that given in the above mechanism for exchange and racemization. Under conditions favoring reduction, iodide ion would then attack iodine to form the sulfide and iodine rather than attacking sulfur to give the diiodide. Alternatively, a reduction mechanism[26] involving rate-determining attack of iodide ion on iodine in a species corresponding to **3** would probably have much the same substituent effect behavior, providing O–S bond rupture proceeds "ahead" of the electron transfer from iodine to sulfur. Such a mechanism would require second-order dependence on iodide ion for the reduction





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[18] G. A. Olah, A. T. Ku, and J. A. Olah, *J. Org. Chem.*, **35**, 3904 (1970), have reported that sulfoxides protonate on sulfur rather than on oxygen in HSO_3F–SbF_5 solutions in SO_2ClF. It is difficult to see how the oxygen-18 exchange, racemization, or reduction reactions of sulfoxides in more conventional acid solutions could proceed through such sulfur protonated species.

[19] S. Oae, T. Kitao, and Y. Kitaoka, *Bull. Chem. Soc. Jap.*, **38**, 543 (1964).

[20] H. J. Shine and D. R. Thompson, *Tetrahedron Lett.*, 1591 (1966).

[21] R. J. Gillespie and J. A. Leisten, *Quart. Rev. (London)*, **8**, 40 (1954); R. J. Gillespie and R. C. Passerini, *J. Chem. Soc.*, 3850 (1956).

[22] T. Zincke and W. Frohneberg, *Chem. Ber.*, **43**, 837 (1909); K. Fries and W. Vogt, *Justus Liebigs Ann. Chem.*, **381**, 337 (1911); E. Fromm, *ibid.*, **396**, 75 (1913); K. Issleib and M. Tzschach, *Z. Anorg. Allg. Chem.*, **305**, 198 (1960).

[23] D. Landini, G. Modena, G. Scorrano, and F. Taddei, *J. Amer. Chem. Soc.*, **91**, 6703 (1969).

[24] S. Oae, K. Sakai, and N. Kunieda, *Bull. Chem. Soc. Jap.*, **42**, 1964 (1969).

[25] R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, **80**, 6355 (1958).

[26] D. Landini, F. Montanari, H. Hogeveen, and G. Maccagnani, *Tetrahedron Lett.*, 2691 (1964).

[27] R. A. Strecker and K. K. Andersen, *J. Org. Chem.*, **33**, 2234 (1968).

TABLE V

COMPARISON OF SUBSTITUENT EFFECTS ON VARIOUS REACTIONS OF SULFOXIDES

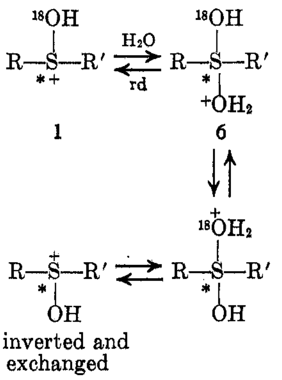
X	p-XC_6H_4SOMe, rel k_{ex} in HCl–dioxane[a]	p-XC_6H_4SOMe, rel $k_{reduction}$ in HOAc–H_2O–HI[b]	p-XC_6H_4SOMe, rel $k_{reduction}$ in $HClO_4$–H_2O–HI[c]	p-XC_6H_4SOPh, rel k_{ex} in 75.4% H_2SO_4[d]	p-XC_6H_4-$SOCH_2Ph$, rel k_{ex} in Ac_2O[e]
CH_3O	2.2	1.5	1.2	6.0	0.9
CH_3	1.6	1.4	1.4	0.8	0.9
H	1.0	1.0	1.0	1.0	1.0
Cl	0.5	0.5	0.5	1.1	0.8
NO_2	0.2	0.2	0.2	1.3	1.1

[a] This research. [b] Reference 26. [c] Reference 27. [d] Reference 2. [e] Reference 3a.

reaction, in contrast to the known[16] first-order iodide ion dependence in a somewhat different reaction medium, but this mechanism could account for the fact that rates of racemization are lower than rates of reduction by a factor of about 30 in some cases.[28]

For racemization and exchange reactions of sulfoxides in 75.4% sulfuric acid in acetic anhydride, $k_{ex}/k_{rac} \cong 0.5$, in contrast to the value of about one for the hydrochloric acid catalyzed reaction (see Table I). The substituent effect pattern is also very different, as can be seen by comparing the smooth trend in the first column of Table V with the erratic results in the last two columns. These two lines of evidence complement each other and are probably best rationalized by a mechanism in which **1** (or the –OAc analog in Ac_2O) can react with water (or AcO^- in Ac_2O) in a rate-determining step to give rapidly equilibrating sulfoxide hydrate conjugate acids (or a symmetrical sulfoxide–Ac_2O addition compound in Ac_2O) (Scheme II). In such a mechanism, every exchange would result in *inversion* at sulfur, so the *racemization* rate would be twice the exchange rate, as observed.[2,3a] Since substituents should have opposite effects on the formation of **1** and its reaction with a nucleophile (Cl^-, H_2O, AcO^-, see above), it is not surprising that erratic substituent effect results should be observed.[2,3a] The results obtained in this research and those of others in dilute acids in the absence of chloride ion seem to be best explained by a mechanism of this type. In the presence of chloride ion, a much better nucleophile than water toward sulfur, **1** reacts to form primarily **2** rather than **6**.

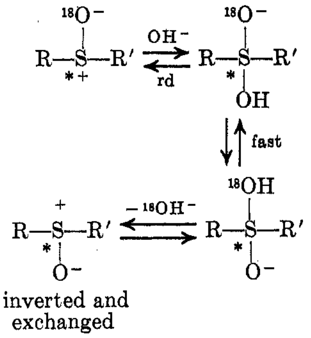
SCHEME II



In more concentrated sulfuric acid,[13] and apparently also in phosphoric acid,[10] trichloroacetic acid,[11] and N_2O_4,[3b] yet another racemization and exchange mechanism is involved, in which **1** is further protonated on oxygen to give, by loss of water or the radical cation $H_2O\cdot^+$ in a rate-determining step, a transitory dication, $R{-}^{+}S^{+}{-}R'$, or radical cation, $R{-}\dot{S}^{+}{-}R'$. Oae and coworkers have discussed the evidence for this mechanism quite extensively.[2,3b,10,11,13,14] A negative ρ behavior would certainly be expected for reactions taking place by this mechanism, and most of the scattered data available are in accord with this view,[3b,10,11,13] although the variation with substituent is surprisingly small, even for radical cation formation. Some esr data appear to favor the radical cation rather than the dication mechanism.[2,13,20]

In addition to the three distinct acid-catalyzed mechanisms for oxygen-18 exchange between sulfoxides and water discussed above, the last entry in Table III makes it clear that a base-catalyzed mechanism is also operative. The simplest mechanism for such a reaction would involve addition of hydroxide ion to the sulfoxide sulfur (numerous other mechanisms, *e.g.*, one involving rate-determining proton abstraction from the sulfoxide methyl group, might be considered, but the one bit of data available does not justify extensive speculation); see Scheme III. Although no substituent effect or comparative k_{ex} *vs.* k_{rac} studies have as yet been carried out under basic conditions, reaction by the above mechanism would be predicted to give $k_{ex}/k_{rac} = 0.5$ and a positive ρ. In a similar manner, a neutral path for the exchange might also be envisioned, but reaction by it should certainly be very slow, and there is currently no experimental evidence to support such speculation.

SCHEME III



It is perhaps noteworthy to mention that the nmr chemical shifts of the methyl protons of the para-substituted phenyl methyl sulfoxides show the expected correlation with substituent, the $\delta_{TMS}^{CHCl_3}$ values being 2.55, 2.55, 2.66, 2.69, and 2.75 for the substituents CH_3O, CH_3, H, Cl, and NO_2, respectively.

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[28] D. Landini, F. Montanari, G. Modena, and G. Scorrano, *Chem. Commun.*, 3 (1969).

Experimental Section

Preparation of Oxygen-18 Enriched Para-Substituted Phenyl Methyl Sulfoxides.—Unenriched *p*-methoxy-, *p*-methyl-, unsubstituted, *p*-chloro-, and *p*-nitrophenyl methyl sulfoxides were prepared by treatment of the corresponding thiophenols with dimethyl sulfate in alkaline solution,[29] followed by oxidation of the sulfides to the sulfoxides using hydrogen peroxide in acetic acid. The sulfoxides were distilled under reduced pressure or recrystallized until their physical constants agreed with those given in the literature. All samples were determined to be at least 99.5% pure by glc and nmr analyses.

The above sulfoxides were prepared in oxygen-18 enriched form by hydrogen chloride catalyzed exchange with water-^{18}O in dioxane solution. A 5-g sample of the unenriched sulfoxide was dissolved in 150 ml of dioxane, and 20 ml of 1.2 *N* hydrochloric acid containing 1.54% oxygen-18 in the water was added. The solution was heated in a 75 ± 0.2° oil bath for 4 hr for the *p*-methoxy and *p*-methyl compounds, and for 20 hr for the *p*-nitro, *p*-chloro, and unsubstituted compounds. The reaction mixture was poured into 100 ml of cold chloroform. The water layer was separated and the chloroform layer was washed with 20 ml of water, with 5% sodium hydroxide, and then with water again. The chloroform solution was dried over sodium sulfate the solvent was removed, and the residue was distilled under reduced pressure or recrystallized from methanol. The purities of the recovered sulfoxides were over 99% as shown by glc analyses or nmr spectroscopy. The oxygen-18 contents were determined to be 1.38, 1.43, 1.54, 1.25, and 1.11 excess atom per cent for the *p*-methoxy-, *p*-methyl-, unsubstituted, *p*-chloro-, and *p*-nitrophenyl compounds, respectively. For the *p*-methoxy compound the excess atom per cent value given is corrected (experimental excess times 2) for dilution by the methoxy oxygen. For the *p*-nitro compound, it seemed possible that the nitro group oxygens might undergo exchange. Fry and Lusser[30] found no oxygen-18 exchange for a group of aromatic nitro compounds under a variety of conditions, but no sulfoxide-substituted nitro compounds were included in their study. Accordingly, the overall oxygen-18 enrichment of the recovered *p*-nitrophenyl methyl sulfoxide was determined, the sulfoxide was reduced to the nitro-substituted sulfide by the procedure of Landini, Montanari, Hogeveen, and Maccagnani,[26] and the oxygen-18 enrichment (now of the nitro group only) was determined again. A small amount of oxygen-18 enrichment (about 5% of the sulfoxide oxygen enrichment in the longest time experiments) was found in the nitro group, and appropriate dilution (experimental excess times 3) and nitro group oxygen enrichment corrections were made.

Oxygen-18 Analyses.—Oxygen-18 analyses were carried out by the method of Rittenberg and Ponticorvo[31] as modified by Anbar and Guttmann[32] and in this laboratory. Samples of about 20 mg of the compounds to be analyzed were pyrolyzed with about 100 mg of a mixture of mercuric cyanide and mercuric chloride in sealed tubes at 500° for 7 hr. The tubes were opened in a vacuum system, and the carbon dioxide was distilled twice, utilizing 5,6-benzoquinoline to remove the hydrogen chloride and other acidic gases formed in the pyrolysis. The purified carbon dioxide was analyzed for oxygen-18 in a mass spectrometer by recording the intensities of the *m/e* 44 and 46 peaks. The oxygen-18 content of the carbon dioxide is given by the formula

$$\text{atom \% oxygen-18} = \frac{R}{2 + R} \times 100$$

where *R* is the 46/44 *m/e* ratio. To correct for day-to-day instrumental variations in the operation of the mass spectrometer, a standard sample of tank carbon dioxide (taken to be 0.204 atom % oxygen-18, the normal abundance ratio) was analyzed prior to each set of analyses, and all samples were normalized to the 0.204 value. These correction factors were seldom very large, being in the range of 1.022–1.041. For each case, the normal abundance atom per cent, 0.204, was substracted from the measured atom per cent value to give the excess atom per cent.

Preliminary Experiments.—In preliminary experiments solutions of about 0.6 mmol of *p*-methoxyphenyl methyl sulfoxide-^{18}O in 3 ml of dioxane were brought to temperature in a constant-temperature bath, and 0.4 ml portions of various aqueous acid solutions were added. After 24 hr in the constant-temperature bath, the mixtures were poured into cold chloroform. The water layers which separated were removed by pipette, and the chloroform solutions were washed with alkali and water. The chloroform solutions were dried over sodium sulfate and the solvent was removed. The residues were kept in a vacuum desiccator. The purities of the recovered sulfoxides were determined by gas chromatography and nmr spectroscopy, and in all cases were over 99%. The results of the oxygen-18 analyses in these preliminary experiments are listed in Table II.

Kinetic Experiments.—The procedure for the kinetic experiments was substantially the same as that used for the preliminary experiments, except that the amounts of the various substrates, solvents, and reagents were increased by a factor of ten, and aliquots were removed from the reaction solution when it had reached bath temperature (zero time sample) and at various appropriate times after that. These aliquots were worked up and analyzed as described above. Representative per cent excess oxygen-18 analytical data as a function of time for the determination of the rate of hydrochloric acid catalyzed exchange between water and *p*-nitrophenyl methyl sulfoxide-^{18}O are as follows: 0.948%, 0 time; 0.873%, 0.5 hr; 0.868%, 1 hr; 0.810%, 2 hr; 0.612%, 5 hr; 0.372%, 10 hr. Individual points were generally reproducible to ±0.005 in excess atom per cent.

Treatment of Kinetic Data.—The first order rate expression for a simple exchange reaction is given[33] by

$$-\ln\,(1 - F) = k_{\text{ex}}t$$

where k_{ex} is the observed first-order rate constant for exchange. *F* is defined as the fraction of exchange and is calculated from the equation

$$F = \frac{(^{18}\text{O}_0) - (^{18}\text{O}_t)}{(^{18}\text{O}_0) - (^{18}\text{O}_\infty)}$$

where $(^{18}\text{O}_0)$ = atom fraction in sulfoxide at time zero, $(^{18}\text{O}_t)$ = atom fraction in sulfoxide at time *t*, and $(^{18}\text{O}_\infty)$ = atom fraction in sulfoxide at infinite time.

The values for the oxygen-18 contents at infinite time were calculated as the percentages of total oxygen-18 to total exchangeable oxygen in the system (not including the dioxane, methoxy, or nitro oxygens). For all cases, the calculated values were used as the infinite time values. Since the nitro group oxygen-18 exchange was so much slower than that of the sulfoxide oxygen, for the purposes of these short time calculations it was assumed that the excess oxygen-18 in the nitro group did not decrease during the reaction.

Plots of $(1 - F)$ *vs.* time were linear up to 60–70% reaction in all cases, with relatively little scatter of the points. The rate constants for the various reactions were calculated from the slopes of the lines in these plots, using the method of least squares. These rate constants are summarized in Tables III and IV.

Registry No.—Hydrogen chloride, 7647-01-0; oxygen-18, 14797-71-8; water, 7732-18-5.

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