Oxidation of Sulfoxides by Hydrogen Peroxide, Catalyzed by Methyltrioxorhenium(VII)

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Dialkyl and diaryl sulfoxides are oxidized to sulfones by hydrogen peroxide using methyltrioxorhenium as the catalyst. The reaction rate is negligible without a catalyst. The kinetics study was performed in CH_3CN-H_2O (4:1 v/v) at 298 K with $[H^+]$ at 0.1 M, conditions which make the equilibration between MTO and its peroxo complexes more rapid than the oxygen-transfer step. The values for the rate constant for the oxygen-transfer step lie in the range 0.1−3 L mol^{-1} s^{-1}. The rate constants were significantly smaller than for the oxidation of sulfides to sulfoxides. A study of ring-substituted diaryl sulfoxides yielded kinetics results that are consistent with nucleophilic attack of the sulfur atom on the peroxide oxygen group since $\rho = -0.65$. The results cited refer to the reactions of the diperoxo from the catalyst, $MeRe(O)(\eta^2\text{-}O_2)_2H_2O$. The monoperoxo complex showed no measurable reactivity toward sulfoxides, in contrast with the situation for nearly every other substrate. That unusual finding suggests a hydrogen-bonded interaction between the substrate and the diperoxorhenium compound which cannot exist with the monoperoxo compound.

Introduction

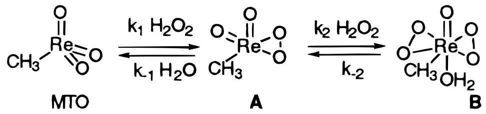
Methyltrioxorhenium (CH_3ReO_3, abbreviated as MTO) is an effective catalyst for reactions in which a substrate, X, usually an electron-rich species, is oxidized to XO by hydrogen peroxide:

$$X + H_2O_2 \rightarrow XO + H_2O \tag{1}$$

In these reactions an oxygen atom is transferred from peroxide to the substrate. The important place of O-atom transfer in industry and biology has been documented,[1] and a common mechanism suggested for inorganic and organic peroxides.[2] The particular place of MTO in this arena has been reviewed.[3−6] In brief, two peroxorhenium compounds play catalytic roles, *usually about equally*; they have been designated **A** and **B**, as shown in Scheme 1. The species **A** and **B** attain their equilibrium concentrations rapidly but not instantaneously; during the operation of the catalytic cycle, the improved steady-state method[7] approximates their concentrations to good accuracy.

In studying the oxidation of alkyl and aryl sulfides ($X = R_2S$, ArSR, Ar_2S) to sulfoxides, it was noted that further oxidation to sulfones ensued over longer times.[8] We were motivated to examine this second oxidation step, not only by its fundamental interest and utility in organic synthesis,[9] but also by certain recent findings with diaryl sulfines, $X = Ar_2CSO$. These compounds show a remarkable U-shaped Hammett plot when aromatic substituents are changed; thioketones, Ar_2CS, presented a regular progression of rates.[10] Since this phenomenon could in part be attributed to the presence of an electronegative oxygen atom on the sulfines, we undertook a study of the kinetics of oxidation of diaryl sulfoxides. The sulfoxides are related to diaryl sulfides as sulfines are to thioketones, whose reactions feature a steady (ordinary) increase in rate as substituents on the aromatic ring are made more electron-donating.[8] A series of substrates, Ar_2SO, was therefore examined as a part of this study.

Scheme 1



Experimental Section

Materials. Reagent-grade acetonitrile was used; laboratory-distilled water was purified by a Milli-Q water system. To maintain homogeneity and afford reasonable solubility for these reagents, particularly the less soluble diaryl sulfoxides, 4:1 acetonitrile−water was used as the solvent. MTO was purchased or prepared from sodium perrhenate.[11] Most sulfoxides were obtained commercially.

Bis(4-dinitrophenyl) sulfoxide was prepared from the sulfide by MTO-catalyzed oxidation. The sulfide (2.5 mmol in 25 mL of acetonitrile) was treated with 1.0 equiv of hydrogen peroxide and 4% MTO. The product was isolated after a 24 h of reaction time by filtration after overnight cooling at ∼10 °C. Anal. ($C_{12}H_8SN_2O_5$) found (calcd): C, 49.09 (49.31); H, 2.61 (2.76); N, 9.48 (9.58).

Kinetics. The progress of most reactions was monitored spectrophotometrically, with NMR used occasionally. The reactions were carried out at 25.0 °C in quartz cuvettes or NMR tubes. The solutions

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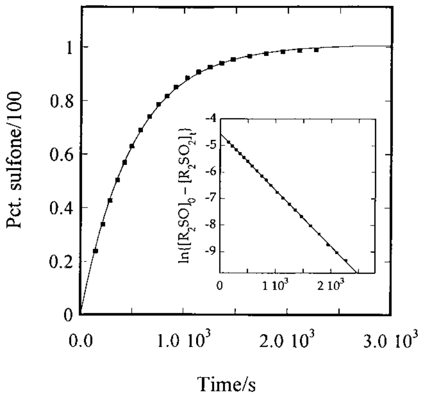

Figure 1. Buildup of bis(dimethyl)sulfone as determined from the integrated intensity of its ^{1}H resonance. The inset shows the fit to first-order kinetics through the linearity of the plot of $\ln\{[Me_2SO]_0 - [Me_2SO_2]_t\}$ with time, which gave $k = 2.07 \times 10^{-3}$ s^{-1}. Initial concentrations were 1.3 mM MTO, 9.9 mM DMSO, and 1.0 M H_2O_2 in 4:1 acetonitrile−water containing 0.1 M HOTf.

contained 0.10 M trifluoromethanesulfonic acid to stabilize MTO−peroxide against deactivation.[12]

Owing to the high molar absorptivities, short-path (0.02−0.1 cm) UV cuvettes were used. Typical reaction conditions were 1 mM sulfoxide, 100 mM hydrogen peroxide, and 0.5 mM MTO. These conditions offer accurate absorbance changes. The recorded absorbance amplitudes agreed with those calculated from the molar absorptivities for the conversion of sulfoxide to sulfone. The NMR method was mandatory for Me_2SO, given the lack of suitable absorptions. The $CH_3-S(O)R$ resonance was monitored with time. Both UV and NMR methods were used for **3** as a double-check. Typical NMR concentrations were 10 mM sulfoxide, 1 M hydrogen peroxide, and 1.0 mM MTO.

Results

Values for equilibrium and rate constants for Scheme 1 pertinent to the interpretation of the data have been determined: $K_1 = k_1/k_{-1} = 347$ L mol^{-1}, $K_2 = 91$ L mol^{-1}, $k_1 = 15.5$ L mol^{-1} s^{-1}, and $k_2 = 0.17$ L mol^{-1} s^{-1}.[10] Most kinetics experiments were carried out with a hydrogen peroxide concentration sufficiently high that essentially all of the rhenium was present as the diperoxo compound **B**. Under such conditions, the contribution of **A** to the kinetics can be entirely ignored. The data consist of absorbance−time (UV) or intensity−time (NMR) values, such as those displayed in Figure 1. Each experiment was fit very well by a first-order rate equation, establishing a first-order dependence on the sulfoxide concentration. As shown in Figure 2 for PhS(O)Me and $(4\text{-}NO_2C_6H_4)_2SO$, the plot of k_{obs} against $[Re]_T$ is linear. This pattern affirms the rate law

$$d[R_2SO_2]\ dt = k_4[R_2SO][Re]_T$$

The rate constant proved independent of the hydrogen peroxide concentration in the range 0.1−1.0 mol/L. These concentration dependences show that the slopes of the lines in Figure 2 afford the values of k_4, the rate constant for the reaction between **B** and R_2SO. The values of k_4 for the various sulfoxides studied are presented in Table 1. For entry 3, data from NMR and spectrophotometry were used to confirm agreement between the two techniques. Thus, the value of k_4 for Me_2SO (which seemed low, given the trends in Table 1) can be trusted. Further, it was redetermined multiple times.

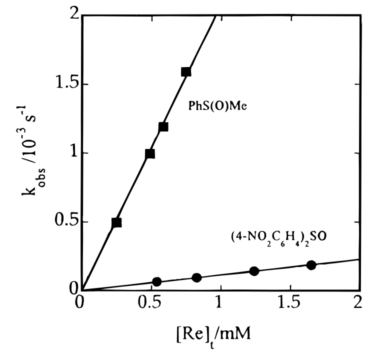

Figure 2. Pseudo-first-order rate constants (k_{obs}) for bis(4-nitrophenyl) sulfoxide (circles) and PhS(O)Me (squares) versus the total initial MTO concentration. The slopes, which represent k_4, are 2.08 and 0.113 L mol^{-1} s^{-1}, respectively.

Kinetics experiments were also carried out at much lower concentrations of hydrogen peroxide. These are the conditions under which k_3 for the reaction between **A** and sulfoxides could be determined. With no immediate success in determining k_3 under the selected conditions, the kinetics simulation program KinSim[13−15] was used to select the optimum conditions, especially the peroxide concentration, that would best elicit the reactivity of **A**. Regardless of any reasonable assumption as to the relative values of k_3 and k_4, no contribution from the k_3 term could be detected experimentally. To ensure that the procedure was sound, experiments were carried out on thioanisole, for which the k_3 step provides the major pathway, as once again confirmed. Then, to be certain that the sulfoxide does not interact with catalytic intermediate **A**, measurements were carried out on a mixture of diphenyl sulfoxide and thioanisole. The results obtained were as if thioanisole alone had been used; the sulfoxide did not alter the rate, and in the time allotted it was itself not oxidized. We thus conclude $k_4/k_3 \geq 250$ for diphenyl sulfoxide: the k_3 path does not enter.

Sulfoxides are much less reactive toward **A** than **B**, and they do not coordinate to MTO (or **A**) to any detectable extent. Thus, they do not affect the oxidation of sulfides by $MTO-H_2O_2$. These points are not out of the ordinary, in that sulfoxides are not strong Lewis bases and sulfides are oxidized more rapidly than sulfoxides. The relative reactivities of **A** and **B** are striking; only for allylic alcohols has such an effect been noted, $k_3 \ll k_4$,[16] which was reasonably ascribed to special hydrogen bonding.

Discussion

Large kinetic differences are found between sulfides and sulfoxides, favoring the sulfides by 10^3, which has been noted for these species before.[17−20] The inductive effect of the oxo group on the sulfoxide must greatly lower the nucleophilicity of the sulfur atom. It is important to contrast kinetics against thermodynamics. For that purpose we use values for thermodynamic functions of the sulfur compounds given.[21] For these

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Table 1. Rate Constants for the Oxidation of Sulfoxides with Hydrogen Peroxide Catalyzed by Methyltrioxorhenium

entry	substrate	k_4/L mol^{-1} s^{-1}	entry	substrate	k_4/L mol^{-1} s^{-1}
1	Me_2SO	1.5 ± 0.1[a]	6	$(4\text{-}MeOC_6H_4)_2SO$	3.10 ± 0.02
2	PhS(O)Me	2.08 ± 0.03	7	$(4\text{-}MeC_6H_4)_2SO$	1.72 ± 0.01
3	$4\text{-}MeC_6H_4S(O)Me$	2.83 ± 0.07 2.9 ± 0.1[a]	8	Ph_2SO	0.91 ± 0.02
			9	$(4\text{-}FC_6H_4)_2SO$	0.68 ± 0.02
4	$PhCH_2S(O)Me$	2.87 ± 0.05	10	$(4\text{-}ClC_6H_4)_2SO$	0.54 ± 0.02
5	$(PhCH_2)_2SO$	2.02 ± 0.02	11	$(4\text{-}NO_2C_6H_4)_2SO$	0.113 ± 0.001

[a] Determined from NMR; others determined from UV−vis measurements.

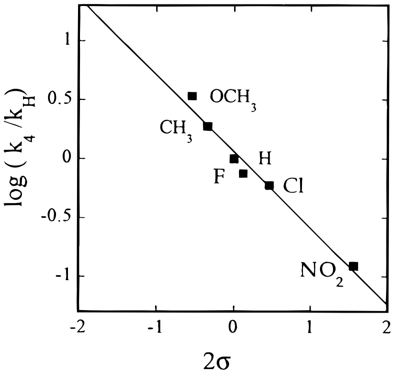

Figure 3. A Hammett plot for the oxidation of substituted diaryl sulfoxides by hydrogen peroxide with MTO as a catalyst. The slope of the line gives $\rho = -0.65$.

two reactions the values of the molar Gibbs energies at 298 K are as shown:

$$Me_2S + H_2O_2 \rightarrow Me_2SO + H_2O \qquad -206\text{ kJ}$$

$$Me_2SO + H_2O_2 \rightarrow Me_2SO_2 + H_2O \qquad -307\text{ kJ}$$

These data apply to $Me_2S(O)_n$ in the gas phase, but the same picture emerges when data are referenced to the condensed state.[22] This trend is more or less independent of the R-group on the sulfur atom; for Ph_2S analogues, for which $\Delta H°$ but not $\Delta G°$ values are known,[21] the $\Delta H°$ values are −221 and −324 kJ, respectively. Thus, it is clear that the thermodynamic trends lie in an order opposite that of the kinetic trends.

The rate constants for the series $(X-C_6H_4)_2SO$ were analyzed by the linear free energy correlation method described by Hammett. For this purpose the *x*-axis is given by 2σ, where σ is the Hammett substituent constant. Twice the value of σ was taken, since two equivalent groups are present in these compounds. The resulting correlation is displayed in Figure 3. The slope of the line gives the reaction constant as $\rho = -0.65$. The linearity of the plot indicates that a common mechanism, and a common rate-controlling step, operates throughout the series.[18] The negative value of ρ shows that the reaction center (the sulfur atom) becomes more positive in the transition state than in the reagent, consistent with a mechanism in which the peroxide group has become electrophilically activated by coordination to the heptavalent rhenium of **B**. In that sense, then, the electron pair of the sulfoxide has it acting as a nucleophile attacking the peroxo oxygen of **B**. This mechanism has been assigned to nearly all reactions in which substrate X is oxidized by hydrogen peroxide under the catalytic influence of MTO.[3,4] (The notable exception is the case of the sulfines, X = Ar_2CSO.[10])

We can make certain comparisons between the diaryl sulfoxides reported here with rate constants for diaryl thioketones,[10] and aryl sulfides.[8] In that case, the available data refer not to Ar_2S but to ArSMe.[8] The Hammett reaction constants are given below:

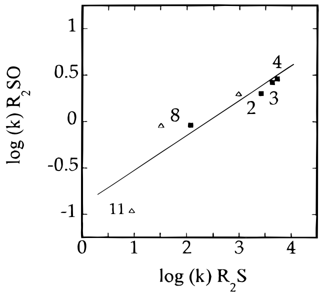

Figure 4. Values of $\log(k_4)$ for selected sulfoxides versus $\log(k_x)$ for the parent sulfide compounds (ref 12). Compounds are numbered according to Table 1. A general linear correlation with a slope of about 0.4 can be seen. Values for the sulfides are k_3 (filled squares) and k_4 (open triangles).

Ar_2SO	Ar_2CS	ArSMe	Ar_2CSO
2σ	2σ	σ	2σ
$\rho = -0.65$	$\rho \approx -1.1$	$\rho = -0.98$	U-shaped

Clearly the same effects operate along each series, except for the thioketones. The fact that the sulfoxides have a smaller ρ-value compared to the sulfides is consistent with the electronegative oxygen atom muting the kinetic effects of the ring substituent, owing to its polarizing effects in the transition state. Much more dominant than those trends, however, are the large changes (~10^3) in reactivity of sulfides to sulfoxides.[19]

Another means of exploring these effects is by means of a linear free energy correlation between parallel sets of compounds, sulfides and sulfoxides. This method allows the inclusion of sets of compounds that cannot be accommodated in a single Hammett correlation. Figure 4 presents a plot of the rate constant k_4 for sulfoxides, ArS(O)Me and Ar_2SO, against the rate constant (k_3 or k_4, as available) for ArSMe and Ar_2S. The number of data points is limited, and the correlation far from perfect. Nonetheless, these results suggest that the same electronic factors are, by-and-large, applicable to all the rate constants for the parallel reactions of sulfoxides and sulfides. The slope of that imperfect correlation is about 0.4 ± 0.1, again showing the electronic effects of the additional oxygen atom on the reaction center. The matter under discussion is not simply that sulfoxides are much less reactive than the sulfides, which was dealt with in the opening part of the Discussion. Rather, this point concerns the *relative* rates along the series, sulfoxide compared to sulfide. Put another way, each sulfoxide is less reactive than its sulfide, but along a series in which the sulfide rate constants rise a given amount, those for the sulfoxide rise less. This effect signals a lessening of the influence of the oxygen atom for the more reactive compounds.

The most notable feature of the kinetic data for the sulfoxides is the lack of a detectable contribution for the k_3 pathway. In

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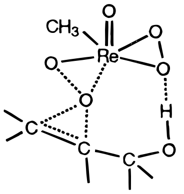
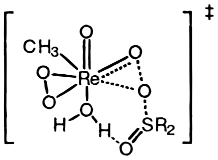
other words, oxidation proceeds entirely through the diperoxorhenium compound **B**, and not at all through **A**. This contrasts with the usual trend for many substrates, where **A** and **B** react at comparable rates ($k_3 \approx k_4$).[3,4] Indeed, in most of those cases **A** carries the much larger portion of the reaction, owing to a rate of regeneration of **B** from **A** that makes the more probable fate of **A** oxygen atom transfer; namely (often) the following inequality holds: $k_3[X] \gg k_2[H_2O_2]$. The single exception to these general statements to date has been the oxidation of allylic alcohols,[16] a reaction that has also been examined by others.[23,24] That unusual finding was interpreted to suggest a hydrogen-bonded interaction between the substrate and the diperoxorhenium compound **B**, which cannot exist with **A**, as conveyed by the structure shown (see ref 15).



Sulfoxides do not offer a parallel pathway. It is however known that **B** has a water molecule bonded to rhenium and **A** does not. Thus, the Re atom in **B** is seven-coordinate,[25] and in **A** five-coordinate.[11] The water molecule can allow for hydrogen bonding in the transition state of the oxidation. The oxo group on the sulfoxide can hydrogen-bond with this water molecule and make a six membered ring:



In support of this suggestion it should be noted that sulfones are formed to a greater extent during sulfide oxidation by MTO$-H_2O_2$ as the water concentration increases.[17]

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