Molecular Rhenium(V) Oxotransferases: Oxidation of Thiols to Disulfides with Sulfoxides. The Case of Substrate-Inhibited Catalysis

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$Re(O)Cl_3(PPh_3)_2$, **1**, and $Re(O)Cl_3(OPPh_3)(Me_2S)$, **2**, catalyze the oxidation of thiols to disulfides with sulfoxides under mild conditions. Catalyst **1** exhibits an induction period which features PPh_3 oxidation to $OPPh_3$ prior to disulfide formation. This lag is absent when **2** is the catalyst precursor. Otherwise, **1** and **2** display comparable kinetics and concentration dependencies. The catalytic reactions are first-order in catalyst, inhibited by thiol, and first-order in sulfoxide at low sulfoxide concentrations. Thiol inhibits the oxygen-transfer reaction because it competes with sulfoxide for coordination on rhenium. Sulfoxides must bind to rhenium in order to be activated for oxo transfer. Ligand substitution reactions of **1** and **2** display kinetics that are consistent with a dissociative (D) mechanism: the substitution rate is zero-order in entering ligand and inhibited by departing ligand. The first-order rate constant for the formation of a 5-coordinate intermediate is 0.06 s^{-1}. As the sulfoxide concentration is increased, the reaction rate increases to reach a maximum and then begins to decline. The catalytic turnover rate at optimal conditions (maximum k_{cat} for PhS(O)Me is 180 h^{-1}) approaches the rate of ligand substitution in these rhenium(V) complexes. Rate retardation at high sulfoxide concentrations is due to catalyst deactivation; sulfoxides oxidize the rhenium(V) catalyst to ReO_4^-, which is inactive. Dimethyl sulfoxide (DMSO) is more efficient than aryl sulfoxides at oxidizing the catalyst, a fact that could be rationalized by the thermodynamics of S−O bond strength. Thus, aryl sulfoxides, such as PhS(O)Me, appear to be more reactive than alkyl ones. The oxygen-transfer reaction, therefore, is not involved in the rate-controlling step and the rate is limited by ligand substitution. The rhenium(V) catalyst in these reactions acts as a Lewis acid and activates the sulfoxide via coordination: the sulfoxide ligand and not the metal is the bearer of the transferred oxygen. A single-crystal X-ray structure of $Re(O)Cl_3(OPPh_3)(Me_2S)$, **2**, has been solved: space group *Pcmn*, $a = 8.863(6)$ Å, $b = 14.269(9)$ Å, $c = 18.45(1)$ Å, $Z = 4$; the structure was refined to final residuals $R = 0.028$ and $R_w = 0.035$.

Introduction

Metal-catalyzed oxygen-atom transfer reactions continue to attract vast attention due to their fundamental role in chemistry and biology.[1−4] The oxidation/reduction of sulfoxides and other organosulfur compounds are particularly interesting from a mechanistic standpoint as well as from a biochemical and environmental perspectives.[5] Many metal-based oxotransferases, such as the molybdenum-containing dimethyl sulfoxide (DMSO) reductase, are known to utilize sulfoxides to oxidize organic substrates.[6−9] Because of their stability in comparison to organic peroxides, sulfoxides are promising environmentally safe oxidants. Thiols are strong reductants and capable of reducing sulfoxides efficiently in vivo;[10] however, chemically high temperature or acid/base catalysis is required.[11,12] We report here on the mechanism of a molecular oxotransferase system that employs $(L)(L')Cl_3Re^{V}{=}O$ complexes for the catalytic oxidation of thiols to disulfides with sulfoxides, eq 1.

$$R_1S(O)R_2 + 2R_3SH \xrightarrow{Re^{V}\ Cat.} R_1SR_2 + R_3SSR_3 + H_2O \qquad (1)$$

With regards to oxygen-transfer chemistry, the literature contains many examples of transition-metal catalysts: Re(VII) and -(V),[13−16] Mo(V) and -(VI),[17,18] and Ru(V) and -(IV),[19] to name few. The ability of rhenium(V) complexes of the general formula $L_2Cl_3Re{=}O$ to catalyze oxygen transfer from DMSO to PPh_3 has been realized previously.[20] While this investigation

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Table 1. Details of X-ray Data Collection and Structure Refinement for $Re(O)Cl_3(OPPh_3)(Me_2S)$

formula	$C_{20}H_{21}ReCl_3S_1P_1O_2$
fw	648.98
cryst syst	orthorhombic
space group	*Pcmn*
cryst color	green
cryst habit	block
a, Å	8.863(6)
b, Å	14.269(9)
c, Å	18.45(1)
Z	4
V, Å^3	2334(3)
ρ(calcd), g cm^{-3}	1.847
radiation; λ, Å	Mo Kα; 0.7107
abs coeff (m), mm^{-1}	5.791
transm factor range (intensity)	0.66−1.00
F(000), e	1256
temp, K	298
diffractometer	Picker (Crystal Logic)
scan mode; speed, deg/min	$\theta-2\theta$; 6.0
2θ range, deg	2.2−60.0
tot. data collcd, unique data used	3845, 2479 ($I > 3\sigma(I)$)
no. of params refined	139
final shift/error, max and av	0.046, 0.002
max resid density, e/Å^3	2.24 (close to Re)
$R = \sum\|\|F_o\| - \|F_c\|\|/\sum\|F_o\|$	0.028
$R_w = (\sum w(\|F_o\| - \|F_c\|)^2/\sum w(\|F_o\|)^2)^{1/2}$	0.035
GOF $= (\sum w(\|F_o\| - \|F_c\|)^2/(N_o - N_v))^{1/2}$	1.108

was underway, a report appeared in the literature in which $(PPh_3)_2Cl_3Re(O)$ was used catalytically in the synthesis of disulfides from thiols.[21] The following report includes kinetics and mechanistic studies on the catalytic reaction shown in eq 1 with a variety of rhenium(V) chloro complexes. A single-crystal X-ray structure of the most active catalyst precursor, $(OPPh_3)(Me_2S)Cl_3Re(O)$, is also reported.

Experimental Section

Materials. The rhenium complexes $(PPh_3)Cl_3Re(O)$,[22] **1**, $(OPPh_3)(Me_2S)Cl_3Re(O)$,[20,23] **2**, and $(Me_2SO)_2ClRe(O)_2$,[23] **3**, were prepared according to literature methods. All solvents used in the kinetics studies were of spectrophotometric grade and used as received. Manipulations were performed without exclusion of air or moisture unless specified otherwise. All of the rhenium compounds employed in this study are stable to prolonged exposure of air. All other chemicals were reagent grade, obtained commercially, and used as received without further purification.

Instrumentation. NMR spectra were obtained on a Bruker AC200 or ARX400 spectrometers. Tetramethylsilane was used as an internal standard for ^{1}H spectra, and 85% H_3PO_4, as external standard for ^{31}P spectra. Infrared spectra were obtained as Nujol mulls on a Perkin-Elmer Paragon 1000 FT-IR spectrometer. UV−vis spectra were recorded on a Shimadzu UV-2501 spectrophotometer.

X-ray Structure Analysis for $Re(O)Cl_3(OPPh_3)(Me_2S)$, 2. A green crystal of $Re(O)Cl_3(OPPh_3)(Me_2S)$, **2**, was grown by slow evaporation of a methylene chloride solution at −5 °C. The solid batch used for growing crystals was prepared from the stoichiometric reaction between **1** and DMSO (1:2) in benzene; the isolated product (78% yield) was shown to be pure by its ^{1}H and ^{31}P spectra (see below).

A suitable crystal of approximate dimensions 0.2 × 0.2 × 0.25 mm was mounted on a glass fiber. X-ray intensity data were recorded at room temperature on a modified Picker diffractometer with graphite monochromated Mo Kα radiation. Crystallographic data are summarized in Table 1. Cell parameters were obtained by least-squares method from the setting angles of 56 reflections. Three standard reflections were monitored during data collection and showed no significant variation in intensities. Reflection data were corrected for Lorentz and polarization effects. An empirical absorption correction was carried out using ψ scans. The structure was solved by Patterson and Fourier techniques. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were calculated at idealized positions and were included in refinement as fixed contributors. Final difference Fourier map was featureless, the largest peak (2.24 e/Å^3) being adjacent to a rhenium atom.

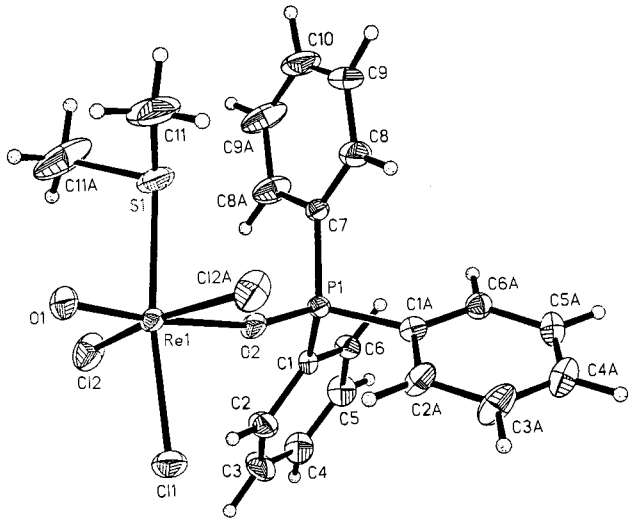

Figure 1. ORTEP drawing of the molecular structure of $Re(O)Cl_3(OPPh_3)(Me_2S)$, **2**.

Kinetics were measured in methylene chloride, deuteriomethylene chloride, or deuteriochloroform; no noticeable differences were observed in the kinetics when $CDCl_3$ was substituted for CD_2Cl_2. Reactions followed by ^{1}H NMR were carried out on a Bruker ARX400 spectrometer at 22 °C in sealed NMR tubes that contained TMS as internal standard. When aromatic sulfoxides were employed, the progress of the reaction was followed by spectrophotometry between 250 and 265 nm at 22 °C using quartz cells of 1.0 mm optical path length. The sulfide product absorbs in this region 3 times as strongly as the starting sulfoxide.[24] Stock solutions of the rhenium(V) catalysts were purged with argon, stored at −20 °C, and used within 5 days. Unless specified otherwise, catalyst was added last to solution mixtures of substrates, thiol and sulfoxide; in the absence of a catalyst, no reaction was observed at ambient temperatures even after 24 h.

Results and Discussion

X-ray Molecular Structure of $Re(O)Cl_3(OPPh_3)(Me_2S)$, 2. The single-crystal X-ray structure of **2** contains isolated molecules with octahedral geometry about the rhenium, Figure 1. The spectroscopic data in solution is also in agreement with this formulation: IR 981, 1130, and 1138 cm^{-1}; ^{1}H NMR in CD_2Cl_2 δ 2.70 (s, 6H, Re−SMe_2), 7.6 (m, 15H, Re−$OPPh_3$); ^{31}P NMR in CD_2Cl_2 δ 48 (s, Re−$OPPh_3$). Interestingly, the stereo-arrangement of the chloride ligands is similar to that in **1**, meridonial, but the neutral ligands are cis in **2** and trans in **1**.[25] This difference could be due to steric hindrance between the bulky PPh_3 ligands. The different arrangement of the neutral ligands in compounds **1** and **2** suggests a low barrier with respect to stereochemical change in a five-coordinate intermediate that must be involved in these reactions (see later).

A preliminary X-ray structural study of **2** has been reported previously.[20] The report stated that "the diffraction data are not of sufficient quality to distinguish between space groups

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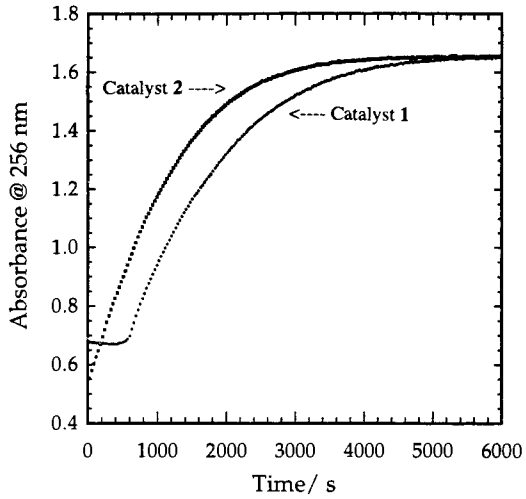


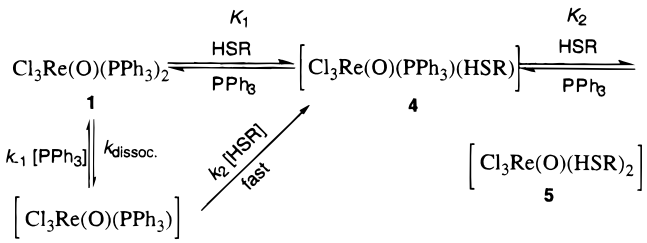
Figure 2. Kinetics profiles for the formation of PhSMe from the reaction of PhS(O)Me and $HSCH_2CH_2OH$ as catalyzed by **1** versus **2**. Conditions: [PhS(O)Me] = 1.5×10^{-3} M, [$HSCH_2CH_2OH$] = 0.010 M, and catalyst [**1**] or [**2**] = 2.0×10^{-4} M in CH_2Cl_2 at 22 °C (1.0 mm optical path length). For catalyst **1** (following the induction period), $k_\psi = 7.71 \times 10^{-4}$ s^{-1} and $V_i = 9.68 \times 10^{-7}$ M s^{-1}. For catalyst **2**, $k_\psi = 9.45 \times 10^{-4}$ s^{-1} and $V_i = 1.06 \times 10^{-6}$ M s^{-1}.

Pnma and *Pna*2_1." The unit cell parameters in this study are the same as reported in the preliminary study; however, as shown in the crystallographic summary table, Table 1, the correct space group is *Pcmn*, a nonstandard setting of *Pnma*.

The Re═O distance of 1.651(4) Å is on the short end for monooxo complexes (range 1.63−1.71 Å).[26] The Re−S distance for the bound DMS is 2.425(2) Å, which is in the range observed for other rhenium thioether compounds.[27] Complete crystallographic tables containing (1) positional and equivalent isotropic thermal parameters, (2) bond lengths, and (3) bond angles are included in the Supporting Information.

Comparison of Catalyst Precursors. When compound **1** is used as catalyst for the reduction of DMSO by 2-mercaptoethanol ($HSCH_2CH_2OH$), $OPPh_3$ was observed in the ^{31}P NMR prior to formation of disulfide ($HOCH_2CH_2S-SCH_2CH_2OH$). In a similar reaction with phenyl methyl sulfoxide (PhS(O)Me) and catalyst **1**, the production of thioanisole (PhSMe) as monitored by UV was delayed by an induction period, Figure 2. On the other hand, when $(OPPh_3)(Me_2S)Cl_3Re(O)$, **2**, was used, thioanisol was produced without a lag, Figure 2. Following the induction period for catalyst **1**, the reaction proceeds with a comparable rate (within ~20%) to that of catalyst **2**, Figure 2, indicating the same active catalyst for both precursors. The induction period for **1** is dependent on thiol concentration: the higher the thiol concentration, the longer the induction period is (Figure S1 in Supporting Information). At high thiol concentrations, the decrease in the absorbance during the induction period for catalyst **1** is well pronounced (Figure S1) and is in agreement with the oxidation of PPh_3 to $OPPh_3$ since $OPPh_3$ has a lower extinction coefficient than PPh_3 in the UV.[28] The inhibitory effect of thiol is enumerated further in the kinetics section below; in short, thiol competes for coordination with sulfoxide. The latter must coordinate to rhenium in order to be activated for oxo transfer.

Scheme 1. Ligand Substitution for $LL'Cl_3Re^V{=}O$ Complexes, Illustrated for **1** and Thiol[a]



[a] See Figure S1 in the Supporting Information for kinetics data and conditions.

Binding of Substrates to Rhenium. Thiols are good ligands, and the rhenium complexes used here are known for their affinity for sulfur.[29] By ^1H NMR 2-mercaptoethanol was found to displace the neutral ligands on both catalysts and coordinate to the metal.[30] Thiol complexes of $TiCl_4$ have been recently reported in the literature.[31] The release of PPh_3 from **1** was verified by ^{31}P NMR (−6.7 ppm versus −16.1 ppm for Re−PPh_3); for compound **2**, free Me_2S (2.1 ppm versus 2.7 ppm for Re−$S(Me)_2$) was observed in the ^1H spectrum and free $OPPh_3$ (33 ppm versus 48 ppm for Re−$OPPh_3$ in CD_2Cl_2) in the ^{31}P spectrum.

The ligand exchange reactions are first order in [Re], inhibited by free [PPh_3], and show no dependence on [thiol], Figure S2 (Supporting Information). The experimental rate law for these substitution reactions supports a dissociative mechanism in which a 5-coordinate rhenium complex is an intermediate, Scheme 1. The k_{dissoc} for the two rhenium complexes **1** and **2** are comparable (~0.06 s^{-1}). DMSO also acts as a ligand for complex **2** displacing both Me_2S and $OPPh_3$. The coordinated dimethyl sulfoxides show a signal in the ^1H NMR spectra at 2.87 ppm in $CDCl_3$ as the major product. Another apparent peak (though weaker than the 2.87 ppm peak) at 2.95 ppm corresponds possibly to $Re(O)_2Cl(DMSO)_2$; *vide infra*. When 1:1 DMSO and **2** are mixed, the ^{31}P spectrum showed approximately 1:1 coordinated to free $OPPh_3$; this is due to a cooperativity effect ($K_2 \gg K_1$). Spectrophotometric titrations of **2** with DMSO and $HSCH_2CH_2OH$ independently demonstrate cooperative binding of these ligands to rhenium.[32] Figure S3 (Supporting Information) shows the titration spectra for the reaction of **2** with $HSCH_2CH_2OH$, and the data are fitted to eq 2; Figure S4 (Supporting Information) displays spectral changes

$$\frac{\text{absorbance}}{[\text{Re}]_T} = \frac{\epsilon_0 + \epsilon_4 K_1[\text{HSR}] + \epsilon_5 K_1 K_2[\text{HSR}]^2}{1 + K_1[\text{HSR}] + K_1 K_2[\text{HSR}]^2} \quad (2)$$

for the titration of complex **2** with DMSO. Since the NMR spectra of the thiol and sulfoxide adducts of $Cl_3Re(O)$ suggest equivalent ligand environment, a *trans* geometry would be postulated. Also "soft" ligands such as thiols are known to favor *cis* coordination relative to metal−ligand multiple bonds.[33−36]

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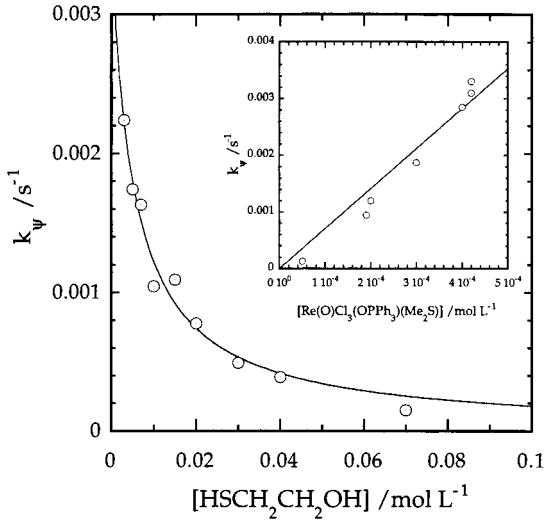

Figure 3. Rate dependences on thiol, $HSCH_2CH_2OH$, and catalyst **2** (inset) concentrations. See text for conditions.

Attempts to isolate thiol adducts of $Re(O)Cl_3$ were not successful because at preparative concentrations an unidentifiable black precipitate was formed over time. As for the sulfoxide adducts, they decompose in solution to ReO_4^- when crystallization was attempted. Thus, when catalytic reactions are performed at high concentrations (preparative scale), it is best to add catalyst last to minimize catalytic degradation.

Kinetics on the Catalytic Reaction. The reduction of PhS(O)Me by $HSCH_2CH_2OH$ was monitored by following the UV absorption of PhSMe, which absorbs much more intensely than PhS(O)Me.[24] Thus PhS(O)Me was limiting and $HSCH_2CH_2OH$ in excess. The products from this reaction were characterized by ^1H NMR to be PhSMe and the disulfide $HOCH_2CH_2S-SCH_2CH_2OH$. The conditions were as follows: [PhS(O)Me] = 0.50−1.50 mM, $[HSCH_2CH_2OH]$ = 0.0050−0.070 M, and $[(OPPh_3)(Me_2S)Cl_3ReO] = 5.0 \times 10^{-5}-4.2 \times 10^{-4}$ M in CH_2Cl_2 with a 1 mm path length quartz cell. The reaction time profiles were exponential (see Figure 2) and thus gave excellent fit to a first-order rate equation. The dependence on the thiol and catalyst concentrations are shown in Figure 3. The rate of reaction is first-order with respect to catalyst and inhibited by substrate, $HSCH_2CH_2OH$. The inhibition by thiol is due to its competitive coordination to rhenium forbidding activation of the sulfoxide. Therefore, the rate-controlling step under these conditions does not involve the oxygen-transfer reaction but instead the coordination of sulfoxide to rhenium. In fact, at optimal conditions (*vide infra*) the catalytic turnover rate never exceeds ~0.05 s^{-1}, which is comparable to the rate of ligand dissociation in these rhenium(V) complexes (*vide supra*). When 27% catalyst (relative to the limiting PhS(O)Me) is used and $HSCH_2CH_2OH$ added last, an immediate surge of PhSMe (~27%) is observed prior to the establishment of steady state (Figure S5). This reconfirms that the oxo-transfer step is fast.

The catalytic reaction with excess PhS(O)Me and limiting $HSCH_2CH_2OH$ was monitored by ^1H NMR and featured zero-order dependence with respect to sulfoxide, Figure 4b.[37] The maximum initial rate observed corresponds to a first-order rate constant ($V_i/[Re]_T$) of 0.052 s^{-1}, which is in agreement with

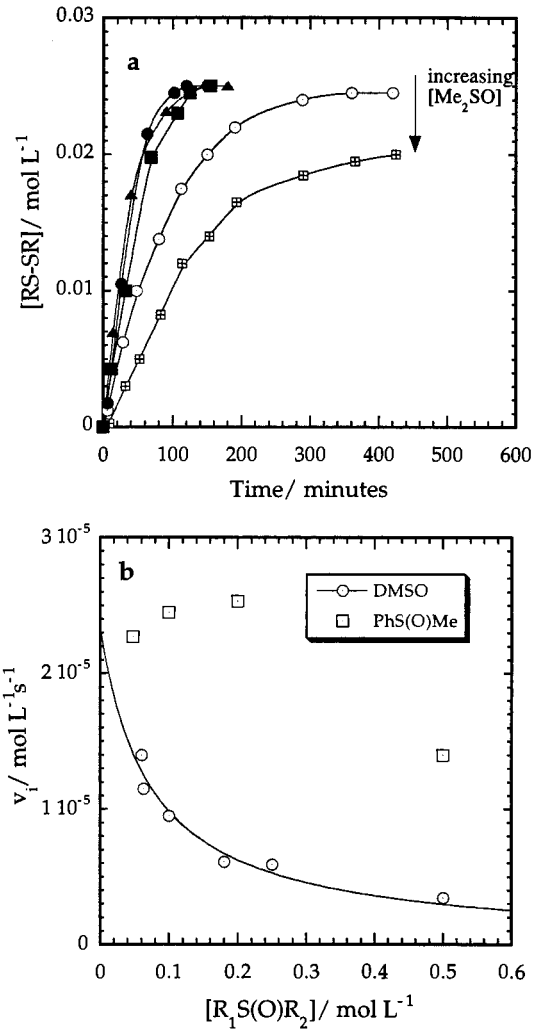

Figure 4. (a) Time profiles depicting disulfide ($HOCH_2CH_2S-SCH_2CH_2OH$) formation at high sulfoxide concentrations from the reaction of DMSO and 2-mercaptoethanol catalyzed by complex **2**. See text for conditions. (b) Plot of the initial rate (V_i) versus sulfoxide concentration (circles for DMSO and squares for PhS(O)Me) showing rate retardation at large sulfoxide concentrations.

k_{dissoc}. for the catalyst. At yet higher concentrations of PhS(O)Me the rate of reaction begins to decline and the time profiles deviate from zeroth-order. This effect was more pronounced for DMSO as discussed next.

The kinetics of the DMSO and $HSCH_2CH_2OH$ reaction were also studied by ^1H NMR. The conditions were the following: $[(OPPh_3)(Me_2S)Cl_3ReO] = 5.0 \times 10^{-4}$ M, $[HSCH_2CH_2OH]$ = 0.050 M, and [DMSO] = 0.040−0.50 M in $CDCl_3$. The kinetics profiles shown in Figure 4a followed zero-order approaching first-order (slowing down) toward the end of the reaction as expected for Michaelis−Menten kinetics.[38] The retardation in the rate was more noticeable for the reactions at larger DMSO concentrations. It is also worth noting that the reaction at 0.50 M DMSO did not reach completion. The inverse dependence on sulfoxide at these concentrations, Figure 4b, was unexpected. We thought perhaps the reaction is sensitive to water and using higher concentrations of DMSO introduces more water into the reaction mixture. Therefore, we repeated one of the runs (0.10 M DMSO) in the presence of 0.20 M D_2O from the beginning of reaction; no change was observed

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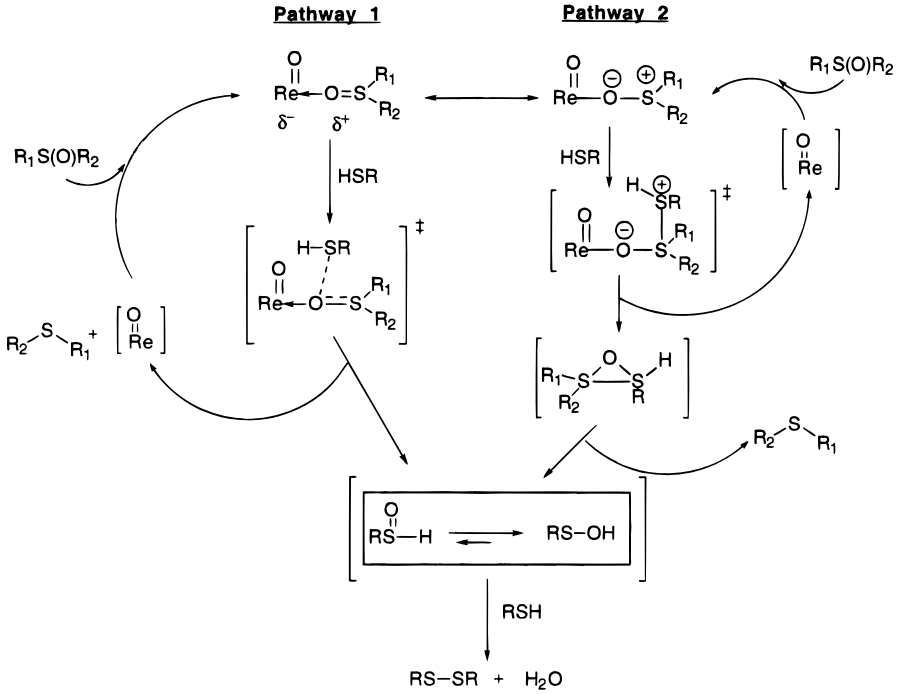
(37) Conditions: $[Re(O)Cl_3(OPPh_3)(Me_2S)] = 5.0 \times 10^{-4}$ M, [HSEtOH] = 0.050 M, and [PhS(O)Me] = 0.050−0.50 M in $CDCl_3$ at 22 °C.
(38) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*; 2nd ed.; McGraw-Hill: New York, 1995.

Scheme 2. Mechanism of Catalytic O-Transfer for the Oxidation of Thiols to Disulfides with Sulfoxide[a]



[a] Two pathways are presented: attack of thiol onto the sulfoxide's (1) oxygen and (2) sulfur. Re═O represents $LCl_3Re{=}O$,where L is either a sulfoxide or a thiol.

in the rate of the reaction. Also drying DMSO over 4 Å molecular sieves gave comparable kinetics to undried DMSO. This led us to investigate the reactions at high DMSO concentrations further to see what influence does DMSO have on the catalyst's stability.

Catalyst Stability. In the presence of excess DMSO, $Re(O)_2Cl(DMSO)_2$ has been synthesized from **1** after a 20 h reaction time.[23] We synthesized $Re(O)_2Cl(DMSO)_2$, **3**, to test its catalytic ability. This compound is polymeric and insoluble in all common organic solvents. A suspension of **3** in $CDCl_3$ gives a weak signal at 2.95 ppm in the ^1H NMR. Besides its IR spectrum,[39] which is in agreement with that reported in the literature,[23] we were unable to characterize **3** any further. Therefore, we adopt the literature's assignment that it is $[(DMSO)_2Re(O)_2Cl]_n$.[23] Compound **3** dissolves in water, however, to give a UV spectrum that is identical to that of an authentic sample of ReO_4^-; electrospray mass spectrometry verified that water solutions of $Re(O)_2Cl(DMSO)_2$ contain ReO_4^- (*m*/*z* 249 and 251 with isotope ratio 3:5). **3** was found to catalyze the reduction of DMSO by $HSCH_2CH_2OH$. Unfortunately, due to its insolubility we could not compare its activity quantitatively to that of $(Me_2S)(OPPh_3)Cl_3Re(O)$. However, when large concentrations of DMSO are used (≥0.50 M), **3** was inactive and the UV spectrum of the solution showed the presence of ReO_4^- as the major rhenium species. $KReO_4$ does not catalyze the oxidation of thiols with sulfoxides. Thus we conclude that, in the presence of large concentrations of DMSO, the catalyst decomposes to ReO_4^- probably via the formation of $Re(O)_2Cl(DMSO)_2$ initially; nevertheless, under our kinetics conditions we do not observe catalyst precipitation, which would be the case if $Re(O)_2Cl(DMSO)_2$ was the major rhenium species at any point during the reaction. Hence **3** must be involved as an intermediate along the catalyst's deactivation pathway. At high DMSO concentrations, **3** perhaps abstracts an oxygen from DMSO, eq 3, to give $ClReO_3$,[40] which is known

$$(Me_2SO)_2Re(O)_2Cl + Me_2SO \rightarrow ClRe(O)_3{\cdot}L_n + Me_2S \quad L = DMSO \quad (3)$$

$$ClRe(O)_3 + H_2O \rightarrow ReO_4^- + 2H^+ + Cl^- \quad (4)$$

to be moisture sensitive and gives ReO_4^- in the presence of H_2O, eq 4.[41] The complete exclusion of water in this system is impossible because water is a byproduct, eq 1. It was also difficult to verify the reaction in eq 3 because compound **3** is only soluble in water and DMS (Me_2S) is not; therefore, we have not been able to quantify the production of DMS away from the catalytic reaction, that is starting from **3** alone. Nevertheless, when dissolved in water, **3** generates approximately 2 equiv of acid [H_3O^+] quantified by pH measurements. The production of 2 equiv of acid supports the proposed reactions in eqs 3 and 4.

Aryl sulfoxides were less effective than DMSO (see Figure 4b) at deactivating the catalyst. This observation could be attributed to thermodynamics since the aryl sulfoxide S═O bonds are typically stronger than alkyl ones by 1−3 kcal mol^{-1}.[42,43] Therefore, the reaction in eq 3 is thermodynamically more favorable for alkyl sulfoxides than aryl ones. In a recent report the enhanced reactivity on a preparative scale of Ph_2SO in the oxidation of thiols catalyzed by **1** was rationalized by invoking an early transition-state and reasoning that the electron-withdrawing ability of the aryl substituents is more significant than the enthalpic effects.[21] In contrast, we have shown in this kinetics study that the oxygen-transfer step in the oxidation of thiols by sulfoxides with catalyst **1** or **2** is not rate-controlling

(39) IR spectral data for **3** in cm^{-1}: 968 (Re═O); 908 and 894 sh (S−O).

(40) $[Re(O)X_4]^-$ compounds are oxidized by sulfoxides to give ReO_4^- as the major product. See for example: Cotton, F. A.; Lippard, S. J. *Inorg. Chem.* **1966**, *5*, 9.

(41) Edwards, P.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1984**, 2695.

(42) Jenks, W. S.; Matsunaga, N.; Gordon, M. *J. Org. Chem.* **1996**, *61*, 1275.

(43) Holm, R. H.; Donahue, J. P. *Polyhedron* **1993**, *12*, 571.

Table 2. Summary of Equilibruim and Rate Constants at 22 °C.

reaction	symbol	value
$Re(O)Cl_3(PPh_3)_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Re(O)Cl_3(PPh_3)] + PPh_3$	k_1	$0.060 \pm 0.005\ s^{-1}$
$[Re(O)Cl_3(PPh_3)] + HSR \xrightarrow{k_2} Re(O)Cl_3(PPh_3)(HSR)$	k_{-1}/k_2	0.0040 ± 0.0004
where $R = -CH_2CH_2OH$		
$Re(O)Cl_3(OPPh_3)(Me_2S) + Me_2SO \overset{K_1}{\rightleftharpoons} [Re(O)Cl_3(OPPh_3)(Me_2SO)] + Me_2S$ $[Re(O)Cl_3(OPPh_3)(Me_2SO)] + Me_2SO \overset{K_2}{\rightleftharpoons} Re(O)Cl_3(Me_2SO)_2 + OPPh_3$	K_1K_2	$(10 \pm 2) \times 10^6$
$Re(O)Cl_3(OPPh_3)(Me_2S) + HSR \overset{K_1'}{\rightleftharpoons} [Re(O)Cl(OPPh_3)(HSR)] + Me_2S$	K_1'	364 ± 80
$[Re(O)Cl_3(OPPh_3)(HSR)] + HSR \overset{K_2'}{\rightleftharpoons} Re(O)Cl(HSR)_2 + OPPh_3$	K_2'	5500 ± 1000
where $R = -CH_2CH_2OH$		
$Re(O)Cl_3(L) + PhS(O)Me \xrightarrow{k_3} [Re(O)Cl_3(L)(PhS(O)Me)]$	k_3	$21 \pm 2\ L\ mol^{-1}\ s^{-1}$
where L = thiol		
$Re(O)Cl_3(L)_2 \underset{k_a}{\overset{k_d}{\rightleftharpoons}} [Re(O)Cl_3(L)] + L$	k_d	$0.060 \pm 0.007\ s^{-1}$
where L = thiol or sulfoxide		

and aryl sulfoxides may appear to be more effective oxo-transfer agents (depending on concentrations) because they are less likely than alkyl sulfoxides to oxidize the rhenium(V) catalyst and hence deactivate it.

The Catalytic Mechanism. In these simple rhenium(V) complexes, **1** and **2**, the chloride ligands are not sufficiently donating (with respect to both σ and π donation) to stabilize rhenium(VII);[44−46] in addition, compounds of the type $L_nRe(O)_2Cl_3$ are not known.[47] It has also been shown previously with ^{18}O-labeled Me_2SO that mainly ^{18}O-labeled $OPPh_3$ is formed over single turnover experiments, demonstrating that the transferred oxygen originates mainly from the sulfoxide.[20] Hence, the activation here is a consequence of sulfoxide coordination to the rhenium(V) Lewis acid center. The result of this association is a polarization of the S=O bond, which becomes more susceptible to nucleophilic attack. Thiols act as nucleophiles in most of their reactions including oxidation to disulfides.[48] The intermediary of sulfenic acid in thiol oxidations has been proposed, eq 5,[5] and recently unequivocally

$$RS{-}H \xrightarrow{\{O\}} \left[RS(O){-}H \rightleftharpoons RS{-}OH \right] \xrightarrow[fast]{RS{-}H} RS{-}SR + H_2O \qquad (5)$$

demonstrated in sterically hindered thiols that are unable of further coupling to yield the disulfide.[49] Sulfenic acids are known to react with C−C multiple bonds. We have attempted to trap sulfenic acid intermediates under catalytic conditions with phenyl acetylene and styrene independently but to no avail.[50]

Precoordination of the thiol is not required since it inhibits the rate of reaction by competing for binding sites with sulfoxide.[51] The remaining mechanistic question is whether the thiol attacks at the coordinated oxygen or the polarized sulfur of the sulfoxide, Scheme 2. The latter is observed for sulfoxides activated by strong acids or electrophiles as in the Swern oxidation of alcohols.[52] The mechanism of nucleophilic attack on the sulfoxide's oxygen would be in agreement with other oxo-transfer mechanisms involving transition-metal complexes.[4,13,16,53] With the kinetics and mechanistic data at hand on this system, we cannot distinguish between the two possibilities.

Concluding Remarks and Future Outlook

We reported here on the use of simple rhenium(V) catalysts, $LL'Cl_3Re(O)$, and sulfoxides for the oxidation of thiols to disulfides under mild conditions. The catalysts are very efficient (maximum $k_{cat} \sim 180\ h^{-1}$) approaching a catalytic rate that is limited by ligand dissociation. When $(PPh_3)_2Cl_3Re(O)$ is used as the catalyst precursor, an induction period is initially observed in which the phosphine is oxidized prior to disulfide formation. The oxygen-transfer step is not rate-controlling, and hence, electronic variations on the thiol have minor effects on the kinetics.[54] The "apparent" enhanced reactivity of aryl sulfoxides in comparison to that of DMSO stems from DMSO's proficiency in deactivating the Re(V) catalyst. The ability of DMSO to

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(48) March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 4th ed.; John Wiley & Sons: New York, 1992.
(49) Goto, K.; Holler, M.; Okazaki, R. *J. Am. Chem. Soc.* **1997**, *119*, 1460.
(50) We used as much as a 20× excess of styrene:thiol without success. This is not surprising since sulfenic acid has never been trapped before in the presence of thiol; usually sulfenic acid is generated thermally from sulfoxides. See for example: Drabowicz, J.; Kielbasinski, P.; Mikolajczyk, M. In *The Chemistry of sulphones and sulphoxides*; Patti, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: New York, 1988; pp 268−270.
(51) It has been shown that ruthenium(IV) oxo complexes with bound phosphine oxidize free phosphine in solution rather than bound phosphine. See for example: Marmion, M. E.; Takeuchi, K. J. *J. Am. Chem. Soc.* **1986**, *108*, 510.
(52) Tidwell, T. T. *Synthesis* **1990**, 857.
(53) Dumez, D. D.; Mayer, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 12416.
(54) Similar kinetics were observed for thiophenol and *p*-methylthiophenol compared to that of $HSCH_2CH_2OH$.

oxidize the Re(V) catalyst more effectively than aryl sulfoxides is consistent with the thermodynamic S═O bond strengths. The equilibrium and rate constants are summarized in Table 2. We are currently investigating coordination complexes containing the Re^{V}═O moiety and chiral ligand auxiliaries for asymmetric oxo-transfer reactions. Our goal is to utilize catalytic oxygen-transfer reactions such as that in eq 1 for kinetic resolution of racemic sulfoxides.

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Supporting Information Available: Five figures for the effect of thiol concentration on induction times with catalyst **1**, kinetics data of thiol substitution reactions with **1** (demonstrating zeroth order in thiol and inhibition by free PPh_3), spectrophotometric titrations and equilibria data for reactions of DMSO and $HSCH_2CH_2OH$ with **2** independently, and time profiles for the catalytic reaction between PhS(O)Me and $HSCH_2CH_2OH$ with different orders of mixing and crystallographic tables for atomic coordinates and equivalent isotropic parameters, bond lengths, and bond angles (9 pages). Ordering information is given on any current masthead page.

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