Stepwise Oxidation of Thiophene and Its Derivatives by Hydrogen Peroxide Catalyzed by Methyltrioxorhenium(VII)

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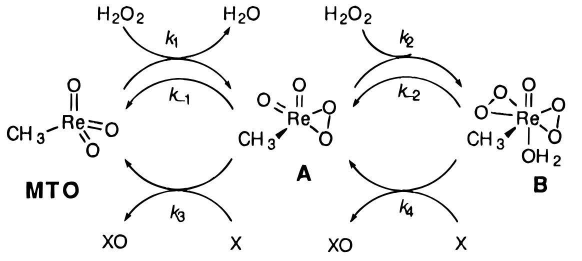
Received May 23, 1996[⊗]

The oxidation of thiophene derivatives by hydrogen peroxide is catalyzed by methyltrioxorhenium(VII) (CH_3ReO_3). This compound reacts with hydrogen peroxide to form 1:1 and 1:2 rhenium peroxides, each of which transfers an oxygen atom to the sulfur atom of thiophene and its derivatives. Complete oxidation to the sulfone occurs readily by way of its sulfoxide intermediate. The rates for each oxidation step of dibenzothiophenes, benzothiophenes, and substituted thiophenes were determined. The rate constants for the oxidation of the thiophenes are 2−4 orders of magnitude smaller than those for the oxidation of aliphatic sulfides, whereas the rate constants are generally the same for the oxidation of the thiophene oxides and aliphatic sulfoxides. The rate constant for conversion of a sulfide to a sulfoxide (thiophene oxide) increases when a more electron-donating substituent is introduced into the molecule, whereas the opposite trend was found for the reaction that converts a sulfoxide to a sulfone (thiophene dioxide). Mechanisms consistent with this are proposed. The first trend reflects the attack of the nucleophilic sulfur atom of a thiophene center on a peroxide that has been electrophilically activated by coordination to rhenium. The second, more subtle, trend arises when both sulfoxide and peroxide are coordinated to rhenium; the inherently greater nucleophilicity of peroxide then takes control.

Introduction

As first recognized by Herrmann, methyltrioxorhenium(VII) (CH_3ReO_3, abbreviated as MTO) has proved an effective catalyst for the oxidation of many substrates by hydrogen peroxide.[1−20] These reactions all take place by oxygen transfer from a peroxorhenium complex to the substrate; indeed, this chemistry appears limited to only those substrates that can be oxidized by the acceptance of an oxygen atom. The mechanism for oxygen transfer using MTO has been addressed previously.[2,3,16] Briefly, MTO binds reversibly one or two molecules of hydrogen peroxide to form mono- and diperoxides, **A** and **B**, respectively. The coordinated peroxides are activated for attack by the nucleophilic substrate **X**. This sequence of events is depicted in Scheme 1, which also presents the numbering of the rate constants.

Scheme 1



The peroxide groups of both **A** and **B** can be attacked by a range of substrates such as chloride[12] and bromide ions,[5] triarylphosphines,[13] triphenylarsine,[13] triphenylstibine,[13] alkenes,[11,17] anilines,[10] alkyl and aryl sulfides,[6,8] cyclic ketones,[18,19] arenes,[7,15] and thianthrene;[19] oxygen atom insertion into C−H bonds has been reported.[20] Thiophene, being difficult to oxidize, presents a challenge. The removal of thiophenes from petroleum feedstocks is an expensive problem, and the oxidation of the sulfur atom might facilitate the removal of thiophenes from the other petroleum components.[21] An exploration of the mechanistic principles involved in such oxidations may assist in the solution of this problem. A study of the MTO-catalyzed oxidation of substituted thiophenes by hydrogen peroxide is presented here.

Experimental Section

Except as otherwise noted, the experiments were performed in a mixture of water−acetonitrile (1:1, v/v) at pH 1, maintained with perchloric acid. The water was purified using deionized water that had been passed through a Millipore-Q water purification system. Some materials were used as received: acetonitrile (HPLC grade, Aldrich), perchloric acid (diluted from 70%, Fisher) hydrogen peroxide (diluted

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[⊗] Abstract published in *Advance ACS Abstracts*, November 1, 1996.

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from 30%, Fisher; standardized iodometrically), and MTO (Aldrich, standardized spectrophotometrically:[2] ϵ_{239} 1900 L mol^{-1} cm^{-1}, ϵ_{270} 1300 L mol^{-1} cm^{-1}). The MTO solutions were protected from light and used within 24 h. Dibenzothiophene, benzothiophene, thiophene, 2-methylthiophene, 2-methoxythiophene, 2,5-dimethylthiophene, tetrahydrothiophene, thioanisole (Aldrich, ~99%), and 3-methylthiophene (Lancaster, 98%) were used as received. 2,8-Dimethyldibenzothiophene and 2-methylbenzothiophene were a gift from John Benson. The purity of each sample was confirmed by ^{1}H NMR and by GC/MS. The dibenzothiophene 5-oxide was prepared by dissolving dibenzothiophene (5.1 g) and MTO (0.23 g) in acetonitrile (750 mL), to which hydrogen peroxide (3 mL of 30% solution) was slowly added. The reaction mixture was stirred for 12 h and was monitored periodically by TLC. The solvent was removed to afford a pale yellow powder, which was subjected to chromatography (silica gel, chloroform) to yield pure dibenzothiophene 5-oxide. The 2,8-dimethyldibenzothiophene 5-oxide was prepared by dissolving 2,8-dimethyldibenzothiophene (0.115 g) and MTO (42 mg) in acetonitrile (22 mL). Hydrogen peroxide (60 μL of 30% solution) was added over 2.5 h and the mixture stirred for a further 4 h. The solvent was removed and the product purified by chromatography (silica gel, chloroform).

Kinetic data were collected using UV/vis and ^{1}H NMR techniques, in the former case with Shimadzu UV-2101 PC and UV-3101 PC spectrophotometers. These reactions were maintained at 25.0 ± 0.2 °C. The solutions contained 0.1 M perchloric acid to stabilize the catalyst.[22] Quartz cuvettes of 0.02−0.2 cm optical path were used. The absorbance changes were monitored at 283.0 and 288.6 nm for the oxidation reactions of dibenzothiophene and 2,8-dimethyldibenzothiophene; the dibenzothiophene 5-oxide oxidation reactions to the corresponding sulfones were monitored at 249.4 and 252.2 nm for dibenzothiophene 5-oxide and 2,8-dimethyldibenzothiophene 5-oxide, respectively. The absorbance changes for the oxidation of benzothiophene, 2-methylbenzothiophene and 3-methylbenzothiophene were monitored at 254.5, 258.8, and 298.8 nm, respectively.

Equation 1 describes the rate law for the depletion of substrate **X**; it was derived by applying the steady state approximation to the concentrations of MTO, **A**, and **B** (where $[\mathrm{Re}]_\mathrm{T} = [\mathrm{MTO}] + [\mathbf{A}] + [\mathbf{B}]$). The values for k_1, k_{-1}, k_2, and k_{-2} in a 1:1 mixture of CH_3CN-H_2O ($[HClO_4] = 0.1$ M) have been determined previously:[11−13]

$$v = -\frac{d[X]}{dt} = \frac{k_1k_3[\mathrm{Re}]_\mathrm{T}[H_2O_2][X] + \dfrac{k_1k_2k_4[\mathrm{Re}]_\mathrm{T}[X][H_2O_2]^2}{k_4[X] + k_{-2}}}{k_{-1} + k_3[X] + k_1[H_2O_2] + \dfrac{k_1k_2[H_2O_2]^2}{k_4[X] + k_{-2}}} \qquad (1)$$

forward rxn k/L mol^{-1} s^{-1}		reverse rxn k/s^{-1}		equil const K/L mol^{-1}	
k_1	32.5	k_{-1}	2.5	K_1	13
k_2	1.05	k_{-2}	0.008	K_2	136

To evaluate the kinetics by **B**, the following conditions were used: $[H_2O_2] \gg [\mathrm{Re}]_\mathrm{T}$, such that $k_2[H_2O_2] \gg k_3[X]$. Pseudo-first-order behavior was applicable, according to the rate law:

$$v = -\frac{d[X]}{dt} = k_4[\mathrm{Re}]_\mathrm{T}[\mathbf{X}] \qquad (2)$$

Hydrogen peroxide was taken in large excess, to maintain **B** at a constant concentration thought the reaction; with this, $[\mathbf{B}] \cong [\mathrm{Re}]_\mathrm{T}$. The depletion of the substrate was monitored and the absorbance−time curves fit to a first-order equation:

$$\mathrm{Abs}_t = \mathrm{Abs}_\infty + (\mathrm{Abs}_0 - \mathrm{Abs}_\infty)(\exp(-k_{\mathrm{obs}}t)) \qquad (3)$$

The rate constants for the reactions with **A** were evaluated from experiments in which the hydrogen peroxide was added last in order to minimize the involvement of **B**. The initial stages of the reactions were used to deduce the initial rates of the reactions. The dependence of the initial rate v_i on the total concentration of the all rhenium species ($[\mathrm{Re}]_\mathrm{T}$) was fit to eq 1, using the values of k_1, k_{-1}, k_2, and k_{-2} defined earlier and the k_4 value which was determined from the experiments where excess hydrogen peroxide had been used.

NMR spectra were acquired with Varian VXR 300 and Bruker 400 spectrometers. For routine NMR spectra, CD_3CN was the solvent. The peak positions were referenced internally to the acetonitrile quintet (1.93 ppm vs Me_4Si). For reactions whose ^{1}H NMR spectral changes were monitored to obtain quantitative kinetic data, the solvent used was 1:1 CD_3CN-D_2O containing 0.1 M $DClO_4$. The integrals of the resonances were calibrated relative to acetonitrile.

Results

The oxidation of thiophenes, benzothiophenes, and dibenzothiophenes by hydrogen peroxide in the absence of MTO do not occur to a measurable extent in a reasonable time. With MTO, the sulfur atom was oxidized to the sulfoxide and then further to the sulfone. In principle this sequence was true for the earlier-studied dialkyl sulfides and alkyl aryl sulfides[6]—in those cases (and unlike this) the second oxidation step was significantly slower than the first, such that it was negligible during the period of sulfide oxidation. Scheme 1 describes the reactions for each oxidation step; however, it is necessary to add two more reactions representing the oxidations of the sulfoxide by **A** (k_5) and by **B** (k_6):

$$\mathbf{A} + \mathbf{X}\mathrm{O} \xrightarrow{k_5} \mathrm{MTO} + \mathbf{X}\mathrm{O}_2 \qquad (4)$$

$$\mathbf{B} + \mathbf{X}\mathrm{O} \xrightarrow{k_6} \mathbf{A} + \mathbf{X}\mathrm{O}_2 \qquad (5)$$

Oxidation of Thiophenes. The peroxide oxidation of a model thiophene, 2,5-dimethylthiophene, in the presence of MTO was examined by ^{1}H NMR spectroscopy, since the absorbance changes for the reaction were minimal. With only an equimolar concentration of hydrogen peroxide, the yellow colored solution characteristic of **B** faded to colorless. The ^{1}H NMR spectrum of the reaction after ~20 min confirmed the absence of peaks for **A** and **B** and showed only the peak for MTO itself. Furthermore, 2,5-dimethylthiophene was only partially consumed. Altering the order of mixing of the reagents gave the same result. With excess hydrogen peroxide the yellow color persisted and the ^{1}H NMR spectra showed that 2,5-dimethylthiophene had been consumed within ~3 h.

However, the ^{1}H NMR spectrum showed that other species besides the 2,5-dimethylthiophene 1-oxide and the 2,5-dimethylthiophene 1,1-dioxide were formed as a result of the oxidation. Similar behavior was noted for thiophene, 2-methylthiophene and 2-methoxythiophene. The oxidation reaction with thiophene itself was slower than the alkyl- and alkoxy-substituted thiophenes.

These observations are consistent with the behavior of thiophene 1-oxides and 1,1-dioxides which readily undergo Diels−Alder cycloaddition to form sesquioxides as depicted in Scheme 2.[23,24] The SO_x ($x = 1, 2$) formed from this cycloaddition is oxidized further by hydrogen peroxide to SO_4^{2-}, which accounts for the need for an excess of hydrogen peroxide for complete consumption of the substrate.[25] Isolation of the intermediate thiophene 1-oxides used in this study has not yet

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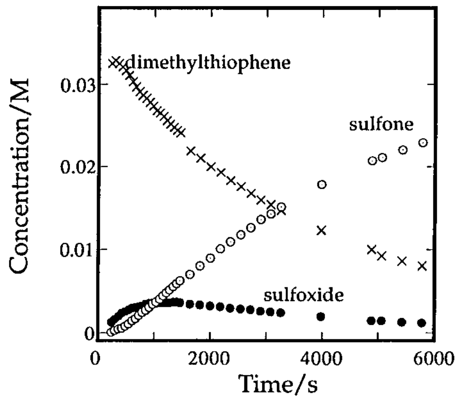
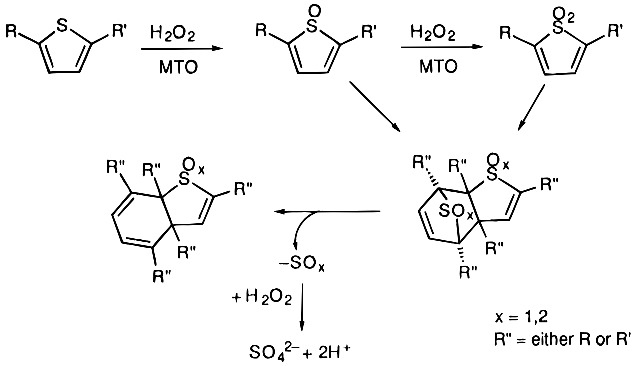


Figure 1. Reaction profile from ^1H NMR for the oxidation of 2,5-dimethylthiophene to 2,5-dimethylthiophene 1-oxide and then to 2,5-dimethylthiophene 1,1-dioxide by hydrogen peroxide in the presence of MTO. Conditions: [2,5-dimethylthiophene] = 3.5×10^{-2} M; [H_2O_2] = 2×10^{-1} M; $[Re]_T = 1.4 \times 10^{-3}$ M.

Scheme 2. Thiophene Oxidation (R = Me, R′ = Me, H; R = OMe, R′ = H)



been successful, due to their tendency to undergo cycloaddition. The experimental concentration−time profile for one experiment depicting the depletion of 2,5-dimethylthiophene, the buildup and decay of sulfoxide, and the buildup of the sulfone is shown in Figure 1.

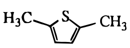
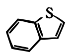
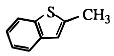
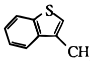
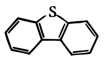
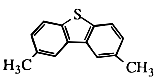
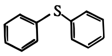
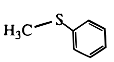
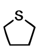
The depletion of the thiophene was fit to a single-exponential decay to estimate the rate constant for the reaction − the observed rate constant was 2.7×10^{-4} s^{-1}. Thus k_4 ~0.2 L mol^{-1} s^{-1}. The buildup and depletion of 2,5-dimethylthiophene 1-oxide were fit to a biexponential expression (eq 6) to obtain

$$\frac{[\mathrm{XO}]}{\mathrm{d}t} = \alpha \mathrm{e}^{-k_a t} + \beta \mathrm{e}^{-k_b t} \tag{6}$$

the pseudo-first-order rate constants k_a and k_b, from which k_6 might be derived and k_4 checked. The values for k_a and k_b were 2.9×10^{-4} and 1.9×10^{-3} s^{-1}. The values for k_4 and k_6 derived from this treatment are approximately 0.2 and 1.4 L mol^{-1} s^{-1}, respectively.

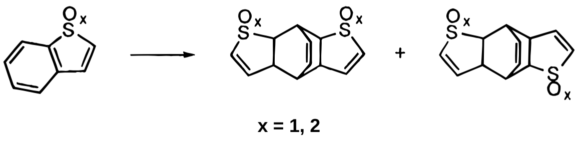
The oxidation of benzothiophene gave rise to spectral changes depicted in Figure S-1 (available in the Supporting Information). To evaluate the kinetics of the first oxidation step by **B**, excess hydrogen peroxide was used such that pseudo-first-order behavior was applicable, according to the rate law described by eq 2. The depletion of benzothiophene was monitored at 254.5 nm and the traces were fit to a single-exponential decay. The values of k_{obs} showed a linear dependence on $[Re]_T$, the slope being k_4 (see Figure S−2, Supporting Information).

Table 1. Rate Constants[a] for the Oxidation of Various Sulfur Substrates to Their Sulfoxides and Sulfones

Substrate	Rate Constants/L mol^{-1} s^{-1}			
	k_3	k_4	k_5	k_6
		~0.2 [b]		~1.4 [b]
		1.75 ± 0.03		1-2 [b]
		4.99 ± 0.05		
		9.4 ± 0.04		
	10.2 ± 0.2	21.8 ± 0.1		0.85 ± 0.03
	20.2 ± 0.9	115 ± 0.3		1.47 ± 0.01
	118[6]	32[6]		
	2650[6]	965[6]	2.8 ± 0.3	1.98 ± 0.01
	24500 ± 1030			

[a] 1:1 CH_3CN-H_2O; 0.1 M $HClO_4$; 25.0 ± 0.2 °C. [b] Values estimated from ^1H NMR reaction profiles.

The first oxidation step by species **B** was about four times faster for 2-methylbenzothiophene than for the unsubstituted benzothiophene (Table 1). Although benzothiophene 1-oxide is stable at the concentrations used in these reactions (<0.1 M), it has not yet been isolated. A dark green-brown oil was formed during evaporation of the solvent. Analysis of this oil by TLC indicated that the benzothiophene 1-oxide was no longer present. Larger scale reactions in methylene chloride, chloroform, carbon tetrachloride, acetonitrile, 1:1 acetonitrile−water (at 0.1 M $HClO_4$) and toluene showed similar behavior; viz., benzothiophene 1-oxide was formed (detected by TLC), but during solvent removal the intensely colored oil formed. Benzothiophene 1-oxide was not detected by TLC or in the ^1H NMR spectra of solutions containing these oils. An alternative oxidation procedure with tetrabutylammonium periodate and a (tetraphenylporphyrin)iron(III) complex also proved unsuccessful. Others have reported similar difficulties in its isolation using other oxidants.[26−30] The oxidized products are good dienophiles and undergo Diels−Alder self-cycloaddition as their concentrations are increased to form compounds such as those exemplified in eq 7.[31,32] Hence independent measurement of



(7)

the rate constants for the second oxidation step proved to be

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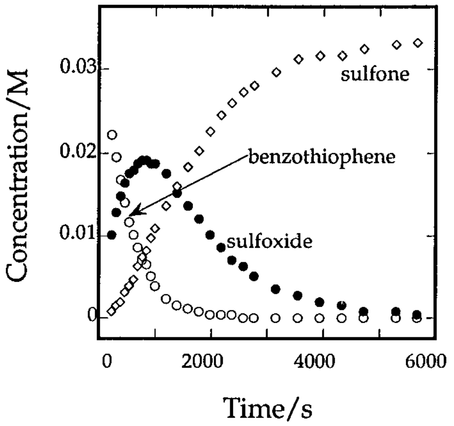

Figure 2. Reaction profile from ^{1}H NMR of the oxidation of benzothiophene. Conditions: [benzothiophene] = 3.5×10^{-2} M; $[Re]_T$ = 1.7×10^{-3} M; $[H_2O_2] = 4 \times 10^{-1}$ M.

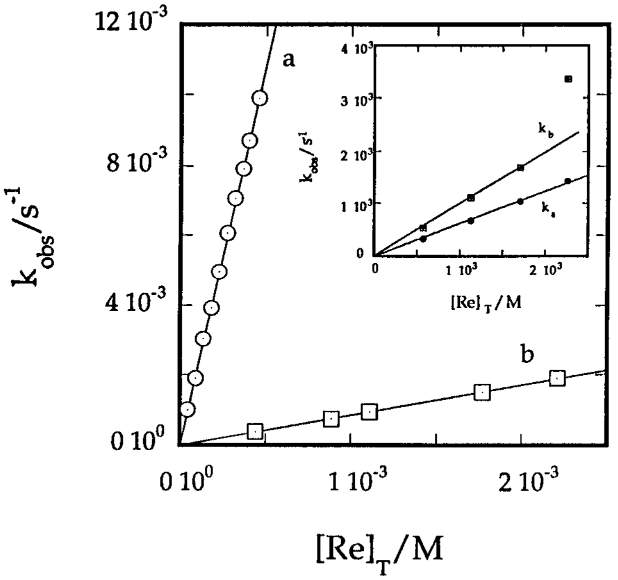

Figure 3. Dependence of the pseudo-first-order rate constants for the **B**-catalyzed oxidation of (a) dibenzothiophene (2.91×10^{-4} M) to dibenzothiophene 5-oxide by hydrogen peroxide ($[Re]_T = (4.56-0.456) \times 10^{-4}$ M; $[H_2O_2] = 9.9 \times 10^{-2}$ M; $\lambda = 282.8$ nm; slope = 21.8 ± 0.07 L mol^{-1} s^{-1}) and (b) dibenzothiophene 5-oxide (4.11×10^{-4} M) to the dioxide ($[Re]_T = (2.21-0.44) \times 10^{-3}$ M; $[H_2O_2] = 0.2$ M; $\lambda = 249.2$ nm; slope = 0.85 ± 0.03). Inset: Similar plot for both oxidation steps for the reaction of benzothiophene. Conditions: [benzothiophene] = 3.5×10^{-2} M; $[Re]_T = (2.26-0.57) \times 10^{-3}$ M; $[H_2O_2] = 4 \times 10^{-1}$ M. (One datum was ignored in the fitting.)

difficult. By monitoring the oxidation of the benzothiophene by ^{1}H NMR spectroscopy, an estimate for the rate constant for the reaction of benzothiophene 1-oxide with **B** was obtained. The reaction profile of the oxidation of benzothiophene to benzothiophene 1-oxide and then to benzothiophene 1,1-dioxide is depicted in Figure 2.

The buildup and depletion of benzothiophene 1-oxide were fitted to a biexponential expression (eq 6) to obtain the pseudo-first-order rate constants k_a and k_b, from which k_4 and k_6 might be derived. The k_a and k_b values are linearly dependent on $[Re]_T$ (see inset to Figure 3). The slopes for these plots are roughly the same, indicating that $k_a \sim k_b$. Under such circumstances, it was not possible to assign accurate values to k_4 and k_6[33,34]—it is meaningful to say only that $k_4 \sim k_6$. Since $k_4 = 1.75 \pm 0.03$ L mol^{-1} s^{-1}, then k_6 is estimated to be ~1−2 L mol^{-1} s^{-1} also.

The oxidation reactions of dibenzothiophenes were then studied, to limit the cycloaddition reactions and also to examine the effect of benzannulation on the relative rates of each oxidation step. The oxidized products were more stable than the thiophenes annd benzothiophenes studied here, and their isolation was straightforward using silica gel chromatography. Good yields of the corresponding oxide were achieved using 1 equiv of hydrogen peroxide per substrate, along with small amounts of the unreacted substrate and the dibenzothiophene 5,5-dioxide. Excess hydrogen peroxide in the presence of MTO produced more of the dioxide. The oxide and the dioxide products were characterized by ^{1}H NMR and by UV/vis spectroscopy. The kinetics for both oxidation steps could therefore be examined independently.

The spectral changes accompanying both steps of oxidation of dibenzothiophene show clean isosbestic points; see Figure S-3 (Supporting Information). The spectral changes for the analogous 2,8-dimethyldibenzothiophenes were similar. For both compounds, the studies of the reactions by **B** were carried out with excess hydrogen peroxide, so that pseudo-first-order behavior would prevail. The kinetic traces were fitted to a single-exponential function. The observed rate constants varied linearly with $[Re]_T$ from which the second-order rate constants for the reactions with **B** could be derived. Figure 3a shows dibenzothiophene oxidation by **B**. The values for the rate constants are summarized in Table 1.

The second oxidation step using **B** was also examined using conditions that would have given rise to pseudo-first-order behavior. The observed rate constants for both dibenzothiophene 5-oxides varied linearly with $[Re]_T$. Figure 3b depicts the example for the dibenzothiophene 5-oxide oxidation. The rate constants for the oxidation of both dibenzothiophene 5-oxides by **B** are listed in Table 1.

Oxidation of Dibenzothiophenes with A. The rate constants for the oxidation by **A** were determined with $k_3[\mathbf{X}] \gg k_2[H_2O_2]$. In the oxidation of the dibenzothiophenes, the initial rates were determined with varying $[Re]_T$. The initial rate, v_i, for each trace was calculated from the initial rate of the absorbance change accompanying the loss of dibenzothiophene (eq 8),

$$v_i = \frac{1}{b\Delta\epsilon_\lambda} \times \frac{\Delta \mathrm{Abs}}{\Delta t} \qquad (8)$$

where $\Delta\epsilon$ is the difference in the molar absorptivities of the reactants and the products at wavelength λ, and b is the optical path length. The initial rate varied linearly with $[Re]_T$; the example of dibenzothiophene is supplied in the Supporting Information, Figure S−4. The rate constant was derived from eq 1, using the values given for other rate constants. The values of k_3 are summarized in Table 1.

Oxidation of Other Sulfoxides. For comparative purposes, the oxidation of methyl phenyl sulfoxide by hydrogen peroxide in the presence of MTO was examined. The rate of oxidation by **B** was determined by monitoring the absorbance changes at 244 nm with varying $[Re]_T$. The traces were fit to a single-exponential decay. Values of k_{obs} varied linearly with $[Re]_T$, and the rate constant for the oxidation by **B** was found to be $k_4 = 1.98 \pm 0.01$ L mol^{-1} s^{-1}. At higher $[Re]_T$:$[H_2O_2]$ ratios the traces did not exhibit first-order decay, indicating that the

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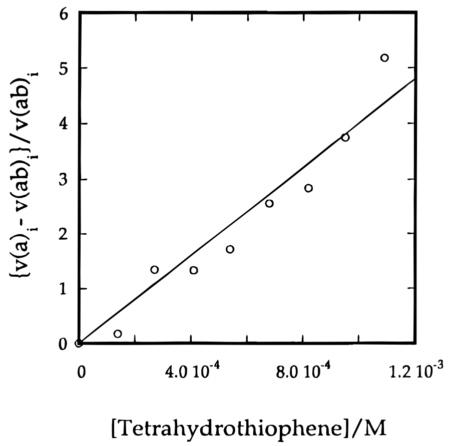


Figure 4. Dependence of the ratio of the initial rates defined in eq 12 on [tetrahydrothiophene]. Conditions: [thioanisole] = 1×10^{-3} M; [tetrahydrothiophene] = $(1.36-0.14) \times 10^{-3}$ M; $[\mathrm{Re}]_T = 6.0 \times 10^{-5}$ M; $[H_2O_2] = 1 \times 10^{-2}$ M. a = thioanisole; ab = both together.

reaction with **A** contributed to the oxidation of the substrate. Under these conditions, the initial rate method was used to derive the rate constant, k_5, for the oxidation by **A** (Table 1).

The oxidation of tetrahydrothiophene by **A** was studied to compare the effect of aromaticity on the rates of oxygen atom transfer to the sulfur atom. Since the oxidation of tetrahydrothiophene did not give rise to significant changes in the absorption spectrum, a competition method was employed to examine this reaction. This method was similar to that described previously for the MTO-catalyzed oxidation of other aliphatic sulfides using hydrogen peroxide.[6] The competing oxidant used was thioanisole, whose $k_3 = 2.65 \times 10^3$ L mol^{-1} s^{-1}.[6] Equations 9−11 describe this system.

$$\mathrm{MTO} + \mathrm{H_2O_2} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{A} + \mathrm{H_2O} \tag{9}$$

$$\mathbf{A} + \text{thioanisole} \xrightarrow{k_{3a}} \mathrm{MTO} + \text{methyl phenyl sulfoxide} \tag{10}$$

$$\mathbf{A} + \text{tetrahydrothiophene} \xrightarrow{k_{3b}} \mathrm{MTO} + \text{tetrahydrothiophene 1-oxide} \tag{11}$$

Equation 12 describes the relationship between the initial rates and the rate constants, where $(v_a)_i$ is the initial rate of the reaction in the absence of tetrahydrothiophene and $(v_{ab})_i$ represents the initial rate of the reaction when both thioanisole and tetrahydrothiophene are present.

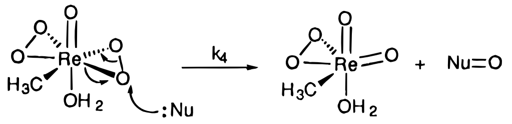
$$\frac{(v_a)_i - (v_{ab})_i}{(v_{ab})_i} = \frac{k_{3b}[\text{tetrahydrothiophene}]}{k_{-1} + k_{3a}[\text{thioanisole}] + k_1[\mathrm{H_2O_2}]} \tag{12}$$

The kinetic traces for the oxidation of tetrahydrothiophene in the presence of thioanisole is shown in Figure S−5 supplied in the Supporting Information, for a range of tetrahydrothiophene concentrations. The initial rate $v_{(ab)i}$ shows a linear dependence on [tetrahydrothiophene] (Figure 4), and the data were fit to eq 12 to deduce k_3 for the oxidation of tetrahydrothiophene by **A** (Table 1). The value for k_3 derived in this way is comparable to those k_3 values reported for simple aliphatic sulfides.[6]

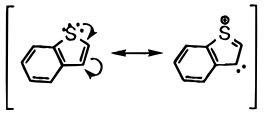
Discussion

The MTO-catalyzed oxidation of thiophene derivatives by hydrogen peroxide can be conducted to allow complete oxidation to the sulfone by way of a sulfoxide (thiophene oxide) intermediate. The rate constants (k_3 and k_4) for the **A**- and **B**-catalyzed reactions for the formation of the thiophene oxides were 2−4 orders of magnitude smaller than those[6] for sulfides where the sulfur atom is not part of an aromatic heterocycle. This pattern is consistent with a mechanism where the substrate behaves as a nucleophile that attacks the electrophilically-activated peroxide coordinated to rhenium (Scheme 3).[5,16,17] Compared to a sulfur atom in "aliphatic" sulfides, the sulfur atom in thiophenes is considerably less nucleophilic, since its electron pairs participate in the aromatic delocalization,[23] and are therefore less available for donation.

Scheme 3. Nucleophilic Attack at a Coordinated Peroxide of **B**



The rate constants for the sulfoxide formation also increase with the degree of benzannulation, which can be attributed to the increase in the nucleophilicity of the sulfur atom.[35,36] The rate constants associated with the first oxidation step were larger for methyl−substituted thiophenes. Similar observations have been reported for alkenes[11] and anilines,[10] where electron-donating substituents enhance the oxidation rates. The larger k_4 values for the 3-methylbenzothiophene compared to the 2−methylbenzothiophene can be explained using resonance stabilization arguments. Electron-donating substituents at the 3-position in benzothiophenes enhance the nucleophilicity of the sulfur atom, since the electron density distribution favors the structures on the left hand side of eq 13.



(13)

For the first oxidation step, the following reactivity trend is: $R_2S > PhSR > Ph_2S \sim$ 2,8-dimethyldibenzothiophene > dibenzothiophene > 3-methylbenzothiophene > 2-methylbenzothiophene > benzothiophene > R$_x$thiophene > thiophene (for R = alkyl, x = 1, 2, and Ph = phenyl, *p*-methylphenyl, *p*-chlorophenyl, *p*-aminophenyl).

Thermodynamic data may be used to support the conclusion that the first oxidation step proceeds by the nucleophilic attack of the sulfur atom of a given thiophene on **A** or **B**. The relative equilibrium constants of binding of various thiophenes to an organoruthenium complex have been accurately evaluated.[36−38] The values of K apply to the reaction

$$[\mathrm{CpRu(CO)(PPh_3)T_1}]^+ + \mathrm{T_2} = [\mathrm{CpRu(CO)(PPh_3)T_2}]^+ + \mathrm{T_1} \tag{14}$$

in which T_1 and T_2 represent two different thiophenes. This allows the definition of a rigorous scale of Lewis basicities. Since kinetic nucleophilicities are often related to thermodynamic basicities, it is reasonable to explore such a correlation. For the four compounds where both parameters were determined, Figure 5 shows that this is a valid relation, supporting the proposed mechanism for nucleophilic attack.

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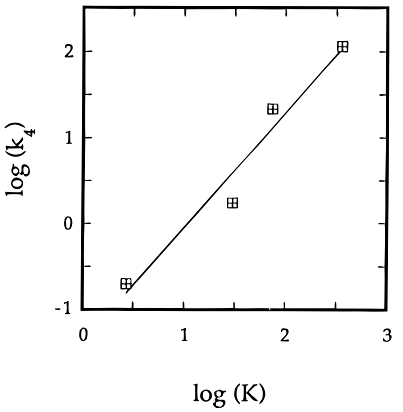
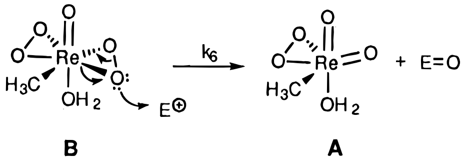


Figure 5. Linear free energy correlation of nucleophilicity vs Lewis basicity. The values of k_4 for four thiophene derivatives are correlated with their binding constants according to eq 14. The four compounds are the first, second, fifth, and sixth entries in Table 1.

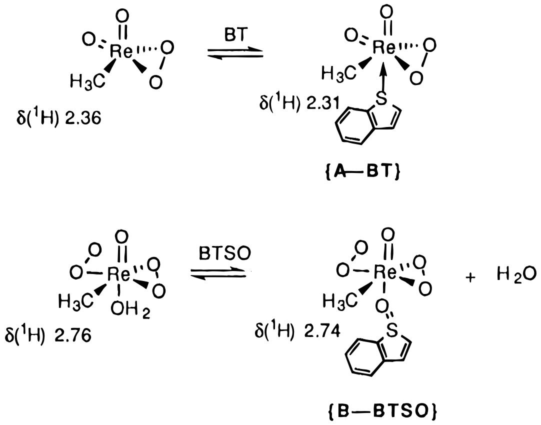
Scheme 4. Attack by Coordinated Peroxide of **B** on an electrophile, E^+



The values of k_6 for the oxidation of the sulfoxides are roughly the same. A precise determination of k_6, however, could not be extended to the thiophene 1-oxides and benzothiophene 1-oxides owing to the difficulty their isolation. However, the relative rates of the first oxidation step for 2,5-dimethylthiophene and benzothiophene stand in the ratio ~1:5 from the ^{1}H NMR data. The rates of oxidation appear to be the same for 2,5-dimethylthiophene 1-oxide and benzothiophene 1-oxide and are comparable with the k_6 values for the dibenzothiophene 5-oxides and the methyl phenyl sulfoxide. Lastly, the effect of the methyl substituents on the oxidation of dibenzothiophene 5-oxides is less pronounced; only a modest rate increase was found for the 2,8-dimethyldibenzothiophene 5-oxide oxidation, in contrast to the first oxidation step, where a 6-fold enhancement was noted.

The similar rates of oxidation of all of the sulfoxides might signal a change in the oxygen-transfer mechanism. Possibly, the substrate no longer behaves like a nucleophile, but is itself attacked by the coordinated peroxide (Scheme 4). Such an argument has been presented for the Baeyer-Villiger oxidation of cyclic ketones[18,19] on the basis of a reversal in direction of the substituent effects and for the reaction of thianthrene 5-oxide.[19]

Scheme 5. Substrate−Catalyst Adducts at High [Benzothiophene]:$[\mathrm{Re}]_T$



The question arises, however, as to whether the electron-deficient Re(VII) center would release sufficient electron density to allow a peroxide group coordinated to it to behave nucleophilically. On the other hand, it is curious that systems appearing to undergo this "electrophilic-attack" mechanism involve substrates having an oxygen atom. The oxygen could conceivably coordinate to the rhenium center of **B**. Such species might be the origin of the new peaks in the ^{1}H NMR spectra of reactions where the concentration of the substrate is high compared to that of $[\mathrm{Re}]_T$. When the ratios [benzothiophene]:$[\mathrm{Re}]_T$:$[\mathrm{H_2O_2}]$ = 47:1:97 were used, two new peaks in the ^{1}H NMR spectrum at 2.74 and 2.31 ppm were detected, but only when hydrogen peroxide was present. The peak at 2.31 ppm disappeared as the benzothiophene was oxidized, suggesting that this peak can be attributed to benzothiophene coordinated to rhenium. Because its peak lies alongside that of **A**, it is tentatively attributed it to a {benzothiophene−$\mathrm{Re}_\mathbf{A}$} adduct (A−BT in Scheme 5). Since the second new signal at 2.74 ppm, near that for **B**, grew during the period in which benzothiophene 1-oxide increased, it is tentatively attributed to a {benzothiophene 1-oxide−$\mathrm{Re}_\mathbf{B}$} adduct (BTSO−B in Scheme 5). An experiment with the reversed order of mixing was carried out, to check any influence of the order in which **A** and **B** form relative to the overall reaction; changing the order of mixing gave the same result. Similar behavior has been observed for the oxidation of cyclobutanone.[19] In order to satisfy the coordination requirement about the rhenium center, this behavior might be rationalized if the labile water ligand of **B** *trans* to Re═O[3,16] is displaced by the substrate. The coordination of the substrate through its oxygen atom might make the rhenium center less electron deficient, allowing the peroxide residue to behave as a nucleophile for either intramolecular attack on the coordinated substrate or intermolecular attack on a nearby substrate.

Acknowledgment. This research was supported by the U. S. Department of Energy, Office of Basic Energy Sciences, Division of Chemical Sciences under contract W-7405-Eng-82. The gift of 2-methylbenzothiophene and 2,8-dimethyldibenzothiophene by J. Benson and R. J. Angelici is greatly appreciated. We also acknowledge helpful discussions with Prof. Angelici concerning the linear free energy correlation presented herein.

Supporting Information Available: Figures showing the spectral changes for the oxidation of benzothiophene, the variation of the observed rate constant with $[\mathrm{Re}]_T$ for the oxidation of benzothiophene, spectral changes for the oxidation of dibenzothiophene and dibenzothiophene 5-oxide, the dependence of the initial rate of oxidation of dibenzothiophene 5-oxide, and the absorbance changes for the oxidation of thioanisole in competition with tetrahydrothiophene (5 pages). See any current masthead page for ordering information and Internet access instructions.

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