Effects of Pyridine and Its Derivatives on the Equilibria and Kinetics Pertaining to Epoxidation Reactions Catalyzed by Methyltrioxorhenium

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Abstract: The coordination of substituted pyridines to MTO (methyltrioxorhenium) is governed by both electronic and steric effects. For example, the binding constant of pyridine to MTO is 200 L mol^{-1}, whereas that of the better donor 4-picoline is 730 L mol^{-1} and that of the sterically encumbered 2,6-di-*tert*-butyl-4-methylpyridine is <1 L mol^{-1}. A Hammett reaction constant $\rho = -2.6$, derived from meta- and para-substituted pyridines, applies to this equilibrium. Pyridine stabilizes the MTO/H_2O_2 system and accelerates the epoxidation of α-methylstyrene. The steady-state concentration of MTO is decreased during the catalytic epoxidation reaction by coordinating a pyridine derivative, thus stabilizing the MTO/H_2O_2 system against irreversible decomposition. Pyridine as a Lewis base accelerates the generation of the peroxorhenium catalysts, whereas coordination of pyridine to the diperoxorhenium complex appears responsible for the acceleration of epoxidation. Ultimately, however, it is the Brønsted basicity of pyridine that lowers the activity of hydronium ion, reducing the rate of epoxide ring opening.

Introduction

This study was prompted by the recent discovery that pyridines greatly enhance the selectivity, and mildly enhance the rate, of epoxide formation from the reaction of alkenes with hydrogen peroxide, catalyzed by MTO (methyltrioxorhenium).[1−3] There are several distinct issues, the ones addressed here being the following: (1) the kinetics and equilibrium for the two stages of complexation of H_2O_2 and MTO; (2) the complexation of pyridines to MTO and other matters relating to the Lewis acidity of MTO; (3) the ternary system, peroxide/pyridine/MTO; and (4) the kinetics of epoxidation reactions under various conditions, inevitably accompanied by the cooxidation of the pyridine.

Experimental Section

Materials and Techniques. Methyltrioxorhenium, CH_3ReO_3 (Aldrich), H_2O_2 (30%, Fisher, standardized by iodometric titration), pyridine and its derivatives (Aldrich), α-methylstyrene (Aldrich), boron trifluoride dimethyl etherate ($(CH_3)_2O{\cdot}BF_3$, Aldrich), trimethyl borate ($B(OCH_3)_3$, Aldrich), CD_3NO_2 (Aldrich), and CD_3CN (CIL) were used as received. High-purity H_2O was obtained by passing laboratory distilled water through a Millipore-Q water purification system. The concentrations of pyridine, its derivatives, boron trifluoride dimethyl etherate, and trimethyl borate were measured volumerically.

A Bruker DRX-400 spectrometer was used to record the ^1H NMR spectra at 400.13 MHz. The ^1H chemical shifts were measured relative to residual ^1H resonance in the deuterated solvents, CD_3NO_2 ($\delta = 4.33$ ppm) and CD_3CN ($\delta = 1.94$ ppm). UV−vis measurements were carried out with a Shimadzu UV-3101PC spectrophotometer.

Determination of Equilibrium Constants. The binding constants between MTO and substituted pyridines were measured by the use of a ^1H NMR spectrometer. Generally a CD_3NO_2 solution containing ∼10 mM MTO was titrated with a concentrated (∼10 M) solution of a pyridine derivative. No extra H_2O was added in these measurements. The observed chemical shift for the CH_3 protons of rhenium complexes (a concentration-weighted average) was recorded after each addition of the pyridine. For solid pyridine derivatives, such as pyridine-*N*-oxide and 3-cyanopyridine, a stock solution (>3 M) was prepared in CD_3NO_2. The titration was generally carried out until [MTO·L] > 90%$[Re]_T$. Since concentrated pyridine was used, the total volume of the solution varied within 2−5% and thus $[Re]_T$ changed only slightly during the titration proceses, particularly for the pyridines with large binding constants. The concentration of uncomplexed ligand, as given in eq 5, was calculated by difference, assuming that $[Re]_T$ is constant.

The binding constants for BF_3 and $B(OMe)_3$ with pyridine were determined in the presence of MTO by the use of the ^1H NMR technique. The weighted-average chemical shift of the rhenium species was observed directly, and the concentration of free pyridine was calculated from the known values for K_{Py}, δ_{MTO}, and $\delta_{MTO{\cdot}Py}$. The concentration of $BX_3{\cdot}Py$ was obtained from the calculated concentration of MTO·Py. The concentration of BX_3 was taken as the difference $[BX_3]_0 - [BX_3{\cdot}Py]$. The equilibrium constants could then be calculated.

Kinetic Studies. The epoxidation of α-methylstyrene by the MTO/H_2O_2 system in the presence of pyridine derivatives was followed by ^1H NMR. A solution with desired concentrations of α-methylstyrene and pyridine derivatives was added into a preequilibrated CD_3CN solution of MTO and H_2O_2 right before the kinetic data were collected. The ortho-protons of pyridine (8.58 ppm) and pyridine-*N*-oxide (8.26 ppm), and the CH_3 protons of α-methylstyrene (2.16 ppm) and its epoxide (1.65 ppm) were integrated. The intensities were then converted to concentrations based on the known initial concentration and mass conservation law. The concentration−time profile for the first 200 s thus obtained is linear, and the slope is the initial rate (mol L^{-1} s^{-1}).

Kinetic studies in the absence of pyridine derivatives were carried out spectrophotometrically under these conditions: 0.070 mM α-methylstyrene, 0.50 M H_2O_2, and 3.4−28 mM Re_T. The absorbance loss at 240 nm, corresponding to the disapperance of α-methylstyrene,

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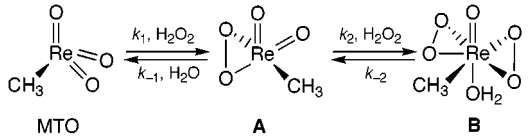
was followed. Quartz cuvettes with an optical path length of 0.010 cm were used to accommodate the use of a large excess of diperoxorhenium species. The slope of the pseudo-first-order plot (k_ψ vs [**B**]) yields the second-order rate constant of 0.086 ± 0.002 L mol^{-1} s^{-1}. The control experiment was also carried out by the use of a ^{1}H NMR spectrometer under the following conditions: [α-methylstyrene] = 1.3 mM, [Re$_T$] = 26 mM, and [H_2O_2] = 0.83 M. The second-order rate constant of 0.060 ± 0.007 L mol^{-1} s^{-1} was obtained.[4]

Kinetic data for the formation of **A** and **B** in methanol were collected by following the absorbance change at 320 (the maximum for **A**) or 360 nm (the maximum for **B**) at 25 °C and [H_2O] = 0.60 M. The biphasic kinetic traces were evaluated as described previously.[5]

Results and Interpretation

MTO−H_2O_2 Interactions in the Absence of Pyridine. Two reactions occur, representing the stepwise complexation reactions, giving rise to **A**, the monoperoxo rhenium complex, and to **B**, the diperoxo complex. The latter species has been well-characterized as $(CH_3)Re(O)(\eta^2\text{-}O_2)_2(H_2O)$, even to the point of a single-crystal diffraction study.[6] **A**, on the other hand, has been characterized only by its ^{1}H NMR and optical spectra, being more elusive owing to the pattern of equilibrium constants, $K_2 > K_1$. To date, these reactions have been studied in methanol,[7] acetonitrile,[5] 1:1 aqueous acetonitrile,[8] and aqueous solution;[9,10] aqueous and semiaqueous solutions were necessarily acidified to minimize MTO decomposition.[11] The rate constants are defined in eq 1, and the equilibrium constants follow from them: $K_1 = k_1/k_{-1}$, $K_2 = k_2/k_{-2}$. The concentration of water is incorporated neither in the values of the reverse rate constants nor in the definitions of the equilibrium constants, because water coordination to **A**, although unlikely,[11] cannot be ruled out absolutely.



(1)

The equilibrium constants are always considerably larger in organic solvents than in aqueous or semiaqueous ones. That trend might arise from the release of water in the coordination reactions, but it is evident in K_2 values as well, where there is no release of water if the extent of hydration of **A** is correctly described in eq 1. The polarity of the medium provides the more likely explanation. The most notable effect in these equilibrium constants, however, is the finding that $K_1 < K_2$ in all of solvents examined. This is an example of a cooperativity effect, and it must signal that the structural rearrangement accompanying conversion of MTO to **A** provides a structure than can coordinate peroxide to yield **B** with a greater spontaneity. Although we have no data to defend this premise, it is tempting to suggest that the gain of multiple bond character in a single Re═O unit poses one thermodynamic barrier and that it occurs to the greatest extent in the second stage.

Table 1. Comparisons of the Thermodynamic and Kinetic Data of the MTO/H_2O_2 System (Equation 1) in Organic ([H_2O] = 0.6 M) and Aqueous Media

solvent	dielectric constant[a]	K_1/M^{-1}	K_2/M^{-1}	k/(10^{-2} L mol^{-1} s^{-1} k_1	k_2
CD_3NO_2	38.6	NA	1300[b]	7.4[b]	1.4[b]
CH_3CN	37.5	210[c]	700[c]	10[c]	1.0[c]
CH_3OH	32.6	261[d]	814[d]	68[b]	1.8[b]
H_2O	78.5	7.7[e]	145[e]	8000[e]	520[e]
1:1 H_2O/CH_3CN	NA	13[f]	136[f]	3250[f]	105[f]

[a] Angelici, R. J. *Synthesis and Technique in Inorganic Chemistry*; 2nd ed.; University Science Books: Mill Valley, CA, 1986; p 215. [b] This work. [c] Reference 5. [d] Reference 7. [e] Reference 9. [f] Reference 8.

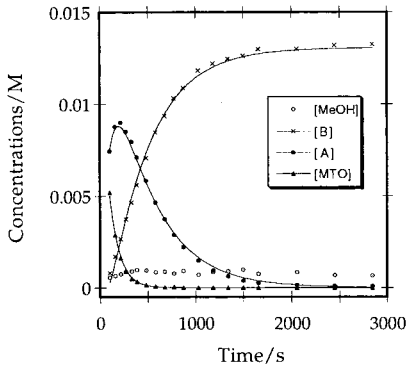


Figure 1. Kinetic curves depicting the buildup of **A** and **B** and the loss of MTO. Also shown is the buildup of methanol, which occurs only during the stage of MTO loss. Conditions: 13.9 mM MTO; 144 mM H_2O_2; 0.6 M H_2O at 296 K. The decrease in MTO followed first-order kinetics, $k = 9.57 \times 10^{-3}$ s^{-1}. The curve for **A** was fit to biphasic kinetics, fixing the one k at 9.57×10^{-3} s^{-1} and floating the other, $k = 2.38 \times 10^{-3}$ s^{-1}. The curve for **B** was also fit to biphasic kinetics, and the second rate constant was refined to $k = 2.42 \times 10^{-3}$ s^{-1}.

We find we must retract the values of the rate constants for peroxorhenium formation (k_1, k_2) and dissociation (k_{-1}, k_{-2}) reported for these reactions in methanol.[7] Only later did we realize these values were unrealistically large ($\times 10^2$−10^3) as compared to other solvents. An examination of the original notebooks brought out the fact that these kinetic determinations were carried out in solutions containing *N*,*N*-dimethylaniline, the substrate for the subsequent catalysis. As we show here for pyridine, peroxorhenium formation is accelerated by bases; this effect is the reason that the values must now be revised. The new values in methanol (Table 1) are in line with rate constants in other organic solvents.

Since the effect of pyridine on the epoxidation reactions was examined in nitromethane,[1] we evaluated the equilibrium and kinetic constants in that solvent by ^{1}H NMR. At this particular set of concentrations, 13.9 mM MTO and 144 mM H_2O_2, the resonances of all three rhenium species were observable: MTO, δ 2.79 ppm; **A**, δ 2.82 ppm; and **B**, δ 2.87 ppm. These chemical shifts move slightly upfield with increasing [H_2O_2], during which [H_2O] necessarily increases as well. The kinetic profiles of these species are displayed in Figure 1.

Most of the methanol was formed in the first 500 s, when MTO was present in the solution. Although a significant amount of **A** remained at that point, practically no more methanol was produced. This result agrees with the deactivation

(4) The quality of the NMR kinetic data with 1.3 mM α-methylstyrene was not as good as those with 0.32 M α-methylstyrene owing to the error associated with the integration of small signals. As pointed out by one reviewer, the initial rate method using the NMR spectrometer could cause a problem, particularly when the signals of reactants and products are not fully resolved. Reasonable kinetic data could be obtained if one integrates the signals of products rather than those of the reactants and uses an internal standard with an intensity similar to that of the products.

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pathway dominated by a reaction in which MTO, but not **A** or **B**, is the reactant:[11]

$$CH_3ReO_3 + HO_2^- \rightarrow ReO_4^- + MeOH \qquad (2)$$

Also, the H^+ that results from eq 2 with the net reaction written for H_2O_2 will increase the acidity of the solution. The increase in acidity would prevent the reaction of **A** with OH^-, that being the kinetically indistinguishable alternative to reaction 2. ^{1}H NMR studies in CD_3NO_2 gave rate constants similar to those obtained in CD_3CN. A summary of the rate and equilibrium constants is given in Table 1.

Adduct Formation between MTO and Pyridines. Ligands, especially those with oxygen or nitrogen donor atoms, form Lewis acid−base adducts with MTO.[12−14] Although both sites of bidentate ligands can bind to the rhenium center to form a distorted octahedral complex, usually only a single monodentate ligand coordinated to the rhenium atom when a monodentate ligand was used. What is the effect of ligand binding on reactivity and selectivity? Selectivity enhancement by the addition of Lewis bases has been observed previously, but catalytic reactivity may be reduced.[15] The effect of pyridine is different: an excess of pyridine over MTO not only increases the selectivity toward epoxide but also accelerates its formation.[1]

A concurrent effect of pyridine arises from its Brønsted basicity. As cited earlier, MTO is much less stable the more neutral or basic the solution becomes. Possible mechanisms for the base-mediated deactivation of the MTO/H_2O_2 system have been proposed on the basis of kinetic studies in aqueous systems.[11] Thus complex formation between pyridine and MTO needs to be explored.

The interaction between MTO and several pyridines was studied by ^{1}H NMR techniques. Only one sharp singlet from CH_3ReO_3 was observed with pyridine/rhenium $\leq$ 1; this resonance remained sharp and shifted upfield with more pyridine. A fully averaged signal was observed even at −40 °C in CD_2Cl_2, which implies that the suggested equilibrium

$$MTO + L \overset{K}{\rightleftharpoons} MTO{\cdot}L \qquad (3)$$

remains rapid relative to the NMR time scale even at the low temperature. Because of that, the observed chemical shift is a concentration-weighted average of the two

$$\delta_{obs} = \frac{\delta_{MTO} + K[L]\delta_{MTO\cdot L}}{1 + K[L]} \qquad (4)$$

where [L] is the free (uncomplexed) concentration of pyridine or other ligand, and is related, with $\xi = 1 + K[Re]_T - K[L]_T$, to the total (starting) concentrations by

$$L = \frac{\sqrt{\xi^2 + 4K[L_T]} - \xi}{2K} \qquad (5)$$

The data fit well to eq 4, affording these values of the parameters: $K = 200 \pm 6$ L mol^{-1} and $\delta_{MTO\cdot L} = 1.86$ ppm in CD_3NO_2 at 296 K. The correlation between its chemical shift and $[Py]_T$ in CD_3NO_2 is shown in Figure 2. The chemical shift of a solution of MTO in pyridine-d_5 is 1.87 ppm, consistent with the fitting result and indicating that only one pyridine is likely coordinated to MTO.

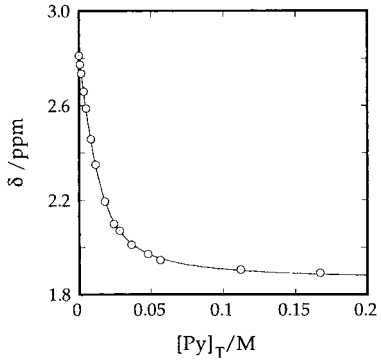

Figure 2. Chemical shift varying with the concentration of pyridine. Conditions: $[MTO]_0 = 14$ mM; 296 K in CD_3NO_2. The line through the data is the fit according to eq 4.

Table 2. Equilibrium Constants for the Coordination of Substituted Pyridines and Related Species to MTO in CD_3NO_2 at 296 K

L	σ_m or σ_p	K/(L mol^{-1})	$\delta_{MTO\cdot L}$/ppm
3-cyanopyridine	0.56	7.21 ± 0.14	2.04 ± 0.007
3-bromopyridine	0.39	23.3 ± 0.2	1.96 ± 0.002
3-chloropyridine	0.37	21.8 ± 0.3	1.95 ± 0.003
4-nicotinaldehyde	0.22	36.8 ± 0.9	1.96 ± 0.006
3-phenylpyridine	0.06	156 ± 4	1.91 ± 0.005
pyridine	0	200 ± 6	1.86 ± 0.005
3-methylpyridine (3-picoline)	−0.07	254 ± 11	1.82 ± 0.007
4-methylpyridine (4-picoline)	−0.17	732 ± 20	1.84
2-chloropyridine		<1	
2,6-di-*tert*-butyl-4-methylpyridine		<1	
pyridine-*N*-oxide		210 ± 4	1.87 ± 0.003
2,6-dimethylpyridine (2,6-lutidine)		<1	
2,6-dimethylpyrazine		20 ± 1.5	1.95 ± 0.03

Derivatives of pyridine, 2-Cl, 3-Cl, 3-CN, 3-Me, 4-Me, 2,6-di-Bu^t-4-Me, also interact with MTO to a greater or lesser extent. These data were also treated by the same procedure used for pyridine. The resulting parameters are summarized in Table 2.

As the data show, the equilibrium constants are sensitive to both steric and electronic effects. Those with steric hindrance, such as 2-Cl and 2,6-di-Bu^t-4-Me, interact only slightly with MTO. On the other hand, electron-rich pyridines, such as 3-Me and 4-Me, are strongly favored over electron-withdrawing ones, such as 3-Cl and 3-CN. An attempted linear free energy relationship (LFER) correlation according to the Hammett equation is displayed in Figure 3. The slope of the line of log (K/K_0) vs σ is −2.6 ± 0.1, which is the reaction constant for this equilibrium.

A related correlation is an attempt to correlate the chemical shift of the adduct, $\delta_{MTO\cdot L}$, with Hammett's σ. Figure 3 also shows a decent but not excellent correlation with the slope of the line being 0.26 ± 0.04. The quality of the correlation and the small value of the slope no doubt reflect the small spread in chemical shifts along the series of substituents. The significant point, however, is this: the trends in K and in δ vary sensibly with the substituent constants and in the direction consistent with the interaction depicted in eq 3.

Other Ligands. The data show that pyridine-*N*-oxide, PyO, binds with MTO as strongly as pyridine does. The Lewis acid−base interactions of these two with MTO are clearly different than those with H_3O^+, where there is a four-order-of-magnitude

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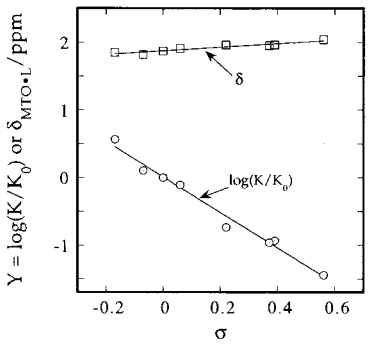

Figure 3. Correlation of the equilibrium constants with the Hammett substituent parameter σ. The reaction constant is -2.6 ± 0.1. The variation of the chemical shift of the MTO·L complex with the Hammett substituent parameter σ is also shown.

difference ($pK_b = 8.75$ and 13.2 for Py and PyO, respectively).[16] The oxophilic character of Re(VII) and less steric interference of PyO possibly account for the similar binding constants with MTO. The ^{17}O NMR data for the MTO adducts with quinuclidine and quinuclidine-*N*-oxide also suggest a comparable equilibrium constant between quinuclidine and quinuclidine-*N*-oxide with MTO.[17]

The association between MTO and 2,6-dimethylpyrazine is much stronger than with its pyridine analogue, Table 2. It is worth noting that the H−D exchange between CH_3ReO_3 and CD_3NO_2 becomes faster as a stronger Lewis base is used. Significant incorporation of deuterium into MTO occurred in an hour when 2,6-dimethylpyridine, the strongest base so far used, was employed.

Lewis Acidity of MTO. MTO is believed to be a hard Lewis acid on the basis of its strong interactions with N- and O-donor ligands and its weak interaction with S-donor ligands. The negative reaction constant for the pyridine equilibria, −2.6, indicates that a positive charge develops on the pyridine nitrogen in the adduct as compared with the free molecule. As expected, the Re(VII) center acts as an electron acceptor, attracting electrons upon coordination.

To put the Lewis acidity of MTO on an external scale, it is necessary to make comparisons with another well-known acid; BF_3 was chosen for this purpose. Against that standard, complexation with pyridines, eq 6, was also chosen. Although

$$BF_3 + L \overset{K_B}{\rightleftharpoons} BF_3{\cdot}L \qquad (6)$$

values of K_B have not been reported, the values of ΔH are known for three substituted pyridines in nitrobenzene.[18] With the reasonable assumption that the ΔS values are the same, the quantity (K/K_0) could be obtained. The Hammett correlation gave $\rho = -2.31 \pm 0.25$. The same procedure for BMe_3, with the use of the calorimetric values of ΔH,[19] also gave $\rho = -2.3$. The same values of ρ appear to arise from the extensive and offsetting π bonding in trifluoroborane, which reduces its acidity significantly, the π component being lost in adduct formation. A value of $\rho = -1.8$ has been reported for the coordination of pyridine derivatives to OsO_4 in acetonitrile.[20] Toward the proton, pyridines have a significantly more negative reaction constant, $\rho = -5.2 \pm 0.3$.

This approach is still lacking, however, in that a reaction's sensitivity to changes in substituent is not synonymous with its thermodynamic driving force. For that reason, we directly studied the binding constants of pyridine with BF_3 and $B(OMe)_3$ with ^1H NMR. The same treatment presented in eq 4 gives these values for Py of K/L mol^{-1}: BF_3 3.3×10^4; $B(OMe)_3$, 1.4×10; MTO, 2.00×10^2; OsO_4, 3.4×10. Although the binding constant for MTO was determined in nitromethane, it can be compared with other *K*'s in acetonitrile, because other equilibrium and kinetic parameters are similar, as given in Table 1.[21] Clearly, MTO is a stronger Lewis acid toward pyridine derivatives than OsO_4.

Effect of H_2O on the Formation of A and B. With 14 mM Py′ (Py′ = 2,6-di-*tert*-butyl-4-methylpyridine) and 1 mM MTO, the observed rate constant for the formation of **B** at 87 mM H_2O_2 varied inversely with [H_2O] in the range 0.3−1.1 M H_2O. This trend is opposite to that in the absence of bases, where added water accelerates the formation of **B** and more so that of **A**. The effect of water with Py′ is not obvious. It is reminiscent of the retarding effect of water on the formation of **A** and **B** in methanol and acetonitrile, found during studies of the oxidation of anilines with MTO/H_2O_2.[7]

MTO/H_2O_2 System in the Presence of Pyridine. If one regards the binding of pyridine and of hydrogen peroxide as separate and sometimes competing reactions, the latter is distinctly more favorable, as the equilibrium constants in Tables 1 and 2 clearly show. Indeed, the yellow color characteristic of **B** rapidly developed when H_2O_2 was added into the colorless solution of MTO·Py in nitromethane or acetonitrile. Interestingly, and important to the catalytic cycle, that color developed more rapidly from MTO·Py than from MTO alone. This phenomenon was more pronounced at low [H_2O_2].

The binding constants for MTO are nearly the same for pyridine ($K = 200$ L mol^{-1}) and pyridine-*N*-oxide ($K = 210$ L mol^{-1}). Pyridine, like amines[7,22−24] and hydroxylamines,[25] is oxidized by the MTO/H_2O_2 system. Thus when pyridine is present, a considerable concentration of PyO develops. In such cases, the interaction of MTO with both Lewis bases must be considered. Though the 4-*tert*-butylpyridine-*N*-oxide adduct of **B** has been isolated,[17] the ^1H spectrum of **B** at high [H_2O_2] was unaffected by the addition of a large excess of PyO. Either the interaction of PyO with **B** is negligible or the chemical shifts of the PyO and H_2O adducts of **B** are the same. We have obtained evidence that the interaction of PyO with **A** forms a complex of appreciable stability. The ^1H spectrum of **A** at lower [H_2O_2] shifts upfield appreciably. Like the reaction between MTO and PyO, the equilibrium between **A** and PyO is established rapidly on the NMR time scale, such that only one *Me*Re resonance could be observed at room temperature.

Addition of hydrogen peroxide to a solution of MTO·Py and free pyridine gave rise to a ^1H spectrum with two observable CH_3−Re resonances. One arises from **B** at 2.87 ppm; the other appears at 2.11 ppm. Reverse addition—Py added to a solution of **B** and excess H_2O_2—gave the same spectrum. The resonance

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(21) The binding constant with MTO was also measured in acetonitrile, $K = 173 \pm 6$ L mol^{-1}, to facilitate comparison with OsO_4. The amount of H_2O (up to 3.1 M) does not affect the binding constant between MTO and pyridine, and the binding constant of H_2O with MTO is small in acetonitrile, 0.4 L mol^{-1}.

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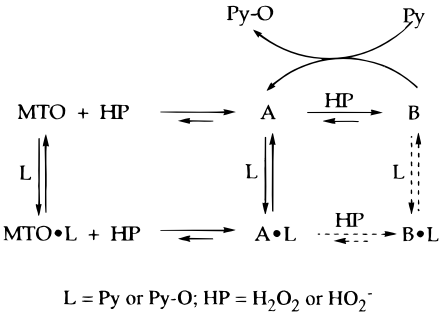
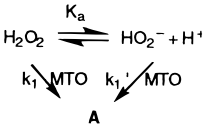
Scheme 1



Scheme 2



at 2.11 ppm is tentatively assigned to A·L (L = Py, PyO), since this signal disappeared and MTO·L appeared at 1.91 ppm when the limiting H_2O_2 had been consumed. Thus it seems that **B** becomes **A** by transferring an O-atom to Py:

$$\mathbf{B} + \mathrm{Py} \rightarrow \mathbf{A} + \mathrm{PyNO\ (or\ A{\cdot}OPy)} + \mathrm{H_2O} \qquad (7)$$

From the description that follows, it is clear that it is not easy to distinguish the adducts of **A** with Py and PyO. The interaction of **B** with pyridine cannot easily be detected owing to the oxidation of Py by **B**, eq 7.

On the basis of these observations, the MTO/H_2O_2/Py system can be described as shown in Scheme 1. The dashed arrows indicate reactions that are plausible but not directly detected. The alternative routes (top and bottom) to **B** cannot be distinguished.

The oxidation of pyridine attracts special attention, since it may and very likely will happen concurrently with epoxidation. The oxidation of Py to PyO occurs mainly when **B** is present, suggesting that pyridine oxidation from A·L is much less effective than that from **B**.

Effects of Pyridines on the Formation of A and B. It is unlikely that the acceleration of these reactions arises only from the coordination of Py to MTO. The bulky and thus noncoordinating pyridine Py′ = 2,6-di-*tert*-butyl-4-methylpyridine accelerates these reactions as well. Although the MTO binding constants for Py and PyO are nearly the same, the accelerating effect for forming **B** is much larger for Py than for PyO. We thus conclude that these accelerations arise from the Brønsted basicity of pyridine: it increases the concentration of HO_2^-, which is much more nucleophilic and thus more reactive than H_2O_2. Scheme 2 shows this effect.

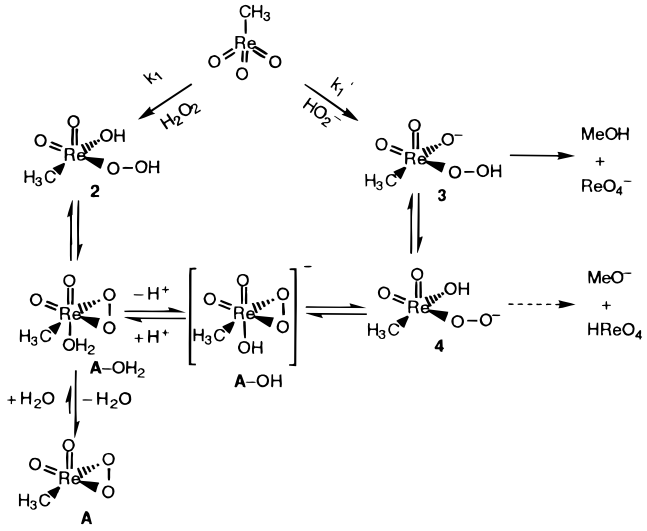
According to this, the reaction rate will be

$$-\frac{\mathrm{d[MTO]}}{\mathrm{d}t} = \frac{k_1[\mathrm{H^+}] + k_1' K_a}{[\mathrm{H^+}] + K_a}[\mathrm{H_2O_2}]_T[\mathrm{MTO}] \qquad (8)$$

On the other hand, the rates of eq 1 are independent of acidity at pH 1−3 in aqueous solution.[9] These formulations are not contradictory, however, since K_a is but 2.5×10^{-12}, such that an acid effect should not be found at pH < 3, even if k_1' were as large as 4×10^8 L mol^{-1} s^{-1}.[11]

A study of the effects of pyridine on the kinetics of the formation of peroxorhenium species must allow for concomitant oxidation of pyridine. Since Py′ and Py have comparable

Scheme 3



pK_b's,[26] but Py′ is noncoordinating and nonoxidizable, its kinetic effect was explored. With 1 mM MTO and 87 mM H_2O_2, the observed rate constant for the buildup of **B** increased with 2−14 mM Py′. The yield of **B** was 40% of $[MTO]_0$, independent of [Py′]. There was significant decomposition of MTO, however, no doubt as a result of its earlier-described reaction with HO_2^-.[11] This factor prevented a meaningful analysis of the kinetic data. The ^{1}H NMR spectrum of this system showed a significant amount of methanol, confirming the decomposition of MTO. This result is different from the system lacking Py′ in these respects: (1) **B** was formed from MTO and H_2O_2 in 95% yield, since MTO remained intact; (2) addition of unsubstituted Py also gave a 95% yield of peroxorhenium species. From that we conclude the coordination of Py to MTO must protect the catalyst from deactivation by the base-mediated pathway.

A plausible mechanism to account for the kinetic enhancement by bases is presented in Scheme 3. The left side of the scheme is the same as that proposed for aqueous acidic solution. The right depicts the basic pathway. Because H_2O_2 (pK_a = 11.6) is more acidic than water (pK_a = 15.7, pK_w = 14.0), the equilibration between **3** and **4** should favor **4**. Products seem likely to arise from **3**, however, because **3** leads directly to MeOH, whereas **4** might release MeO^-. Once **4** forms, then **A** will follow by the sequence **4** → **A**-OH → **A**-OH_2 → **A**. The formation of **B** follows from a closely analogous scheme.

Both H_2O_2 and HO_2^- produce the peroxorhenium complexes **A** and **B**. But HO_2^-, the better nucleophile, should react more rapidly with MTO, leading to a pH effect. Still, an explanation must be produced for the significant decomposition of MTO when the sterically encumbered Py′ is used.

The binding of MTO to Py or PyO stabilizes the system, suggesting that the reaction between MTO·L with H_2O_2 (Scheme 1) is also involved in the generation of the active form of the catalysts. Pyridine coordination may alter the rate of methyl migration; also, the change of the coordination geometry about rhenium may impede methyl migration.

Epoxidation Reactions in the Presence of Pyridine. ^{1}H NMR techniques were used to follow the epoxidation but with two complications: (1) the catalyst is slowly decomposing, and (2) pyridine is being oxidized at a comparable rate. To optimize the information, a relatively reactive olefin, α-methylstyrene, was used. We chose to use 0.83 M H_2O_2 for comparison with

(26) Anne, A.; Morioux, J.; Saveant, J.-M. *J. Am. Chem. Soc.* **1993**, *115*, 10224.

Table 3. Initial Rates of Oxidation of Pyridine and α-Methylstyrene in the Presence of 0.83 M H_2O_2 at 296 K in CD_3CN ($[H_2O] = 3.3$ M)

entry	MTO/ mM	[Py]/ M	α-methylstyrene/ M	$v_i/10^{-5}$ L mol^{-1} s^{-1} PyO	epoxide
1	0.66	0.090	0.52	2.22 ± 0.21	7.63 ± 0.097
2	2.0	0.090	0.52	7.05 ± 0.18	26.4 ± 0.77
3	6.6	0.090	0.52	19.9 ± 1.3	72.8 ± 2.8
4	4.0	0.33	0.20	56.2 ± 2.1	19.2 ± 0.61
5	4.0	0.25	0.20	42.2 ± 1.2	19.8 ± 0.61
6	4.0	0.16	0.20	27.1 ± 0.48	18.8 ± 0.53
7	1.3	0.058	0.12	3.13 ± 0.17	3.74 ± 0.053
8	1.3	0.058	0.071	3.17 ± 0.29	2.30 ± 0.037
9	1.3	0.058	0.020	3.06 ± 0.11	0.67 ± 0.008

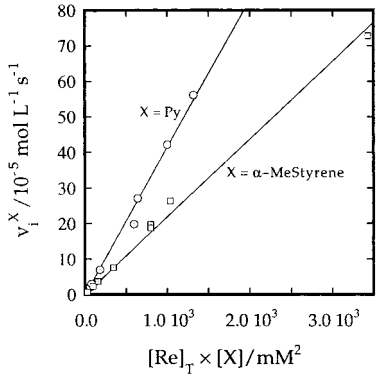


Figure 4. Plots of the initial rates (v_i) for the oxidation of pyridine (circles) and α-methylstyrene (squares) against the product of two concentrations, $[Re]_T[X]$ (X = $[Py]_0$ or $[\alpha\text{-methylstyrene}]_0$). The concentration of H_2O_2 was kept constant at 0.83 M ($[H_2O] = 3.3$ M), while $[Py]_0$ was varied from 0.058 to 0.33 M and $[\alpha\text{-methylstyrene}]_0$ from 0.020 to 0.52 M.

other work,[1] but this precluded the use of nitromethane solvent, where the system was not homogeneous. Thus, for these studies, acetonitrile was the solvent; independent studies confirmed the accelerating effect of pyridine coordination under catalytic conditions. Again, the kinetic data were analyzed by the method of initial rates. The reaction order of each pertinent species was explored by examining the variation of the reactant concentrations, as given in Table 3.

In entries 1−3, the two substrates were held constant while [MTO] was varied; the initial rate of oxidation of each substrate was proportional to $[MTO]_0$. Further, and to no surprise, the rate of pyridine oxidation is first-order with respect to $[Py]_0$, and zero-order with respect to $[\alpha\text{-MeSty}]_0$, entries 4−9. These entries also show that the rate of formation of the epoxide is first-order with respect to $[\alpha\text{-MeSty}]_0$ and zero-order with respect to $[Py]_0$. To display these kinetic effects graphically, for each substrate X (=α-MeSty and Py), a plot was constructed of the initial rate for each substrate (v_i^X) against the product $[Re]_T[X]$, using the data from Table 3. The excellent straight lines *at fixed hydrogen peroxide = 0.83 M*, are shown in Figure 4. The quantitative conclusions of this aspect are

$$v_i^{PyO} = k[MTO]_0[Py]_0; \quad k = 0.42 \pm 0.01 \text{ L mol}^{-1} \text{ s}^{-1}$$

$$v_i^{Epox} = k[MTO]_0[\alpha\text{-MeSty}]_0; \quad k = 0.22 \pm 0.04 \text{ L mol}^{-1} \text{ s}^{-1}$$

As these data show, oxidation of pyridine is favored over the pyridine-present epoxidation of α-methylstyrene. The rate constant for the pyridine-present epoxidation of α-methylstyrene is larger than that for the pyridine-free epoxidation in acetonitrile, with $k = 0.086$ L mol^{-1} s^{-1}. On the other hand, in 1:1 CH_3CN/H_2O, the rate constant is larger, as expected: 0.47 L mol^{-1} s^{-1}; epoxidations of alkenes are always faster in a semiaqueous solvent.[27]

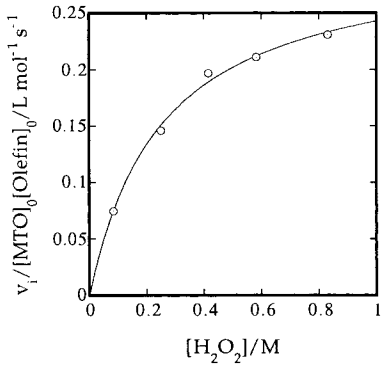


Figure 5. Apparent rate constant for the epoxidation of 0.32 M α-methylstyrene, in CD_3CN at constant $[Py] = 41$ mM, $[Re]_T = 3.3$ mM, and 3.3 M H_2O, varying with the hydrogen peroxide concentration, *c*. The fit takes the form $k = 1.20c/(1 + 3.92c)$.

The data just presented show that the epoxidation rate is independent of [Py]; nonetheless, the pyridine-free epoxidation rate is lower. Since the epoxide produced in the experiment with pyridine, during the first 3 min of reaction, amounts to some 5−15 times $[\mathbf{B}]_0$, a catalytic cycle is clearly effective. The difference in k's might be attributed to a faster reaction of α-methylstyrene with **A** than **B**, as is the case for most styrenes (the difference of the reactivities between **A** and **B** is not significant).[27] If so, and because the ratio of $[\mathbf{A}]_{ss}/[\mathbf{B}]_{ss}$ should increase as $[H_2O_2]$ decreases, then the catalytic rate should increase as $[H_2O_2]$ decreases.

Just the opposite is so, as shown in Figure 5: the "rate constant" for epoxidation at constant [Py] and $[Re]_T$ rises to a plateau with increasing $[H_2O_2]$. This treatment ignores the speciation of the binary and ternary complexes of MTO/Py/H_2O_2, all rate constants being expressed on the basis of $[Re]_T$. Evidence for **A**·L has been presented; the current findings allow us to conclude that **A**·L is much less reactive in epoxidation than **B**. To explore this issue further, the epoxidation reactions were carried out as before with high and constant $[H_2O_2]$, but lower [Py] and varying $[\alpha\text{-MeSty}]$ and $[Re]_T$. As before the rate constants were calculated from the initial rates as $v_i/([Re]_T[\alpha\text{-MeSty}])$. These values rise with increasing [Py], as presented in Figure 6. To account for this, we suggest that the (so far undetected) species **B**·Py is present, and that it epoxidizes the alkene even faster than **B**.

Epoxidation Reactions in the Presence of Pyridine Derivatives. The epoxidation of α-methylstyrene in the presence of 4-methylpyridine, 3-chloropyridine, or pyridine-*N*-oxide was also carried out in a way similar to the experiments presented in Figure 6. As expected the oxidation of 4-methylpyridine by the MTO/H_2O_2 system is faster than that of pyridine (0.59 vs 0.42 L mol^{-1} s^{-1}). Unlike the case with 4-methylpyridine, a much higher concentration of 3-chloro pyridine was needed to achieve high selectivity for epoxide. Compared with the epoxidation reactions in the absence of any ligands, the formation of epoxide is faster in the presence of 4-methylpyridine or 3-chloropyridine. The maximum rate was achieved

(27) Al-Ajlouni, A.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 9243−9250. The inhibitor present in α-methylstyrene, *p-tert*-butylcatechol, did not affect the kinetics in the studies reported in this reference. As pointed out by one reviewer, a problem might exist in the present work, but that seems unlikely considering that the data for α-methylstryene were independent of concentration (Table 3).

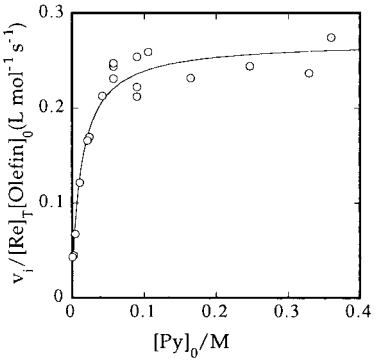


Figure 6. Effect of pyridine on the epoxidation rate constant in CD_3CN at 296 K. Conditions: 0.66−6.6 mM Re_T; 2.1−360 mM Py; 20−560 mM α-methylstyrene; 0.83 M H_2O_2; 3.3 M H_2O.

when the concentration of 4-methylpyridine was greater than 0.05 M; however, the maximum rate was not attained even at 0.2 M 3-chloropyridine. No substantial difference was found between the reactivities of the peroxorhenium species in the presence of pyridine and 4-methylpyridine.

Although PyO does not accelerate the epoxidation of α-methylstyrene, its presence does speed up the formation of **A** and **B**. Since the donor capabilities of the oxygen atoms in PyO and H_2O are probably similar, the reactivities of their peroxorhenium adducts are possibly alike as well. The acceleration of the formation of peroxorhenium species by PyO unlikely results from its Brønsted basicity ($pK_b = 13.2$). It has been suggested on the basis of the IR stretching frequencies that the Re═O bond of MTO is weakened upon coordination of an O- or N-containing ligand.[17] Since the rate-controlling step for the formation of A is believed to be the formation of CH_3ReO_2-(OH)(OOH),[28,29] weakening the Re═O bond in the presence of PyO is likely the main cause of the acceleration for the formation of peroxorhenium species. The selectivity enhancement in the presence of a large excess of pyridine-*N*-oxide possibly results from its replacement of H_2O on the H_2O-solvated rhenium species.

For the epoxidation of α-methylstyrene, the use of a mixture of PyO and a bulky pyridine is better than the use of the bulky pyridine alone. Also, the preliminary results indicate that the use 2,6-dimethylpyrazine, which provides a protected basic function group and a binding site, is better than the use of 2,6-dimethylpyridine. However, none of these is superior to the use of pyridine.

Better Choice than Pyridine Alone? Oxidation of pyridine has to be considered, particularly when one tries to prepare an epoxide from a unreactive olefin.[2,3] As observed in the oxidation of hydroxylamines,[25] protonation of pyridine by adding trifluoromethane sulfonic acid slowed the formation of pyridine-*N*-oxide. When $[Py]_0 > 10[H^+]_0$ ($[Py]_0 = 0.20$ M), as more and more acid was added, the selectivity toward epoxide decreased while the reactivity increased slightly. For α-methylstyrene, whose epoxide is sensitive to the acid-catalyzed ring opening reaction, best results were obatined when the ratio [Py]/[acid] is about 2 for CH_3COOH and about 120 for CF_3SO_3H.

Conclusions. The beneficial effects of pyridine can be traced to these factors: (1) Selectivity for the epoxidation over dihydroxylation is greatly enhanced due to the basicity of pyridine.[1−3,27] Although amines, stronger bases than pyridine, would seem to be a better choice in this regard, it has been shown that the oxidation of amines by the MTO/H_2O_2 system is generally much faster than most of the epoxidation reactions. A bulky pyridine can give a high selectivity of epoxide; however, the noncoordinating pyridine cannot stabilize the MTO/HP system. (2) Stabilization of MTO against decomposition is seen, provided a sufficient pyridine concentration is used. For a pyridine derivative, both the basicity and its binding constant to MTO should be considered. Generally, as the basicity increases, the binding constant increases and the catalyst lifetime decreases. Our results indicate that the basicity of pyridine is probably too strong for the current system and a Py/PyH^+ buffer should be used instead of pyridine alone. (3) Pyridine not only accelerates the generation of the peroxorhenium catalysts but also accelerates the epoxidation reactions. The nature of the latter effect of pyridine is not clear. It is possible that the Re−O (η^2-O_2) bond is weakened upon coordination of pyridine, and as a result the energy barrier for the formation of epoxide is decreased.[30] Acceleration of the epoxidation reactions will benefit all olefins, and acceleration of the regeneration of catalysts will speed up the epoxidation of very reactive olefins.

Acknowledgment. This research was supported by a grant from the National Science Foundation (CHE-9007283). Some experiments were conducted with the use of the facilities of the Ames Laboratory. We are grateful to Dr. A. Yudin and Dr. K. B. Sharpless for helpful discussions and to the latter for making available to us the material in ref 1 prior to publication.

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(28) Pestovsky, O.; van Eldik, R.; Huston, P.; Espenson, J. H. *J. Chem. Soc., Dalton Trans.* **1995**, 133.

(29) Espenson, J. H.; Abu-Omar, M. M. *Adv. Chem. Ser.* **1997**, *253*, 99−134.

(30) The following results favor the involvement of the peroxorhenium complex with a coordinated pyridine, Re(η^2-O_2)Py, instead of the ReO-(PyO) complex. The reaction of pyridine-*N*-oxide with α-methylstyrene in the presence of MTO did not yield the corresponding epoxide in 24 h. Also, pyridine-*N*-oxide does not accelerate the epoxidation of α-methylstyrene by MTO/H_2O_2; see ref 3 as well.