1998

Kinetics and mechanisms of the oxidation of alcohols and hydroxylamines by hydrogen peroxide, catalyzed by methyltrioxorhenium, MTO, and the oxygen binding properties of cobalt Schiff base complexes

Timothy Harlan Zauche
Iowa State University

INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

UMI

A Bell & Howell Information Company
300 North Zeeb Road, Ann Arbor MI 48106-1346 USA
313/761-4700 800/521-0600

Kinetics and mechanisms of the oxidation of alcohols and hydroxylamines by hydrogen peroxide, catalyzed by methyltrioxorhenium, MTO, and the oxygen binding properties of cobalt Schiff base complexes

by

Timothy Harlan Zauche

A dissertation submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Major: Inorganic Chemistry

Major Professor: Dr. James H. Espenson

Iowa State University

Ames, Iowa

1998

Graduate College

Iowa State University

This is to certify that the Doctoral dissertation of

Timothy Harlan Zauche

has met the dissertation requirements of Iowa State University

Signature was redacted for privacy.

Major Professor

Signature was redacted for privacy.

For the Major Program

Signature was redacted for privacy.

For the Graduate College

TABLE OF CONTENTS

GENERAL INTRODUCTION

Introduction

Catalysis is a very interesting area of chemistry, which is currently developing at a rapid pace. A great deal of effort is being put forth by both industry and academia to make reactions faster and more productive. One method of accomplishing this is by the development of catalysts. Enzymes are an example of catalysts that are able to perform reactions on a very rapid time scale and also very specifically; a goal for every man-made catalyst. A kinetic study can also be carried out for a reaction to gain a better understanding of its mechanism and to determine what type of catalyst would assist the reaction. Kinetic studies can also help determine other factors, such as the shelf life of a chemical, or the optimum temperature for an industrial scale reaction.

An area of catalysis being studied at this time is that of oxygenations. Life on this earth depends on the kinetic barriers for oxygen in its various forms. If it were not for these barriers, molecular oxygen, water, and the oxygenated materials in the land would be in a constant equilibrium. These same barriers must be overcome when performing oxygenation reactions on the laboratory or industrial scale. By performing kinetic studies and developing catalysts for these reactions, a large number of reactions can be made more economical, while making less unwanted byproducts. For this dissertation the activation by transition metal complexes of hydrogen peroxide or molecular oxygen coordination will be discussed.

Oxidation of Two Organic Functionalities

The oxidation of secondary hydroxylamines ($(R_2R'C)_2NOH$) and alcohols are two reactions where a mechanistic study would be helpful in understanding the reactions better. When secondary hydroxylamines are oxidized, nitrones ($R_2C=N(O)CR_2R'$), are formed where R' is a hydrogen atom and R can be either a hydrogen atom or an alkyl group. Oxoammonium ions are instead formed as the product if R and R' are alkyl groups. Both of these products are special in their uses. Nitrones can be used as radical trapping agents, allowing a researcher to be able to study a short-lived and reactive species on a longer time scale. Nitrones are also extensively used in the synthesis of natural products. They combine with olefins in a 1,3 dipolar cycloaddition reaction to yield heteroatomic five membered rings that can be converted to a variety of other functionalities. Oxoammonium ions on the other hand, are known as strong oxidizing agents comparable to bromine. The products from alcohol oxidations are either aldehydes or ketones. These two carbonyl compounds have their own specific uses and can be reacted further to produce other functionalities.

Many oxidants have been used to oxidize hydroxylamines and alcohols, such as peracids, dioxiranes, and transition metal oxo and peroxo complexes under stoichiometric and catalytic conditions. The sources of oxygen for the transition metal catalysis are mainly O_2, H_2O_2, alkylperoxides, and PhIO. All of these oxygen donors have good and bad qualities. For example O_2 is the most abundant while H_2O_2 is more soluble under aqueous conditions than O_2 and gives only water as a byproduct. The others are not as favored as oxygen donors due to the goals of waste management. For this study, H_2O_2 is used as the oxygen source with methyltrioxorhenium(VII), CH_3ReO_3, **MTO**, as a high valent metal catalyst. H_2O_2 is activated upon coordination to a high valent transition metal,

such as MTO. The metal acts as a Lewis acid and upon coordination, the peroxide becomes less nucleophilic, increasing the susceptibility of the peroxo oxygens to nucleophilic attack.

MTO has been found to activate H_2O_2 by formation of a bidendate monoperoxide, $CH_3Re(O)_2(\eta_2\text{-}O_2)$, **A**, and a bisperoxide, $CH_3Re(O)(\eta_2\text{-}O_2)_2(H_2O)$, **B**. These compounds will be discussed in detail in the following chapters. For this study, conditions were chosen to make **B** the dominant reactive form of the catalyst, although it has been shown before that both **A** and **B** can oxidize a variety of substrates. A mechanistic study was carried out for both substrates as described in Chapters 1–3. For secondary hydroxylamines a mechanism is proposed where the lone pair of the nitrogen acts as a nucleophile towards the bound peroxo-oxygens and a transfer of an oxygen atom occurs. Depending on the hydroxylamine, either water or hydroxide is eliminated from this intermediate to yield the nitrone or oxoammonium ion, respectively. For the oxidation of alcohols a hydride abstraction mechanism was proposed where the peroxo-oxygen abstracts the alpha hydrogen of the alcohol carbon. A portion of this mechanism also goes through a step where an oxygen atom is inserted into the same C–H bond instead. All reactions were optimized to give products in greater than 90% yields. The activation of H_2O_2 upon coordination to MTO speeds the oxidation of substrates by a factor of 50 to 500,000 compared to the uncatalyzed reaction. In fact the MTO/H_2O_2 system is such a strong oxidizing system that its rates of oxidation are typically only 50 to 100 times slower than those of the strong oxidizing agent Br_2. The MTO/H_2O_2 oxidizing system is also be more beneficial from the standpoint of hazardous waste production as compared to stoichiometric bromine oxidations.

Molecular Oxygen Coordination

The activation of molecular oxygen is a difficult task that not many metal centers can accomplish. Cobalt(II), when pentacoordinated, is one such compound that can coordinate O_2. These Co(II) complexes can usually be described as analogous to cobalamin. The Praxair Corporation is investigating the uses of such compounds for the coordination of oxygen and its subsequent purification on an industrial scale. To have a better understanding of the complexes they had synthesized, scientists at Praxair Inc. collaborated with us to determine the rates of oxygen coordination for each complex. We were to determine these rate constants in solution with hopes of extrapolating to solid state conditions, as needed for the ultimate application There are only a few methods available at this time to determine these rate constants, one of which is laser flash photolysis that has been used extensively at Iowa State. This method was applied to this project as well as some new variations.

Dissertation Organization

This dissertation consists of four chapters. The first three chapters deal with the catalytic oxidation of alcohols and hydroxylamines. Chapters I and III have been submitted for publication in *Inorganic Chemistry* while Chapter II has already been published in the same journal. The last chapter deals with rate constant determinations for the binding of molecular oxygen by Co(II) salen derivatives. This work was supported by Praxair. Each section is self contained with its own equations, tables, figures, and references. Following the last chapter are some general conclusions. All the work in this dissertation was performed by this author.

CHAPTER I
OXIDATION OF ALCOHOLS BY HYDROGEN PEROXIDE, CATALYZED BY METHYLTRIOXORHENIUM (MTO): A HYDRIDE ABSTRACTION

A paper submitted for publication in the journal *Inorganic Chemistry*.

Timothy H. Zauche and James H. Espenson

Abstract: Primary and secondary alcohols are oxidized using hydrogen peroxide as an oxygen donor and methyltrioxorhenium (MTO) as a catalyst. The methylrhenium bis-peroxide, $CH_3Re(O)(\eta_2\text{-}O_2)_2(H_2O)$ was the dominant and reactive form of the catalyst. Representative rate constants k/L mol^{-1} s^{-1},are 1.02 $\times$ 10^{-4} for 4-Me-α-methylbenzyl alcohol and 4.9 $\times$ 10^{-5} for 4-Cl-α-methylbenzyl alcohol. There was a kinetic isotope effect of 3.2 for the α C-H bond. When sec-phenethyl alcohol was labeled with ^{18}O, 80% of the oxygen was retained in the ketone. A mechanism featuring hydride abstraction is proposed which is the first time that the H_2O_2/MTO system is proposed to react in this fashion. Also, a co-catalytic set of reaction conditions has been developed on the synthetic scale, using bromide and MTO as co-catalysts, which cuts the reaction time to minutes instead of hours.

Introduction

The selective oxidation of C-H bonds has always been a challenging task. Typical of this is the oxidation of alcohols to aldehydes or ketones. Usually only the strongest oxidizing agents, such as $KMnO_4$, Br_2, MnO_2, SeO_2, RuO_4, and acid dichromate can perform this reaction.[1] Only a few of these reagents have been

used in a catalytic system; one example is SeO_2.[2] It has recently been shown that methyltrioxorhenium (CH_3ReO_3, or MTO) can catalyze reactions of hydrogen peroxide (HP) with alcohols.[3]

HP used with a catalytic amount of MTO has been shown to oxidize catalytically a variety of substrates besides alcohols, such as sulfides[4], alkenes[5,6], amines[7,8], hydroxylamines[9], and halides[10,11]. The mechanisms of these oxidations follow a general pathway where the substrate acts as a nucleophile and attacks an electron-poor peroxorhenium oxygen.

The previous study of alcohol oxidations by MTO and HP focused on the synthetic aspects of the catalytic system.[3] We were intrigued by these oxidations since the alcohol, unlike other substrates oxidized by MTO and HP, has no center of electron density to act as a nucleophile, nor does it have a site to which an oxygen atom can be easily transferred. Anticipating a new mechanism of oxidation for the catalyst MTO, we undertook a study of the oxidation of alcohols by MTO and HP.

Experimental Section

Materials. Hydrogen peroxide and HPLC grade solvents were purchased from Fisher. Water was purified by distillation and then filtered by a Milli-Q water purification system. The various alcohols, ketones, and aldehydes were purchased either from Aldrich or Lancaster and used as received. The 10% ^{18}O labeled water and MTO were purchased from Aldrich 1-Phenyl ethanol (1,2,2,2 -D_4, 98%) was purchased from Cambridge Isotope Laboratories. The methyl-(1-phenyl)ethyl ether was made by a standard literature procedure.[12]

The products of alcohol oxidation were identified using various methods. ^1H NMR spectra were recorded using a Varian VXR 300 MHz NMR or a Bruker

DRX 400 MHz NMR spectrometer, mass spectra were obtained using a Finnigan TSQ 700 GC-MS, and the UV-Vis spectra were determined using a Shimadzu 2501 or 3101 spectrophotometer.

Kinetics. The experiments were carried out in 20% water-acetonitrile containing 0.1 M $HClO_4$. This solvent mixture was chosen for solubility reasons and because the kinetics and thermodynamics of the HP/MTO system are known under these conditions. The reactions were monitored by the absorbance rise in the region of 240-255 nm, due to the formation of the carbonyl product. The reactions were carried out in a quartz cuvette under air, since there was no effect upon saturating the solutions with air or argon. Because of the large molar absorptivities of the products ($\varepsilon \sim 1 \times 10^4$ L cm^{-1} mol^{-1}) and the background from hydrogen peroxide and MTO, a 0.01 cm pathlength cell from Spectrocell was used throughout the study. Reactant stock solutions were made fresh daily. A typical reaction procedure is as follows: 10-50 mM MTO, 200 mM HP and 0.10 M $HClO_4$ were mixed together in the cell and allowed to stand for one to two minutes to allow the complete formation of the catalytically active form of MTO; 20 - 50 mM of neat alcohol was added at this point and the solution mixed thoroughly (~ 25 sec). Data acquisition was then started and the reaction was kept at a constant temperature of 25 °C. The reactions were typically monitored until 1-2% of the alcohol had reacted, since over longer periods of time the catalyst is susceptible to decomposition. The absorbance versus time data were analyzed by the initial rate method. The absorbance traces were converted to concentrations based on the molar absorptivities of the alcohols and products determined from authentic samples. The data was linear over the time frame used and was fit to a linear least-squares analysis using the computer program KaleidaGraph.

Oxygen Labeling. An ^{18}O isotope labeling experiment was carried out with sec-phenethyl alcohol. The 10% labeled alcohol was synthesized by the standard literature preparation[13] from acetophenone mixed with 10% ^{18}O water and a catalytic amount of acid. After 16 h, the labeled acetophenone was isolated and reduced using sodium borohydride. The resulting alcohol was then purified and stored in a desiccator.

In a typical labeling experiment a reaction solution contained 30 mM of 10% ^{18}O labeled alcohol, 25 - 30 mM MTO and ~ 200 mM urea hydrogen peroxide (UHP) in acetonitrile. Not all of the UHP was dissolved, but enough was dissolved to assure that the dominant form of the catalyst was the bis-peroxorhenium compound, determined by observation of its characteristic 360 nm absorption. UHP was used in these experiments to limit the amount of ^{16}O-bearing water in the reaction solution.

All of the gas chromatography-mass spectrometry experiments were performed using a Finnigan TSQ 700. The system was configured in the electron impact ionization mode. The first quadrupole was used as the analyzer to scan from m/z 35 to m/z 400 at 0.5 sec/scan. The second and third quadrupoles were kept in the RF-only mode. Unit mass resolution was achieved using FC43 as calibration and tuning reference. A DB1701 gas column was used for all experiments. This allowed the ketone to flow through the column first, and any tailing of the larger alcohol peak was not a worry. This was a concern lest tailing from the alcohol peak, were it first off the column (as was the case when a DB5 gas column was used), may overlap with the ketone peak. The ratio of labeled to unlabeled compounds was determined by the ratio of mass to charge peaks for both the alcohol and ketone with each injection by taking an average of three mass spectral scans at the maximum of the GC peak and subtracting a

background scan. This allowed direct comparison of the starting alcohol labeling and the product ketone, eliminating any variations the instrument might have from day to day. Each data point was the average of three injections and each reaction was carried out two to three times.

Synthetic Scale Reactions. These reactions were carried out on the 2.5 mmol alcohol scale. A typical procedure is as follows: 4 mol% MTO and 2 eq of 30% HP were combined. The alcohol was then added and the biphasic mixture stirred at 40 ± 2 °C for one day. No acid was added, to avoid acid catalyzed by-products. Periodically, the NMR spectrum of an aliquot taken from the organic layer was obtained in d-chloroform to monitor the progress of the reaction.

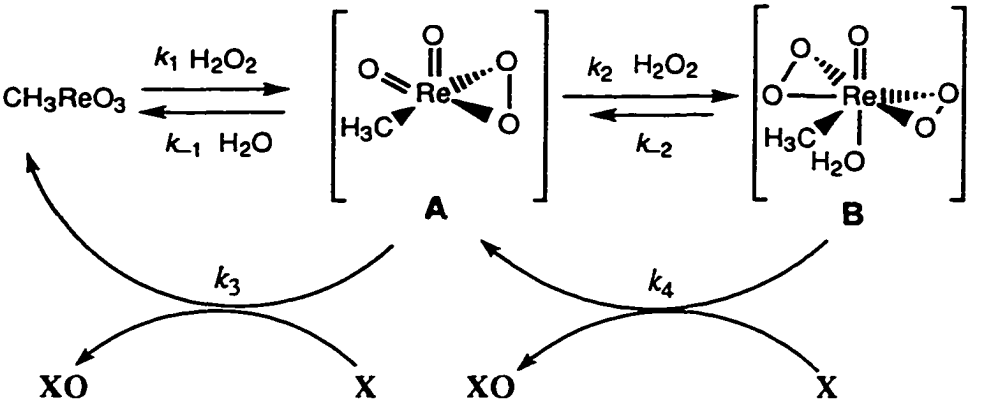
Other synthetic scale reactions were carried out using Br^- as a co-catalyst with MTO. These reactions were performed with an equal volume of acetonitrile as compared to HP and alcohol added, which rendered the reaction mixture homogeneous. The 1.1 eq. of HP were added by syringe pump infusion to limit the amount of peroxide decomposition by bromide species in the solution. For these reactions 4.0 mol% of HBr and 0.50 mol% of MTO (relative to the alcohol) was used as the catalysts with addition of HP over 30-45 mins.

Results

The Catalyst. MTO can reversibly coordinate one or two HPs to yield the corresponding mono and bis-peroxorhenium complexes **A** and **B**, as shown in **Scheme 1**. Without a substrate present MTO, **A**, and **B** will reach equilibrium concentrations governed by [HP] and the values of K_1 (k_1/k_{-1}) and K_2 (k_2/k_{-2}), the equilibrium constants. The same does not hold true during a catalytic reaction cycle where steady-state conditions apply. With the oxidation of a substrate at rates defined by the second order rate constants k_3 and k_4 and the concentration

of substrate, the steady state concentrations of the various rhenium complexes will be obtained.

Scheme 1



With such a number of reactions possible it proved difficult to determine the steady-state concentration of each rhenium complex during the reaction. For example, when the rates of oxidation are larger than the rates of reformation of **A** or **B**, then after a few catalytic cycles the major form of the catalyst will be MTO, with the rate-determining step being the formation of **A**. On the other hand, when the rates of oxidation are slow compared to the formation of **A** or **B**, then the dominant form of the catalyst during the reaction will be **B** at high [HP]. With alcohols the rate of oxidation is much slower than the rate of reformation of the oxidizing species B from A, leading to a well-behaved catalytic system.

Reaction Kinetics. It has been shown that the initial rate method can be applied to catalytic MTO oxidations.[9] Owing to the long reaction times for alcohol oxidations (typically $t_{1/2}$ ~ 30 hr) and the slow decomposition of the catalyst, the initial rate method was employed. For these reactions MTO and HP were equilibrated before addition of the alcohol. With the high concentration of HP used (0.2 - 0.3 M), the predominant form of the catalyst will be **B** in accord with the assumption that [**B**] ≡ $[Re]_T$ = [MTO] + [**A**] + [**B**], which will hold throughout the reaction. This treatment allows the determination of the

bimolecular rate constant k_4 for the reaction of **B** with an alcohol as written in eq 1, expressed by the rate law, eq 2, written in terms of initial rates.[14]

$$\mathbf{B} + R_2CHOH \xrightarrow{k_4} \mathbf{A} + R_2CO + H_2O \quad (1)$$

$$v_i = k_4[\mathbf{B}][R_2CHOH]_0 \cong k_4[Re]_T[R_2CHOH]_0 \quad (2)$$

Based on equations 1 and 2 a plot was made of the initial rates versus the product $[Re]_T \times [R_2CHOH]_0$. According to eq 2 the values of v_i should define a straight line that passes through the origin with the slope equal to k_4. The data for 4-Me-α-methylbenzyl alcohol are displayed in **Figure 1**. The least-squares slope of the line gives the value $k_4 = 1.02 \times 10^{-4}$ L $mol^{-1}s^{-1}$ (25 °C, in 20% water/acetonitrile, 0.1 M $HClO_4$). The determined rate constant k_4 for each alcohol is listed in **Table 1**. The spread of rate constants is not large, all being within a factor of 5. Included in this study was the oxidation of methyl (1-phenyl)-ethyl ether. This compound has the smallest rate constant of all compounds determined and is about 3.3 times slower than its respective alcohol, sec-phenethyl alcohol, entries 3 and 13. The k_4 rate constants could not be determined accurately for some alcohols, but these substrates were also listed to show the widespread applicability of the MTO/HP oxidations.

A linear free energy relationship plot was made of the para substituted α-methylbenzyl alcohols as shown in **Figure 2**. From this plot the slope $\rho = -0.51$ was determined. The negative ρ value implies that electron donating groups increase the reaction rate, while electron withdrawing groups decrease the rate. This agrees well with an oxidation mechanism in which the rhenium peroxo-oxygen performs an electrophilic attack on the C-H bond. One of the 7 substrates used to make the LFER plot did not react as expected. 4-Bromo-α-methylbenzyl alcohol has a rate constant that is approximately half of the expected value. The alcohol sample was pure by ^1H NMR. We have no explanation for this

deviation at this time, but would call attention to this also being one of the compounds giving a low yield (see later).

Isotopic Labeling. A number of reactions were performed using 10% ^{18}O labeled sec-phenethyl alcohol with GC-MS monitoring. When it was treated with MTO/UHP, it was found that 80 ± 5% of the labeled oxygen remains in the ketone. UHP was used for these experiments to limit the amount of added water, by minimizing oxygen exchange between the ketone and solvent. When 30% aqueous HP was used there was significant exchange of the labeled ketone with the solvent oxygens. Even without added acid, when MTO decomposes it forms perrhenic acid which will catalyze exchange. With UHP as the oxygen donor there was no detectable exchange of the labeled ketone over 24 h. Multiple trials were performed and the reactions were monitored over time to verify that the ketone did not exchange its oxygen during the oxidation experiment. A deuterium kinetic isotope study was performed using 1-phenyl ethanol (1,1,1,2-D_4). As shown in Table 1, entries 3 and 11, the k_H/k_D ratio is 3.2.

Radical Mechanism Possibilities. Another strong oxidizing compound, dimethyldioxirane (DMDO) can also oxidize alcohols.[15] The mechanism of C-H bond activation by DMDO has been investigated by a number of groups.[16-19] The intermediate in DMDO oxidations can be described as a biradical trapped within a solvent cage. Under different conditions the radical nature of this intermediate can be exploited. MTO has been compared to DMDO in the past for alkene oxidations,[6] therefore a radical intermediate for MTO oxidations was examined. We first tested whether O_2 affects the reaction rates. For reactions carried out under an air or argon atmosphere, no difference in the rate of the reactions was noted. Another test for radicals was to add freshly distilled $CBrCl_3$.[17] The reaction rate was not changed when 25 to 50 mM $CBrCl_3$ was

added. (No halogenated product was checked for since such a product would rapidly lose HBr to form the ketone.) Other radical trapping agents such as Tempo could not be used for this reaction, because the oxidations were performed under acidic conditions. From these negative results we conclude that radical reactions are not significant in the mechanism of these reactions.

Phase Transfer Reactions. The slow rates of oxidation for the various alcohols reveal the long reaction times required to reach completion. Recently, it was reported that the oxidation of alcohols occurs with WO_4^{2-} and HP under "solvent free" conditions.[20] That study used neat alcohol and dissolved the catalyst in 30% HP while using a phase transfer catalyst (PTC) to assist in WO_4^{2-} transportation between the phases. Since MTO is soluble in many organic solvents, no PTC would be needed were MTO used under similar reaction conditions.

Synthetic preparations of ketones were carried out on the neat alcohol. Typically 2.5 mmol of the alcohol was used with 5 mmol HP as a 30% solution and 4 mol% MTO. The reactions were stirred at 40 °C for 1 day and then the yields were determined by NMR as found in Table 1. As seen in Table 1 many of the yields are often better than 80%. This is a great improvement over the previous report of alcohol oxidations by MTO/HP (< 30% yield, 19 mol% catalyst[3]). The temperature of 40 °C was chosen instead of the previously-used 60 °C, to avoid MTO decomposition at higher temperatures.[21] At 40 °C the decomposition of MTO is less, allowing good yields of the product while shortening the reaction times. The reactions were monitored for up to 24 h, but as seen in the table most of the reactions were almost complete after only 8 h. The percent conversion is also listed in the table demonstrating the low amounts of byproducts in these reactions.

An interesting point is the oxidation of a primary alcohol beyond the aldehyde to the carboxylic acid. When two equivalents of HP were used to oxidize benzyl alcohol, not only was benzaldehyde made but a large portion was further oxidized to benzoic acid (21%). When one equivalent of HP was used, the product ratio became 40% benzaldehyde, 7% benzoic acid. Most of the α-phenyl alcohols were oxidized in good yields in reference to large scale reactions. The only two exceptions were the 4-bromo-α-phenylethanol and the 4-methoxy-α-phenylethanol. The reason for the decreased yield for the 4-bromo could be due to the slower rate of reaction then expected as seen in the LFER plot, while the 4-methoxy compound gave a number of products that were not characterized. The non-α phenyl alcohols varied in amounts of yields from 27% for 1-phenyl-2-propanol to 92% for 1-cyclohexylethanol.

Co-catalysts: MTO and Br. Synthetic scale reactions can be made more environmentally friendly by limiting the number and types of side products. Another goal is for the reactions to be halide-free. We have accomplished this by using non-halogenated solvents and non-halogenated oxidizing agents. Now that the oxidation of alcohols by MTO/HP has been defined, we have explored shortening the reaction time by adding bromide as a co-catalyst.

Previously, MTO/HP has been shown to oxidize catalytically Br^- to OBr^-[10] which can form Br_2 when in the presence of another Br^- and H^+.[22] It is also known that Br_2 can oxidize alcohols.[23] When HBr was added as a co-catalyst for the oxidation of alcohols, the reaction was significantly faster as seen in **Figure 3**. This figure demonstrates that the uncatalyzed reaction of the alcohol with HP is almost non-existent. When MTO (0.5 mole equiv.) is added, the reaction becomes faster. However, if HBr is added as well (2 mol%), the reaction is much

faster. Also if the reaction is done on a synthetic scale, 99% of the ketone can be achieved in just minutes, instead of hours without HBr.

There is a competing decomposition of HP by OBr^- or Br_2.[24] Even when HP was initially added to 5 times excess over the alcohol, it was necessary to add more HP to oxidize all of the alcohol in this co-catalytic system. If the HP was added dropwise though, only 10% excess was needed for the reaction to reach completion.

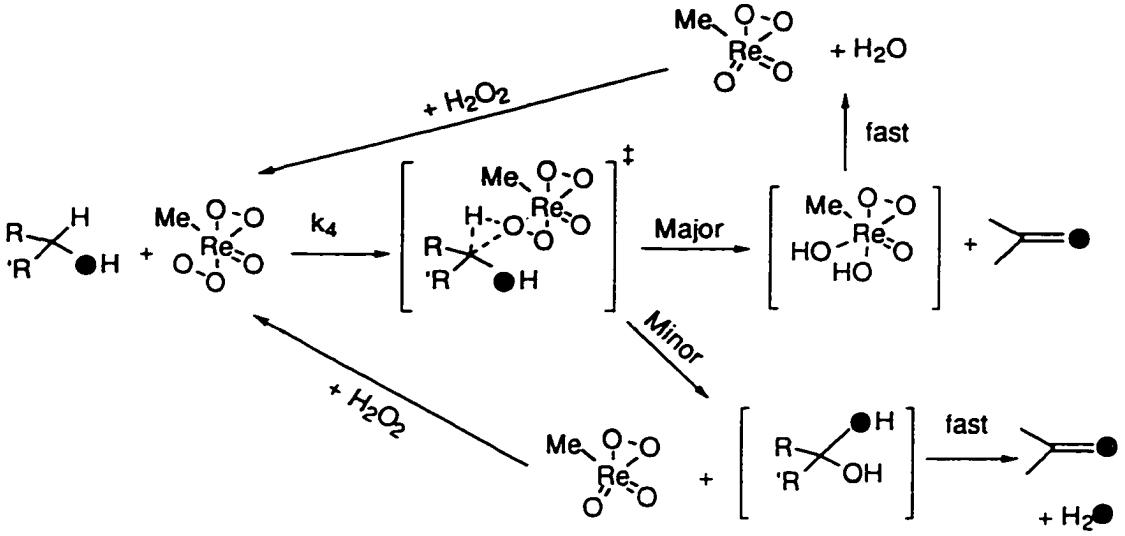
Discussion

Oxidation Mechanism. As stated earlier the oxidation of alcohols by MTO and HP must proceed by a different mechanism then has been determined for other substrates such as sulfides, alkenes, and hydroxylamines. All of these previous compounds had a center of electron density where an oxygen atom can be transferred to. **Scheme 2** best describes the oxidation of alcohols by MTO/HP based on our observations. This mechanism shows the formation of an intermediate in which there are interactions between the peroxorhenium oxygen with both the carbon and the hydrogen of the α C-H bond. This is typically how an hydride abstraction is depicted, supported by the kinetic isotope effect k_H/k_D of 3.2. The electron-poor oxygen performs an electrophilic attack on the electron density of the C-H bond. Based on our observations there is no radical intermediate.

This intermediate can then proceed along two pathways. The major path is followed when the C-H bond is severed, after which the carbocation loses a proton to produce the ketone. This proton could be lost either to the solvent or to the other peroxorhenium oxygen to give a di-hydroxo rhenium product, which rapidly eliminates water to give **A**. The di-hydroxo rhenium species has

not been isolated, but is not unreasonable in that MTO oxygens are known to exchange with those of water, through a similar di-hydroxo rhenium form.[25] This major pathway is further supported by the retention of labeled oxygen in the ketone.

Scheme 2



The minor pathway is proposed to account for the 20% of labeled oxygen that does not remain in the product and to account for the fact that the methyl-ether can be oxidized as well. With a rate constant for the ether and the respective alcohol within a factor of 4, the mechanism for oxidation of both must be somewhat similar. The difference between the major and minor pathway is where the di-hydroxy group resides when the intermediate breaks apart. Since the active oxidizing form of MTO has capabilities similar to those of DMDO, there appear to be similarities between the rhenium center of MTO and the carbon center of DMDO. The pathway with the di-hydroxo rhenium product is preferred in our mechanism over the carbon gem-diol product, showing that the two centers are not truly identical.

Listed in Table 1 are the substrates oxidized by MTO/HP in this study. A LFER plot of the para substituted α-methylbenzyl alcohols demonstrates the

effect of electronic variations. If an electron donating group is at the para position the reaction becomes faster, and vice versa. This also supports a hydride abstraction mechanism. It can also be noticed that steric factors play a role in the rate of the reaction based on the difference in yields for the various non-α-phenyl alcohols. The yields start at 92 % for cyclohexylethanol and decrease with additional steric bulk to 27% for 1-phenyl-2-butanol. A last point of interest is that a primary alcohol is oxidized not only to the aldehyde, but further oxidation occurs with excess peroxide to give the carboxylic acid as seen with benzyl alcohol. This second oxidation can be limited by the amount of peroxide added.

Synthetic Considerations. This study has produced a new synthetic scale preparation of ketones from alcohols in good yields. The yields are somewhat dependent on the starting alcohol, with the majority being above 80%. Further, the use of bromide co-catalytst decreased the reaction times by a factor of at least 1000 with decreased reaction temperatures. We feel that this co-catalytic system[26] has great potential.

References

1) March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure;* 4 ed.; John Wiley & Sons, Inc.: New York, 1992.

2) Larock, R. C. *Comprehensive Organic Transformations;* VCH Publishers, Inc.: New York, 1989.

3) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.* **1995**, *36*, 6415-6418.

4) Vassell, K. A.; Espenson, J. H. *Inorg. Chem.* **1994**, *33*, 5491-5498.

5) Herrmann, W. A.; Fischer, R. W.; Scherer, W.; Rauch, M. U. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1157.

6) Al-Ajlouni, A.; Espenson, J. E. *J. Org. Chem.* **1996**, *61*, 3969-3976.

7) Yamazaki, S. *Bull. Chem. Soc. Jpn.* **1997**, *in press.*

8) Zhu, Z.; Espenson, J. E. *J. Org. Chem.* **1995**, *60*, 1326-1332.

9) Zauche, T. H.; Espenson, J. H. *Inorg. Chem.* **1997**, *36*, 5257-5261.

10) Espenson, J. H.; Pestovsky, O.; Huston, P.; Staudt, S. *J. Am. Chem. Soc.* **1994**, *116*, 2869.

11) Hansen, P. J.; Espenson, J. H. *Inorg. Chem.* **1995**, *34*, 5839-5844.

12) Meinwald, J.; Schneider, R. A.; Thomas, A. F. *J. Am. Chem. Soc.* **1967**, *89*, 70.

13) Stasuik, F.; Sheppard, W. A. *Canadian Journal of Chemistry* **1956**, *34*, 123-127.

14) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*; 2 ed.; McGraw-Hill, Inc.: New York, 1995.

15) Kovac, F.; Baumstark, A. L. *Tetrahedron Lett.* **1994**, *35*, 8751-8754.

16) Baumstark, A. L.; Beeson, M.; Vasquez, P. C. *Tetrahedron Lett.* **1989**, *30*, 5567-5570.

17) Minisci, F.; Zhao, L.; Fontana, F.; Bravo, A. *Tetrahedron Lett.* **1995**, *36*, 1697-1700.

18) Vanni, R.; Garden, S. J.; Banks, J. T.; Ingold, K. U. *Tetrahedron Lett.* **1995**, *36*, 7999-8002.

19) Murray, R. W.; Gu, H. *J. Org. Chem.* **1995**, *60*, 5673-5677.

20) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 12386-12387.

21) Jacob, J.; Espenson, J. H. *unpublished results* .

22) Eigen, M.; Kustin, K. *J. Am. Chem. Soc.* **1962**, *84*, 1355.

23) Stewart, R. *Oxidation Mechanisms*; W.A. Benjamin, Inc.: New York, 1964.

24) Bray, W. C. *Chem. Rev.* **1932**, *10*, 161.

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

26) Zhu, Z.; Espenson, J. H. *unpublished results* .

27) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; 3 ed.; Harper Collins Publishers: New York, NY, 1987.

Table 1. Rate Constants and Yields for the Catalytic Oxidation of Alcohols

Entry	Alcohol	$10^5 \times k_4$ /L $mol^{-1}s^{-1}$ [a]	% Yield on Synthetic Scale[b]		% Conversion
1	4-Me-α-methylbenzylalcohol	10.2	84	92	93
2[c]	4-MeO-α-methylbenzylalcohol	8.85	-	-	-
3	*sec*-phenethyl alcohol	7.7	89	97	98
4	1-phenyl-1-propanol	6.8	69	92	93
5	4-F-α-methylbenzylalcohol	6.2	91	99	99
6	(R)-(+)-2-Methyl-1-phenyl-1-propanol	5.5	64	86	87
7	benzyl alcohol[d]	5.3	41 (7)[e]	40 (12)	54
			28 (21)	16 (38)	55
8	benzhydrol	5.0	46	48	49
9	4-Cl-α-methylbenzylalcohol	4.9	84	95	96
10	4-(CF_3)-α-methylbenzylalcohol	4.4	60	85	85
11	1-phenylethanol-1,2,2,2,-D_4	2.4	-	-	-
12	4-Br-α-methylbenzylalcohol	2.3	58	64	64
13	methyl-(1-phenyl)-ethyl ether	2.3	22	53	53
14	1-cyclohexylethanol		74	92	93
15	4-phenyl-2-butanol		58	61	64
16	1-phenyl-2-propanol		26	27	30

[a] Determined in 20% Water/Acetonitrile, 0.10 M $HClO_4$, at 25 °C.

[b] neat alcohol, 2 mole equivalents HP, 4 mol% MTO, 40 °C. The first column is after 8 hours, the second after 24 hours, based on NMR peak integrations.

Table 1. continued

[c] 4-MeO gave a number of products, which were not identified; entry 11 was not reacted on the synthetic scale due to lack of starting alcohol.

[d] The top entry is with 1 eq of HP, the bottom entry is with 2 eq of HP.

[e] the first value refers to yield of benzaldehyde, while the value in ( ) refer to the yield of benzoic acid.

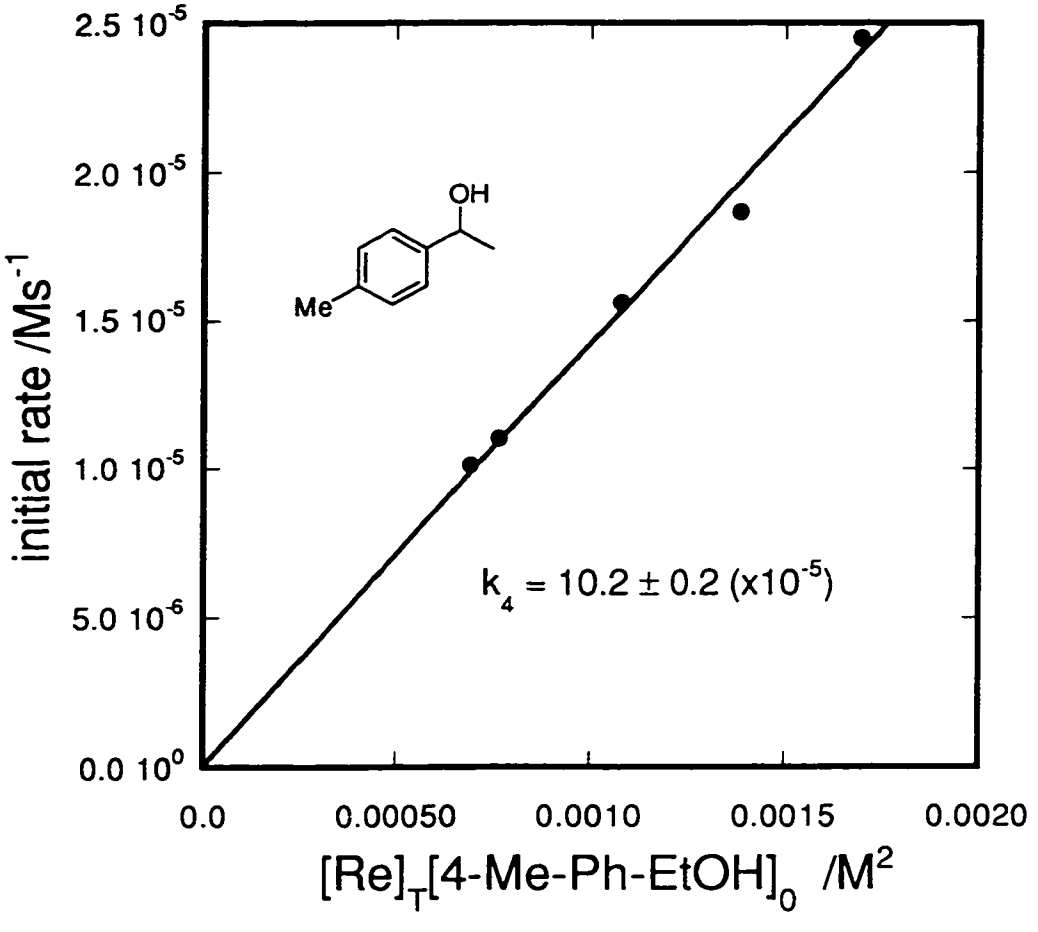


Figure 1. Determination of the rate constant k4 for 4-Me-phenethyl alcohol from the linear dependence of initial rate on total rhenium and alcohol concentrations. Concentrations: 200 mM H_2O_2, 36 - 72 mM 4-Me-phenylethanol, and 10 - 30 mM MTO in 20% H_2O/acetonitrile and 0.10 M $HClO_4$.

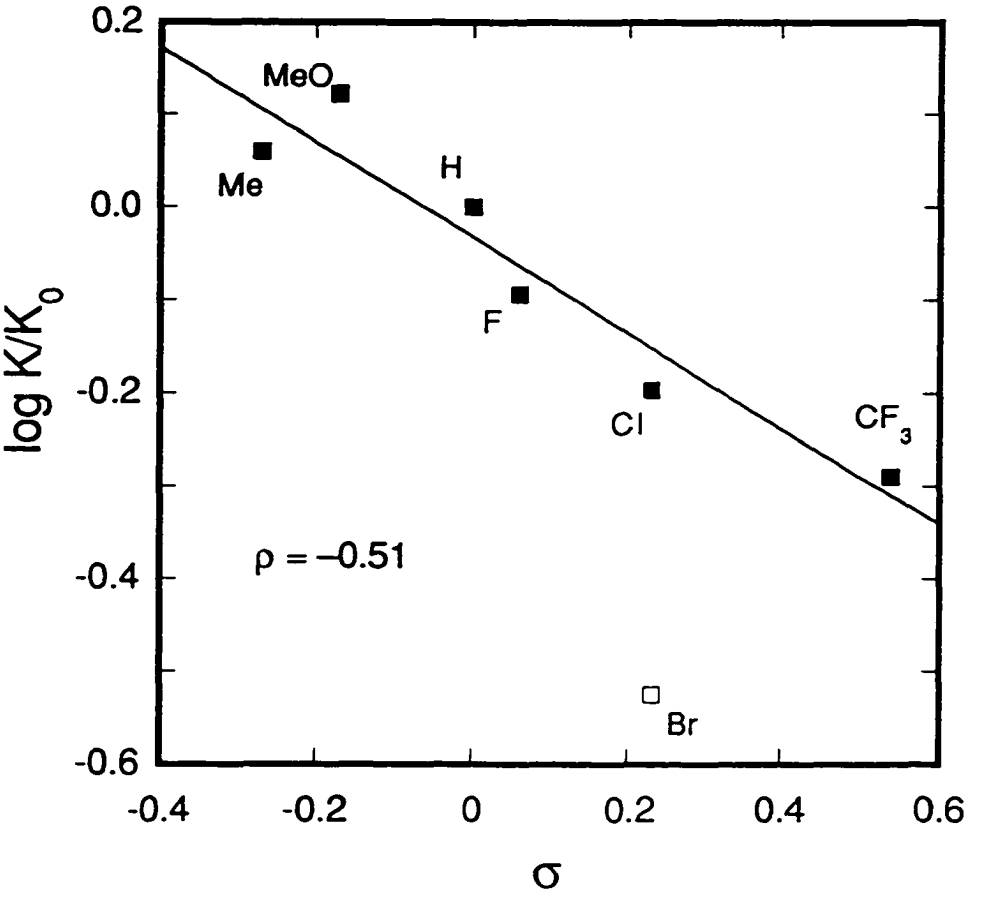


Figure 2. The linear free energy relationship between the rate constant for the oxidation of 4-X-α-methylbenzyl alcohols by MTO and H_2O_2 and the Hammett σ constant for X[27]. K_0 is defined as X = H. The deviant X= Br point was left out of the ρ calculation. The ρ value of –0.51 describes the effect that electron donating and withdrawing groups have on the transition state.

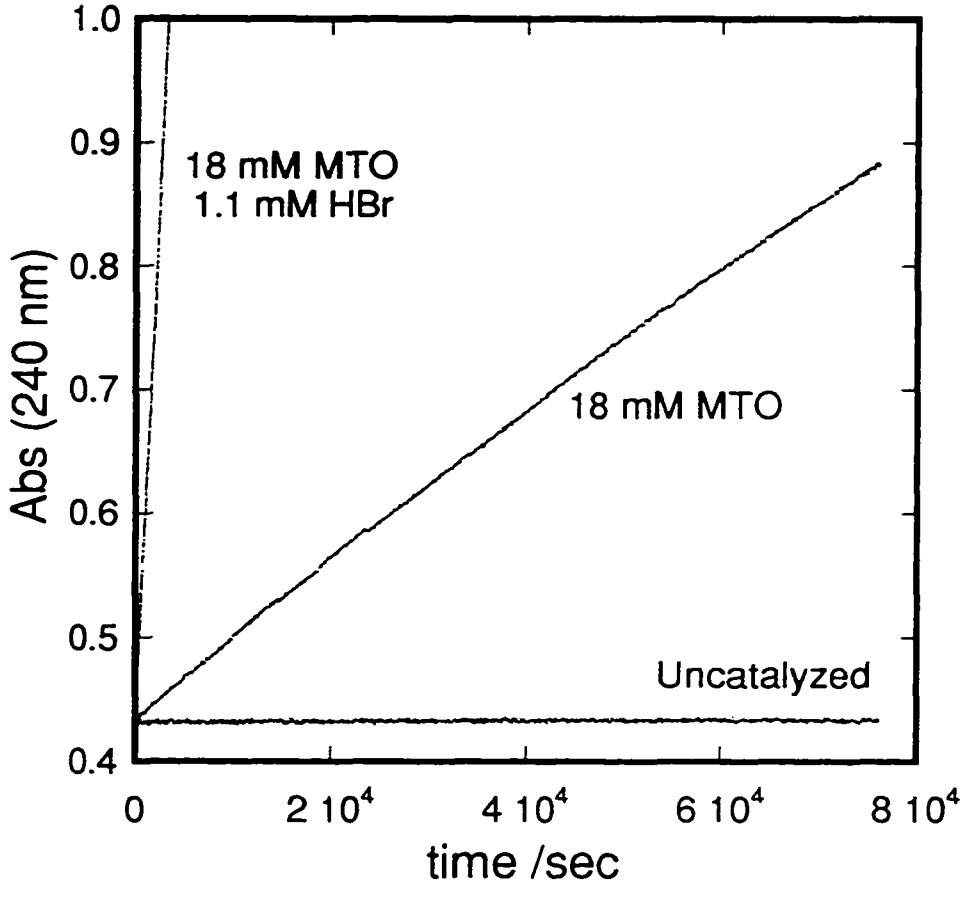


Figure 3. The increase in absorbance at 240 nm accompanying the buildup of the ketone from the reaction of sec-phenethyl alcohol and hydrogen peroxide in 20% water-acetonitrile containing 0.10 M $HClO_4$. Without a catalyst the reaction is nonexistent, while adding MTO or HBr and MTO increases the rate of the reaction to different extents.

CHAPTER II

KINETICS AND MECHANISM OF THE OXIDATION OF SECONDARY HYDROXYLAMINES TO NITRONES WITH HYDROGEN PEROXIDE, CATALYZED BY METHYLTRIOXORHENIUM (MTO)

A paper published in *Inorganic Chemistry*[*]

Timothy H. Zauche and James H. Espenson

Abstract

Secondary hydroxylamines, $(RCH_2)_2NOH$ and $(R_2CH)_2NOH$, are converted to nitrones, $RCH_2N(O)=CHR$ and $R_2CHN(O)=CR_2$, in >94% yield with hydrogen peroxide as an oxygen donor and methylrhenium trioxide (MTO) as a catalyst. High concentrations of hydrogen peroxide were used so that the methylrhenium diperoxide, $CH_3Re(O)(\eta_2\text{-}O_2)_2(H_2O)$, was the dominant and reactive form of the catalyst. Representative rate constants are: $k/L\ mol^{-1}\ s^{-1}$ = 150 (R = Me), 52 (Et), 13.8 (Pr^i) and 3.33 ($PhCH_2$) no H/D kinetic isotope effect on the rate constant for this step. The data are interpreted to infer the intervention of an oxygenated intermediate, $(RCH_2)_2N(O)OH$, which then rapidly dehydrates to yield the nitrone. Two products are formed from unsymmetrical hydroxylamines, the ratio of which establishes the reactivities of the intermediate towards the competing elimination reactions: $(RCH_2)(R'CH_2)NOH \rightarrow \{(RCH_2)(R'CH_2)N(O)OH\} \rightarrow \chi\ RCH_2N(O)=CHR' + (1-\chi)\ R'CH_2N(O)=CHR$.

---

[*] Zauche, Timothy H; Espenson, James H. *Inorg. Chem.* 1997, 36, 23, 5257.

Introduction

Methylrhenium trioxide (CH_3ReO_3, abbreviated as MTO) has proved to be an efficient oxidation catalyst with hydrogen peroxide as the oxygen source. This catalyst, first prepared as a minor side product,[1] can now be obtained easily.[2] The scope of the catalytic oxidations is quite wide, and a considerable diversity of substrates will react.[3-13] Particularly germane to the present studies are the reports that MTO catalyzed the oxidation of primary and secondary amines to hydroxylamines, nitrosoalkyls, nitroalkyls, and nitrones.[14-17] The net reactions of the hydroxylamine, either as the starting material or prepared in-situ from a secondary amine, are given in eq 1, along with the formula of the presumed intermediate that represents the result of the transfer of an oxygen atom so typical of MTO-hydrogen peroxide reactions. Hereinafter, we use one of the two generalized formulas for the hydroxylamines, as the other follows easily from it.

$$(RCH_2)_2NOH + H_2O_2 \xrightarrow{\text{cat. MTO}} \{(RCH_2)_2N(O)OH\} \xrightarrow{-H_2O} RCH_2N(O)=CHR \quad (1)$$

We were attracted to a study of the oxidation of secondary hydroxylamines to nitrones by their value as synthetic intermediates, which is important in medicinal and natural product chemistry.[18-24] Highly functionalized nitrogen heterocycles can be synthesized from nitrones and olefins in 1,3-dipolar cycloaddition reactions.[25,26] Nitrones are also widely used as radical traps.[27-35]

Catalysts other than MTO have been used for the oxidation of amines or hydroxylamines to nitrones; SeO_2 catalyzes the reaction of hydrogen peroxide and amines to form nitrones, but the yields are not always high.[36] Tungstate is effective as a catalyst only for certain amines.[37,38] Imine oxidation also provides nitrones in stoichiometric reactions with permanganate, peroxyacids, and or dimethyldioxirane.[39-41]

Since much of the earlier work with MTO has focused on the preparative aspects,[14-17] we have chosen to explore the mechanism of the MTO system. There are two principal themes of reaction mechanism we have developed in this study, one pertaining to the oxidation step, the other to the dehydration of the first-formed intermediate, previously postulated, but without experimental proof.[36]

Experimental Section

Materials. Certain reagents were purchased: N,N-diethylhydroxylamine, N,N-dimethylhydroxylamine (as a 2 M solution in methanol), N,N-dibenzylhydroxylamine, several secondary amines, 30% hydrogen peroxide, and methylrhenium trioxide (Aldrich); HPLC grade organic solvents (Fisher); $CD_3(CH_3)NH$ (Cambridge Isotopes). N-hydroxypiperidine, di-isopropylamine, N-ethyl-N-isopropyl-hydroxylamine, and N-tert-butyl-N-benzyl-hydroxylamine were prepared according to the literature.[42]

N-Benzyl-N-alkyl-hydroxylamines, with alkyl = Me, Et, and Pr^i, were synthesized by the following procedure based on MTO catalysis. The given amine was oxidized with hydrogen peroxide (1 eq) and 4–8% MTO in 50 mL of methanol by adding the catalyst slowly until a yellow color persisted, signaling an MTO-amine complex and thus indicating that the hydrogen peroxide had entirely reacted. At that point 5 mL of satd. aqueous sodium carbonate was added. The resulting nitrogen compounds were a mixure owing to competing rates of oxidation of the amine and hydroxylamine; they were extracted with 3 × 20 mL ether and concentrated by rotary evaporation to 3 mL. The hydroxylamine was then separated by column chromatography on silica gel, eluting usually with an ethyl acetate-hexane mixture. The pure hydroxylamine was collected in 20-30%

yield; the yield undoubtedly could have been improved, but this procedure sufficed to prepare high-purity hydroxylamines for the kinetic studies.

Stock solutions of the hydroxylamine and MTO were made in methanol and used within two days. The 30% hydrogen peroxide was standardized iodometrically; it was stable for long periods; dilute solutions made from it by dilution in methanol were standardized every 3-4 h.

Kinetics. These experiments were carried out in methanol by spectrophotometry with Shimadzu 2501 and 3101 instruments, monitoring the product buildup of alkyl nitrones at 235 nm and aryl nitrones at 295 nm. The reactions were carried out in a quartz cuvette in air, since this reaction, like other MTO-catalyzed oxidations, showed no effect on changing from an atmosphere of argon to one of air or oxygen. Because the molar absorptivities of the nitrones are so large, ~4×10^3 L mol^{-1} cm^{-1} (235 nm) and ~1.2×10^4 L mol^{-1} cm^{-1} (290 nm), a cell of 0.02 cm was usually used to keep the absorbance change within a permissible range. Except for two special cases discussed later, the reactions reached a final stable absorbance. A typical procedure is the following: MTO and hydrogen peroxide were mixed in the reaction cell, and allowed to stand for 4–5 min until the catalytically active peroxorhenium compounds had formed. The hydroxylamine was then added, the solution thoroughly mixed (~20 s), and the data acquisition started. In addition to these experiments, some measurements were made at 360 nm, where **B** [= $CH_3Re(O)(\eta^2\text{-}O_2)_2(OH_2)$], has a unique absorption band ($\varepsilon \sim 1.2 \times 10^3$ L mol^{-1} cm^{-1}). These measurements allowed us to follow the concentration of one of the active forms of the catalyst with time.

We anticipated a problem might arise from the pH of the medium. If too acidic, protonation of the hydroxylamine would reduce its concentration by some amount and lower the rate as a consequence. If too basic, catalyst decomposition

would set in by several pathways, prominent among them under these conditions being the reaction between MTO and HO_2^-.[43] Experiments with N,N-diethylhydroxylamine gave the same rate constant in methanol as when buffered by an acetic acid-sodium acetate (1.8:1) solution added at ca. 20× the concentration of the hydroxylamine, showing that the buffer was not needed.

Kinetic data. The absorbance-time curves were analyzed by either or both of two methods. Certain sets of kinetic data followed first-order kinetics, and the rate constant was determined by a nonlinear least-squares fit to the equation

$$Abs_t = Abs_\infty + (Abs_0 - Abs_\infty) \times e^{-kt} \qquad (2)$$

More frequently, the initial rate method was used, since the distribution of the catalyst among the forms MTO, **A** [= $CH_3Re(O)_2(\eta^2\text{-}O_2)$] and **B** did not remain completely constant during the course of the experiment; further discussion of this point will be given later. The concentration of the product was calculated from the absorbance at each time, with hundreds or thousands of values collected in each data file. The equation is

$$[\text{Nitrone}]_t = C_t = [(RCH_2)_2NOH]_0 \times \frac{Abs_0 - Abs_t}{Abs_0 - Abs_\infty} \qquad (3)$$

The concentration-time data were then fit to a power series, $C_t = m_0 + m_1 t + ... + m_n t^n$, with the program KaleidaGraph. The initial rate, $(dC/dt)_{t=0}$ or v_i is the value of m_1.[44,45] This procedure is particularly useful when the catalyst species change in proportion to one another during the course of the run, but it is somewhat less accurate than the method based on the integrated rate equation.

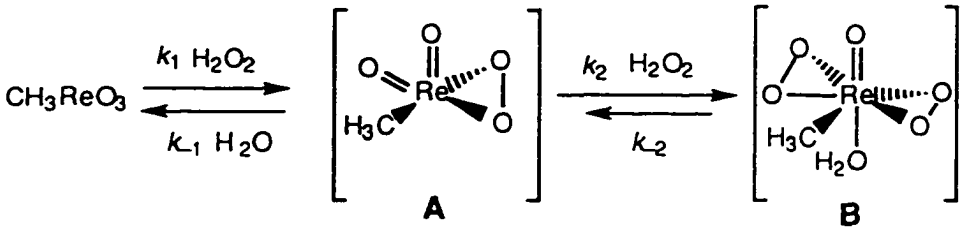
Reaction Products. The nitrones were identified by their ^{1}H–NMR spectra in CD_3OD. Many of these products have been reported previously,[16,17,36-41] for some, NMR data were reported in $CDCl_3$. The chemical shifts are collected in the **Appendix, Table A-1.**

Hydroxylamines with inequivalent R groups produce two nitrones. Their ratio was determined by integrating the NMR signals (cf. tabulated specta in the **Appendix, Table A-2**); triplicate determinations on independent samples were made.

Results

MTO Speciation during the Catalytic Cycles. We refer first to the two reactions with hydrogen peroxide, shown in **Scheme 1.** On their own, MTO, **A**, and **B** will attain *equilibrium* concentrations governed by the values of K_1 and K_2, the equilibrium constants for reactions in that scheme, and the peroxide concentration.

Scheme 1



The same is not true during a catalytic reaction cycle during which steady-state conditions apply. To illustrate this phenomenon, the absorbance was recorded at 360 nm over the time in which dibenzylhydroxylamine was being converted to the nitrone. At this wavelength, **B** is the only absorbing species; the starting material, product, MTO and **A** do not contribute to the light absorption. As shown in **Figure 1**, [**B**] falls to some 80% of its starting value (i.e., from the equilibrium value, MTO and hydrogen peroxide having been allowed to equilibrate before the hydroxylamine was added), and then rises. Then, after nitrone formation was complete, [**B**] rose to the same concentration it had at the start. The reason is simple enough: the steady-state concentration of **B** and of the

other rhenium species are governed not only by the rate constants in **Scheme 1**, but also by the rate constant for the reaction of each peroxorhenium compound with the hydroxylamine. Analysis of the full time course of the kinetics by following the buildup of the nitrone would thus be quite complex, since the proportions of **A** and **B** did not remain constant. This problem was circumvented by the use of initial rates in experiments in which such conditions prevailed.

Reaction Kinetics. It was necessary to show that the two methods for the analysis of kinetic data were equivalent. Experiments carried out on Et_2NOH were analyzed by both methods. Assume that the reaction under the conditions chosen (high $[H_2O_2]$ = 0.2–0.3 M) is dominated by a reaction between **B** and Et_2NOH, eq 4, expressed by the rate law, eq 5, written in terms of initial rates

$$\mathbf{B} + (RCH_2)_2NOH \xrightarrow{k_4} \mathbf{A} + (RCH_2)_2N(O)OH \quad (4)$$

$$v_i = k_4[\mathbf{B}][R_2NOH]_0 \cong k_4[Re]_T[R_2NOH]_0 \quad (5)$$

in which $[\mathbf{B}] \cong [Re]_T = [MTO] + [\mathbf{A}] + [\mathbf{B}]$ and k_4 represents the bimolecular rate constant for the indicated reaction. Experiments were then carried out over a range of MTO concentrations, 0.07–0.52 mM. In each case v_i was evaluated by polynomial fitting. The values of v_i were then correlated with the concentrations of **B** and hydroxylamine. We show the result as a plot of v_i against the product of these concentrations (in this set of experiments, one of the concentrations is constant, however). According to eq 5 the values of v_i should define a straight line that passes through the origin. The data are shown in **Figure 2**. The least-squares slope of the line gives $k_4 = 52 \pm 1$ L mol^{-1} s^{-1} (25 °C in methanol).

The method of pseudo-first-order kinetics was then applied to the same data. The rate constant so evaluated, designated k_ψ, should be directly

proportional to $[Re]_T$ given this rate law. To allow a presentation of the results of this method alongside those of the other, the product $k_\psi \times [Et_2NOH]_0$ is displayed on the y-axis, and the same concentration product on the x-axis. As shown in **Figure 2**, the plots are coincident within the experimental error. The first-order kinetic treatment gives $k_4 = 51 \pm 2$ L mol^{-1} s^{-1}. These findings taken together validate both methods of data treatment and the rate law given in eq 5.

Why are the values of k_4 so close, when it was shown (Figure 1 and accompanying discussion) for a related reaction that [**B**] changed over the course of the reaction? Two reasons can be cited: first, the decrease in $[B]_{ss}$ is governed here by $k_4 = 52$ L mol^{-1} s^{-1}, different from that for the dibenzylhydroxylamine, **Figure 1**, with $k_4 = 3.33$ L mol^{-1} s^{-1}. More importantly, the convergence of the two methods reflects the averaging of the contributions from both peroxorhenium complexes. This reaction is given in eq 6.

$$\mathbf{A} + (RCH_2)_2NOH \xrightarrow{k_3} MTO + (RCH_2)_2N(O)OH \qquad (6)$$

In general, as has been found for many types of substrate, k_3 is about the same as k_4, or a factor of 2–3 larger at most. As such, a change in the proportions of **A** and **B** during the course of the reaction, which is exemplified in Figure 1, will not have a large effect on the kinetic analysis.

Nonetheless, we made it our practice to use preferentially the method of initial rates. The rate constants calculated on that basis for the eleven dialkyl hydroxylamines are given in **Table 1**. An example of a product buildup curve is given in **Figure 3**, which depicts the rise in nitrone concentration from the reaction of N-ethyl-N-isopropylhydroxylamine.

In those instances where two nitrones were formed, Entries 6-7, 9, and 11, the kinetic data were acquired at a wavelength at which only one of the nitrones absorbs. This is critical for the initial rate method. In fact, this work illustrates an

important but subtle distinction between a rate and a rate constant. The value of k_ψ represents the rate constant for forming all the products, in this case the single rate constant leading to the intermediate, irrespective of its partitioning to products and of the relative contributions to the absorbance. On the other hand, the initial rate from the buildup of one nitrone represents just the rate constant leading to that product. The actual value of k_4 requires division of v_i by $[RR'NOH]_0 \times [Re]_T$ *and by F,* the fraction formed of the particular nitrone being monitored. For these cases, the k_4 values summarized in Table 2 were calculated by this procedure. Entry 5 in that table constitutes the single exception: the absorption bands of the two nitrones were not distinct, and thus the pseudo-first-order kinetic treatment was needed.

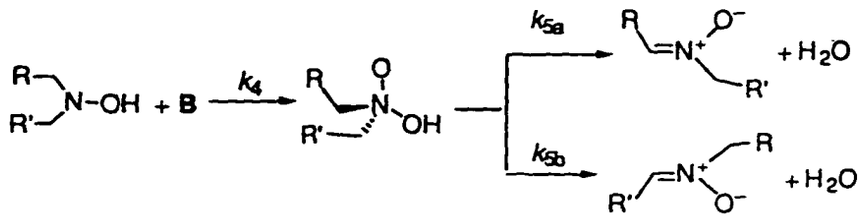
Products. The nitrones from all the reactions were identified by their NMR spectra. These spectra agree with the structure and with literature values, where known. This information is given in the **Appendix, Table A-2.** The chemical shifts are consistent with the structures given. The data presented in **Table 2** shows that in all reactions save two, the yield of nitrone (or nitrone pair, considering the asymmetric hydroxylamines) is quantitative. The nitrone from the oxidation of dimethylhydroxylamine was formed in an 85% yield, based on an in-situ NMR determination. By a similar method, N-benzyl-N-methylhydroxylamine gave but 55% nitrone. This nitrone, N-methylene-N-benzylamine-N-oxide, is subject to the hydrolysis reaction shown in eq 7. The resulting N-benzylhydroxylamine is subject to further MTO-catalyzed oxidation to the oxime.[14]

$$PhCH_2N(O)=CH_2 \xrightarrow{H_2O} HCHO + PhCH_2NHOH \xrightarrow{MTO} PhCH=NOH \qquad (7)$$

Partitioning to the Products. Unsymmetric hydroxylamines give rise to a pair of nitrones, since the subsequent elimination reaction can involve the

hydrogen on either of the α-carbon atoms. **Scheme 2** presents this situation more fully.

Scheme 2



The ratio of the two nitrones determined by ^{1}H–NMR affords the ratio of the rate constants k_{5a}/k_{5b}, which are clearly (because of the concentration dependences that enter the kinetic expression) fast steps following the rate-controlling step.

For the kinetics analysis, the initial rate of formation of product a is

$$(v_i)_a = \frac{k_4[RR'NOH][Re]_T}{1+\frac{k_{5b}}{k_{5a}}} \qquad (7)$$

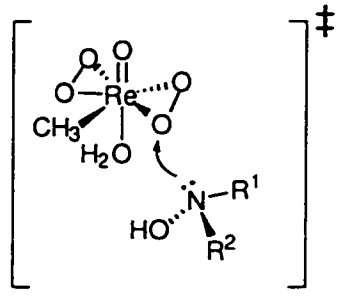
which provides the basis for the evaluation of k_4 in these cases, as described in the preceding section.

Kinetic Isotope Effects. The rate constants for N-hydroxypiperidine and its d_{10} derivative are the same; compare Entries 2 and 3 in Table 2. This is as to be expected, given the mechanistic implications of eq 1 and eq 4: the first step is an oxygenation process, and the C–H bonds on the α-carbons are not involved. On the other hand, there is every reason to anticipate that the second step of the reaction, nitrone formation, will exhibit a significant kie, given the representation in **Scheme 2**. The kinetic isotope effect will not show up in the kinetics. Thus we prepared $(CH_3)(CD_3)NOH$ in-situ by the MTO-catalzyed oxidation of the the commercially-available amine. The ratio of the resulting nitrones could be determined quantitatively from the ^{1}H–NMR spectra, allowing

a resolution of the kinetic isotope effect. The value k_H/k_D (the ratio of k_5 values for elimination from a C–H bond relative to a C–D bond) was found to be 2.9 (**Table 2**, Entry 12).

Discussion

Oxidation Mechanism. Given the many parallels in the kinetic data between the present set of data and the oxidation of other substrates in MTO-catalyzed reactions of hydrogen peroxide, the data suggest that the k_4 step (reaction 4) is rate-controlling. The mechanism of this reaction is then nucleophilic attack of the nitrogen lone pair on one of the four peroxo oxygens of **B**. The peroxide groups have been electrophilically activated by coordination to the electropositive +7 rhenium center. We also note that the rate constants for 1-hydroxypiperidine and its d_{10} derivative are the same, indicating that there is no involvement of a proton on the α-carbon in the transition state. This is a telling point, in that nitrone formation ultimately requires its elimination. The transition state for a nucleophilic process can be depicted like this:



The kinetic trends within the simplest of the series R_2NOH must be considered. The rate constants for $R_1 = R_2$ = Me, Et, Pr^i, and c-C_5H_{10} are 150, 52, 14, and 62 L mol^{-1} s^{-1}, respectively. One wonders at the virtual absence of a parallel effect in the case of a seemingly analogous series of R_2S compounds, the rate constants for which are 2.0×10^4 (R = Et), 1.6×10^4 (R = Pr^i), and 2.0×10^4 (R = C_5H_{10}) L mol^{-1} s^{-1}.[12] It appears that the trend for the hydroxylamines represents

a steric effect. It is not a large trend, of course, the values of $\Delta G^{\ddagger}$ at the extremes differing by only 14 kJ mol^{-1} along the series. Steric effects would, of course, be expected more for trivalent nitrogen than for divalent sulfur. We further note that steric effects have been observed for the oxidation of phosphines; to cite but one example, note the difference between $(p\text{-}MeC_6H_4)_3P$ and $(o\text{-}MeC_6H_4)_3P$, with rate constants of 9×10^5 and 1.9×10^5 L mol^{-1} s^{-1}.[8] Under the conditions adopted for the kinetic experiments the peroxorhenium compound **B** is dominant, with **A** playing a minor role. Nonetheless, we would anticipate a parallel transition state for it which would be more important at lower peroxide concentrations.

The Hydroxylamine-N-Oxide. The immediate product of the oxygen transfer reaction is an intermediate dialkyl-hydroxylamine-N-oxide that has not been directly observed. This species is postulated here on grounds of the operative O-transfer mechanism, and thus the material that can reasonably be obtained from the reaction with **B** . This intermediate, moreover, can yield the nitrone product by a precedented elimination step. Since the product-forming step is much more rapid than the initial reaction, it does not contribute directly to the rate equation. The nitrone-forming step is shown in **Scheme 2**. The hydroxylamine-N-oxide intermediate was previously postulated in the oxidation of secondary amines with hydrogen peroxide catalyzed by selenium dioxide[36] and tungstates.[38] In neither case, however, was it identified or detected during the reaction.

The Elimination Reaction. In light of data from the literature[17] that give a different yield of these products, we examined further the values for Entry 6. As noted, the ^{1}H–NMR data gave one nitrone, $CH_3N(O)=CHPh$, in a yield of 48 ± 7%. By difference, the second nitrone, $PhCH_2N(O)=CH_2$, was formed in 52% yield. This is the ratio reported in **Table 2**. Further checking was required,

however, in that the literature reported an isolated yield of 70% $CH_3N(O)=CHPh$ from the MTO-catalyzed reaction of the parent amine with urea-hydrogen peroxide (UHP) at 0 °C. We obtained an NMR yield of ~40%, the balance being the other nitrone. A repeat determination by UV-vis using hydrogen peroxide gave the yield as 50 ± 10%.

Because nitrone formation makes no direct kinetic contribution, this step must be explored by indirect means. Kinetic isotope effects have afforded a way of examining this mechanism. The reactions of the 1-hydroxypiperidine derivatives (h_{10} and d_{10}) do not speak to this point; each reacts independently (and, as it turns out, at the same rate). A suitable compound was found in $(CH_3)(CD_3)NH$. Two nitrones were easily detected and determined by their ^1H-NMR spectra. The rate constant ratio is $k_H/k_D = 2.9$, for cleavage of a C–H bond relative to a C–D bond.

Different compounds provided other means of exploring the elimination reaction. The data in **Table 2** show the relative rates of formation of the pairs of nitrones that result from the sequence of oxidation and elimination processes. Since oxidation is not the determinant of the product ratio, the relative rates of elimination can be determined. Moreover, it may be useful to compare the relative rates after normalization per α-hydrogen, to correct for statistical effects. This, too, is given in **Table 2.**

For an E2 elimination mechanism,[46] the more conjugated and substituted product is favored. These factors are manifest in the values recorded, in **Table 2,** although for Entry 9 the two factors are in opposition. The effects do appear to be systematic in that a relation such as the following holds among *different* compounds

$$\frac{k_{Et}}{k_{Bn}} \times \frac{k_{Bn}}{k_{Pr}} \approx \frac{k_{Et}}{k_{Pr}} \qquad (8)$$

For example, k_{Bn} in this interpretation can be transferred from one compound to the next. The relative rate for elimination from a given R group appears to be transferable from one compound to another, supporting a common mechanism.

The gist of the elimination mechanism is that a conjugate base attacks the CH proton at almost the same time the conjugate acid attacks the OH group. The kinetic isotope effect establishes that C–H bond breaking is well advanced in the transition state. The conjugate base and acid are most likely H_2O and H_3O^+, although this point remains uncertain.

References

(1) Beattie, I. R.; Jones, P. J. *Inorg. Chem.* **1979**, *18*, 2318.

(2) Herrmann, W. A.; Kühn, F. E.; Fischer, R. W.; Thiel, W. R.; Romão, C. C. *Inorg. Chem.* **1992**, *31*, 4431.

(3) Hansen, P. J.; Espenson, J. H. *Inorg. Chem.* **1995**, *34*, 5839.

(4) Herrmann, W. A.; Fischer, R. W.; Scherer, W.; Rauch, M. U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1157.

(5) Brown, K. N.; Espenson, J. H. *Inorg. Chem.* **1996**, *35*, 7211.

(6) Al-Ajlouni, A.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 9243.

(7) Al-Ajlouni, A.; Espenson, J. H. *J. Org. Chem.* **1996**, *61*, 3969.

(8) Abu-Omar, M. M.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 272.

(9) Abu-Omar, M. M.; Espenson, J. H. *Organometallics* **1996**, *15*, 3543.

(10) Zhu, Z.; Espenson, J. H. *J. Mol. Catal.* **1995**, *103*, 87.

(11) Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 1326.

(12) Vassell, K. A.; Espenson, J. H. *Inorg. Chem.* **1994**, *33*, 5491.

(13) Huston, P.; Espenson, J. H.; Bakac, A. *Inorg. Chem.* **1993**, *32*, 4517.

(14) Yamazaki, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 877.

(15) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.* **1996,** *37,* 805.

(16) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *J. Org. Chem.* **1996,** *61,* 8099.

(17) Goti, A.; Nannelli, L. *Tetrahedron Lett.* **1996,** *37,* 6025.

(18) Asrof Ali, S.; Wazeer, M. I. M. *J. Chem. Soc., Perkin Trans. II* **1986,** 1789.

(19) Asrof Ali, S.; Khan, J. H.; Wazeer, M. I. M. *Tetrahedron* **1988,** *44,* 5911.

(20) Brown, B. R. *The Organic Chemistry of Aliphatic Nitrogen Compounds;* Clarendon Press: Oxford, 1994.

(21) Dicken, C. M.; DeShong, P. *J. Org. Chem.* **1982,** *47,* 2047.

(22) Haran, S.; Mathur, H. H.; Trivedi, G. K. *Ind. J. Chem.* **1988,** *27B,* 994.

(23) Padwa, A. *1,3 Dipolar Cycloaddition Reactions;* John Wiley & Sons: New York, 1984; Vol. 2.

(24) Padwa, A.; Chiacchio, U.; Kline, D. N.; Perumattam, J. *J. Org. Chem.* **1988,** *53,* 2238.

(25) Carruthers, W.; Coggins, P.; Weston, J. B. *J. Chem. Soc., Perkin Trans. I* **1990,** 2323.

(26) Merlin, P.; Braekman, J. C.; Daloze, D. *Tetrahedron* **1991,** *47,* 3805.

(27) Haire, D. L.; Hilborn, J. W.; Janzen, E. G. *J. Org. Chem.* **1986,** *51,* 4298.

(28) Huie, R.; Cherry, W. H. *J. Org. Chem.* **1985,** *50,* 1531.

(29) Janzen, E. G. *Acc. Chem. Res.* **1971,** *4,* 31.

(30) Janzen, E. G.; Oehler, U. M.; Haire, D. L.; Kotake, Y. *J. Am. Chem. Soc.* **1986,** *108,* 6858.

(31) Janzen, E. G.; Haire, D. L.; Coulter, G., A.; Stronks, H. J.; Krygsman, P. H.; Towner, R. A.; Hilborn, J. W. *J. Org. Chem.* **1989,** *54,* 2915.

(32) Janzen, E. G.; Krygsman, P. H.; Lindsay, D. A.; Haire, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 8279.

(33) Kotake, Y.; Janzen, E. G. *J. Am. Chem. Soc.* **1989**, *111*, 2066.

(34) Janzen, E. G.; Zhang, Y.-K.; Haire, D. L. *J. Am. Chem. Soc.* **1994**, *116*, 3738.

(35) Kotake, Y.; Janzen, E. G. *J. Am. Chem. Soc.* **1991**, *113*, 9503.

(36) Murahashi, S.-I.; Shiota, T. *Tetrahedron Lett.* **1987**, *28*, 2383.

(37) Mitsu, H.; Zenki, S.-I.; Shiota, T.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1984**, 874.

(38) Murahashi, S.-I.; Mitsui, H.; Shiota, T.; Tsuda, T.; Watanabe, S. *J. Org. Chem.* **1990**, *55*, 1736.

(39) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739.

(40) Boyd, D. R.; Coulter, P. B.; McGuckin, M. R.; Sharma, N. D.; Jennings, W. B.; Wilson, V. E. *J. Chem. Soc., Perkin Trans. I* **1990**, 301.

(41) Christensen, D.; Jorgensen, K. A. *J. Org. Chem* **1989**, *54*, 126.

(42) Biloski, A. J.; Ganem, B. *Synthesis* **1983**, 537.

(43) Abu-Omar, M.; Hansen, P. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1996**, *118*, 4966.

(44) Hall, K. J.; Quickenden, T. I.; Watts, D. W. *J. Chem. Educ.* **1976**, *53*, 493.

(45) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms, 2d Ed.*; 2 ed.; McGraw-Hill, Inc.: New York, 1995.

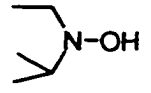
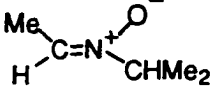
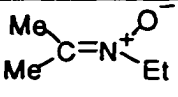
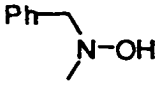
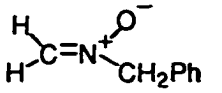
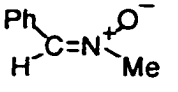
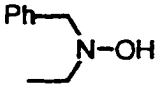
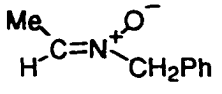
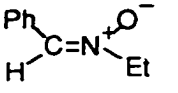
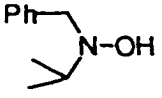
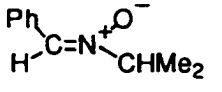
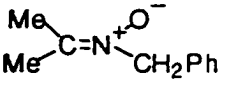
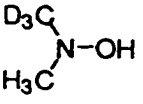
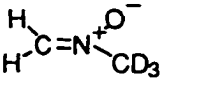
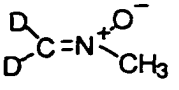
(46) March, J. *Advanced Organic Chemistry*; 4th ed.; Wiley: New York, 1992, p 1167.

Table 1. Rate Constants for the Catalytic Oxygenation of Hydroxylamines in Methanol at 25.0 °C

Entry	Hydroxylamine	k_4/L mol^{-1} s^{-1}	Nitrone (% yield)[a]
1	N,N-Dimethyl	150 ± 6	85
2	1-Hydroxypiperidine	64 ± 1	99
3	d_{10}-1-Hydroxypiperidine	63 ± 2	99
4	N,N-Diethyl	52 ± 1	97
5	N-Ethyl-N-isopropyl	35.4 ± 0.6[b]	98
6	N-Benzyl-N-methyl	26 ± 4	55 [c]
7	N-Benzyl-N-ethyl	15.8 ± 0.3	95
8	N,N-Di-isopropyl	13.8 ± 0.6	94
9	N-Benzyl-N-isopropyl	7.0 ± 0.2	98
10	N,N-dibenzyl	3.33 ± 0.05	99
11	N-Benzyl-N-tert-butyl	0.94 ± 0.05	99

[a] Based on NMR peak integrations; [b] Determined from fit to first-order kinetics; [c] The low yield is a consequence of subsequent nitrone decomposition (see text).

Table 2. Ratio of Nitrone Products From Asymmetric Hydroxylamines

Entry	Hydroxylamine	Major Nitrone	Minor Nitrone	Ratio = k_{5a}/k_{5b}	Normalized ratio[a]
5				6.0	3.0
6				~1.1	~0.7[b]
7				1.6	1.6
9				4.4	2.2
12				2.9	2.9

[a] Normalized based on the number of available protons; [b] This number is imprecise since N-oxide-N-benzylmethyleneamine decomposes under these conditions.

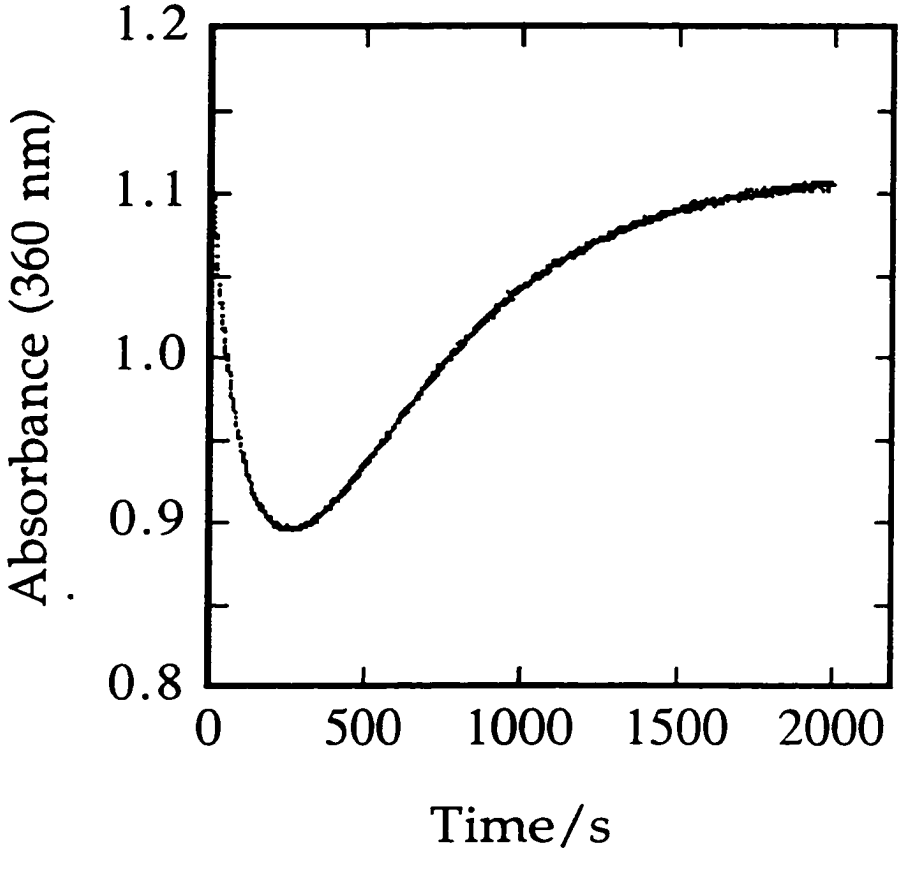


Figure 1. A recording of the concentration of **B**, the catalytically-active methylrhenium diperoxide, during the course of the oxidation of dibenzylhydroxylamine. **B**, the only species in the solution that absorbs at 360 nm, drops to ca. 80% of its initial value during the reaction and is fully restored at the end. Concentrations: 0.98 mM $(PhCH_2)_2NOH$, 200 mM H_2O_2, 0.87 mM MTO.

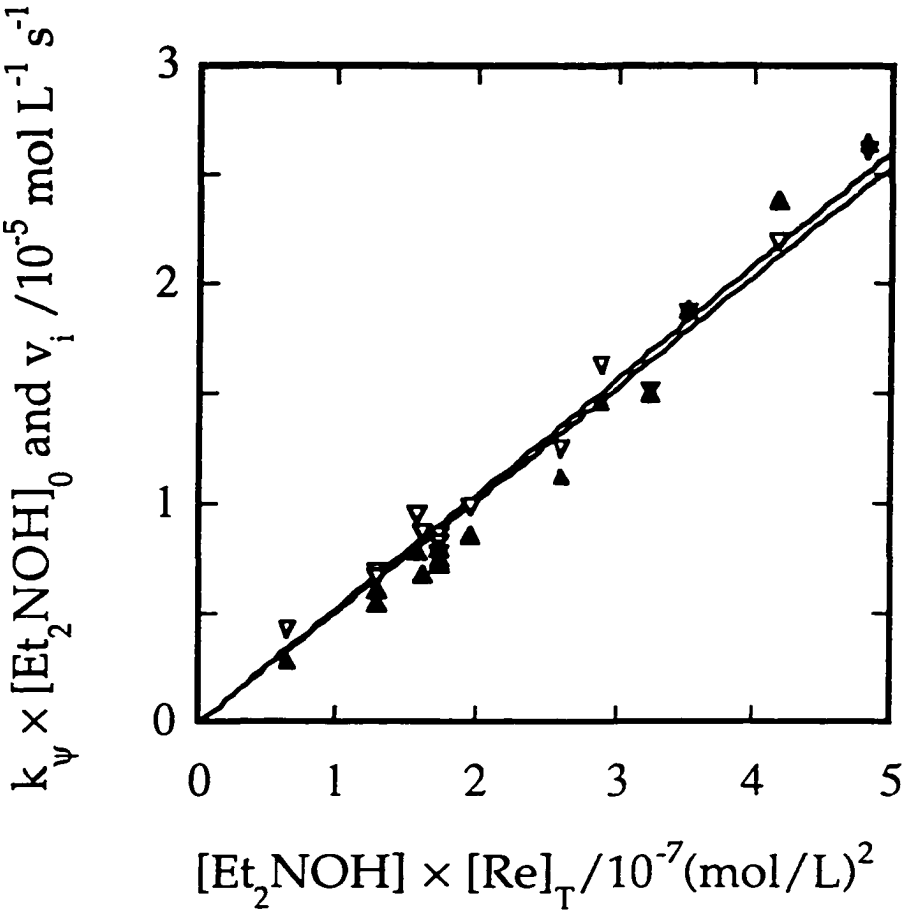


Figure 2. A comparison of two methods (initial rates, filled symbols, and pseudo-first-order kinetics) for the evaluation of the kinetic data for the reaction of Et_2NOH (0.928 mM) and H_2O_2 (0.20–0.30 M) catalyzed by MTO (0.07–0.52 mM). The solutions also contained HOAc (12.1 mM) and NaOAc (8.3 mM).

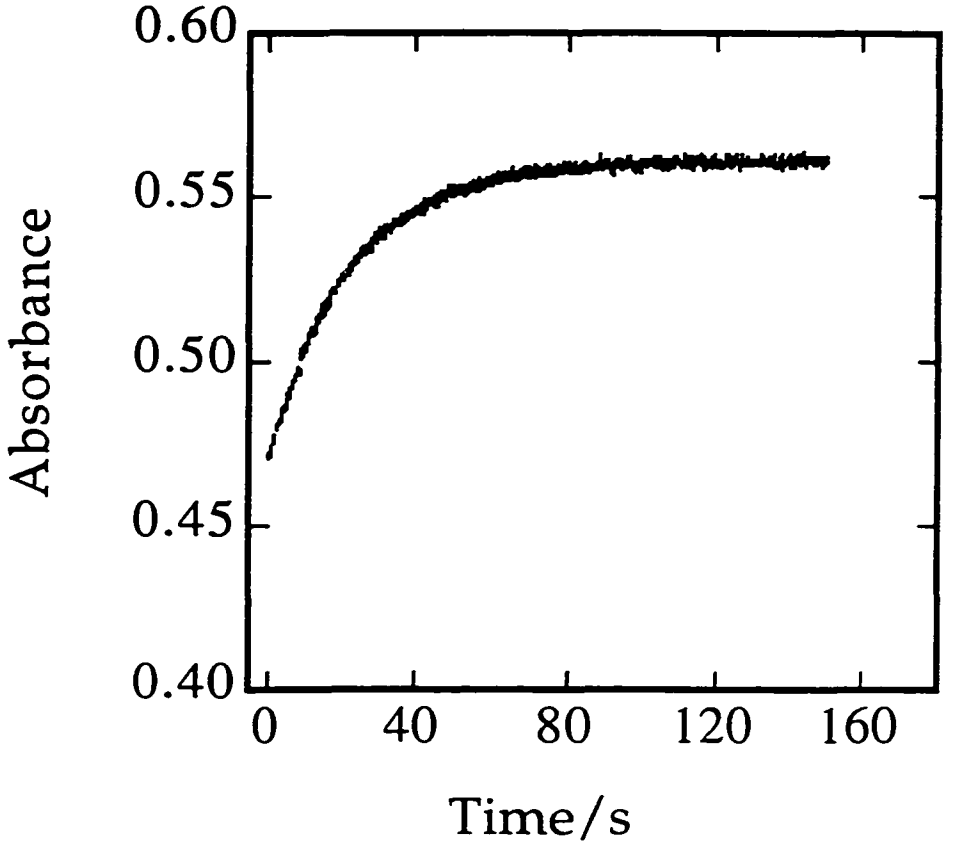


Figure 3. The increase in absorbance at 230 nm accompanying the buildup of the nitrone from the reaction of N-ethyl-N-isopropyl-hydroxylamine and hydrogen peroxide in methanol at 25 °C. Concentrations were 0.20 M H_2O_2, 2.03 mM R_2NOH, and 1.32 mM MTO. The reaction kinetics as shown occur in a single stage; the later partitioning to two nitrones takes place quite rapidly (see text).

APPENDIX: NMR CHEMICAL SHIFTS FOR SELECTED COMPOUNDS

Table A–1: ^{1}H–NMR chemical shifts in CD_3OD

Dialkylhydroxylamines	δ, rel to Me_4Si
Me_2NOH	3.175 (s, 6H)
Et_2NOH	2.66 (broad q, 4H, J 7.2 Hz), 1.13 (t, 6H, J 7.2 Hz)
Pr^i_2NOH	3.06 (hept, 2H, J 6.4 Hz), 1.08 (d, 12H, J 6.4 Hz)
$(PhCH_2)_2NOH$	7.37 (m, 4H), 7.30 (m, 4H), 7.23 (m, 2H), 3.86 (s, 4H)
c-$C_5H_{10}NOH$	3.20 (m, 2H), 2.39 (m, 2H), 1.73 (m, 2H), 1.59 (m, 3H), 1.16 (m, 1H)
$(Et)Pr^iNOH$	2.081 (hept, 1H, J 6.4Hz), 2.67 (broad q, 2H, 7.2 Hz) 1.11 (t, 3H, J 7.2 Hz), 1.06 (d, 6H, J 6.4 Hz)
$(PhCH_2)MeNOH$	7.33 (m, 5H), 3.76 (s, 2H), 2.61 (s, 3H)
$(PhCH_2)EtNOH$	7.30 (m, 5H), 3.78 (s, 2H), 2.72 (broad q, 2H, J 7.2 Hz) 1.15 (t, 3H, J 7.2 Hz)
$(PhCH_2)Pr^iNOH$	7.3 (m, 5H), 3.81 (s, 2H), 2.95 (hept, 1H J 6.3 Hz), 1.16 (d, 6H J 6.3 Hz)
$(PhCH_2)Bu^tNOH$	7.36 (m, 2H), 7.27 (m, 2H), 7.18 (m ,1H), 3.76 (s, 2H), 1.18 (s, 9H)
c-C_5D_9NOH	**^{2}D spectrum** (rel to CH_2DOH = 3.069 ppm): 2.88 (s, 2H), 2.07 (s, 2H), 1.40 (s, 2H), 1.23 (s, 3H), 0.83 (s, 1H)

Table A–2. ^{1}H–NMR spectra for nitrones

Nitrone	δ (rel to Me_4Si) in CD_3OD	Literature in $CDCl_3$
H_2C=N(O)Me	6.74 (s, 1H, J 7.2 Hz), 6.63 (s, 1H, J 7.2 Hz), 3.74 (s, 3H)	This material was independently synthesized [Ref 3]
MeCH=N(O)Et	7.29 (q, 1H, J 6.0 Hz), 3.86 (broad q, 2H, J 7.2 Hz), 2.004 (d, 3H, J 6.0 Hz), 1.42 (t, 3H, J 7.2 Hz)	6.9 (q, 1H, J 6.0 Hz), 3.8 (broad q, 2H, J 7.2 Hz), 1.9 (d, 3H, J 6.0 Hz), 1.4 (t, 3H, J 7.2 Hz) [Ref 1]
Me_2C=N(O)Pr^i	4.63 (hept, 1H, J 6.4 Hz), 2.22 (s, 3H), 2.15 (s, 3H), 1.31 (d, 6H, J = 6.4 Hz)	4.47 (hept, 1H, J 6.5 Hz), 2.14 (s, 6H), 1.37 (d, 6H, J = 6.5 Hz) [Ref 2]
PhCH=N(O)CH_2Ph	8.24 (m, 2H), 8.04 (s, 1H), 7.40 (m, 8H), 5.12 (s, 2H)	8.17-8.25 (m, 2H), 7.36-7.51 (m, 9H), 5.06 (s, 2H) [Ref 1]
c-C_5H_9NO	7.36 (s, 1H), 3.75 (s, 2H), 2.51 (m, 2H), 1.99 (m, 2H) 1.73 (m, 2H)	7.15-7.25 (m, 1H), 3.75-3.85 (m, 2H), 2.4-2.5 (m, 2H), 1.9-2.1 (m, 2H) 1.6-1.8 (m, 2H) [Ref 2]
MeCH=N(O)Pr^i	7.29 (q, 1H, J 5.6 Hz), 4.19 (hept, 1H, J 6.4 Hz), 1.98 (d, 3H, J 5.6 Hz), 1.37 (d, 6H, J 6.4 Hz)	
Me_2C=N(O)Et	3.92 (broad q, 2H, 7.2 Hz), 2.21 (s, 3H), 2.15 (s, 3H), 1.407 (t, 3H, J 7.2 Hz)	
PhCH=N(O)Me	8.25 (m, 2H), 7.84 (s, 1H), 7.40 (m, 3H), 3.87 (s, 3H),	8.22 (dd, 2H), 7.39 (dd, 4H), 3.81 (s, 3H) [Ref 1]
H_2C=N(O)CH_2Ph	7.40 (m, 5H), 6.86 (d, 1H, J 6.8 Hz), 6.66 (d, 1H, J 6.8 Hz), 5.00 (s, 2H)	

Table A–2 cont.

PhCH=N(O)Et	8.26 (m, 2H), 7.89 (s, 1H), 7.4 (m, 3H), 4.03 (broad q, 2H, J 7.2 Hz), 1.53 (t, 3H J 7.2 Hz)	
MeCH=N(O)CH_2Ph	7.4 (m, 6H), 4.96 (s, 2H), 2.01 (d, 3H, J 6 Hz)	
PhCH=N(O)Pr^i	8.27 (m, 2H), 7.90 (s, 1H), 7.46 (m, 3H), 4.37 (hept, 1H J 6.4 Hz), 1.46 (d, 6H J 6.4 Hz)	8.05-8.4 (m, 2H), 7.48 (s, 1H), 7.2-7.56 (m, 3H), 1.58 (s, 9H) [Ref 2]
Me_2C=N(O)CH_2Ph	7.4 (m, 5H), 5.12 (s, 2H), 2.27 (s, 3H), 2.19 (s, 3H)	
PhCH=N(O)Pr^i	8.32 (m, 2H), 7.92 (s, 1H), 7.48 (m, 3H), 1.61 (s, 9H)	
c-C_5D_9NO	**^{2}D spectrum** (rel to CH_2DOH = 3.069 ppm): 7.10 (s, 1H), 3.42 (s, 2H), 2.12 (s, 2H), 1.64 (s, 2H), 1.37 (s, 2H)	

References:

(1) Dicken, C. M.; DeShong, P. *J. Org. Chem.* **1982**, *47*, 2047.

(2) Murahashi, S.-i.; Mitsui, H.; Shiota, T.; Tsuda, T.; Watanabe, S. *J. Org. Chem.* **1990**, *55*, 1736.

(3) Menard *Can. J. Chem.* **1974**, *52*, 2316.

CHAPTER III
TEMPO AND MTO AS CO-CATALYSTS FOR THE OXIDATION OF ALCOHOLS BY HYDROGEN PEROXIDE

A paper submitted for publication in the journal *Inorganic Chemistry*

Timothy H. Zauche and James H. Espenson

Abstract

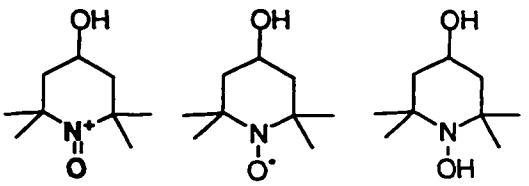
The reactions of the oxammonium ion 4-hydroxy-2,2,66-tetramethylpiperidinium N-oxide, 4-hydroxy-Tempo, abbreviated R_2NO^+, have been studied. The previously unreported triflate salt was used, because Cl^- and Br^- can themselves be oxidized and must be avoided in the part of the research that involves methyltrioxotrhenium, MTO, and H_2O_2. Reactions with R_2NO^+ convert alcohols to their carbonyl compounds; the rate constant for $PhCH_2OH$ is 4.4×10^{-3} L mol^{-1} s^{-1} in acetonitrile at 298 K. The immediate product is the hydroxylamine, R_2NOH, but its further comproportionation reaction with R_2NO^+ yields the stable piperidinyl oxyl radical, $R_2NO^\bullet$. The rate constant of this reaction is 1.78×10^3 L mol^{-1} s^{-1} at 298 K.

Introduction

Oxammonium ions, such as 4-hydroxy-2,2,66-tetramethylpiperidinium N-oxide, R_2NO^+ in **Chart 1**, are strong oxidizing agents. Alcohols are oxidized by R_2NO^+ stoichiometrically and catalytically, both electrochemically[1,2] and with a variety of reagents such as HOCl,[3-5] MCPBA,[6] and Cu(II).[7] Secondary alcohols react preferentially over primaries, possibly for steric reasons.[4,8] During most oxidations R_2NO^+ is converted to R_2NOH without an intermediate piperidinyl oxyl radical, $R_2NO^\bullet$. The comproportionation equilibrium, $R_2NOH + R_2NO^+ =$

$2R_2NO^{\bullet} + H^+$, favors the radical; thus after the initial stage of the reaction $R_2NO^{\bullet}$ predominates.

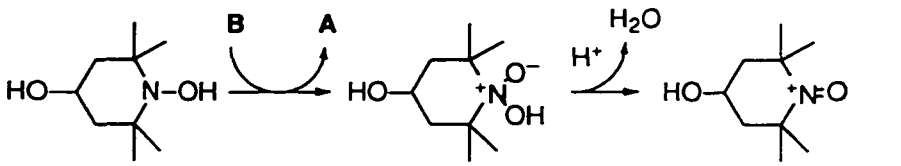
Chart 1



1 = R_2NO^+ **2** = $R_2NO^{\bullet}$ **3** = R_2NOH

Hydrogen peroxide oxidizes secondary hydroxylamines to nitrones when methyltrioxorhenium (CH_3ReO_3, abbreviated as MTO)[9] or Na_2WO_4[10] is used as catalyst. a-Tetrasubstituted amines are converted to N-oxyl radicals with MTO–H_2O_2,[11] perhaps by the same mechanism (**Scheme 1**). Alcohols are oxidized with MTO–H_2O_2,[12,13] albeit very slowly. We have examined the possibility, using alcohol reactions as the test case, that R_2NO^+ might act in concert with MTO to promote certain oxidations.

Scheme 1



hydroxylamine oxoammonium ion

Experimental Section

Some reagents were purchased: TEMPO, 4–hydroxy-TEMPO, MTO, 30% H_2O_2, $AgCF_3SO_3$ and HPLC-grade organic solvents. 2,2,6,6-Tetramethyl-piperidine-1,4-diol and 2,2,6,6-tetramethyl-1-oxo-piperidinium chloride were prepared according to the literature procedures.[8,14,15] They were stored under nitrogen because they are sensitive to moisture and oxygen.[16] Chloride salts cannot be used since hypochlorite formation must be avoided.[17] Silver salts

have been used to oxidize $R_2NO^{\bullet}$, but no product has been isolated. 4-Hydroxy-2,2,6,6-tetramethyl-1-oxo-piperidinium triflate, previously unreported, was prepared by stirring 0.55 mmol silver triflate in 4 mL nitromethane with 0.50 mmol 4-hydroxy-TEMPO. Metallic silver formed within minutes; it was removed and 25 mL ether was added to obtain a yellow solid in 84% yield. Anal.: Calcd. for $C_{10}H_{18}NSO_5F_3$: C, 37.38; N, 4.36; H, 5.65; Found: C, 37.44, N, 4.33, H, 5.67.

Kinetics studies were carried out in acetonitrile without an added Lewis base, once it had been confirmed that 2,6-lutidine had no effect on the rate. Conditions were selected to minimize the amount of protons released during any reaction, owing to the involvement of side reactions that will be discussed.

Results and Interpretation

Several steps to consider are these:

$$MTO + H_2O_2 = \mathbf{A} + H_2O \quad (1)$$

$$\mathbf{A} + H_2O_2 = \mathbf{B} \quad (2)$$

$$\mathbf{B} + R_2NOH \rightarrow \mathbf{A} + R_2NO^+ + OH^- \quad (3)$$

$$R_2NO^+ + R_2CHOH \rightarrow R_2NOH + R_2CO + H^+ \quad (4)$$

In solutions of MTO containing hydrogen peroxide, the two peroxorhenium complexes were formed in equilibrium, **A** [$MeRe(O)_2(h^2\text{-}O_2)$] and **B** [$MeRe(O)(\eta^2\text{-}O_2)_2(H_2O)$], as given in reactions 1 and 2. Reaction **3** was monitored at 240 nm by the buildup of $R_2NO^{\bullet}$, $\varepsilon = 1.85 \times 10^3$ L mol^{-1} cm^{-1}. This radical resulted from the rapid comproportionation reaction between R_2NO^+ and R_2NOH. The concentrations employed were 0.6-3.0 mM MTO, 200 mM H_2O_2, and 0.7-2.0 mM R_2NOH. Since **B** was rapidly regenerated under these conditions, pseudo-first-order conditions applied. The rate constant is $k_3 = 3.0$ L mol^{-1} s^{-1} in

acetonitrile at 298 K. In comparison, the closely-related reaction of **B** with N-benzyl-N-Bu^{t}hydroxylamine has k_3 = 0.94 L mol^{-1} s^{-1} in methanol at 298 K.[9] Based on the similarity of these values, we infer that the two reactions represent the same chemistry.

Rate constants for reaction 4 have not been reported hitherto. The buildup of benzaldehyde was monitored at 244 nm, with 1-5 mM R_2NO^+ and 60-200 mM $PhCH_2OH$. These measurements afforded $k_4 = 4.4 \times 10^{-3}$ L mol^{-1} s^{-1} in acetonitrile at 298K. The reaction stoichiometry was $2R_2NO^+$:1$PhCH_2OH$, evidence for the rapid comproportionation reaction of R_2NO^+ with R_2NOH, reaction 5.

$$R_2NO^+ + R_2NOH \rightarrow 2R_2NO^\bullet + H^+ \qquad (5)$$

The kinetics of the reaction of R_2NO^+ with R_2NOH was monitored by stopped-flow and conventional UV-Vis methods. The initial conditions were 18-32 μM R_2NO^+, 46-416 μM R_2NOH. A few of these experiments were carried out under pseudo-first-order conditions. These data were fit to the form for mixed-second-order kinetics, eq 6 in terms of concentration and eq 7 in terms of absorbance.

$$[R_2NO^+]_t = [R_2NO^+] \times \frac{R-1}{R \times e^{k^* t} - 1} \qquad (6)$$

$$Abs_t = Abs_\infty + \frac{(R-1) \times (Abs_0 - Abs_\infty)}{R \times e^{k^* t} - 1} \qquad (7)$$

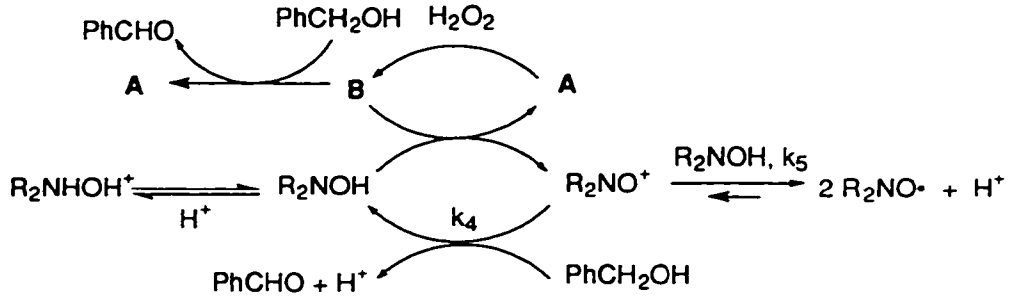
where $R = [R_2NOH]_0/[R_2NO^+]_0$ and the rate constant $k^* = k_5 \times \Delta$, with $\Delta = [R_2NOH]_0 - [R_2NO^+]_0$.

The plot of k against Δ is depicted in **Figure 1**; its slope gave $k_5 = (1.78 \pm 0.05) \times 10^3$ L mol^{-1} s^{-1} in acetonitrile at 298 K. The position of the equilibrium in eq 5 can be shifted by protonation of the hydroxylamine, $R_2NHOH^+ = R_2NOH + H^+$, but doing so provides no advantage here since the protonated hydroxylammonium ion does not react with **B**.[9] The low reactivity of R_2NHOH^+

seems general, which is the reason that catalytic R_2NO^+ oxidations are generally performed under neutral or basic conditions.

With these values and estimates at hand, the construction of the catalytic cycle was possible. **Scheme 2** presents an analysis of the transformations occurring. For sake of simplicity, steps interconverting MTO and A are not shown. At the outset the oxidation of $PhCH_2OH$ by **B** is negligible relative to its oxidation by the oxammonium ion. The cycle cannot be sustained for long, however, because of the rapid comproportionation reaction. These experiments were run without added H^+, so that the equilibrium in eq 5 would lie well to the right. To limit the occurrence of reaction 5, which limits the effectiveness of a catalytic mechanism, [MTO] was increased to 40 mM and $[R_2NO^+]_0$ decreased to 0.1 mM. Aldehyde formation was detected, but it arises mainly from the reaction of **B**, not R_2NO^+, with $PhCH_2OH$.

Scheme 2



It can be recognized that the comproportionation reaction limits the catalytic applicability of this scheme. It is widely recognized that ClO^- is a 2e oxidizing agent. Hypochlorite oxidations succeed, and it appears that under these conditions the MTO-TEMPO co-catalysts are relatively ineffective. It was difficult to sustain the oxidation of alcohol by R_2NO^+ since is being more rapidly consumed in reaction 5. Note that the equilibrium in reaction 5 could be made reversible at higher $[H^+]$. With that, the oxyl radical would be an intermediate

not a dead end. Conditions of high [H^+] are, however, incompatible with the need for R_2NOH, not the nonreactive R_2NHOH^+.

References

(1) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492.

(2) Inokuchi, T.; Matsumoto, S.; Fukushima, M.; Torii, S. *Bull. Chem. Soc. Jpn* **1991**, *64*, 796.

(3) Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem.* **1989**, *54*, 2970.

(4) Siedlecka, R.; Skarzewski, J.; Mochowski, J. *Tetrahedron Lett.* **1990**, *31*.

(5) Leanna, M. R.; Sowin, T. J.; Morton, H. E. *Tetrahedron Lett.* **1992**, *33*, 5029.

(6) Cella, J. A.; McGrath, J. P.; Kelley, J. A.; Soukarry, E. O.; Hilpert, L. *J. Org. Chem.* **1977**, *42*, 2077.

(7) Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 3374.

(8) Yamaguchi, M.; Miyazawa, T.; Takata, T.; Endo, T. *Pure & Appl. Chem.* **1990**, *62*, 217.

(9) Zauche, T. H.; Espenson, J. H. *Inorg. Chem.* **1997**, *22*, 5257.

(10) Sen, V. D.; Golubev, V. A.; Efremova, N. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1982**, 61.

(11) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.* **1996**, *37*, 805.

(12) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.* **1995**, *36*, 6415.

(13) Zauche, T. H.; Espenson, J. H. , submitted for publication.

(14) Paleos, C. M. *J. Chem. Soc., Chem. Commun.* **1977**, 345.

(15) Yamaguchi, M.; Miyazawa, T.; Takata, T.; Endo, T. *Pure and Applied Chemistry* **1990**, *62*, 217-222.

(16) Golubev, V. A.; Sen, V. D.; Kulyk, I. V.; Aleksandrov, A. L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1974**, *10*, 2235-2243.

(17) Hansen, P. J.; Espenson, J. H. *Inorg. Chem.* **1995**, *34*, 5839.

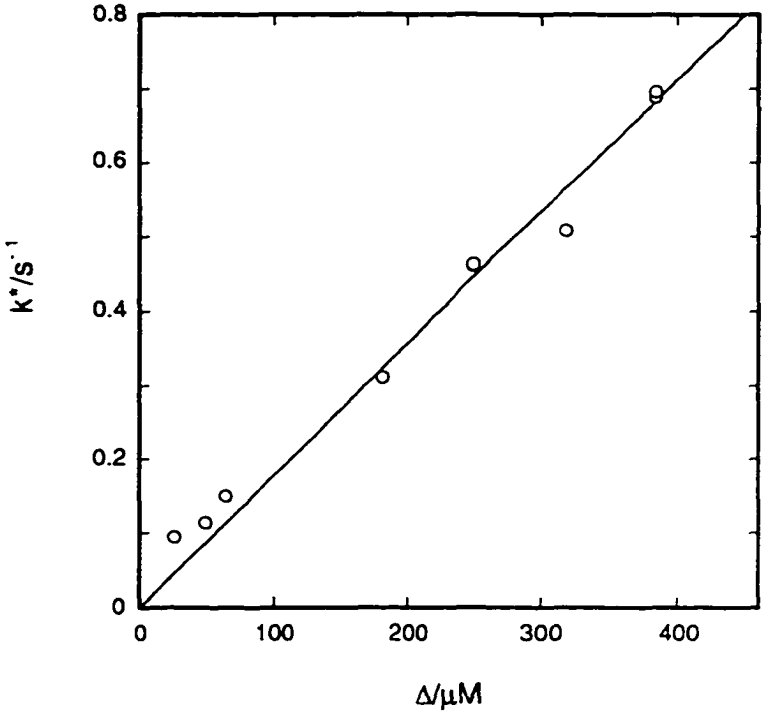


Figure 1. The kinetic analysis of the data for reaction 5 in acetonitrile at 298 K. The values of k*, obtained from eq 7, are shown here as a plot of k* vs. Δ, the difference in the initial concentrations of the reactants; the slope of this plot is k_5.

CHAPTER IV
OXYGEN-SELECTIVE SORBENTS

Introduction

During the preceding two years our group at the Ames Laboratory, Iowa State University has had a research partnership with the Praxair Corporation. This undertaking was centered on various kinetics experiments for the reactions of selected Co(salen) derivatives with molecular oxygen. This chapter summarizes the goals of the project, how these goals were to be achieved, and the results that were obtained during the study.

Five compounds were received from Praxair. The ultimate goal was to obtain the "solvent free" rates of oxygen binding and dissociation for these cobalt complexes. The kinetics were to be determined in solution and then extrapolated to solvent-free conditions since Praxair uses these compound in the non-solvated form.

The methods for determining the rapid rate of molecular oxygen binding to cobalt complexes are few in number. The binding of Lewis bases (B, in eq 1-2) is an important consideration.[1] Many determinations have been made of the equilibrium constant relating the oxygenated to the non-oxygenated cobalt complex, K_{ox},[2] defined as the ratio of k_{on}/k_{off} as described in eq 3. This has been demonstrated the most effectively by Martell et al.[3,4] K_{ox} was determined by monitoring the change in barometric pressure, quantifying the amount of oxygen absorbed by the cobalt complexes. The product of this coordination is a $Co(III)O_2\bullet$, shown here as a superoxo radical. Equation 4 describes the formation of a μ-peroxo bridging two Co(III) atoms.

$$Co(L) + B \overset{K_1}{\rightleftharpoons} Co(L)B \qquad (1)$$

$$Co(L)B + B \overset{K_2}{\rightleftharpoons} Co(L)B_2 \qquad (2)$$

$$Co(L)B + O_2 \overset{K_{Ox}}{\rightleftharpoons} O_2\text{-}Co(L)B \qquad (3)$$

$$O_2\text{-}Co(L)B + Co(L)B \overset{K_{dimer}}{\rightleftharpoons} \mu\text{-}O_2\text{-}[Co(L)B]_2 \qquad (4)$$

It is more difficult to determine the actual rate constants of equations 3, binding (k_{on}) and dissociation (k_{off}) . One method entails the use of polarographic techniques where the rates are determined by the change in redox potentials.[5] This method works well for rate constants in the range of 10^2-10^4 $Lmol^{-1}s^{-1}$. Certain rate constants can be obtained by using a standard stopped-flow instrument, which is valid for rate constants up to 10^4-$10^5 Lmol^{-1}s^{-1}$.[6] The temperature jump technique has been applied to determine several rate constants of eq 3, including those for a few biological derivatives.[7,8] These techniques and corresponding conditions are summarized in Table 1. Recently Busch et al. used a cryogenic stopped-flow apparatus to slow the reactions down to an observable rate. They then extrapolated these rate constants back to room temperature, a procedure not without its problems given the minimal range of experimental temperatures.[9-11] All of these techniques except polarography use UV-Vis to monitor the reaction.

At Ames Laboratory the laser flash-photolysis, LFP, method has been used before to determine k_{on} and k_{off} for Co (cyclam).[12-16] The LFP method has been employed for these studies, for which a few requirements must be met. The Co-O_2 bond must dissociate upon photolysis. There also needs to be a corresponding absorbance change. One concern is the ratio of $k_{on}*[O_2]$ and k_{off}. This ratio cannot be too small other wise only the k_{off} term can be determined by this method. One last requirement, which holds true here as well for the other

techniques, is that the cobalt complex cannot be entirely in the μ-peroxo dimer form. There must be some Co-O_2 present in solution to photodissociate, because the peroxo dimer does not photodissociate.

Results and Discussion

The compounds that were explored in this study are shown in **Figure 1**.. At room temperature the **Co(saltmen)** derivative is converted only to a minor extent to its oxygenated form. This was determined by cooling an oxygenated solution to ~–40°C whereupon a large spectral change accompanying oxygen binding was seen, **Figure 2**. At room temperature, no change in equilibrium was observed upon photolysis. This compound was not explored further at that time. **Co(malophen)** was found to be more fruitful. The compound was photolyzable in LFP experiments, and gave rise to rate constants that were presumably k_{off}, since the rates of reaction were independent of oxygen concentration.

At this time in the study we received from Praxair two additional compounds, **IC–1** and **IC–2, Figure 1**. The structure of IC–2 shows an internal base that might bind via a second IC–2, eliminating the need for added base. The first study was to determine the K_b for IC–2 with another IC-2 acting as the base. Using a program called Specfit and the corresponding UV-Vis data, K_b was determined to be 2×10^3 L mol^{-1}, calculated with the assumption that only the monomer and dimer were present in the solution. Praxair [N. Stephenson] was having experiments carried out to verify this assumption. After the bonding studies were complete, the LFP experiments followed. Unfortunately though, photodissociation of the Co-O_2 bond was not observable for either IC–2 or IC–1.

This approach suggested a need for the carbon analog to IC–2, coined IC–C, **Figure 1**. During the investigation of IC-C, it was found that a similar change in the UV-Vis spectrum occurs for IC–C upon addition of oxygen, with or without added base (pyr). This finding remains unexplained at this time. Some temperature variations were performed on IC–C, but little or no change in absorbance occurred with changes in temperature.

The next logical step was to perform EPR experiments to determine the amount of Co-O_2 adduct present in solution.[17-21] The experiments were performed with 1.2 mM IC–2 or IC–C in toluene with 250 mM pyridine added to the IC–C solution. The solutions were saturated with either Ar or O_2. The spectra were obtained at 125 K with 8 scans per spectrum, **Figure 3**. As seen by the spectra for both species, there is an 80-90% loss in signal upon addition of molecular oxygen. This change in signal intensity was unexpected. The experiment also did not show the typical electronic splitting for a "superoxo" centered radical.[22,23] This may have been due to the lone electron being delocalized throughout the Schiff base ligand. With the large amount of conjugated π-bonding, the π^* orbital may now be accessible to the radical electron. Another possibility could be that the μ-peroxo dimer is the dominant form in solution explaining the large loss of signal.[24]

Little success has been realized in the determination of the k_{on} and k_{off} rate constants for the cobalt Schiff base complexes in this study. This led us to explore an alternative method for LFP based on the well-established photolysis of Co(III)-R complexes.[25,26] This type of cobalt alkyl bonds can be photodissociated.[27] Often, such studies have been performed in order to transfer the alkyl group to another compound with prolonged, low-intensity

photolysis.[28] Our working model has the Co–C bond homolytically cleaved, following which the Co(II) complex reacts with oxygen.

We tested this method with isoPr-Co(III)salen(pyr). Under anaerobic conditions the alkyl radical will dissociate and then reform the parent Co-alkyl species. When oxygen is present the alkyl radical combines with oxygen to make an alkylperoxyl radical that then recombines with Co(II) rather than molecular oxygen. To counteract this reaction, so as to divert the radical in the desired direction, a radical trapping agent (e.g., TEMPO) was added.[29] A summary of known rate constants pertinent to this study are shown in equations 5-10.[30-32]

Co(II)salen +	O_2	⟶	O_2•-Co(III)salen	$k = 5.7 \times 10^5\ M^{-1}s^{-1}$	(5)
Co(II)L +	ROO•	⟶	ROO-Co(III)L	$k = 2 \times 10^9$	(6)
Co(II)L +	R•	⟶	LCo(III)-R	$k = \sim 10^7\text{-}10^9$	(7)
R• +	R•	⟶	R-R	$k = \sim 10^{10}$	(8)
R• +	O_2	⟶	ROO•	$k = 1\text{-}5\ (\times 10^9)$	(9)
TEMPO +	R•	⟶	trapped product	$k = 1 \times 10^9$	(10)

It has long been known that TEMPO is a good trapping agent for alkyl radicals, but not for peroxyl radicals. With this is mind, the reaction conditions (concentrations) were chosen such that the alkyl radical would react with TEMPO and not O_2 (eqns 9 & 10). This meant that since the rate constants for these two reactions are similar, the TEMPO concentration was increased to around 20 mM and the O_2 concentration was decreased to ~1 mM. Under these conditions the LFP experiment was performed. The initial bleaching was observed, but no further reaction could be monitored, **Figure 4.** Most probably, the change in absorbance due to the formation of Co-O_2 was so low that the reaction could not be observed.

In consultation with Dr. N. Stephenson, we asked if they could make the alkylated analogs to IC–2 and IC–C. We were optimistic that with these

compounds the change in absorbance would be great enough to monitor the reaction of Co(II) with O_2. We then performed kinetic simulations of these reactions based on the rate constants for similar compounds. If the k_{on} term is greater than 1×10^6 L mol^{-1} s^{-1}, a radical trap will not have to be added. The molecular oxygen will coordinate faster than the peroxy radical based on concentration differences.

We were, however, notified by Dr. Stephenson that the Praxair group was having some difficulty in synthesizing the alkylated analog. We then proceeded to try the synthesis on our own with the limited amount of IC–2 in hand. I first synthesized the similar cobalt complexes, Co(salen) and Co(salophen), to familiarize myself with the synthetic procedures. I then alkylated the Co(salen) with isopropyl bromide. After the completion of this synthesis, the alkylation of IC–2 was performed. This experiment was unsuccessful in alkylating the Co(II), giving instead the Br-Co(III) derivative of IC-2. After this first trial insufficient IC–2 remained for additional synthetic preparation at the Ames Laboratory.

Conclusion

We have studied five different Co(II) complexes, with the ultimate goal of determining the rate constants for these compounds. Many interesting characteristics of these compounds have been found along the way. One worth mentioning is the disappearance of the EPR signal upon addition of molecular oxygen. Another is the fact that IC–C, a compound with no known Lewis base abilities has similar characteristics of oxygen coordination with or without added base. Similar observations of 4-coordinate cobalt complexes binding oxygen have been reported in the literature, but these are the exceptions. By incorporation of a radical trapping agent into the photolysis of Co(III) alkyls, small amounts of

Co(II) can be made in the presence of O_2. With sufficient difference in UV-Vis spectra, the rate of formation of Co(III)-O_2• should be observable. The radical trapping agent will only be need when the rates of reactions 5, 6, and 7 are comparable.

References

(1) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chemical Reviews* **1979**, *29*, 139.

(2) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chemical Reviews* **1984**, *84*, 137.

(3) Chen, D.; Martell, A. E. *Inorganic Chemistry* **1987**, *26*, 1026.

(4) Chen, D.; Martell, A. E.; Sun, Y. *Inorganic Chemistry* **1989**, *28*, 2674.

(5) Puxeddu, A.; Costa, G. *J.Chem. Soc. Dalton Trans* **1981**, 1115.

(6) Miller, F.; Simplicio, J.; Wilkins, R. G. *JACS* **1969**, *91*, 1962.

(7) Yamamoto, H.; Kayne, F. J.; Yonetani, T. *Journal of Biological Chemistry* **1974**, *249*, 691.

(8) Bigotto, A.; Costa, G.; Mestroni, G.; Pellizer, G.; Puxeddu, A.; Relsenhofer, E.; Stefani, L.; Tauzher, G. *Inorganica Chimica Acta* **1970**, 41.

(9) Ransohoff, S.; Adams, M. T.; Dzugan, S. J.; Busch, D. H. *Inorganic Chemistry* **1990**, *29*, 2945.

(10) Rybak-Akimova, E. V.; Masarwa, M.; Marek, K.; Wartburton, P. R.; Busch, D. H. *J. Chen. Soc. Chemical Communications* **1996**, 1451.

(11) Rybak-Akimova, E. V.; Otto, W.; Deardorf, P.; Roesner, R.; Busch, D. H. *Inorganic Chemistry* **1997**, *36*, 2746.

(12) Bakac, A.; Espenson, J. H. *JACS* **1984**, *106*, 5197.

(13) Bakac, A.; Espenson, J. H. *Inorganic Chemistry* **1989**, *28*, 3901.

(14) Bakac, A.; Espenson, J. H. *Inorganic Chemistry* **1987**, *26*, 4353.

(15) Bakac, A.; Espenson, J. H. *JACS* **1990**, *112*, 2273.

(16) Bakac, A.; Espenson, J. H. *Inorganic Chemistry* **1990**, *29*, 2062.

(17) Stevens, J. C.; Busch, D. H. *JACS* **1980**, *102*, 3285.

(18) Walker, F. A. *JACS* **1970**, *92*, 4235.

(19) Bakac, A. *Progress in Inorganic Chemistry* **1995**, *43*, 267.

(20) Bayston, J. H.; King, N. K.; Looney, F. D.; Winfeld, M. E. *JACS* **1969**, *91*, 2775.

(21) Bottcher, A.; Elias, H.; Jager, E.-G.; Langfelderova, H.; Mazur, M.; Muller, L.; Paulus, M.; Pelikan, P.; Rudolph, M.; Valko, M. *Inorganic Chemistry* **1993**, *32*, 4131.

(22) Hoffman, B. M.; Diemente, D.; Basolo, F. *JACS* **1970**, *92*, 61.

(23) Hoffman, B. M.; Basolo, F.; Diemente, D. *JACS* **1973**, *95*, 6497.

(24) Carter, M. J.; Rillema, D. P.; Basolo, F. *JACS* **1974**, *96*, 392.

(25) Schrauzer, G. N.; Sibert, J. W.; Windgassen, R. J. *J. Am. Chem. Soc.* **1968**, *90*, 6681.

(26) Bakac, A.; Espenson, J. H. *Inorganic Chemistry* **1989**, *28*, 4319.

(27) Ram, M. S.; Riordan, G.; Yap, G. P. A.; Liable-Sands, L.; Rheingold, A. L.; Marchaj, A.; Norton, J. R. *J. Am. Chem. Soc.* **1997**, *119*, 1648.

(28) Branchaud, B. P.; Meier, M. S.; Malekzadeh, M., N. *Journal of Organic Chemistry* **1987**, *52*, 212.

(29) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *Journal of Organic Chemistry* **1988**, *53*, 1629.

(30) Wong, C.-L.; Switzer, J. A.; Balakrishnan, K. P.; Endicott, J. F. *JACS* **1980**, *102*, 5511.

(31) Endicott, J. F.; Ferraudi, G. J. *JACS* **1977**, *99*, 243.

(32) Endicott, J. F.; Netzel, T. L. *JACS* **1979**, *101*, 4000.

(33) Hay, R. W.; Dilworth, J. R.; Nolan, K. B. *Perspectives on Bioinorganic Chemistry*; JAI Press Ltd: Greenwich, Connecticut, 1993; Vol. 2.

Table 1. A summary of cobalt-oxygen binding and dissociation rate constants.

Co-complex	Solvent	Base	Temp	k_{on}	k_{off}	Method	Ref
Salen	py	py	0	5.7×10^5	36	pol	5
Sal(+)pn	py	py	0	7.0×10^3	1.7	pol	" "
Sal(+)bn	py	py	0	320	0.13	pol	" "
Sal(+)bn	py	py	0	760	0.24	pol	" "
Sal(-)ch×n	py	py	0	6.2×10^3	27	pol	" "
Sal(m)ch×n	py	py	0	$< 10^2$	<1.1	pol	" "
Protoporphyrin	Tol	MeIm	23	2.8×10^{-4}			33
" " (2-MeIm)	DMF		-5		$>4\times10^4$	TJ	
[14]aneN$_4$	H_2O	H_2O	25	1.2×10^7	63	FP	15
meso-Me$_6$[14]aneN$_4$	H_2O	H_2O	25	5×10^6	1.7×10^4	FP	" "
(C_5Cyc)	Me_2CO	MeIm	25	2.0×10^6	1.1×10^4	cryo SF	11
(C_5Cyc)	MeCN	MeIm	25	3.7×10^6	9.2×10^3	" "	" "
(C_5Cyc)	MeOH	MeIm	25	2.4×10^6	1.6×10^4	" "	" "
(C_5Cyc)	Me_2CO	py	25	2.3×10^6	1.0×10^5	" "	" "
(C_4Cyc)	Me_2CO	MeIm	25	5.4×10^4	3.6×10^5	" "	" "
(C_6Cyc)	Me_2CO	MeIm	25	$\sim1\times10^8$		" "	" "
Co-Mb	H_2O		25	4.7×10^7	2×10^3	TJ	7

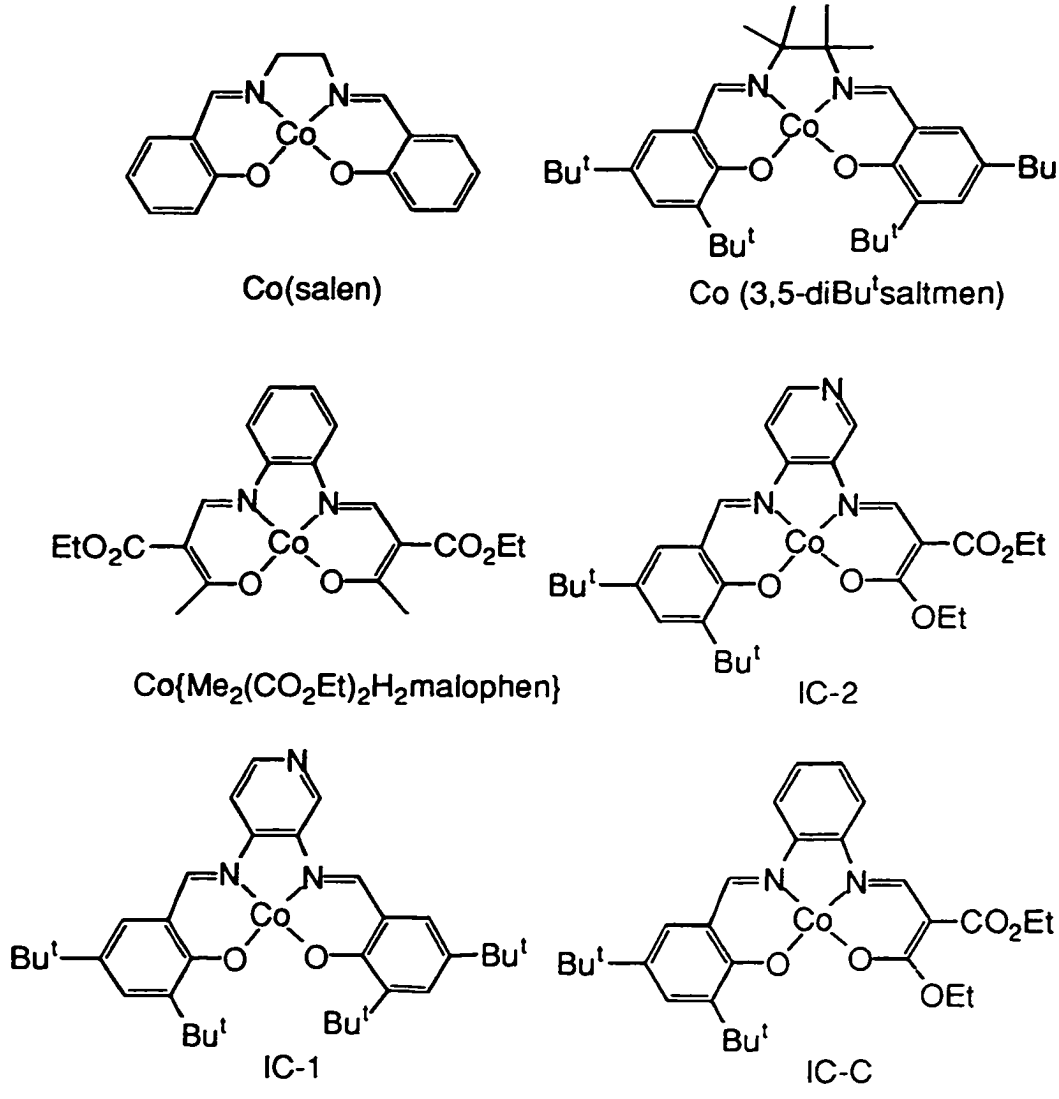


Figure 1. Cobalt complexes

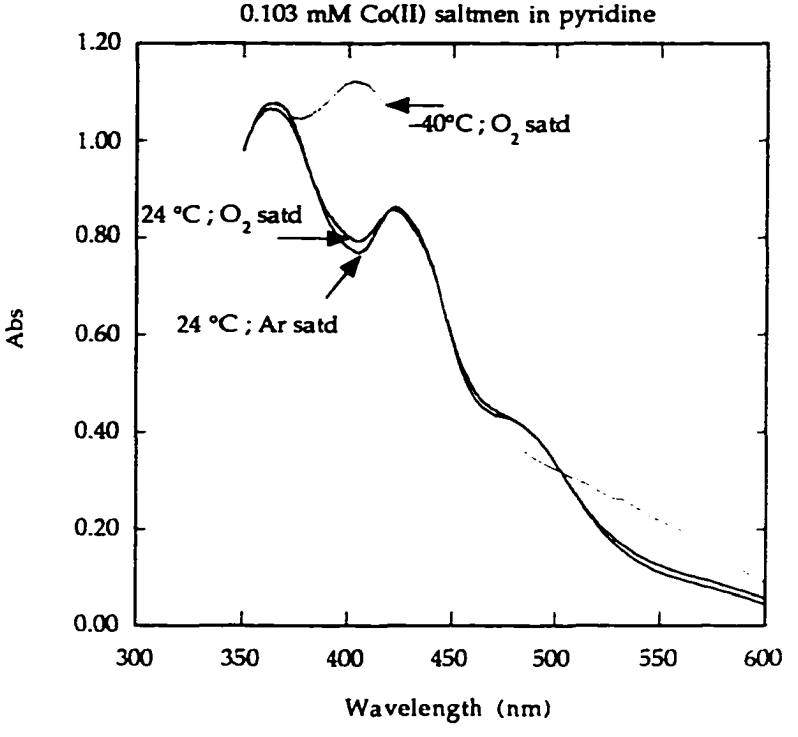


Figure 2. A display of the oxygen binding dependence of Co(II) saltmen on temperature. The –40 °C solution was chilled using an acetone/dry ice bath. As seen be the spectra there is little coordination of oxygen at room temperature while at lower temperatures the binding increases. There was no further absorbance change at temperatures lower than 40 °C.

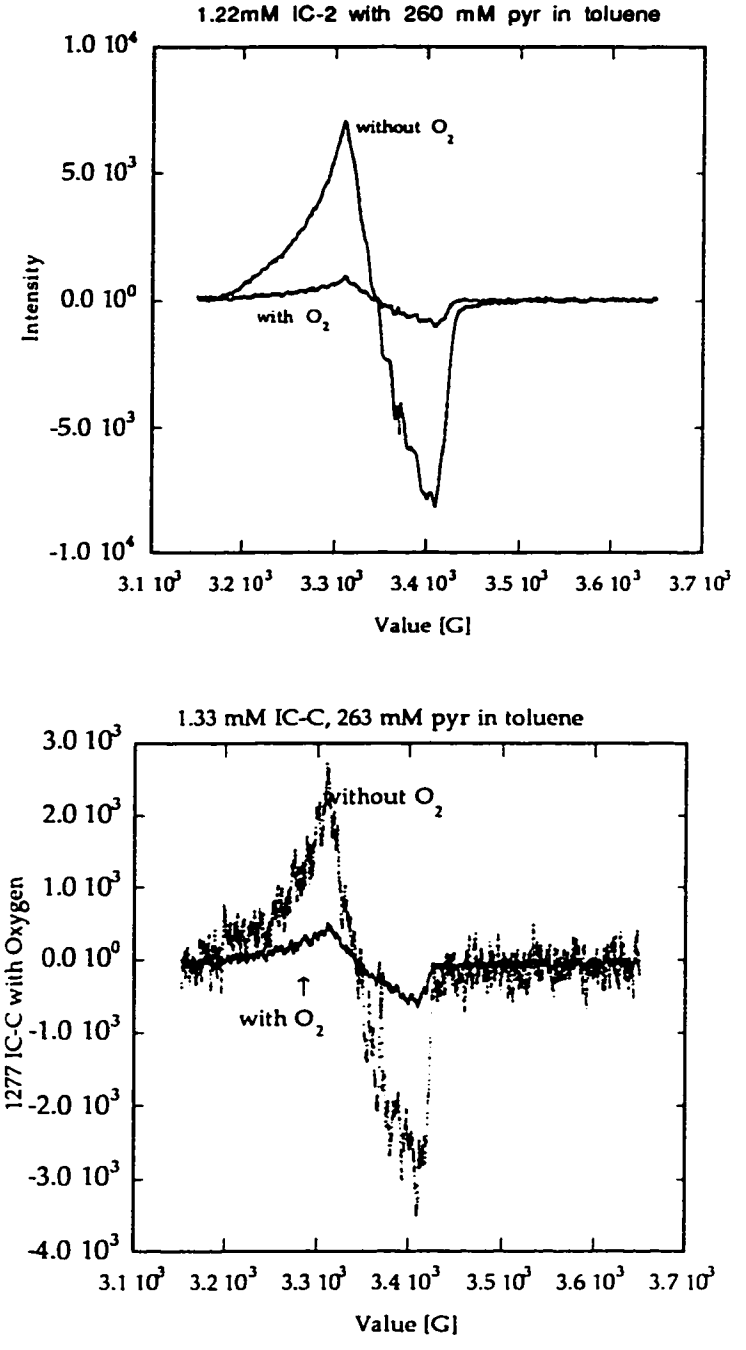


Figure 3. EPR spectra of Co(II) complexes with and without O_2. The upper figure is for IC–2 while the lower is for IC–C. Both figures demonstrate the loss of signal upon addition of oxygen.

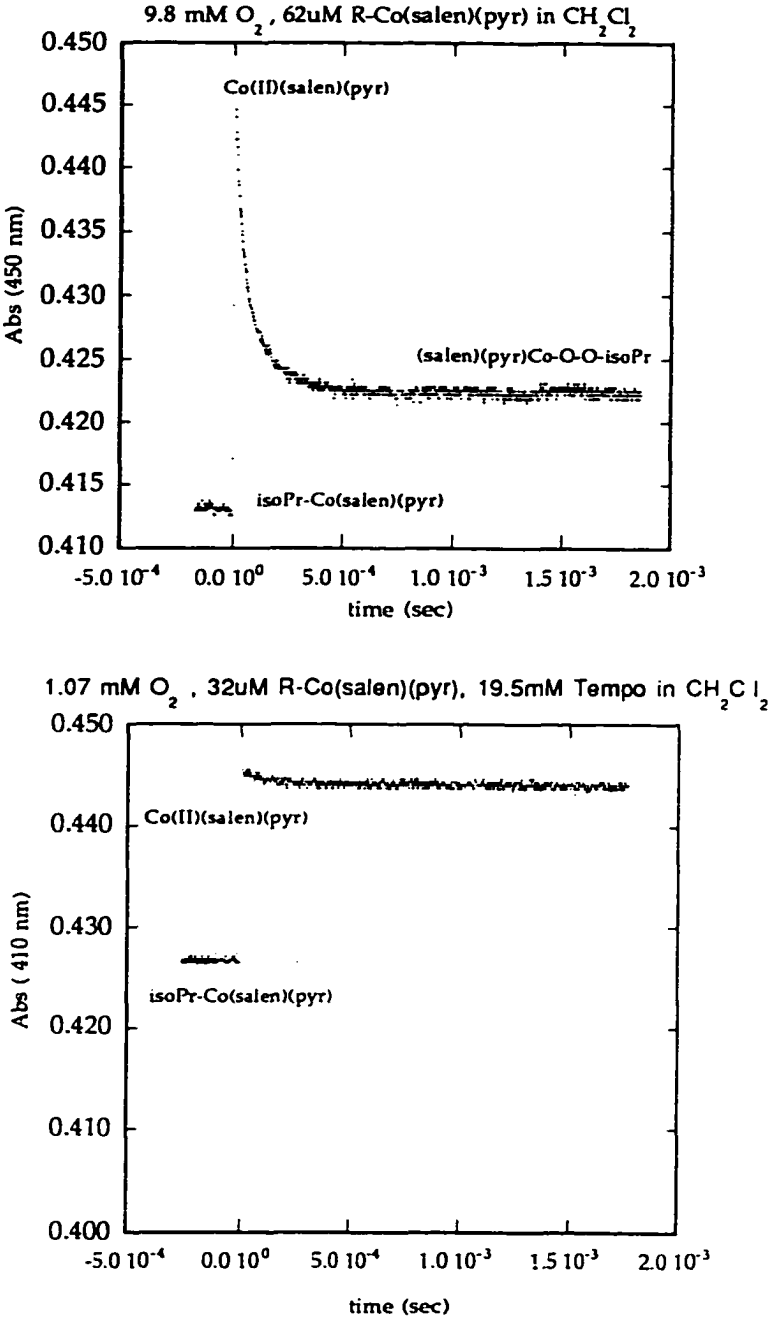


Figure 4. Laser Flash Photolysis of isoPr-Co(salen)(pyr) with and without Tempo. The upper figure shows the growth of the Co-alkylperoxide. The lower figure shows that with the addition of a radical trap, there is almost no Co-alkylperoxide formation.

GENERAL CONCLUSIONS

MTO and hydrogen peroxide continue to be a great asset in the oxidation of organic compounds. The types of reactions that this combination can achieve have now been expanded to hydride abstraction reactions as well as to further oxygen transfer reactions. The oxidation of alcohols proceeds mainly by a hydride abstraction from the alpha carbon. Following the oxidation of primary alcohols, further oxidation of the aldehyde to organic acids proceeds if excess H_2O_2 is present.

The oxidation of secondary hydroxylamines yields nitrones or oxoammonium ions. In methanol these reactions take place by nucleophilic attack of the nitrogen lone pair on the electron–poor peroxo-oxygen coordinated to the rhenium center. The proposed intermediate with the oxygen transferred to the nitrogen is supported by various isotopic labeling experiments. Subsequent rapid loss of water or hydroxide yield the two types of products in excellent yields.

Oxidation reactions using MTO/H_2O_2 as the oxidizing agents achieve great yields with water as the only by-product. The catalyzed reactions are typically thousands of time faster than the uncatalyzed reaction. The use of this catalytic system is also being expanded by the incorporation of co-catalysts with their faster rates and selectivity adding a new dimension to these reactions.

The coordination of oxygen to Co(II)salen compounds was explored by studying the rates of binding. These rates were not obtained to a high degree of accuracy, but led to the development of conditions making the determination of oxygen binding rate constants for other compounds more accessible. By incorporating a radical trapping agent into the reaction solution, the formation

of Co(III)-O_2• can be monitored without interference of the peroxo radicals, upon photolysis of Co(III)–alkyl compounds. This new method is still unproven, but with so few methods available, it should prove to be very useful.

By using different metals, the controlled oxidation of compounds with hydrogen peroxide and activation of molecular oxygen can be achieved. A large amount of work remains to be done in the future of oxidation reactions. This work will continue to be carried out by this researcher as well as many others.

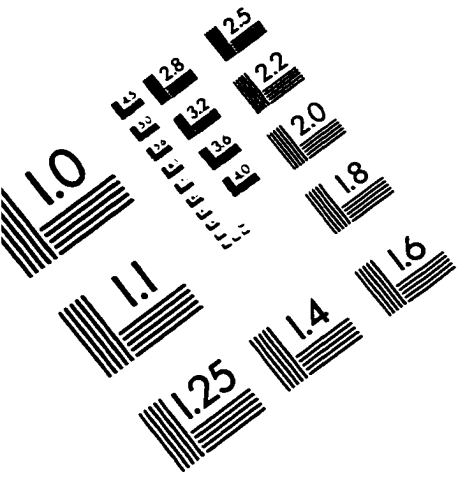
ACKNOWLEDGMENTS

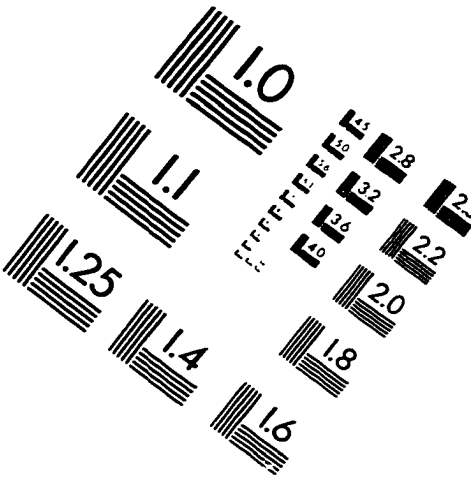
I would like to thank Professor James H. Espenson, Dr. Andreja Bakac, and Dr. Weidong Wang for their guidance or encouragement during my graduate career. I am also thankful to the members of my research group for being a sounding board with insight into my research. I am pleased to acknowledge informative discussions with Professor Walter Trahanovsky and assistance with the GC-MS experiments from Dr. Kamel Harrata.

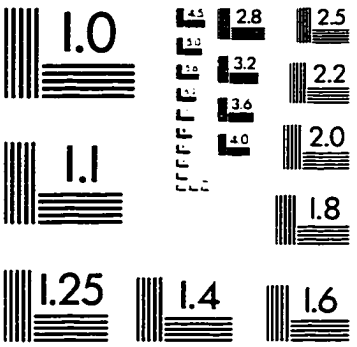
I would like to acknowledge my family for their support and never ending love: my wife Geri and our two children Jared and Sarah. I know with your support that I can achieve the impossible now. I pray that I will not disappoint my family and friends with my future endeavors.

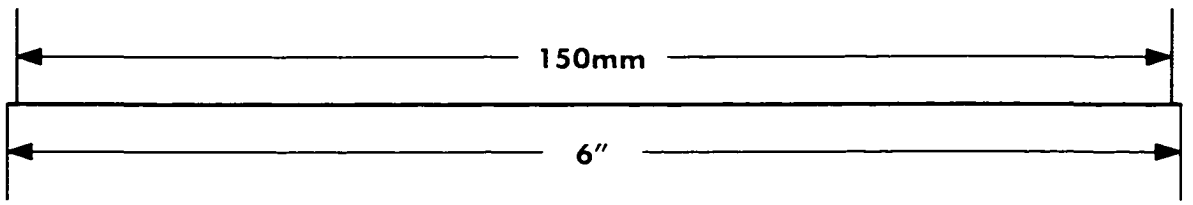
This work was supported by the following: U.S. Department of Energy, Office of Basic Energy Science, Division of Chemical Science under contract W-7405-Eng-82, the National Science Foundation (CHE-9007283), and Praxair. Some of the experiments were done with facilities of Ames Laboratory. The United States government has assigned the DOE report number IS–T 1852 to this thesis.

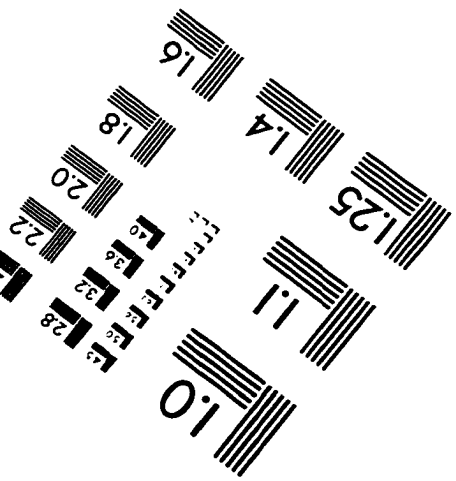
IMAGE EVALUATION TEST TARGET (QA-3)

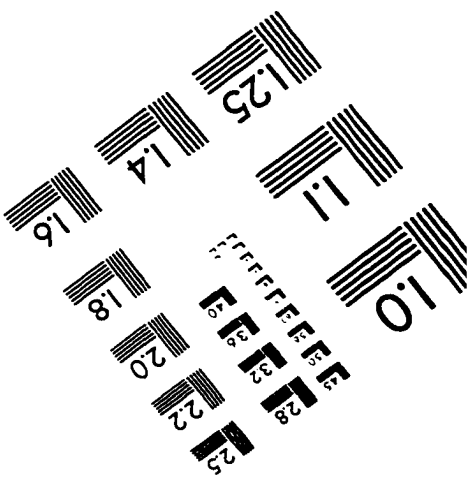












APPLIED IMAGE, Inc
1653 East Main Street
Rochester, NY 14609 USA
Phone: 716/482-0300
Fax: 716/288-5989