Kinetics of Autoxidation of Cobalt(II) Cyclidene Dioxygen Carriers

Mohamad Masarwa,† P. Richard G. Warburton,† Wayne E. Evans,‡ and Daryle H. Busch*,†

Departments of Chemistry, University of Kansas, Lawrence, Kansas 66045, and
The Ohio State University, Columbus, Ohio 43210

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The cobalt(II) cyclidene complexes are known to bind dioxygen reversibly under ambient conditions; however, the lifetime of the dioxygen adduct is limited by autoxidation. This paper describes a study of the autoxidation reactions of the cobalt(II) cyclidenes in nonaqueous media. The kinetics of the autoxidation reaction of the cobalt(II) complex are dependent on the nature of the ligand substituents and dioxygen concentration and on the nature and concentration of added base. Mechanistic details have been explored through isotopic substitution of the ligand. The proposed mechanism involves preequilibrium deprotonation of the ligand in the dioxygen complex, followed by irreversible ligand oxidation.

Introduction

Much effort has been devoted to the design and synthesis of functional mimics of the biological heme-based dioxygen carriers. Historically, the first reversibly formed synthetic dioxygen complex, $[(NH_3)_5Co–O_2–Co(NH_3)_5]^{4+}$, was discovered by Werner,[1] and since then a large number of cobalt(II) and iron(II) complexes have been found to bind dioxygen reversibly. The study of synthetic dioxygen carriers has been summarized in a number of excellent reviews on synthetic transition metal dioxygen carriers.[2]

All dioxygen carriers known to date suffer autoxidation (irreversible oxidation by dioxygen) in solution, including hemoglobin and myoglobin. For example, 1.5–3% of the hemoglobin of the blood is typically oxidized to the iron(III) form, methemoglobin, each day.[3] However the actual concentration of methemoglobin is maintained below about 1% by an enzymatic reduction process.[4]

Autoxidation of dioxygen carriers is known to proceed via many types of mechanism, few of which are understood in any detail. The predominant mechanism depends greatly on both the nature of the dioxygen carrier and the experimental conditions. Details of the autoxidation of dioxygen carriers may be found in a recent review.[5] The rate of autoxidation determines the functional lifetime of the dioxygen carriers and therefore limits the applications to which the dioxygen carriers may be applied. Consequently, there is great interest in determining the mechanisms of autoxidation of dioxygen carriers. In particular, it is hoped that by understanding the autoxidation mechanisms, it may be possible to design ligands resistant to these deleterious processes and hence develop improved dioxygen carriers.

The cobalt(II) and iron(II) cyclidene complexes represent a most successful class of non-porphyrin dioxygen carrier. Reversible dioxygen binding has been achieved for both the cobalt(II) and the iron(II) complexes of some of these ligands, and they display high dioxygen affinities, under normal conditions, even in aqueous solution.[6] The cyclidene complexes contain a sterically protected, hydrophobic cavity, as shown in Figure 1, into which the dioxygen may enter to bind at the axial site of the metal. The other axial site is blocked by a bulky nitrogenous base, for example, 1-methylimidazole, that is usually added in large excess for dioxygen binding experiments. The axial base both increases the electron density on the metal, facilitating dioxygen binding, and prevents dimeric autoxidation reactions, by blocking the open metal axial site. An important feature of the cyclidene dioxygen carriers is that both the dioxygen affinity and rate of autoxidation are highly dependent on the ligand substituents, allowing the possibility of systematically investigating the dependence of reactivity of the complexes on molecular parameters.

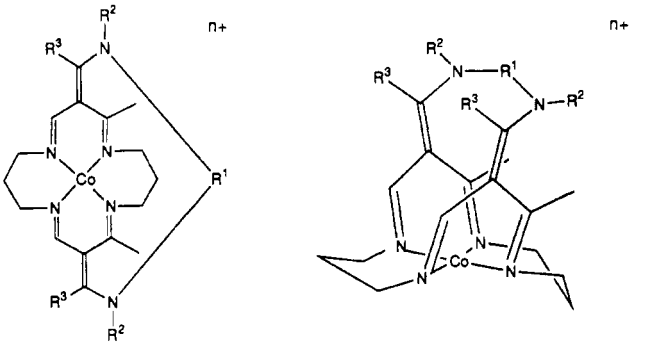

Figure 1. Planar and three dimensional representations of cobalt(II) cyclidene complexes.

For convenience a simplified nomenclature for the cyclidene complexes has been adopted and will be used henceforth in this paper. Since for all of the cyclidene complexes described here, only the ligand substituents are changed, as indicated in Figure 1, the complexes may be described as $M(R^3)_2(R^2)_2(R^1)^{n+}$, where M is the metal. In this paper, the autoxidation of cobalt(II) complexes having $R^3 = R^2 = CH_3$ and $R^1 = (CH_2)_n$, $n = 5$, 6, 7, 8, will dominate the discussion.

Experimental Section

Materials. The solvents and reagents used in these studies were reagent grade or better. Solvents were dried, distilled under nitrogen, and degassed

* To whom correspondence should be addressed.
† University of Kansas.
‡ The Ohio State University.

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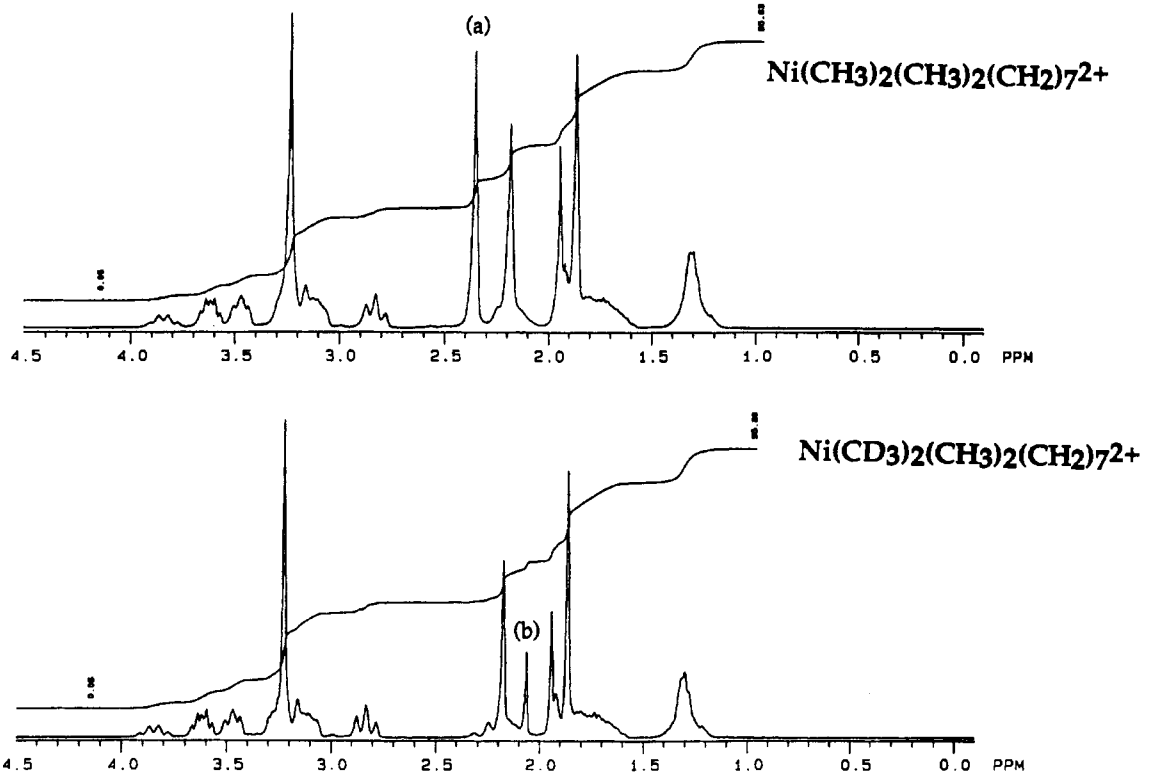

Figure 2. ^1H NMR spectra of $[Ni(CH_3)_2(CH_3)_2(CH_2)_7](PF_6)_2$ and $[Ni(CD_3)_2(CH_3)_2(CH_2)_7](PF_6)_2$ in CD_3CN. The peak labeled (a) corresponds to the protons in the R^3 methyl group of the unsubstituted cyclidene. This peak disappears after deuterium substitution at R^3. The peak labeled (b) probably arises from trace amounts of water.

by successive freeze–pump–thaw cycles prior to use. The syntheses of the complexes have been described previously.[7] Synthesis of cobalt(II) cyclidene complexes substituted with $R^3 = CD_3$ was achieved by two methods. The first procedure involved stirring an acetonitrile/D_2O solution of the corresponding nickel(II) cyclidene complex having $R^3 = CH_3$, which had been made basic (pH ~ 10) by the addition of small amounts of NaOD/D_2O solution. After 1 week, substitution of the R^3 methyl protons by deuterons had reached a steady state, with almost complete conversion, as indicated by ^1H NMR (Figure 2) and FAB mass spectroscopy. In the ^1H NMR spectrum, peak (a), corresponding to the R^3 methyl group of $Ni(CH_3)_2(CH_3)_2(CH_2)_7(PF_6)^+$,[8] disappeared following substitution of the protons by deuterons. The mass spectrum displayed a principal peak (663 amu for $Ni(CD_3)_2(CH_3)_2(CH_2)_7(PF_6)^+$) at 6 mass units greater than that observed for the unsubstituted complex. After neutralization, the nickel complex was isolated by removal of the acetonitrile and filtration of the resulting precipitate. The free ligand was obtained as described previously,[7] by passing HCl gas through an acetonitrile solution of the complex, and precipitating the ligand salt by addition of aqueous ammonium hexafluorophosphate. The product was washed with small amounts of cold water and ether and dried. Under the acidic conditions employed for this procedure, the rate of deuteron/proton substitution at the R^3 position is sufficiently slow that the R^3 groups remained in the deuterated form. Under inert atmosphere, the cobalt(II) cyclidene complex was prepared by mixing solutions of cobalt(II) acetate and the ligand salt together in the presence of sodium acetate; the procedure was similar to that of previous workers,[7] except that deuterated methanol (CH_3OD) was used as solvent. The use of the usual proton form of MeOH was found to result in a significant degree of resubstitution by protons at the R^3 positions, under the basic conditions and high temperature (reflux) employed for this synthetic process. The deuterium substitution was evident from the FAB mass spectrum, which exhibited a dominant peak at 663 amu ($Co(CD_3)_2(CH_3)_2(CH_2)_7(PF_6)^+$), 6 mass units higher than that for the unsubstituted complex.

Substitution at the R^3 position was also achieved on stirring a solution of the cobalt(II) cyclidene complex in basic (pH ~ 10) acetonitrile/D_2O under nitrogen. After 1 week, the acetonitrile was removed and the substituted cobalt(II) cyclidene complex was filtered. FAB mass spectral analysis confirmed that substitution had occurred, almost to completion, as indicated by the presence of predominant peaks at six mass units higher than those for the unsubstituted cobalt(II) complex, (678 amu $[Co(CD_3)_2(CH_3)_2(CH_2)_8](PF_6)^+$).

Solutions of the cobalt(II) cyclidene complexes were always freshly prepared in a glove box prior to their use in the autoxidation studies.

Physical Measurements. UV–visible spectrophotometric studies were conducted using a 1-cm gastight quartz cell, fitted with a gas inlet and a bubbling tube. Spectra were recorded on either a Varian 2300 spectrophotometer or a Hewlett-Packard 8452 diode array spectrophotometer, with a 9000 (300) Hewlett-Packard Chem Station. The Varian 2300 spectrometer was connected via an IEEE interface to an IBM PC, allowing automated instrument control and data collection. Both instruments incorporated flow through temperature regulated cell holders connected to a Neslab constant temperature circulation system, giving a temperature precision of ±0.3 °C. Dioxygen/nitrogen gas mixtures were generated using Tylan FC-260 mass flow controllers. Dioxygen concentrations were maintained at constant value during the kinetic experiments by initially bubbling the solutions for 4 min, with the appropriate gas mixture, and, intermittently, between periods of data collection. Data processing and treatment were either performed using proprietary software accompanying the HP 9000 Series 300 computer or software written by Dr. Naidong Ye of this group, for use with DOS-based computers.

All inert atmosphere manipulations were performed in a nitrogen filled Vacuum Atmospheres Corporation (VAC) glovebox, equipped with a gas circulation and dioxygen removal system either a VAC MO40-1 or HE-493 dry train.

Electrolysis experiments were undertaken within the glovebox, using a divided three-compartment cell. The working electrode was platinum, the secondary electrode was graphite, and the reference electrode was either a silver wire or a silver wire coated with silver chloride. During electrolysis, the solutions were stirred at constant rate. Under these conditions, typical electrolysis times were about 20 min to ~95% completion. The experiments were undertaken using a Princeton Applied Research (PAR) programmer Model 175 and PAR potentiostat Model 173. Conductivity measurements were performed using a YSI Model 35 conductance meter. ESR were recorded on a Varian E-112 spectrometer operating in the X-band, and the magnetic field was calibrated with

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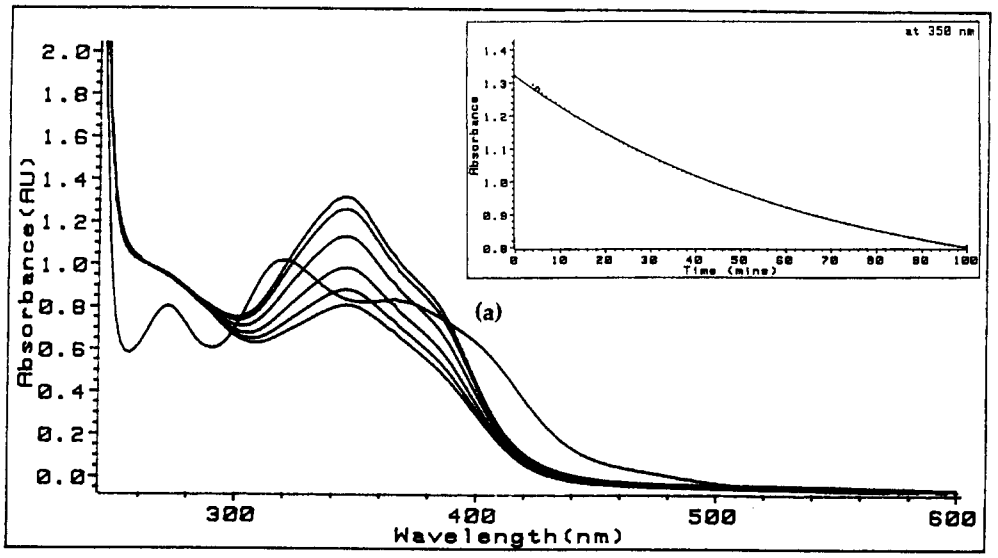

Figure 3. Electronic spectral changes accompanying autoxidation of $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in acetonitrile containing 1.5 M 1-methylimidazole, at 25 °C, 760 Torr, ($[Co^{II}] = 5 \times 10^{-5}$ M), showing the initial spectrum under nitrogen (a), and spectra 10, 15, 30, 55, 80, and 105 min after exposure to dioxygen. Insert shows the kinetic trace at 350 nm and the first-order fit (solid line).

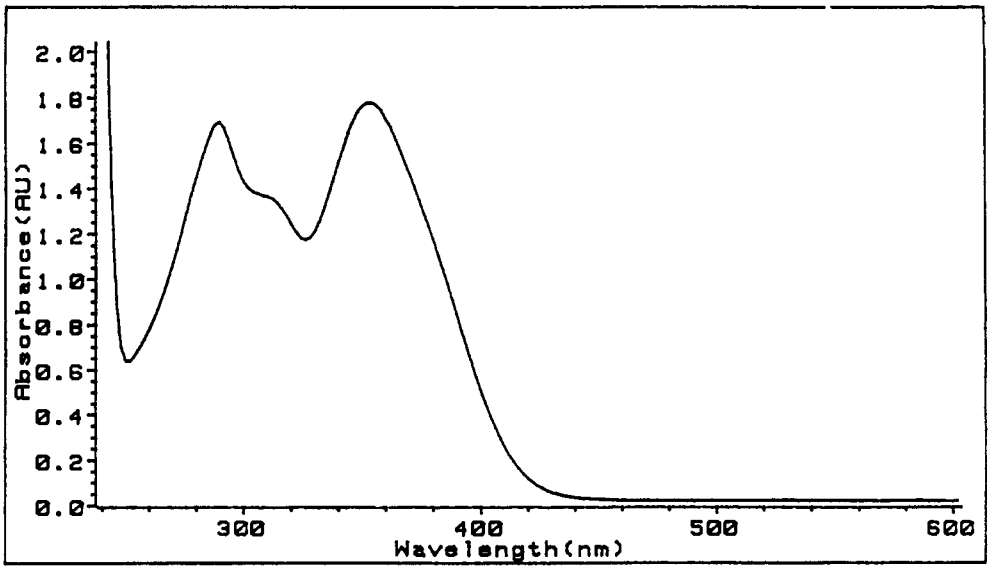

Figure 4. UV–visible spectrum of ligand salt $H_n(CH_3)_2(CH_3)_2(CH_2)_6(PF_6)_n$ in acetonitrile containing 1.5 M 1-methylimidazole.

external DPPH (g = 2.0036). Fast atom bombardment mass spectra (FAB) were obtained with a VG ZAB HS mass spectrometer, using either a mixture of 3:1 dithiothreitol and dithioerythritol (FAB/MB) or 3-nitrobenzyl alcohol (FAB/NBA) as matrices.

Results

UV–Visible Spectral Changes. The autoxidation process of the cobalt cyclidenes is complicated by the fact that the ligand is eventually destroyed for those derivatives that have $R^3 = CH_3$. This ligand destruction proceeds in steps that follow the rate-determining process, and only those first reactions will be considered here. Product analysis will be the subject of a later report.

Solutions of the cobalt(II) cyclidene complex ($\sim 5 \times 10^{-5}$ M, in acetonitrile containing 1.5 M 1-methylimidazole) typically exhibit reversibly dioxygen binding, as indicated by UV–visible spectroscopic and ESR changes, under ambient conditions.[6a] Over extended periods of time, the binding of dioxygen is no longer fully reversibly as the effects of autoxidation become more apparent. This autoxidation process may be conveniently followed by UV–visible spectroscopy (Figure 3); the peak at 345 nm corresponding to the dioxygen adduct, decays in height with time, to about ~60% of the initial absorbance over about 2 h (data for $[Co(CH_3)_2(CH_3)_2(CH_2)_6]^{2+}$/1.5 M MeIM/MeCN, 25 °C, 760 Torr O_2), depending on experimental conditions, with a concomitant shift in λ_{max} to 350 nm.

Closer analysis of the changes in the UV–visible spectrum upon autoxidation is very revealing. While the exact assignments of the electronic transitions are unclear, comparison of the spectrum of the cobalt(II) complex $[Co(II)(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in 1.5 M 1-methylimidazole/acetonitrile with that of the corresponding ligand salt reveals that the two most prominent bands in the spectral envelope between 250 and 450 nm {CoL λ_{max} = ~310, ~370 nm; ligand salt λ_{max} = 290, 310, 352 nm} (Figure 4) are common to both spectra and therefore are derived from ligand transitions, probably π–π^*. The decay of these bands during the autoxidation process may suggest that the ligand is modified during this process. Exposure of the cobalt(II) complex to dioxygen gives similar spectral changes upon autoxidation in pure acetonitrile as in the presence of 1-methylimidazole, except that in the presence of 1-methylimidazole formation of the dioxygen adduct is more pronounced, reflecting the greater dioxygen affinity of the complex in this medium. Formation of the dioxygen adduct is typified by the decay of absorbance bands at 312 and 412 nm and the formation of a new absorbance band

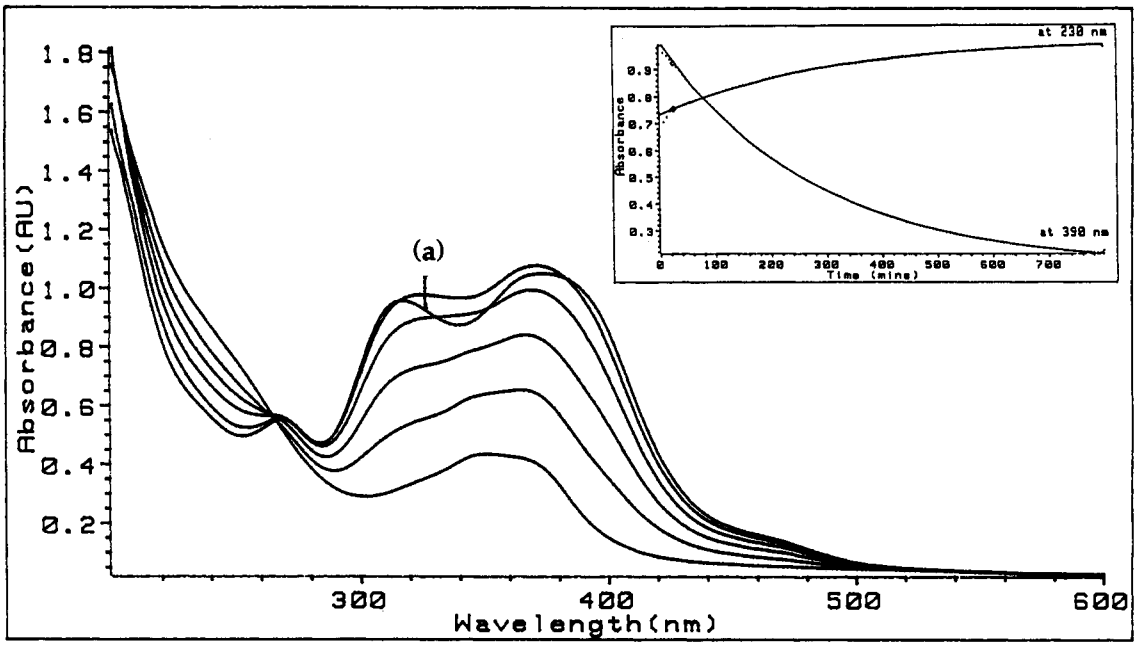

Figure 5. Electronic spectral changes accompanying autoxidation of $[Co(CH_3)_2(CH_3)_2(CH_2)_8](PF_6)_2$ in acetonitrile at 25 °C, 760 Torr of dioxygen ($[Co^{II}] = 5 \times 10^{-5}$ M), showing initial spectrum under nitrogen (a) and spectra after 0.2, 1, 2.5, 5, and 13 h of exposure to dioxygen. Inserts show the kinetic traces at 390 and 230 nm and the first-order fits (solid lines).

at 350 nm, in the spectral range 300–600 nm.[6a] Furthermore, during the autoxidation of the cobalt(II) complexes in the absence of 1-methylimidazole, an increase in absorbance was observed at $\lambda_{max} = 230$ nm, which displayed similar kinetic behavior (Figure 5). In the presence of 1-methylimidazole, this wavelength region is obscured by the strong absorbance of 1-methylimidazole below 290 nm.

Examination of the spectral changes on autoxidation of the cobalt(II) cyclidene complexes over longer time periods (~24 h), at about 25 °C, reveals that the autoxidation process involves at least two reactions. This work has concentrated on the kinetics of the first reaction and its dependence on experimental conditions, since this primary autoxidative process represents removal of the dioxygen carrier from the system. The second reaction was sufficiently slow that the two kinetic processes could be treated independently.

Kinetic Studies. The kinetics of autoxidation of cobalt(II) cyclidene complexes were found to be first order in the presence of a large excess of dioxygen, and the pseudo-first-order rate constant was independent of the cobalt(II) complex concentration under these conditions. This result indicates that the rate-determining step is unimolecular in cobalt(II), in contrast to that found for the autoxidation of many families of cobalt(II) dioxygen carriers, whose second-order dependence on [Co] signals the involvement of dinuclear dioxygen adducts.[9]

The rate of autoxidation of $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in 1.5 M 1-methylimidazole/acetonitrile, saturated with 760 Torr of dioxygen, increased with temperature. A plot of the logarithm of the observed pseudo-first-order rate constant divided by temperature versus the inverse of the temperature was linear ($\ln(k/T) = 10.1 - 7162/T$, $R^2 = 0.99$). From the slope of the graph, the enthalpy of activation is $\Delta H^{\ddagger} = 59.5$ kJ mol^{-1}. From the intercept it may be seen that the entropy of activation for the autoxidation reaction is slightly negative (–0.11 kJ T^{-1} mol^{-1}), indicating a transition state more ordered than the reactants; however, a more detailed interpretation would be equivocal due to the large number of variables in this system.

The dependence of the rate of autoxidation on the concentration of dioxygen, was linear (first order) for low dioxygen concentrations, but reached a plateau for higher dioxygen concentrations, Figure 6a. Such behavior is characteristic of saturation kinetics and consistent with a preequilibrium process. Confirmation of this supposition was provided by a plot of the inverse of the observed rate versus the inverse of the partial pressure of dioxygen, which for $Co(CH_3)_2(CH_3)_2(CH_2)_6^{2+}$ in acetonitrile containing 1.5 M 1-methylimidazole gave a linear plot which intercepted the ordinate axis (Figure 6b).

The saturation dependence on dioxygen concentration suggests that the autoxidation process involves a preequilibrium reaction, presumably the reversible binding of dioxygen by the cobalt(II) cyclidene complex. Conceptually, two reaction sequences may account for this behavior; they involve a dioxygen-binding preequilibrium which is either accompanied by a parallel rate-determining autoxidation reaction or followed by a consecutive autoxidation process.

$$CoLB + O_2 \rightleftarrows CoLBO_2 \; K_{O_2}$$

$$CoLBO_2 \rightarrow \text{products} \; k$$

or

$$CoLB + O_2 \rightleftarrows CoLBO_2$$

$$CoLB + O_2 \rightarrow \text{products} \; k'$$

On the basis of these reaction schemes the rate may be described by the equations

$$k_{obs} = kK_{O_2}[O_2]/(1 + K_{O_2}[O_2])$$

for the consecutive mechanism and

$$k_{obs} = k'[O_2]/(1 + K_{O_2}[O_2])$$

for the parallel mechanism. For both equations, plots of $1/k_{obs}$ vs $1/[O_2]$ would be expected to give a straight line, with K_{O_2} being given by the intercept divided by the slope, where k_{obs} is the pseudo-first-order rate constant. The value obtained from

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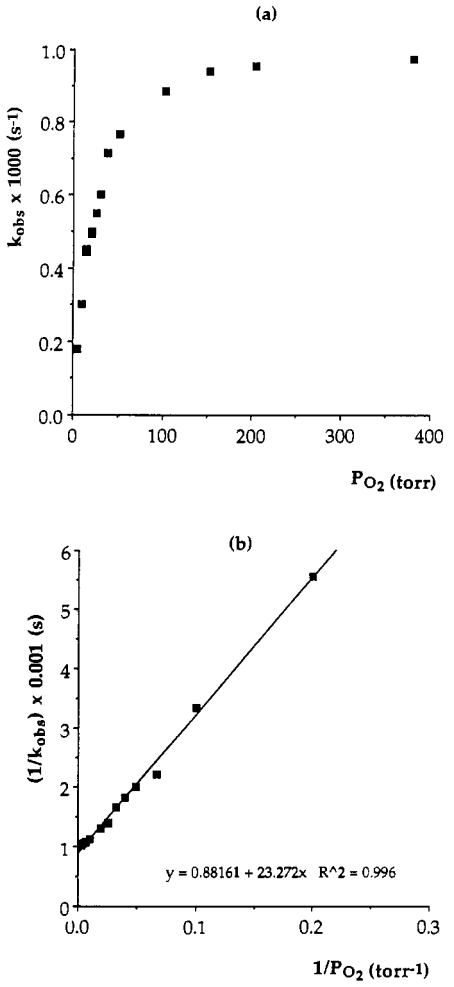

Figure 6. (a) Graph of pseudo-first-order rate constant for the autoxidation of $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in acetonitrile containing 1.5 M 1-methylimidazole at 40 °C ($[Co^{II}] = 5 \times 10^{-5}$ M) versus the partial pressure of dioxygen. (b) Graph of the reciprocal of the pseudo-first-order rate constant versus the reciprocal of the partial pressure of oxygen for the same conditions.

Table I. Observed Pseudo-First-Order Rate Constants for the Autoxidation of Cobalt(II) Cyclidene Complexes in 1.5 M 1-Methylimidazole, Acetonitrile, 30 °C, 760 Torr of Dioxygen

complex	k_{obs} (s^{-1})
$Co(CH_3)_2(CH_3)_2(CH_2)_3^{2+}$	$(2.0 \pm 0.4) \times 10^{-5}$
$Co(CH_3)_2(CH_3)_2(CH_2)_4^{2+}$	$(2.0 \pm 0.4) \times 10^{-5}$
$Co(CH_3)_2(CH_3)_2(CH_2)_5^{2+}$	$(2.0 \pm 0.2) \times 10^{-4}$
$Co(CH_3)_2(CH_3)_2(CH_2)_6^{2+}$	$(4.0 \pm 0.4) \times 10^{-4}$
$Co(CH_3)_2(CH_3)_2(CH_2)_7^{2+}$	$(1.0 \pm 0.1) \times 10^{-3}$
$Co(CH_3)_2(CH_3)_2(CH_2)_8^{2+}$	$(8.0 \pm 1) \times 10^{-4}$
$Co(CH_3)_2(H)_2(CH_2)_8^{2+}$	$(1 \pm 0.1) \times 10^{-2}$
$Co(Ph)_2(CH_3)_2(CH_2)_6^{2+}$	$(2 \pm 0.2) \times 10^{-5}$

either mechanism is the same (0.038 $Torr^{-1}$, 40 °C, for $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in 1.5 M 1-methylimidazole/MeCN), and it is in reasonable agreement with the dioxygen-binding equilibrium constant (K_{O_2}) determined from direct measurements, extrapolated to 40 °C (K_{O_2} = 0.025 $Torr^{-1}$).[6a]

In order to distinguish between the two autoxidation mechanism, the effect of the dioxygen affinity (K_{O_2}) on the rate of autoxidation was examined. It is known that the dioxygen affinity for these complexes depends markedly on the length of the bridging group R^1, increasing systematically with an overall increase by a factor of about 70 on changing n from 5 to 8.[6c] The observed rates of autoxidation for complexes with a variety of ligand substitutions are shown in Table I. For cobalt(II) cyclidene complexes with shorter bridges, n = 3 or 4, the cavity into which dioxygen binds becomes increasingly restricted, such that for n = 4, the dioxygen affinity is greatly diminished,[6c] and for the cobalt(II) cyclidene complex with n = 3, no binding of dioxygen has been observed.[10] The rates of autoxidation of the complexes with n = 3 and 4 are significantly slower than those of the longer bridged complexes (Table I), indicating that the smaller cavity does indeed inhibit the autoxidation process. While this result supports the preequilibrium autoxidation model, it should be noted that the inhibition could also arise from the more positive cobalt(III)/cobalt(II) redox potentials of the shorter bridged complexes,[11] which would be expected to retard the autoxidation reaction associated with the electron transfer/competitive equilibrium mechanism. The striking observation is the insensitivity of the autoxidation rate to changes in cavity size, particularly within the group having penta-, hexa-, hepta-, and octamethylene bridges. That similarity in rates of autoxidation for the cobalt(II) cyclidene complexes with n = 5–8 is best understood if the autoxidation reaction occurs subsequent to dioxygen binding, since for these complexes the cobalt(III)/cobalt(II) potential continues to become more negative as the bridge length increases.

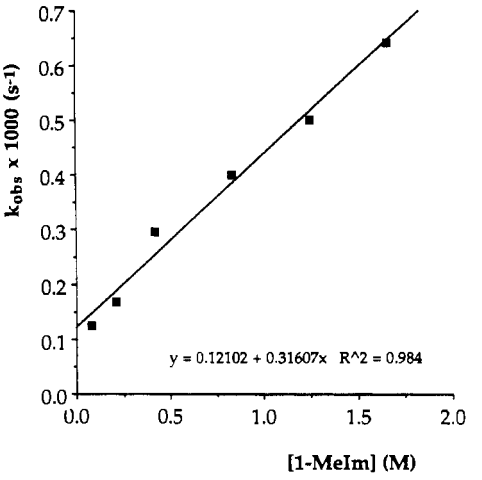

Figure 7. Graph of pseudo-first-order rate constant for the autoxidation of $[Co(CH_3)_2(CH_3)_2(CH_2)_8](PF_6)_2$ in acetonitrile saturated with 760 Torr of dioxygen, at 25 °C ($[Co^{II}] = 5 \times 10^{-5}$ M), versus the concentration of 1-methylimidazole.

Replacement of the methyl group at the R^2 position by hydrogen produces a relatively acidic N–H proton, and this results in a significant increase (12-fold) in the rate of autoxidation. Conversely, conversion of the R^3 methyl to phenyl resulted in a significantly slower (20-fold) rate of autoxidation. These results are summarized in Table I; they are discussed in more detail below.

The effect of base concentration on the autoxidation behavior of the cobalt(II) complexes was investigated by examining the effect of 1-methylimidazole concentration on the rate of reaction. The rate of autoxidation increased dramatically with 1-methylimidazole concentration; over the range from a few tenths molar to almost 2 M, the dependence is approximately linear (Figure 7). Data were obtained up to 15 M. The equilibrium constant for 1-methylimidazole binding to $Co(CH_3)_2(CH_3)_2(CH_2)_6(PF_6)_2$ in acetonitrile has been estimated as 80 mol^{-1} dm^3.[12] However, the base binding equilibrium constant for the dioxygen complex is known to be about 2 orders of magnitude greater than that for the deoxygenated complex,[13] and thus the axial base binding equilibrium will be saturated over the 1-methylimidazole concentration range considered in Figure 7. The linear dependence

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Table II. Effect of Base on the Autoxidation of $Co(CH_3)_2(CH_3)_2(CH_2)_8^{2+}$ (~5×10^{-5} M) in CH_3CN at 30 °C, 760 Torr of O_2

base	[base] (M)	pK_a (25 °C)[14]	rate const (s^{-1})[a]
MeCN	solvent		$(5.0 \pm 0.2) \times 10^{-5}$
pyridine	0.15	5.25	$(7.0 \pm 0.7) \times 10^{-5}$
pyridine	1.5	5.25	$(8.0 \pm 0.8) \times 10^{-4}$
1-methylimidazole	0.15	6.95	$(1.0 \pm 0.1) \times 10^{-4}$
1-methylimidazole	1.5		$(1.0 \pm 0.1) \times 10^{-3}$
collidine	0.15	7.43	$(5.2 \pm 0.5) \times 10^{-4}$
collidine	1.5		$(1.65 \pm 0.2) \times 10^{-3}$
tributylamine	0.15		$(4.9 \pm 0.5) \times 10^{-3}$
diisopropylamine	0.15	10.96 (28.5 °C)	$(4.0 \pm 0.4) \times 10^{-3}$
diisopropylamine	1.5		$(4.0 \pm 0.4) \times 10^{-3}$
diisopropylamine + 1-methylimidazole	1.5 0.15		$(5 \pm 0.5) \times 10^{-3}$
diisopropylamine + 1-methylimidazole	1.5 0.5		$(7 \pm 0.7) \times 10^{-3}$

[a] Apparent first-order rate constant obtained under pseudo-first-order conditions.

of the rate of autoxidation on the base concentration indicates that the autoxidation reaction is first order in base, a result indicative of a ligand deprotonation process affecting the autoxidation rate-determining step. At higher concentrations of 1-methylimidazole the rate of autoxidation continues to increase; however, the slope of the graph decreases. It should be noted that the base concentration as a fraction of solvent extends up to unity and presumably it is those changes in solvent properties which result in the decreased dependence of the rate at very high base concentrations.

The effect of the nature of the added base on the rate of autoxidation was also examined and the results are summarized in Table II. The rate of autoxidation is faster in the presence of stronger bases, and there is no apparent dependence on the steric demands of the bases or on aliphatic and aromatic character. This behavior indicates that the base dependence of the autoxidation rate is due to a deprotonation step in the autoxidation reaction, rather than a result of coordination at the metal.

In order to differentiate the coordinating ability of the added base from its basicity, the rate of autoxidation was measured for $Co(CH_3)_2(CH_3)_2(CH_2)_8(PF_6)_2$ in acetonitrile containing 0.15 M 1-methylimidazole and a range of concentrations of diisopropylamine (0.01–0.1 M), at 25 °C, 760 Torr of O_2. The latter, diisopropylamine, is not expected to coordinate to the cobalt, because of its great steric bulk. The rate of autoxidation increased approximately linearly with diisopropylamine concentration, in a manner similar to that found in the absence of 1-methylimidazole. The rate of autoxidation for a solution containing 1.5 M diisopropylamine with 1-methylimidazole was only slightly higher than that found for the analogous experiment without the 1-methylimidazole: 5.0×10^{-3} vs 4.0×10^{-3} s^{-1}, respectively. When the 1-methylimidazole concentration was increased to 0.5 M, the rate of autoxidation increased to 7×10^{-3} s^{-1}.

In the presence of 1.5 M 1-methylimidazole, little effect on the rate of autoxidation was observed among different aprotic solvents (MeCN, CH_2Cl_2, DMF); however, the rate was significantly reduced in protic media. For example for $Co(CH_3)_2(CH_3)_2(CH_2)_6^{2+}$, at 30 °C, the rates of autoxidation in acetonitrile, methanol, and water were 4.0×10^{-4}, 3.0×10^{-4} and 3.0×10^{-5} s^{-1}, respectively. Ionization of the R^3 = methyl protons is less likely in the presence of a protic solvent; thus a lower rate of autoxidation via a ligand deprotonation mechanism may be expected. The autoxidation of the cobalt(II) cyclidenes in aqueous media will be discussed in more detail in a future publication.[15]

Isotopic Substitution. The mechanisms of reactions involving hydrogen or proton transfer have been investigated by isotopic substitution in either the reactants[16] or the solvent,[17] in particular on enzyme systems.[18] The suspected deprotonation step in the autoxidation reaction of cobalt cyclidenes was examined in more detail by measuring and comparing the pseudo-first-order rate constants for autoxidation of $[Co\{(CH_3)_2(CH_3)_2(CH_2)_7\}](PF_6)_2$ and its deuterium-substituted analog $[Co\{(CD_3)_2(CH_3)_2(CH_2)_7\}](PF_6)_2$, where CD_3 is at the R^3 position, under identical conditions. In an acetonitrile solution of $[Co\{(R^3)_2(CH_3)_2(CH_2)_7\}]^{2+}$, in the presence of 1.5 M 1-methylimidazole and 760 Torr of O_2, the pseudo-first-order rate constants gave a kinetic isotope ratio, $k_H/k_D = 3.5 \pm 0.2$, upon changing R^3 from CH_3 to CD_3, revealing that a carbon–hydrogen bond-breaking process is important to the rate-determining step.

Two probable ligand deprotonation scenarios may be considered, based on the preceding discussion. In the first case, the rate determining step in the autoxidation reaction is deprotonation of the cobalt(II)–dioxygen adduct:

$$CoLH(O_2)^{2+} + B \xrightarrow{\text{slow}} CoL(O_2)^{+} + BH^{+} \xrightarrow{\text{fast}} \text{products}$$

In the second case, the rate-determining step is a ligand oxidation reaction that follows a deprotonation preequilibrium:

$$CoLH(O_2)^{2+} + B \overset{\text{fast}}{\rightleftarrows} CoL(O_2)^{+} + BH^{+} \xrightarrow{\text{slow}} \text{products}$$

Either scenario is consistent with the observed base dependence and related observations, as described above.

In order to distinguish between these two possibilities, the autoxidation reactions were repeated for both the deuterium-substituted and the unsubstituted complexes in solutions of acetonitrile containing 1.5 M 1-methylimidazole and 0.1–0.2 M of either H_2O or D_2O, under 760 Torr of O_2. The kinetic isotope effects observed were independent of water concentration over this concentration range. Low concentrations of water were chosen in order to minimize the effect of changes in the character of the solvent. Under these conditions, the rate of autoxidation is significantly faster than the rate of H/D substitution at the R^3 position, as discussed in the Experimental Section. The rationale for this experiment is that if the first scenario is correct, then the kinetic isotope ratio should be the same for both solvent mixtures, since the rate will be limited by the deprotonation of the R^3 group. If the second scenario is correct, then the rate of autoxidation will

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Table III. Rates of Autoxidation of $Co(R^3)_2(CH_3)_2(CH_2)_7(PF_6)_2$ in Acetonitrile Containing 1.5 M 1-Methylimidazole and 0.2 M of either H_2O or D_2O, 760 Torr of O_2, 25 °C

	$R^3 = CH_3$	$R^3 = CD_3$	k_H/k_D
H_2O	$(1.1 \pm 0.1) \times 10^{-3}$	$(3.5 \pm 0.2) \times 10^{-4}$	3.2 ± 0.2
D_2O	$(1.5 \pm 0.2) \times 10^{-3}$	$(5.0 \pm 0.2) \times 10^{-4}$	3.0 ± 0.2
$k(H_2O)/k(D_2O)$	0.73	0.70	

Table IV. Ratio of the Pseudo-First-Order Rate Constants for $R^3 = CH_3$ and CD_3 for Cobalt(II) Cyclidene Complexes in Acetonitrile at 25 °C, 760 Torr of O_2

base (B)	[B] (mol dm^{-3})	k_H/k_D
	$[Co(R^3)_2(CH_3)_2(CH_2)_7](PF_6)_2$	
acetonitrile	solvent	3.5 ± 0.5
pyridine	0.42	4.2 ± 0.2
pyridine	1.5	4.2 ± 0.2
1-methylimidazole	0.14	6.0 ± 0.2
1-methylimidazole	0.2	4.6 ± 0.2
1-methylimidazole	0.5	3.5 ± 0.2
1-methylimidazole	1.5	3.5 ± 0.2
diisopropylamine	0.03	
+ 1-methylimidazole	1.5	1.5 ± 0.2
tributylamine	0.03	
+ 1-methylimidazole	1.5	2.0 ± 0.2
	$[Co(R^3)_2(CH_3)_2(CH_2)_8](PF_6)_2$	
acetonitrile	solvent	4.0 ± 0.2
1-methylimidazole	0.5 M	3.0 ± 0.2

be dependent upon the cyclidene deprotonation equilibrium, which in turn is dependent upon the relative rates of the forward-deprotonation and back-protonation reactions. The rate of reprotonation of the ligand will be dependent upon the ease of breaking the isotopically sensitive hydrogen/deuterium–B bond. Addition of small amounts of either H_2O or D_2O will ensure that the isotopic distribution of B–H or B–D is saturated with the appropriate hydrogen isotope, and thus the ligand reprotonation rate will be independent of whether the R^3 methyl group is substituted with hydrogen or deuterium. Thus, if the second scenario is correct, then the rate of autoxidation will be faster in the solvent mixture containing the D_2O compared to a similar solution containing H_2O. The results of these experiments (Table III) show that the autoxidation of the cobalt(II) cyclidenes proceeds via a deprotonation preequilibrium, prior to the irreversible ligand oxidation.

Although the results summarized in Table III indicate the presence of a ligand deprotonation preequilibrium, the isotope ratios obtained from Table III are consistent with the proposal that the breaking of the C–H bond is at least partially rate limiting under these conditions, since the kinetic isotope ratio is about 3, significantly higher than that expected for an equilibrium isotope effect.[16b,19g] In contrast, the isotope effects observed for experiments performed in pure H_2O and pure D_2O are much lower, about 1.43, a result that is consistent with an equilibrium isotope effect (expressed in Table III as the inverse, 0.7, since this isotope effect reflects the ligand reprotonation reaction).

Both the nature of the added base and its concentration affect the kinetic isotope ratio. In general, the kinetic isotope ratio decreases for higher base concentrations (1-methylimidazole) and for stronger bases (Table IV).

The observation that the isotope effect on the pseudo-first-order autoxidation rate constants of $[Co(R^3)_2(CH_3)_2(CH_2)_7](PF_6)_2$, for $R^3 = CH_3$ and CD_3, has a significant base dependence, confirms the conclusion that deprotonation affects the rate-determining process. The decrease in the kinetic isotope effect with increasing base strength is in the opposite direction to that predicted by the Westheimer model, supporting the suggestion that deprotonation is not the primary rate-determining step. The Westheimer model describes the kinetic isotope effect in deprotonation reactions and predicts a maximum kinetic isotope ratio k_H/k_D when the difference in pK_a between the acid and the protonated base goes to 0.[16a,19] For the present system, a more satisfactory explanation for the decrease in kinetic isotope ratio under more basic conditions suggests that, under weakly basic conditions, the deprotonation step is predominately rate determining, yielding a full kinetic isotope effect, (0.14 M 1-methylimidazole, k_H/k_D 6.0). From considerations of differences in the zero point energies of C–H and C–D bonds, a kinetic isotope ratio of about 7 may be expected.[16b,h,20] Under more basic conditions, the rate of deprotonation becomes more rapid and the subsequent oxidation reaction gains increasing control over the rate process, with a concomitant decrease in the observed kinetic isotope effect. When the rate of the deprotonation reaction becomes significantly faster than that of the oxidation process, the deprotonation step becomes a preequilibrium process, opening the way to the rate-determining irreversible oxidation. Typically, equilibrium isotope ratios are smaller than kinetic isotope ratios since the differences in zero point energy between the protonated and deuterated forms partially cancel.[16b,19g,20]

Additional Observations. The cobalt(II) cyclidene complexes and the dioxygen adducts both have distinctive ESR spectra,[2f,6a,9c,22d,23] and therefore the ESR spectra were obtained during the autoxidation process. It was found that over the time period expected for the autoxidation reaction to occur at room temperature, the anisotropic cobalt–oxygen adduct spectra, recorded at 77 K, gradually faded away to produce an ESR silent product. This observation is consistent with formation of a diamagnetic cobalt(III) product.

The conductivity change of a cobalt(II) cyclidene complex solution during autoxidation is expected to depend on the number and charges on any ions of the products. In an air-saturated acetonitrile solution of $Co(CH_3)_2(CH_3)_2(CH_2)_6$, over a period of several days at room temperature, no change in conductivity was observed relative to the initial solution of the cobalt(II) cyclidene complex. The half-life of the reaction under these conditions is several hours, and the visible color changes indicated that the autoxidation reaction had proceeded to completion. This observation indicates that there was no significant increase in the number of charge carriers during the process, and thus the product of the autoxidation reaction is also a 2:1 electrolyte and, in that way, is similar to the initial complex.

For comparison to the autoxidation reaction, the UV–visible spectra were recorded after a one electron oxidation of the complex and after exhaustive electrooxidation at a potential more positive than the second (ligand) oxidative wave. As previously described,[8,11] voltammograms of $Co(CH_3)_2(CH_3)_2(CH_2)_6^{2+}$ in acetonitrile exhibit two oxidative processes. The first corresponds to a one-electron metal-centered oxidation and the second corresponds to a ligand oxidation. Bulk electrolysis at a potential 200 mV positive of the first oxidative wave required one electron (0.90e/CoL) as described before;[11] however, electrolysis 200 mV positive of the second ligand oxidation wave (E_p = 1.3 V vs NHE) required ~2.7 electrons per cobalt. The exact electron count is uncertain due to the proximity of this oxidative process to the rising edge of the solvent/electrolyte oxidation.

The spectral properties of the solution after electrooxidation are shown in Figure 8. After oxidation of the complex to cobalt(III), the spectral properties of the complex resemble those of the oxygenated cobalt(II) cyclidene, and this is consistent with the assignment to the dioxygen adduct of a structure involving a cobalt(III)–superoxide complex, as discussed by previous

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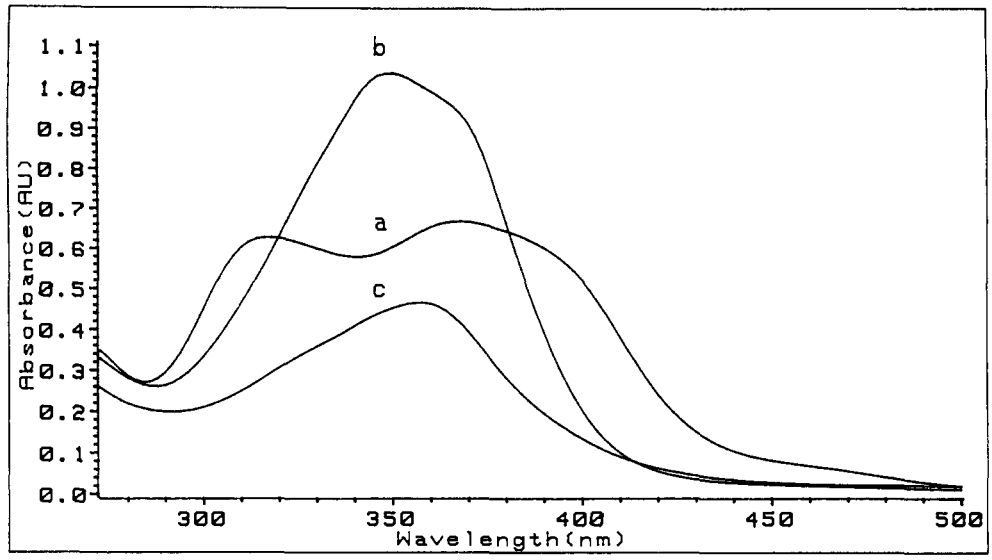

Figure 8. UV–visible spectra (a) of $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in acetonitrile, (b) of the same compound after oxidation by one electron, and (c) of the same compound aftere exhaustive ligand oxidation.

workers.[2f,22d-g,23,24] In contrast, the UV–visible spectrum of the solution after the second electrooxidation, which corresponds to oxidation of the cyclidene ligand, reflects the spectral changes occurring during the autoxidation process. This observation is consistent with the conclusion that the autoxidation reaction involves a ligand oxidation process.

Discussion

The autoxidation of the cobalt(II) cyclidene complexes in acetonitrile in the presence of a base, such as 1-methylimidazole, has been shown to follow first-order kinetics when the concentration of the cobalt complex serves as the reaction variable. The observed saturation kinetics are also consistent with a dioxygen binding preequilibrium prior to the autoxidation reaction. Examination of the effects of 1-methylimidazole concentration and of the basicity of added bases on the rate of autoxidation indicate that the reaction involves deprotonation of the cyclidene ligand, in a step that precedes the irreversible autoxidation reaction. Deuterium substitution of the cyclidene at the R^3 position and the addition of either H_2O or D_2O to the reaction mixture showed that under mildly basic conditions, the rate of deprotonation is rate limiting, with a kinetic isotope effect of about 6, approaching the value predicted based on the calculations of C–H/C–D bond zero point energies.[19] In contrast, in the presence of stronger bases, the rate of deprotonation increases relative to the irreversible ligand oxidation, resulting in a lessor isotope effect that is consistent with a preequilibrium deprotonation reaction.

The similarity of results with relatively high concentrations of diisopropylamine both in the presence and absence of 1-methylimidazole was a remarkable feature of the experiments in which the nature of the added base was varied. The isotope substitution experiments indicated that in the presence of small amounts of water the autoxidation proceeds according to a deprotonation equilibrium of the cobalt–dioxygen complex, prior to a slower irreversible oxidation process. For this mechanism and in the presence of an excess of the strong base diisopropylamine, the presence or absence of 1-methylimidazole would be expected to make a large difference since the dioxygen affinity is expected to be enhanced by the binding of 1-methylimidazole at the axial base site. In turn, a higher K_{O_2}, is expected to increase the equilibrium concentration of both the dioxygen complex and deprotonated dioxygen complex. For $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ in acetonitrile, K_{O_2} is increased by about a factor of 30 upon the addition of 1-methylimidazole. An explanation for the much smaller increase in the rate of autoxidation in excess diisopropylamine on adding 1-methylimidazole is found in the possibility of an alternative autoxidation mechanism.

It is suggested that, under strongly basic conditions, there is a significant degree of deprotonation of the five-coordinate cobalt(II) complex and that this deprotonated species is capable of undergoing rapid reaction with dioxygen to give the autoxidation products. When more 1-methylimidazole was added to the complex in the presence of diisopropylamine, the rate of autoxidation did increase as discussed above. This behavior is consistent with both of the autoxidation pathways being significant under these conditions. In support for this proposal, previous workers have shown that the cobalt(II) complex may be deprotonated with strong bases (sodium methoxide), and they observed that the deprotonated complex autoxidized very rapidly on exposure to dioxygen.[21] It is expected that the cobalt cyclidene dioxygen complex will exhibit a lower pK_a than the corresponding five-coordinate cobalt(II) complex, since the coordination of dioxygen results in at least partial electron transfer from the cobalt to the dioxygen.[22] Consequently, it is reasonable to expect the autoxidation reaction to proceed via the more acidic form under low base conditions (1-methylimidazole/acetonitrile/water), whereas in the presence of high concentrations of significantly stronger bases (nonaqueous/diisopropylamine), deprotonation of the five-coordinate cobalt(II) complex may provide a second significant autoxidation pathway.

It is clear that the autoxidation of the cobalt(II) cyclidene complexes involves deprotonation of the R^3 methyl group when that moiety is present. It is well-known that the $R^3 = CH_3$ substituent is relatively acidic. For example, it has been shown that the nickel(II) complex is readily deprotonated in the presence of strong bases such as sodium methoxide.[8] Furthermore, the analogous neutral doubly deprotonated cobalt(II) complex has been isolated and its structure has been established by X-ray

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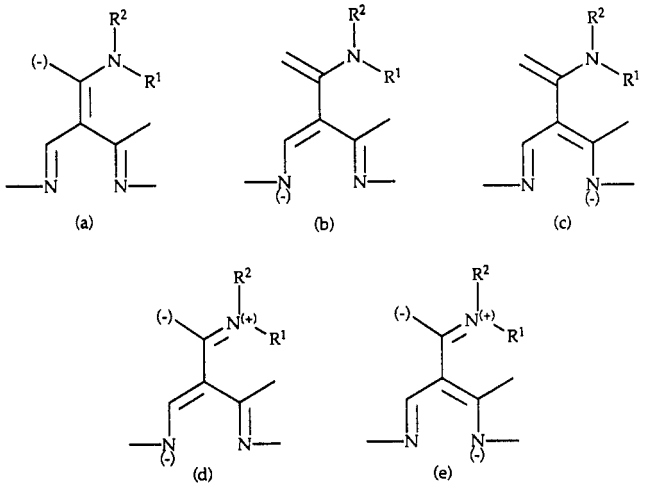

Figure 9. Schematic representation of the major resonance forms of the deprotonated cyclidene ligand.

diffraction studies. The redox potential of the cobalt(III)/cobalt(II) couple was also shifted toward more negative values by about 0.7 V, from +0.31 to −0.42 V versus ferrocene/ferrocenium (in CH_2Cl_2) on deprotonation of the parent $[Co(CH_3)_2(CH_3)(CH_2)_6](PF_6)_2$ cyclidene complexes.[21] (Fc/Fc^+ = 0.41 V vs NHE.[25]) Exposure of the deprotonated complex to dioxygen resulted in rapid autoxidation, approximately 200 times more rapidly than the corresponding nondeprotonated complex $[Co(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$.[21] Deprotonation of the cyclidene ligand may be rationalized in terms of stabilization by extension of the conjugated π system of the cyclidene ligand as illustrated in Figure 9. It may also be noticed that resonance structures (d) and (e) in Figure 9 would stabilize deprotonation of the cyclidenes at the R^2 position if R^2 = H. In the presence of dioxygen, cobalt cyclidene complexes with R^2 = H have been found to undergo notably more rapid autoxidation than their analogs with $R^2 = CH_3$, Table I; this result is consistent with a deprotonation mechanism similar to that discussed above for deprotonation at the R^3 position. Exposure of the manganese(II) cyclidene complex $[Mn(CH_3)_2(CH_3)_2(CH_2)_6](PF_6)_2$ to dioxygen yielded no evidence of a dioxygen adduct, but the complex underwent rapid autoxidation. Analysis of the products revealed net oxidation of the manganese(II) to manganese(III) and deprotonation of the cyclidene ligand at the R^2 position.[26]

Substitution of a phenyl group at the R^3 position, has been found to greatly inhibit the autoxidation process of both the iron(II) and the cobalt(II) cyclidene complexes. In the case of the iron(II) complex, autoxidation was inhibited as illustrated for the iron(II) with $R^2 = CH_2C_6H_5$, and R^2 = *m*-xylyl, for which the half-life of autoxidation changed from ~3 min to ~24 h at 20 °C, in aqueous acetone/1-methylimidazole.[27] A similar enhancement in the resistance to autoxidation has been observed for the cobalt cyclidene complexes on substitution of a phenyl group at the R^3 position, as shown in Table I. This dramatic autoxidative stability on substitution of phenyl for methyl at the R^3 position is consistent with the autoxidation pathway involving initial deprotonation of the R^3 methyl group.

The electron density at the cobalt(II) center may be an important determinant in the autoxidation reaction. The dependence of the rate of autoxidation on the bridge length (R^1), as shown in Table I, is significantly less than the nearly 5 orders of magnitude change in dioxygen affinity obtained on making the same ligand substitutions, a trend that has been correlated to the cyclidene cavity width.[6e] It may be anticipated that the autoxidation process would become easier for more negative Co(III)/Co(II) redox potentials. It is known that the preference of cobalt(III) to be six-coordinate results in the first oxidation of the cobalt(II) complexes being easier in acetonitrile for the longer polymethylene bridging groups ($n > 6$) compared to the shorter bridges (n = 3, 4), a result that is consistent with solvent being able to enter the cavity, upon oxidation, and bind to the cobalt(III) at the sixth coordination site.[11] The rapid autoxidation of the manganese(II) complex is consistent with the negative redox potential of the Mn(III)/Mn(II) couple in acetonitrile (−0.5 V vs Ag/0.1 M $AgNO_3$[26] (Ag/0.1 M $AgNO_3$ = 0.577 V vs NHE)[28]).

A simple electrochemical argument, predicts that the more negative the M(III)/M(II) redox couple, the more facile the autoxidation; however, the more positive the M(III)/M(II) redox couple, the greater the prospect that the ligand will be oxidized. Consequently, from a simplistic electrochemical viewpoint, for a given ligand family, those metals with the most positive M(III)/M(II) redox potential are most likely to undergo ligand oxidation in the autoxidation process. Thus the manganese cyclidene complexes autoxidize more rapidly than those of cobalt, but ligand oxidation is expected to be more facile among the cobalt complexes.

Ligand oxidation is believed to be integral to the autoxidation reaction reported here. Support for this hypothesis comes from the observation that ESR spectra of the one electron oxidation products of the shorter bridged cyclidenes (n = 3, 4, 5) following electrolysis showed the presence of an organic radical.[11] Even though the ESR spectra of the cobalt(II) solutions become diamagnetic following autoxidation, it has been observed that an ESR signal ($g \sim 2$) appears during the autoxidation reaction when the cobalt(II) cyclidene complex is covalently tethered to a solid support.[29] The observed reactivity toward dioxygen of the electrooxidized cobalt(III) cyclidene complexes for n = 5, 6, 7 is most unusual for a cobalt(III) complex and leads to the suspicion that even for the apparently diamagnetic, large cavity cobalt(III) cyclidene complexes, there is an equilibrium between cobalt(III) and cobalt(II)/ligand radical.[11] The absence of reactivity toward dioxygen of the oxidized cobalt cyclidene complexes having a shorter bridge, n = 3 and 4,[11] presents an interesting possibility; perhaps the reaction with dioxygen occurs within the ligand cavity.

There is considerable precedent for autoxidation by outer sphere processes in biological dioxygen carriers such as hemoglobin[5,30] and the iron(II) cyclidene complexes under some conditions.[31] However, from the results presented above, it is clear that the autoxidation of the cobalt(II) cyclidene complexes is not occurring by an outer sphere mechanism.

There are several examples in the chemical literature of the autoxidation of cobalt(II) complexes that involve oxidation of the ligand.[9b,32] For example, it has been found that during the autoxidation of the complex (Co(II)(Pydien), the cobalt μ-peroxo complex, which forms initially, undergoes successive ligand oxidative dehydrogenation reactions, liberating hydrogen peroxide and forming different cobalt(II) complexes, which were able to bind dioxygen.[9b]

During the autoxidation of the cobalt(II) cyclidene complexes, the most probable location for electron removal for a ligand

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oxidation process would be from the conjugated π system. The autoxidation of the cobalt(II) cyclidenes is proposed to proceed via deprotonation of the R^3 methyl group in the dioxygen adduct, followed by a dual metal/ligand oxidation process.

$$[Co(II)(LH)]^{2+} + O_2 \rightleftarrows [(LH)Co(III)O_2^-]^{2+}$$

$$[(LH)Co(III)O_2^-]^{2+} + B \rightleftarrows [(L^-)Co(III)O_2^-]^{+} + BH^+$$

$$[(L^-)Co(III)O_2^-]^{+} \rightarrow \text{autoxidation products}$$

The products of the autoxidation reaction will be described in a later report.

Summary

Kinetics studies on the autoxidation of cobalt(II) cyclidene complexes with $R^3 = CH_3$ (Figure 1) in nonaqueous solution have shown that the rate is dependent upon the partial pressure of dioxygen, the concentration and nature of added base, and ligand substituents. A mechanism has been proposed involving a preequilibrium deprotonation of the dioxygenated cobalt(II) complex to produce the conjugate base, which subsequently undergoes irreversible oxidation of the ligand. An analogous deprotonation mechanism also occurs if $R^2 = H$, resulting in rapid autoxidation; however, if these two relatively acidic sites are blocked, the resistance of the cobalt(II) complexes to autoxidation is greatly enhanced.

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