

Oxygenation of Substituted Phenols Using Molecular Oxygen and Cobalt(II) Cyclidene Complexes

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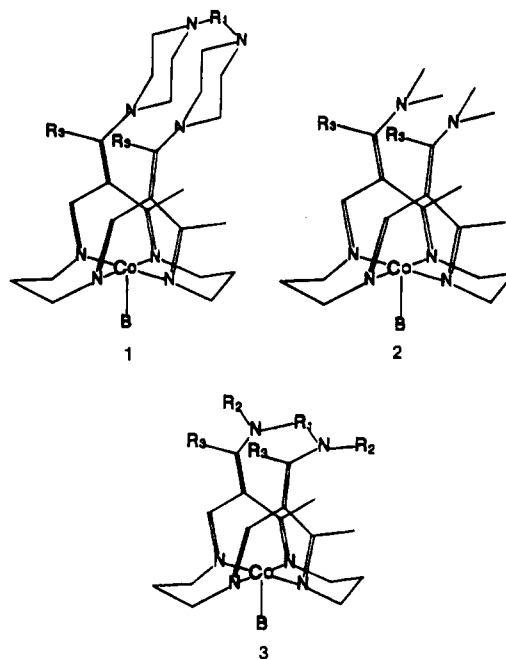
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The superstructured cobalt(II) cyclidene complexes function as both oxidase and oxygenase models in oxygenation of substituted phenols. The catalytic cycle for oxygenation of 2,6-di-*tert*-butylphenol is considered, including the reaction pathways to the two oxygenation products, benzoquinone and diphenoquinone. The product selectivity of the oxygenation reaction varies with the structures and dioxygen binding behavior, providing insight into the reaction mechanism. This, the kinetics of the oxygenation reaction, and modeling studies lead to a minor modification of the previously proposed mechanism, in which electron transfer is suggested for the formation of the intermediate phenoxy radical. The stabilities of the complexes under a dioxygen atmosphere control their catalytic abilities because autoxidation destroys the catalysts.

Introduction

Molecular oxygen is a powerful oxidizing agent for potentially useful oxidation reactions, and because it is freely available, O₂ is often the oxidant of choice. However, the triplet ground state of molecular oxygen provides a significant kinetic barrier toward interaction with singlet organic molecules, making molecular oxygen relatively inert toward many desirable oxidation reactions. The interaction of molecular oxygen with transition metal atoms may reduce this kinetic barrier through spin orbit coupling and facilitated spin state changes.¹ We have previously reported the dioxygen binding and autoxidation properties of many cobalt(II) complexes with the cyclidene family of ligands.² Ease of variation of structural features is an advantage of these compounds, and three variants are important to the work reported here. Structure 1 shows the so-called *vaulted* cyclidene complex. The piperazine risers place a bridging R¹ well above the parent macrocycle, creating a large cavity within which both O₂ and an organic molecule could be bound. In formulas and abbreviations, vaulted ligands are indicated by the sequence R³VR¹; thus the vaulted complex having a durene bridge (=R¹) and R³ = Me is abbreviated MeVD as in [CoMeVD]²⁺. Structure 2 shows the unbridged cyclidene, while Structure 3 illustrates the so-called *lacunar* cyclidene, which contain small cavities that are only large enough for such small ligands as O₂, NCS⁻, or CO. For the unbridged cyclidene, the ligand is merely abbreviated by the list of substituents R¹ and R² on the nitrogens and R³ on the vinyl group; thus the species having only methyl substituents has the abbreviation MeMeMe as in [CoMeMeMe]²⁺. Abbreviations for the lacunar complexes are essentially the same as for the unbridged species, except R¹ is then a bridging group as in [CoMeMeC₆]²⁺, where C₆ indicates a bridging chain having 6 methylene groups.



The structural variant called the vaulted complex³ (Structure 1) was designed to imitate the monooxygenase enzymes, cytochromes P450, with a view toward producing a potent model of the ternary complex that P450 forms with the substrate and O₂.^{3f-g} The vaulted complexes have indeed been shown to form quaternary complexes consisting the metal, ligand, a monodentate axial ligand, and dioxygen (Figure 1).³ Further, the iron, manganese, and chromium complexes all promote P450-like oxygenations using surrogate oxidizing agents in much the same manner as has been so extensively reported for porphyrin

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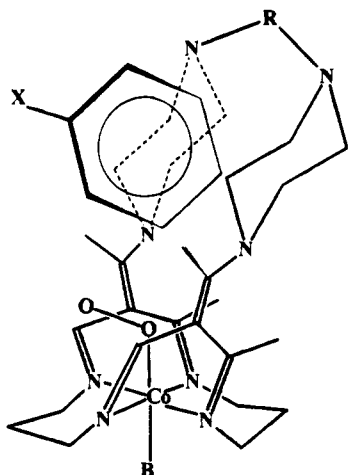


Figure 1. Conceptualization of the quintuple complex containing dioxygen and an organic substrate in the cavity of a vaulted cobalt(II) cyclidene complex.

complexes. However, O_2 has not provided verifiable oxygenation reactions.^{3f,g}

The oxygenation of phenols with cobalt(II) dioxygen complexes has been widely studied. The first such reaction was reported using a cobalt(II) Schiff base complex.⁴ Benzoquinones were found to be the main products, and a phenoxy radical was suggested as a reactive intermediate. The same reactions were later studied in great detail, and a reaction mechanism was proposed.⁵ In the suggested mechanism, the dioxygen complex abstracts a hydrogen atom from the phenol to form the phenoxy radical, and this hypothesis has been followed by many researchers.⁶ This paper reports oxygenation of phenols using as catalysts cobalt(II) cyclidene complexes having greatly varied cavity sizes, ranging from wide-open (unbridged), through large cavities (vaulted), to small cavities (lacunar cyclidenes). This work represents the first example of a systematic study of an oxygenation reaction using totally synthetic superstructured cobalt(II) complexes, and interesting consequences derive from the confinement of the reaction to the cavity within the superstructure.

Experimental Section

Solvents and Materials. The HPLC grade solvents used for HPLC measurements were purchased from either Fisher Scientific or Aldrich Chemical Co., Inc., and used without further treatment. The HPLC grade solvents used for the oxygenation studies were stored over activated 3A Union Carbide molecular sieves. The 2,6-di-*tert*-butylphenol was purchased from Aldrich Chemical Co., Inc., and recrystallized from either hexane or ethanol. Electrometric grade tetrabutylammonium fluoroborate (TBAB) was purchased from Southwestern Analytical Chemicals, Inc., and used as received.

Physical Measurements. Infrared spectra were obtained using a Perkin Elmer 1610 FTIR spectrometer (4000–400 cm^{-1}) calibrated with polystyrene. Samples were run as solutions in a liquid sample cell with KBr windows. Ionization potentials were estimated using a

ZAB HS mass spectrometer (VG Analytical Ltd., Manchester, U.K.). Samples were introduced through a heated septum inlet using the molecular leak technique. Xenon was used as the calibrating gas with an ionization potential equal to 12.13 eV and was introduced through the gas line. Electron energies were measured at ± 0.01 eV with control intervals equal to ± 0.2 eV. Spectroelectrochemical experiments were performed using a Princeton Applied Research Model 173 potentiostat/galvanostat and a Hewlett Packard 8452A diode array spectrophotometer equipped with a Hewlett Packard 9000/300 computer, open to the atmosphere. The spectroelectrochemical quartz cell contained the reaction solution, with 0.1 M TBAB as supporting electrolyte, and three electrodes. The working electrode consisted of a glassy slide coated with In_2O_3 ; the reference electrode was Ag/AgCl in 0.1 M TBAB CH_3CN ; and the auxiliary electrode was platinum gauze. The applied potentials between the working electrode and reference electrode were varied from 0.0 to 2.7 V with an oxidation time of 2 min at each potential. Elemental analyses were performed by the staff at the University of Kansas.

Molecular Mechanics. Molecular mechanics calculations were performed with modified version of MM2/MMP2 program⁷ running on a VAX 9000 computer. The original crystallographic data for the vaulted cyclidene complex were obtained from the Cambridge Structural Data Base. A commercial molecular mechanics software program, Sybyl,⁸ was used for molecular imaging. The image of the dioxygen complex $[Co(MeVD)ClO_2]Cl$ was built from coordinates for the vaulted anthracene complex, $[NiMeVA](PF_6)_2$,^{3a} using Sybyl. The energy minimization of $[Co(MeVD)ClO_2]Cl$ and of the guest molecule, DMP, were carried out with the modified version of MM2/MMP2.

Oxygenation of Phenols. A gas absorption apparatus was constructed for recording pressure changes at constant volume and temperature during the oxygenation reactions. Pressure changes (± 0.001 Torr) were measured using a Texas Instruments Model 145 precision pressure gauge. The system was purged with dioxygen for at least 4 pump/dioxygen cycles at the beginning of each experiment. Samples of the cobalt(II) complexes were weighed inside a dry oxygen-free glove box, removed, dissolved in HPLC grade acetonitrile, and transferred to the reactor through a septum. The solutions were allowed to saturate with dioxygen for 5 min, followed by the addition of the solutions of substrates. The system was then closed, and pressure measurements were started. The gas temperature was recorded using a Micronta digital thermometer (± 0.1 °C). HPLC was used to analyze the organic reactants and products involved in the oxygenation reactions (Waters Model 680 automated gradient controller, Model 510 pumps, a Model U6K injector, a Lambda-Max Model 481 LC spectrophotometer, and a normal phase ES Industry Alumina (N) Chromega column (4.6×150 mm) equipped with a Waters guard column with Waters CORASIL II packing material). Hexane and a mixture of 70% hexane and 30% tetrahydrofuran were employed as mobile phases. All analyses were carried out at ambient temperature. Toluene was chosen as the internal standard and a Hewlett Packard 3394A integrator was used to record peaks and calculate results.

Results and Discussion

Oxygenation of Various Phenols. Several substituted phenols including 2,6-di-*tert*-butylphenol (DTBP), 2,6-dimethylphenol (DMP), 2,6-dimethoxyphenol (DMOP), and 3,5-di-*tert*-butylphenol (35-DTBP) were chosen for qualitative survey of the catalytic oxidation. The reaction products were characterized using GC/MS as well as other analytical techniques, and the qualitative results are summarized in Table 1. For the oxygenation of DTBP, two products, 2,6-di-*tert*-butyl-1,4-benzoquinone (DTBQ) and 3,5,3',5'-tetra-*tert*-butyl-4,4'-diphenoquinone (TT-BDQ), were detected by GC/MS. The diphenoquinone, TT-BDQ, was isolated as a crystalline solid and further characterized by infrared and NMR spectroscopies. Elemental analyses:

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Table 1. Identified Reaction Products from Oxygenation of Various Phenols with O₂ and [CoMeVD](PF₆)₂^a

Phenol	Product
	or
	—
	—
	—

^a In CH₃CN solution at 25.0 °C and 1 atm of O₂ for 24 h.

Table 2. Approximate Ionization Potentials of the Phenols^a

phenol	<i>I</i> (eV)	phenol	<i>I</i> (eV)
DMOP	8.7	DTBP	8.0
DMP	8.4	3,5-DTBP	7.9

^a These data are best considered to be semiquantitative in nature. The uncertainties may exceed 10%.

Calcd for C₂₈H₄₀O₂: C 82.30, H 9.87; found: C 82.10, H 10.18. Only small amounts of the corresponding benzoquinone products were detected by GC/MS in the oxygenation of DMOP and 3,5-DTBP. No reaction product was detected by either GC/MS or HPLC in the attempted oxygenation of DMP. Substantial oxidation with measurable yields of products was only observed for DTBP.

The electron releasing abilities of the three substituent groups follow the order of -C(CH₃)₃ > -OCH₃ ≈ -CH₃.⁹ For the same substituents, the electron donation from the *ortho* position has the greater effect on the reactivities of phenols. These results indicate that the electronic properties of the phenols affect the reaction and that the oxygenation reaction will be favored by good electron releasing groups. This indicates that the cobalt-(II) cyclidene complexes are only capable of catalyzing oxygenation of the more reactive phenols. Additional evidence was sought to support the conclusion that the observations arose from the oxidizability of the phenols.

In order to support the previous inference, the ionization potentials of phenols were estimated by an established technique¹⁰ (Table 2). Because of the limitation of emission current regulation of the mass spectrometer employed, these data may only be treated semiquantitatively. The results suggest that phenol has the highest ionization potential (9.0 eV),¹¹ followed by DMOP, DMP, and the di-*tert*-butyl substituted phenols. This observation indicates that the difficulty of removing one electron from these phenols increases in the order DTBP ≈ 3,5-DTBP

< DMP < DMOP < phenol. This order, like the sequence expected on the basis of the electron releasing effects of the substituents (above), identifies the DTBP as the most easily oxidized phenol in this list and is consistent with the fact that only the DTBP displays a substantial reactivity toward the O₂ adducts of cobalt cyclidenes.

Oxygenation of 2,6-Di-*tert*-butylphenol: Stoichiometry and Analysis of Products. The formation of the oxygenation products was followed by HPLC. When the DTBP/[CoMeVD]-(PF₆)₂ ratio is low, the formation of the benzoquinone product, DTBQ, is enhanced. The second product is the diphenoquinone, TTBDQ, and it precipitates from the acetonitrile solution as a red crystalline solid when its concentration is sufficiently high. The graphs of Figure 2 show dioxygen uptake versus time for the oxygenation of DTBP using (Figure 2a) the vaulted complex [CoMeVD](PF₆)₂ (Structure 1) and (Figure 2b) the unbridged complex [CoMeMeMe](PF₆)₂ (Structure 2) as catalysts. Significantly, the total dioxygen uptake is 2.0 mmol for [CoMeVD]-(PF₆)₂ and 0.46 mmol for [CoMeMeMe](PF₆)₂, respectively, giving a dioxygen uptake ratio between the two complexes of 4.3. This value is close to the reciprocal of the ratio of autoxidation rate constants for their dioxygen complexes, which is 3.9,² suggesting that the extent of reaction is a simple function of the lifetime of the catalyst. This requires similar oxygenation rates for the two systems, and the measured initial dioxygen uptake rates are indeed identical within experimental error (7.1 × 10⁻³ mmol/min and 6.0 × 10⁻³ mmol/min for the [CoMeVD]-(PF₆)₂ and [CoMeMeMe](PF₆)₂, respectively).

Electrochemical investigations of the anodic oxidation of 2,4,6-tri-*tert*-butylphenol and 2,6-di-*tert*-butyl-4-methylphenol in acetonitrile solution indicate that a phenoxy radical forms as a reaction intermediate during the two electron oxidation process,^{12,13} and high yields of cyclohexadienone derivatives were observed in the presence of a nucleophile. In addition, a theoretical study of the phenoxy radical has been carried out,¹⁴ indicating significant delocalization of the unpaired electron

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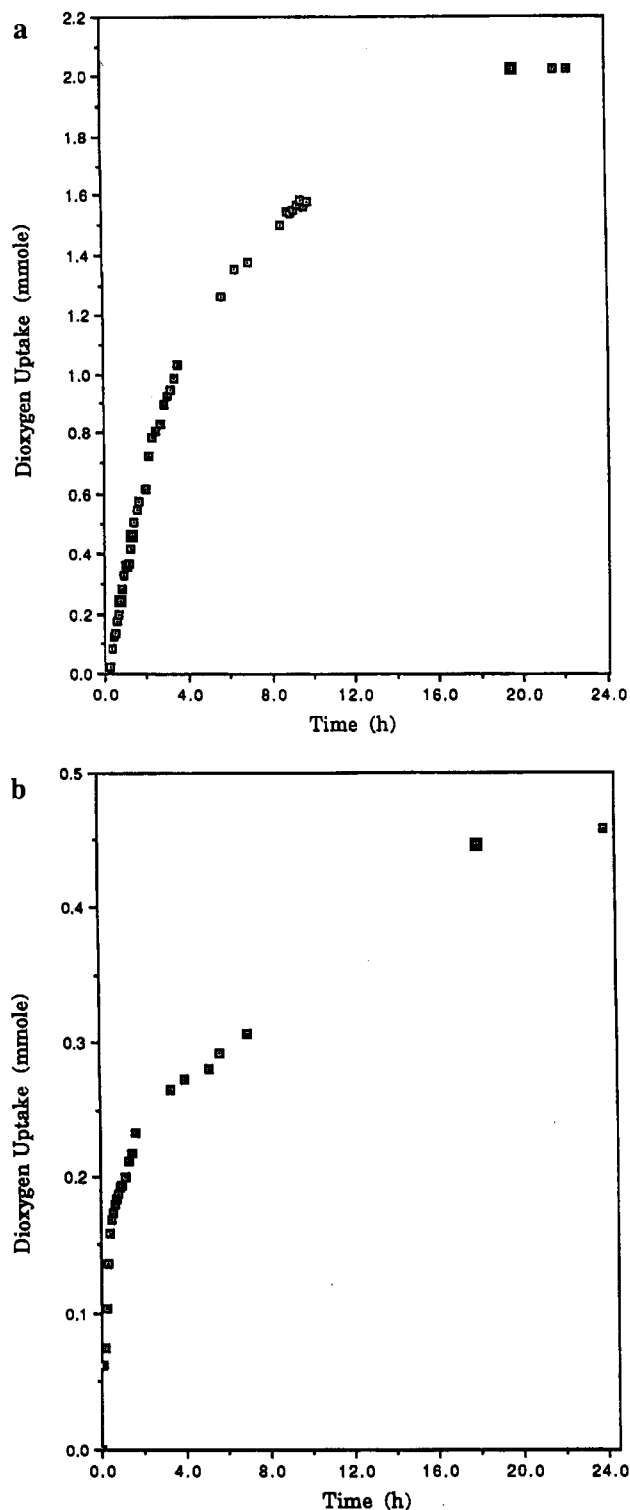


Figure 2. Dioxygen uptake curves for 2,6-di-*tert*-butylphenol (5.9×10^{-1} M) at 1 atm of O_2 and $25.0^\circ C$ in CH_3CN solution with (a) $[CoMeVD](PF_6)_2$ (3.03×10^{-2} M); (b) $[CoMeMeMe](PF_6)_2$ (2.92×10^{-2} M).

around the aromatic ring. The calculated electron spin densities are 0.234e at the *ortho* carbon, 0.461e at the *para* carbon, and only 0.138e at the oxygen. In accord with these considerations, Scheme 1 suggests a reaction pathway for oxygenation of DTBP in which a phenol radical is generated by the dioxygen adduct. Attack at the *para* position by a radical derived from the dioxygen adduct, or by another phenoxyl radical, give respectively benzoquinone or diphenoquinone. The two competitive parallel radical additions determine the distributions of the products. Under conditions of high cobalt dioxygen complex

Scheme 1. Reaction Pathway for Oxygenation of DTBP by Cobalt Cyclidene Dioxygen Complexes

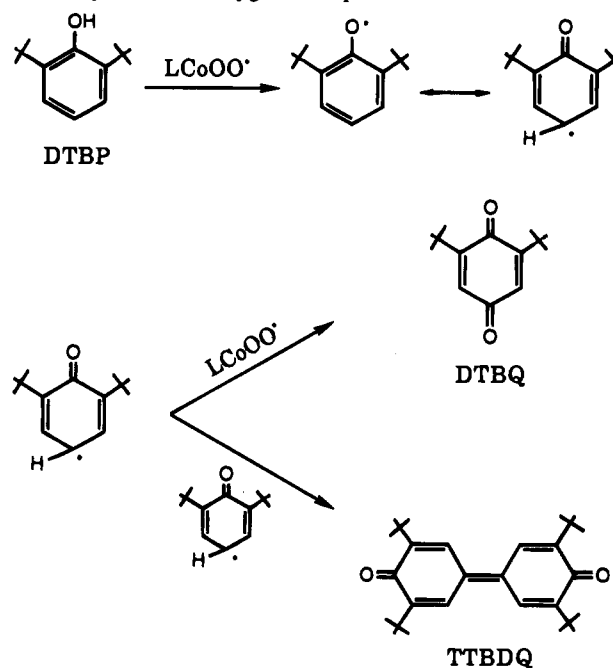


Table 3. Reaction Results for Oxygenation of 2,6-Di-*tert*-butylphenol with O_2 and Cobalt(II) Complexes^{a,c,e}

complex	$[Co]_0$ (M) $\times 10^2$	R_1^b	conv (%)	DTBQ (%)	TTBDQ (%)	R_2^c
$[CoMeVD](PF_6)_2$	3.05	2D	37	5.0	22	0.22
$[CoMeMeMe](PF_6)_2$	3.15	2D	33	2.9	4.6	0.63
$[CoMeVD](PF_6)_2$	1.51	10	37	5.2	14	0.37
$[CoMeVD](PF_6)_2^d$	1.51	10	22	1.3	5.6	0.23

^a At 1 atm of O_2 at the beginning of the reaction and in 13.0 mL of CH_3CN solution at $25.0^\circ C$ for 24 h. ^b Ratio of DTBP/Co. ^c Ratio of DTBQ/TTBDQ. ^d In the presence of 1-methylimidazole. ^e The uncertainties of the % conversions are approximately $\pm 3\%$.

concentration, relatively more benzoquinone product should form, while at low cobalt(II) dioxygen complex concentration, relatively more of the diphenoquinone product should form.

Additional evidence for the proposed reaction pathway is provided by the effect of the manner of binding the dioxygen to the vaulted complex $[CoMeVD](PF_6)_2$.² (1) The dioxygen may bind either inside or outside the cavity if the available axial bases are all relatively small and not too strong; such is the case with acetonitrile. (2) Dioxygen only bonds inside the cavity if a large powerful axial base, such as 1-methylimidazole, is available. The phenoxyl radical has freer access to the bound dioxygen if the latter is outside the cavity. This accounts for a higher product ratio benzoquinone/diphenoquinone for acetonitrile as the axial base when compared to the ratio for 1-methylimidazole (Table 3). The lowest benzoquinone/diphenoquinone ratio, 0.14, was obtained by increasing the 1-methylimidazole concentration to 1.5 M.

The difference in catalytic behavior of the two complexes, $[CoMeVD](PF_6)_2$ and $[CoMeMeMe](PF_6)_2$, supports the proposed reaction pathway in a similar way. It is known that the unbridged complex $[CoMeMeMe](PF_6)_2$ has a totally open structure around the metal atom.² Therefore, during the reaction with the dioxygen adduct of the unbridged complex $[CoMeMeMe](PF_6)_2$, the radical can reach the bound dioxygen without steric restriction, and the benzoquinone/diphenoquinone ratio is expected to be higher than that using vaulted complex $[CoMeVD](PF_6)_2$ (where the O_2 is partially shielded inside the cavity). Table 3 shows about a 3-fold increase of the benzo-

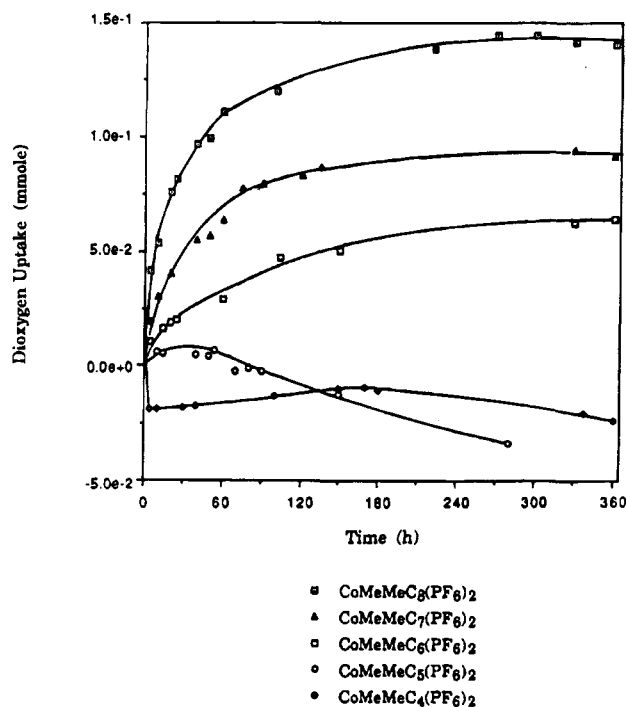
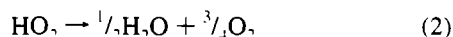
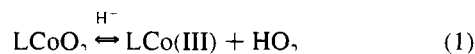


Figure 3. Dioxygen uptake curves for 2,6-di-*tert*-butylphenol (3.85×10^{-2} M) with $[\text{CoMeMeC}_n](\text{PF}_6)_2$ (3.85×10^{-3} M) at 1 atm of O_2 and 25.0°C in CH_3CN solution.

quinone/diphenoxinone ratio when the catalyst is changed from $[\text{CoMeVD}](\text{PF}_6)_2$ to $[\text{CoMeMeMe}](\text{PF}_6)_2$.

The sizes of the cavities of the lacunar cobalt(II) cyclidene complexes (Structure 3) $[\text{CoMeMeC}_n](\text{PF}_6)_2$ ($n =$ number of methylene groups in the polymethylene bridge) can be controlled systematically by variation of the length of a polymethylene bridge across the cavity top. The size of the cavity increases monotonically as n increases from 3 to 8, and the effect of cavity size on O_2 affinity has been thoroughly documented.¹⁵ The curves for dioxygen uptake as a function of time are presented in Figure 3 for oxygenation of DTBP using the lacunar complexes. Both the amount of dioxygen taken up (height of asymptotic line) and the rate of dioxygen uptake (initial slope of curve) increased from $n = 6$ to $n = 8$, a result that is consistent with the previous arguments presented here and with the expected effects of cavity size. Interestingly, the complex with $n = 4$, $[\text{CoMeMeC}_4](\text{PF}_6)_2$, did not catalyze the oxygenation of the substrate; it simply released the dioxygen it had bound before the substrate was added. Autoxidation of the cobalt complex to a cobalt(III) state is expected to liberate $3/4$ of the dioxygen that had been bound to the dioxygen adduct if no dioxygen is used in reaction with other substrates (eqs 1 and 2). The complex $[\text{CoMeMeC}_5](\text{PF}_6)_2$ catalyzed the oxy-



genation slightly and then released dioxygen. These results strongly support the earlier conclusion that oxygenation in these systems is limited by the autoxidation of the catalysts and that the cavities restrict the participation of the dioxygen adduct in substrate oxidation. Viewed from another standpoint, the retarding and yield limiting effects of the cavity prove that the

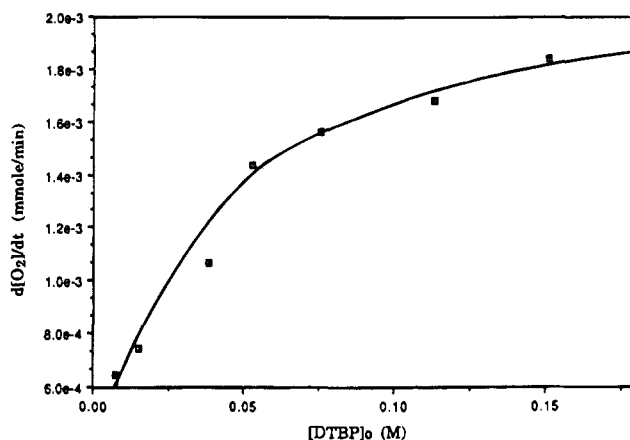


Figure 4. A plot of $d[\text{O}_2]/dt$ versus concentration of 2,6-di-*tert*-butylphenol upon oxygenation with $[\text{CoMeVD}](\text{PF}_6)_2$ (7.55×10^{-3} M) at 1 atm of O_2 at the beginning of the reaction in CH_3CN solution at 25.0°C .

reaction takes place within the cavity, a conclusion that is interesting in its own right.

Kinetic Studies. The rate of oxygenation of DTBP was monitored by the uptake of dioxygen. Initial dioxygen uptake rates were determined with substrate/catalyst ratios of 20:1 at 1 atm of dioxygen. A plot of $d[\text{O}_2]/dt$ versus the cobalt complex concentration for $[\text{CoMeVD}](\text{PF}_6)_2$ gave a straightline, indicating that the reaction is pseudo-first-order in catalyst concentration. The variation of rate with the concentration of DTBP revealed a saturation behavior typical of catalyst/substrate complex formation (Figure 4). At very low substrate concentrations ($[\text{DTBP}] < 4.50 \times 10^{-2}$ M, and $\text{DTBP}/[\text{CoMeVD}](\text{PF}_6)_2 < 6.0$), the dependence of $d[\text{O}_2]/dt$ on $[\text{DTBP}]$ is basically linear, showing the expected first-order kinetics. At high substrate concentrations ($[\text{DTBP}] > 1.50 \times 10^{-1}$ M, and $\text{DTBP}/[\text{CoMeVD}](\text{PF}_6)_2 > 20$), the rate is independent of DTBP. Parenthetically, it has been reported for oxygenation of 2,6-dimethylphenol using $[\text{Co}(\text{saplr})\text{m}]$ that the reaction is zero-order when the ratio of substrate to catalyst $\text{DMP}/[\text{Co}(\text{saplr})\text{m}]$ is equal or larger than 20.^{12b} The overall kinetic rate law for oxygenation of DTBP using vaulted cobalt(II) cyclidene complexes $[\text{CoMeVD}](\text{PF}_6)_2$ in acetonitrile solution can be given as

$$d[\text{O}_2]/dt = \{k_{\text{cat}}[[\text{CoMeVD}](\text{PF}_6)_2][\text{DTBP}](P_{\text{O}_2})^{3/2}\} / (K_m + [\text{DTBP}])$$

for the case where $[\text{CoMeVD}] = 7.55 \times 10^{-3}$ M and $P_{\text{O}_2} = 1$ atm, $k_{\text{cat}} = 0.28$, and $K_m = 0.026$. It must be emphasized that this equation is appropriate only at zero time when autoxidation of the cobalt complex can be neglected. This observed rate behavior is consistent with a reaction pathway in which the formation of the phenoxy radical within a catalyst/substrate complex is the rate determining step.

The dependence of $\ln(d[\text{O}_2]/dt)$ on $\ln(P_{\text{O}_2})$ is shown in Figure 5. It is apparently linear with a slope of 1.66, which is in the vicinity of $3/2$, but the very limited data only indicate the fractional character, not its precise value. This unusual reaction order may be due to a complicated multistep reaction process involving molecular oxygen.

Spectroelectrochemical Results and the Reaction Mechanism. Spectroelectrochemical studies on the electrooxidation of DTBP gave the UV-visible spectral changes in Figure 6. Upon applying anodic potentials, the intensities of the DTBP absorption bands at 270 and 276 nm decreased, and the absorbances characteristic of DTBQ (255 nm) and TTBDQ (420

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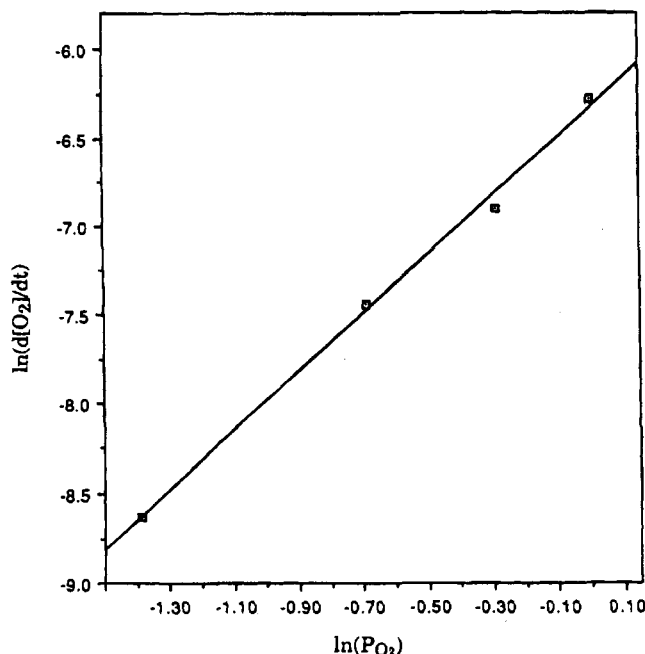


Figure 5. A plot of $\ln(d[O_2]/dt)$ versus $\ln(P_{O_2})$ upon oxygenation of 2,6-di-*tert*-butylphenol (1.13×10^{-1} M) with $[CoMeVD](PF_6)_2$ (7.55×10^{-3} M) in CH_3CN solution at $25.0^\circ C$.

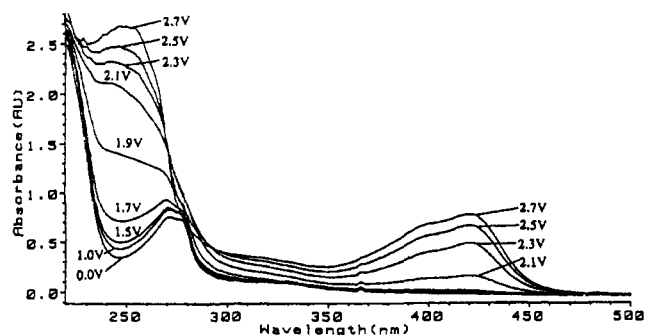


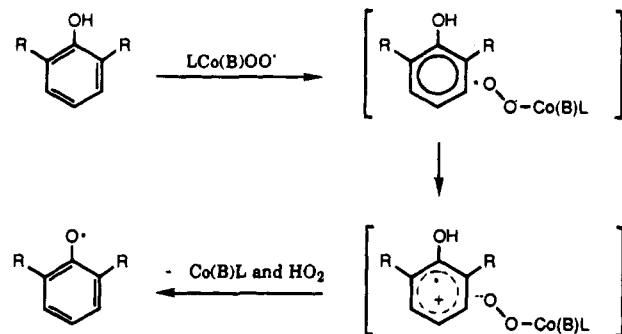
Figure 6. UV-visible spectral changes upon electrochemical oxidation of 2,6-di-*tert*-butylphenol in 0.1 M TBAB CH_3CN solution, open to the atmosphere at room temperature at potentials of 0.0, 1.0, 1.5, 1.7, 1.9, 2.1, 2.4, 2.5, and 2.7 with 2 min intervals.

nm) grew in. Thus, the oxidation of DTBP by either electrochemistry or cobalt cyclidene dioxygen complexes produces the same products, suggesting the two processes may share similar reaction pathways.

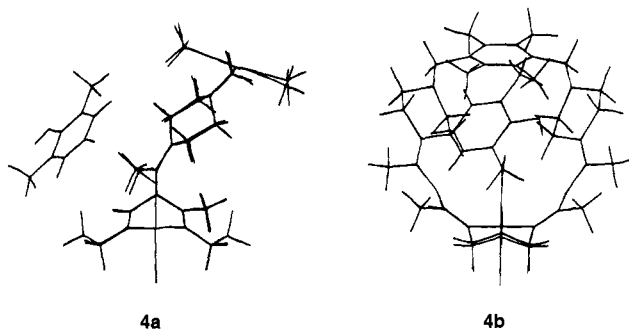
Previous considerations of reactions of this type have assumed that the phenoxy radical is produced by hydrogen atom abstraction. An alternative reaction mechanism for the generation of the phenoxy radical by cobalt cyclidene dioxygen complexes (Scheme 2) involves electron transfer followed by loss of a proton. Several steps of the proposed reaction mechanism deserve consideration: (1) the electron deficient dioxygen adduct of a cobalt cyclidene complex behaves as a radical² and shares an encounter complex with the phenol at the transition state; (2) one electron is transferred from the phenol to the cobalt-bound dioxygen, most likely, through the delocalized $p-\pi$ system on the phenol, resulting in the spontaneous formation of a cationic radical and a bound dioxygen anion; (3) the cationic radical is highly susceptible to deprotonation, and the proton can be captured by the bound dioxygen anion. Subsequent release of HO_2 regenerates the catalytic $Co(II)(B)L$ species. In this scheme, the cobalt dioxygen complex behaves as an oxidase model.

Molecular Mechanics Studies. The interactions of phenols and a vaulted cobalt cyclidene dioxygen complex were modeled

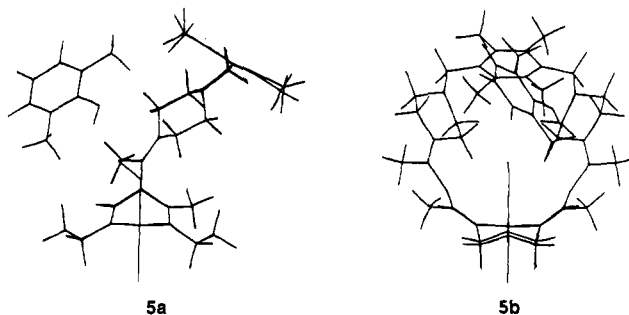
Scheme 2. Proposed Electron Transfer Mechanism for Formation of the Phenoxy Radical



using molecular mechanics in order to visualize the proposed electron transfer process. Structures **4a** and **4b** show the energy



minimized molecular pair for the case where the phenol is initially oriented with the hydroxy group away from the cavity and the phenol ring is above the middle of the cavity and parallel to the piperazine rings of the bridging group. Structure **4a** shows the orientation of the phenol with respect to the complex, while **4b** displays the same docking experiment from a different vantage point; here it is obvious that the phenol lies across the opening to the lacuna. Structures **5a** and **5b** correspond to the



case in which the initial configuration has the hydroxy group pointed toward the bound dioxygen. Remarkably, when the phenolic proton was poised for hydrogen bonding to the coordinated O_2 , energy minimization resulted in a structure in which the phenolic group is moved away from the O_2 and cobalt. The two docking entities are again clearly shown in **5a**, while the more subtle relationships can be seen by study of **5b**. The repulsion of the complex cation and the phenolic dipole may exceed any local advantage due to hydrogen bonding. For the case in which the aromatic ring of the substrate was initially poised above the O_2 and the cavity, energy minimization caused the guest molecule, DMP, to rotate and cover the entrance of the cavity wherein the bound dioxygen pointed toward the phenol ring (Structure **4**). This entrance-covering structure seems suitable for overlap of the electron clouds of the bound

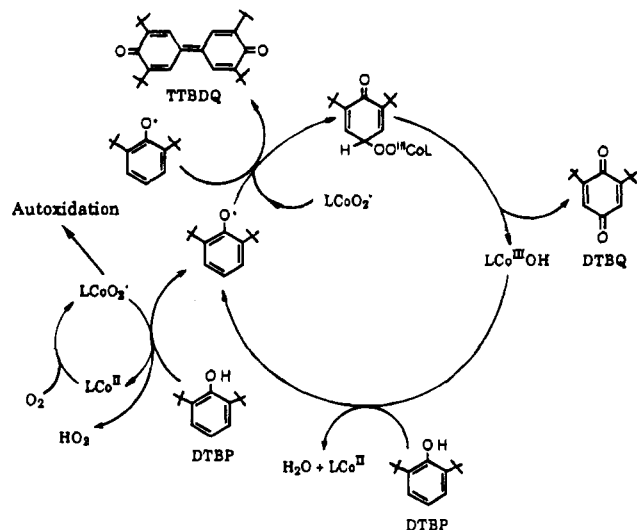
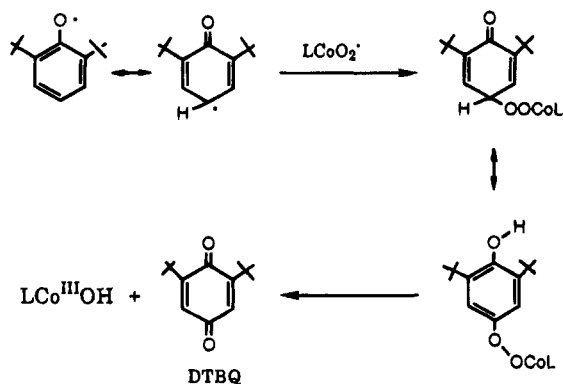


Figure 7. Proposed reaction mechanism for oxygenation of 2,6-di-*tert*-butylphenol by cobalt cyclidene dioxygen complexes.

Scheme 3. Formation of 2,6-Di-*tert*-butyl-1,4-benzoquinone

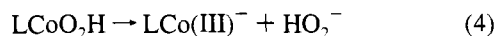
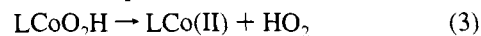


dioxygen and the aromatic ring of the phenol, an arrangement well suited for electron transfer.

Overall Reaction Mechanism. Based on the information obtained from studies of dioxygen binding to cobalt(II) cyclidene complexes and their roles in oxygenation reactions, a catalytic cycle of oxygenation of 2,6-di-*tert*-butylphenol, analogous to that was previously described,^{6a} is presented in Figure 7: (1) the phenoxyl radical generated by one electron transfer process can be attacked by either LCoO_2^* (wherein the cobalt dioxygen complex acts as an oxygenase) or another phenoxyl radical to form either a phenol- O_2CoL adduct or the dipe-

noquinone precursor, respectively; (2) the phenol- O_2CoL adduct releases benzoquinone and forms the Co(III)OH species; (3) this Co(III)OH species may also undergo an electron transfer reaction with another molecule of phenol (which may deprotonate to give a phenoxy radical), subsequently releasing water and the catalyst LCo(II) .

The dioxygen adduct of the cobalt(II) cyclidene complex, LCoO_2 , also undergoes autoxidation,² and autoxidation appears to be promoted by the substrate (recall C4 and C5 bridged species in Figure 3). The following equations ($\text{PhOH} = \text{DTBP}$) rationalize these relationship:



The LCoO_2H species, produced by reaction of the phenol with the dioxygen adduct, LCoO_2 , is believed to undergo two parallel reactions. According to eq 3, this results in liberation of the catalytic LCo(II) species and one molecule of HO_2 . Equation 4 gives the LCo(III) species and a hydrogen peroxide anion HO_2^- , thereby contributing to autoxidation. The LCo(II) species is able to reenter the cycle and bind dioxygen again. However, the LCo(III) species reenters the catalytic cycle by oxidizing phenol (eq 5).¹⁶ Upon adding a large excess of DTBP (20-fold) to a solution of the vaulted complex $[\text{CoMeVD}](\text{PF}_6)_2$ in acetonitrile at 25.0 °C and an atmosphere of dioxygen, the increase in the autoxidation rate constant is arguably imperceptible; the value changed from $4.7 \times 10^{-5} \text{ s}^{-1}$ to $5.1 \times 10^{-5} \text{ s}^{-1}$, indicating that the presence of DTBP does not cause a dramatic acceleration of an irreversible autoxidation process.

According to Scheme 3, the proton migrates to the oxygen atom, producing a hydroquinone analog after addition of LCoO_2 to the phenoxy radical. This is followed by heterolysis of the O-O bond, a reaction that constitutes two-electron oxidation of the substrate. Proton loss completes the process, leaving the quinone and the cobalt(III) complex.

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