

temperature for 2 h. The mixture was extracted with methylene chloride. The organic extract was washed with water, dried over anhydrous MgSO_4 , and concentrated in vacuo. The resulting yellow oil was chromatographed on 10 g of silica gel with 1:1 hexane/ethyl acetate as the eluant giving acetate **36** (0.44 g, 81%): IR (film) 3350, 2960, 1750, 1530, 1220, 1010, 910 cm^{-1} ; ^1H NMR δ 2.14 (3 H, s), 2.2-2.6 (2 H, m), 3.8 (3 H, s), 4.0-4.4 (2 H, m), 4.95-6.5 (7 H, m).

Methyl (3 α ,4 α ,8 β)-4,4a,7,8-Tetrahydro-1-oxo-1H,3H-pyrido[1,2-c][1,3]oxazine-8-carboxylate (37). A solution of acetate **36** (0.387 g, 1.4 mmol) in 8 mL of reagent grade toluene was sealed in a 8 in. \times 1 in. thick walled glass tube and was heated at 210 $^\circ\text{C}$ in an oil bath for 2 h. After cooling, the solution was concentrated in vacuo, and the resultant oil passed through a short column of silica gel (ethyl acetate), giving **37** as an oil which crystallized as white plates (0.239 g, 80%): mp 80-81 $^\circ\text{C}$; IR (KBr) 2960, 2850, 1740, 1690, 1430, 1210, 775 cm^{-1} ; ^1H NMR δ 1.8-2.2 (2 H, m), 2.5-2.7 (2 H, m), 3.74 (3 H, s), 4.3-4.4 (3 H, m), 5.3-5.9 (3 H, m); ^{13}C NMR δ 26.22, 28.89, 50.32, 51.47, 52.50, 65.58, 123.96, 126.55, 153.19, 171.32; mass spectrum, m/e (relative intensity) 211 (11.8) [M^+], 179 (11.0), 152 (74.8), 108 (100), 93 (36.8), 80 (50.2), 67 (38.6), 53 (20.4).

Anal. Calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_4$: C, 56.87; H, 6.20. Found: C, 56.92; H, 6.17.

3 α ,4 α ,8 β -4,4a,7,8-Tetrahydro-1-oxo-1H,3H-pyrido[1,2-c][1,3]oxazine-8-carboxylic Acid (38). A solution of the Diels-Alder adduct **37** (0.27 g, 1.3 mmol) in 25 mL of methanol was treated with 1 mL of 5% aqueous NaOH. The reaction mixture was stirred at room temperature for 2 h. The mixture was neutralized with 5% aqueous HCl, and the solvent was removed in vacuo. The residue was extracted with ethyl acetate, washed with water, dried over anhydrous MgSO_4 , and evaporated. The crude product was crystallized from methanol by slow evaporation, giving acid **38** as leafy, white crystals (0.223 g, 89%): mp 168-170 $^\circ\text{C}$; IR (film) 3400, 1660, 1420, 1023, 1000 cm^{-1} ; ^1H NMR δ 1.6-2.3 (2 H, m), 2.4-2.7 (2 H, m), 4.3-4.4 (3 H, m), 5.4-6.0 (3 H, m); mass spectrum, m/e (relative intensity) 197 [M^+] (16.4), 152 (45.8), 124 (20.5), 108 (100), 80 (91.8).

Anal. Calcd for $\text{C}_9\text{H}_{11}\text{NO}_4$: C, 54.82; H, 5.62. Found: C, 54.49; H, 5.61.

X-ray Crystal Structure Determination of Carboxylic Acid 38.²⁶ Unit cell dimensions determined from 25 reflections at moderate 2θ angles indicated an orthorhombic cell of dimensions: $a = 10.596$ (4) \AA ; $b = 6.693$ (5) \AA ; $c = 12.895$ (2) \AA , and $v = 912.2$ (1.9) \AA^3 . The observed volume is consistent with that expected for $Z = 4$, using a calculated density of 1.43 gm cm^{-3} . Observed systematic absences of $h0l$ for $l = 2n + 1$ and $hk0$ for $h = 2n + 1$ gave possible space group choices as either $Pmca$ or $P2_1ca$. Application of the zero-moment test of Howells, Phillips, and Rogers²⁷ indicated an acentric cell, thereby uniquely determining the space group as $P2_1ca$.

Data were collected using molybdenum $K\alpha$ radiation [$\lambda(\text{Mo } K\alpha)$

0.70930 \AA]. A total of 2310 reflections were collected out to a 2θ of 70 $^\circ$; of these 654 had intensities with $I \geq 3\sigma(I)$ (23.1%) and were considered observed. These data were corrected for Lorentz and polarization factors and used in the refinement of the structure.

Starting positions for the nitrogen, four oxygens, and eight of the carbon atoms were obtained from a MULTAN E -map synthesis where $E_{\text{min}} = 1.35$ and only data out to $\theta = 25^\circ$. Three cycles of isotropic least-squares refinement of these atoms yielded $R_1 = 0.181$ and $R_2 = 0.214$. The difference Fourier constructed at this stage revealed the remaining carbon atom and isotropic refinement of all non-hydrogen atoms resulted in $R_1 = 0.106$ and $R_2 = 0.141$.

Conversion to anisotropic thermal parameters and inclusion of the remaining data ($\theta = 25$ - 35°) lowered $R_1 = 0.098$ and $R_2 = 0.115$ after 3 cycles of least-squares refinement. Subsequent difference Fourier/least-squares refinement located all the hydrogen atoms of the molecule. Inclusion of the hydrogens ($B = 4.0$) and refinement of their positional parameters along with full-matrix anisotropic refinement of the non-hydrogen atoms converged $R_1 = 0.068$ and $R_2 = 0.087$ with esd = 2.179. Convergence was considered complete when all shifts were less than one-tenth their standard deviations.

Final positional and thermal parameters are presented in Table V. Table VII shows observed and calculated structure factors, Table VIII lists bond angles, and Table IX gives bond lengths. (See Supplementary Material.) The final difference Fourier map was smooth with maxima and minima in the range of $\pm 0.22 \text{ e}/\text{\AA}^3$.

Basic Equilibration of Ester 37. To 2 mL of absolute CH_3OD was added 5 mg of sodium metal, and upon cessation of gas evolution, the ester **38** (0.052 g, 0.24 mmol) was added. The mixture was refluxed under N_2 for 24 h, and the solution was neutralized with acidic methanol. The solvent was removed in vacuo, and the crude product extracted with methylene chloride. The organic phase was washed with water, dried over anhydrous MgSO_4 , and concentrated in vacuo affording the monodeuterated ester **39** as a light yellow oil (0.0448 g, 87%): IR (film) 2930, 2850, 1740, 1690, 1430, 1200, 760 cm^{-1} ; ^1H NMR δ 1.8-2.2 (2 H, m), 2.5-2.7 (2 H, m), 3.74 (3 H, s), 4.3-4.4 (3 H, m), 5.4-5.9 (2 H, m); mass spectrum, m/e (relative intensity) 212 [M^+] (13.2), 153 (45.5), 109 (75), 94 (23.9), 81 (100), 68 (33.7), 53 (28.9), 41 (47.6).

Acknowledgment. This research was generously supported by the National Science Foundation (CHE 78-1916). We thank Dr. R. Minard for mass spectra and Mr. A. Freyer for FT-NMR spectra at 200 and 360 MHz. We are extremely grateful to Professor C. H. Eugster for samples of **3**, **4**, and **6**.

Supplementary Material Available: Tables II-IX contain X-ray data on compounds **32** and **38** (16 pages). Ordering information is given on any current masthead page.

Activation of Molecular Oxygen. Mechanistic Studies of the Oxidation of Hindered Phenols with Cobalt-Dioxygen Complexes

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Abstract: Mechanistic studies of the oxidation of various substituted phenols by cobalt(II) bis(3-(salicylideneamino)propyl)methylamine, CoSMDPT, are reported. The reaction is first order in $[\text{O}_2]$, [substrate], and $[\text{Co}]$. A series of experiments are reported to provide strong support for a mechanistic scheme that involves reaction of coordinated dioxygen. Coordination of O_2 to this cobalt(II) complex enhances the ability of the dioxygen to abstract hydrogen atoms and to react with phenoxy radicals. The mechanism provides a rationale for the influence of several variables on the reaction and suggests steps that were taken to retard catalyst deactivation.

Determining the ways dioxygen can be activated by a metal center is important for understanding both biological and commercial systems.^{1,2} Though homogeneous catalytic oxidations

have been classified in many different fashions,^{3,4} they can be separated into four broad categories: (1) free radical autoxidations

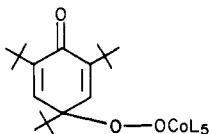
(1) Spiro, T. G. "Metal Ion Activation of Dioxygen"; Wiley: New York, 1980 and references therein.

(2) Dumas, T.; Bulani, W. "Oxidation of Petrochemicals: Chemistry and Technology", Halsted Press, Wiley: New York, 1974 and references therein.
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using simple metal salts; (2) attack by various oxygen-containing nucleophiles on coordinated substrates; (3) oxygen atom transfers from high oxidation state elements; (4) epoxidation of olefins using metal catalysts and alkyl hydroperoxides. Major goals in this field involve controlled, highly selective, oxidations of substrates and demonstration of oxidation capabilities by metal-bound O_2 .

We became interested in investigating the possibility of catalyzing oxidations with metal-dioxygen adducts. There are many complexes that reversibly bind dioxygen,⁵ and the bonding is now understood in terms of the spin-pairing model.⁶ Upon coordination of cobalt(II) to dioxygen,⁷ partial electron transfer from cobalt to oxygen occurs ranging from 0.1 to 0.8 e^- depending on the ligand field surrounding the cobalt.⁸ This should provide for variation in the reactivity of the bound O_2 . Of the many reported oxidations by O_2 , the oxidation of phenols appeared most attractive as a candidate for a process that involves metal-coordinated O_2 . Numerous reagents and catalysts oxidize phenols, and these reactions have been reviewed extensively in the literature.⁹⁻¹¹ Generally, phenols can be oxidized to quinones, coupled products (diphenoquinones), or polymers, depending on the choice of catalyst or reagent. The oxidation of hindered phenols by cobalt salen dioxygen complexes was first described in 1967 by vanDort and Guerson.¹² High yields of the corresponding benzoquinone, BQ, were obtained by using phenols which were not substituted in the para position. Several workers^{13,14} have investigated the effect of various reaction conditions on the product distribution and hypothesize that the monomeric $Co-O_2$ species produces BQ while the μ -peroxo dimer yields DPQ. While it is true that reaction conditions will affect the monomer-dimer equilibrium, Kothari and Tazurma cite evidence to indicate¹⁵ that the active species leading to both BQ and DPQ is the mononuclear adduct. Cobalt phthalocyanine,¹⁵ CoSMDPT,¹⁶ Co-acacen,¹⁷ and cobaloxime derivatives¹⁸ all form dioxygen adducts and have been found to be active catalysts for this oxidation.

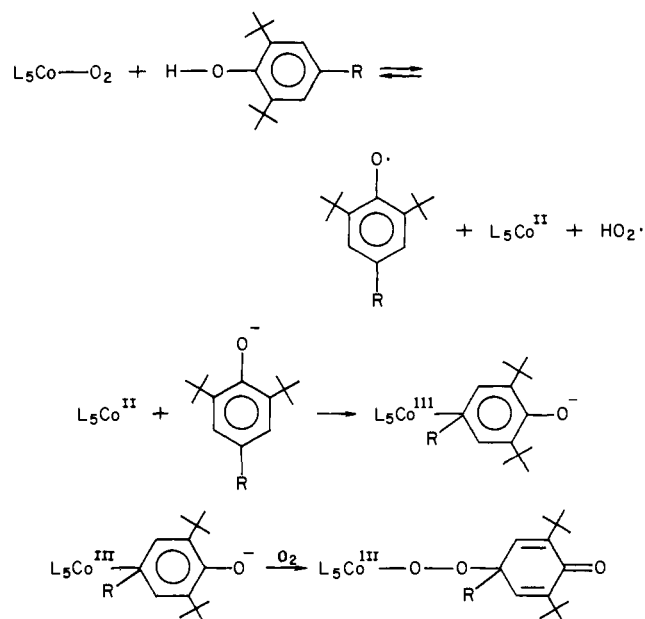
Nishinaga¹⁹ has reported the majority of the recent work on this subject. He has demonstrated²⁰ that the monomeric cobalt-dioxygen complex can abstract a hydrogen atom from a 2,4,6-trisubstituted phenol by showing the simultaneous disappearance of the $Co-O_2$ EPR signal with the appearance of a phenoxy radical signal when the oxygen supply is limited. The product of the reaction of the phenoxy radical with the cobalt(II) complex and O_2 has been isolated and characterized as the species shown.²¹



Nishinaga proposes that this product arises from O_2 attack on

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Scheme I



a cobalt(III) phenolate complex. Nishinaga's proposed mechanism is summarized as shown in Scheme I.

Many unanswered questions remain concerning this important reaction. To date, the reaction schemes presented are based on chemical intuition supported by relatively little mechanistic data. Also, the catalyst undergoes about 70 turnovers and then becomes relatively ineffective for reasons that are unknown. Thus, we began a kinetic investigation to provide insight for both the oxidation of the substrate and the deactivation of the catalyst. We hoped to gain an understanding of the mechanism of this reaction to determine if indeed a true dioxygen-activation pathway is operative and with this understanding evaluate the potential of this catalytic system for more difficult oxidations.

Experimental Section

General Data. The EPR spectra were collected on a Varian Model E-9 spectrometer equipped with a Hewlett-Packard frequency counter. NMR spectra were obtained on a Varian 390 spectrometer. Mass spectra were run by the Mass Spectroscopy Lab at the University of Illinois on a CH-5 instrument. All elemental analyses were performed by the Microanalytical Lab at the University of Illinois.

Materials. The preparation of CoSMDPT, cobalt (II) bis(3-(sali-cylideneamino)propyl)methylamine, by published procedures,²² was verified by elemental analysis. All phenols were obtained from Aldrich and used without further purification. All solvents were stored over 3A molecular sieves.

Deuterated 2,6-Dimethylphenol. A deuterated sample of 2,6-dimethylphenol was prepared by reaction of the starting phenol with methylmagnesium iodide Grignard reagent, followed by subsequent workup in D_2O . Its mass spectrum showed 70% substitution of OD. The OD stretch is observed at 2520 cm^{-1} .

Kinetic Studies. The reaction progress was monitored by following the O_2 consumption. The procedure and apparatus for conducting the oxidation at atmospheric pressure have been described previously.²³ Oxidations performed at elevated pressures were conducted in a Parr pressure bottle fitted with a pressure gauge and placed in a temperature controlled oil bath. Typically, a 250-mL pressure bottle was charged with a 50-mL solution of the phenol (concentrations given in text) and magnetic stir bar. The solid cobalt catalyst would be floated on the solution in a plastic cap. The system was purged several times with O_2 and allowed to equilibrate at the appropriate temperature and pressure (usually 30 min). Reaction began by stirring the solution and spilling the solid catalyst into the solution. All reactions were stirred at a sufficient rate to ensure mass transfer of dioxygen in the solvent was not rate limiting. The O_2 consumption was found to correlate with product formation. This method gave reproducible results within ± 1 psi. Reported rates reproducible to

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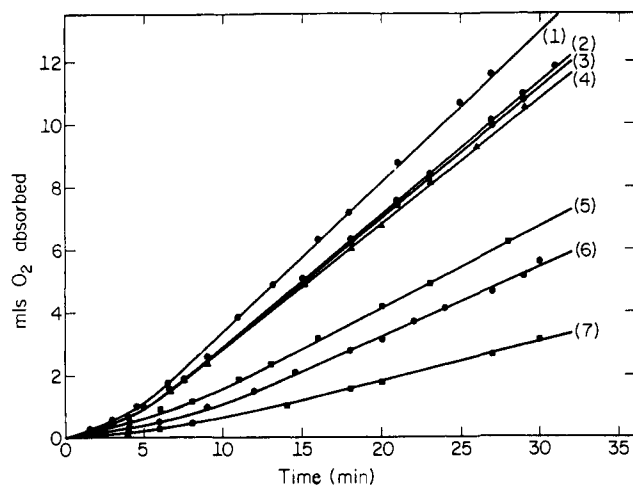


Figure 1. Oxygen uptake curves for oxidation of 2,6-dimethylphenol (4.0×10^{-2} M), with CoSMDPT. Cobalt concentrations are (1) 4.014×10^{-2} M, (2) 2.996×10^{-2} M, (3) 2.202×10^{-2} M, (4) 2.00×10^{-2} M, (5) 1.252×10^{-2} M, (6) 1.014×10^{-2} M, and (7) 0.620×10^{-2} M.

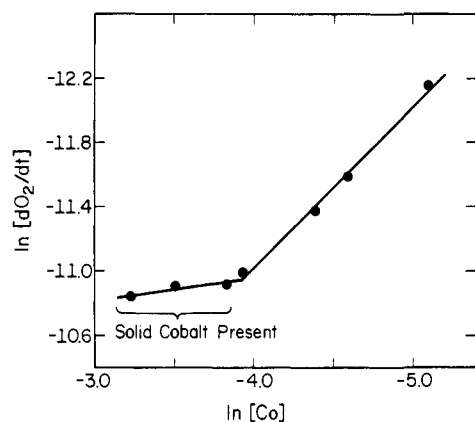


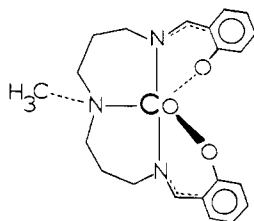
Figure 2. Plot of $\ln [\text{Co}]$ vs. $\ln [d\text{O}_2/dt]$ (from Figure 1). Slope indicates reaction order for cobalt equals 1.0.

within 5% were taken from maximum slopes of the oxygen uptake curves.

Products for the 2,6-di-*tert*-butylphenol oxidation were analyzed by NMR integration of the *tert*-butyl group.²⁴ After completion of the reaction, CHCl_3 was added to ensure all products were in solution.

Results

The cobalt complex used in our study was cobalt(II) bis(3-(salicylideneamino)propyl)methylamine, or CoSMDPT. A representation of the complex is shown.



Kinetic Studies. The reaction orders for cobalt, phenol, and O_2 were obtained by independently varying the concentrations of each and monitoring O_2 uptake. All oxidations were conducted in benzene. The O_2 uptake at atmospheric pressure for the reaction at various cobalt concentrations is shown in Figure 1. A plot of $\ln [\text{Co}]$ vs. $\ln [d[\text{O}_2]/dt]$ yields a straight line with a slope of 1.0 (Figure 2), indicating the reaction is first order in $[\text{Co}]$ as long as the catalyst is completely dissolved. First-order kinetics are observed for phenol concentrations less than 0.09 M (Figure 3). When the ratio of phenol to cobalt becomes greater than 20/1,

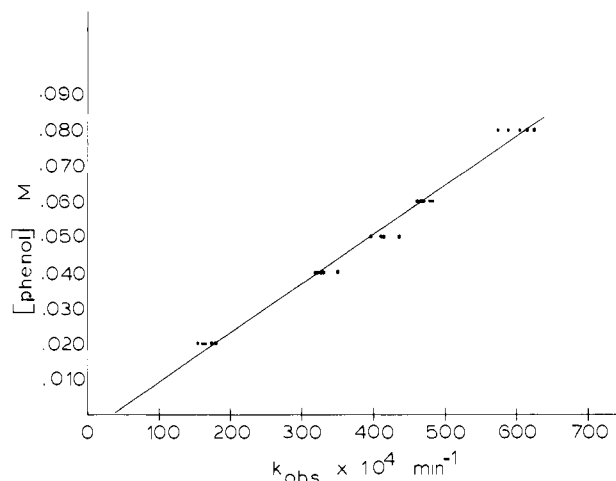


Figure 3. First-order kinetic plot for oxidation of 2,6-dimethylphenol with CoSMDPT (4×10^{-3} M in Co) in 25 mL of benzene.

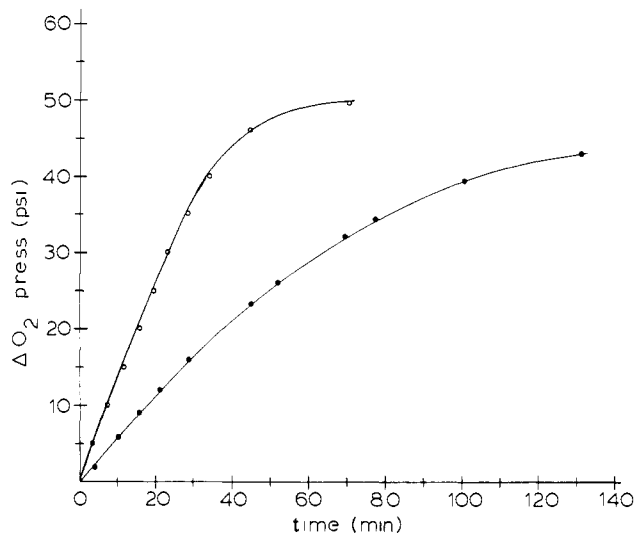


Figure 4. Oxidation of 2,6-dimethylphenol (0.494 M) with CoSMDPT (0.0146 M) in 50 mL of benzene (temperature = 30°C): \circ initial pressure = 120 psi; \bullet , initial pressure = 60 psi.

the rate becomes pseudo zero order in substrate. The reaction was conducted at three different O_2 pressures, while maintaining all other conditions constant. Figure 4 shows the dependence of the rate of the reaction on the oxygen pressure. The initial rates observed at 60 psi (4.1 atm) and 120 psi (8.2 atm) are approximately 4 and 8 times faster, respectively, than the rate of oxidation at atmospheric pressure, indicating a first-order dependence on the O_2 concentration.

When a sample of 2,6-dimethyldeuteriophenol is employed as the substrate at 30°C , the reaction rate is identical, within experimental error, with the undeuterated sample throughout the duration of the reaction. To ensure that the reaction conditions did not convert some of the deuterated phenol to undeuterated phenol since HOD is produced, a reaction was run with excess D_2O (2 mL, 0.11 mol) present with the deuterated phenol. The same rate is found for both the deuterated phenol- D_2O and the undeuterated phenol-water experiment, thus indicating an absence of a deuterium isotope effect for this system.

Various phenols were oxidized with CoSMDPT in benzene at 30°C (Table I). In the absence of the steric effects encountered in the 2,4,6-trisubstituted phenols or the 2,6-di-*tert*-butylphenol, the rate increases as the oxidation potential of the phenol decreases. Unsubstituted phenol is oxidized by CoSMDPT in dimethylformamide at higher temperatures and pressures (Table I).

Increasing temperatures up to 50°C results in a faster oxidation of 2,6-dimethylphenol as seen in Figure 5. Temperatures above 70°C have little or no effect on the rate. This behavior indicates

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Table I^a

phenol	(OP) ₀ ²⁶	ΔP, psi	time, min	total turnovers ^b	turnovers per hour ^c
2,4,6-trimethyl ^d	0.67	26	1190	20.4	1.6
2,6-di- <i>tert</i> -butyl	0.68	33	310	24.9	4.8
2,3,5,6-tetramethyl	0.71	40	97	27.7	13.6
2,6-diisopropyl	0.74	40	188	30.1	15.4
2,6-dimethyl	0.76	43	131	32.3	14.8
2,5-di- <i>tert</i> -butyl	0.83	12	1415	9.1	0.4
3,5-dimethyl	0.86	15	930	11.3	0.4
phenol ^e	0.92	18	1060	14.1	0.8
2,6-dichloro	0	0	300	0	0

^a All oxidations were 0.49 M in phenol and 0.0146 M in CoSMDPT; 50 mL of benzene were used as solvent; temperature = 30 °C; initial pressure of O₂ = 60 psi. ^b Total turnovers = mol of O₂ consumed/mol of Co before rate of O₂ uptake begins to decline. ^c Turnovers per hour = (mol of O₂ consumed/mol of Co)/h, based on initial rates. ^d DMF used as solvent. ^e DMF used as solvent; temperature = 75 °C; initial O₂ pressure = 120 psi.

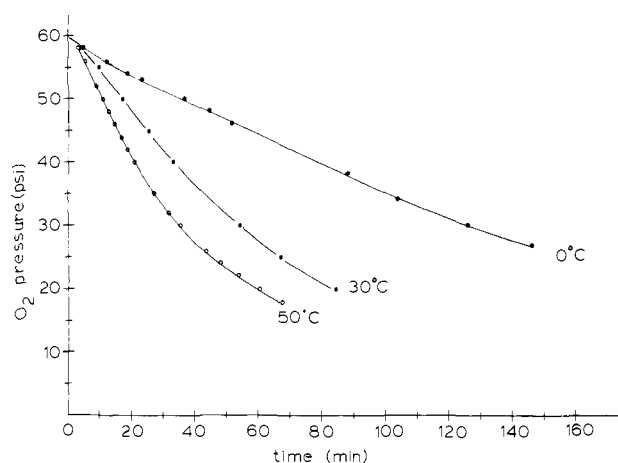


Figure 5. Oxidation of 2,6-dimethylphenol at various temperatures ([Co] = 0.0146 M; [phenol] = 0.49 M in 50 mL of toluene).

the complexity of the reaction mechanism since this increased rate contrasts with the decreased amount of cobalt-dioxygen adduct expected at the higher temperature.²⁵

Solvent variation also yields complicated behavior where the rate follows the order: chloroform ≈ Toluene ≈ benzene > methylene chloride ≈ methanol > DMF.

Catalyst Deactivation. In a typical oxidation with excess phenol, O₂ uptake slows substantially by 70 turnovers and declines to almost zero, in roughly the next 20 turnovers. The deactivation of the catalyst (evidenced by the decrease in reaction rate) is accompanied by the precipitation of a brown solid. Chemical analysis of this solid indicates that a considerable increase in the oxygen content of the spent catalyst has occurred compared to CoSMDPT. Typically a 6/1 ratio of O/Co is found in the former.

Studies were initiated to determine the factors that lead to decline in catalytic activity. The change in catalyst lifetime for different conditions is indicated in Table II by the number of turnovers. In these experiments an oxidation was run at 60 psi with a large excess of phenol to cobalt. Uptake is monitored to 30 psi and then recharged to 60 psi. This cycle is repeated until a noticeable decrease in rate is observed.

The EPR spectrum of a reaction mixture was monitored during the course of an oxidation to determine the correlation of the Co-O₂ signal with catalyst deactivation. Aliquots of the reaction mixture taken at various intervals of O₂ uptake show only a Co-O₂ signal. Interestingly, this signal remains at relatively the same intensity throughout the reaction, even after the noticeable drop in catalyst activity that occurs at 70 turnovers. This result implies

Table II. Oxidation of 2,6-Dimethylphenol. Determination of Catalytic Activity with Various Additives^a

	mmol of additives	ΔP, psi	time, h	total turnovers
no additive		68	20.5	76
2,6-dimethylbenzoquinone	10.5	83	17.5	93
2,6-dimethylbenzoquinone	33.0	86	18	96
2,6-dimethylbenzoquinone + H ₂ O	33.0	82	18	92
Na ₂ CO ₃ slurry ^b	36.7	56	20.5	249
Fe(acac) ₃ Cl	36.7	70	20.5	78
MeOH (solvent) ^c		48	20.5	200
H ₂ O ₂ in MeOH ^c	17.6	51	20.5	46
H ₂ O ₂ in MeOH plus 2,6-dimethylbenzoquinone	17.6	21	20.5	24

^a All oxidations were conducted in 50 mL of benzene, unless stated otherwise, with 7.37×10^{-2} mol of 2,6-dimethylphenol and 4.88×10^{-4} mol of CoSMDPT; temperature = 30 °C. ^b Small amount of a crown ether was added as well to act as a phase-transfer catalyst but was later found not to be necessary. ^c 1.24×10^{-4} mol of CoSMDPT of accommodate the large numbers of turnovers at comparable phenol concentrations.

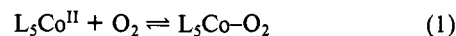
that a product of the oxidation causes a decline in catalytic activity without initially destroying the Co-O₂ species. This period is followed by the subsequent oxidation of cobalt(II) to cobalt(III) and the disappearance of the EPR signal. The major products of the oxidation, BQ and H₂O, do not inhibit the O₂ uptake as shown in Table II. However, acids are found to inhibit catalytic activity. Adding a solution of benzene, saturated with dry HCl, to a solution in the midst of an oxidation reaction results in an immediate end to the O₂ uptake. Inhibition is obtained when solutions of trifluoroethanol or benzoic acid are added. When a weaker acid such as unsubstituted phenol is added to the oxidation reaction, the rate decreases and a large amount of the coupled product DPQ is generated. The EPR of the solution containing TFE and phenol show characteristic Co-O₂ signals, while solutions containing benzoic acid or HCl do not show an EPR signal because rapid oxidation of the cobalt occurs.

Increased turnovers are obtained when the reaction is run in the presence of Na₂CO₃ as seen in Table II. The addition of 2,6-lutidine or polystyrene-bound tertiary amine²⁷ also increases turnover with the Na₂CO₃ slurry being most effective. Peroxides formed from decomposition of metal-dioxygen complexes²⁸ or from HO₂ were suspected as side products that could cause ring cleavage and lead to organic acids that decompose the catalyst. When an aqueous H₂O₂ solution is added to a methanol solution of catalyst, O₂ gas is evolved. When a 30% aqueous H₂O₂ solution is added to a 2,6-dimethylphenol oxidation in methanol solvent, the pressure drop is monitored from the initial increased value of pressure from H₂O₂ decomposition. A decline in the number of turnovers (Table II) is observed.

If H₂O₂ is used as the only oxygen source (the reaction with phenol is run under argon), CoSMDPT catalyzes the decomposition of H₂O₂ to H₂O and O₂ with the simultaneous irreversible oxidation of the cobalt center and no benzoquinone is formed. Thus, the presence of H₂O₂ inhibits the conversion of phenol to quinone.

Discussion

The results of this study clearly indicate that a metal-bound dioxygen is an active species in the oxidation of phenol. The steps shown in eq 1-3 are implicated. Step 2 is supported by earlier



studies in which it is conclusively shown²⁵ that trifluoroethanol, TFE, undergoes a hydrogen-bonding interaction with the terminal oxygen of the cobalt-dioxygen adduct. Although TFE is a stronger acid than 2,6-dimethylphenol,²⁹ they are close enough in acidity to expect the interaction in eq 2 to occur. Step 3 receives support

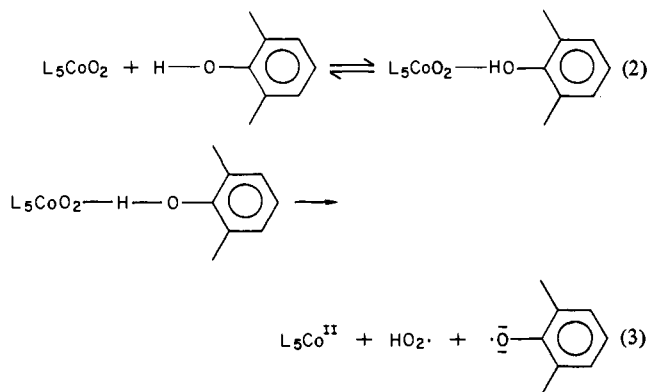
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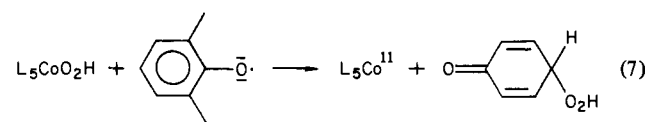
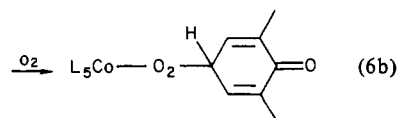
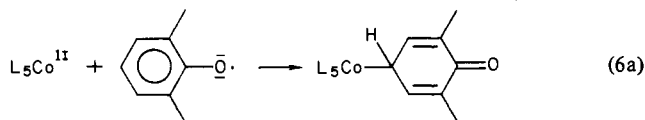
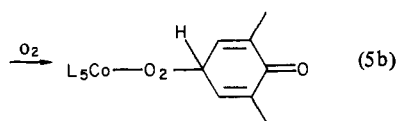
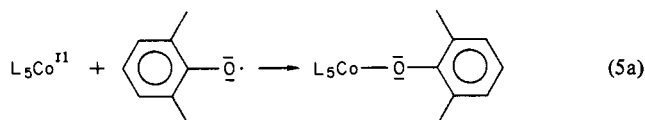
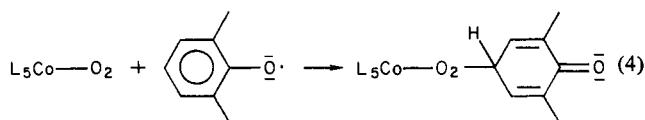


from the EPR identification of the phenoxy radical formed when 2,4,6-tri-*tert*-butylphenol is oxidized with this catalyst.

There are several paths by which the phenoxy radical can be converted to the quinone. The reaction of the phenoxy radical with free O_2 to form benzoquinone (BQ) is ruled out since the free radical reacts faster with itself in the presence of O_2 to form diphenohydroquinone and subsequently diphenoquinone, DPQ, than it reacts with O_2 .⁹ The reaction of the phenoxy radical with HO_2 was proposed earlier in a scheme to account for the products of the reaction.³ This proposal does not seem plausible for the following reason. When HO_2 radicals are intermediates in autoxidations, large deuterium isotope effects are observed³⁰ and this is not the case in our system. Since HO_2 is reported³¹ to decompose at diffusion controlled rates and the slow step in this reaction occurs subsequent to step 3 (vide infra), the fate of HO_2 is decomposition.



The possible reactions of the phenoxy radical with cobalt complexes remain to be considered for the next step.



The kinetic orders found in this study are consistent with several of the reactions listed above. Rate expressions can be derived whose reaction orders are consistent with step 2, or more likely step 3, being rate controlling and step 4, 5, 6, or 7 being fast. Since

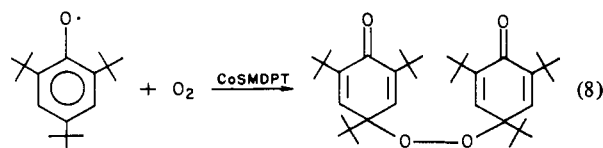
no deuterium isotope effect was observed on the rate of oxidation, we can eliminate step 2 or 3 as the rate-controlling step. Mechanisms in which steps 4, 5a, and 6a are rate controlling are also consistent with the observed rate law if a steady-state concentration of phenoxy radicals is assumed. Rate-controlling steps for steps 5b and 6b can be eliminated for they would lead to a second-order dependence on O_2 . A rate-controlling step, eq 7, is not reasonable in view of the short lifetime of an $\text{L}_5\text{CoO}_2\text{H}$ species³² and because peroxides have not been observed in the reaction medium.²¹ Furthermore, if eq 7 were a key step, catalysis of the hydroxylation of 2,4,6-trimethylphenol by CoSMDPT would have been observed.

Several indirect pieces of evidence suggest that in addition to the hydrogen atom abstraction of the first step, there is involvement of an L_5CoO_2 species in a subsequent reaction with the phenoxy radical (eq 4). The ratio of BQ to DPQ is very informative in this connection. If this step under consideration (eq 4, 5a, or 6a) is inhibited, the phenoxy radical concentration will increase and these radicals will couple to form diphenohydroquinone and be oxidized to diphenoquinone. Data reported earlier²³ on the catalysis of this oxidation by polystyrene-bound CoSMDPT suggest subsequent cobalt involvement (steps 4, 5a, or 6a). The BQ/DPQ ratio is a function of the cobalt loadings on the polymer. At high loadings, where the generated radical has a high probability of encountering another cobalt-dioxygen center, large ratios of BQ/DPQ are obtained. At low cobalt concentrations the ratio is reduced substantially. Encounter of phenoxy radical with a cobalt center leads to BQ while failure to encounter one leads to DPQ. Several reagents including solid PbO_2 will generate phenoxy radicals.³³ When PbO_2 and cobalt(II) bis(acetylacetonate) (which does not form a dioxygen adduct under these conditions) catalyze oxidation of 2,6-dimethylphenol, only diphenoquinone is produced. This result suggests that the phenoxy radical needs to encounter a $\text{Co}-\text{O}_2$ species as shown in step 4 for the production of the quinone. If, as shown in step 5, a cobalt(II) species were sufficient, $\text{Co}(\text{acac})_2$ could have fulfilled this requirement.

When competitive hydrogen-bonding agents are added to the reaction medium for a 2,6-dimethylphenol, CoSMDPT -catalyzed oxidation, the results are readily rationalized in terms of step 4. When unsubstituted phenol, a slightly stronger acid than 2,6-dimethylphenol, is added to the reaction mixture, the rate of reaction is decreased and the BQ/DPQ ratio is decreased. With the phenol competitively hydrogen bonding to L_5CoO_2 , the phenoxy radical attack on this species is inhibited and DPQ is formed at the expense of BQ.

A reaction in progress can be stopped by adding the stronger acid TFE. Since radicals can be generated by $\text{Co}(\text{III})$ (vide infra), this suggests a role of other than a radical initiation step for L_5CoO_2 and we propose eq 4. When stronger acids such as benzoic acid or HCl are added, the reaction stops immediately and this is accompanied by oxidation of cobalt(II) to cobalt(III).

Nishinaga¹⁹ has ruled out the possibility of step 4 being important on the basis of the following experiment: bubbling O_2 through a solution of CoSMDPT and 2,4,6-tri-*tert*-butylphenoxy radical produced only the coupled product that resulted from the reaction of the radical with free O_2 .



Although experimental details are lacking, there may be two potential drawbacks to this conclusion. First, the concentration of free phenoxy radicals in the oxidation of 2,6-dimethylphenol is extremely low under catalytic reaction conditions (as mentioned above), making the reaction in eq 8 much less probable. Second, the concentration of $\text{Co}-\text{O}_2$ in the above experiment is expected

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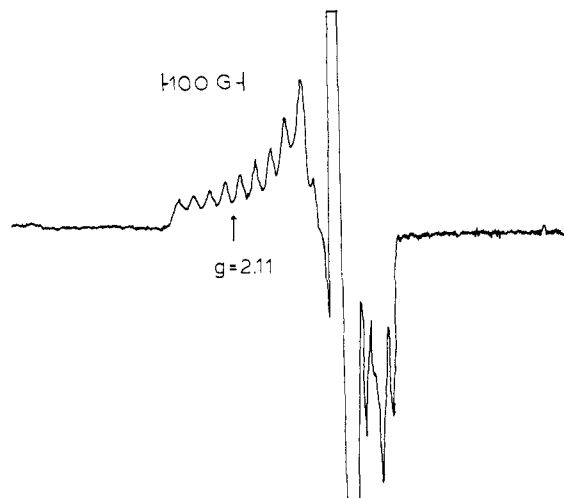
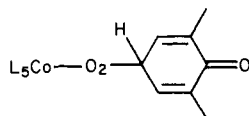


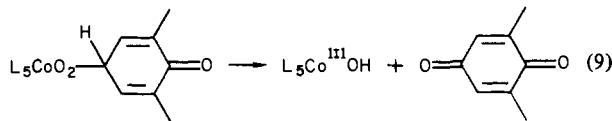
Figure 6. CH_2Cl_2 /toluene frozen-glass EPR (α -band) spectrum of Co-O_2 and the phenoxy radical.

to be lower than that in the phenol oxidation because it has been shown that the equilibrium in step 1 is enhanced²⁵ by the addition of hydrogen-bonding substrates via step 2. Thus, the concentration of L_5CoO_2 in a solution of phenoxy radicals is considerably less than what is found in a typical phenol oxidation. Instead of step 4, steps 6a and 6b are proposed¹⁹ as the mechanism for quinone formation. Formation of a Co-C bond is followed by subsequent O_2 insertion to produce the cobalt-peroxyquinone compound. We prepared the cobalt-peroxyquinone complex of 2,4,6-tri-*tert*-butylphenol reported by Nishinaga²⁰ and observed a very interesting phenomena in the EPR. If a toluene/ CH_2Cl_2 glass of this complex is prepared, the EPR spectrum in Figure 6 is observed. It displays overlapping spectra of the free phenoxy radical and Co-O_2 signal. Thus, the phenoxy radical plus L_5CoO_2 are in equilibrium with the cobalt-peroxyquinone. This is most readily visualized as occurring via the reverse reaction of step 4 and would support the direct pairing of radicals in the oxidation as opposed to an unprecedented reversible O_2 insertion (the reverse of step 6).

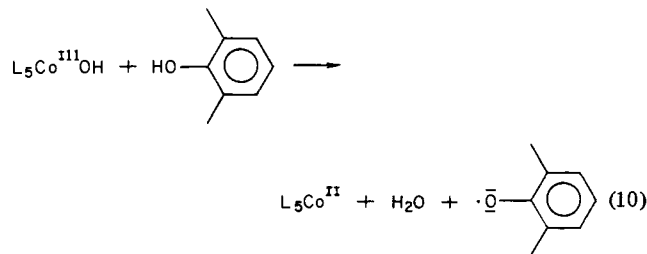
The remaining problem involves the step for converting



to the quinone and regenerating the catalyst. There is no direct information bearing on this problem. By analogy with the decomposition of an organic hydroperoxide, we propose reaction 9



for quinone formation. The Co(II) species could be regenerated by phenol oxidation as shown in eq 10.



The fate of the HO_2 generated in step 3 is worth considering further. The rate of self-reaction of HO_2 approaches the diffusion

PROPOSED MECHANISM

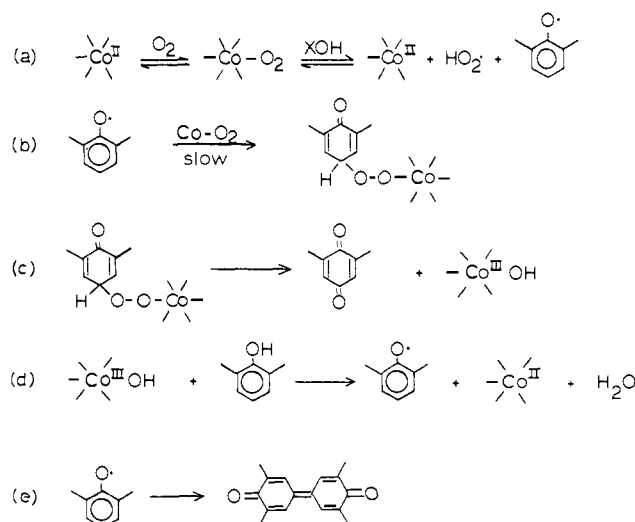


Figure 7. Proposed mechanism for the oxidation of 2,6-dimethylphenol by CoSMDPT .

controlled limit in nonpolar solvents.³¹ It could be converted to hydrogen peroxide by hydrogen atom abstraction from phenol and the peroxide can be decomposed into water and O_2 by the cobalt(II) complex. Minor side reactions involving small amounts of HO_2 radical or hydrogen peroxide are probably implicated in the catalyst degradation reaction. Carboxylic acids formed from ring-opening reactions would block step 2 above and stop oxidation by inhibiting formation of the phenoxy radical. The observation of a cobalt- O_2 EPR of undiminished intensity in the deactivated catalyst is consistent with such a hydrogen-bonded carboxylic acid-cobalt dioxygen adduct. Carboxylic acids can arise by attack of HO_2 on quinones or via Baeyer-Villiger type attacks of peroxides on ketones. Experiments designed to test this speculation led to a very significant improvement in catalyst lifetime. Addition of base to the reaction mixture greatly extended the number of turnovers by the catalyst. The most basic material, Na_2CO_3 , was most effective. The role of a base is not well established; however, since the pK_a of HO_2 is 4.9, it should be converted into a superoxide anion by the addition of these bases.³⁴ Thus we propose that eq 1, 2, 3, 4, 9, and 10 constitute the reaction for both the formation of quinone and the regeneration of the catalyst.

The metal plays two important roles in the catalysis of the oxidation: (1) coordination activates the O_2 molecule and enhances its ability to abstract hydrogen atoms; (2) coordination enhances the activity of the O_2 molecule in a free radical reaction with organic molecules. There are many aspects of the mechanism of this oxidation reaction that remain speculative. We have, however, presented results that rule out many of the possible paths. Our proposed mechanism is summarized in Figure 7. The extension of a reaction pathway for a given system to other substrates is always a dangerous practice, and this lack of generality is one of the shortcomings of kinetic investigations. In this study, we have been able to provide a scheme for the oxidation of 2,6-dimethylphenol that is consistent with the known reactivity of this and analogous substrates. We have also been able to demonstrate that coordination of dioxygen to a metal enhances the rate at which it undergoes the spin-pairing reaction with organic free radicals.

Acknowledgment. We acknowledge the financial support of this research by the National Science Foundation and the Office of Naval Research as well as helpful discussion of this research with Dr. P. M. Burke of the Petrochemicals Department of Du Pont.

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