Cleavage of Carbon–Carbon Bonds. Copper(II)-Induced Oxygenolysis of *o*-Benzoquinones, Catechols, and Phenols. On the Question of Nonenzymatic Oxidation of Aromatics and Activation of Molecular Oxygen

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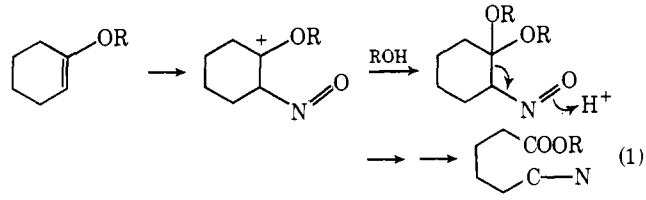
Abstract: *o*-Benzoquinones and catechols undergo the carbon–carbon bond cleavages induced by a particular copper(II) reagent in the presence as well as in the absence of molecular oxygen. The overall anaerobic transformation of catechol to *cis,cis*-muconic acid monomethyl ester involves a two-electron oxidation of catechol to *o*-benzoquinone, followed by a second two-electron oxidation of the *o*-benzoquinone to the muconic acid ester. The active copper(II) species can be generated by reaction of cupric methoxide with water in pyridine and is equivalent to a dimeric cupric methoxy hydroxide complexed with pyridine. The oxidation reagent ("Cu reagent") can also be generated either by reaction of cuprous chloride with oxygen in pyridine in the presence of methanol, by reaction of methanol with a product mixture of the oxidation of cuprous chloride in pyridine, or by addition of 1 molar equiv of water to any of the following reagents: to cupric methoxy chloride in pyridine, to pyridine cupric methoxy chloride in pyridine, to a mixture of cupric methoxide and cupric chloride in pyridine, or to a mixture of cupric methoxide and pyridine hydrochloride in the same solvent. Thus, all the methods provide the same active oxidation agent which in pyridine exists as a mixture of bispyridine cupric chloride and dimeric, oligomeric, or polymeric cupric methoxy hydroxide in equilibrium with each other. During the reaction the active copper(II) agent is being reduced to copper(I) muconate ester and cuprous hydroxide, which under the reaction conditions can efficiently reduce the intermediate *o*-benzoquinone to the copper(II)-catecholate complex that resists further oxidation. However, this undesirable reduction is prevented by the cupric chloride which scavenges cuprous muconate and cuprous hydroxide in situ and converts them into an innocuous mixture of basic cupric muconate and cuprous chloride. In the presence of molecular oxygen, the cuprous chloride is reoxidized to the original active copper(II) reagent. Since in these transformations the active copper(II) species act as electron acceptors from *o*-benzoquinone and cathechol, and since the final transfer of electrons to molecular oxygen occur from the generated copper(I) species, a direct reaction between oxygen and organic substrates does not take place. Consequently, overall oxidation of these substrates does not require a special mechanism for the activation of the molecular oxygen.

Currently one of the most intriguing chemical mysteries is the question of how living organisms circumvent the low kinetic reactivity of molecular oxygen in reaction with organic substrates.[1] Under typical conditions this low reactivity is a consequence of oxygen's ground-state triplet character which makes the reaction with a singlet organic substrate a spin-forbidden process.[1a] The last decade has seen considerable progress in the understanding of the chemical bonding and structures of various transition metal complexes with oxygen,[1c,2] and many chemical models for enzymatic oxidations have been discussed.[1a-d,3-20]

The remarkable ability of certain oxygenases to catalyze oxidative carbon–carbon bond cleavage of various aromatic substrates, most notably of phenols and catechols, is well known.[21,22] While the precise mechanism of these transformations remains uncertain, it is becoming increasingly clear that molecular oxygen is not involved directly in reactions with these substrates.[1a-c,23] It is generally accepted[21a] that the required activation of molecular oxygen in enzyme systems is achieved by reaction of the oxygen with the transition metal bonded to the enzyme molecule. It is then the reaction of these oxygen-containing intermediates with the complexed organic substrate that brings about the observed oxidation reaction. The possible role of superoxide ion in certain biological oxidations is well recognized and the investigations of superoxide ion chemistry in vitro[24-29] as a model for the oxidative carbon–carbon bond cleavage of catechols catalyzed by pyrocatechase and metapyrocatechase has already been carried out.[30,31]

Our interest in new synthetic approaches to caprolactam led us to explore various methods for cleaving carbon–carbon bonds in cyclic C_6 systems. We recently reported on the nitrosolysis reaction—a novel carbon–carbon bond cleavage effected through nitrosation which leads to the formation of a terminal carbon–nitrogen bond.[32-35] The success of this reaction was attributed to an efficient trapping of the α-nitrosoalkoxy carbonium ion intermediates with an alcohol as a nucleophile, and in situ cleavage of the ensuing α-nitroso acetals[32] (eq 1).



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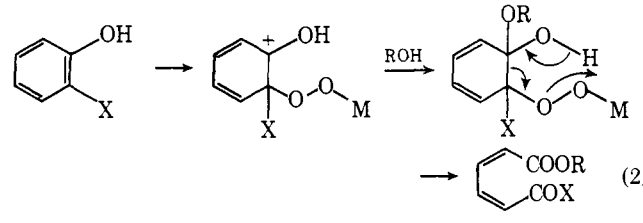
In an effort to streamline the preparation of caprolactam, a more direct route from phenol was sought. The success of the nitrosolysis concept prompted us to investigate possibilities for a similar transformation between phenol or catechol and a system containing "activated oxygen" (eq 2). The present



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paper describes results of these efforts and discusses the chemistry associated with copper(II)-induced carbon–carbon bond cleavage reactions in *o*-benzoquinones, catechols, and phenols, and elucidates the nature of the active copper species and the role of molecular oxygen in these transformations.

Results and Discussion

1. Copper(I) as a Catalyst for "Activation" of Molecular Oxygen. (a) General. In an attempt to imitate the action of the enzyme tyrosinase Brackman and Havinga studied oxidation

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of phenols using copper/amine catalyst.[3] Terentiev and coworkers reported that aromatic amines were converted to the corresponding azo compounds by aerial oxidation in pyridine solution containing cuprous chloride,[36] and Kinoshita described that benzil undergoes the carbon–carbon bond cleavage to benzoic acid under similar conditions.[37] Approximately at the same time Hay, Blanchard, Endres, and Eustance reported that 2,6-disubstituted phenols undergo oxidative polymerization catalyzed by cuprous chloride in nitrobenzene/pyridine solution,[38] and shortly thereafter showed that the pyridine cupric methoxy chloride complex[39e] was an active catalyst for these oxidative polymerizations.[39a-e,40-44]

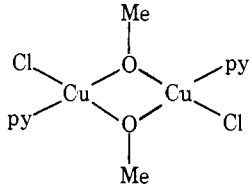
Since oxygen is a four-electron oxidant, most reported oxidations of cuprous chloride involve the expected $4CuCl + O_2$ stoichiometry.[39e,44,47,48] In solvents which do not dissolve cuprous chloride, the reaction with oxygen does not occur. However, in the presence of a cosolvent, e.g., pyridine, methanol, etc., that can act as a coordinating ligand for copper, the oxidation does take place even in benzene,[39e] *o*-dichlorobenzene,[39e] or chloroform.[43,44] While the stoichiometry of the reaction in these solvents was the same, with the exception of methanol, which provides insoluble crystalline cupric methoxy chloride,[39e,49]

$$4CuCl + O_2 \xrightarrow[MeOH]{} 4CuClOMe + 2H_2O \qquad (3)$$

the nature of the oxidation products in other solvents remains uncertain.[39e] Pyridine is atypical as a solvent for copper compounds, because it solvates Cu(I) very effectively, but apparently solvates Cu(II) relatively poorly.[45,46] The oxidation of cuprous chloride in methanol containing pyridine[39e] gives a deep green, insoluble, crystalline pyridine cupric methoxy chloride complex, I.

$$4CuCl + O_2 + 4py \xrightarrow[MeOH]{} \underset{I}{(pyCuClOMe)_n} + 2H_2O \qquad (4)$$

The same complex can also be prepared directly from various copper(II) starting materials.[39e,50] The tentative structure of this complex was criticized and an alternative one was proposed,[54] but a single crystal analysis has now established[55] that the complex I exists as the methoxy bridged dimer analogous to the corresponding α-picoline complex.[56]



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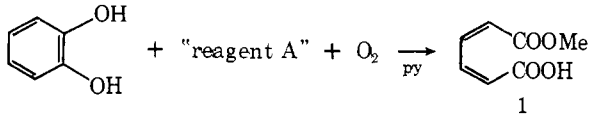
(b) Cuprous Chloride as a Catalyst for Oxidation of Catechol.[57] The reaction of oxygen with 4 molar equiv of cuprous chloride in pyridine solution containing 5 equiv of methanol generates a green, heterogenous mixture ("reagent A"):

$$4CuCl + O_2 + 4MeOH \xrightarrow[py]{} \text{"reagent A"} \qquad (5)$$

When a solution of catechol in pyridine/methanol was added to the "reagent A" under oxygen, approximately 1 molar equiv of oxygen was consumed. Evaporation of solvent, followed by acid hydrolysis and extraction, gave an 80–85% yield of the *cis,cis*-muconic acid monomethyl ester **1** (eq 6). When ethanol, *n*-butyl alcohol, or isopropyl alcohol were used instead of methanol, the corresponding *cis,cis*-muconic acid monoalkyl esters were obtained in 63, 76, and 26% yield, respectively.



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$$+ H_2O \qquad (6)$$

Alternatively, reaction of oxygen with cuprous chloride in pyridine[39e] gives a brown-yellow, heterogeneous reaction mixture. Addition of the required amount of methanol, ethanol, *n*-butyl alcohol, or isopropyl alcohol to this reaction mixture provides the corresponding "reagent(s) B":

$$4CuCl + O_2 \xrightarrow[py]{} [\ \ ] \xrightarrow[py]{4ROH} \text{"reagent B"} \qquad (7)$$

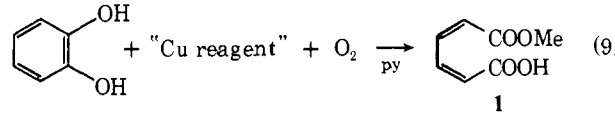
Addition of catechol to "reagent B" under oxygen resulted in formation of the monoalkyl esters in essentially the same yields as when the reaction was carried out with the "reagent(s) A" as above.

Finally, the reaction of complex I in pyridine with 1 equiv of water generates reagent C

$$2(pyCuClOMe)_2 + 2H_2O \xrightarrow[py]{} \text{"reagent C"} \qquad (8)$$

which in the presence of oxygen effectively oxidizes catechol to the monomethyl ester **1** in an 80–85% yield.

Since all three agents, "reagent A", "reagent B", and "reagent C", henceforth referred to as the "Cu reagent", were active in promoting conversion of catechol in the presence of oxygen to the monomethyl ester **1**, *it is reasonable to conclude that all three are the same and contain the same active copper(II) species* (eq 9).



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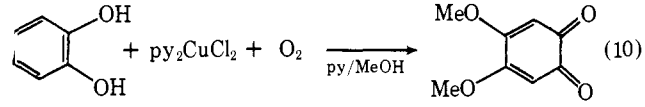
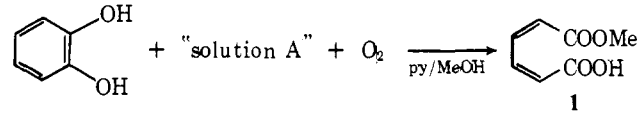
Regardless of the method of preparation, the "Cu reagent" on filtration provided approximately half of the total copper as bispyridine cupric chloride. Addition of catechol to a reaction mixture of bispyridine cupric chloride in pyridine/methanol under oxygen resulted in a very slow oxygen uptake. Workup as above gave 4,5-dimethoxy-1,2-benzoquinone[58] (eq 10).



(10)

Evaporation of the olive-green solution ("CuO solution") after the filtration of the bispyridine cupric chloride gave an amorphous, brown-black material containing a small amount of chloride ion. Addition of catechol either directly to "CuO solution" or to the redissolved brown-black solid in pyridine resulted in a consumption of 1 equiv of oxygen and formation of the monomethyl ester **1** (eq 11). Before returning to this point, it is necessary to consider briefly the nature of the oxidative carbon–carbon bond cleavage of catechol to the *cis,cis*-muconic acid monoalkyl esters.



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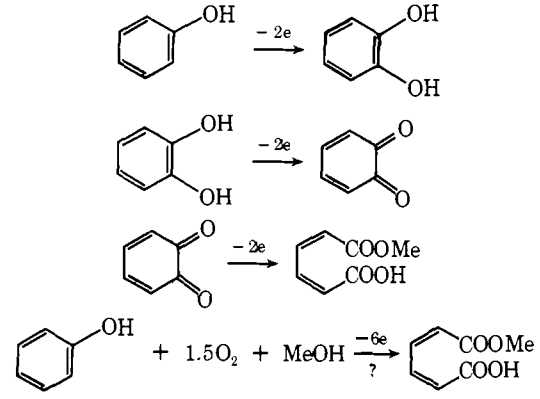
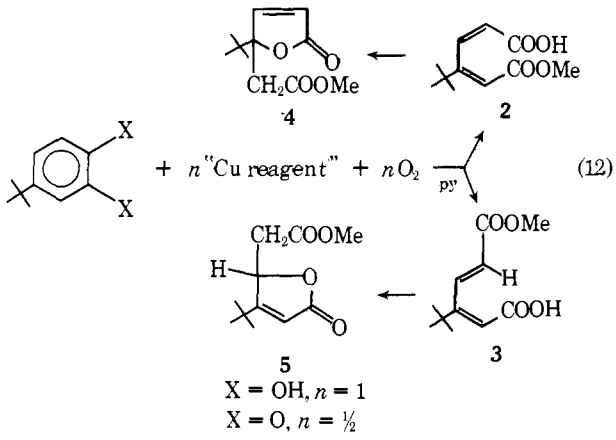
2. Possible Pathways for the Oxidative Carbon–Carbon Bond Cleavage in Catechol. In the oxidation of catechol to *cis,cis*-muconic acid catalyzed by the iron-containing pyrocatechase,[1a-c,21,22] neither *o*-benzoquinone nor hydrogen peroxide was detected as a reaction intermediate. On the other hand, it is well known that tyrosinase is capable of catalyzing oxidation of phenols to the corresponding catechols, and further to *o*-benzoquinones.[59] Oxidation of catechol to *cis,cis*-muconic acid monomethyl ester **1** is a four-electron oxidation and in

Scheme I



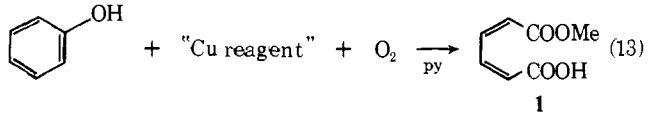
principle the reaction could involve stepwise oxidations of catechol to *o*-benzoquinone, followed by the oxidative cleavage of *o*-benzoquinone to the observed muconic acid monomethyl ester. Consequently, it was of interest to determine whether the overall reaction of catechol involves *o*-benzoquinone as a reaction intermediate, and, more importantly, whether the same reaction can even be carried out with phenol as catechol precursor (Scheme I).

Because 4-*tert*-butyl-1,2-benzoquinone is considerably easier to handle than *o*-benzoquinone itself, we used 4-*tert*-butyl derivatives to test the above possibilities.[57] Thus, addition of 4-*tert*-butylcatechol to the "Cu reagent" (prepared as above) under oxygen resulted in consumption of an equivalent amount of oxygen, and after standard workup gave a mixture of the isomeric 3- and 4-*tert*-butylmuconic acid monomethyl esters **2** (55%) and **3** (40%) (eq 12). Upon attempted chromatography on silica gel both acid esters were converted to the corresponding lactones **4** and **5**. The reaction with 4-*tert*-butyl-1,2-benzoquinone (eq 12) required one-half of the



equivalent amount of the oxygen, and afforded essentially identical yields of the isomeric monomethyl esters **2** and **3**. Careful analysis of the reaction mixtures after oxidation of both 4-*tert*-butylcatechol and 4-*tert*-butyl-1,2-benzoquinone also revealed a small quantity of white, powdery material, mp 228 °C, whose structure will be described later in the text.

Finally, addition of phenol to the "Cu reagent" resulted in slow oxygen uptake to give after 1 day about 50–60% yield of the monomethyl ester **1** (eq 13).

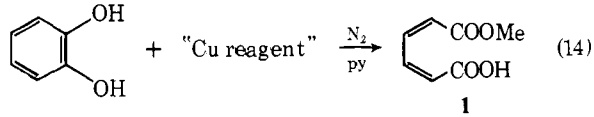


Since both 4-*tert*-butylcatechol and 4-*tert*-butyl-1,2-benzoquinone provided essentially the same mixture of the isomeric monomethyl esters **2** and **3**, it seems reasonable to conclude that corresponding *o*-benzoquinone is the intermediate in conversion of catechol into the monomethyl esters. Moreover, since the oxidation of phenol also provided the monomethyl ester **1**, it appears that the overall oxidation of phenol might indeed be a stepwise process that involves catechol and *o*-benzoquinone as the reaction intermediates,[60] as suggested in Scheme I.

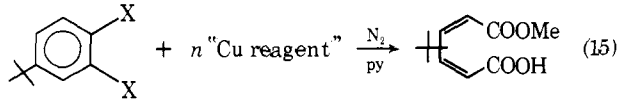
3. Does Oxidation of Catechol to *cis,cis*-Muconic Acid Monomethyl Ester Require Molecular Oxygen? (a) Anaerobic Reaction in the Presence of Water. The salient feature of the carbon–carbon bond cleavage of phenols and catechols in the reaction with oxygen catalyzed by iron-containing oxygenases is that the product contains both atoms of the O_2, one on each carbon of the bond cleaved.[1a-c,21,61] It is generally accepted[1a-c,21a,65,66] that the required activation of molecular oxygen in the enzyme systems is achieved by reaction of the oxygen with the transition metal bonded to the enzyme molecule.

After cursory inspection of our experimental results with catechols and *o*-benzoquinone, one may be tempted to conclude that the "activation" of molecular oxygen in our system is similarly achieved by reaction of oxygen with the "Cu reagent". However, from the observed stoichiometries between cuprous chloride and oxygen it is evident that only the amount of oxygen required to oxidize the available copper(I) to copper(II) is consumed initially. Moreover, the "Cu reagent" does not show any tendency toward further reaction with oxygen.

Addition of a freeze–pump–thaw degassed solution of catechol in pyridine/methanol to a similarly degassed "Cu reagent" prepared as above, followed by the standard workup but under the inert atmosphere, gave the *cis,cis*-muconic acid monomethyl ester **1** in essentially the same yields as when the reaction was carried out in the presence of oxygen (eq 14). Both

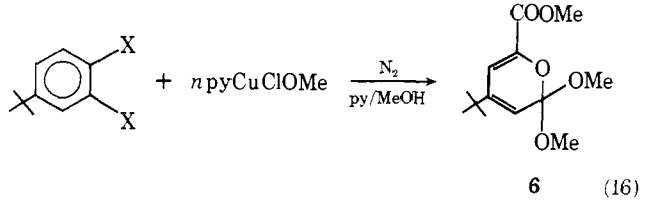


4-*tert*-butylcatechol and 4-*tert*-butyl-1,2-benzoquinone reacted with the "Cu reagent" under nitrogen to give the identical mixture of monomethyl esters **2** and **3** (eq 15; X =



OH, $n = 2$; X = O, $n = 1$) as produced in the presence of oxygen.[58]

(b) Anaerobic Reactions in the Absence of Water. Addition of catechol to a pyridine/methanol solution of the complex I *in the absence of water* under anaerobic conditions led predominantly to polymeric material. However, when reaction of either 4-*tert*-butylcatechol or 4-*tert*-butyl-1,2-benzoquinone was carried out with the complex I under anaerobic and anhydrous conditions, evaporation of the solvent gave a brown, oily material. Pentane extraction of this residue, followed by evaporation of the solvent and distillation, afforded 2,2-dimethoxy-6-carbomethoxy-4-*tert*-butyloxacyclohexa-3,5-diene (**6**) in 65% yield (eq 16; X = OH, $n = 6$; X = O, $n = 3$).



Acid hydrolysis of the ortho ester **6** in chloroform gave quantitatively 6-carbomethoxy-4-*tert*-butyloxacyclohexa-3,5-dien-2-one (**7**), mp 84–85 °C.[57] Heating the lactone ester **7** with an excess of maleic anhydride at 150 °C gave a 70% yield

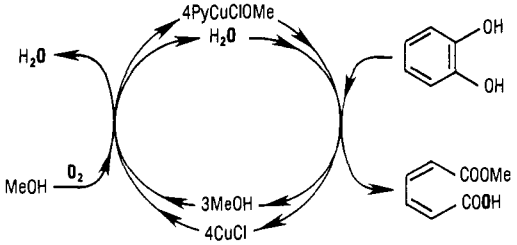


Figure 1. Schematic representation of the relationship between cuprous chloride, methanol, and oxygen on the one hand and the catechol substrate and the product monomethyl ester and water on the other.[71]

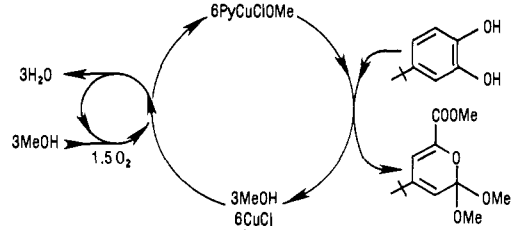
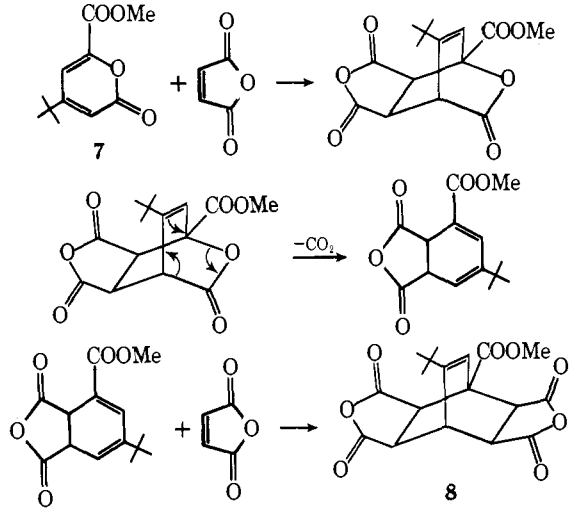


Figure 2. Schematic representation of the cleavage of 4-*tert*-butylcatechol with pyridine cupric methoxy chloride in pyridine under anhydrous and anaerobic conditions. Preparation of the Cu(II) reagent must be carried out in a separate "loop".

Scheme II



of bis adduct **8**, mp 326–329 °C, which is a single isomer by NMR analysis (Scheme II).

Clearly, the oxidative carbon-carbon bond cleavage in catechols and *o*-benzoquinone brought about by reaction with "Cu reagent" under anaerobic conditions conclusively establishes that molecular oxygen is not involved in the cleavage reaction.[15-17] It follows that copper(II) species present in the "Cu reagent" are the active oxidizing agent capable of bringing about the observed conversion of catechol and *o*-benzoquinone into muconic acid monomethyl ester (**1**) even in the absence of oxygen.[67]

When the transformation is being carried out in the presence of oxygen, the role of oxygen is to reoxidize the reduced copper species (generated as the oxidative cleavage progresses) back to the copper(II) reagent with water formed as a by-product (reagent A).[68] Since this oxidation produces 2 equiv of water, one of which is required to generate the active copper(II) species, it is clear that the experiment with isotopically labeled oxygen would incorporate one atom of the labeled oxygen in the carboxylic group of the half ester **1**, and that the other one would end up in the water by-product.[16] These relationships between the oxygen, copper(I), copper(II), methanol, and the substrate on the one hand, and the half ester product and water by-product on the other, are illustrated in Figure 1.

The reaction in the absence of water clearly precludes aerobic conditions and requires that the preparation of the active copper(II) reagent, in this case the complex I, be carried out in a separate "loop" (Figure 2).

It now appears that the general relationships between the copper reagent, substrate, and oxygen have been finally clarified (Figures 1 and 2), and we will now discuss the nature of the active copper species and the mechanism of the carbon-carbon bond cleavage reactions.

4. Nature of the Active Copper(II) Species. (a) Reaction of Cuprous Chloride with Oxygen in Pyridine. Numerous reports

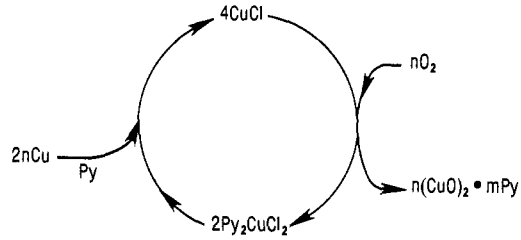


Figure 3. Conversion of copper metal into copper(II)-oxygen-pyridine species by reaction with oxygen in pyridine in the presence of a catalytic amount of cuprous (or cupric) chloride.

have established that 1 equiv of oxygen oxidizes 4 molar equiv of cuprous chloride,[39e,41,43,44,47,48,69] regardless of the solvent/copper(I) ratio. The reaction is first order in oxygen and first order in cuprous chloride.[44,69] The nature of the product(s) in this oxidation is unknown, although in the specific examples where the solvent is methanol[39] or methanol containing pyridine,[39e] well-defined copper(II) complexes are generated (eq 3, 4). More recently Davies and co-workers reinvestigated the reaction of cuprous chloride with oxygen in pyridine.[70] Using gel permeation chromatography they were able to separate from the reaction mixture bispyridine cupric chloride and showed that it accounted for half of the total copper in the products. The remaining pyridine solution contained the other half of the total amount of copper, and according to Davies,[70] this was a pyridine complex of the "copper(I) peroxide" (eq 17).

$$4CuCl + O_2 \xrightarrow[py]{} 2py_2CuCl_2 + (Cu\text{-}O\text{-}OCu) \cdot npy \quad (17)$$

We repeated Davies' experiments and also prepared a similar solution by reaction of oxygen with cuprous chloride in the presence of a large excess of copper metal. The cupric chloride initially produced reacts with copper metal to provide cuprous chloride, which is then again reoxidized by oxygen. When oxygen uptake ceases, the cuprous chloride originally present is converted to bispyridine cupric chloride, and the copper metal is oxidized to the same species present in the Davies solution (Figure 3). Using this technique we were able to prepare pyridine solutions of the copper-oxygen species containing less than 20% of the total copper as bispyridine cupric chloride. Davies' strongest evidence for the existence of pyridine coordinated cuprous peroxide was his report of a characteristic peroxide band at 856 nm in the Raman spectrum of the above pyridine solutions.[70] We were unable to observe this band in solution after separation of bispyridine cupric chloride by chromatography or in the solution prepared from copper metal. Thus, we were skeptical of the copper(I) peroxide assignment of Davies'.

Any mechanism for the oxidation of cuprous chloride in pyridine[71] must take into consideration the following experimental facts:

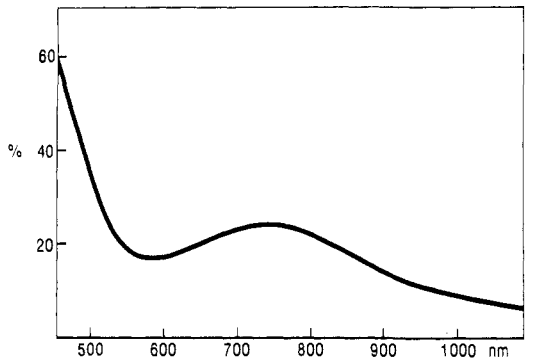


Figure 4. Visible spectrum of the "reagent A". Total copper concentration 2.47×10^{-2} in pyridine; λ_{max} 731 nm, ϵ 90.0. The spectra of the reagents "B" and "C" were the same within experimental error.[73]

(1) One equivalent of oxygen oxidizes 4 equiv of cuprous chloride.[39e,41,43,44,47,48,69,70]

(2) The reaction between oxygen and cuprous chloride is first order in each reactant.[44,69]

(3) One of the reaction products is bispyridine cupric chloride which contains all of the chlorine atoms and half of the total amount of the copper.[70]

(4) The second product contains the other half of the original copper and both oxygen atoms. Neither pyridine solutions of this product nor the amorphous solid remaining after evaporation of the solvent showed any evidence for the peroxide structure.

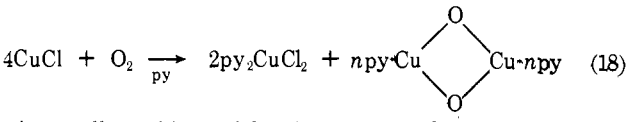
(5) Pyridine solution of the copper-oxygen species is stable for an extended period of time and does not react with oxygen.

(6) Acid-catalyzed hydrolysis of the pyridine solution containing copper-oxygen species provides cupric oxide.[73]

(7) Pyridine solution containing the copper oxygen species is not ESR active.[73]

The absence of the peroxide absorption in the Raman spectrum of the copper-oxygen species, the stability of these species toward oxygen, and the fact that on hydrolysis these species provide cupric oxide strongly argue against the copper(I) peroxide structure,[70] and suggest that the oxygen-oxygen bond in this product has already been broken. The absence of an ESR signal in pyridine solution of this species is certainly not evidence for the presence of copper(I) species, since significant antiferromagnetic coupling of the unpaired electrons on the two adjacent copper(II) centers would also eliminate the necessary condition for the observation of the ESR signal.[52,53] Clearly, this copper-oxygen product cannot be a simple cupric oxide. Most likely this is a copper(II) oxide that exists as a tight di-μ-oxo-bridged copper(II)-pyridine dimer, oligomer, or a polymer effectively solvated with pyridine.

Consequently, oxidation of cuprous chloride in pyridine provides a mixture of bispyridine cupric chloride and the copper(II)-oxygen-pyridine complex described above (eq 18). It should be understood, however, that the structure of the copper-oxygen species given in eq 18 was not determined ex-



perimentally and is used for the purpose of discussion only.

(b) Reaction of Cuprous Chloride with Oxygen in Pyridine in the Presence of Methanol. When reaction of cuprous chloride with oxygen is carried out in pyridine solution in the presence of 4 equiv of methanol (eq 5, "reagent A") both the stoichiometry[39e,44] and the reaction order between the oxygen and cuprous chloride remain the same as in pyridine in the absence of methanol (eq 7, "reagent B"). The apparent chemical equivalency of these "Cu reagents" (vide supra) may be formally explained by assuming that the reaction between oxygen and cuprous chloride in pyridine gives initially the same products (eq 18) regardless of whether methanol is present or not. *The copper-oxygen species then reacts with the methanol to produce cupric methoxy hydroxide which may exist in equilibrium with cupric methoxide and water. More importantly, the products obtained by reaction of the copper-oxygen-pyridine complex with methanol could also be obtained by reaction of cupric methoxide with water in pyridine* (Scheme III). Furthermore, the same overall product mixture also results from the reaction of pyridine cupric methoxy chloride complex I with water in pyridine ("reagent C"), or from the reaction of bispyridine cupric chloride and cupric methoxide with water in the same solvent. Indeed, both the spectroscopic[72] and the chemical properties of these "Cu reagents" ("reagent A", reagent B", or "reagent C") were identical regardless of the method of preparation. For example, freshly prepared pyridine solutions of either of the three reagents (vide supra) had the same visible spectrum (Figure 4). These solutions were undergoing a very slow irreversible change as indicated by the decrease of the maximum at 730 nm and a slight "increase" of the minimum at 565 nm (Figure 4). Whether this slow, irreversible change reflected slow hydrolysis of the cupric methoxy hydroxide to cupric hydroxide or cupric oxide or slow polymerization of some intermediate is not known at this time.

While it is now quite certain that the "Cu reagent" is a

Scheme III

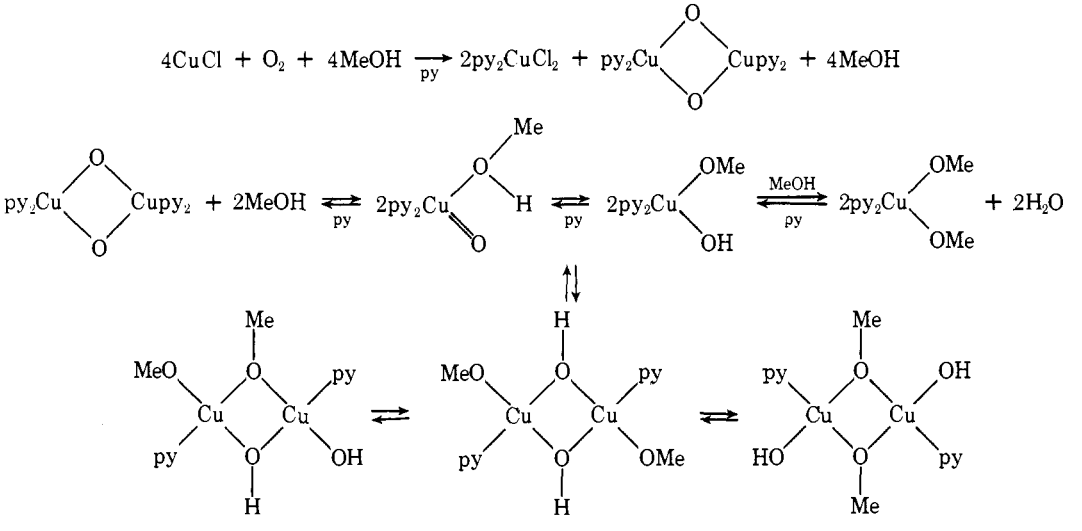


Table I. Reaction of 4-*tert*-Butylcatechol and 4-*tert*-Butyl-1,2-benzoquinone with Copper Reagents in Pyridine[a]

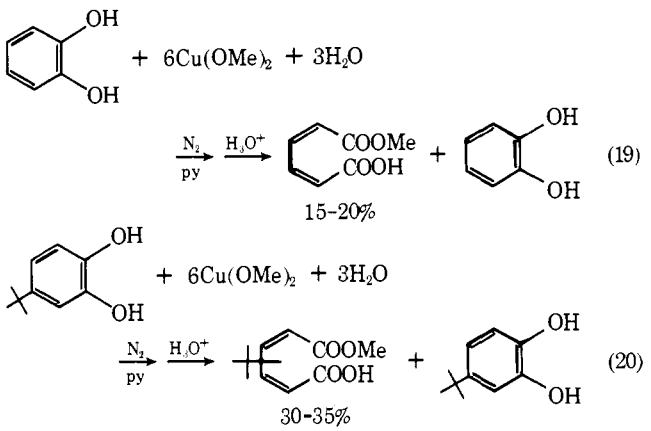
no.	copper reagent,[c] mmol	substrate,[b] mmol	products (%)[d]
1	1CAT	$6Cu(OMe)_2/3H_2O$	HE-1 (15-20); CAT (~80)
2	1TBC	$6Cu(OMe)_2/3H_2O$	HE-2 + 3 (30-35); TBC (~60)
3	1TBC	$6Cu(OMe)_2/3H_2O/O_2$	HE-2 + 3 (~60); TBC (~35)
4	1TBC	$12Cu(OMe)_2/6H_2O$	HE-2 + 3 (30-35); TBC (~60)
5	1TBQ	$6Cu(OMe)_2/3H_2O$	HE-2 + 3 (~57); TBC (~43)
6	1TBQ	$24Cu(OMe)_2/12H_2O$	HE-2 + 3 (~57); TBC (~43)
7	1TBQ	$2Cu(OMe)_2/2H_2O/2CuCl_2$	HE-2 + 3 (95)
8	1TBQ	$2Cu(OMe)_2/2H_2O/1CuCl_2$	HE-2 + 3 (95)
9	1TBQ	$1Cu(OMe)_2/1H_2O/4CuCl_2$	HE-2 + 3 (~35); polymer[e]
10	1TBQ	$1Cu(OMe)_2/1H_2O/12CuCl_2$	HE-2 + 3 (~35); polymer[e]
11	1TBQ	2CuOBu-*t*/$2H_2O$	TBC (100)
12	1TBQ	$6Cu(OMe)_2/3H_2O$/2CuOBu-*t*/$2H_2O$	HE-2 + 3 (~35); TBC (~65)
13	(1TBQ + 2CuOBu-*t*/$3H_2O$)[f]	$6Cu(OMe)_2/3H_2O$	TBC (95)
14	(1TBQ + 2CuOBu-*t*/$2H_2O$)[f]	$6CuCl_2$	polymer[e]
15	1TBQ	4CuOBu-*t*/$4H_2O$/4MeOH/$4CuCl_2$[g]	HE-2 + 3 (95)
16	1TBQ	$2CuCl/2H_2O$/2MeOH	TBC (60)
17	1TBQ	$4CuCl/4H_2O$/4MeOH/$4CuCl_2$	polymer[e]
18	1TBQ	$6Cu(OMe)_2/3H_2O$/2CuCl	HE-2 + 3 (57); TBC (43)
19	1TBQ	$1Cu(OMe)_2/1H_2O$	HE-2 + 3 (~55); TBC (~45)
20	1[Cu(TBC)dipy][h]	$6Cu(OMe)_2/3H_2O$	TBC (95)
21	1[Cu(TBC)(py)][i]	$6Cu(OMe)_2/3H_2O$	TBC (95)
22	1[Cu(TBC)dipy]	$6CuCl_2/3H_2O$/3MeOH	polymer[e]
23	1[Cu(TBC)(py)]	$6CuCl_2/3H_2O$/3MeOH	polymer[e]
24	1[Cu(TBC)dipy]	6pyCuClOMe/$3H_2O$[k]	HE-2 + 3 (95)
25	1[Cu(TBC)(py)]	6pyCuClOMe/$3H_2O$[k]	HE-2 + 3 (95)
26	1[Cu(CAT)dipy][j]	6pyCuClOMe/$3H_2O$[k]	HE-1 (95)

[a] All reactions were carried out at room temperature in a degassed solvent system under an inert atmosphere. Detailed experimental procedure is reported in the Experimental Section. [b] CAT = catechol; TBC = 4-*tert*-butylcatechol; TBQ = 4-*tert*-butyl-1,2-benzoquinone. [c] Copper reagents were generated in situ by mixing indicated molar quantities in pyridine. [d] HE-1 = *cis,cis*-muconic acid monomethyl ester **1**; HE-2 + 3 = a mixture of isomeric 4-*tert*-butylmuconic acid monomethyl esters **2** and **3** in the usual ratio of 5:4.5. The reported yields are by NMR on a crude isolated product. [e] The same polymer was formed in all experiments. [f] A product mixture resulting from the reaction of the *o*-benzoquinone and cuprous *tert*-butoxide/water in pyridine. [g] A product mixture resulting from the reaction of indicated components in pyridine. [h] 4-*tert*-Butylcatecholato-2,2′-dipyridylcopper(II). [i] 4-*tert*-Butylcatecholatopyridinecopper(II). See also ref 82. [j] Catecholato-2,2′-dipyridylcopper(II). [k] "Reagent C".

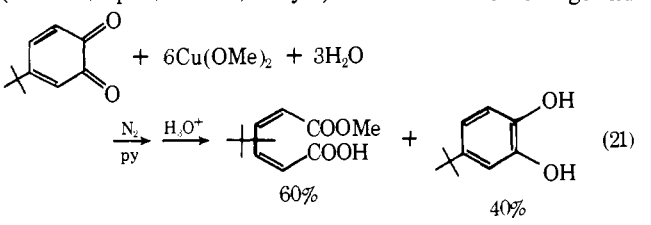
mixture of bispyridine cupric chloride and the copper(II) species generated from cupric methoxide and water in pyridine, the equilibria indicated in Scheme III are probably simplifications of a more complex situation. For example, it is known that cupric methoxide as well as cupric methoxy chloride exists as polymers;[49,51] therefore, cupric methoxy hydroxide pyridine complex would probably exist in pyridine not only as a dimer, but could also be present in oligomeric or polymeric form. Finally, since bispyridine cupric chloride alone in pyridine was not effective in inducing the carbon-carbon bond cleavage,[74] *the actual active copper(II) species in the "Cu reagent" (Scheme III) must come from the reaction of the copper(II)-oxygen-pyridine species with methanol, or from reaction of cupric methoxide with water*, as will be described in the next section.

5. Reaction of Cupric Methoxide/Water in Pyridine with Catechols and *o*-Benzoquinones. (a) Cleavage of the Carbon-Carbon bond. Addition of a pyridine solution of catechol to a mixture of cupric methoxide[75] and water in pyridine under anaerobic conditions, followed by acid hydrolysis and the usual workup, gave a 15–20% yield of the *cis,cis*-muconic acid monomethyl ester **1** and a large quantity of unreacted catechol (eq 19). A similar reaction with 4-*tert*-butylcatechol gave the expected isomeric 4-*tert*-butylmuconic acid monomethyl esters **2** and **3** in a 30–35% yield (eq 20; Table I, entry 2); in the presence of oxygen the yield of the cleavage products increased to ca. 60% (Table I, entry 3).

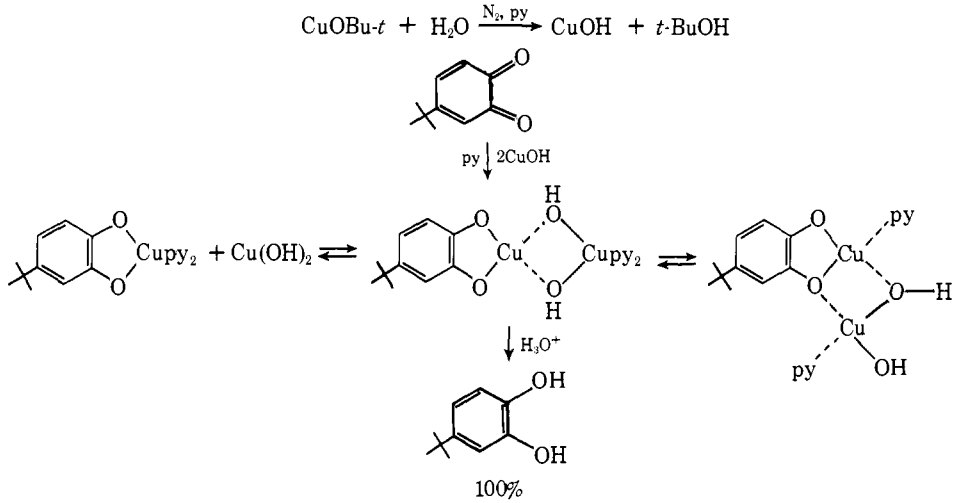
The low yield of the cleavage products in these reactions was attributed to a possible irreversible hydrolysis of the cupric methoxide under the reaction conditions to give inactive cupric



oxide. Increased amounts of cupric methoxide did not lead to a higher yield of the cleavage products (Table I, entry 4). Even more surprising is the reaction of 4-*tert*-butyl-1,2-benzoquinone with an excess of cupric methoxide in pyridine in the presence of water to give a mixture of the half esters **2** and **3** (ca. 60% in the usual ratio of 5:4.5), and 4-*tert*-butylcatechol (ca. 40%, eq 21; Table I, entry 5). The ratio of the cleavage and



Scheme IV



reduction products did not change significantly even when a large excess of cupric methoxide was used (Table I, entry 6). While reaction of 4-*tert*-butyl-1,2-benzoquinone with a mixture of *2 equiv each of cupric methoxide, water, and cupric chloride* (Table I, entry 7), as well as with reduced amounts of cupric chloride (1 equiv; Table I, entry 8), gave the cleavage products only, the reaction with a mixture of *1 equiv of cupric methoxide, water, and 4 or even 12 equiv of cupric chloride* (Table I, entries 9 and 10) gave only 30–40% of the half esters **2** and **3** and polymeric material.

Clearly, the reagent prepared from cupric methoxide and water in pyridine is capable of bringing about the carbon–carbon bond cleavage in both catechols and *o*-benzoquinone. Therefore, it follows that the active copper(II) species responsible for the cleavage reaction is either cupric methoxy hydroxide complexed with pyridine and methanol or a mixture of these with the corresponding di-μ-hydroxy- or di-μ-methoxy-bridged copper(II) dimers or oligomers as suggested in Scheme III.

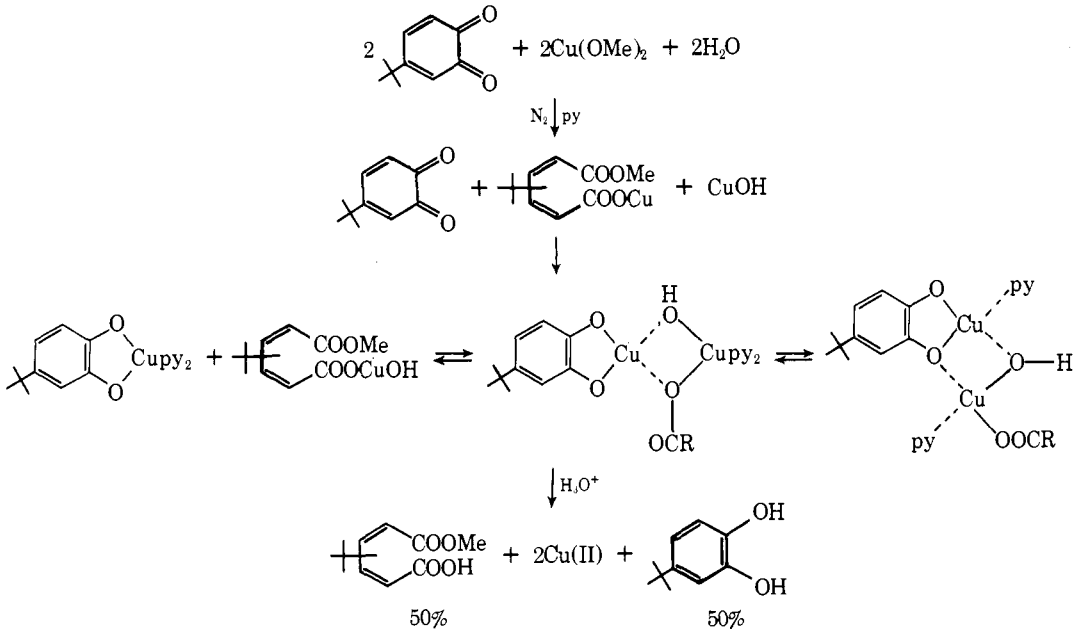
(b) Reduction of *o*-Benzoquinone. The formation of the catechol in the reaction of 4-*tert*-butyl-1,2-benzoquinone with cupric methoxide and water evidently arises as a result of a competitive reduction pathway. Since the only reducing reagent present in the system can be a copper(I) species produced in the cleavage reaction,[76] it appears that this reduction is a very facile process that effectively competes with the cleavage reaction. Possible copper(I) species that can be formed in the course of the cleavage reaction are cuprous hydroxide (or the corresponding oxide) and the copper(I) salt of the muconic acids **2** and **3**. Addition of 4-*tert*-butyl-1,2-benzoquinone to a pyridine solution containing cuprous hydroxide (generated in situ by reaction of cuprous *tert*-butoxide[77] with water[78]) gave either the copper(II) catecholate and cupric hydroxide[79] or the corresponding mixed complexes of copper(II) catecholate and cupric hydroxide, which after acid hydrolysis afforded 4-*tert*-butylcatechol quantitatively (Scheme IV; Table I, entry 11).

Reaction of 4-*tert*-butyl-1,2-benzoquinone with a mixture of 6 equiv of cupric methoxide and 2 equiv of cuprous hydroxide[78] in the presence of water (Table I, entry 12) provided 30–40% cleavage and 60–70% reduction. When 4-*tert*-butyl-1,2-benzoquinone was treated first with cuprous hydroxide, and then with an excess of cupric methoxide and water, only trace amounts of the cleavage products were observed (Table I; compare entries 13 and 12). Similarly, addition of cupric chloride to a product mixture resulting from the reaction of 4-*tert*-butyl-1,2-benzoquinone and cuprous hydroxide also gave only small amounts of cleavage product (Table I, entry 14). On the other hand, addition of 4-*tert*-butyl-1,2-benzoquinone to a mixture of cuprous hydroxide, methanol, and cupric chloride in pyridine[80] led to clean carbon–carbon bond cleavage (Table I, entry 15). Addition of 4-*tert*-butyl-1,2-benzoquinone to a solution of cuprous chloride in pyridine containing methanol and water resulted in a rapid reaction, as indicated by the disappearance of the quinone absorptions in the IR spectrum. If the reaction mixture was quickly hydrolyzed in the presence of acid, the catechol was obtained quantitatively (Table I, entry 16). However, if the reaction mixture was allowed to stand overnight before hydrolysis, or if the attempted reduction was carried out in the presence of cupric chloride, and then hydrolyzed, only polymeric material was observed (Table I, entry 17). Contrary to the experiment with cupric methoxide/water/cuprous hydroxide (Table I, entry 12), in which the presence of cuprous hydroxide increased the amount of the reduction product, the presence of cuprous chloride did not have any significant effect on the reaction of *o*-benzoquinone with cupric methoxide/water[80] (Table I, entry 18; compare with entry 4).

These experiments established that cuprous hydroxide, cuprous chloride, and probably other copper(I) species (e.g., cuprous monomethyl muconate) indeed react very readily with *o*-benzoquinones. Moreover, as one now would expect, the reaction of the 4-*tert*-butyl-1,2-benzoquinone *with 1 equiv of cupric methoxide and water* in pyridine, followed by acid hydrolysis, gave about 55% of the cleavage products **2** + **3** and ca. 45% of catechol (Table I, entry 19). The outcome of this particular reaction is remarkable, *because it requires all of the resulting copper species to exist in a copper(II) state.* In other words, the overall reaction occurred without a net change in the oxidation state of the copper reagent. To account for the isolated products, it is then necessary to conclude that the *o*-benzoquinone was converted into copper(II) catecholate and basic copper(II) monomethylmuconate, which before the hydrolysis were present in solution either as such, or as a mixed copper(II) catecholate/basic copper(II) monomethylmuconate complex[79,81] (Scheme V).

Since the reaction between copper(II) catecholate complex and cupric methoxide/water (Table I, entry 13) or cupric hydroxide (e.g., the reverse of the reaction in Scheme IV) does not generate *o*-benzoquinone, it follows that such a complex must be stable under the reaction conditions. The reaction of the *o*-benzoquinone with cuprous chloride, on the other hand, does not provide a copper(II) catecholate complex that is stable under reaction conditions (Table I, entries 16, 17). Evidently, the equilibrium between the copper(II) catecholate complex and cupric chloride and *o*-benzoquinone and cuprous chloride is readily established and produces some intermediate that on hydrolysis provides catechol. As it will become evident (vide infra), this redox reaction involves a semiquinone radical anion intermediate and under thermodynamic conditions it is this

Scheme V

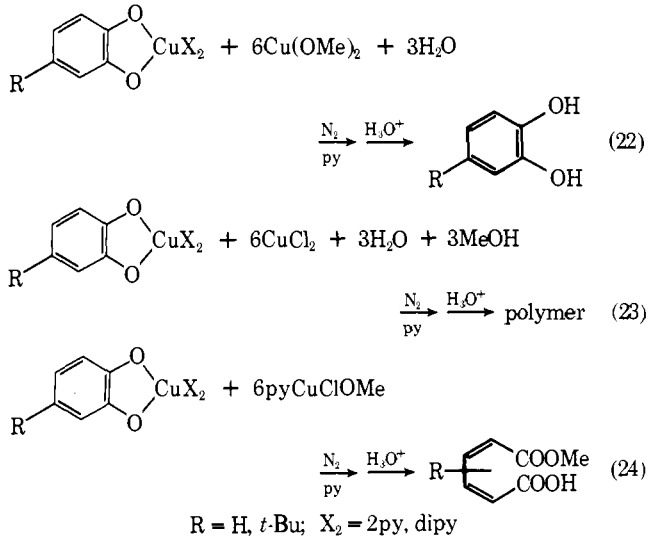


intermediate that undergoes a relatively slow irreversible polymerization.

(c) **Copper(II) Catecholates as Intermediates in the Carbon–Carbon Bond Cleavage Reactions of *o*-Benzoquinones and Catechols.** In order to test the above conclusions unequivocally, we prepared copper(II) 4-*tert*-butylcatecholates both with dipyridyl and with pyridine itself as counter ligands. The reaction of 4-*tert*-butylcatechol with cupric sulfate in the presence of dipyridyl and a base according to Brown's procedure[81] gave the 4-*tert*-butylcatecholato-2,2′-dipyridylcopper(II) as a dark brown-red, powdery solid. The same complex was also prepared by reacting the catechol with cupric methoxide in pyridine containing 1 equiv of dipyridyl. When the latter reaction was carried out in the absence of dipyridyl, the corresponding 4-*tert*-butylcatecholatopyridinecopper(II) complex was obtained as a very soluble, brownish-black solid.[82]

Both copper(II) catecholate complexes[82] were inert to cupric methoxide/water in pyridine (Table I, entries 20, 21; eq 22), and underwent polymerization in the presence of cupric chloride (Table I, entries 22, 23,; eq 23), to provide the same polymeric material as in the previous experiments with cuprous chloride and the *o*-benzoquinone (Table I, entry 17), and cupric chloride[83] (Table I, entry 14). Conversely, the various 4-*tert*-butylcatecholatocopper(II) complexes underwent clean carbon–carbon bond cleavage when treated with excess pyridine cupric methoxy chloride complex (complex I) in pyridine in the presence of water (Table I, entries 24–26; eq 24, R = *tert*-butyl, H; X_2 = dipyridyl, 2py).

The above experiments with copper(II) catecholate complexes (eq 22–24; Table I, entries 20–23) corroborate the previous observations with the copper(II) catecholate complexes generated in situ (Table I, entries 13, 14), and reaffirm that the cupric methoxide/water reagent cannot convert effectively the copper(II) catecholate back to *o*-benzoquinone and cuprous hydroxide (eq 22). The formation of the polymeric material in the reaction between the copper(II) catecholate and cupric chloride (eq 23) suggests that cupric chloride can oxidize the catecholate complex to the same semiquinone radical anion that is being formed in the reaction of the *o*-benzoquinone with cuprous chloride. It is this radical anion which is then responsible for the relatively slow but irreversible formation of the polymer. The carbon–carbon bond cleavage did not occur, simply because these systems lack the active copper(II) species, presumably cupric methoxy hydroxide or its equivalent (see Scheme III), that could affect the oxidative



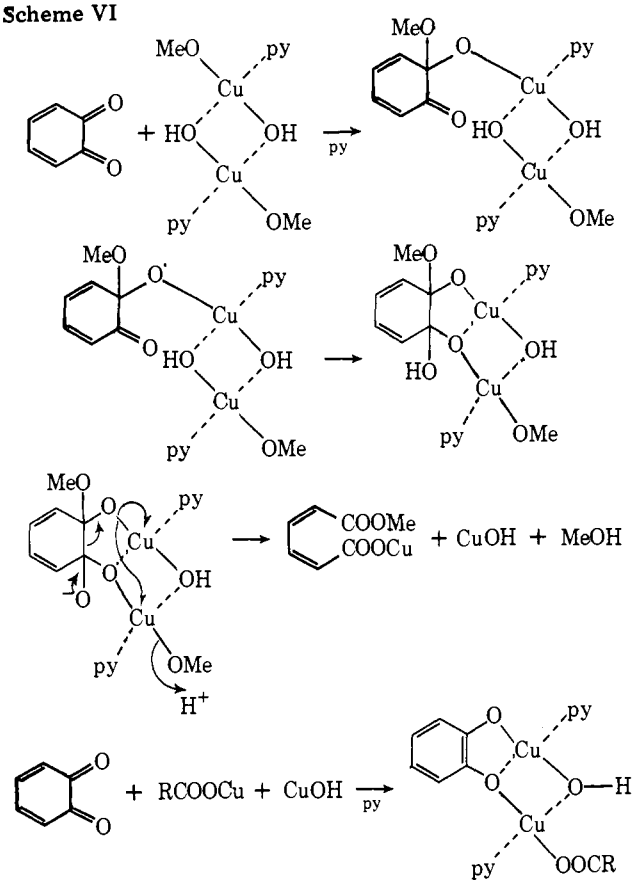
cleavage in the generated *o*-benzoquinone. However, in the reaction of the copper(II) catecholate complexes with pyridine cupric methoxy chloride in the presence of water (eq 24; Table I, entries 24–26), all the requirements for the carbon–carbon bond cleavage are met and this transformation again becomes the exclusive reaction.[85]

The experimental results presented in this section firmly establish that the active copper(II) species responsible for the carbon–carbon bond cleavage reaction can indeed be generated by reaction of cupric methoxide with water in pyridine. However, it is now evident that copper(II) catecholates can be formed as an intermediate from both catechol and *o*-benzoquinone.

In the following section we will first discuss the mechanism of the carbon–carbon bond cleavage of *o*-benzoquinone with cupric methoxide in pyridine in the presence of water; then we shall extend the discussion to the "Cu reagent"; and finally we will outline the details of the overall catechol transformation.

6. Mechanism of the Cleavage of *o*-Benzoquinone with Cupric Methoxide in Pyridine in the Presence of Water. (a) Stepwise One-Electron Oxidations. Considering the ubiquitous propensity of copper(II) toward one-electron oxidations,[86] it may be expected that carbon–carbon bond cleavage of *o*-benzoquinone would proceed by a sequence of two one-electron

Scheme VI

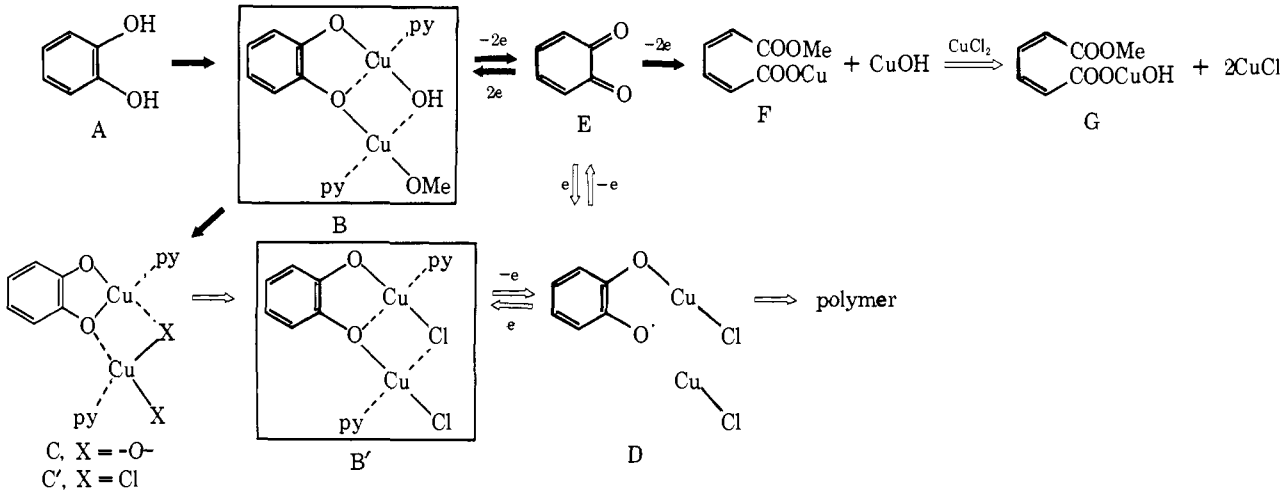


oxidations. However, the conspicuous absence of any products typical for reactions involving free-radical intermediates[87,88] raises serious doubts about such a mechanism. Most of the experimental observations can be adequately explained by an "ionic" mechanism in which the two electrons from the organic substrate are being removed in a single step by two copper(II) centers. This mechanism is considered next.

(b) A Single-Step Two-Electron Oxidation. Another ubiquitous characteristic of many copper compounds[89] is that they exist in the solid state as well as in solution, as polymers or highly clustered aggregates.[49,51-55] We have already alluded to the possibility that the active oxidant, cupric methoxy hydroxide, or its equivalent may exist in solution as methoxy hydroxy bridged dimers or oligomers in mobile equilibrium (see Scheme III). An initial interaction between cupric methoxy hydroxide dimer and *o*-benzoquinone, followed by oxidative cleavage of the carbon-carbon bond accompanied by the other bond reorganization outlined in Scheme VI, can generate directly the copper(I) salt of the muconic acid monomethyl ester, cuprous hydroxide, and methanol. The two electrons provided by the substrate in a single step are distributed between the two copper(II) centers converting them both to the copper(I) state[90,91] According to the experiment summarized in Table I, entry 19, and Scheme VI, the copper(I) salt of the muconic acid monomethyl ester together with cuprous hydroxide can then reduce the *o*-benzoquinone to the copper(II) catecholate and basic copper(II) monomethyl muconate.[79,93] This mechanism satisfactorily explains both the exclusive formation of the monoester and the concomitant conversion of the *o*-benzoquinone into copper(II) catecholate in the absence of cupric chloride. More importantly, the removal of two electrons from the organic substrate in a single step[90,91] does not violate the well-established propensity for single electron oxidations by copper(II).[86] Indeed, the copper-containing oxidase,[21] laccase,[95] which contains four copper(II) centers per molecule,[96] catalyzes the oxidation of organic substrates by removing electrons *in pairs*, accepting a total of four electrons with oxygen being fully reduced to water. It is also known that two of the four copper(II) centers in the fully oxidized laccase molecule, similarly to the cupric methoxide/water system in pyridine, exist as an "EPR-nondetectable copper(II) pair".[95,97,103] The absence of an EPR signal in this case was also attributed to a total antiferromagnetic coupling of the unpaired spins on the two adjacent copper(II) centers.[95,97,98]

(c) The Role of Cupric Chloride in the Cleavage of the Carbon–Carbon Bond of *o*-Benzoquinone. Earlier discussion established that the carbon-carbon bond cleavage of *o*-benzoquinone with cupric methoxide/water in pyridine is followed by a rapid competing reduction of *o*-benzoquinone by copper(I) species produced in the cleavage reaction providing the corresponding copper(II) catecholate complex (Scheme V). It should also be remembered that bispyridine cupric chloride alone in pyridine (with and without added water or methanol) is inactive in cleaving the carbon-carbon bond in both catechol and *o*-benzoquinone. The experimental results summarized in Table I suggest that the main role of cupric chloride in the oxidation of *o*-benzoquinone with the "Cu reagent" is to scavenge cuprous hydroxide (or cuprous oxide) and the copper(I) salt of the monoalkylmuconate as they are generated in the cleavage reaction, and to form an innocuous mixture of cuprous chloride and basic copper(II) monomethylmuconate. This interpretation is summarized in Scheme VII. (The black arrows indicate transformations with cupric methoxy hydroxide dimer or copper(I)-oxygen species, and the white ones represent transformations induced by cupric chloride or cuprous chloride.)

Scheme VII



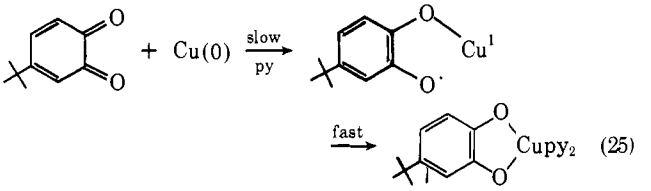
Reaction between *o*-benzoquinone E and cupric methoxy hydroxide or the corresponding dimer, according to the mechanism discussed earlier (Scheme VI), provides copper(I) monomethyl muconate F and cuprous hydroxide (or cuprous oxide). A direct transfer of a pair of electrons from the two generated copper(I) centers (Schemes IV, V) would generate dicopper(II) catecholate intermediate B,[99] which could either return to E or irreversibly collapse[100,101] to copper(II) catecholate complex with cupric methoxy hydroxide C. Reaction between catechol A and dimeric cupric methoxy hydroxide affords again the same dicopper(II) catecholate intermediate B. In this case, however, the net forward reaction is not as efficient as when the substrate was *o*-benzoquinone itself, mainly owing to the parallel but irreversible transformation of the intermediate B into the copper(II) catecholate complex C.

Reaction of copper(II) catecholate with cupric chloride (C′) appears to give irreversibly the dicopper(II) catecholate intermediate B′ (Scheme VII, X = Cl). The reaction of *o*-benzoquinone with cuprous chloride under kinetic conditions leads to the reversible formation[102] of the same intermediate B′. Under thermodynamic conditions both of these reactions provided the same polymer. Presumably, a rapid one-electron transfer from the substrate to one of the copper(II) centers in the intermediate B′ produces the corresponding semiquinone radical anion D, the same intermediate that is being produced by a single-electron reduction of *o*-benzoquinone by cuprous chloride. Under thermodynamic conditions this radical intermediate undergoes a relatively slow but irreversible polymerization.

When, on the other hand, the reaction of either catechol, *o*-benzoquinone, or copper(II) catecholate is being carried out with the active "Cu reagent", e.g., pyridine cupric methoxy chloride complex I in the presence of water, the carbon–carbon bond cleavage reaction becomes exclusive (Table I, entries 24–26). Clearly, the generated active reagent (see Scheme III) now effectively converts the entire *o*-benzoquinone E into the cleavage product F, regardless of whether the *o*-benzoquinone was produced directly from the intermediate B, and hence from catechol A, or from the intermediate B′ and hence from copper(II) catecholate and cupric chloride (C′). In addition to transforming the otherwise stable copper(II) catecholate into the reaction intermediate B′, cupric chloride also acts as an efficent oxidizing agent for converting the copper reduced species generated in the carbon–carbon bond cleavage reaction into cuprous chloride. The cuprous chloride remains innocuous in the present system as long as there is the active copper(II) reagent that can cleave the intermediate *o*-benzoquinone before the thermodynamically controlled formation of polymer via D intervenes. Thus, in effect, by converting the reduced forms of copper into cuprous chloride and basic copper(II) monomethylmuconate G, cupric chloride suppresses the side reactions that would otherwise result from the reduction of the *o*-benzoquinone intermediate E.

The flow of electrons in pairs or singly in rapid succession between the substrate and the attacking copper dimer in the intermediate B, in which the copper(II) centers are held together effectively by the bridging oxygen ligands, is essentially simultaneous.[90,91] Thus, the radical anion intermediate D is by-passed and the side reaction leading to polymeric materials suppressed. On the other hand, the electron transfer between the organic substrate and copper(II) centers in the intermediate B′ occurs in a stepwise manner.[103] The radical anion intermediate D, formed by one-electron transfer, then under thermodynamic conditions can undergo slower but irreversible polymer formation.

(d) Possibilities for a Single-Step Two-Electron Oxidation with a Monomeric Copper(II) Reagent. As a further illustration of the complex chemistry in the present system, we found that 4-*tert*-butyl-1,2-benzoquinone readily undergoes reduction with copper(0) in pyridine to give the copper(II) catecholate pyridine complex (eq 25).



(25)

The question now arises whether the oxidation of catechol to *o*-benzoquinone can also take place by a similar two-electron oxidation with formation of copper(0). Moreover, is it possible that even the carbon–carbon bond cleavage of *o*-benzoquinone involves a similar two-electron oxidation with the generation of copper metal, rather than the previously discussed mechanism in which two copper(II)s are reduced to the copper(I) state?

We have established that bispyridine cupric chloride in pyridine readily oxidizes copper(0) to give stable solutions of cuprous chloride, but the corresponding reaction does not take place between cupric methoxide and copper(0), or between cupric *tert*-butoxide and copper(0) as indicated by the recovery of unchanged copper metal. Cuprous *tert*-butoxide in pyridine

$$py_2CuCl_2 + Cu(0) \xrightarrow[py]{} 2pyCuCl$$

$$Cu(OMe)_2 + H_2O + Cu(0) \xrightarrow[py]{\not\rightarrow} CuOH + CuOMe + MeOH$$

$$Cu(OBu\text{-}t)_2 + Cu(0) \xrightarrow[py]{\not\rightarrow} 2CuOBu\text{-}t$$

failed to disproportionate to copper metal and cupric *tert*-butoxide over a period of several hours. Clearly, the absence of any reaction between copper metal and cupric methoxide, cupric *tert*-butoxide, and cupric hydroxide does not reflect the thermodynamic stabilities of the copper(II) and the corresponding copper(I) species in pyridine solution.[45,46] These copper(II) systems appear to be stable in pyridine because each is polymeric and virtually insoluble in this solvent. Thus, the possibility that the previously discussed reduction of *o*-benzoquinone by cuprous hydroxide or cuprous muconate could actually involve a prior, thermodynamically controlled disproportionation of the copper(I) species to copper(II) and copper(0), which then reduces the *o*-benzoquinone, has to be considered unlikely.

Similarly, the fact that 4-*tert*-butylcatechol reacts rapidly with cuprous *tert*-butoxide in pyridine to form copper(II) catecholate complex and copper(0) in the absence and in the presence of water is most reasonably explained by formation of a dicopper(I) catecholate which then undergoes disproportionation to give copper(II) catecholate and copper(0).

One cannot unequivocally disprove a two-electron transformation involving a single copper species, but all the available experimental observations strongly suggest that the active copper(II) species in the present system do not operate by this mechanism.

Conclusion

For the first time it has been demonstrated conclusively that the cleavage of the carbon–carbon bond in catechol and *o*-benzoquinone can be brought about by a particular copper(II) reagent in the absence of molecular oxygen. The overall transformation of catechol to *cis,cis*-muconic acid monomethyl ester involves a two-electron oxidation of catechol to *o*-benzoquinone, followed by a second two-electron oxidation of the *o*-benzoquinone to the muconic acid ester. The active cop-

per(II) species can be generated by reaction of cupric methoxide with water in pyridine and is equivalent to a dimeric cupric methoxy hydroxide complexed with pyridine. The oxidation agent ("Cu reagent") can also be generated either by reaction of cuprous chloride with oxygen in pyridine in the presence of methanol, by reaction of an alcohol with a product mixture of the oxidation of cuprous chloride in pyridine, or by addition of 1 molar equiv of water to any of the following reagents: to cupric methoxy chloride in pyridine, to pyridine cupric methoxy chloride (complex I) in pyridine, to a mixture of cupric methoxide and cupric chloride in pyridine, or to a mixture of cupric methoxide and pyridine hydrochloride in the same solvent. It appears that all methods provide the same active oxidation agent that exists in pyridine as a mixture of bispyridine cupric chloride and dimeric, olygomeric, or polymeric cupric methoxy hydroxide in eqilibrium with each other. During the reaction the active copper(II) agent is being reduced to copper(I) muconate ester and cuprous hydroxide, which under the reaction conditions can efficiently reduce the intermediate *o*-benzoquinone to the copper(II) catecholate complex that resists further oxidation. However, this undesirable reduction is prevented by the cupric chloride which scavenges cuprous muconate and cuprous hydroxide in situ and converts them into an innocuous mixture of basic cupric muconate and cuprous chloride. In other words, the electrons provided by catechol and *o*-benzoquinone are transferred first to the active copper(II) agent from where, eventually, they could be transported to their ultimate destination, molecular oxygen. In the absence of molecular oxygen the flow of electrons from the organic substrate stops at the copper stage which at the end of the reaction cycle exists in copper(I) state. In the presence of oxygen the electrons continue to flow from the copper(I) centers to the molecular oxygen thus providing thermodynamically stable copper(II)–oxygen species, which are ready to reenter the reaction cycle and accept another set of electrons from the organic substrate.

Since the active copper(II) species rather than molecular oxygen act as electron acceptor in these transformations, and since the final transfer of electrons to molecular oxygen occurs from generated copper(I) species, a direct reaction between oxygen and organic substrate does not take place. Consequently, it is now clear that in the present system overall oxidation of organic substrate does not require a special mechanism for the activation of molecular oxygen. We have only briefly mentioned that phenol also undergoes overall oxidative carbon–carbon bond cleavage with the active copper(II) agent in the presence of molecular oxygen, but at a much slower rate. Discussion of this particular transformation, as well as the discussion of the reaction of pyridine cupric methoxy chloride with catechols and *o*-benzoquinones under anaerobic and anhydrous conditions, will be presented in a subsequent paper.

Experimental Section

Catechol and 4-*tert*-butylcatechol were commercial products which were purified by crystallization and stored under dry and inert atmosphere. 4-*tert*-Butyl-1,2-benzoquinone was prepared by oxidation of the catechol by the literature procedure[104] and was stored in a refrigerator under nitrogen. Pyridine and methanol were freshly distilled before use, and other alcohols were purified similarly. Cuprous chloride was a commercial product which was prereduced by sulfurous acid according to the standard literature procedure.[105] Cupric chloride was an anhydrous commercial product and reaction with pyridine gave bispyridine cupric chloride. Cupric methoxide[44,51] was prepared by reaction of cupric chloride with lithium methoxide in methanol and stored in a drybox. Cuprous *tert*-butoxide was prepared by reaction of lithium *tert*-butoxide with cuprous chloride in tetrahydrofuran and purified by sublimation.[77] Cupric methoxy chloride[39e] was prepared by reaction of cuprous chloride with oxygen in methanol; pyridine cupric methoxy chloride was prepared by (1) reaction of cupric methoxy chloride with pyridine,[39e] (2) reaction of bispyridine cupric chloride with cupric methoxide in methanol,[39e] or (3) reaction of cupric methoxide with pyridine hydrochloride in pyridine. Alternatively, reaction of cuprous chloride with oxygen in methanol containing a slight excess of pyridine also gave the pyridine cupric methoxy chloride complex.[39e]

The reported melting points are uncorrected. GLC analyses were generally carried out on a Hewlett-Packard 5700A instrument using 3- or 6-ft columns of either 10% SE-30 or 10% Carbowax 20M columns packed on Chromosorb W. ^{1}H NMR spectra were recorded on either a Varian A-60 or Varian T60-A 60-MHz or HA-100 MHz instrument, while ^{13}C NMR spectra were measured on a Varian CFT-20 instrument using tetramethylsilane as an internal standard. EPR spectra were taken on a Varian E-12 EPR spectrometer. Routine chemical ionization mass spectra were obtained on a Finnigan 3100D mass spectrometer, while high-resolution mass spectra were obtained on an AEI M.S. 902 instrument.

Oxidation of Catechol to *cis,cis*-Muconic Acid Monomethyl Ester (1). (a) With "Reagent A" in the Presence of Oxygen. A three-neck 500-ml flask equipped with a mechanical stirrer, an addition funnel, and an inlet attached to a gas buret was charged with 5.93 g (60 mmol) of purified cuprous chloride, 2.4 g (75 mmol) of methanol, and 60 mL of pyridine under a blanket of nitrogen. After flushing with oxygen *without stirring*, the system was exposed to the oxygen in the buret and the mechanical stirrer was started. Oxygen uptake ceased after 1 equiv (15 mmol) was consumed, and the resulting green, heterogeneous mixture is referred to as "reagent A". The addition funnel was charged with a solution of catechol (1.10 g, 10 mmol) in pyridine (20 mL) and methanol (0.5 mL). This solution was added dropwise to the reagent A under oxygen over a 60-min period. The rate of oxygen consumption roughly paralleled the rate of addition of catechol with oxygen uptake stopping after ca. 10 mmol was consumed. The reaction mixture was evaporated to dryness and the yellow-brown solid residue was hydrolyzed with dilute hydrochloric acid in chloroform under nitrogen. Drying and evaporation of the chloroform solution afforded the *cis,cis*-muconic acid monomethyl ester (**1**), mp 80–80.5 °C, in an 80–85% yield.[57]

(b) With "Reagent B" in the Presence of Oxygen. The reaction of cuprous chloride with oxygen was carried out in pyridine as above except that the pyridine solution did not contain methanol. After the equivalent amount of oxygen was introduced (15 mmol), further oxygen uptake ceased. To the yellow-brown, heterogenous mixture, 2.4 g of methanol (75 mmol) was added and the resulting "reagent B" was then used in the reaction with catechol and oxygen as above. Similar workup provided an identical yield of the acid ester **1** as in the previous experiment.

(c) With "Reagent C" in the Presence of Oxygen. The "reagent C" was prepared in the same reaction flask as above by adding water (0.5 g, ca. 30 mmol) to a solution of 12.50 g (60 mmol) of pyridine cupric methoxy chloride (complex I) in pyridine (120 mL). The reaction with catechol was then carried out under oxygen and when oxygen uptake ceased (ca. 10 mmol) the reaction mixture was worked up as above. The yield of the monomethyl ester **1** was identical with that in the previous two experiments.

***cis,cis*-Muconic Acid Monoethyl Ester.**[57] The reaction of cuprous chloride with oxygen in pyridine in the presence of *ethanol* also provided a "reagent A" which reacted with catechol under oxygen to give *cis,cis*-muconic acid monoethyl ester, mp 101–102 °C, in 63% yield: NMR ($CDCl_3$) δ 9.98 (bs, 1 H, $-CO_2H$), 8.05 (t, $J \simeq 11$ Hz, 1 H, $-CH{=}CHCO_2H$) overlapping with 7.86 (t, $J \simeq 11$ Hz, 1 H, $-CH{=}CHCO_2Et$), 6.06 ("d", $J \simeq 9$ Hz, 2 H, $C{=}CHCO_2-$), 4.26 (q, $J = 7$ Hz, 2 H), 1.32 (t, $J = 7$ Hz, 3 H); IR (KBr) 2800–2400 ($-CO_2H$), 1720 (conjugated –COOR), 1693 (conjugated $-CO_2H$), 1585 (conjugated C=C), 1245, and 1180 cm^{-1}; UV ($CHCl_3$) 262 nm (ϵ 22 200).

Anal. ($C_8H_{10}O_4$) C, H.

***cis,cis*-Muconic Acid Mono-*n*-butyl Ester.**[57] Oxidation of catechol as above with the "reagent A" prepared with *n*-butyl alcohol instead of methanol provided the *cis,cis*-muconic acid mono-*n*-butyl ester, mp 54.5–56 °C, in 73% yield.

Anal. ($C_{10}H_{14}O_4$) C, H.

Muconic Acid Monoisopropyl Esters (Mixture of Double Bond Isomers).[57] Oxidation of catechol as above with the "reagent A" prepared with isopropyl alcohol gave the muconic acid monoisopropyl esters, mp 51–71 °C, in 26% yield: NMR ($CDCl_3$) δ 11.52 (s, 1, $-CO_2H$), 8.05 (t, $J = 11.2$ Hz, 1 H, $-CH{=}CCOOR$), 7.84 (t, $J =$

11.2 Hz, 1 H, -CH=CCOOR), 6.01 (d, J = 10.5 Hz, 2 H, =$CHCO_2$-), 5.12 (septet, J = 6.5 Hz, 1 H, $CH(CH_3)_2$), 1.29 (d, J = 6.5 Hz, 6 H, $(CH_3)_2C$) (cis,trans isomer(s) noted as minor absorption at δ 8.4, 6.8, 6.1, and 5.2); ^{13}C NMR ($CDCl_3$) δ 170.91 and 170.7 (-CO_2H), 165.15 and 165.8 (-CO_2R), 140.23 and 142.86 (d, -CH=$CHCO_2H$), 137.06 and 137.94 (d, -CH=$CHCO_2R$), 125.81 and 130.61 (d, =$CHCO_2H$), 122.97 and 123.5 (d, =$CHCO_2R$), 68.16 and 68.47 (d, $CH(CH_3)_2$), 21.86 (q, $CH(CH_3)_2$). The second of each of the pairs of chemical shifts is due to the minor double bond isomer.

Anal. ($C_9H_{12}O_4$). C, H.

The same monoalkyl esters were also prepared in a similar yield by carrying out the oxidation of cuprous chloride in neat pyridine and then adding the alcohol to the resulting pyridine product mixture, followed by addition of catechol in the presence of oxygen.

4,5-Dimethoxy-1,2-benzoquinone. The preparation of the "reagent A" was carried out as above using the same quantities of cuprous chloride, methanol, and pyridine. The dark green heterogenous mixture was filtered and the collected blue solid, 3.05 g, was identified as bispyridine cupric chloride by IR and x-ray diffraction. A sample of pure bispyridine cupric chloride (5.85 g, 20 mmol) was suspended in pyridine (100 mL) containing methanol (1 mL) in a 250-mL three-neck flask equipped with mechanical stirrer, addition funnel, and an inlet attached to an oxygen buret. A solution of catechol (1.10 g, 10 mmol) in pyridine (20 mL) and methanol (1 mL) was added to the copper reagent under oxygen with stirring. After 18 h 11-12 mmol of oxygen was consumed and the red mixture was evaporated and hydrolyzed with 20% aqueous hydrochloric acid (2 × 100 mL) in the presence of methylene chloride at 0 °C. The combined organic layers were dried and evaporated to give 0.75 g of yellow-brown solid shown to be ca. 80% pure 4,5-dimethoxy-1,2-benzoquinone by comparison of the NMR spectrum with that of an authentic sample.[106] The other minor products were not identified.

The pyridine solution remaining after filtration of the bispyridine cupric chloride from the "reagent A" (see above) was reacted with catechol (1.10 g, 10 mmol) in pyridine (20 mL) and methanol (1 mL) in the presence of oxygen as above. When the oxygen uptake ceased, the reaction mixture was worked up as above to give the muconic acid monomethyl ester (**1**) in ca. 80% yield.

Reaction of 4-*tert*-Butylcatechol with the "Reagent A" in the Presence of Oxygen. The preparation of the "reagent A" was carried out as above by the oxidation of cuprous chloride (1.98 g, 20 mmol) in pyridine (40 mmol), containing methanol (1 mL). A solution of 4-*tert*-butylcatechol (1.66 g, 10 mmol) in pyridine (20 mL) and methanol (1.0 mL) was then added dropwise over 90 min under oxygen with stirring. The rate of the oxygen uptake roughly paralleled the rate of addition of the catechol solution and ceased after ca. 11 mmol reacted. The reaction mixture was worked up as above to give 2.27 g of amber oil whose GC and 60-Hz NMR spectrum clearly revealed two major components, 3-*tert*-butylmuconic acid monomethyl ester (**2**, 55%) and 4-*tert*-butylmuconic acid monomethyl ester (**3**, 40%). Column chromatography (Sephadex-LH-20/methyl acetate) provided the major isomer **2**: mp 75-76 °C (pentane/methylene chloride); NMR ($CDCl_3$) δ 1.40 (b, 1 H, OH), 6.87 (dd, J = 12.5, 2.0 Hz, 1 H, cis CH=CHCO-), 6.02 (d, J = 12.5 Hz, 1 H, cis CH=CHCO-), 5.85 (d, J = 2.0 Hz, 1 H, =CHCO-) 3.67 (s, 3 H, -OCH_3), and 1.15 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 170.56 (s, -CO_2H), 166.92 (s, -$COOCH_3$), 162.41 (s, $CC(CH_3)_3$), 144.35 (d, -CH=$CHCO_2H$), 121.29 (d, =$CHCO_2H$), 114.65 (d, =$CHCO_2CH_3$), 51.21 (q, -OCH_3), 37.86 (s, $C(CH_3)_3$), 29.14 (q, $C(CH_3)_3$); IR (Nujol) 3200-3230 (b, -CO_2H), 1735 (s, RCO_2CH_3), 1692 (s), 1640 (bs), 1350, 1260, 1235, and 1200 cm^{-1}.

Anal. ($C_{11}H_{16}O_4$) C, H.

The minor isomer **3** was not isolated in analytically pure state:[107] NMR ($CDCl_3$) δ 10.97 (bs, CO_2H, 1 H), 7.57 (dd, J_{23} = 16.8, J_{35} = 1.5 Hz, trans CH=CHCOOMe, 1 H), 5.87 (d, J_{23} = 16.8 Hz, trans CH=CHCOOMe, 1 H), 5.82 (d, J_{35} = 1.5 Hz, C=CHCOOH, 1 H), 3.77 (s, OCH_3, 3 H), 1.13 (s, $C(CH_3)_3$, 9 H).

The crude mixture of **2** and **3** on standing, or during attempted chromotography on silica gel, underwent lactonization to give the corresponding ester lactones **4** and **5**.

5-Carbomethoxymethyl-5-*tert*-butyloxacyclopent-3-en-2-one (4), an oil obtained by column chromatography, (silica gel/$CHCl_3$-EtOAc, 9:1), was evaporatively distilled to give an analytical sample: bp 105-108 °C (0.04 mm); 100-MHz NMR ($CDCl_3$) δ 7.58 (d, J_{34} = 5.9 Hz, CH=CHCOO, 1 H), 6.10 (d, J_{34} = 5.9 Hz, =CHCOO, 1 H), 3.64 (s, OCH_3, 3 H), 2.95 (q, CH_2COOCH_3, 2 H), 1.01 (s, $C(CH_3)$, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.11 (s, COO-), 169.61 (s, CO_2CH_3), 156.84 (d, CH=CCOO), 122.23 (d, =CHCOO-), 92.49 (s, $CC(CH_3)_3$), 51.99 (q, OCH_3), 38.16 (s, $C(CH_3)_3$), 37.75 (t, CH_2COOCH_3), 25.42 (q, $C(CH_3)_3$); IR (neat) 3140, 1780-1730, 1610 cm^{-1}.

Anal. ($C_{11}H_{16}O_4$) C, H.

5-Carbomethoxymethyl-4-*tert*-butyloxacyclopent-3-en-2-one (5), after separation by column chromatography (silica gel/$CHCl_3$-EtOAc, 9:1), was further purified by bulb-to-bulb distillation: bp 105-108 °C (0.04 mm); 100-MHz NMR ($CDCl_3$) δ 5.91 (d, $J_{35} \simeq$ 1.7 Hz, C=CHCOO, 1 H), 5.46 (ddd, J_{ac} = 9.2, J_{bc} = 3.2, J_{3c} = 1.7 Hz, $OCH_cCH_aH_b$-, 1 H), 3.77 (s, 3 H, OCH_3), 3.08 (dd, J_{bc} = 3.2, J_{ab} = 16.0 Hz, 1 H, $OCH_cCH_aH_b$), 2.54 (dd, J_{ab} = 16.0, J_{ac} = 9.2 Hz, $CH_cCH_aH_b$-, 1 H), 1.26 (s, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 179.41 (s, -COO), 153.26 (s, CO_2Me), 124.14 (s, $CC(Me)_3$), 116.14 (d, =CHCOO), 79.33 (d, -CHO-), 52.18 (q, OCH_3), 38.52 (t, CH_2COOMe), 33.63 (s, $C(CH_3)_3$), 29.45 (q, $C(CH_3)_3$); IR (neat) 1780-1740, 1630, 1445, 1380, 1190 cm^{-1}; ^{13}C NMR (CCl_4) 1776 (s, lactone C=O), 1748 (ester C=O), 1625 cm^{-1} (w, C=C).

Anal. ($C_{11}H_{16}O_4$) C, H.

3,10-Di-*tert*-butyl-1,5-dihydroxytricyclododeca-3,9-diene-7,8,-11,12-tetraone. The crude, oily product mixtures resulting from several oxidations of 4-*tert*-butylcatechol were combined and treated with methylene chloride to redissolve the half esters **2** and **3**. The insoluble, white, powdery material, mp 224-226 °C, was filtered off and tentatively identified as a dimer of 5-*tert*-butyl-3-hydroxy-1,2-benzoquinone with the following properties: 100-MHz NMR (Me_2SO-d_6) δ 6.78 (s, OH, 2 H), 6.36 (d, J = 1.7 Hz, -CH=, 2 H), 3.72 (d, J = 1.7 Hz, CHCO, 2 H), 1.12 (s, $C(CH_3)_3$, 18 H); ^{13}C NMR (Me_2SO-d_6) δ 199.83 (s, HOCC=O), 195.06 (s, -CHCO-), 171.44 (s, $(CH_3)_3CC$=), 126.16 (d, -C=CH-), 87.51 (s, -COH-), 59.58 (d, -CHCO-), 37.60 (s, $C(CH_3)_3$), 29.63 (q, CH_3); IR (KBr) 3370 (s, OH), 1757 (s), 1678 (s), 1598 (m), 1400, 1370, and 1365 (*t*-Bu), 1175, 1157, and 867 cm^{-1}; mass spectrum CI (methane) MH^+ at m/e 361 and 181 (monomer + H^+).

Anal. ($C_{20}H_{24}O_6$) C, H.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with "Reagent A" in the Presence of Oxygen. Reaction of cuprous chloride (2.96 g, 30 mmol) with oxygen (7.5 mmol) in pyridine (60 mL) containing methanol (1.2 g, 38 mmol) as above gave the "reagent A". Addition of a solution of 4-*tert*-butyl-1,2-benzoquinone (1.64 g, 10 mmol) in pyridine (20 mL) and methanol (1.0 mL) to the stirred "reagent A" under oxygen over 45 min resulted in consumption of the required amount of oxygen (ca. 5 mmol). The product mixture was isolated as before to give essentially the same yield of the half esters **2** and **3** as obtained in the reaction with 4-*tert*-butylcatechol.

Reaction of Phenol with "Reagent A" in the Presence of Oxygen. The preparation of "reagent A" was carried out as described for the reaction with catechol above. A phenol solution (0.94 g, 10 mmol) in pyridine (10 mL) was added to the "reagent A" dropwise under oxygen. The oxygen uptake was very slow and the complete reaction (15 mmol of oxygen) required about 24 h. Workup as above gave the monomethyl ester **1** in 50-60% yield.

Reaction of Catechol with Copper(II) Reagents in the Absence of Oxygen. (a) With "Reagent A". The preparation of "reagent A" was carried out as before using purified cuprous chloride[105] (5.93 g, 60 mmol) in a three-neck 500-mL flask equipped with a mechanical stirrer, an addition funnel, and an inlet attached to a gas buret or a vacuum line. This mixture was then freeze-pump-thaw degassed three times under nitrogen or argon. A similarly degassed solution of catechol (1.10 g, 10 mmol) in pyridine (20 mL) and methanol (1 mL) was added dropwise from the addition funnel under anaerobic conditions. After complete addition (15-30 min) the reaction mixture was stirred for an additional 15-30 min and then evaporated. The yellow-brown solid residue was hydrolyzed with dilute hydrochloric acid in the presence of chloroform at 0 °C under nitrogen. Drying and evaporation of the chloroform solution afforded *cis,cis*-muconic acid monomethyl ester (**1**) in essentially the same yield as when the reaction was carried out in the presence of oxygen (above).

(b) With "Reagent B". "Reagent B" was prepared as described earlier and then degassed and the reaction with catechol carried out as above. The monomethyl ester **1** was obtained in ca. 80% yield.

(c) With "Reagent C". The same reaction flask as above was charged with pyridine cupric methoxy chloride complex I (6.26 g, 30 mmol) and a solution of methanol (0.3 mL) and water (0.27 g, ca. 15 mmol)

in pyridine (60 mL). The green suspension was then freeze–pump–thaw degassed three times under nitrogen or argon. A similarly degassed solution of catechol (0.55 g, 5 mmol) in pyridine (10 mL) and methanol (0.5 mL) was added dropwise from the addition funnel at room temperature. Following similar reaction conditions and workup the yield of methyl ester **1** was the same as in the preceding experiments.

Reaction of 4-*tert*-Butylcatechol with "Reagent C" in the Absence of Oxygen. As in the preceding experiment the "reagent C" was prepared from 6.26 g (30 mmol) of the complex I and water (0.27 g, ca. 15 mmol) in pyridine/methanol. Addition of 4-*tert*-butylcatechol (0.83 g, 5 mmol) to the degassed "reagent C" under anaerobic conditions, followed by standard workup, gave a mixture of the isomeric 3- and 4-*tert*-butylmuconic acid monomethyl esters **2** and **3** in 55 and 40% yield, respectively.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with "Reagent C" in the Absence of Oxygen. Essentially the same results were obtained when the reaction was carried out with 4-*tert*-butyl-1,2-benzoquinone (0.82 g, 5 mmol) and the "reagent C" prepared from the complex I (3.14 g, 15 mmol) as in the preceding experiment.

Reaction of 4-*tert*-Butylcatechol with Pyridine Cupric Methoxy Chloride under Anaerobic and Anhydrous Conditions. A three-neck 1000-mL flask equipped with a mechanical stirrer, addition funnel, and nitrogen inlet was charged with 56 g (0.268 mol) of complex I and 500 mL of pyridine. This mixture was degassed three times and a solution of 4-*tert*-butylcatechol (7.40 g, 44 mmol) in degassed pyridine (90 mL) and methanol (7 mL) was then added dropwise over 90 min with stirring under a nitrogen atmosphere. The stirring was continued for an additional 60 min and the solvent was removed under reduced pressure. The remaining brown oily material was extracted with pentane (4 × 500 mL) and the combined extracts were concentrated to give 7.20 g (64%) of **6** as a brown oil. This material was evaporatively distilled to give 5.65 g (50%) of 2,2-dimethoxy-6-carbomethoxy-4-*tert*-butyloxacyclohexa-3,5-diene (**6**): bp 100 °C (0.06 mm); NMR ($CDCl_3$) δ 6.55 (d, J = 1.8 Hz, CH=CO–, 1 H), 5.37 (d, J = 1.8 Hz, C*H*=CC(CH_3)$_3$, 1 H), 3.82 (s, CO_2CH_3, 3 H), 3.32 (s, C(OCH_3)$_2$, 6 H), 1.15 (s, C(CH_3)$_3$, 9 H); ^{13}C NMR ($CDCl_3$) δ 162.57 (s, *C*O_2CH_3), 148.28 (s, *C*CO_2CH_3), 142.96 (s, *C*C(CH_3)$_3$), 114.73 (s, –*C*(O)$_3$), 112.38 (d, *C*H=CCO_2CH_3), 106.95 (d, *C*HC(O–)$_3$), 52.30 (q, COO*C*H_3), 50.19 (q, CO*C*H_3), 33.97 (s, *C*(CH_3)$_3$), 28.76 (q, C(*C*H_3)$_3$): IR (neat) 2875 (OCH_3), 1730 (s, CO_2CH_3), 1655 (s, C=CO), 1590 (w), 1443, 1330, 1290, 1255, 1100 cm^{-1}; UV (MeOH) λ_{max} 286 nm (ϵ 8900); mass spectrum CI (methane) MH$^+$ at *m/e* 257.

Anal. ($C_{13}H_{20}O_5$) C, H.

6-Carbomethoxy-4-*tert*-butyloxacyclohexa-3,5-dien-2-one (7). The ortho ester **6** (0.5 g) was dissolved in 10 mL of chloroform containing 1 mL of water and a catalytic amount of concentrated hydrochloric acid. After stirring for 15 min, an excess of sodium bicarbonate was added, the solution filtered, and the solvent evaporated to dryness to give 0.44 g of **7**: mp 84–85 °C (100% yield); 100-MHz NMR ($CDCl_3$) δ 7.21 (d, J = 1.8 Hz, CH=CO–, 1 H), 6.42 (d, J = 1.8 Hz, C=CHCO–, 1 H), 3.97 (s, CH_3O–, 3 H), 1.27 (s, C(CH_3)$_3$, 9 H); IR (CCl_4) 2970, 1755 (s), 1736 (s, CO_2R), 1730 (s), 1643 (w), 1438, 1335, 1272, 1253, 1112 cm^{-1}; UV (MeOH) λ_{max} 297.5 nm (ϵ 6343), 206.5 (19 272); mass spectrum CI (methane/ammonia) MH$^+$ at *m/e* 211.

Anal. ($C_{11}H_{14}O_4$) C, H.

Reaction of the Lactone Ester 7 with Maleic Anhydride. The lactone ester **7** (0.5 g) was mixed with an excess of maleic anhydride (3.5 g) and sealed in a heavy-wall glass tube. The glass ampule was then heated at 150 °C overnight, cooled in dry ice, and opened. Crystallization from acetone/chloroform gave 0.55 g of the bis adduct **8**: mp 326–329 °C (70% yield); NMR ($(CD_3)_2CO$) δ 6.57 (d, J = 1.9 Hz, –CH=, 1 H), 4.4–3.84 (m, methine H's) + 3.97 (s, OCH_3) (total 8 H), 1.03 (s, C(CH_3)$_3$, 9 H); ^{13}C NMR ($(CD_3)_2CO$) δ 171.01 and 170.20 (2 s, 4C, *COOCO*), 169.48 (s, *C*O_2CH_3, 1 C), 154.02 (s, *C*C(CH_3)$_3$), 121.23 (d, –CH=), 52.82 (q, OCH_3), 47.64 and 44.96 (2 d, –CO*C*C*C*O–, 4 C), 33.78 (s, *C*(CH_3)$_3$), 28.53 (q, C(*C*H_3)$_3$) (the bridgehead carbon attached to the carbomethoxy group was not detected); IR (Nujol) 1860 (m) and 1790 (s, anhydride), 1740 (s, COOR), 1225, 1090, 950, 935 cm^{-1}; mass spectrum CI (methane/ammonia) MH$^+$ at *m/e* 363.

Anal. ($C_{18}H_{18}O_8$) C, H.

Reaction of Cuprous Chloride with Oxygen in Pyridine in the Presence of an Excess of Copper Metal. A three-neck 50-mL flask equipped with a magnetic stirring bar and an inlet attached to an oxygen buret was charged with 0.268 g (2 mmol) of anhydrous cupric chloride and 0.635 g (10 mmol) of 99.9999% pure copper metal powder.[108] Addition of dry pyridine (25 mL) under nitrogen resulted in formation of a yellow-olive solution, indicating that the cupric chloride was reduced by copper metal to cuprous chloride. The connecting stopcock in the oxygen buret was opened, the magnetic stirrer started, and the reaction with oxygen begun. After 4 h the theoretical amount of oxygen was consumed (ca. 5 mmol). The resulting pyridine solution was evaporated to dryness to give an amorphous olive-black solid containing pyridine. Unfortunately, elemental analysis indicated nonstoichiometric Cu/pyridine ratio, and the spectrum revealed only pyridine bands. However, the Raman spectrum clearly showed that the previously reported[70] peroxide absorption at 856 mm was not present. The EPR spectrum of the solid as well as of the original pyridine solution indicated the presence of small amounts of bispyridine cupric chloride suggesting that the remaining copper–oxygen species exist in an EPR-undetectable antiferromagnetically coupled copper(II) state.[70,72]

Reaction of Cuprous Chloride with Oxygen in Pyridine Containing Methanol (Visible Spectrum). A solution of cuprous chloride (0.128 g, 1.3 mmol) in dry pyridine (40 mL) containing methanol (0.042 g, 1.3 mmol) was exposed to anhydrous oxygen with stirring. After oxygen uptake ceased, the homogeneous solution ("reagent A") was transferred via syringe into the spectrophotometer cell and the spectrum was recorded as a function of time. The results are summarized in Figure 4.

Reaction of Pyridine Cupric Methoxy Chloride (Complex I) with Water. To a solution of the complex I (0.209 g, 1 mmol) in 40 mL of pyridine, water was added (0.009 g, 0.5 mmol) and the visible spectrum of the resulting homogenous solution, "reagent C", was recorded as a function of time. The spectrum was essentially identical with that of the "reagent A" above (Figure 4).

Reaction of Cupric Methoxide with Cupric Chloride in Pyridine in the Presence of Water. A mixture of cupric methoxide (0.125 g, 1 mmol), cupric chloride (0.134 g, 1 mmol), and water (0.018 g, 1 mmol) was dissolved in 80 mL of pyridine and the visible spectrum of the resulting homogenous solution recorded as before. Within experimental error the spectrum was indistinguishable from those of the "reagents A" and "C" above (Figure 4).

Reaction of Catechol with Cupric Methoxide/Water in Pyridine. Typical Reaction Procedure. A 200-mL Airless-ware[109] flask equipped with a magnetic stirrer was charged with 3.76 g (30 mmol) of cupric methoxide under strictly anhydrous conditions. An Airless-ware[109] addition funnel containing 0.55 g (5 mmol) of catechol was attached and degassed pyridine containing water (0.27 g, 15 mmol) was then distilled into the reaction flask (60 mL) and addition funnel (10 mL) under vacuum. The catechol solution was added dropwise over 30–45 min at room temperature to the stirred suspension of cupric methoxide/water in pyridine. After complete addition the reaction mixture was stirred for an additional 30 min and then the pyridine was removed under vacuum. The brown-black residue was stirred with an excess of chloroform and dilute hydrochloric acid under nitrogen. The chloroform solution was dried and evaporated to give a solid residue which according to GLC and NMR analyses was a mixture of muconic acid monomethyl ester **1** (~15%) and unreacted catechol. Other similar experiments are either summarized in Table I or reported below.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with Cupric Methoxide/Water in Pyridine in the Presence of Cupric Chloride (Table I, Entry 7). A solution of 0.16 g (1 mmol) of 4-*tert*-butyl-1,2-benzoquinone in pyridine (5 mL) was added over 15 min to the stirred suspension of cupric methoxide (0.250 g, 2 mmol), cupric chloride (0.268 g, 2 mmol), methanol (0.064 g, 2 mmol), and water (0.036 g, 2 mmol) in pyridine (40 mL) under nitrogen. After stirring for 90 min at room temperature the mixture was evaporated and hydrolyzed in the standard manner to give 0.16 g of amber oil shown by NMR to be a mixture of 3- and 4-*tert*-butylmuconic acid esters **2** and **3** in the usual 5/4.5 ratio.

Essentially the same result was obtained with the reduced amount of cupric chloride (entry 8). However, the reduced amount of cupric methoxide (Table I, entry 9) gave only 35% yield of **2** and **3** together with a polymeric material which was not characterized.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with a Mixture of Cupric Methoxide/Cuprous *tert*-Butoxide/Water in Pyridine. A solution of 4-*tert*-butyl-1,2-benzoquinone (0.16 g, 1 mmol) in 5 mL of pyridine

was added to a mixture of cupric methoxide (0.75 g, 6 mmol), cuprous *tert*-butoxide (0.272 g, 2 mmol), and water (0.09 g, 5 mmol) in pyridine (60 mL) and the resulting reaction mixture stirred for 30 min at room temperature. Workup as before, followed by GLC and NMR analyses, indicated about 35% of **2** and **3** and about 65% of 4-*tert*-butylcatechol. However, when 4-*tert*-butyl-1,2-benzoquinone was added to the suspension of cuprous *tert*-butoxide/water, and then cupric methoxide was introduced, workup as above showed only 4-*tert*-butylcatechol (95% yield). On the other hand, addition of cupric chloride (0.27 g, 2 mmol) to the reaction mixture obtained by the reaction of cuprous *tert*-butoxide and the *o*-benzoquinone, followed by stirring (overnight) and usual workup, led to the formation of a polymer whose IR spectrum was identical with that of the polymer mentioned above.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with a Mixture of Cuprous *tert*-Butoxide and Cupric Chloride in Pyridine. A mixture of cuprous *tert*-butoxide (0.544 g, 4 mmol), cupric chloride (0.540 g, 4 mmol), methanol (0.13 g, 4 mmol), and water (0.072 g, 4 mmol) in 40 mL of pyridine was stirred at room temperature for ca. 30 min; then a solution of 4-*tert*-butyl-1,2-benzoquinone (0.16 g, 1 mmol) was added. After stirring for an additional 30 min, the reaction mixture was worked up as above. The combined GLC and NMR analyses indicated a 95% yield of the isomeric acid esters **2** and **3**.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with Cuprous Chloride in Pyridine. (a) Kinetic Conditions. A solution of 4-*tert*-butyl-1,2-benzoquinone (0.16 g, 1 mmol) in 5 mL of pyridine was added over 5 min under argon to a solution of cuprous chloride (0.40 g, 4 mmol) in 40 mL of degassed pyridine containing methanol (0.065 g, 2 mmol) and water (0.036 g, 2 mmol). After stirring for 10 min the reaction solution was cooled to 0 °C and hydrolyzed with 10 mL of 20% hydrochloric acid in the presence of methylene chloride (100 mL). After washing with excess dilute hydrochloric acid the organic layer was dried and evaporated to give 0.36 g of red-brown solid shown by NMR to contain 4-*tert*-butylcatechol as the major component (~50–60%) and unidentified, presumably polymeric, materials.

(b) Thermodynamic Conditions. In a similar experiment, the reaction mixture was stirred overnight at room temperature and then worked up as above. Evaporation of the methylene chloride solution gave a crude product whose IR and NMR spectra were identical with those of the polymeric material isolated earlier.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with Cuprous Chloride/Cupric Chloride Mixture. Reaction of *o*-benzoquinone (0.16 g, 1 mmol) with a mixture of cuprous chloride (0.396 g, 4 mmol), cupric chloride (0.540 g, 4 mmol), methanol (0.130 g, 4 mmol), and water (0.072 g, 4 mmol) in 40 mL of pyridine under thermodynamic conditions again gave the same polymer as above.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with a Mixture of Cupric Methoxide/Cuprous Chloride/Water in Pyridine. Addition of a solution of *o*-benzoquinone (0.16 g, 1 mmol) to a mixture of cupric methoxide (0.75 g, 6 mmol), cuprous chloride (0.198 g, 2 mmol), and water (0.042 g, 3 mmol) in 40 mL of pyridine, followed by stirring for 30 min at room temperature, and the usual workup gave a mixture of the muconic acid esters **2** and **3** (57%) and 4-*tert*-butylcatechol (43%) by NMR analysis.

Reaction of 4-*tert*-Butyl-1,2-benzoquinone with 1 Equiv of Cupric Methoxide/Water in Pyridine. Using the standard procedure, the reaction of *o*-benzoquinone (0.16 g, 1 mmol) with cupric methoxide (0.125 g, 1 mmol) in pyridine (30 mL) containing water (0.018 g, 1 mmol), followed by the usual workup, gave 54% of the isomeric muconic acid esters **2** and **3** and 46% of the 4-*tert*-butylcatechol by NMR analysis.

4-*tert*-Butylcatecholato-2,2′-dipyridylcopper(II). 4-*tert*-Butylcatecholato-2,2′-dipyridylcopper(II) was prepared in 93% yield by the procedure of Brown et al.[84] The dark brick red solid had the following combustion analysis.

Anal. Calcd for $C_{20}H_{20}N_2O_2Cu$: C, 62.57; H, N, Cu, 16.55. Found: C, 61.65; H, N, Cu, 17.25.

Catecholato-2,2′-dipyridylcopper(II). Catecholato-2,2′-dipyridylcopper(II) was prepared as a brown solid in 67% yield by the procedure of Walker et al.[110]

Anal. Calcd for $C_{16}H_{12}N_2O_2Cu$: C, 58.62; H, N, Cu, 19.38. Found: C, 57.08; H, N, Cu, 18.49.

4-*tert*-Butylcatecholatopyridinecopper(II). Addition of 4-*tert*-butylcatechol (2.49 g, 15 mmol) in 75 mL of dry pyridine to the suspension of cupric methoxide (1.88 g, 15 mmol) in 75 mL of pyridine, followed by stirring for 2 h and evaporation of the solvent, afforded 4.26 g (93% yield) of 4-*tert*-butylcatecholatopyridinecopper(II) complex as a reddish-black solid: IR (Nujol) 1615, 1265, 940, 810, and 695 cm^{-1}; UV (MeOH) 244, 250 (ϵ 4500), 256, 358 (ϵ 8.3), and 490 nm (ϵ 4.5); (Et_2O) 235, 240 (ϵ 3700) 246, 252, 284 (ϵ 2800), 371 (ϵ 434), 470, and 676 nm; mol wt (osmometry in benzene) 918.

Anal. ($C_{15}H_{17}NO_2Cu$) C, H, N, Cu.

Reaction of 4-*tert*-Butylcatecholato-2,2′-dipyridylcopper(II) Complex with Cupric Methoxide/Water. A solution of the copper(II) catecholate complex (0.383 g, 1 mmol) in 5 mL of pyridine was added to a suspension of cupric methoxide (0.75 g, 6 mmol) and water (0.054 g, 3 mmol) in 40 mL of pyridine at room temperature with stirring. After 1 h the reaction mixture was evaporated to dryness, hydrolyzed, and analyzed as above to give 4-*tert*-butylcatechol in ca. 90% yield by NMR analysis.

Reaction of 4-*tert*-Butylcatecholatopyridinecopper(II) Complex with Cupric Methoxide/Water. A similar reaction with the 4-*tert*-butylcatecholatopyridinecopper(II) complex (0.306 g, 1 mmol) gave only 4-*tert*-butylcatechol in essentially the same yield as above.

Reaction of 4-*tert*-Butylcatecholato-2,2′-dipyridyl- and 4-*tert*-Butylcatecholatopyridinecopper(II) complexes with Cupric Chloride. The reaction of either copper(II) complex (1 mmol) with cupric chloride (0.804 g, 6 mmol), methanol (0.087 g, 3 mmol), and water (0.054 g, 3 mmol) in pyridine (40 mL) gave after 1 h the same polymer isolated in the earlier experiments.

Reaction of 4-*tert*-Butylcatecholatopyridinecopper(II) Complex with "Reagent C". "Reagent C", prepared from the complex I (1.28 g, 6 mmol), water (0.054 g, 3 mmol), and pyridine (40 mL), was reacted with a solution of the copper(II) catecholate (0.306 g, 1 mmol) in 5 mL of pyridine with stirring under nitrogen. After 60 min the reaction mixture was worked up as usual and GLC and NMR analyses again showed the presence of the isomeric acid esters **2** and **3** in greater than 90% yield.

Reduction of 4-*tert*-Butyl-1,2-benzoquinone with Copper(0). To a solution of the *o*-benzoquinone (0.33 g, 2 mmol) in 40 mL of pyridine in excess 99.9999% pure copper powder (0.25 g, 4 mmol) was added under argon. After stirring overnight at room temperature the excess of unreacted copper metal (0.09 g) was filtered off and the pyridine solution evaporated to dryness. There was obtained 0.70 g of red-black solid shown by IR comparisons to contain 4-*tert*-butylcatecholatopyridinecopper(II) as the major component. Hydrolysis gave an amber oil containing at least 60–65% 4-*tert*-butylcatechol by NMR analysis. GC analysis revealed 4-*tert*-butylcatechol (~90%) and four other minor unidentified compounds.

Reaction of Bispyridine Cupric Chloride with Copper(0) in Pyridine. A mixture of bispyridine cupric chloride (0.292 g, 1 mmol) and copper metal (0.635 g, 10 mmol) was placed together with a magnetic stirring bar in a glass ampule. Pyridine (25 mL) was added under nitrogen, the ampule sealed, and the contents stirred overnight. The bright yellow solution was filtered and the unreacted copper metal recovered (0.572 g) indicating complete reduction of cupric chloride to cuprous chloride. Evaporation of the pyridine solution afforded 0.355 g (100% yield) of cuprous chloride identified by x-ray diffraction.

Attempted Reactions between Cupric Methoxide and Cupric *tert*-Butoxide with Copper(0) in Pyridine. A mixture of cupric methoxide (0.125 g, 1 mmol) or cupric *tert*-butoxide (0.21 g, 1 mmol) and an excess of copper metal (0.635 g, 10 mmol) was stirred in pyridine (25 mL) overnight. No color change was observed and the unreacted copper metal was recovered essentially quantitatively, indicating that no reaction had occurred.

Stability of Cuprous *tert*-Butoxide in Pyridine. Cuprous *tert*-butoxide in pyridine does not appear to disproportionate over a period of several hours. Addition of water to a suspension of cuprous *tert*-butoxide in pyridine gives a bright orange precipitate (cuprous hydroxide?) which does not deposit copper metal after 16 h at room temperature.

Reaction of 4-*tert*-Butylcatechol with Cuprous *tert*-Butoxide. Stirring of 4-*tert*-butylcatechol (0.166 g, 1 mmol) under argon with a solution of cuprous *tert*-butoxide (0.273 g, 2 mmol) in pyridine (20 mL) produced a copper mirror after 30 min. After stirring overnight the dark red solution was filtered and the solvent evaporated to give 0.43 g of red-black solid identified as being predominantly the 4-*tert*-butylcatecholatopyridinecopper(II) complex by a comparison of the IR with that of an authentic sample.

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(59) (a) W. H. Venneste and A. Zuberbuhler in ref 1a, Chapter 9; (b) J. M. Nelson and C. R. Dawson, *Adv. Enzymol.*, 4, **99** (1946); (c) A. Bunsen Lerner, *ibid.*, **14**, 73 (1953); (d) A. Bunsen Lerner and T. B. Fitzpatrick, *Physiol. Rev.*, **30**, 91 (1950).

(60) However, a direct cleavage of phenol to *cis,cis*-muconic acid ester aldehyde, followed by rapid oxidation of the latter to the acid ester 1, cannot be completely ruled out at this point.

(61) While cleavage of catechol can in principle occur from the corresponding dioxetane intermediate,[62] the formation of this intermediate would be very endothermic,[63] and the cleavage reaction would be expected to be a very exothermic process which is usually accompanied by chemiluminescence.[64] However, during the enzyme-catalyzed cleavage no light is observed.

(62) O. Hayaishi and K. Hashimoto, *J. Biochem.* (*Tokyo*), **37**, 371 (1950).

(63) H. E. O'Neal and W. H. Richardson, *J. Am. Chem. Soc.*, **92**, 6553 (1970).

(64) R. Hiatt, "Organic Peroxides", Vol. II, D. Swern. Ed., Wiley, New York, N.Y., 1971, p 1.

(65) H. S. Mason, *Adv. Enzymol.*, **19**, 79 (1957).

(66) A. E. Martell, *Proc. Symp. Coord. Chem., 3rd*, **2**, 25 (1970).

(67) As early as 1937 F. Kubowitz proposed [*Biochem. Z.*, **292**, 221 (1937); **299**, 32 (1939)] that in oxidation of catechol to *o*-benzoquinone catalyzed by copper oxidases, the function of oxygen was to regenerate copper(I) enzyme to copper(II) enzyme, which was the actual oxidizing reagent. Similarly, in their studies of copper(II)-catalyzed polymerization of phenols, Hay, Endres, and their co-workers[39e] felt that the role of oxygen was to reoxidize the copper(I) back to copper(II) species which were the actual oxidizing reagent.

(68) It is assumed at this point, for the sake of simplicity, that the oxidation of cuprous chloride in pyridine in the presence of methanol leads to pyridine cupric methoxy chloride complex I and 2 equiv of water, a reagent equivalent to the reagent A. However, as it will become apparent later in the text, the actual oxidizing reagent is a mixture of several species (vide infra).

(69) E. Tsuchida, M. Kaneko, and H. Nishide, *Macromol. Chem.*, **151**, 221 (1972).

(70) C. E. Kramer, G. Davies, R. B. Davis, and R. W. Slaven, *J. Chem. Soc., Chem. Commun.*, 606 (1975).

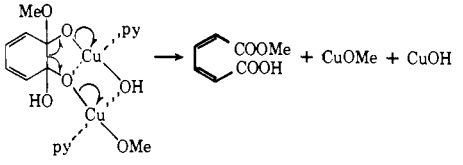
(71) For the mechanism of oxidation of copper(I) by molecular oxygen in perchloric acid–acetonitrile solutions see R. D. Gray, *J. Am. Chem. Soc.*, **91**, 56 (1969); (b) see also A. D. Zuberbuhler, *Helv. Chim. Acta*, **59**, 1448 (1976), and references cited therein.

(72) The EPR spectra of either of the three reagents, reagent A, B, or C in pyridine, clearly showed the presence of approximately 50% of the total amount of copper in a paramagnetic state. The spectrum is consistent with that of bispyridine cupric chloride in pyridine and exhibits general features very similar to that described earlier.[40,43]

(73) It should be remembered, however, that cupric oxide once isolated and "aged" is insoluble in pyridine or methanol. Consequently, if present at all in these solutions, cupric oxide must be stabilized in monomeric or oligomeric but pyridine/methanol soluble form, as it is being formed in situ.

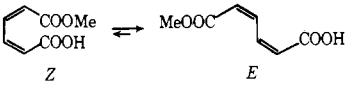
(74) While the positions of various equilibria in Scheme III are not known, it should be recalled that filtration of the "Cu reagent" (vide supra) provided approximately 50% of the total copper in a form of bispyridine cupric chloride. The remaining pyridine solution ("CuO solution") was evidently an active "catalyst" for the cleavage of catechol.

(75) Cupric methoxide was prepared according to the published procedure of ref 49.
(76) However, for the possibility that the reducing reagent might be copper metal see later text.
(77) T. Tsida, T. Hashimoto, and Saegusa, *J. Am. Chem. Soc.*, **94**, 658 (1972).
(78) A reaction of cuprous *tert*-butoxide with water in pyridine does take place. While a solution of the cuprous *tert*-butoxide in pyridine is stable, the resulting reaction mixture after treatment with water does not undergo appreciable disproportionation over several hours. However, an overnight reaction produced appreciable amounts of what appears to be a polymeric cuprous oxide and small amounts of copper(0) and cupric oxide. Presumably, after addition of water the copper(II) species in pyridine are either cuprous hydroxide or cuprous oxide hydrate present in oligomeric form.
(79) The reaction mixture before hydrolysis appears homogenous and does not deposit cupric oxide on standing. Consequently, it is possible that in solution the copper(II) catecholate complex and cupric hydroxide exist as a mixture of the isomeric copper(II) catecholate/cupric hydroxide complexes (vide infra).
(80) While cuprous hydroxide readily reacts with cupric chloride, cuprous chloride does not react with cupric methoxide/water in pyridine (see also Table I, entries 9 and 10).
(81) D. G. Brown, J. T. Reinprecht, and G. C. Vogel, *Inorg. Nucl. Chem. Lett.*, **12**, 399 (1976).
(82) Molecular weight of the 4-*tert*-butylcatecholate pyridinecopper(II) complex in benzene solution was found to be 919.0, indicating that it exists as a trimer. We assume that in pyridine solution the trimer either completely dissociates to the corresponding monomer containing two pyridine ligands, or at least that it exists under the reaction conditions in equilibrium with such a monomer. We will discuss the structure and the EPR spectra of this and other related copper(II) catecholate complexes elsewhere.
(83) Brown and co-workers[84] have shown that 3,5-di-*tert*-butylcatecholato-1,10-phenanthrolinecopper(II) and 3,5-di-*tert*-butylcatecholato-2,2′-dipyridylcopper(II) undergo a reaction with oxygen in solution to give a mixture of a cleavage product and unidentified copper complexes.
(84) D. G. Brown, Z. Beckmann, C. H. Ashby, G. C. Vogel, and J. T. Reinprecht, *Tetrahedron Lett.*, 1363 (1977).
(85) "Cu reagent" prepared by other methods (eq **5**, 7) behaves in the same way.
(86) For a review of oxidation by copper(II) see W. G. Nigh in "Oxidation in Organic Chemistry", W. S. Trahanovsky, Ed., Academic Press, New York, N.Y., 1973; (b) R. A. Sheldon and J. K. Kochi, *Adv. Catal.*, **25**, 272 (1976); (c) J. K. Kochi, "Free Radicals", Vol. 1, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, p 591, and references cited therein.
(87) See, for example, ref 86c and references cited therein.
(88) J. W. Wilt, "Free Radicals", Vol. 1, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, p 333; (b) D. C. Nonhebel and J. C. Walton, "Free-Radical Chemistry", Cambridge University Press, New York, N.Y., 1974, pp 470–552.
(89) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry", 3rd ed, Wiley, New York, N.Y., 1972, p 905.
(90) Alternatively, the carbon–carbon bond cleavage may involve two simultaneous one-electron oxidations to provide the muconic acid ester and copper(I) hydroxide and methoxide, followed by reaction between the acid



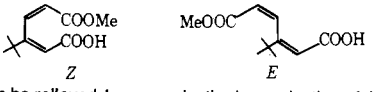
$$RCOOH + CuOMe \longrightarrow RCOOCu + MeOH$$

ester and the copper(I) species to give the copper(I) muconate and methanol (or water).
(91) After this manuscript was submitted for publication Fenton, Schroeder, and Lintvedt described a bimolecular copper(II) system capable of accepting two electrons simultaneously.[92]
(92) D. E. Fenton, R. R. Schroeder, and R. L. Lintvedt, *J. Am. Chem. Soc.*, **100**, 1931 (1978).
(93) We do not have evidence that the copper(II) catecholate indeed exists in solution as the suggested mixed complex with basic copper(II) muconate. The structures of inorganic and simple aliphatic basic cupric salts are usually portrayed as combinations of normal salts, cupric hydroxide, cupric oxide, and water. However, Kaeding and Shulgin[94] have shown that various basic cupric salts exist as such.
(94) W. W. Kaeding and A. T. Shulgin, *J. Org. Chem.*, **27**, 3551 (1962).
(95) For a brief review of the copper-containing oxidases, see R. Malkin in "Inorganic Biochemistry", G. L. Eichhorn, Ed., American Elsevier, New York, N.Y., 1973, Chapter 21.
(96) R. Malkin and B. G. Malmstrom, *Adv. Enzymol.*, **33**, 177 (1970).
(97) J. A. Fee, R. Malkin, B. G. Malmstrom, and T. Vanngard, *J. Biol. Chem.*, **244**, 4200 (1969).
(98) E. I. Solomon, D. M. Dooley, R.-H. Wang, H. B. Gray, M. Cerdonio, F. Moguo, and G. L. Romani, *J. Am. Chem. Soc.*, **98**, 1029 (1976).
(99) The exact nature of bonding in this intermediate of course is not known.
(100) The catecholate C is present in solution either as a mixed complex with cupric hydroxide or basic copper(II) muconate, or as a mixture with these copper(II) species (see Scheme V).
(101) Once formed the copper(II) catecholate complex C is stable because the reverse reaction would require that a relatively soft hydroxide or methoxide anion of cupric methoxy hydroxide replace a much harder catecholate bidentate ligand in the copper(II) catecholate complex C.
(102) Presumably, the harder chloride anion from cupric chloride can replace the relatively softer catecholate anion from the copper catecholate in C′, but reverse reaction, the replacement of one of the harder chloride anions in the intermediate B′ to produce copper(II) catecholate and cupric chloride as in C′, either does not take place readily, or, if it does, the ensuing equilibrium favors the intermediate B′.
(103) It is well known[86] that electron transfer oxidations occur mainly with oxy salts of copper(II), whereas ligand transfer oxidations predominate with copper(II) halides. Accordingly, the singlet state of copper(II) is unreactive in electron transfer reactions. However, the triplet state of the dimeric copper(II) species is largely unreactive and only paramagnetic monomeric copper(II) species function as electron transfer oxidizing reagents.
(104) V. Balogh, M. Fetizon, and M. Golfier, *J. Org. Chem.*, **36**, 1339 (1971).
(105) R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, **2**, 1 (1946).
(106) H. W. Wanzlick and J. Ulrich, *Chem. Abstr.*, 71, 30237r (1969).
(107) During the discussion of the carbon–carbon bond cleavage of 4-*tert*-butylcatechol and 4-*tert*-butyl-1,2-benzoquinone, no explanation was given for the isomerization of the C_2–C_3 double bond in the half ester **3**. The muconic acid ester **1**, according to the ^1H NMR spectrum, exists primarily in the *E* conformation. It appears that the observed thermodynamic



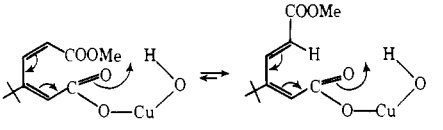
Z *E*

preference stems from the greater steric and dipole–dipole interactions between the carbomethoxy and carboxylic groups in the *Z* conformer. In the case of the half ester **3**, however, similar relief of the unfavorable interactions is not possible because of the pronounced steric interactions between the carbomethoxy and 4-*tert*-butyl groups in the planar conformation of the *E* conformer. The unfavorable interactions in the *Z* con-



Z *E*

former can be relieved, however, by the isomerization of the C_2–C_3 double bond, that may be assisted by chelation in the basic copper(II) salt. The isomer **2** exists in the *Z* conformation, because the isomerization of the C_4–C_5 double bond would not be thermodynamically favored.



(108) Spex Industries, Metuchen, N.J.
(109) Trademark of Kontes, Vineland, N.J.
(110) H. Walker, H. Sigel, and D. G. McCormick, *Inorg. Chem.*, 11, 2756 (1972).