# Novel *tert*-Butyl Migration in Copper-Mediated Phenol *Ortho*-Oxygenation Implicates a Mechanism Involving Conversion of a 6-Hydroperoxy-2,4-cyclohexadienone Directly to an *o*-Quinone

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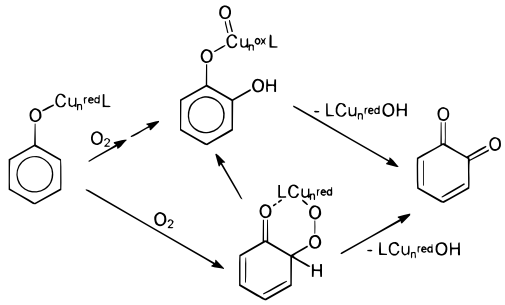
Copper mediated *ortho*-oxygenation of phenolates may proceed through the generation of a 6-peroxy-2,4-cyclohexadienone intermediate. To test this theory, we studied the fate of sodium 4-carbethoxy-2,6-di-*tert*-butylphenolate, where the *ortho*-oxygenation sites are blocked by *tert*-butyl groups. Using the Cu(I) complex of *N*,*N*-bis(2-(*N*-methylbenzimidazol-2-yl)ethyl)benzylamine, isolation of the major oxygenated product and characterization by single-crystal X-ray crystallography and NMR spectroscopy revealed it to be 4-carbethoxy-3,6-di-*tert*-butyl-1,2-benzoquinone, resulting from a 1,2-migration of a *tert*-butyl group. The independently prepared 6-hydroperoxide is transformed by the Cu(I)− (or Cu(II)−) ligand complex to the same *o*-quinone. The observed 1,2-migration of the *tert*-butyl group appears to reflect an electron demand created by rearrangement of the postulated peroxy intermediate. A mechanism proceeding alternatively through a catechol and subsequent oxidation to the *o*-quinone seems ruled out by a control study demonstrating that the requisite intermediate to catechol formation would instead eliminate the 2-*tert*-butyl group.

## Introduction

Copper catalysis of phenol *ortho*-oxygenation is being extensively studied in regard to understanding the mechanism of oxidation of tyrosine to dihydroxyphenylalanine (DOPA) quinone by the cuproenzyme tyrosinase (EC 1.14.18.1)[1] and the oxygenation of the active site tyrosine residue in copper amine oxidases, as the initial step in cofactor biogenesis.[2] In the latter case, oxygenation occurs spontaneously following binding of Cu(II) to its three histidine ligands in the vicinity of the active site tyrosine residue. Synthetic model systems that achieve *ligand-based* arene monooxygenation have been characterized in exquisite detail,[3] but model systems achieving regiospecific *ortho*-oxygenation of *exogenous* phenols[4,5] are mechanistically less defined. In the latter case, it is unclear whether ultimate *o*-quinone formation reflects initial production of catechol with subsequent oxidation, or a dioxygenase-like generation of a peroxy intermediate that can convert to *o*-quinone directly or through intermediacy of catechol (Scheme 1).

Information on the nature of intermediates may be achieved from a determination of the fate of oxygenation of a phenol bearing *o*,*o*′-dialkyl-substituents. Since a subsequent rearrangement would be required to reestablish aromaticity, the properties of this rearrangement would intimately reflect electronic attributes of the oxygenation intermediate. The most well-known rearrangement accompanying oxygenation chemistry, termed the "1,2-NIH shift", occurs for arene monooxygenation mediated by cytochrome P450 systems. An example of the 1,2-NIH shift in copper-mediated oxygenation was reported by Karlin for his *m*-xylyl-bridged binucleating dicopper(I) system upon replacing the hydrogen at the oxygenation site (xylyl C-2 position) with a methyl group.[6]

**Scheme 1**

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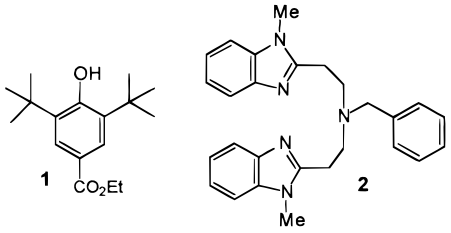
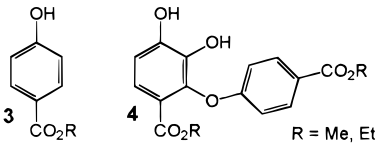
However, there have been no reports of alkyl rearrangements in systems that achieve oxygenation of exogenous phenols. Herein we report a 1,2-shift of a *tert*-butyl group that occurs when the sodium salt of ethyl 3,5-di-*tert*-butyl-4-hydroxybenzoate (**1**) is exposed to the Cu(I) complex of *N*,*N*-bis(2-(*N*-methylbenzimidazol-2-yl)ethyl)-benzylamine (**2**) under $O_2$. Companion studies on the independently prepared 6-hydroperoxy-2,4-cyclohexadienone yield results consistent with a mechanism of copper-mediated phenolate oxygenation to give *o*-quinone via an *o*-peroxy intermediate without obligate intermediacy of catechol.




## Results and Discussion

We previously reported that the reaction of the sodium salt of 4-carbomethoxyphenol (**3**, R = Me) with the dicopper(I) complex of the binucleating ligand *N*,*N*,*N*′,*N*′-tetrakis(2-(*N*-methylbenzimidazol-2-yl)ethyl)-*m*-xylylenediamine in $CH_3CN$, with subsequent exposure to $O_2$, affords as the major product catechol **4** (R = Me), resulting from coupling of the initial *ortho*-oxygenation product with the starting phenolate.[5] Casella and coworkers reported that the copper(I) complex of the simple mononucleating secondary amine, *N*,*N*-bis(2-(*N*-methylbenzimidazol-2-yl)ethyl)amine, was an ineffective oxygenation catalyst.[4f] However, this might be a consequence of the free NH, since we now report that the copper(I) complex of the mononucleating *tertiary* amine **2**, obtained by benzylation of the secondary amine ligand, permits achieving the conversion of **3** to **4** (R = Et) in the best yield so far observed.




To gain information on the nature of the oxygenation, we carried out the same reaction substituting the di-*tert*-butyl analogue **1** for **3**. Compound **1** was synthesized by acid-catalyzed esterification of the commercially available acid in ethanol. Reaction of the sodium salt of **1** with the Cu(I)−**2** complex in $CH_3CN$ followed by exposure to $O_2$ resulted in a single major product which was shown by $^1H$ and $^{13}C$ NMR analysis to contain two nonidentical *tert*-butyl groups. Although the material was colored, suggestive of quinone structure **5**, FAB mass spectral analysis gave an expected mass peak (M + 1) that was 2.6-fold smaller than a peak at M + 3 reflective of the reduced catechol analogue **6**. Nonetheless, the structure was confirmed to be 4-carbethoxy-3,6-di-*tert*-butyl-1,2-benzoquinone (**5**) by single-crystal X-ray diffraction (Figure 1)[7] and clearly indicates that migration of a 1,2-*tert*-butyl has accompanied the oxygenation.

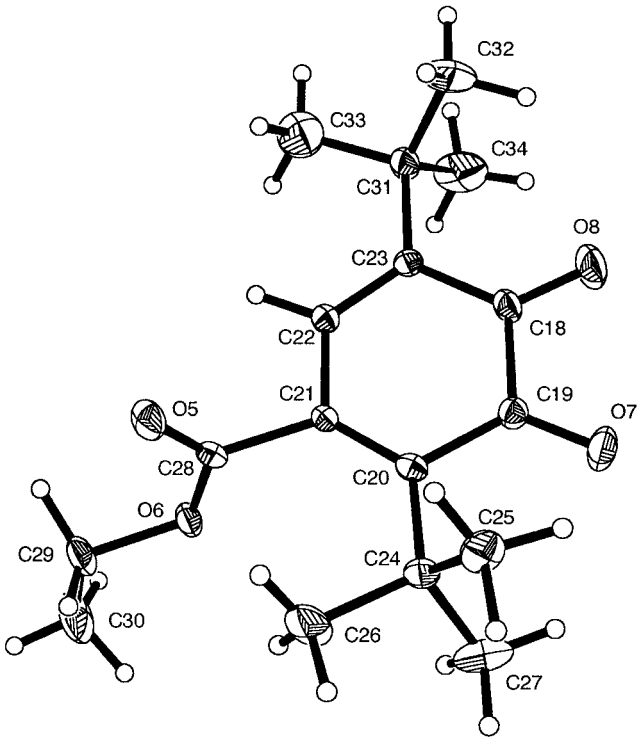
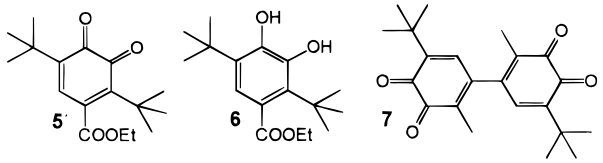



**Figure 1.** ORTEP view (thermal elipsoids at the 30% probability level) of one of the independent molecules of **5** with labeling scheme.

Stannous chloride reduction of oxygenation product (quinone **5**) afforded authentic catechol **6**, which was not colored, had distinct NMR spectral and TLC elution properties, and could thereby be excluded as even a minor product in the oxygenation of **1**. The propensity for **5** to be reduced to **6** in the mass spectrometer may arise from fragmentation and the supply of hydrogens by the *tert*-butyl groups.



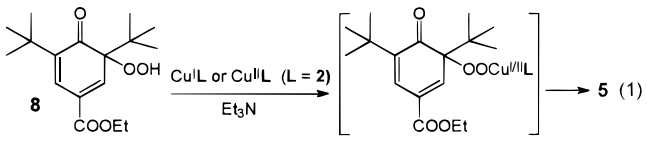

The X-ray structural analysis demonstrated that the bond distances and angles for the two independent

(6) Nasir, M. S.; Cohen, B. I.; Karlin, K. D. *J. Am. Chem. Soc.* **1992**, *114*, 2482.

(7) $C_{17}H_{24}O_4$: $a$ = 10.7440(14) Å, $b$ = 10.5177(13) Å, $c$ = 30.432(4) Å, $\beta$ = 97.702(4)°, $Z$ = 8, two independent molecules per asymmetric unit. X-ray quality crystals were grown by vapor diffusion from ethanol−water mixtures of **5**. A green crystal (0.6 × 0.1 × 0.08 mm$^3$) was mounted on a glass fiber, and a unit cell was determined based on 2585 reflections using the data integration program SAINT. Data were collected at 223(1) K using the Bruker SMART Platform with a CCD 1K detector and Mo radiation with a graphite monochromator (using 3 different settings of Φ to cover a hemisphere, 0.3° increment in omega scans, 2Θ < 58° and 30 s/frame exposure time). Corrections for absorption and decay were applied in SADABS (Sheldrick, G.M., University of Gottingen, 1998) although decay was negligible. The structure was solved by direct methods in the space group $P2_1/c$ (No. 14) and refined by a full matrix least squares on $F^2$ using all 8260 independent reflections. All non-hydrogen atoms were located from Fourier difference maps; hydrogens were placed in ideal calculated positions. Hydrogen atoms were assigned common thermal parameters. Refinement converged at final values of $R$ = 0.0610 and $R_w$ = 0.1070. Crystal data and data collection parameters for compound **5** are available as Supporting Information.

molecules in the unit cell fall into the expected range.[8] No significant hydrogen bonding was observed in the packing diagram. The *o*-benzoquinone rings are virtually planar (average rms deviation from the mean least squares plane 0.027). This planarity and the *o*-benzoquinone C═O bond lengths (1.200(3)−1.213(3) Å) closely match analogous attributes in the published structure of the similar compound 2,2′-dimethyl-5,5′-di-*tert*-butylbiphenyl-3,4,3′,4′-diquinone **7** (1.211(4)−1.220(4) Å).[9,10]

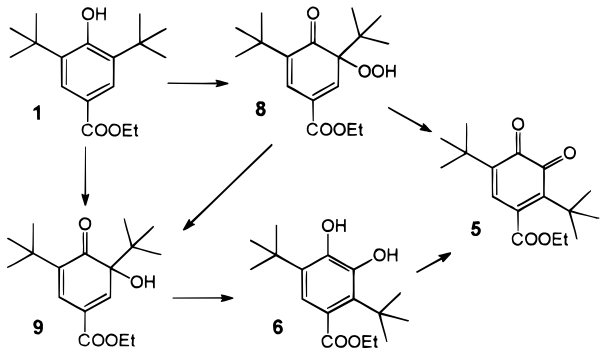
On the basis of our proposal that copper-mediated oxygenation of phenols may proceed through generation of a 6-peroxy-2,4-cyclohexadienone intermediate[5] (e.g., **8**), we hypothesized that the observed *tert*-butyl migration could reflect rearrangement to an electron-deficient center created by structural reorganization of this putative peroxy intermediate. To test this theory we synthesized the hydroperoxide **8** and studied the fate of its coordination to copper. Compound **8** was obtained by filtration over silica gel of the cobalt hydroperoxide arising from oxygenation of **1** mediated by Co(II)(Salpr).[11] We were unable to isolate and characterize the copper peroxide complex of **8** prior to its structural reorganization, but generation of the complex in situ by triethylamine-induced deprotonation of **8** in the presence of either the Cu(I)- or Cu(II)-complex of **2** under argon afforded **5** in good yield (eq 1).




In an effort to demonstrate formation of the copper−**8** salt in the Cu(I)-mediated oxygenation of **1**, the sodium salt of **1** was allowed to react with the Cu(I)−**2** complex in $CH_3CN$ under $O_2$ at −43 °C. At this temperature only **5** was obtained even when the reaction was acid-quenched at short reaction times. Clearly, the intermediate copper−**8** species must be very short-lived. The freezing point (−45.7 °C) of $CH_3CN$ prevented us from exploring the reaction at even lower temperature.

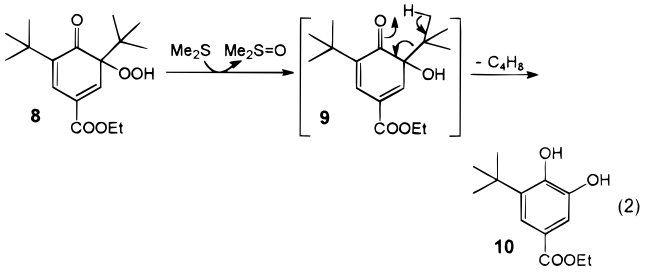
It is noteworthy that during the synthesis[11] of **8** from **1** using Co(II)(Salpr), **5** was also obtained as a side-product, the yield of which slowly increased with increasing reaction time, with a concomitant decrease in yield of **8**. From this observation, it is clear that although Co(II) and/or Co(III)(Salpr) complexes are much less reactive than the above copper complexes toward **8**, the *tert*-butyl migration appears to be a general phenomenon for hydroperoxide **8** in the presence of transition metal complexes.

**Scheme 2**




Possible reaction pathways (omitting details of the role of the metal) consistent with our experimental observations are shown in Scheme 2. Direct reorganization of **8** could lead to **5**. Alternatively, reaction could proceed through **9**, generated from monooxygenation of **1** or reduction of **8** by Cu(I); **9** could then undergo rearrangement to catechol **6** analogous to base-mediated rearrangement of tertiary ketols,[12] and **6** would be oxidized to **5** by the Cu(II) produced during generation of **9**. Both reactions would have the same net stoichiometry and would be catalytic (theoretically) with copper.

Nonetheless, if the reaction proceeded through **9**, the latter might alternatively undergo elimination of isobutylene to give a catechol missing one of the two *tert*-butyl groups. In fact, Nishinaga and co-workers found that dimethyl sulfide-mediated deoxygenation of the 6-hydroperoxy-2,4-cyclohexadienone obtained from Co(II)-mediated oxygenation of 2,4,6-tri-*tert*-butylphenol led to 3,5-di-*tert*-butylcatechol, shown by $^1$H NMR spectroscopy at low temperature to involve the intermediacy of the 6-hydroxy-2,4-cyclohexadienone.[13] These workers also found that 6-hydroperoxy-2,6-di-*tert*-butyl-4-(*tert*-butylcarbonyl)-2,4-cyclohexadienone underwent instant conversion by $Me_2S$ at room temperature to the des-*tert*-butyl catechol.[14] When we dissolved **8** in $Me_2S$ at 0−5 °C, there was immediate evolution of gas, and eventual workup of the reaction indicated quantitative conversion of **8** to catechol **10**. In analogy to the work of Nishinaga et al., we propose a mechanism proceeding via the 6-hydroxy intermediate **9** (eq 2). The facile conversion of **9** to **10** must reflect transformation of a strongly electrophilic dienone into an aromatic system with "push−pull" resonance and could follow the concerted 6-center reaction shown.




*Since this conversion appears to occur so readily, we believe that if* **9** *were an intermediate in the oxygenation*

(8) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2*, **1987**, S1.

(9) Abakumov, G. A.; Nevodchikov, V. I.; Druzhkov, N. O.; Zacharov, L. N.; Abakumova, L. G.; Kurskii, Y. A.; Cherkasov, V. K. *Russ. Chem. Bull.* **1997**, *46*, 771.

(10) Numerous X-ray crystal structures having the 3,6-di-*tert*-butyl-1,2-benzoquinone moiety complexed to various metal centers have been published. The geometry of those quinones, however, is affected by the metal center; in particular, the C═O bonds are considerably elongated. The most recent structures of metal 3,6-di-*tert*-butyl-1,2-benzoquinone complexes are described in: Lange, C. W.; Pierpont, C. G. *Inorg. Chim. Acta* **1997**, *263*, 219. Attia, A. S.; Conklin, B. J.; Lange, C. W.; Pierpont, C. G. *Inorg. Chem.* **1996**, *35*, 1033. Jung, O.-S.; Pierpont, C. G. *J. Am. Chem. Soc.* **1994**, *116*, 2229.

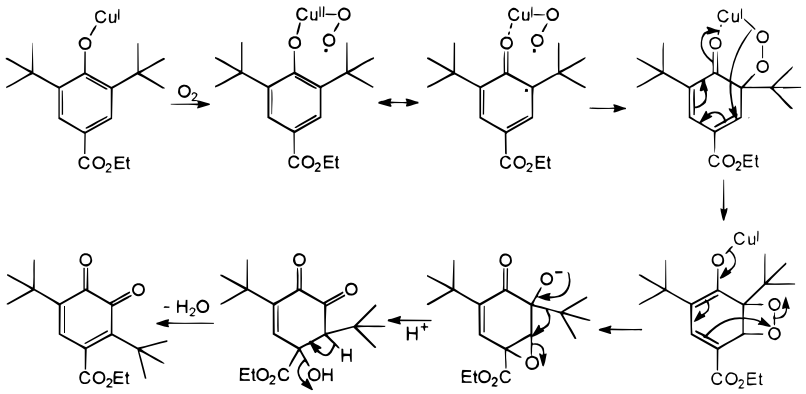
(11) Nishinaga, A.; Shimizu, T.; Toyoda, Y.; Matsuura, T. J.; Hirotsu, K. *J. Org. Chem.* **1982**, *47*, 2278 and references therein.

(12) Selman, S.; Eastham, J. F. *Quart. Rev.* **1960**, *14*, 221.

(13) Nishinaga, A.; Itahara, T.; Shimizu, T.; Matsuura, T. *J. Am. Chem. Soc.* **1978**, *100*, 1820.

(14) Nishinaga, A.; Shimizu, T.; Matsuura, T. *Tetrahedron Lett.* **1981**, *22*, 5293.

**Scheme 3**

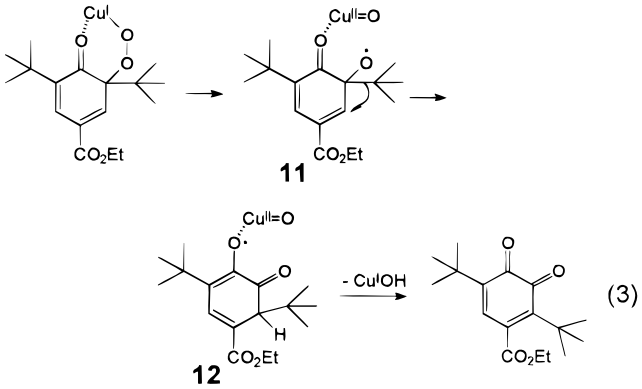


*of* **1** *according to Scheme 2, the product observed would be* **10** *rather than* **5**. However, not even a trace amount of **10** was seen in the copper-mediated oxygenation of **1**. It should be noted that if **9** were the immediate product of copper-mediated oxygenation of **1**, it would probably be produced as the corresponding Cu(II)−alkoxide; but this should not affect the choice between rearrangement to give **6** and elimination to give **10**. We are forced to conclude that observation of **5** as the exclusive identifiable product from copper-mediated oxygenation of **1** implicates a mechanism involving direct reorganization of the 6-hydroperoxide **8** to quinone **5**.

There are no simple mechanisms that would justify such reorganization, but a similar conversion is precedented by the outcome of base-mediated autoxidation of 4,6-di-*tert*-butylguaiacol.[15] In analogy with this work, we consider the intermediacy of a dioxetane that decays to an epoxide, opening of which would provide the "driving" force for migration of the *tert*-butyl group. This mechanism as well as a possible scenario for initial oxygenation are depicted in Scheme 3.[16]

One aspect of Scheme 3 that appears problematic is the putative intermediacy of a Cu(I) peroxide, since Cu(I) might be expected to mediate reductive fission of the O−O bond. However, we argued above that if reduction of the 6-hydroperoxy intermediate **8** to the 6-hydroxy intermediate **9** occurred, the latter would evolve to a different product (**10**) than what is observed (**5**). Thus, although the *two-electron* reduction of **8** to **9** cannot be on the pathway for generation of **5**, one potential mechanistic alternative consistent with redox predictions would call for Cu(I)-induced reductive cleavage of **8** to the radical **11**, which could undergo migration of the *tert*-butyl group to produce another radical **12** that would in turn be oxidized to **5** by the Cu(II) generated in the peroxide reductive cleavage (eq 3). Although we know of no precedent for such putative homolytic 1,2-alkyl shift, this mechanism would avoid having to invoke a metastable Cu(I)−peroxy intermediate.

Further studies will be required to determine whether the mechanistic argument presented here pertains also to phenolate oxygenation in systems lacking blocking *ortho* substituents. If the reactions are judged to be electronically similar, our finding is consistent with possible direct *o*-quinone production from phenols, without the intermediacy of catechols, in biologically important reactions mediated by copper-containing enzymes. In addition, although we have depicted the reactions as



being mediated by mononuclear copper, we cannot exclude a possible binuclear copper involvement. Notwithstanding the need for further mechanistic definition in this system, we note that the 1,2-migration of a *tert*-butyl group driven by a metal ion-mediated oxygenation event is unprecedented. To the best of our knowledge, the present account represents the first example of any copper/$O_2$-mediated 1,2-alkyl migration within an exogenous substrate.

## Experimental Section

**General.** All reagents and solvents were obtained from commercial sources and used as received unless otherwise noted. Acetonitrile was dried according to published procedure[17] and distilled under argon immediately prior to use. All air-sensitive reactions were performed under argon. The salt $[Cu(CH_3CN)_4][BF_4]$[18] was prepared by suspending 10% excess $Cu_2O$ in 95% aq $CH_3CN$ (v/v) containing 2 M $HBF_4$, heating at reflux under argon, hot filtration under argon, cooling to 0 °C, and recrystallization of the resulting colorless crystals from $CH_3CN$. The monosodium salt of ethyl 3,5-di-*tert*-butyl-4-hydroxybenzoate (**1**) was prepared by using 1 equiv of aqueous NaOH solution in EtOH, followed by solvent evaporation, with azeotropic removal of traces of water using EtOH−toluene. The Cu(II)−**2** complex was prepared by using equimolar amounts of $Cu(BF_4)_2 \cdot xH_2O$, 19.6% Cu, and **2** in $CH_3CN$, followed by removal of solvent under reduced pressure at 40 °C and azeotropic removal of traces of water using EtOH−toluene. Triethylamine was dried by refluxing over $LiAlH_4$, distilled, and stored over NaOH. All reactions were carried out at room temperature (25 °C) with magnetic stirring unless otherwise

(15) Gierer, J.; Imsgard, F. *Acta Chim. Scand. B* **1977**, *31*, 546.

(16) Direct formation of the putative dioxetane by a photosensitized production of $^1O_2$ and its reaction with the starting phenolate seems unlikely in that the reaction shows no dependence on light.

(17) Perrin, D. D.; Armarego, W. L. F., Eds. *Purification of Laboratory Chemicals*; Pergamon Press: New York, 1988.

(18) Hathaway, B. J.; Holah, D. G.; Postlethwaite, J. D. *J. Chem. Soc.* **1961**, 3215.

noted, and all evaporations were carried out at reduced pressure with a rotary evaporator. The $^1$H NMR spectra were obtained at 300 MHz ($^{13}$C NMR at 75 MHz), with chemical shifts being referenced to TMS or the solvent peak(s). Thin-layer and preparative-layer chromatography were run on Merck silica gel 60 plates with a 254 nm indicator.

**Preparation of Ethyl 3,5-Di-*tert*-butyl-4-hydroxybenzoate (1).** To a solution of 3,5-di-*tert*-butyl-4-hydroxybenzoic acid (3.8 g, 15.2 mmol) in EtOH (60 mL) was added concentrated $H_2SO_4$ (20 $\mu$L), and the mixture was heated at reflux for 9 days. The solvent was removed, and the solid was triturated with a saturated aqueous solution of $NaHCO_3$ to removed unreacted acids. A $CH_2Cl_2$ solution of the remaining solid was washed with saturated $NaHCO_3$ and then with water. On evaporation of $CH_2Cl_2$, **1**[19] was obtained in 92% yield in pure form. $^1$H NMR ($CDCl_3$) $\delta$ 1.37 (t, 3H, $J$ = 7.12 Hz), 1.46 (s, 18H), 4.36 (q, 2H, $J$ = 7.12 Hz), 5.79 (s, 1H), 7.94 (s, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.37, 30.05, 34.21, 60.36, 121.41, 126.86, 135.61, 157.99, 167.07.

**Preparation of *N*,*N*-Bis(2-(*N*-methyl benzimidazol-2-yl)ethyl)benzylamine (2)**. According to a previously described procedure,[4e] benzyl bromide (1.80 g, 10.5 mmol) and dry sodium carbonate (1.75 g, 16.5 mmol) were added to a solution of *N*,*N*-bis[2-(*N*-methylbenzimidazol-2-yl)ethyl]amine (3.5 g, 10.5 mmol) in anhydrous DMF (60 mL). The mixture was heated with rapid stirring for 42 h at 70 °C. After removal of DMF, the residue was treated with chloroform, the inorganic salts were filtered off, and the solvent was removed. Compound **2** was isolated as a light pink crystals from ethanol−water (1:1, v/v, 0 °C) in 55% yield: $^1$H NMR ($CDCl_3$) $\delta$ 2.97−3.17 (m, 8H), 3.50 (s, 6H), 3.79 (s, 2H), 7.18−7.25 and 7.67−7.68 (m, 13H); $^{13}$C NMR ($CDCl_3$) $\delta$ 25.96, 29.39, 51.81, 58.97, 108.82, 118.83, 121.60, 121.82, 126.93, 128.13, 128.55, 135.52, 139.12, 142.41, 153.55; HRMS (EI) *m*/*z* calcd for $C_{27}H_{29}N_5$ 423.2423, found 423.2410.

**Copper(I)/$O_2$-Mediated Oxygenation of Ethyl 4-Hydroxybenzoate (3)**. To the degassed solution of **2** (0.339 g, 0.80 mmol) in 120 mL of $CH_3CN$ was added $[Cu(CH_3CN)_4][BF_4]$ (0.252 g, 0.80 mmol) under argon. The sodium salt of **3** (0.150 g, 0.80 mmol) was then added anaerobically to the resulting solution, and stirring was continued until it dissolved completely. Dry $O_2$ was then admitted into the flask for 35 min at room temperature. The reaction mixture was then quenched with dilute HCl (0.4 M, 20 mL), followed by removal of solvent. The remaining residue was taken up in ethyl acetate (100 mL) and washed with dilute HCl (0.4 M, 3 × 20 mL) and then with water (3 × 20 mL). The crude product was subjected to preparative thin-layer silica gel chromatography (ethyl acetate−hexane, 2:3, v/v), affording the product ethyl 2-(4-carbethoxyphenoxy)-3,4-dihydroxybenzoate (**4**) in 84% yield (42% oxygenation): $^1$H NMR ($CDCl_3$) $\delta$ 1.05 (t, 3H, $J$ = 7.15 Hz), 1.38 (t, 3H, $J$ = 7.11 Hz), 4.08 (q, 2H, $J$ = 7.10 Hz), 4.35 (q, 2 H, $J$ = 7.14 Hz), 6.88 (d, 2H, $J$ = 8.82 Hz), 6.92 (d, 1H, $J$ = 8.70 Hz), 7.62 (d, 1H, $J$ = 8.70 Hz), 7.98 (d, 2H, $J$ = 8.82 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.78, 14.17, 60.91, 61.09, 112.4, 114.5, 115.9, 123.7, 124.1, 131.5, 137.7, 141.2, 150.4, 161.9, 165.2, 166.7; HRMS (EI) *m*/*z* calcd for $C_{18}H_{18}O_7$ 346.1052, found 346.1053.

**Copper(I)/$O_2$-Mediated Oxygenation of 1**. To a degassed solution of **2** (0.254 g, 0.6 mmol) in 20 mL of $CH_3CN$ was added $[Cu(CH_3CN)_4][BF_4]$ (0.188 g, 0.6 mmol) under argon. The sodium salt of **1** (0.180 g, 0.6 mmol) was added to the resulting solution, and stirring was continued until **1** dissolved completely. Dry $O_2$ was then admitted into the flask for 15 min at room temperature. The reaction mixture was then quenched by glacial acetic acid (0.108 g, 1.8 mmol), followed by removal of solvent. The remaining solid residue was taken up in $CH_2Cl_2$ (20 mL), and the mixture was filtered through a short silica gel column to remove the metal complex. After removal of $CH_2Cl_2$, the $^1$H NMR spectrum of the crude product indicated (average of three experiments) ~40% 4-carbethoxy-3,6-di-*tert*-butyl-1,2-benzoquinone (**5**) and ~55% starting phenol (**1**). Although we see no evidence of any significant single minor product, integration of the *tert*-butyl signals indicates the presence of ~5% of unidentified products. The crude product was subjected to preparative thin-layer silica gel chromatography ($CH_2Cl_2$−hexane, 3:2, v/v), affording analytical quality **5**: $^1$H NMR ($CDCl_3$) $\delta$ 1.24 (s, 9H), 1.29 (s, 9H), 1.41 (t, 3H, $J$ = 7.17 Hz), 4.36 (q, 2 H, $J$ = 7.18 Hz), 6.52 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.78, 28.80, 29.41, 35.01, 36.37, 62.16, 134.73, 138.36, 146.61, 149.73, 169.11, 180.50, 183.72; HRMS (FAB) *m*/*z* calcd for $C_{17}H_{25}O_4$ $(M + 1)^+$ 293.1754, found 293.1744 (rel intensity 38.1). Apart from the molecular ion peak, $(M + 2)^+$ and $(M + 3)^+$ peaks were also observed with relative intensities of 37.69 and 100.00, respectively. X-ray quality crystals were grown at room temperature from an ethanolic solution of **5** in an open vial, which was placed in a closed vial containing water.

The same reaction, when carried out for a longer period of time, produced many unidentified products, along with a lower yield of **5**. In control reactions performed with omission of either ligand **2** or Cu(I), **5** was not detected. Using 2 rather than 1 equiv of the Cu(I)−**2** complex per equivalent of phenolate **1** resulted in an increase in yield of **5** by only 2−3%, whereas 4−6% more starting phenolate was converted to unidentified products.

**Preparation of Ethyl 2,5-Di-*tert*-butyl-3,4-dihydroxybenzoate (6).** A room-temperature $SnCl_2$ reduction of **5** under argon atmosphere in a mixed solvent system (0.2 M aqueous HCl:MeOH 1:2, v/v) afforded catechol **6**, which was purified by preparative thin-layer silica gel chromatography ($CH_2Cl_2$). $^1$H NMR ($CDCl_3$) $\delta$ 1.37 (t, 3H, $J$ = 7.13 Hz), 1.39 (s, 9H), 1.49 (s, 9H), 4.31 (q, 2H, $J$ = 7.13 Hz), 5.59 (s, 2H), 6.70 (s, 1H); HRMS (EI) *m*/*z* calcd for $C_{17}H_{26}O_4$ 294.1832, found 294.1830.

**Preparation of 2,6-Di-*tert*-butyl-4-carbethoxy-6-hydroperoxy-2,4-cyclohexadienone (8)**. Co(II)(Salpr) was prepared and isolated from the reaction of bis(salicylaldehydato)-cobalt(II) dihydrate with bis(3-aminopropyl)amine under $N_2$.[20] To a degassed solution of Co(II)(Salpr) (0.436 g, 1.1 mmol) in 20 mL $CH_2Cl_2$ was added **1** (0.278 g, 1.0 mmol) under argon. Dry $O_2$ was admitted into the flask at room temperature for 4.5 h, at which time the mixture was filtered through a short silica gel column to remove the metal complex. Upon removal of $CH_2Cl_2$, **8** was obtained (65% yield as determined by the $^1$H NMR analysis) as a mixture with recovered starting material **1** (35%). **8**: $^1$H NMR ($CDCl_3$) $\delta$ 0.98 (s, 9H), 1.25 (s, 9H), 1.36 (t, 3H, $J$ = 7.05 Hz), 4.31 (q, 2 H, $J$ = 7.05 Hz), 7.21 (d, 1H, $J$ = 2.26 Hz), 7.53 (d, 1H, $J$ = 2.26 Hz), 9.34 (s, 1H). When the reaction was allowed to proceed for longer than 4.5 h, there was a slow transition of the product mixture to one reflecting less **8**, accompanied by the appearance of **5** and unidentified products. By 5.5 h, the yield (by $^1$H NMR analysis, $CDCl_3$) of **8** decreased to 55%, with 9% **5** appearing, whereas by 10 h, the yield of **8** was 47%, with 23% **5** appearing.

**Reaction of 8 with the Cu(I)− or Cu(II)−2 Complexes**. To a degassed solution of **2** (0.127 g, 0.3 mmol) in 10 mL of $CH_3CN$ was added $[Cu(CH_3CN)_4][BF_4]$ (0.094 g, 0.3 mmol) under argon. Triethylamine (0.030 g, 0.3 mmol) and the crude hydroperoxide product **8** (0.091 g of the mixture of 65% **8** and 35% **1**, 0.3 mmol) in 10 mL of $CH_3CN$ was then added to the Cu(I)−**2** complex solution under argon. The resulting solution was stirred for 2 min anaerobically and was quenched with glacial acetic acid (0.054 g, 0.9 mmol), followed by evaporation of solvents. The residue was taken up into $CH_2Cl_2$, and the mixture was filtered through a short silica gel column to remove the metal complex. Upon removal of $CH_2Cl_2$, $^1$H NMR ($CDCl_3$) analysis of the crude product showed the complete absence of **8**, while compound **5** was detected as a major product along with unreacted **1** and minor amounts of unidentified materials. A control experiment, performed under the identical conditions except for exclusion of the Cu(I)−**2** complex, showed that **8** was unaffected by $Et_3N$, and conversion of **8** to **5** occurred smoothly in the absence of $Et_3N$ anyway. Another experiment, performed under $O_2$ using the Cu(II)−**2** complex, also indicated complete conversion of **8** to **5** within 90 s.

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**Deoxygenation of 8 with Dimethyl Sulfide.** The crude hydroperoxide product **8** (0.182 g of the mixture of 65% **8** and 35% **1**, 0.6 mmol) was placed in an ice-cooled flask. Excess dimethyl sulfide (3 mL) was then added dropwise with stirring. The resulting solution was stirred for 30 min followed by removal of the ice bath and continued stirring for 40 min at room temperature (25 °C). Upon evaporation of dimethyl sulfide under reduced pressure, the crude $^1$H NMR spectrum ($CDCl_3$) revealed the complete disappearance of **8** and quantitative appearance of ethyl 5-*tert*-butyl-3,4-dihydroxybenzoate (**10**), while the fraction of **1** present remained unchanged. The crude product **10** was purified by preparative thin-layer silica gel chromatography (hexanes−ethyl acetate, 3:2, v/v): $^1$H NMR ($CD_3OD$) $\delta$ 1.34 (t, 3H, $J$ = 7.11 Hz), 1.39 (s, 9H), 4.28 (q, 2 H, $J$ = 7.11 Hz), 7.34 (d, 2H, $J$ = 2.04 Hz), 7.50 (d, 2H, $J$ = 2.04 Hz); $^{13}$C NMR ($CD_3OD$) $\delta$ 14.74, 29.84, 35.65, 61.64, 114.56, 121.05, 121.20, 136.69, 145.83, 150.76, 168.95; HRMS (EI) $m/z$ calcd for $C_{13}H_{18}O_4$ 238.1205, found 238.1204 (rel intensity 100).

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**Supporting Information Available:** For compound **5**, tables (six) listing detailed crystal data structure refinement, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters, torsion angles; an ORTEP view of both independent molecules in the unit cell with labeling scheme; $^1$H and $^{13}$C (expect **6** and **8**) NMR spectra of **1**, **2**, **4**−**6**, **8**, and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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