Synthesis, Structure and Reactivity of Phenoxo Copper(II) Complexes, $Cu(OAr)(HB(3,5\text{-}Pr^i_2pz)_3)$ ($Ar = C_6H_4\text{-}4\text{-}F, 2,6\text{-}Me_2C_6H_3, 2,6\text{-}Bu^t_2C_6H_3$)

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Structure and reactivity of novel tetrahedral phenoxo copper(II) complexes have been reported as models for the reaction intermediates of tyrosinase catalyzed oxidation of phenols.

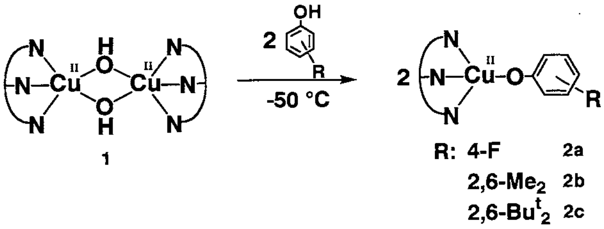
Structure and reactivity of phenoxo copper(II) complex are of interest because of its potential relevance to the tyrosinase catalysis.[1] Tyrosinase is a ubiquitous monooxygenase involved in melanin biosynthesis and has a binuclear copper active site.[2] A phenol (tyrosine) is supposed to interact with the copper(II) ion in the active site where dioxygen is reduced to a peroxide ion. A few interpretations have been made for the mechanistic study of the oxygen incorporation reaction.[3]

Our mechanistic study on the phenol oxidation with a μ-η^2:η^2 peroxo binuclear copper(II) complex suggested the involvement of phenoxo copper(II) intermediate.[4] That is to say, the reaction between nucleophilic μ-η^2:η^2 peroxo copper(II) complex $[[Cu(HB(3,5\text{-}Pr^i_2pz)_3)]_2(O_2)]$[5] ($HB(3,5\text{-}Pr^i_2pz)_3$ = hydrotris(3,5-diisopropyl-1-pyrazolyl)borate) and an acidic phenol yielded the phenoxo copper(II) complex via the acid-base reaction.[4a,6] Therefore, its reaction aspects are of very important to understand the reaction mechanism of tyrosinase catalysis. In this letter, a series of phenoxo copper(II) complexes has been synthesized by the reaction of the bis(μ-hydroxo) copper(II) complex ligated by a hindered tris(pyrazolyl)borate (to stabilize and make these complexes isolable for structural determination) with phenol derivatives. Mononuclear tetrahedral phenoxo copper(II) complexes, of which the structure is unusual for copper(II) ion, were obtained, and the reactivity of these complexes has been examined.

Addition of slightly excess (1.2 equiv.) of 4-fluorophenol, 2,6-dimethylphenol, or 2,6-di-*tert*-butylphenol into a CH_2Cl_2/pentane solution of bis(μ-hydroxo) complex $[[Cu(HB(3,5\text{-}Pr^i_2pz)_3)]_2(OH)_2]$ (**1**)[5] at -50 °C resulted in formation of a deep blue solution (Scheme 1). Removal of the solvent followed by recrystallization from a pentane/octane mixture yielded $[Cu(OC_6H_4\text{-}4\text{-}F)(HB(3,5\text{-}Pr^i_2pz)_3)]$ (**2a**), $[Cu(OC_6H_3\text{-}2,6\text{-}Me_2)(HB(3,5\text{-}Pr^i_2pz)_3)]$ (**2b**), or $[Cu(OC_6H_3\text{-}2,6\text{-}Bu^t_2)(HB(3,5\text{-}Pr^i_2pz)_3)]$ (**2c**), as a deep blue microcrystalline solid, respectively.[7] The molecular structure of **2a** has been determined by X-ray diffraction (Figure 1).[8]

It is apparent that the starting binuclear bis(μ-hydroxo) complex **1** was cleaved to form the first distorted tetrahedral phenoxo copper(II) complex. The Cu-O bond distance (1.731(3) Å) is distinctly shorter than those found in mononuclear phenoxo copper(II) complexes (1.83 Å - 1.94 Å),[9] but this is in accord with the general tendency observed in other tetrahedral copper(II) complexes with the same ligand: $[Cu(Cl)(HB(3,5\text{-}Pr^i_2pz)_3)]$, Cu-Cl = 2.13 Å,[10] and $[Cu(OOC\text{-}(Me)_2C_6H_5)(HB(3,5\text{-}Pr^i_2pz)_3)]$, Cu-O = 1.81 Å.[11]

While **2b** and **2c** are stable below -50 °C for a few months, they gradually decompose even under argon atmosphere at room temperature.[12] During the decomposition, intensity of the characteristic absorption bands declined gradually. The final spectrum is essentially identical with those of the bis(μ-hydroxo) complex, 3,3',5,5'-tetra-alkyldiphenoquinone (diphenoquinone), and 2,6-dialkyl-1,2-benzoquinone (benzoquinone). The products of the spontaneous decomposition under argon or dioxygen atmosphere were analyzed and quantified by GCMS and GC, respectively.[13] The products obtained by these reactions are summarized in Table 1.



Scheme 1

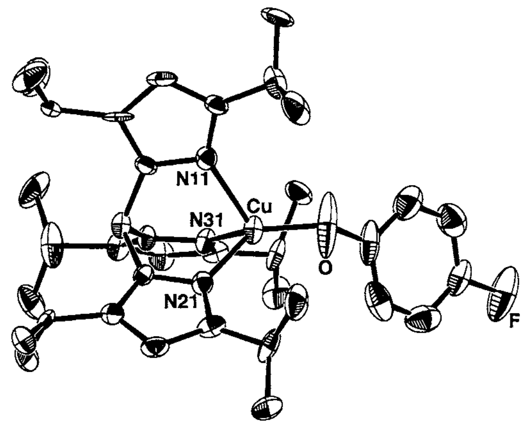
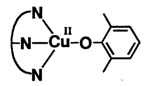
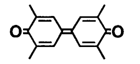
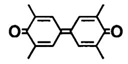
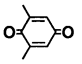
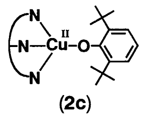
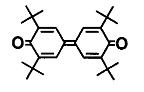
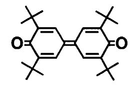
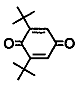


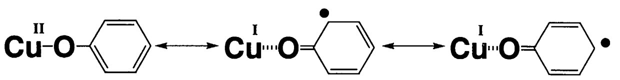
Figure 1. The structure of $[Cu(OC_6H_4\text{-}4\text{-}F)(HB(3,5\text{-}Pr^i_2pz)_3)$ (**2a**)] showing 30% thermal ellipsoids and atom-labeling scheme. For clarity, hydrogen atoms were omitted. Selected bond distances (Å) and angles (deg): Cu-O 1.731(3), Cu-N11 2.043(4), Cu-N21 1.995(4), Cu-N31 2.023(3), O-Cu-N11 120.1(2), O-Cu-N21 129.8(2), O-Cu-N31 121.1(1), N11-Cu-N21 90.9(1), N11-Cu-N31 92.5(1), N21-Cu-N31 92.9(1).

Under anaerobic conditions, only the oxidative coupling products, diphenoquinones, were generated. On the other hand, in the

Table 1. The products of the spontaneous decomposition of **2b** and **2c** under argon or dioxygen atmosphere[13]

	Ar	O_2	
 **(2b)**	 (12 %)	 (34 %)	 (21 %)
 **(2c)**	 (32 %)	 (42 %)	 (10 %)

presence of dioxygen, the benzoquinones were also formed in addition of the coupling product. However, the main products were still the oxidatively coupled products. Moreover, the yields of these products are higher than those of anaerobic reactions. Thus, we would like to address that under dioxygen atmosphere the formations of diphenoquinone and benzoquinone were enhanced due to the resonance structures of the phenoxo copper(II) species:



These results lead to the conclusion that these tetrahedral phenoxo copper(II) complexes, as an intermediate of tyrosinase catalysis,[14] could be accessible to radical species (dioxygen or more activated oxygen species) due to the contribution of the radical resonance. Therefore, this radical resonance structure should be very important for the oxidation of phenols, in relevance to tyrosinase catalysis.

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References and Notes

1 Copper is known as an effective catalyst for oxidative coupling reactions of phenols with dioxygen. The reaction has been explained in terms of free-radical mechanism involving a phenoxo radical, however, the details of the initial mechanism for the formation of the radical from phenol/dioxygen/copper has not been clarified yet.: A. S. Hay, *J. Polym. Sci., Polym. Chem. Ed.*, **36**, 505 (1998).

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6 These μ-η^2:η^2 peroxo copper(II) complexes are effective for the polymerization of phenols. H. Higashimura, K. Fujisawa, Y. Moro-oka, M. Kubota, A. Terahara, A. Shiga, H. Uyama, and S. Kobayashi, *J. Am. Chem. Soc.*, **120**, 8529 (1998).

7 Complex **2a**: Anal. Calcd for $C_{33}H_{50}N_6BCuOF$: C, 61.92; H, 7.87; N, 13.13%; Found: C, 62.34; H, 8.09; N, 13.04%. UV-Vis (CH_2Cl_2, -50 ℃, λmax/nm (ε/cm^{-1}mol^{-1}dm^3) 338(1760), 667(2540), 1020(490). Complex **2b**: Anal. Calcd for $C_{35}H_{55}N_6BCuO$: C, 64.65; H, 8.53; N, 12.93%; Found: C, 64.45; H, 8.89; N, 13.19%. UV-Vis (CH_2Cl_2, -50 ℃, λmax/nm(ε/cm^{-1}mol^{-1}dm^3) 340(1840), 393(1340), 715(2810), 1030(750). Complex **2c**: Anal. Calcd for $C_{41}H_{67}N_6BCuO$: C, 67.06; H, 9.20; N, 11.44%; Found: C, 66.15; H, 9.34; N, 10.90%. UV-Vis (CH_2Cl_2, -50 ℃, λmax/nm(ε/cm^{-1}mol^{-1}dm^3) 310(4450), 345(3230), 568 (1520), 833(3070).

8 Crystal data for **2a** ($C_{33}H_{50}N_6BCuOF$), M = 640.13, monoclinic, space group $P2_1/a$ (no. 14), a = 19.087(7) Å, b = 16.501(7) Å, c = 11.300(2) Å, β = 100.85(2) °, V = 3495(4) Å^3, Z = 4, Dc = 1.22 gcm^{-3}, μ(MoKα) = 6.62 cm^{-1}, 2θmax = 50.0 °, T = -60 ℃. Of 63760 unique reflections measured, 3480 [$I > 5.0\ \sigma(I)$] were used in refinement (R = 0.045, Rw = 0.030).

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12 The complex **2a** is very stable because of 4-F substitution. In the same reaction condition, the characteristic absorption bands did not decline.

13 The typical experiment is as follows: the 20-30 mg of the phenoxo complexes (**2b** - **2c**) was dissolved in 2-3 mL of CH_2Cl_2. The atmosphere was replaced with argon or dioxygen and the solution was allowed to stand at room temperature for one hour.

14 In tyrosinase, only one phenol (tyrosine) can be inserted into the substrate binding pocket in the protein, so the initial intermediate is most likely this mononuclear phenoxo copper(II) intermediate.