salicylaldehyde; Cu(II)-catalyzed racemization of L-glutamic acid. A high value of ρ indicates a more efficient transfer of electronic effects from the substituents to the reactive center. It may be a reflection of the more rigid coordination in the systems we have studied. However, the systems studied by Ando and Emoto had a 10-fold excess of L-glutamic acid. Equilibria are complex, and speciation differences were not analyzed for the different systems. It is possible that their value of ρ reflects not only differences in reactivity but also differences in degrees of complex formations as substituents are varied.

Coupling Constants and Distortions at the Glycine Methylene CH_2. The four-bond proton-proton spin coupling between a glycine methylene proton and the azomethine proton is expected to be a function of the dihedral angle between these bonds. Table III reports those coupling constants. It is observed that the high-field methylene proton is always equally or more strongly coupled than is the low-field proton. These coupling constants can be converted into dihedral angles using $^4J_{H-H} = -2.2 \sin^2 \phi$.[5,22]

Nature of the Stereoselectivity of Proton Exchange at the Glycine Methylene Group. Two explanations may be offered for the reason the glycine methylene protons exchange at different rates. One explanation is electronic in nature and is derived from the Dunathan hypothesis described above. The proton with the greatest dihedral angle with the plane of the π system should be most acidic and exchange more rapidly. This explanation has been suggested for the pyridoxal system in which the glycine proton with the largest coupling to the azomethine proton exchanges most rapidly.[4] An alternate explanation is based on steric factors. In this explanation, steric factors impede the removal of one of the methylenic protons of the reactant and discriminate against reprotonation of the carbanion intermediate from the same side of the ligand plane. This explanation has been offered to explain the selectivity in 3-Me and other related systems.[6-8] In the 3-Me compound, presumably, it is the 3-methyl group of one ligand that impedes the reprotonation on one side of the other ligand. While we hoped that our present study would provide a clear resolution between electronic and steric effects, a review of the results show that evidence can be selected to support either model. For example, 3-Me has the greatest rate difference of any system reported herein. Figure 4 shows that, on a Hammett plot, the slowly exchanging proton rate falls far below the line, indicating, perhaps, that steric effects impede its rate and result in the observed selectivity. On the other hand, space-filling molecular models do not indicate substantial steric problems for reprotonation in aqueous media. Also, if steric factors were operating, the more bulky 3-isopropyl group of Thym, the 3-methoxy group of the 3-MeO, and the 3-ethoxy group of the 3-EtO might be expected to cause even greater selectivity than does the 3-methyl substituent; however, this is not the case. Moreover, in two of the compounds studied in this work, the selectivity in proton exchange is the reverse of the others and there is certainly no obvious steric explanation. Additional work investigating the effect of even more bulky groups in the 3-position is under way.

Chelate ring conformations vary in this series of compounds. It has been demonstrated by X-ray crystallography that the azomethine and glycyl chelate rings are planar in the Sal case[21] but puckered in the pyridoxal case.[5] Puckering results in different dihedral angles between the two glycyl methylene protons and the plane in the π system, which, according to the Dunathan hypothesis, should affect the rate of carbon-hydrogen bond breaking. This difference is revealed in the difference in four-bond coupling constants betwen the azomethine proton and each methylene proton. These coupling constants are nearly identical in the Sal case, in keeping with its observed planarity, but are very different in the 3-Me case, indicating a substantially puckered ring. In the present work, it was hoped that there would be a simple relationship between those coupling constants and the reactivity of the compounds, but this does not appear to be the case. It is possible that the conformations differ in a complicated way from compound to compound. Until structures for a representative group of substituted salicyl chelates have been determined, it will not be possible to provide a detailed assessment of the relative contributions of steric and electronic effects of stereoselectivity in these compounds. However, it appears that, whatever the role of steric factors, electronic factors are important.

Conclusions

1. The rates of glycyl carbon-hydrogen bond breaking are strongly influenced by inductive and resonance effects of substituents on the aromatic ring.
2. In this system, the inductive effects are considerably larger than had been previously reported for an analogous system.
3. For each compound, the glycyl protons exchange at different rates. The degree of stereoselectivity depends on the nature of remote ring substituents.
4. Ring substitutents cause small distortions from planarity of the azomethine and glycyl chelate rings.

Acknowledgment. The complexes studied in this paper were prepared at WNMU by Gail Stanford, Mary Kappel, Phillip Welsh, David Lambert, William VanDran, and J. Antonio Lopez as part of requirements for Chemistry 304 and 485. We also gratefully acknowledge support of this work through a Flinn Foundation—Cottrell College Science Grant C-2511 from the Research Corp. and grants from the WNMU Research Committee at Western New Mexico University and through Grant CHE 7826160 from the National Science Foundation at Montana State University.

Supplementary Material Available: A table, in spreadsheet format, containing a more detailed summary of the kinetic results (1 page). Ordering information is given on any current masthead page.

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Synthesis and Dioxygen Reactivity of Dinuclear Copper-Phenolate and Copper-Phenol Complexes with Pyrazole and Pyridine Donors

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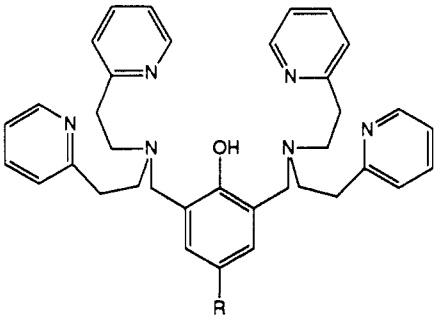
Received September 25, 1989

New hybrid ligands containing pyrazole and pyridine have been prepared; and the reaction chemistry of their copper(I) derivatives has been studied. These dinucleating ligands provide three nitrogen donors to each metal ion, and a phenol or phenolate group to bridge between the metals. The reaction of the different dicopper(I) species with dioxygen follows patterns established previously for analogous pyridyl ligands; and peroxo and hydroperoxo adducts can be generated at low temperature.

There is convincing evidence to suggest that hemocyanin contains an endogenous protein bridging ligand in at least some of its derivatives,[2] and before the crystal structure of deoxyHc had been determined,[3] a phenolate group was considered a likely

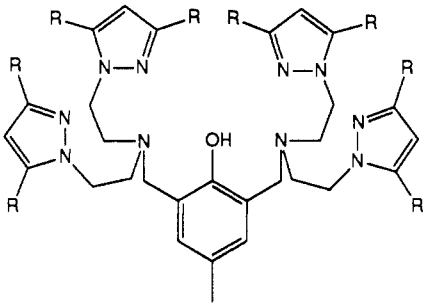
0020-1669/90/1329-1687$02.50/0

candidate. As a result, many phenol- and phenolate-containing ligands[4] have been used as models for the hemocyanin active site. The ligand systems $(Py_4)N6OH$ (**1**),[5] $(Pz_4)N6OH$ (**2a**), and



1a R = H

1b R = CH_3



2a R = H

2b R = CH_3

$(DMP_4)N6OH$ (**2b**), which ultimately provide three nitrogen donors to each Cu ion, have been used to prepare many particularly useful biomimics of the type III copper protein sites.[6-8]

To continue developing the chemistry of this type of dinucleating ligand, we have synthesized and studied the reactivity of the mixed ligands **3** (see Scheme I) with the hope of observing reactivity patterns intermediate between those observed for the copper complexes of **1a** and **2**. In this paper, we compare the reaction chemistry of the copper(I) complexes of ligands **1**–**3**.

Experimental Section

All reagents and solvents were purchased from commercial sources and used as received unless noted otherwise. 2,6-Bis(hydroxymethyl)-*p*-cresol,[9] 2,6-bis(chloromethyl)-*p*-cresol,[10] $(Pz_2)N3H$,[11] and $Cu(CH_3CN)_4PF_6$[12] were prepared according to literature methods. The binucleating ligands **1b**,[13] **2a**, and **2b** were all prepared by the method described previously.[7] The solvents used to prepare the copper(I) complexes were distilled and stored under nitrogen: methanol, from magnesium methoxide under dinitrogen; tetrahydrofuran (THF), from sodium–benzophenone ketyl under argon; acetonitrile and 2-propanol, from calcium hydride under dinitrogen. Carbon monoxide was purified by successive passage of the gas through an acidic chromium(II) solution, concentrated H_2SO_4, NaOH pellets, and $CaSO_4$. Analytical thin-layer chromatography (TLC) was run on Analtech precoated (0.25 mm) silica gel plates. Flash chromatography was performed according to the general procedure of Still.[14] Cu(I) complexes and spectroscopic samples were prepared in a Vacuum Atmospheres drybox (<1 ppm of O_2 and H_2O). Microanalyses were performed by Desert Analytics, Tucson, AZ, or by Atlantic Microlabs, Inc., Norcross, GA.

^1H NMR spectra were recorded on an IBM 200-MHz instrument. All chemical shifts are reported in parts per million (ppm) relative to an internal standard of tetramethylsilane. Infrared spectra were recorded on a Beckman IR 4250 spectrophotometer, and peaks are reported in cm^{-1}.

Dioxygen-uptake measurements were performed at −78 °C by manometric methods similar to those described in the literature.[16]

Absorption Spectra. Methylene chloride was purified by stirring with concentrated H_2SO_4 in the dark for several days, washing with saturated KOH/KCl and distilled water, and then distilling from CaH_2 under dinitrogen. Spectra were recorded on a Hewlett-Packard 8450 diode array spectrophotometer or on a Perkin-Elmer 552 spectrophotometer. Low-temperature spectra were taken by using a sealed quartz cell (1 cm) placed in a Kontes UV–vis variable-temperature glass Dewar flask. The cell was held in place by means of a Teflon collar connected to the cell and to the Dewar flask. The flask was filled with Burdick and Jackson spectral grade MeOH that was cooled by means of a copper coil through which cold dinitrogen was passed. The copper coil was twisted so that the cell fit inside the helix and was of a length that the windows of the Dewar flask were not obscured. The temperature was controlled by adjusting the nitrogen flow and was monitored with an alcohol thermometer. Oxygen was dried by passage through a column of $CaSO_4$, and reactions were conducted under a constant stream of dioxygen. Hydrogen peroxide and HPF_6 were added in CH_2Cl_2 solution to avoid fogging of the cell.

[2-(1-Pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amine [(PyPz)N3H] (4). Under a dinitrogen atmosphere at 0 °C, 5.8 g (0.085 mol) of pyrazole was added slowly to a suspension of 4.3 g (0.180 mol) of sodium hydride in 200 mL of *N*,*N*-dimethylformamide (DMF). The mixture was stirred for 30 min; then 10.0 g (0.086 mol) of chloroethylamine hydrochloride was added slowly. Once the addition was complete, the mixture was warmed to 50 °C and stirred for 2 days. The reaction mixture was evaporated to dryness, the residue was dissolved in 150 mL of methanol, and the solution was filtered. The filtrate was acidified to pH 5 with acetic acid; then 10.0 mL (0.095 mol) of 2-vinylpyridine was added. This mixture was heated under reflux under a dinitrogen atmosphere for 1 week. The reaction mixture was then evaporated to dryness, and the residue was dissolved in 10% sodium hydroxide and extracted with methylene chloride. The extracts were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Flash chromatography on silica using 1:1 methanol–ethyl acetate as the eluent (R_f = 0.16) yielded 6.65 g (36%) of a yellow oil. ^1H NMR ($CDCl_3$): 2.9 (m, 4 H, CH_2CH_2–Py), 3.1 (t, 2 H, NCH_2), 4.2 (t, 2 H, CH_2–Pz), 6.2 (t, 1 H, pyrazolyl C4–H), 7.1 (d, 2 H, pyrazolyl C3,C5–H), 7.4 (d of d, 2 H, pyridyl C3,C5–H), 7.6 (t of d, 1 H, pyridyl C4–H), 8.4 (d, 1 H, pyridyl C6–H).

[2-(3,5-Dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amine [(PyDMP)N3H] (5). Under a dinitrogen atmosphere at 0 °C, 12.4 g (0.129 mmol) of 3,5-dimethylpyrazole was slowly added to a suspension of 6.2 g (0.258 mmol) of sodium hydride in 400 mL of DMF. The reaction was stirred for 30 min; then 15.0 g (0.129 mmol) of chloroethylamine hydrochloride was added slowly. Once the addition was complete, the mixture was warmed to 50 °C and stirred for 2 days. The reaction mixture was evaporated to dryness, the residue was dissolved in 200 mL of methanol, and the solution was filtered. The filtrate was acidified to pH 5 with acetic acid; then 15.0 mL (0.143 mmol) of 2-vinylpyridine was added. The mixture was heated at reflux under a dinitrogen atmosphere for 3 days. It was evaporated to dryness, and the residue was dissolved in 10% sodium hydroxide and extracted with

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(5) Abbreviations used in this paper: DMF, *N*,*N*-dimethylformamide; DMP, 3,5-dimethylpyrazolyl; Hc, hemocyanin; Py, pyridyl; Pz, pyrazolyl; THF, tetrahydrofuran.
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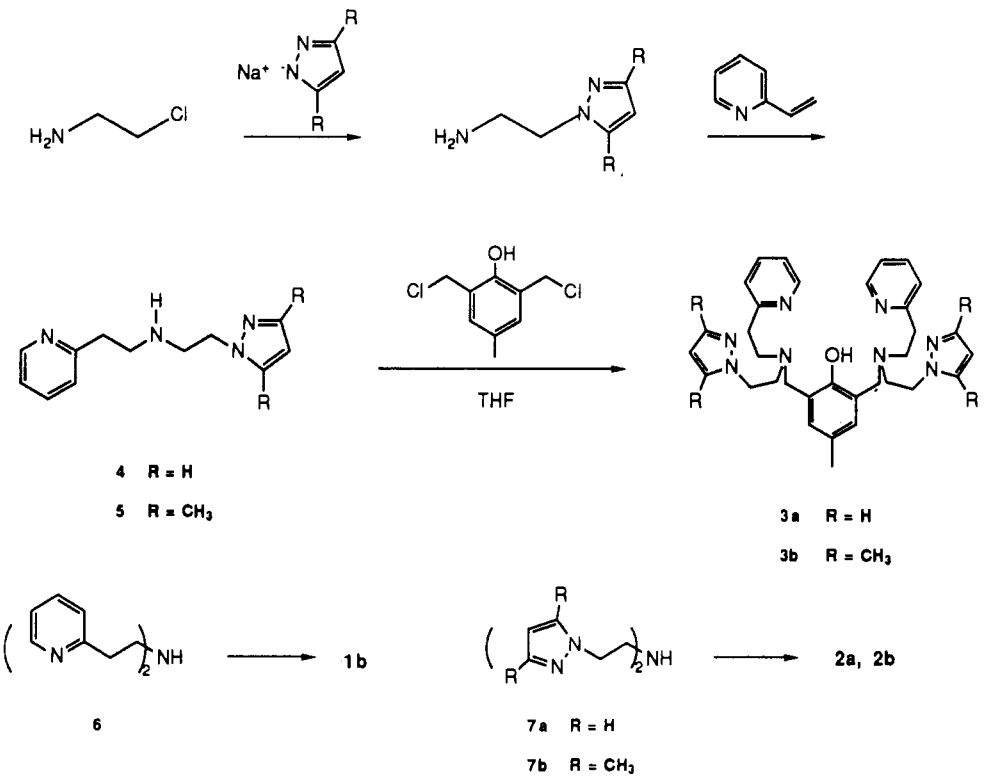
Scheme I



methylene chloride. The extracts were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Flash chromatography on silica using 1:1 methanol–ethyl acetate as the eluent (R_f = 0.20) gave 3.4 g (11%) of a yellow oil. ^{1}H NMR ($CDCl_3$): 2.14 (s, 3 H, pyrazolyl–CH_3), 2.25 (s, 3 H, pyrazolyl–CH_3), 3.2 (t, 2 H, NCH_2), 3.4 (m, 4 H, CH_2CH_2–Py), 4.27 (t, 2 H, CH_2–DMP), 5.79 (s, 1 H, pyrazolyl C4–H), 7.16 (m, 2 H, pyridyl C3,5–H), 7.6 (m, 1 H, pyridyl C4–H), 8.36 (d, 1 H, pyridyl C6–H).

2,6-Bis{[[2-(1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol [(Py_2Pz_2)N6OH] (3a). Under a dinitrogen atmosphere, 1.1 g (5.4 mmol) of 2,6-bis(chloromethyl)-*p*-cresol and 1.1 g (10.9 mmol) of triethylamine were added to 70 mL of THF. A white precipitate formed immediately. A solution of 2.4 g (11.1 mmol) of (PyPz)N3H (4) in 70 mL of THF was added, and the resulting mixture was stirred overnight at room temperature. The reaction mixture was evaporated to dryness, and the residue was dissolved in aqueous saturated sodium bicarbonate. The solution was subsequently neutralized with 15% HCl and extracted with methylene chloride. The extracts were washed with aqueous saturated sodium chloride and dried over sodium sulfate. Flash chromatography on silica using 1:1 methanol–ethyl acetate as the eluent (R_f = 0.58) yielded 0.73 g (24%) of product as a yellow oil. ^{1}H NMR ($CDCl_3$): 2.18 (s, 3 H, $ArCH_3$), 2.93 (s, 8 H, CH_2CH_2–Py), 3.05 (t, 4 H, NCH_2), 3.70 (s, 4 H, $ArCH_2$), 4.20 (t, 4 H, CH_2–Pz), 6.15 (s, 2 H, pyrazolyl C4–H), 6.75 (s, 2 H, Ar H), 7.10 (m, 4 H, pyridyl C3,C5–H), 7.30 (s, 2 H, pyrazolyl C5–H), 7.50 (m, 4 H, pyrazolyl C3–H, pyridyl C4–H), 8.50 (d, 2 H, pyridyl C6–H).

2,6-Bis{[[2-(3,5-dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol [(Py_2DMP_2)N6OH] (3b). Under a dinitrogen atmosphere, 1.0 g (4.9 mmol) of 2,6-bis(chloromethyl)-*p*-cresol and 1.0 g (9.9 mmol) of triethylamine were added to 150 mL of THF. A white precipitate formed immediately. A solution of 2.29 g (9.38 mmol) of (PyDMP)N3H (**5**) in 25 mL of THF was added, and the mixture was stirred at room temperature for 6 h. The reaction mixture was evaporated to dryness, and the residue was dissolved in saturated aqueous sodium bicarbonate. The solution was subsequently neutralized with 10% HCl and extracted with ethyl acetate. The extracts were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Flash chromatography on silica using 1:1 methanol–ethyl acetate as the eluent (R_f = 0.61) yielded 1.05 g (36%) of a yellow oil. ^{1}H NMR ($CDCl_3$): 2.1 (s, 3 H, $ArCH_3$), 2.2 (s, 12 H, pyrazolyl–CH_3), 3.0 (m, 12 H, CH_2CH_2–Py), 3.7 (s, 4 H, $ArCH_2$), 4.0 (t, 4 H, CH_2–DMP), 5.7 (s, 2 H, pyrazolyl C4–H), 6.75 (s, 2 H, Ar H), 7.1 (m, 4 H, pyridyl C3,C5–H), 7.5 (m, 2 H, pyridyl C4–H), 8.45 (d, 2 H, pyridyl C6–H).

{2,6-Bis{[bis[2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(I) Hexafluorophosphate Hydrate {Cu_2[(Py_4)N6O]PF_6·H_2O} (8). In an inert-atmosphere box, a solution of 1.2 g (3.22 mmol) of $Cu(CH_3CN)_4PF_6$ in 12 mL of warm methanol was prepared, allowed to cool to room temperature, and added to a solution of 0.935 g (1.63 mmol) of (Py_4)N6OH (**1b**) and 0.100 g (1.78 mmol) of potassium hydroxide in 3 mL of methanol. The volume of the solution was reduced by half under vacuum, and the orange precipitate that formed was collected. The dark orange product was recrystallized by diffusion of THF into an acetonitrile solution of the compound. IR (KBr): 2950, 2920, 2860, 2840 (Ar H); 870 (PF_6). Anal. Calcd for $C_{37}H_{44}Cu_2F_6N_6O_2P$: C, 50.74; H, 5.02; N, 9.60. Found: C, 50.51; H, 4.77; N, 9.88.

{2,6-Bis{[[2-(1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(I) Hexafluorophosphate {Cu_2[(Py_2Pz_2)N6O]PF_6} (9). In an inert-atmosphere box, a solution of 0.963 g (2.59 mmol) of $Cu(CH_3CN)_4PF_6$ in 10 mL of warm methanol was prepared, allowed to cool to room temperature, and added to a solution of 0.730 g (1.29 mmol) of **3a** and 0.100 g (1.79 mmol) of KOH in 2 mL of methanol. The solution was stirred for 15 min, and the orange precipitate that formed was collected. The crude product was recrystallized by vapor diffusion of THF into a solution of the complex in CH_3CN. IR (KBr): 2960, 2920, 2860, 2840 (Ar H); 835 (PF_6). Anal. Calcd for $C_{33}H_{40}Cu_2F_6N_8OP$: C, 47.42; H, 4.67; N, 13.41. Found: C, 47.33; H, 4.66; N, 13.32.

{2,6-Bis{[[2-(3,5-dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(I) Hexafluorophosphate {Cu_2[(Py_2DMP_2)N6O]PF_6} (10). In an inert-atmosphere box, a solution of 1.10 g (2.96 mmol) of $Cu(CH_3CN)_4PF_6$ in 10 mL of warm methanol was prepared, allowed to cool to room temperature, and added to a solution of 0.938 g (1.51 mmol) of **3b** and 0.100 g (1.79 mmol) of potassium hydroxide in 10 mL of methanol. The resulting mixture was stirred for 20 min, during which an orange precipitate formed. The precipitate was collected and recrystallized from acetonitrile by vapor diffusion with THF. IR (KBr): 2950, 2910 (Ar H); 835 (PF_6). Anal. Calcd for $C_{37}H_{47}Cu_2F_6N_8OP$: C, 49.83; H, 5.27; N, 12.57. Found: C, 49.74; H, 5.29; N, 12.75.

{2,6-Bis{[bis[2-(1-pyrazolyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Bis(hexafluorophosphate) {Cu_2[(Pz_4)N6OH](PF_6)$_2$} (11). In an inert-atmosphere box, a solution of 1.8 g (4.84 mmol) of $Cu(CH_3CN)_4PF_6$ in 15 mL of warm methanol was prepared, allowed to cool to room temperature, and added to a solution of 1.3 g (2.40 mmol) of (Pz_4)N6OH (**2a**) in 3 mL of methanol. A white precipitate formed immediately and was collected and recrystallized from warm methanol. IR (KBr): 3680 (OH); 3140, 2850 (Ar H); 830 (PF_6).

{2,6-Bis{[bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Bis(hexafluorophosphate) {Cu_2[(DMP_4)N6OH](PF_6)$_2$} (12). In an inert-atmosphere box, a solution of 0.910 g (2.45 mmol) of $Cu(CH_3CN)_4PF_6$ in 10 mL of methanol was added to a solution of 0.799 g (1.22 mmol) of (DMP_4)N6OH (**2b**) in 3 mL of methanol. The resulting mixture was evaporated to dryness, and the crude product was

recrystallized from warm methanol, yielding white crystals. IR (KBr): 3570 (OH); 2960, 2920, 2840 (Ar H); 830 (PF_6). Anal. Calcd for $C_{37}H_{54}Cu_2F_{12}N_{10}OP_2$: C, 41.46; H, 5.04; N, 13.07. Found: C, 41.54; H, 4.96; N, 13.26.

{2,6-Bis{[[2-(1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Bis(hexafluorophosphate) {Cu_2[(Py_2Pz_2)N6OH](PF_6)$_2$} (13). In an inert-atmosphere box, a solution of 0.915 g (2.46 mmol) of $Cu(CH_3CN)_4PF_6$ in 15 mL of methanol was added to a solution of 0.694 g (1.23 mmol) of **3a** in 4 mL of methanol. The resulting mixture was stirred for 5 min and evaporated to dryness. The crude product was recrystallized from warm methanol by vapor diffusion of 2-propanol into the solution, yielding yellow crystals. IR (KBr): 3140, 2920, 2960, 2840 (Ar H); 830 (PF_6). Anal. Calcd for $C_{33}H_{40}Cu_2F_{12}N_8OP_2$: C, 40.37; H, 4.08; N, 11.41. Found: C, 40.46; H, 4.20; N, 11.50.

{2,6-Bis{[[2-(3,5-dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Bis(hexafluorophosphate) Trihydrate {Cu_2[(Py_2DMP_2)N6OH](PF_6)$_2$·3H_2O} (14). In an inert-atmosphere box, a solution of 0.95 g (2.5 mmol) of $Cu(CH_3CN)_4PF_6$ in 7 mL of methanol was added to a solution of 0.794 g (1.3 mmol) of **3b** in 3 mL of methanol. The resulting mixture was evaporated to dryness to isolate the product. IR (KBr): 2920, 2860 (Ar H); 820–860 (PF_6). Anal. Calcd for $C_{37}H_{54}Cu_2F_{12}N_8O_3P_2$: C, 40.69; H, 4.94; N, 10.26. Found: C, 40.19; H, 4.36; N, 10.89.

{2,6-Bis{[bis[2-(1-pyrazolyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Dicarbonyl Bis(hexafluorophosphate) Hydrate {Cu_2[(Pz_4)N6OH](CO)$_2$-(PF_6)$_2$·H_2O} (15). In an inert-atmosphere box, a solution of 0.422 g (0.78 mmol) of **2a** in 3 mL of THF was prepared and placed in a Schlenk tube. A solution of 0.580 g (1.56 mmol) of $Cu(CH_3CN)_4PF_6$ in 10 mL of warm methanol was prepared and placed in a second Schlenk tube. The Schlenk tubes were removed from the drybox and purged with CO for 30 min. The solution of the copper complex was added to the ligand solution by cannula, and the volume of the resulting mixture was reduced by half under a stream of CO. The yellow precipitate was separated from the remaining solution by decantation and was dried under a stream of CO. IR (KBr): 3500 (OH); 3040, 2950, 2860 (Ar H); 2090 (CO); 815–880 (PF_6). Anal. Calcd for $C_{31}H_{48}Cu_2F_{12}N_{10}O_4P_2$: C, 35.64; H, 4.64; N, 13.44. Found: C, 35.80; H, 3.78; N, 13.41.

{2,6-Bis{[bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Dicarbonyl Bis(hexafluorophosphate) Hydrate {Cu_2-[(DMP_4)N6OH](CO)$_2$(PF_6)$_2$·H_2O} (16). In an inert-atmosphere box, a solution of 0.314 g (0.48 mmol) of **2b** in 3 mL of THF was prepared and placed in a Schlenk tube. A solution of 0.360 g (0.97 mmol) of $Cu(CH_3CN)_4PF_6$ in 4 mL of warm methanol was also prepared and placed in a second Schlenk tube. The Schlenk tubes were removed from the box and purged with CO for 30 min. The solution of the copper complex was added to the ligand solution by cannula, and the solvent was evaporated under a stream of CO, leaving a powdery yellow solid. IR (KBr): 3580–3530 (OH); 2930, 2860 (Ar H); 2085 (CO); 820–880 (PF_6). Anal. Calcd for $C_{39}H_{56}Cu_2F_{12}N_{10}O_4P_2$: C, 40.87; H, 4.89; N, 12.23. Found: C, 40.45; H, 4.97; N, 12.38.

{2,6-Bis{[[2-(1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Dicarbonyl Bis(hexafluorophosphate) Tetrakis(acetonitrile) Tetrahydrofuranate {Cu_2[(Py_2Pz_2)N6OH](CO)$_2$(PF_6)$_2$·4CH_3CN·THF} (17). In an inert-atmosphere box, a solution of 0.817 g (1.4 mmol) of **3a** in 5 mL of 2:3 methanol–THF was prepared and placed in a Schlenk tube. A solution of 1.0 g (2.7 mmol) of $Cu(CH_3CN)_4PF_6$ in 10 mL of methanol was also prepared and placed in a second Schlenk tube. The Schlenk tubes were removed from the box and purged with CO for 30 min. The solution of the copper complex was added to the ligand solution by cannula, and the solvent was evaporated under a stream of CO, leaving a dark solid. IR (KBr): 3140, 2950, 2870 (Ar H); 2090 (CO); 830–920 (PF_6). Anal. Calcd for $C_{47}H_{60}Cu_2F_{12}N_{12}O_4P_2$: C, 44.30; H, 4.71; N, 13.19. Found: C, 44.15; H, 4.51; N, 13.50.

{2,6-Bis{[[2-(3,5-dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresol}dicopper(I) Dicarbonyl Bis(hexafluorophosphate) {Cu_2[(Py_2DMP_2)N6OH](CO)$_2$(PF_6)$_2$} (18). In an inert-atmosphere box, a solution of 0.493 g (0.795 mmol) of **3b** in 6 mL of 1:1 methanol–THF was prepared and placed in a Schlenk tube. A solution of 0.540 g (1.59 mmol) of $Cu(CH_3CN)_4PF_6$ in 7 mL of methanol was also prepared and placed in a second Schlenk tube. The Schlenk tubes were removed from the box and purged with CO for 30 min. The solution of the copper complex was added to the ligand solution by cannula, and the volume of the solution was reduced by three-fourths, at which time the complex separated as an oil. The remaining solvent was decanted, and the oil was dried under a stream of CO until it solidified. IR (KBr): 2960, 2930, 2870 (Ar H); 2080 (CO); 810–870 (PF_6). Anal. Calcd for $C_{39}H_{48}Cu_2F_{12}N_8O_3P_2$: C, 42.81; H, 4.39; N, 10.25. Found: C, 43.15; H, 4.61; N, 10.36.

(μ-Hydroxo){2,6-bis{[bis[2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(II) Bis(perchlorate) Methanolate {Cu_2[(Py_4)N6O](OH)-(ClO_4)$_2$·CH_3OH} (19). A solution of 0.930 g (2.52 mmol) of Cu(ClO_4)$_2$·6H_2O in 5 mL of methanol was added to a solution of 0.740 g (1.26 mmol) of **1b** in 5 mL of methanol. A 10-mL aliquot of H_2O was added to the solution, which was filtered and allowed to stand open. Dark green crystals formed after several days. IR (KBr): 3360 (OH); 2920, 2860 (Ar H); 1080–1105 (ClO_4). Anal. Calcd for $C_{38}H_{47}Cl_2Cu_2N_6O_{11}$: C, 47.54; H, 4.90; N, 8.76. Found: C, 47.46; H, 4.62; N, 8.80.

(μ-Hydroxo){2,6-bis{[[2-(1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(II) Bis(perchlorate) Tetrahydrate Methanolate {Cu_2[(Py_2Pz_2)N6O]OH(ClO_4)$_2$·3H_2O·CH_3OH} (20). A solution of 0.207 g (0.559 mmol) of Cu(ClO_4)$_2$·6H_2O in 2 mL of methanol was added to a solution of 0.158 g (0.280 mmol) of **3a** in 3 mL of methanol. The resulting mixture was filtered through glass wool. A 5-mL aliquot of H_2O was added to the filtrate, which was allowed to stand for 1 week to give green crystals. IR (KBr): 3400–3700 (OH); 3130, 2920, 2860 (Ar H); 1080–1105 (ClO_4). Anal. Calcd for $C_{33}H_{50}Cl_2Cu_2N_8O_{14}$: C, 41.17; H, 4.74; N, 11.30. Found: C, 40.92; H, 4.39; N, 11.26.

(μ-Hydroxo){2,6-bis{[[2-(3,5-dimethyl-1-pyrazolyl)ethyl][2-(2-pyridyl)ethyl]amino]methyl}-*p*-cresolato}dicopper(II) Bis(perchlorate) Hydrate {Cu_2[(Py_2DMP_2)N6O](OH)(ClO_4)$_2$·H_2O} (21). A solution of 0.884 g (2.39 mmol) of Cu(ClO_4)$_2$·6H_2O in 2 mL of methanol was added to a solution of 0.740 g (1.19 mmol) of **3b** in 3 mL of methanol. A 5-mL aliquot of H_2O was added to the resulting brown solution, which afforded brown crystals after standing in the air for several days. IR (KBr): 3350–3640 (OH); 2960, 2920, 2860 (Ar H); 1090 (ClO_4). Anal. Calcd for $C_{37}H_{50}Cl_2Cu_2N_8O_{11}$: C, 45.35; H, 5.20; N, 11.44. Found: C, 45.50; H, 4.85; N, 11.11.

Results

Synthesis. The N6OH ligands were synthesized by the route outlined in Scheme I. The pyrazole group is introduced via nucleophilic displacement of a chloride ion, and the pyridine donor is added by addition of the amine to 2-vinylpyridine. The "N3" piece is then used to displace the chloride groups from 2,6-bis(chloromethyl)-*p*-cresol. We have used this reaction before to prepare ligands **2a** and **2b**,[6,7] but better results are obtained when the reaction is run at ambient temperature in THF.

The N6OH ligands can be used either protonated or unprotonated to give different types of Cu(I) complexes (Scheme II). When a methanolic solution of $Cu(CH_3CN)_4PF_6$ is added to a methanolic solution of ligand **1a**, **1b**, **3a**, or **3b** and potassium hydroxide, an orange phenolato complex of the form {Cu_2N6O}(PF_6) precipitates. In the case of the pyrazolyl ligands **2a** and **2b**, disproportionation occurs instead.

However, the *phenol* complexes {Cu_2[N_6OH](PF_6)$_2$} can be isolated for each N_6OH ligand if no hydroxide ion is used in the synthesis; and the corresponding carbonyl complexes may be obtained if the reaction of the ligand and Cu(I) precursor is carried out under an atmosphere of CO. All of the complexes can be handled briefly in air in the solid state without decomposition.

For all intents and purposes, the pyridyl complexes **8** and **19** prepared for this study have already been characterized extensively by Karlin.[16] We felt it was necessary to prepare the complex with the methyl group *para* to the phenol group to make sure that the reactivity patterns that we observed were not influenced by that particular substitution. In every way, the copper(I) complexes of ligands **1a** and **1b** react analogously.

Absorption Spectroscopy. The chemistry of the phenol (**11–18**) and phenolate (**8–10**) complexes with dioxygen is summarized in Figure 1, and the spectral data are presented in Table I. At room temperature, all the complexes (both phenolate and phenol) react with dioxygen and are oxidized to the μ-phenoxo–μ-hydroxo Cu(II) complexes, prepared independently from the ligand and copper(II) perchlorate. However, at low temperature (−78 °C) in CH_2Cl_2, more interesting chemistry is observed. It is important to note that this chemistry is observed only if the CH_2Cl_2 has been carefully dried; if not, oxidation to the corresponding μ-phenoxo–μ-hydroxo Cu(II) complex results.

At −78 °C, an orange solution of the Cu(I) phenolate complex **8**, **9**, or **10** reacts very rapidly (<1 min) with dioxygen to form a purple Cu(II)–peroxo adduct (2:1 Cu:O_2), which is characterized by an intense band at ~500 nm (a peroxide to Cu(II) charge-transfer band[15]) in the visible region of the spectrum. Figure 2 shows representative spectra for the {Cu_2[(Py_2Pz_2)N6O]PF_6

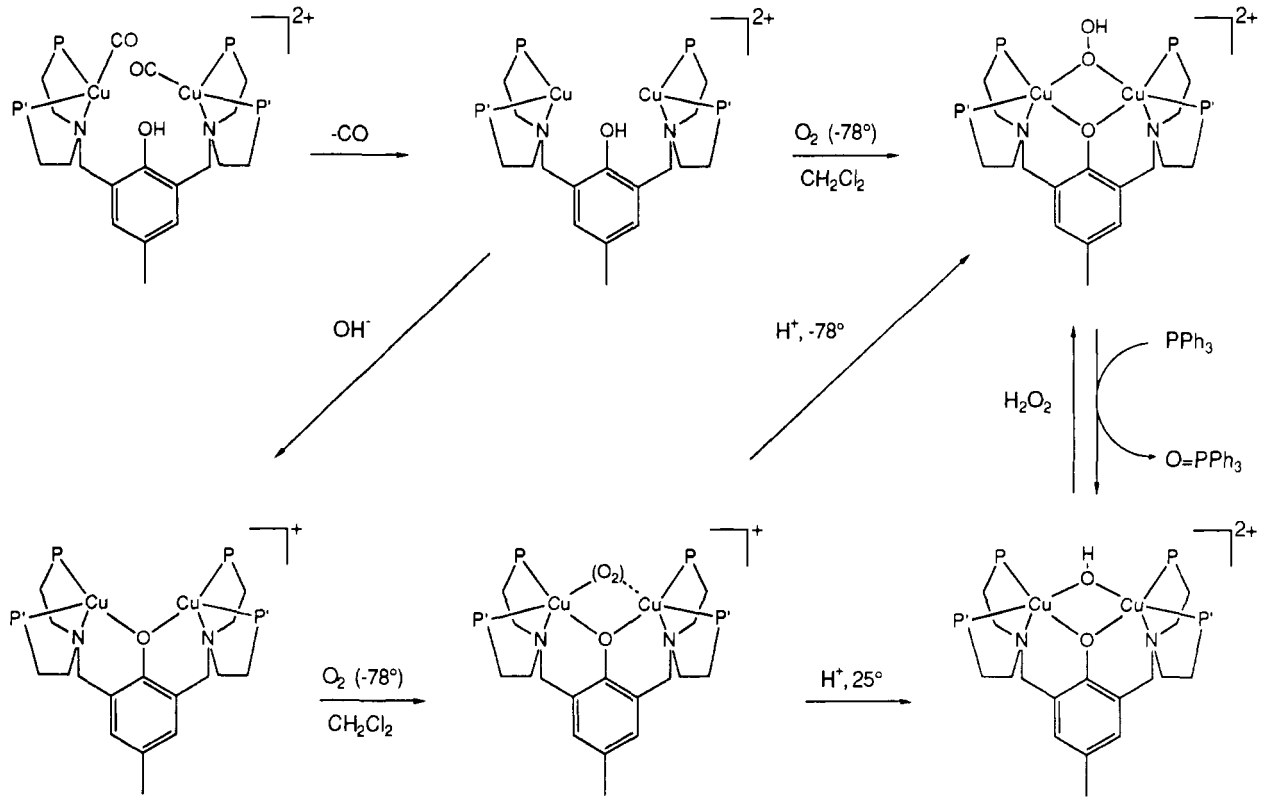


Figure 1. Summary of reactions of $Cu_2(N6O)^+$ and $Cu_2(N6OH)^{2+}$ complexes.

Table I. Spectral Data for Peroxo- and (Hydroperoxo)copper Complexes[a]

	$Cu_2L(O_2)^+$		$Cu_2L(OOH)^{2+}$	
ligand (LH)	λ, nm	ε, M^{-1} cm^{-1}	λ, mn	ε, M^{-1} cm^{-1}
1a[b]	390	2900	395	8000
	505	6000	450	2200
	610	2100	620	450
1b	390	4800	343	8600
	500	6500	396	8300
	630	750	480	3700
2a	*c*		345	2100
			402	4400
			458	900
2b	*c*		345	4900
			404	7600
			506	1000
			658	65
3a	400	2500	344	8600
	505	4900	400	8400
	630	1200	490	3300
3b	390	3400	345	3900
	510	6700	395	5500
	630	1600	470	1300
			630	330

[a] At −78 °C in CH_2Cl_2. [b] Peroxo complex: ref 16; hydroperoxo complex: ref 21. [c] The starting copper(I) complex (Cu_2L^+) disproportionates.

complex. A smaller band at ~395 nm (a phenoxide to Cu(II) charge-transfer band[16]) and a shoulder at ~630 nm (a peroxide to Cu(II) charge-transfer band[16]) are also observed. The Cu(I) complex shows no bands in this region, and the μ-phenoxo–μ-hydroxo Cu(II) complex, while having absorptions in this region, does not have a band at 500 nm. The purple color disappears when the sample is warmed above −50 °C, if dinitrogen is bubbled through the solution, or if a vacuum is applied to a warmed sample. Karlin has been able to show quasi-reversible binding of dioxygen for the pyridyl system by immersing the sample quickly in boiling water while applying a vacuum.[16] Under those conditions, the solution reacts again with dioxygen to regenerate the peroxo species; and the cycle can be repeated several times with only a small amount of decomposition.

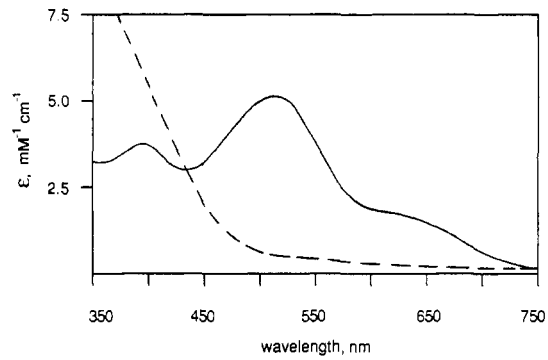


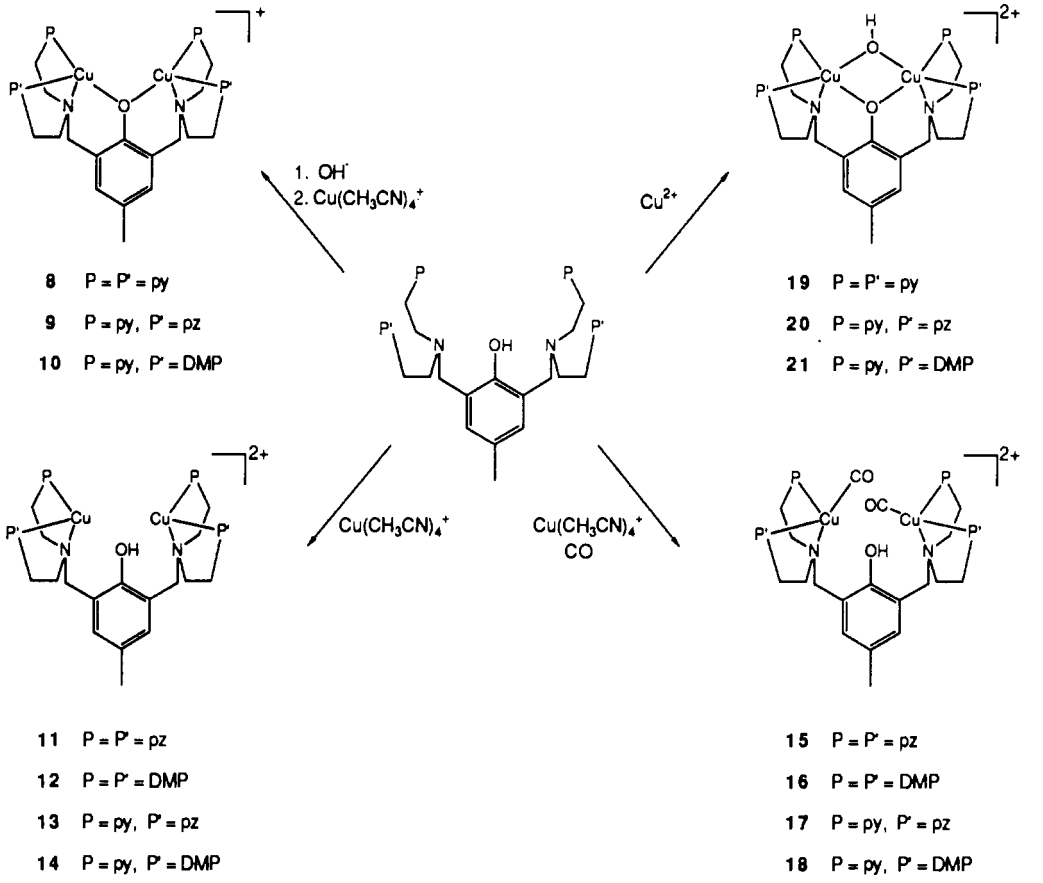
Figure 2. Absorption spectra for $Cu_2[(Py_2Pz_2)N6O]PF_6$ (**9**) in CH_2Cl_2 at −78 °C under N_2 (- - -) and after addition of O_2 (—).

The Cu(I) phenol complexes **11–18** also react at low temperature with dioxygen (2:1 Cu:O_2), this time to form adducts that are characterized by an intense band at ~395 nm in the UV–vis region (Table I). Figure 3 shows representative spectra for the reaction of the $\{Cu_2[(DMP_4)N6OH](CO)_2\}(PF_6)_2$ complex with O_2. Before reaction with dioxygen, the carbonyl groups (if present) must be removed under vacuum. The phenol complexes without coordinated CO react analogously, and reaction with dioxygen gives a product with the same spectrum. Besides the absorption at 395 nm, bands at 345, 480, and 640 nm are also observed. The Cu(I) complex shows no bands in this region, and the Cu(II) complex shows a very broad band centered around 450 nm. The same species can also be obtained by protonation with HPF_6 of the peroxo species formed from **8**, **9**, or **10** or by treatment of the μ-phenoxo–μ-hydroxo copper(II) dimers with H_2O_2.

Discussion

With the N6OH ligands reported here, donor sets able to stabilize Cu(I) give complexes that show interesting patterns of reactivity with dioxygen. The Cu ions in both the N6O and N6OH complexes (Scheme II) are held close to each other by virtue of bonds to the phenol group and the amine nitrogen atoms,

Scheme II



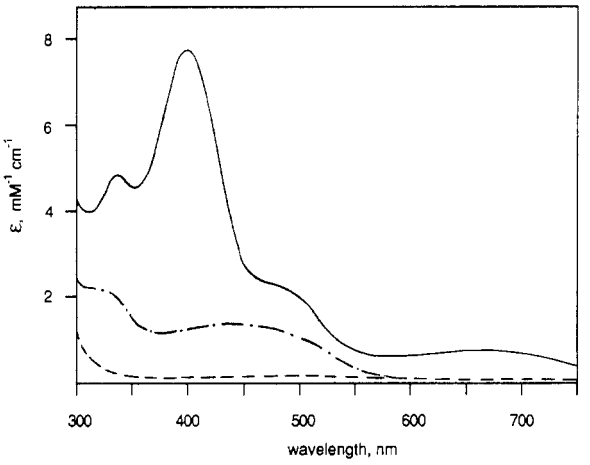


Figure 3. Absorption spectra for $Cu_2[(DMP_4)N6OH](CO)_2(PF_6)_2$ (**16**) in CH_2Cl_2 at −78 °C under N_2 (- - -), after removal of CO ligands under vacuum and addition of O_2 (—), and after warming to 25 °C (-·-).

setting the stereochemistry for the binding of a small molecule such as dioxygen.

Dinuclear Cu(I) phenolate complexes (**8**, **9**, or **10**) form analogous peroxo species, which have been extensively characterized by several spectroscopic methods in the case of the pyridyl derivative.[17,18] Thus, substituting pyrazole or dimethylpyrazole for one of the pyridine groups in the ligand apparently has little, if any, effect on the reactivity of the copper(I) complex toward dioxygen. This is in contrast to structurally related $Cu^I[N]_6$ complexes that lack the phenolate bridge. We have shown[19,20] that the pyrazole-ligated complexes react very much differently from their pyridine analogues by failing to activate dioxygen for hydroxylation of the benzene ring in those cases.

The dinuclear copper(I) phenol complexes **11**–**18** also react with dioxygen at low temperature, this time to form μ-OOH Cu(II) species. The spectral similarity of all of these compounds with a previously characterized pyridine-ligated complex,[21] as well as the reactivity of those adducts with triphenylphosphine to form triphenylphosphine oxide and the corresponding μ-hydroxo–μ-phenoxo copper(II) dimer, provides strong evidence for the formulation of these species as hydroperoxide complexes.

Despite the facile reaction of the various copper(I) complexes with dioxygen to form stable adducts at low temperature, the peroxo and hydroperoxo species generated with these ligands are not good spectroscopic models for the hemocyanin active site. Oxyhemocyanin shows two bands in the UV–vis region at 345 and 580 nm,[2] while these complexes show three or four absorptions at different wavelengths (Table I).

However, we have shown that the identity of the heterocycle has little effect on the reactivity with dioxygen of this type of complex; so it may be possible to prepare other derivatives able to bind dioxygen under less stringent conditions, for example by creating a more protected binding pocket. Another way to affect the stability may be to use the more biologically relevant imidazole group instead of pyrazole or pyridine, a goal we are currently pursuing. Thus, complexes of this type may still help us understand how hemocyanin is able to effect stabilization of bound dioxygen, despite possible shortcomings in mimicking the detailed spectral features of the peroxide adduct.

Acknowledgment is made to the National Science Foundation and to the Alfred P. Sloan Foundation for their generous support of this work.

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