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Synthesis and Reactivity of Dinuclear Copper Complexes Having a *m*-Xylyl Spacer between Coordination Units

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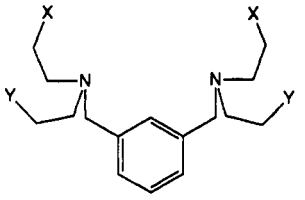
New hybrid ligands containing combinations of pyrazole, pyridine, and imidazole have been prepared, and the reaction chemistry of their copper(I) derivatives has been studied. The dinucleating ligands provide three nitrogen donors to each metal ion, and each coordination unit is separated by a *m*-xylyl group. Except for the case where four of the donor groups are pyridyl, in which the xylyl spacer is hydroxylated, all of the complexes react via four-electron reduction of the dioxygen molecule to give bis(μ-hydroxy)copper(II) dimers.

The crystal structure of deoxyHc[2,3] shows a dinuclear site in which each copper ion is asymmetrically ligated by three histidyl-imidazole groups. The design and synthesis of ligands that might generate suitable mimics of this coordination environment, leading to modeling of the reaction chemistry of hemocyanin and the related enzyme tyrosinase, has therefore become the focus of much effort.[4,5]

The ligand systems $(Pz_4)N6$ (**1**),[6] $((DMP)_4)N6$ (**2**),[7] and $(Py_4)N6$ (**3**),[8] which provide three nitrogen donors to each Cu ion, have been used to prepare biomimics of the type III copper protein sites. The differences in reactivity between those systems (vide infra)[7] have been difficult to reconcile, especially in light of more recent results with Schiff-base ligands in which hydroxylation of the *m*-xylyl spacer appears to be normative.[9]

To continue exploring the chemistry of this type of binucleating ligand, we have synthesized and studied the reactivity of the new complexes $Cu_2(L)^{2+}$ (L = **4**-**7**) with the hope of observing reactivity patterns intermediate between those observed for the copper(I) complexes of ligands **1**-**3**. In this paper, we compare the chemistry of the copper complexes of ligands **1**-**7**.



1 X = Y = 1-pyrazolyl
2 X = Y = 1-(3,5-dimethylpyrazolyl)
3 X = Y = 2-pyridyl
4 X = Y = 2-(*N*-methylimidazolyl)
5 X = 2-pyridyl Y = 1-pyrazolyl
6 X = 2-pyridyl Y = 1-(3,5-dimethylpyrazolyl)
7 X = 2-pyridyl Y = 2-(*N*-methylimidzolyl)

Experimental Section

All reagents and solvents were purchased from commercial sources and used as received unless noted otherwise. α,α'-Dibromo-*m*-xylene,[10] $Cu(CH_3CN)_4PF_6$,[11] and $Cu(CH_3CN)_4BF_4$[11] were prepared according to literature methods. The following solvents used to prepare the Cu(I) complexes were distilled and stored under nitrogen: methanol, from magnesium methoxide under nitrogen; tetrahydrofuran (THF), from sodium benzophenone ketyl under argon; 2-propanol, from calcium hydride under nitrogen. Analytical thin-layer chromatography (TLC) was performed using Analtech precoated (0.25 mm) silica gel plates. Flash chromatography was performed according to the general procedure of Still.[12] Microanalyses were performed by Desert Analytics Laboratories, Inc., Tucson, AZ, or by Atlantic Microlab, Inc., Norcross, GA. Cu(I) complexes and spectroscopic samples were prepared in a Vacuum Atmospheres drybox (<1 ppm O_2 and H_2O).

^1H and ^{13}C NMR spectra were recorded on an IBM AC 200 instrument at 200.132 MHz or a Bruker WM 250 instrument at 250.13 MHz. 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}. Absorption spectra and manometric dioxygen-uptake measurements were performed as described previously;[13] λ values are in nm with ϵ values reported as M^{-1} cm^{-1}.

Electrochemical measurements were conducted in an inert-atmosphere box. Acetonitrile from Burdick and Jackson was used without further purification. The solutions were 0.1 M in tetrabutylammonium perchlorate. A standard three-electrode cell setup was employed. A silver wire was used as the pseudoreference electrode, a Pt-wire coil as the auxiliary electrode, and a Pt disk (A = 0.103 cm^2) as the working electrode. Ferrocenecarboxylic acid was used as a reference to report the potentials vs SSCE.

α,α'-Bis{bis[2-(1'-pyrazolyl)ethyl]amino}-*m*-xylene [$(Pz_4)N6$] (1). Under a dinitrogen atmosphere a solution of α,α'-dibromo-*m*-xylene (2.7 g, 10.2 mmol), bis[2-(1-pyrazolyl)ethyl]amine (4.2 g, 20.5 mmol),[14] and triethylamine (2.1 g, 20.8 mmol) in 300 mL of THF was stirred overnight at room temperature. The reaction mixture was evaporated to dryness, and the residue was dissolved in 10% NaOH and extracted with CH_2Cl_2. The extracts were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Flash chromatography on silica using 10% methanol-ethyl acetate as the eluent (R_f = 0.38) yielded 1.5 g (29%) of a yellow oil. ^1H NMR ($CDCl_3$): 2.9 (t, 8 H, $N-CH_2$), 3.5 (s, 4 H, $ArCH_2$), 4.0 (t, 8 H, CH_2-Pz), 6.2 (s, 4 H, pyrazolyl C4-H), 6.9 (m, 4 H, Ar H), 7.2 (s, 4 H, pyrazolyl C-H), 7.5 (s, 4 H, pyrazolyl C-H).

α,α'-Bis{bis[2-(1'-methyl-2'-imidazolyl)ethyl]amino}-*m*-xylene [(Im_4)-N6] (4). Bis[2-(1'-methyl-2'-imidazolyl)ethyl]amine[15] (1.7 g, 72 mmol) and α,α'-dibromo-*m*-xylene (1.0 g, 37 mmol) were dissolved in 50 mL of 2-propanol. Anhydrous potassium carbonate (1.0 g) and sodium iodide (0.1 g) were added, and the mixture was stirred at ambient temperature for 8 days. The solvent was then evaporated under vacuum. The residue was treated with water and extracted with two, 100-mL portions of chloroform. After drying over Na_2SO_4, the extracts were concentrated to a pale oil, which was purified by flash chromatography with methanol-1% NH_4OH (R_f = 0.30) to afford 0.71 g (34%) of product. ^1H NMR ($CDCl_3$): 2.79 (t, J = 5.9 Hz, 8 H, $N-CH_2-$), 2.96 (t, J = 5.9 Hz, 8 H, $Im-CH_2-$), 3.47 (s, 12 H, imidazolyl N-Me), 3.68 (s, 4 H, $Ar-CH_2-N$), 6.74 (d, J = 4.4 Hz, 4 H, imidazolyl C-H), 7.18 (d, J = 4.4 Hz, 4 H, imidazolyl C-H), 7.15-7.31 (m, 4 H, Ar H). ^{13}C NMR

(1) Fellow of the Alfred P. Sloan Foundation, 1985-89.
(2) Abbreviations used in this paper: DMF, *N,N*-dimethylformamide; DMP, 3,5-dimethyl-1-pyrazolyl; Hc, hemocyanin; Im, 2-imidazolyl; MeIm, *N*-methyl-2-imidazolyl; Py, 2-pyridyl; Pz, 1-pyrazolyl; THF, tetrahydrofuran.
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($CDCl_3$): 24.87 (t), 32.44 (q), 51.95 (t), 58.73 (t), 120.29 (d), 126.76 (d), 127.22 (d), 128.09 (d), 128.89 (d), 139.34 (s), 146.69 (s).

α,α′-Bis{[2-(2′-pyridyl)ethyl][2-(1′-pyrazolyl)ethyl]amino}-*m*-xylene [(Py_2Pz_2)N6] (5). Under a dinitrogen atmosphere, α,α′-dibromo-*m*-xylene (1.5 g, 5.7 mmol), triethylamine (1.2 g, 11.9 mmol), and a solution of (PyPz)N3H[13] (2.5 g, 11.6 mmol) in 50 mL of THF were added to 150 mL of THF and the mixture was allowed to stir overnight at room temperature. The reaction temperature was 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 a 1:1 methanol–ethyl acetate as the eluent (R_f = 0.58) gave 1.07 g (35%) of a yellow oil. ^1H NMR ($CDCl_3$): 2.88 (s, 8 H, N–CH_2–CH_2–Py), 2.94 (t, 4 H, N–CH_2), 3.60 (s, 4 H, ArCH_2), 4.10 (t, 4H, CH_2–Pz), 6.10 (m, 2 H, pyrazolyl C4–H), 7.10 (m, 10 H, Ar H), 7.50 (m, 4 H, pyridyl C3–H and C5–H), 8.5 (d, 2 H, pyridyl C6–H).

α,α′-Bis{[2-(2′-pyridyl)ethyl][2-(3′,5′-dimethyl-1′-pyrazolyl)ethyl]amino}-*m*-xylene [(Py_2DMP_2)N6] (6). Under a dinitrogen atmosphere, α,α′-dibromo-*m*-xylene (1.0 g, 3.8 mmol), triethylamine (0.80 g, 7.9 mmol), and a solution of (PyDMP)N3H[13] (2.0 g, 8.1 mmol) in 50 mL of THF were added to 100 mL of THF and the mixture was stirred overnight at room temperature. The reaction mixture was 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 = 0.65) yielded 1.2 g (54%) of a yellow oil. ^1H NMR ($CDCl_3$): 2.1 (s, 12 H, Pz–CH_3), 2.9 (s, 8 H, N–CH_2–CH_2–Py), 3.3 (t, 4 H, N–CH_2), 3.6 (s, 4 H, ArCH_2), 4.3 (t, 4 H, CH_2-Pz), 5.7 (s, 2 H, pyrazolyl C4–H), 6.8 (d, 2 H, Ar H), 7.0 (m, 4 H, pyridyl C3–H and C5–H), 7.5 (t, 4 H, pyridyl C4–H), 8.5 (d, 2 H, pyridyl C6–H).

[2-(2′-Pyridyl)ethyl][2-(1′-methyl-2′-imidazolyl)ethyl]amine [(PyIm)-N3H]. [2-(1′-Methyl-2′-imidazolyl)ethyl]amine hydrochloride[16] (1.5 g, 8.6 mmol) and 2-vinylpyridine (2.0 g, 21.5 mmol) were dissolved in 200 mL of methanol, and the mixture was allowed to reflux for 42 h. The solution was then evaporated under reduced pressure, and saturated aqueous sodium bicarbonate was added. The product was extracted with three, 100-mL portions of chloroform. The combined extracts were dried over Na_2SO_4 and concentrated. Flash chromatography with methanol afforded 0.42 g (21%) of a pale oil (R_f = 0.25). Longer reaction times or the addition of a large excess of vinylpyridine resulted in production of an inseparable mixture of products. ^1H NMR ($CDCl_3$): 2.81 (t, J = 1.0 Hz, 2 H, N–CH_2), 2.87–3.09 (m, 6 H, Im–CH_2–, –CH_2CH_2Py), 3.57 (s, 3 H, imidazolyl N–Me), 6.78 (d, J = 1.3 Hz, 1 H, imidazolyl C–H), 7.08 (d, J = 1.3 Hz, imidazolyl C–H), 7.08–7.16 (m, 2 H, pyridyl C–H), 7.60 (t of d, J^1 = 7.6 Hz, J^2 = 0.8 Hz, 1 H, pyridyl C–H), 8.50 (d of d, J = 2.5 Hz, J = 1 Hz, 1 H, pyridyl C–H). ^{13}C NMR ($CDCl_3$): 26.55 (t), 32.32 (q), 37.81 (t), 46.94 (t), 48.89 (t), 120.29 (d), 123.12 (d), 126.64 (d), 136.26 (d), 146.30 (s), 148.90 (d), 159.71 (s).

α,α-Bis{[2-(2′-pyridyl)ethyl][2-(1′-methyl-2′-imidazolyl)ethyl]amino}-*m*-xylene [(Py_2Im_2)N6] (7). (PyIm)N3H (430 mg, 1.9 mmol) was dissolved in 70 mL of acetonitrile. Potassium carbonate (1.0 g) and α,α′-dibromo-*m*-xylene (240 mg, 9 mmol) were added, and the reaction mixture was stirred at ambient temperature for 51 h. The acetonitrile was evaporated at reduced pressure, 20 mL of water was added, and the product was extracted with two, 100-mL portions of chloroform. The dried extracts were concentrated to a yellow oil (500 mg, 98%). ^1H NMR ($CDCl_3$): 2.74 (t, J = 6.6 Hz, 4 H, N–CH_2–), 2.91 (t, J = 6.6 Hz, 4 H, –CH_2–Im), 2.96 (s, 8 H, N–CH_2CH_2–Py), 3.36 (s, 6 H, imidazolyl N–Me), 3.67 (s, 4 H, ArCH_2–N), 6.72 (d, J = 1.0 Hz, 2 H, imidazolyl C–H), 6.87 (d, J = 1.0 Hz, 2 H, imidazolyl C–H), 7.04–7.15 (m, 8 H), 7.59 (t of d, J = 7.6 Hz, J = 1 Hz, 4 H, pyridyl C–H), 8.48 (d of d, J = 2.5 Hz, J = 1 Hz, 2 H, pyridyl C–H). ^{13}C NMR ($CDCl_3$): 25.02 (t), 32.24 (q), 35.8 (t), 51.41 (t), 51.68 (t), 120.11 (d), 121.3 (d), 123.15 (d), 126.8 (d), 127.01 (d), 127.64 (d), 128.76 (d), 135.86 (d), 139.32 (s), 146.7 (s), 148.9 (d), 160.39 (s).

{α,α-Bis[bis[2-(1′-methyl-2′-imidazolyl)ethyl]amino}-*m*-xylene}dicopper(I) Bis(hexafluorophosphate) {Cu_2[(Im_4)N6](PF_6)$_2$} (11). Ligand **4** (190 mg, 0.33 mmol) was dissolved in 5 mL of methanol, and the mixture was treated with a solution of tetrakis(acetonitrile)copper(I) hexafluorophosphate (250 mg, 0.67 mmol) in 15 mL of methanol. The white precipitate that formed immediately was collected and dissolved in a minimum of acetonitrile. The product was isolated as colorless crystals by slow diffusion of THF into the acetonitrile solution. ^1H NMR (DMSO-d_6): 2.90 (br m, 8 H), 3.14 (br m, 8 H), 3.62 (s, 12 H, N–Me), 3.86 (s, 4 H, Ar–CH_2–N), 7.03 (d, J = 1.5 H, 4 H, imidazolyl C–H), 7.25–7.31 (m, 4 H, Ar H), 7.30 (d, J = 1.5 Hz, 4 H, imidazolyl C–H). Anal. Calcd for $C_{32}H_{44}Cu_2N_{10}P_2F_{12}$: C, 38.99; H, 4.49; N, 14.20. Found: C, 38.74; H, 4.47; N, 14.12.

{α,α′-Bis[[2-(2′-pyridyl)ethyl][2-(1′-pyrazolyl)ethyl]amino}-*m*-xylene}dicopper(I) Bis(tetrafluoroborate)–Acetonitrile {Cu_2[(Py_2Pz_2)N6](BF_4)$_2$·CH_3CN} (12). This complex was prepared as described for **11**. A yellow precipitate formed, which was collected and recrystallized by diffusion of ether into a methanol solution of the compound. UV/vis (CH_2Cl_2): 262 (13 000); 244 (670). IR (KBr): 3130, 2960, 2840 (Ar); 1050 (BF_4). Anal. Calcd for $C_{34}H_{41}B_2Cu_2F_8N_9$: C, 46.59; H, 4.72; N, 14.38. Found: C, 46.47; H, 4.80; N, 14.38.

{α,α′-Bis[[2-(2′-pyridyl)ethyl][2-(3′,5′-dimethyl-1′-pyrazolyl)ethyl]amino}-*m*-xylene}dicopper(I) Bis(hexafluorophosphate) {Cu_2[(Py_2DMP_2)N6](PF_6)$_2$} (13). This complex was prepared in the same manner as that described for **11**. UV/vis (CH_2Cl_2): 262 (18 000); 352 (1900). IR (KBr): 2860, 2820 (Ar); 880 (PF_6).

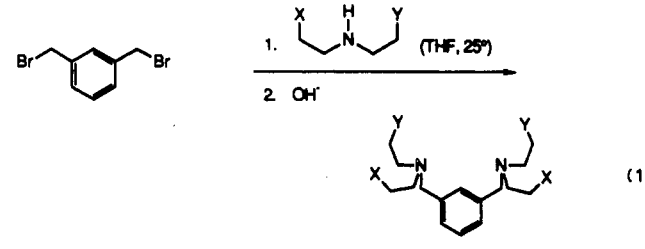
{α,α′-Bis[[2-(2′-pyridyl)ethyl][2-(1′-methyl-2′-imidazolyl)ethyl]amino}-*m*-xylene}dicopper(I) Bis(tetrafluoroborate) {Cu_2[(Py_2Im_2)N6](BF_4)$_2$} (14). This complex was prepared as described for **11**. The crude product was collected and dissolved in a minimum amount of warm methanol, and the mixture was filtered. Pale yellow crystals were obtained by slow diffusion of THF into the methanol solution. UV/vis (CH_2Cl_2): 265 (15 000); 355 (2500). Anal. Calcd for $C_{34}H_{42}N_8Cu_2B_2F_8$: C, 47.29; H, 4.90; N, 12.97. Found: C, 47.36; H, 4.97; N, 12.62.

{α,α′-Bis{bis[2-(3′,5′-dimethyl-1′-pyrazolyl)ethyl]amino}-*m*-xylene}dicopper(II) Tetrakis(tetrafluoroborate) Pentahydrate {Cu_2[($(DMP)_4$)N6](BF_4)$_4$·$5H_2O$}. A solution of 0.843 g (0.020 mol) of $Cu(BF_4)_2$·xH_2O in 10 mL of methanol was added to a solution of 0.812 g (0.020 mol) of $Cu(BF_4)_2$·xH_2O in 10 mL of methanol was added to a solution of 0.812 g (0.013 mol) of ($(DMP)_4$)N6 (**2**) in 3 mL of methanol. Green crystals were formed by diffusion of 2-propanol into the methanol solution. IR (KBr): 3430–3520 (H_2O); 3160, 2980, 2930, 2900, 2870 (Ar); 990–1130 (BF_4). Anal. Calcd for $C_{36}H_{62}B_4Cu_2F_{16}N_{10}O_5$: C, 36.33; H, 5.21; N, 11.77. Found: C, 36.12; H, 5.11; N, 11.70.

Bis(μ-hydroxy){α,α′-bis[[2-(2′-pyridyl)ethyl][2-(1′-pyrazolyl)ethyl]amino}-*m*-xylene}dicopper(II) Bis(hexafluorophosphate) {Cu_2[(Py_2Pz_2)-N6](OH)$_2$(PF_6)$_2$}. In an inert-atmosphere box, 0.800 g (0.84 mmol) of **12** was dissolved in 100 mL of DMF. The yellow solution was stirred under a stream of dioxygen overnight at room temperature. The resulting green solution was evaporated to dryness and the residue was dissolved in acetone. 2-Propanol was added, and the resulting precipitate was collected and washed with 2-isopropanol. IR (KBr): 3640, 3340–3540 (OH); 3140, 2920 (Ar); 820–850 (PF_6). Anal. Calcd for $C_{32}H_{44}Cu_2F_{12}N_8O_4P_2$: C, 37.61; H, 4.31; N, 10.97. Found: C, 36.99; H, 3.50; N, 10.63.

Results

Synthesis. The *m*-xylyl ligands **1**–**7** were synthesized by a sequence previously reported (eq 1) in which a preformed "N_3"



(1)

piece is used to displace the bromide ions from α,α′-dibromo-*m*-xylene. The original procedure employed ethyl acetate as the reaction solvent,[7] but we have since found that running the reaction at room temperature in THF gives higher yields. Attempts to make unsymmetrical N_6 ligands by this method unfortunately have proven unsuccessful.

The corresponding Cu(I) complexes, $Cu_2(L)^{2+}$ (**8**–**14**), were made by treating a methanol or THF solution of $Cu(CH_3CN)_4^+$ with a solution of ligand under an inert atmosphere. The crude products either precipitated or were obtained by evaporating the mixture to dryness; they were subsequently crystallized by the vapor diffusion method.

Nonbridged copper(II) complexes [$Cu_2(L)^{4+}$] could be isolated as crystalline solids only for ligands **2** and **3**, the latter having been reported by Karlin.[17] The Cu(II) complexes of the other dinu-

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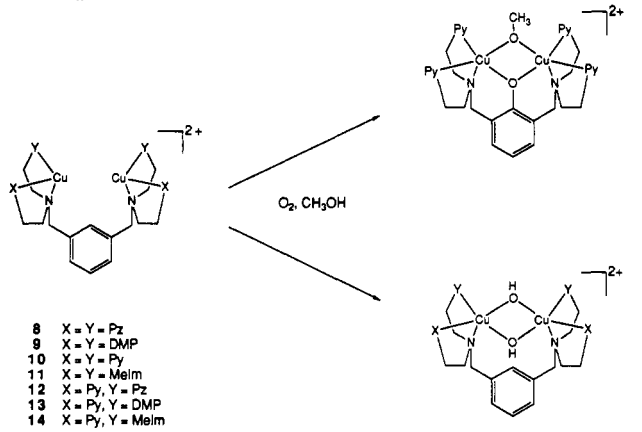
Scheme I



cleating ligands were obtained as oils even though a wide variety of counterions (BF_4^-, ClO_4^-, NO_3^-) and solvent mixtures were tested. However, bis(μ-hydroxy)copper(II) dimers [$Cu_2(L)(OH)_2^{2+}$] could be obtained for the pyrazole-containing ligands by reaction of the copper(I) derivatives with dioxygen in methanol (vide infra).

Dioxygen Reactivity. The reactivity of the dinuclear Cu(I) complexes **8–14** (Scheme I) with dioxygen was examined both at 25 and −78 °C. The lower temperature has no effect on the reactivity of **8–11**, and it only slows the four-electron reduction of O_2 for complexes **12–14** in dichloromethane. The stoichiometry (4:1 Cu:O_2) was demonstrated for **12–14** by manometric uptake measurements at −78 °C in CH_2Cl_2. Unfortunately, complex **11** is not soluble in dichloromethane at −78 °C, and it reacts with solvent at higher temperatures.[15]

The effect of solvent on the oxidation process varies. For example, complex **8** and **9** are inert to dioxygen in CH_2Cl_2, even at 25 °C, but all of the other complexes react with O_2 in dichloromethane. The use of methanol appears to lead to clean production of bis(μ-hydroxy)copper(II) dimers for all but complex **10**. In the latter case, hydroxylation of the benzene ring occurs.[8] In acetonitrile, the complexes are stable to O_2, presumably because of coordination of the solvent to the Cu(I) ion.

In DMF, **12** reacts with dioxygen to form a green solid. An infrared spectrum, showing a peak at 3640 cm^{-1} and a broad band from 3540 to 3340 cm^{-1}, as well as analytical data, shows that the product is $Cu_2(L)(OH)_2^{2+}$ (L = **5**). Bis(μ-hydroxy) species are well-known,[18] and complexes **8** and **9** also give isolable bis(μ-hydroxy) dimers upon reaction with dioxygen in methanol.[7,8] To confirm that **11–14** do not react via oxygen atom insertion into the arene ring to form $Cu_2(L\text{–}O)(OH)^{2+}$ (Scheme I), we extracted the copper ions from the oxidation products using NH_4OH and compared the NMR spectral properties of the ligand before and after reaction with dioxygen. Ligands **4–7** were recovered unchanged. Addition of acid to a CH_2Cl_2 solution did not change the course of the reaction, as has been reported in related systems,[9] and the four-electron reduction of dioxygen still occurred.

The reaction of $Cu_2(L)^{4+}$ (L = **1–3**, **5**) with H_2O_2 in DMF was also studied, and the reactivity appears to be the same in all cases. A solution of Cu(II) and the ligand in DMF treated with aqueous H_2O_2 gives a spectrum which resembles that for previously characterized μ-phenoxo complexes having the same nitrogen donor sets.[13] In particular, there is a new band at 380–390 nm, indicative of hydroxylation of the aromatic ring.[8]

Spectroscopy. The Cu(I) complexes having at least one pyridine donor are yellow and show an absorption at about 350 nm, which is most likely assigned to the π–π^* transitions for the pyridine ring. By contrast, the pyrazole- and imidazole-ligated complexes are colorless and have no absorptions above 300 nm.

Upon reaction with dioxygen, each of the complexes displays new bands in the visible region of the spectrum. The reaction of

Scheme II

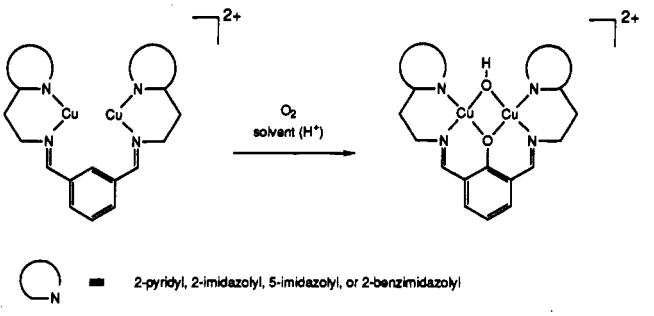


Table I. Electrochemistry Data for Dinuclear Complexes

complex	$E_{1/2}$	ΔE_p, mV
8	0.309	165
9	0.549	295
10	0.335	165
12	0.415	375
13	0.565	235

the copper(I) compounds with O_2 in *methanol* gives the bis(μ-hydroxy)copper(II) dimers, which are characterized by absorptions in the region at about 360 nm. A number of other hydroxy-bridged dinuclear Cu(II) complexes are known to have bands in the region between 350 and 380 nm.[19] Only for complex **10** is the spectrum substantially different, and the strong absorption at 390 nm is characteristic of ligand hydroxylation.[8]

Electrochemistry. Results of cyclic voltammetry studies of complexes **8–10**, **12**, and **13** in CH_3CN solution are shown in the Table I. Of the five complexes, **8** and **10** show the lowest $E_{1/2}$ and the greatest reversibility (the smallest ΔE_p). We were unable to prepare enough of complexes **11** and **14** to obtain analogous electrochemical data.

Discussion

In the *m*-xylyl-bridged dinucleating ligands studied here, the substitution of pyridine by other heterocycles has a pronounced affect on the reactivity of the Cu(I) complexes with dioxygen. In CH_2Cl_2, one of three processes occurs: (1) no reaction, (2) four-electron reduction of dioxygen to two molecules of water (or OH^-), or (3) hydroxylation of the arene ring. The exact factors that account for the different reactivities are obscure and probably encompass both geometric and electronic effects.

In methanol, reaction always occurs, resulting in formation of 2 equiv of hydroxide ion/copper dimer or in hydroxylation of the arene ring (Scheme I). We presume that the reduction of O_2 to water occurs by interaction between two copper(I) dimers, one of which has formed an intermediate peroxo complex. The second dimer then transfers two electrons to produce two oxide ions (O^{2-}), which remove protons from water in the solvent. This results in the overall formation of four hydroxide ions/two copper dimers or two hydroxide ions/dimer.

The low dioxygen reactivity of the pyrazole complexes might be explained by the decreased basicity of that heterocycle relative to pyridine and imidazole; for compounds **8** and **9**, we find no evidence for reaction with dioxygen in dichloromethane. On the other hand, the basicity must only affect the dioxygen reactivity to a small extent, since we have shown that copper(I) imidazole complexes *do* form dioxygen adducts similar to those seen for the pyridyl-ligated species;[15] so we presume that the same type of O_2 adduct is formed from **10** and **11** in dichloromethane. Thus, to explain the difference in product formation between pyridine- and imidazole-ligated species **10** and **11**, we suspect that the geometry must be affected such that the arene cannot approach the bound dioxygen in a way that leads to hydroxylation by donation of electrons into the σ^* orbital of the bound peroxide.[4] Note that whenever a five-membered-ring heterocycle is present in these

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ligands, no hydroxylation of the arene occurs.

Studies on *m*-xylyl-bridged Schiff-base ligands also suggest that ligand basicity has little effect on the oxidation reaction (Scheme II),[9,15] since hydroxylation occurs despite changes in the nature of the heterocycle. Perhaps in those systems the geometry is optimal for correct orientation of the bound peroxo group and the arene ring. On the other hand, H^+ must be added in certain cases in order for hydroxylation to predominate over reduction of O_2 to water, so electronic effects undoubtedly play a role there, too.

Another factor that may influence the formation of a reactive peroxo adduct in complexes **8-14** is the potential of the Cu(I)/Cu(II) couple. From cyclic voltammetry studies, we find that $E_{1/2}$ for **10** is *between* that measured for **8** and **12**, which is incongruous with a simple correlation between ligand basicity and $E_{1/2}$. On the basis of the reactivity, we expected that $E_{1/2}$ for complex **10** might be at one end of the range of $E_{1/2}$ values. However, we do note that the conditions of the electrochemical measurements (CH_3CN) and the quasireversible nature of the scans may not reflect the true redox properties of the complexes in their reaction with dioxygen.

In contrast to the differences in dioxygen reactivity of the Cu(I) complexes, the Cu(II) species seem to react with H_2O_2 to hydroxylate the arene ring. Although a *solid* copper(II) complex could only be isolated for ligands **2** and **3**,[17] solutions of Cu(II) ions and the other ligands appear to react analogously with H_2O_2, as judged by absorption spectra. The difference in overall behavior of the Cu(I) vs the Cu(II) complexes is not surprising when one considers that their reactions occur via two different mechanisms. Through kinetic studies, Karlin has shown that the reaction of **10** with O_2 proceeds through a copper(II) peroxo adduct, but $Cu_2(L)^{4+}$ (L = **3**) reacts with hydrogen peroxide to give a hydroperoxide intermediate formed via association of two dimers.[17] Apparently the geometric and electronic effects are less important in the Cu(II) adducts than they are in the copper peroxo species formed from the analogous copper(I) complexes.

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Synthesis and Reactivity of Imidazolyl- and Benzimidazolyl-Containing Copper Complexes

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New polydentate ligands having (2-imidazolylethyl)amino and (2-benzimidazolylethyl)amino groups have been prepared via the imidate esters derived from *N*-(2-cyanoethyl)benzamides. These chelating ligands form stable copper(I) complexes that react with dioxygen at low temperature to give adducts presumed to be dinuclear peroxo complexes on the basis of the similarity of their electronic spectra with those for analogous pyridine-ligated species. A Schiff-base ligand derived from isophthalaldehyde and (aminoethyl)imidazole is hydroxylated when its copper(I) derivative is treated with dioxygen.

Hemocyanin is a copper protein responsible for transport of molecular oxygen in the hemolymph of many species of molluscs and arthropods. A crystal structure of deoxyhemocyanin[2] and extensive spectroscopic studies on the oxidized form of the protein[3] have contributed much to our knowledge about the *structure* of hemocyanin's dinuclear active site. Understanding how the active site reacts reversibly with O_2 has been a more difficult challenge and has relied on studies of inorganic model compounds that react with dioxygen.[4]

The active site of hemocyanin comprises a dinuclear unit in which each copper ion is ligated by three imidazole groups provided by histidine. One of the imidazole ligands is farther from the copper ions than the other two.[2] Since imidazole groups are relatively difficult to incorporate into synthetic ligands, many researchers have used nitrogen donors other than imidazole in designing copper chelates. Pyridine, pyrazole, and benzimidazole have been investigated extensively as donors in copper complexes, and both mononucleating and dinucleating ligands have been prepared.[5]

Karlin has developed a wealth of chemistry based on pyridyl-ligated copper compounds,[4] and he has been able to generate several dioxygen adducts with bis[2-(2'-pyridyl)ethyl]amine complexes. Although the peroxide complexes do not exhibit all of the spectroscopic properties of hemocyanin, those species constitute the best characterized systems that reversibly bind dioxygen.

The pyrazole derivatives of Karlin's ligands have markedly different reactivity toward oxygen, and many such complexes are inert to dioxygen in methylene chloride.[6] Because of its size, pyrazole is probably a better *structural* analogue for imidazole than is pyridine. However, pyrazole is significantly less basic than histidine, whereas pyridine has approximately the same basicity; so pyridine is possibly a better mimic for the *electronic* features of imidazole. It is noteworthy that incorporation of pyrazole into tris(pyrazolyl)borate ligands affects the electronic features significantly; and Thompson and Kitajima have used those ligands to prepare isolable copper(II) superoxide and peroxide complexes, respectively.[7,8]

The variation observed in the reactivity of copper complexes toward O_2 with respect to the heterocycle prompted us to prepare imidazole-containing ligands. Since imidazole is presumed to be the best model for histidine, we felt that studying the reactivity of the imidazole derivative would be a valuable complement to the work previously reported for the pyridyl and pyrazolyl complexes. The purpose of this work was to develop a general synthetic

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