Hemocyanin and Tyrosinase Models. Synthesis, Azide Binding, and Electrochemistry of Dinuclear Copper(II) Complexes with Poly(benzimidazole) Ligands Modeling the Met Forms of the Proteins

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Received April 22, 1992

The new poly(benzimidazole) ligands α,α'-bis[[bis(1-methyl-2-benzimidazolyl)methyl]amino]-*m*-xylene (L-5,5) and α,α'-bis[bis[2-(1-methyl-2-benzimidazolyl)ethyl]amino]-*m*-xylene (L-6,6) and their dicopper(I) and bis(aquo)-dicopper(II) complexes are reported. The ligands provide one tertiary amino and two benzimidazole nitrogen donors to each metal center; each of the two "arms" of L-5,5 binds the metal with two adjacent five-membered chelate rings, while with L-6,6 these chelate rings are six-membered. The dicopper(I) complexes react with dioxygen to produce the bis(hydroxo)dicopper(II) complexes. The bis(aquo)- and bis(hydroxo)dicopper(II) complexes can be interconverted in a single step by addition of base and acid, respectively. The electrochemical behavior of the bis(aquo)dicopper(II) complex of L-6,6 shows reversible reduction to the corresponding dicopper(I) complex whereas the analogous complex of L-5,5 is irreversibly reduced. The bis(hydroxo)dicopper(II) complexes of both ligands also undergo irreversible reduction. Azide adducts of the dicopper(II) complexes have been isolated; the anion bridges the two coppers in μ-1,1 fashion in the L-5,5 derivative and in μ-1,3 fashion in the L-6,6 derivative. The spectral properties of the two complexes are significantly different. Binding studies performed in solution for the bis(aquo)- and bis(hydroxo)dicopper(II) complexes show that up to four azide molecules can bind to the complexes and the affinity of azide decreases with the charge of the complex. Electrochemistry shows that, upon increasing the number of bound azide groups, the successive reductions of the two copper(II) centers tend to coalesce, thus indicating progressive lowering of the electronic communication between the metal centers. The relevance of the spectroscopic and binding data of these azide complexes to hemocyanin and tyrosinase is discussed.

Introduction

Considerable progress in the modeling of features of the dinuclear (type 3) copper centers of hemocyanin and tyrosinase has recently been made, especially with the characterization of synthetic copper–dioxygen complexes[1] and systems performing model monooxygenase reactions.[1a,2] Dinucleating ligands having *m*-xylyl spacers between coordination units have been widely used in synthetic studies. These ligands generally contain nitrogen donors as substitutes for the protein imidazole groups and, often, additional bridging groups to better fulfill the need to keep the two metal ions in close proximity.[3-7] The presence and the nature of a similar bridge in the protein Cu_2 cores are still a matter of some debate. It may be absent in the reduced forms of the proteins, as shown by the structure of *Panulirus interruptus* hemocyanin,[8] but it seems to be present in the met forms and other derivatives, as shown by EXAFS data[9] and other spectroscopic studies,[10] where it may be necessary to mediate strong antiferromagnetic coupling between the metal centers.

As part of our systematic studies on dinuclear complexes as models for the protein type 3 copper active sites we describe

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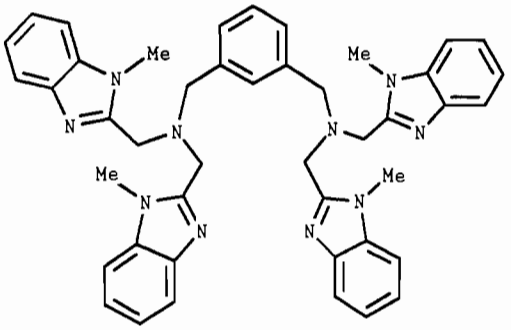
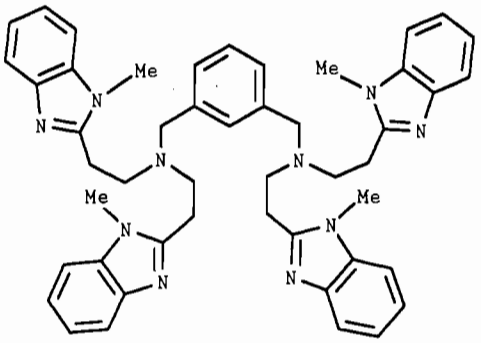
Chart I



L-5,5



L-6,6

herein the synthesis, reactivity, and electrochemistry of the copper(II) complexes derived from poly(benzimidazole) ligands L-5,5 and L-6,6 (Chart I). These two ligands have identical donor groups but provide metal coordination sites with different chelate ring size: five-membered for L-5,5 and six-membered for L-6,6. Our interest focuses on the differences in the properties of the complexes that arise from the different constraints and accessibilities of the metal sites imposed by the ligands. We also report the azide adducts of the copper(II) complexes and binding studies in solution that complement our previous investigation on mononuclear copper(II)–azide model complexes.[11] The relevance of the present complexes to type 3 copper model chemistry is shown by the tyrosinase-like effect exhibited by the copper(I) complex of L-6,6, $[Cu_2(L\text{-}6,6)]^{2+}$, on exogenous phenols, which we recently communicated.[2g] The corresponding $[Cu_2(L\text{-}5,5)]^{2+}$ complex exhibits similar, but lower, activity in the same reaction.[12]

Experimental Section

All reagents were purchased from commercial sources and used as received unless noted otherwise. $[Cu(MeCN)_4]ClO_4$ was prepared by a literature method[13] and recrystallized to analytical purity. Dimethylformamide (DMF) was degassed and distilled under vacuum from calcium hydride. Tetrahydrofuran (THF) was purified through a dry alumina column and distilled from metallic sodium. Acetonitrile for spectral measurements was successively distilled from potassium permanganate, sodium carbonate, and calcium hydride. The synthesis and manipulation of copper(I) complexes were performed with Schlenk and glovebag techniques. Infrared spectra were recorded on a Jasco FT/IR-5000. Elemental analyses were performed at the microanalytical laboratory of the Chemistry Department in Milano. NMR spectra were recorded on Bruker WP-80 and AC-200 spectrometers operating at 80 and 200 MHz, respectively. Optical spectra were obtained on Perkin-Elmer Lambda 5, Cary 2390, and HP 8452A diode array spectrophotometers. Measurements of pH were performed on an Amel Model 328 pH meter. Conductivity measurements were performed in acetonitrile with an Amel Model 133 conductimeter; the concentrations of the solutions were between 0.5 and 1.0 mM, according to the solubility of the complexes. Cyclic voltammetry was performed in a three-electrode cell having a platinum working electrode, surrounded by a platinum-spiral counter electrode, and an aqueous saturated calomel reference electrode (SCE) mounted with a Luggin capillary. A BAS 100A electrochemical analyzer was used as polarizing unit. Controlled-potential coulometric tests were performed in an H-shaped cell with anodic and cathodic compartments separated by a sintered-glass disk. The working macroelectrode was a platinum gauze; a mercury pool was used as counter electrode. An Amel Model 551 potentiostat with an associated coulometer (Amel Model 558 integrator) was employed here. In all electrochemical tests, the temperature was controlled at 20 ± 0.1 °C.

Ligand binding studies of the copper(II) complexes were performed by adding concentrate methanolic solutions of the ligands to solutions of the complexes at 23 °C. The spectral data were analyzed as described previously[11b,14] to deduce equilibrium constants and stoichiometry of formation of the adducts.

Benzene-1,3-dicarbaldehyde Dioxime. A mixture of benzene-1,3-dicarbaldehyde (2.0 g, 15 mmol), hydroxylamine hydrochloride (2.7 g, 40 mmol), sodium hydroxide (1.6 g, 40 mmol), and ethanol (60 mL) was refluxed for 3 h and then left under stirring at room temperature for an additional 4 h. The precipitate present was filtered off, and the solution was evaporated to dryness under vacuum. The residue was treated with a small amount of water, and the mixture was filtered. The solid was dissolved in dry ethanol containing a small amount of toluene, and the mixture was evaporated to dryness in order to remove most of the water. The residue was dried under vacuum (yield 75%). Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.92; N, 17.06. Found: C, 58.55; H, 4.67; N, 16.96.

α,α′-Diamino-*m*-xylene Dihydrochloride. To a suspension of powdered lithium aluminum hydride (1.5 g, 39 mmol) in dry THF (80 mL) was added solid benzene-1,3-dicarbaldehyde dioxime (1.5 g, 9.1 mmol). The flask was protected from light by an aluminum foil, and the mixture was heated to reflux for about 7 h. After the mixture was cooled to room temperature and then cooled in an ice bath, a THF–H_2O solution made basic with NaOH was added dropwise until the evolution of dihydrogen ceased. The mixture was filtered, and the solid was treated two times with additional basic THF–H_2O solution followed by filtration. The combined filtrates were acidified with hydrochloric acid, and the mixture was washed three times with dichloromethane. The aqueous phase was evaporated to dryness under vacuum (yield 50%). The crude diamine dihydrochloride was used as such in the following step. ^1H NMR (D_2O): δ 4.3 (s, 4H, CH_2), 7.6 (~s, 4H, Ph H).

2-(Chloromethyl)-1-methylbenzimidazole. *N*-Methyl-*o*-diaminobenzene dihydrochloride (3.5 g, 18 mmol) and chloroacetic acid (2.6 g, 27 mmol) were refluxed in 6 M aqueous hydrochloric acid (40 mL) for about 8 h. After being cooled first to room temperature and then in an ice bath, the mixture was neutralized by dropwise addition of concentrated ammonia. The precipitated product was collected by filtration and washed with small amounts of cold water. The crude product was purified by column chromatography on alumina using chloroform as eluent (yield

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50%). Anal. Calcd for $C_9H_9N_2Cl$: C, 59.84; H, 5.03; N, 15.50. Found: C, 59.79; H, 4.98; N, 15.31. ^1H NMR ($CDCl_3$): δ 3.95 (s, 3H, NCH_3), 4.90 (s, 2H, CH_2), 7.2–7.4 (m, 3H) 7.6–7.8 (m, 1H) (Ph H).

α,α′-Bis[[bis(1-methyl-2-benzimidazolyl)methyl]amino]-*m*-xylene (L-5,5). A mixture of α,α′-diamino-*m*-xylene dihydrochloride (0.38 g, 1.8 mmol), 2-(chloromethyl)-1-methylbenzimidazole (1.35 g, 7.4 mmol), anhydrous sodium carbonate (1.5 g, 14.2 mmol), and dry DMF (100 mL) was refluxed for about 8 h. After evaporation to dryness under vacuum, the solid residue was treated with chloroform and the inorganic salts were filtered off. The filtrate was concentrated to a small volume, and diethyl ether was added to precipitate the product (yield 70%). Anal. Calcd for $C_{44}H_{44}N_{10}$: C, 74.13; H, 6.22; N, 19.65. Found: C, 74.00; H, 6.20; N, 19.55. ^1H NMR ($CDCl_3$): δ 3.25 (s, 12H, NCH_3), 3.76 (s, 4H, CH_2–phenyl), 3.94 (s, 8H, CH_2–benzimidazolyl), 7.2–7.4 and 7.6–7.8 (m, 16H, Ph H + benzimidazolyl H). UV (MeOH), λ_{max}, nm (ε, M^{-1} cm^{-1}): 258 (29 400), 271 (23 600), 278 (25 900), 286 (22 900), 336 (1340), 350 sh, 376 sh, 400 sh.

α,α′-Bis[bis[2-(1-methyl-2-benzimidazolyl)ethyl]amino]-*m*-xylene (L-6,6). The synthesis of this ligand from α,α′-dibromo-*m*-xylene and bis-[2-(1-methyl-2-benzimidazolyl)ethyl]amine was reported in our previous communication.[2g]

Copper(I) Complexes. The synthesis of the copper(I) complexes was performed under argon as follows. To a solution of the ligand (0.50 mmol) in 20 mL of degassed methanol (L-5,5) or ethanol (L-6,6) was added solid tetrakis(acetonitrile)copper(I) perchlorate (1.05 mmol). The mixture was refluxed for about 0.5 h and then left under stirring at room temperature for additional 0.5 h. The light yellow product was collected by filtration and dried under vacuum. Anal. Calcd for $[Cu_2(L\text{-}5,5)][ClO_4]_2$, $C_{44}H_{44}N_{10}Cl_2Cu_2O_8$: C, 50.87; H, 4.26; N, 13.50. Found: C, 50.65; H, 4.03; N, 13.38. Calcd for $[Cu_2(L\text{-}6,6)][ClO_4]_2$, $C_{48}H_{52}N_{10}Cl_2Cu_2O_8$: C, 52.64; H, 4.79; N, 12.80. Found: C, 52.57; H, 4.74; N, 12.74.

$[Cu_2(L\text{-}5,5)][ClO_4]_4\cdot 6H_2O$. The ligand L-5,5 (0.52 g, 0.73 mmol) was dissolved in hot methanol (30 mL), and a solution of copper(II) perchlorate hexahydrate (0.57 g, 1.53 mmol) in a few milliliters of methanol was added. The resulting green solution was stirred for several minutes and concentrated to a small volume. The green precipitate formed was collected by filtration and dried. Anal. Calcd for $C_{44}H_{56}N_{10}Cl_4Cu_2O_{22}$: C, 39.26; H, 4.19; N, 10.41. Found: C, 39.29; H, 4.04; N, 10.28. UV–vis (MeCN), λ_{max}, nm (ε, M^{-1} cm^{-1}): 247 (33 800), 274 (37 000), 280 (33 500), 300 sh (3800), 390 sh (500), 650 (350). Molar conductivity: Λ_M = 380 Ω^{-1} cm^2 mol^{-1}. IR (Nujol mull), cm^{-1}: 3480 [ν(OH)]; 1618, 1539, 1506, 1487 [ν(ring)]; 1110, 623 [ν(ClO_4)]; 940, 748 [δ(CH)].

$[Cu_2(L\text{-}6,6)][ClO_4]_4\cdot 6H_2O$. To a solution of L-6,6 (0.20 g, 0.26 mmol) in methanol–dichloromethane (1:1, v/v, 30 mL) was added copper(II) perchlorate hexahydrate (0.22 g, 0.60 mmol) dissolved in a small amount of methanol. The mixture was refluxed for a few minutes and then stirred at room temperature for 1 h. The green precipitate was filtered off, washed with methanol, and dried. Anal. Calcd for $C_{48}H_{64}N_{10}Cl_4Cu_2O_{22}$: C, 41.12; H, 4.61; N, 9.98. Found: C, 41.22; H, 4.31; N, 9.92. UV–vis (MeCN), λ_{max}, nm (ε, M^{-1} cm^{-1}): 250 (34 000), 273 (32 200), 280 (30 800), 304 (3900), 410 sh (600), 675 (450), 814 (440), 875 (420). Molar conductivity: Λ_M = 377 Ω^{-1} cm^2 mol^{-1}. IR (Nujol mull), cm^{-1}: 3460 [ν(OH)]; 1620, 1506, 1485 [ν(ring)]; 1100, 623 [ν(ClO_4)]; 930, 868, 750 [δ(CH)].

$[Cu_2(L\text{-}5,5)(OH)_2][ClO_4]_2\cdot H_2O$. A degassed solution of $[Cu_2(L\text{-}5,5)][ClO_4]_2$ (50 mg) in dry acetonitrile (25 mL) was cooled in an ice bath and exposed to a stream of purified dioxygen for 1 h. The resulting green solution was allowed to reach room temperature and then evaporated to dryness. The residue was dissolved in methanol, and the mixture was concentrated until precipitation occurred. The greenish gray precipitate was collected by filtration and dried. Anal. Calcd for $C_{44}H_{48}N_{10}Cl_2Cu_2O_{11}$: C, 48.44; H, 4.44; N, 12.84. Found: C, 48.69; H, 4.32; N, 12.50. UV–vis (MeCN), λ_{max}, nm (ε, M^{-1} cm^{-1}): 250 (31 800), 272 (38 000), 280 (33 500), 300 sh (4300), 335 (3500), 620 (200). Molar conductivity: Λ_M = 222 Ω^{-1} cm^2 mol^{-1}. IR (Nujol mull), cm^{-1}: 3590, 3510 [ν(OH)]; 1620, 1506, 1485 [ν(ring)]; 1095, 623 [ν(ClO_4)]; 932, 745 [δ(CH)].

Demetalation of a sample of the complex by treatment with concentrated ammonia and extraction with chloroform, according to the procedure described by Karlin et al.,[4b] led to isolation of the free ligand, without any detectable trace of ligand hydroxylation products.

$[Cu_2(L\text{-}6,6)(OH)_2][ClO_4]_2\cdot 2H_2O$. A degassed solution of $[Cu_2(L\text{-}6,6)][ClO_4]_2$ (50 mg) in dry acetonitrile (20 mL) was cooled in an ice bath and exposed to a stream of purified dioxygen for a few hours. The product was precipitated at room temperature as a light green powder by addition of diethyl ether. This was filtered off and dried. Anal. Calcd for $C_{48}H_{58}N_{10}Cl_2Cu_2O_{12}$: C, 49.48; H, 5.02; N, 12.02. Found: C, 49.35; H, 4.84; N, 11.95. UV–vis (MeCN/MeOH, 1:1, v/v), λ_{max}, nm (ε, M^{-1} cm^{-1}): 248 (28 000), 274 (32 000), 282 (29 600), 320 sh (3200), 360 (4200), 640 (190). The molar conductivity could not be determined for the insufficient solubility of the compound in acetonitrile. IR (Nujol mull), cm^{-1}: 3620, 3510 [ν(OH)]; 1618, 1518, 1491 [ν(ring)]; 1095, 623 [ν(ClO_4)]; 876, 849, 764, 746 [δ(CH)].

Demetalation of a sample of the complex as described above for $[Cu_2(L\text{-}5,5)(OH)_2][ClO_4]_2$ showed no trace of ligand hydroxylation product.

$[Cu_2(L\text{-}5,5)(N_3)][ClO_4]_3\cdot 2H_2O$. This compound was prepared by mixing equimolar solutions of $[Cu_2(L\text{-}5,5)][ClO_4]_4\cdot 6H_2O$ and sodium azide (0.1 mmol) in methanol. The resulting dark green solution was concentrated to a small volume and left standing until precipitation of the product occurred. This was then filtered off and washed with a small amount of methanol. Anal. Calcd for $C_{44}H_{48}N_{13}Cl_3Cu_2O_{14}$: C, 43.44; H, 3.98; N, 14.97. Found: C, 42.95; H, 3.80; N, 15.04. UV–vis (MeCN), λ_{max}, nm (ε, M^{-1} cm^{-1}): 247 (30 000), 272 (35 000), 279 (31 000), 330 sh (2400), 410 sh (1600), 430 sh (1200), 490 (300), 630 (300). Molar conductivity: Λ_M = 330 Ω^{-1} cm^2 mol^{-1}. IR (Nujol mull), cm^{-1}: 3600 [ν(OH)]; 2056, 1330 [ν(N_3)]; 1615, 1540, 1506, 1490 [ν(ring)]; 1100, 621 [ν(ClO_4)]; 938, 748 [δ(CH)].

A small sample of the azide adduct was prepared similarly using unsymmetrically labeled sodium azide (^{15}N–^{14}N–^{14}N, 99% ^{15}N; Cambridge Isotope Laboratories, Woburn, MA). The IR spectrum of this compound was identical with that of the unlabeled compound except for the position of the azide bands.

$[Cu_2(L\text{-}6,6)(N_3)][ClO_4]_3\cdot H_2O$. This compound was prepared by treating a solution of $[Cu_2(L\text{-}6,6)][ClO_4]_4\cdot 6H_2O$ (~50 mg) in acetonitrile (5 mL) with a concentrated solution of sodium azide in methanol containing slightly more than the equivalent amount of the anion. A crude precipitate of the adduct was obtained by addition of diethyl ether. This was collected by filtration and treated under stirring with a small amount of methanol. Then the product was filtered off and dried under vacuum. Anal. Calcd for $C_{48}H_{54}N_{13}Cl_3Cu_2O_{13}$: C, 45.95; H, 4.34; N, 14.51. Found: C, 46.08; H, 4.01; N, 14.21. UV–vis (MeCN), λ_{max}, nm (ε, M^{-1} cm^{-1}): 247 (30 500), 271 (32 000), 279 (28 000), 305 sh (3800), 435 (2100), 500 sh (1000), 735 br (650). Molar conductivity: Λ_M = 350 Ω^{-1} cm^2 mol^{-1}. IR (Nujol mull), cm^{-1}: 3450 [ν(OH)]; 2042 [ν(N_3)]; 1618, 1502 [ν(ring)]; 1095, 623 [ν(ClO_4)]; 932, 870, 750 [δ(CH)].

A small sample of the azide adduct was prepared with unsymmetrically labeled sodium azide. The IR spectrum of this compound is identical with that of the unlabeled compound except for the position of the azide band.

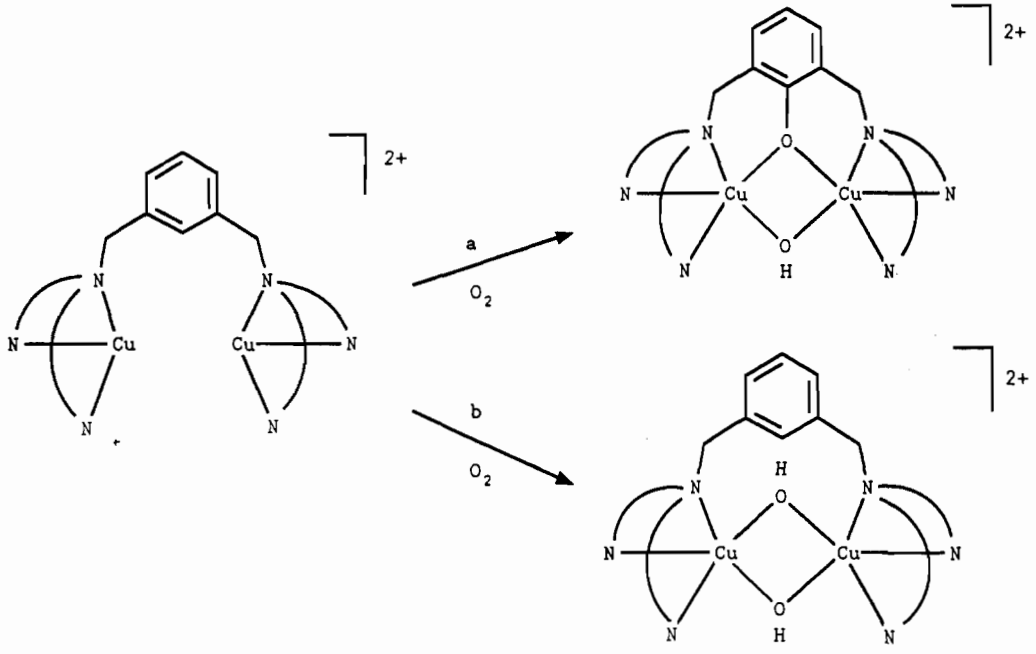
Caution! Although the perchlorate complexes reported in this study were not found to be shock sensitive, the materials should be handled with care and in small quantities.

Results and Discussion

Synthesis. The ligands reported in this paper belong to a family of dinucleating ligands in which a *m*-xylyl spacer carries two "N_3" arms, each containing one tertiary amine and two heterocyclic nitrogen donors. The ligands with arms containing pyridyl, pyrazolyl, and imidazolyl groups have been prepared previously,[4b,6c] together with their dicopper(I) complexes; the choice to extend the investigation to benzimidazole analogues was encouraged by their relatively easy synthetic accessibility, chemical inertness, and steric bulk. In these respects, benzimidazoles are even preferable to the more biomimetically significant imidazole groups. Poly(benzimidazole) dinucleating ligands with additional alkoxy[5a,b] or phenoxy[5d,7e] bridging groups have also been reported previously, but in all cases the synthetic routes were restricted to systems containing single methylene groups between the tertiary amine and benzimidazole groups. For the systems reported in the present investigation, it was possible to find synthetic schemes leading to ligands containing one (L-5,5) or two (L-6,6) methylene bridges between the amine and benzimidazole groups. These involve formation of chelates with relatively rigid, fused five-membered rings and more flexible six-membered rings, respectively, at each metal site.

Reaction of L-5,5 and L-6,6 with copper(II) perchlorate hexahydrate in a 1:2 ratio leads to the dinuclear aquo complexes. These can be converted to the corresponding bis(hydroxo)-dicopper(II) complexes by reaction with alkali or to adducts with anions like azide. A different route to the bis(hydroxo)copper-

Scheme I



(II) dimers involves preparation of the dinuclear copper(I) complexes and reaction with dioxygen. The latter reaction is particularly interesting in view of the model chemistry relevant to hemocyanin and tyrosinase. Of the large series of dicopper(I) complexes derived from *m*-xylyl dinucleating ligands with N_3 donor sets examined so far, only that reported by Karlin[4ab] and containing pyridyl-ligated species is able to effect hydroxylation of the aromatic ring of the ligand by reaction with dioxygen (Scheme I, route a). Replacement of even a single pyridyl group in the side arms of the ligand by other nitrogen heterocycles, as done by Sorrell and co-workers,[6c] or use of benzimidazole groups having basicities virtually identical to that of pyridine (pK_b 8.5 vs 8.6), as is reported here, completely depresses the monooxygenase reactivity on the ligand of the dicopper(I) complex and only the bis(hydroxo)copper(II) dimers[6] are obtained by reaction with dioxygen (Scheme I, route b). Therefore, it is probably a favorable collection of electronic and steric factors that in these model systems restricts the monooxygenase reaction on the ligand to the single complex reported by Karlin. On the other hand, the dicopper(I) complexes reported here are able to transfer their potential monooxygenase reactivity to exogenous phenols,[2g,12] mimicking the reaction catalyzed by tyrosinase.[16]

Aquo and Hydroxo Complexes. The IR spectra of these compounds show relatively sharp bands at about 3470 cm^{-1} for the aquo complexes and 3600 and 3510 cm^{-1} for the hydroxo complexes that can be attributed to coordinated water or hydroxo groups. Since the doublet pattern of IR bands for the hydroxo complexes is very similar to that of the related complexes where pyrazole replaces the benzimidazole residue in the ligand,[6a] we assume a similar bis(hydroxo)-bridged structure for the dinuclear copper(II) centers. Spectroscopic evidence indicates that such bridges are maintained also in solution. For instance the complex $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$ displays a proton NMR spectrum typical for common diamagnetic compounds (Figure 1). Many signals are sharp, and it is even possible to note a signal at low field (δ 10.8) attributable to doublly bridging hydroxo groups. The sharp signals between 3.0 and 4.0 ppm are probably associated with the benzimidazole *N*-methyl groups and some of the methylene protons. The broader signals in the 4.0–5.0 ppm region probably belong to the other methylene protons and to noncoordinated water. Also $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$ and the bis(aquo)dicopper-

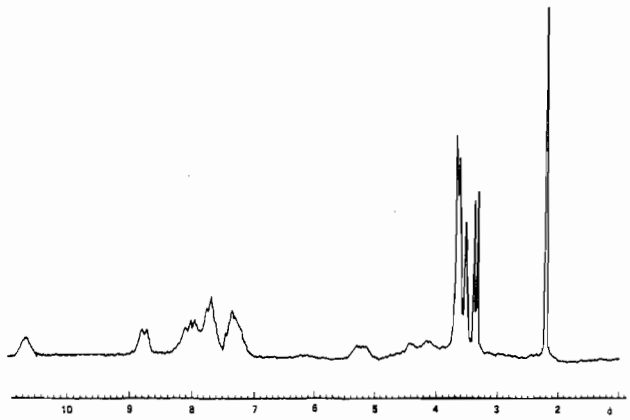


Figure 1. Proton NMR spectrum of a solution of $[Cu_2(L\text{-}5,5)(OH)_2][ClO_4]_2 \cdot H_2O$ in CD_3CN.

(II) complexes display proton NMR spectra with relatively narrow signals, but these are now spread outside the diamagnetic region (from about +25 to −20 ppm). NMR spectra with narrow signals are rare among copper(II) complexes,[17] but they can be observed for dimeric complexes when an effective superexchange interaction occurs between close metal centers. We can therefore assume that water molecules are probably bridging the copper(II) centers also in the aquo complexes.

The electronic spectra of the four complexes are somewhat solvent-dependent, indicating that solvent molecules may bind to the metal centers or affect the geometry of the complexes through interactions with the ligands. Besides the intense absorptions below 300 nm, associated with ligand $\pi \rightarrow \pi^*$ transitions, the spectra of the aquo complexes we formulate as $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ and $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ display two absorptions near 300 and between 350 and 400 nm, occurring as shoulders on the higher energy UV absorption, which can be attributed to σ(amino) → Cu(II)[18] and π(benzimidazole) → Cu(II)[19] LMCT transitions, and further absorptions at lower energy which are basically d–d in nature. The center of gravity of the d–d envelope is found at higher energy for $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ than for $[Cu_2$-

(16) (a) Wilcox, D. E.; Porras, A. G.; Hwang, Y. T.; Lerch, K.; Winkler, M. E.; Solomon, E. I. *J. Am. Chem. Soc.* **1985**, *107*, 4015. (b) Kazandjian, R. Z.; Klibanov, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 5448.

(17) (a) Maekawa, M.; Kitagawa, S.; Munakata, M.; Masuda, H. *Inorg. Chem.* **1989**, *28*, 1904. (b) Kitajima, N.; Koda, T.; Hashimoto, S.; Kitagawa, T.; Moro-oka, Y. *J. Am. Chem. Soc.* **1991**, *113*, 5664.

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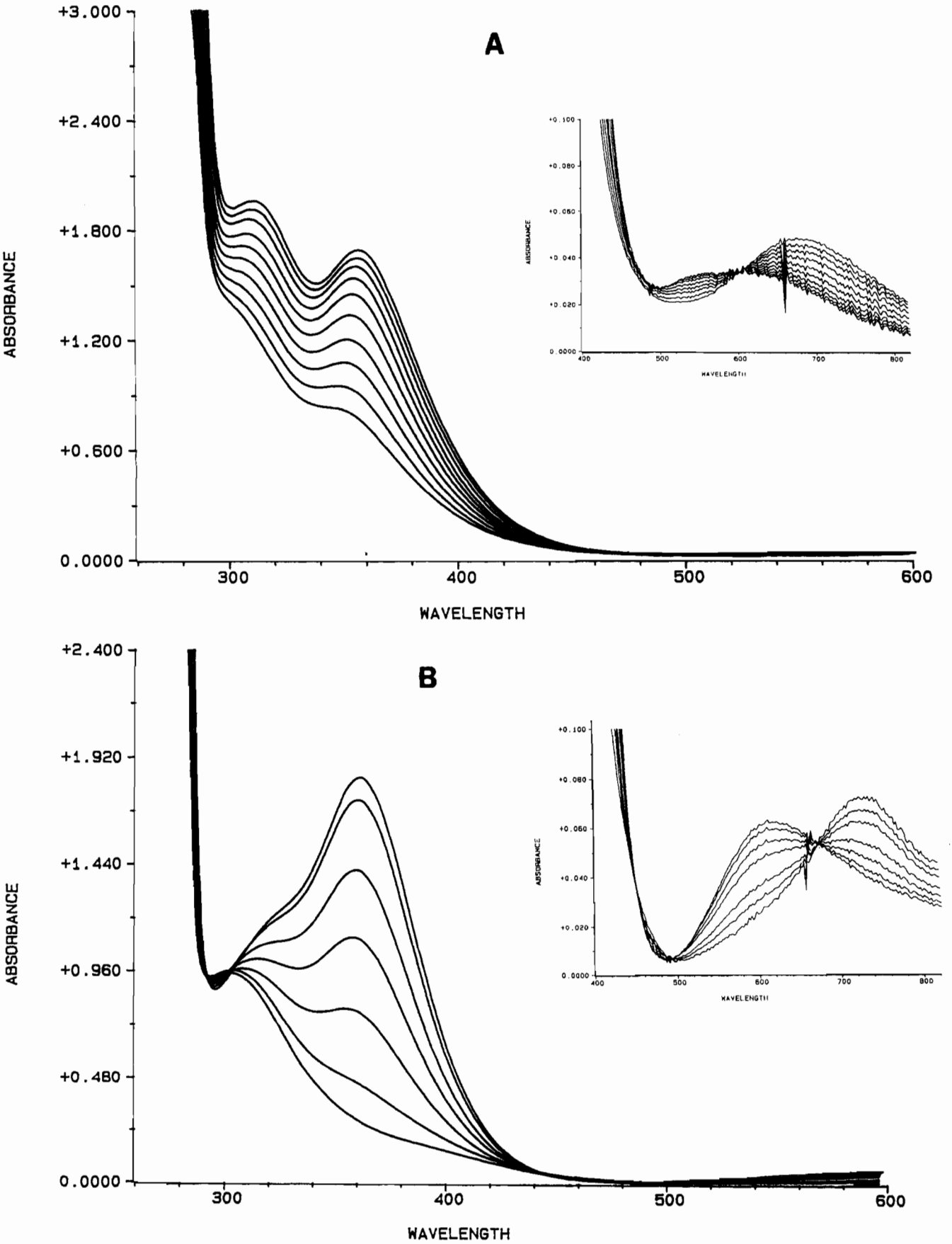
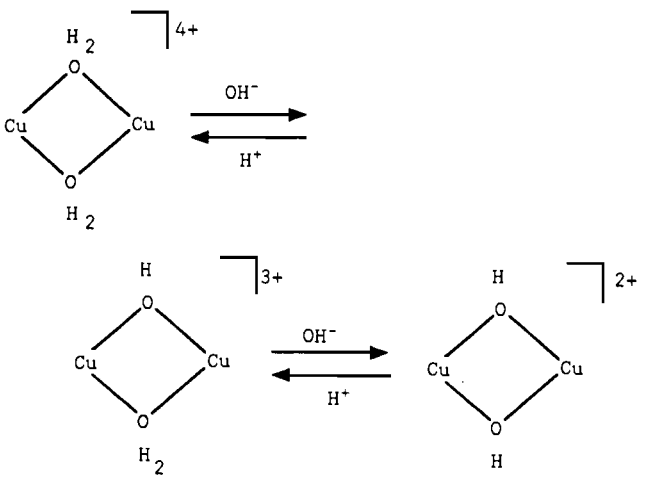


Figure 2. (A) Titration of $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ (3.0×10^{-4} M) in methanol–acetonitrile (4:1, v/v) with methanolic sodium hydroxide (6×10^{-3} M). Representative spectra, normalized for dilution, refer to solutions obtained after addition of successive and equal amounts of OH^- for $[OH^-]$:$[Cu_2]$ ratios from 0.4 to 2.0. (B) Titration of $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ (3.0×10^{-4} M) in methanol–acetonitrile (9:1, v/v) with methanolic sodium hydroxide. Representative spectra, normalized for dilution, refer to solutions containing $[OH^-]$:$[Cu_2]$ ratios of 0.0, 0.2, 0.6, 1.0, 1.4, 1.8, and 2.0.

$(L\text{-}6,6)(H_2O)_2]^{4+}$, consistent with the higher donor strength of the ligand forming five-membered chelate rings. The position of the d–d band observed for $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ (in the 650–680-nm range) is indicative of basic square-pyramidal structure

Scheme II

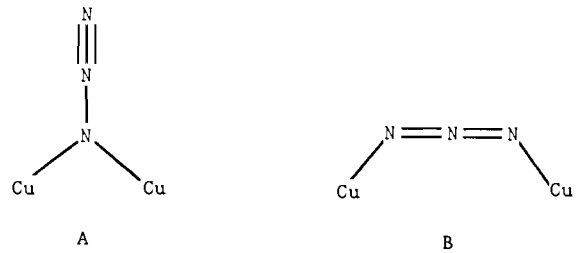


for the copper(II) centers, while for $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ the situation is more complex. In acetonitrile, three separate bands are observed at 675, 814, and 875 nm; the intensity is remarkable for d–d bands considering that there are no intense LMCT transitions at low energy from which they can borrow intensity. We believe that such an unusual spectrum arises from the presence of one basically square-pyramidal and one basically trigonal-bipyramidal metal center in the dinuclear complex. In methanol solution, two bands at 730 and 1020 nm are observed, indicative of distorted trigonal-bipyramidal copper(II) centers.

The dominant feature of the electronic spectra of the bis(hydroxo)dicopper(II) complexes is the presence of intense LMCT absorptions between 320 and 360 nm. The LMCT band occurs at higher energy for $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$ than for $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$, and in both cases the change of solvent from MeCN to MeOH produces a bathochromic shift in and a hyperchromic effect on the LMCT band and development of a more pronounced shoulder or band at higher energy (300–320 nm). While it is clear that these absorptions are largely due to $OH^- \rightarrow Cu(II)$ LMCT transitions, since it is known that for copper(II)–hydroxo complexes LMCT bands occur in this range,[4d,10a] it is possible that some further contribution comes from an enhancement of intensity of the amino-to-copper and benzimidazole-to-copper LMCT transitions due to restrictions on the conformational mobility of the ligand imposed by the tightly bound bis(hydroxo) bridge. Interestingly, the d–d band envelope of both bis(hydroxo) complexes occurs in the 600-nm range, consistent with square-pyramidal structures for the copper(II) centers, although the maximum is still found at higher energy for the L-5,5 system with respect to the L-6,6 system.

The bis(aquo)dicopper(II) and bis(hydroxo)dicopper(II) species can be interconverted by addition of base and acid, respectively. Spectral titrations show that the exchange of two protons occurs in a single step, as shown by the presence of isosbestic points (Figure 2), so that the amount of the intermediate aquohydroxodicopper(II) species at equilibrium must be negligible (Scheme II). Interestingly, while the bis(aquo) → bis(hydroxo) conversion is immediate, the reverse reaction is slower and the equilibrium after each addition of acid during the spectral titration is reached after some time (up to about 1 h). This finding supports the view that the $Cu_2(OH)_2$ units must be tightly packed and impose conformational rigidity on the poly(benzimidazole) ligands.

Azide Complexes. The bis(aquo)dicopper(II) complexes of L-5,5 and L-6,6 exhibit high affinity for small anionic ligands such as azide that can replace bridging water molecules. The mono(azido)dicopper(II) complexes of L-5,5 and L-6,6, however, exhibit IR and electronic spectra which are significantly different from each other, suggesting that the modes of coordination of the anion are different in the two cases. The asymmetric stretching of the coordinate azide ion occurs at 2056 cm^{-1} for the L-5,5 derivative and 2042 cm^{-1} for the L-6,6 derivative. But in the former case a band at 1330 cm^{-1}, absent in the spectrum of the bis(aquo) complex, can be assigned to the symmetric stretch, while no similar band of significant intensity can be detected in the IR spectrum of $[Cu_2(L\text{-}6,6)(N_3)]^{3+}$. The higher energy of $\nu_{as}(N_3)$ and the occurrence of $\nu_s(N_3)$ agrees with the presence of a μ-1,1 azide bridge in $[Cu_2(L\text{-}5,5)(N_3)]^{3+}$ (structure A), while



the lower energy of ν_{as} and the lack or low intensity of ν_s suggest the presence of the symmetrical μ-1,3 bridge in $[Cu_2(L\text{-}6,6)(N_3)]^{3+}$ (structure B), according to the expected trends.[4c,20] This interpretation is confirmed by the IR spectra of the azide adducts prepared with unsymmetrically labeled azide ($^{15}N^{14}N^{14}N$). For the L-5,5 adduct the asymmetric stretching of the coordinated $^{14}N_2{}^{15}N$ splits into two components at 2044 and 2054 cm^{-1}, while the symmetric stretch occurs at 1321 cm^{-1}. For the L-6,6 adduct a single asymmetric stretch of bound $^{14}N_2{}^{15}N$ is observed at 2034 cm^{-1}. It is likely that a second aquo bridge is maintained in these adducts so that these azido complexes can be formulated as $[Cu_2(L\text{-}5,5)(N_3)(H_2O)]^{3+}$ and $[Cu_2(L\text{-}6,6)(N_3)(H_2O)]^{3+}$. Unfortunately, we could not obtain crystals suitable for X-ray investigation to fully clearify the structure of these complexes.

The electronic spectra of the azide–dicopper(II) complexes derived from L-5,5 and L-6,6 show multicomponent structures and solvent dependence in the near-UV LMCT bands associated with the azide-to-copper transitions. In general, the spectra can be rationalized by assuming the existence of two basic components, the most intense of which lies at higher energy. However, this higher energy component is clearly split (1000–2000 cm^{-1}) in some of the spectra. The low-energy component usually occurs as a weak shoulder on the main band, except for $[Cu_2(L\text{-}5,5)(N_3)]^{3+}$ in acetonitrile, where it occurs as a separate band at 490 nm. A distinct azide-to-copper(II) LMCT band at such low energy has been observed only in the spectrum of met-azide arthropod hemocyanin.[21] Although up to four components in the LMCT band are predicted for a bridging azide, only two were apparent in the spectra of several μ-1,1 or μ-1,3 azide dinuclear complexes.[22] The $[Cu_2(L\text{-}5,5)(N_3)]^{3+}$ acetonitrile spectrum mentioned above features two partially resolved high-energy components at 410 and 430 nm generating an overall broad absorption extending from 350 to 470 nm. The spectrum of the same compound is markedly different in methanol where a single high-energy component occurs at 360 nm, with low-energy component near 440 nm. The blue shift of the LMCT bands in the more polar solvent cannot simply be due to solvent coordination, since the d–d bands are less affected and the change is in the opposite direction (λ_{max} 630 nm in MeCN, λ_{max} 660 nm in MeOH). Although it is possible that the aquo bridge is replaced by methanol in this solvent, we believe that the main reason for the blue shift of the LMCT bands is solvation of the μ-1,1 azide moiety as the polarity of the environment increases. We noted

(20) (a) Drew, M. G. B.; Nelson, J.; Esho, F.; McKee, V.; Nelson, S. M. *J. Chem. Soc., Dalton Trans.* **1982**, 1837. (b) Pate, J. E.; Ross, P. K.; Thamann, T. J.; Reed, C. A.; Karlin, K. D.; Sorrell, T. N.; Solomon, E. I. *J. Am. Chem. Soc.* **1989**, *111*, 5198. (c) Nakao, Y.; Takagi, Y.; Okazaki, H.; Itho, T.; Mori, W.; Suzuki, S. *Inorg. Chim. Acta* **1990**, *175*, 17.

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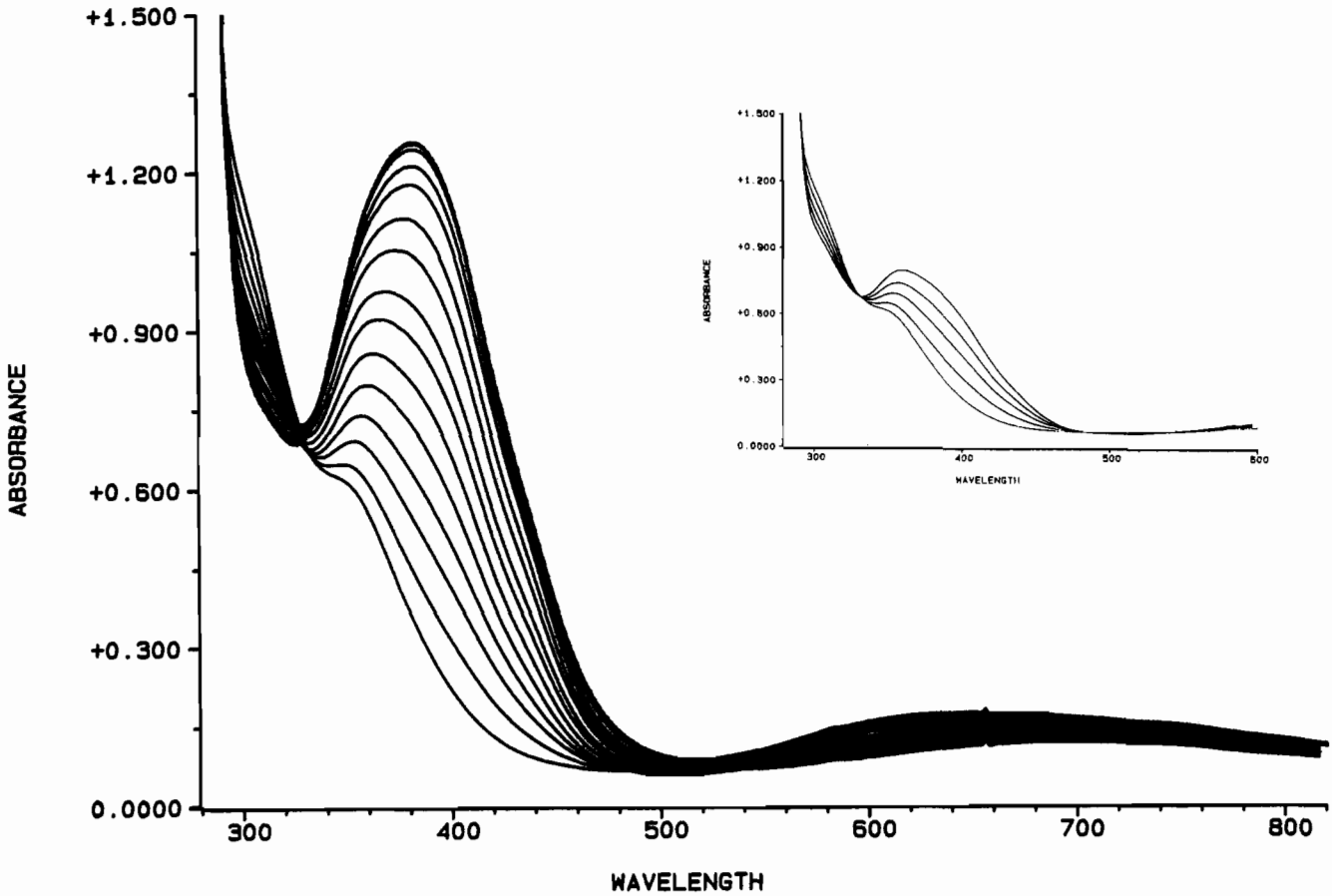


Figure 3. Titration of $[Cu_2(L\text{-}5,5)(H_2O)]^{4+}$ (3.0×10^{-4} M) with sodium azide (6.0×10^{-3} M) in methanol solution. The spectra, normalized for dilution, refer to addition of equal amounts of azide for $[N_3]:[Cu_2]$ ratios from 0.0 to 3.0. The insert shows the initial part of the titration where the [azide]:$[Cu_2]$ ratio varies from 0.0 to 0.8.

a similar effect for terminal azide bound to mononuclear copper(II) complexes.[11b] As a matter of fact, much smaller solvent effects for the azide-to-copper(II) LMCT bands occur in the $[Cu_2(L\text{-}6,6)(N_3)]^{3+}$ system, where a less exposed, μ-1,3-bridged azide is present. Here the high-energy component occurs at 435 nm in MeCN and is split into two well-defined components at 412 and 442 nm in MeOH. In both cases a low-energy component near 500 nm is observed. The ligand field spectrum of this derivative suggests other differences with respect to the L-5,5 system. Two d–d bands occur at ~730 and 1000 nm for $[Cu_2(L\text{-}6,6)(N_3)]^{3+}$, with little solvent dependence, indicating distorted trigonal-bipyramidal structures for the copper(II) centers, whereas for $[Cu_2(L\text{-}5,5)(N_3)]^{3+}$ the structures are of the more typical square-pyramidal type.

To get an estimate of the affinity of azide for the various dinuclear complexes we performed spectrophotometric titrations on the aquo and hydroxo complexes in methanol and acetonitrile solutions. In all cases, multiphase behavior was observed, with several azide molecules binding to the dinuclear complexes. In acetonitrile, it was difficult to separate the various binding steps because the affinity of several azide molecules for the dinuclear centers was very high, whereas, in methanol, it was possible to differentiate the binding modes of successive azide molecules in several instances. When a solution of $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ in methanol is titrated with azide, the spectrum undergoes marked changes up to a ratio $[N_3^-]:[Cu_2] \sim 2.5:1$ (Figure 3). The spectrum of the monoazide adduct (λ_{max} 360 nm, with a shoulder near 440 nm) is evident in the first half of the titration, but isosbestic points at 312 and 330 nm are maintained only with the initial additions of the titrant (up to about $[N_3^-]:[Cu_2] \sim 0.8:1$). Then the second azide molecule begins to bind significantly with a slightly different spectrum (λ_{max} 382 nm, with a shoulder near 440 nm) so that the isosbestic points are lost. An estimate of the binding constant of the first azide obtained from the titration data at 360 nm and the molar extinction coefficient of the complex $[Cu_2(L\text{-}5,5)(N_3)(H_2O)][ClO_4]_3$ yields $K_1 > 5 \times 10^4$ M^{-1}, but it is clear that the binding constant of the second azide molecule must be also high (Scheme III). The ligand field spectrum shows that the d–d bands shift to higher energy, consistent with binding of the azide ligands in equatorial positions.[11b] We thus conclude that a double-azide bridge replaces the aquo bridges in the dinuclear complex.

Binding of further azide to the species $[Cu_2(L\text{-}5,5)(N_3)_2]^{2+}$ occurs with much lower affinity and can be followed with additions of the ligand above $[N_3^-]:[Cu_2] \sim 10:1$.[23] The LMCT band increases progressively in intensity with a shift of the maximum to 390 nm. Although it is difficult to extract accurate binding constants from the titration data, estimates of K_3 and K_4 can be obtained from the data for $[N_3^-]:[Cu_2]$ between 10 and 20 and between 30 and 200, respectively. In these intervals, isosbestic points at the wavelengths 292 and 350 nm, respectively, are maintained, and it seems therefore reasonable to assume that they represent separate steps for binding of the third and fourth azide molecules to the dinuclear complex. The values of K_3 (115 M^{-1}, Hill coefficient[11b] $n = 1.00$) and K_4 (15 M^{-1}, $n = 0.99$) indicate low affinity of these azide molecules and we assume they bind to the coppers in the terminal mode. It is interesting to note that the d–d bands shift to lower energy (690 nm) on binding of these azide molecules to the coppers, which is consistent with binding in the axial positions.[11]

A similar azide titration experiment performed on $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ shows that also in this case two azide molecules replace water molecules with high affinity (Figure 4). The spectral features of these adducts consist of LMCT bands at 412 and 442 nm with a weak shoulder near 520 nm. An estimate of K_1 using the spectral data up to $[N_3^-]:[Cu_2] = 1.0$, showing isosbestic

(23) Supplementary material.

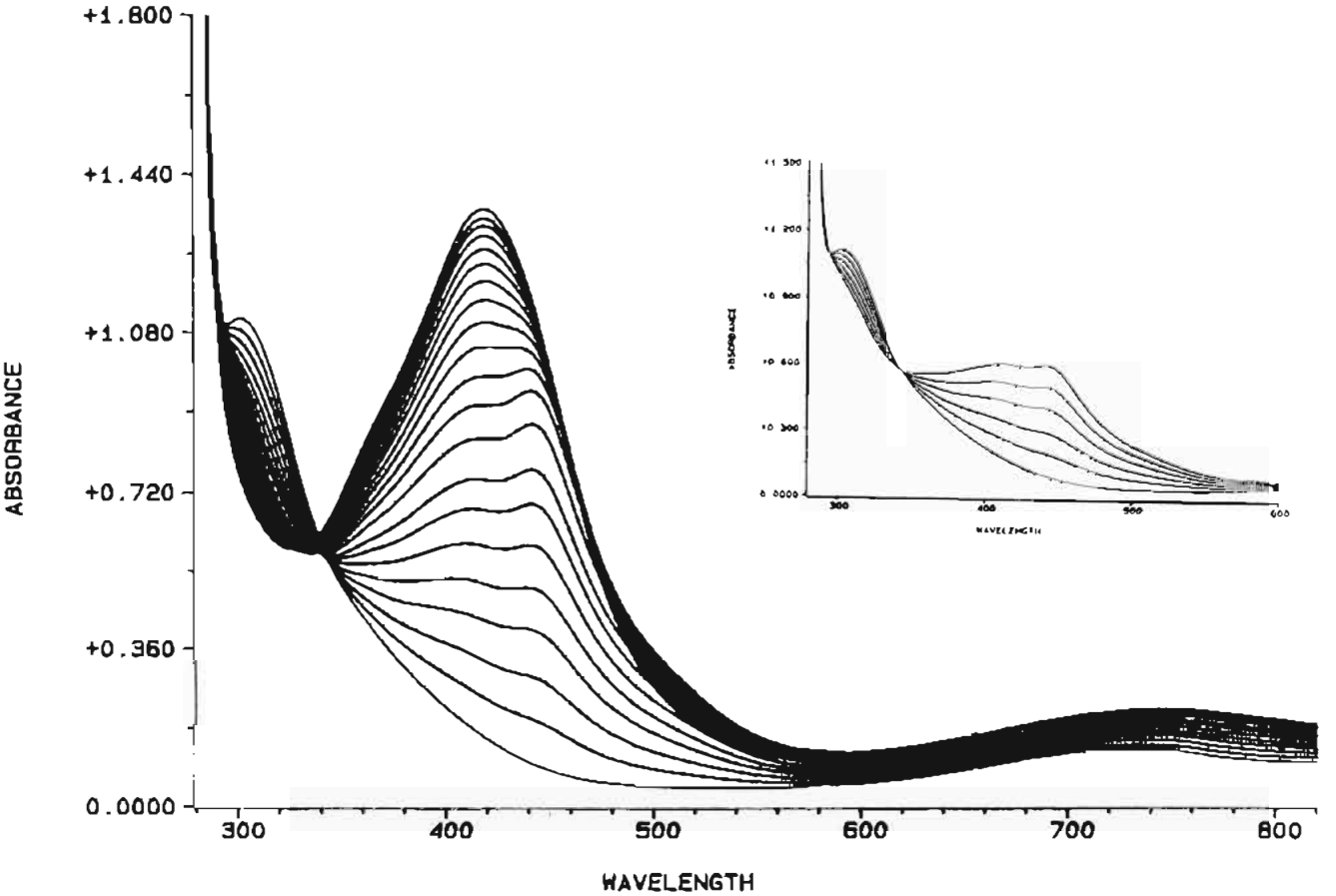
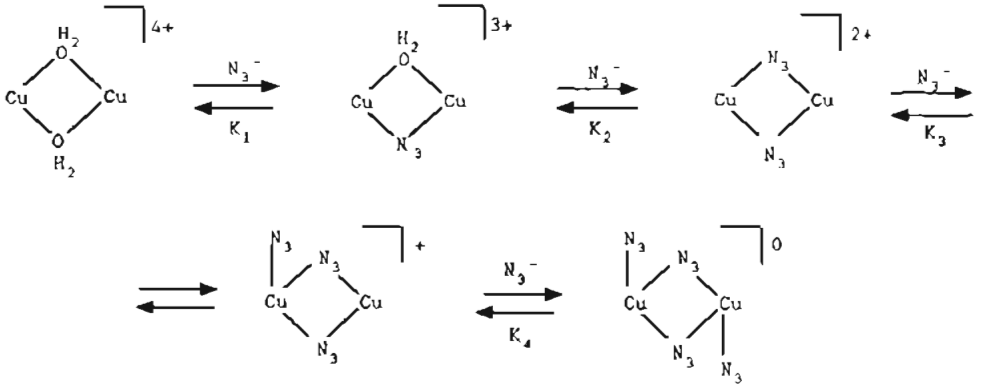


Figure 4. Titration of $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ (3.1×10^{-4} M) with sodium azide in methanol solution. The spectra, normalized for dilution, refer to 20 successive and equal additions of azide for [azide]:[Cu_2] ratios from 0.2 to 4.0. The insert shows the initial part of the titration, with [azide]:[Cu_2] ratios of 0.0, 0.2, 0.4, 0.6, 0.8, and 1.0.

Scheme III



points at 294 and 344 nm (see insert of Figure 4), yields $K_1 > 5 \times 10^4$ M^{-1}. This confirms that the affinity depends primarily on the charge of the complex and much less on the mode of binding of the anion. The affinity of the second azide molecule must also be high since saturation is achieved at $[N_3^-]:[Cu_2] \sim 5:1$. However, binding of this second azide produces the loss of the 520-nm shoulder and the merging of the two higher energy components into a single, more symmetrical band at 425 nm. It can be proposed that the binding of the second azide causes a cleavage of the existing μ-1,3 bridge so that the $[Cu_2(L\text{-}6,6)(N_3)_2]^{2+}$ species contains two terminal azide moieties (Scheme IV). Two additional azide molecules can bind to $[Cu_2(L\text{-}6,6)(N_3)_2]^{2+}$ with low affinity,[23] in analogy with the behavior of the corresponding L-5,5 system. Separating the titration steps for $[N_3]:[Cu_2]$ between 8 and 15 (isosbestic points at 290, 376, and 500 nm) and between 30 and 90 (isosbestic points at 292, 354, and 486 nm) yields the binding constants $K_3 = 170$ M^{-1} (n = 0.95) and $K_4 = 90$ M^{-1} (n = 1.01). Also in this case, the d–d bands shift to lower energy on binding of the anion.

The azide titration experiments performed on the bis(hydroxo) complexes show reduced affinity of the anion for the dicopper cores with respect to the aquo complexes. In the case of $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$, replacement of the hydroxo bridges is accompanied by progressive extinction of the two near-UV bands at 310 and 353 nm, the latter of which is replaced by a single absorption band that moves progressively to 390 nm (Figure 5). The binding process can be separated into two steps. In the first half of the titration, occurring with disappearance of the 310-nm band, the LMCT spectrum features a maximum between 360 and 370 nm, with shoulder at 440 nm, which is similar to the spectra of the monoazide and bis(azide) adducts obtained from $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$. Analysis of the spectral data at 354 nm at the beginning of the titration, with $[N_3]:[Cu_2]$ between 5 and 90, showing two isosbestic points at 292 and 374 nm (see insert

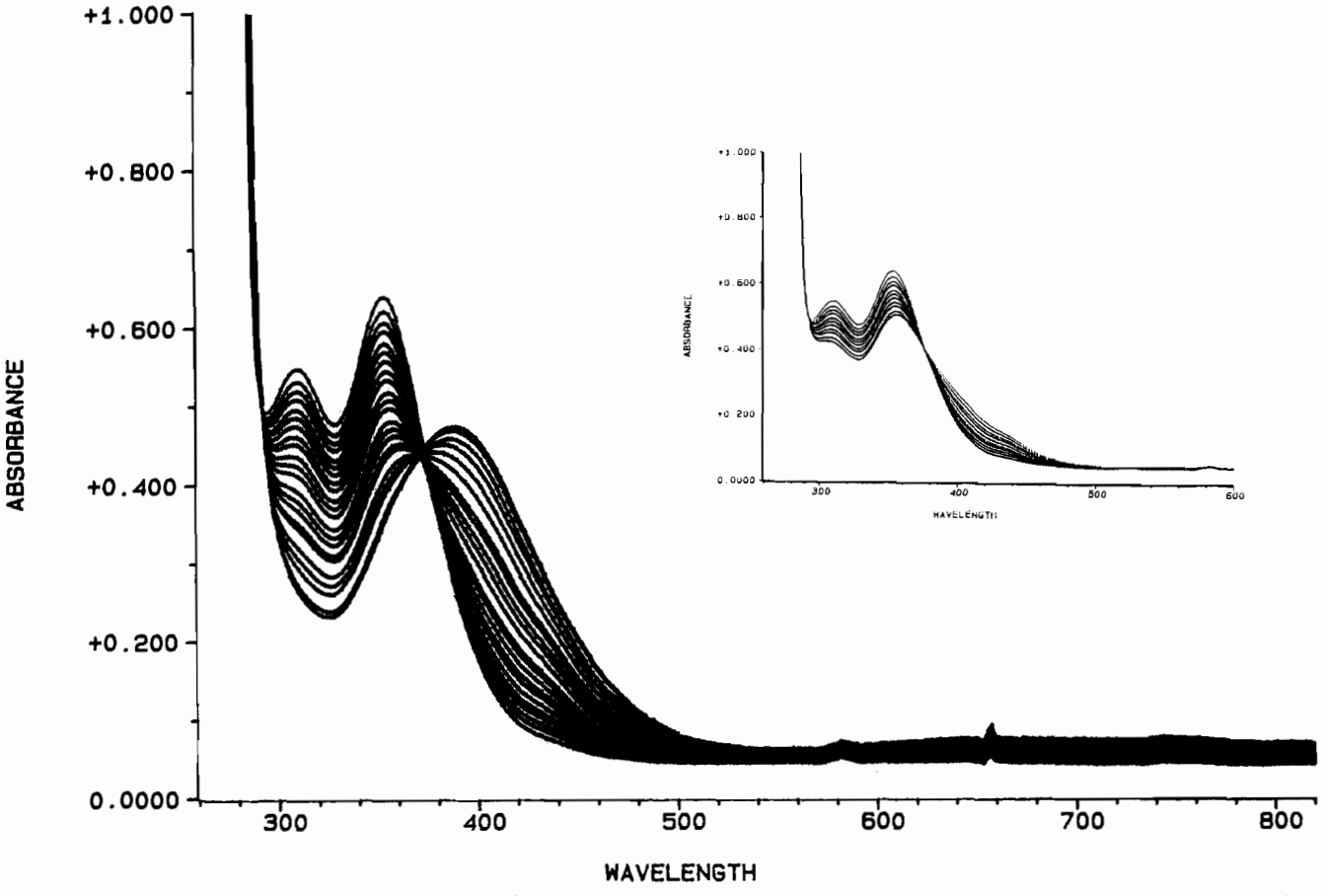
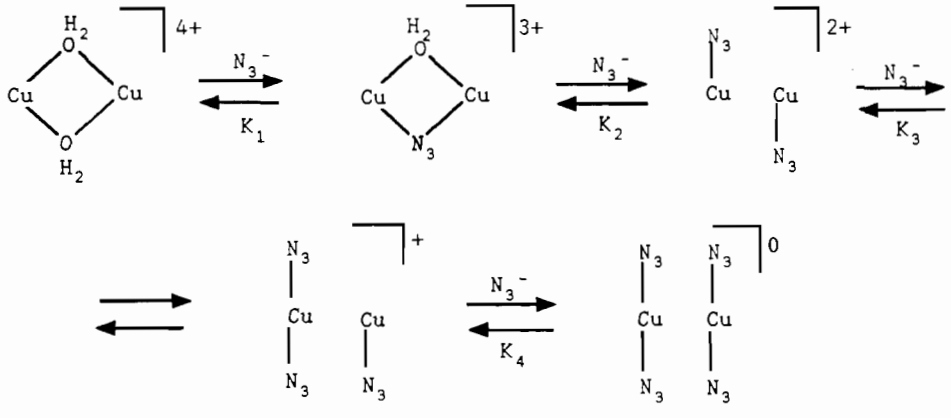


Figure 5. Titration of $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$ (9.3×10^{-5} M) with sodium azide in methanol solution. The spectra, normalized for dilution, refer to solutions containing [azide]:$[Cu_2]$ ratios of 0, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 100, 120, 140, 160, 200, 250, 300, 350, 400, 500, and 600. The insert shows the initial part of the titration with [azide]:$[Cu_2]$ ratios from 0 to 70.

Scheme IV



of Figure 5), enables one to obtain a binding constant of 250 M^{-1} (n = 1.07) for the first azide molecule. In the second part of the titration, the LMCT band moves from 370 to 390 nm with no isosbestic points. This band comprises several absorptions due to species containing two or more bound azide molecules. These species cannot be differentiated in the titration because of similar affinities and the relatively large amount of azide present in solution.

Also for $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$, the addition of azide produces the disappearance of the LMCT bands of the hydroxo bridges and the appearance of new absorptions at lower energy (Figure 6). Initially, the addition produces a broad absorption near 440 nm that resembles the better resolved azide-to-copper LMCT bands of $[Cu_2(L\text{-}6,6)(N_3)(H_2O)]^{3+}$ occurring in the same region. Isosbestic points are observed at 295 and 388 nm (see insert in Figure 6) so that an estimate of the binding constant can be made. Analysis of the data at 360 nm yields K = 280 M^{-1} (n = 1.13), a value similar to that found for the corresponding bis(hydroxo)dicopper(II) complex of L-5,5. Further addition of azide leads to the development of an intense band centered at 418 nm encompassing the absorptions of species containing multiple bound azide molecules.

Electrochemistry. The thermodynamic aspects of the redox propensity of the complexes separate the L-6,6 and L-5,5 copper(II)–aquo complexes from the corresponding hydroxo derivatives, whereas the kinetic aspects differentiate the L-6,6 complexes from the L-5,5 analogues. The complex $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ undergoes, in acetonitrile solution, a chemically reversible single-stepped reduction process at rather positive potential value, which proved, by coulometric tests (E_w = 0.0 V), to involve two electrons per molecule. A second irreversible reduction step is present at more negative potential values; its irreversibility is associated with the demetalation reaction, as illustrated by the appearance of an anodic stripping peak (E_p = –0.3 V) on the reverse scan.

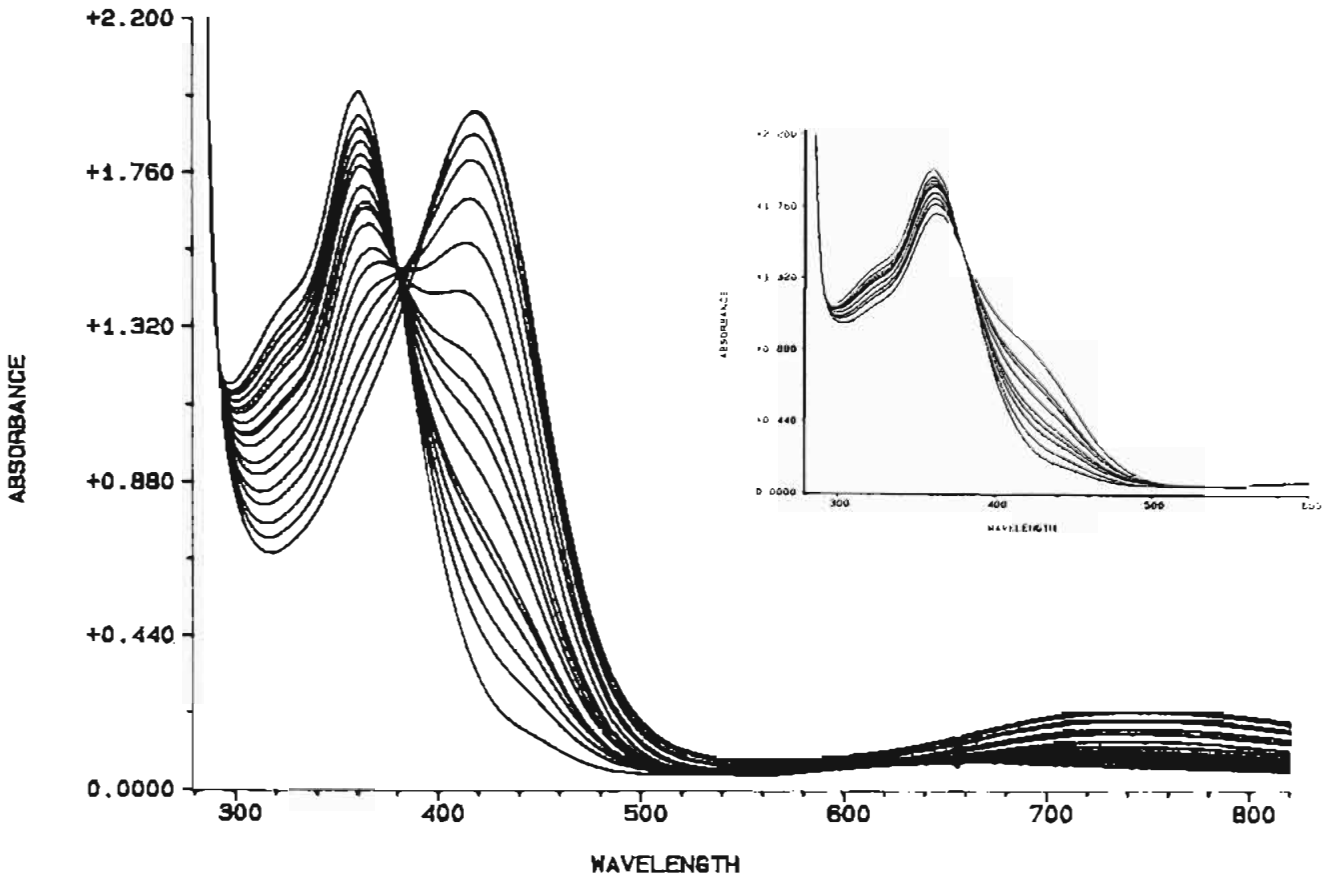


Figure 6. Titration of $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$ (3.0×10^{-4} M) with sodium azide in methanol solution. The spectra, normalized for dilution, refer to solutions containing [azide]:[Cu_2] ratios of 0, 2, 6, 10, 14, 18, 20, 30, 40, 50, 60, 80, 100, 120, 140, 160, 180, and 200. The insert shows the initial part of the titration with [azide]:[Cu_2] ratios from 0 to 30.

The overall reduction path can be schematized as follows:

$$Cu^{II}Cu^{II} \underset{-2e}{\overset{E^{0\prime} = +0.40\ V;\ +2e}{\rightleftarrows}} Cu^{I}Cu^{I} \xrightarrow{E_p = -1.30\ V;\ +2e} Cu^{0}Cu^{0}$$

In contrast, $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$ undergoes two distinct, irreversible one-electron reduction processes at notably negative potential values. Deeper electrochemical investigations are prevented by the low solubility of the complex; nevertheless, the lack of the anodic stripping peak in the reverse scan after traversing the most cathodic step, even at the lowest scan rate (0.02 V s^{-1}), seemingly allows the following reduction sequence to be assigned:

$$Cu^{II}Cu^{II} \xrightarrow{E_p = -1.08\ V;\ +e} Cu^{II}Cu^{I} \xrightarrow{E_p = -1.70\ V;\ +e} Cu^{I}Cu^{I}$$

As far as the complexes $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ and $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$ are concerned, the aquo complex is reduced through two closely spaced one-electron steps at relatively high potential values, irreversible in character, according to the sequence

$$Cu^{II}Cu^{II} \xrightarrow{E_p = +0.21\ V;\ +e} Cu^{II}Cu^{I} \xrightarrow{E_p = +0.10\ V;\ +e} Cu^{I}Cu^{I}$$

whereas the hydroxy complex undergoes two closely spaced two-electron steps at relatively low potential values, according to the overall process

$$Cu^{II}Cu^{II} \xrightarrow{E_p = -0.85\ V;\ +2e} Cu^{I}Cu^{I} \xrightarrow{E_p = -1.10\ V;\ +2e} Cu^{0}Cu^{0}$$

Reduction metallic copper evidenced by the reoxidation stripping peak present in the reverse scan.

Two points deserve some comments. (i) The bis(aquo) complexes undergo reduction at relatively high potential values, whereas the bis(hydroxo) complexes undergo reduction at notably low potential values. This behavior is not unusual[3c,24] and may be ascribed to the poor ability of the hydroxo bridge to bind the instantaneously electrogenerated copper(I) center, as well as to the reduced electrostatic effect of the relevant cationic copper(II) complexes. (ii) Within the bis(aquo) assemblies, which thermodynamically favor access to copper(I), the presence of the more flexible six-membered ligand L-6,6 kinetically stabilizes the dicopper(I) complex, likely supporting the structural reorganization involved in the Cu^{II}_2/Cu^{I}_2 redox change. A rough evaluation of the barrier energy to such a geometrical rearrangement can be gained by the trend of the peak-to-peak separation of the relevant reduction process with the scan rate.[25] In the case of $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$, the ΔE_p values progressively increase from 104 mV at 0.02 V s^{-1} to 289 mV at 5.12 V s^{-1}. If one considers that a two-electron step, electrochemically reversible (i.e., not involving important structural effects), is expected to display a constant ΔE_p of 29 mV,[26] it seems evident that, although there are possible effects of uncompensated solution resistances, particularly at high scan rate, the actual reduction process is accompanied by a somewhat large steric strain.

Figure 7 shows the cyclic voltammetric responses exhibited by the azide derivatives $[Cu_2(L\text{-}6,6)(N_3)(H_2O)]^{3+}$, $[Cu_2(L\text{-}6,6)(N_3)_2]^{2+}$, and $[Cu_2(L\text{-}6,6)(N_3)_4]$. It is evident that, with an increase in the number of azide groups, the one-electron reduction process of the two copper centers tends to convert from two separated to two almost coincident steps. All these processes show features of chemical reversibility, at least in the short times of cyclic voltammetry. In addition, in all cases, the successive

(24) Christou, G.; Perlepes, S. P.; Libby, E.; Folting, K.; Huffman, J. C.; Webb, R. J.; Hendrikson, D. N. *Inorg. Chem.* **1990**, *29*, 3657.
(25) Cinquantini, A.; Opromolla, G.; Zanello, P. *J. Chem. Soc., Dalton Trans.* **1991**, 3161 and references therein.
(26) Brown, E. R.; Sandifer, J. R. In *Physical Methods of Chemistry. Electrochemical Methods*; Rossiter, B. W.; Hamilton, J. F., Eds.; Wiley-Interscience: New York, 1986; Vol. 2, Chapter 4.

one-electron reduction of the two copper(I) centers proceeds through a single step, irreversible in character, because of the subsequent demetalation reaction, as illustrated in Figure 7a for $[Cu_2(L\text{-}6,6)(N_3)(H_2O)]^{3+}$. The overall redox pathway can hence be so schematized:

$$Cu^{II}Cu^{II}(N_3) \underset{-e}{\overset{E^{\circ\prime} = +0.36\ V,\ +e}{\rightleftarrows}} Cu^{II}Cu^{I}(N_3) \underset{-e}{\overset{E^{\circ\prime} = +0.17\ V,\ +e}{\rightleftarrows}} Cu^{I}Cu^{I}(N_3) \overset{E_p = -1.23\ V,\ +2e}{\longrightarrow} Cu^{0}Cu^{0}(N_3)$$

$$Cu^{II}Cu^{II}(N_3)_2 \underset{-e}{\overset{E^{\circ\prime} = +0.21\ V,\ +e}{\rightleftarrows}} Cu^{II}Cu^{I}(N_3)_2 \underset{-e}{\overset{E^{\circ\prime} = +0.04\ V,\ +e}{\rightleftarrows}} Cu^{I}Cu^{I}(N_3)_2 \overset{E_p = -1.00\ V,\ +2e}{\longrightarrow} Cu^{0}Cu^{0}(N_3)_2$$

$$Cu^{II}Cu^{II}(N_3)_4 \underset{-2e}{\overset{E^{\circ\prime} = +0.00\ V,\ +2e}{\rightleftarrows}} Cu^{I}Cu^{I}(N_3)_4 \overset{E_p = -1.17\ V,\ +2e}{\longrightarrow} Cu^{0}Cu^{0}(N_3)_4$$

Speculatively, it is difficult to attribute either to different geometrical factors or to the reduced electrostatic effects the shift of the redox potentials toward less positive values with the increase of the number of azide groups.

As shown in Figure 8, a similar trend in redox propensity is displayed by the azide-substituted copper(II) complexes of the five-membered L-5,5 ligand, namely $[Cu_2(L\text{-}5,5)(N_3)(H_2O)]^{3+}$ and $[Cu_2(L\text{-}5,5)(N_3)_2]^{2+}$. Also in this case, the increase of the number of azide groups tends to induce coalescence between the two one-electron reductions of the copper(II) centers. The reduction pathways are

$$Cu^{II}Cu^{II}(N_3) \underset{-e}{\overset{E^{\circ\prime} = +0.40\ V,\ +e}{\rightleftarrows}} Cu^{II}Cu^{I}(N_3) \underset{-e}{\overset{E^{\circ\prime} = +0.00\ V,\ +e}{\rightleftarrows}} Cu^{I}Cu^{I}(N_3) \overset{E_p = -0.70\ V,\ +2e}{\longrightarrow} Cu^{0}Cu^{0}(N_3)$$

$$Cu^{II}Cu^{II}(N_3)_2 \underset{-2e}{\overset{E^{\circ\prime} = -0.03\ V,\ +2e}{\rightleftarrows}} Cu^{I}Cu^{I}(N_3)_2 \overset{E_p = -0.70\ V,\ +2e}{\longrightarrow} Cu^{0}Cu^{0}(N_3)_2$$

The chemical reversibility of the copper(II)/copper(I) redox change in the different azide complexes of both L-6,6 and L-5,5 ligands shows that an increased flexibility around the coordination sphere of each copper center is obtained upon substitution of aquo bridges for azide groups. Most importantly, it must be taken into account that the successive addition of one electron to two noncommunicating sites of a molecule should lead to two

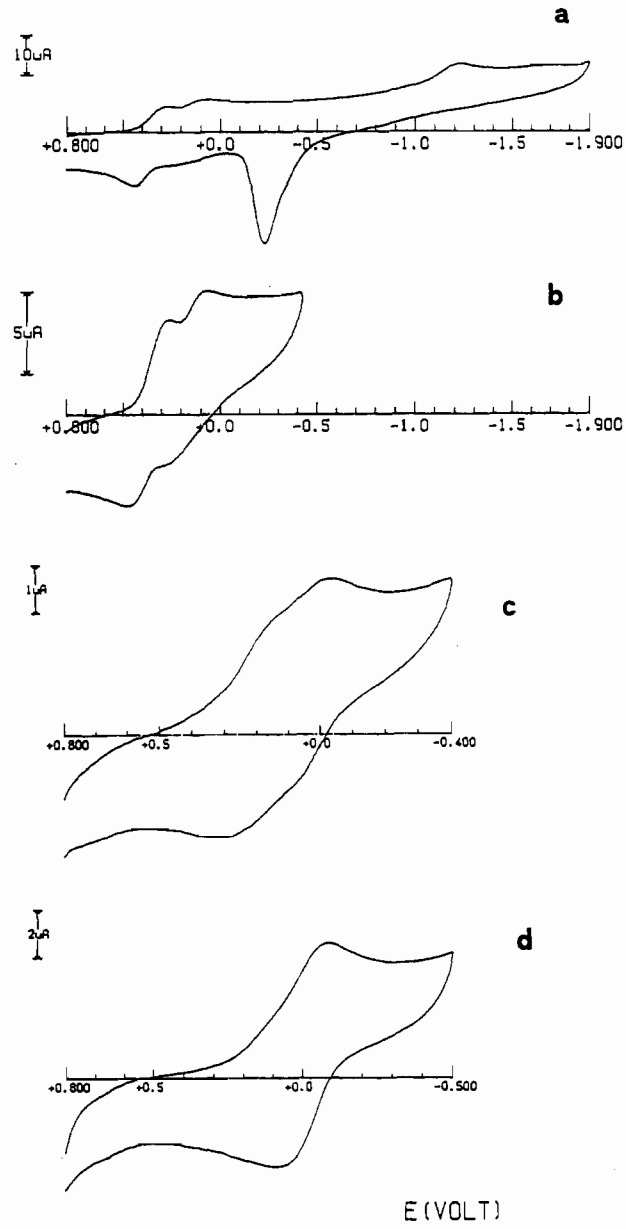


Figure 7. Cyclic voltammograms recorded at a platinum electrode for MeCN solutions containing $[NEt_4][ClO_4]$ (0.1 M) and the following: (a, b) $[Cu_2(L\text{-}6,6)(N_3)(H_2O)]^{3+}$ (1.1×10^{-3} M); (c) $[Cu_2(L\text{-}6,6)(N_3)_2]^{2+}$ (8.0×10^{-4} M); (d) $[Cu_2(L\text{-}6,6)(N_3)_4]$ (9.0×10^{-3} M). Scan rate = 0.2 V s^{-1}.

essentially overlapping reduction processes, the expected separation in redox potentials being 36 mV.[3c] This means that, at a first approximation,[27] in the present case, the highest electronic conjugation between the two metal ions is reached upon substituting one water bridge for one azide bridge apparently independently of its μ-1,1 or μ-1,3 coordination mode. Finally, it is noteworthy that the Cu^{II}_2/Cu^{I}_2 reduction processes of the aquo complexes of the L-6,6 ligand as well as of the azido complexes of both L-6,6 and L-5,5 ligands occur at relatively high potential values, just in the range from 0 to +0.3 V (vs SCE), which characterizes the redox activity of the type 3 copper proteins.[28]

Biological Relevance. The binuclear complexes derived from L-5,5 and L-6,6 exhibit several features that are relevant to the biomimetic chemistry of hemocyanin and tyrosinase. Besides the fact that monooxygenase reactivity on exogenous phenols is exhibited by the dicopper(I) complexes, the bis(hydroxo)dicopper(II) complexes can be considered as good models for the met

(27) One reviewer has rightly pointed out that the precise assessment of the extent of communicability between two equivalent centers of a molecule by electrochemical measurements depends upon many factors (interactions between the two centers, Coulombic repulsions in the sequential oxidation states, Nernstian behavior of the relevant electron transfers, and reorganizations of the coordination spheres of the metal centers as a consequence of such multiple redox changes). In view of the substantial chemical and electrochemical reversibility of the present redox changes, we confide that allowance is made to draw conclusions about the whole series of azido complexes even if they differ in charge and composition, because of the widely accepted conclusion that the electronic interaction between the two centers is the major source of the wave splitting. (See for instance: Flanagan, J. B.; Margel, S.; Bard, A. J.; Anson, F. C. *J. Am. Chem. Soc.* **1978**, *100*, 4248.)

(28) Fee, J. A. *Struct. Bonding (Berlin)* **1975**, *23*, 1.

Table I. Comparison of the Spectral Features of the Azide Adducts of the Dicopper(II) Complexes Derived from L-5,5 and L-6,6 in Methanol Solution with Those of Met-Hemocyanin (Hc) and Met-Tyrosinase

species	$N_3^- \rightarrow Cu(II)$ LMCT λ_{max}, nm (ϵ, M^{-1} cm^{-1})	Cu/N_3^- d–d λ_{max}, nm (ϵ M^{-1} cm^{-1})	Cu/H_2O–Cu/OH^- d–d λ_{max}, nm (ϵ, M^{-1} cm^{-1})	K, M^{-1}
$[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$	360 (2300) 440 sh (650)	660 (300)	680 (280)	$>5 \times 10^4$
$[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$	412 (2300) 442 (2300) 520 sh (700)	735 (700) 985 (400)	730 (450) 1020 (650)	$>5 \times 10^4$
$[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$	360[a] 440 sh	650 (300)	590 (230)	250
$[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$	440 br (2200)	720 (320)	620 (200)	280
met-Hc (*Busycon*)[b]	380 (1500) 450 sh (~500)	720 (~200) 870 sh (~160)	680 (~200) 870 sh (~150)	500
met-Hc (*Limulus*)[b]	≤375 (>1500) 500 (~500)	720 (~200)	650 (~200) 900 sh (~100)	10
met-Hc (*Cancer*)[b]	430 (~1500) 520 sh	670 (~200) 820 sh (~100)	635 (~200)	100
met-tyrosinase[c]	360 (2100) 420 sh (1400)	690	680	3000

[a] The intensity is contributed by LMCT from the hydroxo group to Cu(II). [b] Data taken from: Himmelwright, R. S.; Eickman, N. C.; LuBien, C. D.; Solomon, E. I. *J. Am. Chem. Soc.* **1980**, *102*, 5378. [c] Data taken from: Himmelwright, R. S.; Eickman, N. C.; LuBien, C. D.; Lerch, K.; Solomon, E. I. *J. Am. Chem. Soc.* **1980**, *102*, 7339.

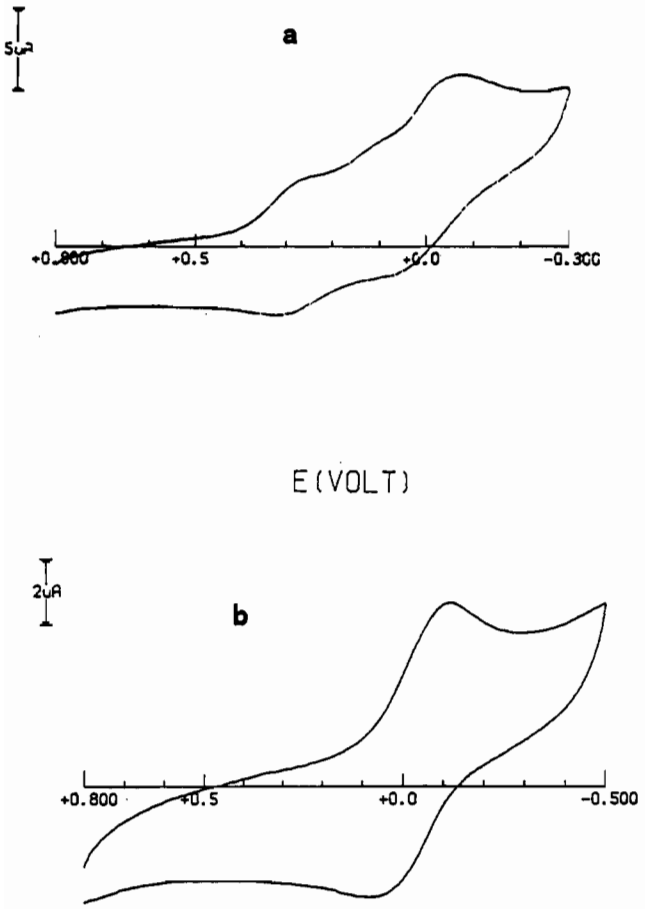


Figure 8. Cyclic voltammograms recorded at a platinum electrode for MeCN solutions containing $[NEt_4][ClO_4]$ (0.1 M) and the following: (a) $[Cu_2(L\text{-}5,5)(N_3)(H_2O)]^{3+}$ (7×10^{-4} M); (b) $[Cu_2(L\text{-}5,5)(N_3)_2]^{2+}$ (8.0×10^{-4} M). Scan rate = 0.2 V s^{-1}.

forms of the proteins. Of particular significance is the strong antiferromagnetic coupling of $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$, where alignment of the copper magnetic orbitals may be realized. Here the tendency of the L-5,5 ligand to impose two rigid coplanar chelate rings on each copper(II) center is clearly important, whereas the higher flexibility of the L-6,6 ligand is more advantageous when oxidative reactivity, and hence redox state changes between Cu(I) and Cu(II), is involved. Also, the LMCT features of the azide adducts bear resemblance to those of the protein derivatives (Table I), which also contain a second "endogenous" bridge.[29] In particular, the spectra of the L-5,5 systems, for both the aquo and the hydroxo derivatives, where the azide bridges in the μ-1,1 mode, are similar to those of met-azide *Busycon*-Hc, met-azide *Limulus*-Hc, and met-azide tyrosinase, while those of the L-6,6 systems, where azide binds in the μ-1,3 mode, are similar to that of met-azide *Cancer*-Hc. These findings contrast with the current view[22] on the formation of μ-1,3 azide bridges by the proteins, but it is worth emphasizing that there are still inconsistencies in the interpretation of the protein spectroscopic data. The affinity of azide for the various dicopper(II) complexes merits a final comment. The binding constants confirm that hydroxo bridges must be present in the met-protein sites; the rather high value of K found for met-tyrosinase probably results from a low-polarity environment of the Cu_2 core in the active site.

Acknowledgment. This work was supported by a grant from the Italian MPI.

Supplementary Material Available: Figures and captions for the spectrophotometric titration of $[Cu_2(L\text{-}5,5)(N_3)_2]^{2+}$ (Figure S1) and $[Cu_2(L\text{-}6,6)(N_3)_2]^{2+}$ (Figure S2) with sodium azide and the cyclic voltammetry of $[Cu_2(L\text{-}6,6)(H_2O)_2]^{4+}$ and $[Cu_2(L\text{-}6,6)(OH)_2]^{2+}$ (Figure S3) and of $[Cu_2(L\text{-}5,5)(H_2O)_2]^{4+}$ and $[Cu_2(L\text{-}5,5)(OH)_2]^{2+}$ (Figure S4) (6 pages). Ordering information is given on any current masthead page.

(29) Wilcox, D. E.; Long, J. R.; Solomon, E. I. *J. Am. Chem. Soc.* **1984**, *106*, 2186.