Polynuclear Complexes of Copper(I) and the 2-(3(5)-Pyrazolyl)-6-methylpyridine Ligand: Structures and Reactivity toward Small Molecules

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The reactivity of trinuclear copper(I) centers vis-à-vis diagnostic diatomic and other small molecules, including carbon monoxide and dioxygen, is examined as part of an effort to unravel the pattern of dioxygen activation at multiscopic sites of potential biological significance. The reaction of [Cu(CH3CN)4][PF6] with deprotonated 2-(3(5)-pyrazolyl)-6-methylpyridine (2-(3(5)-pz,6-Mepy), 1) affords the trinuclear copper(I) compound [Cu3-py(2-(3(5)-pz,6-Mepy))3]0.5py (2) from pyridine solutions. Species 2 rearranges in toluene to yield a tetrameric unit that precipitates as the molecular pair [Cu2(2-(3(5)-pz,6-Mepy)])2·3tol (3). The two units are symmetry-related by virtue of a C2 axis and are coupled via a unique Cu(I)...Cu(I) contact at 3.0405(13) Å. Compound 2 or 3 reacts with carbon monoxide to generate reversibly the trinuclear species [Cu(CO)(2-(3(5)-pz,6-Mepy)])3 (4), featuring coordination of one CO molecule per copper ion on the same face of a nine-membered Cu6N6 ring framework. Compound 2 reacts with dioxygen in tetrahydrofuran to yield the dinuclear species [Cu2(2-(3(5)-pz,6-Mepy)]2·thf (5) and an as yet uncharacterized green-brown crystalline material. In the presence of the hexafluorophosphate anion (PF6−) in CH3CN, the reaction with dioxygen affords the tetranuclear compound [Cu4(2-(3(5)-pz,6-Mepy)]2(CH3CN)2(3)[PF6]2·CH3CN (6). An analogous dinuclear species, [Cu2(2-(3(5)-pz,6-Mepy)](MeOH)2(CF3SO3)2 (7), is formed in wet methanol from Cu(CF3SO3)2 and the deprotonated ligand 1. The nuclearity of the resulting species upon dioxygen activation and the fact that no compounds are observed containing the Cu5(μ3-O(H)) unit are discussed.

Introduction

A remarkable series of multicopper-containing oxygenases and oxidases have been intensively studied in recent years to reveal synergism between two or more copper sites in the activation of dioxygen.1 An important subset of this category is composed of copper enzymes that have a minimum requirement of one trinuclear copper cluster participating in their dioxygen activating apparatus. Well-characterized members of this group are the oxidases laccase,2 ceruloplasmin,3 and ascorbate oxidase,4 all of which couple the four-electron reduction of dioxygen to the one-electron-at-a-time oxidation of 4 equiv of substrate. The electron-transfer cycle is conveniently mediated by four copper sites which apparently store oxidizing power upon complete reduction of dioxygen to water prior to delivering oxidizing equivalents to substrate in a sequential manner. As indicated by the crystallographic determination of ascorbate oxidase,3 three of these copper ions are intimately engaged in a cluster arrangement considered to be the site of dioxygen reduction. The fourth copper ion is a distinct type-1 (or “blue”) copper center that most likely contributes to the overall stoichiometry by long-range (~12.5 Å in ascorbate oxidase)5 electron transfer to the trinuclear cluster. Interestingly, human ceruloplasmin, which has been recently characterized crystallographically at a 3.1-Å resolution,3 features two additional type-1 copper sites. Typically, the trinuclear cluster of these oxidases includes a “normal”, type-2 copper site in close proximity (~3.7 Å in oxidized ascorbate oxidase)4 to an antiferromagnetically coupled, type-3 binuclear copper center.

Trinuclear copper clusters functioning in the oxygenase mode have not been unambiguously characterized, but a prominent example, which is a source of inspiration for the present work, is the putative tricopper center of particulate methane monoxygenase (pMMO).5 By virtue of quantitative EPR and magnetic data, a ferromagnetically coupled (S = 5/2) trinuclear copper cluster has been proposed to exist in “as isolated” and ferricyanide-oxidized preparations of pMMO. Interestingly, an unusually high copper content (~70%) remains at the Cu(I) level in “as isolated” pMMO or even after extensive dioxygen treatment of dithionite-reduced preparations of pMMO (40–

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5 (3) Zaitseva, I.; Zaitsev, V.; Card, G.; Moskov, K.; Bax, B.; Ralph, A.; Lindley, P. JBC. 1996, 1, 15.
50%). This finding calls into question the stoichiometry of the Cu/3O interaction, but without a clear knowledge of the number of copper sites that act as electron-transfer rather than catalytic centers, the issue cannot be easily resolved. If the trinuclear copper hypothesis holds (especially with respect to an alternative dinuclear copper–iron model proposed and to recent reexamination of the type of copper involved by low-frequency EPR), then the electronic and potentially geometric features of this cluster would be intrinsically different from those attributed to the coupled type-2/type-3 tricopper cluster found in the oxidases. In passing, we note that copper-containing ammonia monoxygenase, which shows extensive sequence homology with pMMO and similar chemical behavior vis-à-vis substrates and inhibitors,11 may be another good candidate for possessing an analogous copper cluster.

To systematically investigate the reactivity of reduced Cu3 cores with respect to dioxygen and other small, diagnostic molecules, we have initiated a study to explore pathways of generating trinuclear copper sites by employing a class of ligands derived from the parent 2-(3(5)-pyrazolyl)pyridine (2-(3(5)-pyzH)py) structure. Reported in the present work is exploitation of one member of this group, namely, the pyridine-substituted 2-(3(5)-pyzH),6-Mepy ligand. These nitrogen-rich ligands are attractive both by virtue of their pyrazolyl moiety, which has been known to stabilize multinuclear Cu3(pz)n (n = 3, 4) clusters, and by their ability to impose planar copper coordination that may facilitate generation of the Cu3(tris-O(H)) core structures upon oxidation. The latter unit has been observed in a number of complexes and reported to display primarily antiferromagnetic coupling, although in rare cases population of the $S = \frac{3}{2}$ level has been noted.

**Experimental Section**

**General Considerations.** All operations were performed under a pure dinitrogen or argon atmosphere using Schlenk techniques on an inert gas/vacuum manifold or in a drybox (O2, H2O < 1 ppm). Hexane, petroleum ether, and toluene were distilled over Na; THF and diethyl ether were distilled over Na2P2O5. Acetonitrile and methylene chloride were distilled over CaH2. Ethanol and methanol were distilled over Na; petroleum ether, and toluene were distilled over Na2; THF and diethyl ether were distilled over CaH2. Solutions at a flow rate of 5 ml/min from a syringe pump (Harvard Apparatus). The electrospray probe capillary was maintained at a potential of 3.0 kV, and the orifice to skimmer potential (“cone voltage”) was varied from 15 to 30 V. Spectra were collected in the multichannel acquisition mode. EI and CI mass spectra were obtained on a Finnigan MAT-90 mass spectrometer. Microanalyses were done by H. Kolbe, Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany.

**Preparation of 2-(3(5)-pyrazolyl)-6-methylpyridine (1).** Synthesis of the ligand involved five steps, starting from commercially available 2,6-dimethyl pyridine (2,6-lutidine). 2,6-Lutidine was first oxidized to 6-methyl-2-picolinic acid (49%) by the method of Black et al. The acid thus obtained was converted to ethyl 6-methyl-2-picolinate (37%) and subsequently to 2-acetyl-6-methylpyridine (69%) by a standard procedure. 2-Acetyl-6-methylpyridine was then treated with N,N-dimethylformamide diethyl acetal in a ratio of 1:1.3, and the mixture was refluxed for 12 h to yield 3-(dimethylamino)-1-(6-methylpyridyl)-2-propan-1-one (80%) after solvent removal and recrystallization from ethanol. This product was then treated with hydrazine monohydrate (ratio 1:1.3) in methanol, and the mixture was refluxed for 1 h. The solvent was removed under reduced pressure and the residue sublimed at 80–90 °C (0.001 Torr) to afford ligand (95%). Mp: 118 °C.

**NMR spectra** were recorded on Varian XL-400 and JEOL GSX-270 NMR spectrometers. Peaks were assigned on the basis of chemical shift, integration, and coupling patterns in 2D NMR (1H observed/13C (de)-coupled) and APT spectra. IR spectra were recorded on a Perkin-Elmer 1800 FT-IR instrument. UV–vis spectra were obtained on a Hewlett-Packard 8452A diode array spectrophotometer. Electrospray mass spectra were recorded using a Platform II MS (Micromass Instruments, Danvers, MA). Samples were introduced from the corresponding solutions at a flow rate of 5 μL/min from a syringe pump (Harvard Apparatus).

(3) Cu[pz(py)-2-(3(5)-pyrazolyl)-6-methylpyridine]2·3H2O (3). Yellow crystals of 3 were obtained by recrystallization of 2 from toluene upon cooling at 10 °C overnight. Mp: 210 °C (dec). 1H NMR (270 MHz, 27 °C, CDCl3): δ 1.81 (br, 3H, CH3), 2.65 (br, 3H, CH3), 6.69 (br, 1H, 4-H(pz)), 6.75 (br, 1H, 4-H(pz)), 6.89 (δ, JH,H = 7.32 Hz, 1H, 5-H(pz)), 7.10 (δ, JH,H = 6.84 Hz, 1H, 5-H(pz)), 7.36 (δ, JH,H = 7.32 Hz, 1H, 5-H(pz)), 7.46 (δ, JH,H = 7.35 Hz, 1H, 3-H(pz)), 7.54–7.68 (m, 2H, 4-H(pz)), 7.64 (br, 1H, 5-H(pz)), 7.18 (3H, 2-CH3) and 7.96 (4H, 2-H(pz)). 13C NMR (270, 1H, 77 MHz, CDCl3): δ 135.8 (d, J = 123.7 Hz, CH3), 146.7 (d, J = 125.7 Hz, CH3), 137.8 (d, J = 126.4 Hz, C=[CH]), 145.5 (s, 3-C(pz)), 149.3 (s, 2-C(pz)), 158.3 (s, 6-C(pz)). CI–HRMS M + H + (calcd for C42H34N8O2): 558.2333. Found: 558.2333.
Table 1. Crystallographic Data for [Cu(CO)(2-(3(5)-pz,6-Mepy)]3 (4). Carbon monoxide was passed for 5 min through a yellow-orange solution of 2 (100 mg, 0.13 mmol) in toluene (20 mL) to generate a light yellow solution. Cooling the CO-saturated solution to 10 °C afforded colorless crystals of 4. Application of reduced pressure to 4 either in the solid state or in solution should be avoided due to loss of coordinated carbon monoxide. 1H NMR (70 MHz, CDCl3): δ 24.7 (br, CH3), 102.0 (4-C(pz)), 117.2 (3-C(pz)), 122.3 (5-C(pz)), 137.7 (4-C(pz)), 142.1 (br, 5-C(pz)), 150.9 (br, 3-C(pz)), 151.6 (2-C(pz)), 157.6 (6-C(pz)). ES-MS (toluene): 886 ([CuL]+), 1207 ([Cu2L2]+), 1488 ([CuL2]+). Anal. Caled for C24H24Cu2F6N6O10S2: C, 54.28; H, 4.32; N, 16.40. Found: C, 54.29; H, 4.35; N, 16.35.

Crystallographic Data for Polynuclear Complexes of Copper(I)

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Crystal structure determinations are deposited as Supporting Information.

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Polynuclear Complexes of Copper(I)

The ligand 2-(3(5)-pzH)₆-Mepy (I) is obtained in a five-step synthetic process (Scheme 1) starting from 2,6-dimethylpyridine. The conversion of this starting material to the intermediate 2-acetyl,6-Mepy is accomplished by following published literature procedures.16,17 The

1. Synthesis of the Ligand. The ligand 2-(3(5)-pzH)₆-Mepy (I) is obtained in a five-step synthetic process (Scheme 1) starting from 2,6-dimethylpyridine. The conversion of this starting material to the intermediate 2-acetyl,6-Mepy is accomplished by following published literature procedures.16,17 The

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3. Characterization of the Complex. The complex 2-(3(5)-pzH)₆-Mepy (I) is characterized by various spectroscopic techniques such as 1H NMR, 13C NMR, and mass spectrometry.16,17 The

4. Electrochemical Studies. The complex 2-(3(5)-pzH)₆-Mepy (I) is studied by cyclic voltammetry and square wave voltammetry in dry DMF containing 0.1 M tetrabutylammonium hexafluorophosphate as the supporting electrolyte.16,17 The

5. Physical Measurements. The complex 2-(3(5)-pzH)₆-Mepy (I) is characterized by powder X-ray diffraction and single crystal X-ray diffraction.16,17 The

6. Biological Activity. The complex 2-(3(5)-pzH)₆-Mepy (I) is tested for its activity against various bacterial and fungal strains.16,17 The

7. Theoretical Studies. The complex 2-(3(5)-pzH)₆-Mepy (I) is studied by density functional theory (DFT) calculations at the B3LYP/6-31G(d,p) level of theory.16,17 The
subsequent two steps, leading to ligand 1, are executed according to methodology implemented in the synthesis\(^{12}\) of the parent compound 2-(3(5)-pzH)py from 2-acetylpyridine. The ligand can be purified by sublimation or recrystallization from hexanes. The solubility of the ligand and its copper complexes in common organic solvents is superior to that observed for the unsubstituted 2-(3(5)-pzH)py and corresponding complexes.

**Synthesis and Characterization of Complexes from Cu(I) Precursor Species.** Reaction of \([\text{Cu(CHCN)}_2][\text{PF}_6]\) with 1 equiv of deprotonated 1 in MeOH/CH\(_3\)CN leads to the formation of a yellow-orange powder, which upon recrystallization from pyridine affords yellow-orange crystals of \([\text{Cu}_3(\text{py})(2-(3(5)-pz,6-Mepy})_3]0.5\text{py}(2)\). The compound is exceedingly air-sensitive, especially in solution (vide infra).

Room-temperature \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra of concentrated solutions of 2 in \(\text{C}_2\text{D}_2\text{N}\) or \(\text{CD}_2\text{Cl}_2\) exhibit one set of ligand resonances, although the methyl resonance in the \(^1\text{H}\) NMR spectrum (\(\delta = 2.53\) (\(\text{C}_2\text{D}_2\text{N}\)), 2.30 (\(\text{CD}_2\text{Cl}_2\))) is particularly broad. Under these conditions, the pyridine solvent appears to be free (noncoordinating) in solution. Variable-temperature \(^1\text{H}\) NMR data reveal a more complex pattern at lower temperatures. Upon cooling (196–296 K) in \(\text{CD}_2\text{Cl}_2\), gradual resolution of three methyl resonances (\(\delta = 2.71, 2.32, 1.75\) (256 K)) is observed, originating from three independent species. The relative amounts of these components vary substantially with temperature, the low-field methyl resonance (\(\delta = 2.65\) (s) at 196 K) dominating at low temperatures. Importantly, the 2.32- and 1.75-ppm resonances split at temperatures below 236 K into patterns composed of three (\(\delta = 2.30, 2.25, 2.22\) at 216 K; relative ratio 3:1:2) and two (\(\delta = 1.71, 1.69\) at 216 K; relative ratio 1:2) bands, respectively. Moreover, resonances assigned to free pyridine at room temperature lose their fine structure upon cooling, indicating coordination of pyridine to copper sites. Tentatively, we assign the aforementioned three features, from low to high field, to \(\text{Cu}_3\text{L}_3\), \(\text{Cu}_2\text{L}_3\), and \(\text{Cu}_3\text{L}_3(\text{py})_3\) (\(n = 1\) or 2) clusters. Electrospray MS data obtained from dilute solutions of 2 in \(\text{CH}_2\text{Cl}_2\) (dilution has an effect similar to cooling) according to \(^1\text{H}\) NMR indicate the presence of, among others, \([\text{Cu}_3\text{L}_3]^{+}\) (665), \([\text{Cu}_2\text{L}_3]^{+}\) or \([\text{Cu}_2\text{L}_3(\text{py})_2]^{+}\) (823), and \([\text{Cu}_3\text{L}_3]^{-}\) or \([\text{Cu}_3\text{L}_3(\text{py})_3])^{-}\) (1267) fragments exhibiting appropriate isotopic patterns. The variable-temperature (240–295 K) \(^1\text{H}\) NMR spectrum of 2 in \(\text{C}_2\text{D}_2\text{N}\) indicates that a new methyl resonance (\(\delta = 1.84\) at 265 K) progressively evolves below 275 K, accompanied by a half-intensity band (\(\delta = 2.79\) at 245 K) that resolves upon further cooling (\(<260\) K). Peaks assigned to pyridine (solvent) are also broadened at lower temperatures. These features are consistent with resolution of the three- and four-coordinate copper environments in emerging 2, although further analysis is precluded by the limits of the available temperature range. However, the single broad methyl resonance observed at room temperature remains the dominant feature in this region of the \(^1\text{H}\) NMR spectrum, sharpening upon cooling in accord with the presence of equivalent copper sites assigned tentatively to \(\text{Cu}_3\text{L}_3\). Electrospray MS data obtained from solutions of 2 in pyridine demonstrate the existence of \([\text{Cu}_3\text{L}_3]^{+}\) (665) and \([\text{Cu}_3\text{L}_3(\text{py})_3])^{-}\) (823) fragments, although higher nuclearity clusters are not observed.

Single-crystal X-ray analysis of 2 reveals a structure (Figure 1) that features an asymmetric trinuclear copper cluster composed of two three-coordinate sites and one unique four-coordinate copper site. The pyrazolyl-bridged copper ions are positioned according to 1 Hz NMR) indicate the presence of, among others, \([\text{Cu}(\text{py})(2-(3(5)-pz,6-Mepy})_3]0.5\text{py}(2)\). The compound is exceedingly air-sensitive, especially in solution (vide infra).

**Scheme 1**

![Scheme 1](Image)

**Figure 1.** Structure of \([\text{Cu}_3(\text{py})(2-(3(5)-pz,6-Mepy})_3]0.5\text{py}(2)\), showing 30% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): \(\text{Cu}(1)–\text{N}(10)\) 1.974(7), \(\text{Cu}(1)–\text{N}(3)\) 1.995(7), \(\text{Cu}(1)–\text{N}(1)\) 2.038(8), \(\text{Cu}(1)–\text{N}(2)\) 2.232(6), \(\text{Cu}(2)–\text{N}(4)\) 1.894(7), \(\text{Cu}(2)–\text{N}(6)\) 1.921(6), \(\text{Cu}(2)–\text{N}(5)\) 2.370(7), \(\text{Cu}(3)–\text{N}(7)\) 1.860(6), \(\text{Cu}(3)–\text{N}(9)\) 1.870(6), \(\text{Cu}(3)–\text{N}(8)\) 2.430(6), \(\text{N}(10)–\text{Cu}(1)–\text{N}(3)\) 116.7(3), \(\text{N}(10)–\text{Cu}(1)–\text{N}(1)\) 119.5(3), \(\text{N}(3)–\text{Cu}(1)–\text{N}(1)\) 116.3(3), \(\text{N}(10)–\text{Cu}(1)–\text{N}(2)\) 106.4(2), \(\text{N}(3)–\text{Cu}(1)–\text{N}(2)\) 78.6(2), \(\text{N}(1)–\text{Cu}(1)–\text{N}(2)\) 110.6(3), \(\text{N}(4)–\text{Cu}(2)–\text{N}(6)\) 160.3(3), \(\text{N}(4)–\text{Cu}(2)–\text{N}(5)\) 121.4(3), \(\text{N}(6)–\text{Cu}(2)–\text{N}(5)\) 76.5(3), \(\text{N}(7)–\text{Cu}(3)–\text{N}(9)\) 161.9(3), \(\text{N}(7)–\text{Cu}(3)–\text{N}(8)\) 122.0(2), \(\text{N}(9)–\text{Cu}(3)–\text{N}(8)\) 75.1(2).

with an in-plane distortion from a T-shaped geometry, as evidenced by the deviation of the N(pz)-Cu-N(pz) angles (average 161.1(8)°) from linearity. For these copper sites the average Cu-N(pz) distance (1.89(4) Å) is shorter than the one observed for the four-coordinate site (1.985(11) Å), reflecting the difference in the coordination number, although, due to the T-shaped geometry, the Cu-N(py) distance (average 2.400(30) Å) is longer by comparison to the corresponding Cu(1)-N(2) distance (2.232(6) Å) of the tetrahedral copper atom.

Recrystallization of 2 from toluene affords yellow plates of \([\text{Cu}_4(2-(3(5)-pz,6-Mepy))_4\]\(_2\)·3tol (3). Rearrangement has also been suggested by virtue of \(^1\)H NMR spectra of 2 in \(\delta_6\)-toluene or CD\(_2\)Cl\(_2\) (27 °C) demonstrating broad bands associated with ligand-based protons, the most discernible feature being two equally populated resonances (\(\delta = 2.65, 1.81\)) assigned to the methyl substituent. Close inspection of the 6.5-8 ppm region reveals that bands assigned to pyridyl/pyrazolyl moieties are also split in appropriate patterns of equal intensity. Variable-temperature \(^1\)H NMR data in CD\(_2\)Cl\(_2\) suggest that both methyl resonances partly resolve in two closely spaced components.

The structure of 3 (Figure 2) reveals an unusual molecular pair composed of two tetranuclear copper units coupled via a unique Cu-Cu interaction (Cu(1)-Cu(1′) = 3.0045(13) Å). The two units are symmetry-related by virtue of a crystallographically imposed \(C_2\) axis. The tetranuclear Cu(pz)\(_4\) core structure is composed of a 12-membered atom ring (Cu(N)\(_9\)) which folds into a trapezoidal or saddle-type conformation. The mean deviation from a least-squares plane defined by the tetrametallic core is 0.119 Å, although the square is somewhat puckered, such that Cu(1) and Cu(3) are 0.12 Å above the plane, while Cu(2) and Cu(4) are 0.12 Å below the plane. The average intermetallic Cu-Cu distance is 3.58(12) Å, a value that precludes any Cu-Cu interactions. A somewhat similar arrangement is found in the tetrameric \([\text{Cu}_4(3,5-	ext{Ph}_2\text{pz})]_4\) compound\(^{13b}\) that features a strictly planar tetracopper core structure. In this compound, the exclusively two-coordinate copper sites are most likely further stabilized by Cu-Cu interactions (average distance 3.12 Å). In contrast, the coordination sphere of the copper ions in 3 is highly variable, with two copper atoms being three-coordinate and the other two being four- and two-coordinate. As in the case of 2, the three-coordinate copper sites in 3 show an in-plane distorted T-shaped coordination geometry (N(4)-Cu(3)-N(8) = 167.4(2)°, N(7)-Cu(4)-N(11) = 164.2(2)°). The two coordination planes are oriented in a mutually orthogonal fashion. The four-coordinate copper center displays a distorted \(C_2\)_\(_v\)_-type geometry involving a Cu(pz)\(_2\)N(py)\(_2\) local environment. This unusual “sesaw” configuration accommodates two planar T-shaped coordination geometries which are orthogonal with respect to each other but are otherwise similarly distorted (N(5)-Cu(2)-N(6) = 76.8(2)°, N(2)-Cu(2)-N(3) = 78.3(2)°). The preference for the N(3) atom of the pyridyl moiety to associate with Cu(2) rather than Cu(1), thus interrupting a potentially symmetric coordination, may be partially assigned to stabilization achieved due to the Cu(1)-Cu(1′) contact.

![Figure 2. Structure of the tetranuclear \([\text{Cu}_4(2-(3(5)-pz,6-Mepy))_4\]\(_2\)·3tol unit (top) and the molecular pair \([\text{Cu}_4(2-(3(5)-pz,6-Mepy))_4\] unit (bottom) in 3, showing 30% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): Cu(1)-N(1) 1.857(4), Cu(1)-N(10) 1.859(4), Cu(2)-N(5) 1.904(4), Cu(2)-N(2) 1.913(4), Cu(2)-N(3) 2.307(4), Cu(2)-N(6) 2.366(4), Cu(3)-N(4) 1.878(4), Cu(3)-N(8) 1.886(4), Cu(4)-N(7) 1.800(4), Cu(4)-N(11) 1.899(4). Cu(4)-N(12) 2.297(5), N(1)-Cu(1)-N(10) 174.1-2(2), N(1)-Cu(1)-Cu(1′) 93.43(13), N(10)-Cu(1)-Cu(1′) 92.41(13), N(5)-Cu(2)-N(2) 160.4(2), N(5)-Cu(2)-N(3) 116.6(2), N(2)-Cu(2)-N(3) 78.3(2), N(5)-Cu(2)-N(6) 76.8(2), N(2)-Cu(2)-N(6) 118.3(2), N(3)-Cu(2)-N(6) 87.4(2), N(4)-Cu(3)-N(8) 167.4(2), N(4)-Cu(3)-N(9) 115.9(2), N(8)-Cu(3)-N(9) 76.3(2), N(7)-Cu(4)-N(11) 164.2(2), N(7)-Cu(4)-N(12) 117.2(2), N(11)-Cu(4)-N(12) 78.5(2).](image-url)

The reactivity of compounds 2 and 3 has been tested with a variety of small molecules. The side-on approaching dihydrogen, ethylene, and 2-butyne have shown no signs of reactivity vis-à-vis these complexes. In contrast, the potentially end-on oriented carbon monoxide and dioxygen react readily with the Cu(I) compounds, even at low temperatures. These reactions are described in the present section.
Figure 3. Structure of [Cu(CO)(2-(3(5)-pz,6-Mepy)] (4), showing 50% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): Cu(1)–C(1) 1.779(5), Cu(1)–N(2) 2.019(3), Cu(1)–N(6) 2.014(3), Cu(1)–O(1) 1.128(5), Cu(2)–C(2) 1.778(4), Cu(2)–N(5) 2.007(3), Cu(2)–N(9) 2.003(3), Cu(2)–N(4) 2.104(3), Cl(2)–O(2) 1.171(5), Cl(3)–C(3) 1.778(5), Cu(3)–N(3) 1.994(3), Cu(3)–N(8) 2.005(3), Cu(3)–N(7) 2.130(3), C(3)–O(3) 1.128(5), Cl(1)–Cu(1)–N(2) 121.2(2), Cl(1)–Cu(1)–N(1) 128.3(2), O(1)–C(1)–Cu(1) 172.8(4), C(2)–Cu(2)–N(5) 120.7(2), C(2)–Cu(2)–N(9) 121.4(2), C(2)–Cu(2)–N(4) 119.4(2), C(2)–C(2)–Cu(2) 177.6(5), C(3)–Cu(3)–N(3) 120.2(2), C(3)–Cu(3)–N(8) 126.3(2), C(3)–Cu(3)–N(7) 120.2(2), O(3)–C(3)–Cu(3) 176.6(5).

(a) Carbon Monoxide. Bubbling CO through a yellow-orange solution of 2 in toluene under ambient conditions leads to a light yellow solution from which colorless crystals of the air-sensitive [Cu(CO)(2-(3(5)-pz,6-Mepy)] (4) slowly precipitate. Applying reduced pressure to solutions of 4 or solid 4 results in immediate restoration of the original yellow-orange coloration, suggesting reversible CO binding.1 H and 13C NMR results in immediate restoration of the original yellow-orange state. Applying reduced pressure to solutions of 1 (Figure 3) reveals a trinuclear copper compound, which is residing on an inversion center, is composed of two symmetry-related dicopper units arranged in a manner similar to that found in compound 5. However, the coordination sphere of each copper site is now completed by a different set of ligand-derived resonances. In the case of Cu(1), chelation of a ligand bridging between the two dicopper units generates a distorted square pyramidal geometry with vector Cu(1)–N(6) 1.124(7) Å.)

Figure 4. Structure of [Cu4(2-(3(5)-pz,6-Mepy)] (5), showing 30% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): Cu–N(5) 1.940(6), Cu–N(2) 1.951(6), Cu–N(1′) 2.033(6), Cu–N(3) 2.210(6), Cu–N(6) 2.287(6), N(5)–Cu–N(2) 170.5(2), N(5)–Cu–N(1′) 89.6(2), N(2)–Cu–N(1′) 92.0(2), N(5)–Cu–N(3) 95.6(2), N(2)–Cu–N(3) 79.3(2), N(1′)–Cu–N(5) 156.5(2), N(5)–Cu–N(6) 78.6(2), N(2)–Cu–N(6) 109.9(2), N(1′)–Cu–N(6) 106.2(2), N(3)–Cu–N(6) 97.3(2).

(b) Dioxygen. Bubbling dioxygen through solutions of 2 in tetrahydrofuran under ambient conditions results in an immediate change of the solution color from yellow-orange to brown-green. Crystallization affords green blocks of paramagnetic [Cu4(2-(3(5)-pz,6-Mepy)] (5) followed by deposition of dichroic green-brown crystals. The latter material cannot be easily separated from 5 by fractional crystallization, thus hampering efforts to characterize this compound. In addition, its crystals are unsuitable for X-ray analysis.

The structure of 5 (Figure 4) reveals a dinuclear copper species residing on a C2 rotational axis. The two five-coordinate copper centers display a distorted square pyramidal geometry. They are bridged by two symmetry-related pyrazolyl moieties in the usual μ-1,2 coordination mode to generate a quasi-planar CuL2 arrangement, while each copper site is further chelated by a perpendicularly oriented ligand that surprisingly remains uncoordinated at the distal pyrazolyl nitrogen atom N(4). It is unlikely that this nitrogen is protonated, since that would reduce the formal oxidation state of the metal to Cu(1), an assignment which is not supported by the paramagnetism, color, coordination number, and Cu–N bond distances demonstrated by the present compound.

In the presence of hexafluorophosphate as a potential counteranion, solutions of [Cu(CH3CN)4][PF6] and deprotonated ligand 1 in MeCN/MeOH which have been exposed to dioxygen afford green crystals of [Cu4(2-(3(5)-pz,6-Mepy)] (6) (PF6)2(CH3CN) (6).

The structure of 6 (Figure 5) reveals that the tetranuclear compound, which is residing on an inversion center, is composed of two symmetry-related dinuclear copper units that are facially bound to each other via two pyrazolyl-derived bridges. Each dicopper unit features an asymmetric pair of five-coordinate copper ions. These copper sites are bridged in an almost planar fashion by two ligand-derived moieties arranged in a manner similar to that found in compound 5. However, the coordination sphere of each copper site is now completed by a different set of contributing residues. In the case of Cu(1), chelation of a ligand bridging between the two dicopper units generates a distorted square pyramidal geometry with vector Cu(1)–N(6) 1.124(7) Å.)
metal for the complete reduction of dioxygen to water. Further, the fact that a Cu₃O unit has not been observed in any of the present structures suggests that a strict requirement for fitting an sp²-hybridized oxo group in the trinuclear copper cavity may be the planar arrangement of the molecular framework. This is clearly unattainable with the present methyl-substituted ligand but may be feasible with the parent nonsubstituted ligand or 4-R-pyridyl substituted derivatives thereof. The stability of the Cu₃O unit may be of importance, especially if switching from a 4:1 to a 6:1 Cu₂O₂ interaction is desirable in order to activate dioxygen between two trinuclear copper clusters which retain their integrity. In addition, the 6:1 stoichiometry circumvents the need for generating a high-valent copper-oxo unit upon dioxygen cleavage, which otherwise will be required in a 3:1 stoichiometric ratio, as witnessed in a recently reported case. Whether a copper(III)-oxo moiety is needed for oxygenation purposes in a biological setting is a point of current debate.

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Supporting Information Available: Variable-temperature ¹H NMR spectra of 2 in Cd₂N₂ and CdCl₂; and tables containing Listings of crystal and data collection parameters, atomic coordinates and isotropic thermal parameters, interatomic distances, bond angles, and anisotropic displacement parameters for complexes 2 and 7 (26 pages). X-ray crystallographic files in CIF format for the structure determinations of complexes 3, 4, 5, and 6 are available on the Internet only.

Conclusions

Although the goal of retaining the trinuclear integrity of the copper species upon dioxygen activation has not been realized with the present ligand, some useful conclusions can be drawn from the reported results. First, the overwhelming tendency to form dinuclear or tetranuclear structures most likely arises from the requirement of four copper sites to deliver one electron per

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Figure 5. Structure of [Cu₄(2-(3(5)-pz,6-Mepy)(CH₃CN)₂](PF₆)₂ (5), showing 30% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): Cu(1)−N(5) 1.945(7), Cu(1)−N(7) 1.949(7), Cu(1)−N(8) 1.965(7), Cu(2)−N(9) 2.059(7), Cu(2)−N(4′) 2.063(7), Cu(2)−N(10) 2.222(8), N(5)−Cu(1)−N(2) 167.8(3), N(7)−Cu(1)−N(3) 175.0(3), N(5)−Cu(1)−N(7) 88.8(3), N(5)−Cu(1)−N(6) 77.4(3), N(3)−Cu(1)−N(6) 89.7(3), N(1)−Cu(2)−N(9) 172.3(3), N(1)−Cu(2)−N(10) 85.5(3), N(8)−Cu(2)−N(10) 120.0(3), N(4′)−Cu(2)−N(10) 114.6(3), N(8)−Cu(2)−N(4′) 125.1(3).

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Figure 6. Structure of [Cu₃(2-(3(5)-pz,6-Mepy)(MeOH)₂](CF₃SO₃)₂ (7), showing 30% probability ellipsoids and the atom-labeling scheme. Selected interatomic distances (Å) and angles (deg): Cu−N(1) 2.018(3), Cu−N(2) 1.987(3), Cu−N(3) 1.933(3), Cu−O(1) 2.166(2), Cu−O(2) 2.129(2), N(3′)−Cu−N(2) 99.32(10), N(3′)−Cu−N(1) 179.29(9), N(2)−Cu−N(1) 81.35(10), N(3)−Cu−O(2) 89.48(11), N(2)−Cu−O(2) 121.36(11), N(1)−Cu−O(2) 89.98(10), N(3′)−Cu−O(1) 86.79(10), N(2)−Cu−O(1) 114.81(11), N(1)−Cu−O(1) 93.13(10), O(2)−Cu−O(1) 123.55(11).

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