

Copper–Dioxygen Reactivity Using Dinucleating Ligands with Activated Methylene or Ketone Function

Dong-Heon Lee,*[1] Narasimha N. Murthy,[2] and Kenneth D. Karlin*[3]

[1]Department of Chemistry, Chonbuk National University, Jeonju 561-756, Korea

[2]Department of Chemistry, IIT Madras, Madras 600036, India

[3]Department of Chemistry, The Johns Hopkins University, Charles and 34th Streets, Baltimore, MD 21218, U.S.A.

Received September 11, 2006; E-mail: karlin@jhu.edu

Copper(I)–dioxygen reactivity studies utilizing new binucleating ligands are described. When catalytic quantities of either Cu^{I} or Cu^{II} salts were introduced to $\mathbf{LH_2}$, which is a dinucleating ligand with two tridentate donors connected via a methylene group at a bis(2-pyridyl)methane junction, dioxygen addition caused complete oxygenation to give bis(2-pyridyl)ketone product **L=O**. Isolated dicopper(I) complex $[Cu^{I}_2(\mathbf{LH_2})]^{2+}$ (**1**) also reacted with excess O_2 to give **L=O**. Additional observations were consistent with a mechanism that does not involve "oxygen-activation" in this process. Ketone hydration and *gem*-diol(ate) copper(II)-coordination occurred by addition of copper(II)–perchlorate to **L=O**, giving $[Cu^{II}_2\{\mathbf{L(OH)(O^-)}\}Cu_2{}^{II}(^-OClO_3)]^{2+}$ (**4**), with a bridging alkoxide moiety (X-ray). Oxygenation of $[Cu^{I}_2(\mathbf{L=O})(CH_3CN)_2]^{2+}$ (**2**) (**2**/O_2 = 0.5, i.e., Cu/O_2 = 4:1 manometry), gave $[Cu^{II}_2\{\mathbf{L(O^-)_2}\}(^-OClO_3)]^{+}$ (**5**), where both oxygen atoms of the doubly deprotonated *gem*-diolate bind separate copper(II) ions; mass spectrometric data showed that one of the two oxygen atoms of the *gem*-diolate $\mathbf{L(O^-)_2}$ came from O_2. An oxo–dicopper(II) species is suggested as an important intermediate, which is supported by the observation that reaction of **2** with NO or iodosylbenzene also produced **5** in high yields. Complexes **4** and **5** are acid–base conjugate pairs and can be readily interconverted using Et_3N or $HClO_{4(aq)}$ reagents.

Investigations of copper(I)–O_2 interactions[1–3] are of interest because they can provide insights into the copper–oxidase or oxygenase enzyme,[4–7] active-site structure, spectroscopy, the nature of reactive intermediates, and oxidative mechanisms. The potential for the future development of catalysts or reagents for oxidative transformations is also apparent. The use of binucleating ligands in such studies[1–3,8] is relevant due to the presence of dicopper centers in copper proteins, such as hemocyanin (O_2-transport in mollusks and arthropods),[4,9,10] the monooxygenase tyrosinase (phenol → *o*-quinone),[4,11] and the enzyme catechol oxidase (*o*-catechol → *o*-quinone).[12]

One approach we have utilized in studying biologically relevant copper–dioxygen chemistry has been to design, synthesize and investigate the dicopper chemistry employing binucleating ligands which internally already possess moieties which may act as oxidizable substrates. One example is the monooxygenase model systems, in which two bis[2-(2-pyridyl)-ethyl]amine (PY2) moieties are linked by a xylyl group.[13–18] In such systems, it has been demonstrated that two three-coordinate copper(I) moieties in close proximity react (reversibly) with O_2 to give a side-on μ-η^2:η^2-peroxo–dicopper(II) adduct, which subsequently reacts (as an electrophile) with the xylyl linker to give a hydroxylated product.[14] Analogues of this xylyl system have also been studied.[2,13] Another approach used by several groups,[1,2] especially Itoh et al.[19,20] and Réglier et al.,[21,22] has been to utilize related pyridine–alkylamine ligands with internal benzylic potential substrates, in modeling the monooxygenase reaction observed for dopamine β-monooxygenase.[6] The side-on dioxygen bound μ-η^2:η^2-peroxo–dicopper(II) moiety, or bis-μ-oxo–dicopper(III) species derived or in equilibrium with it,[2,3,23,24] is thought to be the relevant oxidant species.

In this report, we describe the chemistry involving either active methylene or ketonic groups as potential internal substrates within dinucleating ligands. The focus will be on ligands $\mathbf{LH_2}$ and **L=O**, where two unsymmetrical tridentate ligand are connected by a methylene or ketone group, respectively (Chart 1). The particular tridentate groups in $\mathbf{LH_2}$ and **L=O** were chosen for their ease of synthesis and analogy to the PY2 moieties used in the xylyl ligands (vide supra) and other methylene chain linked PY2 dinucleating ligands (Nn), of which dicopper(I) complexes $[Cu^{I}_2(Nn)]^{2+}$ reversibly form O_2-adducts.[3,25,26] In $\mathbf{DH_2}$ and **D=O**, tetradentate moieties are also linked by a methylene or ketone function (Chart 1); we have separately extensively investigated the copper(I)/O_2 reversible dioxygen binding chemistry of tris[2-pyridylmethyl]-amine (TMPA), as well as a variety of analogues.[13,27–29]

In addition to ligand synthetic procedures, we describe the catalytic oxygenation of the methylene groups in $\mathbf{LH_2}$ and $\mathbf{DH_2}$ using copper(I) and copper(II), which affords **L=O** or **D=O**, respectively. In particular, the subsequent use of **L=O** as a copper ion dinucleating ligand is detailed. Copper(II) salts reacted with **L=O** and its ketone group, affording an alcohol-μ-alkoxide dicopper(II) product, $[Cu^{II}_2\{\mathbf{L(OH)(O^-)}\}Cu_2{}^{II}(^-OClO_3)]^{2+}$ (**4**). This is related by acid–base chemistry to the product of oxygenation of a dicopper(I) complex of **L=O**, $[Cu^{I}_2(\mathbf{L=O})(CH_3CN)_2]^{2+}$ (**2**), which affords the *gem*-diolate $[Cu^{II}_2\{\mathbf{L(O^-)_2}\}(^-OClO_3)]^{+}$ (**5**). In reactions of **2** with nitro-

Published on the web April 13, 2007; doi:10.1246/bcsj.80.732

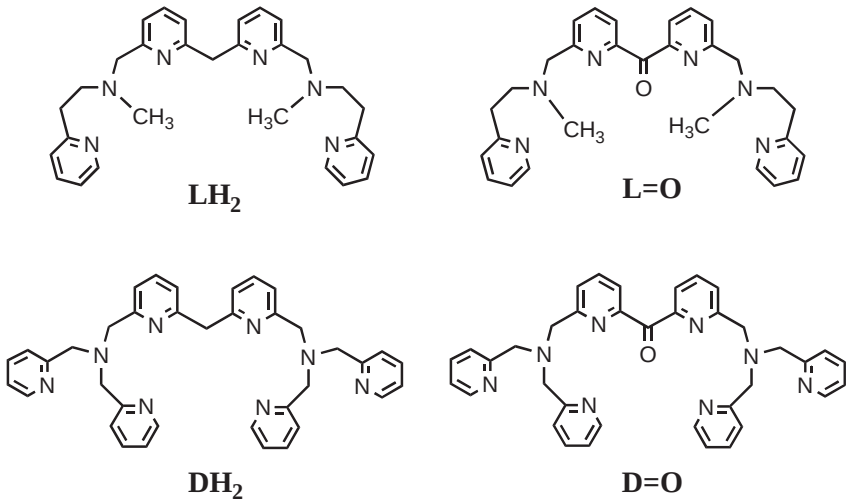


Chart 1.

gen monooxide or iodosylbenzene, the same product was observed, and the relevance of these findings is described. A preliminary report on some aspects of the work has appeared.[30]

Experimental

Warning. Although we experienced no difficulties with the perchlorate complexes described, these should be regarded as potentially explosive and handled accordingly.

Materials and Methods. Reagents and solvents used were of commercially available reagent grade quality unless otherwise stated. Dioxygen (O_2) gas was dried by passing through a short column of supported P_4O_{10} (Aquasorb, Mallinkrodt). Nitric oxide was purified by passing it through a copper coil tube immersed in an acetone–liquid nitrogen bath. Acetonitrile was stirred over CaH_2 and then freshly distilled from CaH_2 under argon. Anhydrous diethyl ether was distilled from sodium/benzophenone under argon or freshly dried by passing it through a 50 cm long column of activated alumina.

All air-sensitive copper complexes were prepared and handled under an argon atmosphere using standard Schlenk techniques. Solvents and solutions were deoxygenated by bubbling argon (20–30 min) directly through the solution. Solid samples were stored and transferred, and samples for NMR and IR spectra were prepared in a Vacuum/Atmospheres dry box filled with argon.

Elemental analysis were performed by Desert Analytics, Tucson, AZ and/or National Chemical Consulting Inc., Tenafly, NJ. Electro ionization and chemical ionization mass spectra were obtained on a double-focusing Vacuum Generator 70-S (VG-70S) gas chromatography/mass spectrometer. Electrospray ionization mass spectrometry experiments were performed at the University of Texas Health Science Center at San Antonio. Infrared (IR) spectra were recorded neat or in Nujol mulls on a Mattson Galaxy 4030 FT-IR spectrometer. ^{1}H NMR spectra were obtained in $CDCl_3$, CD_3CN, or CD_3NO_2 on a Bruker (300 MHz) spectrometer. All spectra were recorded in 5 mm-o.d. NMR tubes. Chemical shifts were reported as δ values downfield from an internal standard of Me_4Si. X-band EPR measurements were taken using a Varian E-4 spectrometer equipped with a liquid nitrogen Dewer insert. The field was calibrated with a powder sample of diphenylpicrylhydrazyl (DPPH; $g = 2.0037$). Frozen DMF solutions of the copper complexes at $\approx 10^{-3}$ M in 4 mm o.d. quartz tubes were used. The signal obtained was roughly integrated by comparing the intensity observed ($I = h_{1/2}(w_{1/2h})^2$) with that of a known concentration of $[Cu^{II}(tepa)(Cl)](PF_6)$ (tepa = tris[2-(2-pyridyl)-ethyl]amine)[31] in DMF. Electronic absorption spectra were acquired on a Shimadzu UV-160 UV–vis using quartz cuvettes (1 cm). Room temperature magnetic susceptibility was recorded with a Johnson Mathey magnetometer, which was calibrated with $Hg[Co(SCN)_4]$. Measurements of the solution state magnetic moment at room temperature were performed according to the Evans method[32] using coaxial NMR tubes and nitromethane-d_3 or acetonitrile-d_3 as a solvent. Diamagnetic corrections were calculated from tabulated values of Pascal's Constants.[33] Gas chromatography was carried out on a Hewlett-Packard 5890 gas chromatograph. For determination of N_2O gas, a stainless steel column (12 ft × 1/8 inch) packed with Porapak Q (80/100) was used with a thermal conductivity detector. A small precolumn filled with silica and glass wool was fitted along with the stainless steel column. Helium and hydrogen were used as carrier and reference gases respectively. Quantitative measurement of the uptake of O_2 at 0 °C and constant pressure (1 atm) for the catalytic oxidation of **LH$_2$** with $[Cu^I(CH_3CN)_4](PF_6)$ was carried out with a gas burette system as previously described.[34]

Synthesis of Ligands. Bis(6-methyl-2-pyridyl)methanone and Bis[6-(bromomethyl)-2-pyridyl]methanone:[35] These compounds were synthesized by a literature method.

L=O: To a solution of bis[6-(bromomethyl)-2-pyridyl]methanone (1.1 g, 2.96 mmol) in 30 mL of tetrahydrofuran (THF) was added 2-(2-methylaminoethyl)pyridine (1.18 g, 5.92 mmol) in 5 mL of THF dropwise at 0 °C with stirring. To this mixture was then added diisopropylethylamine ((*i*Pr)$_2$EtN) (2.29 g, 17.7 mmol). Stirring at room temperature for 2 days gave a white precipitate, and the color of the solution changed to yellowish brown. Filtration and concentration in vacuo gave a brown oil, which was chromatographed on alumina with a 97/3 (v/v) mixture of ethyl acetate/MeOH ($R_f = 0.35$). The purified ligand was obtained as a brown oil in 70% yield (0.99 g). ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6H), 2.87 (t, 4H, $J = 6.9$ Hz), 3.02 (t, 4H, $J = 6.9$ Hz), 3.78 (s, 4H), 7.14 (m, 4H), 7.48 (d, 2H, $J = 4.8$ Hz), 7.58 (m, 2H), 7.72 (t, 2H, $J = 7.4$ Hz), 7.93 (d, 2H, $J = 7.4$ Hz), 8.5 (d, 2H, $J = 4.8$ Hz). IR (neat, cm^{-1}) 2953–2795 (C–H), 1686 (vs, C=O), 1591 (vs, C=C). Mass spectrum (CI) (m/z) 481 $(M + 1)^+$.

LH(OH): L=O (6.0 g, 12.5 mmol) in ethanol (100 mL) was stirred with 20 mL of 20% aqueous NaOH solution and zinc dust

(16.3 g, 250 mmol) under reflux for 12 h. The reaction mixture was cooled to room temperature and filtered, and after removal of the ethanol, the filtrate was extracted with CH_2Cl_2 (50 mL) twice. The organic extract was washed with water (100 mL), dried over anhydrous $MgSO_4$, and concentrated to give **LH(OH)** (5.2 g, 86% yield), which was used directly in the next step without further purification. ^{1}H NMR ($CDCl_3$) δ 2.56 (s, 6H), 2.87 (t, 4H, $J = 6.9$ Hz), 3.03 (t, 4H, $J = 6.9$ Hz), 3.78 (s, 4H), 5.86 (s, 1H), 6.15 (s, 1H), 7.10–7.19 (m, 6H), 7.35 (d, 2H, $J = 7.5$ Hz), 7.54 (m, 4H), 8.50 (d, 2H, $J = 4.8$ Hz). Mass spectrum (CI) (m/z) 483 $(M + 1)^+$.

LH(Cl): Freshly distilled thionyl chloride (6.4 g, 53.8 mmol) in anhydrous methylene chloride (300 mL) was added to **LH(OH)** (5.2 g, 10.8 mmol) in anhydrous CH_2Cl_2 (10 mL) at 0 °C with vigorous stirring. The color of the solution changed from bright yellow to dark brown, and some thick unstirrable syrup also formed. The reaction mixture was warmed to room temperature, stirred for 8 h and then made basic with saturated sodium carbonate solution (200 mL). The solution was then washed with water (100 mL) twice. Drying over anhydrous $MgSO_4$ and removal of methylene chloride yielded ≈5 g of brown oil (≈90% yield). The crude material was used for the next step without further purification. ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 6H), 2.86 (t, 4H, $J = 6.9$ Hz), 3.03 (t, 4H, $J = 6.9$ Hz), 3.78 (s, 4H), 6.17 (s, 1H), 7.12 (m, 4H), 7.22 (m, 2H), 7.44 (d, 2H, $J = 4.8$ Hz), 7.57 (m, 4H), 8.50 (d, 2H, $J = 4.8$ Hz). Mass spectrum (CI) (m/z) 501, 503 $(M + 1)^+$.

LH_2: LH(Cl) (crude, ≈5 g, ≈10 mmol) in ethanol (150 mL) was stirred with $NaOH_{(aq)}$ (20%, 15 mL) and zinc dust (10 g, 153 mmol) at reflux for 12 h. The reaction mixture was cooled to room temperature and filtered, and after removal of the ethanol, the filtrate was extracted with CH_2Cl_2 (2 × 100 mL). The organic extract was washed with water (100 mL), dried over anhydrous $MgSO_4$, and concentrated to give a brown oil, which was columned on alumina with a 98/2 (v/v) mixture of ethyl acetate/MeOH ($R_f = 0.30$) to yield 1.35 g (≈30% yield) of pure yellow oil. ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6H), 2.87 (t, 4H, $J = 6.6$ Hz), 3.03 (t, 4H, $J = 6.6$ Hz), 3.75 (s, 4H), 4.33 (s, 2H), 7.03 (d, 2H, $J = 6.9$ Hz), 7.12 (m, 6H), 7.44 (t, 2H, $J = 7.4$ Hz), 7.52 (t, 2H, $J = 7.4$ Hz), 8.50 (d, 2H, $J = 4.8$ Hz). Mass spectrum (CI) (m/z) 467 $(M + 1)^+$.

D=O, DH(OH), DH(Cl), and DH_2: These compounds were synthesized by reactions analogous to those for **L=O**, **LH(OH)**, **LH(Cl)**, and **LH_2**. **D=O**: 67.7% yield. ^{1}H NMR ($CDCl_3$) δ 3.86 (two s, 12H), 7.10 (t, 4H, $J = 7.4$ Hz), 7.55 (m, 8H), 7.76 (m, 4H), 7.93 (d, 2H, $J = 4.8$ Hz), 8.5 (d, 4H, $J = 4.8$ Hz). IR (neat, cm^{-1}) 2796 (C–H), 1685 (vs, C=O), 1591 (vs, C=C). Mass spectrum (CI) (m/z) 607 $(M + 1)^+$. **DH(OH)**: ≈94% yield. ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 12H), 5.85 (s, 1H), 6.13 (s, 1H), 7.13 (m, 4H), 7.38 (d, 4H, $J = 6.4$ Hz), 7.60 (m, 10H), 8.52 (d, 4H, $J = 4.8$ Hz). Mass spectrum (CI) (m/z) 609 $(M + 1)^+$. **DH(Cl)**: ≈60% yield. ^{1}H NMR ($CDCl_3$) δ 3.82 (s, 4H), 3.84 (s, 8H), 6.15 (s, 1H), 7.11 (m, 4H), 7.60 (m, 14H), 8.50 (d, 4H, $J = 4.8$ Hz). **DH_2**: 36% yield. ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 4H), 3.88 (s, 8H), 4.30 (s, 2H), 7.11 (m, 4H), 7.38 (d, 2H, $J = 4.9$ Hz), 7.59 (m, 14H), 8.50 (d, 2H, $J = 4.8$ Hz). Mass spectrum (CI) (m/z) 593 $(M + 1)^+$.

Synthesis of Cu^I Complexes. $[Cu^I_2(LH_2)](ClO_4)_2 \cdot CH_3CN \cdot 1/3Et_2O$ (1-$(ClO_4)_2 \cdot CH_3CN \cdot 1/3Et_2O$): The ligand **$LH_2$** (0.22 g, 0.46 mmol) was dissolved in 15 mL of argon saturated CH_3CN and added dropwise to $[Cu^I(CH_3CN)_4](ClO_4)$ (0.29 g, 0.89 mmol) while stirring under argon for 30 min. To the yellow solution was added air free diethyl ether (ca. 20 mL) until the solution became cloudy. Filtration through a medium porosity frit and addition of another 50 mL of diethyl ether gave a dark yellow oil, which was subsequently dried in vacuo and washed with diethyl ether twice. The resulting solid was dried in vacuo to yield 0.29 g (74% yield) of a yellow powder. Anal. Calcd for $Cu_2C_{32.33}H_{40.33}N_7Cl_2O_{8.33}$: C, 45.24; H, 4.74; N, 11.42%. Found: C, 44.94; H, 4.56; N, 10.93%. IR (Nujol, cm^{-1}) 1603 (C=C, aromatic), 1084 (ClO_4^-). ^{1}H NMR (CD_3NO_2) δ 1.03 (t, CH_3 of ether), 1.03 (t, CH_3 of ether), 2.06 (s, 3H), 2.35 (s, 6H), 3.07 (br, 8H), 3.30 (q, CH_2 of ether), 3.33–4.30 (br, 4H), 7.27 (t, 2H, $J = 7.4$ Hz), 7.40–7.45 (m, 6H), 7.83–7.93 (m, 4H), 8.36–8.38 (d, 2H, $J = 4.8$ Hz).

$[Cu^I_2(L{=}O)(CH_3CN)_2](ClO_4)_2$ (2-$(ClO_4)_2$): The ligand **L=O** (0.35 g, 0.73 mmol) was dissolved in 30 mL of argon saturated CH_3CN and added dropwise to 0.23 g (0.73 mmol) of $[Cu^I(CH_3CN)_4](ClO_4)$ while stirring under argon for 30 min. To the resulting dark brown solution was added air free diethyl ether (ca. 25 mL) until the solution became cloudy. Filtration through a medium porosity frit was followed by precipitation using diethyl ether (40 mL). The resulting supernatant was decanted, and the complex was washed with 50 mL of additional diethyl ether. The solid was dried in vacuo to yield 0.54 g (83% yield) of a bright red powder. Anal. Calcd for $Cu_2C_{33}H_{38}N_8Cl_2O_9$: C, 44.60; H, 4.32; N, 12.61%. Found: C, 44.59; H, 4.28; N, 12.58%. IR (Nujol, cm^{-1}) 2004 (ClO_4^- overtone), 1672 (C=O), 1598 (C=C, aromatic), 1084 (ClO_4). ^{1}H NMR (CD_3NO_2) δ 2.05 (s, 6H, $2CH_3CN$), 2.51 (s, 6H, $2CH_3$), 2.70–3.3 (br, 8H, $2CH_2CH_2$), 3.80–4.25 (br, 4H, $2CH_2$), 7.22–7.37 (m, 4H), 7.69–7.82 (m, 4H), 8.03–8.10 (m, 6H). ^{1}H NMR (CD_3CN) δ 2.53 (s, 6H, $2CH_3$), 2.81 (s, 8H, $2CH_2CH_2$), 3.79 (s, 4H, $2CH_2$), 7.18–7.22 (t, 2H, $J = 7.3$ Hz), 7.29–7.32 (d, 2H, $J = 4.8$ Hz), 7.48–7.80 (t, 2H, $J = 7.3$ Hz), 7.56–7.59 (d, 2H, $J = 4.8$ Hz), 7.97–8.10 (m, 6H).

$[Cu^I_2(DH_2)(CH_3CN)_2](ClO_4)_2$ (3-$(ClO_4)_2$): This complex was prepared in an identical manner as **1-$(ClO_4)_2 \cdot CH_3CN \cdot 1/3Et_2O$** by adding a solution of **DH_2** (0.16 g, 0.27 mmol) in 25 mL of acetonitrile to solid $[Cu(CH_3CN)_4](ClO_4)$ (0.17 g, 0.52 mmol) under argon. Recrystallization from CH_3CN/Et_2O yielded 0.20 g (83%) of a light yellow powder. Anal. Calcd for $Cu_2C_{41}H_{42}N_{10}Cl_2O_8$: C, 49.20; H, 4.23; N, 13.99%. Found: C, 49.21; H, 4.33; N, 13.52%. IR (Nujol, cm^{-1}) 1600 (C=C, aromatic), 1084 (ClO_4^-). ^{1}H NMR (CD_3CN) δ 1.98 (s, 6H, CH_3CN), 3.95 (br, 10H), 4.48 (br, 2H), 7.29 (br), 7.74 (m), 8.45 (br).

Low-Temperature Reaction of $[(DH_2)Cu^I_2(CH_3CN)_2]^{2+}$ (3) with Dioxygen. Complex **3-$(ClO_4)_2$** (0.11 g, 0.18 mmol) was dissolved in dioxygen free propionitrile solvent, and the solution was cooled to −80 to −90 °C by using a methanol liquid nitrogen slush bath. Upon bubbling with dioxygen, the yellow Cu^I solution immediately changed to an intense purple color. The solution was completely oxygenated by bubbling with O_2 throughly for 5 min, and then dioxygen was removed by repeated vacuum/argon purging, followed by Ar bubbling (5 min). The resulting solution was slowly warmed to room temperature for 2 h, followed by solvent removal in vacuo. The green species that was obtained was redissolved in degassed CH_2Cl_2 and extracted with O_2-free concentrated aqueous ammonia. The CH_2Cl_2 layer was dried over $MgSO_4$ and concentrated in vacuo. The product was identified by NMR spectroscopy as **DH_2**.

Reaction of L=O with $Cu(ClO_4)_2 \cdot 6H_2O$. Synthesis of $[Cu^{II}_2\{L(OH)(O^-)\}(^-OClO_3)](ClO_4)_2$ (4-$(ClO_4)_2$). A 100-mL Schlenk flask was charged with copper perchlorate hexahydrate ($Cu(ClO_4)_2 \cdot 6H_2O$) (0.52 g, 1.4 mmol) and a magnetic stirring bar. A 100-mL addition funnel was attached to the flask via a standard 14/20 joint and the whole system was evacuated and purged three times with argon. An acetonitrile solution (30 mL) with **L=O** (0.35 g, 0.73 mmol) was bubbled with argon and added

to the flask dropwise. The resulting solution was stirred overnight at room temperature. Argon saturated diethyl ether was added until the solution became cloudy (ca. 30 mL), and the solution was filtered through a medium porosity frit. Addition of another 75 mL of ether to the filtrate resulted in the separation of a blue solid, which was collected, and washed throughly with ether. The light blue powder obtained was vacuum dried for 24 h to give 0.54 g product (83% yield). Anal. Calcd for $Cu_2C_{29}H_{33}N_6Cl_3O_{14}$: C, 37.73; H, 3.60; N, 9.10%. Found: C, 37.17; H, 3.71; N, 8.71%. IR (Nujol; cm^{-1}): 1613 (C=C, aromatic), 1084 (ClO_4^-). EPR (DMF): silent. Solid-state magnetic moment (room temperature): $\mu_{eff} = 1.11 \pm 0.1\,\mu_B$/Cu. Solution-state magnetic moment (Evans method): $\mu_{eff} = 1.06 \pm 0.1\,\mu_B$/Cu.

Reaction of 2-$(ClO_4)_2$ with O_2. Synthesis of [Cu^{II}_2{$L(O^-)_2$}-($^-OClO_3$)](ClO_4) (5-(ClO_4)). Complex **2-$(ClO_4)_2$** (0.24 g, 0.27 mmol) was dissolved in 40 mL of air-free CH_3CN. The flask was evacuated and purified O_2 was admitted, resulting in a color change from brown to blue in ≈5 min. The solution was stirred at room temperature for 1 h and then diethyl ether (30 mL) was added until it became cloudy. At this stage, the solution was filtered through a medium porosity frit and 70 mL of diethyl ether was added to precipitate a blue solid, which was washed thoroughly with 30 mL diethyl ether and then dried under vacuum. The solid was recrytallized from CH_3CN/Et_2O and dried in vacuo to produce 0.17 g of **5-(ClO_4)** in 75% yield. Anal. Calcd for $Cu_2C_{29}H_{34}N_6Cl_2O_{11}$ (calculated for **5-(ClO_4)** plus H_2O) C, 41.44; H, 4.08; N, 10.00%. Found: C, 41.42; H, 3.95; N, 9.75%. Electrospray mass spectrum: 723 (M − (ClO_4)), IR (Nujol, cm^{-1}) 2010 (ClO_4^- overtone), 1603 (C=C, aromatic), 1084 (ClO_4^-). UV–Vis (CH_3CN; λ_{max}/nm ($\varepsilon/M^{-1}\,cm^{-1}$)): 604 (420). EPR (DMF): silent. Solid-state magnetic moment (room temperature): $\mu_{eff} = 1.22 \pm 0.1\,\mu_B$/Cu. Solution-state magnetic moment (Evans method): $\mu_{eff} = 1.23 \pm 0.1\,\mu_B$/Cu. The ^{18}O-labeled sample of **5-(ClO_4)** was prepared by an analogous reaction of **2-$(ClO_4)_2$** with ^{18}O-labeled O_2. Electrospray mass spectrum: 725 (M − (ClO_4)), IR (Nujol, cm^{-1}) 2010 (ClO_4^- overtone), 1603 (C=C, aromatic), 1084 (ClO_4^-). UV–Vis (CH_3CN; λ_{max}/nm ($\varepsilon/M^{-1}\,cm^{-1}$)): 605 (420).

Reaction of Iodosylbenzene with 1-$(ClO_4)_2$. Complex **1-$(ClO_4)_2$** (0.25 g, 0.28 mmol) and iodosylbenzene (0.06 g, 0.28 mmol)[36] were placed in a 50-mL Schlenk flask under argon and air free CH_3CN (30 mL) was added to it while stirring. The solids quickly dissolved, and the brown solution slowly changed to green and then finally to blue. The resulting blue solution was filtered through a medium porosity frit, and the product was precipitated with 100 mL of diethyl ether under Ar. The liquid was decanted and the precipitates were washed with diethyl ether several times under argon and then dried under vaccum to give 0.18 g of a blue solid. This was characterized by UV–vis and IR spectroscopies and found to be identical to authentic [($L(O^-)_2$)Cu^{II}_2($^-OClO_3$)]$^+$ (**5**) (79% yield). The decanted solution was concentrated to give 0.05 g (90%) of liquid, which was identified (TLC and ^1H NMR spectroscopy) as iodobenzene (PhI).

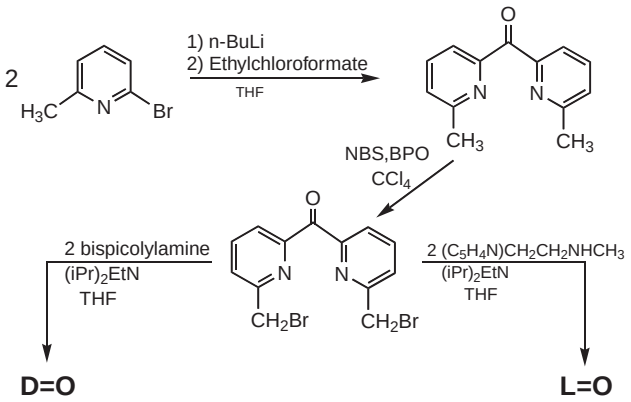
Reaction of NO(g) Gas with 2-$(ClO_4)_2$. Complex **2-$(ClO_4)_2$** (0.19 g, 0.21 mmol) was dissolved in of air-free CH_2Cl_2 (15 mL) under argon and cooled to −80 °C. The flask was evacuated and purified NO(g) was introduced into the flask. The solution turned from brown to a darker brown color in 10 min. It was then stirred at −80 °C for 30 min, after which the excess nitrogen monoxide gas was removed by evacuating and purging the solution with argon. After stirring for another hour with the stopcock of the Schlenk flask closed, the solution was allowed to warm to room temperature during which a blue solid precipitated. Generation of N_2O gas from the reaction was demonstrated by removal of head-space gases (via syringe) and carrying out gas chromatographic analysis, and comparing with authentic N_2O. On the other hand the blue solid was filtered and washed with diethyl ether several times under argon and then dried in vacuo to give 0.16 g (84% yield) of a blue solid, which was characterized as **5** by UV–visible and IR spectroscopy.

X-ray Structure Determinations. X-ray quality blue, plate-like crystals of **4-$(ClO_4)_2$** were grown by adding diethyl ether over an acetonitrile solution of the copper complex and allowing the solution to stand several days at room temperature. These crystals were mounted on glass fibers. All measurements were made on a Rigaku AFC6S diffractometer with a graphite monochromated Mo Kα source (λ (Mo Kα) = 0.71069 Å). Cell constants and an orientation matrix for data collection were obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $31.62 < 2\theta < 38.74°$ for **4-$(ClO_4)_2$**. All the data for **4-$(ClO_4)_2$** were collected at a temperature of 23 ± 1 °C using ω scan technique to a maximum 2θ value of 50°. The intensities of three representative reflections which were measured after every 150 reflections remained constant throughout data collection, indicating crystal and electronic stability. Thus, no decay correction was applied. All ORTEP diagrams were created by using the Johnson Programs. Crystal data, data collection methods, and refinement procedures are listed in Table 1. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre: Deposition numbers CCDC-620643, for compound **4-$(ClO_4)_2$**. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Table 1. Crystal Data and Details of the Structure Determination for **4-$(ClO_4)_2$**

Formula	$C_{29}H_{32}N_6O_{14}Cl_3Cu_2$
Temperature/K	296
MW	922.05
Cryst system	orthorhombic
Space group	*Pbca*
a/Å	17.276(7)
b/Å	26.333(7)
c/Å	15.900(5)
V/Å^3	7234(4)
F(000)	3752
Z	8
λ(Mo Kα)/Å	0.71069
D_{calcd}/g cm^{-3}	1.693
Abs coeff/cm^{-1}	14.7
Scan type	ω
Reflections measured	$+h, +k, \pm l$
Reflections collected	7011
Independent reflections	7010
No. of variables	325
R[a)]	0.069
R_w[b)]	0.069
Goodness of fit[c)]	3.94

a) $R = \Sigma[F_o| - |F_c|/\Sigma|F_o|]$. b) $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$. c) GOF = $[\Sigma w(|F_o| - |F_c|)^2/(NO - NV)]^{1/2}$.



Scheme 1.

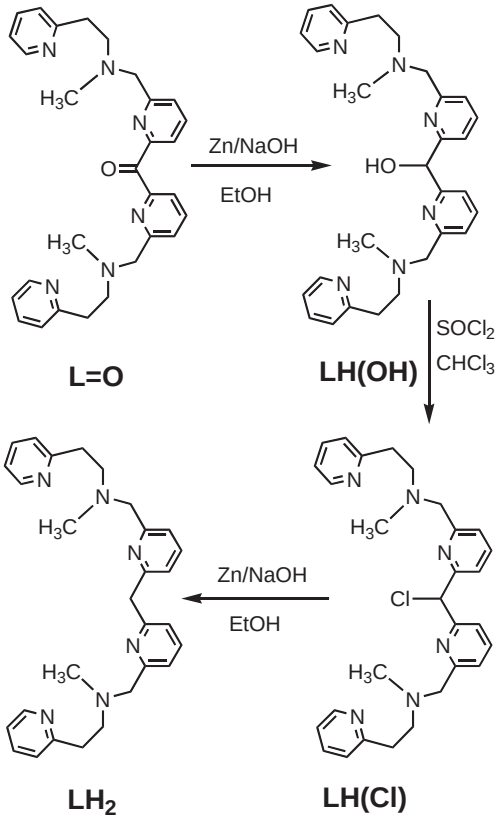
Results and Discussion

Synthesis of Ligands. Dinucleating ligands **L=O** and **D=O** were prepared by the reaction of bis[6-(bromomethyl)-2-pyridyl]methanone[35] with either 2-(2-methylaminoethyl)-pyridine or bispicolylamine (PY1),[37] respectively (Scheme 1). Ligand $\mathbf{LH_2}$ was synthesized by reducing the carbonyl groups of **L=O** to the corresponding methylene compounds. A direct one-step reduction of the carbonyl group to the alkane was attempted by known methods,[38] however, the secondary alcohol was always obtained, rather than an alkane. Thus, $\mathbf{LH_2}$ was prepared by the multi-step synthesis shown in Scheme 2. $\mathbf{DH_2}$ was prepared from **D=O** in a similar manner.

Synthesis of Copper(I) Complexes of L=O, LH_2, and DH_2. The synthesis and handling of copper(I) complexes was carried out exclusively either in an inert atmosphere box or under an inert atmosphere using standard Schlenk techniques. A copper(I) complex of ligand $\mathbf{LH_2}$ was synthesized by reacting 2 equiv of $[Cu(CH_3CN)_4](ClO_4)$ and $\mathbf{LH_2}$ in acetonitrile solvent and obtained as a yellow powder. Based on elemental analysis and ^{1}H NMR spectroscopy, the complex was formulated as $[Cu^I_2(\mathbf{LH_2})](ClO_4)_2\cdot CH_3CN\cdot 1/3Et_2O$ ($\mathbf{1\text{-}(ClO_4)_2\cdot CH_3CN\cdot 1/3Et_2O}$). The reaction of the dinucleating ligand **L=O** with 2 equiv of $[Cu(CH_3CN)_4](ClO_4)$ in an organonitrile solvent gave the dinuclear copper(I) complex, $[Cu^I_2(\mathbf{L{=}O})(CH_3CN)_2](ClO_4)_2$ ($\mathbf{2\text{-}(ClO_4)_2}$) in good yield. The color of the complex was bright red. From elemental analysis, NMR, and IR spectroscopic studies, it was confirmed that in the solid state, the dicopper complex possesses two acetonitrile molecules. Despite the lack of direct structural evidence, it is thought that the acetonitrile molecules in the complex are bound to each Cu^I ion. This has been observed in many other cases of copper complexes with alkylamine/pyridyl ligands.[34,39]

In the IR spectra of $\mathbf{2\text{-}(ClO_4)_2}$, the carbonyl C=O stretching frequency of the complexed ligand was 1672 cm^{-1}, while that of free base was 1684 cm^{-1}. The lower frequency of the complex might be due to some weak interaction between the Cu^I ion and the carbonyl oxygen and consequently reduced bond order of the C=O, which has been reported for all of the copper(II) and zinc(II) complexes of *N*,*O*-chelated 2-benzoylpyridine (PhCOpy).[40]

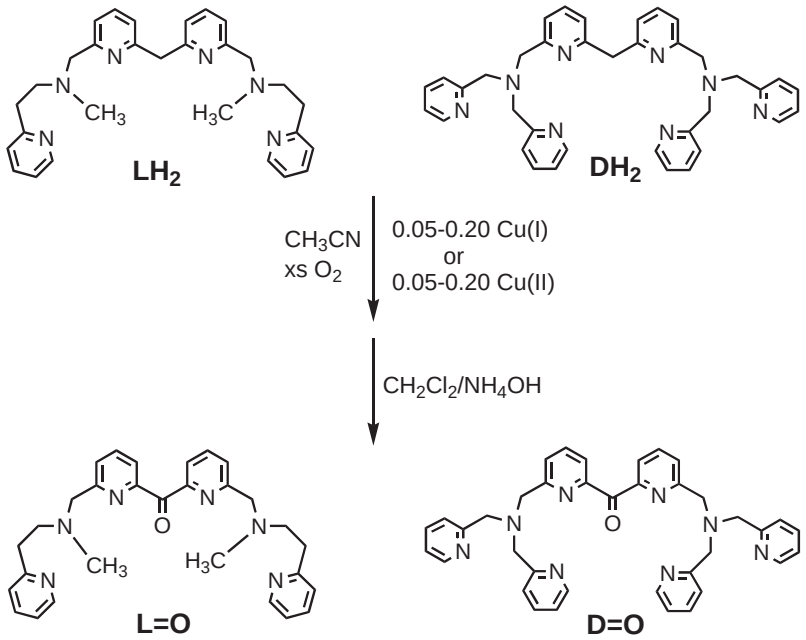
The dinuclear copper(I) complex $\mathbf{3\text{-}(ClO_4)_2}$ was synthesized by reacting the ligand $\mathbf{DH_2}$ and two equiv of $[Cu(CH_3CN)_4](ClO_4)$ in acetonitrile. This complex was very air sensitive, but the oxygen-free solution was stable indefinitely in nitrile solvents, e.g., MeCN, EtCN. Like other copper(I) complexes containing tris[2-(2-pyridyl)methyl]amine(tmpa) unit(s), such as $[(tmpa)Cu^I(CH_3CN)](PF_6)$[32] or $[(D^1)Cu^I_2(CH_3CN)_2](ClO_4)_2$ (D^1 contains $-CH_2CH_2-$ linked tmpa moities, and is dinucleating),[28] this compound probably has one acetonitrile molecule bound to each copper ion. The isolation of a dicopper(I) complex of **D=O** was not attempted.



Scheme 2.

Sharp ^{1}H NMR spectra of the ligands and their Cu^I complexes have been obtained in $CDCl_3$, CD_3NO_2, and/or CD_3CN, except for $\mathbf{3\text{-}(ClO_4)_2}$, and as like other copper(I) systems,[15] the ^{1}H resonances shifted downfield upon coordination to the positively charged copper(I) ion. Extreme line broadening was observed for $\mathbf{3\text{-}(ClO_4)_2}$ in CD_3NO_2. Since Cu^I is diamagnetic (d^{10} system), its complexes usually exhibit sharp ^{1}H NMR spectra. However, there are quite a few other systems that exhibit line broadening effects and dynamics behavior, e.g., ligand exchange or dimerization is usually responsible.[16,28,41]

Catalytic Oxidation of LH_2 and DH_2 with Copper Salts and Dioxygen. Exposure of O_2 to an acetonitrile solution of ligands $\mathbf{LH_2}$ or $\mathbf{DH_2}$ containing sub-stoichiometric amounts of either a copper(I) or copper(II) salt caused the rapid transformation of the central methylene group of the ligands between two pyridine rings of the ligands to ketone products. Typically, 0.05–0.2 mole equivalent of either a copper(I) ($[Cu^I(CH_3CN)_4](PF_6)$ or $[Cu^I(CH_3CN)_4](ClO_4)$) or copper(II) salt ($Cu^{II}(ClO_4)_2\cdot 6H_2O$) and $\mathbf{LH_2}$ or $\mathbf{DH_2}$ ($\approx$0.5 g) were dissolved in CH_3CN and stirred under an O_2 atmosphere at



Scheme 3.

25 °C for several hours. The reaction mixtures were evaporated, redissolved in CH_2Cl_2, and extracted with a concentrated aqueous ammonia solution (Scheme 3). The phases were separated, the CH_2Cl_2 layers were dried over $MgSO_4$, and then, the solvent evaporated in vacuo. The identity of the product was determined by ^{1}H NMR spectroscopy and the turnover numbers (≈20 for both ligands) were calculated from the molar ratio of the ligand to the copper salts. The yields of the oxygenated ligands (**L=O** and **D=O**) were greater than 85% (isolated), based on the ratio of the amount of the products to the starting ligands.

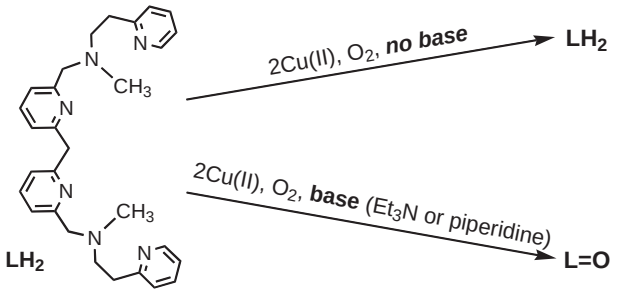
Manometric O_2-uptake for the catalytic reaction at 0 °C was carried out in order to confirm the stoichiometry of the reaction with O_2 in the presence of 0.05 equivalent of Cu^{II} salt. The results showed that the absorption ratio of O_2 by **LH_2** was $L/O_2 \approx 1{:}1$. This oxygenation reaction can also occur non-catalytically, such as in a stoichiometric reaction when $[Cu^{I}_2(\mathbf{LH_2})(CH_3CN)_2]^{2+}$ (**1**) is reacted with excess O_2 in acetonitrile. The yield of ketone in the stoichiometric reaction was essentially quantitative, and utilization of $^{18}O_2$ in the reaction with **1** resulted in exclusive formation of **L=^{18}O** on the basis of mass spectrometry. Combined with the O_2-uptake experiment, this suggested that the ketonic oxygen atom was derived from one of two atoms in O_2. The detection of water as product was not attempted, but the data suggest the overall reaction can be expressed as

$$\mathbf{LH_2} + O_2 \rightarrow \mathbf{L{=}O} + H_2O. \quad (1)$$

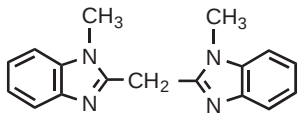
To explore the possible role of Cu_2O_2 adducts (formally peroxo–dicopper(II) species) in its reactivity, a yellow solution of **1** in acetonitrile was exposed to one equiv O_2 at −45 °C through a gas tight syringe. The reaction mixture changed to green immediately. Uptake of one equivalent of O_2 by dicopper(I) complexes often results in the formation of Cu_2O_2 adducts which are stable at −80 °C.[8,13,27,42] In the present case, however, spectrophotometric monitoring by using UV–vis indicated no sign of build-up of any low-temperature stable species, but only rapid formation of green Cu^{II} species. Even after warming to room-temperature followed by work-up with CH_2Cl_2/NH_3 (aq) no ketone was present, and the central methylene group of the ligand remained intact, as analyzed by NMR spectroscopy. However, further exposure of the green species to excess O_2 with stirring did result in good yields of **L=O**. Along the same lines, a **3**–O_2 adduct was generated by bubbling dried O_2 into a cold propionitrile solution of **3-(ClO_4)$_2$** at −90 °C. Formation of a dioxygen adduct, i.e., μ-peroxo–dicopper(II), was evidenced by its low-temperature UV–vis features ($\lambda_{max} = 518$ nm, ≈600 nm (sh)), which are analogous to those previously reported for $[\{(tmpa)Cu^{II}\}_2(O_2^{2-})]^{2+}$ ($\lambda_{max} = 525$ nm, ≈600 nm (sh)).[32] Even when the excess O_2 was removed at the same temperature and the solution was warmed to room temperature, the substrate was not oxidized. However, like the reaction of **1** with O_2, further exposure of O_2 causes quantitative ketone formation. Thus, it seems unlikely that a Cu_2O_2 adduct directly attacks the ligand substrates giving product; rather, the reaction of subsequently added O_2 to thermal decomposition products, such as oxo–copper(II) or hydroxo–copper(II) species, are probably responsible for the ketone formation (vide infra).

In addition, the efficiency of the oxygenation reaction decreased with an increase in the amount of the copper ion present. Excess copper(II), e.g., two equivalents of $Cu^{II}(ClO_4)_2 \cdot 6H_2O$, completely inhibited the oxygenation reaction and no ketone was formed (Scheme 4). However, the reaction proceeded upon addition of an external base, such as triethylamine or piperidine, and the ligand was subsequently completely converted to ketone (Scheme 4). Thus, it appears that the presence of a base is required for ketone formation.

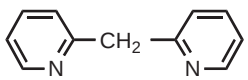
Kinetic studies, performed by Zuberbühler and co-workers,[43] who investigated copper ion mediated catalytic oxygenation of the activated methylenes of bis(1-methylbenzimidazol-2-yl)methane and bis(2-pyridyl)methane (Scheme 5),



Scheme 4.



bis(1-methylbenzimidazol-2-yl)methane



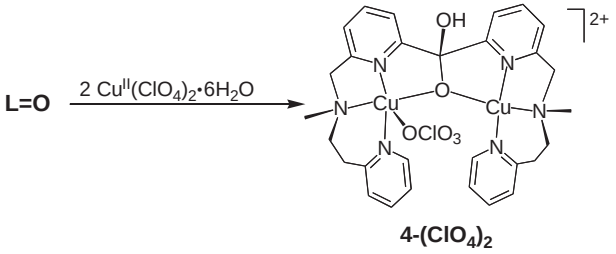
bis(2-pyridyl)methane

Scheme 5.

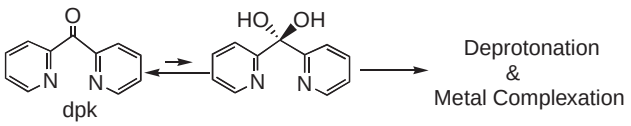
have revealed that the most important step prior to reaction with O_2 is deprotonation of the active methylene group by a base and the rate of the oxygenation reaction is proportional to the concentration of either free ligand, buffer base, or hydroxide ions.[43,44] In the current study, the polyamine ligand itself could behave as a base for the catalytic reaction with sub-stoichiometric amounts of copper(II) ions. Upon addition of a stoichiometric amount of Cu^{II} salt, there is no free base (ligands) available, so that deprotonation is completely blocked. On the other hand, the non-catalytic Cu^{I}/O_2 reactions probably produce copper(II)–oxide or hydroxide species, which, as a base, might aid carbanion formation. In any case, activated methylene oxygenation is likely to occur by metal-mediated or direct O_2 attack on a carbon radical, generated by transient oxidation of the Cu^{II} present.[43–45] Kodera and coworkers[45] also recently describe related chemistry for a sterically hindered tripyridine copper(II) complex, which is active toward C–H oxygenation. A number of cobalt complexes are of related interest.[46,47]

Hydration of Ketone Function of L=O with $Cu(ClO_4)_2 \cdot 6H_2O$. Mixing **L=O** with two equiv $Cu^{II}(ClO_4)_2 \cdot 6H_2O$ in acetonitrile gave a blue solution, and the monoalkoxide bridged product **4-$(ClO_4)_2$** was isolated in >90% yield (Scheme 6). The product, characterized by X-ray crystallography (discussed below), was EPR silent (dimethylformamide solvent, 77 K), indicating that the two copper ions are magnetically coupled. The solution and solid-state magnetic moments were $1.06 \pm 0.1\,\mu_B$/Cu and $1.11 \pm 0.1\,\mu_B$/Cu, respectively, well below the "spin only" value of $1.73\,\mu_B$/Cu (theoretical), and consistent with the EPR results and the presence of strong magnetic coupling. The extent of coupling can be estimated to be $-2J \cong 450\,cm^{-1}$ ($H = -2JS_1 \cdot S_2$).[48]

In this reaction, hydration of the ketone double bond in the ligand and ligation of one of the hydrate oxygens to the copper



Scheme 6.



Scheme 7.

ions to form the alkoxy-bridged complex occur. Evidence for the hydration reaction comes from the X-ray structure of **4-$(ClO_4)_2$**, and the disappearance of the ketonic carbonyl C=O stretching frequency at $1685\,cm^{-1}$ and the appearance of a band at $\approx 3500\,cm^{-1}$ in the infrared spectra, assigned to an O–H stretching vibration.

The hydration of a carbonyl group leads to a 1,1-diol (*gem*-diol).[49–56] However, in general, such hydrates are unstable since the hydration reaction is reversible and the equilibrium generally lies on the carbonyl side. Stabilization of hydrates occurs when the diol is flanked by very strong electron-withdrawing groups, such as trichloromethyl or trifluoromethyl groups, such as in chloral hydrate ($Cl_3CC(OH)_2H$) and hexafluoropropane-2-diol.[49] Di-2-pyridyl ketone (dpk) also undergoes nucleophilic addition reactions at the carbon of the carbonyl group in the presence of various transition metals, and the diol(ate) form is stabilized by deprotonation and metal coordination (Scheme 7).[50–56] With **L=O**, we think that hydration and subsequent deprotonation are meditated by a juxtaposed Cu^{II}_n–Cu^{II}_n–OH_2 or Cu^{II}_n–OH^- moiety, yielding **4-$(ClO_4)_2$**.

Structure of $[Cu^{II}_2\{L(OH)(O^-)\}(^-OClO_3)](ClO_4)_2$ (4-$(ClO_4)_2$). A summary of crystal data and refinement results for **4-$(ClO_4)_2$** is given in Table 1 and selected bond distances and angles listed in Table 2. A structure plot of the cationic portion of the compound is presented in Fig. 1.

In **4-$(ClO_4)_2$** the two cupric ions are separated by a distance of 3.567(2) Å and bridged by an alkoxide oxygen atom. The two coppers are in different ligand environments; one (Cu1) is penta-coordinate environment, while the other is tetra-coordinate. Cu1 is ligated to two pyridyl nitrogen atoms, a nitrogen atom from an aliphatic amine, an oxygen atom from the alkoxide oxygen, and a perchlorate anion. Cu2 is ligated to two pyridyl nitrogen atoms, a nitrogen atom from a tertiary amine, and an alkoxy oxygen atom on its equatorial position. The axial coordination sites are vacant, but atoms O2 and O3 of the perchlorate bound to Cu1 appear to approach one such position with Cu2–O3 and Cu2–O2 distances of 3.41 and 3.62 Å, respectively.

Oxo-Transfer to the Ketone of L=O. Reactivity of 2-$(ClO_4)_2$ with O_2. To explore Cu^{I}/O_2 reactivity, **2** was reacted with O_2 in acetonitrile at room temperature, the result being

Table 2. Selected Bond Distances (Å) and Angles (°) for **4** and **5**

Intermolecular distances/Å			
4		**5**	
Cu1–Cu2	3.467(2)	Cu1–Cu2	5.683(3)
Cu1–O3	2.266(8)	Cu1–O2	2.612(4)
Cu1–O13	2.021(7)	Cu1–O10	1.917(3)
Cu1–N1	2.076(9)	Cu1–N1	2.040(4)
Cu1–N2	1.909(9)	Cu1–N2	1.899(4)
Cu1–N3	1.976(9)	Cu1–N3	1.969(4)
Cu2–N4	2.034(9)	Cu2–N4	2.084(4)
Cu2–N5	1.894(9)	Cu2–N5	1.943(4)
Cu2–N6	1.968(9)	Cu2–N6	2.084(4)
Cu2–O13	1.995(7)	Cu2–O9	2.073(3)
Intermolecular bond angles/°			
4		**5**	
O13–Cu1–O3	94.3(3)	O10–Cu1–O2	105.5(2)
O13–Cu1–N3	100.1(3)	O10–Cu1–N3	99.6(2)
O13–Cu1–N1	157.7(3)	O10–Cu1–N1	157.9(2)
O13–Cu1–N2	81.6(3)	O10–Cu1–N2	83.3(1)
O3–Cu1–N3	91.9(3)	O2–Cu1–N3	78.0(3)
O3–Cu1–N1	106.1(3)	O2–Cu1–N1	92.0(2)
O3–Cu1–N2	109.1(3)	O2–Cu1–N2	94.5(2)
N3–Cu1–N1	88.4(4)	N3–Cu1–N1	97.2(2)
N3–Cu1–N2	158.8(4)	N3–Cu1–N2	172.4(2)
N1–Cu1–N2	83.2(4)	N1–Cu1–N2	81.9(2)
Cu1–O13–Cu2	119.3(3)	Cu1–O2–Cl1	134.9(2)
Cu1–O3–Cl1	123.7(5)	N4–Cu2–N5	81.5(2)
N4–Cu2–N5	83.3(4)	N4–Cu2–O9	101.9(2)
N4–Cu2–O13	154.9(4)	N4–Cu2–N6	97.0(2)
N4–Cu2–N6	98.0(4)	N5–Cu2–O9	81.3(1)
N5–Cu2–O13	80.8(4)	N5–Cu2–N6	132.4(2)
N5–Cu2–N6	166.5(4)	O9–Cu2–N6	101.5(1)
O13–Cu2–N6	102.0(4)		
Cu1–O13–C1	114.0(6)		
Cu2–O13–C1	111.1(6)		

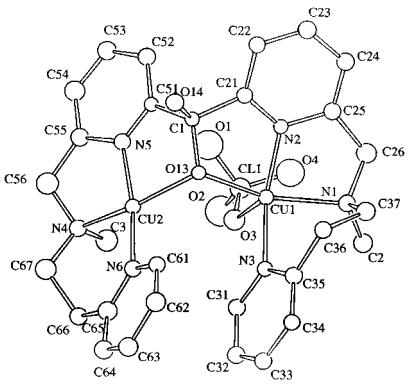
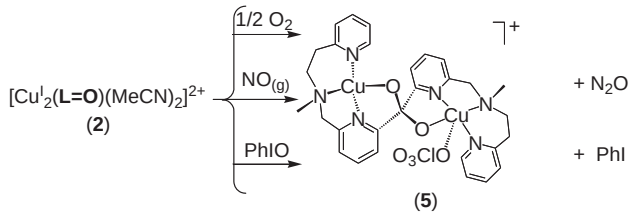


Fig. 1. Structure plot of the cationic portion of **4**.

an immediate color change from brown to green (Experimental Section; Scheme 8). Diethyl ether addition resulted in the isolation of **5** in >95% yield.

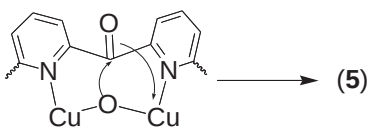
An X-ray structure analysis, published in a preliminary



Scheme 8.

communication[30] and also discussed further below, revealed a μ-1,3-bridged *gem*-diolate dicopper(II) complex with Cu···Cu = 5.583(3) Å. **5** was EPR silent, suggesting that the two copper(II) ions are magnetically coupled. Solution (Evans method) and solid-state magnetic moment measurements afforded magnetic moments of $1.23 \pm 0.1\,\mu_B$/Cu and $1.22 \pm 0.1\,\mu_B$/Cu, respectively, in accord with the EPR results. These results are consistent with the solid-state structure. Thus, net ketone hydration (and deprotonation) was achieved with Cu^I–O_2 reactivity.

For the transformation **2** to **5**, manometry indicated a reaction stoichiometry of $\mathbf{2}/O_2 = 0.5$, i.e., $Cu/O_2 = 4{:}1$, while electrospray mass spectrometric comparisons of samples of **2** reacted with $^{16}O_2$ versus $^{18}O_2$ were consistent with inclusion of one atom of O_2 into the product (the peak at 723 corresponding to $M[(^{16}O–^{16}O) - (ClO_4)]$ for $\mathbf{2} + {}^{16}O_2$ shifts to 725 with incorporation of one ^{18}O (≈70% incorporation)). Thus, the diolate oxygen atoms are derived from the one ketone moiety and one from O_2.[30] These observations point to the complete utilization and incorporation of both oxygen atoms from O_2, suggesting that it is not an initially formed Cu_2O_2 (peroxo–dicopper(II)) adduct, but rather an oxo–dicopper(II) species, which affects the ketone oxygenation reaction. Initial formation of an unstable Cu_2O_2 adduct $[Cu^I{}_2(\mathbf{L{=}O})(O_2)]^{2+}$ was not observed in the current system, but considered to be involved in the reaction as an intermediate. Even though many Cu_2O_2 species have been synthesized and stabilized in synthetic systems,[1–3] they are often difficult to detect, since they generally decompose rapidly because of their thermal instability. A number of mechanisms have been proposed for the course of decomposition reaction of peroxide species,[57–62] which include peroxide disproportionation, equivalent to the further reaction of the initially formed Cu_2O_2 adduct with an additional mole equiv of reducing dicopper(I) complex. Thus, this reaction could lead to an intermediate Cu^{II}–O–Cu^{II} species, i.e., $\{[Cu^{II}{}_2(\mathbf{L{=}O})(O^{2-})]^{2+}\}$ which could account for the observed $Cu/O_2 = 4{:}1$ stoichiometry (Scheme 9). However, this oxo species $\{[Cu^{II}{}_2(\mathbf{L{=}O})(O^{2-})]^{2+}\}$ should be unstable with respect to nucleophilic attack of the proximate carbonyl group, resulting in the production of the **5**.



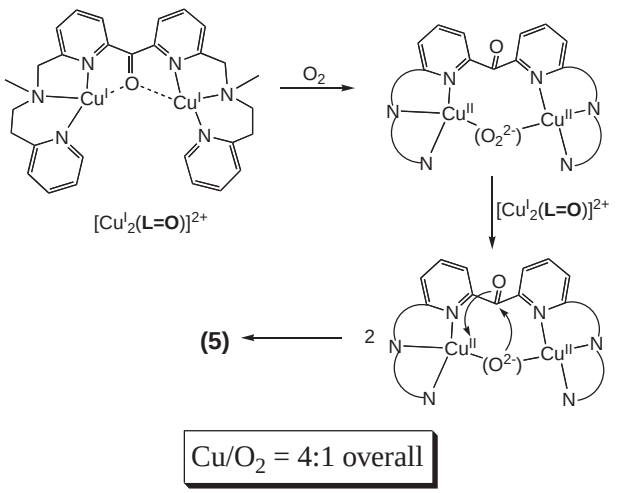
(2)

Support for the proposition that a Cu^{II}–O–Cu^{II} species is responsible for the observed chemistry comes from two other lines of evidence (Scheme 8). Aside from $Cu/O_2 = 4{:}1$ reactions of O_2 with copper(I) compounds as a means of forming Cu^{II}–O–Cu^{II} entities,[59–62] oxo–dicopper(II) complexes have al-

so been generated by other routes, such as by reacting copper(I) compounds with iodosylbenzene (PhIO)[61,63] or nitrogen monoxide.[64,65] Indeed, reaction of **2** with one equivalent of PhIO under Ar gave **5** in 79% isolated yield; iodobenzene was detected qualitatively (i.e., by NMR spectroscopy and thin-layer chromatography) as the reaction byproduct (Scheme 10). Thus, an oxo–dicopper(II) species may form and react according to Scheme 10.

Reaction of **2** with NO(g) at $-80\,^{\circ}C$ gave an intensely brown solution; removal of excess nitric oxide in vacuo, followed by warming also gives dialkoxide **5** (86% yield) (Scheme 11). N_2O was detected in the head-space of the final reaction mixture, consistent with previous observations,[64,65] suggesting the following course of reaction.

Higher nuclearity oxo–copper(II) (sometimes with Cu^{I}) clusters have been well described,[58,66–73] and recent advances show that bis-μ-oxo–dicopper(III) species can result from the oxygenation of certain copper(I) complexes.[3,23] However, to the best of our knowledge, no X-ray structures of discrete dinuclear Cu^{II}–O–Cu^{II} compounds exist.[74,75] Oxo–dicopper(II) species are known to transfer an oxygen-atom to phosphines,[60,61,64,67,76] and they are implicated in (catalytic) oxidative dehydrogenation reactions.[60,76–80] The chemistry described above strongly suggests a discrete Cu^{II}–O–Cu^{II} in the reaction process and subsequent novel oxo-transfer to the ligand carbonyl group.

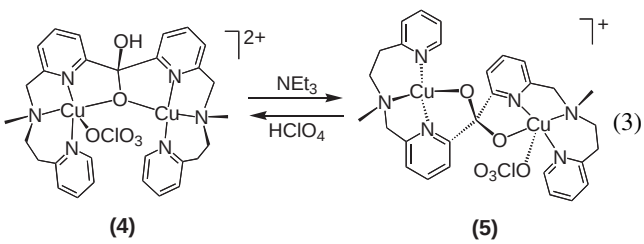


Scheme 9.

Structure of $[Cu^{II}_2\{L(O^-)_2\}(^-OClO_3)](ClO_4)\cdot 4CH_3CN$ (5-(ClO_4))$\cdot 4CH_3CN$). We previously published this structure, and that report[30] contains the details of the X-ray analysis, tables, etc. A diagram of the structure (Fig. 2) and selected bond lengths and angles (Table 2) are presented here again, for side-by-side comparison with the structure of **4-$(ClO_4)_2$**.

The two Cu^{II} ions of **5** are in inequivalent chemical environments. One of the copper(II) centers (Cu1) is penta-coordinate with coordination by two pyridyl nitrogen atoms, a nitrogen atom from a tertiary amine, an alkoxy oxygen atom, and a perchlorate anion. The other Cu^{II} ion (Cu2) is four coordinate and coordinated by two pyridyl nitrogen atoms, a nitrogen atom from a tertiary amine, and an alkoxy oxygen atom. The Cu···Cu separation is 5.683 Å.

Acid–Base Interconversion of 5 and 4. Since **4** and **5** are different only by one perchloric acid in the formula, acid–base titration by Et_3N and perchloric acid was attempted to see if they could be interconverted.



(3)

Chemical changes upon addition of triethylamine to a solution of **4** in acetonitrile were monitored by UV–vis spectroscopy. The d–d absorption of monoalkoxy dicopper(II) complex **4** in the visible region was broad and weak with $\lambda_{max} = 641$ nm ($\varepsilon = 313\,M^{-1}\,cm^{-1}$), while λ_{max} for dialkoxy complex **5** was 604 nm ($\varepsilon = 420\,M^{-1}\,cm^{-1}$). As triethylamine was added to

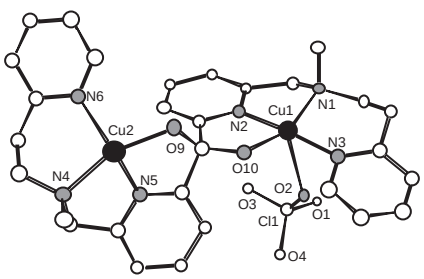
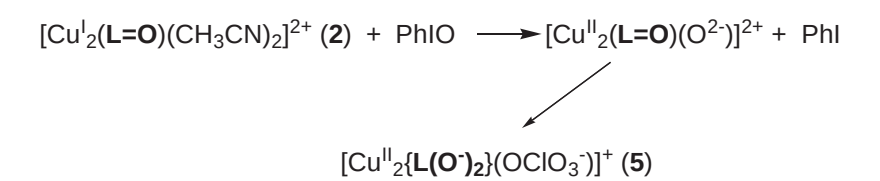
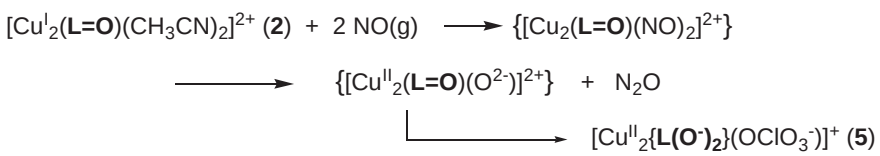


Fig. 2. Chem-3D View of the cationic portion of **5**.



Scheme 10.



Scheme 11.

the blue solution of **4** in increments, the solution became a greenish color, and λ_{max} blue-shifted to 604 nm. The reverse reaction occurred when perchloric acid was added to the solution of **5**. Analysis of the product isolated after the titration was carried out on a synthetic scale indicated that it was indeed conjugate pair of the starting compound. Thus, **4** and **5** are acid–base conjugate pairs, and they can be reversibly interconverted using stoichiometric amount of $HClO_4$(aq) or Et_3N.

Summary and Conclusion

New dinucleating ligands **L=O**, **D=O**, **LH_2**, **DH_2**, and copper complexes were designed and synthesized. **LH_2** and **DH_2** were catalytically oxidized with small quantities of either Cu^I or Cu^{II} salts, forming bis(2-pyridyl) ketone product **L=O** and **D=O**, respectively. Isolated dicopper(I) complex **1** also reacted with excess O_2 to give **L=O**. Experiments using $^{18}O_2$ isotope indicated that the oxygen atom in the product was derived from one O_2 molecule; however; additional observations ruled out a mechanism involving "oxygen-activation."

The ketone function of the **L=O** ligand was "hydrated" with stoichiometric addtion of 2 copper(II) perchlorates, with subsequent coordination to give the *gem*-diol(ate) complex **4**. Oxygenation of **2** gave complex **5**, in which one of the two oxygen atoms of the *gem*-diolate came from O_2. An oxo–dicopper(II) species was implicated as an important intermediate; supporting evidence was provided by the observation that reaction of **1** with NO or PhIO, which produced N_2O or PhI byproducts, repectively, also gave **5** in high yields. Complexes **4** and **5** are acid–base conjugate pairs and easily interconverted using NEt_3 or $HClO_4$ (aq).

The new ligand systems designed as analogs of the previously described dinucleating ligands exhibited rich chemistry and gave new insights into Cu/O_2 chemistry. This demonstrates how specific ligand design is important in defining the nature of observable chemistry.

DHL thanks Chonbuk National University & KRF (2002-070-C00053). KDK is grateful to the National Institutes of Health, U.S.A. (NIH GM28962) for support of this research.

References

1 L. Quant Hatcher, K. D. Karlin, *J. Biol. Inorg. Chem.* **2004**, *9*, 669.
2 E. A. Lewis, W. B. Tolman, *Chem. Rev.* **2004**, *104*, 1047.
3 L. M. Mirica, X. Ottenwaelder, T. D. P. Stack, *Chem. Rev.* **2004**, *104*, 1013.
4 E. I. Solomon, P. Chen, M. Metz, S.-K. Lee, A. E. Palmer, *Angew. Chem., Int. Ed.* **2001**, *40*, 4570.
5 S. Itoh, *Curr. Opin. Chem. Biol.* **2006**, *10*, 115.
6 J. P. Klinman, *J. Biol. Chem.* **2006**, *281*, 3013.
7 I. Bento, M. Carrondo, P. Lindley, *J. Biol. Inorg. Chem.* **2006**, *11*, 539.
8 M. Suzuki, H. Furutachi, H. Okawa, *Coord. Chem. Rev.* **2000**, *200–202*, 105.
9 M. E. Cuff, K. I. Miller, K. E. van Holde, W. A. Hendrickson, *J. Mol. Biol.* **1998**, *278*, 855.
10 K. A. Magnus, B. Hazes, H. Ton-That, C. Bonaventura, J. Bonaventura, W. G. J. Hol, *Proteins: Struct., Funct., Genet.* **1994**, *19*, 302.
11 Y. Matoba, T. Kumagai, A. Yamamoto, H. Yoshitsu, M. Sugiyama, *J. Biol. Chem.* **2006**, *281*, 8981.
12 C. Gerdemann, C. Eicken, B. Krebs, *Acc. Chem. Res.* **2002**, *35*, 183.
13 K. D. Karlin, A. D. Zuberbühler, in *Formation, Structure and Reactivity of Copper Dioxygen Complexes*, ed. by J. Reedijk, E. Bouwman, New York, **1999**.
14 E. Pidcock, H. V. Obias, C. X. Zhang, K. D. Karlin, E. I. Solomon, *J. Am. Chem. Soc.* **1998**, *120*, 7841.
15 K. D. Karlin, M. S. Nasir, B. I. Cohen, R. W. Cruse, S. Kaderli, A. D. Zuberbühler, *J. Am. Chem. Soc.* **1994**, *116*, 1324.
16 M. Becker, S. Schindler, K. D. Karlin, T. A. Kaden, S. Kaderli, T. Palanche, A. D. Zuberbühler, *Inorg. Chem.* **1999**, *38*, 1989.
17 M. S. Nasir, B. I. Cohen, K. D. Karlin, *J. Am. Chem. Soc.* **1992**, *114*, 2482.
18 M. S. Nasir, K. D. Karlin, D. McGowty, J. Zubieta, *J. Am. Chem. Soc.* **1991**, *113*, 698.
19 S. Itoh, M. Taki, H. Nakao, P. L. Holland, W. B. Tolman, L. Que, Jr., S. Fukuzumi, *Angew. Chem., Int. Ed.* **2000**, *39*, 398.
20 S. Itoh, H. Nakao, L. M. Berreau, T. Kondo, M. Komatsu, S. Fukuzumi, *J. Am. Chem. Soc.* **1998**, *120*, 2890.
21 I. Blain, P. Bruno, M. Giorgi, E. Lojou, D. Lexa, M. Réglier, *Eur. J. Inorg. Chem.* **1998**, 1297.
22 I. Blain, M. Giorgi, I. De Riggi, M. Réglier, *Eur. J. Inorg. Chem.* **2000**, 393.
23 L. Que, Jr., W. B. Tolman, *Angew. Chem., Int. Ed.* **2002**, *41*, 1114.
24 L. Q. Hatcher, M. A. Vance, A. A. NarducciSarjeant, E. I. Solomon, K. D. Karlin, *Inorg. Chem.* **2006**, *45*, 3004.
25 E. Pidcock, H. V. Obias, M. Abe, H.-C. Liang, K. D. Karlin, E. I. Solomon, *J. Am. Chem. Soc.* **1999**, *121*, 1299.
26 H.-C. Liang, K. D. Karlin, R. Dyson, S. Kaderli, B. Jung, A. D. Zuberbühler, *Inorg. Chem.* **2000**, *39*, 5884.
27 K. D. Karlin, S. Kaderli, A. D. Zuberbühler, *Acc. Chem. Res.* **1997**, *30*, 139.
28 D.-H. Lee, N. Wei, N. N. Murthy, Z. Tyeklár, K. D. Karlin, S. Kaderli, B. Jung, A. D. Zuberbühler, *J. Am. Chem. Soc.* **1995**, *117*, 12498.
29 C. X. Zhang, S. Kaderli, M. Costas, E.-i. Kim, Y.-M. Neuhold, K. D. Karlin, A. D. Zuberbühler, *Inorg. Chem.* **2003**, *42*, 1807.
30 D.-H. Lee, N. N. Murthy, K. D. Karlin, *Inorg. Chem.* **1996**, *35*, 804.
31 K. D. Karlin, J. C. Hayes, J. Shi, J. P. Hutchinson, J. Zubieta, *Inorg. Chem.* **1982**, *21*, 4106.
32 D. Ostfield, I. A. Cohen, *J. Chem. Educ.* **1972**, *49*, 829.
33 C. J. O'Connor, *Prog. Inorg. Chem.* **1982**, *29*, 203.
34 K. D. Karlin, M. S. Haka, R. W. Cruse, G. J. Meyer, A. Farooq, Y. Gultneh, J. C. Hayes, J. Zubieta, *J. Am. Chem. Soc.* **1988**, *110*, 1196.
35 G. R. Newkome, G. E. Kiefer, Y. A. Frere, M. Onishi, V. K. Gupta, F. R. Fronczek, *Organometallics* **1986**, *5*, 348.
36 H. Saltzman, J. G. Sharefkin, *Iodosobenzene*, New York, **1973**.
37 J. K. Romary, R. D. Zachariasen, J. D. Garger, H. Schiesser, *J. Chem. Soc.* **1968**, 2884.
38 R. C. Larock, *Comprehensive Organic Transformations*, 2nd ed., Wiley-VCH, New York, **1999**.
39 K. D. Karlin, Z. Tyeklár, A. Farooq, M. S. Haka, P. Ghosh, R. W. Cruse, Y. Gultneh, J. C. Hayes, P. J. Toscano, J. Zubieta, *Inorg. Chem.* **1992**, *31*, 1436.

40 R. R. Osborne, W. R. McWhinnie, *J. Chem. Soc. A* **1967**, 2075.
41 D. K. Coggin, J. A. Gonzalez, A. M. Kook, D. M. Stanbury, L. J. Wilson, *Inorg. Chem.* **1991**, *30*, 1115.
42 A. G. Blackman, W. B. Tolman, *Struct. Bonding (Berlin)* **2000**, *97*, 179.
43 F. L. Urbach, U. Knopp, A. D. Zuberbühler, *Helv. Chim. Acta* **1978**, *61*, 1097.
44 C. A. Sprecher, A. D. Zuberbühler, *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 189.
45 M. Kodera, Y. Tachi, T. Kita, H. Kobushi, Y. Sumi, K. Kano, M. Shiro, M. Koikawa, T. Tokii, M. Ohba, H. Okawa, *Inorg. Chem.* **2000**, *39*, 226.
46 M. C. Weiss, V. L. Goedken, *J. Am. Chem. Soc.* **1976**, *98*, 3389.
47 J. A. Switzer, J. F. Endicott, *J. Am. Chem. Soc.* **1980**, *102*, 1181.
48 L. K. Thompson, B. S. Ramaswamy, *Inorg. Chem.* **1986**, *25*, 2664.
49 A. T. Morse, P. B. Ayscough, L. C. Leitch, *Can. J. Chem.* **1955**, *33*, 453.
50 G. Bandoli, A. Dolmella, T. I. A. Gerber, J. G. H. du Preez, H. J. Kemp, *Inorg. Chim. Acta* **1994**, *217*, 141.
51 S. Sommerer, W. P. Jensen, R. A. Jacobson, *Inorg. Chim. Acta* **1990**, *172*, 3.
52 S. O. Sommerer, J. D. Baker, W. P. Jensen, A. Hamza, R. A. Jacobson, *Inorg. Chim. Acta* **1993**, *210*, 173.
53 P. K. Byers, A. J. Canty, L. M. Engelhardt, J. M. Patrick, A. H. White, *J. Chem. Soc., Dalton Trans.* **1985**, 981.
54 T. I. A. Gerber, H. J. Kemp, J. G. H. Du Preez, G. Bandoli, *J. Coord. Chem.* **1993**, *28*, 329.
55 S.-L. Wang, J. Richardson, J. W. S. J. Briggs, R. A. Jacobson, W. P. Jenson, *Inorg. Chim. Acta* **1986**, *111*, 67.
56 Z. Serna, M. G. Barandika, R. Gortés, M. Karmele Urtiaga, M. I. Arriortua, *Polyhedron* **1998**, *18*, 249.
57 G. Davies, M. A. EI-Sayed, *Comments Inorg. Chem.* **1985**, *4*, 151.
58 K. G. Caulton, G. Davies, E. M. Holt, *Polyhedron* **1990**, *9*, 2319.
59 C. Lapinte, H. Riviere, J. Roselli, C. Fabre, *J. Chem. Soc., Chem. Commun.* **1981**, 1109.
60 S. M. Nelson, F. Esho, A. Lavery, M. G. B. Drew, *J. Am. Chem. Soc.* **1983**, *105*, 5693.
61 N. Kitajima, T. Koda, S. Hashimoto, T. Kitagawa, Y. Moro-oka, *J. Am. Chem. Soc.* **1991**, *113*, 5664.
62 E. Monzani, G. Battaini, A. Perotti, L. Casella, M. Gullotti, L. Santagostini, G. Nardin, L. Randaccio, S. Geremia, P. Zanello, G. Opromolla, *Inorg. Chem.* **1999**, *38*, 5359.
63 K. D. Karlin, Y. Gultneh, J. C. Hayes, J. Zubieta, *Inorg. Chem.* **1984**, *23*, 519.
64 P. P. Paul, K. D. Karlin, *J. Am. Chem. Soc.* **1991**, *113*, 6331.
65 H. V. Obias, Y. Lin, N. N. Murthy, E. Pidcock, E. I. Solomon, M. Ralle, N. J. Blackburn, Y.-M. Neuhold, A. D. Zuberbühler, K. D. Karlin, *J. Am. Chem. Soc.* **1998**, *120*, 12960.
66 S. Wang, Z. Pang, J.-C. Zheng, M. J. Wagner, *Inorg. Chem.* **1993**, *32*, 5975.
67 M. Håkansson, M. Örtendahl, S. Jagner, M. P. Sigalas, O. Eisenstein, *Inorg. Chem.* **1993**, *32*, 2018.
68 F. S. Keij, J. G. Haasnoot, A. J. Oosterling, J. Reedijk, C. J. O'Connor, J. H. Zhang, A. L. Spek, *Inorg. Chim. Acta* **1991**, *181*, 185.
69 V. McKee, S. S. Tandon, *J. Chem. Soc., Dalton Trans.* **1991**, 221.
70 J. T. Guy, J. C. Cooper, R. D. Gilardi, J. L. Flippen-Anderson, C. F. George, *Inorg. Chem.* **1988**, *27*, 635.
71 J. Reim, R. Werner, W. Haase, B. Krebs, *Chem. Eur. J.* **1998**, *4*, 289.
72 A. M. Atria, A. Vega, M. Contreras, J. Valenzuela, E. Spodine, *Inorg. Chem.* **1999**, *38*, 5681.
73 M. Y. Han, K. S. Min, M. P. Suh, *Inorg. Chem.* **1999**, *38*, 4374.
74 P. Chaudhuri, D. Ventur, K. Wieghardt, E.-M. Meters, K. Peters, A. Simon, *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 57.
75 M. Ruf, H. Vahrenkamp, *J. Chem. Soc., Dalton Trans.* **1995**, 1915.
76 G. A. Ardizzoia, M. A. Angaroni, G. La Monica, F. Cariati, S. Cenini, M. Moret, N. Masciocchi, *Inorg. Chem.* **1991**, *30*, 4347.
77 H. Gampp, A. D. Zuberbühler, *J. Mol. Catal.* **1980**, *7*, 81.
78 H. Gampp, D. Haspra, W. Spieler, A. D. Zuberbühler, *Helv. Chim. Acta* **1984**, *67*, 1019.
79 M. A. El-Sayed, A. Abu-Raqabah, G. Davies, A. El-Toukhy, *Inorg. Chem.* **1989**, *28*, 1909.
80 C. Jallabert, C. Lapinte, H. Riviere, *J. Mol. Catal.* **1980**, *7*, 127.