Tuning Copper−Dioxygen Reactivity and Exogenous Substrate Oxidations via Alterations in Ligand Electronics

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The chemistry of copper(I)−dioxygen adducts are of intrest owing to their importance in biological and industrial processes.[1,2] Although several Cu_n−O_n binding modes have been described, the best represented are the binuclear Cu^{II}_2−peroxo species, which can bind either in the μ-1,2- (end-on) or the μ-η^2-η^2- (side-on) fashion, depending on the ligand donor type and chelate denticity.[1−5] The side-on peroxo−Cu_2^{II} complexes can exist in equilibrium with isomeric bis-μ-oxo $Cu^{III}_2(\mu$-O$)_2$ species.[1,5,6] While the position and existence of this equilibrium has been shown to be influenced by ligand identity, steric bulk, counterion, and solvent effects,[1,5,7] there has been no information concerning how pure variations in ligand electronics can influence the peroxo/bis-μ-oxo equilibrium and substrate reactivity. To better understand this aspect of Cu^I_n−O_2 chemistry, a series Cu^I complexes containing 4-pyridyl substituted tridentate bis[2-(2-pyridyl)ethyl]methylamine ligands were prepared, ([Cu^I(R-MePY2)]B(C_6F_5)$_4$ (1^R- B(C_6F_5)$_4$, R = Cl-, H-, MeO-, Me$_2$N-).[8] Here we report that the different electronic effects imposed by varying the R-group considerably influences Cu^I/O_2 reactivity and the nature of the adduct formed. These complexes are also observed to perform 2-electron oxidations of atypical exogenous substrates, exhibiting dramatically enhanced reaction rates as the R-group is made more electron-donating.

An X-ray crystal structure of 1^{Me2N}-B(C_6F_5)$_4$ (Figure 1B) shows that the copper center is contained in a distorted three-coordinate geometry, as has been previously observed with similar ligands.[5,9] This differs from the other derivatives of 1^R (R = Cl, H, MeO), possessing less electron-donating 4-pyridyl substituents, where pseudotetrahedral (MeCN fourth ligand) coordination is observed (Figure 1A).[10] The effects of incremental increases in the electron-donating ability of the ligands to the Cu^I center are also evident in the Cu^{II}−Cu^I redox potentials of the 1^R series. Copper(I) complex 1^{Me2N} ($E_{1/2} = -440$ mV vs FeCp$_2$/FeCp$_2^+$) is measurably easier to oxidize than the MeO, H, and Cl derivatives of 1^R, which possess $E_{1/2}$ values of −360, −310, and −270 mV, respectively. The CO stretching frequencies ([Cu^I(R-MePy2)(CO)](B(C_6F_5)$_4$) (1^R-CO, generated by bubbling CO through CH_2Cl_2 solutions of 1^R) display modest but expected systematic shifts in ν_{CO}, ranging from 2093 cm^{-1} for 1^{Cl}-CO to 2075 cm^{-1} for 1^{Me2N}-CO.

The Cu^I complexes 1^R are stable in O_2 free CH_2Cl_2 for days. For R = H, MeO, and Me$_2$N, bubbling of O_2 through solutions of 1^R at −80 °C results in the rapid and full production (seconds to minutes) of the corresponding O_2 adducts (Scheme 1), which are stable in the absence of exogenous substrate (decomposition rates at −80 °C are <10^{-7} s^{-1}). As previously observed for 1^H,[11] and
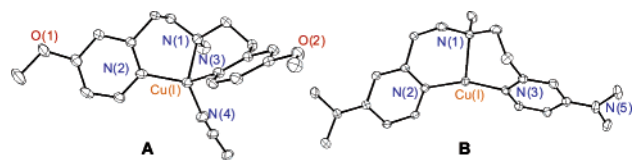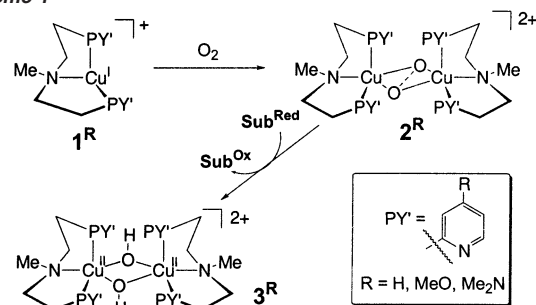
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Figure 1. ORTEP diagrams: [Cu^I(MeO-MePY2)(MeCN)]$^+$ (A, 1^{MeO}) and [Cu^I(Me$_2$N-MePY2)]$^+$ (B, 1^{Me2N}).

Scheme 1

confirmed by resonance Raman studies in solution,[12] the products [{Cu^{II}(R-MePY2)}$_2$(O$_2$)](B(C_6F_5)$_4$)$_2$ (2^R) are primarily μ-η^2-η^2-side-on peroxo−Cu^{II}_2 complexes ($\lambda_{max} \approx 360$ nm), with small amounts of bis-μ-oxo−Cu_2^{III} species present.[12]

The formation of 2^{Me2N} from 1^{Me2N} in O_2-saturated CH_2Cl_2 solutions was monitored by stopped-flow kinetics,[8] and fit to an overall third-order reaction (first-order in O_2, second-order in 1^{Me2N}) with $k_{on} = 8.2(6) \times 10^4$ M^{-2} s^{-1} (183 K). Although no intermediates were observed, the negative enthalpy ($\Delta H^{\ddagger} = -20.3(6)$ kJ mol^{-1}) and entropy ($\Delta S^{\ddagger} = -219(3)$ J mol^{-1} K^{-1}) of activation are indicative of the initial formation of an unstable superoxo species ($Cu/O_2 = 1:1$) in a rapid left-lying equilibrium.[5,11,13,14] No O_2 adduct forms when bubbling dioxygen through solutions of 1^{Cl} (−80 °C to room temperature (RT)); only slow oxidation (hours) of 1^{Cl} occurs at RT. This is clearly an electronic effect imposed by the electron-withdrawing abilities of the Cl group, which makes electron transfer from Cu(I)-to-O_2 less favorable.

Solutions of 2^R readily oxidize a variety of substrates, forming the corresponding bis-μ-hydroxy−Cu^{II}_2 complexes [{Cu^{II}(R-MePY2)}$_2$(OH)$_2$](B(C_6F_5)$_4$)$_2$ (3^R, R = H, OMe, Me$_2$N)[8,15] and the 2-electron oxidation products (Scheme 1, Table 1). These reactions are noncatalytic even when excess O_2 and substrate are present in solution. Oxidation of 9,10-dihydroanthracene (DHA) to anthracene proceeds in high yields for all three 2^R complexes. Efficient tetrahydrofuran (THF) oxidation to 2-hydroxytetrahydro-furan (THF-OH) is also observed. Such reactivity has been observed with manganese,[16] vanadium,[17] cobalt,[18] and iron[19] complexes (with

Table 1. Products, Yields, and Rate Constants for Substrate Oxidations Induced by 2^R in Dichloromethane at -80 °C

	H^a	MeO^a	Me_2N^a
9,10(DHA) → anthracene	81%	93%	98%
THF → THF−OH	67%	82%	84%
	$2(1) \times 10^{-5}$	$7(1) \times 10^{-4}$	$3(1) \times 10^{-2}$
DMA → *N*-methylaniline + $CH_2{=}O^b$	69%	83%	96%
$PhCH_2OH \rightarrow PhCH{=}O$	72%	88%	quant.
$Ph_2CHOH \rightarrow Ph_2C{=}O$	79%	92%	quant.
$MeOH \rightarrow CH_2{=}O$	31%	38%	37%
	$5(1) \times 10^{-5}$	$9(1) \times 10^{-4}$	$1(1) \times 10^{-1}$

^{a} Top values are yields determined by GC, and bottom values are pseudo-first-order reaction rate constants given in s^{-1}. ^{b} Based on the amount of *N*-methylaniline produced.

low yields and side products). The oxidation of THF has never been observed with a copper species, but with 2^R this reaction is both high-yielding (Table 1) and results in mainly THF-OH formation.[20] When THF is oxidized with ^{18}O-incorporated 2^R, over 80% of the THF-OH formed contains an ^{18}OH moiety, indicating that the hydroxylation of THF involves the transfer of oxygen from the dicopper complex to the substrate. There is a dramatic substituent effect; yields of THF-OH increase and oxidation rates are enhanced by ~1500-fold (Table 1) as the ligand 4-pyridyl group is made more electron-donating.[34]

N,N′-Dimethylaniline (DMA) was also examined as a substrate for 2^R. Extensive work has been accomplished using DMA as a substrate for oxidation events in cytochrome P450 metalloenzymes,[21-23] and models.[24] Intramolecular oxidative N-dealkylations have been observed in $Cu^{II}_2{-}O_2$ species (i.e., ligand degradation),[25-27] but DMA has never been used as a potential substrate for Cu_nO_n complexes. Solutions of 2^R all readily oxidatively N-dealkylate DMA, forming methylaniline, formaldehyde, and 3^R in excellent yields, with 2^{Me2N} being the significantly more efficient oxidant (Table 1).

Benzyl alcohol and benzhydrol, which have previously been utilized in $Cu^{II}_n{-}O_n$ substrate oxidation chemistry,[28-32] are both readily oxidized by 2^R to benzaldehyde and benzophenone, respectively. Surprisingly, the relatively inert alcohol methanol[31] is also oxidized by dichloromethane solutions of 2^R. Only the 2-electron oxidation products are obtained (aldehydes and ketones), with no further oxidation products observed. The general trends in reactivity of 2^R follows that noted above; as R is made more electron-donating, yields substantially improve, and oxidation rates increase by ~2000× going from R = H to R = Me_2N (Table 1).

In summary, we have shown for the first time clear ligand electronic influences on the formation and subsequent reactivity of dioxygen adducts of copper(I) complexes with tridentate ligands. In particular, 2^{Me2N} exhibits exceptionally high reactivity toward newly examined and interesting exogenous substrates such as THF and DMA. It will be of interest to determine the origin of the enhanced reactivity for 2^{Me2N} relative to those of 2^{MeO} and 2^H.[12,33]

Supporting Information Available: Contains a detailed Experimental Section, UV/vis spectra of 2^H, 2^{MeO}, and 2^{Me2N}, and kinetics plots (PDF). Crystallographic data for 1^{Me2N} and 1^{MeO} (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(33) The increased amount of bis-μ-oxo−Cu^{III}_2 in solution (ref 12) alone cannot account for the >3 order of magnitude increase in oxidation rates.

(34) It appears that trace water is required for this reaction, to proceed to final bis-hydroxo complex 3^R (Scheme 1), and primary isotope effects are observed (for THF vs THF-d_8), indicating that the reaction is proceeding via a rate-limiting oxidative C−H bond cleavage. Studies are in progress.

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