Dioxygen–Copper Reactivity: Intermediacy of a Peroxo–Dicopper(II) (Dioxygen–Copper) Complex in the Hydroxylation Reaction of a Model Mono-Oxygenase System

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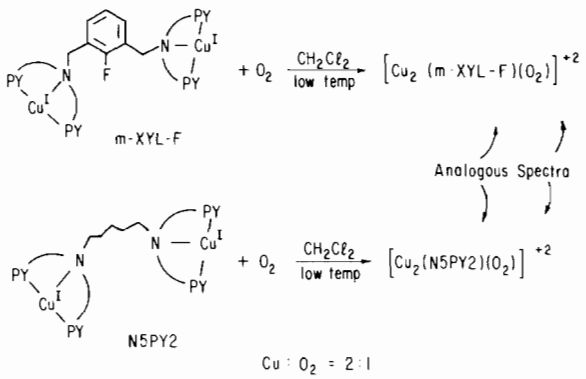
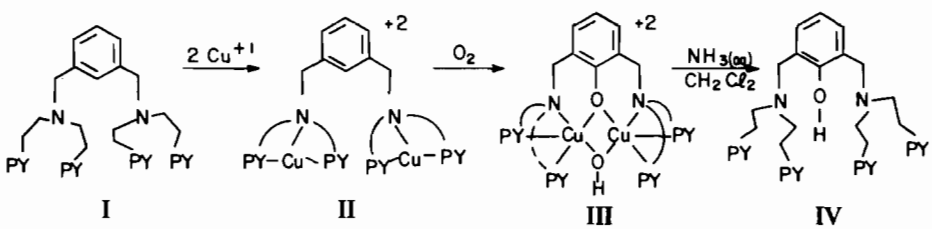
We have previously described a copper monooxygenase model system in which an aromatic ring, which is part of a dinucleating ligand, is hydroxylated [1, 2]. Thus, a three-coordinate dinuclear copper(I) complex, **II**, of the dinucleating ligand *m*-XYL (**I**) reacts with dioxygen (O_2), resulting in the oxygenation of the ligand and concomitant formation of the phenoxo- and hydroxo-bridged dinuclear Cu(II) complex **III**. The free phenol, **IV**, can be isolated by extraction from compound **III**. The reaction of **II** + O_2 → **III** is reminiscent of the action of the copper monooxygenases such as tyrosinase [3] and dopamine β-hydroxylase [3b, 4] since one atom of O_2 is incorporated into the organic substrate and the stoichiometry of the reaction is $Cu:O_2 = 2:1$.

Mechanistic studies of this reaction are ongoing [5] and we have also presented some evidence for the intermediacy of a peroxo–dicopper(II) complex through the observation that the reaction of a dicopper(II) species of **I** with hydrogen peroxide results in the same product **III** [6]. Here, we present further indication for the same intermediate, but the evidence is derived from the observed reactivity of dioxygen with dicopper(I) complexes of analogs of **I**. The ligands are *m*-XYL-F and N5PY2, both of which contain the same amine-pyridyl tridentate unit (PY2) as is found in **I**. In the case of *m*-XYL-F, the only difference between this and **I** is that the C–H bond which is cleaved in the reaction of **II** with O_2 is replaced by a C–F moiety, rendering the copper(I) complex of *m*-XYL-F much less reactive. N5PY2 possesses a 5-carbon methylene chain between the amine nitrogen atoms of the PY2 units, instead of the xylyl group. Both *m*-XYL-F and N5PY2 are close analogs of **I** since they have five-carbon units separating the PY2 groups of the dinucleating ligands.

The ligand *m*-XYL-F was prepared by synthesizing 2,6-bis-(bromomethyl)fluorobenzene via the diazotization of 2,6-dimethylaniline using standard procedures and flourination with HF/pyridine followed by bromination which was effected by using *N*-bromosuccinamide in CCl_4. Addition of PY2 in the presence of base afforded the desired dinucleating ligand after column chromatography. The dicopper(I) complex, $[Cu_2(m\text{-XYL-F})](PF_6)_2$, was prepared by the anaeorbic addition of two equivalents of $Cu(CH_3CN)_4PF_6$ to the ligand in methanol, followed by evaporation and crystallization at 0 °C. Recrystallization from dichlormethane/Et_2O afforded pure light yellow crystalline material†. The ligand N5PY2 and the dicopper(I) complex $[Cu_2(N5PY2)(CO)_2)]^{+2}$ were prepared as described elsewhere [7].



†*Anal.* for $[Cu_2(m\text{-XYL-F})](PF_6)_2$. Calc. for $C_{36}H_{39}Cu_2F_{13}N_6P_2$: C, 43.60; H, 3.96; N, 8.47. Found: C, 43.63; H, 3.94; N, 8.61%.



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We have recently shown that a dicopper(I) complex of N5PY2 and other similar ligands can bind both CO and O_2 reversibly [7]. Thus, the reaction of $[Cu_2(N5PY2)]^{+2}$ (generated *in situ* from the dicarbonyl adduct) with O_2 at −80 °C in CH_2Cl_2 gives a dark brown colored solution which is due to a compound formulated as $[Cu_2(N5PY2)(O_2)]^{+2}$ and best described as a peroxo–dicopper(II) complex [7]. Here, manometric measurements at low temperature indicate that $Cu:O_2 = 2:1$ and the complex is characterized by three strong absorptions in the UV–Vis region which can be assigned to $O_2^{2-} \rightarrow$ Cu(II) charge-transfer transitions: λ_{max} (ϵ, M^{-1} cm^{-1}), 360 nm (21 400), 425 nm (3600), 520 nm (1200). Interestingly, the dicopper(I) complex of *m*-XYL-F exhibits a very similar spectrum when it is oxygenated under similar conditions with λ_{max} (ϵ, M^{-1} cm^{-1}), 360 nm (18 700), 435 nm (4400), 515 nm (1300). Since $Cu:O_2 = 2:1$ is observed in this case as well, we suggest that a complex formulated as $[Cu_2(m\text{-XYL-F})(O_2)]^{+2}$ is generated here and that this and the N5PY2 analog are very similar in nature. Furthermore, if we oxygenate the 'native' compound, $[Cu_2(m\text{-XYL})]^{+2}$, at low temperature we are able to see transient intense absorptions at 360 nm (*) and 435 nm (*) although even at −80 °C the oxygenation reaction involving **II** → **III** is very rapid[§]. It is also notable that the UV–Vis spectra of these dioxygen/copper species are more similar to each other than they are to complexes of ligands containing other than a five-carbon unit which separates the PY2 groups [7].

[§]While the intensity of the absorptions appears to be comparable to those observed for complexes of *m*-XYL-F and N5PY2, accurate extinction coefficients cannot be obtained.

The analogy of the ligands *m*-XYL-F and N5PY2 with **I**, the stoichiometry of dioxygen uptake ($Cu:O_2 = 2:1$) and the close similarity of the spectra of oxygenated dicopper(I) complexes of these ligands provide further evidence that the hydroxylation reaction **II** + O_2 → **III** initially proceeds via the formation of a peroxo–$Cu(II)_2$ species. Investigations which may give additional insights into the mechanism of the hydroxylation reaction are currently in progress.

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