Functional Analogues of Cytochrome *c* Oxidase Active Site: Possible Effects of the Histidine-Tyrosine Cross-link and Cu_B

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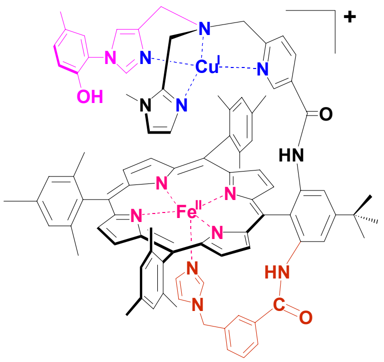
Cytochrome *c* oxidase (C*c*O), a terminal enzyme of the respiratory chain, catalyzes the reduction of molecular oxygen to water and harness the energy from this reaction to pump protons across the membrane. Since the discovery of the presence of the histidine-tyrosine cross-link in the proximity of the heme a_3/Cu_B binuclear active site, several functional/structural roles played by this unique cross-link have been proposed and it triggered many chemists to model this moiety in the hope of understanding its exact role(s) involved during the catalytic cycle. It remains uncertain whether Cu_B serves mainly as an electron storage site or just as nonredox role to provide a reaction pathway that is not accessible for the O-O bond activation by the heme alone.

Biomimetic models that faithfully reproduce the active site of the heme a_3/Cu_B center will be indispensable to address questions that cannot be probed by working with the enzyme itself. We report herein the preparation of a novel heme/Cu C*c*O model, in which the heme is axially ligated by a covalently appended imidazole group and the copper binds to a cross-linked Tyr-His mimic.[1] The spectroscopic evidence demonstrates the unique transformation of the formed heme-μ-peroxo-Cu^{II} species to the heme-superoxo/Cu^{I} intermediate in the course of the oxygenation reaction at low temperature. The heme-superoxo/Cu^{I} intermediate, which derives from its precursor, a peroxo bridged Fe^{III}-O_2^{2-}-copper^{II} species, is more stable than the heme-only heme-superoxide. The results suggest that the binding and activation of dioxygen catalyzed by this heme/copper model compound, the copper ion not only plays a role as a redox center but also stabilizes the heme-superoxide intermediate; the cross-linked phenolic hydroxyl group is responsible for the generation of the corresponding superoxide intermediate, possibly collaborating with water molecules.



1. J.-G. Liu, Y. Naruta, F. Tani, *Angew. Chem. Int. Ed.* **2005**, *44*, 1836.