Theoretical perspective on C-H/O-H activation by Cu-O in biological and synthetic systems

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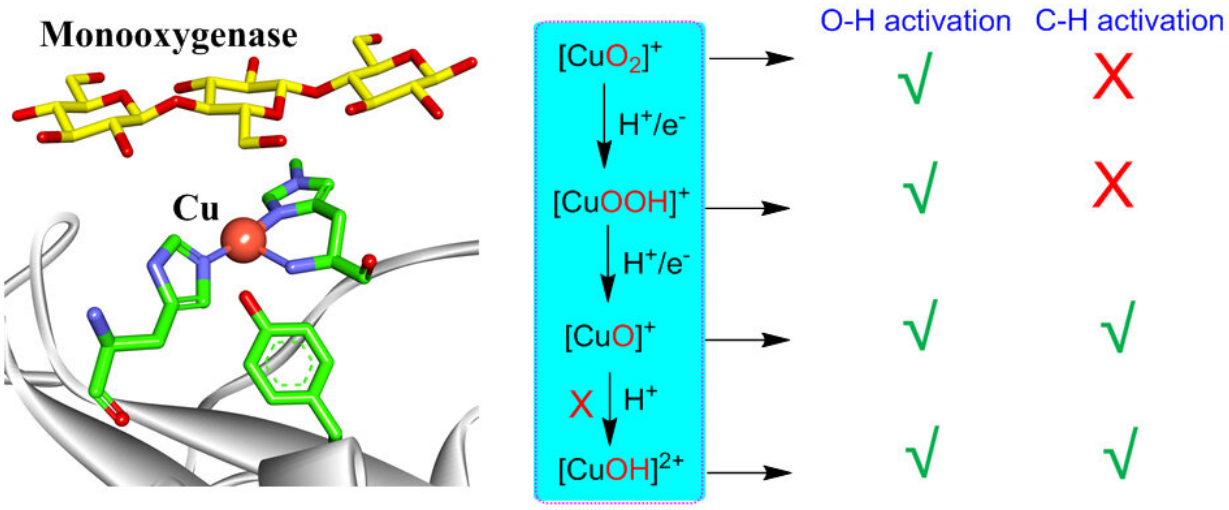

Dioxygen activation by mononuclear copper in biological and synthetic systems may generate various copper-oxygen intermediates including $[CuO_2]^+$, $[CuOOH]^+$, $[CuO]^+$, $[CuOH]^{2+}$. All these species are able to perform O-H activation, while only $[CuO]^+$ and $[CuOH]^{2+}$ are reactive for C-H activation. However, the formation of $[CuOH]^{2+}$ is highly unfavorable in monooxygenases, leaving $[CuO]^+$ as the only active intermediate responsible for C-H activation in monooxygenases. These insights can provide consistent understanding on reactivities of various copper-oxygen active species in biological and synthetic systems. Credit: *Chinese Journal of Catalysis*

Dioxygen activations constitute one of the core issues in copper-dependent metalloenzymes. Upon O_2 activation, copper-dependent metalloenzymes, including particulate methane monooxygenases (pMMOs), lytic polysaccharide monooxygenases (LPMOs) and binuclear copper enzymes PHM and DBM, are able to perform challenging C-H/O-H bond activations.

Meanwhile, copper-oxygen core-containing complexes have been synthetized to mimic the active species of metalloenzymes. Dioxygen activation by mononuclear copper active site may generate copper-oxygen intermediates, including Cu(II)-superoxo, Cu(II)-hydroperoxo, Cu(II)-oxyl as well as the Cu(III)-hydroxide species.

Intriguingly, all these species have been invoked as the potential active intermediates for C-H/O-H activations in either biological or synthetic systems. Due to the poor understanding of the reactivities of the copper-oxygen complex, the nature of active species in both biological and synthetic systems are highly controversial.

Recently, a research team led by Prof. Binju Wang from Xiamen University, China, gaged the reactivities of various mononuclear copper-oxygen species in both biological systems and the synthetic systems. The study shows:

- (a) the MN15 functional is highly accurate for mononuclear copper-oxygen complexes, in which the experimental kinetics of various C-H/O-H activations can be well reproduced with MN15.
- (b) Cu(II)-superoxo shows the consistent reactivities in both biological and synthetic systems: It is highly reactive for O-H bond activations but shows low reactivities for C-H bond activations. Thus, Cu(II)-superoxo could not be the active species for C-H activations in both biological and synthetic systems.
- (c) Cu(II)-hydroperoxo is inert for C-H bond activations, but its

radical character on the proximal O enables it to perform HAA from moderate O-H bonds or couple with another Cu(I) to form the dinuclear copper species. Thus, Cu(II)-hydroperoxo represents a key intermediate along the O_2 activation pathways rather than an oxidant for C-H activation in both biological and synthetic systems.

- (d) Cu(II)-oxyl is highly reactive for C-H bond activations and thus could be responsible for C-H activation in mononuclear copper monoxygenases.
- (e) Though the highly reactivities of copper(III)-hydroxide toward C-H bond activations have been well established, the formation of such species in monoxygenases is highly unfavorable thermodynamically.

These insights are expected to provide the consistent understanding on reactivities of various copper-oxygen active species in both biological and synthetic systems.

The review was published in the *Chinese Journal of Catalysis*.

More information: Peng Wu et al, Theoretical perspective on mononuclear copper-oxygen mediated C–H and O–H activations: A comparison between biological and synthetic systems, *Chinese Journal of Catalysis* (2022). DOI: 10.1016/S1872-2067(21)63974-8

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