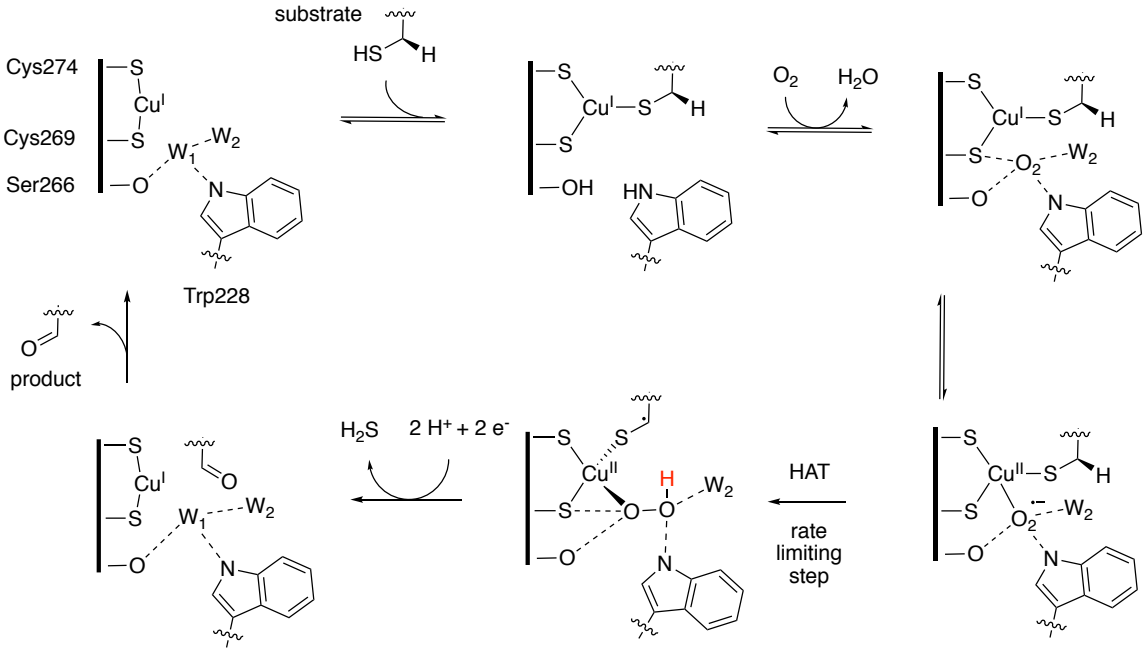
O_2-activation by the copper-dependent formylglycine-generating enzyme

Florian P. Seebeck[1]
[1]*Department of Chemistry, University of Basel, Mattenstrasse 24a, Basel 4002, Switzerland*
florian.seebeck@unibas.ch

Reductive activation of O_2 to superoxide is the first catalytic step in O_2-utilization by mononuclear copper enzymes.[1] To facilitate the difficult electron transfer from Cu^I to O_2, this step is usually coupled to the thermodynamically favorable formation of a Cu^{II} superoxide coordination species. To minimize the activation barrier for this concerted process, the ligand sets and geometries of the copper centers in enzymes such as the lytic polysaccharide monooxygenases or the peptidyl-glycine-α-hydroxylating monooxygenase are tuned to stabilize Cu^{II} relative to Cu^I, and allow coordination of superoxide with minimal structural reorganization. The formylglycine generating enzyme (FGE) does not seem to follow this paradigm. This enzyme catalyzes conversion of specific cysteine residues in client proteins to formylglycine in a O_2-dependent two-electron oxidation reaction. In this presentation I will discuss our recent efforts to understand as to how the tris-thiolate coordinated Cu^I in FGE may react with O_2 and form a species that is reactive enough to mediate hydrogen atom abstraction from its substrate.[2, 3]



References

1. E. I. Solomon, D. E. Heppner, E. M. Johnston, J. W. Ginsbach, J. Cirera, M. Qayyum, M. T. Kieber-Emmons, C. H. Kjaergaard, R. G. Hadt and L. Tian, **114**, *Chem. Rev.*, 3659 - 3853 (2014)
2. F. Leisinger, D. A. Miarzlou and F. P. Seebeck, **60,** *Angew. Chem. Int. Ed. Engl.*, 6154 - 6159. (2021)
3. D. A. Miarzlou, F. Leisinger, D. Joss, D. Häussinger and F. P. Seebeck, **10,** *Chem. Sci.*, 7049 - 7058 (2019)