Unveiling selectivity in indole oxidation catalyzed by artificial heme-enzymes

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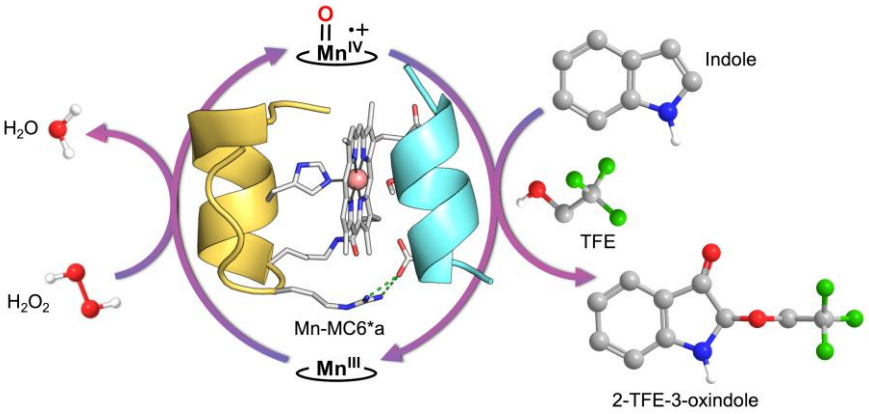
Selective oxidation of small molecules holding multiple reactive positions is a prevailing challenge in organic synthesis. Indole oxidation is an emblematic example of the difficulty to obtain a single product starting from a simple molecular scaffold.[1] This reaction has attracted considerable interest among researchers, owing that oxindole is a widely diffused structural motifs in bioactive compounds.[2] Recent advances in the field of enzyme design and engineering have significantly expanded the synthetic chemist's toolbox, providing a collection of catalysts featuring exceptional stereo- and/or regio-selectivity.[3] In this context, we have tackled the challenge of selectivity in indole oxidation by exploiting miniaturized metalloporphyrin-containing proteins, named "Mimochromes" (MCs). Among them, we have identified MC6*a as the most promising candidate for catalysis, and have screened its iron, manganese, and cobalt complexes for diverse reactivities.[4]



Here, we report indole oxidation catalyzed by Mn-MC6*a and show that this catalyst is able to regioselectively convert the substrate, promoting indole oxidation at the C3 position.[5] Notably, Mn-MC6*a outperforms natural and artificial heme-enzymes in terms of product selectivity. Interestingly, the presence of 2,2,2-trifluoroethanol (TFE) as a cosolvent, required for enhancing MCs peptide folding and catalytic performances, allowed us to trap a highly reactive 3-oxindole derivative. Further, we have performed a comparative analysis between the iron and manganese complexes of MC6*a through experimental and theoretical approaches, unravelling the role of the metal ion identity in the reaction pathway.

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