

ENZYME ACTIVITY BY DESIGN: AN ARTIFICIAL RHODIUM HYDROFORMYLASE FOR LINEAR ALDEHYDES

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The development of artificial enzymes is an emerging field driven by the prospect of highly selective and active catalytic chemical conversions for which natural enzymes are unavailable.¹ Nature exploits the molecular recognition properties of proteins to perform chemical transformations with high product specificity and excellent activity under benign conditions. Meanwhile, industry still relies on traditional transition metal catalysis due to a lack of enzymes for desired reactions such as CO and alkene insertion reactions. Artificial metalloenzymes (ArMs) combine synthetic metal catalysts with selective substrate binding protein scaffolds, thereby adding to the catalytic toolbox. Despite the rapidly increasing number of successful applications in unnatural reactions, most ArMs do not meet the rates and performances achieved by natural enzymes. In particular, the full power of enzymes in the form of strong molecular recognition and shape selectivity has not been fully exploited. We have combined robust site specific phosphine bioconjugation methodology² with a lipid-binding protein (SCP-2L)³ aiming at rational design of an artificial rhodium hydroformylase. This novel ArM displays remarkable activities and selectivities for the production of higher linear aldehydes under benign aqueous conditions. The ArM provides enzyme-like rate enhancement when compared to the traditional Rh-TPPTS system. Extensive characterization of the rhodium environment in this ArM by MS, IR, and XAFS, as well as selenium incorporation using SeMet, supports the presence of a monophosphine-rhodium center stabilized by methionine residues within the protein scaffold accounting for the high selectivities observed. Overall, our study demonstrates that specific protein binding scaffolds can be adapted to obtain enzymes that provide the reactivity of the introduced metal center combined with specifically intended product selectivity. Such approaches should inspire the development of new catalytic systems that utilize the powerful substrate binding capabilities of proteins.