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Dative coordination of a di-rhodium cofactor in a de novo protein

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PURPOSE OF THE ABSTRACT
Metal catalysts facilitate challenging chemical reactions such as C-C bond formations [1]. However, their regio- and enantioselectivity must often be dictated by large ligands that usually require multi-step syntheses. Combining a powerful metal catalyst such as di-rhodium(II,II) with the chiral environment of a protein to yield an artificial metalloenzyme allows for easier fine-tuning of the metal's microenvironment and is the basis for a large field of research [2]. Previous work has reported novel catalysts that consist of (i) Rh2 coordinated to peptides [3] or (ii) proteins linked to a Rh2 catalyst [4], which both exhibited improved regio- or enantioselectivity compared to conventional ligands.

Here we show a de novo designed protein scaffold with four central glutamic acid residues [5] that form an ideal coordination geometry to harbor a di-rhodium cofactor. By datively coordinating the metal to the amino acids of the protein, we envision a direct control over the reactivity of the metal by altering its second and third coordination spheres. Analytical methods, such as dynamic light scattering and analytical ultracentrifugation, show distinct changes in the shape of the protein upon metal addition. Inductively coupled plasma mass spectrometry indicates binding of the metal to the protein that cannot be observed in knockout variants.

We aim to demonstrate the correct placement of the metal by elucidating the structure of the holo-protein and through mass spectrometric analysis. Additionally, computational redesign of the protein surface will be used to minimize off-target binding of the metal. The envisioned reactions catalyzed by this artificial metalloenzyme include reactions not observed in natural enzymes, such as cyclopropanations or heteroatom-H insertions.

FIGURES

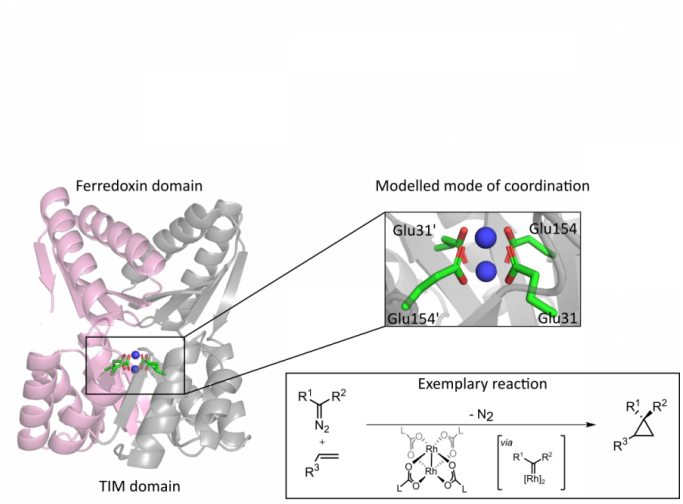

FIGURE 1

Artificial di-rhodium enzyme

Left: Model of the protein with a central di-rhodium cofactor. Bottom right: Exemplary reaction.

FIGURE 2

KEYWORDS

artificial metalloenzymes

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