BIOTRANS
LA ROCHELLE 2023

N°1137 / PC
TOPIC(s) : Artificial enzymes and de-novo enzyme design

Design and Optimisation of a De Novo Gold Artificial Metalloenzyme

AUTHORS
Elinor MORRIS / UNIVERSITY OF BASEL, MATTENSTRASSE 24A, BASEL

PURPOSE OF THE ABSTRACT

The ability to design and produce metalloenzymes from scratch could enable chemists to engineer artificial metalloenzymes with a vastly superior biocatalytic toolbox than is currently accessible. Such an ability may allow for the creation of an ‘ideal' enzyme for a given transformation, which could be expressed in high yields and with high (thermo)stabilities. The field of enzyme design has, however, lagged behind that of protein design in recent years, owing principally to the inherent computational challenges involved, as well as the many unknowns we still face with respect to how an enzyme's structure relates to its function [1].

Herein, we present preliminary results showcasing a thermostable de novo tandem repeat scaffold [2], computationally designed to bind to an artificial NHC-Au cofactor. We demonstrate that this scaffold binds the cofactor with micromolar affinity and effects gold-catalyzed hydroamination with higher turnover numbers (TONs) than the cofactors alone. Moreover, we show that mutation of active site residues in the protein scaffold can improve the enzyme's catalytic activity.

FIGURES

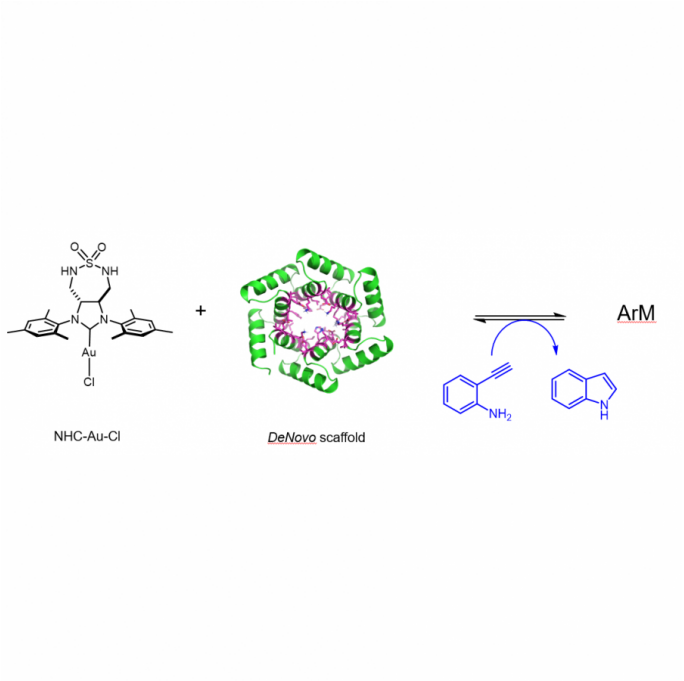

FIGURE 1

Artificial metalloenzyme (ArM) formation

Incubation of the NHC-Au cofactor with the computationally designed protein leads to the formation of an artificial metalloenzyme (ArM) which can effect gold catalysis. For example, the hydroamination reaction presented here.

FIGURE 2

KEYWORDS

Artificial Metalloenzyme | de novo design | gold catalysis | thermostable

BIBLIOGRAPHY

[1] Lovelock, S. L.; Crawshaw, R.; Basler, S.; Levy, C.; Baker, D.; Hilvert, D.; Green, A. P., Nature 2022, 606, 49-58

[2] Doyle, L.; Hallinan, J.; Bolduc, J.; Parmeggiani, F.; Baker, D.; Stoddard, B. L.; Bradley., Nature 2015, 528, 585-588