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Artificial [Mn]-hydrogenase for Asymmetric Transfer Hydrogenation

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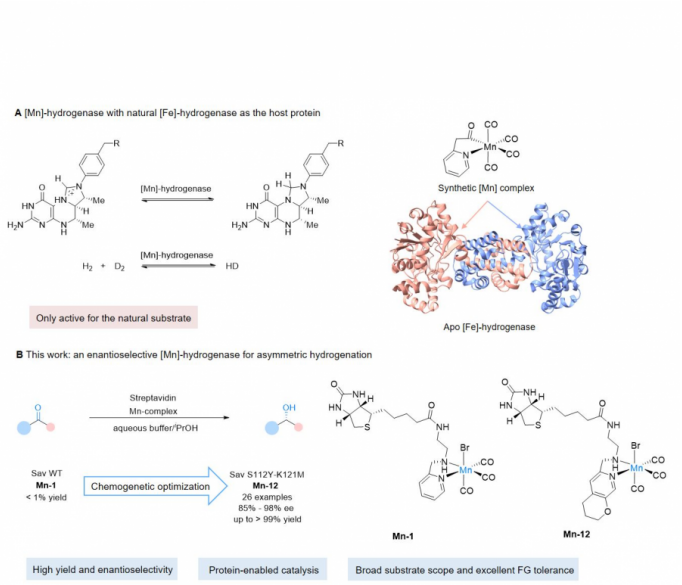
PURPOSE OF THE ABSTRACT
Natural hydrogenases exclusively choose Ni and Fe in [NiFe]-, [FeFe]- and [Fe]-hydrogenases for (asymmetric) hydrogenation reactions. However, these enzymes are generally with limited substrate scope. In contrast, artificial metalloenzymes (ArMs) can incorporate abiotic metal complexes into a protein scaffold, leading to a wider substrate diversity. Although synthetic Mn complexes have been successfully incorporated into natural [Fe]-hydrogenase (Fig. 1A), achieving enantioselective hydrogenation reactions has remained a challenge. Herein, we report the development of an enantioselective [Mn]-hydrogenase based on biotin-streptavidin technology (Fig. 1B). Through chemogenetic optimzation of the reaction conditions, we achieved up to 98% enantiomeric excess (ee) and > 99% yield. Additionally, this artificial metalloenzyme displayed excellent functional group tolerance and broad substrate scope, catalyzing asymmetric transfer hydrogenation of ketones with high yield and enantioselectivity (Fig. 2). By combining QM/MM calculation and X-ray crystallography, out findings suggest that the S112Y-K121M mutations, along with the chemical structure of the Mn cofactor, play critical roles in enhancing the reactivity and enantioselectivity of the enzyme. These results highlight the potential of manganese as a metal cofactor in the development of artificial metalloenzymes, and demonstrate the power of chemogenetic optimization for enzyme engineering.

FIGURES



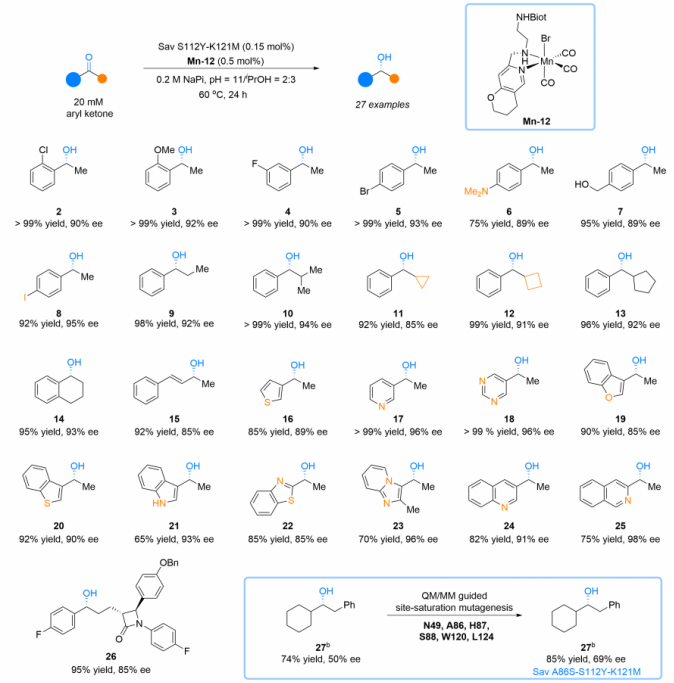


FIGURE 1

Development of artificial [Mn]-hydrogenase

A, previous work on artificial [Mn]-hydrogenase with natural [Fe]-hydrogenase as the host protein; B, this work: an enantioselective [Mn]-hydrogenase for asymmetric hydrogenation

FIGURE 2

Substrate scope of [Mn]-hydrogenase

This artificial metalloenzyme displayed excellent functional group tolerance and broad substrate scope, catalyzing asymmetric transfer hydrogenation of ketones with high yield and enantioselectivity

KEYWORDS

Biocatalysis | Artificial hydrogenase | Manganese catalysis

BIBLIOGRAPHY