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Artificial Metalloenzyme-Catalyzed Enantioselective Amidation via Nitrene Insertion in Unactivated C(sp3)-H Bonds

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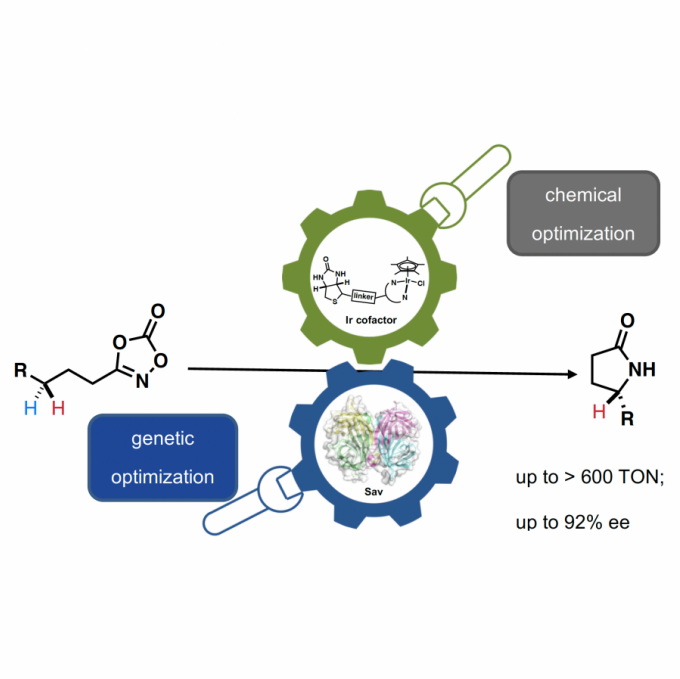
PURPOSE OF THE ABSTRACT

Enantioselective C-H amidation offers attractive means to assemble C-N bonds to synthesize high-added value, nitrogen-containing molecules. In the past few decades, complementary enzymatic and homogeneous-catalytic strategies for C-H amidation have been reported. Herein, we report on an Artificial Metalloenzyme (ArM) resulting from anchoring a biotinylated Ir-complex within streptavidin (Sav). The resulting ArM catalyzes the enantioselective amidation of unactivated C(sp3)-H bonds. Chemogenetic optimization of the Ir cofactor and Sav led to significant improvement in both activity and enantioselectivity. Up to > 600 TON and 92% ee for the amidation of unactivated C(sp3)-H bonds was achieved. X-ray analysis of the artificial nitrene insertase (ANIase) along the evolutionary trajectory sheds light on critical second coordination sphere contacts leading to improved catalytic performance.

FIGURES



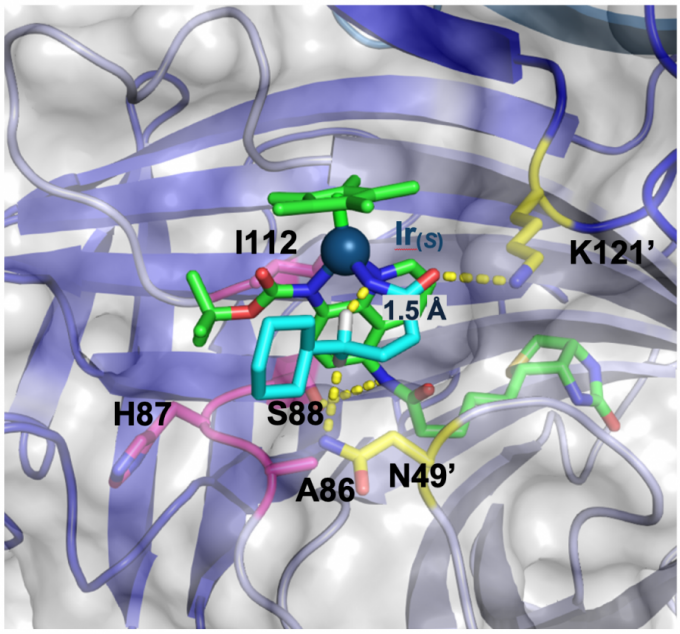


FIGURE 1

Artificial Metalloenzyme-Catalyzed Enantioselective Amidation via Nitrene Insertion in Unactivated C(sp3)-H Bonds

FIGURE 2

Computational study

QM-MM calculations of the reaction path leading to the enantiopure product based on crystal structures of the ANIase.

KEYWORDS

Artificial Metalloenzyme | Nitrene insertion | C-H activation | Chemogenetic optimization

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