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Novel Artificial Metalloenzymes for Copper-Catalyzed Enantioselective Michael Addition to Nitroalkenes

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PURPOSE OF THE ABSTRACT

To combine the attractive features of transition metal catalysis and biocatalysis, artificial enzymes, which consist of abiological catalytic moieties incorporated into protein scaffolds, have emerged as a promising strategy to realize non-natural reactions in biocatalysis. LmrR, a small, homodimeric protein that contains a large hydrophobic pore at its dimer interface, is a privileged scaffold for artificial metalloenzyme (ArM) design. Here, we incorporated the metal binding unnatural amino acid bipyridine alanine (BpyAla) into the protein scaffold LmrR through in vivo stop codon suppression and created a proficient and stereoselective artificial metalloenzyme (LmrR_XBpy) for catalytic asymmetric Michael addition of 2-acetyl azaarenes to nitroalkenes (up to 89±0% yield, 96±1% ee) (Fig 1). In our design, 2-acetyl azaarene 1 is activated by the new created [Cu-Bpy] site to form the enolate, whereas the aryl substituted nitroalkene 2 is the Michael acceptor, which is bound by the tryptophan residues (W96 and W96') via π-stacking interactions, to give the addition product 3. Furthermore, derivatizing the nitro compounds 3 into potential natural products or drug targets renders this methodology attractive for the green synthesis.

FIGURES

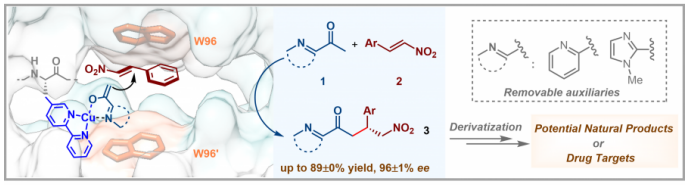

FIGURE 1

Fig. 1 Cu-catalyzed asymmetric Michael addition of 2-acetyl azaarenes to nitroalkenes in an artificial enzyme

This figure shows that our reaction design, inculding reaction mechanism and derivatization of products.

FIGURE 2

KEYWORDS

artificial metalloenzyme | copper catalysis | Michael addition of nitroalkenes | enantioselectivity

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