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Biosynthesis of valuable hydroxyl compounds via C=O/C-H asymmetric oxidoreductive reactions: Engineering of enzymatic selectivity

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PURPOSE OF THE ABSTRACT
Selective synthesis of valuable hydroxyl compounds has become as an attractive field due to the increasing demands of pharmaceuticals and biologically active natural products. In the pharmaceutical industry, hydroxyl compounds including chiral cyclic and heterocyclic alcohols and hydroxyl derivatives can serve as intermediates of many chiral drugs such as flossonol, (−)- prosopinine, (R)-ladostigil, sertraline, fosamprenavir, sulopenem, ezetimibe, aprepitant, and ibrutinib, etc. To date, the main strategies to selectively produce hydroxyl compounds are chemical and enzymatic methods. Most chemical methods apply complex chiral catalysts for asymmetric redox, addition, and ring opening reactions under harsh conditions. In turn, most enzymatic methods use alcohol dehydrogenase/reductases to catalyze C=O bond asymmetric reduction, P450 enzymes or dioxygenases for C−H bond asymmetric hydroxylation, and lipases to catalyze C−O bond asymmetric hydrolysis [1,2]. In this work, we highlight the development of the strategies for enzymes catalyzing selective synthesis of various valuable hydroxyl compounds, with focus on the asymmetric reduction of C=O bonds by ketoreductases [3,4] and the asymmetric hydroxylation of C−H bonds by hydroxylases [5], involving identification and engineering of the functional enzymes and construction of the enzymatic systems. These works present green and powerful strategies for the selective synthesis of valuable hydroxyl compounds.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

Hydroxyl compounds | Asymmetric biosynthesis | Ketoreductases | Hydroxylases

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