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anti-selective Epoxidation of α,β-unsaturated Aldehyde Enabled by Engineered Aldolase DERA

AUTHORS

Hangyu ZHOU / UNIVERSITY OF GRONINGEN, ANTONIUS DEUSINGLAAN 1, GRONINGEN
Corresponding author : Gerrit POELARENDS / g.j.poelarends@rug.nl

PURPOSE OF THE ABSTRACT

Chiral epoxides are versatile building blocks which are essential for the synthesis of biologically active compounds and chiral pharmaceuticals. The development of efficient catalysts for the synthesis of chiral epoxides has received considerable attention in recent times. We herein describe the anti-selective epoxidation of α,β-unsaturated aldehydes promoted by an engineered 2-deoxy-D-ribose-5-phosphate aldolase (DERA). After 5 rounds of directed evolution, the archetypical class I aldolase DERA was engineered into an efficient non-natural cofactor-independent peroxygenase. The resulting mutant DERA-EP has 277-fold enhanced peroxygenase activity over the DERA wild-type. In addition, DERA-EP accepts a broad array of α,β-unsaturated aldehydes and enables the 100 milligram-scale synthesis of the epoxy aldehyde in good to excellent crude yield (75-98%) with excellent conversion (>96%), enantiopurity (>95% e.r.) and high anti-diastereoselectivities for most of the cinnamaldehyde derivatives analyzed. This enzymatic strategy is complementary to numerous methodologies previously developed, such as syn-selective metal and amine catalysis, thus opening up a manifold of novel prospects for producing previously inaccessible compounds. From a broader perspective, these studies represent attractive starting points for further expanding the toolbox of enzymes for the practical synthesis of important chiral synthons.

FIGURES

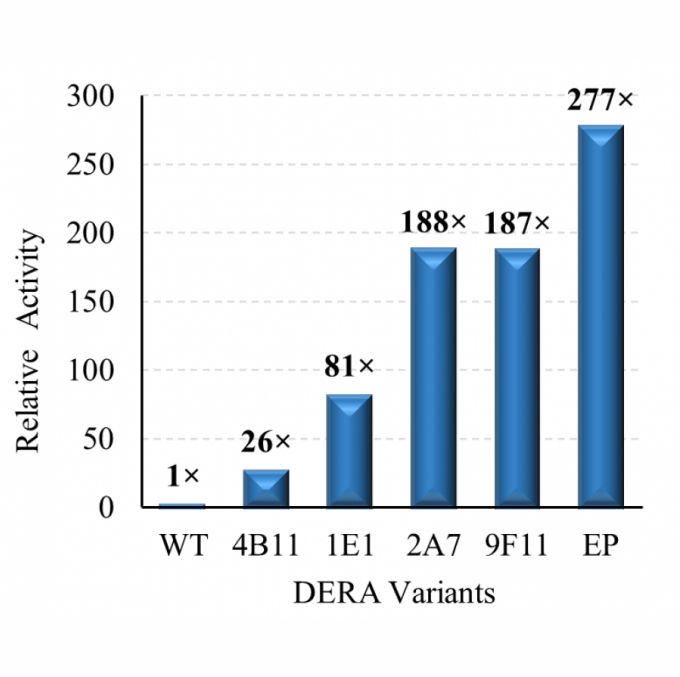

FIGURE 1

Comparison of the peroxygenase activity of wild-type DERA (WT) and engineered DERA variants.

no

FIGURE 2

KEYWORDS

anti-selectivity | enzyme engineering | catalytic promiscuity | peroxidation

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