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Development and Application of Amine and Imine Biocatalysts for the Synthesis of privileged Motifs

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PURPOSE OF THE ABSTRACT

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The synthesis of important amine-containing privileged motifs via a chemo-enzymatic route offers high chemo-, regio- and stereoselectivity with fewer synthetic steps and higher conversions. As opposed to traditional resolution techniques of racemic mixtures that are used in industry, the enzymatic reaction cascade of amine oxidase (AO) and imine reductase (IRED) uses less hazardous reaction conditions and reduces waste production. The chemo-enzymatic route combines the chemical synthesis of the enzymatic substrate, a substituted 1,2,5,6-tetrahydropyridine (THP) with a biocatalytic cascade. The cascade comprises of an AO which oxidises the THP to a conjugated iminium ion. Subsequent double reduction of the iminium by an IRED via an enamine leads to a desired substituted piperidine enantiomer. The chemo-enzymatic route is applied to the synthesis of Niraparib which exemplifies the opportunity this cascade provides for new synthetic strategies of known active pharmaceutical ingredients.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

amine oxidase | imine reductase | biocatalytic cascade | stereoselective reduction

BIBLIOGRAPHY