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Biocatalytic alkene isomerization for asymmetric synthesis

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PURPOSE OF THE ABSTRACT
Nowadays, the pharma and chemical industries are increasingly looking for cleaner routes to accessing chiral synthons in enantiopure form. For this reason, it is essential to control the stereochemistry of a chemical reaction while maximising the performance of the process and minimising waste[1].

The angelica lactones and gamma-valerolactones are versatile bio-based building blocks derived from glucose and represent platform chemicals with broad industrial applications, such as solvent production, fuel additives, precursors of bio-based polymers, building blocks of natural products and drugs, and fragrance/flavouring agents[2]. Unfortunately, most chemical methods available to isomerise the prochiral alpha-angelica lactone into the chiral beta-angelica lactone and, subsequently, access the reduced chiral gamma-valerolactone require harsh acid and base conditions and produce racemic products with low yields. Furthermore, only a few organocatalytic protocols can isomerise stereoselectively beta,gamma-unsaturated butenolides into the corresponding chiral gamma-substituted alpha,beta-unsaturated butenolides[3].

Recently, the promiscuous behaviour of flavin-dependent Old Yellow Enzymes (OYEs) able to isomerise asymmetrically alpha-angelica lactone in the absence of nicotinamide was identified[4]. We coupled this redox-neutral step with a nicotinamide-dependent bioreduction using originally two separate OYEs. The system was improved by designing a fusion bi-molecular protein to generate a one-pot enzymatic cascade for the formal stereo-divergent reduction of alpha-angelica lactone[2]. We are now exploring this synthetic platform on a range of non-activated C=C bonds to provide access to various chiral molecules in enantiopure form and with possible additional chiral centres.

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FIGURES

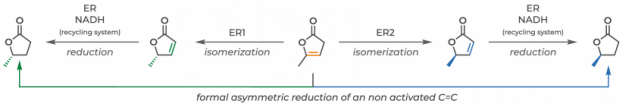

FIGURE 1

General approach to generate chiral lactones in a one-pot cascade.

FIGURE 2

Stereocomplementary isomerisation-reduction cascade catalysed by ene-reductases (ER) applied to alpha-angelica lactone.

KEYWORDS

Biocatalysis | One-pot enzymatic cascade | Flavin-dependent Old Yellow Enzymes (OYEs) | Stereocomplementary cascade

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