BIOTRANS
LA ROCHELLE 2023

N°1642 / PC
TOPIC(s) : (Chemo)enzymatic strategies

One-Pot Deracemization of sec-Alcohols Combining Photocatalytic Oxidation and Biocatalytic Reduction

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PURPOSE OF THE ABSTRACT

Chiral alcohols are versatile building blocks and have gained a particular interest in the asymmetric synthesis of non-racemic active pharmaceutical ingredients, agrochemicals, fragrances, flavors, natural products, etc. Herein we report on a practical and sustainable "one-pot" oxidation-reduction photo-biocatalytic process to synthesize enantiomerically enriched alcohols. In this regard, a relatively new ultra-efficient photocatalytic system, based on irradiation of the reaction mixtures with 440 nm blue LEDs in the presence of inexpensive 9-fluorenone as a metal-free photocatalyst and molecular oxygen as the terminal oxidant in dry DMSO as the solvent and hydrogen peroxide-neutralizing agent at once, was used to oxidize a broad range of (hetero)aromatic-aliphatic racemic alcohols into prochiral ketones quantitively (>99% conv.). The in situ formed carbonyl compounds were subsequently converted into corresponding chiral alcohols via a sequential biotranshydrogenation catalyzed by lyophilized E. coli cells overexpressing highly stereoselective and stereocomplementary recombinant short-chain alcohol dehydrogenases (ADHs) originated from Rhodococcus ruber (E. coli/ADH-A) or Rhodococcus erythropolis (E. coli/ReADH) to obtain (S)-alcohols and Lactobacillus kefir (E. coli/Lk-ADH) to obtain (R)-alcohols, respectively. Overall, the elaborated photo-biocatalytic deracemization of racemic alcohols using 9-fluorenone-O2-blue LED-DMSO-E. coli/ADH system carried out on a semi-preparative scale (0.25 mmol; 63 mM final conc. in 4 mL) yielded non-racemic alcohols with 82–99.9% conv., in up to 92% isolated yield, with high-to-excellent optical purity (97–99.9% ee), and complementary chirality.

FIGURES

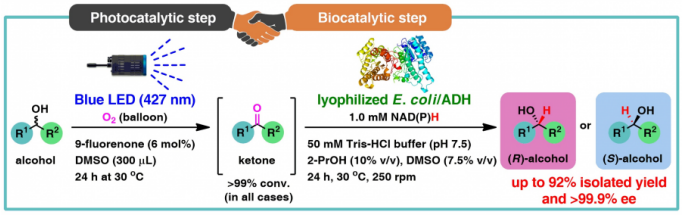

FIGURE 1

Figure 1.

"One-pot" photo-biocatalytic deracemization of sec-alcohols using 9-fluorenone-O2-blue LED-E. coli/ADH system

FIGURE 2

KEYWORDS

Photoredox catalysis | Biocatalysis | Chemo(enzymatic) cascades | Chiral alcohols

BIBLIOGRAPHY