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TOPIC(s) : (Chemo)enzymatic strategies

Enantiopure Sulfoxides via Cyclic Photobiocatalytic Deracemization

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PURPOSE OF THE ABSTRACT

The combination of biocatalysis and photocatalysis facilitates access to novel synthetic strategies which correspond very well to the requirements of more sustainable and resource-efficient synthesis concepts.[1] In here, we present a cyclic deracemization process combining an enantioselective enzyme-catalyzed sulfoxide reduction with an unselective photocatalyzed sulfide oxidation to yield the desired non-racemic sulfoxide targets.[2] The latter are valuable structural motifs, which occur in many active pharmaceutical ingredients, particularly in proton pump inhibitors such as omeprazole® and its derivatives, as well as in flavor and fragrance compounds.[3]

The enantioselective sulfoxide reduction of the racemic model substrate methyl-p-tolyl sulfoxide (MPTSO, R = CH₃) was achieved using an (S)-selective methionine sulfoxide reductase from *Pseudomonas alcaliphila* (paMsr),[4] yielding the corresponding methyl-p-tolyl sulfide, while leaving the unreacted (R)-MPTSO behind. The combination with a subsequent oxidation using various photocatalysts enabled a successful deracemization process towards (R)-MPTSO with enantiomeric excesses (ee) in the range of 56-99%. The biosynthesized photocatalyst protochlorophyllide[5] gave the best results in the deracemization process, yielding optically pure (R)-MPTSO (ee >99%). The concept was further extended by using the commercially available Eosin Y (EY) as photocatalyst for which the deracemization was run in a step-wise fashion in order to overcome incompatible reaction conditions since EY was found to not only degrade dithiothreitol (DTT), but also inactivate paMsr.

The generality of the system was demonstrated by applying a small library of biocatalysts as well as structurally diverse substrates to produce the desired optical pure sulfoxides.

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FIGURES

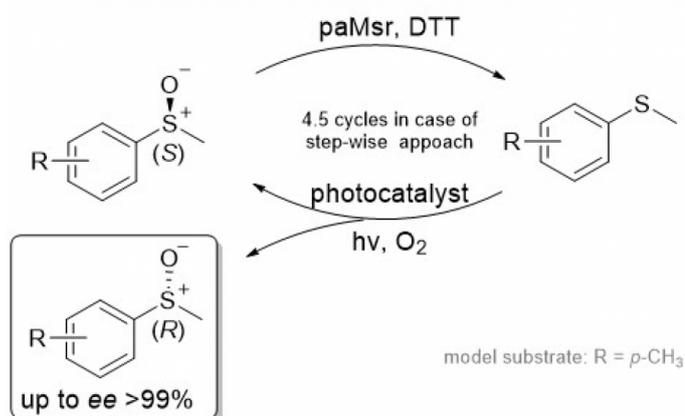


FIGURE 1

Cyclic Photobiocatalytic Deracemization

Figure 1. Cyclic (stepwise) deracemization of rac-sulfoxides via biocatalytic enantioselective reduction and subsequent unselective photocatalyzed oxidation.

FIGURE 2

KEYWORDS

cyclic deracemization | photobiocatalysis | sulfoxides

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