BIOTRANS
LA ROCHELLE 2023

N°1027 / PC
TOPIC(s) : Biocatalytic cascade reactions

A mild and chemoselective CALB biocatalysed synthesis of sulfoxides exploiting the dual role of AcOEt as solvent and reagent

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PURPOSE OF THE ABSTRACT
Sulfoxides are an important class of organic compounds that often are seen used in organic synthesis as chiral auxiliaries, synthons for C–C bond forming reactions, directing groups in C–H bond functionalisation and can partake in numerous other functionalisation reactions. Moreover, sulfoxides are widely found in pharmaceutically active ingredients such as the blockbuster drug omeprazole. Sulfoxides are commonly obtained through the oxidation of the corresponding sulfide precursor.1 However, the current methodologies adopted for their synthesis rely on the use of harsh chemicals such as nitric acid, hypohalites, peroxides and oxone, all of which present limited industrial use as can be shock sensitive and explosive, hence unsuitable for large scale production.2

Following our interest in the development of new and industrially applicable green methodologies for the synthesis of sulfur-containing drugs and drug-like synthons, herein we report a facile, chemoselective and scalable biocatalytic protocol for the synthesis of sulfoxides using immobilised Candida antarctica lipase B (CALB), a very robust enzyme which retains its activity in both aqueous and organic solvents, and AcOEt with a dual role of more environmentally friendly reaction solvent and enzyme substrate.3 A series of 27 sulfides that included alkyl, aryl, carbonyl and alkene bearing compounds as well as omeprazole were successfully oxidised in high yields and with excellent E-factors to the corresponding sulfoxides with little to no overoxidation by-products. In addition, a large-scale experiment starting from 3 g of sulfide substrate afforded the corresponding sulfoxide in excellent yield. Finally, a series of enzyme recyclability experiments were carried out to further confirm the industrial potentiality of the methodology.

This method proves to be cost effective, robust and selective with few side-reactions. Furthermore, we show that the use of AcOEt as solvent and CALB substrate improves the industrial sustainability of the method, providing an overall greener methodology.

FIGURES

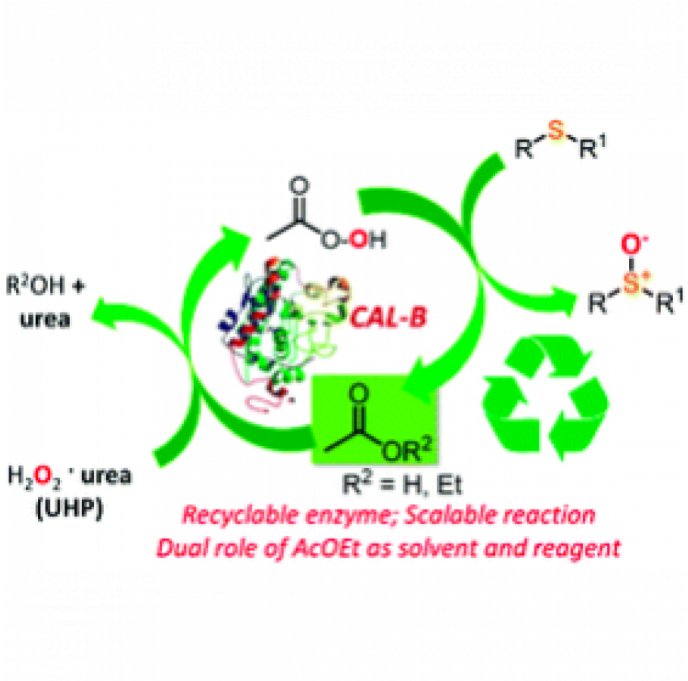

FIGURE 1

CALB for the biocatalytic synthesis of sulfoxides

A mild, chemoselective and sustainable biocatalysed synthesis of sulfoxides has been developed exploiting CALB and using AcOEt with a dual role of more environmentally friendly reaction solvent and enzyme substrate. A series of sulfoxides, including the d

FIGURE 2

KEYWORDS

sulfoxides | CALB | biocatalysis

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