Production of isophorone derivatives by fungal peroxygenases

CSIC has developed a biocatalytic transformation of isophorone (3,5,5-trimethylcyclohex-2-en-1-one) and 4-hydroxyisophorone (4HIP) to selectively produce 4-hydroxyisophorone and 4-ketoisophorone (4KIP), valuable products for pharmaceutical, flavor and fragrance industry. The biocatalysts employed are unspecific peroxygenases from the fungi or recombinant proteins expressed in *Aspergillus oryzae*. Industrial partners from pharmaceutical, flavour or fragance industry are being sought to collaborate through a patent licence agreement.

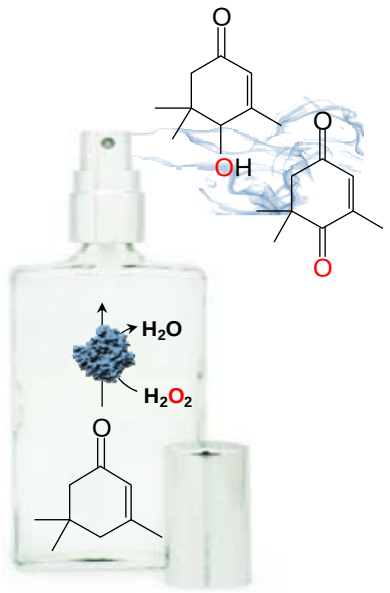
An offer for Patent Licensing

Environmentally friendly route

A direct chemical oxidation process of isophorone to 4HIP is not available in literature and this compound is usually synthesized by reduction of 4KIP which can be expensive as starting material. The route often employed for the synthesis of these molecules starts with the isomer β-isophorone but the rearrangement to isophorone is the main disadvantage.

Fungal peroxygenases are able to transfer an oxygen atom from H_2O_2 to isophorone selectively in C-4 to produce 4HIP and 4KIP generating H_2O as the only by-product.

The selection of the biocatalyst is important since the peroxygenase from *Chaetomium globosum* produced mainly 4HIP, the recombinant peroxygenase from *Humicola insolens* fastly produced 4KIP while the peroxygenase from *Agrocybe aegerita* was the most stereoselective enzyme producing (S)-4HIP with 88% enantiomeric excess. In addition, the (R)-enantiomer could be produced by kinetic resolution of the racemic 4HIP by the first two enzymes.



Enzymatic synthesis of F&F molecules 4HIP and 4KIP by fungal peroxygenases

Main innovations and advantages

- Novel simple and environmentally friendly route for the production of isophorone derivatives.
- These biocatalysts only require H_2O_2 or organic peroxides for activation, being H_2O the only by-product.
- Both (S) and (R) enantiomers of 4-hydroxyisophorone could be obtained with 88 and 100% enantiomeric excess, respectively.

Patent Status

Priority patent application suitable for international extension

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