From Micro to Macro: Oxyfunctionalization with UPOs using continuous flow techniques

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Abstract

Unspecific peroxygenases (UPOs, EC 1.11.2.1) are heme-thiolate oxidoreductases originating from fungi, tracing back to their initial discovery over two decades ago.[1] They predominantly catalyze selective oxyfunctionalization reactions using only hydrogen peroxide,[2] eliminating cofactor recycling burdens intrinsic to P450 monooxygenases.[3] Kara and colleagues have demonstrated significant expertise in the innovative use of UPOs for catalysis and bioprocessing, making substantial contributions to enzyme immobilization[4–6] and their application in continuous bioreactor[4,7] and flow technologies.[8] Automated fed-batch fermentation of the UPO mutant PaDa-I from the Alcalde lab[9] in *Komagatella phaffii* eliminates manual control, enabling reproducible large-scale UPO synthesis with consistent enzyme titers.[10] Immobilization platforms – including synthetic hydrogels, 3D-printed microfluidics, and commercial carriers – are tailored to specific reactor geometries such as packed-bed, microfluidic, and rotating-bed systems.[4,5,8,11] For example, the immobilized PaDa-I[5] was effectively applied in a rotating-bed reactor for continuous enantiopure synthesis of (*R*)-1-phenylethanol from ethylbenzene, achieving a productivity of 436 $mg \cdot L^{-1} \cdot h^{-1}$ and turnover numbers (TONs) of ~900,000, which is the maximum TON reported so far for UPOs.[4] Apart from this aromatic oxidation, a complex sesquiterpene mixture was oxidized to potential olfactory or pharmaceutically relevant hemiacetals and oxiranes.[12] These integrated advances establish a coherent technical framework for the use of UPOs in fine chemical synthesis, positioning them as credible alternatives to P450 monooxygenases and traditional chemical oxidation methods.

Literature

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