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Selective peroxygenase-catalysed oxidation of toluene derivatives to benzaldehydes

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PURPOSE OF THE ABSTRACT

In recent years, unspecific peroxygenases (UPOs) have emerged as promising biocatalysts in the selective activation of C-H bonds,[1] which is still challenging for organic chemistry. However, for the conversion of toluene, the selectivity of the archetypal UPO from *Agrocybe aegerita* (AaeUPO) is rather poor comprising both ring-hydroxylation and oxidation of the alkyl substituent.[2] In contrast, the AaeUPO-catalyzed hydroxylations of the toluene homologue ethyl benzene proceed highly selectively with (R)-1-phenyl ethanol as the sole product.[3]

Inspired by the smart-substrate strategy, we hypothesize that substitution of aromatic ring might influence the selectivity of AaeUPO-catalyzed oxyfunctionalization of toluene derivatives. In silico docking studies suggest that indeed, further substituents at the aromatic ring should improve the substrate binding selectivity, leading to a preferable position for benzylic oxyfunctionalization. In fact, a range of ring-substituted toluene derivatives were highly selectively converted to corresponding benzaldehydes with a selectivity above 92%, while the overoxidation to benzoic acids were hardly detected.

Due to the poor aqueous solubility of the starting materials, a neat system was employed with the toluene derivatives as sole solvent and AaeUPO immobilized on a solid carrier. The immobilized AaeUPO was stable in the organic phase under high peroxide dosing, giving on average 100 mM of the desired benzaldehyde products, corresponding to more than 10 g L⁻¹. A highest product concentration of 185 mM was achieved in the formation of p-nitro-benzaldehyde.

FIGURES

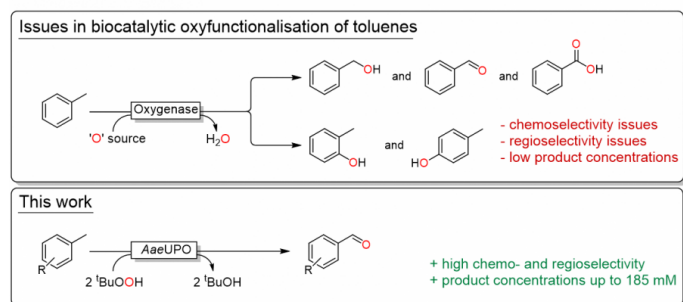


FIGURE 1

Scheme

Selective issues and low product concentration in the biocatalytic oxyfunctionalisation of toluene (derivates) addressed by the combined substrate- and reaction engineering approach.

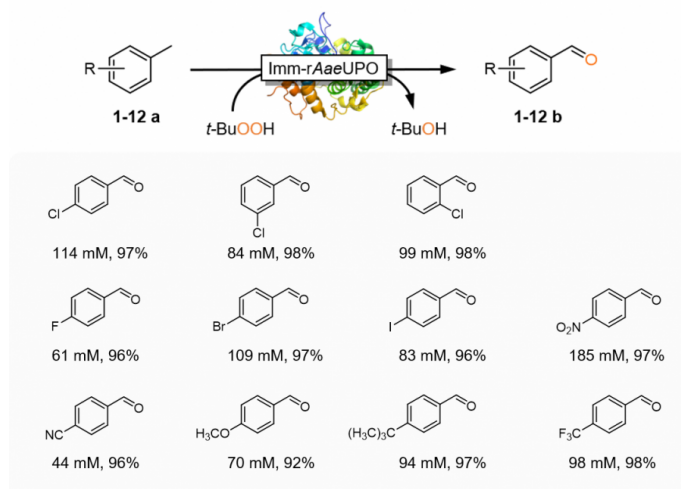


FIGURE 2

Substrate scope

Substrate scope is shown along with product concentration and selectivity. All reactions were conducted under neat condition using immobilised peroxygenase (imm-UPO).

KEYWORDS

Biocatalytic oxidation | Selective oxyfunctionalisation | Peroxygenase | Solvent-free biocatalysis

BIBLIOGRAPHY

- [1] Hobisch, M.; Holtmann, D.; Gomez de Santos, P.; Alcalde, M.; Hollmann, F.; Kara, S., *Biotechnol. Adv.* 2021, 51, 107615.
- [2] Ullrich, R.; Hofrichter, M., *FEBS Lett.* 2005, 579 (27), 6247-6250.
- [3] Kluge, M.; Ullrich, R.; Scheibner, K.; Hofrichter, M., *Green Chem.* 2012, 14 (2), 440-446.