Force feeding PaDa-I: a hybrid nest for selective chemo-enzymatic oxyfunctionalization

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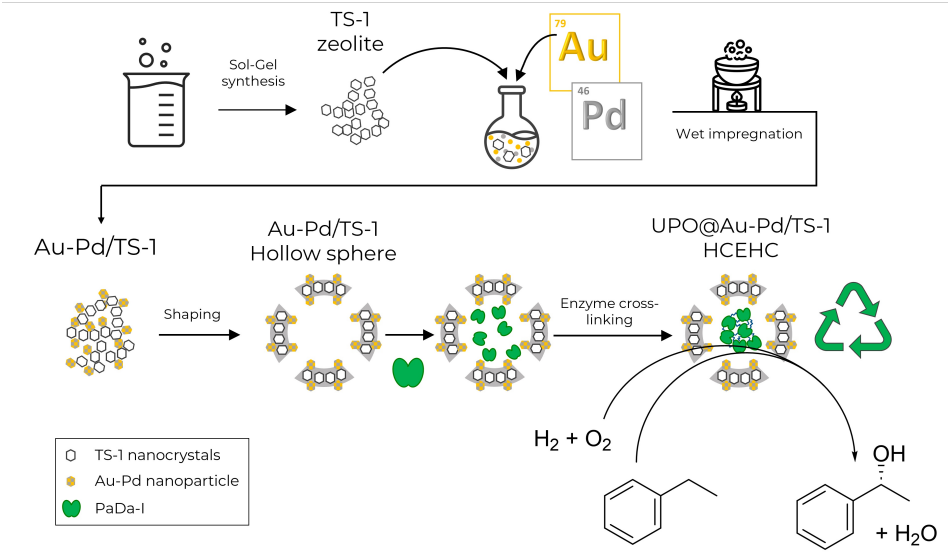
In biocatalysis, unspecific peroxygenases (UPO) are a promising class of enzymes. They enable regio-and-enantioselective oxyfunctionalizations with minimal hydrogen peroxide, without needing additional cofactors[1]. However, adding excessive H_2O_2 externally can denature the enzyme, and the industrial, high-grade production of hydrogen peroxide is highly energy intensive. Thankfully, H_2O_2 can be produced *in situ* by gold-palladium catalysts at room temperature in water under low H_2 pressure. Freakley et al. recently showed that combining Au-Pd catalysts with UPO enables one-pot cascade reactions without interference between catalysts.[2]

Learning from their work, and leaning on our group's experience in the fabrication of chemo-enzymatic heterogeneous catalysts (HCEHC)[3,4] we recreated those Au-Pd catalysts and combined them with a commercially available UPO (PaDa-I) in a single solid material. The resulting HCEHC, produced through an "enzyme-in-a-cage" strategy, was shown to be reusable and highly stereo-and regioselective for the hydroxylation of ethylbenzene to (R)-phenylethanol. Working in an acetone-rich reaction medium, a single gram per liter of our most active HCEHC manages the full conversion of 14mM of ethylbenzene into (R)-phenylethanol in less than 4 hours. This activity is on par with the free enzyme but allows for its recovery and reuse in a high atom-economy, one-pot, one-step chemo-enzymatic cascade reaction. In this work, we explore the effects of synthesis and operational parameters on both the activity of the catalysts and the quality of immobilization, as we search for a subtle balance between activity and robustness.



Schematic representation of the proposed system. PaDa-I is added into preformed hollow spheres of Au-Pd/TS-1 catalyst and sequestrated by cross-linking, creating a reusable HCEHC. H2 and O2 gases react on the metals to form the H2O2 used by PaDa-I for the oxyfunctionalization of ethylbenzene to (R)- phenylethanol.

[1] Markus Hobisch, Dirk Holtmann, Patricia Gomez de Santos, Miguel Alcalde, Frank Hollmann, Selin Kara. (**2021**). *Biotechnology Advances*, 107615. DOI: 10.1016/j.biotechadv.2020.107615
[2] Simon J. Freakley, Svenja Kochius, Jacqueline van Marwijk, Caryn Fenner, Richard J. Lewis, Kai Baldenius, Sarel S. Marais, Diederik J. Opperman, Susan T. L. Harrison, Miguel Alcalde, Martha S. Smit, Graham J. Hutchings. (**2019**). *Nat Commun*, *1*, DOI: 10.1038/s41467-019-12120-w
[3] Valentin Smeets, Walid Baaziz, Ovidiu Ersen, Eric M. Gaigneaux, Cédric Boissière, Clément Sanchez, Damien P. Debecker. (**2020**). *Chem. Sci.*, *4*, 954. DOI: 10.1039/C9SC04615A
[4] Damien P. Debecker, Valentin Smeets, Margot Van der Verren, Hippolyte Meersseman Arango, Marty Kinnaer, François Devred. (**2021**). *Current Opinion in Green and Sustainable Chemistry*, 100437. DOI: 10.1016/j.cogsc.2020.100437