Heterogeneous Bio- and Hybrid catalysts for greener organic synthesis

Damien P. Debecker

[1] *UCLouvain, Institute of Condensed Matter and Nanosciences, Louvain-la-Neuve, Belgium*

Here, we aim to underscore the critical importance of innovative enzyme immobilization techniques and reactor designs in bridging the gap between enzymatic and traditional heterogeneous catalysis. By integrating robust supports, continuous flow operations, and efficient separation mechanisms, these approaches represent significant steps toward the development of sustainable and efficient catalytic systems for industrial applications.

Exploiting the immobilization of enzymes via covalent grafting using glutaraldehyde, we prepared monolithic flow reactors, where immobilized transaminases are used for biocatalytic transamination reactions.[1] The covalent anchoring strategy enhances the robustness of the enzymes, thereby enabling their repeated use and supporting the transition from discontinuous batch processes to continuous flow biocatalytic applications. This methodology directly addresses the challenges of enzyme leaching and operational stability, which are critical for industrial applications. Expanding on the integration of enzymatic catalysis with reactor technology, we discuss the pertinence of enzyme-membrane reactors,[2] in particular for the production of fine chemicals and pharmaceutical intermediates. Membrane technology facilitates downstream recovery, which is crucial for process intensification. The membranes can either serve strictly as separation units or – more interestingly – also serve as a support to fixate the enzyme. This dual strategy requires ad-hoc strategies for enzyme immobilization on flat polymeric membranes.[3] We argue it provides a clean and efficient approach to produce high-purity compounds, emphasizing the synergy between reaction engineering and separation technology, as shown in the example of chiral amines production. Another way to improve the sustainability score of biocatalytic organic synthesis is by coupling equilibrated reactions with crystallization.[4] This can drive the yield towards completion and markedly facilitate product purification.

We also present recent achievements based on strategies for developing and employing hybrid heterogeneous catalysts that merge the fields of chemo- and biocatalysis.[5] Using a "Lego-like" strategy, a spray drying process was exploited to form hollow zeolite microspheres that serve as robust nests for trapping enzymes.[6] These hierarchically structured supports can facilitate multistep chemo-enzymatic cascade reactions, providing a pathway to design catalysts that combine the selectivity of enzymes with the durability of inorganic frameworks. This approach not only leverages the high surface area and tunable pore environments of zeolites but also overcomes issues related to enzyme stability and reusability in traditional homogeneous systems. The proof of concept is presented for an epoxidation reaction, using enzymatically produced H_2O_2; it is expanded to the industrially-relevant synthesis of chiral alcohols using unspecific peroxygenase fed with chemo-catalytically produced H_2O_2.

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