Process Considerations for the Asymmetric Synthesis of Chiral Amines using ω-Transaminase - DTU Orbit (03/10/2019)

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The implementation of new biocatalytic processes can be a very challenging procedure, which can require several stages of screening, characterization and evaluation prior to scale-up. Indeed, several process parameters, with different weights on the final process costs, need to be considered side-by-side. Process design and economic evaluation represent a very important part of the early process development stage. However, often the parameters set at these initial stages are based on assumptions. Therefore, a laboratory scale characterization of the biocatalyst and different process options are important in order to eliminate infeasible routes. This work illustrates the Laboratory scale characterization of different process options for the asymmetric synthesis of chiral amines catalysed by ω-transaminase (ω –TAm). The studied process options include: (i) the immobilization of the biocatalyst to improve its stability and allow recycling and easy separation; (ii) the use of controlled release of substrate (fed-batch) or in situ substrate supply – (ISSS) to decrease substrate inhibition and deal with the substrate low solubility; and (iii) the use of in situ product (ISPR) and co-product removal (IScPR) to respectively alleviate product inhibition and shift the reaction equilibrium. From an academic point of view, more important than the implementation of these technologies to a specific example, is the development of a general methodology that can be later applied in other cases. Hence, this work has also focused on development of comprehensive screening methodologies and guidelines to aid (i) the selection and characterization of suitable biocatalysts for the process; (ii) the selection and characterization of suitable carriers for immobilization of (S)- and (R)-selective ω-TAm; and (iii) the selection of suitable polymeric resins for product removal. The work has been performed in collaboration with c-LEcta GmbH (Leipzig, Germany) and DSM Innovative Synthesis (Geleen, The Netherlands) who supplied the enzymes for the case study, making possible the successful demonstration of the screening methodologies developed. Furthermore, the work addresses several practical questions regarding to the implementation of the process strategies mentioned above.

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