Process strategies in the enzymatic resolution of enantiomers

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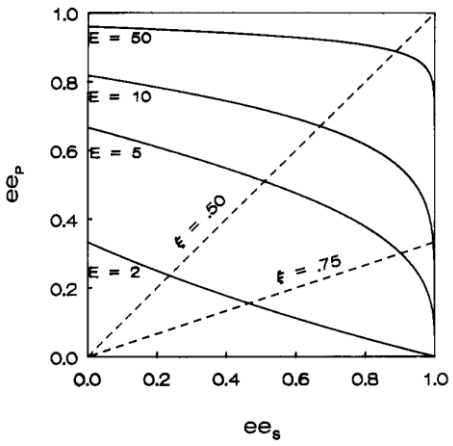
Description

Asymmetry is often involved in the interaction of pharmaceuticals, agrochemicals and food chemicals with a biochemical system of the living organism. There is a need for organic building blocks in order to synthesize such biologically active compounds. Chemical synthesis of a chiral building block usually results in a racemate, although in the last decade some progress has been achieved in chiral synthesis. Enzymatic kinetic resolution is a promising technique to resolve a chemically produced racemate. The lack of a wide range of cheap, commercially available enzymes with high enantioselectivity is a bottleneck, however. Many enzyme-substrate combinations with poor enantioselectivity exist. In order to improve a kinetic resolution, several approaches may be adopted, as substrate-, medium- and enzyme-engineering. These methods often focus on a particular specific reaction and are currently limited by the lack of predictive models for selectivity enhancement.
As an alternative, more structured, option a process engineering approach is suggested. From this point of view, one is not occupied with modification of substrate, enzyme or medium, but employs the available tools, that is, easily available enzymes, substrates and solvents, and optimizes the process conditions by considering and (possibly) changing the standard situation. So far, this approach has hardly been addressed as a principle of improving a kinetic resolution process. Its elegance is its general applicability, which mainly resides in the generality of the concepts and the useful properties of the mathematical predictive models. The standard formulation compares as follows with possible alternatives:



1. Uni-uni kinetics ←→ bi-bi kinetics
2. Batch reactor ←→ continuous reactor
3. Single reaction ←→ multiple reactions
4. Single enzyme ←→ multiple enzymes

The application of this approach requires proper methods to quantify the enzymatic resolution process.

Dissertation

J.L.L. Rakels, Process strategies in the enzymatic resolution of enantiomers. PhD thesis, Delft University of Technology, 1994. http://resolver.tudelft.nl/uuid:fcfebca9-5541-4274-a007-86453ed4cdd5

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