The combined use of active and stable catalysts with micro flow conditions is recognized as one of the ten essentials for fine chemical syntheses in the flow mode. [1] Moreover, enzymatic microreactors enable increased productivity and (enantio)selectivity, intensified mass transfer between enzymes and substrates, while relatively small amounts of enzyme are needed. However, up to now limited number of enzymatic processes has been commercialized, due to limited enzyme stability, reaction efficiency and cost. [2] At first, stability issues are diminished and cost-competitive reaction is enabled through enzyme immobilization on a solid support.

Following our starting work in the field of enzyme immobilization for micro-flow applications and its economy [3], we continued with focusing on reactor engineering and long term operation in a packed bed microreactor using the commercial Novozym 435 lipase form. The aim of this work was to demonstrate the potential of enzymatic microreactors for commercial scale production.

The transesterification reaction between ethyl butyrate and 1-butanol to give butyl butyrate has been used as a model reaction. The reaction is in conventional reactors kinetically and mass transfer limited. The microreactor packed with Novozym 435 proved to reduce mass transfer limitations, what was also confirmed with comparing the modeled and experimental conversion values. Tenfold increase in reaction rate and overall higher conversion was achieved on a micro scale (Figure) compared to the batch experiments, which is mainly due to higher specific enzyme loading (400 g/l) and increased liquid-solid mass transport. No loss of enzyme activity was observed over a period of 12 hours at 70°C. This allowed for the production of 40 g of the product per gram of enzyme, what is already a commercial range for production of pharmaceuticals. [4] Multiple 12 hours periods were run with the same packing of enzymes, showing no signs of enzyme deactivation.

This efficient transesterification reaction, together with our recent patent research in this field [5], contributes to solve the issue of applicability of enzymatic microreactors, by supplying a positive answer for low-volume high-value chemicals. Significant amounts of even lower valued chemicals could be produced by further numbering up, where good enzyme stability and activity, like in the case reported here, ensure the cost-effective production.

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