BIOTRANS
LA ROCHELLE 2023

N°1610 / PC
TOPIC(s) : (Chemo)enzymatic strategies

Preparative implementation of in situ-product crystallization in semi-continuous amine transaminase-catalyzed reactions

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PURPOSE OF THE ABSTRACT

Chiral amines are valuable compounds for the synthesis of various synthetically interesting intermediates and APIs. Here transaminases in particular have established themselves as industrially relevant biocatalysts, which are available with both (R)- and (S)-selectivity. Aside chiral resolution the direct (asymmetric) synthesis of these compounds is often applied due to a theoretic maximum yield of 100%. Such a complete conversion is theoretically possible, but often prevented by an unfavorable reaction equilibrium or other limitations that must be overcome with secondary (bio)chemical reactions, yielding further waste and additional effort during downstream-processing.[1]

As a potent alternative we present the preparative implementation of the previously developed integrated use of selective crystallization, which allow an apparent shift of the reaction equilibrium to the product side.[2] The product amine is herein (semi-)continuously removed from the unfavorable biocatalytic reaction equilibrium in the form of a salt, which is precipitated directly from solution (Figure 1). The concept was shown primarily at (S)-3-methoxy-1-phenylethylamine with >1.2 mol/l, which is a valuable intermediate for the synthesis of rivastigmine.[3] The concept was subsequently expanded successfully to a wider range of chiral amines and charcterized regarding choice of counterion, solid phase behavior and synthetic applicability.[3]

FIGURES

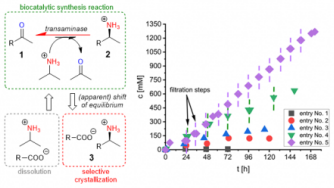

FIGURE 1

Figure 1

Figure 1: Representation of the integrated selective crystallization of the product (salt) in transaminase-catalyzed reactions

FIGURE 2

KEYWORDS

transaminase | amine | crystallization | in situ product removal

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