Preparation of chiral *prim*-, and *sec*-amines employing biocatalysts

Wolfgang Kroutil[1], Robert C. Simon[1], Eduardo Busto[1], Nina Richter[2], Katharina Tauber[1], Christine S. Fuchs[2], Desiree Pressnitz[1], Eva-Maria Fischereder[1], Horst Lechner[1], Ferdinand Zepeck[3]

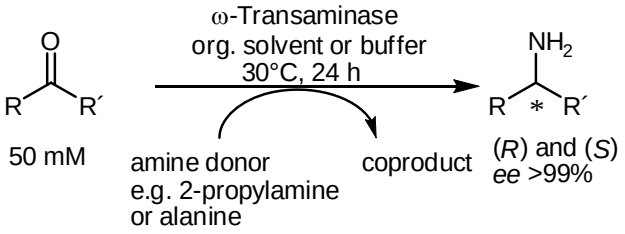
[1] Department of Chemistry, University of Graz, Graz (8010), Austria. [2] Austrian Centre of Industrial Biotechnology ACIB c/o University of Graz, Graz (8010), Austria. [3] Sandoz, Kundl, Austria.

**e-mail corresponding author*:

Keywords: asymmetric synthesis, amines, biocatalysis

Abstract Speech

Optically pure α-chiral primary amines can be prepared by reductive amination employing metal-, ogano- or biocatalysis. Using biocatalysts such a ω-transaminases [1,2], α-chiral primary amines were prepared with e.e. up to >99% at a substrate concentration of 50 mM (Scheme 1). The formal asymmetric reductive amination of ketones was achieved giving access to the (*S*)-as well as the (*R*)-enantiomer. By this methodology various building blocks for bioactive compounds were prepared in aqueous buffer [3].



Scheme 1. Biocatalytic amination of ketones to access primary amines.

Using appropriate conditions it was shown that the amination can also be performed in organic solvents, thereby simplifying workup of the amine compared to reactions in aqueous phase [4]. Furthermore, it was demonstrated, that the biocatalyst can perfectly differentiate between different keto groups within a single molecule; for instance, when transforming 1,5-diketones only the keto moiety in (ω-1)-position was aminated avoiding thereby sophisticated protection strategies [5,6]. The obtained mono-aminated intermediate underwent spontaneous cyclization giving access to secondary amines after chemical diastereoselective reduction.

The amination of primary alcohols represents a challenging task for chemistry. Nature has not foreseen this reaction to be performed by a single enzyme in one step. Consequently, we designed an artificial biocatalytic pathway transforming *prim*-alcohol to the corresponding amine via oxidation followed by reductive amination. The pathway was set up in that way that the hydride abstracted in the oxidation step is reused in the reductive amination. By employing such an enzyme cascade alcohols were successfully as demonstrated for the preparation of 1,ω-alkyldiamines as building blocks for polymers (Figure 1) [7].

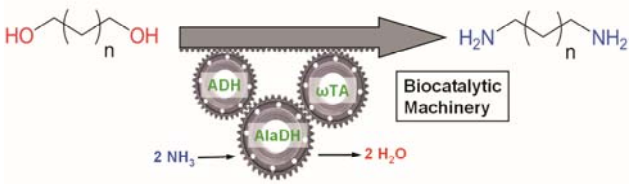


Figure 1. Bio-amination of alcohols.

Acknowledgement

Funding from the European Union's Seventh Framework Programme FP7/2007-2013 was received under grant agreement n° 245144 (AmBioCas), grant agreement n° 289646 (KyroBio) and grant agreement n° PIEF-GA-2011-298030 (Biocascade). The DK "Molecular Enzymology" and financial support by the FWF (Project W9) is acknowledged. We acknowledge the Federal Ministry of Economy, Family and Youth (BMWFJ), the Federal Ministry of Traffic, Innovation and Technology (bmvit), the Styrian Business Promotion Agency SFG, the Standortagentur Tirol and ZIT - Technology Agency of the City of Vienna through the COMET-Funding Program managed by the Austrian Research Promotion Agency FFG.

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