Over the last decades transaminases (TAs) have been proven to be powerful catalysts for the enzymatic synthesis of chiral amines from achiral ketones via an asymmetric reductive amination.1,2 While (S)-configured amines are easily accessible using the (S)-selective enzyme together with cheap L-alanine as the amine donor, for an efficient (R)-selective transamination the far more expensive D-alanine is required. We present the combination of an alanine racemase with the classical amination system, addressing the described limitation for the application of (R)-selective TAs (Scheme 1). By using this approach, the required d-alanine can be provided by in situ racemization of the employed L-alanine.2

A suitable alanine racemase (AlaR) catalyzing the racemization of L-alanine was identified from Streptomyces coelicolor. The enzyme was characterized concerning its activity and stability in the desired cascade reaction in order to identify optimal conditions. Results have shown that the racemization proceeds efficiently within 30 min, with AlaR being a rather stable catalyst under process conditions (Figure 1 and 2).

The AlaR catalyzed racemization of L-alanine was coupled with the (R)-selective reductive amination mediated by TAs. In order to shift the equilibrium, the co-product pyruvate was either recycled by an alanine dehydrogenase (AlaDH; Scheme 2) or removed by a lactate dehydrogenase (LDH; Scheme 3). Comparable conversions were obtained using either d-alanine as amine donor or L-alanine together with AlaR, leading to an economically improved and greener (R)-amination system.