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TOPIC(s) : Biocatalytic cascade reactions

recycling cascades combining aldolases and transaminases for the highly selective synthesis of hydroxylated amino acids

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PURPOSE OF THE ABSTRACT

The combination of aldolases (AL) and transaminases (TA) in bi-enzymatic cascades constitutes a straightforward approach to prepare 1,3-amino-alcohols with high stereoselectivity: a ketol, selectively obtained from achiral carbonyl compounds through AL-catalysis is further converted with high stereoselectivity into 1,3-amino alcohol by action of a TA in the presence of an amino donor substrate.[1,2] In the course of a project devoted to the discovery of new AL and TA from microbial diversity using a genome mining approach,[3,4] we have identified a set of AL and TA suitable for the synthesis of various valuable γ-amino alcohols. Moreover, we have developed a recycling cascade model, in which the nucleophilic substrate of AL is generated from the amino donor substrate of TA (see figure). This process thus brings the benefit of optimal atom economy. whereas the thermodynamically favoured aldolisation, affords an equilibrium shift for the transamination reaction thus solving the reversibility problem encountered with TA-catalysed reactions. Moreover We have also demonstrated that the dynamic nature of the recycling cascade affords a large increase in stereoselectivity through various ways that will be discussed.

AL with complementary enantioselectivities were thus combined with L- or a D-α-TA to prepare in high yield a variety of 4-hydroxy-2-amino acids including all four stereomers of 4-hydroxy-glutamic acid, L-syn and D-syn-4-hydroxynorvaline and D-anti-4,5-dihydroxynorvaline. Furthermore, the stereocontrol afforded by the recycling cascade was extended to 3 chiral centers with the synthesis of the bioactive (2S,3R,4S)-4-hydroxy-isoleucine (Hil) as well as 3 new β-branched 4-hydroxyamino acids analogues of Hil.

FIGURES

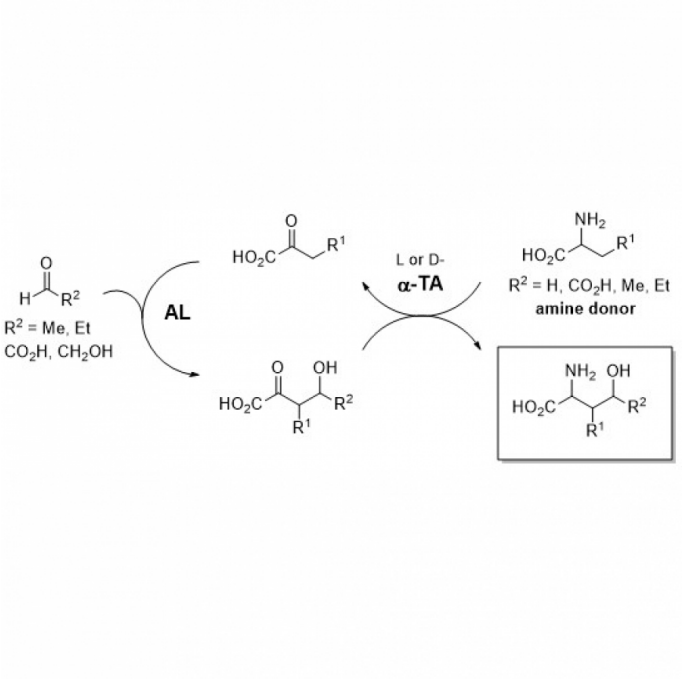

FIGURE 1

AL-TA recycling cascades

A variety of 4-hydroxy-2-amino acids were prepared with high yield and selectivity.

FIGURE 2

KEYWORDS

aldolases | transaminases | recycling cascades | genome mining

BIBLIOGRAPHY

[1] C. Gu□rard-H□laine, E. Heuson, M. Ndiaye,L. Gourbeyre, M. Lemaire, V. H□laine, F. Charmantray, J.L. Petit, M. Salanoubat, V. De Berardinis, T. Gefflaut, Chem. Commun. 2017, 53 (39), 5465.

[2] C. J. Moreno, K. Hern□ndez, S.J. Charnok, S. Gittings, M. Bolte, J. Joglar, J. Bujons, T. Parella, P. Clap□s, ACS Catal. 2021, 11 (8), 4660.

[3] V. De Berardinis, C. Gu□rard-H□laine, E. Darii, K. Bastard, V. H□laine, A. Mariage, J.-L. Petit, N. Poupard, I. S□nchez-Moreno, M Stam, T. Gefflaut, M. Salanoubat, M. Lemaire, Green Chem. 2017, 19 (2), 519.

[4] E. Heuson, J.-L. Petit, A. Debard, A. Job, F. Charmantray, V. De Berardinis, T. Gefflaut, Appl. Microbiol. Biotechnol. 2016, 100, 397.