ENZYMATIC SYNTHESIS OF CYCLIC IMINO ACIDS

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Optically active cyclic imino acids are widely used as important pharmaceutical intermediates and it is necessary to develop cost effective synthetic method for their production.

We have already established one-pot synthesis of L-cyclic imino acids from diamino acids by using *N*-methyl-L-amino acid dehydrogenase (NMAADH) from *Pseudomonas putida*. In order to make this process more efficient, we established a recombinant *Escherichia coli* which expresses NMAADH, lysine racemase from *P. putida* and D-lysine dehydrogenase from *Selenomonas ruminantium* in a single cell. The recombinant *E. coli* makes it possible to recycle NADPH by combination of reductive reaction using NMAADH and oxidative reaction using D-lysine dehydrogenase (Fig.1).

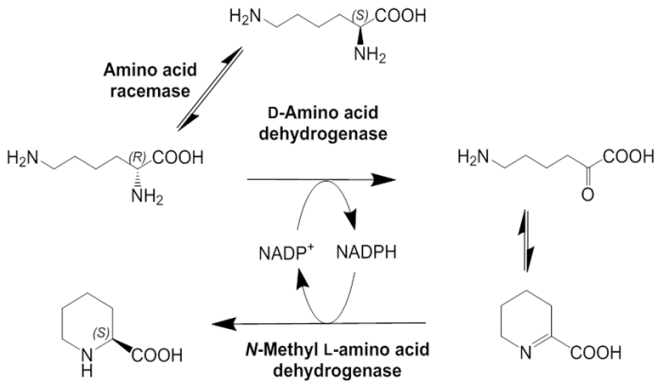

Fig. 1 One-pot synthesis of L-pipecolic acid

In addition to the L-imino acids synthetic process, novel lysine hydroxylases and pipecolic acid hydroxylases were applied to synthesize optically-active hydroxy imino acids. We can separately produce optical isomers by several types of amino acid hydroxylase that we have acquired originally (Fig. 2).

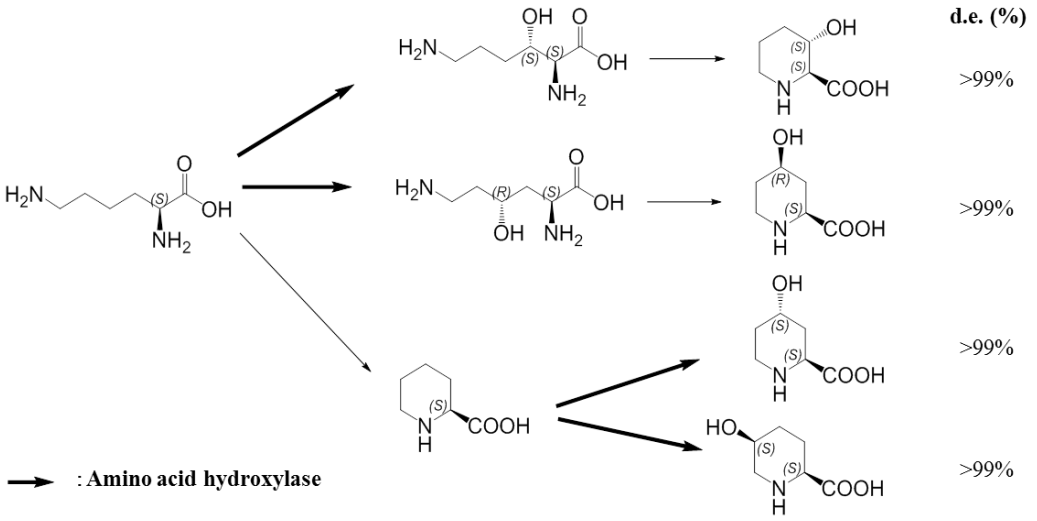

Fig. 2 Synthesis of hydroxypipecolic acid by application of amino acid hydroxylase