ENZYMATIC SYNTHESIS OF CYCLIC IMINO ACIDS

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Key Words: N-methyl-L-amino acid dehydrogenase, D-amino acid dehydrogenase, L-pipecolic acid, Fe(II)/α-ketoglutarate-dependent dioxygenases

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).

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. 1 One-pot synthesis of L-pipecolic acid

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