Biocatalytic Stereoselective Deuteration Of Alpha-Amino Acids

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BACKGROUND

Deuterated amino acids are valuable building blocks for developing deuterated drugs and are important tools for studying biological systems. Biocatalytic deuteration represents an attractive strategy to directly access enantiopure deuterated amino acids. The importance of deuterated compounds has hence spurred great interests to develop synthetic methods to incorporate deuteration into common building blocks. Although a few chemical approaches have been developed, these methods often have limited functional group tolerance, incomplete deuteration, and sometimes modest site- and/or stereoselectivity. Therefore, it is crucial to explore cost-effective methods for incorporating deuterium labels into amino acids. In comparison, biocatalytic deuteration represents an attractive strategy and offers several advantages, including excellent selectivity, green, and sustainable reaction conditions.

Deuterated compounds have very different chemical and physical properties from their nondeuterated counterparts, and have found wide applications in chemistry, biology, and medicine. Deuterium incorporation plays a very important role in drug discovery: to date two deuterated drugs have been approved by the FDA, while many others are currently under clinical trials.

DESCRIPTION

Researchers at the University of California, Santa Barbara have developed a cost-efficient process to create deuterated amino acids by catalyzing a reversible proton exchange at a Cα amino acid substrate on L-amino acids in a stereo-retentive manner. The enzyme LolT, which is dependent on the cofactor pyridoxal 5'-phosphate (PLP), can catalyze a deprotonation of the amino acid substrates to produce α-deuterated amino acids. Using this enzyme, complete deuteration can be achieved with diverse L-amino acids bearing assorted functional groups, e.g. from lysine to glutamic acid. In addition, the broad substrate scope and strict stereoselectivity make LolT a powerful biocatalyst for the preparation of α-deuterated L-amino acids. Using this new, innovative method complete deuteration can be achieved within minutes with exquisite control on the site- and stereoselectivity.

This process presents a promising approach to meet the growing demand for deuterium-labeled amino acids by enabling the creation of a wider range of such amino acids compared to existing methods. Not only is it more cost-efficient, but it also offers a simpler process with fewer steps involved. These advantages position it as a compelling solution to address the increasing demand for deuterium-labeled amino acids.

ADVANTAGES

▶ Presents a cost-efficient method to create deuterium-labeled amino acids
▶ Offers a simpler approach to creating deuterium-labeled amino acids
▶ Enables the creation of a wider range of deuterium-labeled amino acids compared to existing methods

APPLICATIONS

▶ Pharmaceuticals

PATENT STATUS

Patent Pending

RELATED CASES

2023-99T-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Biocatalytic Asymmetric Synthesis Of Heterocyclic Alpha, Alpha-Disubstituted Amino Acids
▶ Chemoenzymatic Synthesis Of Exo-Amino-Izidine Alkaloids