Enzymatic Syntheses of Aromatic Amino Acids Labeled with Carbon and Hydrogen Isotopes

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Abstract

Aromatic amino acids are of great importance in biochemistry. Their isotopomers can be applied in different studies, i.e., in metabolic or mechanistic investigations, and also in nuclear medicine. Thus, the syntheses of specifically labeled aromatic amino acids have become our goal. Such amino acids can be invaluable tools for studying mechanisms of enzymatic reactions.

L-phenylalanine was obtained via the Knoevenagel condensation of malonic acid with benzaldehyde to give (*E*)-cinnamic acid, and subsequent stereoselective addition of ammonia catalyzed by phenylalanine ammonia lyase (PAL). Specifically, carbon labeled L-phenylalanines in positions 1, 2, and 3 were obtained using this route[1]. In addition, hydrogen (both deuterium and tritium isotopomers) was incorporated into 2, 3*R* and 3*S* positions.

L-tyrosine was obtained via oxidation of previously obtained L-phenylalanine using L-phenylalanine monooxygenase from rat liver. L-tyrosines were obtained starting from above mentioned isotopomers of L-phenylalanine[2,3]. Novel approaches were undertaken to the syntheses of the following compounds: (I) 3*S*-hydrogen labeled L-tyrosines using PAL-catalyzed ammonia addition, and (II) 2-hydrogen isotopomers using the proton exchange with solvent catalyzed by tryptohanase. Labeled L-tyrosine will be used as the precursor of L-dopa.

L-tryptophan and 5'-hydroxy-L-tryptophan were labeled with carbon-14 in the carboxylic group using the condensation of [1-^{14}C]-D,L-alanine with indole and 5-hydroxyindole catalyzed by tryptophanase[4]. 2-deuteriated and tritiated L-tryptophan and 5'-hydroxy-L-tryptophan were synthesized via the similar condensation of indole or its 5-hydroxy derivative with *S*-methyl-L-cysteine in heavy or tritiated water, respectively[5].

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