

Syntheses of Carbon and Hydrogen Isotopomers of L-Tyrosine

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Abstract

Isotopomers of L-tyrosine are very attractive tools for radiochemical synthesis, due to their potential application in biochemical studies of metabolic processes, or of mechanisms (e.g. by the determination of kinetic isotope effects). The syntheses of these isotopomers may also be used for nuclear medicine purposes.

[1-¹⁴C]-, and [2-¹⁴C]-L-tyrosines were obtained using the Knoevenagel condensation of [1- or 2-¹⁴C]-malonic acid, respectively, with benzaldehyde to give (*E*)-cinammic acid, followed by the addition of ammonia catalyzed by L-phenylalanine ammonia-lyase. The products, e.g. [1-¹⁴C]- and [2-¹⁴C]-L-phenylalanines, were then oxidized to corresponding L-tyrosines using L-phenylalanine monooxygenase¹.

[2-³H]-L-tyrosine was obtained in the similar manner to the above mentioned carbon isotopomers starting from [2-³H]-malonic acid, obtained via the exchange of α -protons with the solvent². The same hydrogen (both deuterium and tritium) label was also incorporated into the L-tyrosine by the proton exchange with solvent catalyzed by tryptophanase.

[3*R*-³H]- and [3*R*-²H]-L-tyrosines were obtained analogously to their carbon isotopomers starting from labeled benzaldehyde. The stereospecific labeling is possible here due to the properties of L-phenylalanine ammonia-lyase, which places the β -proton of cinamic acid in the 3*R* position during the addition of ammonia².

[3*S*-³H]-L-tyrosine was also obtained using the above synthetic strategy; the hydrogen label was incorporated into 3*S* position from the solvent during the enzymatic addition of ammonia². The synthetic route was also simplified by the analogous addition of ammonia to *p*-coumaric acid catalyzed by L-phenylalanine ammonia-lyase to give L-tyrosine labeled in the 3*S* position. Deuteriated and tritiated amino acids were obtained using heavy or tritiated water, respectively.

1. W. Augustyniak, R. Kański, M. Kańska, *Synthesis of carbon-14 labeled [1-¹⁴C]-, and [2-¹⁴C]-L-tyrosine*, J. Label. Compd. Radiofarm., 44, 553-560, 2001
2. W. Augustyniak, P. Suchecki, J. Jemielity, R. Kański, M. Kańska, *Syntheses of tritium labelled isotopomers of L-tyrosine*, J. Label. Compd. Radiofarm., J. Label. Compd. Radiofarm., 45, 559-567, 2002