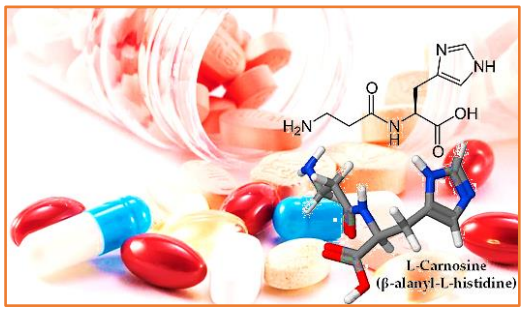
CATALYTIC STRATEGIES FOR THE SYNTHESIS OF CARNOSINE DERIVATIVES

Giorgio Facchetti, Giulia Coffetti, Isabella Rimoldi

Department of Pharmaceutical Sciences, via Golgi 19, 20133-Milan, Italy

giorgio.facchetti@unimi.it; isabella.rimoldi@unimi.it



L-Carnosine is a naturally occurring endogenous dipeptide formed by the combination of β-alanine and L-histidine, particularly in tissues with high oxidative metabolism such as muscles and the brain. By neutralizing free radicals and reducing oxidative stress—factors associated with various age-related conditions—it is believed to offer cellular protection[1]. The Global L-Carnosine Market size was estimated to be around USD 35.87 million in 2022, with projections indicating future growth at a compound annual growth rate of 6.45% until 2030. Thus, the development of synthetic methods able to afford L-Carnosine and its derivatives in enantiopure form is attracting interest and investments from both academia and industry. The contribution offers both the points of view applied to the attempt to achieve such a goal. The first part was focused on the development of a second-generation process for the synthesis of L-Carnosine. A series of nitrile precursor reduction studies was performed utilized gaseous H_2 and commercially available (Pd, Rh, etc). As final scope, the optimization of the reaction conditions was performed, including a method for the isolation of the product as chromatographic separation and/or crystallization of the corresponding salt. Asymmetric hydrogenation using transition metal catalysts is a significant transformation in both academia and industry. Its high efficiency, atom economy, and broad substrate scope make this methodology appealing for both fields. In the second part, starting from an unsaturated precursor, different rhodium catalysts based on non-commercially available diphosphine were applied to the synthesis of enantiopure L-Carnosine derivatives with e.e. up to 95%. [2,3,4]

References:

1. *Pharmaceuticals* **2023**, 16, 778
2. *Tetrahedron: Asymmetry*, **2008**, 19, 273
3. *Synlett.*, **2016**, 27, 2734
4. *New J. Chem.*, **2021**, 45, 18769