ENANTIOSELECTIVE ACCESS TO *L*-CARNOSINE VIA ONE-POT CATALYTIC PROTOCOL

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The worldwide demand for *L*-Carnosine continues to rise, fuelled by its increasing use in nutritional supplements, pharmaceutical formulations, and cosmetic products. This naturally occurring dipeptide, consisting of β-alanine and *L*-histidine, is well known for its antioxidant properties and its role in energy metabolism, and it has shown promising therapeutic relevance in disorders including diabetes, Alzheimer's disease, and Parkinson's disease.[1]

To address the need for a more sustainable and high-performing synthetic approach capable of delivering *L*-Carnosine with excellent yield and enantiomeric purity, we designed an efficient one-pot synthetic strategy (Figure 1) based on ethyl methyl (Z)-2-(2-cyanoacetamido)-3-(1H-imidazol-4-yl)acrylate, selected as a Privileged Precursor (PP) for *L*-Carnosine production. The methodology involves an initial asymmetric hydrogenation of the C=C double bond of the PP catalysed by [RhCOD(*R*,*R*)-Ephos]$^{+}$TfO^{-}, followed by reduction of the cyano group using a heterogeneous Rh/C catalyst under basic conditions.[2,3] Both transformations were conducted sequentially in a single reaction vessel without intermediate purification, enabling the direct formation of *L*-Carnosine with an overall yield of 68% and enantiomeric excess value reaching 73%, as determined by HPLC-MS analysis. Although this approach markedly simplifies the synthetic and downstream processing steps, ongoing optimization efforts are aimed at enhancing its suitability for industrial-scale implementation.[4]

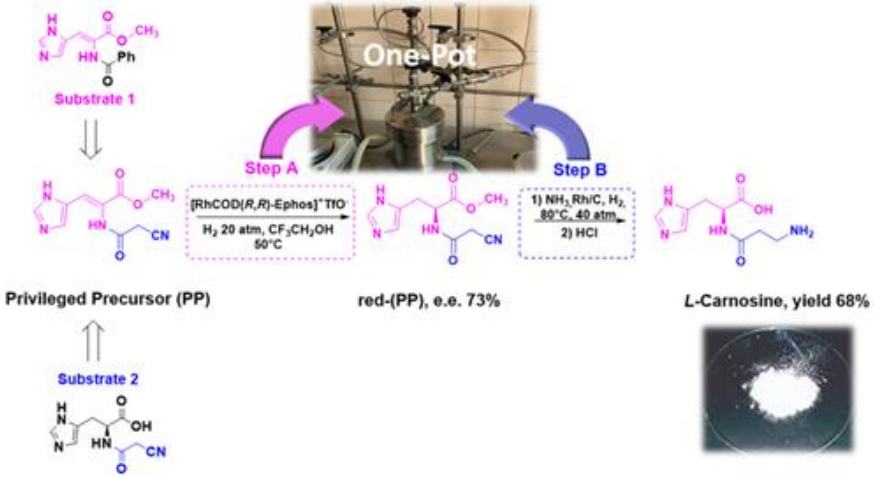

Figure 1. One pot protocol for the synthesis of *L*-Carnosine under optimized reaction conditions.

[1] Gasmi, A. et al. *Current Medicinal Chemistry* **2025**, *32*, 6-22.
[2] Facchetti, G. et al. *New J. Chem*. **2021**, *45,* 18769-18775.
[3] Yenare, P.P. et al. *Catal. Sci. Technol.* **2025**, 15, 7295.
[4] Facchetti, G. et al. *Mol. Catal* **2025**, *584, 115246.*