# Catalytic synthesis of versatile chiral heterocycles: En route to γ-Amino Acid derivatives

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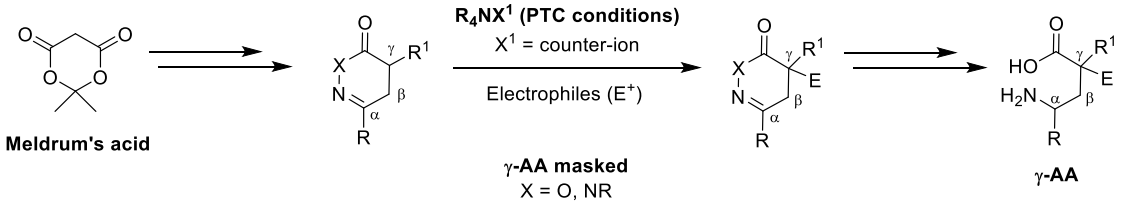
Despite decades of investigations, syntheses and applications of novel chiral **Amino Acids** (**AA**) and peptides derived thereof are still research topics of major importance. Compared to classical α-**AA**, the introduction of γ-**AA**, into the corresponding peptides can lead to peptidomimetics with different secondary structures and improved hydrolytic stability towards peptidases, thus allowing for better biological properties/activities.[1]
Furthermore, γ-Aminobutyric acid (GABA), is the major inhibitory neurotransmitter in the mammalian central nervous system (CNS) and plays a significant role in several brain disorders.[2] Modulation of GABA signaling is the basis of many pharmacologic treatments. γ$^{2,2}$-**AA** are useful building blocks for the elaboration of original small chiral molecules and heterocycles allowing the exploration of the 3D-chemical space in search of selectivity in biological properties,[3] and prevent any racemization event at the α-position of the carbonyl functional group.

Catalytic synthesis of versatile chiral heterocycles: en route to γ-Amino Acid derivatives is a collaborative project featuring Jean-François Brière group and Mario Waser group. This project aims at the development of versatile chiral heterocycles as building blocks to access γ-**AA**, using Meldrum acid chemistry and new developments in eco-efficient and environmentally friendly Phase-Transfer Catalysis (PTC) approaches (Scheme 1). The results of this study will be presented.




Scheme 1. Our strategy for accessing γ-Amino Acids.

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[1] For illustrative reviews on γ-AA: (a) M. Ordóñez, C. Cativiela, Tetrahedron: *Asymmetry* **2007**, 18, 3. (b) M. Ordóñez, C. Cativiela, I. Romero-Estudillo, *Tetrahedron: Asymmetry* **2016**, 27, 999.

[2] (a) K. M. Brown, K. K. Roy, G. H. Hockerman, R. J. Doerksen, D. A. Colby J. *Med. Chem.* **2015**, 58, 6336; (b) H. Abdel-Halim, J. R. Hanrahan, D. E. Hibbs, G. A. R. Johnston, M. Chebib, *Chem. Biol. Drug Des.* **2008**, 71, 306; (c) M. Filip, M. Frankowska, *Pharmacol. Rep.* **2008**, 60, 755.

[3] For a pioneering report in the field, see: D. Seebach, S. Abele, T. Sifferlen, M. Hänggi, S. Gruner, P. Seiler *Helv. Chim. Acta* **1998**, 81, 2218.