

# HIGHLY ENANTIOSELECTIVE PHASE-TRANSFER CATALYZED ADDITION OF ISOXAZOLIDIN-5-ONES TO MBH CARBONATES AND PARA QUINONE METHIDES: ACCESS TO FUNCTIONALIZED $\beta^{2,2}$ -AMINO ACIDS

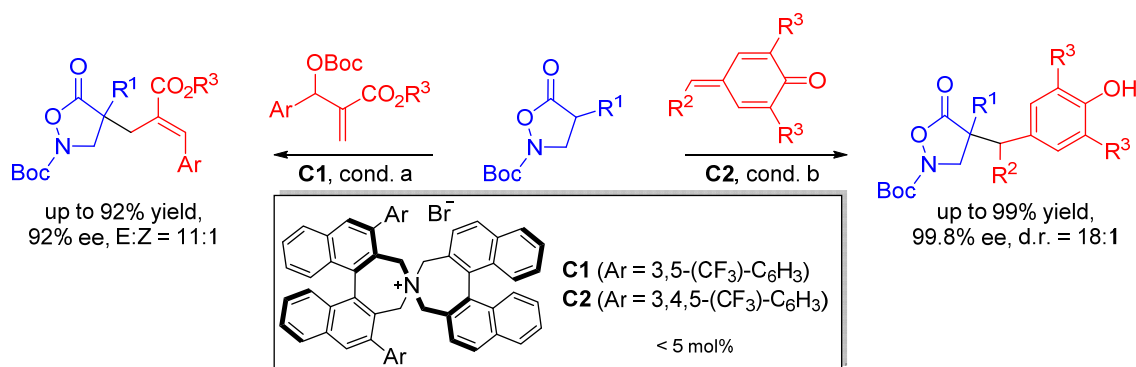
Andreas Eitzinger<sup>a</sup>, Vito Capaccio<sup>b</sup>, Johannes Schörghumer<sup>a</sup> and Mario Waser<sup>a</sup>

<sup>a</sup>Institute of Organic Chemistry, Johannes Kepler University, 4040 Linz, Austria

<sup>b</sup>Dipartimento di Chimica e Biologia, Università di Salerno, 84084 Fisciano, Italy

$\beta$ -amino acids are present in a vast number of natural products and pharmaceuticals. It is therefore of great interest to access these structural motives in a stereochemically defined fashion. Isoxazolidin-5-ones, a class of  $\beta$ -amino acid precursors, show susceptibility towards different modes of asymmetric (organo)catalytic activation, as was impressively shown by the groups of Briere [1], Shibasaki [2] and Cossy [3].

In this work, we demonstrate an asymmetric phase transfer catalyzed allylation protocol for isoxazolidin-5-ones by employing a *Maruoka*-type catalyst and MBH-carbonates as acceptors [4]. Furthermore, the 1,6-addition of isoxazolidin-5-ones to para-quinone methides was explored and slight modifications of the reaction conditions gave the products in excellent yields and enantioselectivities. Subsequent hydrogenation under mild conditions yielded highly enantioenriched  $\beta^{2,2}$ -amino acid derivatives.



In addition, a new type of para-quinone methide with  $R^2 = CF_3$  is introduced and successfully tested within this context. DFT calculations of the proposed transition states based on the abs. configuration rationalize the high selectivity of the 1,6-addition.

[1] T. Cadart, C. Berthonneau, V. Levacher, S. Perrio, J.-F. Briere, *Chem. Eur. J.*, **2016**, 22, 15261-15254

[2] J.-S. Yu, H. Noda, M. Shibasaki, *Chem. Eur. J.*, **2018**, 24, 15796-15800

[3] M. N. Oliveira, S. Arseniyadis, J. Cossy, *Chem. Eur. J.*, **2018**, 24, 4810-4814

[4] V. Capaccio, K. Zielke, A. Eitzinger, A. Massa, L. Palombi, K. Faust, M. Waser, *Org. Chem. Front.*, **2018**, 5, 3336-3340