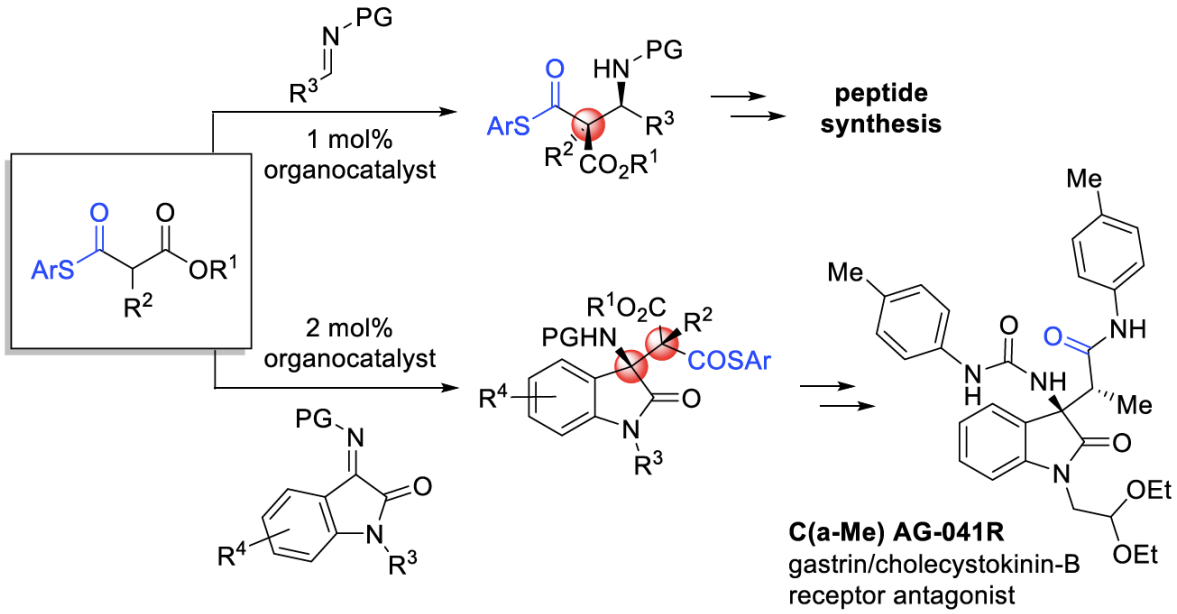
Stereoselective Organocatalytic Synthesis of *β*-Amino Thioesters and their Synthetic Application

Oliver D. Engl, Helma Wennemers

ETH Zurich, Laboratory for Organic Chemistry, D-CHAB, HCI H314, Vladimir-Prelog-Weg 3, 8093 Zurich, Switzerland

Thioesters are versatile building blocks for subsequent transformations into other functional groups such as ketones, aldehydes or amides. Nature utilizes malonic acid half thioesters (MAHTs) as thioester enolate equivalents in the biosynthesis of fatty acids and polyketides. MAHTs have also been used in organic synthesis but suffer from uncontrolled decarboxylation. Our group introduced mono thiomalonates (MTMs) as protected variants of MAHTs and versatile surrogates of thioester enolates.1 Herein we present highly stereoselective synthesis of *β*-amino thioesters that proceed under mild organocatalytic conditions through Mannich-type addition reactions of MTMs to *N*-Cbz and *N*-Boc protected imines. The method provides valuable building blocks for coupling-reagent-free peptide synthesis.2,3 In addition, this methodology also allowed for the synthesis of 3-substituted 3-amino-2-oxindoles containing two adjacent tetrasubstituted stereocenters. We show the synthetic value of the differentially functionalized oxindoles for the synthesis of derivatives of the bioactive *β*-amino acid AG-041R.4



[1] a) O. D. Engl, S. P. Fritz, A. Käslin, H. Wennemers, *Org. Lett.* **2014**, *16*, 5454-5457. b) A. Kolarovic, A. Käslin, H. Wennemers, *Org. Lett.* **2014**, *16*, 4236-4239. c) Y. Arakawa, S. P. Fritz, H. Wennemers, *J. Org. Chem.* **2014**, *79*, 3937-3945. d) P. Clerici, H. Wennemers, *Org. Biomol. Chem.* **2012**, *10*, 110-113. e) J. Lubkoll, H. Wennemers, *Angew. Chem. Int. Ed.* **2007**, *46*, 6841- 6844.

[2] A. Bahlinger, S. P. Fritz, H. Wennemers, *Angew. Chem. Int. Ed.* **2014**, *53*, 8779-8783.

[3] *E. Cosimi, *O. D. Engl, J. Saadi, M.-O. Ebert, H. Wennemers, *manuscript submitted.*

[4] O. D. Engl, S. P. Fritz, H. Wennemers, *Angew. Chem. Int. Ed.* **2015**, *54*, 8193-8197. ***(Selected as Hot Paper and Highlighted in Synfacts)***