

## Organocatalytic Addition Reactions of Malonates to Cyclic Imines: Short Total Synthesis of Tetraponerines

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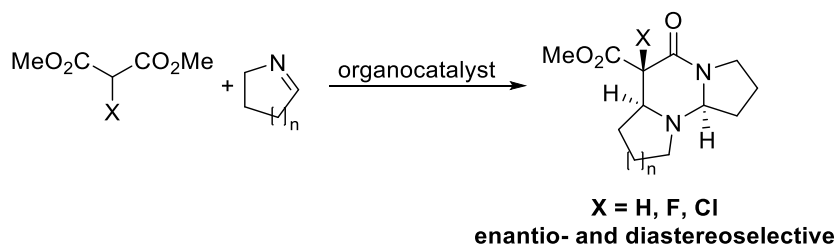
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Cyclic amines are widespread motives in natural products and bioactive molecules. [1] Nature uses cyclic imines for the biosynthesis of, e.g. alkaloids. Cyclic imines are highly reactive electrophiles and therefore useful but also difficult to handle reaction partners. As a result, few enantioselective catalytic methods have been established.

The Wennemers group has developed stereoselective, organocatalytic addition reactions that use malonic acid-derived thioesters. These thioacetate equivalents react in the presence of catalytic amounts of cinchona alkaloid derivatives with different electrophiles, including aldehydes, nitroolefins, and imines. [2]

Herein, we present the enantioselective addition of malonates to cyclic imines. The reaction proceeds in the presence of chiral hydrogen-bond donor catalysts to yield chiral amines with high stereoselectivity (>90% ee) and excellent diastereoselectivity (d.r. >20:1). This methodology allowed for the shortest enantioselective total synthesis of the natural product Tetraponerine T-2 achieved to date. [3]



[1] a) R. D. Taylor, M. MacCoss, A. D. Lawson, *J. Med. Chem.* 2014, 57, 5845; b) E. Vitaku,; D. T. Smith; J. T. Njardarson *J. Med. Chem.* 2014, 57, 10257.

[2] a) J. Lubkoll, H. Wennemers, *Angew. Chem. Int. Ed. Engl.* 2007, 46, 6841; b) A. Bahlinger, S. P. Fritz, H. Wennemers, *Angew. Chem. Int. Ed.* 2014, 53, 8779; c) J. Saadi, H. Wennemers, *Nature Chem.* 2016, 8, 276 d) D. Zetschok, L. Heieck, H. Wennemers, *Org. Lett.* 2021, 23, 1753.

[3] F. Kölblin, J. W. Rackl, T. Egger, H. Wennemers, manuscript in preparation.