

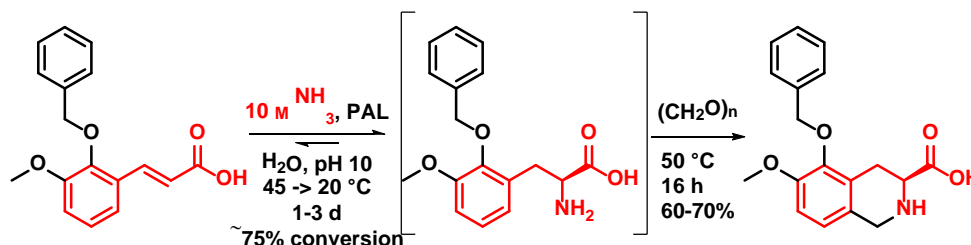
Use of Phenylalanine Ammonia Lyase (PAL) enzymes in the manufacture of EMA401 (olodanrigan)

Leo A. Hardegger, Pascal Beney, Dominique Bixel, Christian Fleury, Feng Gao, Alexandre Grand-Guillaume-Perrenoud, Xingxian Gu, Julien Haber, Tao Hong, Roger Humair, Andreas Kägi, Michael Kibiger, Florian Kleinbeck, Van Tong Luu, Lukas Padeste, Florian A. Rampf, Thomas Ruch, Thierry Schlama, Eric Sidler, Anikó Udvarhelyi, Bernhard Wietfeld, Yao Yang

Novartis Pharma AG, Technical Research and Development, Chemical and Analytical Development, Lichtstrasse 35, 4056 Basel, Switzerland
leo.hardegger@novartis.com

We present our results from process research and development using phenylalanine ammonia lyase (PAL) enzymes for the manufacture of the analgesic EMA401 (olodanrigan), a phenylalanine derivative which was used in clinical studies for the treatment of postherpetic neuralgia and neuropathic pain.¹

The results of our quest for the optimal reaction conditions of this biocatalytic hydroamination reaction are presented, with a detailed analysis of the most important parameters and the challenges encountered in the development of a reaction, which is thermodynamically not favored. We will also present our investigation of various work-up strategies and report the results from a successful scale-up.



[1] *Org. Process Res. Dev.* **2020**, *24*, 1763–1771