## **BIOCATALYTICAL ACCESS TO AMIDES**

Erna Zukic, acib, Krenngasse 37, Austria erna.zukic@uni-graz.at Christian Willrodt, BASF, Ludwigshafen, Germany Klaus Ditrich, BASF, Ludwigshafen, Germany Wolfgang Kroutil, Institute of Chemistry, University of Graz, Austria

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Amide formation is one of the most important reactions in industrial pharmaceutical synthesis.<sup>[1]</sup> Although the synthetic approaches appear to be simple, they suffer in fact from many drawbacks. The synthesis requires toxic or hazardous reagents to activate the ester or acid component and have a poor atom economy.<sup>[2]</sup> So far, many strategies to obtain amides have been published, but several problems have not been solved, yet.<sup>[3,4]</sup> Challenges are for example the direct transformation of carboxylic acids or esters with amines. Known chemical strategies require the hydrolysis of the ester, activation of the carboxylic acid via SOCl<sub>2</sub> leading to a reactive acyl chloride which reacts with the amine.

For these challenges, biocatalysis may offer a solution, especially because biocatalysis is known for using harmless reagents and working under mild conditions.



Figure 1 – Amide formation starting from a bulky acyl donor.

Our aim is to identify a biocatalytic access to amide formation, especially by the help of hydrolases starting from bulky acyl donors. Screening several hydrolases, one promising candidate is the lipase from *Sphingomonas sp.* HXN-200 also known as SpL.<sup>[5]</sup> The lipase was discovered and expressed by Li and co-workers in 2018. SpL shows high activity in aminolysis towards various acid and esters with amines in organic solvents. New substrates have been tested and functional studies on this protein shall be conducted to understand its reaction behavior with the help of the Loschmidt tools.

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References

[1] D. J. Constable, P. J. Dunn, J. D. Hayler, G. R. Humphrey, J. L. Leazer, R. J. Linderman, K. Lorenz, J. Manley, B. A. Pearlman, A. Wells, A. Zaks, T. Y. Zhang, *Green Chem.* 2007, *9*, 411–420.

[2] M. Petchey, A. Cuetos, B. Rowlinson, S. Dannevald, A. Frese, P. W. Sutton, S. Lovelock, R. C. Lloyd, I. J. Fairlamb, G. Grogan, *Angew. Chem. Int. Ed.* 2018, *57*, 11584–11588.

[3] J. Pitzer, K. Steiner, J. Biotechnol. 2016, 235, 32–46 2018, 57, 11584–11588.

[4] V. R. Pattabiraman, J. W. Bode, Nature 2011, 480, 471-479.

[5] S. Zeng, J. Liu, S. Anankanbil, M. Chen, Z. Guo, J. P. Adams, R. Snajdrova, Z. Li, ACS Catal. 2018, 8, 8856–8865.