Biocatalysis for the Sustainable Synthesis of Small Molecules Intermediates for APIs

Francesco G. Mutti

Van' t Hoff Institute for Molecular Science, HIMS-Biocat, University of Amsterdam, Science Park 904, 1098 XH, Amsterdam, The Netherlands
E-mail: f.mutti@uva.nl

The sustainable synthesis of small molecules as intermediates for APIs remains a challenge in the pharmaceutical industry. Traditional chemical synthesis often relies on harsh conditions and toxic reagents, generating significant waste and leading to environmental and economic concerns. Biocatalysis, which employs enzymes as catalysts, offers a green alternative for the synthesis of small molecules.[1] Enzymes are highly regio- and stereoselective, operate under mild conditions, and produce fewer, if any, by-products. This lecture will illustrate emerging trends and methodologies in biocatalysis and its application in the synthesis of small molecule intermediates for APIs. Various enzymatic transformations will be covered for the synthesis of e.g., (chiral) alcohols, amines, amides, carboxylic acids, nitriles and epoxides using oxidoreductases, transaminases, and hydrolases. Examples from my research group will be provided, such as the development of a new family of enzymes, called amine dehydrogenases (AmDHs), for the synthesis of chiral amines from ketones using only ammonia and generating water as the sole by-product.[2] Other examples include the engineering of a styrene monooxygenase to catalyze the asymmetric epoxidation of styrene,[3] and the enzymatic conversion of alcohols into nitriles.[4] These enzymes, along with others studied in my group, have been incorporated into biocatalytic cascade reactions for the synthesis of compounds such as chiral amines, amino alcohols, diols, and α-substituted chiral carboxylic acids with up to two stereogenic centers, starting from inexpensive and readily available materials (e.g., alcohols and alkenes). These biocatalytic cascades involve the use of multiple enzymes operating in one-pot, without the need to isolate intermediates. This approach leads to higher yields and purity of products, better selectivity and atom economy, reduced solvent and energy consumption, simplified process development, and lower costs.

References

[1] S. Simić, E. Zukić, L. Schmermund, K. Faber, C. K. Winkler, W. Kroutil, *Chem. Rev.* **2022**, *122*, 1052-1126.
[2] V. Tseliou, T. Knaus, M. F. Masman, M. L. Corrado, F. G. Mutti, *Nat. Commun.* **2019**, *10*, 3717.
[3] M. L. Corrado, T. Knaus, F. G. Mutti, *ChemBioChem* **2018**, *19*, 679-686.
[4] J. Vilim, T. Knaus, F. G. Mutti, *Angew. Chem. Int. Ed.* **2018**, *57*, 14240-14244.