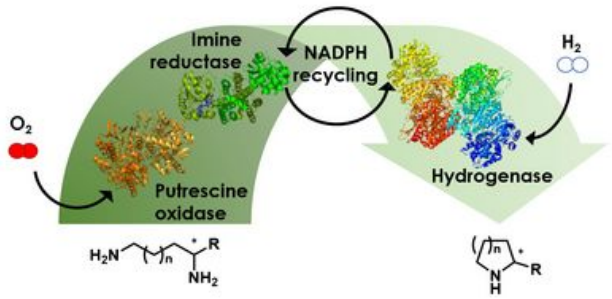
Synthesis of N-heterocycles from diamines via H2-driven NADPH recycling in presence of O2



Start Time: Wednesday, January 30, 2019

End Time:

2019 Jan 30

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Enzymatic cascades enable the regioselective and stereroselective synthesis of fine chemicals and pharmaceutics in a series of coupled reactions, which is of core interest of UniSysCat. In a joined collaboration, the groups of Lauterbach and Nestl designed an enzymatic cascade for the H_2-driven synthesis of nitrogen-heterocycles. Saturated nitrogen-heterocycles, especially pyrrolidines and piperidines, are attractive scaffolds for agrochemicals and pharmaceuticals. The newly developed enzymatic cascade included an O_2-dependent putrescine oxidase, a NADPH-dependent imine reductase and an O_2-tolerant $NADP^+$-reducing hydrogenase. The incorporation of a hydrogenase made the reducing power of H_2 available for biosynthesis. Enzyme engineering approaches were combined to optimize the specificity and activity of the putrescine oxidase from *Rhodococcus erythropolis* for the transformation of substituted diamines to the corresponding pyrrolidines and piperidines. The one-pot reaction resulted in up to 97% product formation. Furthermore, high selectivities up to 93% ee were obtained by exploiting the kinetic resolution of the putrescine oxidase. The prevention of organic solvents, toxic compounds or purification of intermediates demonstrates the “greeness” of this approach.

Green Chem. **2019** | Accepted Manuscript | DOI:10.1039/C8GC03798A