

Catalytic Cascade Reactions Inspired by Polyketide Biosynthesis

Christof Sparr
University of Basel

The biosynthesis of aromatic polyketides by non- or partially reducing polyketide synthases involves the controlled folding of poly- β -carbonyl chains by a fascinatingly intricate enzymatic machinery. In relation to polyene cyclizations and epoxide-opening cascades, an extraordinary number of folds thereby leads to tremendous structural variability. Given the versatility of the processes, directing the folding mode in biomimetic polyketide cyclizations with catalyst-control is a formidable challenge, guided by outstanding seminal work on stoichiometric reactions.

The talk will outline our stepwise approach to catalyst-controlled biomimetic polyketide cyclizations by gradually increasing the complexity of poly- β -carbonyl substrates. Analogously, noncanonical polyketide chains were selectively converted into aromatic products with a new-to-nature oxygenation pattern. A catalyst that controls the folding by an extended hydrogen-bond network is proposed and various applications of the products will be presented.

By taking inspiration from early stereochemistry and in particular the concepts of macrocyclic stereocontrol, transannular cyclizations of cyclic poly- β -carbonyl substrates, leading to structurally unique products with catalyst-control, were investigated as a next step. The presentation will highlight selected reaction cascades observed upon transannular aldol reactions of macrocyclic polyketides together with tailoring steps to reenter biosynthetic sequences.

