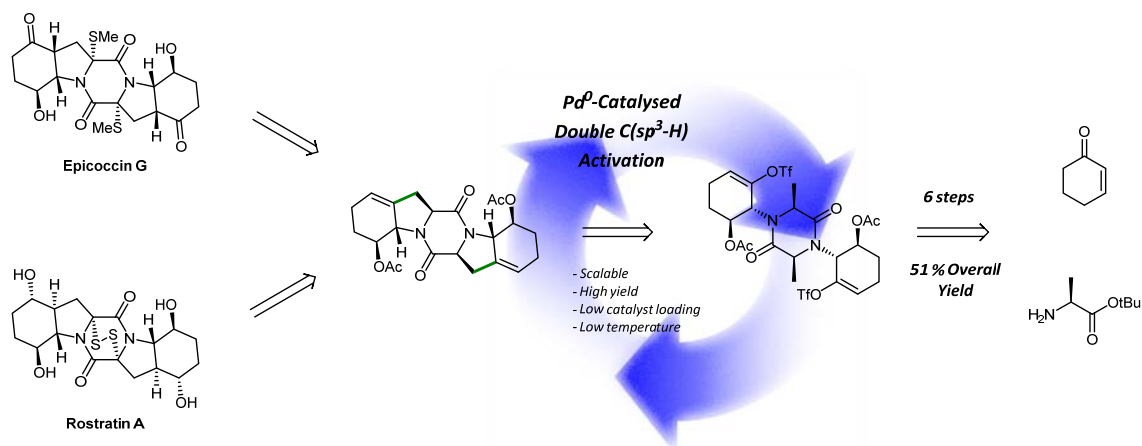


DIVERGENT TOTAL SYNTHESIS OF (+)-EPICOCCIN G AND (-)-ROSTRATIN A ENABLED BY DOUBLE C(sp³)-H ACTIVATION

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Dithiodiketopiperazine (DTP) natural products comprise a large number of metabolites, which display a wide range of biological activities including antiviral, antibacterial, antiallergic, antimalarial and cytotoxic properties.¹ DTPs, characterized by sulfur atoms on a fused diketopiperazine (DKP) structure, have gained significant interest from the synthetic community, due to their unique structural and biological properties. In particular, the groups of Nicolaou, Reisman and Tokuyama have reported elegant total syntheses of DTP molecules containing a pentacyclic ring system.^{2,3,4} The innovative strategy reported herein is based on a Pd(0)-catalysed double C(sp³)-H activation key step allowing straightforward, high-yielding and concise access to a common advanced intermediate bearing the pentacyclic DKP scaffold.^{5,6} The latter can be readily derivatised into several DTP natural products. Herein, we report the application of this C(sp³)-H activation-based strategy to the divergent enantioselective synthesis of epicoccin G and rostratin A, which are synthesized for the second and first time, respectively.



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