

# Enzymatic Polyketide Chain Branching to Give Substituted Lactone, Lactam, and Glutarimide Heterocycles.

Heine D, Bretschneider T, Sundaram S, Hertweck C (2014) Enzymatic Polyketide Chain Branching to Give Substituted Lactone, Lactam, and Glutarimide Heterocycles. *Angew Chem Int Ed Engl* 53(43), 11645-11649.

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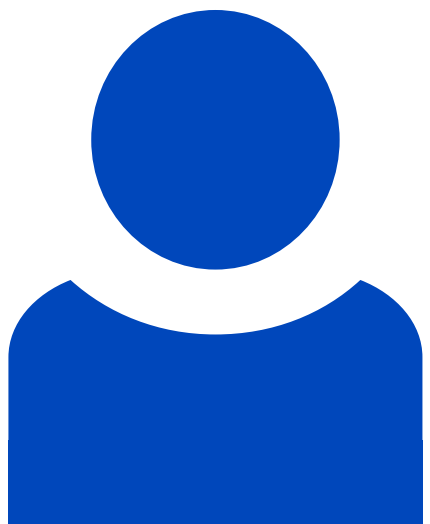
## Abstract

Polyketides typically result from head-to-tail condensation of acyl thioesters to produce highly functionalized linear chains. The biosynthesis of the phytotoxin rhizoxin, however, involves a polyketide synthase (PKS) module that introduces a  $\delta$ -lactone chain branch through Michael addition of a malonyl extender to an  $\alpha,\beta$ -unsaturated intermediate unit. To evaluate the scope of the branching module, polyketide mimics were synthesized and their biotransformation by the reconstituted PKS module from the *Rhizopus* symbiont *Burkholderia rhizoxinica* was monitored in vitro. The impact of the type and configuration of the  $\delta$ -substituents was probed and it was found that amino-substituted surrogates yield the corresponding lactams. A carboxamide analogue was transformed into a glutarimide unit, which can be found in many natural products. Our findings illuminate the biosynthesis of glutarimide-bearing polyketides and also demonstrate the utility of this branching module for synthetic biology.

## Beteiligte Forschungseinheiten

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**doi:** 10.1002/anie.201407282

**PMID:** 25214315