

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

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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 δ -lactone chain branch through Michael addition of a malonyl extender to an α,β -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 δ -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

[Biomolekulare Chemie](#) [Christian Hertweck](#) [Mehr erfahren](#)

Leibniz-HKI-Autor*innen



Daniel Heine

[Details](#)



Christian Hertweck

[Details](#)



Srividhya Sundaram

[Details](#)

Identifier

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