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. PubMed

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Projects

Biochemical characterisation of bacterial terpene cyclases
Details

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.

Identifier

doi: 10.1002/anie.201407282 PMID: 25214315