

Discovery of an Extended Austinoid Biosynthetic Pathway in *Aspergillus calidoustus*.

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Abstract

Filamentous fungi produce a wide range of natural products that are commonly used in various industrial contexts (e.g., pharmaceuticals and insecticides). Meroterpenoids are natural products of interest because of their various biological activities. Among the meroterpenoids, there is a group of insecticidal compounds known as the austinoids. These compounds have also been studied because of their intriguing spiro-lactone ring formation along with various modifications. Here, we present an extension of the original austinol/dehydroaustinol biosynthesis pathway from *Aspergillus nidulans* in the recently identified filamentous fungus *Aspergillus calidoustus*. Besides the discovery and elucidation of further derivatives, genome mining led to the discovery of new putative biosynthetic genes. The genes involved in the biosynthesis of later austinoid products were characterized, and among them was a second polyketide synthase gene in the *A. calidoustus* cluster that was unusual because it was a noninteractive polyketide synthase producing a diketide. This diketide product was then loaded onto the austinoid backbone, resulting in a new insecticidal

derivative, calidodehydroaustin.

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Leibniz-HKI-Autor*innen



Axel A. Brakhage

[Details](#)



Reinhard Guthke

[Details](#)



Christian Hertweck

[Details](#)



Fabian Horn

[Details](#)



Derek J. Mattern

[Details](#)



Markus Nett

[Details](#)



Kirstin Scherlach

[Details](#)



Vito Valiante

[Details](#)



Grit Walther

[Details](#)

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