

Discovery of clostrubin, an exceptional polyphenolic polyketide antibiotic from a strictly anaerobic bacterium.

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Abstract

Genome mining of the strictly anaerobic bacterium *Clostridium beijerinckii*, an industrial producer of solvents, revealed the presence of several cryptic gene clusters for secondary metabolite biosynthesis. To unearth its metabolic potential, a *C. beijerinckii* strain was cultured under various conditions, which led to the discovery of a deep purple pigment. This novel metabolite, named clostrubin (1), was isolated and its structure was fully elucidated. The pentacyclic polyphenol features a benzo[a]tetraphene ring topology that is unprecedented for natural products. Stable-isotope labeling experiments showed that 1 is an aromatic polyketide that folds in a noncanonical manner to form the unusual perifused ring system. In addition to being the first reported polyketide from an anaerobic bacterium, 1 is a potent antibiotic with pronounced activity against various pathogenic bacteria, such as MRSA, VRE, and mycobacteria, with minimum inhibitory concentrations (MIC) of 0.12-0.97 μM .

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