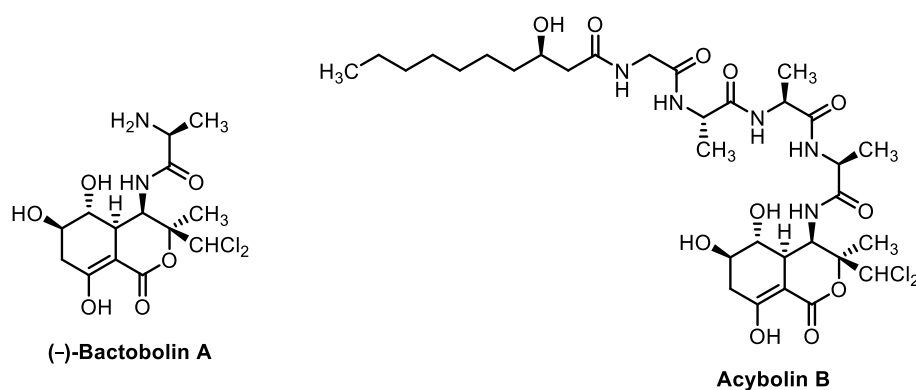


Total Synthesis of the Cryptic Secondary Metabolite Acybolin B

Raju Hazra, Prabhakara R. Tharra, and Jakub Švenda*

Masaryk University, Faculty of Science, Department of Chemistry, Kamenice 5/A8, 623 00 Brno, Czech Republic.

rajuhazra@mail.muni.cz; svenda@chemi.muni.cz



Bactobolin A is a member of the polyketide–non-ribosomal peptide family of natural products, first isolated in the late 1970s. This secondary metabolite inhibits the growth of several Gram-positive and Gram-negative bacterial strains. It is also cytotoxic toward various cancer cell lines. Bactobolin A acts as a protein synthesis inhibitor by targeting a unique binding site within the bacterial and the eukaryotic ribosomes.

Acybolins are so-called cryptic secondary metabolites that have been identified only recently. Seyedsayamdost group at Princeton University used sublethal concentrations of the antibiotic trimethoprim to elicit the normally silent biosynthetic gene cluster of acybolins. Little is currently known about the roles of these cryptic metabolites in the context of regulated protein synthesis and bacterial communities. Acybolins are structurally related to bactobolins though significantly more complex. They are available only through isolation, as no semisynthetic or synthetic route was reported to date. In this contribution, I am going to highlight different approaches we have taken to successfully prepare acybolin B in laboratory, prioritizing high convergency of the synthetic approach.

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