Bioactivity and mode of action of bacterial tetramic acids.

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Details

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Abstract

Microbially produced 3-acyltetramic acids display a diverse range of biological activities. The pyreudiones are new members of this class that were isolated from bacteria of the genus Pseudomonas. Here, we performed a structure-activity relationship study and determined their mode of action. An efficient biomimetic synthesis was developed to synthesize pyreudione A. Pyreudiones and synthetic analogs thereof were tested for their amoebicidal, antibacterial, antiproliferative, and cytotoxic activities. The length of the alkyl side chain and the nature of the amino acid residues within the tetramic acid moiety strongly affected activity, in particular against mycobacteria. The mode of action was shown to correlate with the ability of pyreudiones to act as protonophores. Removal of the acidic proton by methylation of pyreudione A resulted in a loss of bioactivity.

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