Sulfonium acids loaded onto an unusual thiotemplate assembly line construct the cyclopropanol warhead of a *Burkholderia* virulence factor.

Trottmann F, Ishida K, Franke J, Stanišić A, Ishida-Ito M, Kries H, Pohnert G, Hertweck C (2020) Sulfonium acids loaded onto an unusual thiotemplate assembly line construct the cyclopropanol warhead of a *Burkholderia* virulence factor. *Angew Chem Int Ed* 59(32), 13511-13515.

Details

Abstract

Pathogenic bacteria belonging to the Burkholderia pseudomallei group cause severe infectious diseases such as glanders and melioidosis. Malleicyprols were identified as important bacterial virulence factors, yet the biosynthetic origin of their cyclopropanol warhead that is crucial for bioactivity has remained enigmatic. By a combination of mutational analysis and metabolomics we found that sulfonium acids, dimethylsulfoniumpropionate (DMSP) and gonyol, known as osmolytes and as crucial components in the global organosulfur cycle, are key intermediates en route to the cyclopropanol unit. Functional genetics and in vitro analyses uncover a specialized pathway to DMSP involving a rare prokaryotic SET-domain methyltransferase for a cryptic methylation, and show that DMSP is loaded onto the NRPS-PKS hybrid assembly line by an adenylation domain

dedicated to zwitterionic starter units. Then, the megasynthase transforms DMSP into gonyol, as demonstrated by heterologous pathway reconstitution in E. coli .

Beteiligte Forschungseinheiten

Biomolekulare Chemie Christian Hertweck Mehr erfahren

Biosynthetisches Design von Naturstoffen Hajo Kries Mehr erfahren

Leibniz-HKI-Autor*innen

Jakob Franke

Details

Christian Hertweck

Details

Keishi Ishida

Details

Mie Ishida-Ito

Details

Hajo Kries

Details

Felix Trottmann

Details

Identifier

doi: 10.1002/anie.202003958

PMID: 32314848