Synthesis of ramariolide natural products and discovery of their targets in mycobacteria

Ramariolides A-D are natural products with antibacterial activity. To exploit their cellular mechanism, we here devise the first total synthesis and prepare a photoprobe for target identification. Antibacterial testing against several pathogenic strains including Mycobacterium tuberculosis revealed the highest potency for ramariolide A. Chemical proteomics unraveled binding to essential proteins for amino acid anabolism.