

Biomimetic Thioesters as Probes for Enzymatic Assembly Lines: Synthesis, Applications, and Challenges.

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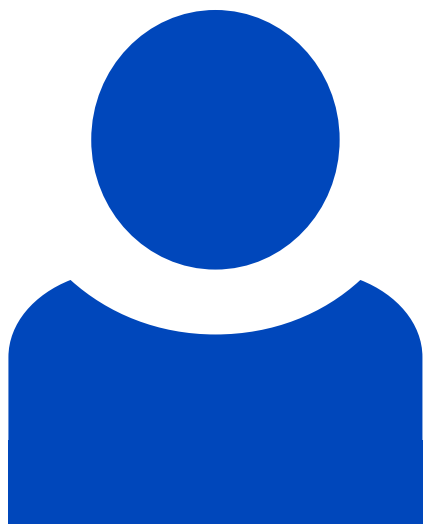
Abstract

Thioesters play essential roles in many biosynthetic pathways to fatty acids, esters, polyketides, and non-ribosomal peptides. Coenzyme A (CoA) and related phosphopantetheine thioesters are typically employed as activated acyl units for diverse C-C, C-O, and C-N coupling reactions. To study and control these enzymatic assembly lines in vitro and in vivo structurally simplified analogs such as N-acetylcysteamine (NAC) thioesters have been developed. This review gives an overview on experimental strategies enabled by synthetic NAC thioesters, such as the elucidation of complex biosynthetic pathways and enzyme mechanisms as well as precursor-directed biosynthesis and mutasynthesis. The review also summarizes synthetic protocols and protection group strategies to access these versatile synthetic tools, which are reactive and often unstable compounds. In addition, alternative phosphopantetheine thioester mimics are presented that can be used as protein tags or suicide inhibitors for protein crosslinking and off-loading probes to elucidate polyketide intermediates.

Beteiligte Forschungseinheiten

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