Towards the total synthesis of the bacteriocin Nisin A on solid support

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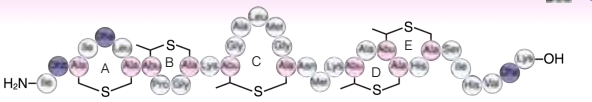


Background

What is nisin?

Nisin A is an antimicrobial peptide produced by *Lactococcus lactis*. It is active against a broad spectrum of Gram-positive bacteria at nanomolar concentrations. Nisin has been widely used as a food preservative (E234) in the past 50 years.

Why bother to synthesize it chemically if bacteria can produce it?

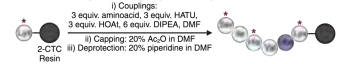
Despite its antimicrobial activity, nisin A is not used as a drug (yet)! It is unstable *in vivo* and is degraded very fast by proteases. The total synthesis of nisin A on solid support would allow us to conduct structure-activity relationship studies and potentially find analogues more suitable as antibiotic drugs.

Why hasn't anyone synthesized nisin A on the solid phase yet?

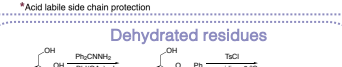
Nisin A's chemical structure contains dehydrated amino acids and (methyl)lanthionine rings, which are challenging to synthesize and incorporate in solid phase peptide synthesis. Take a look at our approach!

Our approach

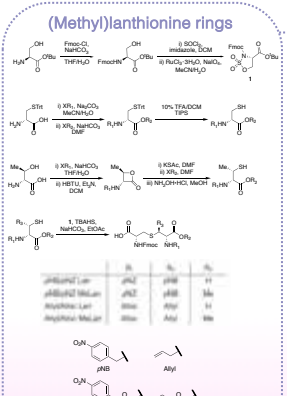
Solid phase peptide synthesis (SPPS)

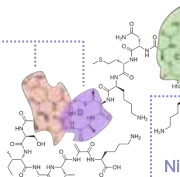


Dehydrated residues

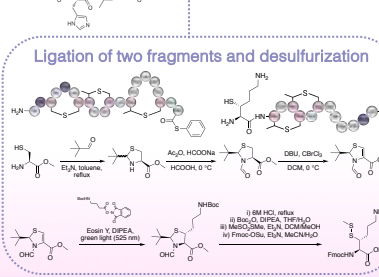


(Methyl)lanthionine rings





Ligation of two fragments and desulfurization



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