Rufomycins are cyclic heptapeptides which exhibit potent biological activity against multidrug-resistant isolates of Mycobacterium tuberculosis. They contain four non-proteinogenic amino acids: 2-amino-4-hexenoic acid (AHA) is unique and has not been observed in any other natural product, 3-nitrotyrosine is a structural motif rarely found in peptides, γ-hydroxyeucine as well as the tryptophan unit are also found in the structurally related Cyclomarins. In the 1960s, the first Rufomycins were isolated from Streptomyces atratus nov. sp. or Streptomyces islandicus. To date, several more Rufomycins have been discovered.

**Synthesis of the non-proteinogenic Amino Acids**

![Synthesis of the non-proteinogenic Amino Acids](image)

**Synthesis of the Rufomycin Derivatives**

For the assembly of the heptapeptides, a linear linkage strategy from the C- to the N-terminus starting from leucine was chosen. Consequently, the macrolactamisation was carried out between the Leu and the AHA unit. Subsequent oxidations to derivatives 16 and 17 were performed according to the experimental procedure of Guo and Ye, who published the total synthesis of Rufomycins 21 and 23 in 2018.