
Jörg Erdsack, Norbert Krause†

Introduction

The nonproteinogenic α-amino acid (–)-furanomycin (Figure 1) is one of very few natural products containing a 2,5-dihydrofuran ring. It was first isolated in 1967 by Katagiri et al. 1 from Streptomyces threomyceticus and it is one of the smallest antibiotic natural products, inhibiting bacterial protein synthesis by mimicking isoleucine. 2 Due to its activity and moderate chemical complexity, several syntheses of furanomycin and derivatives thereof 3 have been disclosed, often using sugars as the starting material.

By taking advantage of the high reactivity and axial chirality of allenes, 4 we have recently extended the gold-catalyzed cyclization of functionalized allenes. 5 This provides an efficient access to somatostatin, pure target molecules, and it is one of the smallest antibiotic natural products, inhibiting bacterial protein synthesis by mimicking isoleucine. 2 Due to its activity and moderate chemical complexity, several syntheses of furanomycin and derivatives thereof 3 have been disclosed, often using sugars as the starting material.

The results show that the gold-catalyzed cycloisomerization of α-hydroxyallenes is a powerful tool in multistep synthesis. In conjunction with the allenylation of carbonyl compounds we are able to synthesize quickly a wide range of natural product derivatives, which find application in pharmaceutical screening programs.

Results

The following two-step oxidation with Dess-Martin Periodinane 6 and Pinnick oxidation of the aldehyde intermediate with NaClO₂ in buffered solution in the presence of 2-methyl-2-butene 7 was insufficient, because chlorolactonization of the boc-protected amino acids by hypochloric acid, the degradative product of the oxidant, takes place. In a control experiment, the oxidation in the absence of any scavenger for dichlorophosphate allows the expected lactone 7a in 53 % yield (scheme 2). 8b Simple crystals of the bicyclic lactones were used for establishment of the stereochemistry 16a,b to prove the anti selectivity of the allenylation step 1a/b → 2a/b (scheme 2). Replacement of 2-methyl-2-butene by resorcinol (scheme 1) and an improved work-up procedure developed by us affords the acids 5a/b in 36 and 41 % yield, respectively, which gave after deprotection with trifluoroacetic acid the amino acids 6a/b in good yield.

Scheme 1 Synthesis of the furanomycin derivatives 4a/b by gold-catalyzed cycloisomerization of α-hydroxyallenes 2a/b

Scheme 2 Chlorolactonization of the hydroxycarbamate 4b and X-ray structure of lactone 7a.

In our working group, we are currently involved in the extension of this method to cyclize the corresponding α-aminoaldehydes which provides an access to nitrogem-containing derivatives ("Azafuranomycins"). Results from these research will be published elsewhere.

References

1 Dortmund University, Organic Chemistry II, D-44221 Dortmund, Germany (e-mail: norbert.krause@uni-dortmund.de).