Synthesis of Bacillamide C analogues

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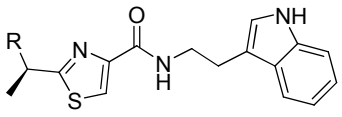
INTRODUCTION

The Bacillamide A (**1**) recently isolated from the marine bacterium *Bacillus* sp. SY-1, is a compound with algaecide activity against the harmful dinoflagellate *Cochlodinium polykrikoides*. The bacillamide C (**2**) isolated from a Bahamian hypersaline microbial mat, has not been tested for algicidal activity due to a lack of sufficient material.[1] Different synthesis of this compound were described in literature.[2] In this work we prepare the Bacillamide **2,** by eight steps starting from L-alanine.

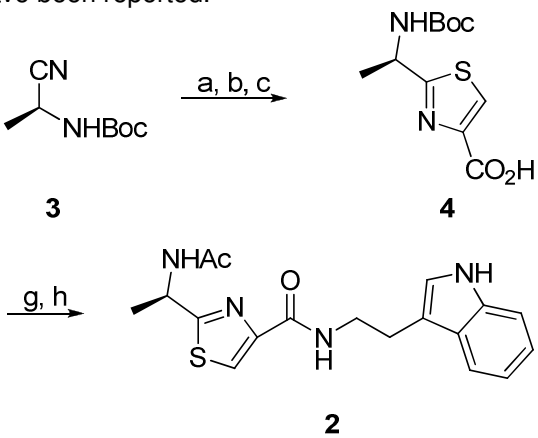


1 R=O
2 R=NHAc

Figure 1. Bacillamides structure

RESULTS AND DISCUSSION

The thiazole ring has been subject of much interest in chemistry due to it presence in many naturally occurring compounds. Several methods for the preparation of thiazoline and thiazole ring have been reported.[3]



3 **4**

2

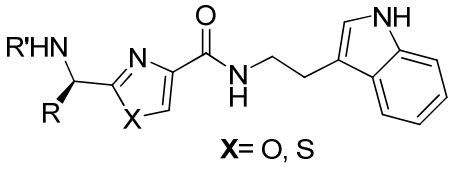
a) Cys ethyl ester, pH 6; b) DBU, BrCCl3; c) KOH, THF; g) tryptamine, ClCO2Et; h) Ac2O, Py

Scheme 1. Synthesis of Bacillamide C

The N-Boc aminoacetonitrile **3** was prepared in three steps starting from L-alanine. Then thiazoline ring was obtained by addition of cysteine ethyl ester in pH 6 phosphate buffer, the reaction mixture was stirred overnight at 60°C. The thiazoline was oxidized to thiazole using bromotrichloromethane-DBU. Finally ester hydrolysis using KOH in THF afforded compound **4**.[4] The condensation between **4** and tryptamine gave the N-Boc bacillamide. Finally, **2** was obtained after Boc-deprotection and N-acetylation**.**

In order to synthesize new analogues, we applied this methodology starting from different amino acids besides L-alanine, Figure 2.

The preparation of analogues containing the oxazole ring, were prepared employing the methodology reported by Wipf.[5]



X= O, S

Figure 2. Bacillamides analogues.

CONCLUSION

The bacillamide C and analogues containing oxazole ring were synthesized, nevertheless some steps of synthesis should be optimized for best performance, and then test their biological activities.

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