Synthesis of the C1-C13 fragment of Nhatrangin A

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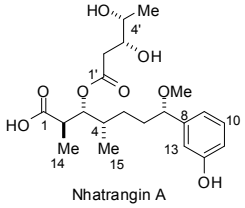
INTRODUCTION

Nhatrangin A (**1**) is a polyketide metabolite containing 6 stereogenic centers, isolated in 2010 from a Vietnamese collection of marine cyanobacterium *Lyngbya majuscula*. Its structure was assigned based on spectrometric and spectroscopic methods including 2D NMR experiments.[1]

Figure 1. Nhatrangin A



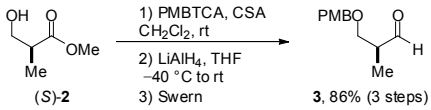
Nhatrangin A

This work aimed to the synthesis of the C1-C13 fragment of nhatrangin A.

RESULTS AND DISCUSSION

Our studies began with the preparation of aldehyde **3** (Scheme 1). Treatment of (*S*)-Roche ester **2** with PMB 2,2,2-trichloroacetimidate (PMBTCA) and camphorsulfonic acid (CSA) followed by reduction with $LiAlH_4$ and Swern oxidation provided aldehyde **3** in 86% yield (3 steps).

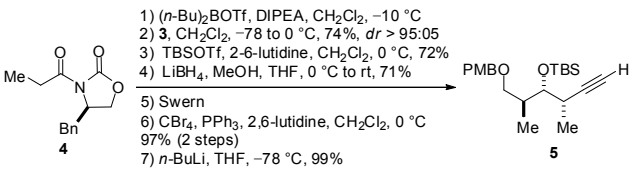
Scheme 1. Preparation of aldehyde **3**



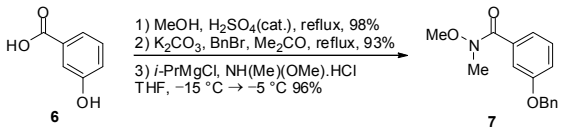
The aldol reaction between the boron enolate of acyloxazolidinone **4** and aldehyde **3** (74%, *dr* > 95:05) followed by treatment with TBSOTf and 2,6-lutidine (72%), reduction with $LiBH_4$ in MeOH/THF (71%), Swern oxidation, treatment with CBr_4, PPh_3, and 2,6-lutidine (97%, 2 steps), and treatment with *n*-BuLi in THF provided the formation of alkyne **5** (99%) (Scheme 2).[2]

The esterification of 3-hydroxy benzoic acid (**6**) (98%) followed by treatment with benzyl bromide and K_2CO_3 (93%), provided an intermediate protected ester that was treated with *i*-PrMgCl and NH(Me)(OMe).HCl to provide the Weinreb amide **7** (96%) (Scheme 3).

Scheme 2. Preparation of alkyne **5**

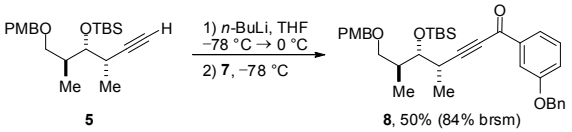


Scheme 3. Preparation of Weinreb amide **7**



Finally, the coupling of alkyne **5** with Weinreb amide **7**, mediated by *n*-BuLi, gave the ketone **8** in 50% yield (84% brsm) (Scheme 4).

Scheme 4. Preparation of ketone **8**



CONCLUSION

In summary, we have achieved a stereoselective synthesis of the C1-C13 fragment of nhatrangin A in 10 steps with an overall yield of 16%.

ACKNOWLEDGEMENTS

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