Synthesis of the C5-C17 fragment of saliniketal A

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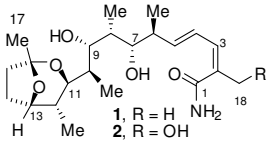
INTRODUCTION

The marine-derived saliniketals A (**1**) and B (**2**) were isolated from the marine actinomycete *Salinispora arenicola* by Fenical and co-workers.[1a] Their structures were confirmed by total synthesis in 2007.[1b] We wish to describe here our synthetic strategy for the synthesis of saliniketal A.

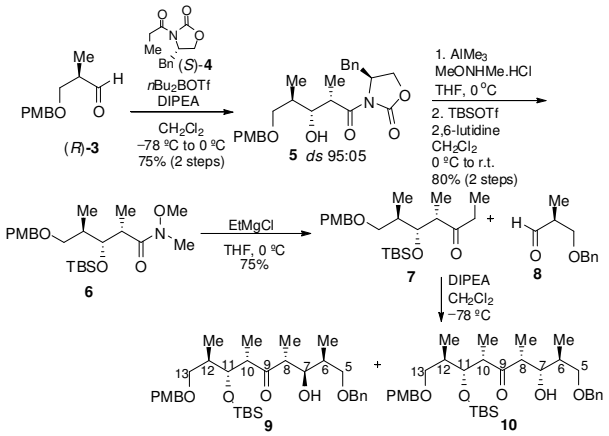


RESULTS AND DISCUSSION

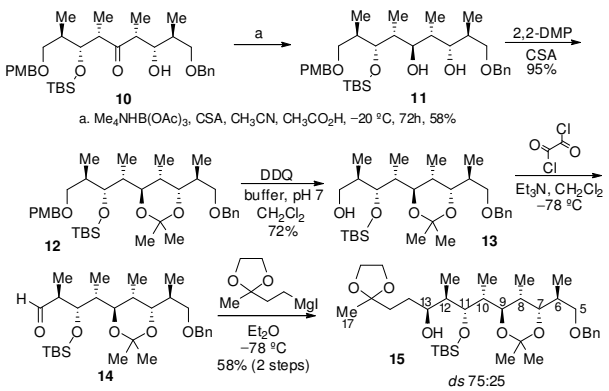
Our approach began with an asymmetric aldol addition of the boron enolate derived from oxazolidinone (*S*)-**4** with aldehyde (*R*)-**3** to give aldol adduct **5** (75%, *ds* 95:5). Transamidation followed by protection of the alcohol functionality provided Weinreb amide **6** (80%, 2 steps), which was treated with EtMgCl providing **7** (75%). Three different attempts of a double stereodifferentiating aldol reaction were performed using diferent Lewis acids (Table 1) and a selectivity inversion was observed when Ti(*i*PrO)Cl_3 was employed. The relative stereochemistry was assigned by applying the method of Murata and co-workers's for conformational analysis of acyclic systems, based on proton-carbon coupling constants.[2-4] These results allowed us to attribute the desired 6,7-*anti* and 7,8-*syn* configuration for compound **10** (Scheme 1). Stereoselective reduction of β-hydroxy ketone **10** delivered *anti*-diol **11** in 58% yield and 85:15 diastereoselectivity. The conversion of diol to the corresponding isopropylidene acetal according to the Rychnovsky methodology,[5] confirmed the 1,3-*syn* relative stereochemistry. Removal of the PMB group and Swern oxidation provided aldehyde **14,** which was treated with the corresponding Grignard reagent providing **15** in 58% yield for the two steps.

Table 1. Lewis acids used in aldol reactions between **7** and **8**.

Lewis Ac.	Yield (2 steps)	*dr* (**9:10**)
$TiCl_4$	52%	72:28
$SnCl_4$	58%	83:17
Ti(*i*PrO)Cl_3	60%	15:85



Scheme 1. Preparation of C5-C13 fragment.



Scheme 2. Preparation of C5-C17 fragment.

CONCLUSION

The synthesis of the C5-C17 fragment (**15**) of saliniketal was achieved in 11 steps and 6% overall yield.

ACKNOWLEDGEMENTS

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