

Preparation of an Intermediate for the Synthesis of Prostaglandins and Analogues

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Abstract

Prostaglandins are important molecules with a wide range of biological activities. In this work, a precursor for the synthesis of these compounds was synthesized and its potential use in the synthesis of an anti-tumor agent (TEI-9826) is currently being evaluated.

Key words:

Prostaglandins, Synthesis, Morita-Baylis-Hillman

Introduction

Prostaglandins are lipid molecules derived from arachidonic acid, and are produced in almost all animal cells. This class of compounds participates in a variety of organism functions.¹ Due to the similarity between this nucleus and the one obtained from the Morita-Baylis-Hillman Reaction (MBH) of 2-cyclopentenones with aliphatic aldehydes, we decided to explore the potentiality of MBH adducts as prostaglandin precursors (Figure 1).

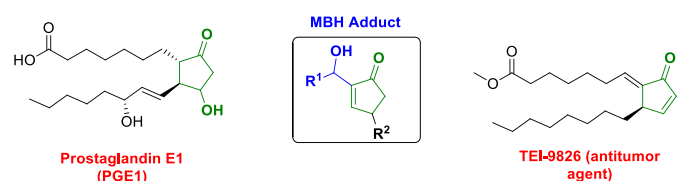
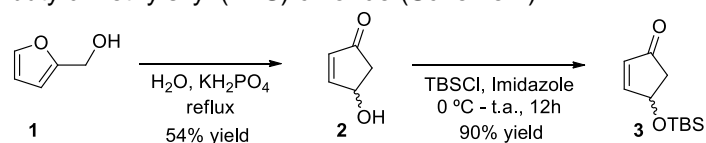


Figure 1. A Natural Prostaglandin and TEI-9826.

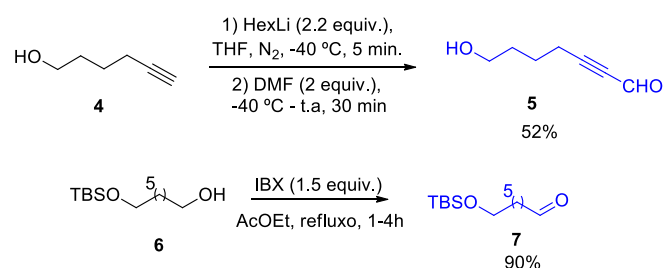
Results and Discussion

To synthesize adducts which could serve as precursors for the three compounds shown in Figure 1, 4-hydroxy-2-cyclopenten-1-one was obtained via Piancatelli rearrangement, and was protected in sequence with *tert*-butyldimethylsilyl (TBS) chloride (Scheme 1).



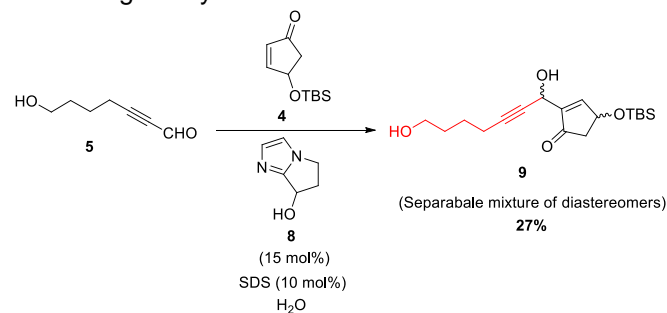
Scheme 1. Synthesis of Protected 4-hydroxy-2-cyclopent-1-one.

An alkyl and a propargylic aldehyde were synthesized to be tested in the MBH reaction with both, 2-cyclopenten-1-one and the 4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopenten-1-one (Scheme 2).²



Scheme 2. Synthesis of 7-hydroxyhept-2-ynal and 7-[(*tert*-butyldimethylsilyl)oxy]heptanal.

In order to test the viability of the reaction, aldehyde **5** was subjected to the MBH reaction with cycloenone **4** in previously optimized conditions, to obtain a separable mixture of diastereomers in 3:2 ratio (Scheme 3).³ The relative stereochemistry of the products could not be determined using NOESY techniques. Further optimization should be done to improve the yield before continuing the synthesis.



Scheme 3. MBH Reaction between Aldehyde **5** and Cycloenone **4**.

Conclusions

As demonstrated above, the synthesis of common intermediate **9** was accomplished. Other aldehydes and adducts, as well as other MBH reaction conditions, are being tested, and the total synthesis of TEI-9826 and natural prostaglandins is already ongoing.

Acknowledgement

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