Preparation of an Intermediate for the Synthesis of Prostaglandins and Analogues

Lucas A. Zeoly*, Fernando Coelho.

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.](image)

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.](image)

An alkyl and a propargylic aldehyde were synthesized to be tested in the MBH reaction with both, 2-cyclopentenone 4 in previously optimized conditions, to obtain a separable mixture of diastereomers in 3:2 ratio (Scheme 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.](image)

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
The authors thank the São Paulo Research Foundation and the Brazilian Council for Scientific and Technological Development (CNPq) for financial support.

References