Synthetic studies towards Ambrox and analogues from coronarin-D

Paulo M. Imamura*, Márcia Y. Okubo, Lúcia Helena B. Baptistella

Instituto de Química – UNICAMP, C. Postal 6154, CEP 13.084-970, Campinas, S. Paulo, Brazil

**e-mail: imam@iqm.unicamp.br*

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INTRODUCTION

Tetranorlabdane oxide (**1**)[1] is a synthetic substitute of ambergris and is known in the market under the trade names Ambrox® (Firmenich), Amberlyn® (Quest) and Ambroxan® (Henkel).[2] The number of publications on this topic in the last years still demonstrate the great interest and importance of ambergris derivatives nowadays.[3] As part of our current interest on organic synthesis using natural products as chiral templates, we undertook the synthesis of Ambrox® (**1**) from readily available coronarin-D (**2**), isolated from *Hedychium coronarium*.[4]

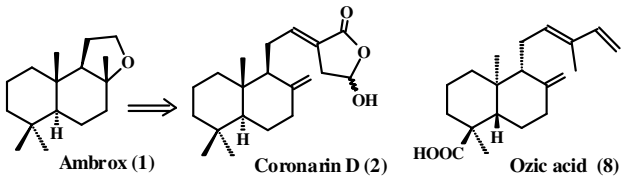
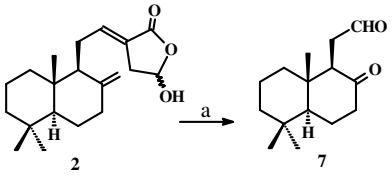


Figure 1. Structures of Ambrox (**1**) and coronarin-D (**2**)

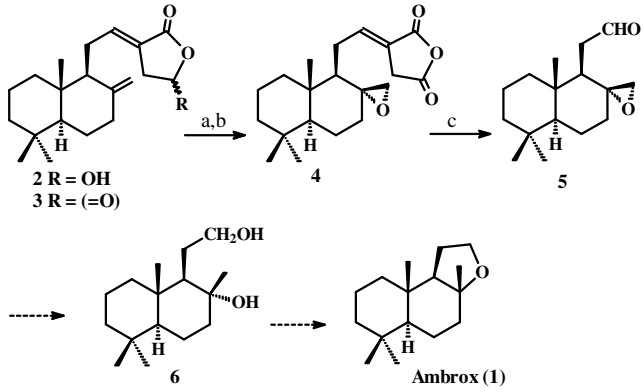
RESULTS AND DISCUSSION

Looking at the structures of **1** and **2**, we proposed manipulations on the side chain on C-9 of **2** to construct the tetrahydrofuran moiety on **1**. In the first essay, an epoxidation reaction of the terminal double bond of **2** with MCPBA was tried, but it led to an intractable mixture of compounds. Thus, the hemiketal was first oxidized with PCC and the corresponding anhydride **3,** isolated in 56% yield, was treated with MCPBA. The epoxide **4**, obtained in 40% yield, was submitted to an ozonolysis reaction to furnish the epoxy-aldehyde **5**. Further sequence to the synthesis of Ambrox® (**1**) is in progress.

Alternatively, the keto-aldehyde **7** was obtained in one step through ozonolysis of **2**, but only in a modest yield of 25%. The enantiomer of **7** was already prepared from ozic acid (**8**) and was an important intermediate used for the synthesis of ambrox analogous.[5]



Scheme 2. a). O_3, CH_2Cl_2, then $P(OCH_3)_3$



Scheme 1. a). PCC, CH_2Cl_2; b). MCPBA, CH_2Cl_2; c). O_3, CH_2Cl_2, then $P(OCH_3)_3$

CONCLUSION

Coronarin-D (**2**), the major constituent of the rhizome extract of *Hedychium coronarium* showed to be a suitable starting material for the synthesis of ambergris type odorants. The yields presented here still need to be optimized, but the intermediates **5** and **7** represent versatile synthons for ambrox analogous.

ACKNOWLEDGEMENTS

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