Selective oxidations of organoboron compounds catalyzed by Baeyer-Villiger monooxygenases

Patrícia B. Brondani,[a] Gonzalo de Gonzalo,[b] Marco W. Fraaije[b] and Leandro H. Andrade[a*]

[a]*Universidade de São Paulo, Av. Prof. Lineu Prestes 748, SP 05508-900, São Paulo, Brazil.*

[b]*University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands.*

**e-mail leandroh@iq.usp.br*

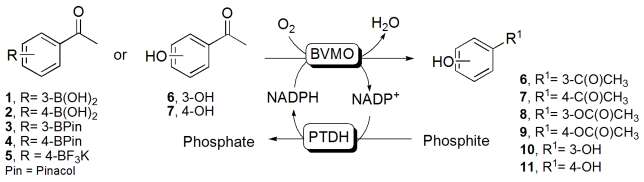
Keywords: Baeyer-Villiger monooxygenases; boron compounds; oxidation reactions.

INTRODUCTION

BVMOs are known for performing the oxidation of aldehydes and ketones to their corresponding esters, the oxygenation of heteroatoms (sulfur, nitrogen, phosphorus, boron, selenium) and even epoxidation reactions.[1,2] In this work we have explored BVMOs and organoboron compounds as well as racemic ones as target substrates in BVMOs-catalyzed oxidation reaction.

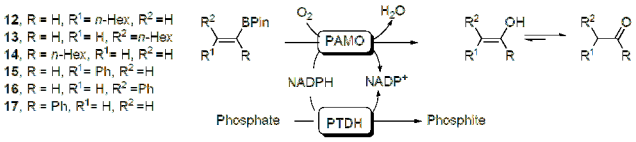
RESULTS AND DISCUSSION

Initially, five boron-containing acetophenones (**1-5**) and hydroxyacetophenones (**6** and **7**) were selected as substrates (Scheme 1). When PAMO was used as biocatalyst, the boron oxidation was observed for all substrates affording the corresponding phenols. However, the B-V reaction was achieved only for the 4-substituted substrates. The M446G PAMO mutant presented a similar behavior for all substrates. On the other hand, in all HAPMO-catalyzed reactions, both oxidations occurred (boron oxidation and B-V reaction). The CHMO showed a high chemoselectivity, in favor of boron oxidation, but low activity.



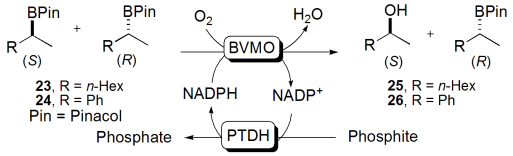
Scheme 1- Oxidation of boron-containing acetophenones catalyzed by BVMOs.

We have also explored the BVMO-catalyzed oxidation of vinyl boron compounds **12-17** (Scheme 2). It was observed that no epoxidation was achieved for any of the substrates and no reaction was observed for compounds **12-14**. Nevertheless, only for compounds **15-17** the boron oxidation was observed.



Scheme 2- Oxidation of vinyl boron compounds **12-17** catalyzed by BVMOs.

We also decided to evaluate the enzymatic kinetic resolution of chiral boron-compounds (**23** and **24**) catalyzed by PAMO (Scheme 3). After 24 h no reaction was observed for compound **23.** However, the enzymatic oxidation of **24** showed excellent results in which the (*S*)-borane was oxidized to the corresponding (*S*)-alcohol (ee = 91%) in 5h and pH=7.5 (conv. = 49%).



Scheme 3- Kinetic resolution of chiral boron-compounds catalyzed by PAMO.

CONCLUSION

We have found that the boron oxidation catalyzed by the studied BVMOs occurs rather than the Baeyer-Villiger reaction or the epoxidation process. This study also revealed that PAMO is very well suited to perform enantioselective boron oxidations.

ACKNOWLEDGEMENTS

CNPq, CAPES, FAPESP and EU-FP7 Oxygreen project for financial support.

REFERENCES

[1] a)Torres Pazmiño, D. E.; Dudek, H.; Fraaije, M. W.; *Curr. Opin. Chem. Biol.* **2010**, *14*, 138. b) Nolan, L. C.; O'Connor, K. E. *Biotechnol. Lett.* **2008**, *30*, 1879. c) Van Berkel, W. J. H.; Kamerbeek, N. M.; Fraaije, M. W. *J. Biotechnol.* **2006**, *124*, 670. [2] a) Colonna, S.; Gaggero,N.; Carrea, G. Ottolina, P.; Pasta,P.; Zambianchi, F. *Tetrahedron: Lett.* **2002**, *43*, 1797. b) Branchaud, B. P.; Walsh, C. T. *J. Am. Chem. Soc.* **1985**, *107*, 2153.
[3] Patti, A.; Pedotti, S.; Sanfilippo,C. *Chirality* **2007**, 19, 344.