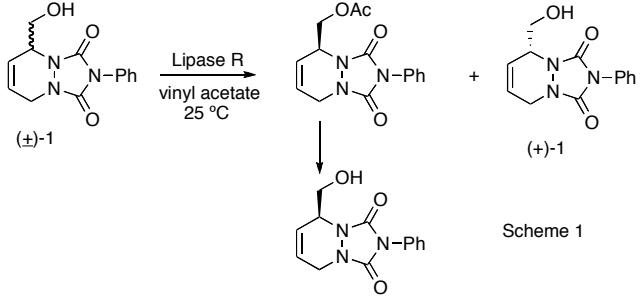
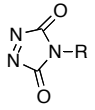
Chemoenzymatic Synthesis of 1-Azafagomine Analogues

R. Mendes, Vera C. M. Duarte, A. Gil Fortes, M. J. Alves, J. A. Martins, N. M. Micaelo
University of Minho, Chemistry Research Centre, Campus de Gualtar, 4700-057, Braga, Portugal
tec.raquelmendes@gmail.com

The synthesis of cycloadduct **1** is described in the literature in 87 % yield [1]. The kinetic enzymatic resolution of adduct **1** leads to both enantiomers **(+)-1** and **(-)-1** in high enantiomeric excess (> 96 % *ee*) according to scheme 1. [1]



Scheme 1



2

a R= C_6H_5 (PTAD)
b R = *p*-$NO_2C_6H_4$
c R = CH_2-*p*-FC_6H_4
d R = *p*-CNC_6H_4

Figure 1

In this work this methodology is applied to analogues of PTAD **2b-d** (Figure 1). The interest of this structural modification is based on molecular modelling studies, which predicted a higher inhibitory activity for the final products due to the possibility of forming extra hydrogen bonds. The homochiral 1-azafagomine analogues will be evaluated as α- and β-glycosidases; the type of inhibition and the inhibition constants (K_i) will be determined for all compounds.

Acknowledgements: *The authors thank to FCT (PTDC/QUI/67407/*2006*),* QREN, COMPETE and POPH for financial support and to the Portuguese NMR Network *RNRMN* (Bruker Avance II 400). *V.C.M.D. also thanks for a PhD grant (SFRH/BD/61290/2009).*

References:

[1] X. Liang, M. Bols *J. Org. Chem. 64*, **1999**, 8485-8488.