Lipase-mediated Desymmetrization of 1,3-di-O-Benzyl-myoinositol

Karla C. Pais, Evelin A. Manoel, Denise M. G. Freire and Alessandro B. C. Simas*

*Universidade Federal do Rio de Janeiro (UFRJ), Instituto de Pesquisas de Produtos Naturais (IPPN), Lab. Roderick A. Barnes, CCS, bloco H and aUFRJ, Instituto de Quimica, Depto. Bioquímica, CT, bloco A, 5º andar - Ilha do Fundão, Rio de Janeiro, RJ, Brazil

e-mail corresponding author: abcsimas@nppn.ufrj.br

Keywords: desymmetrization, myo-inositol, lipase

INTRODUCTION

The phosphorylated myo-inositols play key roles in fundamental biological phenomena such as cellular signal transduction. Notwithstanding the efficiency and practicality of catalytic reactions, most syntheses of chiral inositols have relied on chiral derivatizations. In this context, few reports in the literature have explored lipases for desymmetrisations and kinetic resolutions of myo-inositol derivatives.

In this work, we report the enzymatic desymmetrization of 1,3-di-O-benzyl-myoinositol 1 (Scheme 2).

RESULTS AND DISCUSSION

Our group has managed to prepare meso-diether 1 through the direct controlled di-O-benzylation of myo-inositol 2 via stannylene acetal catalysis (Scheme 1).

![Scheme 1. One-pot synthesis of diether 1 from myo-inositol 2.](https://via.placeholder.com/150)

Compound 1 was screened against nine lipases in vinyl acetate (solvent and acyl donor) for transesterification. (Scheme 2, Table 1).

Table 1. Screening of different enzymes in the desymmetrization of 1.

<table>
<thead>
<tr>
<th>Lipase</th>
<th>Time(h)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS-D</td>
<td>96</td>
<td>-</td>
</tr>
<tr>
<td>A-Amano</td>
<td>96</td>
<td>-</td>
</tr>
<tr>
<td>PS-C amano</td>
<td>96</td>
<td>-</td>
</tr>
<tr>
<td>Novozyme 435</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>Lipozyme RM-IM</td>
<td>72</td>
<td>4</td>
</tr>
<tr>
<td>Lipozyme TL-IM</td>
<td>48</td>
<td>4</td>
</tr>
</tbody>
</table>

Lipases Lipozyme TL-IM and Lipozyme RM-IM were active with total conversion to chiral product 4. The enantiomeric excesses were > 99% e 85.5%, respectively. Conversely, lipases Lipomod 34P and Novozyme 435 led to achiral ester 3, and their conversions approached 100%. In all cases, HPLC analysis showed formation of a single regioisomeric acetate.

![Scheme 2. Desymmetrization of 1.](https://via.placeholder.com/150)

CONCLUSION

The use of a lipase-catalyzed desymmetrization enabled the preparation of a useful chiral precursor of bioactive inositols.

ACKNOWLEDGEMENTS

We thank CNPq, UFRJ and FAPERJ for funding and fellowships.

REFERENCES