ENANTIOSELECTIVE REDUCTION OF ALPHA-KETOPHOSPHONATES BY CANDIDA ALBICANS CCT 5847

Paulo J. S. Moran (PQ), J. Augusto R. Rodrigues (PQ), Lucidio C. Fardelone (PQ), Letícia M. Sato (IC), Taisa N. Kitamura (IC).

Abstract
Enantioselective reduction of alpha-ketophosphonates 1a-d by Candida albicans CCT 5847 afforded (R)-alpha-hydroxy phosphonates (R)-2a-d that are valuable building blocks for pharmaceutical and agrochemical compounds.

Key words: alpha-ketophosphonates, biocatalysis, asymmetric synthesis.

Introduction
The optically active alpha-hydroxy phosphonates are important compounds in the organophosphate class, due to their biological properties, such as enzyme inhibitors, antibiotics, antiviral agents, antitumor and agrochemicals. The organophosphorus compounds have a direct phosphorus-carbon bond (PC), forming molecules with chiral centers, whose specific spatial configuration directly influences the activity of the molecule, as these organophosphorus compounds are analogous to amino acids. In this work, we report the preliminary enantioselective reduction of alpha-ketophosphonates 1a-d by using whole cells of Candida albicans CCT 5847 in excellent isolated yield, Table 1.

Results and Discussion
The alpha-ketophosphonates 1a-d were synthesized according to the methodology of Vahdat et al. by using benzaldehyde, 4-chlorobenzaldehyde, 4-methoxybenzaldehyde and 3,4-dimethoxy benzaldehyde, 1.1 equivalent of trimethyl phosphite and oxalic acid (catalyst), without solvent, at 60 °C, and subsequent oxidation with IBX providing alpha-ketophosphonates 1a-d. Alpha-hydroxy phosphonates (R)-(+)-2a-d were obtained by bioreduction of alpha-ketophosphonates 1a-d by using whole cells of Candida albicans CCT 5847, Figure 1.

Table 1. Enantioselective reduction of alpha-ketophosphonates 1a-d by Candida albicans CCT 5847.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Isolated Yield (%)</th>
<th>[α]D 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>(R)-2a</td>
<td>88 +44.6</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>(R)-2b</td>
<td>82 +37</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>(R)-2c</td>
<td>90 +48</td>
<td></td>
</tr>
<tr>
<td>1d</td>
<td>(R)-2d</td>
<td>84 +15</td>
<td></td>
</tr>
</tbody>
</table>

* 6 mmol of substrate in 0.5 mL of ethanol was added to a suspension of 4 g of whole cells in 100 mL of water. Reaction time: 18h; temperature: 30°C; orbital shaker: 200 rpm. The configuration of alpha-hydroxy phosphonates was determined by comparison of the [α]D 20 with literature.

Conclusions
The bioreduction of 1a-d by Candida albicans CCT 5847 furnished (R)-alpha-hydroxy phosphonates (R)-2a-d in excellent isolated yields. Those compounds are valuable building blocks for pharmaceutical and agrochemical products.

Acknowledgement
We thank CAPES, FAPESP (2014/00108-9) and CNPq for financial support.