Enzymatic Kinetic Resolution of Hydroxy Furan and Thiophene 2-substituted

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INTRODUCTION

Chiral non racemic secondary alcohols containing 2-Furan and Thiophene rings are widely widespread compounds in the environment and they also play important role in biochemical processes.¹ In addition these compounds can be employed as building blocks in the synthesis of bioactive molecules. However, environmentally harmful reagents and many reaction steps are generally assigned to synthetic methodologies that employ it.² Here, we propose a chemoenzymatic methodology to prepare enantiopure secondary alcohols containing furan and thiophene heterocyclic group.

RESULTS AND DISCUSSION

Initially a set of sec-alcohols containing furan and thiophene rings 1a-h (Figure 1) were prepared according with the literature³ in good yields.

Figure 1. Furan and thiophene derivatives

The racemic compound 1b was submitted to the enzymatic kinetic resolution (EKR) using vinyl acetate as acyl donor, the enzyme Candida antarctica lipase (CAL-B) and n-hexane as a non-polar organic solvent (Scheme 1).

Scheme 1. Analytical scale EKR of (R,S)-1b

The bioreolution of racemic substrate by CAL-B showed an anti Kaslauskas rule preference obtaining the free alcohol (R)-1b and ester (S)-2b in its enantiopure form (e.e. > 99%).

With this, the initial parameters were extended to EKR of the alcohols 1a-h (Scheme 2 and Table 1).

Table 1. EKR of the racemac alcohols 1a-h.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>n</th>
<th>x</th>
<th>Time (min)</th>
<th>(R)-1a-h (%)</th>
<th>Yield (%)</th>
<th>(S)-2a-h (%)</th>
<th>Yield (%)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>40</td>
<td>35</td>
<td>78</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>45</td>
<td>40</td>
<td>75</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>45</td>
<td>40</td>
<td>79</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>50</td>
<td>40</td>
<td>80</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>50</td>
<td>45</td>
<td>90</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>50</td>
<td>45</td>
<td>90</td>
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<td></td>
</tr>
<tr>
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<td>1a</td>
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<td>0</td>
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<td>45</td>
<td>96</td>
<td>54</td>
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<tr>
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<td>1a</td>
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<td>0</td>
<td>50</td>
<td>45</td>
<td>97</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>

As can be seen in the table 1, the chiral non racemic (S)-substrates and (R)-esters were obtained in an excellent enantioselectivity. Actually the enantiopure compound (S)-1g has been employed as key intermediate in the enantioselective synthesis of bioactive Pyrerenphorine.⁴

CONCLUSION

The alcohols (R)-1a-h and esters (S)-2a-h have been acquired in high (>99%) and moderated (from 68% to 99%) enantiomeric excess, respectively. The preliminary results have shown that alcohols containing furan and thiophene as heterocyclic compounds could be resolved by CAL-B.

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REFERENCES