Lipase Catalyzed Dynamic Kinetic Resolution of some 5-Hydroxy-2(5H)-Furanones

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Abstract: Lipase PS was successfully applied in the dynamic kinetic resolution of 5-hydroxy-2(5H)-furanones 4a-d (quantitative conversions, e.e.'s 78-86%) Copyright © 1996 Elsevier Science Ltd

The naturally occurring strigolactones, e.g. 1, and their synthetic analogs, e.g. 2, are highly potent germination stimulants of seeds of several parasitic weeds, such as *Striga* and *Orobanche* spp. In connection with our interest in the stereocontrolled synthesis of these germination stimulants, enantiopure D-ring precursors are required. Recently, we reported the preparation of the four diastereomers of GR7 using the latent D-ring 3b, which was resolved in its enantiomers via the menthylxy derivative 3a.

![Chemical Structures](image)

This paper deals with an enzymatic approach for the preparation of potential D-ring precursors of high enantiopurity by the kinetic resolution of 5-hydroxy-2(5H)-furanones 4a-d as is depicted in scheme 1.

![Scheme 1](image)

In this lipase mediated dynamic kinetic resolution vinyl acetate was used as the irreversible acyl donor. As a consequence of the labile stereogenic center at C-5, it was expected that a single enantiomer of 5 can be obtained in a theoretical yield of 100%. The interconversion of both enantiomers of 4 by mutarotation allows a dynamic kinetic resolution. The highly rewarding results are collated in the Table. The retro-reaction, *viz*...
transesterification of rac. 5a in the presence of a lipase to give rac. 4a and either enantiopure 5a or ent. 5a, has recently been reported. However, this conventional kinetic resolution suffers from an inherent drawback that the maximum yield of a single enantiomer is only 50%.

Table. Dynamic Kinetic Resolution of 5-Hydroxy-2(5H)-Furanones 4a-d

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>reaction time</th>
<th>temp. (°C)</th>
<th>e.e. (%)</th>
<th>enantiomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>100 h</td>
<td>32</td>
<td>83</td>
<td>(-) 5a^d</td>
</tr>
<tr>
<td>2</td>
<td>4a</td>
<td>150 h</td>
<td>20</td>
<td>84</td>
<td>(-) 5a^d</td>
</tr>
<tr>
<td>3</td>
<td>4b</td>
<td>28 d</td>
<td>35</td>
<td>78</td>
<td>(-) 5b^e</td>
</tr>
<tr>
<td>4</td>
<td>4c</td>
<td>166 h</td>
<td>30</td>
<td>84</td>
<td>(-) 5c^d</td>
</tr>
<tr>
<td>5</td>
<td>4d</td>
<td>168 h</td>
<td>30</td>
<td>86</td>
<td>(-) 5d^e</td>
</tr>
</tbody>
</table>

a) reaction time after 100% conversion as determined by capillary G.C. b) determined by chiral G.C., using a β-DEX 120 Capillary Column. c) sign of [γ]D of major enantiomer in dichloromethane. d) absolute stereochemistry established by comparison with authentic sample. e) absolute stereochemistry established by comparison of the CD-spectrum with that of 5a and 5c (same sign of Cotton effect). f) A typical procedure is as follows: Lipase PS (200 mg) and powdered molecular sieves (4A) were added to a stirred solution containing 4a (2.0 mmol), vinyl acetate (10 eq.) and biphenyl (50 mg) as internal standard, in dichloromethane (10 mL). At several time intervals samples (0.5 mL) were taken, filtered over hyflo and analyzed for conversion and e.e.

The data in the Table reveal that the asymmetric transformation of 4a-d takes place with 100% conversion and with high enantioselectivity. Methyl substituents (entries 3-5) have a negative effect on the reaction rate. Higher temperatures enhance the reaction rate considerably, without affecting the e.e.'s (entries 1-2). Other solvents such as THF or CH3CN instead of CH2Cl2 result in slower reactions and slightly lower e.e.'s (data not shown). It is important to note that the e.e.'s remain constant throughout the reactions as was established by analyzing aliquots at several time intervals. This implies that the stereoinversion (k_inv) is infinitely faster than the acetylation reaction (k_{R} >> k_{S}; Scheme 1).

In conclusion, the dynamic kinetic resolution of 4a-d offers an attractive route to the enantioselective synthesis of a series of 5-acetoxy-2(5H)-furanones 5a-d with optimal chiral economy. The compounds 5a-d can be used for the introduction of various D-rings into strigolactones and their analogs in an enantiocontrolled manner. In addition these compounds are chiral synthons with rich prospects.

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REFERENCES AND NOTES


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