

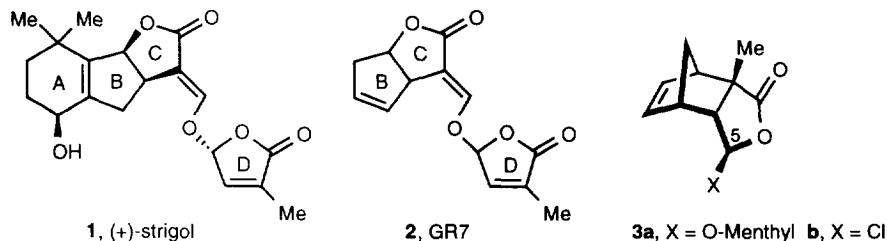
Lipase Catalyzed Dynamic Kinetic Resolution of some 5-Hydroxy-2(5H)-Furanones

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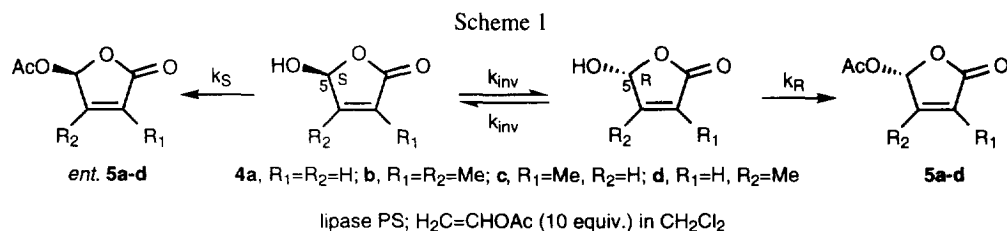
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Abstract: Lipase PS was successfully applied in the dynamic kinetic resolution of 5-hydroxy-2(5H)-furanones **4a-d** (quantitative conversions, e.e.'s 78-86%) Copyright © 1996 Elsevier Science Ltd

The naturally occurring strigolactones, e.g. **1**, and their synthetic analogs, e.g. **2**, are highly potent germination stimulants of several parasitic weeds, such as *Striga* and *Orobanchae* spp.¹⁻³. In connection with our interest in the stereocontrolled synthesis of these germination stimulants⁴, 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 menthyloxy derivative **3a**⁵.



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.



In this lipase mediated dynamic kinetic resolution vinyl acetate was used as the irreversible acyl donor⁶. 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 resolution⁷. 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 reported⁸. 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**^f

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

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 $[\alpha]_D$ 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 ($k_{inv} \gg k_R$ and 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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