Tetrahedron: Asymmetry Vol. 4, No. 5, pp. 957-958, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Diastereo- and Enantioselective Esterification of Butane-2,3-diol Catalysed by the Lipase from *Pseudomonas fluorescens*.

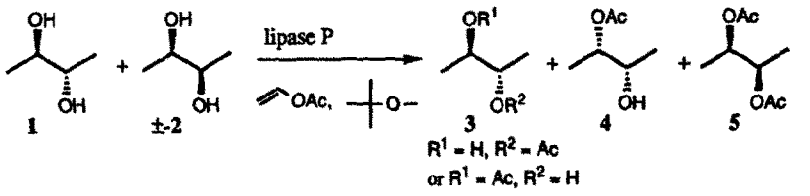
Kirpal S. Bisht and Virinder S. Parmar*
Department of Chemistry, University of Delhi, Delhi-110 007, India
and
David H.G. Crout*
Department of Chemistry, University of Warwick, Coventry CV4 7AL, U.K.

(*Received* 16 *March* 1993; *accepted* 5 *April* 1993)

Abstract: Butane-2,3-diol was converted into the (2*R*, 3*R*)-diacetate **5** with 91% de and >98% ee on esterification with vinyl acetate catalysed by the lipase from *Pseudomonas fluorescens* (Amano P).

Enantiomerically pure 1,2-diols are of considerable interest for many applications, for example in the synthesis of optically active macromolecules, as auxiliaries for the preparation of bidentate ligands and in the synthesis of organometallic catalysts. Partially protected polyols or their simple derivatives are important starting materials for the synthesis of various compounds useful in medicine, industry and biology as antimicrobial agents,[21] fungicides,[2] biosurfactants[3] etc.

Esterhydrolases (esterases and lipases) are well known for their ability to differentiate between enantiomeric alcohols and esters.[4] We have recently used the lipases from porcine pancreas and *Candida cylindracea* (*Candida rugosa*) to study regioselectivity in esterolytic reactions involving 1,2-diols.[5] We here report a method for obtaining the diacetate **5** of (2*R*, 3*R*)-butane-2,3-diol of high optical purity from a commercial mixture of *meso*-, **1**, and racemic, **2**, butane-2,3-diol (Scheme).



Scheme

In a general procedure, to a mixture of the diol (0.1 g) and vinyl acetate (0.18 cm^3) in *tert*-butyl methyl ether (15 cm^3) was added lipase P (0.2 g). The mixture was stirred at 20°C and the reaction was monitored by g.l.c. and t.l.c. When the diol was essentially consumed, the mixture was filtered and the solvent was evaporated under reduced pressure. The product mixture was separated by flash chromatography (EtOAc:light petroleum (b.p. 40-60°) 1:9 (v/v)). A preparative reaction was carried out in the same way on a 7 g scale.
The diacetate fraction (>90% yield based on the content of (*R*,*R*)isomer in the starting mixture) was found to consist of the (*R*, *R*)-diacetate **5** of >98% ee and 91% de ($[\alpha]_D^{20}$ 14.6 (c 2.1, $CHCl_3$)) as determined by chiral g.l.c. using a 3-acetyl-2,6-di-*O*-butyl-β-cyclodextrin column (Fig. 1b). The absolute configuration of the product was established by co-injection of racemic material and authentic material obtained by acetylation of commercially available (Fluka) (2*R*, 3*R*)-butane-2,3-diol.

The starting mixture (Fig. 1a) consisted of 54% *meso*-and 46% racemic butane-2,3-diol.[6] In the monoacetate fraction from the lipase-catalysed esterification, the ratio of monoacetate **3** of the *meso*-diol to the monoacetate **4** of the (2*S*, 3*S*)-diol was approximately 2.3:1 as estimated by integration of the signals attributable to H-2 and

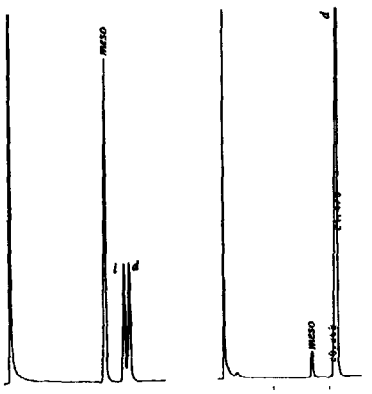


Figure 1. Chiral g.l.c. of diacetates of butane-2,3-diol.

a) Diacetate mixture from acetylation of a commercial mixture of *meso*- and racemic butane-2,3-diol.

b) Diacetate mixture from esterification of the mixture of butane-2,3-diol enantiomers using vinyl acetate as acyl donor and catalysed by lipase P.

H-3 (Fig. 2). If all of the (2*R*, 3*R*)-diol had been converted into diacetate **5**, the ratio expected would have been 2.4:1 confirming that essentially all of the (2*R*, 3*R*)-diol had been converted into diacetate.

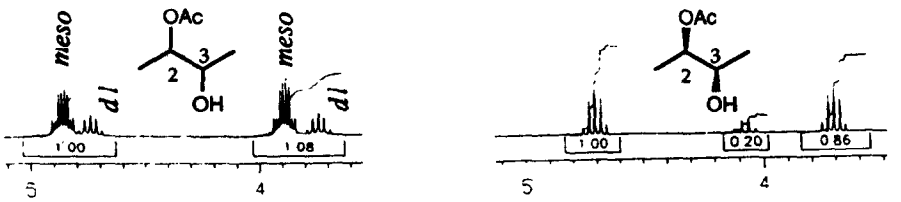


Figure 2. Partial n.m.r. spectra of the monoacetate fraction from the lipase-catalysed esterification of a mixture of *meso*- and racemic butane-2,3-diol, and the monoacetate obtained by acetylation (Ac_2O/C_5H_5N) of authentic (2*R*, 3*R*)-butane-2,3-diol. In each case, the downfield groups of signals are attributable to H-2 and the upfield groups to H-3.

The monoacetate of the chiral diol was clearly the (2*S*, 3*S*)-enantiomer. The absolute configuration of the monoacetate of the *meso*-diol remains to be determined.

Lipase P thus demonstrates enantio- and diastereoselectivity of an unusually high order in its catalysis of the esterification of stereoisomers of butane-2,3-diol.

Acknowledgements: We thank the CSIR (New Delhi) and the British Council for financial assistance.

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6. Purchased from Fluka, >99% pure.
7. The ^1H n.m.r. spectra were determined for solutions in C_6D_6 using a Bruker ACF (250 MHz) spectrometer. For the (2*R*, 3*R*)-diacetate **5**: d_H 1.02 (d, 6 H, 2 x CH_3), 1.70 (s, 6 H, 2 x CH_3CO_2), 5.02 (m, 2 H, 2 x CHO).