Tetrahedron Letters, Vol.31, No.25, pp 3603-3604, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

KINETIC RESOLUTION OF (η^6-ARENE)CHROMIUM COMPLEXES BY A LIPASE

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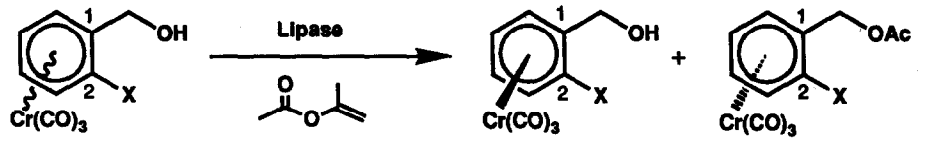
Abstract: Tricarbonylchromium complexes of *ortho*-substituted benzyl alcohol derivatives were kinetically resolved by asymmetric esterification with a lipase.

Nowadays, preparation of optically active tricarbonyl(η^6-arene)chromium species is a subject of absorbing interest. Since the $Cr(CO)_3$ moiety has strong electron-withdrawing ability and has large steric bulkiness, a chiral $Cr(CO)_3$ complex is quite promising in asymmetric syntheses.[1] In this paper, we would like to report kinetic resolution of planar-chiral tricarbonyl(η^6-arene)chromium complexes by the aid of a lipase.[2] Tricarbonyl(η^6-arene)chromium can exist in two enantiomeric forms when the phenyl ring is *ortho*- or *meta*-disubstituted. This planar chirality can be transferred into new central chirality with a high e.e. by means of an appropriate organic reaction.[1,3] After the transformation, the $Cr(CO)_3$ moiety can be removed easily from the product. Since an tricarbonyl(η^6-arene)chromium complex is sensitive to air and light, and is difficult to be dissolved into water, a method to dealt with these complexes is restricted to those that can cover up the disadvantages mentioned above. It is also desirable that a reagent or a catalyst can be separated easily from the products after the reaction. The use of a lipase as a catalyst for resolution of enantiomers provides a good method because the lipase works in an organic solvent under an anaerobic atmosphare, and it is easily separated from the product on filtration of the reaction mixture.

We subjected the $Cr(CO)_3$ complexes of *o*-methyl, *o*-methoxy, and *o*-trimethylsilyl (TMS) derivatives of benzyl alcohol as the substrates to be resolved. The reaction of racemic tricarbonyl(*o*-methylbenzyl alcohol)chromium (rac-$\mathbf{1_{Me}}$) with isopropenyl acetate in the presence of a lipase from *Pseudomonas* sp. (Amano P) gave the corresponding (*S*)-acetate[4] ((*S*)-$\mathbf{2_{Me}}$, 98 % e.e., 48 % chemical yield, $[\alpha]_D^{20}$ = +38.9°, $CHCl_3$) remaining the (*R*)-alcohol ((*R*)-$\mathbf{1_{Me}}$, 100 % e.e., 47 % chemical yield, $[\alpha]_D^{20}$ = –5.2°, $CHCl_3$). *o*-Methoxy and *o*-TMS-substituted substrate were also transacylated enantioselectively. Among lipases studied, Amano AK and Toyobo Type A (both from *Pseudomonas* sp.) gave the best result in the acylation of the *o*-OMe and the *o*-TMS derivatives, respectively, as listed in the Table.

These lipases reacted with the (*S*)-alcohol in all the substrates employed for the present study with excellent enantioselectivity, which is opposite to the stereoselectivity observed in the reductive resolution of $Cr(CO)_3$ complex mediated by bakers' yeast or HLADH where the (*R*)-aldehyde was reduced preferentially.[5)]



(*R*,*S*)-1 (*R*)-1 (*S*)-2

X in Substrate	Lipase	(*R*)-1 Chem. Yield, %	(*R*)-1 e.e., %	(*S*)-2 Chem. Yield, %	(*S*)-2 e.e., %
Me	Amano P	47	100	48	98
OMe	Amano AK	46	95	47	97
$SiMe_3$	Toyobo Type A	48	85	45	84

In a typical run, racemic tricarbonyl(*o*-methylbenzyl alcohol)chromium (50 mg, 0.2 mmol) was reacted with isopropenyl acetate (350 μl) in the presence of a lipase (Amano P, 100 mg) in an argon atmosphere at room temperature (25 °C) in the dark for 6 h. Dichloromethane (3 ml) was added to the reaction mixture and the resulted mixture was filtered through a short column of silica gel (Bond Elut) to remove the lipase. (*S*)-Acetate (98 % e.e.) and (*R*)-alcohol (100 % e.e.) were obtained in 48 % and 47 % chemical yields, respectively, after the filtrate was subjected to column chromatography on silica gel with dichloromethane as an eluent.

Acknowledgment. We are indebted to Amano Pharmaceutical Co., Ltd. and Toyobo Co., Ltd. for kind supply of lipases.

References and Footnotes

1) A. Solladié-Cavallo, "Chiral Arene-chromium-carbonyl complexes in Asymmetric Synthesis," in "Advances in Metal-Organic Chemistry," ed. by L. S. Liebeskind, Vol. 1, JAI Press Inc. 1989, pp 99-131.

2) Kinetic resolution of a secondary alcohol with a ferrocenyl moiety by a lipase has been reported: Y.-F, Wang, J. J. Lanonde, M. Momongan, D. E. Bergbreiter, and H.-H. Wong, *J. Am. Chem. Soc.*, **110**, 7200 (1988); N. W. Boaz, *Tetrahedron Lett.*, **30**, 2061 (1989).

3) M. Uemura, H. Nishimura, and Y. Hayashi, *J. Organomet. Chem.*, **376**, C3 (1989).

4) The e.e. of the acetate was determined by ^{1}H-NMR analysis in the presence of $Pr(hfc)_3$ or by HPLC analysis on Daicel Chiralcel OF. To determine the e.e. of the alcohol, it was converted chemically into the corresponding acetate by acetic anhydride.

5) S. Top, G. Jaouen, J. Gillois, C. Baldoli, and S. Maiorana, *J. Chem. Soc., Chem. Commun.*, 1284 (1988); Y. Yamazaki and K. Hosono, *Tetrahedron Lett.*, **30**, 5313 (1989).

(Received in Japan 16 March 1990)