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CRUDE CHICKEN LIVER ESTERASE MEDIATED RESOLUTION OF HOMOALLYL ALCOHOLS[†]

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ABSTRACT: Racemic acetates of homoallyl alcohols have been enantioselectively hydrolyzed by crude chicken liver esterase (liver acetone powder) to provide homoallyl alcohols in 72-98% optical purities.

Synthesis of optically pure homoallyl alcohols has been the subject of increasing interest in recent years because these structural units are useful in the synthesis of numerous biologically active natural products.¹⁻³ In continuation of our research program⁴⁻⁶ on enantioselective synthesis using crude enzymes we herein report enantioselective hydrolysis of racemic acetates of homoallyl alcohols with crude chicken liver esterase (liver acetone powder) to provide the desired homoallyl alcohols in high optical purities.

Synthesis of enantiomerically pure molecules using chemicoenzymatic methodology is of current interest.^{7,8} We recently reported⁵ that pig liver acetone powder (PLAP) hydrolyzes the racemic acetates of homoallyl alcohols to produce homoallyl alcohols in moderate to good (56-72%) enantiomeric purities. During our search for

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a suitable crude enzyme for obtaining homoallyl alcohols of high optical purity we have found that crude chicken liver esterase (CCLE) (liver acetone powder)⁹ enantioselectively hydrolyzes the acetates of racemic homoallyl alcohols¹⁰ thus providing the required homoallyl alcohols in high (72-98%) enantiomeric purities (Table 1).



Ar = a) Phenyl, b) 4-Tolyl, c) 4-Chlorophenyl, d) 1-Naphthyl, e) 2,4-Dichlorophenyl, f) 3,4-Dichlorophenyl

The following procedure for hydrolysis of (+)-1-acetoxy-1-(4-tolyl)-3-butene is representative. To 40 mL of 0.5 M, pH 8.0, KH_2PO_4/K_2HPO_4 aqueous buffer 1.02 g (5 mM) of racemic acetate in 10 mL of ether was added with stirring at room temperature. After 15 minutes 1 g of crude chicken liver esterase (liver acetone powder) was added and the stirring was continued. The progress of the reaction was monitored by HPLC. After 40 hours (conversion ratio 41:59) the reaction was quenched with 2N HCl. Usual work up followed by column chromatography (silica gel, 10% ethyl acetate in hexane) afforded 0.3g (90%) of (+)-1-(4-tolyl)-3-buten-1-ol, $[\alpha]_{D}^{20}$ + 44.62 (c 3.83, PhH), $\{\text{lit}^{11} [\alpha]_{D}^{25}$ - 37.3 (c 2.0, PhH) 82% e.e in 98% enantiomeric purity and 0.53 g (91%) of unhydrolyzed acetate.

This methodology represents a simple procedure for preparation of homoallyl alcohols in high optical purities using crude chicken liver Downloaded by [University of Bristol] at 03:48 26 November 2014

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Substrate	Time	Conversion ^b		(+)-Alcohol		Recove	red 1
(7)-1	in hrs.	ratio OH:OAC	Yield ^c	۲ ₀ ما 22	Е.е. ^d	Yield ^c	Е.е.
			(%)		(%)	(%)	(%)
1a	35	30:70	98	+ 34.08 (c 1.11, PhH)	72	93	38
dI	40	41:59	06	+ 44.62 (c 3.83, PhH)	98	16	73
1c	22	32:68	75	+ 32.18 (c 3.20, PhH)	95	89	51
1d	20	28:72	89	+ 92.90 (c 1.26, PhH)	96	93	32
1e	40	42:58	92	+ 56.70 (c 1.30, PhH)	85	93	569
1f	20	31:69	88	+ 23.30 (c 2.06, PhH)	92 ^f	91	46 ⁹
a) All rea	ctions	s were carrie	ed out	in 5 mM scale with 1 g	of ccL	E. b) 0	conver-
sion ratio	was (determined by	/ НРLС	analysis. c) Yield	ls of]	pure is	solated
products a	nd are	e based on co	nversio	on ratio. d) Based on	literat	ure valu	les ¹¹ :
(i) $Ar = p$	henyl	, [α] ²¹ -39.	. D) 6.	2.48, PhH), 84% e.e.;	(ii)	Ar = 4-	-tolyl,
[α] _D ²⁵ - 37	.3 (c	2.0, PhH), 8	328 e.e	.; (iii) Ar = 4-chloro	phenyl,	$\left[\alpha\right]_{D}^{23}$	- 28.4

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- 77.5 (c 2.98, PhH), of (-)-alcohols, obtained after hydrolysis with KOH/MeOH, with that of literature values. f) E.e. was determined by ¹H NMR (200 MHz) analysis of corresg) Based on $[\alpha]_{D}$ value of corresponding (+)-alcohol. e) Determined by comparing observed specific rotations (iv) Ar = 1-naphthyl, $[\alpha]_{D}^{24}$ 84% e.e.; ponding Mosher's ester. (c 3.03, PhH), 80% e.e.; 54

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esterase. Further applications of crude chicken liver esterase in a variety of organic transformations are underway in our laboratory.

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- 9. Preparation of crude chicken liver esterase (CCLE) : Freshly purchased chicken liver (500g) is homogenized in cold acetone using kitchen juicer. The mass obtained after filteration was washed again with cold acetone. The residue obtained was air

dried at room temperature and powdered in a juicer. Sieving afforded brown powder (80-90g). This powder (chicken liver acetone powder) can be stored in refrigerator for 2-3 months without significant loss in activity.

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